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Supporting Information

Total Syntheses and Biological Reassessment of Lactimidomycin, Isomigrastatin and Congener Glutarimide Antibiotics

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Contents

Bioassays

Cell lines: 4T1 (murine breast carcinoma), MDA-MB-231 (human breast carcinoma), and LoVo (human colon carcinoma) cell lines were obtained from ATCC. 4T1 cells were grown in RPMI 1640 (Life Technologies Cat # 22400-089) supplemented with 10 % FBS and non-essential amino acids. MDA-MB-231 cells were grown in MEM (Life Technologies Cat # 11095-080) supplemented with 10 % FBS, non-essential amino acids and sodium pyruvate. LoVo were grown in DMEM/ F-12 (1:1) medium (Life Technologies Cat # 10565-018) supplemented with 10 % FBS.

Cytotoxicity assay: Cells in 100 µL medium were cultured in a 96-well plate at the following cell densities such that confluence upon cell harvest was approximately 80 %: For 1 day assay, 4T1 cells = 3000 cells per well; MDA-MB-231 cells = 8000 cells per well; LoVo cells = 12000 cells per well. For 4 day assay, 4T1 cells = 1000 cells per well; MDA-MB-231 cells = 4000 cells per well; LoVo cells = 5000 cells per well. Cells were maintained in a humidified chamber (37ºC, 5 % CO2) overnight, then the cells were treated with compounds by adding 50 µL of 3X stocks in duplicate at 10 concentrations. Cells were incubated with compounds for one or four days. On the specified harvest day, 30 µL of Celltiter 96 Aqueous One Solution (MTS reagents; Promega, Cat # G3582) was added to the cells and incubated 1.5 h at 37ºC, then absorbance was measured at 490 nm on a Victor plate reader (Perkin Elmer, Waltham, MA). Relative cell viability was determined as a percentage of untreated control wells. IC_{50} values were calculated using four parameter logistic model #203 with XLfit v4.2 (IDBS, Guildford, Surry, UK).

Scratch wound healing assay: Cells (200,000 cells per well) were seeded into a 24-well-tissue culture plate and allowed to grow in a humidified chamber (37ºC, 5 % CO2). The next day, the confluent monolayer of cells was scratched with a sterile pipette tip using a straight edge to create an empty space of approximately 1 mm width in the middle of the well. Cells were then washed once with media to remove debris. Fresh media containing compounds at various concentrations were added to wells and incubated overnight in a humidified chamber. Migration was quantified by computer-based pixel calculation of the clearing, and data are reported as percent of control vs. DMSO treated wells.

Platypus cell migration assay: Cells were seeded into a 96-well Collagen-coated Platypus plate (Platypus technologies Cat No. CMACC1.101) with cell seeding stoppers in place and incubated overnight in a humidified chamber (37ºC, 5 % CO_2). Stoppers were removed and the cells washed gently with 100 µL sterile PBS to remove unattached cells. Fresh media (100 µl) with or without compounds in DMSO (6 replicates/compound) was added to each well and the plates were incubated for 24 h in a humidified chamber to allow migration. Reference wells for pre-migration controls (time = 0) were obtained by leaving the cell stoppers in place until the end of the migration period. Migration was stopped by removing the media then cells were washed gently with 100 µL PBS containing Ca^{++} and Mg^{++}. Cells were then fluorescently stained with 0.5 µg/mL calcein AM (R&D Systems, Cat No. 4892-010-K) in PBS with Ca^{++} and Mg^{++} for 30-60 min at 37ºC. The Oris Detection Mask was attached to the

plate bottom and fluorescence from the migrated cells was read in a microplate reader at 485/528 nm excitation /emission. Data are normalized to DMSO-treated control wells.

Transwell migration assay: Cells were starved overnight in serum-free media then collected by trypsinization, counted, and aliquoted into 1.5 mL centrifuge tubes (0.5 million cells in 1.5 mL serum-free medium). Compounds in DMSO were added to the cells in quadruplicate and incubated for one hour at room temperature. These pre-treated cells were then added to the inserts of a 24-multiwell Insert System (BD Falcon, Cat No. 351185) at 300 µL/insert. Migration was started by lowering the inserts onto a 24-well plate containing complete medium (1 mL) with the same drug concentration used for the corresponding insert. Blank samples received DMSO in serum-free media in both inserts and bottom wells. Plates were incubated for 24 h in a humidified chamber (37ºC, 5 % CO_2) to allow cell migration. At the harvest time point, media in inserts and bottom wells were discarded and the inserts were dipped quickly into a feeder tray (BD Falcon, Cat No. 351186) containing PBS to wash the outside of the inserts. Inserts were carefully washed twice with PBS, then lowered into a 24-well plate (BD Falcon 353047) containing 0.5 mL of 1.7 µg/mL calcein AM (R&D Systems, Cat No. 4892-010-K) in cell dissociation solution (Gibco, Cat No. 13151-014). After 30 min incubation at 37ºC, the inserts were removed and fluorescence at 485/528 nm excitation/emission was read in a fluorescence plate reader. Migration is calculated by comparing signal in the lower chamber of compound treated samples vs. DMSO-only control samples.

Crystallographic Abstract

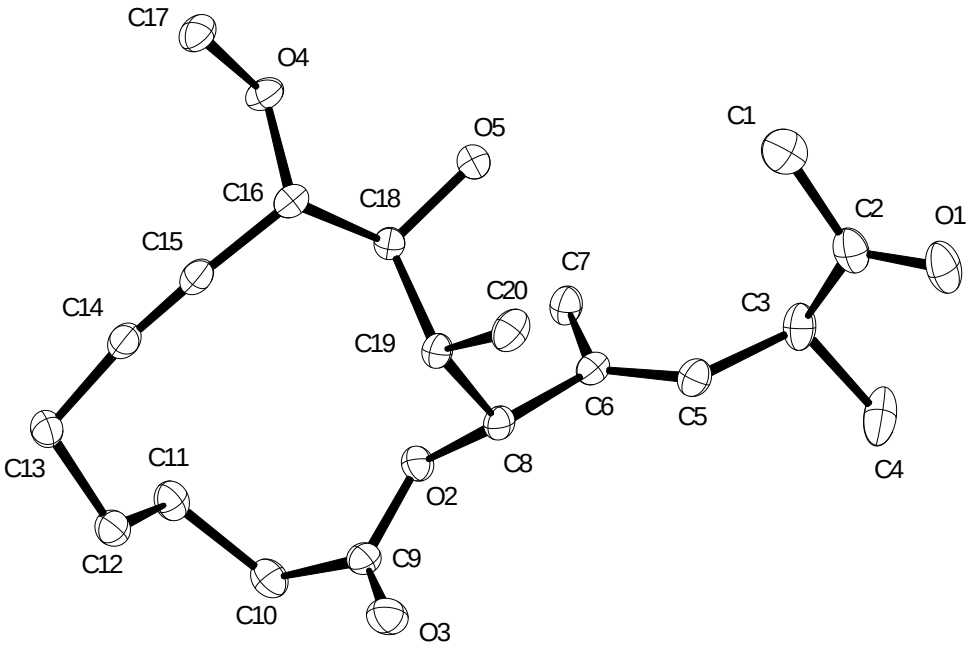


Figure S-1. Structure of cycloalkyne **63** in the solid state.

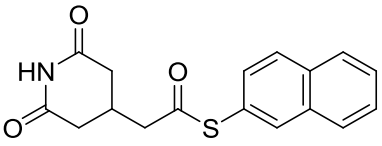
C_{20} H_{30} O_5, M_r = 350.44 g·mol^{-1}, colorless block, crystal size 0.33 x 0.32 x 0.15 mm, orthorhombic, space group $P2_12_12_1$, a = 7.7235(3) Å, b = 14.4643(6) Å, c = 16.7847(7) Å, V = 1875.10(13) Å^3, T = 100 K, Z = 4, D_{calc} = 1.241 g·cm^3, λ = 1.54178 Å, $\mu(Cu\text{-}K_\alpha)$ = 0.712 mm^{-1}, Semi-empirical absorption correction (T_{min} = 0.76, T_{max} = 0.91), Bruker AXS X8 Proteum diffractometer, diffractometer, 4.03 < θ < 67.05°, 42749 measured reflections, 3326 independent reflections, 3243 reflections with $I > 2\sigma(I)$, Structure solved by direct methods and refined by full-matrix least-squares against F^2 to R_1 = 0.026 [$I > 2\sigma(I)$], wR_2 = 0.064, 232 parameters, H atoms riding, S = 1.067, absolute structure parameter = –0.04(13), residual electron density +0.1 / –0.2 e Å^{-3}.

The anisotropic displacement parameters are drawn at the 50 % probability level; hydrogen atoms are omitted for clarity. **CCDC 913898** contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

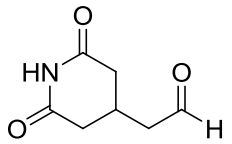
General. All reactions were carried out under Ar in flame-dried glassware. The solvents used were purified by distillation over the drying agents indicated and were transferred under Ar: THF, Et_2O, CH_2Cl_2, HMPA (CaH_2), hexane, toluene (Na/K), MeOH (Mg). Flash chromatography (FC): Merck silica gel 60 (230–400 mesh). NMR: Spectra were recorded on Bruker AMX 300, AV 400, or AVIII 600 spectrometer in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (*J*) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: $\delta_C \equiv 77.0$ ppm; residual $CHCl_3$ in $CDCl_3$: $\delta_H \equiv 7.26$ ppm). IR: Spectrum One (Perkin-Elmer) spectrometer, wavenumbers ($\tilde{\nu}$) in cm^{-1}. MS (EI): Finnigan MAT 8200 (70 eV), ESI-MS: ESQ3000 (Bruker), accurate mass determinations: Bruker APEX III FT-MS (7 T magnet) or Mat 95 (Finnigan). Unless stated otherwise, all commercially available compounds (Fluka, Lancaster, Aldrich) were used as received.

The preparation of compounds **26**-**33** is described in detail in the Supporting Information of our preliminary communication, cf. ref. [1]

Compound S1: O-(Benzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HBTU, 243 mg, 0.64 mmol) and triethylamine (120 µL, 0.87 mmol) were added to a solution of 2-(2,6-dioxopiperidin-4-yl)acetic acid **41a** (100 mg, 0.58 mmol)[2] in THF (6 mL). The mixture was stirred at ambient temperature for 2 h before naphthalene-2-thiol (103 mg, 0.64 mmol) was added. Stirring was continued for 1.5 h before all volatile materials were evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 2/1) to give product **S1** as a white solid (200 mg, quant.). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (br s, 1H), 7.94 (s, 1H), 7.91–7.82 (m, 3H), 7.58–7.51 (m, 2H), 7.43 (dd, *J* = 8.5, 1.8 Hz, 1H), 2.84 (d, *J* = 4.0 Hz, 1H), 2.81–2.71 (m, 4H), 2.47–2.37 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.0 (C), 170.9 (C), 134.5 (CH), 133.5 (C), 133.4 (C), 130.6 (CH), 129.0 (CH), 128.0 (CH), 127.8 (CH), 127.4 (CH), 126.7 (CH), 123.9 (C), 47.3 (CH_2), 37.1 (CH_2), 27.6 ppm (CH); MS (EI): *m*/*z* (%): 313 (9) $[M]^+$, 160 (100), 128 (4), 115 (22), 112 (10), 55 (8); HRMS (ESI): *m*/*z:* calcd for $C_{17}H_{15}NO_3SNa$ $[M + Na]^+$: 336.0665; found 336.0667.



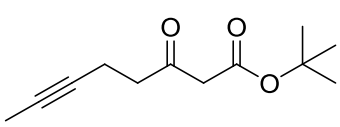
Compound 41b: Palladium on charcoal (5 % *w*/*w*, 180 mg) and triethylsilane (2.2 mL, 13.4 mmol) were added to a solution of thioester **S1** (420 mg, 1.34 mmol) in THF (5 mL) and the resulting suspension was stirred for 7 h before it was diluted with acetone (20 mL) and filtered through a pad of Celite. The filtrate was evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 2/8 → 1/9) to give aldehyde **41b** as a white solid (125 mg, 60 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.78 (s, 1H), 8.10 (br s, 1H), 2.82–2.71 (m, 3H), 2.61 (d, *J* = 6.1 Hz, 2H), 2.36 ppm (dd, *J* = 17.5, 10.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.6 (C), 171.1 (C), 47.8 (CH_2), 37.2 (CH_2), 24.6 ppm (CH); MS (EI): *m*/*z* (%): 155



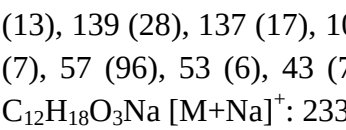
[1] K. Micoine, A. Fürstner, *J. Am. Chem. Soc*. **2010**, *132*, 14064-14066.
[2] Y. Egawa, M. Suzuki, T. Okuda. *Chem. Pharm. Bull.* **1963**, *11*, 589-586.

(< 1) $[M]^+$, 127 (82), 112 (17), 99 (23), 84 (16), 69 (15), 55 (32), 42 (100), 39 (38), 29 (24); HRMS (EI): *m/z:* calcd for $C_7H_9NO_3Na$ $[M]^+$: 155.0582; found 155.0581.

Compound S2. NaH (855 mg, 35.6 mmol) was added in several portions to a solution of *tert*-butyl acetoacetate **34** (5.3 mL, 32.4 mmol) in THF (65 mL) at 0 °C. After the gas evolution had ceased, *n*BuLi (1.6 M in hexanes, 21.3 mL, 34.0 mmol) was added dropwise before a solution of 1-bromo-2-butyne (5.39 g, 40.5 mmol) was slowly introduced via canula. Stirring was continued for 1 h at 0 °C before the resulting mixture was poured into a mixture of Et_2O and HCl (2 M). The aqueous layer was extracted with Et_2O and the combined organic layers were dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 95/5 → 80/20) to afford product **S2** as a yellow oil (6.56 g, 96 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.37 (s, 2H), 2.73 (t, *J* = 7.3 Hz, 2H), 2.41 (tq, *J* = 7.3, 2.5 Hz, 2H), 1.75 (t, *J* = 2.5 Hz, 3H), 1.47 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.7 (C), 166.4 (C), 82.2 (C), 77.5 (C), 76.3 (C), 50.8 (CH_2), 42.3 (CH_2), 28.1 (CH_3), 13.4 (CH_2), 3.6 ppm (CH_3); IR (film): 2979, 2923, 1725, 1393, 1353, 1254, 1150, 1172, 1030, 966, 907, 841, 795, 670 cm^{-1}; MS (EI): *m/z* (%): 195 (0.6), 155 (2), 154 (10), 153 (13), 139 (28), 137 (17), 109 (6), 108 (14), 96 (7), 95 (100), 94 (5), 67 (25), 66 (6), 65 (6), 59 (7), 57 (96), 53 (6), 43 (7), 41 (31), 39 (8), 29 (10), 27 (5); HRMS (ESI): *m/z:* calcd for $C_{12}H_{18}O_3Na$ $[M+Na]^+$: 233.1147; found 233.1148.



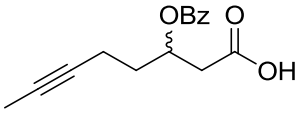
Compound S3. $NaBH_4$ (3.93 g, 103.8 mmol) was added in several portions to a solution of ketone **S2** (7.29 g, 34.6 mmol) in THF (200 mL) at 0 °C. After stirring for 3 h at ambient temperature, the reaction was quenched with sat. aq. NH_4Cl and diluted with *tert*-butyl methyl ether. The aqueous layer was extracted with *tert*-butyl methyl ether and the combined extracts were dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 95/5 → 90/10) to give product **S3** as a colorless oil (5.15 g, 70 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.09 (dddd, *J* = 12.4, 8.4, 4.1, 4.1 Hz, 1H), 3.15 (d, *J* = 3.5 Hz, 1H), 2.44 (dd, *J* = 16.4, 3.3 Hz, 1H), 2.35 (dd, *J* = 16.4, 8.8 Hz, 1H), 2.28 (tq, *J* = 7.3, 2.5 Hz, 2H), 1.77 (t, *J* = 2.5 Hz, 3H), 1.70-1.54 (m, 2H), 1.47 ppm (s, 9H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4 (C), 81.4 (C), 78.5 (C), 76.1 (C), 67.2 (CH), 42.3 (CH_2), 35.6 (CH_2), 28.2 (CH_3), 15.2 (CH_2), 3.6 ppm (CH_3); IR (film): 3464, 2978, 2921, 1723, 1435, 1393, 1367, 1304, 1253, 1147, 1071, 943, 844, 761 cm^{-1}; MS (EI): *m/z* (%): 197 (0.4), 139 (6), 138 (18), 121 (6), 110 (5), 97 (39), 96 (28), 95 (11), 93 (17), 81 (6), 79 (7), 69 (8), 67 (9), 59 (14), 57 (100), 56 (10), 55 (7), 53 (10), 43 (20), 41 (41), 39 (12), 29 (16), 27 (7); HRMS (ESI): *m/z:* calcd for $C_{12}H_{20}O_3Na$ $[M+Na]^+$: 235.1305; found 235.1304.



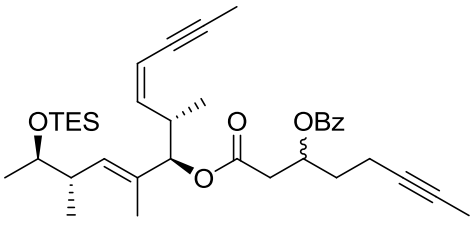
Compound S4. Triethylamine (5.0 mL, 36.2 mmol), benzoyl chloride (4.2 mL, 36.2 mmol), and DMAP (4.42 g, 36.2 mmol) were successively added to a solution of alcohol **S3** (5.13 g, 24.1 mmol) in CH_2Cl_2 (120 mL) at 0 °C. The mixture was stirred for 20 h at ambient temperature before the reaction was quenched with sat. aq. NH_4Cl. The aqueous layer was extracted with *tert*-butyl methyl ether and the combined extracts were dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 95/5 → 90/10) to give product **S4** as a colorless oil (6.77 g, 89 %). ^{1}H NMR

(400 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 7.1 Hz, 2H), 7.55 (tt, *J* = 7.5, 1.6 Hz, 1H), 7.43 (tt, *J* = 7.5, 1.5 Hz, 2H), 5.52 (dddd, *J* = 7.5, 7.3, 5.8, 5.1 Hz, 1H), 2.70 (dd, *J* = 15.1, 7.3 Hz, 1H), 2.62 (dd, *J* = 15.1, 5.8 Hz, 1H), 2.26 (tq, *J* = 7.3, 2.5 Hz, 2H), 2.03-1.90 (m, 2H), 1.71 (t, *J* = 2.5, 3H), 1.38 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.3 (C), 165.7 (C), 132.9 (CH), 130.2 (C), 129.6 (CH), 128.3 (CH), 81.0 (C), 77.7 (C), 76.2 (C), 70.6 (CH), 40.5 (CH_2), 33.4 (CH_2), 27.9 (CH_3), 15.0 (CH_2), 3.7 ppm (CH_3); IR (film): 2978, 2921, 1718, 1602, 1585, 1451, 1392, 1367, 1314, 1270, 1217, 1150, 1109, 1069, 1041, 1025, 948, 842, 709, 687 cm^{-1}; MS (EI): *m*/*z* (%): 261 (7), 260 (39), 259 (14), 243 (8), 174 (6), 138 (75), 123 (9), 121 (34), 110 (8), 106 (8), 105 (100), 95 (10), 93 (30), 91 (8), 79 (11), 77 (34), 57 (34), 51 (5), 41 (9) ; HRMS (ESI): *m*/*z:* calcd for $C_{19}H_{24}O_4Na$ $[M+Na]^+$: 339.1564; found 339.1567.

Compound 35. Trifluoroacetic acid (9.8 mL, 132 mmol) was added to a solution of ester **S4** (6.98 g, 22 mmol) in CH_2Cl_2 (100 mL) at 0 °C. The mixture was stirred at ambient temperature for 10 h. H_2O (80 mL) was then added, the aqueous layer was extracted with ethyl acetate, and the combined organic phases were dried over $MgSO_4$ and evaporated. The residue was dissolved in a small amount of toluene and the solution was evaporated to remove residual trifluoroacetic acid by aceotropic distillation; this operation was repeated five times to give product **35** as an orange oil (5.78 g, quant.). ^1H NMR (400 MHz, $CDCl_3$): δ = 10.54 (br s, 1H), 8.02 (d, *J* = 7.1, 2H), 7.56 (tt, *J* = 7.4, 1.2 Hz, 1H), 7.43 (t, *J* = 7.4, 2H), 5.53 (ddt, *J* = 5.8, 6.8, 6.3 Hz, 1H), 2.84 (dd, *J* = 15.9, 6.8 Hz, 1H), 2.77 (dd, *J* = 15.9, 5.8 Hz, 1H), 2.31-2.25 (m, 2H), 2.06-1.93 (m, 2H), 1.71 ppm (t, *J* = 2.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.2 (C), 165.8 (C), 133.0 (CH), 130.0 (C), 129.6 (CH), 128.3 (CH), 77.5 (C), 76.5 (C), 70.0 (CH), 38.7 (CH_2), 33.1 (CH_2), 15.0 (CH_2), 3.3 ppm (CH_3); IR (film): 2922, 1790, 1712, 1602, 1584, 1451, 1316, 1270, 1211, 1158, 1110, 1070, 1041, 1026, 935, 844, 805, 709, 685 cm^{-1}; MS (EI): *m*/*z* (%): 260 (5) $[M]^+$, 259 (15), 199 (5), 174 (5), 139 (6), 138 (61), 123 (6), 110 (6), 106 (8), 105 (100), 95 (13), 93 (29), 92 (5), 91 (11), 79 (10), 78 (5), 77 (46), 53 (6), 51 (9); HRMS (ESI): *m*/*z:* calcd for $C_{15}H_{17}O_4$ $[M+H]^+$: 261.1127; found 261.1124.

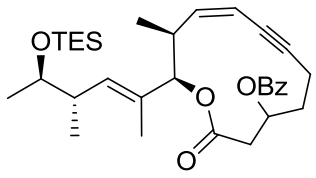


Compound 36. 2,4,6-Trichlorobenzoyl chloride (2.05 mL, 14.4 mmol) and triethylamine (1.85 mL, 14.4 mmol) were successively added to a solution of acid **35** (2.9 g, 11.3 mmol) in toluene (100 mL) at 0 °C. The resulting mixture was stirred at this temperature for 20 min before a solution of alcohol **33** (3.6 g, 10.3 mmol) was added, followed by DMAP (0.63 g, 5.0 mmol). The mixture was stirred at ambient temperature for 1 h 15 min before it was diluted with ethyl acetate and aq. citric acid solution (10 %). The organic layer was successively washed with brine, saturated $NaHCO_3$ solution, and brine prior to drying over $MgSO_4$ and evaporation. The residue was purified by flash chromatography (hexanes/EtOAc, 98/2 → 95/5) to give ester **36** as a yellow oil (5.0 g, 82 %). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 7.4 Hz, 4 H, 2 *dia.*), 7.54 (t, *J* = 7.4 Hz, 2 H, 2 *dia.*), 7.46–7.37 (m, 4 H, 2 *dia.*), 5.59–5.50 (m, 2 H, 2 *dia.*), 5.46 (dd, *J* = 10.2, 10.2 Hz, 1 H, 1 *dia.*), 5.44 (dd, *J* = 10.5, 10.5 Hz, 1 H, 1 *dia.*), 5.31 (dq, *J* = 10.7, 2.2 Hz, 1 H, 1 *dia.*), 5.29 (dq, *J* = 10.6, 2.2 Hz, 1 H, 1 *dia.*), 5.25 (d, *J* = 10.1 Hz, 1 H, 1 *dia.*), 5.23 (d, *J* = 9.7 Hz, 1 H, 1 *dia.*), 5.03 (d, *J* = 9.0 Hz, 2 H, 2 *dia.*),



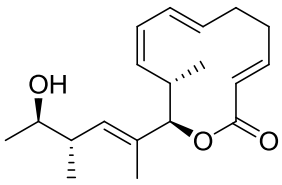
3.71–3.62 (m, 2 H, 2 *dia.*), 3.18–3.05 (m, 2 H, 2 *dia.*), 2.84 (dd, *J* = 15.3, 6.7 Hz, 2 H, 2 *dia.*), 2.73 (dd, *J* = 15.4, 6.1 Hz, 2 H, 2 *dia.*), 2.38–2.30 (m, 2 H, 2 *dia.*), 2.30–2.22 (m, 4 H, 2 *dia.*), 2.04–1.92 (m, 4 H, 2 *dia.*, overlap), 1.96 (d, *J* = 2.0 Hz, 6 H, 2 *dia.*, overlap), 1.70 (t, *J* = 2.5 Hz, 6 H, 2 *dia.*), 1.59 (d, *J* = 1.2 Hz, 3 H, 1 *dia.*), 1.54 (d, *J* = 1.2 Hz, 3 H, 1 *dia.*), 0.98-0.90 (m, 30 H, 2 *dia.*), 0.89 (d, *J* = 6.8 Hz, 3 H, 1 *dia.*), 0.84 (d, *J* = 6.8 Hz, 3 H, 1 *dia.*), 0.60–0.52 ppm (m, 12 H, 2 *dia.*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.2 (C), 169.1 (C), 165.8 (C), 165.7 (C), 143.0 (CH, 2 *dia.*), 132.9 (CH, 2 *dia.*), 132.4 (CH), 132.4 (CH), 131.9 (C, 2 *dia.*), 130.2 (C, 2 *dia.*), 129.6 (CH, 2 *dia.*), 128.3 (CH, 2 *dia.*), 109.6 (CH), 109.6 (CH), 90.0 (C, 2 *dia.*), 83.1 (CH, 2 *dia.*), 77.6 (C, 2 *dia.*), 76.3 (C, 2 *dia.*), 76.1 (C, 2 *dia.*), 71.1 (CH), 71.1 (CH), 70.5 (CH), 70.4 (CH), 39.3 (CH_2), 39.3 (CH_2), 39.2 (CH), 39.1 (CH), 36.9 (CH), 36.8 (CH), 33.2 (CH_2), 33.1 (CH_2), 20.3 (CH_3), 20.2 (CH_3), 16.5 (CH_3), 16.5 (CH_3), 15.4 (CH_3), 15.3 (CH_3), 15.0 (CH_2), 15.0 (CH_2), 12.1 (CH_3), 12.1 (CH_3), 6.9 (3 x CH_3, 2 *dia.*), 5.0 (3 x CH_2, 2 *dia.*), 4.3 (CH_3, 2 *dia.*), 3.4 ppm (CH_3, 2 *dia.*); IR (film): 3419, 2956, 2917, 2877, 1789, 1721, 1452, 1370, 1315, 1266, 1212, 1173, 1111, 1071, 1017, 998, 910, 869, 733, 704 cm^{-1}; HRMS (ESI): *m*/*z:* calcd for $C_{36}H_{52}O_5SiNa$ $[M + Na]^+$: 615.3476; found 615.3471.

Compound 37. Activated molecular sieves (5 Å, ca. 20 g) were added to a solution of diyne **36** (2.00 g, 3.4 mmol) in toluene (1.2 L) and the resulting suspension was heated to 80 °C before a solution of complex **21** (0.22 g, 0.17 mmol) in toluene (10 mL) was introduced. The mixture was stirred at 80 °C for 3 h before it was allowed to reach ambient temperature. Insoluble materials were filtered off through a pad of silica which was carefully rinsed with ethyl acetate. The combined filtrates were evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 1/0 → 95/5) to give cycloalkyne **37** as a yellow oil (1.56 g, 85 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 8.2 Hz, 2 H, 1 *dia.*), 8.02 (d, *J* = 8.2 Hz, 2 H, 1 *dia.*), 7.59–7.51 (m, 2 H, 2 *dia.*), 7.48–7.39 (m, 4 H, 2 *dia.*), 5.73–5.66 (m, 1 H, 1 *dia.*), 5.60–5.51 (m, 2 H, 2 *dia.*, overlap), 5.55–5.47 (m, 2 H, 2 *dia.*, overlap), 5.41–5.34 (m, 1 H, 1 *dia.*, overlap), 5.34 (d, *J* = 9.8 Hz, 2 H, 2 *dia.*, overlap), 5.23 (d, *J* = 3.5 Hz, 1 H, 1 *dia.*), 5.19 (d, *J* = 4.2 Hz, 1 H, 1 *dia.*), 3.79–3.71 (m, 2 H, 2 *dia.*), 3.37–3.26 (m, 2 H, 2 *dia.*), 3.17 (dd, *J* = 17.3, 11.4 Hz, 1 H, 1 *dia.*), 3.10 (dd, *J* = 17.3, 3.4 Hz, 1 H, 1 *dia.*), 2.93 (dd, *J* = 17.2, 4.3 Hz, 1 H, 1 *dia.*), 2.83 (dd, *J* = 17.3, 5.4 Hz, 1 H, 1 *dia.*), 2.70–2.54 (m, 2 H, 2 *dia.*), 2.52–2.31 (m, 6 H, 2 *dia.*), 2.10–1.98 (m, 2 H, 2 *dia.*), 1.64 (d, *J* = 1.1 Hz, 3 H, 1 *dia.*), 1.62 (d, *J* = 1.1 Hz, 3 H, 1 *dia.*), 1.06 (d, *J* = 6.2 Hz, 6 H, 2 *dia.*), 1.03 (d, *J* = 7.1 Hz, 3 H, 1 *dia.*), 1.00 (d, *J* = 6.8 Hz, 3 H, 1 *dia.*), 0.99-0.91 (m, 24 H, 2 *dia.*), 0.62–0.54 ppm (m, 12 H, 2 *dia.*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.0 (C), 169.1 (C), 165.9 (C), 165.3 (C), 144.2 (CH), 144.0 (CH), 135.2 (C, 2 *dia.*), 134.1 (CH), 133.7 (CH), 133.0 (CH), 133.0 (CH), 130.3 (C), 129.7 (CH), 129.5 (CH), 129.4 (C), 128.4 (CH), 128.3 (CH), 110.8 (CH), 110.5 (CH), 93.8 (C), 93.1 (C), 83.0 (CH), 82.2 (CH), 80.0 (C), 79.6 (C), 71.4 (CH, 2 *dia.*), 70.9 (CH), 70.7 (CH), 39.5 (CH_2), 39.5 (CH_2), 37.5 (CH), 37.2 (CH), 37.0 (CH_2, 2 *dia.*), 30.5 (CH_2), 30.2 (CH_2), 21.1 (CH_3), 21.0 (CH_3), 17.3 (CH_3), 17.1 (CH_3), 16.2 (CH_3), 16.2 (CH_3), 16.1 (CH_2), 14.5 (CH_3), 14.4 (CH_3), 13.6 (CH_2), 6.9 (3 x CH_3, 2 *dia.*), 5.0 ppm (3 x CH_2, 2 *dia.*); IR (film): 2959, 2933, 2875, 1721, 1451, 1414, 1376, 1334, 1271, 1189, 1166, 1108, 1068, 1025, 963, 943, 880, 804, 740, 709 cm^{-1}; MS (EI): *m*/*z* (%): 494 (2), 416 (8), 282 (5), 207 (10), 160 (100), 159 (56), 131



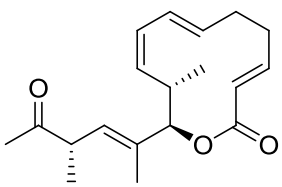
(31), 115 (36), 105 (55), 87 (18), 59 (5); HRMS (ESI): *m/z:* calcd for $C_{32}H_{46}O_5SiNa$ [M + Na]$^+$: 561.3007; found 561.3003.

Compound 39. [Cp*Ru(MeCN)$_3$]PF$_6$ (38 mg, 0.074 mmol) and benzyldimethylsilane (0.47 mL, 2.97 mmol) were successively added to a solution of cycloalkyne **37** (400 mg, 0.74 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C. The mixture was stirred at this temperature for 10 min until the catalyst had fully dissolved and then for 1 h at ambient temperature. Next, the solvent was slowly evaporated by a stream of Ar over ca. 30 min, at which point TLC control indicated complete conversion. The residue was purified by flash chromatography (hexanes/EtOAc, 98/2 → 95/5) to give product **38**, which was directly used in the next step.



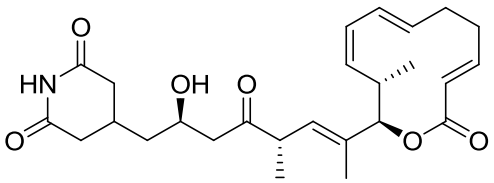
A solution of anhydrous TBAF (1 M in THF, 3.0 mL, 3.0 mmol) was added at 0 °C to a solution of alkenylsilane **38** in THF (1.0 mL) and the resulting orange mixture stirred at ambient temperature for 2 h. For work up, the solution was filtered through a pad of silica which was carefully rinsed with ethyl acetate. The combined filtrates were evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 90/10) to remove traces of the undesired (*Z*,*Z*)-diene isomer. Product **39** was thus obtained as a colorless oil (165 mg, 73 %). $[\alpha]_D^{20}$ = −232.7 (c = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.47 (ddd, *J* = 16.0, 10.4, 5.4 Hz, 1H), 6.04 (dd, *J* = 10.8, 10.8 Hz, 1H), 5.74 (dd, *J* = 15.6, 10.6 Hz, 1H), 5.55 (d, *J* = 16.1 Hz, 1H), 5.40 (ddd, *J* = 15.3, 8.8, 6.6 Hz, 1H), 5.35 (d, *J* = 4.5 Hz, 1H, overlap), 5.33 (d, *J* = 9.5 Hz, 1H, overlap), 5.10 (dd, *J* = 10.9, 10.9 Hz, 1H), 3.60 (qd, *J* = 6.2, 6.2 Hz, 1H), 3.09 (ddq, *J* = 11.7, 6.2, 5.8 Hz, 1H), 2.59-2.49 (m, 2H), 2.44 (dqd, *J* = 9.4, 6.5, 3.7 Hz, 1H), 2.01-1.84 (m, 2H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.55 (br s, 1H), 1.18 (d, *J* = 6.1 Hz, 3H), 0.99 (d, *J* = 6.7 Hz, 3H), 0.94 ppm (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.7 (C), 146.4 (CH), 134.5 (CH), 133.1 (CH), 131.9 (C), 131.7 (CH), 128.9 (CH), 128.3 (CH), 127.7 (CH), 83.3 (CH), 71.5 (CH), 40.0 (CH), 35.7 (CH), 32.2 (CH_2), 31.1 (CH_2), 20.3 (CH_3), 17.5 (CH_3), 16.4 (CH_3), 14.9 ppm (CH_3); IR (film): 3453, 2964, 2928, 2872, 1709, 1641, 1451, 1376, 1336, 1313, 1259, 1190, 1141, 1085, 1005, 957, 923, 848, 800, 736, 691 cm^{-1}; MS (EI): *m/z* (%): 304 (2) [*M*$^+$], 162 (7), 94 (100), 79 (41), 68 (12), 55 (4), 41 (9); HRMS (ESI): *m/z:* calcd for $C_{19}H_{28}O_3Na$ [M + Na]$^+$: 327.1931; found 327.1931.

Compound 19. Oxalyl chloride (88 µL, 1.02 mmol) was added to a solution of DMSO (0.14 mL, 2.0 mmol) in CH_2Cl_2 (5 mL) at –78 °C before a solution of alcohol **39** (62 mg, 0.20 mmol) in CH_2Cl_2 (3 mL) was added. After 1 h at this temperature, triethylamine (0.42 mL, 3.1 mmol) was introduced and stirring continued for 30 min at this temperature and for 1.5 h at 0 °C. The reaction was quenched with sat. aq. NH_4Cl, the aqueous phase was extracted with CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 90/10) to furnish product **19** as a pale yellow solid (51 mg, 82 %). $[\alpha]_D^{20}$ = −3.9 (c = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.48 (ddd, *J* = 16.0, 10.4, 5.4 Hz, 1H), 6.05 (dd, *J* = 10.8, 10.8 Hz, 1H), 5.73 (dd, *J* = 15.6, 10.7 Hz, 1H), 5.55 (d, *J* = 16.1 Hz, 1H), 5.41 (ddd, *J* = 15.6, 8.9, 6.5 Hz, 1H, overlap), 5.39-5.31 (m, 2H, overlap), 5.08 (dd, *J* = 10.9, 10.9 Hz, 1H), 3.43 (dq, *J* = 9.4, 6.9 Hz, 1H), 3.10 (dqd, *J* = 11.7, 6.4, 3.2



Hz, 1H), 2.60-2.46 (m, 2H), 2.14 (s, 3H), 2.02-1.85 (m, 2H), 1.78 (d, *J* = 1.3 Hz, 3H), 1.17 (d, *J* = 6.8 Hz, 3H), 0.92 ppm (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.0 (C), 166.5 (C), 146.6 (CH), 134.5 (CH), 133.3 (C), 131.4 (CH), 129.8 (CH), 129.1 (CH), 128.2 (CH), 127.8 (CH), 82.6 (CH), 46.8 (CH), 36.0 (CH), 32.2 (CH_2), 31.2 (CH_2), 27.9 (CH_3), 17.3 (CH_3), 16.1 (CH_3), 14.9 ppm (CH_3); IR (film): 2965, 2931, 2872, 1713, 1642, 1453, 1373, 1353, 1313, 1244, 1188, 1140, 1088, 1001, 957, 872, 848, 829, 799, 768, 733, 701 cm^{-1}; MS (EI): *m*/*z* (%): 302 (1) [*M*$^+$], 162 (8), 94 (100), 79 (42), 68 (12), 53 (2), 43 (11); HRMS (ESI): *m*/*z:* calcd for $C_{19}H_{26}O_3Na$ [M + Na]$^+$: 325.1774; found 327.1775.

Lactimidomycin (1). Me_3SiCl (0.80 mL, 6.20 mmol) and triethylamine (0.86 mL, 6.20 mmol) were added to a solution of ketone **39** (186 mg, 0.61 mmol) in THF (15 mL) at –78 °C. Next, LiHMDS (1 M in THF, 1.23 mL, 1.23 mmol) was slowly introduced and the resulting mixture stirred at –78 °C for 1 h. The reaction was then quenched with pH 7 phosphate buffer and the product extracted with CH_2Cl_2 (3 x 10 mL). The combined organic phases were dried over $MgSO_4$ and evaporated to give the corresponding silyl enol ether **40**, which was immediately used in the next step without further purification.



Molecular sieves (4 Å, ca. 1.5 g) and aldehyde **41b** (97 mg, 0.61 mmol) were added to a solution of the crude silyl enol ether in propionitrile (10 mL). The mixture was cooled to –78 °C before a solution of compound **42** [prepared upon stirring of a solution of $PhBCl_2$ (94 µL, 0.70 mmol) and N-tosyl-D-tryptophane (245 mg, 0.70 mmol) in CH_2Cl_2 (4.5 mL) for 1 h, followed by removal of the solvent][3] in propionitrile (4.5 mL) was added dropwise. After stirring for 35 h at –78 °C, the reaction was quenched with sat. aq. $NaHCO_3$ (15 mL), the aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL), and the combined organic layers were dried over $MgSO_4$ and evaporated. The resulting crude product was dissolved in THF (100 mL) at 0 °C and treated with 11.0 mL of buffered HF·pyridine solution [prepared from THF (7.98 mL), pyridine (2.96 mL) and HF·pyridine complex (0.65 mL, 70 % *w*/*w*)]. The mixture was stirred at 0 °C for 2 h and warmed to ambient temperature for 30 min to complete the desilylation. Dilution with CH_2Cl_2 (100 mL), washing of the organic layer with sat. aq. $NaHCO_3$ (50 mL) and aq. $CuSO_4$ solution (1 M, 3 x 50 mL), drying over $MgSO_4$ and evaporation of the solvents left a residue, which was purified by flash chromatography (EtOAc/hexanes, 50/50 → 100/0) to give product **1** as a white solid (138 mg, 50 %). $[\alpha]_D^{20}$ = +6.9 (c = 0.5, DMSO);[4] $[\alpha]_D^{20}$ = −7.0 (c = 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): see Table S-1; ^{13}C NMR (150 MHz, $CDCl_3$): see Table S-2; IR (film): 3481, 3239, 2925, 2852, 1695, 1453, 1376, 1259, 1190, 1145, 1084, 1003, 829, 796, 767, 733, 701 cm^{-1}; HRMS (ESI): *m*/*z:* calcd for $C_{26}H_{35}NO_6Na$ [M + Na]$^+$: 480.2357; found 480.2363.

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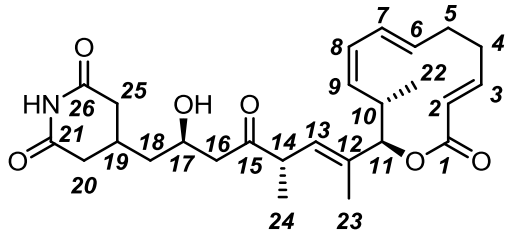
[3] K. Ishihara, S. Kondo, H. Yamamoto, *J. Org. Chem*. **2000**, *65*, 9125-9128.

[4] The original isolation paper reports: $[\alpha]_D^{20}$ = −20 (c = 0.5, DMSO), cf. K. Sugawara, Y. Nishiyama, S. Toda, N. Komiyama, M. Hatori, T. Moriyama, Y. Sawada, H. Kamei, M. Konishi, T. Oki, *J. Antibiot*. **1992**, *45*, 1433-1441. It seems, however, that this value is incorrect. Prof. B. Shen, University of Wisconsin, kindly informed us that the optical rotation of authentic lactimidomycin produced by the original strain deposited at ATCC is in fact positive in DMSO.

Table S-1. Comparison of the recorded ^{1}H NMR data ($CDCl_3$) of lactimidomycin (**1**) with those reported in the literature;[5] numbering scheme as shown in the Insert.



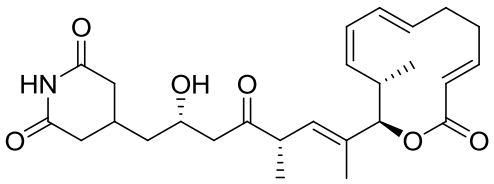
Position	Literature (500 MHz) δ (ppm) mult. (*J* in Hz)	Experimental (600 MHz) δ (ppm) mult. (*J* in Hz)	Δδ
2	5.53 d (16.0)	5.54 d (16.1)	+0.01
3	6.49 ddd (16.0, 10.0, 5.0)	6.47 ddd (16.1, 10.2, 5.2)	-0.02
4	1.96 m/2.56 m	1.95 m/2.56 m	-0.01/0
5	1.96 m/2.54 m	1.92 m/2.52 m	-0.04/-0.02
6	5.42 m	5.41 ddd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

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

Table S-2. Comparison of the recorded ^{13}C NMR data (δ in ppm, $CDCl_3$) of lactimidomycin (**1**) with those reported in the literature.[5]

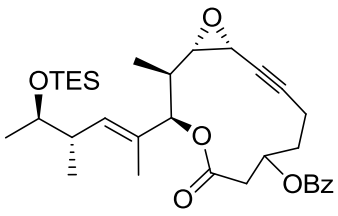
Position	Literature (125 MHz)	Experimental (150 MHz)	Δδ
1	166.7	166.7	0
2	128.4	128.3	-0.1
3	147.0	147.0	0
4	32.4	32.4	0
5	31.4	31.3	-0.1
6	128.2	128.2	0
7	134.6	134.5	-0.1
8	129.6	129.5	-0.1
9	131.1	131.2	+0.1
10	36.1	36.0	-0.1
11	82.5	82.4	-0.1
12	134.1	134.0	-0.1
13	129.1	129.0	-0.1
14	46.8	46.7	-0.1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

15-*epi*-Lactimidomycin (15-*epi*-1). Prepared analogously using *ent*-**42** [prepared upon stirring of a solution of $PhBCl_2$ (11 µL, 0.083 mmol) and N-tosyl-*L*-tryptophane (30 mg, 0.083 mmol) in CH_2Cl_2 (1 mL) for 1 h, followed by removal of the solvent][3] as promoter for the Mukaiyama aldol reaction. White solid (7 mg, 18 %, *dr* 85/15). ^1H NMR (600 MHz, $CDCl_3$): δ = 7.92 (br s, 1H), 6.48 (ddd, *J* = 16.0, 10.4, 5.4 Hz, 1H), 6.05 (dd, *J* = 10.8, 10.8 Hz, 1H), 5.71 (dd, *J* = 15.6, 10.7 Hz, 1H), 5.54 (d, *J* = 16.1 Hz, 1H), 5.42 (ddd, *J* = 15.4, 9.2, 6.2 Hz, 1H), 5.36-5.32 (m, 2H, overlap), 5.04 (dd, *J* = 10.9, 10.9 Hz, 1H), 4.13-4.08 (m, 1H), 3.42 (dq, *J* = 9.9, 6.7 Hz, 1H),



3.14-3.06 (m, 1H), 2.81-2.72 (m, 2H), 2.66-2.62 (m, 2H), 2.59-2.54 (m, 1H), 2.54-2.46 (m, 2H), 2.37-2.27 (m, 2H), 2.02-1.85 (m, 2H), 1.77 (d, *J* = 1.3 Hz, 3H), 1.61 (ddd, *J* = 14.1, 10.6, 4.9 Hz, 1H), 1.31 (ddd, *J* = 14.0, 8.9, 2.8 Hz, 1H), 1.18 (d, *J* = 6.8 Hz, 3H), 0.91 ppm (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 212.5 (C), 172.2 (C), 172.0 (C), 166.7 (C), 147.0 (CH), 134.5 (CH), 134.0 (C), 131.2 (CH), 129.5 (CH), 129.0 (CH), 128.2 (CH), 128.2 (CH), 82.4 (CH), 64.9 (CH), 47.4 (CH_2), 46.8 (CH), 40.8 (CH_2), 38.5 (CH_2), 37.2 (CH_2), 36.0 (CH), 32.4 (CH_2), 31.3 (CH_2), 27.2 (CH), 17.6 (CH_3), 16.2 (CH_3), 15.4 ppm (CH_3); IR (film): 3422, 2929, 2856, 1698, 1454, 1376, 1265, 1190, 1143, 1087, 1024, 829, 795, 766, 734, 702 cm^{-1}; HRMS (ESI): *m/z:* calcd for $C_{26}H_{35}NO_6Na$ $[M + Na]^+$: 480.2357; found 480.2358.

Compound 66. A solution of buffered NaOCl (0.55 M, 50 mL) was prepared by mixing 14 mL of commercial bleach[6] and Na_2HPO_4 (36 mL, 0.05 M in water). This solution was cooled to 4 °C before a solution of enyne **37** (2.1 g, 3.9 mmol) and (*R,R*)-(–)-[1,2-cyclohexane-diamino-*N,N'*-bis(3,5-di-*tert*-butylsalicylidene] manganese chloride (0.5 g, 0.78 mmol) in CH_2Cl_2 (25 mL) was added. The resulting biphasic mixture was vigorously stirred at 4 °C for 20 h. It was then diluted with *tert*-butyl methyl ether and brine, the aqueous phase was extracted with *tert*-butyl methyl ether, and the combined extracts were dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 95/5 → 90/10) to give epoxide **66** as a yellow oil (1.36 g, 63 %). The two diastereomers (at C3) are separable by flash chromatography (hexanes/EtOAc, 95/5). *First diastereomer*: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 8.4 Hz, 2H), 7.57 (tt, *J* = 7.5, 1.3 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 5.65 (dddd, *J* = 11.5, 4.6, 4.6, 2.6 Hz, 1H), 5.43 (d, *J* = 9.7 Hz, 1H), 5.24 (d, *J* = 3.5 Hz, 1H), 3.75 (qd, *J* = 6.1, 3.5 Hz, 1H), 3.52–3.49 (m, 1H), 3.15 (dd, *J* = 17.0, 11.4 Hz, 1H), 2.97 (dd, *J* = 17.1, 4.6 Hz, 1H), 2.88 (dd, *J* = 9.9, 3.8 Hz, 1H), 2.56 (dd, *J* = 17.7, 11.6 Hz, 1H), 2.48–2.37 (m, 2H), 2.31–2.20 (m, 1H), 2.13 (ddq, *J* = 10.5, 6.8, 3.5 Hz, 1H), 2.04–1.94 (m, 1H), 1.73 (d, *J* = 1.2 Hz, 3H), 1.17 (d, *J* = 7.1 Hz, 3H), 1.07 (d, *J* = 6.3 Hz, 3H), 1.00-0.92 (m, 12H), 0.58 ppm (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.7 (C), 165.4 (C), 134.4 (CH), 133.3 (CH), 130.4 (C), 129.7 (CH), 128.6 (CH), 128.5 (C), 86.8 (C), 81.0 (CH), 77.5 (C), 71.6 (CH), 70.5 (CH), 60.3 (CH), 46.5 (CH), 39.8 (CH), 38.6 (CH), 37.3 (CH_2), 30.1 (CH_2), 21.5 (CH_3), 16.6 (CH_3), 15.3 (CH_3), 14.8 (CH_3), 13.0 (CH_2), 7.1 (3 x CH_3), 5.2 ppm (3 x CH_2).

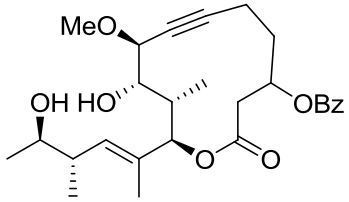


Second diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 8.5 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 5.46–5.37 (m, 1H, overlap), 5.43 (d, *J* = 10.1 Hz, 1H, overlap), 5.25 (d, *J* = 3.0 Hz, 1H), 3.76 (qd, *J* = 6.1, 3.4 Hz, 1H), 3.54–3.51 (m, 1H), 3.08 (dd, *J* = 17.2, 3.2 Hz, 1H), 2.97 (dd, *J* = 17.1, 4.6 Hz, 1H), 2.88–2.80 (m, 2H), 2.57–2.49 (m, 1H), 2.43 (ddq, *J* = 10.0, 6.5, 3.3 Hz, 1H), 2.30–2.21 (m, 2H), 2.13 (dqd, *J* = 10.5, 6.8, 3.3 Hz, 1H), 2.05–1.97 (m, 1H), 1.75 (d, *J* = 1.2 Hz, 3H), 1.20 (d, *J* = 7.1 Hz, 3H), 1.06 (d, *J* = 6.2 Hz, 3H), 1.00-0.92 (m, 12H), 0.58 ppm (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7 (C), 166.0 (C), 134.0 (CH), 133.3 (CH), 130.4 (C), 129.9 (CH), 128.8 (C), 128.5

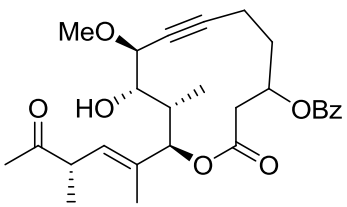
[6] From Fisher Scientific UK. Ref. S/5042/15 - Sodium hypochlorite min 14 % available chlorine

(CH), 85.7 (C), 81.3 (CH), 77.4 (C), 71.6 (CH), 70.7 (CH), 60.4 (CH), 46.6 (CH), 39.8 (CH), 38.9 (CH), 37.9 (CH_2), 30.5 (CH_2), 21.5 (CH_3), 16.6 (CH_3), 15.6 (2 x CH_3), 14.7 (CH_2), 7.1 (3 x CH_3), 5.2 ppm (3 x CH_2); IR (film): 2958, 2931, 2875, 1720, 1451, 1376, 1313, 1271, 1170, 1108, 1068, 1016, 949, 878, 836, 710 cm^{-1}; MS (EI): *m*/*z* (%): 510 (6), 304 (2), 207 (15), 159 (100), 131 (46), 115 (46), 105 (39), 87 (17); HRMS (ESI): *m*/*z:* calcd for $C_{32}H_{46}O_6SiNa$ $[M + Na]^+$: 577.2956; found 577.2951.

Compound 67. *p*-Toluenesulfonic acid (0.23 g, 1.23 mmol) was added to a solution of epoxide **66** (1.36 g, 2.45 mmol) in MeOH (50 mL) and the resulting mixture was stirred at 60 °C for 6 h. The methanol was evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 9/1 → 6/4) to give diol **67** as a white solid (0.85 g, 73 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.4 Hz, 2 H, 1 *dia.*), 8.00 (d, *J* = 8.3 Hz, 2 H, 1 *dia.*), 7.60–7.54 (m, 2 H, 2 *dia.*), 7.48–7.41 (m, 4 H, 2 *dia.*), 5.70 (dddd, *J* = 11.1, 8.6, 2.6, 2.6 Hz, 1 H, 1 *dia.*), 5.59 (dddd, *J* = 10.5, 5.2, 5.2, 2.8 Hz, 1 H, 1 *dia.*), 5.27 (d, *J* = 2.5 Hz, 1 H, 1 *dia.*), 5.18–5.12 (m, 1 H, 1 *dia.*, overlap), 5.18–5.12 (m, 2 H, 2 *dia.*, overlap), 4.17 (d, *J* = 9.3 Hz, 1 H, 1 *dia.*), 3.97 (dd, *J* = 9.9, 2.3 Hz, 1 H, 1 *dia.*), 3.67–3.59 (m, 2 H, 2 *dia.*), 3.48–3.36 (m, 2 H, 2 *dia.*, overlap), 3.45 (s, 3 H, 1 *dia.*, overlap), 3.41 (s, 3 H, 1 *dia.*, overlap), 3.14–2.96 (m, 2 H, 2 *dia.*), 2.58–2.45 (m, 4 H, 2 *dia.*), 2.45–2.33 (m, 4 H, 2 *dia.*), 2.33–2.22 (m, 4 H, 2 *dia.*), 2.13–1.99 (m, 2 H, 2 *dia.*), 1.91 (d, *J* = 1.0 Hz, 3 H, 1 *dia.*), 1.80 (d, *J* = 1.1 Hz, 3 H, 1 *dia.*), 1.19 (d, *J* = 6.3 Hz, 3 H, 1 *dia.*), 1.18 (d, *J* = 6.2 Hz, 3 H, 1 *dia.*), 0.96 (d, *J* = 7.2 Hz, 3 H, 1 *dia.*, overlap), 0.95 (d, *J* = 6.6 Hz, 3 H, 1 *dia.*, overlap), 0.95 ppm (d, *J* = 6.0 Hz, 3 H, 1 *dia.*, overlap); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.6 (C), 168.8 (C), 166.1 (C), 165.4 (C), 133.3 (CH), 133.3 (CH), 133.1 (C), 132.5 (C), 131.6 (CH), 131.3 (CH), 130.3 (C), 130.1 (C), 129.7 (CH), 129.7 (CH), 128.6 (CH), 128.6 (CH), 88.2 (C), 87.7 (C), 80.6 (CH), 79.0 (CH), 77.4 (C), 77.3 (C), 74.5 (CH), 73.6 (CH), 72.5 (CH), 72.1 (CH), 71.8 (CH), 71.2 (CH), 70.8 (CH), 70.2 (CH), 57.1 (CH_3), 57.0 (CH_3), 40.9 (CH), 40.8 (CH_2), 40.6 (CH), 39.8 (CH), 38.1 (CH), 37.0 (CH_2), 33.3 (CH_2), 30.5 (CH_2), 20.2 (CH_3), 20.1 (CH_3), 16.9 (CH_3), 16.8 (CH_3), 16.0 (CH_2), 14.0 (CH_3), 13.8 (CH_3), 12.9 (CH_2), 10.9 ppm (CH_3, 2 *dia.*); IR (film): 3495, 2968, 2930, 2875, 1719, 1450, 1377, 1315, 1270, 1191, 1174, 1105, 1070, 1049, 1025, 984, 940, 881, 850, 735, 711 cm^{-1}; HRMS (ESI): *m*/*z:* calcd for $C_{27}H_{36}O_7Na$ $[M + Na]^+$: 495.2353; found 495.2357.

