Catalytic Alkene Cyclization Reactions for the Stereoselective Synthesis of Complex "Terpenoid-like" Heterocycles

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Supporting information

Table of contents **page**

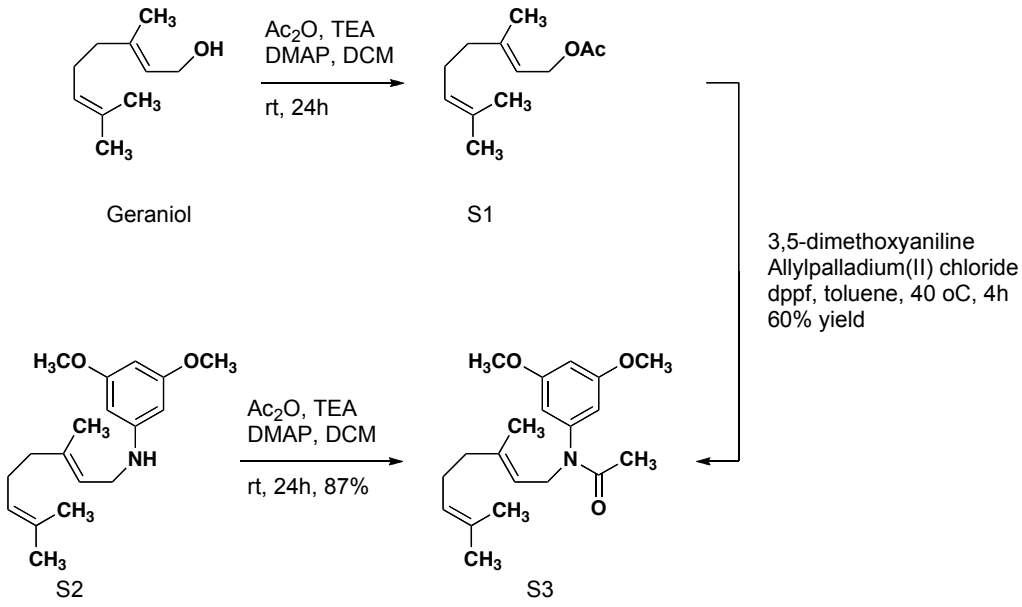
1. General Information

All reactions were carried out under an atmosphere of argon in flame dried glassware with magnetic stirring. Dichloromethane (CH_2Cl_2) diethylether (Et_2O), and tetrahydrofuran (THF) were purified by passage through a bed of activated alumina. Nitromethane was purified by distillation from calcium chloride ($CaCl_2$) and stored under argon. Purification of reaction products was carried out by flash chromatography using Silicycle Reagent silica gel F60 (230-400 mesh) and Dynamic Absorbants, inc. Reagent silica gel. Analytical thin layer

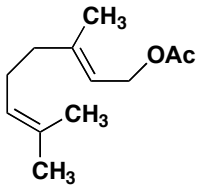
chromatography was performed on Dynamic Absorbants, inc. Reagent 0.25 mm silica gel F-254 plates. Visualization was accomplished with UV light, aqueous potassium permanganate ($KMnO_4$) stain and acidic ceric ammonium molybdate (CAM) followed by heating. ^{1}H NMR spectra and proton-decoupled ^{13}C NMR spectra were obtained on a 300, 400, or 600 MHz Varian NMR spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) relative to residual undeuterated $CHCl_3$, CH_2Cl_2, C_6H_6, DMSO ($CHCl_3$, δ_H = 7.26; CH_2Cl_2, δ_H = 5.32; C_6H_6, δ_H = 7.16; DMSO, δ_H = 2.50) and $CDCl_3$, CD_2Cl_2, DMSO-*d*$_6$ ($CDCl_3$, δ_C = 77.16; CD_2Cl_2, δ_C = 53.84; DMSO-*d*$_6$, δ_C = 39.52). Multiplicities are given as: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), td (triplet of doublet), ddd (doublet of doublet of doublets), m (multiplet), br s (broad singlet) and sep (septet). High-resolution mass spectra were recorded on positive ESI mode in methanol or acetonitrile. Melting points were taken on an EZ-melting apparatus and were uncorrected. Infrared spectra were taken on a Bruker Tensor 27 spectrometer. Gas chromatography-mass spectrometry data was recorded on a GCMS-QP 2010 Shimadzu spectrometer. High performance liquid chromatography data was recorded on a Prominence Shimadzu HPLC with a UV/Vis detector and an Xterra (RP 18, 5 um, 4.6X50mm) waters column. Products were eluted with acetonitrile/water (0.2% TFA) mobile phase and detected at 254 nm. Reagent phenylselenenyl chloride was purchased from commercial source (Alfa Aesar) and sulfur reagents phenylsulfenyl chloride and phenylsulfenyl methoxyde were prepared according procedures previously

reported.[1] Methylbenzene sulfenate was prepared according to procedures previously reported by Chang and coworkers (1977).[2] All other compounds and solvents were used as purchased without further purification.

2. Procedures for the synthesis of the N-Acetyl-N-geranyl aniline



Geranyl Acetate S1:

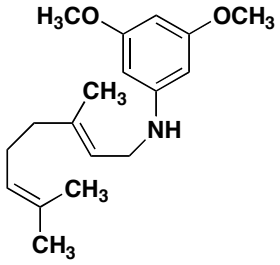


Geraniol was first acetylated according procedures previously reported by Felpin

[1] Barrett, A. G. M.; Dhanak, D.; Graboski, G. G.; Taylor, S. J. *Org. Synth.* **1990**, *68*, 8-13.
[2] Chang, L. L.; Denney, D. B.; Denney, D. Z.; Kazior, R. J. *J. Am. Chem. Soc.* **1977**, *99*, 2293-2297.

and coworkers (2007)[3] and the product was obtained in 92% yield. ^{1}H NMR matches with data previously described. ^{1}H NMR (300 MHz, $CDCl_3$) 5.31 (t, *J* = 7.2 Hz, 1H), 5.04 (t, *J* = 6.3 Hz, 1H), 4.55 (d, *J* = 7.2 Hz, 2H), 2.02-2.06 (m, 4H), 2.01(s, 3H), 1.67 (s, 3H), 1.65 (s, 3H), 1.57 (s, 3H).[3]

N-geranyl Aniline S2:

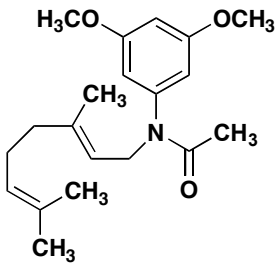


Geranyl acetate was aminated according to the procedure previously reported by Nguyen and coworkers (2006).[4] A solution of 1,1'-bis(diphenylphosphino) ferrocene (dppf) (0.31 g, 0.56 mmol) and allylpalladium(II) chloride dimer (0.18 g, 0.50 mmol) in toluene (13.0 mL, 0.1 M) was stirred at rt. After one hour, geranyl acetate (1.3 mL, 6.1 mmol) and 3,5-dimethoxyaniline (1.12 g, 7.3 mmol) were added dropwise by syringe dissolved in a minimal amount of toluene. The mixture was heated (40 °C) and stirred for 4 h. After the mixture was cooled to 25 °C, it was washed with an equal volume of hydrochloric acid (1 M). The aqueous layer was extracted with 2 x 20 mL of ether. The combined organic layers were washed with 20 mL of sodium bicarbonate solution and 20 mL of brine, dried with

[3] Felpin, F. X.; Lory, C.; Sow, H.; Acherar, S. *Tetrahedron* **2007**, *63*, 3010-3016.
[4] Nguyen, D. H.; Urrutigoity, M.; Fihri, A.; Hierso, J. C.; Meunier, P.; Kalck, P. *Appl. Organomet. Chem.* **2006**, *20*, 845-850.

Na_2SO_4, and concentrated *in vacuo* to afford a red/orange oil. The alkylated aniline was purified using 10% EtOAc:hexanes (R*f* = 0.33) to afford a yellow/orange oil (1.05 g, 60%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 (t, *J* = 2.1 Hz, 1H), 5.81 (d, *J* = 2.0 Hz, 2H), 5.32 (t, *J* = 6.8 Hz, 1H), 5.09 (t, *J* = 6.8 Hz, 1H), 3.75 (s, 6H), 3.67 (d, *J* = 5.6 Hz, 2H), 3.62 (br s, 1H), 2.14-1.99 (m, 4H), 1.70 (s, 3H), 1.68 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 150.6, 139.2, 131.9, 124.2, 121.7, 92.0, 90.0, 55.3, 42.3, 39.8, 26.7, 25.9, 18.0, 16.6; IR (neat) 3401, 2961, 2929 cm^{-1}; HRMS (ESI) m/z calcd for $C_{18}H_{28}NO_2$ $(M + H)^+$ 290.2115, found 290.2115.

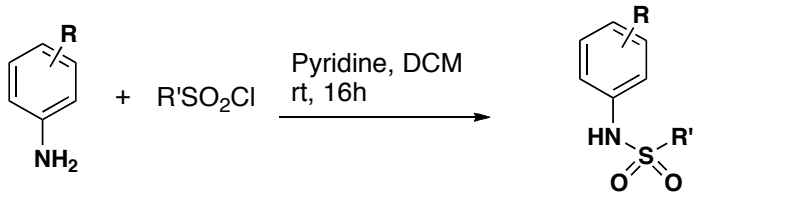
N-acetyl-N-geranyl Aniline S3:



To a solution of N-geranyl aniline 1.2 (0.20 g, 0.69 mmol) in dichloromethane (7.0 mL, 0.1 M) was added acetic anhydride (0.13 mL, 1.38 mmol), triethylamine (0.19 mL, 1.38 mmol), and 4-Dimethylaminopyridine (0.002 g). After 24 h, the mixture was washed with H_2O, brine, dried with Na_2SO_4, and concentrated *in vacuo* to afford a clear oil. The alkylated aniline was purified using 25% EtOAc:hexanes (R*f* = 0.15) to afford a yellow oil (0.20 g, 87%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.40 (t, *J* = 2.2 Hz, 1H), 6.28 (d, *J* = 2.2 Hz, 2H), 5.24 (t, *J* = 7.1 Hz, 1H), 5.03 (t, *J* = 7.1 Hz, 1H), 4.25 (d, *J* = 7.1 Hz, 2H), 3.76 (s, 6H), 1.99 (m,

4H), 1.88 (s, 3H), 1.65 (s, 3H), 1.56 (s, 3H), 1.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 161.1, 144.7, 139.3, 131.4, 123.9, 119.4, 106.4, 99.4, 55.3, 46.4, 39.5, 26.4, 25.5, 22.4, 17.5, 16.0; IR (neat) 2965, 2928, 1657 cm^{-1}; HRMS (ESI) m/z calcd for $C_{20}H_{30}NO_3$ $(M + H)^+$ 332.2220, found 332.2210

3. General Procedure A. Synthesis of sulfonylated anilines



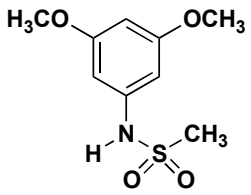
R' = CH_3 or *o*-$NO_2C_6H_5$

S4 (R'=CH_3)
S5-S16 (R'= *o*-$NO_2C_6H_5$)

Anilines were sulfonylated according to the procedure previously described by Choi and coworkers (2006).[5] Pyridine (3.0 equiv) was added to a cooled (0 °C) solution of aniline (0.5 M) in CH_2Cl_2. The mixture was stirred for ten minutes before the sulfonyl chloride (1.0 - 1.2 equiv) was added. The reaction was stirred overnight at room temperature. The solvent and excess pyridine was removed *in vacuo.* The purple or brown colored crude mixture was purified by flash chromatography (DCM/hexanes or EtOAc/hexanes) to yield the product as a white to slightly yellow crystalline solid.

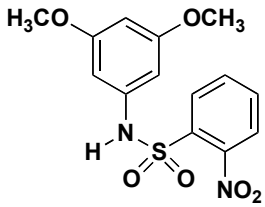
[5]Choi, S.; Jung, K.; Ryu, J. *Arch. Pharmacal Res.* **2006**, *29*, 369-374.

N-methanesulfonyl aniline S4:



This compound was prepared according to general procedure A using 3,5-dimethoxyaniline (1.530 g, 10.0 mmol), pyridine (2.42 mL, 30.0 mmol), and methanesulfonyl chloride (0.93 mL, 12.0 mmol). The compound was purified by flash chromatography (33:67 EtOAc/hexanes) to give the product as a white solid (2.272 g, 99%): ^{1}H NMR (400 MHz, $CDCl_3$) 6.49 (br s, 1H), 6.39 (d, *J* = 2.2 Hz, 2H), 6.28 (t, *J* = 2.2 Hz, 1H), 3.78 (s, 6H), 3.03 (s, 3H). ^{1}H NMR spectrum matches those reported in the literature.[5]

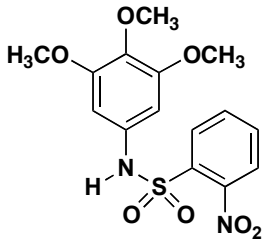
N-nosyl aniline S5:



This compound was prepared according to general procedure A using 3,5-dimethoxyaniline (1.531 g, 10 mmol), pyridine (2.42 mL, 30 mmol), and 2-nitrobenzenesulfonyl chloride (2.66 g, 12 mmol). The product was purified by flash chromatography (CH_2Cl_2) to give a white solid (2.907 g, 86 %): mp 167 – 169 °C; ^{1}H NMR (400 MHz, DMSO-d_6) 10.75 (br s, 1H), 8.04 ‑7.91 (m, 2H), 7.91 ‑7.78 (m, 2H), 6.28 (d, *J* = 2.0 Hz, 2H), 6.21 (t, *J* = 2.0 Hz, 1H), 3.65 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) 160.9, 148.1, 138.5, 134.8, 132.6, 131.2, 129.9,

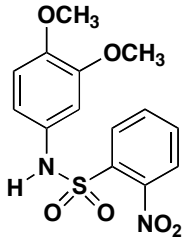
124.6, 98.1, 95.9, 55.2; IR (neat) 3334, 3100, 1608 cm^{-1}; HRMS (ESI) m/z calcd for $C_{14}H_{15}N_2O_6S$ $(M + H)^+$ 339.0646, found 339.0637.

N-nosyl aniline S6:



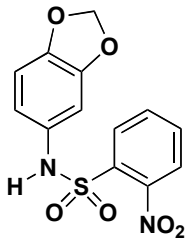
This compound was prepared according to general procedure A using 3,4,5-trimethoxyaniline (0.916 g, 5 mmol), pyridine (1.16 mL, 15 mmol), and 2-nitrobenzenesulfonyl chloride (1.11 g, 5 mmol). The product was purified by flash chromatography (35:65 EtOAc/Hex) to give a brown solid (1.461 g, 79 %): mp 132 - 134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.0 Hz, 2H), 7.72 (td, *J* = 7.9 Hz, 1.4 Hz, 1H), 7.61 (t, *J* = 7.7 Hz, 1H), 7.11 (br s, 1H), 6.41 (s, 2H), 3.78 (s, 3H), 3.76 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 148.1, 136.4, 134.2, 132.6, 131.8, 131.8, 131.2, 125.2, 100.8, 60.8, 56.1; IR (neat) 3286, 3093, 1551 cm^{-1}; HRMS (ESI) m/z calcd for $C_{15}H_{17}N_2O_7S$ $(M + H)^+$ 369.0751, found 369.0752.

N-nosyl aniline S7:



This compound was prepared according to general procedure A using 3,4-dimethoxyaniline (0.767 g, 5 mmol), pyridine (1.16 mL, 15 mmol), and 2-nitrobenzenesulfonyl chloride (1.11 g, 5 mmol). The product was purified by flash chromatography (CH_2Cl_2) to give a yellow solid (1.05 g, 62 %): mp 153 - 156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 8.0 Hz, 1.2 Hz, 1H), 7.77 (dd, *J* = 7.8 Hz, 1.4 Hz, 1H), 7.70 (td, *J* = 7.8 Hz, 1.4 Hz, 1H), 7.57 (td, *J* = 7.7 Hz, 1.2 Hz, 1H), 7.10 (br s, 1H), 6.80 (d, *J* = 2.4 Hz, 1H), 6.69 (d, *J* = 8.6 Hz, 1H), 6.62 (dd, *J* = 8.5 Hz, 2.4 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.4, 148.3, 148.2, 134.0, 132.6, 132.2, 132.1, 128.3, 125.2, 116.5, 111.2, 108.8, 56.1, 56.0; IR (neat) 3291, 3096, 1516 cm^{-1}; HRMS (ESI) m/z calcd for $C_{14}H_{18}N_3O_6S$ $(M + NH_4)^+$ 356.0911, found 356.0912.

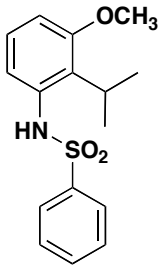
N-nosyl aniline S8:



This compound was prepared according to general procedure A using 3,4-(methylenedioxy)aniline (0.686 g, 5 mmol), pyridine (1.16 mL, 15 mmol), and 2-nitrobenzenesulfonyl chloride (1.10 g, 5 mmol). The product was purified by flash chromatography (70:30 CH_2Cl_2/hexanes) to give a yellow solid (1.085 g, 67 %): mp 160 - 163 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 8.0 Hz, 1.1 Hz, 1H), 7.81 (dd, *J* = 7.8 Hz, 1.4 Hz, 1H), 7.71 (td, *J* = 7.7 Hz, 1.4 Hz, 1H), 7.60 (td, *J* = 7.7 Hz, 1.2 Hz, 1H), 7.09 (br s, 1H), 6.77 (d, *J* = 2.1 Hz, 1H), 6.64 (d, *J* = 8.2 Hz,

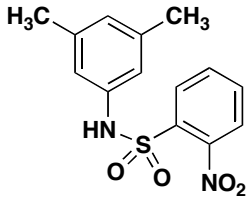
1H), 6.56 (dd, *J* = 8.2 Hz, 2.1 Hz, 1H), 5.95 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.1, 147.7, 145.2, 134.5, 132.5, 131.4, 130.2, 130.2, 124.6, 115.7, 108.4, 104.2, 101.6; IR (neat) 3336, 3110, 1542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{13}H_{11}N_2O_6S$ $(M + H)^+$ 323.0333, found 323.0334.

N-nosyl aniline S9:



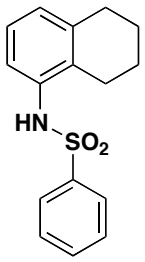
This compound was prepared according to general procedure A using 3-methoxy-2-*iso*-propylaniline (100.0 mg, 0.6 mmol), pyridine (0.15 mL, 1.81 mmol), and 2-nitrobenzenesulfonyl chloride (147.6 mg, 0.7 mmol). The product was purified by flash chromatography using 30% of ethyl acetate in hexanes as eluent to give an amorphous white solid (193.3 mg, 91 %): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 1.2 Hz, 8.0 Hz, 1H), 7.80 (dd, *J* = 1.4 Hz, 7.9 Hz, 1H), 7.72 (s, 1H), 7.61 (td, *J* = 1.2 Hz, 7.7 Hz, 1H), 7.11 (s, 1H), 7.03 (t, *J* = 8.1 Hz, 1H), 6.80 (d, *J* = 8.3 Hz, 1H), 6.70 (dd, *J* = 1.1 Hz, 8.0 Hz, 1H), 3.79 (s, 3H), 3.40 (sep, *J* = 7.0 Hz 1H), 1.12 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.7, 148.1, 133.9, 133.8, 133.6, 133.1, 132.8, 131.6, 126.7, 125.4, 120.3, 111.3, 55.4, 27.4, 20.3 (2C); IR (neat) 3299, 2965, 1604, 1367 cm^{-1}; HRMS (ESI) m/z calcd for $C_{16}H_{18}N_2O_5S$ $(M + H)^+$ 351.1009, found 351.1010.

N-nosyl aniline S10:



This compound was prepared according to general procedure A using 3,5-dimethylaniline (500.0 mg, 4.1 mmol), pyridine (0.9 mL, 12.4 mmol), and 2-nitrobenzenesulfonyl chloride (1.007 g, 4.5 mmol). The product was purified by flash chromatography using 20% of ethyl acetate in hexanes as eluent to give a white solid (908.4.2 mg, 67 %): mp 151.5 - 152.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84 (m, 2H), 7.69 (td, *J* = 1.4 Hz, 7.8 Hz, 1H), 7.58 (td, *J* = 1.2 Hz, 7.7 Hz, 1H), 7.16 (br s, 1H), 6.80 (br s, 3H), 2.22 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.3, 139.3, 135.4, 134.0, 132.6, 132.4, 131.9, 128.3, 125.4, 120.7, 21.3; IR (neat) 3342, 3095, 1607, 1532, 1380 cm^{-1}; HRMS (ESI) m/z calcd for $C_{14}H_{14}N_2O_4S$ $(M + H)^+$ 307.0747, found 307.0751.

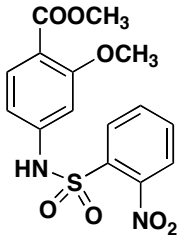
N-nosyl aniline S11:



This compound was prepared according to general procedure A using 5,6-7,8-tretrahydro-1-naphtylamine (500.0 mg, 3.4 mmol), pyridine (0.8 mL, 10.18 mmol), and 2-nitrobenzenesulfonyl chloride (827.9 mg, 3.7 mmol). The product was

purified by flash chromatography using 20% of ethyl acetate in hexanes as eluent to give a white solid (600.2 mg, 53 %): mp 164.0 - 165.2 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 1.4 Hz, 7.7 Hz, 1H), 7.88 (dd, *J* = 1.4 Hz, 7.8 Hz, 1H), 7.73 (td, *J* = 1.5 Hz, 7.8 Hz, 1H), 7.64 (td, *J* = 1.3 Hz, 7.7 Hz, 1H), 7.01 (m, 4H), 2.74 (d, *J* = 5.4 Hz, 2H), 2.61 (d, *J* = 5.8 Hz, 2H), 1.70 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.0, 139.1, 133.9, 133.7, 133.6, 132.8, 132.2, 131.5, 128.2, 125.9, 125.5, 122.0, 29.8, 24.8, 22.8, 22.5; IR (neat) 3274, 2931, 1542, 1369 cm^{-1}; HRMS (ESI) m/z calcd for $C_{16}H_{16}N_2O_4S$ $(M + H)^+$ 333.0904, found 303.0903.

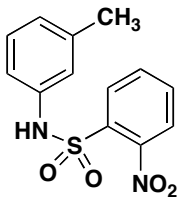
N-nosyl aniline S12:



This compound was prepared according to general procedure A using 4-carboxymethyl-3-methoxyl-aniline (300.0 mg, 1.6 mmol), pyridine (0.4 mL, 4.97 mmol), and 2-nitrobenzenesulfonyl chloride (404.1 mg, 1.8 mmol). The crude product was filtered through a plug of silica and washed with ethyl acetate/hexanes (1:1) solution. Then, the solvent was removed under reduced pressure and the product was crystallized from methanol as a white solid (422.5 mg, 70 %): mp 150.3 - 151.8 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (m, 1H), 7.84 (s, 1H), 7.69 (m, 2H), 7.62 (m, 1H), 7.52 (s, 1H), 6.93 (d, *J* = 1.7 Hz, 1H), 6.75 (dd, *J* = 1.7 Hz, 8.2 Hz, 1H), 3.86 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.4, 140.6, 134.5, 133.2, 132.9, 132.1, 131.9, 125.6, 117.6, 112.9,

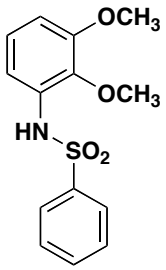
105.6, 56.3, 52.2; IR (neat) 3171, 2954, 1689, 1548 cm^{-1}; HRMS (ESI) m/z calcd for $C_{15}H_{14}N_2O_7S$ $(M + H)^+$ 367.0595, found 367.0597.

N-nosyl aniline S13:



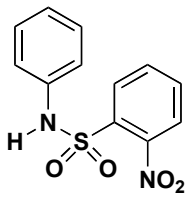
This compound was prepared according to general procedure A using 3-methylaniline (500.0 mg, 4.6 mmol), pyridine (1.2 mL, 13.9 mmol), and 2-nitrobenzenesulfonyl chloride (1.137 g, 5.1 mmol). The product was purified by flash chromatography using 25% of ethyl acetate in hexanes as eluent to give a white solid (908.4.2 mg, 67 %): mp 114.4 - 114.9 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 1.3 Hz, 7.8 Hz, 1H), 7.82 (dd, *J* = 1.3 Hz, 7.9 Hz, 1H), 7.68 (td, *J* = 1.4 Hz, 7.9 Hz, 1H), 7.57 (td, *J* = 1.2 Hz, 7.8 Hz, 1H), 7.26 (s, 1H), 7.13 (t, *J* = 7.7 Hz, 1H), 6.99 (m, 3H), 2.27 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.2, 139.6, 135.4, 134.1, 132.6, 132.2, 131.8, 129.3, 127.4, 125.4, 123.8, 120.1, 21.3; IR (neat) 3299, 3090, 1541, 1350 cm^{-1}; HRMS (ESI) m/z calcd for $C_{13}H_{12}N_2O_4S$ $(M + H)^+$ 293.0591, found 293.0591.

N-nosyl aniline S14:



This compound was prepared according to general procedure A using 2,3-dimethoxyaniline (0.466 g, 3.04 mmol), pyridine (0.737 mL, 9.13 mmol), and 2-nitrobenzenesulfonyl chloride (0.741 g, 3.34 mmol). The product was purified by flash chromatography (35:65 EtOAc/Hex) to give a white solid (0.723 g, 70 %): mp112.0-115.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.98 (dd, *J* = 7.9 Hz, 1.4 Hz, 1H), 7.86 (dd, *J* = 7.9 Hz, 1.2 Hz, 1H), 7.68 (td, *J* = 7.8 Hz, 1.5 Hz, 1H), 7.62 (td, *J* = 7.7 Hz, 1.3 Hz, 1H), 7.31 (dd, *J* = 8.3 Hz, 1.3 Hz, 1H), 7.01 (t, *J* = 8.4 Hz, 1H), 6.68 (dd, *J* = 8.4 Hz, 1.3, 1H), 3.80 (s, 3H), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 148.0, 139.3, 134.1, 132.7, 132.6, 131.4, 129.7, 125.4, 124.1, 113.2, 109.2, 61.0, 55.8; IR (neat) 3313, 3101, 1537 cm^{-1}; HRMS (ESI) m/z calcd for $C_{14}H_{15}N_2O_6S$ $(M + H)^+$ 339.0646, found 339.0649.

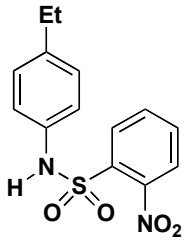
N-nosyl aniline S15:



This compound was prepared according to general procedure A using aniline (0.511 g, 5.5 mmol), pyridine (1.33 mL, 16.5 mmol), and 2-nitrobenzenesulfonyl

chloride (1.22 g, 5.5 mmol). The product was purified by flash chromatography (20:80 EtOAc/hexanes) to give a white solid (1.110 g, 73 %): mp 118 - 121 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85 (dt, *J* = 8.0 Hz, 1.0 Hz, 1H), 7.82 (dt, *J* = 7.9 Hz, 1.2 Hz, 1H), 7.70 – 7.66 (m, 1H), 7.59 - 7.55 (m, 1H), 7.29 – 7.25 (m, 2H), 7.24 (br s, 1H), 7.22 – 7.16 (m, 3H). ^{1}H NMR spectrum matches those reported in the literature.[6]

N-nosyl aniline S16:

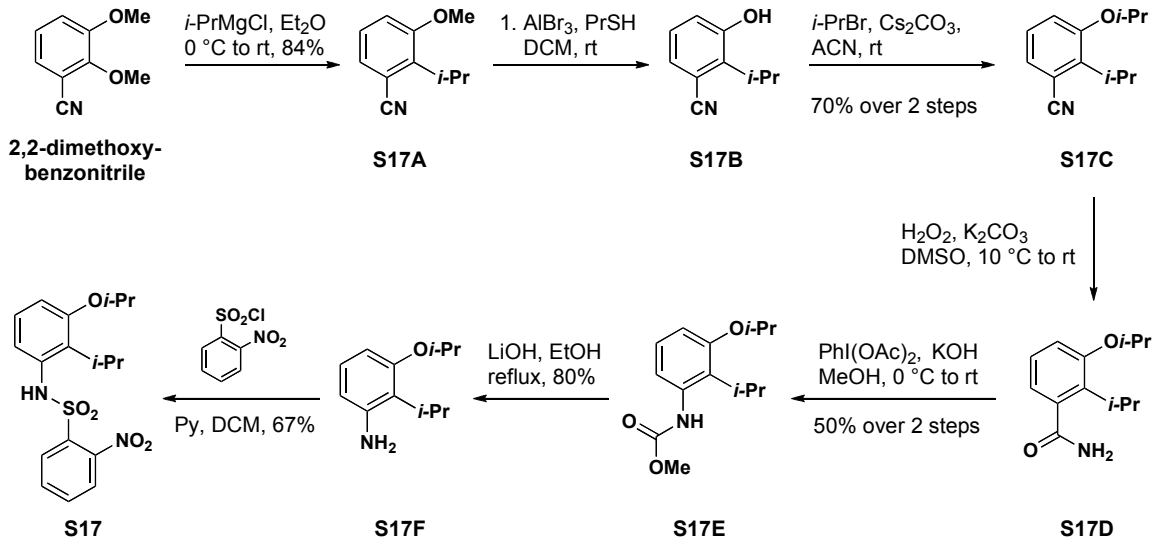


This compound was prepared according to general procedure A using 4-ethylaniline (1.003 g, 8.25 mmol), pyridine (1.985 mL, 24.6 mmol), and 2-nitrobenzenesulfonyl chloride (1.828 g, 8.25 mmol). The product was purified by flash chromatography (20:80 EtOAc/Hex) to give a white solid (1.539 g, 61 %): mp 105 - 108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 8.0 Hz, 1.2 Hz, 1H), 7.81 (dd, *J* = 7.8 Hz, 1.4 Hz, 1H), 7.68 (td, *J* = 7.8 Hz, 1.4 Hz, 1H), 7.57 (td, *J* = 7.7 Hz, 1.3 Hz, 1H), 7.16 (br s, 1H), 7.09 (s, 4H), 2.58 (q, *J* = 7.6 Hz, 2H), 1.18 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 143.1, 134.0, 133.0, 132.7,

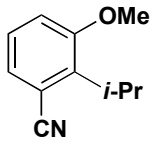
[6]Kurkin, A. V.; Bernovskaya, A. A.; Yurovskaya, M. A. *Tetrahedron: Asymmetry* **2009**, *20*, 1500-1505.

132.3, 131.9, 128.9, 125.4, 123.8, 28.3, 15.4; IR (neat) 3246, 3100, 1531 cm^{-1}; HRMS (ESI) m/z calcd for $C_{14}H_{15}N_2O_4S$ $(M + H)^+$ 307.0747, found 307.0747.

4. Preparation of Sulfonylated Aniline S17



Isopropyl benzonitrile S17A

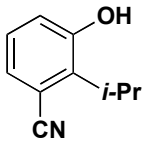


The compound **S17A** was prepared from 2,2-dimethoxybenzonitrile according procedure previously described by Kim et al (2010).[7] ^{1}H NMR (300 MHz, $CDCl_3$) 7.20 (dd, *J* = 7.8 Hz, 1H), 7.15 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.04 (dd, *J* = 7.8, 1.5 Hz, 1H), 3.82 (s, 3H), 3.54 (m, 1H), 1.37 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz,

[7] Kim, M. B.; Shaw, J. T. *Org. Lett.* **2010**, *12*, 3324-3327.

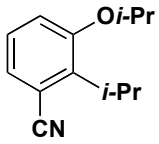
$CDCl_3$) 159.4, 140.3, 127.6, 125.5, 118.9, 115.6, 112.6, 55.8, 31.1, 20.8; ^{1}H NMR corresponds to published data.[7]

Phenol S17B



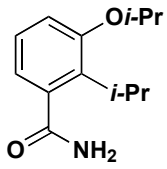
To a flame dried flask was added a solution of aluminum tribromide (44.0 mL, 44.0 mmol, 1.0M in CH_2Cl_2). To this solution was added CH_2Cl_2 (100 mL) and 1-propanethiol (4.0 mL, 44.1 mmol). After the mixture was cooled (0 °C), a solution of compound **S16A** (2.544 g, 14.5 mmol) in CH_2Cl_2 (5.0 mL) was added slowly. The solution was allowed to warm (23 °C) and stirred overnight. The reaction mixture was cooled (0 °C) and quenched dropwise with methanol until the solution became red and clear. The solution was washed with hydrochloric acid (50 mL, 10 %). The aqueous layer was extracted 3 X 20 mL CH_2Cl_2. The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo* to afford a yellow oil. The oil was purified by flash chromatography (18:82 EtOAc/hexanes) to yield the product as a white solid (2.075 g, 87 %): mp 175 - 178 °C; ^{1}H NMR (400 MHz, DMSO) 10.07 (s, 1H), 7.21 – 7.14 (m, 2H), 7.08 (dd, J = 7.0, 2.5, 1H), 3.41 (dt, J = 14.0, 7.1, 1H), 1.34 (d, J = 7.0, 6H). ^{13}C NMR (100 MHz, DMSO) 156.0, 136.5, 127.8, 124.0, 120.7, 118.7, 111.2, 29.9, 20.4; IR (neat) 3310, 2983, 2966, 2238 cm^{-1}; HRMS (ESI) m/z calcd for $C_{10}H_{12}NO$ $(M + H)^+$ 162.0914, found 162.0910.

Isopropoxy benzonitrile S17C



To a solution of compound **S17C** (1.977 g, 12.3 mmol) in acetonitrile (70 mL) was added cesium carbonate (12.0 g, 36.8 mmol) followed by isopropyl bromide (3.5 mL, 36.8 mmol) at room temperature. The solution was stirred for 24 h. The reaction mixture was filtered and concentrated *in vacuo* to afford a yellow oil. The oil was purified by flash chromatography (10:90) EtOAc/hexanes) to yield the product as a clear oil (2.034 g, 81 %): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.19 – 7.16 (m, 1H), 7.15 – 7.12 (m, 1H), 7.03 (d, *J* = 8.1, 1H), 4.64 – 4.54 (m, 1H), 3.58 - 3.49 (m, 1H), 1.38 (d, *J* = 7.0, 6H), 1.36 (d, *J* = 6.0, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.4, 140.7, 127.3, 125.0, 118.9, 117.3, 112.8, 70.2, 31.2, 22.0, 20.7; IR (neat) 2979, 2934, 2224, cm^{-1}; HRMS (ESI) m/z calcd for $C_{13}H_{18}NO$ $(M + H)^+$ 204.1383, found 204.1379.

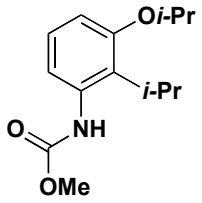
Benzamide S17D



To a cooled (0 °C) solution of benzonitrile **S17C** (2.045 g, 10.0 mmol) dissolved in DMSO (100 mL, 0.1 M) was added K_2CO_3 (2.073 g, 15.0 mmol) and 30% H_2O_2 (40 mL) slowly. The solution was slowly warmed to rt and stirred for 24 h. The reaction mixture was diluted with H_2O (200 mL) and then extracted with EtOAc (3

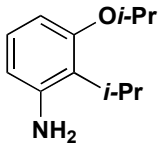
x 150 mL). Approximately 90 % of the solvent was removed *in vacuo* and the remaining mixture was washed with 3 x 10 mL of H_2O and 5 mL of brine, dried (Na_2SO_4), and concentrated *in vacuo* to afford the amide as a white solid (1.571 g). The crude product was submitted to the next step without further purification.

Carbamate S17E



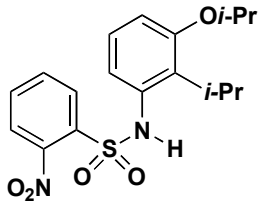
To a cooled (0 °C) solution of the crude product **S17D** and KOH (1.402 g, 25.0 mmol) dissolved in methanol (100 mL) was added $PhI(OAc)_2$ (3.877 g, 12.0 mmol) and stirred for 30 min. The solution was allowed to warm to 25 °C and continued to stir for 3 h. The mixture was diluted with EtOAc (100 mL) and washed with 3 x 20 mL brine, dried (Na_2SO_4), and concentrated *in vacuo* to afford an orange solid. The solid was purified using 8% EtOAc:hexanes to give an orange solid (1.140 g, 50 % over two steps): mp 110 - 112 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.10 (t, *J* = 7.9, 1H), 6.71 (d, *J* = 8.4, 1H), 6.34 (br s, 1H), 4.59 – 4.55 (m, 1H), 3.76 (s, 3H), 3.34 (s, 1H), 1.34 (d, *J* = 6.0, 6H), 1.32 (d, *J* = 7.1, 6H); ^{13}C NMR (151 MHz, DMSO) δ 156.2, 155.1, 135.9, 131.9, 125.5, 119.2, 110.5, 68.4, 51.0, 26.0, 21.4, 20.2; IR (neat) 3300, 2974, 1726 cm^{-1}; HRMS (ESI) m/z calcd for $C_{14}H_{22}NO_3$ $(M + H)^+$ 252.1594, found 252.1593.

Aniline S17F



To a solution of carbamate **S17E** (1.14 g, 4.5 mmol) in ethanol (45 mL, 0.1 M) was added LiOH (1.077 g, 45.0 mmol) and the mixture was refluxed for 24 h. The solution was concentrated to 15 mL *in vacuo* and then diluted with CH_2Cl_2 (100 mL). The resulting solution was washed with 3 x 20 mL H_2O, and the aqueous phase was extracted with 2 x 40 mL CH_2Cl_2. The combined organic phase was washed with 20 mL brine, dried (Na_2SO_4), and concentrated *in vacuo* to afford orange/red oil that was not purified further (0.839 g). This material was taken forward into the nosyl protection without purification.

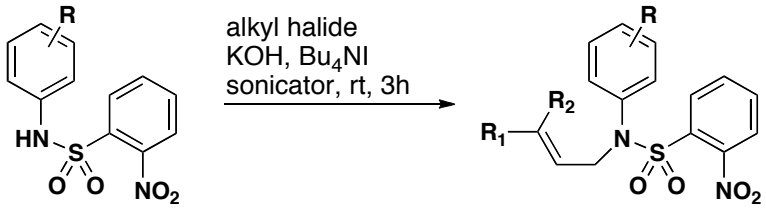
N-nosyl aniline S17



Pyridine (1.09 mL, 12.5 mmol) was added to a cooled (0 °C) solution of crude aniline **S17F** in CH_2Cl_2 (9.0 mL). The mixture was stirred for ten minutes before sulfonyl chloride (1.201 g, 5.42 mmol) was added. The reaction was stirred overnight at room temperature. The solvent and excess pyridine was removed *in vacuo.* The purple colored crude mixture was purified by flash chromatography (70:30 DCM/hexanes) to yield the product as a white to slightly yellow crystalline solid, (1.147 g, 67 %): mp 127 - 129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, *J*

= 8.0 Hz, 1.1 Hz, 1H), 7.82 (dd, *J* = 7.8 Hz, 1.4 Hz, 1H), 7.72 (td, *J* = 7.8 Hz, 1.4 Hz, 1H), 7.61 (td, *J* = 7.7 Hz, 1.2 Hz, 1H), 7.09 (br s, 1H), 7.00 (t, *J* = 8.1 Hz, 1H), 6.76 (d, *J* = 8.2 Hz, 1H), 6.65 (d, *J* = 7.6 Hz, 1H), 4.62 - 4.52 (m, 1H), 3.43 - 3.33 (m, 1H), 1.33 (d, *J* = 6.0 Hz, 6H), 1.13 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.5, 148.2, 134.1, 133.8, 133.7, 133.4, 132.8, 131.7, 126.6, 125.4, 119.7, 112.2, 69.4, 27.4, 22.0, 20.3; IR (neat) 3342, 2978, 1541 cm^{-1}; HRMS (ESI) m/z calcd for $C_{18}H_{23}N_2O_5S$ $(M + H)^+$ 379.1322, found 379.1323.

5. General procedure B: preparation of *N*-alkyl sulfonylanilines



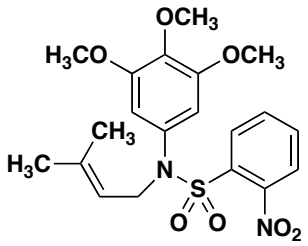
S5-S14 **15, 19-27, 37-40**

Sulfonylanilines were alkylated according procedure previously described by Keusenkothen and Smith (1992).[8] A solution of the sulfonylaniline (1.0 eq.) and the alkyl halide (1.5 eq.) in anhydrous THF was added to a sonicated suspension of grounded KOH (2.2 eq.) and tetrabutylammonium iodide (0.4 eq.) in anhydrous THF. The reaction mixture was stirred at room temperature (23 ^{o}C) for 3 hours. The crude reaction was then filtered through a plug of celite, which was washed with ethyl acetate. The filtrate was washed with water followed by brine and the organic layer was dried over sodium sulfate. The solvent was removed

[8]Keusenkothen, P. F.; Smith, M. B. *Tetrahedron Lett.* **1989**, *30*, 3369-3372.

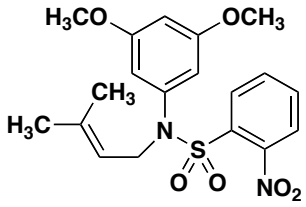
under reduced pressure and product was purified by recrystallization or by flash chromatography using a mixture of hexanes:ethyl acetate as the eluent.

N-prenyl-N-nosyl aniline 15



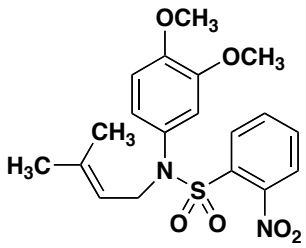
Compound **15** was prepared from a solution of sulfonylaniline **S6** (440.0 mg, 1.19 mmol) and prenyl bromide (267.0 mg, 1.79 mmol) in 4.7 mL of anhydrous THF which was combined to a sonicated suspension of grounded KOH (147.4 mg, 2.63 mmol) and Bu_3NI (176.5 mg, 0.48 mmol) in 5.6 ml of anhydrous THF. Purification by recrystallization from methanol:hexanes (~9:1) afforded the title compound in 77% yield (403.1 mg) as a white solid. mp 93.7 - 94.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (m, 3H), 7.51 (m, 1H), 6.34 (s, 2H), 5.18 (t, *J* = 7.2 Hz, 1H), 4.27 (d, *J* = 7.2 Hz, 2H), 3.80 (s, 3H), 3.68 (s, 6H), 1.62 (s, 3H), 1.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2, 148.1, 138.1, 137.8, 133.7, 133.5, 132.2, 132.0, 131.1, 123.8, 118.9 107.2, 61.0, 56.2, 50.3, 25.8, 17.7. IR (neat) cm^{-1} 2926, 1594, 1540, 1127; HRMS (ESI) m/z calcd for $C_{20}H_{24}N_2O_7S$ $(M + H)^+$ 437.1377, found 437.1375.

N-prenyl-N-nosyl aniline 19



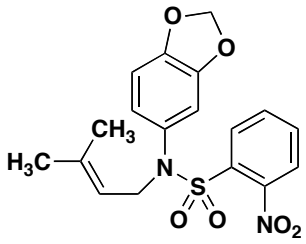
Compound **19** was prepared from a solution of sulfonylaniline **S5** (141.8 mg, 0.42 mmol) and prenyl bromide (93.7 mg, 0.63 mmol) in 1.7 mL of anhydrous THF which was combined to a sonicated suspension of grounded KOH (51.7 mg, 0.92 mmol) and Bu_4NI (61.9 mg, 0.17 mmol) in 2.0 ml of anhydrous THF. Purification by flash chromatography using 30% of ethyl acetate in hexanes as eluent afforded the title compound in 86% yield colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (m, 3H), 7.51 (m, 1H), 6.39 (t, *J* = 2.2 Hz, 2H), 6.33 (d, *J* = 2.2 Hz, 2H), 5.19 (t, *J* = 7.3 Hz, 1H), 4.33 (d, *J* = 7.3 Hz, 2H), 3.70 (s, 6H), 1.64 (s, 3H), 1.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 148.0, 139.8, 137.6, 133.7, 132.1, 131.8, 131.2, 123.8, 118.9, 107.6, 100.5, 55.5, 50.1, 25.7, 17.7. IR (neat) cm^{-1} 2939, 1603, 1539, 1161; HRMS (ESI) m/z calcd for $C_{19}H_{22}N_2O_6S$ $(M + H)^+$ 407.1272, found 407.1269.

N-prenyl-N-nosyl aniline 20



Compound **20** was prepared from a solution of sulfonylaniline **S7** (200.0 mg, 0.59 mmol) and prenyl bromide (132.1 mg, 0.89 mmol) in 2.4 mL of anhydrous THF which was combined to a sonicated suspension of grounded KOH (72.9 mg, 1.30 mmol) and Bu_3NI (87.3 mg, 0.23 mmol) in 2.8 ml of anhydrous THF. Purification by flash chromatograpy using a solution of 20% of ethyl acetate in hexanes as eluent, afforded the product as a slightly green oil in 88% yield (212.2 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (m, 3H), 7.51 (dt, *J* = 1.4, 7.3 Hz, 1H), 6.75 (d, *J* = 8.6 Hz, 1H), 6.70 (m, 2H), 5.20 (t, *J* = 7.3 Hz, 1H), 4.31 (d, *J* = 7.3 Hz, 2H), 3.86 (s, 3H), 3.75 (s, 3H), 1.64 (s, 3H), 1.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 148.9, 148.0, 137.7, 133.5, 132.2, 131.9, 131.1, 130.5, 123.8, 122.2, 118.93, 113.27, 110.70, 55.96, 55.86, 50.26, 25.70, 17.60. IR (neat) cm^{-1} 2945, 1601, 1551, 1508, 1163; HRMS (ESI) m/z calcd for $C_{19}H_{22}N_2O_6S$ $(M + H)^+$ 407.1272, found 407.1270.

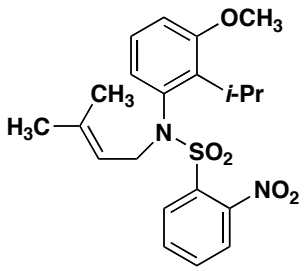
N-prenyl-N-nosyl aniline 21



Compound **21** was prepared from a solution of sulfonylaniline **S8** (190.3 mg, 0.59 mmol) and prenyl bromide (132.1 mg, 0.89 mmol) in 2.4 mL of anhydrous THF which was combined to a sonicated suspension of grounded KOH (72.9 mg, 1.30 mmol) and Bu_3NI (87.3 mg, 0.23 mmol) in 2.8 ml of anhydrous THF. Purification by flash chromatography using a solution of 20% of ethyl acetate in hexanes as

eluent afforded the product as white solid in 85% yield (194.3 mg). mp 95.0 - 95.4 ^{0}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (m, 3H), 7.54 (dt, *J* = 1.4 Hz, 8.0 Hz, 1H), 6.67 (m, 2H), 6.59 (dd, *J* = 2.0 Hz, 8.4 Hz, 1H), 5.97 (s, 2H), 5.18 (t, *J* = 7.3 Hz, 1H), 4.29 (d, *J* = 7.3, 2H), 1.64 (s, 3H), 1.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 147.9, 147.6, 137.8, 133.7, 132.1, 131.8, 131.4, 131.2, 123.8, 123.5, 118.8, 110.8, 108.0, 101.8, 50.4, 25.7, 17.6. IR (neat) cm^{-1} 2930, 1541, 1484, 1356, 1153; HRMS (ESI) m/z calcd for $C_{18}H_{18}N_2O_6S$ $(M + H)^+$ 391.0959, found 391.0961.

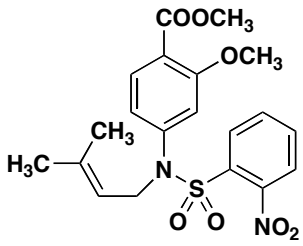
N-prenyl-N-nosyl aniline 22



Compound **22** was prepared from a solution of sulfonylaniline **S9** (150.0 mg, 0.43 mmol) and prenyl bromide (95.8 mg, 0.64 mmol) in 1.7 mL of anhydrous THF which was combined to a sonicated suspension of grounded KOH (52.9 mg, 0.94 mmol) and Bu_3NI (63.3 mg, 0.17 mmol) in 2.0 ml of anhydrous THF. Purification by flash chromatography using a solution of 20% of ethyl acetate in hexanes as eluent afforded the product as colorless oil in 93% yield (166.7 mg). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65 (td, *J* = 1.4 Hz, 7.8 Hz, 1H), 7.60 (dd, *J* = 1.4 Hz, 7.8 Hz, 1H), 7.57 (dd, *J* = 1.4 Hz, 8.0 Hz, 1H), 7.49 (td, *J* = 1.4 Hz, 8.0 Hz, 1H), 7.02 (t, *J* = 8.1 Hz, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 6.56 (d, *J* = 7.9 Hz, 1H), 5.20 (t, *J* =

8.2 Hz, 1H), 4.29 (d, *J* = 7.5 Hz, 2H), 3.80 (s, 3H), 3.42 (m, 1H), 1.63 (s, 3H), 1.39 (s, 3H), 1.23 (d, *J* = 7.0 Hz, 4H), 1.04 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.8, 148.2, 137.9, 137.6, 136.4, 133.5, 132.88, 132.3, 131.2, 126.3, 123.8, 122.9, 118.9, 112.0, 55.3, 51.1, 27.7, 25.9, 20.6, 19.7, 17.6. IR (neat) 2927, 1582, 1553, 1358 cm^{-1}; HRMS (ESI) m/z calcd for $C_{21}H_{26}N_2O_5S$ $(M + H)^+$ 419.1635, found 419.1635.

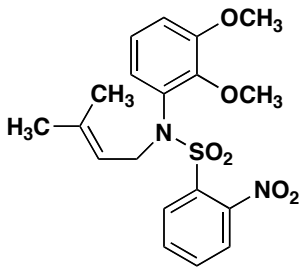
N-prenyl-N-nosyl aniline 23



Compound **23** was prepared from a solution of sulfonylaniline **S12** (222.2 mg, 0.61 mmol) and prenyl bromide (135.9 mg, 0.91 mmol) in 2.4 mL of anhydrous THF which was combined to a sonicated suspension of grounded KOH (5.0 mg, 1.33 mmol) and Bu_3NI (89.8 mg, 0.24 mmol) in 2.8 ml of anhydrous THF. Purification by flash chromatography using a solution of 30% of ethyl acetate in hexanes as eluent afforded the product as colorless solid in 94% yield (248.0 mg). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 1.2 Hz, 8.4 Hz, 1H), 7.63 (m, 1H), 7.57 (m, 2H), 7.48 (m, 1H), 6.84 (br s, 1H), 6.71 (dd, *J* = 1.7 Hz, 10.0 Hz, 1H), 5.10 (t, *J* = 7.2 Hz, 1H), 4.32 (d, *J* = 7.2 Hz, 2H), 3.81 (d, *J* = 1.2 Hz, 3H), 3.75 (s, 3H), 1.57 (s, 3H), 1.42 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.9, 159.4, 148.0, 142.9, 138.1, 133.9, 132.1, 131.8, 131.6, 131.3, 124.0, 120.0, 119.6, 118.5,

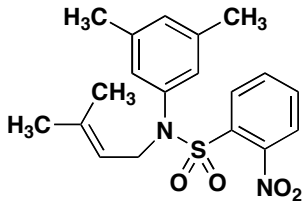
113.5, 56.2, 52.08, 49.8, 25.6, 17.7; IR (neat) 2962, 1726, 1601, 1536 1166 cm^{-1}; HRMS (ESI) m/z calcd for $C_{20}H_{22}N_2O_7S$ $(M + H)^+$ 435.1221, found 435.1219.

N-prenyl-N-nosyl aniline 24



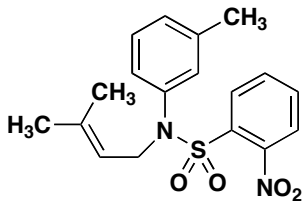
Compound **24** was prepared from a solution of sulfonylaniline **S14** (200.0 mg, 0.59 mmol) and prenyl bromide (132.1 mg, 0.89 mmol) in 2.4 mL of anhydrous THF which was combined to a sonicated suspension of grounded KOH (72.9 mg, 1.30 mmol) and Bu_3NI (87.3 mg, 0.23 mmol) in 2.8 ml of anhydrous THF. Purification by flash chromatography using a solution of 30% of ethyl acetate in hexanes as eluent afforded the product as yellow oil in 92% yield (212.9 mg). ^1H NMR (600 MHz, $CDCl_3$) δ 7.76 (bd, *J* = 7.9 Hz, 1H), 7.62 (m, 1H), 7.57 (m, 1H), 7.54 (m, 1H), 6.90 (m, 2H), 6.75 (dd, *J* = 1.9 Hz, 9.6 Hz, 1H), 5.14 (t, *J* = 6.9 Hz, 1H), 4.33 (br s, 2H), 3.79 (s, 3H), 3.59 (s, 3H), 1.56 (s, 3H), 1.37 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.3, 148.3, 147.7, 137.4, 133.9, 133.3, 131.4, 131.2, 130.8, 124.6, 123.8, 122.7, 119.2, 113.7, 60.5, 56.2, 49.5, 25.6, 17.5. IR (neat) 2925, 1601, 1536, 1356, 1175 cm^{-1}; HRMS (ESI) m/z calcd for $C_{19}H_{22}N_2O_6S$ $(M + H)^+$ 407.1272, found 407.1272.

N-prenyl-N-nosyl aniline 25



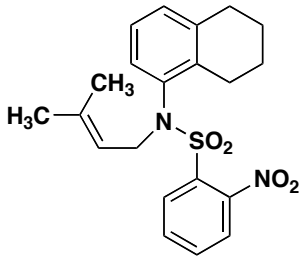
Compound **25** was prepared from a solution of sulfonylaniline **S10** (180.9 mg, 0.59 mmol) and prenyl bromide (132.6 mg, 0.89 mmol) in 2.4 mL of anhydrous THF which was combined to a sonicated suspension of grounded KOH (72.9 mg, 1.30 mmol) and Bu_3NI (87.3 mg, 0.23 mmol) in 2.8 ml of anhydrous THF. Purification by flash chromatography using a solution of 20% of ethyl acetate in hexanes as eluent afforded the product as white solid in 90% yield (198.7 mg). mp 102.2 - 103.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (td, *J* = 1.4 Hz, 7.8 Hz, 1H), 7.57 (dd, *J* = 1.4 Hz, 8.0 Hz, 1H), 7.52 (dd, *J* = 1.3 Hz, 7.2 Hz, 1H), 7.48 (dt, *J* = 1.3 Hz, 7.2 Hz, 1H), 6.89 (br s, 1H), 6.75 (br s, 2H), 5.14 (t, *J* = 7.1 Hz, 1H), 4.29 (d, *J* = 7.1 Hz, 2H), 2.20 (s, 6H), 1.59 (s, 3H), 1.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 138.7, 137.8, 137.3, 133.6, 132.2, 131.6, 131.0, 130.0, 127.1, 123.7, 118.9, 50.0, 25.6, 21.1, 17.6. IR (neat) 2907, 1680, 1541, 1330, 1148 cm^{-1}; HRMS (ESI) m/z calcd for $C_{19}H_{22}N_2O_4S$ $(M + H)^+$ 375.1373, found 375.1377.

N-prenyl-N-nosyl aniline 26



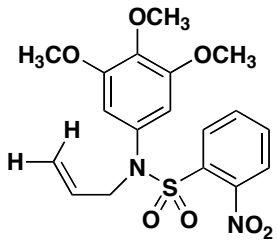
Compound **26** was prepared from a solution of sulfonylaniline **S13** (200.0 mg, 0.68 mmol) and prenyl bromide (152.9 mg, 1.03 mmol) in 2.7 mL of anhydrous THF which was combined to a sonicated suspension of grounded KOH (84.4 mg, 1.30 mmol) and Bu_3NI (101.1 mg, 0.27 mmol) in 3.2 ml of anhydrous THF. Purification by flash chromatography using a solution of 20% of ethyl acetate in hexanes as eluent afforded the product as colorless oil in 95% yield (195.3 mg). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (dt, *J* = 1.2 Hz, 8.0 Hz, 1H), 7.57 (dd, *J* = 1.2 Hz, 8.0 Hz, 1H), 7.53 (dd, *J* = 1.4 Hz, 8.0 Hz, 1H), 7.47 (dt, *J* = 1.4 Hz, 8.0 Hz, 1H), 7.14 (t, *J* = 7.8 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.98 (s, 1H), 6.91 (d, *J* = 7.3 Hz, 1H), 5.15 (t, *J* = 7.2 Hz, 1H), 4.32 (d, *J* = 7.2 Hz, 2H), 2.26 (s, 3H), 1.59 (s, 3H), 1.41 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.1, 139.1, 137.9, 137.5, 133.6, 132.21, 131.6, 131.1, 130.4, 129.1, 128.8, 126.4, 123.8, 118.9, 50.1, 25.6, 21.2, 17.6. IR (neat) 2914, 1624, 1544, 1359 cm^{-1}; HRMS (ESI) m/z calcd for $C_{18}H_{20}N_2O_4S$ $(M + H)^+$ 361.1217, found 361.1219.

N-prenyl-N-nosyl aniline 27



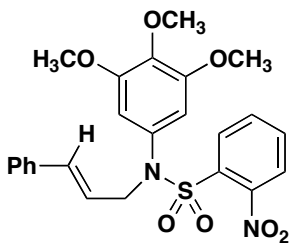
Compound **27** was prepared from a solution of sulfonylaniline **S11** (196.3 mg, 0.59 mmol) and prenyl bromide (132.1 mg, 0.89 mmol) in 2.4 mL of anhydrous THF which was combined to a sonicated suspension of grounded KOH (72.9 mg, 1.30 mmol) and Bu_3NI (87.3 mg, 0.23 mmol) in 2.8 ml of anhydrous THF. Purification by flash chromatography using a solution of 20% of ethyl acetate in hexanes as eluent afforded the product as slightly yellow solid in 93% yield (220.8 mg). mp 88.7 - 89.1 ^{0}C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (dt, *J* = 1.5 Hz, 8.1 Hz, 1H), 7.58 (dd, *J* = 1.5 Hz, 8.1 Hz, 1H), 7.56 (dd, *J* = 1.4 Hz, 8.1 Hz, 1H), 7.51 (dt, *J* = 1.4 Hz, 8.1 Hz, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 6.99 (t, *J* = 7.6 Hz, 1H), 6.73 (d, *J* = 7.6, 1H), 5.19 (t, *J* = 7.6 Hz, 1H), 4.31 (dd, *J* = 7.6 Hz and 14.5 Hz, 1H), 4.23 (dd, *J* = 7.6 Hz and 14.5 Hz, 1H), 2.75 (t, *J* = 6.5 Hz, 2H), 2.66 (m, 2H), 1.71 (m, 2H), 1.60 (m, 5H), 1.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 139.1, 138.8, 138.1, 136.2, 133.5, 132.6, 131.7, 131.0, 129.7, 127.7, 125.4, 123.6, 118.3, 49.9, 29.4, 25.6, 25.3, 22.6, 22.5, 17.3. IR (neat) cm^{-1} 2919, 2854, 1547, 1145; HRMS (ESI) m/z calcd for $C_{21}H_{24}N_2O_4S$ $(M + H)^+$ 401.1530, found 401.1530.

N-allyl-N-nosyl aniline 37



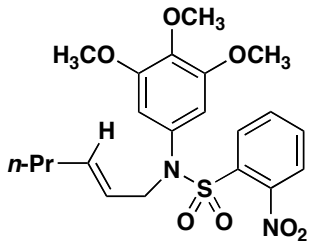
Compound **37** was prepared from a solution of sulfonylaniline **S6** (200.0 mg, 0.54 mmol) and allyl bromide (98.5 mg, 0.81 mmol) in 2.2 mL of anhydrous THF which was combined to a sonicated suspension of grounded KOH (67.0 mg, 1.19 mmol) and Bu_3NI (80.2 mg, 0.21 mmol) in 2.6 ml of anhydrous THF. Purification by recrystallization from methanol:hexanes (~9:1) afforded the title compound in 98% yield (217.8 mg) as a white solid. mp 92.3 - 93.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (m, 1H), 7.59 (dd, *J* = 1.4, 5.3 Hz, 1H), 7.57 (dd, *J* = 1.3, 5.2 Hz, 1H), 7.47 (m, 1H), 6.31 (s, 2H), 5.77 (m, 1H), 5.09 (dd, *J* = 1.3, 15.9 Hz, 1H), 5.05 (dd, *J* = 1.3, 8.8, 1H), 4.27 (d, *J* = 6.4 Hz, 2H), 3.75 (s, 3H), 3.64 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 147.9, 138.0, 133.9, 133.2, 132.9, 131.9, 131.7, 131.13, 123.8, 119.1, 106.9, 60.8, 56.1, 55.1. IR (neat) cm^{-1} 2981, 1601, 1356, 1122; HRMS (ESI) m/z calcd for $C_{18}H_{20}N_2O_7S$ $(M + H)^+$ 409.1064, found 409.1062.

N-(*E*)-cinnamyl-N-nosyl aniline 38



Compound **38** was prepared from a solution of sulfonylaniline **S6** (108.7 mg, 0.29 mmol) and cinnamyl bromide (87.0 mg, 0.44 mmol) in 1.2 mL of anhydrous THF which was combined to a sonicated suspension of grounded KOH (36.5 mg, 0.65 mmol) and Bu_3NI (43.7 mg, 0.12 mmol) in 1.4 ml of anhydrous THF. Purification by flash chromatography using a solution of 20% of ethyl acetate in hexanes as eluent afforded the product as slightly yellow solid in 76% yield (108.0 mg). mp 80.0 - 80.8 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (m, 3H), 7.52 (m, 1H), 7.29 (m, 4H), 7.24 (m, 1H), 6.42 (d, *J* = 16.0 Hz, 1H), 6.40 (s, 2H), 6.22 (m, 1H), 4.49 (d, *J* = 6.7 Hz, 2H), 3.83 (s, 3H), 3.67 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 148.0, 138.3, 136.4, 133.8, 133.3, 132.4, 132.3, 131.3, 128.7, 128.1, 126.6, 124.2, 124.0, 107.3, 61.0, 56.3, 55.1. IR (neat) cm^{-1} 2933, 1601, 1544, 1126; HRMS (ESI) m/z calcd for $C_{24}H_{24}N_2O_7S$ $(M + H)^+$ 485.1377, found 485.1377.

N-(*E*)-2,3-hexenyl-N-nosyl aniline E39

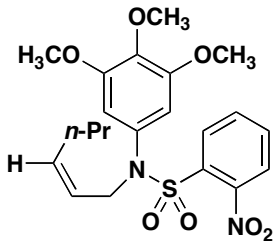


(*E*)- isomer

Compound **E39** was prepared from a solution of sulfonylaniline **S6** (217.7 mg, 0.59 mmol) and *trans*-2,3-hexenyl bromide (144.5 mg, 0.89 mmol) in 2.4 mL of anhydrous THF which was combined to a sonicated suspension of grounded KOH (72.9 mg, 1.30 mmol) and Bu_3NI (87.3 mg, 0.24 mmol) in 2.8 ml of

anhydrous THF. Purification by flash chromatography using a solution of 20% of ethyl acetate in hexanes as eluent afforded the product as a slightly yellow oil in 86% yield (227.6 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (m, 3H), 7.53 (ddd, *J* = 1.6 Hz, 7.2 Hz, 8.0 Hz, 1H), 6.35 (s, 2H), 5.46 (m, 2H), 4.26 (d, *J* = 5.5 Hz, 2H), 3.82 (s, 3H), 3.71 (s, 6H), 1.93 (m, 2H), 1.28 (m, 2H), 0.76 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 147.9, 138.0, 136.4, 133.7, 133.2, 132.0, 131.9, 131.1, 124.5, 123.8, 107.3, 60.8, 56.1, 54.7, 34.1, 22.0, 13.30. IR (neat) cm^{-1} 2969, 1601, 1551, 1128; HRMS (ESI) m/z calcd for $C_{21}H_{26}N_2O_7S$ $(M + H)^+$ 451.1534, found 451.1532.

N-(*Z*)-2,3-hexenyl-N-nosyl aniline Z39

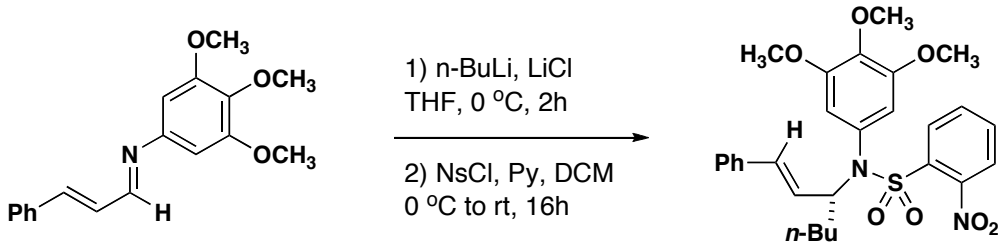


(*Z*)- isomer

Compound **Z39** was prepared from a solution of sulfonylaniline **S6** (217.7 mg, 0.59 mmol) and *trans*-2,3-hexenyl bromide (144.5 mg, 0.89 mmol) in 2.4 mL of anhydrous THF which was combined to a sonicated suspension of grounded KOH (72.9 mg, 1.30 mmol) and Bu_3NI (87.3 mg, 0.24 mmol) in 2.8 ml of anhydrous THF. Purification by flash chromatography using a solution of 20% of ethyl acetate in hexanes as eluent afforded the product as white solid in 90% yield (240.3 mg). mp 66.2 - 66.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (m, 3H), 7.56 (ddd, *J* = 1.4 Hz, 7.6 Hz, 8.0 Hz, 1H), 6.39 (s, 2H), 5.48 (m, 2H), 4.37 (d, *J* =

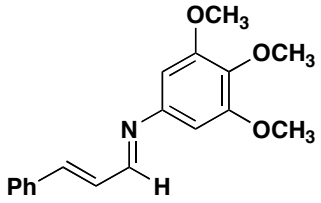
6.8 Hz, 2H), 3.82 (s, 3H), 3.72 (s, 6H), 1.87 (m, 2H), 1.18 (hex, *J* = 7.4 Hz, 2H), 0.75 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2, 148.0, 138.1, 135.0, 133.8, 133.3, 132.0, 132.0, 131.1, 123.8, 107.2, 107.1, 60.8, 56.1, 49.1, 29.1, 22.4, 13.6. IR (neat) 2931, 1590,1550, 1121 cm^{-1}; HRMS (ESI) m/z calcd for $C_{21}H_{26}N_2O_7S$ $(M + H)^+$ 451.1534, found 451.1532.

Procedures for the preparation of alkene 38



imine 40A **40**

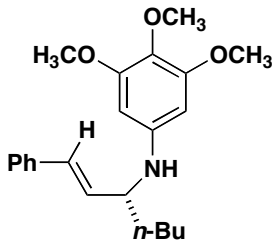
imine 40A



Imine compound **40A** was prepared according procedure previously described by Pace and co-workers (2011). Cinnamaldehyde (300.5 mg, 2.27 mmol) was dissolved in 7 mL of anhydrous toluene under argon atmosphere. Then, anhydrous magnesium sulfate (273.7 mg, 2.27 mmol) and 3,4,5-trimethoxyanline (500.0 mg, 2.73 mmol) were added at room temperature (23 °C). The reaction mixture was stirred at room temperature for 2 hours. After filtration to remove

magnesium sulfate, the solvent was removed under reduced pressure yielding 587.7 mg (87%) of product as a yellow solid, which was used in the next step without further purification. mp 95.1 - 95.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 6.8 Hz, 2H), 7.40 (m, 3H), 7.19 (d, *J* = 15.8 Hz, 1H), 7.10 (dd, *J* = 8.4 Hz, 15.8 Hz, 1H), 6.48 (s, 2H), 3.90 (s, 6H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 153.7, 147.6, 144.1, 136.8, 135.7, 129.8, 129.1, 128.6, 127.6, 98.4, 61.1, 56.3. IR (neat) cm^{-1} 3004, 2924, 1632, 1574; HRMS (ESI) m/z calcd for $C_{18}H_{19}NO_3$ $(M + H)^+$ 298.1438, found 298.1441.

N-alkyl aniline 40B

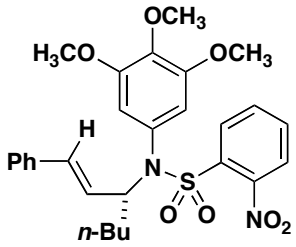


Amine compound **40B** was prepared according procedure previously described by Pace and co-workers (2011).[9] To a suspension of the imine **40A** (100.0 mg, 0.34 mmol) in 1.0 mL of anhydrous THF and LiCl (21.4 mg, 0.50 mmol) at 0 °C, was added *n*-BuLi (0.25 mL, 2.17 M, 0.504 mmol) within five minutes. The reaction mixture was stirred at 0 °C for 90 minutes. Then, after quenching with NH_4Cl aqueous solution at 1.0 M (10 mL), crude product was extracted using ethyl acetate (3x 15 mL). The combined organic layers were dried over sodium

[9] Pace, V.; Castoldi, L.; Hoyos, P.; Sinisterra, J. V.; Pregnolato, M.; Sanchez-Montero, J. M. *Tetrahedron* **2011**, *67*, 2670-2675.

sulfate and the solvent was removed under reduced pressure. Flash chromatography purification using 20% of ethyl acetate in hexanes as eluent afforded 86.8 mg (73%) of product as pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) 7.35 (d, *J* = 7.0 Hz, 2H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.21 (d, *J* = 7.2 Hz, 1H), 6.58 (d, *J* = 16.0 Hz, 1H), 6.11 (dd, *J* = 6.7 Hz, 16.0 Hz, 1H), 5.90 (s, 2H), 3.90 (m,1H), 3.78 (s, 6H), 3.75 (s, 3H), 1.67 (s, 2H), 1.38 (s, 4H), 0.92 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 144.5, 137.0, 132.7, 130.4, 129.9, 128.6, 127.4, 126.3, 90.9, 61.1, 56.4, 55.9, 36.1, 28.2, 22.7, 14.1. IR (neat) 3385, 2933, 1614, 1508, 1130 cm^{-1}; HRMS (ESI) m/z calcd for $C_{22}H_{29}NO_3$ $(M + H)^+$ 356.2220, found 356.2227.

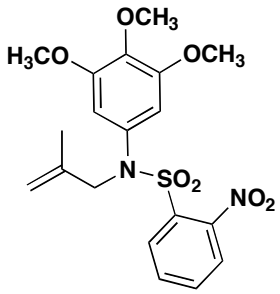
N-alkyl-N-nosyl aniline 40



Compound **38** was prepared according general procedure described in the general procedure 3. To a solution of the amine compound (80.0 mg, 0.24 mmol) in dichloromethane (0.5 mL) at 0^{o}C was added pyridine (56.1 mg, 0.71 mmol) and nosyl chloride (57.7 mg, 0.26 mmol). The reaction mixture was allowed to reach the room temperature and was stirred for 16 hours. Purification by flash chromatography using 20% of ethyl acetate in hexanes as eluent afforded 87.2 mg (71%) of product as a slightly brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 1.1 Hz, 7.9 Hz, 1H), 7.63 (m, 2H), 7.51 (ddd, *J* = 1.9 Hz, 6.9 Hz and 8.0

Hz, 1H), 7.30 (m, 4H), 7.23 (m, 1H), 6.66 (d, *J* = 16.0 Hz, 1H), 6.31 (s, 2H), 5.95 (dd, *J* = 8.6 Hz, 16.0 Hz, 1H), 4.96 (td, *J* = 6.4 Hz, 8.6 Hz, 1H), 3.87 (s, 3H), 3.63 (s, 6H), 1.79 (m, 1H), 1.52 (m, 1H), 1.35 (m, 4H), 0.89 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.9, 148.0, 138.8, 136.6, 133.6, 133.6, 133.2, 132.1, 131.1, 129.8, 128.7, 128.0, 127.8, 126.5, 123.9, 110.2, 62.0, 61.0, 56.2, 33.8, 28.5, 22.5, 14.1. IR (neat) 2939, 1593, 1550 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{32}N_2O_7S$ $(M + H)^+$ 541.2003, found 541.2008.

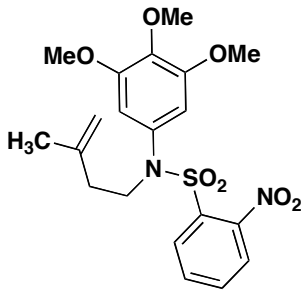
N-methallyl-N-nosyl aniline 46



To a cooled (0 °C) solution of the aniline **S6** (0.368 g, 1.0 mmol) in tetrahydrofuran (10 mL, 0.1 M) was added triphenylphosphine (0.323 g, 1.2 mmol). The solution was stirred for 10 min. β-methallyl alcohol (0.085 mL, 1.0 mmol) was added to the solution followed by Diisopropyl azodicarboxylate (0.236 mL, 1.2 mmol) dropwise. The reaction was stirred overnight at room temperature. The solvent was removed *in vacuo* to afford a yellow oil. The product was purified by flash chromatography (01:01:198 MeOH/TEA/CH_2Cl_2) to give the product as a yellow oil (0.2074 g, 50 %); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.61 (m, 2H), 7.59 (d, *J* = 8.2, 1H), 7.51 – 7.45 (m, 1H), 6.39 (s, 2H), 4.85 (s, 1H), 4.81 (s, 1H), 4.30 (s, 2H), 3.82 (s, 3H), 3.70 (s, 6H), 1.83 (s, 3H). ^{13}C NMR (100

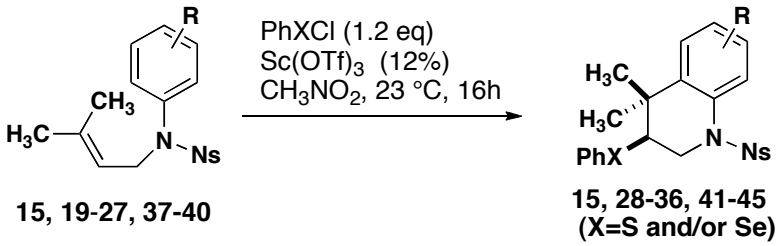
MHz, $CDCl_3$) δ 153.0, 147.8, 139.9, 137.9, 133.8, 133.2, 132.0, 131.4, 131.0, 123.7, 115.3, 106.5, 60.8, 58.6, 56.1, 19.7; IR (neat) 3017, 2940, 2840, 1543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{19}H_{23}N_2O_7S$ $(M + H)^+$ 423.1220, found 423.1213.

N-homomethallyl-N-nosyl aniline 47



To a cooled (0 °C) solution of the aniline **S6** (0.184 g, 0.50 mmol) in tetrahydrofuran (5 mL, 0.1 M) was added triphenylphosphine (0.162 g, 0.60 mmol). The solution was stirred for 10 min. 3-methyl-3-buten-1-ol (0.050 mL, 0.50 mmol) was added to the solution followed by Diisopropyl azodicarboxylate (0.118 mL, 0.60 mmol) dropwise. The reaction was stirred overnight at room temperature. The solvent was removed *in vacuo* to afford a yellow oil. The product was purified by flash chromatography (01:99 $MeOH/CH_2Cl_2$) to give the product as a yellow solid (0.211 g, 97 %): mp 160 - 163 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.40 (m, 4H), 6.36 (s, 2H), 4.77 (s, 1H), 4.65 (s, 1H), 3.82 (d, *J* = 7.2, 2H), 3.79 (s, 3H), 3.67 (s, 6H), 2.17 (t, *J* = 7.3, 2H), 1.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2, 148.0, 141.9, 138.1, 133.7, 133.1, 132.0, 131.6, 131.0, 123.7, 112.8, 107.0, 60.9, 56.2, 50.4, 36.9, 22.2; IR (neat) 3095, 2946, 1547 cm^{-1}; HRMS (ESI) m/z calcd for $C_{20}H_{25}N_2O_7S$ $(M + H)^+$ 437.1377, found 437.1377.

6. General procedure C: monocyclizations



15, 19-27, 37-40 → **15, 28-36, 41-45 (X=S and/or Se)**

In a flamed dried flask under an argon atmosphere containing $Sc(OTf)_3$ (12 mol%) in the reported solvent (0.3 M), and sodium hexafluoroantimonate (0 - 1.2 eq), was added at room temperature the PhXCl (X= S or Se) or PhSOMe (1.2 eq). The alkene substrate (1.0 eq) was added last. When the alkene was an oil, a portion of the solvent (1/2) was saved to dissolve and deliver the substrate as a solution. The reaction mixture was stirred at room temperature for 16 hours. Then, the crude product was filtered through a plug of silica and washed using dichloromethane. The solvent was removed under reduced pressure and the product was purified by flash chromatography.

Optimization of monocyclizations mediated by sulfur electrophiles

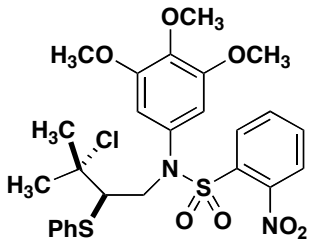
In an effort to synthesize compound **18a,** the alkene **15** (28.0 mg, 0.064 mmol) was added to a solution of scandium triflate (25 mol%, 7.8 mg, 0.016 mmol) and PhSCl (17.9 mg, 0.128 mmol) in anhydrous dichloromethane (3.2 mL). After work up and purification by flash chromatography using 20% of ethyl acetate in hexanes as eluent, no desired product was obtained. Instead, compound **16** was obtained as the only product in 20% yield (7.5 mg) as colorless oil. Total

conversion of starting material to the side product **13** was observed by TLC. It is possible the product degraded on silica gel upon purification.

In another experiment, the alkene **15** (28.0 mg, 0.064 mmol) was added to a solution of scandium triflate (25 mol%, 7.8 mg, 0.016 mmol) and PhSOMe (17.9 mg, 0.128 mmol) in anhydrous dichloromethane (3.2 mL). Purification by flash chromatography using 20% of ethyl acetate in hexanes as eluent afforded compound **18a** in 16% yield (5.5 mg) and by-product **17** in 55% yield (20.4 mg).

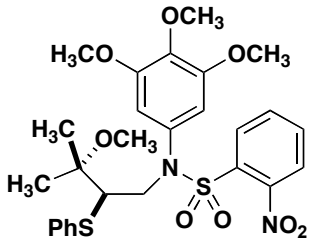
Fortunately, changing the conditions to more polar solvents such as acetonitrile and nitromethane resulted solely in the formation of the desired product **18a** as a slighly yellow solid. To accomplish this alkene **15** (14.0 mg, 0.032 mmol) was added to a solution of scandium triflate (12 mol%, 1.8 mg, 0.004 mmol) and PhSCl (5.4 mg, 0.038 mmol) in anhydrous acetonitrile or nitromethane (1.0 mL). After work up and purification by flash chromatography using 20% of ethyl acetate in hexanes as eluent, the product **18a** was isolated in 73% yield (12.7 mg) from the reaction carried out in acetonitrile and in 87% yield (15.2 mg) from the reaction carried out in nitromethane.

By-product 16



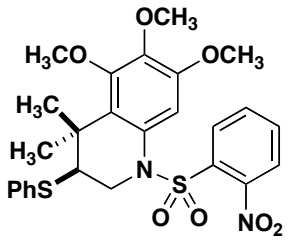
^{1}H NMR (400 MHz, $CDCl_3$): 7.64 (m, 2H), 7.60 (dd, *J* = 1.2 Hz, 7.9 Hz, 1H), 7.51 (dd, *J* = 1.3 Hz, 8.0 Hz, 1H), 7.46 (m, 2H), 7.35 (m, 2H), 7.25 (s, 2H), 6.34 (s, 2H), 4.50 (dd, *J* = 2.7 Hz, 14.4 Hz, 1H), 4.16 (dd, *J* = 10.8 Hz, 14.4 Hz, 1H), 3.83 (s, 3H), 3.56 (s, 6H), 3.33 (dd, *J* = 2.7 Hz, 10.8 Hz, 1H), 1.70 (s, 3H), 1.69 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 147.23, 136.4, 135.6, 132.8, 131.6, 131.4, 130.6, 130.1, 129.6, 128.1,125.9, 122.9, 105.5, 72.3, 60.11, 58.7, 55.3, 52.7, 32.0, 27.2. IR (neat) 2940, 1599, 1546, 1375, 1133 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{29}ClN_2O_7S_2$ $(M + H)^+$ 581.1178, found 581.1162.

By-product 17



^{1}H NMR (400 MHz, $CDCl_3$): 7.63 (m, 1H), 7.58 (dd, *J* = 1.4 Hz, 7.9 Hz, 1H), 7.50 (dd, *J* = 1.4 Hz, 8.0 Hz, 1H), 7.45 (m, 1H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.24 (t, *J* = 7.6 Hz, 2H), 7.16 (t, *J* = 7.3 Hz, 1H), 6.23 (s, 2H), 4.33 (dd, *J* = 3.3 Hz, 14.5 Hz, 1H), 3.98 (dd, *J* = 10.3 Hz, 14.5 Hz, 1H), 3.81 (s, 3H), 3.52 (s, 6H), 3.23 (dd, *J* = 3.3 Hz, 10.3 Hz, 1H), 3.08 (s, 3H), 1.33 (s, 3H), 1.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2, 148.2, 138.0, 137.3, 133.6, 133.3, 132.3, 131.8, 131.0, 130.5, 129.0, 126.4, 123.7, 106.7, 78.2, 61.1, 56.2, 53.7, 49.7, 23.9, 22.3. IR (neat) cm^{-1} 2938, 2833, 1596, 1553, 1124; HRMS (ESI) m/z calcd for $C_{27}H_{32}N_2O_8S_2$ $(M + H)^+$ 599.1492, found 599.1488.

Cyclized compound 18a



mp 149.4-151.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): 7.60 (m, 2H), 7.54 (dd, *J* = 1.1 Hz, 8.0 Hz, 1H), 7.46 (m, 2H), 7.39 (ddd, *J* = 1.5 Hz, 7.3 Hz, 8.0 Hz, 1H), 7.33 (m, 3H), 6.65 (s, 1H), 4.07 (dd, *J* = 3.5 Hz, 14.1 Hz, 1H), 3.95 (s, 3H), 3.82 (s, 3H), 3.71 (s, 3H), 3.47 (dd, *J* = 12.1 Hz, 14.1 Hz, 1H), 3.21 (dd, *J* = 3.5 Hz, 12.1 Hz, 1H), 1.70 (s, 3H), 1.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4, 151.5, 145.0, 141.1, 136.7, 134.3, 134.0, 133.3, 132.9, 131.8, 131.0, 130.2, 129.3, 127.8, 124.6, 103.9, 77.4, 77.2, 77.0, 60.9, 60.6, 57.7, 55.8, 47.5, 37.7, 26.1, 23.6. IR (neat) cm^{-1} 2942, 1593, 1556, 1337; HRMS (ESI) m/z calcd for $C_{25}H_{25}N_2O_7S_2$ $(M + H)^+$ 545.1411, found 545.1410.

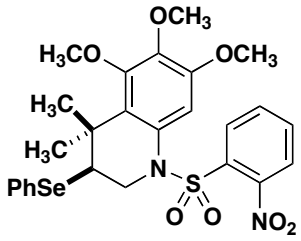
Optimization of monocyclizations mediated by phenylselenenyl chloride (PhSeCl)

Compound **18b** was easily prepared from phenylselenenyl chloride. Initially, the desired product was obtained from the reaction using alkene **15** (28.0 mg, 0.064 mmol), phenylselenenyl chloride (24.57 mg, 0.128 mmol), $Sc(OTf)_3$ (25 mol%, 7.8 mg, 0.016 mmol) in dichloromethane (3.2 mL). Work up and purification by flash chromatography afforded 29.5 mg (78%) of product as yellow solid.

The yield was improved when the reaction was carried out using the alkene **12** (14.0 mg, 0.032 mmol) in acetonitrile (1.0 mL), scandium triflate (12 mol%, 1.8 mg, 0.004 mmol), sodium hexafluorantimonate (9.9 mg, 0.038 mmol) and PhSeCl (7.3 mg, 0.038 mmol). Purification by flash chromatography using 20% of ethyl acetate in hexanes as eluent afforded 15.8 mg (83%) of desired product.

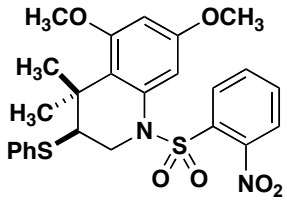
When this reaction was carried out in nitromethane (7.6 mL) using the alkene **12** (100.0 mg, 0.23 mmol), phenylselenenyl chloride (52.7 mg, 0.27 mmol) and scandium triflate (12 mol%, 13.5 mg, 0.03 mmol), the product was obtained in 95% yield (129.0 mg).

Cyclized compound 18b



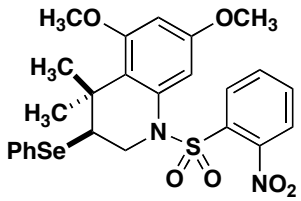
mp 148.5-149.0 ^{o}C. ^{1}H NMR (600 MHz, $CDCl_3$): 7.61 (d, *J* = 7.0 Hz, 3H), 7.56 (dd, *J* = 1.1 Hz, 7.9 Hz, 1H), 7.47 (dd, *J* = 0.9 Hz, 8.0 Hz, 1H), 7.38 (m, 4H), 6.67 (s, 1H), 4.16 (dd, *J* = 3.5 Hz, 14.2 Hz, 1H), 3.95 (s, 3H), 3.83 (s, 3H), 3.73 (s, 3H), 3.61 (dd, *J* = 12.5 Hz, 14.2 Hz, 1H), 3.29 (dd, *J* = 3.5 Hz, 12.5 Hz, 1H), 1.68 (s, 3H), 1.34 (s, 3H).). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.4, 151.6, 135.8, 133.9, 131.7, 131.1, 130.2, 129.5, 128.6, 128.3, 124.6, 124.4, 104.2, 61.0, 60.6, 55.9, 55.3, 48.7, 37.8, 26.5, 25.10. IR (neat) 2934, 1607, 1546, 1372 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{28}N_2O_7SSe$ $(M + H)^+$ 593.0855, found 593.0857.

Cyclized compound 28a



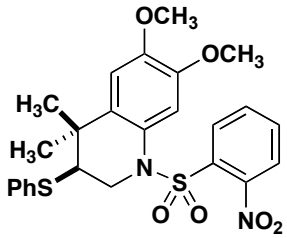
Compound **28a** was prepared from alkene **19** (13.0 mg, 0.032 mmol), phenylsulfenyl chloride (5.3 mg, 0.038 mmol) and scandium triflate (12 mol%, 1.8 mg, 0.004 mmol) in anhydrous nitromethane (1.0 mL). After work up and purification by flash chromatography using 20% of ethyl acetate in hexanes as eluent, the product **28a** was obtained in 88% yield (14.5 mg) as a white solid. mp 129.4-131.0 ^{o}C. ^{1}H NMR (600 MHz, $CDCl_3$): 7.65 (d, *J* = 7.8 Hz, 1H), 7.63 (m, 2H), 7.47 (m, 2H), 7.44 (m, 1H), 7.32 (m, 3H), 6.42 (d, *J* = 2.5 Hz, 1H), 6.35 (d, *J* = 2.5 Hz, 1H), 4.19 (dd, *J* = 3.4 Hz, 14.0 Hz, 1H), 3.82 (s, 3H), 3.66 (s, 3H), 3.51 (dd, *J* = 12.0 Hz, 14.0 Hz, 1H), 3.23 (dd, *J* = 3.4 Hz, 12.0 Hz, 1H), 1.70 (s, 3H), 1.37 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.7, 158.3, 148.0, 136.6, 134.5, 133.9, 133.8, 133.1, 132.0, 130.8, 129.4, 127.7, 124.7, 119.3, 100.6, 98.0, 58.4, 55.4, 55.4, 47.7, 37.5, 25.6, 22.4. IR (neat) cm^{-1} 2971, 1625, 1592, 1541, 1344; HRMS (ESI) m/z calcd for $C_{25}H_{26}N_2O_6S_2$ $(M + H)^+$ 515.1305, found 515.1303.

Cyclized compound 28b



Compound **28b** was prepared from alkene **19** (13.0 mg, 0.032 mmol), phenylsulfenyl chloride (5.3 mg, 0.038 mmol), sodium hexafluoroantimonate (9.9 mg, 0.038 mmol) and scandium triflate (12 mol%, 1.8 mg, 0.004 mmol) in anhydrous acetonitrile (1.0 mL). After work up and purification by flash chromatography using 20% of ethyl acetate in hexanes as eluent, the product **28b** was obtained in 71% yield (12.8 mg) as slightle yellow solid. mp 137.3-139.1 ^{o}C. ^{1}H NMR (600 MHz, $CDCl_3$): 7.60 (m, 5H), 7.38 (m, 2H), 7.32 (m, 2H), 6.45 (d, *J* = 2.5 Hz, 1H), 6.35 (d, *J* = 2.5 Hz, 1H), 4.28 (dd, *J* = 3.5 Hz, 13.9 Hz, 1H), 3.81 (s, 3H), 3.67 (s, 3H), 3.64 (dd, *J* = 12.5 Hz, 13.9 Hz, 1H), 3.29 (dd, *J* = 3.5 Hz, 12.5 Hz, 1H), 1.69 (s, 3H), 1.36 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.6, 158.3, 148.0, 136.6, 135.5, 133.8, 133.7, 131.9, 130.8, 129.4, 128.7, 128.2, 124.6, 119.0, 100.8, 98.1, 56.0, 55.4, 55.4, 48.8, 37.6, 25.9, 23.8. IR (neat) 2958, 1616, 1580, 1544, 1342 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{26}N_2O_6SSe$ $(M + H)^+$ 563.0750, found 563.0749.

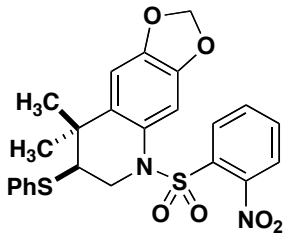
Cyclized compound 29



Compound **29** was prepared from alkene **20** (13.0 mg, 0.032 mmol), phenylsulfenyl chloride (5.3 mg, 0.038 mmol), and scandium triflate (12 mol%, 1.8 mg, 0.004 mmol) in anhydrous nitromethane (1.0 mL). After work up and purification by flash chromatography using 30% of ethyl acetate in hexanes as

eluent, the product **29** was obtained in 75% yield (12.4 mg) as a slightly yellow solid. mp 176.6-178.1 ^{o}C. ^{1}H NMR (600 MHz, $CDCl_3$): 7.62 (td, *J* = 1.2 Hz, 7.6 Hz, 1H), 7.55 (m, 2H), 7.44 (m, 2H), 7.39 (m, 1H), 7.33 (m, 3H), 6.96 (s, 1H), 6.79 (s, 1H), 4.11 (dd, *J* = 3.8 Hz, 14.1 Hz, 1H), 3.88 (s, 3H), 3.79 (s, 3H), 3.56 (dd, *J* = 11.7 Hz, 14.1 Hz, 1H), 3.20 (dd, *J* = 3.8 Hz, 11.7 Hz, 1H), 1.55 (s, 3H), 1.26 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.2, 147.5, 147.3, 134.2, 133.9, 133.3, 132.7, 131.7, 131.0, 130.3, 129.4, 127.9, 127.2, 124.5, 109.9, 107.7, 56.3, 56.0, 55.4, 47.8, 37.7, 28.4, 27.3. IR (neat) cm^{-1} 2964, 1548, 1512, 1336, 1149; HRMS (ESI) m/z calcd for $C_{25}H_{26}N_2O_6S_2$ $(M + H)^+$ 515.1305, found 515.1303.

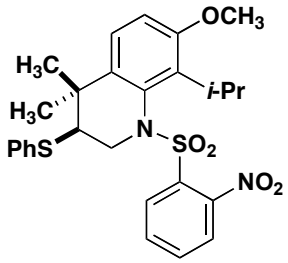
Cyclized compound 30



Compound **30** was prepared from alkene **21** (12.5 mg, 0.032 mmol), phenylsulfenyl chloride (5.3 mg, 0.038 mmol), and scandium triflate (12 mol%, 1.8 mg, 0.004 mmol) in anhydrous nitromethane (1.0 mL). After work up and purification by flash chromatography using 25% of ethyl acetate in hexanes as eluent, the product **30** was obtained in 75% yield (12.4 mg) as a yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$): 7.63 (m, 1H), 7.59 (m, 2H), 7.43 (m, 2H), 7.39 (m, 1H), 7.32 (m, 3H), 6.85 (s, 1H), 6.81 (s, 1H), 4.10 (dd, *J* = 3.7 Hz, 14.1 Hz, 1H), 3.54 (dd, *J* = 11.7 Hz, 14.1 Hz, 1H), 3.19 (dd, *J* = 3.7 Hz, 11.7 Hz, 1H), 1.52 (s, 3H), 1.25 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.0, 146.1, 146.1, 134.2, 133.9,

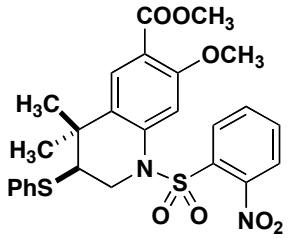
133.3, 132.8, 132.1, 131.9, 131.0, 129.4, 128.0, 127.9, 124.6, 106.7, 105.2, 101.7, 55.4, 48.0 38.2, 28.3, 27.3. IR (neat) 2961, 1539, 1481, 1361 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{22}N_2O_6S_2$ $(M + H)^+$ 499.0992, found 499.0992.

Cyclized compound 31



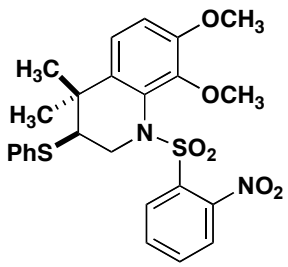
Compound **31** was prepared from alkene **22** (26.8 mg, 0.064 mmol), phenylsulfenyl chloride (10.8 mg, 0.077 mmol), and scandium triflate (12 mol%, 3.8 mg, 0.008 mmol) in anhydrous nitromethane (2.1 mL). After work up and purification by flash chromatography using 25% of ethyl acetate in hexanes as eluent, the product **31** was obtained in 78% yield (26.4 mg) as a colorless oil. ^1H NMR (600 MHz, $CDCl_3$): 7.55 (m, 2H), 7.51 (dd, *J* = 1.4 Hz, 8.2 Hz, 1H), 7.42 (dd, *J* = 3.2 Hz, 6.3 Hz, 2H), 7.32 (m, 4H), 7.20 (d, *J* = 8.8 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 1H), 4.28 (dd, *J* = 4.1 Hz, 14.3 Hz, 1H), 3.79 (s, 3H), 3.58 (dd, *J* = 12.2 Hz, 14.3, 1H), 3.35 (dd, *J* = 4.1 Hz, 12.2, 1H), 3.18 (sep, *J* = 6.9 Hz, 1H), 1.52 (s, 3H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.22 (s, 3H), 1.06 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.7, 148.1, 134.0, 133.6, 133.5, 133.4, 133.4, 132.9, 131.5, 130.6, 129.2, 127.8, 125.4, 124.3, 111.1, 55.3, 55.0, 50.0, 38.1, 29.8, 29.4, 27.9, 22.0, 19.6. IR (neat) 2982, 1676, 1553, 1358 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{30}N_2O_5S_2$ $(M + H)^+$ 527.1669, found 527.1669.

Cyclized compound 32



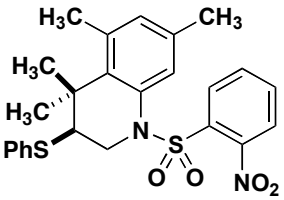
Compound **32** was prepared from alkene **23** (27.8 mg, 0.064 mmol), phenylsulfenyl chloride (10.8 mg, 0.077 mmol) and scandium triflate (12 mol%, 3.8 mg, 0.008 mmol) in anhydrous nitromethane (2.1 mL). After work up and purification by flash chromatography using 40% of ethyl acetate in hexanes as eluent, the product **32** was obtained in 71% yield (24.7 mg) as a slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): 7.86 (s, 1H), 7.67 (m, 2H), 7.62 (m, 1H), 7.43 (s, 3H), 7.33 (s, 3H), 7.06 (s, 1H), 4.19 (dd, *J* = 3.8 Hz, 13.8 Hz, 1H), 3.88 (s, 3H), 3.78 (s, 3H), 3.67 (dd, *J* = 11.2 Hz, 13.8 Hz, 2H), 3.17 (dd, *J* = 3.8 Hz, 11.2 Hz, 1H), 1.57 (s, 3H), 1.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 157.6, 147.9, 139.0, 134.3, 133.9, 133.2, 132.4, 132.0, 131.4, 130.8, 129.4, 128.8, 128.0, 124.7, 116.6, 106.5, 55.4, 52.2, 47.8, 37.4, 28.3, 27.1. IR (neat) cm^{-1} 2979, 1721, 1545, 1259; HRMS (ESI) m/z calcd for $C_{26}H_{26}N_2O_7S_2$ $(M + H)^+$ 543.1254, found 543.1259.

Cyclized compound 33



Compound **33** was prepared from alkene **24** (26.0 mg, 0.064 mmol), phenylsulfenyl chloride (10.8 mg, 0.077 mmol), and scandium triflate (12 mol%, 3.8 mg, 0.008 mmol) in anhydrous nitromethane (2.1 mL). After work up and purification by flash chromatography using 15% of ethyl acetate in hexanes as eluent, the product **33** was obtained in 76% yield (25.0 mg) as a slightly yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$): 8.13 (dd, *J* = 1.5 Hz, 7.8 Hz, 1H), 7.69 (dd, *J* = 1.5 Hz, 7.6 Hz, 1H), 7.63 (m, 4H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.26 (m, 1H), 7.08 (d, *J* = 8.9 Hz, 1H), 6.79 (d, *J* = 8.9 Hz, 1H), 4.43 (dd, *J* = 3.1 Hz, 13.3 Hz, 1H), 3.79 (s, 3H), 3.60 (dd, *J* = 3.1 Hz, 11.7 Hz, 1H), 3.54 (dd, *J* = 11.8 Hz, 13.3 Hz, 1H), 3.04 (s, 3H), 1.66 (s, 3H), 1.34 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 150.8, 147.1, 141.7, 136.5, 134.4, 133.1, 132.4, 132.3, 131.7, 130.9, 130.2, 129.2, 127.5, 123.9, 122.6, 110.6, 59.3, 57.3, 55.9, 50.4, 37.8, 28.6, 27.6. IR (neat) cm^{-1} 2936, 1605, 1544, 1353; HRMS (ESI) m/z calcd for $C_{25}H_{26}N_2O_6S_2$ $(M + H)^+$ 515.1305, found 515.1305.

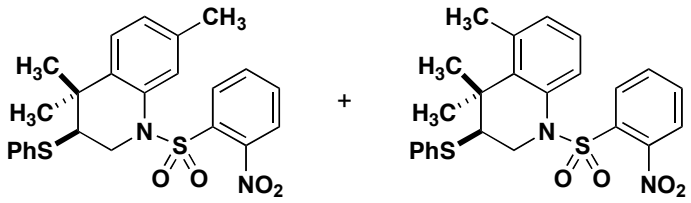
Cyclized compound 34



Compound **34** was prepared from alkene **25** (23.9 mg, 0.064 mmol), phenylsulfenyl chloride (10.8 mg, 0.077 mmol) or phenylselenenyl chloride (14.7 mg, 0.077 mmol), and scandium triflate (12 mol%, 3.8 mg, 0.008 mmol) in anhydrous nitromethane (2.1 mL). After work up and purification by flash

chromatography using 20% of hexanes in ethyl acetate as eluent, the product **34** was obtained in 86% yield (26.5 mg) as yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$): 7.70 (m, 1H), 7.65 (m, 2H), 7.48 (m, 3H), 7.32 (m, 3H), 6.86 (d, *J* = 1.8 Hz, 1H), 6.84 (d, *J* = 1.9 Hz, 1H), 4.22 (dd, *J* = 3.6 Hz, 13.9 Hz, 1H), 3.61 (dd, *J* = 11.4 Hz, 13.9 Hz, 1H), 3.33 (dd, *J* = 3.6 Hz, 11.4 Hz, 1H), 2.53 (s, 3H), 2.17 (s, 3H), 1.75 (s, 3H), 1.41 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.0, 137.4, 135.8, 135.2, 134.4, 134.0, 133.8, 133.7, 132.8, 132.2, 132.0, 130.8, 129.4, 127.7, 124.7, 123.0, 59.4, 47.5, 38.5, 26.5, 24.3, 24.1, 20.8. IR (neat) 2929, 1618, 1547, 1361, 1172 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{26}N_2O_4S_2$ $(M + H)^+$ 483.1407, found 483.1403.

Cyclized compound 35

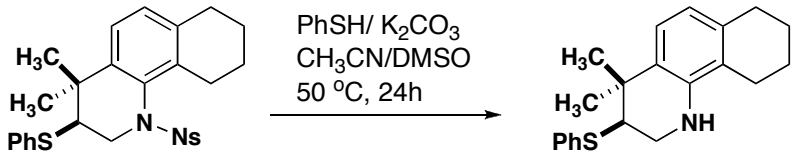


major product

Compound **35** was prepared from alkene **26** (23.0 mg, 0.064 mmol), phenylsulfenyl chloride (10.8 mg, 0.077 mmol), and scandium triflate (12 mol%, 3.8 mg, 0.008 mmol) in anhydrous nitromethane (2.1 mL). After work up and purification by flash chromatography using 15% of ethyl acetate in hexanes as eluent, the product **35** was obtained in 88% yield (26.4 mg) as an inseparable mixture of diastereomers (73:23). ^{1}H NMR (600 MHz, $CDCl_3$) distinctive major diastereomer peaks: 7.27 (d, *J* = 8.1 Hz, 1H), 7.00 (m, 2H), 4.20 (dd, *J* = 3.8 Hz,

13.9 Hz, 1H), 3.62 (dd, *J* = 11.5 Hz, 13.8 Hz, 1H), 3.27 (dd, *J* = 3.8 Hz, 11.5 Hz, 1H), 2.27 (s, 3H), 1.57 (s, 3H), 1.29 (s, 3H). Distinctive minor diastereomer peaks: 4.24 (dd, *J* = 3.7 Hz, 13.9 Hz, 1H), 3.33 (dd, *J* = 3.6 Hz, 11.4 Hz, 1H), 2.57 (s, 3H), 1.77 (s, 3H), 1.44 (s, 3H). Mixture of diastereomers: 7.69 (m, 1H), 7.64 (m, 1H), 7.62 (m, 1H), 7.45 (m, 4H), 7.32 (dd, *J* = 1.8, 5.1, 4H), 7.15 (d, *J* = 0.7 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.1, 136.6, 134.8, 134.31, 133.9, 132.95, 132.8, 132.0, 130.7, 129.4, 127.7, 127.5, 126.7, 124.7, 123.7, 120.2, 55.6, 47.9, 37.7, 28.3, 27.3, 21.2 IR (neat) cm^{-1} 2972, 1623, 1541, 1358; HRMS (ESI) m/z calcd for $C_{24}H_{24}N_2O_4S_2$ $(M + H)^+$ 469.1250, found 469.1248.

Cyclized compound 36



36 **36A**

Compound **36** was prepared from alkene **27** (50.0 mg, 0.125 mmol), phenylsulfenyl chloride (21.0 mg, 0.150 mmol), and scandium triflate (12 mol%, 7.4 mg, 0.015 mmol) in anhydrous nitromethane (4.2 mL). After work up and purification by flash chromatography using 15% of ethyl acetate in hexanes as eluent, the product **36** was obtained in 82% yield (51.9 mg) as colorless oil.

Small peaks from an impurity were detected in the ^{13}C NMR. Efforts to remove the side product by flash chromatography were not successful. Thus, nosyl deprotection was carried out in order to obtain clean spectra suitable for

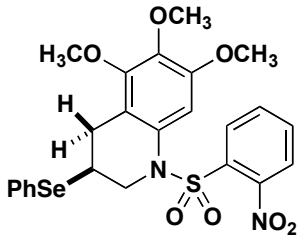
publication. The nosyl group was removed according to the procedure previously reported by Carballo et al. (2010).[10] To a solution of **36** (20.0 mg, 0.039 mmol) in anhydrous CH_3CN/DMSO (0.5 mL/18.3 μL) were added, at room temperature, potassium carbonate (21.8 mg, 0.157 mmol) and thiophenol (13.0 mg, 0.118 mmol). The reaction mixture was heated to 50 ^oC and stirred for 24 hours. The reaction mixture was allowed to cool down to room temperature, the crude mixture was filtered, the solvent was removed under reduced pressure and the product was purified by flash chromatography using 5% of ethyl acetate in hexanes as eluent. The clean product **36A** was obtained in 74% yield (9.4 mg, 60% over 2 steps) as colorless oil.

Cyclized compound 36 - ^1H NMR (600 MHz, $CDCl_3$): 7.66 (dd, *J* = 1.3 Hz, 8.0 Hz, 1H), 7.52 (m, 2H), 7.40 (m, 2H), 7.28 (m, 4H), 7.18 (d, *J* = 8.1 Hz, 1H), 7.01 (d, *J* = 8.1, 1H), 4.20 (dd, *J* = 3.8 Hz, 14.3 Hz, 1H), 3.59 (t, *J* = 13.8 Hz, 1H), 3.38 (dd, *J* = 3.6 Hz, 12.2 Hz, 1H), 2.74 (m, 2H), 2.58 (m, 2H), 1.78 (m, 2H), 1.60 (s, 3H), 1.34 (m, 2H), 1.23 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.1, 138.5, 136.6, 135.7, 134.1, 133.6, 133.5, 133.3, 133.1, 131.8, 130.5, 129.3, 128.3, 127.8, 124.7, 124.5, 55.0, 49.5, 38.2, 29.1, 29.0, 27.9, 27.8, 22.9, 22.3. IR (neat) cm^{-1} 2938, 1584, 1548, 1364; HRMS (ESI) m/z calcd for $C_{27}H_{28}N_2O_4S_2$ $(M + H)^+$ 509.1563, found 509.1558.

[10]Carballo, R. M.; Valdomir, G.; Purino, M.; Martin, V. S.; Padron, J. I. *Eur. J. Org. Chem.* **2010**, 2304-2313.

Deprotected cyclized compound 36A - ^{1}H NMR (400 MHz, $CDCl_3$): 7.45 (m, 2H), 7.29 (m, 2H), 7.22 (m, 1H), 7.06 (d, *J* = 8.0 Hz, 1H), 6.50 (d, *J* = 8.0 Hz, 1H), 3.76 (s, 1H), 3.55 (dd, *J* = 4.0 Hz, 11.6 Hz, 1H), 3.47 (t, *J* = 14.5 Hz, 1H), 3.39 (dd, *J* = 4.0 Hz, 9.6 Hz, 1H), 2.70 (t, *J* = 6.0 Hz, 2H), 2.30 (t, *J* = 6.3 Hz, 2H), 1.84 (m, 2H), 1.72 (m, 2H), 1.58 (s, 3H), 1.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.4, 136.1, 135.7, 131.6, 129.1, 126.8, 126.2, 123.8, 120.4, 118.3, 55.4, 44.3, 37.1, 29.9, 29.1, 27.7, 24.0, 23.2, 22.7. IR (neat) cm^{-1} 3434, 2933, 1609, 1591, 1478; HRMS (ESI) m/z calcd for $C_{21}H_25N_S$ $(M + H)^+$ 324.1781, found 324.1788.

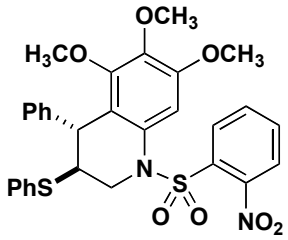
Cyclized compound 41b



Compound **41b** was prepared from alkene **37** (13.0 mg, 0.032 mmol), phenylselenenyl chloride (7.3 mg, 0.038 mmol), and scandium triflate (12 mol%, 1.9 mg, 0.004 mmol) in anhydrous nitromethane (1.0 mL). After work up and purification by flash chromatography using 30% of ethyl acetate in hexanes as eluent, the product **41b** was obtained in 69% yield (12.5 mg) as a slightly yellow solid. No product **(41a)** was detected from the reaction using phenylsulfenyl chloride. mp 105.1-106 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): 7.65 (m, 2H), 7.58 (m, 3H), 7.49 (m, 1H), 7.32 (m, 3H), 6.80 (s, 1H), 4.33 (dd, *J* = 3.2 Hz, 12.9 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.76 (s, 3H), 3.38 (t, *J* = 11.6 Hz, 1H), 3.29 (m, 1H), 3.13 (dd, *J* = 5.6 Hz, 17.3 Hz, 1H), 2.55 (dd, *J* = 10.8 Hz, 17.3 Hz, 1H). ^{13}C NMR

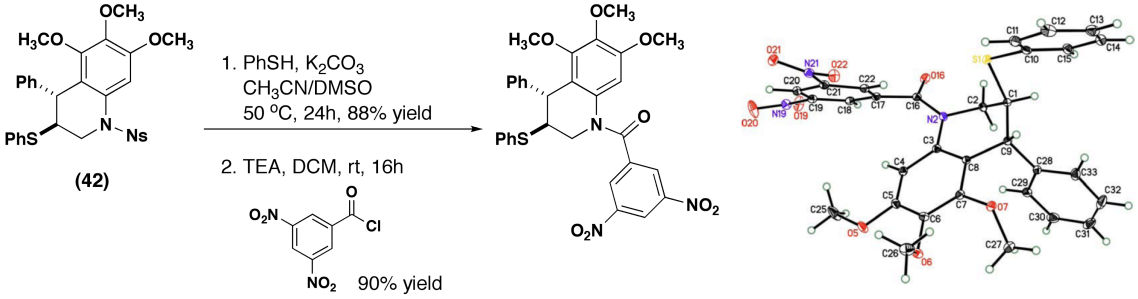
(100 MHz, $CDCl_3$) δ 151.8, 150.9, 148.0, 140.1, 135.6, 134.1, 132.7, 131.7, 130.9, 130.8, 129.4, 128.4, 127.1, 124.5, 116.1, 104.1, 61.0, 60.7, 56.1, 51.7, 34.7, 28.2. IR (neat) cm^{-1} 2925, 1612, 1537, 1355; HRMS (ESI) m/z calcd for $C_{24}H_{24}N_2O_7SSe$ $(M + H)^+$ 565.0542, found 565.0549.

Cyclized compound 42 and crystallographic data



Compound **42** was prepared from alkene **38** (15.5 mg, 0.032 mmol), phenylsulfenyl chloride (10.8 mg, 0.038 mmol), and scandium triflate (12 mol%, 1.9 mg, 0.004 mmol) in anhydrous nitromethane (1.0 mL). After work up and purification by flash chromatography using 30% of ethyl acetate in hexanes as eluent, the product **42** was obtained in 98% yield (18.7 mg) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$): 7.91 (m, 1H), 7.68 (m, 2H), 7.56 (m, 1H), 7.26 (m, 5H), 7.19 (m, 3H), 7.07 (m, 2H), 6.71 (s, 1H), 4.24 (dd, *J* = 3.8 Hz, 13.7 Hz, 1H), 4.12 (d, *J* = 8.2 Hz, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.56 (dd, *J* = 10.3 Hz, 13.7 Hz, 1H), 3.41 (ddd, *J* = 3.8 Hz, 8.2 Hz, 10.3 Hz, 1H), 3.10 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6, 152.0, 148.1, 145.0, 140.5, 134.2, 133.8, 133.6, 132.7, 132.3, 132.0, 130.8, 129.2, 128.3, 127.8, 126.6, 124.6, 118.7, 102.5, 60.7, 59.77, 56.0, 51.2, 50.4, 45.2. IR (neat) cm^{-1} 2945, 1615, 1543, 1373, 1107; HRMS (ESI) m/z calcd for $C_{30}H_{28}N_2O_7S_2$ $(M + H)^+$ 593.1411, found 593.1412.

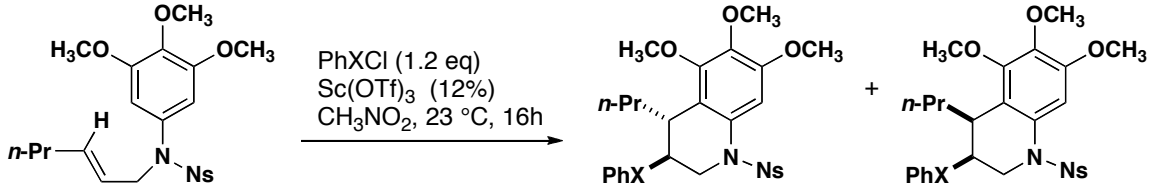
The relative stereochemistry was determined by analysis of the crystal structure obtained from the N-3,5-dinitrobenzoyl derivative.



