Se-(9-Fluorenylmethyl) Selenoesters; Preparation, Reactivity and Use as Convenient Synthons for Selenoacids

Fabien Fécourt,[a] Bernard Delpech,[a] Oleg Melnyk,[b] and David Crich,[*,c]

a. Centre de Recherche de Gif, Institut de Chimie des Substances Naturelles, CNRS, 1 Avenue de la Terrasse, 91190 Gif-sur-Yvette, France. b. CNRS UMR 8161, Univ. Lille Nord de France, Institut Pasteur de Lille, 59021, Lille, France. c. Department of Chemistry, Wayne State University, 5101 Cass Avenue, Detroit, MI 48202, USA.

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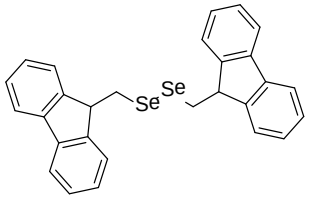
General information

Reactions were performed using oven dried glasswares under an atmosphere of argon. All separations were carried out under flash-chromatographic conditions on silica gel (Interchim Puriflash Silica Std IR 50 UM prepacked column) with use of a CombiFlash Companion. Reactions were monitored by thin-layer chromatography on Merck silica gel plates (60 F254 aluminum sheets) which were rendered visible by ultraviolet light and/or spraying with phosphomolybdic acid (10%) in EtOH or ninhydrin in *n*-butanol followed by heating. CH_3CN, THF, DMF, CH_2Cl_2 and MeOH were purchased from Acros Organics at the highest commercial quality and used without further purification.

Reagent-grade chemicals were obtained from diverse commercial suppliers (Sigma-Aldrich, Acros Organics, Merck-Novabiochem and Alfa-Aesar) and were used as received.

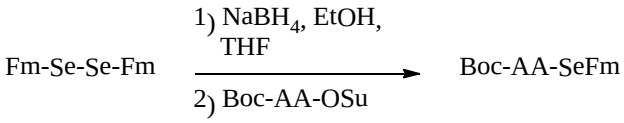
^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on Bruker Avance spectrometers at 298 K unless otherwise stated. Chemical shifts (δ) are given in ppm and are referenced to the internal solvent signal or to TMS used as an internal standard. Multiplicities are declared as follow: *s* (singlet), *br s* (broad singlet), *d* (doublet), *t* (triplet), *q* (quadruplet), *dd* (doublet of doublet), *ddd* (doublet of doublet of doublet), *dt* (doublet of triplet), *m* (multiplet). Coupling constants *J* are given in Hz.
Infrared spectra (IR) were recorded on a Perkin-Elmer FT-IR system using diamond window Dura SamplIR II and the data are reported in reciprocal centimeters (cm^{-1}).
Optical rotations were measured on a Anton Paar MCP 300 polarimeter at 589 nm. $[\alpha]^{25}_D$ is expressed in $deg.cm^3.g^{-1}.dm^{-1}$ and *c* is expressed in g/100 cm^3.
Melting points were recorded in open capillary tubes on a Büchi B-540 apparatus and are uncorrected.
High resolution mass spectra (HRMS) were recorded using a Micromass LCT Premier XE instrument (Waters) and were determined by electrospray ionization (ESI).

1,2-bis((9*H*-fluoren-9-yl)methyl)diselane (2)



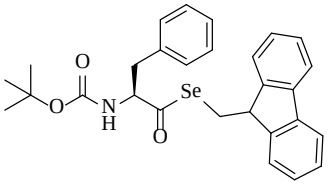
To a cold suspension of elemental selenium (901 mg, 11.41 mmol, 0.5 equiv.) in water (8.5 mL) was added dropwise a solution of $NaBH_4$ (0.864 g, 22.82 mmol, 1 equiv) in water (8.5 mL). The resulting mixture was stirred for 20 min at room temperature. Then, additional selenium (902 mg, 11.41 mmol, 0.5 equiv.) was added. The mixture was stirred for 10 min and then warmed briefly to dissolve selenium. The resulting brown-red Na_2Se_2 solution was ready for further use.
A solution of (9*H*-fluoren-9-yl)methyl 4-methylbenzenesulfonate[1] **1** (8 g, 22.82 mmol, 1 equiv) in DMF (50 mL) was added to the previous aqueous solution. The resulting solution was stirred 2 h at room temperature before to be heat 16 h at 40 °C. *tert*-Butylmethylether was added followed by water. The organic layer was extracted and the aqueous layer was washed with MTBE (× 3). Combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The crude was purified by flash chromatography (Heptane/CH_2Cl_2 8/2) to furnish FmSe-SeFm **2** (4.07 g, 69%) as a yellow solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.47 (d, J = 6.1 Hz, $J^2_{Se\text{-}H}$ = 19.5 Hz, 2H); 4.27 (t, J = 5.9 Hz, 1H); 7.28 (t, J = 7.4 Hz, 1H); 7.28 (t, J = 7.4 Hz, 1H); 7.38 (t, J = 7.3 Hz, 2H); 7.60 (d, J = 7.3 Hz, 2H); 7.75 (d, J = 7.2 Hz, 2H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 34.8 (2 CH_2); 47.9 (2 CH); 120.1 (4 CH); 124.9 (4 CH); 127.2 (4 CH); 127.8 (4 CH); 141.3 (2 Cq); 146.3 (2 Cq).
Mp = 106 °C. IR υ_{max} (cm^{-1}) : 1443; 738. HRMS (Maldi): *m/z* calcd for $C_{28}H_{22}Se_2$ [M] 518.00464, found 518.00288.

General procedure for the synthesis of (9*H*-fluoeren-9-yl)methyl *tert*-butoxy carbonylaminoselenoester (Boc-AA-SeFm):



To a cold solution of Fm-Se-Se-Fm (400 mg, 0.775 mmol, 1 equiv.) in anhydrous THF (4 mL) at 0°C were added successively at $NaBH_4$ (58.6 mg, 1.549 mmol, 2 equiv.) and absolute EtOH (1.2 mL, 20.53 mmol, 26.5 equiv.). The resulting yellow solution was stirred for 10-20 min at room temperature. Then, a solution of Boc-AA-OSu (1.549 mmol, 2 equiv.) in anhydrous THF (4 mL) was added. The resulting mixture was stirred for 4 h at room temperature. The reaction mixture was diluted with EtOAc followed by the addition of saturated aqueous NH_4Cl. The organic layer was extracted with EtOAc (× 3), dried over Na_2SO_4, filtered and concentrated in vacuum. A flash chromatography (Heptane/EtOAC: 9/1) gave the corresponding Boc-AA-SeFm as a solid.

(*S*)-*Se*-((9*H*-fluoren-9-yl)methyl) 2-((*tert*-butoxycarbonyl)amino)-3-phenylpropaneselenoate (Boc-Phe-SeFm) (3)

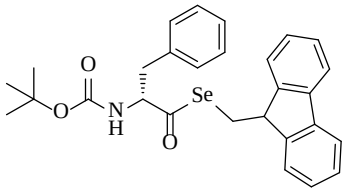


Yield: 77% (601 mg) as a white solid.

[1] Gu, X.; Ying, J.; Agnes, R. S.; Navratilova, E.; Davis, P.; Stahl, G.; Porreca, F.; Yamamura, H. I.; Hruby, V. J. *Org. Lett.* **2004**, *6*, 3285-3288.

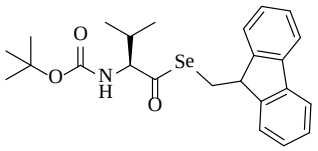
^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.26 (rotamer) + 1.33 (s, 9H); 2.73 (dd, *J* = 14.4, 8.0 Hz, 1H); 2.94 (dd, *J* = 14.4, 4.8 Hz, 1H); 3.51 (dd, *J* = 11.5, 6.2 Hz, 1H); 3.61 (dd, *J* = 11.5, 6.2 Hz, 1H); 4.28 (t, *J* = 5.2 Hz, 1H); 4.38-4.45 (m, 1H); 4.66 (d, *J* = 8.2 Hz, 1H); 6.99-6.01 (m, 2H); 7.19-7.24 (m, 3H); 7.27 (td, *J* = 7.4, 1.2 Hz, 1H); 7.29 (td, *J* = 7.4, 1.2 Hz, 1H); 7.37 (br t, *J* = 7.4 Hz, 2H); 7.59 (d, 7.1 Hz, 1H); 7.60 (d, *J* = 7.1 Hz, 1H); 7.72 (d, *J* = 7.4 Hz, 2H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 28.37 (CH_2); 28.43 (3 CH_3); 37.7 (CH_2); 47.2 (CH); 63.7 (CH); 80.8 (Cq); 119.96 (CH); 120.05 (CH); 124.7 (CH); 124.9 (CH); 127.2 (CH); 127.3 (2 CH); 127.8 (2 CH); 128.9 (2 CH); 129.4 (2 CH); 135.6 (Cq); 141.3 (2 Cq); 146.1 (Cq); 146.4 (Cq); 155.2 (Cq); 205.5 (Cq).
Mp = 141 °C. $[\alpha]^{25}_{D}$ = -38.3 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3345; 1691; 1514; 1162; 750; 704. HRMS (ESI): *m/z* calcd for $C_{28}H_{29}NNaO_3Se$ [M + Na] 530.1210 found 530.1226.

(*R*)-*Se*-((9*H*-fluoren-9-yl)methyl) 2-((*tert*-butoxycarbonyl)amino)-3-phenylpropaneselenoate (Boc-D-Phe-SeFm) (4)



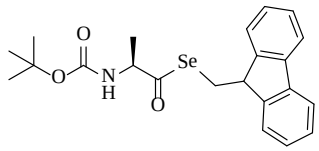
Yield: 74% (582 mg) as a yellowish solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.28 (rotamer) + 1.34 (s, 9H); 2.74 (dd, *J* = 13.8, 8.9 Hz, 1H); 2.95 (dd, *J* = 14.1, 5.2 Hz, 1H); 3.51 (dd, *J* = 11.9, 5.2 Hz, 1H); 3.61 (dd, *J* = 11.9, 5.2 Hz, 1H); 4.28 (t, *J* = 5.4 Hz, 1H); 4.39-4.46 (m, 1H); 4.67 (d, *J* = 8.1 Hz, 1H); 7.19-7.26 (m, 3H); 7.28 (td, *J* = 7.4, 1.1 Hz, 1H); 7.29 (td, *J* = 7.4, 1.1 Hz, 1H); 7.37 (br t, *J* = 7.4 Hz, 2H); 7.59 (d, *J* = 7.5 Hz, 1H); 7.60 (d, *J* = 7.4 Hz, 1H); 7.72 (d, *J* = 7.6 Hz, 2H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 28.37 (CH_2); 28.45 (CH_3); 37.8 (CH_2); 47.2 (CH); 63.7 (CH); 80.8 (Cq); 119.96 (CH); 120.05 (CH); 124.7 (CH); 124.9 (CH); 127.2 (CH); 127.3 (2 CH); 127.8 (2 CH); 128.9 (2 CH); 129.4 (2 CH); 135.6 (Cq); 141.30 (2 Cq); 141.34 (Cq); 146.1 (Cq); 146.4 (Cq); 155.2 (Cq); 205.5 (Cq).
Mp = 138 °C. $[\alpha]^{25}_{D}$ = +39.1 (*c* 1.02, $CHCl_3$). IR υ_{max} (cm^{-1}): 3341; 1690; 1511; 1159; 740; 703. HRMS (ESI): *m/z* calcd $C_{28}H_{29}NNaO_3Se$ [M + Na] 530.1210, found 530.1217.

(*S*)-*Se*-((9*H*-fluoren-9-yl)methyl) 2-((*tert*-butoxycarbonyl)amino)-3-methylbutaneselenoate (Boc-Val-SeFm) (5)



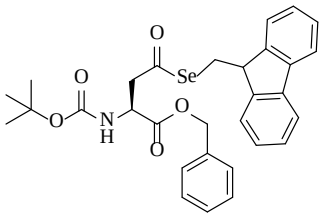
Yield: 81% (575 mg) as a white solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.59 + 0.66 (rotamer) (d, *J* = 6.9 Hz, 3H); 0.83 (d, *J* = 6.9 Hz, 3H); 1.34 (rotamer) + 1.41 (s, 9H); 1.99-2.17 (m, 1H); 3.53 (dd, *J* = 12.7, 4.9 Hz, 1H); 3.62 (dd, *J* = 12.7, 4.9 Hz, 1H); 4.08 (dd, *J* = 9.3, 4.0 Hz, 1H); 4.27 (t, *J* = 5.3 Hz, 1H); 4.80 (br d, *J* = 9.3 Hz, 1H); 7.28 (2 t, *J* = 7.1 Hz, 1H); 7.34 (t, *J* = 7.4 Hz, 1H); 7.36 (t, *J* = 7.5 Hz, 1H); 7.58 (d, *J* = 6.6 Hz, 1H); 7.60 (d, *J* = 6.1 Hz, 1H); 7.69 (d, *J* = 6.7 Hz, 1H); 7.71 (d, *J* = 7.1 Hz, 1H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.6 (CH_3); 19.6 (CH_3); 28.0 (CH_2); 28.5 (3 CH_3); 30.7 (CH); 47.2 (CH); 68.0 (CH); 80.2 (Cq); 119.9 (CH); 120.0 (CH); 124.6 (CH); 124.9 (CH); 127.2 (CH); 127.3 (CH); 127.7 (2 CH); 141.3 (2 Cq); 146.0 (Cq); 146.4 (Cq); 155.7 (Cq); 205.4 (Cq).
Mp = 95 °C. $[\alpha]^{25}_{D}$ = -14.5 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3389; 1715; 1679; 1494; 1160; 735. HRMS (ESI): *m/z* calcd $C_{24}H_{29}NNaO_3Se$ [M + Na] 482.1210, found 482.1228.

(*S*)-*Se*-((9*H*-fluoren-9-yl)methyl) 2-((*tert*-butoxycarbonyl)amino)propaneselenoate (Boc-Ala-SeFm) (6)



Yield: 75% (502 mg) as a yellowish solid
^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.08 (d, *J* = 7.4 Hz, 3H); 1.32 (rotamer) + 1.41 (s, 9H); 3.48-3.60 (m, 2H) ; 4.12-4.21 (m, 1H); 4.27 (t, *J* = 5.5 Hz, 1H); 4.76 (br d, *J* = 6.9 Hz, 1H); 7.24-7.31 (m, 2H); 7.33-7.39 (m, 2H); 7.59 (d, *J* = 7.4 Hz, 2H); 7.72 (d, *J* = 7.4 Hz, 2H); 7.73 (d, *J* = 7.4 Hz, 2H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.0 (CH_3); 28.0 (CH_2); 28.5 (3 CH_3); 47.3 (CH); 59.3 (CH); 80.7 (Cq); 119.9 (CH); 120.0 (CH); 124.7 (CH); 124.9 (CH); 127.2 (CH); 127.3 (CH); 127.8 (2 CH); 141.3 (2 Cq); 146.1 (Cq); 146.4 (Cq); 155.0 (Cq); 206.1 (Cq).
Mp = 139 °C. $[\alpha]^{25}_D$ = -8.3 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3358; 1683; 1501; 1157; 752; 732. HRMS (ESI): *m/z* calcd for $C_{22}H_{25}NNaO_3Se$ [M + Na] 454.0897, found 454.0926.

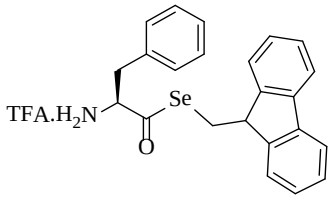
(*S*)-benzyl 4-(((9*H*-fluoren-9-yl)methyl)selanyl)-2-((*tert*-butoxycarbonyl)amino)-4-oxobutanoate (Boc-Asp(γSeFm)-OBn) (7)



Yield: 60% (525 mg) as a white solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.42 (s, 9H); 3.04 (dd, *J* = 16.6, 3.8 Hz, 1H); 3.17 (dd, *J* = 16.6, 3.8 Hz, 1H); 3.55 (d, *J* = 5.7 Hz, 2H); 4.23 (t, *J* = 5.2 Hz, 1H); 4.44-4.48 (m, 1H); 5.09 (d, *J* = 12.2 Hz, 1H); 5.12 (d, *J* = 12.2 Hz, 1H); 5.27 (d, *J* = 7.8 Hz, 1H); 7.26-7.31 (m, 7H); 7.36 (t, *J* = 6.9 Hz, 1H); 7.37 (t, *J* = 7.3 Hz, 1H); 7.56 (d, *J* = 7.4 Hz, 1H); 7.57 (d, *J* = 7.4 Hz, 1H); 7.71 (2 d, *J* = 7.4 Hz, 1H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 28.5 (3 CH_3); 29.1 (CH_2) ; 47.1 (CH); 49.5 (CH_2); 50.6 (CH); 67.7 (CH_2); 80.4 (Cq); 120.1 (2 CH); 124.64 (CH) ; 124.71 (CH); 127.3 (2 CH) ; 127.9 (2 CH); 128.5 (2 CH) ; 128.6 (CH); 128.7 (2 CH); 135.3 (Cq); 141.2 (2 Cq); 146.01 (Cq); 146.07 (Cq); 155.4 (Cq); 170.6 (Cq); 199.2 (Cq).
Mp = 99 °C. $[\alpha]^{25}_D$ = 11.3 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3382; 1750; 1714; 1697; 1510; 1337; 1165; 738; 726. HRMS (ESI); *m/z* calcd $C_{30}H_{31}NNaO_5Se$ [M + Na] 588.1265, found 588.1262.

Synthesis of (9*H*-flueren-9-yl)methyl aminoselenoester trifluoroacetic salt (TFA.H-AA-SeFm)

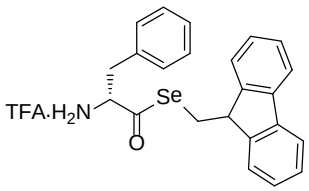
(*S*)-*Se*-((9*H*-fluoren-9-yl)methyl) 2-amino-3-phenylpropaneselenoate trifluoroacetic acid salt (TFA.H-Phe-SeFm) (8)



To a solution of Boc-Phe-SeFm **3** (300 mg, 0.592 mmol) in CH_2Cl_2 (4 mL) was added TFA (0.8 mL). The resulting solution was stirred for 1 h at room temperature. The solvent was evaporated and excess of TFA was azeotroped with CH_2Cl_2 (× 3). Then, the crude oil was triturated with Et_2O to give the ammonium salt TFA.H-Phe-SeFm **8** (290 mg, 94%) as a white solid without further purification.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.87 (dd, *J* = 14.7, 7.6 Hz, 1H); 2.99 (dd, *J* = 14.7, 5.8 Hz 1H); 3.66 (dd, *J* = 12.3, 4.9 Hz, 1H); 3.80 (dd, *J* = 12.4, 4.6 Hz, 1H); 4.22 (dd, *J* = 7.5, 5.9 Hz, 1H); 4.30 (t, *J* =

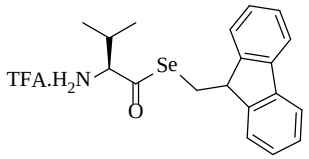
4.7 Hz, 1H); 6.95-7.00 (m, 2H); 7.21-7.24 (m, 2H); 7.25-7.34 (m, 2H); 7.38 (d, *J* = 7.1 Hz, 1H); 7.39 (t, *J* = 7.1 Hz, 1H); 7.48 (br d, *J* = 7.3 Hz, 2H); 8.20 (br s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) *δ*: 30.1 (CH_2); 37.1 (CH_2); 46.5 (CH); 63.6 (CH); 120.19 (CH); 120.25 (CH); 124.4 (CH); 124.6 (CH); 127.5 (CH); 127.6 (CH); 128.3 (2 CH); 128.6 (CH); 129.5 (2 CH); 129.6 (2 CH); 132.1 (Cq); 141.3 (Cq); 141.5 (Cq); 145.1 (Cq); 145.4 (Cq); 199.1 (Cq).
Mp = 166 °C. $[\alpha]^{25}_D$ = -30.5 (*c* 1, MeOH). IR υ_{max} (cm^{-1}): 3354; 2935; 1653; 1182; 1142; 740; 721; 703. HRMS (ESI): *m/z* calcd $C_{23}H_{22}NOSe$ [M - $CF_3CO_2^-$] 408.0867, found 408.0864.

(*R*)-*Se*-((9*H*-fluoren-9-yl)methyl) 2-amino-3-phenylpropaneselenoate trifluoroacetic acid salt (TFA.H-D-Phe-SeFm) (9)



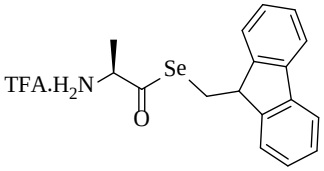
To a solution of Boc-D-Phe-SeFm **4** (300 mg, 0.592 mmol) in CH_2Cl_2 (4 mL) was added TFA (0.8 mL). The resulting solution was stirred for 1 h at room temperature. The solvent was evaporated and excess of TFA was azeotroped with CH_2Cl_2 (× 3). Then, the crude oil was triturated with Et_2O to give the ammonium salt TFA.H-D-Phe-SeFm **9** (277 mg, 90%) as a yellowish solid without further purification.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.97 (br d, *J* = 6.0 Hz, 2H); 3.58 (dd, *J* = 12.6, 5.1 Hz, 1H); 3.72 (dd, *J* = 12.6, 5.1 Hz, 1H); 4.16 (d, *J* = 6.4 Hz, 1H); 4.26 (t, *J* = 5.0 Hz, 1H); 6.78 (br s, 2H); 6.99-7.02 (m, 2H); 7.19-7.32 (m, 5H); 7.37 (t, *J* = 7.2 Hz, 1H); 7.39 (t, *J* = 7.0 Hz, 1H); 7.47 (d, *J* = 7.4 Hz, 1H); 7.48 (d, *J* = 7.4 Hz, 1H); 7.72 (d, *J* = 7.4 Hz, 2H).
^{13}C NMR (75 MHz, $CDCl_3$) *δ*: 29.9 (CH_2); 37.3 (CH_2); 46.6 (CH); 63.5 (CH); 120.1 (CH); 120.2 (CH); 124.5 (CH); 124.7 (CH); 127.5 (CH); 127.6 (CH); 128.2 (2 CH); 128.3 (CH); 129.4 (2 CH); 129.7 (2 CH); 132.9 (Cq); 141.3 (Cq); 141.4 (Cq); 145.3 (Cq); 145.6 (Cq); 199.6 (Cq).
Mp = 165 °C. $[\alpha]^{25}_D$ = +30.8 (*c* 1, MeOH). IR υ_{max} (cm^{-1}): 2921; 1653; 1191; 1145; 743; 725; 709. HRMS (ESI): *m/z* calcd $C_{23}H_{22}NOSe$ [M - $CF_3CO_2^-$] 408.0867; found 408.0871.

(*S*)-*Se*-((9*H*-fluoren-9-yl)methyl) 2-amino-3-methylbutaneselenoate trifluoroacetic acid salt (TFA.H-Val-SeFm) (10)



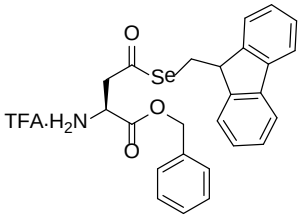
To a solution of Boc-Val-SeFm **5** (300 mg, 0.654 mmol) in CH_2Cl_2 (4 mL) was added TFA (0.8 mL). The resulting solution was stirred for 1 h at room temperature. The solvent was evaporated and excess of TFA was azeotroped with CH_2Cl_2 (× 3). Then, the crude oil was triturated with Et_2O to give the ammonium salt TFA.H-Val-SeFm **10** (294 mg, 95%) as a white solid without further purification.
^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 0.72 (d, *J* = 7.0 Hz, 3H); 0.93 (d, *J* = 7.0 Hz, 3H); 0.90-0.96 (m, 1H); 3.65 (dd, *J* = 12.5, 4.8 Hz, 1H); 3.79-3.85 (m, 1H); 3.84 (d, *J* = 3.8 Hz, 1H); 4.31 (t, *J* = 4.7 Hz, 1H); 7.22-7.43 (m, 4H); 7.40 (br s, 3H); 7.51 (d, *J* = 7.0 Hz, 1H); 7.54 (d, *J* = 7.1 Hz, 1H); 7.70 (d, *J* = 7.3 Hz, 1H); 7.73 (d, *J* = 7.1 Hz, 1H).
^{13}C NMR (75 MHz, $CDCl_3$) *δ*: 16.2 (CH_3); 18.3 (CH_3); 29.5 (CH_2); 30.5 (CH); 46.7 (CH); 67.7 (CH); 120.0 (CH); 120.2 (CH); 124.4 (CH); 124.7 (CH); 127.47 (CH); 127.51 (CH); 128.04 (CH); 128.10 (CH); 141.4 (2 Cq); 145.2 (Cq); 145.8 (Cq); 198.9 (Cq).
Mp = 155 °C. $[\alpha]^{25}_D$ = -49.4 (*c* 1, MeOH). IR υ_{max} (cm^{-1}): 2959; 1651; 1525; 1188; 1132; 737; 721. HRMS (ESI): *m/z* calcd $C_{19}H_{22}NOSe$ [M - $CF_3CO_2^-$] 360.0867; found 360.0877.

(*S*)-*Se*-((9*H*-fluoren-9-yl)methyl) 2-aminopropaneselenoate trifluoroacetic acid salt (TFA.H-Ala-SeFm) (11)



To a solution of Boc-Ala-SeFm **6** (300 mg, 0.697 mmol) in CH_2Cl_2 (4 mL) was added TFA (0.8 mL). The resulting solution was stirred for 1 h at room temperature. The solvent was evaporated and excess of TFA was azeotroped with CH_2Cl_2 (× 3). Then, the crude oil was triturated with Et_2O to give the ammonium salt TFA.H-Ala-SeFm **11** (288 mg, 94%) as a white solid without further purification.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.31 (d, *J* = 7.2 Hz, 3H); 3.60 (dd, *J* = 13.4, 5.2 Hz, 1H); 3.70 (dd, *J* = 13.4, 5.2 Hz, 1H); 3.96 (q, *J* = 7.2 Hz, 1H); 4.26 (t, *J* = 5.0 Hz, 1H); 7.21-7.27 (m, 2H); 7.34 (t, *J* = 7.4 Hz, 1H); 7.35 (t, *J* = 7.2 Hz, 1H); 7.47 (2 d, *J* = 7.2 Hz, 1H); 7.68 (d, *J* = 7.4 Hz, 1H); 7.69 (d, *J* = 7.4 Hz, 1H); 7.96 (br s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.1 (CH_3); 29.6 (CH_2); 46.6 (CH); 58.6 (CH); 120.1 (CH); 120.2 (CH); 124.4 (CH); 124.6 (CH); 127.4 (CH); 127.5 (CH); 128.1 (2 CH); 141.3 (2 Cq); 145.2 (Cq); 145.6 (Cq); 200.2 (Cq).
Mp = 136 °C. $[\alpha]^{25}_D$ = -30.3 (*c* 1, MeOH). IR υ_{max} (cm^{-1}): 2843; 1654; 1521; 1184; 1133; 956; 742; 720. HRMS (ESI): *m/z* calcd $C_{17}H_{18}NOSe$ [M - $CF_3CO_2^-$] 332.0554; found 332.0562.

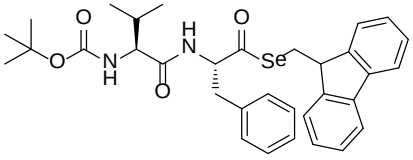
(*S*)-benzyl 4-(((9*H*-fluoren-9-yl)methyl)selanyl)-2-amino-4-oxobutanoate trifluoroacetic acid salt (TFA.H-Asp(γSeFm)-OBn) (12)



To a solution of Boc-Asp(γSeFm)-OBn **7** (300 mg, 0.531 mmol) in CH_2Cl_2 (4 mL) was added TFA (0.8 mL). The resulting solution was stirred for 1 h at room temperature. The solvent was evaporated and excess of TFA was azeotroped with CH_2Cl_2 (× 3). Then, the crude oil was triturated with Et_2O to give the ammonium salt TFA.H-Asp(γSeFm)-OBn **12** (280 mg, 91%) as a white solid without further purification.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.24-3.26 (m, 2H); 3.55 (d, 5.2 Hz, 2H); 4.20 (t, *J* = 9.9 Hz, 2H); 5.04 (d, *J* = 11.9 Hz, 1H); 5.09 (d, *J* = 11.9 Hz, 1H); 5.06 (d, *J* = 2.0 Hz, 2H); 6.01 (br s, 3H); 7.18-7.28 (m, 7H); 7.31-7.38 (m, 2H); 7.50 (d, *J* = 7.7 Hz, 2H); 7.68 (dd, *J* = 7.7, 3.3 Hz, 2H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 29.6 (CH_2); 46.0 (CH); 46.8 (CH); 69.1 (CH_2); 120.1 (2 CH); 124.6 (2 CH); 127.4 (2 CH); 128.0 (2 CH); 128.1 (2 CH); 128.9 (2 CH); 129.1 (CH); 134.1 (Cq); 141.2 (2 Cq); 145.7 (2 Cq); 167.8 (Cq); 200.0 (Cq).
Mp = 158 °C. $[\alpha]^{25}_D$ = +4.1 (*c* 1, MeOH). IR υ_{max} (cm^{-1}): 2904; 1746; 1693; 1656; 1204; 1139; 740; 721. HRMS (ESI): *m/z* calcd $C_{25}H_{24}NO_3Se$ [M - $CF_3CO_2^-$] 466.0921; found 466.0923.

Synthesis of dipeptidoselenoester Fm

(*S*)-*Se*-((9*H*-fluoren-9-yl)methyl) 2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methylbutanamido)-3-phenylpropaneselenoate (Boc-Val-Phe-SeFm) (13)



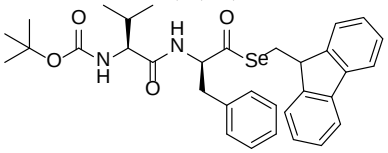
To a solution of Boc-Val-OH (81 mg, 0.375 mmol, 1.3 equiv.) in DMF (2 mL) were added HBTU (142 mg, 0.375 mmol, 1.3 equiv.) and dropwise DIEA (0.121 mL, 0.692 mmol, 2.4 equiv). The resulting solution was stirred for 20 min at room temperature. Then, a solution of TFA.H-Phe-SeFm **8** (150 mg, 0.288 mmol, 1 equiv) in DMF (0.5 mL) was added. After stirring overnight at room temperature, DMF was removed under high vacuum. A flash purification (Heptane/EtOAc: 9/1) of the crude gave Boc-Val-Phe-SeFm **13** (139 mg, 80%) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.78 (br s, 3H); 0.87 (d, *J* = 6.9 Hz, 3H); 1.41 (s, 9H); 2.05-2.16 (m, 1H); 2.81-2.94 (m, 1H); 3.02 (dd, *J* = 14.5, 5.2 Hz, 1H); 3.51-3.64 (m, 2H); 3.83 (dd, *J* = 8.3, 6.0 Hz, 1H); 4.28 (t, *J* = 5.2 Hz, 1H); 4.82 (dt, *J* = 8.0, 5.5 Hz, 2H); 6.25 (d, *J* = 7.9 Hz, 1H); 7.03-7.07 (m, 2H); 7.21-7.34 (m, 5H); 7.40 (t, *J* = 7.4 Hz, 2H); 7.60 (d, *J* = 7.4 Hz, 2H); 7.75 (d, *J* = 7.4 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.7 (CH_3); 19.6 (CH_3); 28.5 (3 CH_3); 28.8 (CH_2); 30.3 (CH); 37.9 (CH_2); 47.1 (CH); 60.3 (CH); 62.3 (CH); 80.3 (Cq); 120.02 (CH); 120.07 (CH); 124.7 (CH); 124.8 (CH); 127.2 (CH); 127.3 (CH); 127.4 (CH); 127.8 (2 CH); 128.9 (2 CH); 129.4 (2 CH); 135.4 (Cq); 141.2 (Cq); 141.3 (Cq); 146.1 (Cq); 146.2 (Cq); 155.8 (Cq); 172.0 (Cq); 203.5 (Cq).

Mp = 192 °C. $[\alpha]^{25}_D$ = -47.5 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3324; 3270; 1699; 1666; 1525; 1244; 1169; 730. HRMS (ESI): *m/z* calcd $C_{33}H_{39}N_2O_4Se$ [M + H] 607.2075; found 607.2070.

(*R*)-*Se*-((9*H*-fluoren-9-yl)methyl) 2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methylbutanamido)-3-phenylpropaneselenoate (Boc-Val-D-Phe-SeFm) (14)



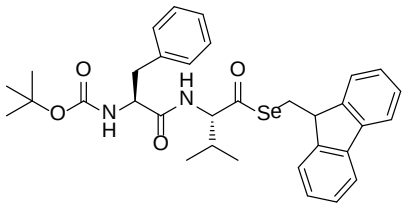
To a solution of Boc-Val-OH (81 mg, 0.375 mmol, 1.3 equiv.) in DMF (2 mL) were added HBTU (142 mg, 0.375 mmol, 1.3 equiv.) and dropwise DIEA (0.121 mL, 0.692 mmol, 2.4 equiv). The resulting solution was stirred for 20 min at room temperature. Then, a solution of TFA.H-D-Phe-SeFm **9** (150 mg, 0.288 mmol, 1 equiv) in DMF (0.5 mL) was added. After stirring overnight at room temperature, DMF was removed under high vacuum. A flash purification (Heptane/EtOAc: 9/1) of the crude gave Boc-Val-D-Phe-SeFm **14** (141 mg, 81%) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.74 (d, *J* = 6.9 Hz, 3H); 0.78 (br s, 3H); 1.42 (s, 9H); 1.98-2.11 (m, 1H); 2.78 (dd, *J* = 14.2, 8.6 Hz, 1H); 3.01 (dd, *J* = 14.2, 5.6 Hz, 1H); 3.56 (dd, *J* = 12.2, 5.3 Hz, 1H); 3.63 (dd, *J* = 12.2, 5.3 Hz, 1H); 3.85 (dd, *J* = 9.0, 5.9 Hz, 1H); 4.29 (t, *J* = 5.4 Hz, 1H); 4.80 (dt, *J* = 8.2, 5.2 Hz, 1H); 4.89 (d, *J* = 8.3 Hz, 1H); 6.24 (d, *J* = 8.0 Hz, 1H); 7.02-7.05 (m, 2H); 7.21-7.30 (m, 3H); 7.33 (tt, *J* = 7.4, 1.4, Hz, 2H); 7.41 (t, *J* = 7.4 Hz, 2H); 7.60 (d, *J* = 7.1 Hz, 1H); 7.62 (d, *J* = 7.3 Hz, 1H); 7.76 (d, *J* =7.5 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.6 (CH_3); 19.3 (CH_3); 28.5 (3 CH_3); 28.7 (CH_2); 30.5 (CH); 37.8 (CH_2); 47.2 (CH); 60.0 (CH); 62.5 (CH); 80.3 (Cq); 120.0 (CH); 120.1 (CH); 124.7 (CH); 124.9 (CH); 127.2 (CH); 127.3 (CH); 127.4 (CH); 127.9 (2 CH); 129.0 (2 CH); 129.3 (2 CH); 135.4 (Cq); 141.26 (Cq); 141.33 (Cq); 146.0 (Cq); 146.2 (Cq); 156.0 (Cq); 172.0 (Cq); 203.6 (Cq).

Mp = 175 °C. $[\alpha]^{25}_D$ = +23.4 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3324; 3287; 1699; 1664; 1521; 1164; 735. HRMS (ESI): *m/z* calcd $C_{33}H_{39}N_2O_4Se$ [M + H] 607.2075; found 607.2073.

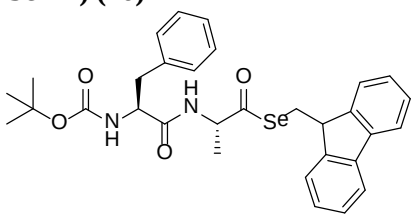
(*S*)-*Se*-((9*H*-fluoren-9-yl)methyl) 2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-phenylpropanamido)-3-methylbutaneselenoate (Boc-Phe-Val-SeFm) (15)



To a solution of Boc-Phe-OH (110 mg, 0.413 mmol, 1.3 equiv.) in DMF (2 mL) were added HBTU (157 mg, 0.413 mmol, 1.3 equiv.) and dropwise DIEA (0.133 mL, 0.762 mmol, 2.4 equiv). The resulting solution was stirred for 20 min at room temperature. Then, a solution of TFA.H-Val-SeFm

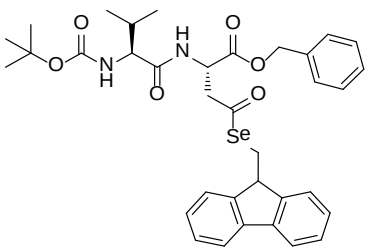
10 (150 mg, 0.318 mmol, 1 equiv) in DMF (0.5 mL) was added. After stirring overnight at room temperature, DMF was removed under high vacuum. A flash purification (Heptane/EtOAc: 9/1) of the crude gave Boc-Phe-Val-SeFm **15** (170 mg, 88%) as a white solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.61 (d, *J* = 7.0 Hz, 3H); 0.79 (d, *J* = 7.0 Hz, 3H); 1.41 (s, 9H); 2.09-2.21 (m, 1H); 3.05 (dd, *J* = 14.0, 6.7 Hz, 1H); 3.13 (dd, *J* = 14.0, 6.7 Hz, 1H); 3.53 (dd, *J* = 11.9, 5.3 Hz, 1H); 3.60 (dd, *J* = 11.9, 5.3 Hz, 1H); 4.28 (t, *J* = 5.3 Hz, 1H); 4.34 (q, *J* = 7.3 Hz, 1H); 4.44 (dd, *J* = 8.8, 4.6 Hz, 1H); 4.97 (br s, 1H); 6.53 (br s, 1H); 7.18-7.35 (m, 7H); 7.38 (t, *J* = 7.0 Hz, 1H); 7.40 (t, *J* = 7.0 Hz, 1H); 7.59 (d, *J* = 6.8 Hz, 1H); 7.61 (d, *J* = 7.1 Hz, 1H); 7.73-7.76 (m, 2H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.5 (CH_3); 19.5 (CH_3); 28.36 (CH_2); 28.46 (3 CH_3); 30.8 (CH); 37.2 (CH_2); 47.2 (CH); 56.1 (CH); 66.7 (CH); 80.7 (Cq); 120.00 (CH); 120.04 (CH); 124.6 (CH); 124.7 (CH); 127.1 (CH); 127.22 (CH); 127.28 (CH); 127.8 (2 CH); 128.9 (2 CH); 129.5 (2 CH); 136.7 (Cq); 141.3 (2 Cq); 146.0 (Cq); 146.2 (Cq); 155.9 (Cq); 172.0 (Cq); 203.5 (Cq).
Mp = 144 °C. $[\alpha]^{25}_D$ = -41.1 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3320; 1668; 1656; 1520; 1167; 741; 733. HRMS (ESI): *m/z* calcd $C_{33}H_{39}N_2O_4Se$ [M + H] 607.2075; found 607.2082.