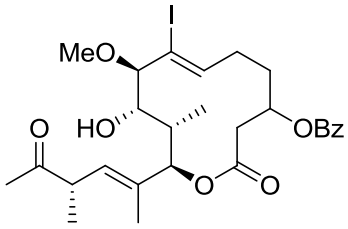


Compound 68. Dess-Martin periodinane (2.3 g, 5.4 mmol) was added to a solution of diol **67** (850 mg, 1.8 mmol) in CH_2Cl_2 (50 mL) at 0 °C. The mixture was stirred at this temperature for 4 h before the reaction was quenched with a few drops of EtOH. The solvents were evaporated and the residue was purified by flash chromatography (hexanes/EtOAc, 9/1 → 7/3), affording ketone **68** as a white solid (740 mg, 87 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.2 Hz, 2 H, 1 *dia.*), 8.00 (d, *J* = 8.5 Hz, 2 H, 1 *dia.*), 7.59–7.53 (m, 2 H, 2 *dia.*), 7.47–7.40 (m, 4 H, 2 *dia.*), 5.68 (dddd, *J* = 10.7, 7.6, 3.2, 3.2 Hz, 1 H, 1 *dia.*), 5.58 (dddd, *J* = 10.5, 5.2, 5.2, 2.7 Hz, 1 H, 1 *dia.*), 5.28 (d, *J* = 8.6 Hz, 1 H, 1 *dia.*), 5.26 (d, *J* = 7.3 Hz, 1 H, 1 *dia.*), 5.23 (d, *J* = 3.6 Hz, 1 H, 1 *dia.*), 5.16 (d, *J* = 4.2 Hz, 1 H, 1 *dia.*), 4.15 (d, *J* =



8.8 Hz, 1 H, 1 *dia.*), 3.97 (dd, *J* = 9.8, 2.5 Hz, 1 H, 1 *dia.*), 3.61 (d, *J* = 9.8 Hz, 1 H, 1 *dia.*, overlap), 3.61 (d, *J* = 9.8 Hz, 1 H, 1 *dia.*, overlap), 3.48–3.38 (m, 2 H, 2 *dia.*, overlap), 3.46 (s, 3 H, 1 *dia.*, overlap), 3.43 (s, 3 H, 1 *dia.*, overlap), 3.12–2.98 (m, 2 H, 2 *dia.*), 2.60–2.45 (m, 4 H, 2 *dia.*), 2.45–2.33 (m, 2 H, 2 *dia.*), 2.33–2.21 (m, 2 H, 2 *dia.*), 2.13 (s, 3 H, 1 *dia.*), 2.11 (s, 3 H, 1 *dia.*), 2.08–1.95 (m, 2 H, 2 *dia.*), 1.92 (d, *J* = 1.0 Hz, 3 H, 1 *dia.*), 1.85 (d, *J* = 1.1 Hz, 3 H, 1 *dia.*), 1.14 (d, *J* = 6.8 Hz, 3 H, 1 *dia.*, overlap), 1.13 (d, *J* = 6.8 Hz, 3 H, 1 *dia.*, overlap), 0.94 (d, *J* = 7.3 Hz, 3 H, 1 *dia.*), 0.92 ppm (d, *J* = 7.3 Hz, 3 H, 1 *dia.*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.6 (C), 209.5 (C), 169.4 (C), 168.5 (C), 166.0 (C), 165.4 (C), 134.1 (C), 133.7 (C), 133.3 (CH), 133.3 (CH), 130.2 (C), 130.1 (C), 129.7 (CH), 129.7 (CH), 128.5 (CH, 2 *dia.*), 128.5 (CH), 128.3 (CH), 88.1 (C), 87.3 (C), 80.8 (CH), 80.5 (CH), 77.4 (C, 2 *dia.*), 74.5 (CH), 74.0 (CH), 71.3 (CH), 70.7 (CH), 70.6 (CH), 70.3 (CH), 57.0 (CH_3), 57.0 (CH_3), 46.8 (CH), 46.8 (CH), 40.4 (CH_2), 39.4 (CH), 38.0 (CH), 37.1 (CH_2), 32.9 (CH_2), 30.6 (CH_2), 28.1 (CH_3, 2 *dia.*), 16.1 (CH_3), 15.9 (CH_3), 15.9 (CH_2), 13.5 (CH_3), 13.4 (CH_3), 13.0 (CH_2), 10.8 ppm (CH_3, 2 *dia.*); IR (film): 3551, 2968, 2931, 2875, 1713, 1450, 1354, 1314, 1271, 1190, 1170, 1104, 1070, 1049, 1025, 983, 942, 884, 850, 711 cm^{-1}; MS (EI): *m*/*z* (%): 470 (<1) $[M]^+$, 399 (3), 289 (38), 239 (12), 204 (7), 181 (14), 167 (25), 121 (13), 109 (29), 105 (100), 77 (21), 43 (21); HRMS (ESI): *m*/*z:* calcd for $C_{27}H_{34}O_7Na$ $[M + Na]^+$: 493.2197; found 493.2195.

Compound 69: Triphenylstannane (1.68 g, 4.8 mmol) and AIBN (158 mg, 1.0 mmol) were added to a carefully degassed solution of alkyne **68** (450 mg, 1.0 mmol) in toluene (13 mL) and the resulting mixture was stirred at 80 °C for 3 h. The mixture was concentrated under vacuum and the residue purified by flash chromatography (hexanes/EtOAc, 9/1 → 7/3) to give the corresponding alkenylstannane as a white solid.

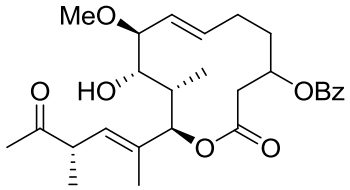


Iodine (295 mg, 1.2 mmol) was added to a solution of this compound in CH_2Cl_2 (25 mL) at 0 °C. The resulting mixture was warmed to ambient temperature for 1 h before the solvent was evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 8/2 → 7/3) to furnish the two diastereomers of iodoalkene **69**. The fast eluting diastereomer (71 mg, 12 %) and the slow eluting one (186 mg, 33 %) were both obtained as white solids. *First diastereomer*: $[\alpha]_D^{20}$ = +86.0 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.5 Hz, 2H), 7.58 (tt, *J* = 7.4, 1.5 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 6.49 (t, *J* = 7.6 Hz, 1H), 5.54–5.45 (m, 1H), 5.23 (d, *J* = 9.6 Hz, 1H), 5.20 (d, *J* = 3.5 Hz, 1H), 3.97 (d, *J* = 9.0 Hz, 1H), 3.72 (d, *J* = 9.0 Hz, 1H), 3.46–3.37 (m, 1H, overlap), 3.38 (s, 3H, overlap), 2.95 (dd, *J* = 14.4, 3.3 Hz, 1H), 2.73 (s, 1H), 2.55 (dd, *J* = 14.4, 10.6 Hz, 1H), 2.41–2.22 (m, 2H), 2.17–2.09 (m, 1H, overlap), 2.14 (s, 3H, overlap), 2.09–1.99 (m, 1H), 1.90 (d, *J* = 1.3 Hz, 3H), 1.86–1.72 (m, 1H), 1.13 (d, *J* = 6.6 Hz, 3H), 0.97 ppm (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.6 (C), 168.1 (C), 166.3 (C), 138.5 (CH), 134.0 (C), 133.4 (CH), 130.1 (C), 129.8 (CH), 128.6 (CH), 128.1 (CH), 90.0 (CH), 81.0 (CH), 73.9 (CH), 69.5 (CH), 56.9 (CH_3), 46.8 (CH), 40.6 (CH_2), 39.0 (CH), 33.3 (CH_2), 30.7 (CH_2), 28.1 (CH_3), 15.9 (CH_3), 13.4 (CH_3), 10.8 ppm (CH_3); IR (film): 3515, 2969, 2936, 2875, 1725, 1703, 1449, 1356, 1314, 1248, 1190, 1172, 1146, 1095, 1064, 1043, 1025, 977, 905, 874, 845, 714 cm^{-1}; MS (EI): *m*/*z* (%): 527 (5), 471 (2), 429 (7), 295 (17), 210 (11), 181 (27), 169 (13), 151 (55), 121

(23), 109 (61), 105 (100), 77 (29), 43 (45); HRMS (ESI): *m/z:* calcd for $C_{27}H_{35}O_7INa$ [M + Na]$^+$: 621.1320; found 621.1321.

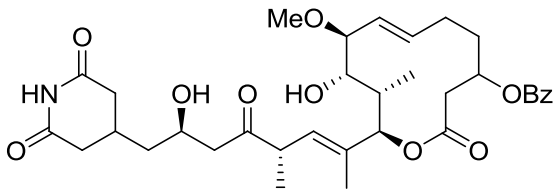
Second diastereomer: $[\alpha]_D^{20}$ = +62.5 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.5 Hz, 2H), 7.56 (tt, *J* = 7.5, 1.4 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 5.96 (dd, *J* = 9.1, 5.1 Hz, 1H), 5.57–5.50 (m, 1H), 5.29 (d, *J* = 9.9 Hz, 1H), 5.09 (d, *J* = 3.8 Hz, 1H), 3.86 (d, *J* = 9.1 Hz, 1H), 3.41 (qd, *J* = 9.6, 6.8 Hz, 1H), 3.34 (s, 3H), 3.13 (d, *J* = 9.1 Hz, 1H), 2.97 (dd, *J* = 17.6, 4.9 Hz, 1H), 2.87 (dd, *J* = 17.7, 11.1 Hz, 1H), 2.70 (s, 1H), 2.38–2.21 (m, 2H), 2.17–2.08 (m, 1H, overlap), 2.11 (s, 3H, overlap), 2.08–2.01 (m, 2H), 1.85 (d, *J* = 1.3 Hz, 3H), 1.13 (d, *J* = 6.8 Hz, 3H), 0.95 ppm (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.4 (C), 169.0 (C), 165.4 (C), 140.7 (CH), 133.4 (C), 133.2 (CH), 130.3 (C), 129.7 (CH), 128.5 (CH), 128.5 (CH), 88.7 (CH), 80.9 (CH), 70.2 (CH), 69.4 (CH), 56.7 (CH_3), 46.7 (CH), 38.3 (CH), 36.7 (CH_2), 30.0 (CH_2), 29.6 (CH_2), 28.1 (CH_3), 16.0 (CH_3), 13.8 (CH_3), 10.9 ppm (CH_3); IR (film): 3511, 2969, 2928, 2875, 1713, 1450, 1353, 1314, 1270, 1191, 1169, 1105, 1067, 1025, 981, 936, 852, 711 cm^{-1}; MS (EI): *m/z* (%): 527 (2), 471 (2), 429 (7), 295 (17), 210 (9), 181 (31), 169 (13), 151 (58), 121 (24), 109 (65), 105 (100), 77 (29), 43 (46); HRMS (ESI): *m/z:* calcd for $C_{27}H_{35}O_7INa$ [M + Na]$^+$: 621.1320; found 621.1324.

Compound 70. Triphenylstannane (434 mg, 1.24 mmol) and AIBN (51 mg, 0.31 mmol) were added to a carefully degassed solution of iodoalkene **69** (370 mg, 0.62 mmol) in toluene (15 mL) and the resulting mixture was stirred at 70 °C for 2 h. The solvents were evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 9/1 → 7/3) to give macrolactone **70** (300 mg, quant.) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 8.6 Hz, 2 H, 1 *dia.*), 8.01 (d, *J* = 8.3 Hz, 2 H, 1 *dia.*), 7.59–7.53 (m, 2 H, 2 *dia.*), 7.47–7.39 (m, 4 H, 2 *dia.*), 5.80–5.67 (m, 2 H, 2 *dia.*), 5.56–5.49 (m, 2 H, 2 *dia.*), 5.47 (dd, *J* = 16.2, 7.0 Hz, 1 H, 1 *dia.*), 5.36 (dd, *J* = 15.9, 7.3 Hz, 1 H, 1 *dia.*), 5.25 (d, *J* = 9.6 Hz, 1 H, 1 *dia.*), 5.23 (d, *J* = 9.6 Hz, 1 H, 1 *dia.*), 5.16 (d, *J* = 3.3 Hz, 1 H, 1 *dia.*), 5.02 (d, *J* = 3.8 Hz, 1 H, 1 *dia.*), 3.79 (dd, *J* = 9.3, 0.9 Hz, 1 H, 1 *dia.*), 3.69 (dd, *J* = 9.5, 3.2 Hz, 1 H, 1 *dia.*), 3.46–3.35 (m, 2 H, 2 *dia.*), 3.31 (s, 3 H, 1 *dia.*), 3.30 (s, 3 H, 1 *dia.*), 3.28–3.21 (m, 2 H, 2 *dia.*), 3.00 (s, 1 H, 1 *dia.*), 2.96 (s, 1 H, 1 *dia.*), 2.93 (dd, *J* = 17.3, 4.2 Hz, 1 H, 1 *dia.*), 2.87 (dd, *J* = 13.1, 3.0 Hz, 1 H, 1 *dia.*), 2.71 (dd, *J* = 17.2, 11.4 Hz, 1 H, 1 *dia.*), 2.54 (dd, *J* = 13.1, 10.6 Hz, 1 H, 1 *dia.*), 2.49–2.37 (m, 1 H, 1 *dia.*), 2.35–2.14 (m, 3 H, 2 *dia.*), 2.14–1.93 (m, 4 H, 2 *dia.*, overlap), 2.14–1.93 (m, 1 H, 1 *dia.*, overlap), 2.13 (s, 3 H, 1 *dia.*, overlap), 2.10 (s, 3 H, 1 *dia.*, overlap), 1.90 (d, *J* = 1.3 Hz, 3 H, 1 *dia.*), 1.81 (d, *J* = 1.3 Hz, 3 H, 1 *dia.*), 1.75–1.60 (m, 1 H, 1 *dia.*), 1.12 (d, *J* = 6.8 Hz, 6 H, 2 *dia.*), 0.95 (d, *J* = 7.1 Hz, 3 H, 1 *dia.*), 0.93 ppm (d, *J* = 7.1 Hz, 3 H, 1 *dia.*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.7 (C), 209.5 (C), 169.2 (C), 168.7 (C), 166.1 (C), 165.5 (C), 136.5 (CH), 136.4 (CH), 134.1 (C), 133.7 (C), 133.3 (CH), 133.2 (CH), 131.7 (CH), 130.4 (C), 130.2 (C), 129.7 (CH), 129.6 (CH), 128.8 (CH), 128.5 (CH), 128.5 (CH), 128.0 (CH, 2 *dia.*), 83.4 (CH), 82.6 (CH), 80.7 (CH), 80.5 (CH), 71.3 (CH, 2 *dia.*), 71.1 (CH), 69.7 (CH), 56.7 (CH_3), 56.5 (CH_3), 46.8 (CH), 46.7 (CH), 40.9 (CH_2), 38.4 (CH), 37.5 (CH), 37.4 (CH_2), 33.4 (CH_2), 30.2 (CH_2), 28.2 (CH_3), 28.1 (CH_3), 27.2 (CH_2), 26.4 (CH_2), 16.1 (CH_3), 15.9 (CH_3), 13.7 (CH_3), 13.5 (CH_3), 11.2 (CH_3), 11.0 ppm (CH_3); IR (film): 3524, 2968, 2931, 2875, 1716, 1451, 1354, 1315, 1272, 1187, 1109, 1070, 1026, 982, 935, 713 cm$^-$



[1]; MS (EI): *m*/*z* (%): 472 (<1) $[M]^+$, 401 (2), 303 (6), 291 (29), 181 (10), 169 (100), 152 (33), 137 (22), 123 (12), 121 (11), 109 (47), 105 (59), 84 (51), 77 (13), 43 (22); HRMS (ESI): *m*/*z:* calcd for $C_{27}H_{36}O_7Na$ $[M + Na]^+$: 495.2353; found 495.2354.

Compound 73: Me_3SiCl (110 µL, 0.85 mmol) and triethylamine (120 µL, 0.85 mmol) were added to a solution of ketone **70** (40 mg, 0.085 mmol) in THF (2 mL) at –78 °C before LiHMDS (1 M in THF, 0.34 mL, 0.34 mmol) was slowly introduced and the resulting mixture stirred at –78 °C for 1 h. The reaction was then quenched with pH 7 phosphate buffer and the product extracted with CH_2Cl_2 (3 x 2 mL). The combined organic phases were dried over $MgSO_4$ and evaporated to give the corresponding silyl enol ether, which was immediately used in the next step without further purification.



Molecular sieves (4 Å, ca. 200 mg) and aldehyde **41b** (13 mg, 0.085 mmol)[2] were added to a solution of the crude silyl enol ether in propionitrile (1 mL). The mixture was cooled to –78 °C before a solution of compound **42** [prepared upon stirring of a solution of $PhBCl_2$ (22 µL, 0.17 mmol) and N-tosyl-D-tryptophane (61 mg, 0.17 mmol) in CH_2Cl_2 (1 mL) for 1 h, followed by removal of the solvent][3] in propionitrile (0.3 mL) was added dropwise. After stirring for 20 h at –78 °C, the reaction was quenched with sat. aq. $NaHCO_3$ (2 mL), the aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL), and the combined organic layers were dried over $MgSO_4$ and evaporated. The resulting material was dissolved in THF (5 mL) at 0 °C and treated with 2.5 mL of a stock solution of buffered HF·pyridine [prepared from THF (7.25 mL), pyridine (2.69 mL) and HF·pyridine complex (0.54 mL, 70 % *w*/*w*)]. The mixture was stirred at 0 °C for 30 min and then at ambient temperature for 4 h to complete the desilylation. Dilution with CH_2Cl_2 (20 mL), washing of the organic layer with sat. aq. $NaHCO_3$ (10 mL) and aq. $CuSO_4$ solution (1 M, 3 x 10 mL), drying over $MgSO_4$ and evaporation of the solvents left a residue, which was purified by flash chromatography (EtOAc/hexanes, 80/20) to give product **73** as a white solid (30 mg, 57 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (br s, 1 H, 1 *dia.*, overlap), 8.17 (br s, 1 H, 1 *dia.*, overlap), 8.04 (d, *J* = 8.2 Hz, 2 H, 1 *dia.*), 8.00 (d, *J* = 8.3 Hz, 2 H, 1 *dia.*), 7.60–7.53 (m, 2 H, 2 *dia.*), 7.48–7.41 (m, 4 H, 2 *dia.*), 5.81–5.64 (m, 2 H, 2 *dia.*), 5.54–5.46 (m, 2 H, 2 *dia.*, overlap), 5.49–5.42 (m, 1 H, 1 *dia.*, overlap), 5.37 (dd, *J* = 15.9, 7.3 Hz, 1 H, 1 *dia.*), 5.18–5.12 (m, 2 H, 2 *dia.*, overlap), 5.18–5.12 (m, 1 H, 1 *dia.*, overlap), 4.97 (d, *J* = 3.4 Hz, 1 H, 1 *dia.*), 4.11–4.01 (m, 2 H, 2 *dia.*), 3.79 (dd, *J* = 9.3, 0.9 Hz, 1 H, 1 *dia.*), 3.66 (dd, *J* = 9.4, 3.6 Hz, 1 H, 1 *dia.*), 3.46–3.34 (m, 2 H, 2 *dia.*), 3.32 (s, 3 H, 1 *dia.*), 3.31 (s, 3 H, 1 *dia.*), 3.29–3.23 (m, 2 H, 2 *dia.*), 3.16 (s, 1 H, 1 *dia.*), 3.11 (s, 1 H, 1 *dia.*), 2.93 (dd, *J* = 17.2, 3.9 Hz, 1 H, 1 *dia.*), 2.87 (dd, *J* = 13.2, 3.0 Hz, 1 H, 1 *dia.*), 2.82–2.67 (m, 6 H, 2 *dia.*), 2.67–2.55 (m, 2 H, 2 *dia.*), 2.55–2.39 (m, 6 H, 2 *dia.*), 2.38–2.23 (m, 6 H, 2 *dia.*), 2.22–2.11 (m, 2 H, 2 *dia.*), 2.10–1.99 (m, 4 H, 2 *dia.*), 1.90 (d, *J* = 0.9 Hz, 3 H, 1 *dia.*), 1.79 (d, *J* = 1.0 Hz, 3 H, 1 *dia.*), 1.63–1.51 (m, 2 H, 2 *dia.*), 1.42–1.33 (m, 2 H, 2 *dia.*), 1.13 (d, *J* = 6.8 Hz, 6 H, 2 *dia.*), 0.93 (d, *J* = 7.3 Hz, 3 H, 1 *dia.*, overlap), 0.92 ppm (d, *J* = 7.2 Hz, 3 H, 1 *dia.*, overlap); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 212.1 (C), 211.9 (C), 172.5 (C), 172.5 (C), 172.4 (C), 172.4 (C), 169.3 (C), 168.7 (C), 166.2 (C), 165.6 (C), 136.7 (CH), 136.4 (CH), 134.8 (C), 134.5 (C), 133.3 (CH), 133.2 (CH),

131.7 (CH), 130.3 (C), 130.1 (C), 129.8 (CH), 129.7 (CH), 128.8 (CH), 128.6 (CH), 128.5 (CH), 126.8 (CH, 2 *dia.*), 83.1 (CH), 82.4 (CH), 80.6 (CH), 80.0 (CH), 71.7 (CH), 71.4 (CH), 71.4 (CH), 69.7 (CH), 65.1 (CH, 2 *dia.*), 56.7 (CH_3), 56.5 (CH_3), 47.5 (CH_2), 47.2 (CH_2), 46.7 (CH), 46.7 (CH), 41.2 (CH_2), 41.1 (CH_2), 40.9 (CH_2), 38.6 (CH_2), 38.5 (CH_2), 38.4 (CH), 37.7 (CH), 37.5 (CH_2), 37.4 (CH_2), 37.3 (CH_2), 37.3 (CH_2), 33.5 (CH_2), 27.3 (CH), 27.2 (CH), 26.5 (CH_2, 2 *dia.*), 15.8 (CH_3), 15.5 (CH_3), 14.0 (CH_3), 13.7 (CH_3), 11.3 (CH_3), 11.0 ppm (CH_3); IR (film): 3469, 2968, 2930, 2875, 1697, 1450, 1374, 1314, 1260, 1190, 1150, 1106, 1069, 1025, 980, 932, 752, 712 cm^{-1}; HRMS (ESI): *m/z:* calcd for $C_{34}H_{45}NO_{10}Na$ $[M + Na]^+$: 650.2936; found 650.2936.

Compound 74. Imidazole (53 mg, 0.78 mmol) and resin-supported triphenylphosphine (3 mmol/g on polystyrene, 53 mg, 0.16 mmol) were added to a solution of diol **73** (33 mg, 0.052 mmol) in CH_2Cl_2 (3 mL) at 0 °C. Next, iodine (46 mg, 0.18 mmol) was introduced and the resulting mixture stirred at ambient temperature for 1.5 h. The reaction was diluted with CH_2Cl_2 (10 mL) and the resin filtered off. The filtrate was extracted with pH 7 phosphate buffer and the aqueous phase extracted with CH_2Cl_2 (10 mL). The combined organic phases were dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography (EtOAc/hexanes, 5/5 → 2/8) to give product **74** as a white solid (19 mg, 60 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08–7.97 (m, 6 H, 2 *dia.*), 7.60–7.53 (m, 2 H, 2 *dia.*), 7.48–7.41 (m, 4 H, 2 *dia.*), 6.79–6.68 (m, 2 H, 2 *dia.*), 6.31 (d, *J* = 15.4 Hz, 1 H, 1 *dia.*), 6.22 (d, *J* = 15.6 Hz, 1 H, 1 *dia.*), 5.81–5.67 (m, 2 H, 2 *dia.*), 5.55–5.46 (m, 2 H, 2 *dia.*, overlap), 5.50–5.43 (m, 1 H, 1 *dia.*, overlap), 5.38 (dd, *J* = 15.9, 7.2 Hz, 1 H, 1 *dia.*), 5.18 (d, *J* = 9.7 Hz, 2 H, 2 *dia.*), 5.15 (d, *J* = 3.3 Hz, 1 H, 1 *dia.*), 4.98 (d, *J* = 3.7 Hz, 1 H, 1 *dia.*), 3.81 (dd, *J* = 9.3, 1.1 Hz, 1 H, 1 *dia.*), 3.67 (dd, *J* = 9.4, 3.6 Hz, 1 H, 1 *dia.*), 3.58–3.47 (m, 2 H, 2 *dia.*), 3.33 (s, 3 H, 1 *dia.*, overlap), 3.31 (s, 3 H, 1 *dia.*, overlap), 3.31–3.22 (m, 2 H, 2 *dia.*, overlap), 2.92 (dd, *J* = 17.2, 3.9 Hz, 1 H, 1 *dia.*), 2.87 (dd, *J* = 13.0, 2.7 Hz, 1 H, 1 *dia.*), 2.75–2.64 (m, 6 H, 2 *dia.*), 2.54 (dd, *J* = 13.3, 10.7 Hz, 1 H, 1 *dia.*), 2.49–2.38 (m, 2 H, 2 *dia.*), 2.38–2.22 (m, 12 H, 2 *dia.*), 2.21–2.12 (m, 2 H, 2 *dia.*), 2.10–1.96 (m, 5 H, 2 *dia.*), 1.93 (d, *J* = 1.0 Hz, 3 H, 1 *dia.*), 1.82 (d, *J* = 1.0 Hz, 3 H, 1 *dia.*), 1.15 (d, *J* = 6.8 Hz, 6 H, 2 *dia.*), 0.90 (d, *J* = 7.3 Hz, 3 H, 1 *dia.*, overlap), 0.83 ppm (d, *J* = 7.1 Hz, 3 H, 1 *dia.*, overlap); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.8 (C), 199.6 (C), 171.7 (C, 2 *dia.*), 171.7 (C, 2 *dia.*), 169.3 (C), 169.2 (C), 165.6 (C, 2 *dia.*), 141.6 (CH), 141.3 (CH), 136.7 (CH), 136.5 (CH), 134.3 (C), 133.9 (C), 133.3 (CH), 133.2 (CH), 131.4 (CH), 131.1 (CH), 130.4 (C, 2 *dia.*), 129.8 (CH), 129.7 (CH), 129.0 (CH), 128.8 (CH), 128.6 (CH), 128.5 (CH), 127.5 (CH, 2 *dia.*), 83.2 (CH), 82.6 (CH), 80.3 (CH, 2 *dia.*), 71.7 (CH, 2 *dia.*), 71.4 (CH, 2 *dia.*), 56.7 (CH_3), 56.5 (CH_3), 44.9 (CH_2, 2 *dia.*), 44.8 (CH), 44.8 (CH), 37.7 (CH_2, 2 *dia.*), 37.6 (CH_2, 2 *dia.*), 37.5 (CH, 2 *dia.*), 37.3 (CH_2, 2 *dia.*), 30.5 (CH_2, 2 *dia.*), 29.8 (CH), 29.8 (CH), 26.6 (CH_2), 22.7 (CH_2), 15.8 (CH_3, 2 *dia.*), 13.9 (CH_3, 2 *dia.*), 11.3 ppm (CH_3, 2 *dia.*); IR (film): 3493, 3226, 2968, 2926, 2875, 1695, 1627, 1450, 1374, 1315, 1268, 1191, 1150, 1107, 1069, 1043, 1025, 979, 931, 804, 712 cm^{-1}; HRMS (ESI): *m/z:* calcd for $C_{34}H_{43}NO_9Na$ $[M + Na]^+$: 632.2830; found 632.2829.

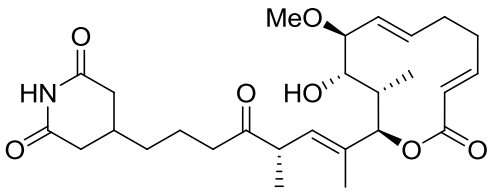
Compound 76. A solution of the copper complex **75** (1 M in toluene, 1.8 mL, 1.8 mmol) was added to enone **74** (11 mg, 0.018 mmol). The solvent was slowly evaporated by a stream of argon until a precipitate formed. After stirring for 14 h at ambient temperature, the mixture was diluted with CH_2Cl_2 and the solvents were evaporated. The residue was purified by flash chromatography (EtOAc/hexanes, 15/85 → 70/30) to give product **76** as a white solid (6.5 mg, 59 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06-8.00 (m, 4 H, 2 *dia.*) 7.85 (br s, 1 H, 1 *dia*), 7.81 (br s, 1 H, 1 *dia*), 7.60-7.59 (m, 2 H, 2 *dia.*) 7.48-7.42 (m, 4 H, 2 *dia.*), 5.79-5.69 (m, 2 H, 2 *dia.*), 5.54-5.48 (m, 2 H, 2 *dia.*, overlap), 5.47 (dd, *J* = 15.7, 6.8 Hz, 1 H, 1 *dia*,overlap), 5.38 (dd, *J* = 16.0, 7.3 Hz, 1 H, 1 *dia*,overlap), 5.18 (d, *J* = 9.8 Hz, 2 H, 2 *dia*.), 5.14 (d, *J* = 3.2 Hz, 1 H, 1 *dia*.), 4.98 (d, *J* = 3.8 Hz, 1 H, 1 *dia*.), 3.79 (d, *J* = 9.0 Hz, 1 H, 1 *dia*.), 3.66 (dd, *J* = 9.4, 3.6 Hz, 1 H, 1 *dia*.), 3.46-3.36 (m, 2 H, 2 *dia*.), 3.33 (s, 3 H, 1 *dia.*, overlap), 3.31 (s, 3 H, 1 *dia.*, overlap), 3.33-3.34 (m, 2 H, 2 *dia.*, overlap), 3.06 (s, 1 H, 1 *dia.*), 2.96 (s, 1 H, 1 *dia.*), 2.92 (dd, *J* = 17.3, 4.0 Hz, 1 H, 1 *dia.*), 2.87 (dd, *J* = 13.3, 3.0 Hz, 1 H, 1 *dia*), 2.74-2.66 (m, 4 H, 2 *dia.*, overlap), 2.68 (dd, *J* = 16.8, 4.2 Hz, 1 H, 1 *dia*, overlap), 2.63-2.57 (m, 1 H, 1 *dia.*, overlap), 2.61-2.43 (m, 4 H, 2 *dia*., overlap), 2.47-2.31 (m, 4 H, 2 *dia.*, overlap), 2.33-2.20 (m, 4 H, 2 *dia.*, overlap), 2.18-2.09 (m, 2 H, 2 *dia.*, overlap), 2.16-2.00 (m, 2 H, 2 *dia.*, overlap), 2.15-1.93 (m, 4 H, 2 *dia.*, overlap), 1.90 (d, *J* = 1.2 Hz, 3 H, 1 *dia.*), 1.81 (d, *J* = 1.2 Hz, 3 H, 1 *dia.*), 1.61-1.54 (m, 4 H, 2 *dia.*), 1.38-1.32 (m, 4 H, 2 *dia.*), 1.12 (d, *J* = 6.6 Hz, 3 H, 1 *dia.*, overlap), 1.12 ppm (d, *J* = 6.8 Hz, 3 H, 1 *dia.*, overlap), 0.91 (d, *J* = 7.2 Hz, 6 H, 2 *dia.*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 210.8 (C), 210.7 (C), 172.2 (C, 2 *dia.*), 172.2 (C, 2 *dia.*), 169.3 (C), 168.7 (C), 166.2 (C), 165.6 (C), 136.6 (CH), 134.4 (CH), 134.1 (C), 133.7 (C), 133.3, (CH), 133.2 (CH), 131.7 (CH), 130.4 (C), 130.2 (C), 129.8 (CH), 129.7 (CH), 128.8 (CH), 128.6 (CH), 128.5 (CH), 128.1 (CH), 127.7 (CH), 83.2 (CH), 82.5 (CH), 80.8 (CH), 80.2 (CH), 71.6 (CH), 71.4 (CH, 2 *dia.*), 69.7 (CH), 56.7 (CH_3), 56.5 (CH_3), 46.2 (CH, 2 *dia.*), 41.0 (CH_2), 40.1 (CH_2), 38.4 (CH), 37.9 (CH), 37.9 (CH_2, 2 *dia.*), 37.7 (CH_2), 37.6 (CH_2), 34.3 (CH_2, 2 *dia.*), 30.5 (CH_2, 2 *dia*.), 30.4 (CH_2), 30.3 (CH_2), 27.3 (CH_2), 26.6 (CH_2), 20.4 (CH_2, 2 *dia*.), 16.1 (CH_3), 15.9 (CH_3), 13.9 (CH_3), 13.5 (CH_3), 11.3 (CH_3), 11.0 ppm (CH_3); IR (film): 3522, 3230, 2931, 1704, 1601, 1450, 1372, 1314, 1270, 1191, 1150, 1108, 1069, 1044, 1026, 982, 932, 851, 804, 713 cm^{-1}; HRMS (ESI): *m/z:* calcd for $C_{34}H_{45}NO_9Na$ $[M + Na]^+$: 634.2987; found 634.2988.

Compound 77: $NaBH_4$ (2.5 mg, 0.065 mmol) was added to a solution of ketone **76** (8.0 mg, 0.013 mmol) in THF (0.5 mL) at 0 °C. After stirring for 1 h at this temperature, a second portion of $NaBH_4$ (2.5 mg, 0.065 mmol) was introduced and stirring continued at ambient temperature for 2 h. The reaction was quenched with sat. aq. NH_4Cl and diluted with CH_2Cl_2. The aqueous layer was extracted with CH_2Cl_2 and the combined organic phases were dried over Na_2SO_4 and evaporated.

DBU (30 μL, 0.20 mmol) was added to a solution of the crude alcohol in THF (0.6 mL). The resulting mixture was stirred at ambient temperature for 18 h before the solvents were

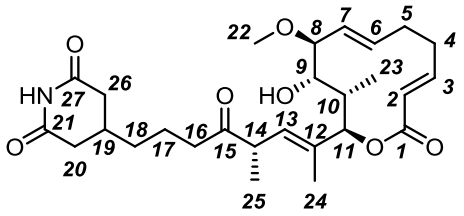
evaporated and the residue was purified by flash chromatography (hexanes/EtOAc, 80/20 → 25/75) to give product **77** as a white solid (4.7 mg, 73 % over two steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (br s, 2 H, 2 *dia*.), 6.69 (dt, *J* = 16.1, 8.1 Hz, 2 H, 2 *dia*.), 5.72 (d, *J* = 16.1 Hz, 1 H, 1 *dia*.), 5.70 (d, *J* = 15.9 Hz, 1 H, 1 *dia*.), 5.66-5.58 (m, 2 H, 2 *dia*.), 5.24 (d, *J* = 3.2 Hz, 1 H, 1 *dia*.), 5.21 (d, *J* = 3.6 Hz, 1 H, 1 *dia*.), 5.15-5.09 (m, 2 H, 2 *dia*., overlap), 5.11-5.03 (m, 2 H, 2 *dia*., overlap), 3.75 (d, *J* = 9.0 Hz, 1 H, 1 *dia.)*, 3.75 (d, *J* = 9.2 Hz, 1 H, 1 *dia*.), 3.47-3.43 (m, 3 H, 2 *dia*.), 3.32 (s, 3 H, 1 *dia*.), 3.29 (s, 3 H, 1 *dia*.), 3.22-3.19 (m, 3 H, *2 dia*.), 3.12 (s, 1 H, 1 *dia*.), 2.99 (s, 1 H, 1 *dia*.), 2.79-2.68 (m, 5 H, 2 *dia*., overlap), 2.72 (dd, *J* = 16.7, 3.8 Hz, 2 H, 2 *dia*.), 2.67-2.60 (m, 2 H, 2 *dia*.), 2.48-2.40 (m, 2 H, 2 *dia*., overlap), 2.46-2.39 (m, 1 H, 1 *dia*., overlap), 2.31-2.18 (m, 4 H, 2 *dia*., overlap), 2.20-2.12 (m, 1 H, 1 *dia*., overlap), 2.18-2.10 (m, 2 H, 2 *dia*., overlap), 1.97 (dtd, *J* = 11.9, 11.9, 4.6 Hz, 2 H, 2 *dia*.), 1.87-1.80 (m, 1 H, 1 *dia*., overlap), 1.86 (s, 6 H, 2 *dia*., overlap), 1.65-1.52 (m, 4 H, 2 *dia*.), 1.47-1.34 (m, 6 H, 2 *dia*.), 1.34-1.21 (m, 2 H, 2 *dia*.), 0.99 (d, *J* = 6.8 Hz, 3 H, 1 *dia*.), 0.94 (d, *J* = 6.6 Hz, 3 H, 1 *dia*.), 0.94 (d, *J* = 7.2 Hz, 3 H, 1 *dia*.), 0.91 ppm (d, *J* = 7.4 Hz, 3 H, 1 *dia*.); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3 (C, 2 *dia*.), 172.3 (C, 2 *dia*.), 168.3 (C), 168.1 (C), 151.0 (CH), 150.9 (CH), 133.7 (C), 133.6 (C), 130.8 (CH), 130.3 (CH), 130.1 (CH), 129.6 (CH), 129.5 (CH), 129.4 (CH), 125.2 (CH), 125.1 (CH), 82.6 (CH), 82.2 (CH), 81.6 (CH), 81.3 (CH), 76.1 (CH), 75.9 (CH), 74.3 (CH), 74.1 (CH), 57.2 (CH_3, 2 *dia*.), 39.2 (CH), 38.5 (CH), 38.3 (CH), 38.1 (CH), 38.0 (CH_2, 2 *dia*.), 38.0 (CH_2, 2 *dia*.), 35.2 (CH_2), 34.9 (CH_2), 33.8 (CH_2), 33.1 (CH_2), 33.1 (CH_2), 32.5 (CH_2), 30.6 (CH), 30.3 (CH_2), 30.0 (CH), 30.0 (CH_2), 23.2 (CH_2), 22.8 (CH_2), 16.8 (CH_3), 16.7 (CH_3), 13.9 (CH_3), 13.7 (CH_3), 10.8 (CH_3), 10.8 ppm (CH_3); IR (film): 3458, 3221, 2930, 2857, 1695, 1645, 1438, 1378, 1325, 1249, 1188, 1146, 1102, 1034, 995, 974, 922, 874, 849, 831, 749, 721, 695, 665 cm^{-1}; HRMS (ESI): *m/z:* calcd for $C_{27}H_{41}NO_7Na$ $[M + Na]^+$: 514.2775; found 514.2781.

Isomigrastatin (2). Dess-Martin periodinane (10 g, 0.024 mmol) was added to a solution of alcohol **77** (4.0 mg, 0.008 mmol) in CH_2Cl_2 (0.5 mL) at 0 °C. After stirring for 1 h at this temperature, a few drops of EtOH were added and the solvents evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 5/5 → 4/6), to afford product **2** as a white solid (2.5 mg, 64 %). $[\alpha]_D^{20}$ = +182° (*c* = 0.21, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.74 (br s, 1H), 6.65 (ddd, *J* = 16.0, 9.0, 7.1 Hz, 1H), 5.68 (d, *J* = 16.0 Hz, 1H), 5.59 (ddd, *J* = 15.8, 11.0, 4.7 Hz, 1H), 5.21-5.18 (m, 2H), 5.09 (dd, *J* = 15.8, 3.7 Hz, 1H), 3.74 (d, *J* = 9.2 Hz, 1H), 3.48-3.41 (m, 2H), 3.33 (s, 3H), 2.84 (br s, 1H), 2.70 (dd, *J* = 17.3, 4.1 Hz, 2H), 2.65-2.59 (m, 2H), 2.45 (dddd, *J* = 11.6, 7.6, 3.9, 3.9 Hz, 1H), 2.38 (dt, *J* = 17.9, 6.9 Hz, 1H), 2.24 (ddd, *J* = 17.3 , 10.6, 2.9 Hz, 2H), 2.19-2.09 (m, 2H), 1.95 (qd, *J* = 12.2, 4.5 Hz, 1H), 1.90 (d, *J* = 1.1 Hz, 3H), 1.87-1.82 (m, 1H), 1.61-1.56 (m, 2H), 1.39-1.33 (m, 2H), 1.13 (d, *J* = 6.8 Hz, 3H), 0.84 ppm (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 210.9 (C), 172.2 (C), 167.8 (C), 150.8 (CH), 134.2 (C), 130.4 (CH), 129.2 (CH), 128.1 (CH), 125.1 (CH), 82.3 (CH), 81.7 (CH), 73.3 (CH), 57.2 (CH_3), 46.1 (CH), 40.1 (CH_2), 38.2 (CH), 37.9 (CH_2), 37.9 (CH_2), 34.3 (CH_2), 32.9 (CH_2), 30.3 (CH), 30.2 (CH_2), 20.4 (CH_2), 15.9 (CH_3), 13.4 (CH_3), 10.7 ppm (CH_3); IR (film): 3500, 3223, 2961, 2929, 1698, 1443, 1405, 1359, 1325, 1259, 1187, 1147, 1100, 1034, 995, 974, 941, 922,



872, 800, 734, 694, 675 cm^{-1}; HRMS (ESI): *m/z:* calcd for $C_{27}H_{39}NO_7Na$ $[M + Na]^+$: 512.2619; found: 512.2622.

Table S-3. Comparison of the recorded ^1H NMR data ($CDCl_3$) of isomigrastatin (**2**) with those reported in literature;[7] numbering scheme as shown in the Insert.



Position	Literature (500 MHz) δ (ppm) mult. (*J* in Hz)	Experimental (600 MHz) δ (ppm) mult. (*J* in Hz)	Δδ
2	5.68 d (16.0)	5.68 d (16.0)	0
3	6.65 ddd (16.0, 9.1, 7.2)	6.65 ddd (16.0, 9.0, 7.1)	0
4	2.46 m	2.45 dddd (11.6, 7.6, 3.9, 3.9)	-0.1
	2.15 m	2.14 m	-0.1
5	2.62 m	2.62 m	0
	1.96 qd (12.0, 4.7)	1.95 qd (12.2, 4.5)	-0.1
6	5.60 ddd (15.7, 10.9, 4.7)	5.59 ddd (15.8, 11.0, 4.7)	-0.1
7	5.10 dd (15.7, 3.9)	5.09 dd (15.8, 3.7)	-0.1
8	3.46 m	3.45 m	-0.1
9	3.74 d (9.2)	3.74 d (9.2)	0
10	1.86 m	1.85 m	-0.1
11	5.20 m	5.19 m	-0.1
13	5.20 m	5.19 m	-0.1
14	3.46 m	3.45 m	-0.1
16	2.62 m	2.62 m	0
	2.39 dt (17.9, 6.9)	2.38 dt (17.9, 6.9)	-0.1
17	1.59 m	1.59 m	0
18	1.36 m	1.36 m	0
19	2.15 m	2.14 m	-0.1
20	2.70 dd (17.0, 4.0)	2.70 dd (17.3, 4.1)	0
	? dd (17.0, 10.8)	2.24 ddd (17.3 , 10.6, 2.9)	?
22	3.33 s	3.33 s	0
23	0.84 d (7.2)	0.84 d (7.1)	0
24	1.91 d (1.2)	1.90 d (1.1)	-0.1
25	1.14 d (6.7)	1.13 d (6.8)	-0.1
26	2.70 dd (17.3, 4.1)	2.70 dd (17.3, 4.1)	0
	2.24 ddd (17.3 , 10.6, 2.9)	2.24 ddd (17.3 , 10.6, 2.9)	?

[7] I. J. Krauss, M. Mandal, S. J. Danishefsky, *Angew. Chem.* **2007**, *119*, 5672-5675; *Angew. Chem. Int. Ed.* **2007**, *46*, 5576-5579.

NH	7.71 br s	7.74 br s	+0.3
OH	2.84 br s	2.84 br s	0

Table S-4. Comparison of the recorded ^{13}C NMR data (δ in ppm, $CDCl_3$) of isomigrastatin (**2**) with those reported in the literature.[7]

Position	Literature (125 MHz)	Experimental (150 MHz)	Δδ
1	167.8	167.8	0
2	125.2	125.1	-0.1
3	150.8	150.8	0
4	30.3	30.2	-0.1
5	32.9	32.9	0
6	129.3	129.2	-0.1
7	130.5	130.4	-0.1
8	81.8	81.7	-0.1
9	73.4	73.3	-0.1
10	38.3	38.2	-0.1
11	82.4	82.3	-0.1
12	134.3	134.2	-0.1
13	128.2	128.1	-0.1
14	46.2	46.1	-0.1
15	211.0	210.9	-0.1
16	40.2	40.1	-0.1
17	20.5	20.4	-0.1
18	34.4	34.3	-0.1
19	30.4	30.3	-0.1
20	37.9	37.9	0
21	172.2	172.2	0
22	57.3	57.2	-0.1
23	10.7	10.7	0
24	13.5	13.4	-0.1
25	15.9	15.9	0
26	38.0	37.9	-0.1
27	172.2	172.2	0

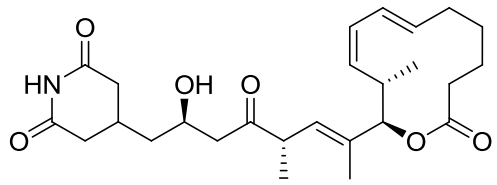
Compound 44. Catecholborane (26 μL, 0.24 mmol) was added to a solution of compound **1** (11.2 mg, 0.024 mmol) in THF (0.8 mL) at –78 °C. The mixture was warmed to –5 °C and stirred for 2 h at this temperature before the mixture was diluted with pH 7 phophate buffer and CH_2Cl_2. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 5/5 → 0/1) to give *syn*-diol **44** as a white solid (6.4 mg, 58 %). $[\alpha]_D^{20} = -1.9°$ (*c* = 0.31, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.76 (s, 1H), 6.45 (ddd, *J* = 16.1, 10.2, 5.1 Hz, 1H), 6.03 (t, *J* = 10.8 Hz, 1H), 5.70 (dd, *J* = 10.7, 15.6 Hz, 1H), 5.53 (d, *J* = 16.7 Hz. 1H), 5.40 (ddd, *J* = 15.6, 9.0, 6.2 Hz, 1H), 5.32 (d, *J* = 4.8 Hz, 1H), 5.28 (d, *J* = 9.9 Hz, 1H), 5.06 (t, *J* = 10.9 Hz, 1H), 3.96-3.91 (m, 1H), 3.91 (br s, 1H), 3.67-3.63 (m, 1H), 3.13-3.07 (m, 1H), 2.79 (dd, *J* = 17.1, 4.1 Hz, 1H), 2.74 (dd, *J* = 17.1, 4.2 Hz, 1H), 2.58-2.54 (m, 1H), 2.54-2.45 (m, 3H), 2.32 (dd, *J* = 17.1, 10.1 Hz, 1H), 2.31 (dd, *J* = 17.1, 10.3 Hz, 1H), 2.15 (br s, 1H), 1.99-1.88 (m, 2H), 1.71 (d, *J* = 1.3 Hz, 3H), 1.64-1.59 (m, 2H), 1.47 (ddd, *J* = 14.3, 10.7, 9.7 Hz, 1H), 1.37 (ddd, *J* = 13.8, 9.1, 3.0 Hz, 1H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.91 ppm (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 172.3 (C), 172.3 (C), 166.8 (C), 146.8 (CH), 134.6 (CH), 133.6 (C), 131.8 (CH), 131.4 (CH), 129.4 (CH), 128.4 (CH), 128.1 (CH), 82.9 (CH), 69.3 (CH), 69.1 (CH), 42.4 (CH_2), 40.7 (CH_2), 39.8 (CH), 38.7 (CH_2), 37.3 (CH_2), 35.7 (CH), 32.4 (CH_2), 31.3 (CH_2), 27.0 (CH), 17.8 (CH_3), 16.6 (CH_3), 15.5 ppm (CH_3); IR (film): 3268, 2970, 1720, 1693, 1454, 1365, 1261, 1178, 1151, 1068, 1035, 962, 926, 847, 770, 724 cm^{-1}; HRMS (ESI): *m/z:* calcd for $C_{26}H_{37}NO_6Na$ $[M + Na]^+$: 482.2513; found: 482.2514.

Compound 45. A solution of MsCl (63 μL, 0.2 M in CH_2Cl_2) and triethylamine (7.6 μL, 0.055 mmol) was added to a solution of compound **1** (5.0 mg, 0.011 mmol) in CH_2Cl_2 (0.2 mL) at 0 °C. After stirring for 2 h at this temperature, pH 7 phophate buffer and CH_2Cl_2 were added, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 50/50 → 30/70) to give enone **45** as a white solid (3.5 mg, 72 %). $[\alpha]_D^{20} = +41.5°$ (*c* = 0.35, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88 (s, 1H), 6.78 (dt, *J* = 15.0, 7.5 Hz, 1H), 6.47 (ddd, *J* = 16.0, 10.5, 5.4 Hz, 1H), 6.24 (d, *J* = 15.4 Hz, 1H), 6.04 (t, *J* = 10.8 Hz, 1H), 5.71 (dd, *J* = 10.0, 15.5 Hz, 1H), 5.54 (s, *J* = 16.1 Hz, 1H), 5.41 (ddd, *J* = 15.5, 9.2, 6.2 Hz, 1H), 5.37 (d, *J* = 9.5 Hz, 1H), 5.34 (d, *J* = 4.6 Hz, 1H), 5.05 (t, *J* = 10.9 Hz, 1H), 3.57-3.51 (m, 1H), 3.12-3.05 (m, 1H), 2.71 (d, *J* = 13.9 Hz, 2H), 2.59-2.54 (m, 1H), 2.54-2.49 (m, 1H), 2.38-2.27 (m, 5H), 1.99-1.87 (m, 2H), 1.77 (d, *J* = 1.3 Hz, 3H), 1.20 (d, *J* = 6.8 Hz, 3H), 0.88 ppm (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 199.3 (C), 171.3 (C), 171.2 (C), 166.7 (C), 146.8 (CH), 141.9 (CH), 134.6 (CH), 133.6 (C), 131.5 (CH), 130.8 (CH), 129.4 (CH), 129.3 (CH), 128.3 (CH), 128.1 (CH), 82.7 (CH), 45.1 (CH), 37.5 (CH_2), 37.5 (CH_2), 37.4 (CH_2), 36.0 (CH), 32.4 (CH_2), 31.3 (CH_2), 29.8 (CH), 17.5 (CH_3), 16.3 (CH_3), 15.3 ppm (CH_3); IR (film): 3241, 2962, 2931, 1694, 1626, 1451, 1374, 1259, 1189, 1144, 1087, 988, 915, 798, 727 cm^{-1}; HRMS (ESI): *m/z:* calcd for $C_{26}H_{33}NO_5Na$ $[M + Na]^+$: 462.2251; found: 462.2254.

Compound 46. Acid **41a** (11 mg, 0.064 mmol), DMAP (8 mg, 0.064 mmol) and EDCI (12 mg, 0.064 mmol) were successively added to solution of alcohol **39** (15 mg, 0.049 mmol) in THF (0.5 mL) at 0 °C. After stirring for 2 h at ambient temperature, the reaction was quenched with pH 7 phophate buffer and CH_2Cl_2. The aqueous layer was extracted with CH_2Cl_2, and the combined organic phases were dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 85/15 → 70/30) to give ester **46** as a white solid (9 mg, 55 % brsm). $[\alpha]_D^{20} = -47°$ (*c* = 1.0, THF); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (s, 1H), 6.47 (ddd, *J* = 16.0, 10.4, 5.4 Hz, 1H), 6.04 (t, *J* = 10.8 Hz, 1H), 5.73 (dd, *J* = 15.6, 10.7 Hz, 1H), 5.54 (d, *J* = 16.1 Hz, 1H), 5.41 (ddd, *J* = 15.5, 9.1, 6.2 Hz, 1H), 5.32 (d, *J* = 4.9 Hz, 1H), 5.29 (d, *J* = 9.6 Hz, 1H), 5.09 (t, *J* = 10.9 Hz, 1H), 4.92-4.86 (m, 1H), 3.11-3.05 (m, 1H), 2.78 (dd, *J* = 17.3, 4.2 Hz, 2H), 2.69-2.59 (m, 2H), 2.58-2.49 (m, 2H), 2.42-2.33 (m, 4H), 2.01-1.87 (m, 2H), 1.71.(d, *J* = 1.5 Hz, 3H), 1.19 (d, *J* = 6.4 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.91 ppm (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.7 (C), 170.7 (C), 169.8 (C), 166.4 (C), 146.2 (CH), 134.1 (CH), 131.6 (CH), 131.4 (C), 131.3 (CH), 128.7 (CH), 127.9 (CH), 127.5 (CH), 82.8 (CH), 74.3 (CH), 38.6 (CH_2), 36.9 (CH_2), 36.9 (CH_2), 36.5 (CH), 35.3 (CH), 31.9 (CH_2), 30.9 (CH_2), 26.8 (CH), 17.1 (CH_3), 17.0 (CH_3), 15.8 (CH_3), 14.3 ppm (CH_3); IR (film): 3224, 2964, 2932, 2875, 1699, 1642, 1452, 1377, 1327, 1289, 1259, 1189, 1142, 1087, 1067, 998, 957, 912, 848, 828, 795, 766, 728 cm^{-1}; HRMS (ESI): *m*/*z:* calcd for $C_{26}H_{35}NO_6Na$ $[M + Na]^+$: 480.2357; found: 480.2362.