First, compound **42** was submitted to nosyl deprotection using procedure previously described by Carballo et al. (2010).[10] To a solution of **42** (40.0 mg, 0.067 mmol) in anhydrous CH_3CN/DMSO (0.8 mL/30.0 μL) potassium carbonate (37.3 mg, 0.207 mmol) and thiophenol (22.3 mg, 0.203 mmol) were added at room temperature, The reaction mixture was heated to 50 °C and stirred for 24 hours. After the reaction mixture cooled down to room temperature, the crude mixture was filtered, the solvent was removed under reduced pressure and the product was purified by flash chromatography using 10% of ethyl acetate in hexanes as eluent. The N-deprotected product **42A** was obtained in 88% yield (24.4 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$): 7.48 (m, 2H), 7.32 (m, 2H), 7.25 (m, 3H), 7.16 (s, 1H), 7.04 (d, 2H), 6.02 (s, 1H), 4.36 (broad s, 1H), 3.92 (broad s, 1H), 3.84 (s, 3H), 3.74 (s, 3H), 3.57 (dd, *J* = 2.6 Hz, 5.3 Hz, 1H), 3.42 (dd, *J* = 2.6 Hz, 12.4 Hz, 1H), 3.38 (s, 3H), 3.17 (ddd, *J* = 1.7 Hz, 3.0 Hz, 12.4 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.4, 152.9, 146.5, 139.7, 135.3, 134.6, 132.1, 129.2, 128.4, 128.3, 127.2, 126.5, 106.1, 93.9, 61.0, 60.3, 55.8, 48.5, 42.5, 40.8. IR (neat) cm^{-1} 3397, 2938, 1607, 1493, 1244; HRMS (ESI) m/z calcd for $C_{24}H_{25}NO_3S$ $(M + H)^+$ 408.1628, found 408.1621.

Then, the N-deprotected compound was submitted to acylation using 3,5-dinitrobenzoyl chloride. To a solution of the N-deprotected compound **42A** (23.0 mg, 0.056 mmol) in anhydrous DCM, under argon atmosphere, triethylamine (1.7 mg, 0.017 mmol) and 3,5-dinitrobenzoyl chloride (19.5 mg, 0.084 mmol) were added at room temperature. The reaction mixture was stirred for 16 hours at room temperature. Then, the crude mixture was quenched with water (5 mL) and the product was extracted with dichloromethane (3x 5 mL). The organic layers were combined, dried over sodium sulfate and the solvent was removed under reduced pressure. Purification by flash chromatography using 30% of ethyl acetate in hexanes afforded 30.6 mg (90% yield) of product **42B** as a yellow solid. The product was dissolved in a mixture of methanol:chloroform (1:1) and a crystalline solid was obtained by slow evaporation of the solvent at room temperature (see crystallographic document for data). mp 142.8-144.0 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d_6, 70 ^{o}C): 8.82 (t, J = 2.1 Hz, 1H), 8.55 (d, J = 2.1 Hz, 2H), 7.35 (d, J = 7.6 Hz, 2H), 7.31 (t, J = 7.5 Hz, 2H), 7.26 (t, J = 7.5 Hz, 2H), 7.21 (t, J = 7.1 Hz, 2H), 7.09 (d, J = 7.6 Hz, 2H), 6.64 (br s, 1H), 4.32 (d, J = 3.5 Hz, 1H), 4.00 (dd, J = 2.6 Hz, 12.9 Hz, 1H), 3.91 (m, 2H), 3.08 (s, 9H). ^{13}C NMR (150 MHz, DMSO-d_6, 70 ^{o}C) δ 165.7, 152.1, 151.9, 148.3, 144.9, 140.4, 139.4, 133.8, 133.0, 131.4, 129.6, 128.9, 128.8, 128.1, 127.6, 127.0, 120.1, 116.6, 106.1, 79.6, 60.8, 60.3, 56.5, 49.8, 46.1, 44.0. IR (neat) cm^{-1} 2930, 1739, 1650, 1546, 1349; HRMS (ESI) m/z calcd for $C_{31}H_{27}N_3O_8S$ $(M + H)^+$ 602.1592, found 602.1594.

Cyclized compounds 43a and 43b



alkene E39

43a-*trans* (X = S)
43b-*trans* (X = Se)

43a-*cis* (X = S)
43b-*cis* (X = Se)

43a: 50%; >95:05 dr (*trans* : *cis*)
43b: 87%; >95:05 dr (*trans* : *cis*)

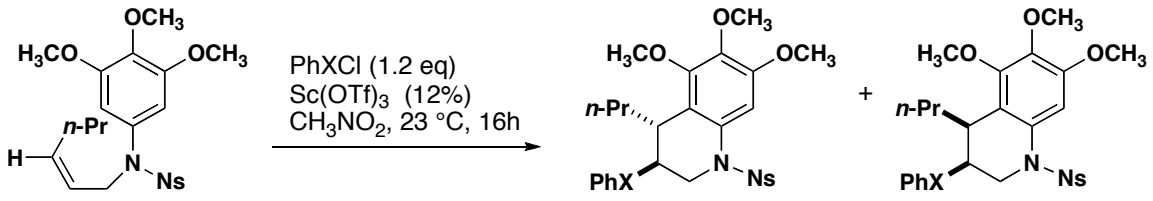
Compounds **43a and 43b** were prepared from alkene **E39** (14.4 mg, 0.032 mmol), phenylsulfenyl chloride (10.8 mg, 0.038 mmol) or phenylselenenyl chloride (7.3 mg, 0.038 mmol), and scandium triflate (12 mol%, 1.9 mg, 0.004 mmol) in anhydrous nitromethane (1.0 mL). After work up and purification by flash chromatography using 25% of ethyl acetate in hexanes as eluent, the product **43a-trans** was obtained in 50% yield (8.0 mg, >95:05 dr) as a yellow oil. Compound **43b-trans** was obtained in 87% yield (16.9 mg, >95:05 dr) as yellow oil.

Data for 43a *trans* - ^{1}H NMR (400 MHz, $CDCl_3$): 7.89 (dd, *J* = 1.2 Hz, 7.9 Hz, 1H), 7.71 (m, 1H), 7.68 (m, 1H), 7.61 (m, 1H), 7.44 (m, 2H), 7.31 (m, 3H), 6.73 (s, 1H), 4.18 (dd, *J* = 7.9 Hz, 16.4 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.72 (s, 3H), 3.59 (m, 2H), 3.11 (m, 1H), 1.44 (m, 1H), 1.25 (s, 2H), 1.14 (m, 1H), 0.76 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.1, 151.8, 148.3, 140.2, 134.1, 134.2, 133.8, 132.5, 131.8, 131.7, 130.6, 129.3, 127.7, 124.5, 119.9, 103.1, 61.0, 60.9, 56.1, 50.2, 47.0, 38.0, 37.2, 19.9, 14.1. IR (neat) cm^{-1} 2933, 1612, 1554,

1371; HRMS (ESI) m/z calcd for $C_{27}H_{30}N_2O_7S_2$ $(M + H)^+$ 559.1567, found 559.1569.

Data for 43b *trans* - ^{1}H NMR (600 MHz, $CDCl_3$): 7.85 (dd, *J* = 1.3 Hz, 8.0 Hz, 1H), 7.69 (m, 1H), 7.63 (dd, *J* = 1.3 Hz, 8.0 Hz, 1H), 7.58 (m, 3H), 7.29 (d, *J* = 8.4 Hz, 3H), 6.75 (s, 1H), 4.24 (dd, *J* = 4.9 Hz, 13.6 Hz, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 3.72 (s, 3H), 3.71 (dd, *J* = 4.9 Hz, 13.6 Hz, 1H), 3.60 (dt, *J* = 4.9 Hz, 7.6 Hz, 1H), 3.20 (dt, *J* = 4.8 Hz, 7.6 Hz, 1H), 1.39 (m, 1H), 1.21 (s, 2H), 1.08 (m, 1H), 0.72 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 151.9, 151.5, 148.1, 139.8, 135.1, 134.0, 133.3, 131.8, 131.5, 130.4, 129.3, 128.4, 128.2, 124.4, 119.9, 102.9, 60.9, 60.9, 56.0, 50.7, 42.1, 37.8, 37.5, 19.8, 14.1. IR (neat) cm^{-1} 2958, 1596, 1541, 1360; HRMS (ESI) m/z calcd for $C_{27}H_{30}N_2O_7SSe$ $(M + H)^+$ 607.1012, found 6907.1018.

Cyclized compounds 44a and 44b



alkene Z39

44a-*trans* (X = S)
44b-*trans* (X = Se)

44a-*cis*(X = S)
44b-*cis* (X = Se)

44a: 17% yield; >05:95 dr (*trans* : *cis*)
44b: 50% yield; 35:65 dr (*trans* : *cis*)

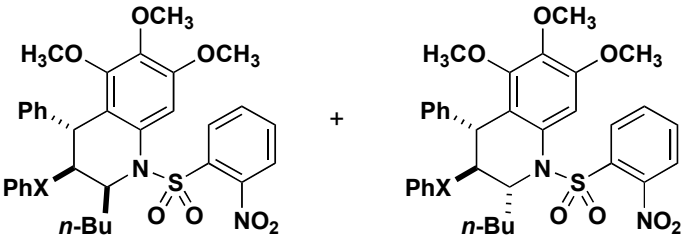
Compounds **44a and 44b** were prepared from alkene **Z39** (28.8 mg, 0.064 mmol), phenylsulfenyl chloride (10.3 mg, 0.077 mmol) or phenylselenenyl chloride (14.7 mg, 0.064 mmol), and scandium triflate (12 mol%, 3.8 mg, 0.008 mmol) in anhydrous nitromethane (2.1 mL). After work up and purification by flash chromatography using 25% of ethyl acetate in hexanes as eluent, the product **44a-*cis*** was obtained in 10% yield (6.2 mg, >95:05 dr) as a yellow oil. Compound **44b** was obtained in 50% yield (19.6 mg, 65:35 cis:trans dr) as a mixture of diastereomers.

Data for 44a *cis* - ^{1}H NMR (600 MHz, $CDCl_3$): 7.81 (dd, *J* = 1.4 Hz and 7.9 Hz, 1H), 7.70 (td, *J* = 1.3 Hz and 7.7 Hz, 1H), 7.61 (td, *J* = 1.4 Hz, 7.9 Hz, 1H), 7.59 (dd, *J* = 1.3 Hz, 7.7 Hz, 1H), 7.42 (m, 2H), 7.29 (m, 3H), 7.08 (s, 1H), 3.98 (ddd, *J* = 1.2 Hz, 6.5 Hz, 11.8 Hz, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.76 (s, 3H), 3.74 (t, *J* = 12.3 Hz, 1H), 3.34 (ddd, *J* = 3.4 Hz, 6.5 Hz, 12.3 Hz, 1H), 3.25 (dt, *J* = 3.4 Hz, 6.5 Hz, 1H), 1.50 (m, 1H), 1.20 (m, 1H), 0.98 (m, 1H), 0.57 (t, *J* = 7.3 Hz, 3H), 0.45 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.2, 150.3, 148.4, 139.7, 134.1, 134.0, 132.3, 131.5, 131.4, 130.9, 130.0, 129.3, 127.8, 124.2, 121.4, 104.5, 61.1, 61.0, 56.3, 48.5, 48.0, 35.6, 30.8, 21.0, 15.3. IR (neat) cm^{-1} 2968, 1613, 1552, 1377; HRMS (ESI) m/z calcd for $C_{27}H_{30}N_2O_7S_2$ $(M + H)^+$ 559.1567, found 559.1568.

Data for 44b *cis* - ^{1}H NMR (600 MHz, $CDCl_3$): 7.71 (dd, *J* = 1.1 Hz, 7.9 Hz, 1H), 7.63 (td, *J* = 1.3 Hz, 7.7 Hz, 1H), 7.50 (m, 4H), 7.20 (m, 3H), 7.01 (s, 1H), 3.96

(ddd, *J* = 1.2 Hz, 6.5 Hz, 11.7 Hz, 1H), 3.84 (t, *J* = 12.2 Hz, 1H), 3.77 (s, 3H), 3.74 (s, 3H), 3.69 (s, 3H), 3.25 (m, 2H), 1.33 (m, 1H), 1.13 (m, 1H), 0.89 (m, 1H), 0.50 (t, *J* = 7.3 Hz, 3H), 0.42 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.9, 152.2, 150.2, 148.4, 139.7, 134.8, 134.0, 131.5, 131.4, 130.9, 129.8, 129.4, 128.7, 128.3, 124.2, 121.6, 104.5, 61.0, 60.9, 56.3, 48.9, 43.8, 36.2, 31.8, 21.0, 14.3. IR (neat) 2967, 1600, 1545, 1365 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{30}N_2O_7SSe$ $(M + H)^+$ 607.1012, found 607.1014.

Cyclized compounds 45a and 45b



45a *trans/cis* (X=S)
45b *trans/cis* (X=Se)

45a *trans/trans* (X=S)
45b *trans/trans* (X=Se)

Compounds **45a and 45b** were prepared from alkene **40** (17.3 mg, 0.032 mmol), phenylsulfenyl chloride (5.3 mg, 0.038 mmol) or phenylselenenyl chloride (7.3 mg, 0.038 mmol), and scandium triflate (12 mol%, 1.9 mg, 0.004 mmol) in anhydrous nitromethane (1.0 mL) at -20 °C. After work up and purification by flash chromatography using 20% of ethyl acetate in hexanes as eluent, the product **45a** was obtained in 68% yield (28 mg, 80:20 dr trans/cis : trans/trans) as colorless oil. Compound **45b** was obtained in 70% yield (15.7 mg, >95:05 dr) as colorless oil. When the reactions were carried out at room temperature, compound **45a** was obtained in 41% (8.4 mg; 70:30 dr) and compound **45b** was obtained in 62% yield (13.7 mg; 75:25 dr).

Data for 45a trans/cis - ^{1}H NMR (600 MHz, $CDCl_3$): 7.54 (td, *J* = 1.2 Hz, 7.8 Hz, 1H), 7.46 (m, *J* = 8.1 Hz, 2H), 7.23 (m, 1H), 7.13 (m, 6H), 7.09 (s, 1H), 6.98 (m, 2H), 6.82 (m, 2H), 4.35 (ddd, *J* = 3.4 Hz, 4.4 Hz, 7.3 Hz, 1H), 3.89 (s, 3H), 3.85 (d, *J* = 11.4 Hz, 1H), 3.78 (s, 3H), 3.14 (dd, *J* = 4.4 Hz, 11.4 Hz, 1H), 2.99 (s, 3H), 2.02 (m, 1H), 1.37 (m, 1H), 1.28 (m, 4H), 0.84 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.8, 151.2, 148.2, 145.1, 141.1, 134.7, 133.8, 133.3, 132.3, 131.5, 131.1, 129.0, 128.9, 128.7, 127.9, 127.8, 126.3, 123.9, 120.2, 106.2, 60.7, 59.7, 59.4, 57.6, 56.3, 44.2, 28.3, 25.1, 22.2, 14.1. IR (neat) 2924, 2856, 1604, 1547 cm^{-1}; HRMS (ESI) m/z calcd for $C_{34}H_{36}N_2O_7S_2$ $(M + H)^+$ 649.2037, found 649.2044.

Data for 45a trans/trans - ^{1}H NMR (600 MHz, $CDCl_3$): 8.47 (dd, *J* = 0.8 Hz and 8.6 Hz, 1H), 7.68 (m, 2H), 7.59 (m, 1H), 7.46 (m, 2H), 7.36 (m, 3H), 7.19 (m, 3H), 6.93 (m, 2H), 6.89 (s, 1H), 4.70 (ddd, *J* = 2.1 Hz, 6.6 Hz and 9.0 Hz, 1H), 4.37 (d, *J* = 1.6 Hz, 1H), 3.76 (s, 3H), 3.69 (s, 3H), 3.42 (s, 3H), 1.62 (m, 1H), 1.46 (m, 1H), 0.95 (m, 2H), 0.55 (t, *J* = 7.2 Hz, 3H). ^{1}H NMR (400 MHz, C_6D_6): 8.64 (dd, *J* = 1.2 Hz, 8.0 Hz, 1H), 7.53 (dd, *J* = 1.3 Hz, 8.2 Hz, 2H), 7.00 (m, 8H), 6.71 (dd, *J* = 1.2 Hz, 7.9 Hz, 1H), 6.59 (td, *J* = 1.2 Hz, 8.0 Hz, 1H), 6.45 (td, *J* = 1.2 Hz, 7.9 Hz, 1H), 6.14 (s, 1H), 5.12 (ddd, *J* = 2.3 Hz, 6.6 Hz, 9.3 Hz, 1H), 4.75 (d, *J* = 1.4 Hz, 1H), 4.10 (t, *J* = 2.2 Hz, 1H), 3.60 (s, 3H), 3.52 (s, 3H), 3.33 (s, 3H), 1.90 (m, 1H), 1.61 (m, 1H), 0.80 (m, 2H), 0.64 (m, 1H), 0.53 (t, *J* = 7.3 Hz, 3H), 0.41 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.7, 152.6, 149.5, 144.4, 138.7, 134.1,

133.8, 133.7, 133.5, 131.8, 130.8, 130.6, 129.5, 128.4, 128.3, 127.7, 126.6, 124.3, 111.7, 100.6, 60.9, 60.8, 59.1, 56.0, 53.1, 42.3, 34.9, 27.9, 22.1, 13.7. IR (neat) 2938, 2870, 1610, 1548 cm^{-1}; HRMS (ESI) m/z calcd for $C_{34}H_{36}N_2O_7S_2$ $(M + H)^+$ 649.2037, found 649.2047.

Data for 45b trans/cis - ^1H NMR (600 MHz, $CDCl_3$): 7.46 (m, 2H), 7.40 (m, 1H), 7.22 (m, 1H), 7.08 (m, 7H), 6.92 (m, 2H), 6.82 (m, 2H), 4.51 (ddd, *J* = 2.6 Hz, 4.4 Hz, 10.6 Hz, 1H), 4.00 (d, *J* = 11.4 Hz, 1H), 3.90 (s, 3H), 3.77 (s, 3H), 3.11 (dd, *J* = 4.4 Hz, 11.4 Hz, 1H), 2.97 (s, 3H), 1.92 (m, 1H), 1.29 (m, 5H), 0.84 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.8, 151.1, 148.1, 145.3, 141.1, 135.1, 133.6, 132.3, 131.4, 131.0, 129.5, 129.0, 128.9, 128.7, 128.0, 127.9, 126.3, 123.8, 120.3, 106.3, 60.8, 60.7, 59.4, 56.3, 53.9, 45.0, 28.4, 26.29, 22.2, 14.1. IR (neat) cm^{-1} 2936, 1603, 1550, 1177; HRMS (ESI) m/z calcd for $C_{34}H_{36}N_2O_7SSe$ $(M + H)^+$ 697.1481, found 697.1492.

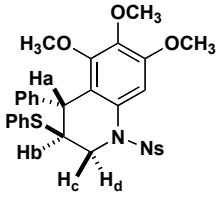
Relative stereochemistry assignment for compounds 42-45

The relative stereochemistry for compound **42** was confirmed as *trans* by crystal structure analysis. For compounds **43-45**, the relative stereochemistry was determined based on the coupling constants between Ha/Hb, Hb/Hc and Hb/Hd. Figure 1 shows *J* values, lowest energy conformer and dihedral angles for all sulfide products. The lowest energy conformer and dihedral angles were calculated to have a reference of the conformation of the structures. This helped to suggest the stereochemistry for the different diastereomers obtained. The

software ChemBio 3D, which is a part of the CambridgeSoft package, was used to minimize the energy and calculate the dihedral angles for all diastereomers. For diastereomers **43a** and **44a**, we observed a $J_{Ha/Hb}$ = 7.6 Hz for one of the diastereomers and a $J_{Ha/Hb}$ = 3.4 Hz for the other diastereomer. The larger *J* value is consistent with the coupling constant observed for compound **42** ($J_{Ha/Hb}$ = 8.2 Hz) so that we can propose the structure of **43a** as *trans* and **44a**, with a small *J* value, as *cis*. For **45a,** we assumed the relative stereochemistry between Ha and Hb is *trans* as we know, from product **42**, that the cyclization of cinnamyl alkene produces the single diastereomer *trans*. Although, a small coupling constant ($J_{Ha/Hb}$ = 1.4 Hz) was observed for one of the diastereomers, we still believe they are *trans,* as we were able to find only two of the four possible diastereomers which are distinguishable by ^{1}H NMR. In this case, the presence of the *n*-butyl group may be changing the conformation of the ring moving the Ph- and PhS- groups to pseudo-axial direction and leaving Ha and Hb in a pseudo-equatorial position. For the major diastereomer, we found $J_{Hb/Hd}$ = 4.4 Hz. This would be consistent with the dihedral angle of approximately 61^o between Hb and Hd, which leads us to believe the *n*-butyl is pseudo-axial/*cis* in relation to the PhS- group. For the minor diastereomer, we found a $J_{Ha/Hb}$ = 1.4 Hz and a $J_{Hb/Hc}$ = 2.3 Hz (as a triplet) which is consistent with all hydrogen atoms in a pseudo-equatorial position and the *n*-butyl group pseudo-axial/*trans* in relation to PhS- group. This data suggests that the major diastereomer has a relative stereochemistry of *trans/cis* and the minor diastereomer of *trans/trans*. The coupling constants for the selenide products were found to be very similar to the

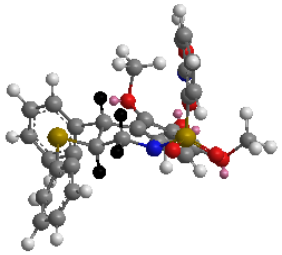
J values for the sulfide products and the stereochemistry was assigned by comparison.

Ha (d): $J_{Ha/Hb}$ **= 8.2 Hz**
Hb (ddd): $J_{Hb/Ha}$ **= 8.2 Hz**
$J_{Hb/Hc}$ **= 10.2 Hz**
$J_{Hb/Hd}$ **= 3.8 Hz**
Hc (dd): $J_{Hc/Hb}$ **= 10.2 Hz**
$J_{Hc/Hd}$ **= 13.8 Hz**
Hd (dd): $J_{Hd/Hb}$ **= 3.8 Hz**
$J_{Hd/Hc}$ **= 13.8 Hz**



42

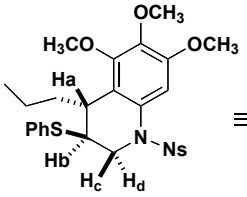
≡



Dihedral angle

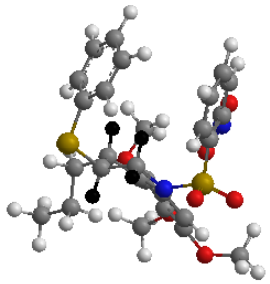
Ha/Hb = 165°
Hb/Hc = 173°
Hb/Hd = 64°

Ha (dt): $J_{Ha/Hb}$ **= 7.6 Hz**
$J_{Ha/CH2}$ **= 5.2 Hz**
Hb (dt): $J_{Hb/Ha}$ **= 7.6 Hz**
$J_{Hb/Hc-Hd}$ **= 5.2 Hz**
Hc (dd): $J_{Hc/Hb}$ **= 4.9 Hz**
$J_{Hc/Hd}$ **= 13.6 Hz**
Hd (dd): $J_{Hd/Hb}$ **= 5.2 Hz**
$J_{Hd/Hc}$ **= 13.6 Hz**



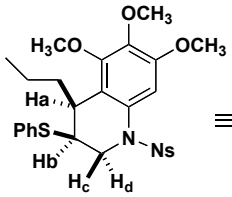
43a (trans)

≡



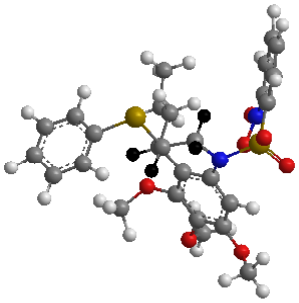
Ha/Hb = 158°
Hb/Hc = 179°
Hb/Hd = 54°

Ha (dt): $J_{Ha/Hb}$ **= 3.4 Hz**
$J_{Ha/CH2}$ **= 6.5 Hz**
Hb (ddd): $J_{Hb/Ha}$ **= 3.4 Hz**
$J_{Hb/Hc}$ **= 12.4 Hz**
$J_{Hb/Hd}$ **= 6.5 Hz**
Hc (t): $J_{Hc/Hd-Hb}$ **= 12.3 Hz**
Hd (ddd): $J_{Hd/Hb}$ **= 6.5 Hz**
$J_{Hd/Hc}$ **= 11.8 Hz**
$J_{Hd/Ha}$ **= 1.2 Hz (W)**



44a (*cis*)

≡



Ha/Hb = 55°
Hb/Hc = 175°
Hb/Hd = 62°

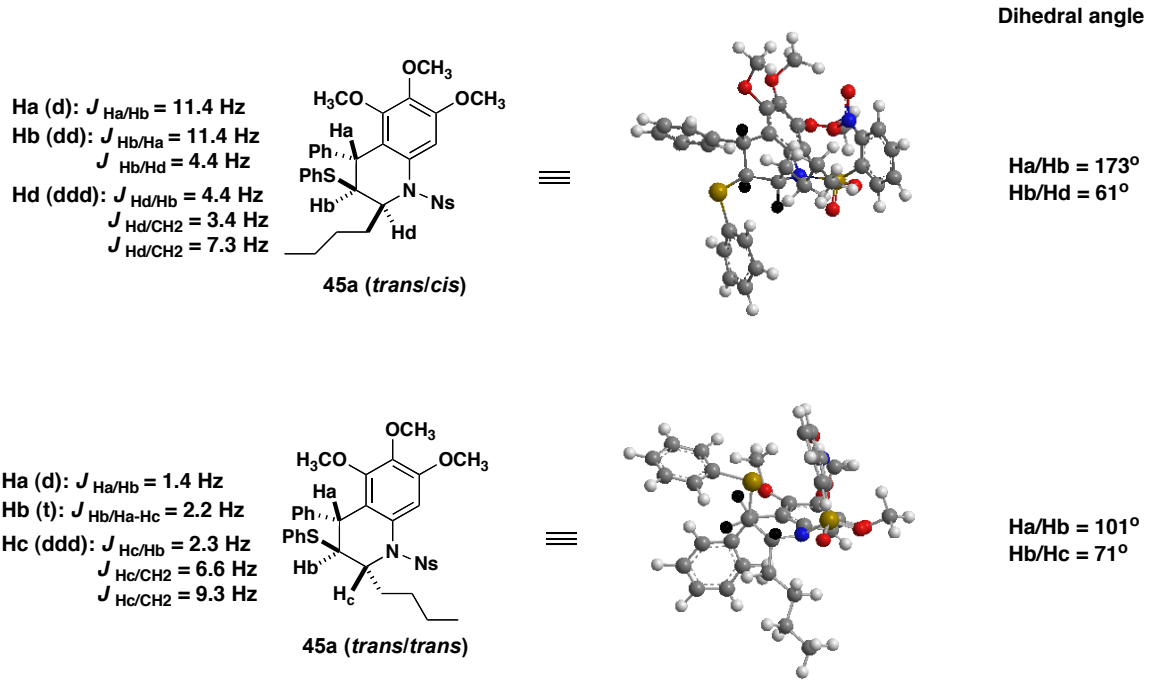
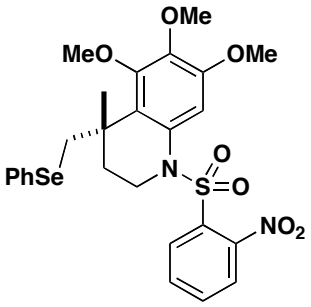


Figure 1 - Coupling constants and dihedral angles for compounds **42-45**.

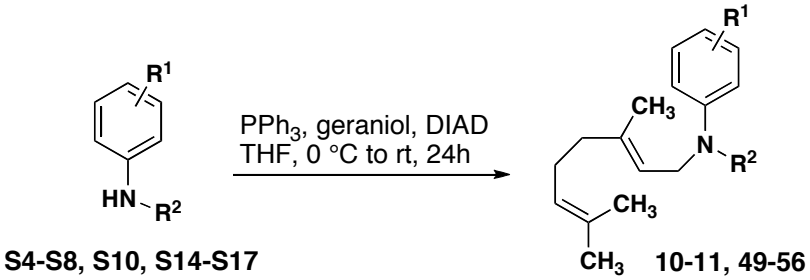
Cyclized compound 48



To a solution of scandium triflate (3.0 mg, 0.006 mmol) in nitromethane (/2.5 mM) was added phenylsulfenyl chloride (9.6 mg, 0.05 mmol). The solution was cooled to -20 °C. After 20 min, compound **47** (21.8 mg, 0.05 mmol) dissolved in nitromethane (0.2 M) added to the reaction mixture. The reaction mixture stirred overnight at -20 °C. The reaction mixture was filtered through a pad of silica gel (50:50 EtOAc/hexanes) to remove the Lewis acid. The solvent was removed *in*

vacuo. The product was purified by flash chromatography (30:70 EtOAc/hexanes) to give the product as a white amorphous solid (19.9 mg, 67%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.8 Hz, 1H), 7.64 – 7.48 (m, 3H), 7.36 – 7.31 (m, 2H), 7.22 – 7.15 (m, 3H), 7.02 (s, 1H), 4.09 – 3.99 (m, 1H), 3.92 (s, 3H), 3.81 (d, *J* = 1.2, 6H), 3.64 – 3.55 (m, 1H), 3.52 (d, *J* = 11.4 Hz, 1H), 3.22 (d, *J* = 11.4 Hz, 1H), 2.20 – 2.10 (m, 1H), 1.59 – 1.50 (m, 1H), 1.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4, 152.0, 148.2, 140.7, 133.9, 133.3, 132.3, 132.0, 131.8, 131.7, 131.0, 129.1, 126.7, 124.2, 122.0, 104.2, 60.9, 60.7, 56.0, 44.1, 40.6, 37.6, 36.8, 27.7; IR (neat) 3084, 2942, 1543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{29}N_2O_7SSe$ $(M + H)^+$ 593.0855, found 593.0859.

7. General Procedure D: Mitsunobu alkylation of sulfonyl anilines



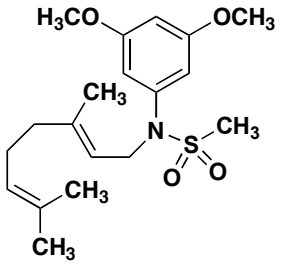
S4-S8, S10, S14-S17 **10-11, 49-56**

R^2 = Ms or Ns

To a cooled (0 °C) solution of the aniline (**S4-S8, S10, S14-S17**) in tetrahydrofuran (0.1 M) was added triphenylphosphine (1.2 equiv). The solution was stirred for 10 min. Geraniol (1.0 equiv) was added to the solution followed by Diisopropyl azodicarboxylate (1.2 equiv) dropwise. The reaction was stirred overnight at room temperature. The solvent was removed *in vacuo* to afford a yellow oil. The oil was purified by flash chromatography to yield the product as a

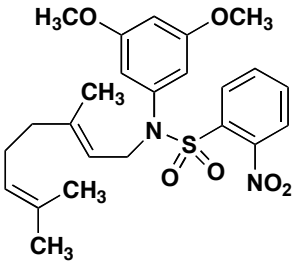
yellow oil.

N-geranyl-methanesulfonyl aniline 10



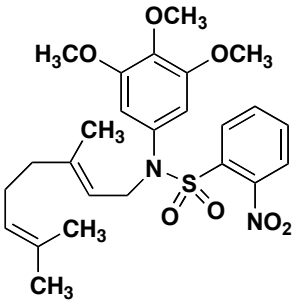
This compound was prepared according to general procedure D using **S4** (1.502 g, 6.5 mmol), triphenylphosphine (3.505 g, 13.0 mmol), geraniol (1.128 mL, 6.5 mmol), and diisopropyl azodicarboxylate (1.53 mL, 7.8 mmol). The product was purified by flash chromatography (20:80 EtOAc/hexanes) to give a yellow oil (2.173 g, 91 %): ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.49 (d, *J* = 2.2 Hz, 2H), 6.40 (t, *J* = 2.2 Hz, 1H), 5.23 (ddd, *J* = 8.3 Hz, 5.8 Hz, 1.3 Hz, 1H), 5.01 – 4.96 (m, 1H), 4.25 (d, *J* = 7.0 Hz, 2H), 3.78 (s, 6H), 2.91 (s, 3H), 2.05 - 1.94 (m, 4H), 1.64 (s, 3H), 1.58 (s, 3H), 1.56 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.0, 141.5, 140.8, 131.8, 123.8, 118.9, 106.8, 99.8, 55.5, 48.8, 39.6, 38.3, 26.4, 25.7, 17.7, 16.3; IR (neat) 2966, 2932 cm^{-1}; HRMS (ESI) m/z calcd for $C_{19}H_{30}NO_4S$ $(M + H)^+$ 368.1890, found 368.1890.

N-geranyl-N-nosyl aniline 11



This compound was prepared according to general procedure D using **S5** (0.338 g, 1.0 mmol), triphenylphosphine (0.539 g, 2.0 mmol), geraniol (0.175 mL, 1.0 mmol), and diisopropyl azodicarboxylate (0.24 mL, 1.2 mmol). The product was purified by flash chromatography (60:40 CH_2Cl_2/hexanes) to give a yellow oil (0.388 g, 82 %): ^{1}H NMR (400 MHz, $CDCl_3$) 7.65 (t, *J* = 8.7, 2H), 7.64 – 7.59 (m, 1H), 7.54 – 7.47 (m, 1H), 6.38 (t, *J* = 2.2, 1H), 6.33 (d, *J* = 2.2, 2H), 5.19 (s, 1H), 4.98 (s, 1H), 4.35 (d, *J* = 7.2, 2H), 3.70 (s, 6H), 1.95 (dd, *J* = 14.2, 5.4, 4H), 1.64 (s, 3H), 1.56 (s, 3H), 1.49 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.8, 148.1, 141.2, 139.8, 133.7, 132.2, 131.8, 131.6, 131.1, 123.8, 123.7, 118.7, 107.7, 100.5, 55.4, 49.9, 39.5, 26.4, 25.6, 17.6, 16.1; IR (neat) 3003, 2965, 1543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{31}N_2O_6S$ $(M + H)^+$ 475.1898, found 475.1897.

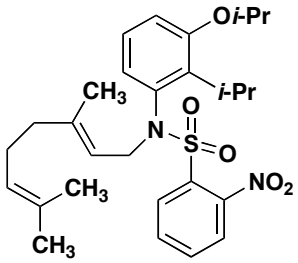
N-geranyl-N-nosyl aniline 49



This compound was prepared according to general procedure D using **S6** (0.368

g, 1.0 mmol), triphenylphosphine (0.323 g, 1.2 mmol), geraniol (0.174 mL, 1.0 mmol), and diisopropyl azodicarboxylate (0.236 mL, 1.2 mmol). The product was purified by flash chromatography (30:70 EtOAc/hexanes) to give the product as a yellow oil (0.250 g, 50 %): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 11.6 Hz, 4.6 Hz, 2H), 7.63 (d, *J* = 7.5 Hz, 1H), 7.52 (dd, *J* = 8.1 Hz, 7.0 Hz, 1H), 6.37 (s, 2H), 5.21 (t, *J* = 7.3 Hz, 1H), 5.03 – 4.96 (m, 1H), 4.33 (d, *J* = 7.2 Hz, 2H), 3.83 (s, 3H), 3.70 (s, 6H), 2.03 – 1.89 (m, 4H), 1.65 (s, 3H), 1.55 (s, 3H), 1.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 148.1, 141.4, 138.1, 133.7, 133.5, 132.2, 132.0, 131.8, 131.1, 123.8, 123.7, 118.7, 107.2, 60.7, 56.2, 50.1, 39.6, 26.5, 25.7, 17.8, 16.2; IR (neat) 2965, 1544 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{33}N_2O_7S$ $(M + H)^+$ 505.2003, found 505.2003.

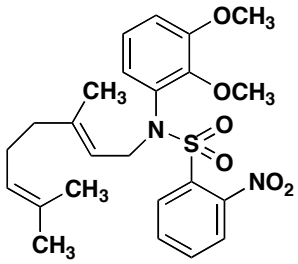
N-geranyl-N-nosyl aniline 50



This compound was prepared according to general procedure D using **S16** (0.186 g, 0.26 mmol), triphenylphosphine (0.159 g, 0.59 mmol), geraniol (0.085 mL, 0.49 mmol), and Diisopropyl azodicarboxylate (0.116 mL, 0.59 mmol) dropwise. The oil was purified by flash chromatography (70:30 CH_2Cl_2/hexanes) to yield a yellow oil (0.234 g, 94 %): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.57 (m, 3H), 7.52 - 7.46 (m, 1H), 6.98 (t, *J* = 8.1 Hz, 1H), 6.80 (d, *J* = 8.2 Hz, 1H), 6.56

(d, *J* = 7.9 Hz, 1H), 5.23 (t, *J* = 7.3 Hz, 1H), 5.01 (t, *J* = 6.7 Hz, 1H), 4.64 - 4.53 (m, 1H), 4.40 (dd, *J* = 14.8 Hz, 7.3 Hz, 1H), 4.22 (dd, *J* = 14.8 Hz, 7.6 Hz, 1H), 3.43 - 3.30 (m, 1H), 2.05 – 1.87 (m, 4H), 1.66 (s, 3H), 1.56 (s, 3H), 1.39 (s, 3H), 1.35 (d, *J* = 4.0 Hz, 3H), 1.33 (d, *J* = 4.0 Hz, 3H), 1.25 (d, *J* = 7.0 Hz, 3H), 0.97 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 148.1, 141.0, 137.4, 136.5, 133.6, 132.7, 132.1, 131.5, 131.1, 126.0, 123.8, 123.7, 122.4, 118.6, 112.8, 69.0, 50.85, 39.66, 27.48, 26.20, 25.62, 21.85, 21.76, 20.65, 19.66, 17.59, 15.83; IR (neat) 2975, 2930, 1545 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{39}N_2O_5S$ $(M + H)^+$ 515.2574, found 515.2581.

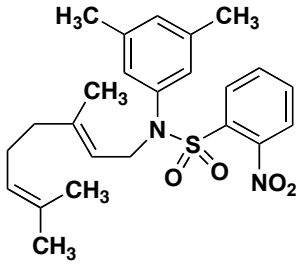
N-geranyl-N-nosyl aniline 51



This compound was prepared according to general procedure D using **S13** (0.338 g, 1.0 mmol), triphenylphosphine (0.323 g, 1.2 mmol), geraniol (0.174 mL, 1.0 mmol), and diisopropyl azodicarboxylate (0.236 mL, 1.2 mmol). The product was purified by flash chromatography (CH_2Cl_2) to give the product as a yellow oil (0.452 g, 95 %): 1H NMR (600 MHz, $CDCl_3$) δ 7.80 (dt, *J* = 7.9 Hz, 1.2, 1H), 7.66 – 7.59 (m, 2H), 7.57 – 7.53 (m, 1H), 6.96 – 6.92 (m, 1H), 6.90 (dd, *J* = 8.3 Hz, 1.7 Hz, 1H), 6.79 (dd, *J* = 7.8 Hz, 1.7 Hz, 1H), 5.16 (t, *J* = 7.4 Hz, 1H), 4.96 (t, *J* = 7.3 Hz, 1H), 4.38 (s, 2H), 3.82 (s, 3H), 3.61 (s, 3H), 1.96 – 1.84 (m, 4H), 1.64 (s, 3H),

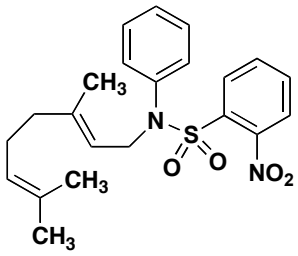
1.54 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 148.1, 147.4, 141.1, 133.7, 133.3, 131.5, 131.3, 131.3, 130.5, 124.7, 123.9, 123.8, 122.7, 118.8, 113.3, 60.5, 56.0, 49.2, 39.5, 26.3, 25.7, 17.6, 15.9; IR (neat) 3023, 2937, 1543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{31}N_2O_6S$ $(M + H)^+$ 497.1717, found 497.1715.

N-geranyl-N-nosyl aniline 52



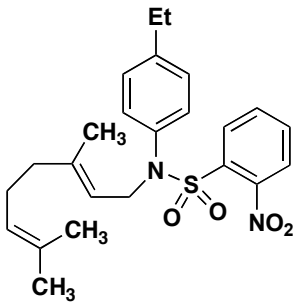
This compound was prepared according to general procedure D using **S10** (0.306 g, 1.0 mmol), triphenylphosphine (0.323 g, 1.2 mmol), geraniol (0.174 mL, 1.0 mmol), and diisopropyl azodicarboxylate (0.236 mL, 1.2 mmol). The product was purified by flash chromatography (60:40 CH_2Cl_2/hexanes) to give the product as a yellow oil (0.416 g, 94 %): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.55 (m, 3H), 7.51 – 7.45 (m, 1H), 6.91 (s, 1H), 6.75 (s, 2H), 5.17 (t, *J* = 7.2 Hz, 1H), 4.98 (t, *J* = 6.7 Hz, 1H), 4.32 (d, *J* = 7.2 Hz, 2H), 2.22 (s, 6H), 1.99 – 1.86 (m, 4H), 1.65 (s, 3H), 1.55 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 141.0, 138.6, 137.8, 133.5, 132.2, 131.7, 131.5, 131.0, 130.0, 127.2, 123.8, 123.7, 118.8, 49.9, 39.5, 26.4, 25.6, 21.1, 17.6, 16.0; IR (neat) 2918, 1543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{31}N_2O_4S$ $(M + H)^+$ 465.1818, found 465.1817.

N-geranyl-N-nosyl aniline 53



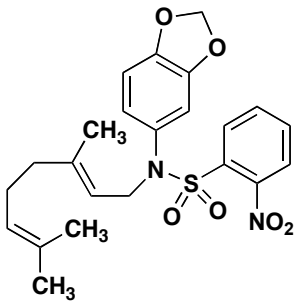
This compound was prepared according to general procedure D using **S14** (0.557 g, 2.0 mmol), triphenylphosphine (0.646 g, 2.4 mmol), geraniol (0.416 mL, 2.0 mmol), and diisopropyl azodicarboxylate (0.473 mL, 2.4 mmol). The product was purified by flash chromatography (15:85 EtOAc/hexanes) to give the product as a yellow oil (0.688 g, 83 %): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (m, 2H), 7.55 (dd, *J* = 8.0 Hz, 1.3 Hz, 1H), 7.50 – 7.44 (m, 1H), 7.32 – 7.27 (m, 3H), 7.19 – 7.13 (m, 2H), 5.18 (td, *J* = 7.3 Hz, 1.1 Hz, 1H), 5.00 – 4.90 (m, 1H), 4.37 (d, *J* = 7.3 Hz, 2H), 2.00 – 1.86 (m, 4H), 1.65 (s, 3H), 1.55 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 141.4, 138.0, 133.6, 132.3, 131.8, 131.7, 131.2, 129.9, 129.1, 128.4, 123.8, 123.8, 118.7, 50.0, 39.5, 26.2, 25.7, 17.7, 16.0; IR (neat) 3093, 2967, 2918, 1542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{22}H_{27}N_2O_4S$ $(M + H)^+$ 415.1686, found 415.1686.

N-geranyl-N-nosyl aniline 54



This compound was prepared according to general procedure D using **S15** (0.306 g, 1.0 mmol), triphenylphosphine (0.323 g, 1.2 mmol), geraniol (0.173 mL, 1.0 mmol), and diisopropyl azodicarboxylate (0.236 mL, 1.2 mmol). The product was purified by flash chromatography (70:30 CH_2Cl_2/hexanes) to give the product as a yellow oil (0.404 g, 91 %): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.59 (m, 2H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.51 – 7.45 (m, 1H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 7.6 Hz, 2H), 5.18 (t, *J* = 7.2 Hz, 1H), 4.97 (t, *J* = 7.3 Hz, 1H), 4.34 (d, *J* = 7.2 Hz, 2H), 2.62 (q, *J* = 7.6 Hz, 2H), 1.99 – 1.86 (m, 4H), 1.65 (s, 3H), 1.55 (s, 3H), 1.41 (s, 3H), 1.21 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, cdcl3) δ 148.2, 144.7, 141.2, 135.5, 133.5, 132.6, 131.9, 131.7, 131.1, 129.8, 128.6, 123.9, 123.8, 118.9, 50.1, 39.6, 28.5, 26.3, 25.8, 17.8, 16.1, 15.4; IR (neat) 2966, 2927,1544 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{31}N_2O_4S$ $(M + H)^+$ 443.1999, found 443.1999.

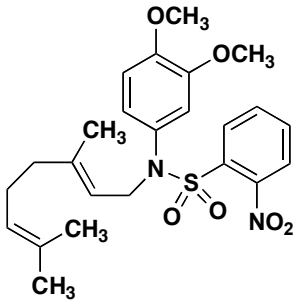
N-geranyl-N-nosyl aniline 55



This compound was prepared according to general procedure D using **S8** (0.322 g, 1.0 mmol), triphenylphosphine (0.323 g, 1.2 mmol), geraniol (0.174 mL, 1.0 mmol), and diisopropyl azodicarboxylate (0.236 mL, 1.2 mmol). The product was purified by flash chromatography (50:50 CH_2Cl_2/hexanes) to give the product as

a yellow oil (0.422 g, 92 %): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.59 (m, 3H), 7.55 – 7.48 (m, 1H), 6.67 (d, *J* = 5.4 Hz, 1H), 6.66 (s, 1H), 6.59 (t, *J* = 8.3 Hz, 2.0 Hz, 1H), 5.97 (s, 2H), 5.19 (dd, *J* = 7.3 Hz, 6.2 Hz, 1H), 4.98 (d, *J* = 6.7 Hz, 1H), 4.30 (d, *J* = 7.3 Hz, 2H), 2.03 – 1.90 (m, 4H), 1.66 (s, 3H), 1.57 (s, 3H), 1.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 147.9, 147.7, 141.5, 133.6, 132.4, 132.1, 131.8, 131.6, 131.2, 123.9, 123.9, 123.8, 118.7, 111.1, 108.1, 101.8, 50.4, 39.6, 26.4, 25.8, 17.8, 16.1; IR (neat) 2968, 1542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{27}N_2O_6S$ $(M + H)^+$ 459.1585, found 459.1585.

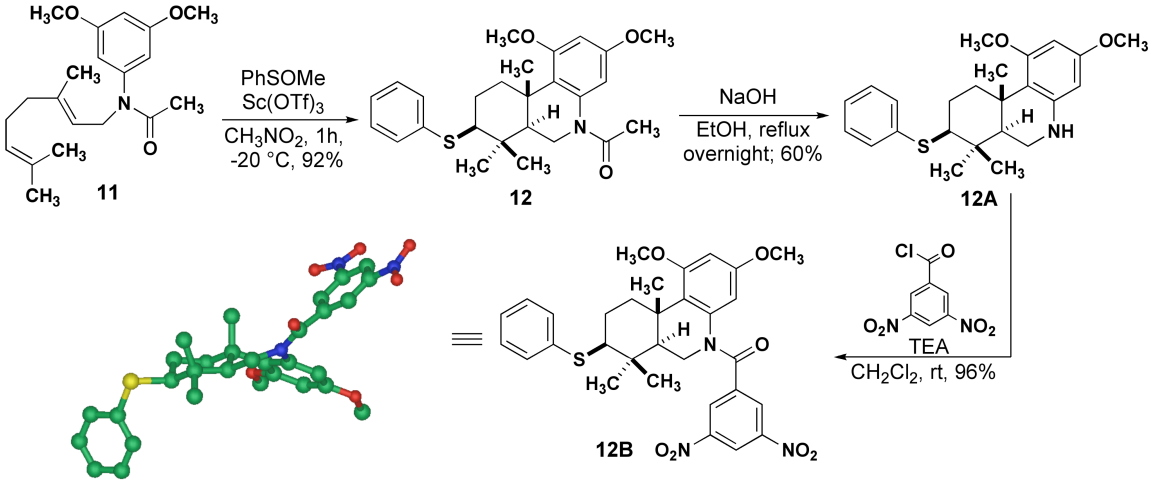
N-geranyl-N-nosyl aniline 56



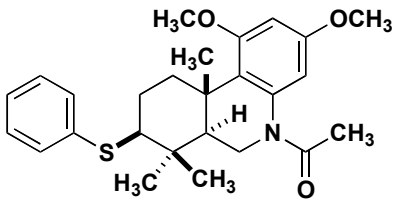
This compound was prepared according to general procedure D using **S7** (0.338 g, 1.0 mmol), triphenylphosphine (0.323 g, 1.2 mmol), geraniol (0.174 mL, 1.0 mmol), and diisopropyl azodicarboxylate (0.236 mL, 1.2 mmol). The product was purified by flash chromatography (75:25 CH_2Cl_2/hexanes) to give the product as a yellow oil (0.400 g, 84 %): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 – 7.57 (m, 3H), 7.51 – 7.45 (m, 1H), 6.75 – 6.65 (m, 3H), 5.20 (t, *J* = 7.3 Hz, 1H), 5.02 – 4.95 (m, 1H), 4.33 (d, *J* = 7.3 Hz, 2H), 3.85 (s, 3H), 3.73 (s, 3H), 1.94 (m, 4H), 1.64 (s, 3H), 1.55 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.0, 148.9, 148.0, 141.3, 133.5, 132.3, 132.0, 131.6, 131.1, 130.5, 123.8, 123.7, 122.3, 118.8,

113.3, 110.7, 56.0, 55.9, 50.1, 39.5, 26.4, 25.6, 17.7, 16.0; IR (neat) 3091, 2964, 1544 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{31}N_2O_6S$ $(M + H)^+$ 475.1898, found 475.1897.

Preparation of Crystalline Tricycle Derivatives:



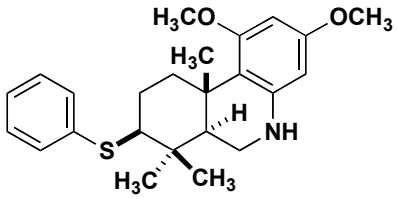
Bicyclized compound 12



To a solution of methyl benzenesulfenate (0.145 g, 1.03 mmol)) in nitromethane (14.7 mL, 0.07 M) was added scandium (III) triflate (0.49 g, 1.00 mmol). The solution was cooled to -20 °C and after 10 min, **9** (0.349 g, 1.05 mmol) dissolved in nitromethane (1.0 mL, 1.05 M) and cooled to -20 °C was added to the reaction mixture. After 1 h, the reaction mixture was quenched with saturated 1 x 5 mL Na_2CO_3. The organic layer was washed with 20 mL H_2O, 20 mL brine, dried with

Na_2SO_4, and concentrated *in vacuo* to afford a yellow oil. The product was purified by flash chromatography using 35 % EtOAc:hexanes to afford a white amorphous solid (0.425 g, 92%): ^{1}H NMR (600 MHz, $CDCl_3$, - 30 °C) δ 7.38 (d, *J* = 7.7 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 2H), 7.21 (t, *J* = 7.2 Hz, 1H), 6.27 (s, 1H), 6.15 (s, 1H), 3.99 (t, *J* = 12.6 Hz, 1H), 3.77 (s, 3H), 3.71 (s, 3H), 3.68 (dd, *J* = 13.1 Hz, 7.5 Hz, 1H), 2.88 (t, *J* = 8.5 Hz, 1H), 2.72 (d, *J* = 14.1 Hz, 1H), 2.15 (s, 3H), 1.94 – 1.89 (m, 2H), 1.75 – 1.67 (m, 1H), 1.65 (dd, *J* = 12.1 Hz, 7.2 Hz, 1H), 1.25 (s, 3H), 1.13 (s, 3H), 1.12 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$, 45 °C) δ 170.4, 158.2, 158.1, 139.7, 137.0, 131.8, 129.0, 126.6, 124.9, 103.6, 97.3, 61.2, 55.7, 55.5, 53.7, 43.0, 39.3, 39.0, 38.8, 30.0, 28.1, 23.6, 19.2, 17.8; IR (neat) 2965, 2935, 1656, cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{34}NO_3S$ $(M + H)^+$ 440.2254, found 440.2251.

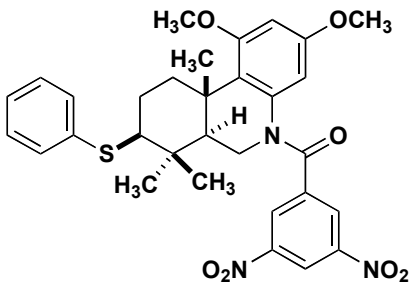
Deprotected bicyclized compound 12A



To a solution of **12** (0.022 g, 0.05 mmol) in EtOH (0.15 M) was added sodium hydroxide solution (2.5 mL, 2 M). The reaction mixture was heated to reflux for 4 h. Upon cooling, the solvent was removed *in vacuo.* The residue was dissolved in 30 mL CH_2Cl_2 and washed with H_2O, brine, dried (Na_2SO_4), and concentrated *in vacuo.* The product was purified by flash chromatography (20:80 EtOAc:hexanes) to afford a white amorphous solid (0.012 g, 60%): ^{1}H NMR (600

MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 2H), 7.30 – 7.24 (m, 2H), 7.22 – 7.16 (m, 1H), 5.82 (d, *J* = 2.4 Hz, 1H), 5.69 (d, *J* = 2.4 Hz, 1H), 4.32 (br s, 1H), 3.71 (s, 3H), 3.70 (s, 3H), 3.33 (dd, *J* = 11.1 Hz, 2.6 Hz, 1H), 3.23 (t, *J* = 11.2 Hz, 1H), 3.06 (dt, *J* = 13.8 Hz, 3.5 Hz, 1H), 2.96 – 2.91 (m, 1H), 1.99 – 1.89 (m, 2H), 1.63 (dd, *J* = 11.3 Hz, 2.7 Hz, 1H), 1.38 – 1.34 (m, 1H), 1.34 (s, 3H), 1.31 (s, 3H), 1.01 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.1, 159.1, 145.3, 136.9, 131.4, 128.9, 126.4, 113.7, 91.8, 89.2, 60.9, 55.0, 54.9, 52.7, 39.0, 38.2, 37.4, 37.4, 30.5, 28.3, 21.4, 18.6; IR (neat) 3406, 3059, 2935 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{32}NO_2S$ $(M + H)^+$ 398.2148, found 398.2148

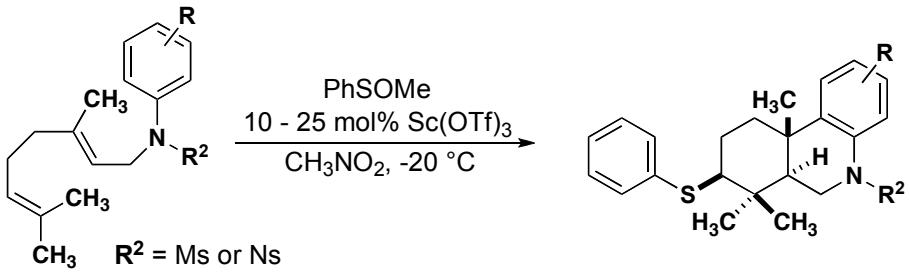
N-acylated bicyclized compound 12B



To a solution of **12A** (0.058 g, 0.147 mmol) in CH_2Cl_2 (0.1 M) was added 3,5-dinitrobenzoyl chloride (0.10 g, 0.441 mmol) and TEA (0.061 mL, 0.441 mmol). After 18 h, the reaction mixture was washed with H_2O and brine, dried (Na_2SO_4), and concentrated *in vacuo* to afford a yellow solid. The product was purified by flash chromatography using (20:80 EtOAc:hexanes) to afford a yellow crystals (0.083 g, 96%). This compound provided a crystal suitable for x-ray crystallography, proving the predicted relative stereochemistry was correct; mp 203 - 205 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.95 (t, *J* = 2.0 Hz, 1H), 8.38 (d, *J* =

1.6 Hz, 2H), 7.42 (d, *J* = 7.6 Hz, 2H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 6.23 (d, *J* = 2.4 Hz, 1H), 5.60 (s, 1H), 4.04 (d, *J* = 9.5 Hz, 2H), 3.78 (s, 3H), 3.39 (s, 3H), 2.98 – 2.89 (m, 2H), 2.03 (dd, *J* = 9.4 Hz, 6.5 Hz, 2H), 1.83 (t, *J* = 9.5 Hz, 1H), 1.79 – 1.70 (m, 1H), [1.46 (s, 3H), 1.34 (s, 3H), 1.21 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.7, 158.5, 158.0, 148.0, 139.9, 138.0, 136.6, 131.8, 129.0, 128.8, 126.7, 124.3, 119.7, 105.0, 97.6, 61.0, 55.8, 55.3, 52.6, 44.5, 39.3, 39.0, 38.6, 29.8, 27.8, 19.0, 17.7; IR (neat) 3088, 2941, 1646 cm^{-1}, 1547; HRMS (ESI) m/z calcd for $C_{31}H_{34}N_3O_7S$ $(M + H)^+$ 592.2112, found 592.2110.

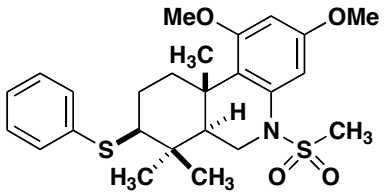
8. General Procedure E: bicyclization using PhSOMe



10-11, 50 **13-14, 58**

To a solution of methyl benzenesulfenate (PhSOMe) (1.0 equiv) in nitromethane (0.07 M) cooled (-20 °C) was added scandium triflate. After 20 min, protected geranylated aniline (1.0 equiv) (**10-11**) dissolved in nitromethane (0.4 M) and cooled (-20 °C) was added to the reaction mixture. The reaction mixture stirred overnight. The reaction mixture was filtered through a pad of silica gel (50:50 EtOAc/hexanes) to remove the Lewis acid. The solvent was removed *in vacuo,* and the crude mixture was purified by flash chromatography.

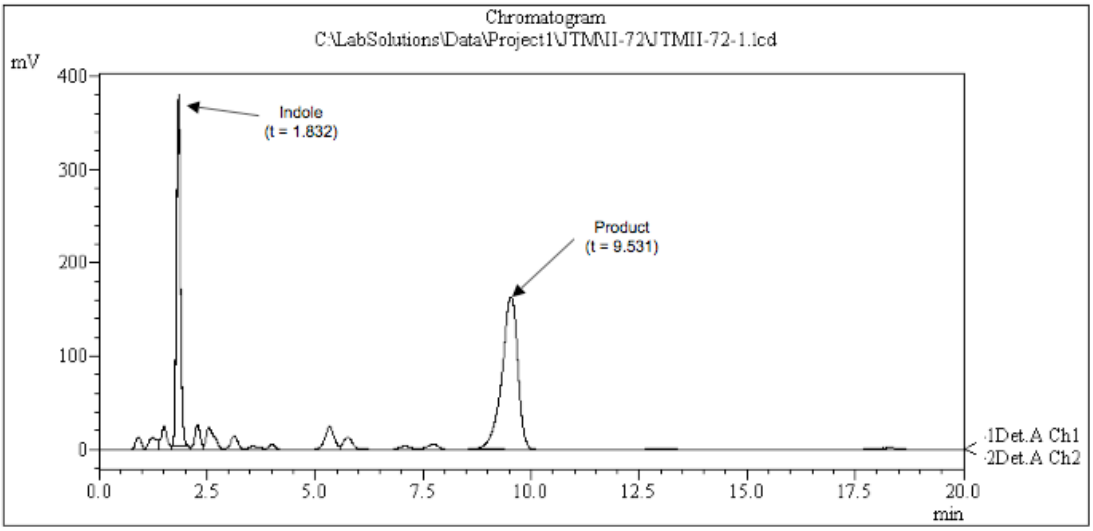
Bicyclized compound 13



This compound was prepared according to general procedure E with some modifications. The yield of this reaction was optimized by changing substrate concentration and catalyst loading. Reaction mixtures were analyzed by an HPLC assay with an internal standard.

General reaction procedure: To a solution of methyl benzenesulfenate (PhSOMe) (4.2 mg, 0.03 mmol) in nitromethane (0.05 mL) cooled (-20 °C) was added scandium triflate (0.1 to 1.0 equiv). Prior to protected geranylated aniline addition, nitromethane was added to the reaction mixture to correct to the desired volume. After 20 min, protected geranylated aniline **10** (11.0 mg, 0.03mmol) dissolved in nitromethane (0.4 M) and cooled (-20 °C) was added to the reaction mixture. The reaction mixture stirred overnight and was filtered through a pad of silica gel (50:50 EtOAc/hexanes) to remove the Lewis acid. The solvent was removed *in vacuo.* The remaining residue was dissolved and diluted in an indole:methanol mixture (0.1077 mg/mL indole) to 25mL in a volumetric flask. The mixture was analyzed by HPLC (0.8 mL/min, 40:60 water:CH_3CN). The data was compared to both external and internal calibration curves to determine conversion. Cyclization reactions utilizing triflic acid, triflimide, and *p*-toluenesulfonic acid replaced scandium triflate as the acid source and utilized the same general procedure.

Figure 2: Example Chromatograph (Entry 8)



PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	1.832	2451249	377377	37.146	69.773
2	9.531	4147666	163486	62.854	30.227
Total		6598914	540863	100.000	100.000

HPLC Data (For Table 1. Optimization of Sulfur-mediated Bicyclization):

Entry number (from Table 1.)	Acid Catalyst Source	Catalyst Loading %	Reaction concentration [Starting material]	AUC (Area Under the curve) Product	AUC indole	Internal Calibration Curve Yield%	External Calibration curve Yield%
3	$Sc(OTf)_3$	100	0.1 M	0	2,357,273	0	0
4	$Sc(OTf)_3$	30	0.1 M	2,333,096	2,263,104	31.5	32.0
5	$Sc(OTf)_3$	10	0.1 M	3,765,953	2,228,123	51.6	51.7
6	$Sc(OTf)_3$	10	0.02 M	14,278,604	2,254,074	85.1	86.3
7*	$Sc(OTf)_3$	10	0.02 M	0	2,262,841	0	0

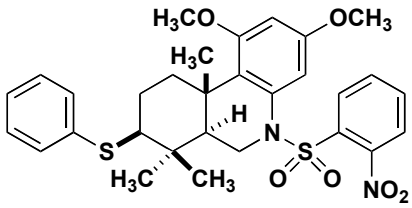
8	TfOH	5	0.02 M	4,147,666	2,451,249	52.0	56.9
9	*p*TSA	20	0.02 M	1,319,092	2,226,284	18.1	18.1
10	Tf_2NH	10	0.02 M	3,147,594	2,201,304	43.6	43.2

0.1 eq of DTBP (a proton scavenger) was added to this reaction mixture.

Characterization information for compound **13**:

white amorphous solid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 – 7.40 (m, 2H), 7.31 – 7.25 (m, 2H), 7.23 – 7.18 (m, 1H), 7.10 (d, *J* = 2.5 Hz, 1H), 6.23 (d, *J* = 2.5 Hz, 1H), 4.32 (dd, *J* = 12.7 Hz, 2.1 Hz, 1H), 3.77 (s, 3H), 3.74 (s, 3H), 3.32 (t, *J* = 12.1 Hz, 1H), 3.06 (dt, *J* = 13.8 Hz, 3.3 Hz, 1H), 2.89 (s, 3H), 2.89 – 2.85 (m, 1H), 1.98 – 1.91 (m, 2H), 1.54 (dd, *J* = 7.2 Hz, 1.2 Hz, 1H), 1.41 (s, 3H), 1.32 (s, 3H), 1.29 – 1.21 (m, 1H), 1.03 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.7, 158.8, 137.7, 136.6, 131.9, 129.0, 126.7, 120.7, 98.1, 96.1, 60.9, 55.5, 55.3, 52.5, 43.9, 38.8, 38.4, 38.1, 37.2, 30.5, 28.2, 20.1, 18.4; IR (neat) 2996, 2934 cm^{-1}; HRMS (ESI) m/z calcd for $C_{25}H_{34}NO_4S_2$ $(M + H)^+$ 476.1924, found 476.1920.

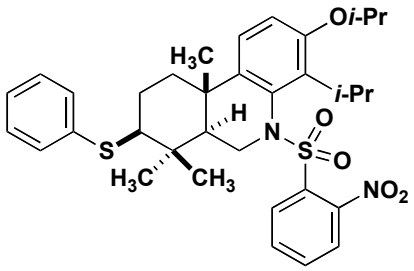
Bicyclized compound 14a



This compound was prepared according to general procedure E using **11** (14.2 mg, 0.03 mmol), methyl benzenesulfenate (4.2 mg, 0.03 mmol), and scandium

triflate (1.5 mg, 0.003 mmol). The product was purified by flash chromatography (28:72 EtOAc/hexanes) to give the product as a white amorphous solid (15.6 mg, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.1 Hz, 1H), 7.73 – 7.68 (m, 2H), 7.68 – 7.62 (m, 1H), 7.40 (d, *J* = 7.2 Hz, 2H), 7.27 (t, *J* = 7.2 Hz, 2H), 7.20 (t, *J* = 6.9 Hz, 1H), 6.46 (d, *J* = 2.4 Hz, 1H), 6.22 (d, *J* = 2.4 Hz, 1H), 4.28 (dd, *J* = 12.7 Hz, 2.4 Hz, 1H), 3.71 (s, 3H), 3.74-3.68 (m, 1H), 3.62 (s, 3H), 3.43 (t, *J* = 12.1 Hz, 1H), 2.99 (dt, *J* = 13.6 Hz, 3.5 Hz, 1H), 2.91 – 2.84 (m, 1H), 1.96 – 1.87 (m, 2H), 1.69 (dd, *J* = 11.5 Hz, 2.4 Hz, 1H), 1.39 (s, 3H), 1.13 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 158.1, 148.2, 136.8, 136.5, 134.0, 133.8, 132.0, 131.7, 130.4, 129.0, 126.6, 124.6, 121.5, 99.4, 96.7, 60.6, 55.3, 55.3, 53.2, 44.5, 38.7, 38.5, 37.0, 30.2, 28.1, 19.7, 18.5; IR (neat) 2935, 1543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{35}N_2O_6S_2$ $(M + H)^+$ 583.1931, found 583.1930.

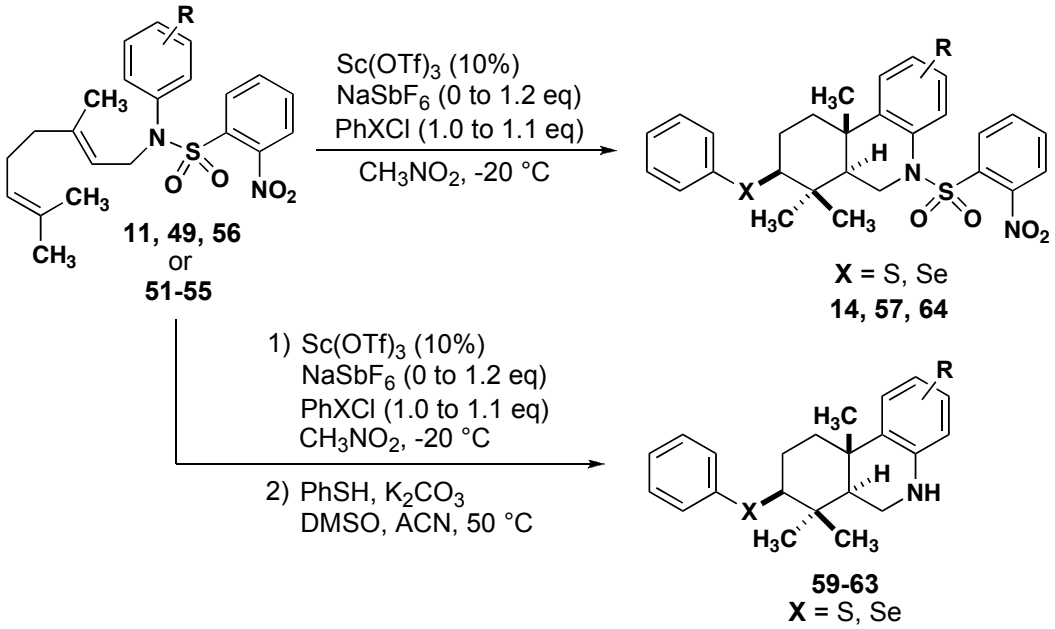
Bicyclized compound 58



This compound was prepared according to general procedure E using **50** (0.051 g, 0.1 mmol), Methyl benzenesulfenate (0.014 g, 0.1 mmol), and scandium triflate (0.012 g, 0.025 mmol). The product was purified by flash chromatography (15:85 EtOAc/hexanes) to give a yellow amorphous solid (0.050 g, 80 %): ^{1}H NMR (600 MHz, $CDCl_3$) 7.94 (d, *J* = 7.4 Hz, 1H), 7.69 (d, *J* = 4.1 Hz, 2H), 7.68 – 7.64 (m,

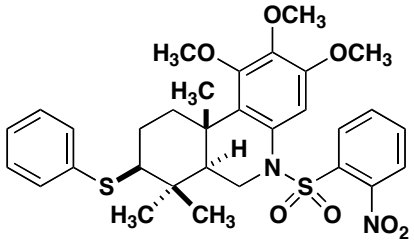
1H), 7.38 (d, *J* = 7.5 Hz, 2H), 7.30 – 7.23 (m, 1H), 7.20 (t, *J* = 7.4 Hz, 1H), 6.90 (d, *J* = 8.6 Hz, 1H), 6.68 (d, *J* = 8.7 Hz, 1H), 4.58 – 4.49 (m, 1H), 4.42 (t, *J* = 11.4 Hz, 1H), 3.75 (dd, *J* = 12.2 Hz, 8.4 Hz, 1H), 2.95 – 2.86 (m, 1H), 2.83 – 2.76 (m, 1H), 2.11 (dt, *J* = 12.7 Hz, 3.0 Hz, 1H), 2.05 – 1.98 (m, 2H), 1.53 (dd, *J* = 10.3 Hz, 9.1 Hz, 1H), 1.51 – 1.45 (m, 1H), 1.33 (d, *J* = 6.0 Hz, 3H), 1.30 (d, *J* = 6.0 Hz, 3H), 1.24 (s, 3H), 1.20 (s, 3H), 1.18 (s, 3H), 1.07 (d, *J* = 6.7, 3H), 1.01 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.7, 147.8, 140.4, 136.7, 135.3, 134.3, 133.7, 133.3, 131.6, 131.5, 130.0, 129.0, 126.6, 124.3, 120.8, 110.5, 69.0, 60.9, 53.2, 47.8, 39.8, 39.0, 36.5, 29.7, 29.1, 27.6, 22.3, 21.9, 21.87, 20.6, 19.7, 17.1.; IR (neat) 2972, 1544 cm^{-1}; HRMS (ESI) m/z calcd for $C_{34}H_{43}N_2O_5S_2$ $(M + H)^+$ 623.2608, found 623.2610.

9. General Procedure F: bicyclization using PhSCl and PhSeCl



To a solution of scandium triflate (0.1 equiv) in nitromethane (2.5 mM) was added sodium hexafluoroantimonate (0-1.2 equiv) and phenylsulfenyl chloride or phenylselenenyl chloride (1.0 equiv). The solution was cooled to -20 °C. After 20 min, protected geranylated aniline (1.0 equiv) (**11, 49-56**) dissolved in nitromethane (0.2 M) added to the reaction mixture. The reaction mixture stirred overnight at -20 °C. The reaction mixture was filtered through a pad of silica gel (50:50 EtOAc/hexanes) to remove the Lewis acid. The solvent was removed *in vacuo,* and the crude mixture was purified by flash chromatography.

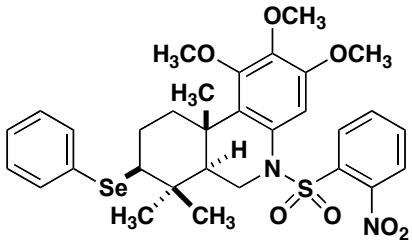
Bicyclized compound 57a



This compound was prepared according to general procedure F using **49** (15.1 mg, 0.03 mmol), phenylsulfenyl chloride (4.3 mg, 0.03 mmol), scandium triflate (1.5 mg, 0.003 mmol), and sodium hexafluoroantimonate (7.8 mg 0.03 mmol). The product was purified by flash chromatography (35:65 EtOAc/hexanes) to give the product as a yellow amorphous solid (16.9 mg, 92%): ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.78 – 7.72 (m, 2H), 7.72 – 7.67 (m, 1H), 7.66 – 7.61 (m, 1H), 7.42 – 7.38 (m, 2H), 7.31 – 7.25 (m, 2H), 7.21 (dt, *J* = 9.5 Hz, 4.2 Hz, 1H), 6.69 (s, 1H), 4.13 (dd, *J* = 12.6 Hz, 3.3 Hz, 1H), 3.79 (s, 3H), 3.75 (s, 3H), 3.65 (s, 3H), 3.46 (t, *J* = 12.2 Hz, 1H), 2.94 – 2.82 (m, 2H), 1.96 – 1.88 (m, 2H), 1.66 (dd, *J* = 11.8 Hz, 3.2 Hz, 1H), 1.40 (dd, *J* = 17.5 Hz, 13.9 Hz, 1H), 1.34 (s, 3H), 1.03

(s, 3H), 1.02 (s, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 153.2, 151.7, 148.6, 140.7, 136.9, 134.6, 133.1, 132.2, 131.9, 131.0, 130.5, 129.3, 127.7, 126.9, 124.8, 103.1, 61.3, 60.7, 56.1, 56.0, 52.8, 44.8, 39.3, 38.8, 37.9, 30.2, 28.3, 20.7, 18.3; IR (neat) 2967, 2936, 1544 cm^{-1}; HRMS (ESI) m/z calcd for $C_{31}H_{37}N_2O_7S_2$ $(M + H)^+$ 613.2037, found 613.2036.

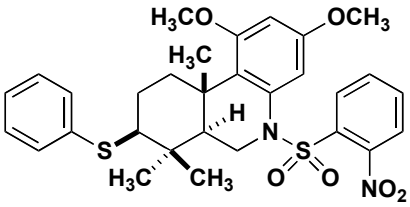
Bicyclized compound 57b



This compound was prepared according to general procedure F using **49** (74.6 mg, 0.15 mmol), phenylselenenyl chloride (28.7 mg, 0.15 mmol), and scandium triflate (7.4 mg, 0.015 mmol). The product was purified by flash chromatography (32:68 EtOAc/hexanes) to give the product as a yellow amorphous solid (93.1 mg, 94%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.9 Hz, 1H), 7.71 (t, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.61 (ddd, *J* = 8.0 Hz, 7.4 Hz, 0.7 Hz, 1H), 7.56 – 7.54 (m, 2H), 7.26 - 7.23 (m, 3H), 6.75 (s, 1H), 4.13 (dd, *J* = 12.6 Hz, 3.2 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.69 (s, 3H), 3.47 (t, *J* = 12.2 Hz, 1H), 3.01 (dd, *J* = 12.7 Hz, 4.5 Hz, 1H), 2.83 (dt, *J* = 13.5 Hz, 3.5 Hz, 1H), 2.14 – 1.98 (m, 2H), 1.68 (dd, *J* = 11.9 Hz, 3.2 Hz, 1H), 1.44 – 1.37 (m, 1H), 1.35 (s, 3H), 1.05 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 152.8, 151.3, 148.4, 140.3, 134.6, 134.1, 132.9, 131.7, 130.7, 130.5, 130.4, 129.1, 127.6, 127.4, 124.4, 102.9, 61.0, 60.7, 59.3, 55.9, 52.1, 44.8, 39.0, 38.8, 38.8, 31.1, 29.2, 20.6, 19.3; IR (neat)

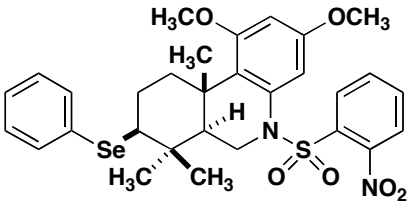
2935, 1543 cm^{-1}; HRMS (ESI) m/z calcd for $C_{31}H_{37}N_2O_7SSe$ $(M + H)^+$ 661.1481, found 661.1485.

Bicyclized compound 14a



This compound was prepared according to general procedure F using **11** (14.2 mg, 0.03 mmol), phenylsulfenyl chloride (4.3 mg, 0.03 mmol), and scandium triflate (1.5 mg, 0.003 mmol). The product was purified by flash chromatography (28:72 EtOAc/hexanes) to give the product as a white amorphous solid (14.9 mg, 85%). See previous characterization data in section 8 (general procedure E).

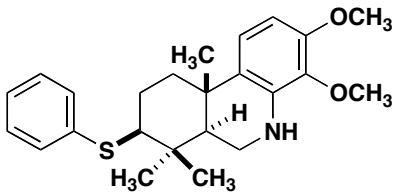
Bicyclized compound 14b



This compound was prepared according to general procedure F using **11** (14.2 mg, 0.03 mmol), phenylselenenyl chloride (5.7 mg, 0.03 mmol), and scandium triflate (1.5 mg, 0.003 mmol). The product was purified by flash chromatography

(30:70 EtOAc/hexanes) to give the product as a white amorphous solid (15.9 mg, 84%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.4 Hz, 1H), 7.75 – 7.68 (m, 2H), 7.68 – 7.61 (m, 1H), 7.58 – 7.53 (m, 2H), 7.26 – 7.22 (m, 3H), 6.46 (d, *J* = 2.4 Hz, 1H), 6.22 (d, *J* = 2.4 Hz, 1H), 4.28 (dd, *J* = 12.8 Hz, 2.4 Hz, 1H), 3.71 (s, 3H), 3.61 (s, 3H), 3.42 (t, *J* = 12.1 Hz, 1H), 3.03 (dd, *J* = 12.7 Hz, 4.5 Hz, 1H), 2.96 (dt, 13.6 Hz, 3.2 Hz, 1H), 2.15 – 2.03 (m, 1H), 2.02 – 1.94 (m, 1H), 1.70 (dd, *J* = 11.4 Hz, 2.1 Hz, 1H), 1.38 (s, 3H), 1.32 – 1.22 (m, 1H), 1.13 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.3, 158.2, 148.2, 136.9, 134.6, 134.0, 133.8, 132.0, 130.4, 130.4, 129.1, 127.3, 124.6, 121.6, 99.4, 96.7, 59.5, 55.3, 55.3, 52.9, 44.8, 38.9, 38.8, 38.1, 31.2, 29.3, 19.7, 19.6; IR (neat) 2995, 2964, 1545 cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{35}N_2O_6SSe$ $(M + H)^+$ 631.1376, found 631.1374.

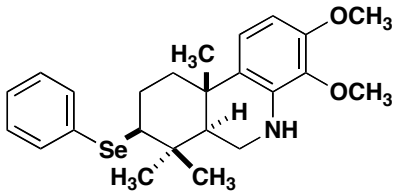
Deprotected bicyclized compound 59a



This compound was prepared according to general procedure F using **51** (95 mg, 0.20 mmol), phenylsulfenyl chloride (0.026 mL, 0.21 mmol), and scandium triflate (10.0 mg, 0.020 mmol). The product was purified by flash chromatography (30:70 EtOAc/hexanes) to give the product as an impure yellow amorphous solid (72 mg). This impure material was dissolved in acetonitrile (2 mL) and stirred under argon. To this solution was added thiophenol (0.038 mL, 0.372 mmol), potassium

carbonate (69 mg, 0.5 mmol), and dimethyl sulfoxide (0.060 mL). The solution was heated to 50 °C and stirred for 24 h. The solvent was removed *in vacuo,* and the crude mixture was purified by flash chromatography (10:90 EtOAc/hexanes) to afford the product as a white amorphous solid (42 mg, 53% over two steps): ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.41 (d, *J* = 7.3 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.20 (t, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 8.6 Hz, 1H), 6.13 (d, *J* = 8.6 Hz, 1H), 4.45 (s, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 3.51 (dd, *J* = 11.3 Hz, 4.0 Hz, 1H), 3.36 (t, *J* = 11.6 Hz, 1H), 2.98 – 2.88 (m, 1H), 2.24 (dt, *J* = 13.1 Hz, 3.3 Hz, 1H), 2.05 – 1.93 (m, 2H), 1.56 (dd, *J* = 11.9 Hz, 4.0 Hz, 1H), 1.53 – 1.44 (m, 1H), 1.31 (s, 3H), 1.17 (s, 3H), 1.03 (s, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 150.9, 137.2, 136.9, 133.8, 131.6, 129.3, 127.9, 126.7, 118.7, 99.6, 61.4, 59.9, 55.9, 49.6, 39.3, 38.5, 38.0, 35.8, 30.2, 28.2, 24.0, 18.1; IR (neat) 3429, 2963, 2932 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{32}NO_2S$ $(M + H)^+$ 398.2148, found 398.2142.

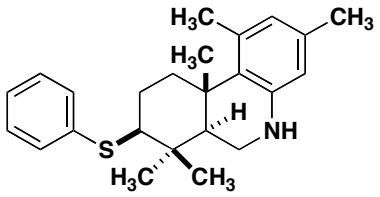
Deprotected bicyclized compound 59b



This compound was prepared according to general procedure F using **51** (142 mg, 0.30 mmol), phenylselenenyl chloride (59.4 mg, 0.31 mmol), scandium triflate (14.8 mg, 0.030 mmol), and sodium hexafluoroantimonate (93.1 mg, 0.36 mmol). The product was purified by flash chromatography (30:70 EtOAc/hexanes) to give the product as an impure yellow amorphous solid (184

mg). This impure material was dissolved in acetonitrile (3 mL) and stirred under argon. To this solution was added thiophenol (0.090 mL, 0.88 mmol), potassium carbonate (0.162, 1.17 mmol), and dimethyl sulfoxide (0.150 mL). The solution was heated to 50 °C and stirred for 24 h. The solvent was removed *in vacuo,* and the crude mixture was purified by flash chromatography (9:91 EtOAc/hexanes) to afford the product as a white amorphous solid (74 mg, 55% over two steps): ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.56 (dd, *J* = 6.4 Hz, 3.0 Hz, 2H), 7.29 – 7.23 (m, 3H), 6.66 (d, *J* = 8.6 Hz, 1H), 6.12 (d, *J* = 8.6 Hz, 1H), 4.48 (s, 1H), 3.75 (s, 3H), 3.73 (s, 3H), 3.50 (dd, *J* = 11.3 Hz, 4.0 Hz, 1H), 3.35 (t, *J* = 11.6 Hz, 1H), 3.08 (dd, *J* = 12.3 Hz, 4.5 Hz, 1H), 2.21 (dt, *J* = 7.4 Hz, 3.4 Hz, 1H), 2.18 – 2.11 (m, 1H), 2.11 – 2.06 (m, 1H), 1.56 (dd, *J* = 11.9 Hz, 4.0 Hz, 1H), 1.47 (td, *J* = 13.0 Hz, 4.2 Hz, 1H), 1.31 (s, 3H), 1.16 (s, 3H), 1.03 (s, 3H); ^{13}C NMR (151 MHz, CD_2Cl_2) δ 150.9, 136.9, 134.5, 133.9, 131.1, 129.4, 127.9, 127.4, 118.7, 99.7, 60.4, 59.9, 55.9, 49.4, 39.6, 39.5, 38.3, 35.9, 31.3, 29.4, 24.1, 19.2; IR (neat) 3429, 2962, 2932 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{32}NO_2Se$ $(M + H)^+$ 446.1593, found 446.1588.

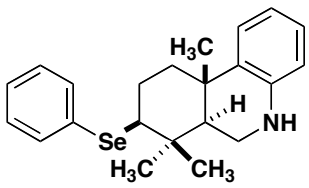
Deprotected bicyclized compound 60



This compound was prepared according to general procedure F using **52** (132.8 mg, 0.30 mmol), phenylsulfenyl chloride (47.7 mg, 0.33 mmol), and scandium

triflate (14.8 mg, 0.030 mmol). The product was purified by flash chromatography (20:80 EtOAc/hexanes) to give the product as an impure yellow amorphous solid (137.6 mg). This impure material was dissolved in acetonitrile (3 mL) and stirred under argon. To this solution was added thiophenol (0.077 mL, 0.75 mmol), potassium carbonate (0.138, 1.0 mmol), and dimethyl sulfoxide (0.150 mL). The solution was heated to 50 °C and stirred for 24 h. The solvent was removed *in vacuo,* and the crude mixture was purified by flash chromatography (55:45 CH_2Cl_2/hexanes) to afford the product as a white amorphous solid (53.6 mg, 49% over two steps): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 8.3 Hz, 1.2 Hz, 2H), 7.29 (t, *J* = 7.7 Hz, 2H), 7.21 (t, *J* = 7.4 Hz, 1H), 6.23 (s, 1H), 6.18 (s, 1H), 4.16 (s, 1H), 3.38 (dd, *J* = 11.0 Hz, 2.7 Hz, 1H), 3.29 (t, *J* = 11.3 Hz, 1H), 2.91 (dd, *J* = 9.7 Hz, 7.1 Hz, 1H), 2.74 (dt, *J* = 13.4 Hz, 3.5 Hz, 1H), 2.36 (s, 3H), 2.14 (s, 3H), 1.99 – 1.93 (m, 2H), 1.64 (dd, *J* = 11.5 Hz, 3.1 Hz, 1H), 1.56 – 1.49 (m, 1H), 1.35 (s, 3H), 1.33 (s, 3H), 1.02 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.8, 136.7, 136.2, 136.1, 131.6, 129.0, 128.2, 126.5, 123.1, 113.8, 60.6, 51.8, 39.0, 38.6, 38.3, 38.2, 30.5, 28.0, 24.9, 21.2, 20.6, 18.4; IR (neat) 3402, 2965, 2861 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{32}NS$ $(M + H)^+$ 366.2250, found 366.2254.

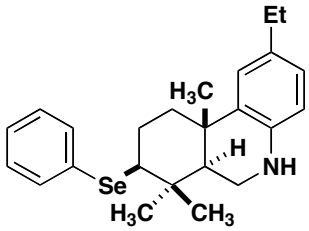
Deprotected bicyclized 61



This compound was prepared according to general procedure F using **53** (124.4

mg, 0.30 mmol), phenylselenenyl chloride (61.3 mg, 0.32 mmol), scandium triflate (15.0 mg, 0.030 mmol), and sodium hexafluoroantimonate (99 mg, 0.38 mmol). The product was purified by flash chromatography (20:80 EtOAc/hexanes) to give the product as an impure yellow amorphous solid (130 mg). This impure material was dissolved in acetonitrile (3 mL) and stirred under argon. To this solution was added thiophenol (0.071 mL, 0.69 mmol), potassium carbonate (0.127, 0.92 mmol), and dimethyl sulfoxide (0.115 mL). The solution was heated to 50 °C and stirred for 24 h. The solvent was removed *in vacuo,* and the crude mixture was purified by flash chromatography (5:95 EtOAc/hexanes) to afford the product as a white amorphous solid (37.2 mg, 32% over two steps): ^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.61 – 7.57 (m, 2H), 7.30 – 7.26 (m, 4H), 7.00 (d, *J* = 7.7 Hz, 1H), 6.91 (t, *J* = 8.1 Hz, 1H), 6.54 (t, *J* = 7.5 Hz, 1H), 6.41 (d, *J* = 7.9 Hz, 1H), 3.95 (br s, 1H), 3.46 (dd, *J* = 11.2 Hz, 4.0 Hz, 1H), 3.37 (t, *J* = 11.5 Hz, 1H), 3.10 (dd, *J* = 12.7 Hz, 4.1 Hz, 1H), 2.27 (dt, *J* = 13.0 Hz, 3.3 Hz, 1H), 2.24 – 2.16 (m, 1H), 2.16 – 2.09 (m, 1H), 1.61 (dd, *J* = 11.9 Hz, 3.9 Hz, 1H), 1.51 (td, *J* = 13.1 Hz, 3.8 Hz, 1H), 1.33 (s, 3H), 1.21 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (151 MHz, CD_2Cl_2) δ 142.9, 134.6, 133.6, 131.1, 129.4, 127.5, 127.0, 124.1, 116.5, 113.5, 60.3, 49.1, 40.2, 39.4, 38.3, 36.1, 31.3, 29.40, 24.0, 19.2; IR (neat) 3407, 2963 cm^{-1}; HRMS (ESI) m/z calcd for $C_{22}H_{28}NSe$ $(M + H)^+$ 386.1387, found 386.1378.

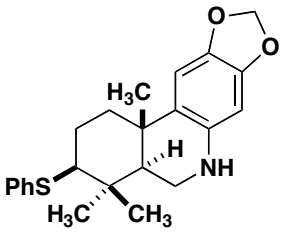
Deprotected bicyclized 62



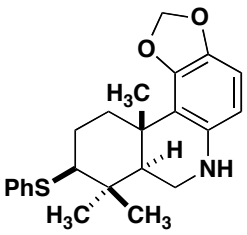
This compound was prepared according to general procedure F using **54** (133 mg, 0.30 mmol), phenylselenenyl chloride (58 mg, 0.30 mmol), scandium triflate (15.0 mg, 0.030 mmol), and sodium hexafluoroantimonate (93 mg, 0.36 mmol). The product was purified by flash chromatography (12:88 EtOAc/hexanes) to give the product as an impure yellow amorphous solid (114 mg). A portion of this impure material (44.1 mg, 0.074 mmol) was dissolved in acetonitrile (1 mL) and stirred under argon. To this solution was added thiophenol (0.023 mL, 0.22 mmol), potassium carbonate (0.042, 0.3 mmol), and dimethyl sulfoxide (0.037 mL). The solution was heated to 50 °C and stirred for 24 h. The solvent was removed *in vacuo,* and the crude mixture was purified by flash chromatography (4:96 EtOAc/hexanes) to afford the product as a white amorphous solid (24.4 mg, 51% over two steps): ^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.59 – 7.56 (m, 2H), 7.29 – 7.25 (m, 3H), 6.84 (d, *J* = 1.7 Hz, 1H), 6.76 (dd, *J* = 8.0 Hz, 1.5 Hz, 1H), 6.37 (d, *J* = 8.0 Hz, 1H), 3.97 (br s, 1H), 3.44 (dd, *J* = 11.1 Hz, 3.9 Hz, 1H), 3.35 (t, *J* = 11.5 Hz, 1H), 3.10 (dd, *J* = 12.7 Hz, 4.2 Hz, 1H), 2.47 (q, *J* = 7.6 Hz, 2H), 2.27 (dt, *J* = 13.1 Hz, 3.4 Hz, 1H), 2.23 - 2.14 (m, 1H), 2.14 - 2.09 (m, 1H), 1.60 (dd, *J* = 11.9 Hz, 3.9 Hz, 1H), 1.50 (td, *J* = 13.2 Hz, 3.9 Hz, 1H), 1.32 (s, 3H), 1.21 (s, 3H), 1.14 (t, *J* = 7.2, 3H), 1.04 (s, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 140.5, 134.5, 133.9, 132.6, 131.1, 129.4, 127.4, 126.3, 123.6, 113.8, 60.3, 49.4, 40.2, 39.5, 38.3, 36.2, 31.3, 29.4, 28.6, 24.1, 19.2, 16.5; IR (neat) 3405, 2961, 2930

cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{32}NSe$ $(M + H)^+$ 414.1700, found 414.1691.

Deprotected bicyclized Compounds 63a major and minor isomers



major isomer



minor isomer

These compounds were prepared as an inseparable mixture according to general procedure F using **55** (92 mg, 0.3 mmol), phenylsulfenyl chloride (0.026 mL, 0.21 mmol), and scandium triflate (10.0 mg, 0.02 mmol). The oil was purified by flash chromatography (20:80 EtOAc/hexanes) to give the product as an impure yellow amorphous solid (84 mg). This impure material was dissolved in acetonitrile (2 mL) and stirred under argon. To this solution was added thiophenol (0.046 mL, 0.45 mmol), potassium carbonate (0.083, 0.60 mmol), and dimethyl sulfoxide (0.075 mL). The solution was heated to 50 °C and stirred for 24 h. The solvent was removed *in vacuo,* and the crude mixture was purified by flash chromatography (10:90 EtOAc/hexanes) to afford the products as a white amorphous solid (17 mg, 22% over two steps, 76:24 major:minor):

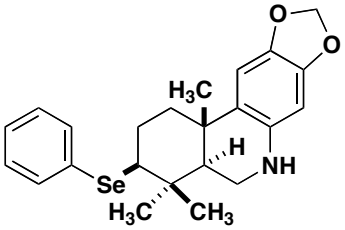
Major isomer: ^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.44 – 7.41 (m, 2H), 7.32 – 7.28 (m, 2H), 7.24 – 7.20 (m, 1H), 6.57 (s, 1H), 6.03 (s, 1H), 5.76 (d, *J* = 3.2 Hz, 2H), 3.40 (dd, *J* = 11.1 Hz, 3.7 Hz, 1H), 3.32 (t, *J* = 11.5 Hz, 1H), 2.94 (dd, *J* = 11.7 Hz, 4.9

Hz, 1H), 2.17 (dt, *J* = 13.1 Hz, 3.4 Hz, 1H), 2.03 – 1.96 (m, 2H), 1.57 (dd, *J* = 11.9 Hz, 3.8 Hz, 1H), 1.46 (td, *J* = 12.9 Hz, 5.0 Hz, 1H), 1.32 (s, 3H), 1.19 (s, 3H), 1.01 (s, 3H);

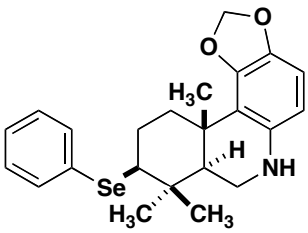
Minor isomer: ^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.44 – 7.41 (m, 2H), 7.32 – 7.28 (m, 2H), 7.24 – 7.20 (m, 1H), 6.48 (d, *J* = 8.3 Hz, 1H), 5.93 (d, *J* = 8.2 Hz, 1H), 5.74 (s, 2H), 3.37 – 3.34 (m, 1H), 3.26 (t, *J* = 11.3 Hz, 1H), 2.98 (dd, *J* = 9.6 Hz, 7.3 Hz, 1H), 2.72 (dt, *J* = 13.7 Hz, 3.4 Hz, 1H), 2.03 – 1.96 (m, 2H), 1.64 (dd, *J* = 11.5 Hz, 3.1 Hz, 1H), 1.54 – 1.49 (m, 1H), 1.34 (s, 3H), 1.31 (s, 3H), 1.01 (s, 3H);

Mixture of isomers: ^{13}C NMR (151 MHz, $CDCl_3$) δ 146.4, 144.9, 139.5, 139.3, 139.1, 137.8, 137.2, 137.2, 131.7, 131.6, 129.3, 129.2, 126.8, 126.7, 125.8, 118.1, 107.1, 105.6, 104.7, 100.7, 100.2, 95.6, 61.3, 61.1, 51.3, 50.0, 39.9, 39.7, 38.8, 38.2, 38.0, 37.7, 36.8, 36.1, 30.2, 30.2, 30.1, 28.2, 24.3, 22.1, 18.5, 18.1; IR (neat) 3414, 2865, 2964, 2932 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{28}NO_2S$ $(M + H)^+$ 382.1835, found 382.1836.

Deprotected bicyclized Compounds 63b major and minor isomers



major isomer



minor isomer

These compound were prepared as an inseparable mixture according to general procedure F using **55** (78 mg, 0.17 mmol), phenylselenenyl chloride (32.6mg, 0.17 mmol), scandium triflate (8.6 mg, 0.017 mmol), and sodium

hexafluoroantimonate (53 mg, 0.20 mmol). The oil was purified by flash chromatography (30:70 EtOAc/hexanes) to give the product as an impure yellow amorphous solid (75 mg). This impure material was dissolved in acetonitrile (2 mL) and stirred under argon. To this solution was added thiophenol (0.025 mL, 0.24 mmol), potassium carbonate (0.45 mg, 0.324 mmol), and dimethyl sulfoxide (0.037 mL). The solution was heated to 50 °C and stirred for 24 h. The solvent was removed *in vacuo,* and the crude mixture was purified by flash chromatography (15:85 EtOAc/hexanes) to afford the product as a white amorphous solid (51 mg, 70% over two steps, 39:61 a:b):

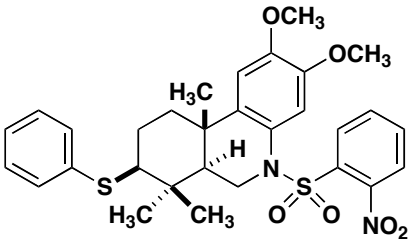
Major isomer: ^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.60 – 7.54 (m, 2H), 7.28 – 7.24 (m, 3H), 6.54 (s, 1H), 6.01 (s, 1H), 5.74 (d, *J* = 2.8 Hz, 2H), 3.39 (dd, *J* = 11.0 Hz, 3.4 Hz, 1H), 3.30 (t, *J* = 11.5 Hz, 1H), 3.07 (dd, *J* = 12.3 Hz, 4.3 Hz, 1H), 2.19 – 2.02 (m, 3H), 1.56 (dd, *J* = 11.9 Hz, 3.8 Hz, 1H), 1.42 (dd, *J* = 13.3 Hz, 9.7 Hz, 1H), 1.31 (s, 3H), 1.18 (s, 3H), 1.01 (s, 3H);

Minor isomer: ^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.60 – 7.54 (m, 2H), 7.28 – 7.24 (m, 3H), 6.46 (d, *J* = 8.2 Hz, 1H), 5.91 (d, *J* = 8.2 Hz, 1H), 5.72 (s, 2H), 3.34 (dd, *J* = 11.1 Hz, 2.7 Hz, 1H), 3.24 (t, *J* = 11.3 Hz, 1H), 3.11 (dd, *J* = 12.9 Hz, 4.3 Hz, 1H), 2.69 (dt, *J* = 13.6 Hz, 3.5 Hz, 1H), 2.19 – 2.02 (m, 2H), 1.63 (dd, *J* = 11.5 Hz, 3.1 Hz, 1H), 1.49 (dd, *J* = 13.5 Hz, 3.8 Hz, 1H), 1.33 (s, 3H), 1.30 (s, 3H), 1.01 (s, 3H);

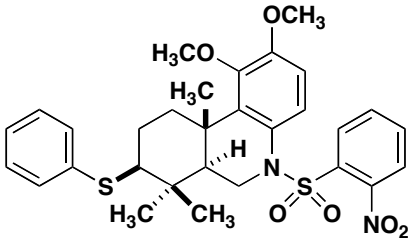
Mixture of isomers: ^{13}C NMR (151 MHz, CD_2Cl_2) δ 146.4, 139.5, 139.3, 139.1, 137.8, 134.6, 134.5, 131.1, 131.0, 129.4, 129.3, 127.5, 127.4, 125.8, 118.1, 107.1, 105.6, 104.6, 100.7, 100.1, 95.6, 60.2, 60.1, 51.0, 49.7, 40.2, 40.0, 39.8,

38.7, 38.5, 38.2, 36.9, 36.2, 31.3, 31.2, 30.1, 29.4, 29.4, 24.3, 22.1, 19.6, 19.2; IR (neat) 3414, 2963, 2931, 2864 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{28}NO_2Se$ $(M + H)^+$ 430.1285, found 430.1281.

Bicyclized compounds 64a major and minor isomers



major isomer



minor isomer

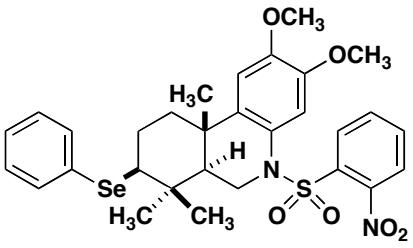
These compounds were prepared as regioisomers according to general procedure F using **56** (62.0 mg, 0.13 mmol), phenylsulfenyl chloride (0.016 mL, 0.13 mmol), scandium triflate (6.4 mg, 0.013 mmol), and sodium hexafluoroantimonate (40 mg 0.16 mmol). The product was purified by flash chromatography (30:70 EtOAc/hexanes) to give the products as yellow amorphous solids.

Major isomer: (24.3 mg, 32%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68 – 7.63 (m, 2H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.29 (s, 1H), 7.28 – 7.24 (m, 2H), 7.20 (t, *J* = 7.1 Hz, 1H), 6.58 (s, 1H), 4.00 (dd, *J* = 12.0 Hz, 5.1 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 3.78 (t, *J* = 11.8 Hz, 1H), 2.80 (dd, *J* = 12.4 Hz, 3.1 Hz, 1H), 2.09 (d, *J* = 13.0 Hz, 1H), 2.03 – 1.85 (m, 2H), 1.57 (dd, *J* = 13.2 Hz, 4.4 Hz, 1H), 1.49 (td, *J* = 13.3 Hz, 3.4 Hz, 1H), 1.30 (s, 3H), 1.09 (s, 3H), 0.71 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.5, 147.3, 146.3, 136.4, 135.1, 134.0, 131.8, 131.7, 131.4, 130.4, 129.1, 127.1, 126.9, 124.0, 107.3,

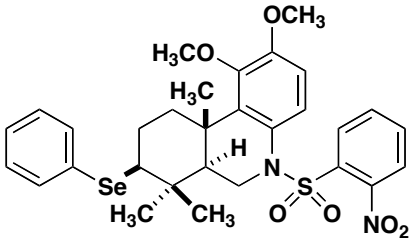
107.2, 61.0, 56.2, 56.2, 51.0, 45.1, 38.6, 38.3, 36.1, 29.7, 27.5, 21.4, 17.5; IR (neat) 2998, 2966, 1543, cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{35}N_2O_6S_2$ $(M + H)^+$ 583.1931, found 583.1934.

Minor isomer: (22.0 mg, 29%): ^1H NMR (600 MHz, $CDCl_3$) δ 7.72 – 7.67 (m, 2H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.61 – 7.58 (m, 1H), 7.40 (dd, *J* = 8.3 Hz, 1.1 Hz, 2H), 7.29 – 7.27 (m, 2H), 7.22 – 7.18 (m, 1H), 7.10 (d, *J* = 9.0 Hz, 1H), 6.72 (d, *J* = 9.0 Hz, 1H), 4.10 (dd, *J* = 12.4 Hz, 3.7 Hz, 1H), 3.82 (s, 3H), 3.75 (s, 3H), 3.57 (t, *J* = 12.1 Hz, 1H), 2.91 (dt, *J* = 13.5 Hz, 3.3, 1H), 2.87 (dd, *J* = 11.6 Hz, 5.2 Hz, 1H), 1.98 – 1.87 (m, 2H), 1.70 (dd, *J* = 12.0 Hz, 3.5 Hz, 1H), 1.50 (td, *J* = 13.2 Hz, 5.2 Hz, 1H), 1.35 (s, 3H), 1.06 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.1, 148.4, 147.8, 136.6, 135.9, 133.9, 133.0, 131.8, 131.7, 130.5, 129.1, 128.5, 126.7, 124.3, 118.8, 110.3, 60.9, 60.7, 56.0, 52.2, 44.6, 39.6, 38.8, 37.9, 30.1, 28.1, 20.2, 18.2; IR (neat) 2967, 2935, 1546 cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{35}N_2O_6S_2$ $(M + H)^+$ 583.1931, found 583.1923.

Bicyclized compounds 64b major and minor isomers



major isomer



minor isomer

These compounds were prepared as regioisomers according to general procedure F using **56** (62.0 mg, 0.13 mmol), phenylselenenyl chloride (25 mg, 0.13 mmol), scandium triflate (6.4 mg, 0.013 mmol), and sodium

hexafluoroantimonate (40 mg 0.16 mmol). The product was purified by flash chromatography (26:74 EtOAc/hexanes) to give the products as yellow amorphous solids.

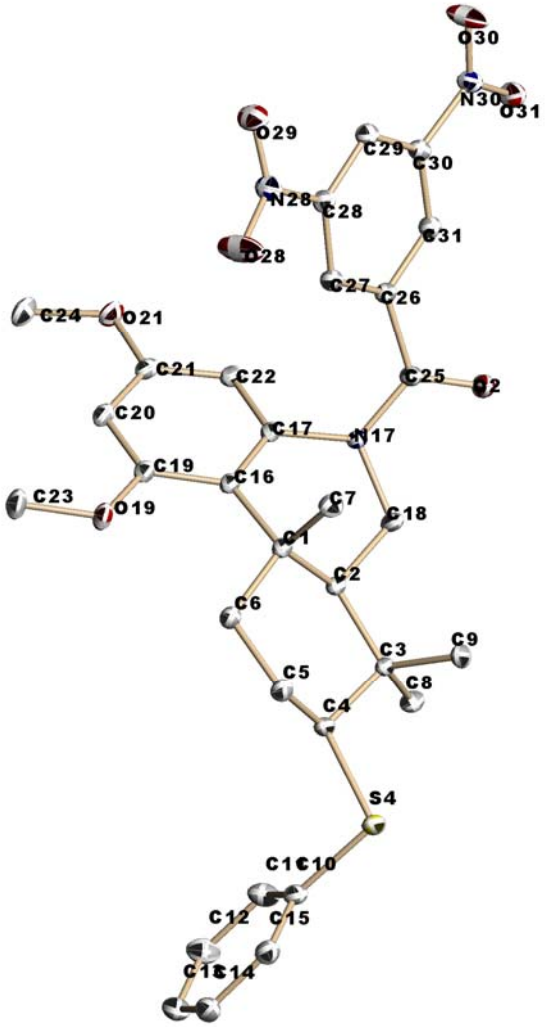
Major isomer: (32.5 mg, 55%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.56 (m, 4H), 7.55 – 7.50 (m, 2H), 7.29 (s, 1H), 7.27 – 7.23 (m, 3H), 6.57 (s, 1H), 4.00 (dd, *J* = 12.0 Hz, 5.0 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 3.75 (d, *J* = 11.9 Hz, 1H), 2.97 – 2.90 (m, 1H), 2.12 – 2.03 (m, 3H), 1.58 (dd, *J* = 12.5 Hz, 5.0 Hz, 1H), 1.52 – 1.41 (m, 1H), 1.30 (s, 3H), 1.10 (s, 3H), 0.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.4, 147.2, 146.3, 135.1, 134.6, 134.0, 131.6, 131.4, 130.4, 129.2, 129.1, 127.5, 127.0, 123.9, 107.2, 107.0, 59.4, 56.2, 56.1, 50.6, 45.4, 39.6, 38.5, 36.1, 30.8, 28.6, 21.3, 18.6; IR (neat) 3059, 2965, 1544, cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{35}N_2O_6SSe$ $(M + H)^+$ 631.1376, found 631.1374.

Minor isomer: (26.6 mg, 45%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.57 (m, 4H), 7.56 – 7.51 (m, 2H), 7.27 – 7.22 (m, 3H), 7.09 (d, *J* = 9.0 Hz, 1H), 6.71 (d, *J* = 9.1, 1H), 4.09 (dd, *J* = 12.4 Hz, 3.5 Hz, 1H), 3.81 (s, 3H), 3.74 (s, 3H), 3.55 (t, *J* = 12.2 Hz, 1H), 3.01 (dd, *J* = 12.1 Hz, 4.8 Hz, 1H), 2.88 (dt, *J* = 13.5 Hz, 3.1 Hz, 1H), 2.15 – 1.97 (m, 1H), 1.71 (dd, *J* = 11.9 Hz, 3.5 Hz, 1H), 1.48 (td, *J* = 13.2 Hz, 4.5 Hz, 1H), 1.34 (s, 3H), 1.06 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.0, 148.3, 147.7, 135.9, 134.6, 133.9, 133.0, 131.7, 130.4, 129.1, 128.4, 127.4, 124.3, 118.8, 110.3, 110.3, 60.9, 59.3, 55.9, 51.9, 44.8, 39.6, 39.0, 38.9, 31.2, 29.2, 20.2, 19.3; IR (neat) 2964, 2932, 1542 cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{35}N_2O_6SSe$ $(M + H)^+$ 631.1376, found 631.1375.

8 November, 2010

JF1975

A yellow block with approximate orthogonal dimensions 0.39 x 0.29 x 0.16mm^3 was placed and optically centered on the Bruker APEX Duo[1] CCD system at –183°C(90K). Indexing of the unit cell was attempted using a random set of reflections collected from three series of 0.5° wide ω-scans, 5 seconds per frame, and 18 frames per series that were well distributed in reciprocal space. Five ω-scan data frame series were collected [MoKα] with 0.3° wide scans, 20 seconds per frame and 606 frames were collected, at varying phi angles (phi=0°, 72°, 144°, 216°, 288°), for each series, respectively. The crystal to detector distance was 4.96cm, thus providing a complete sphere of data with processing to $2\theta_{max}$=63.32°.



Structural determination and Refinement:

All crystallographic calculations were performed on a Personal computer (PC) with a Pentium 3.20GHz processor and 4GB of extended memory. A total of 60727 reflections were collected and corrected for Lorentz and polarization effects with SAINT[1] and absorption using Blessing's method as incorporated into the program SADABS[2,3] with 10001 unique. The SHELXTL[4] program package was implemented to determine the probable space group and set up the initial files. System symmetry, systematic absences, and intensity statistics indicated the centrosymmetric monoclinic space group C2/c (no.15). The structure was determined by direct methods with the successful location of nearly all of the non-hydrogen atoms using the program XS[5]. The structure was refined with XL[5]. The 60727 data collected were merged based upon identical indices to 36520 data [R(int)=0.0157], then truncated to $2\theta_{max}$=55.00°, yielding 24881 reflections and then merged for least squares refinement to 6467 unique data [R(int)=0.0142]. A single least-squares difference-Fourier cycle was required to locate the remaining non-hydrogen atoms. Hydrogen atoms were initially idealized and then allowed to refine freely throughout the final refinement stages. The final structure was refined to convergence with R(F)=3.28%, wR(F^2)=8.32%, GOF=1.052 for all 6467 unique reflections [R(F)=3.00%, wR(F^2)=8.15% for those 5941 data with Fo > 4σ(Fo)]. The final difference-Fourier map was featureless indicating that the structure is both correct and complete. An

empirical correction for extinction was also attempted but found to be one sigma and therefore not applied.

References:

1. Bruker (2010) APEX (Version 2010-1) and SAINT (Version 7.68a). Bruker AXS Inc., Madison, Wisconsin, USA.

2. An Empirical Correction for Absorption Anisotropy, Blessing, R. H. (1995). Acta Cryst., A51, 33-38.

3. Sheldrick, G.M., SADABS (2008) Version 2008/2, 'Siemens Area Detector Absorption Correction' Universität Göttingen: Göttingen, Germany.

4. Sheldrick, G.M., (2002). SHELXTL. Version 6.1. Bruker AXS Inc., Madison, Wisconsin, USA.

5. Sheldrick, G. M., (1997). SHELXS97 and SHELXL97. Universität Göttingen: Göttingen, Germany.

Acknowledgment: We thank the National Science Foundation (Grant 0840444) for the Dual source X-ray diffractometer.

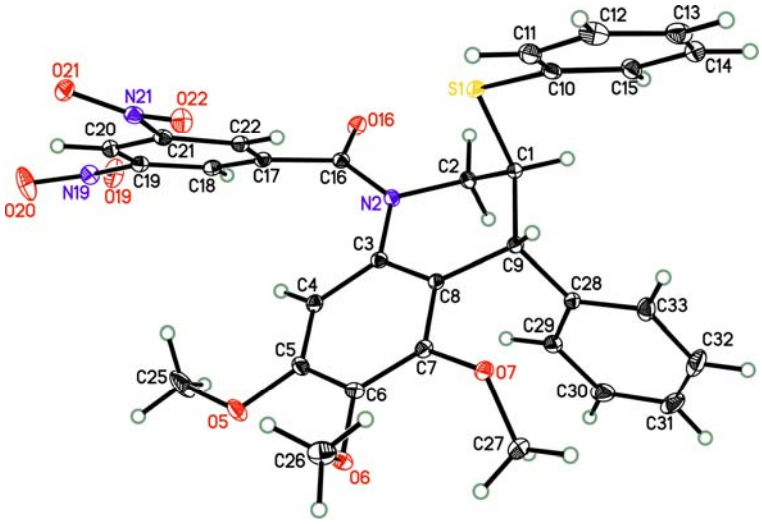
29 March, 2012

JF2117

A faint yellow plate with approximate orthogonal dimensions 0.31 x 0.25 x 0.09mm^3 was placed and optically centered on the Bruker Duo APEXII[1] CCD diffractometer at –183°C. All of the crystals exhibited the same behavior and appeared twinned. The initial unit cell was indexed using a least-squares analysis of a random set of reflections collected from three series of 0.3° wide ω-scans, 10 seconds per frame, and 30 frames per series that were well distributed in reciprocal space. Five ω-scan data frame series were collected [MoKα] with 0.3° wide scans, 25 seconds per frame and 606, 483, 606, 483, 606 frames collected per series at varying φ angles (φ=0°, 72°, 144°, 216°, 288°), respectively. The crystal to detector distance was 4.96cm, thus providing a complete sphere of data to $2\theta_{max}$=55.37°.

Structural determination and Refinement:

All crystallographic calculations were performed on an iMac with an Intel Core i7 2.80GHz processor and 8GB of extended memory at 1067MHz DDR3. Data collected were corrected for Lorentz and polarization effects with Saint[1] and absorption using Blessing's method and merged as incorporated with the program Sadabs[2,3]. The SHELXTL[4] program package was now implemented to determine based upon intensity statistics, the centrosymmetric triclinic space group P-1 (no. 2). The structure was determined by direct methods with a majority of the non-hydrogen atoms being located directly using the program XS[5]. Refinement of the structure was achieved using the program XL[5]. Difference-Fourier refinement cycles were required to locate the remaining non-hydrogen atoms. Refinement converged to approximately R_F=17.0% for all data. It was evident from the outset that the structure possessed more than a single domain when examining the individual frames and the data were additionally quite weak so reflections were thresholded in APEX[1] and these reflections were input into Cellnow[6] that determined the twin relationship between the two components and generated the orientation matrices for the components and output a useable multiple matrice input file for the integration program SAINT[1]. Saint was run three times using the output optimized merged matrix file from the previous run. Data collected were now corrected for absorption using TWINABS[2,7] and Blessing's method and merged generating both HKLF4 and HKLF5 files. Convergence of the structure proceeded quickly using both the HKLF5 and HKLF4 files. All of the non-hydrogen atoms were refined anisotropically with



Acknowledgment: We thank the National Science Foundation (Grant 0840444) for the Dual source X-ray diffractometer.

the two domains being present as follows: major:minor component 74:26. Since the HKLF4 format file yielded nearly identical results compared with the HKLF5 file, it was chosen for structure completion. All of the hydrogen atoms were idealized throughout the final convergence cycles. The final structure was refined to convergence with R(F)=5.19%, wR(F^2)=9.69%, GOF=1.022 for all 12572 reflections [R(F)=3.93%, wR(F^2)=9.19% for those 10453 data with Fo > 4σ(Fo)]. A final difference-Fourier map was featureless indicating that the structure is therefore both correct and complete.