(*S*)-*Se*-((9*H*-fluoren-9-yl)methyl) 2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-phenylpropanamido) propaneselenoate (Boc-Phe-Ala-SeFm) (16)



To a solution of Boc-Phe-OH (116 mg, 0.439 mmol, 1.3 equiv.) in DMF (2 mL) were added HBTU (166 mg, 0.439 mmol, 1.3 equiv.) and dropwise DIEA (0.142 mL, 0.810 mmol, 2.4 equiv). The resulting solution was stirred for 20 min at room temperature. Then, a solution of TFA.H-Ala-SeFm **11** (150 mg, 0.338 mmol, 1 equiv) in DMF (0.5 mL) was added. After stirring overnight at room temperature, DMF was removed under high vacuum. A flash purification (Heptane/EtOAc: 9/1) of the crude gave Boc-Phe-Val-SeFm **16** (154 mg, 79%) as a white solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.10 (d, *J* = 7.1 Hz, 3H); 1.38 (s, 9H); 3.01 (dd, *J* = 14.0, 7.3 Hz, 1H); 3.09 (dd, *J* = 14.0, 6.4 Hz, 1H); 3.50-3.61 (m, 2H); 4.27 (t, *J* = 5.4 Hz, 1H); 4.34 (q, *J* = 7.2 Hz, 1H); 4.44-4.54 (m, 1H); 4.93 (br s, 1H) ; 6.45 (br s, 1H); 7.16-7.33 (m, 7H); 7.38 (t, *J* = 7.4 Hz, 2H); 7.57 (d, J = 7.3 Hz, 1H); 7.59 (d, *J* = 7.5 Hz, 1H); 7.73 (d, *J* = 7.5 Hz, 2H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.1 (CH_3); 28.4 (3 CH_3 + CH_2); 37.8 (CH_2); 47.2 (CH); 55.8 (CH); 58.1 (CH); 80.6 (Cq); 120.0 (CH); 120.03 (CH); 124.66 (CH); 124.74 (CH); 127.2 (2 CH); 127.3 (CH); 127.8 (2 CH); 128.9 (2 CH); 129.5 (2 CH); 136.6 (Cq); 141.3 (2 Cq); 146.01 (Cq); 146.15 (Cq); 155.6 (Cq); 171.5 (Cq); 203.9 (Cq).
Mp = 97 °C. $[\alpha]^{25}_D$ = -21.0 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3283; 1693; 1656; 1525; 1164; 737. HRMS (ESI): *m/z* calcd $C_{31}H_{35}N_2O_4Se$ [M + H] 579.1762; found 579.1767.

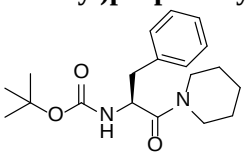
(*S*)-benzyl 4-(((9*H*-fluoren-9-yl)methyl)selanyl)-2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methyl butanamido)-4-oxobutanoate (Boc-Val-Asp(γSeFm)-OBn (17)



To a solution of Boc-Val-OH (73.2 mg, 0.337 mmol, 1.3 equiv.) in DMF (2 mL) were added HBTU (128 mg, 0.337 mmol, 1.3 equiv.) and dropwise DIEA (0.109 mL, 0.622 mmol, 2.4 equiv). The resulting solution was stirred for 20 min at room temperature. Then, a solution of TFA.H-Asp(γSeFm)-OBn **12** (150 mg, 0.259 mmol, 1 equiv) in DMF (0.5 mL) was added. After stirring

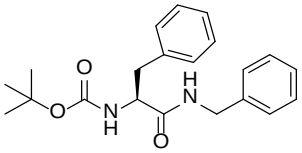
overnight at room temperature, DMF was removed under high vacuum. A flash purification (Heptane/EtOAc: 9/1) of the crude gave Boc-Val-Asp(γSeFm)-OBn **17** (121 mg, 70%) as white solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.85 (d, *J* = 7.0 Hz, 3H); 0.96 (d, *J* = 7.0 Hz, 3H); 1.47 (s, 9H); 2.07-2.18 (m, 1H); 3.09 (dd, *J* = 16.6, 4.7 Hz, 1H); 3.27 (dd, *J* = 17.0, 4.7 Hz, 1H); 3.59 (d, *J* = 5.4 Hz, 2H); 3.99 (dd, *J* = 7.6, 5.1 Hz, 1H); 4.27 (t, *J* = 5.4 Hz, 1H); 4.76 (dt, *J* = 8.0, 4.3 Hz, 1H); 5.03 (d, *J* = 8.3 Hz, 1H); 5.11 (d, *J* = 11.9 Hz, 1H); 5.17 (d, *J* = 11.9 Hz, 1H); 6.65 (d, *J* = 7.6 Hz, 1H); 7.28-7.37 (m, 7H); 7.40 (t, *J* = 7.4 Hz, 1H); 7.43 (t, *J* = 7.6 Hz, 1H); 7.59 (t, *J* = 6.4 Hz, 1H); 7.62 (t, *J* = 6.9 Hz, 1H); 7.75 (d, *J* = 7.2 Hz, 1H); 7.76 (d, *J* = 7.4 Hz, 1H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.6 (CH_3); 19.3 (CH_3); 28.5 (3 CH_3); 29.1 (CH_2); 31.4 (CH); 47.1 (CH); 49.0 (CH); 49.1 (CH_2); 59.7 (CH); 68.0 (CH_2); 80.1 (Cq); 120.1 (2 CH); 124.6 (CH); 124.7 (CH); 127.29 (CH); 127.32 (CH); 128.0 (2 CH); 128.68 (2 CH); 128.73 (CH); 128.77 (2 CH); 135.1 (Cq); 141.24 (Cq); 141.27 (Cq); 146.0 (2 Cq); 155.9 (Cq); 170.0 (Cq); 171.4 (Cq); 199.4 (Cq).
Mp = 154 °C. $[\alpha]^{25}_D$ = +19.1 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3331; 1734; 1694; 1651; 1518; 1276; 1186; 740. HRMS (ESI): *m/z* calcd $C_{35}H_{41}N_2O_6Se$ [M + H] 665.2130; found 665.2125.

(*S*)-*tert*-butyl (1-oxo-3-phenyl-1-(piperidin-1-yl)propan-2-yl)carbamate (18)[2,3]



To a solution of Boc-Phe-SeFm **3** (100 mg, 0.197 mmol) in DMF (1 mL) was added piperidine (0.2 mL). The mixture was stirred at room temperature for 1 h, diluted with EtOAc and hydrolyzed with a saturated aqueous NH_4Cl solution. After filtration through a pas of celite, the organic layer was dried over Na_2SO_4 and concentrated in vacuum. A flash chromatography (Heptane/EtOAc: 95/5 to 8/2) of the crude furnished amide **18** (45.9 mg, 70%) as a colorless oil.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.87-0.97 (m, 1H); 1.34 (s, 9H); 1.39-1.49 (m, 5H); 2.88 (d, *J* = 7.0 Hz, 2H); 2.88-2.98 (m, 1H); 3.12-3.21 (m, 1H); 3.41 (dd, *J* = 5.4, 3.8 Hz, 2H); 4.78 (q, *J* = 7.8 Hz, 1H); 5.39 (br d, *J* = 8.4 Hz, 1H); 7.11-7.23 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 24.5 (CH_2); 25.3 (CH_2); 25.9 (CH_2); 28.3 (3 CH_3); 40.3 (CH_2); 43.0 (CH_2); 46.6 (CH_2); 50.9 (CH); 79.5 (Cq); 126.80 (CH); 128.4 (2 CH); 129.6 (2 CH); 136.6 (Cq); 155.0 (Cq); 169.7 (Cq).
$[\alpha]^{25}_D$ = +22.6 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3290; 1702; 1630; 1447; 1166. HRMS (ESI): *m/z* calcd $C_{19}H_{29}N_2O_3$ [M + H] 333.2178; found 333.2181.

(*S*)-*tert*-butyl (1-(benzylamino)-1-oxo-3-phenylpropan-2-yl)carbamate (19)[4,5]



From Benzylamine

To a solution of Boc-Phe-SeFm **3** (100 mg, 0.197 mmol) in DMF (1.5 mL) was added benzylamine (54 µL, 0.494 mmol, 2.5 equiv.). The resulting mixture was stirred overnight at room temperature. EtOAc was added and the solution was filtered through celite, which was washed with EtOAc. The

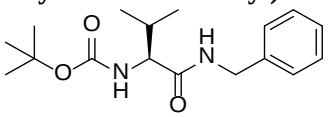
[2] Richmond, M. L.; Seto, C. T. *J. Org. Chem.* **2003**, *68*, 7505-7508.
[3] Ribeiro, L.; Silva, N.; Iley, J.; Rautio, J.; Järvinen, J.; Mota-Filipe, H.; Moreira, R.; Mendes, E. *Arch. Pharm. Chem. Life Sci.* **2007**, *340*, 32-40.
[4] Hagiwara, D.; Miyake, H.; Morimoto, H.; Murai, M.; Fujii, T.; Matsuo, M. *J. Med. Chem.* **1992**, *35*, 3184-3191.
[5] Saito, Y.; Ouchi, H.; Takahata, H. *Tetrahedron* **2008**, *64*, 11129-11135.

filtrate was evaporated in vacuum. The crude was purified by flash chromatography (Heptane/EtOAc: 9/1 to 8/2) to give **19** (61 mg, 87%) as white solid.

From Benzylazide

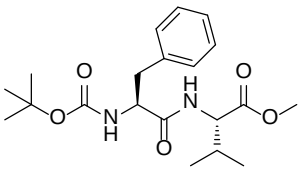
To a solution of Boc-Phe-SeFm **3** (200 mg, 0.395 mmol) in DMF (2 mL) was added added DBU (63 µL, 0.421 mmol, 1.07 equiv.). After stirring for 3 min at room temperature, benzylazide (71 mg, 0.534 mmol, 1.35 equiv.) was added. The resulting solution was stirred overnight at room temperature. EtOAc was added and the solution was filtered through celite, which was washed with EtOAc. The filtrate was evaporated in vacuum. The crude was purified by flash chromatography (Heptane/EtOAc: 9/1 to 8/2) to give **19** (37 mg, 26%) as a white solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.39 (s, 9H); 3.02-3.15 (m, 2H); 4.30-4.41 (m, 1H); 4.35 (d, *J* = 5.5 Hz, 2H); 5.11 (br s, 1H); 6.20 (br t, *J* = 5.4 Hz, 1H); 7.10 (d, *J* = 5.6 Hz, 2H); 7.18-7.31 (m, 7H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 28.4 (3 CH_3); 38.8 (CH_2); 43.6 (CH_2); 56.2 (CH); 80.4 (Cq); 127.1 (CH); 127.6 (CH); 127.8 (2 CH); 128.8 (2 CH); 128.9 (2 CH); 129.5 (2 CH); 136.9 (Cq); 137.9 (Cq); 155.6 (Cq); 171.3 (Cq).
mp = 127 °C. $[\alpha]^{25}_D$ = +3.5 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3338; 3304; 1676; 1658; 1520; 1169; 694. HRMS (ESI): *m/z* calcd $C_{21}H_{27}N_2O_3$ [M + H] 355.2022; found 355.2023.

(*S*)-*tert*-butyl (1-(benzylamino)-3-methyl-1-oxobutan-2-yl)carbamate (20)[6,7]



To a solution of Boc-Val-SeFm **5** (100 mg, 0.218 mg) in DMF (1.5 mL) was added benzylamine (60 µL, 0.545 mmol, 2.5 equiv.). The resulting mixture was stirred overnight at room temperature. EtOAc was added and the solution was filtered through celite, which was washed with EtOAc. The filtrate was evaporated in vacuum. The crude was purified by flash chromatography (Heptane/EtOAc: 9/1 to 8/2) to give **20** (48 mg, 72%) as a white solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.93 (d, *J* = 6.9 Hz, 3H); 0.97 (d, *J* = 6.9 Hz, 3H); 1.42 (s, 9H); 2.12-2.23 (m, 1H); 3.94 (dd, *J* = 9.0, 6.0 Hz, 1H); 4.41 (dd, *J* = 15.0, 5.9 Hz, 1H); 4.48 (dd, *J* = 15.0, 5.9 Hz, 2H); 5.12 (br d, *J* = 6.4 Hz, 1H); 6.47 (t, *J* = 5.0 Hz, 1H); 7.24-7.35 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.0 (CH_3); 19.6 (CH_3); 28.5 (3 CH_3); 30.9 (CH); 43.6 (CH_2); 60.4 (CH); 80.1 (Cq); 127.7 (CH); 127.9 (2 CH); 128.9 (2 CH); 138.2 (Cq); 156.1 (Cq); 171.8 (Cq).
Mp = 117 °C. $[\alpha]^{25}_D$ = -9.6 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3307; 1683; 1646; 1520; 1244; 1162. HRMS (ESI): *m/z* calcd $C_{17}H_{27}N_2O_3$ [M + H] 307.2022; found 307.2018.

(*S*)-methyl 2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-phenylpropanamido)-3-methylbutanoate (Boc-Phe-Val-OMe) (25)[8]

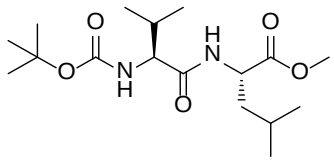


To a solution of HCl.H-Val-OMe (39.7 mg, 0.237 mmol, 1.2 equiv) in DMF (0.5 mL) was added Et_3N (36 µL, 0.257 mmol, 1.3 equiv.) and the mixture was stirred for 10 min to obtain a solution of H-Val-OMe.
To a solution of Boc-Phe-SeFm **3** (100 mg, 0.197 mmol, 1 equiv.) in a degassed DMF (1.5 mL) was added DBU (36 µL, 0.237 mmol, 1.2 equiv). The resulting solution was stirred for 2-3 min. Then, the previous prepared solution of H-Val-OMe in DMF was added. After stirring overnight at room

[6] Figlus, M.; Tarruella, A. C.; Messer, A.; Sollis, S. L. ; Hartley, R. C. *Chem. Commun.*, **2010**, *46*, 4405-4407.
[7] Ramalingam, B.; Neuburger, M.; Pfaltz, A. *Synthesis*, **2007**, 572-582.
[8] Suaifan, G. A.R. Y.; Arafat, T.; Threadgill, M. D. *Bioorg. Med. Chem.* **2007**, *15*, 3474-3488.

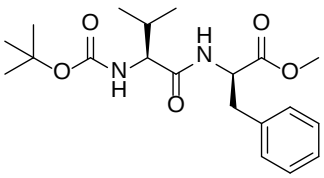
temperature, the solution was filtered through celite, which was washed with EtOAc and concentrated in vacuum. The crude was purified by flash chromatography (Heptane/EtOAc: 8/2 to 7/3) to furnish Boc-Phe-Val-OMe **25** (48 mg, 64%) as a yellowish solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.85 (d, J = 7.0 Hz, 3H); 0.89 (d, J = 6.8 Hz, 3H); 1.43 (s, 9H); 2.04-2.20 (m, 1H); 309 (d, J = 7.0 Hz, 2H); 3.71 (s, 3H); 4.37 (q, J = 6.9 Hz, 1H); 4.48 (dd, J = 8.5, 4.9 Hz, 1H); 5.04 (br s, 1H); 6.38 (d, J = 8.5 Hz, 1H); 7.22-7.34 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.9 (CH_3); 19.0 (CH_3); 28.4 (3 CH_3); 31.5 (CH); 38.2 (CH_2); 52.3 (CH_3); 56.1 (CH); 57.4 (CH); 80.4 (Cq); 127.1 (CH); 128.9 (2 CH); 129.5 (2 CH); 136.8 (Cq); 155.6 (Cq); 171.3 (Cq); 172.0 (Cq).
Mp = 116 °C. $[\alpha]^{25}_D$ = -7.1 (*c* 1.02, $CHCl_3$). IR υ_{max} (cm^{-1}): 3291; 1741; 1680; 1654; 1528; 1253; 1167; 1145; 1018; 694. HRMS (ESI): *m/z* calcd $C_{20}H_{31}N_2O_5$ [M + H] 379.2233; found 379.2228.

(*S*)-methyl 2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methylbutanamido)-4-methylpentanoate (Boc-Val-Leu-OMe) (26)[9]



To a solution of HCl.H-Leu-OMe (47.5 mg, 0.262 mmol, 1.2 equiv) in DMF (0.5 mL) was added Et_3N (40 µL, 0.284 mmol, 1.3 equiv.) and the mixture was stirred for 10 min to obtain a solution of H-Leu-OMe.
To a solution of Boc-Val-SeFm **5** (100 mg, 0.218 mmol, 1 equiv.) in a degassed DMF (1.5 mL) was added DBU (39 µL, 0.262 mmol, 1.2 equiv). The resulting solution was stirred for 2-3 min. Then, the previous prepared solution of H-Leu-OMe in DMF was added. After stirring overnight at room temperature, the solution was filtered through celite, which was washed with EtOAc and concentrated in vacuum. The crude was purified by flash chromatography (Heptane/EtOAc: 8/2 to 7/3) to furnish Boc-Val-Leu-OMe **26** (42 mg, 56%) as a white solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.90 (d, J = 6.1 Hz, 9H); 0.94 (d, J = 6.7 Hz, 3H); 1.42 (s, 9H); 1.49-1.67 (m, 3H); 2.03-2.14 (m, 1H); 3.70 (s, 3H); 3.85 (dd, J = 6.5, 8.8 Hz, 1H); 4.60 (td, J = 6.2, 8.8 Hz, 1H); 5.03 (br d, J = 8.3 Hz, , 1H); 6.22 (br d, J = 8.3 Hz, 1H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.1 (CH_3); 19.4 (CH_3); 21.0 (CH_3); 23.0 (CH_3); 25.0 (CH); 28.5 (3 CH_3); 31.0 (CH); 41.7 (CH_2); 50.8 (CH); 52.5 (CH_3); 60.2 (CH); 80.1 (Cq); 156.0 (Cq); 171.6 (Cq); 173.3 (Cq).
Mp = 130 °C. $[\alpha]^{25}_D$ = -23.0 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3324; 3266; 1753; 1685; 1649; 1520; 1246; 1159. HRMS (ESI): *m/z* calcd $C_{17}H_{32}N_2NaO_5$ [M + Na] 367.2209; found 367.2208.

(*R*)-methyl 2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methylbutanamido)-3-phenylpropanoate (Boc-Val-D-Phe-OMe) (27)[10]

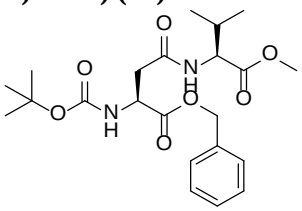


To a solution of HCl.H-D-Phe-OMe (56.5 mg, 0.262 mmol, 1.2 equiv) in DMF (0.5 mL) was added Et_3N (40 µL, 0.284 mmol, 1.3 equiv.) and the mixture was stirred for 10 min to obtain a solution of H-D-Phe-OMe.
To a solution of Boc-Val-SeFm **5** (100 mg, 0.218 mmol, 1 equiv.) in a degassed DMF (1.5 mL) was added DBU (39 µL, 0.262 mmol, 1.2 equiv). The resulting solution was stirred for 2-3 min. Then, the previous prepared solution of H-D-Phe-OMe in DMF was added. After stirring overnight at room temperature, the solution was filtered through celite, which was washed with EtOAc and concentrated

[9] Declerck, A.; Nun, P.; Martinez, J.; Lamaty, F. *Angew. Chem. Int. Ed.* **2009**, *48*, 9318-9321.
[10] Crich, D.; Sana, K.; Guo, S. *Org. Lett.*, **2007**, *9*, 4423-4426.

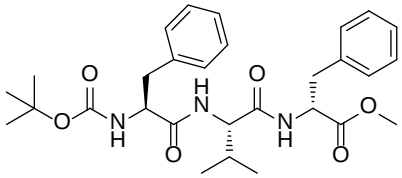
in vacuum. The crude was purified by flash chromatography (Heptane/EtOAc: 8/2 to 7/3) to furnish Boc-Val-D-Phe-OMe **27** (53 mg, 64%) as a white solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.80 (d, J = 6.8 Hz, 3H); 0.88 (d, J = 6.6 Hz, 3H); 1.43 (s, 9H); 2.05-2.19 (m, 1H); 3.04-3.17 (m, 1H); 3.71 (s, 3H); 3.98 (dd, J = 6.4, 5.8 Hz, 1H); 4.89 (q, J = 7.0 Hz, 1H); 4.96 (br d, J = 7.0 Hz, 1H); 6.43 (br d, J = 7.0 Hz, 1H); 7.11 (d, J = 7.0 Hz, 2H); 7.23-7.31 (m, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.3 (CH_3); 19.5 (CH_3); 28.5 (3 CH_3); 30.8 (CH); 38.2 (CH_2); 52.5 (CH_3); 53.2 (CH); 59.8 (CH); 80.1 (Cq); 127.4 (CH); 128.9 (2 CH); 129.4 (2 CH); 135.9 (Cq); 156.0 (Cq); 171.4 (Cq); 172.0 (Cq).
Mp = 174 °C. $[\alpha]^{25}_D$ = 39.6 (*c* 1.02, $CHCl_3$). IR υ_{max} (cm^{-1}): 3314; 1728; 1683; 1648; 1522; 1242; 1162; 696. HRMS (ESI): *m/z* calcd $C_{20}H_{31}N_2O_5$ [M + H] 379.2233; found 379.2241.

(*S*)-benzyl 2-((*tert*-butoxycarbonyl)amino)-4-(((*S*)-1-methoxy-3-methyl-1-oxobutan-2-yl)amino)-4-oxobutanoate (Boc-Asp-(γ-Val-OMe)-OBn) (28)[11]



To a solution of HCl.H-Val-OMe (35.6 mg, 0.213 mmol, 1.2 equiv) in DMF (0.5 mL) was added Et_3N (35 µL, 0.248 mmol, 1.4 equiv.) and the mixture was stirred for 10 min to obtain a solution of H-Val-OMe.
To a solution of Boc-Asp(γSeFm)-OBn **7** (100 mg, 0.177 mmol, 1 equiv.) in a degassed DMF (1 mL) was added DBU (32 µL, 0.213 mmol, 1.2 equiv). The resulting solution was stirred for 2-3 min. Then, the previous prepared solution of H-Val-OMe in DMF was added. After stirring overnight at room temperature, the solution was filtered through celite, which was washed with EtOAc and concentrated in vacuum. The crude was purified by flash chromatography (Heptane/EtOAc: 8/2) to furnish Boc-Asp-(γ-Val-OMe)-OBn **28** (60 mg, 78%) as a yellowish solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.79 (d, J = 6.0 Hz, 3H); 0.81 (d, J = 6.6 Hz, 3H); 1.34 (s, 9H); 1.98-2.09 (m, 1H); 2.68 (dd, J = 15.7, 4.2 Hz, 1H); 2.91 (dd, J = 16.0, 4.0 Hz, 1H); 3.66 (s, 3H); 4.44 (dd, J = 8.7, 4.7 Hz, 1H); 4.46-4.53 (m, 1H); 5.09 (s, 2H); 5.71 (d, J = 8.0 Hz, 1H); 6.08 (d, J = 8.6 Hz, 1H); 7.22-7.28 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.9 (CH_3); 19.0 (CH_3); 28.5 (3 CH_3); 31.5 (CH); 38.0 (CH_2); 50.7 (CH); 52.4 (CH_3); 57.3 (CH); 67.5 (CH_2); 80.1 (Cq); 128.3 (2 CH); 128.4 (CH); 128.7 (2 CH); 135.6 (Cq); 155.8 (Cq); 170.0 (Cq); 171.5 (Cq); 172.4 (Cq).
Mp = 95 °C. $[\alpha]^{25}_D$ = +13.3 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3382; 1750; 1714; 1697; 1510; 1338; 1166; 738; 727. HRMS (ESI): *m/z* calcd $C_{22}H_{33}N_2O_7$ [M + H] 437.2288; found 437.2277.

(6*S*, 9*S*, 12*R*)-methyl 6,12-dibenzyl-9-isopropyl-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (Boc-Phe-Val-D-Phe-OMe) (29)

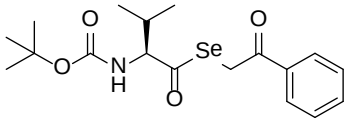


To a solution of HCl.H-D-Phe-OMe (42.7 mg, 0.198 mmol, 1.2 equiv.) in DMF (0.5 mL) was added Et_3N (30 mL, 0.215 mmol, 1.3 equiv.) and the mixture was stirred for 10 min to obtain a solution of H-D-Phe-OMe in DMF.
To a solution of Boc-Phe-Val-SeFm **15** (100 mg, 0.165 mmol, 1 equiv.) in a degassed DMF (1 mL) was added DBU (30 µL, 0.198 mmol, 1.2 equiv.). The resulting solution was stirred for 2-3 min. Then, the previous prepared solution of H-D-Phe-OMe in DMF was added. After stirring overnight at room temperature, the solution was filtered through celite, which was washed with EtOAc and concentrated

[11] Kumar, A.; Singh, M.; Chauhan, V.S. *J. Antibiot.* **1985**, *38*, 1420-1422.

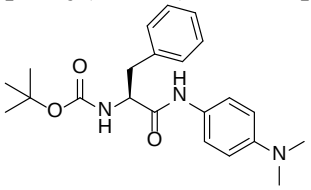
in vacuum. The crude was purified by flash chromatography (Heptane/EtOAc: 8/2 to 7/3) to furnish tripeptide Boc-Phe-Val-D-Phe-OMe **29** as a white solid (51 mg, 59 %).
^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.77 (d, *J* = 6.8 Hz, 3H); 0.81 (d, *J* = 6.8 Hz, 3H); 1.42 (s, 9H); 2.06-2.19 (m, 1H); 3.05 (dd, *J* = 13.7, 7.4 Hz, 1H); 3.07 (d, *J* = 7.5 Hz, 2H); 3.16 (dd, *J* = 13.7, 5.8 Hz, 1H); 3.71 (s, 3H); 4.27 (dd, *J* = 8.5, 5.4 Hz, 1H); 4.34 (q, *J* = 6.7 Hz, 1H); 4.84 (q, *J* = 7.0 Hz, 1H); 5.05 (br d, *J* = 6.4 Hz, 1H); 6.50 (br d, *J* = 8.9 Hz, 1H); 6.71 (br d, *J* = 7.0 Hz, 1H); 7.13-7.33 (m, 10H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.4 (CH_3); 19.4 (CH_3); 28.4 (3 CH_3); 30.7 (CH); 37.9 (CH_2); 38.1 (CH_2); 52.5 (CH_3); 53.6 (CH); 56.2 (CH); 58.4 (CH); 80.8 (Cq); 127.2 (CH); 127.3 (CH); 128.8 (2 CH); 129.0 (2 CH); 129.38 (2 CH); 129.43 (2 CH); 136.2 (Cq); 136.6 (Cq); 155.9 (Cq); 170.6 (Cq); 171.4 (Cq); 172.0 (Cq).
Mp = 173 °C. $[\alpha]^{25}_D$ = -35.1 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3287; 1736; 1690; 1639; 1520; 1220; 1249; 1167; 698. HRMS (ESI): *m/z* calcd $C_{29}H_{40}N_3O_6$ [M + H] 526.2917; found 526.2915.

(*S*)-*Se*-(2-oxo-2-phenylethyl) 2-((*tert*-butoxycarbonyl)amino)-3-methylbutaneselenoate (30)



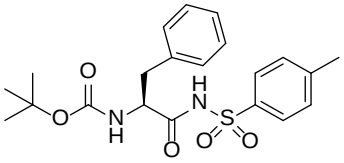
To a solution of Boc-Val-SeFm **5** (100 mg, 0.218 mmol) in degassed DMF (1.5 mL) was added DBU (39 µL, 0.262 mmol, 1.2 equiv.). The resulting solution was stirred for 2-3 min. Then, 2-bromoacetophenone (52 mg, 0.262 mmol, 1.2 equiv.) was added. After stirring overnight at room temperature, the solution was filtered through celite, which was washed with EtOAc and concentrated in vacuum. The crude was purified by flash chromatography (Heptane/EtOAc: 9/1) to furnish **30** (74 mg, 85%) as a white solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.84 (d, *J* = 7.0 Hz, 3H); 0.96 (d, *J* = 7.0 Hz, 3H); 1.45 (s, 9H); 2.26-2.37 (m, 1H); 4.18-4.25 (m, 2H); 4.34 (d, *J* = 13.4 Hz, 1H); 4.94 (d, *J* = 9.7 Hz, 1H); 7.43 (t, *J* = 7.5 Hz, 2H); 7.52-7.58 (m, 1H); 7.95 (d, *J* = 6.8 Hz, 2H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.9 (CH_3); 19.6 (CH_3); 28.5 (3 CH_3); 30.7 (CH); 31.0 (CH_2); 68.0 (CH); 81.1 (Cq); 128.9 (4 CH); 133.7 (CH); 135.7 (Cq); 155.7 (Cq); 195.8 (Cq); 204.6 (Cq).
Mp = 104 °C. $[\alpha]^{25}_D$ = -1.4 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3338; 1717; 1683; 1668; 1505; 1271; 1154; 1055; 1009; 710; 663. HRMS (ESI): *m/z* calcd $C_{18}H_{25}NNaO_4Se$ [M + Na] 422.0846; found 422.0854.

(*S*)-*tert*-butyl (1-((4-(dimethylamino)phenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (31)



To a solution of Boc-Phe-SeFm **3** (150 mg, 0.296 mmol) in degassed DMF (2 mL) was added DBU (54 µL, 0.355 mmol, 1.2 equiv.). The resulting solution was stirred for 2-3 min. Then, 4-azido-*N*,*N*-dimethylaniline (57.6 mg, 0.355 mmol, 1.2 equiv.) was stirred. After stirring overnight at room temperature, the solution was filtered through celite, which was washed with EtOAc and concentrated in vacuum. The crude was purified by flash chromatography (Heptane/EtOAc: 8/2) to furnish amide **31** (49 mg, 43%) as a yellow solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.45 (s, 9H); 2.93 (s, 6H); 3.08-3.22 (m, 2H); 4.44 (q, *J* = 6.8 Hz, 1H); 5.19 (br s, 1H); 6.69 (d, *J* = 9.0 Hz, 2H); 7.21 (d, *J* = 9.0 Hz, 2H); 7.26-7.36 (m, 6H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 28.5 (3 CH_3); 38.9 (CH_2); 41.2 (CH_2); 56.8 (CH); 80.6 (Cq); 113.4 (2 CH); 122.2 (2 CH); 127.2 (CH); 127.4 (CH); 129.0 (2 CH); 129.6 (2 CH); 137.0 (Cq); 148.1 (Cq); 155.8 (Cq); 169.2 (Cq).
Mp = 178 °C. $[\alpha]^{25}_D$ = -1.5 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3321; 3297; 1687; 1651; 1518; 1247; 1162; 703. HRMS (ESI): *m/z* calcd $C_{22}H_{30}N_3O_3$ [M + H] 384.2287; found 384.2250.

(*S*)-*tert*-butyl (1-(4-methylphenylsulfonamido)-1-oxo-3-phenylpropan-2-yl)carbamate (32) [12,13]



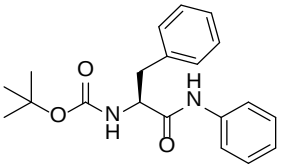
To a solution of Boc-Phe-SeFm **3** (100 mg, 0.197 mmol) in degassed DMF (1.5 mL) was added DBU (36 µL, 0.237 mmol, 1.2 equiv.). The resulting solution was stirred for 2-3 min. Then, *p*-toluenesulfonyl azide 15% w/w in toluene (0.346 mL, 0.237 mmol, 1.2 equiv.) was added. After stirring overnight at room temperature, the solution was filtered through celite, which was washed with EtOAc and concentrated in vacuum. The crude was purified by flash chromatography (CH_2Cl_2/MeOH: 10/1) to furnish **32** (54 mg, 65%, purity > 95%) as a white foam.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.40 (s, 9H); 2.48 (s, 3H); 2.97 (dd, *J* = 14.2, 7.6 Hz, 1H); 3.08 (dd, *J* = 13.9, 6.0 Hz, 1H); 4.29 (br s, 1H); 4.81 (d, *J* = 7.4 Hz, 1H); 7.06 (m, 2H); 7.25-7.28 (m, 3H); 7.36 (d, *J* = 8.4 Hz, 2H); 7.95 (d, *J* = 8.4 Hz, 2H); 9.15 (br s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.9 (CH_3); 28.3 (3 CH_3); 36.9 (CH_2); 56.2 (CH); 81.7 (Cq); 127.5 (CH); 128.8 (2 CH); 129.1 (2 CH); 129.4 (2 CH); 129.7 (2 CH); 135.6 (Cq); 145.3 (Cq); 156.0 (Cq); 169.5 (Cq).

IR υ_{max} (cm^{-1}): 3232; 1678; 1448; 1346; 1157; 1087; 812; 733; 699. HRMS (ESI): *m/z* calcd $C_{21}H_{26}N_2NaO_5S$ [M + Na] 441.1460; found 441.1449.

Synthesis of (*S*)-*tert*-butyl (1-oxo-3-phenyl-1-(phenylamino)propan-2-yl)carbamate (33)[14,15]



From phenyl isocyanate:

To a solution of Boc-Phe-SeFm **3** (100 mg, 0.197 mmol) in degassed DMF (1.5 mL) was added DBU (36 µL, 0.237 mmol, 1.2 equiv.). The resulting solution was stirred for 2-3 min. Then, phenyl isocyanate (26 µL, 0.237 mmol, 1.2 equiv.) was stirred. After stirring overnight at room temperature, the solution was filtered through celite, which was washed with EtOAc and concentrated in vacuum. The crude was purified by flash chromatography (Heptane/EtOAc: 7/3) to furnish **33** (32 mg, 48%) as a white solid.

From phenyl isothiocyanate:

To a solution of Boc-Phe-SeFm **3** (184 mg, 0.363 mmol) in degassed DMF (3 mL) was added DBU (66 µL, 0.436 mmol, 1.2 equiv.). The resulting solution was stirred for 2-3 min. Then, phenyl isothiocyanate (52 µL, 0.436 mmol, 1.2 equiv.) was stirred. After stirring overnight at room temperature, the solution was filtered through celite, which was washed with EtOAc and concentrated in vacuum. The crude was purified by flash chromatography (Heptane/EtOAc: 7/3) to furnish **33** (104 mg, 84%) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.38 (s, 9H); 3.04-3.20 (m, 2H); 4.61 (br s, 1H); 5.53 (d, *J* = 7.9 Hz, 1H); 7.05 (t, *J* = 7.1 Hz, 1H); 7.18-7.29 (m, 7H); 7.36 (d, *J* = 7.9 Hz, 2H); 8.42 (br s, 1H).

[12] Wu, X.; Chen, Y.; Hu, L. *Tetrahedron Lett.* **2009**, *50*, 5585-5588.

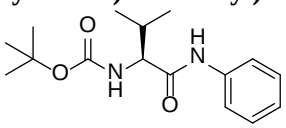
[13] Raz, R.; Rademann, J. *Org. Lett.* **2012**, *14*, 5038-5941.

[14] Pelagatti, P.; Calbiani, F.; Carcelli, M.; Cassi, C.; Eviri, L.; Pelizzi, C.; Rizzotti, U.; Rogolino, D. *Organometallics* **2005**, *24*, 5836-5844.

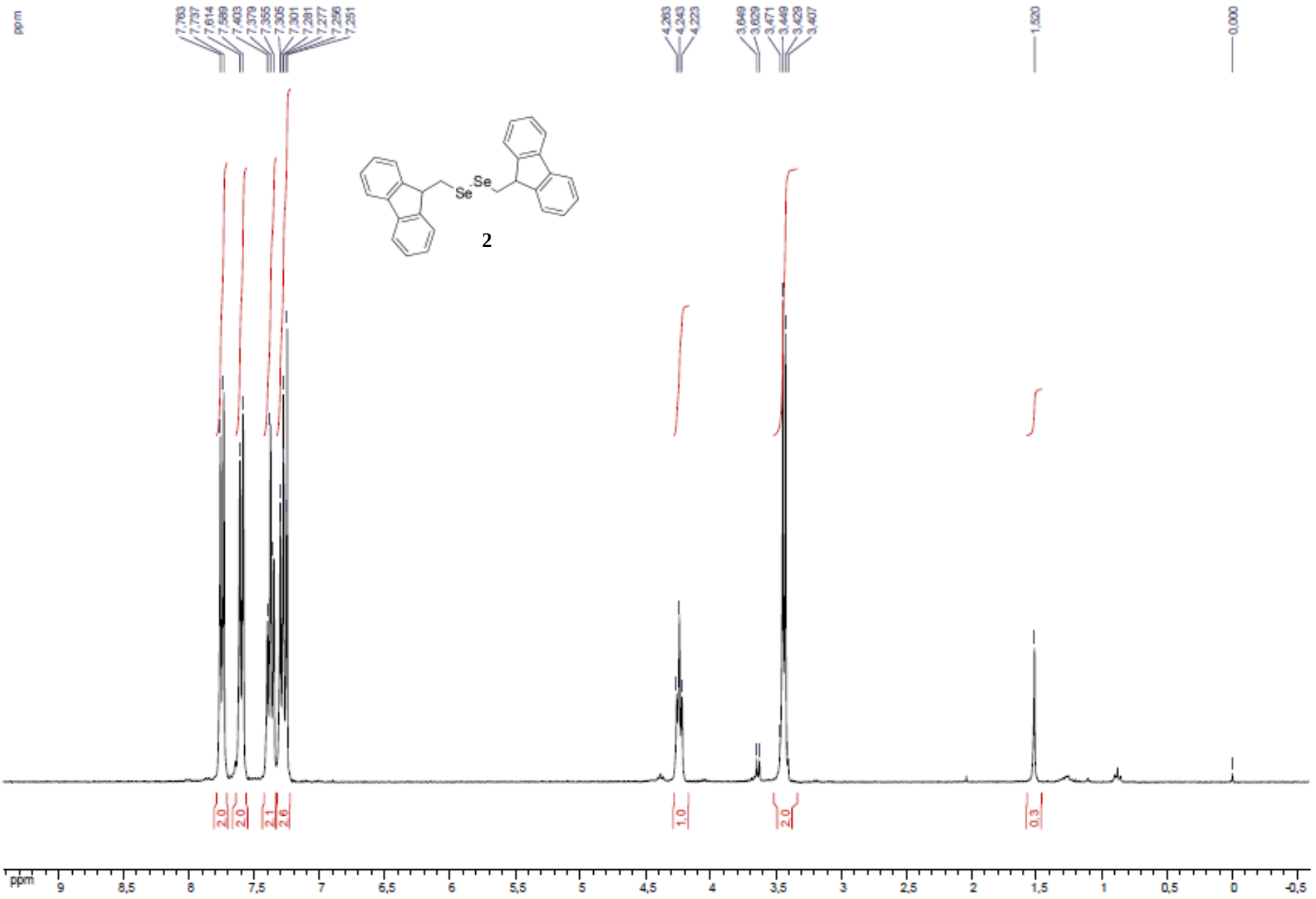
[15] Desai, A. A.; Wulff, W. D. *J. Am. Chem.* **2010**, *132*, 13100-13103.

^{13}C NMR (75 MHz, $CDCl_3$) δ: 28.4 (3 CH_3); 38.8 (CH_2); 56.9 (CH); 80.6 (Cq); 120.2 (2 CH); 124.5 (CH); 127.1 (CH); 128.8 (2 CH); 129.0 (2 CH); 129.5 (2 CH); 136.9 (Cq); 137.6 (Cq); 156.2 (Cq); 170.7 (Cq).
Mp = 125 °C. $[\alpha]^{25}_D$ = -13.0 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3283; 1659; 1533; 1496; 1442; 1246; 1162; 750; 691. HRMS (ESI): *m/z* calcd $C_{20}H_{25}N_2O_3$ [M + H] 341.1865; found 341.1857.

(*S*)-*tert*-butyl (3-methyl-1-oxo-1-(phenylamino)butan-2-yl)carbamate (34)[11]



To a solution of Boc-Val-SeFm **5** (100 mg, 0.218 mmol) in degassed DMF (1.5 mL) was added DBU (39 µL, 0.262 mmol, 1.2 equiv.). The resulting solution was stirred for 2-3 min. Then, phenyl isothiocyanate (31 µL, 0.262 mmol, 1.2 equiv.) was added. After stirring overnight at room temperature, the solution was filtered through celite, which was washed with EtOAc and concentrated in vacuum. The crude was purified by flash chromatography (Heptane/EtOAc: 7/3) to furnish **34** (55 mg, 86%) as a white solid.
^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.03 (d, *J* = 6.8 Hz, 3H); 1.07 (d, *J* = 6.8 Hz, 3H); 1.46 (s, 9H); 2.17-2.28 (m, 1H); 4.12 (t, *J* = 7.2 Hz, 1H); 5.42 (d, *J* = 8.5 Hz, 1H); 7.07 (t, *J* = 7.3 Hz, 1H); 7.25 (t, *J* = 7.5 Hz, 2H); 7.50 (d, *J* = 8.0 Hz, 2H); 8.51 (br s, 1H).
^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.4 (CH_3); 19.6 (CH_3); 28.5 (3 CH_3); 31.0 (CH); 61.2 (CH); 80.4 (Cq); 120.2 (2 CH); 124.5 (CH); 129.0 (2 CH); 137.8 (Cq); 156.6 (Cq); 170.7 (Cq).
Mp = 174 °C. $[\alpha]^{25}_D$ = -73.1 (*c* 1, $CHCl_3$). IR υ_{max} (cm^{-1}): 3307; 1683; 1646; 1520; 1244; 1162. HRMS (ESI): *m/z* calcd $C_{16}H_{25}N_2O_3$ [M + H] 293.1865; found 293.1870.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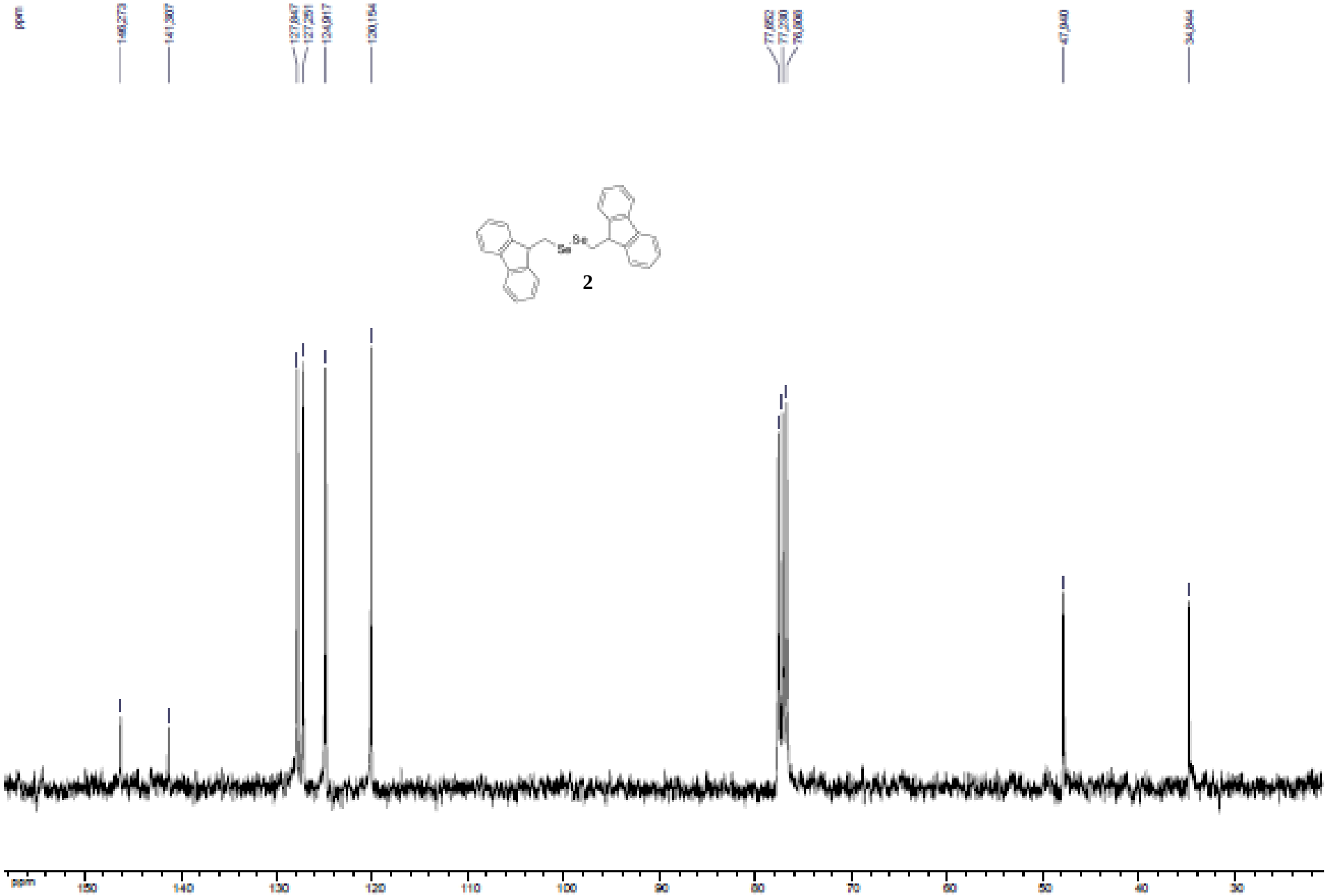
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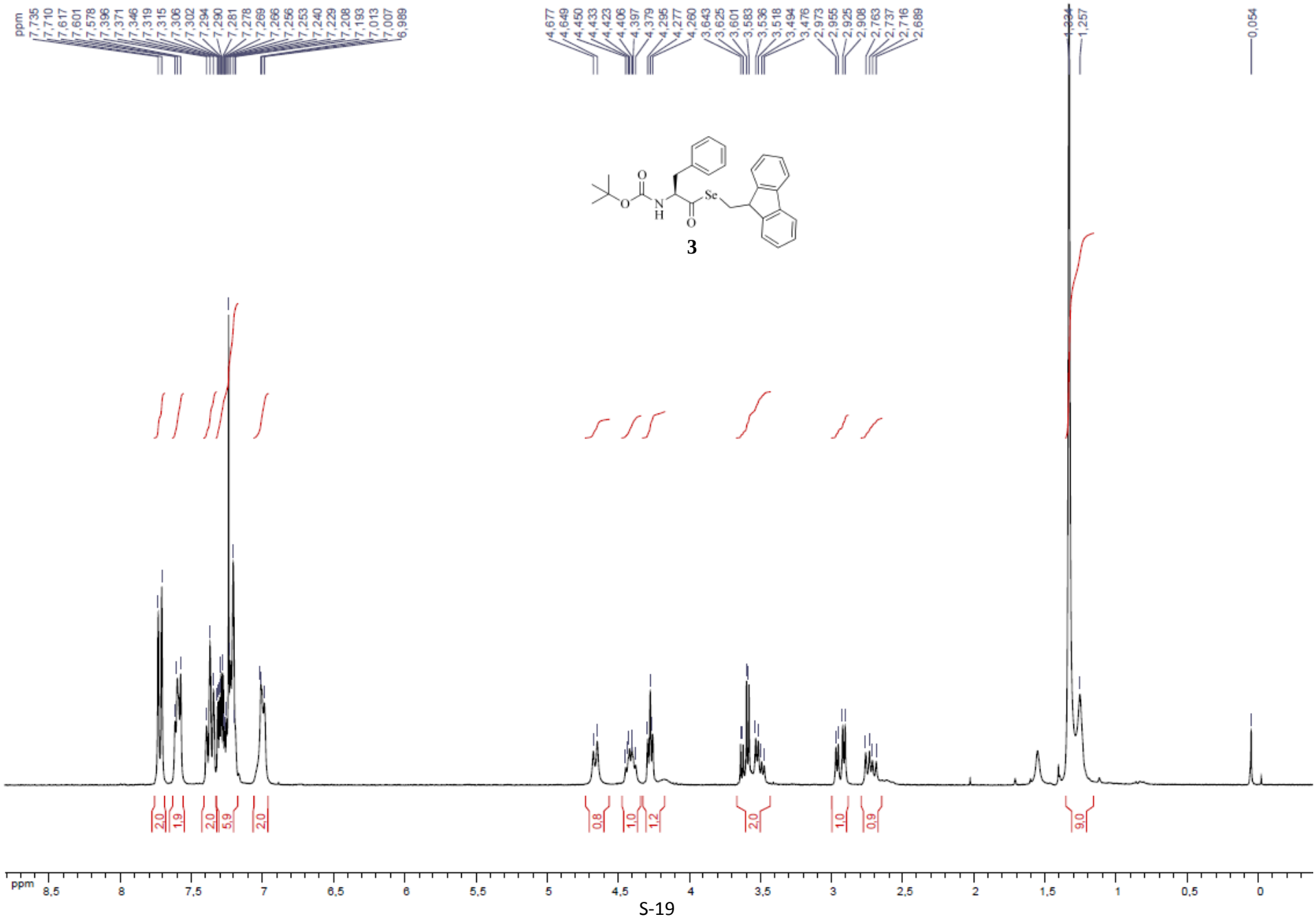
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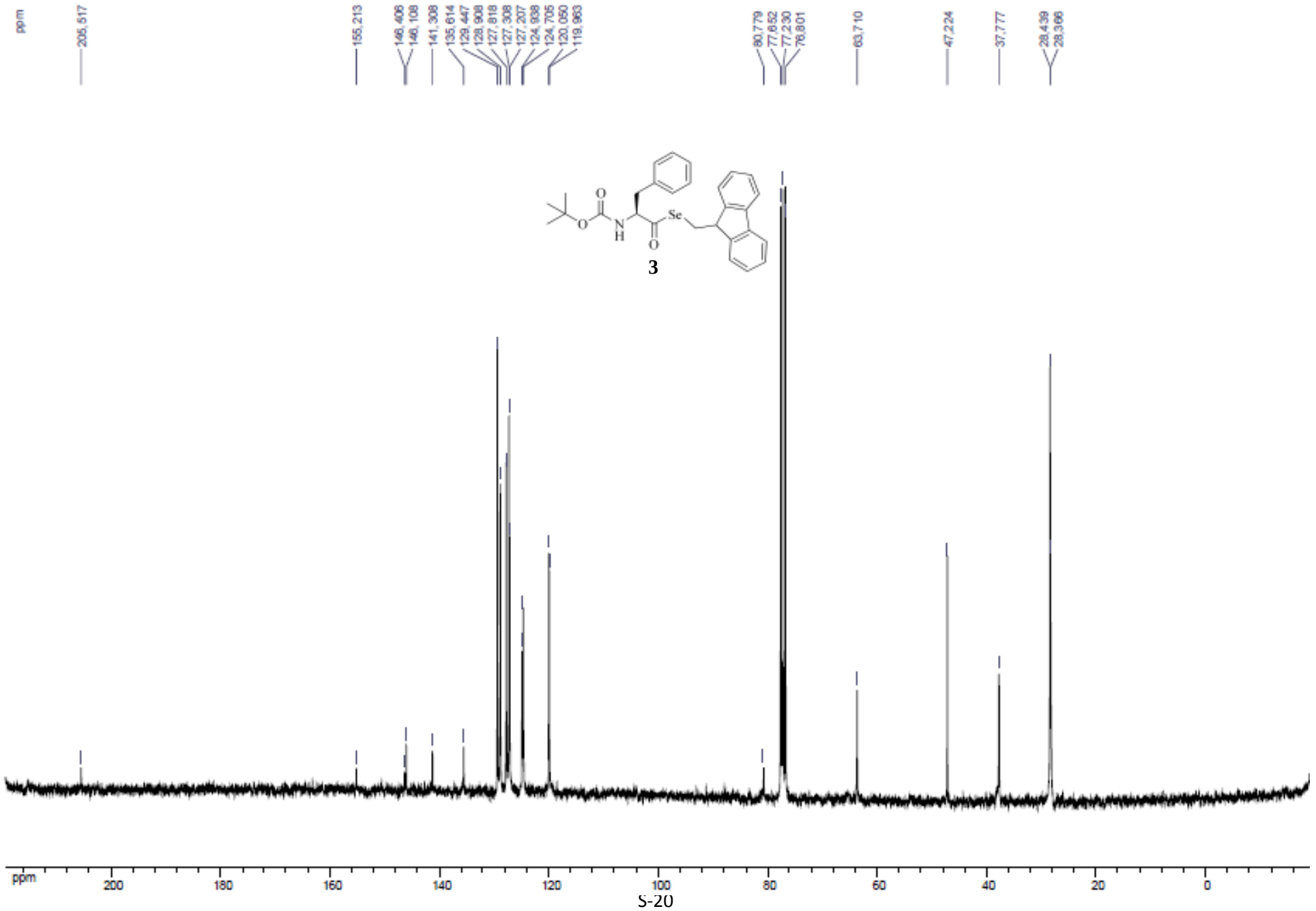
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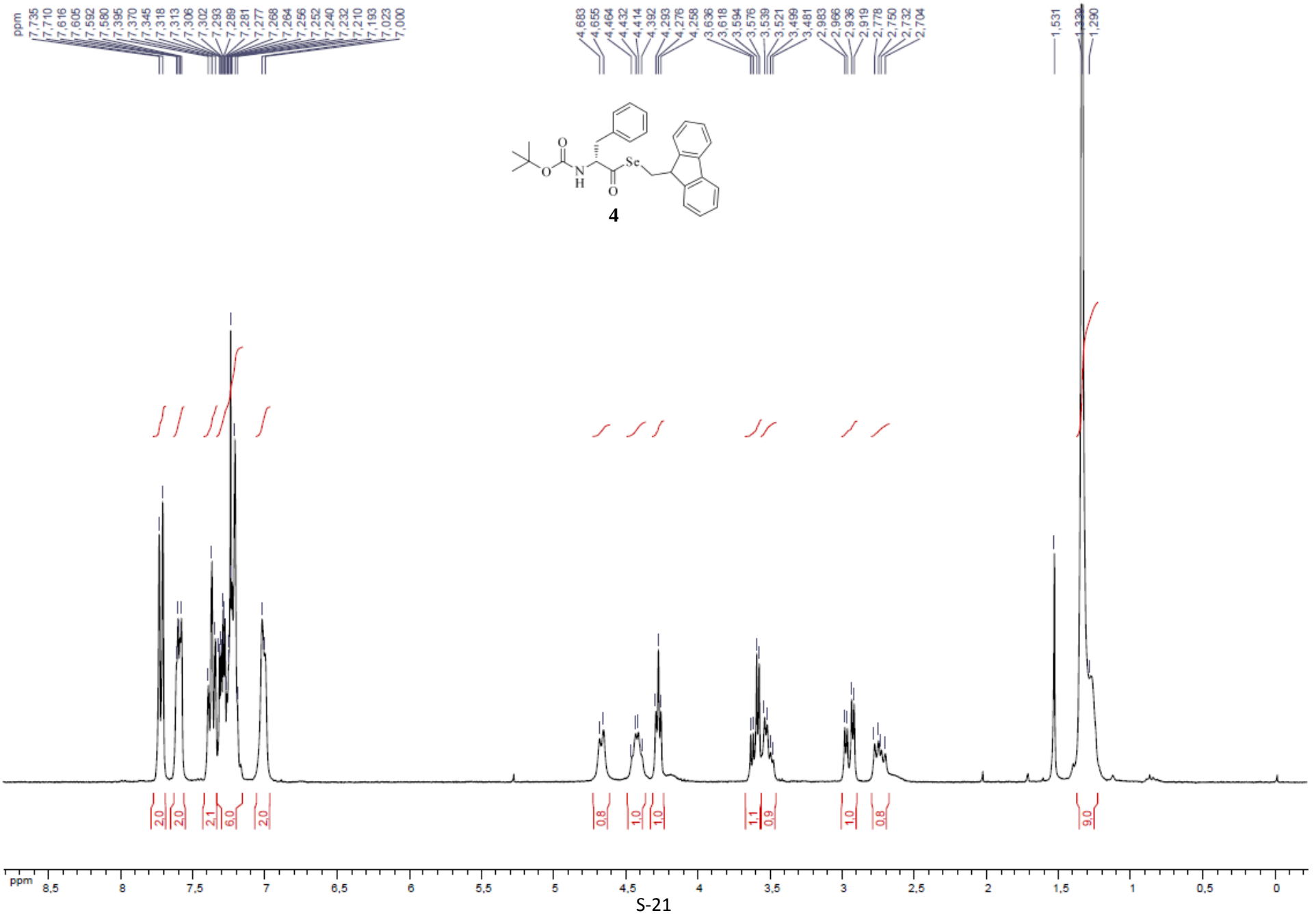
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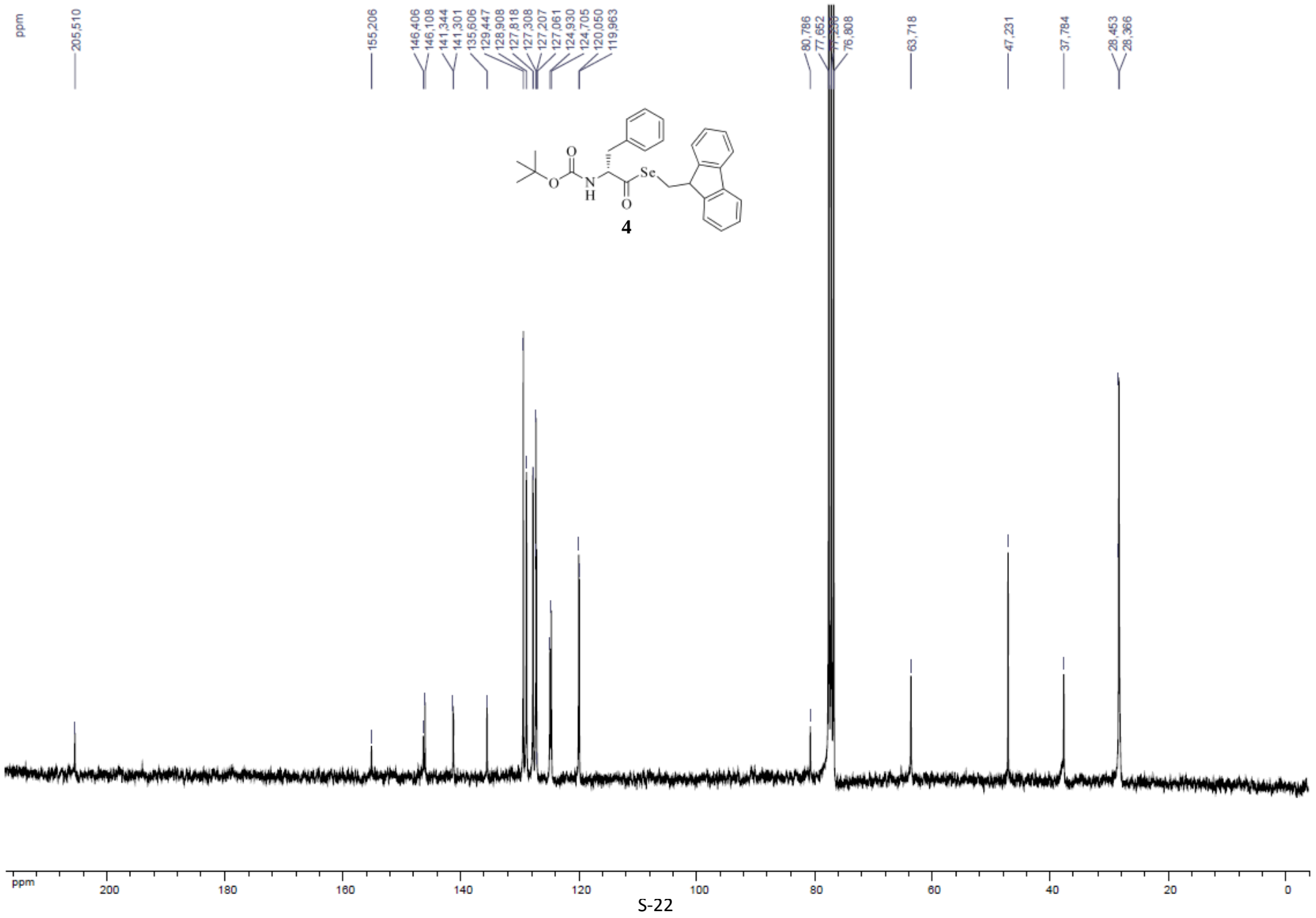
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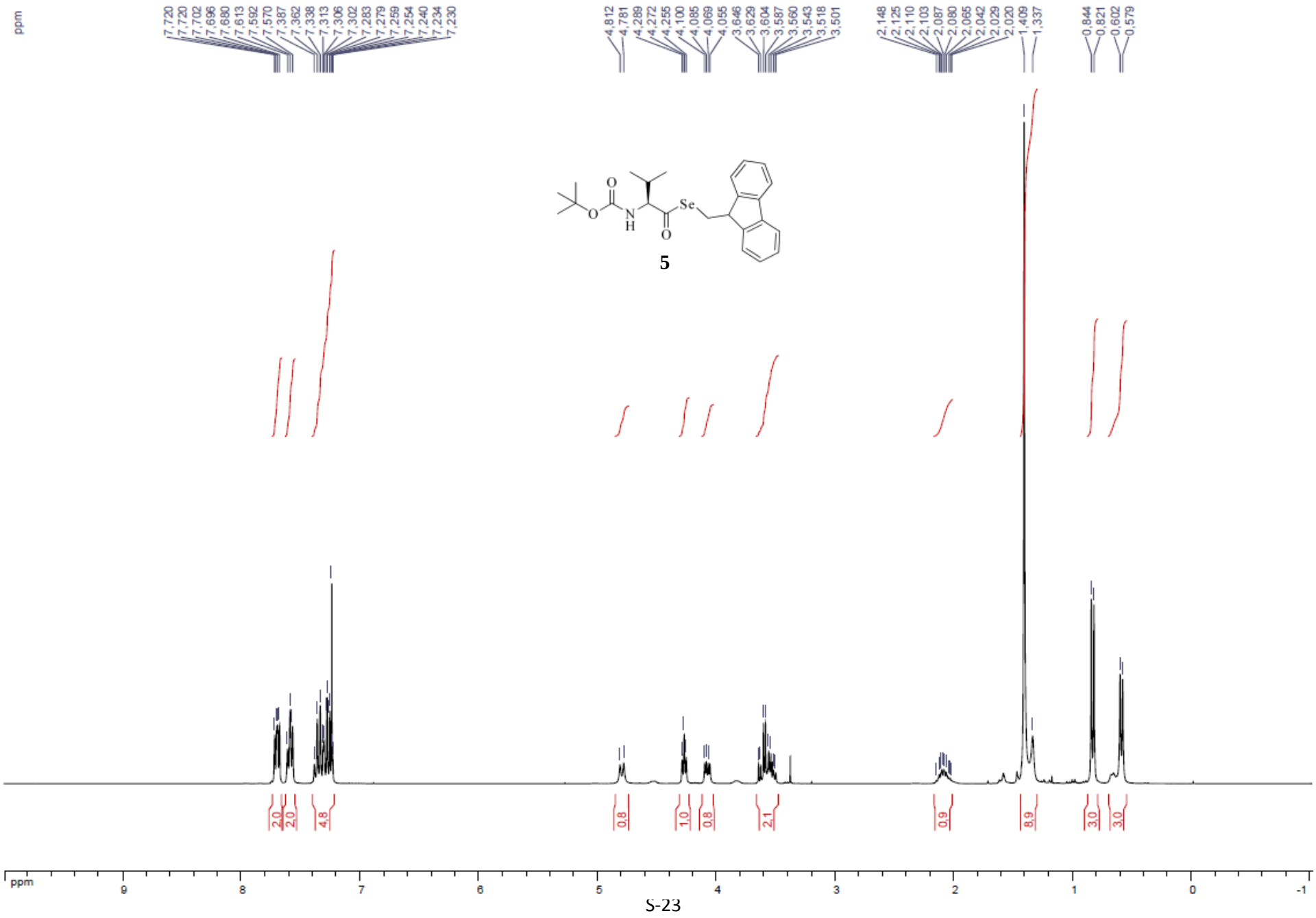
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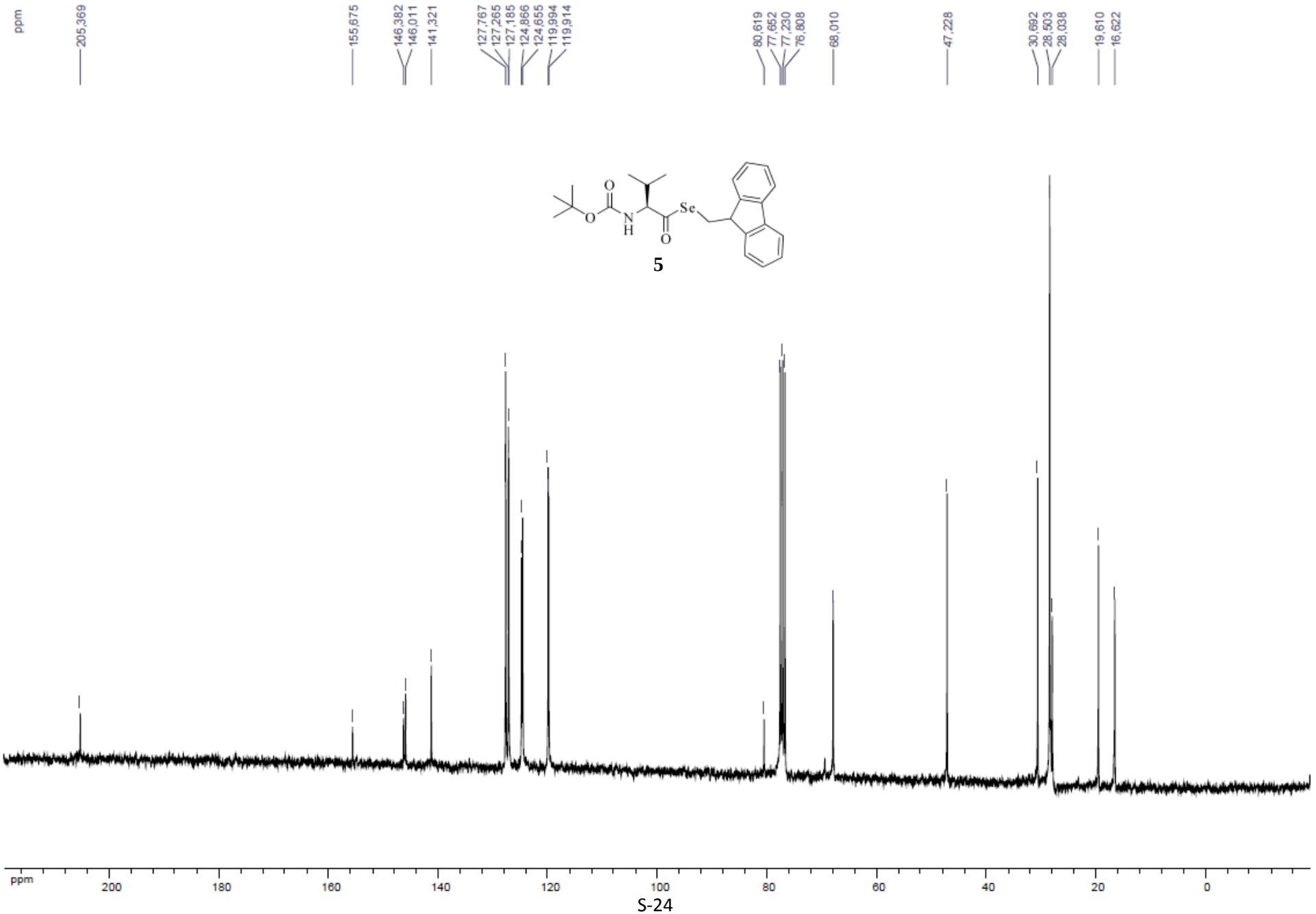
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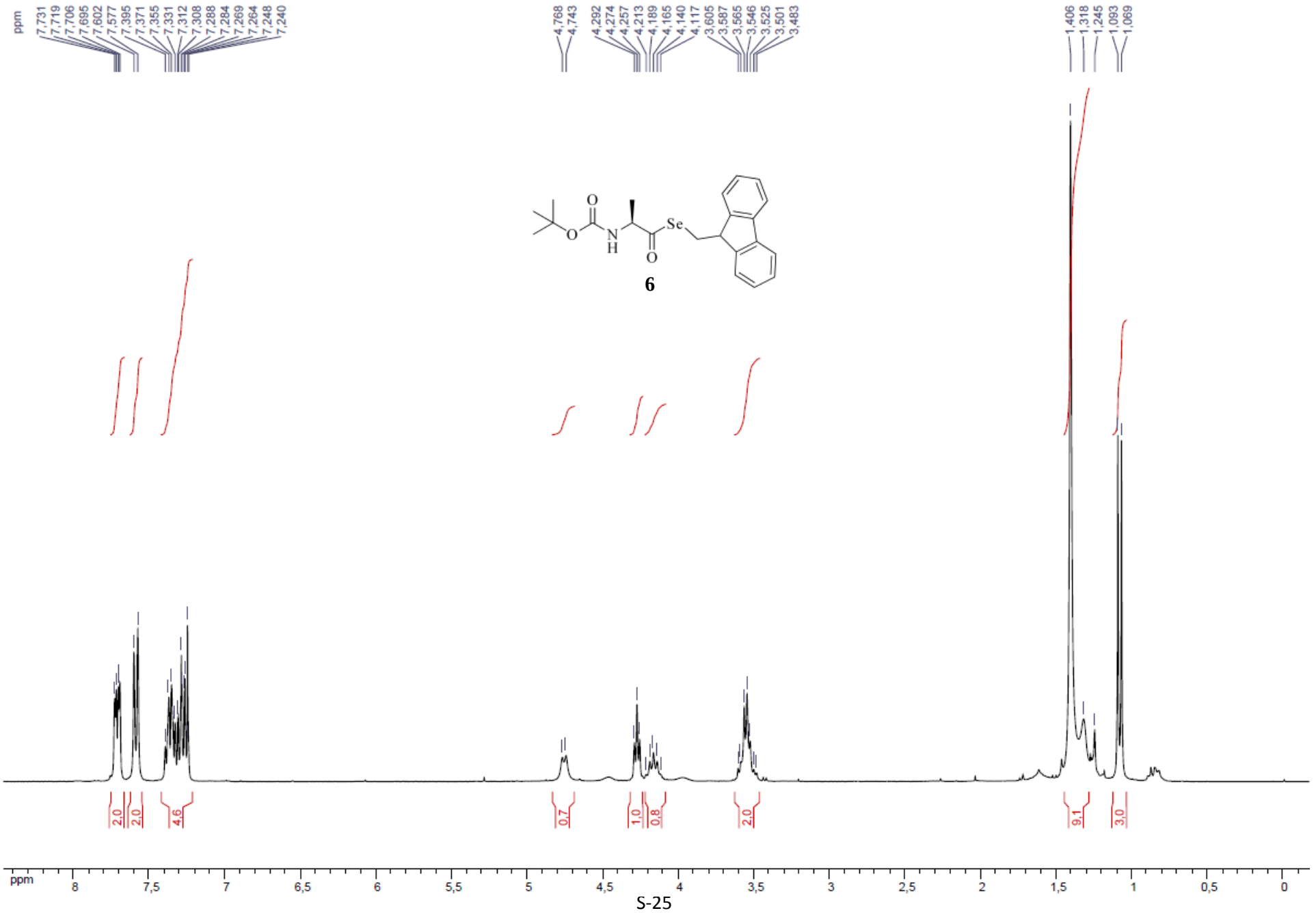
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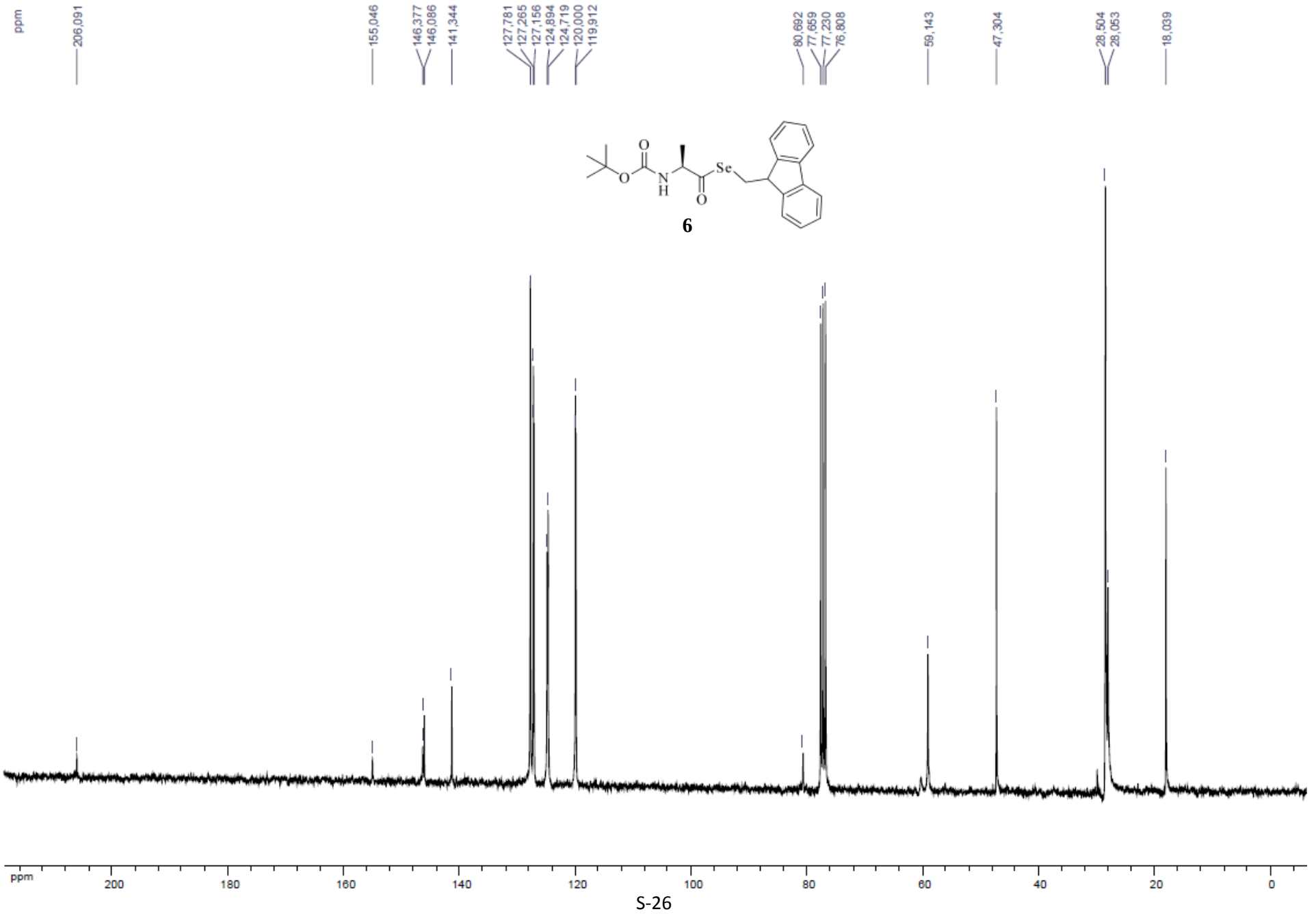
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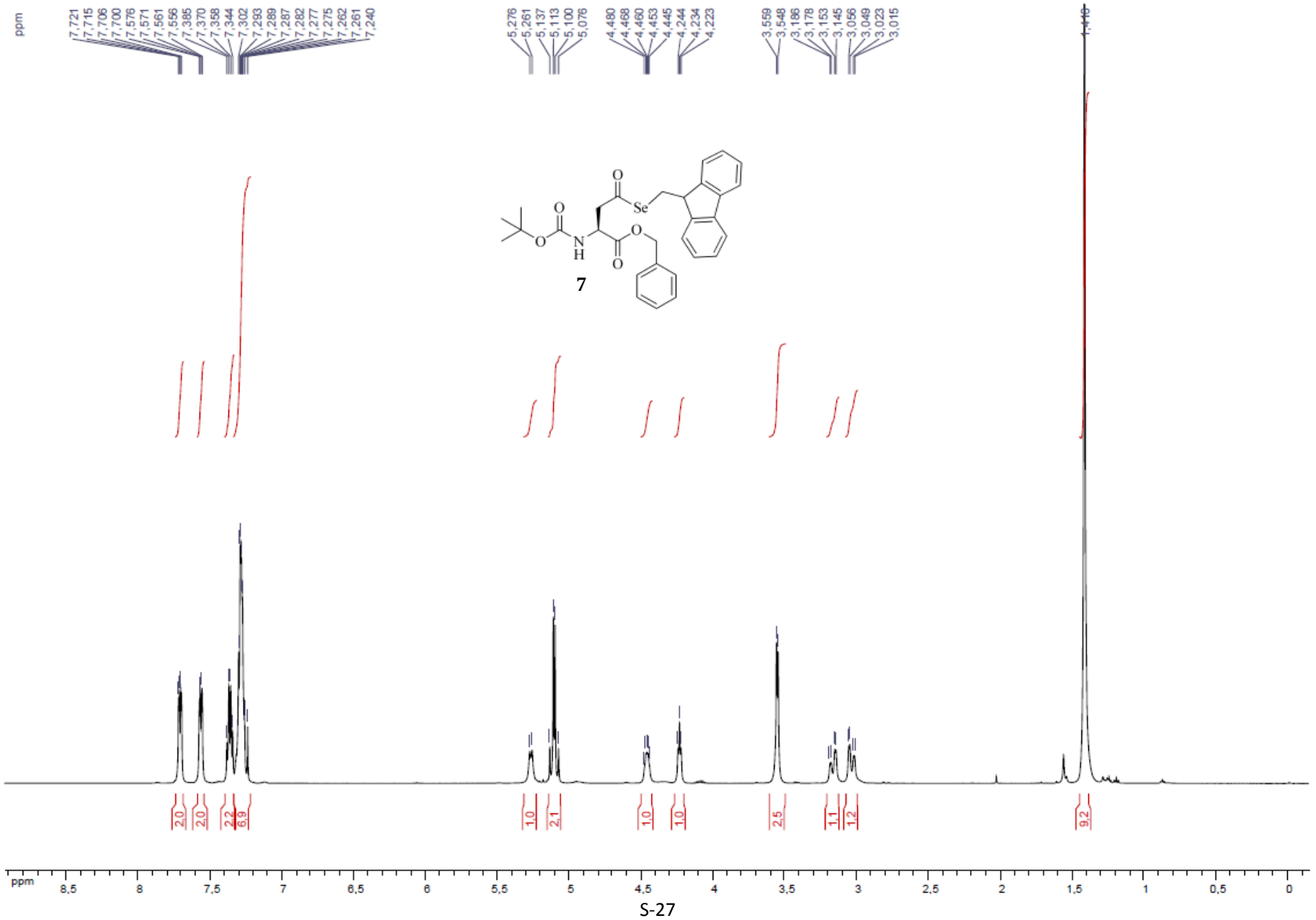
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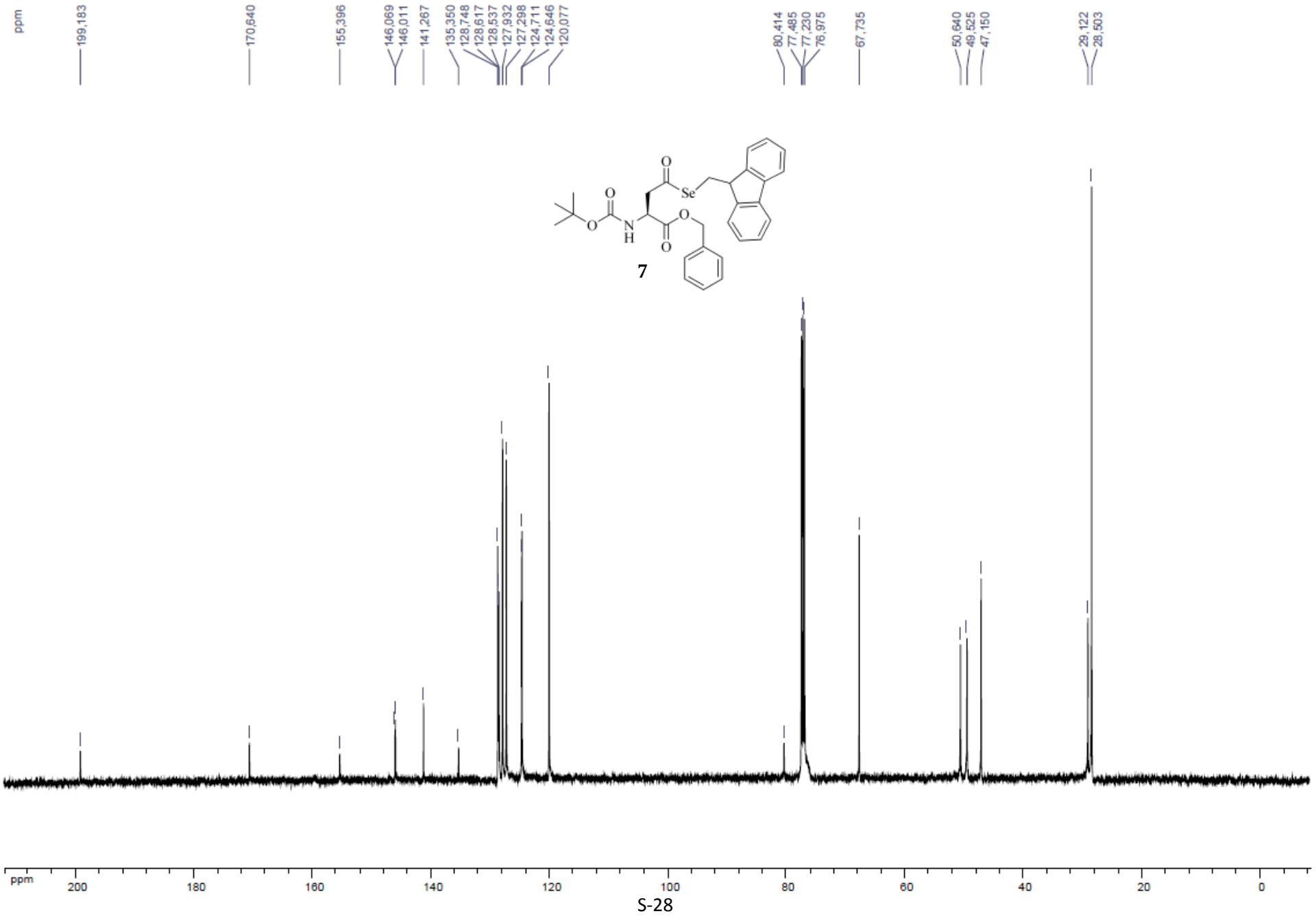
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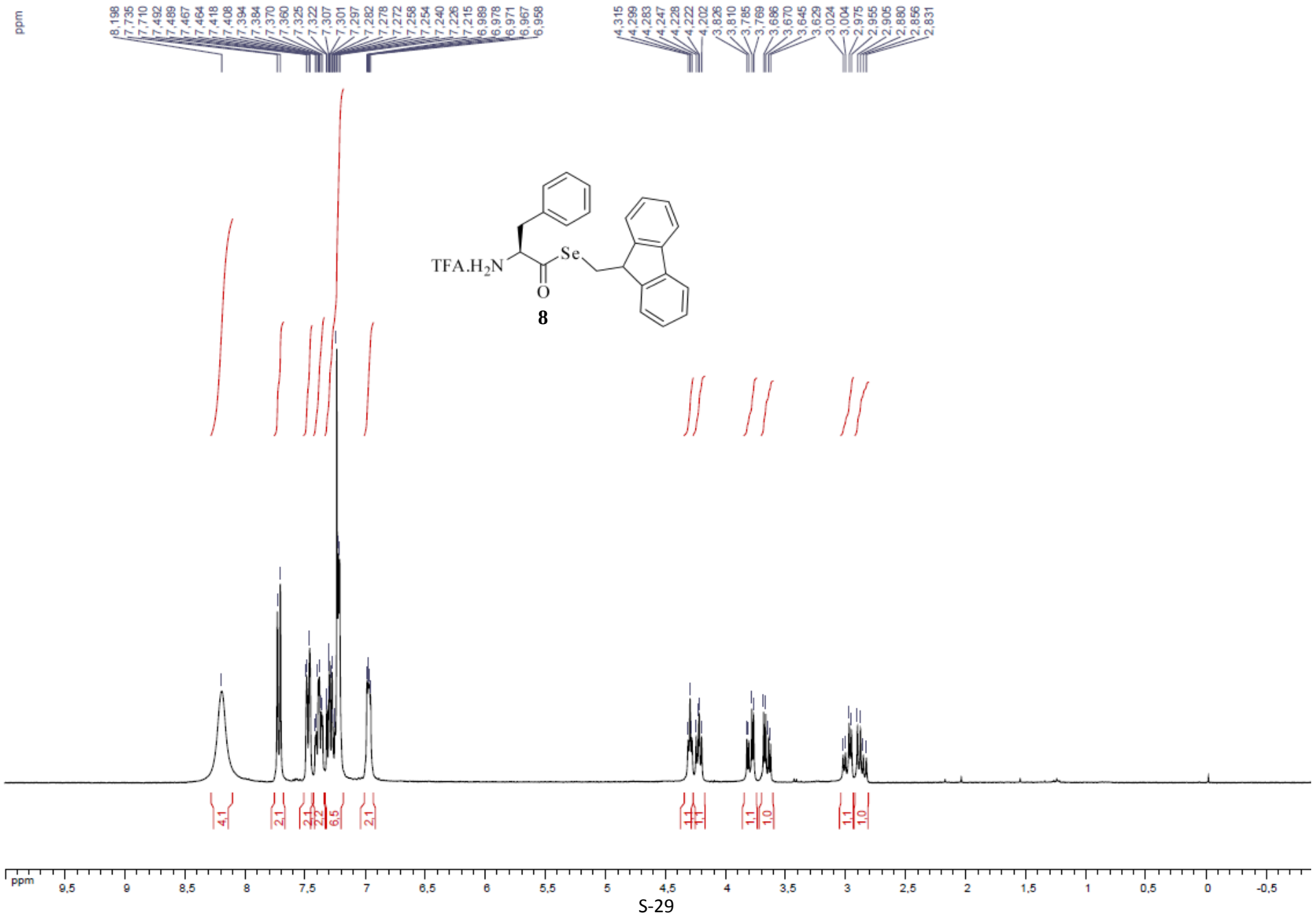
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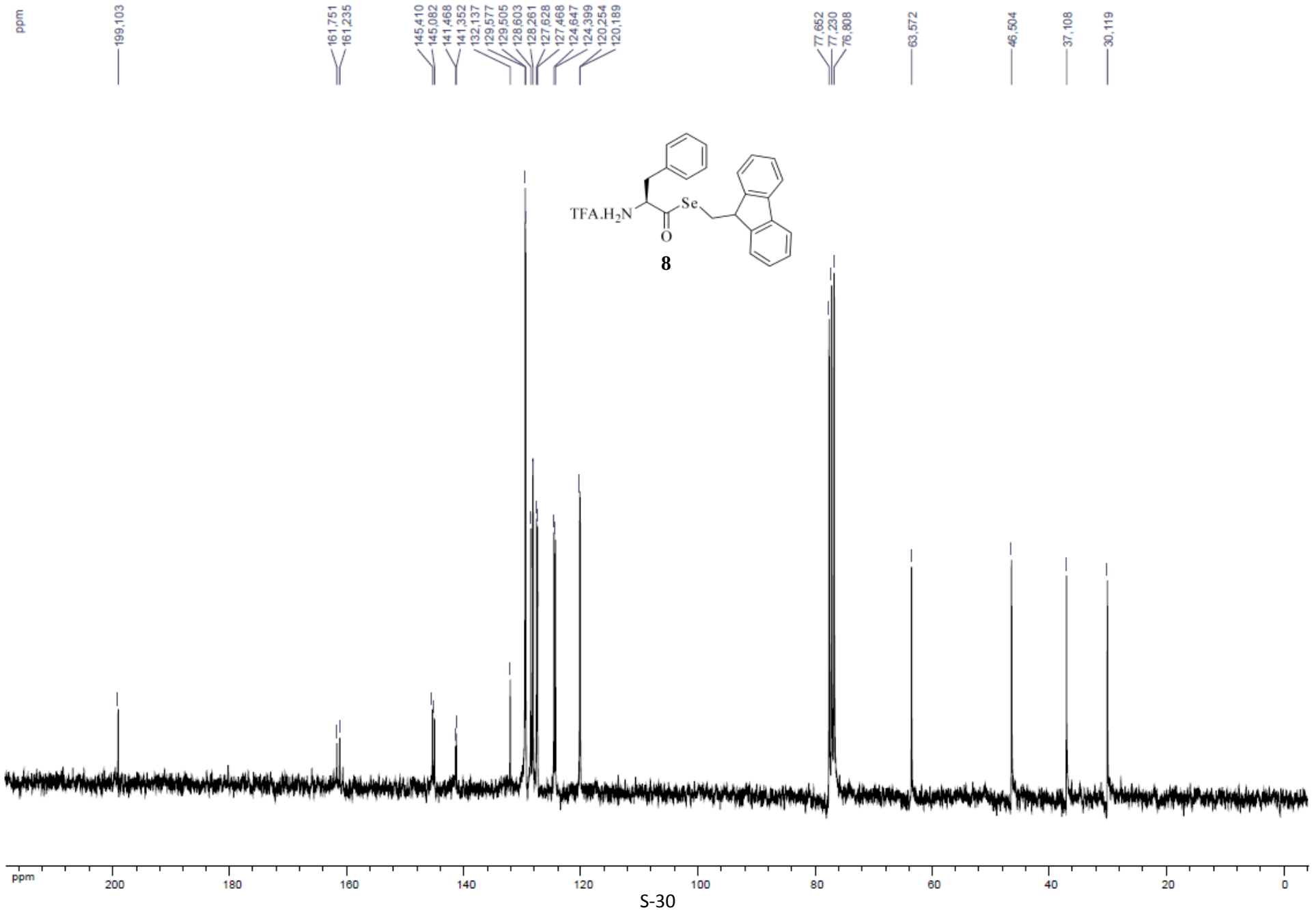
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129,577
129,505
128,603
128,261
127,628
127,468
124,647
124,399
120,254
120,189
77,652
77,230
76,808
63,572
46,504
37,108
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Se
O
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140
120
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60
40
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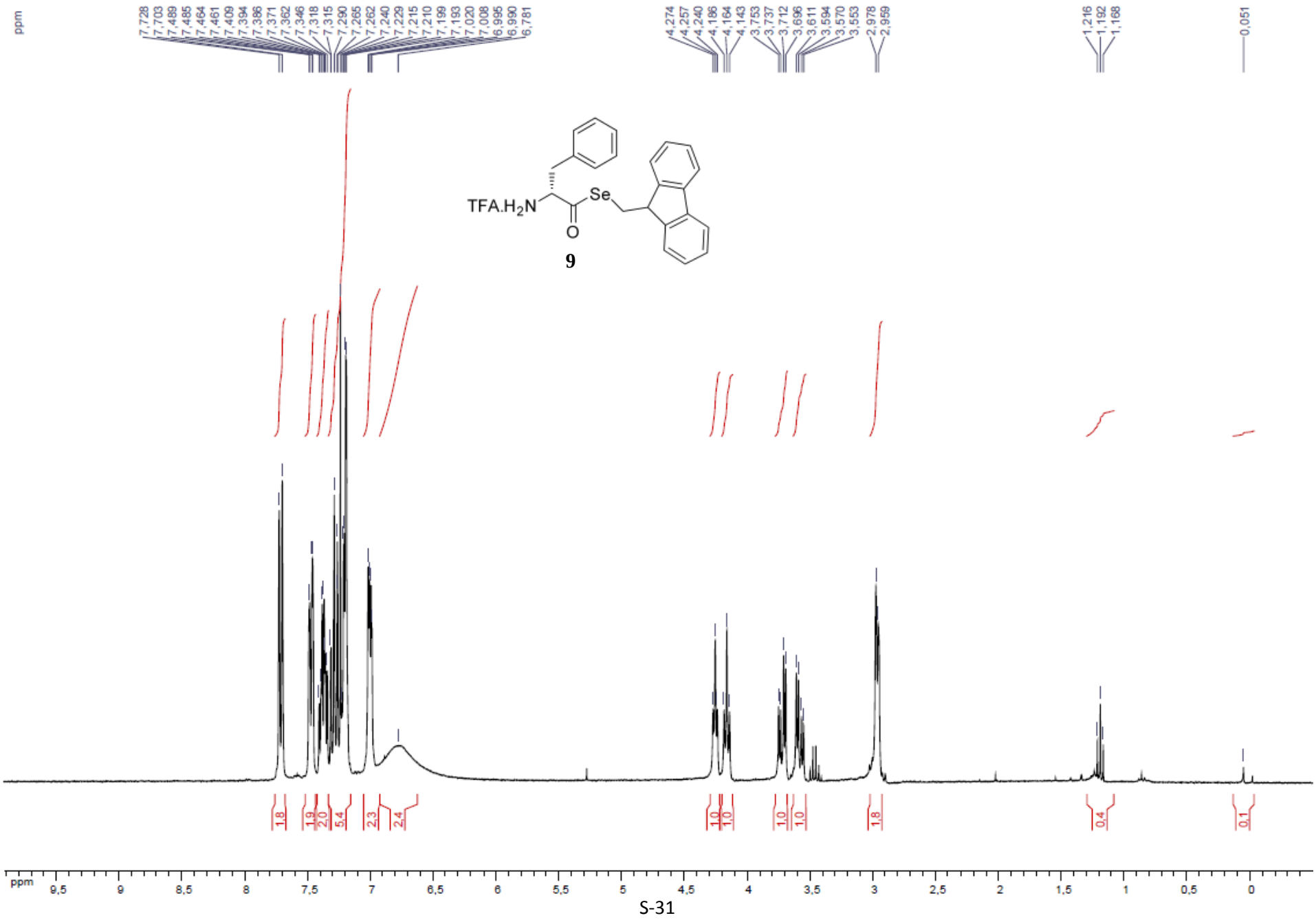
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7,386
7,371
7,362
7,346
7,318
7,315
7,290
7,265
7,262
7,240
7,229
7,215
7,210
7,199
7,193
7,020
7,008
6,995
6,990
6,781
4,274
4,257
4,240
4,186
4,164
4,143
3,753
3,737
3,712
3,696
3,611
3,594
3,570
3,553
2,978
2,959
1,216
1,192
1,168
0,051
TFA.H2N
Se
O
9
1,8
1,9
2,0
5,4
2,3
2,4
1,0
1,0
1,0
1,0
1,8
0,4
0,1
ppm
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8,5
8
7,5
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5,5
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3,5
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2,5
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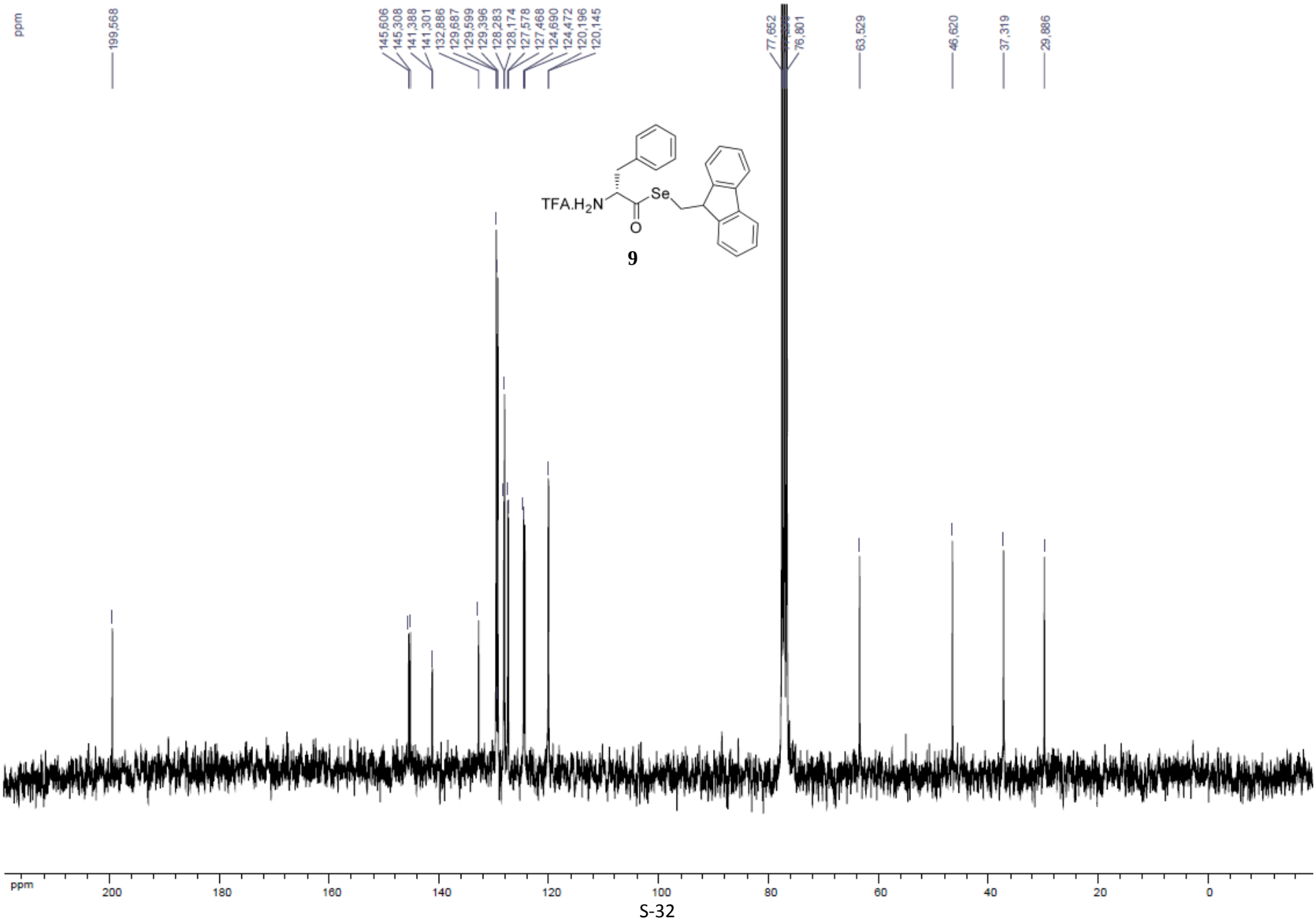
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129,396
128,283
128,174
127,578
127,468
124,690
124,472
120,196
120,145
77,652
76,801
63,529
46,620
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29,886
TFA.H2N
Se
O
9
ppm
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140
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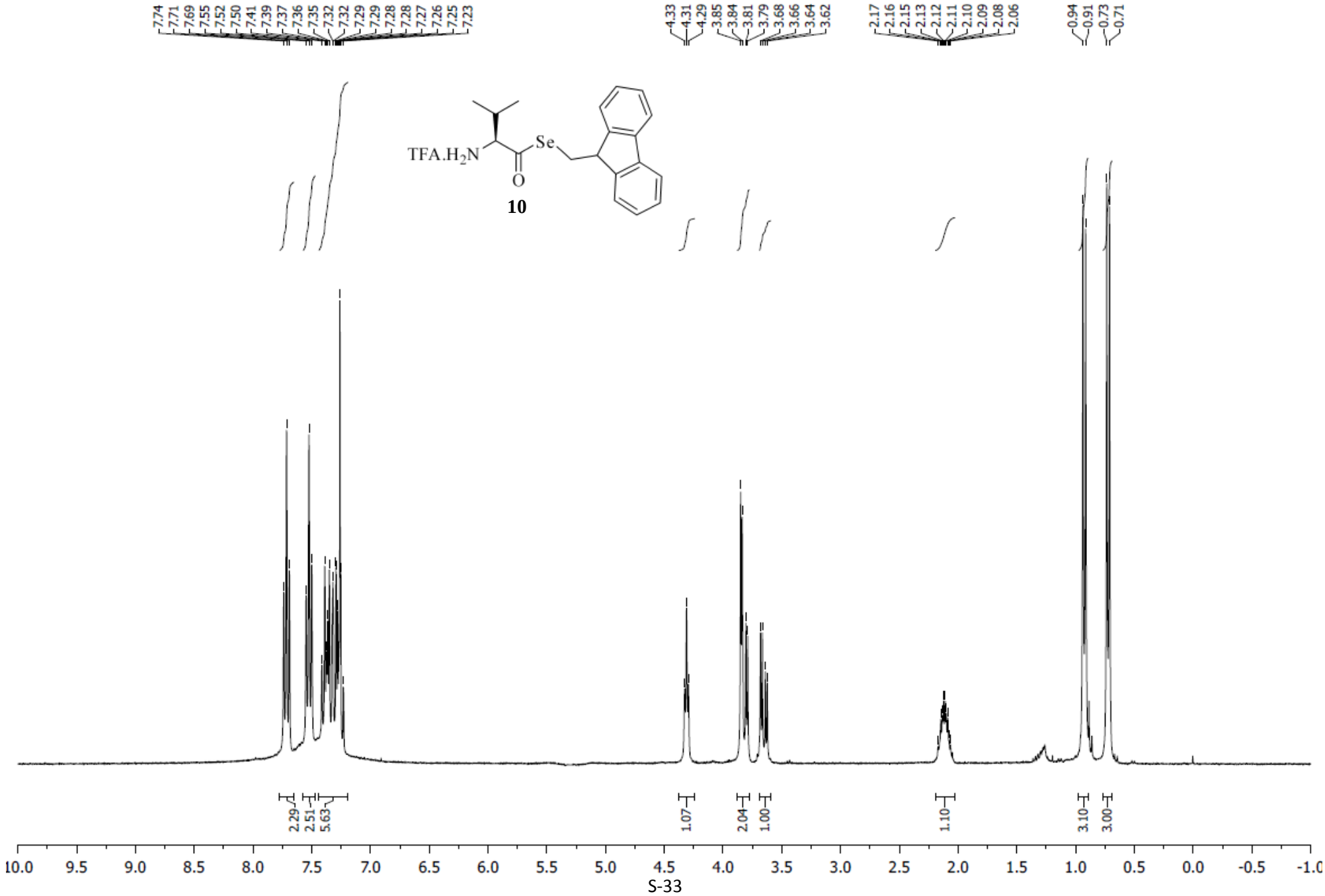
20
0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7.69
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7.39
7.37
7.36
7.35
7.32
7.32
7.29
7.29
7.28
7.28
7.27
7.26
7.25
7.23
4.33
4.31
4.29
3.85
3.84
3.81
3.79
3.68
3.66
3.64
3.62
2.17
2.16
2.15
2.13
2.12
2.11
2.10
2.09
2.08
2.06
0.94
0.91
0.73
0.71
TFA.H2N
Se
O
10
2.29
2.51
5.63
1.07
2.04
1.00
1.10
3.10
3.00
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
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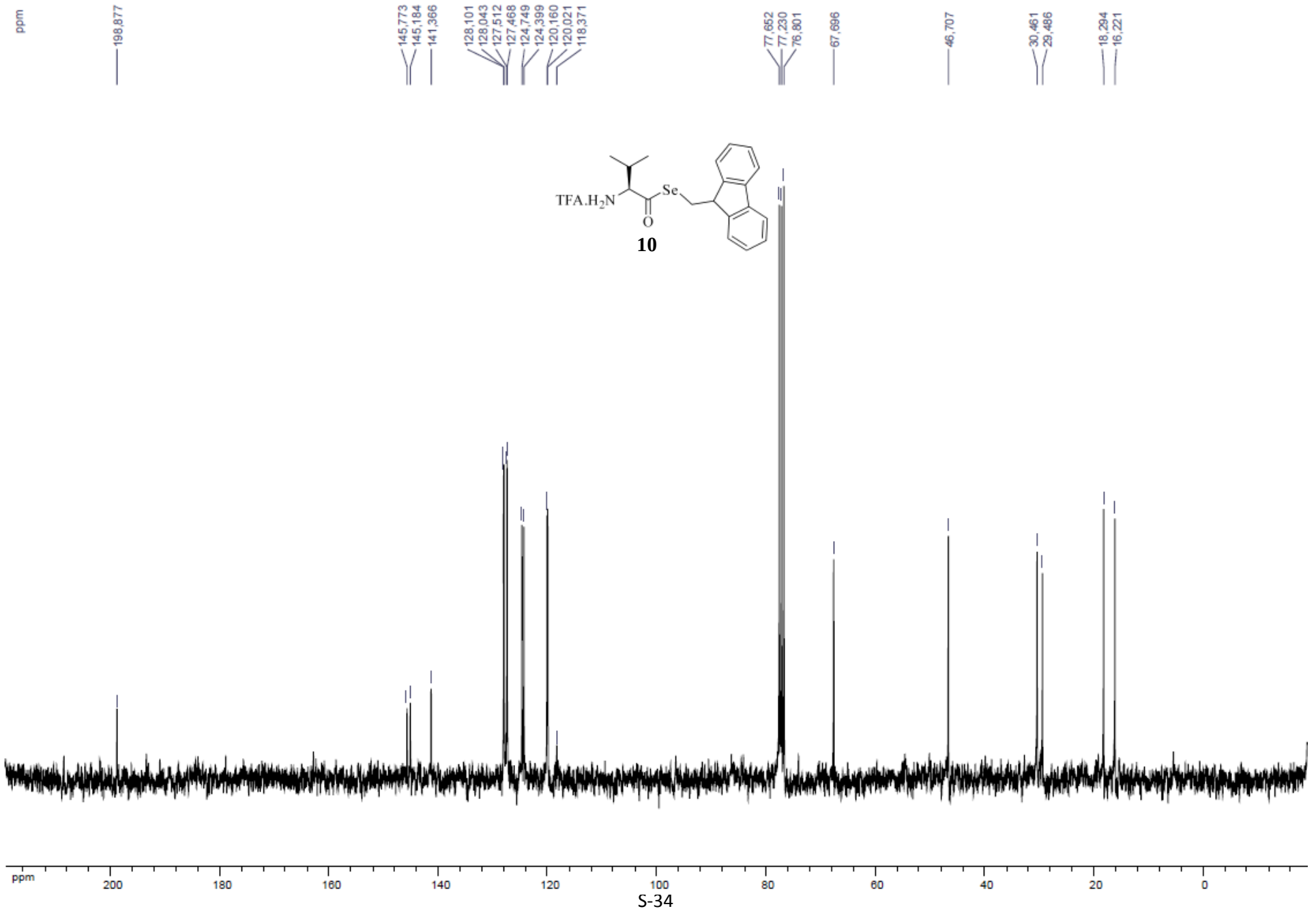
0.0
-0.5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124,399
120,160
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118,371
77,652
77,230
76,801
67,696
46,707
30,461
29,486
18,294
16,221
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Se
O
10
ppm
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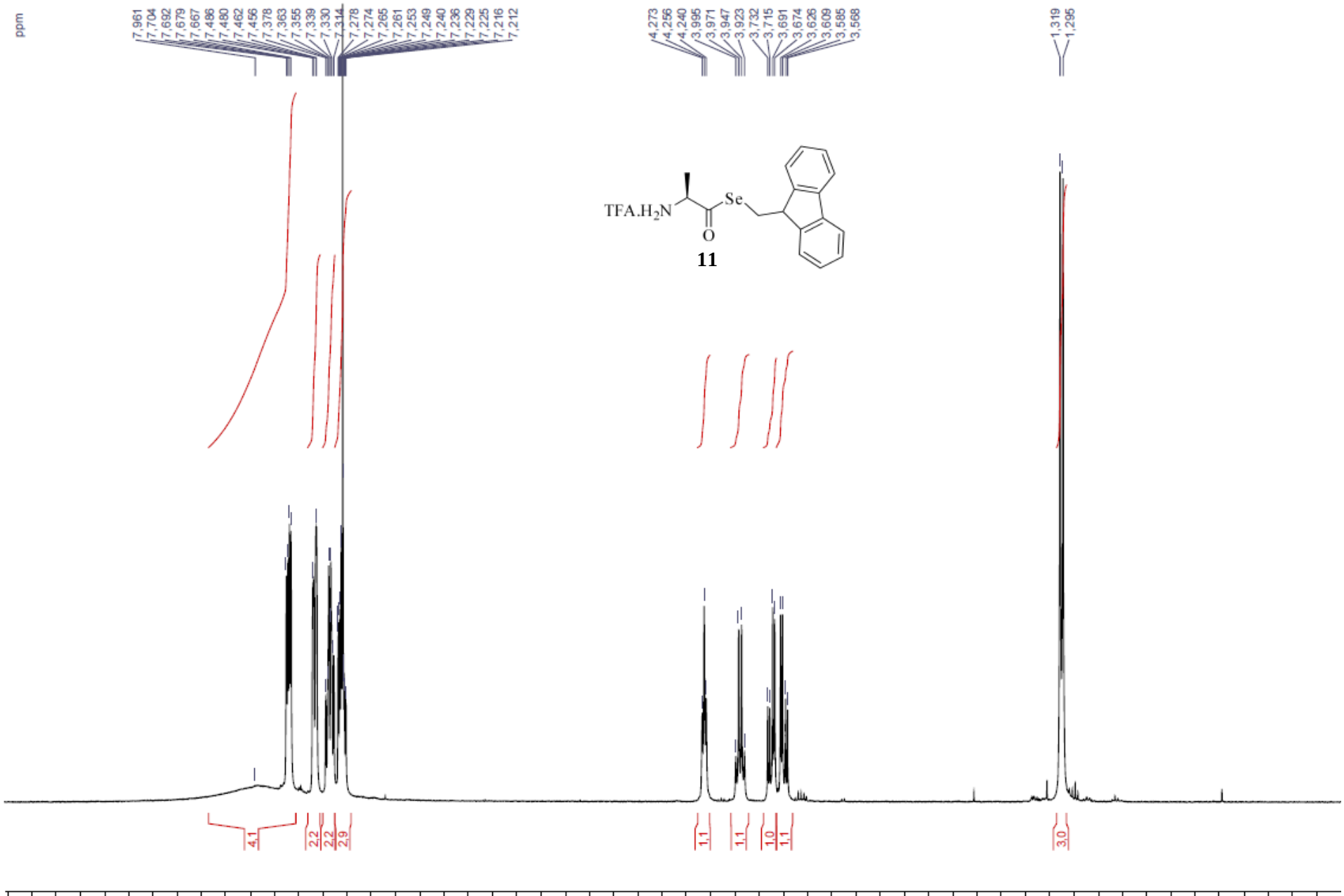
160
140
120
100
80
60
40
20
0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7,692
7,679
7,667
7,486
7,480
7,462
7,456
7,378
7,363
7,355
7,339
7,330
7,314
7,278
7,274
7,265
7,261
7,253
7,249
7,240
7,236
7,229
7,225
7,216
7,212
4,273
4,256
4,240
3,995
3,971
3,947
3,923
3,732
3,715
3,691
3,674
3,626
3,609
3,585
3,568
1,319
1,295
TFA.H2N
Se
O
11
4,1
2,2
2,2
2,9
1,1
1,1
1,0
1,1
3,0
ppm
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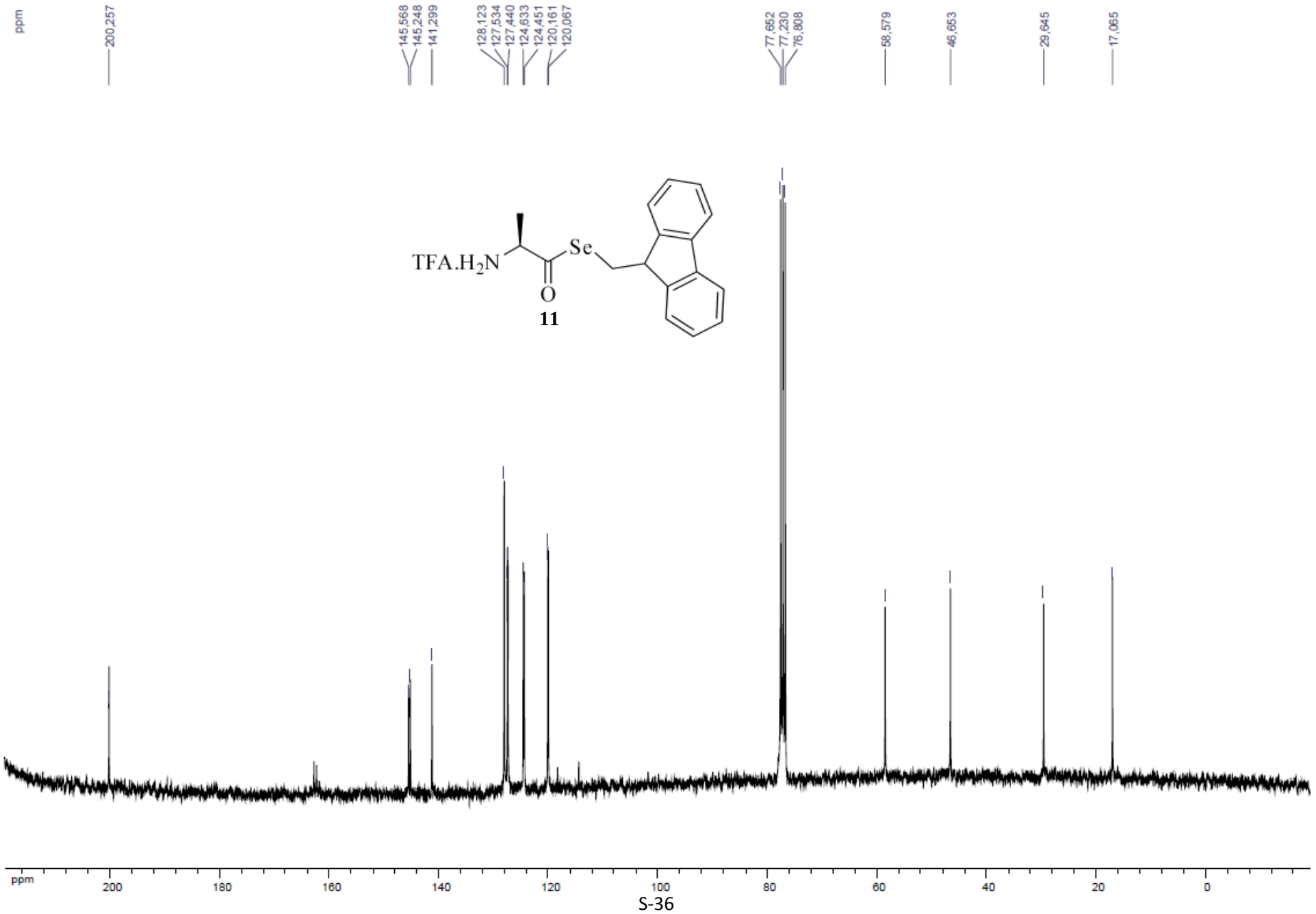
8
7
6
5
4
3
2
1
0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200,257
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145,248
141,299
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127,534
127,440
124,633
124,451
120,161
120,067
77,652
77,230
76,808
58,579
46,653
29,645
17,065
TFA.H2N
Se
O
11
ppm
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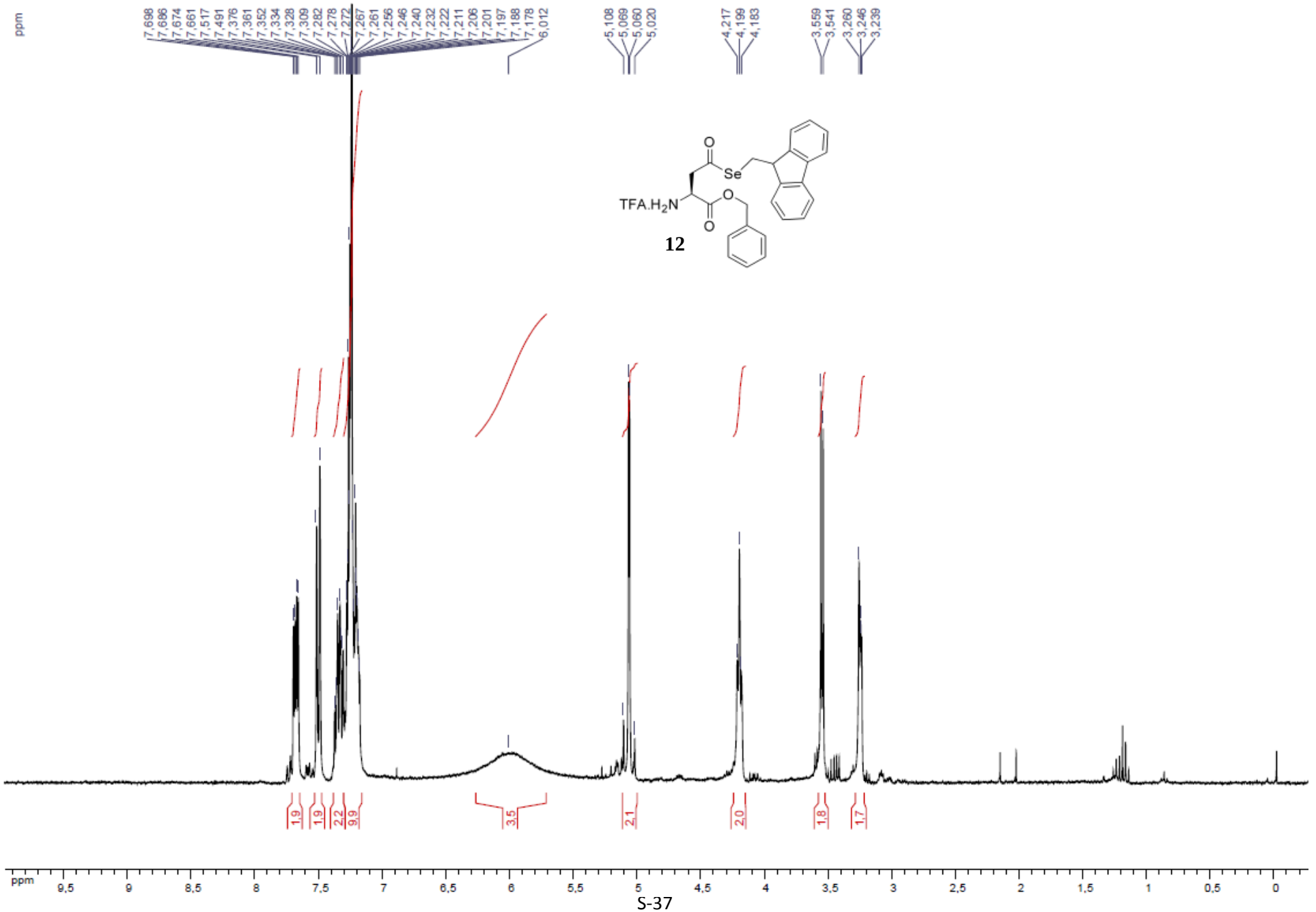
160
140
120
100
80
60
40
20
0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7,698
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7,674
7,661
7,517
7,491
7,376
7,361
7,352
7,334
7,328
7,309
7,282
7,278
7,272
7,267
7,261
7,256
7,246
7,240
7,232
7,222
7,211
7,206
7,201
7,197
7,188
7,178
6,012
5,108
5,069
5,060
5,020
4,217
4,199
4,183
3,559
3,541
3,260
3,246
3,239
TFA.H2N
Se
O
O
O
1,9
1,9
2,2
9,9
3,5
2,1
2,0
1,8
1,7
ppm
9,5
9
8,5
8
7,5
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6,5
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5,5
5
4,5
4
3,5
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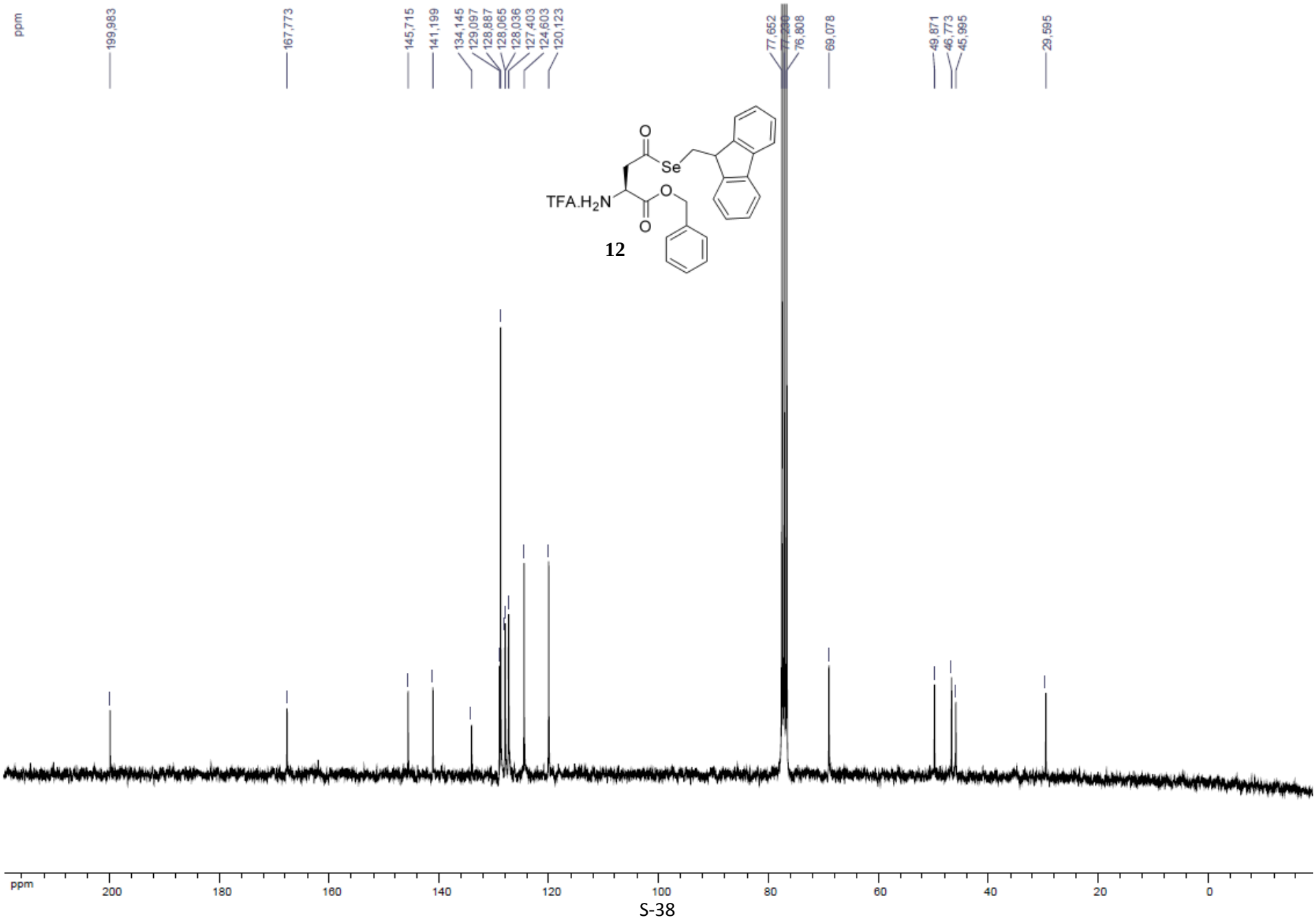
2,5
2
1,5
1
0,5
0