Compound 47. Dess-Martin periodinane (61 mg, 0.14 mmol) was added to solution of alcohol **23** (36 mg, 0.12 mmol) in CH_2Cl_2 (5 mL) at 0 °C. After stirring for 1 h at ambient temperature, the solvent was evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 95/5) to give ketone **47** as a yellowish solid (32 mg, 89 %). M.p. 75-76 °C; $[\alpha]_D^{20} = +113°$ (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.18-6.05 (m, 2H), 5.69 (dt, *J* = 15.2, 5.3 Hz, 1H), 5.20 (d, *J* = 10.4 Hz, 1H), 5.08 (d, *J* = 5.0 Hz, 1H), 4.98 (t, *J* = 9.8 Hz, 1H), 3.36-3.29 (m, 2H), 2.32-2.20 (m, 3H), 2.06 (s, 3H), 1.99-1.89 (m, 2H), 1.85-1.76 (m, 1H), 1.64 (d, *J* = 1.3 Hz, 3H), 1.54-1.42 (m, 2H), 1.07 (d, *J* = 6.8 Hz, 3H), 0.88 ppm (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 208.7 (C), 172.6 (C), 133.8 (C), 131.2 (CH), 130.5 (CH), 130.0 (CH), 129.5 (CH), 126.1 (CH), 82.1 (CH), 46.5 (CH), 33.4 (CH), 32.8 (CH_2), 29.9 (CH_2), 27.6 (CH_3), 23.5 (CH_2), 22.6 (CH_2), 17.2 (CH_3), 15.8 (CH_3), 14.3 ppm (CH_3);); IR (film): 2970, 2932, 2878, 1726,1706, 1451, 1417, 1375, 1353, 1334, 1254, 1196, 1158, 1142, 1074, 1053, 1002, 967, 909, 967, 881, 831, 795, 760 cm^{-1}; MS (EI): *m*/*z* (%): 304 (4) [*M*+], 165 (12), 164 (100), 149 (7), 136 (19), 135 (18), 123 (7), 121 (22), 120 (61), 108 (5), 107 (22), 120 (61), 108 (5), 107 (22), 105 (10), 95 (9), 94 (23), 93 (18), 92 (5), 91 (13), 82 (5), 81 (14), 80 (7), 79 (31), 77 (11), 69 (6), 68 (27), 67 (15), 55 (12), 53 (7), 43 (28), 41 (19), 29 (6); HRMS (ESI): *m*/*z:* calcd for $C_{19}H_{28}O_3$ $[M]^+$: 304.2038; found: 304.2040.

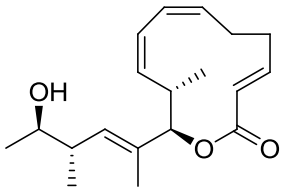
Compound 48. Me_3SiCl (58 µL, 0.45 mmol) and triethylamine (63 µL, 0.45 mmol) were added to a solution of ketone **47** (13.6 mg, 0.045 mmol) in THF (1.6 mL) at –78 °C. Next, LiHMDS (1 M in THF, 90 µL, 0.090 mmol) was slowly introduced and the resulting mixture stirred at –78 °C for 1 h. The reaction was then quenched with pH 7 phosphate buffer and the product extracted with CH_2Cl_2 (3 x 2 mL). The combined organic phases were dried over $MgSO_4$ and evaporated to give the corresponding silyl enol ether, which was used in the next step without further purification.



Molecular sieves (4 Å, ca. 150 mg) and aldehyde **41b** (7.0 mg, 0.045 mmol) were added to a solution of the crude silyl enol ether in propionitrile (0.8 mL). The mixture was cooled to –78 °C before a solution of compound **42** [prepared upon stirring of a solution of $PhBCl_2$ (6 µL, 0.045 mmol) and N-tosyl-D-tryptophane (16.1 mg, 0.045 mmol) in CH_2Cl_2 (0.4 mL) for 1 h, followed by removal of the solvent][3] in propionitrile (0.3 mL) was slowly added. After stirring for 35 h at –78 °C, the reaction was quenched with sat. aq. $NaHCO_3$, the aqueous phase extracted with CH_2Cl_2 (3 x 2 mL), and the combined organic layers were dried over Na_2SO_4 and evaporated. The resulting material was dissolved in THF (8 mL) at 0 °C and treated with 0.85 mL of buffered HF·pyridine solution [prepared from THF (7.25 mL), pyridine (2.69 mL) and HF·pyridine complex (0.59 mL, 70 % *w*/*w*)]. The mixture was stirred at 0 °C for 2 h and warmed to ambient temperature for 30 min to complete the desilylation. Dilution with CH_2Cl_2 (25 mL), washing of the organic layer with sat. aq. $NaHCO_3$ (15 mL) and $CuSO_4$ solution (1 M, 3 x 15 mL), drying over Na_2SO_4 and evaporation of the solvents left a residue, which was purified by preparative TLC (EtOAc/hexanes, 4/1) to give product **48** as a white solid (6.3 mg, 31 %). $[\alpha]_D^{20}$ = +73° (*c* = 0.21, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.81 (s, 1H), 6.11-6.02 (m, 2H), 5.66 (dt, *J* = 15.2, 5.3 Hz, 1H), 5.13 (d, *J* = 9.6 Hz, 1H), 5.03 (d, *J* = 5.1 Hz, 1H), 4.91 (t, *J* = 9.8 Hz, 1H), 4.02-3.96 (m, 1H), 3.31-3.24 (m, 2H), 3.13 (br s, 1H), 2.69-2.63 (m, 2H), 2.45 (d, *J* = 5.7 Hz, 2H), 2.42-2.36 (m, 1H), 2.26-2.15 (m, 5H), 1.93-1.86 (m, 2H), 1.79-1.73 (m, 1H), 1.59 (d, *J* = 1.3 Hz, 3H), 1.52-1.40 (m, 3H), 1.23-1.17 (m, 1H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.83 ppm (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 212.3 (C), 173.0 (C), 172.0 (C), 171.8 (C), 134.8 (C), 131.7 (CH), 130.5 (CH), 130.5 (CH), 128.9 (CH), 126.3 (CH), 82.1 (CH), 64.6 (CH), 47.3 (CH_2), 46.5 (CH), 40.6 (CH_2), 38.4 (CH_2), 37.0 (CH_2), 33.6 (CH), 33.0 (CH_2), 30.2 (CH_2), 27.0 (CH), 23.9 (CH_2), 22.8 (CH_2), 17.6 (CH_3), 16.0 (CH_3), 14.9 ppm (CH_3); IR (film): 3451, 3223, 2927, 1698, 1454, 1375, 1258, 1200, 1145, 1074, 1013, 994, 970, 872, 829, 789 cm^{-1}; MS (EI): *m*/*z* (%): 459 (0.16) [*M*+], 165 (13), 164 (100), 149 (7), 146 (5), 136 (22), 135 (17), 121 (19), 120 (49), 107 (19), 105 (9), 96 (8), 95 (6), 94 (19), 93 (16), 91 (11), 82 (5), 81 (14), 80 (6), 79 (26), 77 (7), 69 (7), 68 (20), 67 (13), 55 (14), 53 (5), 43 (12), 41 (19), 29 (5); HRMS (ESI): *m*/*z:* calcd for $C_{26}H_{37}NO_6Na$ $[M + Na]^+$: 482.2513; found: 482.2511.

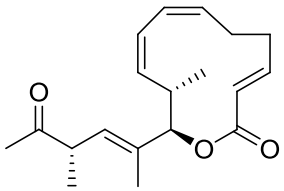
Compound S5. The Pt-catalyst **49** (15 mg, 0.022 mmol) and $BnMe_2SiH$ (0.35 mL, 2.23 mmol) were dissolved in THF (1.5 mL) and heated to 60 °C for 3 h prior to addition of cycloalkyne **37** (240 mg, 0.445 mmol) as a solution in THF (2 mL). The mixture was stirred for 14 h at 60 °C. The solvent was evaporated and the residue purified by flash

chromatography (hexanes/EtOAc, 98/2 → 96/4) to give the alkenylsilane **50**, which was directly used in the next step.

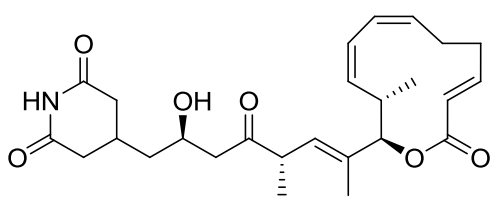


A solution of TBAF (1 M in THF, 1.78 mL, 1.78 mmol) was added at 0 °C to a solution of alkenylsilane **50** in THF (0.5 mL) and the resulting mixture was stirred at ambient temperature for 1 h. For work up, the solvent was evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 85/15 → 75/25) to give (*Z*,*Z*)-alkene **S5** as a colorless oil, which contained small impurites of (*Z*,*E*)-alkene (111 mg, 82 %). $[\alpha]_D^{20} = -60°$ (*c* = 0.82, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.86 (ddd, *J* = 15.7, 12.2, 3.5 Hz, 1H), 6.16 (t, *J* = 9.4 Hz, 1H), 6.10 (t, *J* = 9.4 Hz, 1H), 5.56 (d, *J* = 15.5 Hz, 1H), 5.42-5.29 (m, 4H), 3.60 (qd, *J* = 6.3, 6.2 Hz, 1H), 2.92-2.83 (m, 1H), 2.60-2.26 (m, 1H), 2.50-2.40 (m, 2H), 2.25-2.21 (m, 1H), 2.10 (qd, *J* = 12.3, 3.9 Hz, 1H), 1.79 (d, *J* = 1.3 Hz, 3H), 1.61 (br s, 1H), 1.19 (d, *J* = 6.3 Hz, 3H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.91 ppm (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.6 (C), 151.6 (CH), 134.0 (CH), 132.7 (CH), 132.3 (C), 131.2 (CH), 127.8 (CH), 126.9 (CH), 123.9 (CH), 82.6 (CH), 71.7 (CH), 40.4 (CH), 37.0 (CH), 32.6 (CH_2), 26.8 (CH_2), 20.4 (CH_3), 16.8 (CH_3), 16.7 (CH_3), 15.5 ppm (CH_3); IR (film): 3466, 2967, 2928, 2872, 1708, 1451, 1376, 1319, 1247, 1199, 1154, 1081, 997, 919, 851, 829, 731cm^{-1}; MS (EI): *m*/*z* (%): 162 (30), 133 (10), 95 (8), 94 (100), 93 (6), 91 (5), 79 (51), 77 (6), 68 (13), 41 (5); HRMS (ESI): *m*/*z:* calcd for $C_{19}H_{28}O_3Na$ $[M + Na]^+$: 327.1931; found: 327.1929.

Compound 51. Dess-Martin periodinane (75 mg, 0.18 mmol) was added to a solution of alcohol **S5** (30 mg, 0.410mmol) in CH_2Cl_2 (3.5 mL) at 0 °C. After stirring for 4 h at ambient temperature the solvent was evaporated and the residue was purified by flash chromatography (hexanes/EtOAc, 90/10) to give ketone **51** as a colorless oil that contained small impurites of the (*Z*,*E*)-isomer (23 mg, 77 %). $[\alpha]_D^{20} = +143°$ (*c* = 0.89, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.86 (ddd, *J* = 15.6, 12.1, 3.5 Hz, 1H), 6.15 (t, *J* = 7.8 Hz, 1H), 6.11 (t, *J* = 7.6 Hz,1H), 5.54 (dd, *J* = 15.6, 1.4 Hz, 1H), 5.41-5.29 (m, 4H), 3.44 (dq, *J* = 9.6, 6.8 Hz, 1H), 2.88 (dqd, *J* = 12.2, 6.4, 5.2 Hz, 1H), 2.60-2.56 (m, 1H), 2.44 (qd, *J* = 12.1, 4.4 Hz, 1H), 2.26-2.19 (m, 1H), 2.13 (s, 3H), 2.11-2.08 (m, 1H), 1.84 (d, *J* = 1.2 Hz, 3H), 1.18 (d, *J* = 6.8 Hz, 3H), 0.89 ppm (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 208.8 (C), 165.9 (C), 151.5 (CH), 133.2 (CH), 133.1 (CH), 130.9 (CH), 129.1 (C), 127.3 (CH), 126.6 (CH), 123.3 (CH), 81.6 (CH), 46.6 (CH), 36.9 (CH), 32.1 (CH_2), 27.6 (CH_3), 26.3 (CH_2), 16.2 (CH_3), 15.9 (CH_3), 15.0 ppm (CH_3); IR (film): 2968, 2930, 1707, 1452, 1353, 1318, 1245, 1181, 1150, 999, 828, 731 cm^{-1}; MS (EI): *m*/*z* (%): 162 (33), 133 (11), 95 (8), 94 (100), 93 (5), 79 (52), 77 (6), 68 (12), 43 (7); HRMS (ESI): *m*/*z:* calcd for $C_{19}H_{26}O_3Na$ $[M + Na]^+$: 325.1774; found: 325.1775.



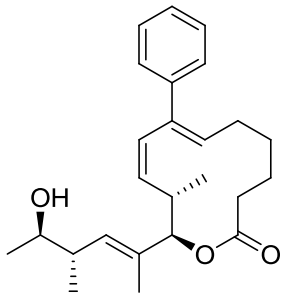
Compound 52: Me_3SiCl (88 µL, 0.69 mmol) and triethylamine (96 µL, 0.69 mmol) were added to a solution of ketone **51** (21 mg, 0.069 mmol) in THF (2 mL) at –78 °C. Next, LiHMDS (1 M in THF, 140 µL, 0.14 mmol) was slowly introduced and the resulting mixture stirred at –78 °C for 1 h. The reaction was then quenched with pH 7 phosphate



buffer and the product extracted with CH_2Cl_2 (3 x 5 mL). The combined organic phases were dried over $MgSO_4$ and evaporated to give the corresponding silyl enol ether, which was used in the next step without purification.

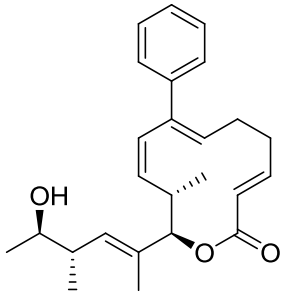
Molecular sieves (4 Å, ca. 200 mg) and aldehyde **41b** (11 mg, 0.069 mmol) were added to a solution of the crude silyl enol ether in propionitrile (1.4 mL). The mixture was cooled to –78 °C before a solution of compound **42** [prepared upon stirring of a solution of $PhBCl_2$ (13 µL, 0.080 mmol) and N-tosyl-D-tryptophane (30 mg, 0.080 mmol) in CH_2Cl_2 (2.5 mL) for 1 h, followed by removal of the solvent][3] in propionitrile (0.6 mL) was added dropwise. After stirring for 20 h at –78 °C, the reaction was quenched with sat. aq. $NaHCO_3$, the aqueous phase extracted with CH_2Cl_2 (3 x 5 mL), and the combined organic layers were dried over Na_2SO_4 and evaporated. The resulting crude product was dissolved in THF (10 mL) at 0 °C and treated with 1.3 mL of buffered HF·pyridine solution [prepared from THF (3.6 mL), pyridine (1.35 mL) and HF·pyridine complex (0.27 mL, 70 % *w*/*w*)]. The mixture was stirred at 0 °C for 2 h and warmed to ambient temperature for 30 min. Dilution with CH_2Cl_2, washing of the organic layer with sat. aq. $NaHCO_3$ and aq. $CuSO_4$ solution (1 M), drying over Na_2SO_4 and evaporation of the solvents left a residue, which was purified by preparative TLC (EtOAc/hexanes, 8/2) to give product **52** as a white solid (22 mg, 69 %) which contained small impurites of the (*Z*,*E*)-isomer. $[\alpha]_D^{20}$ = +75° (*c* = 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.97 (s, 1H), 6.84 (ddd, *J* = 15.6, 12.2, 3.5 Hz, 1H), 6.14-6.09 (m, 2H), 5.53 (dd, *J* = 15.6, 1.2 Hz, 1H), 5.37-5.30 (m, 4H), 4.11-4.06 (m, 1H), 3.42 (dq, *J* = 9.7, 6.8 Hz, 1H), 3.25 (br s, 1H), 2.90-2.83 (m, 1H), 2.80-2.70 (m, 2H), 2.60-2.57 (m, 1H), 2.57-2.54 (m, 2H), 2.50-2.38 (m, 2H), 2.31 (t, *J* = 10.4 Hz, 1H), 2.28 (t, *J* = 10.4 Hz, 1H), 2.25-2.18 (m, 1H), 2.09 (qd, *J* = 12.4, 3.9 Hz, 1H), 1.81 (d, *J* = 1.3 Hz, 3H), 1.58 (ddd, *J* = 14.1, 10.6, 4.9 Hz, 1H), 1.33-1.26 (m, 1H), 1.18 (d, *J* = 6.8 Hz, 3H), 0.87 ppm (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 212.4 (C), 172.1 (C), 172.0 (C), 166.3 (C), 152.1 (CH), 134.3 (C), 133.4 (CH), 131.5 (CH), 128.6 (CH), 127.7 (CH), 127.3 (CH), 123.7 (CH), 81.7 (CH), 65.0 (CH), 47.4 (CH_2), 46.8 (CH), 40.9 (CH_2), 38.6 (CH_2), 37.3 (CH), 37.2 (CH_2), 32.6 (CH_2), 27.3 (CH), 26.8 (CH_2), 16.8 (CH_3), 16.3 (CH_3), 15.8 ppm (CH_3); IR (film): 3250, 2962, 2932, 2874, 1697, 1453, 1374, 1249, 1149, 1065, 1034, 999, 917, 851, 829, 729 cm^{-1}; HRMS (ESI): *m*/*z:* calcd for $C_{26}H_{35}O_6NNa$ $[M + Na]^+$: 480.2357; found: 480.2354.

Compound S6: A solution of TBAF.3H_2O (1 M in THF, 0.51 mL, 0.51 mmol) was added at 0 °C to a solution of alkenylsilane **53** (240 mg, 0.42 mmol) in THF (2.5 mL). The resulting orange mixture was stirred at 0 °C for 5 min before H_2O (68 µL, 3.8 mmol) and TBAF·3H_2O (1 M in THF, 1.2 mL, 1.2 mmol) were added. After stirring for 5 min at this temperature, iodobenzene (141 µL, 1.26 mmol) and (Pd_2dba_3)·$CHCl_3$ (43 mg, 0.042 mmol) were successively introduced. The mixture was stirred for 30 min at 0 °C and for 6 h at ambient temperature, before it was filtered through a pad of silica which was carefully rinsed with ethyl acetate. The combined filtrates were evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 95/5 → 90/10) to give product **S6** as a pale brown oil (87 mg, 54 %). $[\alpha]_D^{20}$ = +48.5 (c = 0.42, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.27 (m, 2H), 7.27–7.21 (m, 1H), 7.20–7.14 (m, 2H), 6.08–6.00 (m, 2H),



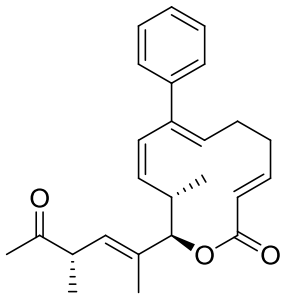
5.32 (d, *J* = 9.8 Hz, 1H), 5.26 (d, *J* = 2.3 Hz, 1H), 5.19 (dd, *J* = 10.9, 10.9 Hz, 1H), 3.63 (qd, *J* = 6.2, 6.2 Hz, 1H), 3.23-3.12 (m, 1H), 2.55-2.30 (m, 4H), 2.06-1.90 (m, 2H), 1.81 (d, *J* = 1.2 Hz, 3H), 1.75-1.61 (m, 2H), 1.43-1.31 (m, 1H), 1.21 (d, *J* = 6.1 Hz, 3H), 1.07 (d, *J* = 7.0 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3 (C), 139.3 (C), 136.7 (C), 133.1 (CH), 132.6 (CH), 132.3 (C), 132.0 (CH), 131.5 (CH), 128.8 (CH), 128.0 (CH), 126.8 (CH), 83.1 (CH), 71.5 (CH), 40.0 (CH), 36.3 (CH), 33.7 (CH_2), 27.8 (CH_2), 26.9 (CH_2), 24.0 (CH_2), 20.3 (CH_3), 19.7 (CH_3), 16.5 (CH_3), 14.7 (CH_3); IR (film): 3444, 2964, 2928, 2873, 1725, 1492, 1444, 1373, 1339, 1252, 1221, 1196, 1149, 1086, 995, 966, 912, 873, 759, 731, 699 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{25}H_{34}O_3Na$ [M + Na]$^+$: 405.2400; found 405.2405.

Compound S7: *n*BuLi (1.6 M in hexane, 0.35 mL, 0.56 mmol) was added dropwise to a solution of diisopropylamine (79 µL, 0.56 mmol) in THF (2 mL) at –78 °C. The resulting yellow solution was stirred at that temperature for 15 min before a solution of compound **S6** (52 mg, 0.14 mmol) in THF (1 mL + 0.5 mL rinse) was added via canula. The resulting mixture was warmed to 0 °C, causing a color change to orange. After 10 min, the mixture was cooled to –78 °C and PhSeBr (50 mg, 0.21 mmol) was introduced. The solution was slowly warmed to 0 °C and stirred for 2 h before the reaction was quenched with sat. aq. NH_4Cl. The aqueous phase was extracted with *tert*-butyl methyl ether, and the combined organic layers were dried over $MgSO_4$ and evaporated to give the corresponding phenylselenide as a yellow syrup, which was directly used in the next step.

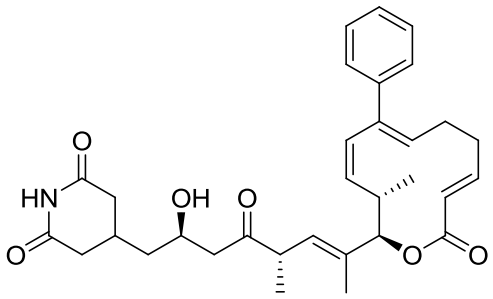


A solution of *m*-chloroperbenzoic acid (70 % *w*/*w*, 69 mg, 0.28 mmol) in CH_2Cl_2 (0.5 mL) was added to a solution of the crude selenide in CH_2Cl_2 (3 mL) at –78 °C. After stirring for 30 min at this temperature, diisopropylethylamine (0.14 mL, 0.84 mmol) was introduced and the mixture warmed to ambient temperature. After stirring for 1 h, hexane was added, the solvents were evaporated, and the residue was purified by flash chromatography (hexanes/EtOAc, 90/10 → 80/20) to give product **S7** as a yellow oil (20 mg, 38 %). $[\alpha]_D^{20}$ = –201 (c = 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (t, *J* = 7.2 Hz, 2H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 6.78 (ddd, *J* = 16.2, 10.9, 5.3 Hz, 1H), 6.49 (d, *J* = 11.3 Hz, 1H), 5.84 (d, *J* = 15.9 Hz,1H), 5.28–5.20 (m, 2H), 5.17–5.09 (m, 2H), 3.56 (dq, *J* = 6.3, 6.2 Hz, 1H), 2.68–2.60 (m, 1H), 2.52–2.37 (m, 3H), 2.37–2.22 (m, 2H), 1.73 (d, *J* = 1.2 Hz, 3H), 1.62 (br s, 1H), 1.16 (d, *J* = 6.3 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.50 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.9 (C), 145.7 (CH), 140.0 (C), 137.7 (C), 133.4 (CH), 132.8 (CH), 132.5 (CH), 132.0 (C), 130.4 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 126.5 (CH), 82.6 (CH), 71.5 (CH), 40.1 (CH), 37.1 (CH), 31.6 (CH_2), 27.5 (CH_2), 20.2 (CH_3), 16.6 (CH_3), 16.5 (CH_3), 15.1 (CH_3); IR (film): 3486, 2966, 2929, 2872, 1717, 1640, 1492, 1450, 1376, 1331, 1189, 1148, 1083, 1006, 766, 703 cm^{-1}; MS (EI): *m*/*z* (%): 380 (1) [M]$^+$, 238 (14), 170 (100), 155 (47), 142 (15), 91 (10), 68 (5), 41 (5); HRMS (ESI): *m*/*z* calcd for $C_{25}H_{32}O_3Na$ [M + Na]$^+$: 403.2244; found 403.2244.

Compound 54. Dess-Martin periodinane (40 mg, 0.10 mmol) was added to a solution of alcohol **S7** (30 mg, 0.08 mmol) in CH_2Cl_2 (2 mL) at 0 °C. The mixture was stirred at ambient temperature for 30 min before the solvent was evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 90/10 → 80/20) to afford product **54** as a colorless oil (22 mg, 74 %). $[\alpha]_D^{20} = -27$ (c = 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (t, *J* = 7.1 Hz, 2H), 7.18 (t, *J* = 7.3 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 2H), 6.79 (ddd, *J* = 16.2, 10.9, 5.3 Hz, 1H), 6.50 (d, *J* = 11.2 Hz, 1H), 5.83 (d, *J* = 15.9 Hz,1H), 5.29 (d, *J* = 9.6 Hz, 1H), 5.24 (dd, *J* = 13.4, 4.0 Hz, 1H), 5.13 (d, *J* = 4.0 Hz, 1H, overlap), 5.10 (dd, *J* = 11.2, 11.2 Hz, 1H, overlap), 3.47–3.37 (m, 1H), 2.69–2.60 (m, 1H), 2.55–2.39 (m, 2H), 2.38–2.22 (m, 2H), 2.10 (s, 3H), 1.79 (d, *J* = 1.3 Hz, 3H), 1.16 (d, *J* = 6.8 Hz, 3H), 0.48 ppm (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.2 (C), 166.8 (C), 145.9 (CH), 139.9 (C), 137.7 (C), 133.7 (CH), 133.2 (C), 132.6 (CH), 130.5 (CH), 129.3 (CH), 128.1 (CH), 128.0 (CH), 127.6 (CH), 126.5 (CH), 82.1 (CH), 46.8 (CH), 37.5 (CH), 31.7 (CH_2), 27.9 (CH_3), 27.5 (CH_2), 16.5 (CH_3), 16.1 (CH_3), 15.1 ppm (CH_3); IR (film): 3402, 2971, 2931, 2871, 1713, 1598, 1493, 1448, 1355, 1245, 1160, 1075, 1005, 765, 735, 702 cm^{-1}; HRMS (ESI): *m/z:* calcd for $C_{25}H_{30}O_3Na$ $[M + Na]^+$: 401.2087; found 401.2093.



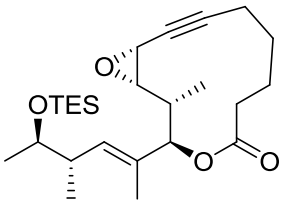
Compound 55. Me_3SiCl (74 µL, 0.58 mmol) and triethylamine (81 µL, 0.58 mmol) were added to a solution of ketone **54** (22 mg, 0.058 mmol) in THF (2 mL) at –78 °C. Next, LiHMDS (1 M in THF, 0.12 mL, 0.12 mmol) was slowly introduced and the resulting mixture stirred at –78 °C for 1 h. The reaction was then quenched with pH 7 phosphate buffer and the product extracted with CH_2Cl_2 (3 x 1 mL). The combined organic phases were dried over $MgSO_4$ and evaporated to give the corresponding silyl enol ether, which was immediately used in the next step without further purification.



Molecular sieves (4 Å, ca. 200 mg) and aldehyde **41b** (9 mg, 0.058 mmol) were added to a solution of the crude silyl enol ether in propionitrile (2 mL). The mixture was cooled to –78 °C before a solution of compound **42** [prepared upon stirring of a solution of $PhBCl_2$ (8 µL, 0.058 mmol) and N-tosyl-D-tryptophane (21 mg, 0.058 mmol) in CH_2Cl_2 (1 mL) for 1 h, followed by removal of the solvent][3] in propionitrile (0.5 mL) was introduced. After stirring for 18 h at –78 °C, the reaction was quenched with sat. aq. $NaHCO_3$ (2 mL), the aqueous phase extracted with CH_2Cl_2 (3 x 5 mL), and the combined organic layers were dried over $MgSO_4$ and evaporated. The resulting crude product was dissolved in THF (5 mL) at 0 °C and treated with 1.5 mL of a stock solution of buffered HF·pyridine [prepared from THF (7.25 mL), pyridine (2.69 mL) and HF·pyridine complex (0.54 mL, 70 % *w*/*w*)]. The mixture was stirred at 0 °C for 30 min and warmed to ambient temperature for 30 min to complete the desilylation. Dilution with CH_2Cl_2 (20 mL), washing of the organic layer with sat. aq. $NaHCO_3$ (10 mL) and aq. $CuSO_4$ solution (1 M, 3 x 10 mL), drying over $MgSO_4$ and evaporation of the solvents left a residue, which was purified by preparative TLC (EtOAc/hexanes, 80/20) to give product **55** as a white solid (20 mg, 65 %). The product was

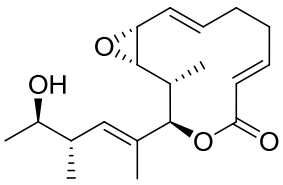
further purified by preparative HPLC to isolate an analytically pure fraction (5 mg). $[\alpha]_D^{20}$ = –144 (c = 0.42, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.86 (br s, 1H), 7.28 (t, *J* = 7.6 Hz, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.11 (d, *J* = 8.3 Hz, 2H), 6.80 (ddd, *J* = 16.1, 11.0, 5.4 Hz, 1H), 6.52 (dt, *J* = 11.2, 1.3 Hz, 1H), 5.82 (d, *J* = 16.1 Hz, 1H), 5.26 (d, *J* = 10.1 Hz, 1H), 5.24 (ddd, *J* = 12.4, 4.1, 1.4 Hz, 1H), 5.11 (d, *J* = 4.4 Hz, 1H), 5.07 (dd, *J* = 11.3, 11.3 Hz, 1H), 4.12–4.05 (m, 1H), 3.41 (dq, *J* = 9.7, 6.8 Hz, 1H), 3.22 (s, 1H), 2.77 (ddd, *J* = 11.4, 4.3, 1.7 Hz, 1H), 2.74 (ddd, *J* = 11.5, 4.3, 1.6 Hz, 1H), 2.68–2.63 (m, 1H), 2.56–2.53 (m, 2H), 2.53–2.40 (m, 3H), 2.36–2.25 (m, 4H), 1.77 (d, *J* = 1.4 Hz, 3H), 1.58 (ddd, *J* = 14.1, 10.6, 4.9 Hz, 1H), 1.32–1.24 (m, 1H), 1.17 (d, *J* = 6.8 Hz, 3H), 0.46 ppm (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 212.5 (C), 172.1 (C), 172.0 (C), 166.9 (C), 146.3 (CH), 140.0 (C), 137.7 (C), 134.1 (CH), 134.0 (C), 132.4 (CH), 130.7 (CH), 128.5 (CH), 128.2 (CH), 128.2 (CH), 127.7 (CH), 126.7 (CH), 81.8 (CH), 64.8 (CH), 47.4 (CH_2), 46.7 (CH), 40.8 (CH_2), 38.5 (CH_2), 37.5 (CH), 37.2 (CH_2), 31.8 (CH_2), 27.7 (CH_2), 27.1 (CH), 16.7 (CH_3), 16.2 (CH_3), 15.6 ppm (CH_3); IR (film): 3486, 3225, 2966, 2928, 1697, 1640, 1442, 1373, 1330, 1313, 1263, 1186, 1145, 1085, 1005, 833, 766, 733, 702 cm^{-1}; HRMS (ESI): *m/z:* calcd for $C_{32}H_{39}NO_6Na$ $[M + Na]^+$: 556.2670; found 556.2672.

Compound 57. A solution of enyne **22** (150 mg, 0.36 mmol) and (*R*,*R*)-(–)-[1,2-cyclohexanediamino-*N,N'*-bis(3,5-di-*tert*-butylsalicylidene]-manganese chloride (23 mg, 0.036 mmol)[8] in CH_2Cl_2 (2 mL) was added to an aqueous solution of NaOCl [2 mL (prepared from a commercial solution of bleach (0.56 mL, 2 M)] and a solution of Na_2HPO_4 (1.44 mL, 0.05 M) at 4 °C. 2 Drops of NaOH (1 M) were added to reach pH 11-12 and the resulting mixture was stirred for 17 h at this temperature before a second portion of the catalyst (40 mg, 0.063 mmol) and of the NaOCl solution (4 mL) were added. The reaction mixture was stirred at 4 °C until TLC showed complete conversion. For work up, the mixture was diluted with water and CH_2Cl_2, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 10/0 → 95/5) to give epoxide **57** as a syrup (104 mg, 66 %). $[\alpha]_D^{20}$ = +13° (*c* = 0.55, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.40 (d, *J* = 9.2 Hz, 1H), 5.21 (d, *J* = 3.6 Hz, 1H), 3.75 (qd, *J* = 6.1, 3.5 Hz, 1H), 3.47-3.46 (m, 1H), 2.85 (dd, *J* = 9.8, 3.8 Hz, 1H), 2.71 (dd, *J* = 17.3, 12.3, 2.6 Hz, 1H), 2.46-2.33 (m, 3H), 2.33-2.17 (m, 3H), 1.79-1.69 (m, 1 H, *overlap*), 1.73 (d, *J* = 1.3 Hz, 3 H, *overlap*), 1.67-1.54 (m, 2H), 1.15 (t, *J* = 7.1 Hz, 3H), 1.06 (d, *J* = 6.2 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.95 (t, *J* = 7.8 Hz, 9H), 0.57 ppm (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3 (C), 133.7 (CH), 128.9 (C), 87.3 (C), 80.5 (CH), 76.6 (C), 71.4 (CH), 60.2 (CH), 46.4 (CH), 39.6 (CH), 38.4 (CH), 32.4 (CH_2), 25.8 (CH_2), 23.9 (CH_2), 21.2 (CH_3), 18.0 (CH_2), 16.4 (CH_3), 15.2 (CH_3), 14.7 (CH_3), 7.0 (CH_3), 5.2 ppm (CH_2); IR (film): 2955, 2931, 2875, 1732, 1456, 1375, 1340, 1239, 1196, 1150, 1088, 1064, 1006, 975, 878, 833, 741, 723 cm^{-1}; MS (EI): *m/z* (%): 161 (5), 160 (14), 159 (100), 131 (27), 116 (6), 115 (51), 109 (9), 103 (9), 91 (8), 87 (23), 79 (5), 77 (7), 75 (13), 67 (5), 59 (10), 55 (7), 43 (6), 41 (7), 40 (6); HRMS (ESI): *m/z:* calcd for $C_{25}H_{42}O_4SiNa$ $[M + Na]^+$: 457.2745; found: 475.2747.



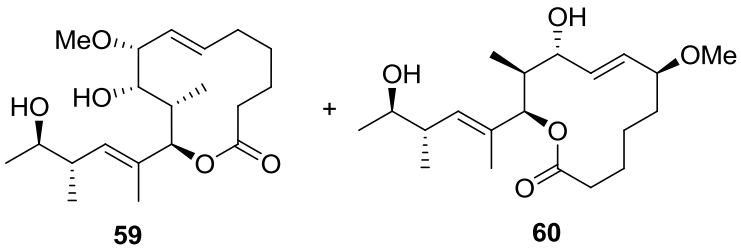
[8] E. N. Jacobsen, W. Zhang, A. R. Muci, J. R. Ecker, L. Deng, *J. Am. Chem. Soc* **1991**, *113*, 7063-7064.

Compound 58: $[Cp^*Ru(MeCN)_3]PF_6$ (4.3 mg, 0.0085 mmol) and benzyldimethylsilane (40 µL, 0.26 mmol) were successively added to a solution of cycloalkyne **57** (37 mg, 0.085 mmol) in CH_2Cl_2 (0.5 mL) at 0 °C. The mixture was stirred for 1 h at this temperature and then warmed to ambient temperature. Next, the solvent was slowly evaporated by a stream of Ar. After 30 min a second portion of $[Cp^*Ru(MeCN)_3]PF_6$ (3.0 mg, 0.006 mmol) and benzyldimethylsilane (20 µL, 0.13 mmol) were added and the reaction mixture was stirred until TLC indicated complete conversion (ca. 30 min). The residue was purified by flash chromatography (hexanes/EtOAc, 90/10) to give the corresponding alkenylsilane, which was directly used in the next step.



A solution of anhydrous TBAF (1 M in THF, 0.44 mL, 0.44 mmol) was added to a solution of this alkenylsilane in THF (0.5 mL) and the resulting mixture stirred at ambient temperature for 1 h and at 50 °C for 45 min. The solvent was evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 60/40) to give alkene **58** as a colorless oil (25 mg, 91 %). $[\alpha]_D^{20} = -38°$ (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.00 (dt, J = 15.8, 6.1 Hz, 1H), 5.30 (d, J = 9.1 Hz, 1H), 5.26 (dd, J = 15.6, 8.5 Hz, 1H), 5.08 (d, J = 4.6 Hz, 1H), 3.61 (dq, J = 6.2, 6.2 Hz, 1H), 3.46 (dd, J = 8.6, 4.2 Hz, 1H), 2.90 (dd, J = 10.1, 4.2 Hz, 1H), 2.49-2.40 (m, 1H), 2.40-2.30 (m, 1H), 2.30-2.18 (m, 2H), 2.17-2.01 (m, 2H), 2.00-1.88 (m, 1H), 1.73 (d, J = 1.1 Hz, 3H), 1.65-1.49 (m, 2H), 1.17 (d, J = 6.3 Hz, 3H), 1.10 (d, J = 6.9 Hz, 3H), 0.98 ppm (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.7 (C), 135.5 (CH), 133.4 (CH), 131.4 (C), 126.3 (CH), 81.4 (CH), 71.4 (CH), 60.2 (CH), 58.3 (CH), 39.9 (CH), 36.0 (CH), 33.4 (CH_2), 30.5 (CH_2), 25.4 (CH_2), 23.5 (CH_2), 20.4 (CH_3), 16.4 (CH_3), 15.5 (CH_3), 14.9 ppm (CH_3); IR (film): 3491, 2968, 2931, 1727, 1454, 1375, 1336, 1255, 1202, 1170, 1147, 1089, 973, 933, 874, 825 cm^{-1}; HRMS (ESI): *m/z:* calcd for $C_{19}H_{30}O_4Na$ $[M + Na]^+$: 345.2036; found: 345.2035.

Compounds 59 and 60: A solution of *p*-TsOH (0.2 mg, 0.0011 mmol) in methanol (0.1 mL) was added to a solution of epoxide **58** (7.0 mg, 0.022 mmol) in methanol (0.3 mL) at 0 °C. The mixture was stirred for 45 min at this temperature and then directly purified by flash chromatography (hexanes/EtOAc, 80/20 → 70/30) to give compound **59** (2.5 mg, 32 %) and compound **60** (4.0 mg, 52 %) as a colorless oil each.



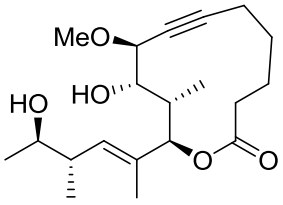
59 **60**

Spectral data of compound **59**: ^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.62 (ddd, J = 15.7, 9.3, 4.1 Hz, 1H), 5.43 (dd, J = 15.8, 7.9 Hz, 1H), 5.13 (s, 1H), 4.95 (d, J = 10.1 Hz, 1H), 3.82 (d, J = 7.4 Hz, 1H), 3.72 (dd, J = 6.0, 2.1 Hz, 1H), 3.36 (dq, J = 6.2, 7.3 Hz, 1H), 3.25 (s, 3H), 2.37-2.29 (m, 2H), 2.22-2.15 (m. 2H), 2.13-2.06 (m, 2H), 1.84-1.70 (m, 2H), 1.68 (d, J = 1.2 Hz, 3H), 1.63-1.54 (m, 4H), 1.13 (d, J = 6.1 Hz, 3H), 0.97 (d, J = 7.2 Hz, 3H), 0.91 ppm (d, J = 6.7 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 173.2 (C), 136.0 (CH), 135.1 (C), 128.4 (CH), 127.1 (CH), 84.5 (CH), 77.2 (CH), 76.8 (CH), 71.8 (CH), 56.5 (CH_3), 40.3 (CH), 37.2 (CH), 34.7 (CH_2), 30.0 (CH_2), 28.9 (CH_2), 22.8 (CH_2), 19.9 (CH_3), 16.8 (CH_3), 14.6 (CH_3), 11.1 ppm (CH_3); IR (film): 3433, 2967, 2928, 1727, 1448, 1373, 1251, 1188, 1155, 1092, 1042,

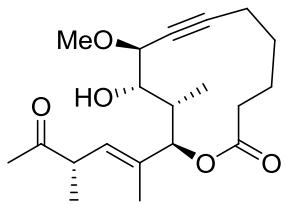
1013, 983, 969, 919, 703 cm^{-1}; MS (EI): *m*/*z* (%): 183 (10), 172 (30), 171 (100), 169 (13), 154 (20), 153 (17), 151 (23), 139 (25), 137 (11), 126 (10), 125 (15), 123 (11), 121 (19), 112 (35), 111 (15), 110 (37), 109 (56), 97 (25), 95 (29), 94 (10), 93 (11), 81 (10), 79 (16), 71 (28), 69 (15), 67 (14), 55 (15), 45 (11), 43 (18), 41 (14); HRMS (ESI): *m*/*z:* calcd for $C_{20}H_{34}O_5Na$ [M + Na]$^+$: 377.2298; found: 377.2297.

Spectral data of compound **60**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.00 (dd, *J* = 15.8, 1.9 Hz, 1H), 5.38 (ddd, *J* = 15.7, 9.3, 2.2 Hz, 1H), 5.01 (s, 1H), 4.89 (d, *J* = 10.4 Hz, 1H), 4.43-4.38 (m, 1H), 3.79 (td, *J* = 9.9, 5.8 Hz, 1H), 3.33 (dq. *J* = 6.8, 6.4 Hz, 1H), 3.26 (s, 3H), 2.48 (dt, *J* = 13.1, 4.2 Hz, 1H), 2.41-2.30 (m, 1H), 2.15-2.02 (m, 2H), 1.85-1.52 (m, 4 H, *overlap*), 1.69 (d, *J* = 0.9 Hz, 3 H, *overlap*) 1.47-1.41 (m, 2H), 1.41-1.36 (m, 2H), 1.15 (d, *J* = 6.0 Hz, 3H), 1.03 (d, *J* = 7.4 Hz, 3H), 0.93 ppm (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.9 (C), 137.1 (C), 134.7 (CH), 126.5 (CH), 125.6 (CH), 82.2 (CH), 74.5 (CH), 72.4 (CH), 72.0 (CH), 56.2 (CH_3), 40.7 (CH), 40.6 (CH), 35.9 (CH_2), 31.2 (CH_2), 24.0 (CH_2), 22.0 (CH_2), 20.0 (CH_3), 17.1 (CH_3), 15.5 (CH_3), 10.1 ppm (CH_3).

Compound 62. *p*-TsOH (17 mg, 0.09 mmol) was added to a solution of epoxide **57** (79 mg, 0.18 mmol) in methanol (6 mL). The mixture was heated to 60 °C for 2 h before the solvent was evaporated. The residue was purified by flash chromatography (hexanes/EtOAc, 60/40) to give compound **62** as a pale yellow oil (60 mg, 94 %). $[\alpha]_D^{20}$ = +70° (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.18 (d, *J* = 2.7 Hz, 1H), 5.07 (dt, *J* = 9.3, 0.9 Hz, 1H), 4.03 (dd, *J* = 9.7, 1.4 Hz, 1H), 3.64-3.58 (m, 1H), 3.41 (s, 3H), 3.37 (dq, *J* = 8.6, 6.1 Hz, 1H), 2.89 (br s , 1H), 2.58 (ddd, *J* = 13.9, 7.1, 2.4 Hz, 1H), 2.41-2.30 (m, 2H), 2.25-2.14 (m, 2H), 2.10-1.96 (m, 2H), 1.81 (d, *J* = 1.1 Hz, 3H), 1.80-1.64 (m, 2H), 1.53-1.40 (m, 1H), 1.17 (d, *J* = 6.1 Hz, 3H), 0.96 (d, *J* = 7.2 Hz, 3H), 0.92 ppm (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4 (C), 133.4 (C), 130.9 (CH), 89.0 (C), 79.5 (CH), 77.8 (C), 73.9 (CH), 72.4 (CH), 72.2 (CH), 57.1 (CH_3), 40.9 (CH), 39.5 (CH), 34.7 (CH_2), 27.0 (CH_2), 23.7 (CH_2), 20.1 (CH_3), 18.4 (CH_2), 16.8 (CH_3), 13.9 (CH_3), 10.9 (CH_3); IR (film): 3450, 2924, 2854, 1728, 1452, 1376, 1252, 1146, 1101, 1046, 983, 904, 832, 761, 699 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{20}H_{32}O_5Na$ [M + Na]$^+$: 375.2142; found: 375.2143.

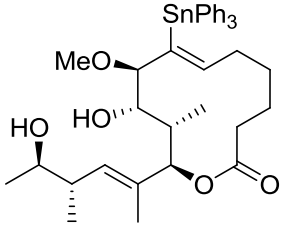


Compound 63: Dess-Martin periodinane (119 mg, 0.28 mmol) was added to a solution of alcohol **62** (50 mg, 0.14 mmol) in CH_2Cl_2 (3 mL) at 0 °C. After stirring for 3 h at this temperature, the solvent was slowly evaporated by a stream of Ar and the residue purified by flash chromatography (hexanes/EtOAc, 80/20 → 70/30) to give ketone **63** as a white solid (36 mg, 73 %). M.p.: 131-132 °C; $[\alpha]_D^{20}$ = +285° (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.20 (d, *J* = 9.7 Hz, 1H), 5.15 (d, *J* = 3.6 Hz, 1H), 3.99 (dd, *J* = 9.7, 2.0 Hz, 1H), 3.60 (dq, *J* = 9.5, 1.1 Hz, 1H), 3.43 (s, 3H), 3.43-3.35 (m, 1H), 2.74 (br s, 1H), 2.57 (ddd, *J* = 14.9, 8.1, 2.4 Hz, 1H), 2.36 (ddt, *J* = 17.1, 7.1, 2.7 Hz, 1H), 2.27-2.16 (m, 2H), 2.15-2.04 (m, 1 H, *overlap*), 2.11 (s, 3 H, *overlap*), 2.03-1.91 (m, 1H), 1.84 (d, *J* = 1.1 Hz, 3H), 1.82-1.75 (m, 1H), 1.73-1.61 (m, 1H), 1.57-1.45 (m, 1H), 1.11 (d, *J* = 6.6 Hz, 3H), 0.93 ppm (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.6 (C), 172.1 (C), 134.3 (C), 127.3 (CH), 88.6 (C), 79.4 (CH), 77.7 (C),

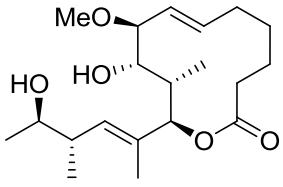


74.1 (CH), 71.6 (CH), 56.8 (CH_3), 46.6 (CH), 39.0 (CH), 34.2 (CH_2), 28.0 (CH_3), 26.8 (CH_2), 23.3 (CH_2), 18.1 (CH_2), 15.8 (CH_3), 13.5 (CH_3), 10.7 ppm (CH_3); IR (film): 3534, 2931, 2873, 1717, 1703, 1445, 1409, 1346, 1328, 1312, 1248, 1223, 1167, 1143, 1107, 1039, 979, 875, 760 cm^{-1}; MS (EI): *m*/*z* (%): 350 (2) [*M*+], 181 (11), 170 (15), 169 (100), 149 (11), 137 (37), 125 (12), 123 (23), 121 (28), 111 (15), 110 (10), 109 (82), 95 (16), 93 (21), 92 (10), 91 (23), 85 (65), 84 (62), 81 (20), 79 (31), 77 (15), 69 (19), 67 (21), 55 (20), 53 (13), 43 (67), 41 (24); HRMS (ESI): *m*/*z*: calcd for $C_{20}H_{30}O_5Na$ [M + Na]$^+$: 373.1985; found: 373.1984.

Compound 61b. Ph_3SnH (200 mg, 0.57 mmol) and AIBN (7 mg, 0.042 mmol) were added to a solution of alkyne **62** (50 mg, 0.14 mmol) in degassed toluene (6 mL). The mixture was stirred at 80 °C for 4 h before additional Ph_3SnH (50 mg, 0.14 mmol) and AIBN (7 mg, 0.042 mmol) were added. After stirring for 7 h at this temperature, the solvent was evaporated and the residue was purified by flash chromatography (hexanes/EtOAc, 90/10 → 80/20) to give stanane **61b** (64 mg, 65 %) as a colorless oil. $[\alpha]_D^{20}$ = +13.4° (*c* = 0.79, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63-7.55 (m, 6H), 7.43-7.31 (m, 9H), 6.77 (t, *J* = 7.8 Hz, 1H), 5.19 (d, *J* = 2.5 Hz, 1H), 5.04 (d, *J* = 10.0 Hz, 1H), 3.91 (d, *J* = 9.0 Hz, 1H), 3.61 (d, *J* = 9.0 Hz, 1H), 3.38-3.29 (m, 1H), 3.20 (br s, 1H), 3.14 (s, 3H), 2.88 (br s, 1H), 2.41-2.28 (m, 2H), 2.20-2.03 (m, 3H), 2.03-1.88 (m, 1H), 1.80 (d, *J* = 0.8 Hz, 3H), 1.74-1.60 (m, 2H), 1.48-1.30 (m, 2H), 1.18 (d, *J* = 6.0 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.78 ppm (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.9, 148.2, 142.0, 138.7, 137.2, 133.3, 131.1, 129.1, 128.9, 85.4, 79.6, 73.2, 72.5, 57.2, 40.8, 38.6, 35.1, 32.3, 28.2, 21.9, 19.9, 16.7, 13.5, 10.7 ppm; IR (film): 3499, 2928, 1728, 429, 1251, 1094, 1073, 1044, 977, 729, 699 cm^{-1}; MS (EI): *m*/*z* (%): 628 (10), 627 (31), 626 (16), 625 (24), 624 (11), 623 (13), 445 (17), 444 (12), 443 (32), 442 (16), 441 (29), 440 (12), 439 (16), 367 (19), 366 (13), 365 (25), 364 (14), 363 (22), 361 (10), 355 (19), 353 (16), 352 (19), 351 (100), 350 (39), 349 (76), 348 (30), 347 (43), 289 (12), 287 (10), 275 (12), 197 (23), 195 (18), 194 (15), 193 (10), 109 (14); HRMS (ESI): *m*/*z*: calcd for $C_{38}H_{48}O_5SnNa$ [M + Na]$^+$: 727.2415; found: 727.2424.



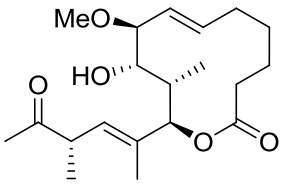
Compound 61a: Iodine (19 mg, 0.073 mmol) was added to a solution of stanane **61b** (43 mg, 0.061 mmol) in CH_2Cl_2 (2 mL) at –78 °C. After 10 min, the reaction was warmed to ambient temperature and stirred for 20 min before the solvent was slowly evaporated by a stream of Ar. The residue was purified by flash chromatography (hexanes/EtOAc, 80/20 → 70/30) to give iodide **61c** as a yellow oil (24 mg, 82 %).



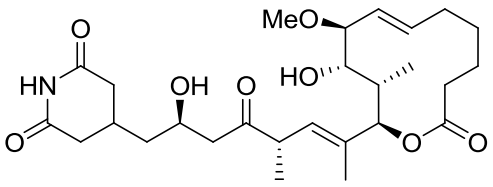
Bu_3SnH (22 µL, 0.082 mmol) and AIBN (4 mg, 0.024 mmol) were successively added to a solution of this iodide in degassed toluene (1 mL). The mixture was stirred at 65 °C for 2 h prior to evaporation of the solvent. The residue was purified by flash chromatography (hexanes/EtOAc, 80/20 → 60/40) to give alkene **61a** as a colorless oil (12 mg, 63 %). $[\alpha]_D^{20}$ = +44° (*c* = 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.66 (ddd, *J* = 15.8, 8.6, 6.9 Hz, 1H), 5.26 (dd, *J* = 16.0, 7.1 Hz, 1H), 5.11 (d, *J* = 2.3 Hz, 1H), 5.06 (d, *J* = 10.0 Hz, 1H), 3.67 (dd, *J* = 9.4, 1.3 Hz, 1H), 3.43-3.34 (m, 1H), 3.32-3.23 (m, 1 H, *overlap*), 3.30 (s, 3H), 3.14 (br s, 1H), 3.09 (br s, 1H), 2.46 (dt, *J* = 13.5, 4.5 Hz, 1H), 2.41-2.30 (m, 1H), 2.26-2.17 (m, 1H), 2.15-2.06 (m, 1H), 1.94-1.86 (m, 1H), 1.82 (d, *J* = 1.1 Hz, 3H), 1.78-1.55 (m, 5H), 1.18

(d, *J* = 6.3 Hz, 3H), 0.97 (d, *J* = 7.3 Hz, 3H), 0.93 ppm (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4 (C), 135.4 (CH), 133.2 (C), 130.9 (CH), 130.3 (CH), 82.2 (CH), 79.5 (CH), 72.4 (CH), 71.7 (CH), 56.6 (CH_3), 40.8 (CH), 38.3 (CH), 34.9 (CH_2), 30.2 (CH_2), 26.5 (CH_2), 22.4 (CH_2), 20.0 (CH_3), 16.7 (CH_3), 13.8 (CH_3), 10.9 ppm (CH_3); IR (film): 3481, 2926, 2855, 1729, 1452, 1377, 1252, 1190, 1142, 1100, 1041, 982 cm^{-1}; MS (EI): *m*/*z* (%): 278 (25), 172 (18), 171 (100), 170 (12), 169 (15), 154 (24), 153 (19), 151 (28), 139 (21), 137 (19), 126 (26), 125 (14), 123 (17), 121 (21), 112 (17). 11 (25), 110 (40), 109 (69), 107 (10), 98 (16), 97 (54), 96 (22), 95 (37), 94 (22), 93 (23), 91 (10), 81 (20), 79 (31), 71 (45), 69 (26), 67 (34), 57 (15), 55 (35), 53 (11), 45 (25), 43 (36), 41 (38); HRMS (ESI): *m*/*z*: calcd for $C_{20}H_{34}O_5Na$ [M + Na]$^+$: 377.2298; found: 377.2299.

