SUPPORTING INFORMATION

Catalysis-Based Total Syntheses of Pateamine A and DMDA-Pat A

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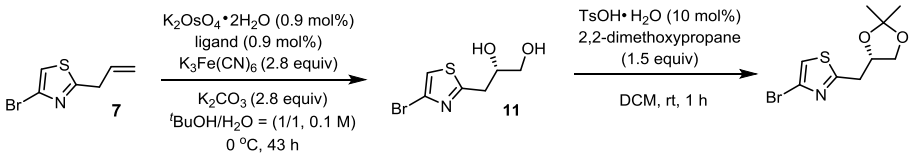
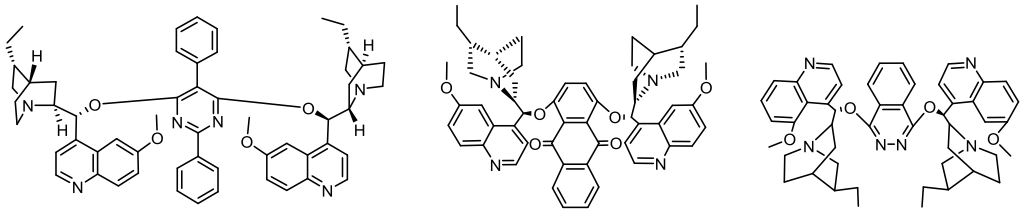
Attempted Preparation of Diol 10 and the Derived Isopropylidene Acetal

by Sharpless Asymmetric Dihydroxylation





$(DHQ)_2PYR$

0 °C, 43 h, 99%, **33% ee**

$(DHQD)_2AQN$

0 °C, 4 h, 99%, **-65% ee**

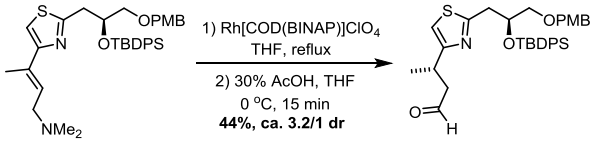
-10 °C, 26 h, 95%, **-62% ee**

$(DHQD)_2PHAL$

0 °C, 7.5 h, 99%, **-4% ee**

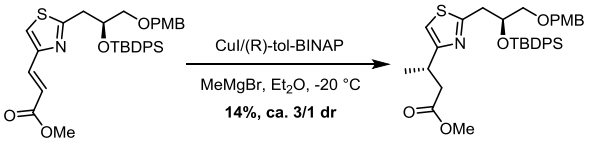
Different Methods Tested for Setting the Methyl-Branched Chiral Center C5

1) Rh-catalyzed enantioselective allylic migration:



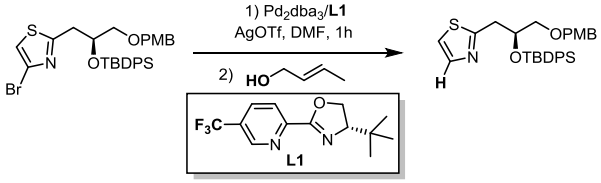
K. Tani, S. Otsuka, R. Noyori et al., *J. Am. Chem. Soc.* **1984**, *106*, 5208.

2) Enantioselective Cu-catalyzed 1,4-addition:



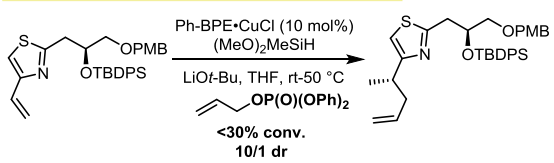
T.-P. Loh et al., *Adv. Synth. Catal.* **2008**, *350*, 673.

3) Enantioselective Heck arylations using a redox-relay strategy:



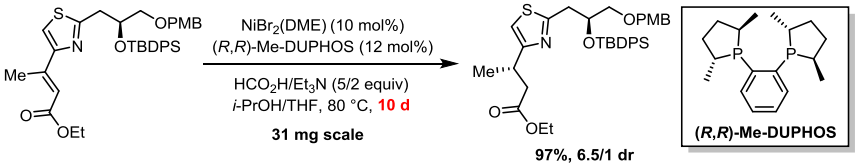
M. S. Sigman et al., *Science*, **2012**, *338*, 1255.

4) Enantioselective Cu-catalyzed hydroallylation:



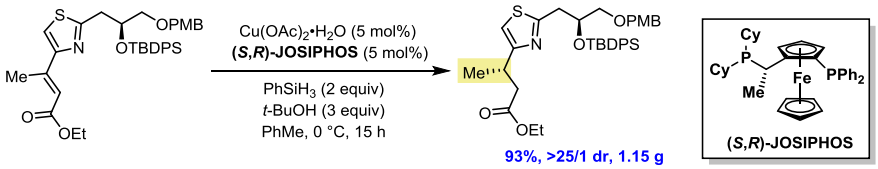
S. L. Buchwald et al., *J. Am. Chem. Soc.* **2016**, *138*, 5024.

5) Enantioselective Ni-catalyzed transfer hydrogenation:



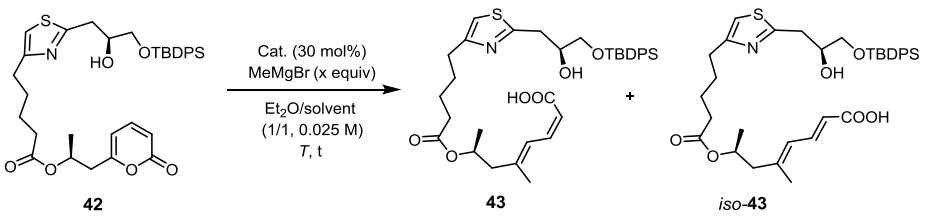
J. Zhou et al., *Chem. Commun.* **2015**, *51*, 12115.

6) Enantioselective Cu-catalyzed 1,4-reduction:



H. W. Lam et al., *J. Am. Chem. Soc.* **2009**, *131*, 10386.

Optimization of the Iron Catalyzed Pyrone Ring Opening/Cross Coupling en route to DMDA Pat A

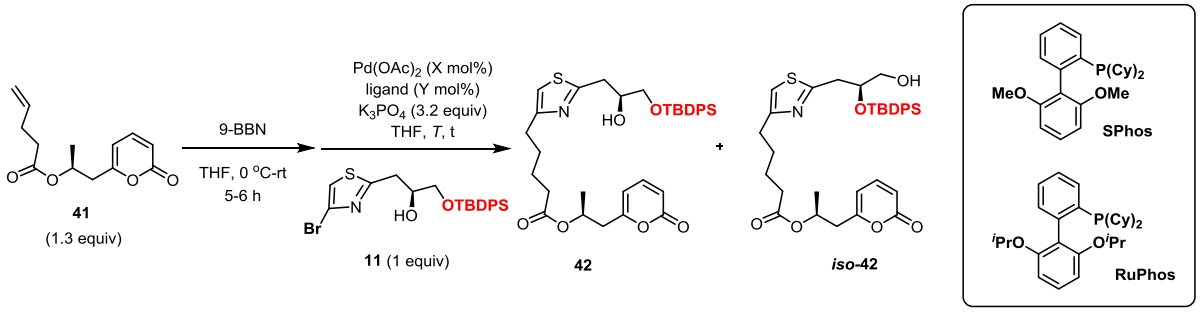


42 43 *iso*-43

Entry[a]	Cat.	X (equiv)	Co-Solvent[a]	*T* (°C)	t (h)	Conv. (%)[b]	43:*iso*-43[b]
1	$Fe(acac)_3$	5	toluene	-50	2	70	17/1
2	$FeCl_2 \cdot 1.5THF$[c]	7	toluene	-60	5.5	75	11/1
3	$FeBr_2$	5	toluene	-50	3[d]	<5	ND
4	$Fe(acac)_3$	7	toluene	-60	4	82	12/1
5	$Fe(acac)_3$	7	toluene	-60	2.5[d]	51	>30/1
6	$Fe(acac)_3$	10	toluene	-50	3.5	87	10/1
7	$Fe(acac)_3$	10	CPME	-30	17[e]	92	10/1
8	$Fe(acac)_3$	8.4	CPME	-30	3.5[f]	86 (75)	18/1

[a] MeMgBr (0.5 M in Et_2O, added via syringe pump (0.14 mmol/h), Et_2O/co-solvent (1:1, 0.025 M). [b] Determined by LC-MS. [c] 68 mol% of the iron precatalyst was used. [d] The MeMgBr was added by syringe. [e] The addition rate of MeMgBr was 0.88 mmol/h. [f] The adding rate of MeMgBr was 0.79 mmol/h.

Optimization of the Alkyl-Suzuki Coupling en route to DMDA Pat A[a]



41 (1.3 equiv) 11 (1 equiv) 42 *iso*-42

Entry	$Pd(OAc)_2$ (mol%)	ligand (mol%)	*T* (°C)	t (min)	42:*iso*-42[b]	Yield (%)[c]
1	14	$AsPh_3$, 30	50	60	84/16	61
2	14	SPhos, 30	65	10	87/13	77
3	6	SPhos, 10	rt	150	89/11	73
4	5	RuPhos, 10	50	30	88/12	82[d]

[a] Reaction conditions: (i) **41** (0. 2 mmol), 9-BBN (0.5 mL, 0.5 M in THF), THF, 0 °C to rt; (ii) **11** (0. 15 mmol), $Pd(OAc)_2$ (X mol%), ligand (Y mol%), K_3PO_4 (3.2 equiv), THF. [b] Determined by LC-MS analysis. [c] Isolated yield of analytically pure **42**. [d] The reaction was performed on a 1.3 g scale.

Experimental details and characterization data

General. Unless stated otherwise, all reactions were carried out in flame-dried glassware using anhydrous solvents under argon. The solvents were purified by distillation over the following drying agents and were transferred under argon: THF, Et_2O (Mg/anthracene), CH_2Cl_2, toluene (Na/K), MeOH (Mg, stored over MS 3 Å), EtOAc (CaH_2, stored over MS 4 Å); DMF, DMSO, Et_3N and pyridine were dried by an adsorption solvent purification system based on molecular sievess; anhydrous (99.9%) cyclopentyl methyl ether (CPME) purchased from Aldrich was kept in a flame-dried Schlenk flask containing MS 4 Å under argon. HCl (4 M in 1,4-dioxane, 99%) was purchased from Alfa Aesar and kept in a flame-dried Schlenk flask under argon. Thin layer chromatography (TLC): Macherey-Nagel precoated plates (POLYGRAM®SIL/UV254); Preparative TLC: Macherey-Nagel precoated plates (SIL G-100 UV 254; silica gel layer: 1.0 mm); Flash chromatography: Merck silica gel 60 (40–63 µm) with predistilled or HPLC grade solvents. Amino column chromatography was performed using 500-mg Bakerbond™ spe amino (NH_2) disposable extraction columns (3 mL solid phase extraction columns, 500 mg per column). NMR: Spectra were recorded on Bruker DPX 300, AV 400, AV 500 or AVIII 600 spectrometers in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (*J*) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: δ_C = 77.0 ppm; residual $CHCl_3$ in $CDCl_3$: δ_H = 7.26 ppm; [D_6]-acetone: δ_C = 206.3, 29.8 ppm; residual acetone: δ_H = 2.05 ppm). IR: Spectrum One (Perkin-Elmer) spectrometer, wavenumbers ($\tilde{\nu}$) in cm^{-1}. MS (EI): Finnigan MAT 8200 (70 eV), ESI-MS: ESQ3000 (Bruker), accurate mass determinations: Bruker APEX III FTMS (7 T magnet) or Mat 95 (Finnigan). Optical rotations ($[\alpha]_D^{20}$) were measured with a Perkin-Elmer Model 343 polarimeter. LC-MS analyses were conducted on a Shimadzu LC-MS 2020 instrument (pumps LC-20AD, autosampler SIL-20AC, column oven CTO-20AC, diode array detector SPD-M20A, controller CBM-20A, ESI detector and software Labsolutions) with a ZORBAX Eclipse Plus column (C18 1.8 µm, 4.6 mm ID × 50 mm (Agilent)) or a YMC-Pack Pro C18 column (S-5 µm, 120 Å, 2.1 mm ID × 150 mm). A binary gradient of MeCN or MeOH in water, aq. triethylammonium acetate buffer (10 mmol, pH 8) or aq. trifluoroacetatic acid buffer (0.1 %) were used as eluents at a flow rate of 0.2 mL/min (2.1 mm ID), or 0.8 mL/min (4.6 mm ID). The oven temperature was kept at 35 °C. Conditions for each compound are specified below. Chiral HPLC analyses were conducted on a Shimadzu LC 20 instrument (pumps LC-20AB, autosampler SIL-20AC, column oven CTO-20AC, diode array detector SPD-M20A, controller CBM-20A, and software Labsolutions) with a Daicel Chiralpak IC-3 or IG-3 column (4.6 mm × 150 mm). Unless stated otherwise, all commercially available compounds (Alfa Aesar, Aldrich, TCI, Strem Chemicals) were used as received.

$[Ph_2PO_2][NBu_4]$ was prepared and purified as previously described in the Supporting Information of a previous publication from our group;[1] the material was stored under Ar.

Detailed experimental procedures for the preparation of compounds **7**, **11**, **29**, **30**, **31**, **41**, **42**, **43**, **44**, **45** and DMDA-Pat A (**2**) together with copies of their spectra are contained in the Supporting Information to our Preliminary Communication.[2]

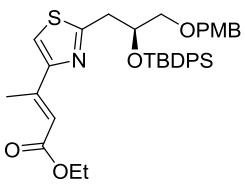
(*S*)-3-(4-Bromothiazol-2-yl)propane-1,2-diol (**10**). A pressure tube equipped with a magnetic stir bar was charged with $Pt(dba)_3$ (0.15 mmol, 134.6 mg), ligand **8** (0.18 mmol, 163.6 mg), and $B_2(pin)_2$ (9.75 mmol, 2.47 g). The tube was evacuated and refilled with argon. THF (7.5 mL) was added via syringe and the resulting solution stirred at 80 °C for 30 min. The tube was cooled to room temperature before 2-allyl-4-bromothiazole **7** (7.50 mmol, 1.53 g, freshly distilled before use)[2] was introduced. The tube was sealed and stirring continued at 60 °C for 27 h. For work up, the mixture was cooled to ambient temperature and transferred into a 100 mL two-necked round bottom flask, rinsing with THF (2 × 5 mL). The mixture was cooled to 0 °C before aq. NaOH (3 M, 21.0 mL) was added, followed by dropwise addition of hydrogen peroxide (30% *w/w*, 10.6 mL). The mixture was gradually warmed to room temperature and stirring continued for 5 h before the reaction was quenched at 0 °C by dropwise addition of sat. aq. sodium thiosulfate (10 mL) over 10 min. The mixture was diluted with ethyl acetate and the aqueous layer extracted with ethyl acetate (6 × 30 mL). The combined extracts were dried over $MgSO_4$, filtered, and concentrated, and the residue was purified by flash chromatography on silica gel (hexane/EtOAc = 1/1 to 1/3, then EtOAc/MeOH = 25/1) to yield the title compound (1.63 g, 91%, 91% ee).[2] After recrystallization twice in hexane/EtOAc, 1.17 g of the diol with an ee of 96.7% were obtained. [Conditions for HPLC analysis: Daicel Chiralpak IC-3 (4.6 mm × 150 mm), *n*-heptane/2-propanol = 80/20, *v* = 1.0 mL·min^{-1}, λ = 250 nm, t (minor) = 7.93 min, t (major) = 5.75 min]; $[\alpha]_D^{20} = -14.0$ (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.13 (s, 1H), 4.19-4.13 (m, 1H), 3.74 (dd, *J* = 11.6, 4.0 Hz, 1H), 3.66 (br. s, 1H), 3.60 (dd, *J* = 11.2, 6.0 Hz, 1H), 3.18 (d, *J* = 6.0 Hz, 2H), 2.67 (br. s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 124.3, 116.6, 70.8, 65.6, 36.6. IR (film, cm^{-1}): 3341, 3167, 3125, 3063, 2918, 2863, 1477, 1256, 1072, 1035, 899, 624, 436. MS (EI): *m*/*z* (%) 239 (1.5), 208 (65), 179 (100), 138 (10), 99 (12). HRMS (ESI): *m*/*z*: calcd for: $C_6H_8NO_2BrSNa$ [*M*+Na$^+$]: 259.93515, found: 259.93503.

(*S*)-1-(4-Bromothiazol-2-yl)-3-((4-methoxybenzyl)oxy)propan-2-ol (**S1**). *p*-Anisaldehyde dimethyl acetal (9.14 mmol, 1.67 g, freshly distilled) and (±)-10-camphorsulfonic acid (0.84 mmol, 193.9 mg) were added at ambient temperature to a suspension containing compound **10** (4.15 mmol, 0.989 g, 96.7% ee) and molecular sieves (5 Å, 2.2 g) in CH_2Cl_2 (46 mL). The resulting mixture was gently stirred at reflux temperature for 17 h. The mixture was cooled to ambient temperature, filtrated through a pad of Celite and the reaction was quenched with sat. aq. Na_2CO_3. The aqueous phase was extracted with CH_2Cl_2 (4 × 25 mL) and the combined organic layers were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated to an oily residue, which was purified by flash chromatography on silica gel (hexane/EtOAc = 20/1 to 4/1) to yield the corresponding *p*-methoxybenzylideneacetal as a mixture of diastereoisomers (1.48 g, quant.). This material was directly used in the next step.

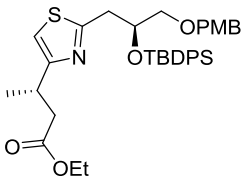
Diisobutylaluminum hydride (11.2 mL, 1 M in CH_2Cl_2) was added dropwise over 2.5 h via syringe pump to a solution of the crude acetal (3.73 mmol, 1.33 g) in CH_2Cl_2 (40 mL) at −78 °C. Stirring was continued for 25 min at this temperature before the reaction was quenched by dropwise addition of MeOH (2 mL), followed by slow addition of sat. aq. Rochelle salt (40 mL). The mixture was slowly warmed to ambient temperature and poured into a 250 mL flask containing ca. 100 mL of *tert*-butyl methyl ether and ca. 20 mL of sat. aq. Rochelle salt. The resulting mixture was vigoriously stirred at ambient temperature for 4 h.

The aqueous phase was extracted with *tert*-butyl methyl ether (4 × 50 mL) and the combined organic layers were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated to an oily residue, which was purified by flash chromatography on silica gel (hexane/EtOAc = 8/1 to 2/1) to yield the title compound as a yellow oil (1.15 g, 86%). $[\alpha]_D^{20} = -10.1$ (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 – 7.21 (m, 2H), 7.10 (s, 1H), 6.91 – 6.84 (m, 2H), 4.48 (s, 2H), 4.27 – 4.12 (m, 1H), 3.80 (s, 3H), 3.51 (dd, *J* = 9.6, 4.4 Hz, 1H), 3.45 (dd, *J* = 9.6, 6.0 Hz, 1H), 3.21 (dd, *J* = 15.2, 4.4 Hz, 1H), 3.18 – 3.17 (m, 1H), 3.13 (dd, *J* = 15.2, 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5, 159.3, 129.7, 129.4, 124.1, 116.6, 113.8, 73.0, 72.6, 69.4, 55.2, 37.2. IR (film, cm^{-1}): 3401, 3118, 2907, 2858, 1611, 1511, 1477, 1243, 1079, 832. MS (ESI): *m*/*z*: 380 [*M*+*Na*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{14}H_{16}NO_3SBrNa$ [*M*+*Na*$^+$]: 379.99266, found: 379.99292.

Ethyl (*S*,*E*)-3-(2-(2-((*tert*-butyldiphenylsilyl)oxy)-3-((4-methoxybenzyl)oxy)propyl)thiazol-4-yl)but-2-enoate (**13**). *tert*-Butyldiphenylchlorosilane (4.35 mmol, 1.2 g) was added to a solution of compound **S1** (3.63 mmol, 1.3 g), imidazole (10.9 mmol, 0.74 g), and 4-(dimethylamino)pyridine (0.44 mmol, 0.054 g) in CH_2Cl_2 (40 mL) at ambient temperature. The resulting mixture was stirred for 15 h before the reaction was quenched with H_2O. The aqueous phase was extracted with EtOAc (4 × 25 mL) and the combined organic layers were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated to an oily residue, which was purified by flash chromatography on silica gel (hexane/EtOAc = 30/1 to 20/1) to yield the silyl ether **12** (contaminated with ca. 15% of *tert*-butyldiphenylsilanol) as a yellow oil (2.3 g). This material was directly used in the next step.



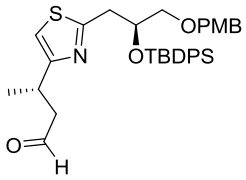
Alkenylboronic acid ester **16** (3.79 mmol, 0.91 g)[3] was added to a solution of compound **12** (2.006 g), K_3PO_4 (9.5 mmol, 2.02 g), H_2O (0.3 mL), 1,1'-bis(di-*tert*-butylphosphino)ferrocene (0.11 mmol, 53.9 mg) and $Pd(OAc)_2$ (0.095 mmol, 21.2 mg) in toluene (30 mL) at ambient temperature. The resulting mixture was stirred at 88 °C for 2 h before it was cooled to ambient temperature and diluted with EtOAc and H_2O. The aqueous phase was extracted with EtOAc (4 × 25 mL) and the combined organic layers were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc = 20/1 to 15/1) to yield the title compound as a yellow oil (1.753 g, 88%). $[\alpha]_D^{20} = -22.8$ (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 6.8 Hz, 2H), 7.58 (d, *J* = 7.2 Hz, 2H), 7.46 – 7.30 (m, 6H), 7.29 (s, 1H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.92 (s, 1H), 6.82 (d, *J* = 8.8 Hz, 2H), 4.38-4.32 (m, 1H), 4.29 – 4.17 (m, 4H), 3.80 (s, 3H), 3.39 – 3.31 (m, 2H), 3.27 (dd, *J* = 14.8, 6.0 Hz, 1H), 3.21 (dd, *J* = 14.8, 4.8 Hz, 1H), 2.55 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 3H), 0.98 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.5, 166.7, 159.0, 155.7, 146.4, 135.9, 135.8, 134.0, 133.2, 130.2, 129.7, 129.6, 129.2, 127.6, 127.5, 117.7, 117.3, 113.6, 72.7, 72.6, 71.5, 59.7, 55.2, 38.3, 26.8, 19.2, 15.6, 14.3. IR (film, cm^{-1}): 3070, 2930, 2856, 1708, 1626, 1512, 1247, 1110, 700, 507. MS (ESI): *m*/*z*: 630 [*M*+*H*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{36}H_{44}NO_5SSi$ [*M*+*H*$^+$]: 630.27040, found: 630.27078.



Ethyl (*S*)-3-(2-((*S*)-2-((*tert*-butyldiphenylsilyl)oxy)-3-((4-methoxybenzyl)oxy)-propyl)thiazol-4-yl)butanoate (**14**). A solution of compound **13** (1.83 mmol, 1.15 g), *t*-BuOH (5.5 mmol, 0.52 mL), (*S*)-(*R*)-JOSIPHOS (**17**) (0.091 mmol, 58.5 mg), $Cu(OAc)_2 \cdot H_2O$ (0.091 mmol, 18.2 mg) and toluene (10 mL) was stirred at 0 °C for 15 min. Phenylsilane (3.65 mmol, 395.4 mg) was added dropwise at 0 °C and

stirring was continued at this temerature for 15 h. The reaction was quenched by the dropwise addition of H_2O. The aqueous layer was extracted with *tert*-butyl methyl ether (4 × 20 mL) and the combined organic layers were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc = 20/1 to 10/1) to yield the title compound as a colorless oil [1.07 g, 93%, > 25/1 dr (determined by HPLC analysis)]. [Conditions for HPLC analysis: Daicel Chiralpak IG-3 (4.6 mm × 150 mm), *n*-heptane/2-propanol = 99/1, *v* = 1.0 mL·min^{-1}, λ = 220 nm]. $[\alpha]_D^{20} = -23.2$ (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 – 7.69 (m, 2H), 7.64 – 7.56 (m, 2H), 7.46 – 7.29 (m, 6H), 7.09 (d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 6.79 (s, 1H), 4.36 – 4.28 (m, 1H), 4.22 (q, *J* = 11.2 Hz, 2H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.80 (s, 3H), 3.50 – 3.39 (m, 1H), 3.39 – 3.30 (m, 2H), 3.30 – 3.16 (m, 2H), 2.82 (ddd, *J* = 15.0, 6.0, 1.2 Hz, 1H), 2.50 (ddd, *J* = 15.2, 8.4, 1.2 Hz, 1H), 1.35 (d, *J* = 6.8 Hz, 3H), 1.23 (t, *J* = 7.2 Hz, 3H), 0.99 (d, *J* = 1.2 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4, 166.5, 159.9, 158.9, 135.9, 135.8, 134.1, 133.3, 130.3, 129.6, 129.5, 129.1, 127.5, 127.4, 113.5, 111.9, 72.7, 72.6, 71.8, 60.1, 55.2, 41.3, 38.2, 32.9, 26.8, 19.8, 19.2, 14.2. IR (film, cm^{-1}): 3070, 2930, 2856, 1732, 1612, 1513, 1246, 1104, 700, 506. MS (ESI): *m*/*z*: 632 [*M*+*H*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{36}H_{46}NO_5SSi$ [*M*+*H*$^+$]: 632.28605, found: 632.28582.

(*S*)-3-(2-((*S*)-2-((*tert*-Butyldiphenylsilyl)oxy)-3-((4-methoxybenzyl)oxy)propyl)thiazol-4-yl)butanal



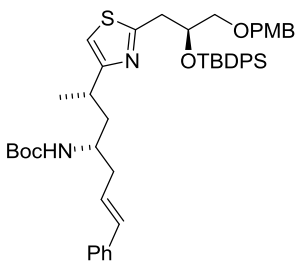
(**15**). Diisobutylaluminum hydride (0.88 mmol, 0.88 mL, 1 M in CH_2Cl_2) was added dropwise via syringe pump over 25 min to a solution of compound **14** (0.863 mmol, 545.1 mg) in CH_2Cl_2 (14 mL) at −80 °C. Stirring was continued for 1 h at this temperature before the reaction was quenched by the dropwise addition of MeOH (0.28 mL), followed by slow addition of sat. aq. Rochelle salt (15 mL). The mixture was slowly warmed to ambient temperature before it was poured into a 250 mL flask containing ca. 100 mL of *tert*-butyl methyl ether and ca. 20 mL of sat. aq. Rochelle salt. The resulting mixture was vigoriously stirred at ambient temperature for 4 h. The aqueous layer was extracted with *tert*-butyl methyl ether (4 × 30 mL) and the combined organic layers were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated. The oily residue was purified by flash chromatography on silica gel (hexane/EtOAc = 4/1 to 2/1) to yield the title compound as a colorless oil (493.3 mg, 97%). $[\alpha]_D^{20} = -26.2$ (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.74 (t, *J* = 2.0 Hz, 1H), 7.69 – 7.66 (m, 2H), 7.62 – 7.54 (m, 2H), 7.46 – 7.28 (m, 6H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.81 (d, *J* = 8.4 Hz, 2H), 6.78 (s, 1H), 4.30 (app quint, *J* = 5.6 Hz, 1H), 4.21 (q, *J* = 11.6 Hz, 2H), 3.80 (s, 3H), 3.52 – 3.44 (m, 1H), 3.37 – 3.28 (m, 2H), 3.27 – 3.17 (m, 2H), 2.86 (ddd, *J* = 16.8, 6.4, 1.6 Hz, 1H), 2.60 (ddd, *J* = 16.8, 7.2, 2.0 Hz, 1H), 1.34 (d, *J* = 6.8 Hz, 3H), 0.98 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.9, 166.9, 159.5, 159.0, 135.9, 135.8, 134.1, 133.4, 130.3, 129.6, 129.5, 129.2, 127.5, 127.4, 113.6, 112.2, 72.7, 72.6, 71.7, 55.2, 50.2, 38.3, 30.8, 26.8, 20.0, 19.2. IR (film, cm^{-1}): 3071, 2930, 2856, 1723, 1612, 1513, 1246, 1104, 700, 506. MS (ESI): *m*/*z*: 588 [*M*+*H*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{34}H_{42}NO_4SSi$ [*M*+*H*$^+$]: 588.25984, found: 588.2594.

***tert*-Butyl ((4*S*,6*S*,*E*)-6-(2-((*S*)-2-((*tert*-butyldiphenylsilyl)oxy)-3-((4-methoxybenzyl)oxy)propyl)thiazol-4-yl)-1-phenylhept-1-en-4-yl)carbamate** (**25**). A solution of aldehyde **15** (0.33 mmol, 195.5 mg) in CH_2Cl_2 (4 mL) was added to a Schlenk tube charged with 9*H*-fluoren-9-amine (0.34 mmol, 61.3 mg)[4] and molecular sieves (4 Å, 450 mg). The Schlenk tube was sealed and the mixture gently stirred at 25 °C for 12 h. For work up, the mixture was filtrated through a short pad of Celite, which was carefully rinsed

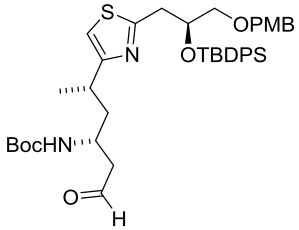
with *tert*-butyl methyl ether. The combined filtrates were concentrated to give the corresponding imine **22** as an oily residue, which was directly used in the next step.

A flame-dried Young Schlenk tube was charged with $[Ir(cod)Cl]_2$ (9.98 μmol, 6.7 mg), ligand **27** (19.95 μmol, 12.0 mg), THF (1.0 mL) and *n*-propylamine (0.5 mL, freshly distilled over CaH_2 under argon). The mixture was stirred at 50 °C for 30 min and the volatile solvents were removed *in vacuo* to yield a yellow solid. The allylic carbonate **23** (0.40 mmol, 93.5 mg),[5] THF (1.0 mL) and DBU (0.40 mmol, 60 μL, freshly distilled over CaH_2 under argon) were successively added. The resulting mixture was cooled to 0 °C before a solution of imine **22** in THF (2.1 mL, rinsing the flask with 3 × 0.5 mL of THF) was added dropwise at 0 °C. The Schlenk tube was sealed and the mixture stirred at 50 °C for 58 h. The crude mixture was cooled to ambient temperature before it was diluted with EtOAc and concentrated. The residue was purified by flash chromatography on basic Al_2O_3 (hexane/EtOAc = 10/1 to 6/1) to yield compound **24** as a yellow oil, which was directly used in the next step.

A solution of hydroxylamine hydrochloride (3.7 mL, 0.5 M in $EtOH/H_2O$ = 4/1) was added to a solution of compound **24** in CH_2Cl_2 (3.6 mL). The mixture was stirred at ambient temperature for 20 min before the reaction was quenched with sat. aq. Na_2CO_3. The aqueous phase was extracted with EtOAc (5 × 25 mL) and the combined organic layers were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated to an oily residue **S2**, which was directly used in the next step.



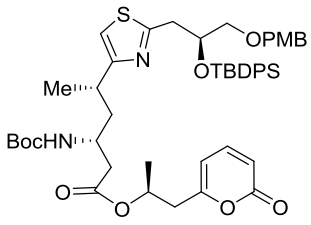
Boc_2O (1.67 mmol, 364 mg) and Et_3N (1.67 mmol, 0.23 mL) were added to a solution of compound **S2** in CH_2Cl_2 (3.6 mL). Stirring was continued for 22 h at ambient temperature before the reaction was concentrated to dryness. The residue was purified by flash chromatography on silica gel (hexane/EtOAc = 20/1 to 6/1) to yield compound **25** as a yellow oil [235.9 mg, 88%, > 25/1 dr (determined by ^{1}H NMR analysis)]. $[\alpha]_D^{20} = -5.2$ (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, [D_6]-Acetone): δ = 7.74 – 7.71 (m, 2H), 7.67 – 7.65 (m, 2H), 7.50 – 7.31 (m, 8H), 7.26 (t, *J* = 7.2 Hz, 2H), 7.19 – 7.15 (m, 1H), 7.11 – 7.08 (m, 2H), 6.98 (s, 1H), 6.86 – 6.80 (m, 2H), 6.39 (d, *J* = 15.6 Hz, 1H), 6.22 (dt, *J* = 16.0, 6.8 Hz, 1H), 5.84 (d, *J* = 9.2 Hz, 1H), 4.36 (app quint, *J* = 5.2 Hz, 1H), 4.24 (d, *J* = 11.6 Hz, 1H), 4.19 (d, *J* = 11.6 Hz, 1H), 3.76 (s, 3H), 3.69 – 3.57 (m, 1H), 3.43 – 3.36 (m, 2H), 3.27 – 3.18 (m, 2H), 3.12 – 3.03 (m, 1H), 2.40 – 2.27 (m, 2H), 1.98 (ddd, *J* = 13.6, 9.2, 4.0 Hz, 1H), 1.75 (ddd, *J* = 14.4, 9.6, 5.2 Hz, 1H), 1.38 (s, 9H), 1.29 (d, *J* = 6.8 Hz, 3H), 0.98 (s, 9H). ^{13}C NMR (100 MHz, [D_6]-Acetone): δ = 166.6, 161.7, 156.3, 138.7, 136.7, 136.6, 135.0, 134.2, 132.6, 131.3, 130.6, 130.5, 130.0, 129.2, 128.5, 128.4, 128.1, 127.7, 126.8, 114.3, 113.4, 78.3, 73.6, 73.2, 73.1, 55.5, 49.7, 42.5, 40.0, 38.9, 34.1, 28.7, 27.3, 21.6, 19.8. IR (film, cm^{-1}): 3070, 2930, 2857, 1710, 1613, 1513, 1246, 1111, 700, 506. MS (ESI): *m*/*z* 805 [$M+H^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{48}H_{61}N_2O_5SSi$ [$M+H^+$]: 805.406508, found: 805.40728.



Compound S3. 2,6-Lutidine (1.46 mmol, 169.6 μL), OsO_4 (4% in water, 29.1 μmol, 185 μL), and $NaIO_4$ (2.62 mmol, 560 mg) were added to a solution of compound **25** (0.58 mmol, 469 mg) in 1,4-dioxane/H_2O (3/1, 12 mL). The solution was stirred at ambient temperature for 21 h. The reaction was quenched with aq. sat. $Na_2S_2O_3$ and the resulting mixture stirred for 30 min.

After dilution with *tert*-butyl methyl ether and H_2O, the aqueous phase was extracted with *tert*-butyl methyl ether (5 × 25 mL). The combined organic layers were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated to an oily residue, which was purified by flash chromatography on silica gel (hexane/EtOAc = 6/1 to 3/1) to yield the title compound as a colorless oil (380.5 mg, 89%). $[\alpha]_D^{20} = -6$ (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.67 (t, *J* = 2.0 Hz, 1H), 7.71 – 7.63 (m, 2H), 7.62 – 7.56 (m, 2H), 7.44 – 7.37 (m, 2H), 7.37 – 7.28 (m, 4H), 7.10 – 7.03 (m, 2H), 6.84 – 6.73 (m, 3H), 4.85 (d, J = 8.8 Hz, 1H), 4.28 (app quint, J = 5.5 Hz, 1H), 4.23 (d, *J* = 11.6 Hz, 1H), 4.17 (d, *J* = 11.6 Hz, 1H), 3.94 – 3.87 (m, 1H), 3.79 (s, 3H), 3.36 – 3.26 (m, 2H), 3.26 – 3.16 (m, 2H), 3.04 – 2.93 (m, 1H), 2.53 (d, *J* = 4.8 Hz, 2H), 1.95 – 1.86 (m, 1H), 1.86 – 1.76 (m, 1H), 1.40 (s, 9H), 1.29 (d, *J* = 6.8 Hz, 3H), 0.98 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 201.2, 166.7, 159.9, 159.0, 155.2, 135.9, 135.8, 134.1, 133.4, 130.3, 129.6, 129.5, 129.1, 127.5, 127.4, 113.6, 112.8, 79.3, 72.7, 72.6, 71.7, 55.2, 49.1, 44.9, 41.5, 38.3, 33.1, 28.3, 26.9, 20.8, 19.2. IR (film, cm^{-1}): 2961, 2930, 2856, 1711, 1513, 1247, 1111, 702, 507. MS (ESI): *m*/*z* 729 [*M*-*H*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{41}H_{53}N_2O_6SSi$ [*M*-*H*$^+$]: 729.33991, found: 729.34048.

Compound 32. A solution of sodium chlorite (1.56 mmol, 141.0 mg) and sodium dihydrogen orthophosphate hydrate (4.16 mmol, 498.9 mg) in water (1.9 mL) was added dropwise to a stirred solution of aldehyde **S3** (0.52 mmol, 380 mg) in *tert*-butyl alcohol/THF (1/1, 7.4 mL) and 2-methyl-2-butene (23.4 mmol, 2.49 mL) at 0 °C. Stirring was continued at 0 °C for 30 min before the reaction was quenched with sat. aq. $Na_2S_2O_3$. The mixture was diluted with EtOAc and H_2O, the aqueous phase was extracted with EtOAc (5 × 25 mL) and the combined organic layers were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated. The residue, which was purified by flash chromatography on silica gel (hexane/EtOAc = 4/1 to 2/1 with 1% of AcOH) to give the desired carboxylic acid **26** as a pale yellow oil, which was directly used in the next step.



1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.16 mmol, 222 mg) and 4-(dimethylamino)pyridine (0.93 mmol, 114 mg) were added to a Schlenk tube containing (*S*)-6-(2-hydroxypropyl)-2*H*-pyran-2-one (0.74 mmol, 114 mg)[2] and acid **26** in CH_2Cl_2 (7.3 mL) at ambient temperature. Stirring was continued for 2 h before the reaction was quenched with H_2O (10 mL). The mixture was diluted with EtOAc and H_2O, the aqueous phase was extracted with EtOAc (5 × 15 mL) and the combined organic layers were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc = 4/1 to 1/1) to yield the title compound as a yellow oil (331.3 mg, 72% over two steps). $[\alpha]_D^{20} = +13$ (*c* = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 – 7.63 (m, 2H), 7.62 – 7.54 (m, 2H), 7.44 – 7.36 (m, 2H), 7.35 – 7.29 (m, 4H), 7.21 (dd, *J* = 9.6, 6.8 Hz, 1H), 7.06 – 7.03 (m, 2H), 6.83 – 6.76 (m, 3H), 6.17 (d, *J* = 9.6 Hz, 1H), 5.99 (d, *J* = 6.4 Hz, 1H), 5.26 – 5.15 (m, 1H), 4.98 (d, *J* = 9.2 Hz, 1H), 4.27 (app quint, *J* = 5.2 Hz, 1H), 4.22 (d, *J* = 11.2 Hz, 1H), 4.16 (d, *J* = 11.2 Hz, 1H), 3.81-3.73 (m, 1H), 3.79 (s, 3H), 3.35-3.26 (m, 2H), 3.27 – 3.14 (m, 2H), 2.99 – 2.94 (m, 1H), 2.72 (dd, *J* = 14.8, 7.2 Hz, 1H), 2.65 (dd, *J* = 14.8, 5.2 Hz, 1H), 2.44 – 2.41 (m, 2H), 1.87 (ddd, *J* = 13.6, 8.4, 4.8 Hz, 1H), 1.80 – 1.75 (m, 1H), 1.41 (s, 9H), 1.28 (d, *J* = 7.2 Hz, 3H), 1.27 (d, *J* = 6.4 Hz, 3H), 0.97 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.8, 166.5, 162.2, 162.0, 160.0, 159.0, 155.1, 143.3, 135.9, 135.8, 134.1, 133.4, 130.3, 129.6, 129.5, 129.2, 127.5, 127.4, 114.0, 113.6, 112.8, 104.4, 79.1, 72.7, 72.6, 71.8, 68.3, 55.2, 46.0, 41.1, 40.0, 39.5, 38.3, 33.1, 28.4, 26.8, 20.7, 19.8, 19.2. IR (film, cm^{-1}): 2930, 2857, 1731, 1707, 1513, 1246, 1104,

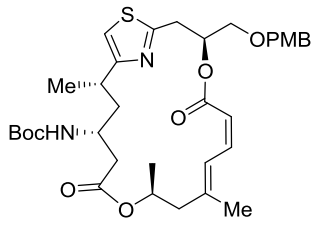
701, 507. MS (ESI): *m*/*z* 905 [*M*+*Na*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{49}H_{62}N_2O_9SSiNa$ [*M*+*Na*$^+$]: 905.38375, found: 905.38466.

Compound 33. MeMgBr (2.96 M in Et_2O, 104.5 µL) was quickly added via syringe to a rapidly stirred mixture of $Fe(acac)_3$ (16.7 µmol, 5.9 mg) and compound **32** (0.055 mmol, 48.8 mg) in Et_2O/cyclopentyl methyl ether (1/1, 2.2 mL) at –60 °C. Stirring was continued for 2.5 h at this temperature before the reaction was quenched with aq. sat. NH_4Cl and the pH of the aqueous layer was adjusted to ~2-3 upon addition of aq. HCl (1 M). The aqueous phase was extracted with EtOAc (5 × 25 mL) and the combined organic layers were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc = 4/1 to 2/1 with 0.5% of AcOH) to yield the title compound as a yellow oil [36.1 mg, 73%, 2*Z*/2*E* = 17/1 (^{1}H NMR)]. Unreacted pyrone **32** was recovered in 25% yield (12.2 mg) when the eluent was switched to hexane/EtOAc = 1/1 to 1/2. $[\alpha]_D^{20}$ = –26.1 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 – 7.64 (m, 2H), 7.62 – 7.56 (m, 2H), 7.44 – 7.36 (m, 2H), 7.36 – 7.28 (m, 4H), 7.14 (d, *J* = 11.6 Hz, 1H), 7.07 – 7.03 (m, 2H), 6.88 (dd, *J* = 12.0, 11.2 Hz, 1H), 6.83 (s, 1H), 6.80 – 6.78 (m, 2H), 5.62 (d, *J* = 11.2 Hz, 1H), 5.20 – 5.05 (m, 1H), 5.03 – 4.96 (m, 1H), 4.27 (app quint, *J* = 5.2 Hz, 1H), 4.22 (d, *J* = 11.6 Hz, 1H), 4.16 (d, *J* = 11.2 Hz, 1H), 3.84 – 3.74 (m, 1H), 3.79 (s, 3H), 3.40 – 3.18 (m, 4H), 3.07 – 2.95 (m, 1H), 2.48 – 2.41 (m, 3H), 2.28 (dd, *J* = 14.4, 4.4 Hz, 1H), 1.93 – 1.87 (m, 1H), 1.86 (s, 3H), 1.83 – 1.69 (m, 1H), 1.42 (s, 9H), 1.28 (d, *J* = 6.8 Hz, 3H), 1.21 (d, *J* = 6.0 Hz, 3H), 0.98 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 171.0, 170.0, 167.1, 160.0, 158.9, 155.2, 145.1, 140.5, 135.9, 135.8, 134.1, 133.4, 130.3, 129.6, 129.5, 129.2, 127.6, 127.4, 124.0, 116.3, 113.5, 112.9, 79.1, 72.7, 72.6, 71.8, 68.8, 55.2, 46.4, 46.0, 41.2, 39.6, 38.1, 33.0, 28.4, 26.9, 20.9, 20.1, 19.2, 17.3. IR (film, cm^{-1}): 3070, 2931, 2857, 1695, 1631, 1513, 1246, 1169, 1110, 702, 509. MS (ESI): *m*/*z* 921 [*M*+*Na*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{50}H_{66}N_2O_9SSiNa$ [*M*+*Na*$^+$]: 921.41505, found: 921.41585.