References:

1. Bruker (2010) SMART APEX (2010.9-1) and (2009) SAINT (Version 7.68a). Bruker AXS Inc., Madison, Wisconsin, USA.

2. An Empirical Correction for Absorption Anisotropy, Blessing, R. H. (1995). Acta Cryst., A51, 33-38.

3. Sheldrick, G.M., SADABS (2008/1), 'Siemens Area Detector Absorption Correction' Universität Göttingen: Göttingen, Germany.

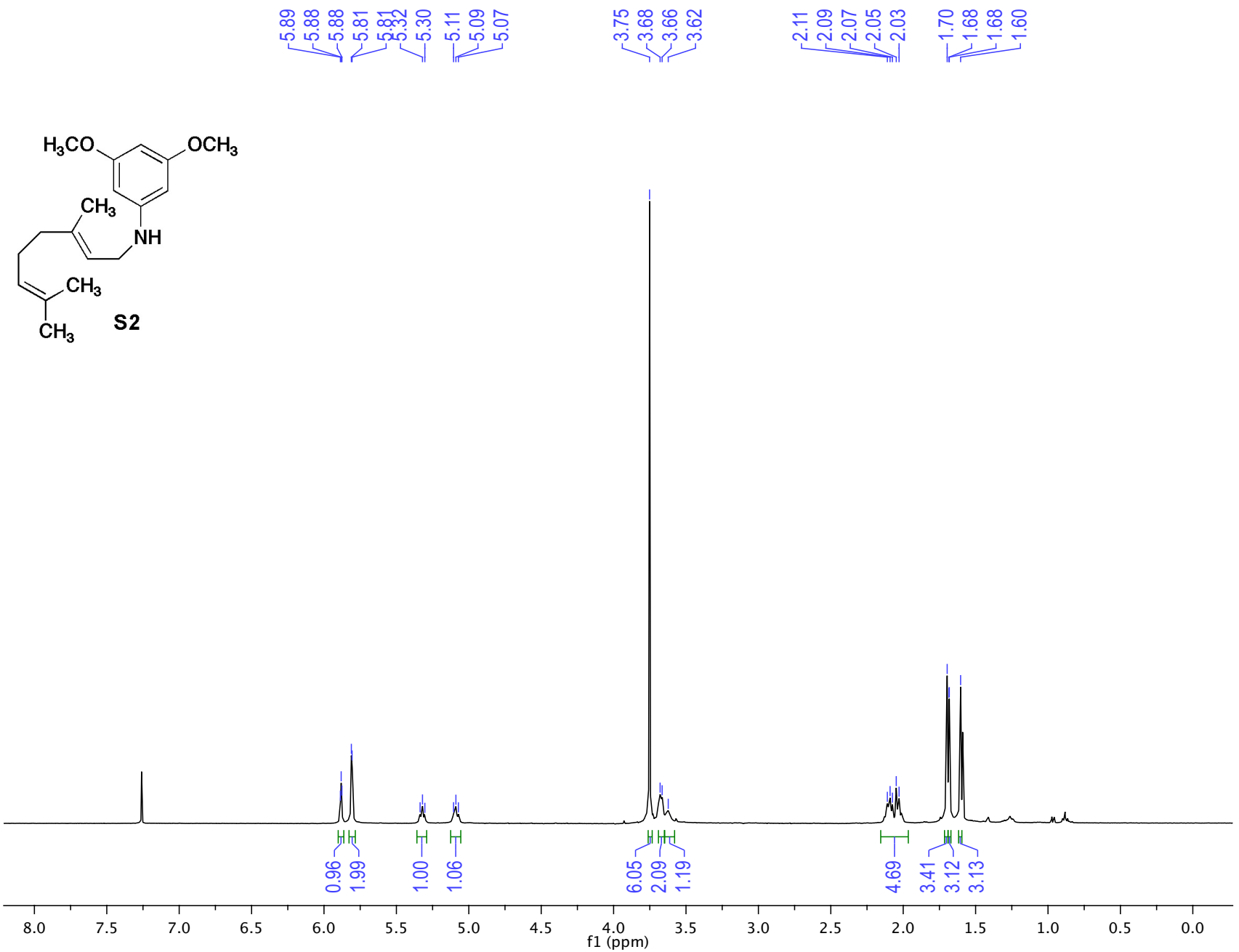
4. Sheldrick, G.M., (2002). SHELXTL. Version 6.1. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

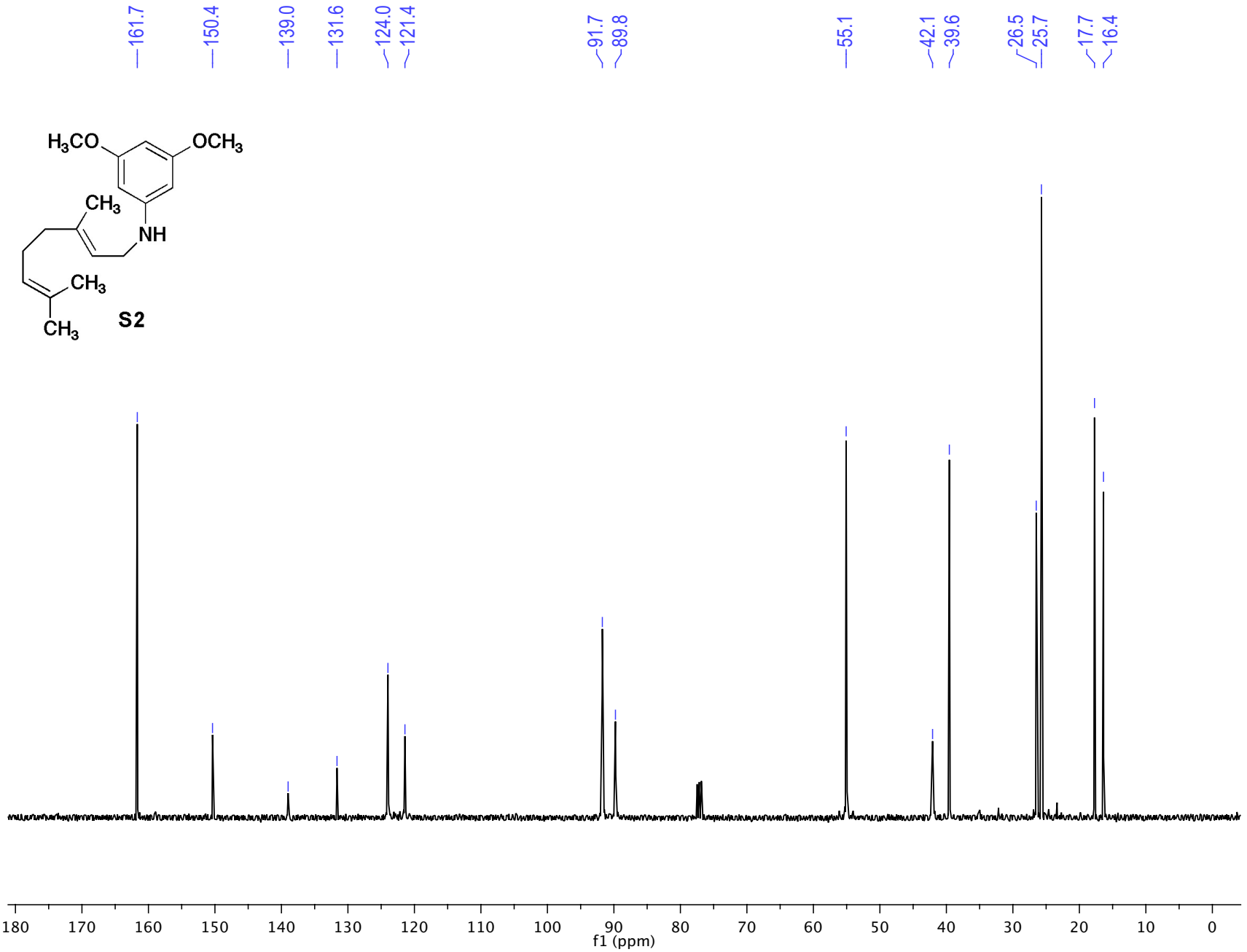
5. Sheldrick, G. M., (1997). SHELXS97 and SHELXL97. Universität Göttingen: Göttingen, Germany.

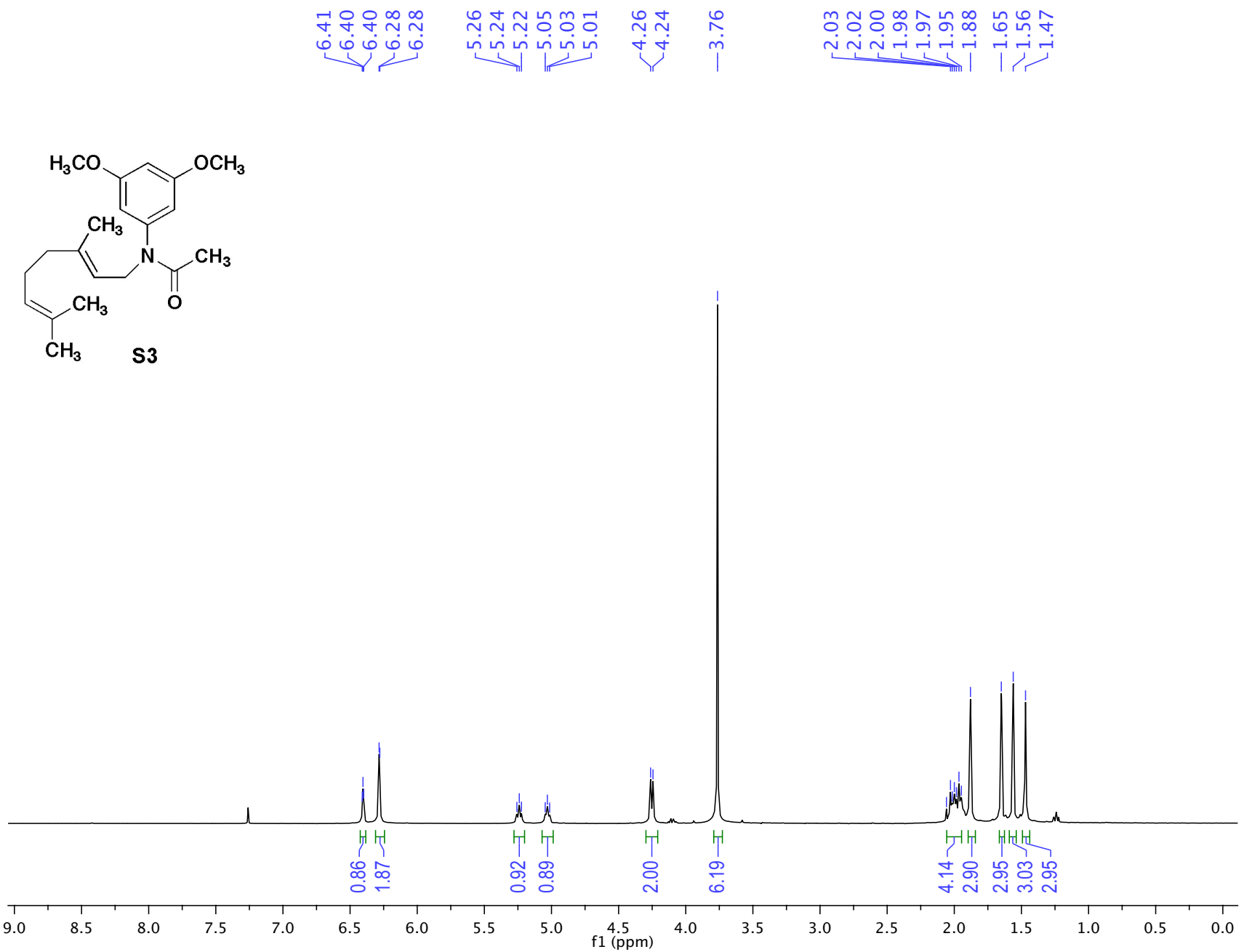
6. Sheldrick, G.M., CELLNOW, Twin matrix determination program, Universität Göttingen: Göttingen, Germany, Version 2008/3.

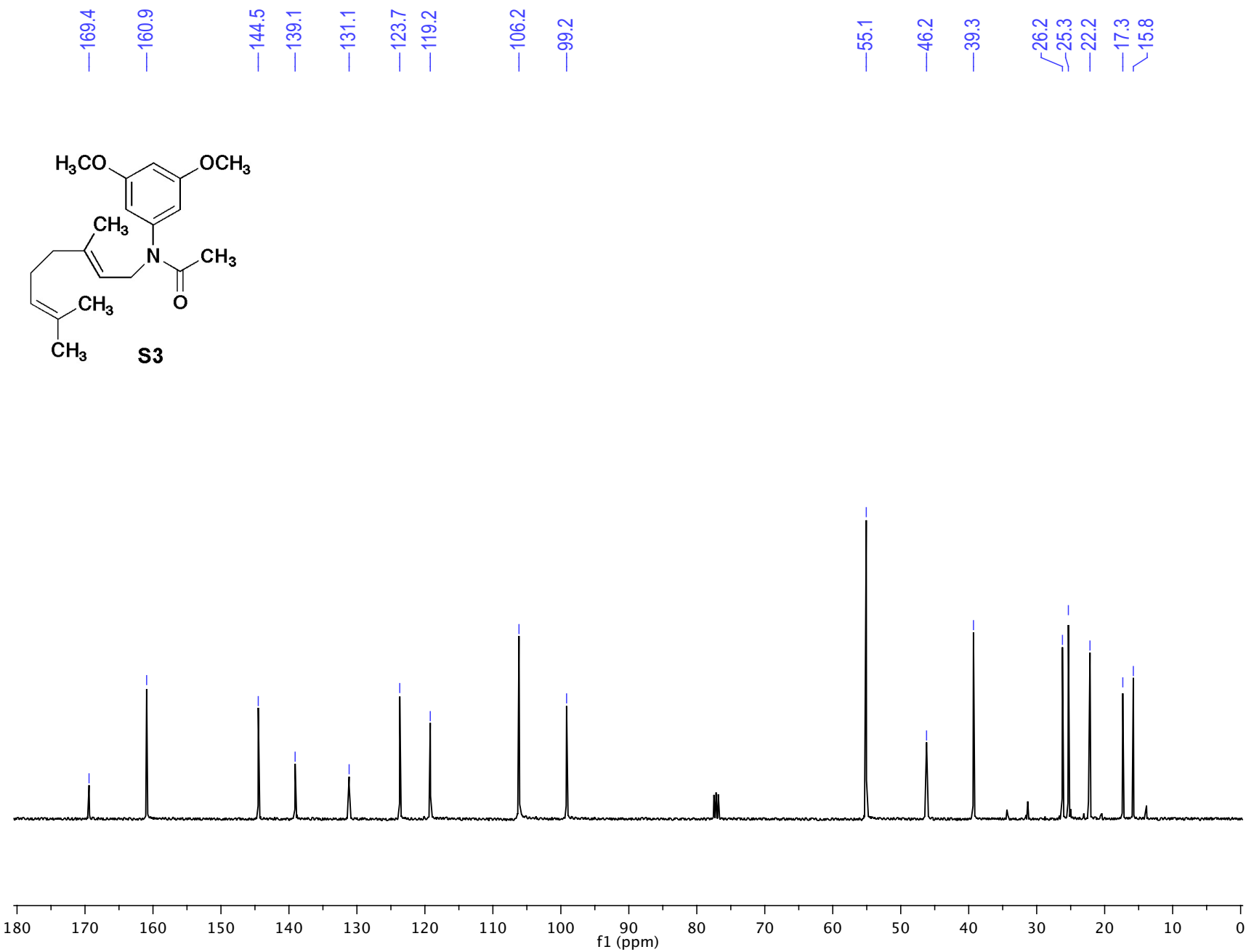
7. Sheldrick, G.M., TWINABS Version 2008/4 'An Empirical Correction for Absorption Anisotropy applied to Twinned crystals'. Universität Göttingen: Göttingen, Germany, 2003.

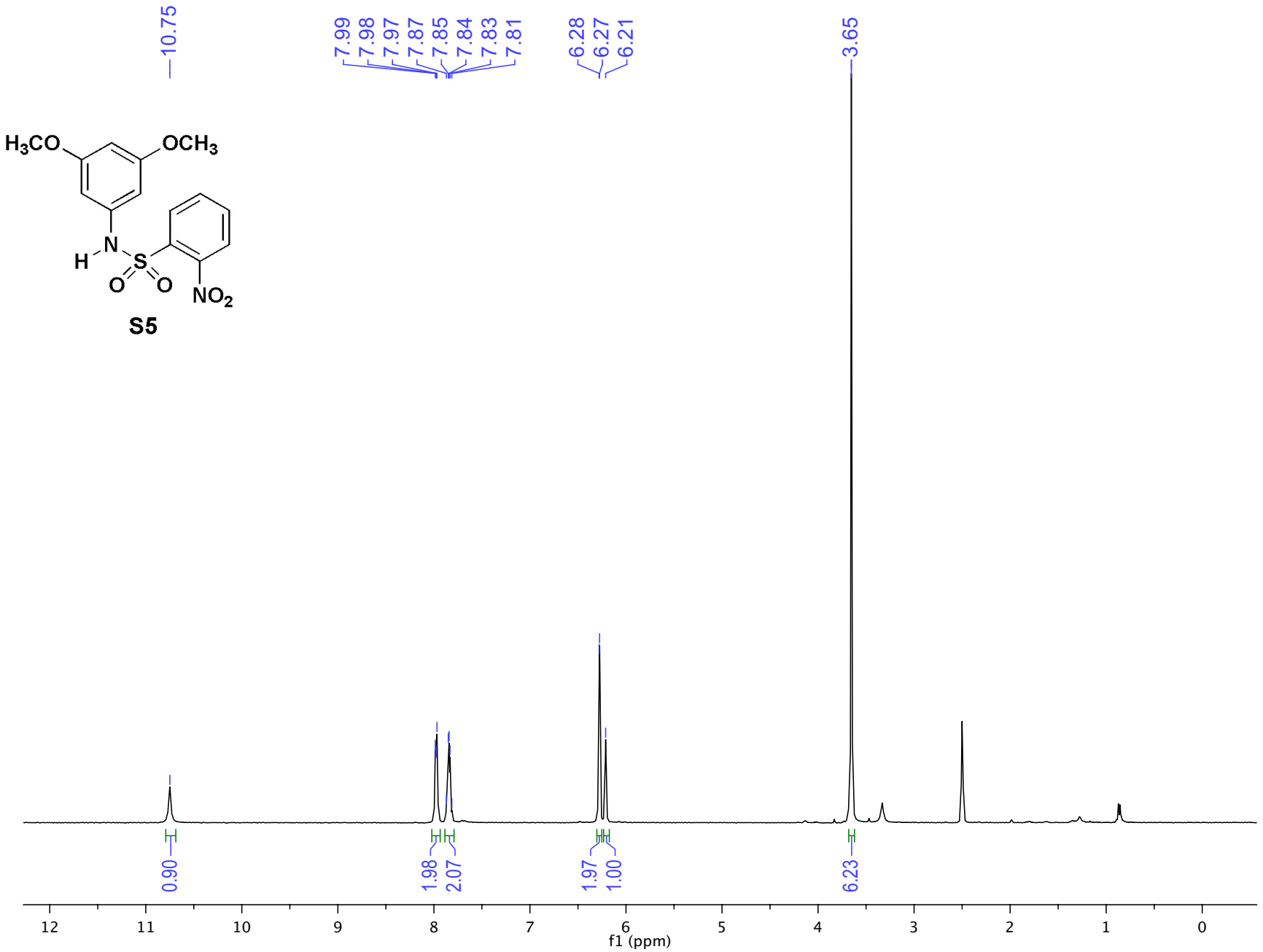
Acknowledgment: We thank the National Science Foundation (Grant 0840444) for the Dual source X-ray diffractometer.











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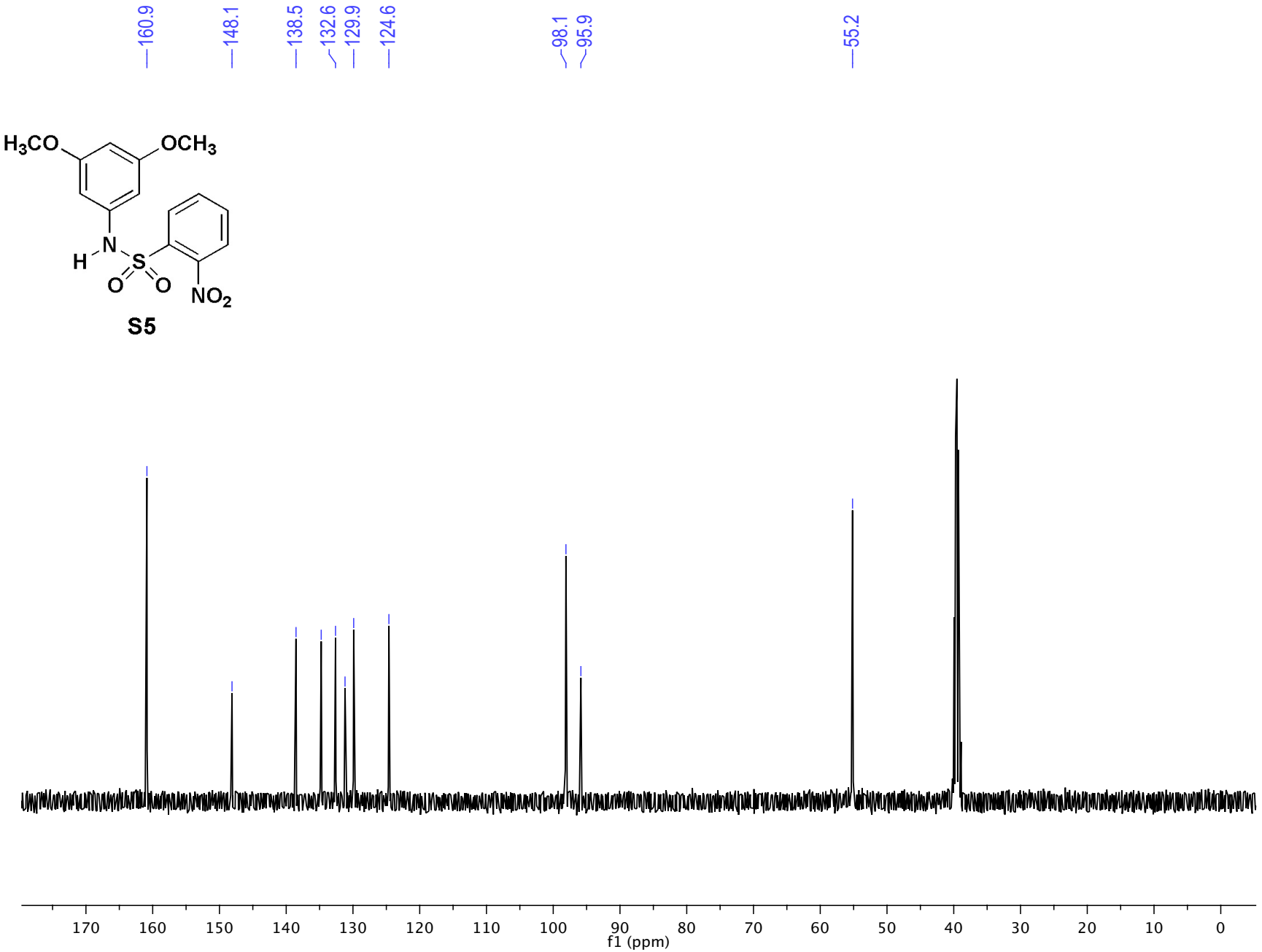

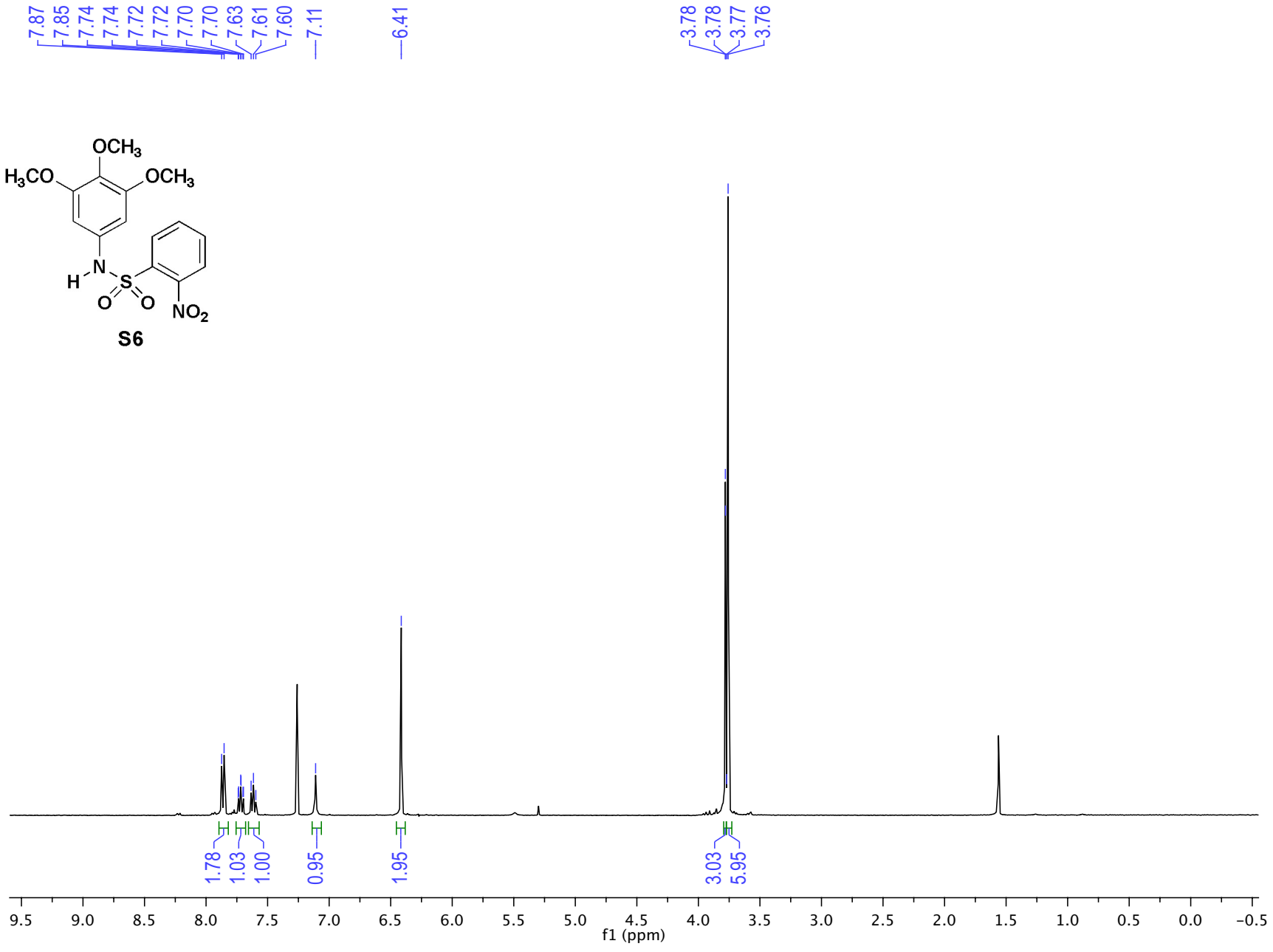

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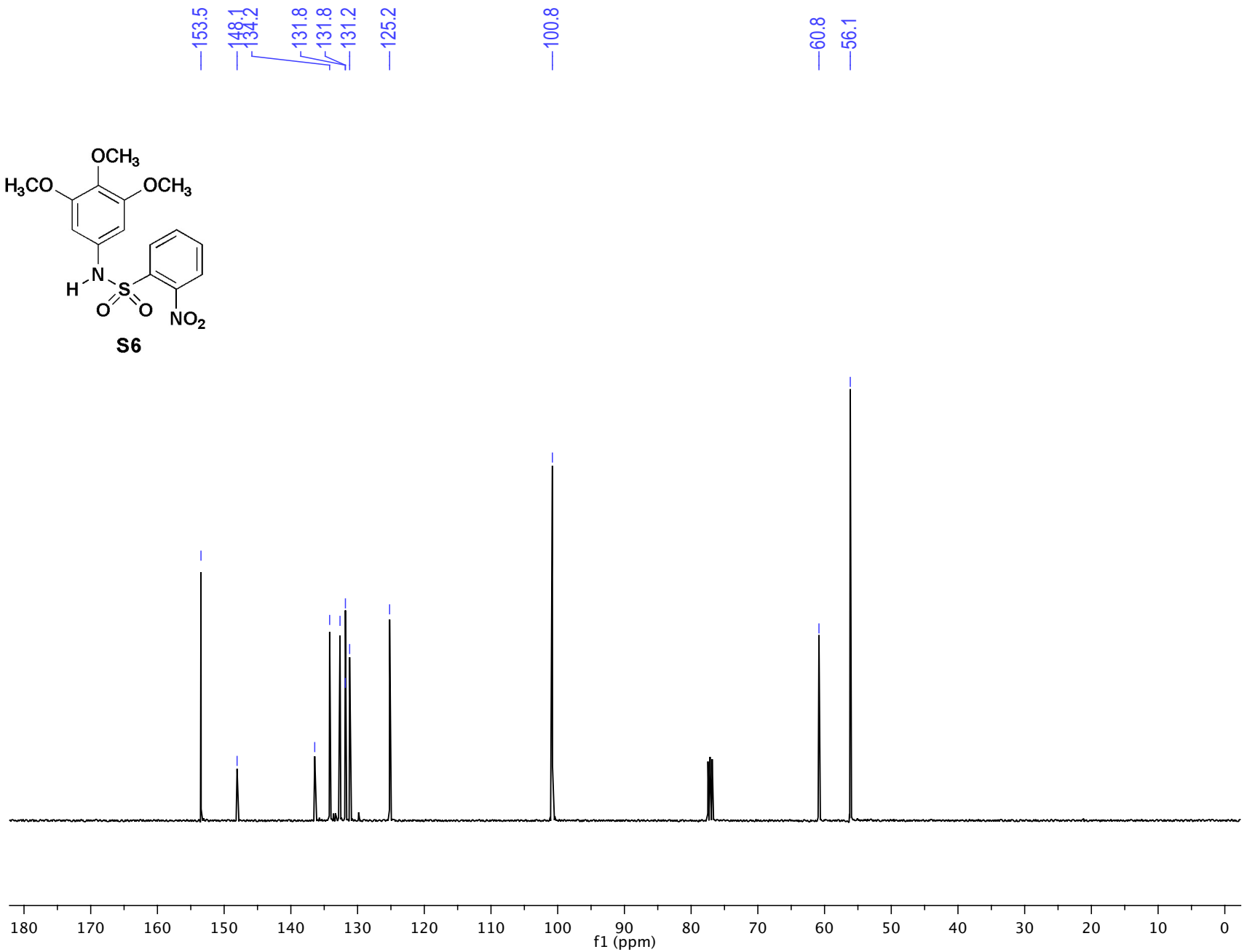

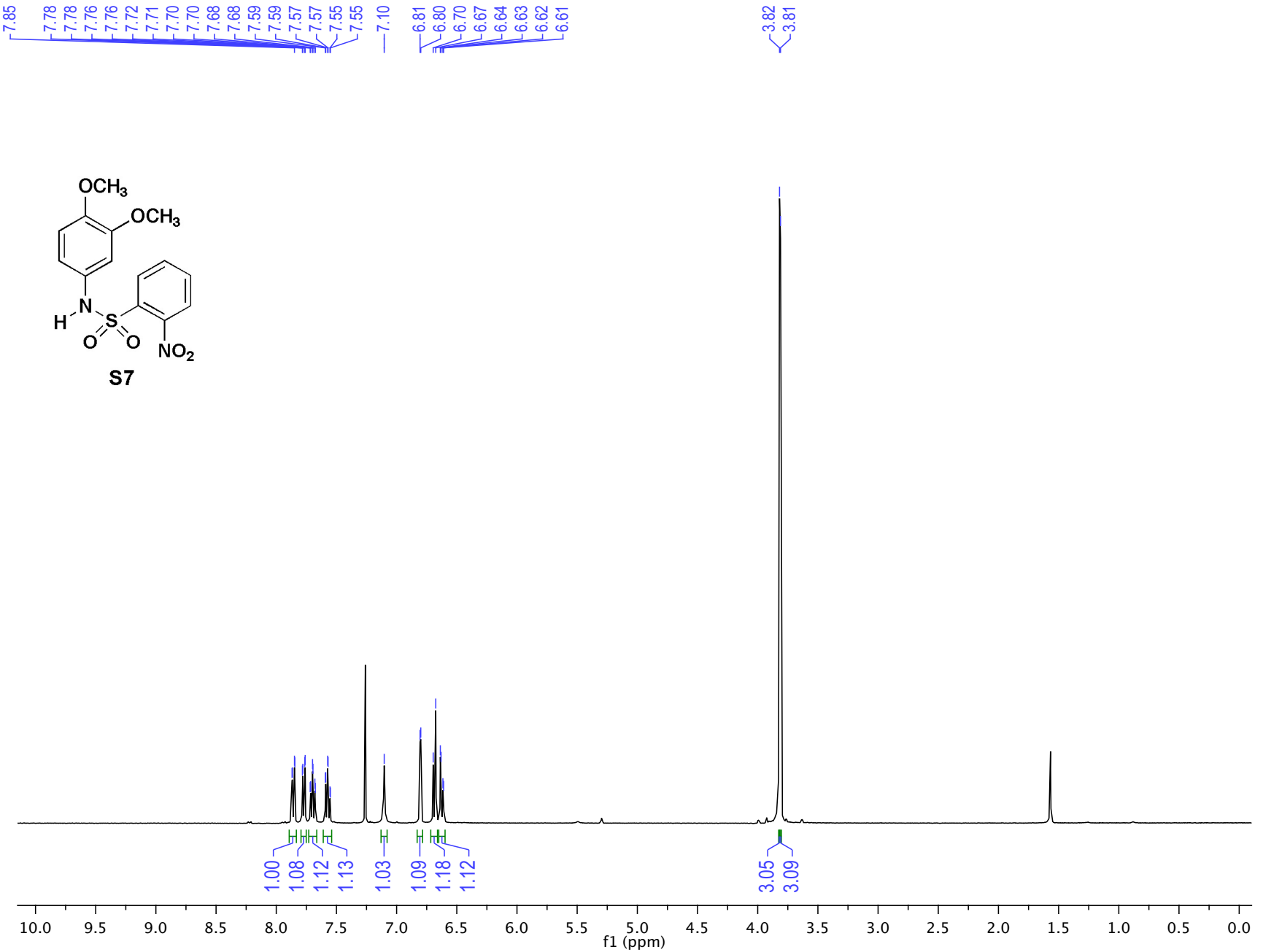

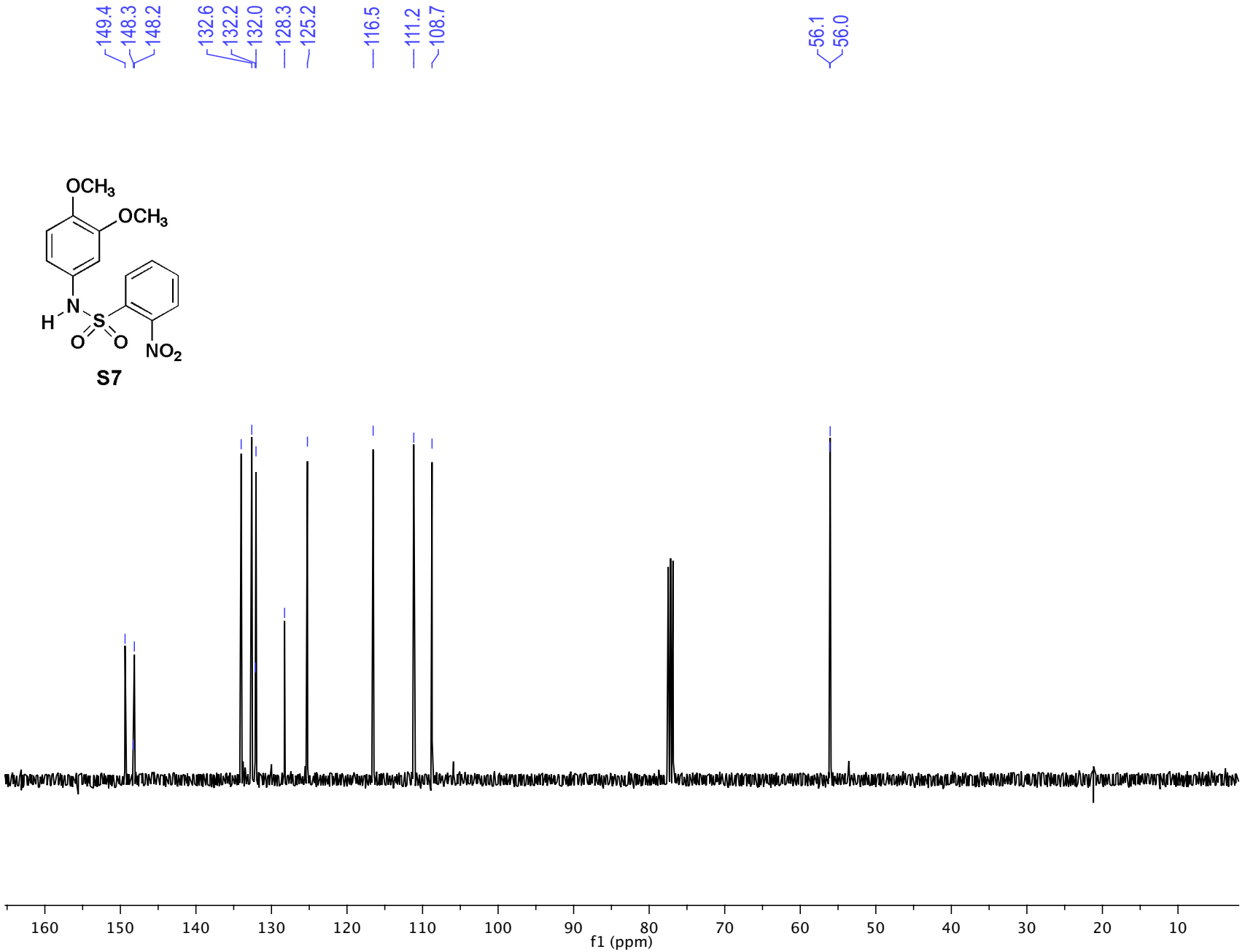

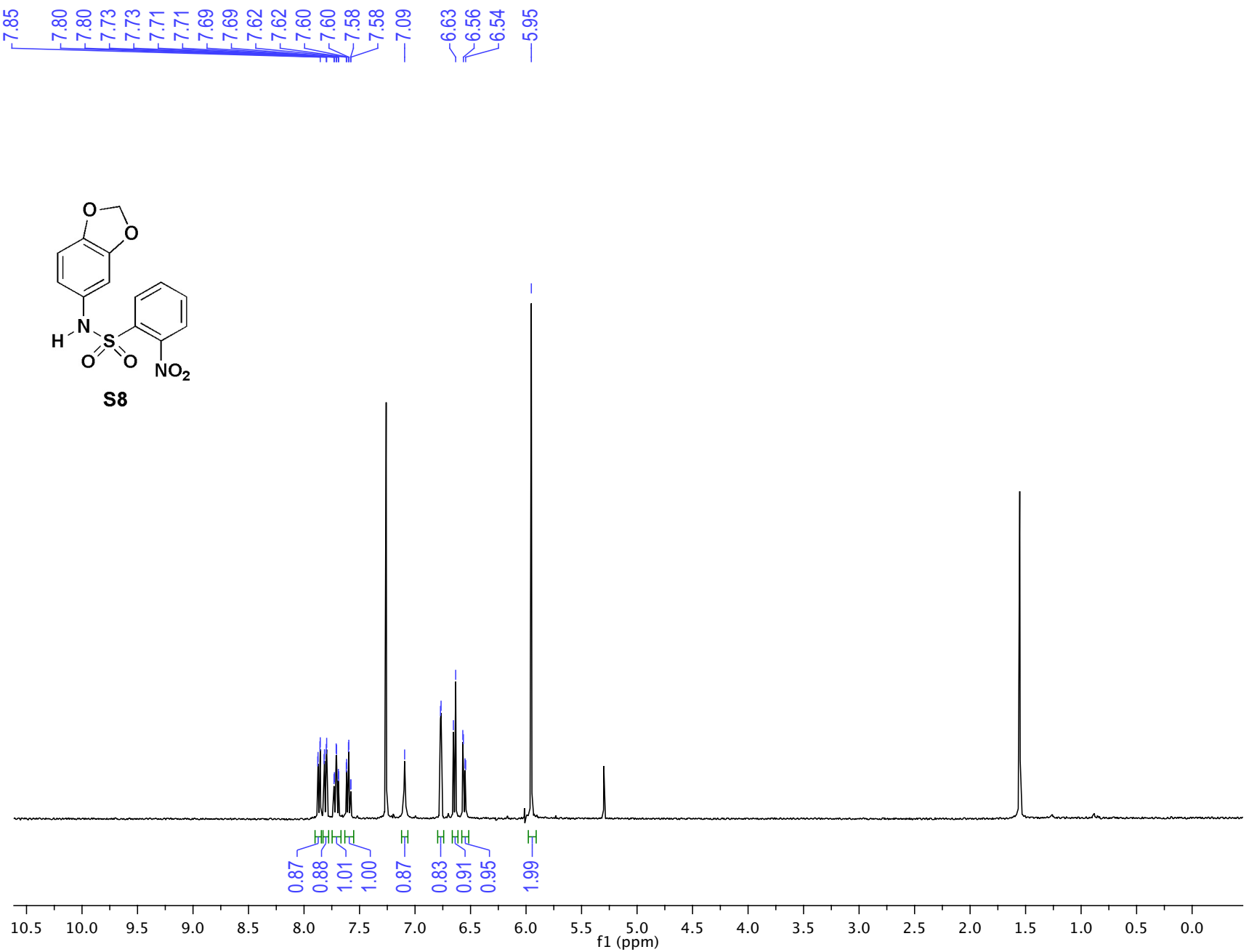

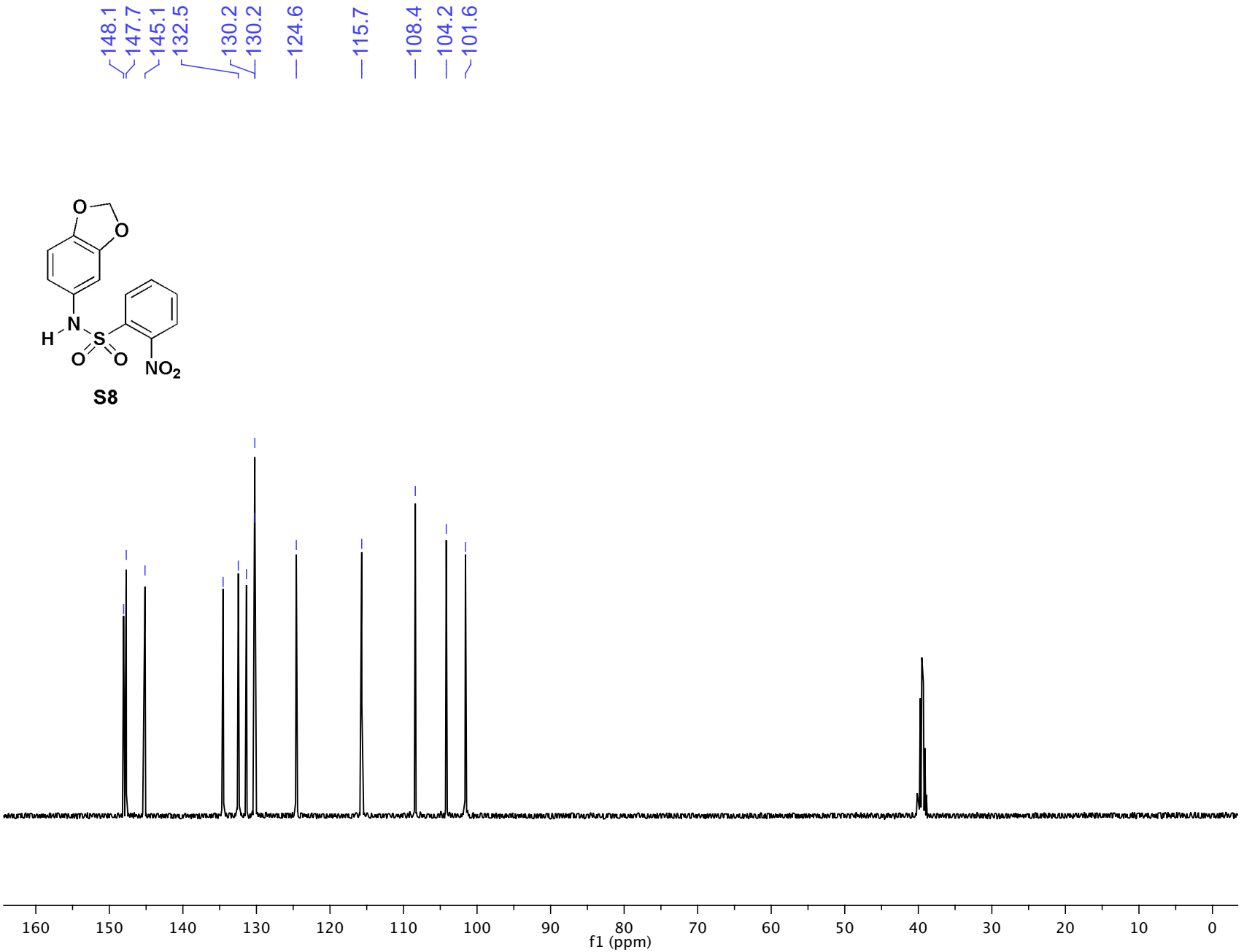

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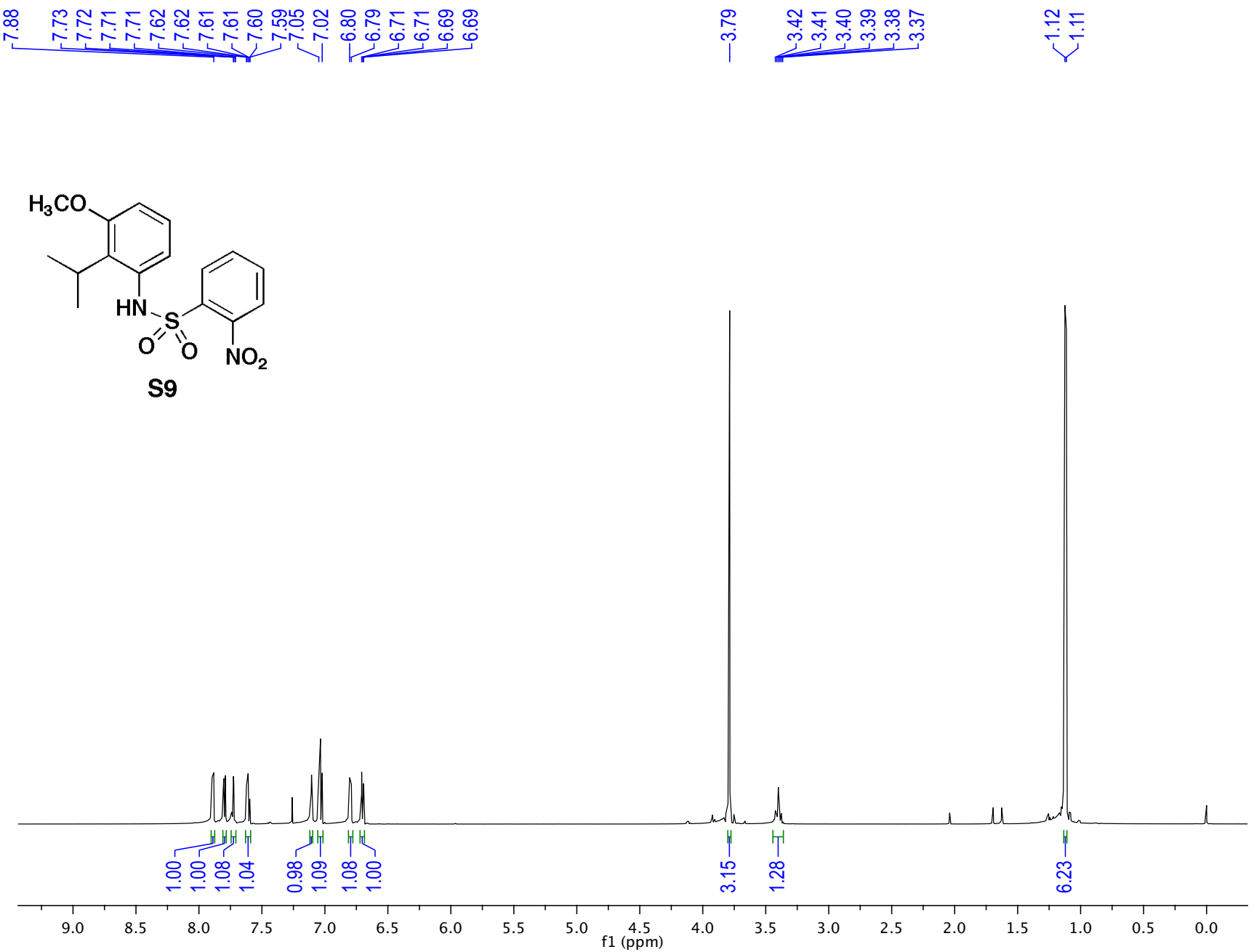

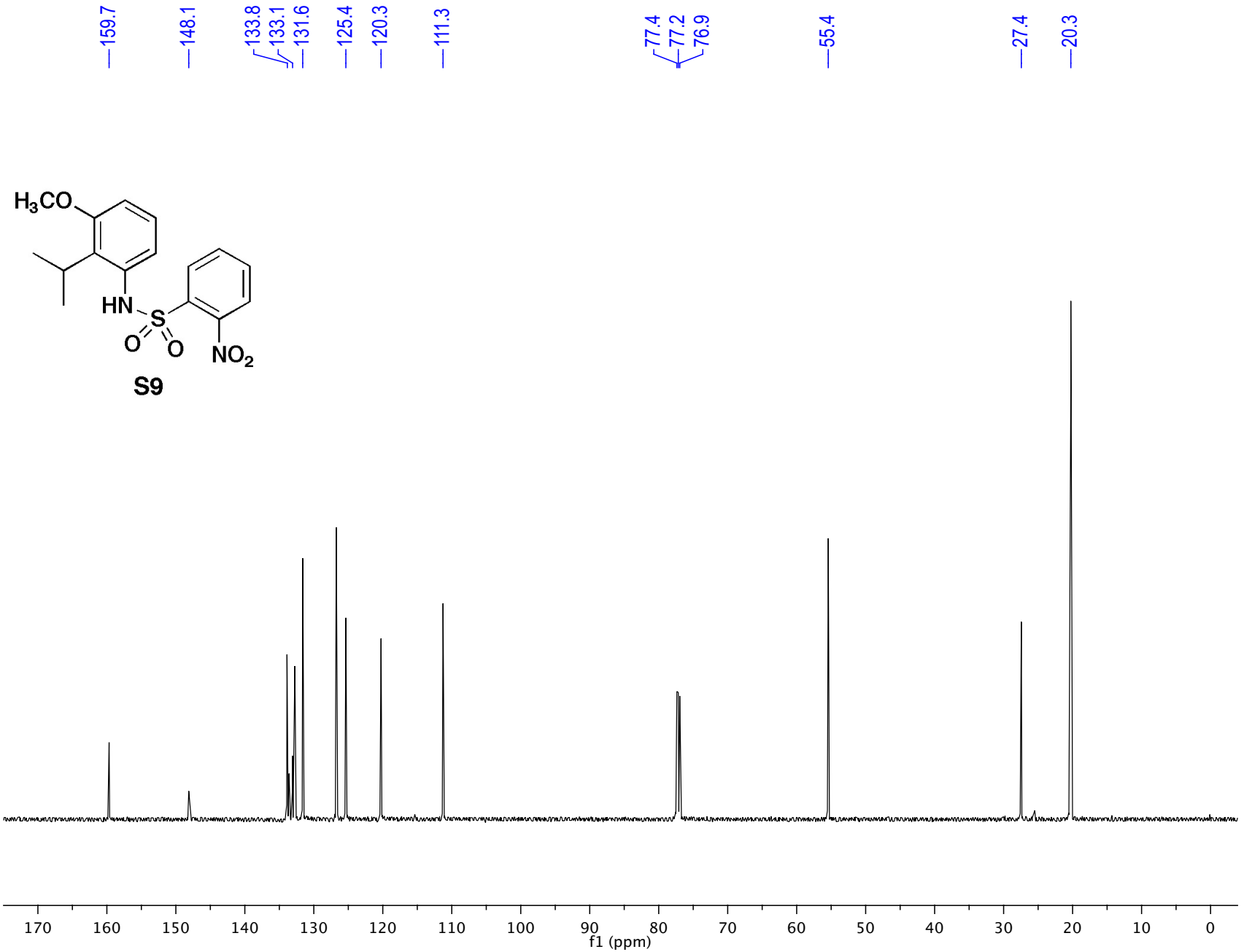

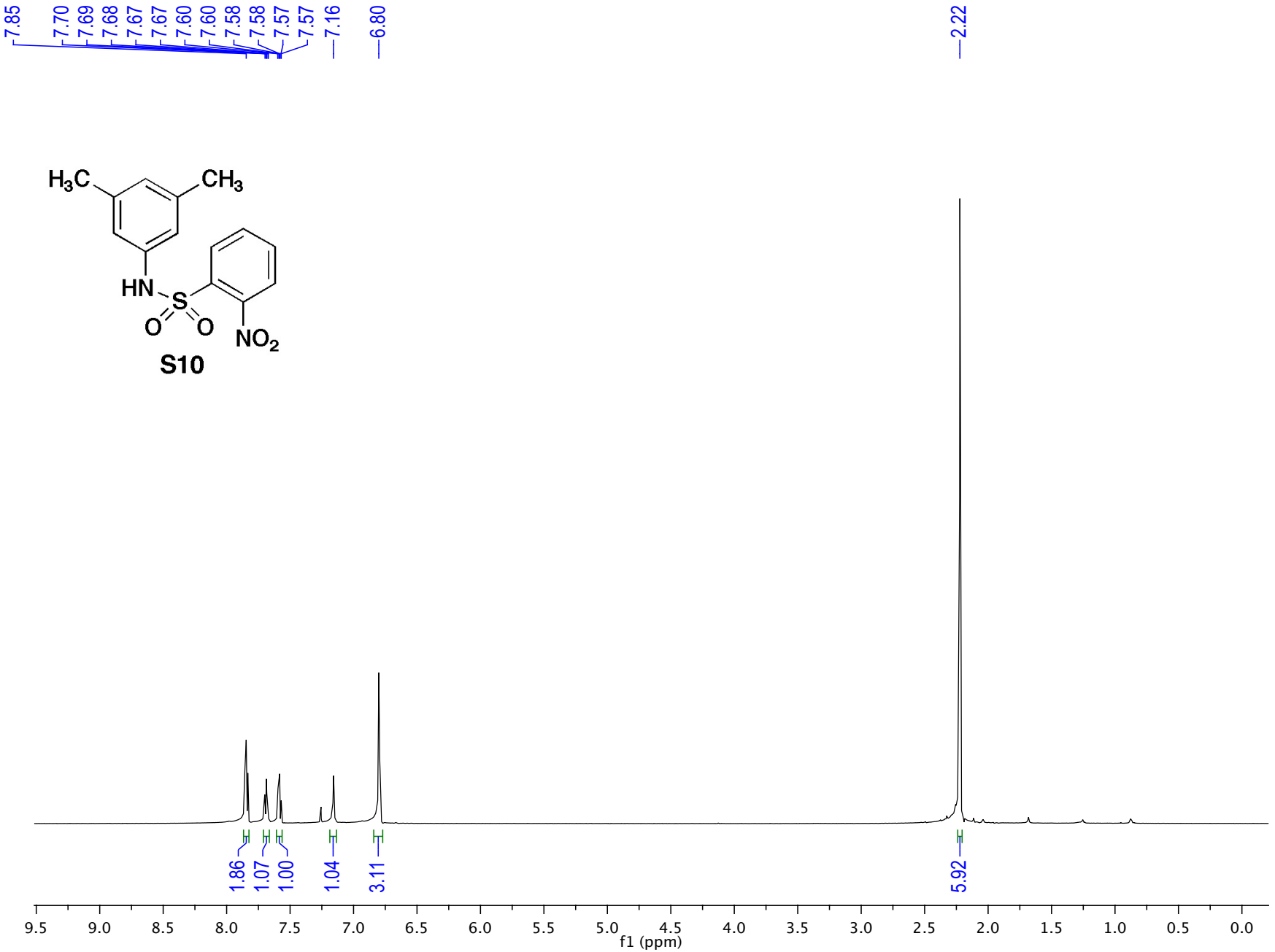

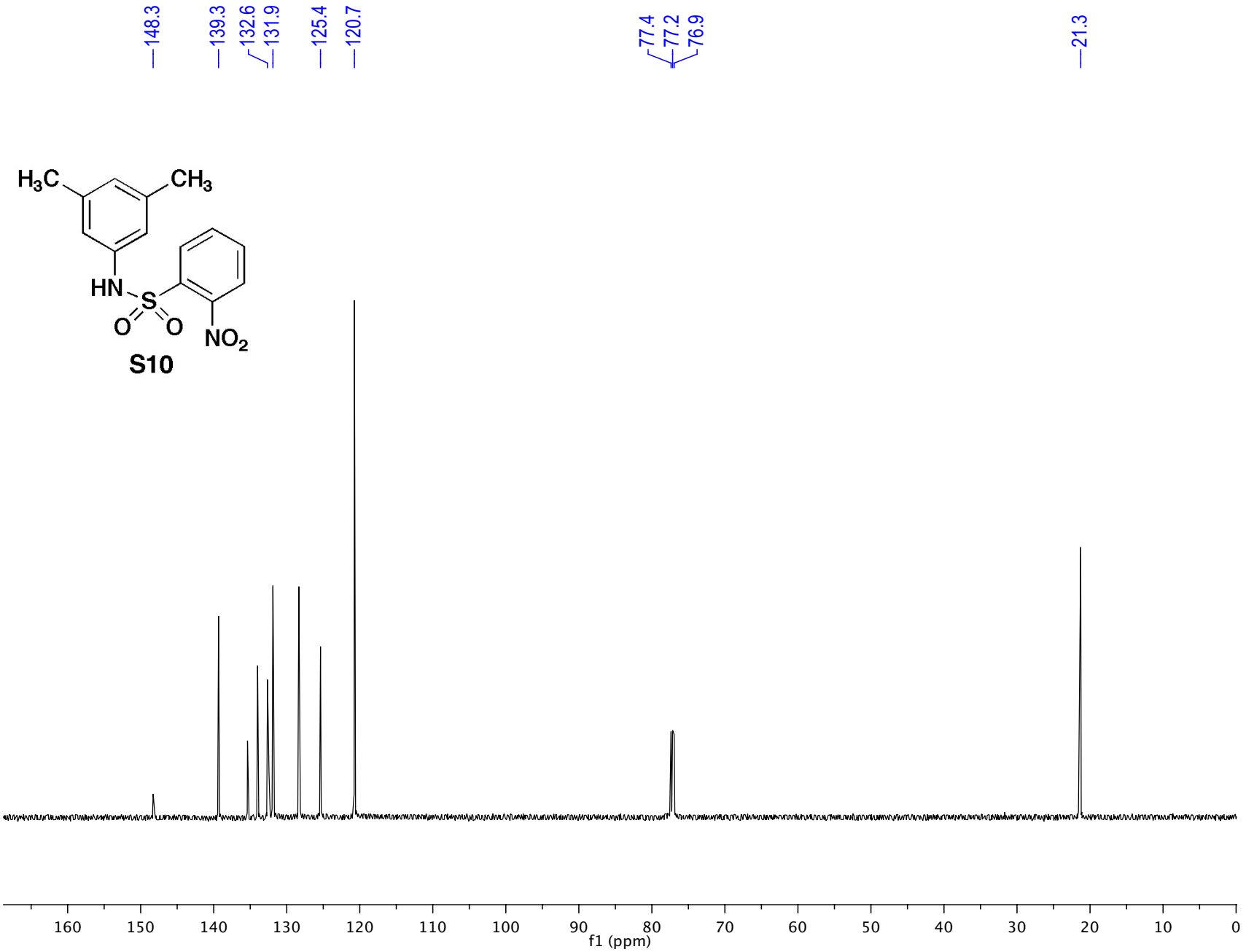

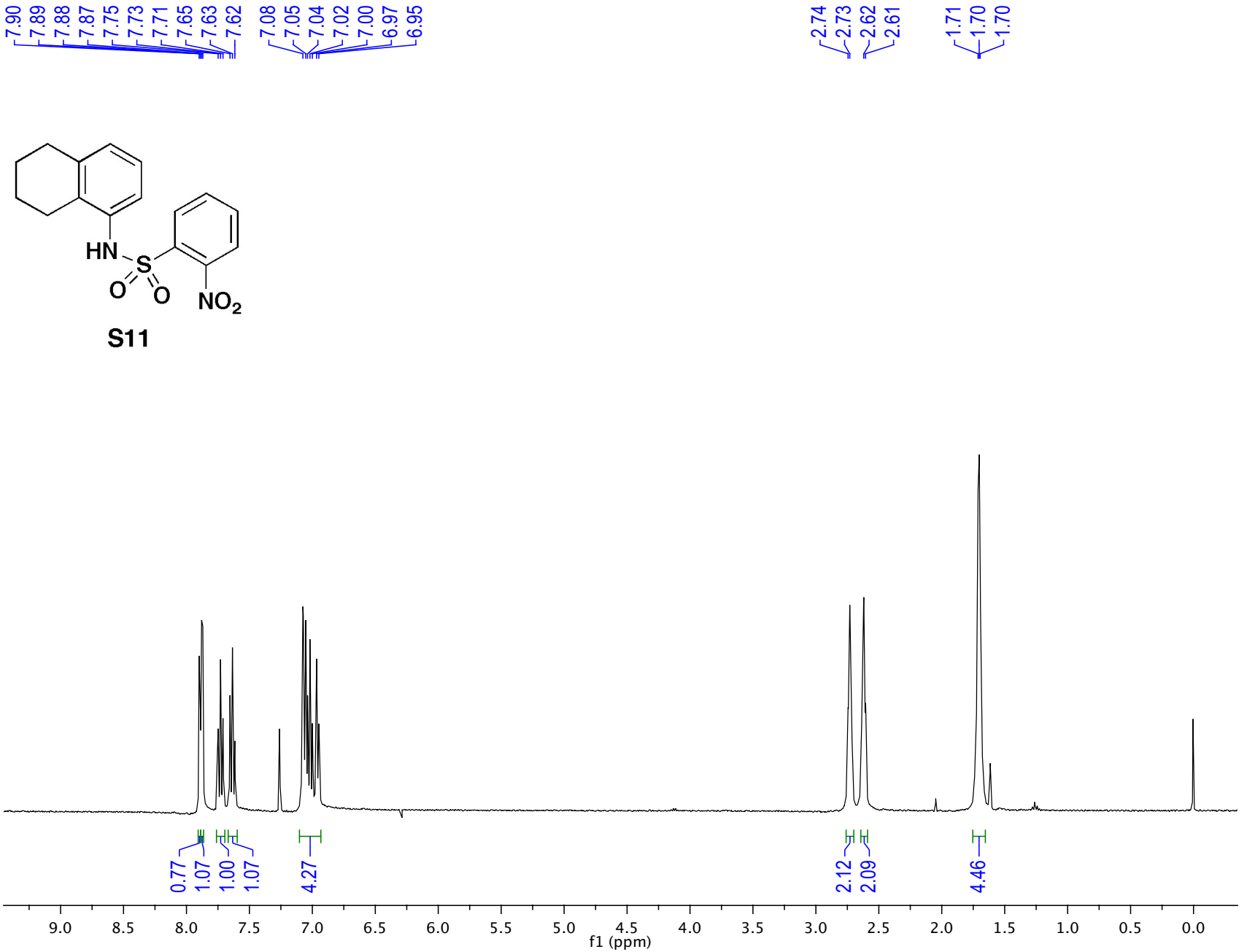

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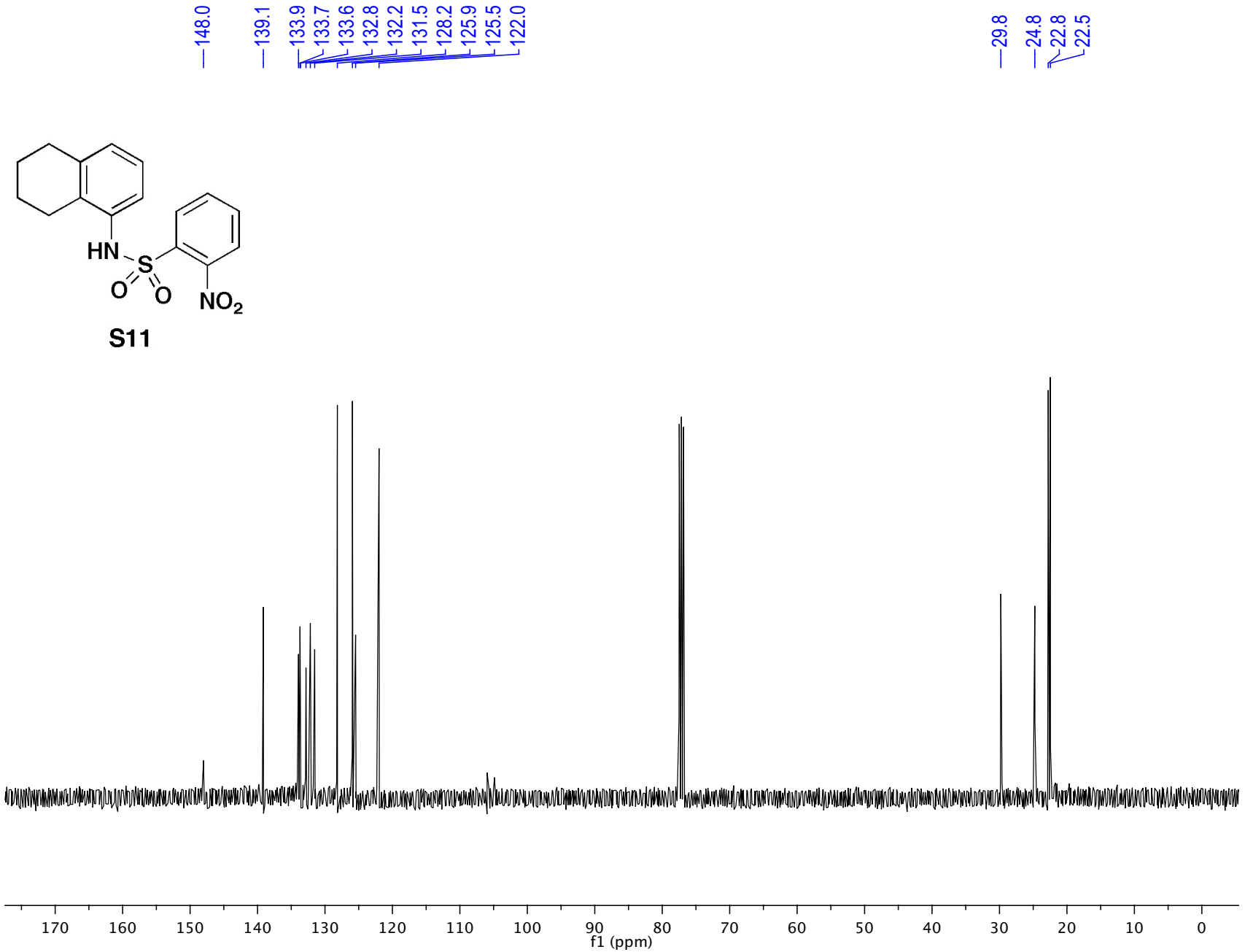

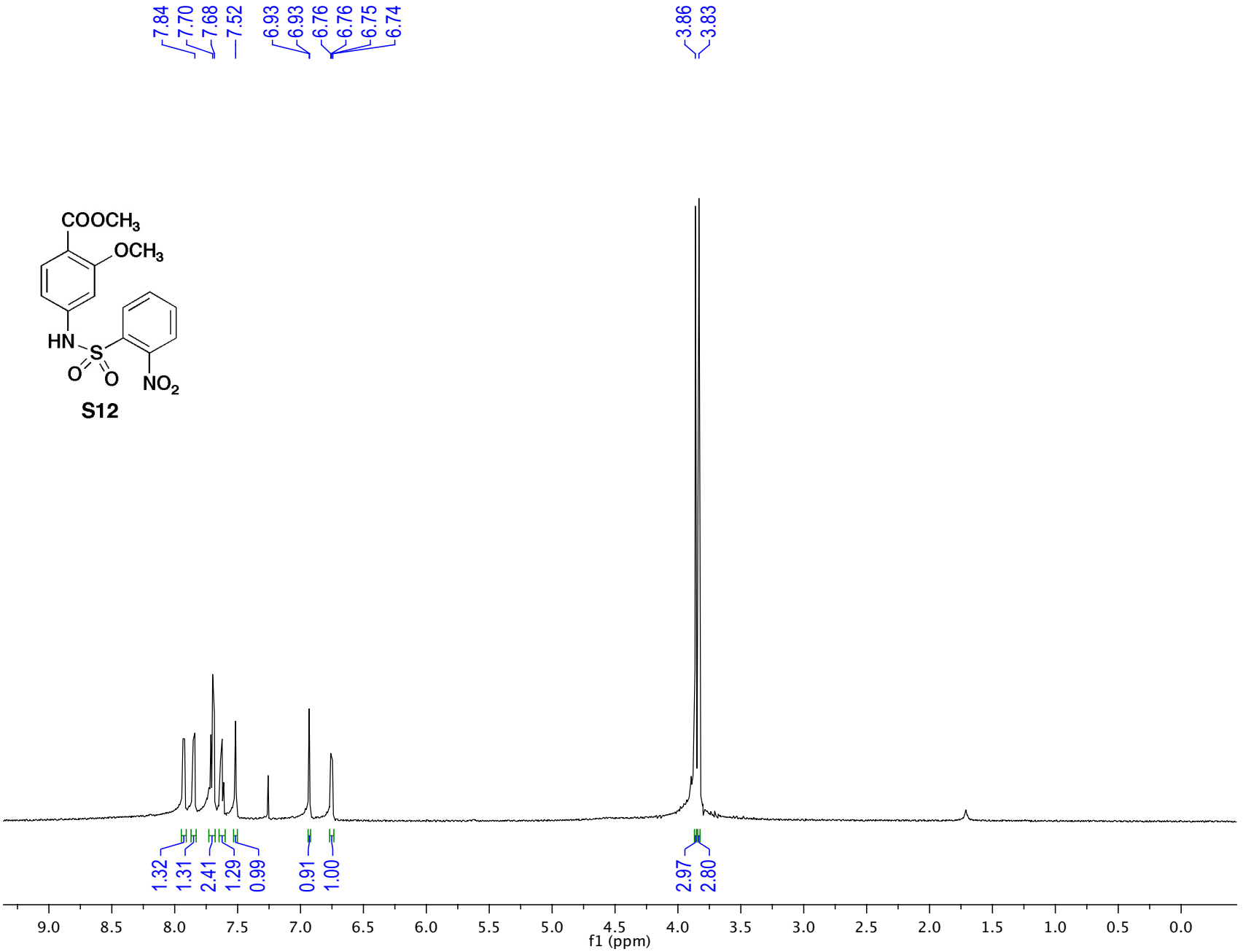

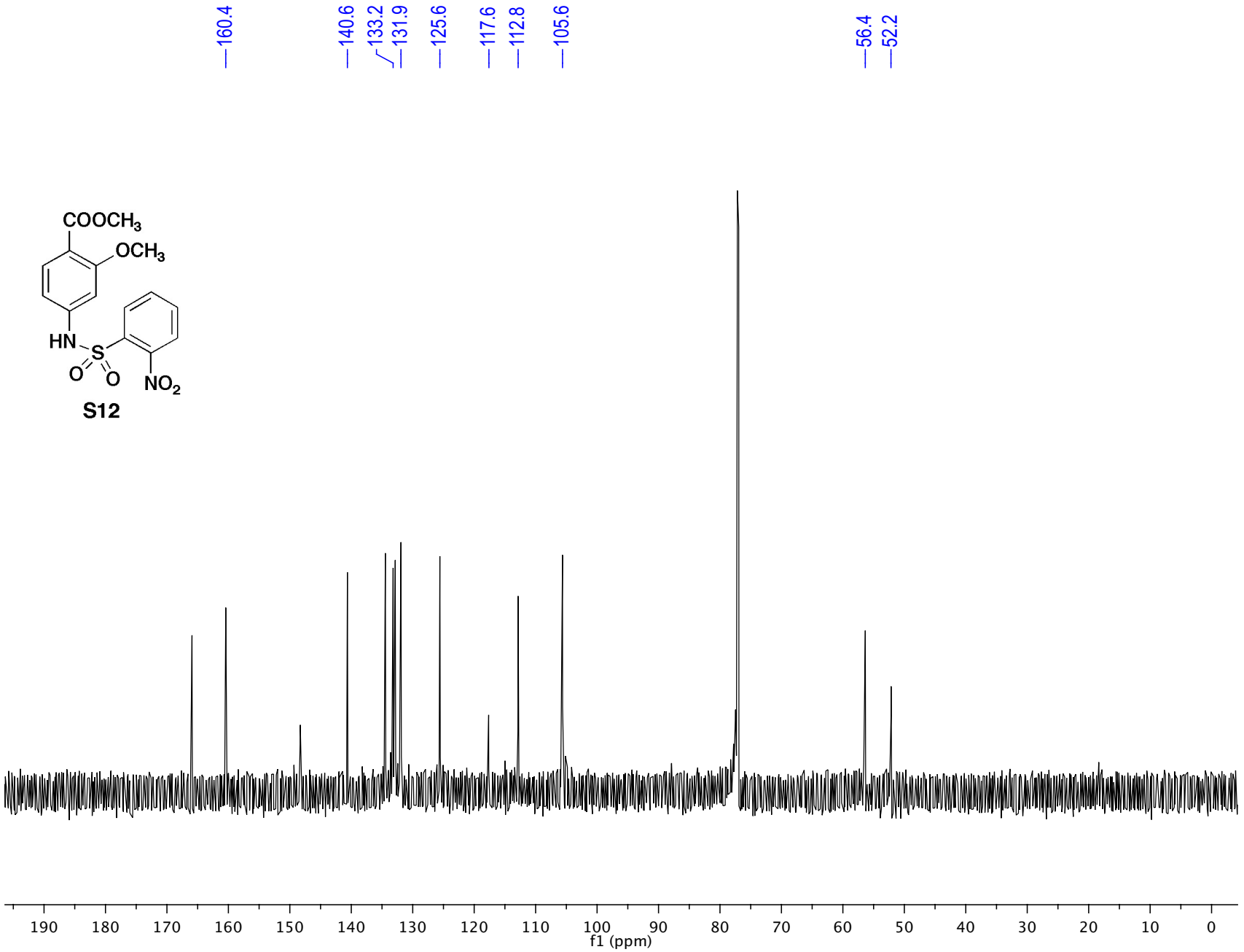

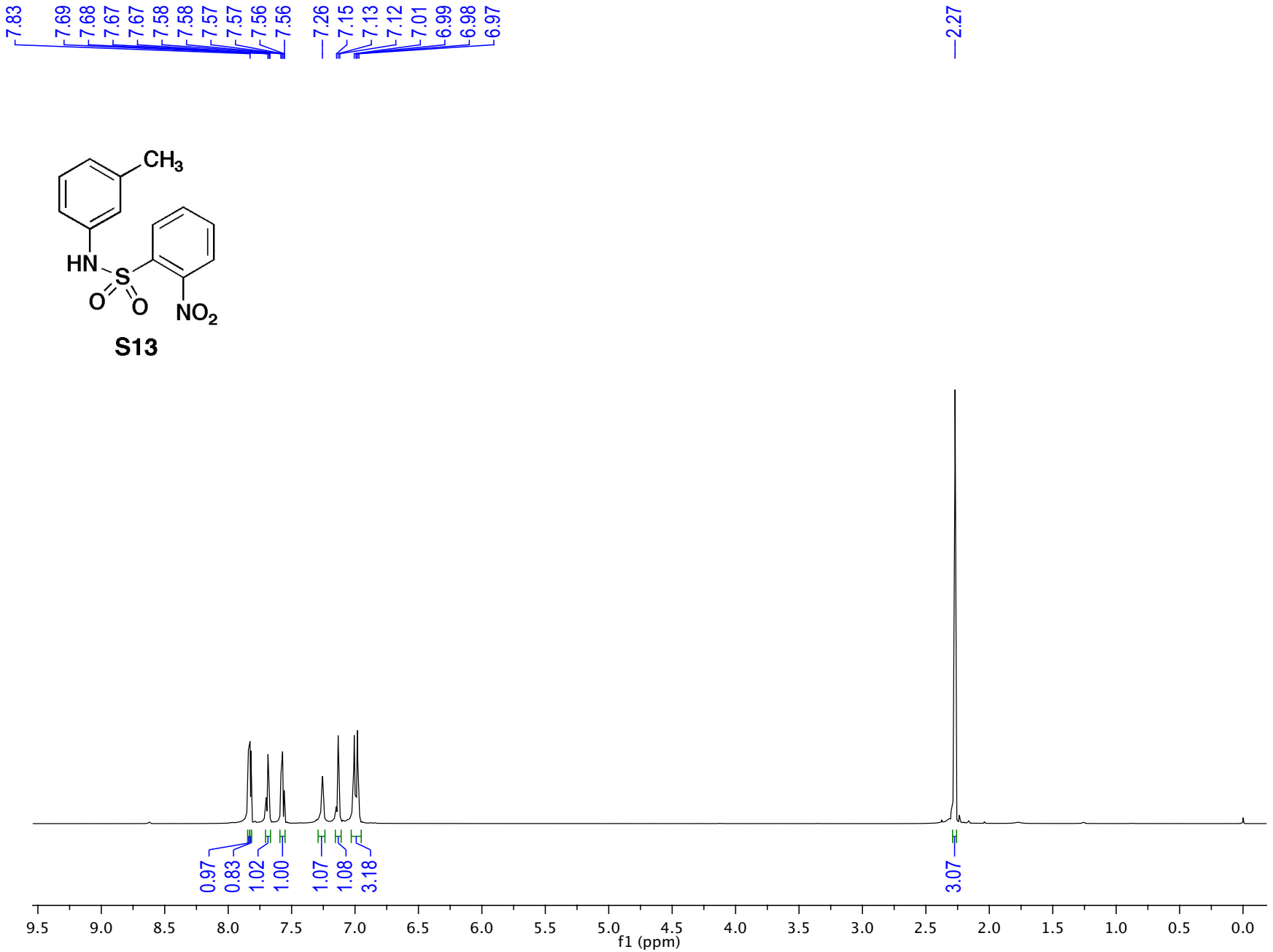

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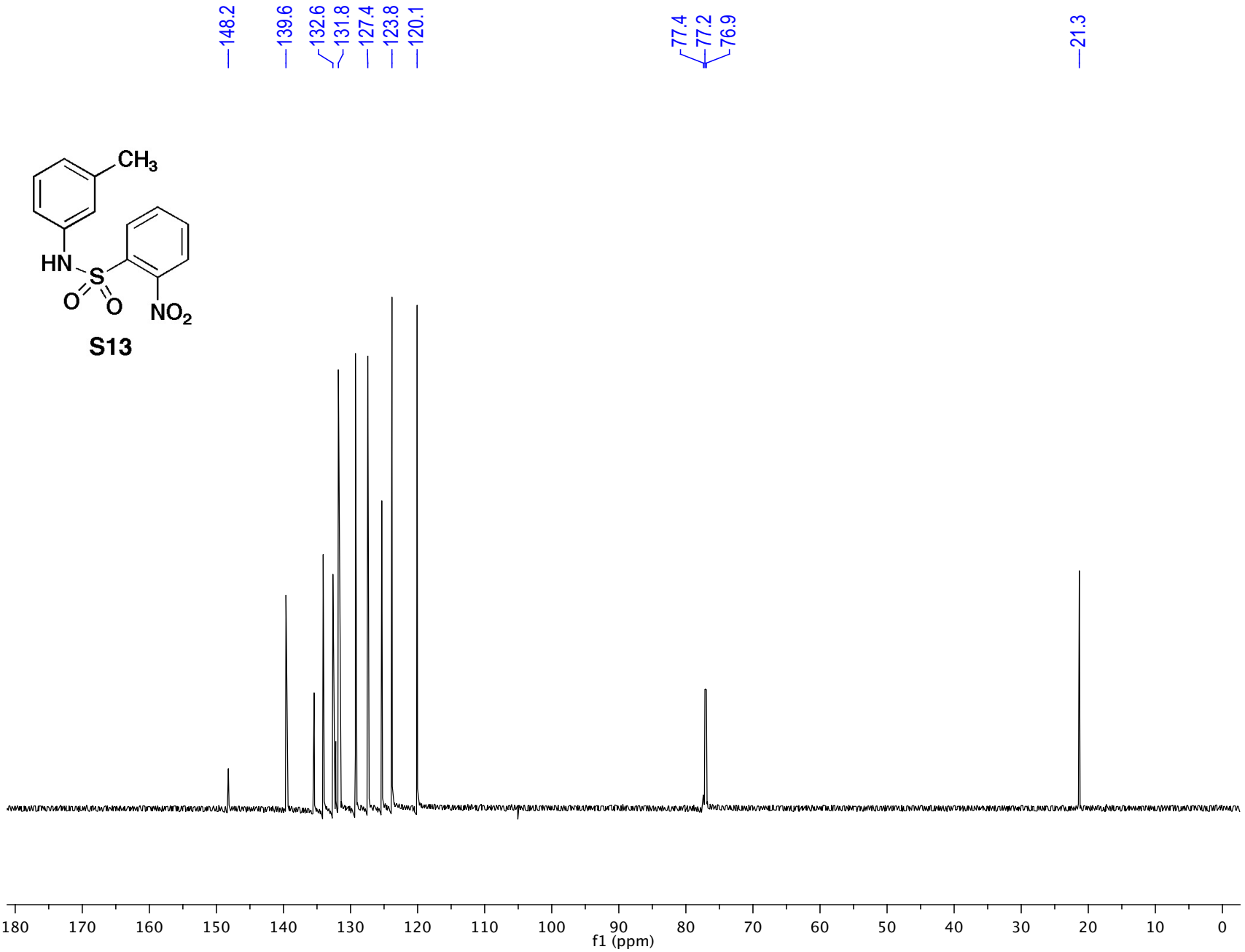

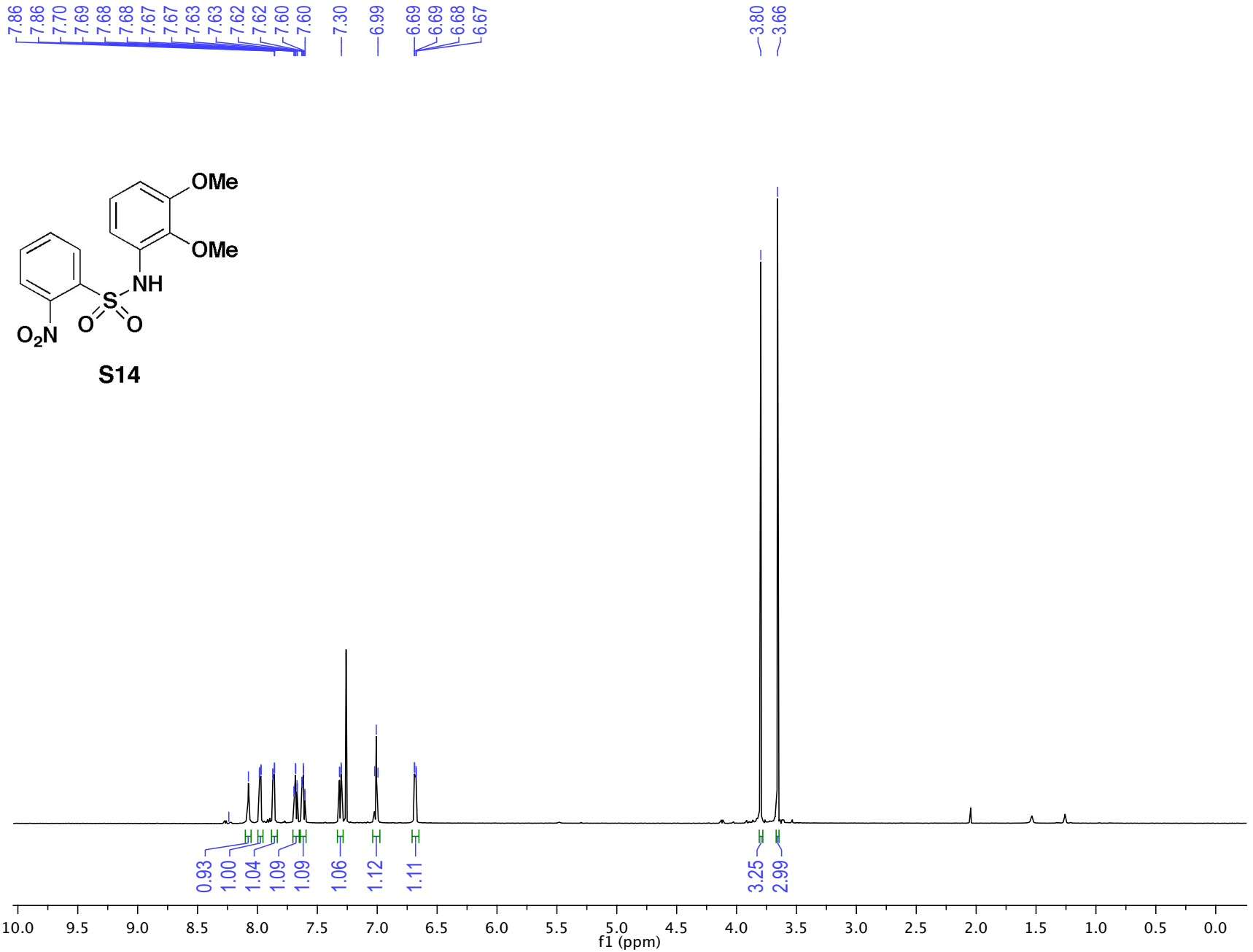

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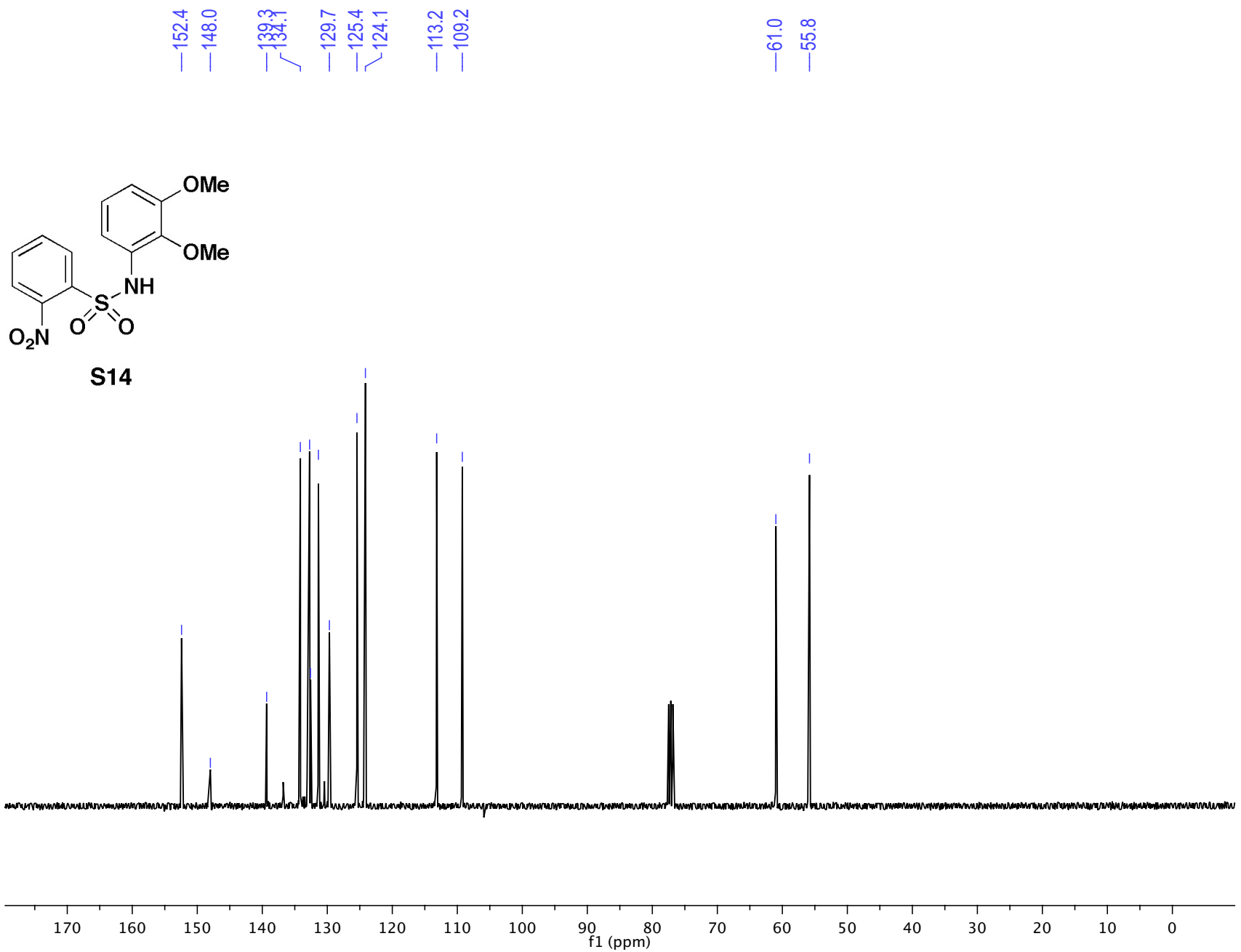