Compound 65: Dess-Martin periodinane (45 mg, 0.11 mmol) was added to a solution of alcohol **61a** (15 mg, 0.042 mmol) in CH_2Cl_2 (2 mL) at 0 °C. After stirring for 4 h at this temperature, the solvent was evaporated and the residue purified by flash chromatography (hexanes/EtOAc, 80/20 → 70/30) to give ketone **65** as a white solid (10 mg, 68 %). $[\alpha]_D^{20}$ = +192° (*c* = 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.68 (dt, *J* = 15.5, 7.4 Hz, 1H), 5.30 (dd, *J* = 16.0, 6.9 Hz, 1H), 5.19 (d, *J* = 9.6 Hz, 1H), 5.05 (d, *J* = 3.0 Hz, 1H), 3.65 (dd, *J* = 9.3, 2.8 Hz, 1H), 3.40 (dq, *J* = 9.6, 6.8 Hz, 1H), 3.31 (s, 3H), 3.31-3.23 (m, 1H), 2.99 (br s, 1H), 2.46-2.38 (m, 1H), 2.27-2.15 (m, 2H), 2.11 (s, 3H), 1.98-1.89 (m, 2H), 1.83 (d, *J* = 1.0 Hz, 3H), 1.78-1.66 (m, 3H), 1.40-1.27 (m, 1H), 1.12 (d, *J* = 6.8 Hz, 3H), 0.95 ppm (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.8 (C), 172.3 (C), 135.5 (CH), 134.3 (C), 129.5 (CH), 127.0 (CH), 82.6 (CH), 79.3 (CH), 72.2 (CH), 56.5 (CH_3), 46.6 (CH), 38.2 (CH), 34.4 (CH_2), 30.2 (CH_2), 28.1 (CH_3), 26.5 (CH_2), 22.6 (CH_3), 15.9 (CH_3), 13.7 (CH_3), 11.0 ppm (CH_3); IR (film): 3526, 2931, 1715, 1449, 1430, 1355, 1251, 1185, 1151, 1102, 1040, 981, 872, 731, 699 cm^{-1}; MS (EI): *m*/*z* (%): 181 (7), 172 (10), 171 (100), 155 (7), 154 (19), 153 (20), 151 (6), 139 (23), 126 (7), 125 (8), 123 (9), 121 (24), 111 (13), 110 (19), 109 (31), 98 (5), 97 (20), 95 (11), 94 (10), 93 (10), 81 (7), 79 (15), 71 (22), 69 (8), 67 (12), 57 (6), 55 (11), 45 (7), 43 (31), 41 (13); HRMS (ESI): *m*/*z*: calcd for $C_{20}H_{32}O_5Na$ [M + Na]$^+$: 375.2142; found: 375.2138.

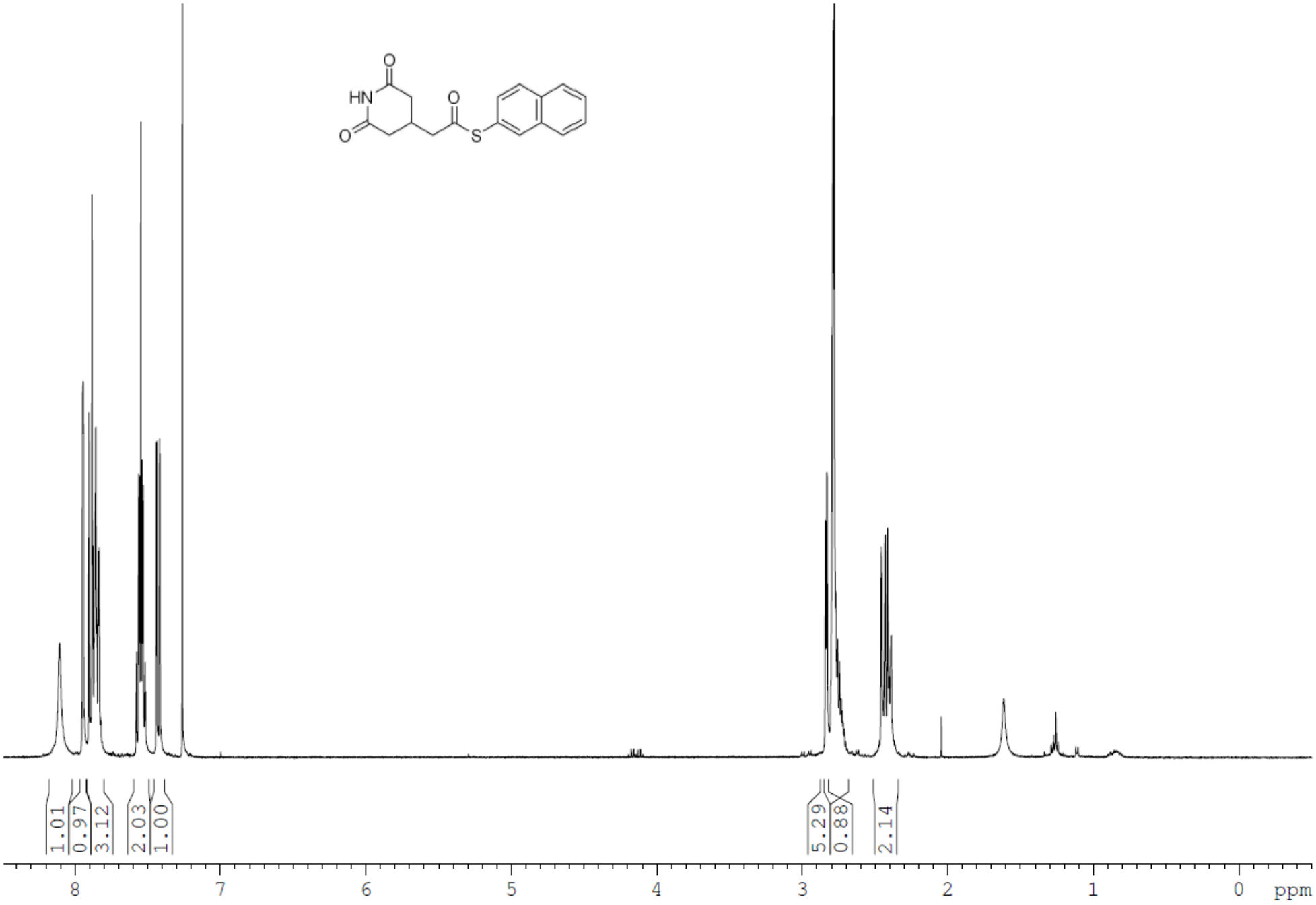


Compound 56: Me_3SiCl (18 µL, 0.14 mmol) and triethylamine (20 µL, 0.14 mmol) were added to a solution of ketone **65** (5.0 mg, 0.014 mmol) in THF (0.5 mL) at –78 °C. Next, LiHMDS (1 M in THF, 84 µL, 0.084 mmol) was slowly introduced and the resulting mixture stirred at –78 °C for 1 h. The reaction was then quenched with pH 7 phosphate buffer and the product extracted with CH_2Cl_2 (3 x 2 mL). The combined organic phases were dried over $MgSO_4$ and evaporated to give the corresponding silyl enol ether, which was used in the next step without further purification.



Molecular sieves (4 Å, ca. 100 mg) and aldehyde **41b** (2.2 mg, 0.014 mmol) were added to a solution of the crude silyl enol ether in propionitrile (0.4 mL). The mixture was cooled to –78 °C before a solution of compound **42** [prepared upon stirring of a solution of $PhBCl_2$ (1.8 µL, 0.014 mmol) and N-tosyl-D-tryptophane (5 mg, 0.014 mmol) in CH_2Cl_2 (0.5 mL) for 1 h,

followed by removal of the solvent][3] in propionitrile (0.1 mL) was added. After stirring for 18 h at –78 °C, the reaction was quenched with sat. aq. $NaHCO_3$, the aqueous phase was extracted with CH_2Cl_2 (3 x 2 mL), and the combined organic layers were dried over Na_2SO_4 and evaporated. The resulting crude product was dissolved in THF (4 mL) at 0 °C and treated with 0.5 mL of buffered HF·pyridine solution [prepared from THF (3.6 mL), pyridine (1.35 mL) and HF·pyridine complex (0.27 mL, 70 % *w*/*w*)]. The mixture was stirred at 0 °C for 1 h and warmed to ambient temperature for 30 min, before a second portion of buffered HF·pyridine solution (0.5 mL) was added and the solvent was slowly evaporated by a stream of Ar. After stirring of the remaining syrup for 2h, the mixture was diluted with CH_2Cl_2, the organic phase was washed with sat. aq. $NaHCO_3$ and $CuSO_4$ solution (1 M) before it was dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography (EtOAc/hexanes, 8/2) to give product **56** as a white solid (2.1 mg, 30 %). $[\alpha]_D^{20}$ = +129° (*c* = 0.4, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.76 (s, 1H), 5.66 (ddd, *J* = 16.0, 7.2, 7.2 Hz, 1H), 5.26 (dd, *J* = 16.0, 7.0 Hz, 1H), 5.06 (d, *J* = 9.6 Hz, 1H), 5.03 (d, *J* = 2.9 Hz, 1H), 4.06-4.00 (m, 1H), 3.63 (dd, *J* = 9.4, 2.4 Hz, 1H), 3.39 (dq, *J* = 9.7, 6.7 Hz, 1H), 3.30 (s, 3H), 3.27 (dd, *J* = 7.0, 9.2 Hz, 1H), 2.77 (dd, *J* = 17.1, 4.0, Hz, 1H), 2.73 (dd, *J* = 17.1, 4.0 Hz, 1H), 2.66 (dd, *J* = 17.7, 8.5 Hz, 1H), 2.48 (dd, *J* = 17.7, 2.9 Hz, 1H), 2.46-2.38 (m, 2H), 2.30 (dd, *J* = 17.1, 10.9 Hz, 1H), 2.28 (dd, *J* = 17.1, 10.7 Hz, 1H), 2.23-2.16 (m, 1H), 2.16-2.10 (m, 1H), 1.94-1.88 (m, 1H), 1.88-1.83 (m, 1H), 1.82 (d, *J* = 1.2 Hz, 3H), 1.75-1.66 (m, 3H), 1.55 (ddd, *J* = 14.0, 10.2, 5.1 Hz, 1H), 1.36 (ddd, *J* = 14.0, 8.8, 3.1 Hz, 1H), 1.32-1.24 (m, 1H), 1.11 (d, *J* = 6.7 Hz, 3H), 0.90 ppm (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 212.2, 172.5, 172.2, 171.9, 135.9, 135.2, 129.7, 126.5, 82.5, 79.3, 72.2, 65.1, 56.6, 47.4, 46.7, 41.1, 38.6, 38.3, 37.3, 34.7, 30.3, 27.2, 26.5, 22.7, 15.6, 13.9, 11.2 ppm; IR (film): 2981, 2934, 1733, 1591, 1490, 1380, 1360, 1276, 1183, 1135, 1100, 1052, 1024, 1003, 979, 769, 689 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{27}H_{41}NO_8Na$ $[M + Na]^+$: 530.2724; found: 530.2727.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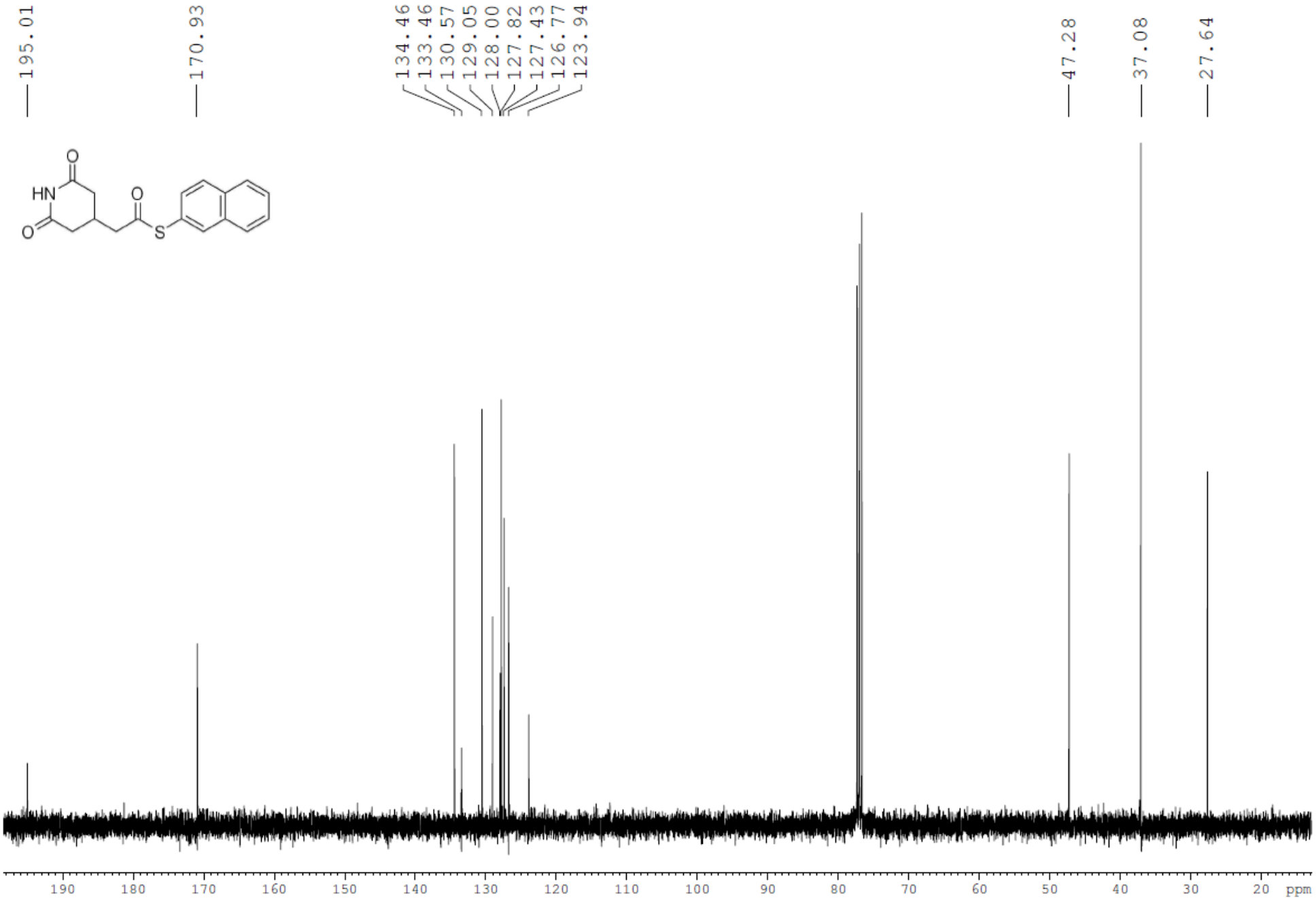
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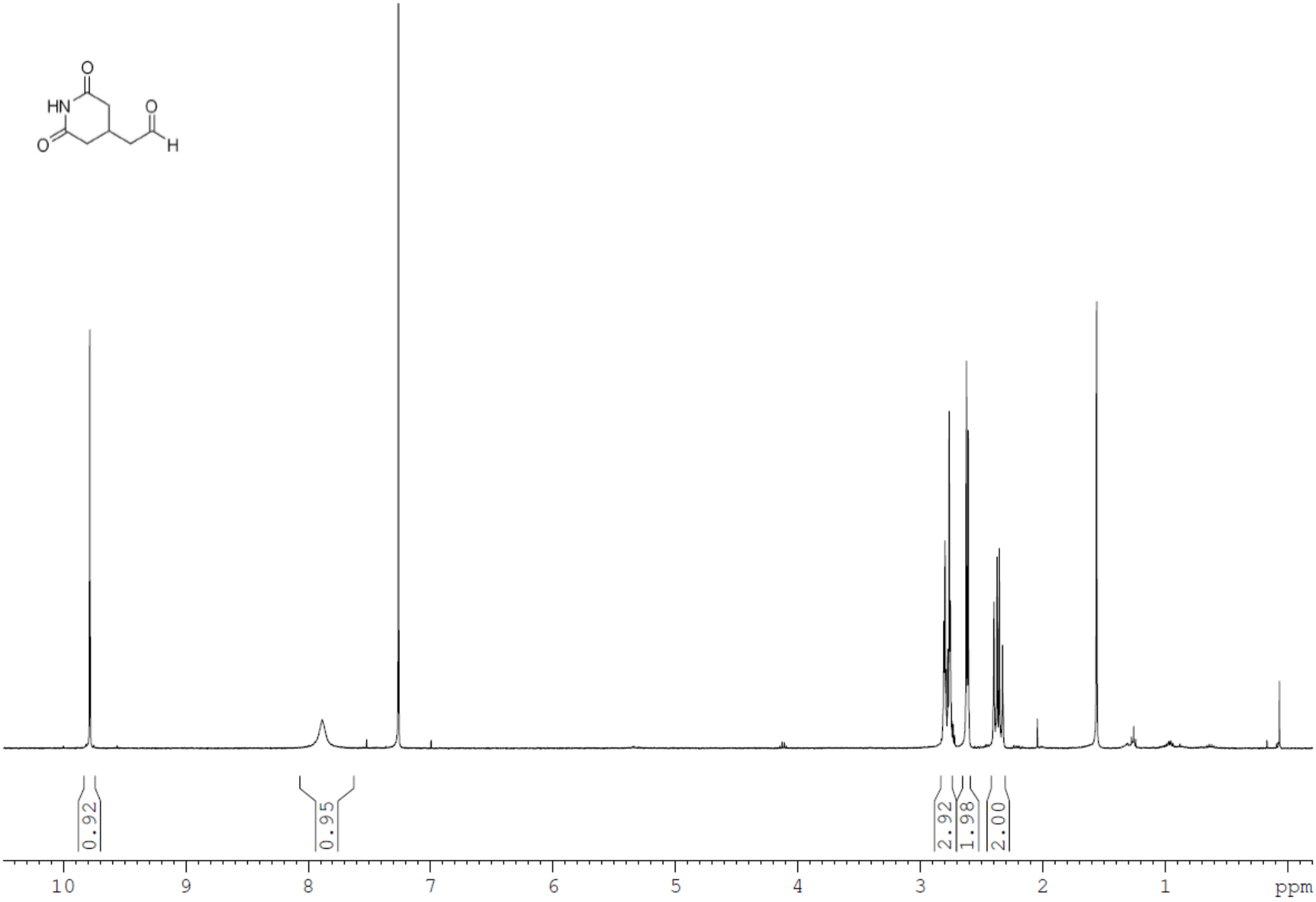
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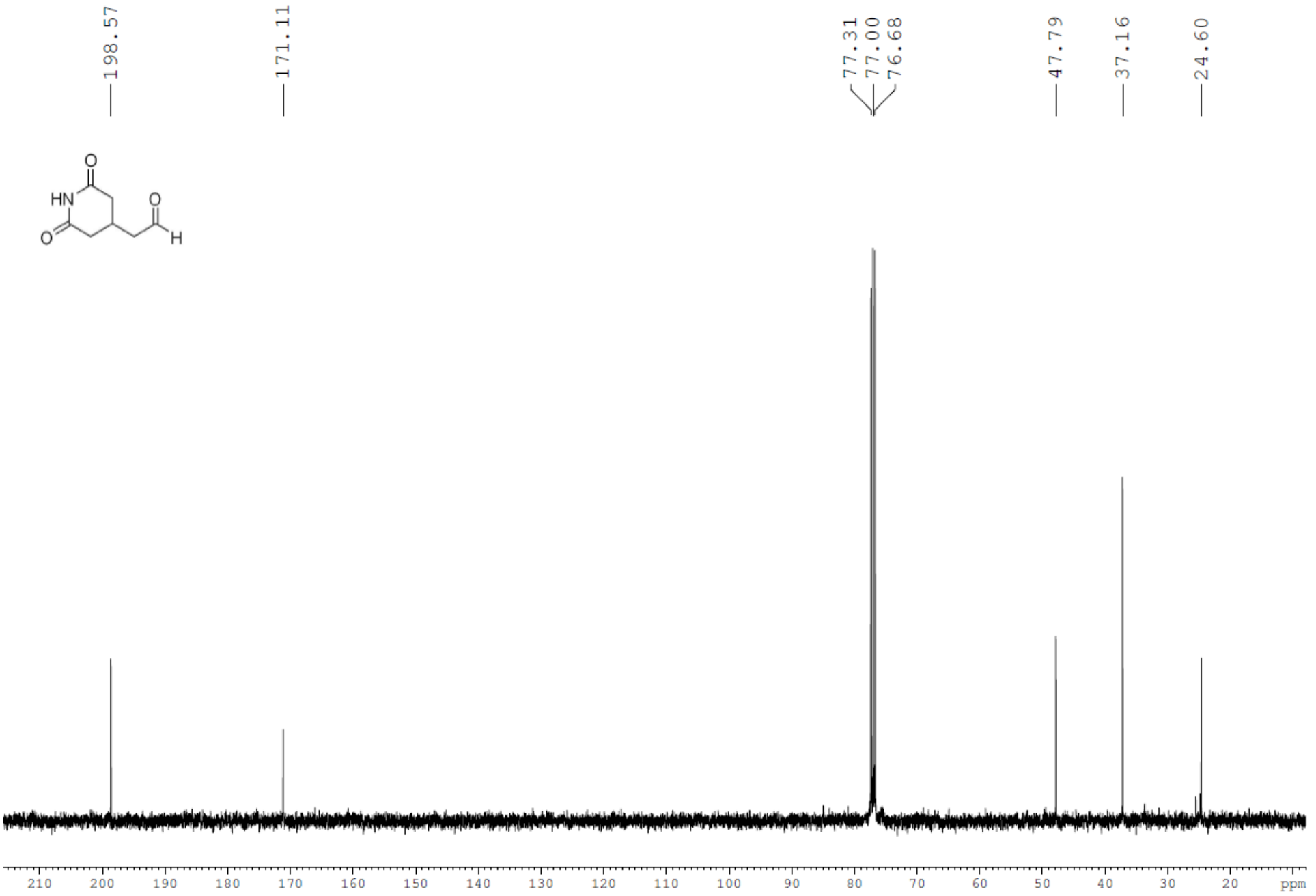
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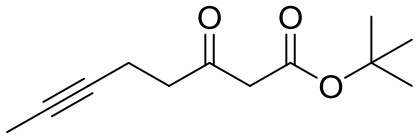
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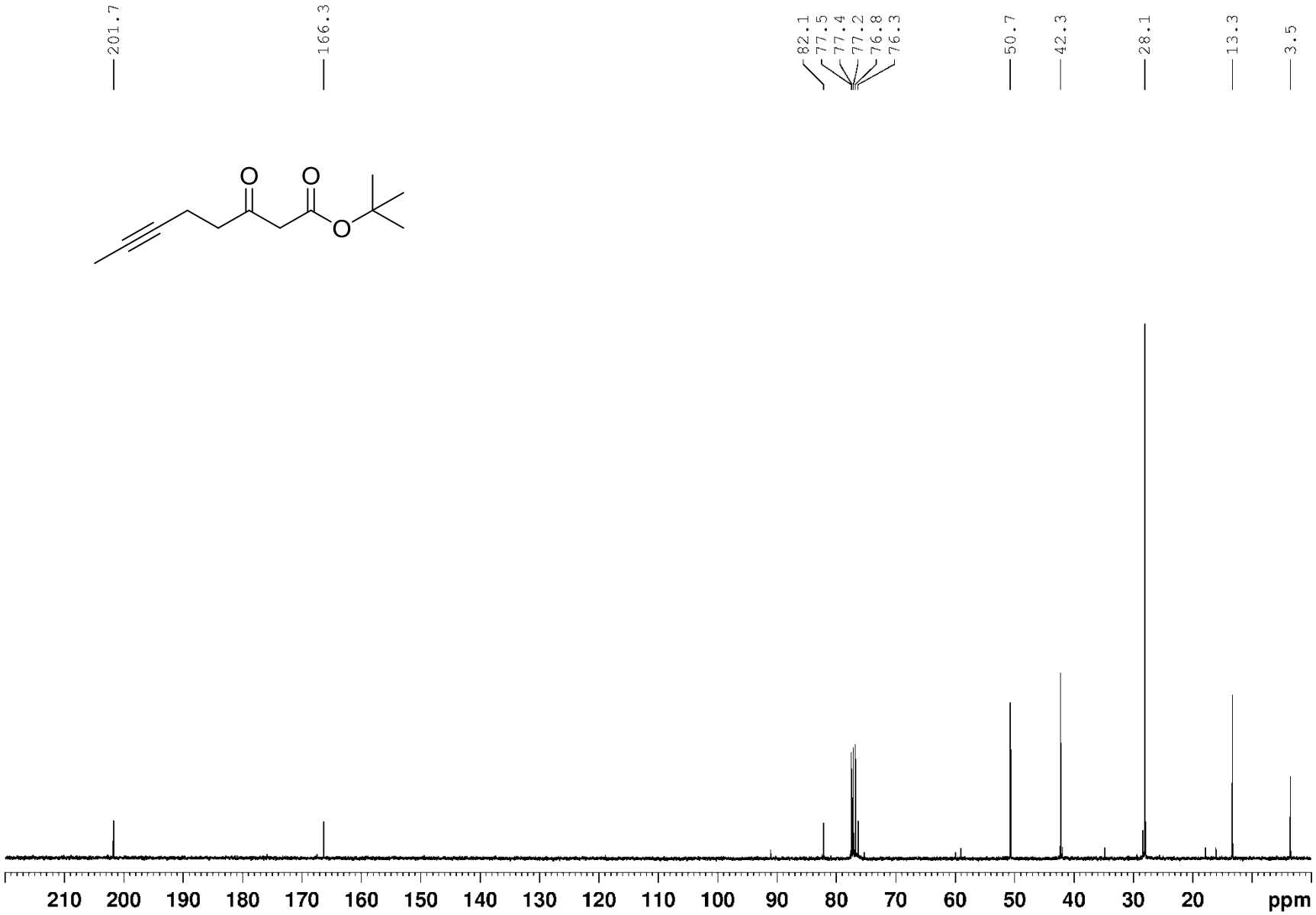
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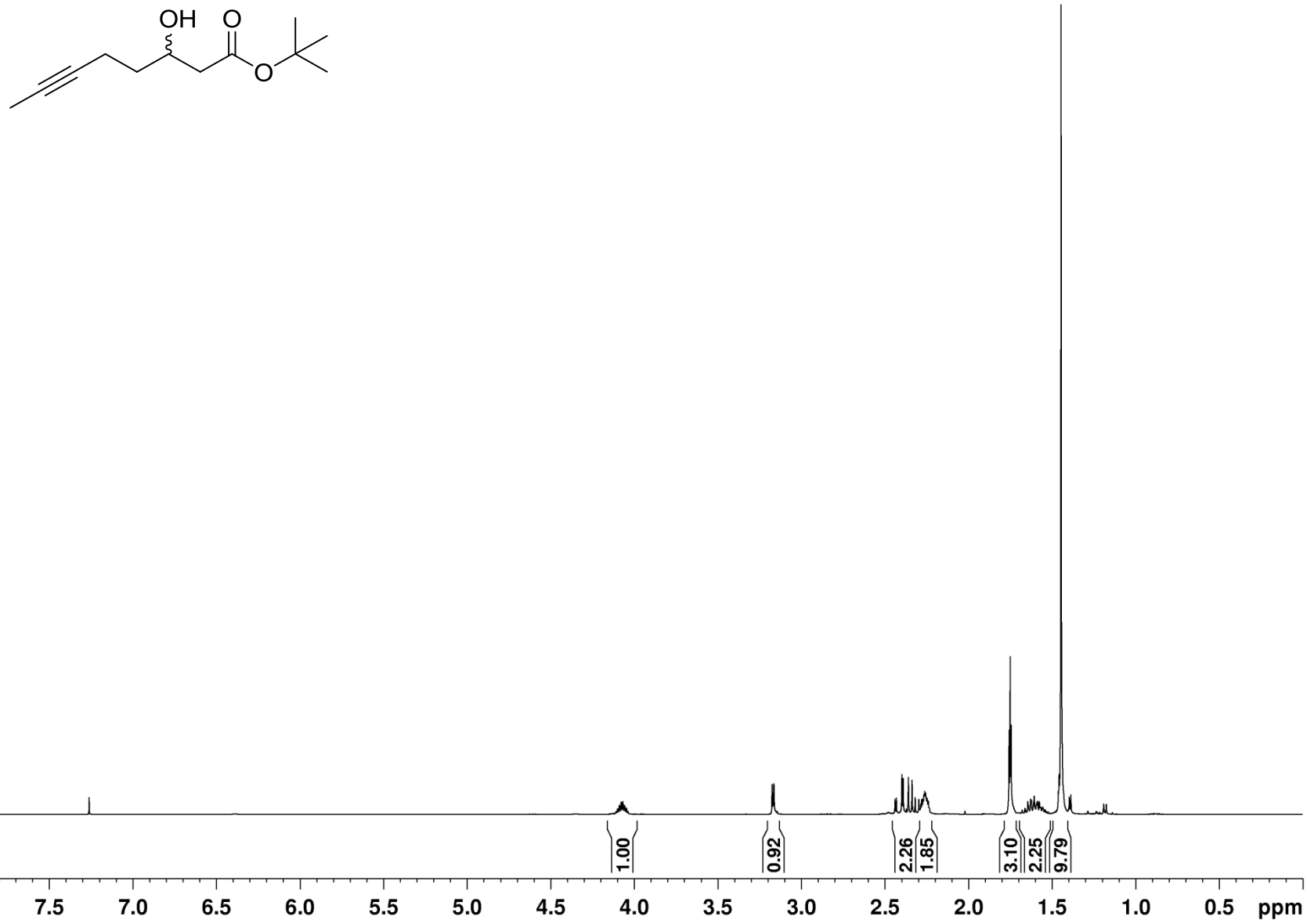
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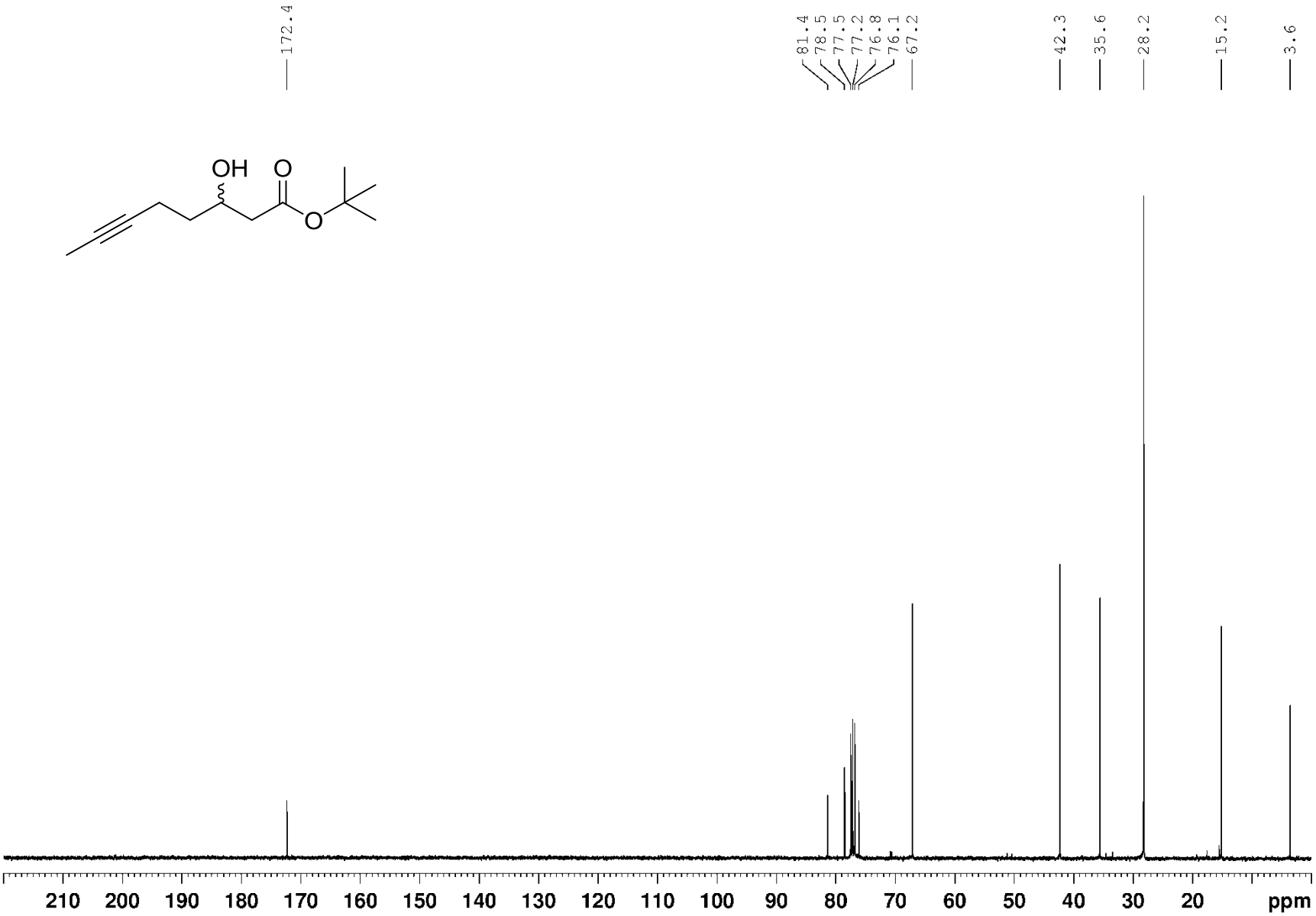
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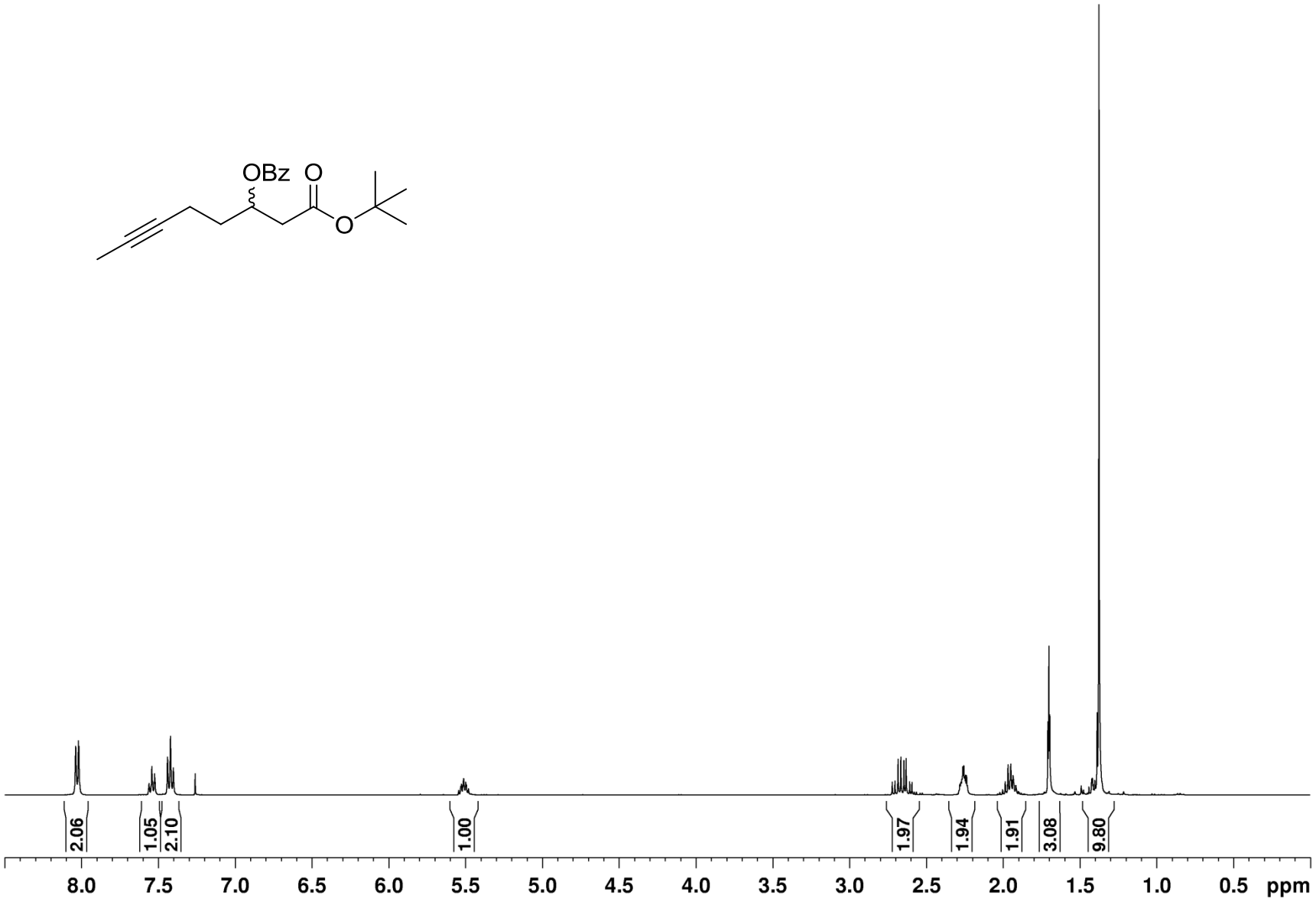
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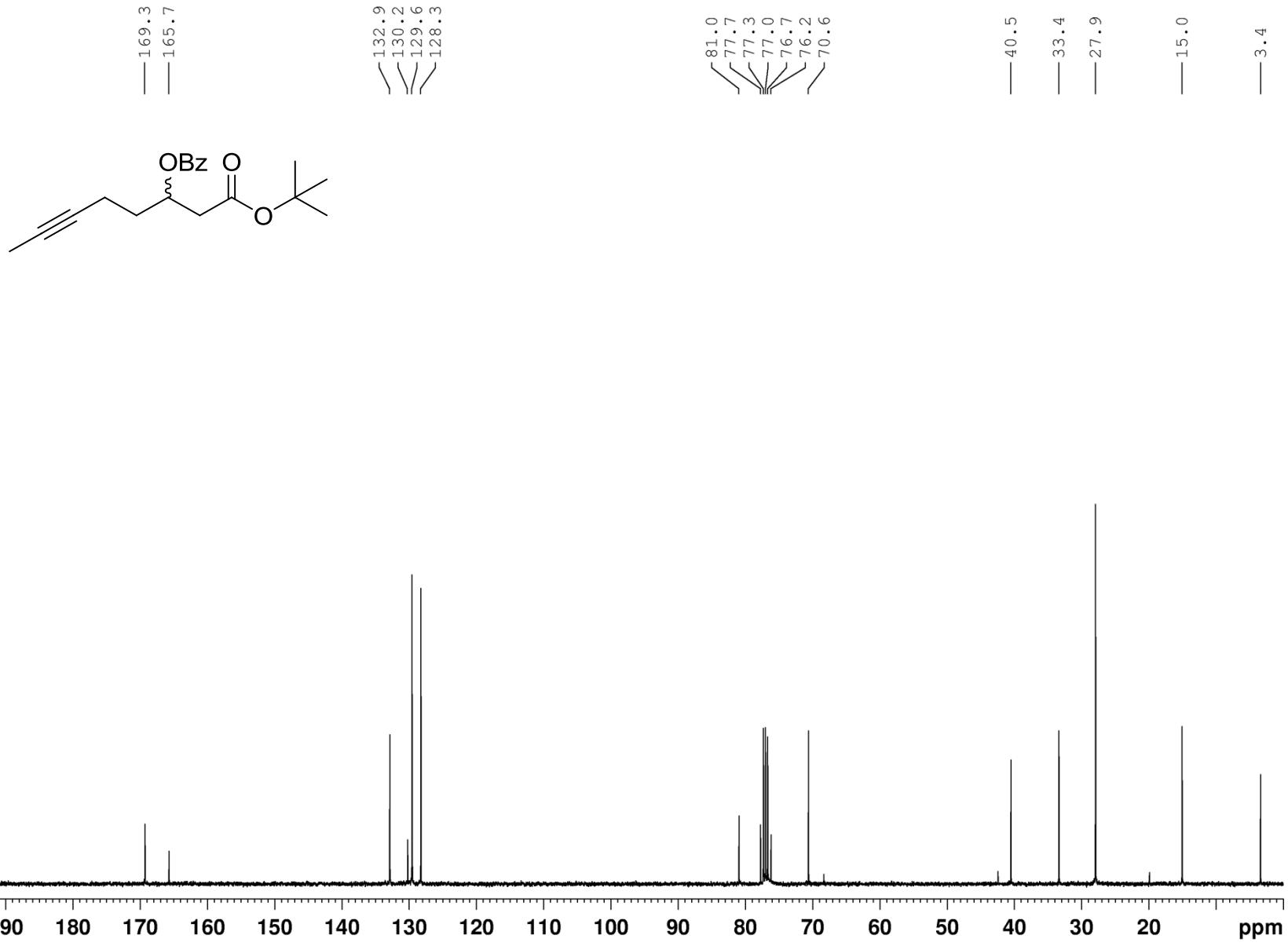
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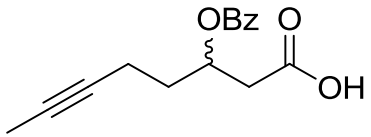
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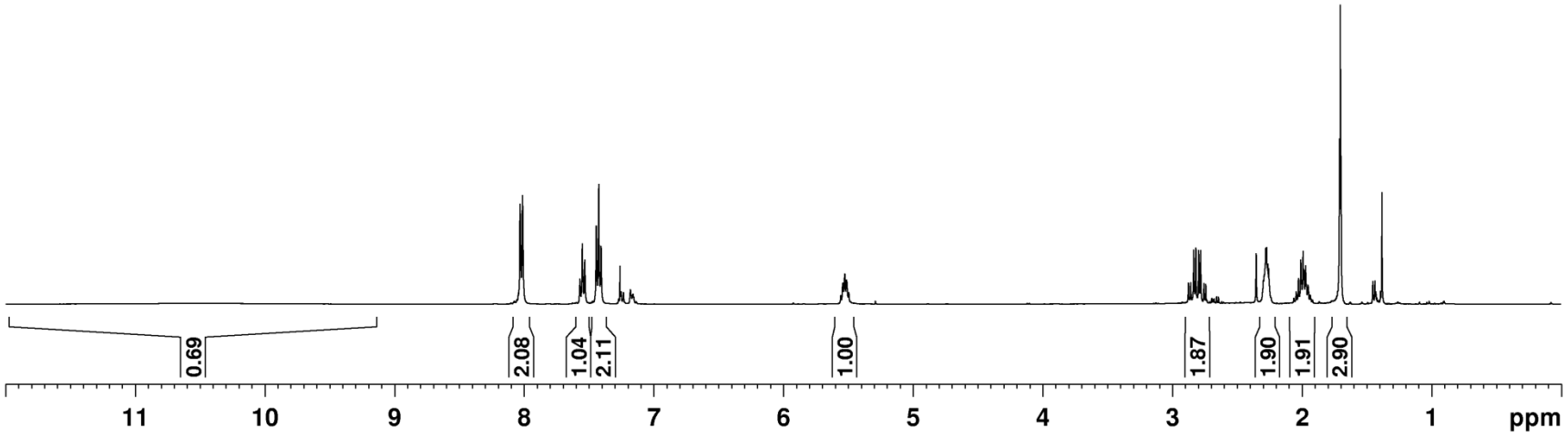
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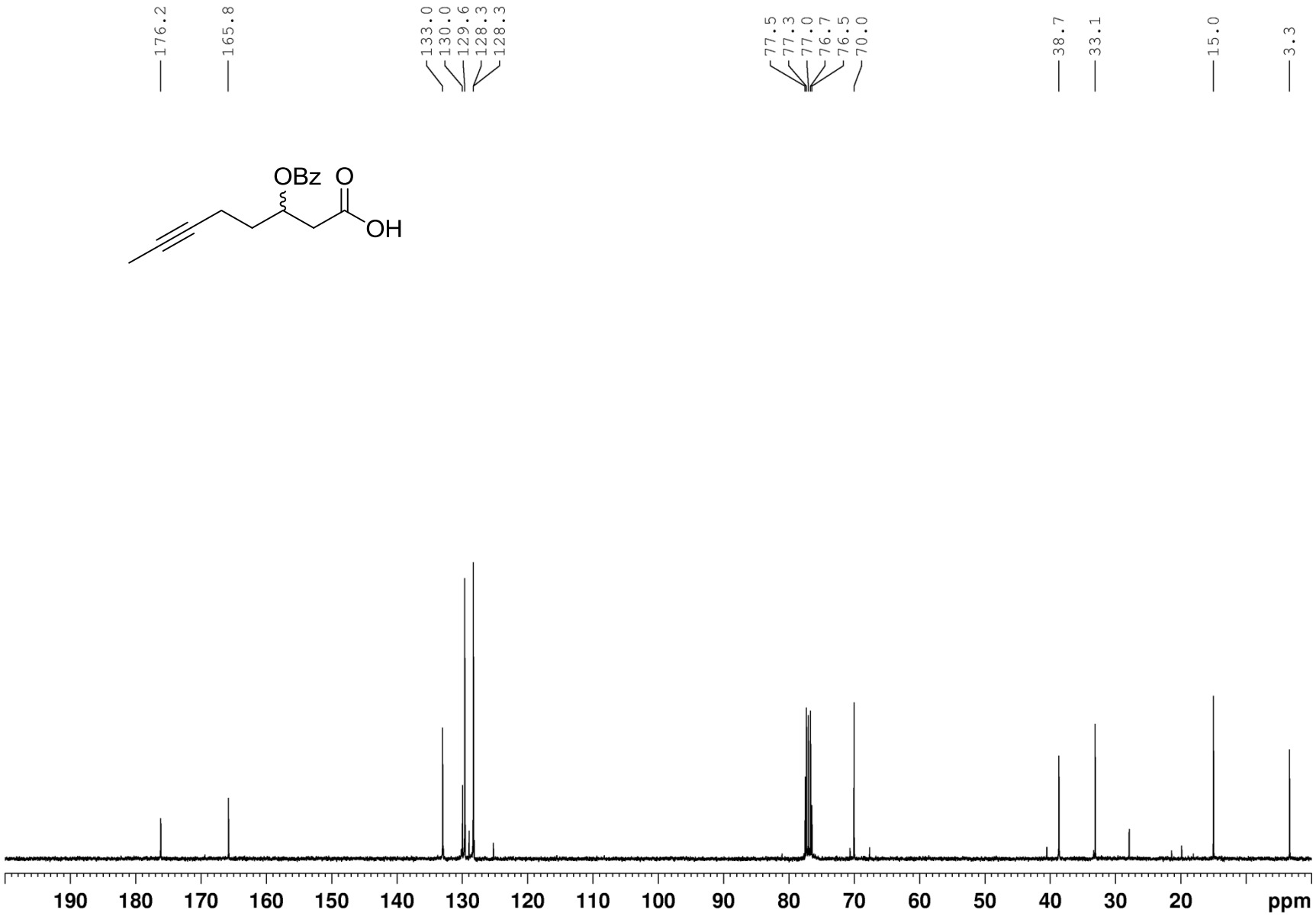
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180
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160
150
140
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120
110
100
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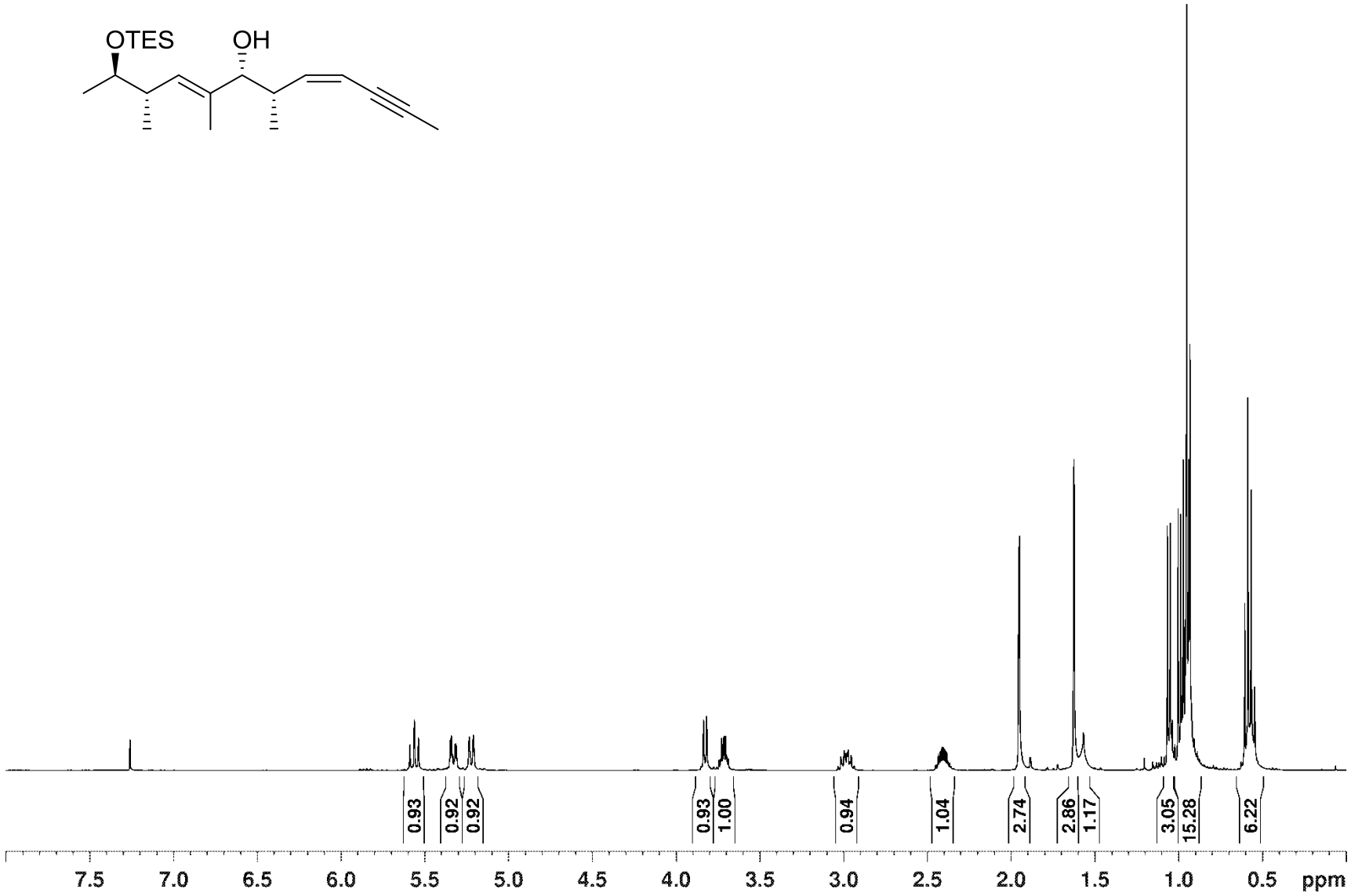
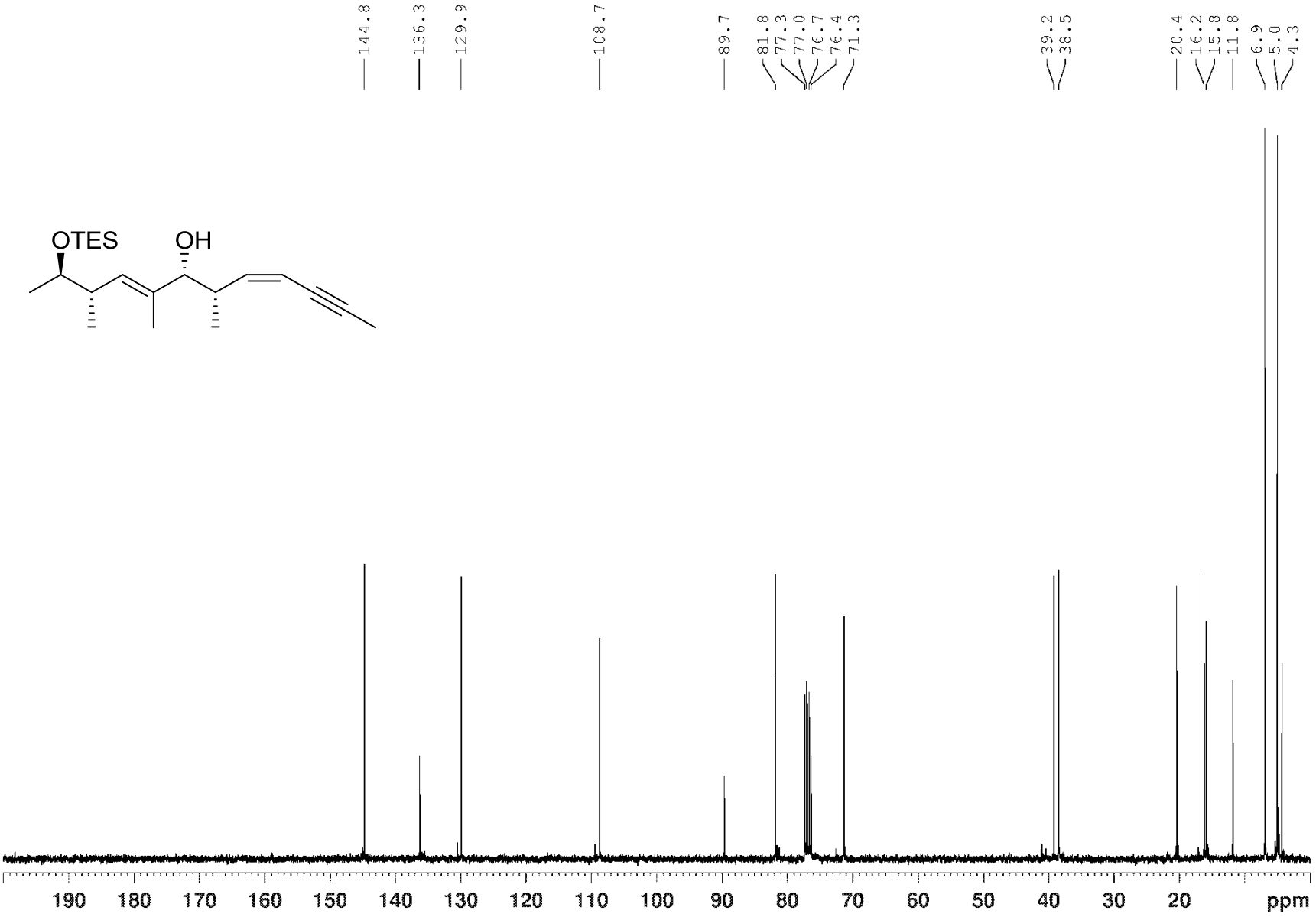
80
70
60
50
40
30
20
ppm