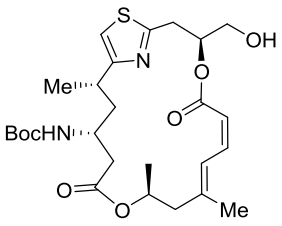
***Seco*-Acid 34**. TBAF (0.17 mmol, 1 M in THF, 0.17 mL) was added to a solution of compound **33** (68.2 µmol, 61.3 mg) in THF (1.4 mL). After stirring for 63 h, the mixture was cooled to 0 °C and the reaction quenched with sat. aq. NH_4Cl (0.5 mL), followed by slow addition of aq. HCl (1 M, 0.4 mL) and H_2O (5 mL). The aqueous phase was extracted with ethyl acetate (5 × 10 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The crude material was purified by flash chromatography on silica gel (hexane/EtOAc = 2/1 to 1/2 with 0.5% of AcOH) to yield the title compound as a colorless oil (39.3 mg, 87%). $[\alpha]_D^{20}$ = –17.2 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 – 7.25 (m, 2H), 7.10 (d, *J* = 11.6 Hz, 1H), 6.95 – 6.77 (m, 4H), 5.61 (d, *J* = 11.6 Hz, 1H), 5.17 (br s, 1H), 4.77 (d, *J* = 9.2 Hz, 1H), 4.50 (s, 2H), 4.31 – 4.26 (m, 1H), 3.80 (s, 3H), 3.73 (br s, 1H), 3.55 (dd, *J* = 9.6, 5.6 Hz, 1H), 3.49 (dd, *J* = 9.6, 5.2 Hz, 1H), 3.27 (dd, *J* = 15.2, 3.6 Hz, 1H), 3.13 (dd, *J* = 14.8, 8.8 Hz, 1H), 3.01 (br s, 1H), 2.52 – 2.38 (m, 3H), 2.24 (dd, *J* = 16.0, 3.2 Hz, 1H), 1.99 (ddd, *J* = 13.6, 9.6, 3.6 Hz, 1H), 1.85 (s, 3H), 1.71 (ddd, *J* = 14.0, 9.6, 4.4 Hz, 1H), 1.42 (s, 9H), 1.30 (d, *J* = 6.8 Hz, 3H), 1.30 – 1.26 (m, 1H), 1.21 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.9, 169.7, 167.8, 160.0, 159.2, 155.1, 144.9, 140.2, 130.1, 129.3, 123.3, 116.5, 113.8, 113.0, 79.2, 73.0, 72.9, 69.8, 68.6, 55.2, 46.0, 45.7, 41.4, 39.9, 36.6, 33.0, 28.4, 20.9, 20.2, 17.5. IR (film, cm^{-1}):

3432, 3338, 2974, 2931, 2870, 1692, 1631, 1512, 1245, 1165, 1127, 751, 582. MS (ESI): *m*/*z* 683 [*M*+*Na*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{34}H_{48}N_2O_9SNa$ [*M*+*Na*$^+$]: 683.29727, found: 683.29783.

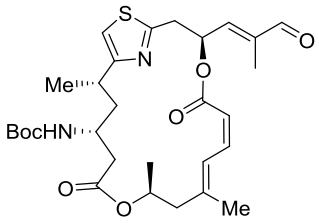
Compound 36. 2-Bromo-1-ethyl-pyridinium tetrafluoroborate **35** (0.76 mmol, 208.4 mg) was added to a solution of compound **34** (37.7 µmol, 24.9 mg) and $NaHCO_3$ (9.5 mmol, 0.79 g) in CH_2Cl_2 (81 mL). The mixture was stirred for 17 h in the dark. The reaction was quenched with H_2O (20 mL), the aqueous phase was extracted with *tert*-butyl methyl ether (4 × 50 mL) and the combined organic phases were dried over $MgSO_4$, filtered, and evaporated. The residue was purified by flash chromatography on silica gel (CH_2Cl_2/*tert*-butyl methyl ether = 20/1 to 10/1) to yield the product as a mixture of isomers (ca. product/Σ of isomers $\geq$ 11/1), which was further purified by preparative LC (Kromasil 100-5C18 5µm, 150 mm × 30 mm, MeOH:H_2O = 75:25, 35 mL/min, λ = 254 nm, t = 20.9 min) to yield the title compound as a colorless oil (19.9 mg, 82%). $[\alpha]_D^{20}$ = −179 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 – 7.23 (m, 2H), 7.04 (d, *J* = 11.6 Hz, 1H), 6.86 – 6.85 (m, 2H), 6.75 (s, 1H), 6.74 (dd, *J* = 12.0, 11.2 Hz, 1H), 5.57 – 5.51 (m, 1H), 5.53 (d, *J* = 11.6 Hz, 1H), 5.12 – 5.05 (m, 1H), 4.55 (d, *J* = 11.6 Hz, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 4.48 – 4.43 (m, 1H), 3.79 (s, 3H), 3.68 – 3.48 (m, 2H), 3.39 – 3.08 (m, 3H), 3.04 – 2.91 (m, 1H), 2.60 – 2.43 (m, 1H), 2.38 – 2.09 (m, 3H), 2.07 – 1.88 (m, 1H), 1.81 (s, 3H), 1.40 (s, 9H), 1.26 – 1.16 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 165.7, 164.8, 161.1, 159.2, 154.9, 145.9, 140.8, 129.8, 129.3, 124.0, 115.2, 113.8, 112.5, 78.8, 72.9, 70.9, 70.86, 67.4, 55.2, 47.5, 47.4, 41.0, 39.3, 35.4, 33.5, 28.3, 22.6, 20.8, 16.7. IR (film, cm^{-1}): 2971, 2926, 2853, 1712, 1512, 1427, 1246, 1157, 814, 750. MS (ESI): *m*/*z* 665 [*M*+*Na*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{34}H_{46}N_2O_8SNa$ [*M*+*Na*$^+$]: 665.28671, found: 665.28697.



Compound S4. DDQ (225.2 µmol, 51.1 mg) was added to a solution of **36** (102.4 µmol, 65.8 mg) in CH_2Cl_2/aq. phosphate buffer (pH 7, 10/1, 3.3 mL) at 0 °C. Stirring was continued for 5 h at ambient temperature before the reaction was quenched with aq. phosphate buffer (pH 7, 10 mL) and the mixture was diluted with EtOAc (15 mL). The aqueous phase was extracted with EtOAc (4 × 25 mL) and the combined organic layers were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc = 2/1 to 1/2) to yield the title compound as a colorless oil (51.6 mg, 96%). $[\alpha]_D^{20}$ = −183.5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.01 (d, *J* = 11.6 Hz, 1H), 6.76 (dd, *J* = 11.2, 12.0 Hz, 1H), 6.77 (s, 1H), 5.53 (d, *J* = 11.6 Hz, 1H), 5.51 – 5.46 (m, 1H), 5.15 – 5.01 (m, 1H), 4.50 (br s, 1H), 3.87 – 3.73 (m, 2H), 3.38 – 3.17 (m, 3H), 3.05 – 2.93 (m, 1H), 2.53 – 2.42 (m, 2H), 2.31 (dd, *J* = 13.6, 10.8 Hz, 1H), 2.22 (dd, *J* = 15.6, 4.0 Hz, 1H), 2.16 (d, *J* = 13.2 Hz, 1H), 2.02 – 1.96 (m, 1H), 1.84 – 1.80 (m, 1H), 1.81 (s, 3H), 1.40 (s, 9H), 1.23 (d, *J* = 2.8 Hz, 3H), 1.21 (d, *J* = 2.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 165.7, 165.1, 161.1, 154.9, 146.2, 141.1, 123.9, 115.0, 112.7, 78.9, 72.9, 67.5, 64.5, 47.5, 47.4, 41.2, 39.4, 34.8, 33.5, 28.4, 22.6, 20.8, 16.8. IR (film, cm^{-1}): 3370, 2975, 2930, 2872, 1711, 1511, 1366, 1158, 816, 751. MS (ESI): *m*/*z* 523 [*M*+*H*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{26}H_{39}N_2O_7S$ [*M*+*H*$^+$]: 523.24725, found: 523.24764.

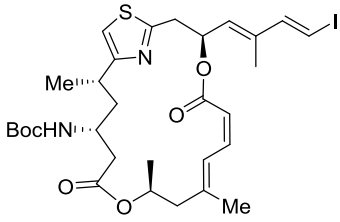


Aldehyde S6. Sulfur trioxide pyridine complex (0.292 mmol, 46.5 mg) and anhydrous *i*Pr_2NEt (0.682 mmol, 118.7 µL) were successively added to a solution of compound **S4** (0.0966 mmol, 50.5 mg) in CH_2Cl_2 (1.5 mL) at −20 °C. The resulting mixture was stirred for 5 min before anhydrous DMSO (0.974 mmol, 69.2 µL) was added dropwise. Stirring was continued for 40 min at −20 °C before the mixture was poured into a mixture of *tert*-butyl methyl ether (8 mL) and aq. phosphate buffer (pH 7, 8 mL). The aqueous layer was extracted with *tert*-butyl methyl ether (3 × 15 mL) and the combined organic phases were washed with phosphate buffer, dried over $MgSO_4$, filtered, and concentrated to give a syrup, which was dried in high vacuum for 3 h (2×10^{-3} mbar); this crude material (**S5**) was directly used in the next step.



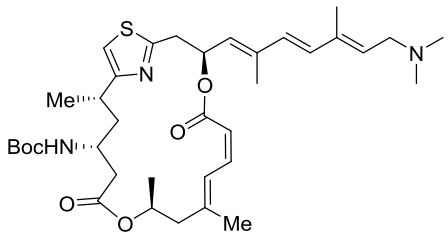
2-(Triphenylphosphoranylidene)-propionaldehyde (0.156 mmol, 49.6 mg) was added to a solution of the crude product **S5** in toluene (3.5 mL) and the resulting solution was stirred at 80 °C for 2.5 h. Once the reaction was complete (monitored by TLC), the mixture was allowed to reach ambient temperature and the reaction was quenched by H_2O (5 mL). The aqueous phase was extracted with *tert*-butyl methyl ether (4 × 10 mL) and the combined organic extracts were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc = 4/1 to 2/1) to yield the title compound as a yellow oil (43.9 mg, 81%). $[\alpha]_D^{20} = -212.1$ (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.47 (s, 1H), 7.00 (d, *J* = 11.6 Hz, 1H), 6.81 (s, 1H), 6.77 (app t, *J* = 11.6 Hz, 1H), 6.44 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.35 – 6.25 (m, 1H), 5.49 (d, *J* = 11.6 Hz, 1H), 5.17 – 5.05 (m, 1H), 4.49 (br s, 1H), 3.40 – 3.27 (m, 1H), 3.25 (d, *J* = 6.8 Hz, 2H), 3.06 – 2.92 (m, 1H), 2.62 – 2.39 (m, 1H), 2.31 (dd, *J* = 13.2, 10.8 Hz, 1H), 2.23 (dd, *J* = 15.6, 3.6 Hz, 1H), 2.16 (d, *J* = 13.2 Hz, 1H), 1.94 (d, *J* = 1.6 Hz, 3H), 1.90 – 1.81 (m, 2H), 1.82 (s, 3H), 1.41 (s, 9H), 1.24 (d, *J* = 6.0 Hz, 3H), 1.22 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.5, 170.3, 164.4, 163.9, 161.5, 155.0, 147.8, 146.7, 141.5, 140.7, 123.8, 114.4, 113.0, 78.9, 68.5, 67.5, 47.7, 47.3, 41.4, 39.3, 37.6, 33.6, 28.4, 22.5, 20.9, 16.9, 9.9. IR (film, cm^{-1}): 2975, 2931, 1694, 1632, 1507, 1150, 1050, 751. MS (ESI): *m*/*z*: 583 [*M*+Na^+]. HRMS (ESI): *m*/*z*: calcd for: $C_{29}H_{40}N_2O_7SNa$ [*M*+Na^+]: 583.24484, found: 583.24467.

Compound 37. A mixture of CHI_3 (0.44 mmol, 175 mg) and aldehyde **S6** (63.8 µmol, 35.8 mg) in degassed THF (1.2 mL, rinsing the flask with 3 × 0.5 mL of THF) was added dropwise to a slurry of $CrCl_2 \cdot 1.05$ THF (1.69 mmol, 329 mg) in degassed THF (1.5 mL) at 0 °C. The mixture was stirred at this temperature for 1.5 h. Once the reaction was complete (monitored by TLC), the mixture was diluted with *tert*-butyl methyl ether (8 mL) and H_2O (8 mL). The aqueous layer was extracted with *tert*-butyl methyl ether (3 × 10 mL) and the combined extracts were dried over $MgSO_4$, filtered, and evaporated. The crude material was purified by flash chromatography on silica (hexane/EtOAc = 8/1 to 4/1) to yield the title compound as a colorless oil (39.3 mg, 90%, product/Σ of isomers = 94/6) [Conditions for LC-MS analysis: 4.6 × 50 mm Zorbax Eclipse Plus C18, 1.8 µm, Nr USUXG06443, MeCN/H_2O = 80:20, *v* = 0.8 mL/min, λ = 257 nm, 35 °C]; $[\alpha]_D^{20} = -297.1$ (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.06 (d, *J* = 14.8 Hz, 1H), 7.02 (d, *J* = 11.6 Hz, 1H), 6.78 (s, 1H), 6.73 (app t, *J* = 11.6 Hz, 1H), 6.44 (d, *J* = 14.8 Hz, 1H), 6.23 – 6.05 (m, 1H), 5.51 (d, *J* = 9.2 Hz, 1H), 5.48 (d, *J* = 11.2 Hz, 1H), 5.16 – 5.01 (m, 1H), 4.50 (br s, 1H), 3.40 – 3.25 (m, 1H), 3.18 (d, *J* = 7.2 Hz, 2H), 3.07 –

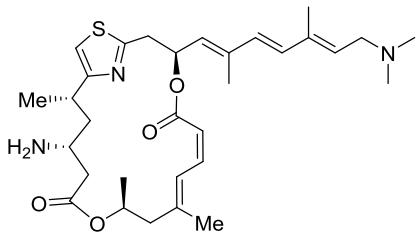


2.92 (m, 1H), 2.62 – 2.46 (m, 1H), 2.32 (dd, *J* = 13.2, 10.8 Hz, 1H), 2.22 (dd, *J* = 15.2, 3.6 Hz, 1H), 2.16 (d, *J* = 13.2 Hz, 1H), 1.92 (s, 3H), 1.87 – 1.81 (m, 1H), 1.81 (s, 3H), 1.41 (s, 9H), 1.28 – 1.20 (m, 1H), 1.24 (d, *J* = 3.2 Hz, 3H), 1.21 (d, *J* = 2.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 165.0, 164.6, 161.3, 155.0, 148.4, 146.0, 140.7, 138.0, 129.8, 123.9, 115.2, 112.7, 78.9, 77.7, 68.5, 67.5, 47.7, 47.5, 41.0, 39.3, 38.7, 33.6, 28.4, 22.7, 20.9, 16.7, 12.8. IR (film, cm^{-1}): 2974, 2928, 2869, 1709, 1632, 1365, 1156, 1050, 814, 752. MS (ESI): *m*/*z*: 707 [*M*+Na^+]. HRMS (ESI): *m*/*z*: calcd for: $C_{30}H_{41}N_2O_6SINa$ [*M*+Na^+]: 707.16223, found: 707.16229.

Boc-Pateamine A (39). Flame-dried $[Ph_2PO_2][NBu_4]$ (0.053 mmol, 24.2 mg) was dissolved in degassed DMF (0.42 mL) and the resulting solution was added to a Schlenk tube containing compound **37** (0.029 mmol, 20.0 mg). (*E*)-*N*,*N*-Dimethyl-3-(tributylstannyl)but-2-en-1-amine (0.055 mmol, 21.2 mg)[6] and copper thiophene carboxylate (CuTC, 0.044 mmol, 8.4 mg) were then introduced, followed by $Pd(PPh_3)_4$ (2.95 µmol, 3.4 mg). The resulting mixture was stirred for 1 h before the reaction was quenched with water (5 mL). After dilution with EtOAc (5 mL), the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined extracts were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered, and evaporated. The residue was purified by flash chromatography on silica (pretreated with 1% Et_3N in hexane, hexane/EtOAc = 1/1 then EtOAc/Et_3N = 120/1 to 80/1) to yield the title compound as a pale yellow oil (16.0 mg, 84%). $[\alpha]_D^{20} = -254.8$ (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.05 (d, *J* = 11.6 Hz, 1H), 6.79 (s, 1H), 6.73 (dd, *J* = 12.0, 11.2 Hz, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 6.22 (d, *J* = 16.4 Hz, 1H), 6.24 – 6.18 (m, 1H), 5.64 (t, *J* = 6.8 Hz, 1H), 5.56 (d, *J* = 9.2 Hz, 1H), 5.51 (d, *J* = 11.6 Hz, 1H), 5.15 – 5.07 (m, 1H), 4.51 (br s, 1H), 3.39 – 3.26 (m, 1H), 3.26 – 3.16 (m, 2H), 3.06 (d, *J* = 7.2 Hz, 2H), 3.11 – 2.98 (m, 1H), 2.65 – 2.50 (m, 1H), 2.39 – 2.12 (m, 4H), 2.25 (s, 6H), 1.98 (d, *J* = 1.2 Hz, 3H), 1.94 – 1.87 (m, 1H), 1.81 (d, *J* = 1.6 Hz, 6H), 1.42 (s, 9H), 1.24 (d, *J* = 2.0 Hz, 3H), 1.22 (d, *J* = 0.8 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.4, 165.4, 164.7, 161.3, 154.9, 145.9, 140.4, 138.2, 135.9, 134.1, 130.6, 130.5, 128.3, 123.9, 115.6, 112.5, 78.8, 69.2, 67.5, 57.2, 47.7, 47.6, 45.4, 40.7, 39.4, 39.1, 33.6, 29.7, 28.4, 22.9, 20.9, 16.6, 13.4, 12.7. IR (film, cm^{-1}): 2970, 2927, 2871, 1709, 1632, 1427, 1261, 1156, 1120, 813, 733. MS (ESI): *m*/*z*: 656 [*M*+H^+]. HRMS (ESI): *m*/*z*: calcd for: $C_{36}H_{54}N_3O_6S$ [*M*+H^+]: 656.37278, found: 656.37311.

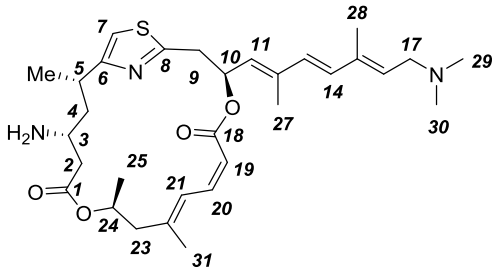


(–)-Pateamine A (1). HCl (0.89 mmol, 0.223 mL, 4 M in 1,4-dioxane) was added dropwise to a solution of Boc-pateamine A **39** (19.8 µmol, 13 mg) in EtOAc (0.65 mL) and H_2O (12.5 µL) at −20 °C (ice-NaCl-acetone bath in a Dewar flask) and the solution was stirred for 3 h while the bath temperature was slowly raised to −9 °C. After dilution with MeOH (2 mL), the mixture was loaded onto an amino cartridge (pre-equilibrated with three column length volume of MeOH, H_2O, MeOH successively) and then eluted with MeOH to give a yellow oil, which was purified by passing it through another amino cartridge (pre-equilibrated with three column length volume of MeOH, H_2O, MeOH successively) with MeOH as eluting solvent to yield (–)-pateamine A (**1**) as a pale yellow oil (8.6 mg, 78%). Analytically pure (–)-pateamine A could be obtained via preparative LC separation (YMC Triart C18 5 µm, 150 mm × 10 mm, MeCN: 20 mM NH_4HCO_3 pH 8.0 = 75:25, 3.0 mL/min, λ = 256 nm, t = 9.1 min). $[\alpha]_D^{20} = -380$ (*c* = 0.49,



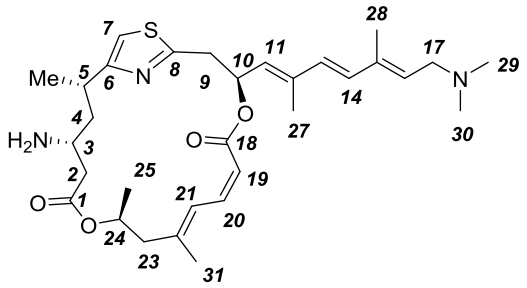
MeOH); {lit.[6] $[\alpha]_D^{26} = -302.8$ (*c* = 0.21, MeOH); lit.[7,8] $[\alpha]_D^{26} = -253.0$ (*c* = 0.29, MeOH); lit.[8] $[\alpha]_D^{26} = -214.5$ (*c* = 0.31, MeOH)}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.00 (d, *J* = 11.7 Hz, 1H), 6.73 (s, 1H), 6.67 (app t, *J* = 11.6 Hz, 1H), 6.37 (d, *J* = 15.9 Hz, 1H), 6.26 (ddd, *J* = 9.9, 9.0, 4.1 Hz, 1H), 6.22 (d, *J* = 15.6 Hz, 1H), 5.64 (t, *J* = 7.0 Hz, 1H), 5.52 (d, *J* = 9.0 Hz, 1H), 5.41 (d, *J* = 11.4 Hz, 1H), 5.15 – 5.10 (m, 1H), 3.23 – 3.14 (m, 2H), 3.12 – 3.05 (m, 3H), 2.60 – 2.55 (m, 1H), 2.40 (dd, *J* = 16.8, 2.5 Hz, 1H), 2.32 (dd, *J* = 13.2, 10.9 Hz, 1H), 2.24 (s, 6H), 2.14 – 1.88 (m, 3H), 2.02 (d, *J* = 1.3 Hz, 3H), 1.83 (s, 3H), 1.81 (s, 3H), 1.33 (ddd, *J* = 13.1, 10.2, 2.4 Hz, 2H), 1.27 (d, *J* = 7.0 Hz, 3H), 1.24 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ = 172.3, 165.5, 164.5, 161.2, 145.5, 140.6, 138.1, 135.9, 134.1, 130.7, 130.4, 128.5, 123.8, 115.1, 112.4, 69.3, 67.3, 57.2, 48.2, 45.5, 45.3, 45.1, 42.9, 38.9, 33.3, 22.8, 21.1, 16.8, 13.4, 12.7. MS (ESI): *m*/*z*: 556 [*M*+H^+]. HRMS (ESI): *m*/*z*: calcd for: $C_{31}H_{46}N_3O_4S$ [*M*+H^+]: 556.32035, found: 556.32044.

Table S-1. Comparison of the ^{1}H NMR data of (–)-pateamine A (**1**) with those reported in the literature



Position	Natural product [7]	Romo group[8]	Pattenden group[6]	This work
	δ (ppm)/*J* (Hz)	**δ (ppm)/*J* (Hz)**	**δ (ppm)/*J* (Hz)**	**δ (ppm)/*J* (Hz)**
25 (3H)	1.22, d, 6.3	1.24, d, 6.6	1.25, d, 6.7	1.24, d, 6.4
26 (3H)	1.24, d, 7.3	1.27, d, 7.2	1.27, d, 7.8	1.27, d, 7.0
4‘ (1H)	1.31, ddd, 13.6, 10.3, 2.4	1.24-1.38, m	1.26-1.39, m	1.33, ddd, 13.1, 10.2, 2.4
NH_2	--	1.50-1.70, br s	1.65-1.80, br s	--
28 (3H)	1.79, d, 1.1	1.81, s	1.82, s	1.81, s
31 (3H)	1.83, d, 1.2	1.83, s	1.84, s	1.83, s
4 (1H)	1.92, ddd, 13.6, 10.0, 2.5	--	--	--
27 (3H)	2.00, d, 1.2	2.02, d, 1.2	2.02, s	2.02, d, 1.3
2‘(1H)	2.07, dd, 16.8, 11.4	--	--	--
23‘(1H)	2.10, dd, 13.1, 1.8	1.88-2.18, m, 3H	1.91-2.20, m, 3H	1.88-2.14, m, 3H
29, 30 (6H)	2.23, s	2.24, s	2.26, s	2.24, s
23 (1H)	2.30, dd, 13.1, 10.7	2.30, dd, 12.9, 10.8	2.36-2.26, m	2.32, dd, 13.2, 10.9
2 (1H)	2.38, dd, 16.8, 2.6	2.40, dd, 16.8, 2.7	2.41, dd, 16.7, 2.4	2.40, dd, 16.8, 2.5
3 (1H)	2.55, dddd, 11.4, 10.3, 2.6, 2.5	2.54-2.61, m	2.55, app t, 10.6	2.55-2.60, m
17 (2H)	3.05, m	3.0-3.12, m	3.10, d, 6.7	3.05-3.12, m
5 (1H)	3.07, m	--	3.14-3.05, m	--
9 (2H)	3.20, m	3.14-3.26, m	3.16-3.25, m	3.14-3.23, m
24 (1H)	5.11, ddq, 10.7, 6.3, 1.8	5.06-5.20, m	5.09-5.18, m	5.10-5.15, m
19 (1H)	5.39, d, 11.4	5.41, d, 11.4	5.41, d, 11.4	5.41, d, 11.4
11 (1H)	5.51, dq, 9.3, 1.2	5.52, d, 9.3	5.53, d, 8.8	5.52, d, 9.0
16 (1H)	5.62, tq, 7.5, 1.1	5.64, t, 6.9	5.65, t, 7.0	5.64, t, 7.0
13 (1H)	6.21, d, 16.0	6.22, d, 15.0	6.23, d, 15.8	6.22, d, 15.6
10 (1H)	6.24, ddd, 9.3, 9.0, 5.3	6.22-6.30, m	6.22-6.30, m	6.26, ddd, 9.9, 9.0, 4.1
14 (1H)	6.35, d, 16.0	6.37, d, 15.9	6.38, d, 15.9	6.37, d, 15.9
20 (1H)	6.66, dd, 11.7, 11.4	6.68, dd, 11.7, 11.4	6.68, t, 11.5	6.67, app t, 11.6
7 (1H)	6.72, s	6.74, s	6.75, s	6.73, s
21 (1H)	6.94, dq, 11.7, 1.2	7.01, d, 11.7	7.00, d, 11.7	7.00, d, 11.7

Table S-2. Comparison of the ^{13}C NMR data of (–)-pateamine A with those reported in the literature



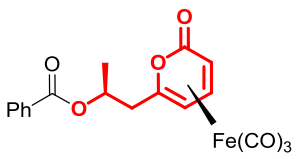
Position	Natural product[7]	Romo group[8]	Pattenden group[6]	This work
	δ (ppm)/*J* (Hz)	δ (ppm)	δ (ppm)	δ (ppm)
28	12.7, q	12.7	12.7	12.7
27	13.4, q	13.4	13.4	13.4
31	16.8, q	16.8	16.8	16.8
25	21.1, q	21.1	21.1	21.1
26	22.8, q	22.8	22.8	22.8
5	33.3, d	33.3	33.3	33.3
9	38.9, t	38.9	39.1	38.9
2	42.9, t	42.9	42.9	42.9
4	45.1, t, 127	45.1	45.1	45.1
29,30	45.3, q	45.4	--	45.3
3	45.5, t, 135	45.4	45.4	45.5
23	48.2, t, 122	48.2	48.2	48.2
17	57.2, t, 132	57.2	57.2	57.2
24	67.3, d, 149	67.3	67.2	67.3
10	69.3, d, 149	69.2	69.2	69.3
7	112.4, d, 190	112.4	112.4	112.4
19	115.1, d, 166	115.1	115.1	115.1
21	123.8, d	123.8	123.8	123.8
11	128.5, d	128.5	128.5	128.5
16 *or* 13	130.3, d	130.5	130.5	130.4
16 *or* 13	130.7, d	130.7	130.7	130.7
14	134.0, d	134.1	134.0	134.1
15	135.9, s	135.8	135.9	135.9
12	138.1, s	138.2	138.1	138.1
20	140.6, d, 148	140.7	140.6	140.6
22	145.4, s	145.5	145.5	145.5
6	161.2, s	161.2	161.2	161.2
18	164.5, s	164.5	164.5	164.5
8	165.5, s	165.4	165.5	165.5
1	172.3, s	172.2	172.3	172.3

Model Studies using Pyrone Tricarbonyliron Complexes.

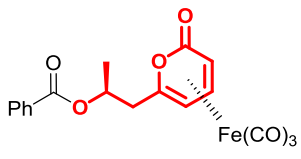
(S)-1-(2-Oxo-2H-pyran-6-yl)propan-2-yl benzoate (**50**). 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.83 mmol, 350.4 mg) and 4-(dimethylamino)pyridine (1.50 mmol, 182.9 mg) were added to a Schlenk tube containing (*S*)-6-(2-hydroxypropyl)-2H-pyran-2-one (0.83 mmol, 127.5 mg)[1] and benzoic acid (0.87 mmol, 107 mg) in CH_2Cl_2 (8.3 mL). Stirring was continued at ambient temperature for 2 h before the reaction was quenched with H_2O (10 mL). The mixture was diluted with EtOAc and H_2O, the aqueous phase was extracted with EtOAc (4 × 20 mL) and the combined organic layers were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered and concentrated. Purification of the residue by flash chromatography on silica gel (hexane/EtOAc = 8/1 to 4/1) yielded the title compound as a yellow oil (193.3 mg, 91%). $[\alpha]_D^{20}$ = +119 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.93 – 7.84 (m, 2H), 7.51 – 7.41 (m, 1H), 7.36 – 7.32 (m, 2H), 7.12 (dd, *J* = 9.6, 6.4 Hz, 1H), 6.01 (d, *J* = 9.6 Hz, 1H), 5.96 (d, *J* = 6.4 Hz, 1H), 5.42 – 5.27 (m, 1H), 2.80 (dd, *J* = 14.7, 7.5 Hz, 1H), 2.72 (dd, *J* = 14.7, 5.1 Hz, 1H), 1.33 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, CD_2Cl_2): δ = 165.5, 162.1, 162.0, 143.4, 133.0, 130.3, 129.4, 128.4, 113.8, 104.5, 68.8, 40.3, 19.7. IR (film, cm^{-1}): 3063, 2982, 1709, 1636, 1557, 1267, 1096, 796, 709. MS (ESI): *m*/*z*: 281 [*M*+*Na*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{15}H_{14}O_4Na$ [*M*+*Na*$^+$]: 281.07843, found: 281.07866.

Iron Complexes 51. A Schlenk flask was charged with $Fe_2(CO)_9$ (0.232 mmol, 84.5 mg) and **50** (0.465 mmol, 120 mg) under Ar. Degassed anhydrous *n*-Bu_2O/THF (5/1, 6 mL) was added via cannula and the mixture was stirred at 65 °C for 0.5 h while argon was slowly bubbled through the mixture. Two further portions of $Fe_2(CO)_9$ (0.232 mmol, 84.5 mg) were added at 0.5 h intervals. After stirring for another 2 h, the mixture was allowed to reach ambient temperature before the solvent was removed in vacuo. Purification of the residue by flash chromatography on silica gel (hexane/EtOAc = 10/1 to 4/1) yielded complexes **51a** and **51b**. The absolute configuration of the iron complex **51a** was assigned by X-ray diffraction.

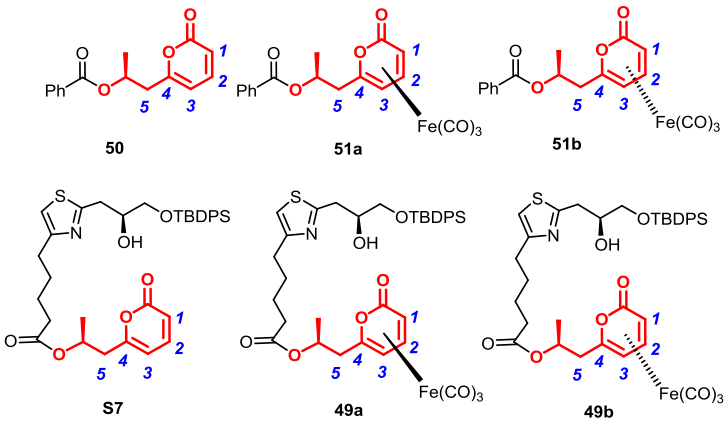
Analytical and spectral data of **51a**: Yellow solid (22.9 mg, 12%). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.99 (d, *J* = 7.2 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 6.04 (dd, *J* = 6.0, 4.1 Hz, 1H), 5.55 (d, *J* = 3.5 Hz, 1H), 5.26 – 5.18 (m, 1H), 2.82 (d, *J* = 5.6 Hz, 1H), 2.60 (dd, *J* = 15.0, 3.0 Hz, 1H), 2.09 (dd, *J* = 14.9, 9.7 Hz, 1H), 1.31 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, CD_2Cl_2): δ = 208.5, 170.1, 166.1, 133.6, 131.0, 130.0, 129.1, 104.2, 88.2, 78.0, 69.7, 49.5, 44.3, 20.8. IR (film, cm^{-1}): 3093, 2058, 2009, 1985, 1731, 1712, 1266, 1108, 1068, 715, 608, 569. MS (ESI): *m*/*z*: 421 [*M*+*Na*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{18}H_{14}FeO_7Na$ [*M*+*Na*$^+$]: 420.9981, found: 420.9987.



Analytical and spectral data of **51b**: Yellow solid (18.3 mg, 9%). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.05 – 7.90 (m, 2H), 7.52 – 7.49 (m, 1H), 7.40 – 7.36 (m, 2H), 6.14 (dd, *J* = 6.1, 4.1 Hz, 1H), 5.51 (dd, *J* = 4.1, 1.4 Hz, 1H), 5.29 (app pent., *J* = 6.3 Hz, 1H), 2.85 (dd, *J* = 6.1, 1.4 Hz, 1H), 2.58 (dd, *J* = 14.9, 6.1 Hz, 1H), 2.20 (dd, *J* = 14.9, 6.3 Hz, 1H), 1.35 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, CD_2Cl_2): δ = 208.3, 170.1, 166.3, 133.5, 131.1, 130.0, 128.9, 104.2, 88.4, 77.5, 69.9, 49.5, 43.0, 20.2. IR (film, cm^{-1}): 3079, 2967, 2002, 1975, 1729, 1709, 1275, 1260, 1112, 1093, 1051, 796, 709, 603, 568. MS (ESI): *m*/*z*: 421 [*M*+*Na*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{18}H_{14}FeO_7Na$ [*M*+*Na*$^+$]: 420.9981, found: 420.9986.



Iron Complexes 49. Prepared analogously from 2-pyrone derivative **42** (0.170 mmol, 108.1 mg);[2] The crude product was purified by flash chromatography on silica gel (hexane/EtOAc = 8/1 to 1/1) to yield the iron-pyrone complexes **49a,b** as a mixture of diastereoisomers, which were separated by preparative LC (Kromasil 100-5C18 5µm, 150 mm × 30 mm, MeCN:H_2O = 80:20, 35 mL/min, λ = 254 nm, t_1 = 16.3 min, t_2 = 17.9 min) The configuration of the iron complexes was tentatively assigned by comparison of the ^{13}C NMR spectra with those of the iron complexes **51a,b**, for one of which X-ray data were available:



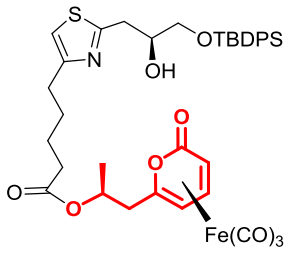
Compound	H1	H2	H3	H5a,b
50	6.01	7.12	5.96	2.80 / 2.72
51a	2.82	6.04	5.55	2.82 / 2.60
51b	2.85	6.14	5.51	2.85 / 2.58
S7	6.01	7.12	5.90	2.61
49a	2.84	6.12	5.47	2.37 / 2.05
49b	2.81	6.06	5.51	2.47 / 1.89

^1H NMR shifts (CD_2Cl_2) in ppm; arbitrary numbering scheme as shown in the Insert

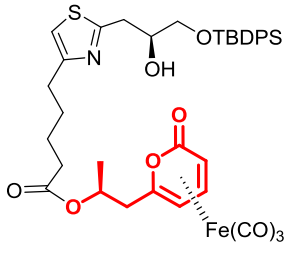
Compound	C1	C2	C3	C4	C5
50	113.8	143.4	104.5	162.1	40.3
51a	49.5	88.2	78.0	104.2	44.3
51b	49.5	88.4	77.5	104.2	43.0
S7	114.3	143.9	104.9	162.6	40.7
49a	49.4	88.1	78.0	104.2	44.1
49b	49.4	88.4	77.5	104.3	43.0

^{13}C NMR shifts (CD_2Cl_2) in ppm; arbitrary numbering scheme as shown in the Insert

Analytical and spectral data of complex **49a**. Yellow oil (8.7 mg, 7%). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.60 – 7.57 (m, 4H), 7.38 – 7.29 (m, 6H), 6.73 (s, 1H), 6.06 (dd, *J* = 6.0, 4.1 Hz, 1H), 5.51 (dd, *J* = 4.1, 1.4 Hz, 1H), 4.97 – 4.89 (m, 1H), 4.08 – 4.01 (m, 1H), 3.74 (d, *J* = 4.3 Hz, 1H), 3.63 (dd, *J* = 10.1, 5.5 Hz, 1H), 3.57 (dd, *J* = 10.2, 5.7 Hz, 1H), 3.15 (dd, *J* = 15.4, 3.7 Hz, 1H), 3.02 (dd, *J* = 15.5, 8.1 Hz, 1H), 2.81 (dd, *J* = 6.0, 1.4 Hz, 1H), 2.66 (t, *J* = 7.0 Hz, 2H), 2.47 (dd, *J* = 14.9, 3.0 Hz, 1H), 2.29 (t, *J* = 6.9 Hz, 2H), 1.89 (dd, *J* = 14.9, 9.8 Hz, 1H), 1.71 – 1.56 (m, 4H), 1.16 (d, *J* = 6.2 Hz, 3H), 0.98 (s, 9H). ^{13}C NMR (101 MHz, CD_2Cl_2): δ = 208.4, 173.1, 170.1, 167.7, 157.2, 136.1, 133.9, 133.8, 130.3, 128.3, 112.9, 104.2, 88.1, 78.0, 71.8, 68.7, 67.5, 49.4, 44.1, 36.9, 34.8, 31.6, 29.2, 27.2, 25.1, 20.7, 19.7. IR (film, cm^{-1}): 3072, 2931, 2858, 2065, 1986, 1737, 1427, 1112, 1067, 702, 609, 504. MS (ESI): *m*/*z*: 796 [*M*+*Na*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{38}H_{43}FeNO_9SSiNa$ [*M*+*Na*$^+$]: 796.16694, found: 796.16712.



Analytical and spectral data of complex **49b** Yellow oil (8.5 mg, 6%). ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 7.63 – 7.53 (m, 4H), 7.41 – 7.26 (m, 6H), 6.72 (d, *J* = 0.9 Hz, 1H), 6.12 (dd, *J* = 6.1, 4.1 Hz, 1H), 5.47 (dd, *J* = 4.1, 1.4 Hz, 1H), 5.03 – 5.01 (m, 1H), 4.08 – 3.99 (m, 1H), 3.75 (d, *J* = 4.3 Hz, 1H), 3.62 (dd, *J* = 10.1, 5.5 Hz, 1H), 3.57 (dd, *J* = 10.1, 5.7 Hz, 1H), 3.14 (dd, *J* = 15.4, 3.8 Hz, 1H), 3.02 (dd, *J* = 15.4, 8.1 Hz, 1H), 2.84 (dd, *J* = 6.0, 1.4 Hz, 1H), 2.64 (t, *J* = 7.0 Hz, 2H), 2.37 (dd, *J* = 14.8, 6.5 Hz, 1H), 2.26 (t, *J* = 7.1 Hz, 2H), 2.05 (dd, *J* = 14.8, 5.9 Hz, 1H), 1.67 – 1.55 (m, 4H), 1.20 (d, *J* = 6.3 Hz, 3H), 0.98 (s, 9H). ^{13}C NMR (101 MHz, CD_2Cl_2): δ = 208.1, 173.2, 170.1, 167.6, 157.2, 136.1, 133.9, 133.8, 130.3, 128.3, 112.8, 104.4, 88.4, 77.5, 71.7, 69.1, 67.4, 49.4, 43.0, 36.9, 34.8, 31.5, 29.1, 27.2, 25.0, 20.2, 19.7. IR (film, cm^{-1}): 3071, 2929, 2857, 2066, 1991, 1735, 1428, 1112, 1067, 703, 610, 505. MS (ESI): *m*/*z*: 796 [*M*+*Na*$^+$]. HRMS (ESI): *m*/*z*: calcd for $C_{38}H_{43}FeNO_9SSiNa$ [*M*+*Na*$^+$]: 796.16694, found: 796.16703.



References:

[1] N. Huwyler, K. Radkowski, S. M. Rummelt, A. Fürstner, *Chem. Eur. J.* **2017**, *23*, 12412-12419.

[2] C.-X. Zhuo, A. Fürstner, *Angew. Chem. Int. Ed.* **2016**, *55*, 6051-6056.

[3] H.-Y. Jung, X. Feng, H. Kim, J. Yun, *Tetrahedron* **2012**, *68*, 3444-3449.

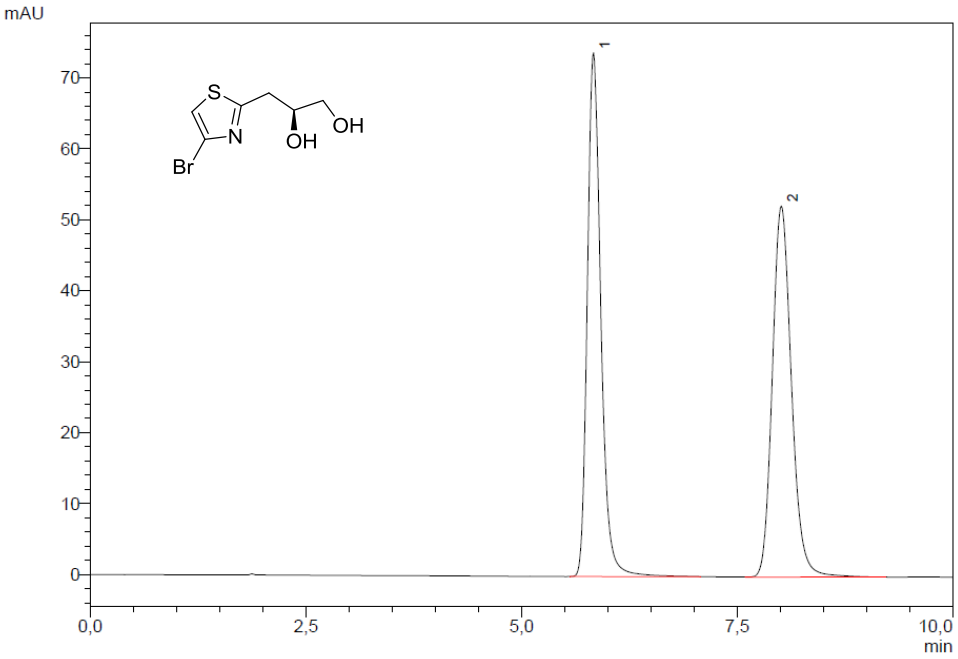
[4] Y. Zhu, S. L. Buchwald, *J. Am. Chem. Soc.* **2014**, *136*, 4500-4053.

[5] L. M. Stanley, J. F. Hartwig, *Angew. Chem. Int. Ed*. **2009**, *48*, 7841-7844.

[6] a) M. J. Remuiñán, G. Pattenden, *Tetrahedron Lett.* **2000**, *41*, 7367-7371; b) G. Pattenden, D. J. Critcher, M. Remuiñán, *Can. J. Chem*. **2004**, *82*, 353-365.

[7] P. T. Northcote, J. W. Blunt, M. H. G. Munro, *Tetrahedron Lett*. **1991**, *32*, 6411-6414.

[8] a) R. M. Rzasa, H. A. Shea, D. Romo, *J. Am. Chem. Soc*. **1998**, *120*, 591-592; b) D. Romo, R. M. Rzasa, H. A. Shea, K. Park, J. M. Langenhan, L. Sun, A. Akhiezer, J. O. Liu, *J. Am. Chem. Soc.* **1998**, *120,* 12237-12254.