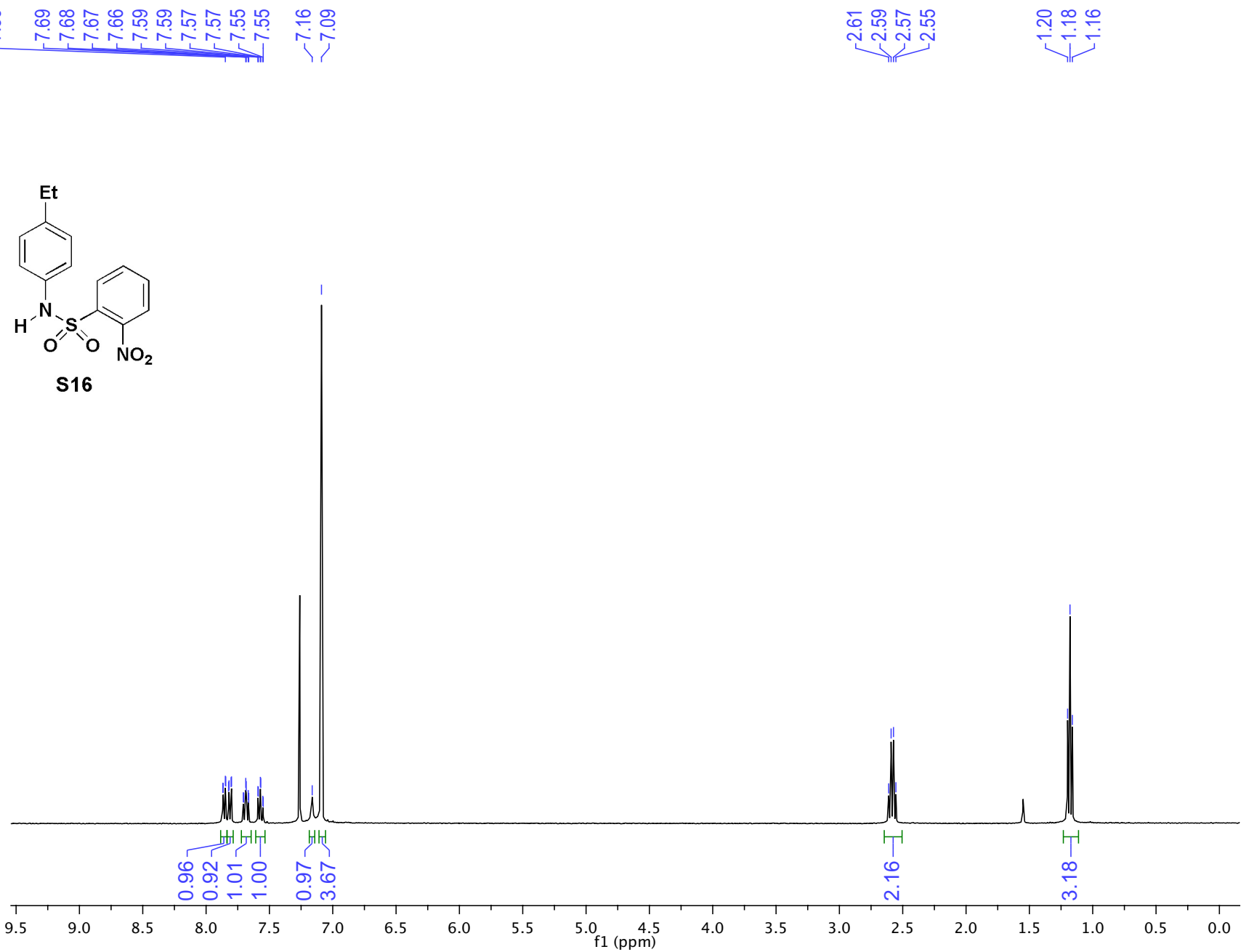

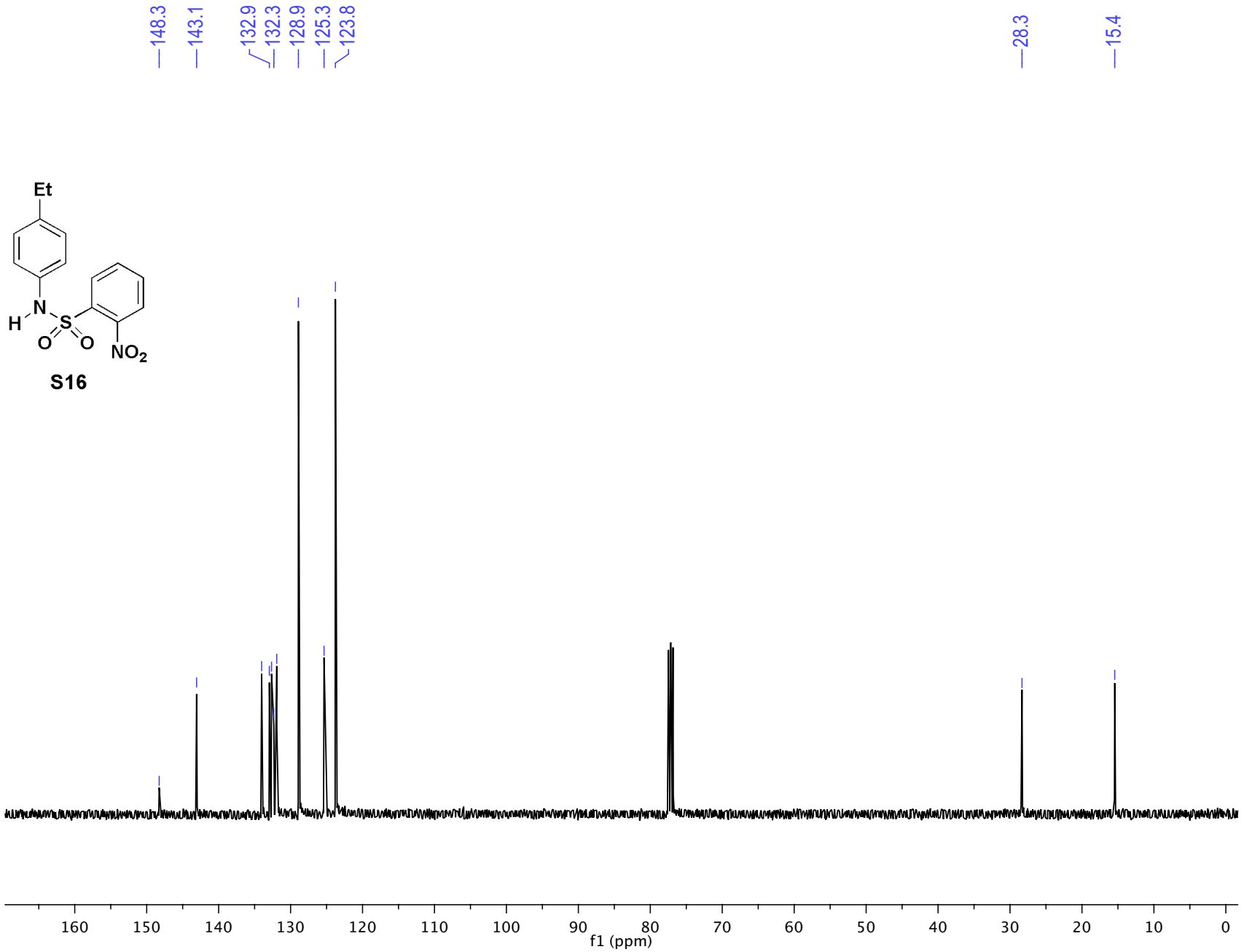

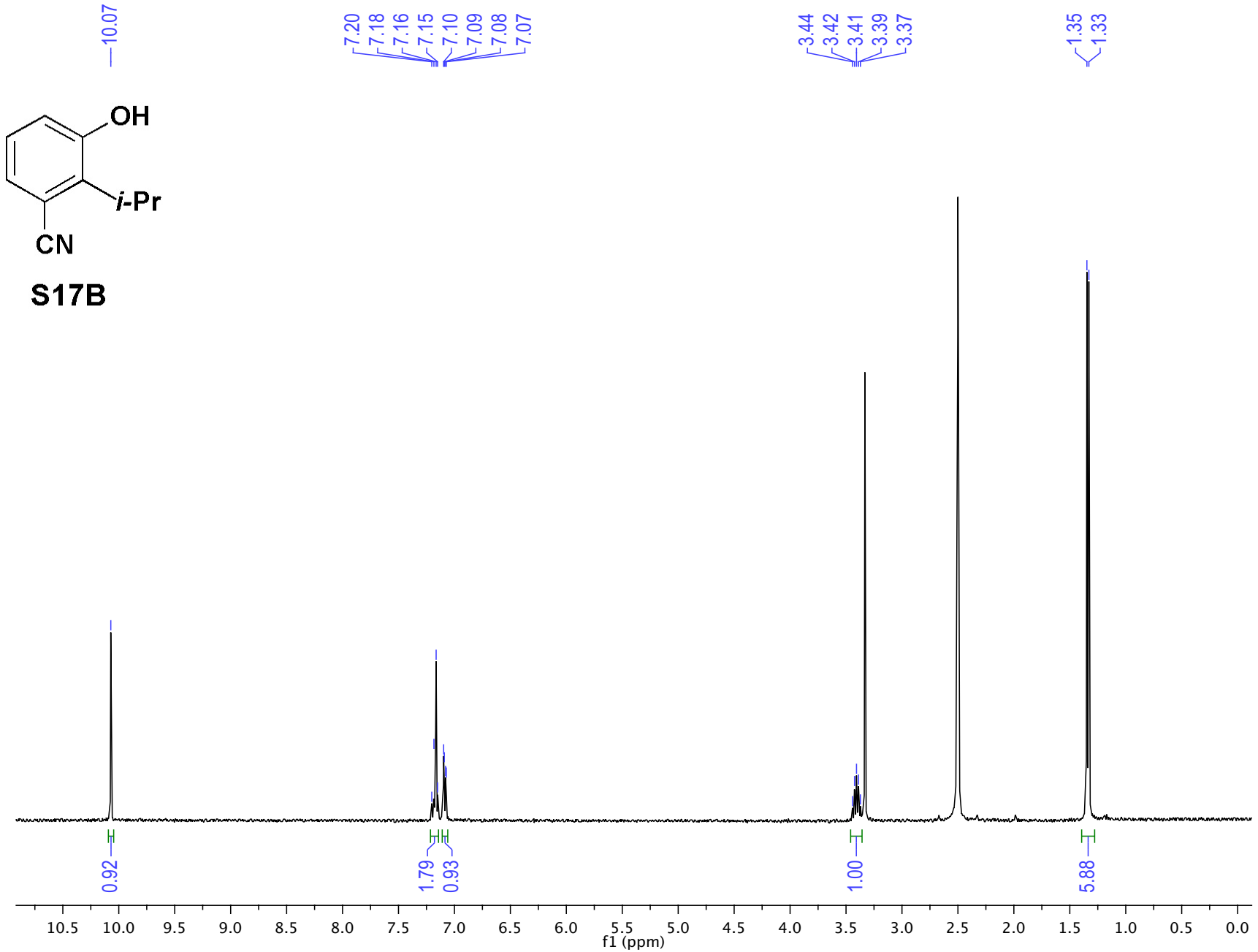

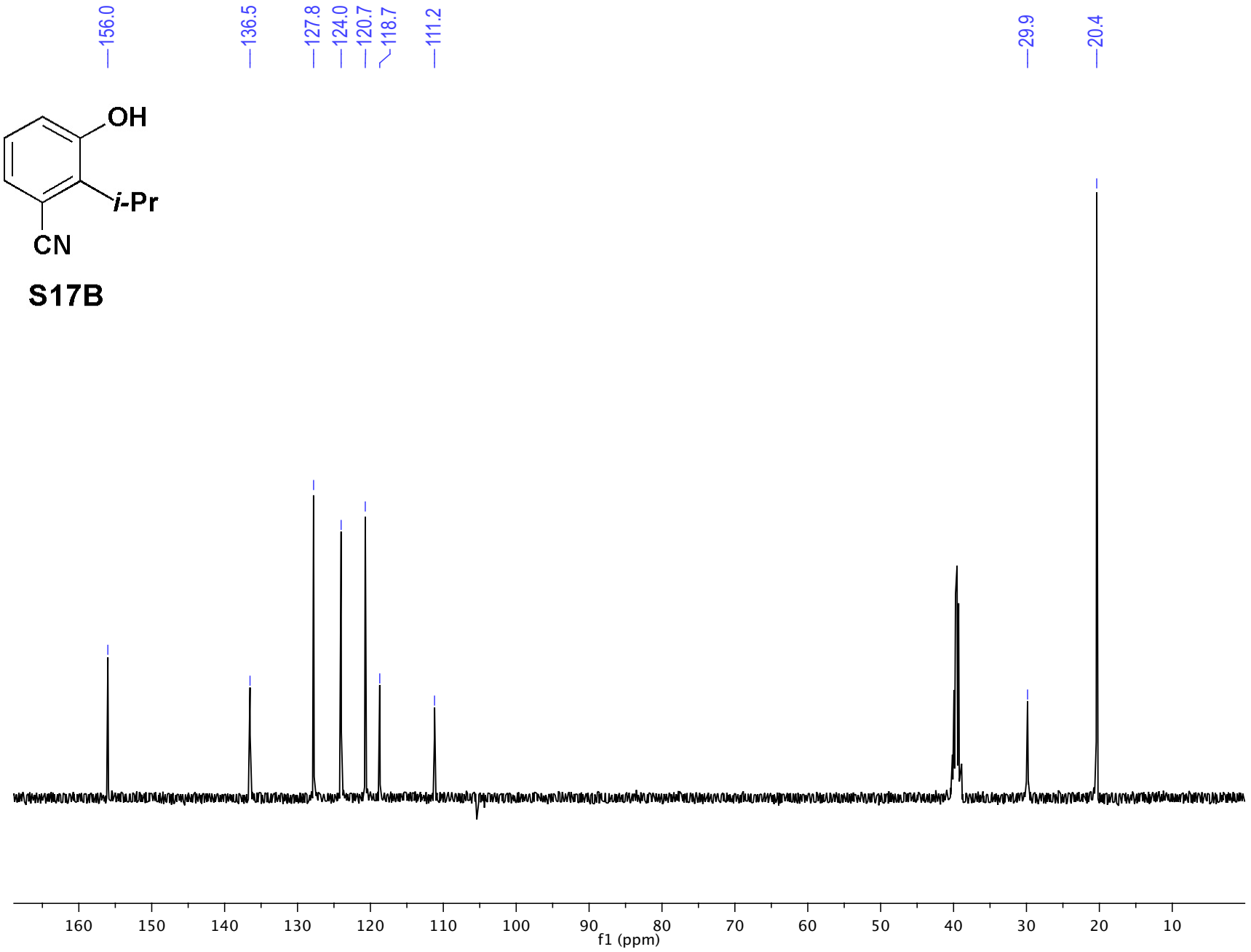

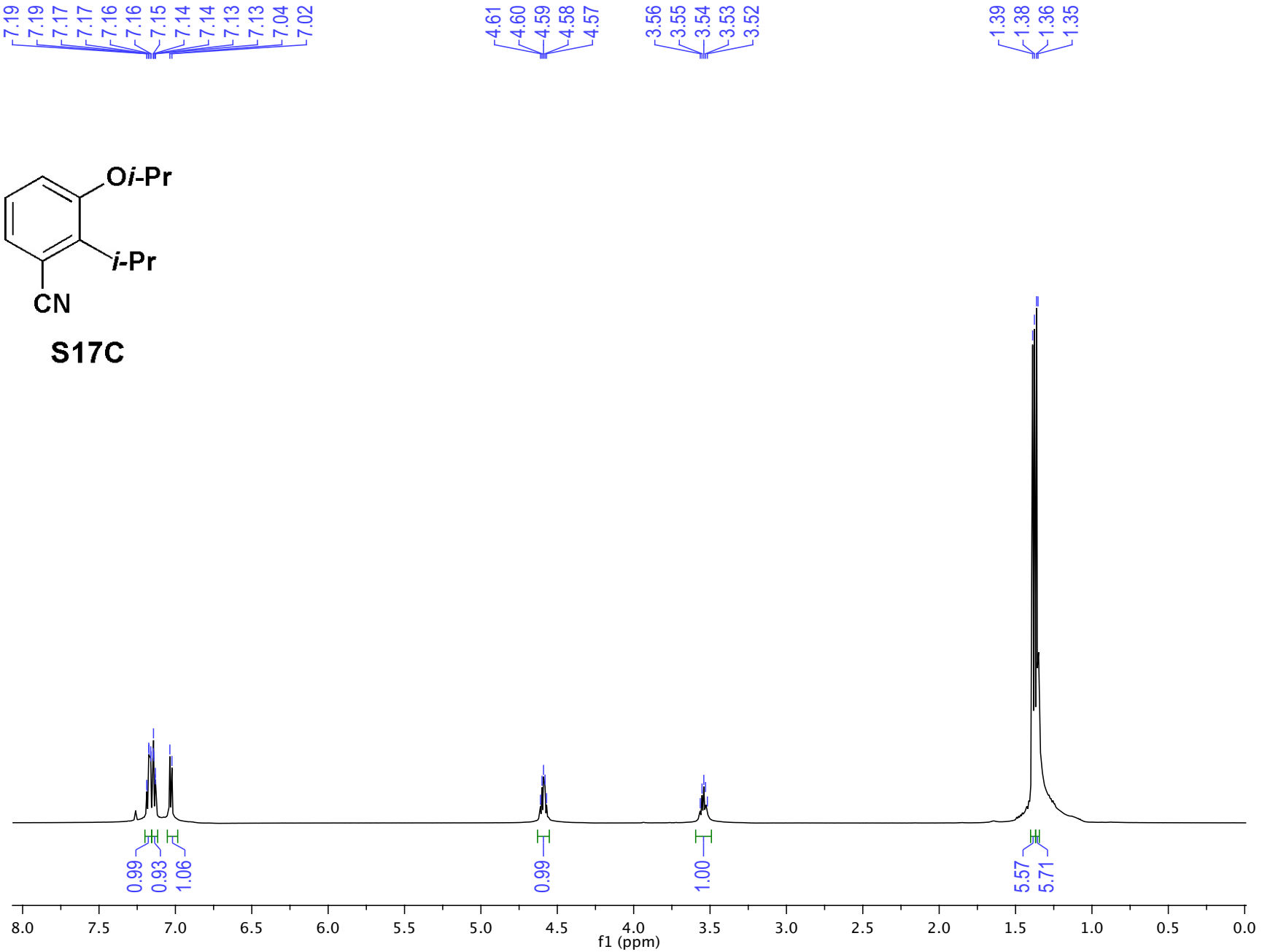

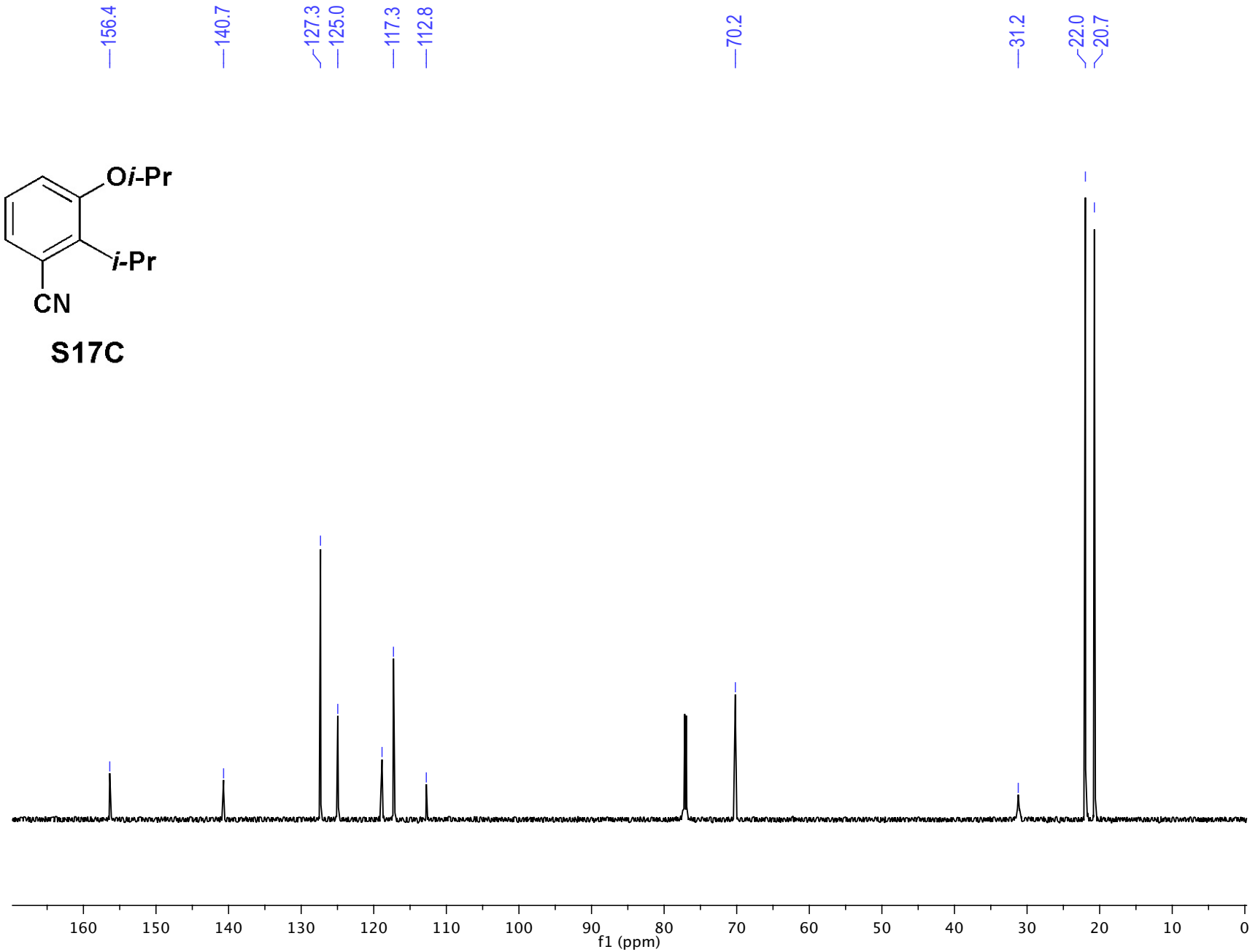

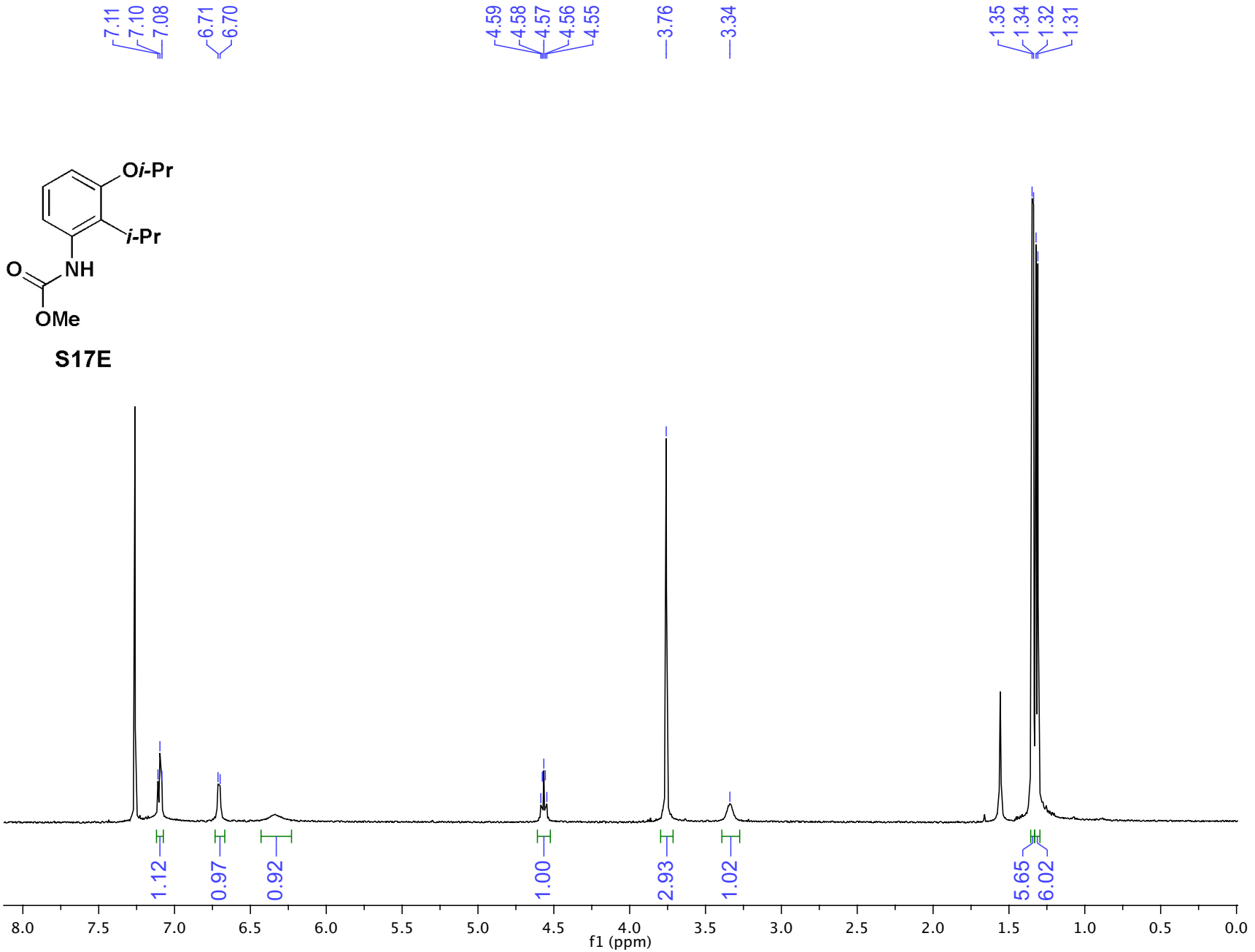

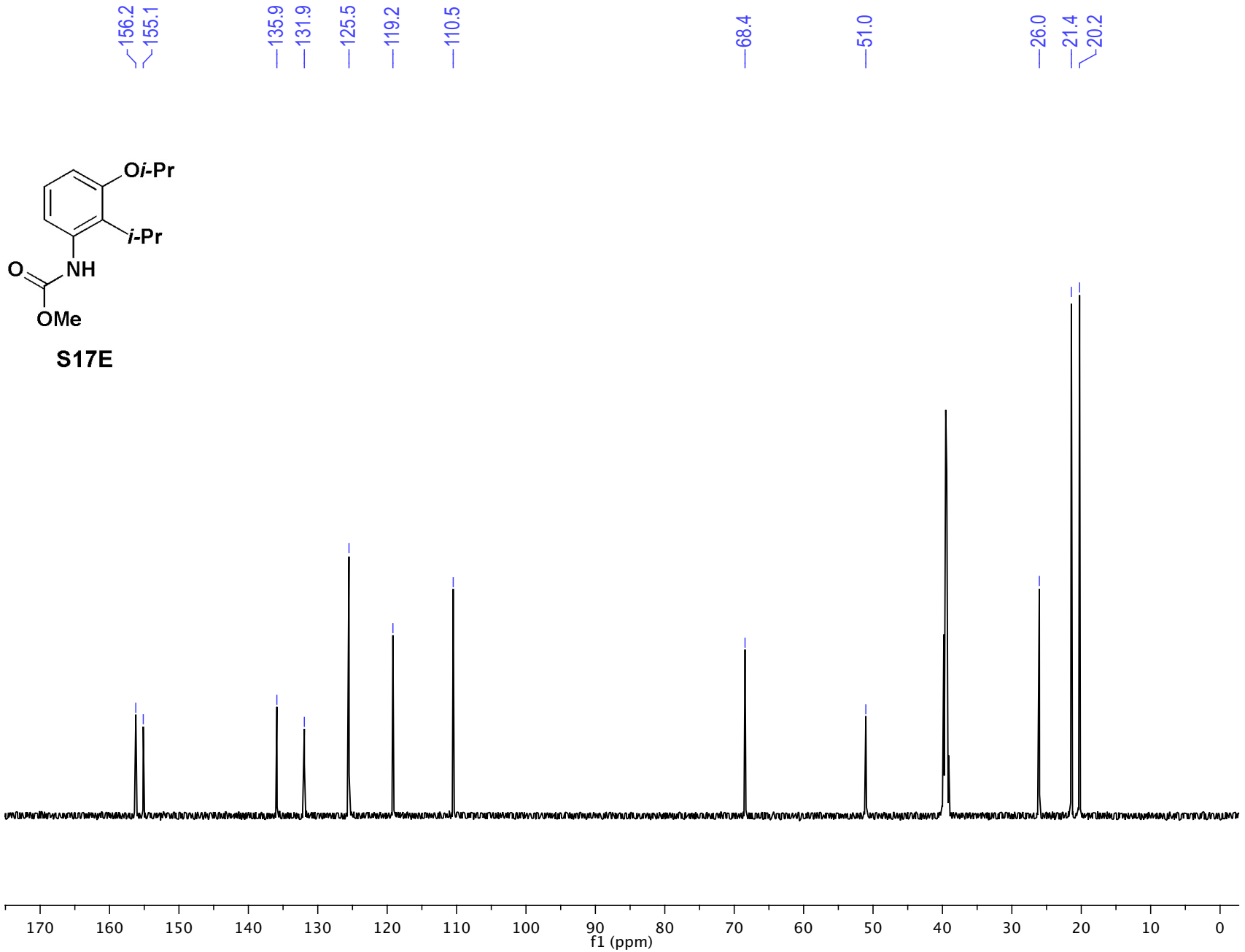

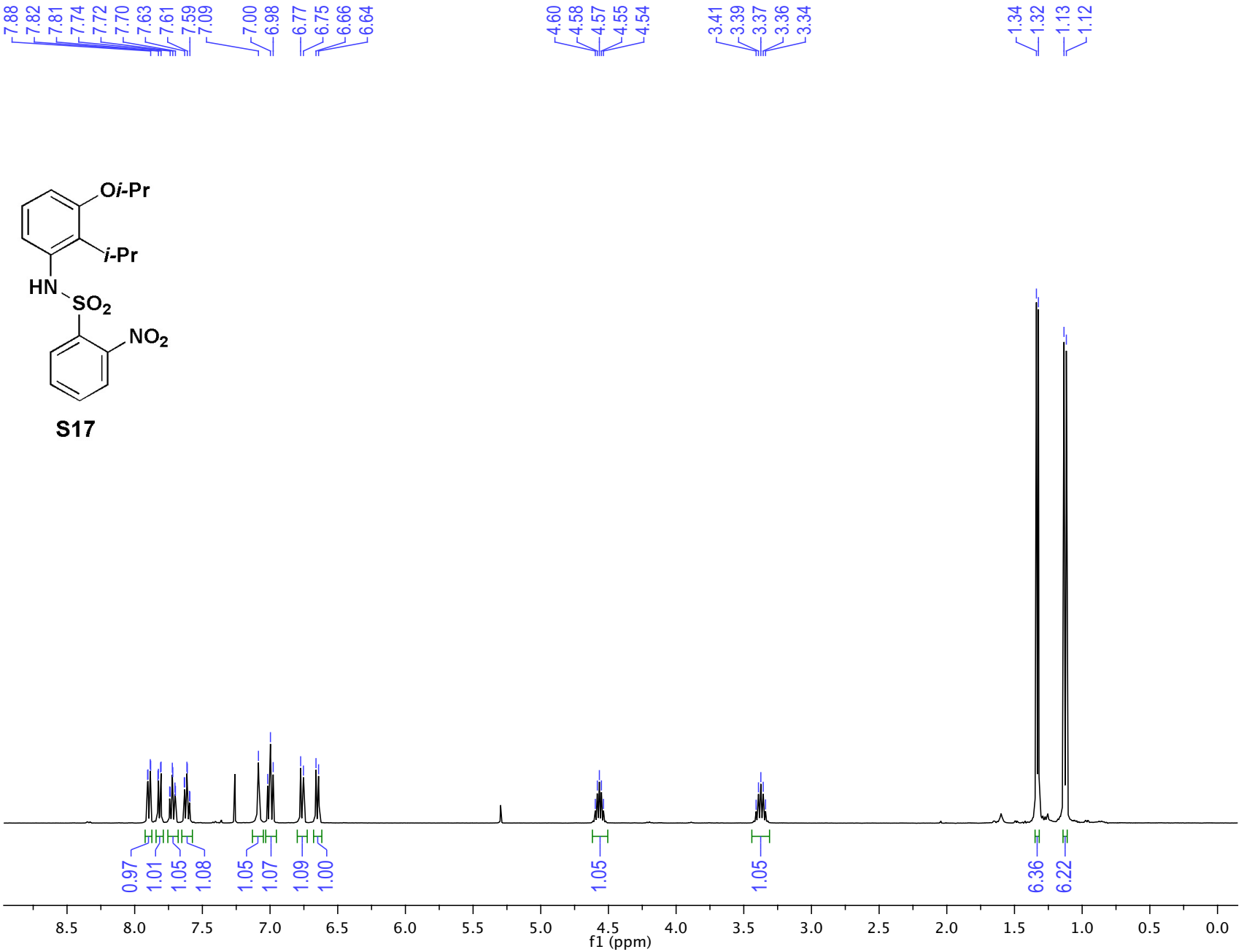

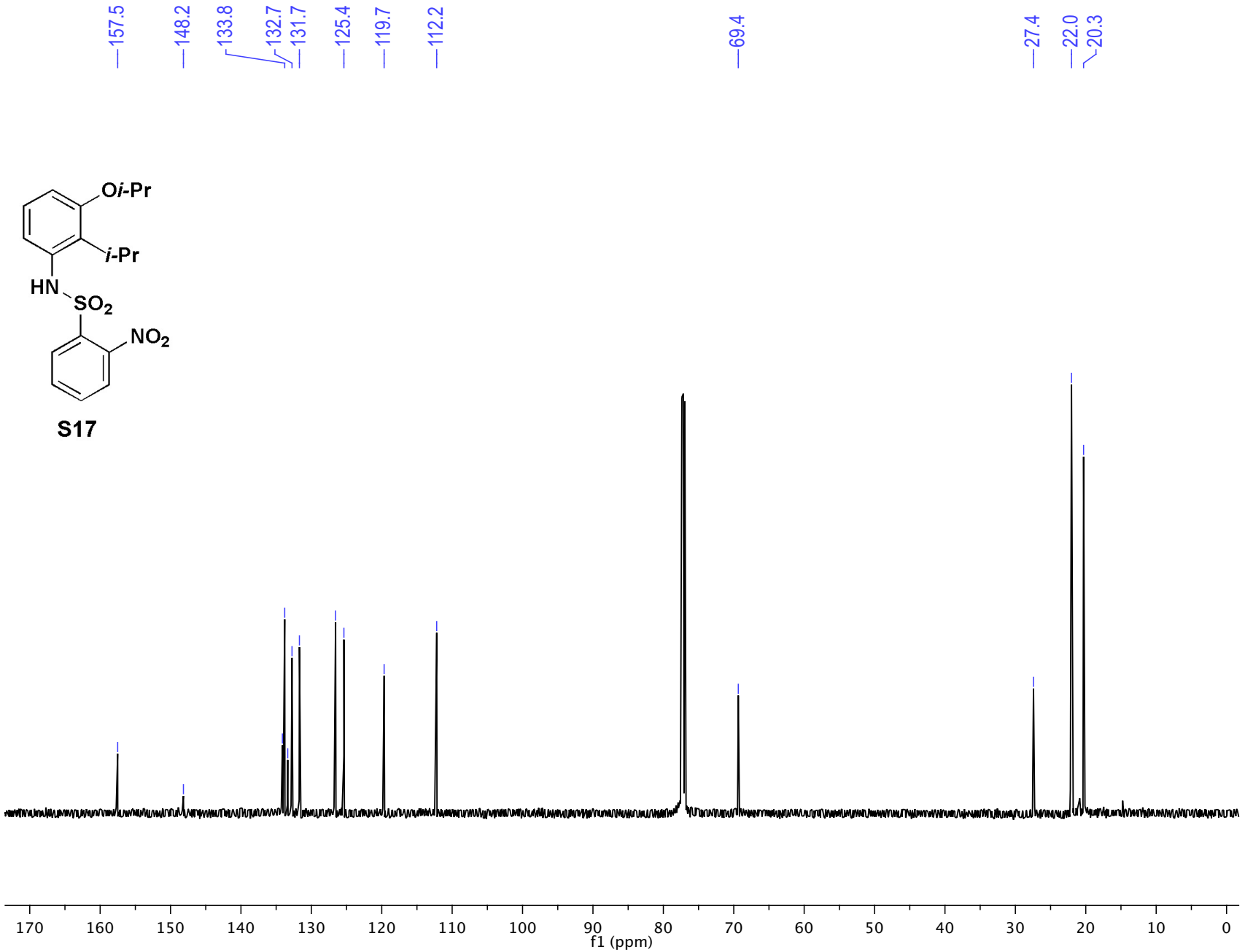

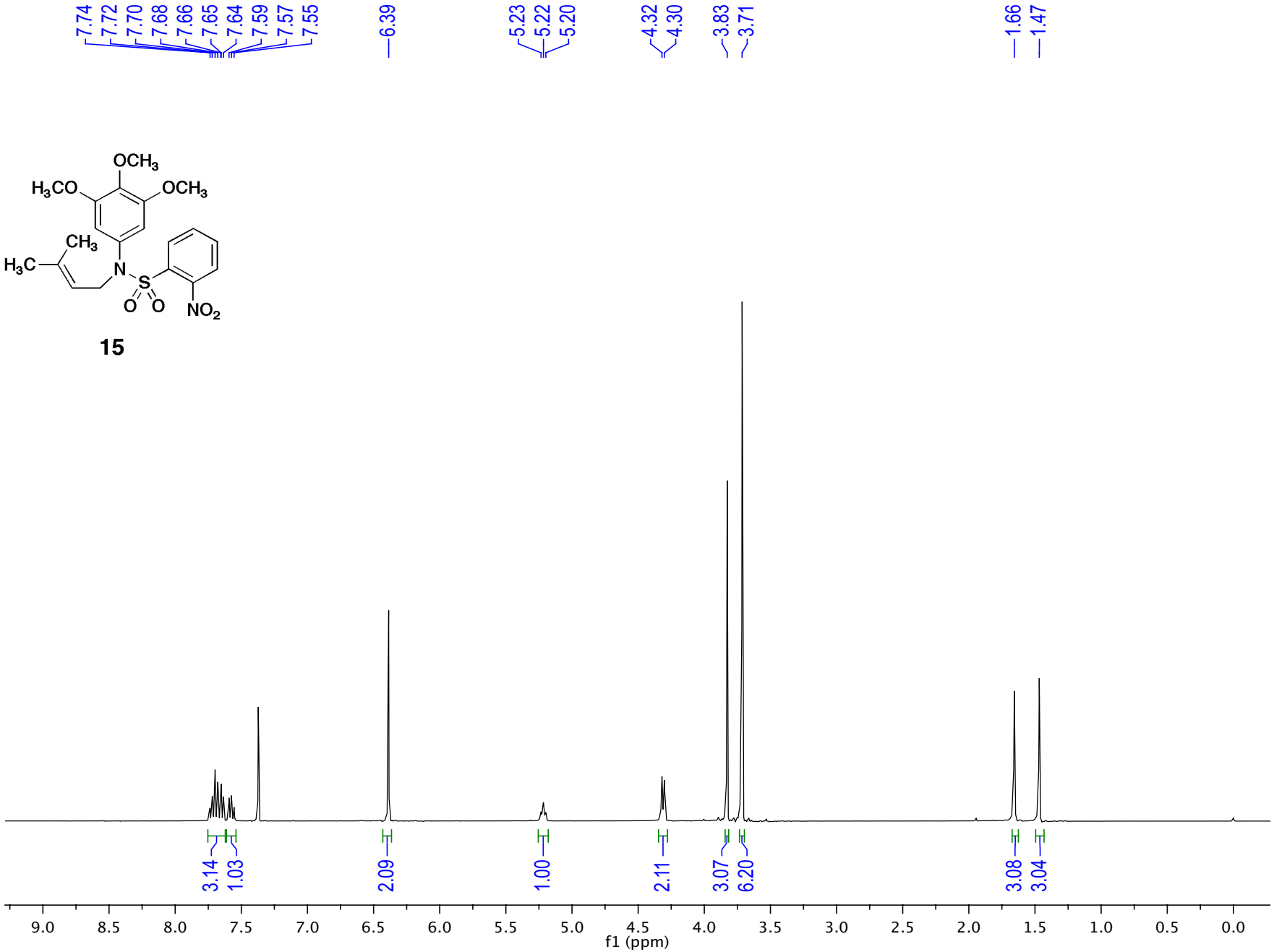

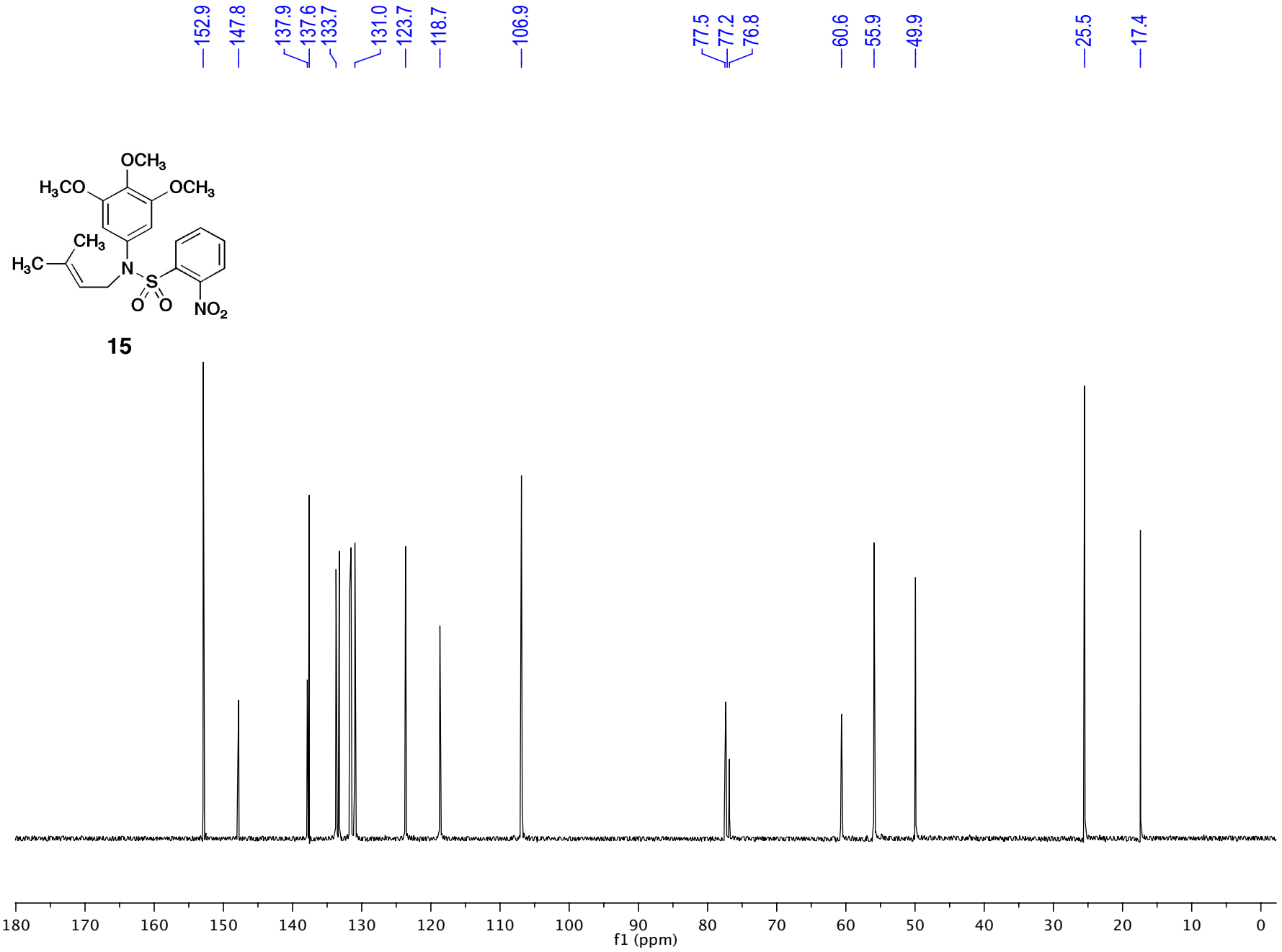

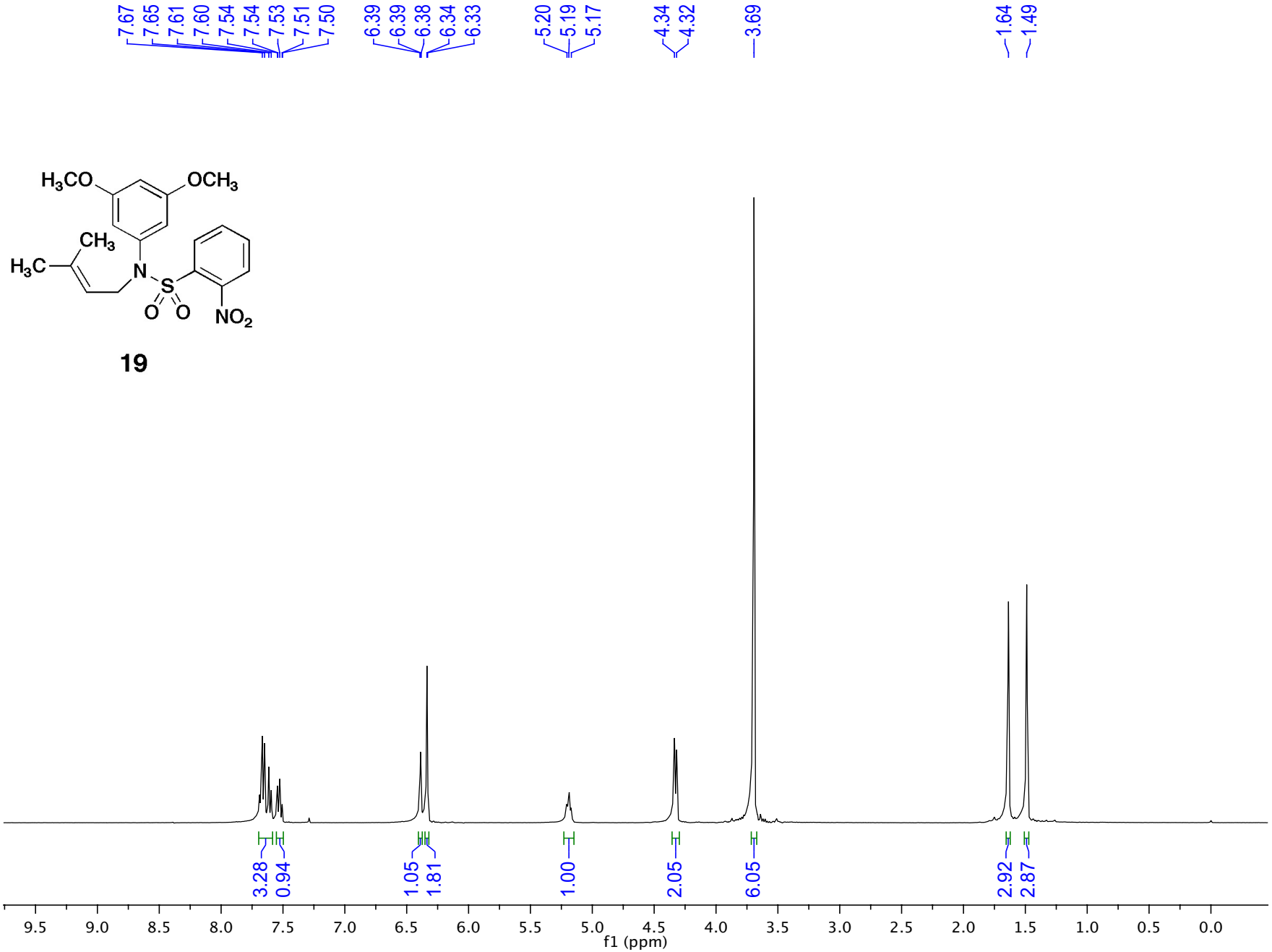

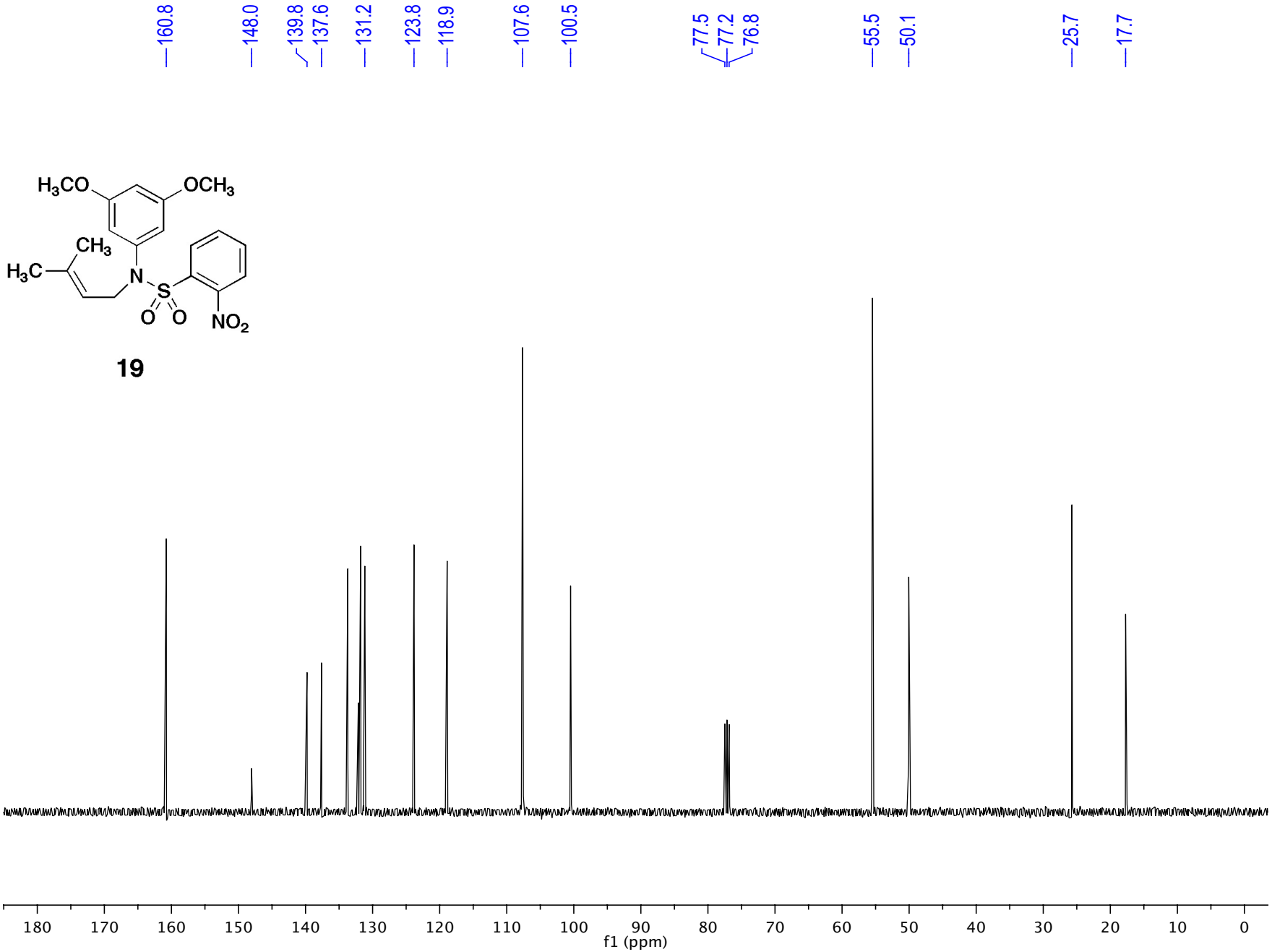

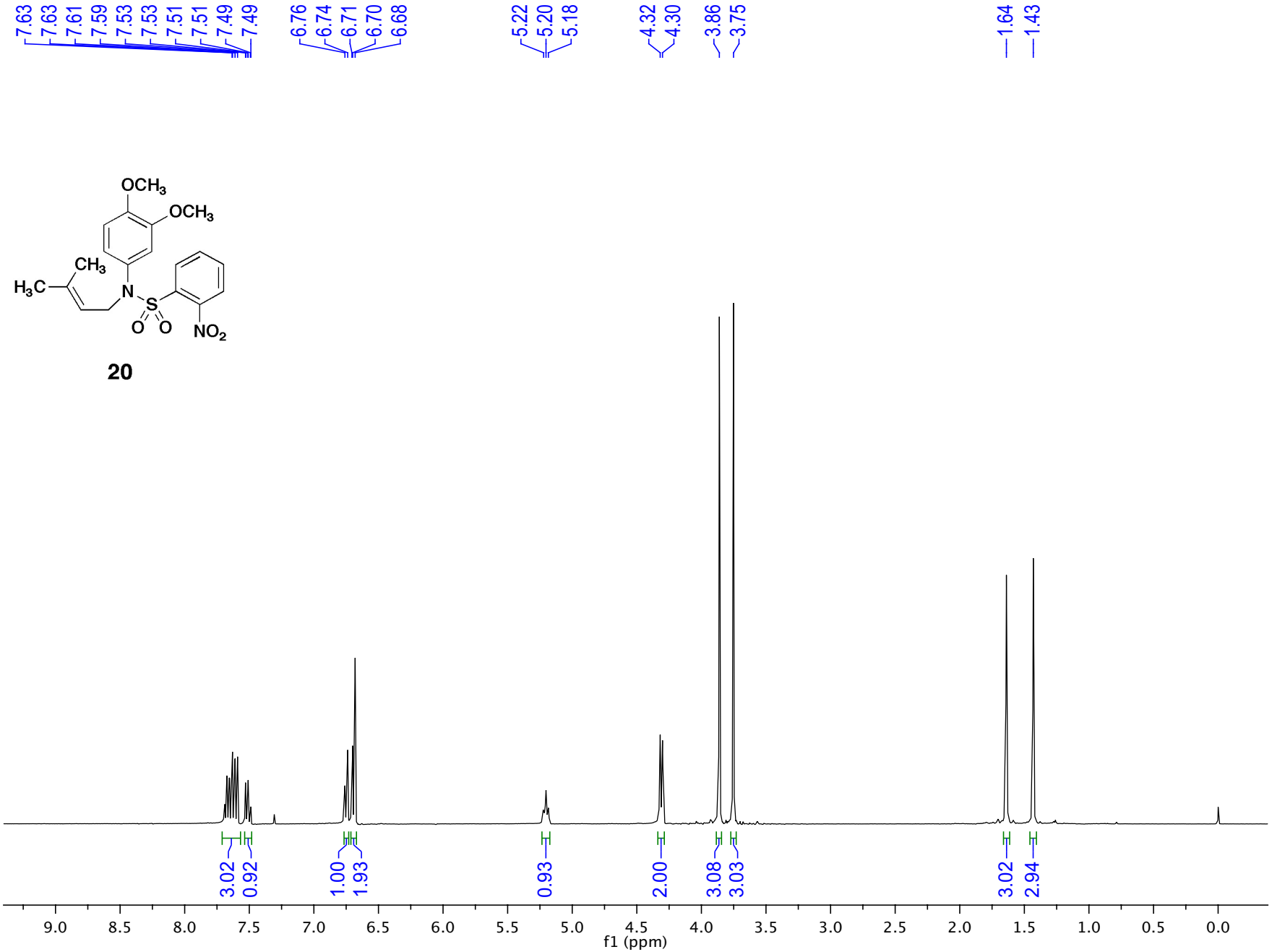

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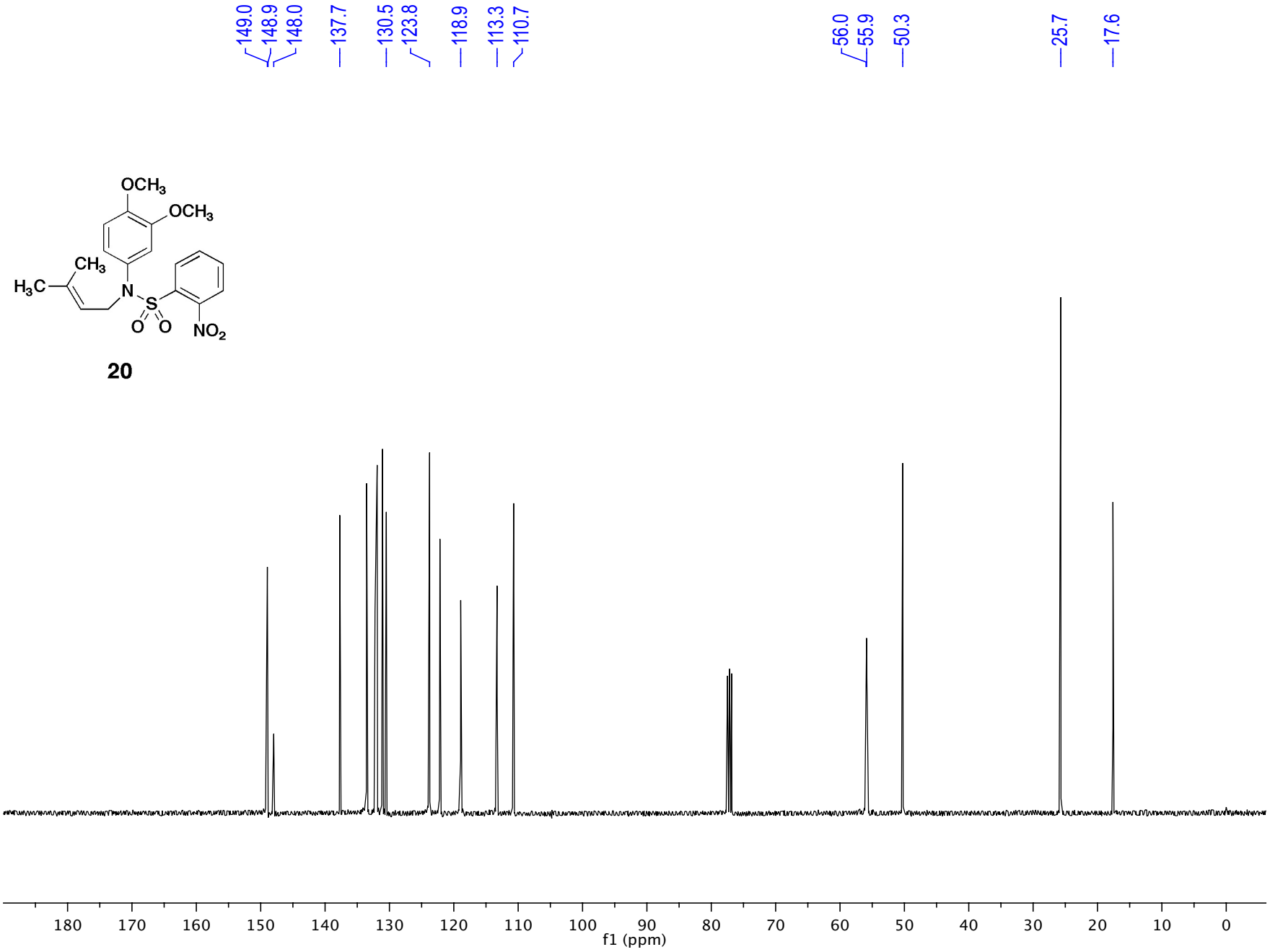

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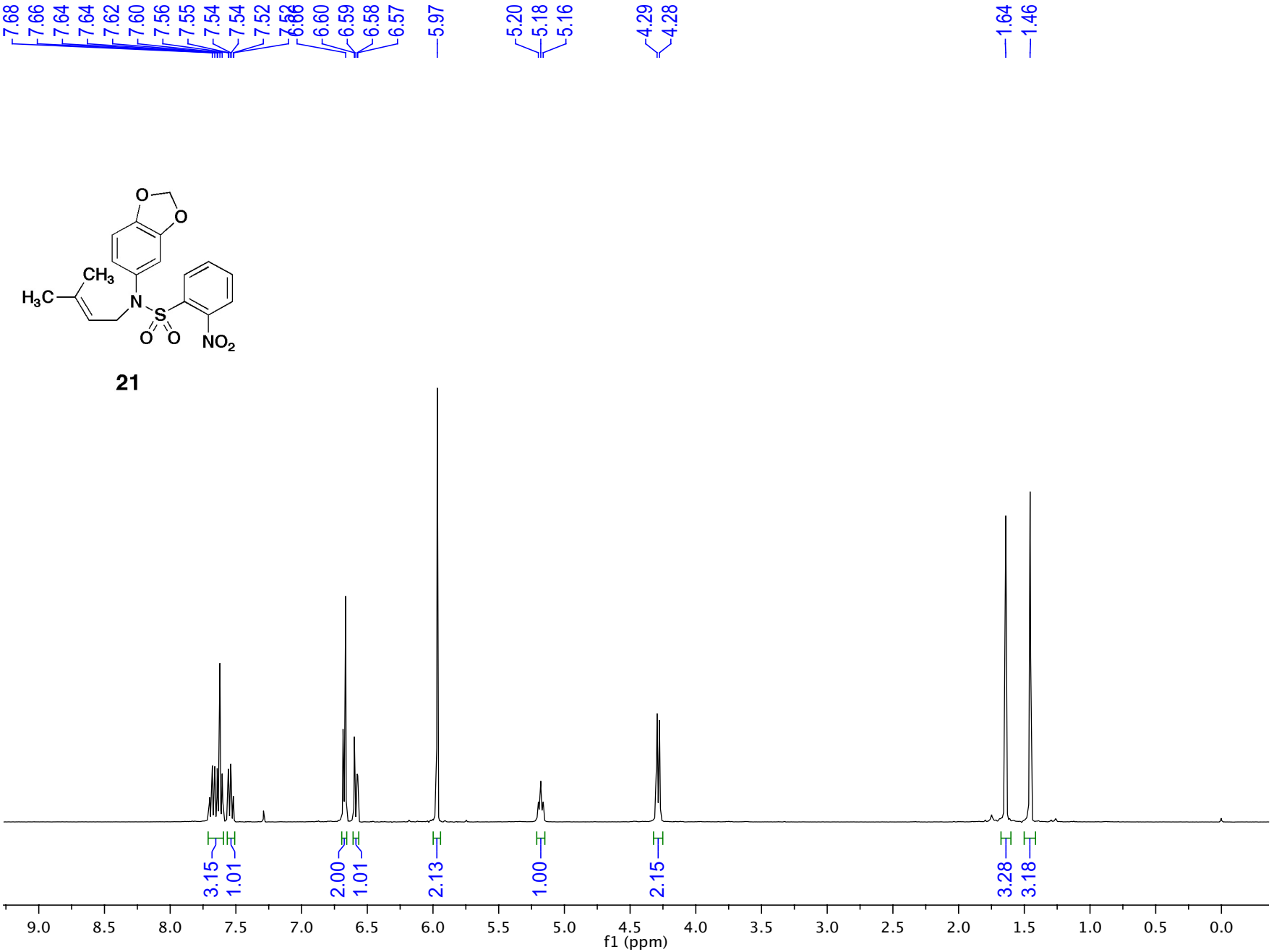

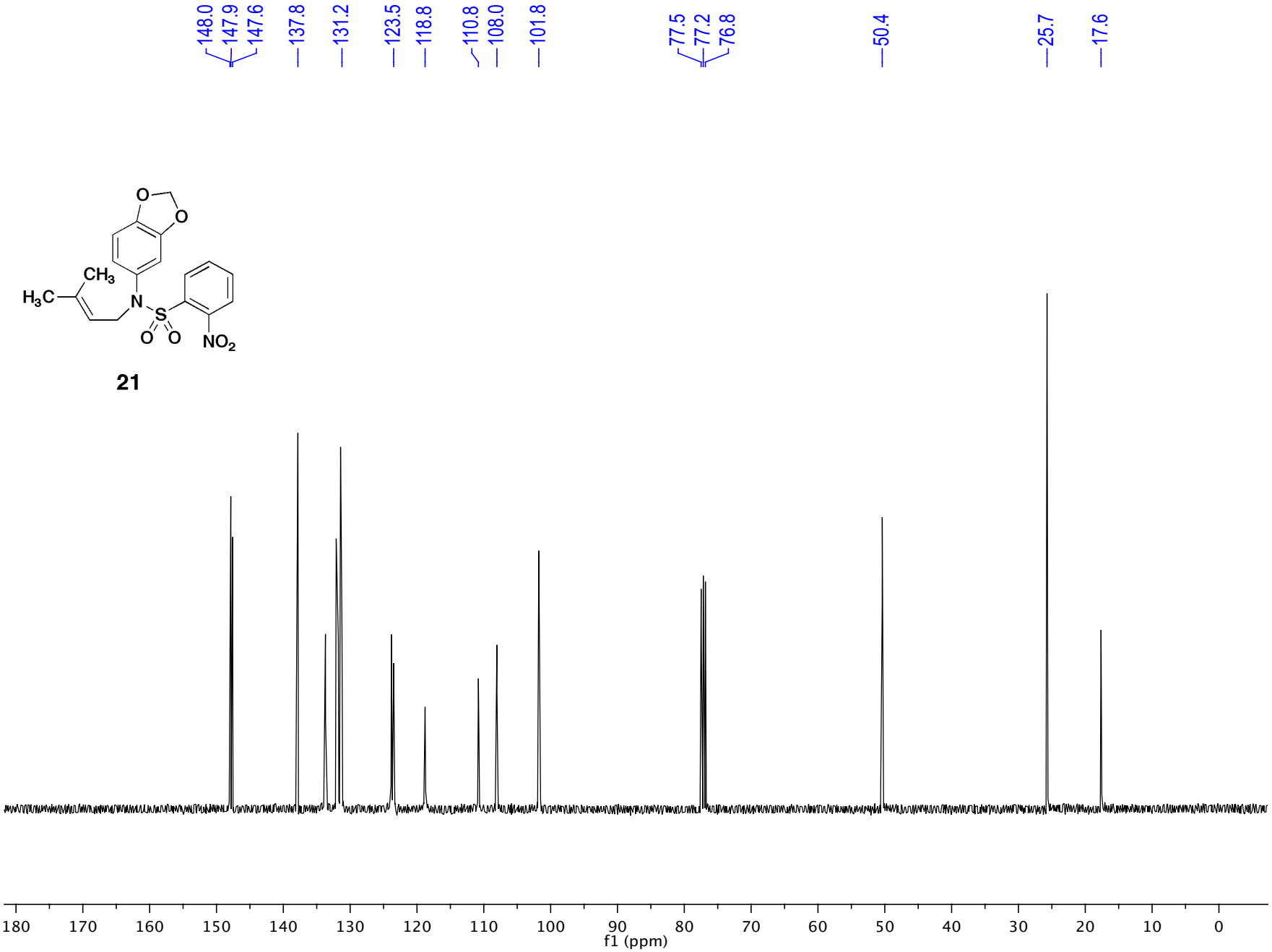

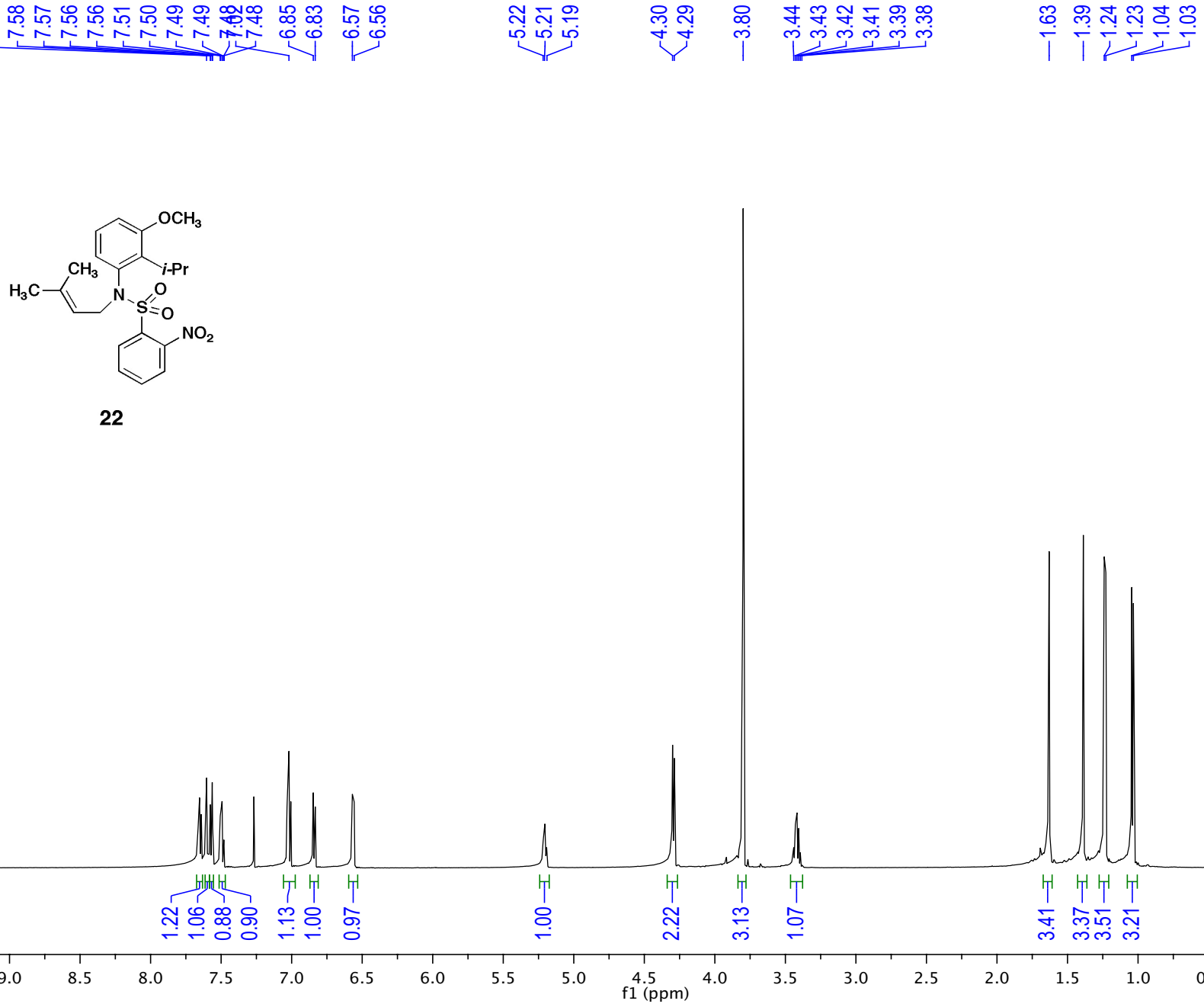

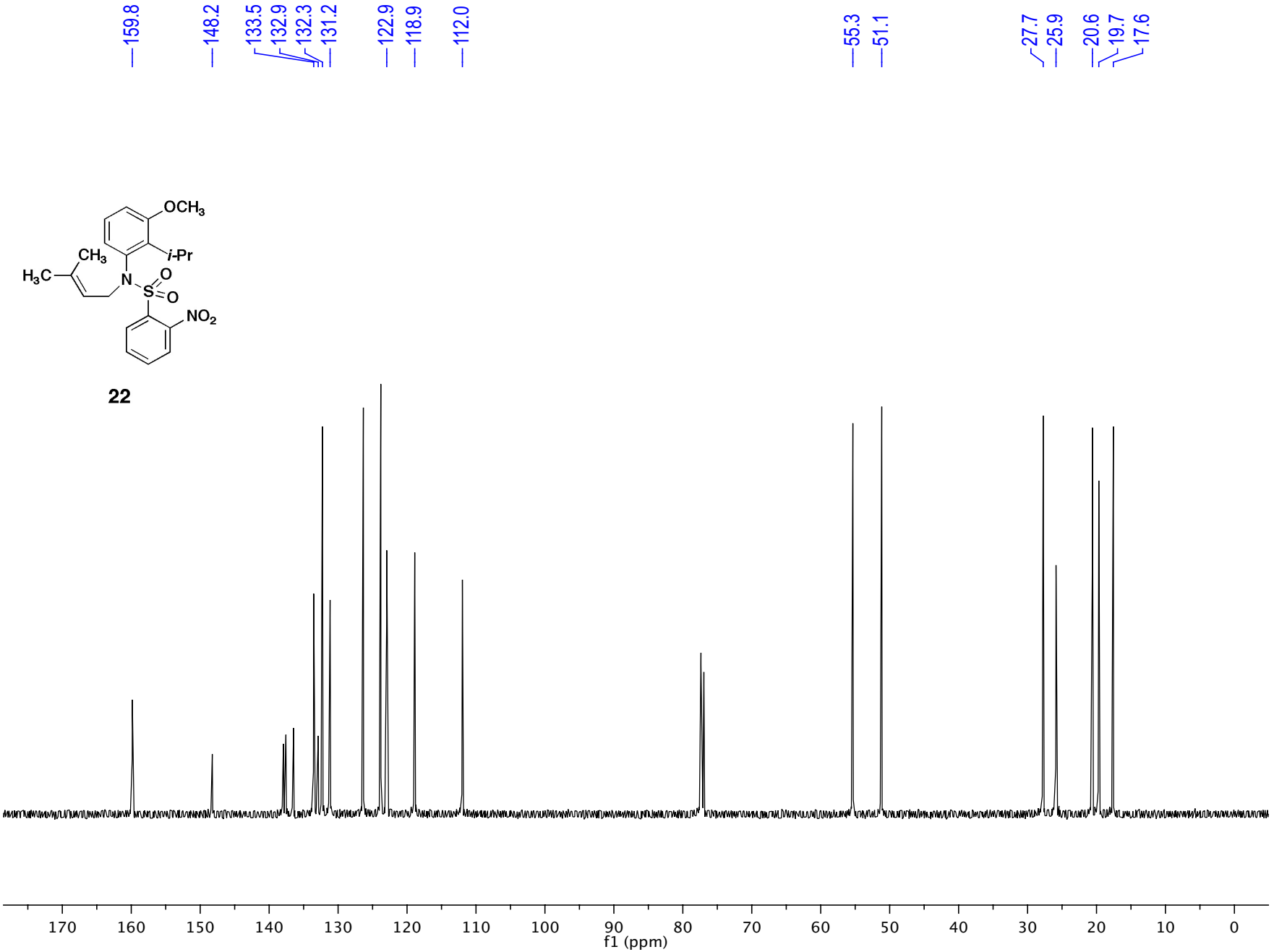

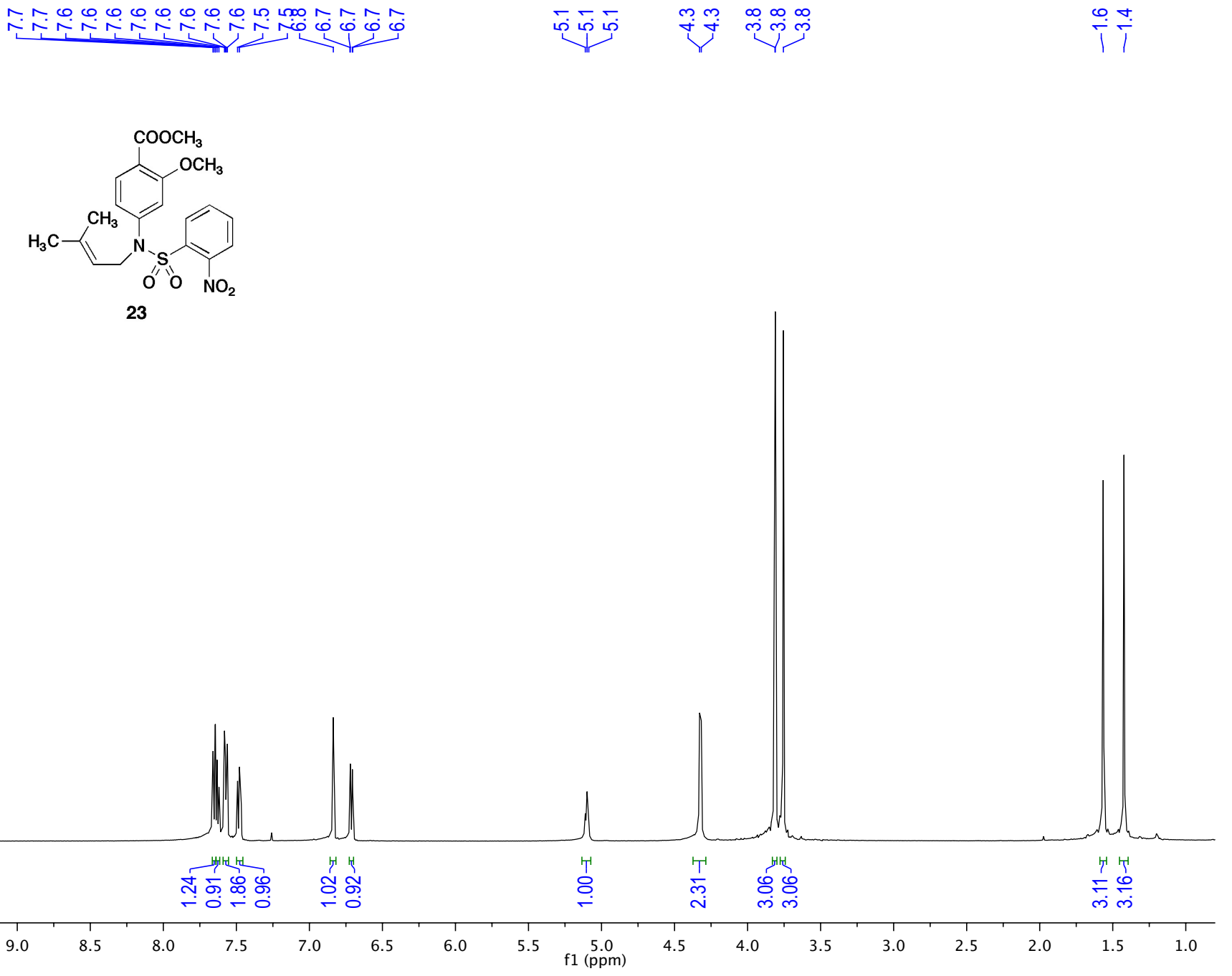

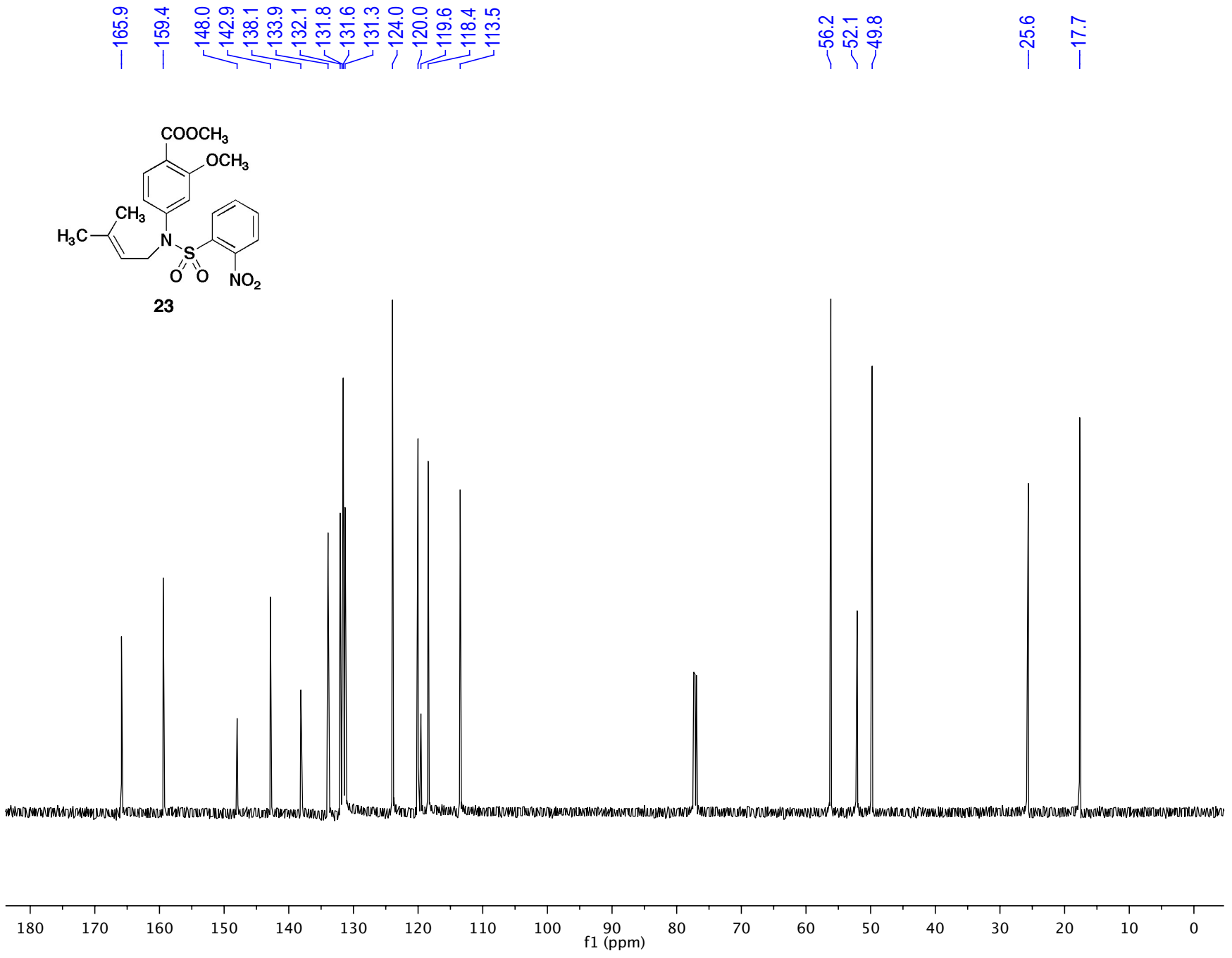

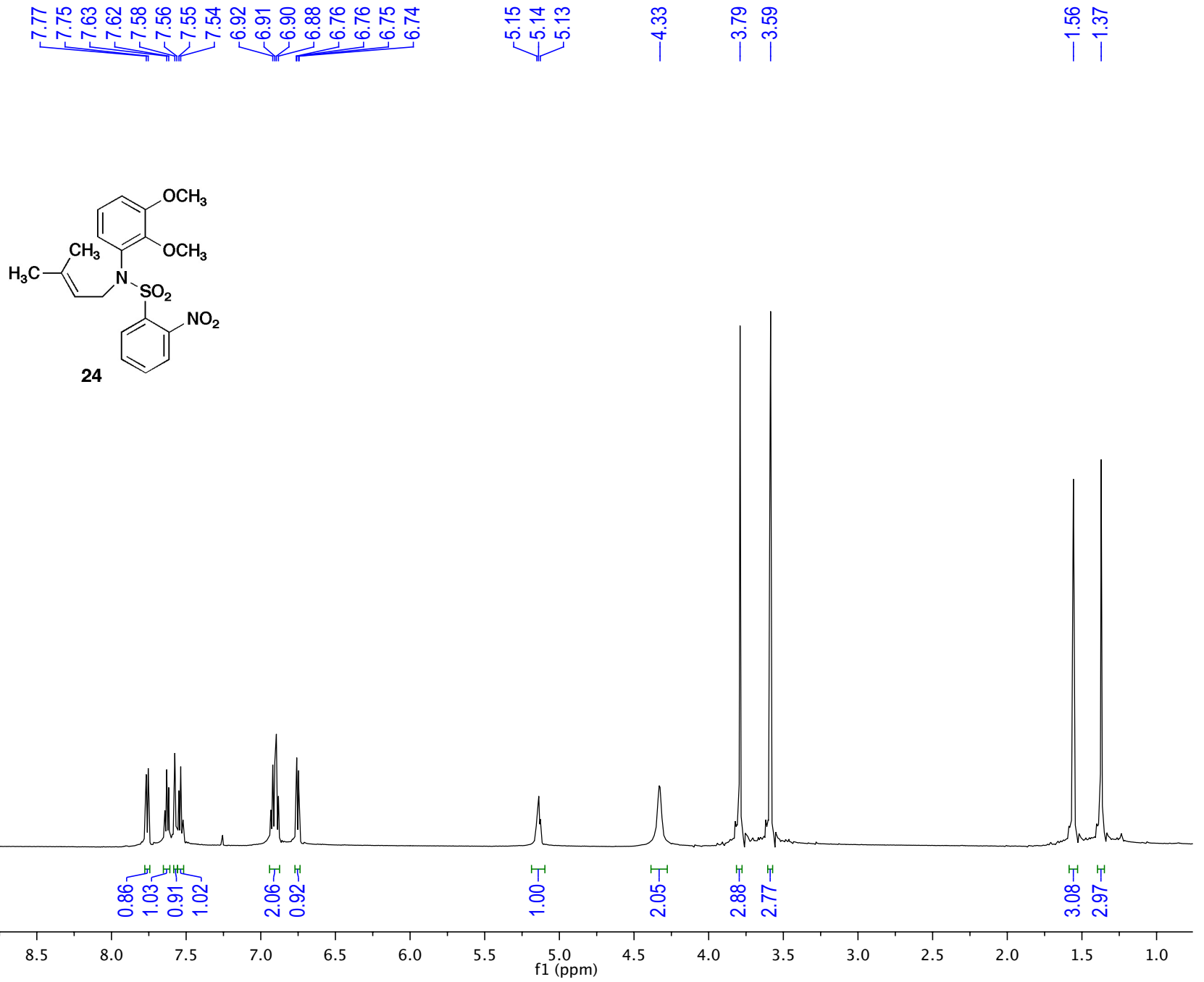

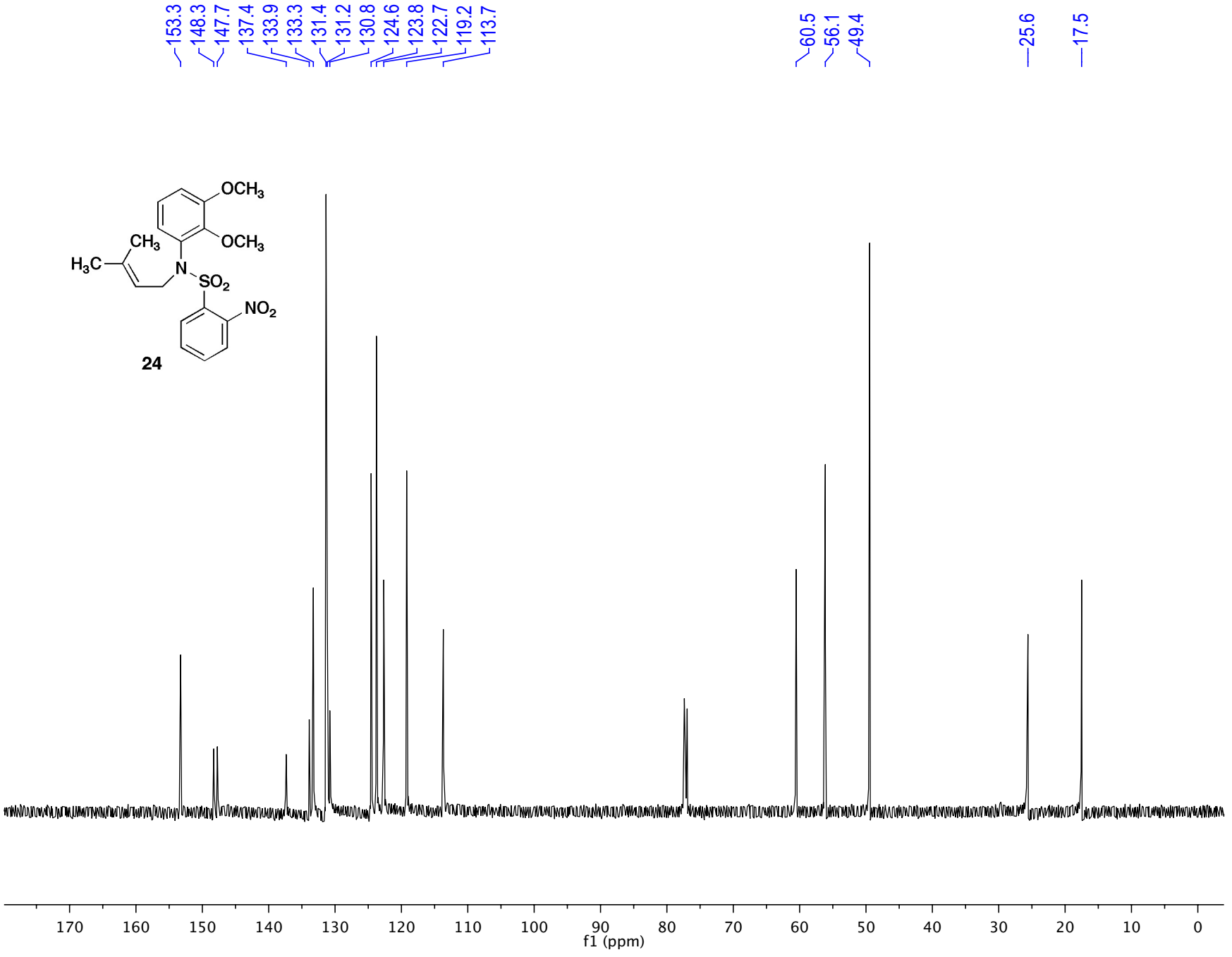

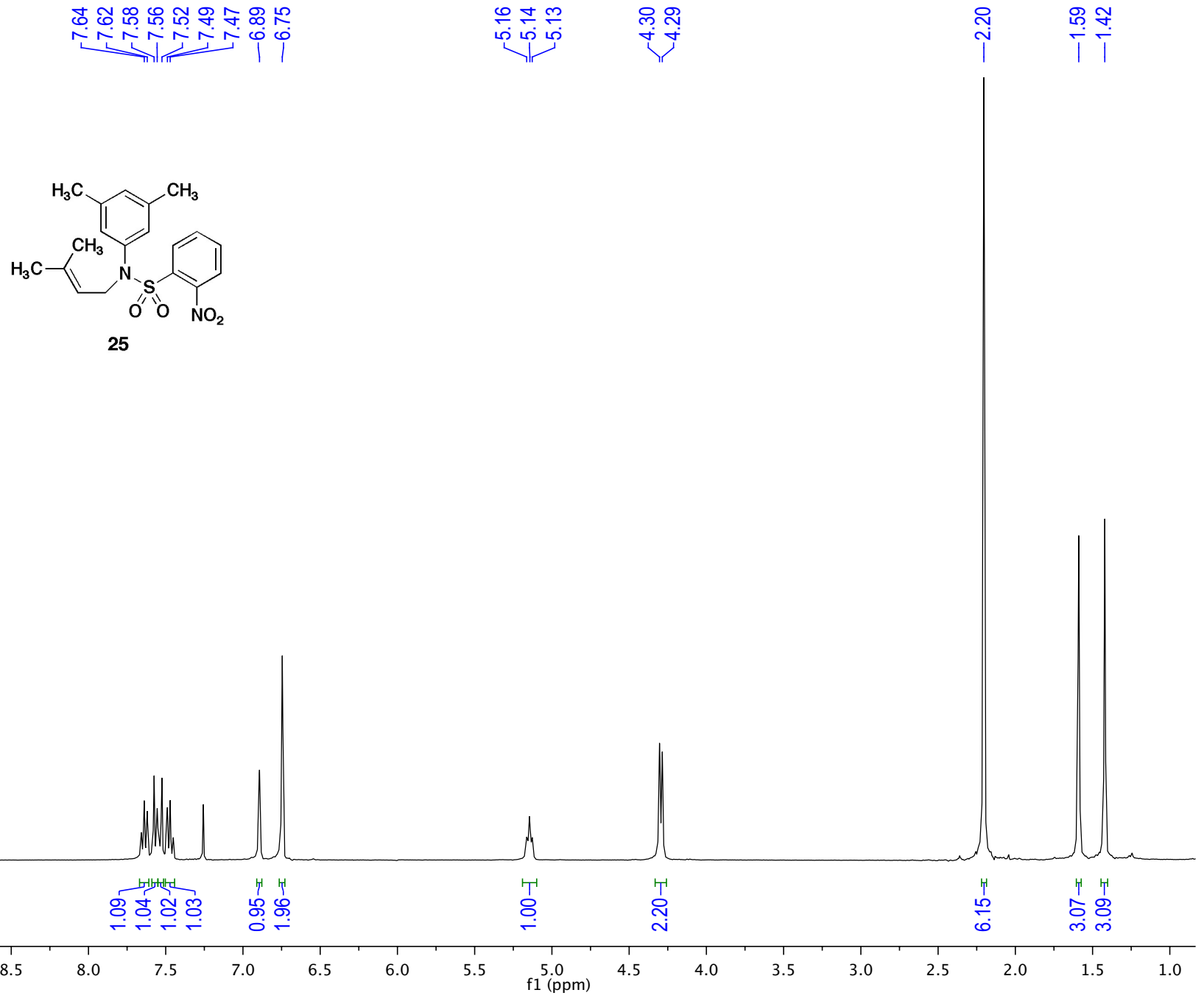

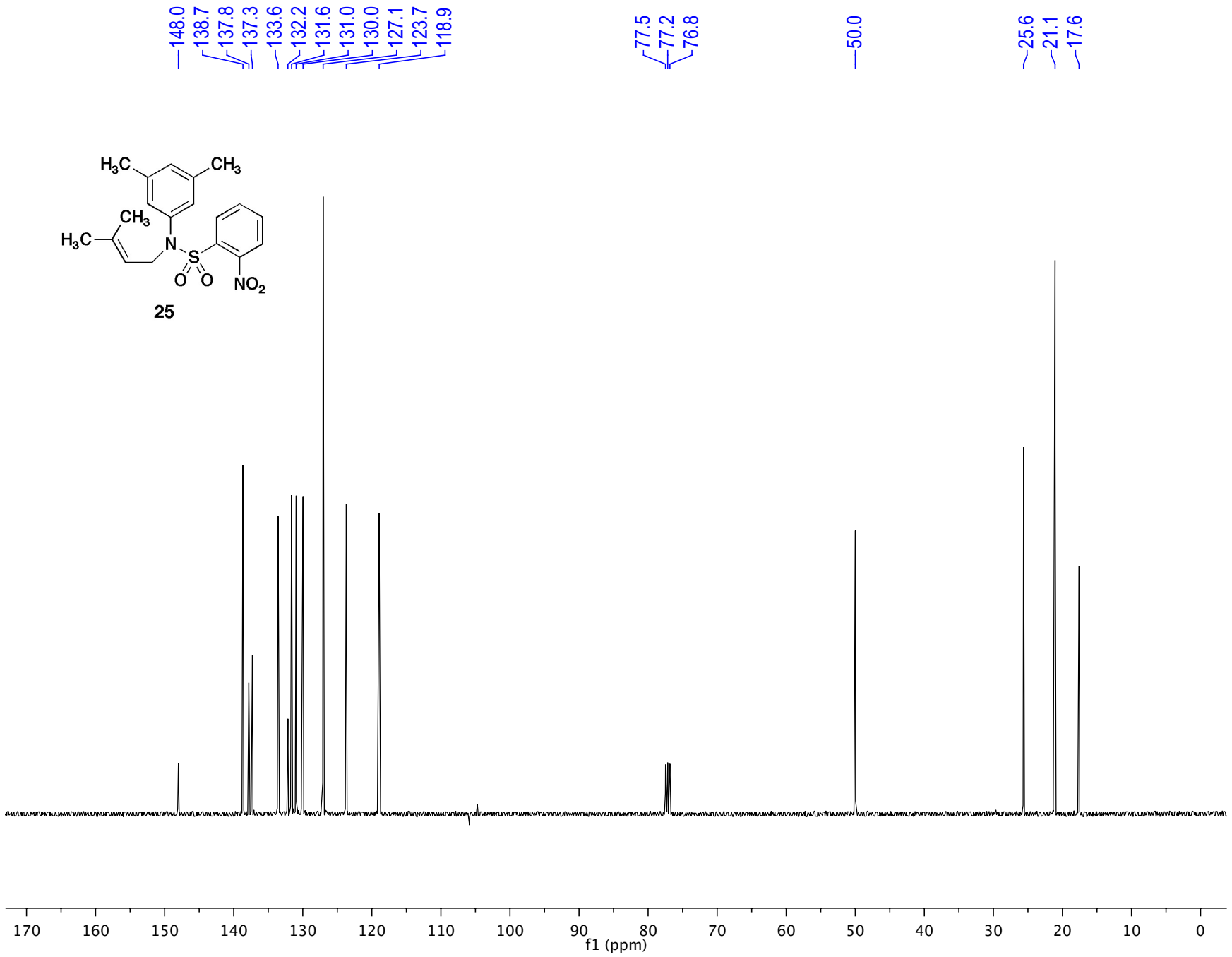

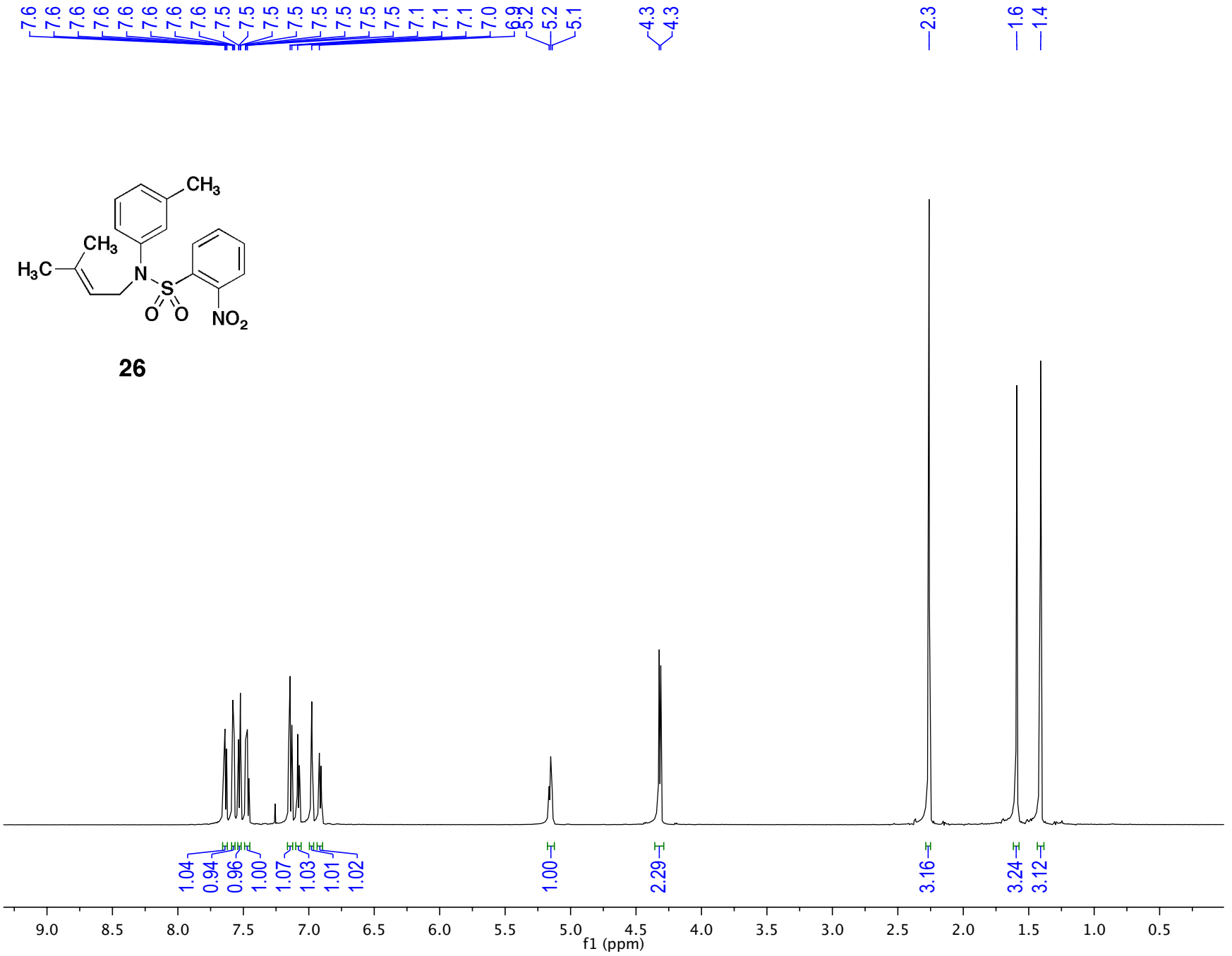

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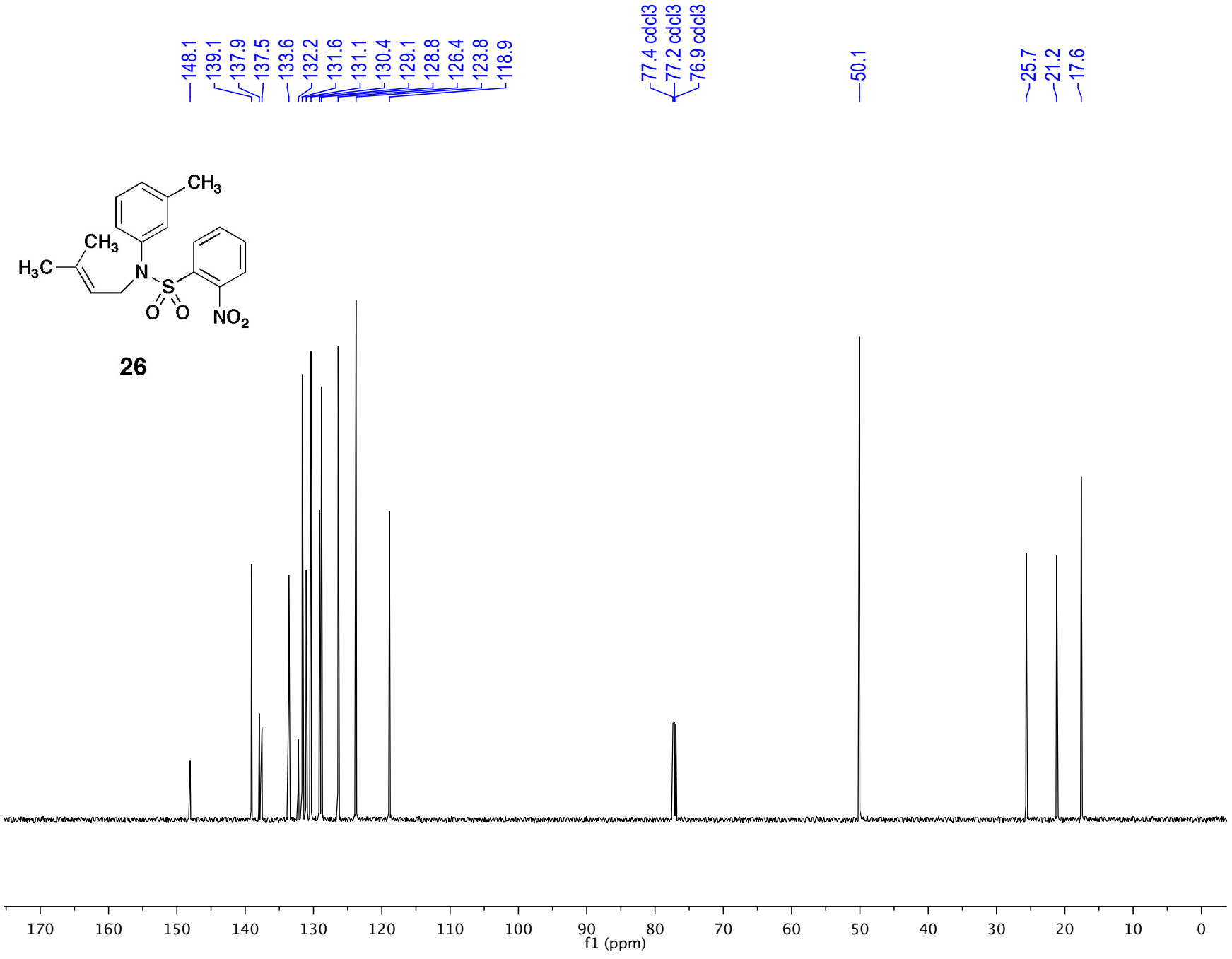

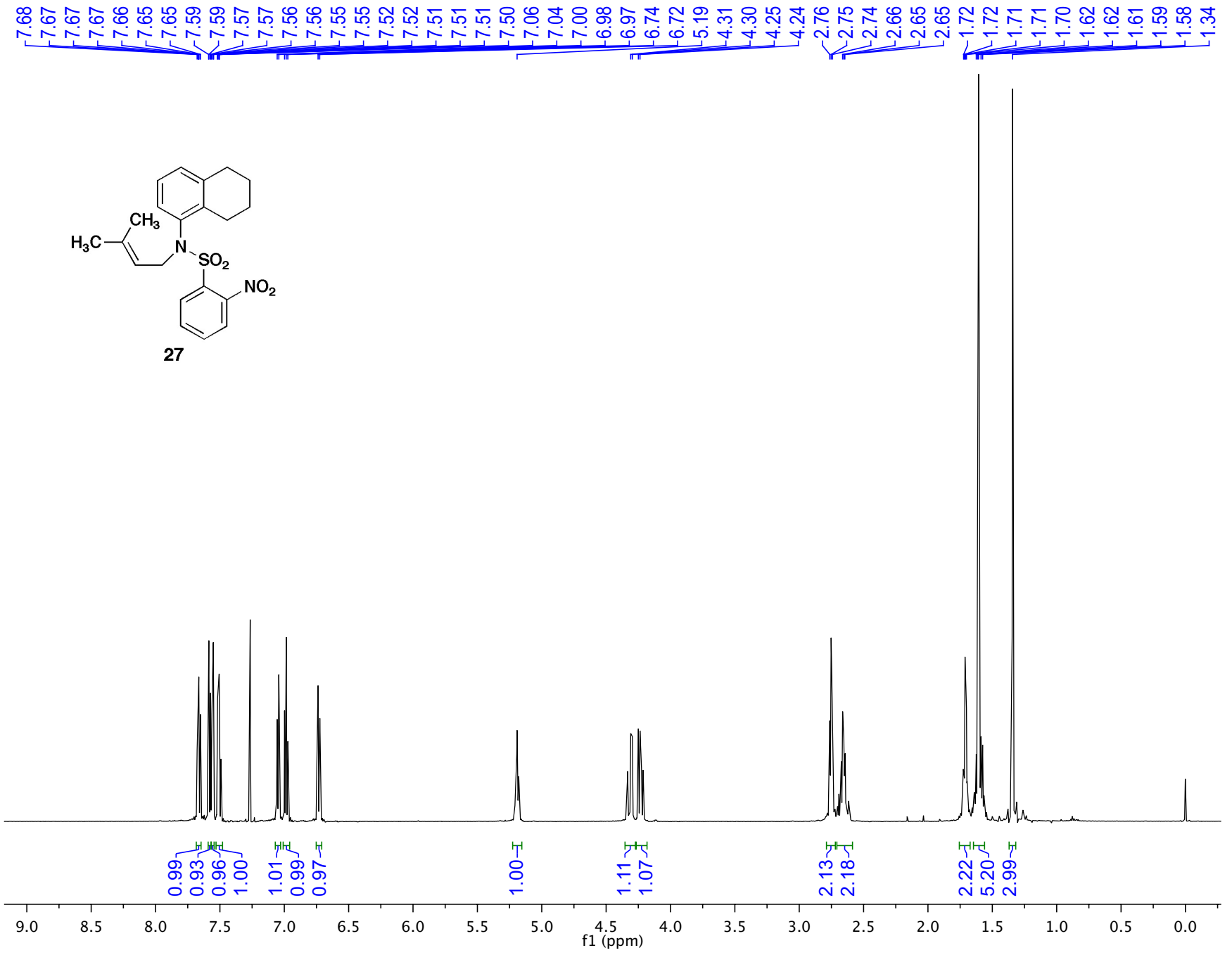

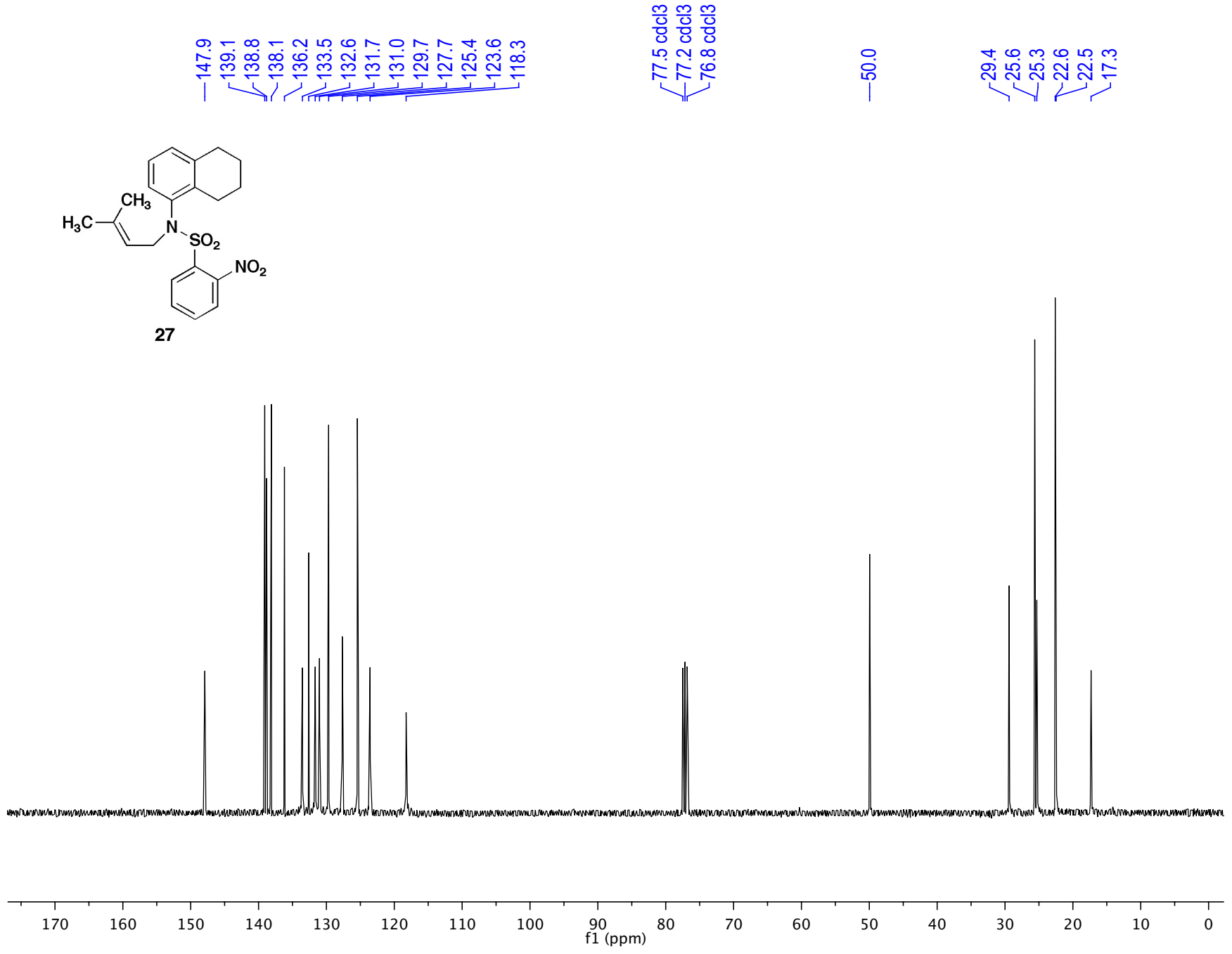

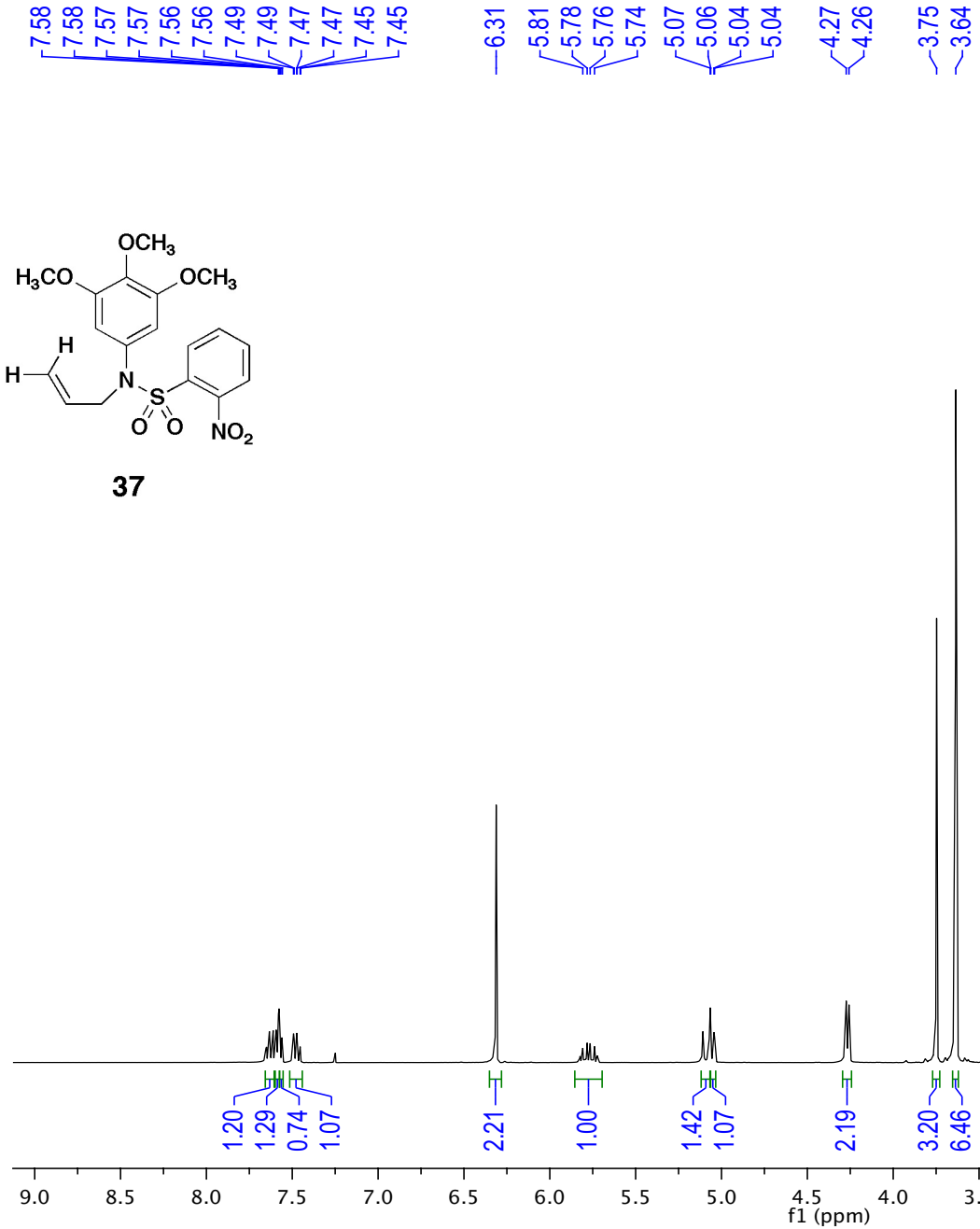

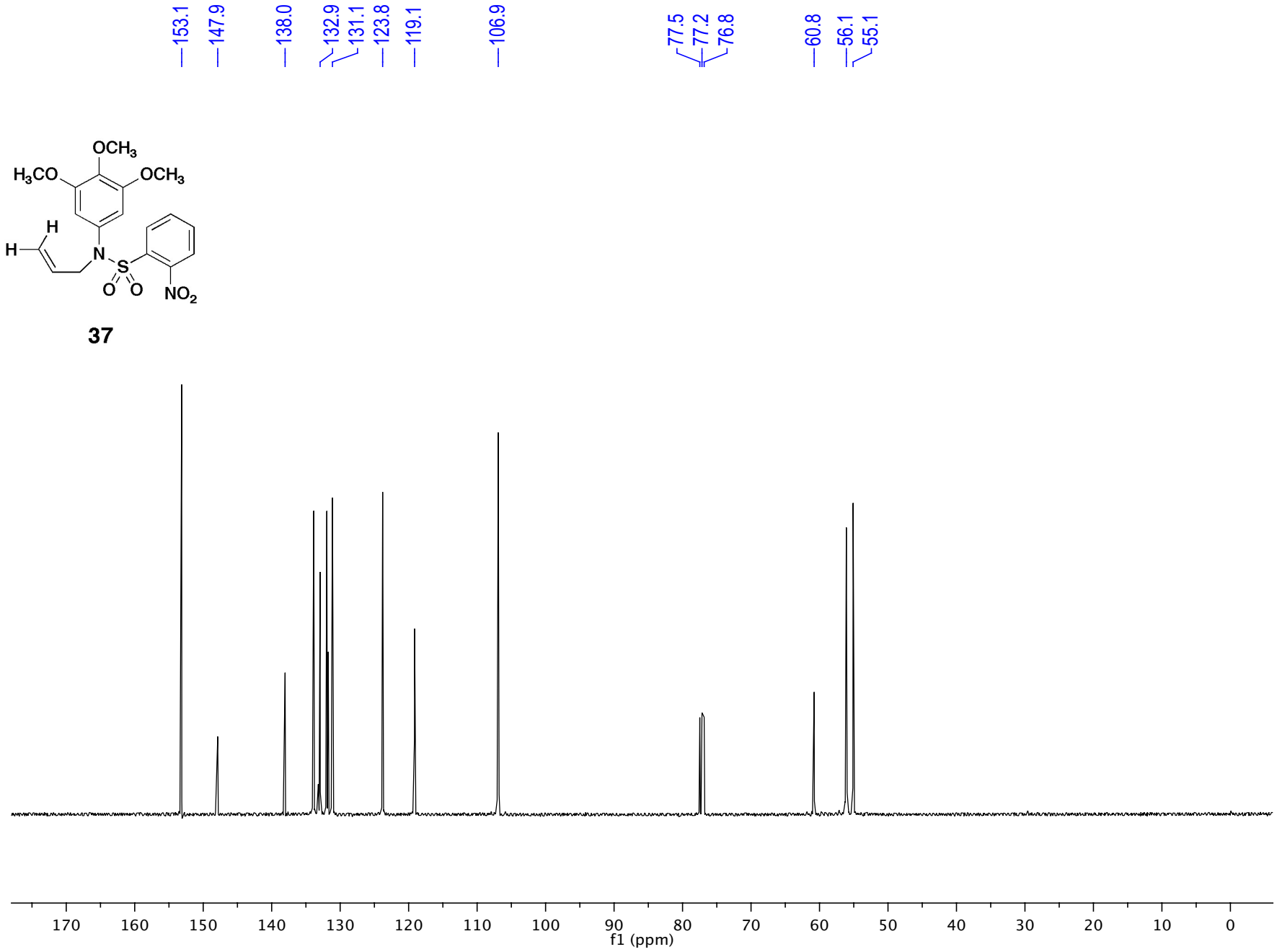

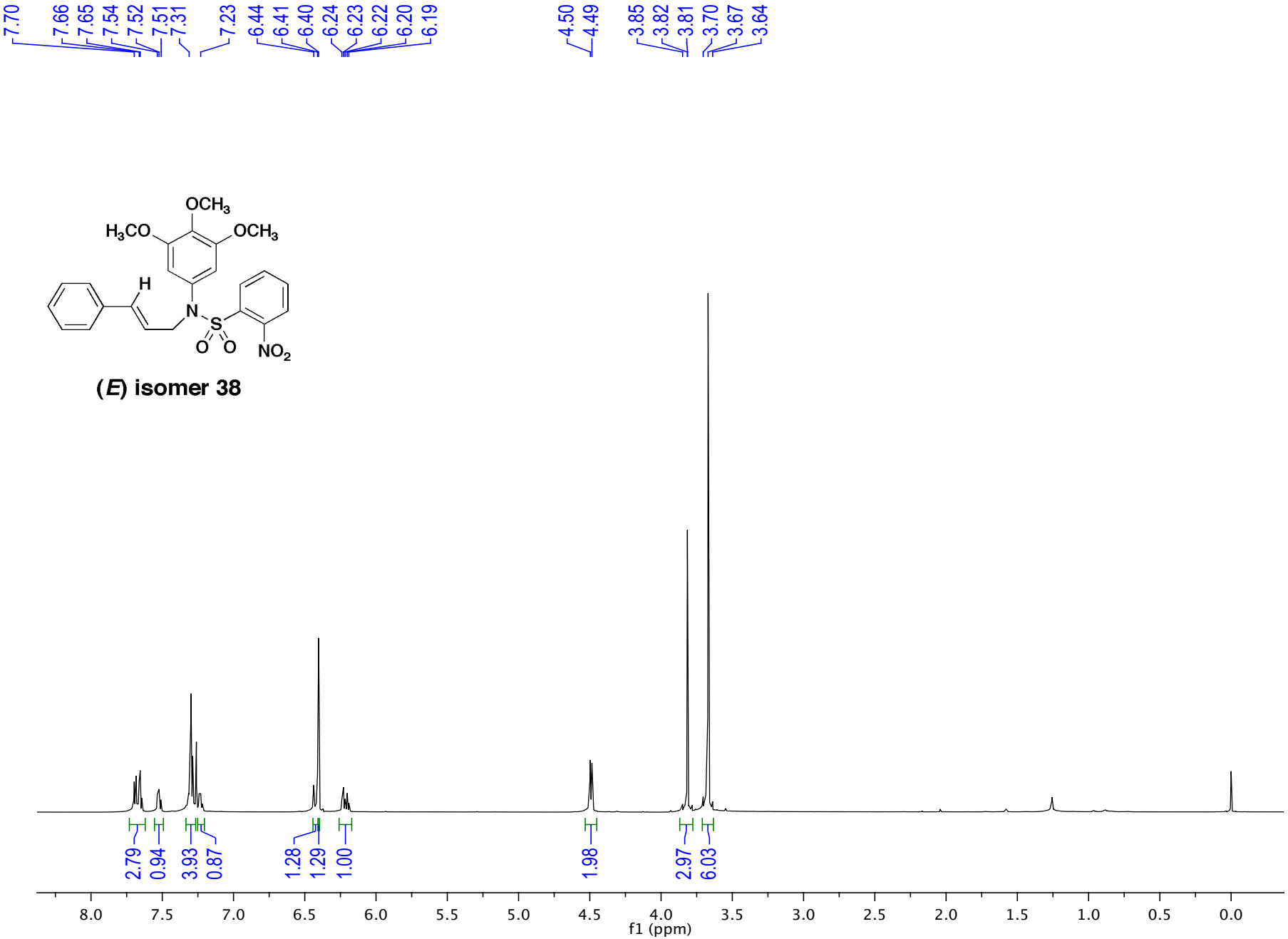

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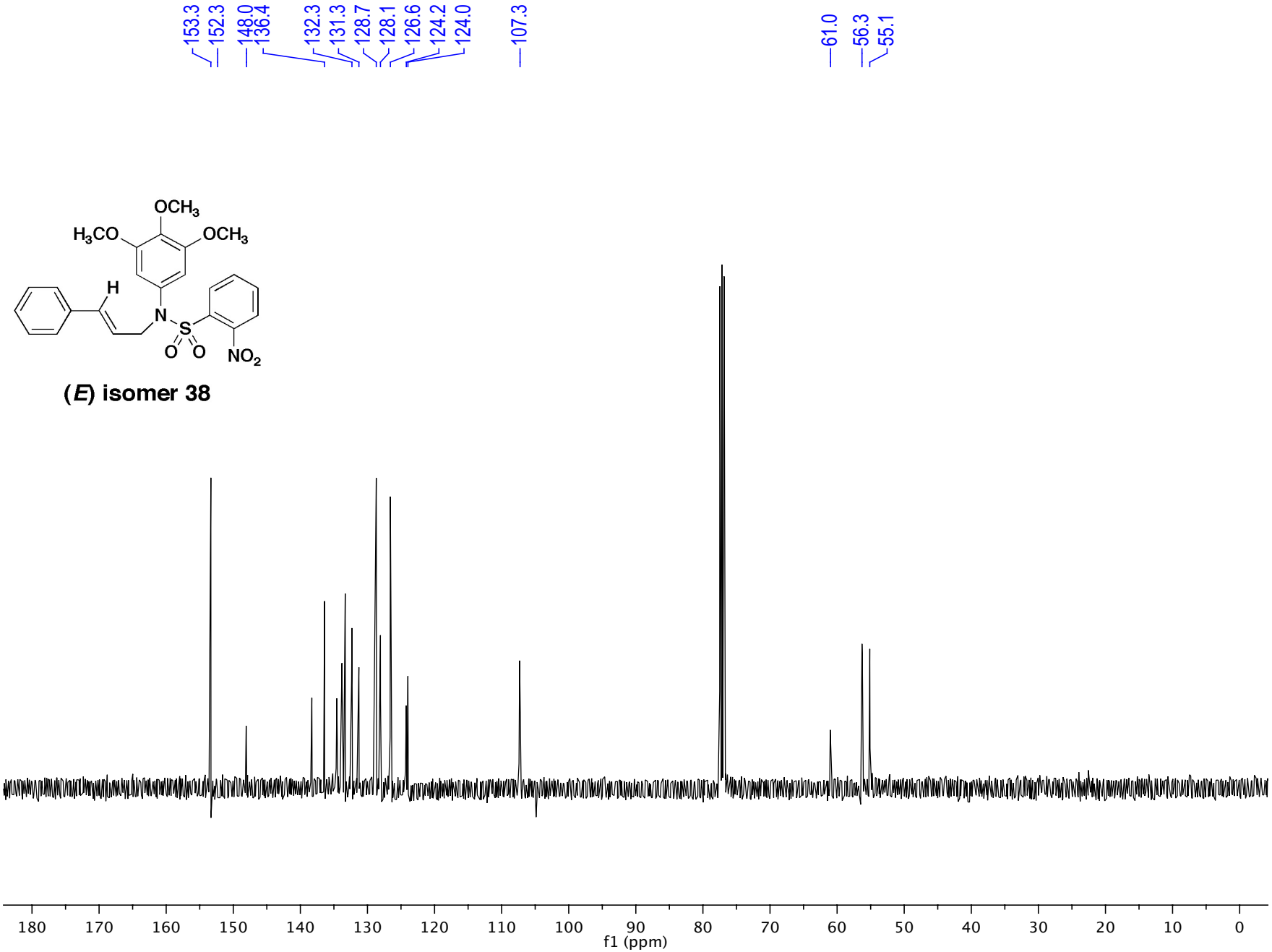

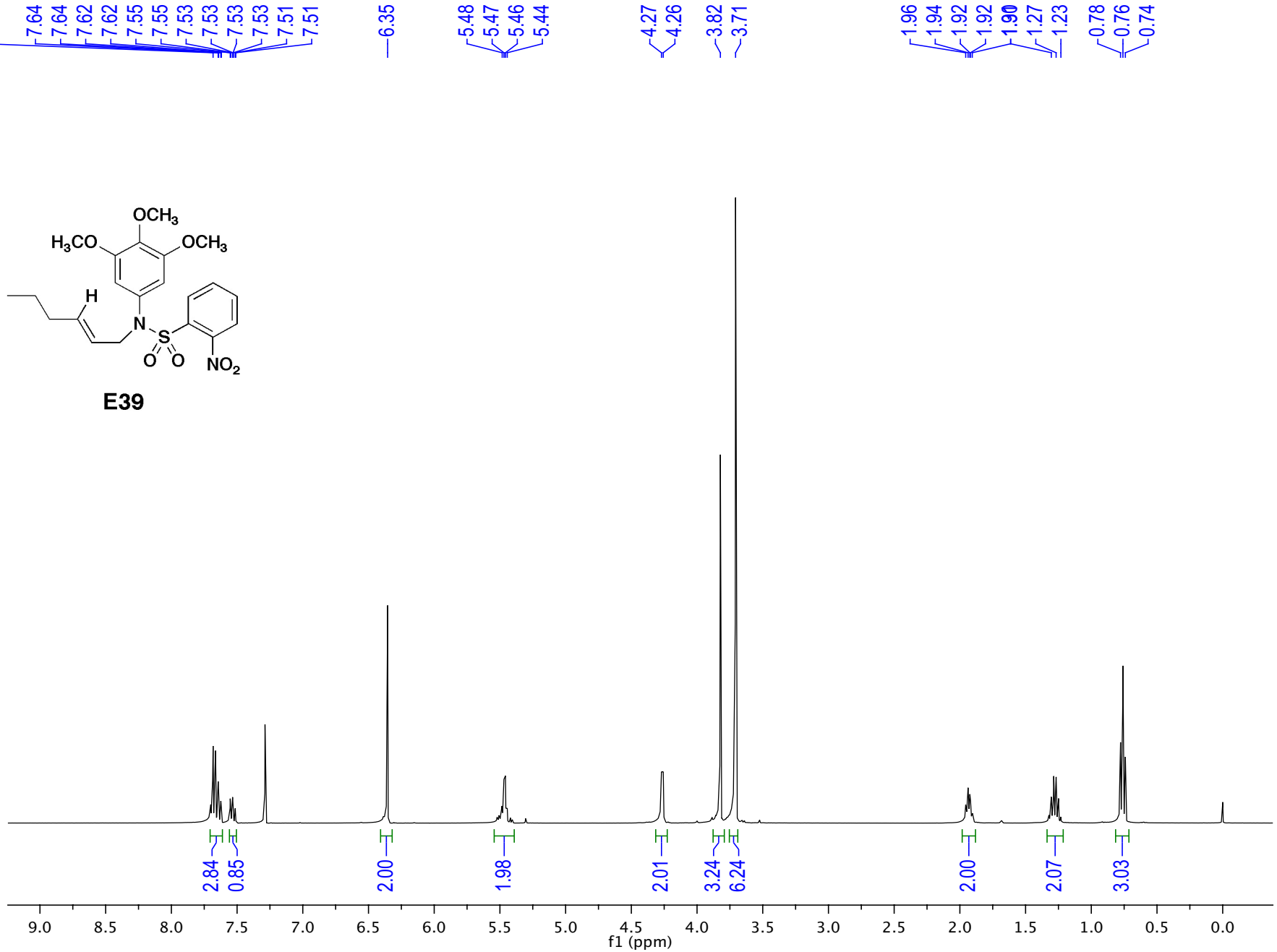

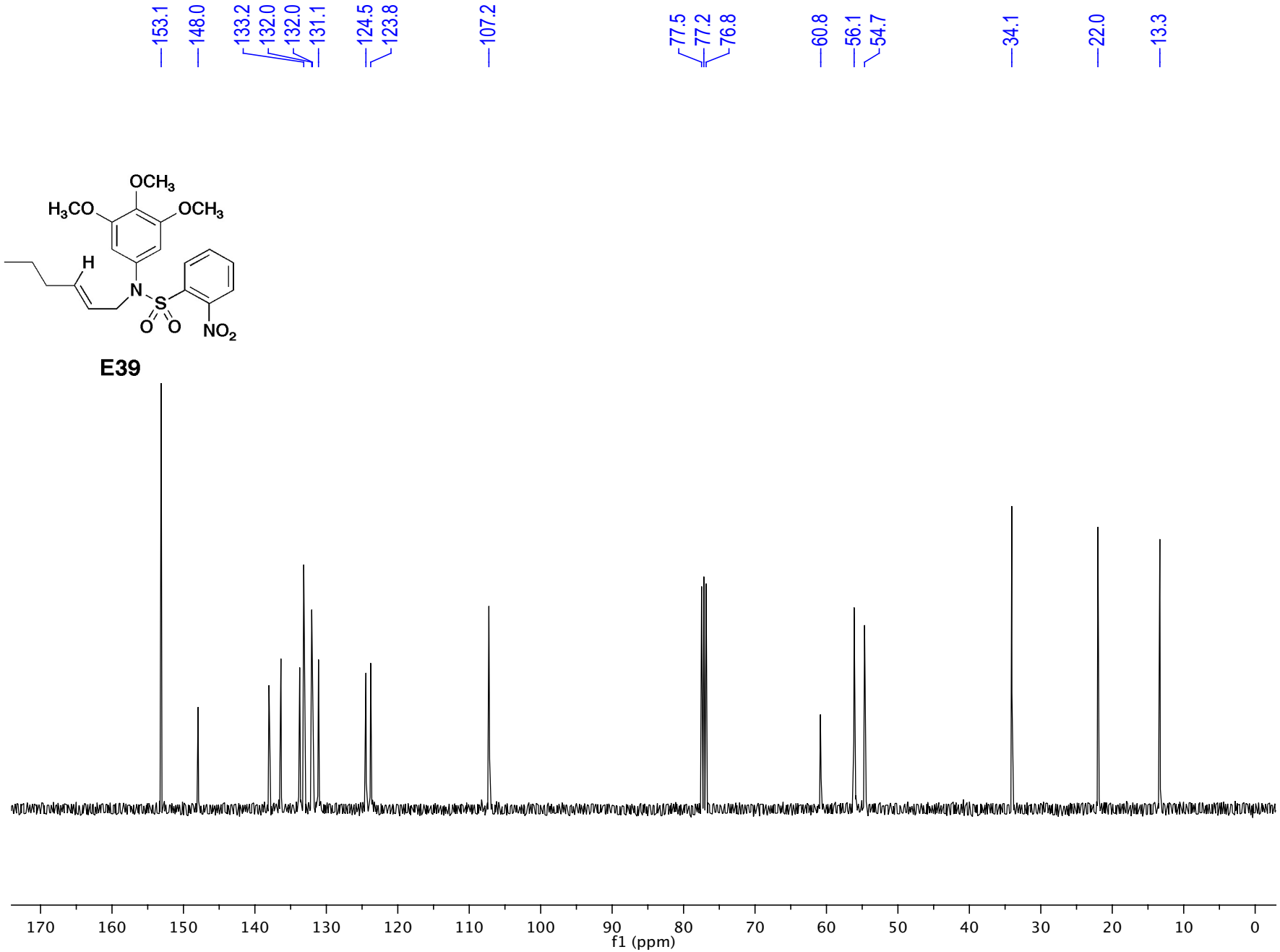

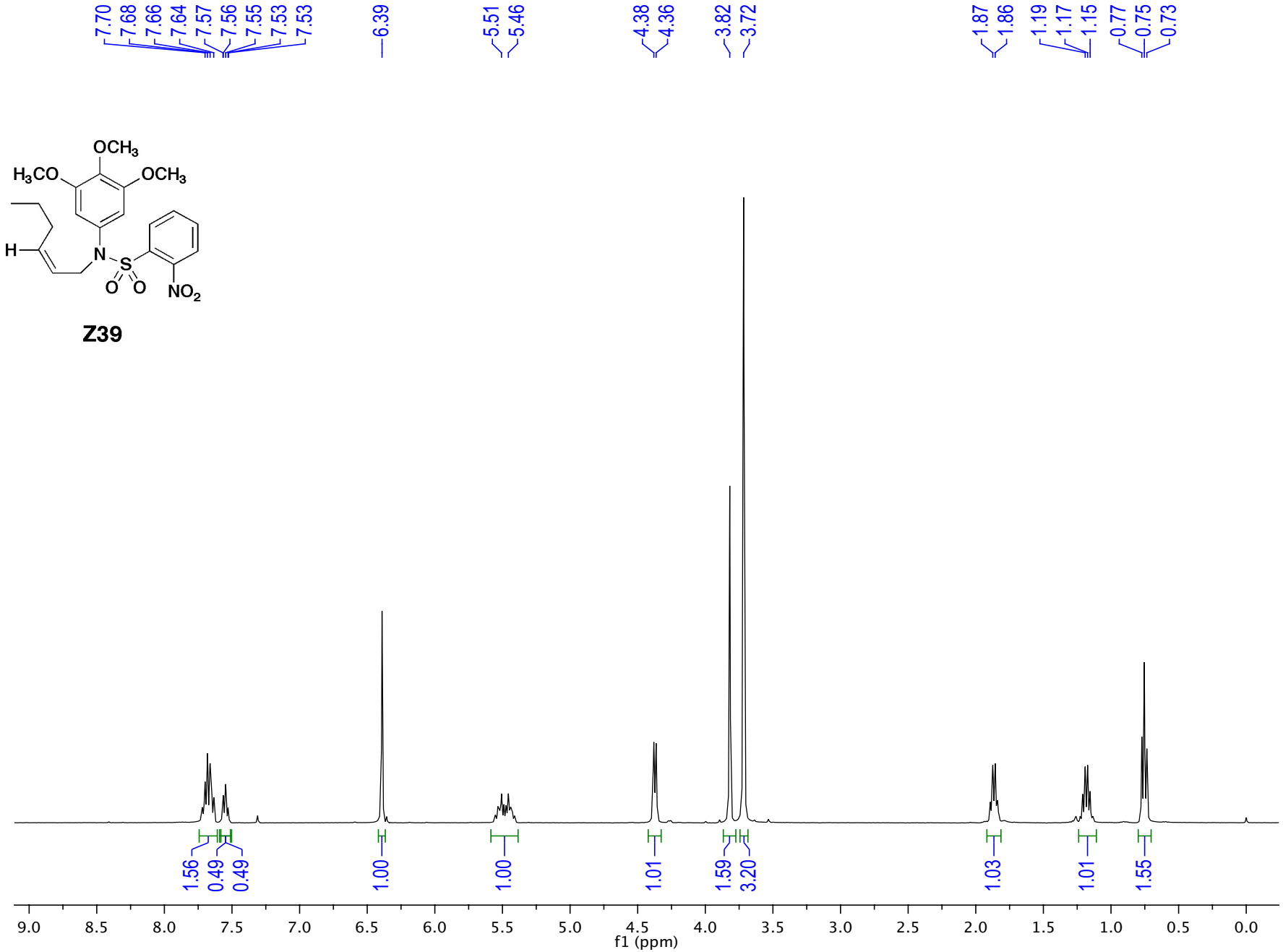

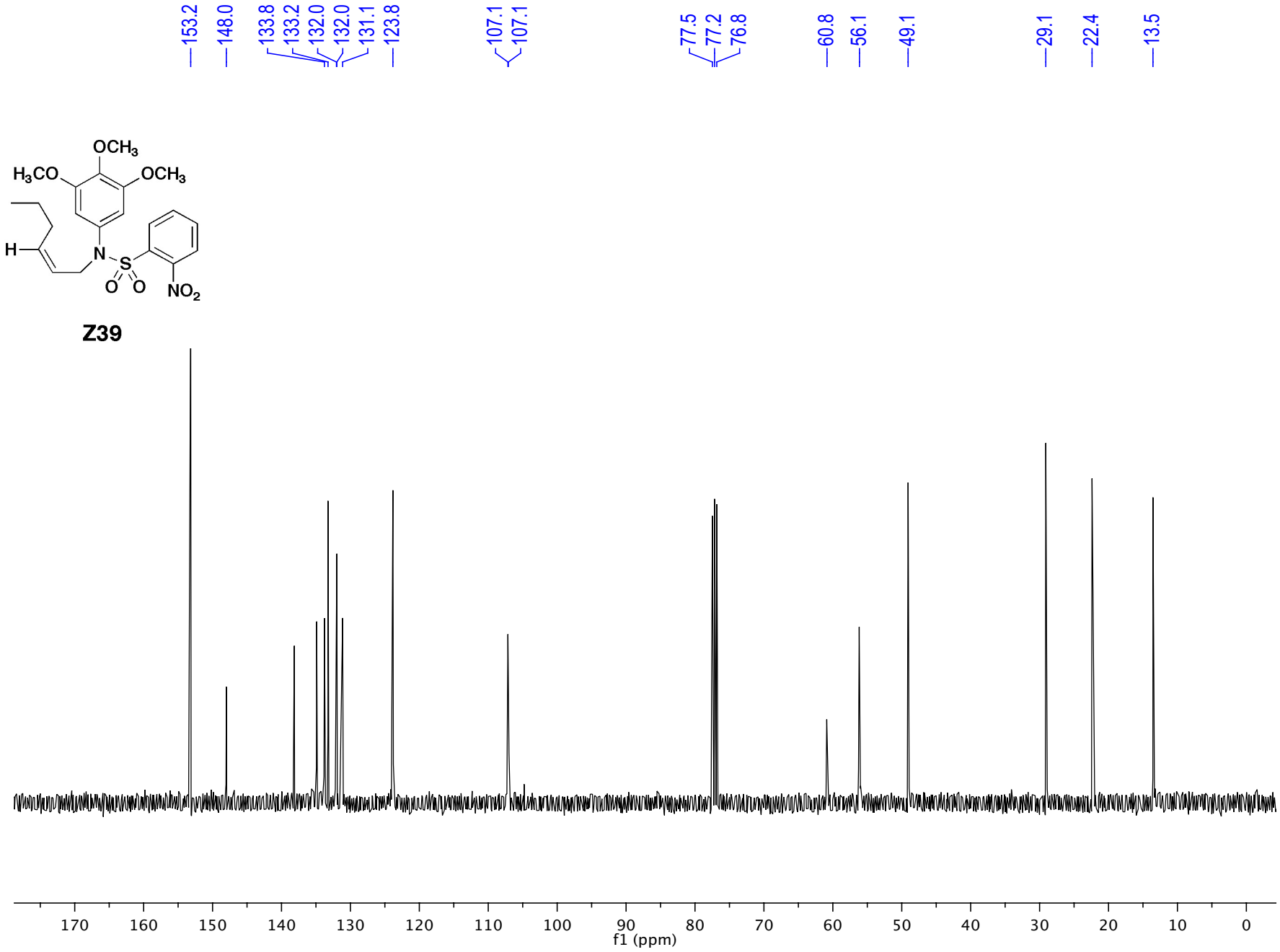

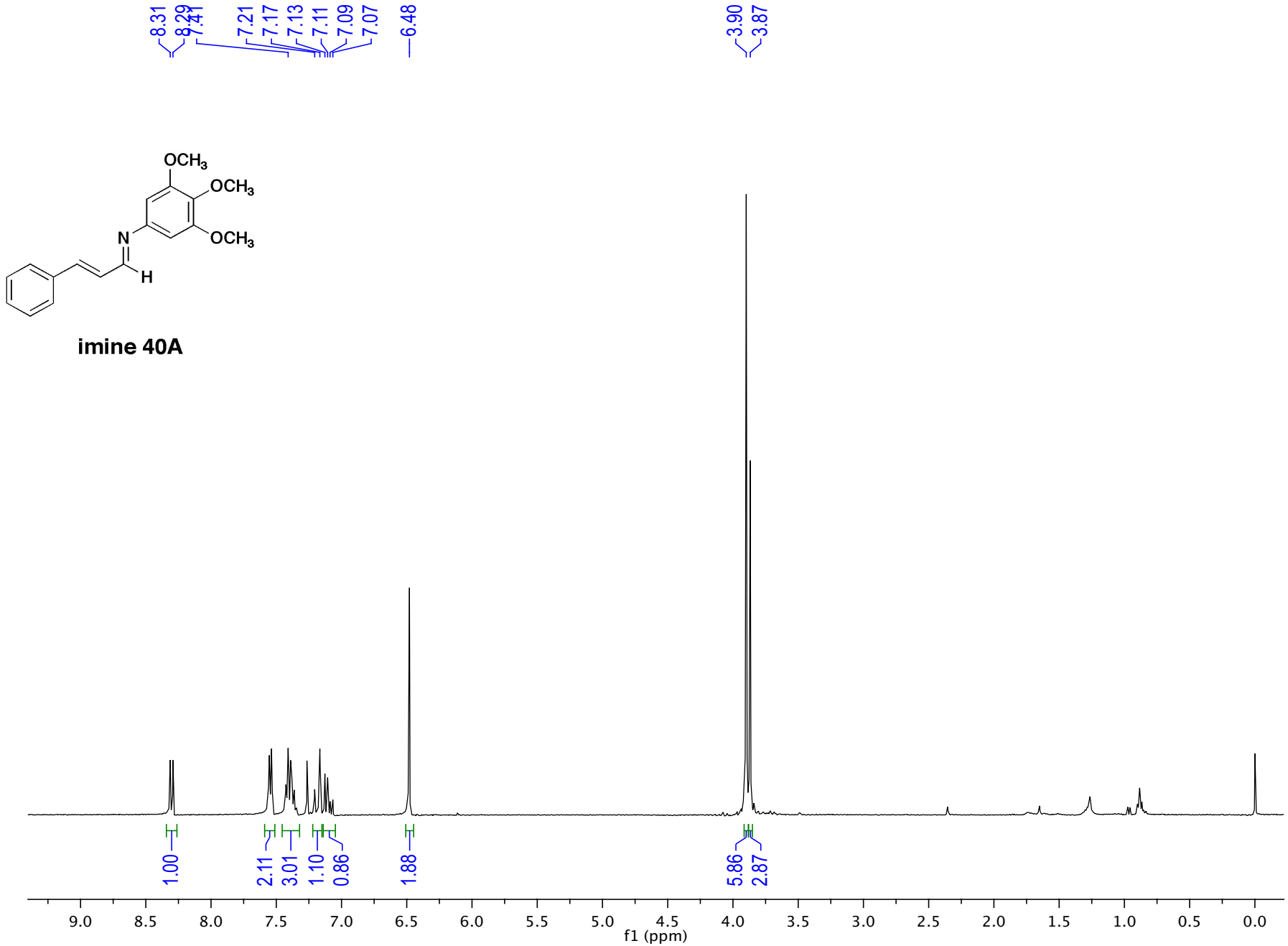

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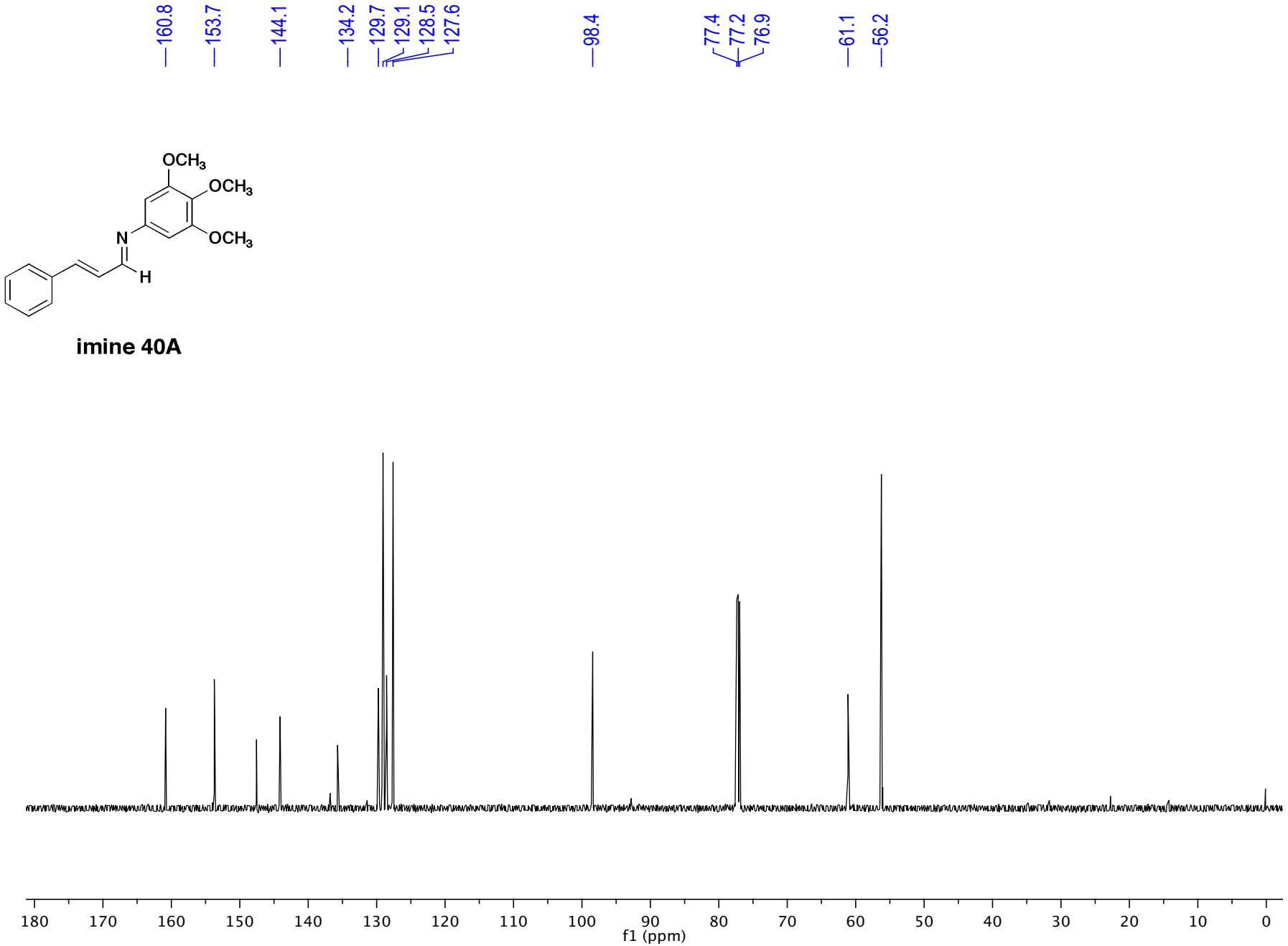

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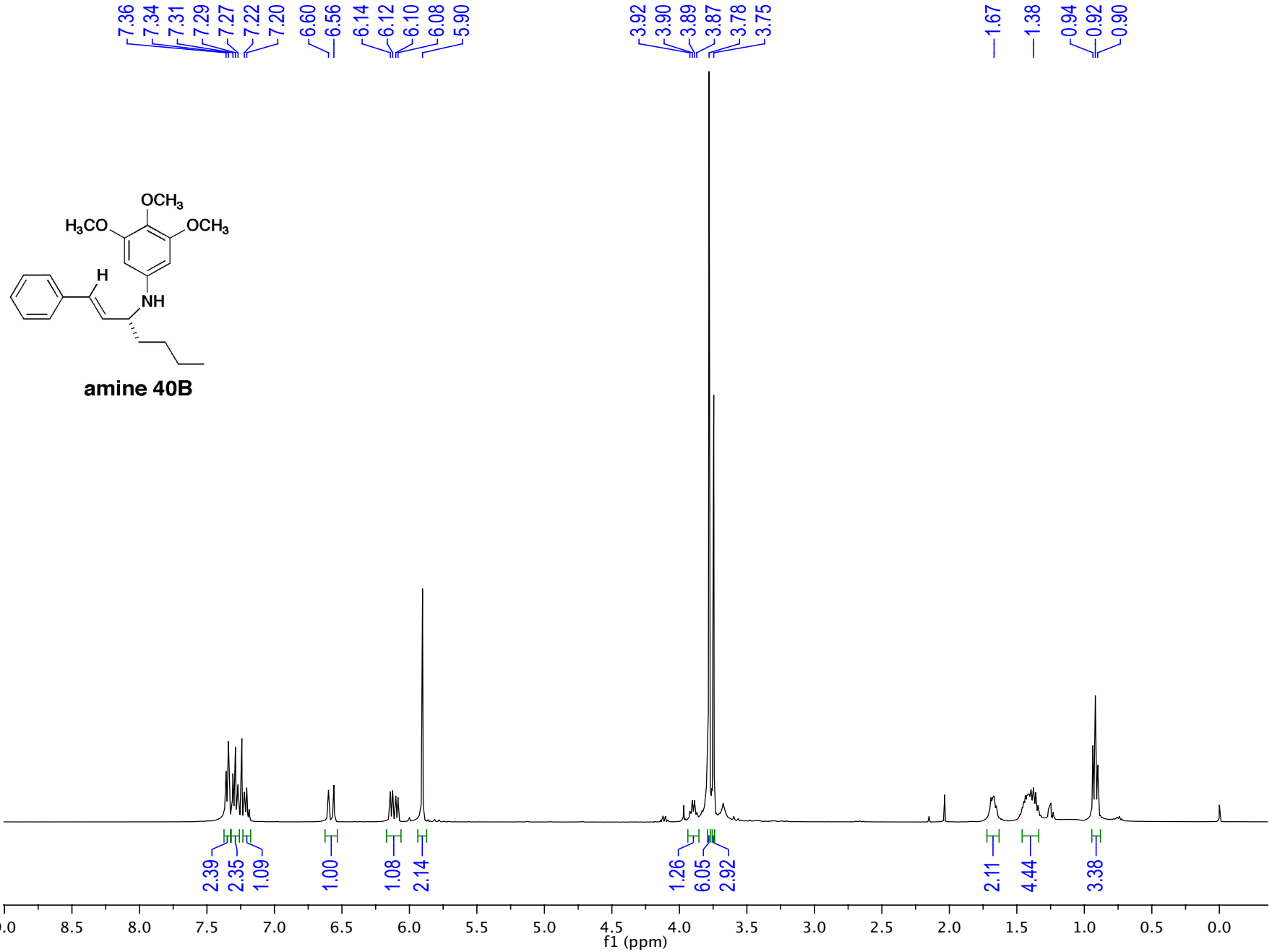

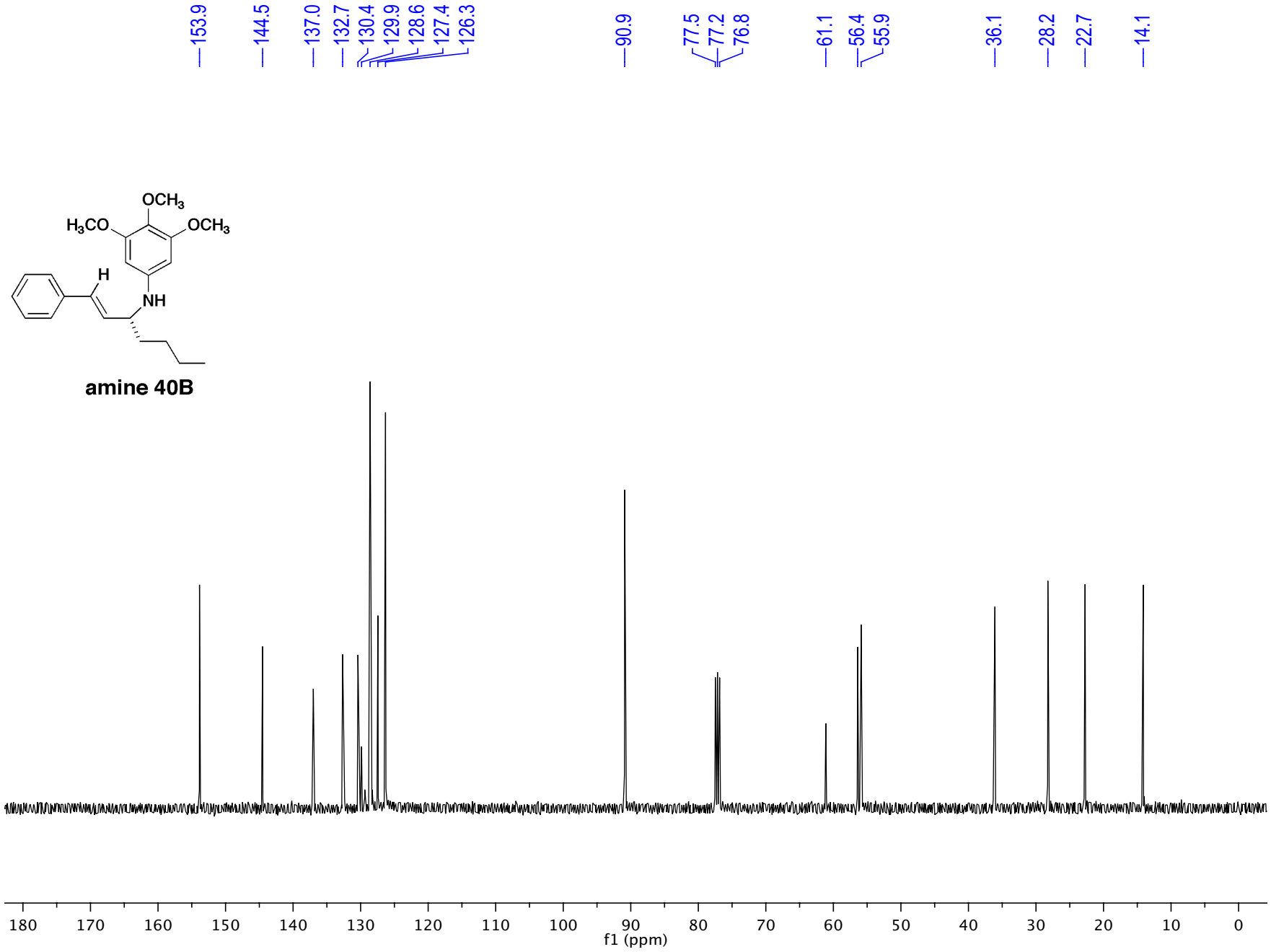

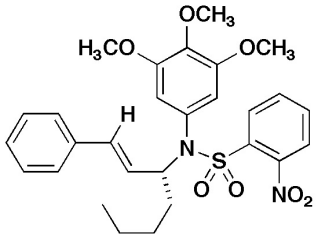

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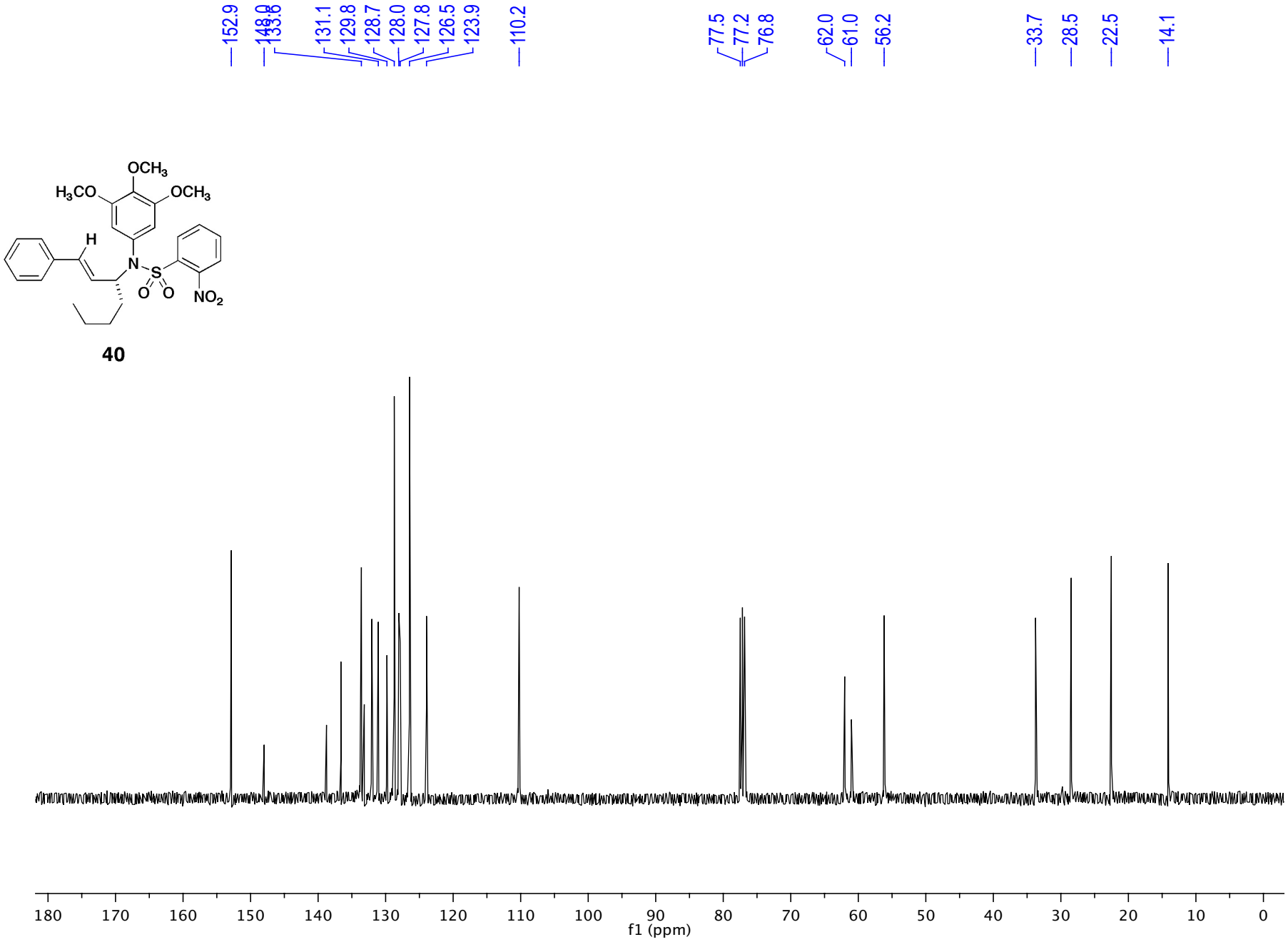

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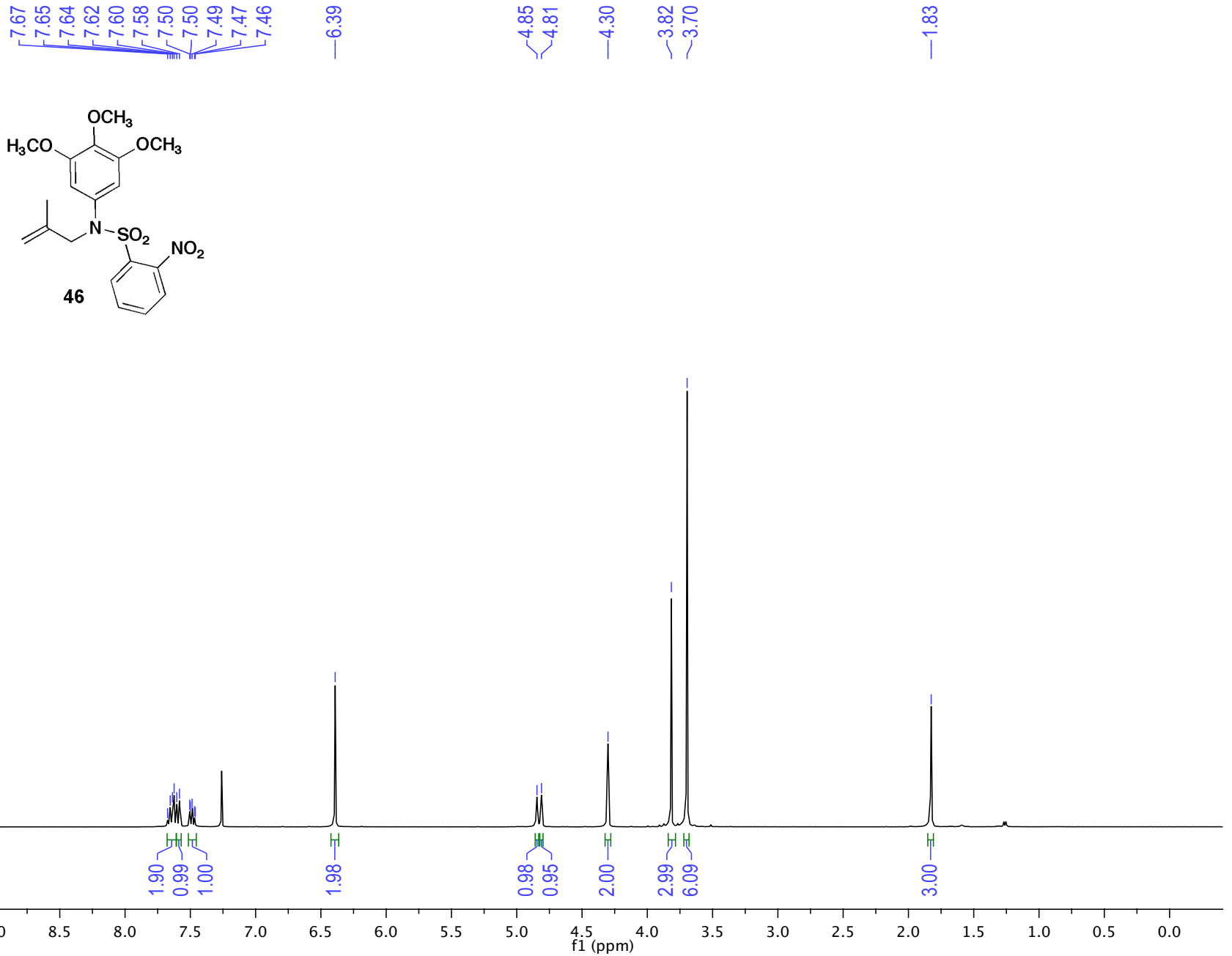

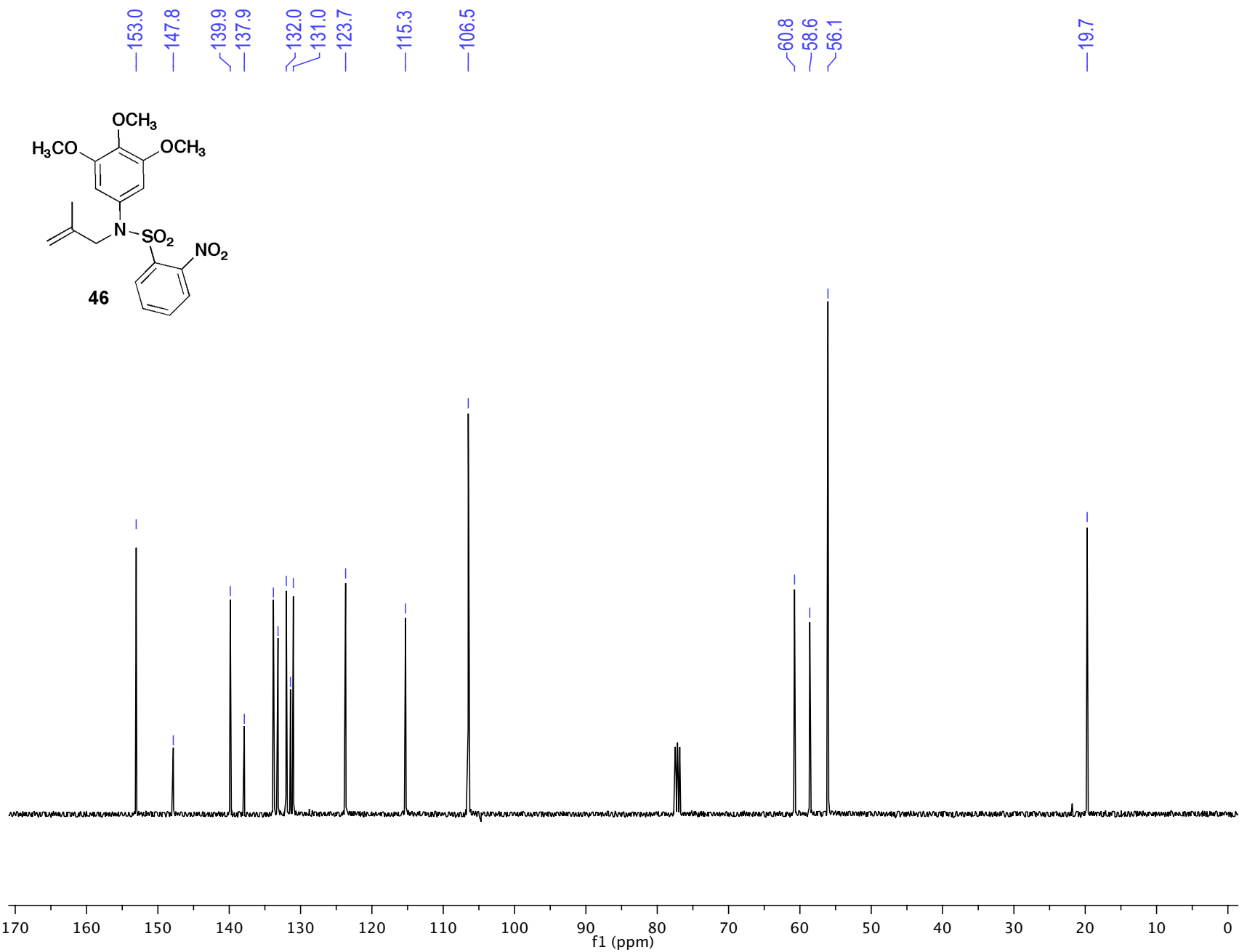

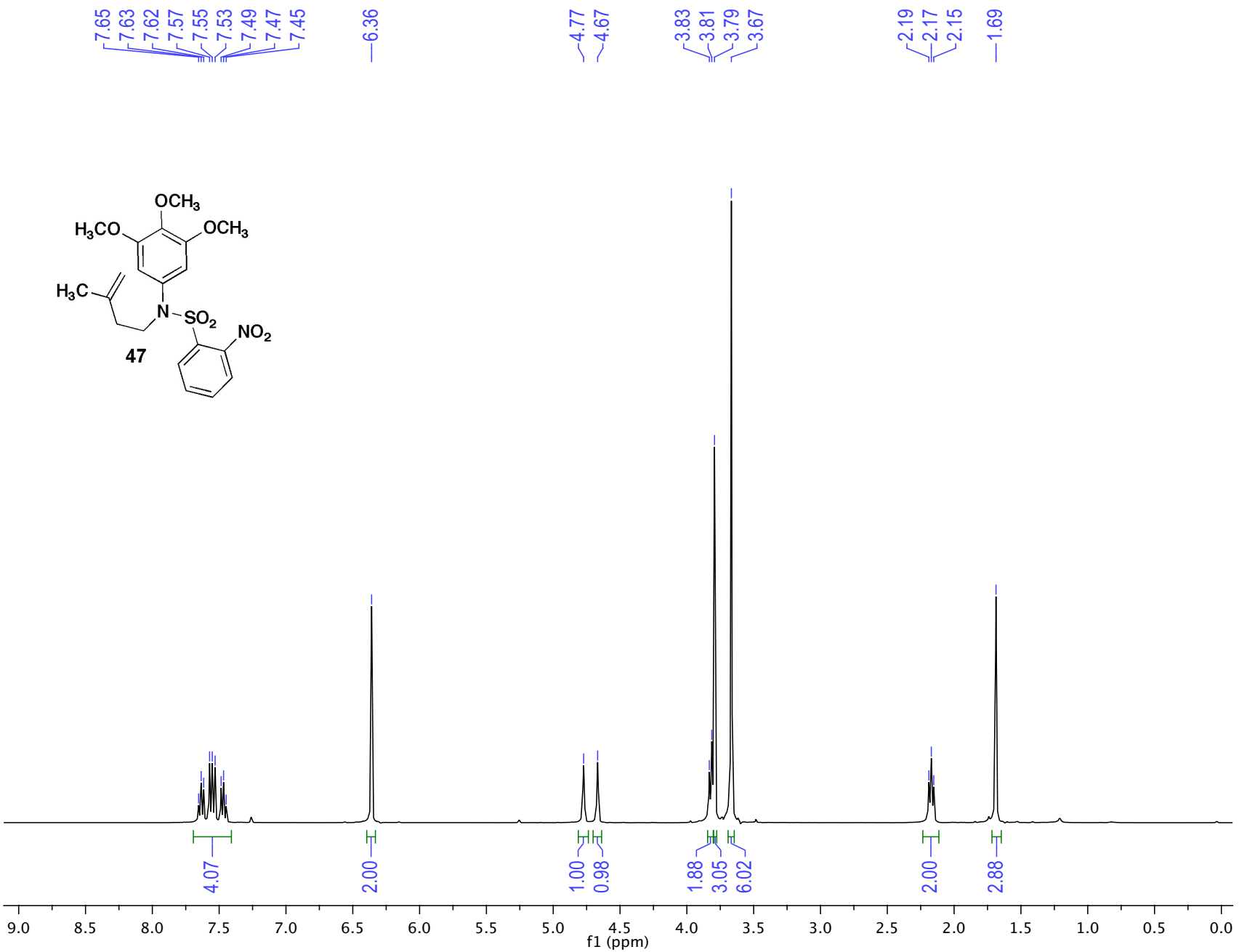

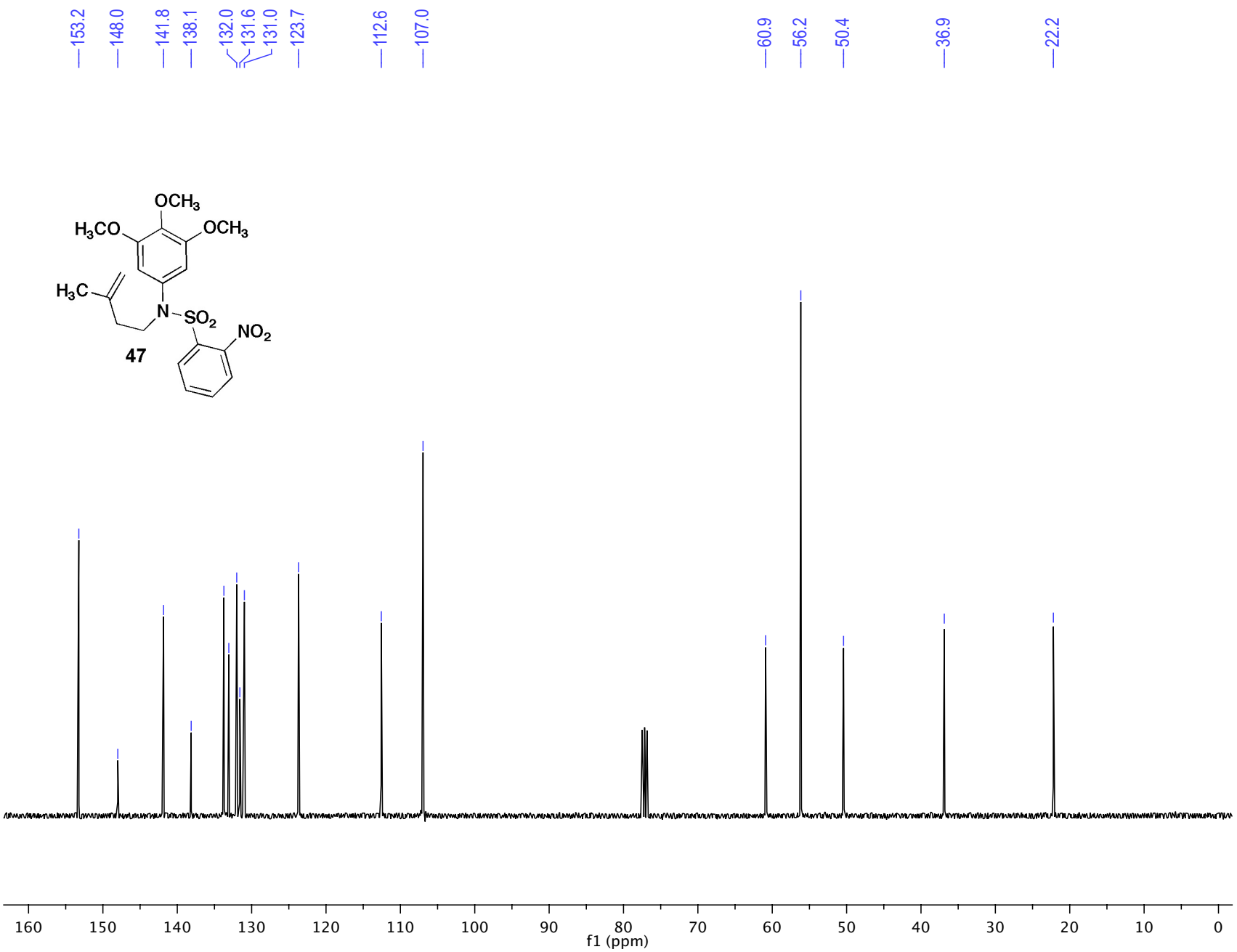

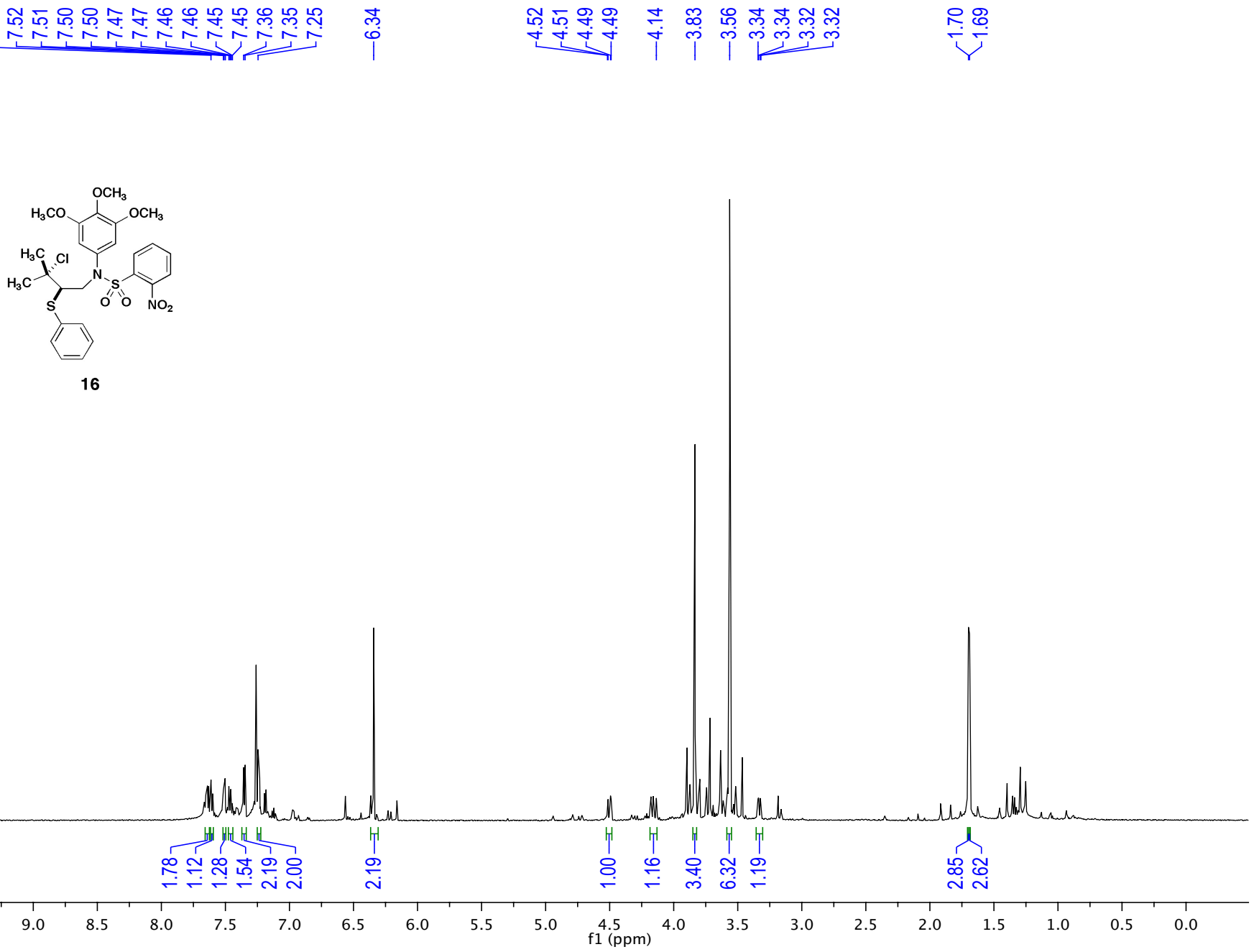

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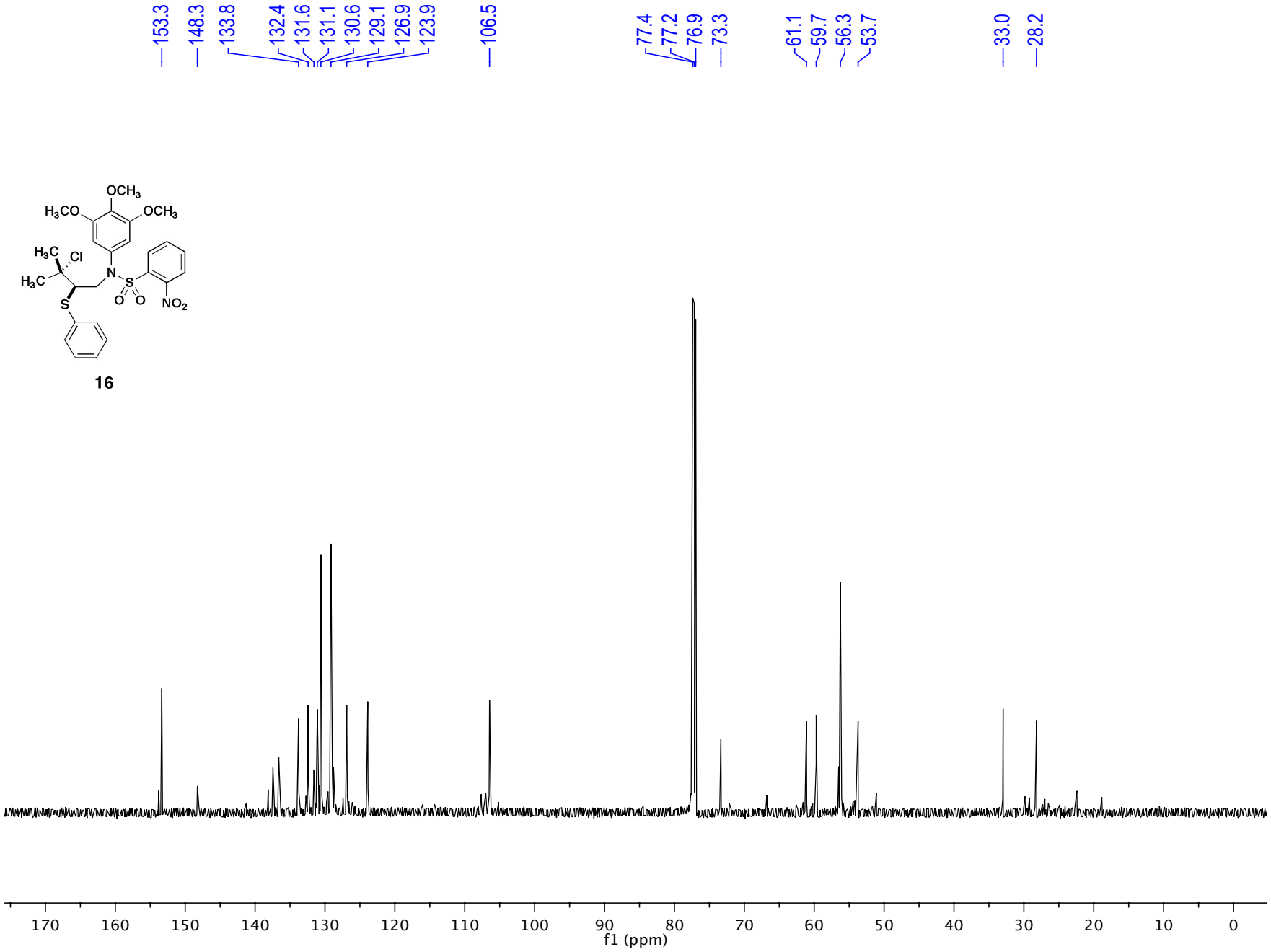

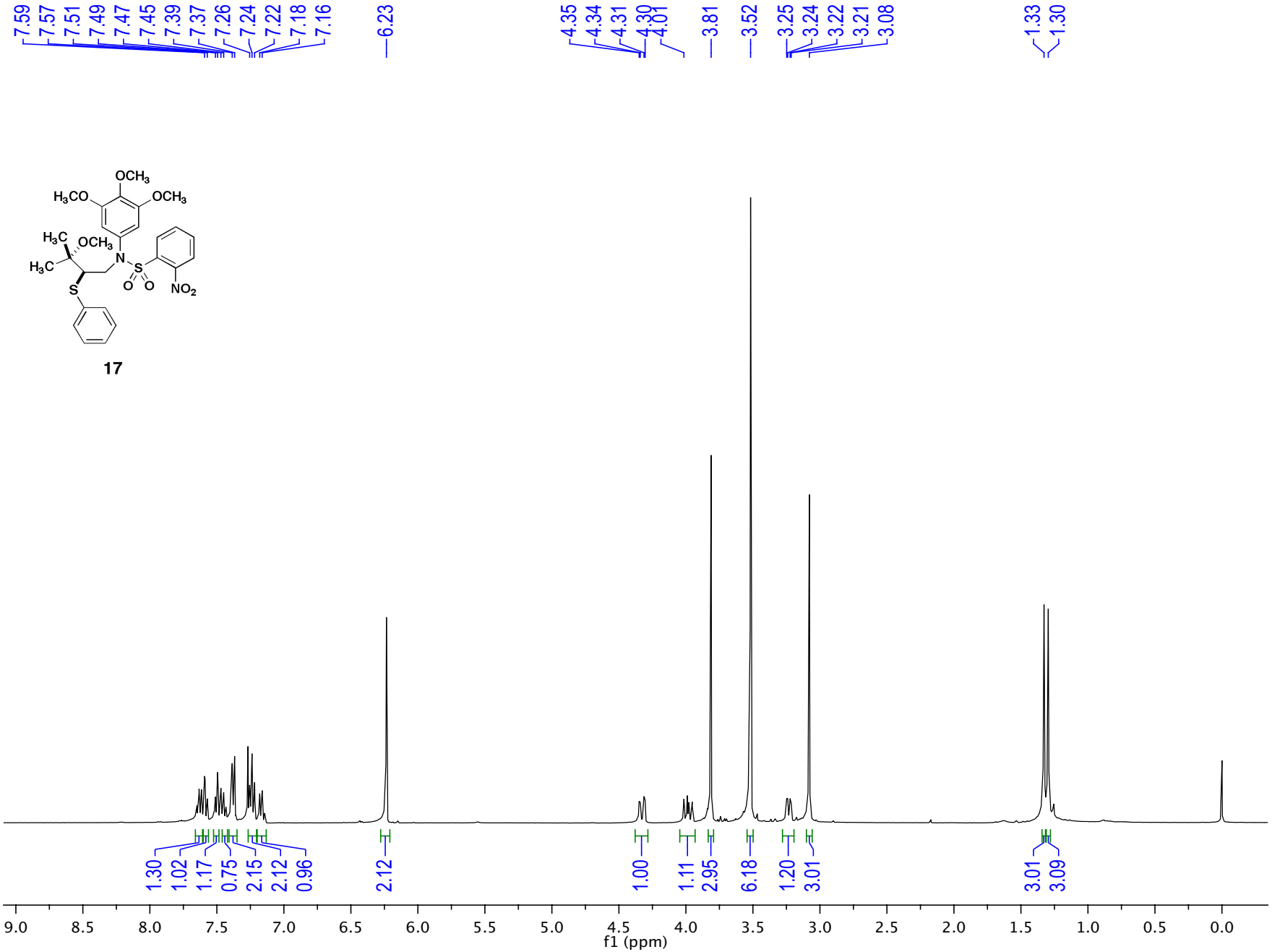

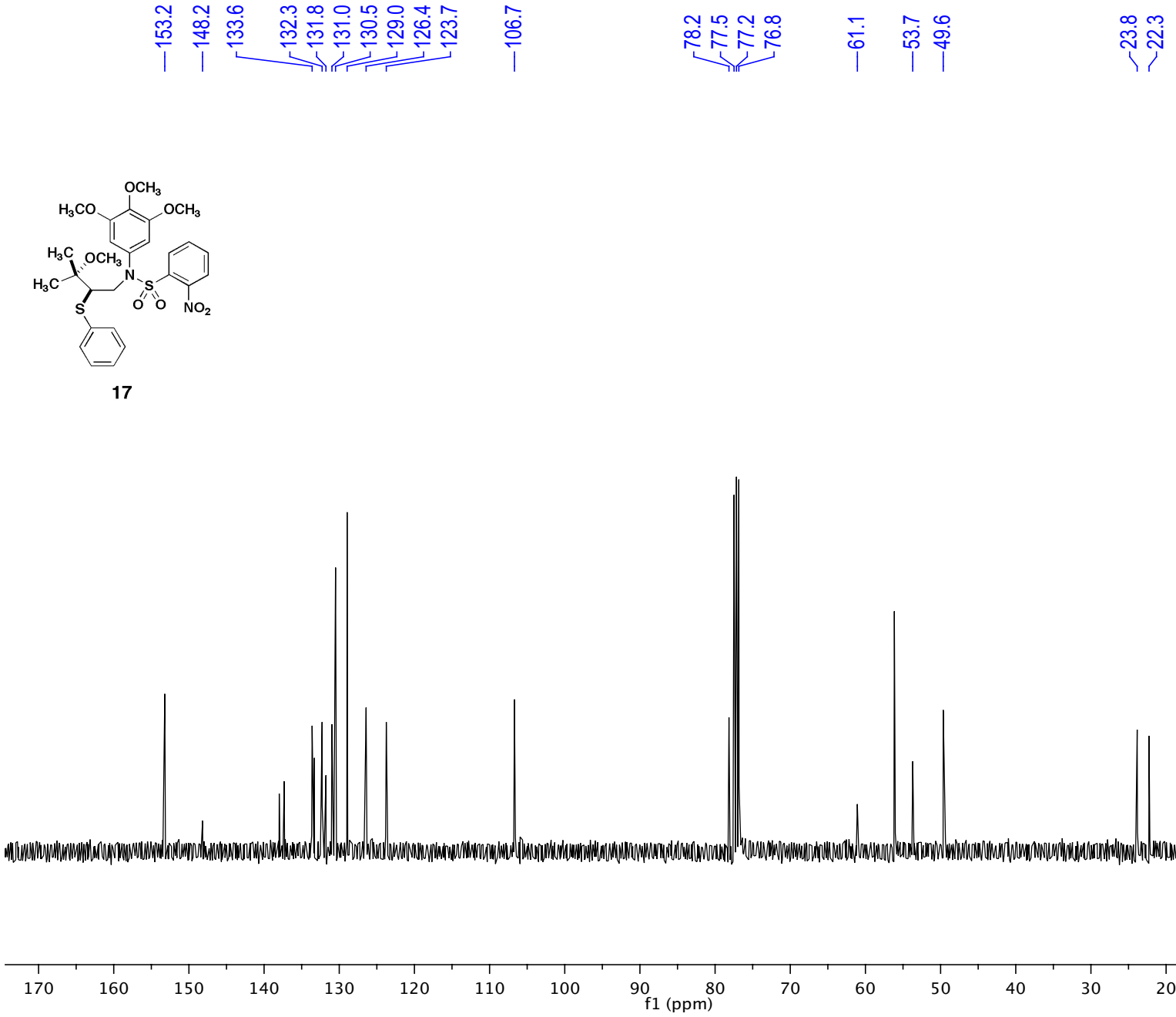

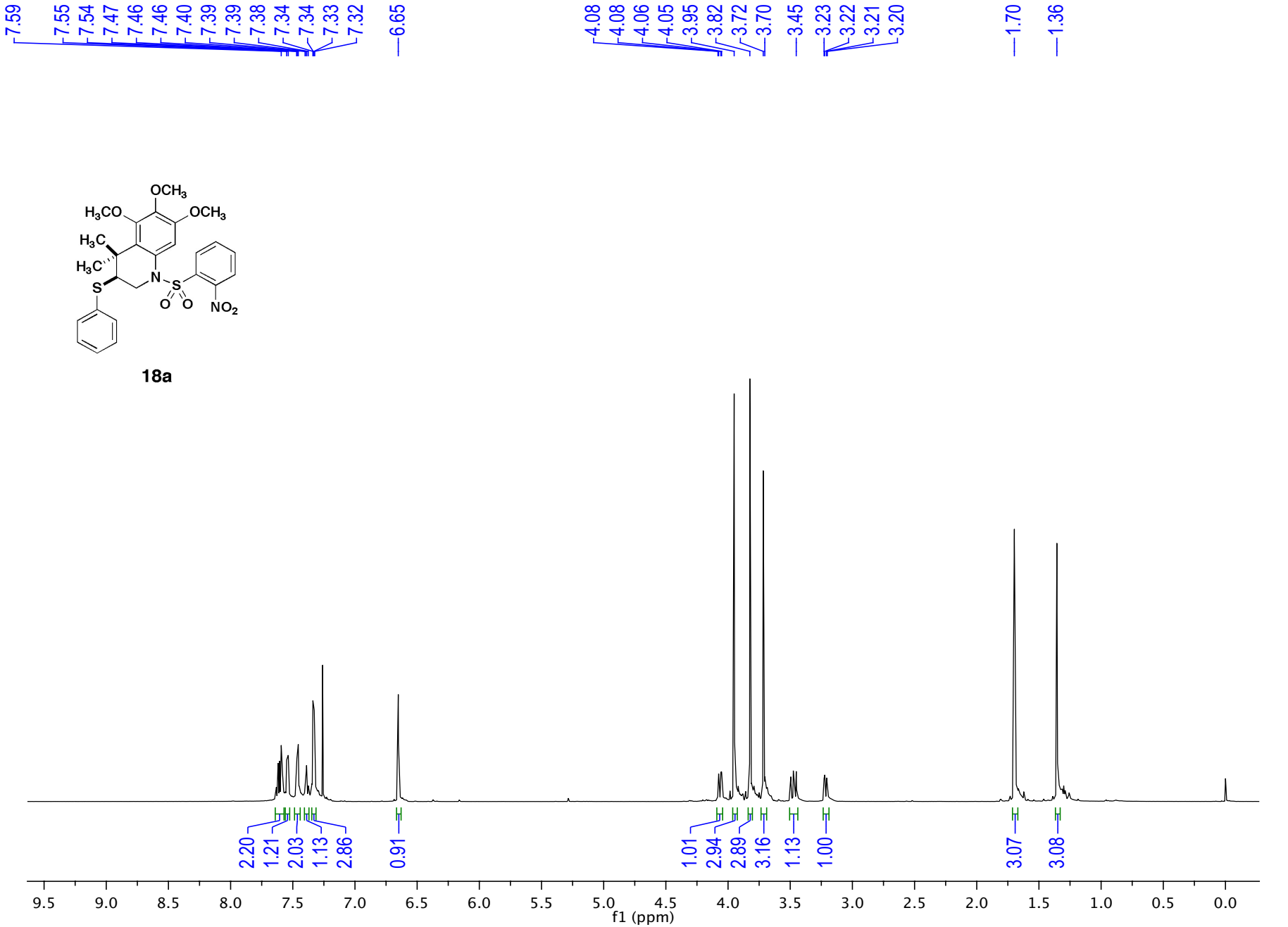

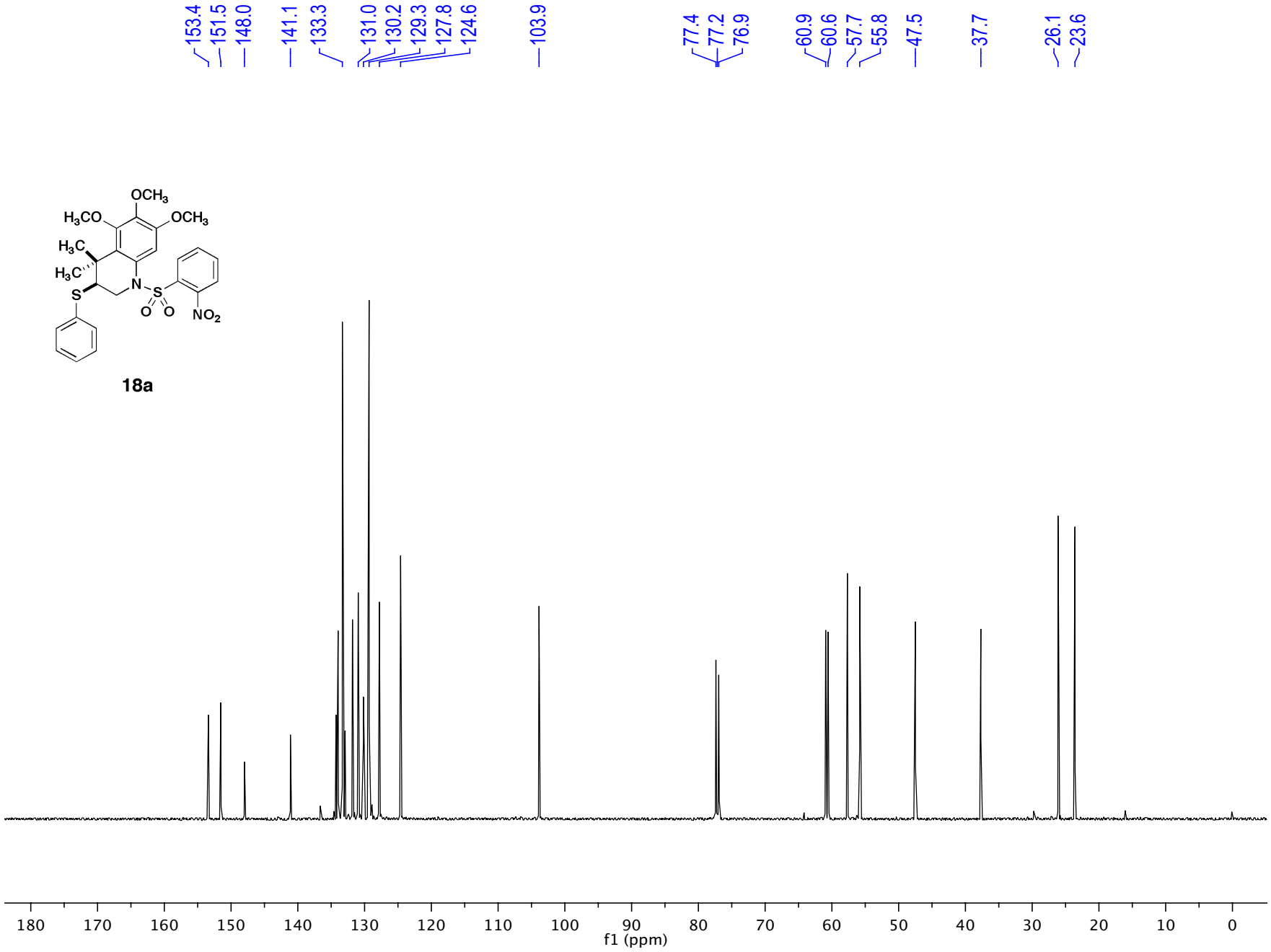

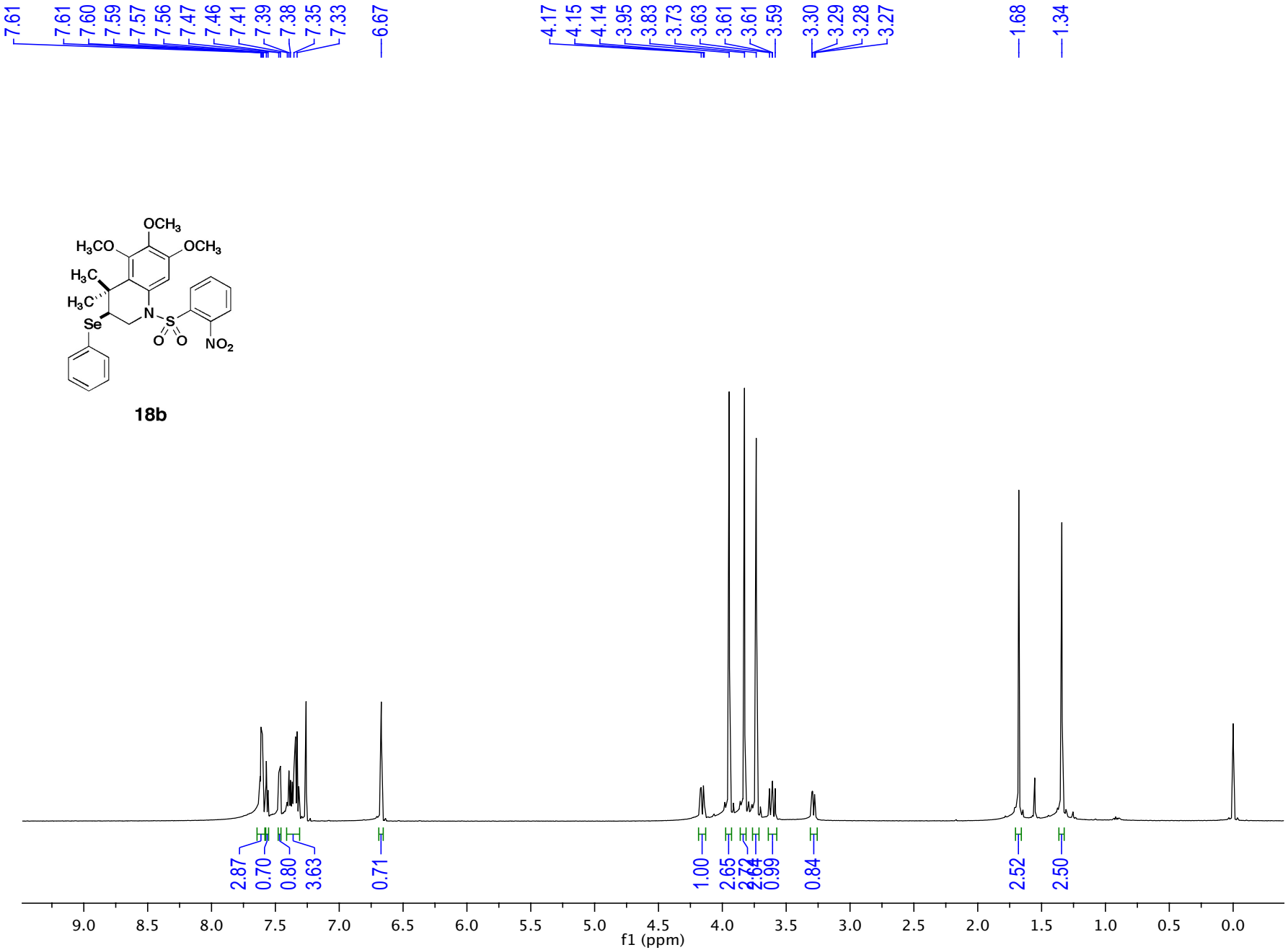

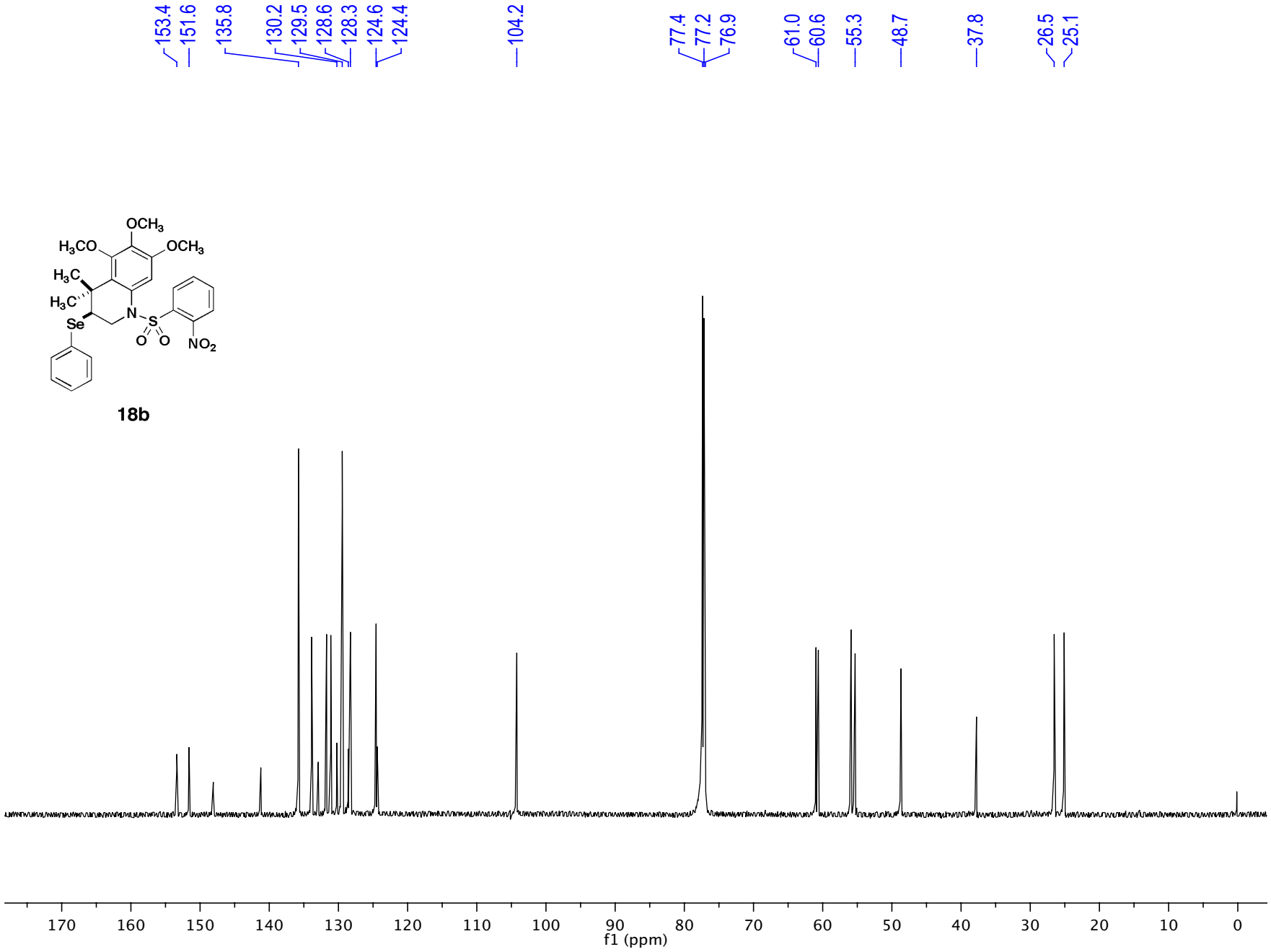

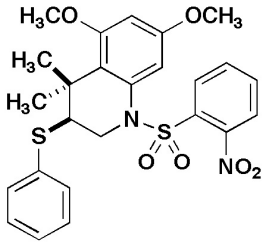

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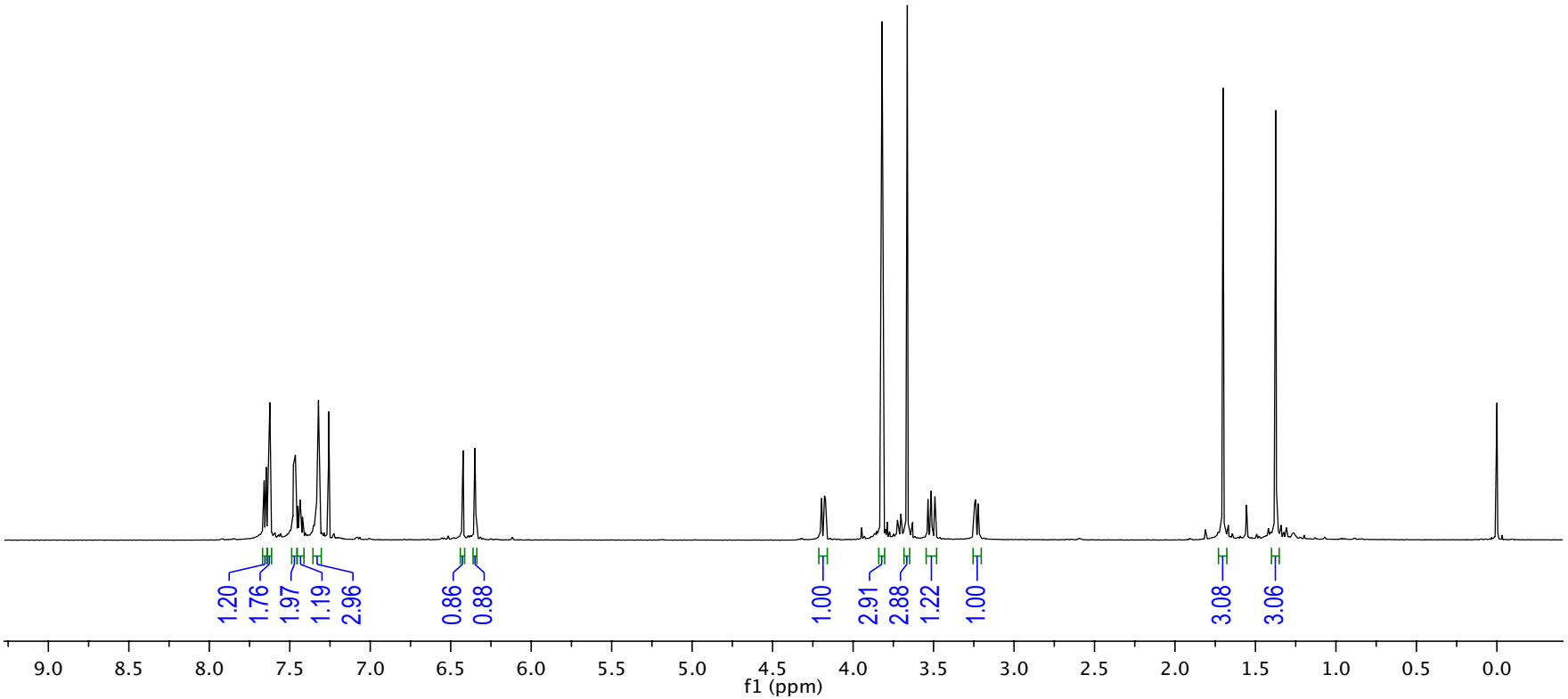

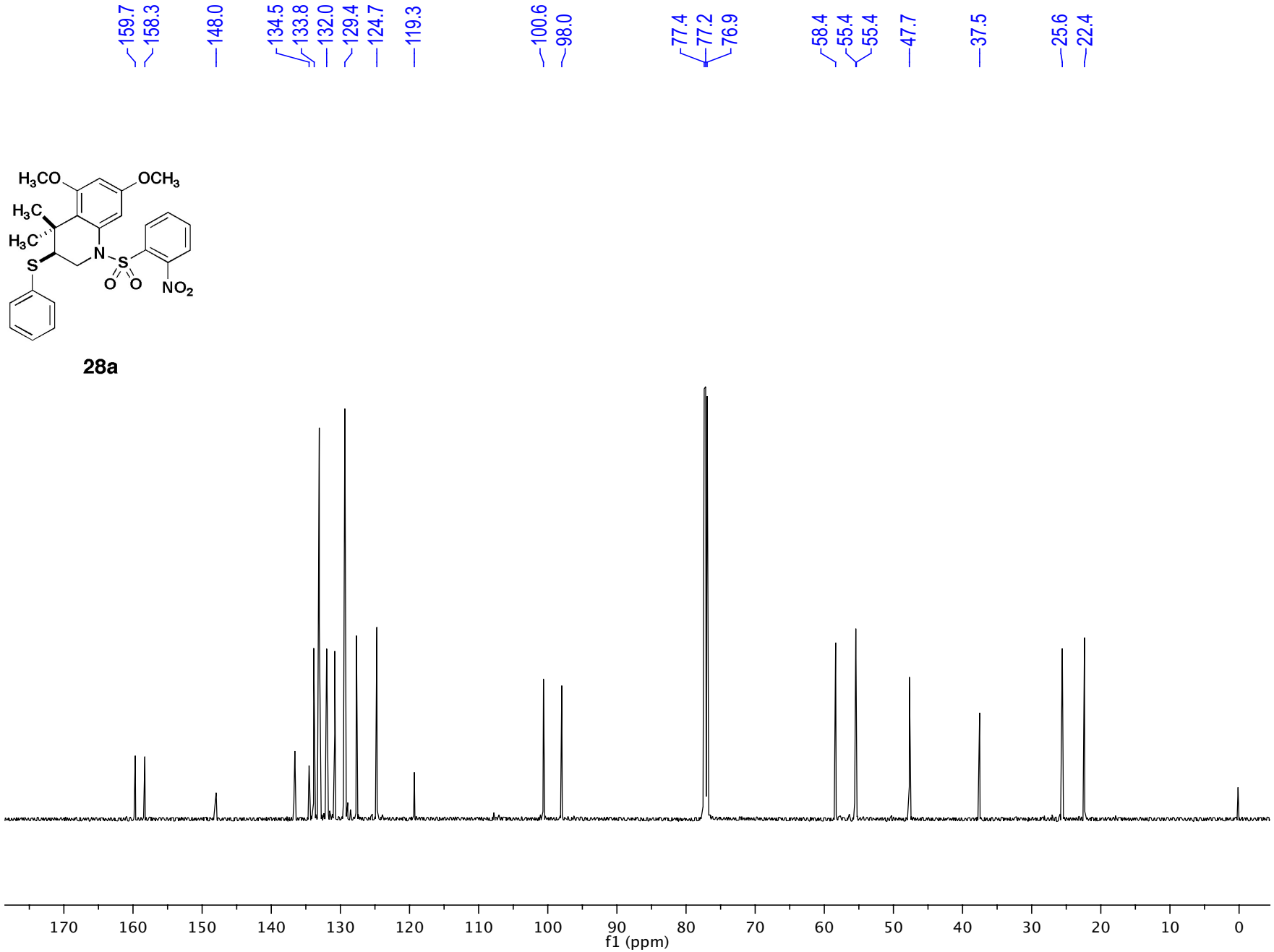

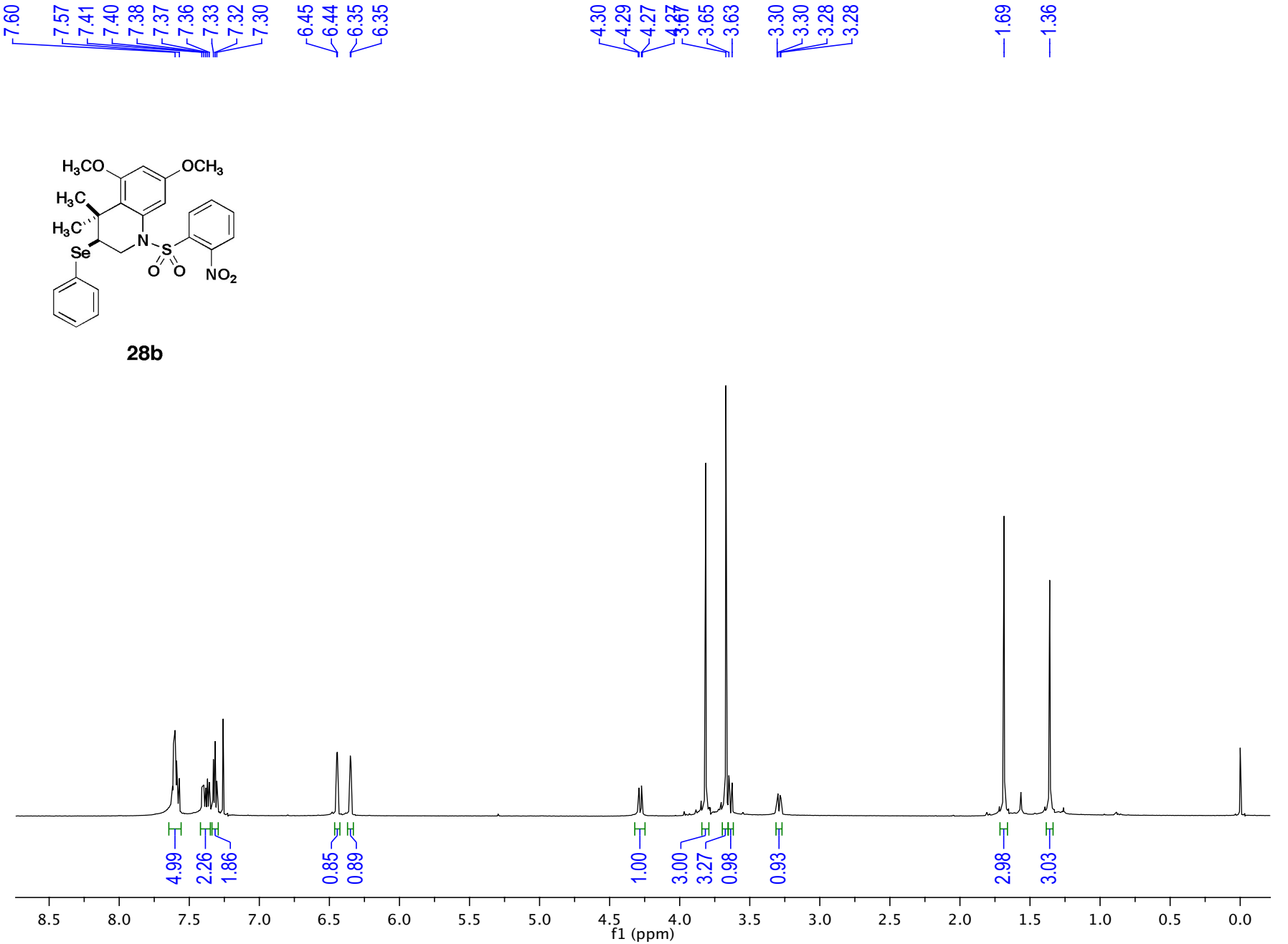

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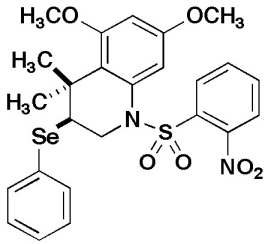

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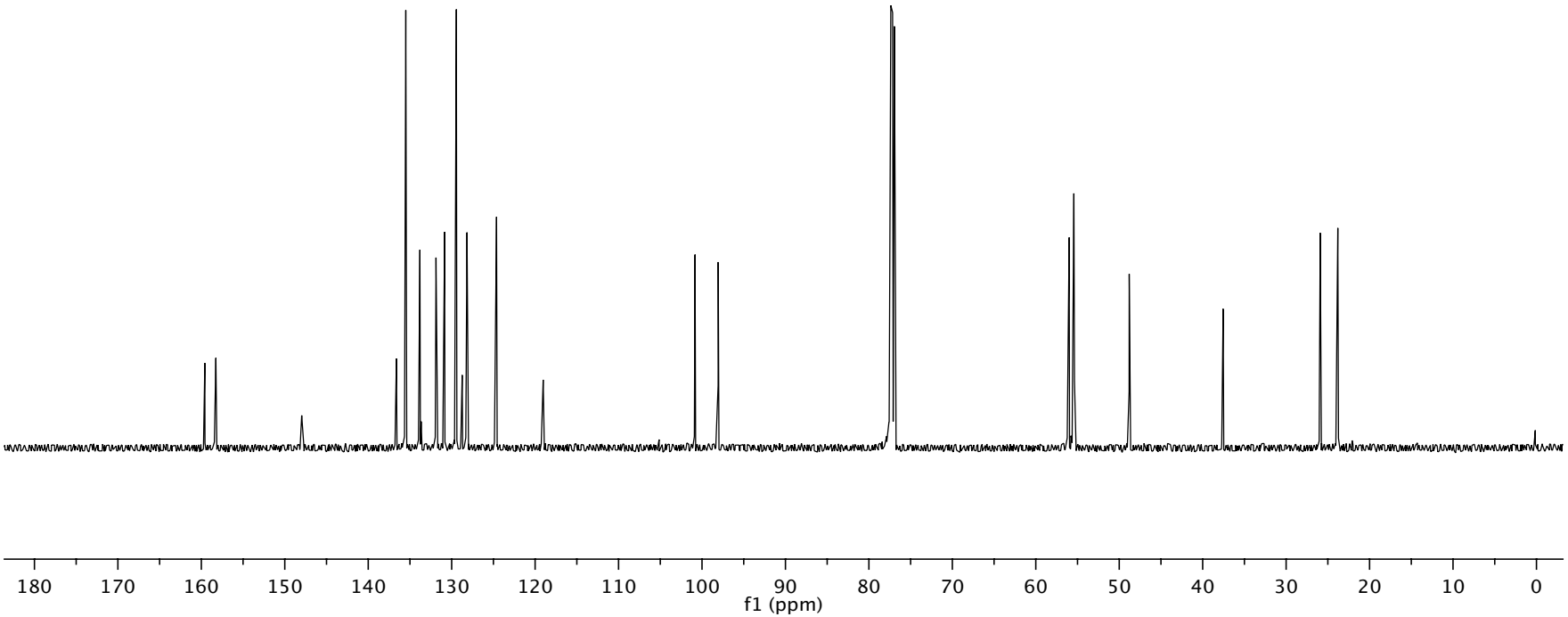

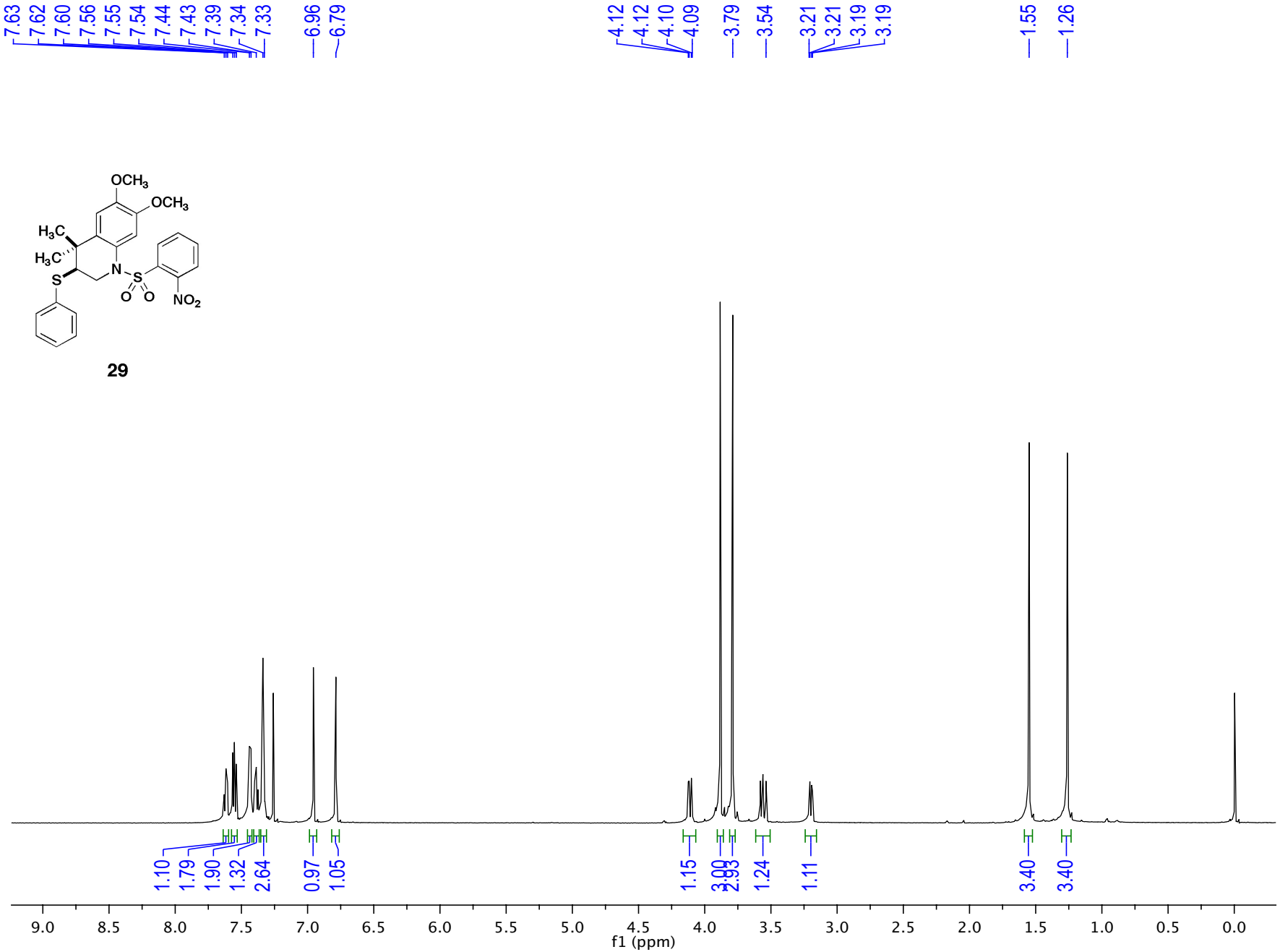

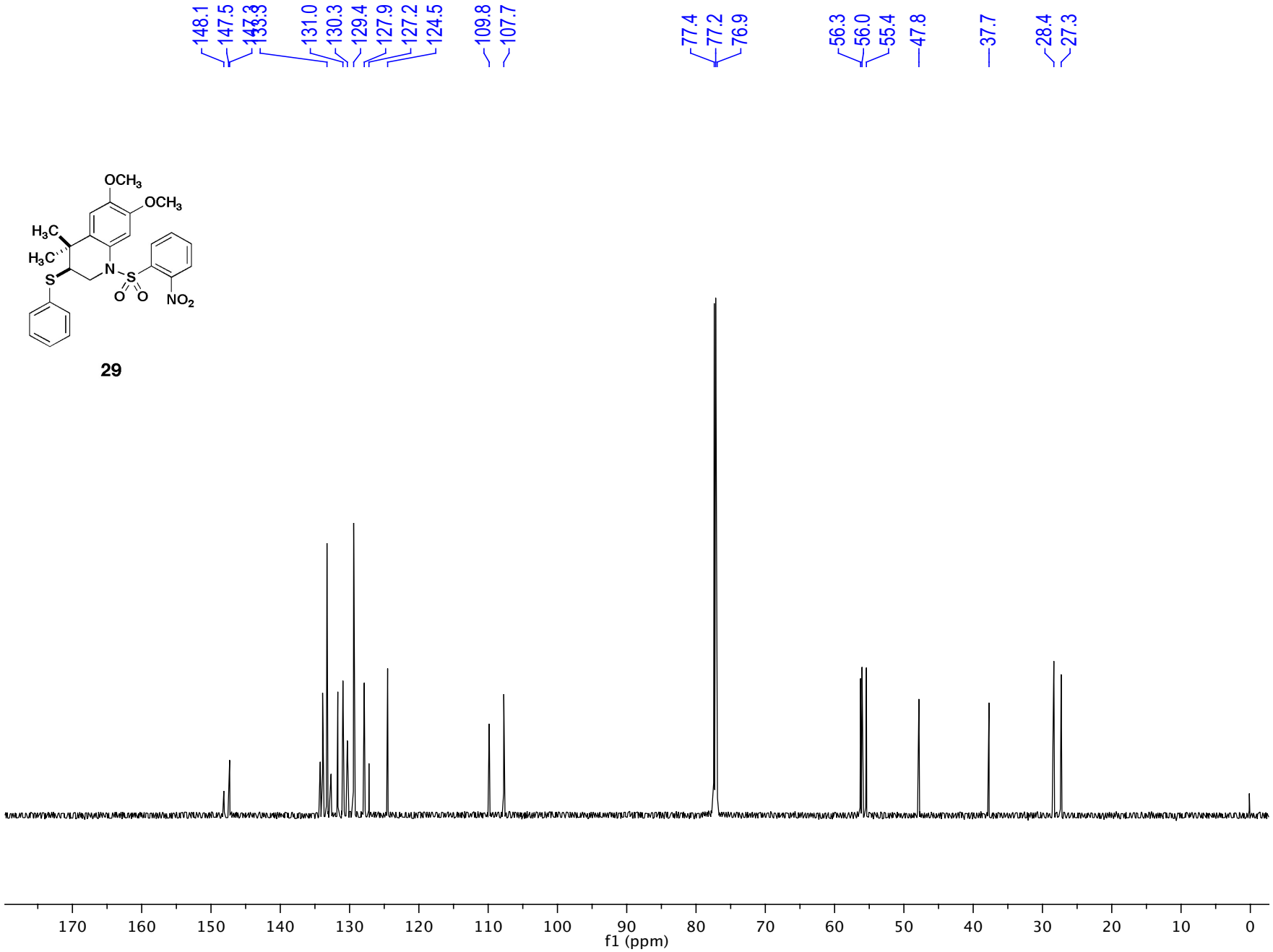

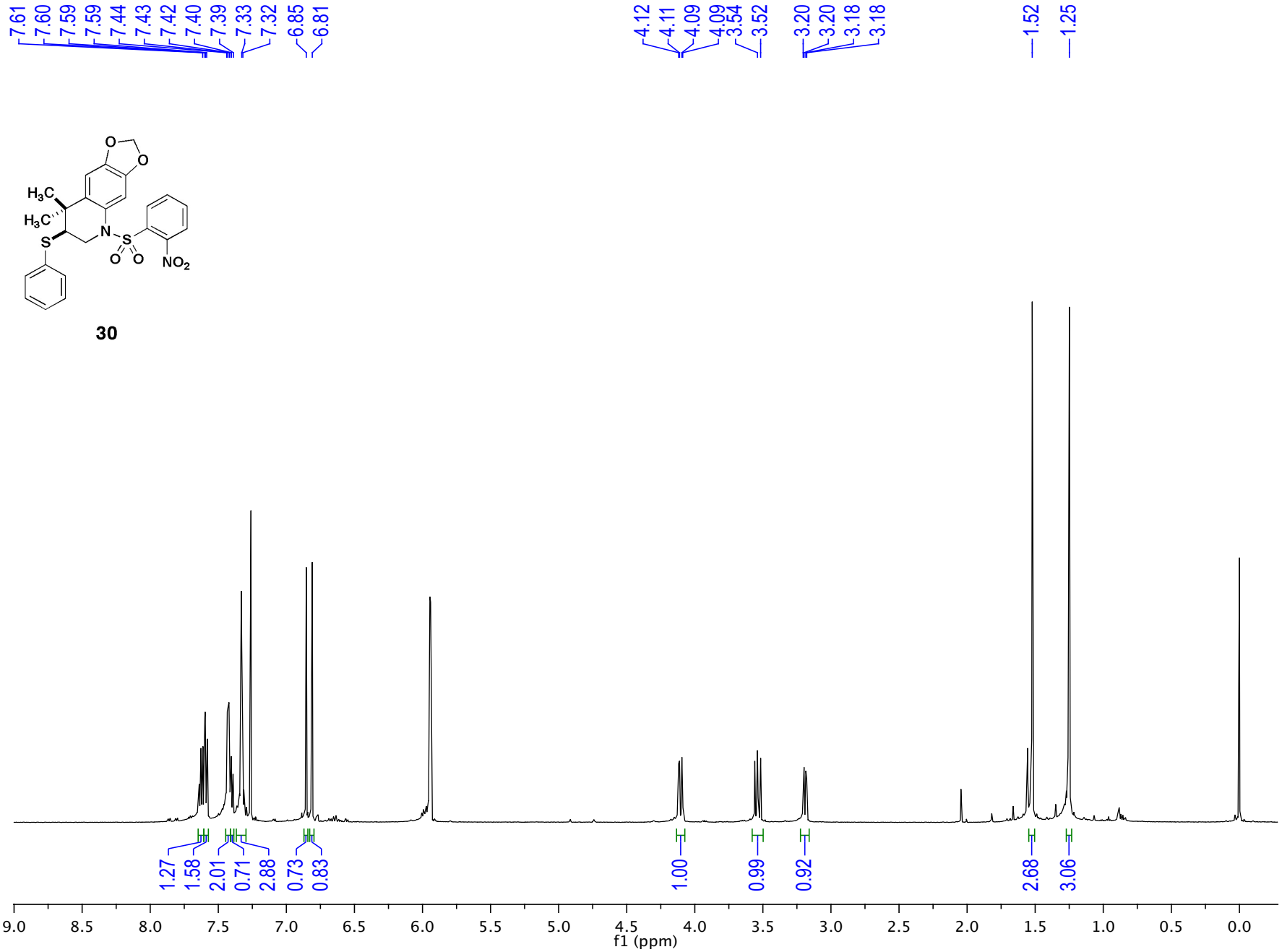

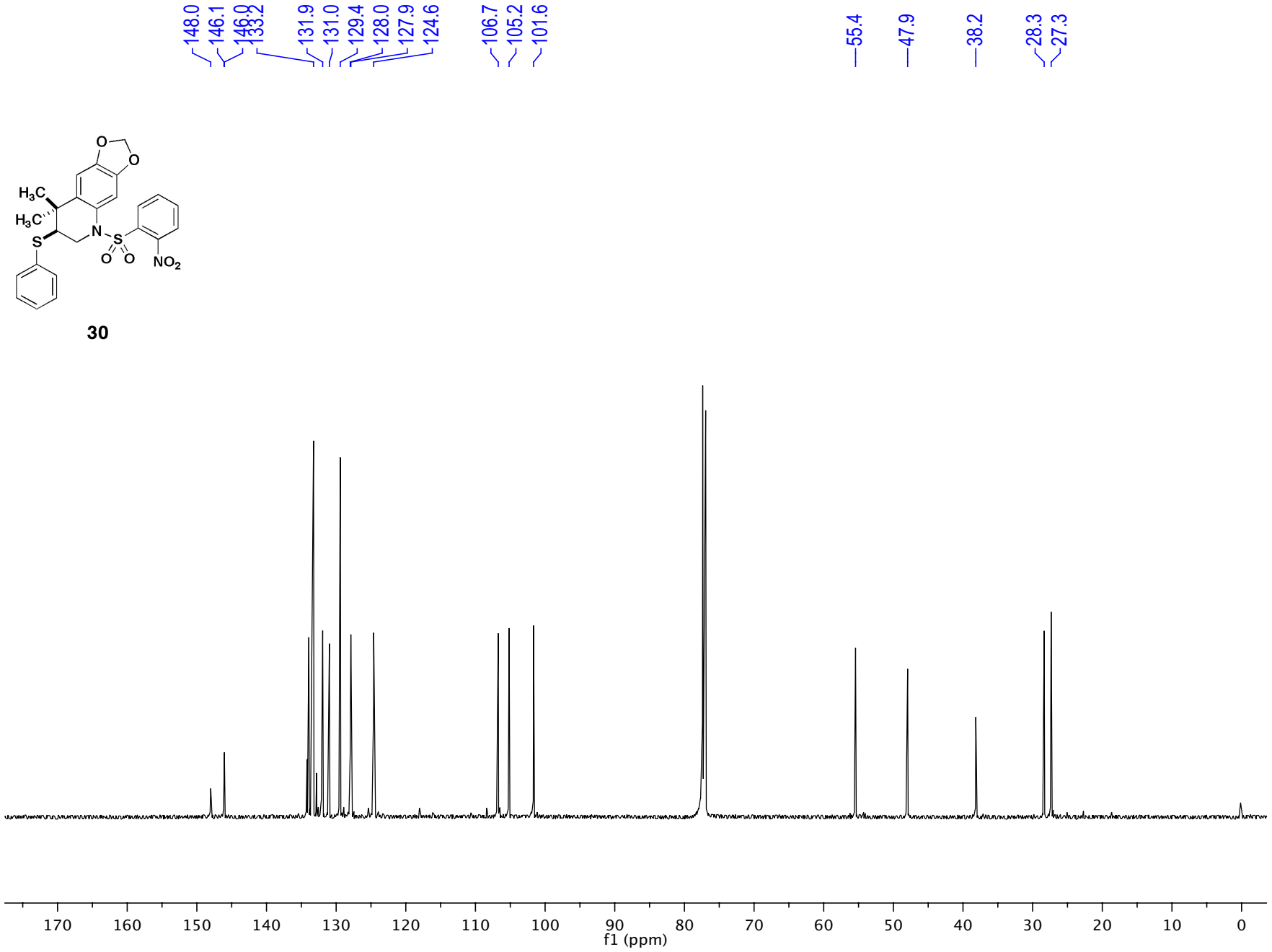

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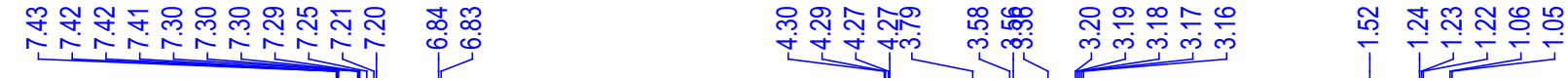

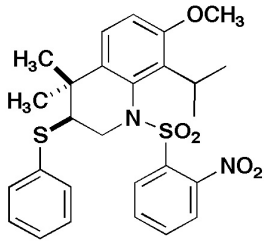

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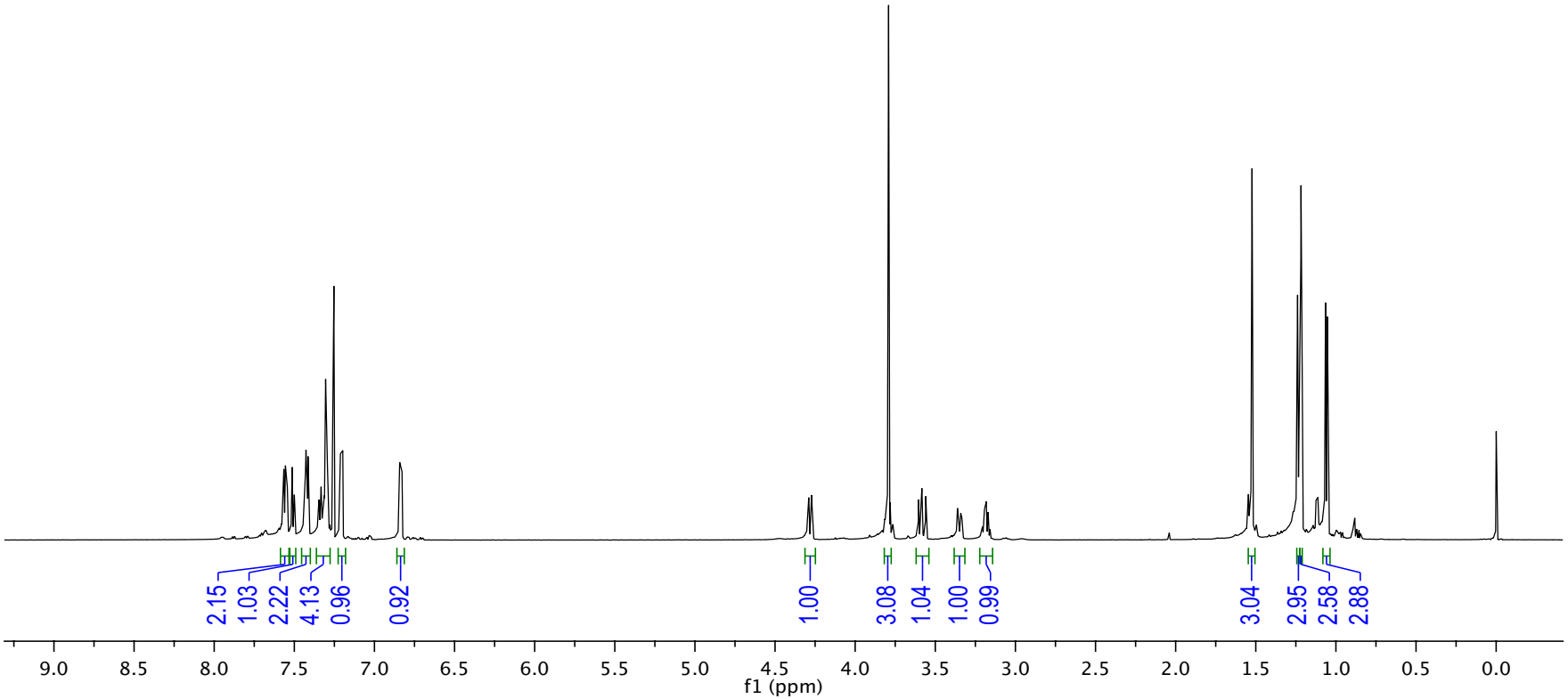
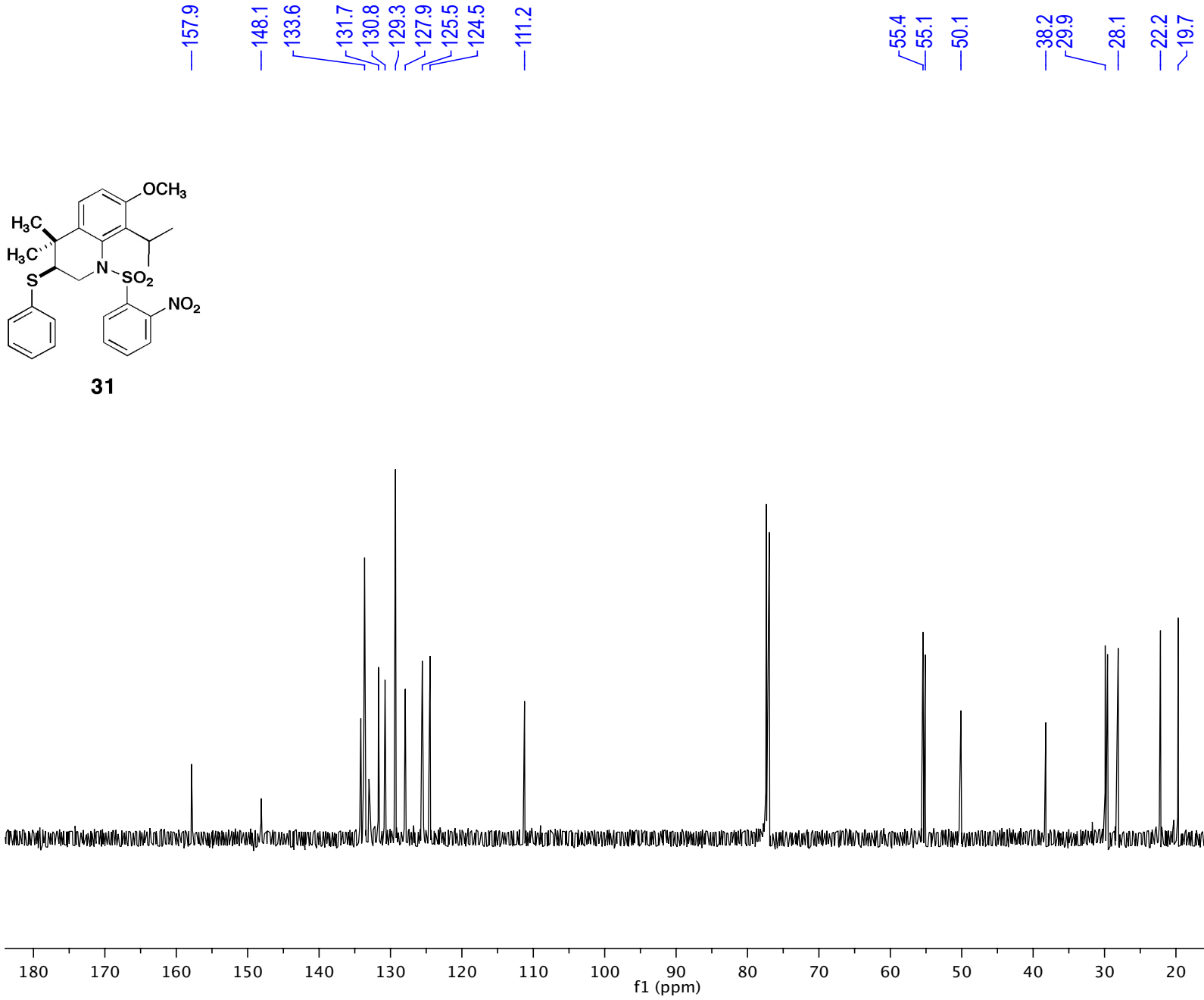
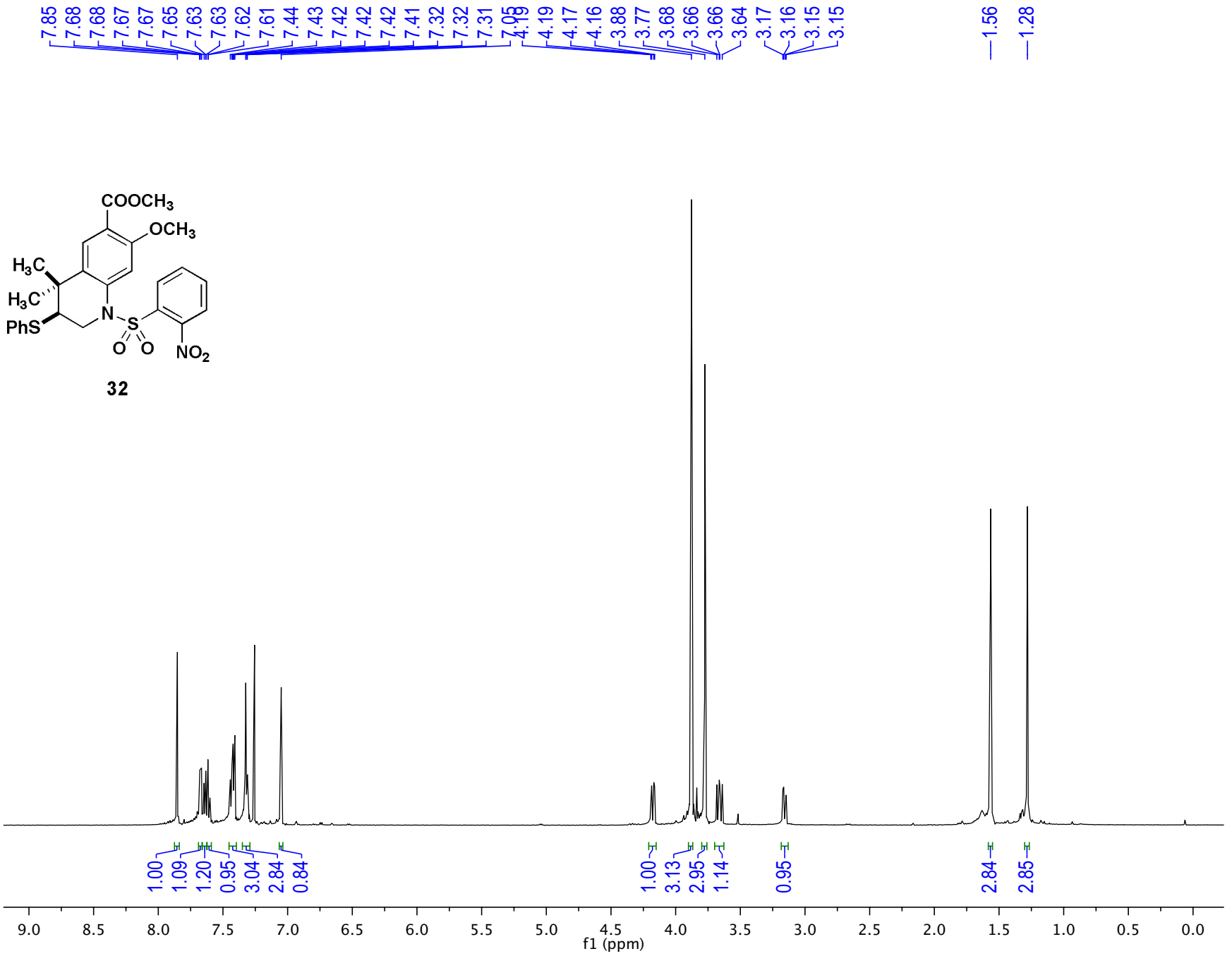
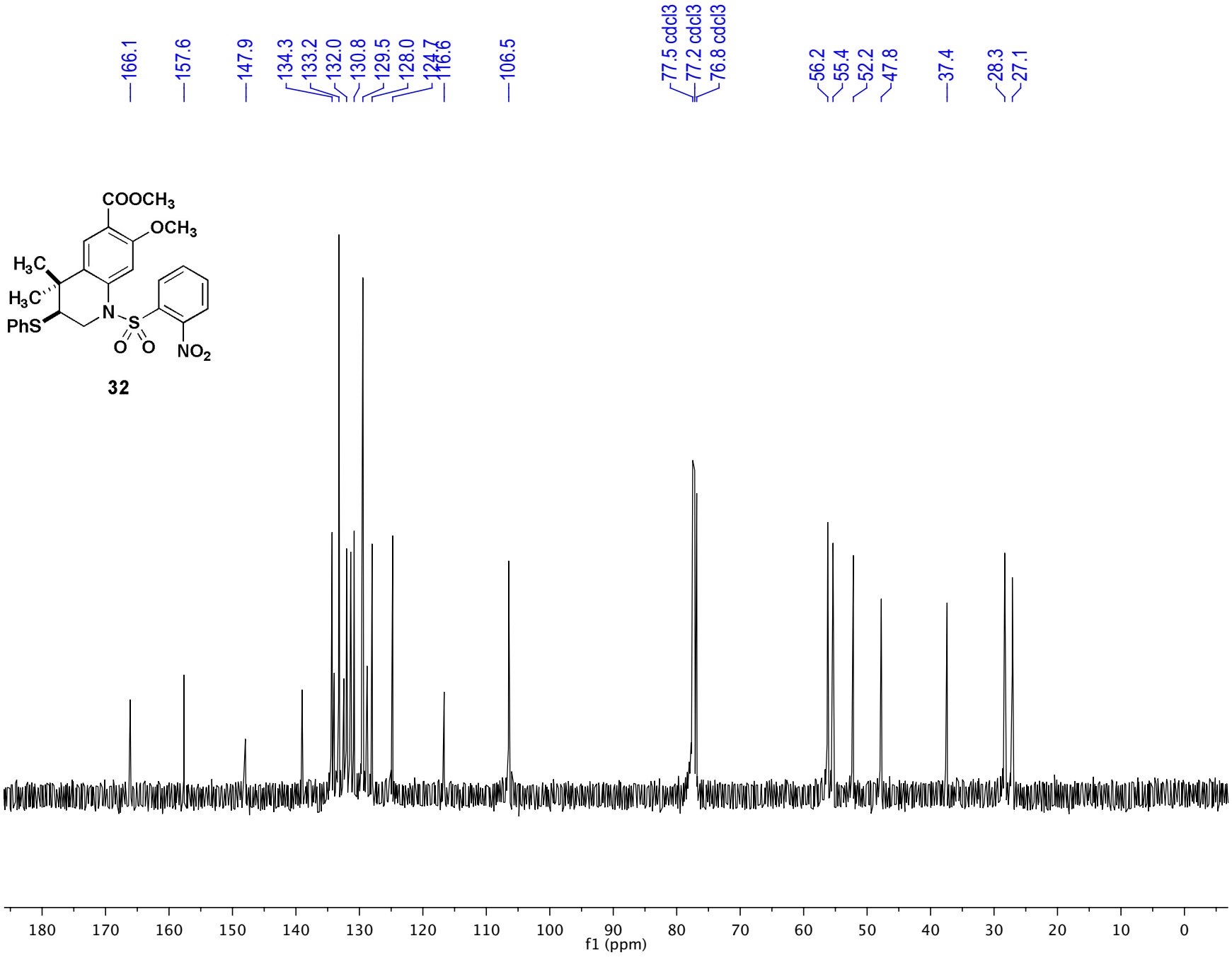
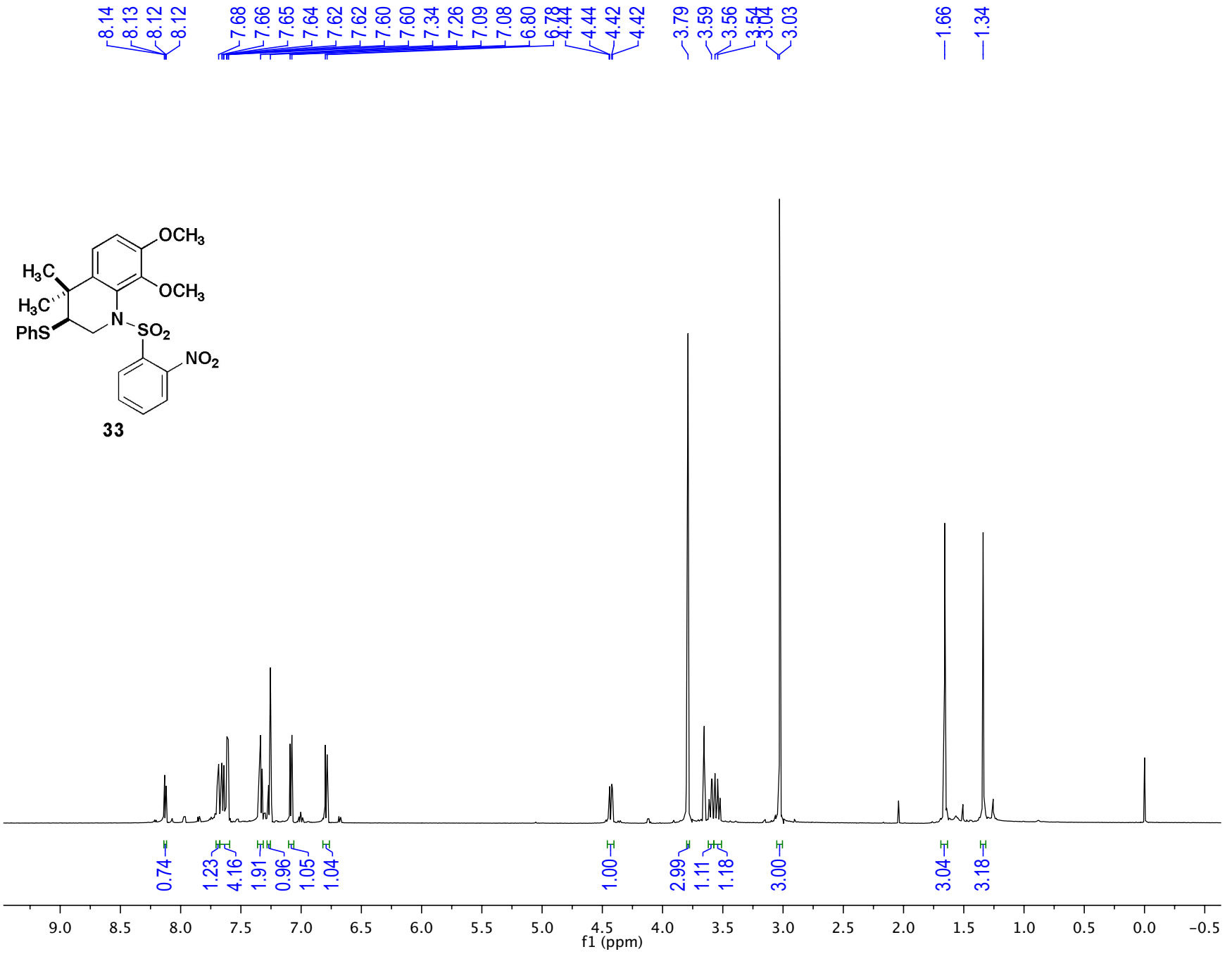
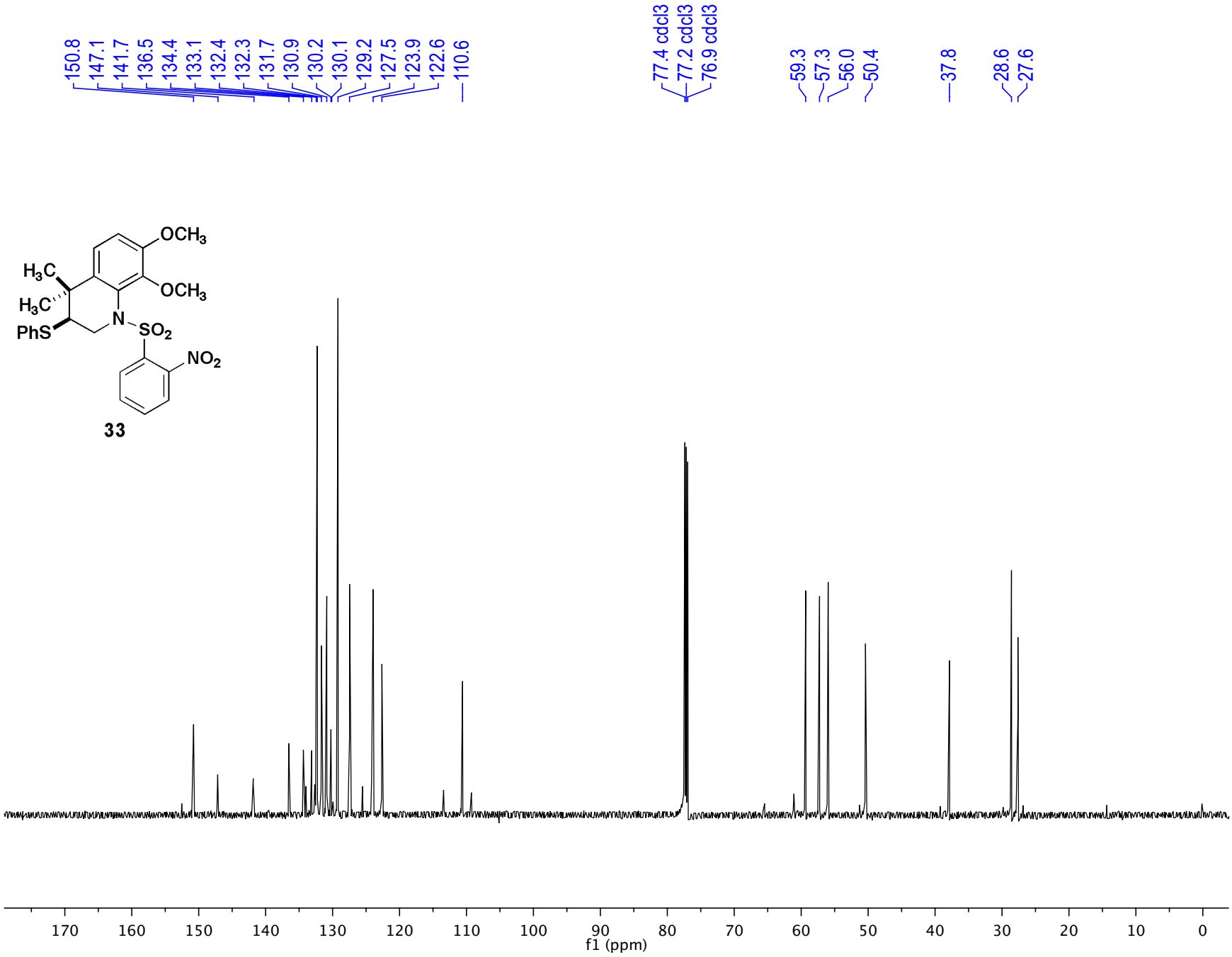


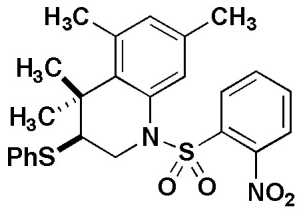




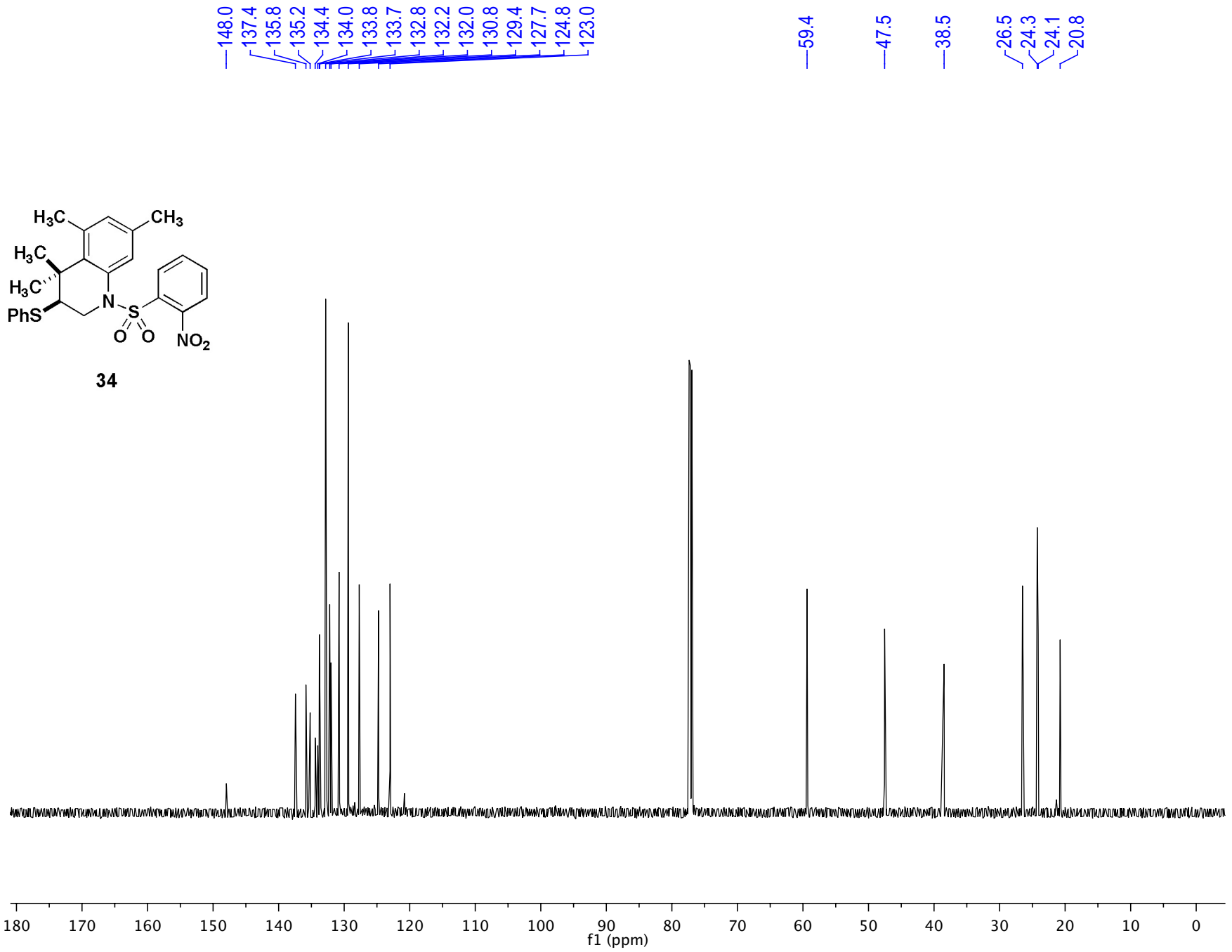


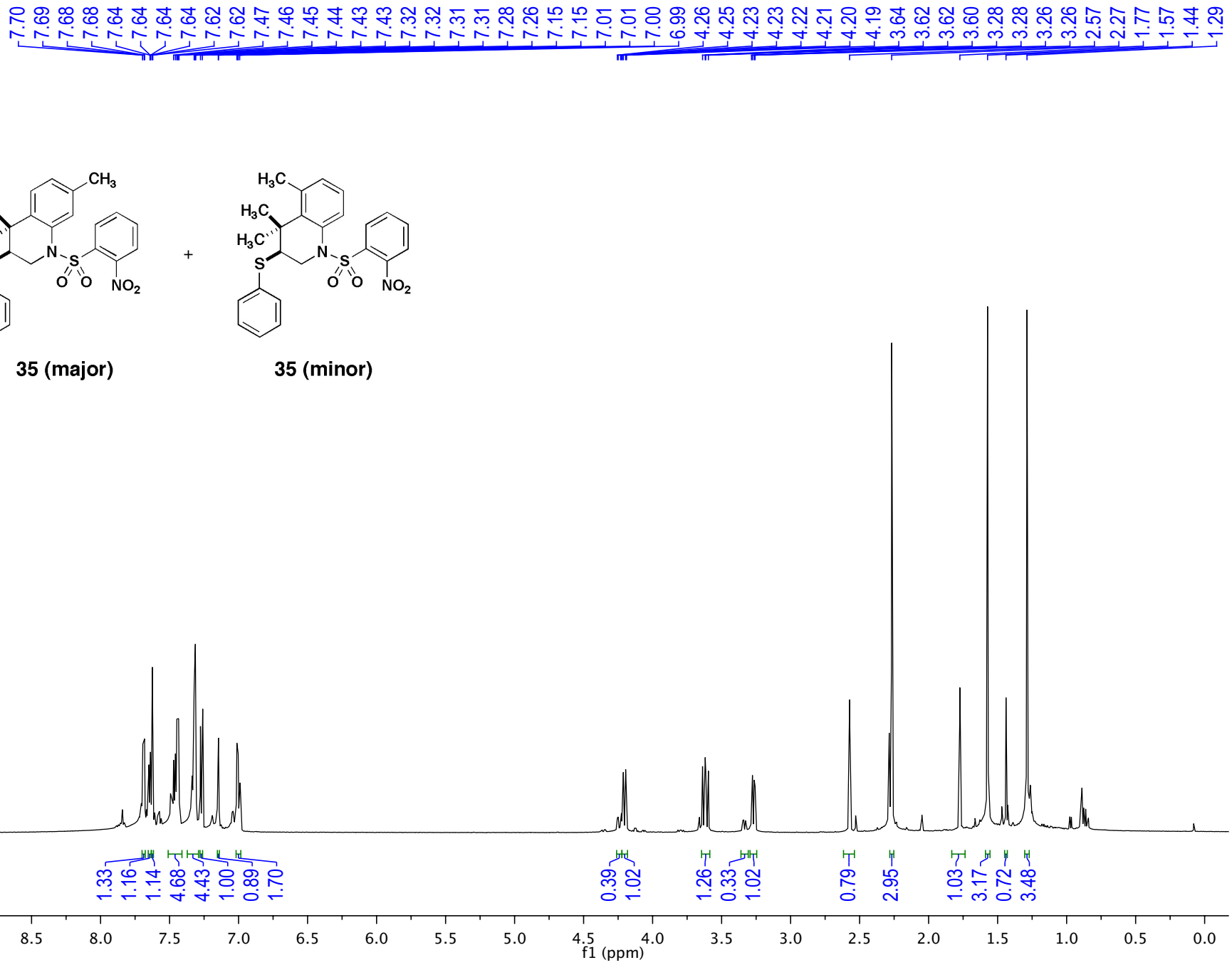






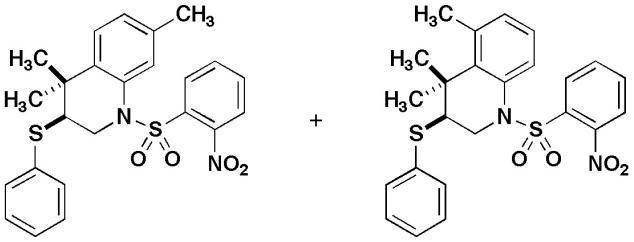
34





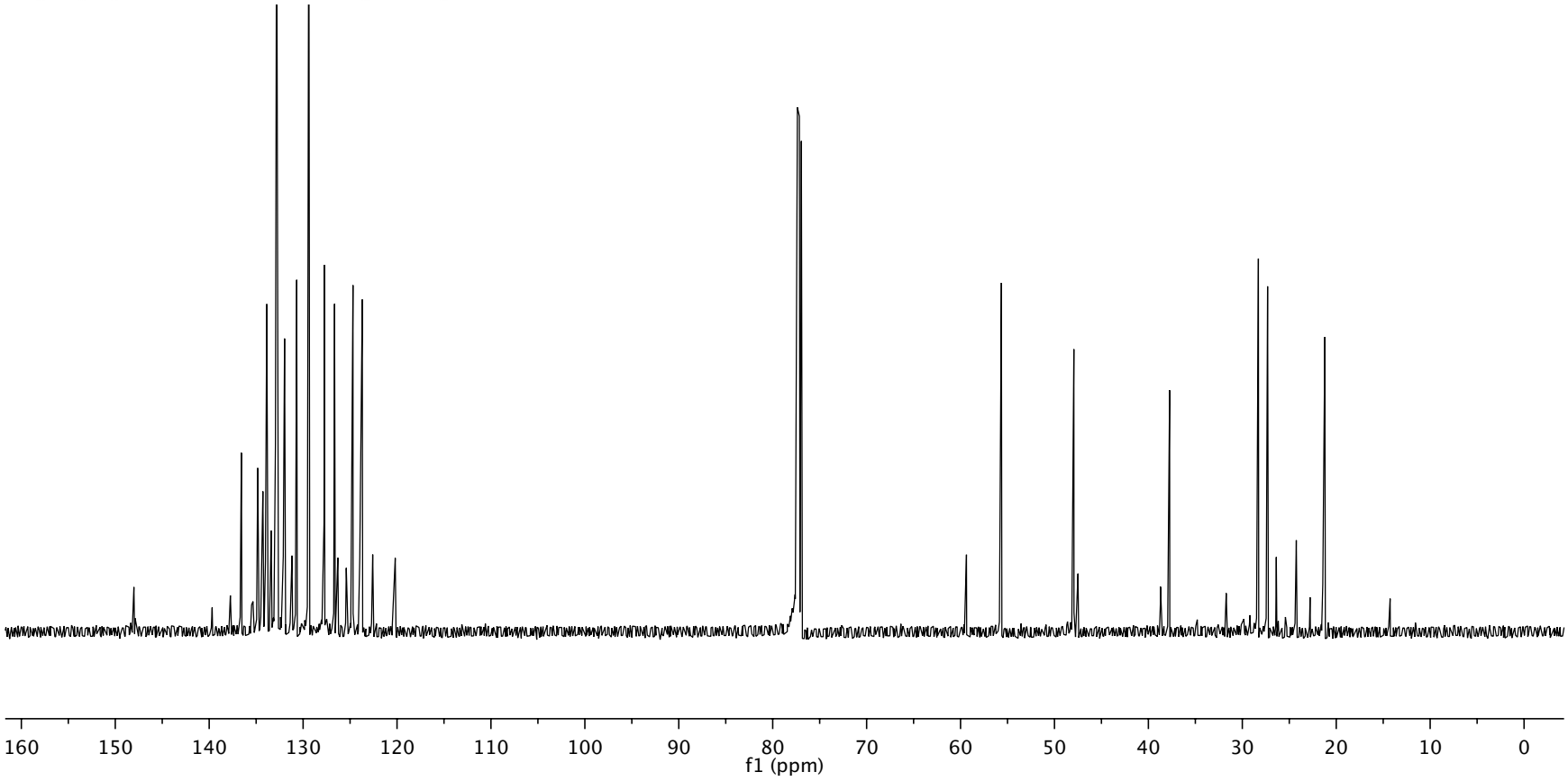
148.1 146.7 136.6 134.8 134.3 133.9 132.9 132.8 132.0 130.7 129.4 127.7 127.5 126.7 124.7 123.7 120.2

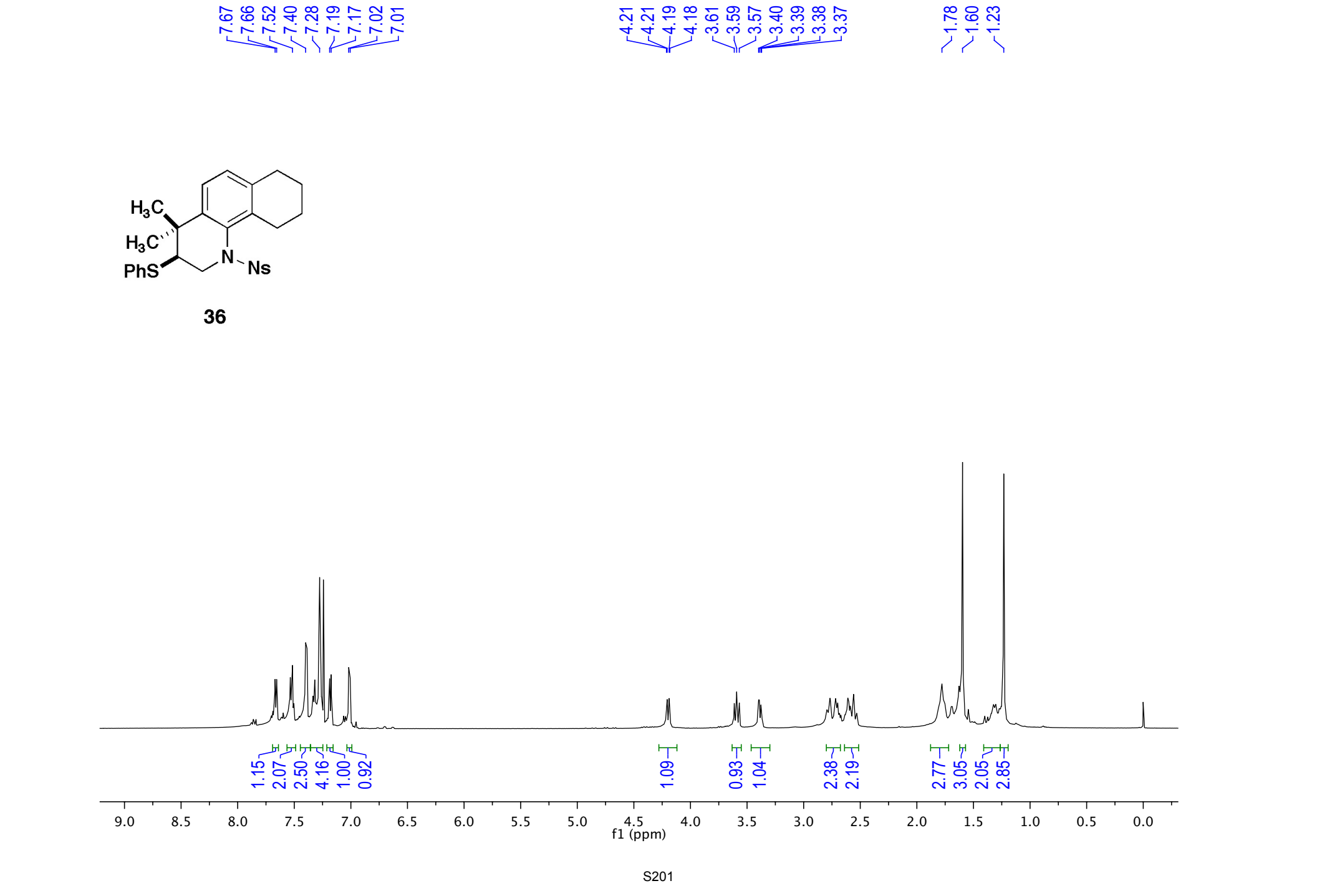
55.7 47.9 37.7 28.3 27.3 21.2



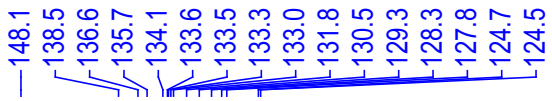
+

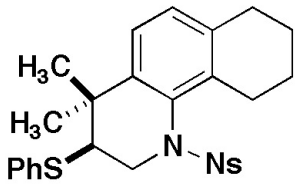
35 (major) **35 (minor)**



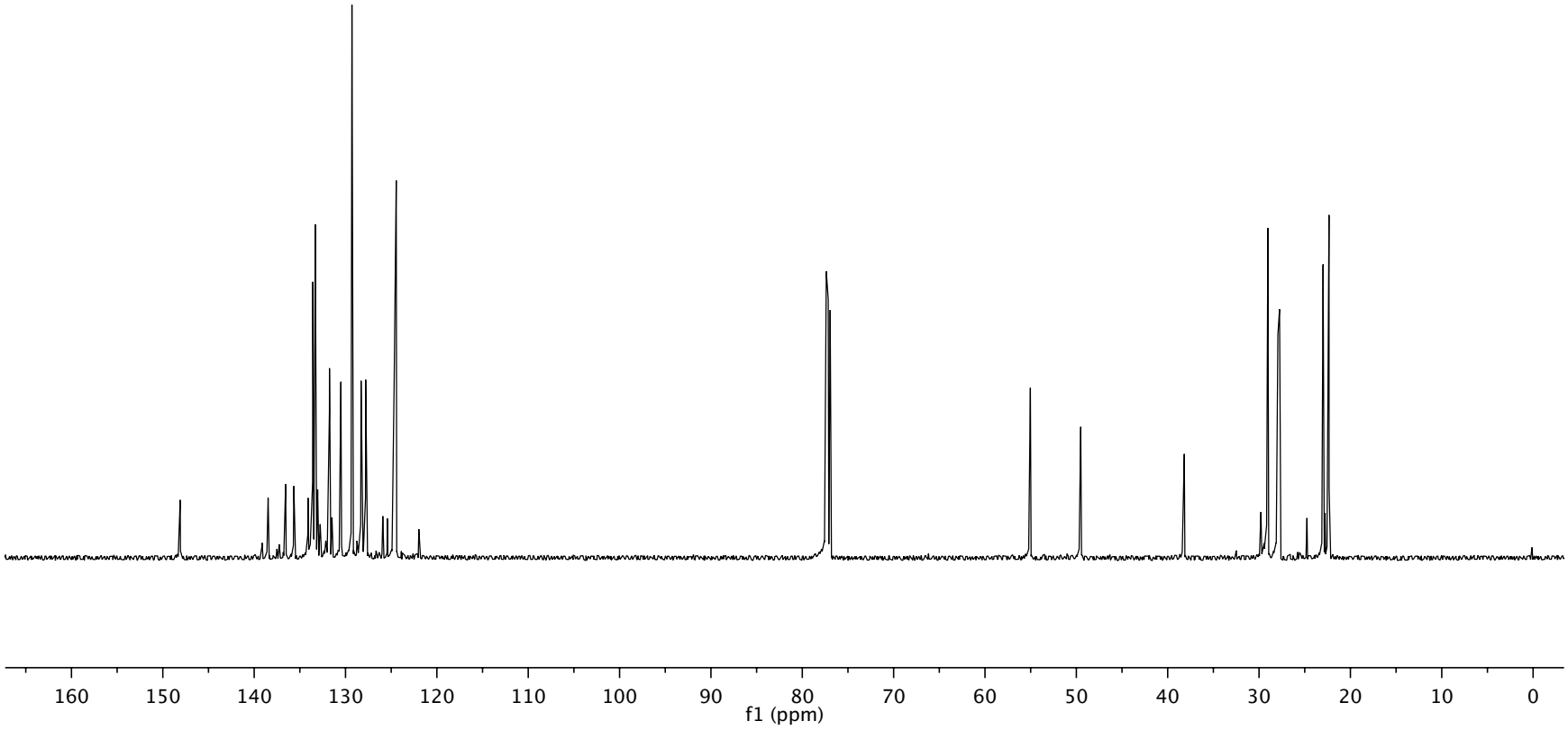


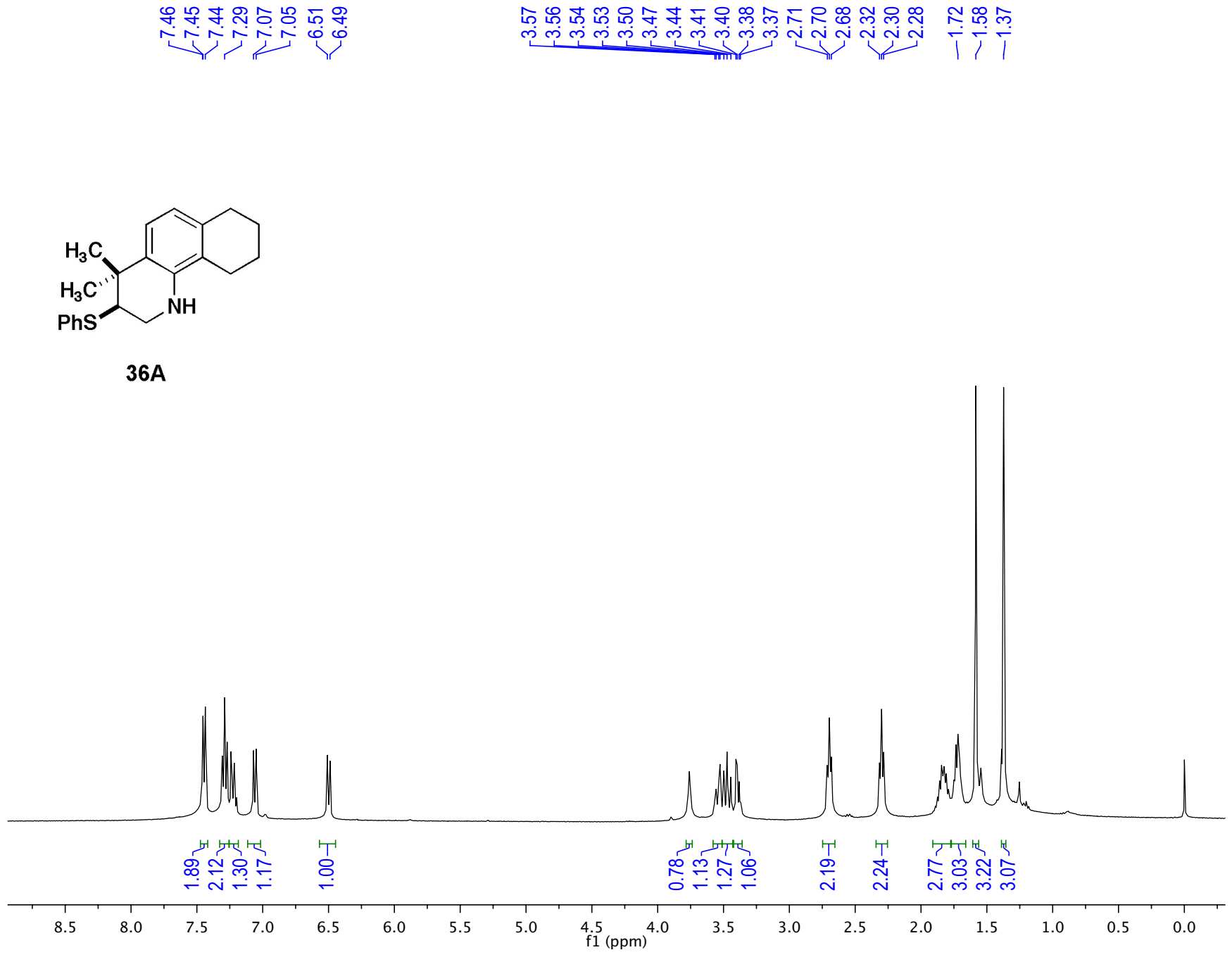
36



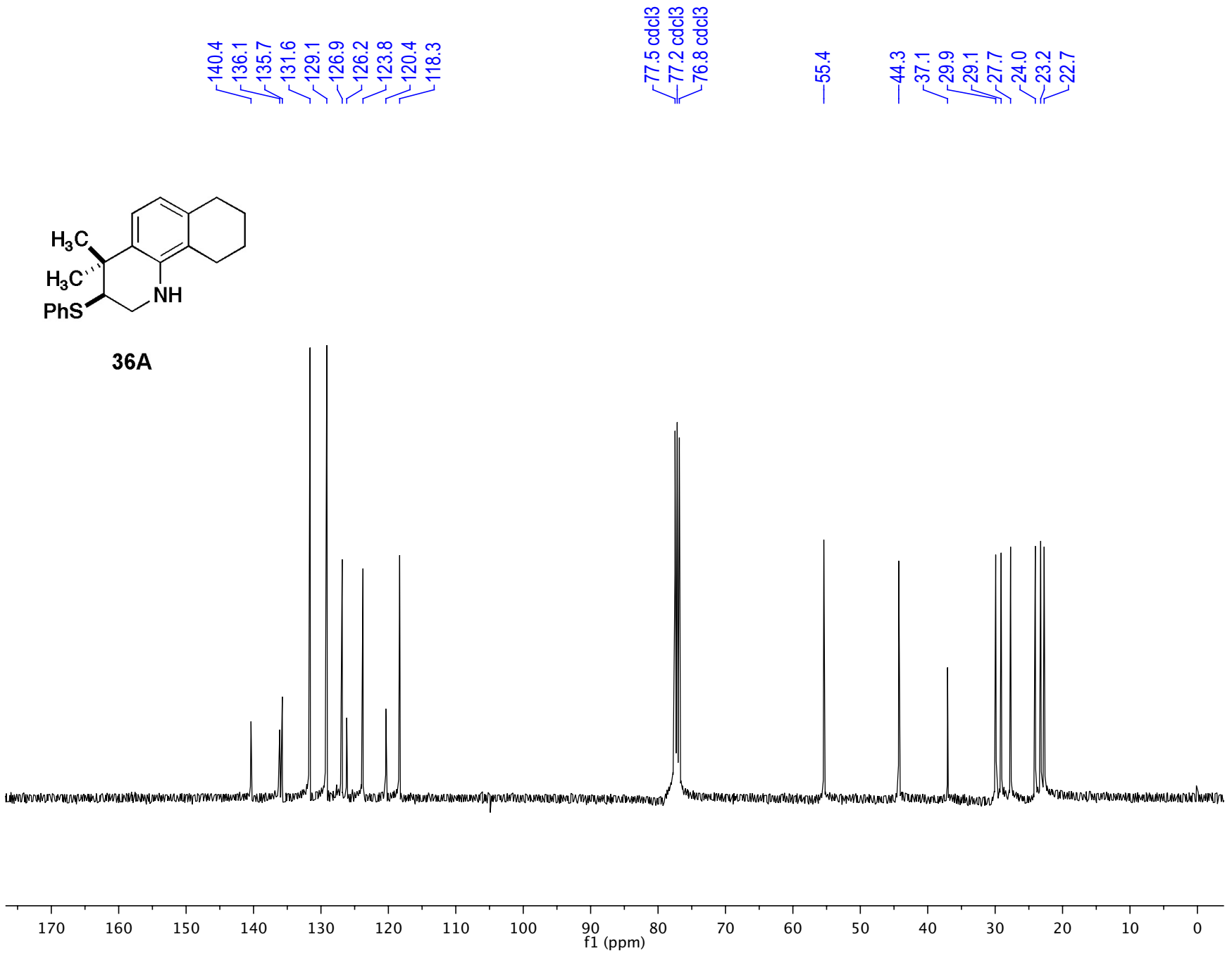


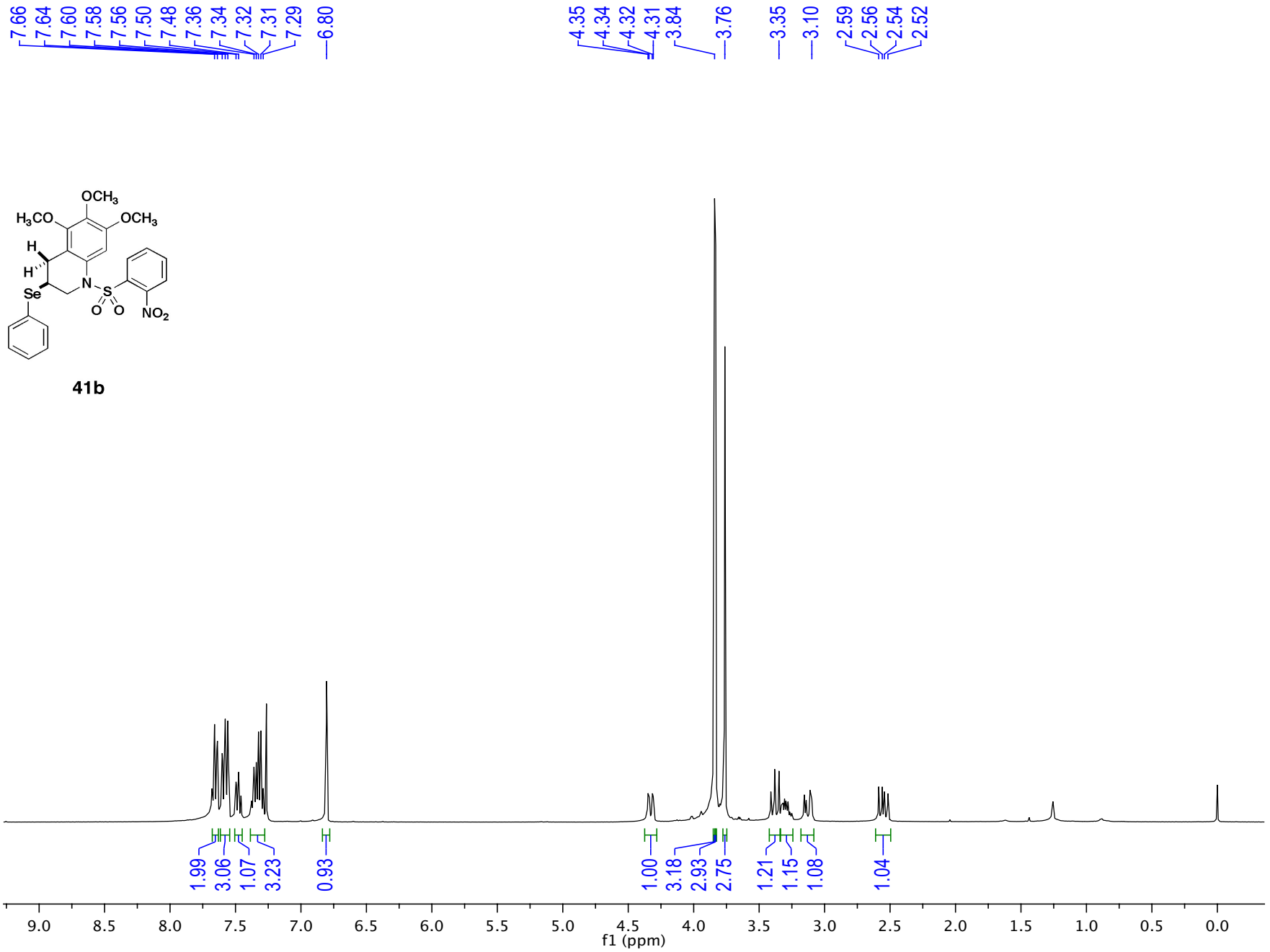
36

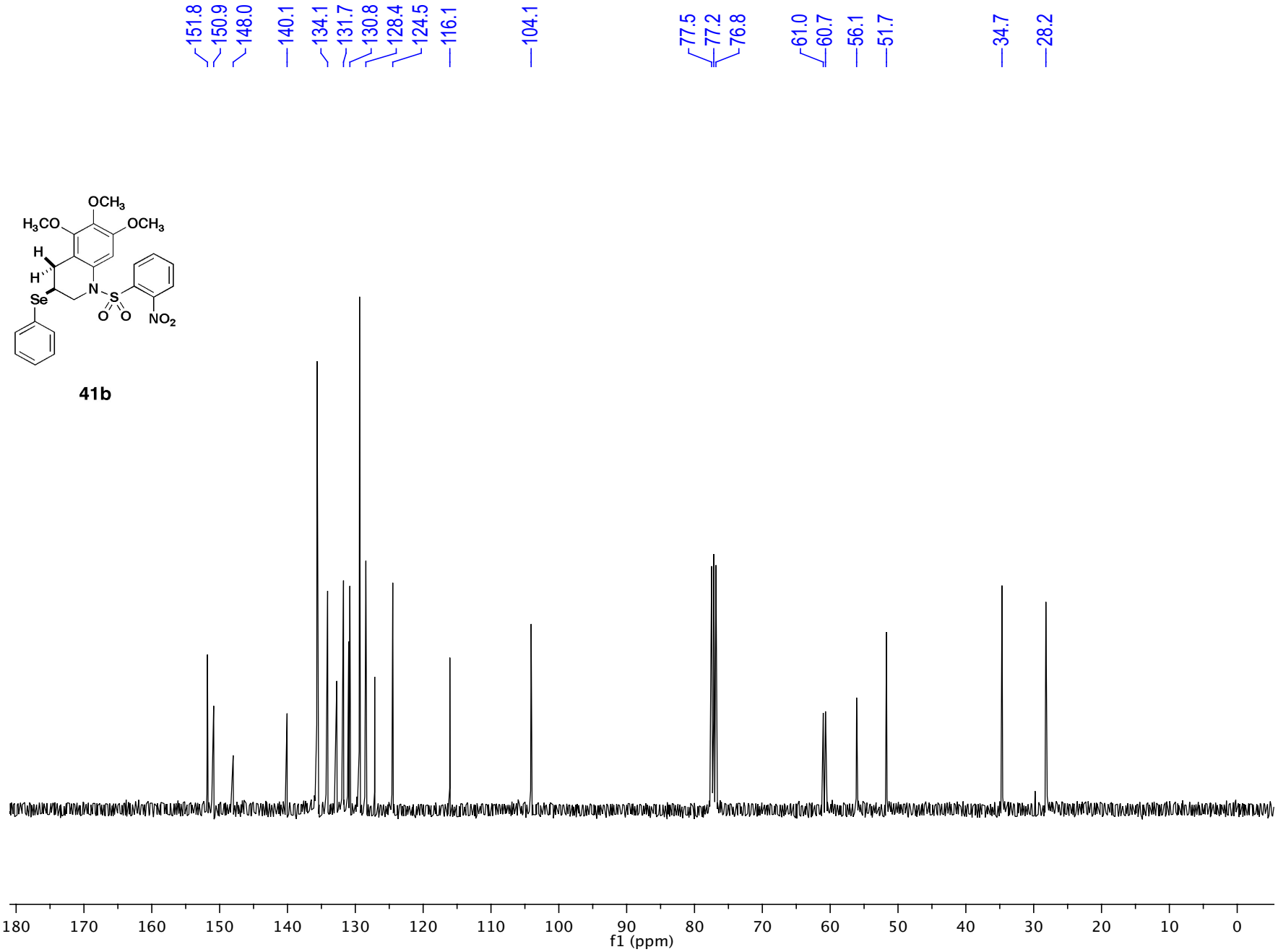


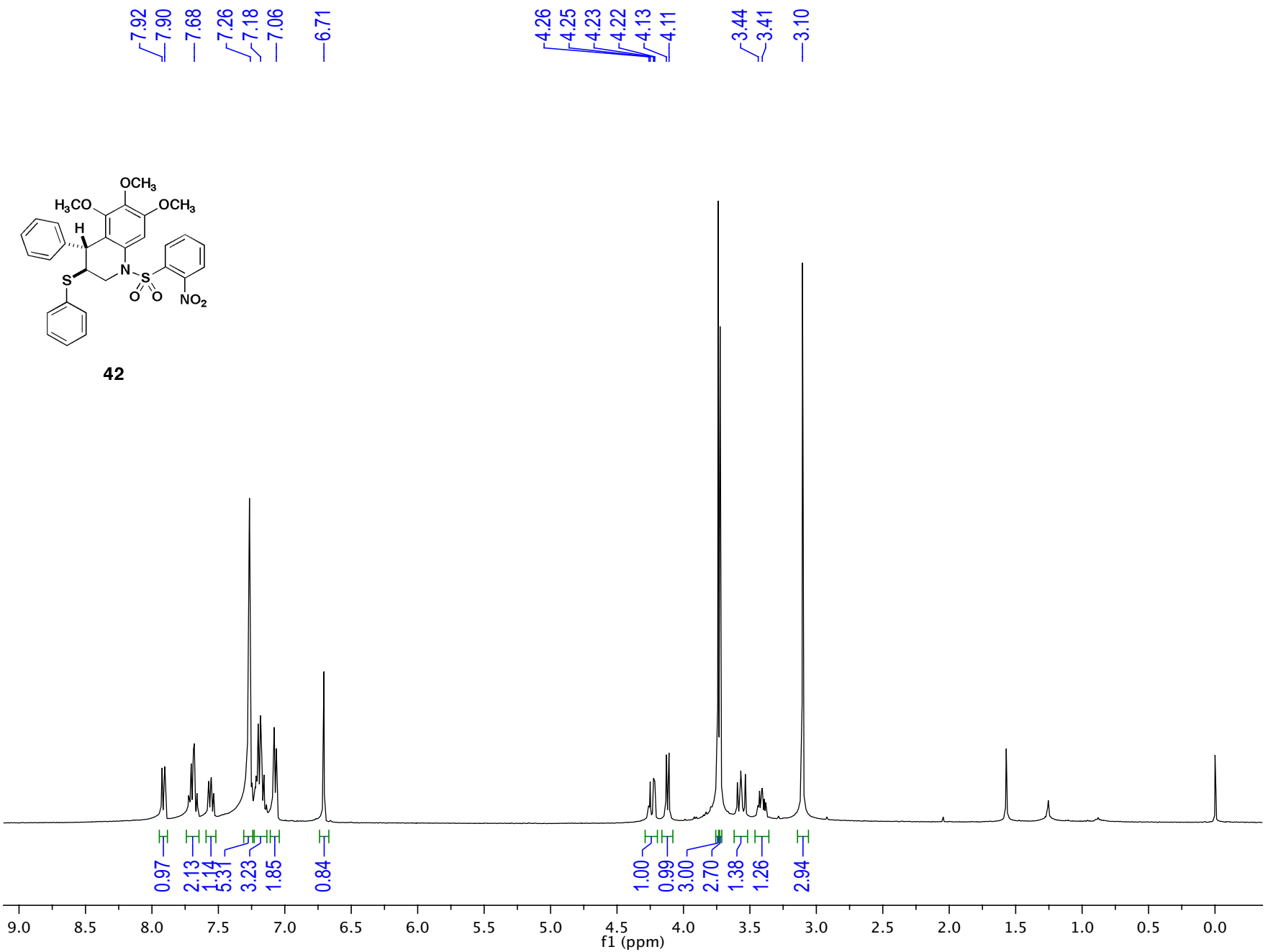


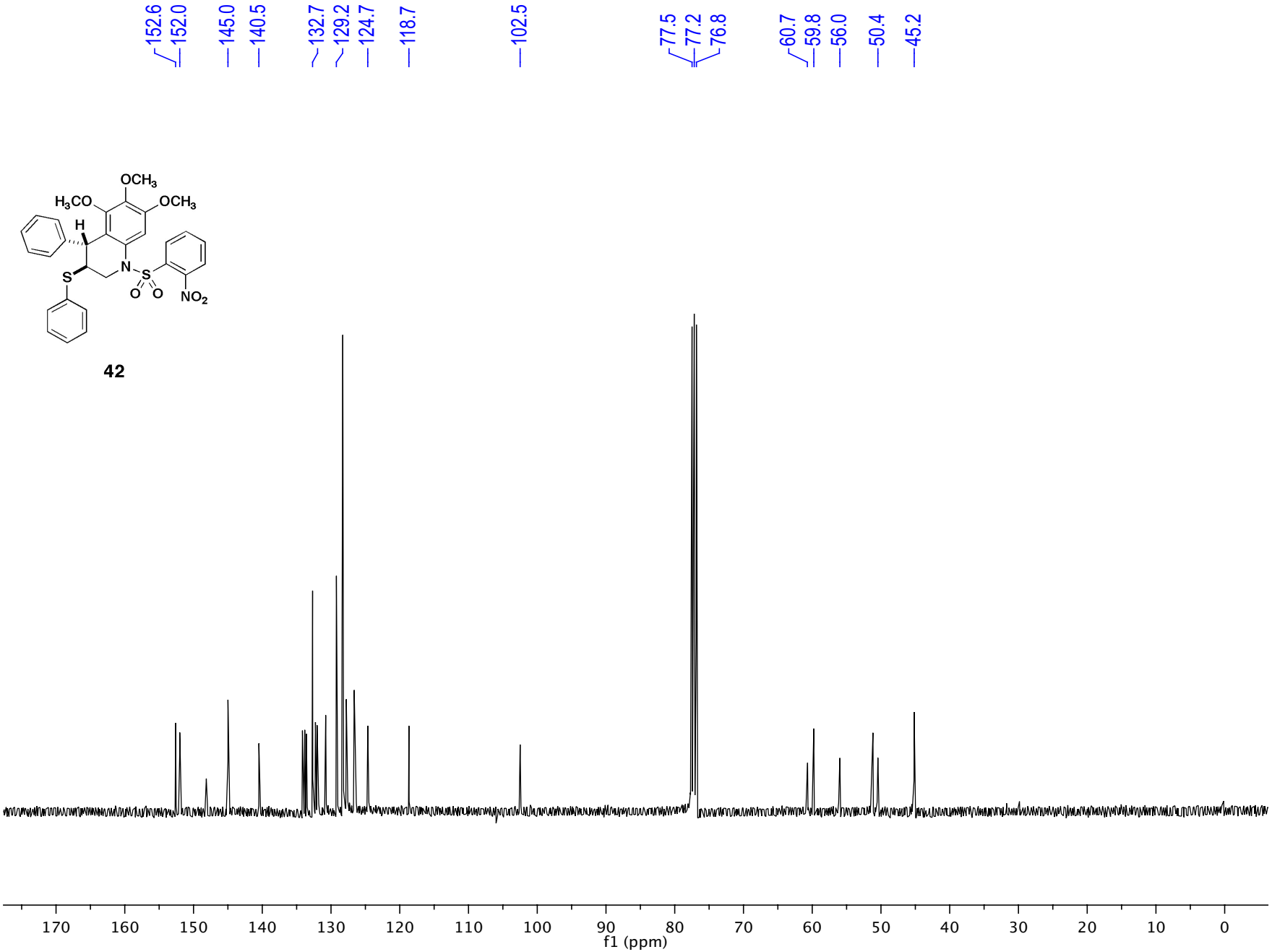
36A

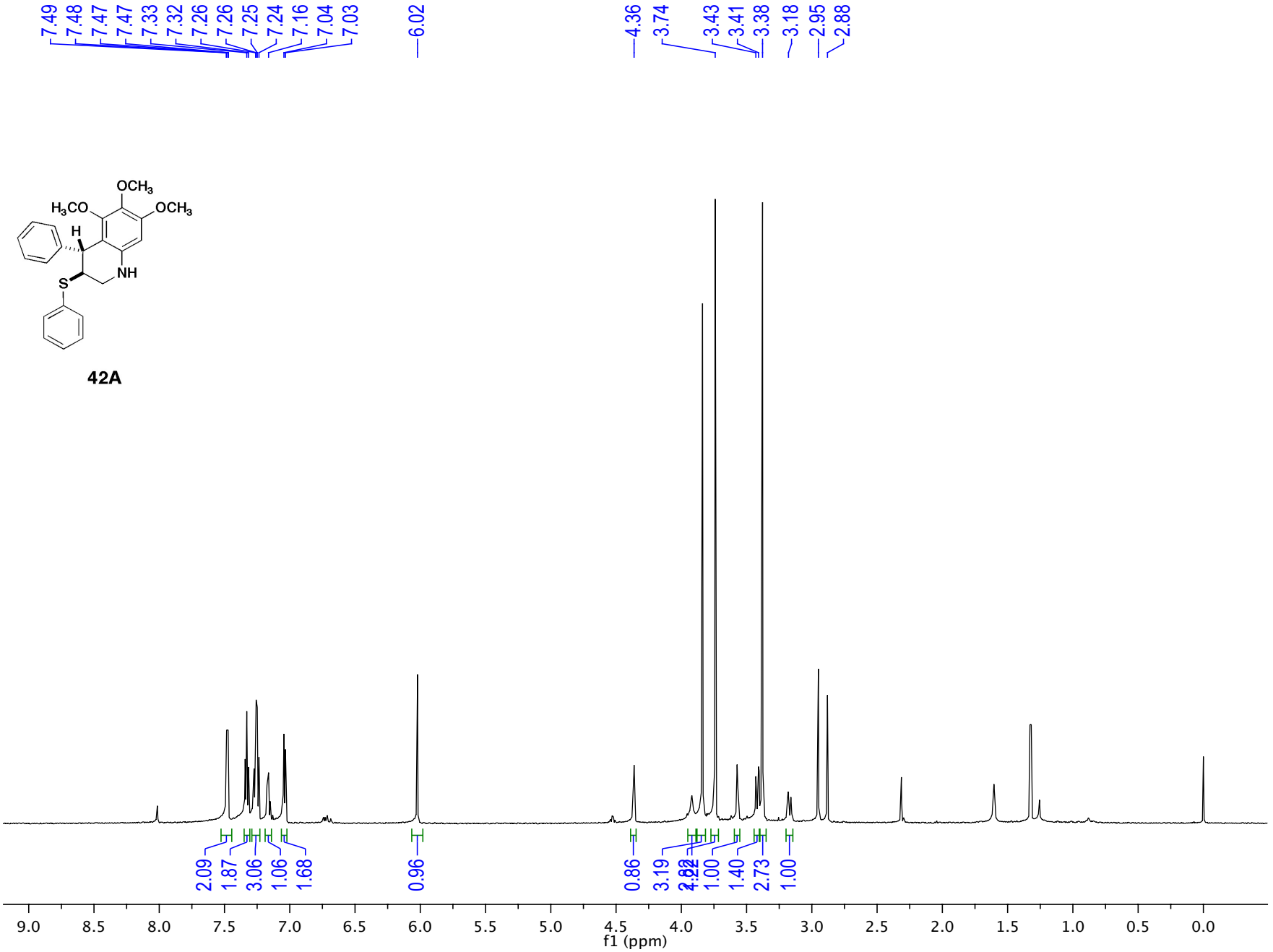


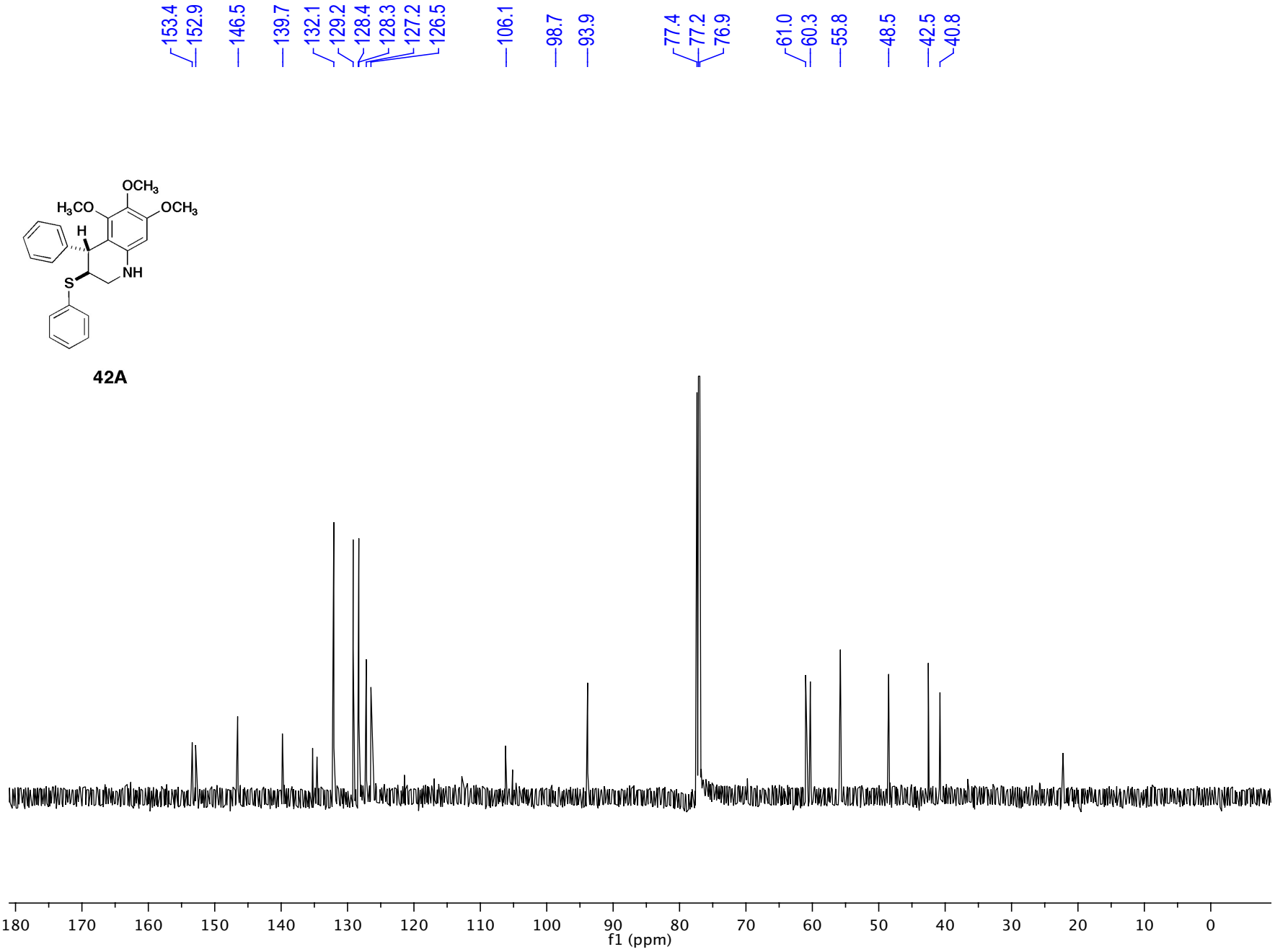




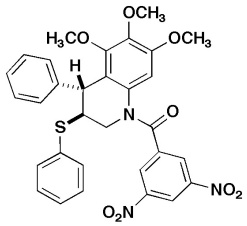




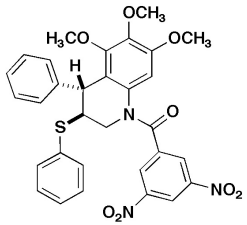




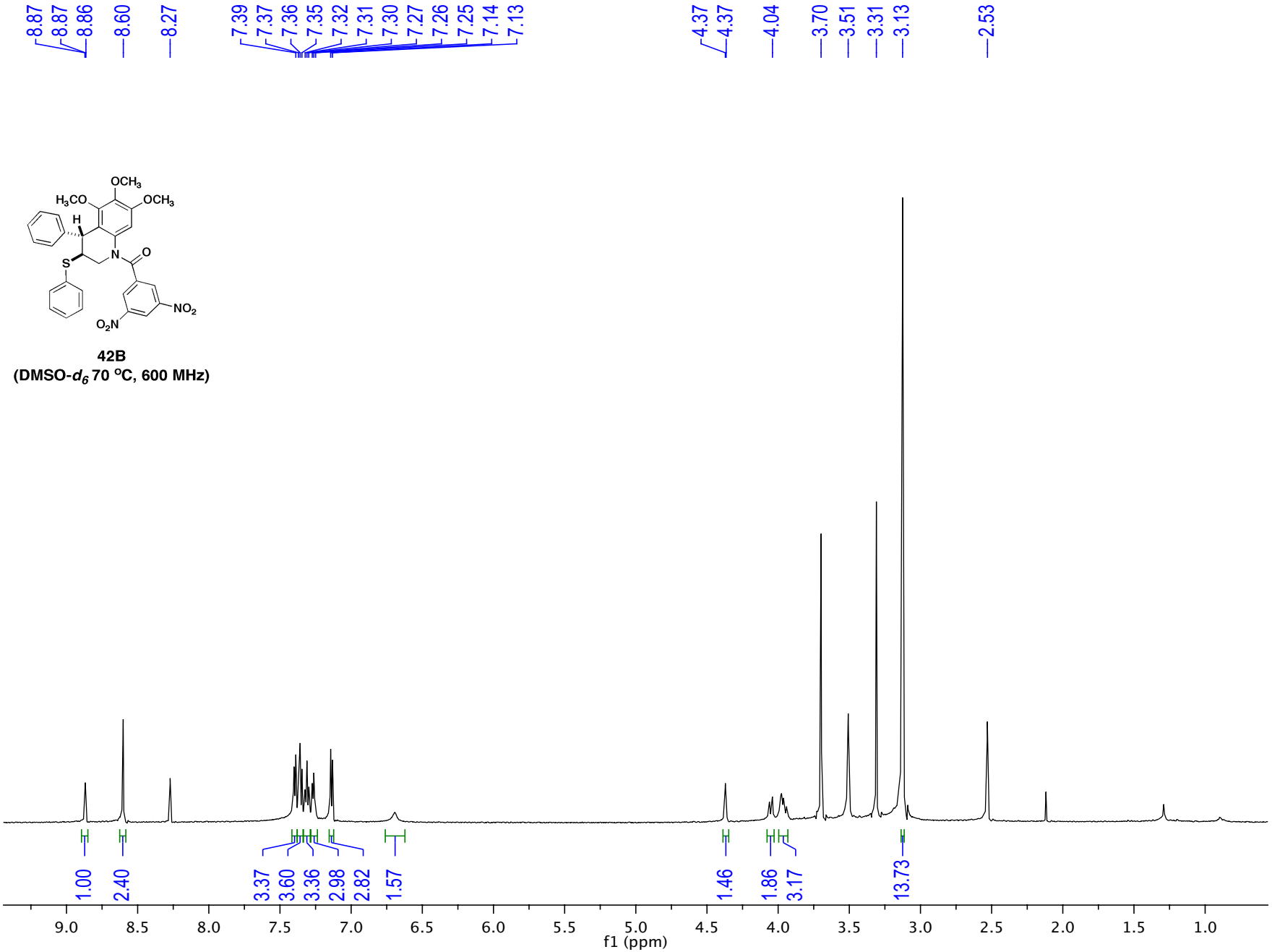
42A



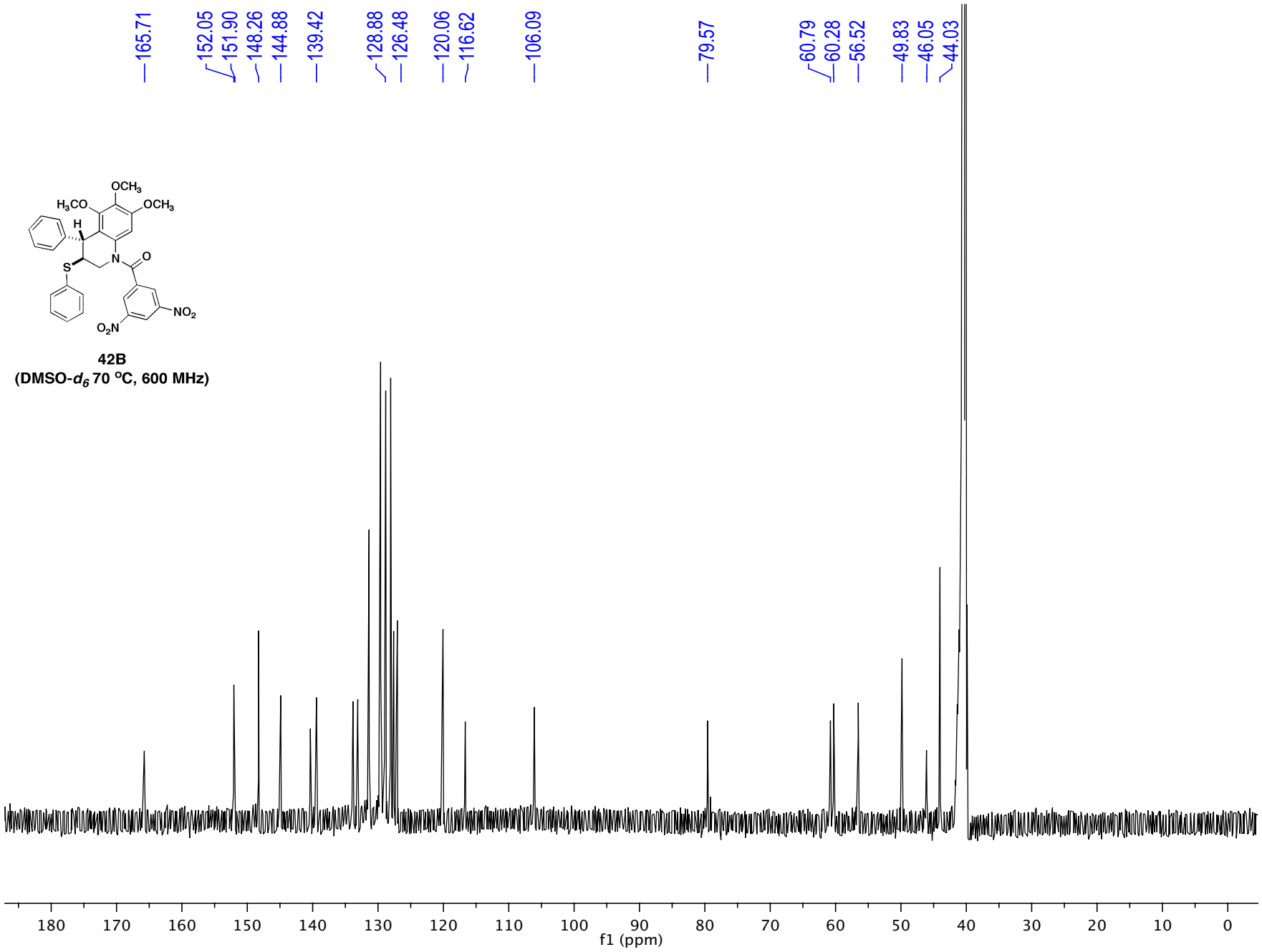
42B
($CHCl_3$ rt, 600 MHz)



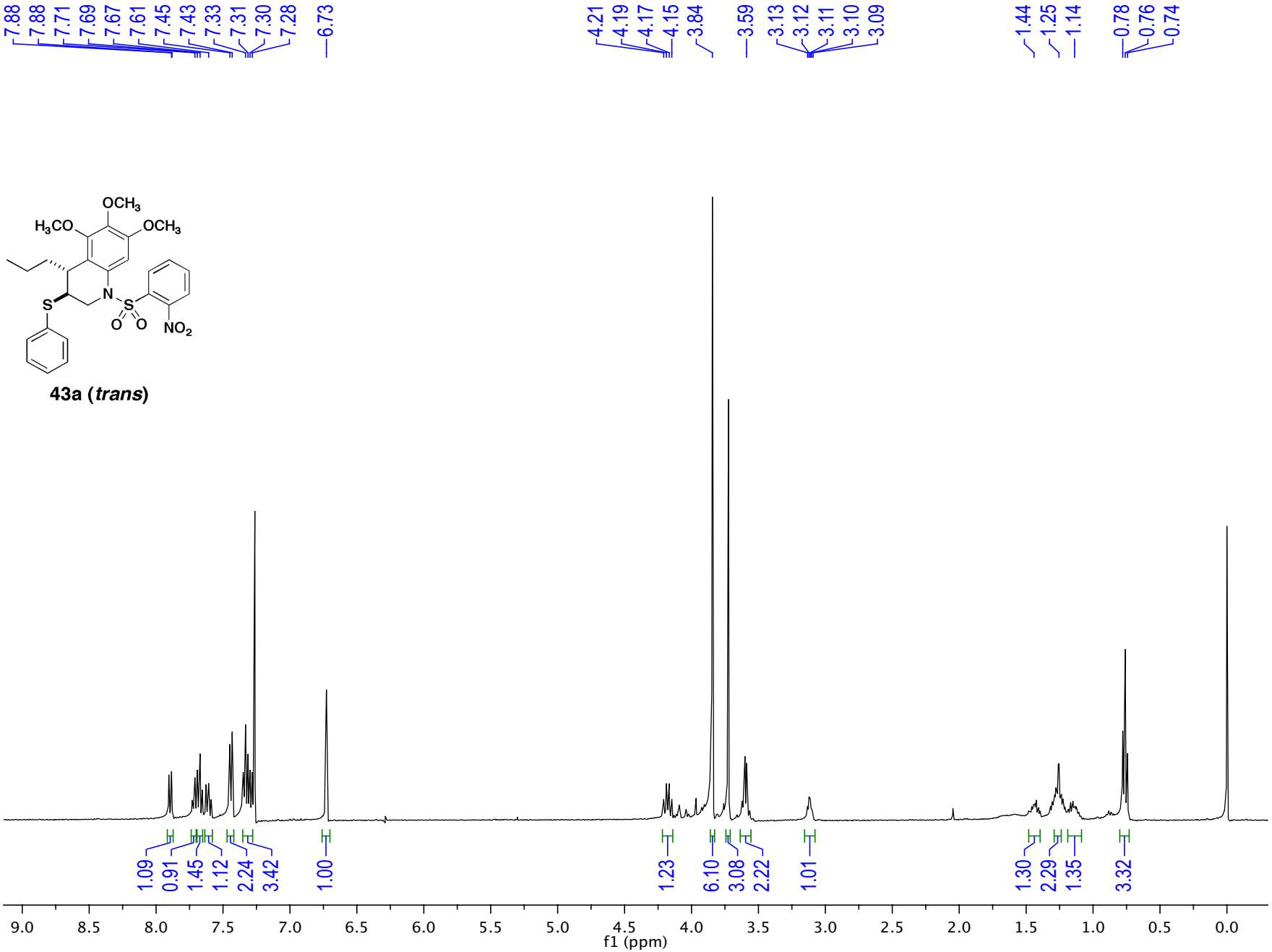
42B
($CHCl_3$ rt, 600 MHz)

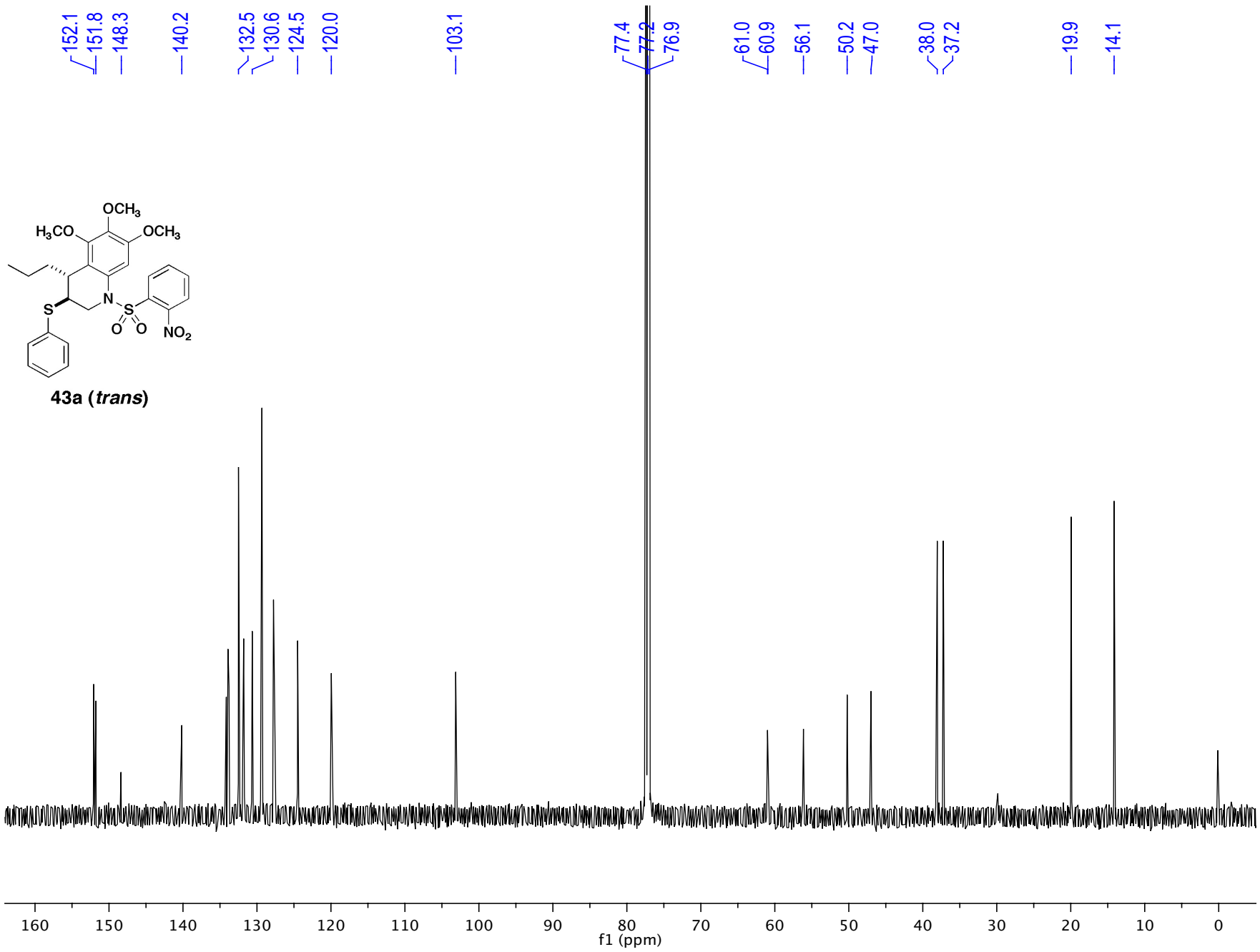


42B
(DMSO-d_6 70 °C, 600 MHz)

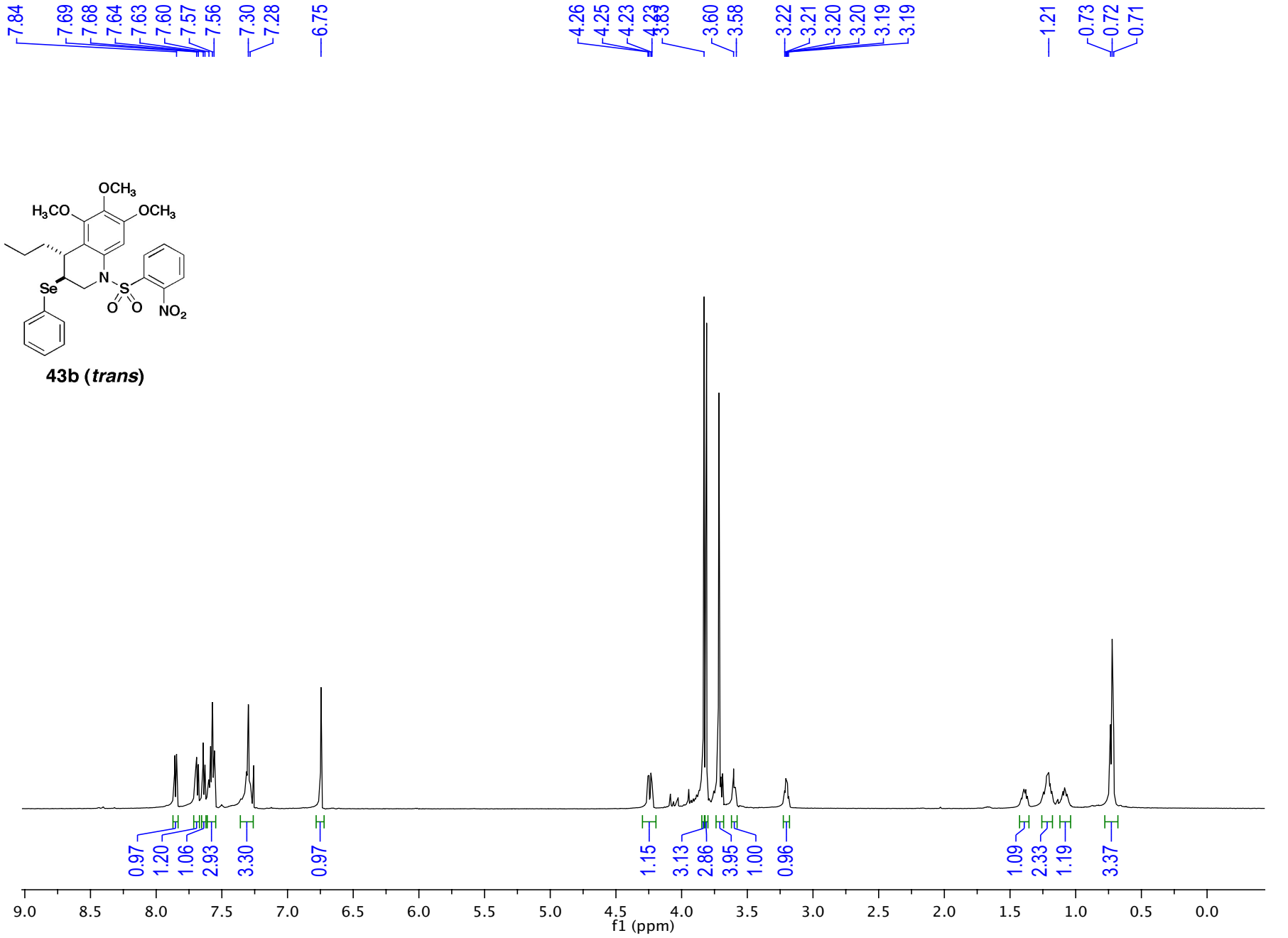


42B
(DMSO-d_6 70 °C, 600 MHz)

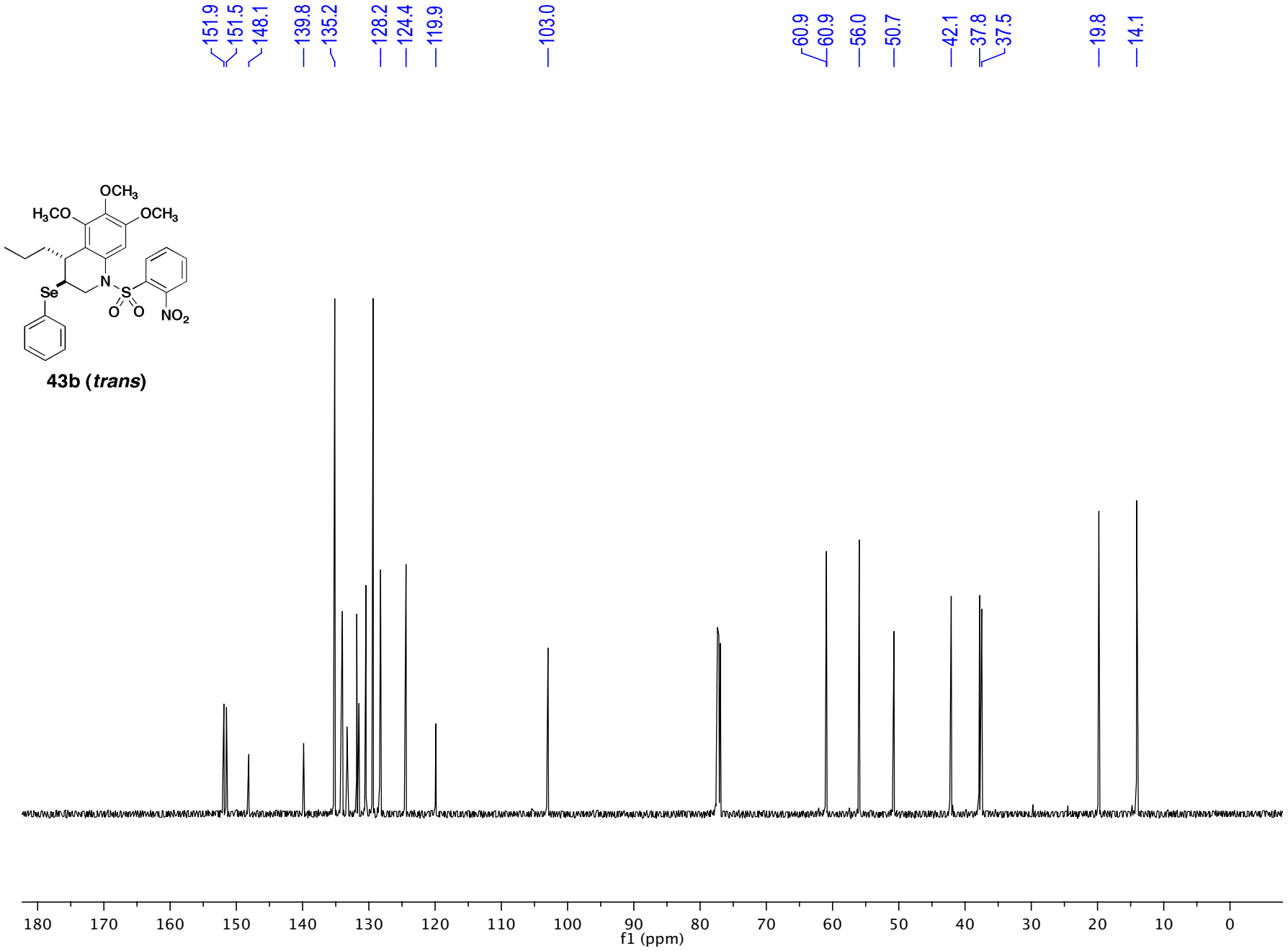


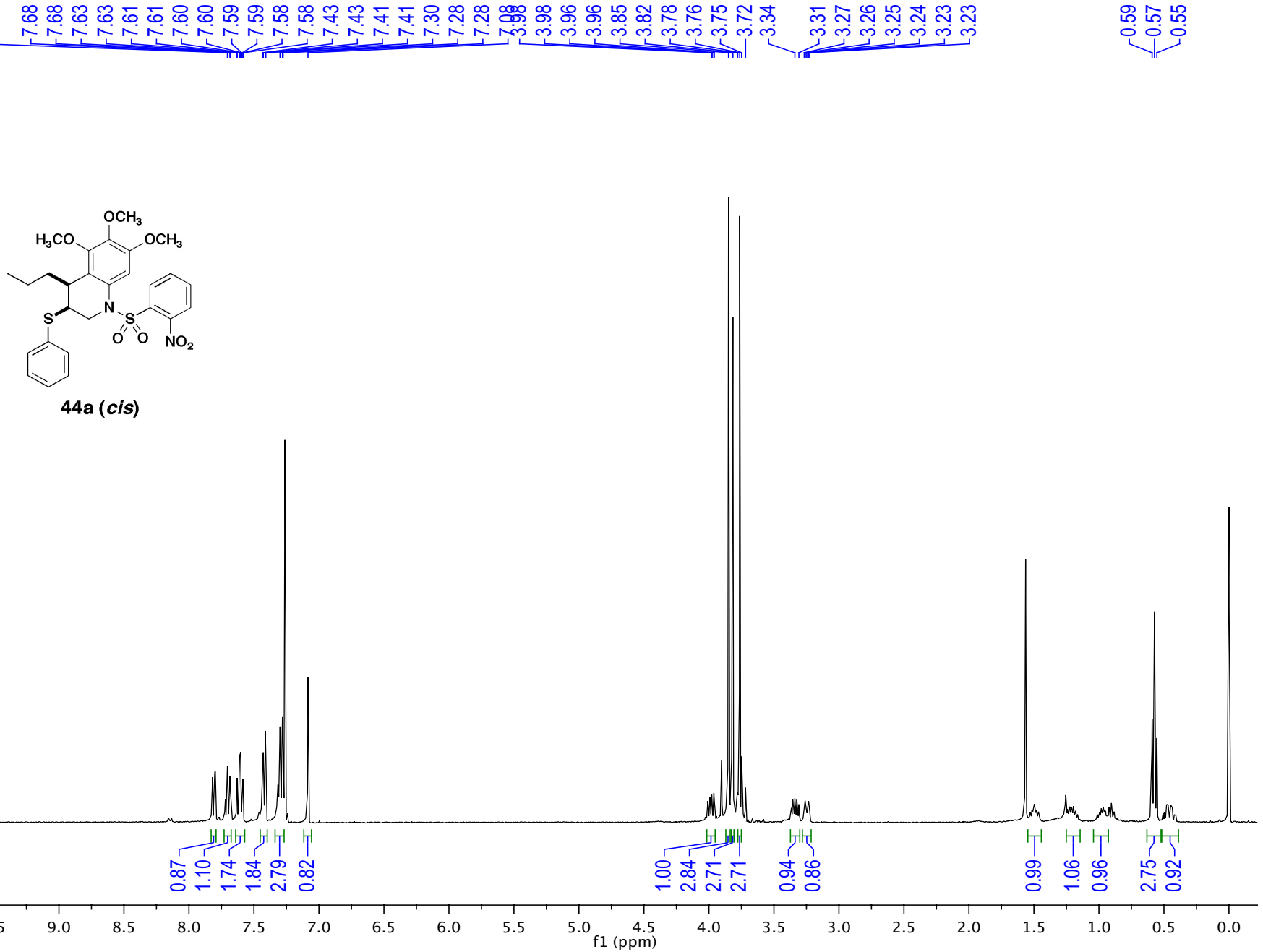


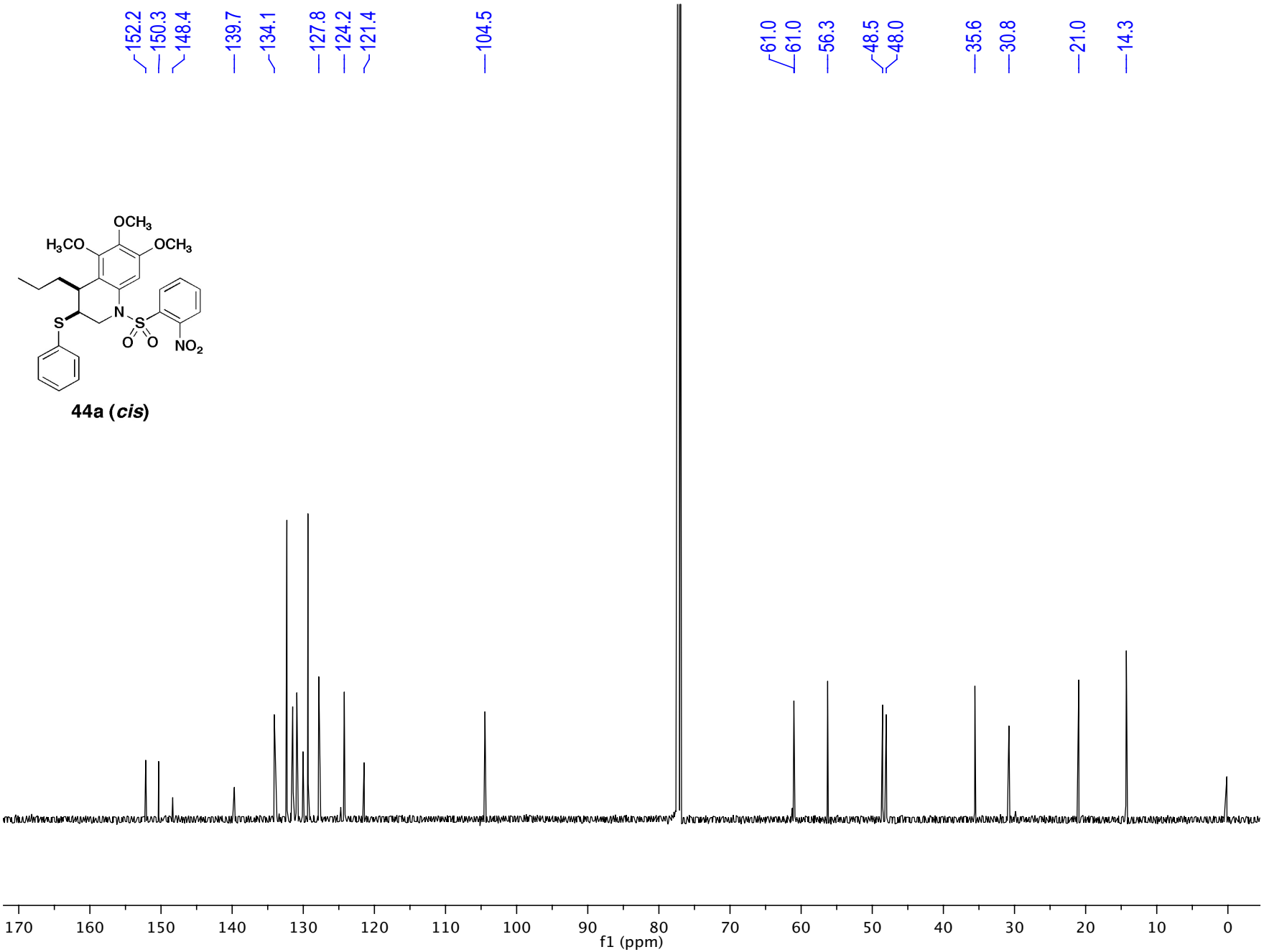
43a (*trans*)



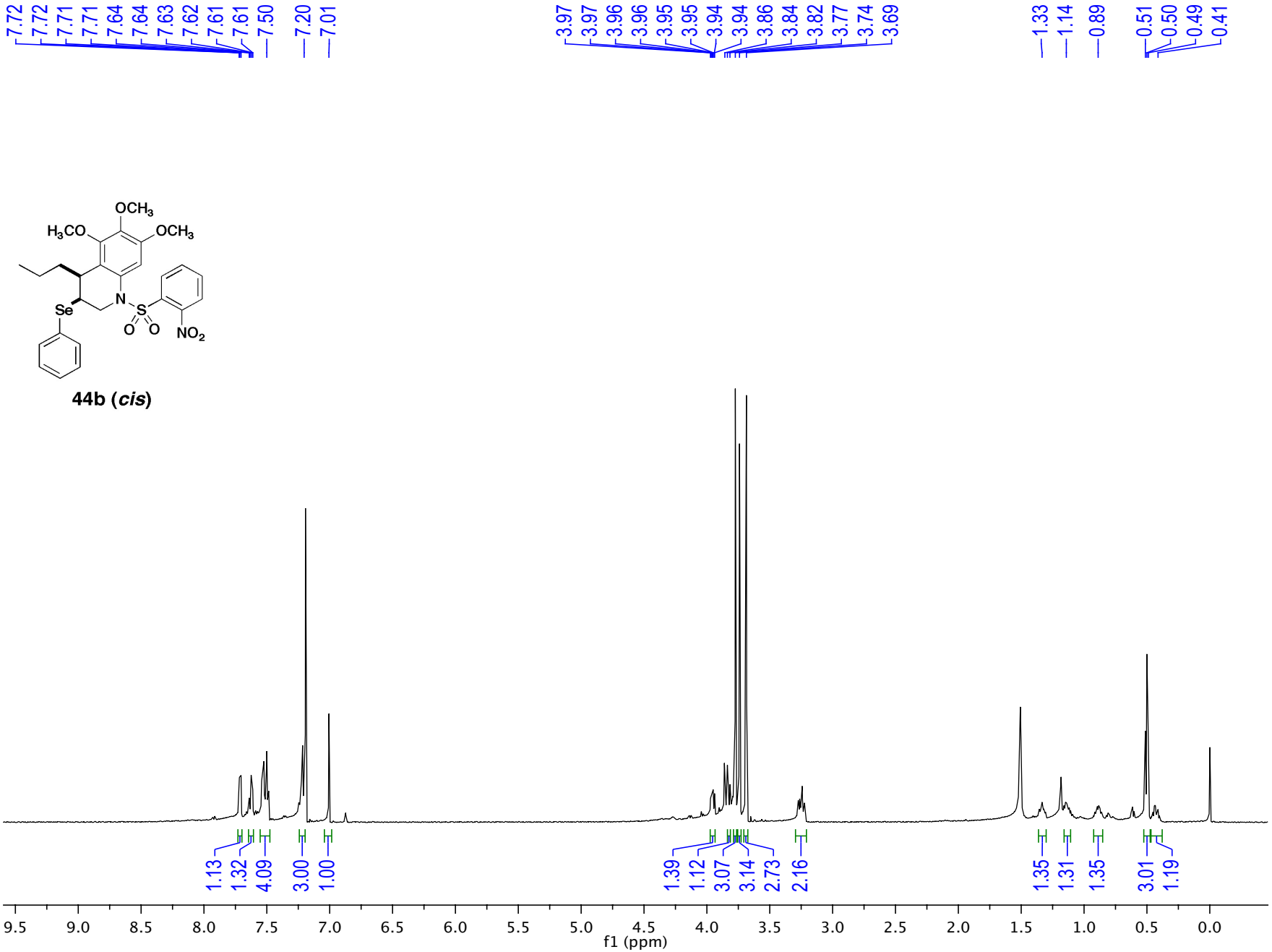
43b (*trans*)



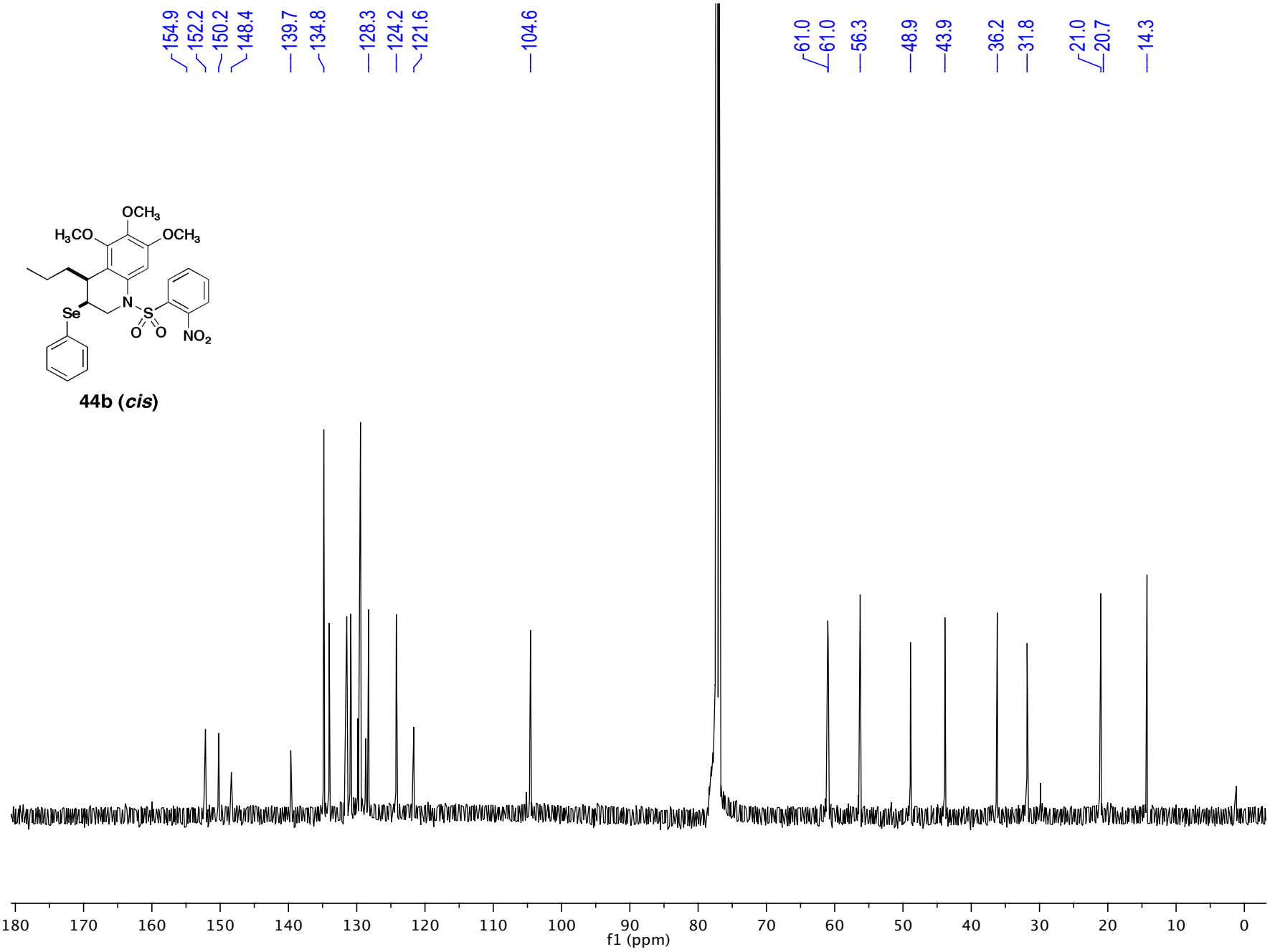




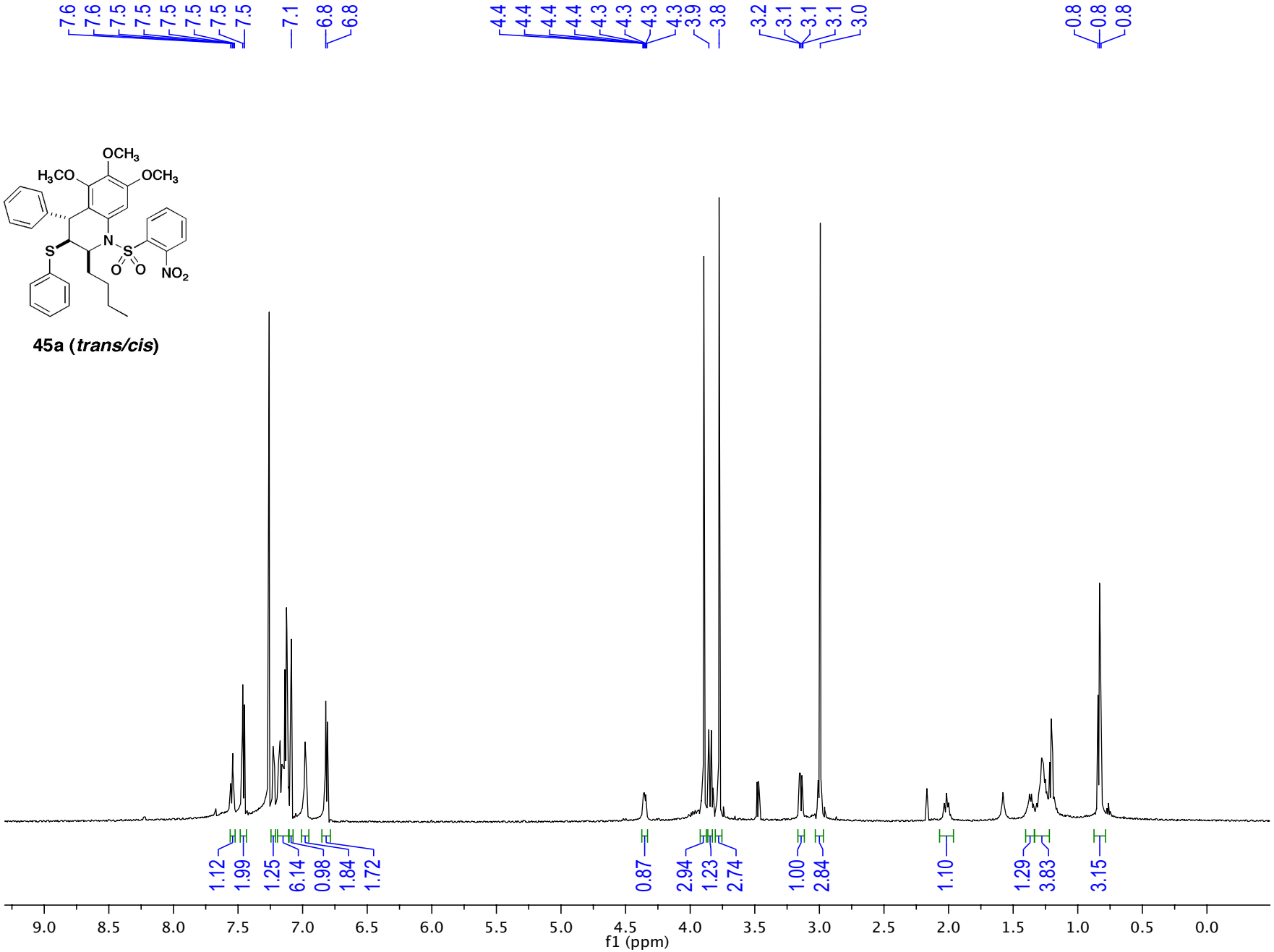
44a (*cis*)

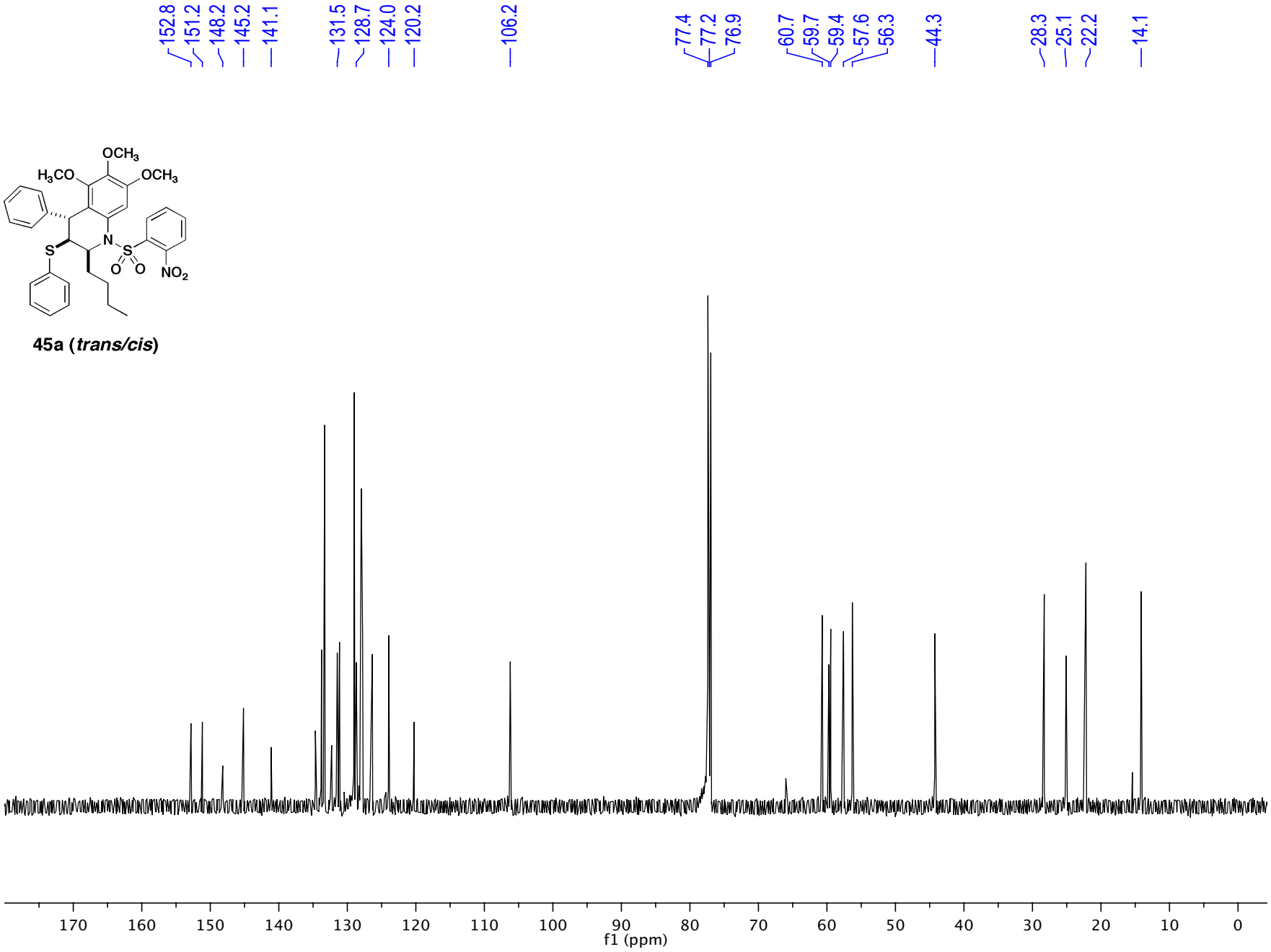


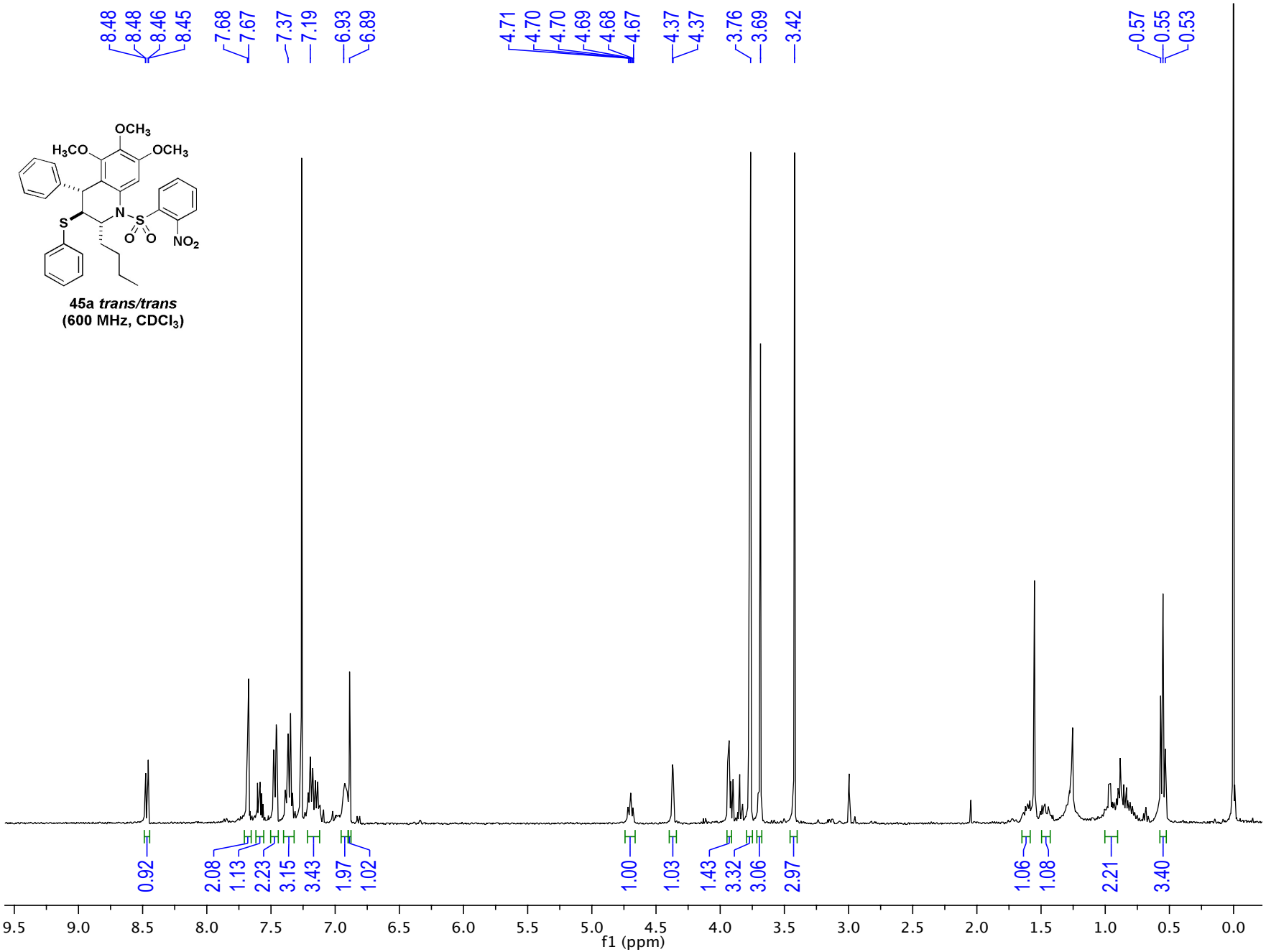
44b (*cis*)

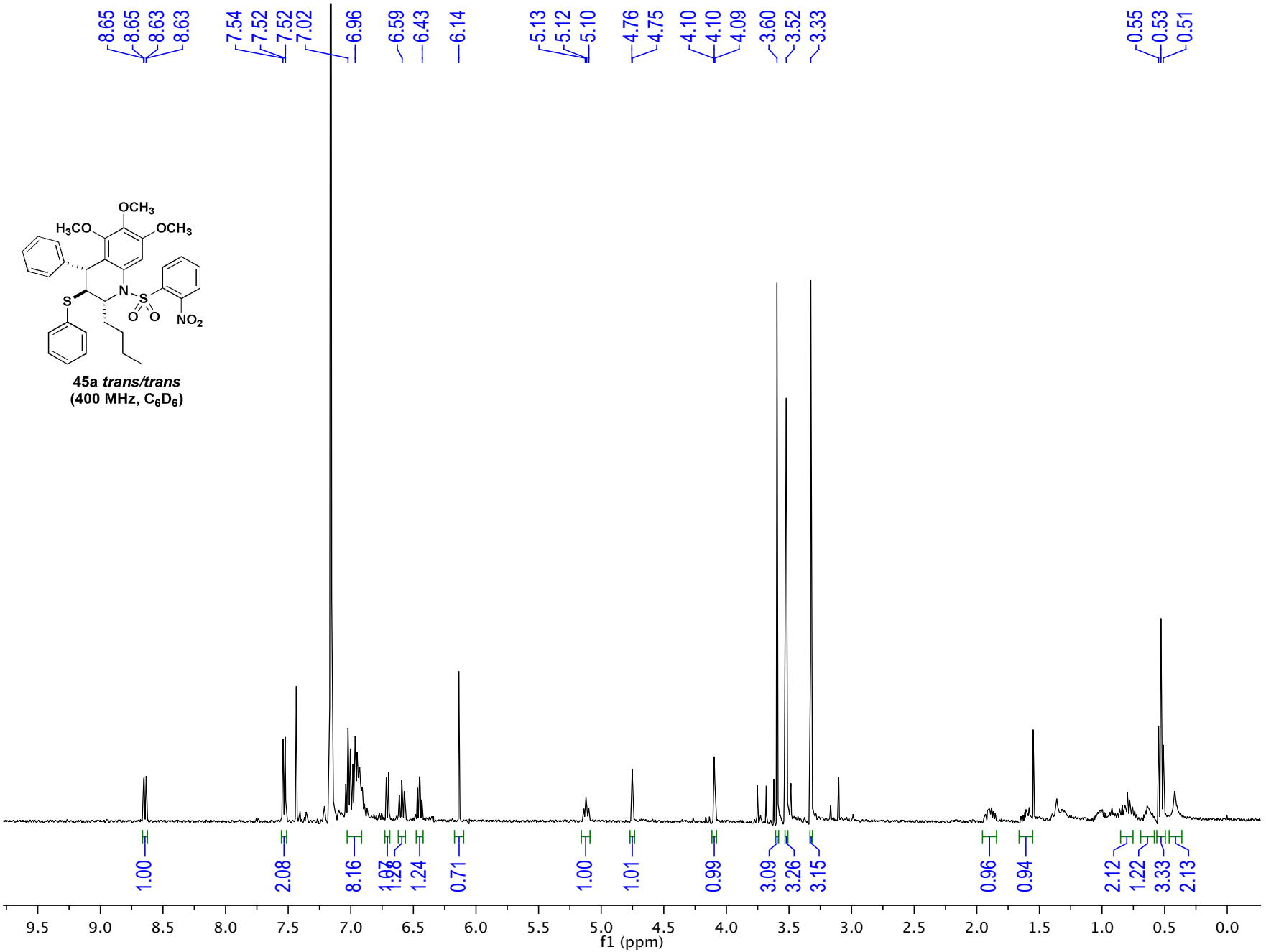


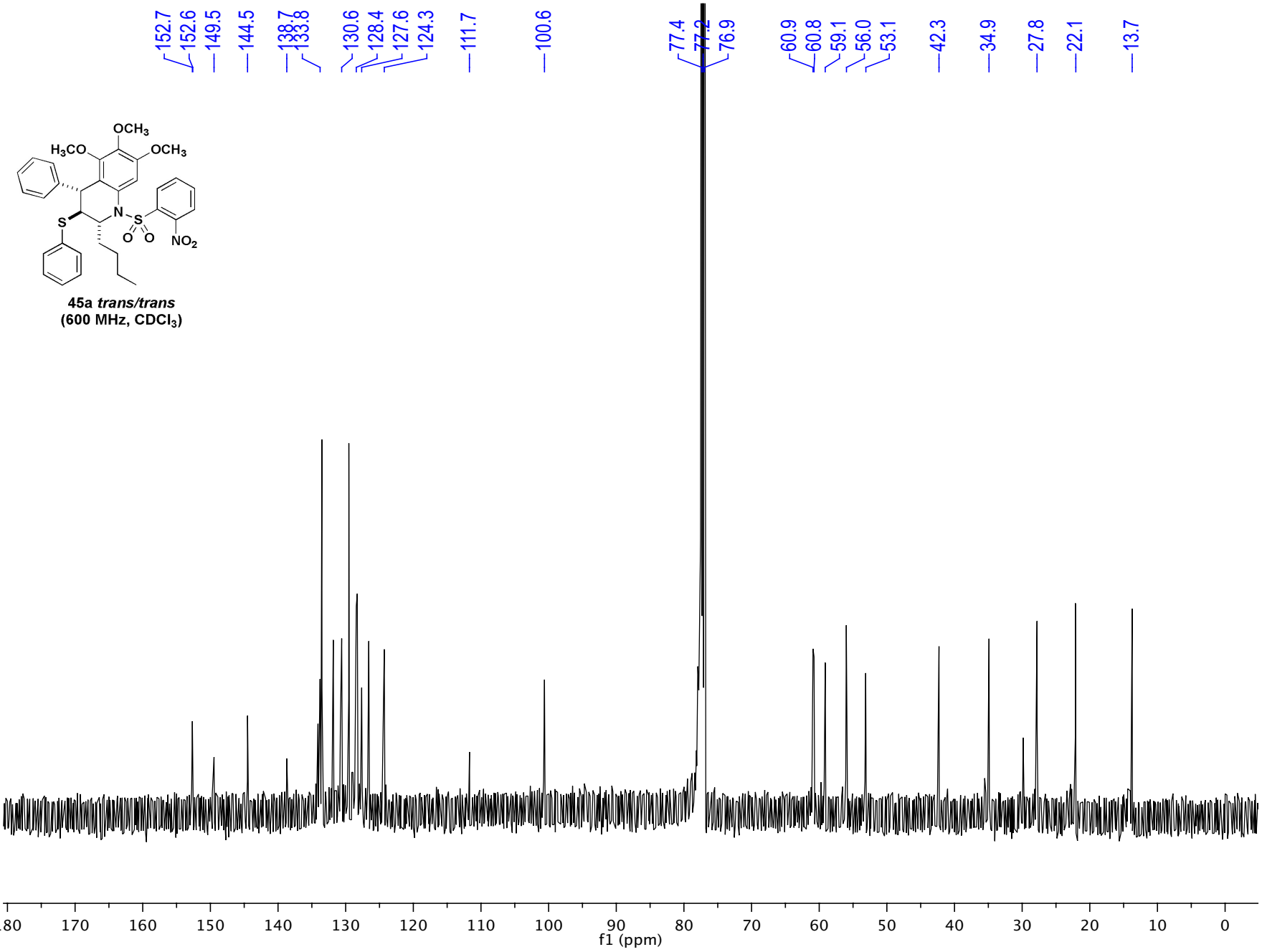
44b (*cis*)

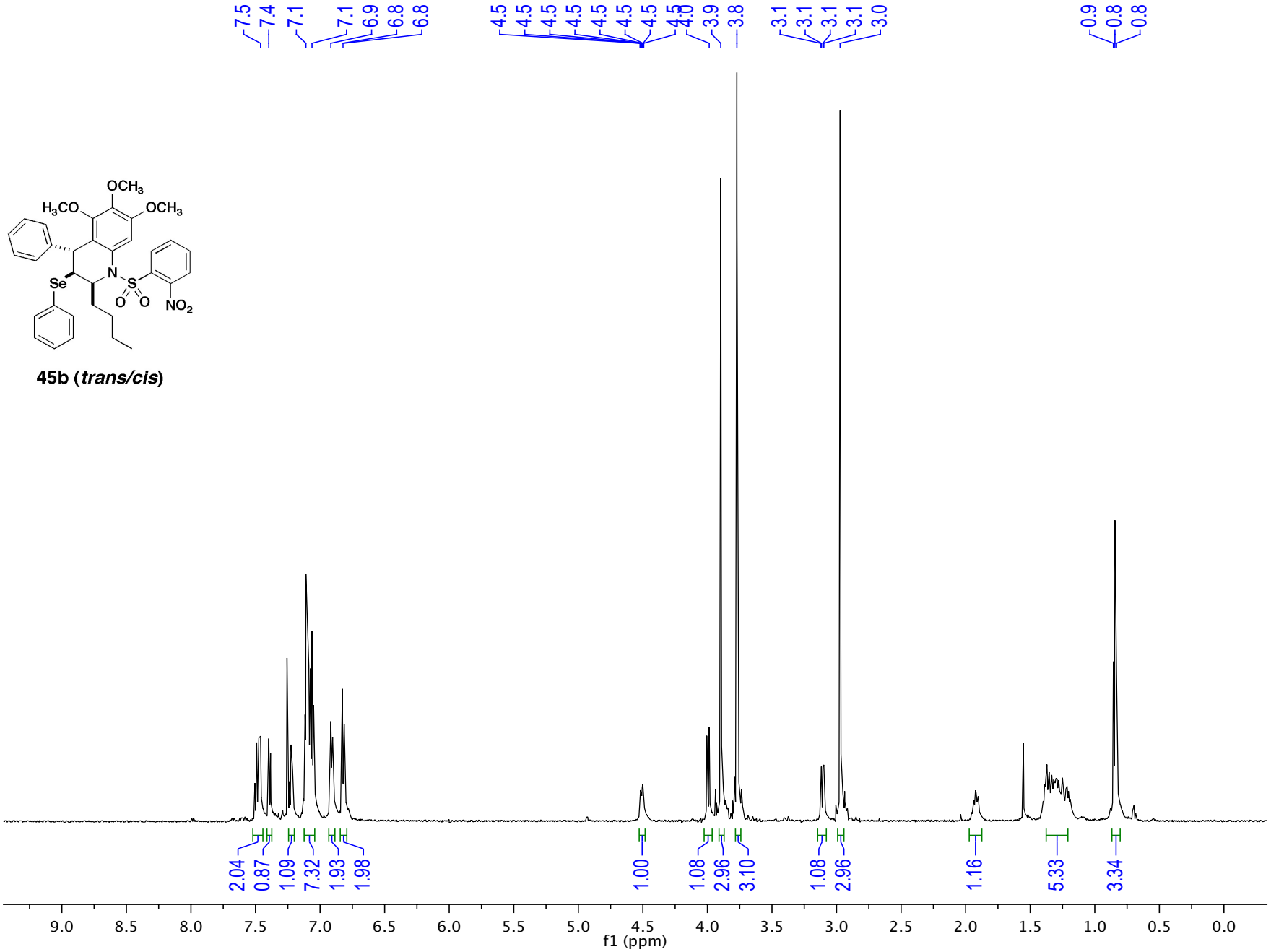




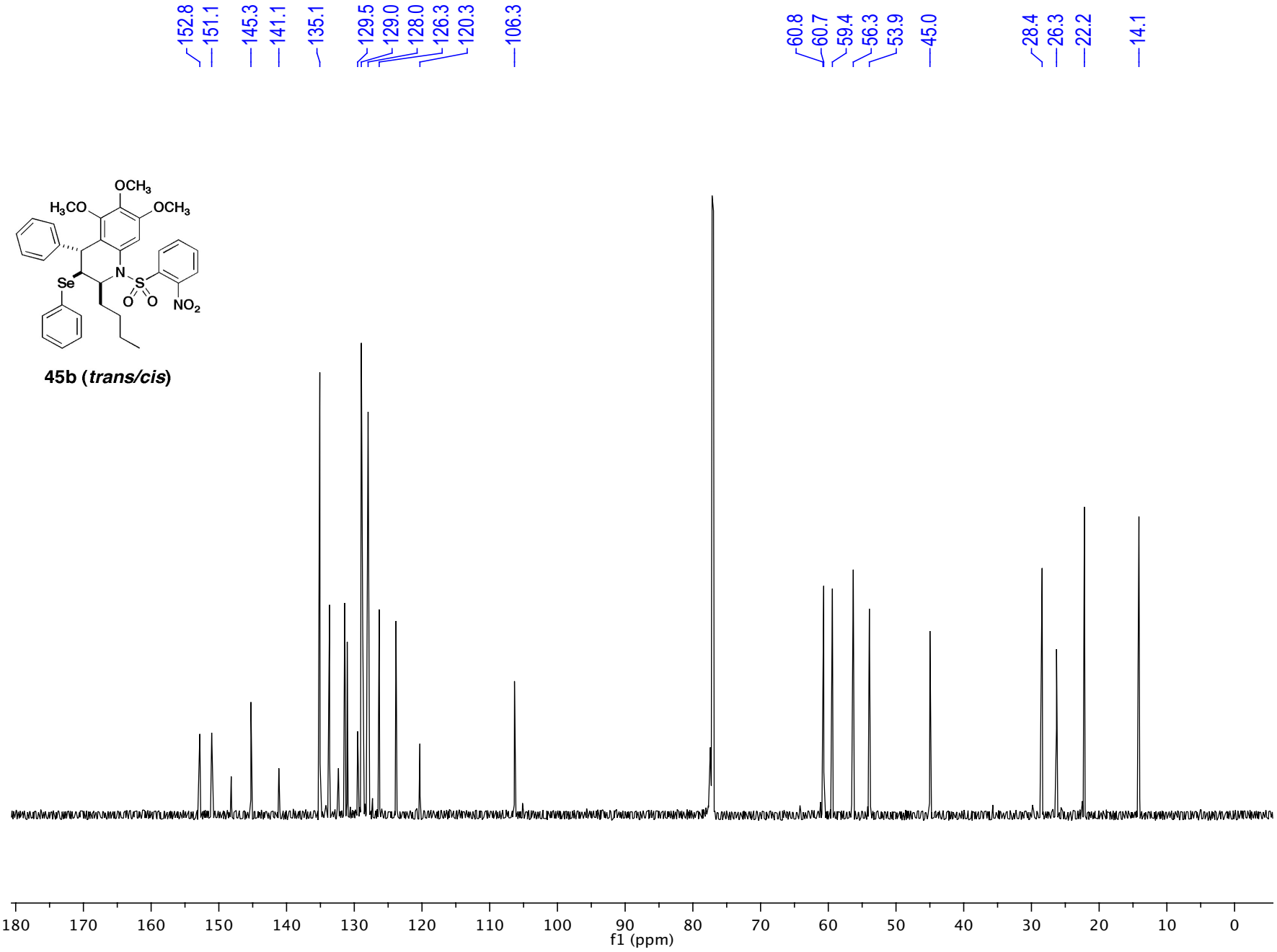


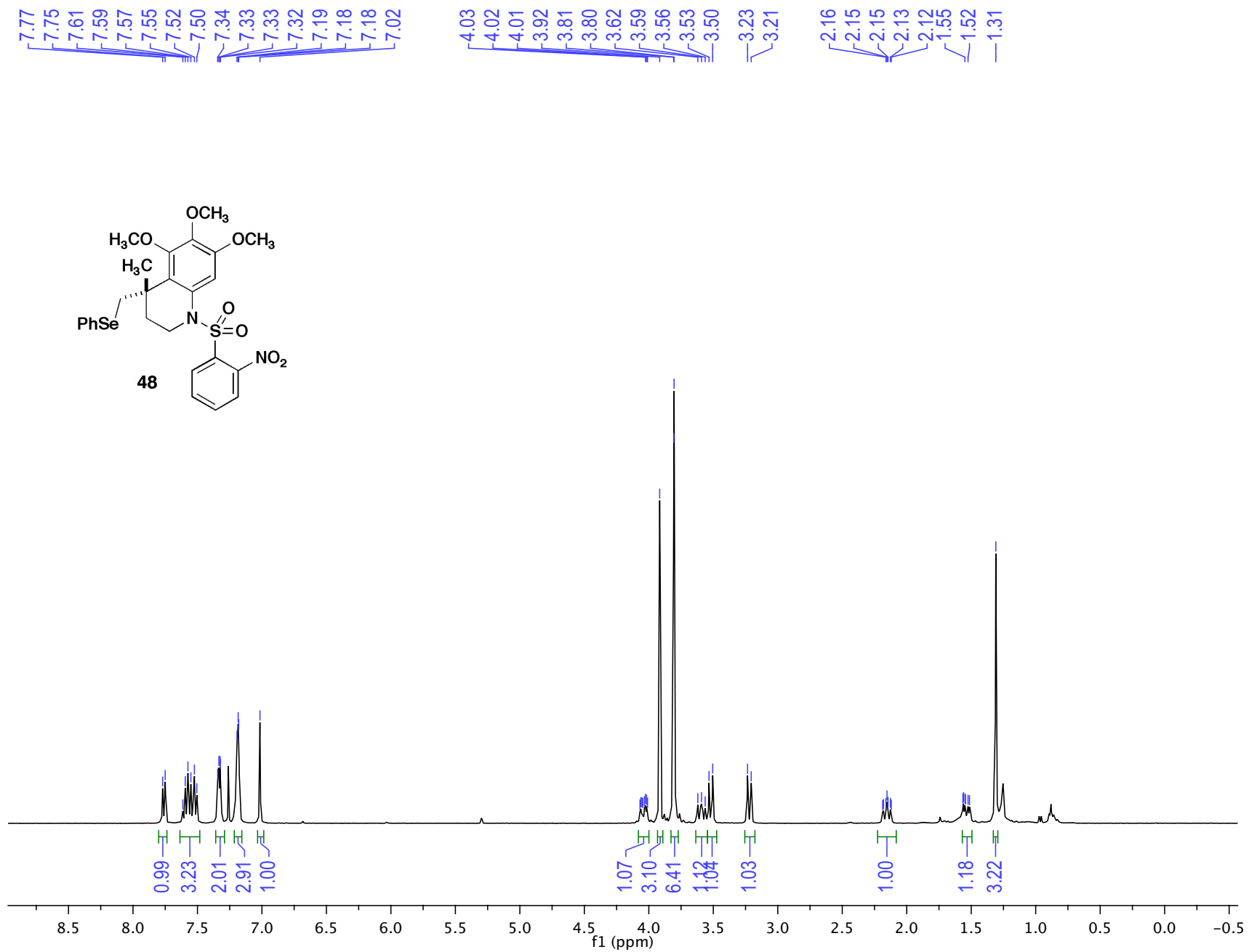


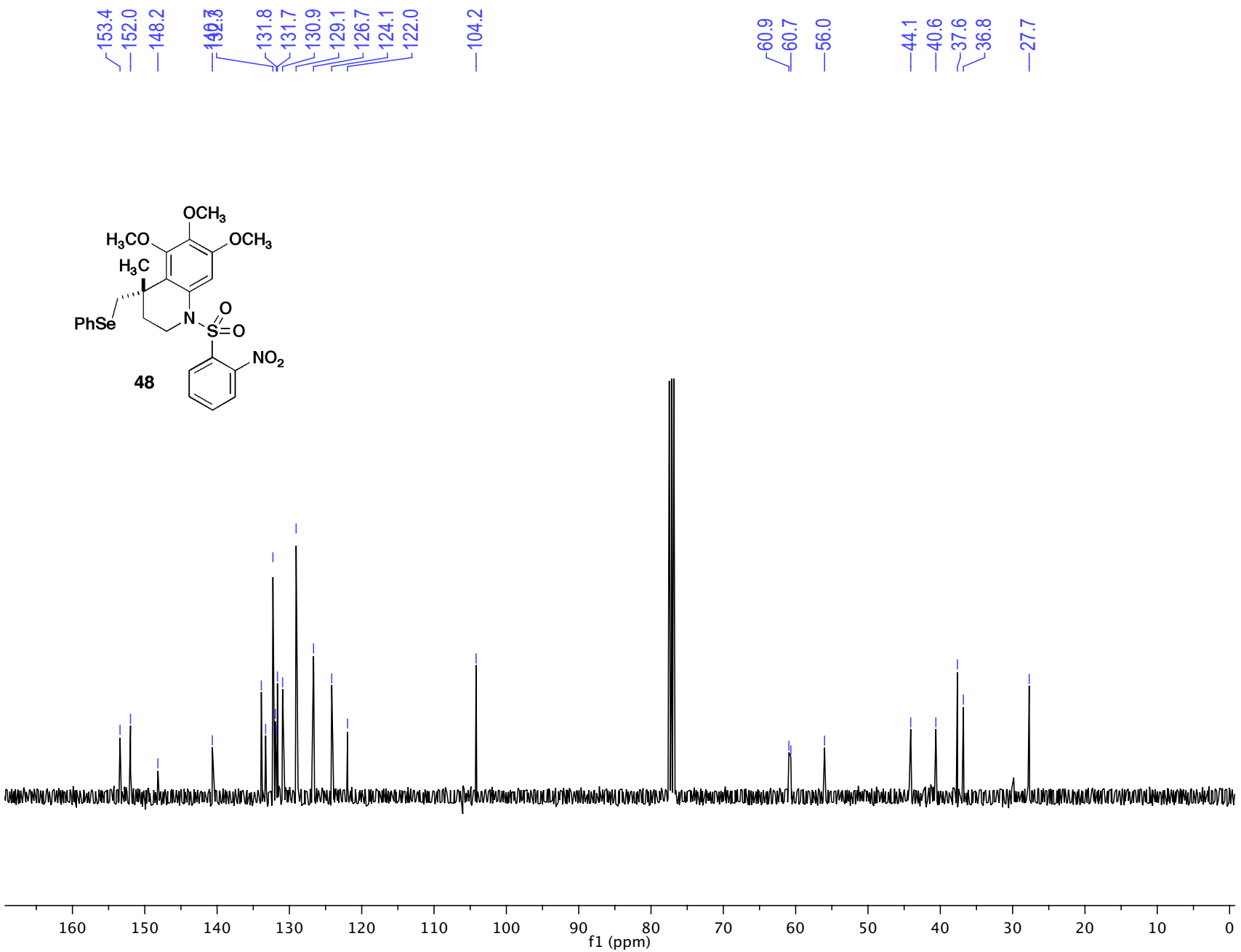


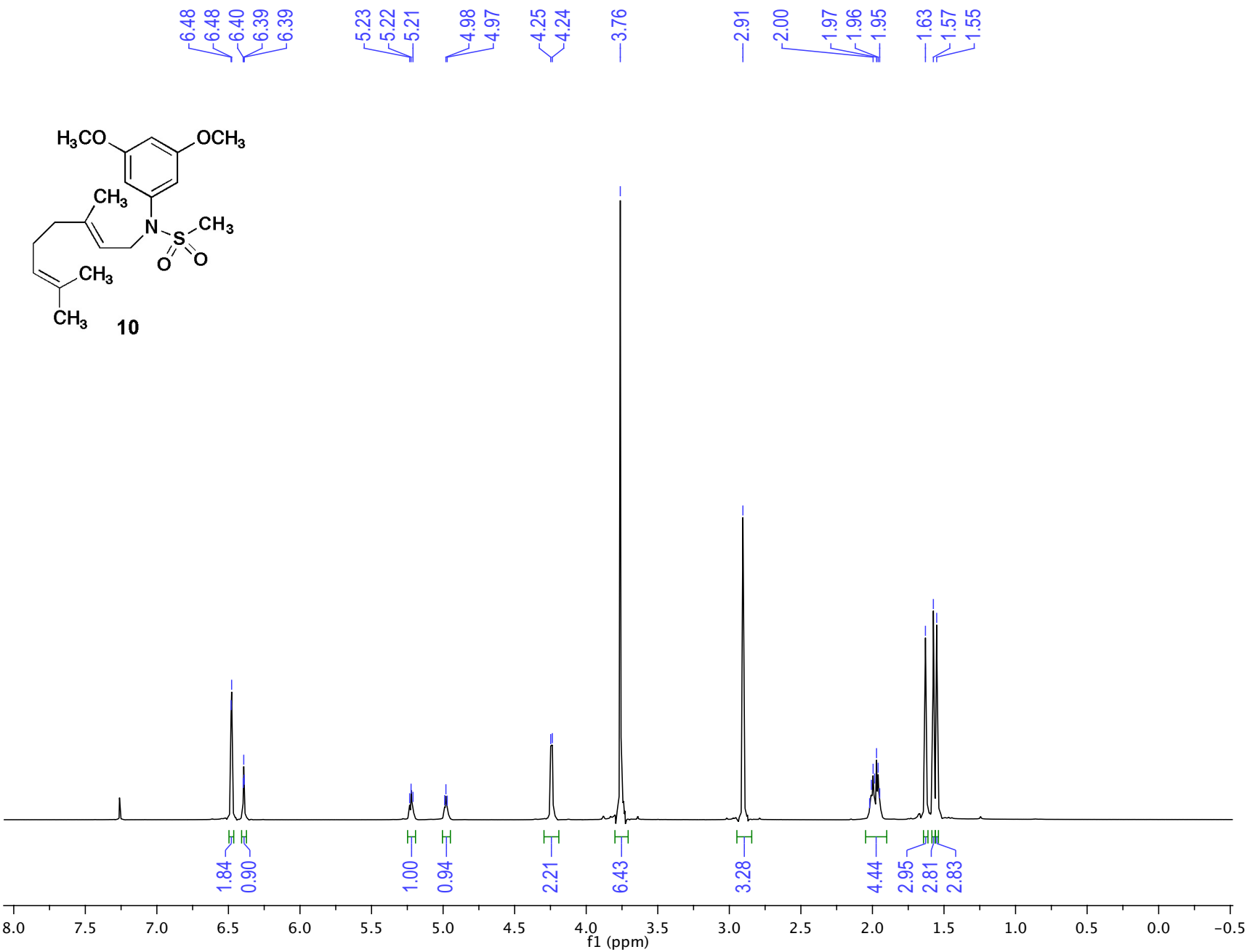


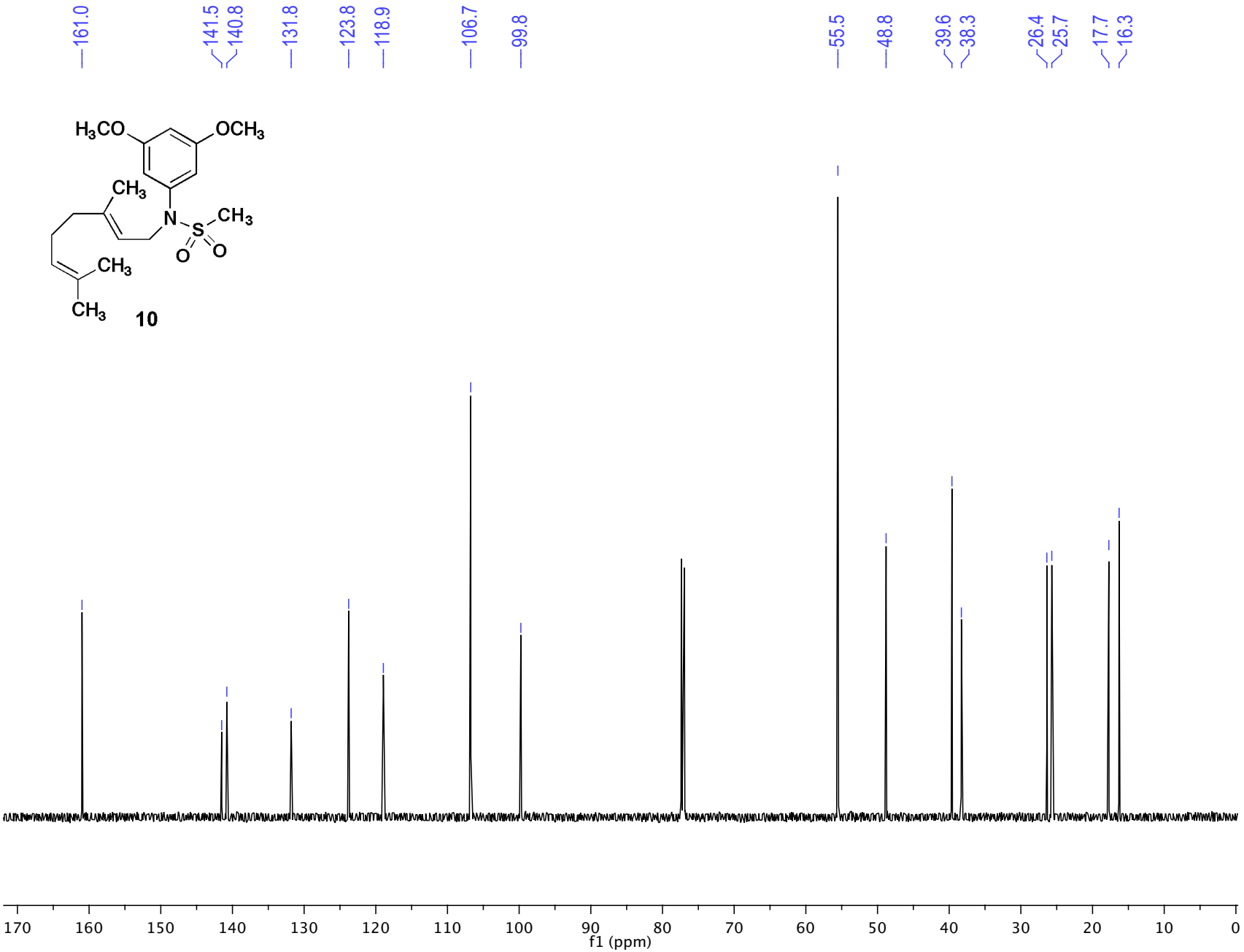
45b (*trans/cis*)

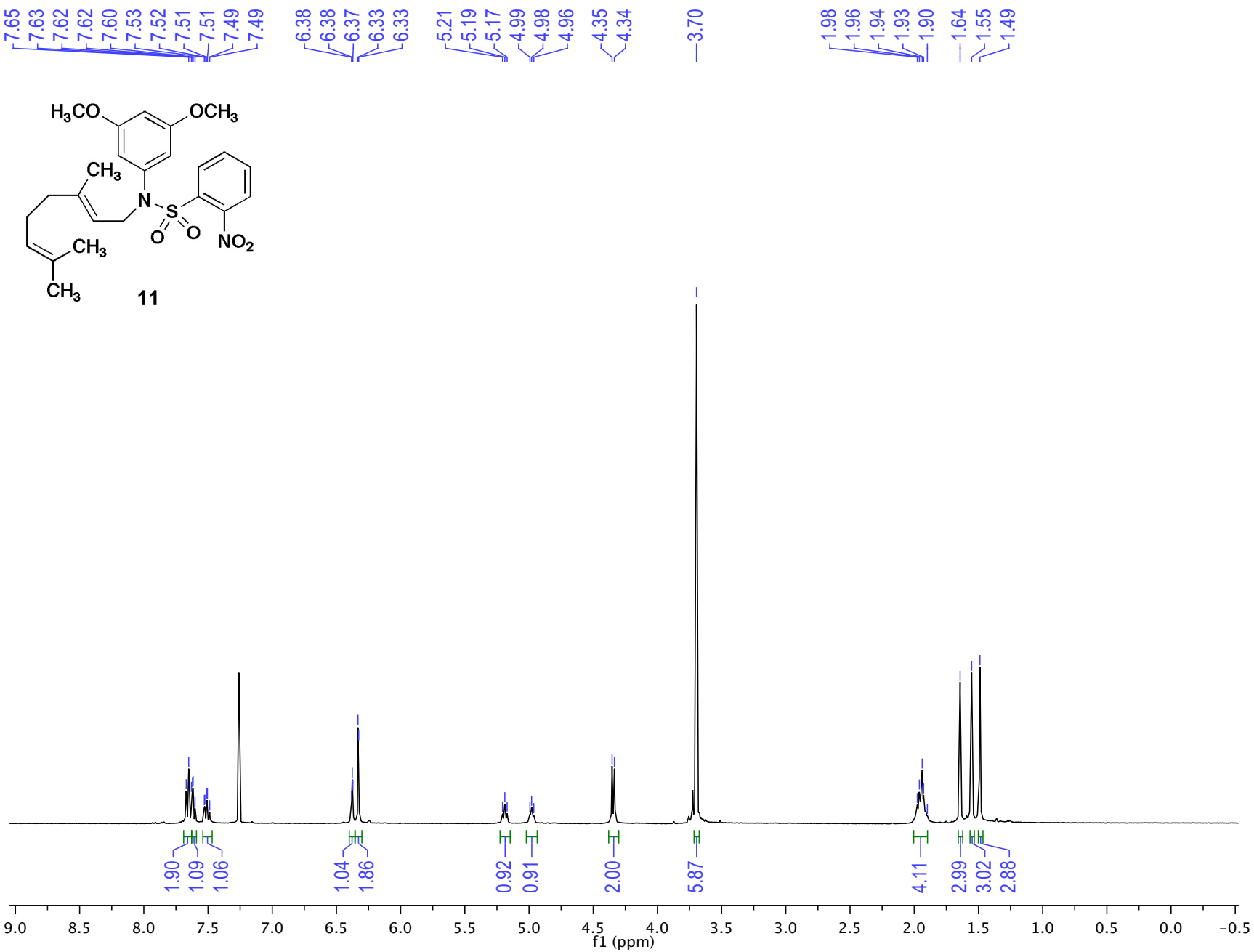


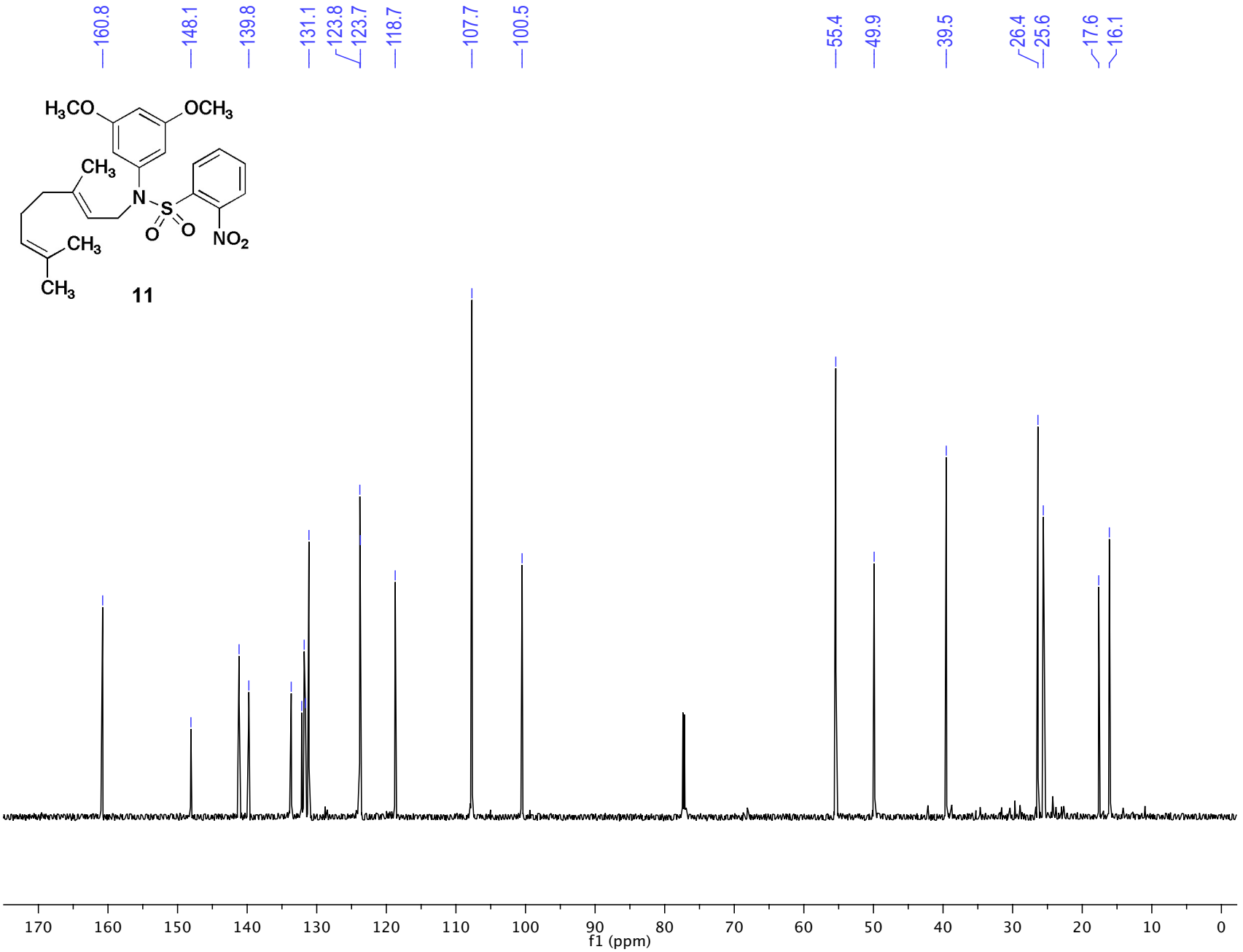


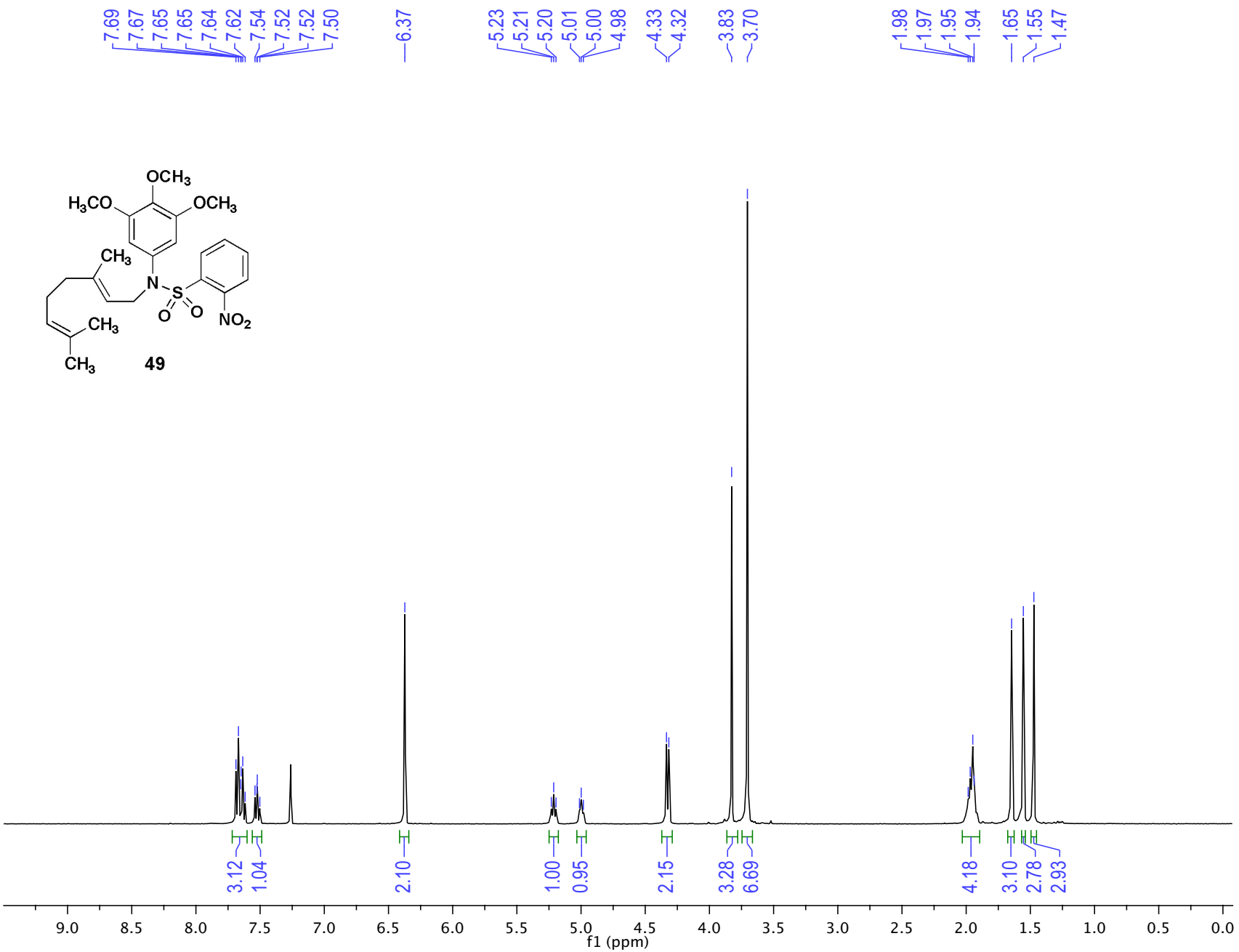


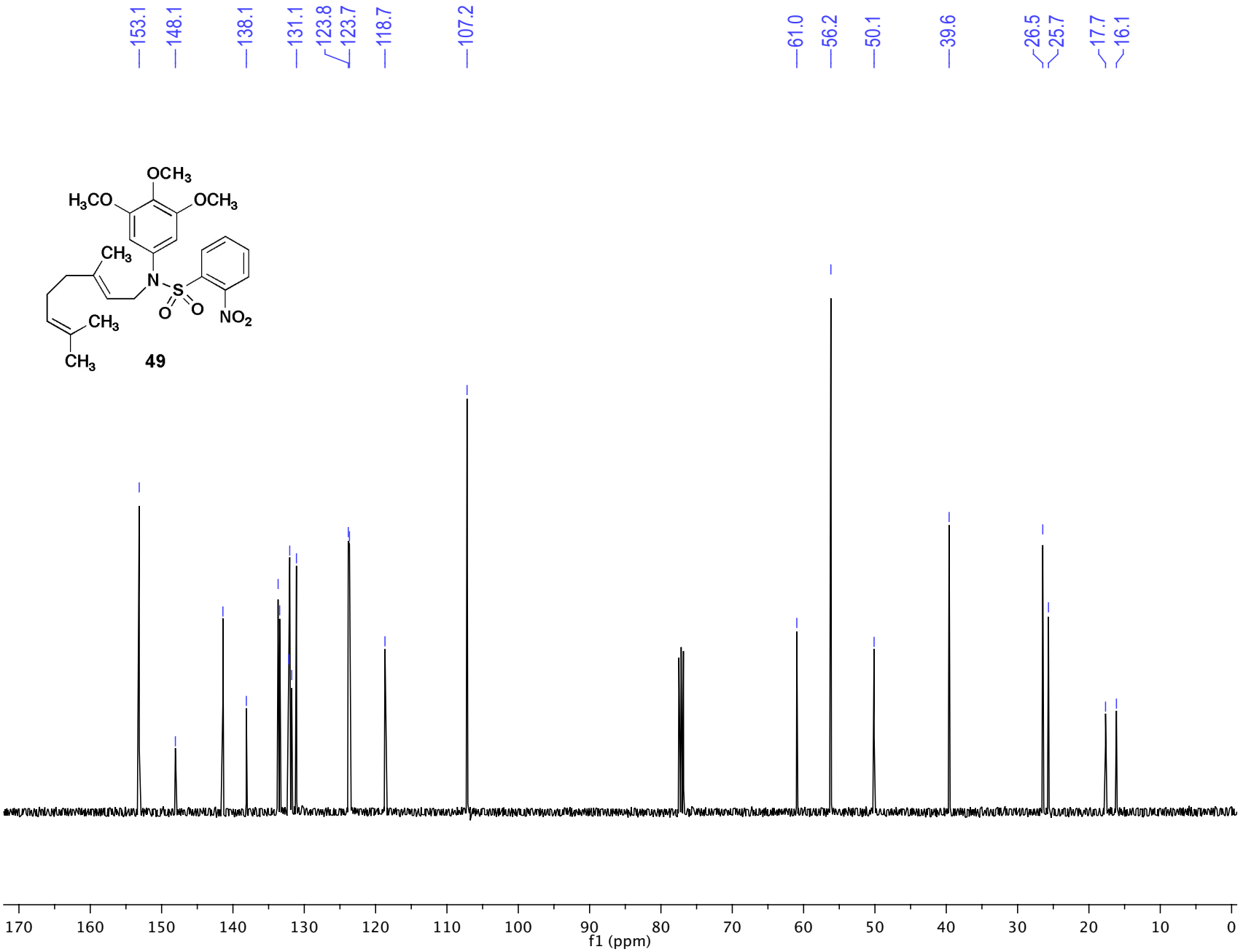


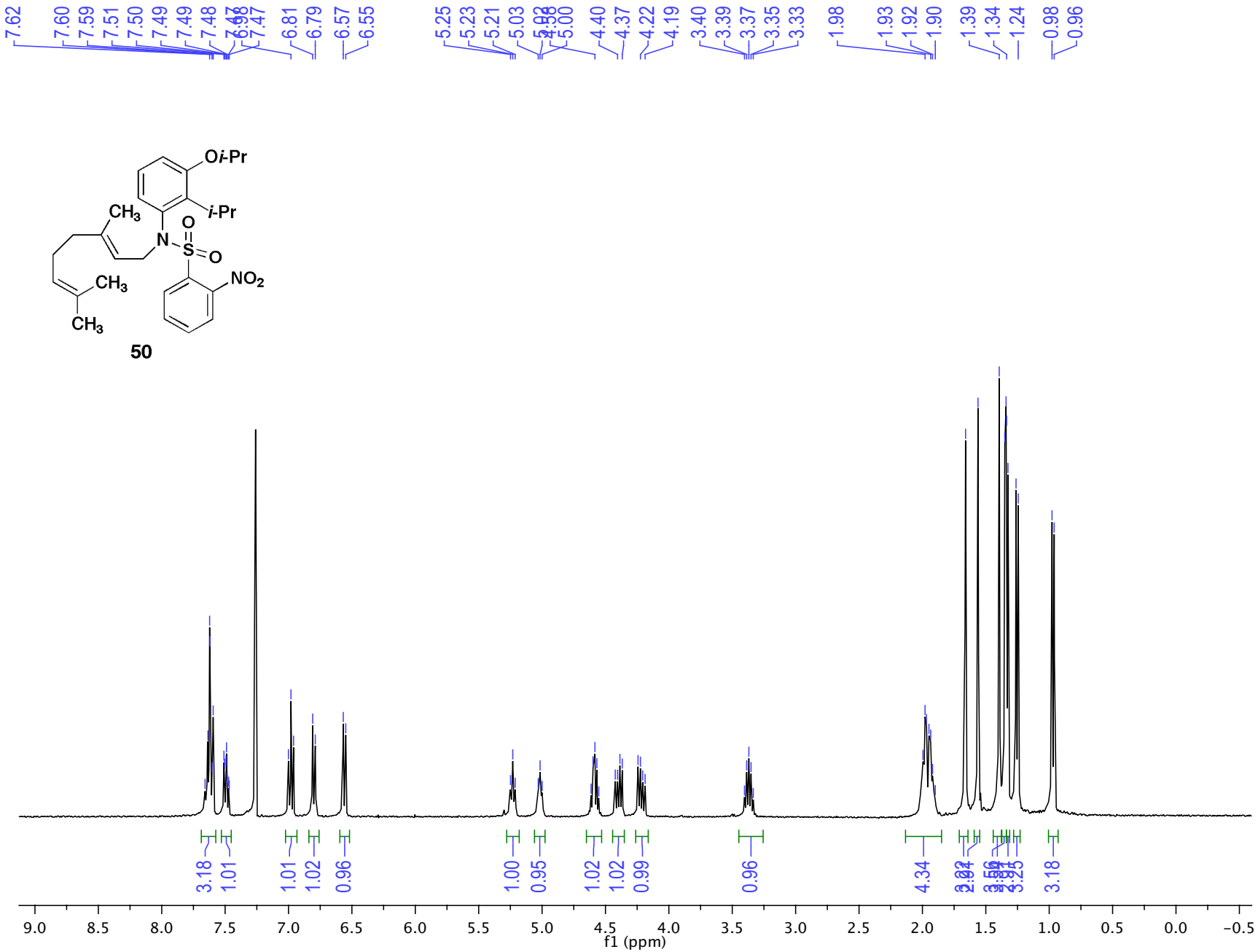


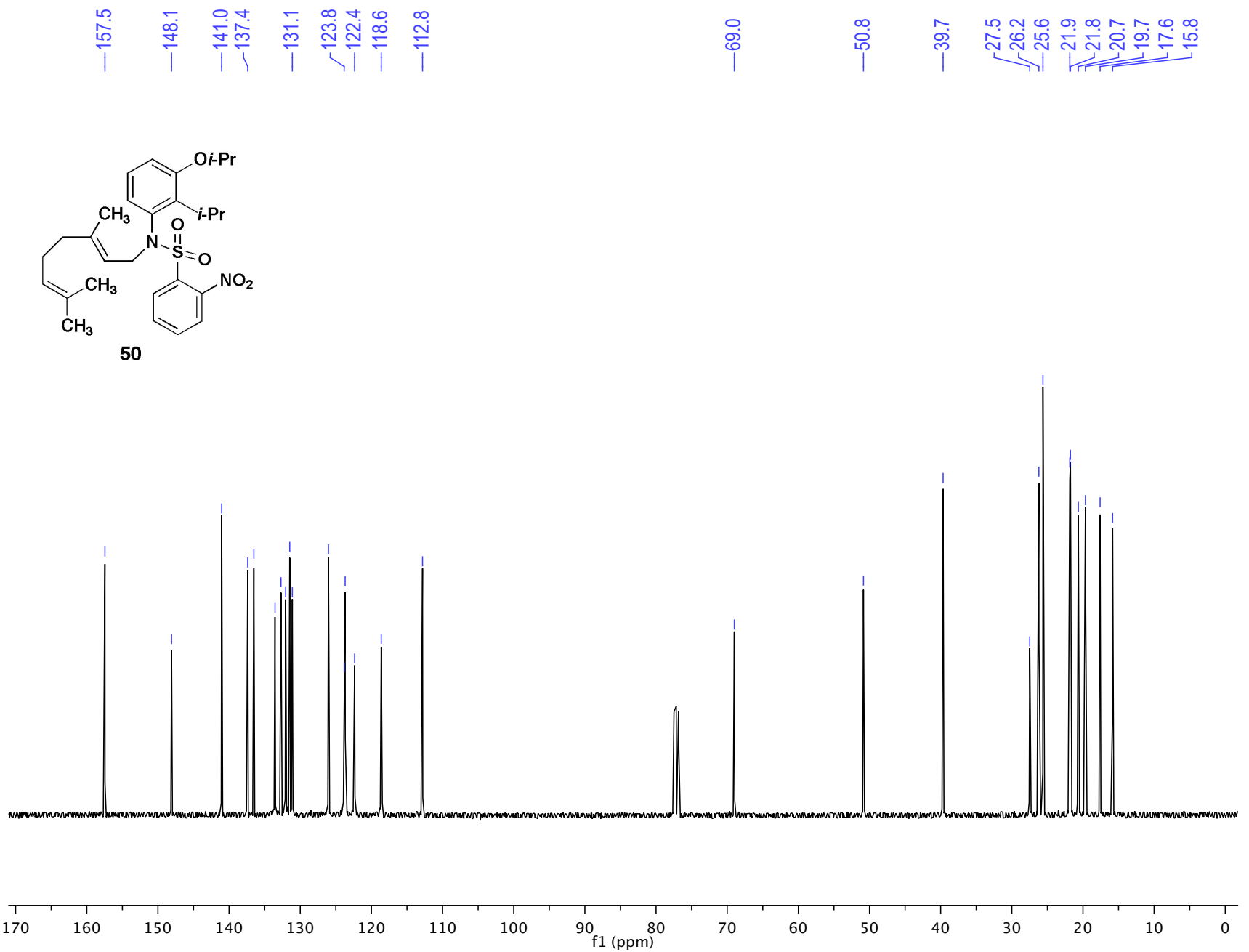


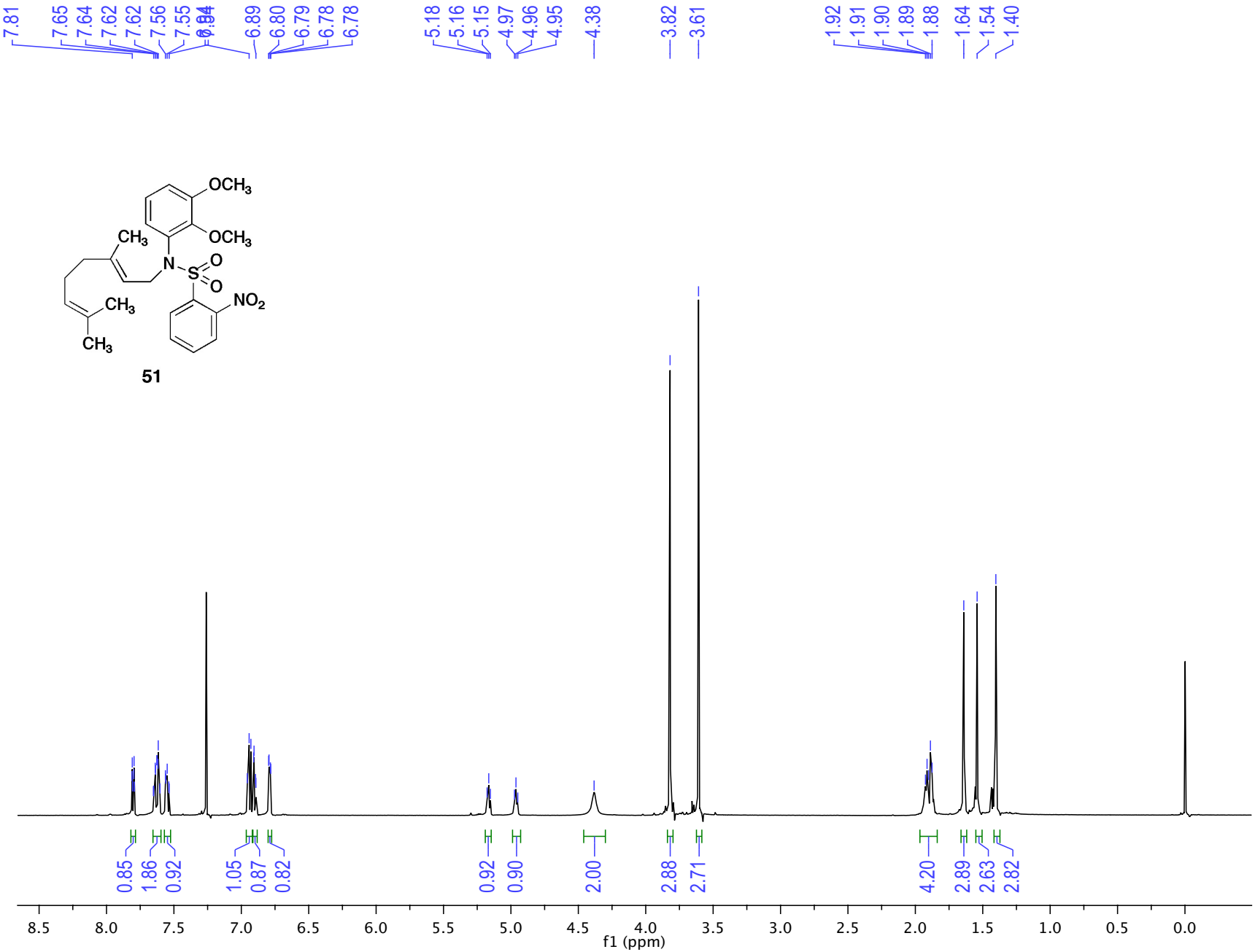




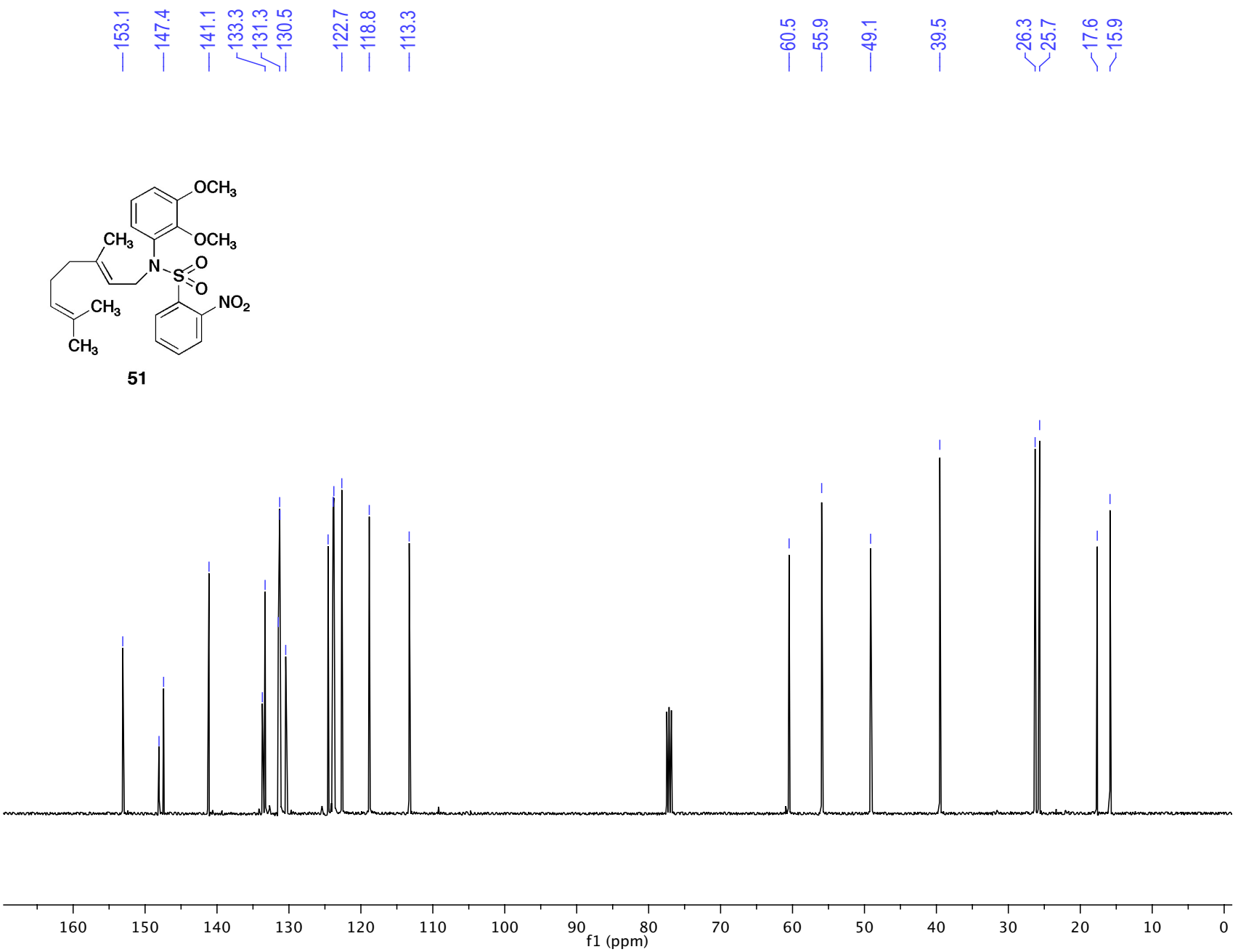




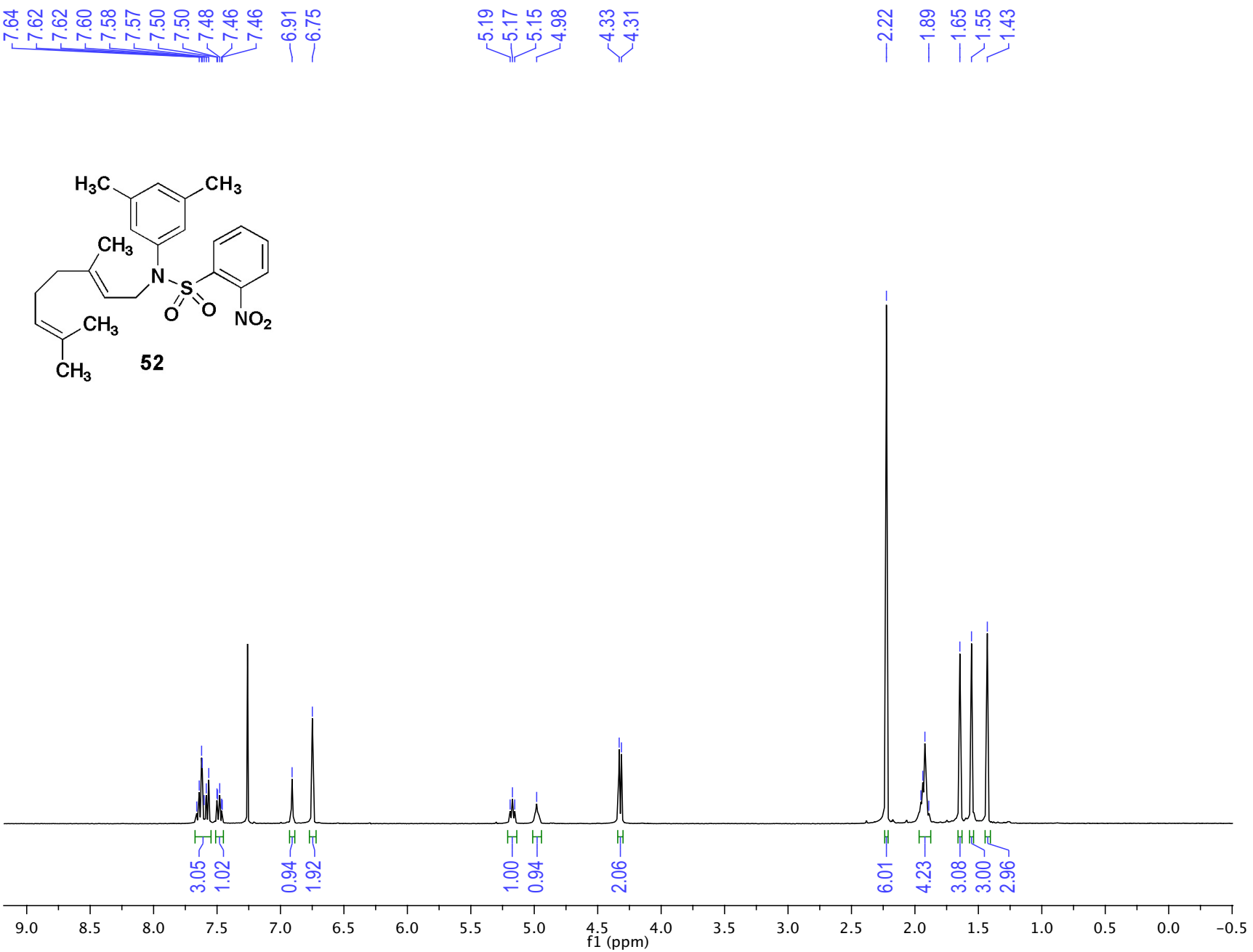




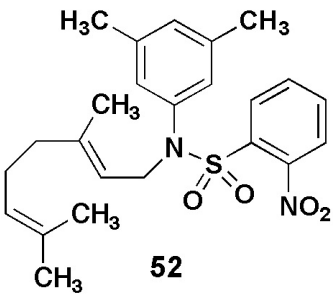
51



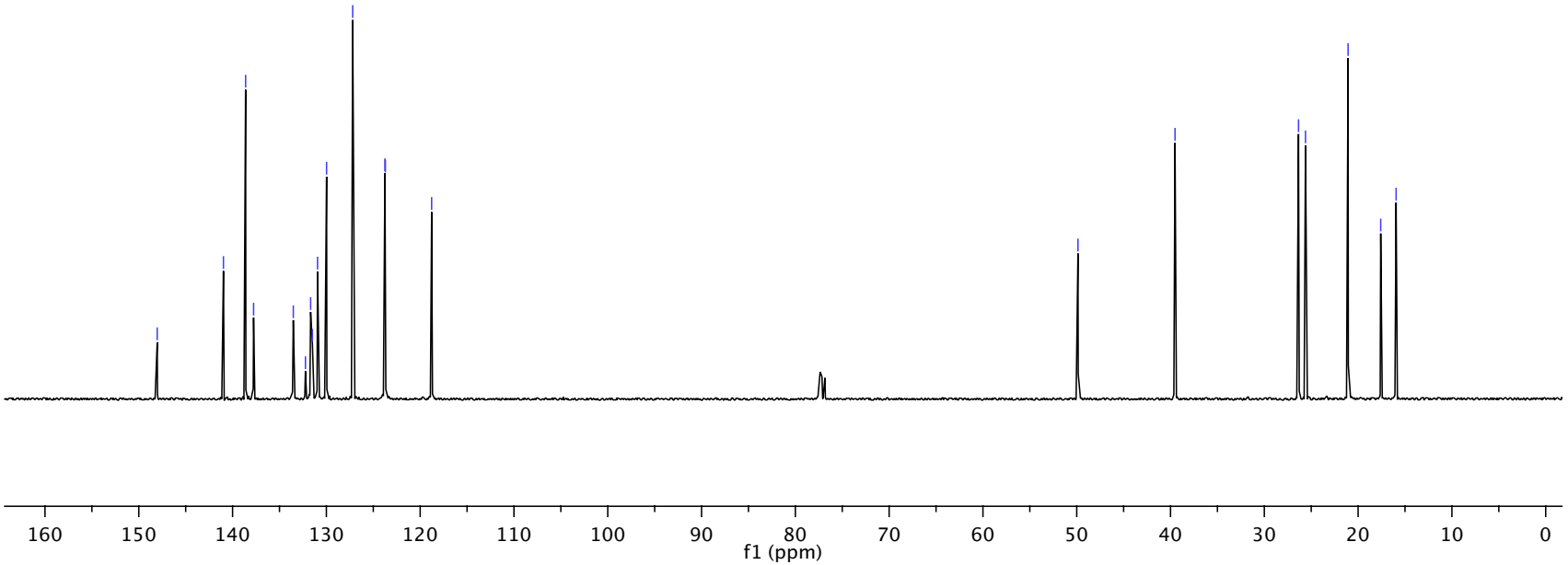
51

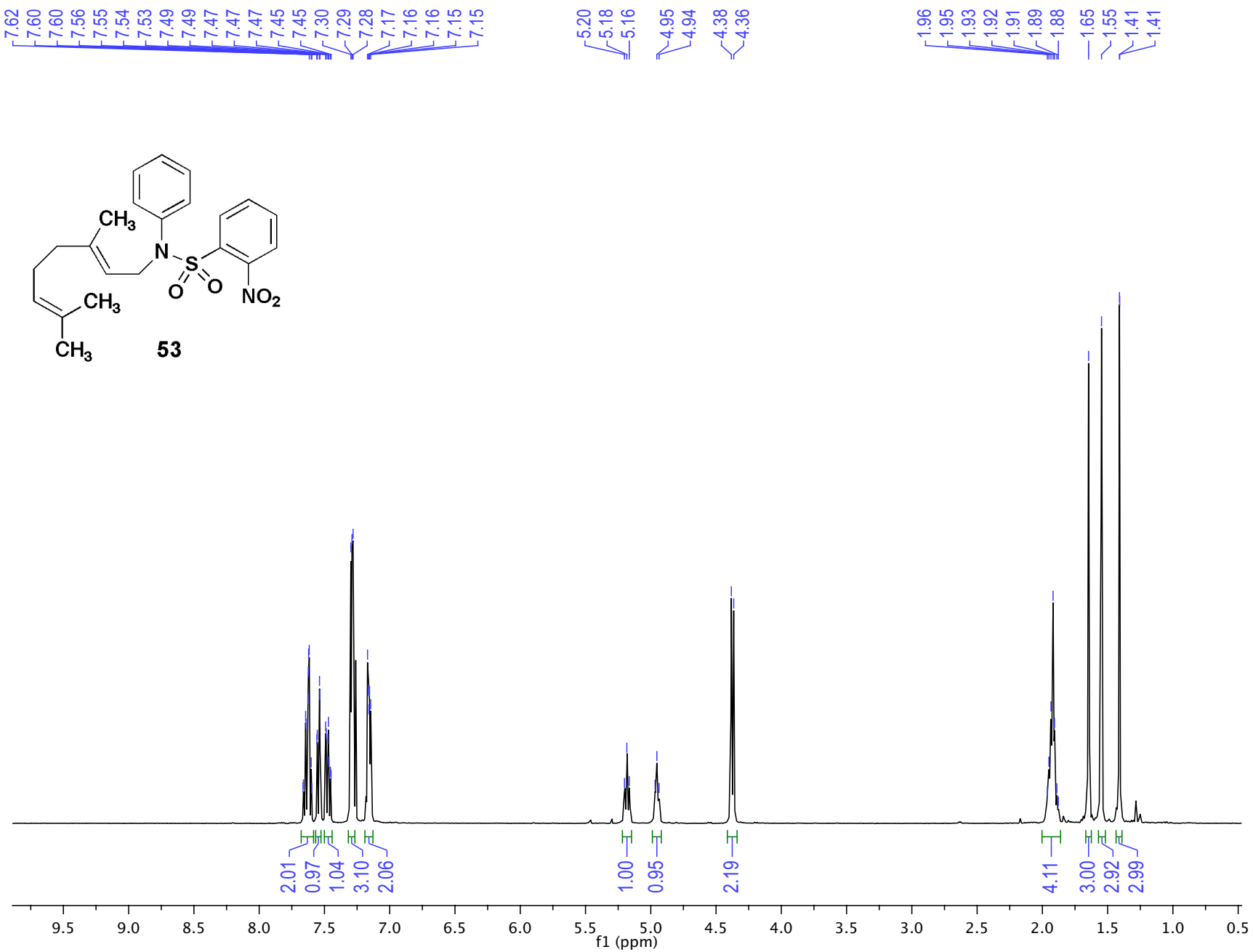


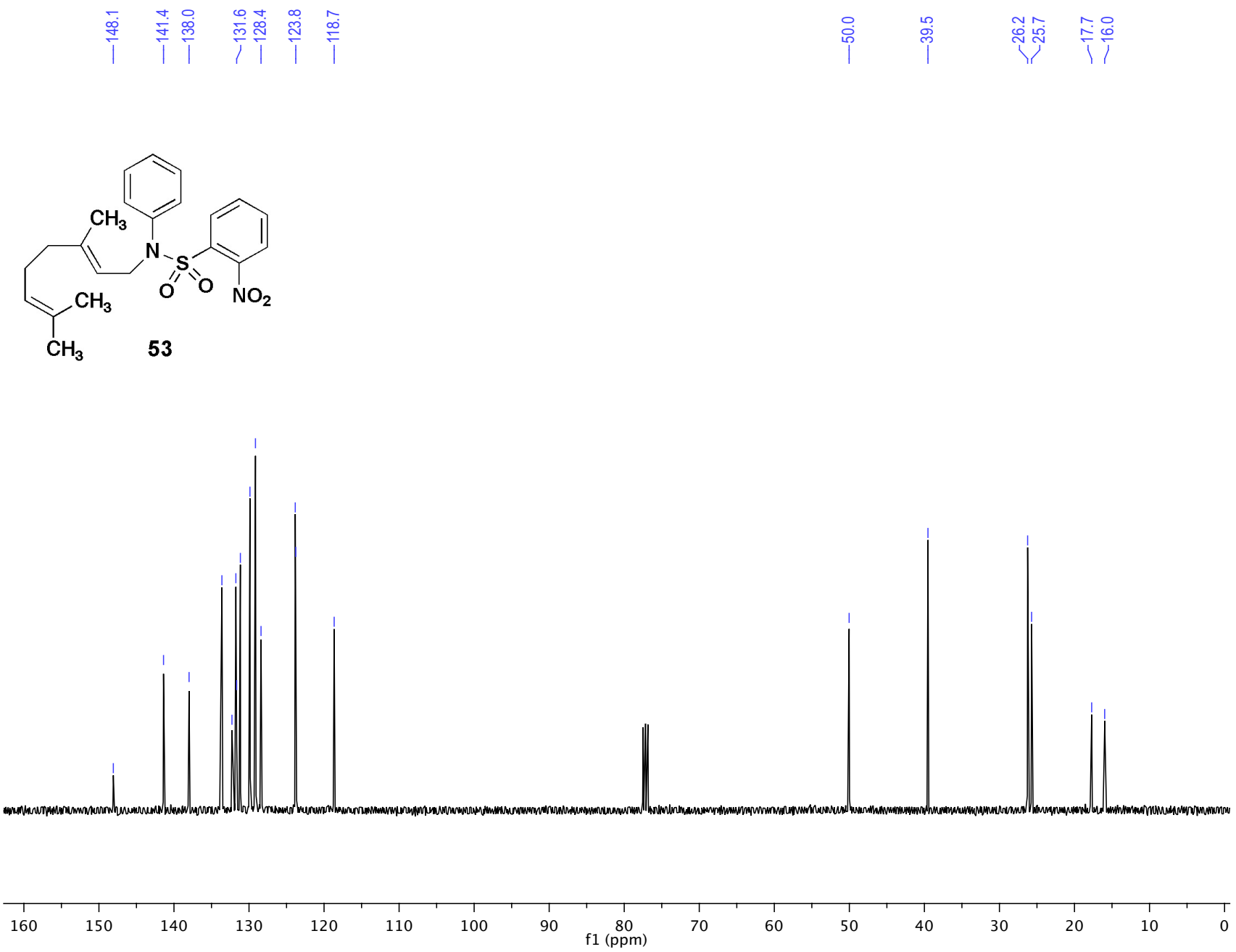
148.0 141.0 138.6 137.8 133.5 127.2 123.7 118.8 49.9 39.5 26.4 25.6 21.1 17.6 15.9

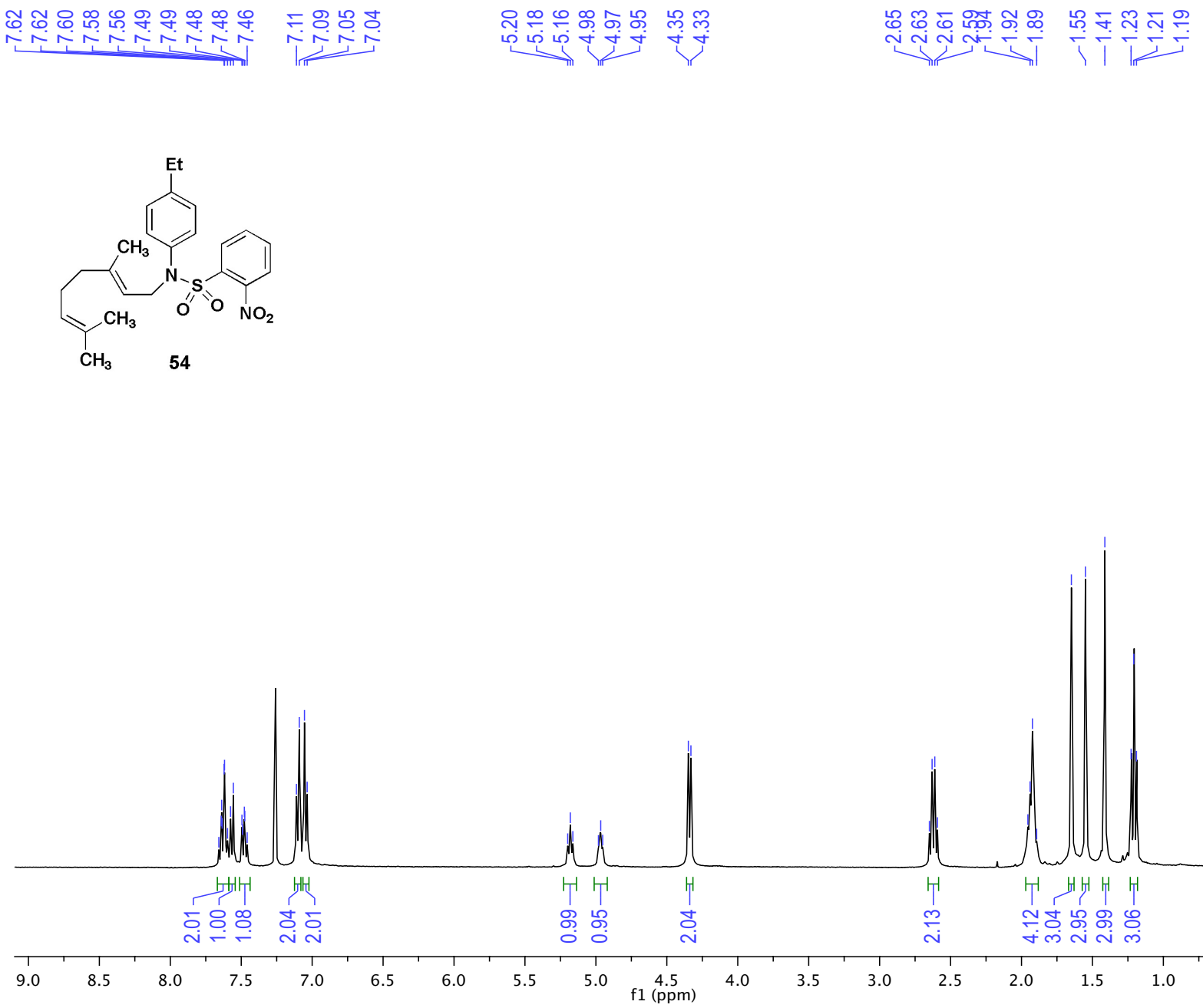


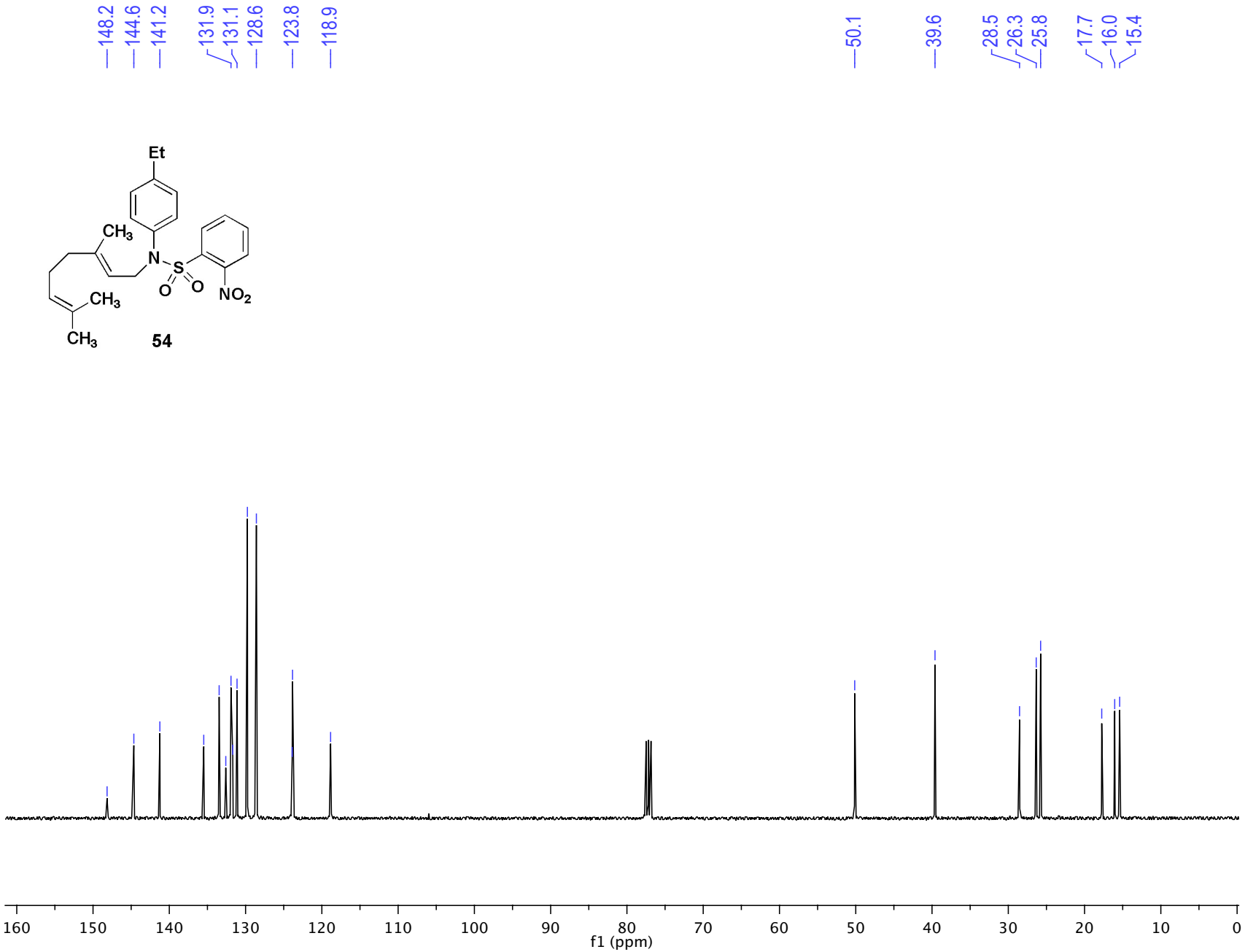
52











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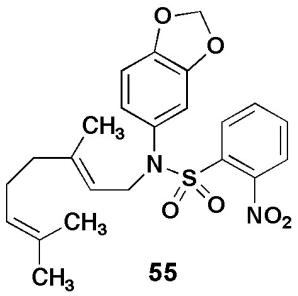

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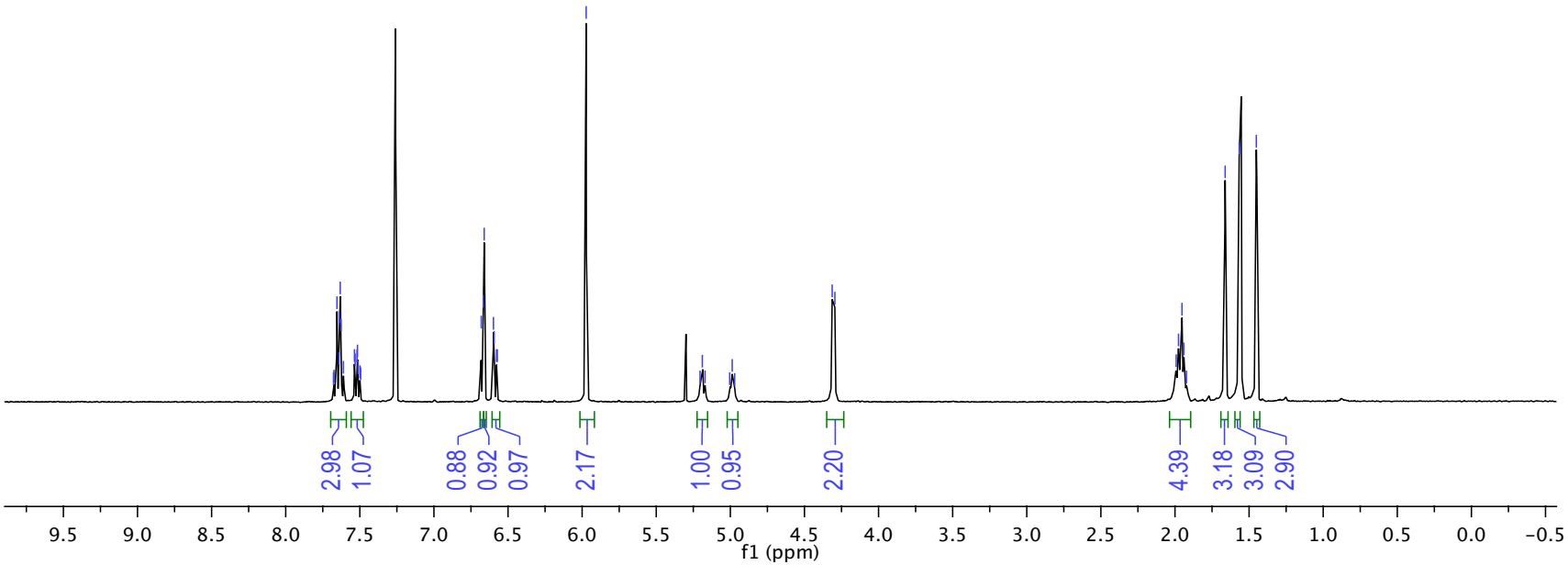

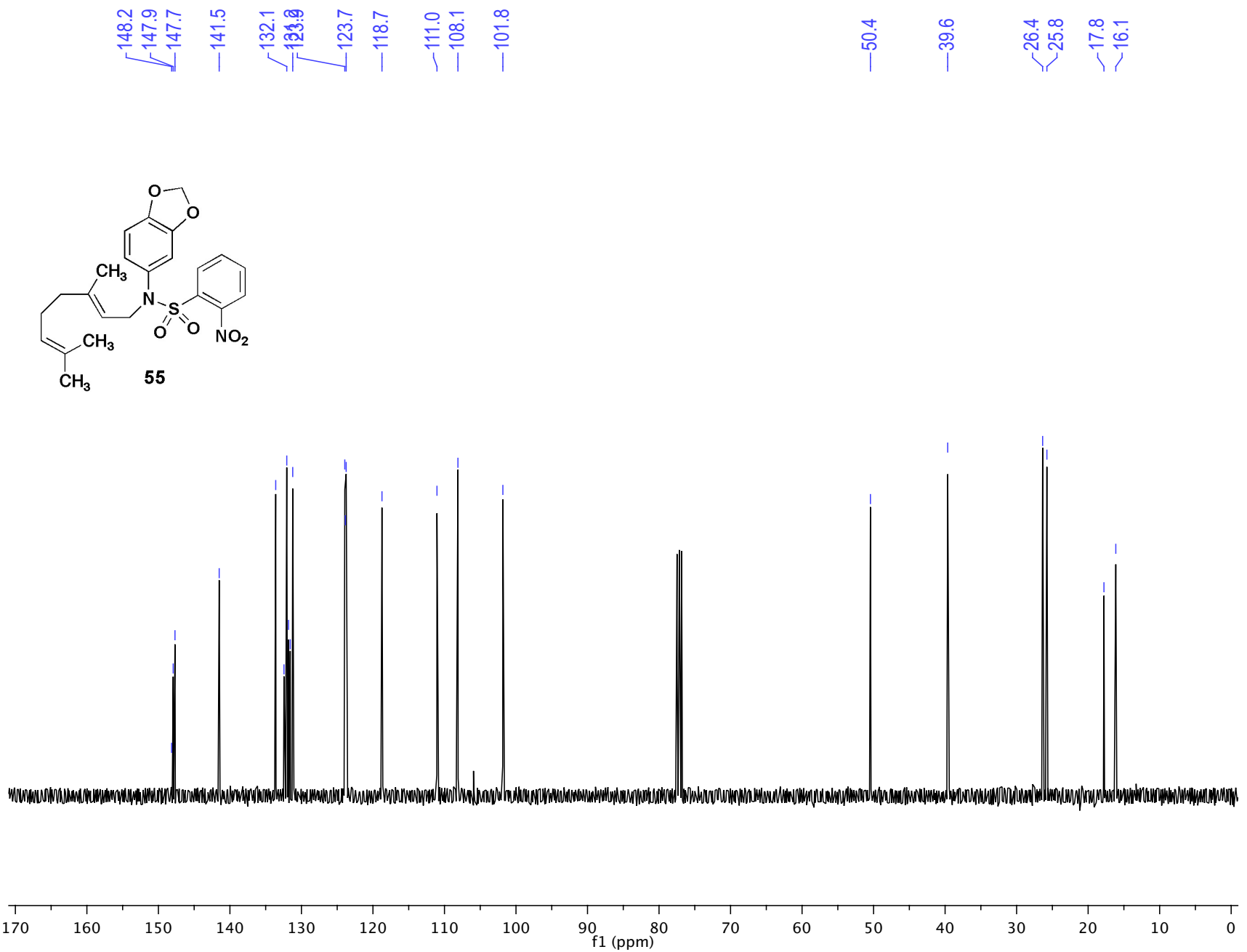

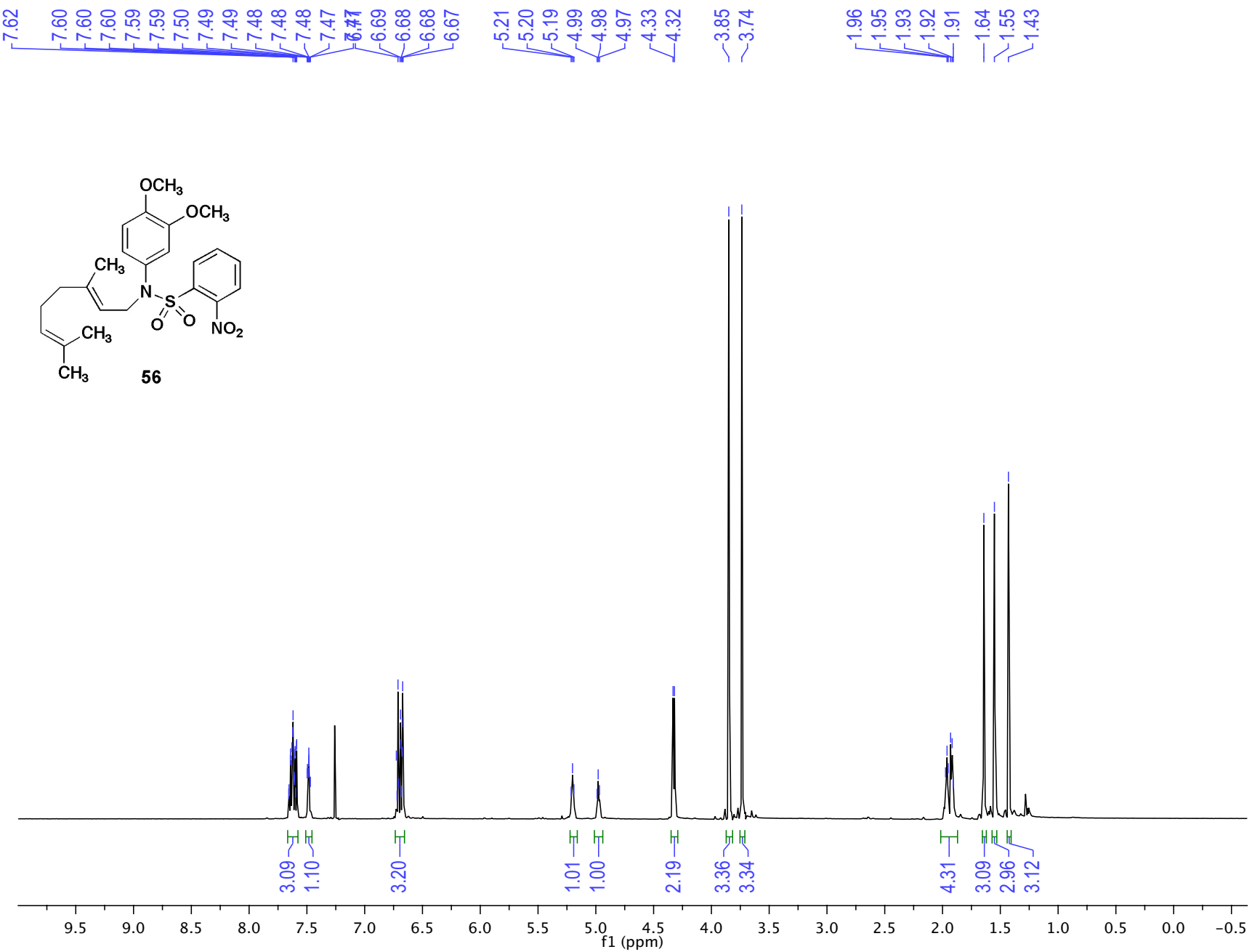

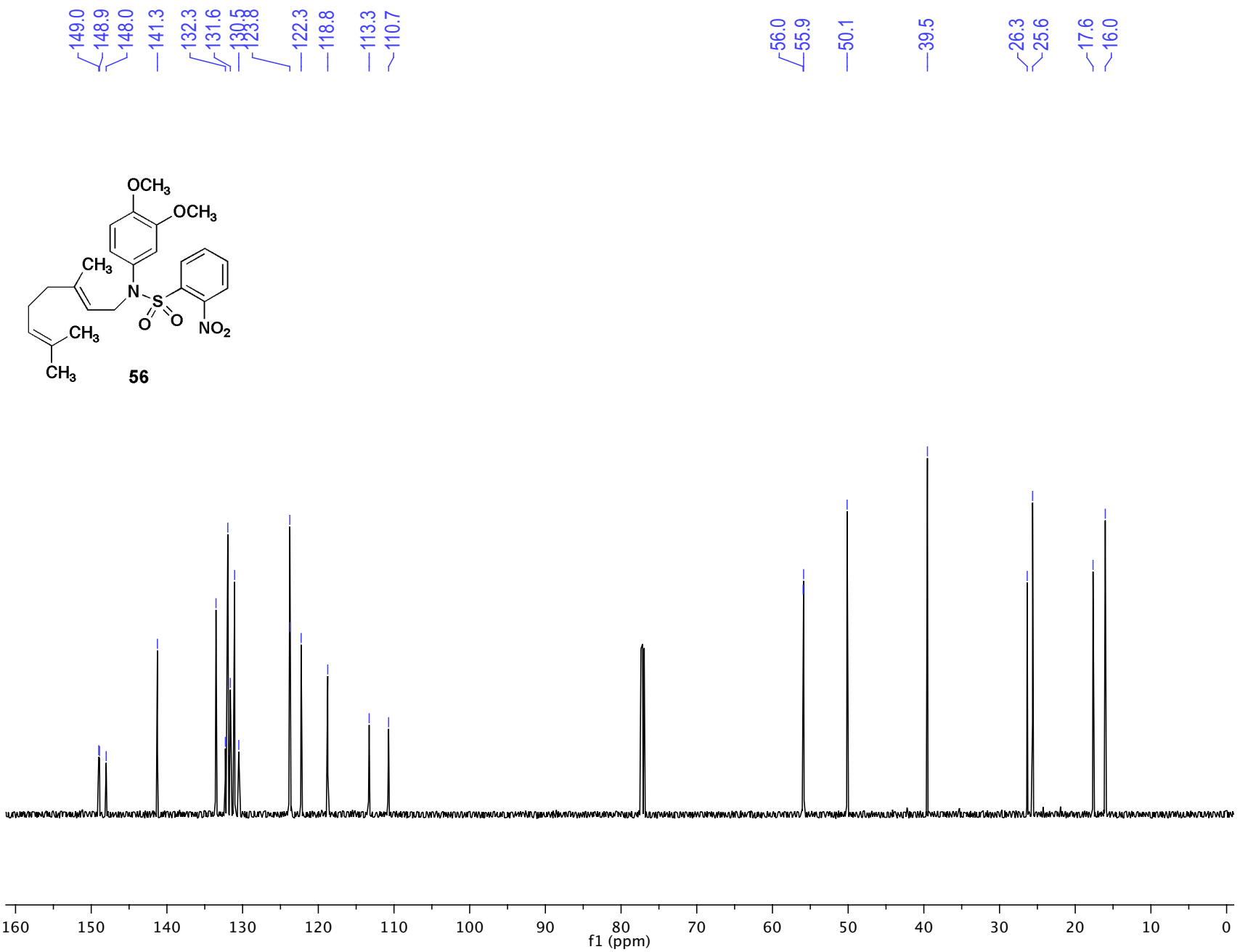

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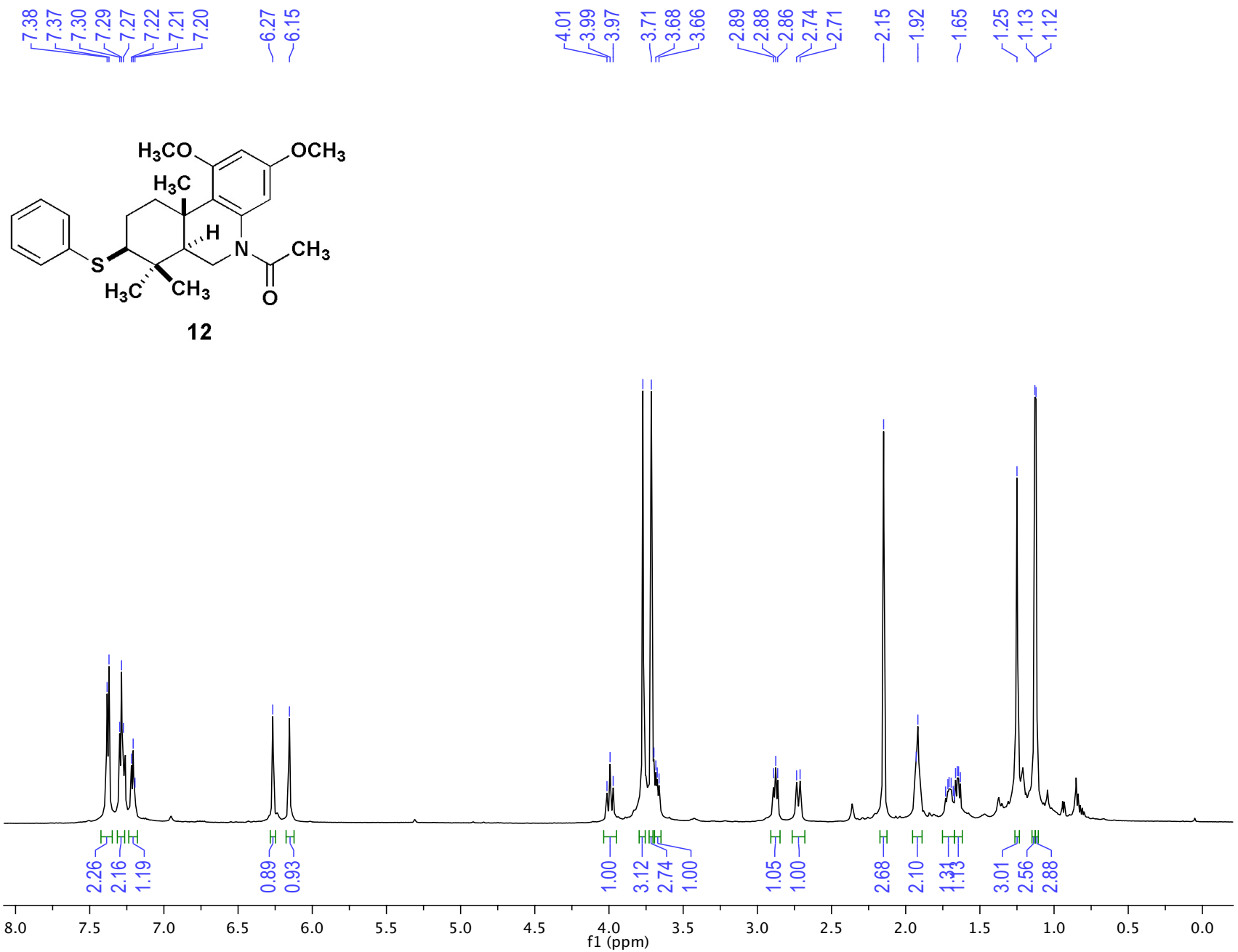

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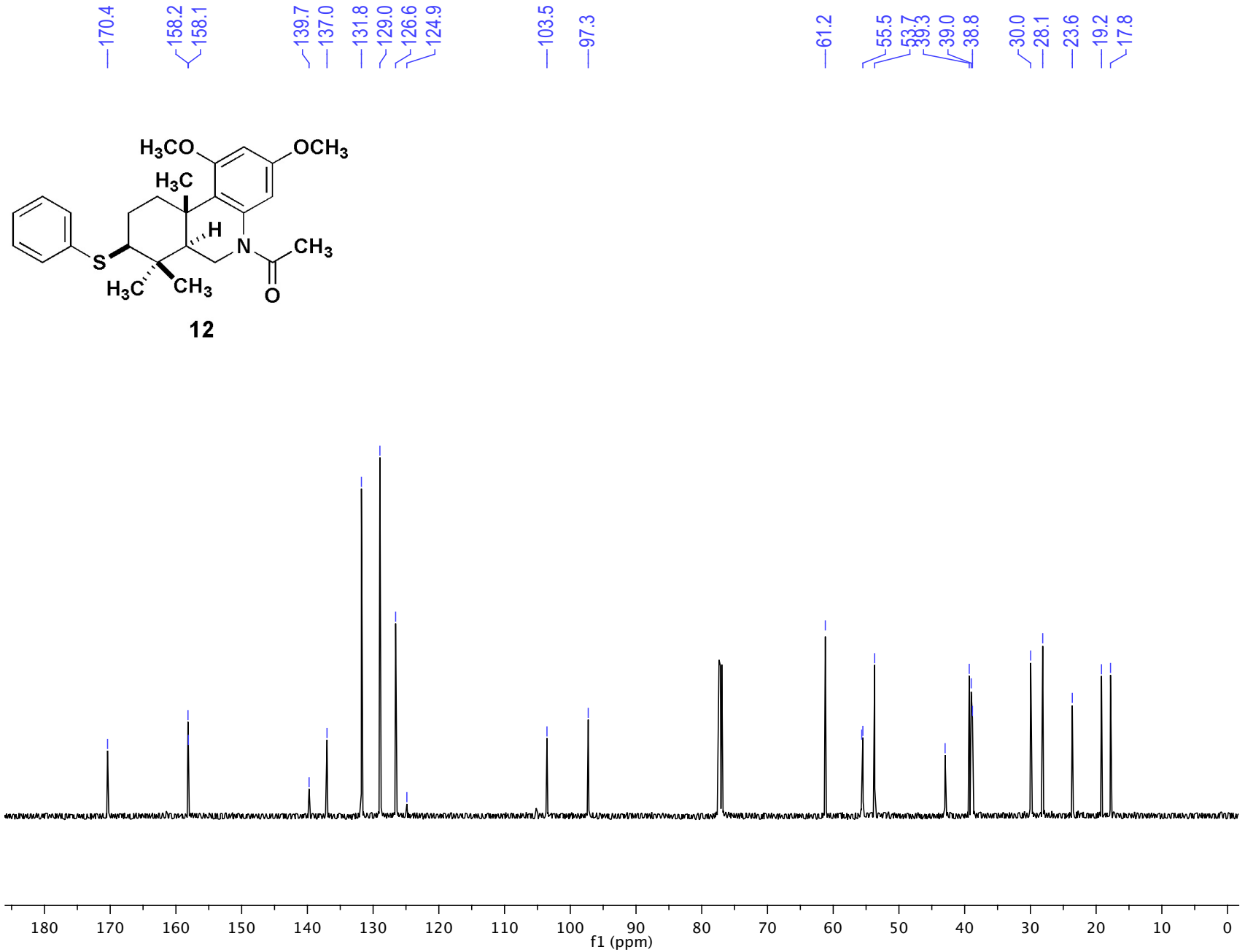

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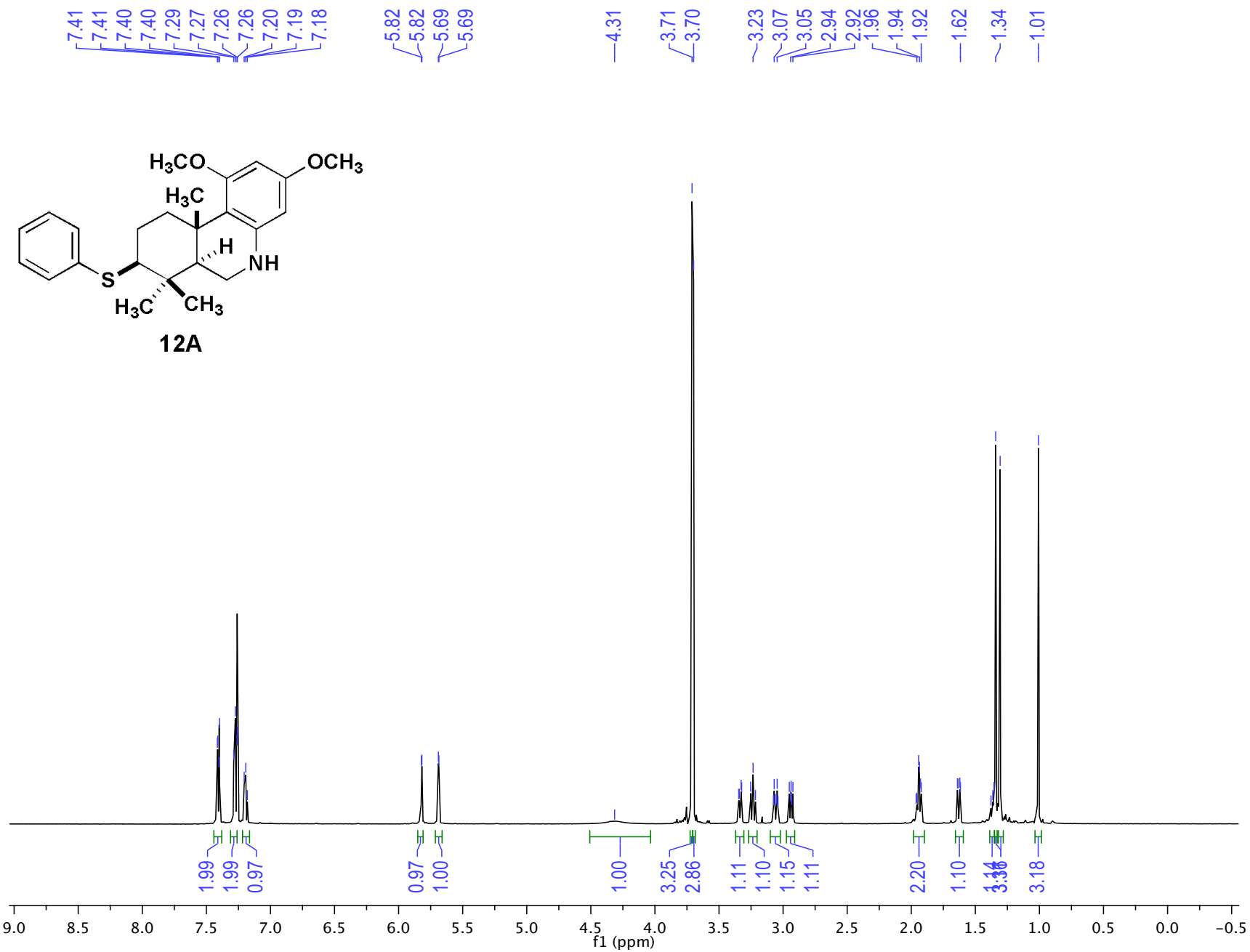

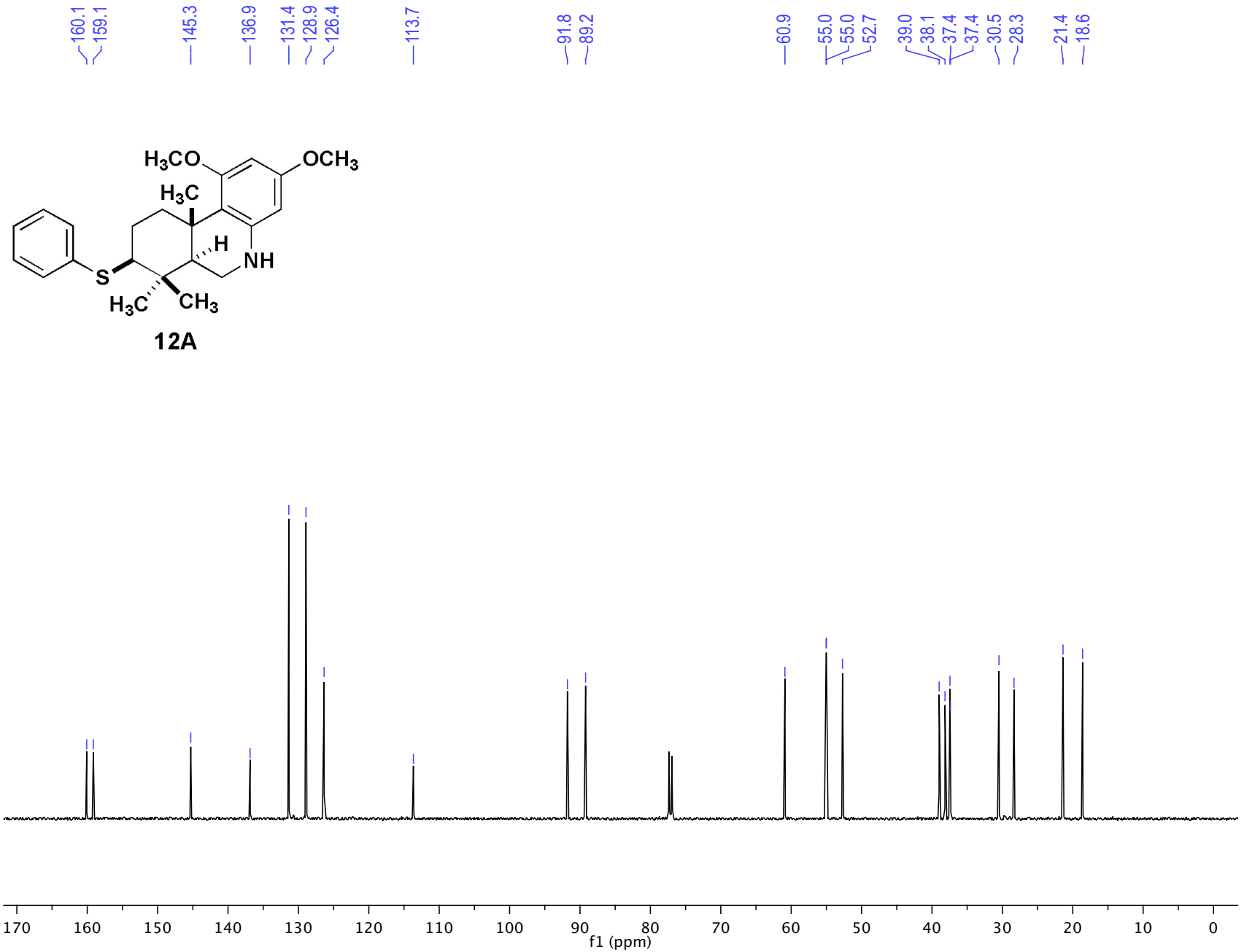

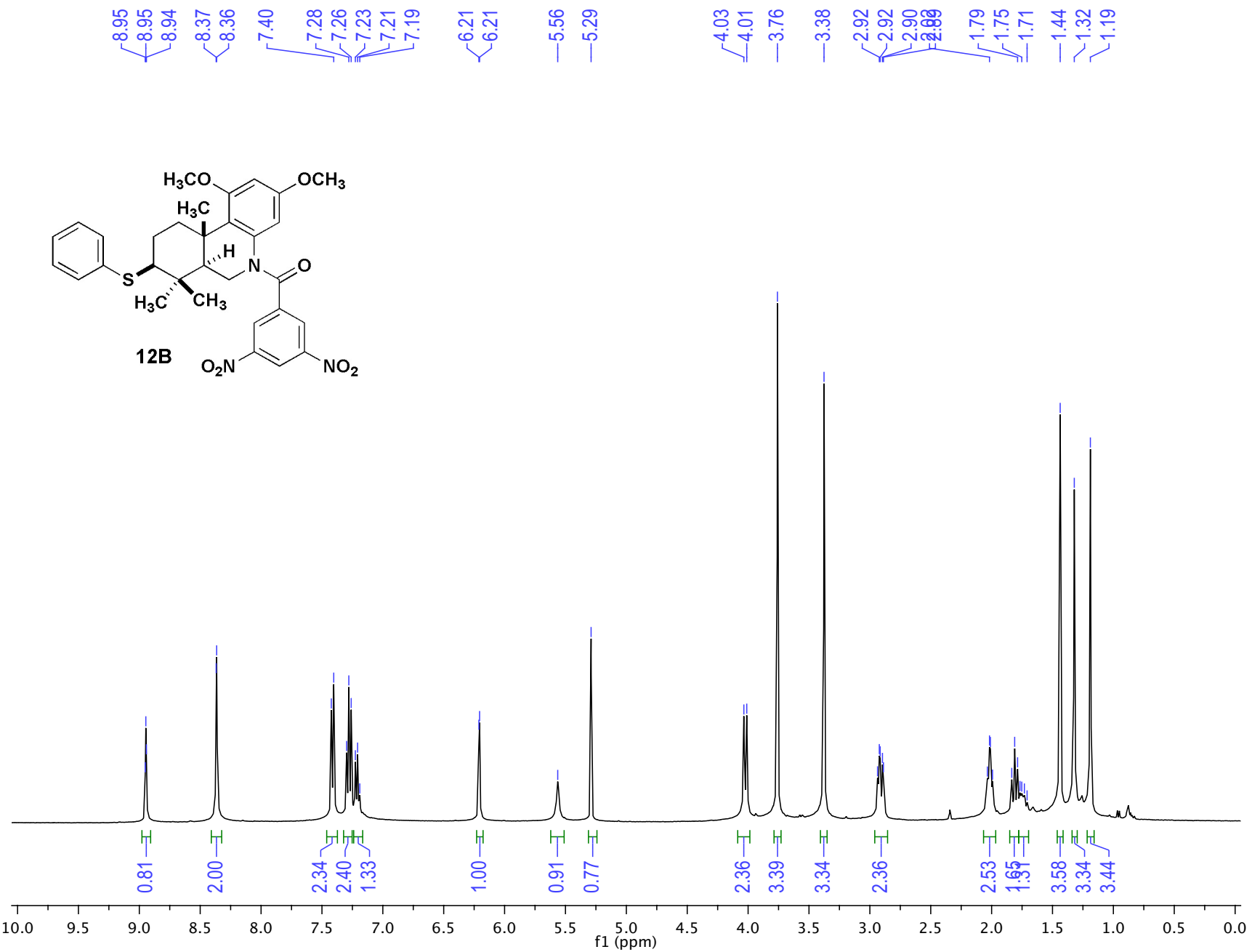

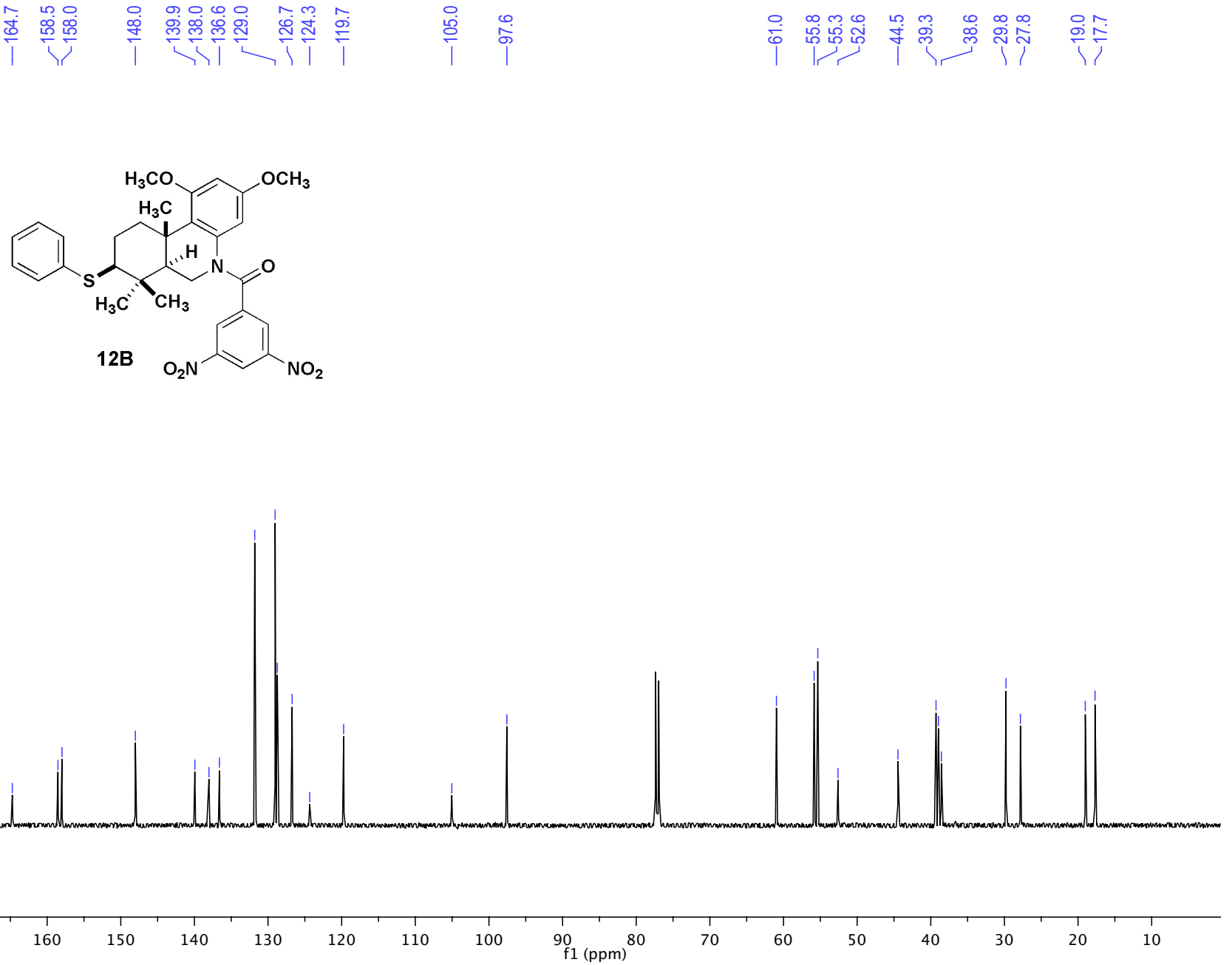

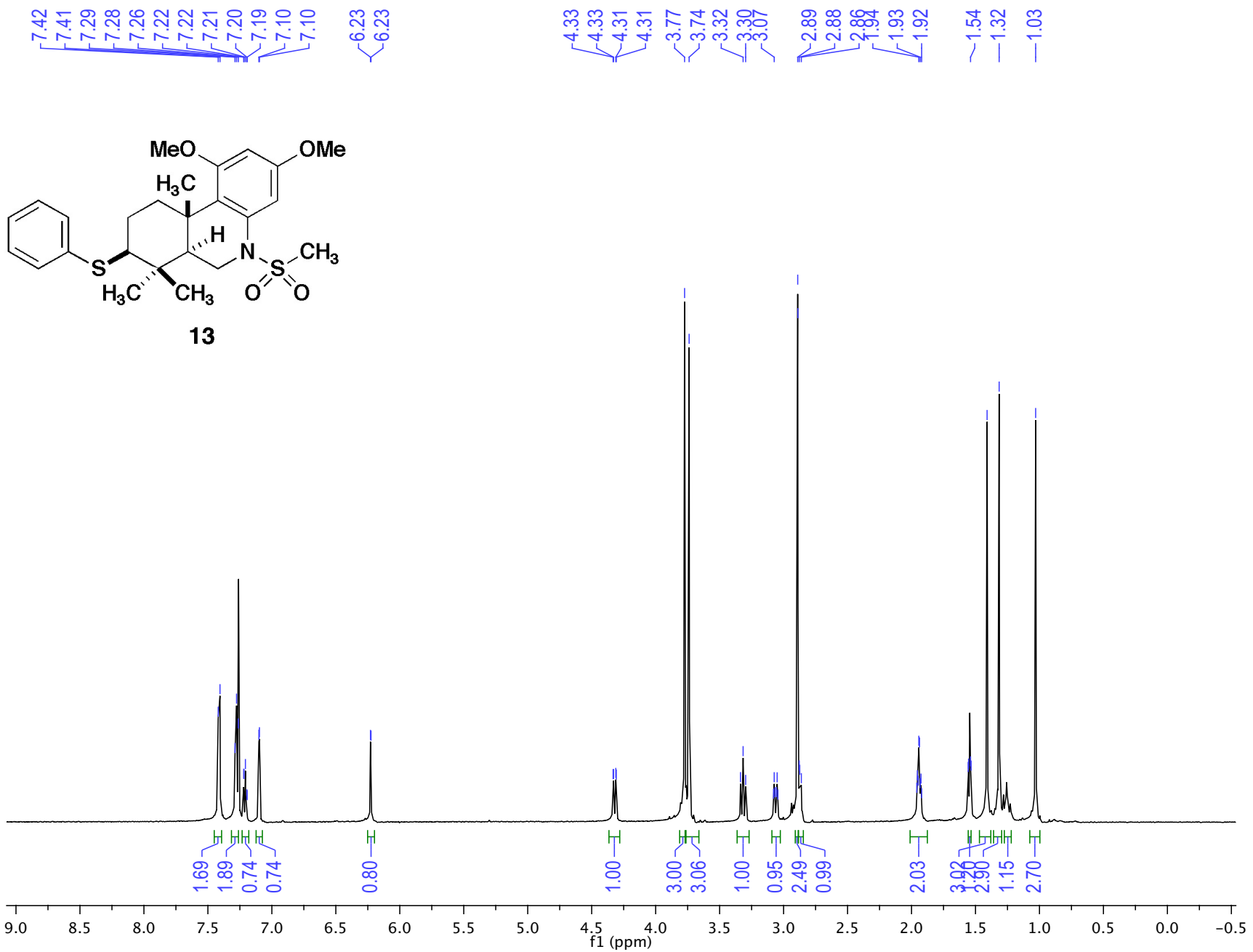

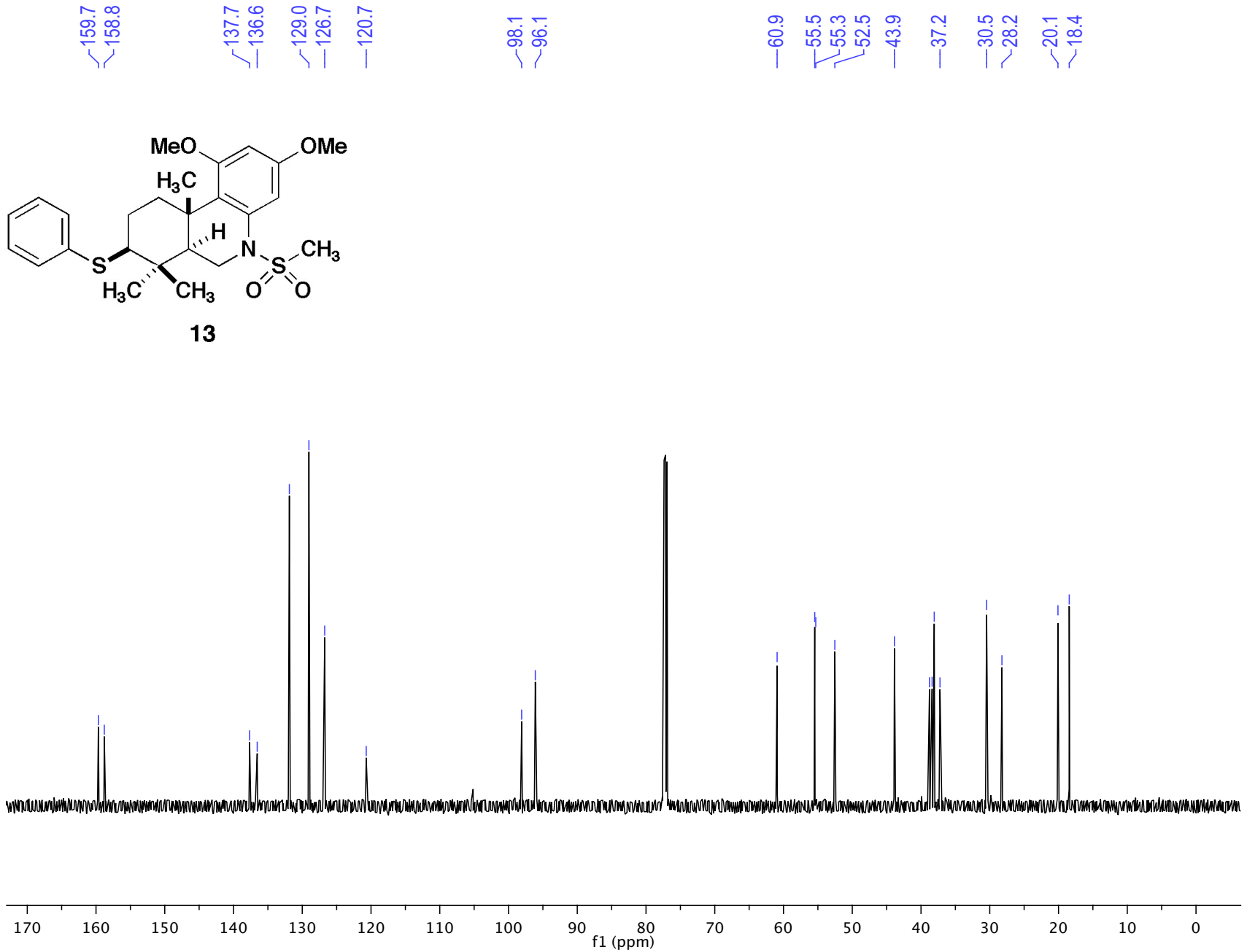

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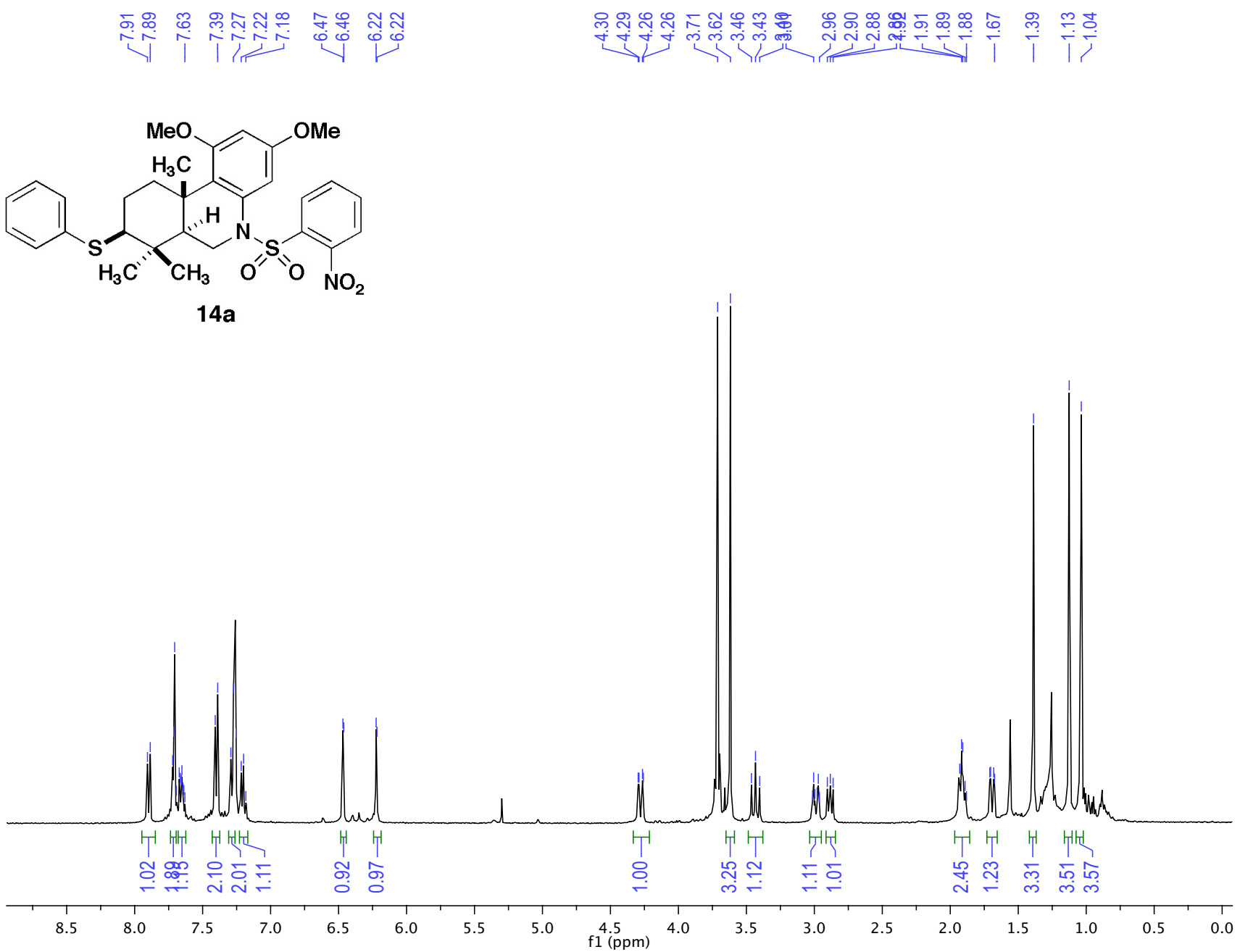

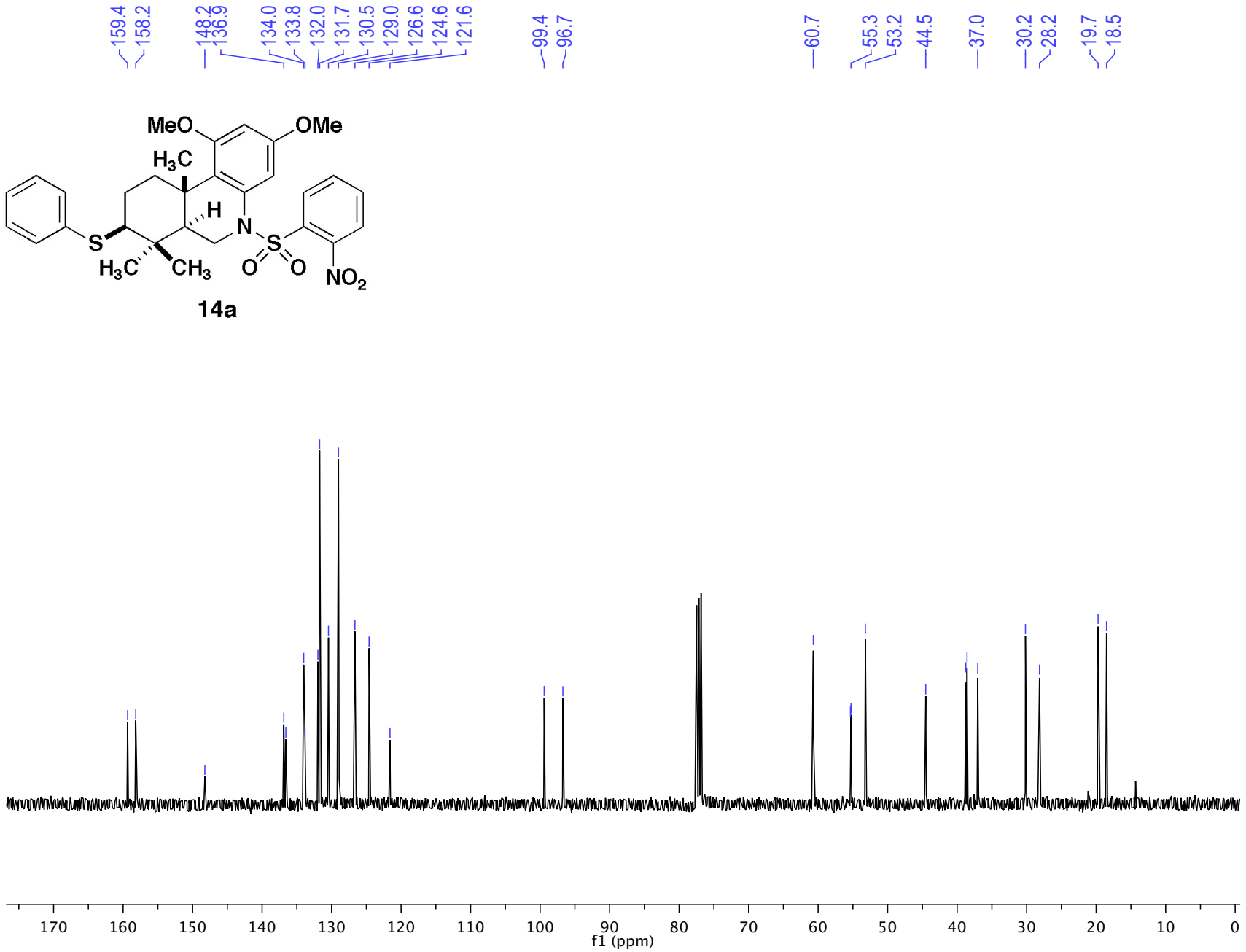

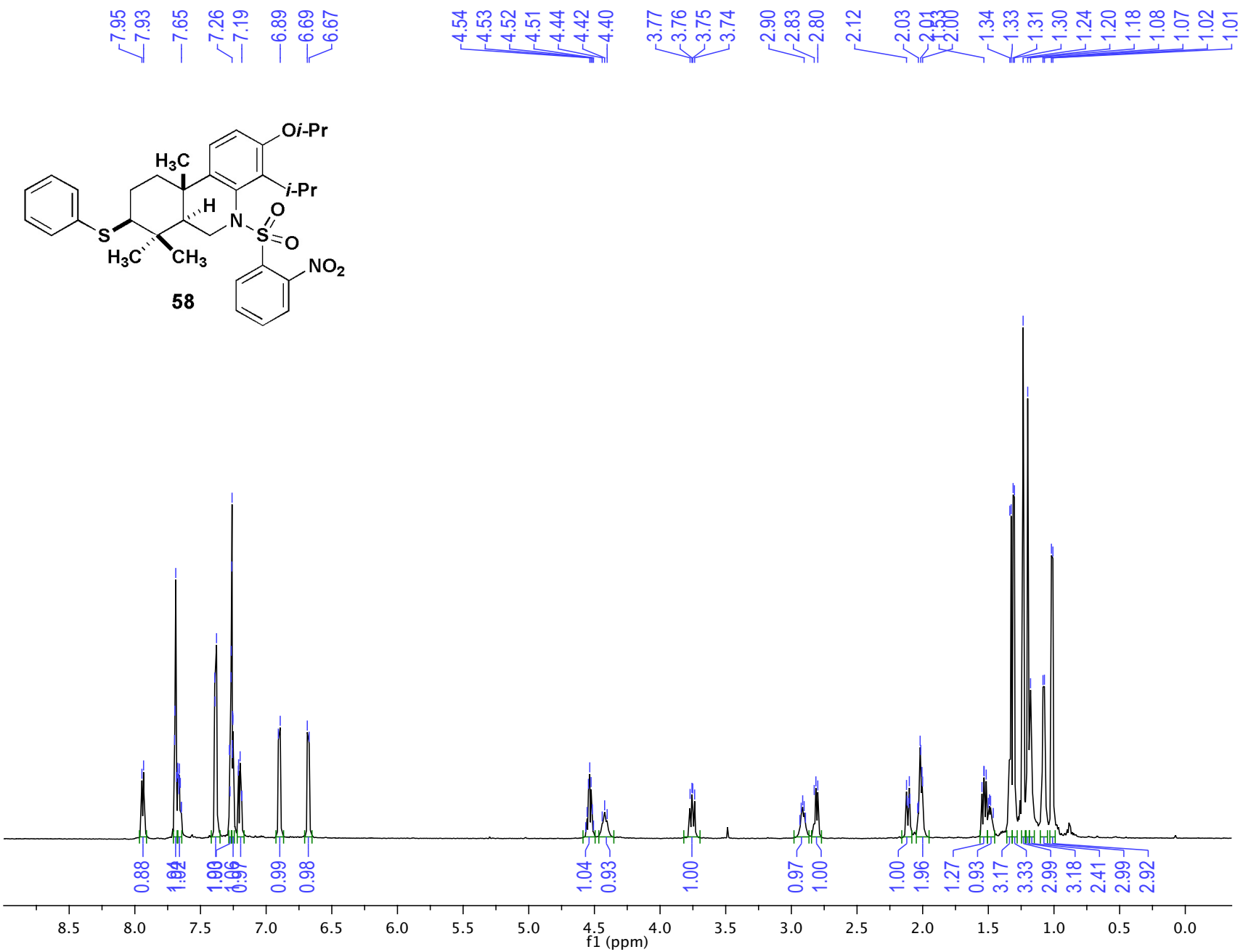

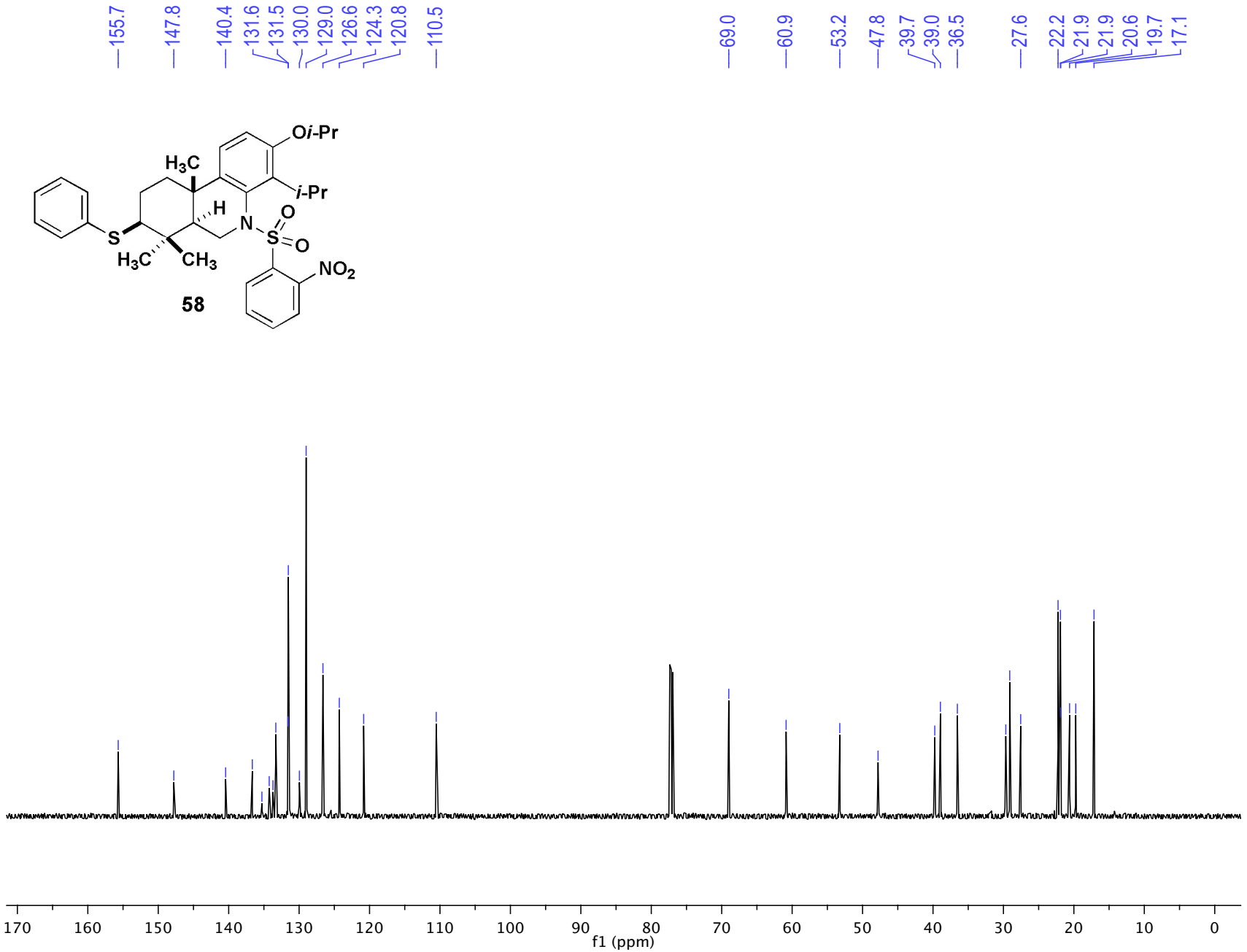

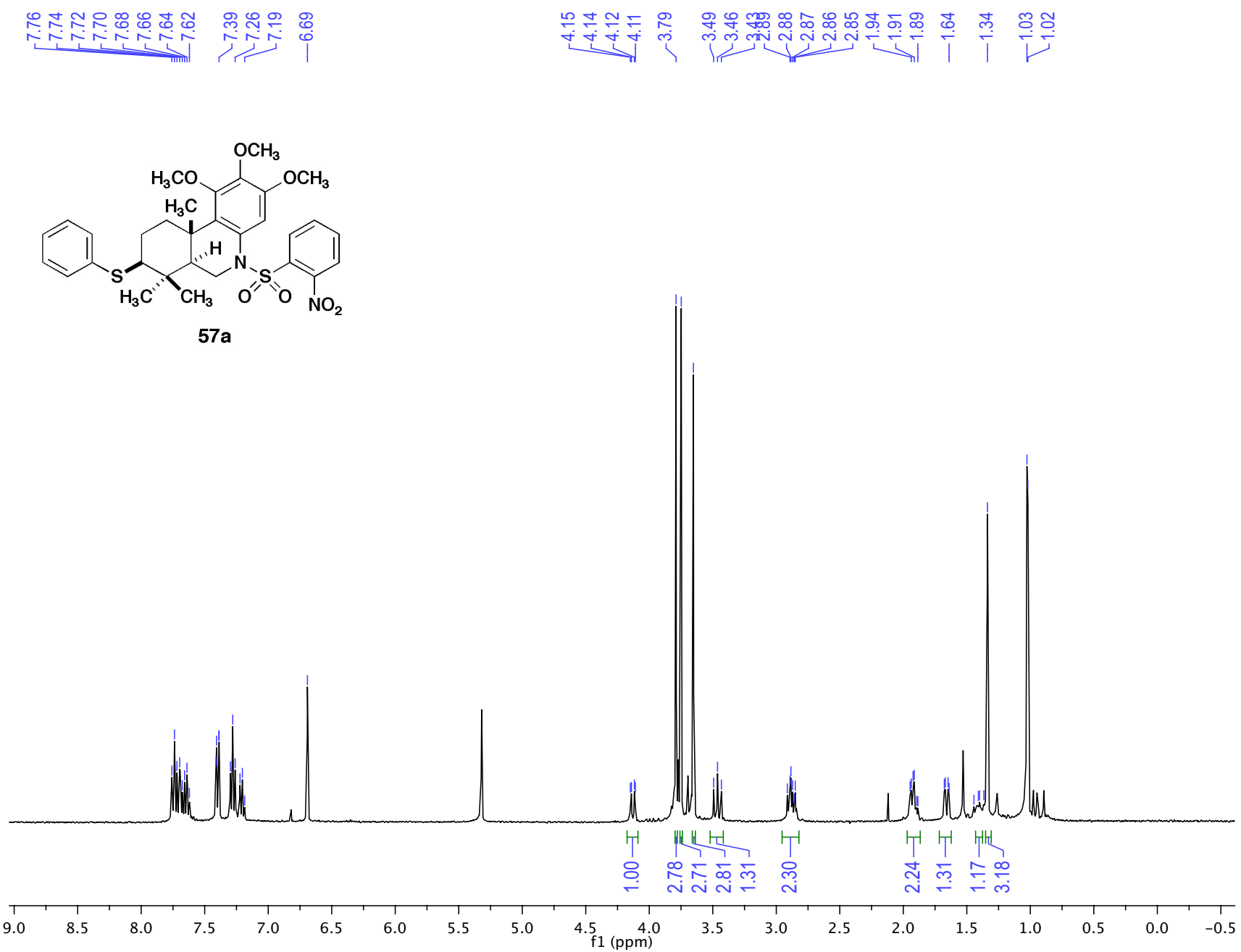

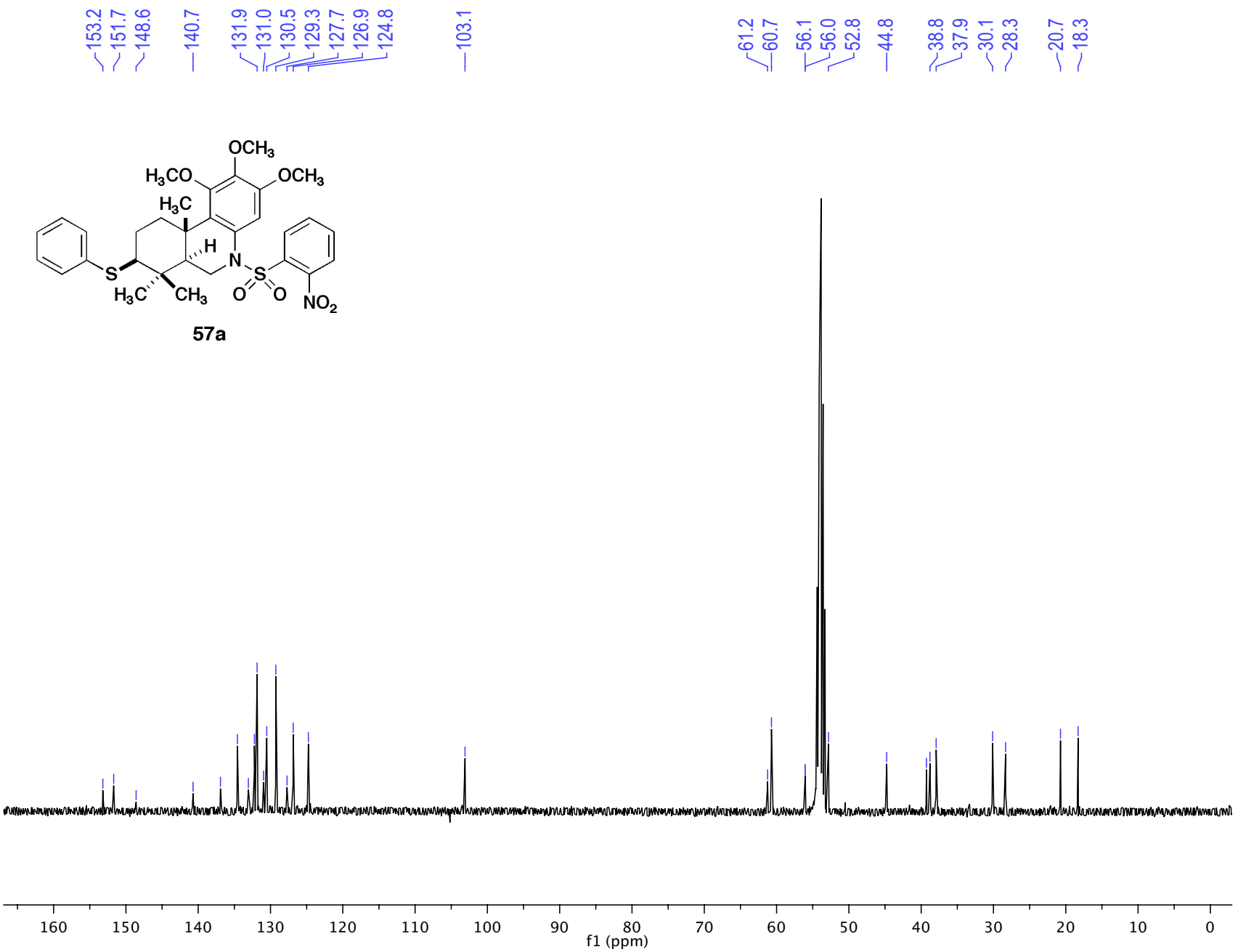

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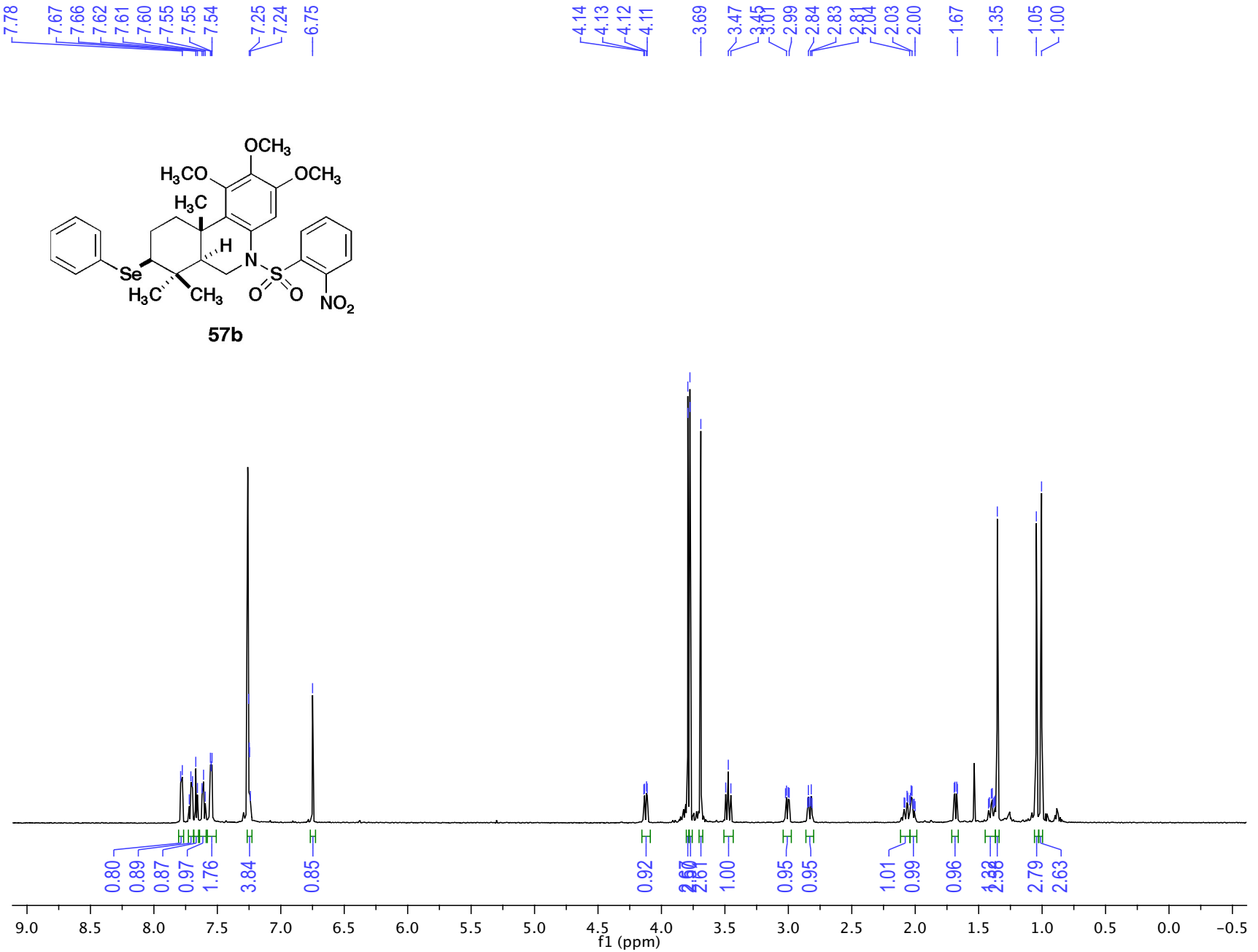

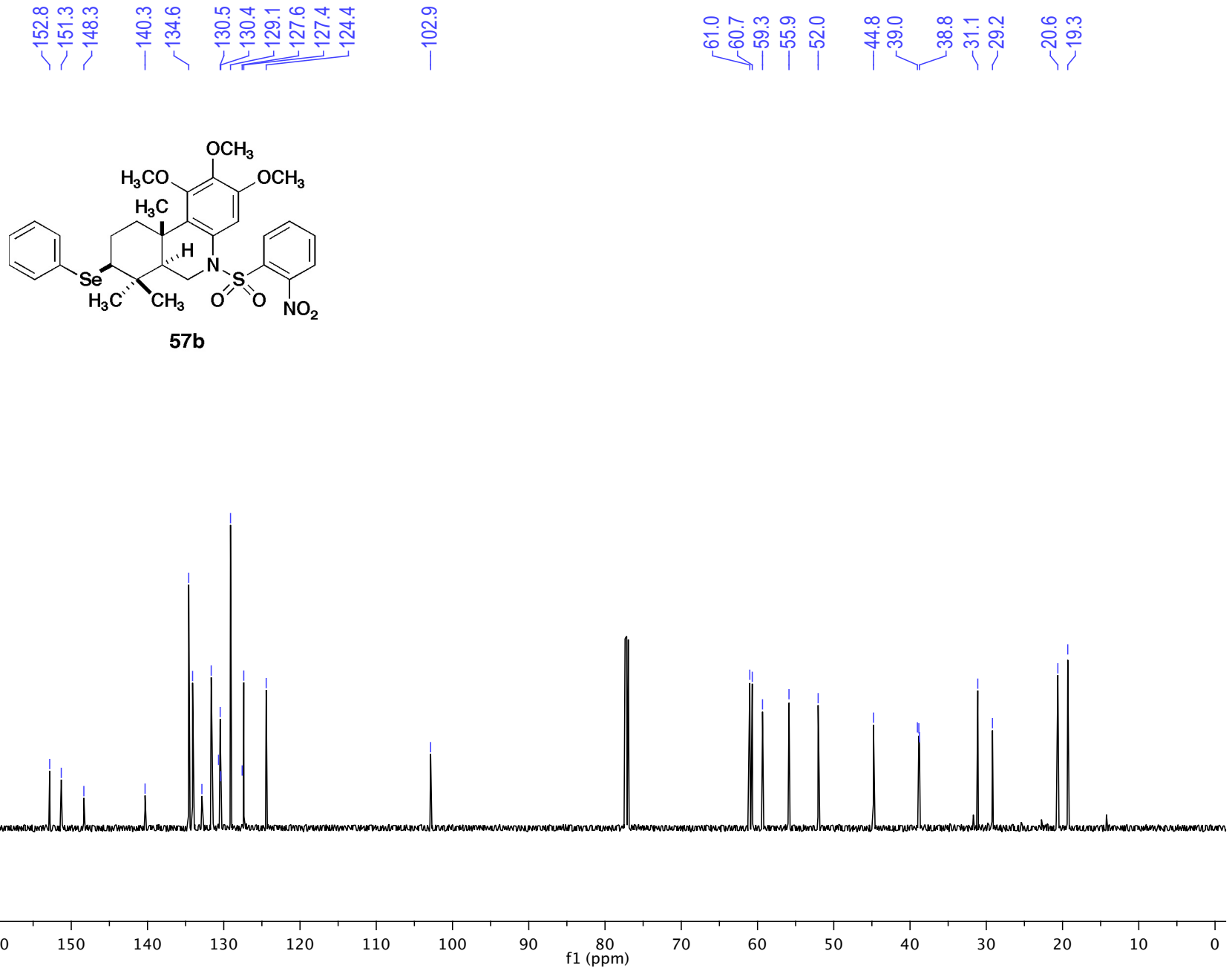

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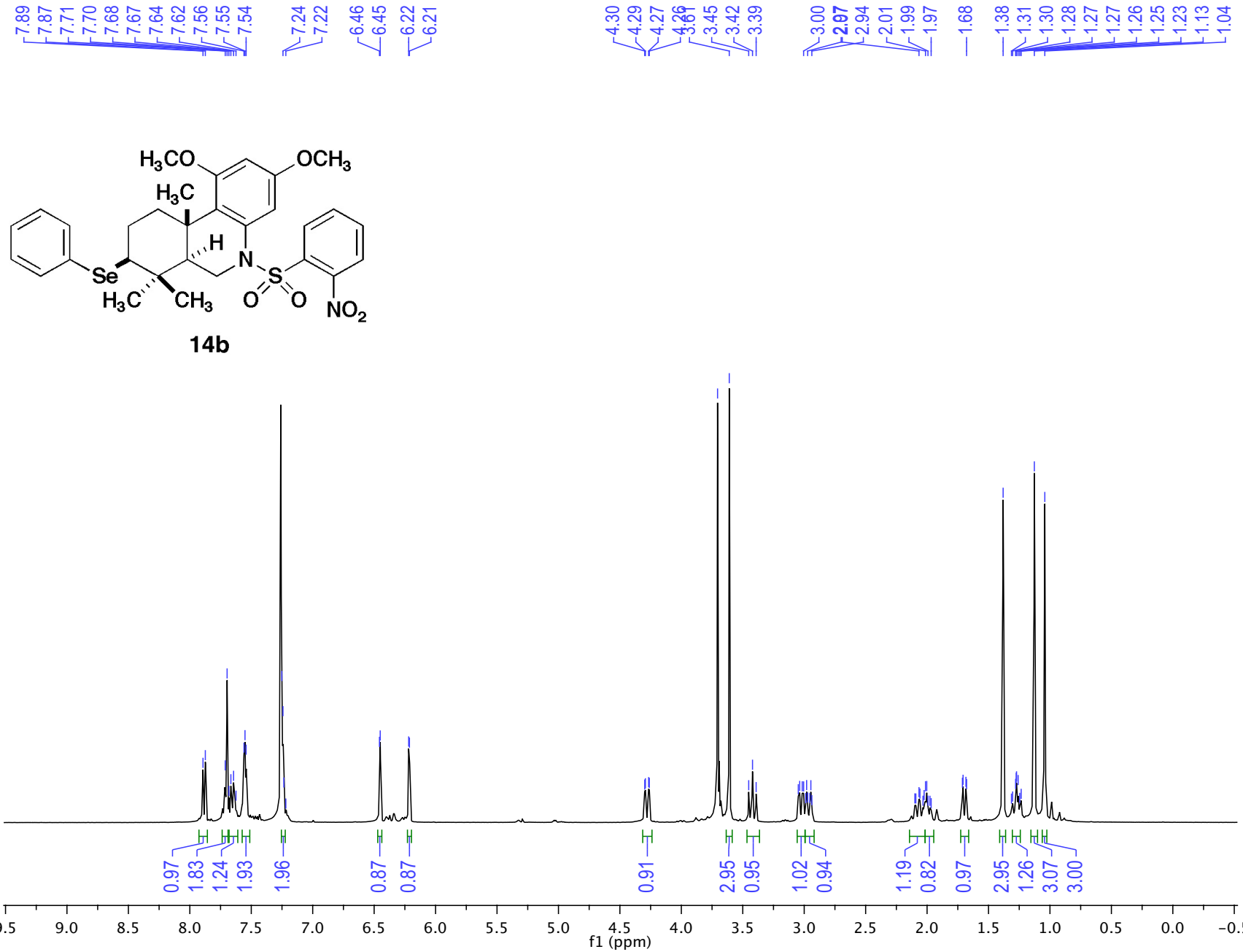

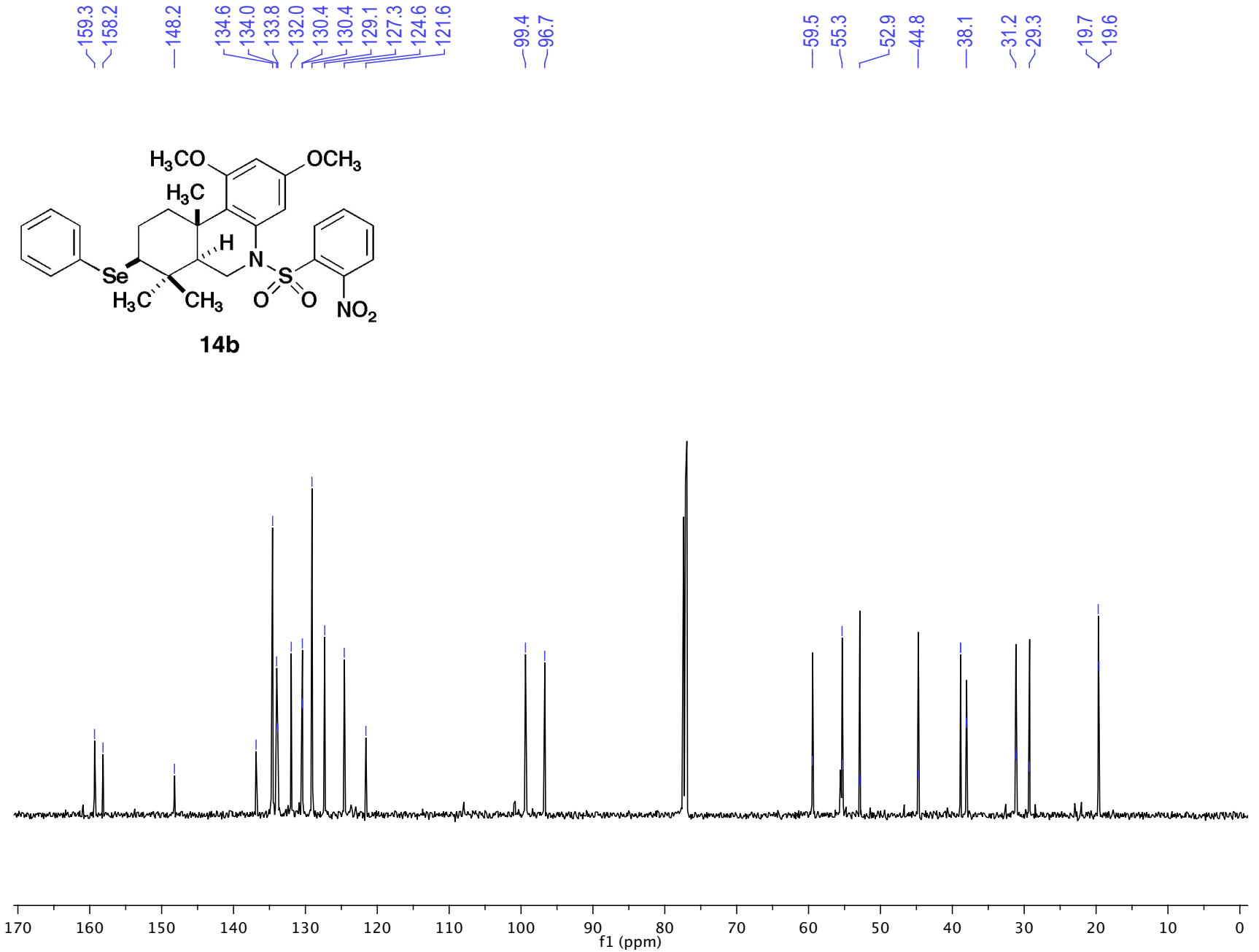

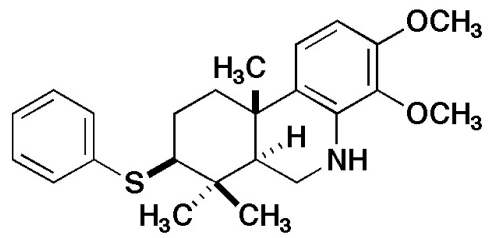

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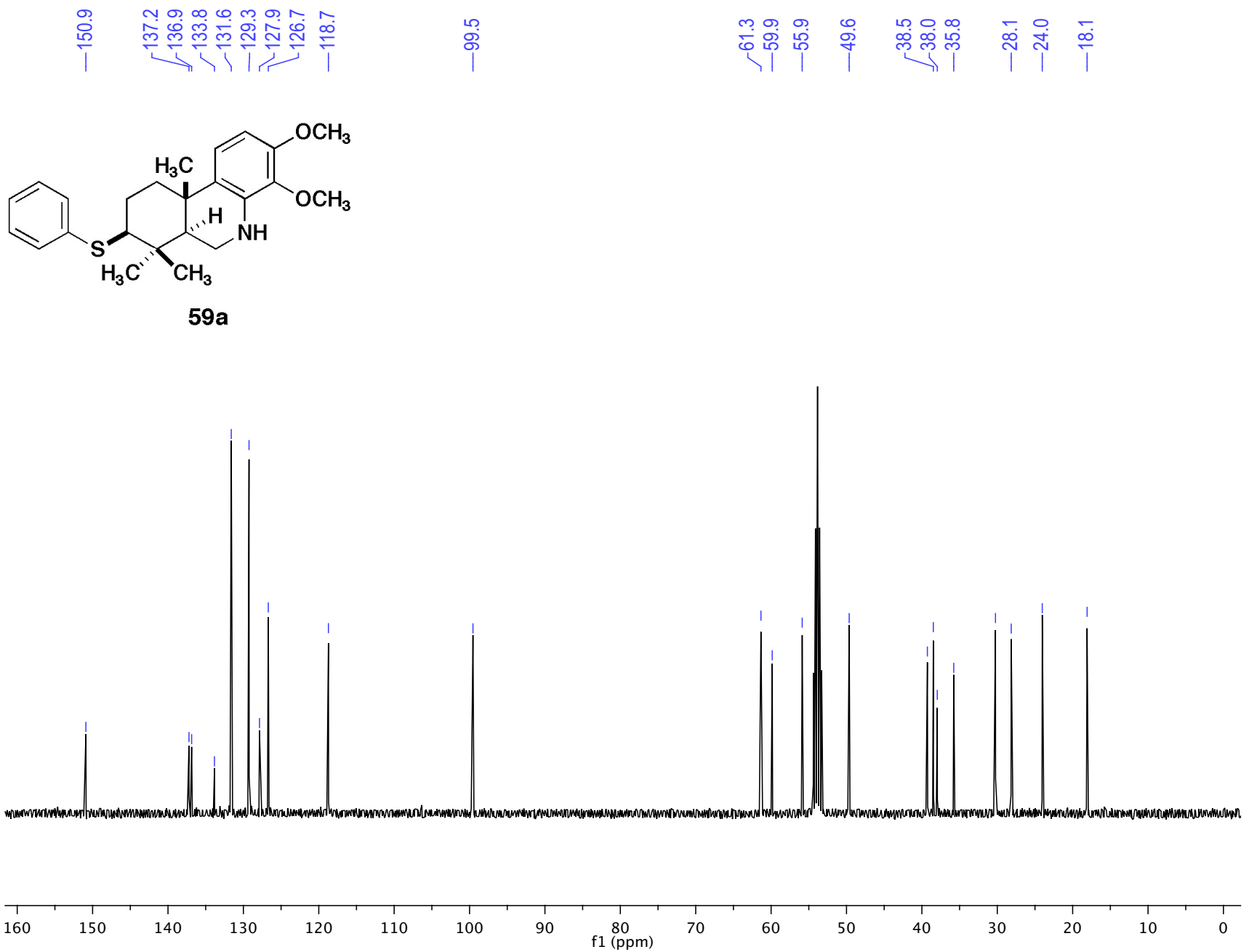

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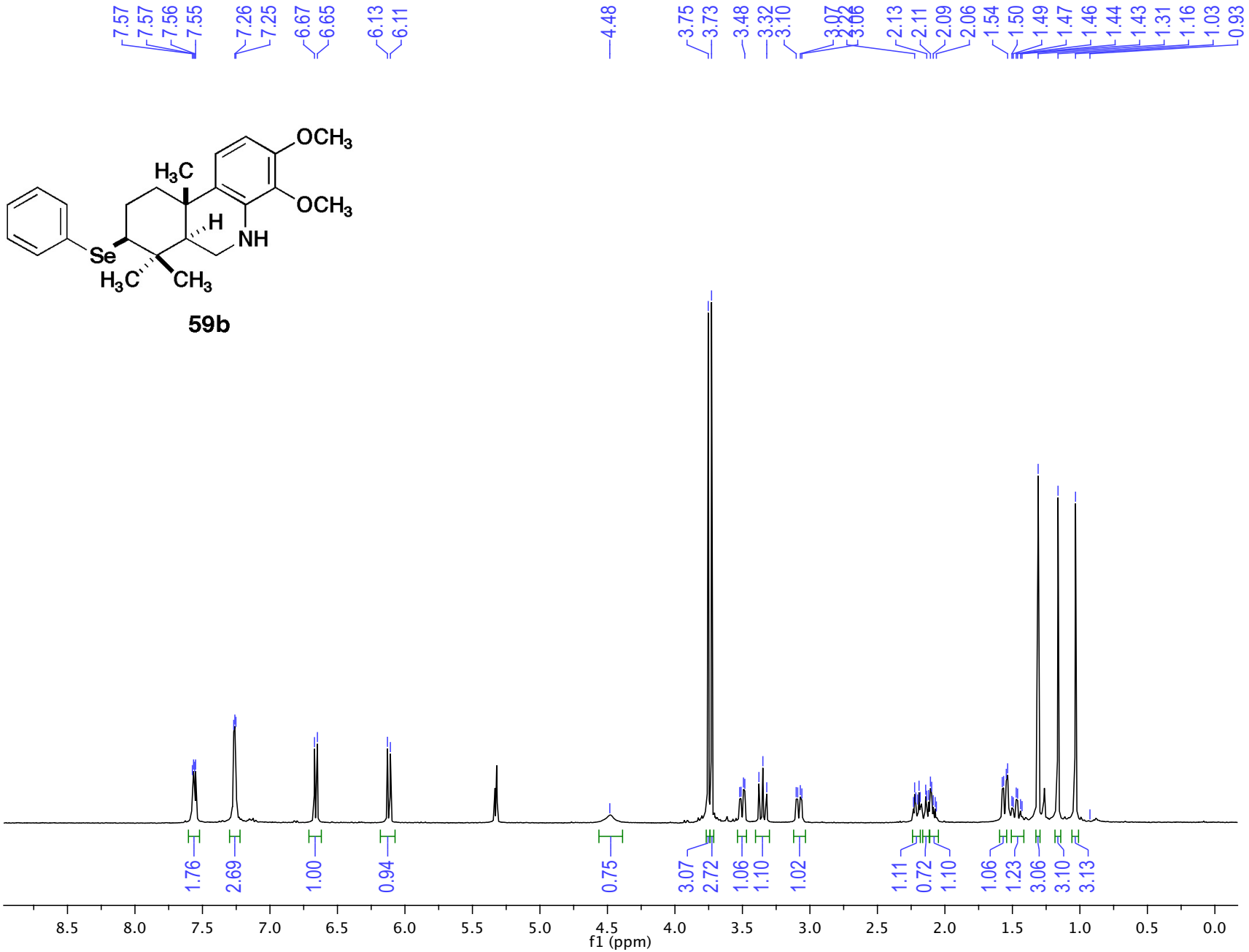

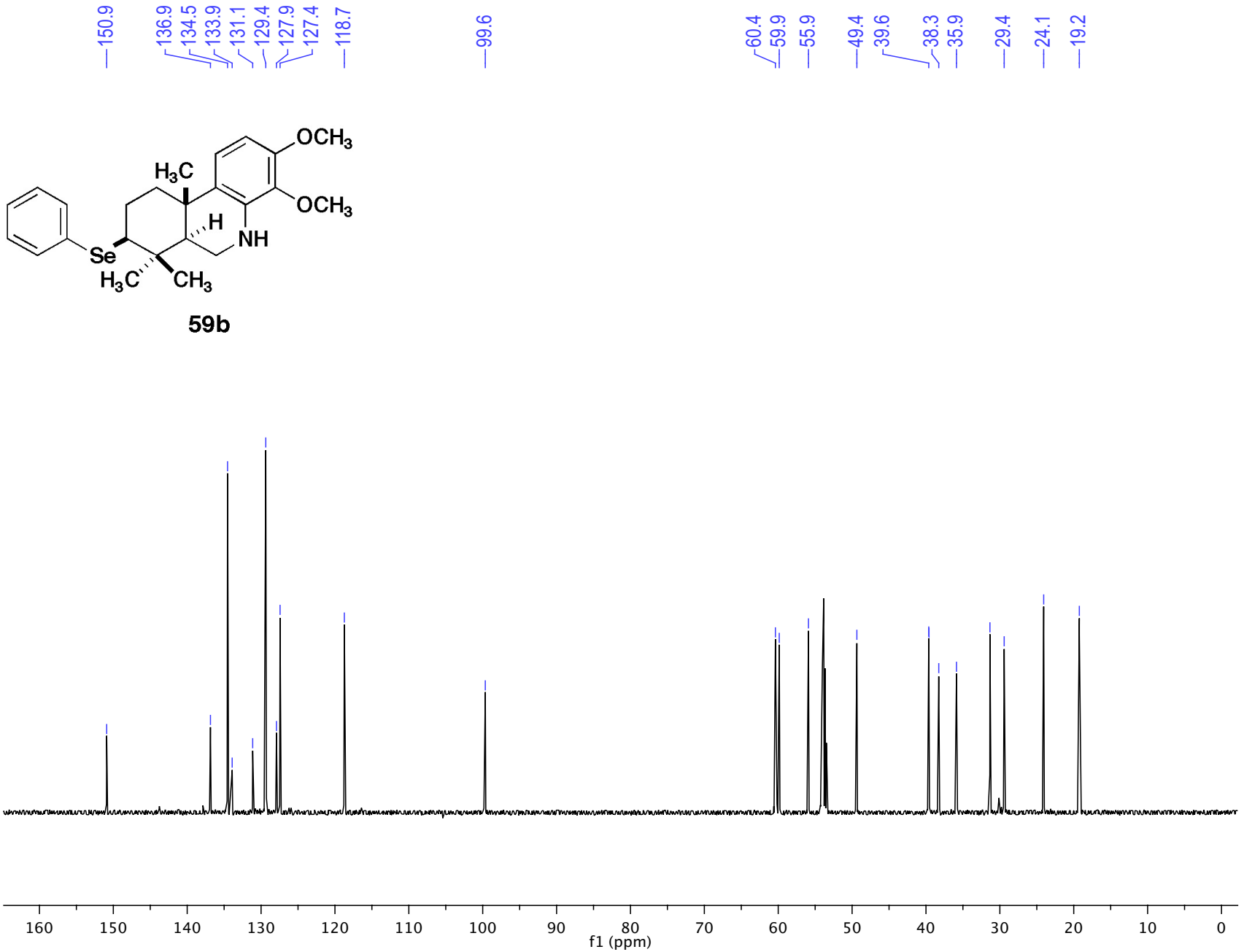

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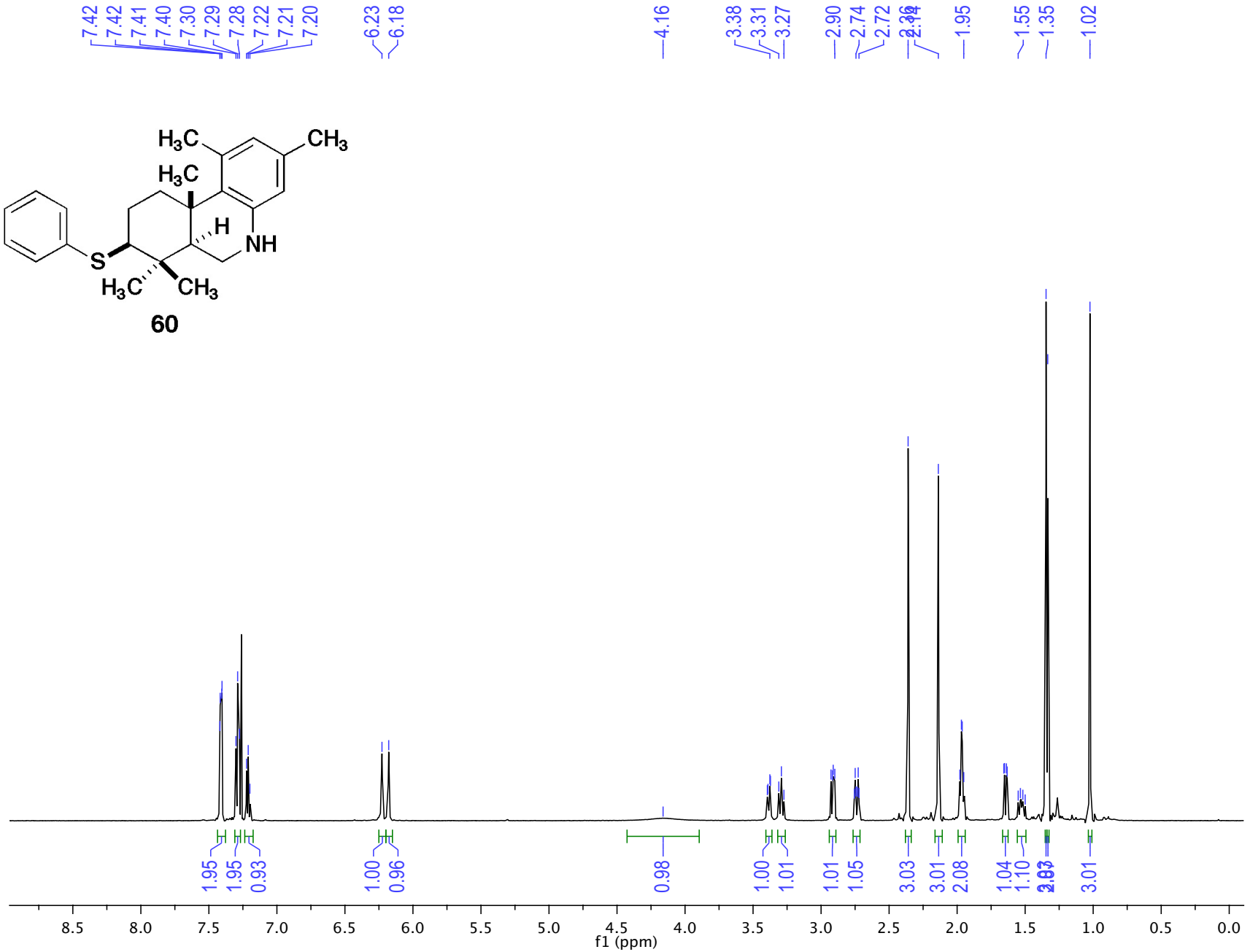

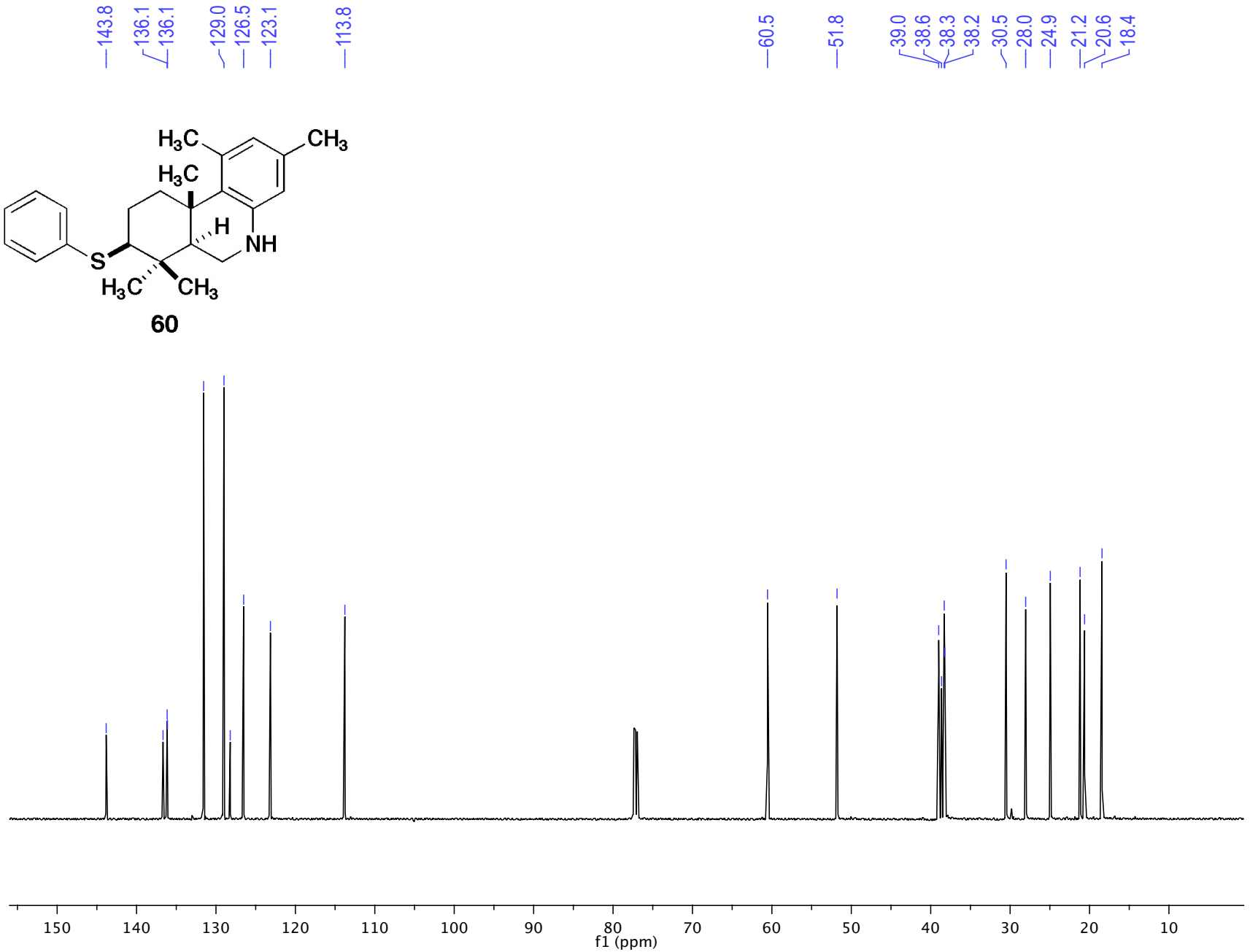

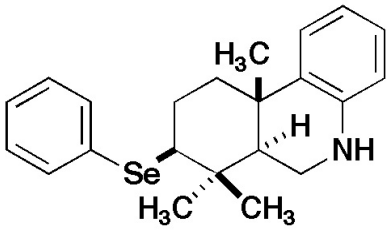

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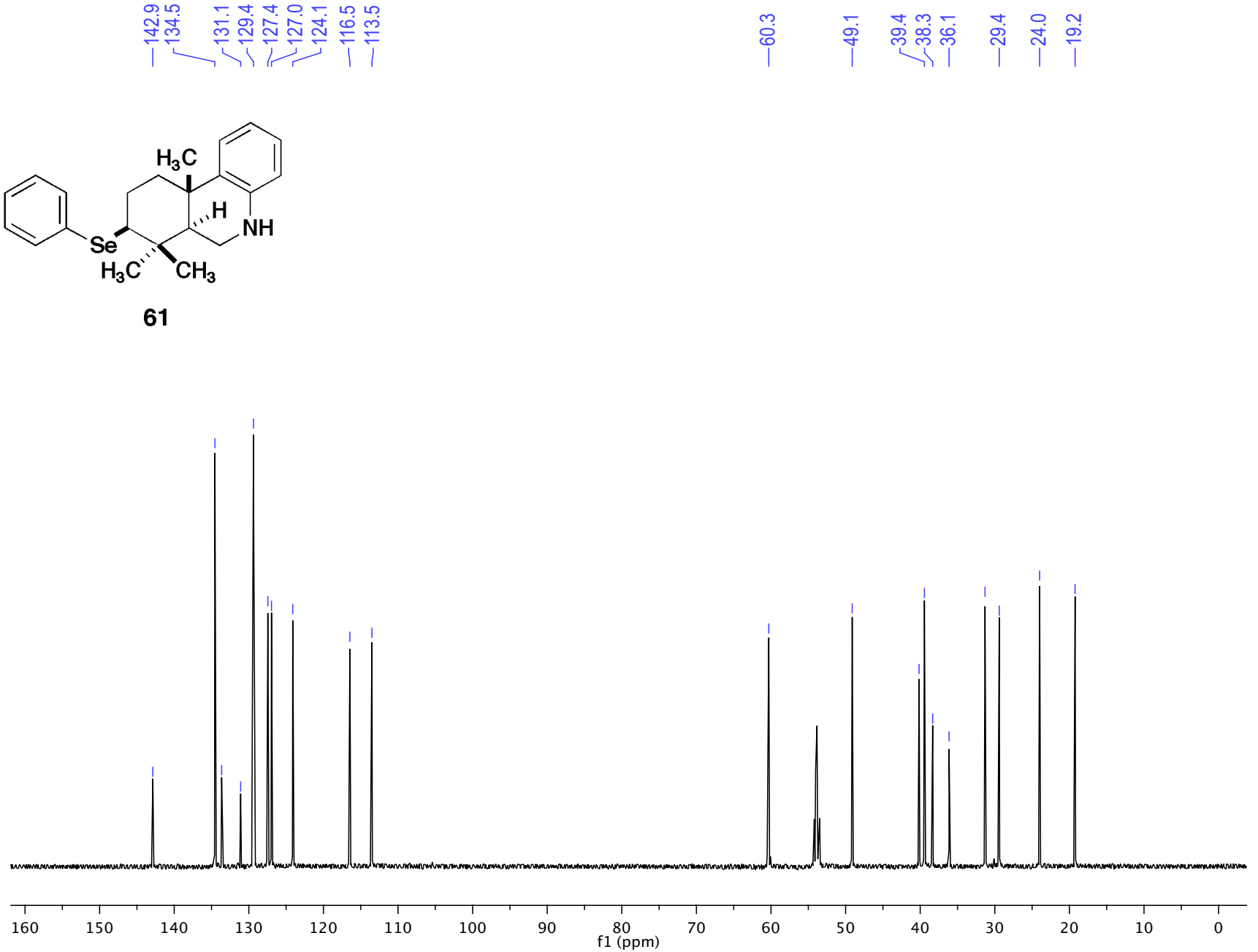

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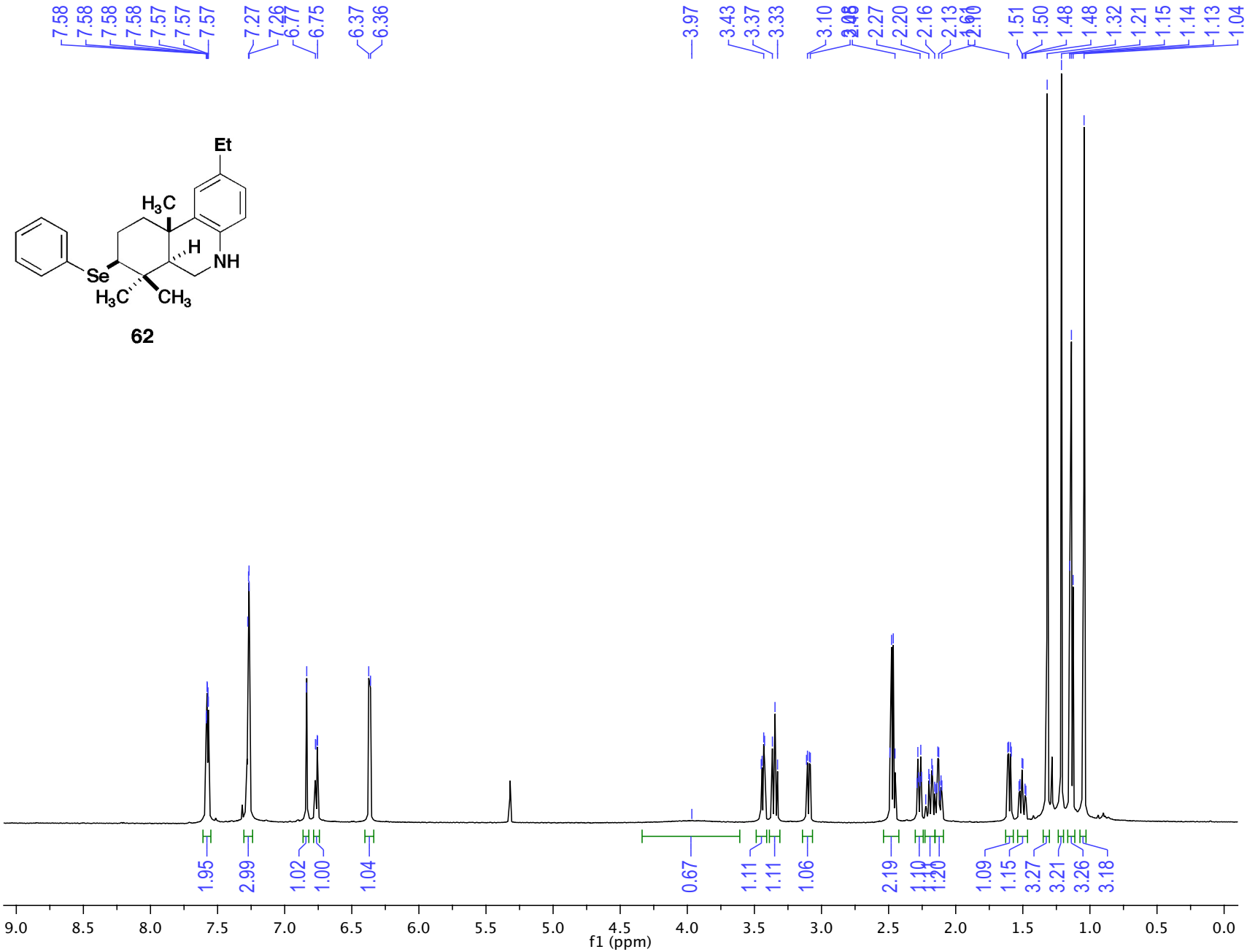

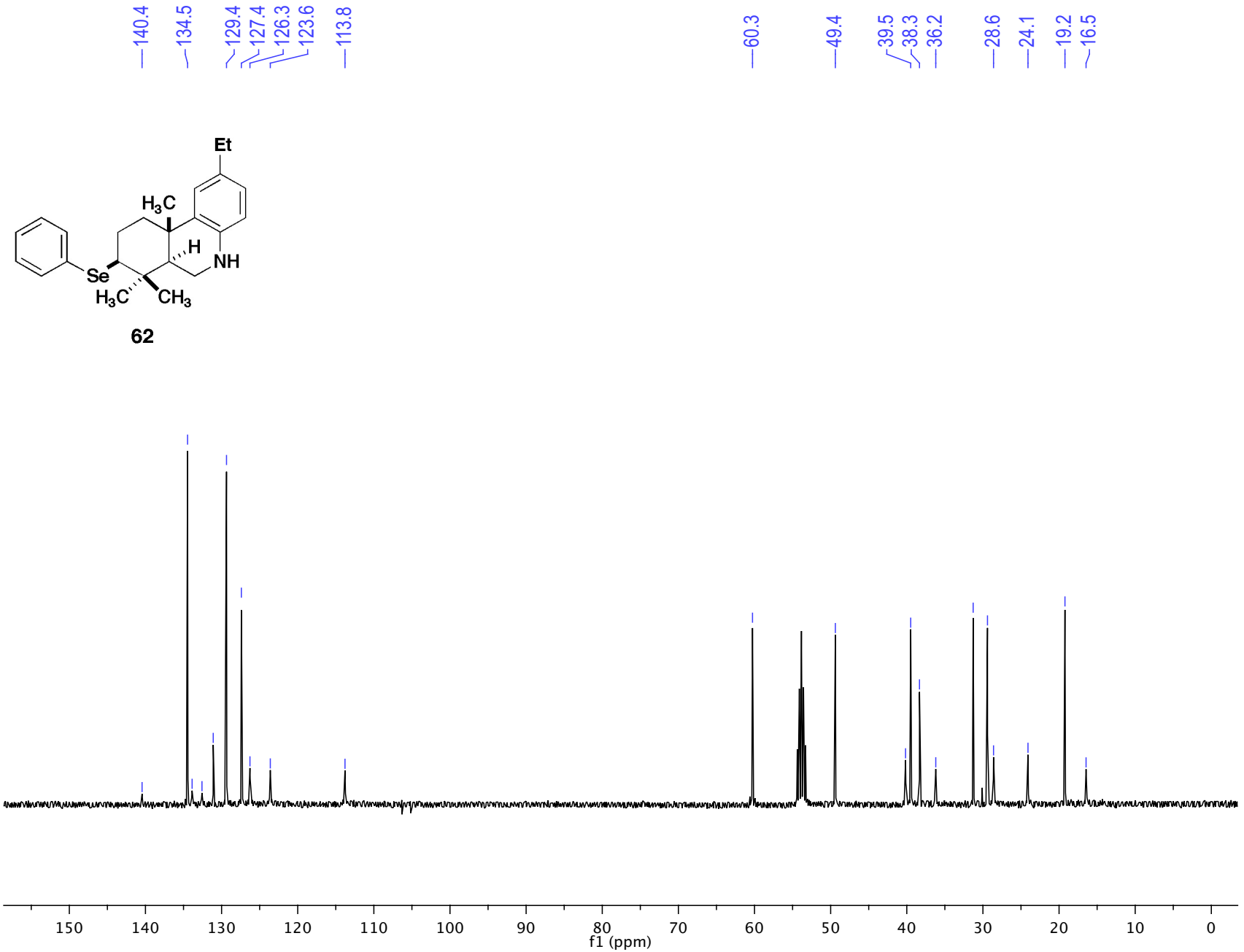

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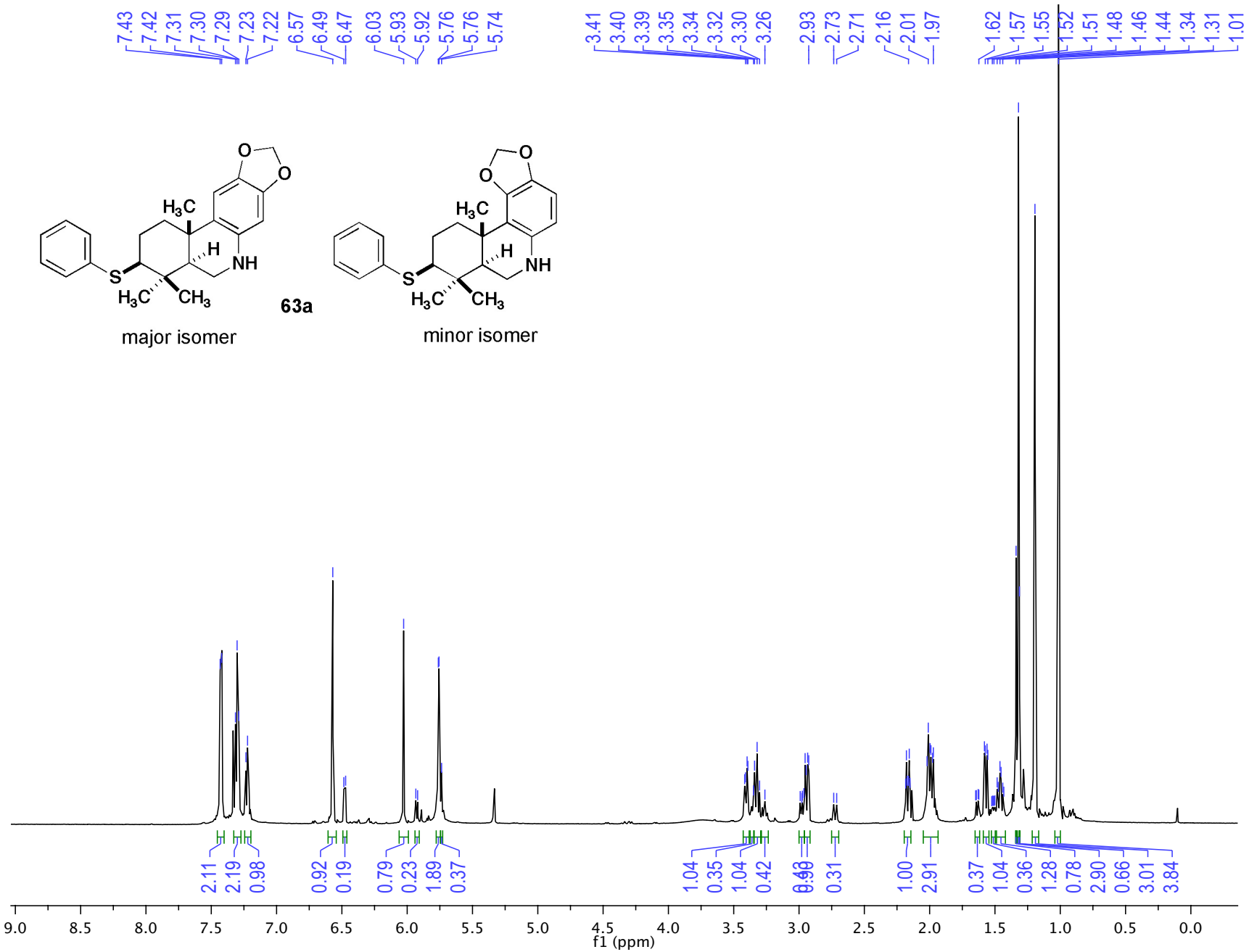
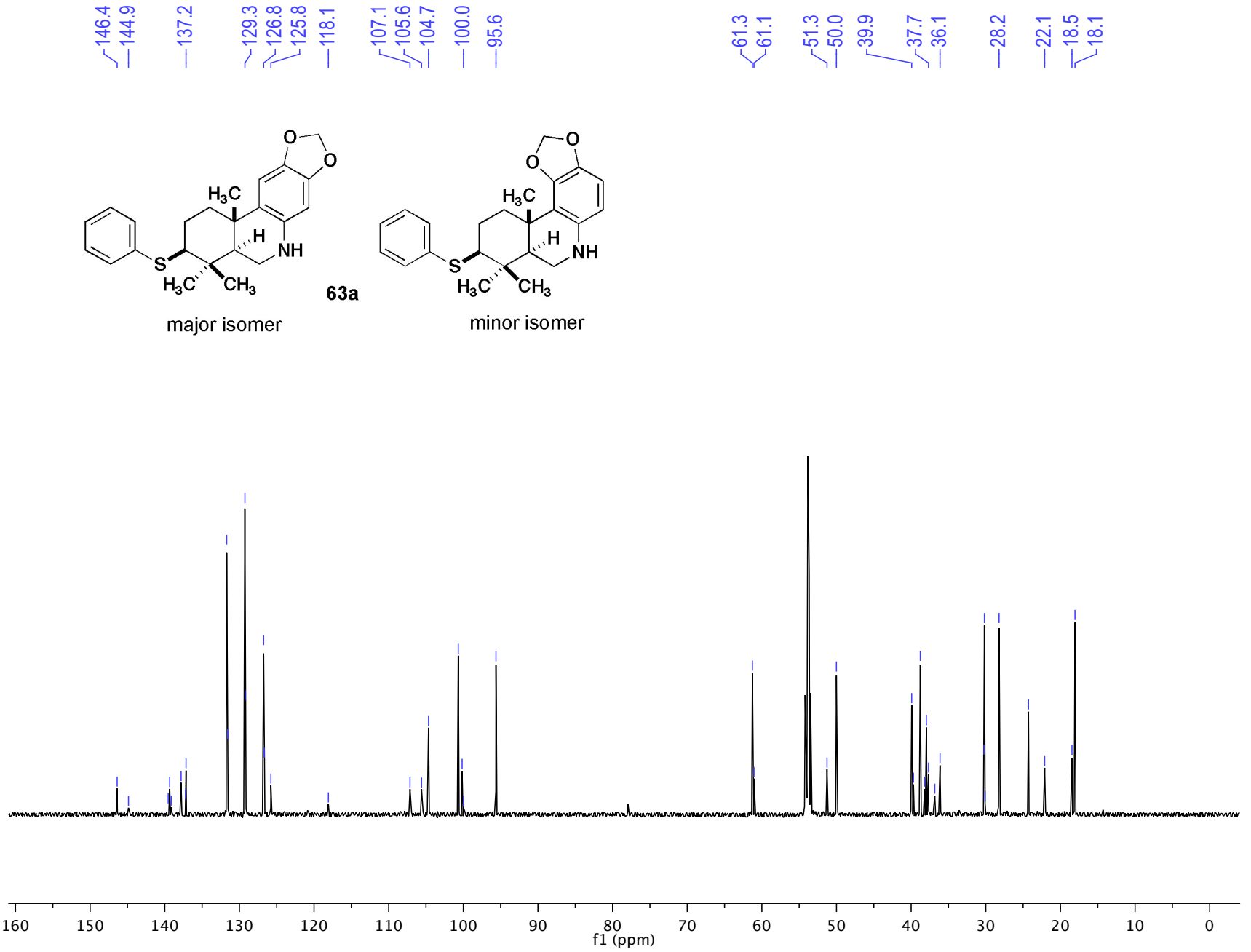
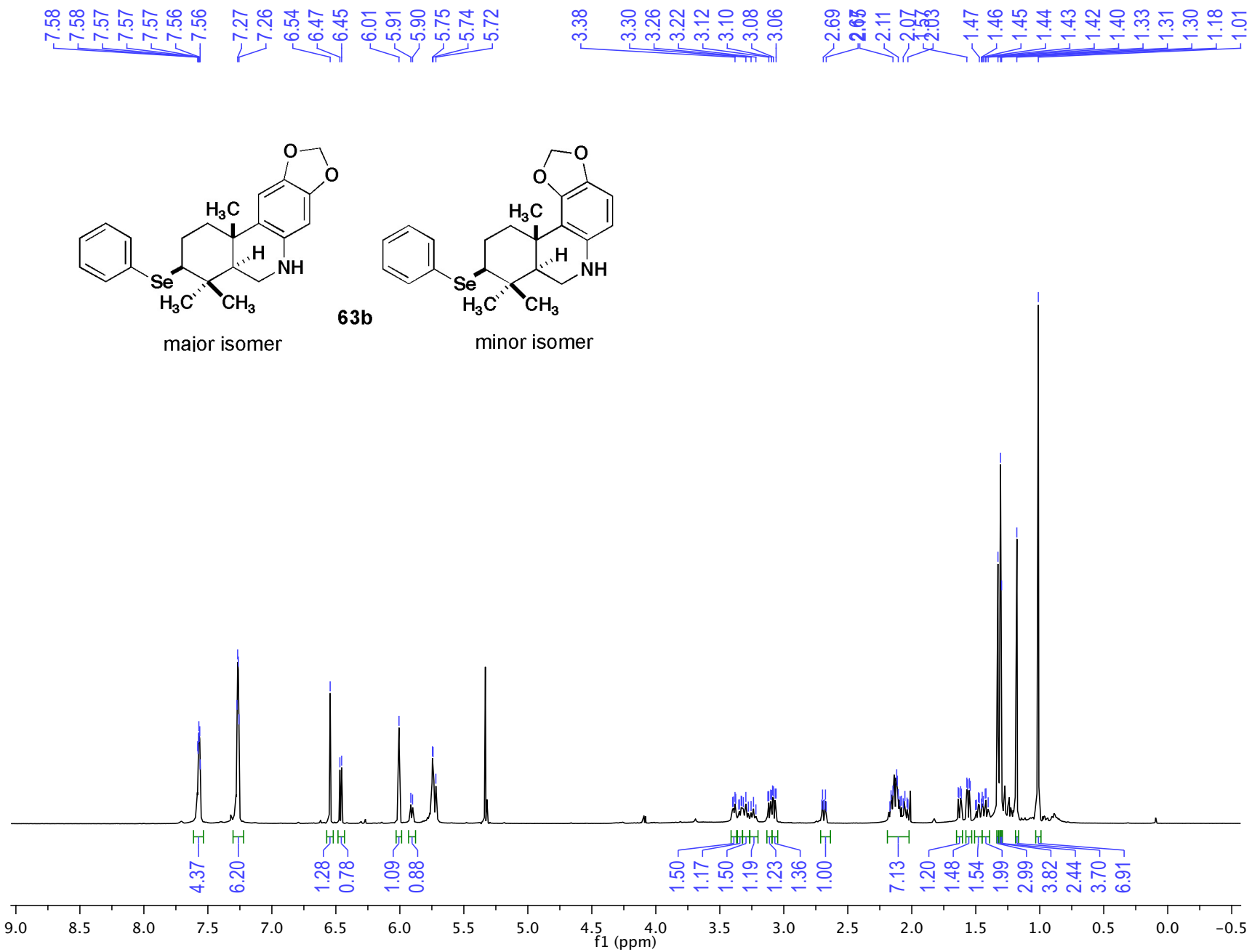
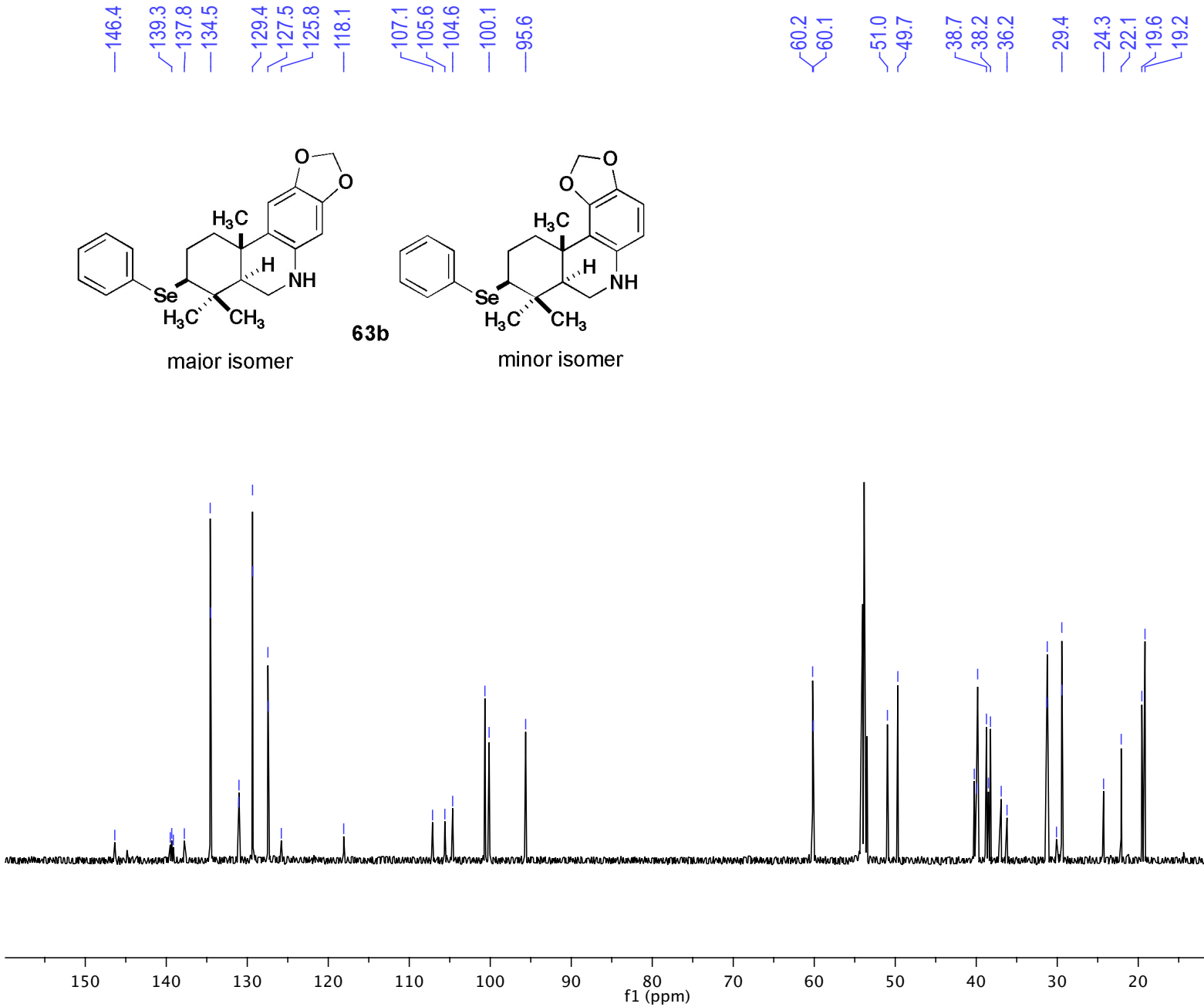
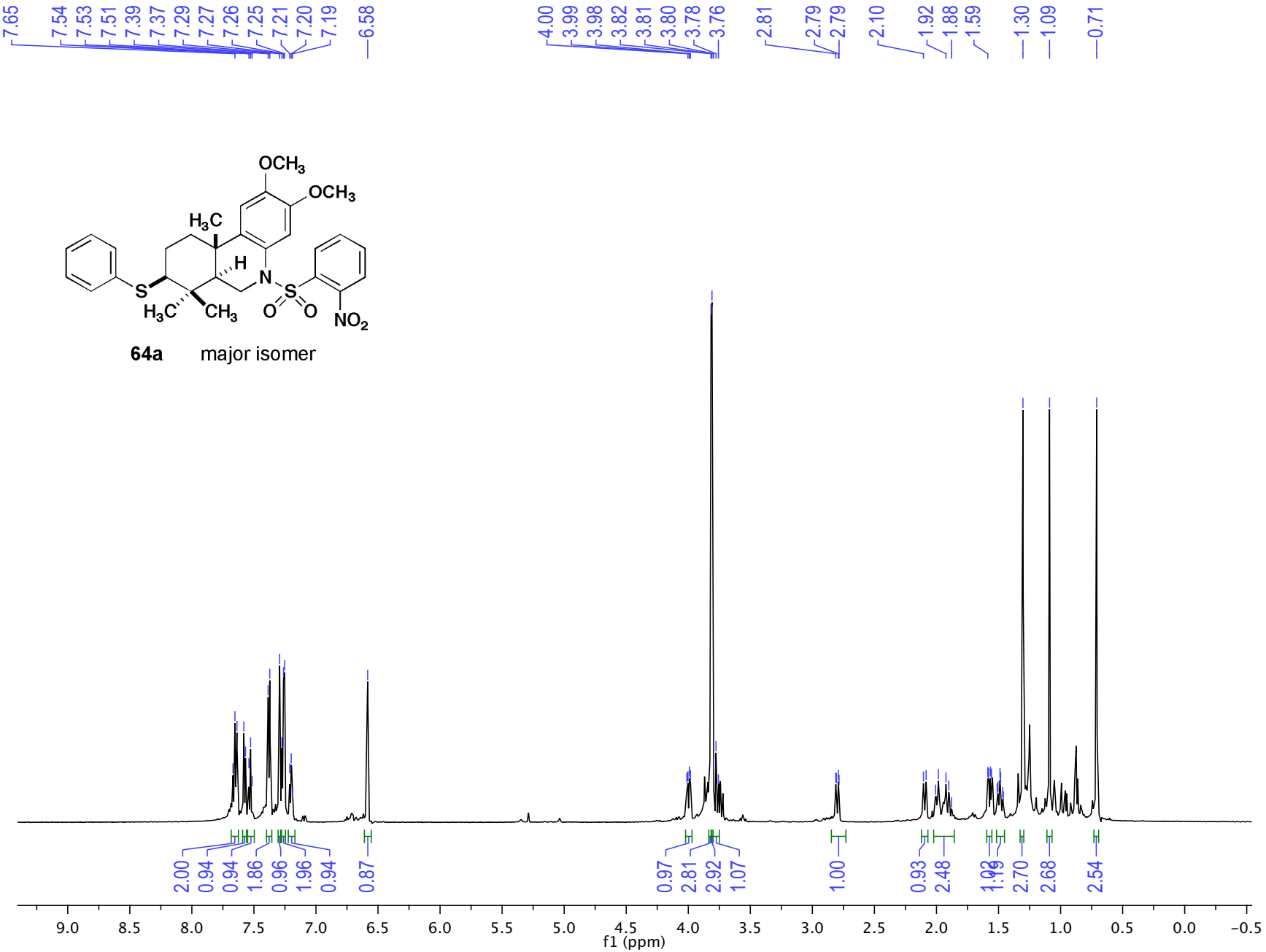
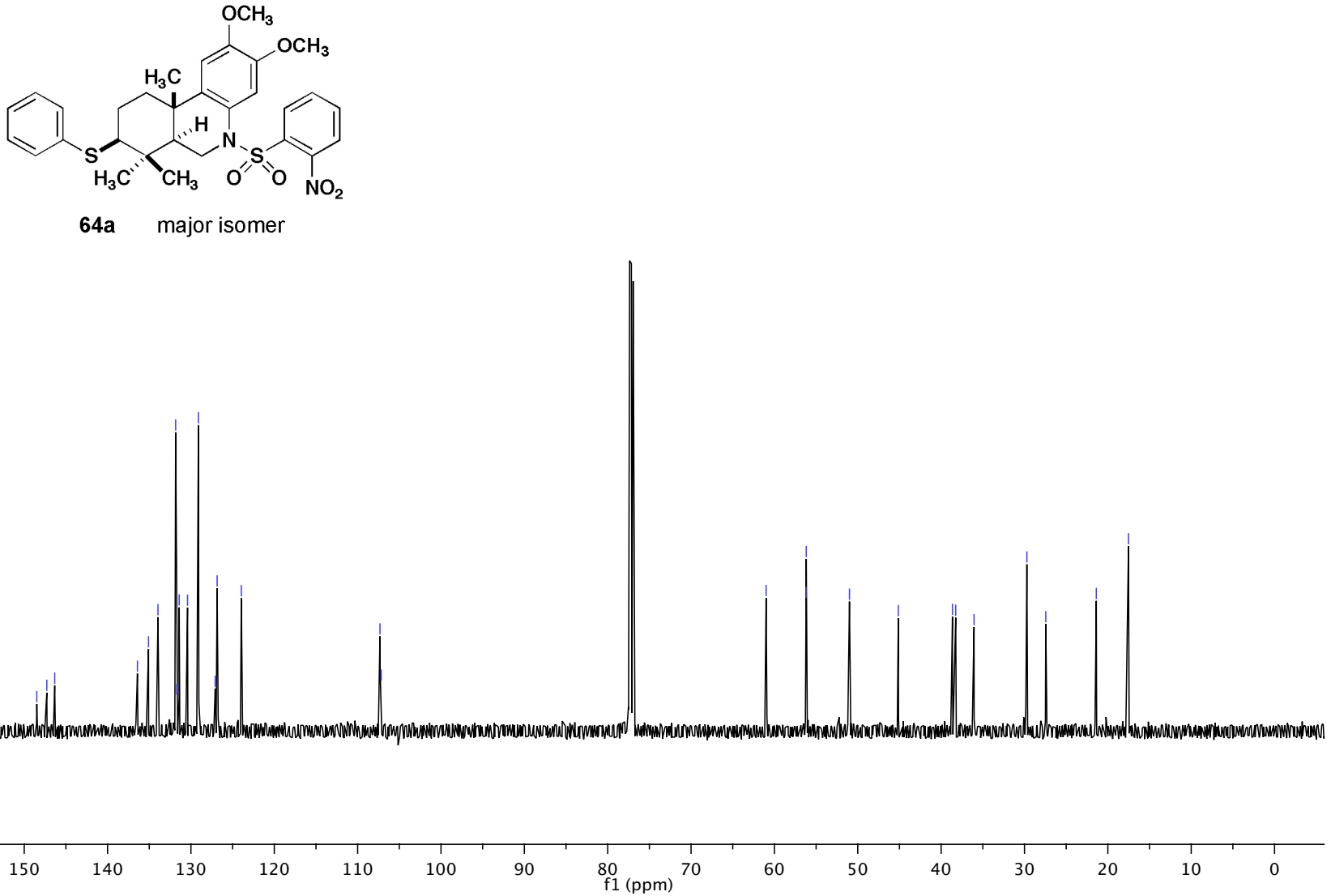




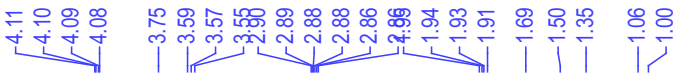


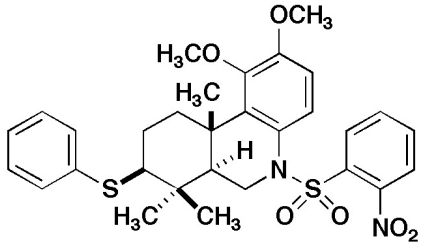




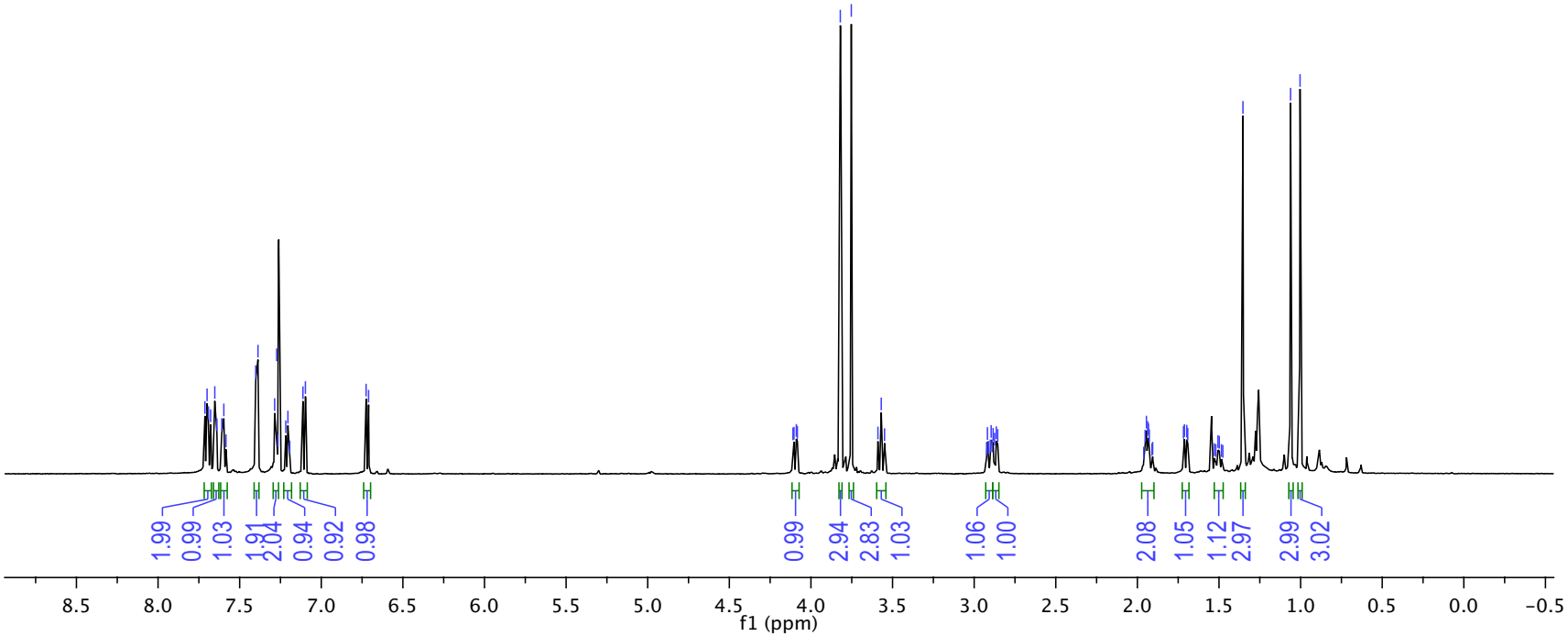


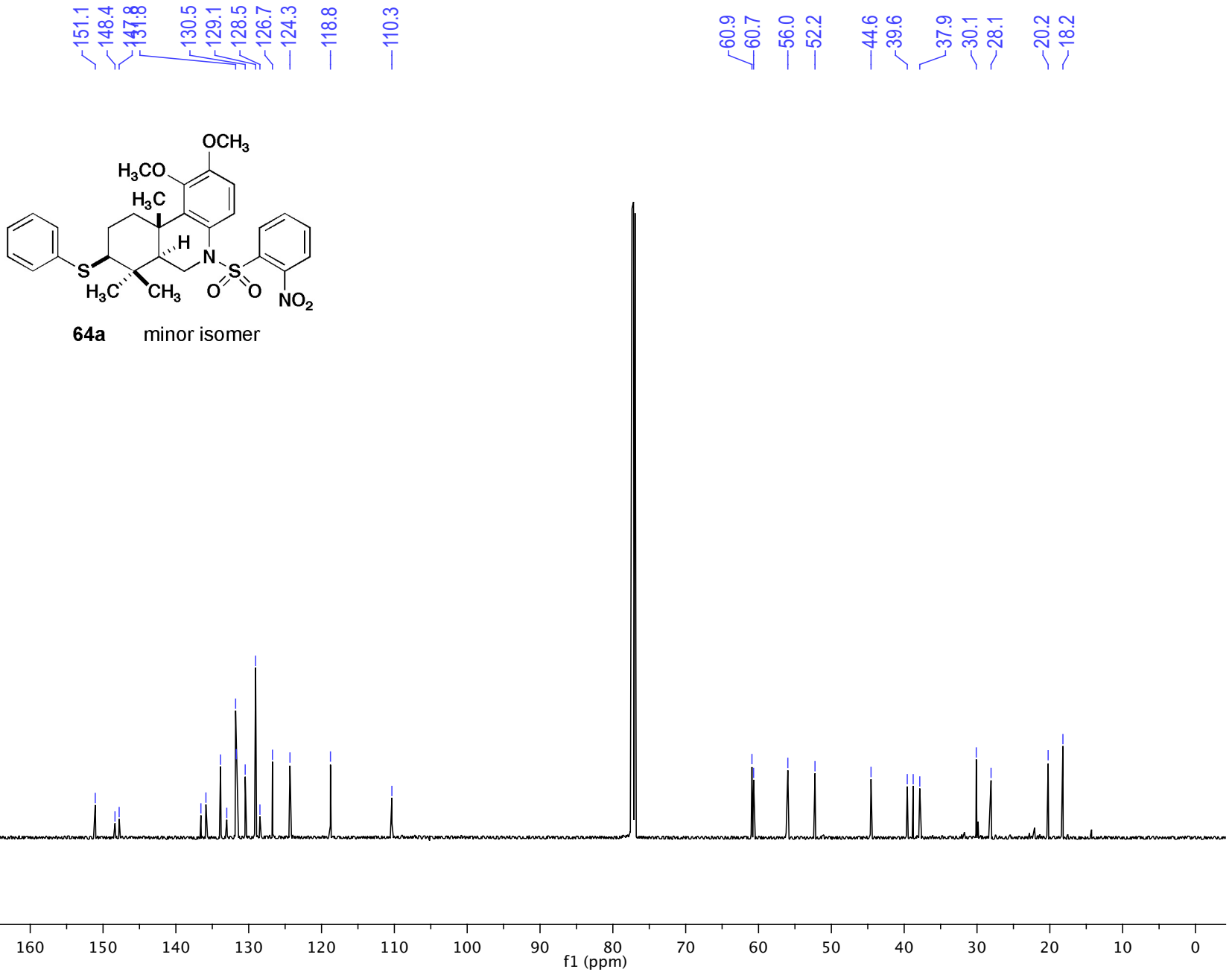
64a major isomer



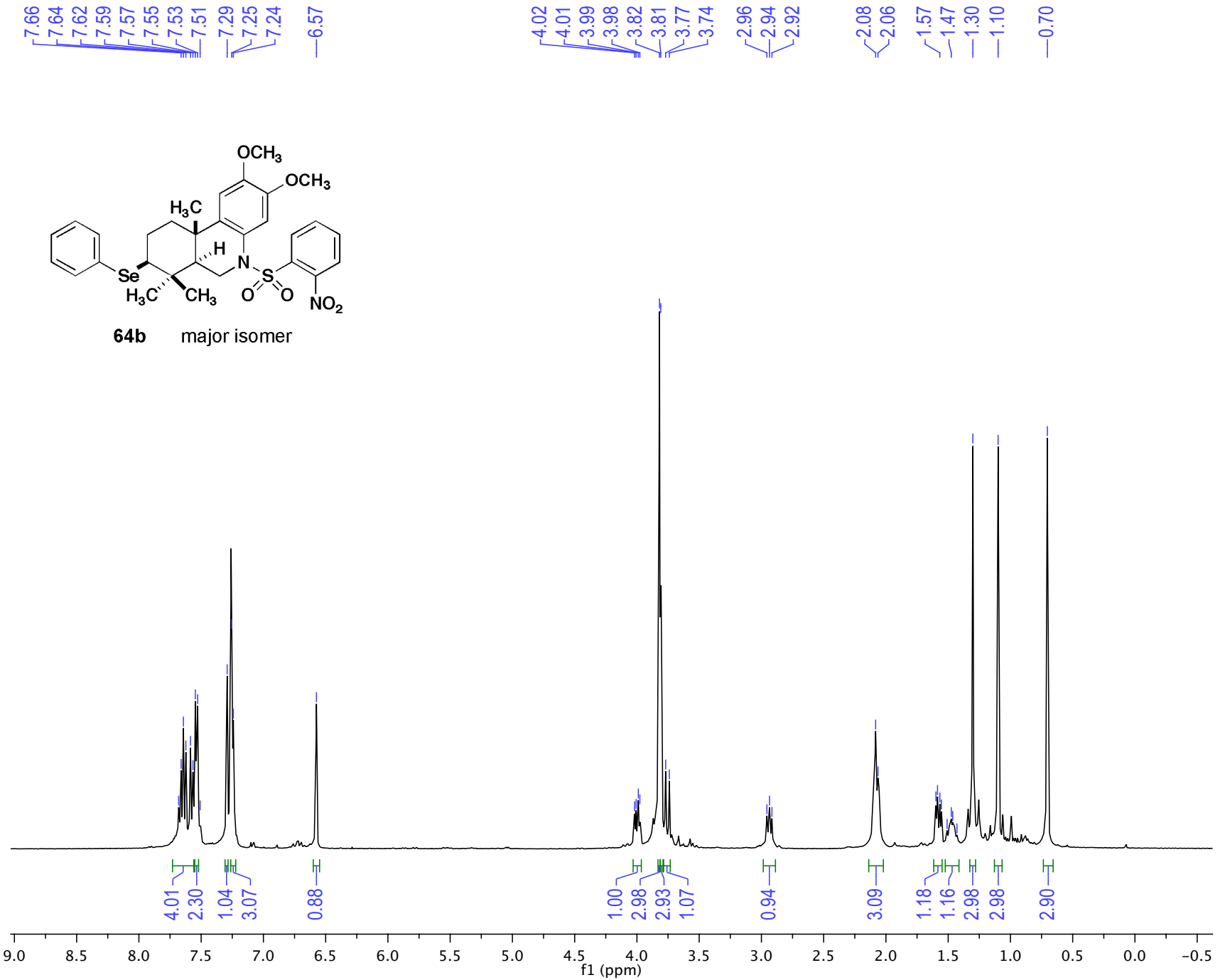


64a minor isomer

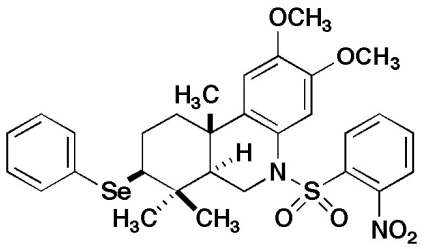




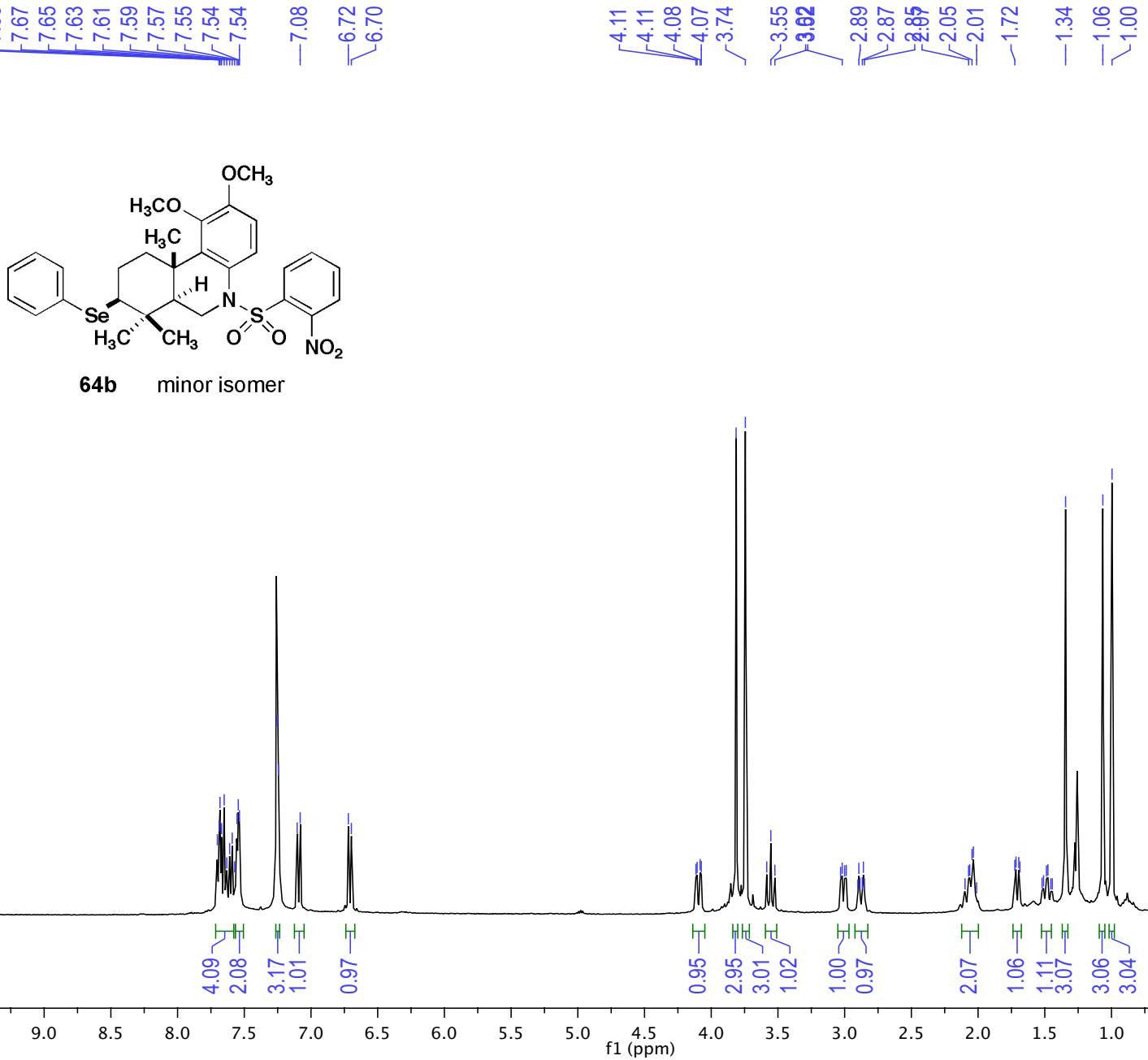
64a minor isomer



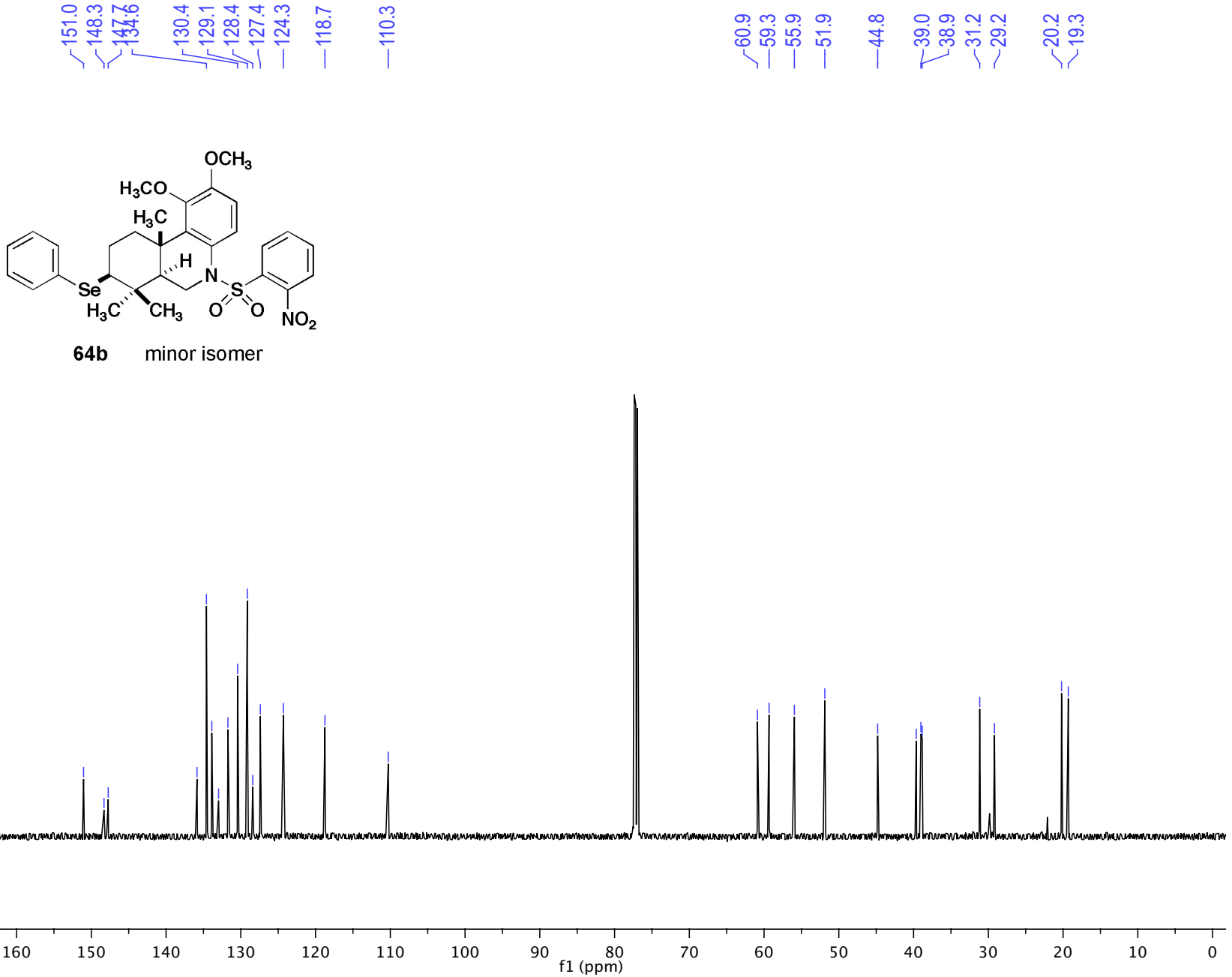
64b major isomer



64b major isomer



64b minor isomer



64b minor isomer