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


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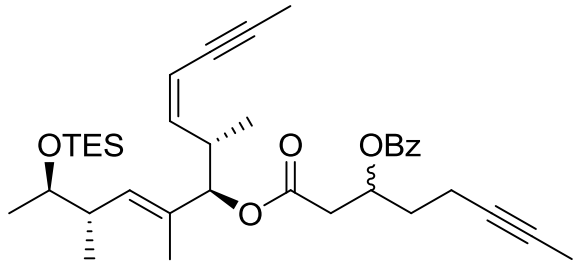
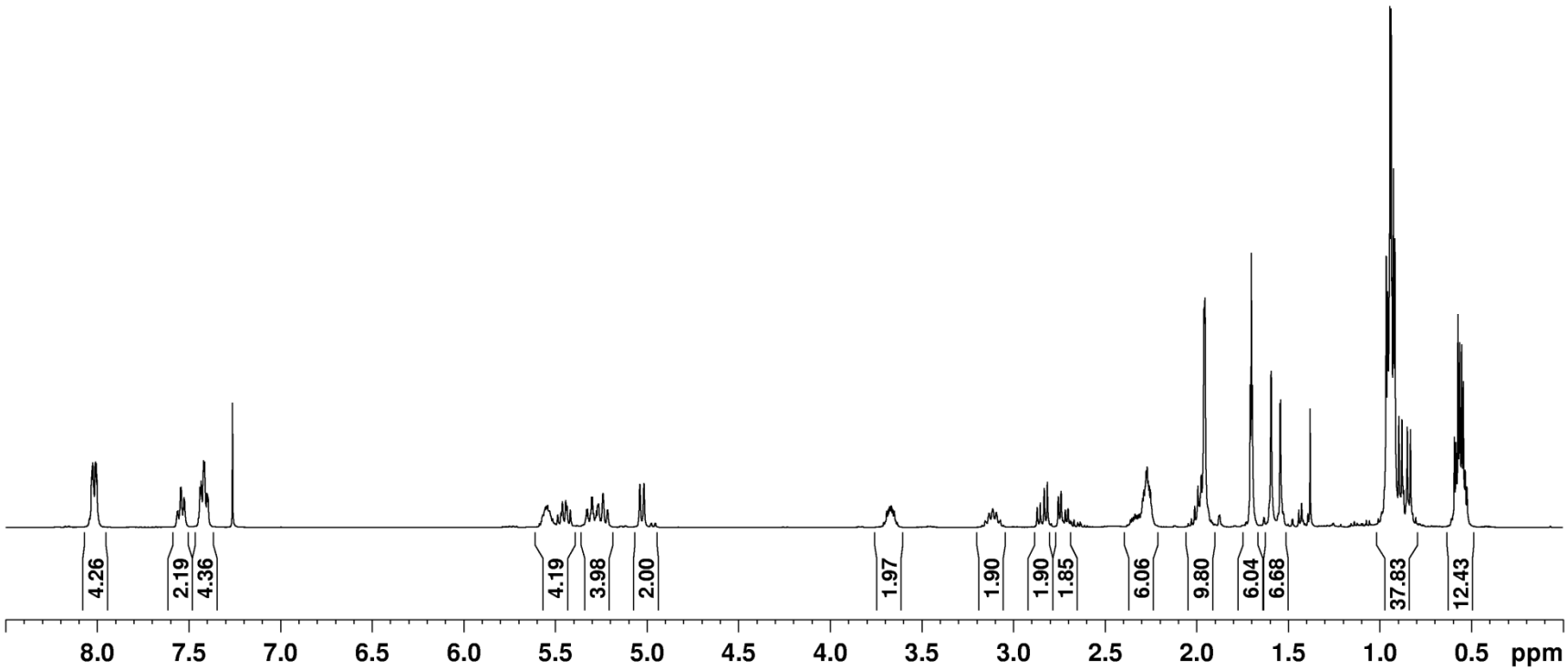
50
40
30
20
ppm


OTES
O
OBz
O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2.19
4.36
4.19
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2.00
1.97
1.90
1.90
1.85
6.06
9.80
6.04
6.68
37.83
12.43
8.0
7.5
7.0
6.5
6.0
5.5
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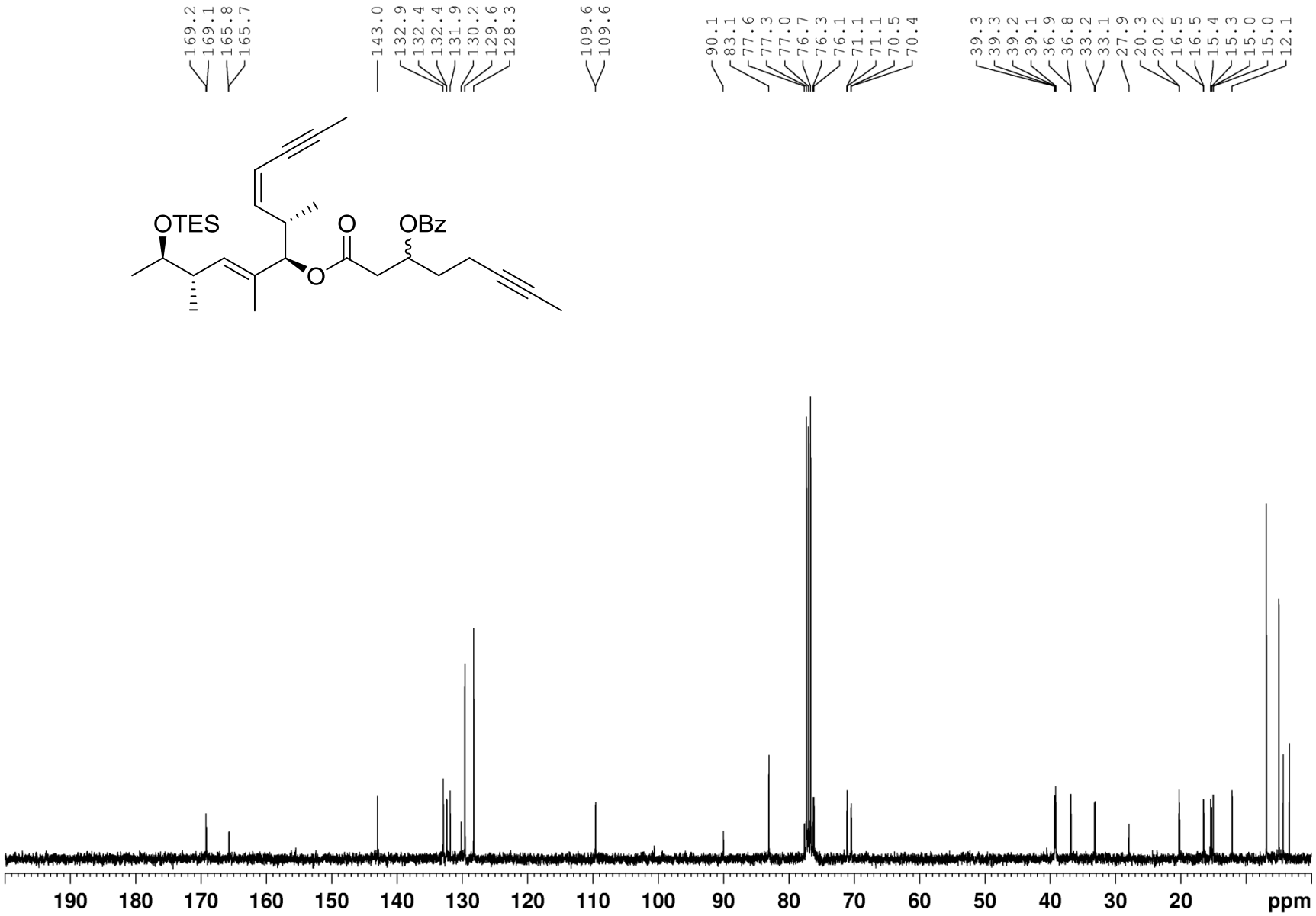
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm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165.8
165.7
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132.9
132.4
132.4
131.9
130.2
129.6
128.3
109.6
109.6
90.1
83.1
77.6
77.3
77.0
76.7
76.3
76.1
71.1
71.1
70.5
70.4
39.3
39.3
39.2
39.1
36.9
36.8
33.2
33.1
27.9
20.3
20.2
16.5
16.5
15.4
15.3
15.0
15.0
12.1
OTES
O
OBz
O
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170
160
150
140
130
120
110
100
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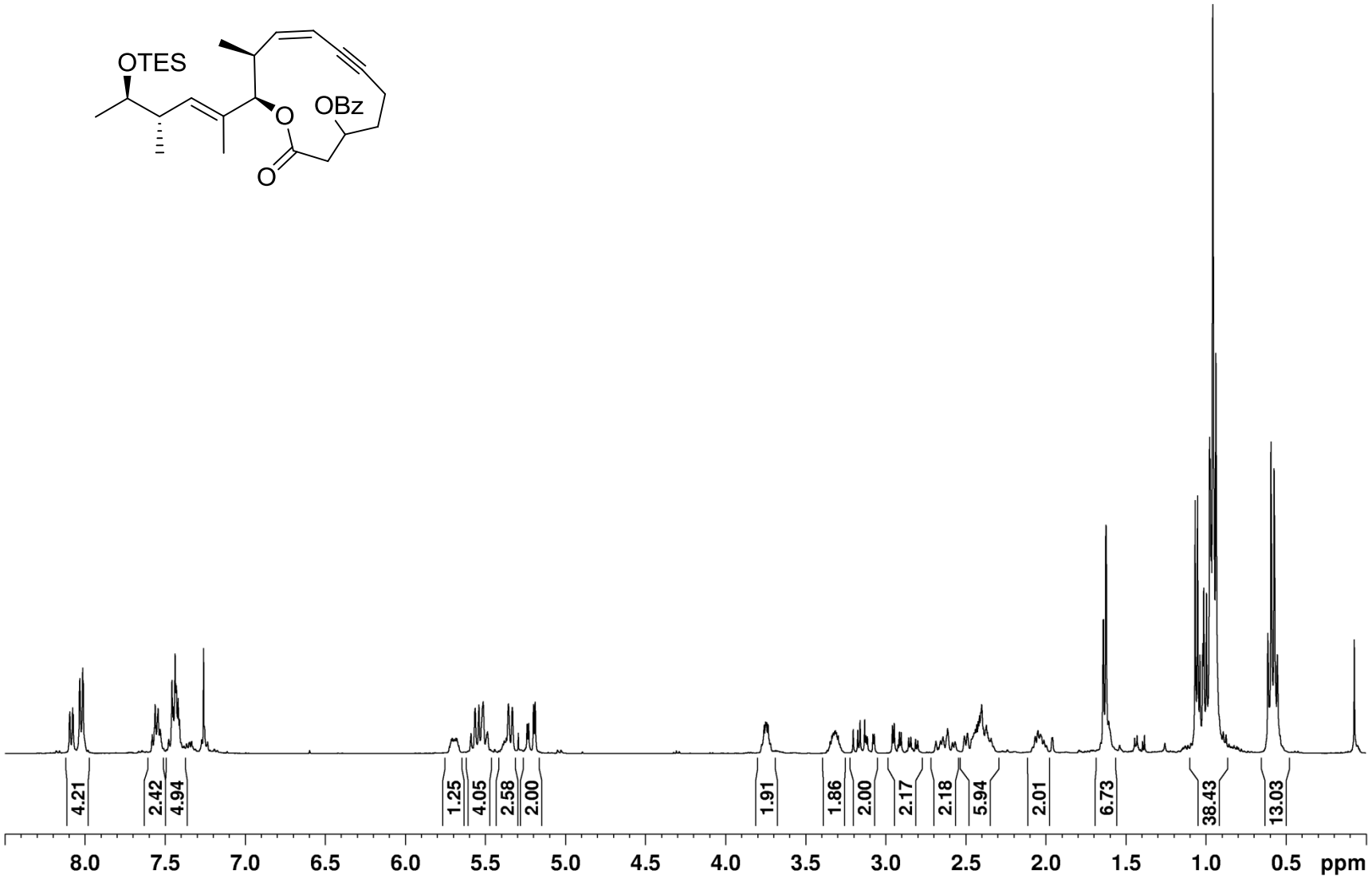
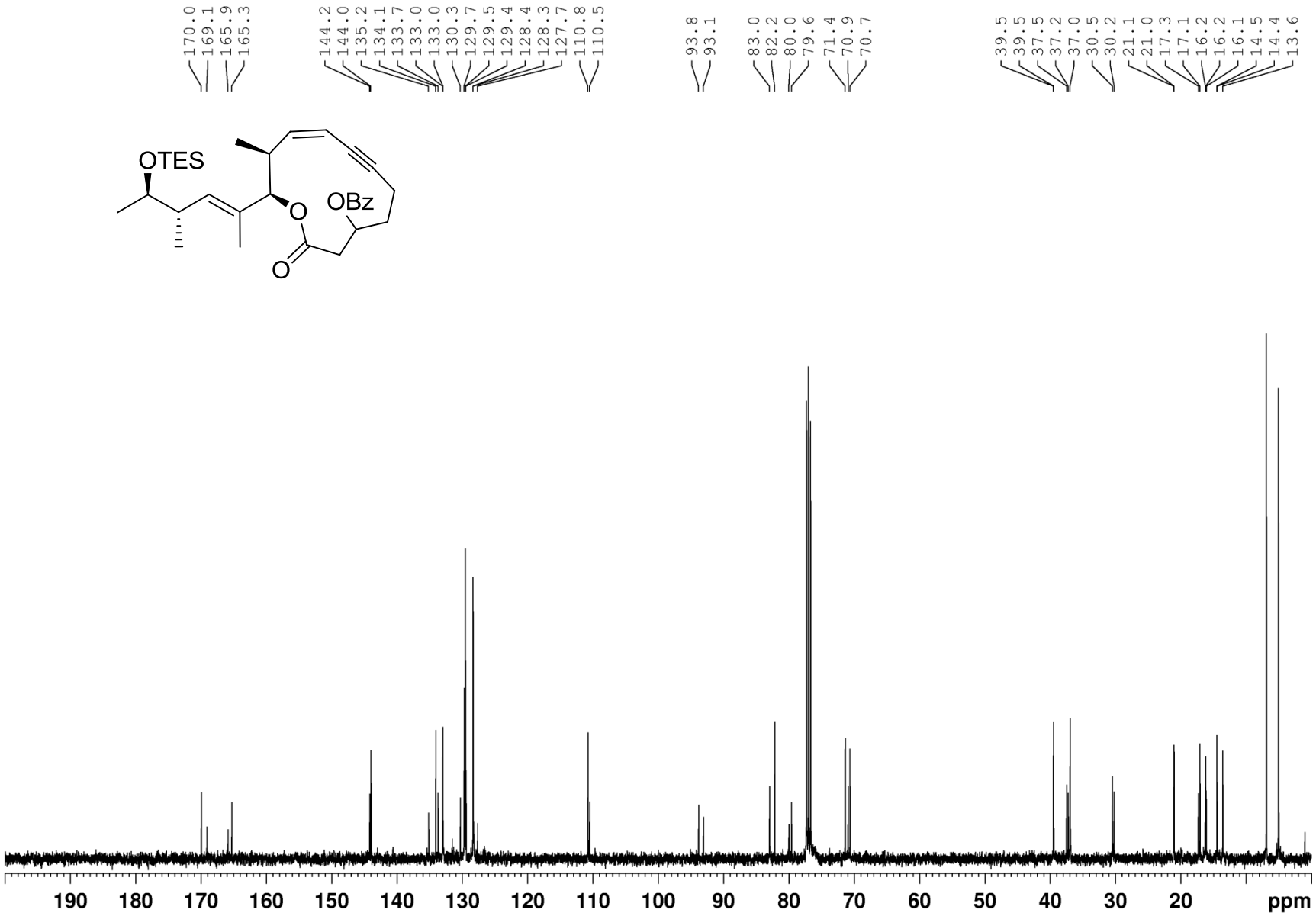
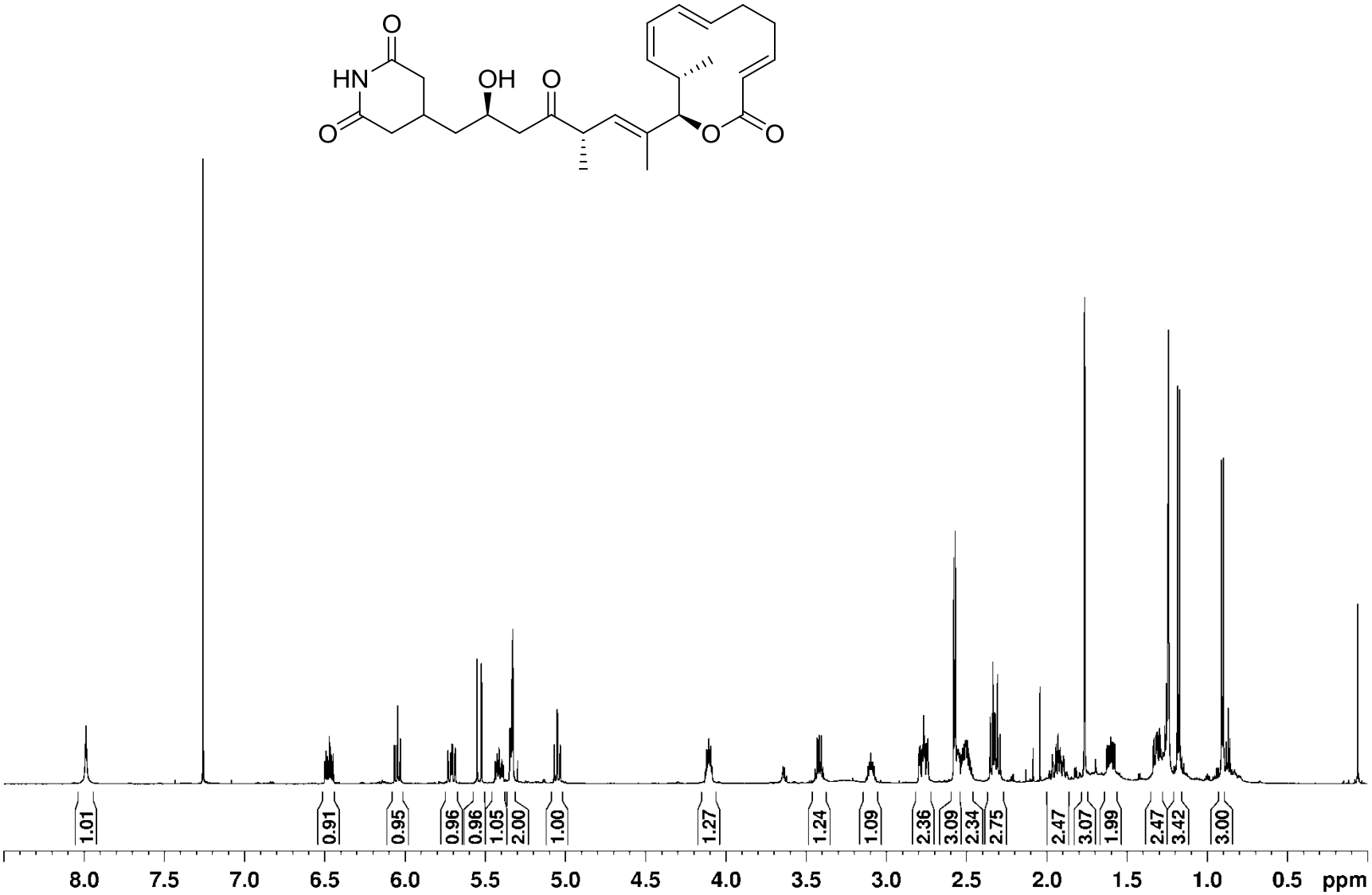
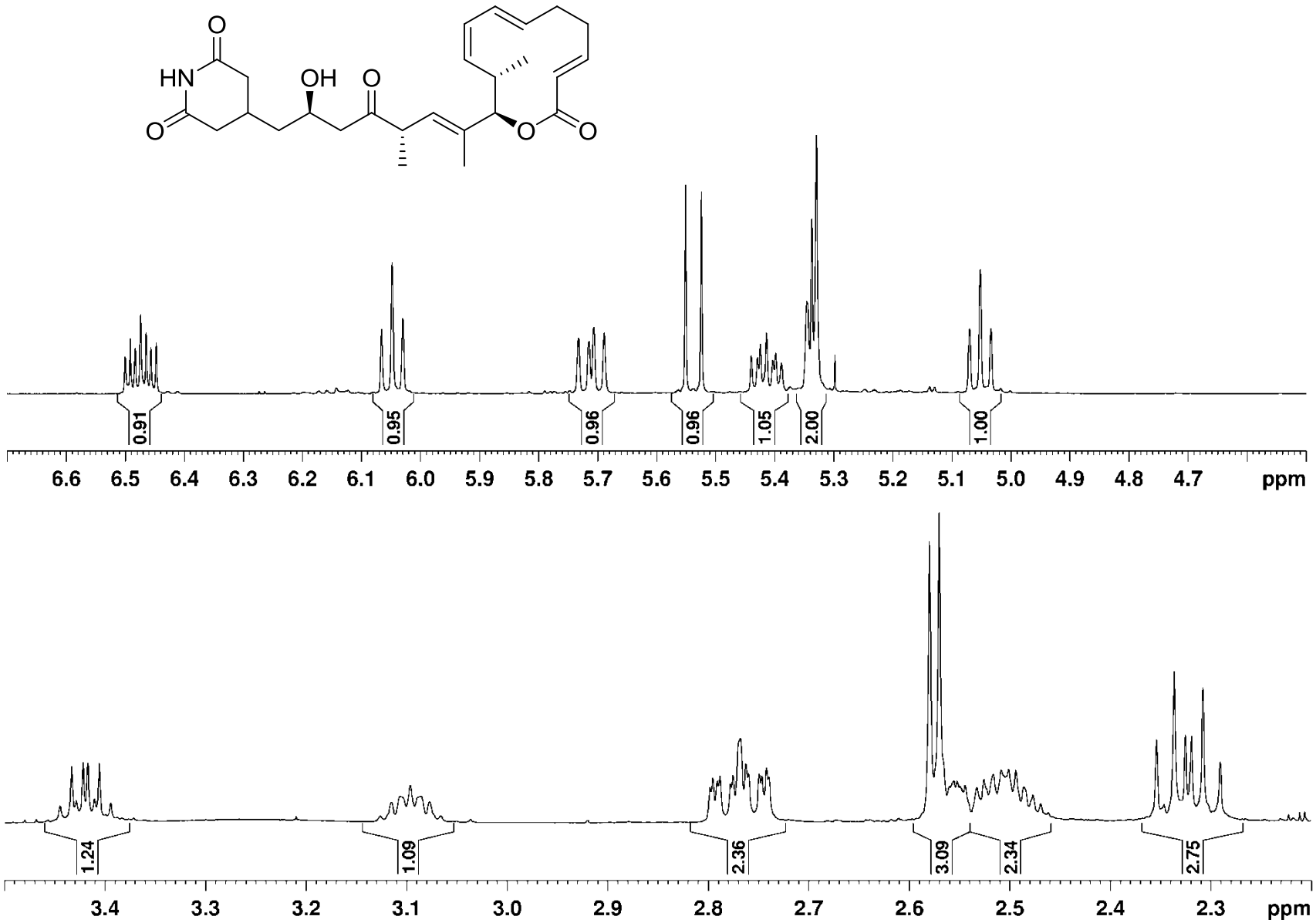
80
70
60
50
40
30
20
ppm

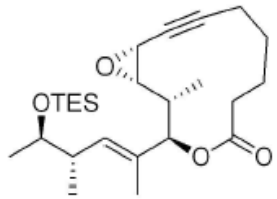

OTES
O
OBz
O
4.21
2.42
4.94
1.25
4.05
2.58
2.00
1.91
1.86
2.00
2.17
2.18
5.94
2.01
6.73
38.43
13.03
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


170.0
169.1
165.9
165.3
144.2
144.0
135.2
134.1
133.7
133.0
133.0
130.3
129.7
129.5
129.4
128.4
128.3
127.7
110.8
110.5
93.8
93.1
83.0
82.2
80.0
79.6
71.4
70.9
70.7
39.5
39.5
37.5
37.2
37.0
30.5
30.2
21.1
21.0
17.3
17.1
16.2
16.2
16.1
14.5
14.4
13.6
OTES
O
OBz
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

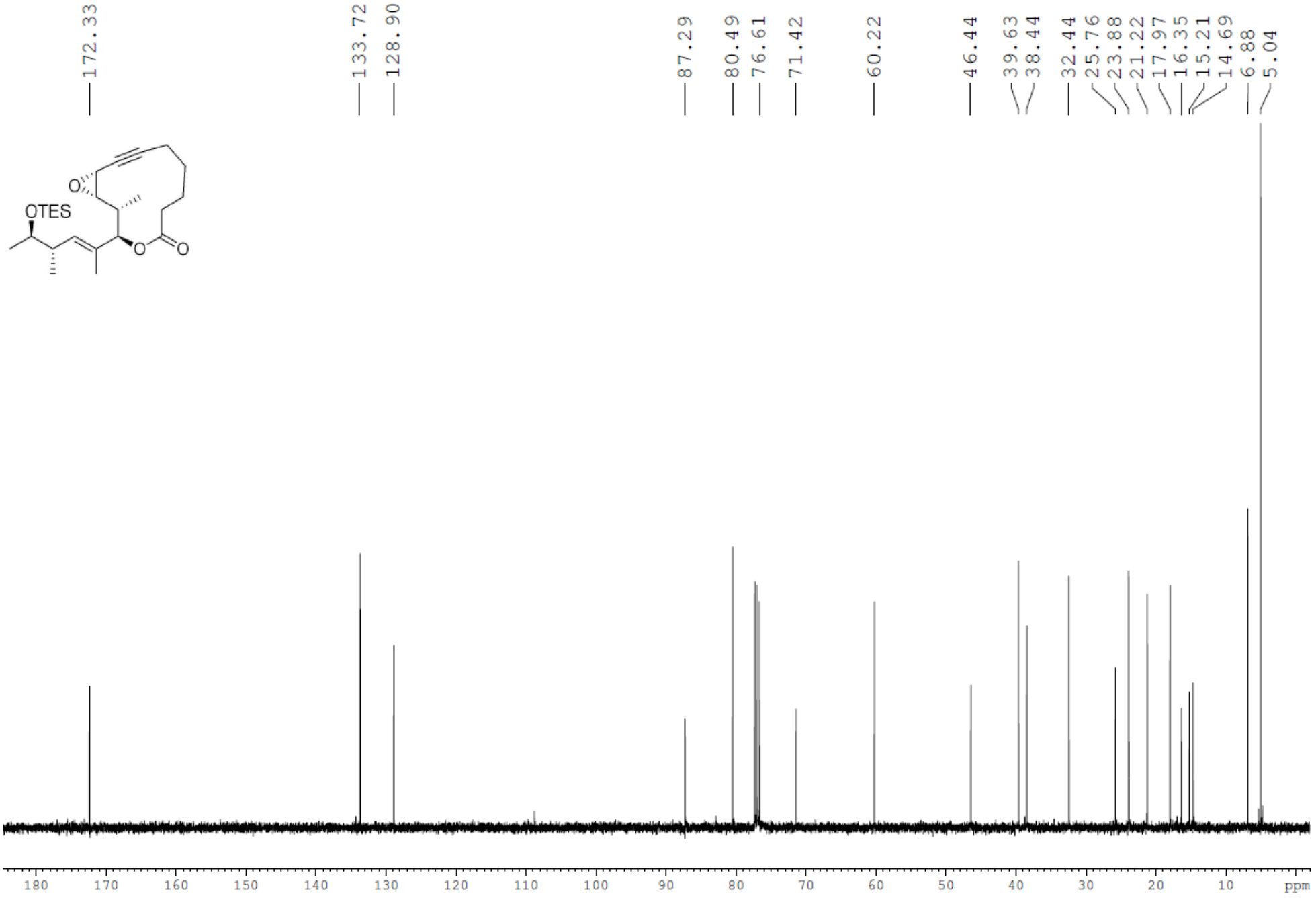

HN
O
O
OH
O
O
O
1.01
0.91
0.95
0.96
0.96
1.05
2.00
1.00
1.27
1.24
1.09
2.36
3.09
2.34
2.75
2.47
3.07
1.99
2.47
3.42
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

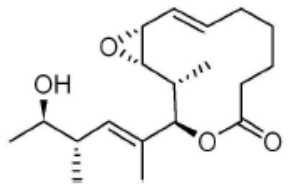

O
HN
OH
O
O
O
O
0.91
0.95
0.96
0.96
1.05
2.00
1.00
6.6 6.5 6.4 6.3 6.2 6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 ppm
1.24
1.09
2.36
3.09
2.34
2.75
3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 ppm

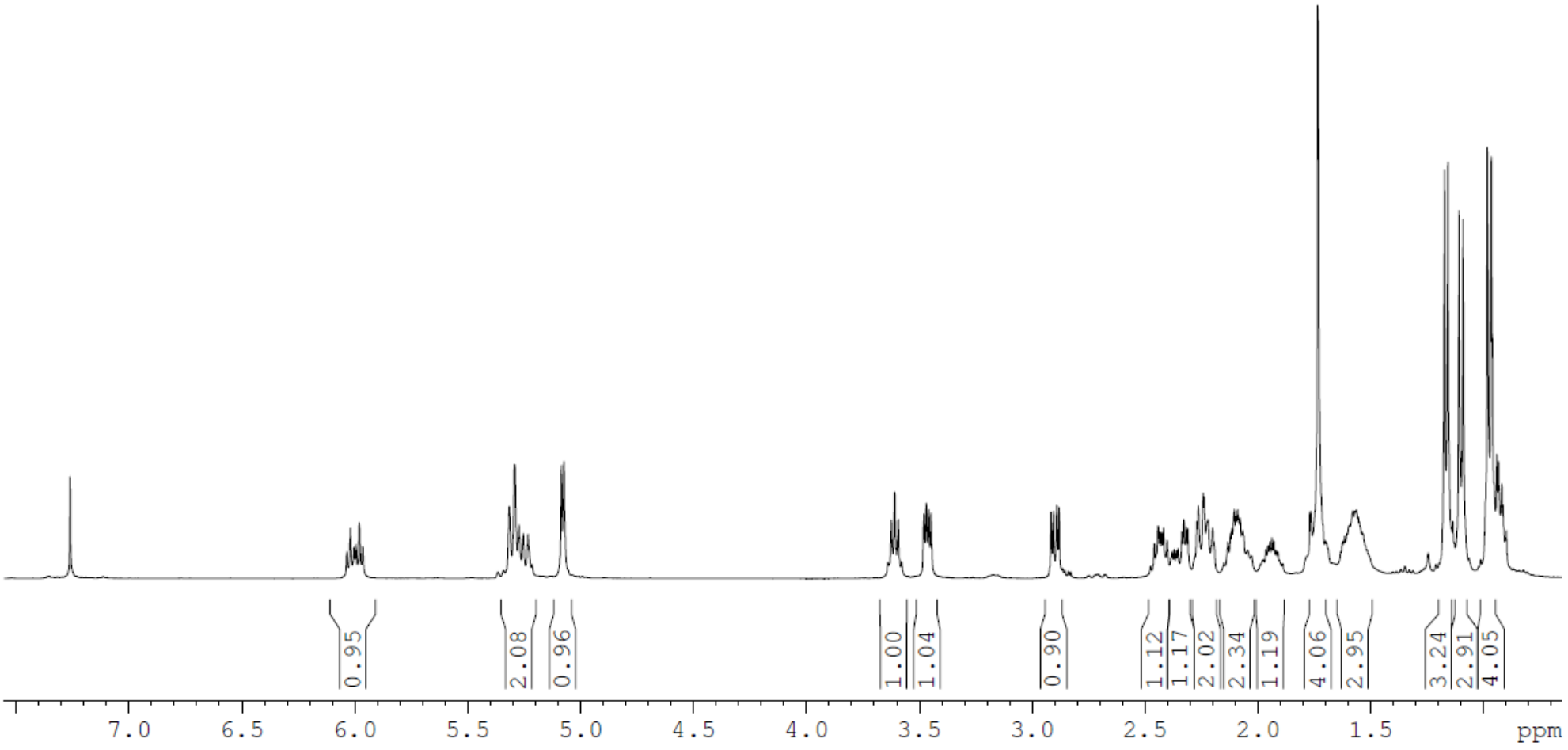

212.5
172.2
172.1
166.7
147.0
134.5
134.0
131.2
129.5
129.0
128.3
128.2
82.4
64.8
47.5
46.7
40.8
38.5
37.2
36.0
32.4
31.3
29.8
27.1
17.6
16.2
15.4
HN
O
OH
O
O
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

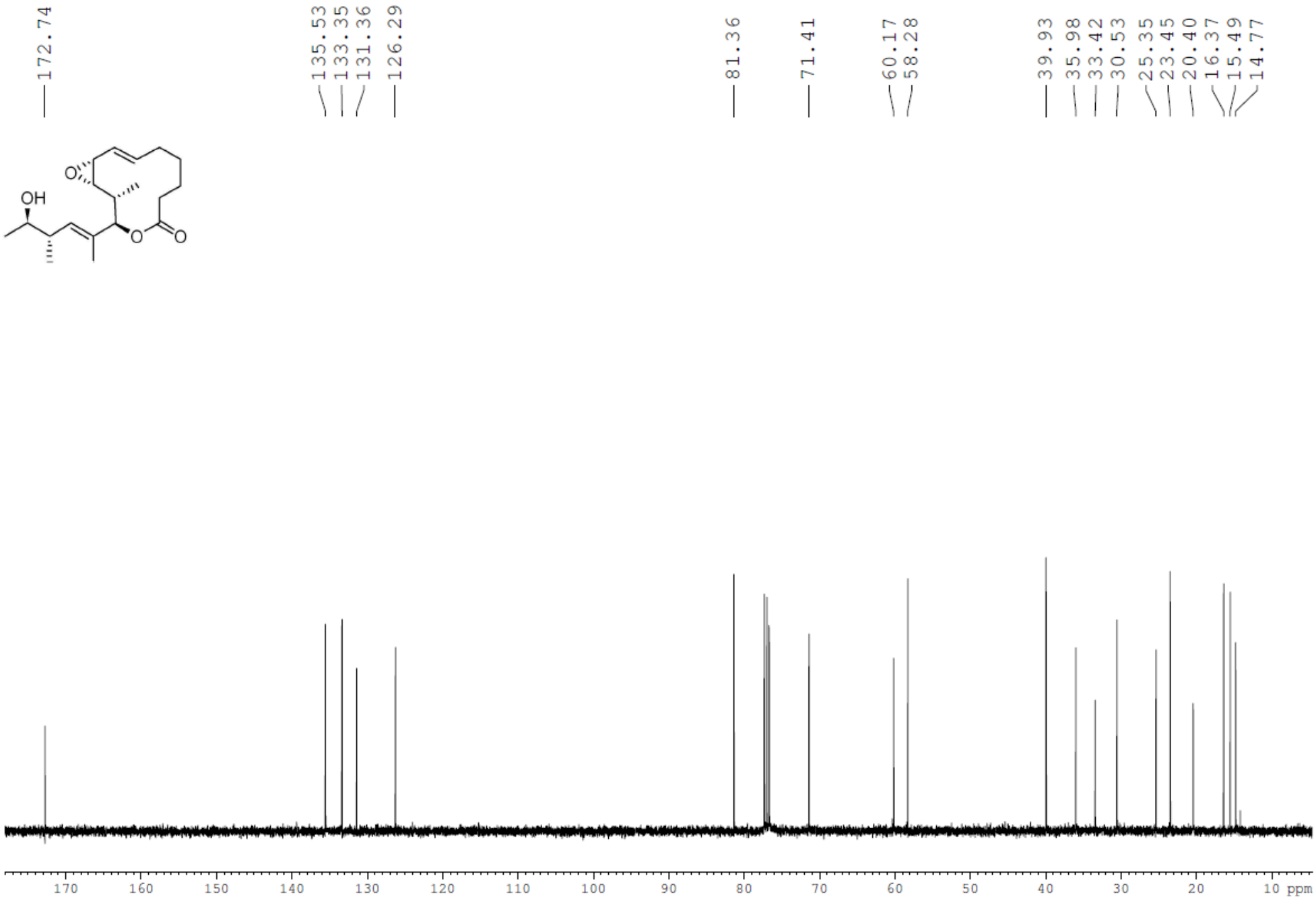

OTES
O
O
O

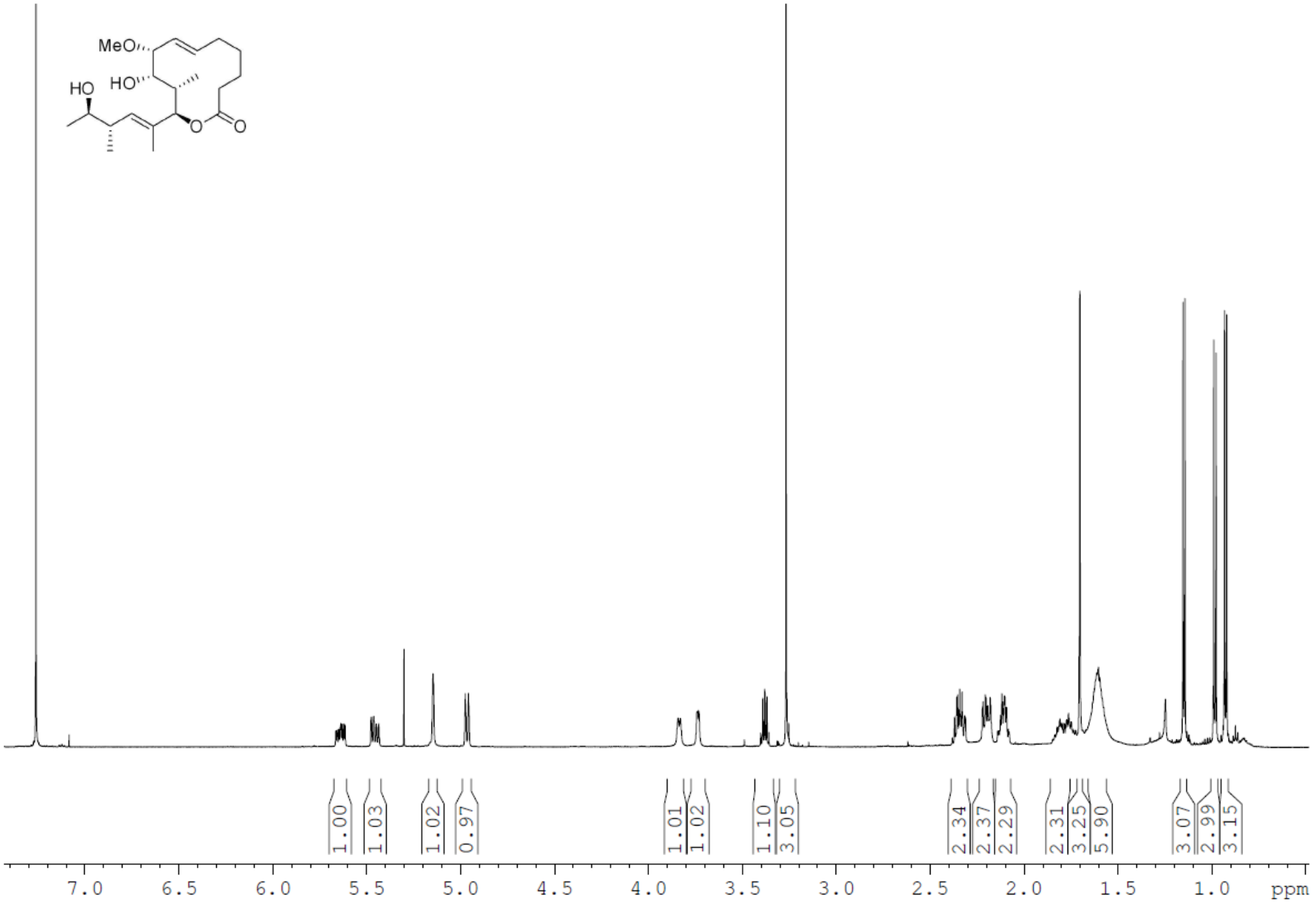
0.96
0.97
1.00
0.96
0.97
1.04
3.14
3.03
3.46
2.53
3.00
3.16
12.82
6.40
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm


172.33
133.72
128.90
87.29
80.49
76.61
71.42
60.22
46.44
39.63
38.44
32.44
25.76
23.88
21.22
17.97
16.35
15.21
14.69
6.88
5.04
OTES
O
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


OH
O
O
O


0.95
2.08
0.96
1.00
1.04
0.90
1.12
1.17
2.02
2.34
1.19
4.06
2.95
3.24
2.91
4.05
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm


172.74
135.53
133.35
131.36
126.29
81.36
71.41
60.17
58.28
39.93
35.98
33.42
30.53
25.35
23.45
20.40
16.37
15.49
14.77
OH
O
O
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm


MeO
HO
HO
O
O
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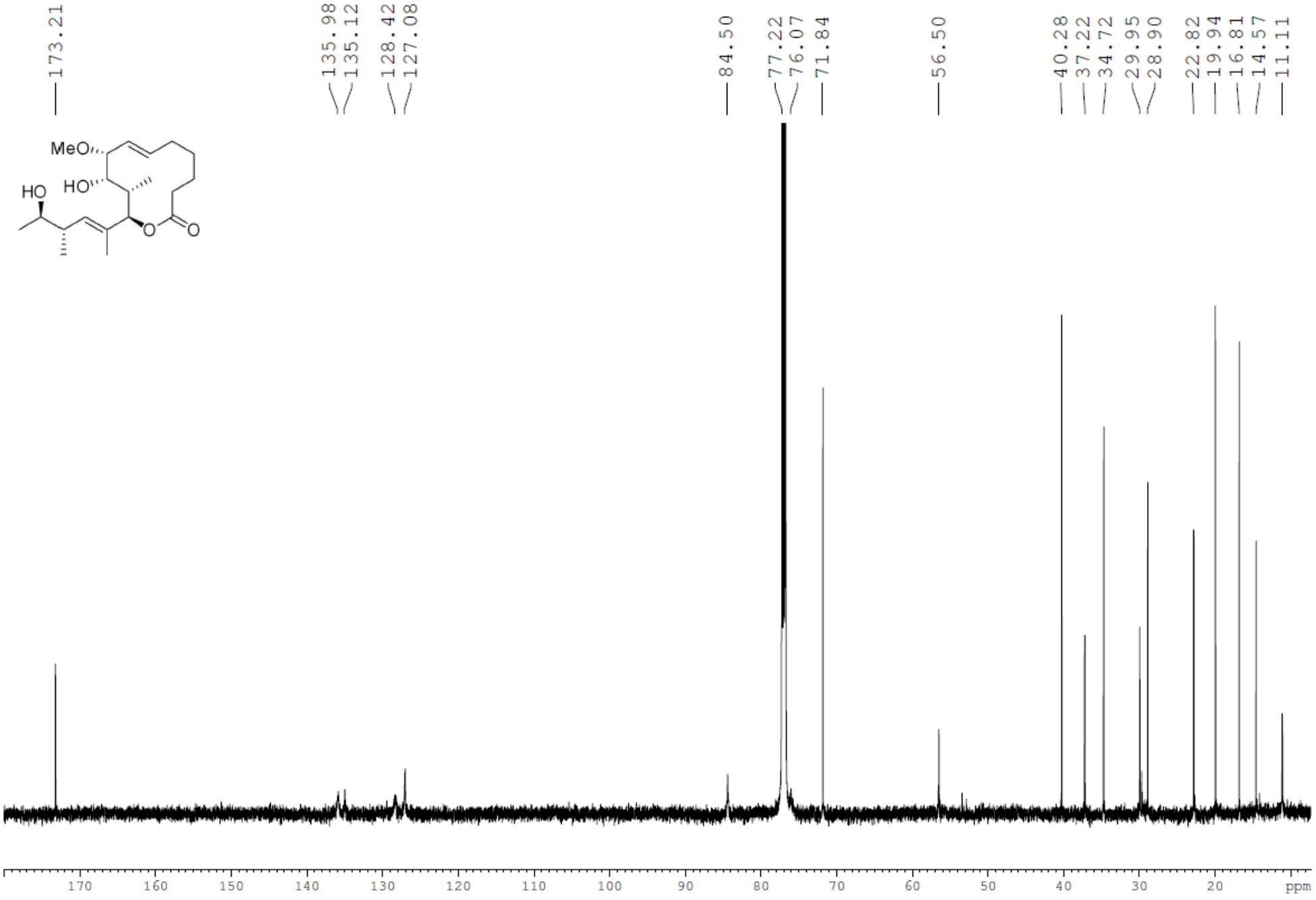
1.03
1.02
0.97
1.01
1.02
1.10
3.05
2.34
2.37
2.29
2.31
3.25
5.90
3.07
2.99
3.15
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm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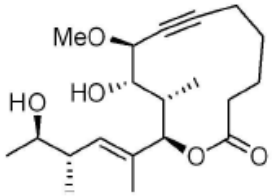
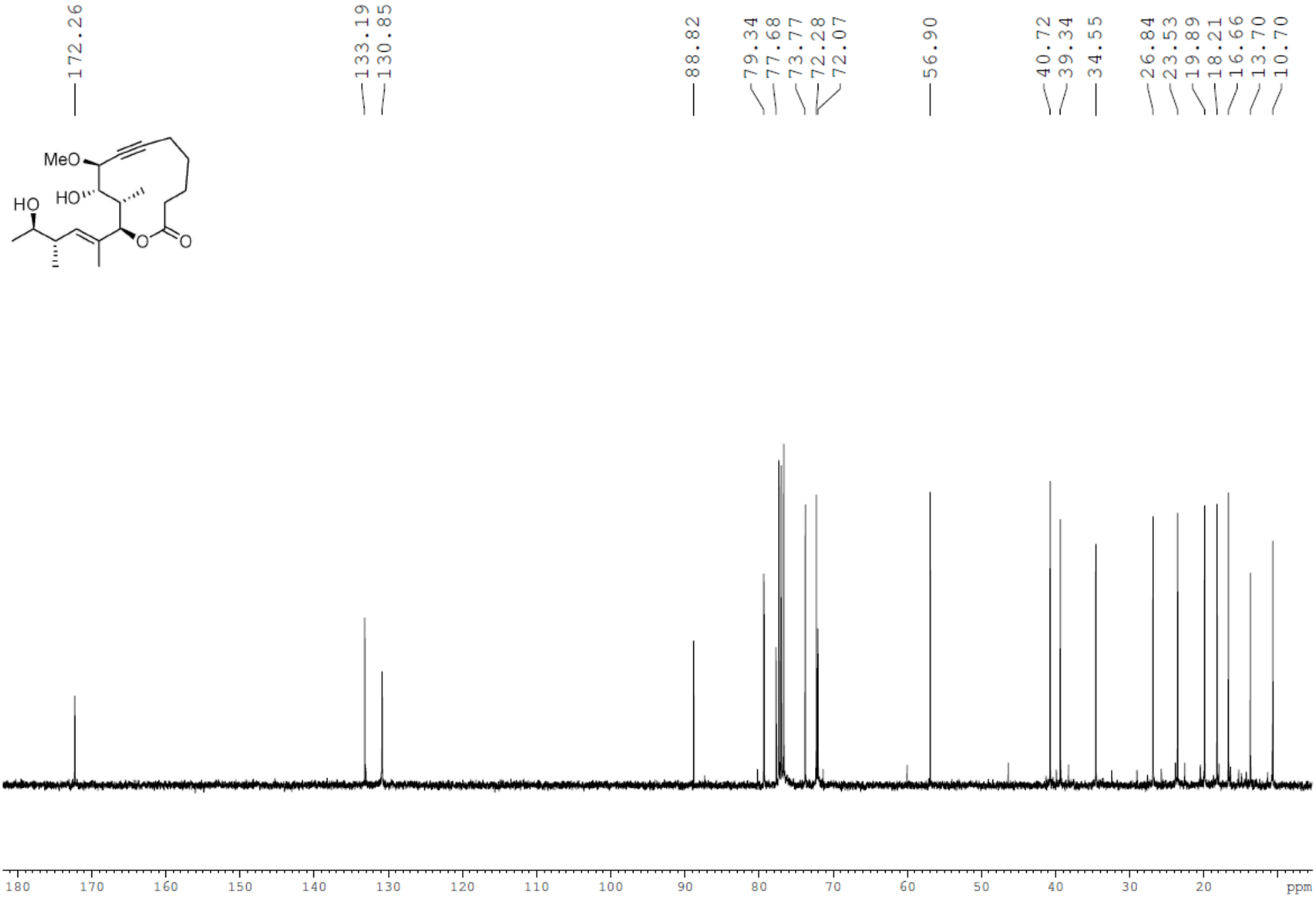
135.12
128.42
127.08
84.50
77.22
76.07
71.84
56.50
40.28
37.22
34.72
29.95
28.90
22.82
19.94
16.81
14.57
11.11
MeO
HO
HO
O
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