1 250nm,4nm

PDA Ch1 250nm

Peak #	Ret. Time	Area %	Name
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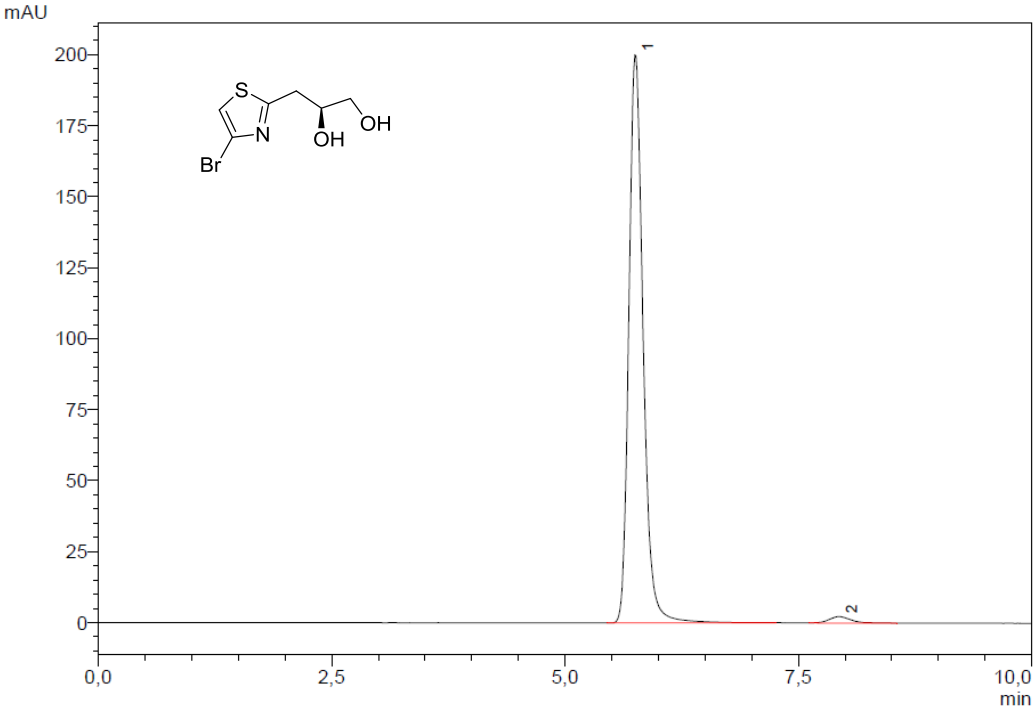
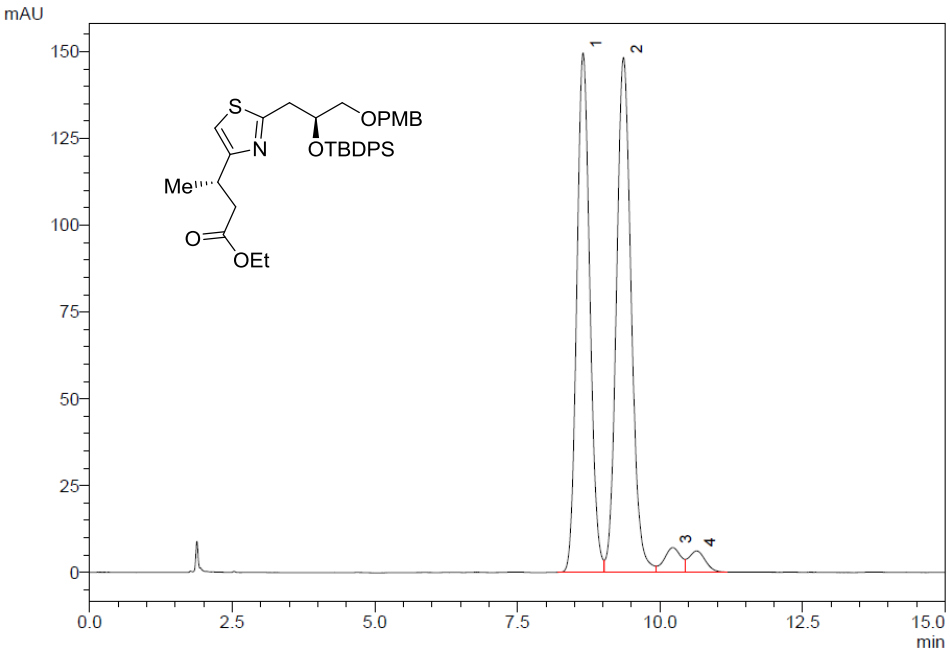
2	8,01	50,03	
Total		100,00	



1 254nm,4nm

PDA Ch1 254nm

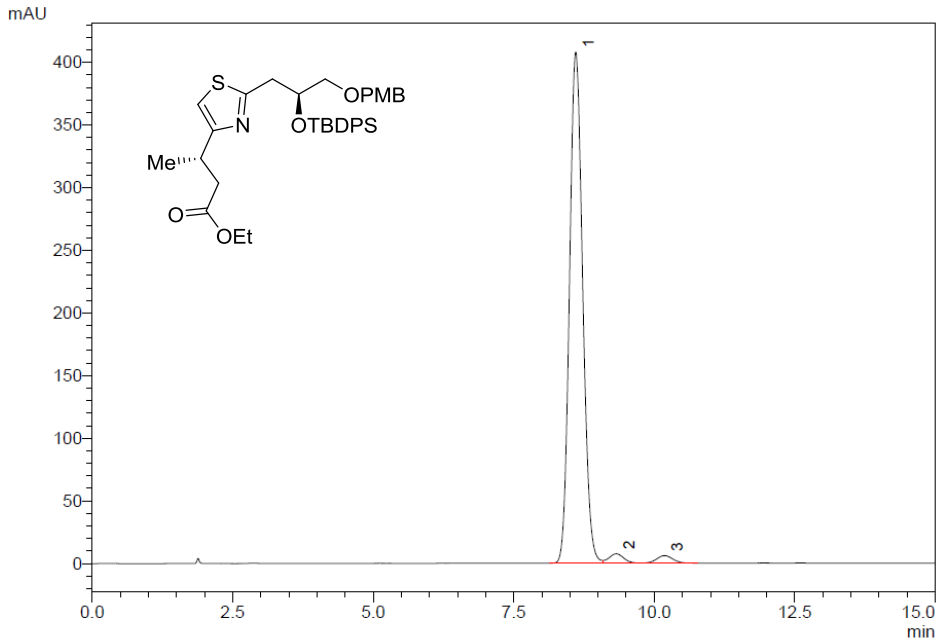
Peak #	Ret. Time	Area %
1	5,75	98,35
2	7,93	1,65
Total		100,00



1 220nm,4nm

PDA Ch1 220nm

Peak #	Ret. Time	Area %
1	8.65	44.74
2	9.36	50.24
3	10.22	2.71
4	10.64	2.31
Total		100.00



1 220nm,4nm

PDA Ch1 220nm

Peak #	Ret. Time	Area %
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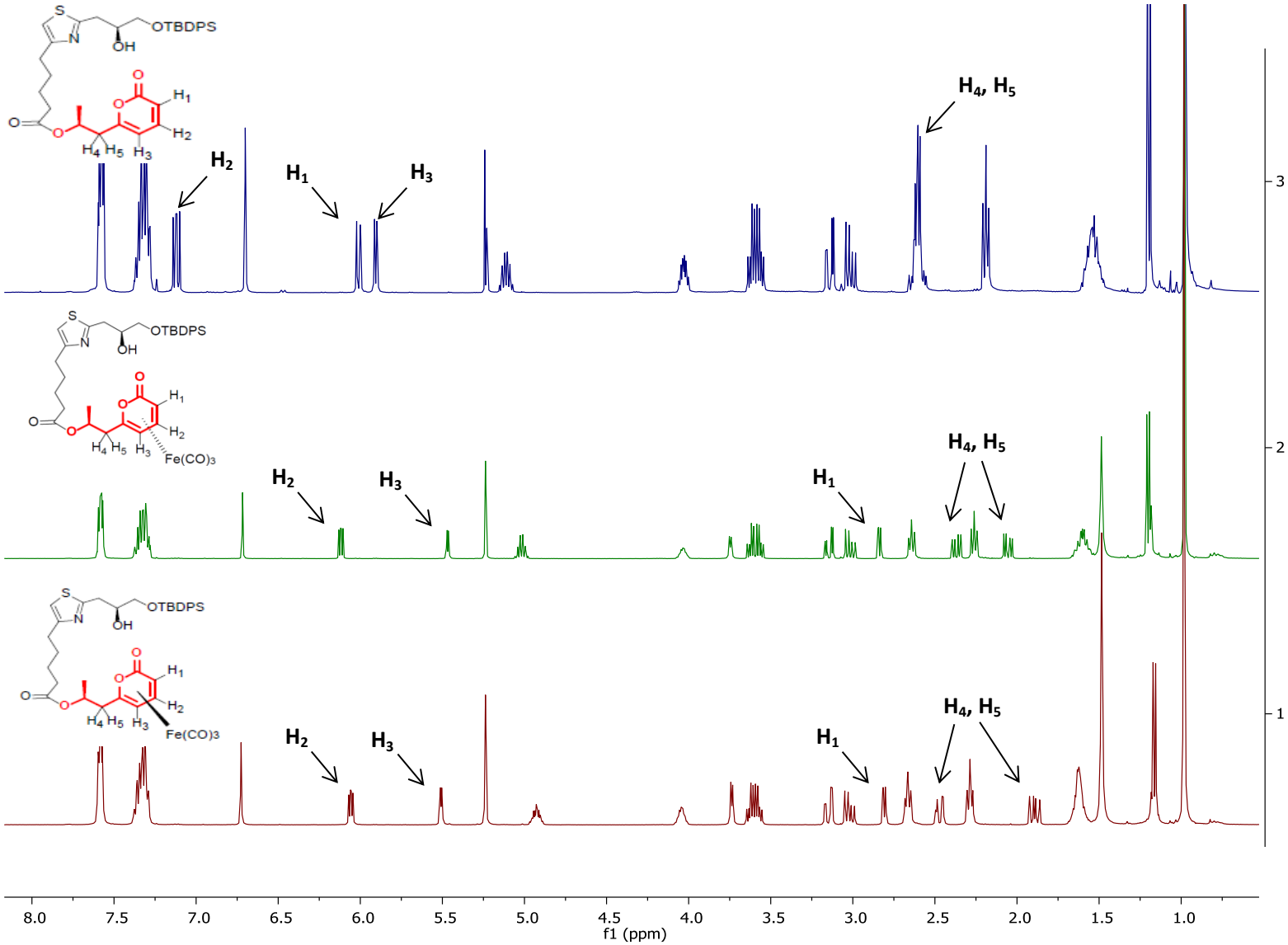
2	9.32	2.00
3	10.18	1.79
Total		100.00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H2
H4 H5 H3
H2
H1
H3
H4, H5
3
OTBDPS
OH
H1
H2
H4 H5 H3
Fe(CO)3
H2
H3
H1
H4, H5
2
OTBDPS
OH
H1
H2
H4 H5 H3
Fe(CO)3
H2
H3
H1
H4, H5
1
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7.5
7.0
6.5
6.0
5.5
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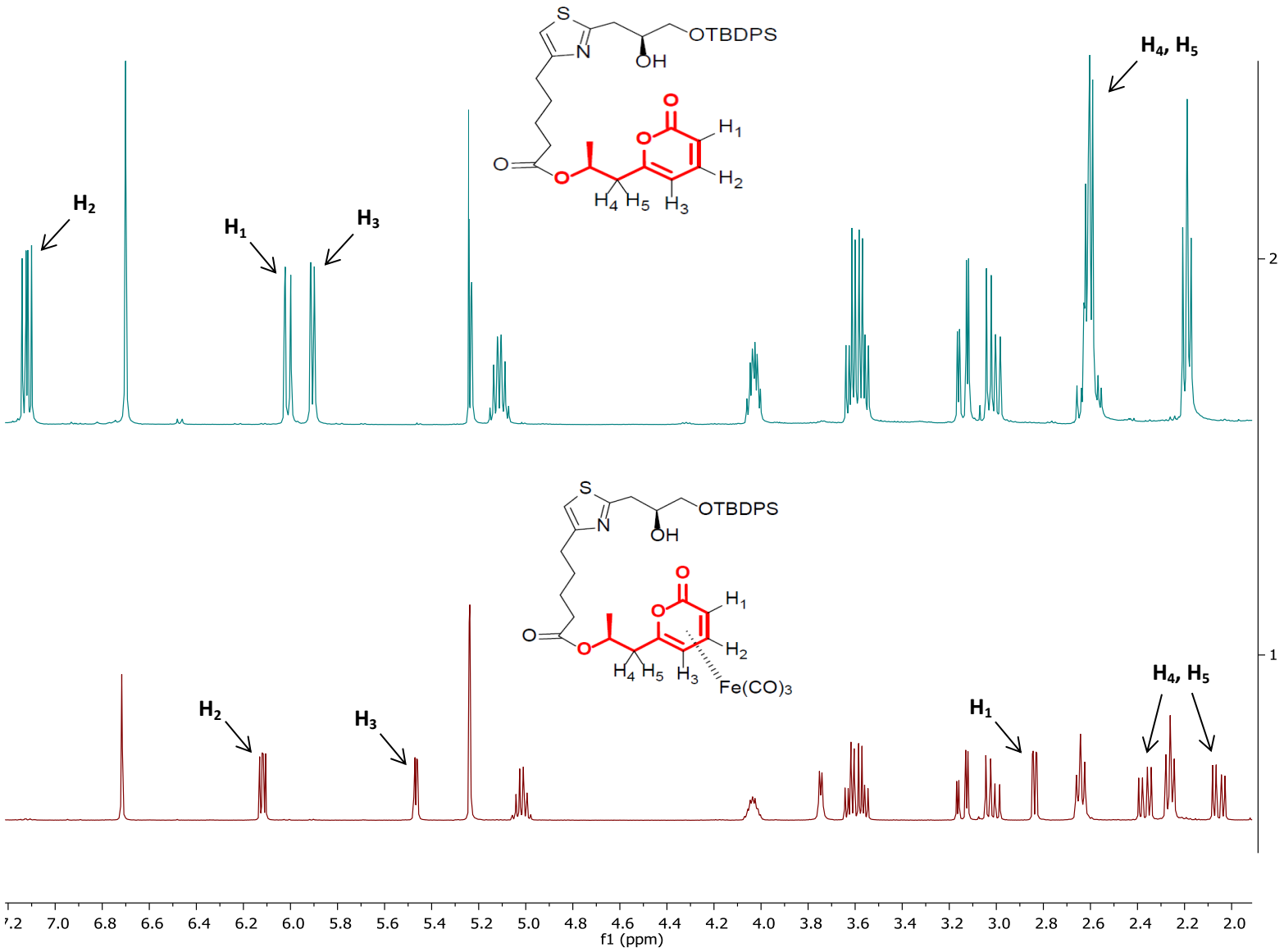
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


S
N
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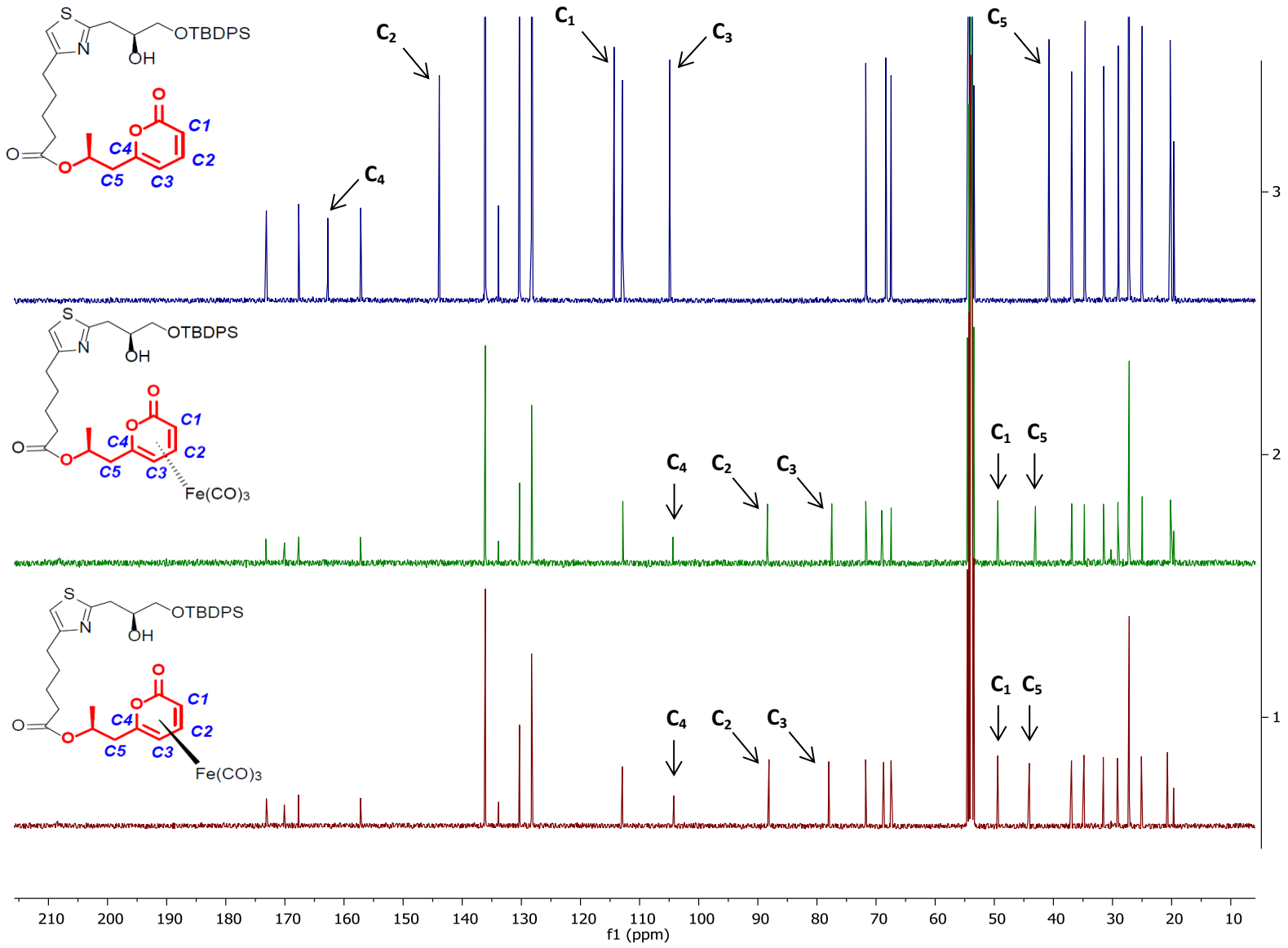
OH
O
O
O
H1
H2
H4 H5 H3
H4, H5
H2
H1
H3
2
S
N
OTBDPS
OH
O
O
O
H1
H2
H4 H5 H3
Fe(CO)3
H2
H3
H1
H4, H5
1
7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0
f1 (ppm)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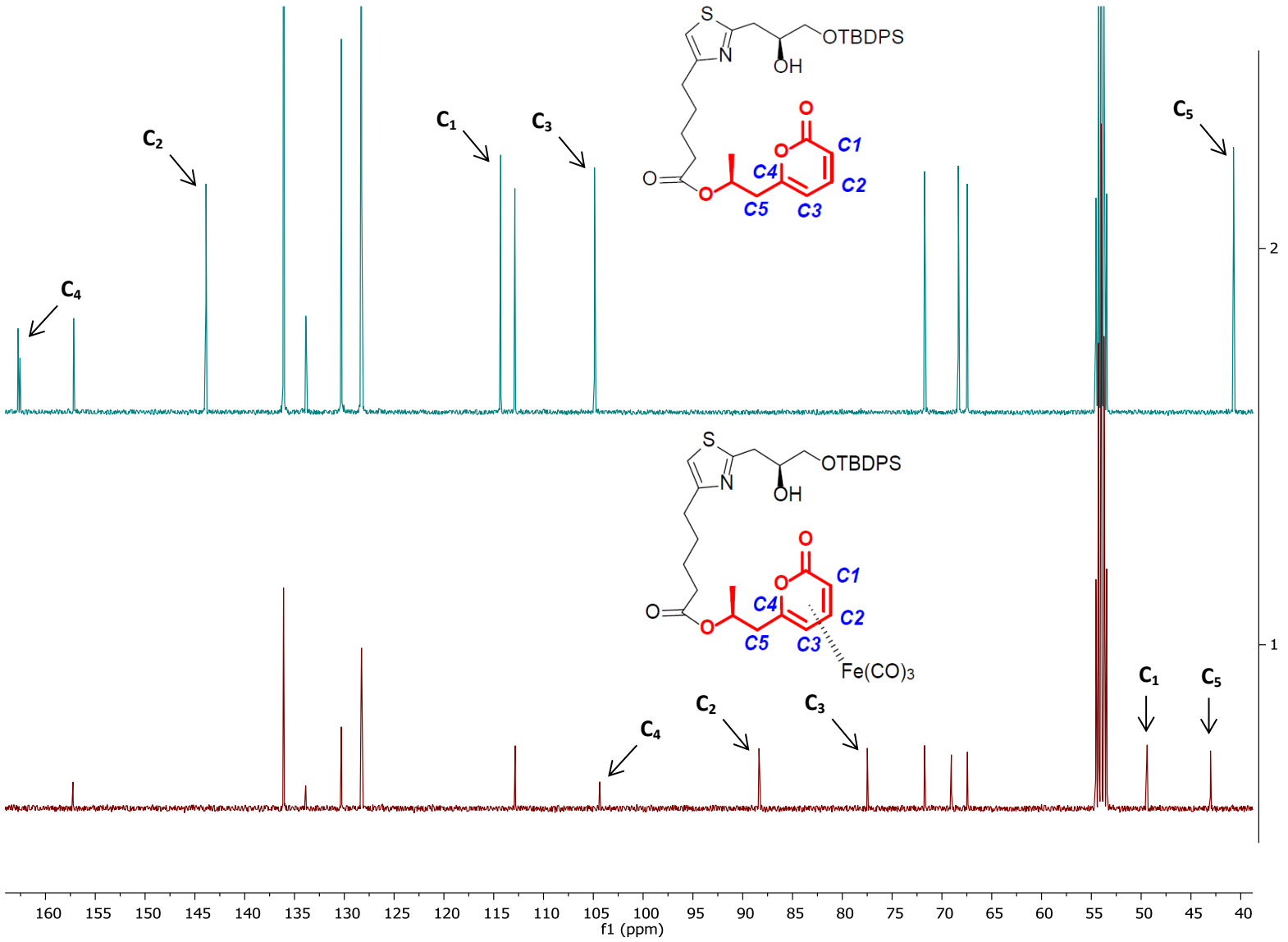
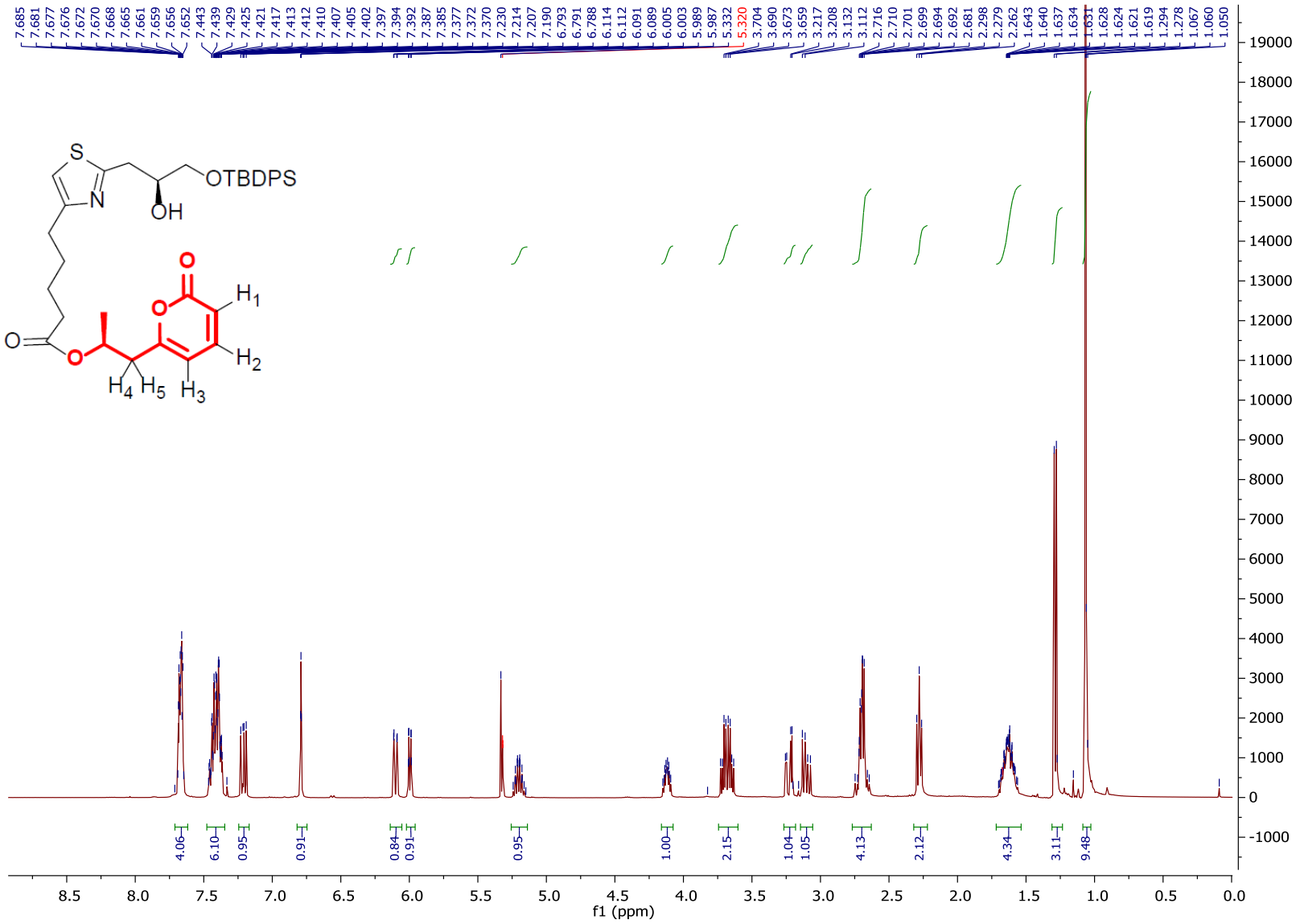
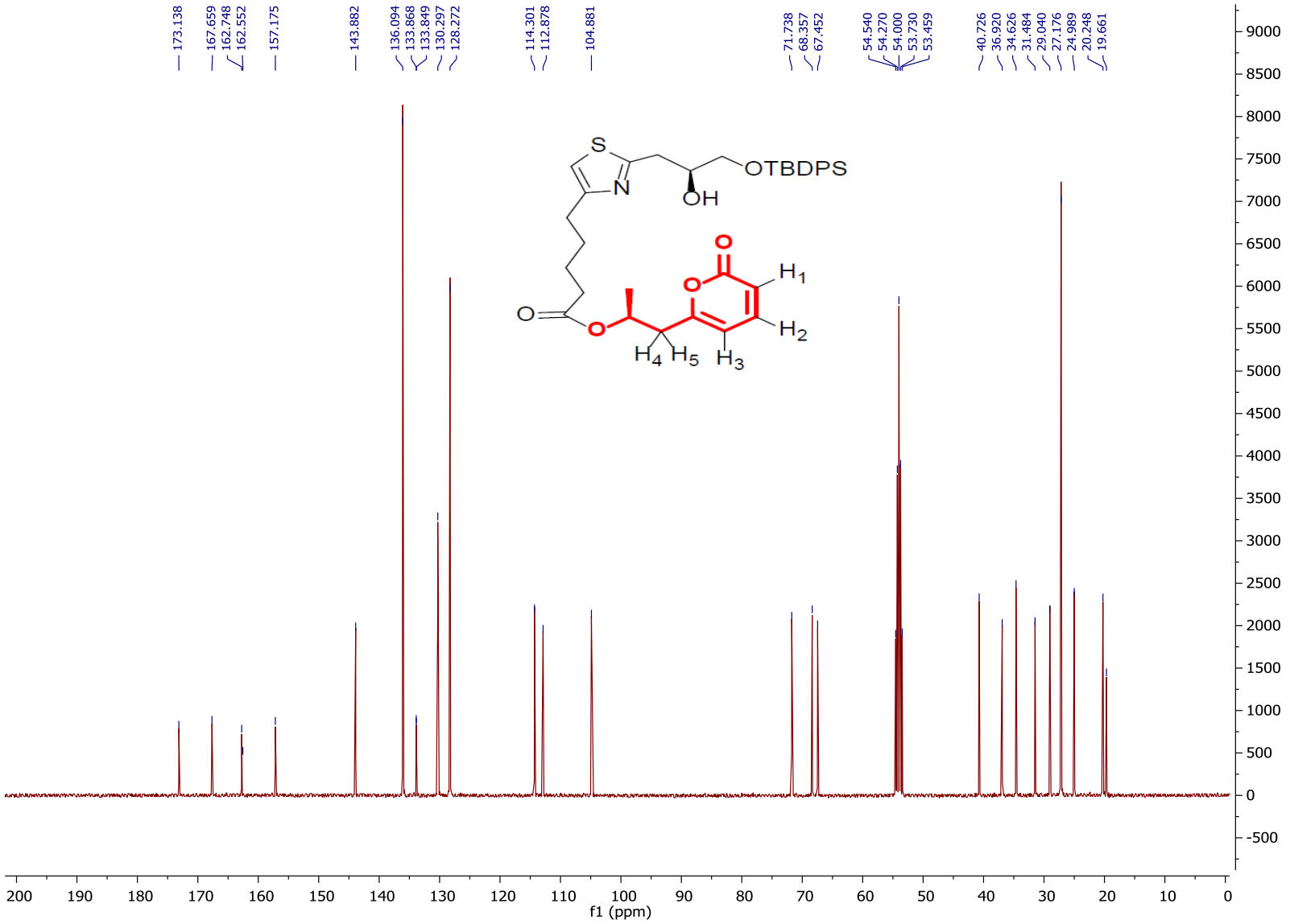
S
N
O
C1
C2
C3
C4
C5
C2
C1
C3
C5
C4
C4
C2
C3
C1
C5
Fe(CO)3
C4
C2
C3
C1
C5
Fe(CO)3
3
2
1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


C1
C2
C3
C4
C5
OTBDPS
OH
S
N
O
Fe(CO)3
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
f1 (ppm)
2
1


S
N
OTBDPS
OH
O
O
O
H1
H2
H3
H4
H5
f1 (ppm)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S
N
OH
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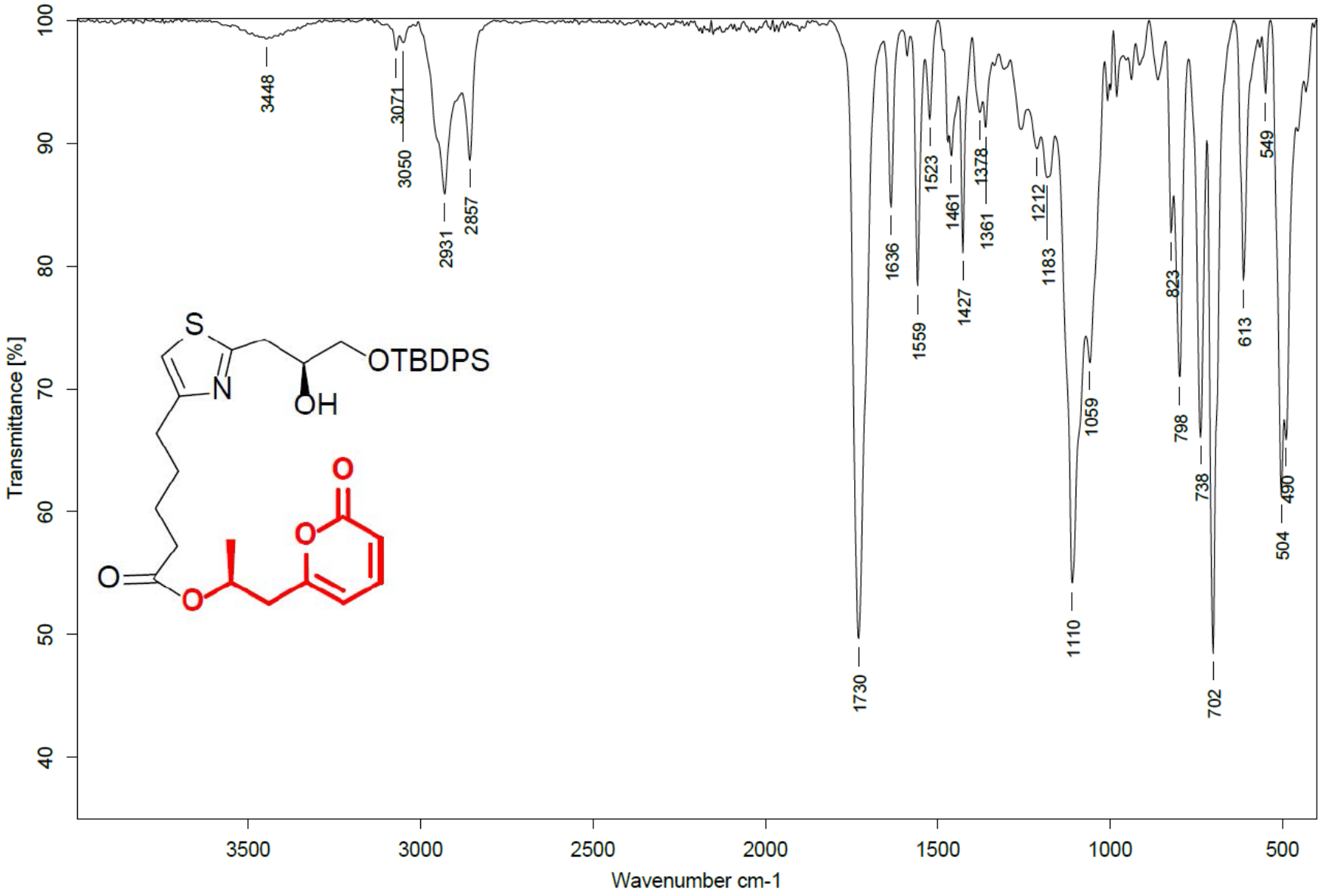
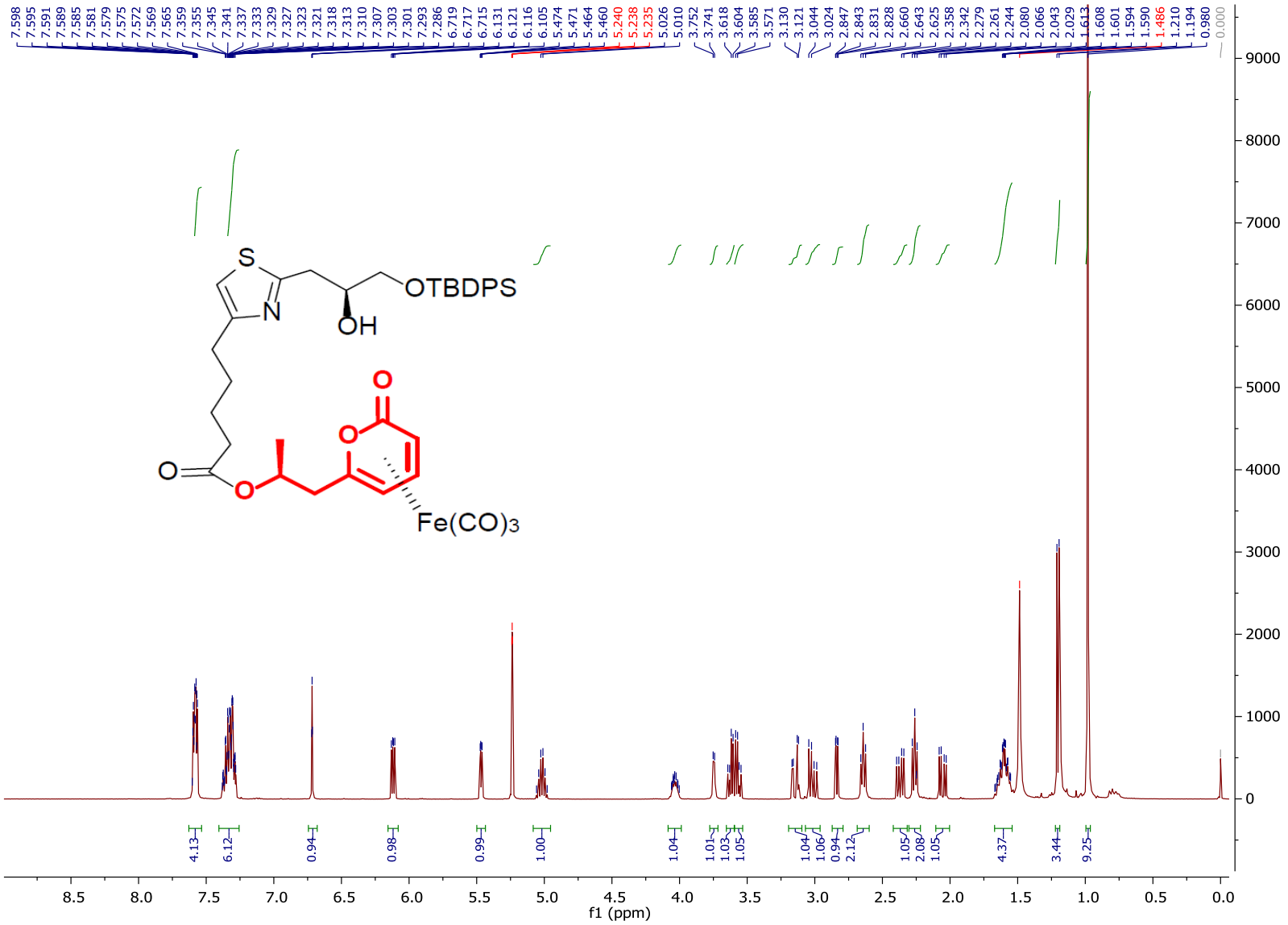
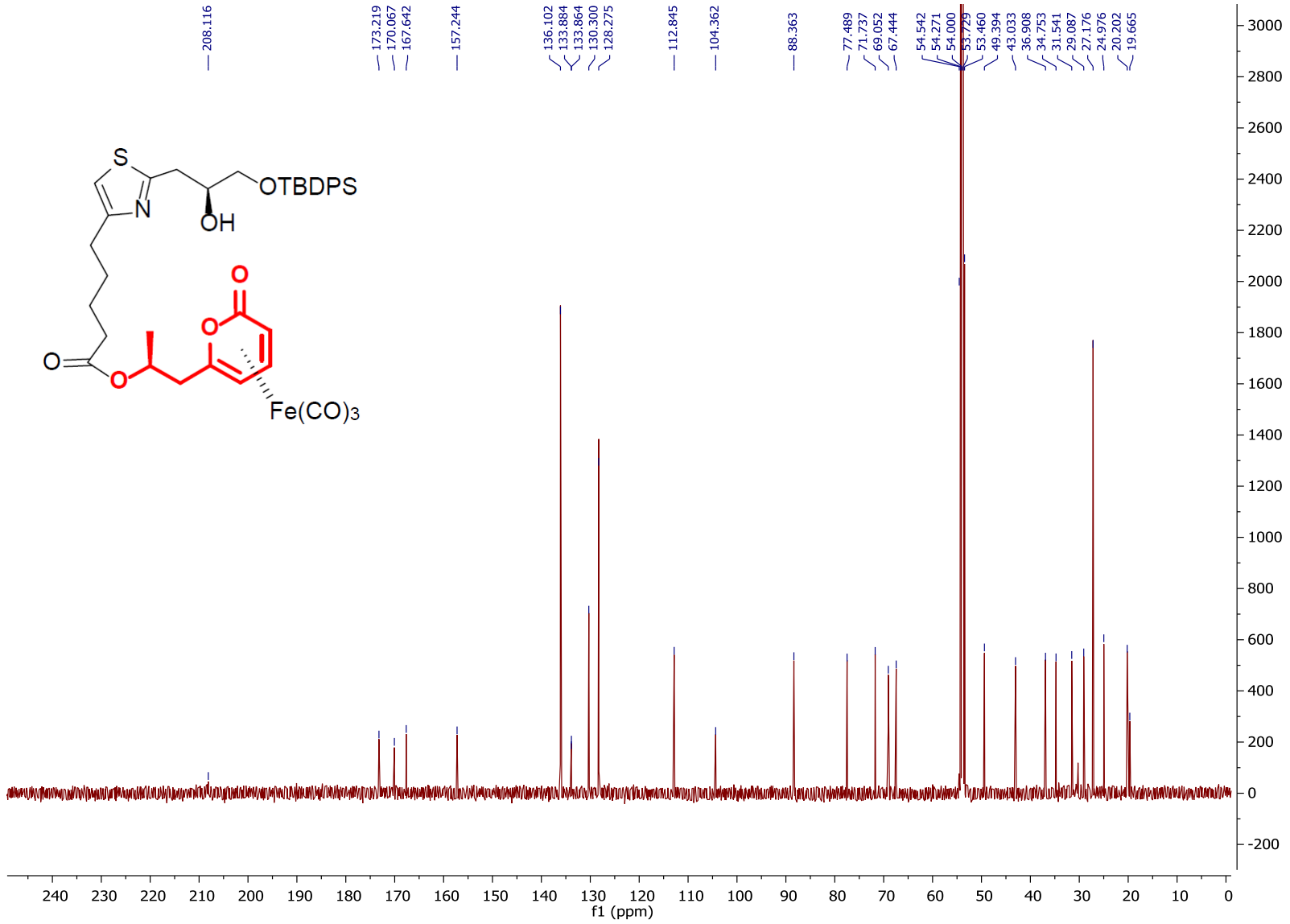
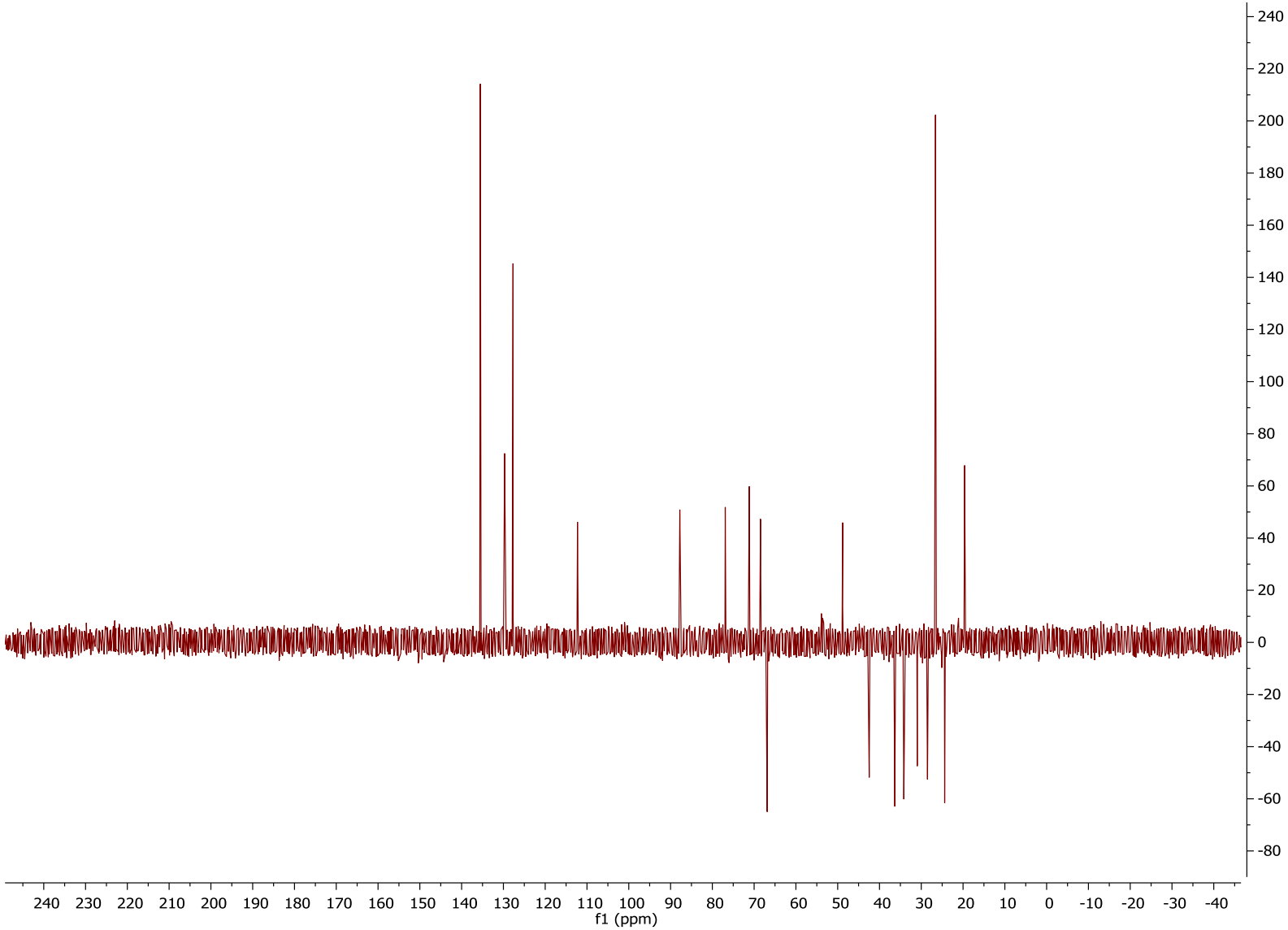
O
O
O
H1
H2
H4
H5
H3
9000
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