12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199,983
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145,715
141,199
134,145
129,097
128,887
128,065
128,036
127,403
124,603
120,123
77,652
77,230
76,808
69,078
49,871
46,773
45,995
29,595
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Se
O
O
12
ppm
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140
120
100
80
60
40
20
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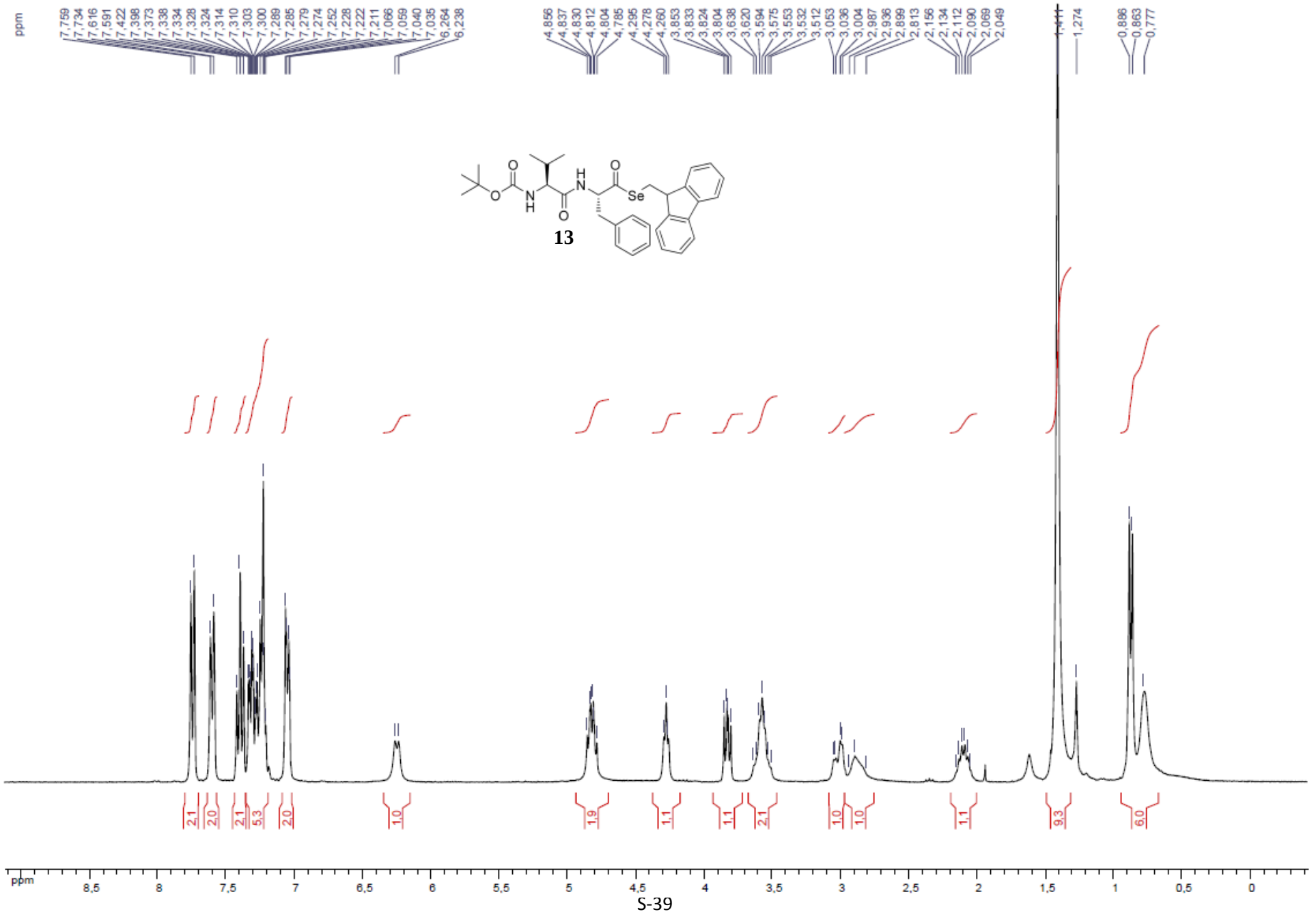
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7,591
7,422
7,398
7,373
7,338
7,334
7,328
7,324
7,314
7,310
7,303
7,300
7,289
7,285
7,279
7,274
7,252
7,228
7,222
7,211
7,066
7,059
7,040
7,035
6,264
6,238
4,856
4,837
4,830
4,812
4,804
4,785
4,295
4,278
4,260
3,853
3,833
3,824
3,804
3,638
3,620
3,594
3,575
3,553
3,532
3,512
3,053
3,036
3,004
2,987
2,936
2,899
2,813
2,156
2,134
2,112
2,090
2,069
2,049
1,411
1,274
0,886
0,863
0,777
O
O
N
H
H
N
O
O
Se
13
2,1
2,0
2,1
5,3
2,0
1,0
1,9
1,1
1,1
2,1
1,0
1,0
1,1
9,3
6,0
ppm
8,5
8
7,5
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6,5
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5,5
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4,5
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3,5
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2,5
2
1,5
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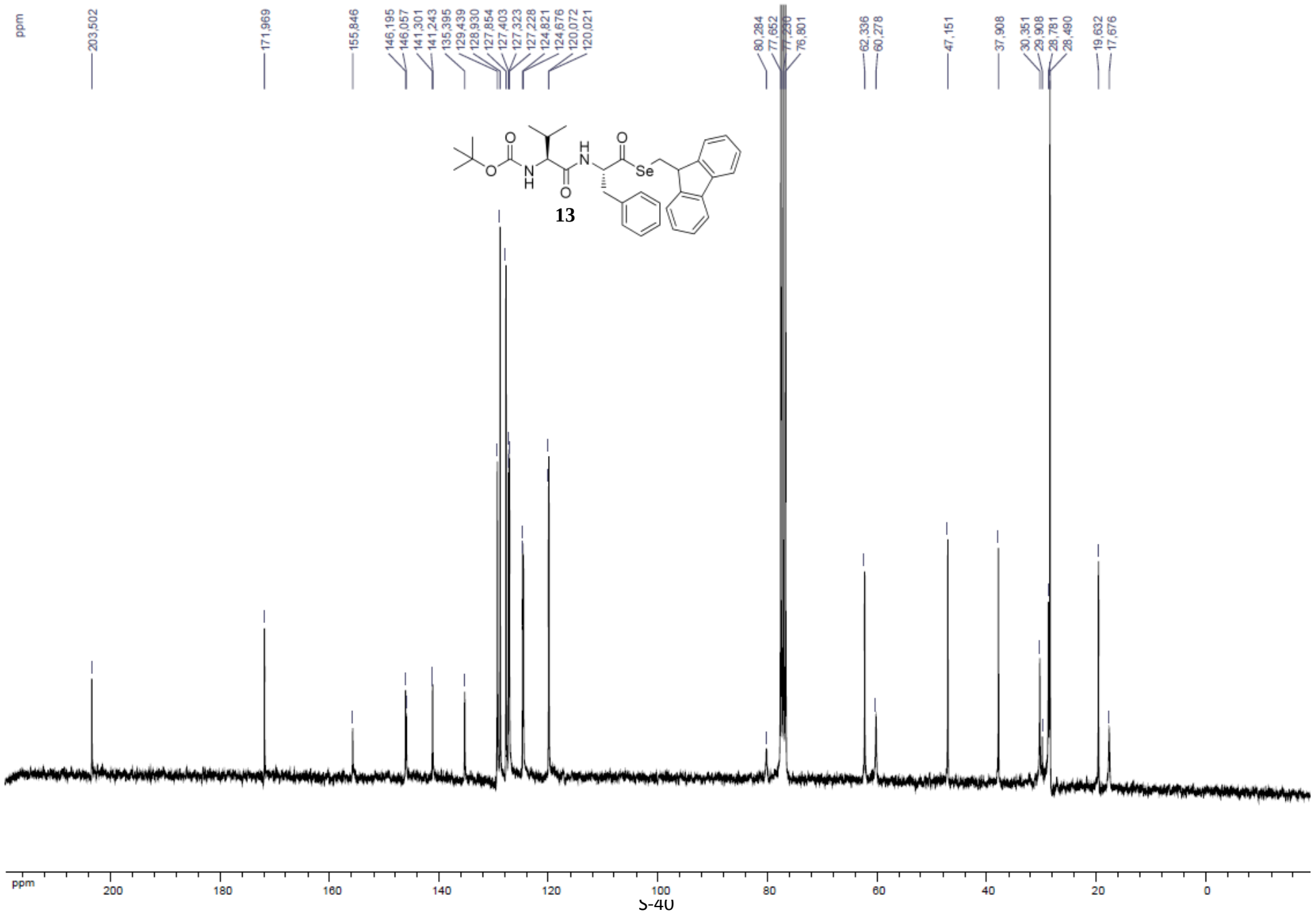
ppm
203,502
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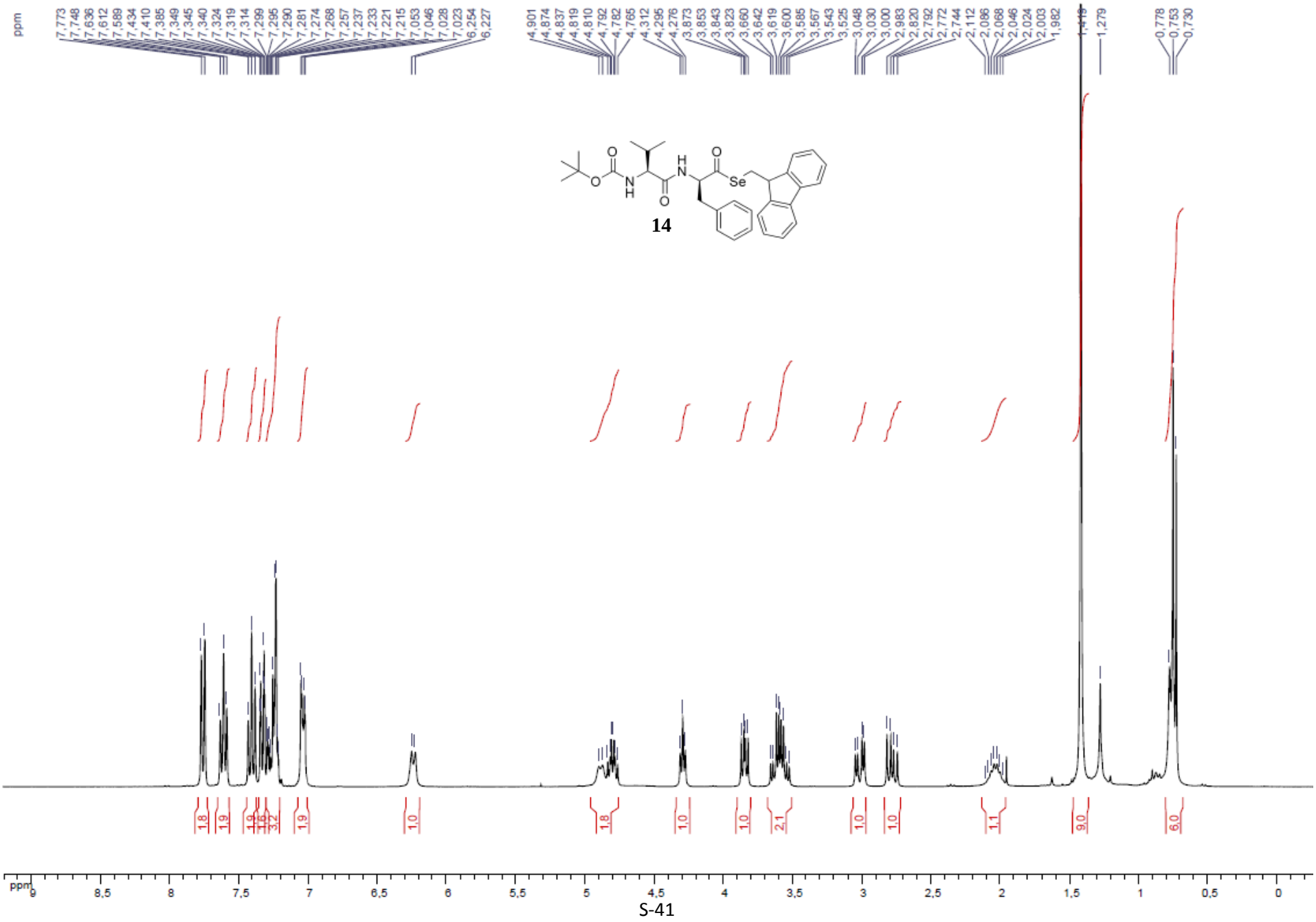
155,846
146,195
146,057
141,301
141,243
135,395
129,439
128,930
127,854
127,403
127,323
127,228
124,821
124,676
120,072
120,021
80,284
77,652
77,236
76,801
62,336
60,278
47,151
37,908
30,351
29,908
28,781
28,490
19,632
17,676
13
Se
ppm
200
180
160
140
120
100
80
60
40
20
0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7,589
7,434
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7,385
7,349
7,345
7,340
7,324
7,319
7,314
7,299
7,295
7,290
7,281
7,274
7,268
7,257
7,237
7,233
7,221
7,215
7,053
7,046
7,028
7,023
6,254
6,227
4,901
4,874
4,837
4,819
4,810
4,792
4,782
4,765
4,312
4,295
4,276
3,873
3,853
3,843
3,823
3,660
3,642
3,619
3,600
3,585
3,567
3,543
3,525
3,048
3,030
3,000
2,983
2,820
2,792
2,772
2,744
2,112
2,086
2,068
2,046
2,024
2,003
1,982
1,419
1,279
0,778
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0,730
O
O
N
H
O
N
H
O
Se
14
1,8
1,9
1,9
1,6
3,2
1,9
1,0
1,8
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1,0
2,1
1,0
1,0
1,1
9,0
6,0
ppm
9
8,5
8
7,5
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5,5
5
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2,5
2
1,5
1
0,5
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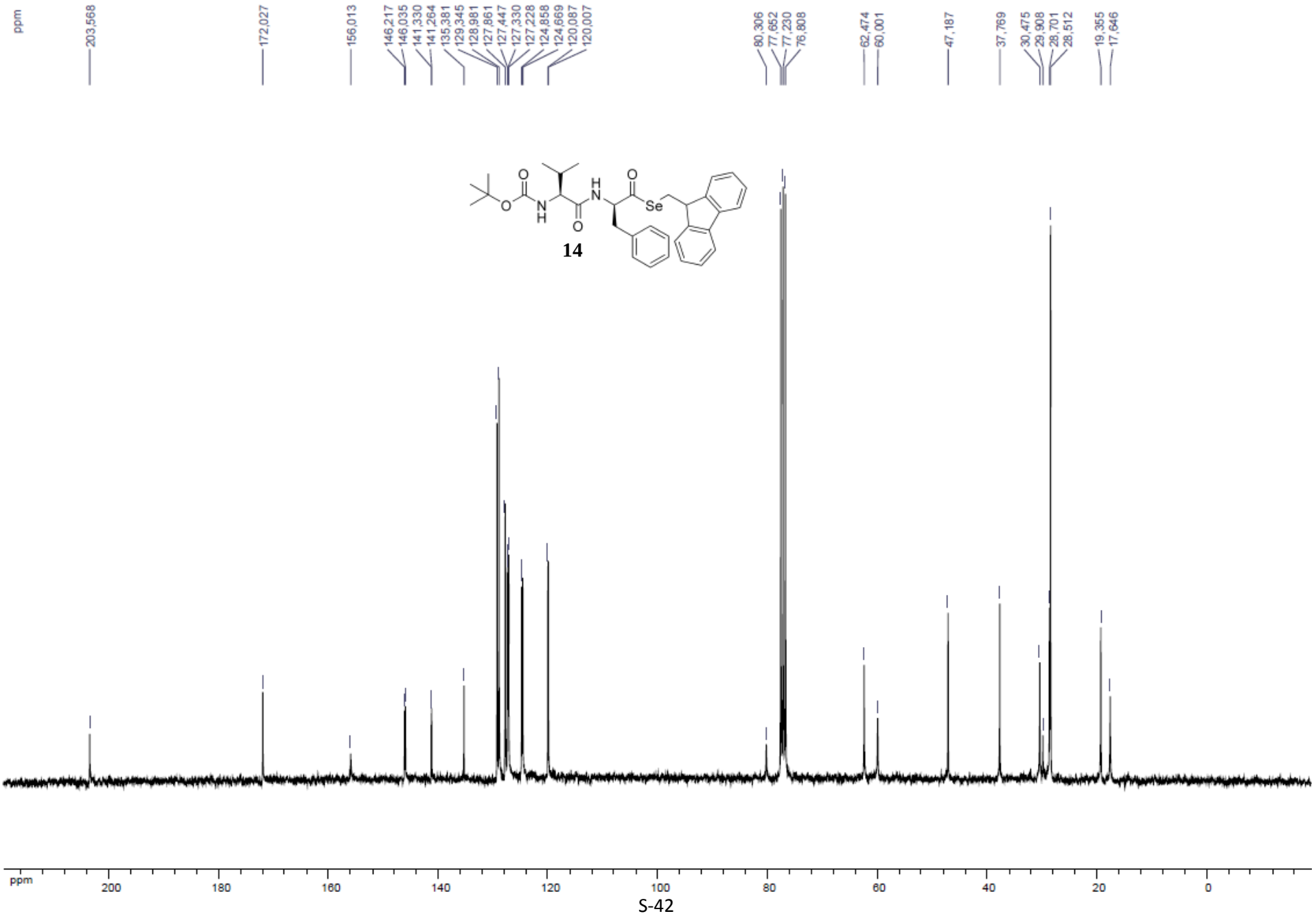
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146,217
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135,381
129,345
128,981
127,861
127,447
127,330
127,228
124,858
124,669
120,087
120,007
80,306
77,652
77,230
76,808
62,474
60,001
47,187
37,769
30,475
29,908
28,701
28,512
19,355
17,646
Se
14
ppm
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140
120
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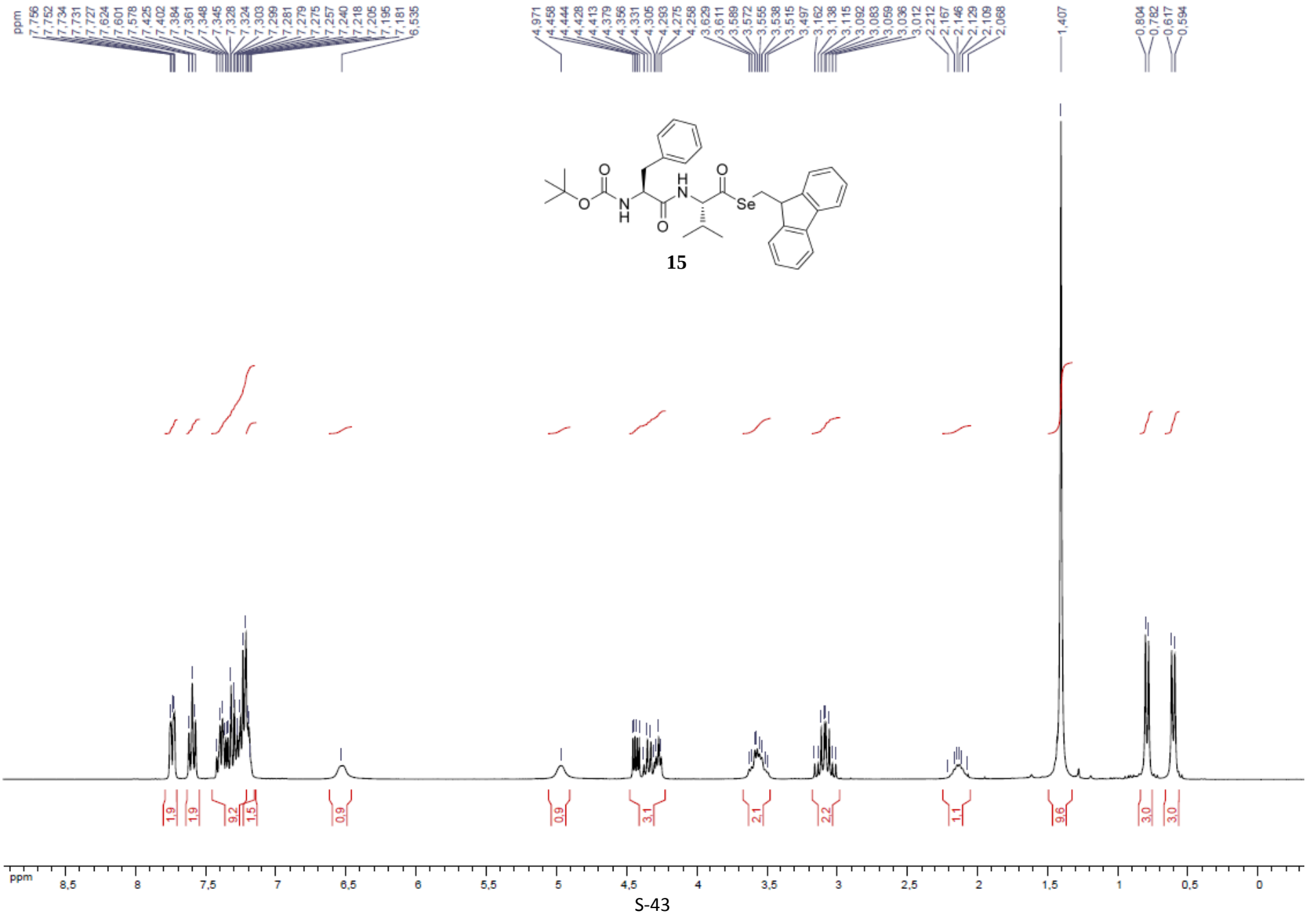
60
40
20
0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7,727
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7,425
7,402
7,384
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7,345
7,328
7,324
7,303
7,299
7,281
7,279
7,275
7,257
7,240
7,218
7,205
7,195
7,181
6,535
4,971
4,458
4,444
4,428
4,413
4,379
4,356
4,331
4,305
4,293
4,275
4,258
3,629
3,611
3,589
3,572
3,555
3,538
3,515
3,497
3,162
3,138
3,115
3,092
3,083
3,059
3,036
3,012
2,212
2,167
2,146
2,129
2,109
2,068
1,407
0,804
0,782
0,617
0,594
O
O
N
H
O
H
N
O
Se
1,9
1,9
9,2
1,5
0,9
0,9
3,1
2,1
2,2
1,1
9,6
3,0
3,0
ppm
8,5
8
7,5
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4,5
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2,5
2
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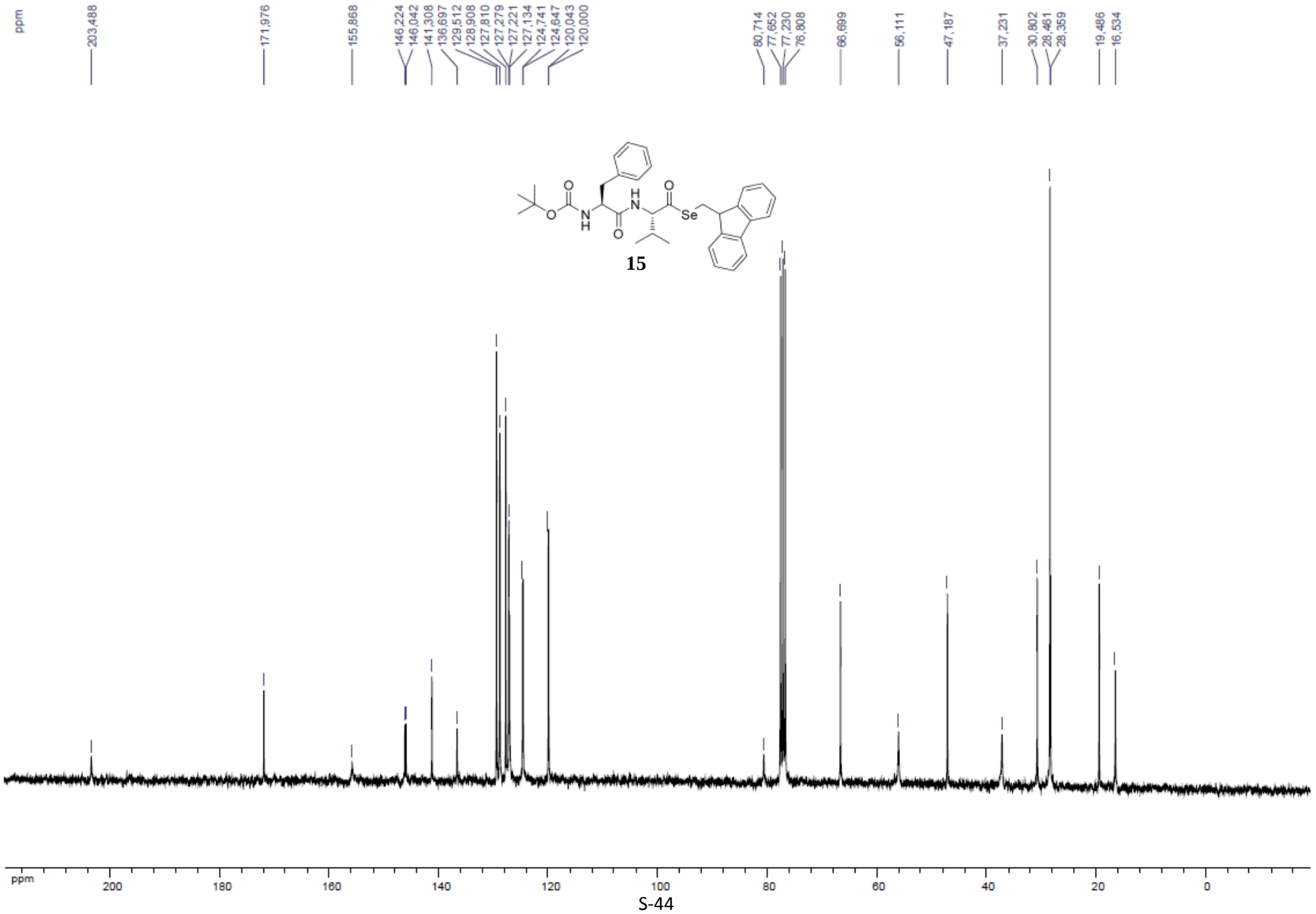
0,5
0

15


ppm
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146,042
141,308
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128,908
127,810
127,279
127,221
127,134
124,741
124,647
120,043
120,000
80,714
77,652
77,230
76,808
66,699
56,111
47,187
37,231
30,802
28,461
28,359
19,486
16,534
O
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N
O
Se
15
ppm
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140
120
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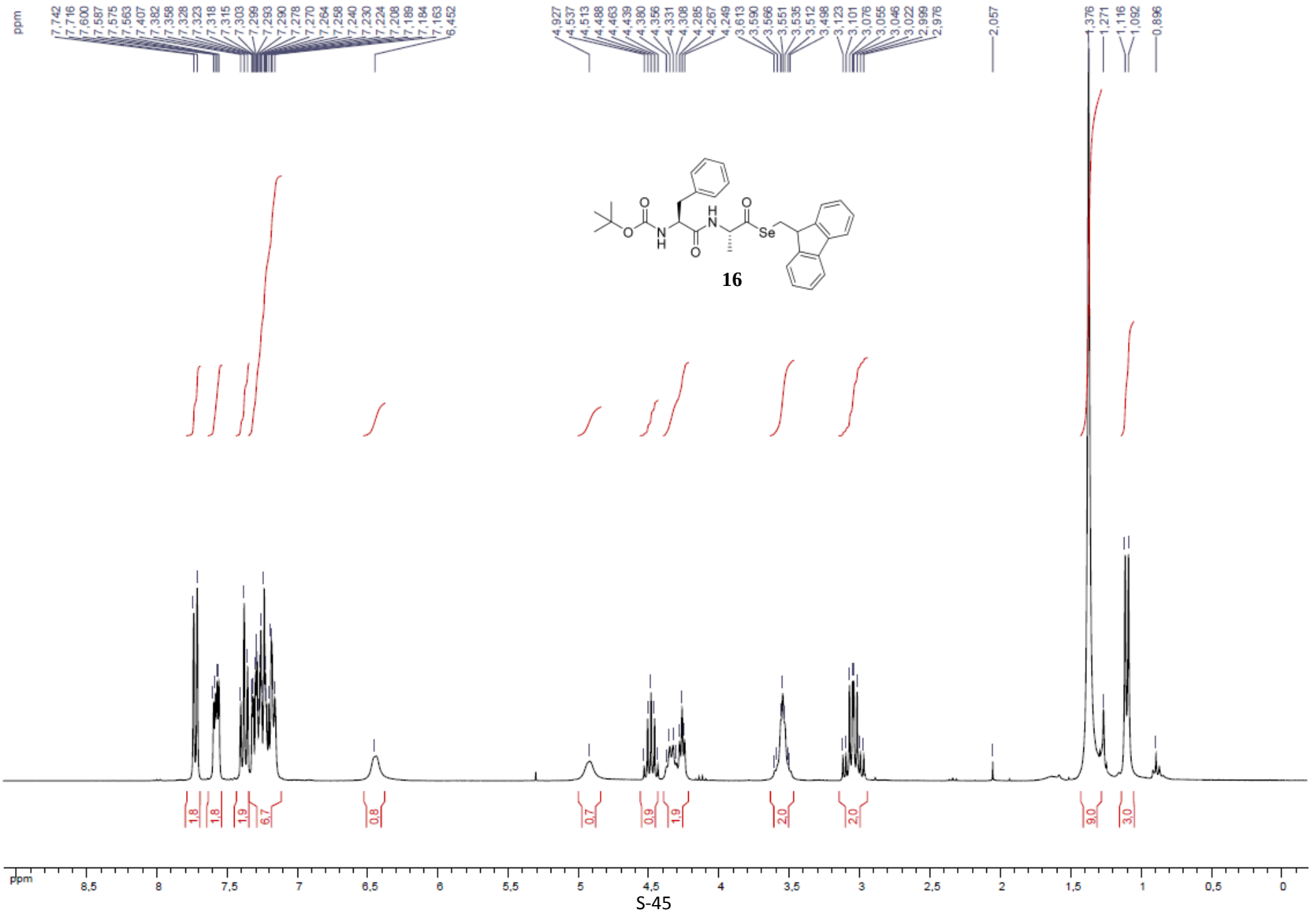
60
40
20
0


ppm
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7,328
7,323
7,318
7,315
7,303
7,299
7,293
7,290
7,278
7,270
7,264
7,258
7,240
7,230
7,224
7,208
7,189
7,184
7,163
6,452
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4,537
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4,488
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4,380
4,356
4,331
4,308
4,285
4,267
4,249
3,613
3,590
3,566
3,551
3,535
3,512
3,498
3,123
3,101
3,076
3,055
3,046
3,022
2,999
2,976
2,057
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1,092
0,896
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O
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O
N
H
O
Se
1,8
1,8
1,9
6,7
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0,9
1,9
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2,0
9,0
3,0
ppm
8,5
8
7,5
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5
4,5
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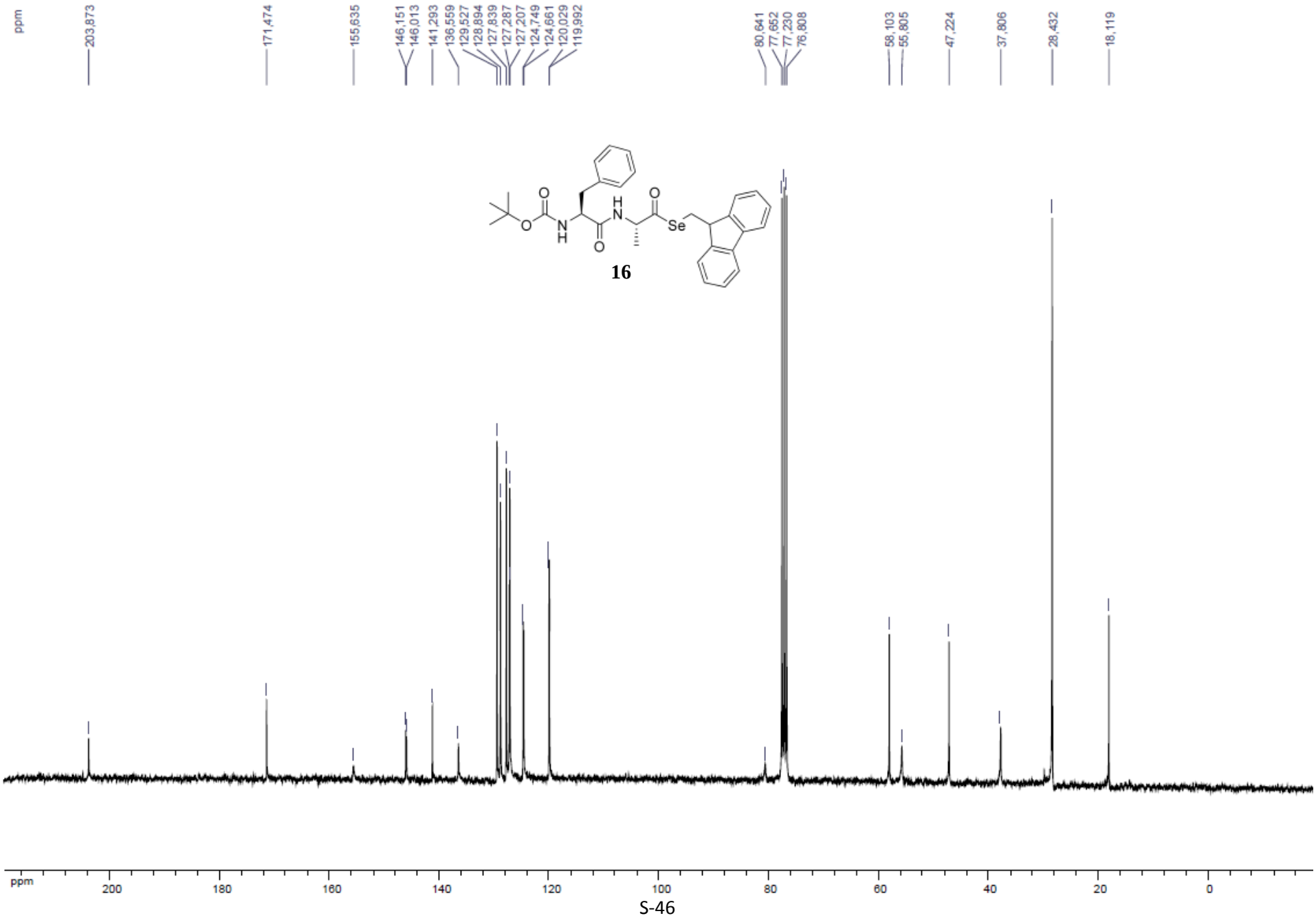
16


ppm
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128,894
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127,287
127,207
124,749
124,661
120,029
119,992
80,641
77,652
77,230
76,808
58,103
55,805
47,224
37,806
28,432
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O
O
N
H
O
H
N
O
Se
16
ppm
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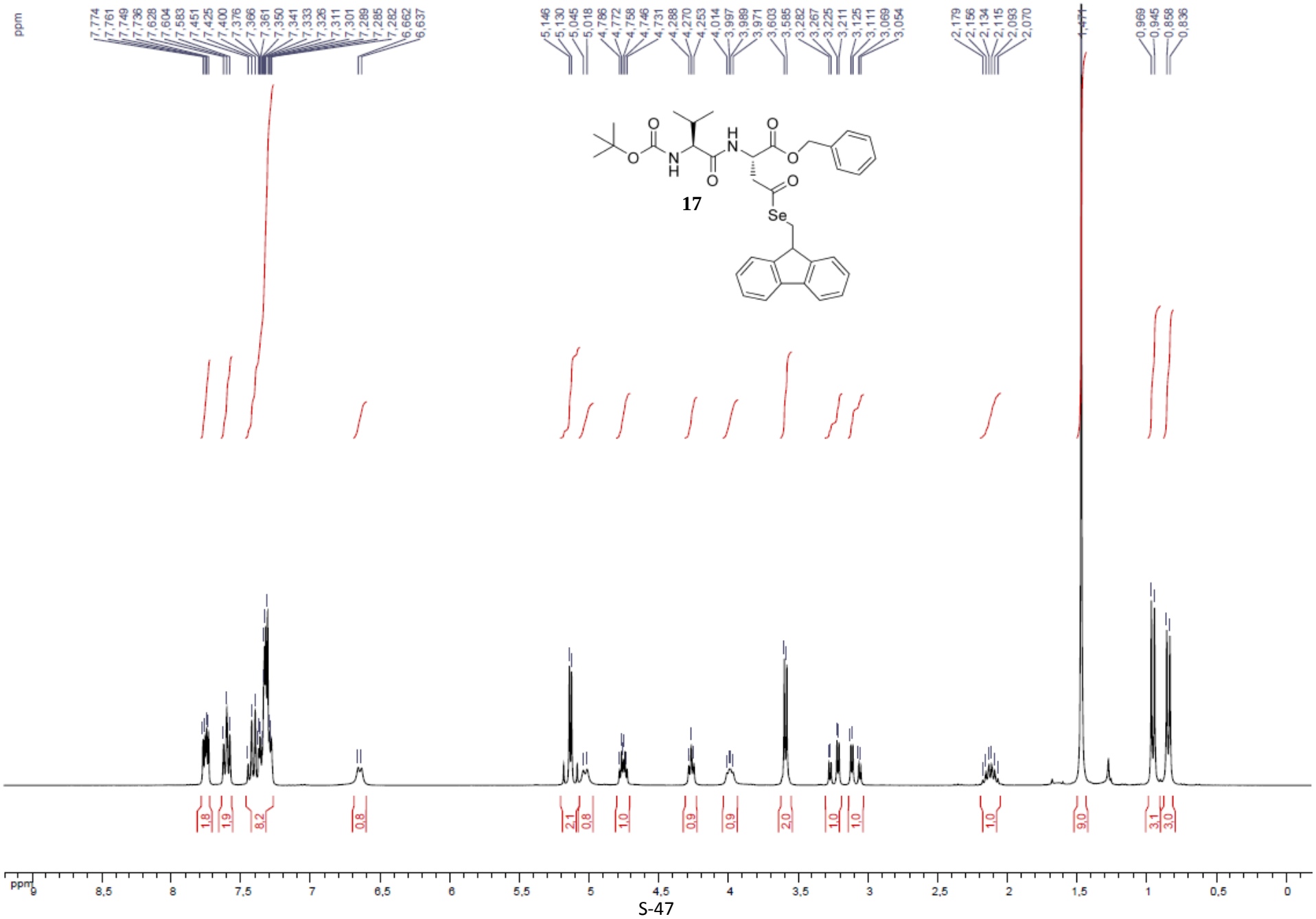
140
120
100
80
60
40
20
0


ppm
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7,400
7,376
7,366
7,361
7,350
7,341
7,333
7,326
7,311
7,301
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7,285
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3,603
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2,134
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2,070
1,471
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0,945
0,858
0,836
17
Se
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1,9
8,2
0,8
2,1
0,8
1,0
0,9
0,9
2,0
1,0
1,0
1,0
9,0
3,1
3,0
ppm
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8
7,5
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5,5
5
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4
3,5
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2,5
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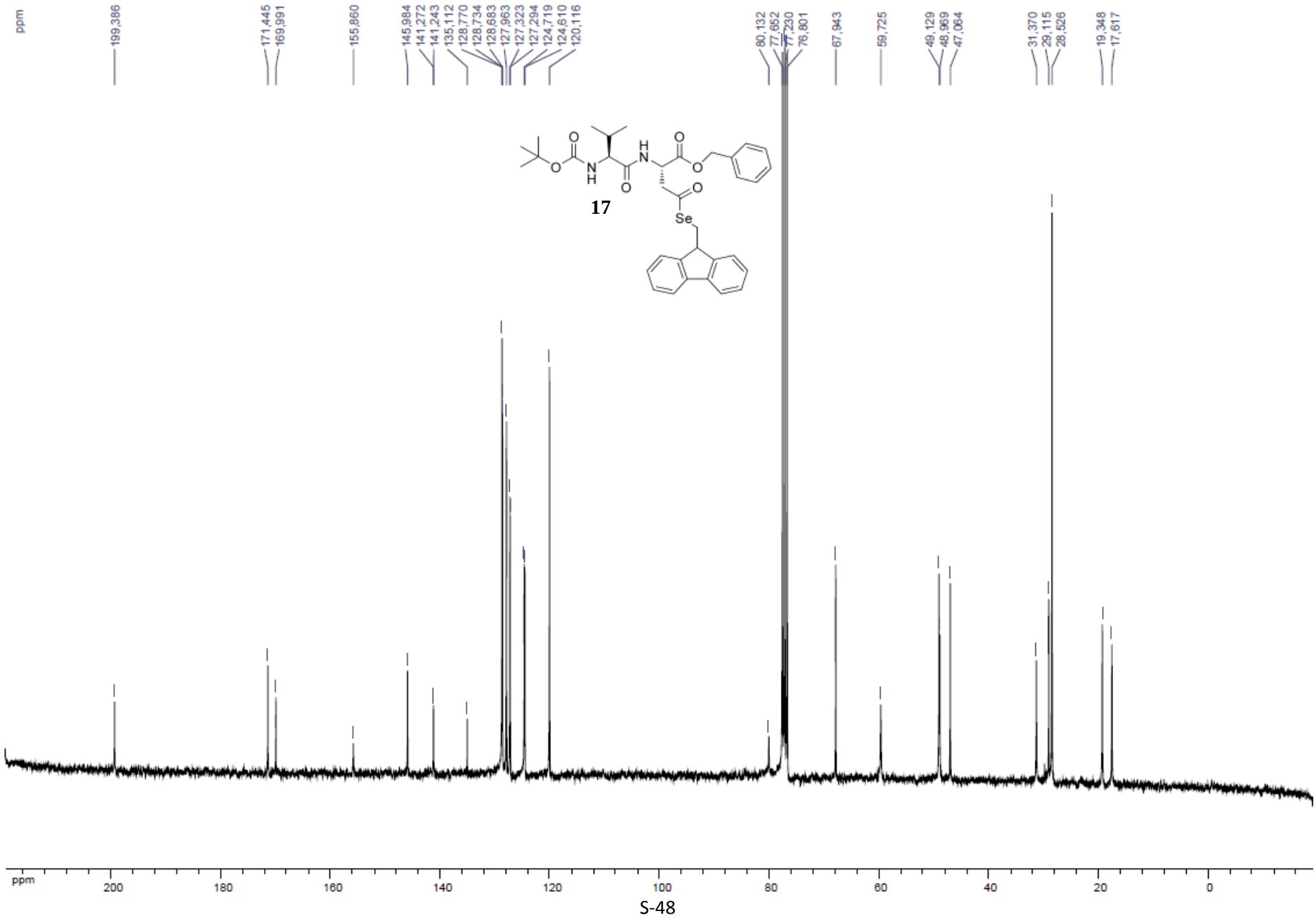
ppm
199,386
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135,112
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128,683
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127,294
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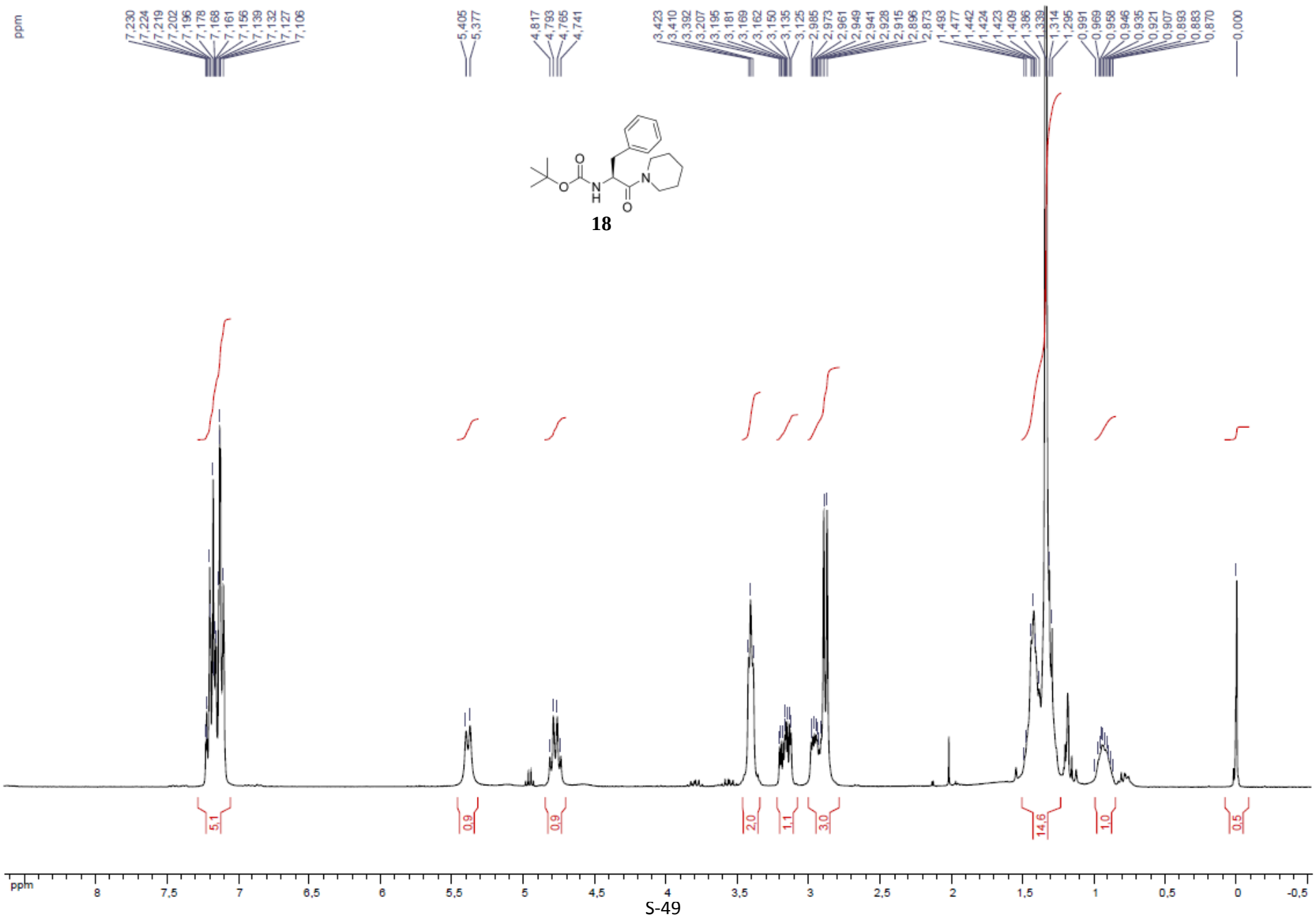
124,610
120,116
80,132
77,652
77,230
76,801
67,943
59,725
49,129
48,969
47,064
31,370
29,115
28,526
19,348
17,617
17
Se
ppm
200
180
160
140
120
100
80
60
40
20
0


ppm
7,230
7,224
7,219
7,202
7,196
7,178
7,168
7,161
7,156
7,139
7,132
7,127
7,106
5,405
5,377
4,817
4,793
4,765
4,741
3,423
3,410
3,392
3,207
3,195
3,181
3,169
3,162
3,150
3,135
3,125
2,985
2,973
2,961
2,949
2,941
2,928
2,915
2,896
2,873
1,493
1,477
1,442
1,424
1,423
1,409
1,386
1,339
1,314
1,295
0,991
0,969
0,958
0,946
0,935
0,921
0,907
0,893
0,883
0,870
0,000
5,1
0,9
0,9
2,0
1,1
3,0
14,6
1,0
0,5
ppm
8
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
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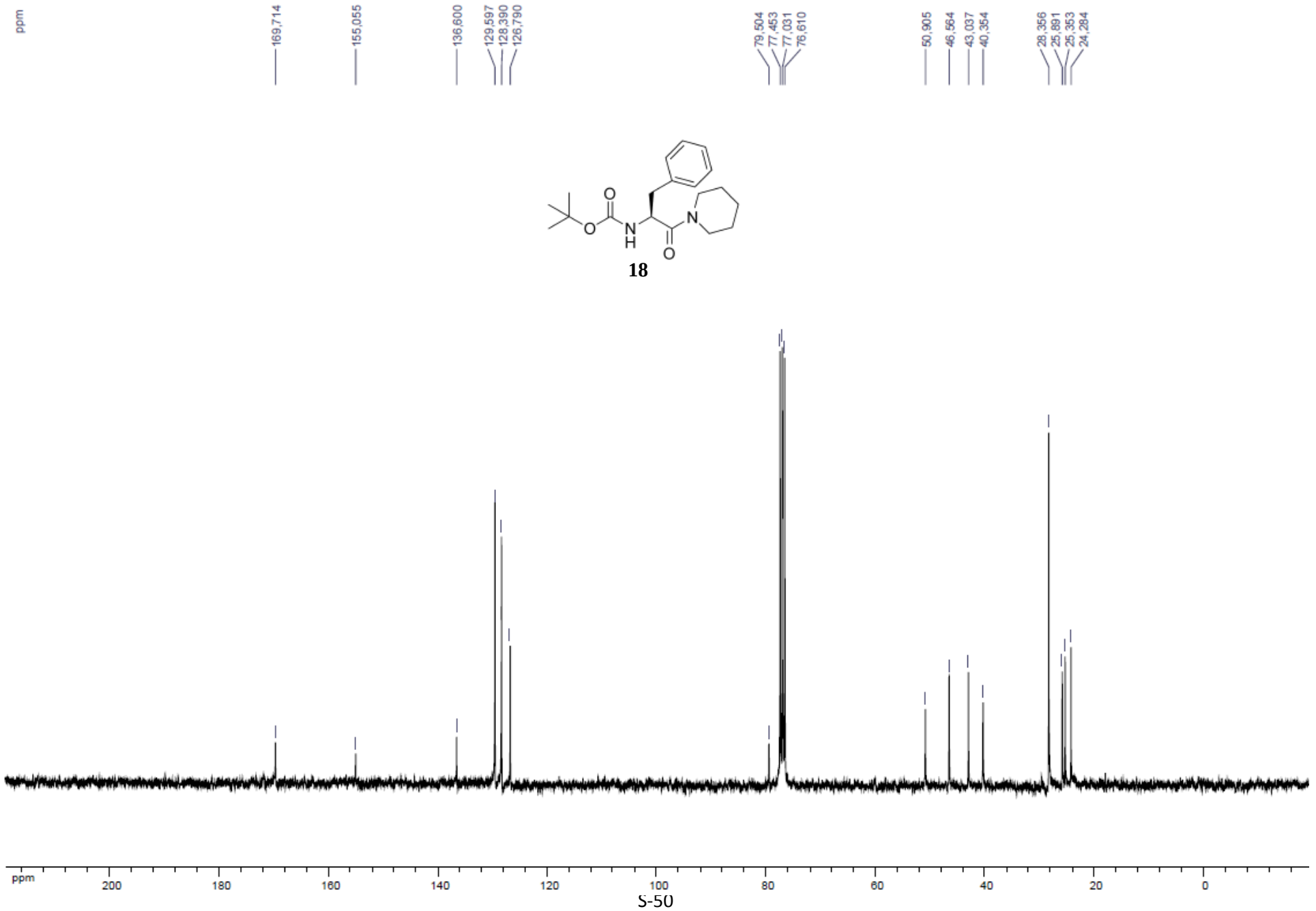
1,5
1
0,5
0
-0,5

18


ppm
169,714
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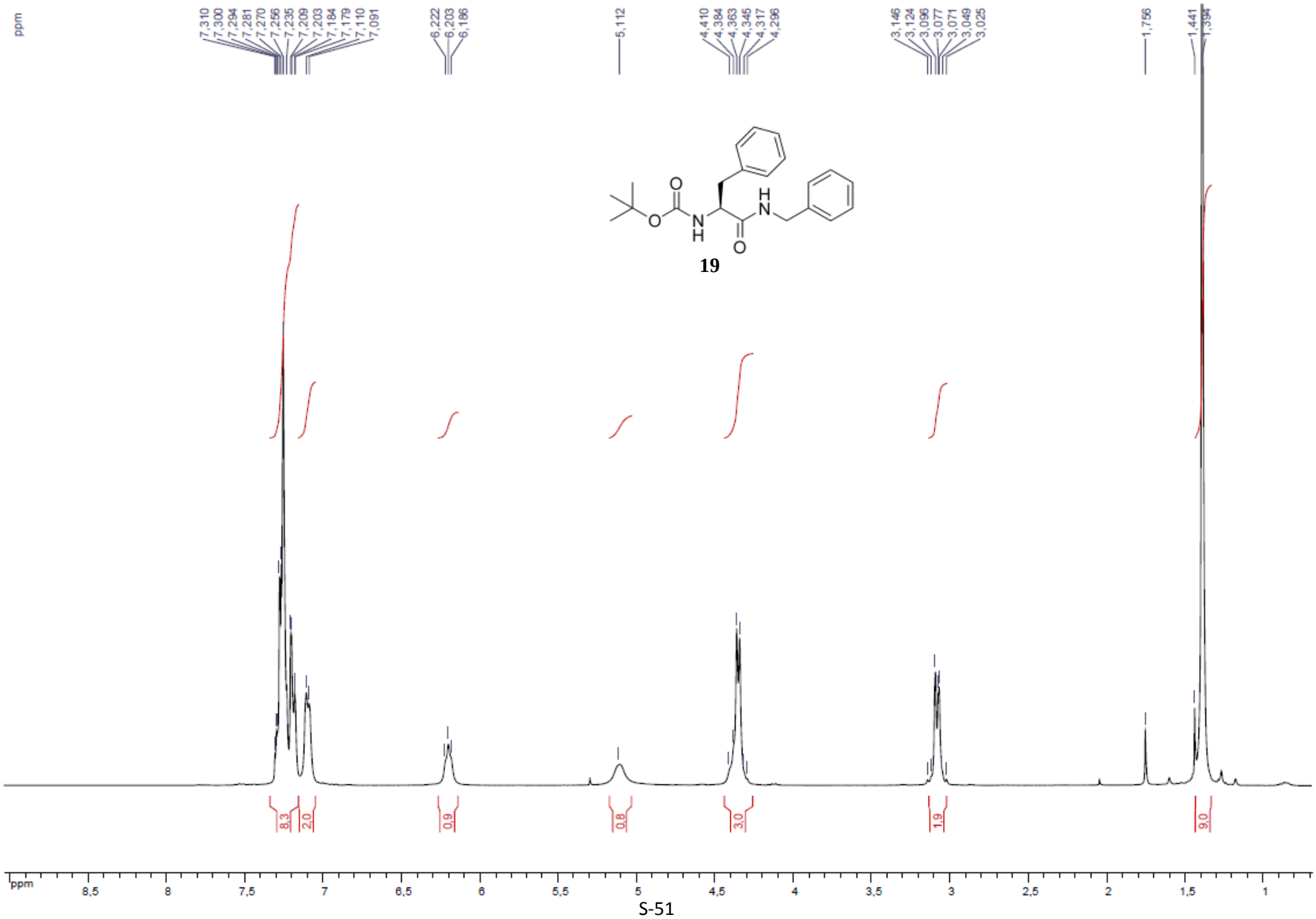
136,600
129,597
128,390
126,790
79,504
77,453
77,031
76,610
50,905
46,564
43,037
40,354
28,356
25,891
25,353
24,284
O
O
N
H
O
N
ppm
200
180
160
140
120
100
80
60
40
20
0

18


ppm
7,310
7,300
7,294
7,281
7,270
7,256
7,235
7,209
7,203
7,184
7,179
7,110
7,091
6,222
6,203
6,186
5,112
4,410
4,384
4,363
4,345
4,317
4,296
3,146
3,124
3,096
3,077
3,071
3,049
3,025
1,756
1,441
1,394
8,3
2,0
0,9
0,8
3,0
1,9
9,0
ppm
8,5
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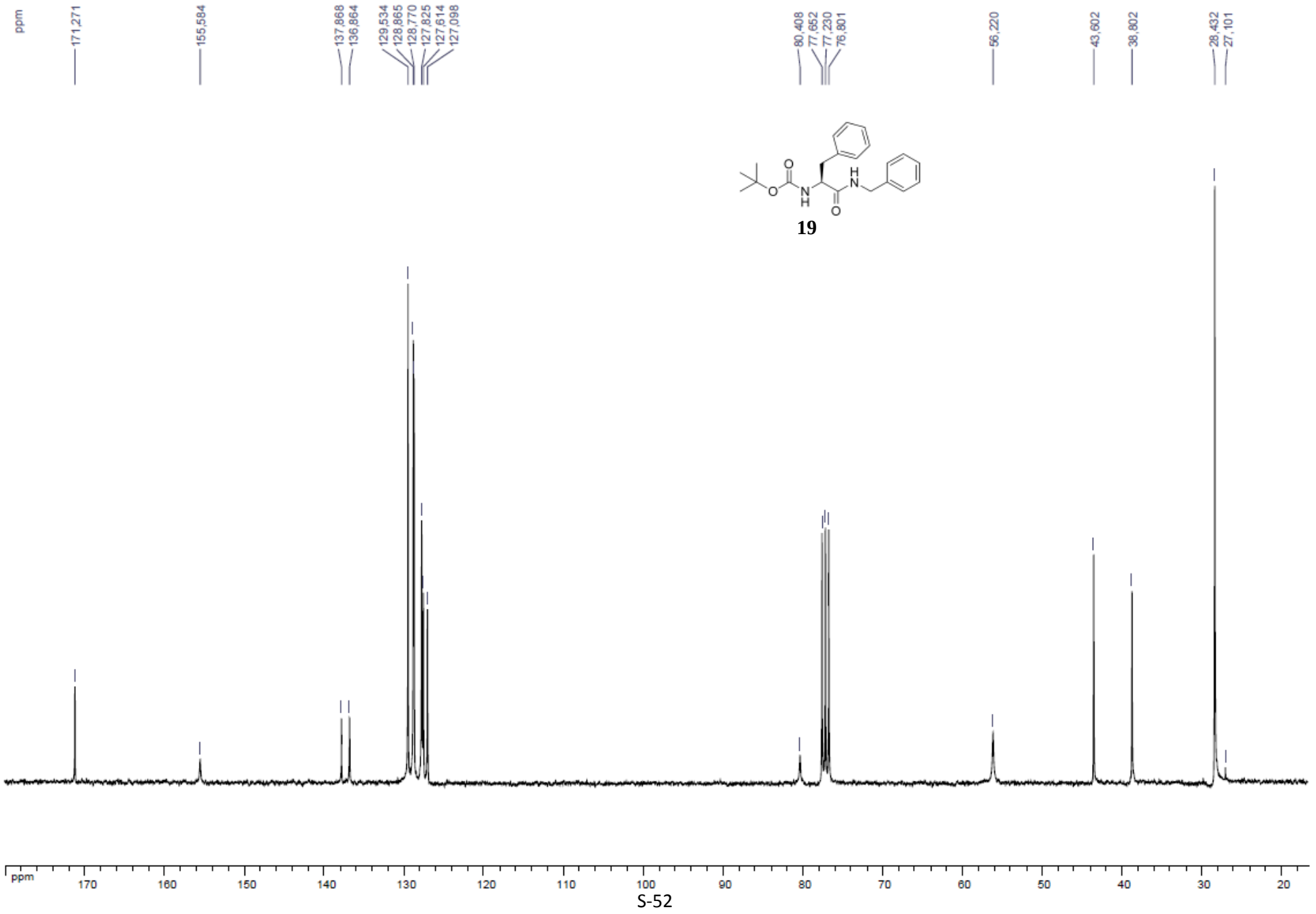
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1

19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171,271
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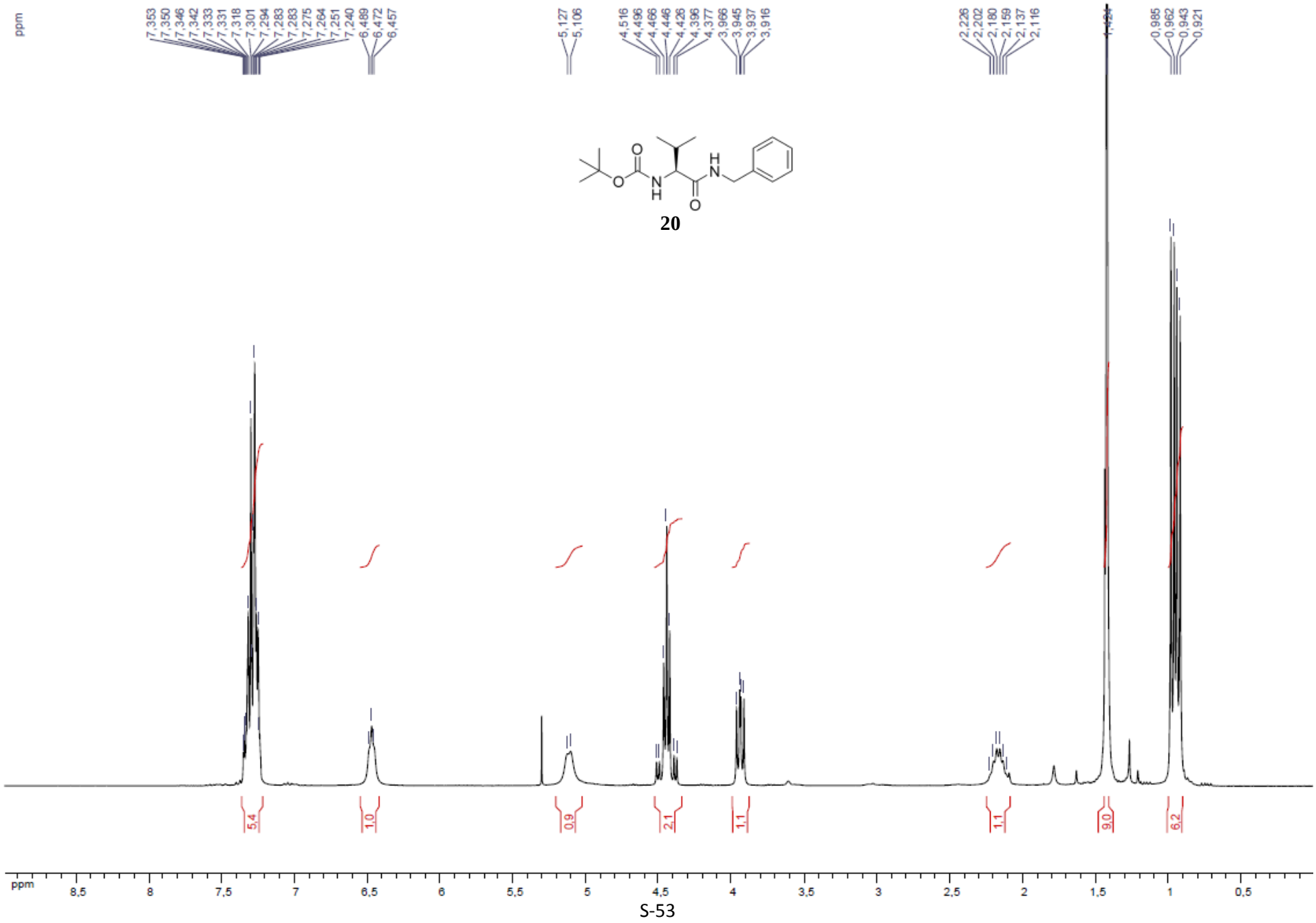
136,864
129,534
128,865
128,770
127,825
127,614
127,098
80,408
77,652
77,230
76,801
56,220
43,602
38,802
28,432
27,101
19
ppm
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20


ppm
7,353
7,350
7,346
7,342
7,333
7,331
7,318
7,301
7,294
7,283
7,283
7,275
7,264
7,251
7,240
6,489
6,472
6,457
5,127
5,106
4,516
4,496
4,466
4,446
4,426
4,396
4,377
3,966
3,945
3,937
3,916
2,226
2,202
2,180
2,159
2,137
2,116
1,424
0,985
0,962
0,943
0,921
5,4
1,0
0,9
2,1
1,1
1,1
9,0
6,2
ppm
8,5
8
7,5
7
6,5
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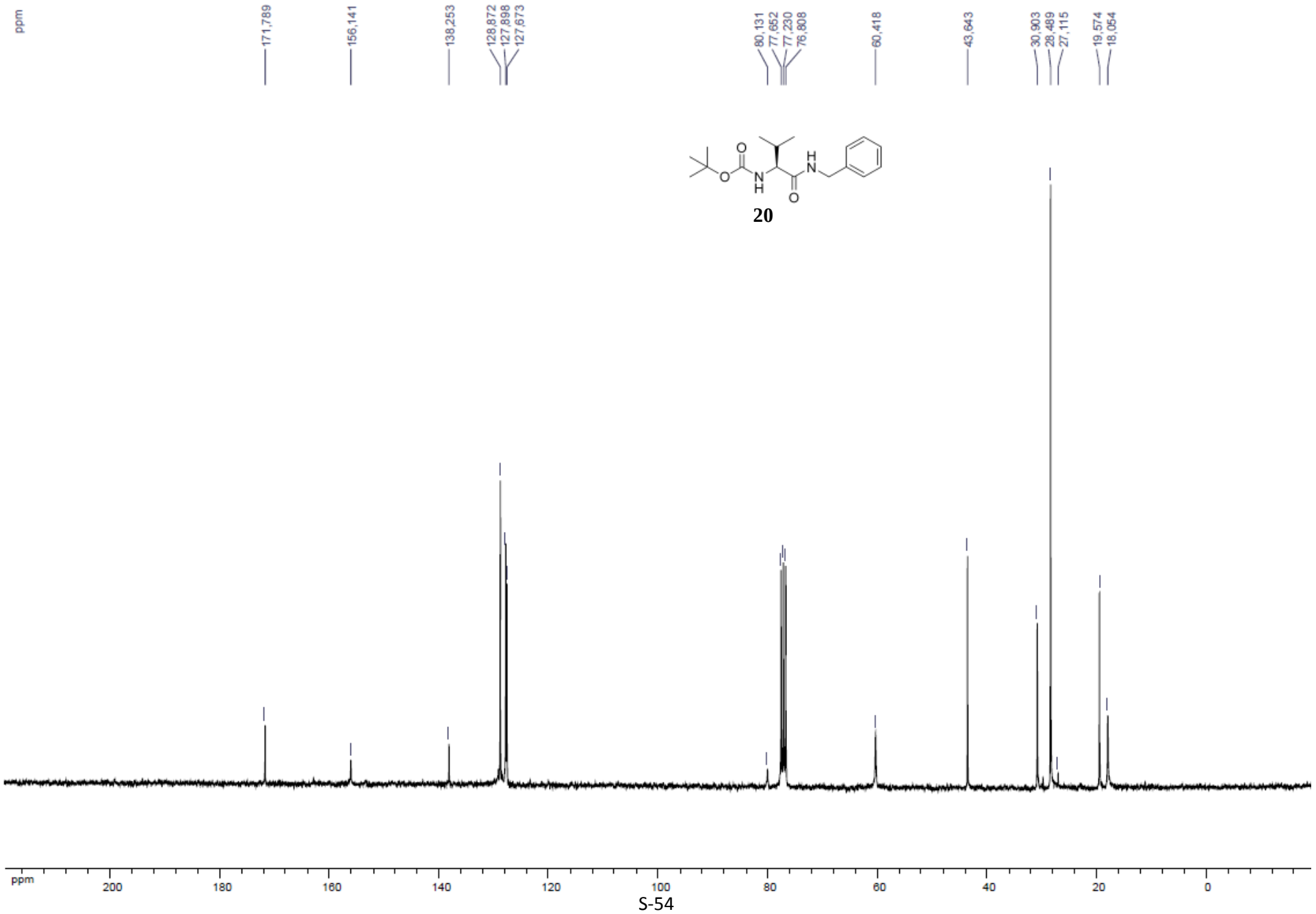
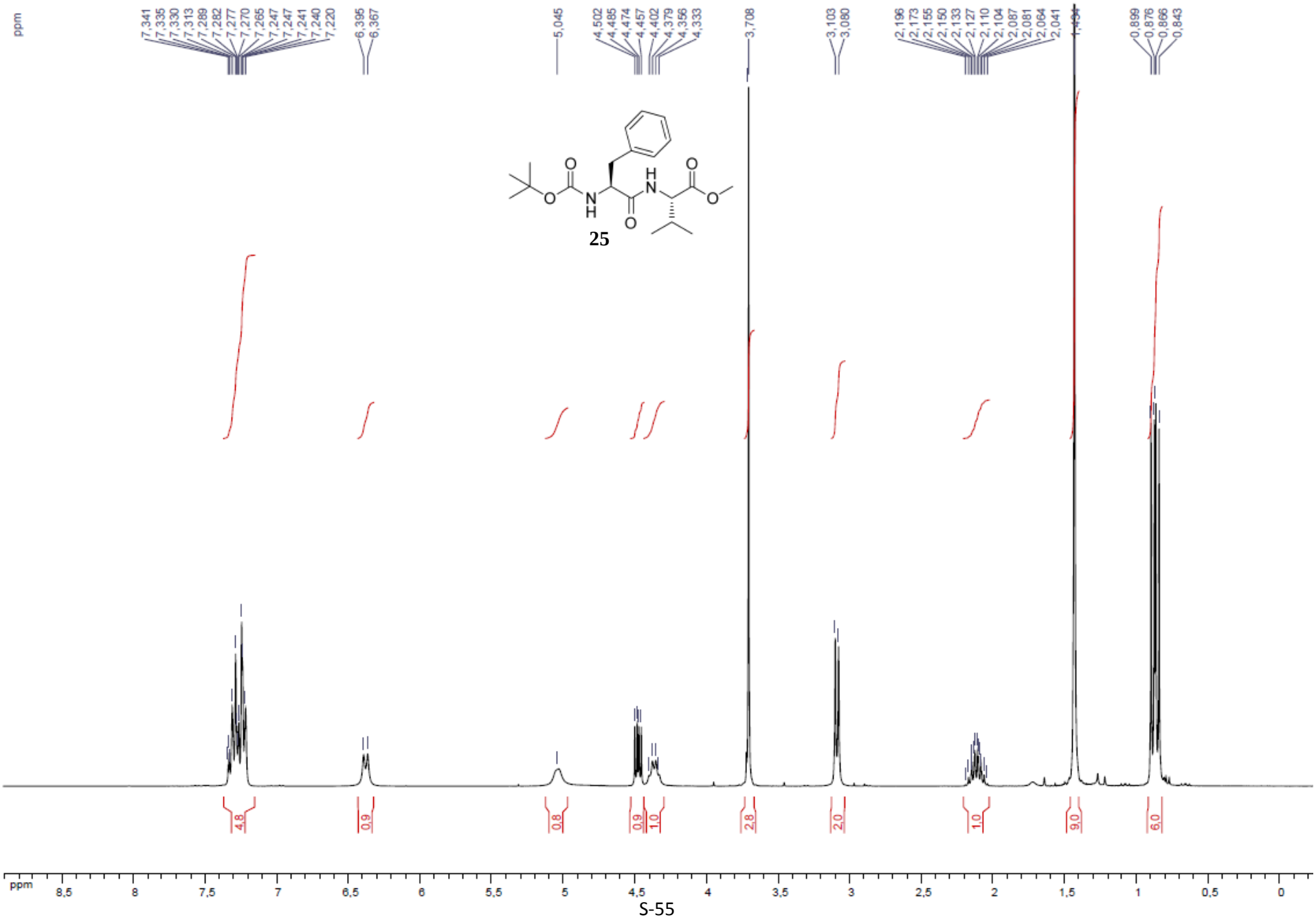
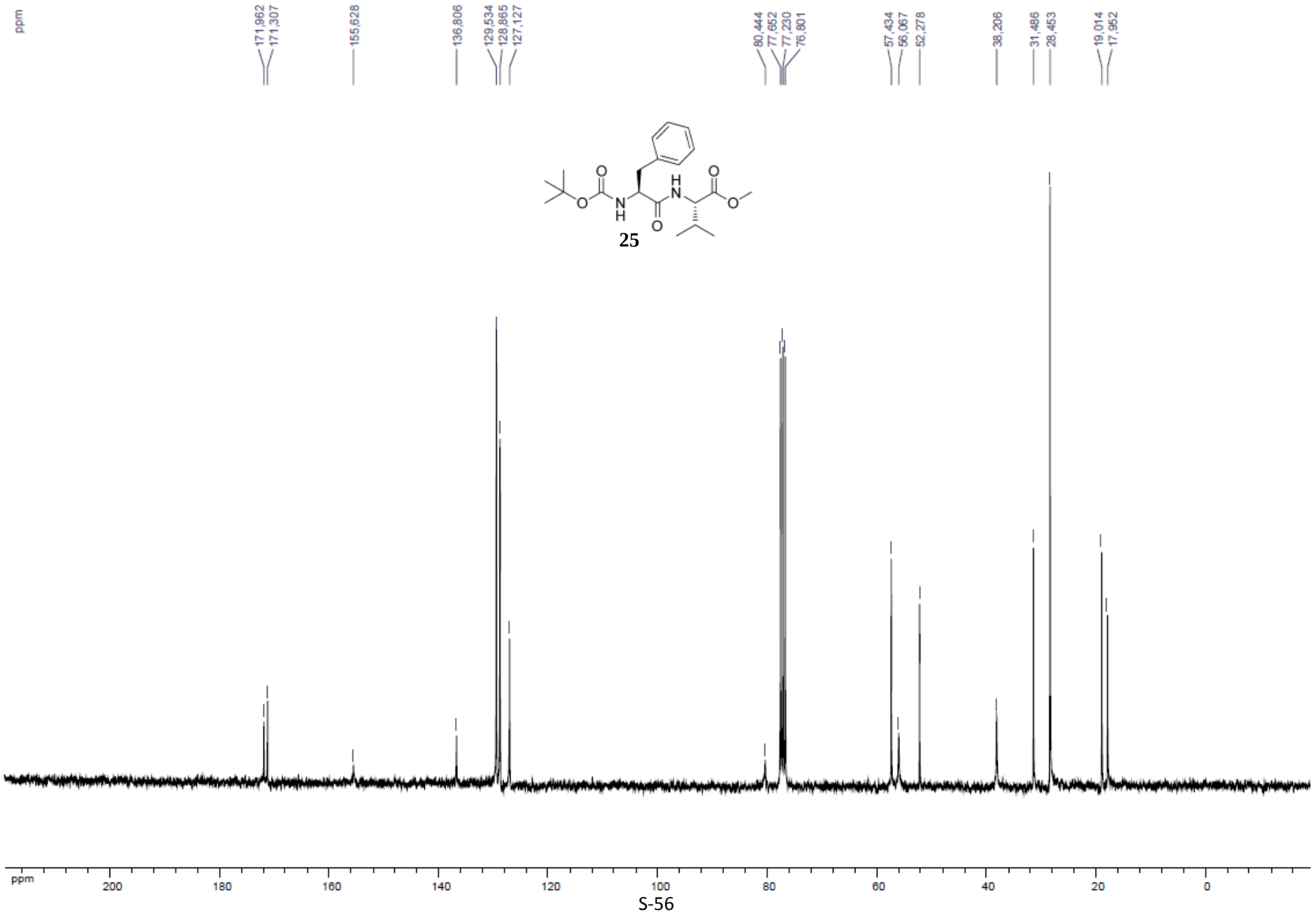
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5

20


ppm
171,789
156,141
138,253
128,872
127,898
127,673
80,131
77,652
77,230
76,808
60,418
43,643
30,903
28,489
27,115
19,574
18,054
20
ppm
200
180
160
140
120
100
80
60
40
20
0


ppm
7,341
7,335
7,330
7,313
7,289
7,282
7,277
7,270
7,265
7,247
7,247
7,241
7,240
7,220
6,395
6,367
5,045
4,502
4,485
4,474
4,457
4,402
4,379
4,356
4,333
3,708
3,103
3,080
2,196
2,173
2,155
2,150
2,133
2,127
2,110
2,104
2,087
2,081
2,064
2,041
1,434
0,899
0,876
0,866
0,843
4,8
0,9
0,8
0,9
1,0
2,8
2,0
1,0
9,0
6,0
ppm
8,5
8
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5
0

25


ppm
171,962
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155,628
136,806
129,534
128,865
127,127
80,444
77,652
77,230
76,801
57,434
56,067
52,278
38,206
31,486
28,453
19,014
17,952
25
ppm
200
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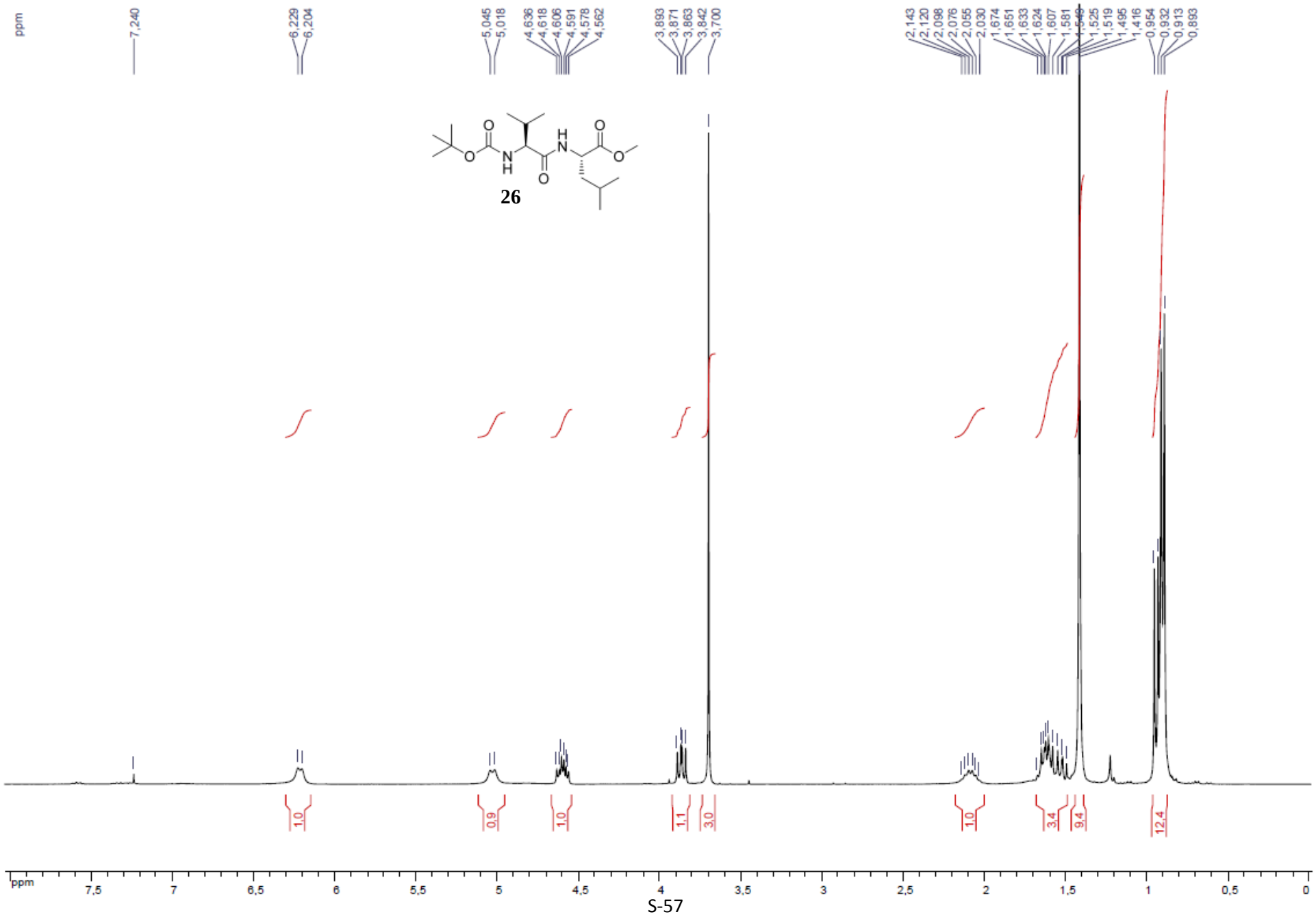
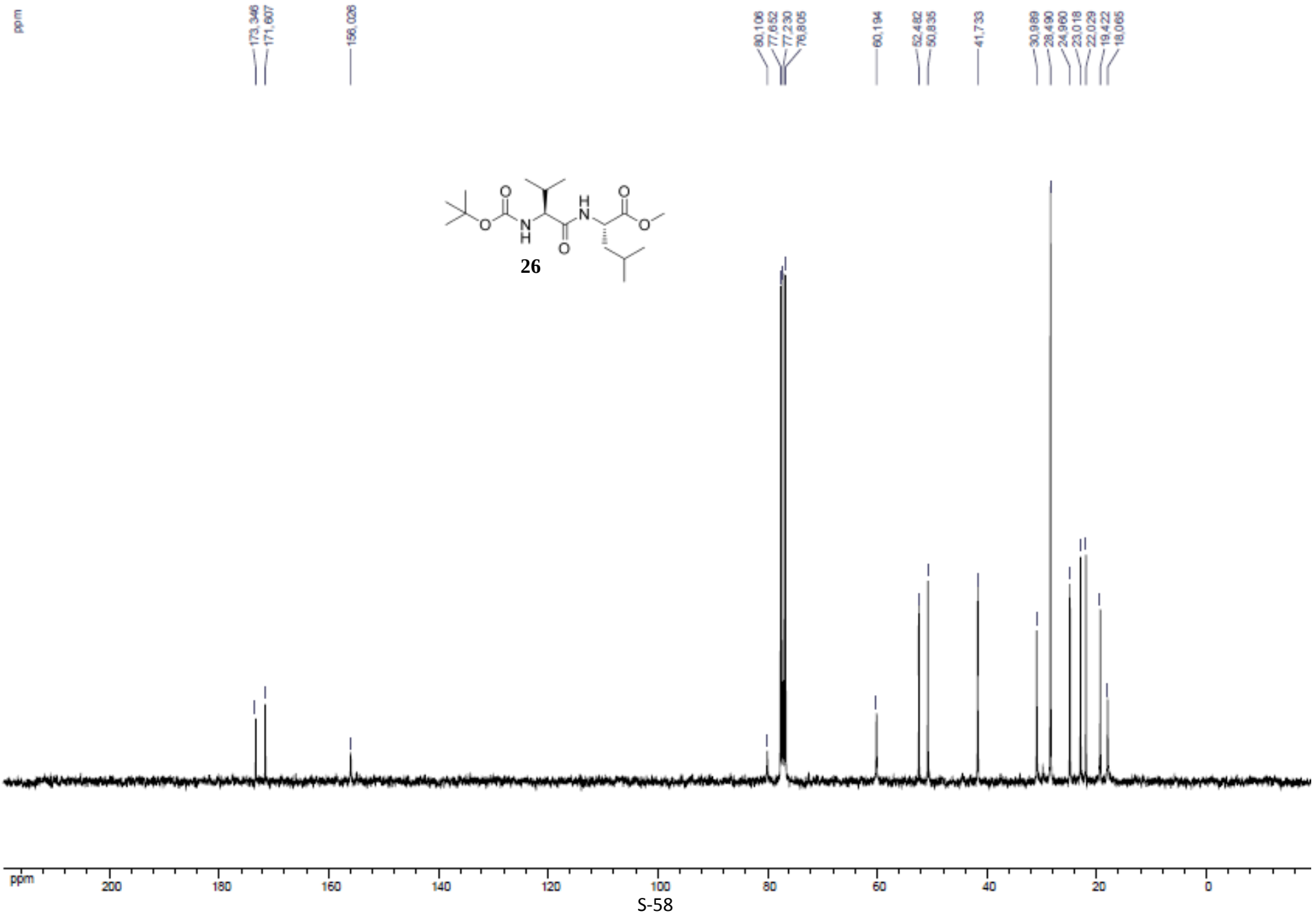
160
140
120
100
80
60
40
20
0


ppm
7,240
6,229
6,204
5,045
5,018
4,636
4,618
4,606
4,591
4,578
4,562
3,893
3,871
3,863
3,842
3,700
2,143
2,120
2,098
2,076
2,055
2,030
1,674
1,651
1,633
1,624
1,607
1,581
1,549
1,525
1,519
1,495
1,416
0,954
0,932
0,913
0,893
1,0
0,9
1,0
1,1
3,0
1,0
3,4
9,4
12,4
ppm
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5
0

26


ppm
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156,026
80,106
77,652
77,230
76,805
60,194
52,482
50,835
41,733
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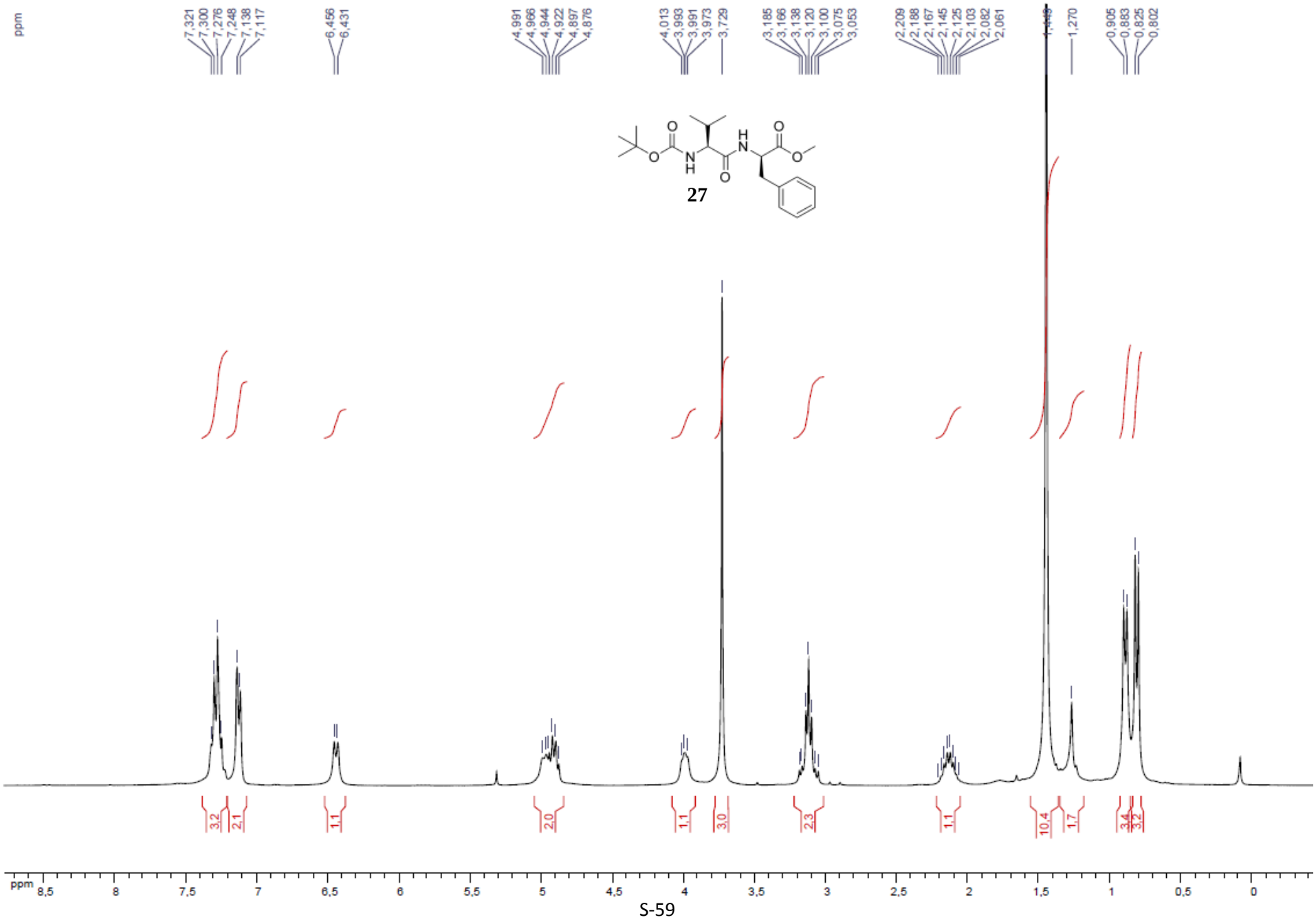
28,490
24,960
23,018
22,029
19,422
18,065
26
ppm
200
180
160
140
120
100
80
60
40
20
0


ppm
7,321
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7,276
7,248
7,138
7,117
6,456
6,431
4,991
4,966
4,944
4,922
4,897
4,876
4,013
3,993
3,991
3,973
3,729
3,185
3,166
3,138
3,120
3,100
3,075
3,053
2,209
2,188
2,167
2,145
2,125
2,103
2,082
2,061
1,443
1,270
0,905
0,883
0,825
0,802
27
3,2
2,1
1,1
2,0
1,1
3,0
2,3
1,1
10,4
1,7
3,4
3,2
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8
7,5
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6,5
6
5,5
5
4,5
4
3,5
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2,5
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1,5
1
0,5
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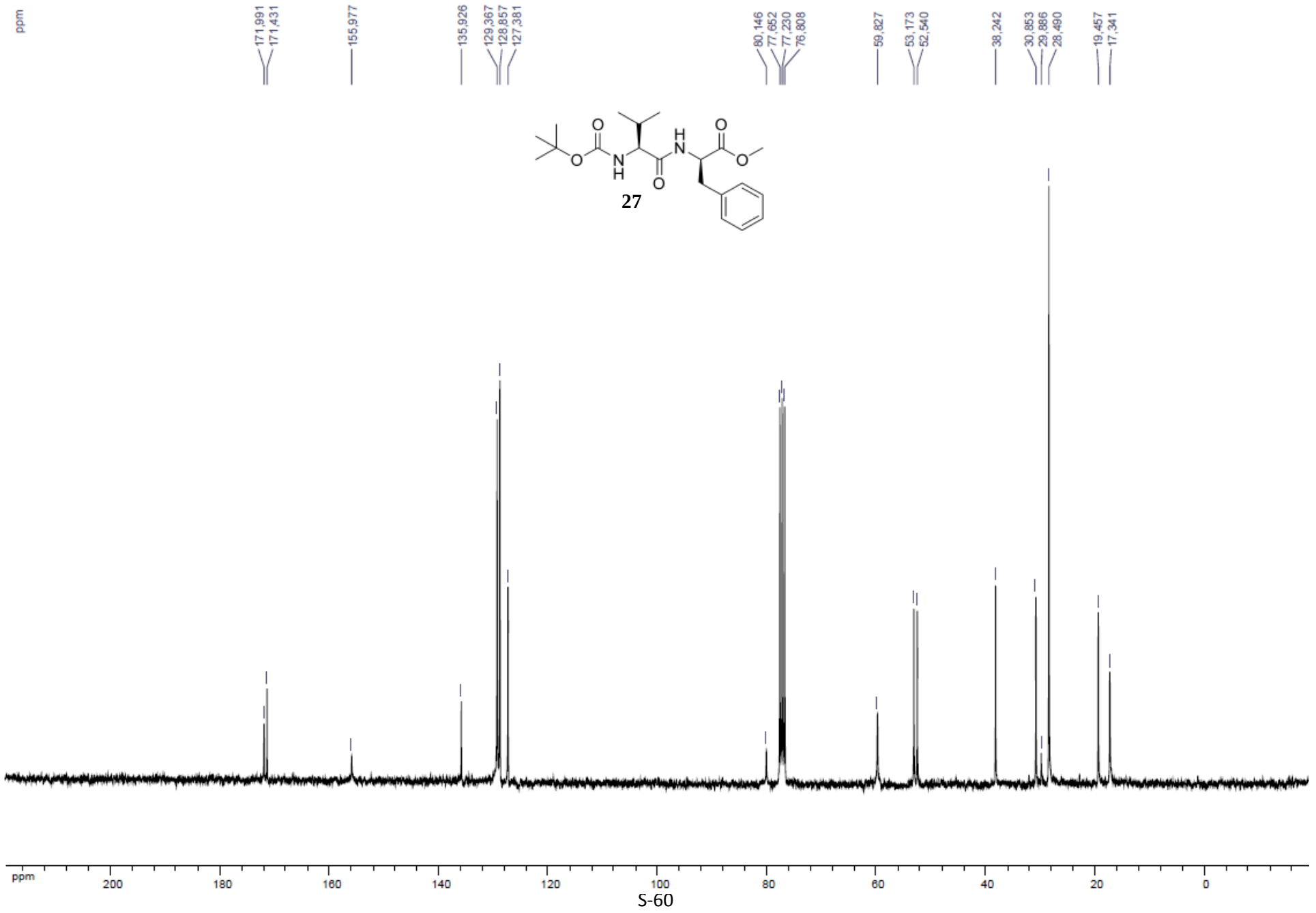
ppm
171,991
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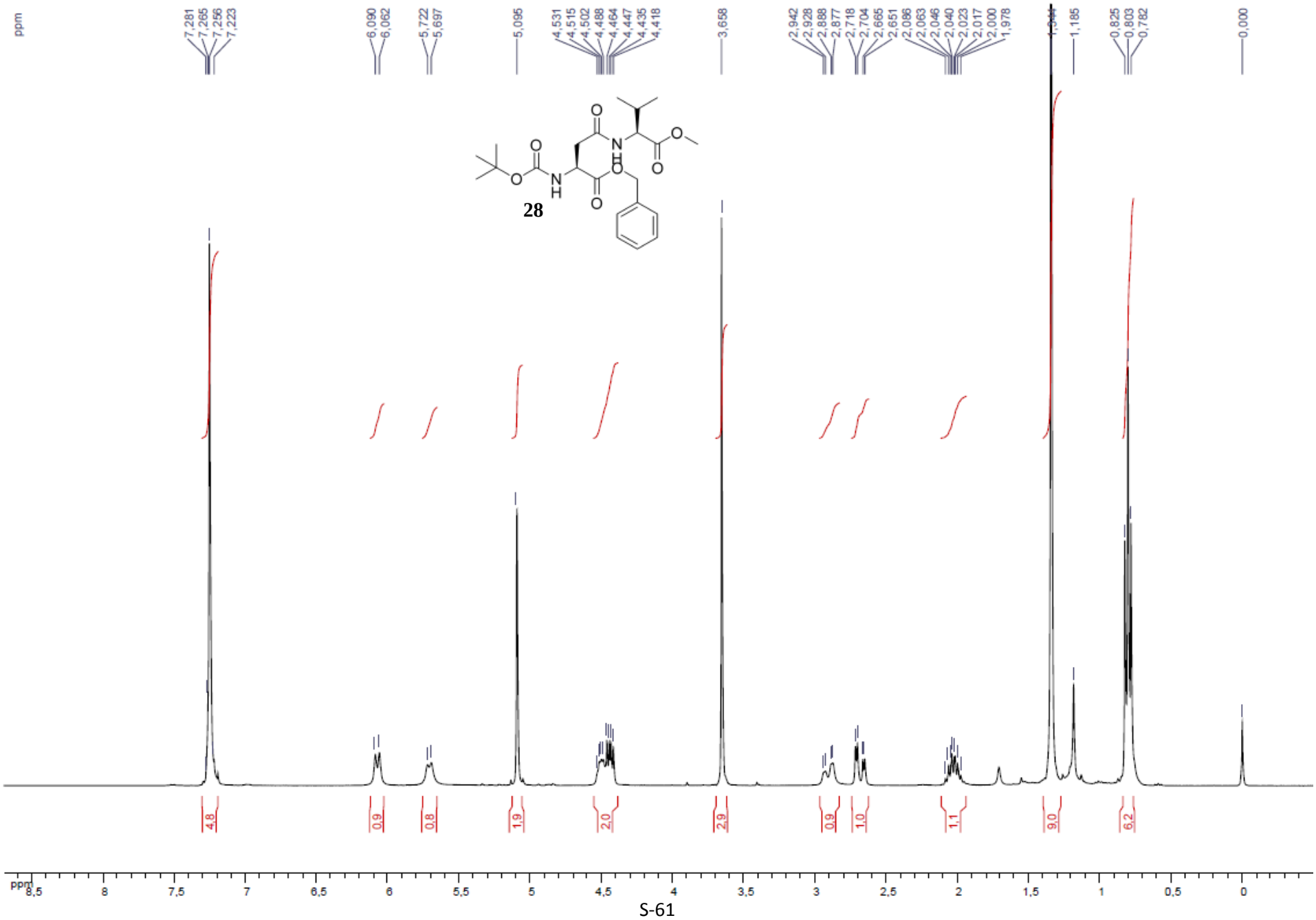
155,977
135,926
129,367
128,857
127,381
80,146
77,652
77,230
76,808
59,827
53,173
52,540
38,242
30,853
29,886
28,490
19,457
17,341
27
ppm
200
180
160
140
120
100
80
60
40
20
0


ppm
7,281
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7,256
7,223
6,090
6,062
5,722
5,697
5,095
4,531
4,515
4,502
4,488
4,464
4,447
4,435
4,418
3,658
2,942
2,928
2,888
2,877
2,718
2,704
2,665
2,651
2,086
2,063
2,046
2,040
2,023
2,017
2,000
1,978
1,185
0,825
0,803
0,782
0,000
28
4,8
0,9
0,8
1,9
2,0
2,9
0,9
1,0
1,1
9,0
6,2
ppm
8,5
8
7,5
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6,5
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5,5
5
4,5
4
3,5
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2,5
2
1,5
1
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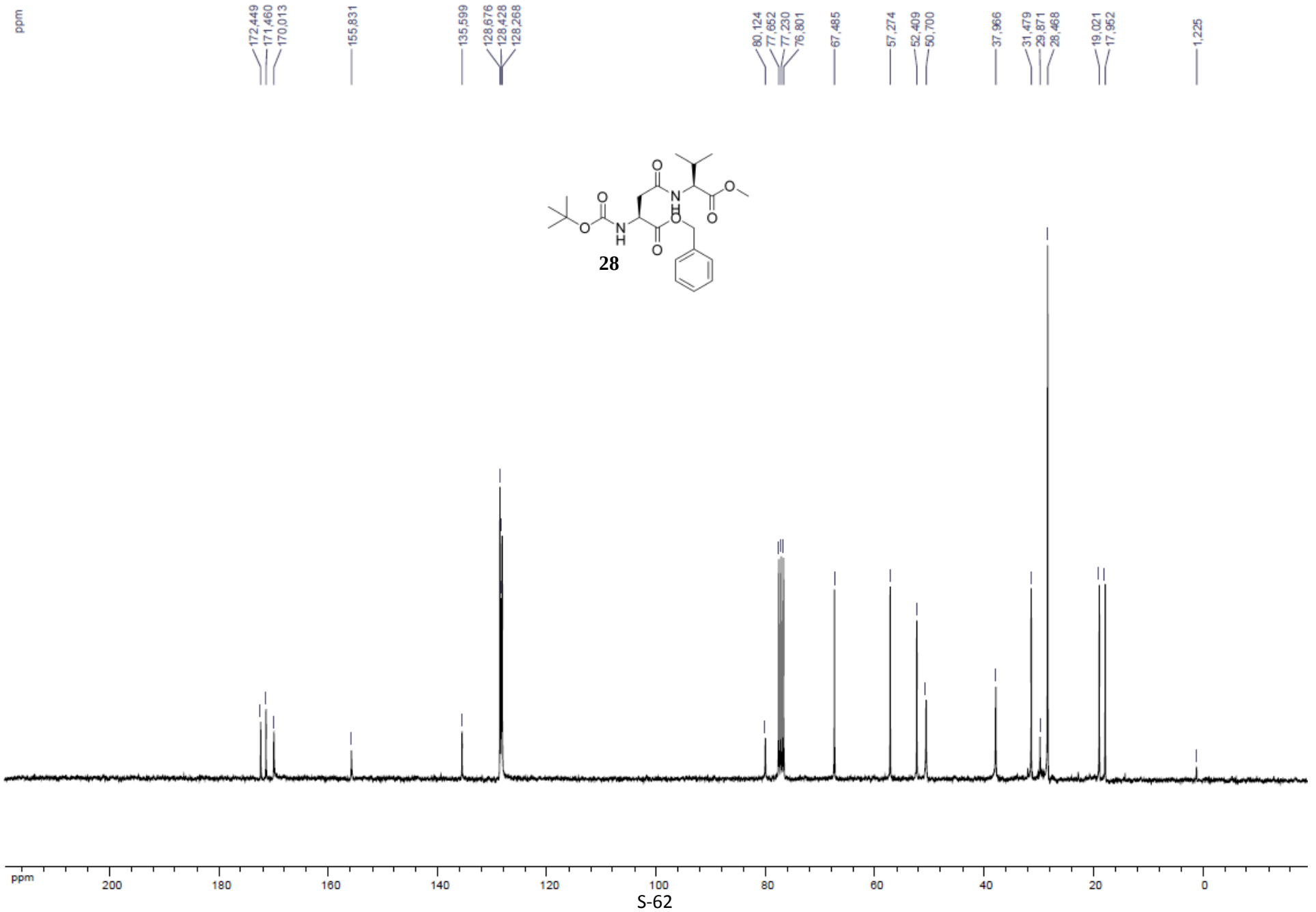
ppm
172,449
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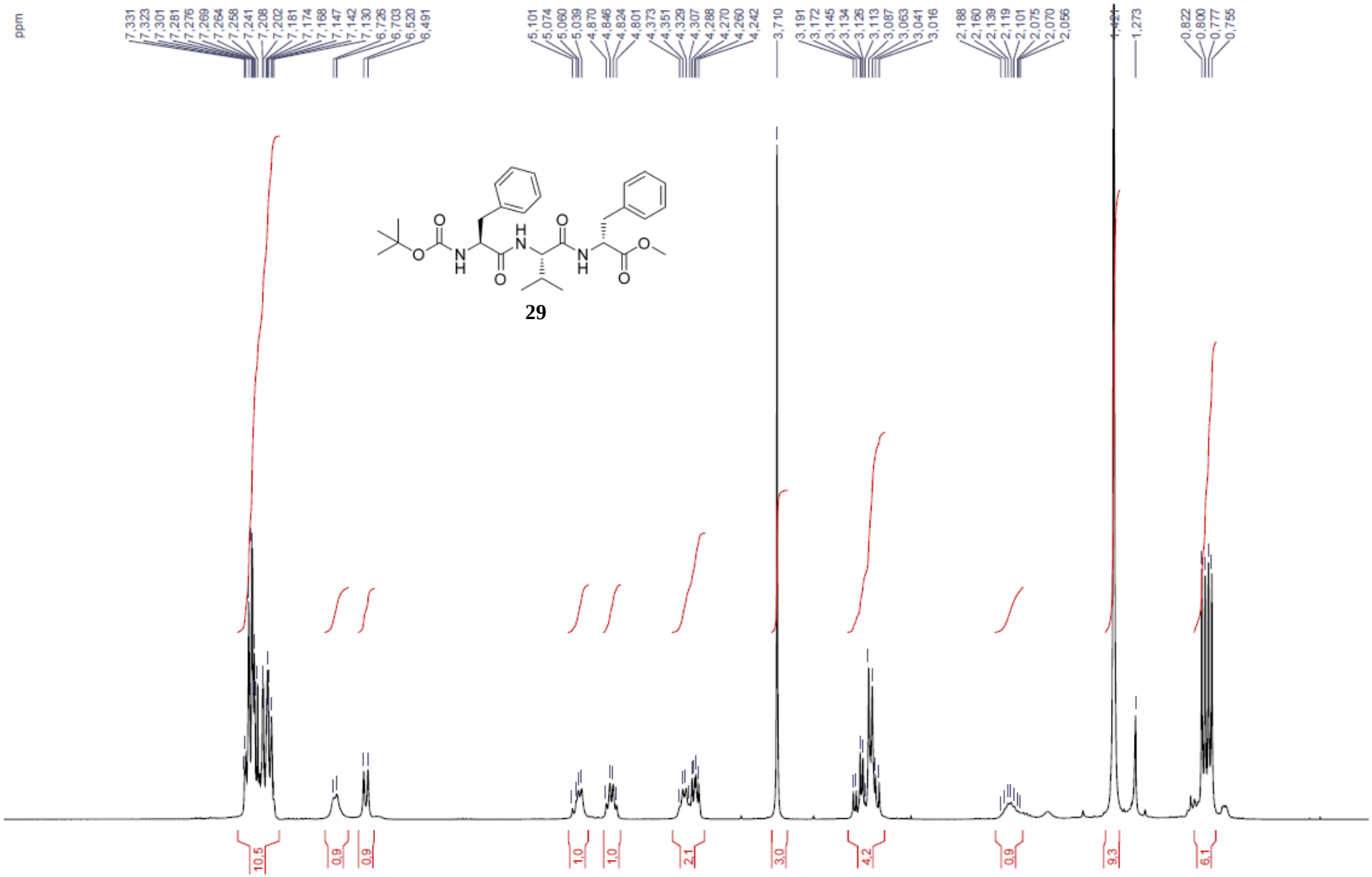
135,599
128,676
128,428
128,268
80,124
77,652
77,230
76,801
67,485
57,274
52,409
50,700
37,966
31,479
29,871
28,468
19,021
17,952
1,225
28
ppm
200
180
160
140
120
100
80
60
40
20
0


ppm
7,331
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7,276
7,269
7,264
7,258
7,241
7,208
7,202
7,181
7,174
7,168
7,147
7,142
7,130
6,726
6,703
6,520
6,491
5,101
5,074
5,060
5,039
4,870
4,846
4,824
4,801
4,373
4,351
4,329
4,307
4,288
4,270
4,260
4,242
3,710
3,191
3,172
3,145
3,134
3,126
3,113
3,087
3,063
3,041
3,016
2,188
2,160
2,139
2,119
2,101
2,075
2,070
2,056
1,421
1,273
0,822
0,800
0,777
0,755
10,5
0,9
0,9
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1,0
2,1
3,0
4,2
0,9
9,3
6,1
ppm
8,5
8
7,5
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5
4,5
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2
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0,5
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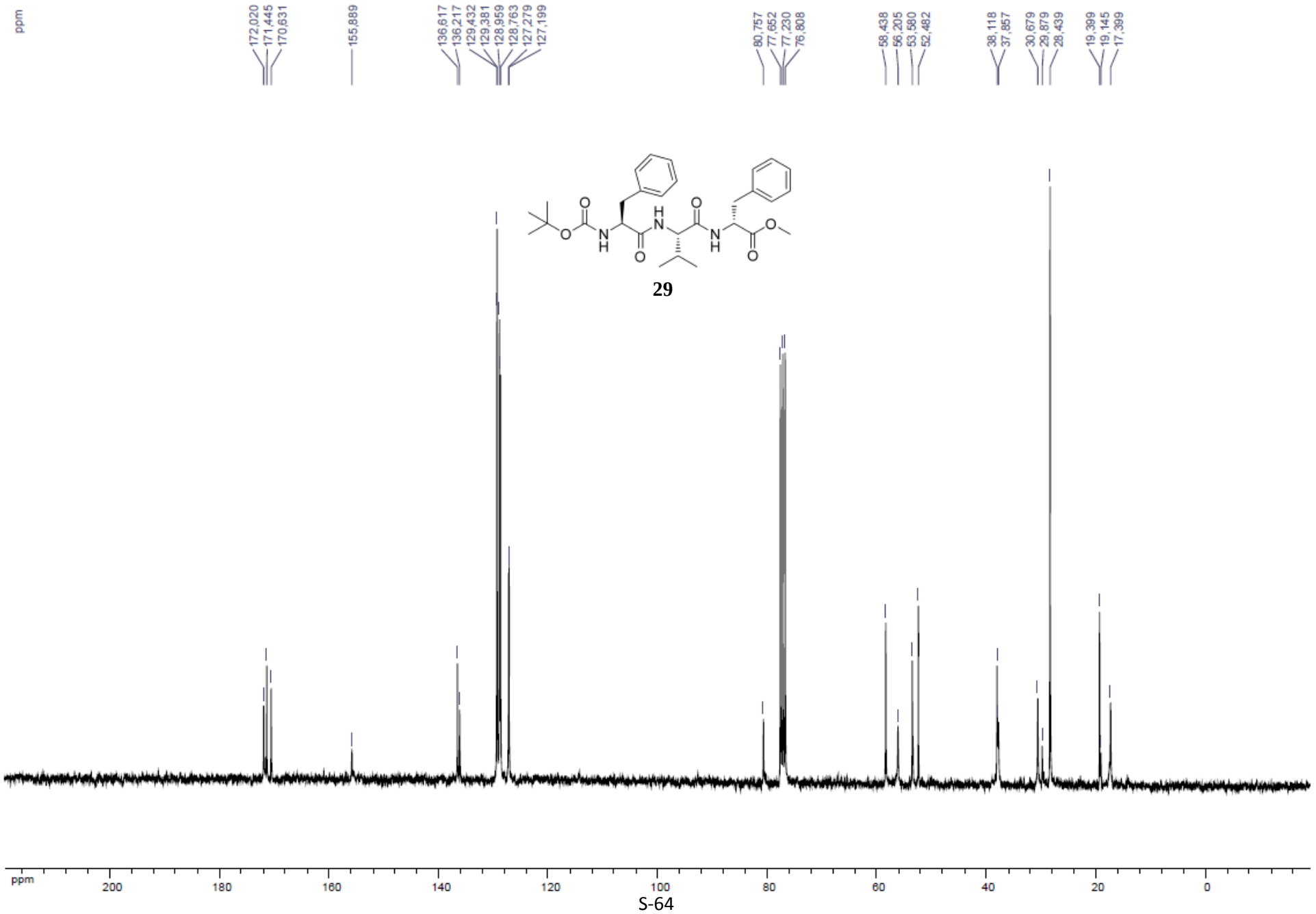
29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172,020
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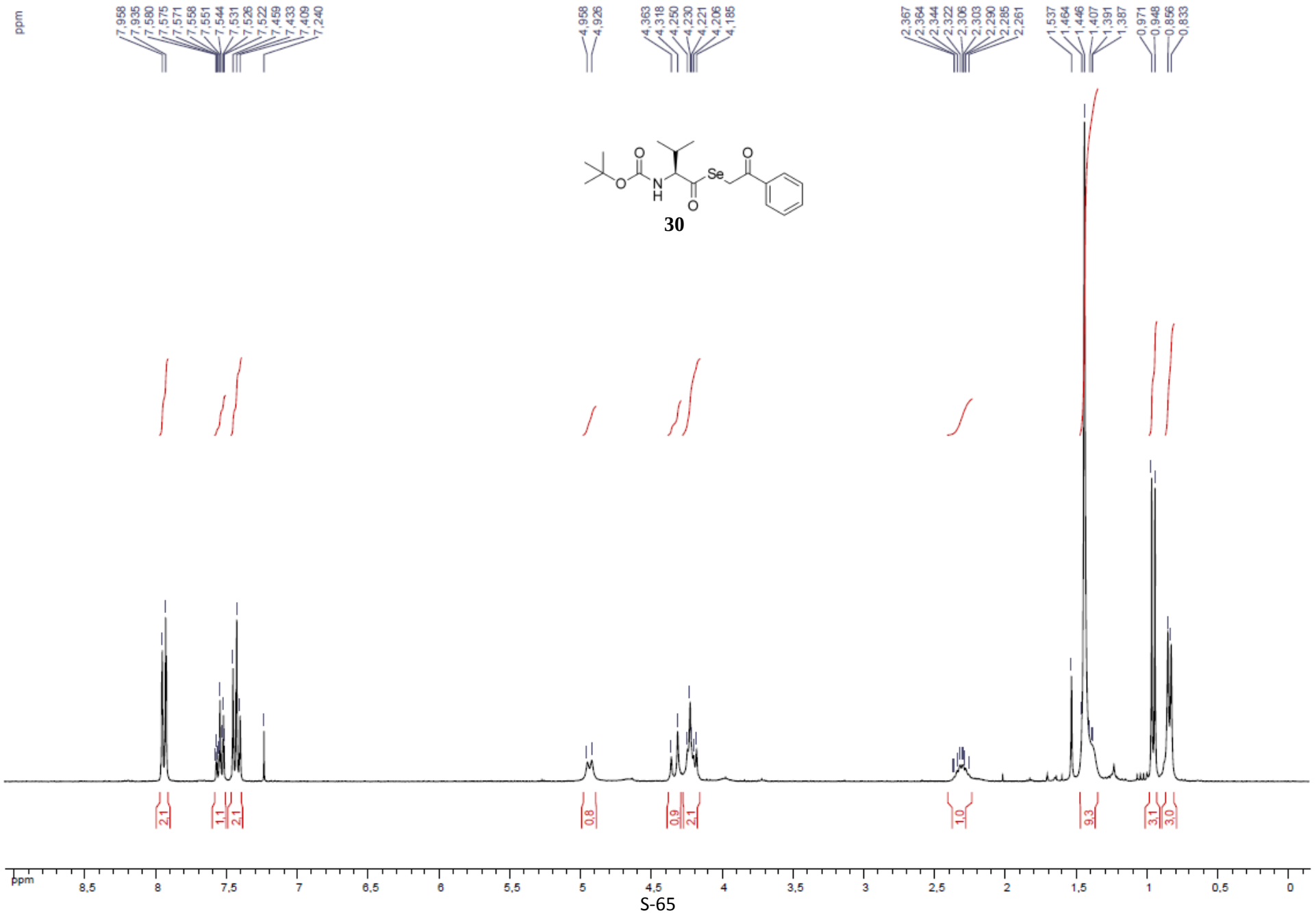
129,381
128,959
128,763
127,279
127,199
80,757
77,652
77,230
76,808
58,438
56,205
53,580
52,482
38,118
37,857
30,679
29,879
28,439
19,399
19,145
17,399
ppm
200
180
160
140
120
100
80
60
40
20
0

29


ppm
7,958
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7,575
7,571
7,558
7,551
7,544
7,531
7,526
7,522
7,459
7,433
7,409
7,240
4,958
4,926
4,363
4,318
4,250
4,230
4,221
4,206
4,185
2,367
2,364
2,344
2,322
2,306
2,303
2,290
2,285
2,261
1,537
1,464
1,446
1,407
1,391
1,387
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0,948
0,856
0,833
O
O
N
H
O
Se
O
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1,1
2,1
0,8
0,9
2,1
1,0
9,3
3,1
3,0
ppm
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4,5
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2
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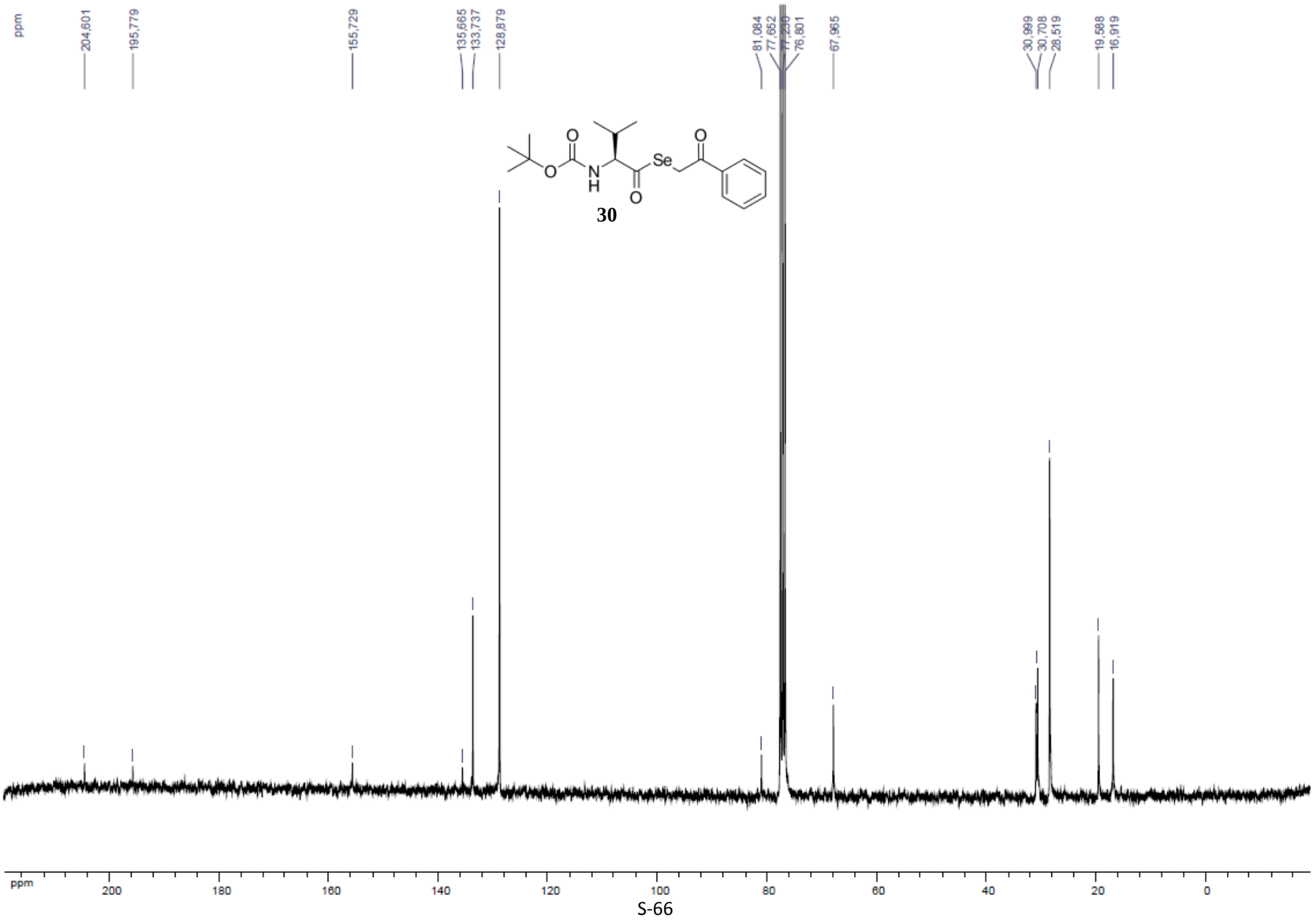
30


ppm
204,601
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135,665
133,737
128,879
81,084
77,652
77,236
76,801
67,965
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O
O
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H
O
O
Se
O
30
ppm
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180
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140
120
100
80
60
40
20
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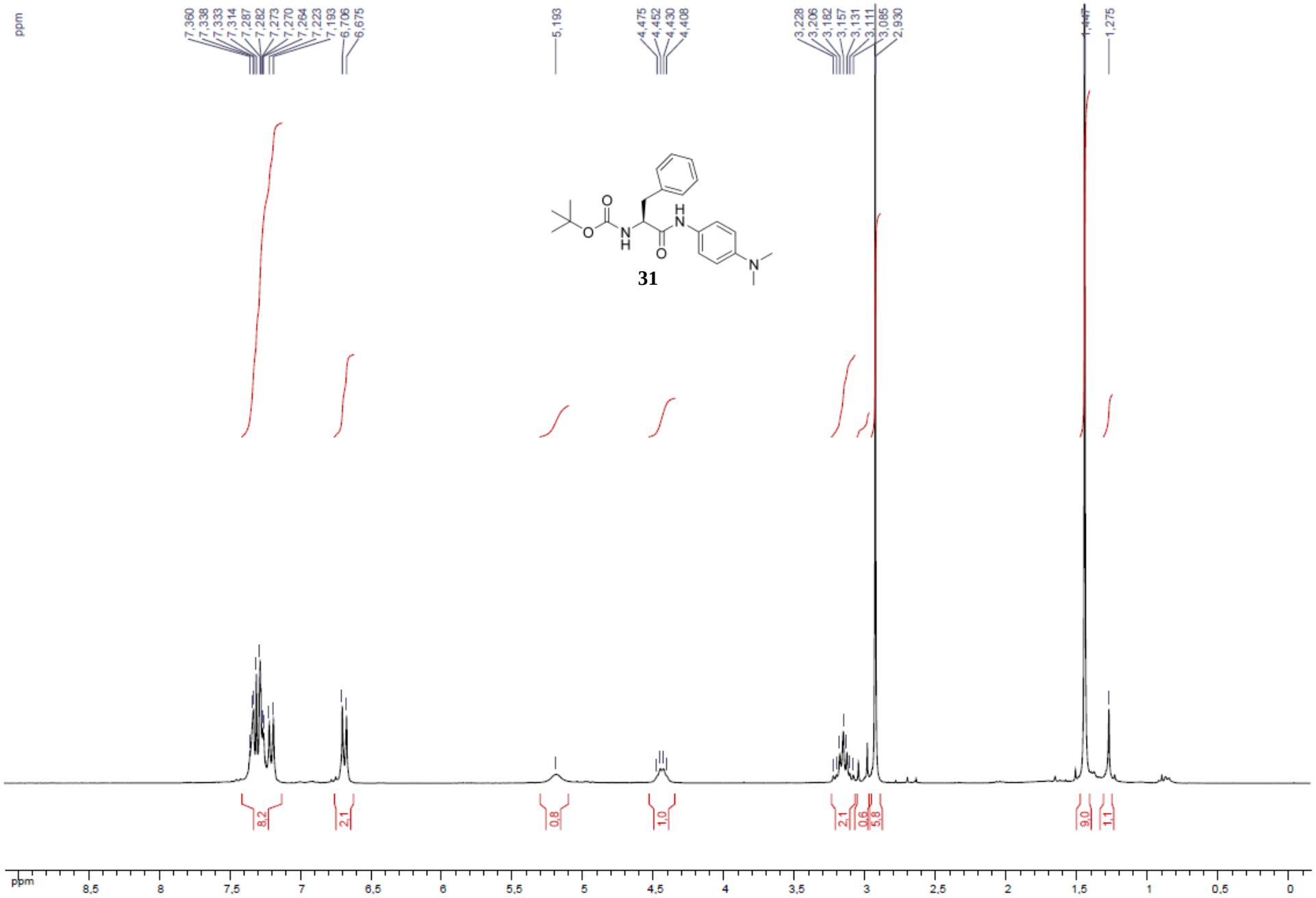
ppm
7,360
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7,314
7,287
7,282
7,273
7,270
7,264
7,223
7,193
6,706
6,675
5,193
4,475
4,452
4,430
4,408
3,228
3,206
3,182
3,157
3,131
3,111
3,085
2,930
1,447
1,275
8,2
2,1
0,8
1,0
2,1
0,6
5,8
9,0
1,1
ppm
8,5
8
7,5
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6,5
6
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5
4,5
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3,5
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0,5
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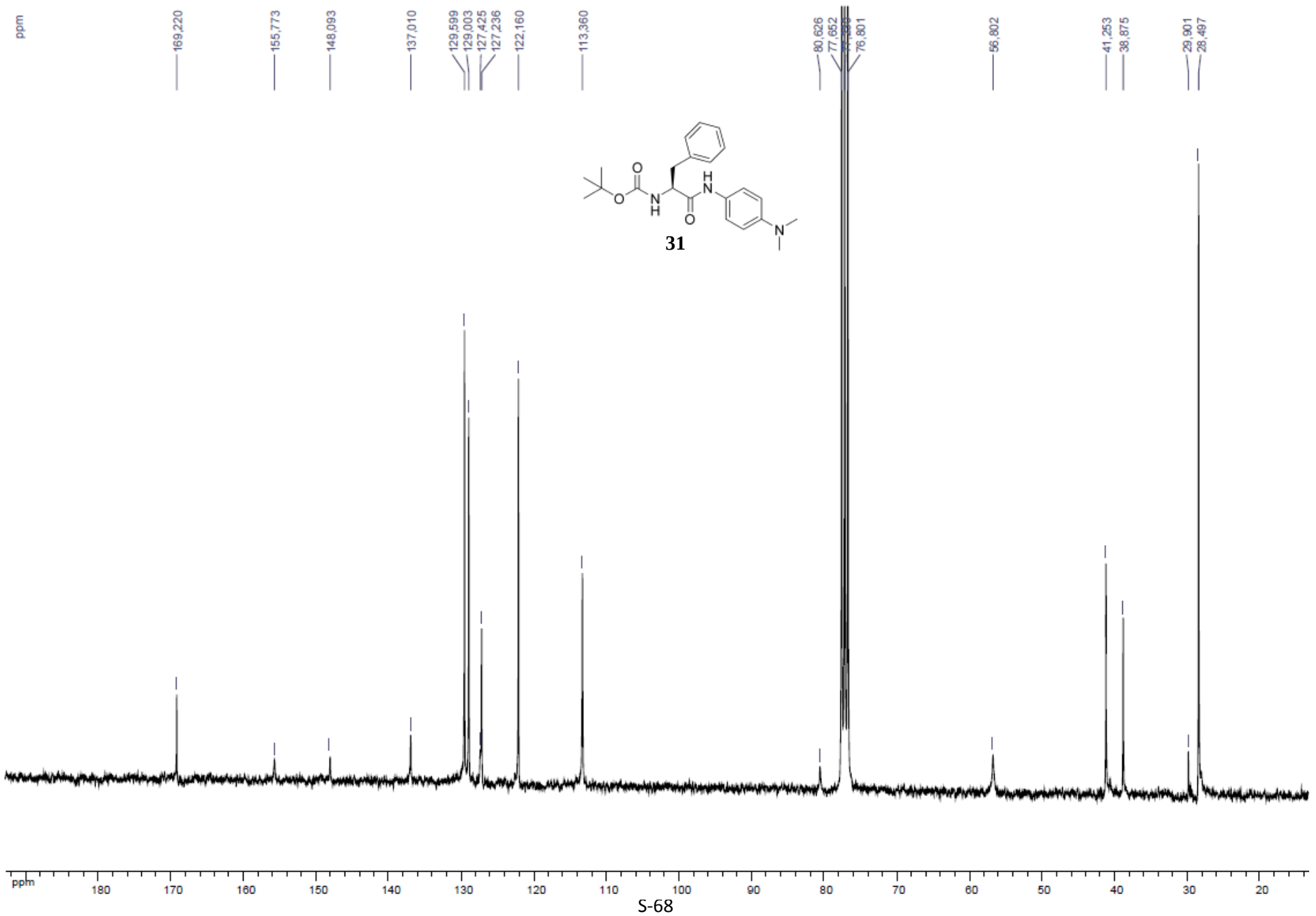
31


ppm
169,220
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127,236
122,160
113,360
80,626
77,652
76,801
56,802
41,253
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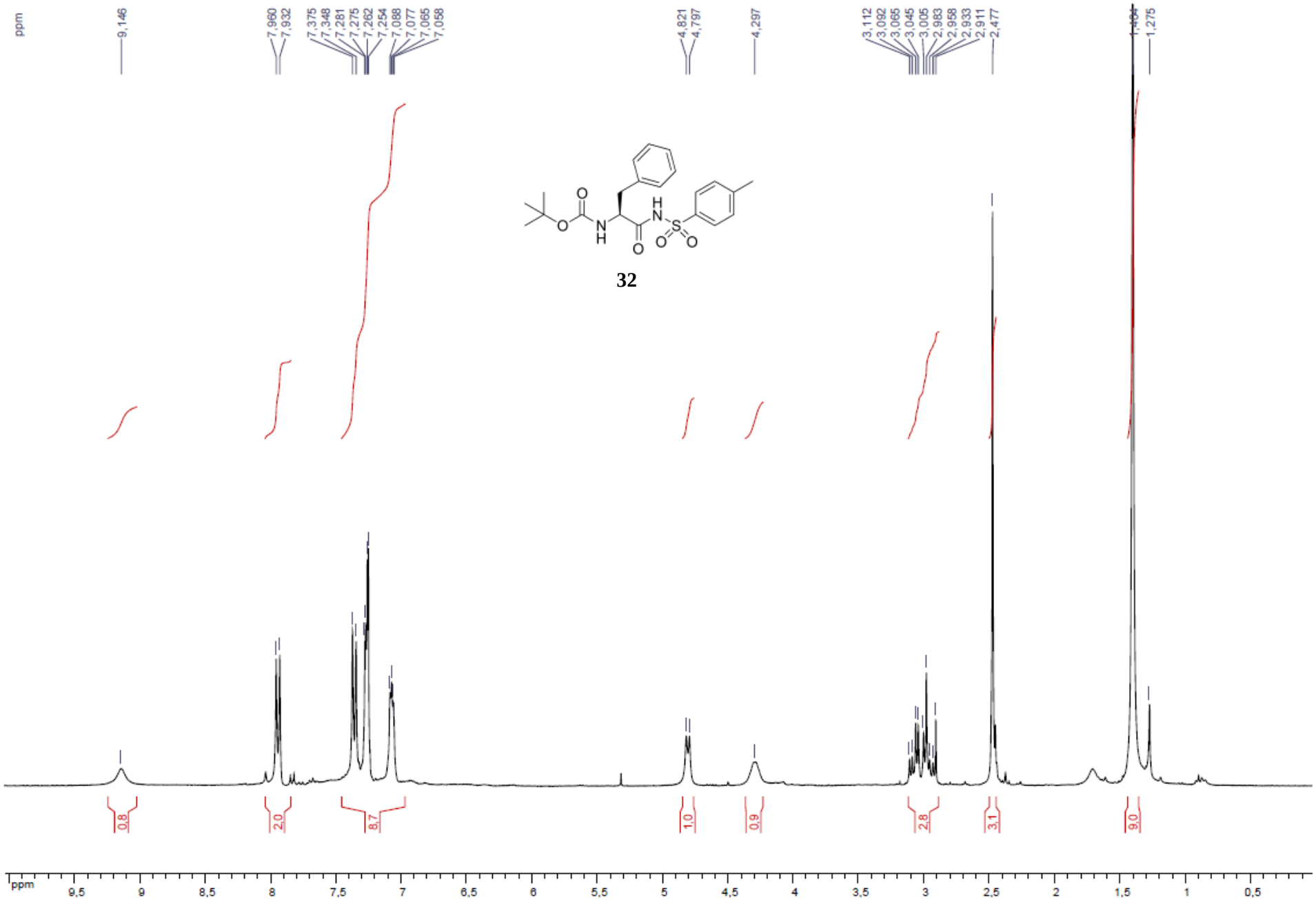
ppm
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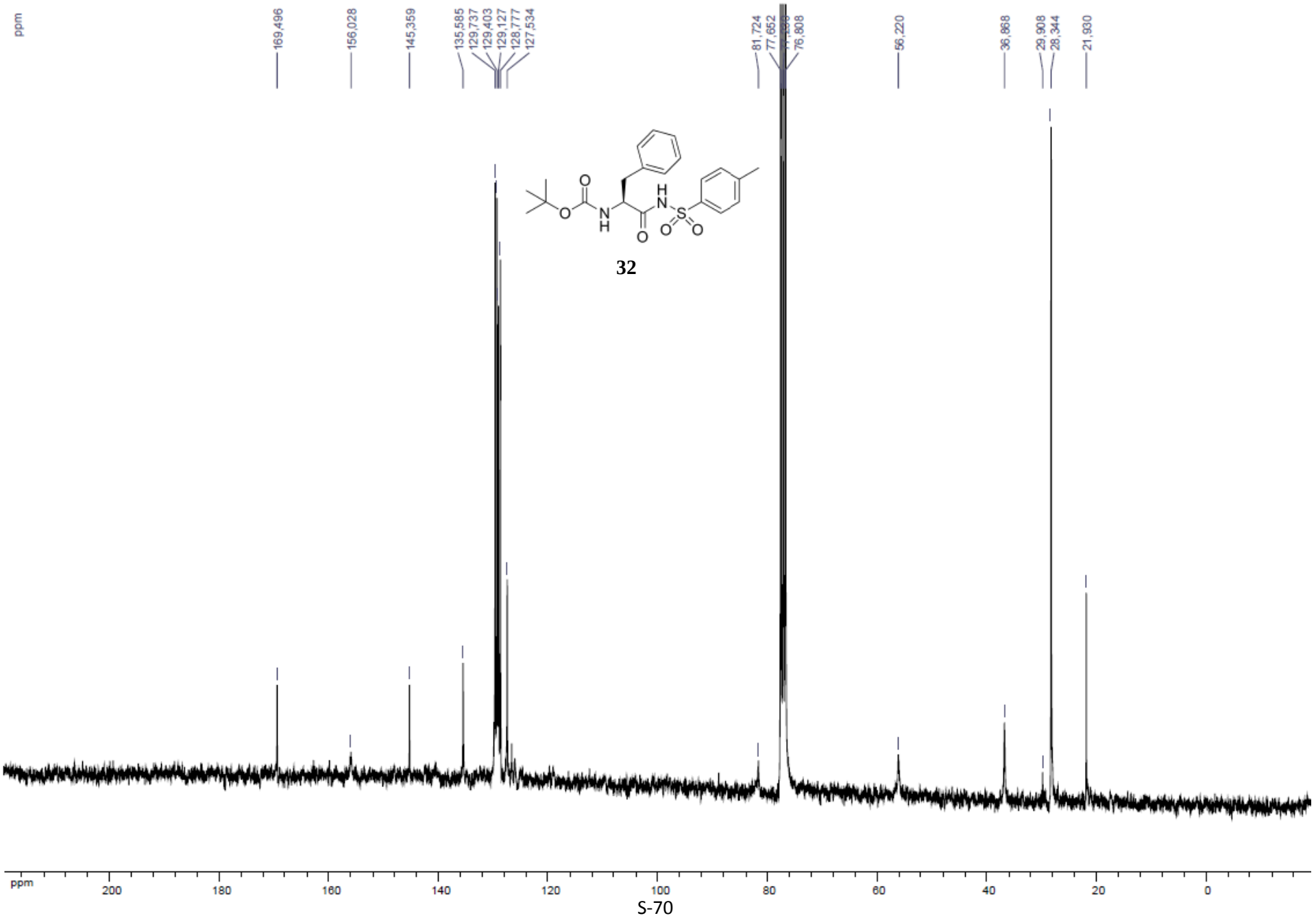
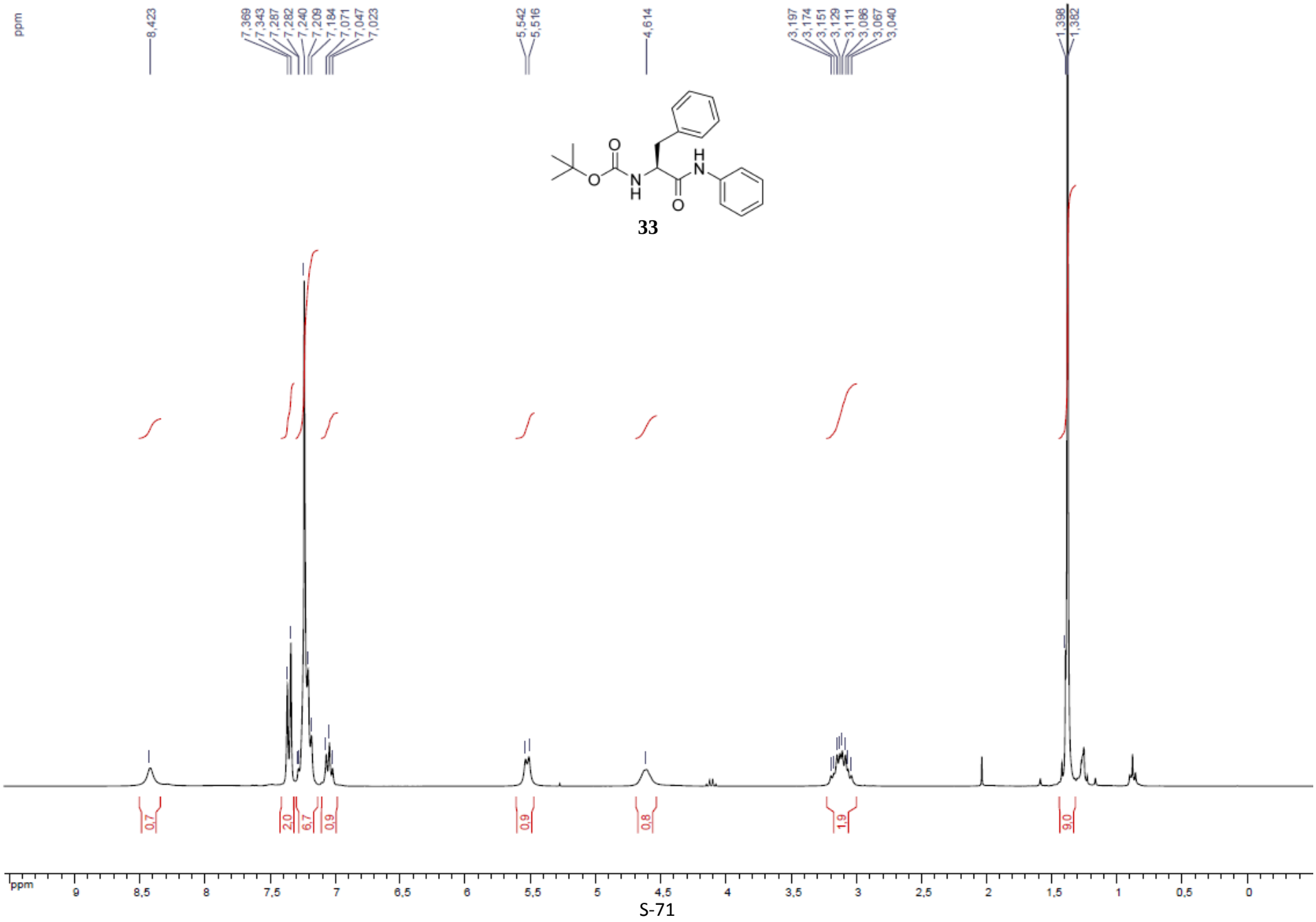
7,275
7,262
7,254
7,088
7,077
7,065
7,058
4,821
4,797
4,297
3,112
3,092
3,065
3,045
3,005
2,983
2,958
2,933
2,911
2,477
1,462
1,275
0,8
2,0
8,7
1,0
0,9
2,8
3,1
9,0
ppm
9,5
9
8,5
8
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5

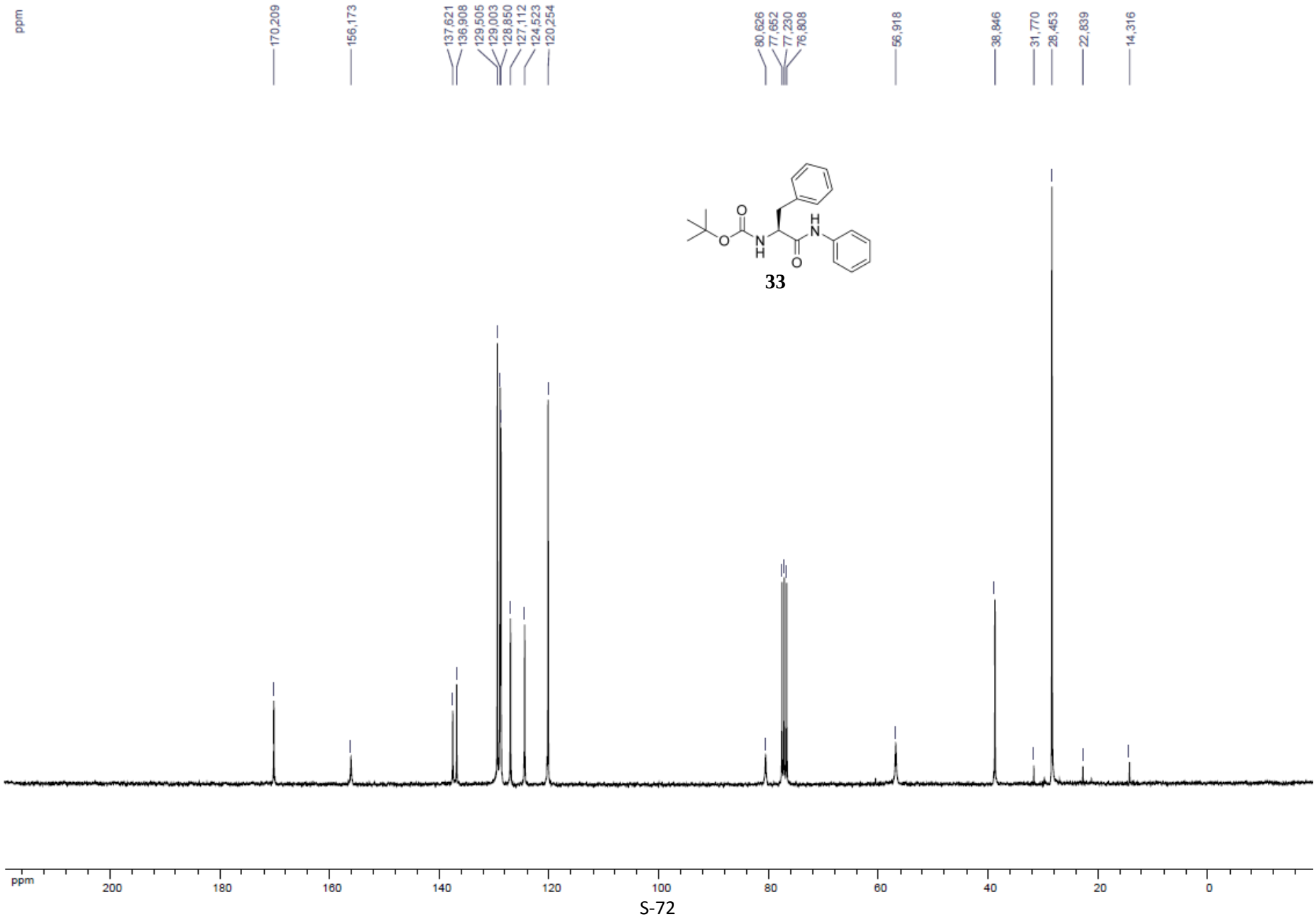
32

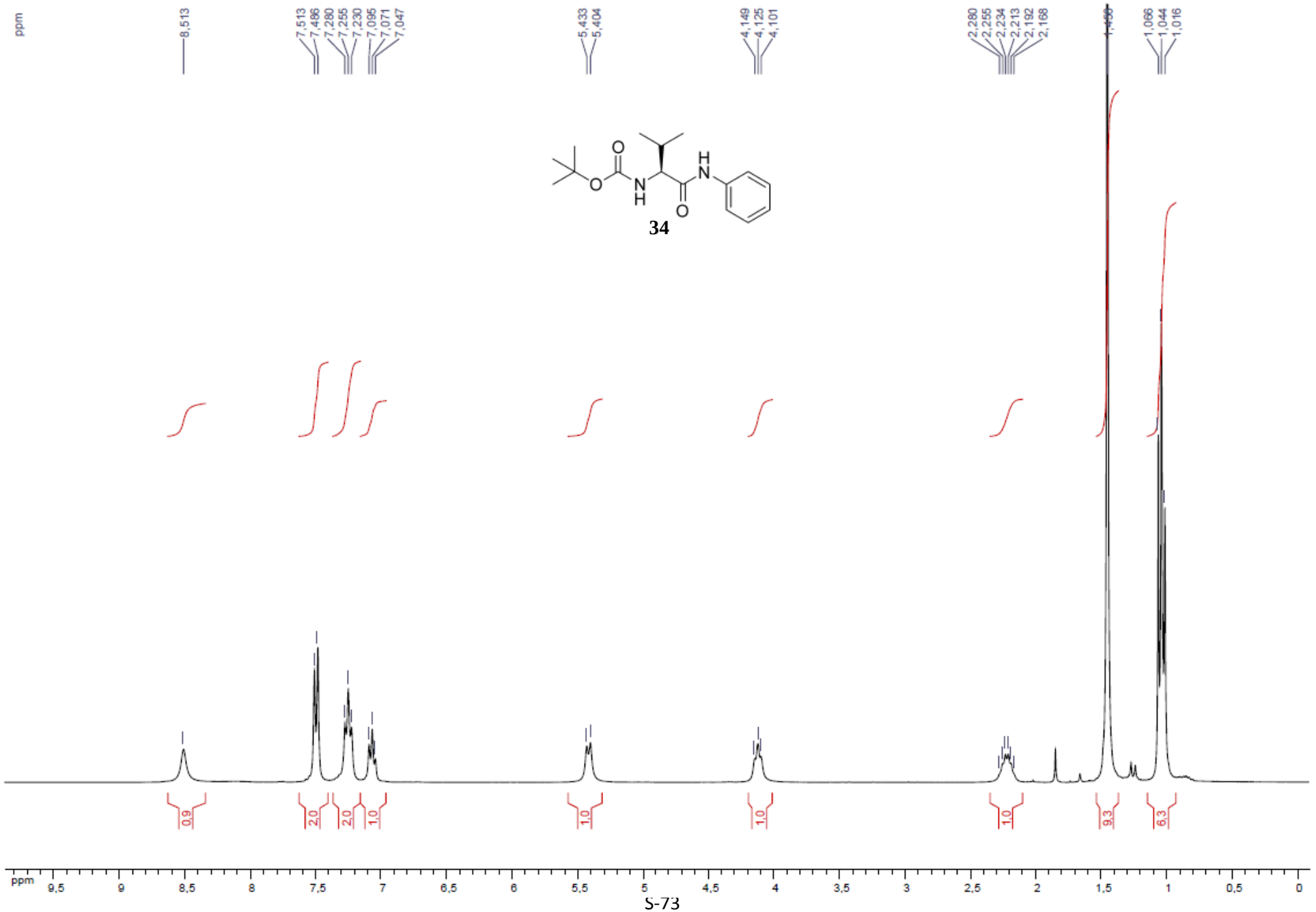

ppm
169,496
156,028
145,359
135,585
129,737
129,403
129,127
128,777
127,534
81,724
77,652
76,808
56,220
36,868
29,908
28,344
21,930
ppm
200
180
160
140
120
100
80
60
40
20
0

32

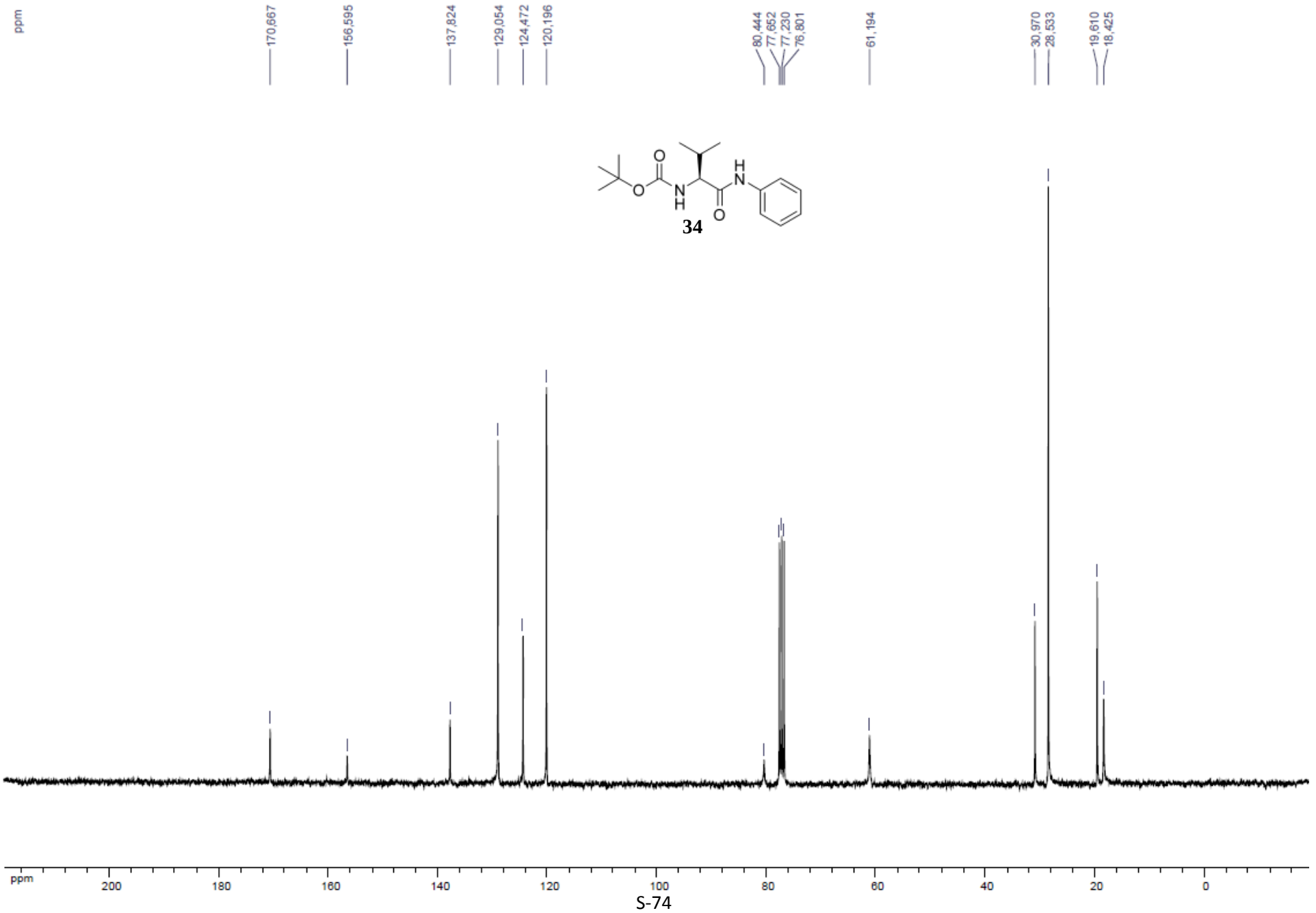

ppm
8,423
7,369
7,343
7,287
7,282
7,240
7,209
7,184
7,071
7,047
7,023
5,542
5,516
4,614
3,197
3,174
3,151
3,129
3,111
3,086
3,067
3,040
1,398
1,382
0,7
2,0
6,7
0,9
0,9
0,8
1,9
9,0
ppm
9
8,5
8
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5
0

33


ppm
170,209
156,173
137,621
136,908
129,505
129,003
128,850
127,112
124,523
120,254
80,626
77,652
77,230
76,808
56,918
38,846
31,770
28,453
22,839
14,316
33
ppm
200
180
160
140
120
100
80
60
40
20
0


ppm
8,513
7,513
7,486
7,280
7,255
7,230
7,095
7,071
7,047
5,433
5,404
4,149
4,125
4,101
2,280
2,255
2,234
2,213
2,192
2,168
1,066
1,044
1,016
0,9
2,0
2,0
1,0
1,0
1,0
1,0
9,3
6,3
ppm
9,5
9
8,5
8
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5
0

34


ppm
170,667
156,595
137,824
129,054
124,472
120,196
80,444
77,652
77,230
76,801
61,194
30,970
28,533
19,610
18,425
34
ppm
200
180
160
140
120
100
80
60
40
20
0