MeO
HO
HO
O
O

1.00
0.92
0.92
1.06
3.88
1.15
1.06
2.12
2.07
2.04
2.90
2.47
1.04
3.55
6.10
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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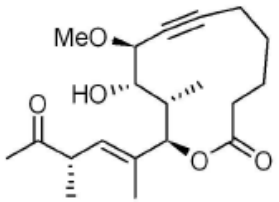
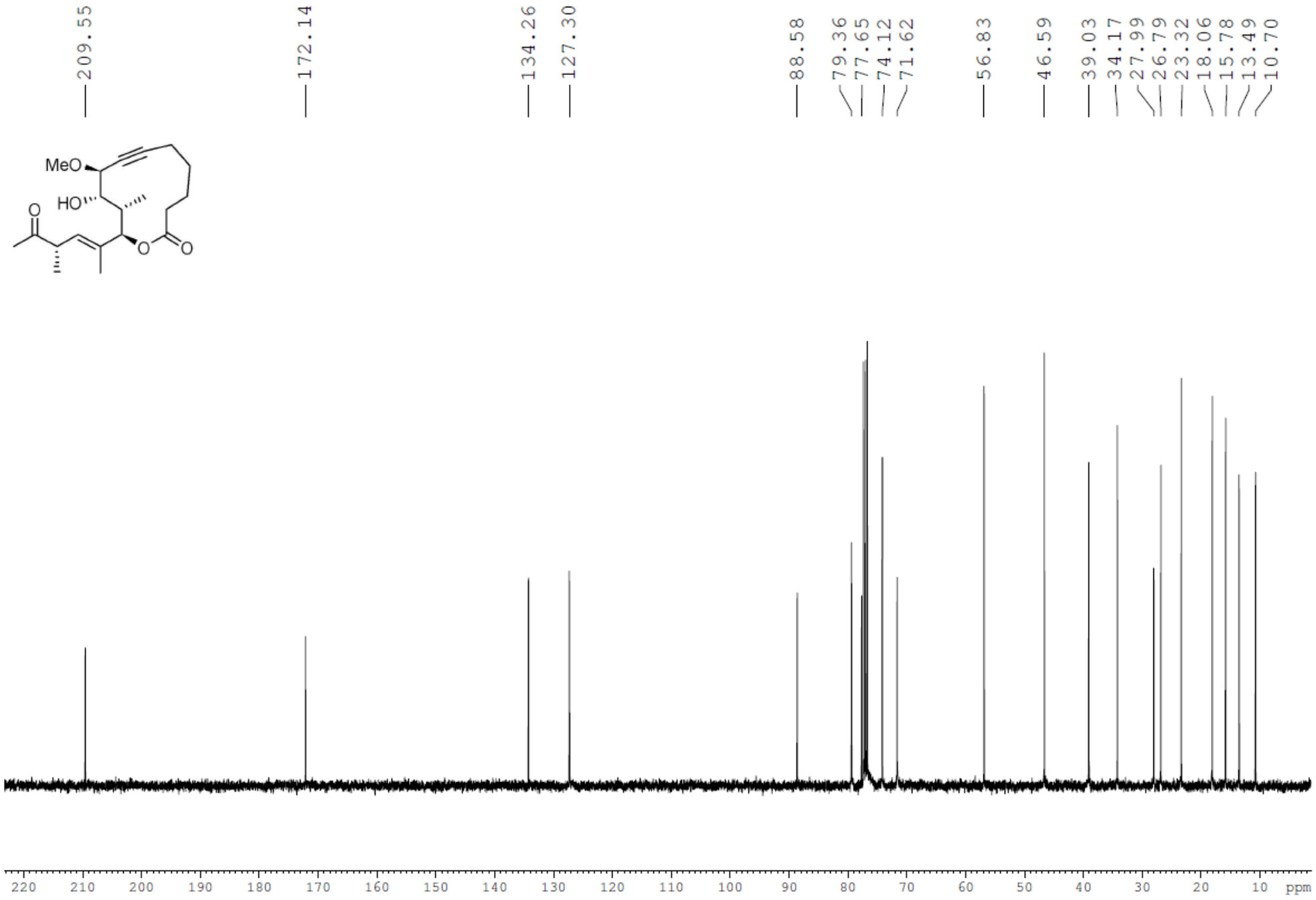
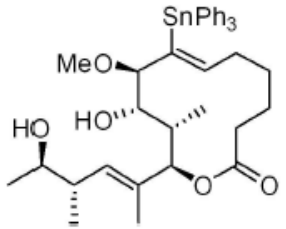
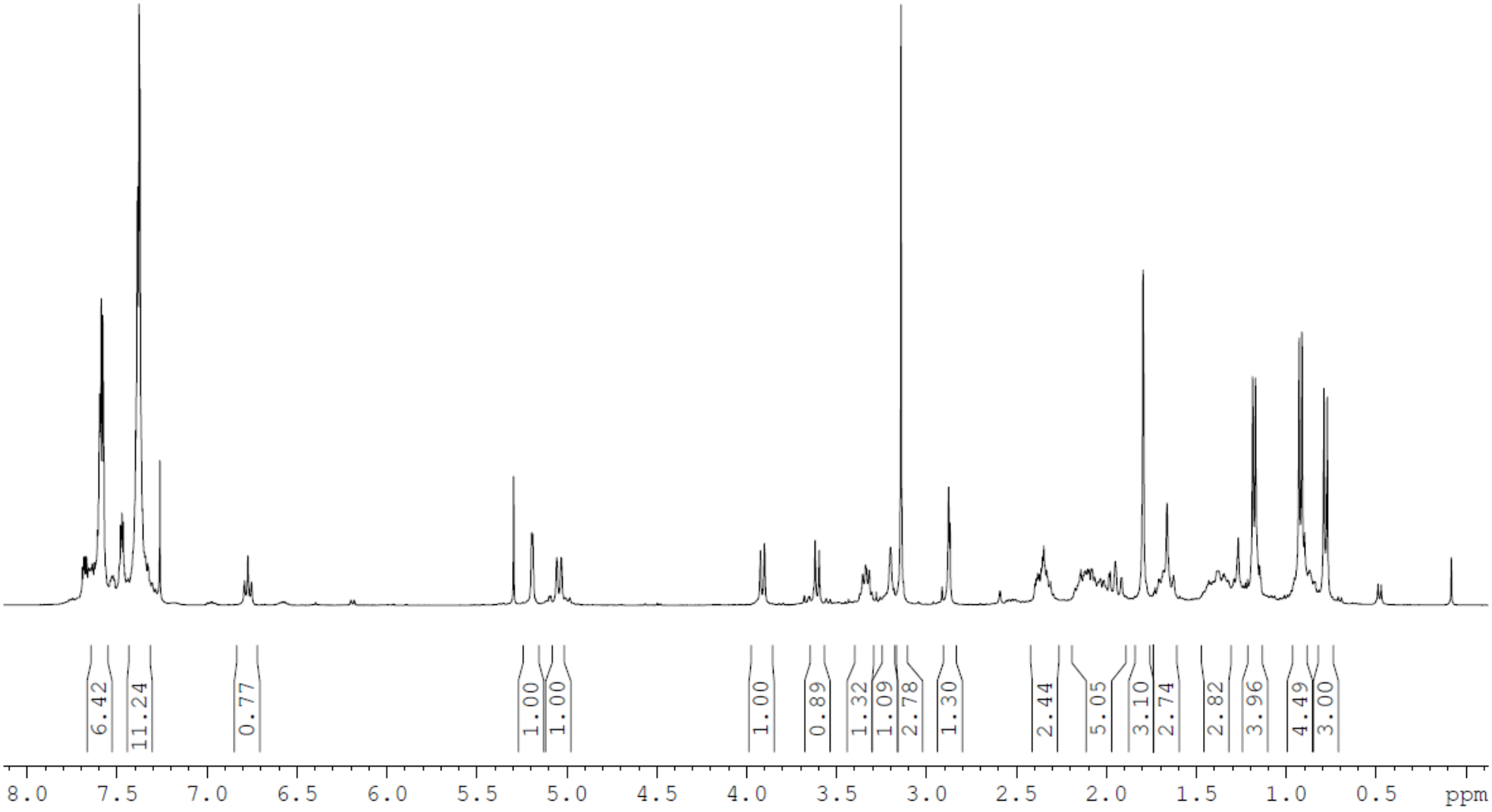
88.82
79.34
77.68
73.77
72.28
72.07
56.90
40.72
39.34
34.55
26.84
23.53
19.89
18.21
16.66
13.70
10.70
MeO
HO
HO
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

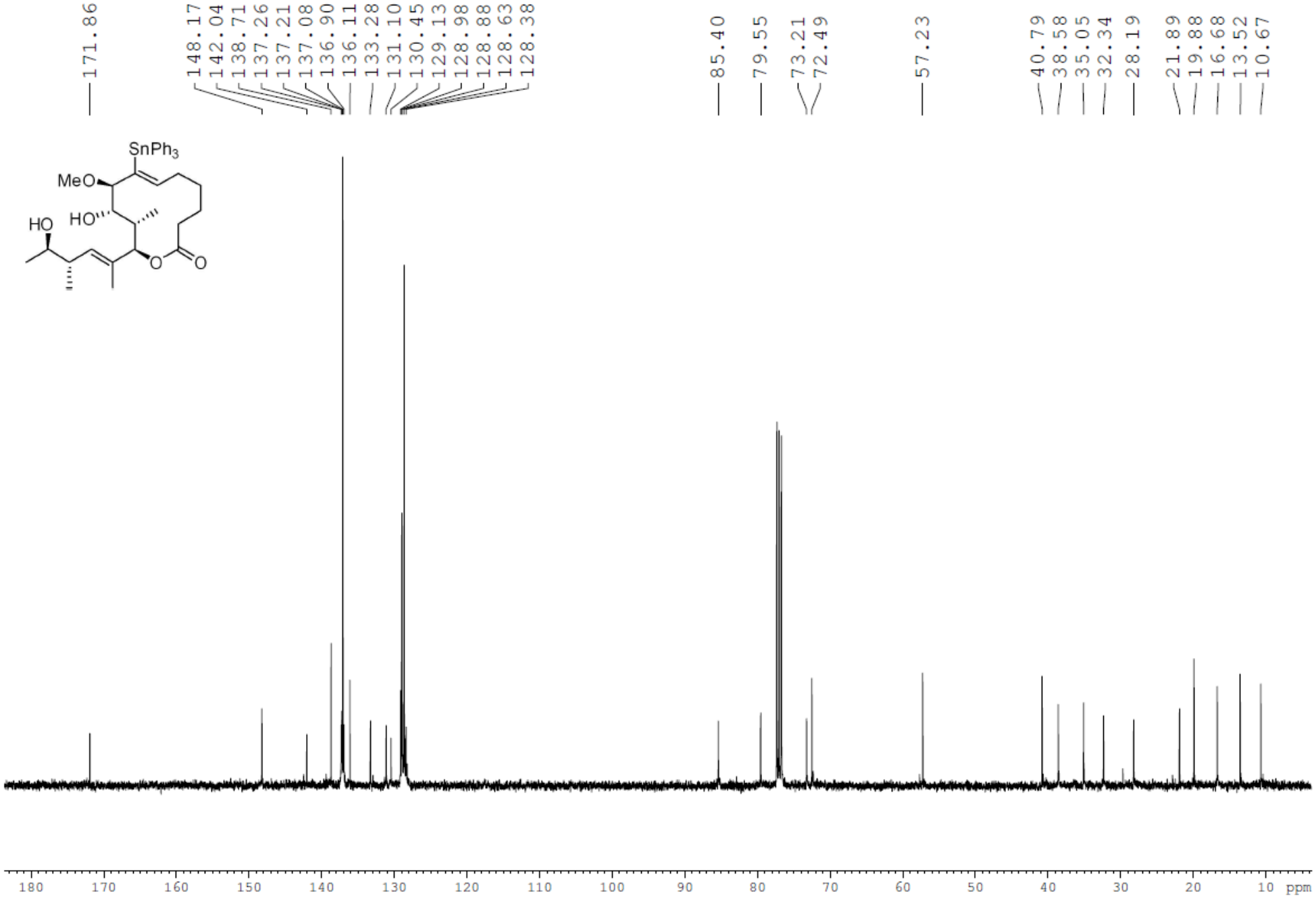

MeO
HO
O
O
O

1.96
0.96
1.00
3.98
0.90
1.00
1.05
2.01
3.98
1.13
4.05
1.36
1.08
3.25
3.08
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


209.55
172.14
134.26
127.30
88.58
79.36
77.65
74.12
71.62
56.83
46.59
39.03
34.17
27.99
26.79
23.32
18.06
15.78
13.49
10.70
MeO
HO
O
O
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


SnPh3
MeO
HO
HO
O
O


6.42
11.24
0.77
1.00
1.00
1.00
0.89
1.32
1.09
2.78
1.30
2.44
5.05
3.10
2.74
2.82
3.96
4.49
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm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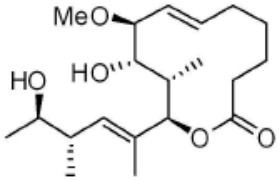
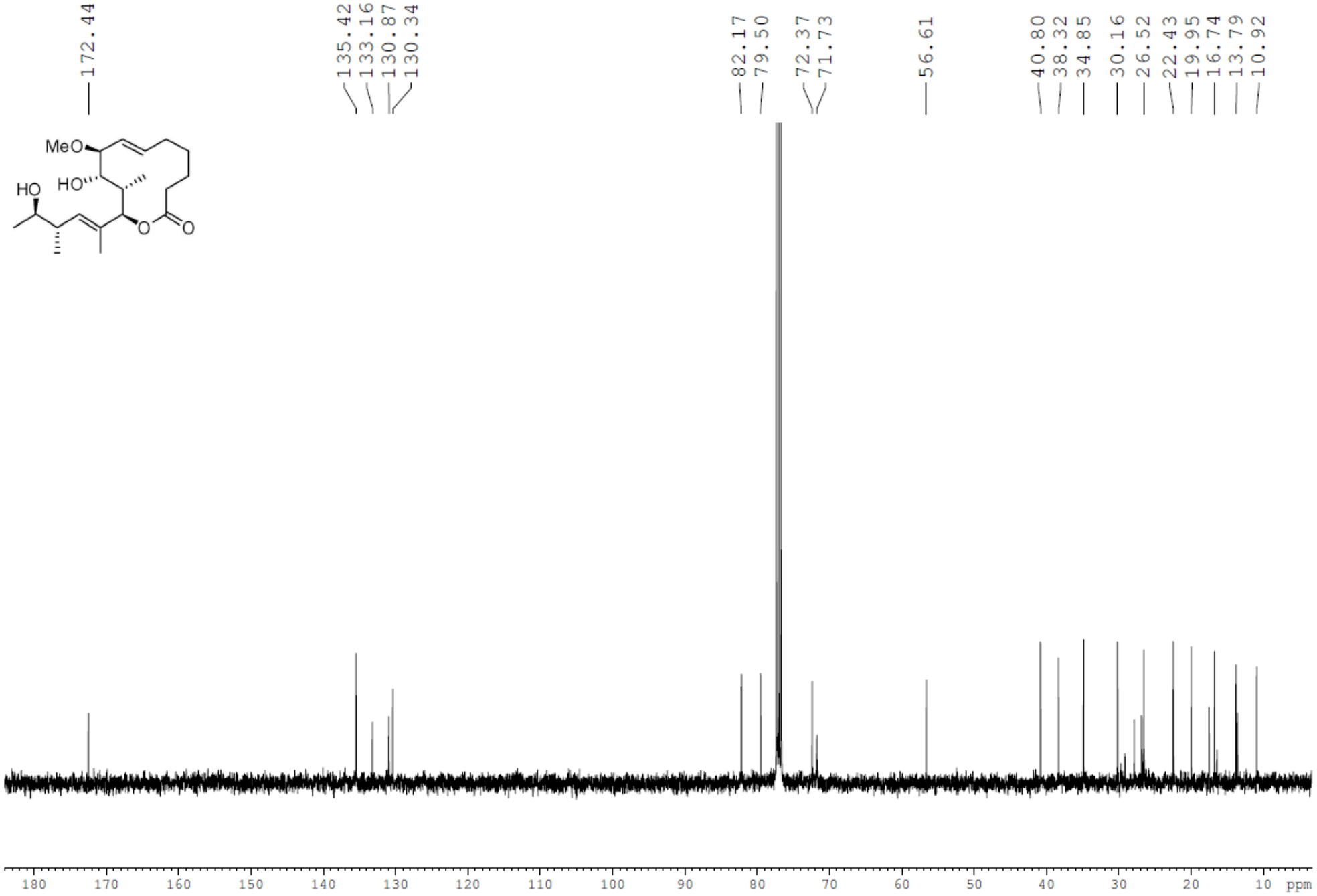
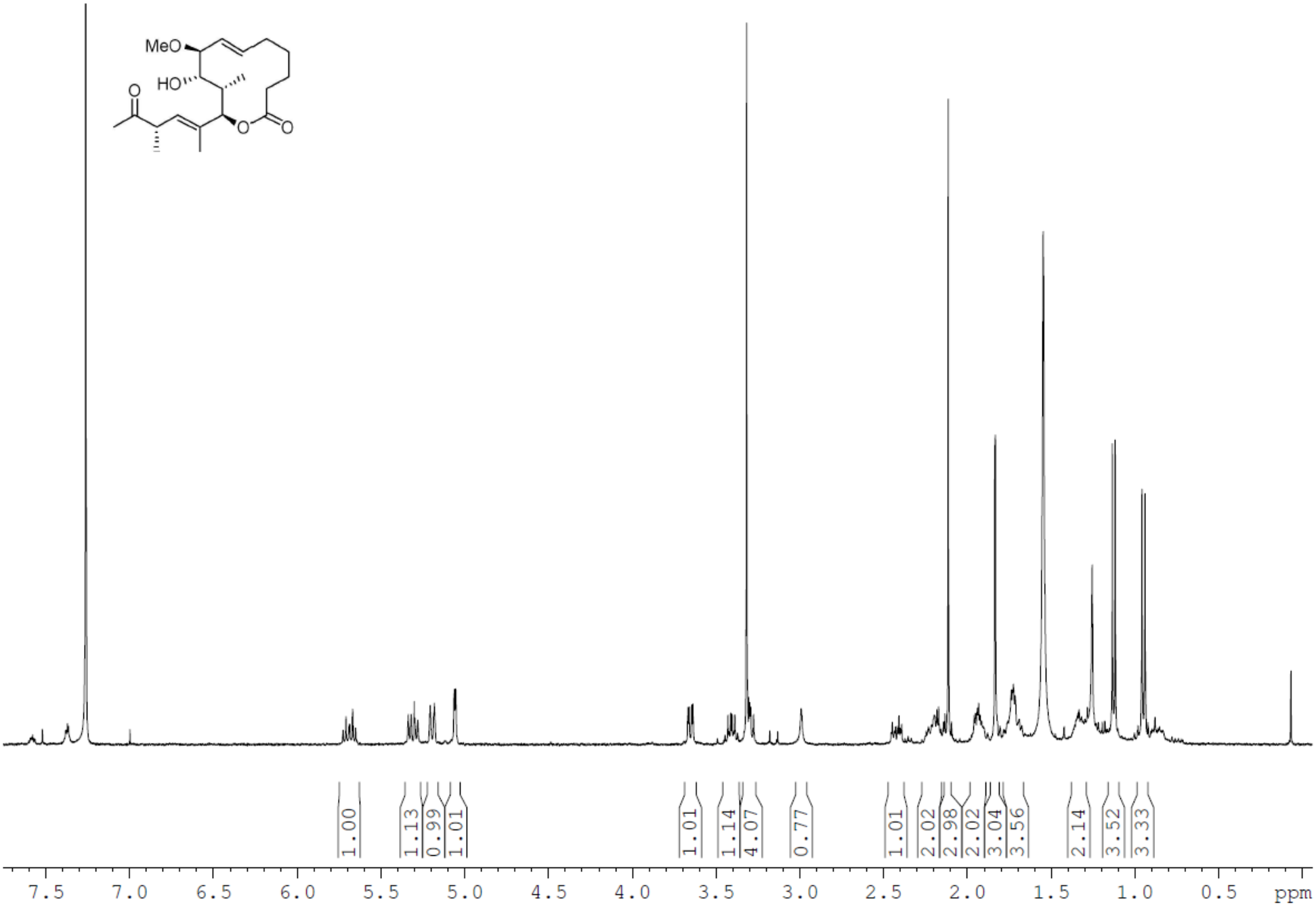
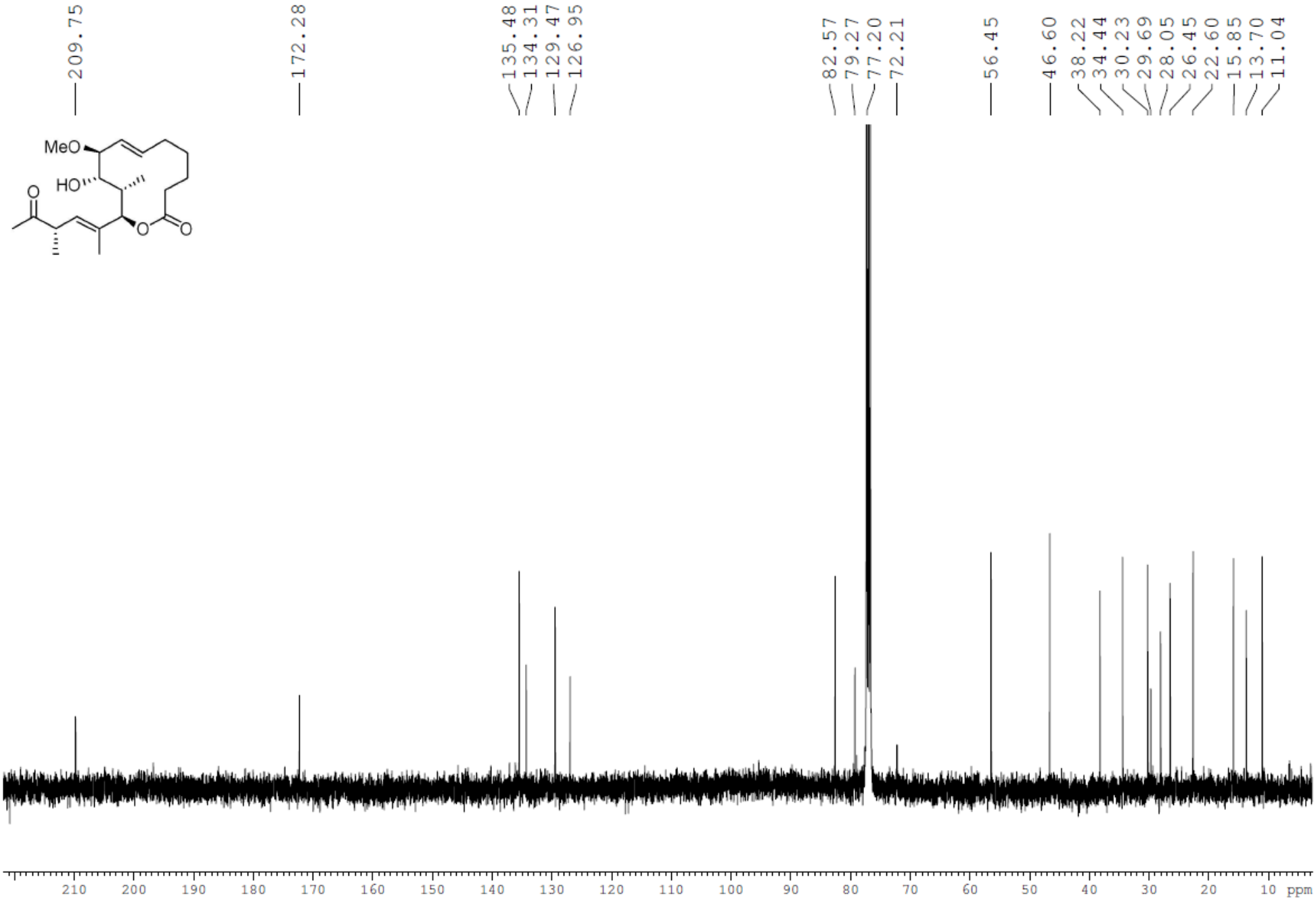
148.17
142.04
138.71
137.26
137.21
137.08
136.90
136.11
133.28
131.10
130.45
129.13
128.98
128.88
128.63
128.38
85.40
79.55
73.21
72.49
57.23
40.79
38.58
35.05
32.34
28.19
21.89
19.88
16.68
13.52
10.67
SnPh3
MeO
HO
HO
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


MeO
HO
HO
O
O

1.00
0.97
1.87
1.00
1.14
3.91
1.65
2.07
2.31
1.16
3.03
6.59
4.15
3.04
4.20
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


172.44
135.42
133.16
130.87
130.34
82.17
79.50
72.37
71.73
56.61
40.80
38.32
34.85
30.16
26.52
22.43
19.95
16.74
13.79
10.92
MeO
HO
HO
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


MeO
HO
O
O
O
1.00
1.13
0.99
1.01
1.01
1.14
4.07
0.77
1.01
2.02
2.98
2.02
3.04
3.56
2.14
3.52
3.33
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


209.75
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134.31
129.47
126.95
82.57
79.27
77.20
72.21
56.45
46.60
38.22
34.44
30.23
29.69
28.05
26.45
22.60
15.85
13.70
11.04
MeO
HO
O
O
O
210
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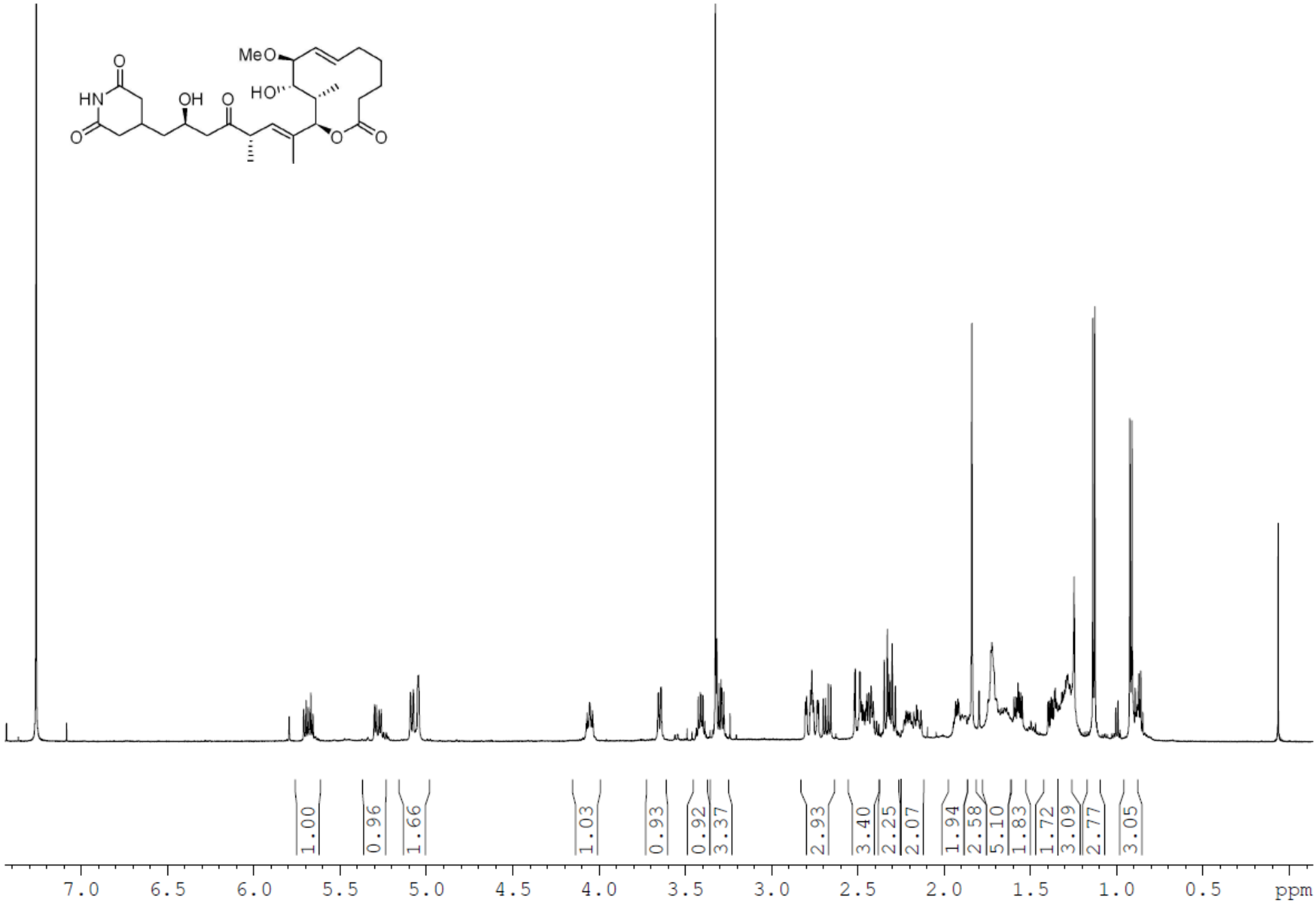
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HO
HN
OH
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2.25
2.07
1.94
2.58
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1.83
1.72
3.09
2.77
3.05
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6.5
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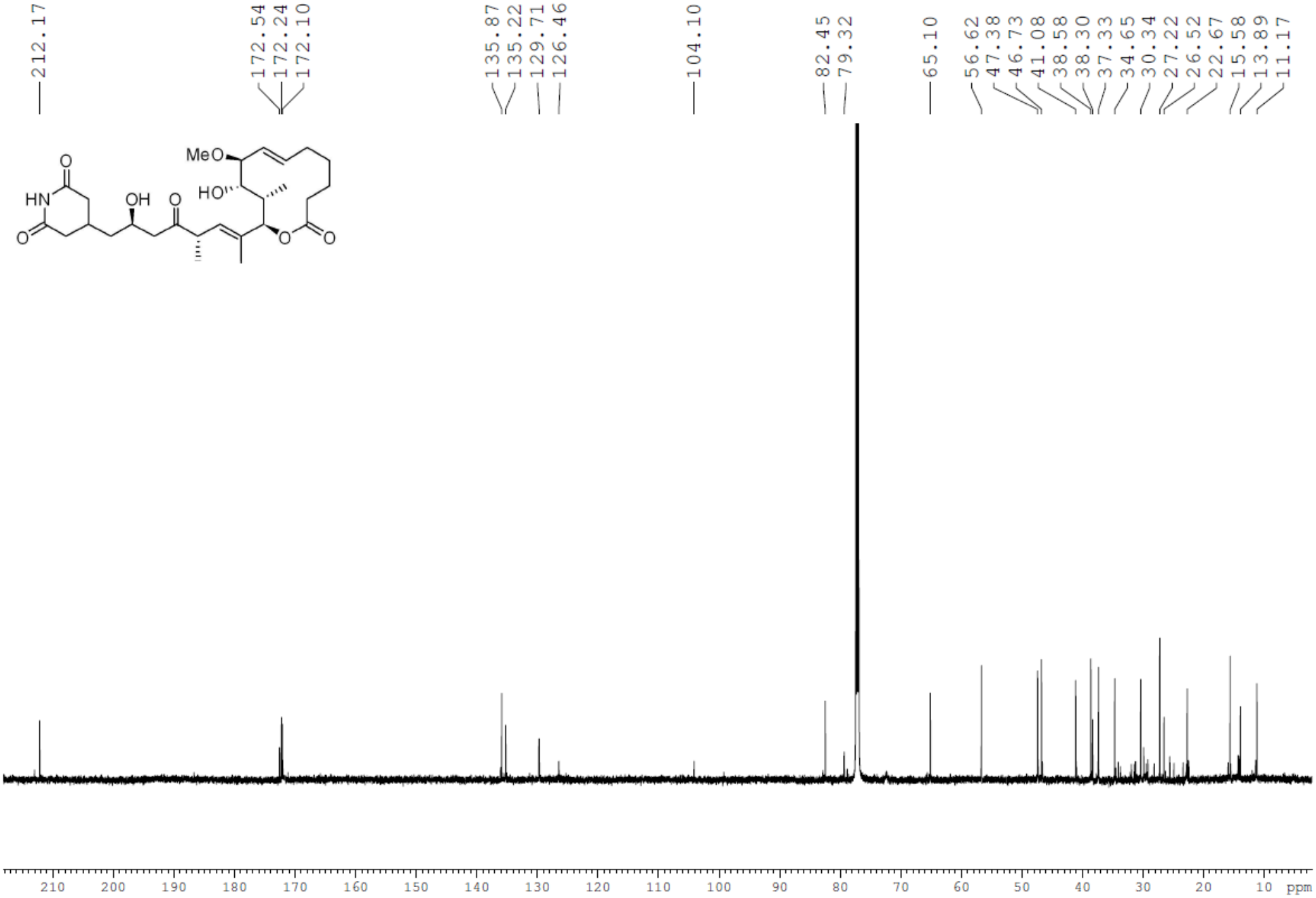
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46.73
41.08
38.58
38.30
37.33
34.65
30.34
27.22
26.52
22.67
15.58
13.89
11.17
MeO
HO
HN
OH
O
O
O
O
O
210
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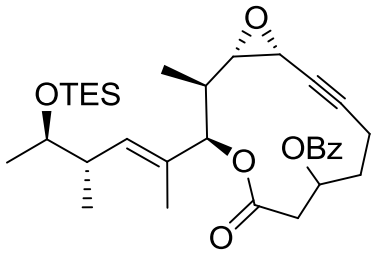
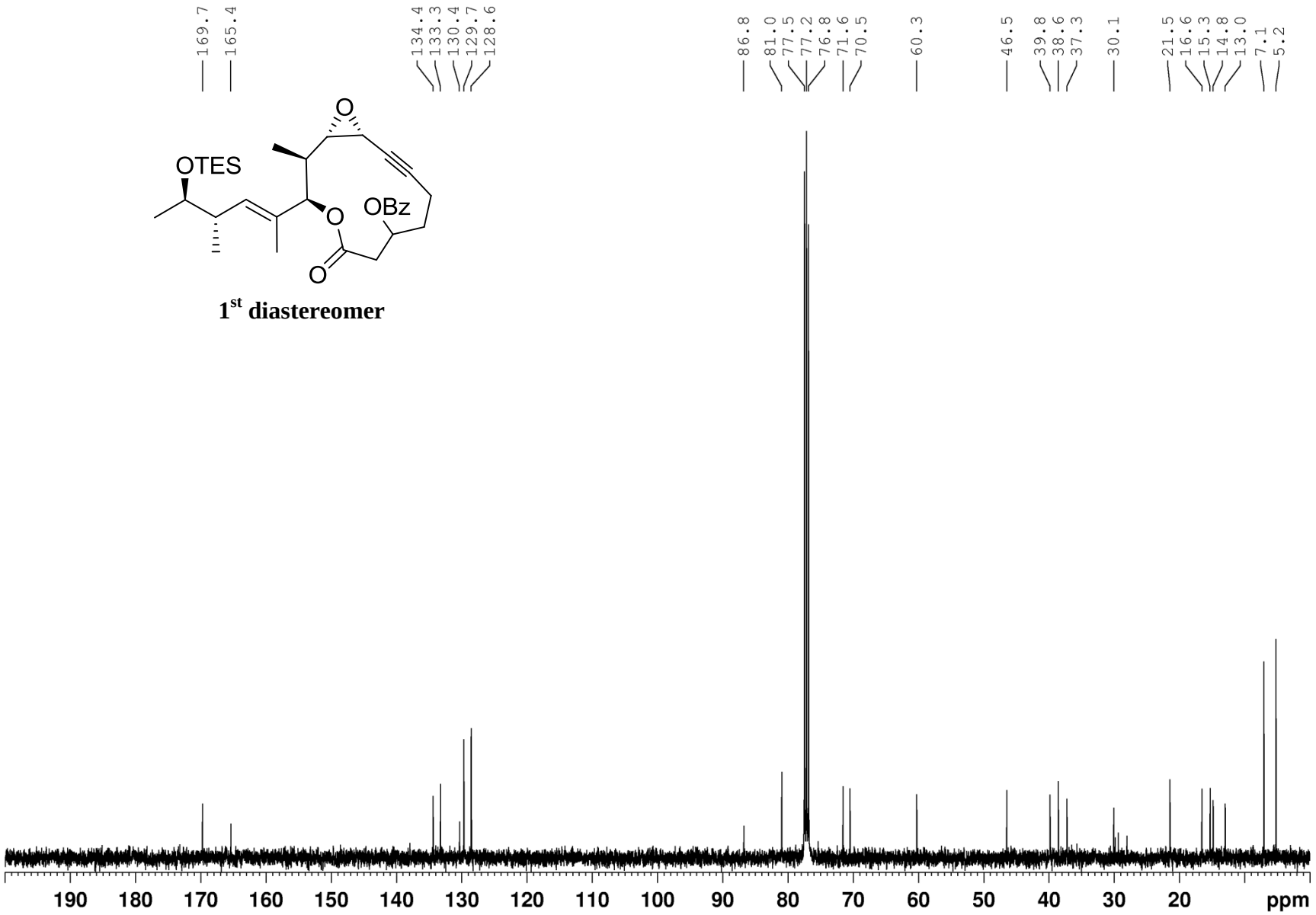
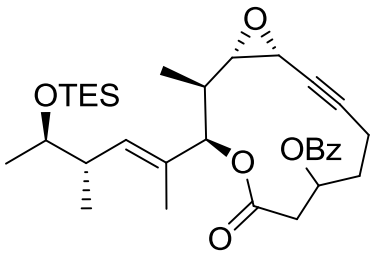
30
20
10
ppm



1st diastereomer



1st diastereomer



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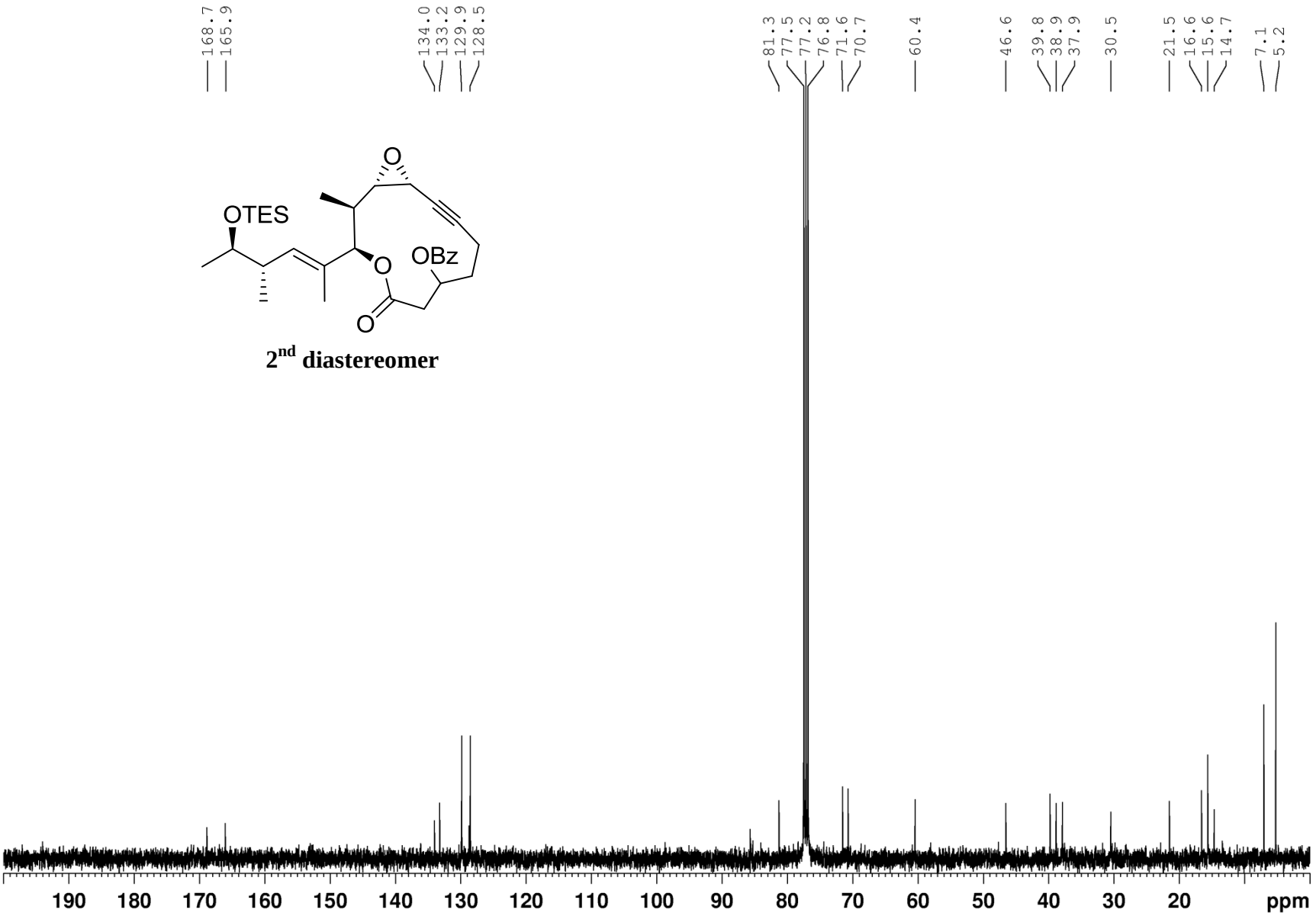
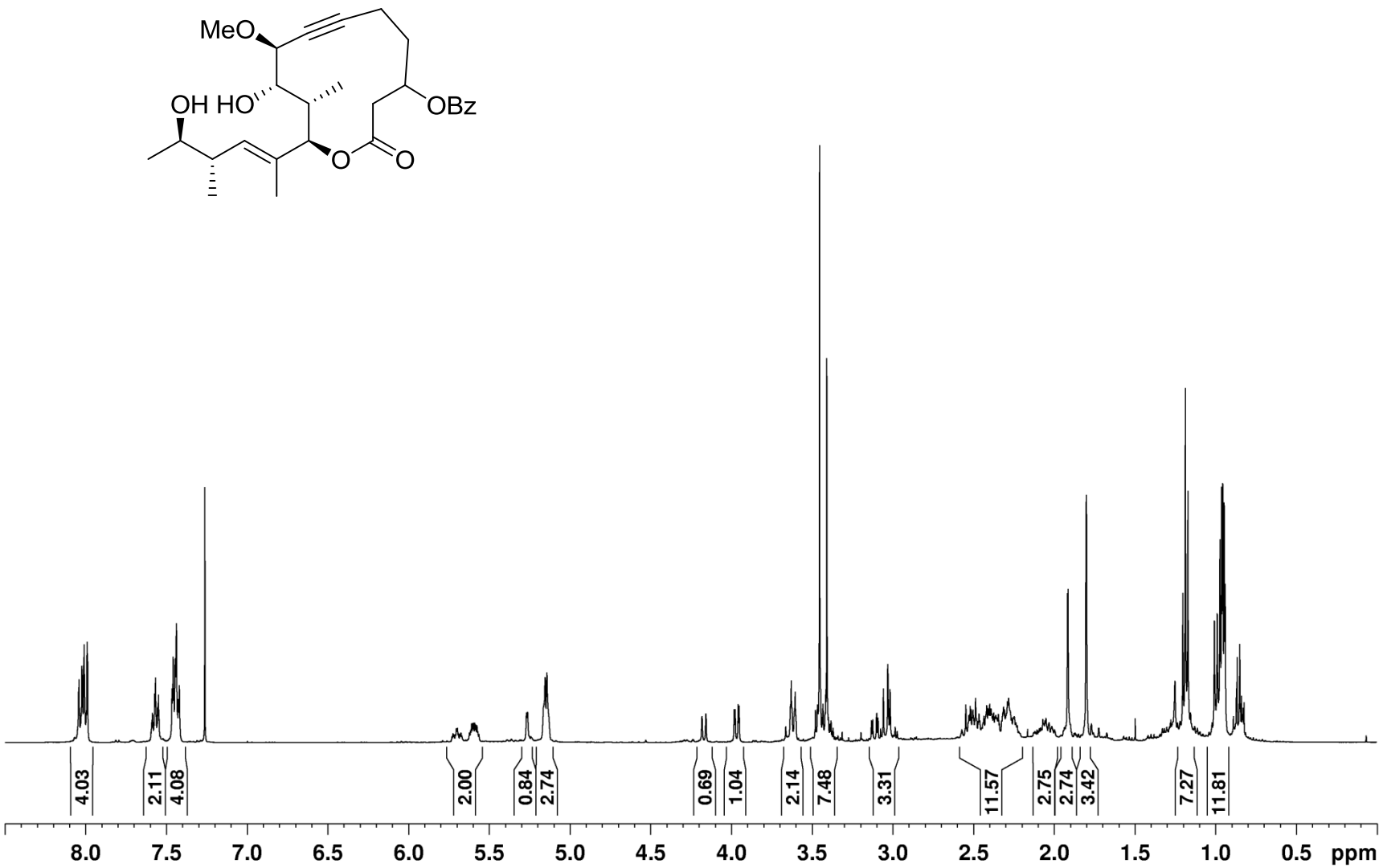


2nd diastereomer


MeO
OH HO
OBz
O
O
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4.08
2.00
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2.74
0.69
1.04
2.14
7.48
3.31
11.57
2.75
2.74
3.42
7.27
11.81
8.0
7.5
7.0
6.5
6.0
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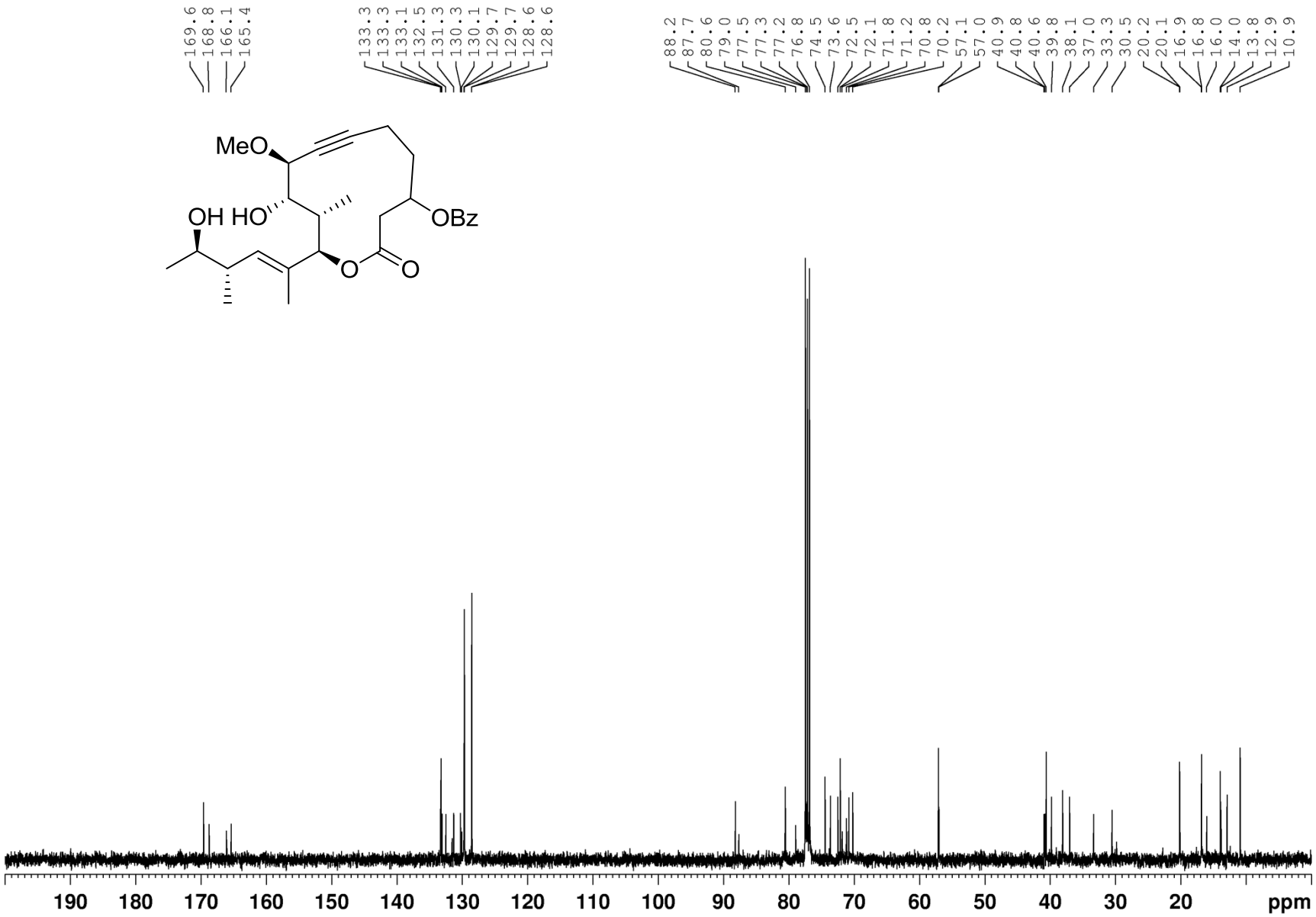
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm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129.7
129.7
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128.6
88.2
87.7
80.6
79.0
77.5
77.3
77.2
76.8
74.5
73.6
72.5
72.1
71.8
71.2
70.8
70.2
57.1
57.0
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40.8
40.6
39.8
38.1
37.0
33.3
30.5
20.2
20.1
16.9
16.8
16.0
14.0
13.8
12.9
10.9
MeO
OH HO
OBz
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O
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80
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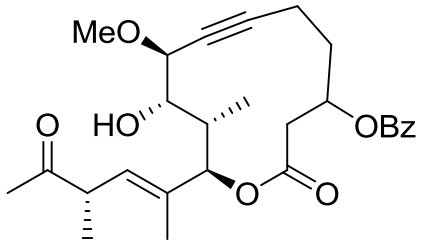
40
30
20
ppm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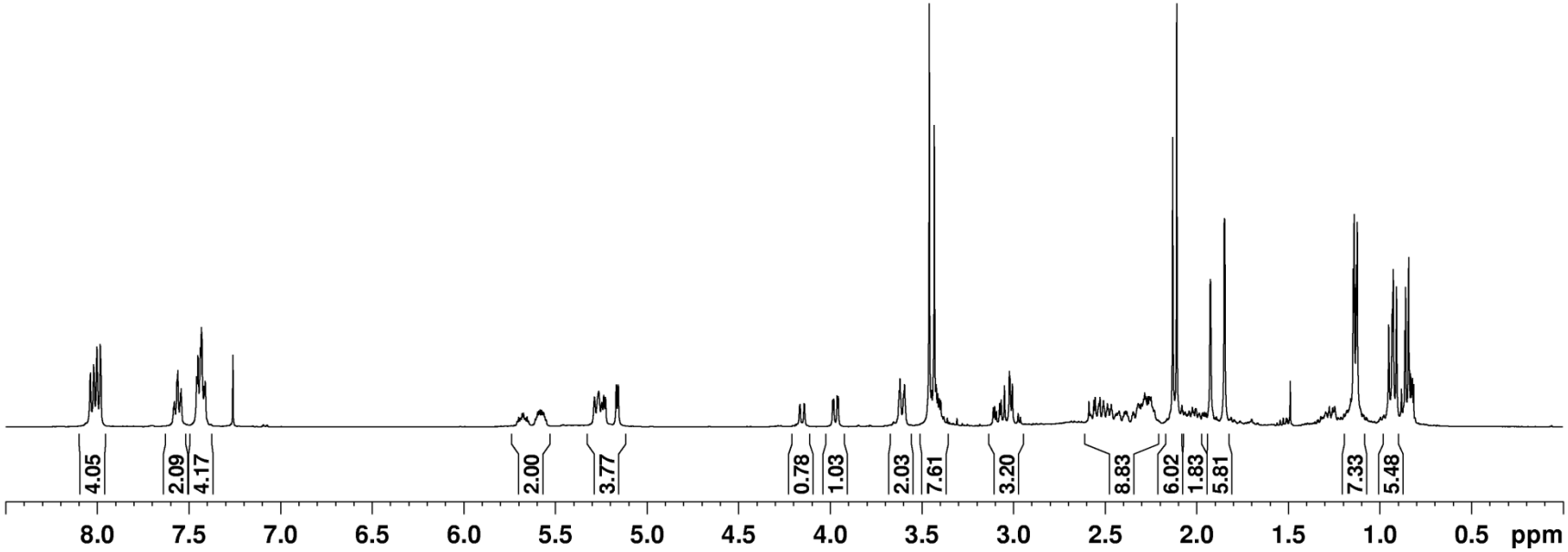
HO
O
OBz
O
O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2.03
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3.20
8.83
6.02
1.83
5.81
7.33
5.48
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

209.6
209.5
169.4
168.5
166.0
165.4
134.1
133.7
133.3
133.3
130.2
130.1
129.7
129.7
128.5
128.5
128.3
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80.8
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70.6
70.3
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57.0
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46.8
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39.4
38.0
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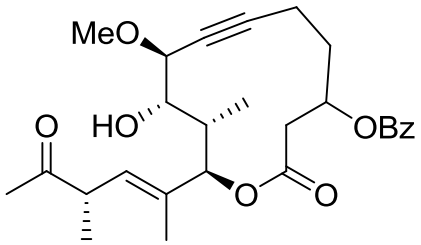
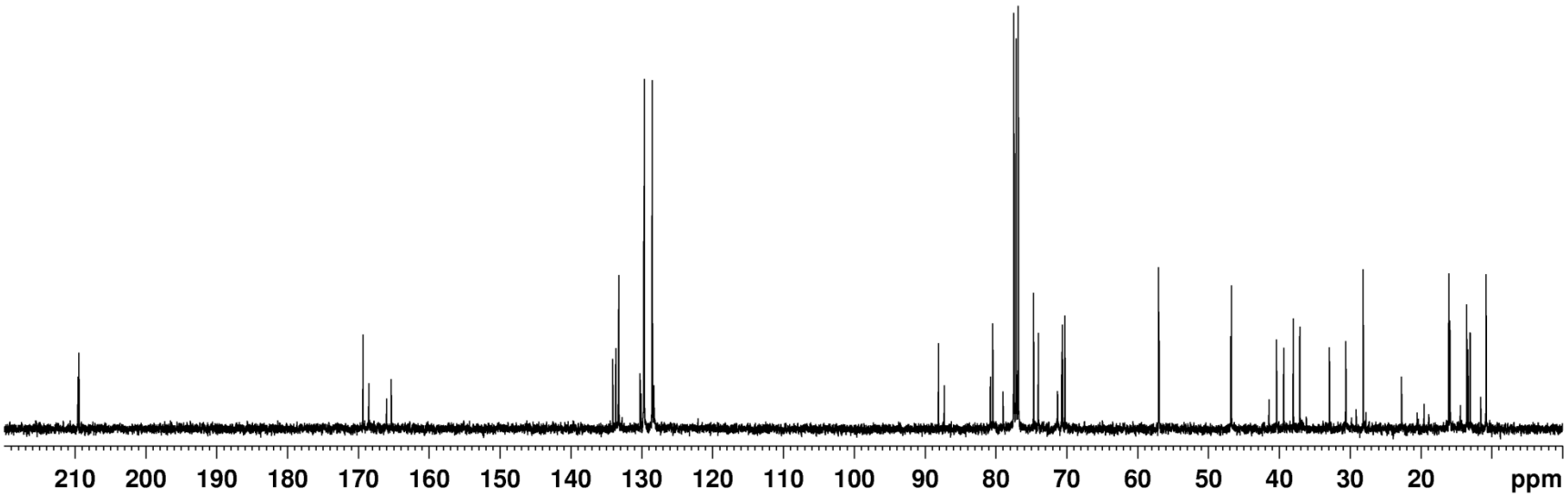
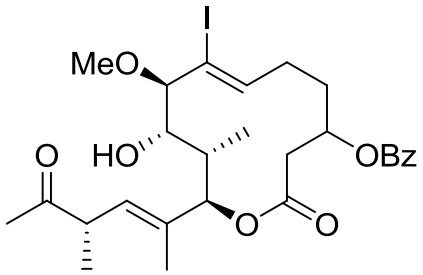
13.4
13.0
10.8







1st diastereomer

209.6
168.1
166.3
138.5
134.0
133.4
130.1
129.8
128.6
128.1
106.9
90.0
81.0
77.5
77.4
77.2
76.8
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56.9
46.8
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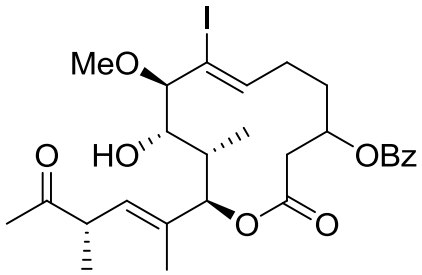
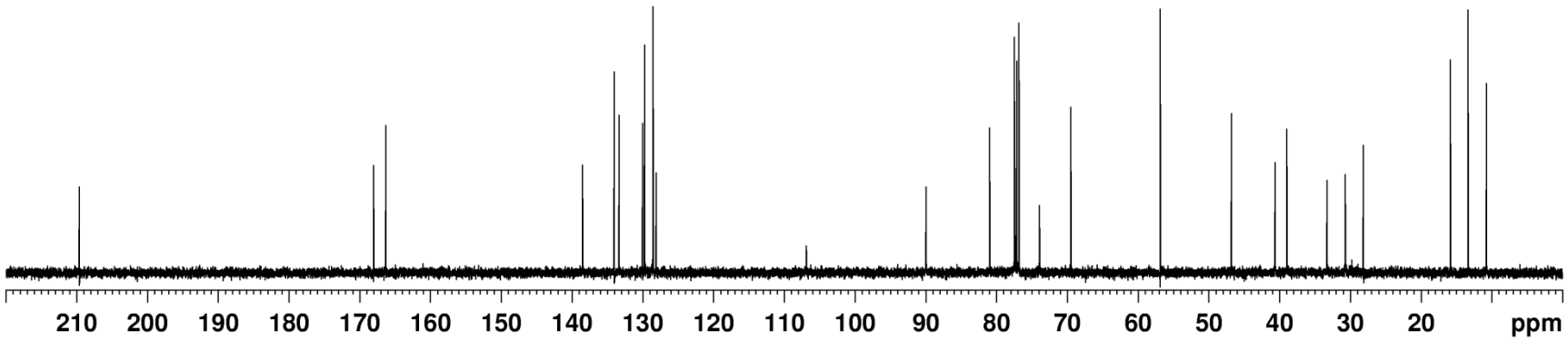
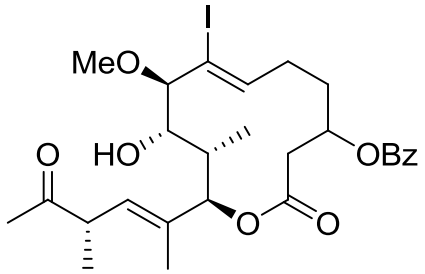
33.3
30.7
28.1
15.9
13.4
10.8