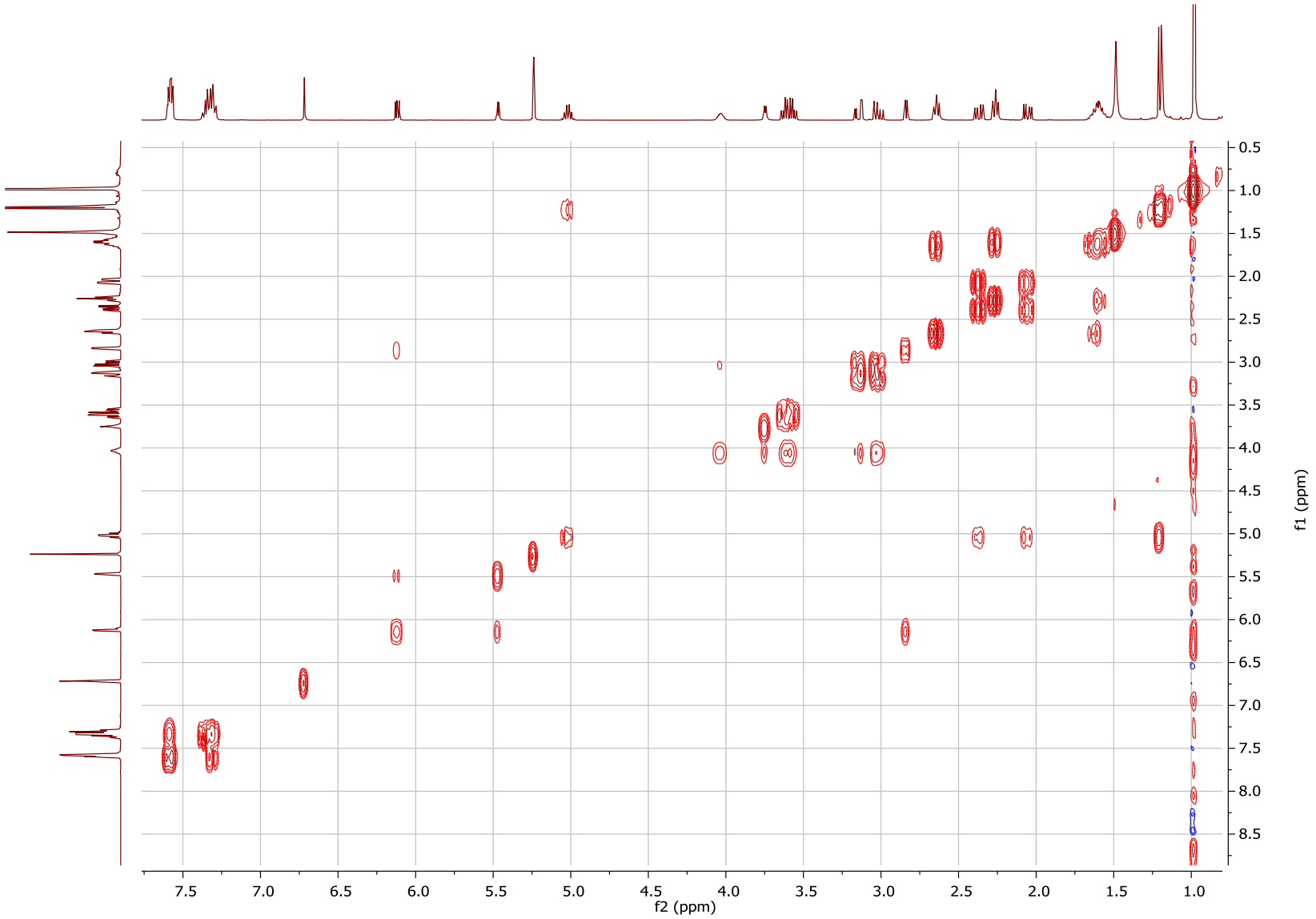

Transmittance [%]
100
90
80
70
60
50
40
3448
3071
3050
2931
2857
1730
1636
1559
1523
1461
1427
1378
1361
1212
1183
1110
1059
823
798
738
702
613
549
504
490
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
S
N
OTBDPS
OH
O
O
O
O

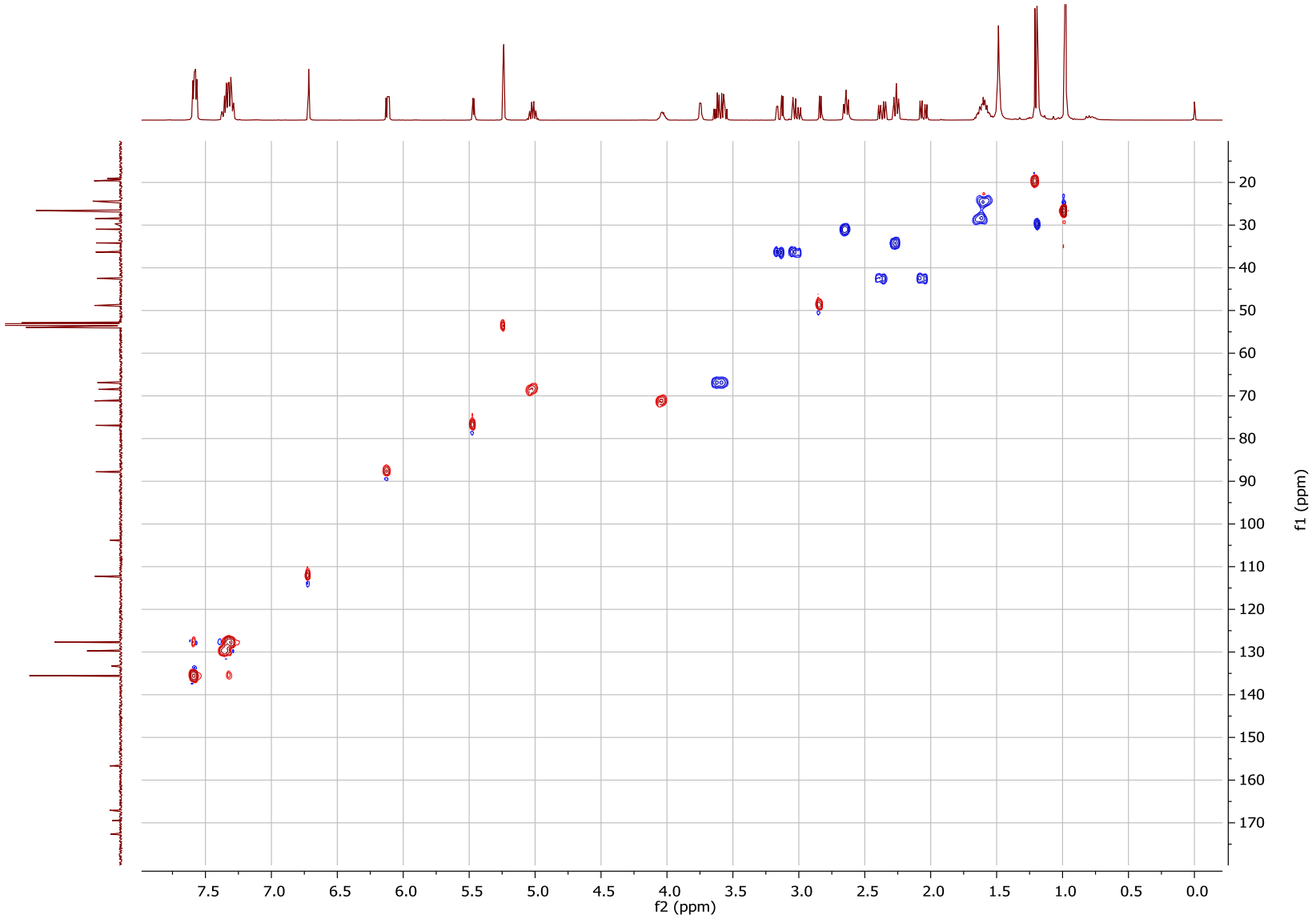
Iron Complex: First diastereomer

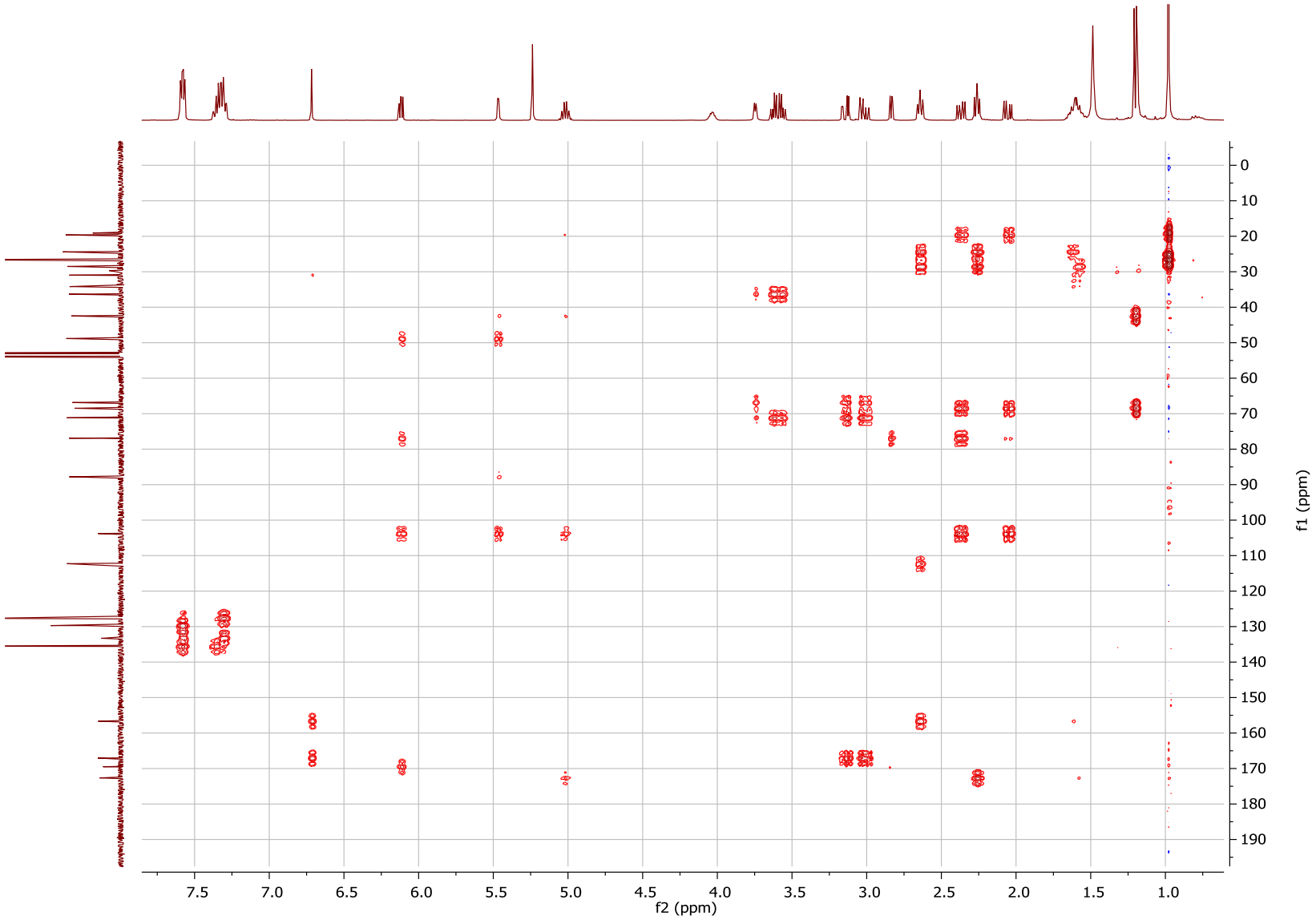


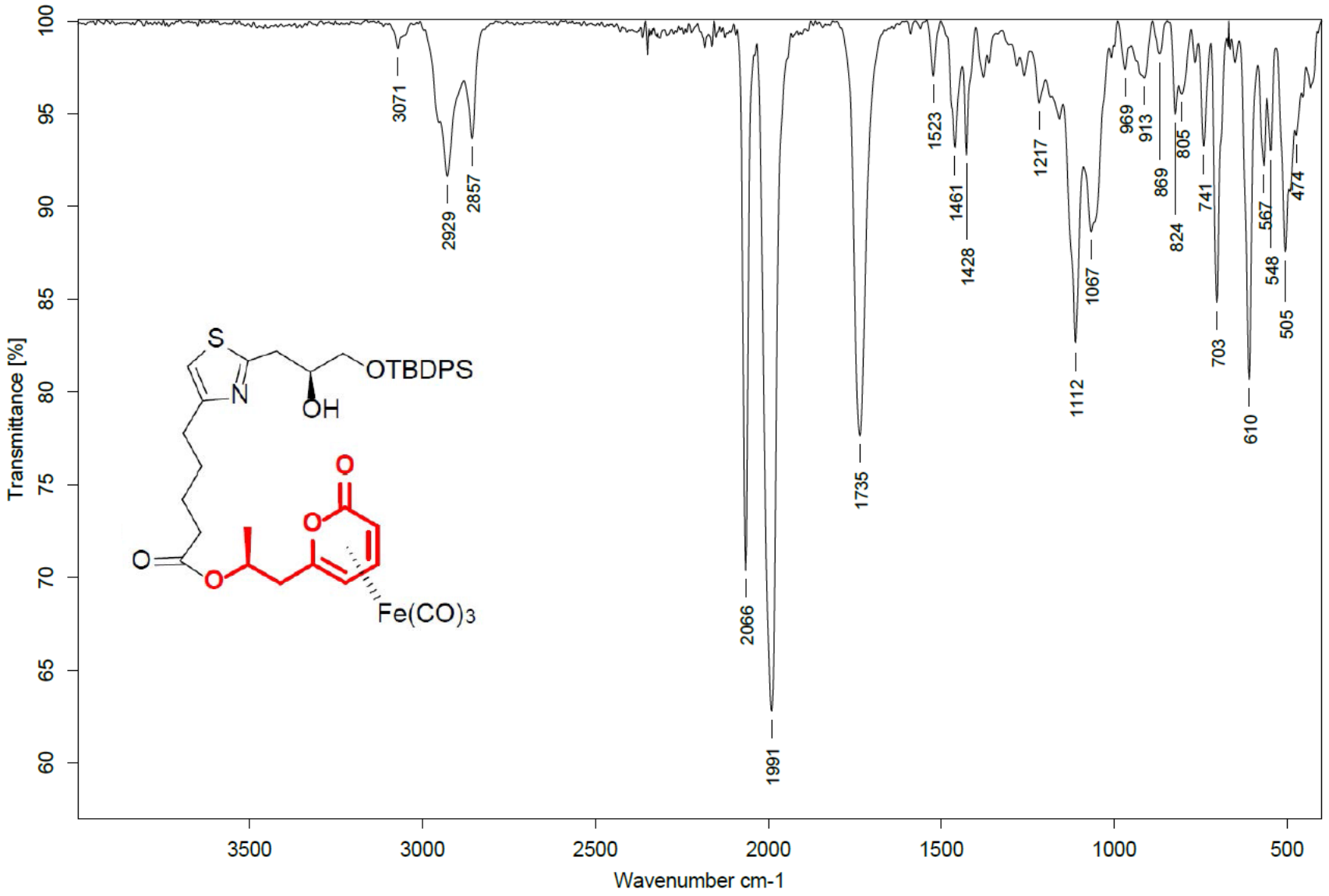

208.116
173.219
170.067
167.642
157.244
136.102
133.884
133.864
130.300
128.275
112.845
104.362
88.363
77.489
71.737
69.052
67.444
54.542
54.271
54.000
53.729
53.460
49.394
43.033
36.908
34.753
31.541
29.087
27.176
24.976
20.202
19.665
S
N
OTBDPS
OH
O
O
O
O
Fe(CO)3
f1 (ppm)


240
220
200
180
160
140
120
100
80
60
40
20
0
-20
-40
-60
-80
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

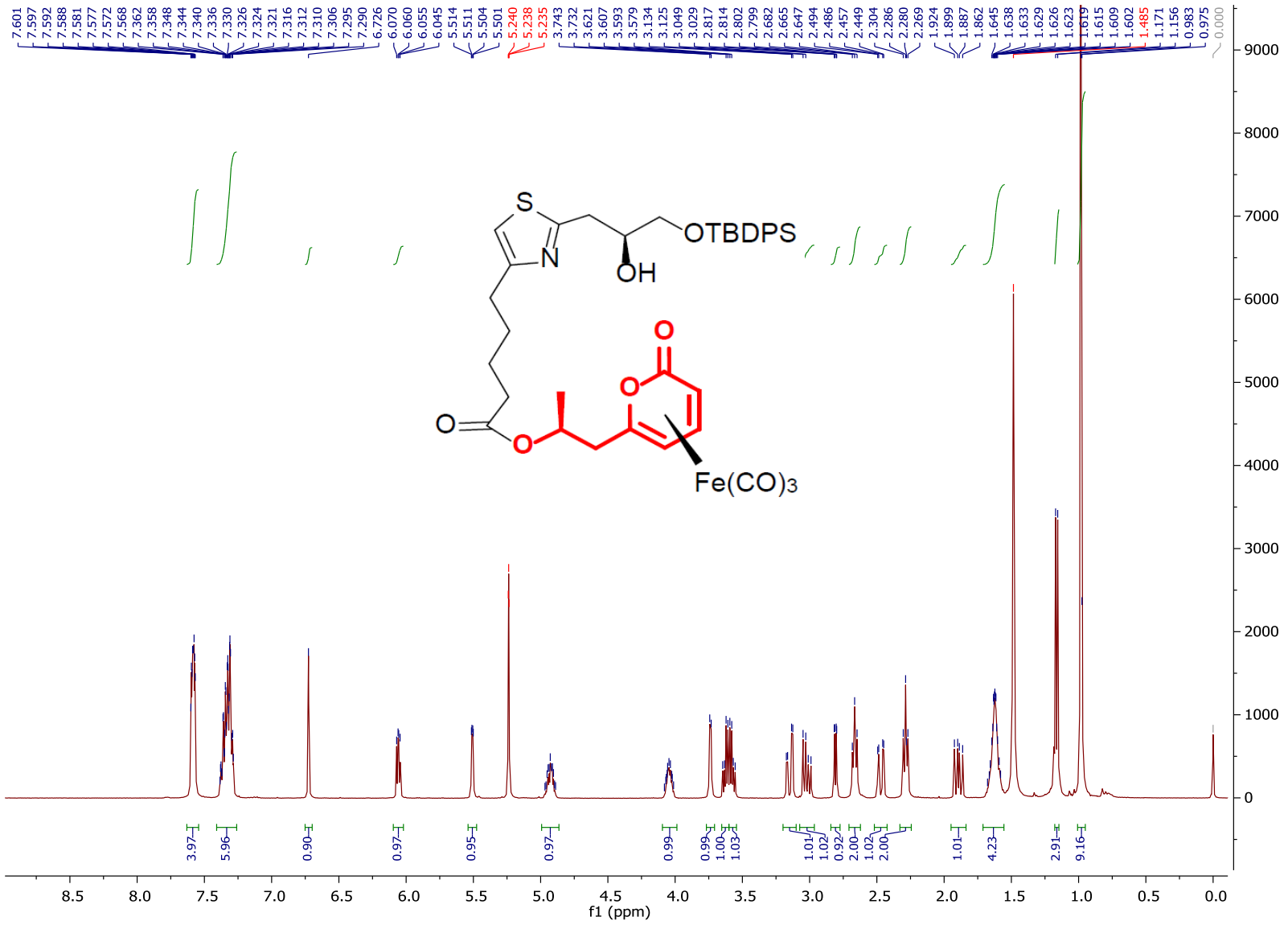

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
f1 (ppm)

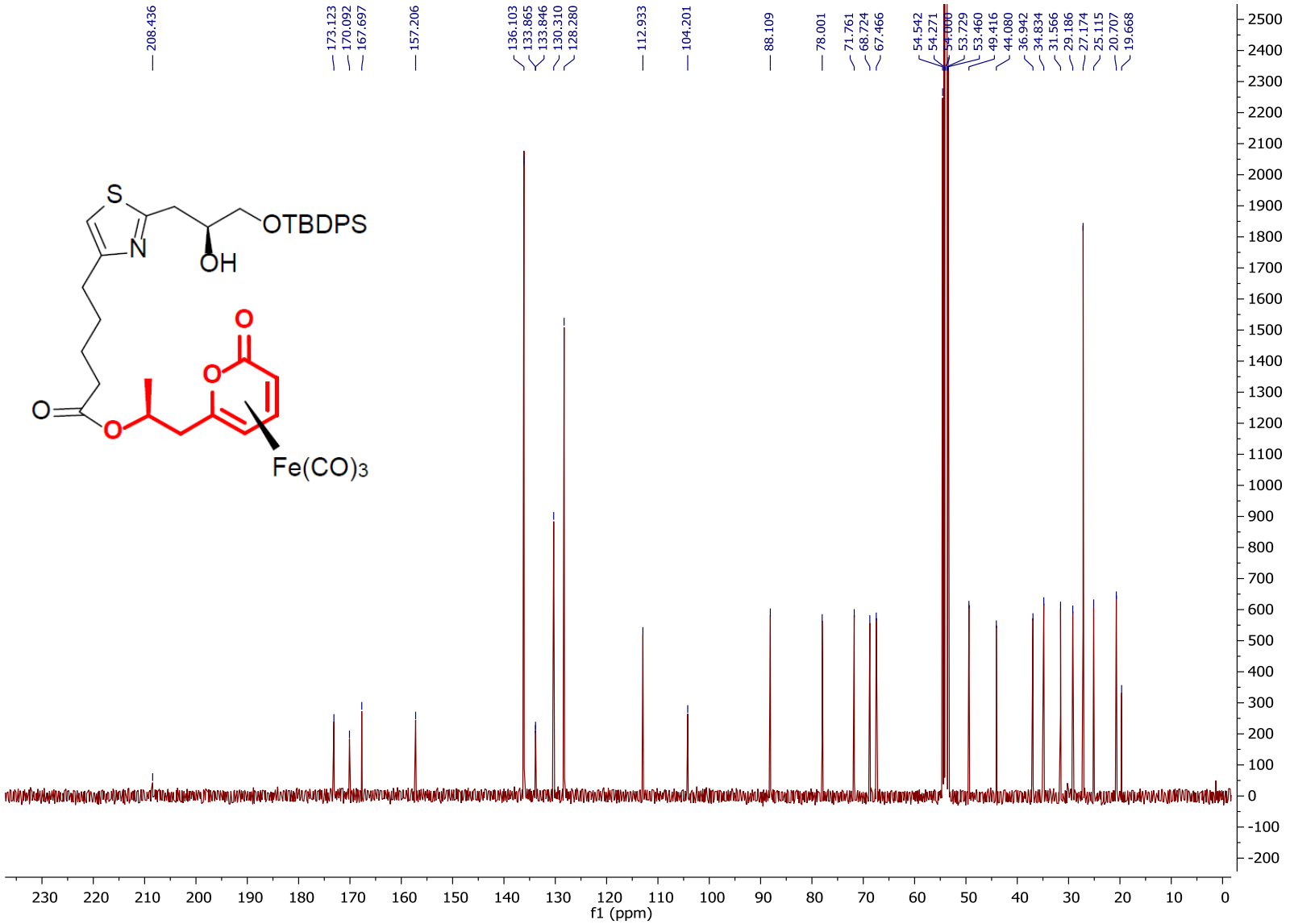

f2 (ppm)
f1 (ppm)

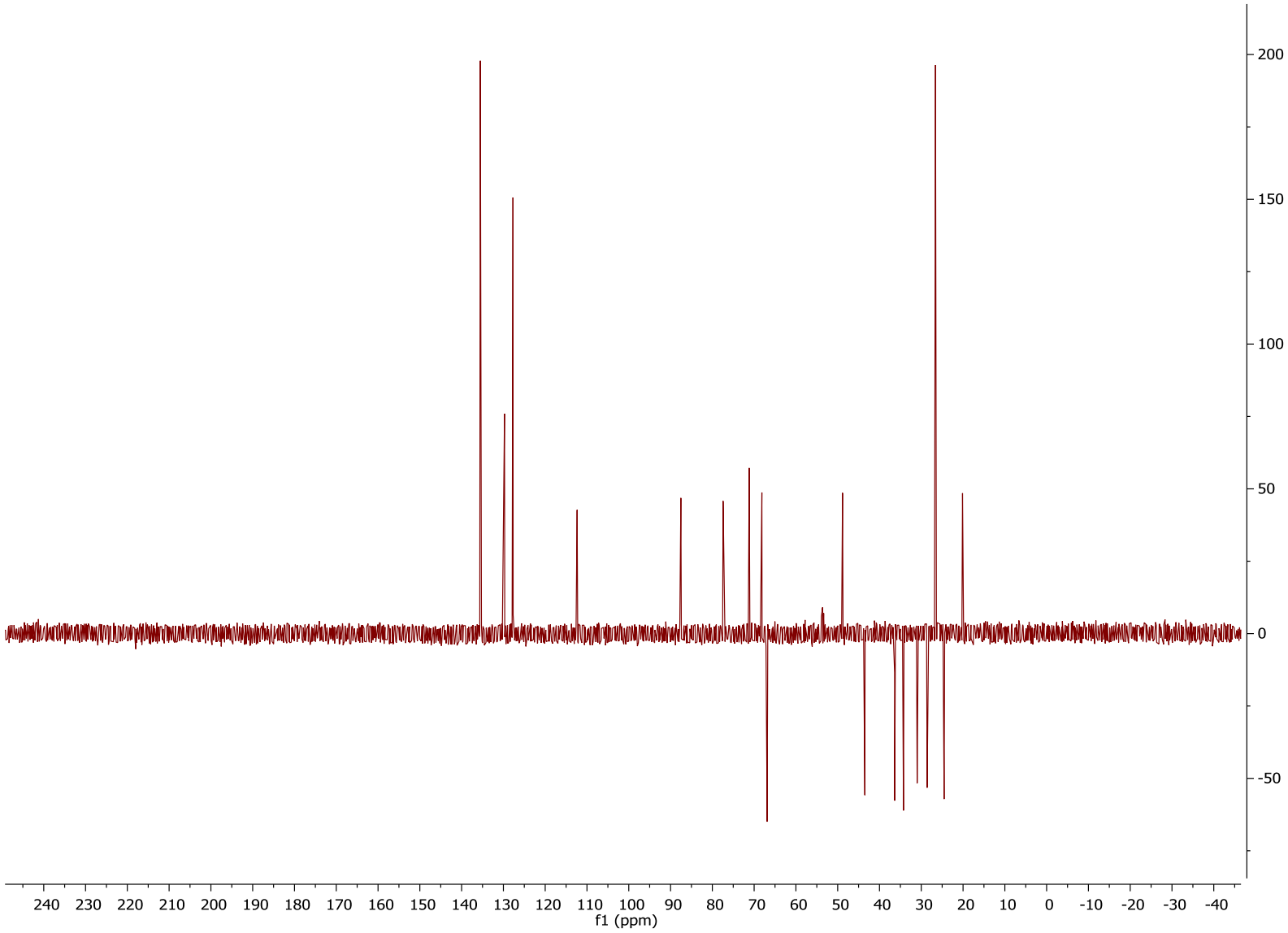

f2 (ppm)
f1 (ppm)

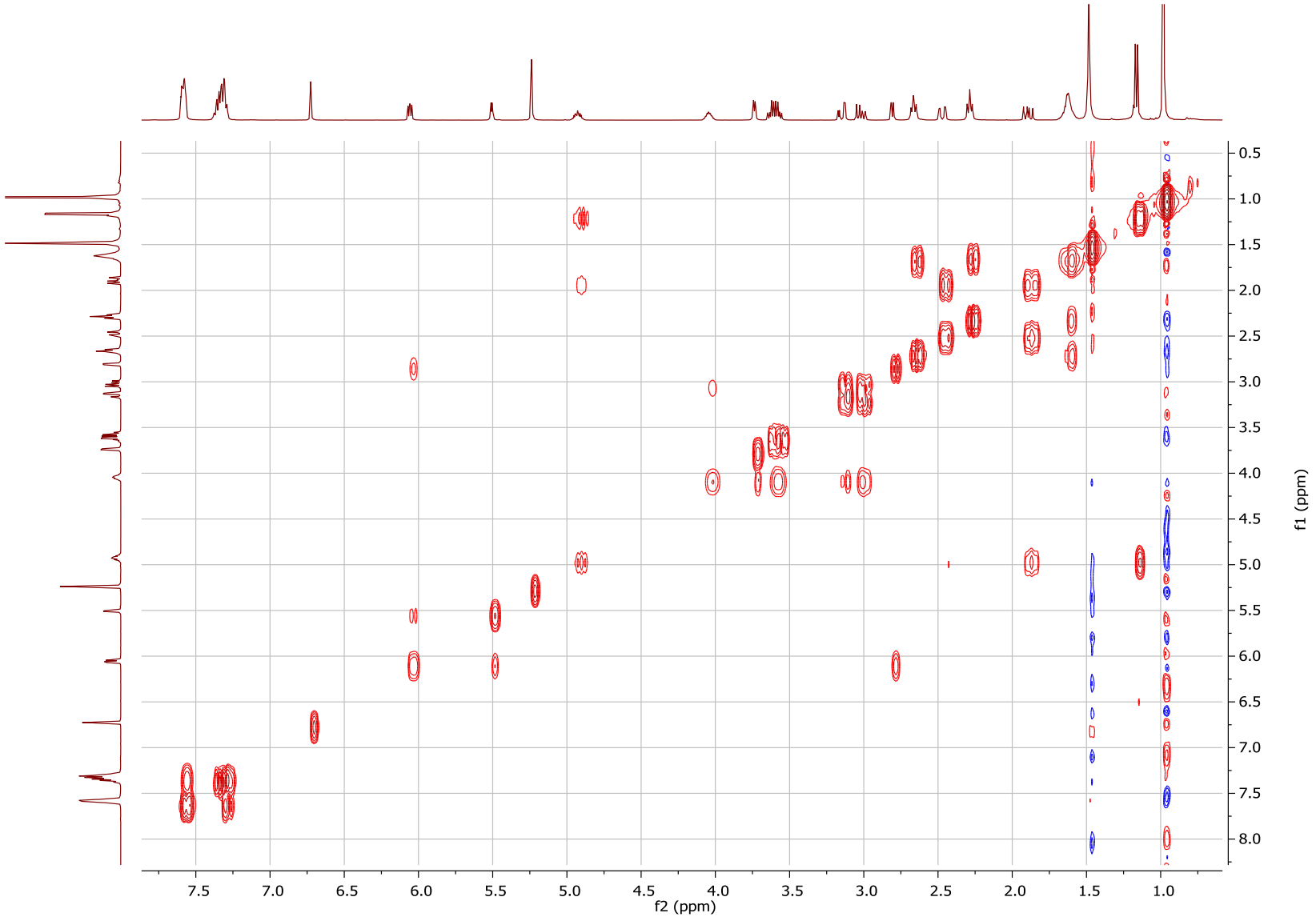

Transmittance [%]
100
95
90
85
80
75
70
65
60
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
3071
2929
2857
2066
1991
1735
1523
1461
1428
1217
1112
1067
969
913
869
824
805
741
703
610
567
548
505
474
S
N
OTBDPS
OH
O
O
O
O
Fe(CO)3

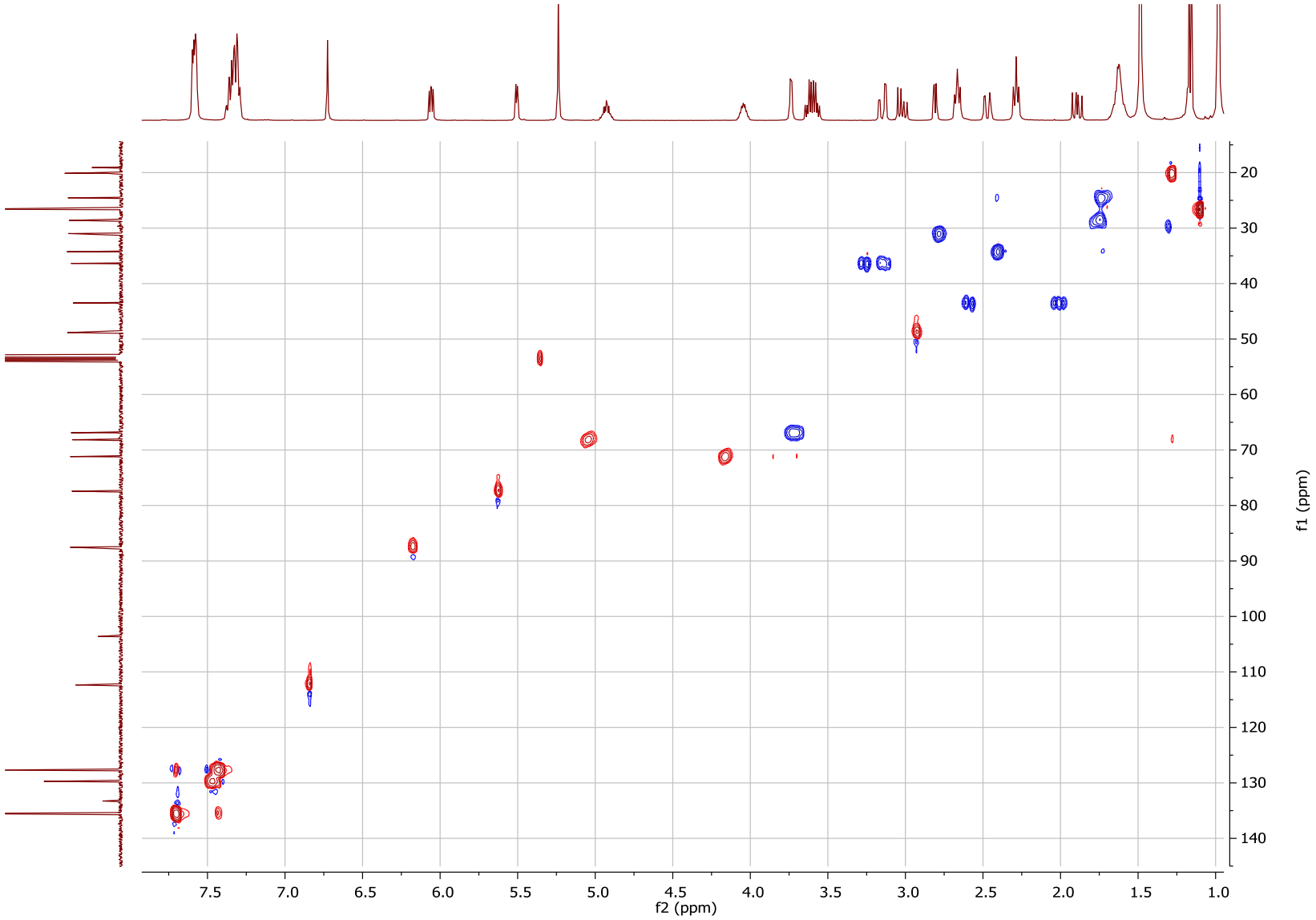
Iron Complex: Second diastereomer

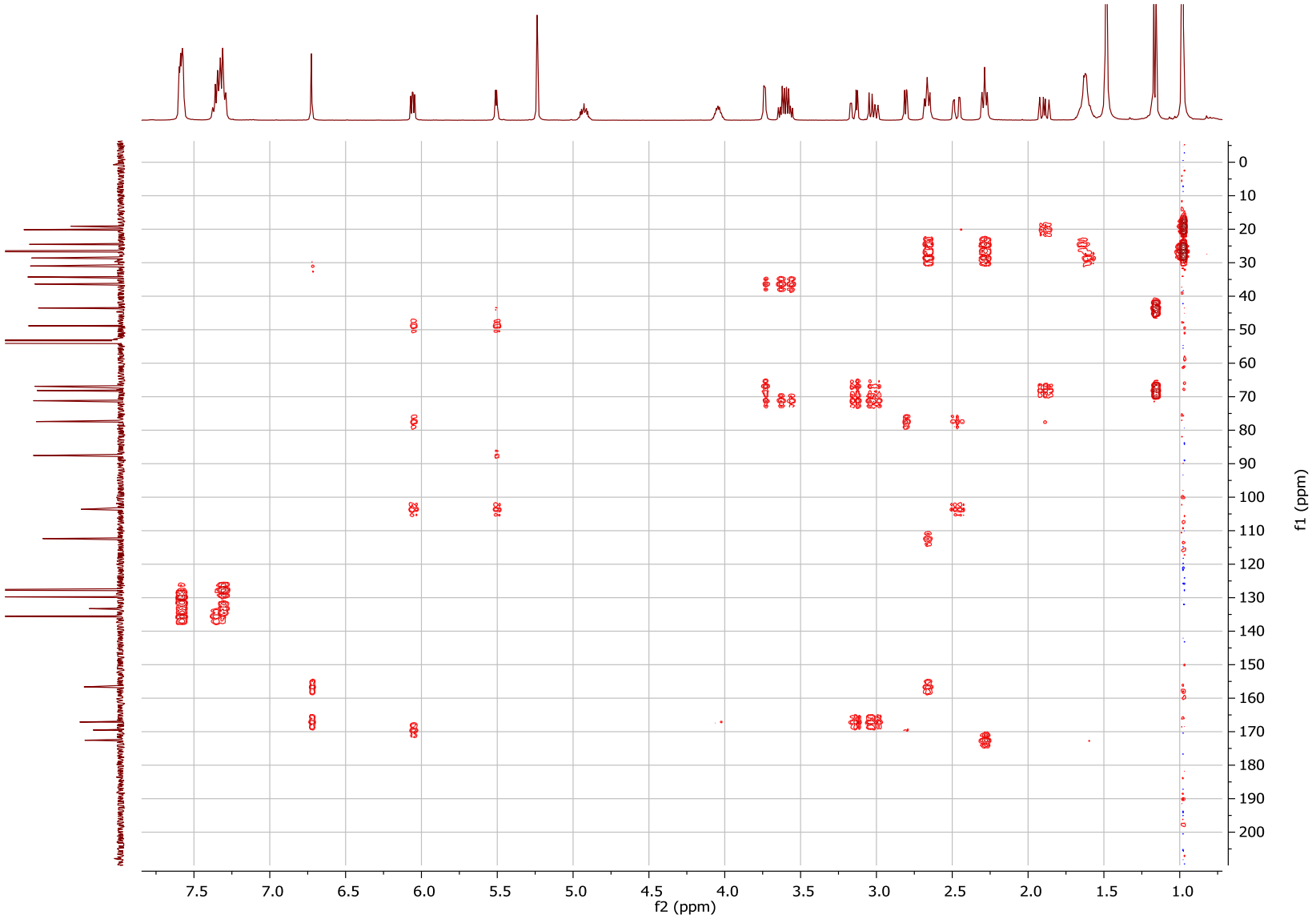


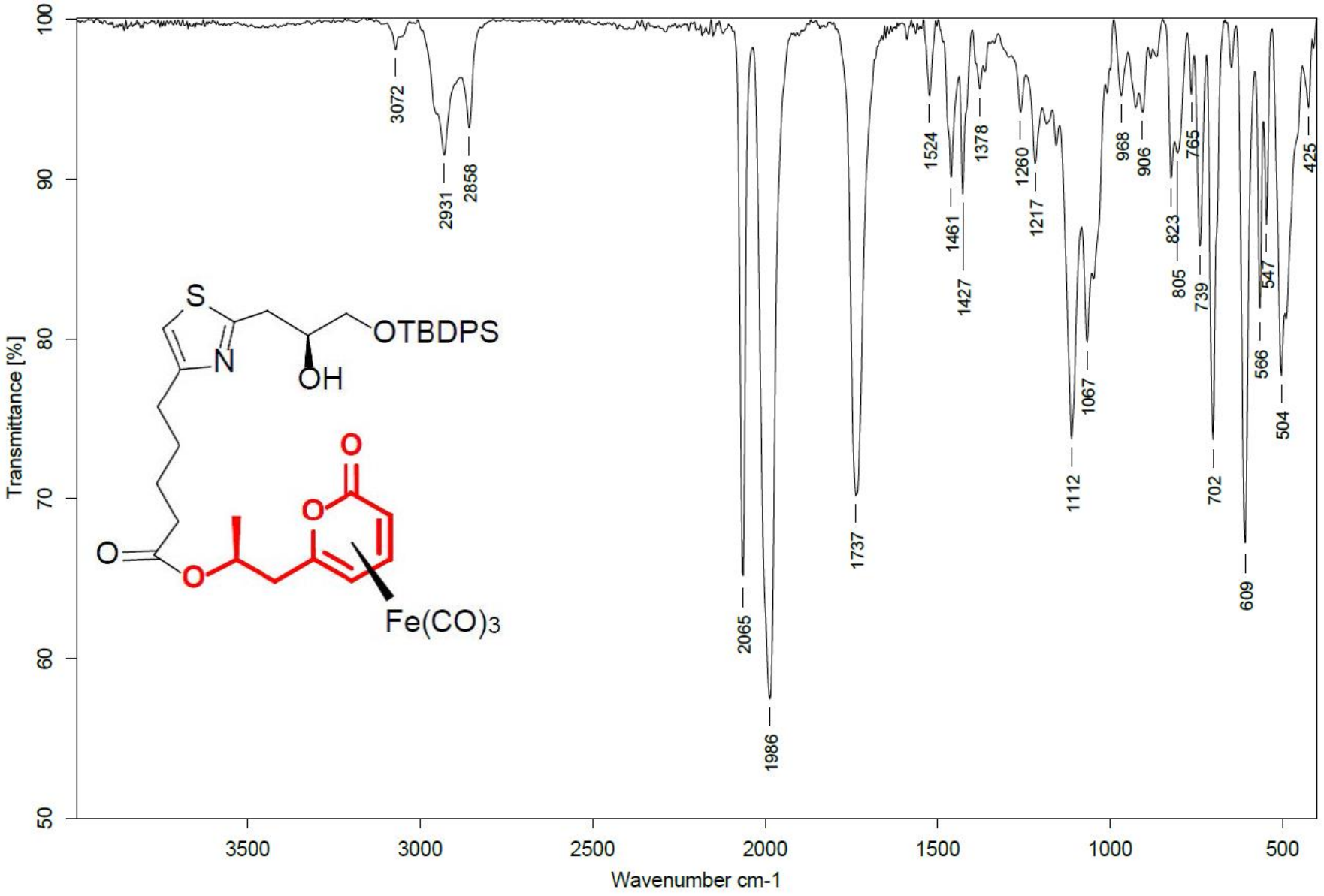

208.436
173.123
170.092
167.697
157.206
136.103
133.865
133.846
130.310
128.280
112.933
104.201
88.109
78.001
71.761
68.724
67.466
54.542
54.271
54.000
53.729
53.460
49.416
44.080
36.942
34.834
31.566
29.186
27.174
25.115
20.707
19.668
S
N
OH
OTBDPS
O
O
O
O
Fe(CO)3
f1 (ppm)

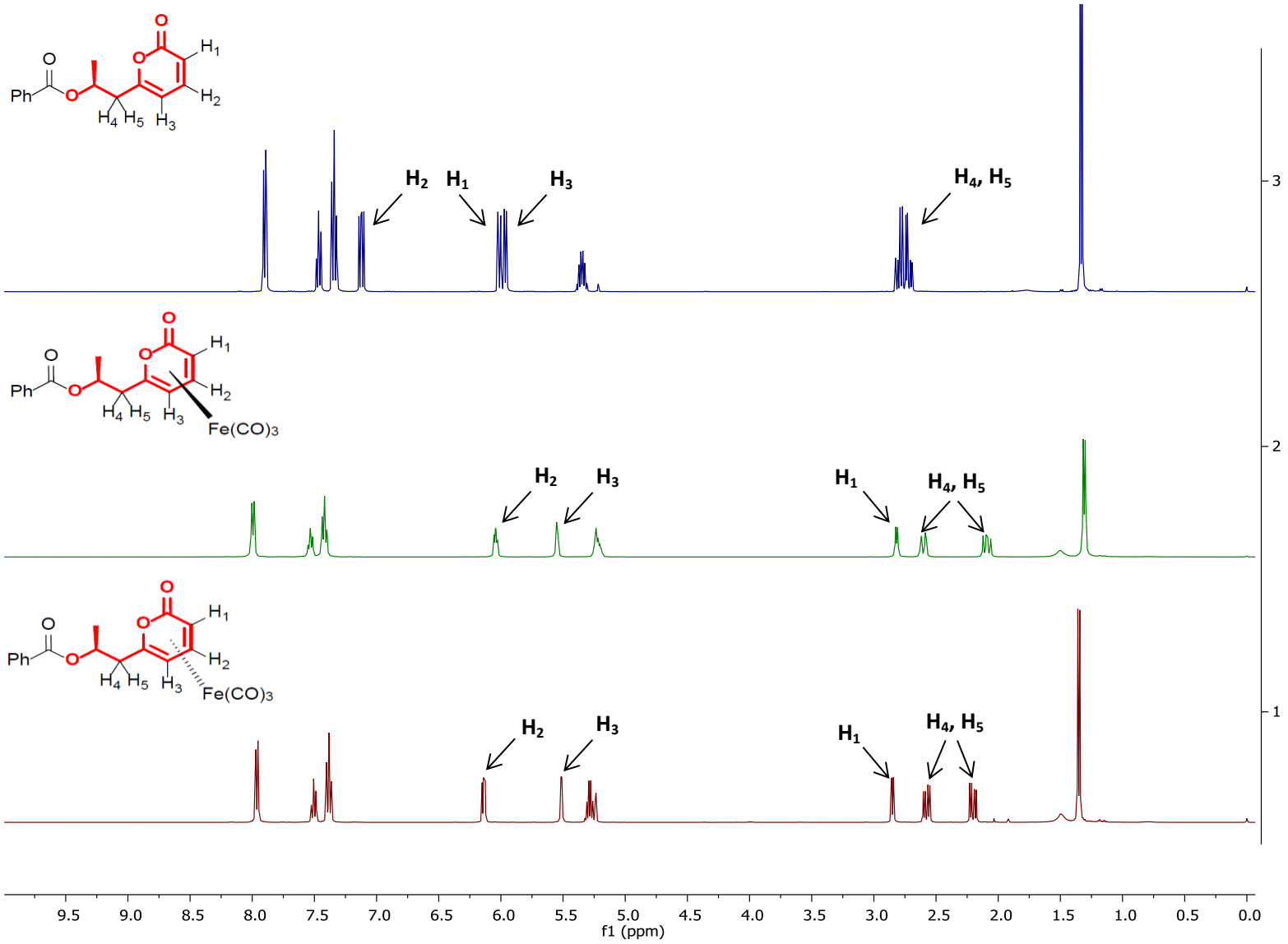

200
150
100
50
0
-50
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

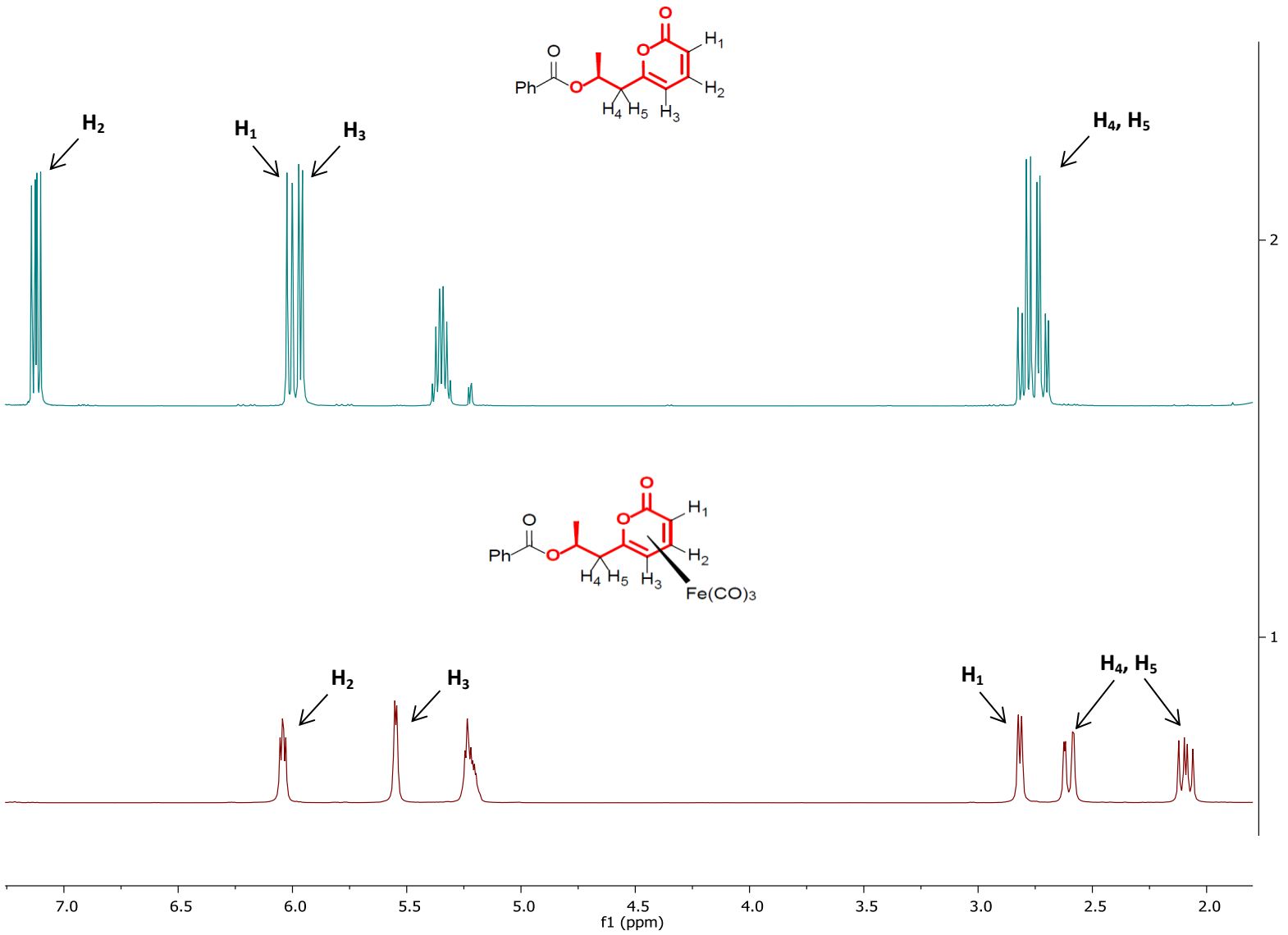

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
f1 (ppm)

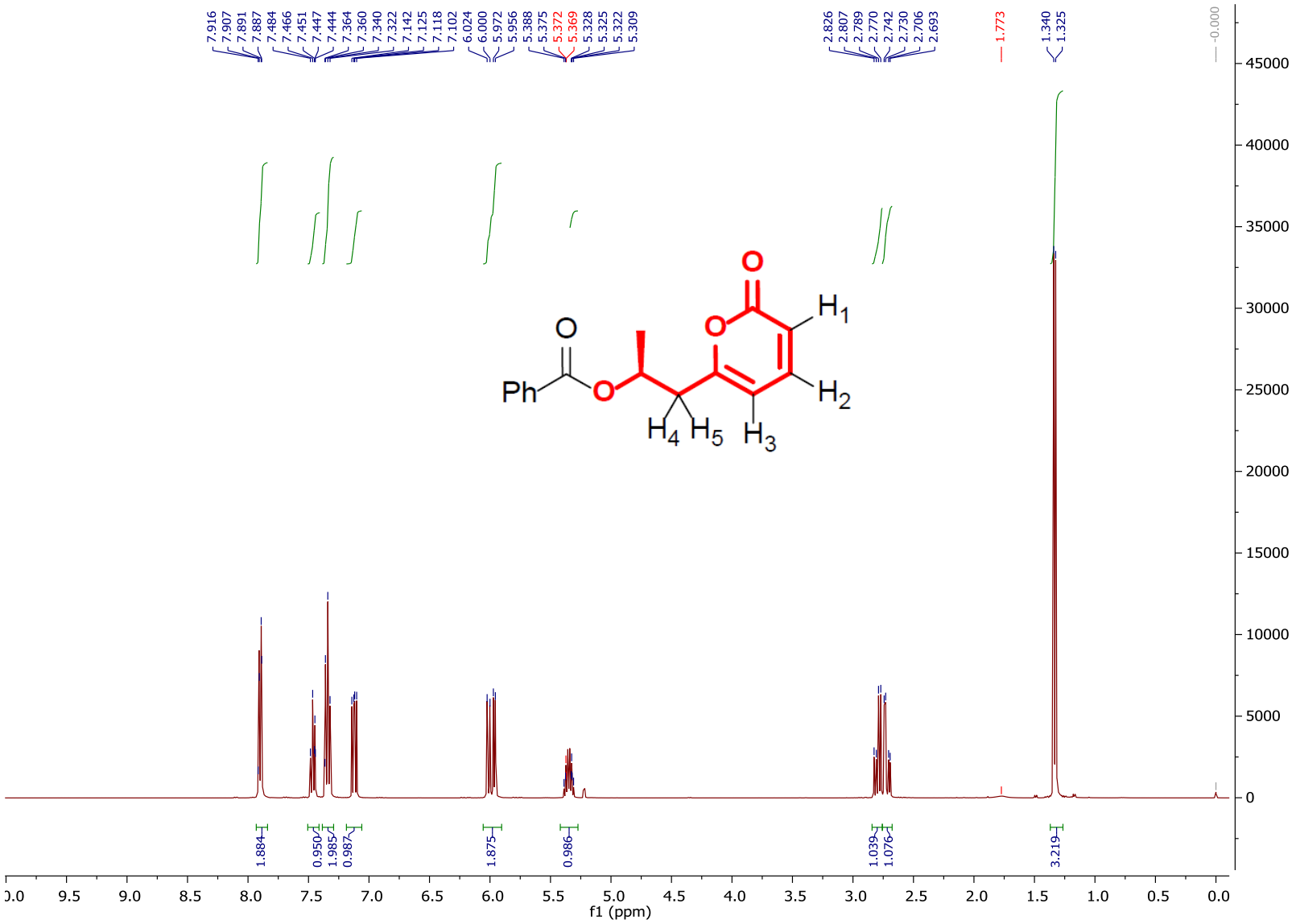

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)
20
30
40
50
60
70
80
90
100
110
120
130
140
f1 (ppm)

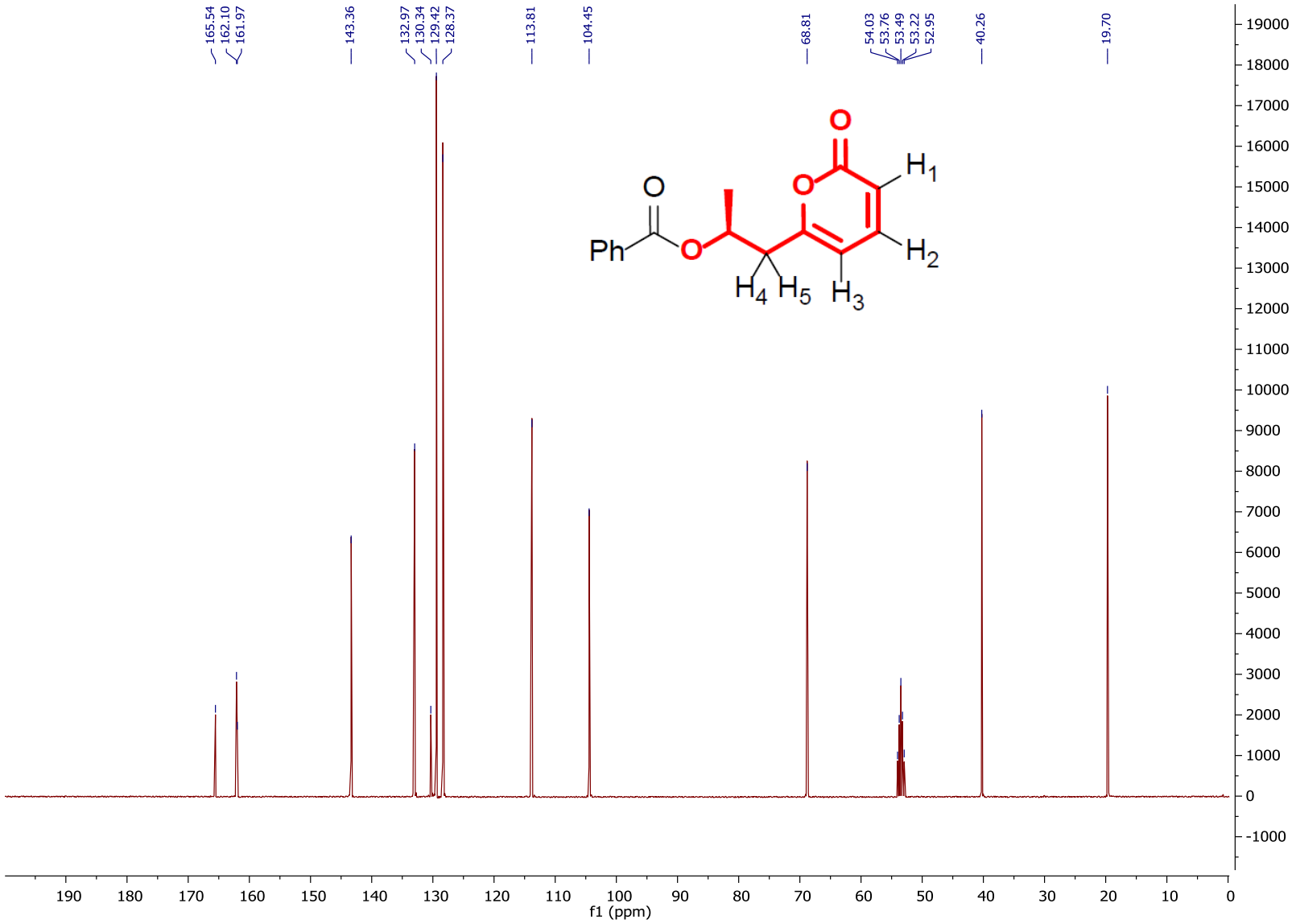

f2 (ppm)
f1 (ppm)

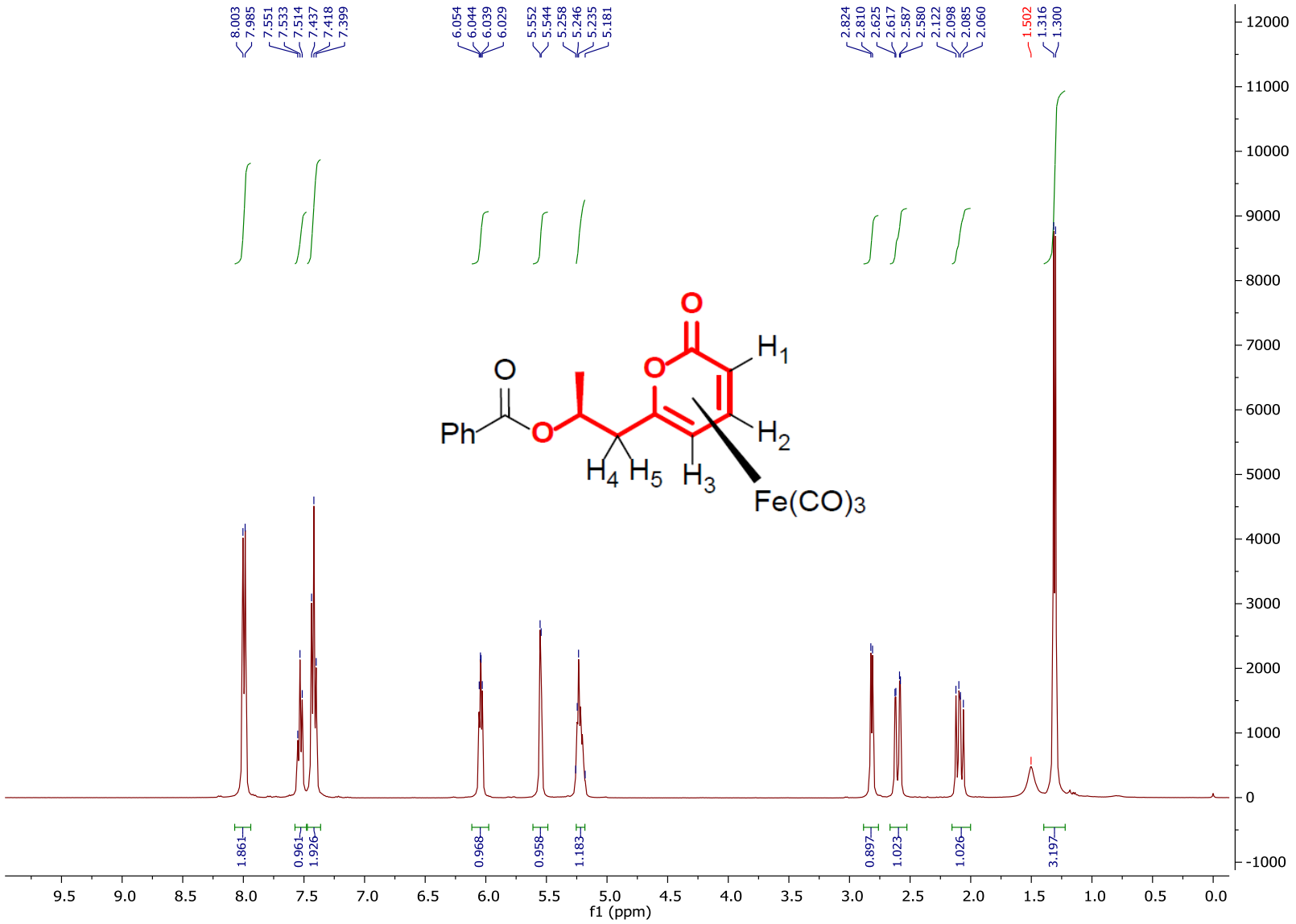

Transmittance [%]
100
90
80
70
60
50
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
3072
2931
2858
2065
1986
1737
1524
1461
1427
1378
1260
1217
1112
1067
968
906
823
805
765
739
702
609
566
547
504
425
S
N
OH
OTBDPS
O
O
O
O
Fe(CO)3

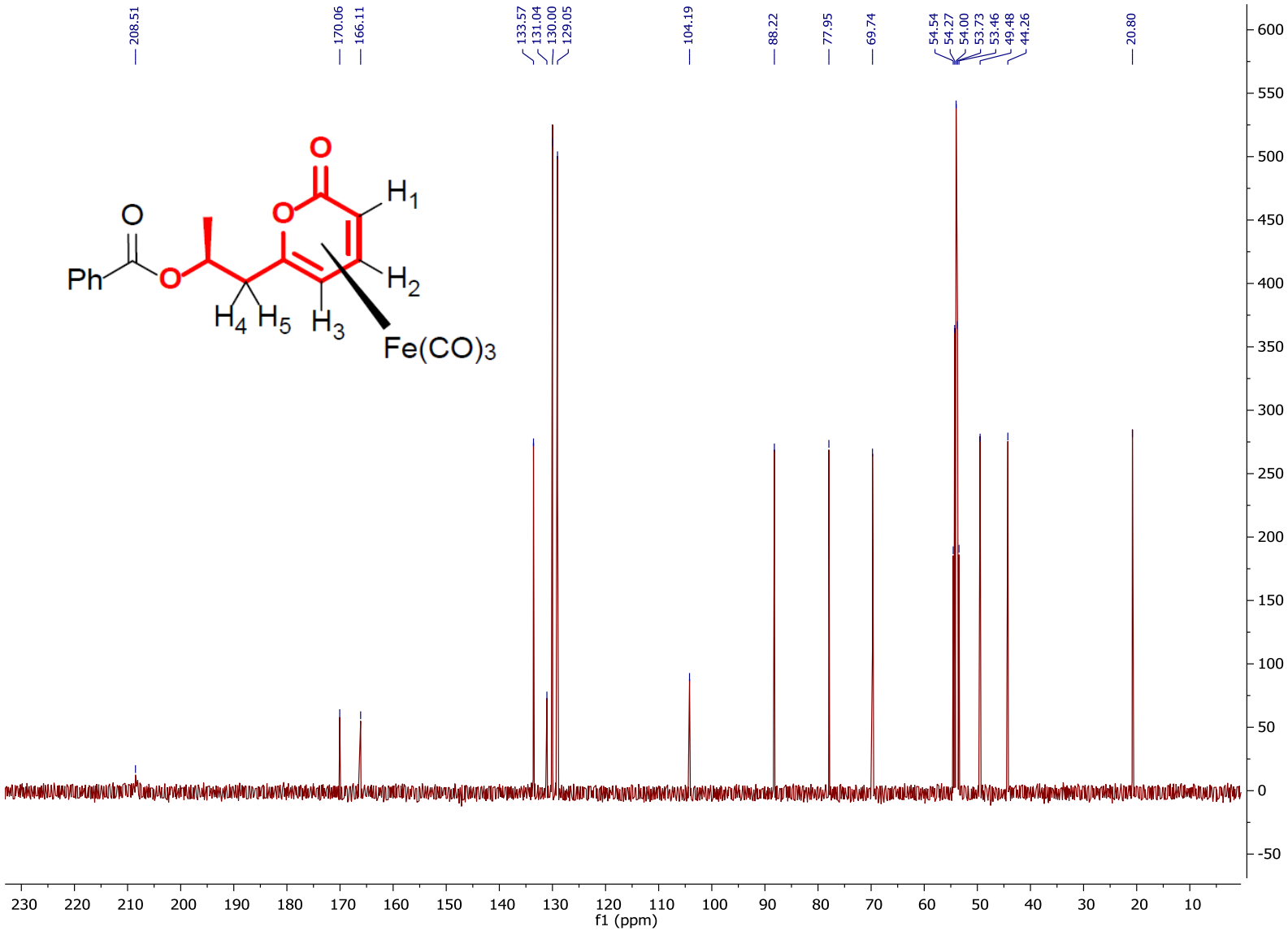

Ph
O
O
O
H1
H2
H4 H5 H3
H2 H1 H3
H4, H5
3
Fe(CO)3
H2 H3
H1
H4, H5
2
H2 H3
H1
H4, H5
1
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

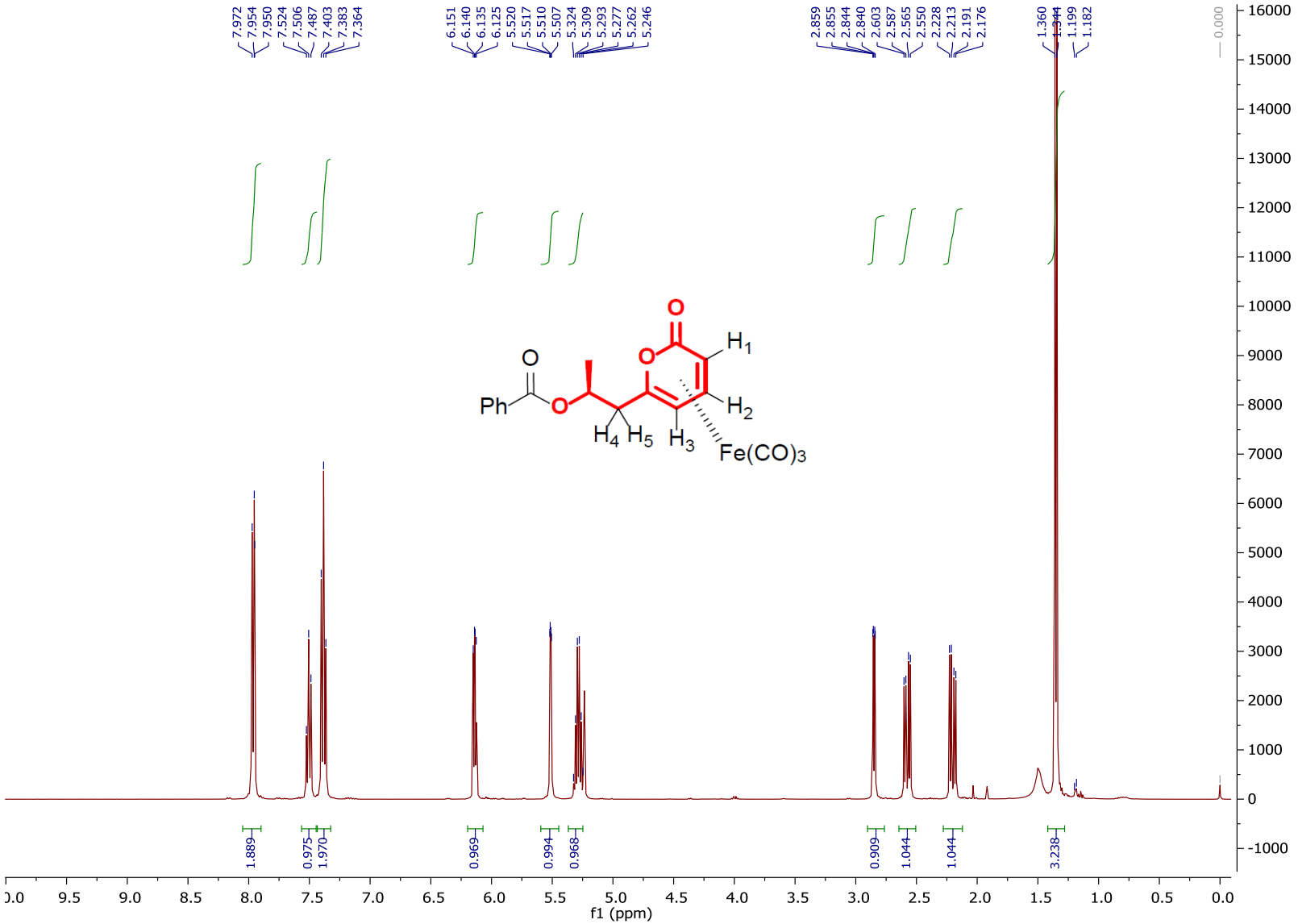

H2
H1
H3
H4, H5
Ph
O
H1
H2
H4 H5 H3
2
H2
H3
H1
H4, H5
Ph
H1
H2
H4 H5 H3
Fe(CO)3
1
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)

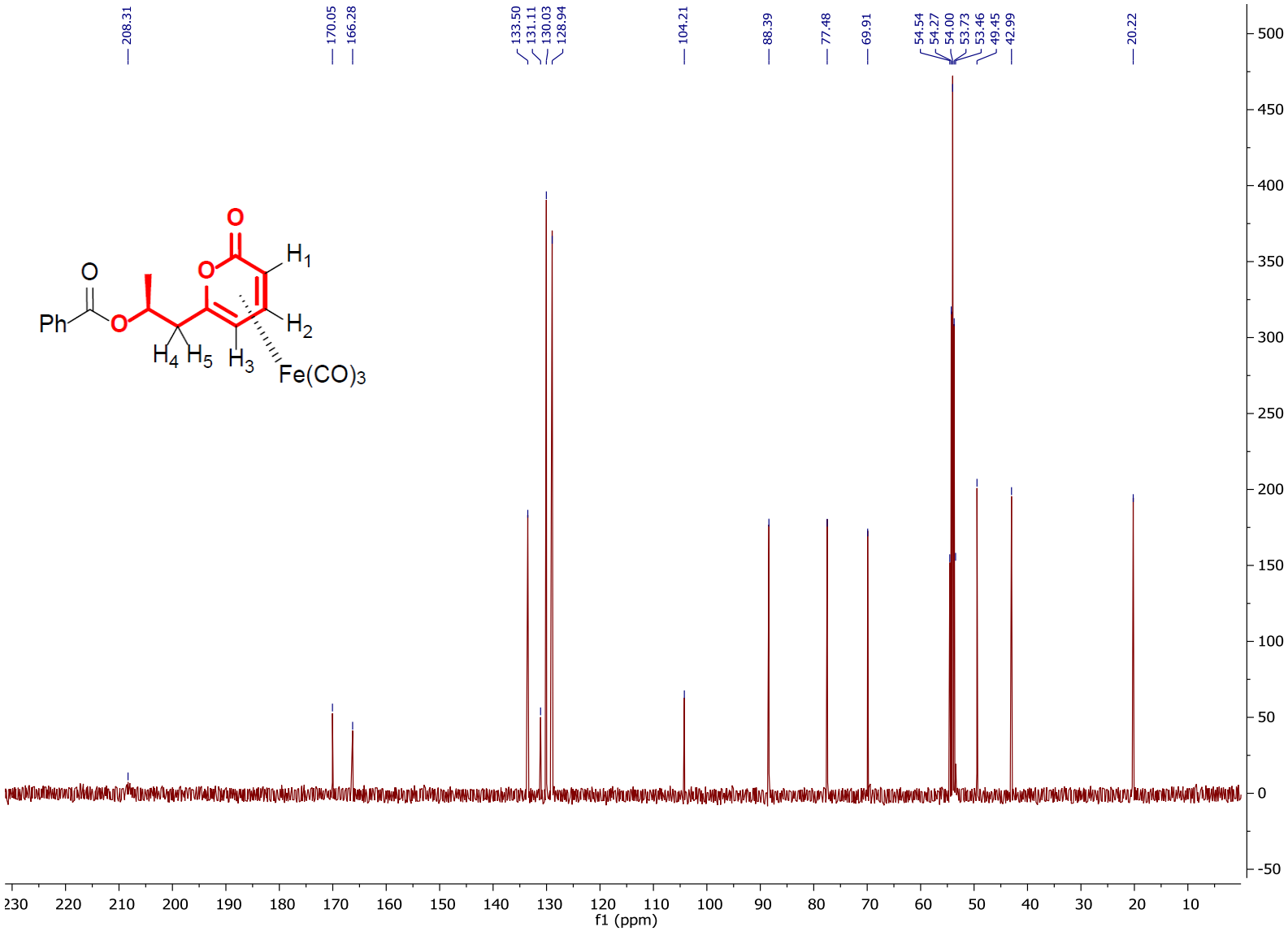

7.916
7.907
7.891
7.887
7.484
7.466
7.451
7.447
7.444
7.364
7.360
7.340
7.322
7.142
7.125
7.118
7.102
6.024
6.000
5.972
5.956
5.388
5.375
5.372
5.369
5.328
5.325
5.322
5.309
2.826
2.807
2.789
2.770
2.742
2.730
2.706
2.693
1.773
1.340
1.325
-0.000
O
O
H1
O
Ph
O
H2
H4 H5
H3
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
1.884
0.950
1.985
0.987
1.875
0.986
1.039
1.076
3.219
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

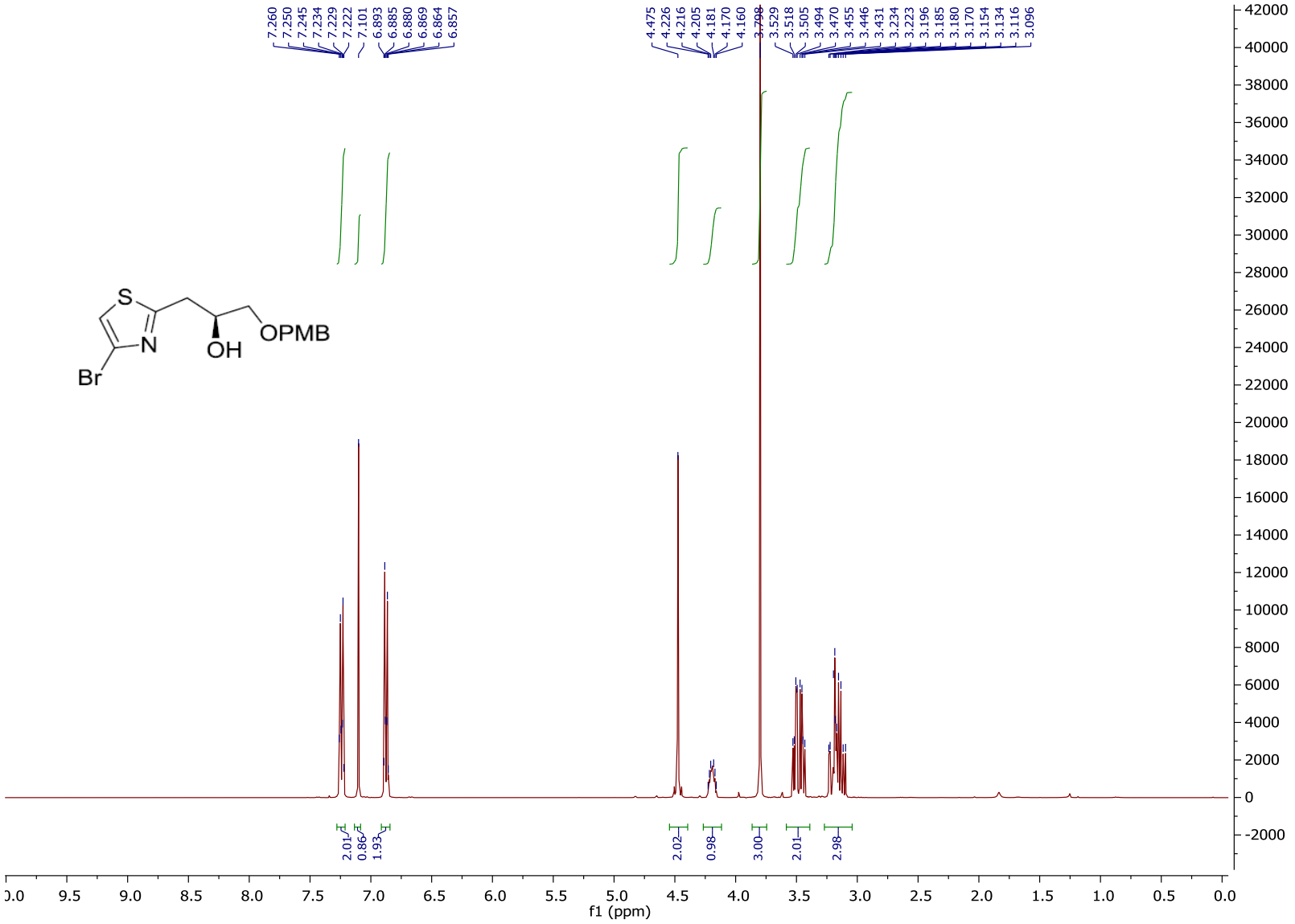

165.54
162.10
161.97
143.36
132.97
130.34
129.42
128.37
113.81
104.45
68.81
54.03
53.76
53.49
53.22
52.95
40.26
19.70
O
O
Ph
O
H1
H2
H4
H5
H3
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

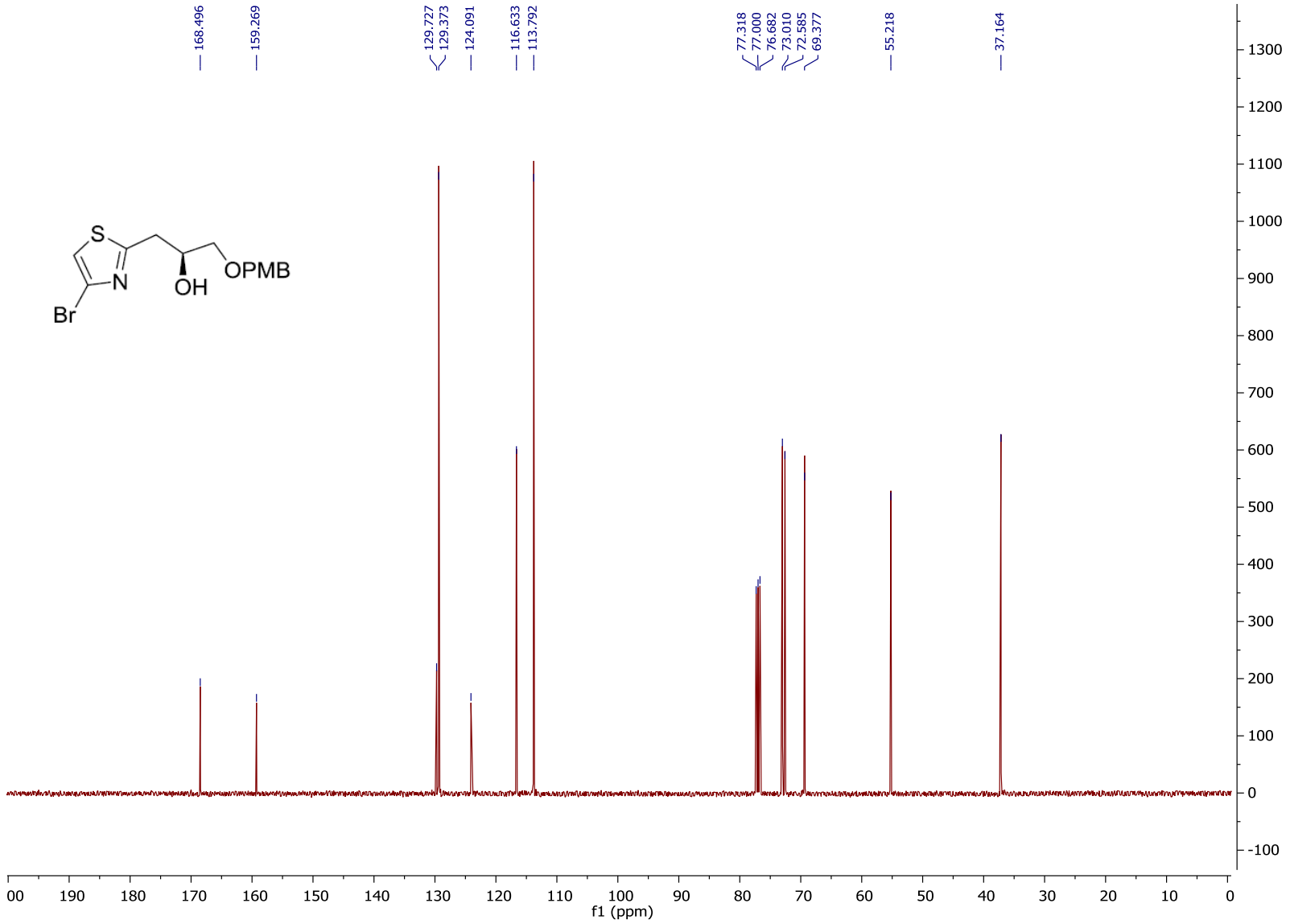

8.003
7.985
7.551
7.533
7.514
7.437
7.418
7.399
6.054
6.044
6.039
6.029
5.552
5.544
5.258
5.246
5.235
5.181
2.824
2.810
2.625
2.617
2.587
2.580
2.122
2.098
2.085
2.060
1.502
1.316
1.300
O
O
O
Ph
H1
H2
H4
H5
H3
Fe(CO)3
1.861
0.961
1.926
0.968
0.958
1.183
0.897
1.023
1.026
3.197
f1 (ppm)

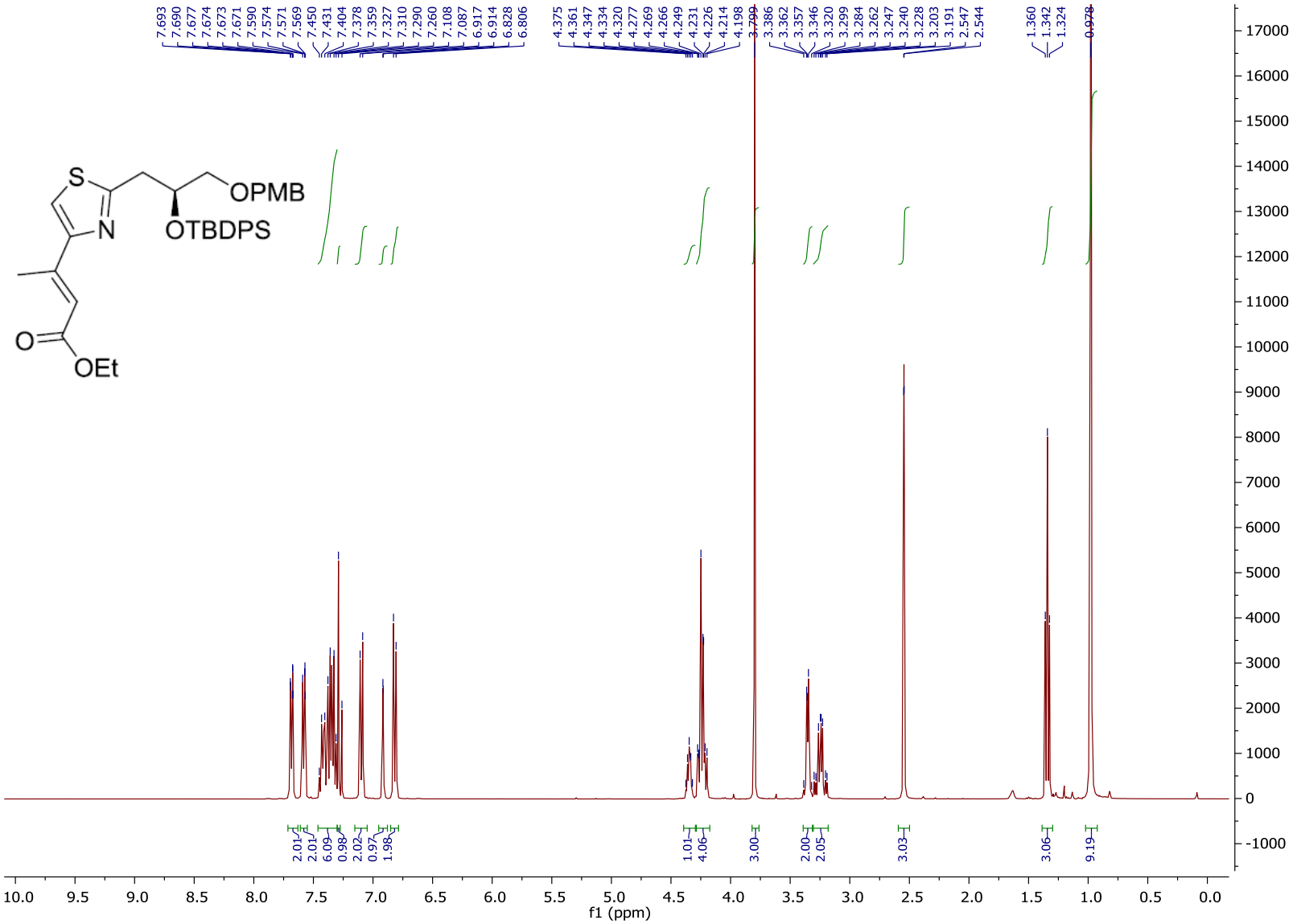

208.51
170.06
166.11
133.57
131.04
130.00
129.05
104.19
88.22
77.95
69.74
54.54
54.27
54.00
53.73
53.46
49.48
44.26
20.80
O
O
O
Ph
O
H1
H2
H4
H5
H3
Fe(CO)3
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

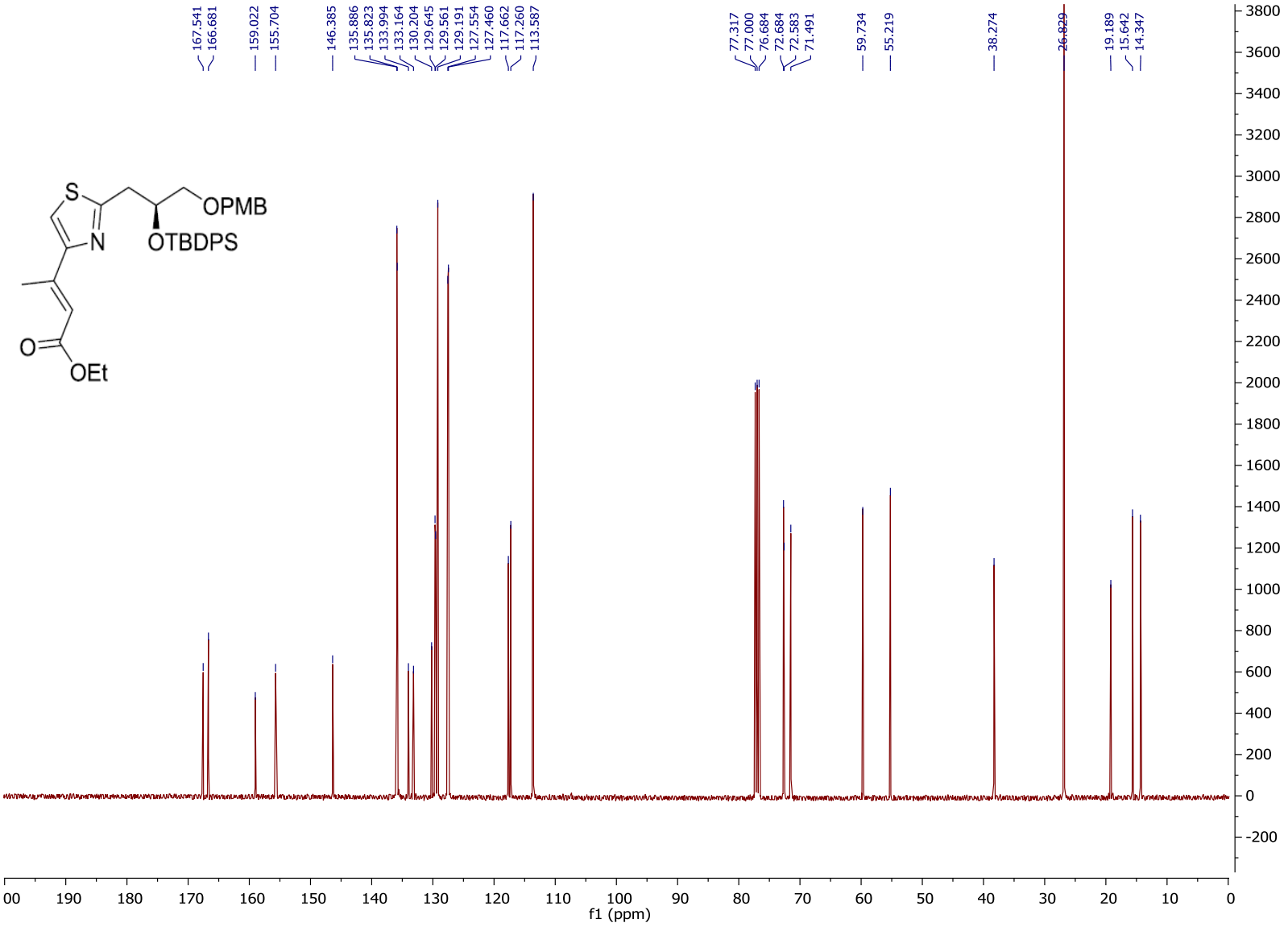

7.972
7.954
7.950
7.524
7.506
7.487
7.403
7.383
7.364
6.151
6.140
6.135
6.125
5.520
5.517
5.510
5.507
5.324
5.309
5.293
5.277
5.262
5.246
2.859
2.855
2.844
2.840
2.603
2.587
2.565
2.550
2.228
2.213
2.191
2.176
1.360
1.344
1.199
1.182
0.000
O
O
O
Ph
H1
H2
H3
H4
H5
Fe(CO)3
1.889
0.975
1.970
0.969
0.994
0.968
0.909
1.044
1.044
3.238
f1 (ppm)


208.31
170.05
166.28
133.50
131.11
130.03
128.94
104.21
88.39
77.48
69.91
54.54
54.27
54.00
53.73
53.46
49.45
42.99
20.22
O
O
O
Ph
H1
H2
H3
H4
H5
Fe(CO)3
500
450
400
350
300
250
200
150
100
50
0
-50
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.260
7.250
7.245
7.234
7.229
7.222
7.101
6.893
6.885
6.880
6.869
6.864
6.857
4.475
4.226
4.216
4.205
4.181
4.170
4.160
3.798
3.529
3.518
3.505
3.494
3.470
3.455
3.446
3.431
3.234
3.223
3.196
3.185
3.180
3.170
3.154
3.134
3.116
3.096
S
N
OH
OPMB
Br
2.01
0.86
1.93
2.02
0.98
3.00
2.01
2.98
f1 (ppm)


168.496
159.269
129.727
129.373
124.091
116.633
113.792
77.318
77.000
76.682
73.010
72.585
69.377
55.218
37.164
S
N
OH
OPMB
Br
f1 (ppm)


7.693
7.690
7.677
7.674
7.673
7.671
7.590
7.574
7.571
7.569
7.450
7.431
7.404
7.378
7.359
7.327
7.310
7.290
7.260
7.108
7.087
6.917
6.914
6.828
6.806
4.375
4.361
4.347
4.334
4.320
4.277
4.269
4.266
4.249
4.231
4.226
4.214
4.198
3.799
3.386
3.362
3.357
3.346
3.320
3.299
3.284
3.262
3.247
3.240
3.228
3.203
3.191
2.547
2.544
1.360
1.342
1.324
0.978
S
N
OPMB
OTBDPS
O
OEt
2.01
2.01
6.09
0.98
2.02
0.97
1.98
1.01
4.06
3.00
2.00
2.05
3.03
3.06
9.19
f1 (ppm)


167.541
166.681
159.022
155.704
146.385
135.886
135.823
133.994
133.164
130.204
129.645
129.561
129.191
127.554
127.460
117.662
117.260
113.587
77.317
77.000
76.684
72.684
72.583
71.491
59.734
55.219
38.274
26.829
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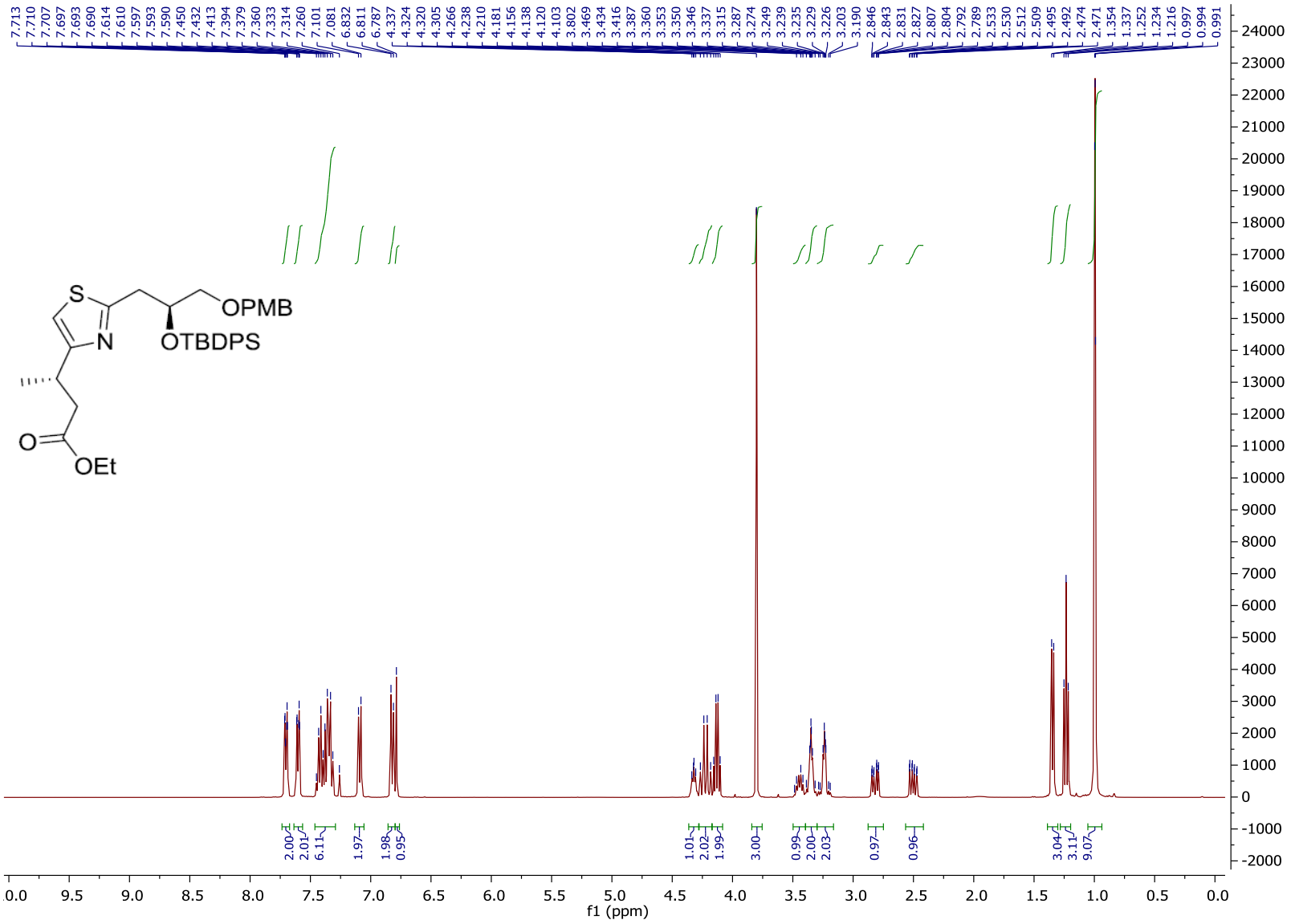
OPMB
OTBDPS
O
OEt
f1 (ppm)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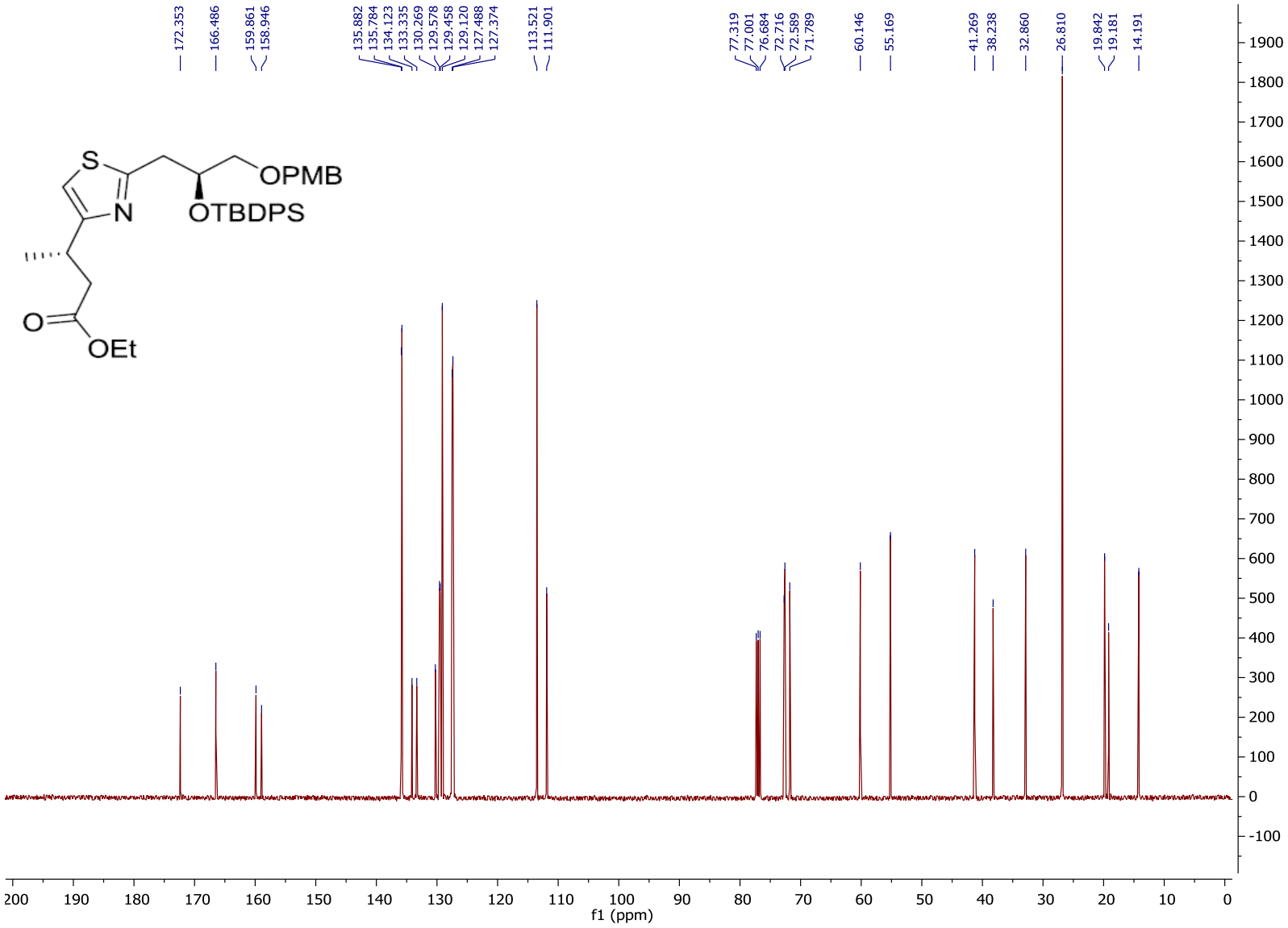
OPMB
OTBDPS
O
OEt
f1 (ppm)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129.120
127.488
127.374
113.521
111.901
77.319
77.001
76.684
72.716
72.589
71.789
60.146
55.169
41.269
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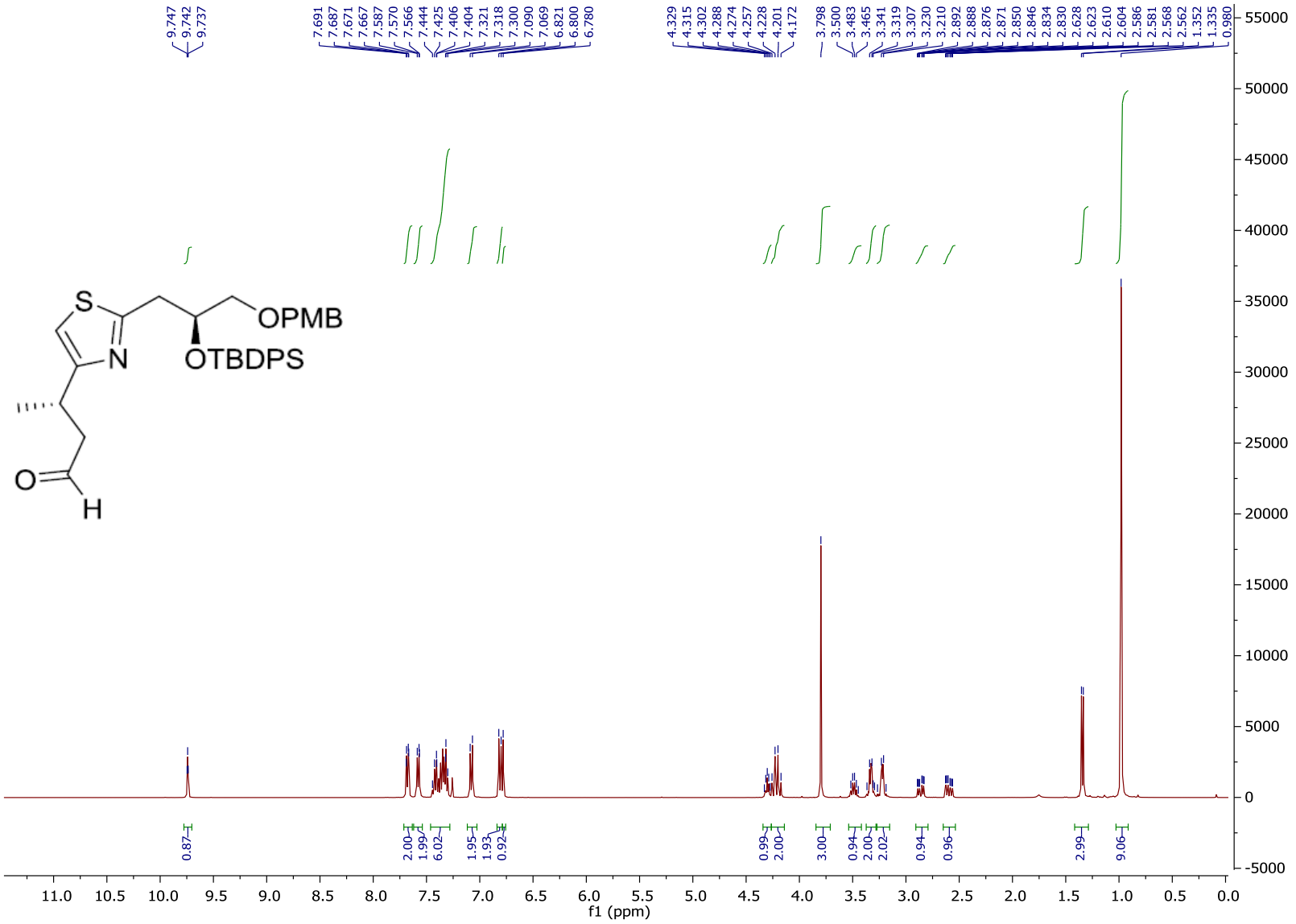
N
OPMB
OTBDPS
O
OEt
f1 (ppm)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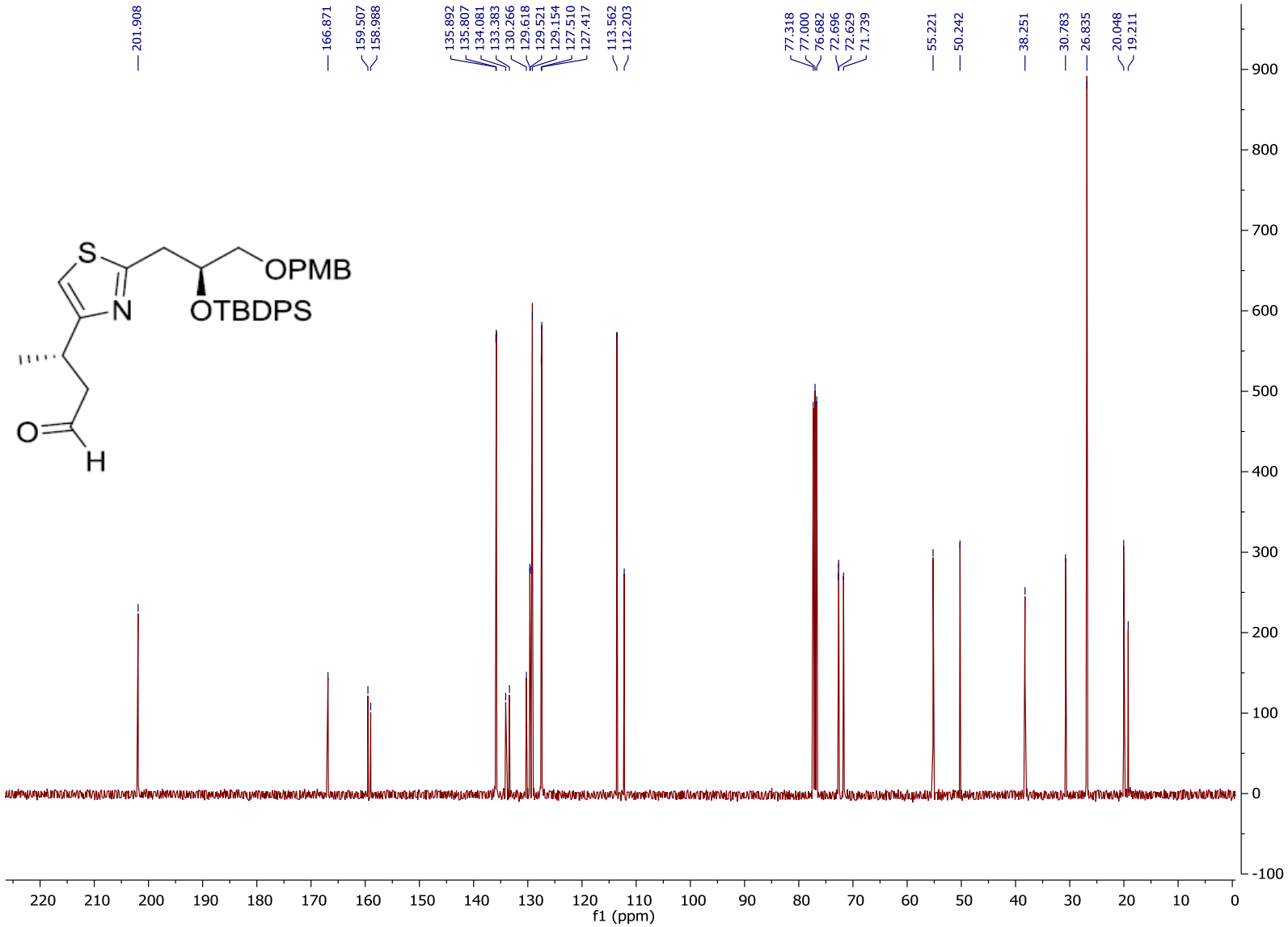
OPMB
OTBDPS
O
H
f1 (ppm)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127.417
113.562
112.203
77.318
77.000
76.682
72.696
72.629
71.739
55.221
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30.783
26.835
20.048
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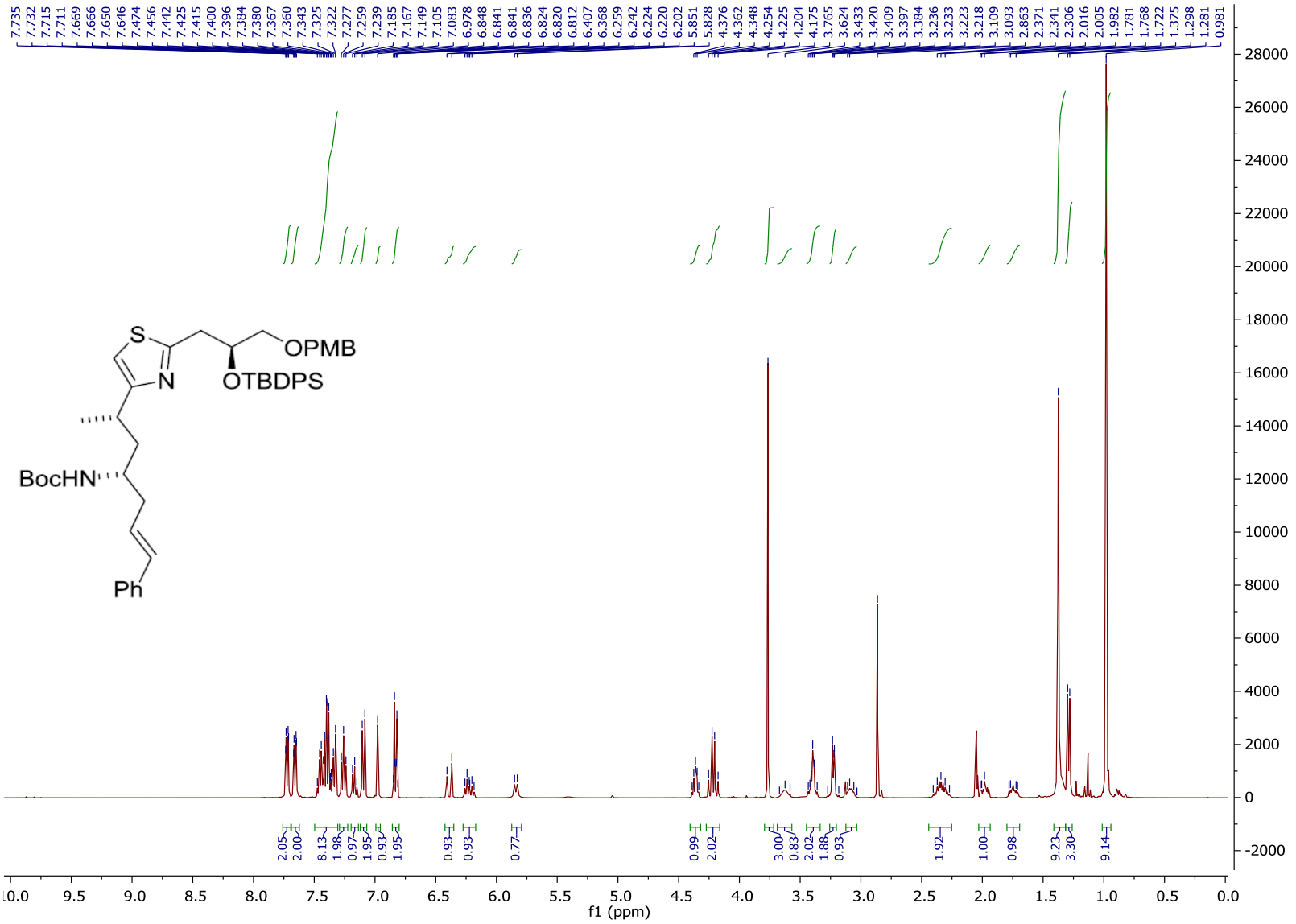
S
N
OPMB
OTBDPS
O
H
f1 (ppm)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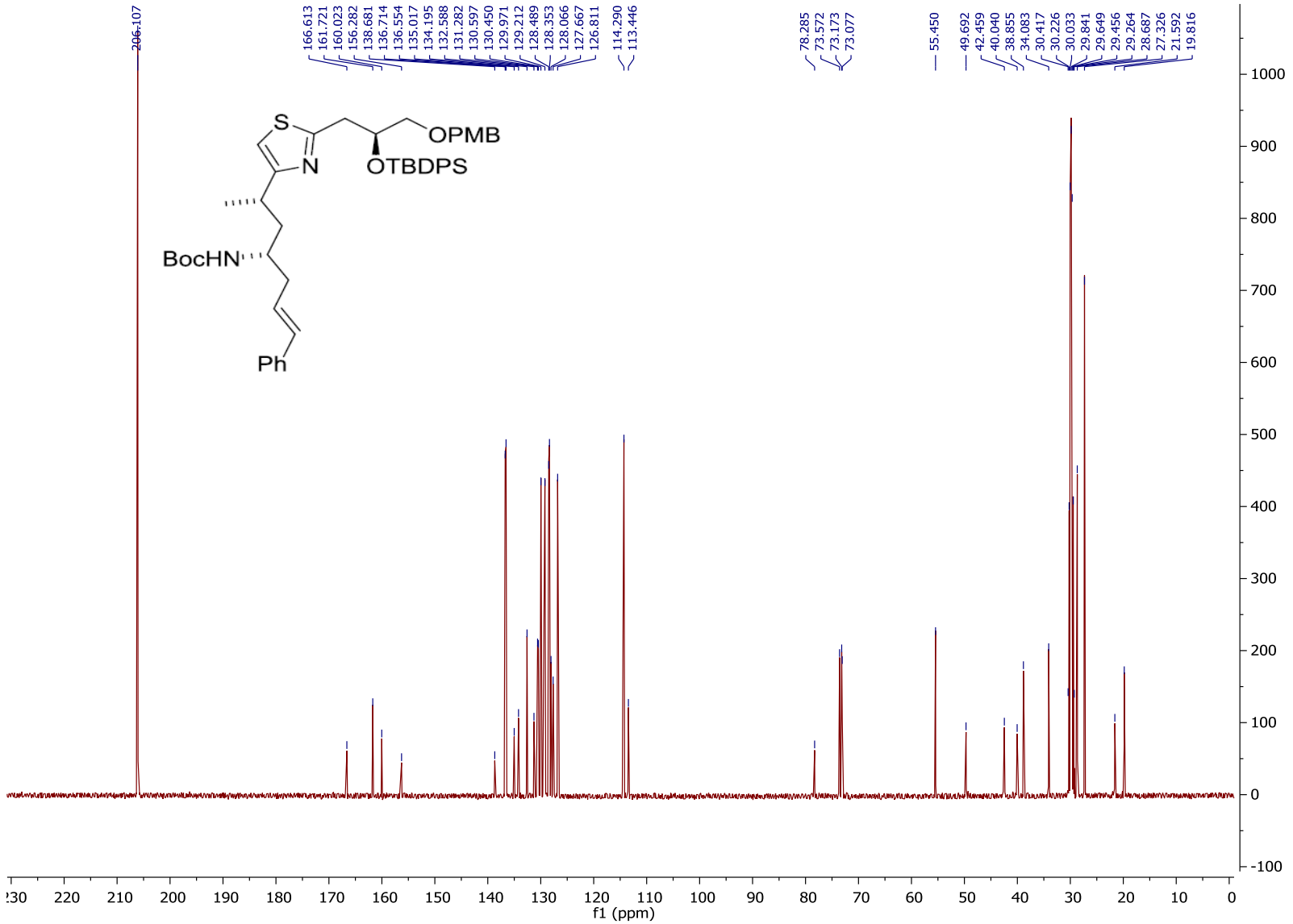
S
N
OPMB
OTBDPS
BocHN
Ph
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
2.05 2.00 8.13 1.98 0.97 1.95 0.93 1.95 0.93 0.93 0.77 0.99 2.02 3.00 0.83 2.02 1.88 0.93 1.92 1.00 0.98 9.23 3.30 9.14
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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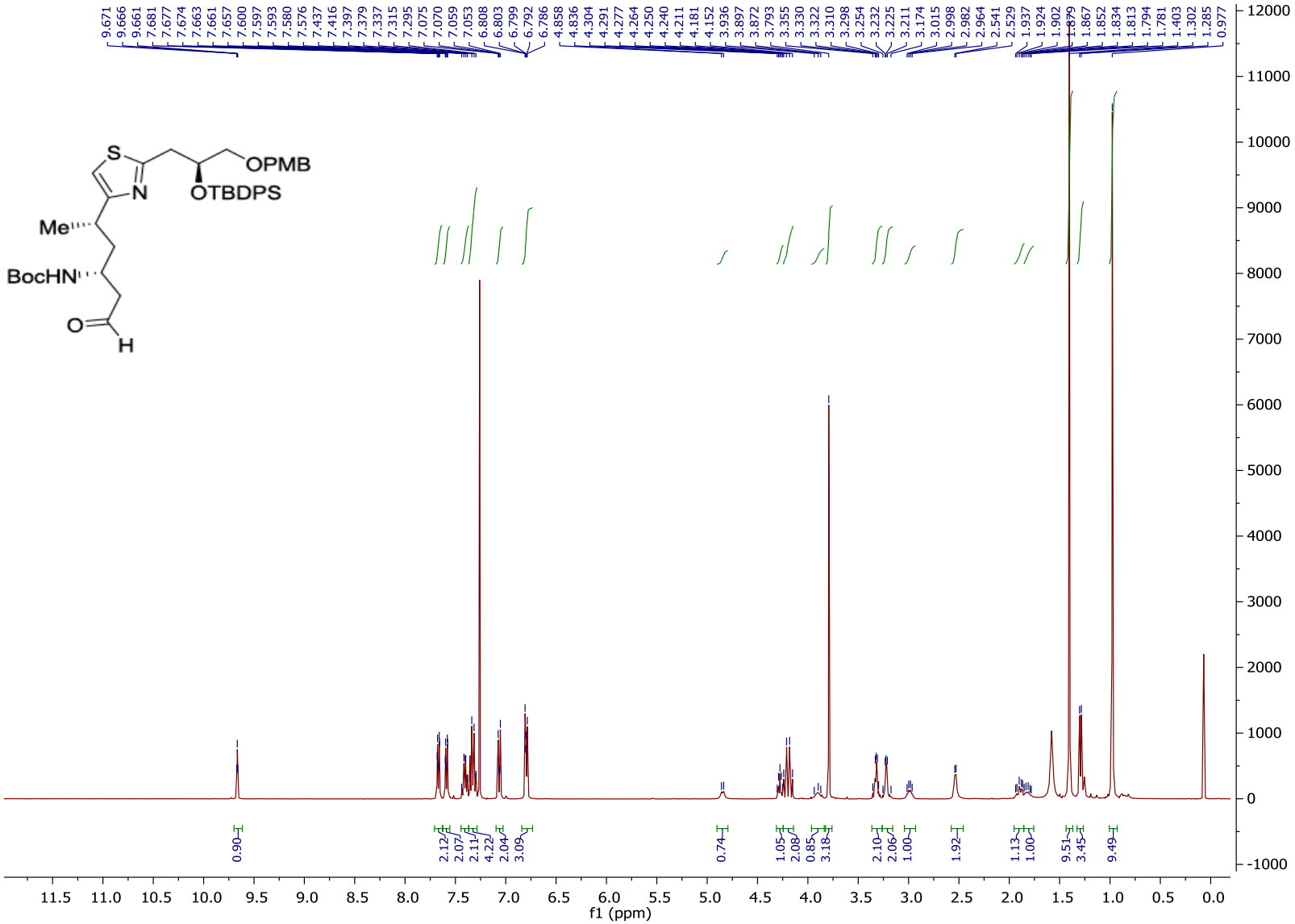
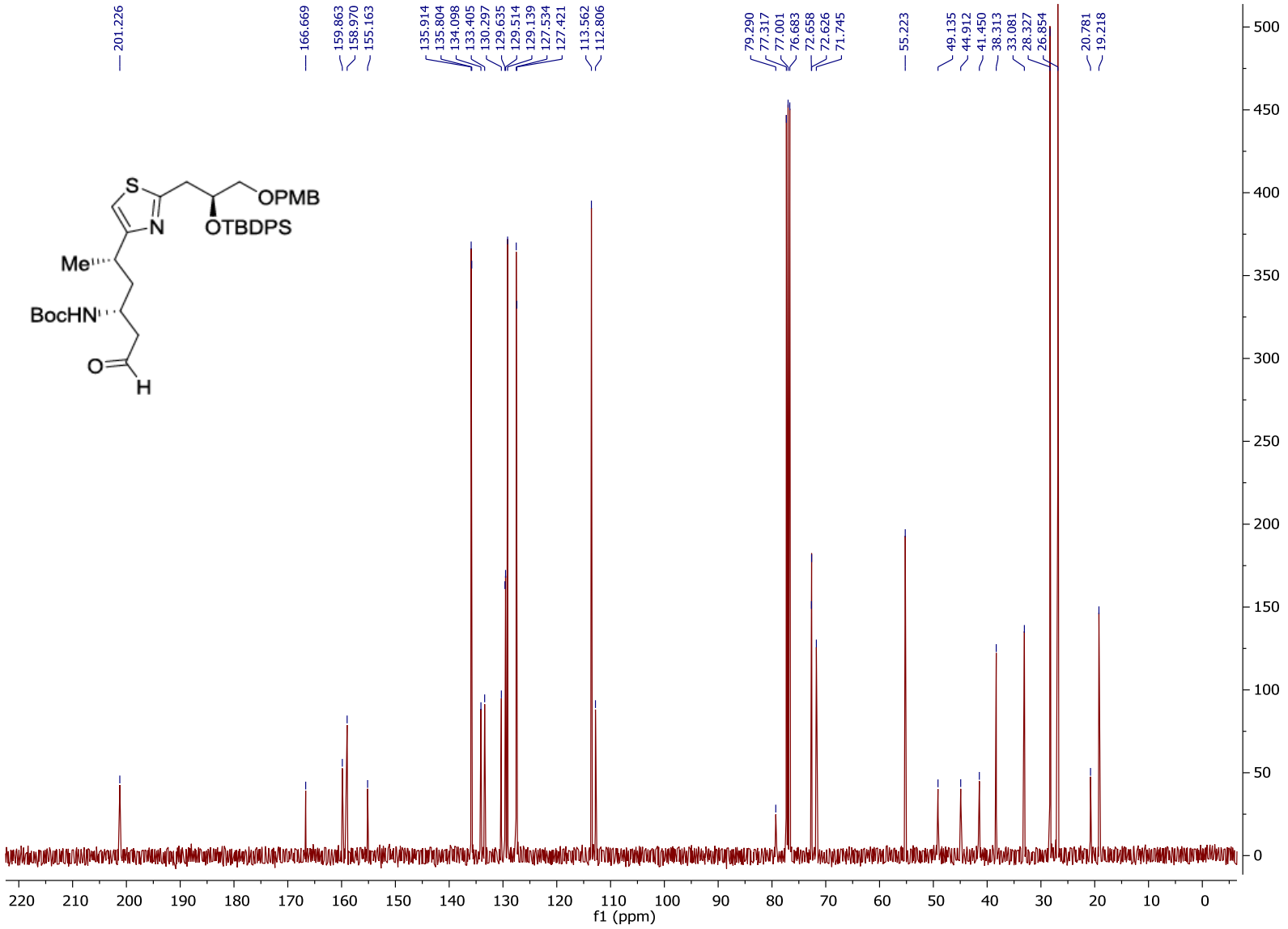
130.597
130.450
129.971
129.212
128.489
128.353
128.066
127.667
126.811
114.290
113.446
78.285
73.572
73.173
73.077
55.450
49.692
42.459
40.040
38.855
34.083
30.417
30.226
30.033
29.841
29.649
29.456
29.264
28.687
27.326
21.592
19.816
S
N
OPMB
OTBDPS
BocHN
Ph
1000
900
800
700
600
500
400
300
200
100
0
-100
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


S
N
OPMB
OTBDPS
Me
BocHN
O
H
f1 (ppm)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135.804
134.098
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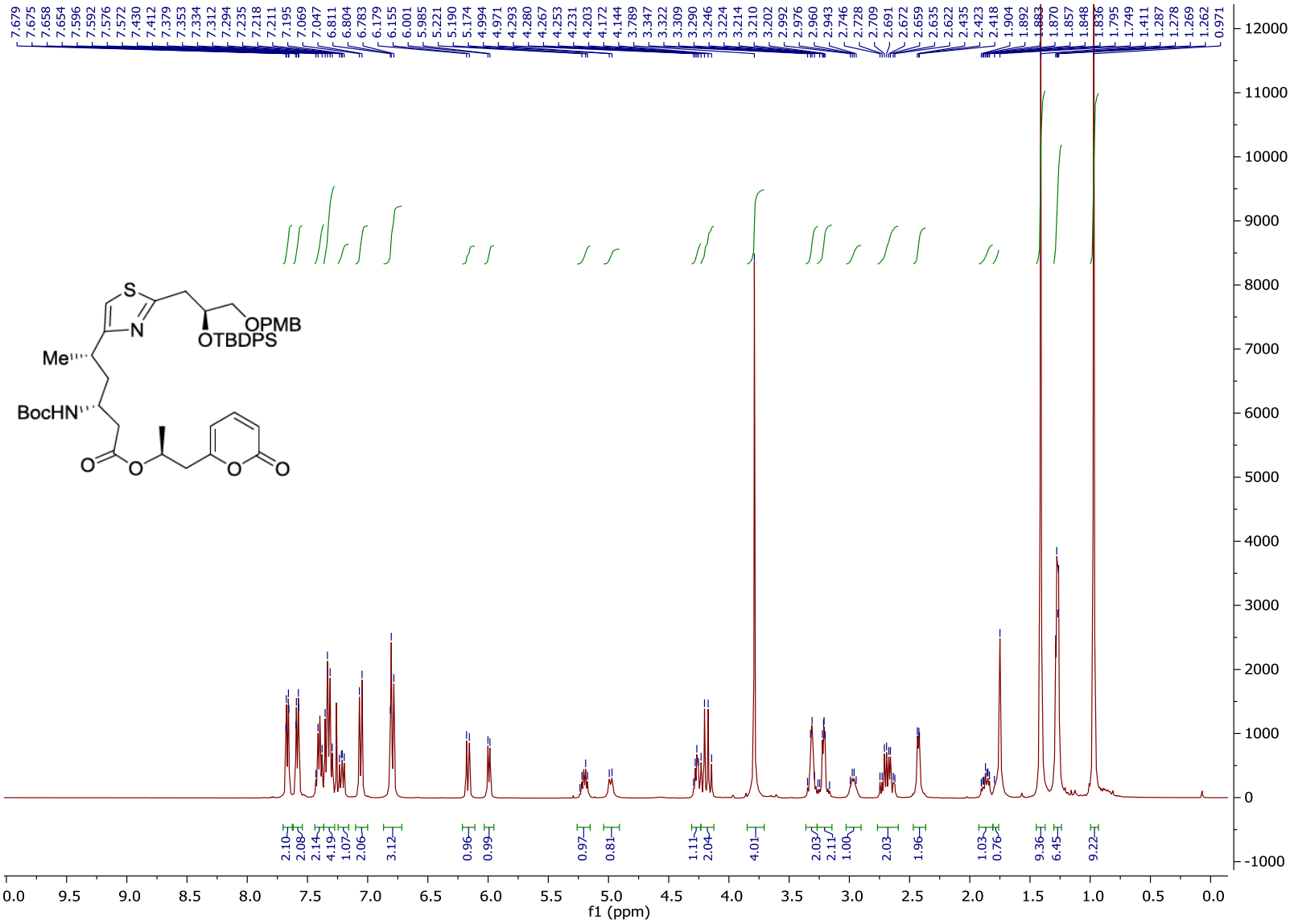
129.139
127.534
127.421
113.562
112.806
79.290
77.317
77.001
76.683
72.658
72.626
71.745
55.223
49.135
44.912
41.450
38.313
33.081
28.327
26.854
20.781
19.218
S
N
OPMB
OTBDPS
Me
BocHN
O
H
f1 (ppm)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7.658
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7.592
7.576
7.572
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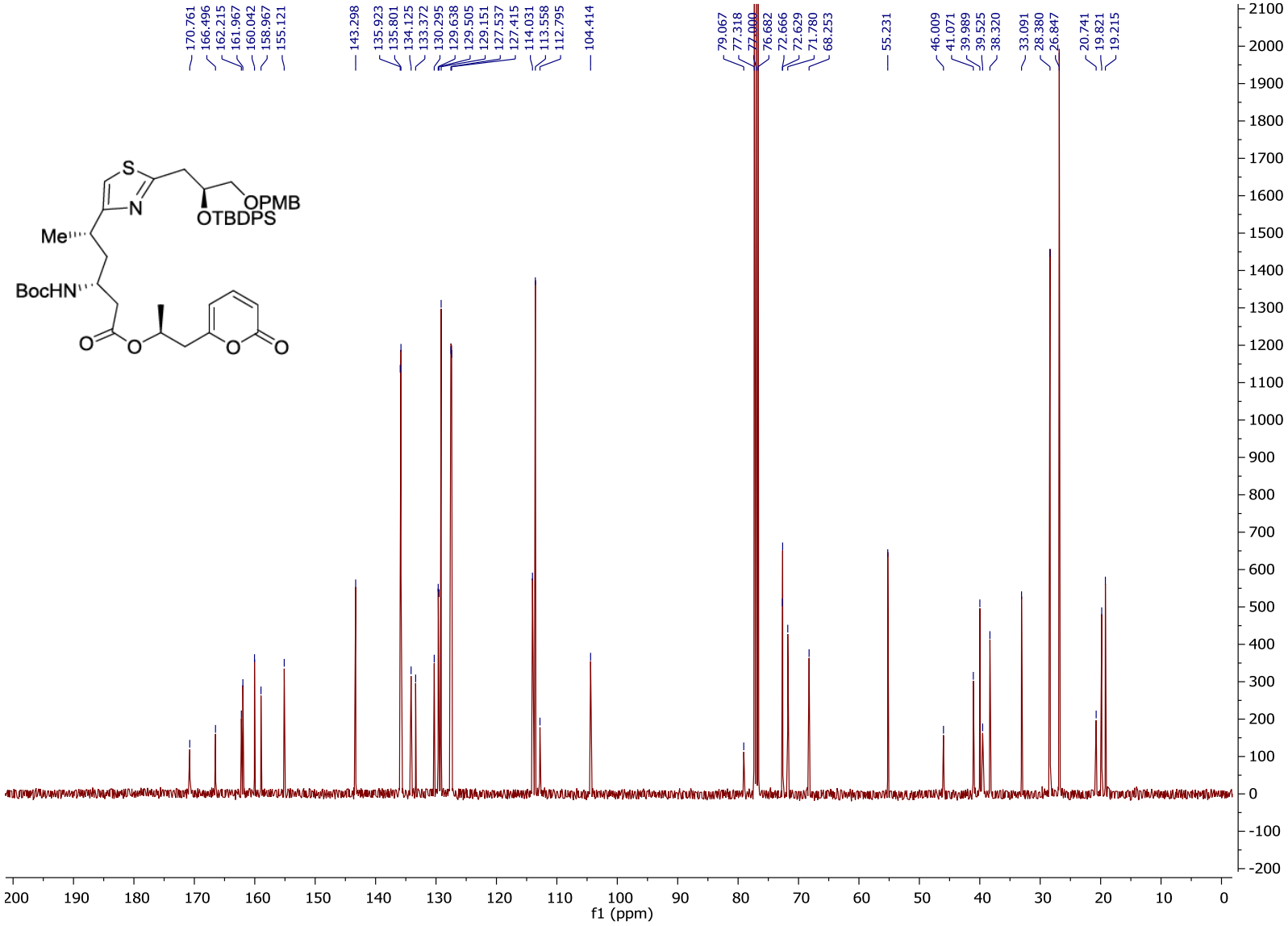
7.412
7.379
7.353
7.334
7.312
7.294
7.235
7.218
7.211
7.195
7.069
7.047
6.811
6.804
6.783
6.179
6.155
6.001
5.985
5.221
5.190
5.174
4.994
4.971
4.293
4.280
4.267
4.253
4.231
4.203
4.172
4.144
3.789
3.347
3.322
3.309
3.290
3.246
3.224
3.214
3.210
3.202
2.992
2.976
2.960
2.943
2.746
2.728
2.709
2.691
2.672
2.659
2.635
2.622
2.435
2.423
2.418
1.904
1.892
1.883
1.870
1.857
1.848
1.836
1.795
1.749
1.411
1.287
1.278
1.269
1.262
0.971
S
N
OPMB
OTBDPS
Me
BocHN
O
O
O
O
2.10
2.08
2.14
4.19
1.07
2.06
3.12
0.96
0.99
0.97
0.81
1.11
2.04
4.01
2.03
2.11
1.00
2.03
1.96
1.03
0.76
9.36
6.45
9.22
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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77.000
76.682
72.666
72.629
71.780
68.253
55.231
46.009
41.071
39.989
39.525
38.320
33.091
28.380
26.847
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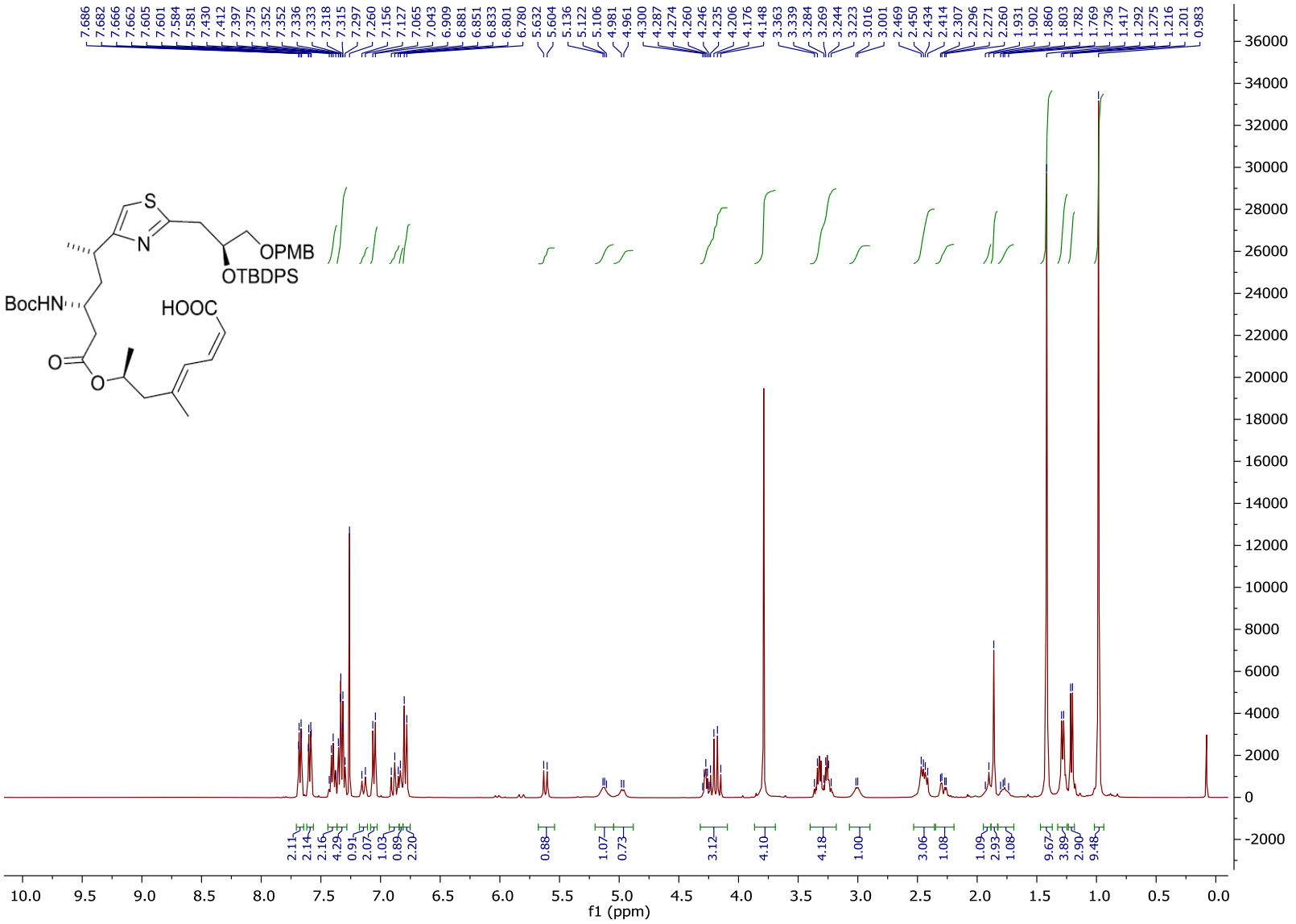
19.215
S
N
OPMB
OTBDPS
Me
BocHN
O
O
O
O
f1 (ppm)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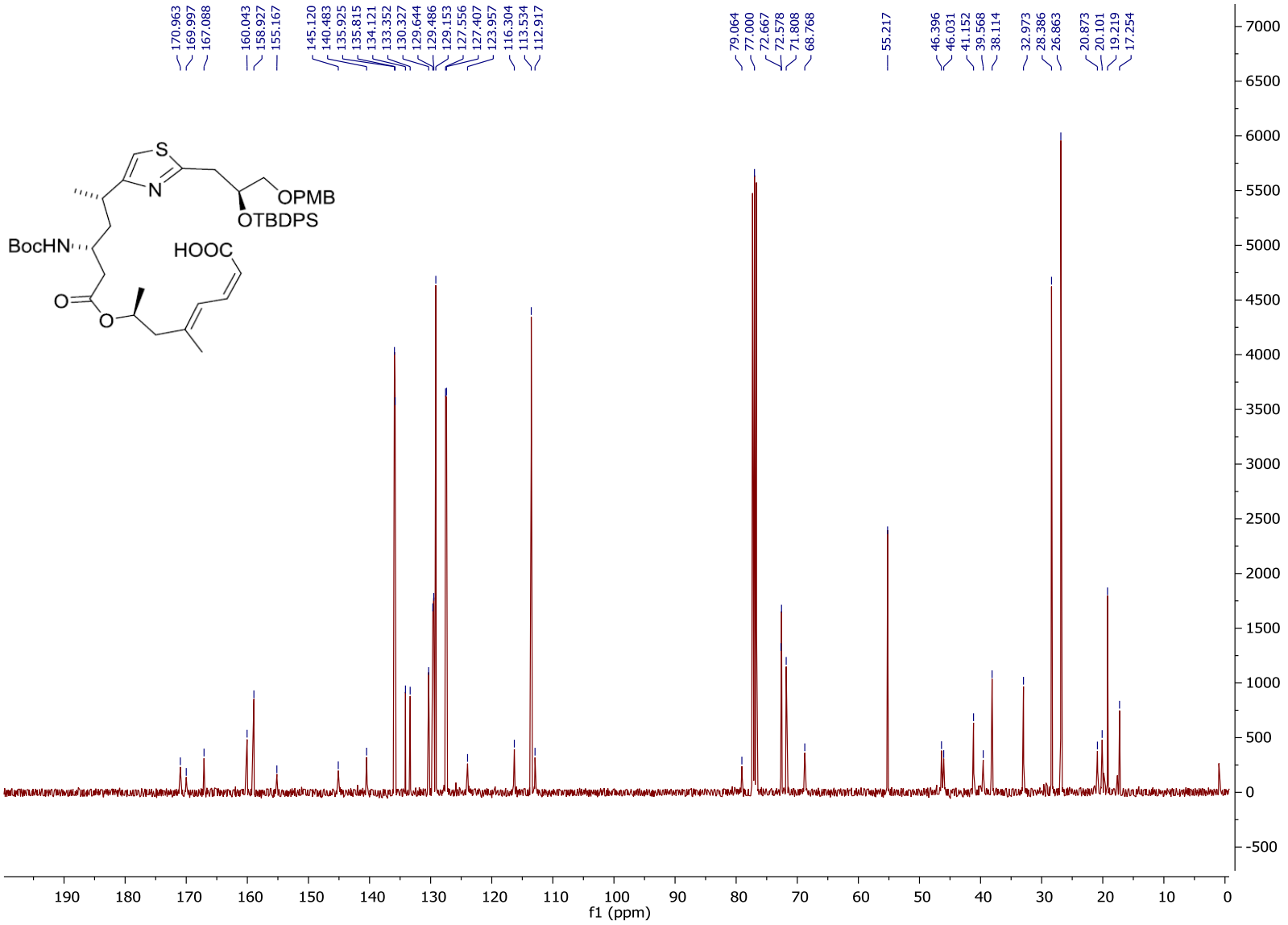
S
N
OPMB
OTBDPS
BocHN
HOOC
O
O
2.11 2.14 2.16 4.29 0.91 2.07 1.03 0.89 2.20 0.88 1.07 0.73 3.12 4.10 4.18 1.00 3.06 1.08 1.09 2.93 1.08 9.67 3.89 2.90 9.48
36000 34000 32000 30000 28000 26000 24000 22000 20000 18000 16000 14000 12000 10000 8000 6000 4000 2000 0 -2000
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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129.486
129.153
127.556
127.407
123.957
116.304
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112.917
79.064
77.000
72.667
72.578
71.808
68.768
55.217
46.396
46.031
41.152
39.568
38.114
32.973
28.386
26.863
20.873
20.101
19.219
17.254
S
N
OPMB
OTBDPS
BocHN
HOOC
O
O
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
190
180
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150
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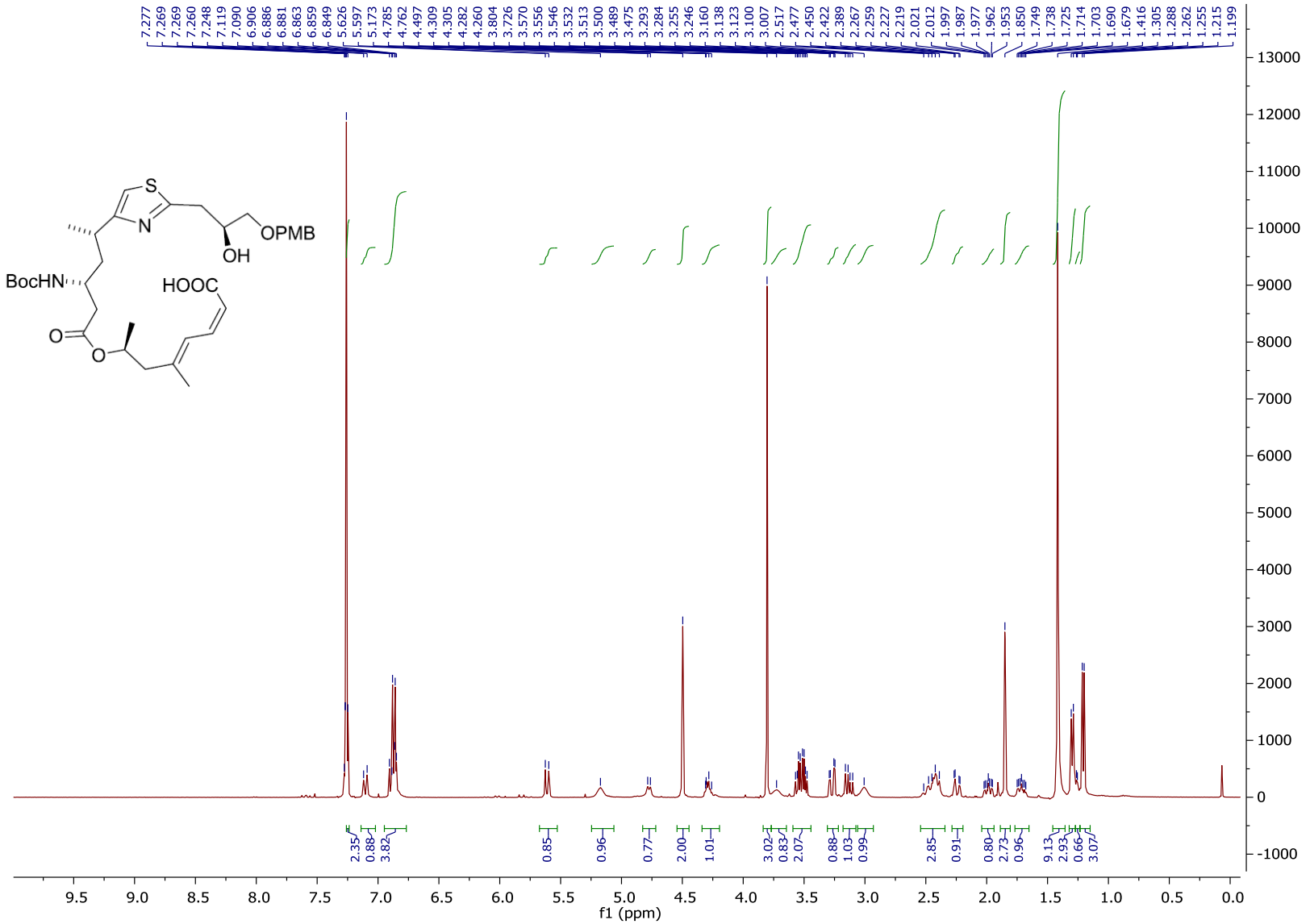
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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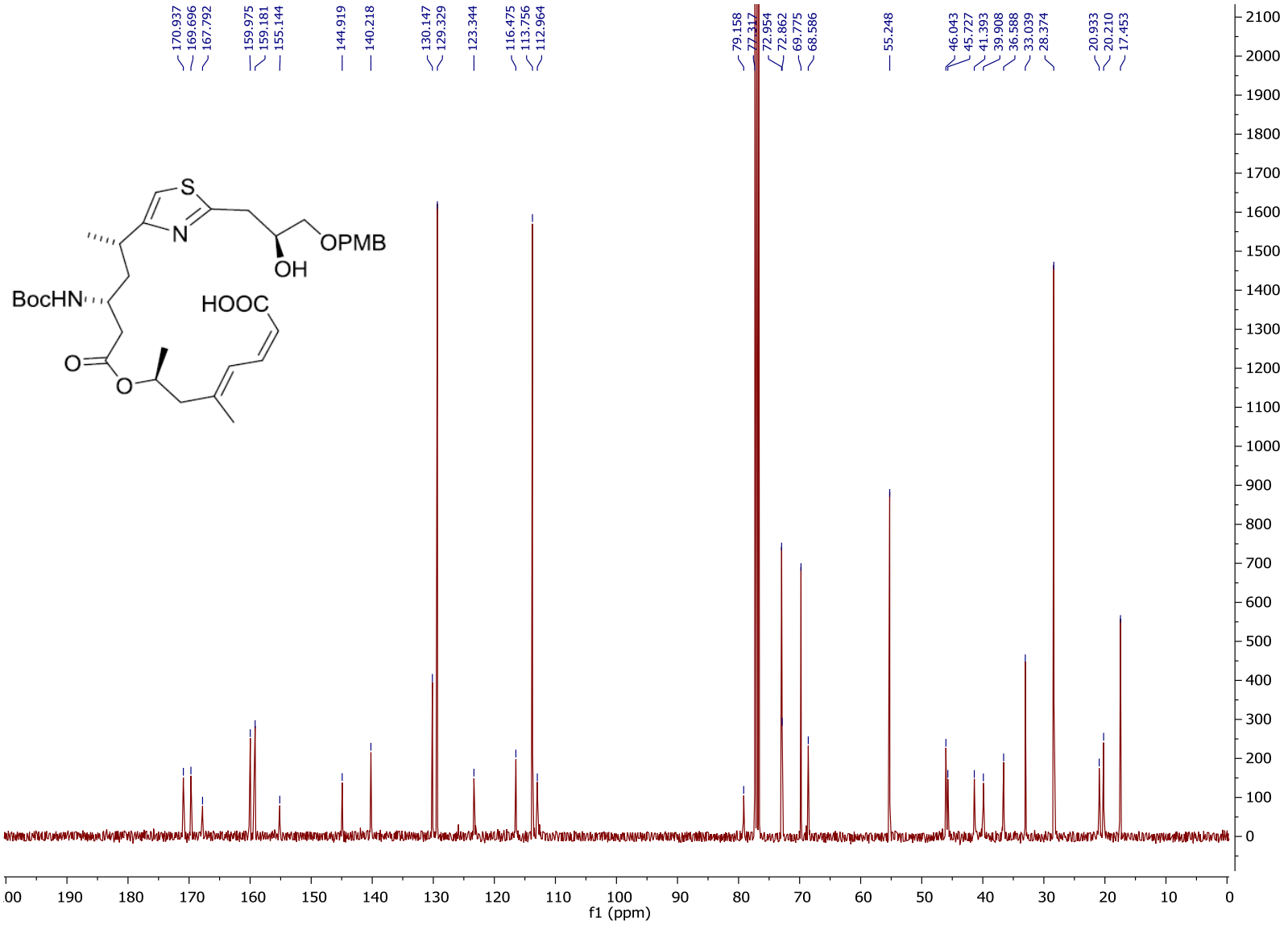
OPMB
OH
BocHN
HOOC
O
O
f1 (ppm)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77.317
72.954
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68.586
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46.043
45.727
41.393
39.908
36.588
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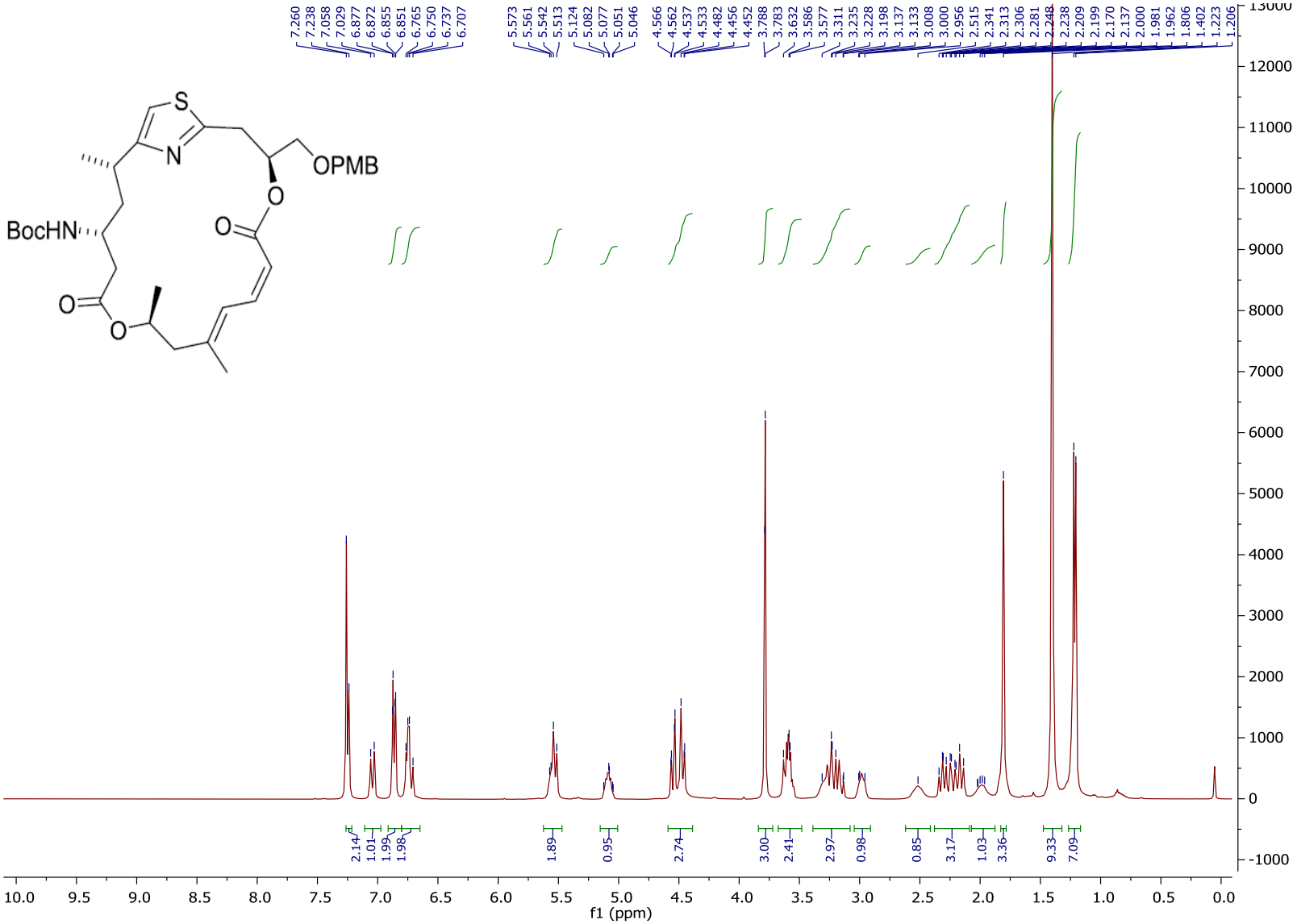
S
N
OPMB
OH
BocHN
HOOC
O
O
f1 (ppm)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5.573
5.561
5.542
5.513
5.124
5.082
5.077
5.051
5.046
4.566
4.562
4.537
4.533
4.482
4.456
4.452
3.788
3.783
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3.586
3.577
3.311
3.235
3.228
3.198
3.137
3.133
3.008
3.000
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2.515
2.341
2.313
2.306
2.281
2.248
2.238
2.209
2.199
2.170
2.137
2.000
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1.962
1.806
1.402
1.223
1.206
S
N
OPMB
O
O
BocHN
O
O
2.14
1.01
1.99
1.98
1.89
0.95
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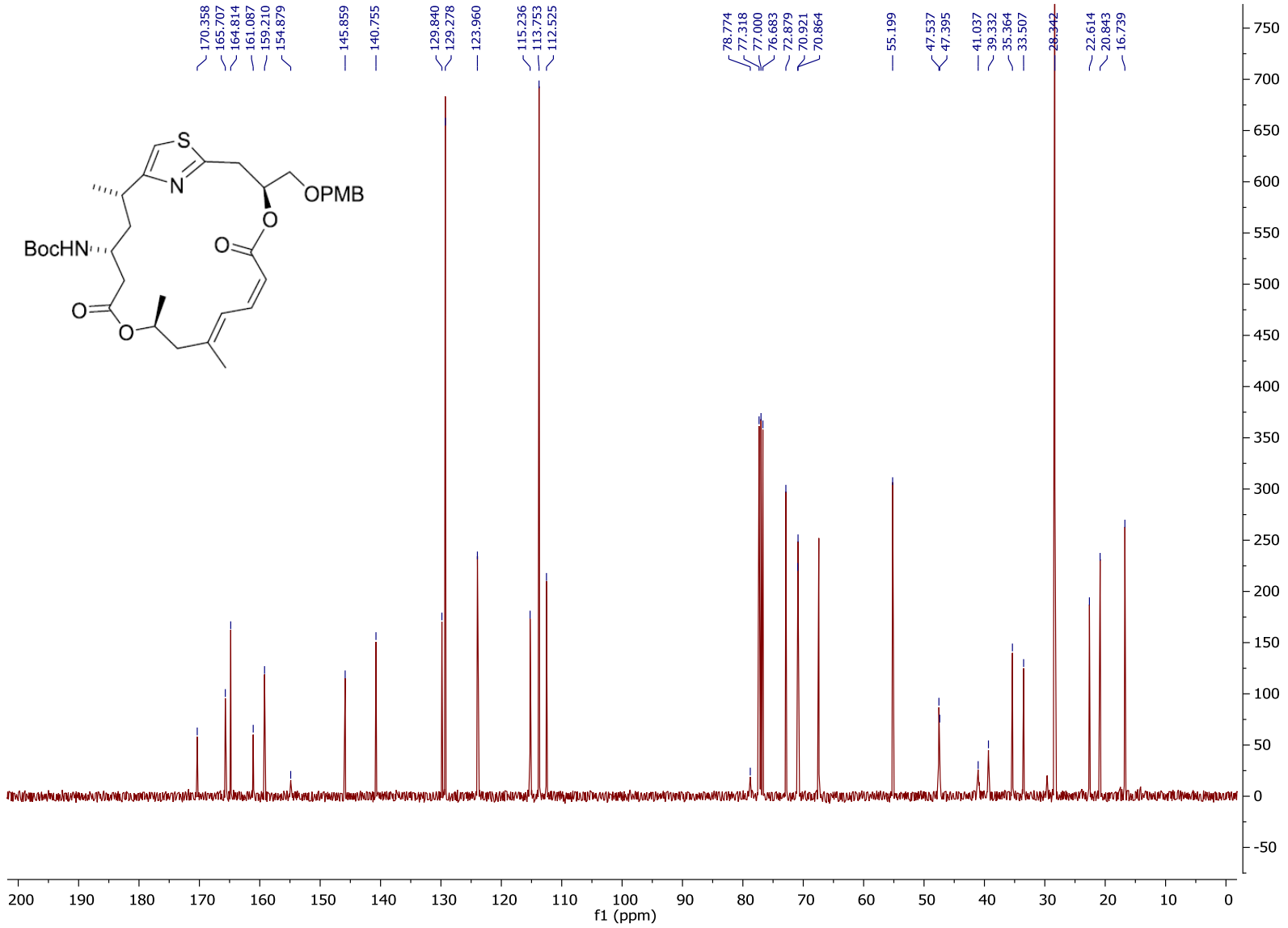
3.00
2.41
2.97
0.98
0.85
3.17
1.03
3.36
9.33
7.09
f1 (ppm)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77.318
77.000
76.683
72.879
70.921
70.864
55.199
47.537
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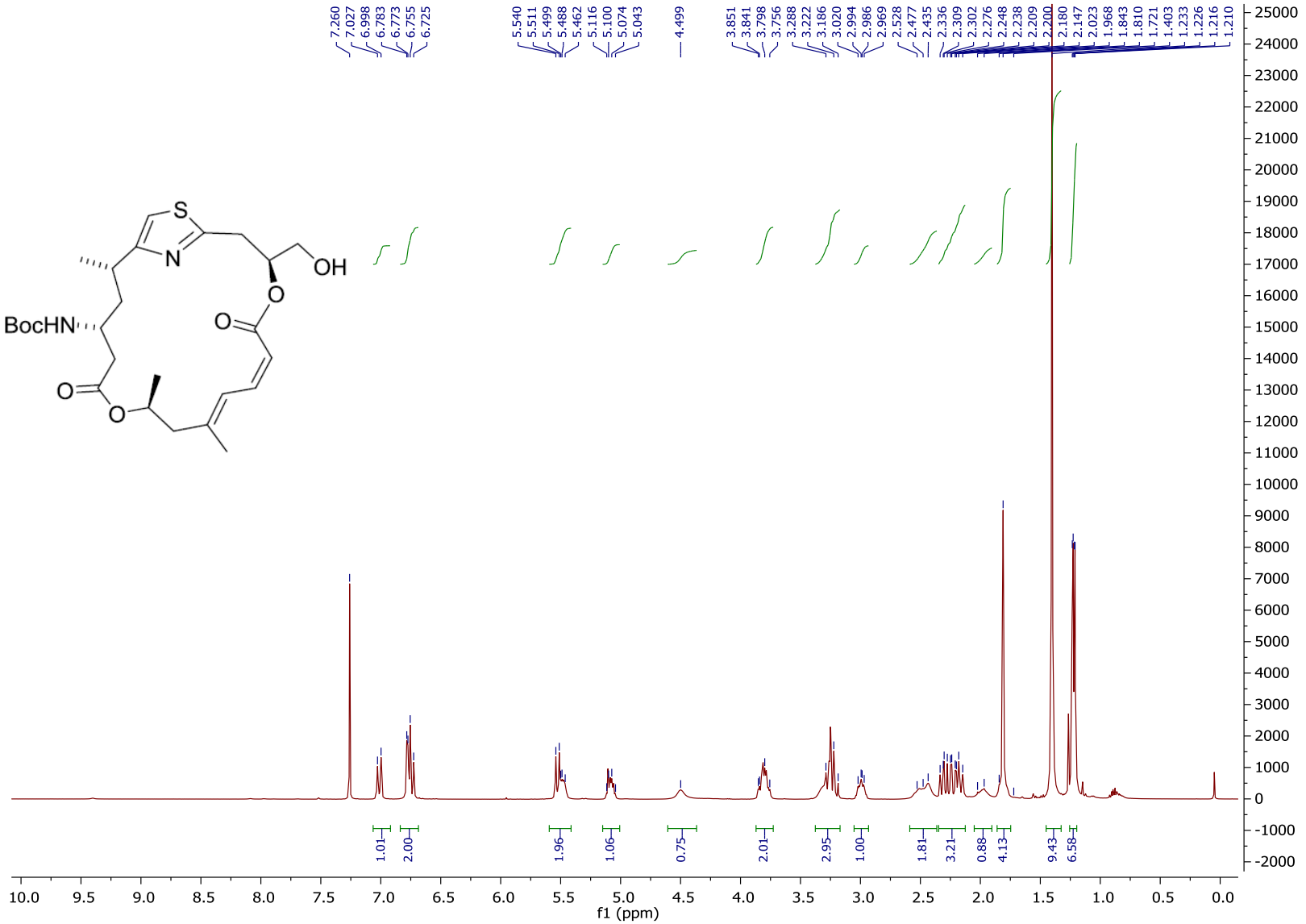
BocHN
OPMB
f1 (ppm)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5.499
5.488
5.462
5.116
5.100
5.074
5.043
4.499
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3.841
3.798
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3.288
3.222
3.186
3.020
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2.435
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2.302
2.276
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2.209
2.200
2.180
2.147
2.023
1.968
1.843
1.810
1.721
1.403
1.233
1.226
1.216
1.210
S
N
OH
O
O
BocHN
O
O
1.01
2.00
1.96
1.06
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2.95
1.00
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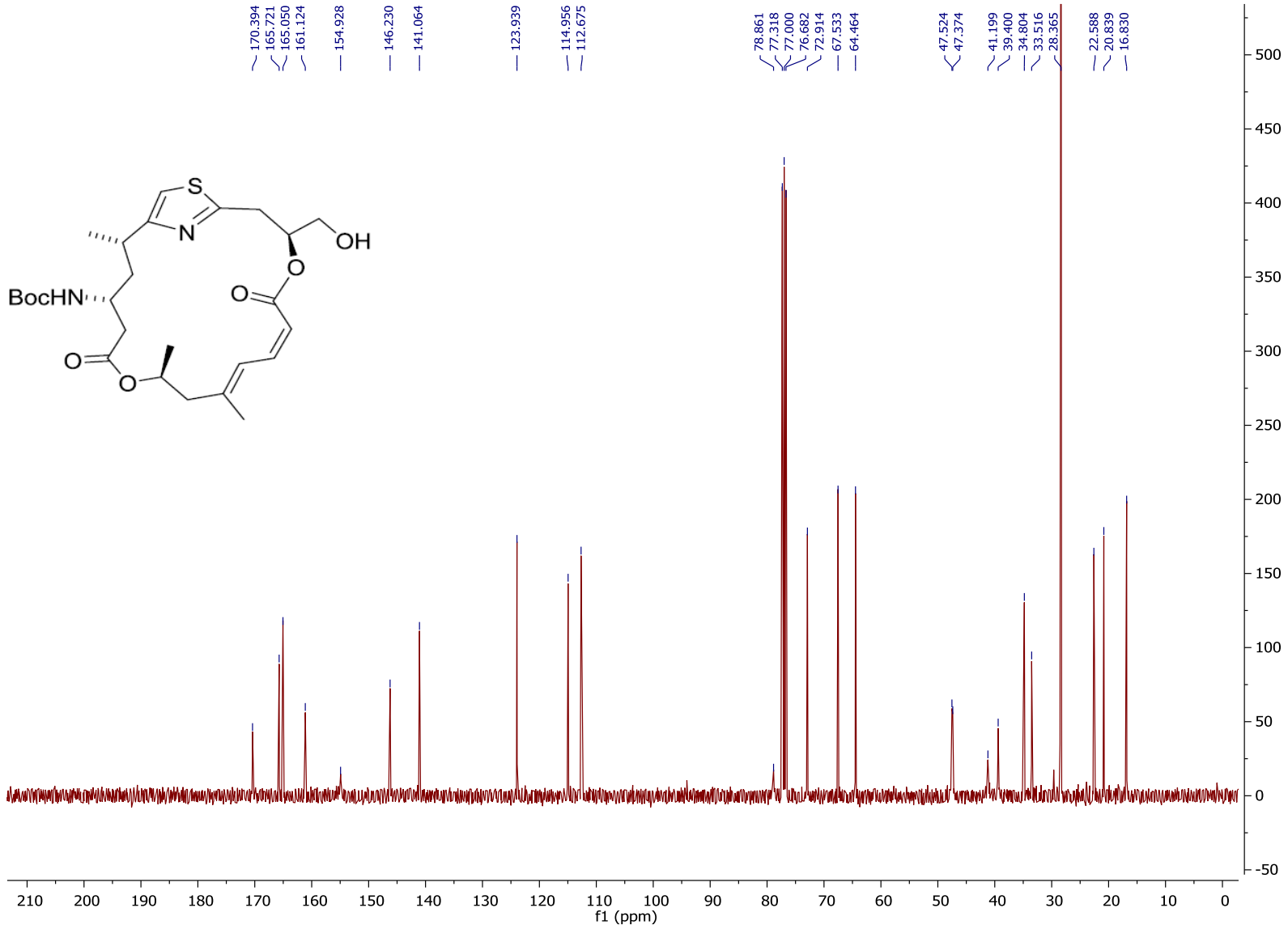
0.88
4.13
9.43
6.58
f1 (ppm)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112.675
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77.318
77.000
76.682
72.914
67.533
64.464
47.524
47.374
41.199
39.400
34.804
33.516
28.365
22.588
20.839
16.830
BocHN
S
N
O
OH
O
O
O
500
450
400
350
300
250
200
150
100
50
0
-50
210
200
190
180
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150
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50
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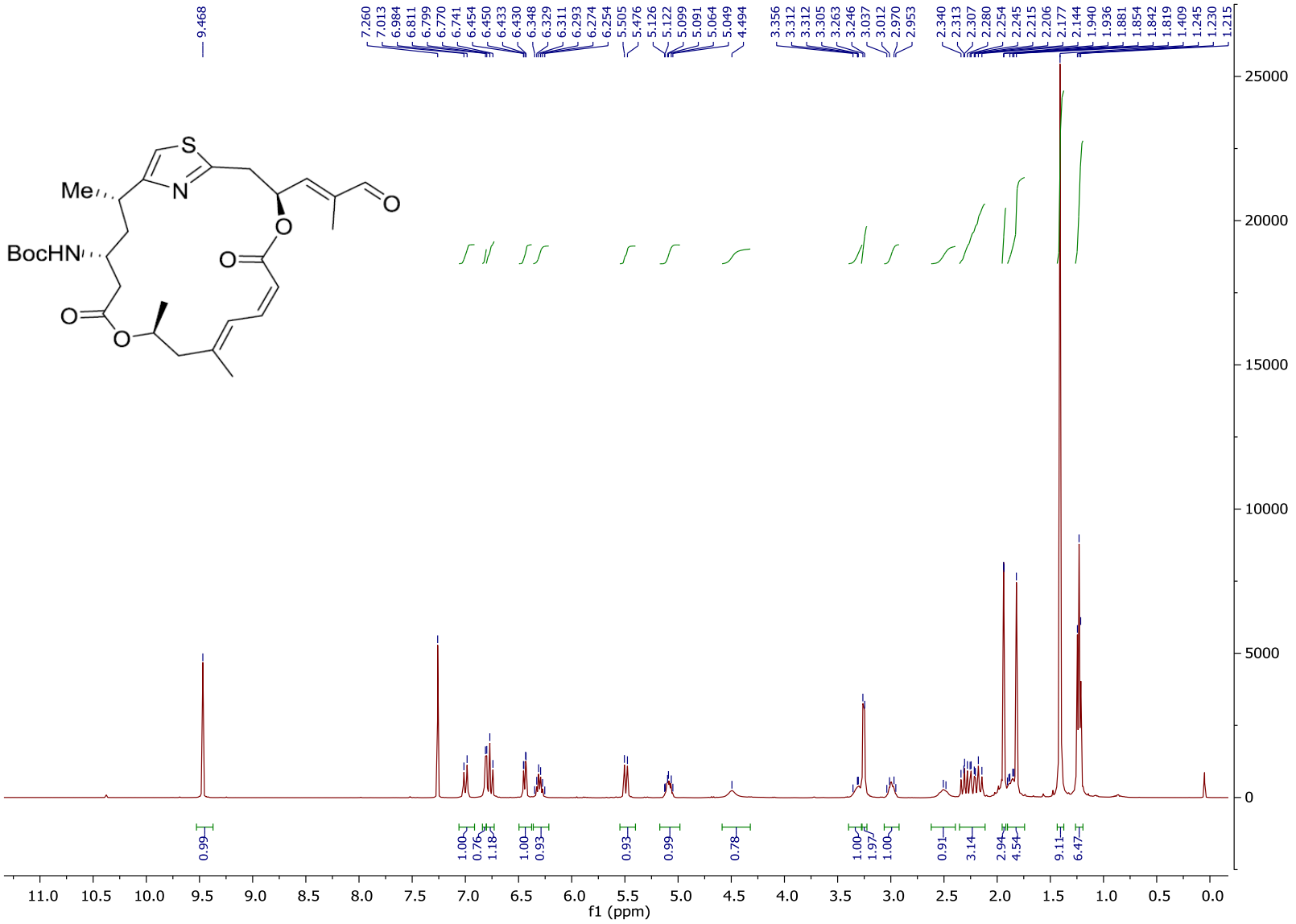
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6.293
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5.476
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5.122
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5.091
5.064
5.049
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3.312
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2.307
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2.215
2.206
2.177
2.144
1.940
1.936
1.881
1.854
1.842
1.819
1.409
1.245
1.230
1.215
S
N
Me
BocHN
O
O
O
O
O
25000
20000
15000
10000
5000
0
0.99
1.00
0.76
1.18
1.00
0.93
0.93
0.99
0.78
1.00
1.97
1.00
0.91
3.14
2.94
4.54
9.11
6.47
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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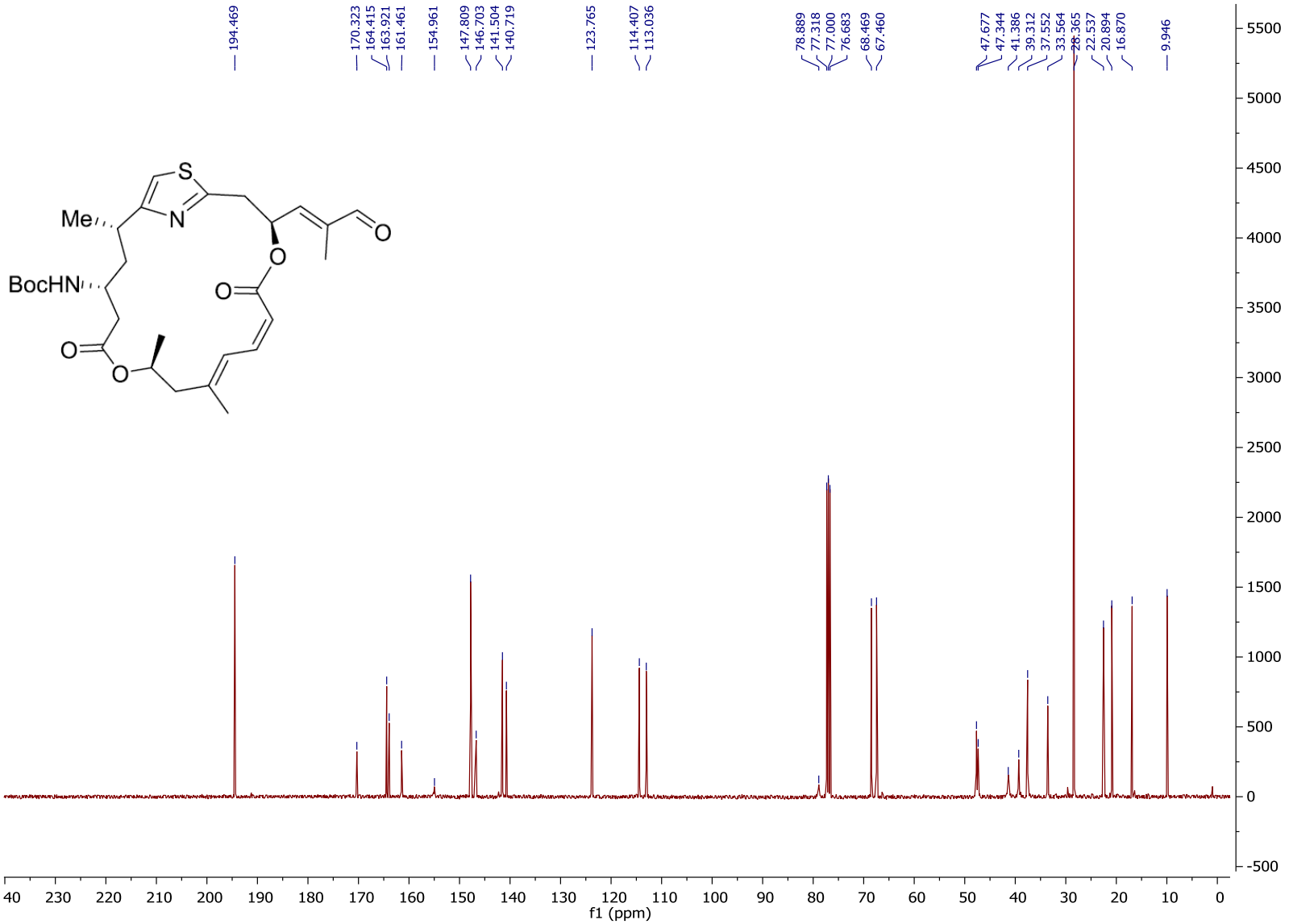
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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47.677
47.344
41.386
39.312
37.552
33.564
28.365
22.537
20.894
16.870
9.946
Me
BocHN
S
N
O
O
O
O
O
O
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
40
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
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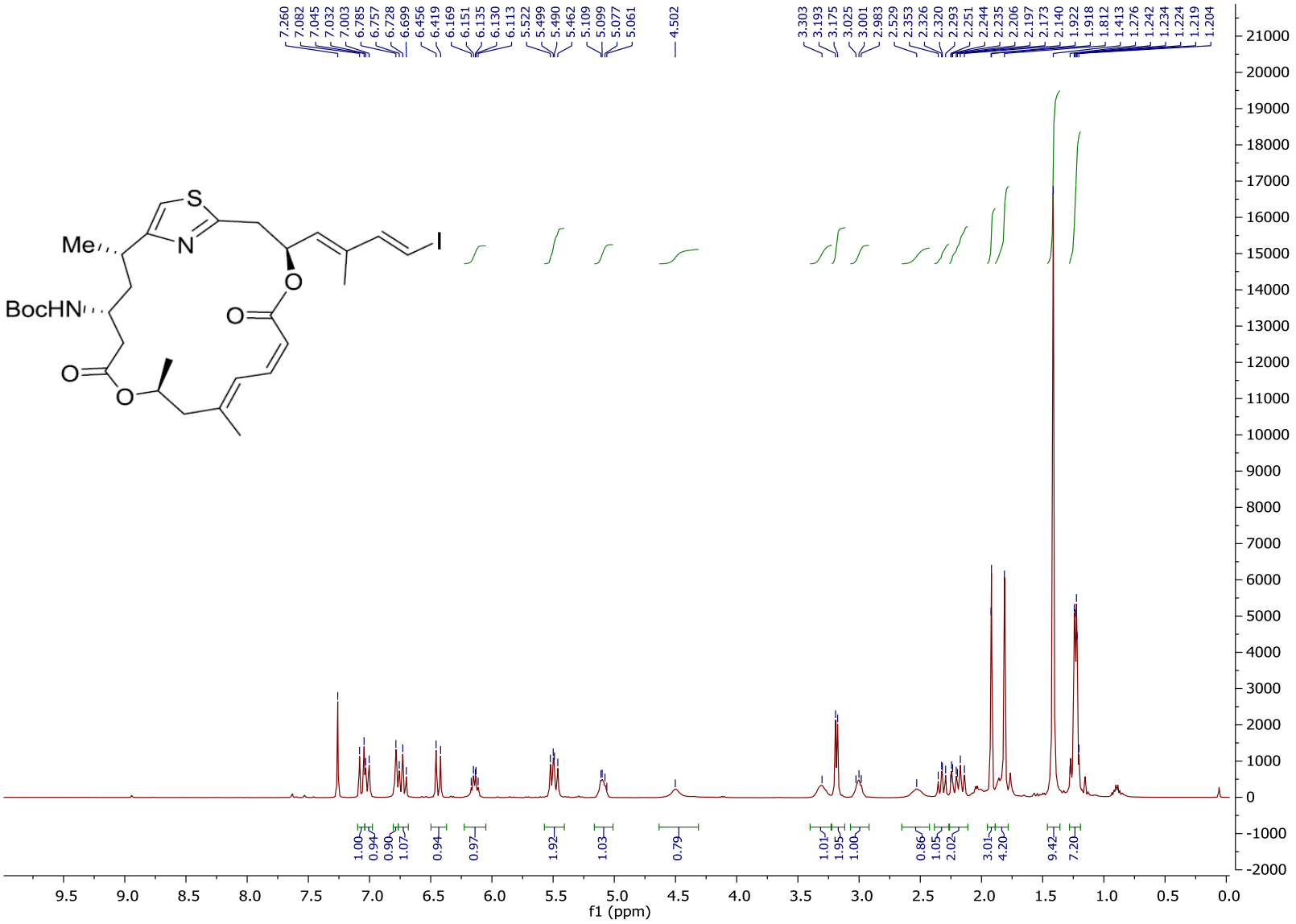
f1 (ppm)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7.082
7.045
7.032
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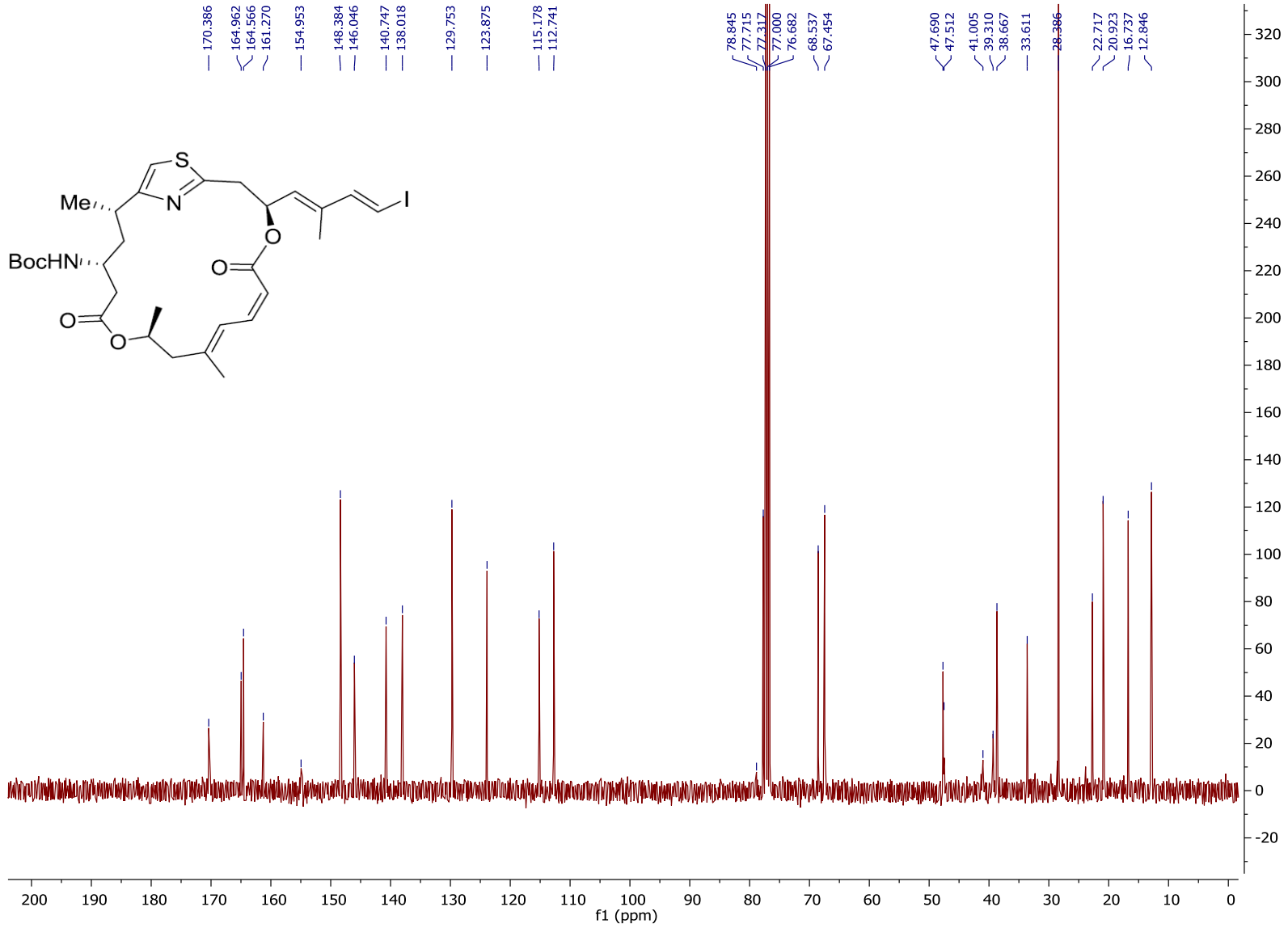
6.728
6.699
6.456
6.419
6.169
6.151
6.135
6.130
6.113
5.522
5.499
5.490
5.462
5.109
5.099
5.077
5.061
4.502
3.303
3.193
3.175
3.025
3.001
2.983
2.529
2.353
2.326
2.320
2.293
2.251
2.244
2.235
2.206
2.197
2.173
2.140
1.922
1.918
1.812
1.413
1.276
1.242
1.234
1.224
1.219
1.204
Me
S
N
I
BocHN
O
O
O
O
1.00
0.94
0.90
1.07
0.94
0.97
1.92
1.03
0.79
1.01
1.95
1.00
0.86
1.05
2.02
3.01
4.20
9.42
7.20
f1 (ppm)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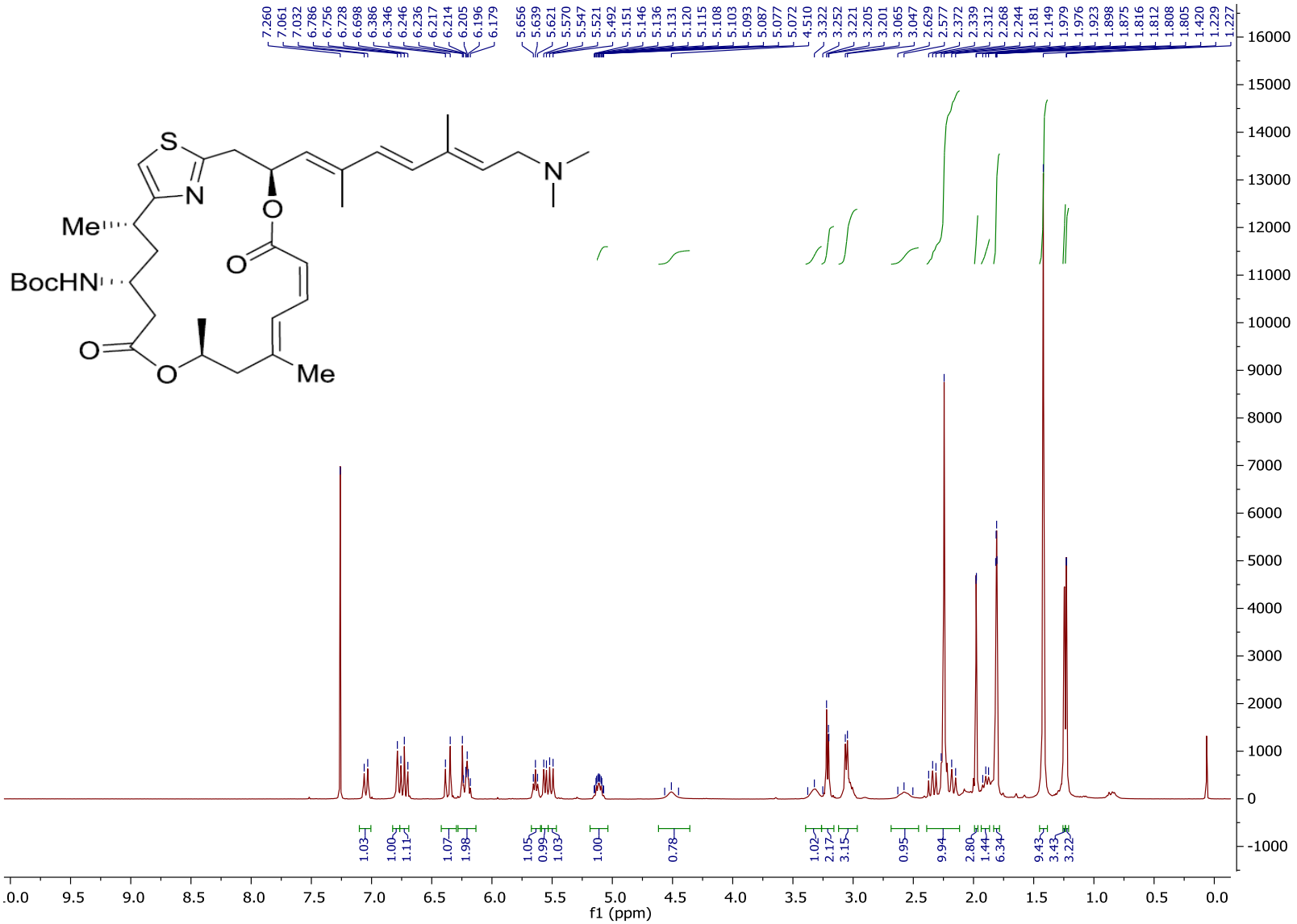
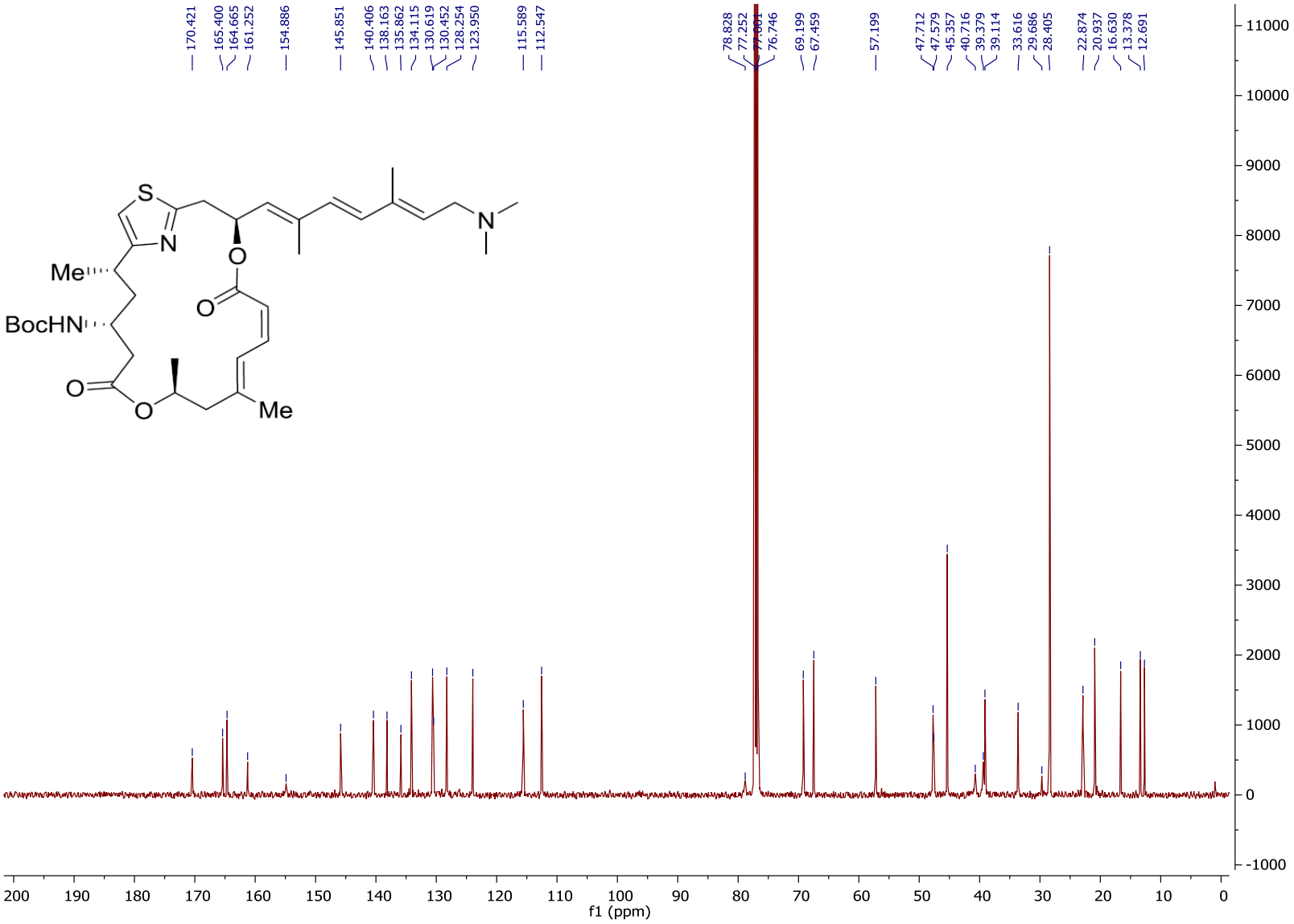
164.962
164.566
161.270
154.953
148.384
146.046
140.747
138.018
129.753
123.875
115.178
112.741
78.845
77.715
77.317
77.000
76.682
68.537
67.454
47.690
47.512
41.005
39.310
38.667
33.611
28.386
22.717
20.923
16.737
12.846
Me
BocHN
S
N
O
O
O
O
I
f1 (ppm)


7.260
7.061
7.032
6.786
6.756
6.728
6.698
6.386
6.346
6.246
6.236
6.217
6.214
6.205
6.196
6.179
5.656
5.639
5.621
5.570
5.547
5.521
5.492
5.151
5.146
5.136
5.131
5.120
5.115
5.108
5.103
5.093
5.087
5.077
5.072
4.510
3.322
3.252
3.221
3.205
3.201
3.065
3.047
2.629
2.577
2.372
2.339
2.312
2.268
2.244
2.181
2.149
1.979
1.976
1.923
1.898
1.875
1.816
1.812
1.808
1.805
1.420
1.229
1.227
S
N
O
N
Me
BocHN
O
O
O
Me
1.03
1.00
1.11
1.07
1.98
1.05
0.99
1.03
1.00
0.78
1.02
2.17
3.15
0.95
9.94
2.80
1.44
6.34
9.43
3.43
3.22
f1 (ppm)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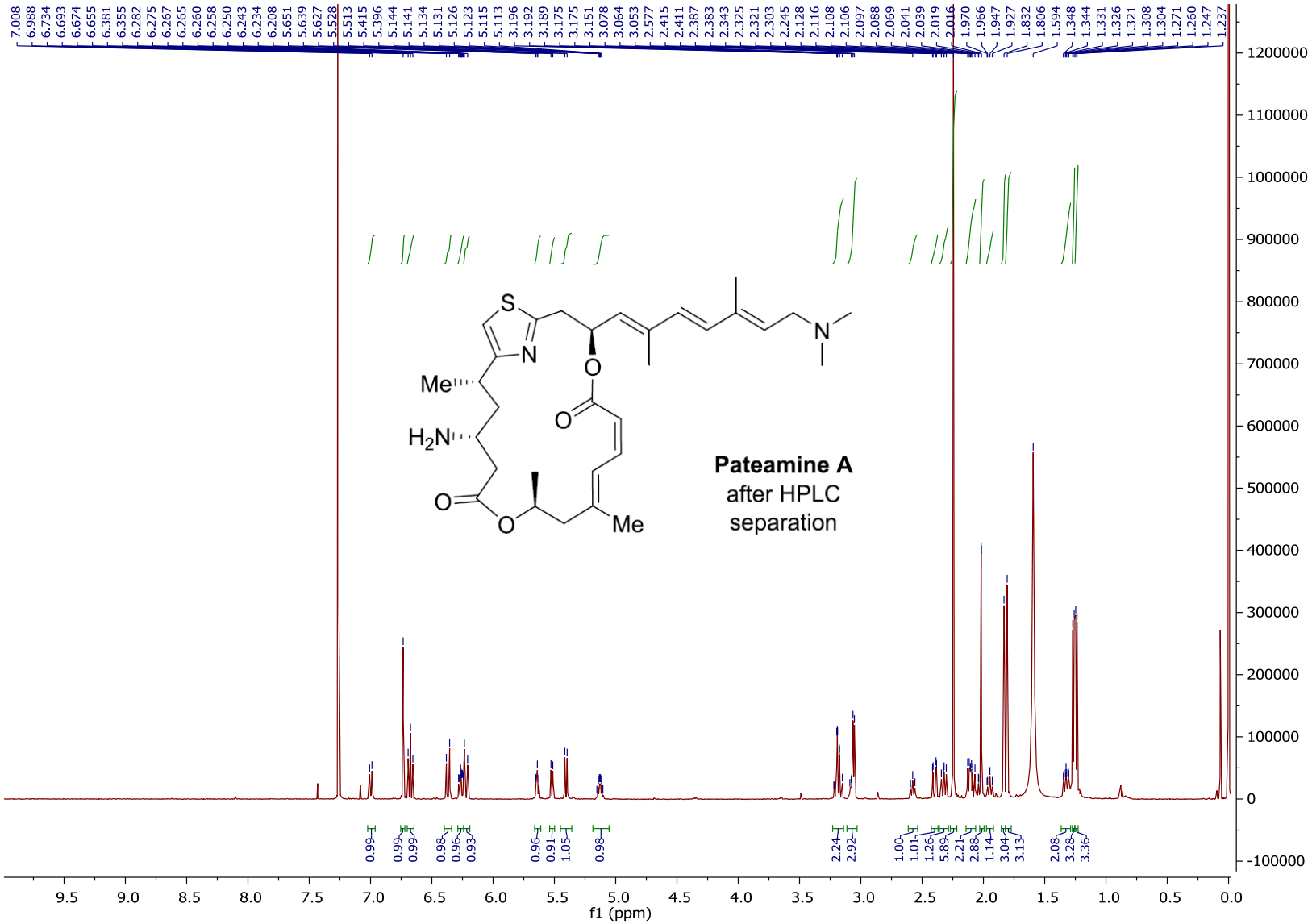
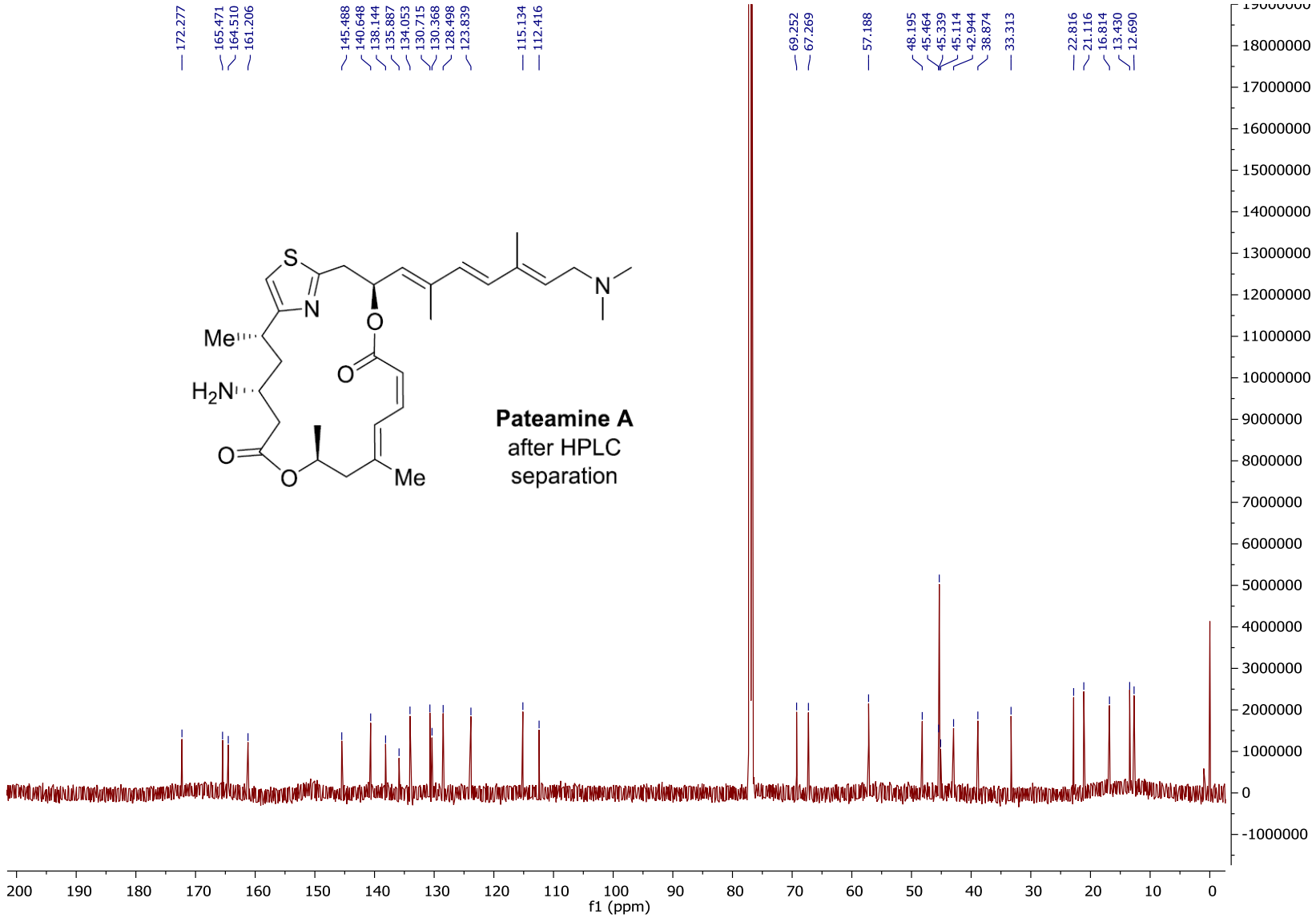
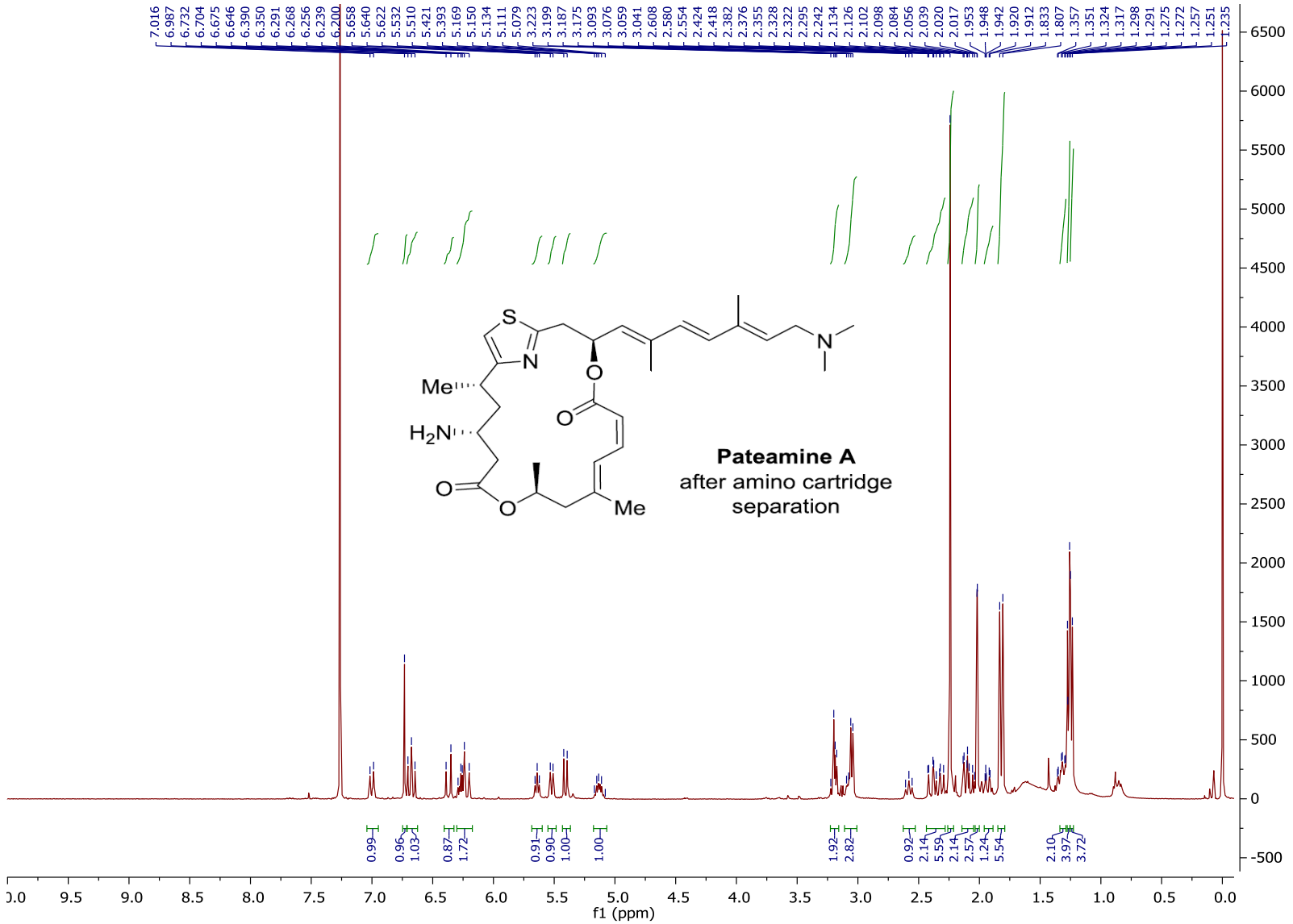
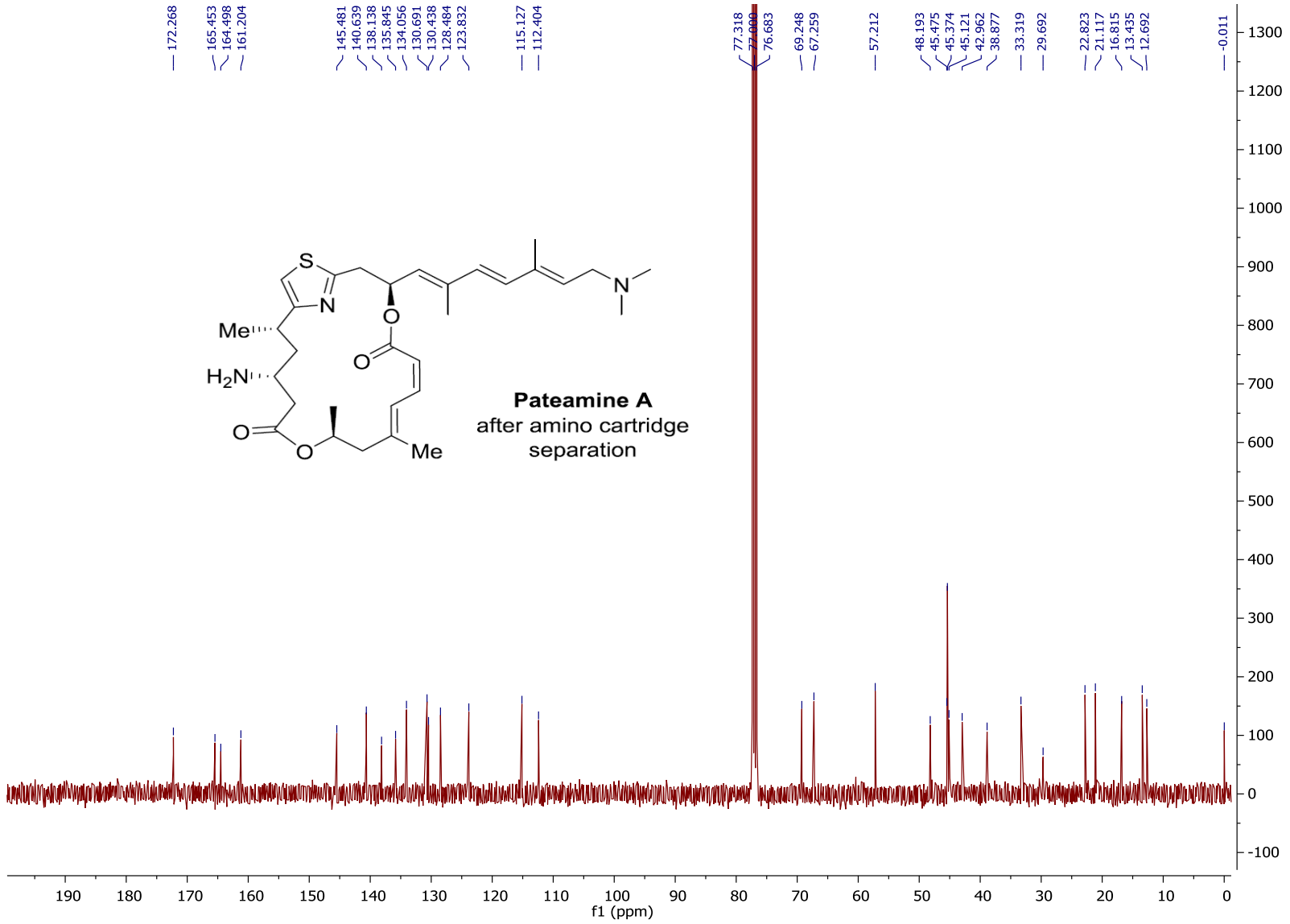
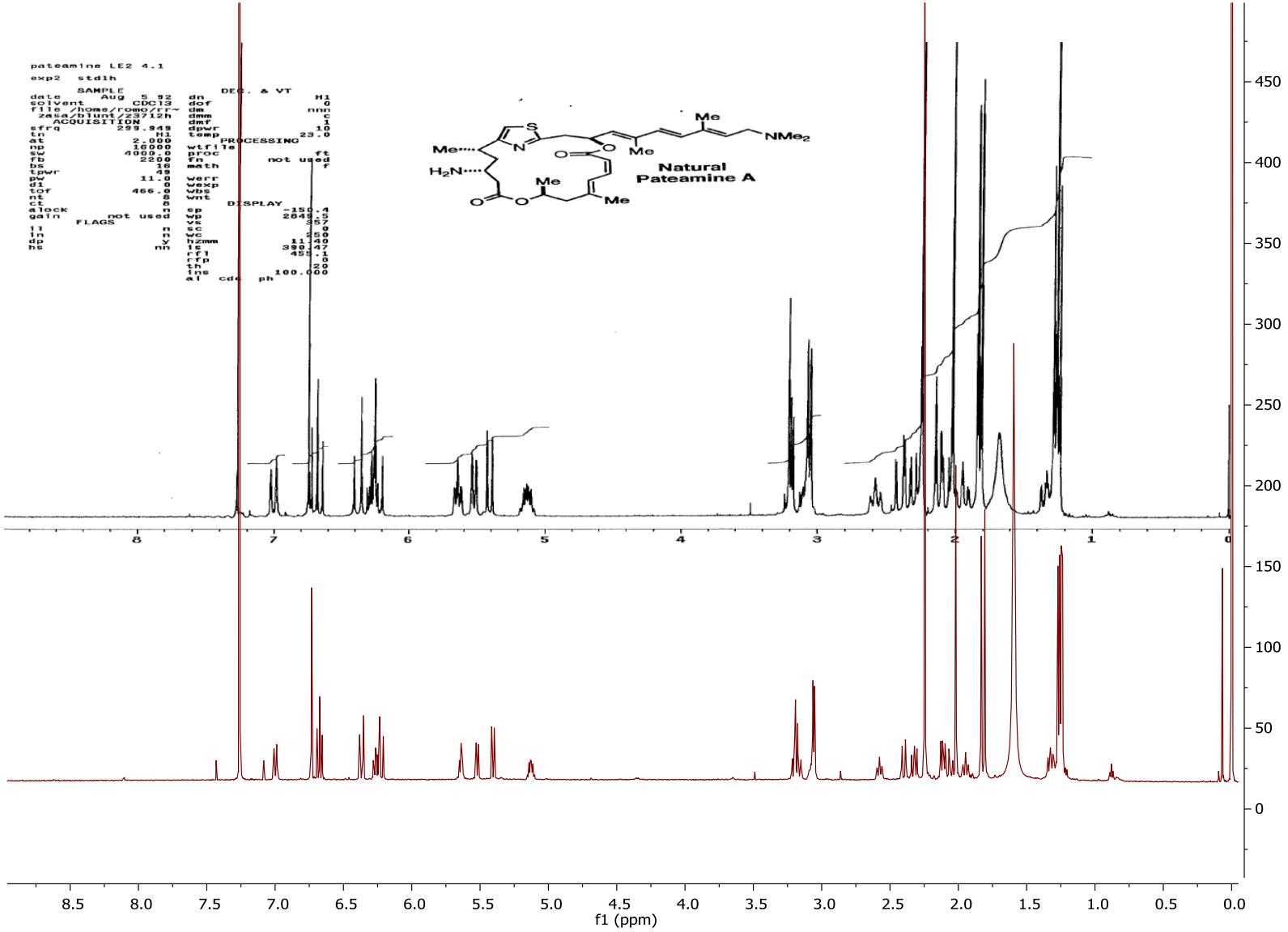
165.400
164.665
161.252
154.886
145.851
140.406
138.163
135.862
134.115
130.619
130.452
128.254
123.950
115.589
112.547
78.828
77.252
77.001
76.746
69.199
67.459
57.199
47.712
47.579
45.357
40.716
39.379
39.114
33.616
29.686
28.405
22.874
20.937
16.630
13.378
12.691
S
N
O
N
Me
BocHN
O
O
O
Me
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Pateamine A
after HPLC
separation
f1 (ppm)

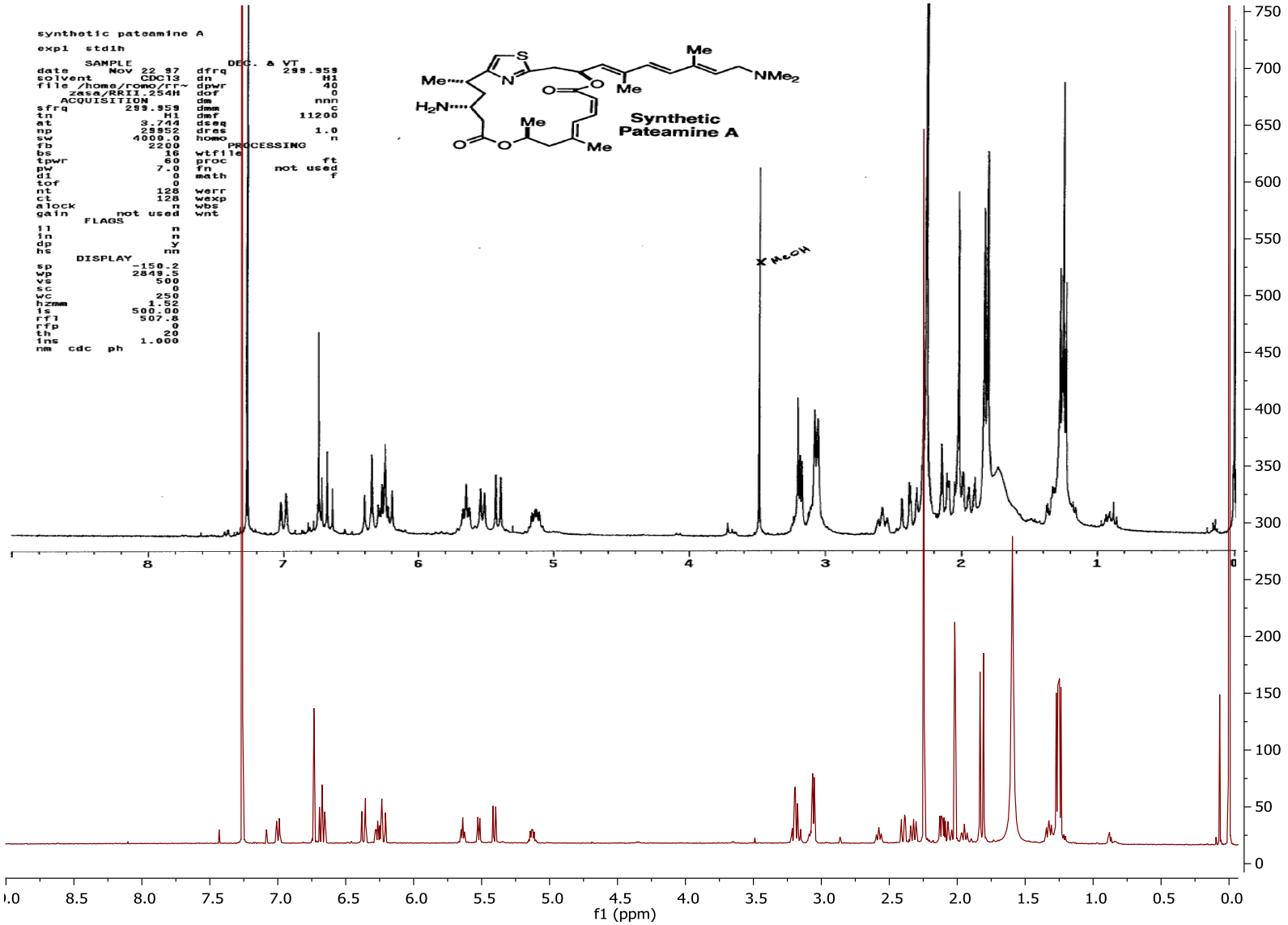

172.277
165.471
164.510
161.206
145.488
140.648
138.144
135.887
134.053
130.715
130.368
128.498
123.839
115.134
112.416
69.252
67.269
57.188
48.195
45.464
45.339
45.114
42.944
38.874
33.313
22.816
21.116
16.814
13.430
12.690
Me
H2N
S
N
O
O
O
O
N
Me
Pateamine A
after HPLC
separation
f1 (ppm)


Pateamine A
after amino cartridge
separation
f1 (ppm)

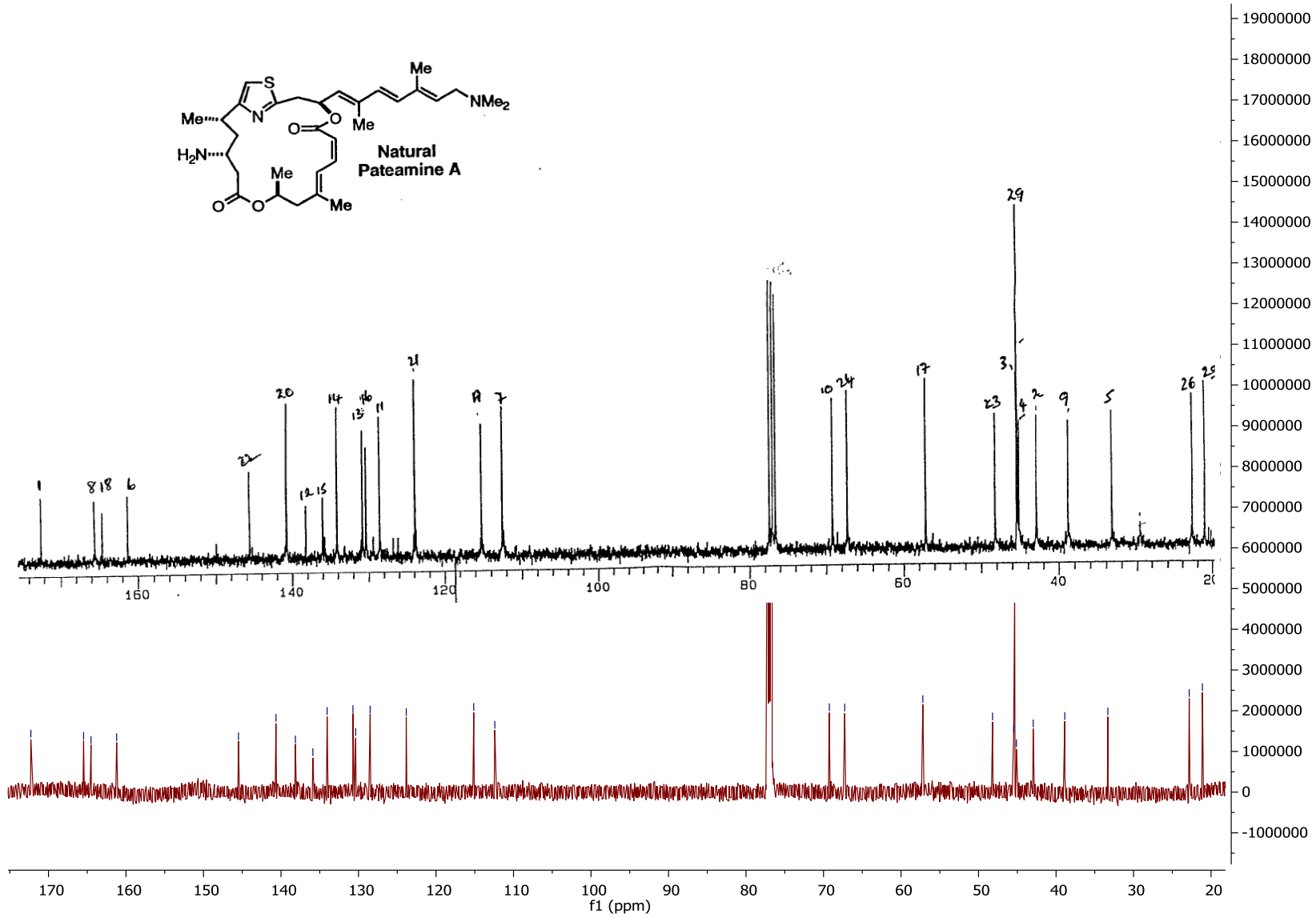

172.268
165.453
164.498
161.204
145.481
140.639
138.138
135.845
134.056
130.691
130.438
128.484
123.832
115.127
112.404
77.318
77.000
76.683
69.248
67.259
57.212
48.193
45.475
45.374
45.121
42.962
38.877
33.319
29.692
22.823
21.117
16.815
13.435
12.692
-0.011
Me
H2N
Me
Pateamine A
after amino cartridge
separation
f1 (ppm)



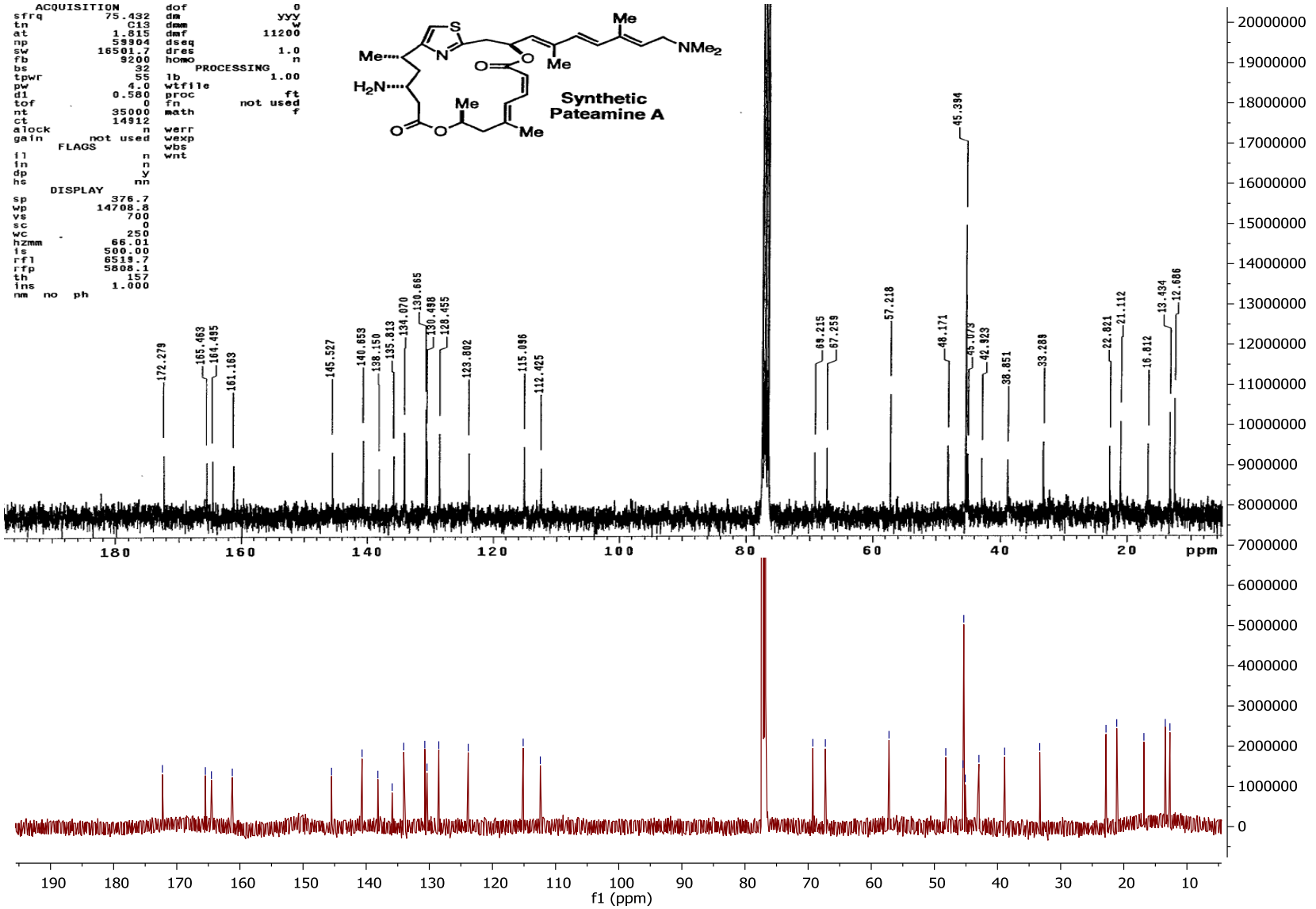
^{1}H NMR Spectrum comparison of natural pateamine A (top) and synthetic sample from this work (bottom)



^{1}H NMR Spectrum comparison of synthetic pateamine A from the Romo group (top) and the Fürstner group (bottom)



^{13}C NMR Spectrum comparison of natural pateamine A (top) and synthetic sample from this work (bottom)



^{13}C NMR Spectrum comparison of synthetic pateamine A from the Romo group (top) and the Fürstner group (bottom