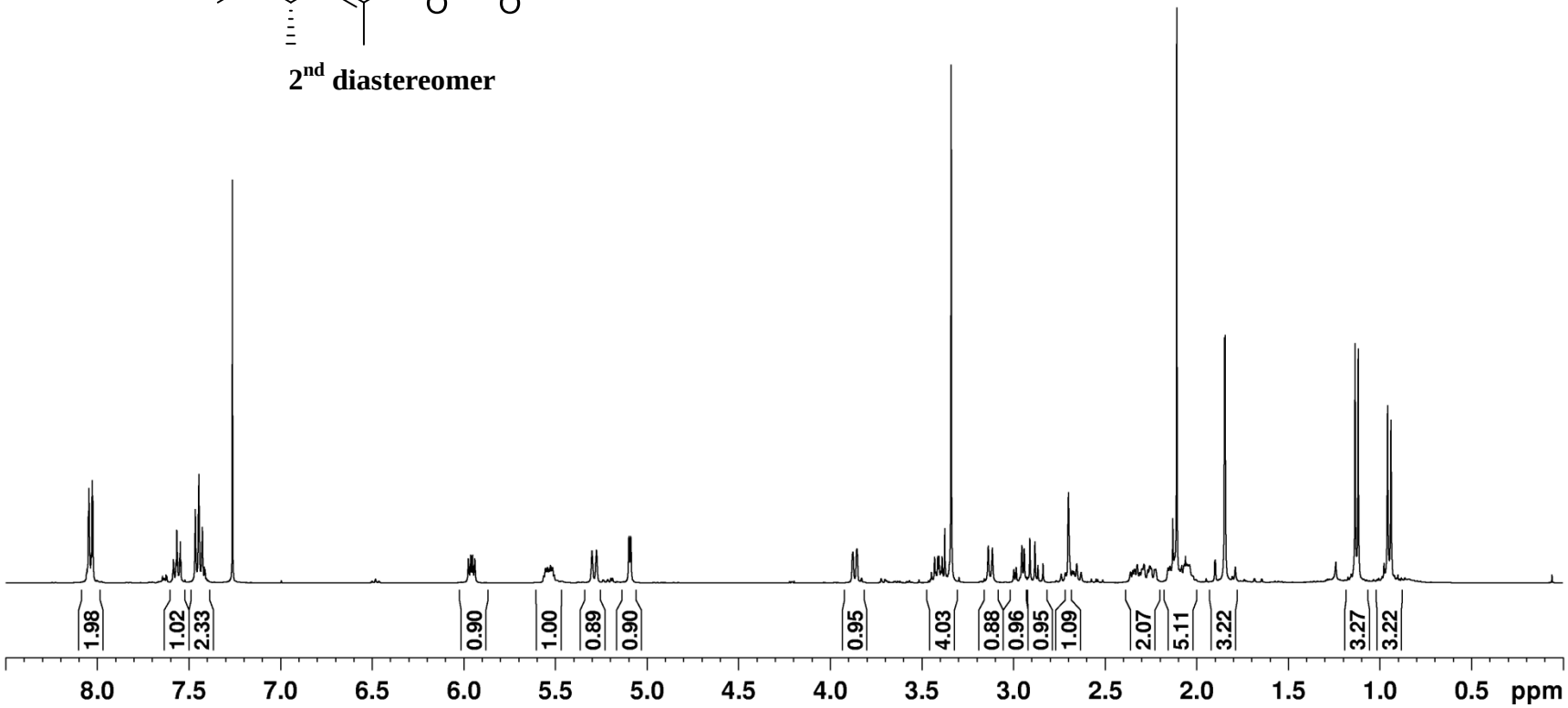


1st diastereomer





2nd diastereomer



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165.4
140.7
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133.4
133.2
130.3
129.7
129.7
129.1
128.5
128.5
111.0
88.7
80.9
77.5
77.4
77.2
76.8
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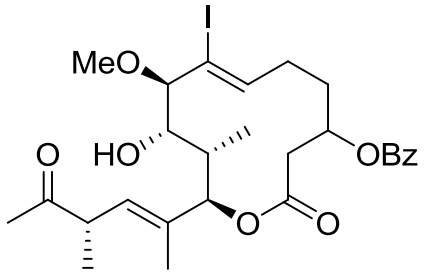
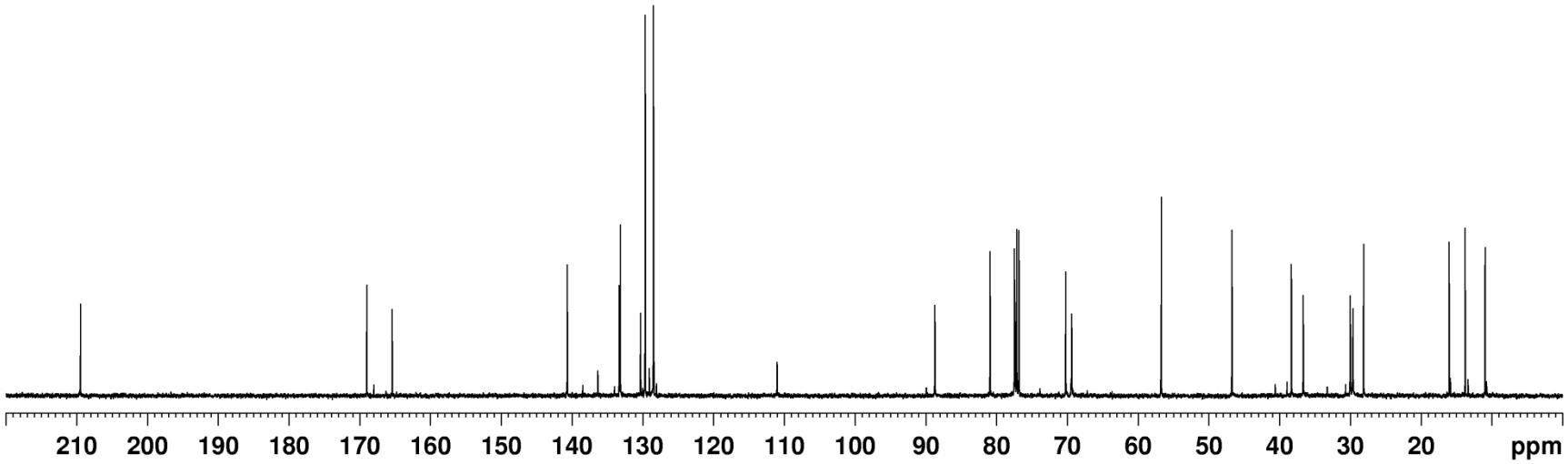
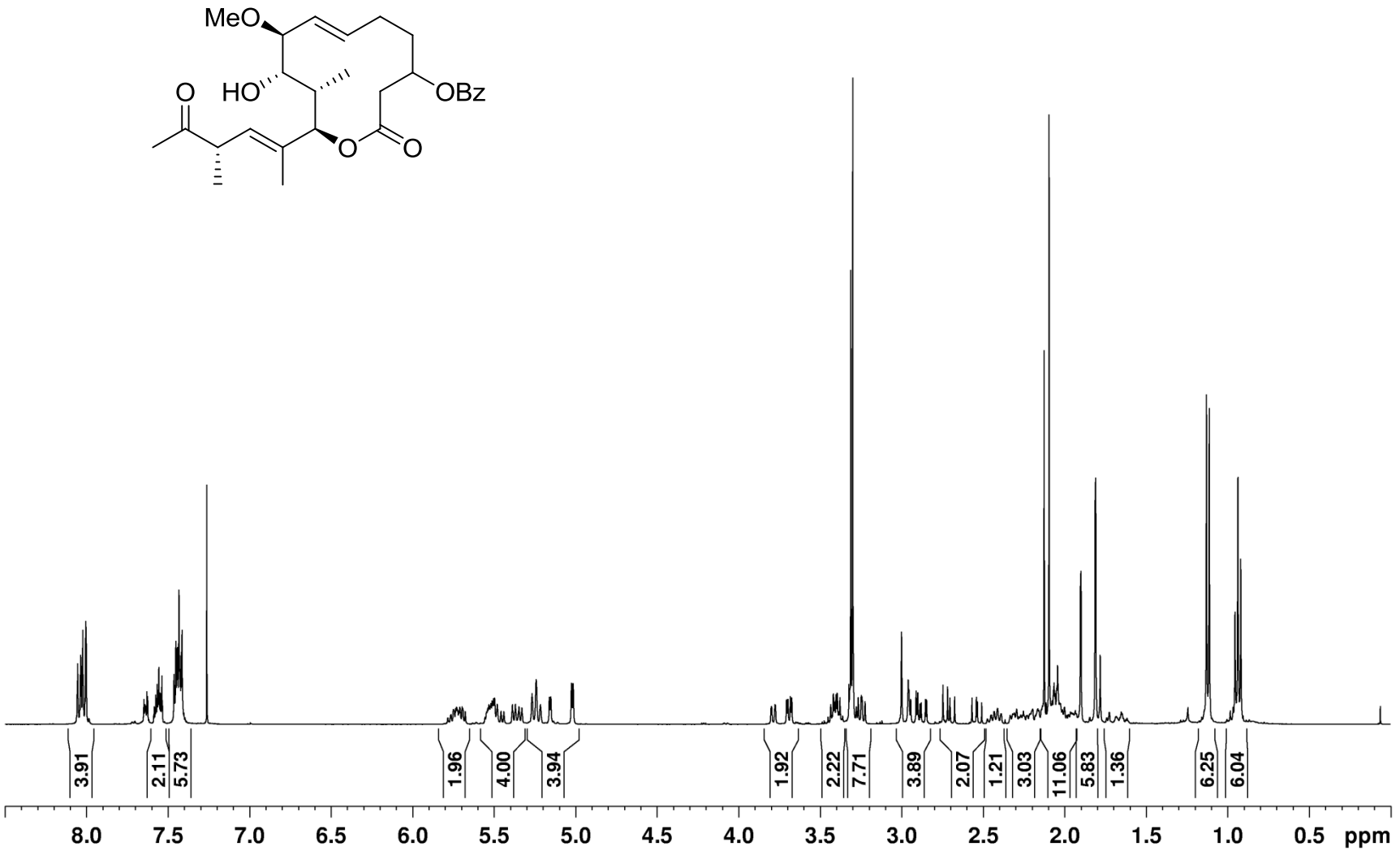
56.7
46.7
38.3
36.7
30.0
29.6
28.1
16.0
13.8
10.9



2nd diastereomer

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HO
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OBz
O
O
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3.94
1.92
2.22
7.71
3.89
2.07
1.21
3.03
11.06
5.83
1.36
6.25
6.04
8.0
7.5
7.0
6.5
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4.5
4.0
3.5
3.0
2.5
2.0
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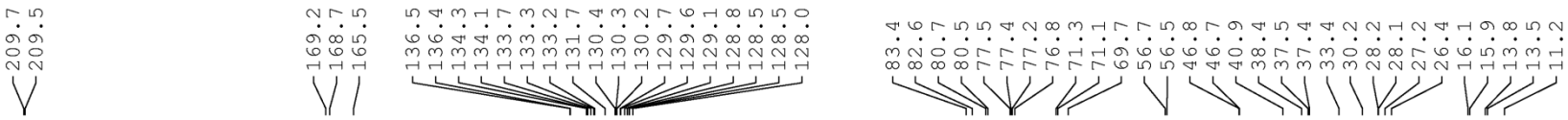
1.0
0.5
ppm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133.7
133.3
133.2
131.7
130.4
130.3
130.2
129.7
129.6
129.1
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128.5
128.0
83.4
82.6
80.7
80.5
77.5
77.4
77.2
76.8
71.3
71.1
69.7
56.7
56.5
46.8
46.7
40.9
38.4
37.5
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27.2
26.4
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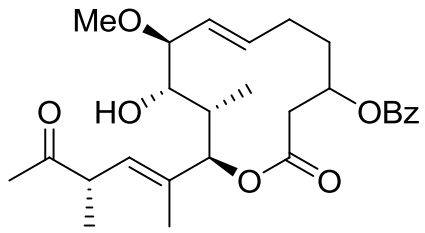
15.9
13.8
13.5
11.2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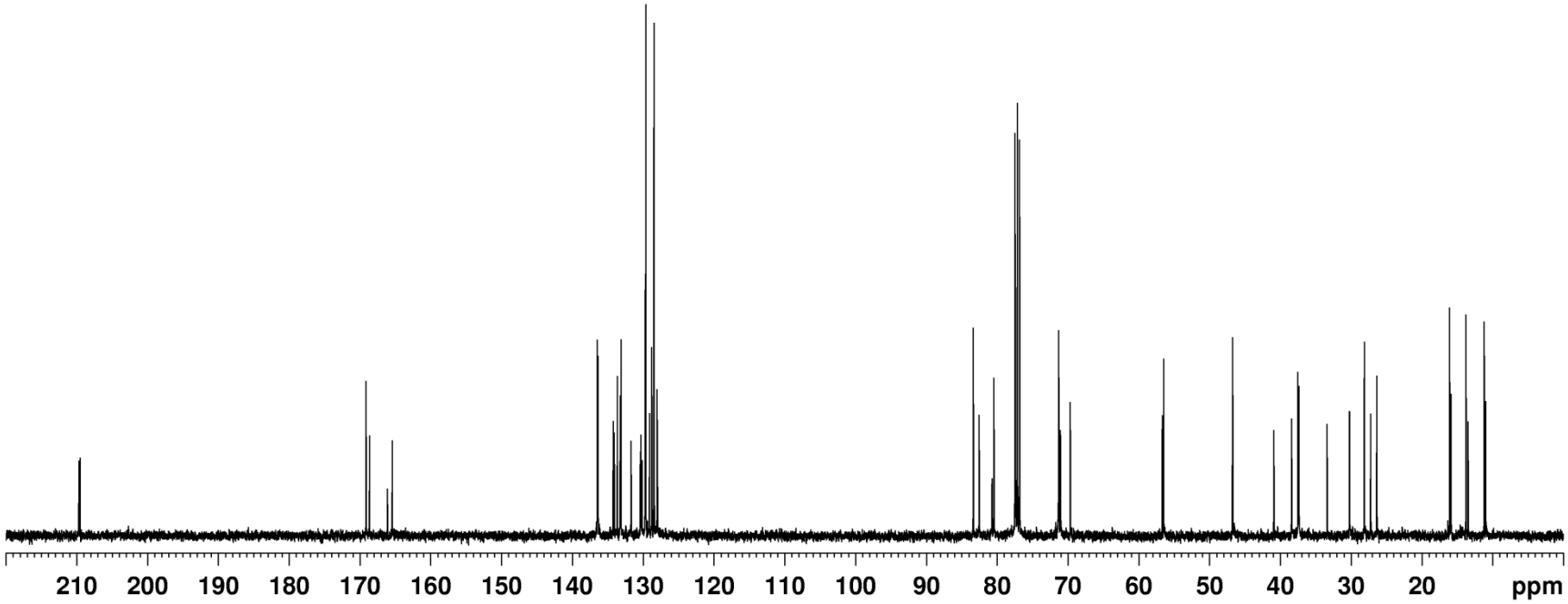
HO
O
OBz
O
O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120
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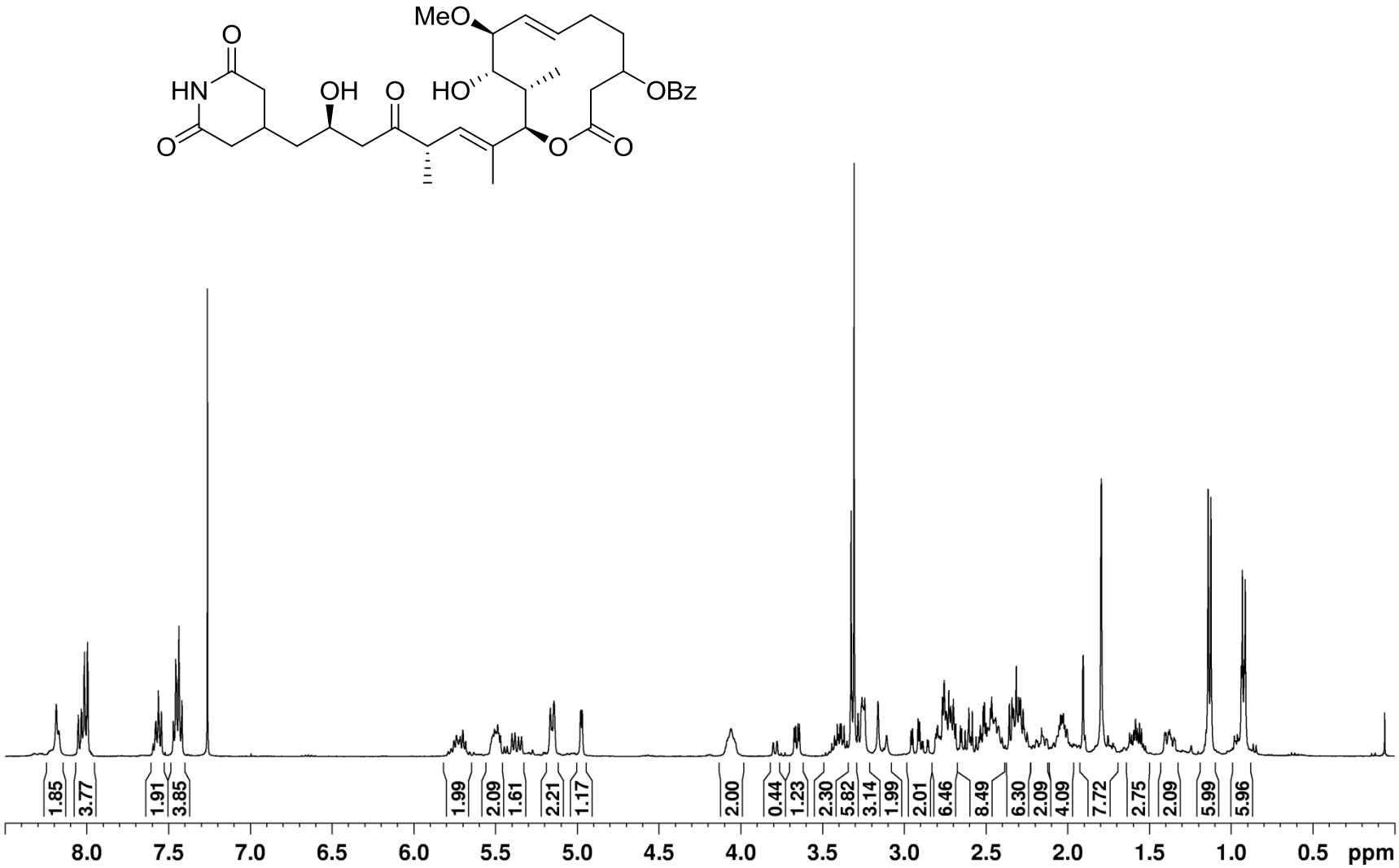
40
30
20
ppm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OH
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HO
OBz
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O
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1.61
2.21
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2.30
5.82
3.14
1.99
2.01
6.46
8.49
6.30
2.09
4.09
7.72
2.75
2.09
5.99
5.96
8.0
7.5
7.0
6.5
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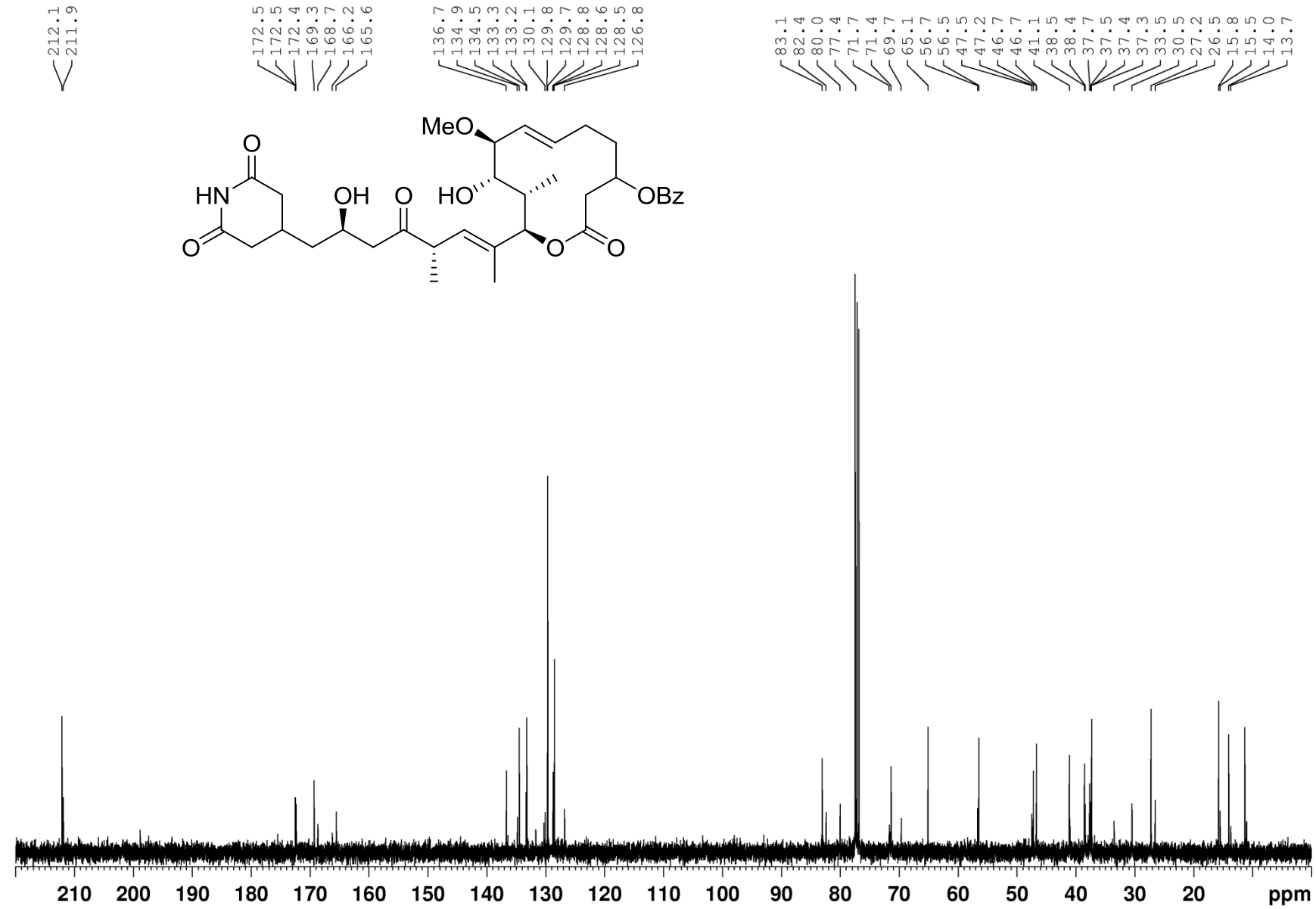
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm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172.4
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133.2
130.1
129.8
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128.8
128.6
128.5
126.8
83.1
82.4
80.0
77.4
71.7
71.4
69.7
65.1
56.7
56.5
47.5
47.2
46.7
46.7
41.1
38.5
38.4
37.7
37.5
37.4
37.3
33.5
30.5
27.2
26.5
15.8
15.5
14.0
13.7
MeO
HO
OBz
HN
OH
O
O
O
O
O
O
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150
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130
120
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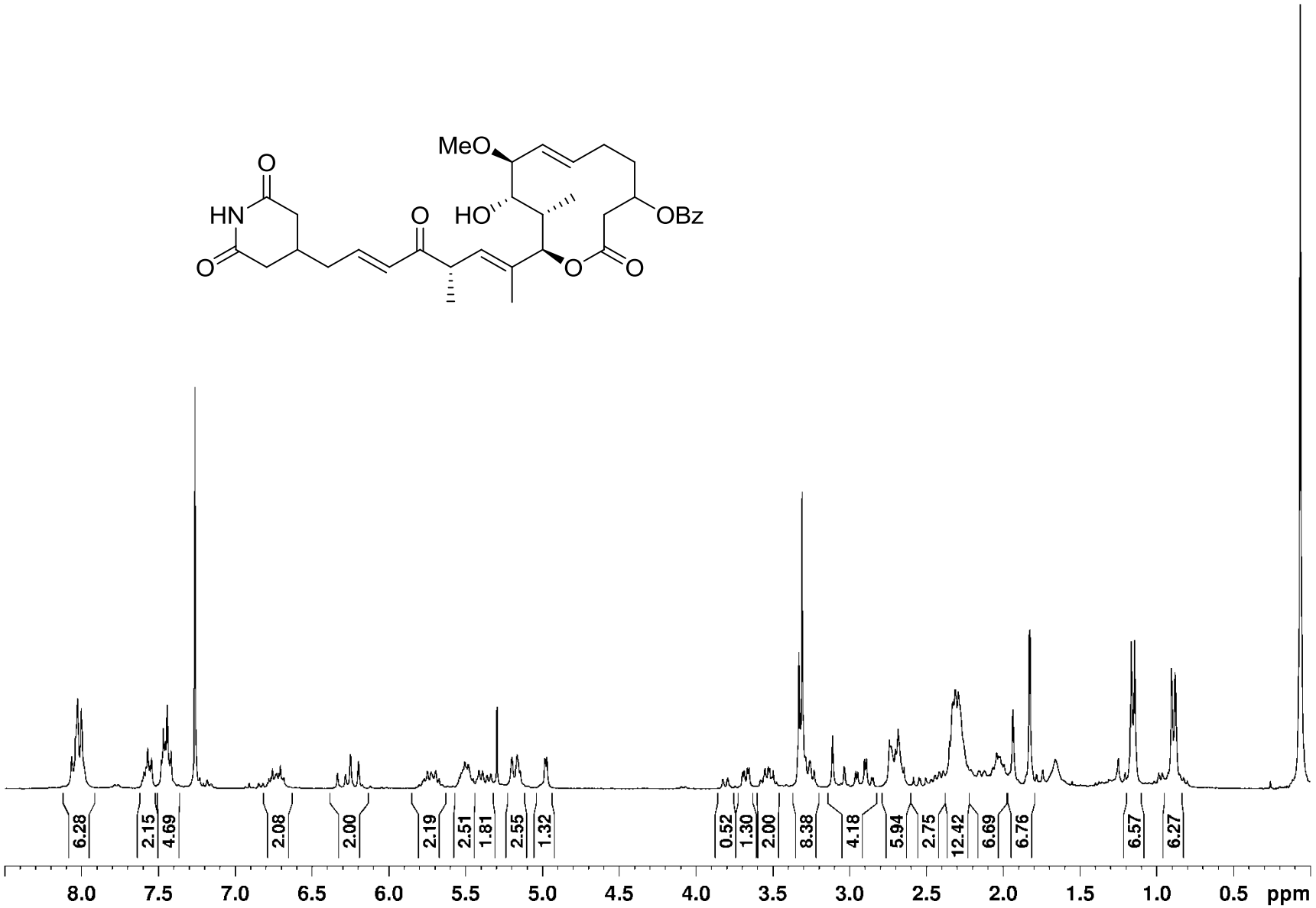
20
ppm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OBz
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12.42
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7.5
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6.5
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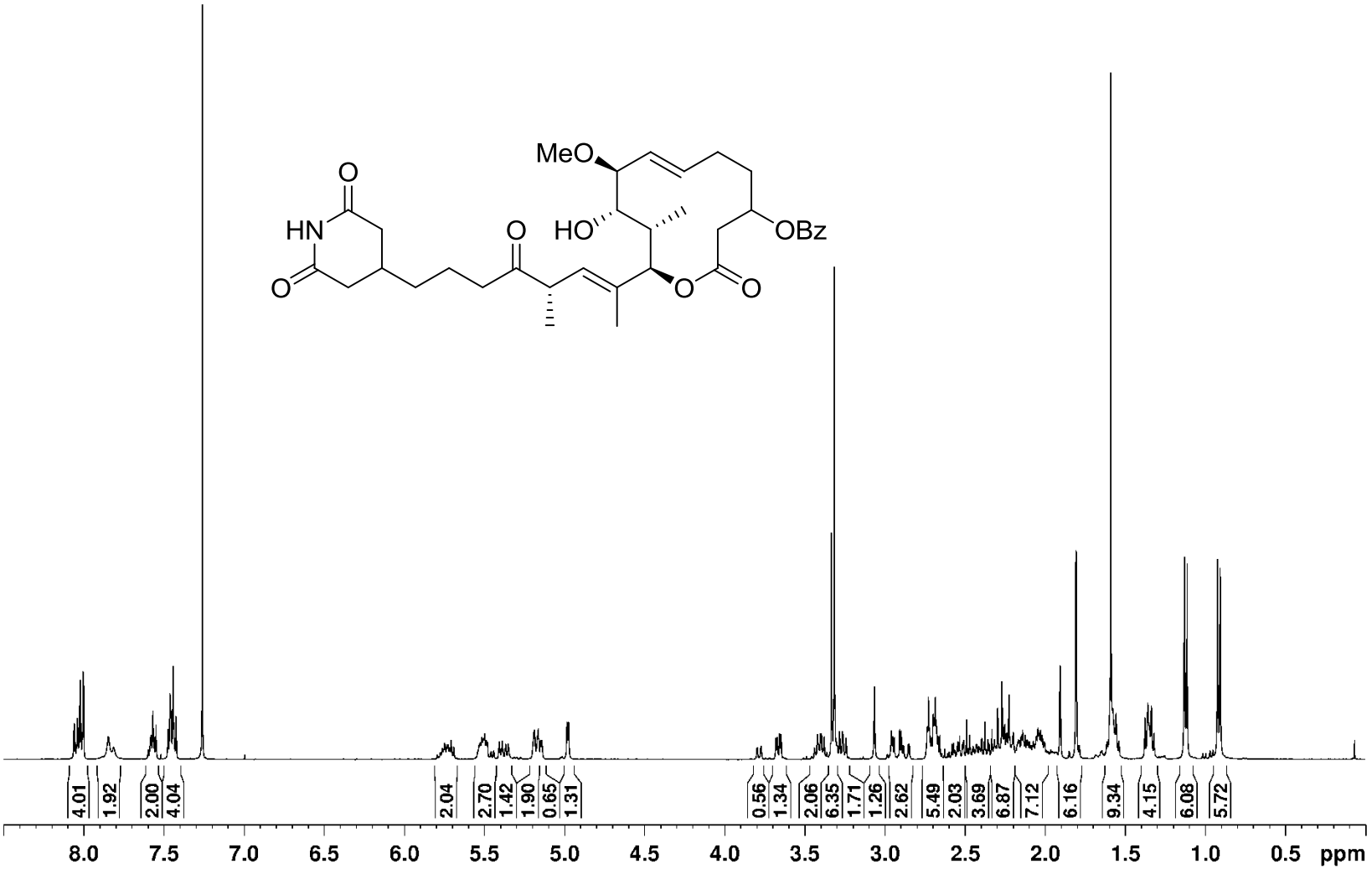
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OBz
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2.04
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1.71
1.26
2.62
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2.03
3.69
6.87
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6.16
9.34
4.15
6.08
5.72
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6.5
6.0
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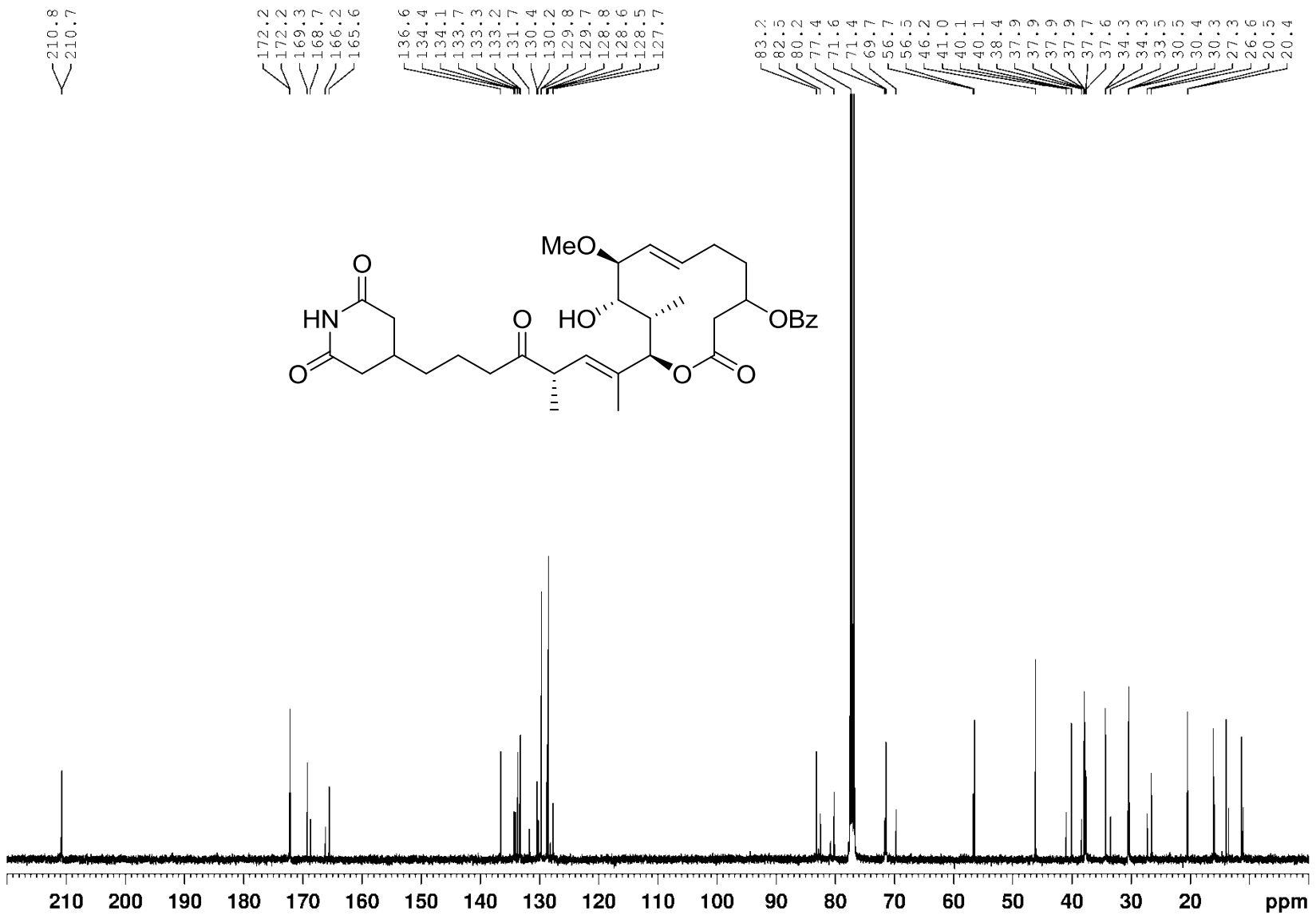
0.5
ppm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133.7
133.3
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130.2
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129.7
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128.6
128.5
127.7
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82.5
80.2
77.4
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71.4
69.7
56.7
56.5
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37.9
37.7
37.6
34.3
34.3
33.5
30.5
30.4
30.3
27.3
26.6
20.5
20.4
MeO
HO
OBz
HN
O
O
O
O
O
O
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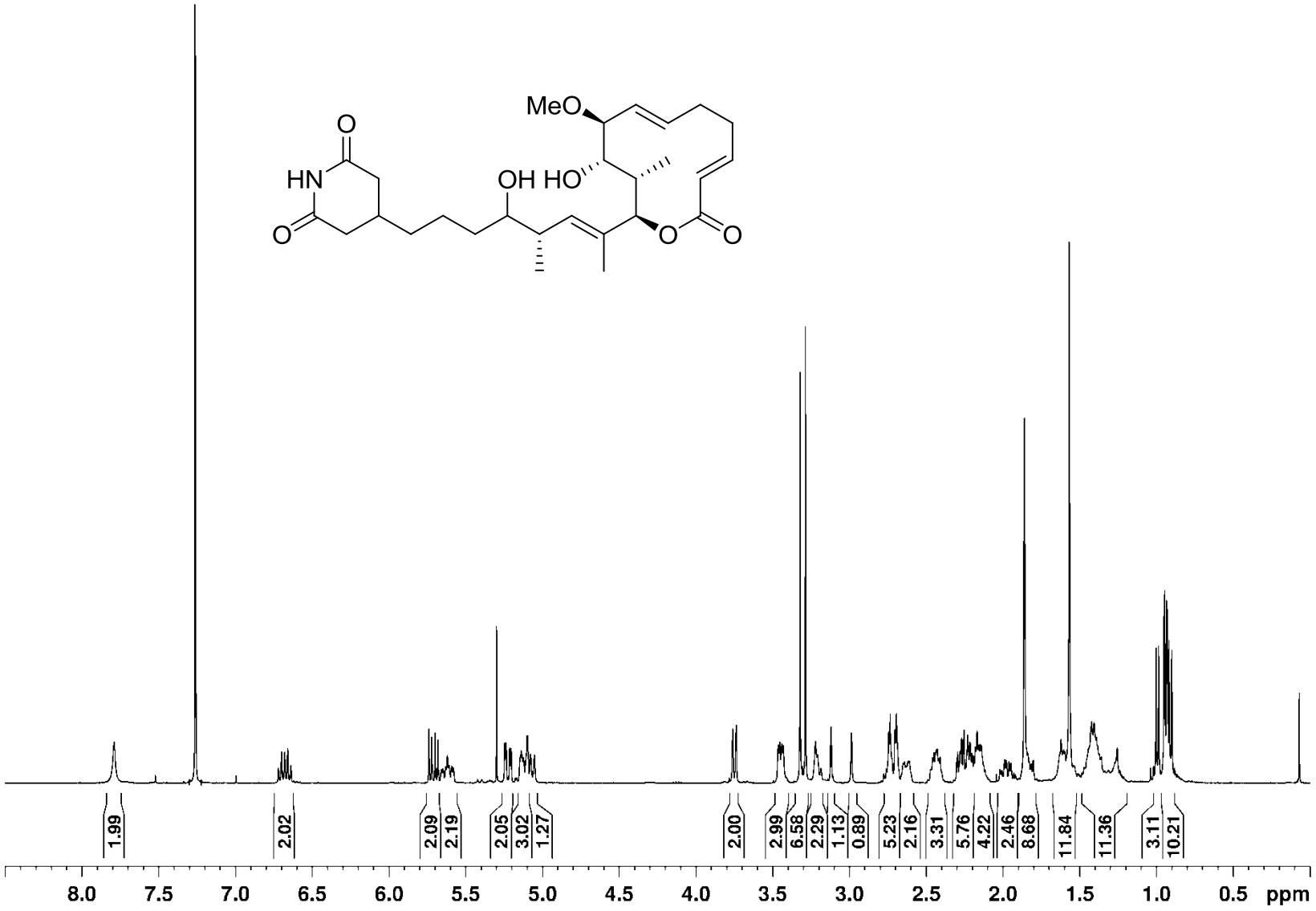
20
ppm


MeO
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HN
OH HO
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2.19
2.05
3.02
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2.00
2.99
6.58
2.29
1.13
0.89
5.23
2.16
3.31
5.76
4.22
2.46
8.68
11.84
11.36
3.11
10.21
8.0
7.5
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6.5
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4.5
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2.0
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1.0
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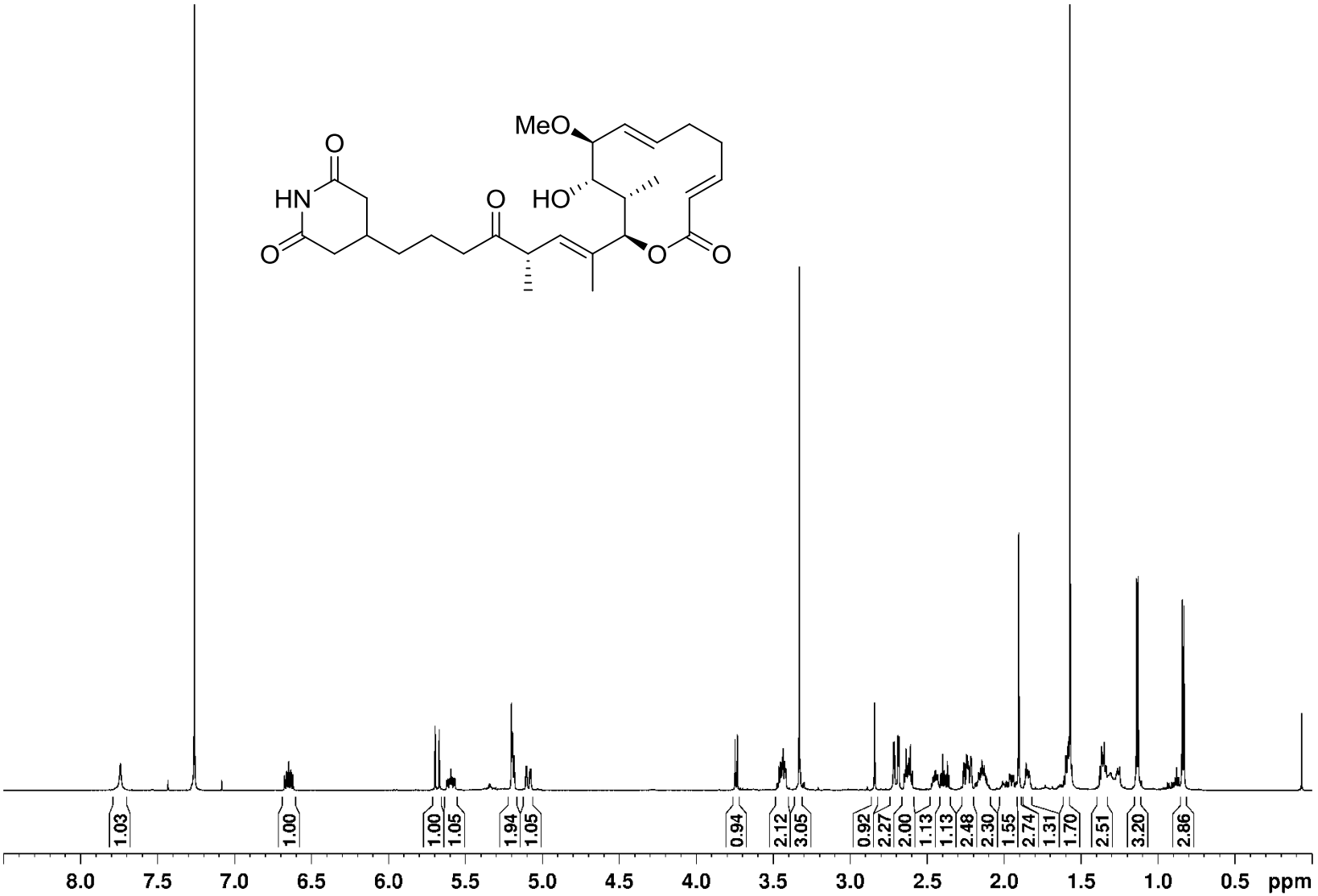
ppm


MeO
HO
HN
O
O
O
O
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1.00
1.05
1.94
1.05
0.94
2.12
3.05
0.92
2.27
2.00
1.13
1.13
2.48
2.30
1.55
2.74
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3.20
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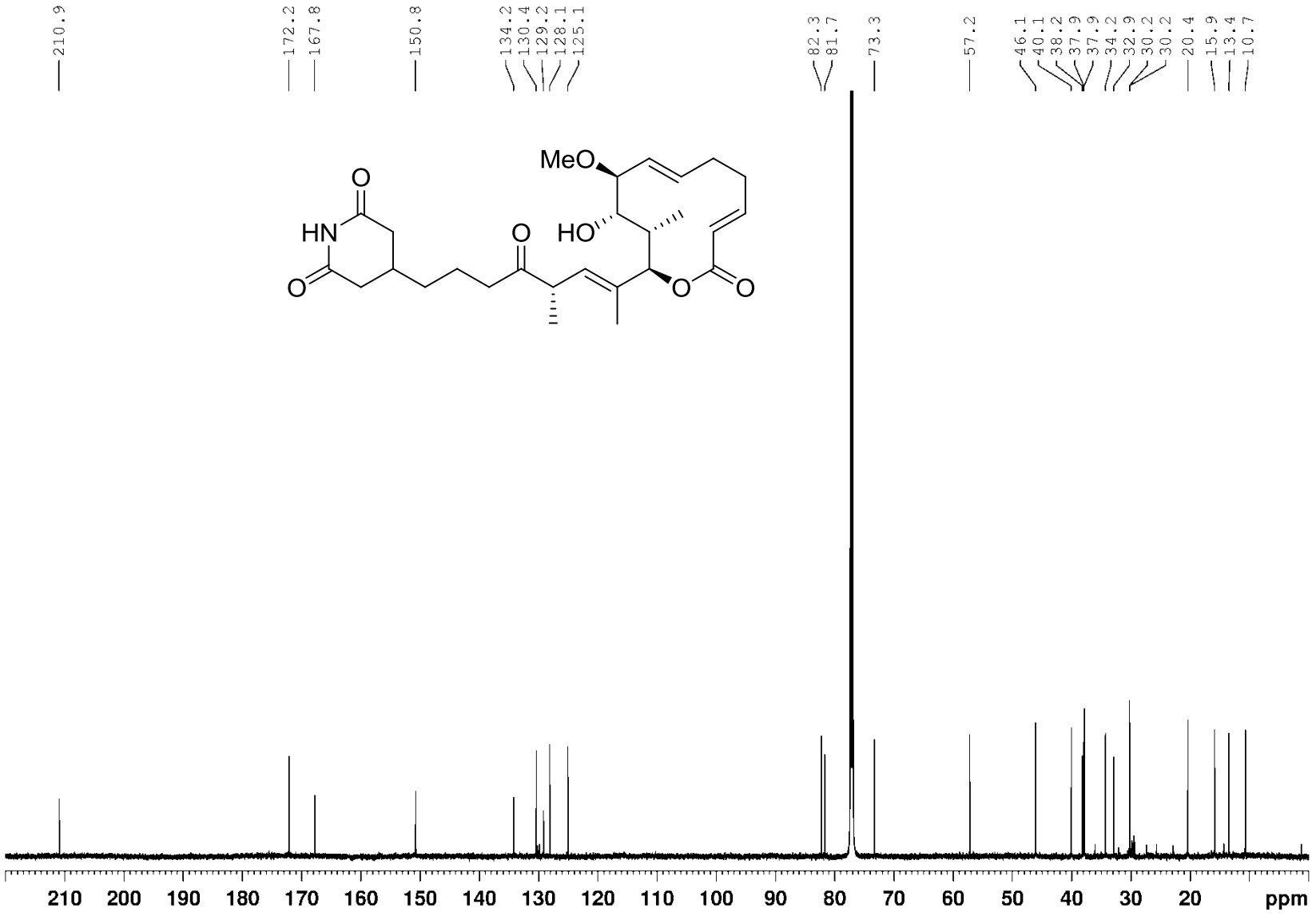
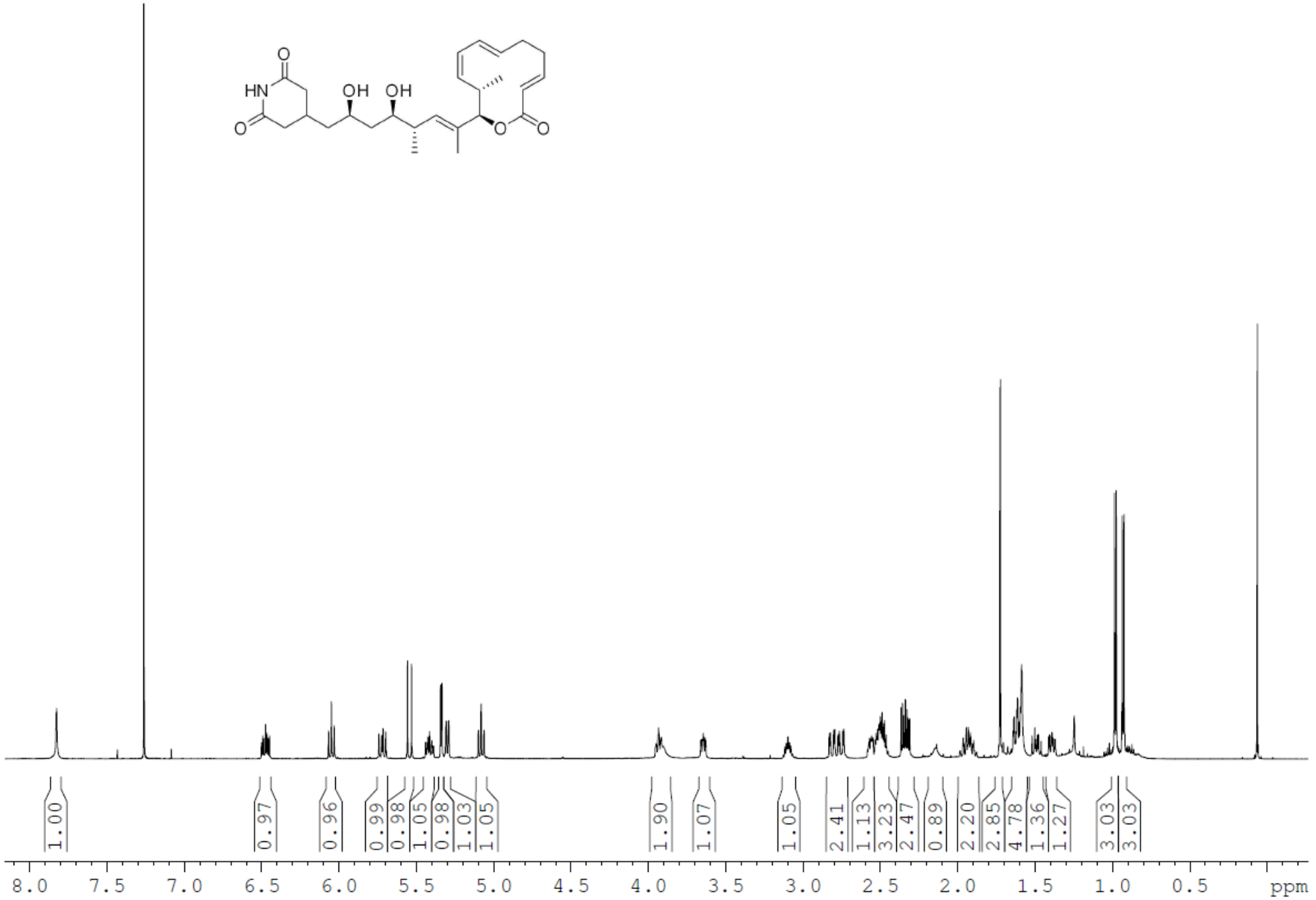
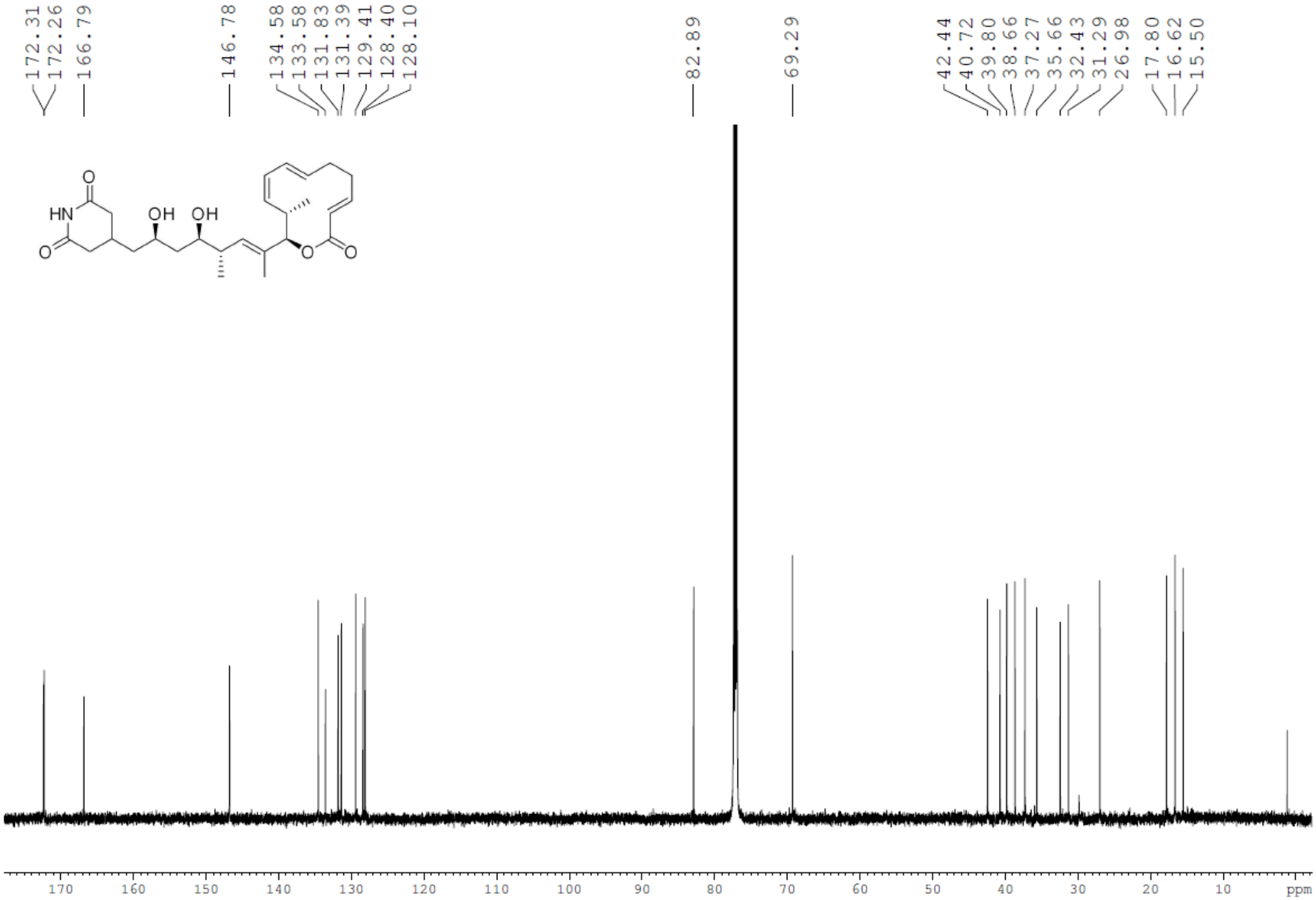
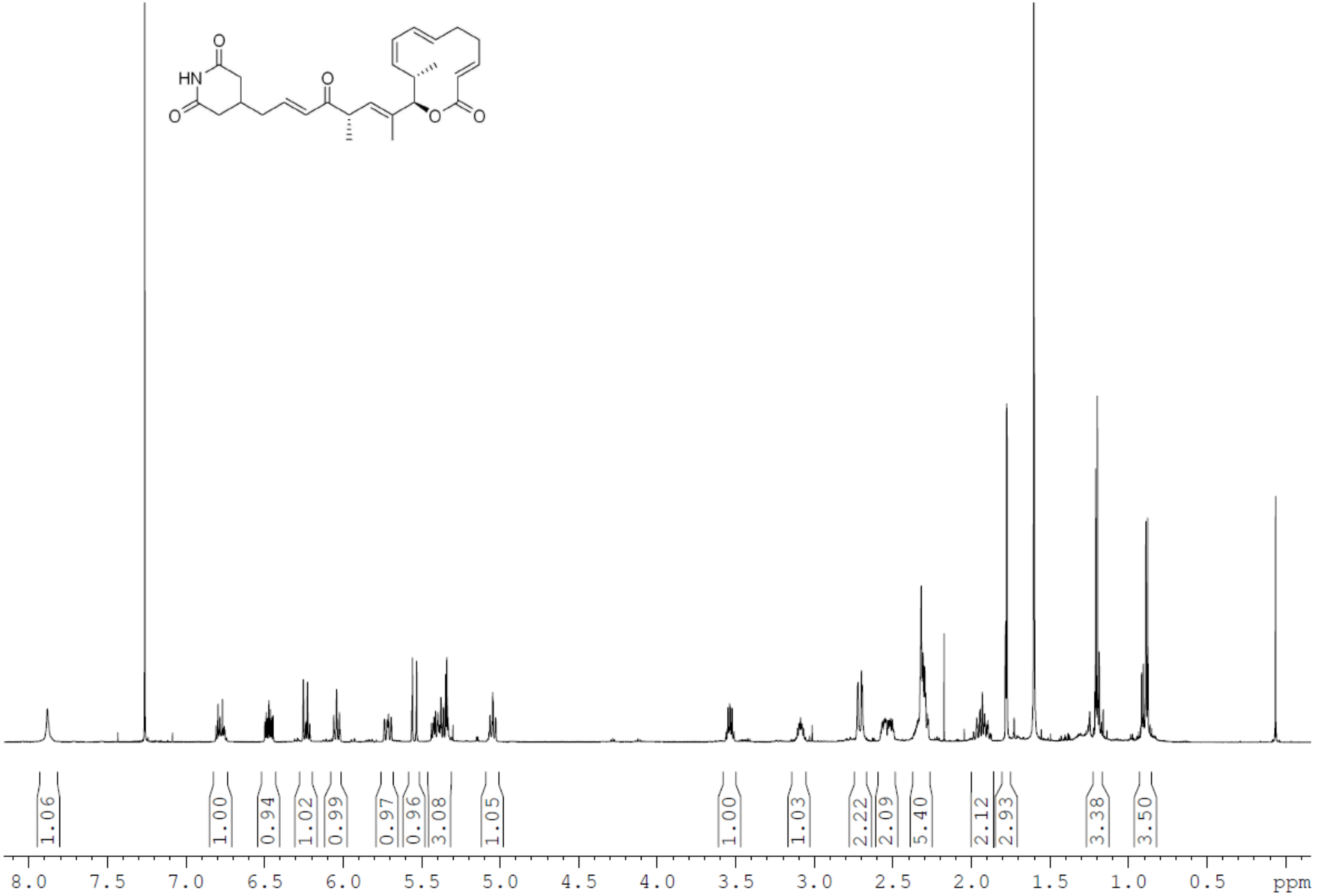
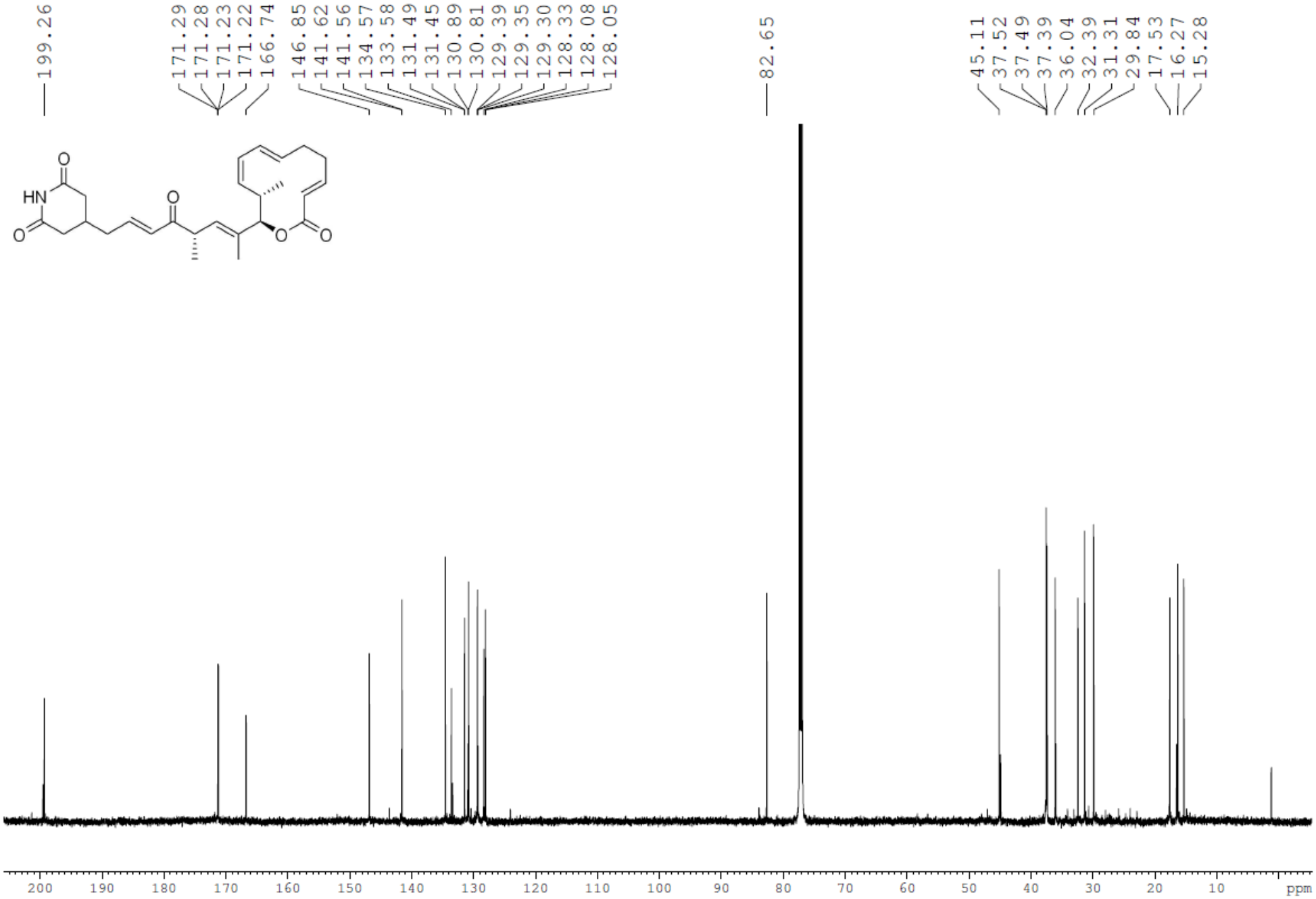
2.0
1.5
1.0
0.5
ppm

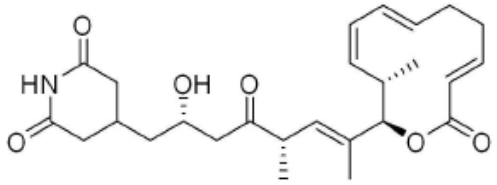

210.9
172.2
167.8
150.8
134.2
130.4
129.2
128.1
125.1
82.3
81.7
73.3
57.2
46.1
40.1
38.2
37.9
37.9
34.2
32.9
30.2
30.2
20.4
15.9
13.4
10.7
MeO
HO
HN
O
O
O
O
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


HN
O
O
OH
OH
O
O
1.00
0.97
0.96
0.99
0.98
1.05
0.98
1.03
1.05
1.90
1.07
1.05
2.41
1.13
3.23
2.47
0.89
2.20
2.85
4.78
1.36
1.27
3.03
3.03
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

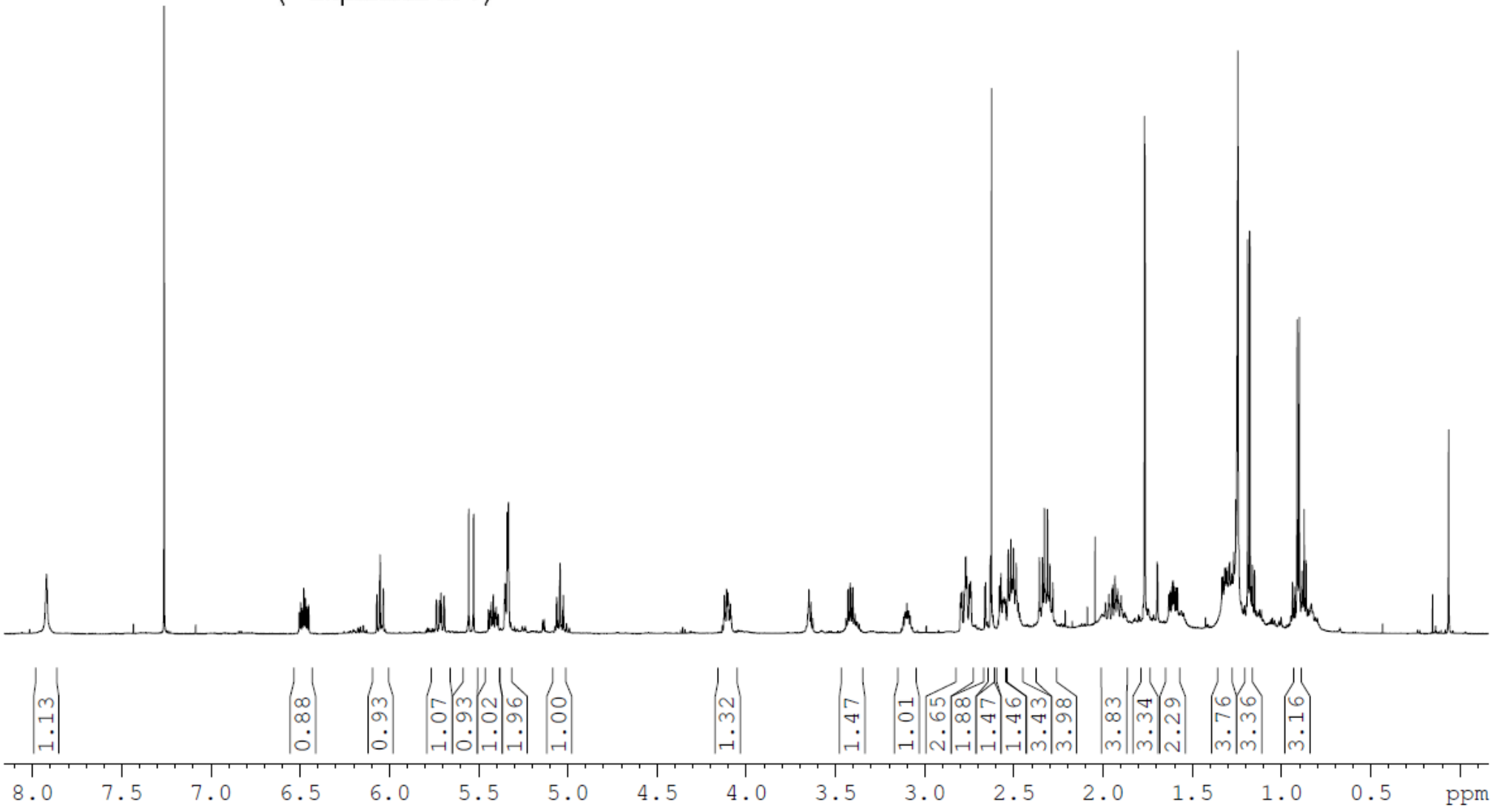

172.31
172.26
166.79
146.78
134.58
133.58
131.83
131.39
129.41
128.40
128.10
82.89
69.29
42.44
40.72
39.80
38.66
37.27
35.66
32.43
31.29
26.98
17.80
16.62
15.50
HN
OH
OH
O
O
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

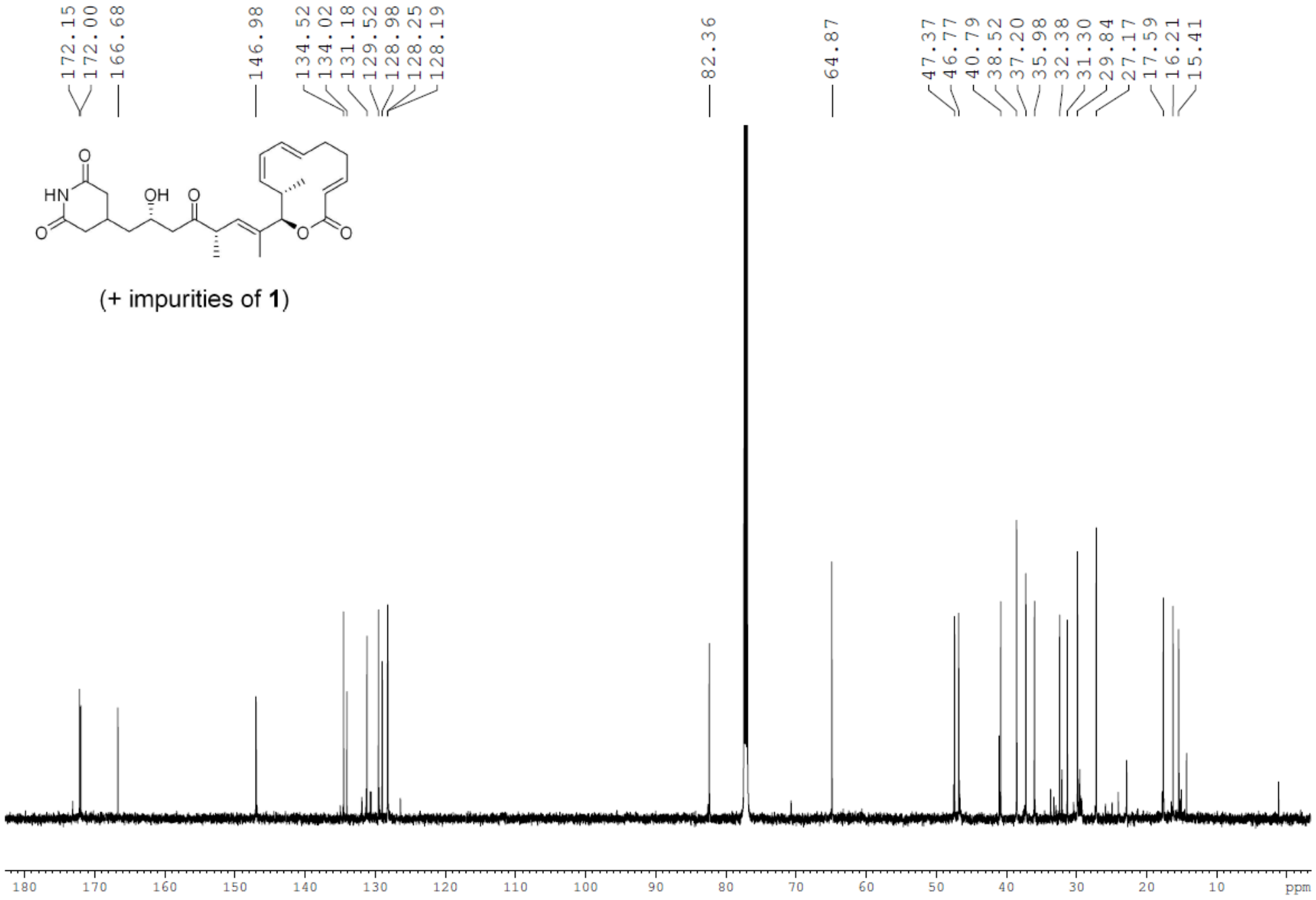

HN
O
O
O
O
O
1.06
1.00
0.94
1.02
0.99
0.97
0.96
3.08
1.05
1.00
1.03
2.22
2.09
5.40
2.12
2.93
3.38
3.50
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


199.26
171.29
171.28
171.23
171.22
166.74
146.85
141.62
141.56
134.57
133.58
131.49
131.45
130.89
130.81
129.39
129.35
129.30
128.33
128.08
128.05
82.65
45.11
37.52
37.49
37.39
36.04
32.39
31.31
29.84
17.53
16.27
15.28
HN
O
O
O
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

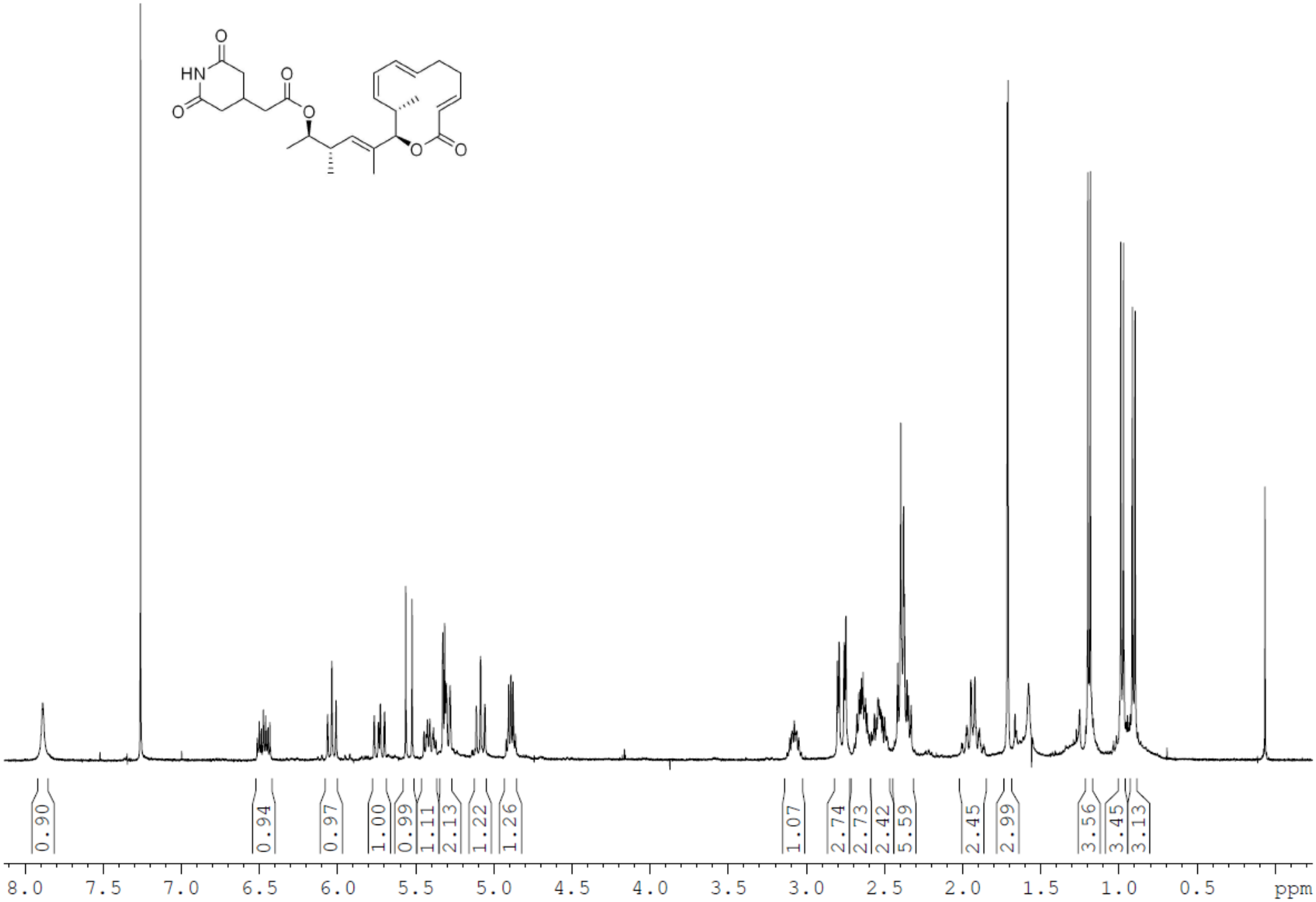


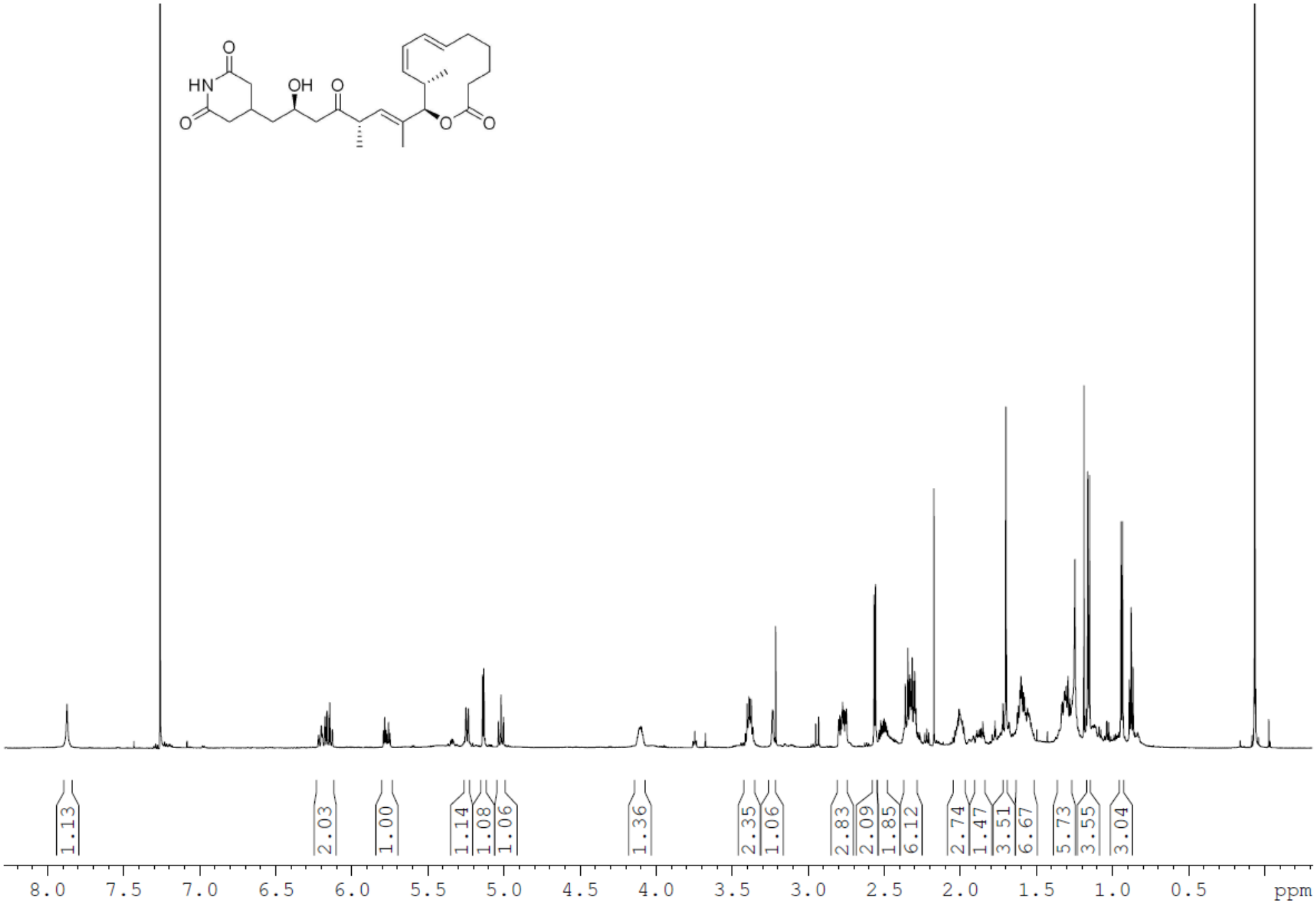
(+ impurities of **1**)

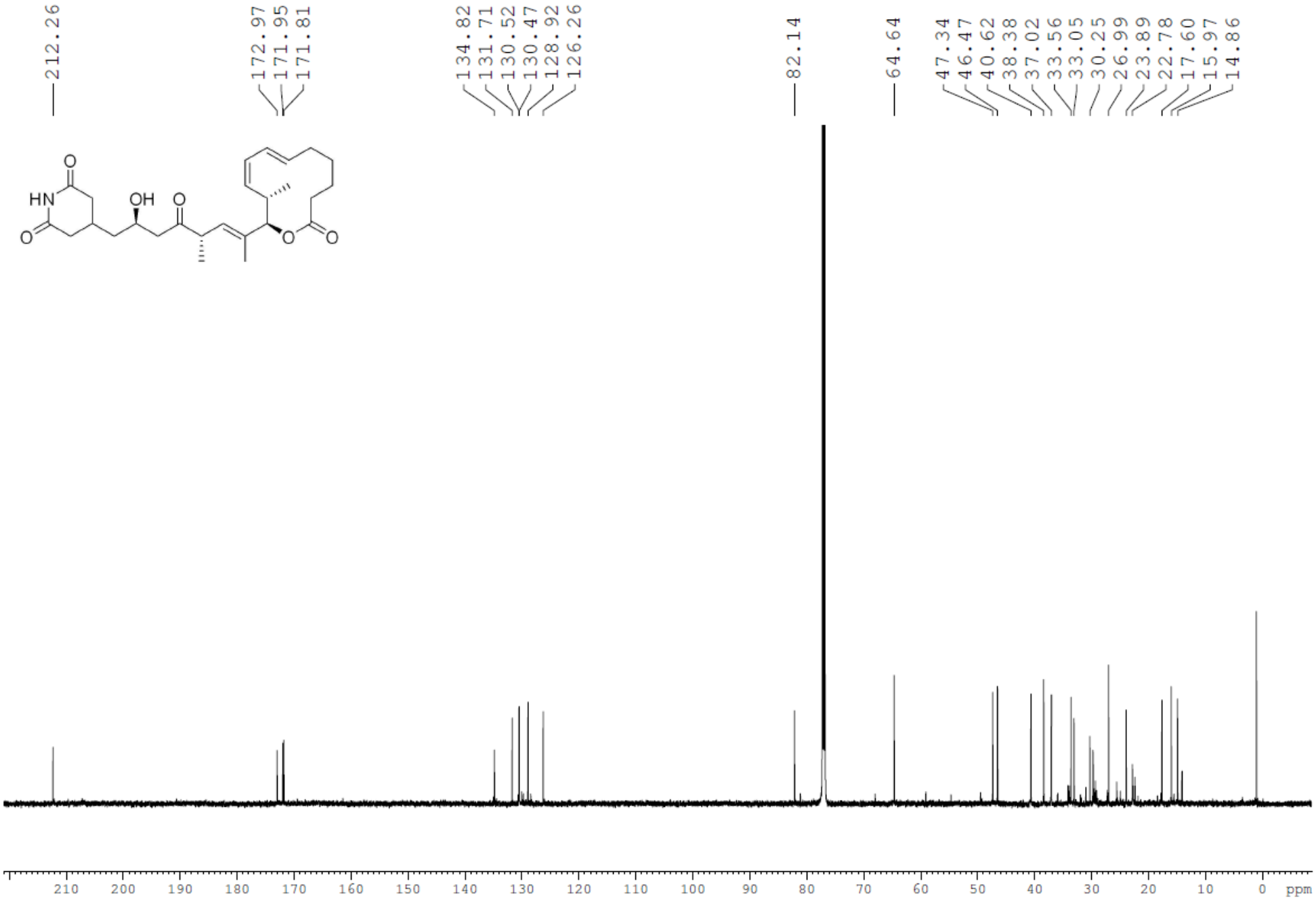


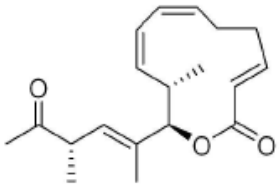


(+ impurities of **1**)

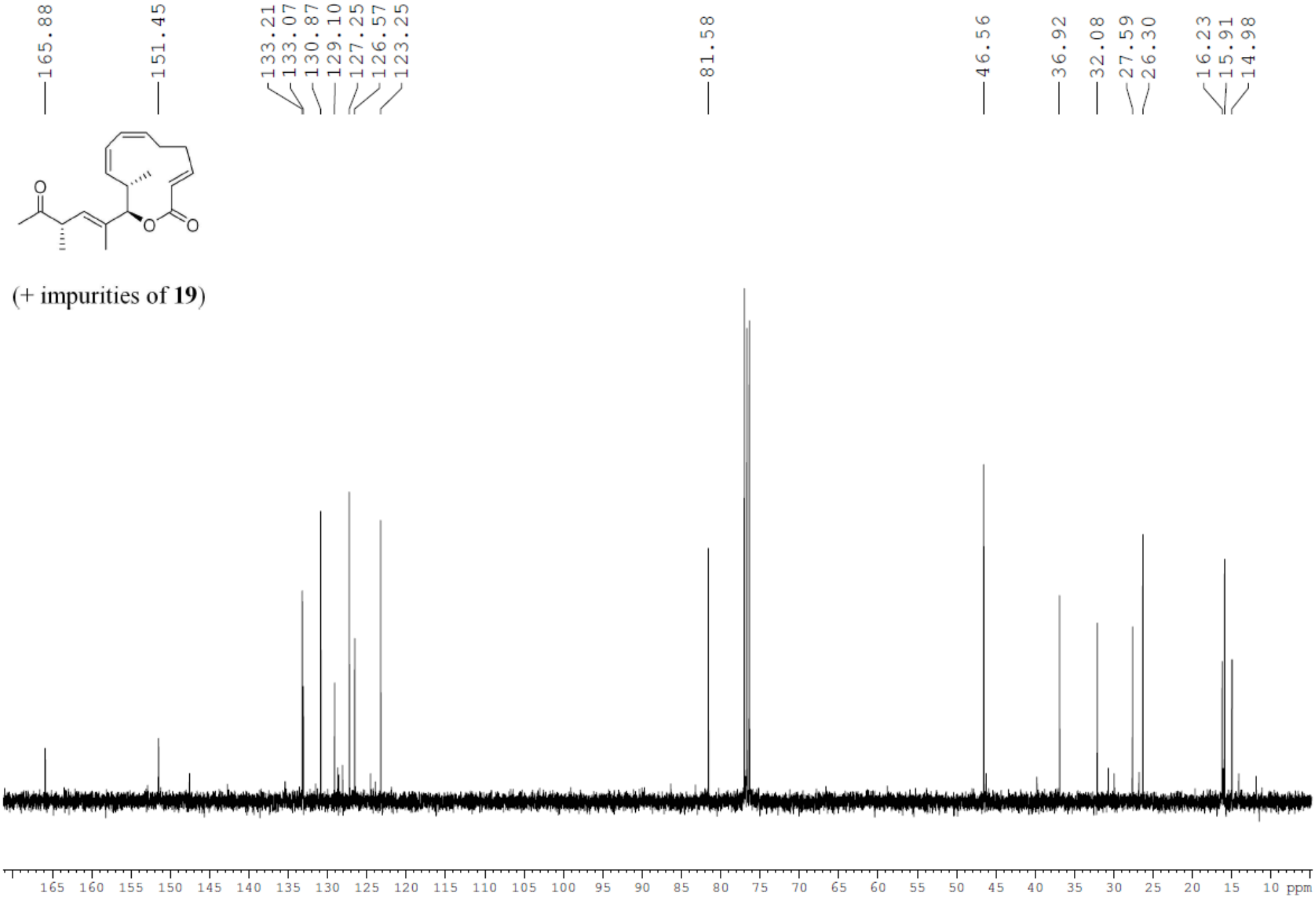

HN
O
O
O
O
O
O
0.90
0.94
0.97
1.00
0.99
1.11
2.13
1.22
1.26
1.07
2.74
2.73
2.42
5.59
2.45
2.99
3.56
3.45
3.13
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

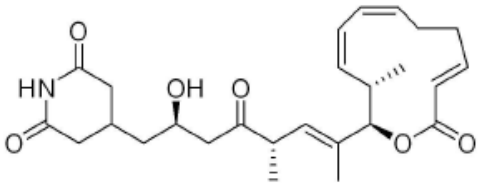

HN
OH
O
O
O
O
O
1.13
2.03
1.00
1.14
1.08
1.06
1.36
2.35
1.06
2.83
2.09
1.85
6.12
2.74
1.47
3.51
6.67
5.73
3.55
3.04
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


212.26
172.97
171.95
171.81
134.82
131.71
130.52
130.47
128.92
126.26
82.14
64.64
47.34
46.47
40.62
38.38
37.02
33.56
33.05
30.25
26.99
23.89
22.78
17.60
15.97
14.86
HN
OH
O
O
O
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

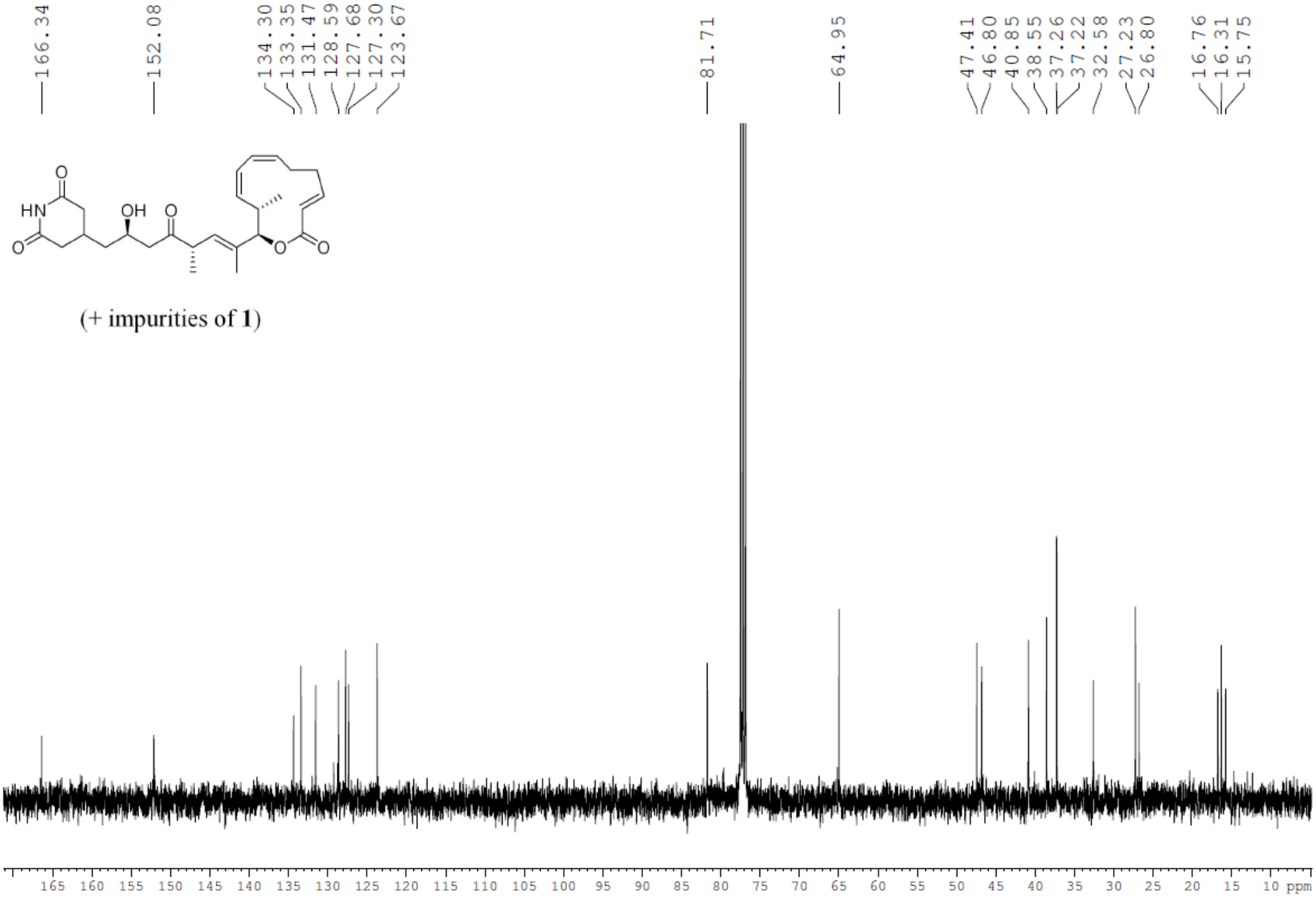


(+ impurities of **19**)

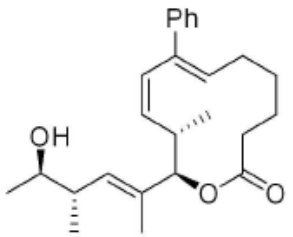

165.88
151.45
133.21
133.07
130.87
129.10
127.25
126.57
123.25
81.58
46.56
36.92
32.08
27.59
26.30
16.23
15.91
14.98
O
O
O
(+ impurities of 19)
165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 ppm

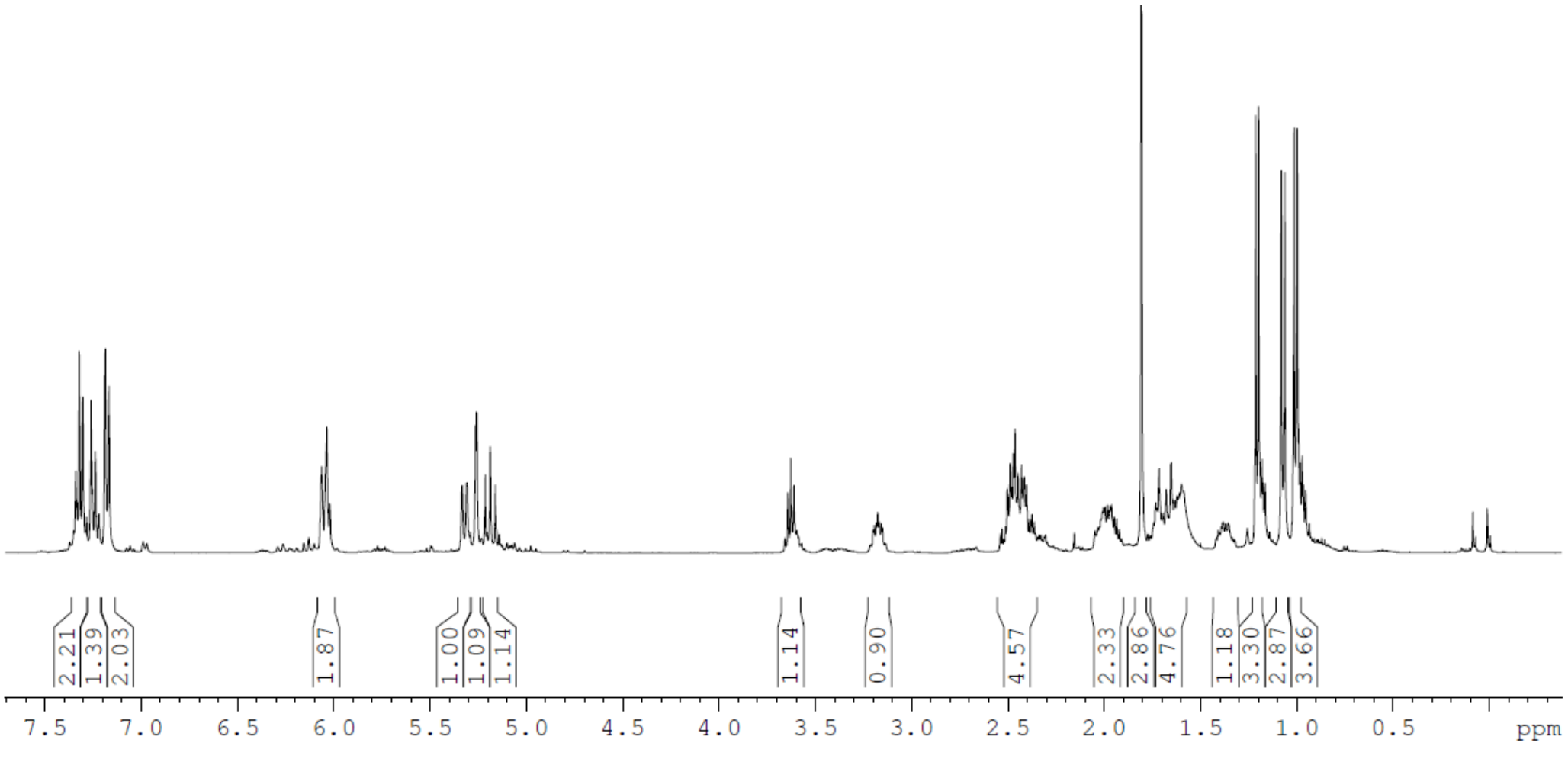


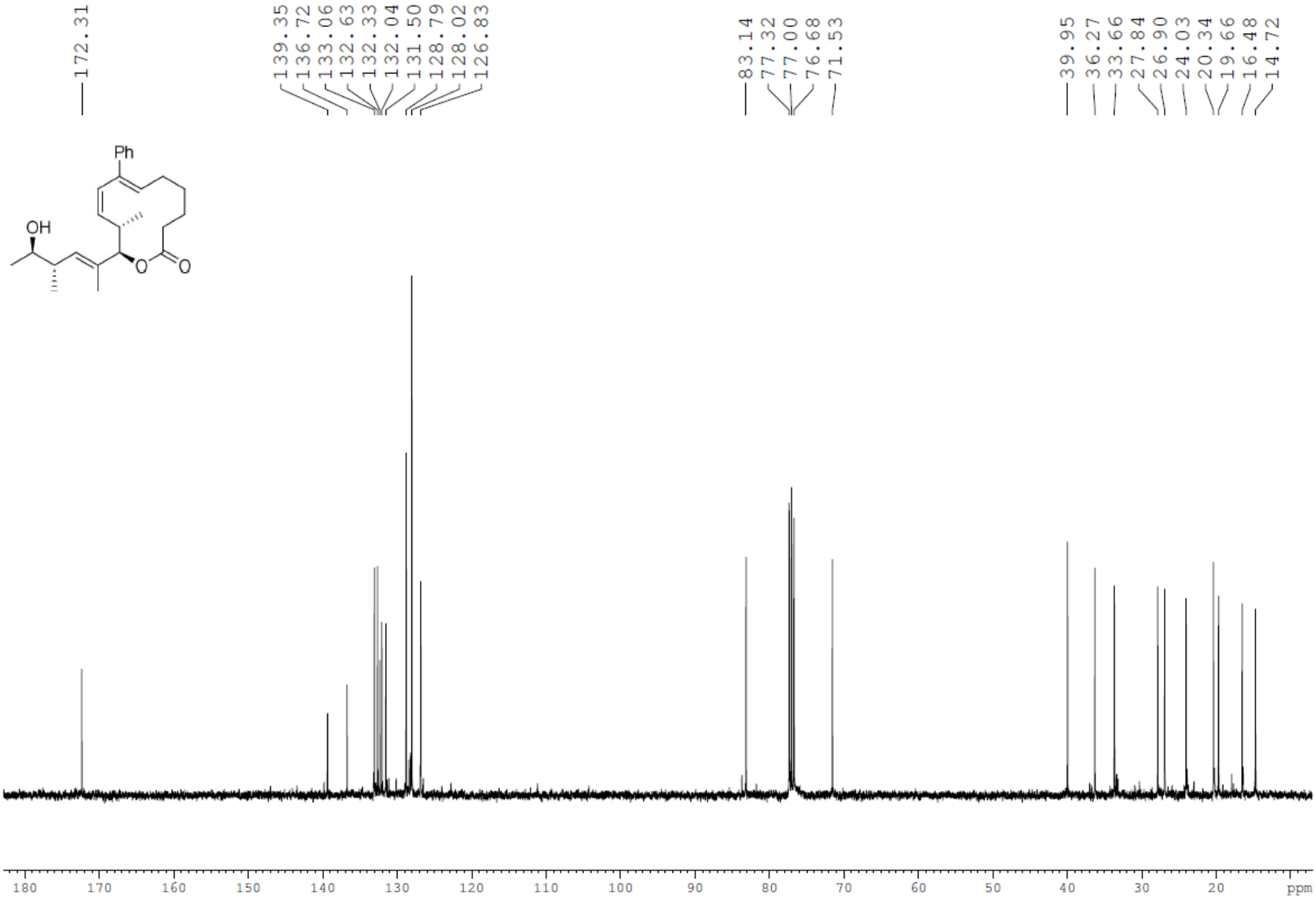
(+ impurities of **1**)

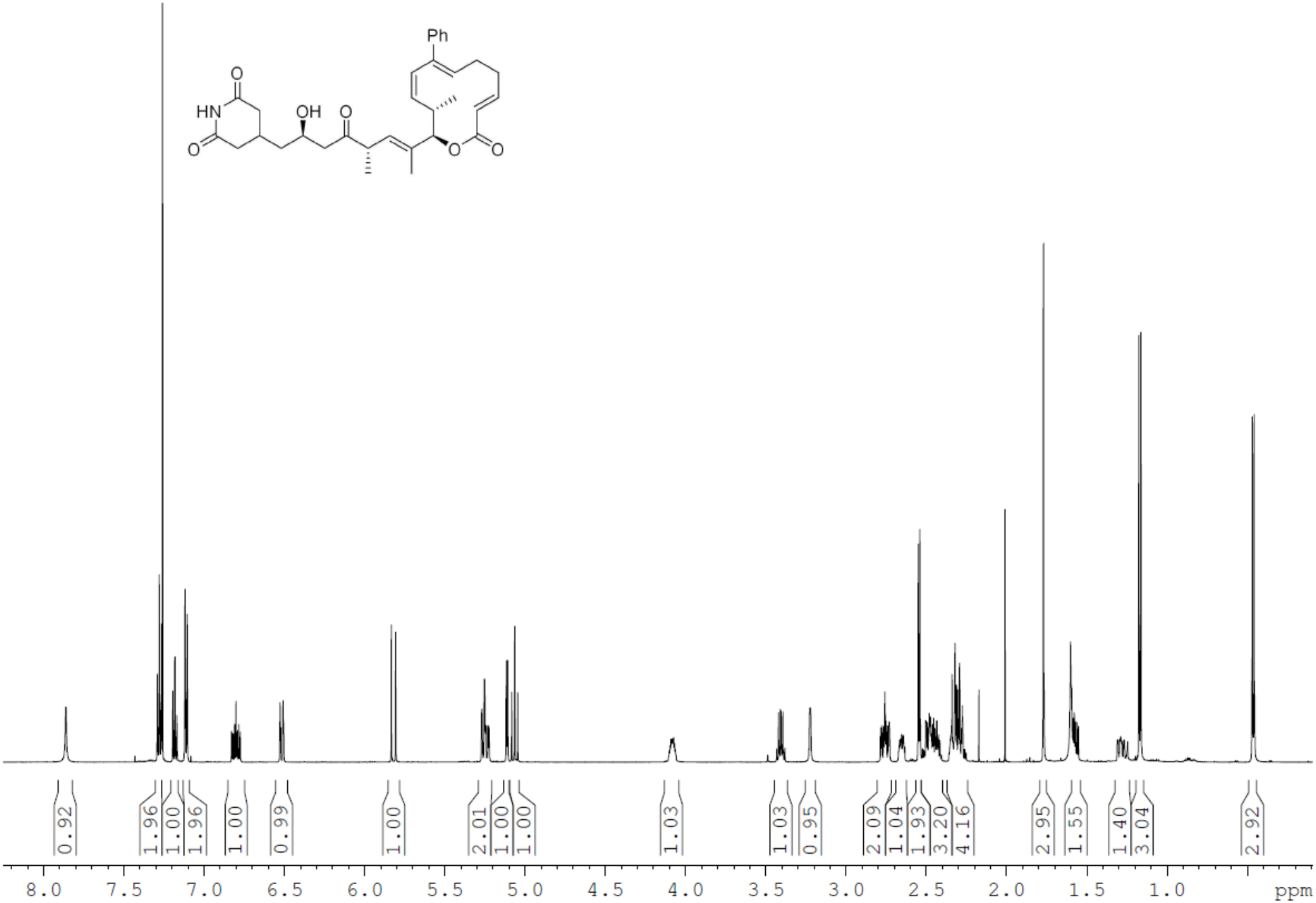


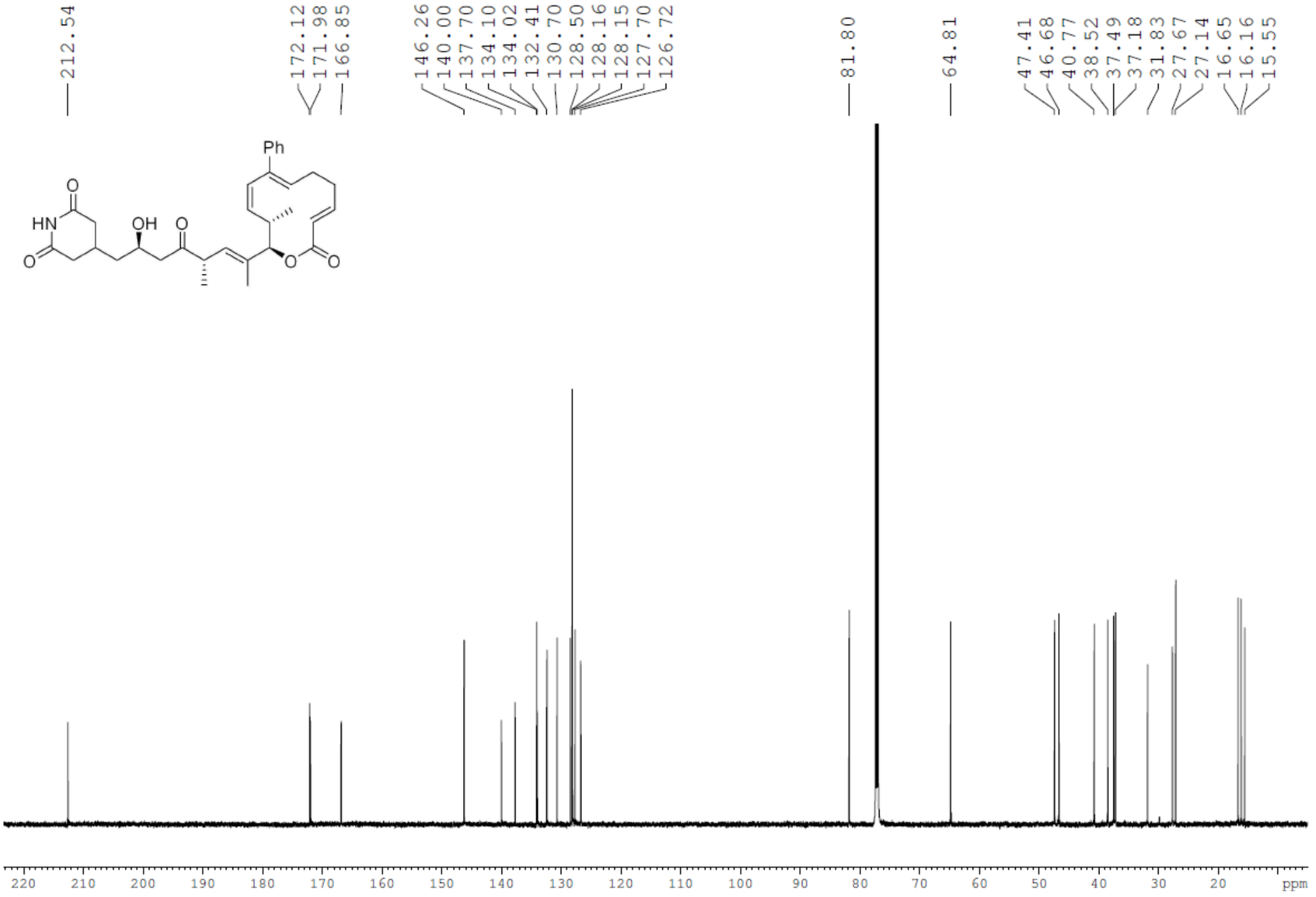
(+ impurities of **1**)


Ph
OH
O
O


2.21
1.39
2.03
1.87
1.00
1.09
1.14
1.14
0.90
4.57
2.33
2.86
4.76
1.18
3.30
2.87
3.66
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


172.31
139.35
136.72
133.06
132.63
132.33
132.04
131.50
128.79
128.02
126.83
83.14
77.32
77.00
76.68
71.53
39.95
36.27
33.66
27.84
26.90
24.03
20.34
19.66
16.48
14.72
Ph
OH
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


Ph
HN
OH
O
O
O
O
O
0.92
1.96
1.00
1.96
1.00
0.99
1.00
2.01
1.00
1.00
1.03
1.03
0.95
2.09
1.04
1.93
3.20
4.16
2.95
1.55
1.40
3.04
2.92
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


212.54
172.12
171.98
166.85
146.26
140.00
137.70
134.10
134.02
132.41
130.70
128.50
128.16
128.15
127.70
126.72
81.80
64.81
47.41
46.68
40.77
38.52
37.49
37.18
31.83
27.67
27.14
16.65
16.16
15.55
Ph
HN
OH
O
O
O
O
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm