Practical and Scalable Synthesis of Orthogonally Protected-2-Substituted Chiral Piperazines

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Supporting Information
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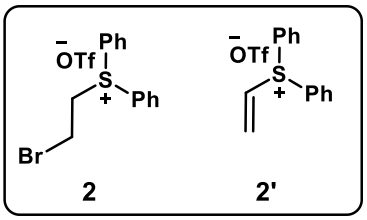
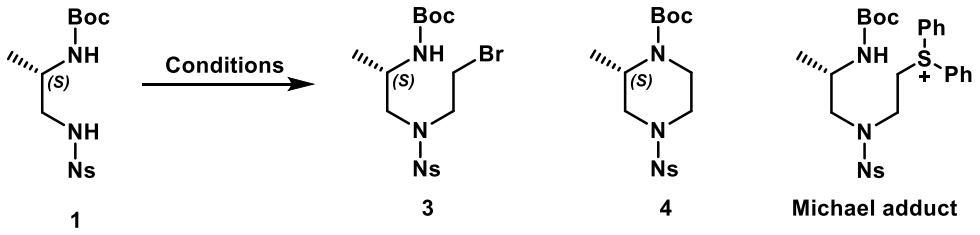
General Methods.

All starting materials and reagents were purchased from commercial sources and used without further purification. Solvents were purchased as either anhydrous grade products in sealed containers or reagent grade and used as received. All reactions were carried out in dry glassware under a nitrogen atmosphere using standard disposable or gastight syringes, disposable or stainless steel needles, and septa. Stirring was achieved with magnetic stir bars. Flash column chromatography was performed with SiO_2 (230-400 mesh) or by using an automated chromatography instrument with an appropriately sized column. Thin layer chromatography was performed on silica gel $60F_{254}$ plates (E. Merck). Non-UV active compounds were visualized on TLC using one of the following stains: $KMnO_4$, ninhydrin, *p*-anisaldehyde. ^{1}H and ^{13}C NMR spectra were recorded on an instrument operating at either 600MHz, and 151MHz respectively. LCMS data were collected using an HPLC instrument coupled to a low resolution mass spectrometer with single quadrupole ionization operating in either positive or negative ion mode. The analytical method utilized a C_{18} column (2.1 × 50 mm, 1.8 μm) eluting with a linear gradient of 95%/5% water/CH_3CN (modified with 0.05% formic acid; T = 0 min flow = 0.35 mL/min) to 95%/5% CH_3CN/water (T = 3.5 min flow = 0.5 mL/min) then 95%/5% CH_3CN/water to T = 5min (0.5 mL/min). Peak detection was done at 254 nm and 230 nm for UV active compounds. For non-UV active compounds total ion count was used. High-resolution mass spectrometry (HRMS) spectra were obtained on a Thermo Scientific Q Exactive hybrid quadrupole-Orbitrap mass spectrometer equipped with a HESI source and using lock masses for correction. Samples were introduced into the HRMS via reversed phase HPLC on an Accucore Vanquish C18+ column (2.1 × 100 mm, 1.5 μm) eluting with a linear gradient of 95%/5% water/acetonitrile (modified with 0.1% formic acid) to 10%/90% water/acetonitrile over 8 min. Chiral HPLC analysis of piperazines was carried out on an instrument with automated 6-column array (Daicel ChiralPak I-series, IA through IF, 4.6 × 150 mm, 5 μm). Racemates were screened using a heptane (A)/ethanol (B) gradient (flow = 1 mL/min) as follows: T = 0 min (%A/%B) 95/5, T = 1 min 95/5, T = 11 min 10/90 (linear gradient), T = 13 min 10/90, T = 13.1min 95/5, T = 15min 95/5. Racemates that gave unsatisfactory resolution of enantiomers were rescreened using the above gradient with *i*PrOH instead of EtOH. Additional editing of the gradient or the use of an isocratic mobile phase to optimize separation was carried out as needed. Chiral materials were analyzed using optimized conditions and their traces were compared to the racemic traces for determination of enantiomeric ratio (er).

To determine our limit of detection (LOD) by chiral HPLC, 5 μL aliquots of 2 mg/mL stocks (10 ng injections) of purified protected scaffolds were subjected to chiral HPLC analysis to resolve and quantify enantiomers and determine enantiomeric ratios. Scouting solvent conditions across six 4.6 mm x 150 mm chiral columns (ChiralPak IA-IE) identified chromatographic conditions for every compound that successfully effected baseline resolution of the enantiomers of the racemic products. Absorbance at 254 nm (nosyl or benzyl) was used to detect and quantify the amount of scaffold. Serial dilutions of the 2 mg/mL stocks established that our LOD is approximately 0.02 ng/injection, or 0.2% of the total material loaded under these conditions. Therefore, the limit of our detection of enantiomeric ratio is ≥99.8:0.2. All chiral traces of the scaffolds are included in the Supplementary Information.

All NMR chemical shifts are quoted on the δ scale and were referenced to residual non-deuterated solvent as an internal standard. Signal multiplicities are described using the following abbreviations: s = singlet, d = doublet, t = triplet, b = broad, quar = quartet, quin = quintet, m = multiplet, v = very; abbreviations are combined, *e.g.* vbs = very broad singlet.





S.No	Reagent	Condition	Outcome	Remarks
1	2	DBU, DCM, rt	3	Slow, not clean
2	2	NaH, DCM, rt	no product	-
3	2	NaH, THF, rt	no product	-
4	2	NaH, THF, 60 °C	complex mixture	-
5	2	DIPEA, ACN, rt	Michael adduct	very slow
6	2	DIPEA, DMF, rt	Michael adduct	slow
7	2	DIPEA, DCM, rt	3	-
8	2	Cs_2CO_3, DCM, rt	3	-
9	2′	NaH, DCM, rt	no product	-
10	2′	NaH, THF, rt	no product	-
11	2′	DBU, DCM, rt	Michael adduct	-
12	2′	DIPEA, DCM, rt	Michael adduct	-

Table S1: Reaction optimization

General Experimental Procedures:

Synthesis of Bromide Intermediate: Into a round bottom flask equipped with magnetic stir bar and septum under nitrogen, the bisprotected chiral diamine (**1 equiv.**) was dissolved in dichloromethane and 2-bromoethyl-diphenylsulfonium triflate (**1.25 equiv.**) was added followed by diisopropylethylamine (**3 equiv.**). The reaction was allowed to stir at room temperature under nitrogen for 16h, after which time the TLC and LCMS showed no starting material remaining. The reaction was worked up by diluting with dichloromethane and washed with water and brine. The organic phase was collected and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give the crude residue. Purification by silica gel chromatography (ethyl acetate/ hexanes) provided the pure bromide product.

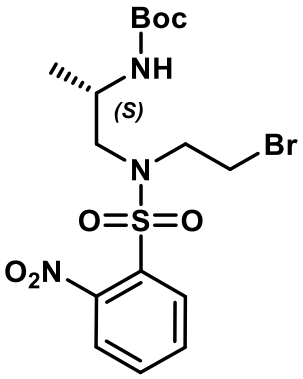
Method A: Into a round bottom flask equipped with magnetic stir bar and septum, the bromide compound (**1 equiv.**) was dissolved in dry THF and NaH (**2 equiv.**) was added at room temperature and the reaction was allowed to stir at room temperature under nitrogen. After 5h, LCMS and TLC showed complete consumption of the starting material. The reaction was quenched by adding cold water and then diluted

with ethyl acetate and washed with brine solution. The organic phase was collected and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give the crude residue. Purification by silica gel chromatography (ethyl acetate/ hexanes) provided the pure piperazine product.

Method B: Into a round bottom flask equipped with magnetic stir bar and septum, the bromide compound (**1 equiv.**) was dissolved in dichloromethane and TFA (10% TFA in DCM, V/V, 10 mL/mmol) was added and allowed to stir at room temperature under nitrogen. After 2h the starting material was consumed according to TLC and LCMS. The volatiles were evaporated under reduced pressure and then redissolved in toluene and evaporated to remove excess TFA. The mixture was diluted with DCM and washed with saturated aq $NaHCO_3$ solution. The organic phase was collected and dried over anhydrous Na_2SO_4. and the solvent was removed under reduced pressure to give the crude residue. Purification by silica gel chromatography (methanol:DCM) provided pure piperazine product.

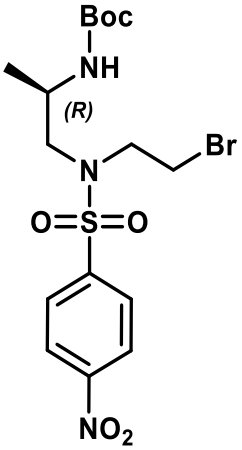
Method C: Into a round bottom flask equipped with magnetic stir bar and septum, the bromide compound (**1 equiv.**) was dissolved at room temperature in dichloromethane and tetrabutylammonium iodide (TBAI; **equiv.**) added. Upon complete dissolution, trimethylsilyltrifluoromethanesulfonate (TMSOTf; **2 equiv.**) was added dropwise by syringe. The reaction allowed to stir at room temperature for 1h under nitrogen, after which time TLC and LCMS indicated complete consumption of starting material. The reaction was diluted with DCM (50 mL) and the organic phase was washed by saturated aq $NaHCO_3$ and then sat aq $Na_2S_2O_3$ solution (30 mL). The organic phase was collected and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give the crude residue. Purification by silica gel chromatography (methanol:DCM) provided pure piperazine product.

Method D: Into a round bottom flask equipped with magnetic stir bar and septum, the bromide compound (**1 equiv.**) was dissolved in dichloromethane and TFA (10% TFA in DCM, V/V, 10 mL/mmol) was added and allowed to stir at room temperature under nitrogen. After 2h the starting material was consumed according to TLC and LCMS. The volatiles were evaporated under reduced pressure and then redissolved in toluene and evaporated to remove excess TFA. The mixture was dissolved in dry THF and K_2CO_3 (**5 equiv.**) was added at room temperature and the reaction was allowed to stir at room temperature under nitrogen. After 16h, LCMS and TLC showed complete consumption of the starting material. The reaction was quenched by adding water and then diluted with ethyl acetate and washed with brine solution. The organic phase was collected and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give the crude residue. Purification by silica gel chromatography (methanol:DCM) provided the pure product.



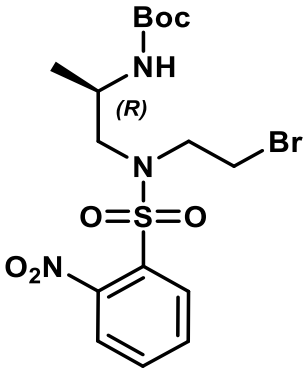
3a

Tert-butyl (*S*)-(1-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)propan-2-yl)carbamate (**3a**): Molecular Formula: $C_{16}H_{24}BrN_3O_6S$; Rf (40% ethyl acetate/hexanes): 0.35; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.04-8.01 (m, 1H), 7.75-7.69 (m, 2H), 7.67-7.64 (m, 1H), 4.62-4.54 (m, 1H), 3.92-3.87 (m, 1H), 3.76-3.65 (m, 2H), 3.52-3.39 (m, 3H), 3.26 (dd, *J* = 14.8, 5.9 Hz, 1H), 1.41 (s, *J* = 3.3 Hz, 9H), 1.16 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 155.4, 148.0, 133.9, 133.0, 131.9, 131.0, 124.4, 79.7, 53.0, 49.2, 44.4, 28.4, 18.7. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 466.0647 and 468.0627, found 466.0645, 468.0623 and 366.012, 368.0096 (-Boc).



3b

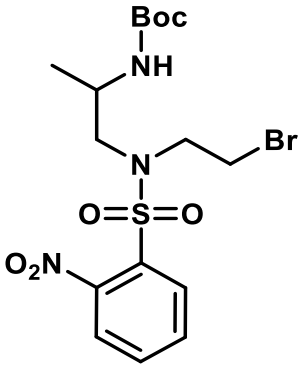
Tert-butyl (*R*)-(1-((N-(2-bromoethyl)-4-nitrophenyl)sulfonamido)propan-2-yl)carbamate (**3b**): Molecular Formula: $C_{16}H_{24}BrN_3O_6S$; Rf (40% ethyl acetate/hexanes): 0.25; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.41 – 8.36 (m, 2H), 8.05 – 7.98 (m, 2H), 4.61 (d, *J* = 7.9 Hz, 1H), 3.89-3.84 (m, 1H), 3.59-3.49 (m, 4H), 3.31-3.28 (m, 1H), 3.15 (dd, *J* = 14.1, 6.1 Hz, 1H), 1.44 (s, 9H), 1.21 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 155.4, 150.2, 145.0, 128.5, 124.5, 79.9, 53.9, 50.5, 45.1, 28.6, 28.4, 18.6. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 466.0647 and 468.0627, found 466.0641, 468.0619 and 366.0116, 368.0092 (-Boc).



3d

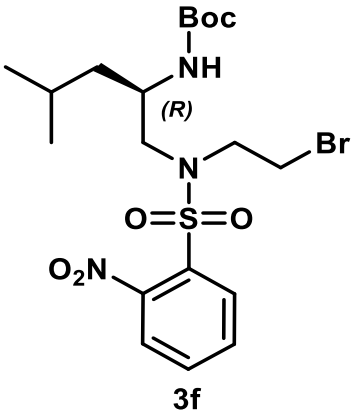
Tert-butyl (*R*)-(1-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)propan-2-yl)carbamate (**3d**): Molecular Formula: $C_{16}H_{24}BrN_3O_6S$; Rf (40% ethyl acetate/hexanes): 0.35; **^{1}H NMR (600 MHz, $CDCl_3$)**

δ 8.04-8.01 (m, 1H), 7.75 – 7.68 (m, 2H), 7.66-7.63 (m, 1H), 4.60 (d, *J* = 8.5 Hz, 1H), 3.93-3.85 (m, 1H), 3.78 – 3.61 (m, 2H), 3.48-3.45 (m, 3H), 3.26 (dd, *J* = 14.8, 5.9, 1H), 1.41 (s, 9H), 1.15 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 155.4, 148.0, 133.9, 133.0, 131.9, 131.0, 124.4, 79.7, 53.0, 49.2, 44.4, 28.4, 28.1, 18.7. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 466.0647 and 468.0627 found 466.0640, 468.0618 and 366.0116, 368.0093 (-Boc).



3e

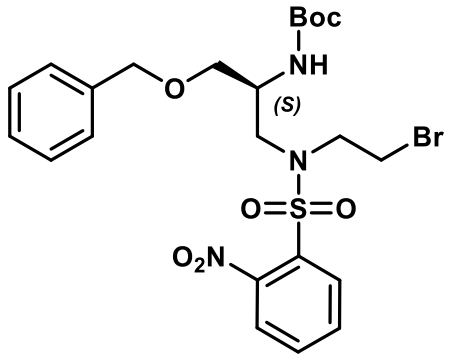
Tert-butyl-(1-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)propan-2-yl)carbamate (**3e**): Molecular Formula: $C_{16}H_{24}BrN_3O_6S$; Rf (40% ethyl acetate/hexanes): 0.35; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.05 – 8.01 (m, 1H), 7.75 – 7.68 (m, 2H), 7.67 – 7.63 (m, 1H), 4.59 (d, *J* = 8.6 Hz, 1H), 3.94-3.85 (m, 1H), 3.77-3.64 (m, 2H), 3.50-3.43 (m, 3H), 3.27 (dd, *J* = 14.8, 5.8 Hz, 1H), 1.42 (s, 9H), 1.17 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 155.4, 148.0, 133.9, 133.0, 131.9, 131.0, 124.4, 79.7, 53.0, 49.8, 44.5, 28.3, 18.7. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 466.0647 and 468.0627 found 466.0641, 468.0618 and 366.0114, 368.0090 (-Boc).



3f

Tert-butyl (*R*)-(1-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)-4-methylpentan-2-yl)carbamate (3f); Molecular Formula: $C_{19}H_{30}BrN_3O_6S$; Rf (40% ethyl acetate/hexanes): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.06 – 8.01 (m, 1H), 7.74 – 7.68 (m, 2H), 7.66-7.63 (m, 1H), 4.42 (d, *J* = 9.4 Hz, 1H), 3.89-3.82 (m, 1H), 3.79-3.68 (m, 2H), 3.50-3.45 (m, 3H), 3.27 (dd, *J* = 14.9, 5.4 Hz, 1H), 1.74 – 1.64 (m, 1H), 1.40 (s, 9H), 1.32 – 1.19 (m, 2H), 0.91 (t, *J* = 6.3 Hz, 7H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 155.7, 148.0, 133.7,

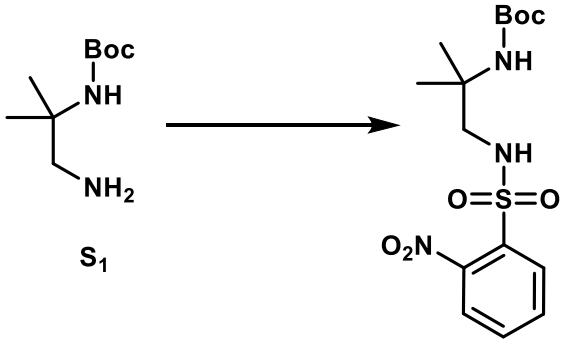
133.3, 131.9, 131.0, 129.2, 124.4, 79.6, 52.3, 49.0, 46.7, 42.1, 28.3, 24.8, 23.3, 21.9. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 508.1117 and 510.1096, found 508.1107, 510.1084 and 408.0581, 410.0558 (-Boc).

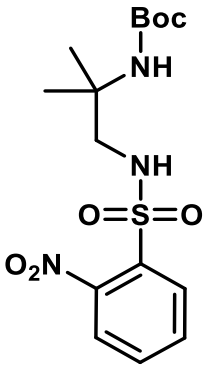


3g

Tert-butyl (*S*)-(1-(benzyloxy)-3-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)propan-2-yl)carbamate (3g); Molecular Formula: $C_{23}H_{30}BrN3O_7S$; Rf (40% ethyl acetate/hexanes): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.03 (d, *J* = 7.9 Hz, 1H), 7.72-7.68 (m, 1H), 7.67 – 7.61 (m, 2H), 7.39 – 7.35 (m, 2H), 7.34-7.29 (m, 3H), 4.94 (d, *J* = 8.8 Hz, 1H), 4.55 – 4.43 (m, 2H), 3.98-3.93 (m, 1H), 3.78 – 3.68 (m, 2H), 3.61 (dd, *J* = 9.6, 3.2 Hz, 1H), 3.55 – 3.44 (m, 5H), 1.41 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 155.49, 148.06, 137.69, 133.84, 132.80, 131.83, 131.17, 128.50, 127.91, 127.85, 124.37, 79.84, 73.46, 69.33, 49.59, 49.19, 48.59, 28.34. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 572.1066 and 574.1046 found 572.1064, 574.1041 and 472.0539, 474.0516 (-Boc).

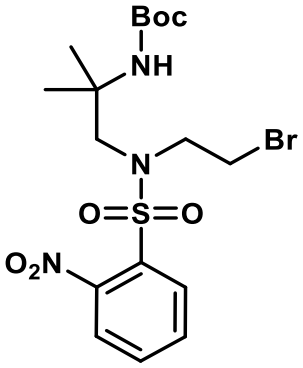
General Procedure for the Nosylation (sulfonylation): Into a round bottom flask equipped with magnetic stir bar and septum, the Boc-protected amine (**1 equiv.**) was dissolved in dichloromethane and TEA (**2 equiv.**) was added followed by 2-nitrobenzene sulfonylchloride (2-Nosylchloride, **1.2 equiv.**). The reaction was stirred at room temperature for 2h under nitrogen, after which time TLC and LCMS indicated complete consumption of the starting material. The reaction was diluted with dichloromethane and washed with saturated aq $NaHCO_3$ and brine solution. The organic phase was collected and dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give the crude residue. Purification by silica gel chromatography (ethyl acetate/ hexanes) provided the pure product.





1h

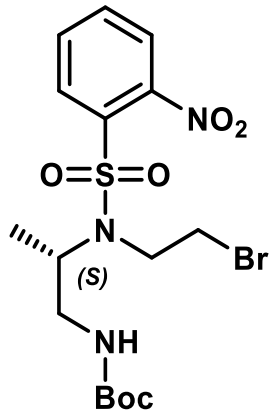
Tert-butyl (2-methyl-1-((2-nitrophenyl)sulfonamido)propan-2-yl)carbamate (**1h**)**:** Molecular Formula: $C_{15}H_{23}N_3O_6S$; Rf (40% ethyl acetate/hexanes): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.13 – 8.09 (m, 1H), 7.86 – 7.82 (m, 1H), 7.75-7.72 (m, 2H), 5.85 (s, 1H), 4.51 (s, 1H), 3.27 (d, *J* = 6.4 Hz, 2H), 1.38 (s, 9H), 1.28 (s, 6H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 154.6, 148.1, 133.5, 132.8, 131.1, 125.4, 79.8, 52.5, 50.6, 28.3, 25.7. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 374.1386, found 374.1376, 274.0853 (-Boc).



3h

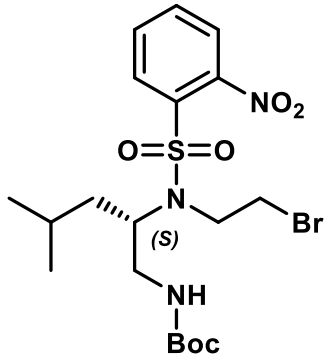
Tert-butyl (1-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)-2-methylpropan-2-yl)carbamate (**3h**)**:** Molecular Formula: $C_{17}H_{26}BrN_3O_6S$; Rf (40% ethyl acetate/hexanes): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.95 (d, *J* = 7.6 Hz, 1H), 7.77 – 7.70 (m, 2H), 7.66 (dd, *J* = 7.5, 1.7 Hz, 1H), 4.49 (s, 1H), 3.74 (s, 2H), 3.62 (dd, *J* = 9.2, 7.0 Hz, 2H), 3.50 (dd, *J* = 9.4, 6.9 Hz, 2H), 1.44 (s, 9H), 1.30 (s, 6H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 154.7, 148.4, 134.0, 132.2, 131.8, 130.5, 124.5, 80.0, 54.6, 53.8, 51.0, 28.4, 26.0. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 480.0804 and 482.0783 found 480.0796, 482.0773 and 380.0271, 382.0247 (-Boc).

Note: 3**k** not purified. After reaction work up, reaction mixture passed through a pad of silica (to eliminate diphenylsulfide by product) and subjected to next reaction.



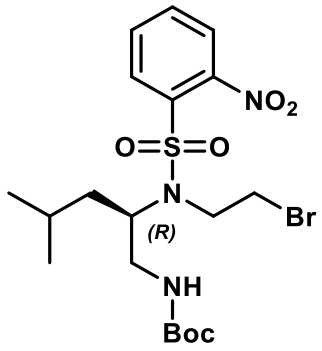
3m

Tert-butyl (*S*)-(2-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)propyl)carbamate (3m); Molecular Formula: $C_{16}H_{24}BrN_3O_6S$; Rf (50% ethyl acetate/hexanes): 0.35; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.08 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.73 (dp, *J* = 7.5, 1.7 Hz, 2H), 7.65 (dd, *J* = 7.5, 1.7 Hz, 1H), 4.92-4.88 (m, 1H), 4.05 – 3.96 (m, 1H), 3.64 – 3.55 (m, 2H), 3.53 – 3.47 (m, 2H), 3.29-3.22 (m, 1H), 3.16-3.10 (m, 1H), 1.38 (s, 9H), 1.16 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 155.7, 147.9, 134.0, 133.1, 131.9, 131.4, 124.4, 79.7, 54.3, 44.9, 43.8, 29.9, 28.3, 16.8. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 466.0647 and 468.0627 found 466.0639, 468.0616 and 366.0113, 368.0091 (-Boc).



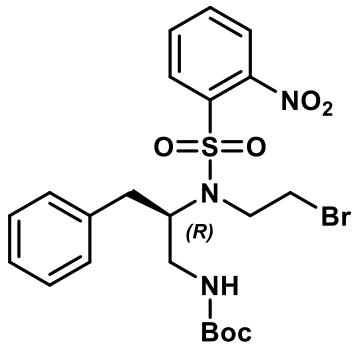
3n

Tert-butyl (*S*)-(2-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)-4-methylpentyl)carbamate (3n); Molecular Formula: $C_{19}H_{30}BrN_3O_6S$; Rf (50% ethyl acetate/hexanes): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.10 – 8.06 (m, 1H), 7.76-7.70 (m, 2H), 7.64 (dd, *J* = 7.4, 1.8 Hz, 1H), 4.94 (t, *J* = 6.0 Hz, 1H), 3.88-3.81 (m, 1H), 3.64-3.54 (m, 3H), 3.46-3.41 (m, 1H), 3.36-3.29 (m, 1H), 3.06 (ddd, *J* = 14.7, 9.6, 5.5 Hz, 1H), 1.63-1.54 (m, 1H), 1.40-1.31 (m, 11H), 0.88 – 0.81 (m, 6H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 156.2, 155.7, 148.0, 134.0, 133.1, 131.9, 131.7, 124.4, 79.6, 56.7, 45.4, 42.4, 40.8, 30.0, 28.3, 28.2, 24.7, 22.6, 22.3. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 508.1117 and 510.1096 found 508.1108, 510.1084 and 408.0579, 410.0557 (-Boc).



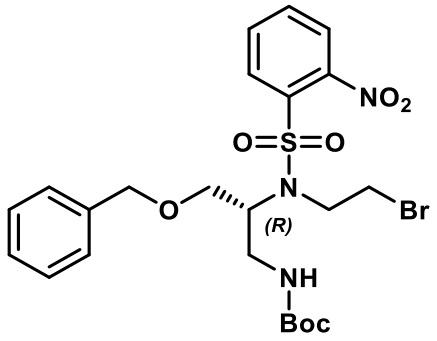
3o

Tert-butyl (*R*)-(2-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)-4-methylpentyl)carbamate (3o); Molecular Formula: $C_{19}H_{30}BrN_3O_6S$; Rf (50% ethyl acetate/hexanes): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.10 – 8.06 (m, 1H), 7.76-7.70 (m, 2H), 7.64 (dd, *J* = 7.5, 1.7 Hz, 1H), 4.93 (t, *J* = 6.0 Hz, 1H), 3.87-3.82 (m, 1H), 3.64-3.55 (m, 3H), 3.48 – 3.40 (m, 1H), 3.35-3.30 (m, 1H), 3.06 (ddd, *J* = 14.7, 9.6, 5.5 Hz, 1H), 1.62-1.55 (m, *J* = 12.5, 6.2 Hz, 1H), 1.35 (s, 13H), 0.90 – 0.79 (m, 6H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 155.7, 147.9, 134.0, 133.1, 131.9, 131.7, 124.4, 79.6, 56.7, 45.4, 42.4, 40.8, 30.0, 28.3, 28.2, 24.7, 22.6, 22.3. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 508.1117 and 510.1096 found 508.1106, 510.1084 and 408.0581, 410.0558 (-Boc).



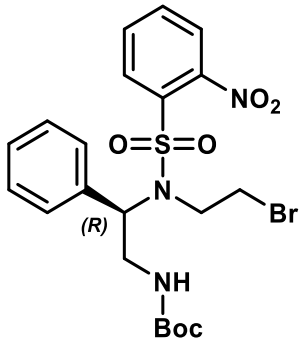
3p

Tert-butyl (*R*)-(2-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)-3-phenylpropyl)carbamate (3p); Molecular Formula: $C_{22}H_{28}BrN_3O_6S$; Rf (50% ethyl acetate/hexanes): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.92 (d, *J* = 7.9 Hz, 1H), 7.69 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.62 (ddd, *J* = 14.6, 7.8, 1.3 Hz, 2H), 7.20-7.13 (m, 3H), 7.07 (d, *J* = 7.3 Hz, 2H), 4.88 (d, *J* = 5.9 Hz, 1H), 4.16 – 4.05 (m, 1H), 3.83 – 3.66 (m, 1H), 3.58-3.49(m, 2H), 3.31 – 3.21 (m, 2H), 2.92 (dd, *J* = 13.8, 5.9 Hz, 1H), 2.76 (dd, *J* = 13.8, 8.8 Hz, 1H), 1.36 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 155.7, 147.8, 136.6, 134.0, 133.0, 132.0, 131.3, 129.1, 128.9, 128.8, 128.8, 127.0, 124.5, 79.6, 59.9, 45.6, 42.0, 38.4, 29.7, 28.3. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 542.0960 and 544.0940 found 542.0959, 544.0938 and 442.0431, 444.0410 (-Boc)



3q

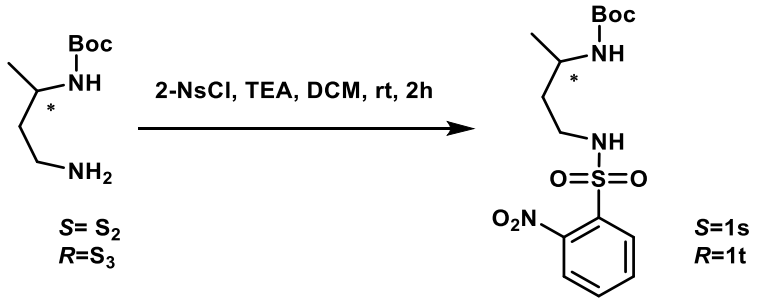
Tert-butyl (*R*)-(3-(benzyloxy)-2-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)propyl)carbamate (3q); Molecular Formula: $C_{22}H_{28}BrN_3O_6S$; Rf (50% ethyl acetate/hexanes): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.07 – 8.03 (m, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.57 – 7.48 (m, 2H), 7.37 – 7.28 (m, 3H), 7.23 – 7.16 (m, 2H), 4.87 (t, *J* = 6.0 Hz, 1H), 4.46 – 4.31 (m, 2H), 4.13-4.07 (m, 1H), 3.71 – 3.65 (m, 2H), 3.58 (d, *J* = 5.2 Hz, 2H), 3.54 – 3.45 (m, 2H), 3.39-3.30 (m, 2H), 1.38 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 155.88, 148.12, 137.13, 133.82, 133.10, 131.83, 131.37, 128.64, 128.14, 128.08, 124.28, 79.84, 73.66, 69.48, 58.08, 46.42, 40.43, 29.89, 28.44. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 572.1066 and 574.1046 found 572.1069, 574.1048 and 472.0540, 474.0578 (-Boc).

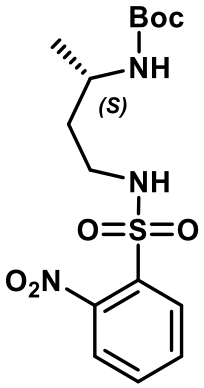


3r

Tert-butyl (*R*)-(2-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)-2-phenylethyl)carbamate (3r); Molecular Formula: $C_{21}H_{26}BrN_3O_6S$; Rf (50% ethyl acetate/hexanes): 0.35; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.03 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.75 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.71-7.65 (m, 2H), 7.35 (s, 5H), 5.12 (dd, *J* = 8.9, 6.8 Hz, 1H), 4.88-4.83 (m, 1H), 3.80 – 3.68 (m, 2H), 3.67-3.59 (m, 1H), 3.56-3.49 (m, 1H), 3.33-3.28 (m, 1H), 2.73-2.67 (m, 1H), 1.34 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 155.6, 147.9, 135.8, 133.9, 133.5, 132.0, 131.1, 129.2, 129.1, 127.9, 124.3, 79.8, 59.9, 46.4, 40.6, 29.2, 28.3. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 528.0804 and 530.0783 found 528.0807, 530.0784 and 428.0260, 430.0241 (-Boc).

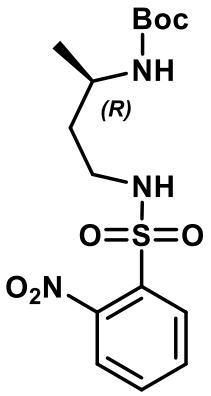
1s and **1t** was prepared according to above discussed general procedure (sulfonylation).





1s

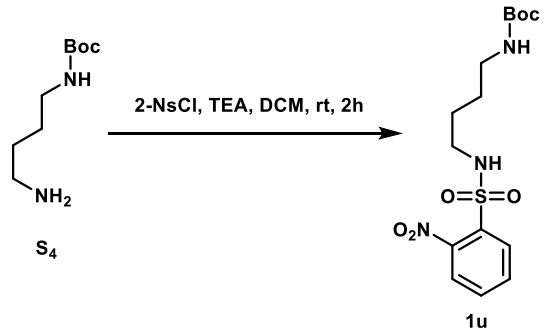
Tert-butyl (*S*)-(4-((2-nitrophenyl)sulfonamido)butan-2-yl)carbamate (1s); Molecular Formula: $C_{15}H_{23}N_3O_6S$; Rf (50% ethyl acetate/hexanes): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.14 – 8.08 (m, 1H), 7.84-7.81 (m, 1H), 7.73-7.69 (m, 2H), 6.26-6.21 (m, 1H), 4.32 (d, *J* = 8.7 Hz, 1H), 3.79 – 3.66 (m, 1H), 3.3-3.22 (m, 1H), 3.07-2.98 (m, 1H), 1.76 – 1.69 (m, 1H), 1.50 – 1.40 (m, 3H), 1.39 (s, 9H), 1.10 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 156.0, 148.1, 134.3, 133.3, 132.6, 130.7, 125.1, 79.7, 43.8, 40.8, 38.2, 28.3, 21.5. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 374.1386, found 374.1374 and –Boc 274.0852.

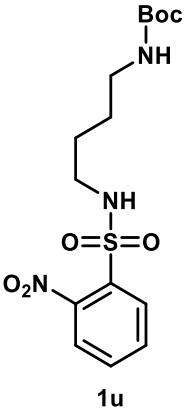


1t

Tert-butyl (*R*)-(4-((2-nitrophenyl)sulfonamido)butan-2-yl)carbamate (1t); Molecular Formula: $C_{15}H_{23}N_3O_6S$; Rf (50% ethyl acetate/hexanes): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.14 – 8.08 (m, 1H), 7.85 – 7.79 (m, 1H), 7.74-7.67 (m, 2H), 6.26-6.21 (bs, 1H), 4.35 – 4.22 (m, 1H), 3.80 – 3.66 (m, 1H), 3.31-3.22 (m, 1H), 3.06-2.99 (m, 1H), 1.77 – 1.68 (m, 1H), 1.39 (s, 9H), 1.10 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 156.0, 148.1, 134.3, 133.3, 132.5, 131.6, 130.8, 125.1, 124.1, 79.7, 44.3, 43.8, 40.8, 38.2, 28.3, 21.5, 13.7. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 374.1386, found 374.1374 and –Boc 274.0850.

1u was prepared according to above discussed general procedure (sulfonylation).

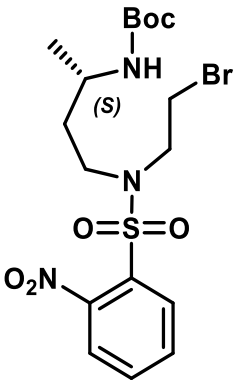




1u

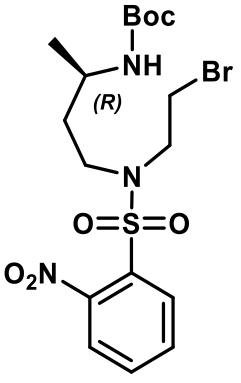
Tert-butyl (4-((2-nitrophenyl)sulfonamido)butyl)carbamate (1u); Molecular Formula: $C_{15}H_{23}N_3O_6S$; Rf (50% ethyl acetate/hexanes): 0.2; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.14 – 8.09 (m, 1H), 7.87 – 7.83 (m,

1H), 7.76 – 7.72 (m, 2H), 5.41-5.36 (m, 1H), 4.54 (bs, 1H), 3.13-3.06 (m, 4H), 1.62 – 1.54 (m, 2H), 1.54 – 1.47 (m, 2H), 1.42 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 156.0, 148.1, 133.7, 133.6, 132.8, 131.1, 125.4, 79.3, 43.4, 39.8, 28.4, 27.2, 26.9. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 374.1386, found 374.1377 and -Boc 274.0850.



3s

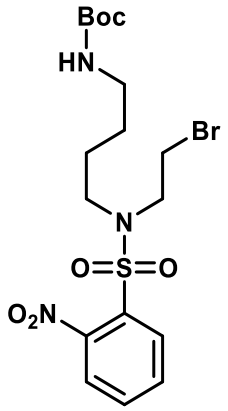
Tert-butyl (*S*)-(4-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)butan-2-yl)carbamate (3s); Molecular Formula: $C_{17}H_{26}BrN_3O_6S$; Rf (50% ethyl acetate/hexanes): 0.45; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.04-8.0 (m, 1H), 7.75-7.69 (m, 2H), 7.65 (d, *J* = 7.6 Hz, 1H), 4.44-4.36 (m, 1H), 3.75 – 3.57 (m, 3H), 3.451-3.41 (m, 3H), 3.39 – 3.28 (m, 1H), 1.81 – 1.65 (m, 2H), 1.44 (s, 9H), 1.14 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 155.4, 148.1, 133.9, 132.8, 131.8, 130.8, 124.3, 79.4, 49.6, 46.1, 44.5, 36.4, 28.7, 28.4, 21.3. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 480.0804 and 482.0783 found 480.0786, 482.07641 and 380.026, 382.0241 (-Boc).



3t

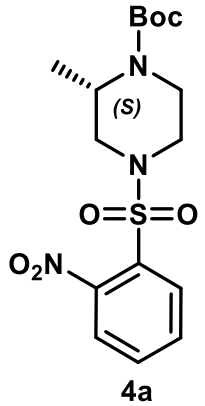
Tert-butyl (*R*)-(4-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)butan-2-yl)carbamate (3t); Molecular Formula: $C_{17}H_{26}BrN_3O_6S$; Rf (50% ethyl acetate/hexanes): 0.45; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.04 – 8.00 (m, 1H), 7.75-7.68 (m, 2H), 7.65 (dd, *J* = 7.4, 1.9 Hz, 1H), 4.42-4.37 (m, 1H), 3.70-3.67 (m,

2H), 3.65 – 3.58 (m, 1H), 3.49-3.41 (m, 3H), 3.39-3.31 (m, 1H), 1.81 – 1.65 (m, 2H), 1.44 (s, 9H), 1.14 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 155.4, 148.1, 133.8, 132.9, 131.8, 130.9, 124.3, 79.4, 49.6, 46.2, 44.5, 44.2, 36.4, 28.4, 21.3, 13.7. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 480.0804 and 482.0783 found 480.0792, 482.077 and 380.0268, 382.0246 (-Boc) .



3u

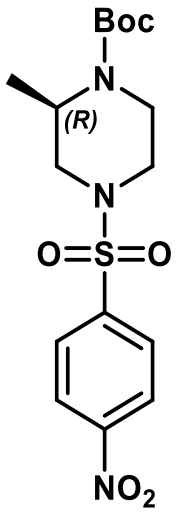
Tert-butyl (4-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)butyl)carbamate (3u); Molecular Formula: $C_{17}H_{26}BrN_3O_6S$; Rf (50% ethyl acetate/hexanes): 0.5; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.05 – 8.01 (m, 1H), 7.76 – 7.69 (m, 2H), 7.65 (dd, *J* = 7.1, 2.1 Hz, 1H), 4.61 – 4.54 (m, 1H), 3.66 (t, *J* = 7.5 Hz, 2H), 3.46 (t, *J* = 7.5 Hz, 2H), 3.37 (t, *J* = 7.6 Hz, 2H), 3.14-3.06 (m, 2H), 1.60 (p, *J* = 7.5 Hz, 2H), 1.50-1.45 (m, 2H), 1.44 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 156.0, 148.1, 133.8, 133.0, 131.8, 130.8, 124.3, 79.3, 49.1, 48.3, 39.7, 28.5, 28.4, 27.2, 25.7. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 480.0804 and 482.0783 found found 480.0791, 482.0769 and 380.0267, 382.0244 (-Boc).



4a

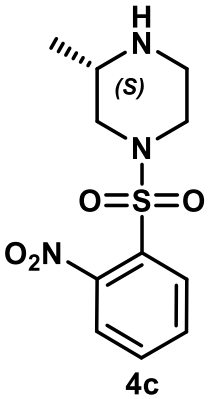
Tert-butyl (*S*)-2-methyl-4-((2-nitrophenyl)sulfonyl)piperazine-1-carboxylate (4a); Molecular Formula: $C_{16}H_{23}N_3O_6S$; Rf (40% ethyl acetate/hexanes): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.95 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.78 – 7.67 (m, 2H), 7.62 (dd, *J* = 7.6, 1.6 Hz, 1H), 4.38 (d, *J* = 9.1 Hz, 1H), 3.95 (d, *J* = 13.6 Hz, 1H), 3.79 (ddt, *J* = 12.3, 3.9, 2.0 Hz, 1H), 3.59 (dt, *J* = 12.3, 1.9 Hz, 1H), 3.18 (td, *J* = 13.0, 3.5 Hz, 1H), 2.94 (dd, *J* = 12.4, 3.7 Hz, 1H), 2.75 (td, *J* = 12.3, 3.5 Hz, 1H), 1.44 (s, 9H), 1.21 (d, *J* = 6.8 Hz,

3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 154.2, 148.4, 133.8, 131.5, 131.1, 131.0, 124.1, 80.4, 50.2, 45.8, 28.3, 14.9. $[\alpha]_D^{25}$ -2.7 (c 1.0, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 386.1386, found 286.0849 (-Boc).



4b

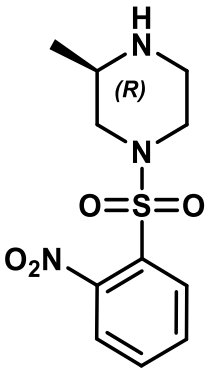
Tert-butyl (*R*)-2-methyl-4-((4-nitrophenyl)sulfonyl)piperazine-1-carboxylate (4b); Molecular Formula: $C_{16}H_{23}N_3O_6S$; Rf (50% ethyl acetate/hexanes): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.42 – 8.37 (m, 2H), 7.96 – 7.91 (m, 2H), 4.37 (s, 1H), 3.95 (d, *J* = 13.6 Hz, 1H), 3.76-3.73 (m, 1H), 3.56-3.54 (m, 1H), 3.18 (dt, *J* = 13.0, 3.6 Hz, 1H), 2.49 (dd, *J* = 11.5, 3.8 Hz, 1H), 2.31 (dt, *J* = 11.8, 3.5 Hz, 1H), 1.42 (s, 9H), 1.29 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 154.0, 150.3, 141.8, 128.8, 124.4, 80.4, 50.3, 45.9, 29.4, 28.3, 15.0. $[\alpha]_D^{25}$ -15 (c 0.5, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 386.1386, found 286.0844 (-Boc).



4c

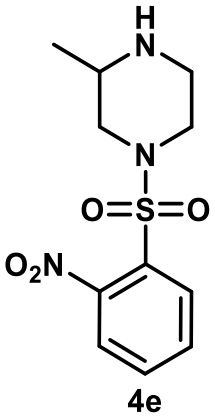
(*S*)-3-methyl-1-((2-nitrophenyl)sulfonyl)piperazine (4c); Molecular Formula: $C_{11}H_{15}N_3O_4S$; Rf (3% methanol/DCM): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.95 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.69 (dp, *J* = 7.5, 1.7 Hz, 2H), 7.60 (dd, *J* = 7.3, 1.9 Hz, 1H), 3.74 – 3.61 (m, 2H), 3.03 (dt, *J* = 12.2, 2.6 Hz, 1H), 2.94 – 2.82 (m, 2H), 2.77 (td, *J* = 11.8, 3.1 Hz, 1H), 2.40 (dd, *J* = 11.9, 10.2 Hz, 1H), 1.06 (d, *J* = 6.4 Hz, 3H). **^{13}C**

NMR (151 MHz, $CDCl_3$) δ 148.5, 133.7, 131.5, 131.2, 130.9, 124.1, 52.5, 50.5, 46.1, 45.5, 19.3. $[\alpha]_D^{25}$ +63.8 (c 1.0, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 286.0862, found 286.0851.



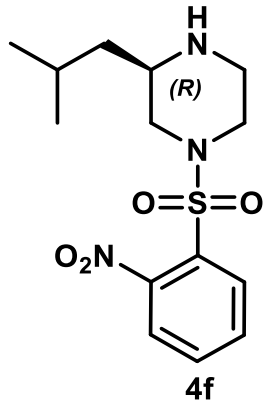
4d

(*R*)-3-methyl-1-((2-nitrophenyl)sulfonyl)piperazine (4d); Molecular Formula: $C_{11}H_{15}N_3O_4S$; Rf (3% methanol/DCM): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.96 – 7.93 (m, 1H), 7.69 (dp, *J* = 7.5, 1.7 Hz, 2H), 7.60 (dd, *J* = 7.6, 1.7 Hz, 1H), 3.70-3.64 (m, 2H), 3.03 (dt, *J* = 12.1, 2.6 Hz, 1H), 2.93 – 2.81 (m, 2H), 2.76 (dt, *J* = 11.8, 3.1 Hz, 1H), 2.38 (dd, *J* = 11.9, 10.2 Hz, 1H), 1.05 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 148.5, 133.7, 131.5, 130.9, 124.1, 52.5, 50.5, 46.1, 45.5, 19.3. $[\alpha]_D^{25}$ +9.1 (c 2.4, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 286.0862, found 286.0851.



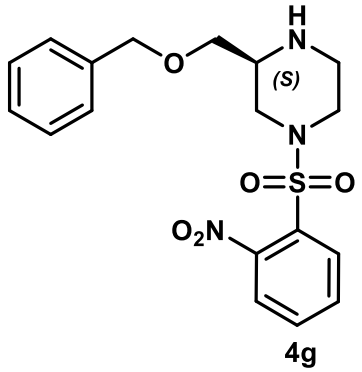
4e

3-methyl-1-((2-nitrophenyl)sulfonyl)piperazine (4e); Molecular Formula: $C_{11}H_{15}N_3O_4S$; Rf (3% methanol/DCM): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.97 (dd, *J* = 7.3, 1.9 Hz, 1H), 7.70 (dp, *J* = 7.5, 1.7 Hz, 2H), 7.61 (dd, *J* = 7.3, 1.8 Hz, 1H), 3.74 – 3.65 (m, 2H), 3.05 (td, *J* = 12.1, 2.6 Hz, 1H), 2.95 – 2.85 (m, 2H), 2.80 (dt, *J* = 11.8, 3.0 Hz, 1H), 2.42 (dd, *J* = 12.0, 10.2 Hz, 1H), 1.08 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 148.5, 133.6, 131.5, 130.9, 124.1, 52.4, 50.5, 46.0, 45.4, 19.2. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 286.0862, found 286.0854.



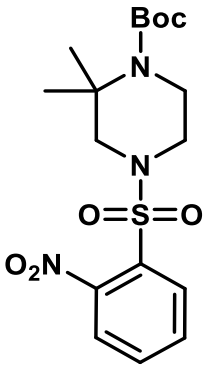
4f

(*R*)-3-isobutyl-1-((2-nitrophenyl)sulfonyl)piperazine (4f); Molecular Formula: $C_{14}H_{21}N_3O_4S$; Rf (3% methanol/DCM): 0.35; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.97 – 7.94 (m, 1H), 7.75 – 7.68 (m, 2H), 7.65 – 7.61 (m, 1H), 3.80-3.74 (m, 2H), 3.19 (dt, *J* = 12.2, 2.7 Hz, 1H), 3.09 – 3.01 (m, 1H), 3.0-2.93 (m, 2H), 2.71 – 2.61 (m, 1H), 1.77-1.69 (m, 1H), 1.44-1.39 (m, 1H), 1.38-1.31 (m, 1H), 0.92 (t, *J* = 7.1 Hz, 6H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 148.4, 133.9, 131.7, 131.3, 130.9, 124.3, 53.4, 50.3, 45.2, 44.7, 41.5, 24.2, 22.6, 22.5. $[\alpha]_D^{25}$ -20.0 (c 1.0, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 328.1331, found 328.1322.



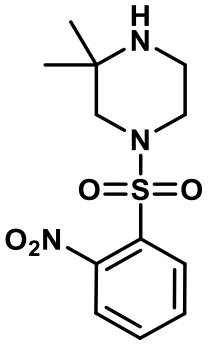
4g

(*S*)-3-((benzyloxy)methyl)-1-((2-nitrophenyl)sulfonyl)piperazine (4g); Molecular Formula: $C_{18}H_{21}N_3O_5S$; Rf (3% methanol/DCM): 0.4; **^{1}H NMR (600 MHz, MeOD)** δ 8.07 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.90-7.80 (m, 3H), 7.40 – 7.34 (m, 4H), 7.33-7.29 (m, 1H), 4.58 (d, *J* = 2.8 Hz, 2H), 3.94 – 3.81 (m, 2H), 3.63 (dd, *J* = 10.2, 4.6 Hz, 1H), 3.58 (dd, *J* = 10.3, 5.8 Hz, 1H), 3.34 – 3.23 (m, 2H), 3.13 – 3.02 (m, 2H), 2.96 (dd, *J* = 13.1, 10.4 Hz, 1H). **^{13}C NMR (151 MHz, MeOD)** δ 148.4, 137.4, 134.6, 132.0, 130.8, 130.0, 128.2, 127.8, 127.7, 124.2, 73.2, 67.9, 54.4, 46.1, 43.7, 43.4. $[\alpha]_D^{25}$ +4.4 (c 2.0, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 392.1280, found 392.1279.



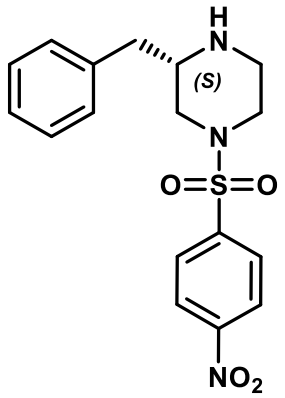
4h

Tert-butyl 2,2-dimethyl-4-((2-nitrophenyl)sulfonyl)piperazine-1-carboxylate (**4h**)**:** Molecular Formula: $C_{17}H_{25}N_3O_6S$; Rf (40% ethyl acetate/hexanes): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.00 (dd, *J* = 7.3, 1.9 Hz, 1H), 7.74-7.69 (m, 2H), 7.64 (dd, *J* = 7.3, 1.9 Hz, 1H), 3.65 (t, *J* = 5.6 Hz, 2H), 3.41 (t, *J* = 5.6 Hz, 2H), 3.25 (s, 2H), 1.46 (s, 9H), 1.42 (s, 6H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 154.3, 147.1, 132.7, 130.6, 130.6, 130.0, 123.2, 79.5, 54.8, 54.3, 44.3, 39.45, 28.7, 27.4, 23.7. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 400.1542, found 300.1008 (-Boc).



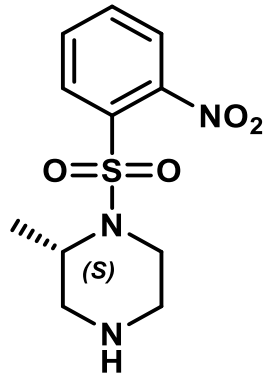
4j

3,3-dimethyl-1-((2-nitrophenyl)sulfonyl)piperazine (4j): Molecular Formula: $C_{12}H_{17}N_3O_4S$; Rf (5% methanol/DCM): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.93 (dd, *J* = 7.3, 1.9 Hz, 1H), 7.72-7.67 (m, 2H), 7.61 (dd, *J* = 7.2, 1.9 Hz, 1H), 3.22-3.21 (m, 2H), 3.06 – 2.95 (m, 4H), 1.17 (s, 6H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 148.4, 133.6, 131.5, 130.9, 124.0, 56.2, 49.7, 46.4, 40.6, 29.7, 25.6. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 300.1018, found 300.1010.



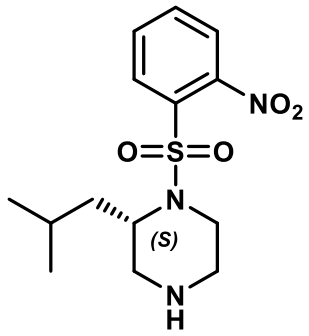
4k

(*S*)-3-benzyl-1-((4-nitrophenyl)sulfonyl)piperazine (4k); Molecular Formula: $C_{17}H_{19}N_3O_4S$; Rf (3% methanol/DCM): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.40 (d, *J* = 8.7 Hz, 1H), 7.94 (d, *J* = 8.8 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.28 – 7.22 (m, 1H), 7.18 – 7.12 (m, 1H), 3.74 – 3.62 (m, 1H), 3.02-2.97 (m, 1H), 2.87 – 2.70 (m, 1H), 2.5-2.44 (m, 1H), 2.18 (t, *J* = 10.4 Hz, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 150.2, 141.9, 136.9, 129.1, 128.8, 127.0, 124.3, 55.8, 51.3, 46.3, 45.0, 39.9. $[\alpha]_D^{25}$ -25.8 (c 0.5, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 362.1175, found 362.1158.



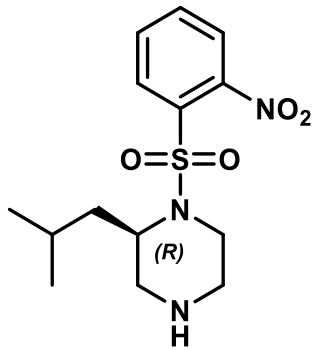
4m

(*S*)-2-methyl-1-((2-nitrophenyl)sulfonyl)piperazine (4m); Molecular Formula: $C_{11}H_{15}N_3O_4S$; Rf (3% methanol/DCM): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.08 – 8.05 (m, 1H), 7.72 – 7.63 (m, 3H), 4.07 (s, 1H), 3.51 (d, *J* = 13.2 Hz, 1H), 3.31 (dt, *J* = 12.7, 2.9 Hz, 1H), 3.04 – 2.93 (m, 2H), 2.84 – 2.69 (m, 2H), 1.31 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 147.8, 133.7, 133.6, 132.1, 132.0, 131.9, 130.9, 128.7, 128.6, 124.5, 49.8, 49.0, 45.2, 40.5, 29.7, 15.5. $[\alpha]_D^{25}$ +90.6 (c 0.75, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 286.0862, found 286.0851.



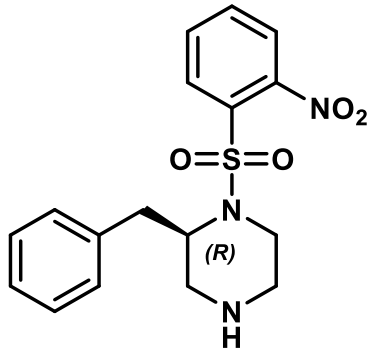
4n

(*S*)-2-isobutyl-1-((2-nitrophenyl)sulfonyl)piperazine (4n); Molecular Formula: $C_{14}H_{21}N_3O_4S$; Rf (3% methanol/DCM): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.07 (dd, *J* = 7.0, 2.2 Hz, 1H), 7.72 – 7.61 (m, 3H), 3.93-3.89 (m, 1H), 3.63 – 3.56 (m, 1H), 3.31 – 3.24 (m, 1H), 2.93 – 2.82 (m, 3H), 2.67 (dt, *J* = 12.4, 3.5 Hz, 1H), 1.79-1.75 (t, 1H), 1.54-1.49 (m, 1H), 1.47-1.43 (m, 1H), 0.87 (t, *J* = 6.2 Hz, 6H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 147.8, 134.3, 133.4, 131.7, 131.0, 124.3, 52.3, 47.9, 45.7, 41.9, 37.7, 24.9, 23.1, 22.1. $[\alpha]_D^{25}$ +79.7 (c 1.9, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 328.1331, found 328.1323.



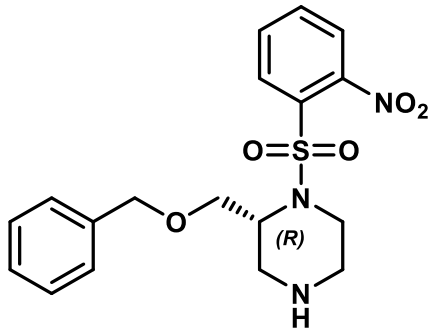
4o

(*S*)-2-isobutyl-1-((2-nitrophenyl)sulfonyl)piperazine (4o); Molecular Formula: $C_{14}H_{21}N_3O_4S$; Rf (3% methanol/DCM): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.07 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.74 – 7.65 (m, 3H), 4.02-3.96 (m, 1H), 3.69 (dd, *J* = 14.0, 3.5 Hz, 1H), 3.39 (td, *J* = 14.3, 13.4, 3.0 Hz, 1H), 3.07 (d, *J* = 12.5 Hz, 1H), 3.04 – 2.93 (m, 2H), 2.77-2.72 (m, 1H), 1.87 – 1.78 (m, 1H), 1.58 – 1.44 (m, 2H), 0.88 (t, *J* = 6.6 Hz, 6H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 147.7, 133.9, 133.7, 131.9, 131.0, 124.5, 51.4, 46.9, 44.8, 40.5, 37.8, 24.9, 22.9, 22.0. $[\alpha]_D^{25}$ -76.2 (c 2.6, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 328.1331, found 328.1319.



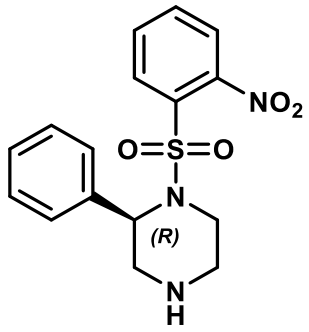
4p

(*R*)-2-benzyl-1-((2-nitrophenyl)sulfonyl)piperazine (4p); Molecular Formula: $C_{17}H_{19}N_3O_4S$; Rf (3% methanol/DCM): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.95 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.68 – 7.58 (m, 3H), 7.24 – 7.18 (m, 4H), 7.15 (t, *J* = 6.9 Hz, 1H), 4.10-4.05 (m, 1H), 3.70 – 3.63 (m, 1H), 3.44 (dt, *J* = 12.9, 3.1 Hz, 1H), 3.26 (dd, *J* = 13.2, 9.8 Hz, 1H), 3.02 (d, *J* = 12.0 Hz, 1H), 2.95 (dd, *J* = 13.2, 5.4 Hz, 1H), 2.84 (d, *J* = 12.3 Hz, 1H), 2.81-2.75 (m, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 147.6, 138.1, 134.0, 133.3, 131.8, 130.9, 129.4, 128.5, 126.6, 124.4, 55.9, 46.8, 46.1, 42.2, 35.2. $[\alpha]_D^{25}$ -84.6 (c 2.3, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 362.1175, found 362.1173.



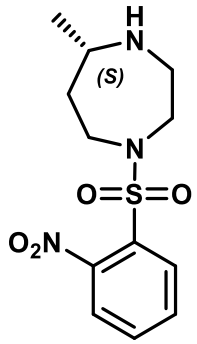
4q

(*R*)-2-((benzyloxy)methyl)-1-((2-nitrophenyl)sulfonyl)piperazine (4q); Molecular Formula: $C_{18}H_{21}N_3O_5S$; Rf (3% methanol/DCM): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.06 (td, *J* = 7.7, 1.1 Hz, 1H), 7.61 – 7.54 (m, 3H), 7.33 – 7.27 (m, 3H), 7.24 – 7.21 (m, 2H), 4.49 – 4.36 (dd, 2H), 4.03 (q, *J* = 5.8 Hz, 1H), 3.81 (dd, *J* = 9.6, 6.9 Hz, 1H), 3.71 (dd, *J* = 9.6, 6.1 Hz, 1H), 3.65 – 3.59 (m, 1H), 3.28 (dt, *J* = 13.0, 3.1 Hz, 1H), 3.14 (d, *J* = 12.6 Hz, 1H), 2.98 – 2.86 (m, 2H), 2.72 (dt, *J* = 12.3, 3.5 Hz, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 147.70, 137.85, 134.05, 133.27, 131.64, 131.25, 131.07, 129.34, 128.42, 127.73, 127.69, 124.81, 124.24, 73.32, 68.44, 52.61, 46.41, 45.74, 42.81. $[\alpha]_D^{25}$ +82 (c 0.5, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 392.1280, found 392.1278.



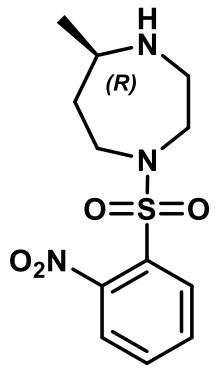
4r

(*R*)-1-((2-nitrophenyl)sulfonyl)-2-phenylpiperazine (4r); Molecular Formula: $C_{16}H_{17}N_3O_4S$; Rf (3% methanol/DCM): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.88 (d, *J* = 7.9 Hz, 1H), 7.65 (d, *J* = 4.3 Hz, 2H), 7.56 (dq, *J* = 8.5, 4.3 Hz, 1H), 7.36 (d, *J* = 7.2 Hz, 2H), 7.29-7.25 (m, 5H), 7.21 (t, *J* = 7.3 Hz, 1H), 5.05-5.03 (m, 1H), 3.75 – 3.66 (m, 1H), 3.51 (dd, *J* = 13.3, 2.8 Hz, 1H), 3.41 (ddd, *J* = 14.0, 11.2, 3.4 Hz, 1H), 3.22 (dd, *J* = 13.3, 4.1 Hz, 1H), 2.96-2.91 (m, 1H), 2.84 (ddd, *J* = 12.7, 11.2, 3.6 Hz, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 147.7, 137.5, 134.2, 133.3, 131.7, 130.8, 128.7, 127.5, 127.4, 124.2, 56.9, 49.5, 45.6, 43.4. $[\alpha]_D^{25}$ -89.2 (c 0.9, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 348.1018, found 348.1006.



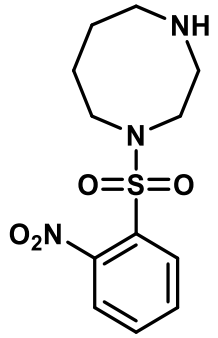
4s

(*S*)-5-methyl-1-((2-nitrophenyl)sulfonyl)-1,4-diazepane (4s); Molecular Formula: $C_{12}H_{17}N_3O_4S$; Rf (5% methanol:DCM): 0.5; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.04 – 7.98 (m, 1H), 7.71-7.66 (m, 2H), 7.64 – 7.60 (m, 1H), 3.64 (td, *J* = 13.8, 3.6 Hz, 1H), 3.56 – 3.41 (m, 2H), 3.31 (ddd, *J* = 13.8, 10.3, 3.5 Hz, 1H), 3.16 (td, *J* = 14.0, 3.7 Hz, 1H), 3.00 – 2.87 (m, 2H), 2.00-1.95 (m, 1H), 1.59-1.52 (m, 1H), 1.15 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 148.1, 133.4, 133.1, 131.6, 130.8, 124.1, 54.2, 51.4, 48.9, 46.6, 38.3, 29.7, 23.2. $[\alpha]_D^{25}$ +10.9 (c 2.0, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 300.1018, found 300.1005.



4t

(*R*)-5-methyl-1-((2-nitrophenyl)sulfonyl)-1,4-diazepane (4t); Molecular Formula: $C_{12}H_{17}N_3O_4S$; Rf (5% methanol:DCM): 0.5; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.02 – 7.99 (m, 1H), 7.72-7.66 (m, 2H), 7.64 – 7.61 (m, 1H), 3.65 (td, *J* = 13.9, 3.6 Hz, 1H), 3.55 – 3.43 (m, 2H), 3.33 (ddd, *J* = 13.8, 10.3, 3.4 Hz, 1H), 3.18 (td, *J* = 14.0, 3.7 Hz, 1H), 3.03 – 2.91 (m, 2H), 2.01-1.96 (m, 1H), 1.62-1.56 (m, 1H), 1.17 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 148.0, 133.4, 133.1, 131.6, 130.8, 124.1, 54.2, 51.1, 48.8, 46.5, 38.1, 29.7, 23.0. $[\alpha]_D^{25}$ -11.8 (c 2.3, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 300.1018, found 300.1009.



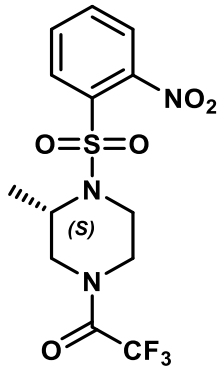
4u

1-((2-nitrophenyl)sulfonyl)-1,4-diazocane (4u); Molecular Formula: $C_{12}H_{17}N_3O_4S$; Rf (5% methanol:DCM): 0.5; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.94 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.74-7.68 (m, 3H), 7.64 (dd, *J* = 7.4, 1.9 Hz, 1H), 3.59 – 3.49 (m, 4H), 3.22-3.17 (m, 4H), 2.00 – 1.85 (m, 4H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 148.3, 133.7, 132.0, 131.7, 130.7, 124.3, 49.8, 48.8, 48.4, 47.4, 25.8, 24.8. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 300.1018, found 300.1007.

General Experimental Procedure for Annulation: Into a round bottom flask equipped with magnetic stir bar and septum under nitrogen, the bisprotected chiral diamine (**1 equiv.**) was dissolved in dichloromethane and 2-bromoethyl-diphenylsulfonium triflate (**1.25 equiv.**) was added followed by diisopropylethylamine (**3 equiv.**). The reaction was allowed to stir at room temperature under nitrogen for 5h, after which time the TLC and LCMS showed no starting material remaining. The reaction was worked up by diluting with dichloromethane and washed with water and brine. The organic phase was collected and dried over

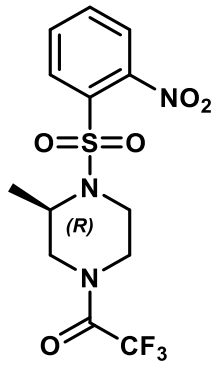
anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give the crude residue. Purification by silica gel chromatography (ethyl acetate/ hexanes) provided the pure piperazine product.

Note: Multiple signals of ^{1}H- and ^{13}C-NMR are due to rotamers



6a

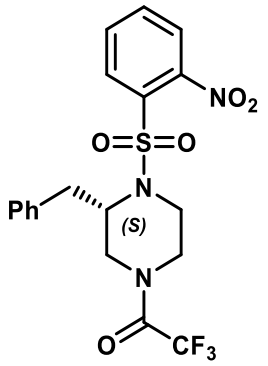
(*S*)-2,2,2-trifluoro-1-(3-methyl-4-((2-nitrophenyl)sulfonyl)piperazin-1-yl)ethan-1-one (6a); Molecular Formula: $C_{13}H_{14}F_3N_3O_5S$; Rf (40% ethyl acetate/hexanes): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.11 (td, *J* = 7.5, 1.9 Hz, 1H), 7.78 – 7.69 (m, 3H), 4.54-4.50 (m, 1H), 4.37-4.33 (m, 1H), 4.29 – 4.20 (m, 1H), 4.0-3.95 (m, 1H), 3.78 (dd, *J* = 13.8, 1.8 Hz, 1H), 3.70-3.66 (m, 1H), 3.70 – 3.63 (m, 1H), 3.49 (dd, *J* = 13.8, 3.6 Hz, 1H), 3.40 – 3.27 (m, 2H), 3.07 (dd, *J* = 13.4, 3.7 Hz, 1H), 2.89 (dt, *J* = 13.0, 3.9 Hz, 1H), 1.25 (d, *J* = 6.8 Hz, 2H), 1.19 (d, *J* = 6.9 Hz, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 156.56, 156.45, 156.32, 156.21, 147.72, 134.11, 134.09, 133.09, 133.04, 132.15, 131.12, 131.08, 124.66, 124.65, 117.19, 115.31, 50.08, 50.05, 49.58, 49.00, 47.86, 45.85, 45.82, 42.91, 40.50, 39.74, 29.71, 14.90, 14.86, 14.12. $[\alpha]_D^{25}$ +47.6 (c 0.75, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 382.0685, found 382.0672.



6b

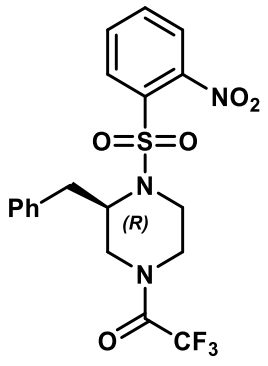
(*R*)-2,2,2-trifluoro-1-(3-methyl-4-((2-nitrophenyl)sulfonyl)piperazin-1-yl)ethan-1-one (6b); Molecular Formula: $C_{13}H_{14}F_3N_3O_5S$; Rf (40% ethyl acetate/hexanes): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.10 (td, *J* = 7.5, 1.8 Hz, 1H), 7.78 – 7.67 (m, 3H), 4.53-4.49 (m, 1H), 4.37-4.33 (m, 1H), 4.29 – 4.20 (m, 1H), 4.00 – 3.93 (m, 1H), 3.81 – 3.70 (m, 1H), 3.7-3.66 (m, 1H), 3.48 (dd, *J* = 13.8, 3.6 Hz, 1H), 3.41 – 3.26 (m, 2H), 3.06 (dd, *J* = 13.4, 3.7 Hz, 1H), 2.89 (dt, *J* = 13.0, 3.9 Hz, 1H), 1.25 (d, *J* = 6.8 Hz, 2H), 1.18 (d, *J* = 6.9 Hz, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 156.55, 156.45, 156.31, 156.21, 147.71, 134.12, 134.10,

133.07, 133.02, 132.16, 131.10, 131.06, 124.66, 124.65, 117.22, 117.19, 115.31, 115.28, 50.07, 50.05, 50.03, 49.57, 48.99, 47.85, 45.84, 45.82, 45.80, 42.91, 40.49, 39.73, 29.70, 14.89, 14.85. $[\alpha]_D^{25}$ -56.2 (c 1.0, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 382.0685, found 382.0673.



6c

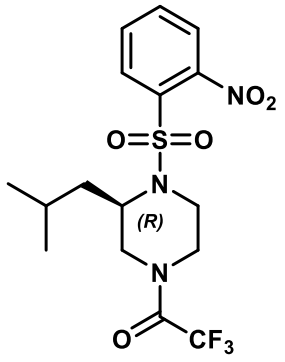
(*R*)-1-(3-benzyl-4-((2-nitrophenyl)sulfonyl)piperazin-1-yl)-2,2,2-trifluoroethan-1-one (6c); Molecular Formula: $C_{19}H_{18}F_3N_3O_5S$; Rf (40% ethyl acetate/hexanes): 0.5; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.96 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.72 – 7.57 (m, 4H), 7.22 – 7.18 (m, 2H), 7.18 – 7.13 (m, 3H), 7.09-7.04 (m, 2H), 4.60 – 4.54 (m, 1H), 4.51-4.46 (m, 1H), 4.38-4.34 (m, 1H), 4.23-4.19 (m, 1H), 4.12 – 3.98 (m, 2H), 3.97 – 3.87 (m, 2H), 3.59 (dd, *J* = 13.7, 3.8 Hz, 1H), 3.54 – 3.42 (m, 2H), 3.35 (dt, *J* = 13.1, 3.3 Hz, 1H), 3.04 – 2.94 (m, 2H), 2.88-2.79 (m, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 147.47, 136.42, 133.92, 133.60, 133.22, 132.21, 131.17, 130.84, 129.41, 128.97, 128.65, 128.48, 127.08, 124.78, 124.71, 56.22, 55.39, 45.98, 44.93, 43.42, 41.37, 40.50, 35.75, 35.47, 29.71, 14.13. $[\alpha]_D^{25}$ -58.0 (c 1.0, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 458.0998, found 458.0994.



6d

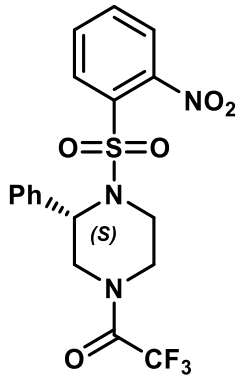
(*R*)-1-(3-benzyl-4-((2-nitrophenyl)sulfonyl)piperazin-1-yl)-2,2,2-trifluoroethan-1-one (6d); Molecular Formula: $C_{19}H_{18}F_3N_3O_5S$; Rf (40% ethyl acetate/hexanes): 0.5; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.96 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.73 – 7.58 (m, 4H), 7.23 – 7.18 (m, 2H), 7.18 – 7.12 (m, 3H), 7.09-7.04 (m, 2H), 4.60 – 4.55 (m, 1H), 4.51-4.47 (m, 1H), 4.38-4.33 (m, 1H), 4.23-4.19 (m, 1H), 4.09 – 3.97 (m, 2H), 3.98 – 3.87 (m, 2H), 3.59 (dd, *J* = 13.7, 3.8 Hz, 1H), 3.54-3.44 (m, 2H), 3.38-3.32 (m, 1H), 3.06 – 2.94 (m, 2H), 2.88-

2.79 (m, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 156.65, 147.46, 136.42, 133.92, 133.61, 133.21, 132.22, 132.17, 131.17, 130.83, 129.41, 128.97, 128.65, 128.48, 127.08, 124.78, 124.70, 56.22, 55.39, 48.65, 46.00, 45.97, 44.93, 43.42, 41.37, 40.50, 35.75, 35.46, 29.71, 14.13. $[\alpha]_D^{25}$ +60.0 (c 1.3, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 458.0998, found 458.0991



6e

(*R*)-2,2,2-trifluoro-1-(3-isobutyl-4-((2-nitrophenyl)sulfonyl)piperazin-1-yl)ethan-1-one (6e); Molecular Formula: $C_{16}H_{20}F_3N_3O_5S$; Rf (40% ethyl acetate/hexanes): 0.45; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.12-8.09 (m, 1H), 7.78 – 7.68 (m, 3H), 4.49-4.43 (m, 1H), 4.13 – 4.02 (m, 1H), 3.96-3.92 (m, 1H), 3.85 – 3.78 (m, 2H), 3.46 (dd, *J* = 13.8, 3.7 Hz, 1H), 3.40 – 3.20 (m, 2H), 3.01 (dd, *J* = 13.5, 3.7 Hz, 1H), 2.81 (dt, *J* = 13.1, 3.9 Hz, 1H), 1.58-1.53 (m, 1H), 1.50-1.41 (m, 2H), 1.30 – 1.21 (m, 1H), 0.87 (dd, *J* = 14.1, 6.3 Hz, 3H), 0.81 (dd, *J* = 6.4, 2.4 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 156.67, 156.43, 156.34, 156.10, 147.69, 134.11, 134.09, 133.45, 133.43, 133.39, 132.12, 132.10, 131.17, 131.15, 130.97, 124.71, 124.70, 117.22, 117.18, 115.31, 115.27, 52.30, 51.47, 48.20, 48.18, 45.90, 45.87, 45.85, 45.83, 45.68, 42.78, 40.93, 40.19, 37.92, 37.47, 24.72, 24.49, 22.86, 22.40, 22.38, 22.00. $[\alpha]_D^{25}$ -71.6 (c 3.7, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 424.1154, found 424.1149.

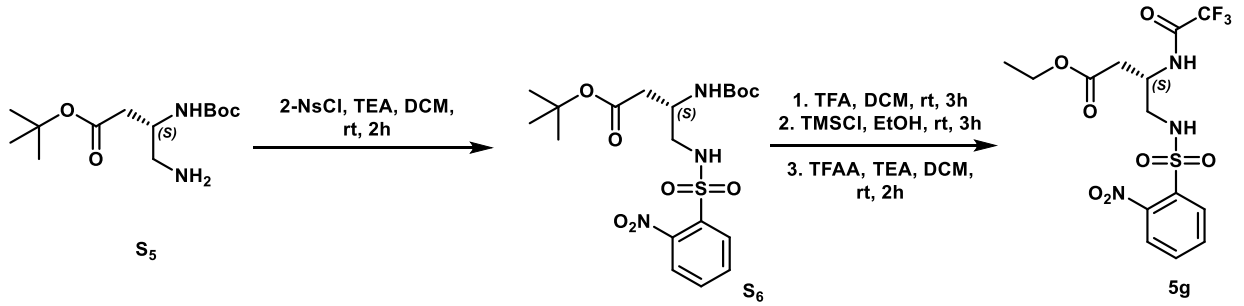


6f

(*S*)-2,2,2-trifluoro-1-(4-((2-nitrophenyl)sulfonyl)-3-phenylpiperazin-1-yl)ethan-1-one (6f); Molecular Formula: $C_{18}H_{16}F_3N_3O_5S$; Rf (40% ethyl acetate/hexanes): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.94-7.91 (m, H), 7.73-7.70 (m, 2H), 7.67 – 7.56 (m, 2H), 7.27-7.24 (m, 5H), 7.22 – 7.14 (m, 2H), 5.30 (t, *J* = 3.8 Hz, 1H), 5.13 (t, *J* = 5.2 Hz, 1H), 4.87-4.82 (m, 1H), 4.06-4.01 (m, 1H), 4.00 – 3.92 (m, 2H), 3.91 – 3.80 (m, 2H), 3.60 – 3.49 (m, 2H), 3.49 – 3.39 (m, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 156.40, 156.18, 155.94,

147.59, 135.78, 134.93, 133.99, 133.71, 133.67, 133.46, 132.16, 131.73, 130.99, 130.91, 128.95, 128.73, 128.52, 128.28, 127.18, 126.84, 124.57, 124.30, 117.05, 115.15, 58.13, 57.12, 48.65, 45.69, 45.66, 45.07, 43.78, 42.11, 41.92. $[\alpha]_D^{25}$ +74.7 (c 2.6, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 444.0841, found 444.0832.

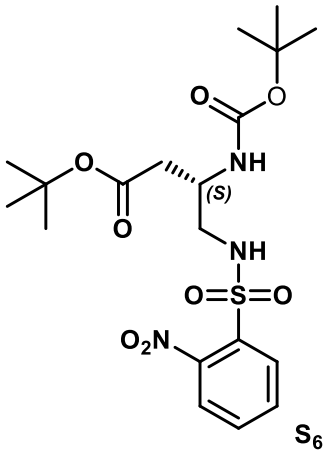
Procedure for the Synthesis of 5g:



S_6 was prepared according to above discussed general procedure (sulfonylation).

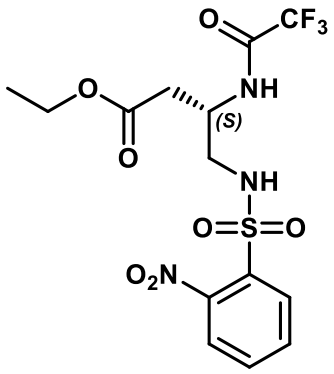
Into a round bottom flask equipped with magnetic stir bar and septum, the compound S_6 (**1 equiv.**) was dissolved in dichloromethane and TFA (10% TFA in DCM, V/V, 10 mL/mmol) was added and allowed to stir at room temperature under nitrogen. After 3h the starting material was consumed according to LCMS. The volatiles were evaporated under reduced pressure and then redissolved in toluene and evaporated to remove excess TFA. The mixture was dissolved in EtOH and TMSCl (**3 equiv.**) was added at room temperature and the reaction was allowed to stir at room temperature under nitrogen. After 3h, LCMS and TLC showed complete consumption of the starting material. The solvent was removed under reduced pressure to give the crude residue. The crude mixture was diluted with ethyl acetate and washed with saturated aq $NaHCO_3$ solution. The organic phase was collected and dried over anhydrous Na_2SO_4. and the solvent was removed under reduced pressure to give the crude product which was carried forward to the next step without purification.

Next, into a round bottom flask equipped with magnetic stir bar and septum, the crude amine (**1 equiv.**) was dissolved in dichloromethane and cooled to 0 °C, TEA (**3 equiv.**) and TFAA (**2 equiv.**) was added. The reaction was immediately allowed to come to room temperature and stirred for 2h under nitrogen, after which time LCMS indicated complete consumption of the starting material. The reaction was diluted with dichloromethane and washed with saturated aq. $NaHCO_3$ and brine solution. The organic phase was collected and dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give the crude residue. Purification by silica gel chromatography (ethyl acetate/ hexanes) provided the pure product **5g** (78% yield over three steps).



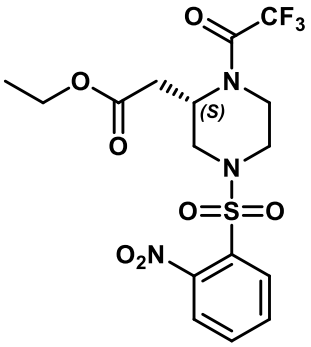
S_6

Tert-butyl (*S*)-3-((tert-butoxycarbonyl)amino)-4-((2-nitrophenyl)sulfonamido)butanoate (S_6); Molecular Formula: $C_{19}H_{29}N_3O_8S$; Rf (50% ethyl acetate/hexanes): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.12 – 8.09 (m, 1H), 7.88 – 7.84 (m, 1H), 7.76 – 7.70 (m, 2H), 5.88 – 5.75 (m, 1H), 5.16 (d, *J* = 7.9 Hz, 1H), 3.98-3.92 (m, 1H), 3.34-3.28 (m, 1H), 3.23-3.19 (m, 1H), 2.55-2.48 (m, 2H), 1.44 (s, 9H), 1.39 (s, 9H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 170.4, 155.4, 148.1, 133.7, 133.6, 132.9, 131.0, 125.5, 81.7, 80.0, 47.4, 46.5, 37.4, 28.3, 28.0. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 460.1754, found 460.1740.



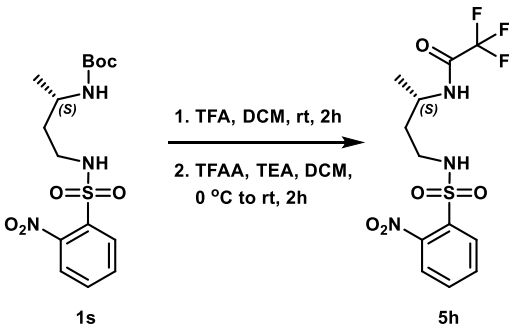
5g

Ethyl (*S*)-4-((2-nitrophenyl)sulfonamido)-3-(2,2,2-trifluoroacetamido)butanoate (5g); Molecular Formula: $C_{14}H_{16}F_3N_3O_7S$; Rf (50% ethyl acetate/hexanes): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.14 – 8.09 (m, 1H), 7.92 – 7.86 (m, 1H), 7.81 – 7.75 (m, 2H), 7.59 (d, *J* = 8.3 Hz, 1H), 5.92 (t, *J* = 6.7 Hz, 1H), 4.40-4.35 (m, 1H), 4.21-4.17 (m, 2H), 3.39 (t, *J* = 6.3 Hz, 2H), 2.82 (dd, *J* = 16.9, 5.0 Hz, 1H), 2.72 (dd, *J* = 16.8, 6.3 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.1, 157.3, 157.1, 148.0, 134.0, 133.1, 131.0, 125.6, 116.5, 114.6, 61.5, 46.8, 45.0, 34.6, 14.0. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 428.0739, found 428.0728.



6g

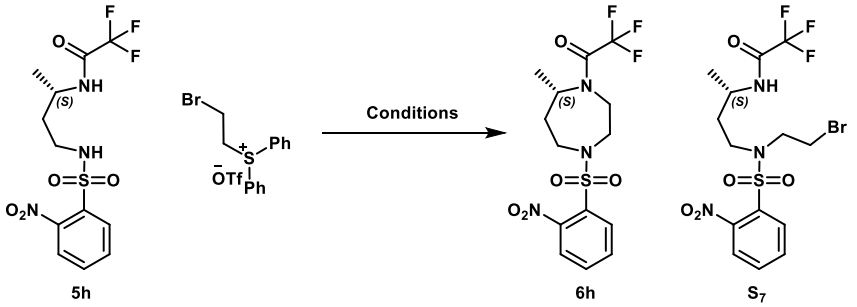
Ethyl (*S*)-2-(1-((2-nitrophenyl)sulfonyl)-4-(2,2,2-trifluoroacetyl)piperazin-2-yl)acetate (6g); Molecular Formula: $C_{16}H_{18}F_3N_3O_7S$; Rf (50% ethyl acetate/hexanes): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.99-7.96 (m, 1H), 7.78 – 7.70 (m, 2H), 7.69-7.66 (m, 1H), 5.12 – 5.01 (m, 1H), 4.59 – 4.46 (m, 1H), 4.20 – 4.05 (m, 2H), 3.99-3.88 (m, 3H), 3.59-3.53 (m, 1H), 3.23 – 3.02 (m, 2H), 2.98 – 2.89 (m, 1H), 2.82 (dd, *J* = 15.9, 8.4 Hz, 1H), 2.70 – 2.44 (m, 1H), 1.27-1.21 (m, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.7, 148.2, 134.3, 131.9, 131.9, 131.2, 131.1, 124.5, 61.3, 61.2, 48.3, 48.0, 46.9, 45.6, 45.3, 41.3, 38.5, 34.0, 33.0, 14.0. $[\alpha]_D^{25}$ +14.7 (c 1.0, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 454.0896, found 454.0892.



1s 5h

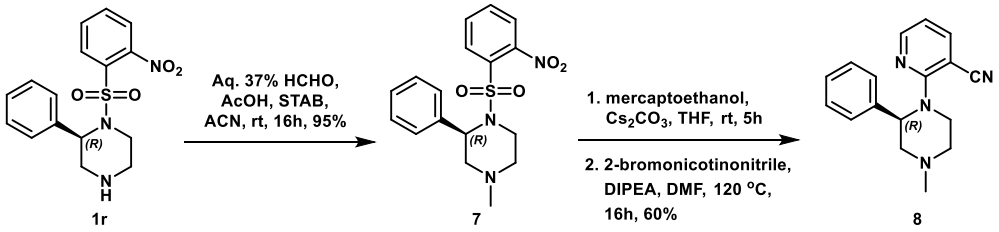
(*S*)-2,2,2-trifluoro-N-(4-((2-nitrophenyl)sulfonamido)butan-2-yl)acetamide (5h); Into a round bottom flask equipped with magnetic stir bar and septum, Compound **1s** (**1 equiv.**) was dissolved in dichloromethane and TFA (10% TFA in DCM, V/V, 10 mL/mmol) was added and allowed to stir at room temperature under nitrogen. After 2h the starting material was consumed according to TLC and LCMS. The volatiles were evaporated under reduced pressure and then redissolved in toluene and evaporated to remove excess TFA. The mixture was dissolved in dichloromethane and cooled to 0 °C, TEA (**4 equiv.**) and TFAA (**2 equiv.**) was added. The reaction was immediately allowed to come to room temperature and stirred for 2h under nitrogen, after which time LCMS indicated complete consumption of the starting material. The reaction was diluted with dichloromethane and washed with saturated aq. $NaHCO_3$ and brine solution. The organic phase was collected and dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give the crude residue. Purification by silica gel chromatography (ethyl acetate/ hexanes) provided the pure product **5h** (80% yield over two steps). Molecular Formula: $C_{12}H_{14}F_3N_3O_5S$; Rf (50% ethyl acetate/hexanes): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.13 – 8.06 (m, 1H), 7.89 – 7.81 (m, 1H), 7.77 – 7.72 (m, 2H), 6.68 (d, *J* = 8.5 Hz, 1H), 5.89 – 5.79 (m, 1H), 4.12-4.09 (m, 1H), 3.23-3.17 (m, 1H), 3.07 – 3.02 (m, 1H), 1.89 – 1.80 (m, 1H), 1.78-1.72 (m, 1H), 1.24 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 157.5, 157.34, 157.1, 156.8, 147.9, 133.8, 133.4, 132.9, 130.7, 125.4, 118.6, 116.7, 114.8, 112.8, 44.2, 40.5, 36.5, 20.2. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 370.0685, found 370.0702.

5h was subjected to annulation described above.



S. No	Conditions	Isolated
1	DIPEA, DCM, rt, 5h	S_7
2	DIPEA, DCM, 80 °C, 48h	S_7

(*S*)-N-(4-((N-(2-bromoethyl)-2-nitrophenyl)sulfonamido)butan-2-yl)-2,2,2-trifluoroacetamide (S_7); Molecular Formula: $C_{14}H_{17}BrF_3N_3O_5S$; Rf (50% ethyl acetate/hexanes): 0.4; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.01 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.78 – 7.69 (m, 2H), 7.66 (dd, *J* = 7.5, 1.6 Hz, 1H), 6.42 (d, *J* = 8.2 Hz, 1H), 4.05-3.98 (m, 1H), 3.76 – 3.61 (m, 2H), 3.50 – 3.45 (m, 2H), 3.45-3.40 (m, 1H), 3.38-3.33 (m, 1H), 1.98 – 1.86 (m, 2H), 1.31 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 156.7, 148.1, 134.1, 132.3, 131.9, 130.8, 124.4, 116.6, 49.8, 45.8, 44.67, 35.2, 28.7, 20.2. HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 476.0103, 478.0082 found 476.0125 and 478.0103.

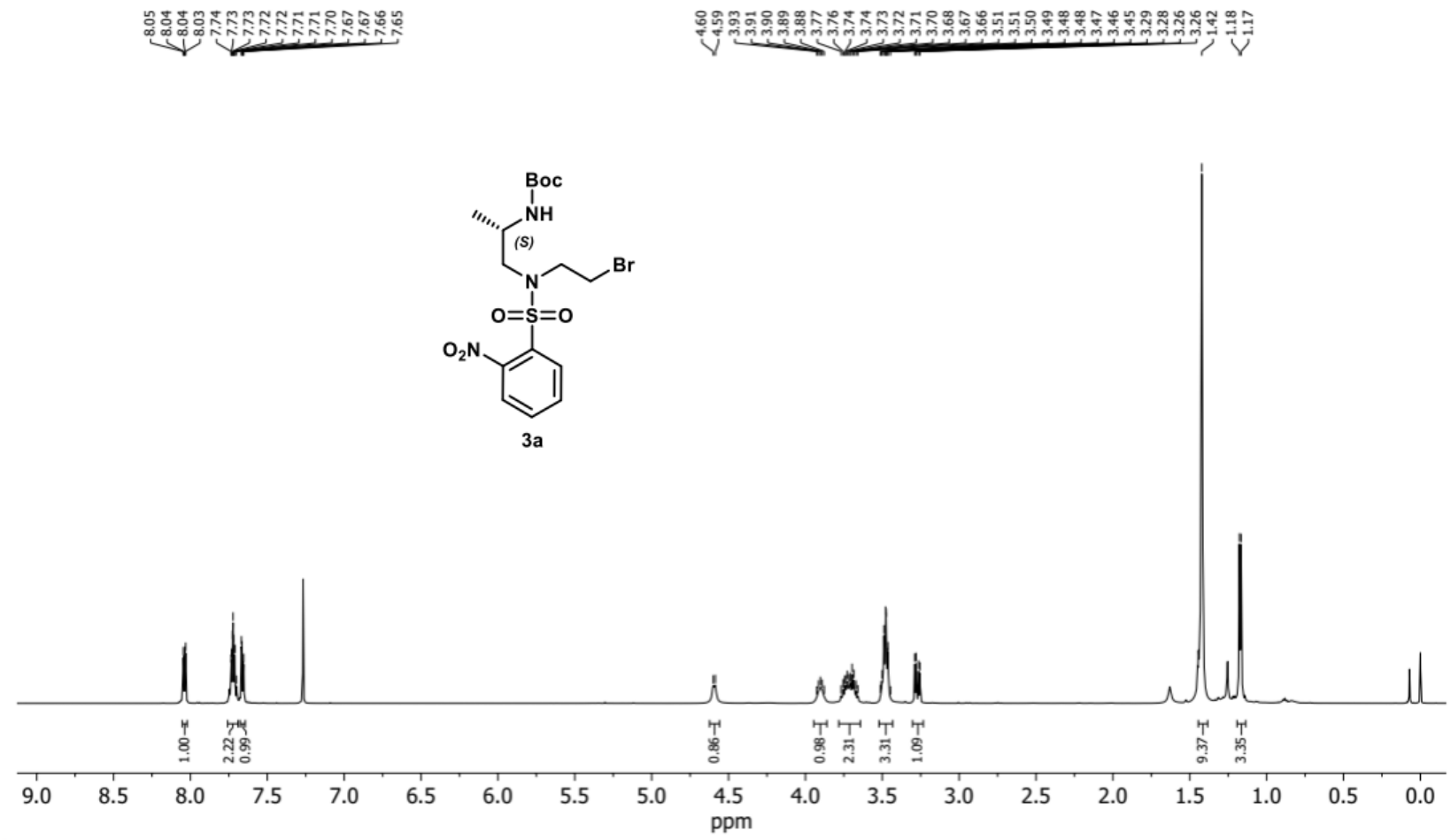


Synthesis of compound **7** and denosylation of 7 was achieved by following the literature protocol (ref no. 26 in manuscript).

(*R*)-4-methyl-1-((2-nitrophenyl)sulfonyl)-2-phenylpiperazine (7); Molecular Formula: $C_{17}H_{19}N_3O_4S$; Rf (60% ethyl acetate/hexanes): 0.3; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.85 – 7.80 (m, 1H), 7.68 – 7.60 (m, 2H), 7.55-7.53 (m, 1H), 7.43 – 7.41 (m, 2H), 7.24 – 7.18 (m, 3H), 5.08 (t, *J* = 3.6 Hz, 1H), 3.75- 3.72 (m, 1H), 3.48-3.44 (m, 1H), 3.18-3.16 (m, 1H), 2.70-2.67 (m, 1H), 2.51 (dd, *J* = 12.0, 4.1 Hz, 1H), 2.24 (s, 3H), 2.15 (td, *J* = 11.3, 3.3 Hz, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 147.7, 138.1, 134.3, 133.3, 131.7, 130.6, 128.3, 127.9, 127.5, 124.2, 58.1, 56.9, 54.7, 46.2, 42.9. $[\alpha]_D^{25}$ -67.7 (c 1.0, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 362.1175 found 362.1162.

(*R*)-2-(4-methyl-2-phenylpiperazin-1-yl)nicotinonitrile (8); Into a round bottom flask equipped with magnetic stir bar and septum under nitrogen, (*R*)-1-methyl-3-phenylpiperazine hydrochloride (**1 equiv.**) was dissolved in DMF, added diisopropylethylamine (**5 equiv.**) and 2-bromonicotinonitrile (**2 equiv.**) The reaction was allowed to stir at 120 °C under nitrogen for 16h, after which time the LCMS showed no

starting material remaining. The reaction was worked up by diluting with ethylacetate and washed with water and brine. The organic phase was collected and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give the crude residue. Purification by silica gel chromatography (ethyl acetate/ hexanes) provided the pure product (60% from 7). Molecular Formula: $C_{17}H_{18}N_4$; Rf (80% ethyl acetate/hexanes): 0.2; **^{1}H NMR (600 MHz, $CDCl_3$) ; ^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.29 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.77 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.29 – 7.22 (m, 2H), 7.20 – 7.13 (m, 1H), 6.77 (dd, *J* = 7.7, 4.8 Hz, 1H), 5.46 (t, *J* = 4.7 Hz, 1H), 3.88 – 3.77 (m, 1H), 3.62-3.58 (m, 1H), 2.96 (dd, *J* = 11.9, 5.6 Hz, 1H), 2.78-2.75 (m, 1H), 2.73 (dd, *J* = 11.8, 3.8 Hz, 1H), 2.56-2.52 (m, 1H), 2.34 (s, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 161.7, 151.9, 143.5, 140.6, 128.3, 127.3, 126.8, 117.7, 115.2, 60.0, 58.0, 55.2, 46.2. $[\alpha]_D^{25}$ +63.8 (c 1.0, MeOH). HRMS (HESI-TOF) m/z calcd for $(M + H)^+$ 279.1610 found 279.1602.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1.17
Boc
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(S)
N
Br
O=S=O
O2N
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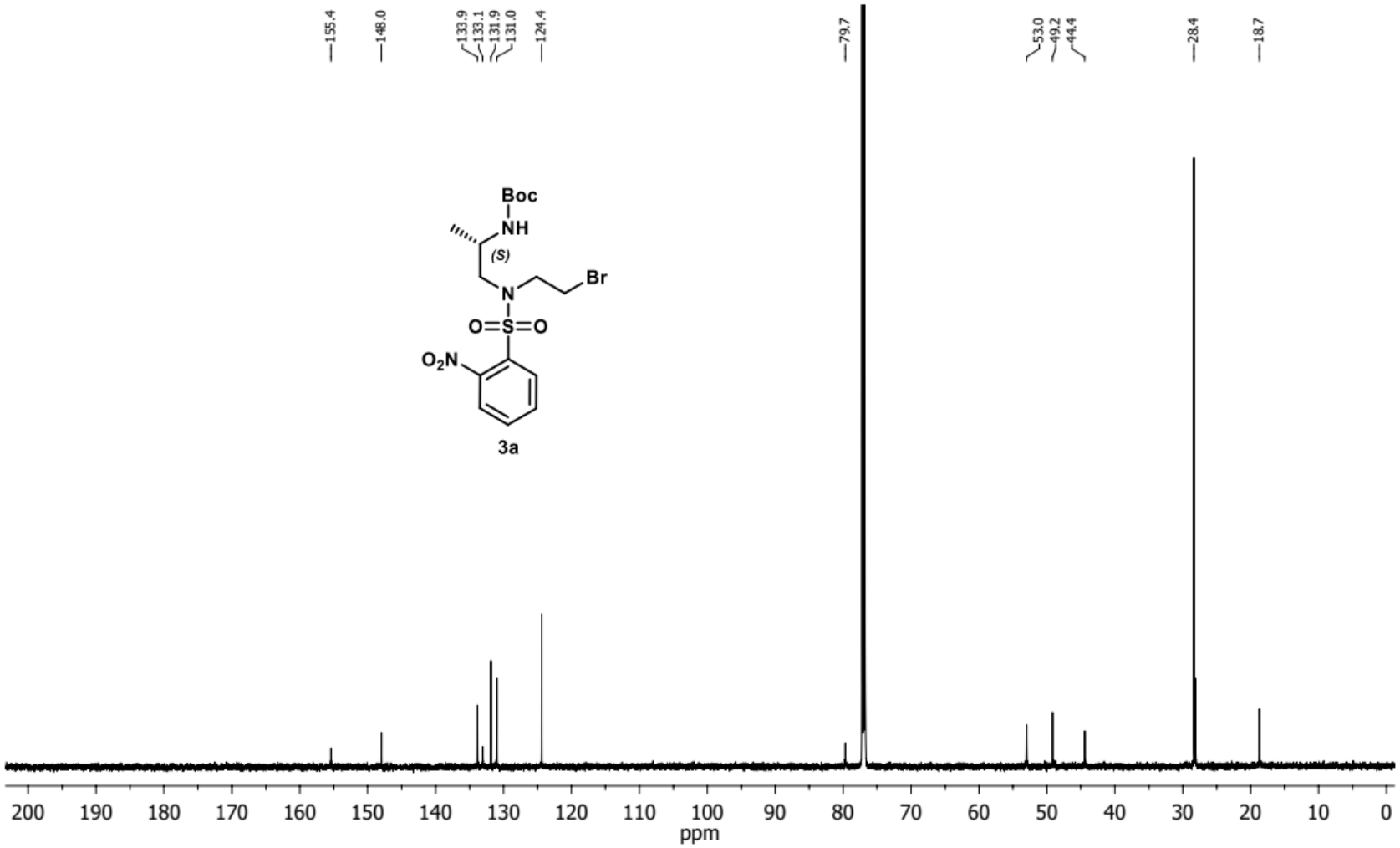
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49.2
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28.4
18.7
Boc
NH
(S)
N
Br
O=S=O
O2N
3a
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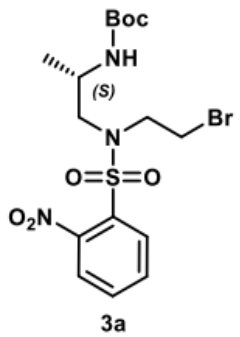
COSY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Br
O=S=O
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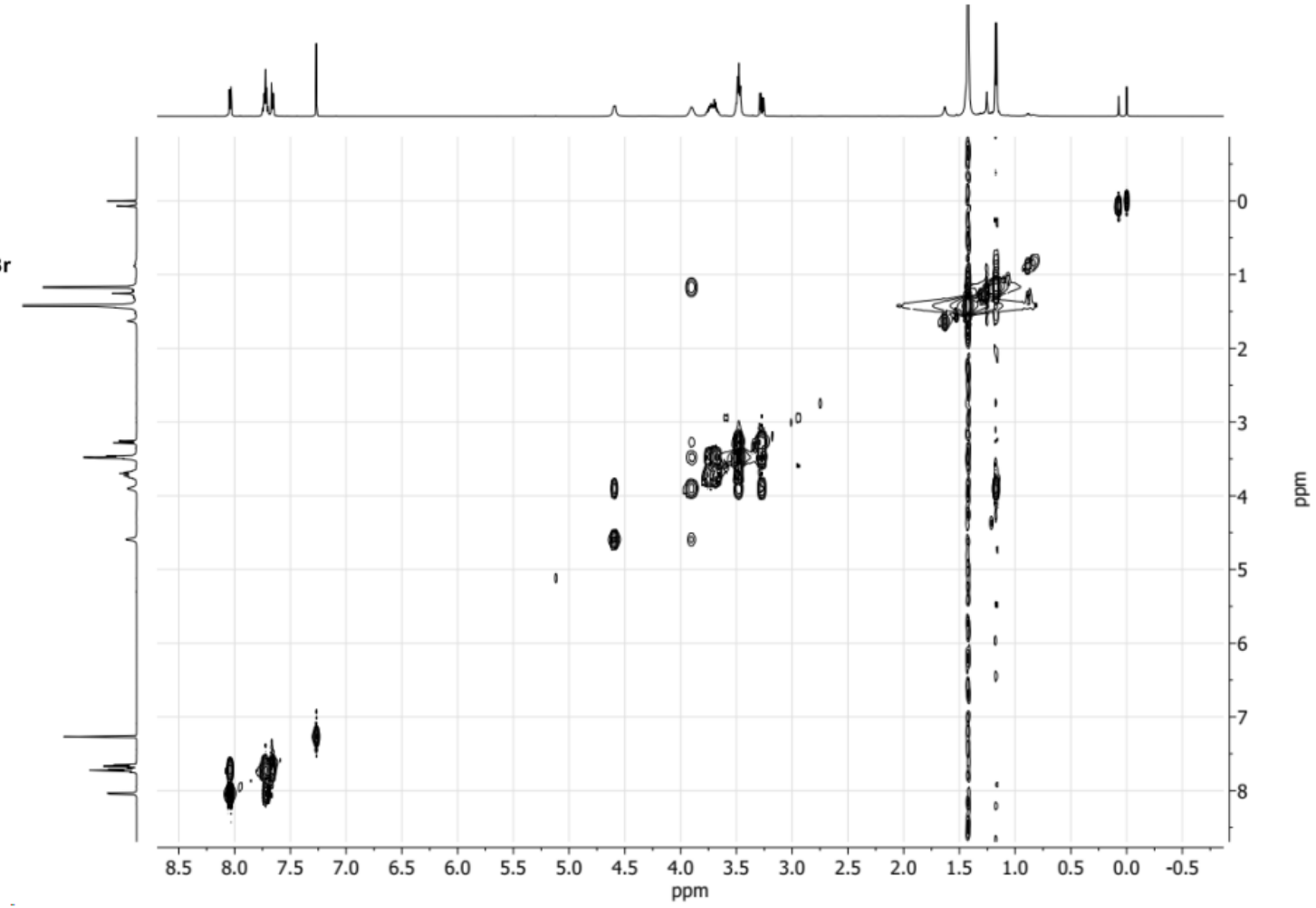
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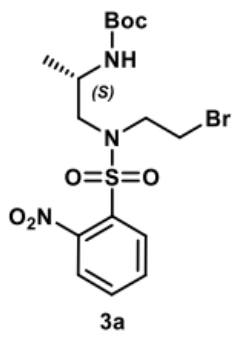
ppm

^{1}H, ^{13}C-HMBC



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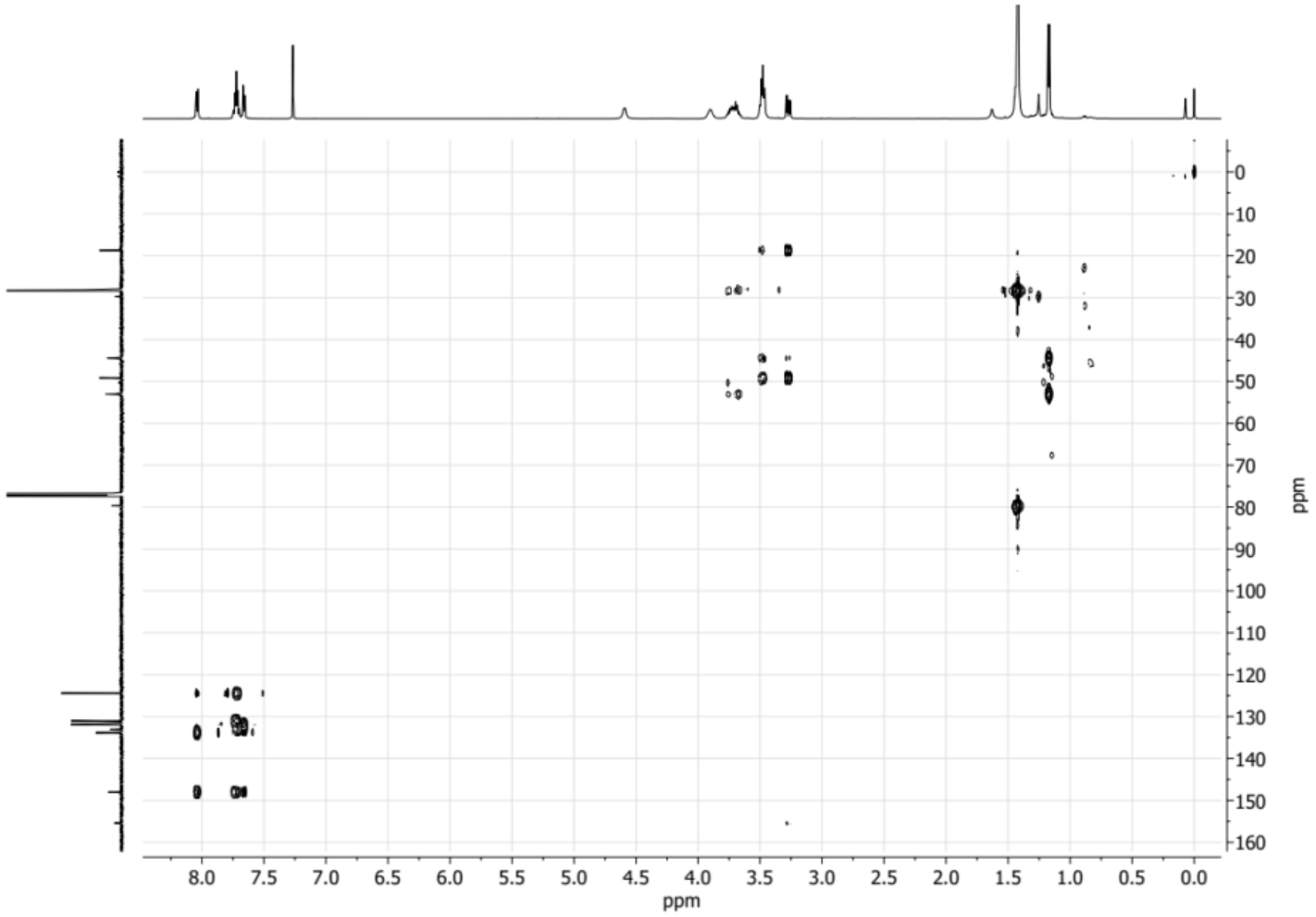
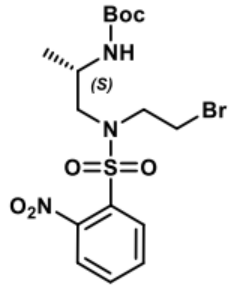


DEPTQ-135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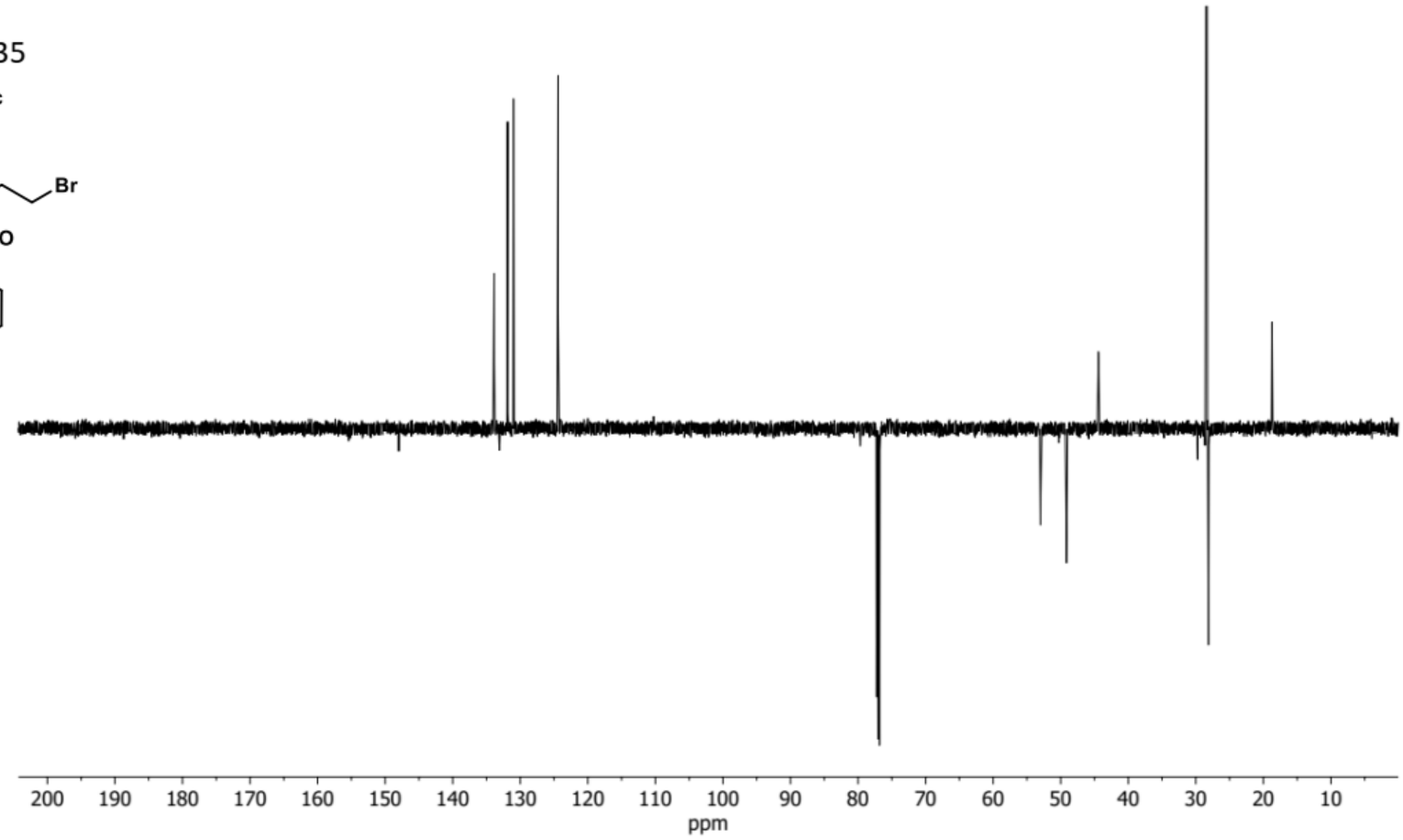
Br
N
O=S=O
O2N

3a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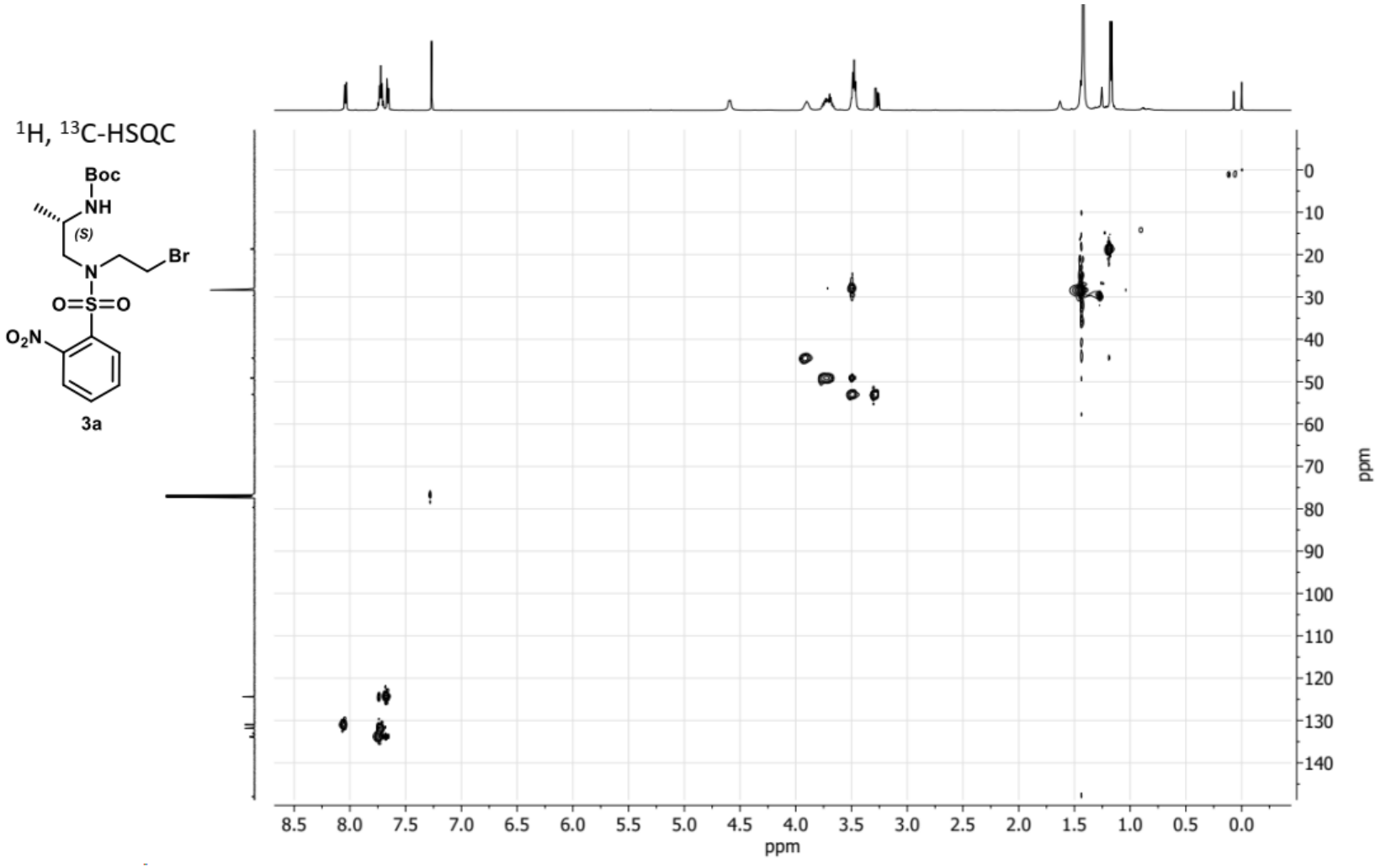
ppm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(S)
Br
N
O=S=O
O_2N
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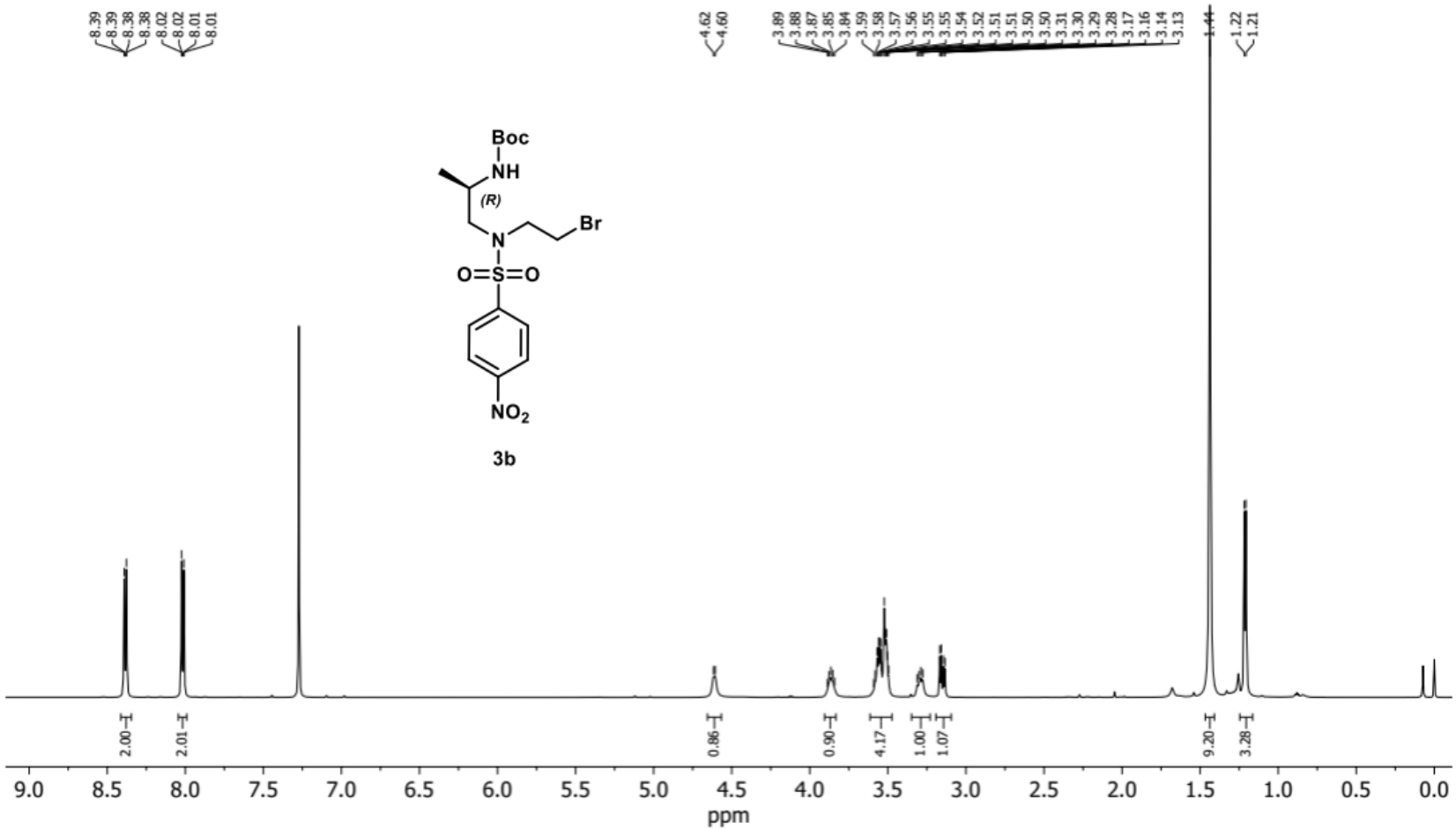
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Br
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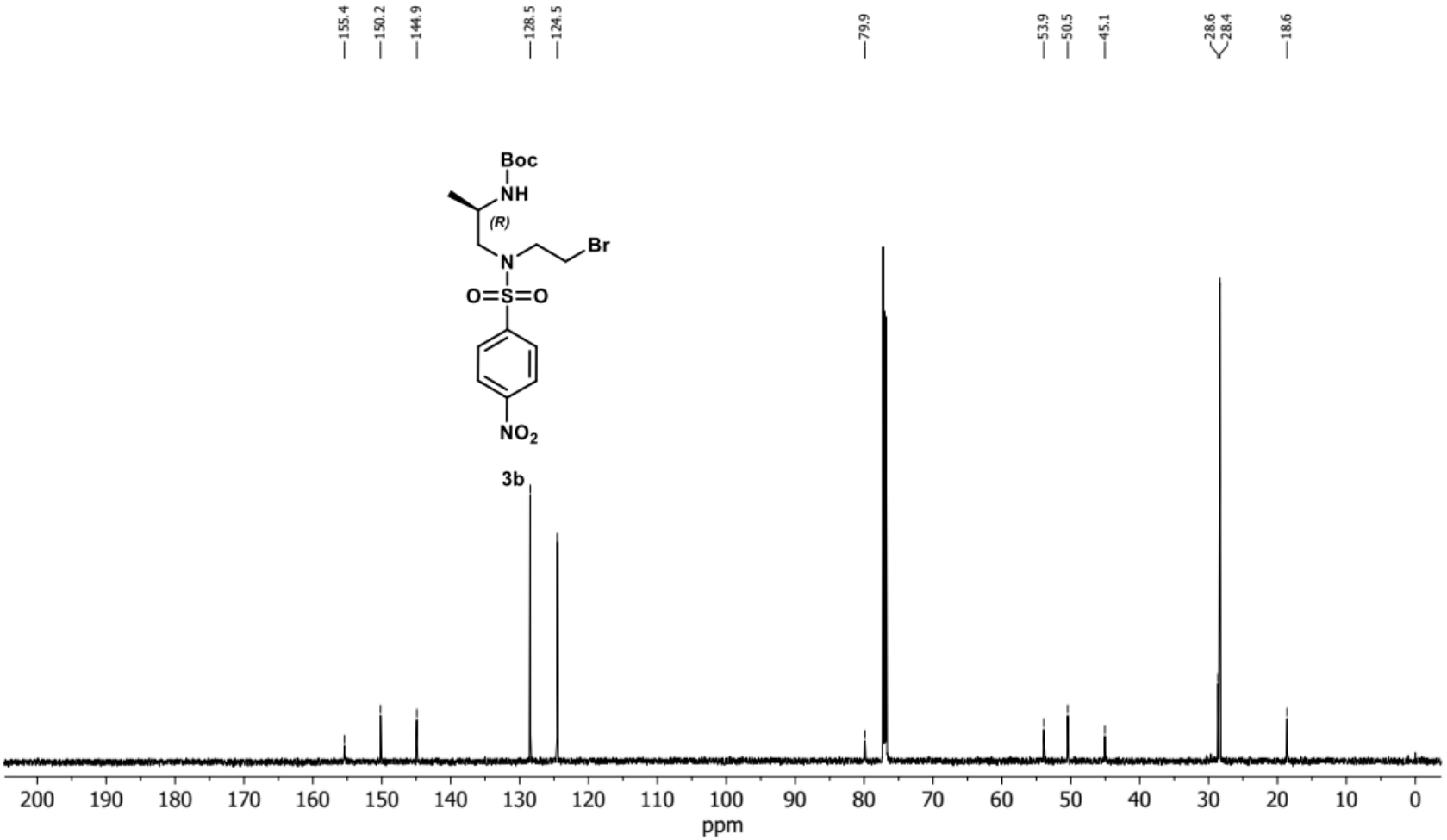
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(R)
Br
N
O=S=O
NO2
3b
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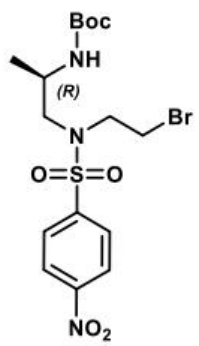
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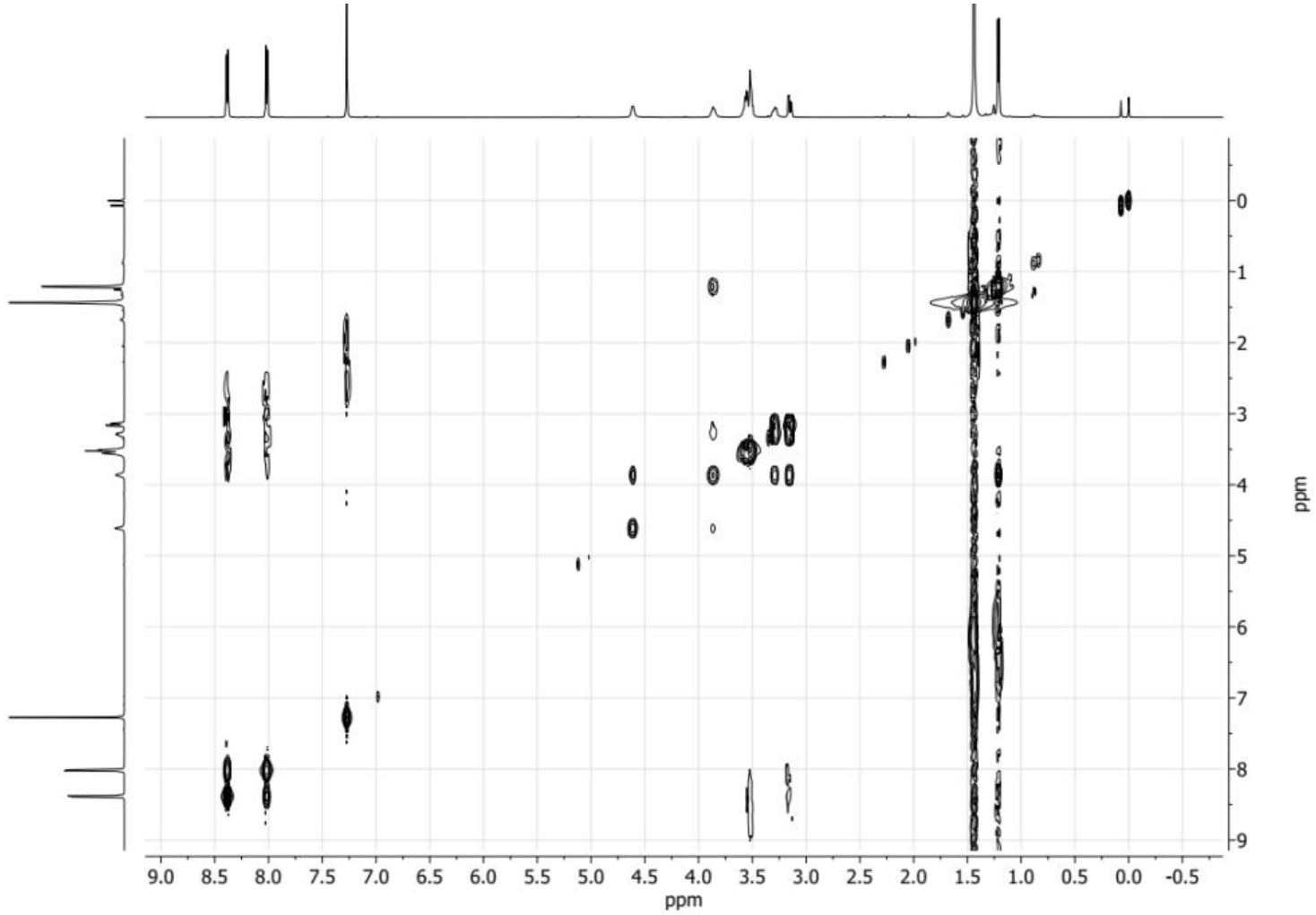
3b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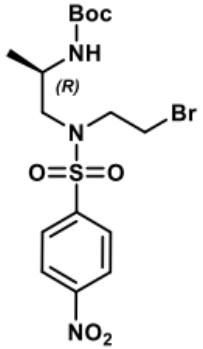
ppm

^{1}H, ^{13}C-HMBC



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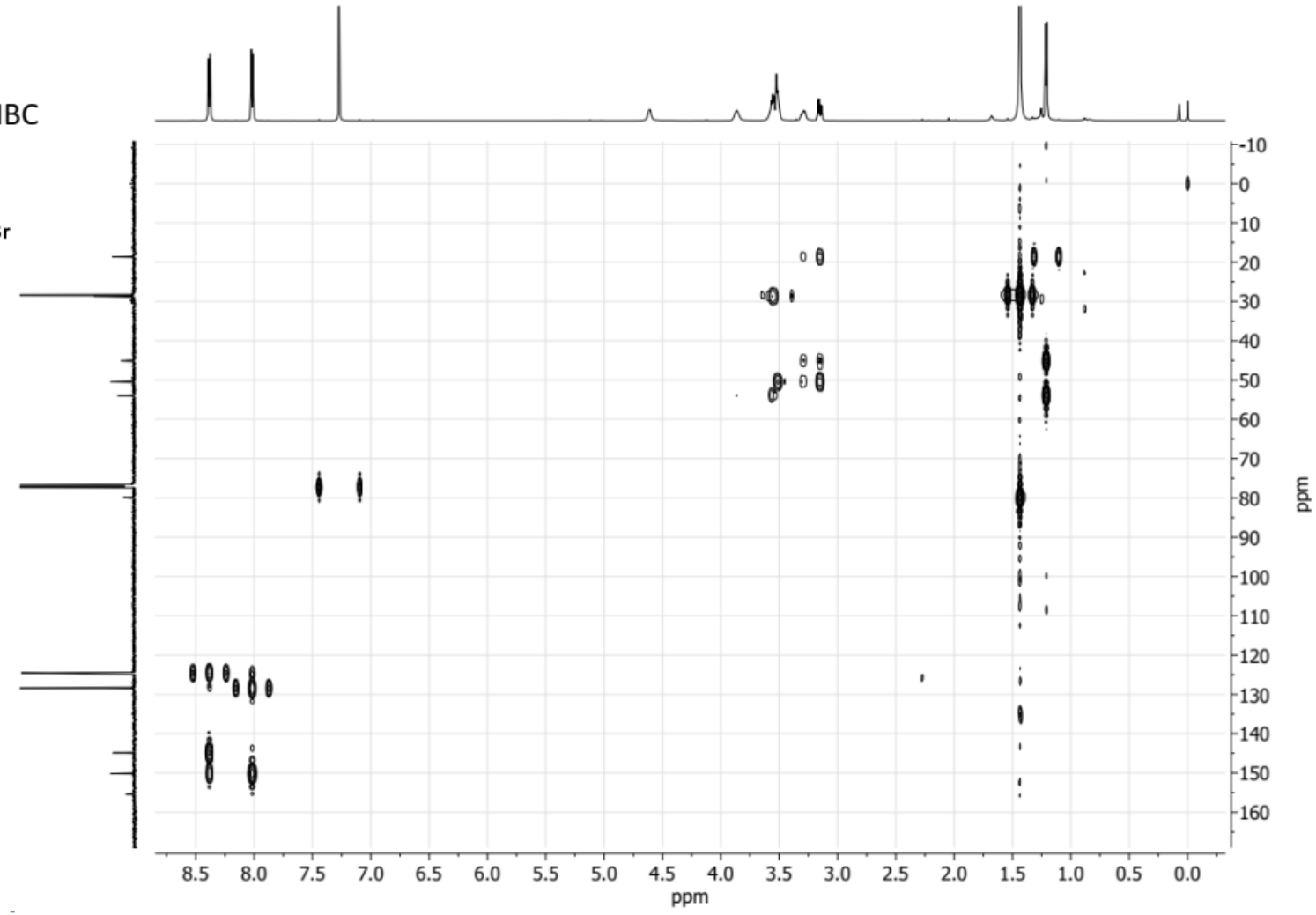

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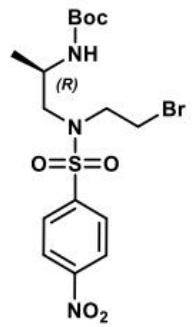
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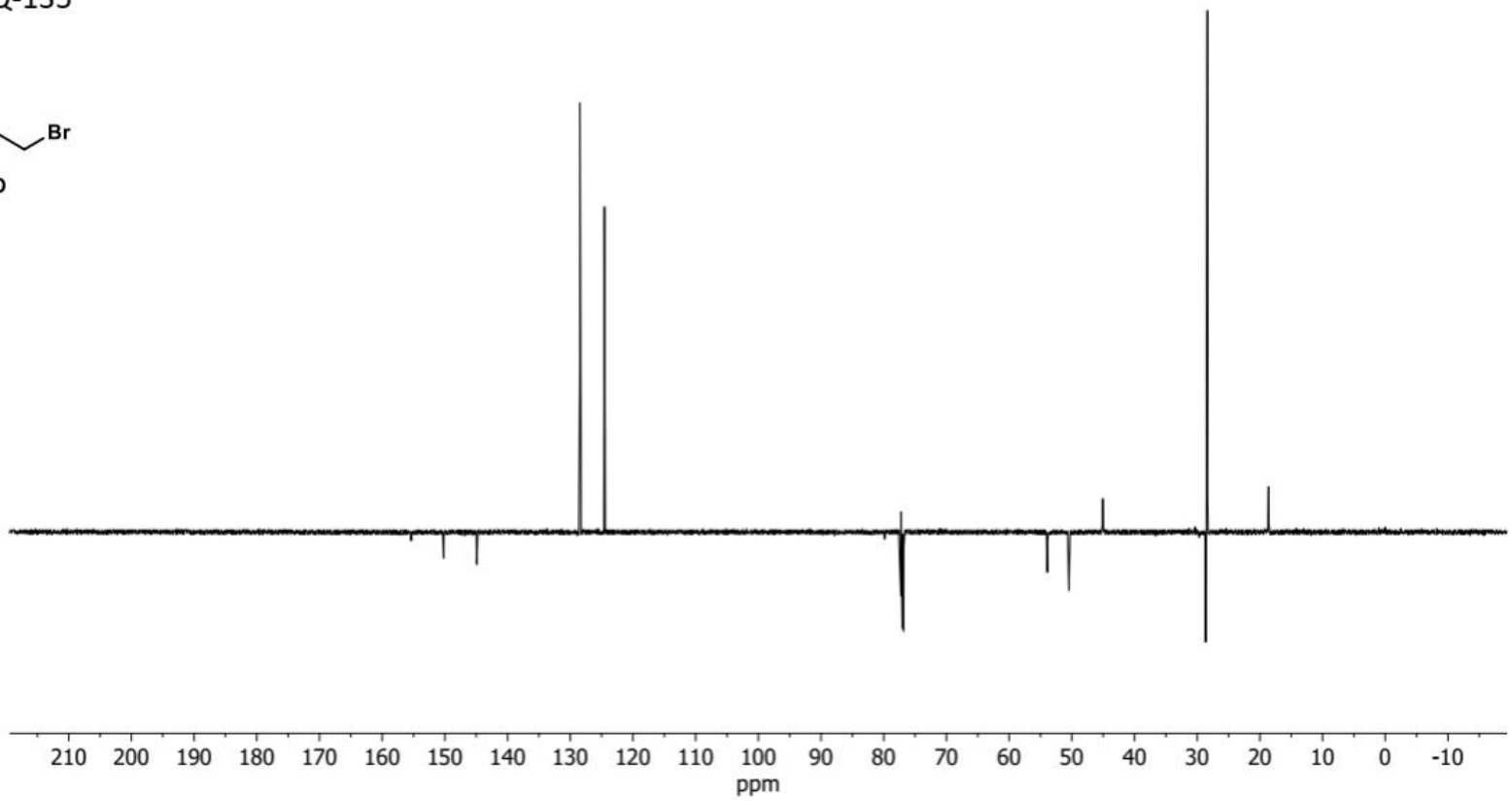
NO2

3b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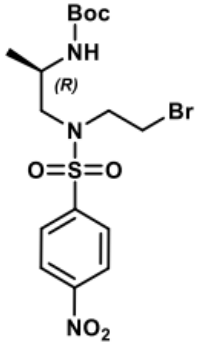
^{1}H, ^{13}C-HSQC



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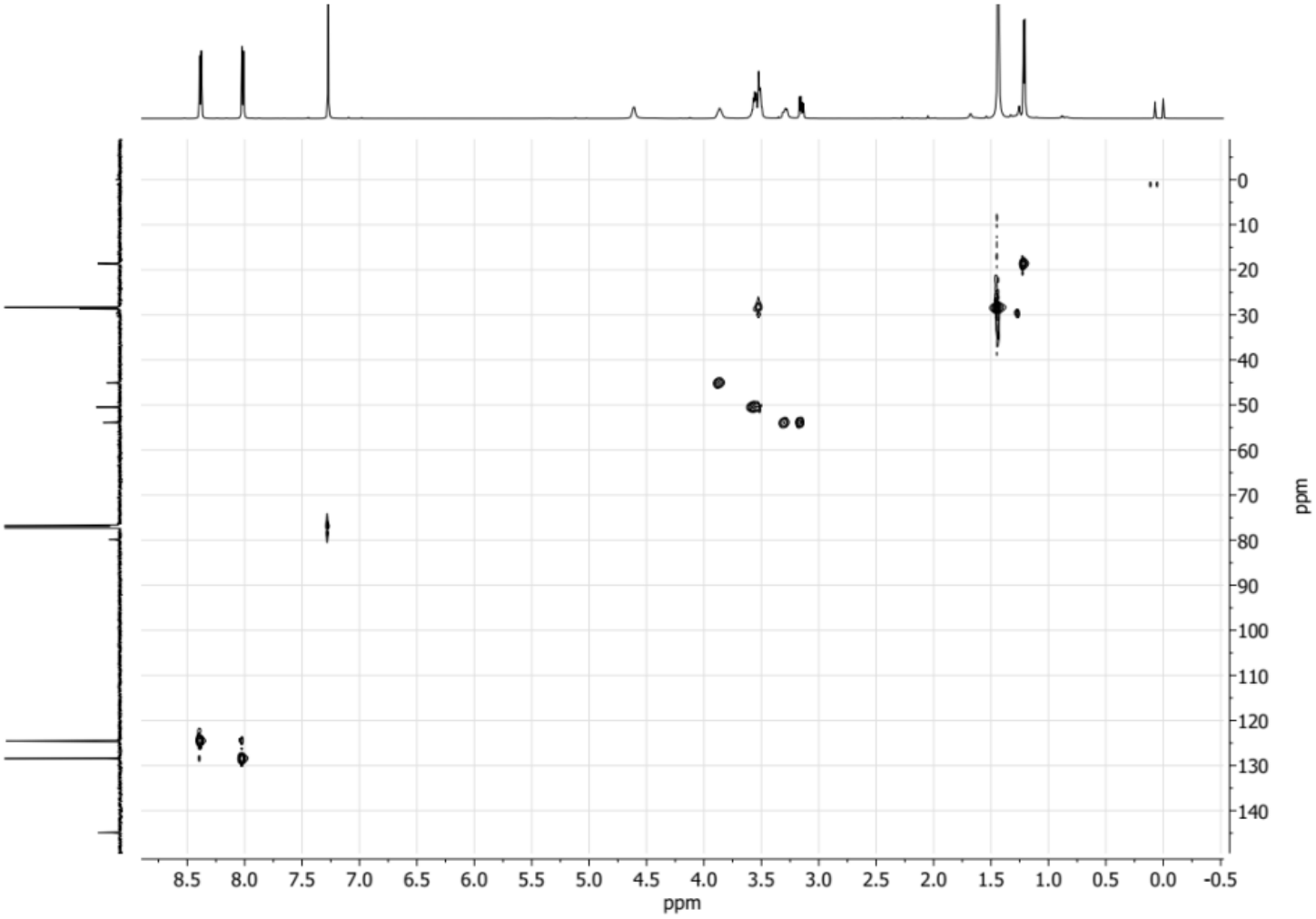

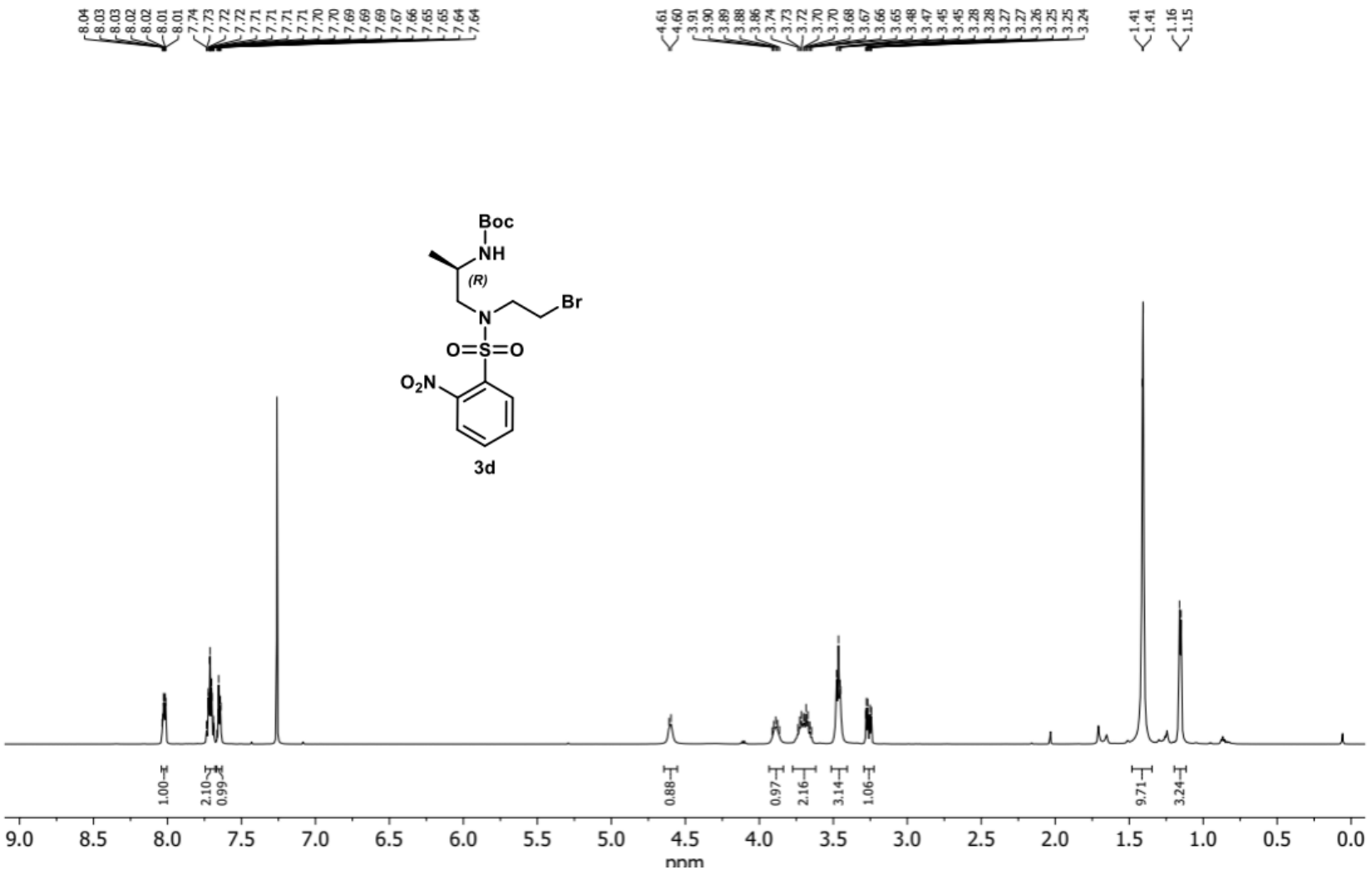
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Br
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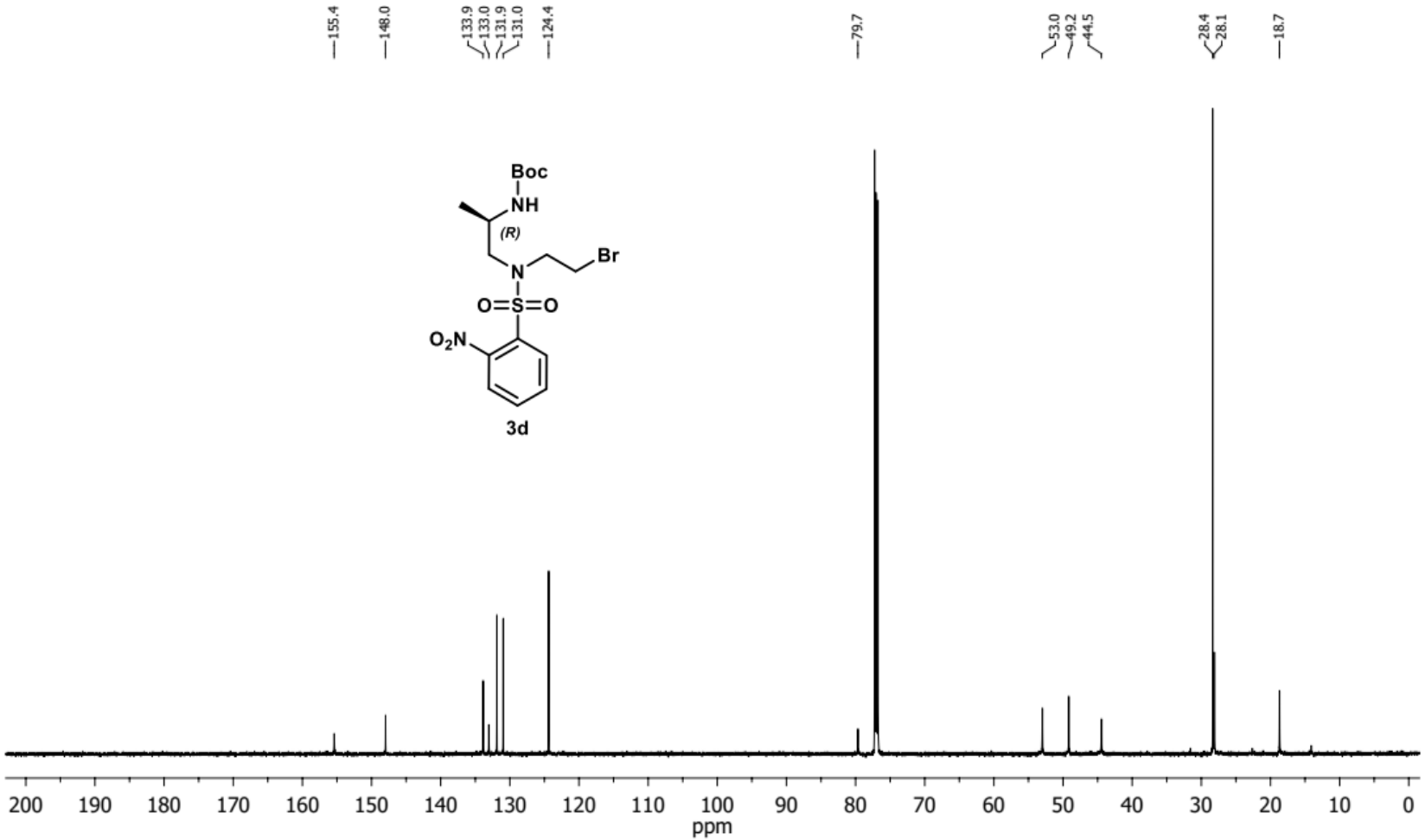
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18.7
Boc
NH
(R)
Br
N
O=S=O
O2N
3d
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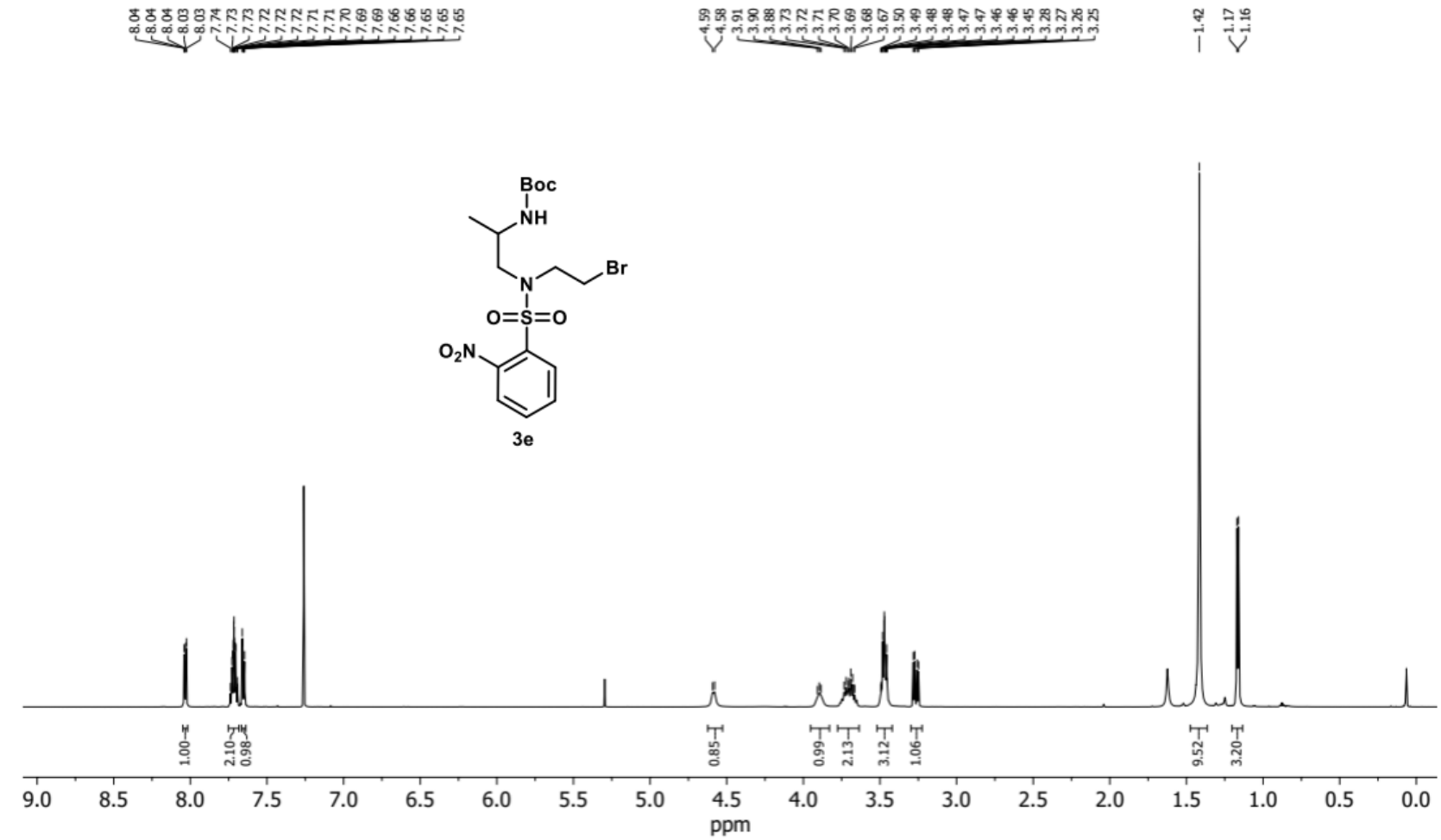
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Br
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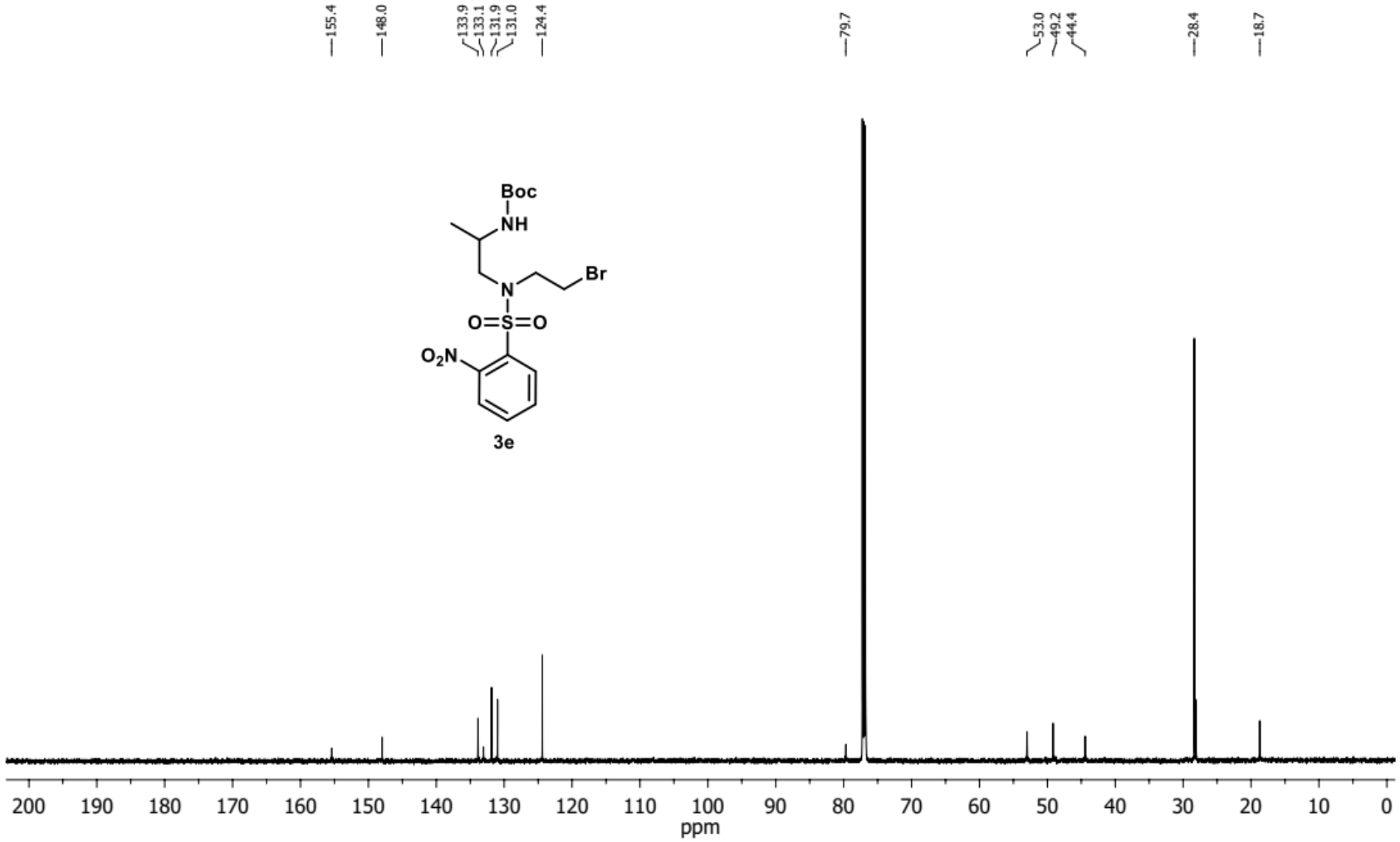
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Br
N
O=S=O
O2N
3e
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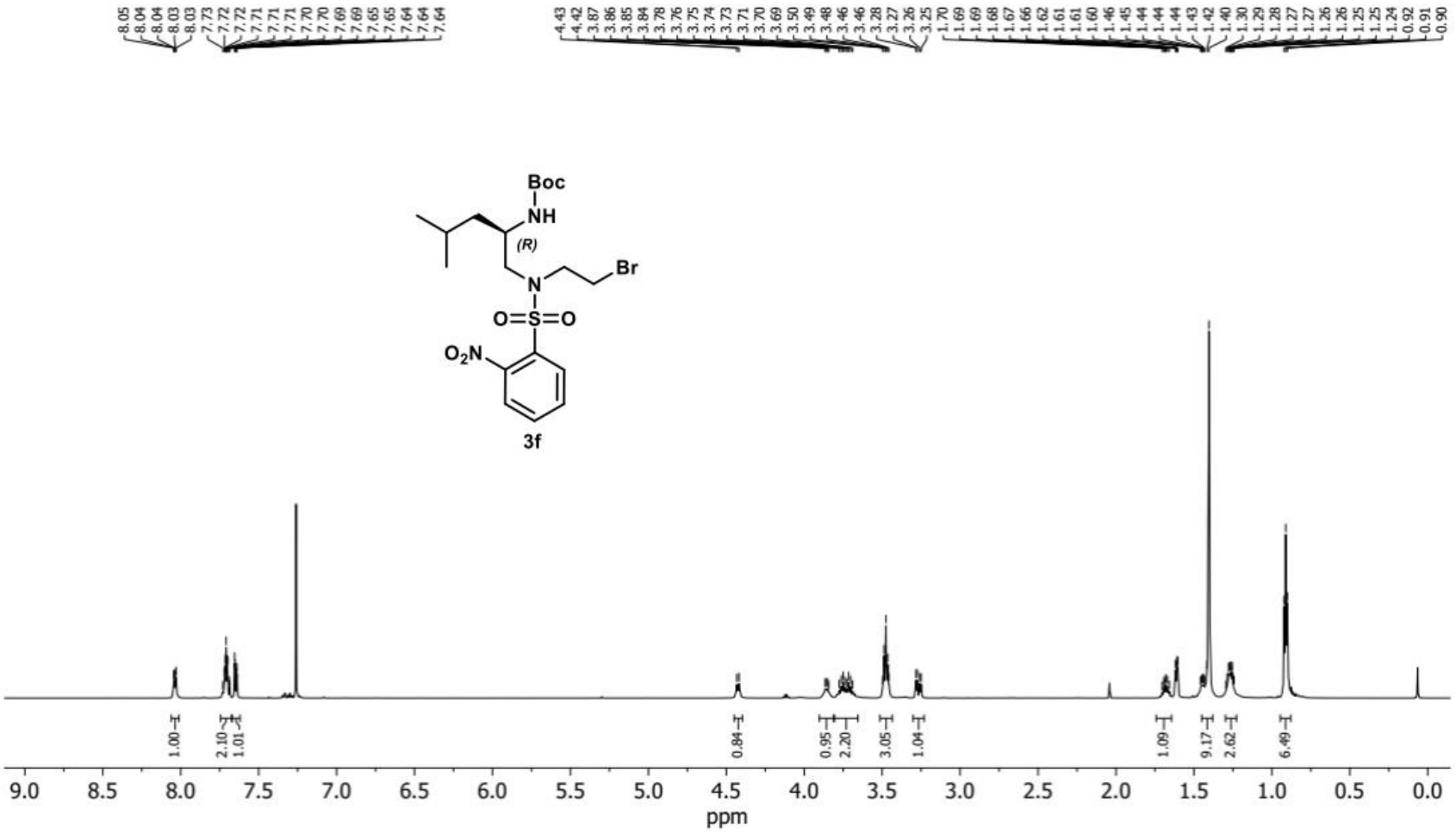
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0.91
0.90
Boc
NH
(R)
N
Br
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O2N
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0.95
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6.5
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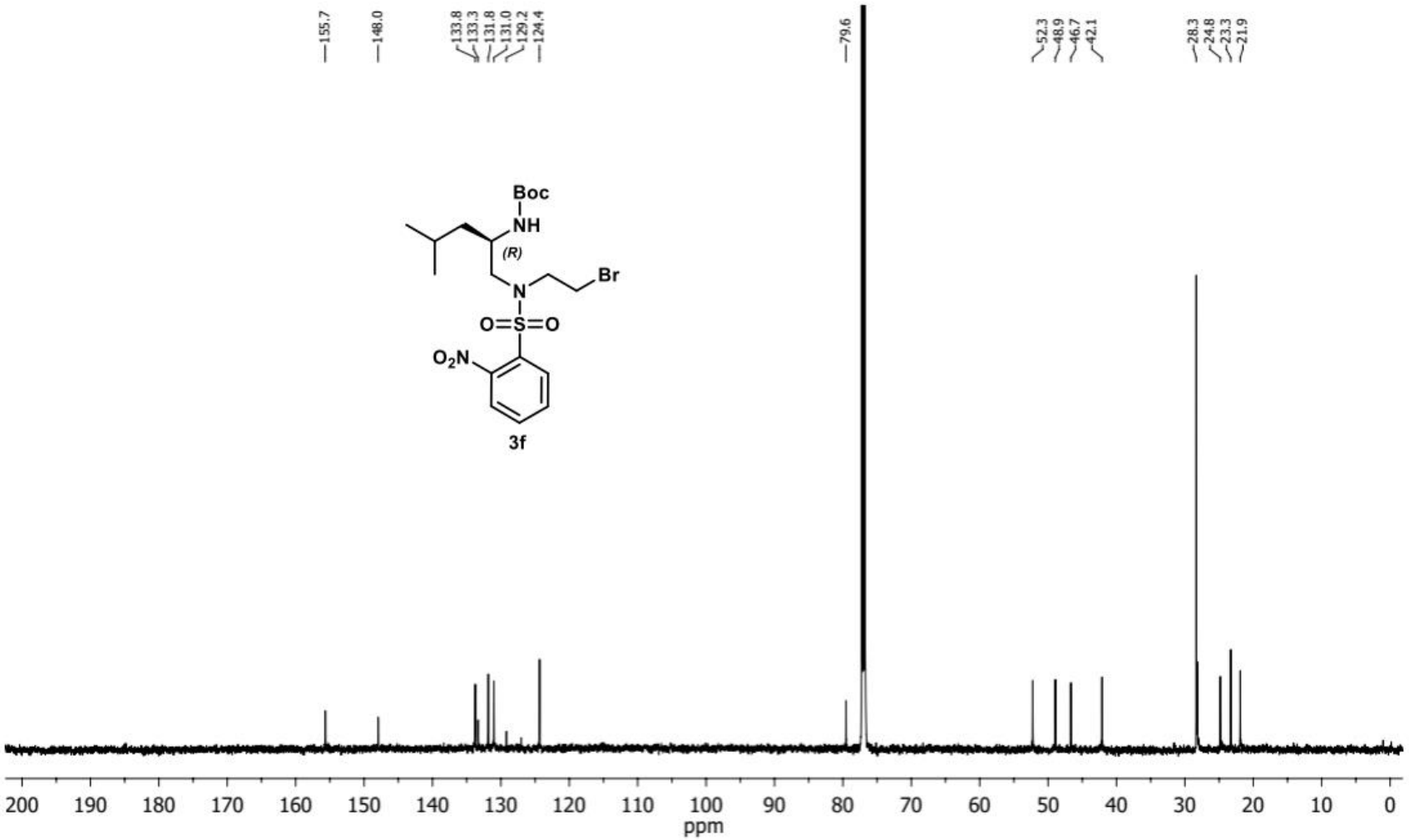
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79.6
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48.9
46.7
42.1
28.3
24.8
23.3
21.9
Boc
NH
(R)
N
Br
O=S=O
O2N
3f
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
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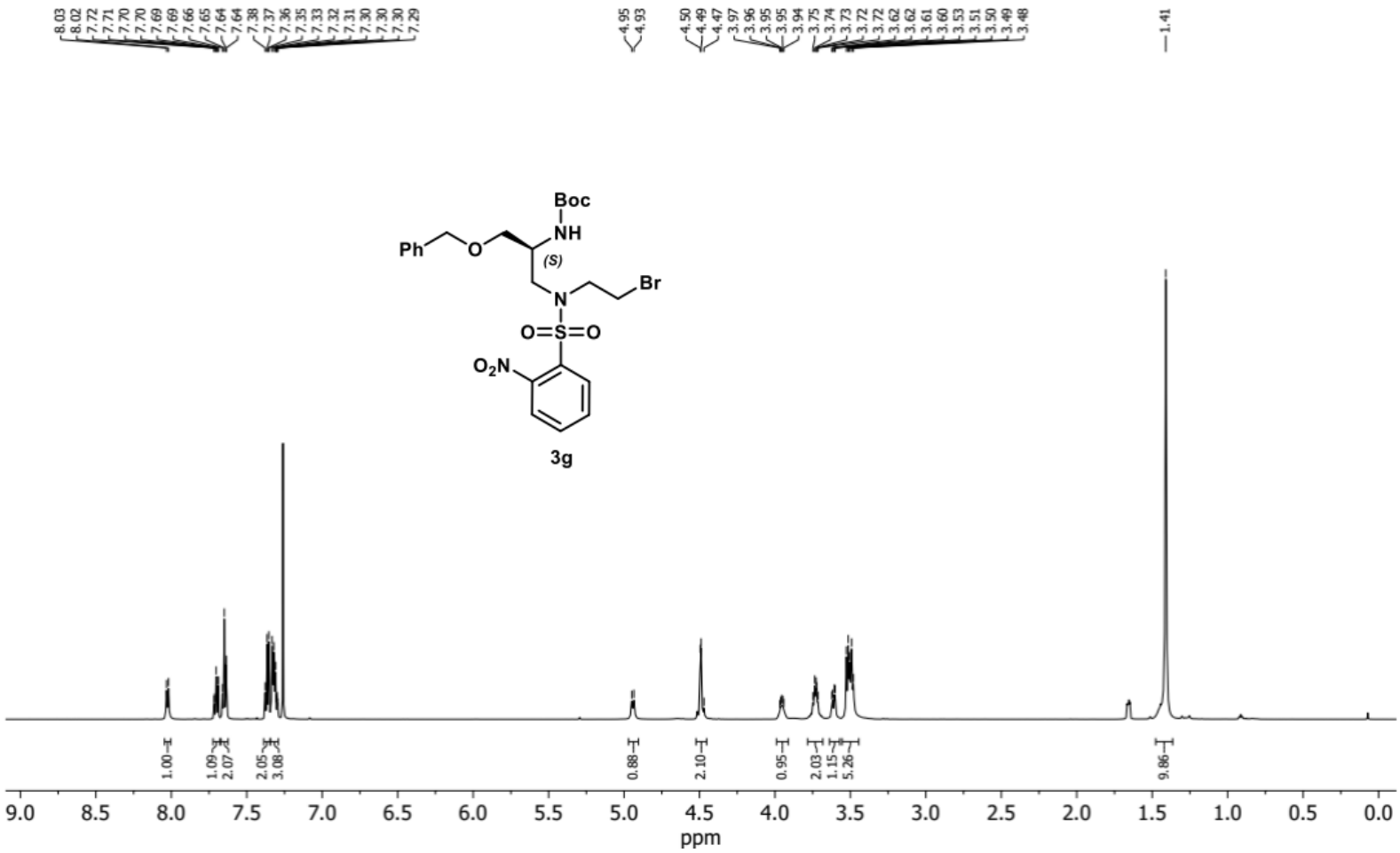
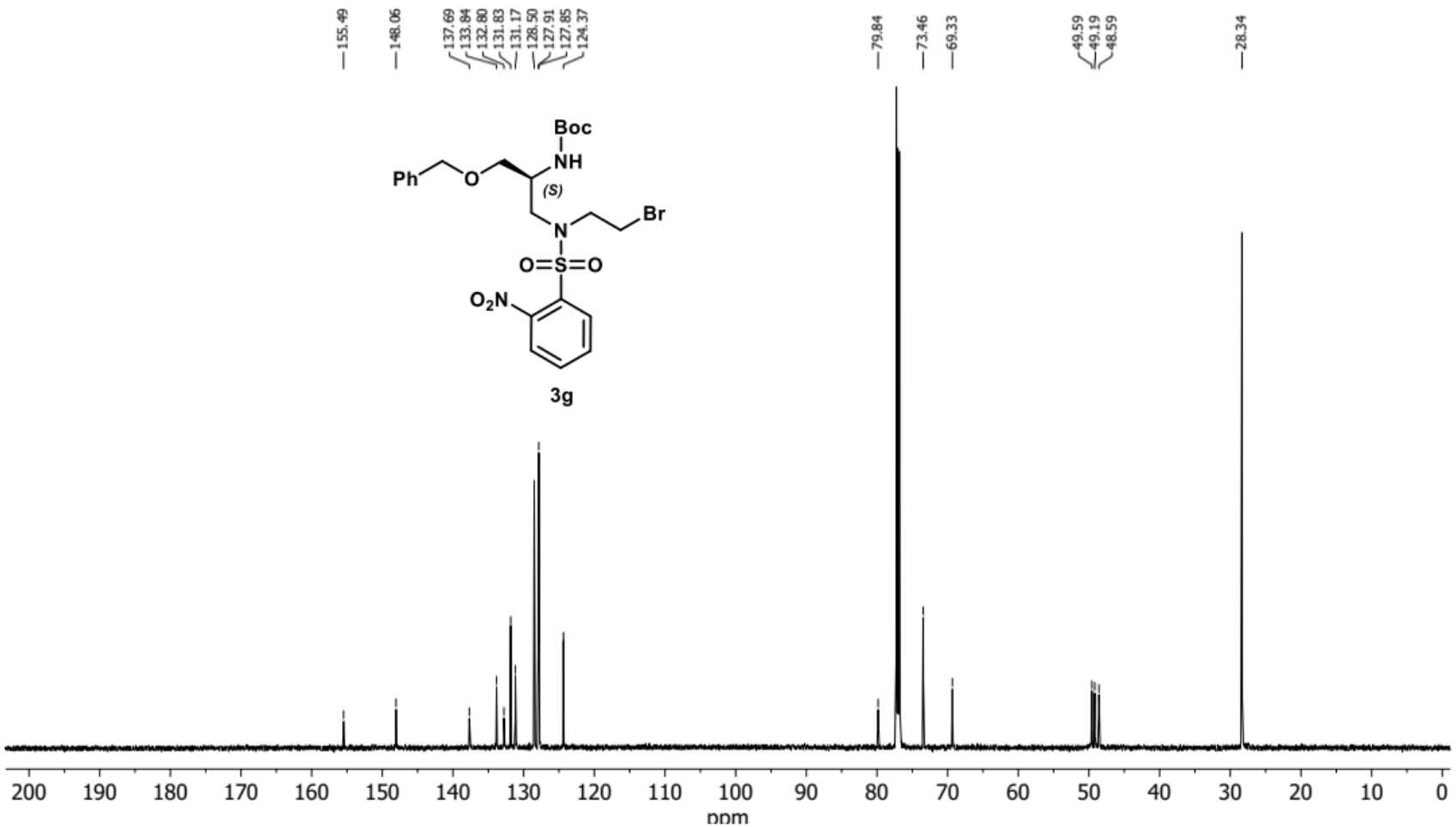
30
20
10
0
ppm


8.03
8.02
7.72
7.71
7.70
7.70
7.69
7.69
7.66
7.65
7.64
7.64
7.38
7.37
7.36
7.35
7.33
7.32
7.31
7.30
7.30
7.30
7.29
4.95
4.93
4.50
4.49
4.47
3.97
3.96
3.95
3.95
3.94
3.75
3.74
3.73
3.72
3.72
3.62
3.62
3.61
3.60
3.53
3.51
3.50
3.49
3.48
1.41
Boc
NH
(S)
Ph
O
N
Br
O=S=O
O2N
3g
1.00
1.09
2.07
2.05
3.08
0.88
2.10
0.95
2.03
1.15
5.26
9.86
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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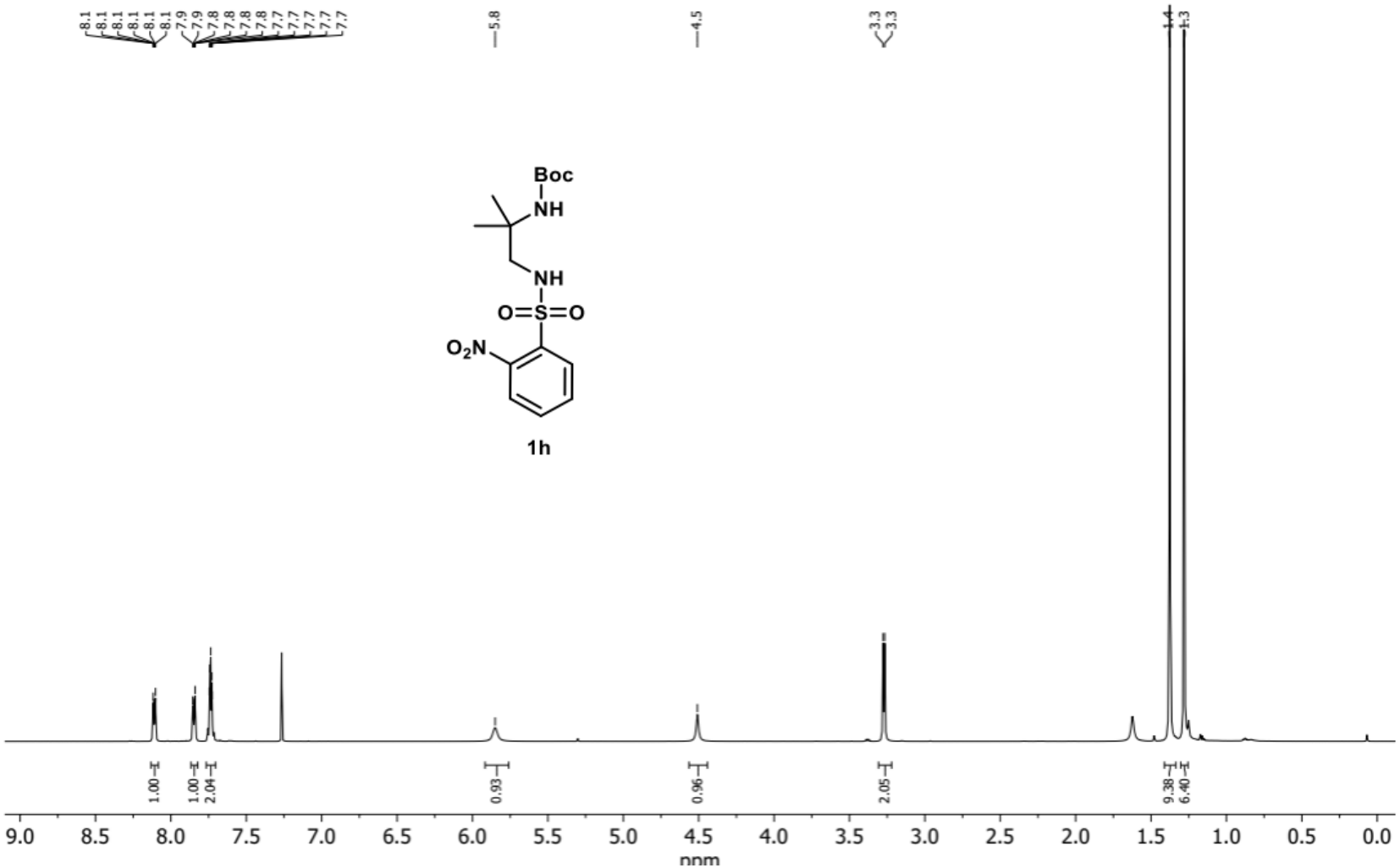
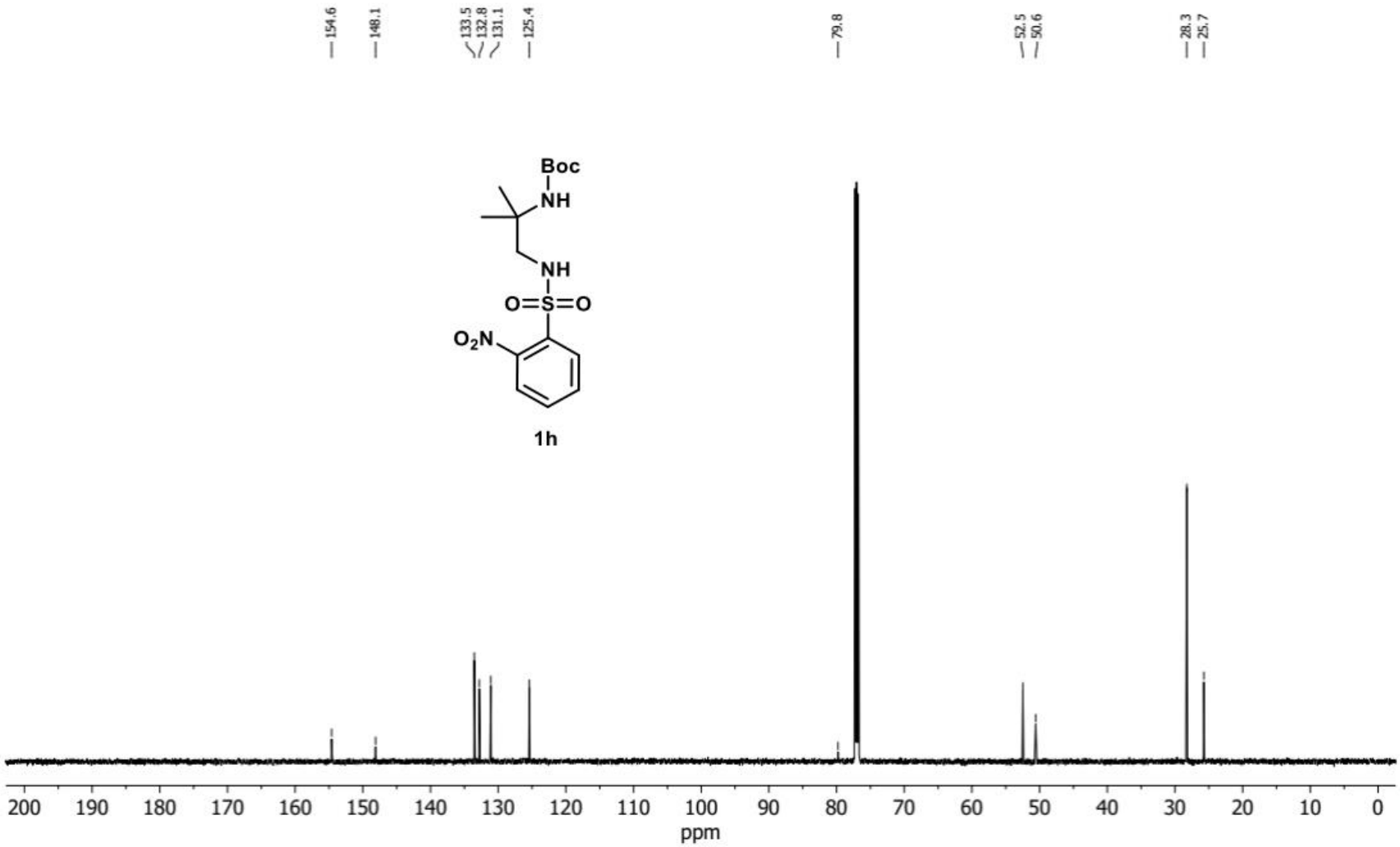
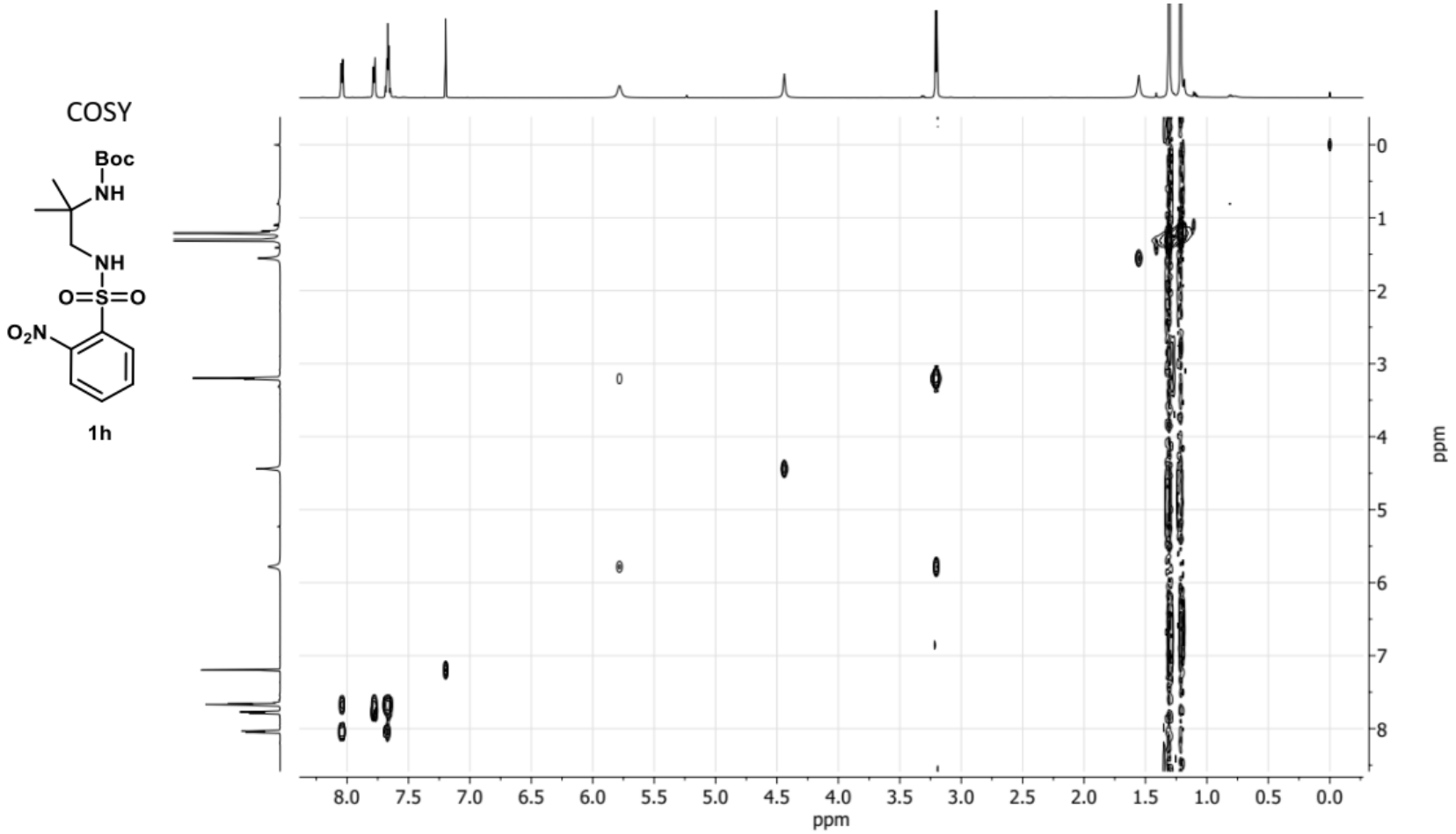
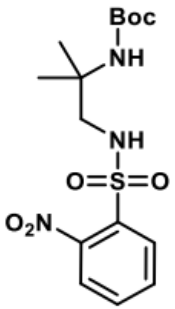
148.06
137.69
133.84
132.80
131.83
131.17
128.50
127.91
127.85
124.37
79.84
73.46
69.33
49.59
49.19
48.59
28.34
Boc
NH
Ph
O
(S)
N
Br
O=S=O
O2N
3g
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


8.1
8.1
8.1
8.1
8.1
7.9
7.9
7.8
7.8
7.8
7.8
7.7
7.7
7.7
7.7
7.7
5.8
4.5
3.3
3.3
1.4
1.3
Boc
NH
NH
O=S=O
O2N
1h
1.00
1.00
2.04
0.93
0.96
2.05
9.38
6.40
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

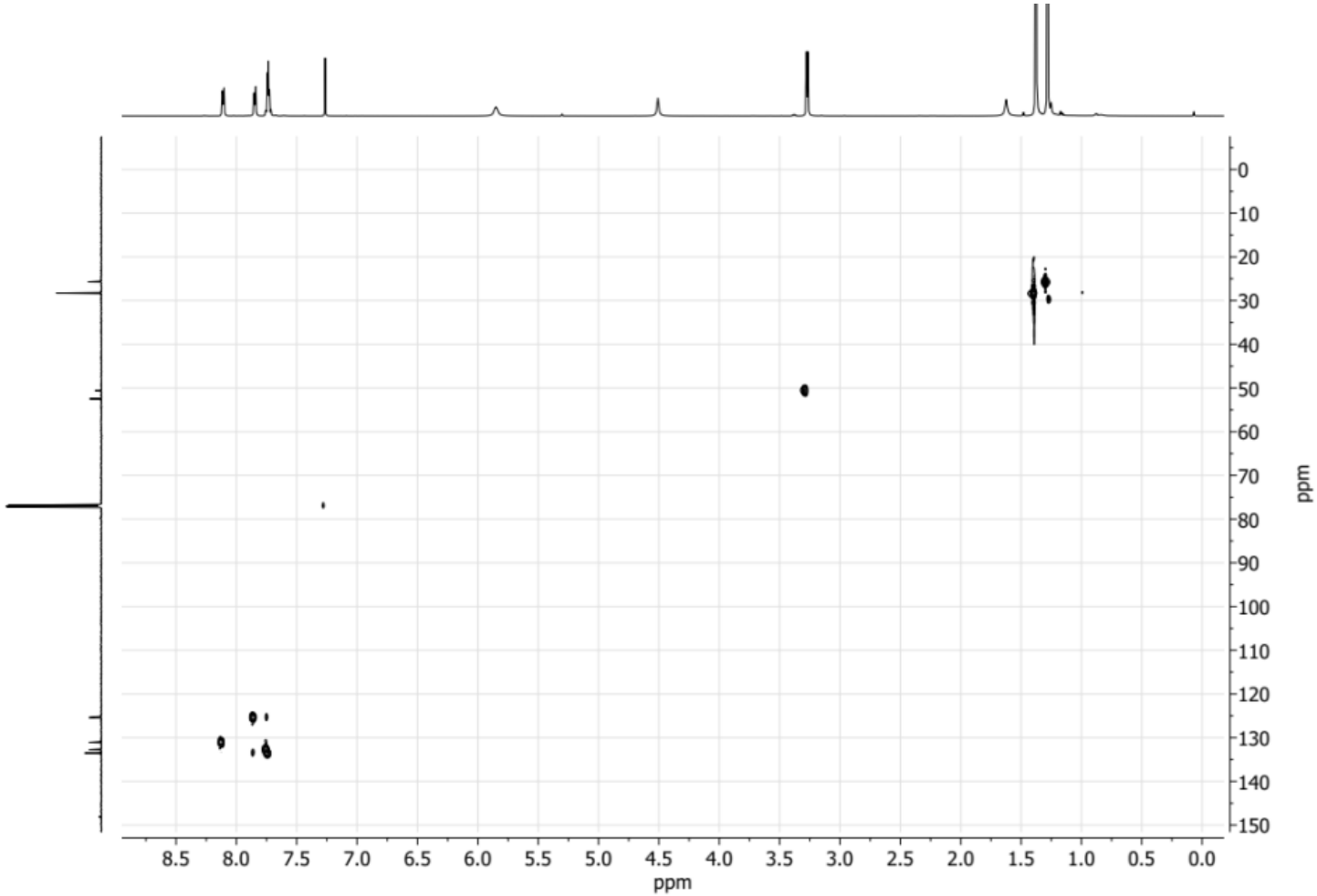

154.6
148.1
133.5
132.8
131.1
125.4
79.8
52.5
50.6
28.3
25.7
Boc
NH
NH
O=S=O
O2N
1h
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

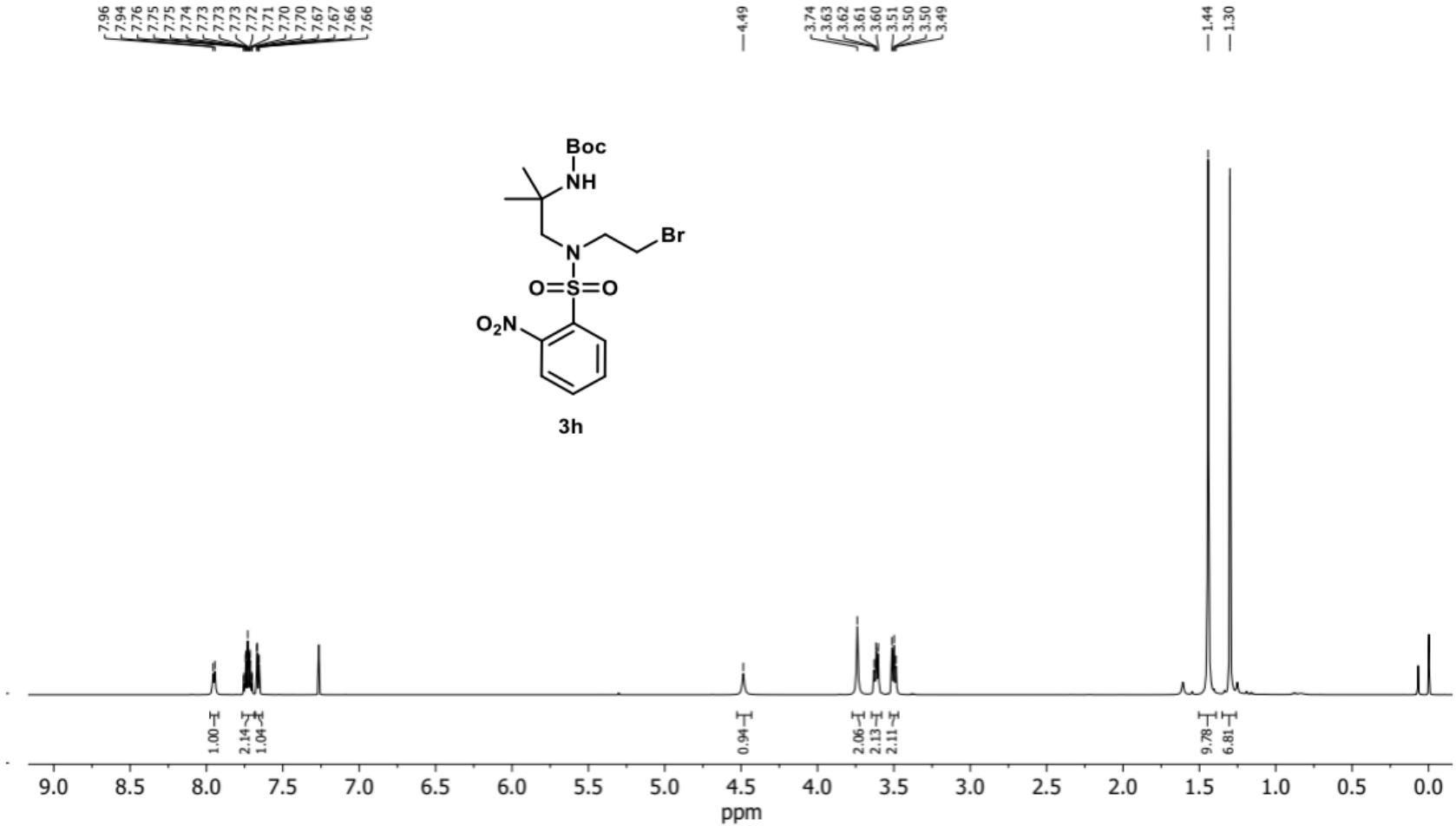

COSY
Boc
NH
NH
O=S=O
O2N
1h
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0
1
2
3
4
5
6
7
8
ppm

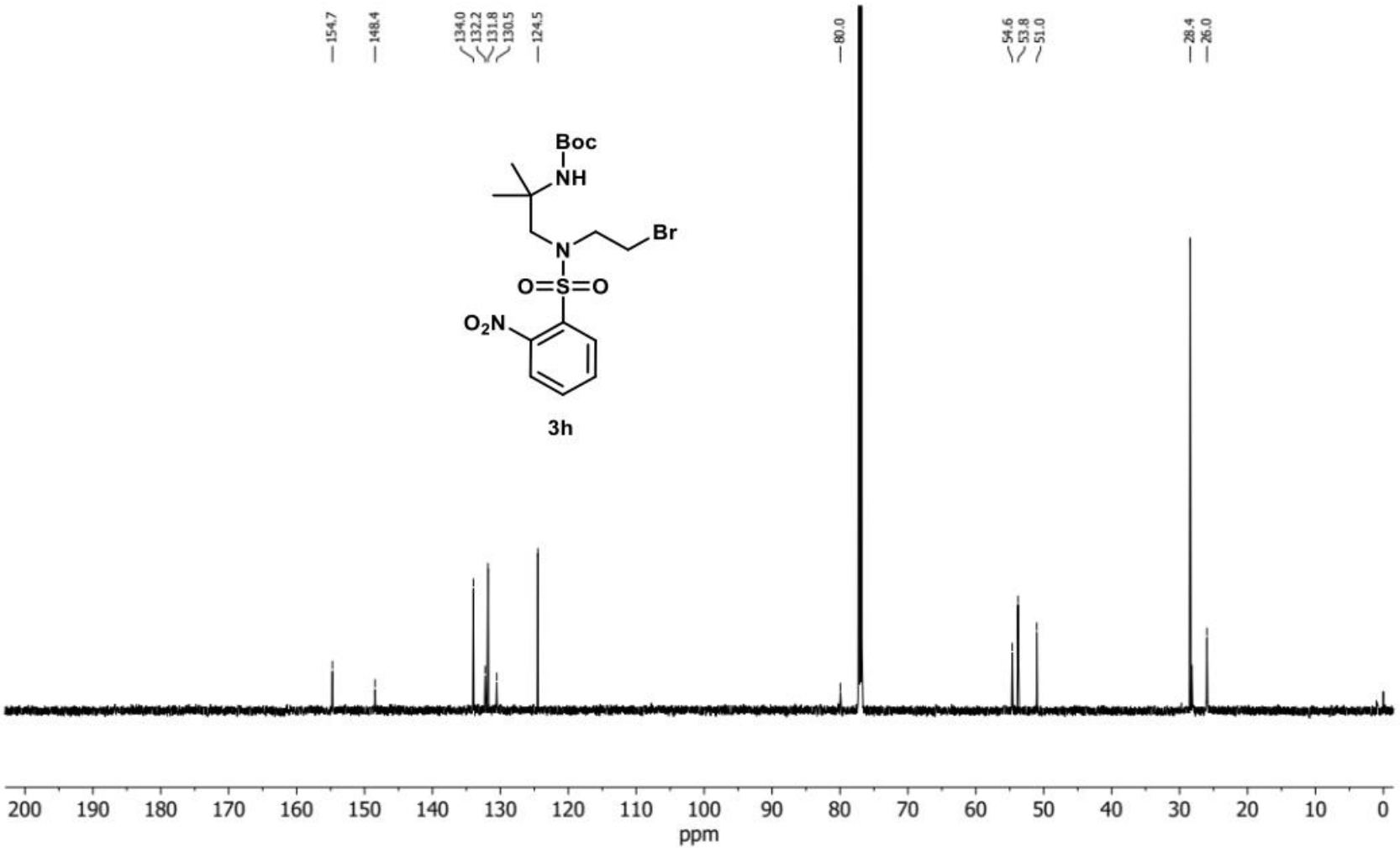
^{1}H, ^{13}C-HSQC

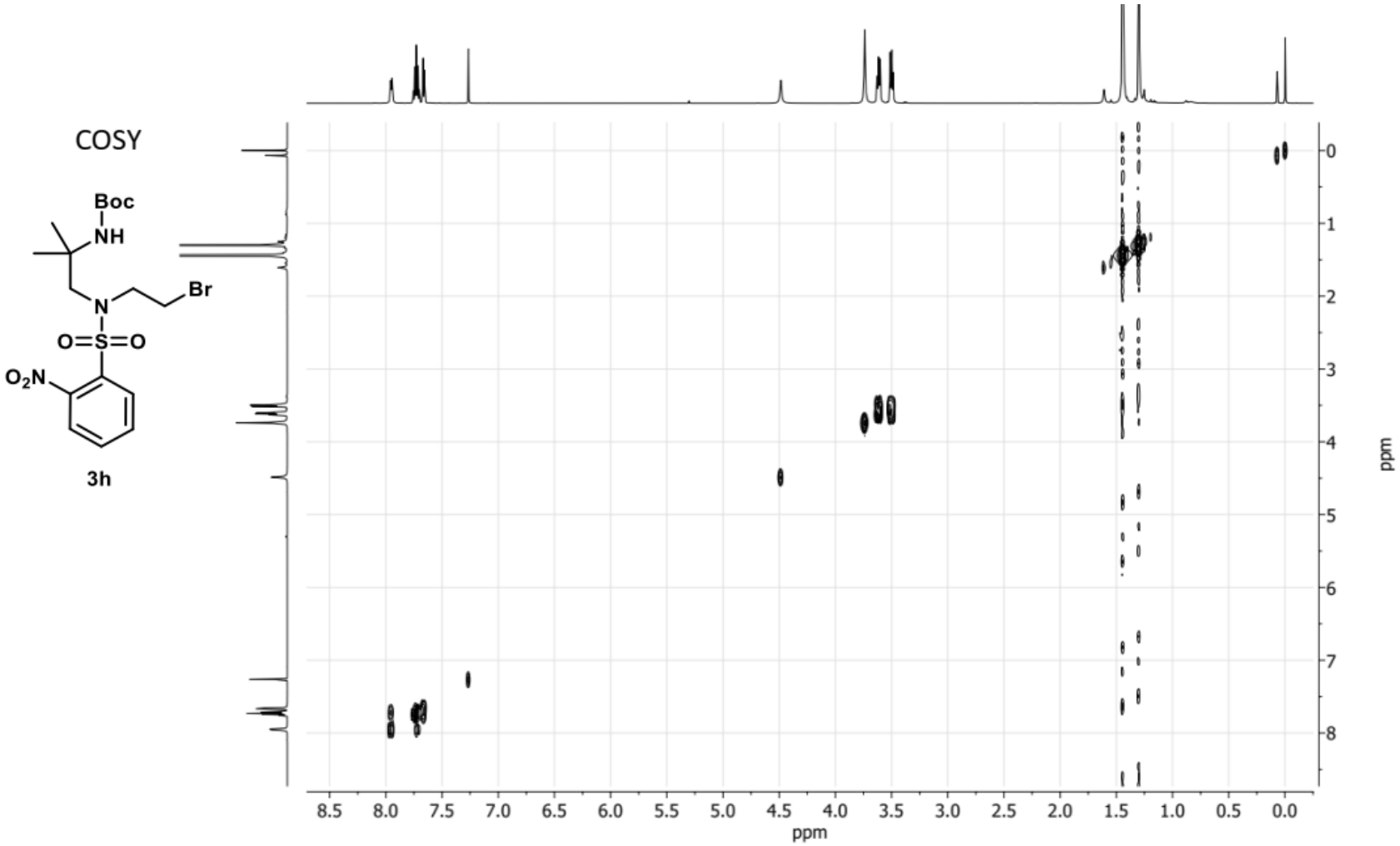


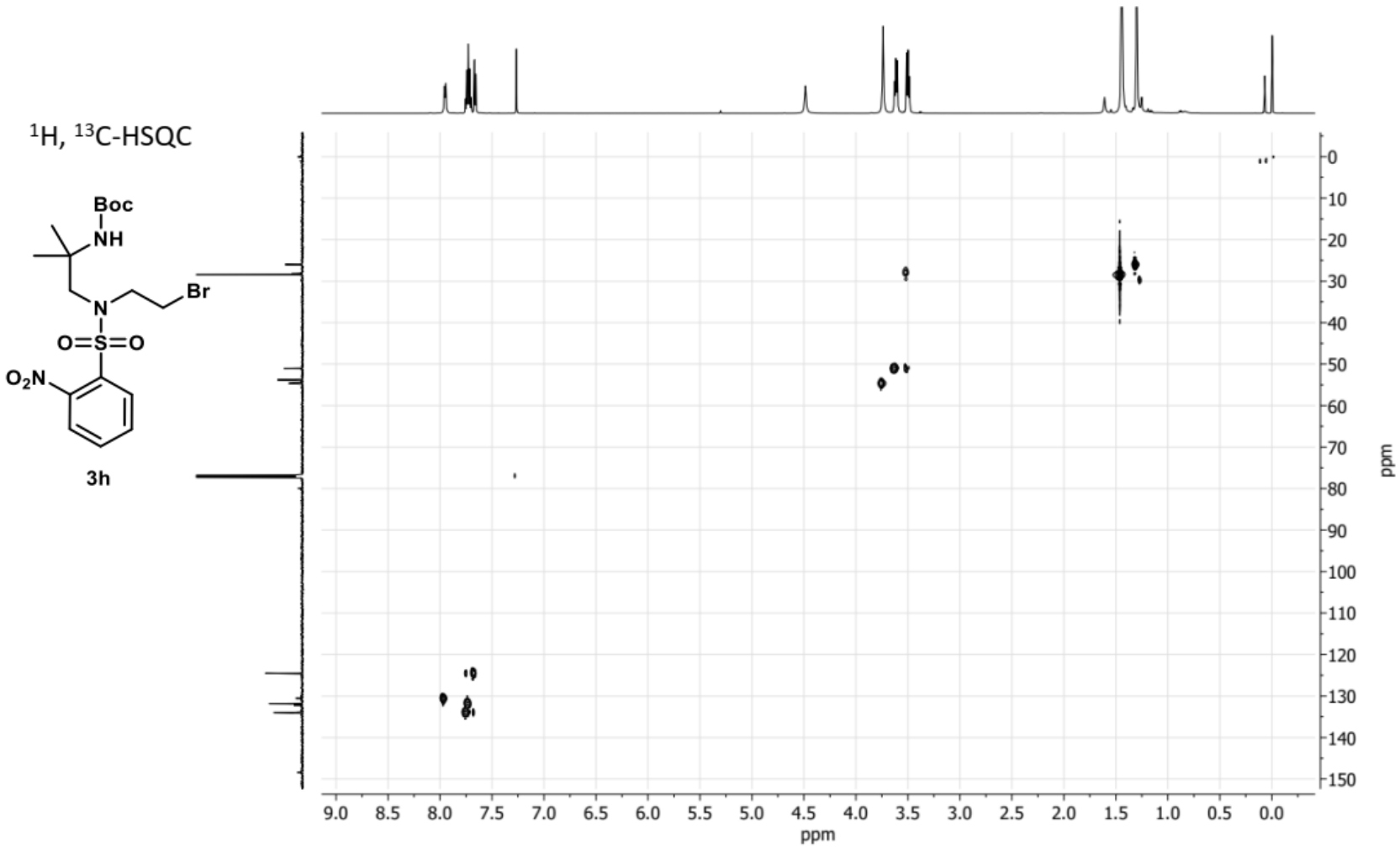
1h

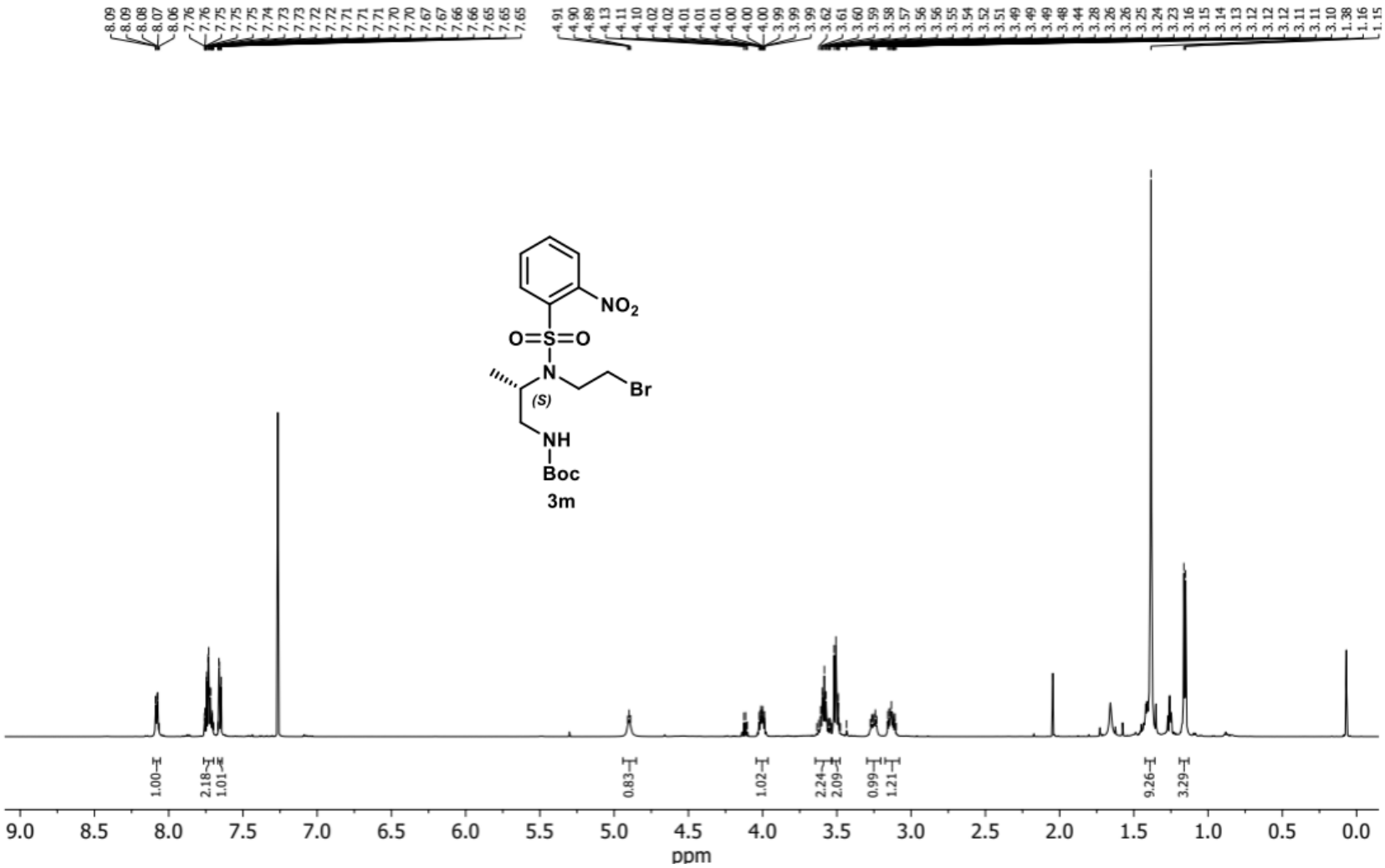


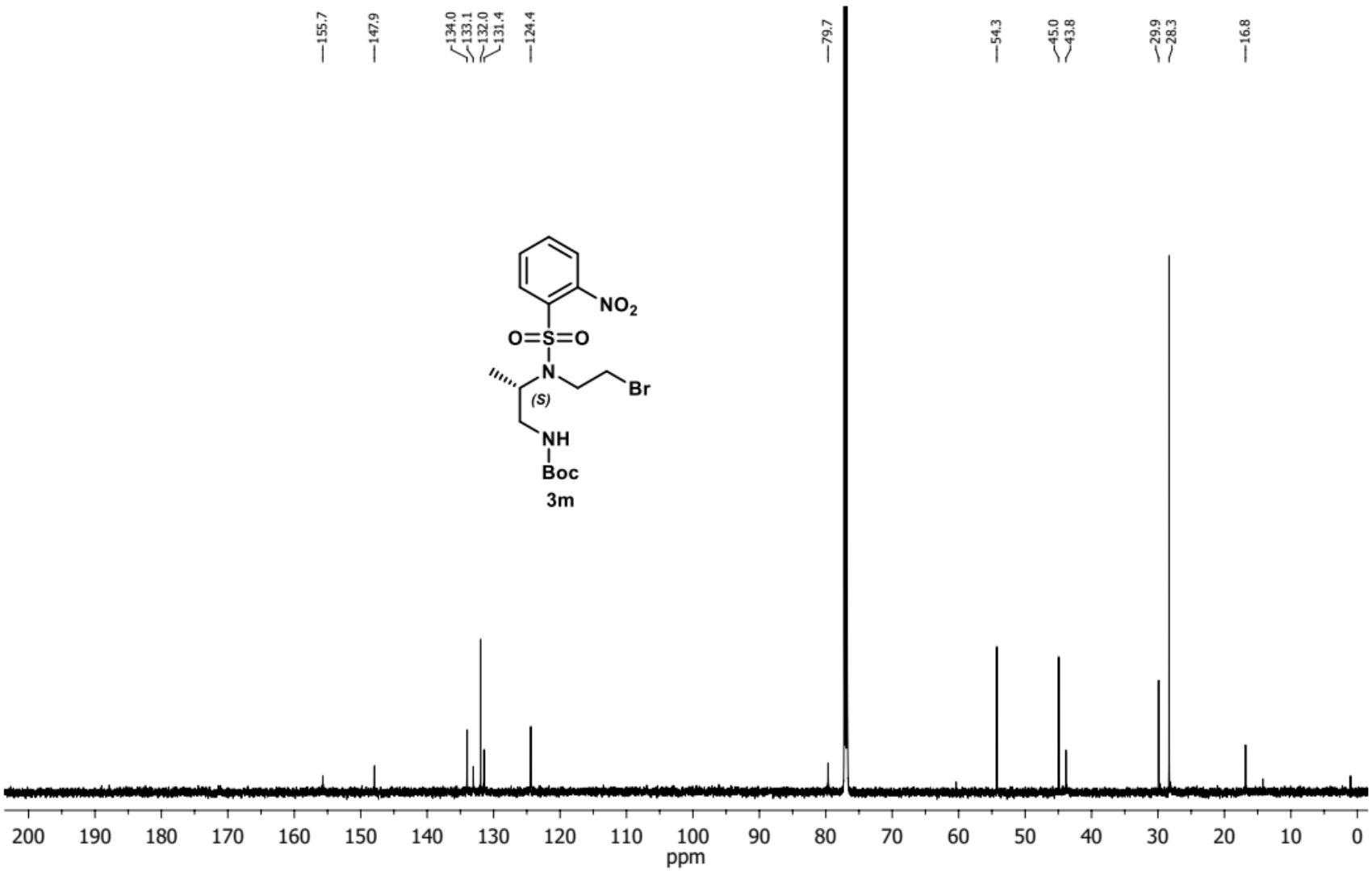

7.96
7.94
7.76
7.75
7.75
7.74
7.73
7.73
7.73
7.72
7.71
7.70
7.70
7.67
7.67
7.66
7.66
4.49
3.74
3.63
3.62
3.61
3.60
3.51
3.50
3.50
3.49
1.44
1.30
Boc
NH
N
Br
O=S=O
O2N
3h
1.00
2.14
1.04
0.94
2.06
2.13
2.11
9.78
6.81
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

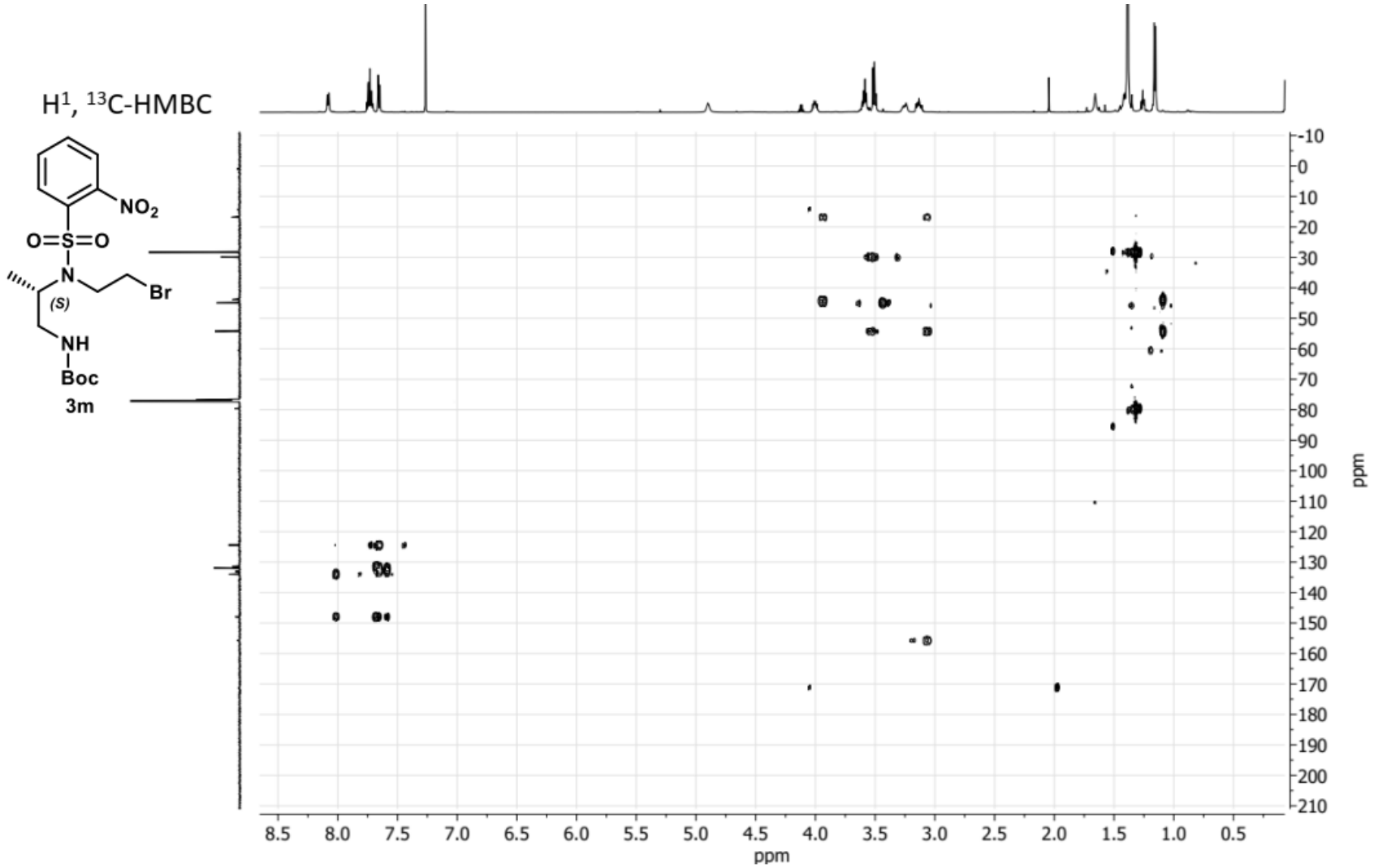

154.7
148.4
134.0
132.2
131.8
130.5
124.5
80.0
54.6
53.8
51.0
28.4
26.0
Boc
NH
N
Br
O=S=O
O2N
3h
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


COSY
Boc
NH
N
Br
O=S=O
O2N
3h
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0
1
2
3
4
5
6
7
8
ppm

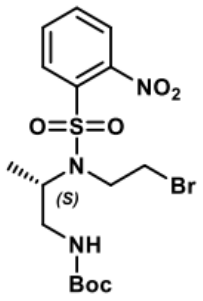

^{1}H, ^{13}C-HSQC
Boc
NH
N
Br
O=S=O
O_2N
3h
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
ppm


8.09 8.09 8.08 8.07 8.06 7.76 7.76 7.75 7.75 7.75 7.74 7.73 7.73 7.72 7.72 7.71 7.71 7.71 7.70 7.70 7.67 7.67 7.66 7.66 7.65 7.65 7.65
4.91 4.90 4.89 4.13 4.11 4.10 4.02 4.02 4.01 4.01 4.01 4.00 4.00 4.00 3.99 3.99 3.99
3.62 3.61 3.60 3.59 3.58 3.57 3.56 3.56 3.55 3.54 3.52 3.51 3.49 3.49 3.49 3.48 3.44 3.28 3.26 3.26 3.25 3.24 3.23 3.16 3.15 3.14 3.13 3.12 3.12 3.11 3.10 1.38 1.16 1.15
NO2
O=S=O
N
Br
(S)
NH
Boc
3m
1.00 2.18 1.01 0.83 1.02 2.24 2.09 0.99 1.21 9.26 3.29
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm


155.7
147.9
134.0
133.1
132.0
131.4
124.4
79.7
54.3
45.0
43.8
29.9
28.3
16.8
NO2
O=S=O
N
Br
(S)
NH
Boc
3m
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

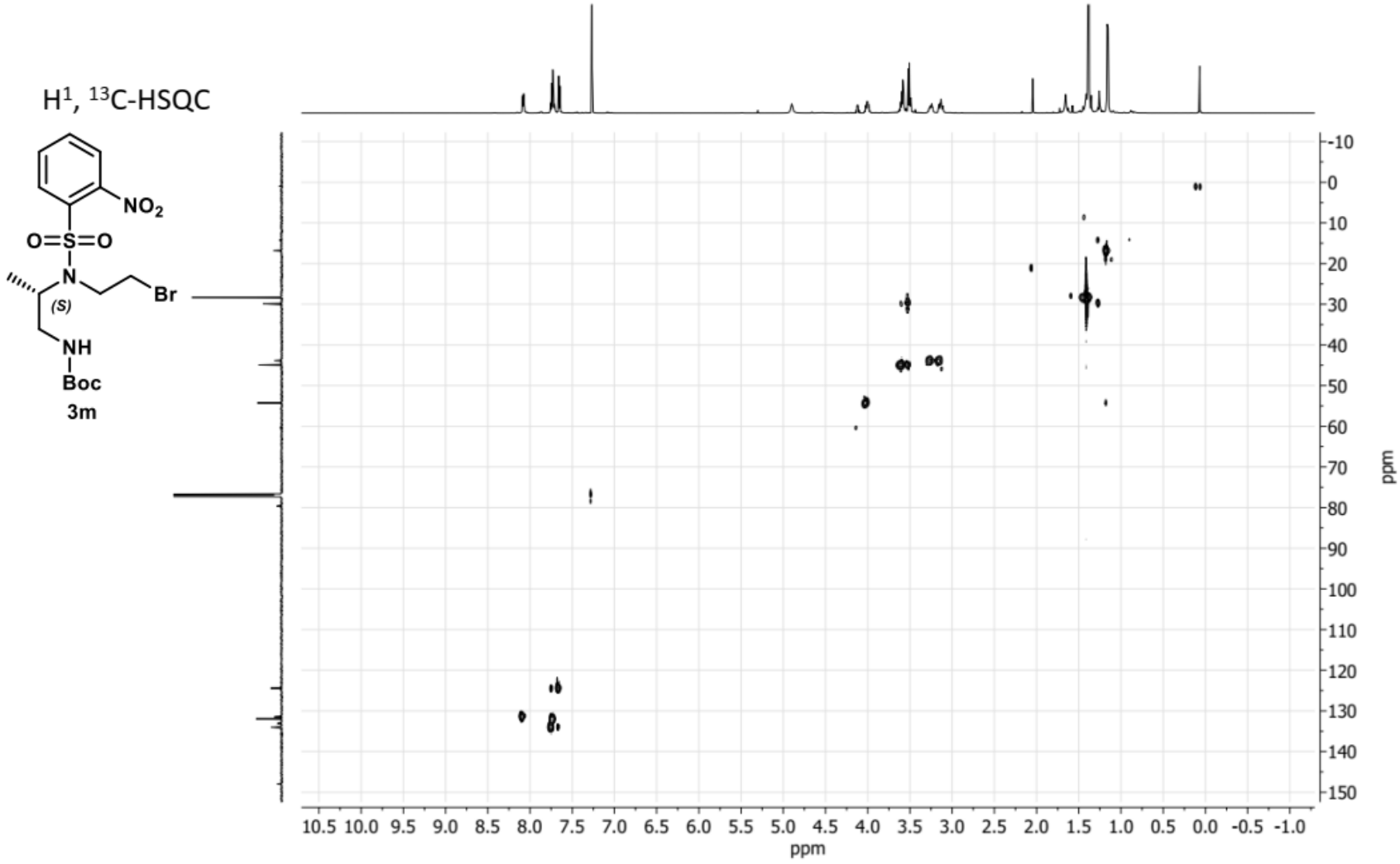

H1, 13C-HMBC
NO2
O=S=O
N
Br
(S)
NH
Boc
3m
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
-10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210
ppm

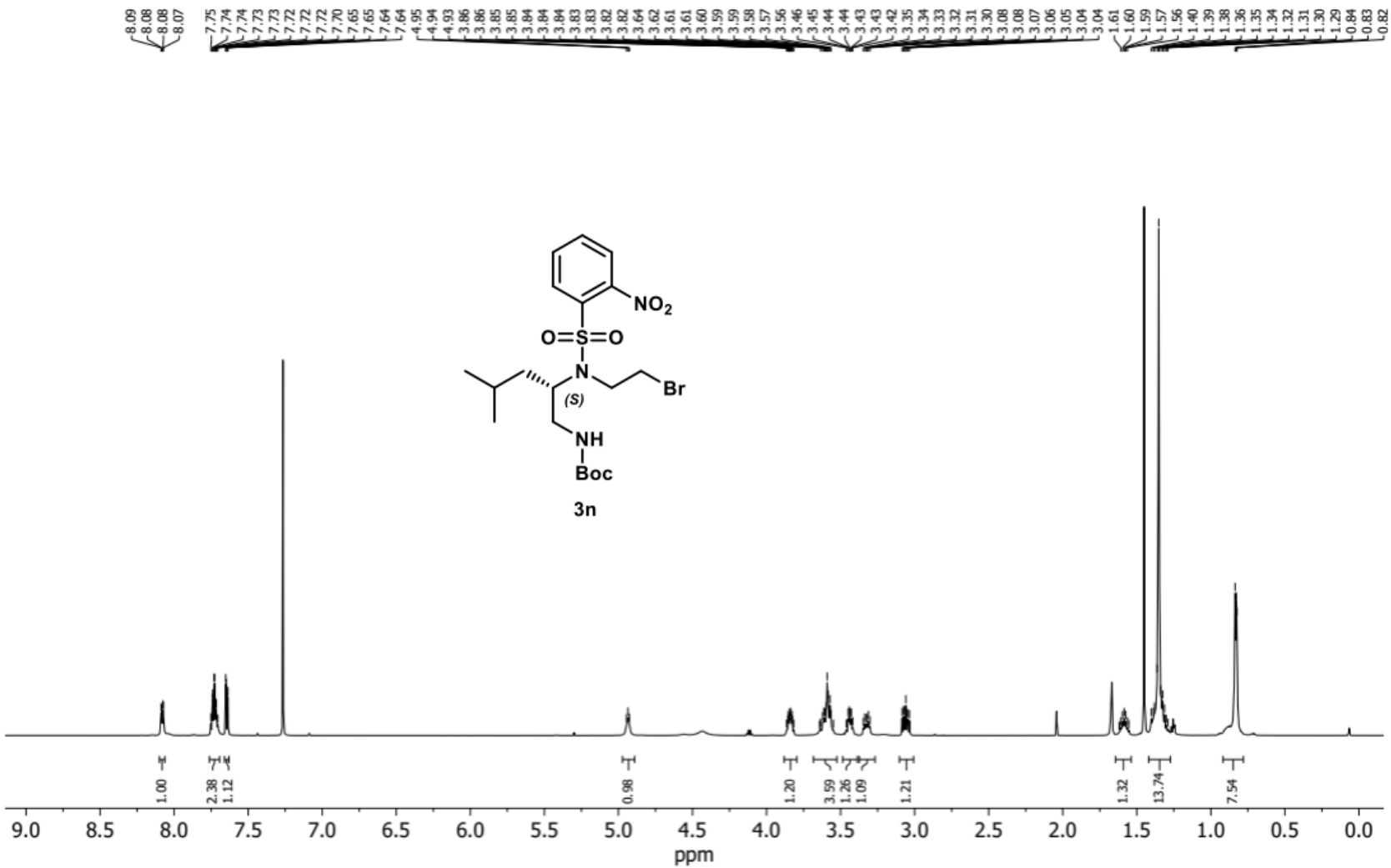
DEPTQ-135

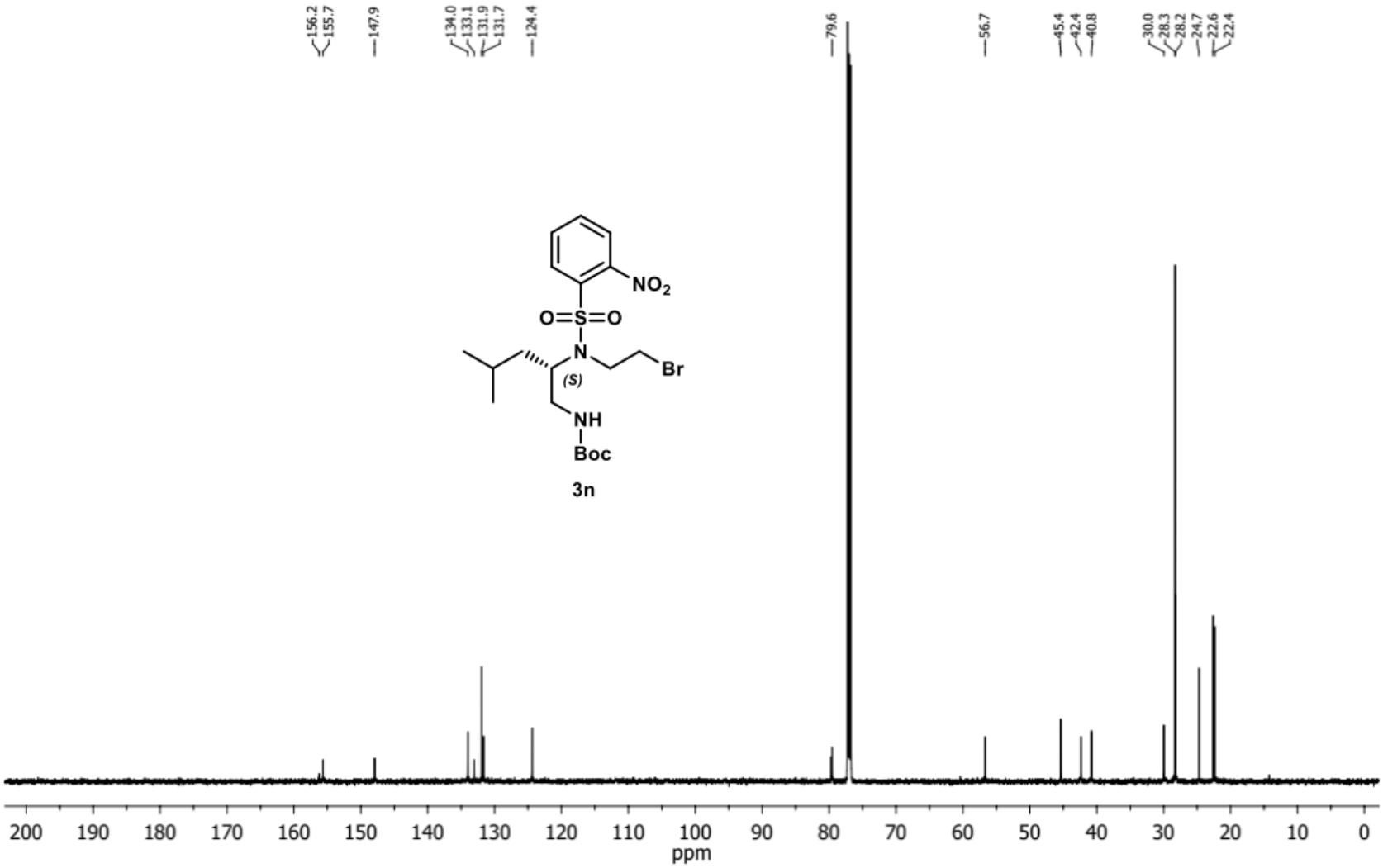

NO2
O=S=O
N
Br
(S)
NH
Boc

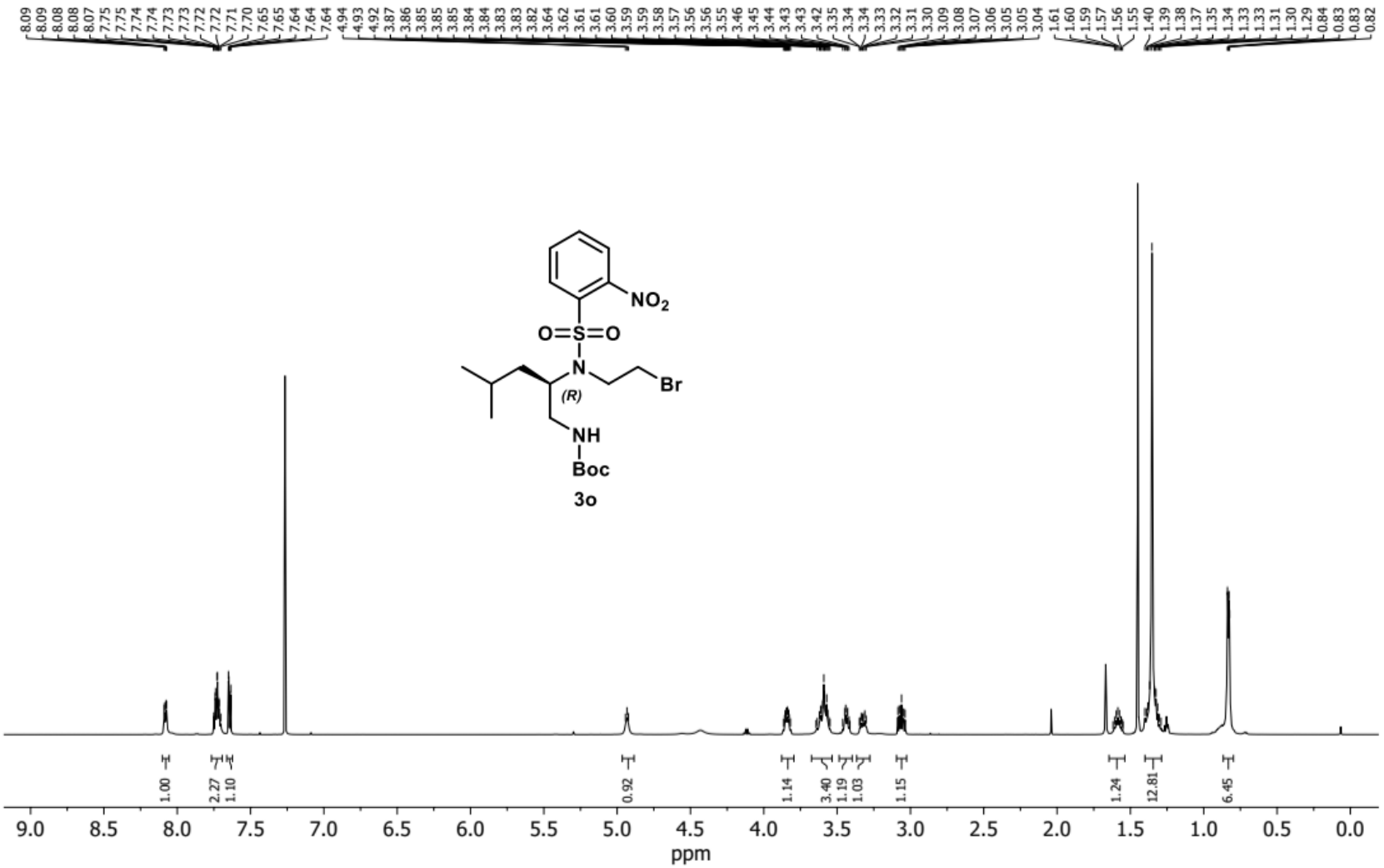
3m

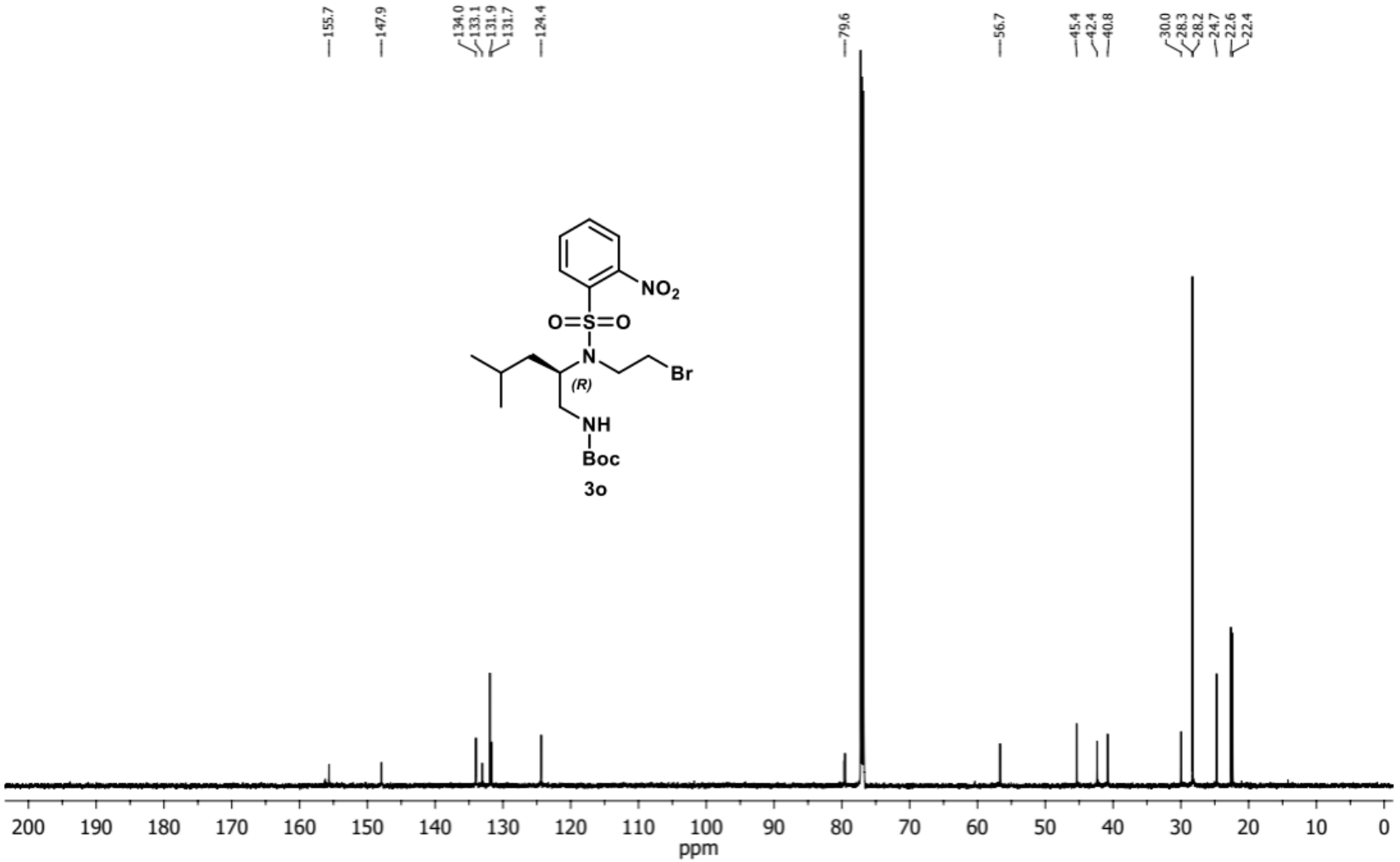
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm

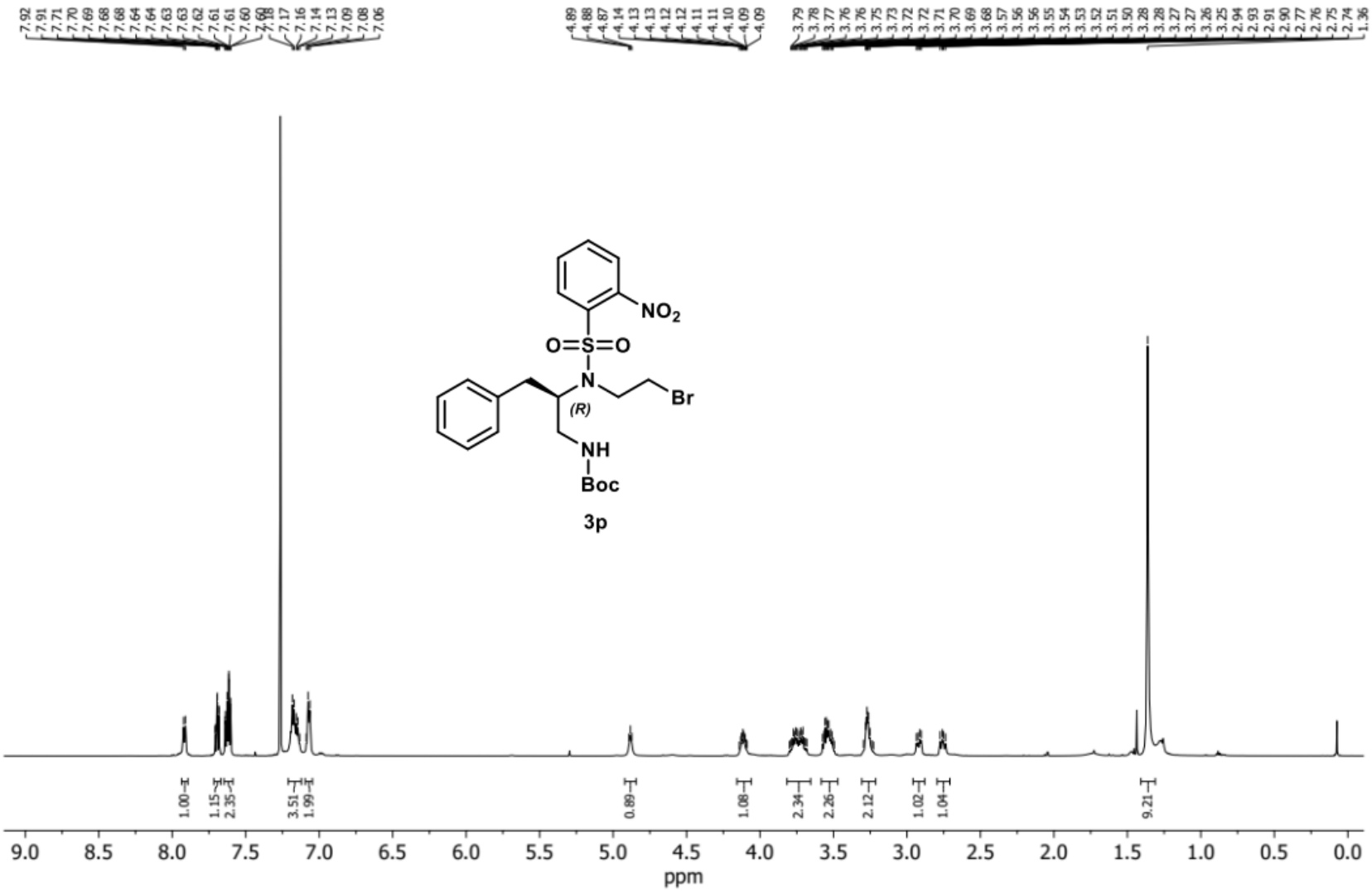

H1, 13C-HSQC
NO2
O=S=O
N
(S)
Br
NH
Boc
3m
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
ppm
-10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
ppm

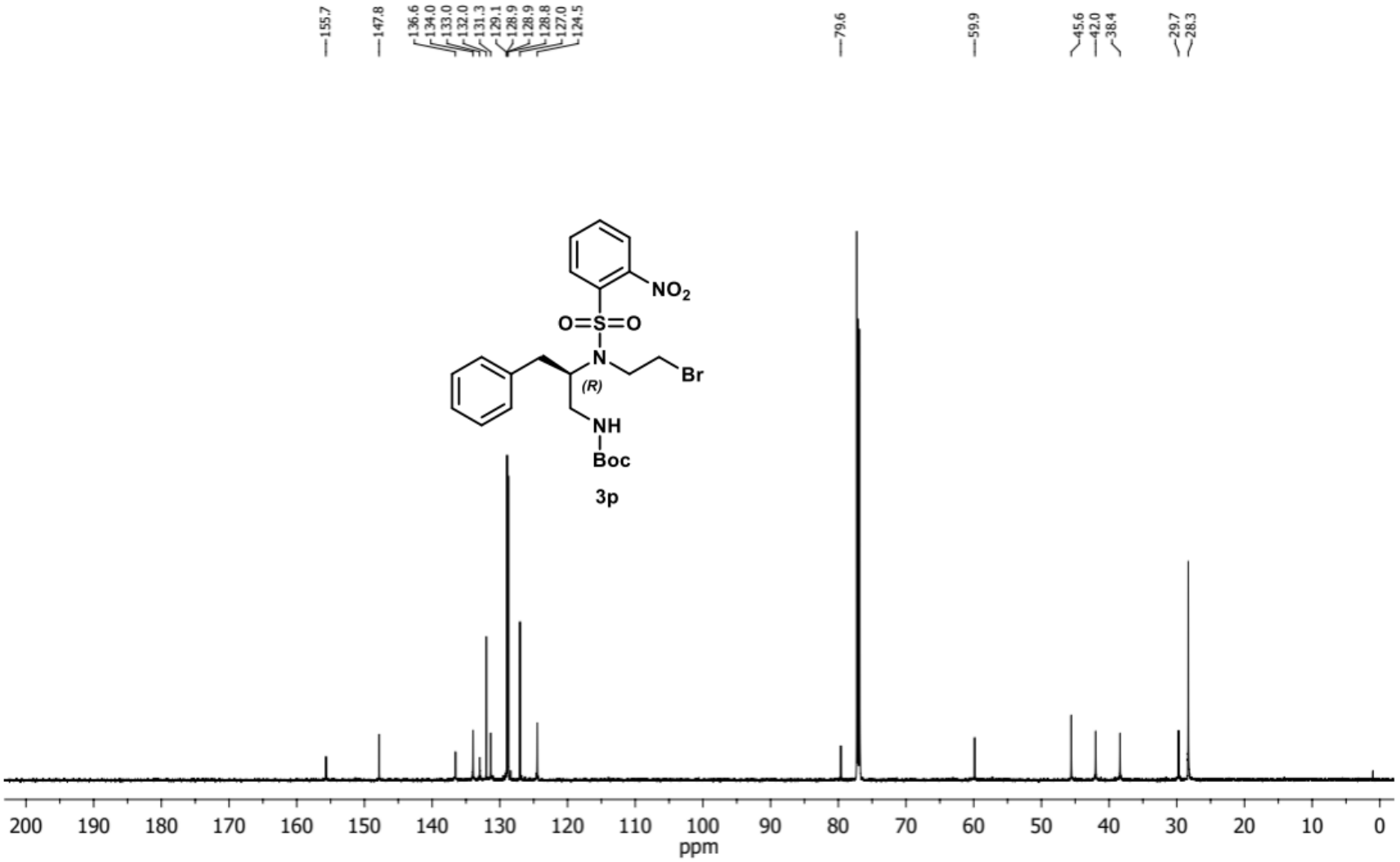

8.09 8.08 8.08 8.07 7.75 7.74 7.74 7.73 7.73 7.72 7.72 7.72 7.70 7.65 7.65 7.64 7.64 4.95 4.94 4.93 3.86 3.86 3.85 3.85 3.84 3.84 3.84 3.84 3.83 3.83 3.82 3.82 3.64 3.62 3.61 3.61 3.60 3.59 3.59 3.58 3.57 3.56 3.46 3.45 3.44 3.44 3.43 3.43 3.42 3.35 3.34 3.33 3.32 3.31 3.30 3.08 3.08 3.07 3.06 3.05 3.04 3.04 1.61 1.60 1.59 1.57 1.56 1.40 1.39 1.38 1.36 1.35 1.34 1.32 1.31 1.30 1.29 0.84 0.83 0.82
NO2
O=S=O
N
Br
(S)
NH
Boc
3n
1.00 2.38 1.12 0.98 1.20 3.59 1.26 1.09 1.21 1.32 13.74 7.54
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm


156.2
155.7
147.9
134.0
133.1
131.9
131.7
124.4
79.6
56.7
45.4
42.4
40.8
30.0
28.3
28.2
24.7
22.6
22.4
NO2
O=S=O
N
Br
(S)
NH
Boc
3n
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

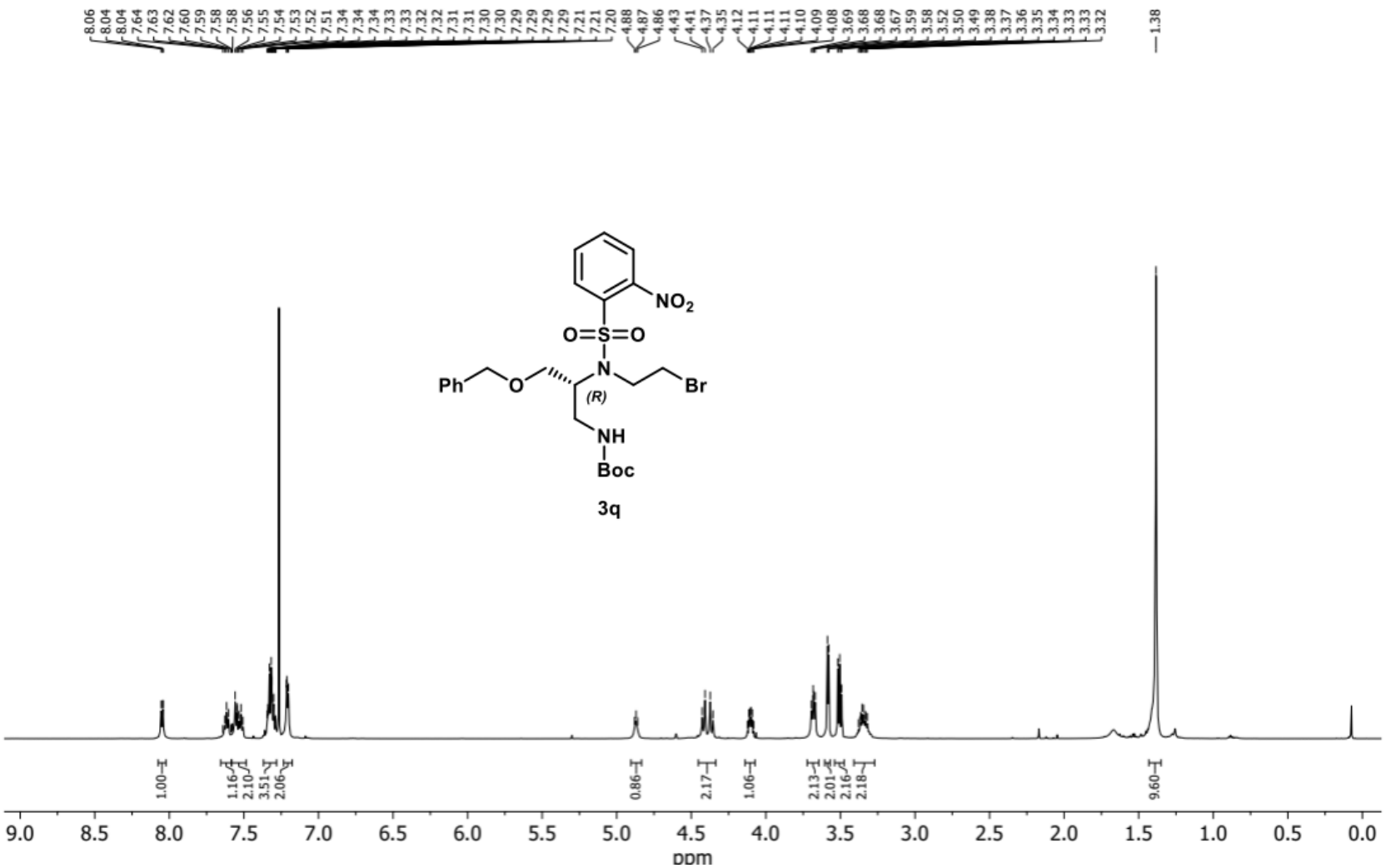

NO2
O=S=O
N
Br
(R)
NH
Boc
3o
1.00
2.27
1.10
0.92
1.14
3.40
1.19
1.03
1.15
1.24
12.81
6.45
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

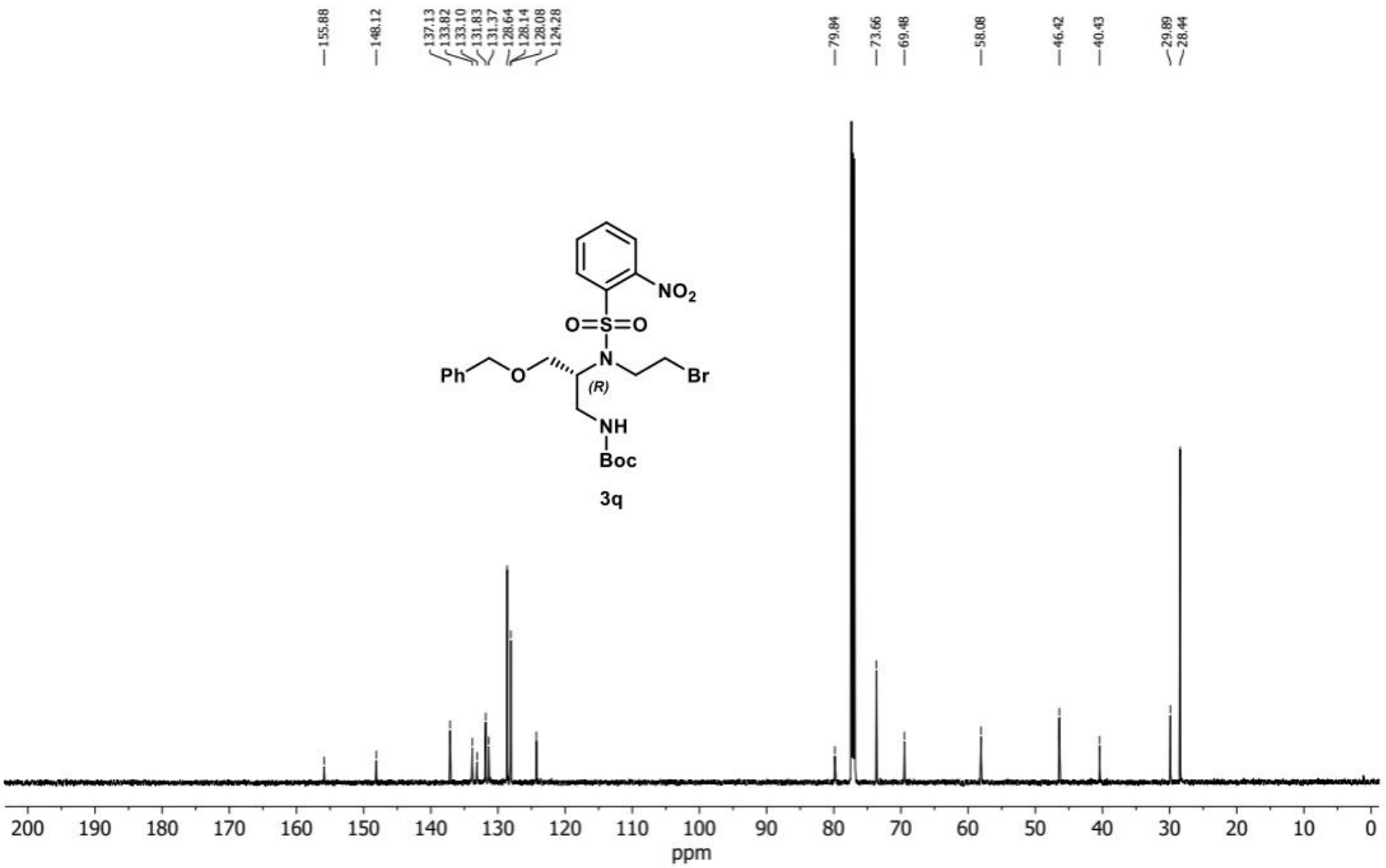

155.7
147.9
134.0
133.1
131.9
131.7
124.4
79.6
56.7
45.4
42.4
40.8
30.0
28.3
28.2
24.7
22.6
22.4
NO2
O=S=O
N
Br
(R)
NH
Boc
3o
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

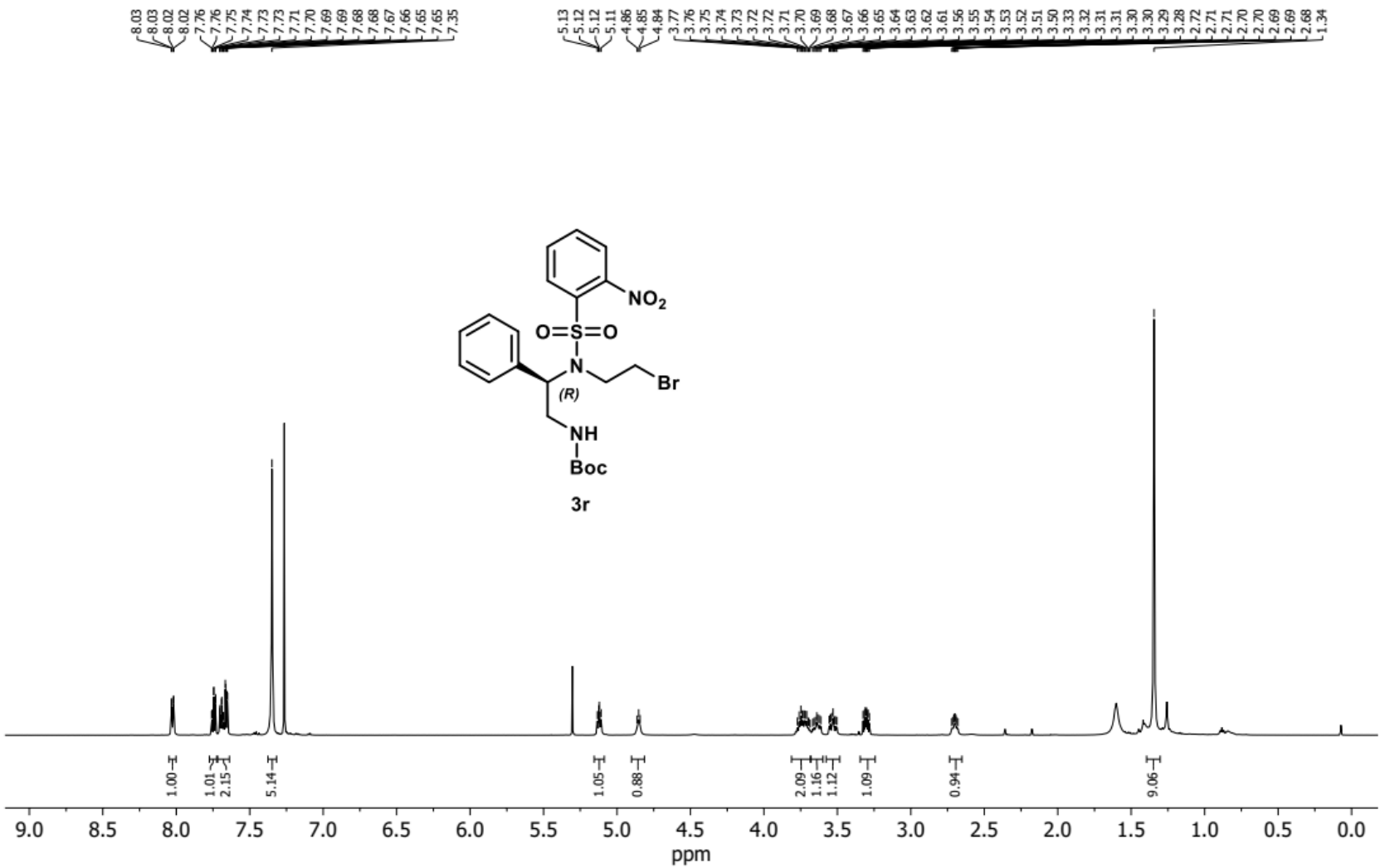

7.92 7.91 7.71 7.70 7.69 7.68 7.68 7.64 7.64 7.63 7.63 7.62 7.61 7.61 7.60 7.60 7.18 7.17 7.16 7.14 7.13 7.09 7.08 7.06
4.89 4.88 4.87 4.14 4.13 4.13 4.12 4.12 4.11 4.11 4.10 4.09 4.09
3.79 3.78 3.77 3.76 3.76 3.75 3.73 3.72 3.72 3.71 3.70 3.69 3.68 3.57 3.56 3.56 3.55 3.54 3.53 3.52 3.51 3.50 3.28 3.28 3.27 3.27 3.26 3.25 2.94 2.93 2.91 2.90 2.77 2.76 2.75 2.74 1.36
NO2
O=S=O
N
Br
(R)
NH
Boc
3p
1.00 1.15 2.35 3.51 1.99 0.89 1.08 2.34 2.26 2.12 1.02 1.04 9.21
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm


155.7
147.8
136.6
134.0
133.0
132.0
131.3
129.1
128.9
128.9
128.8
127.0
124.5
79.6
59.9
45.6
42.0
38.4
29.7
28.3
NO2
O=S=O
N
Br
(R)
NH
Boc
3p
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

,


8.06 8.04 8.04 7.64 7.63 7.62 7.60 7.59 7.58 7.58 7.56 7.55 7.54 7.53 7.52 7.51 7.34 7.34 7.34 7.33 7.33 7.32 7.32 7.31 7.31 7.30 7.30 7.29 7.29 7.29 7.29 7.21 7.21 7.20 4.88 4.87 4.86 4.43 4.41 4.37 4.35 4.12 4.11 4.11 4.11 4.10 4.09 4.08 3.69 3.68 3.68 3.67 3.59 3.58 3.52 3.50 3.49 3.38 3.37 3.36 3.35 3.34 3.33 3.33 3.32 1.38
NO2
O=S=O
N
Ph
O
(R)
Br
NH
Boc
3q
1.00 1.16 2.10 3.51 2.06 0.86 2.17 1.06 2.13 2.01 2.16 2.18 9.60
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm


155.88
148.12
137.13
133.82
133.10
131.83
131.37
128.64
128.14
128.08
124.28
79.84
73.66
69.48
58.08
46.42
40.43
29.89
28.44
NO2
O=S=O
N
Ph
O
(R)
Br
NH
Boc
3q
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


8.03
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8.02
8.02
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7.74
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7.73
7.71
7.70
7.69
7.69
7.68
7.68
7.67
7.66
7.65
7.65
7.35
5.13
5.12
5.12
5.11
4.86
4.85
4.84
3.77
3.76
3.75
3.74
3.73
3.72
3.72
3.71
3.70
3.69
3.68
3.67
3.66
3.65
3.64
3.63
3.62
3.61
3.56
3.55
3.54
3.53
3.52
3.51
3.50
3.33
3.32
3.31
3.31
3.30
3.30
3.29
3.28
2.72
2.71
2.71
2.70
2.70
2.69
2.69
2.68
1.34
NO2
O=S=O
N
Br
(R)
NH
Boc
3r
1.00
1.01
2.15
5.14
1.05
0.88
2.09
1.16
1.12
1.09
0.94
9.06
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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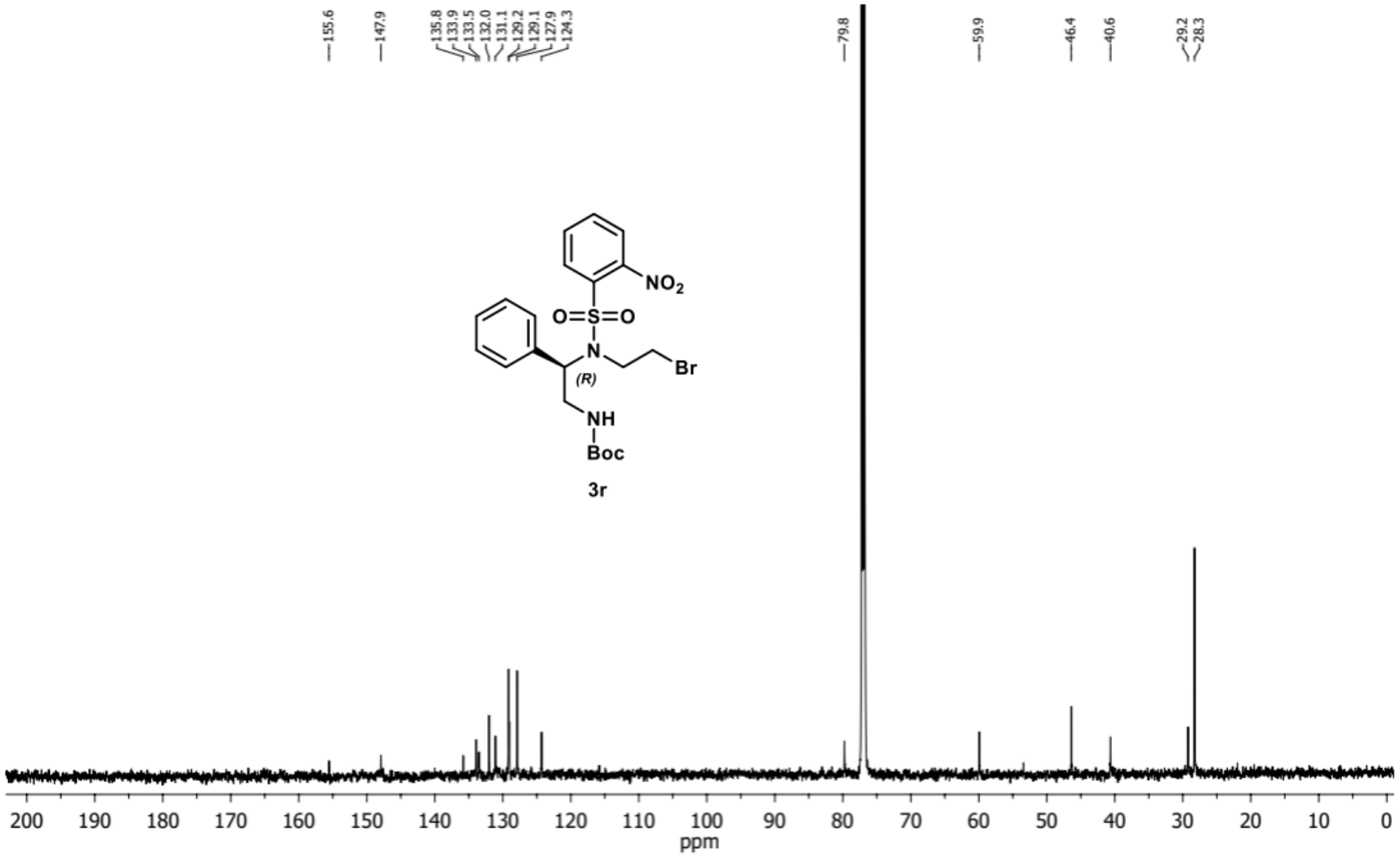
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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129.2
129.1
127.9
124.3
79.8
59.9
46.4
40.6
29.2
28.3
NO2
O=S=O
N
Br
(R)
NH
Boc
3r
200
190
180
170
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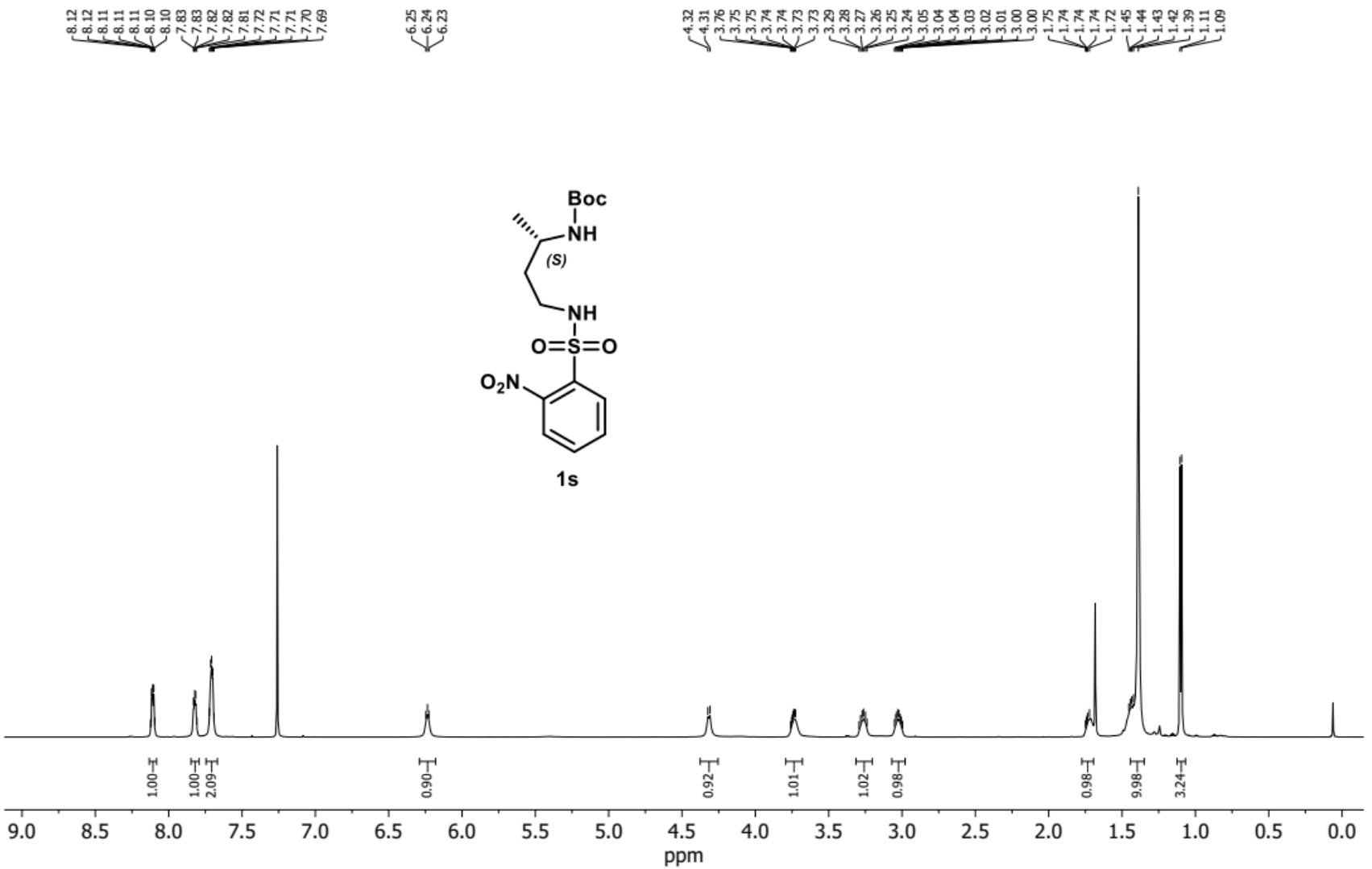
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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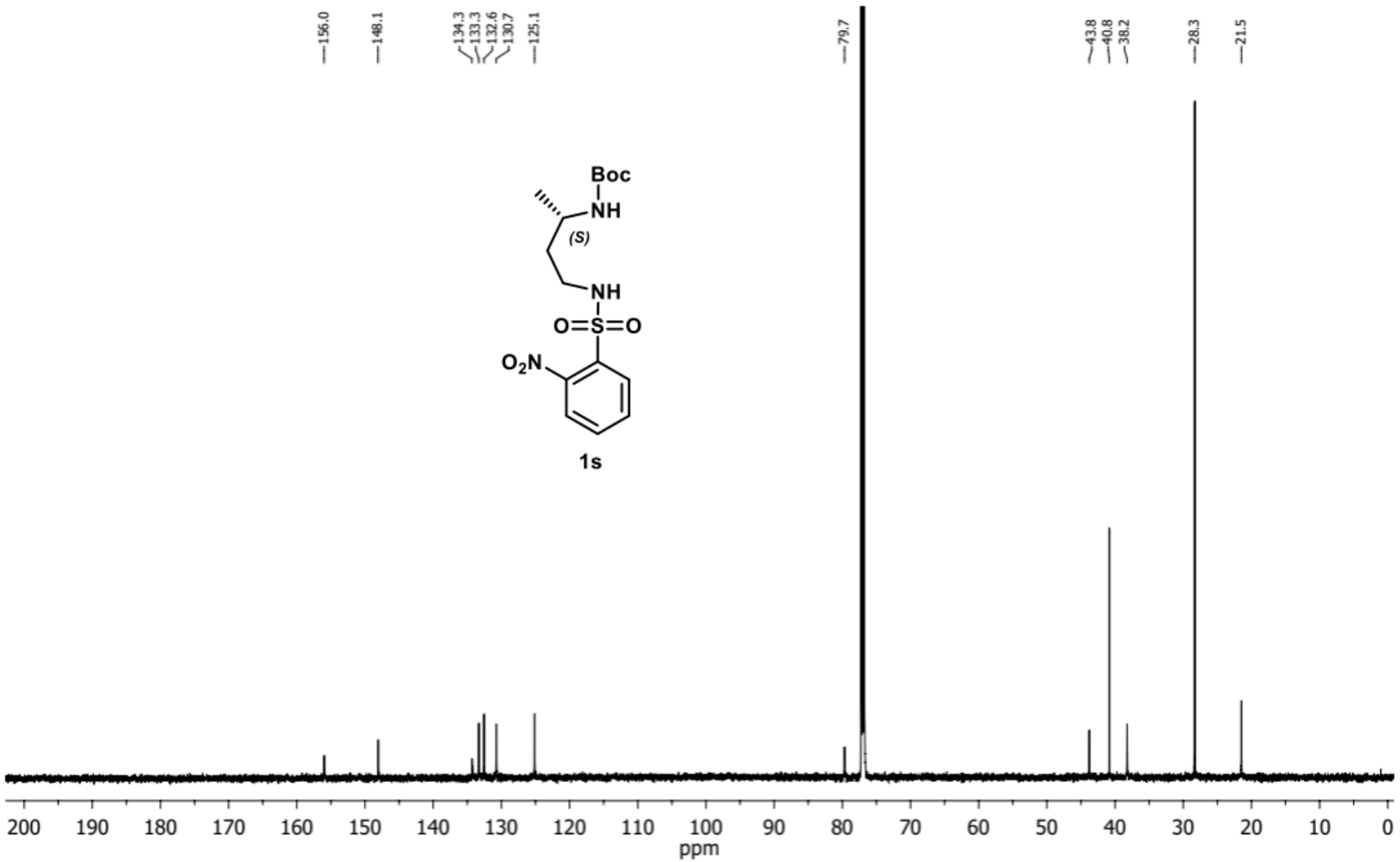
7.82
7.82
7.81
7.72
7.71
7.71
7.70
7.69
6.25
6.24
6.23
4.32
4.31
3.76
3.75
3.75
3.74
3.74
3.73
3.73
3.29
3.28
3.27
3.26
3.25
3.24
3.05
3.04
3.04
3.03
3.02
3.01
3.00
3.00
1.75
1.74
1.74
1.74
1.72
1.45
1.44
1.43
1.42
1.39
1.11
1.09
Boc
NH
(S)
NH
O=S=O
O2N
1s
1.00
1.00
2.09
0.90
0.92
1.01
1.02
0.98
0.98
9.98
3.24
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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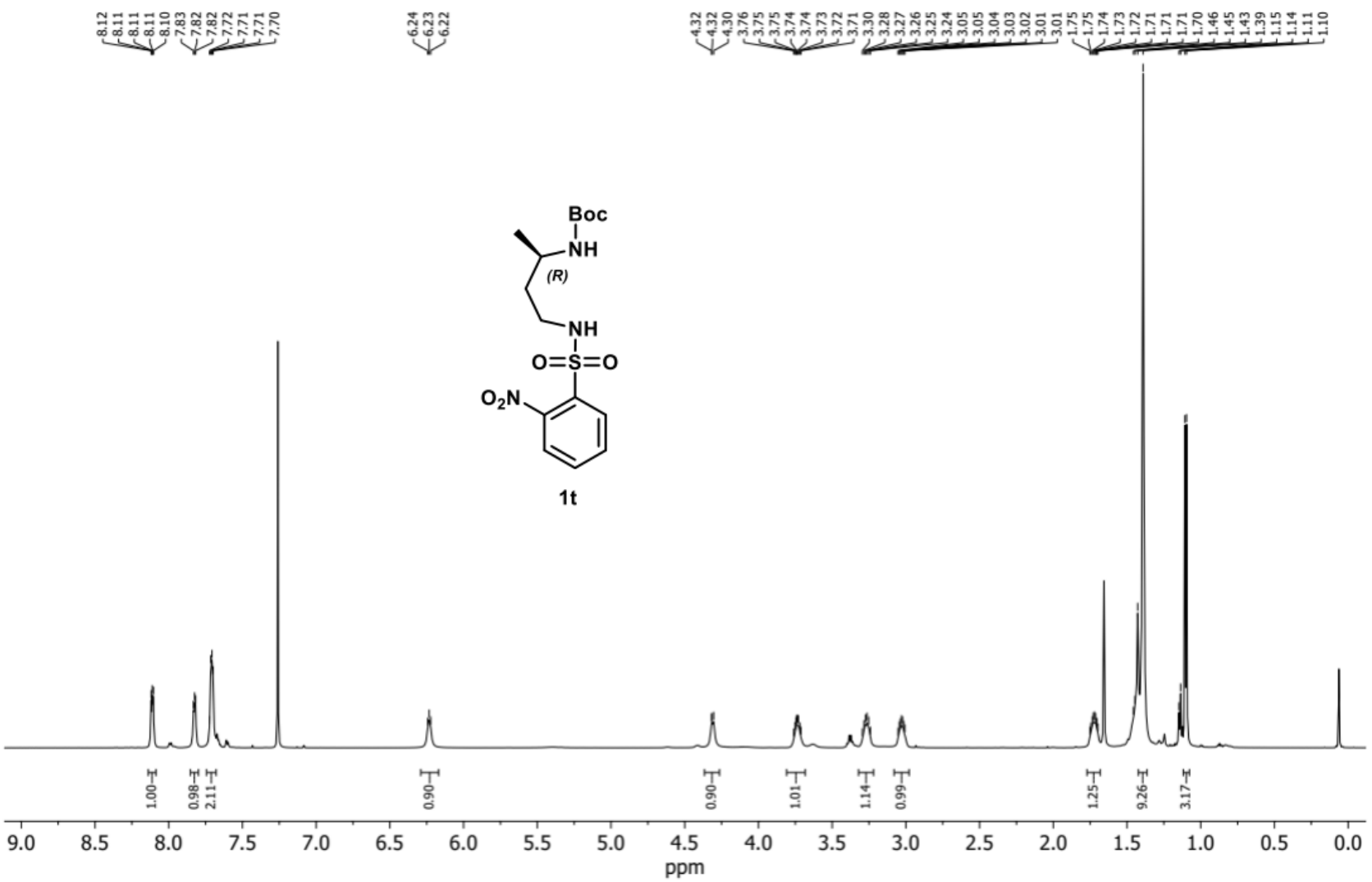
148.1
134.3
133.3
132.6
130.7
125.1
79.7
43.8
40.8
38.2
28.3
21.5
Boc
NH
(S)
NH
O=S=O
O2N
1s
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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8.11
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7.82
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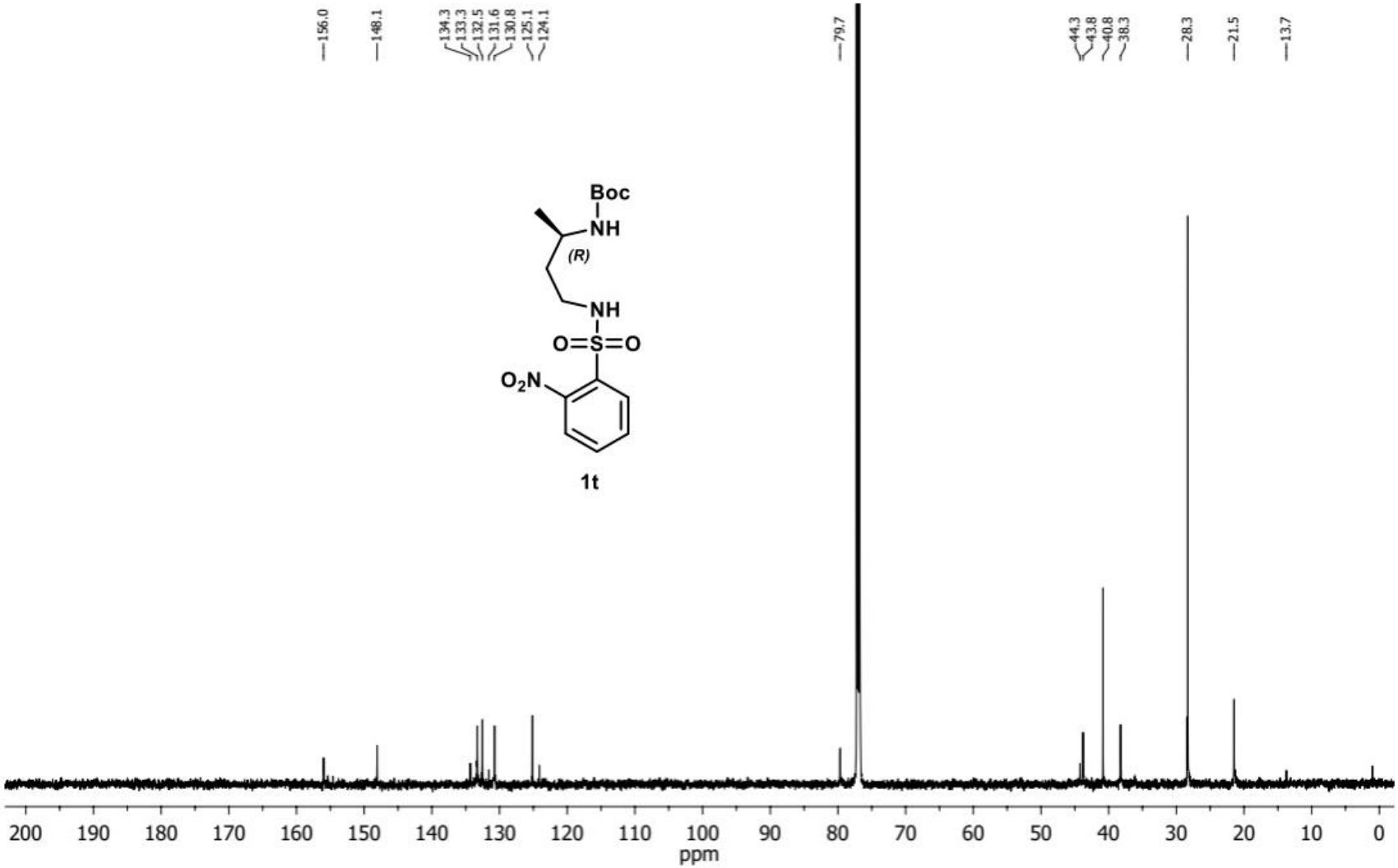
7.71
7.71
7.70
6.24
6.23
6.22
4.32
4.32
4.30
3.76
3.75
3.75
3.74
3.74
3.73
3.72
3.71
3.30
3.28
3.27
3.26
3.25
3.24
3.05
3.05
3.04
3.03
3.02
3.01
3.01
1.75
1.75
1.74
1.73
1.72
1.71
1.71
1.71
1.70
1.46
1.45
1.43
1.39
1.15
1.14
1.11
1.10
Boc
NH
(R)
NH
O=S=O
O2N
1t
1.00
0.98
2.11
0.90
0.90
1.01
1.14
0.99
1.25
9.26
3.17
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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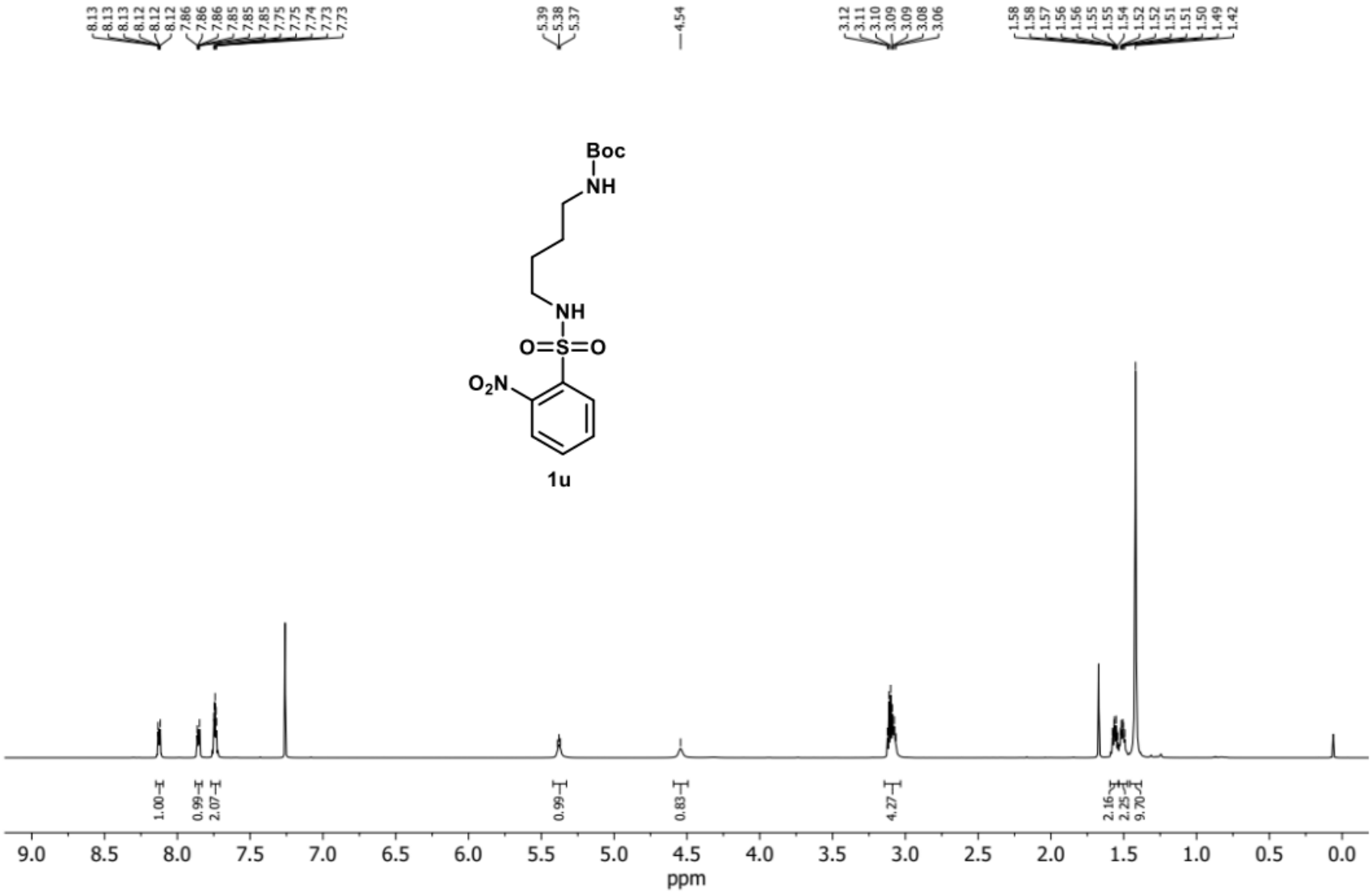
134.3
133.3
132.5
131.6
130.8
125.1
124.1
79.7
44.3
43.8
40.8
38.3
28.3
21.5
13.7
Boc
NH
(R)
NH
O=S=O
O2N
1t
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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8.13
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7.86
7.86
7.85
7.85
7.85
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7.75
7.74
7.73
7.73
5.39
5.38
5.37
4.54
3.12
3.11
3.10
3.09
3.09
3.08
3.06
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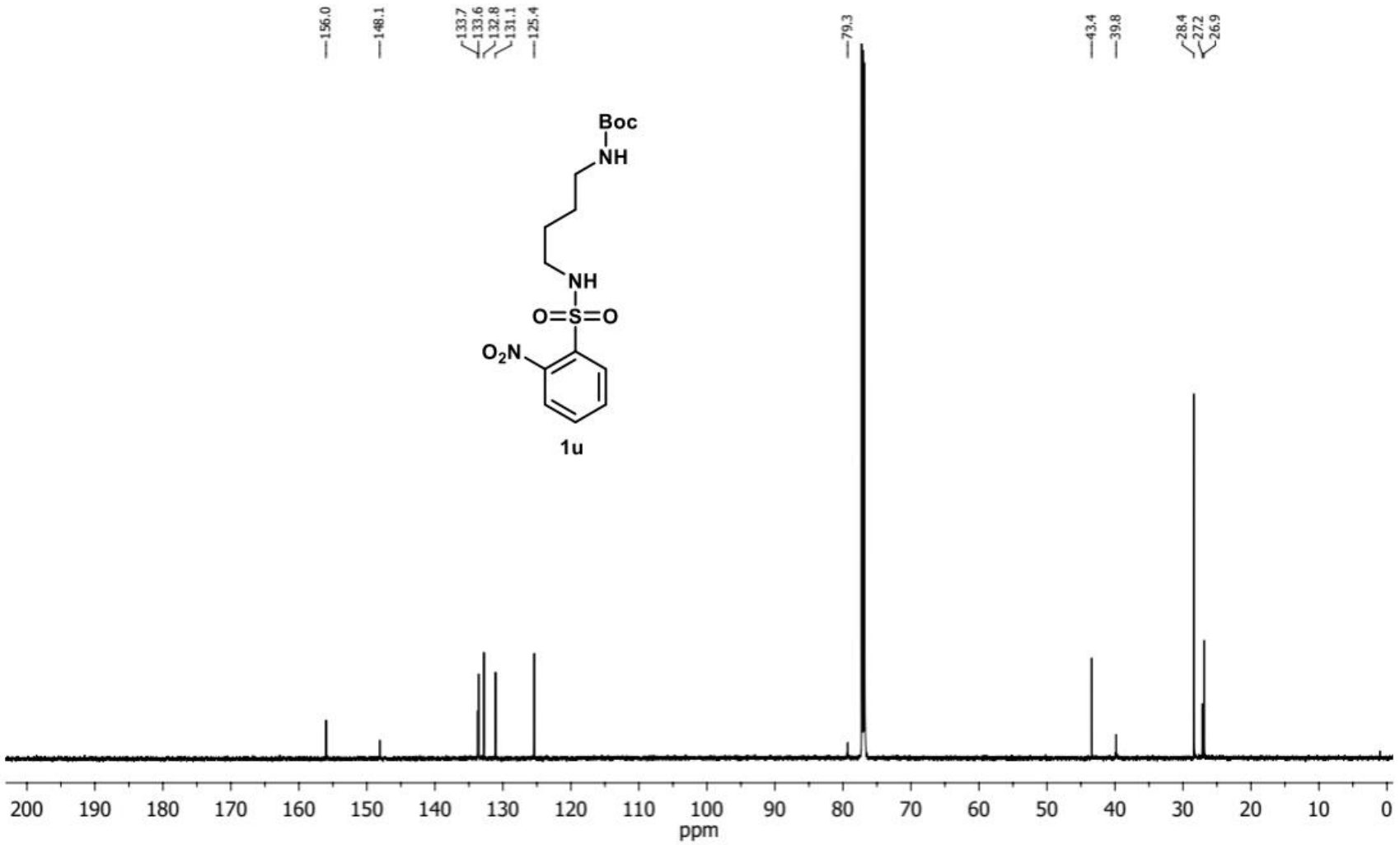
1.58
1.57
1.56
1.56
1.55
1.55
1.54
1.52
1.52
1.51
1.51
1.50
1.49
1.42
Boc
NH
NH
O=S=O
O2N
1u
1.00
0.99
2.07
0.99
0.83
4.27
2.16
2.25
9.70
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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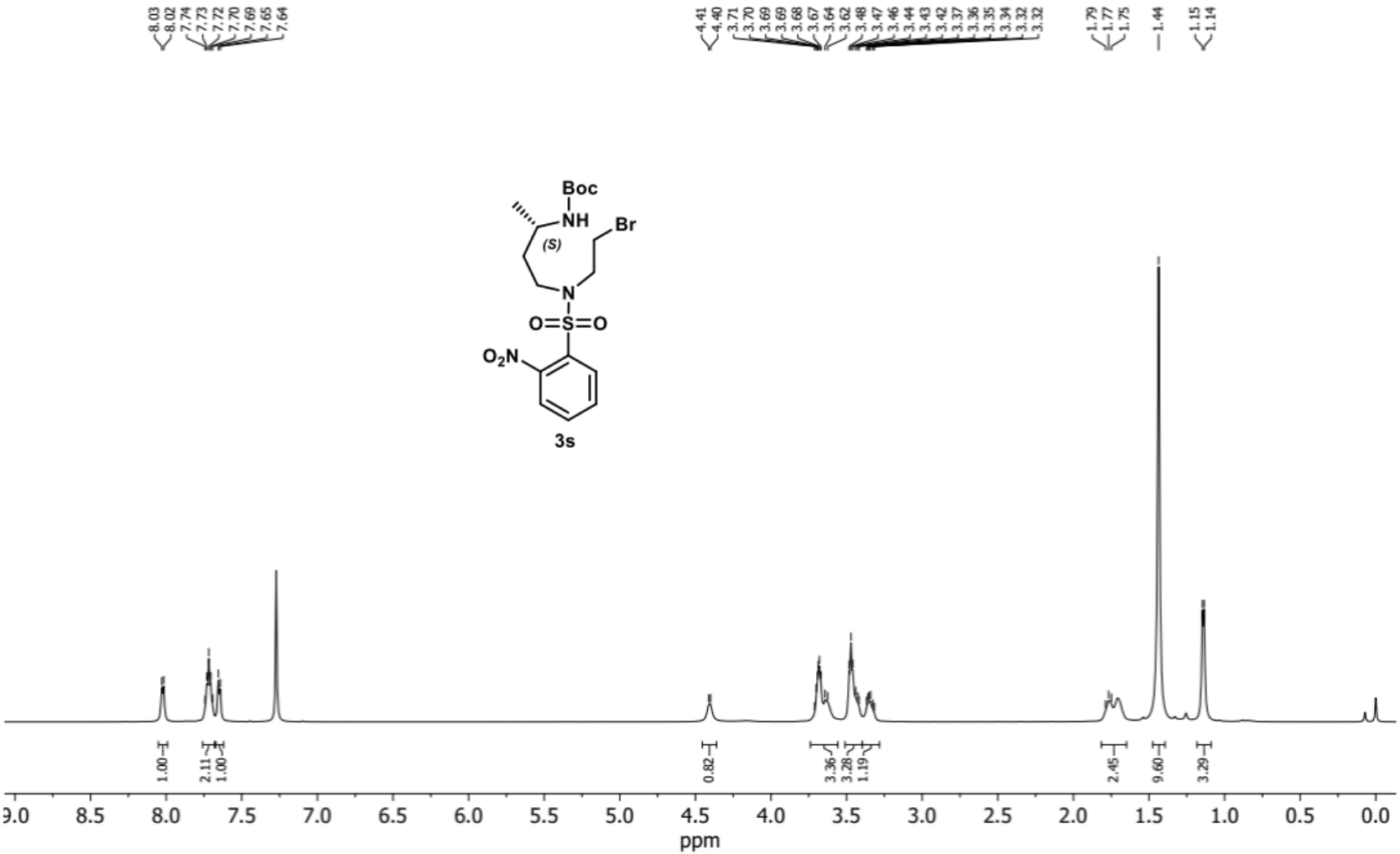
133.7
133.6
132.8
131.1
125.4
79.3
43.4
39.8
28.4
27.2
26.9
Boc
NH
NH
O=S=O
O2N
1u
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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8.02
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7.70
7.69
7.65
7.64
4.41
4.40
3.71
3.70
3.69
3.69
3.68
3.67
3.64
3.62
3.48
3.47
3.46
3.44
3.43
3.42
3.37
3.36
3.35
3.34
3.32
3.32
1.79
1.77
1.75
1.44
1.15
1.14
Boc
NH
(S)
Br
N
O=S=O
O2N
3s
1.00
2.11
1.00
0.82
3.36
3.28
1.19
2.45
9.60
3.29
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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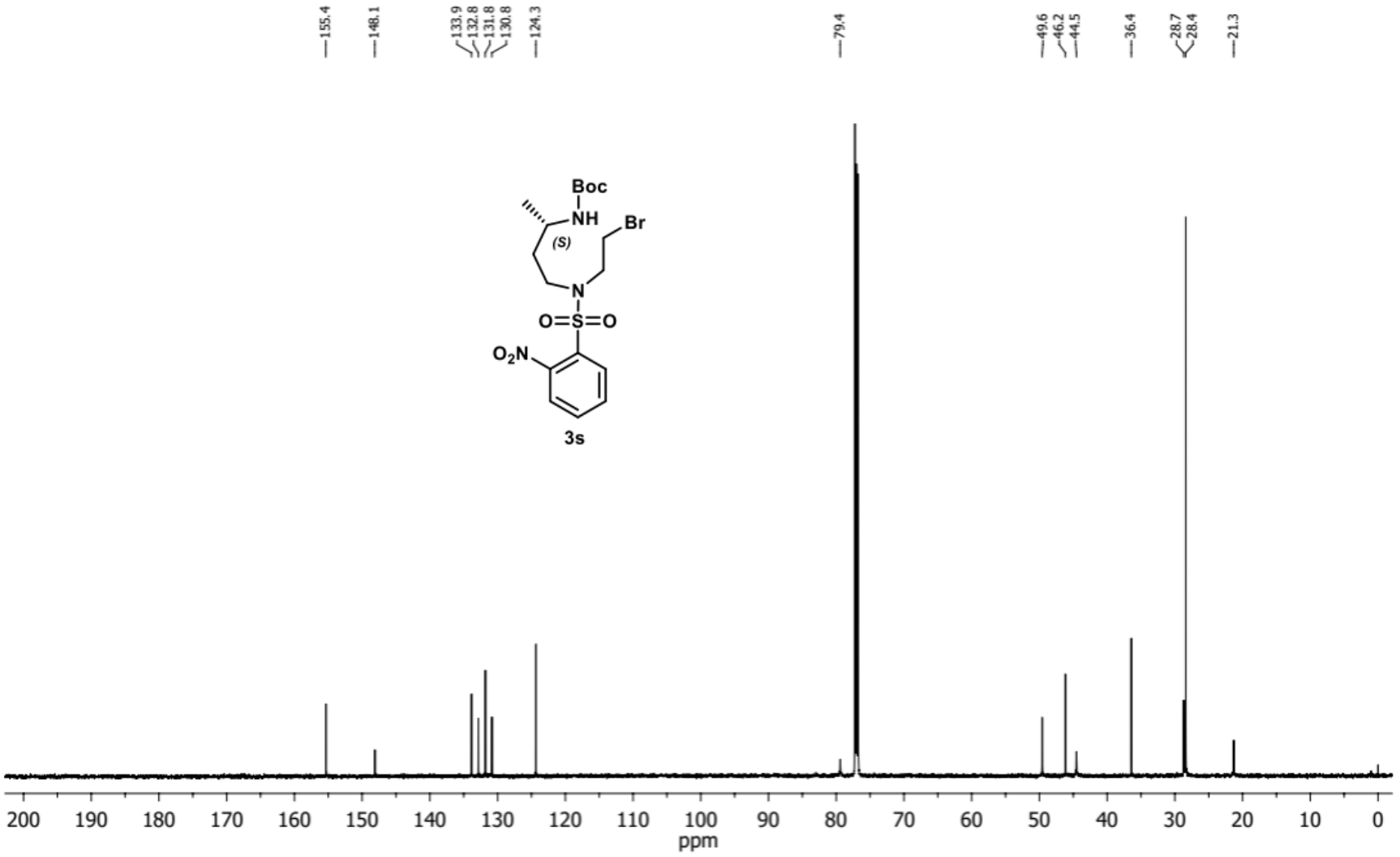
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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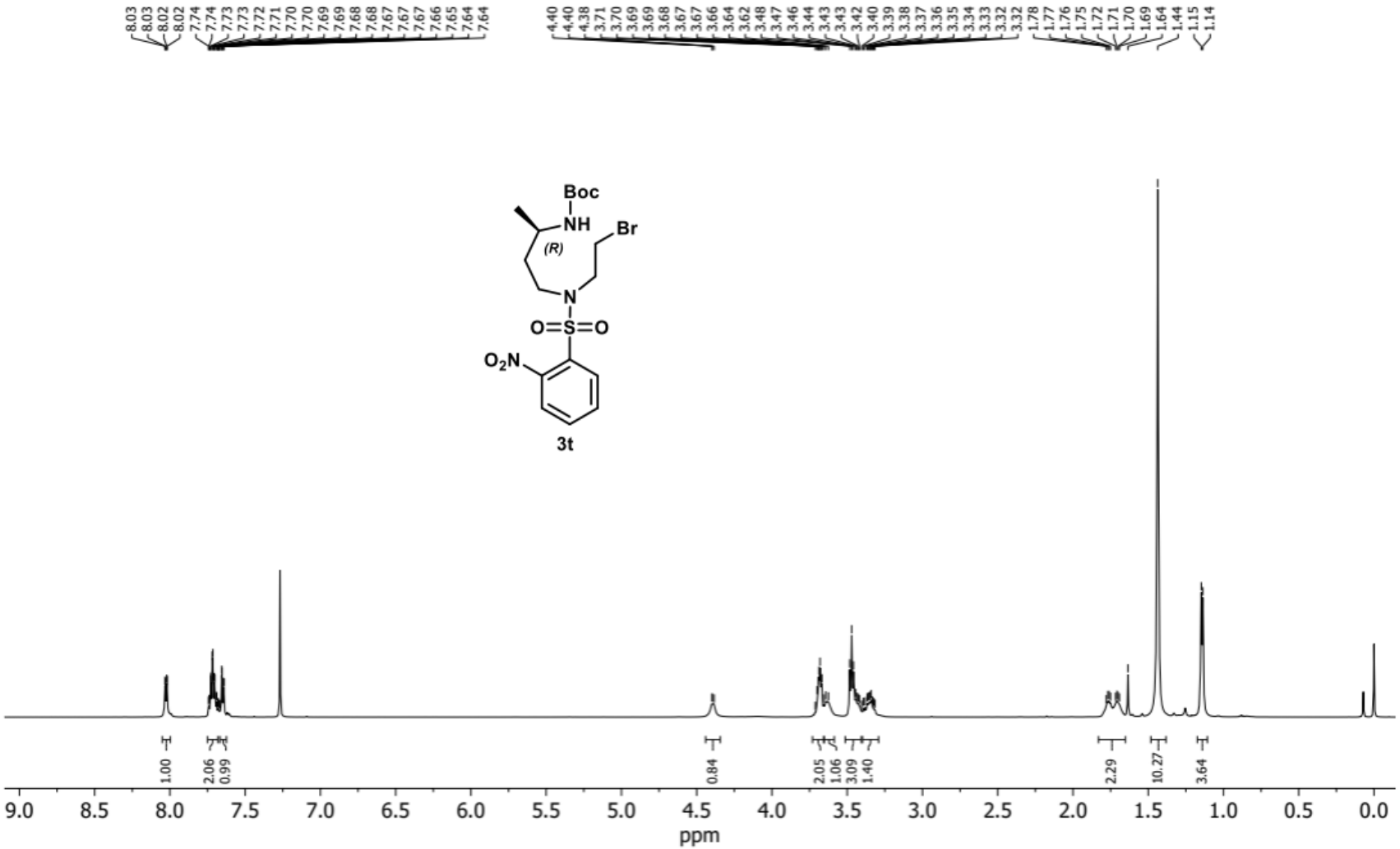
132.8
131.8
130.8
124.3
79.4
49.6
46.2
44.5
36.4
28.7
28.4
21.3
Boc
NH
Br
(S)
N
O=S=O
O2N
3s
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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8.03
8.02
8.02
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7.74
7.73
7.73
7.72
7.71
7.70
7.70
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7.69
7.68
7.68
7.67
7.67
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7.66
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4.40
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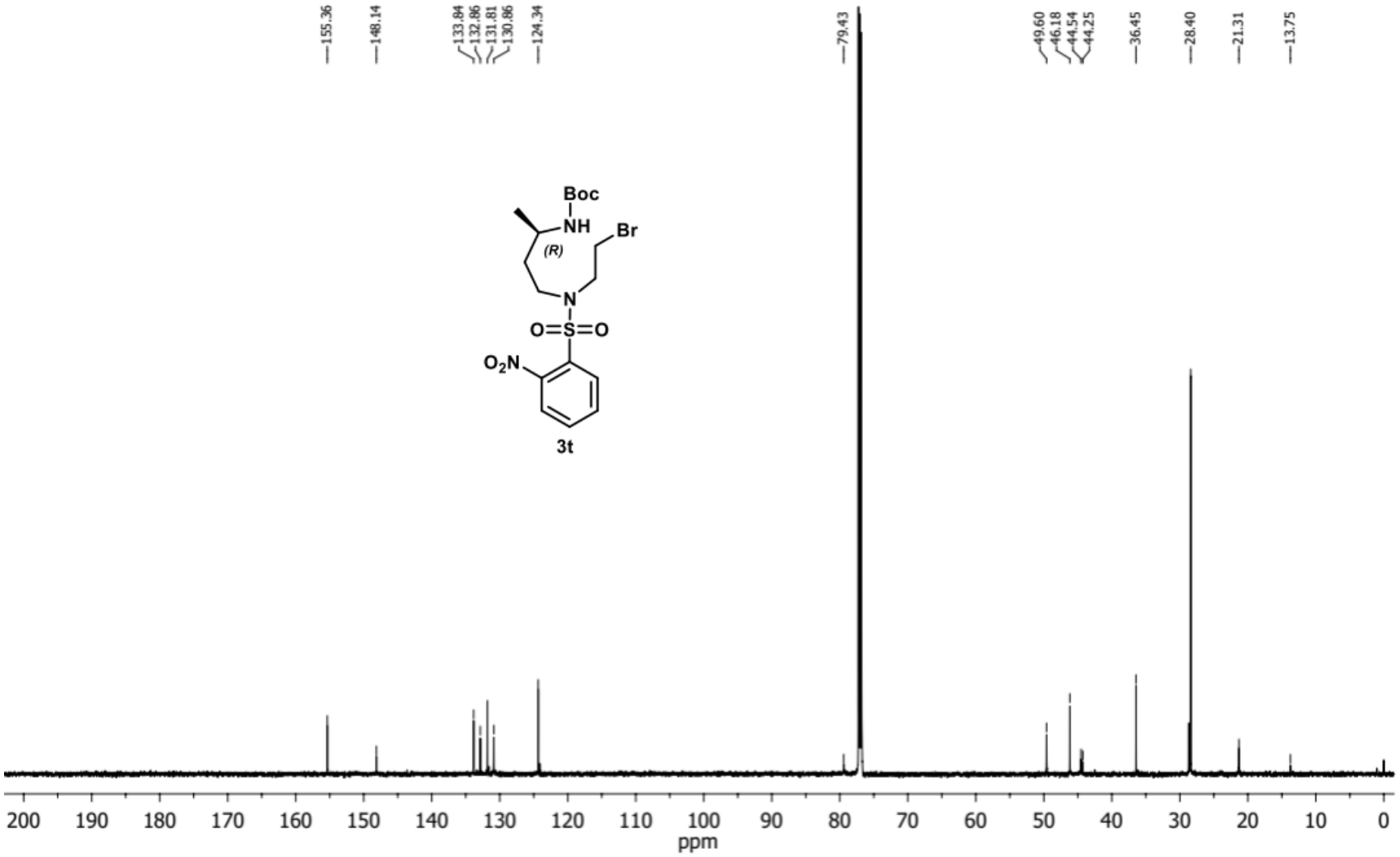
3.70
3.69
3.69
3.68
3.67
3.67
3.66
3.64
3.62
3.48
3.47
3.46
3.44
3.43
3.43
3.42
3.40
3.39
3.38
3.37
3.36
3.35
3.34
3.33
3.32
3.32
1.78
1.77
1.76
1.75
1.72
1.71
1.70
1.69
1.64
1.44
1.15
1.14
Boc
NH
(R)
Br
N
O=S=O
O2N
3t
1.00
2.06
0.99
0.84
2.05
1.06
3.09
1.40
2.29
10.27
3.64
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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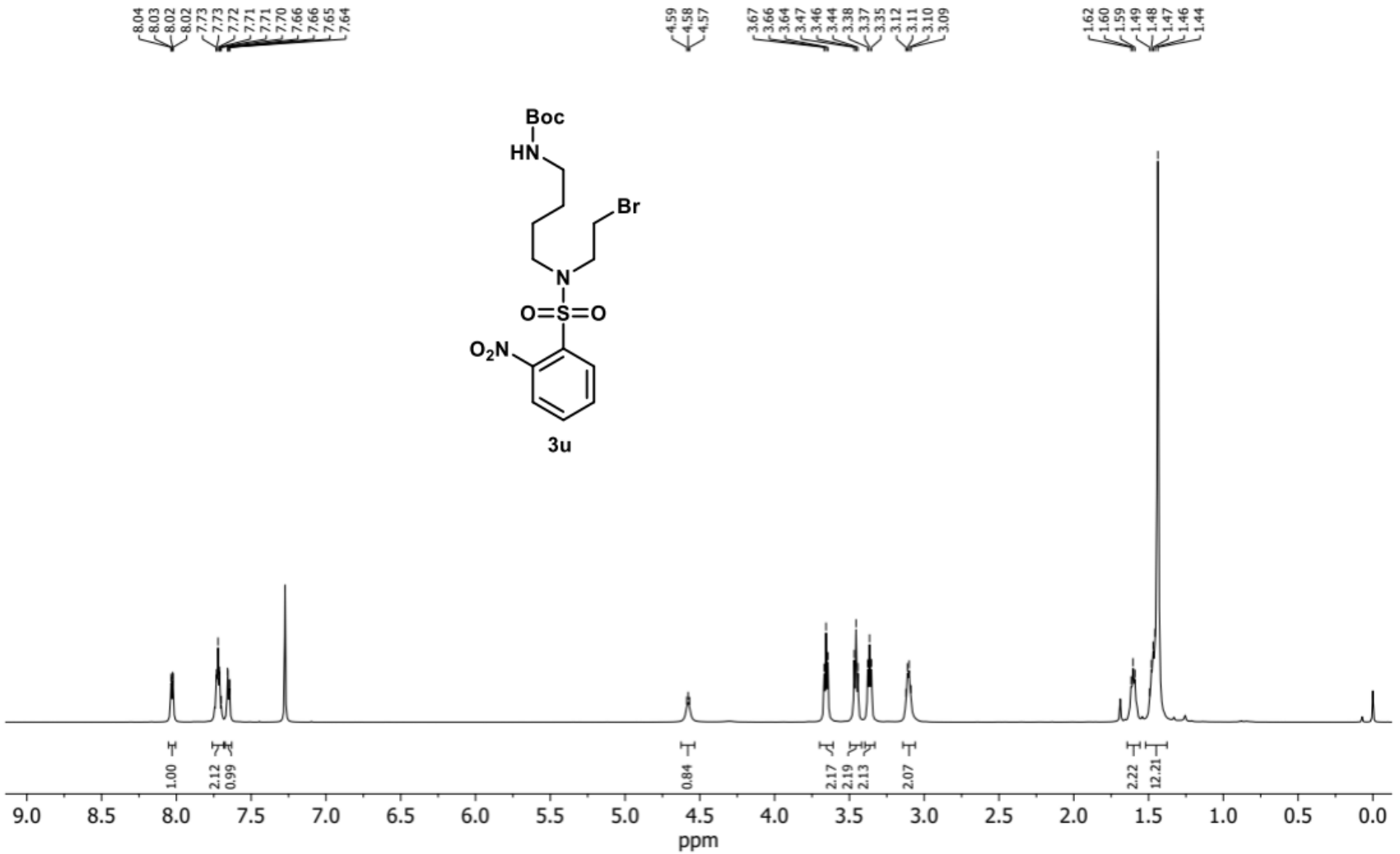
124.34
79.43
49.60
46.18
44.54
44.25
36.45
28.40
21.31
13.75
Boc
NH
(R)
Br
N
O=S=O
O2N
3t
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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7.66
7.65
7.64
4.59
4.58
4.57
3.67
3.66
3.64
3.47
3.46
3.44
3.38
3.37
3.35
3.12
3.11
3.10
3.09
1.62
1.60
1.59
1.49
1.48
1.47
1.46
1.44
Boc
HN
Br
N
O=S=O
O2N
3u
1.00
2.12
0.99
0.84
2.17
2.19
2.13
2.07
2.22
12.21
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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4.0
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3.0
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1.5
1.0
0.5
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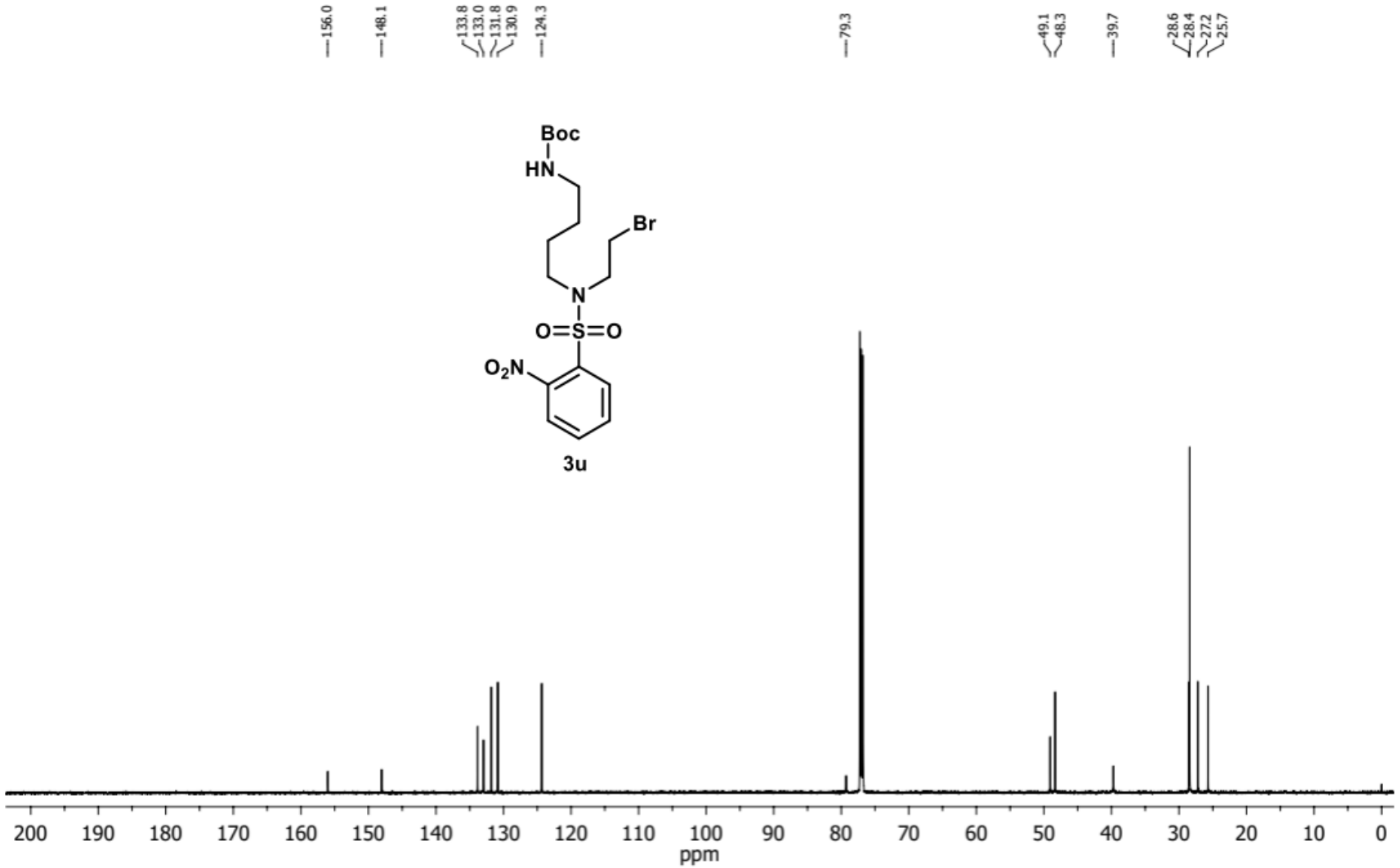
ppm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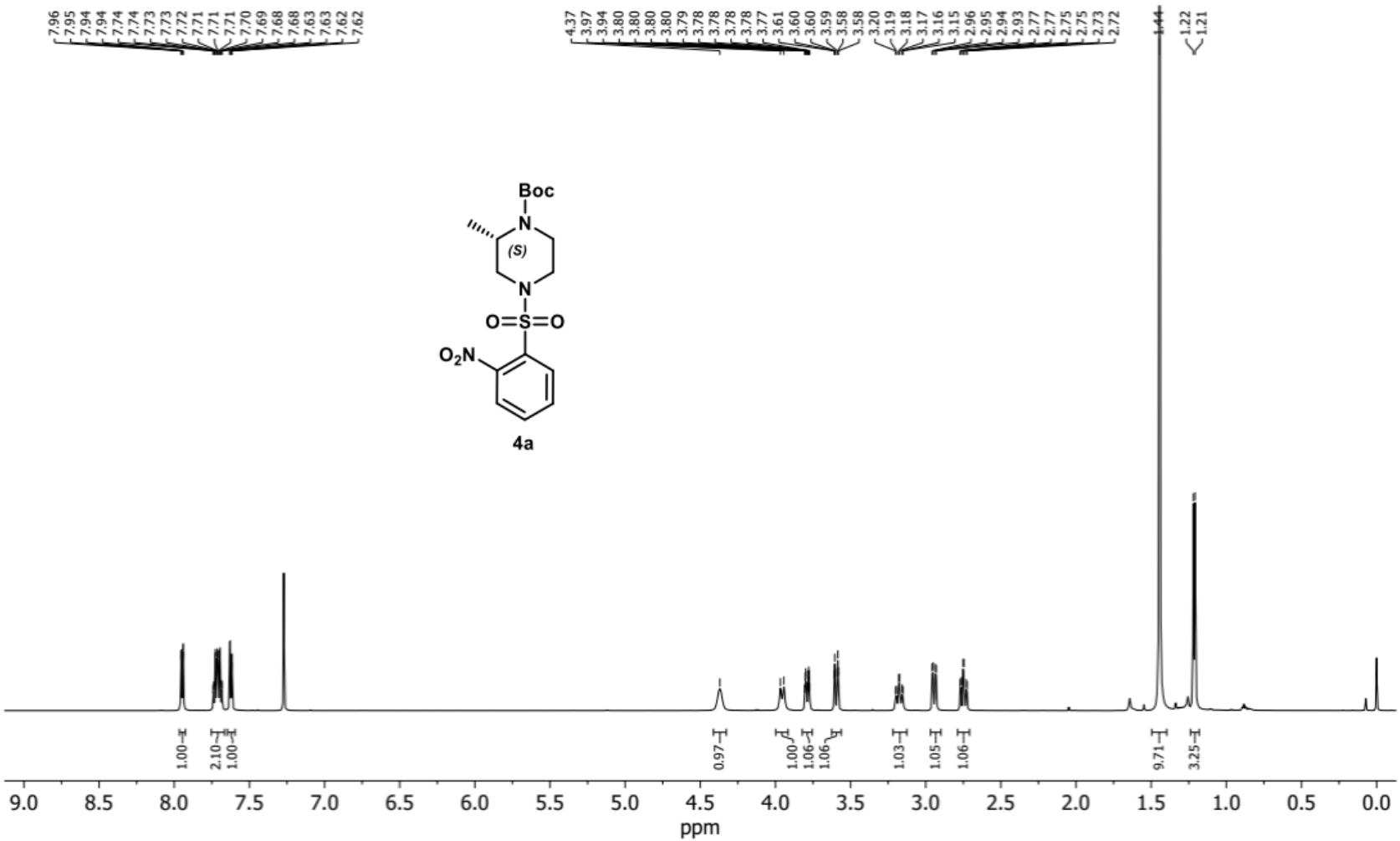
133.8
133.0
131.8
130.9
124.3
79.3
49.1
48.3
39.7
28.6
28.4
27.2
25.7
Boc
HN
Br
N
O=S=O
O2N
3u
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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7.71
7.71
7.71
7.70
7.69
7.68
7.68
7.63
7.63
7.62
7.62
4.37
3.97
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3.80
3.80
3.80
3.79
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3.78
3.78
3.78
3.77
3.61
3.60
3.60
3.59
3.58
3.58
3.20
3.19
3.18
3.17
3.16
3.15
2.96
2.95
2.94
2.93
2.77
2.77
2.75
2.75
2.73
2.72
1.44
1.22
1.21
Boc
N
(S)
N
O=S=O
O2N
4a
1.00
2.10
1.00
0.97
1.00
1.06
1.06
1.03
1.05
1.06
9.71
3.25
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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4.0
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2.0
1.5
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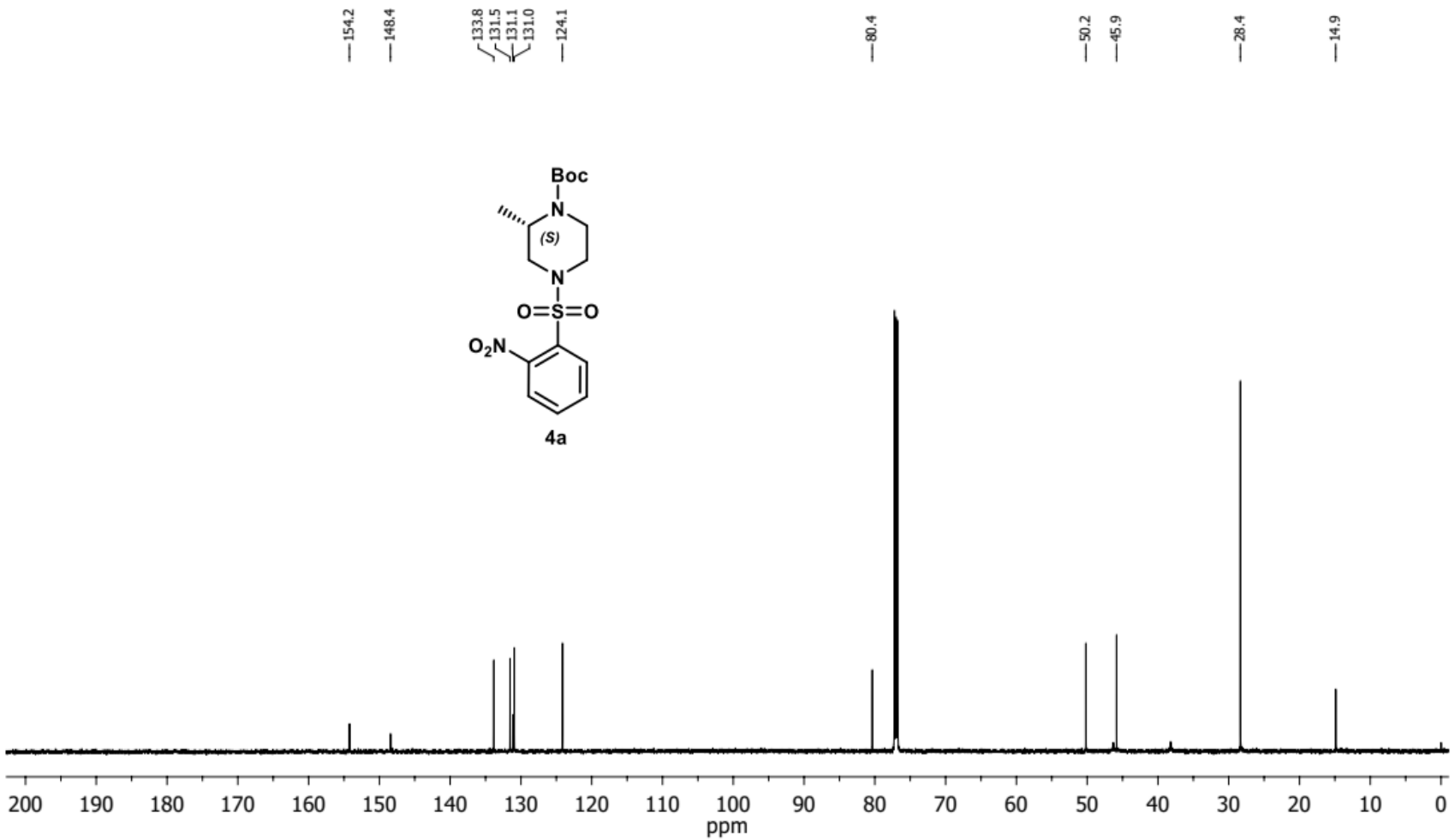
ppm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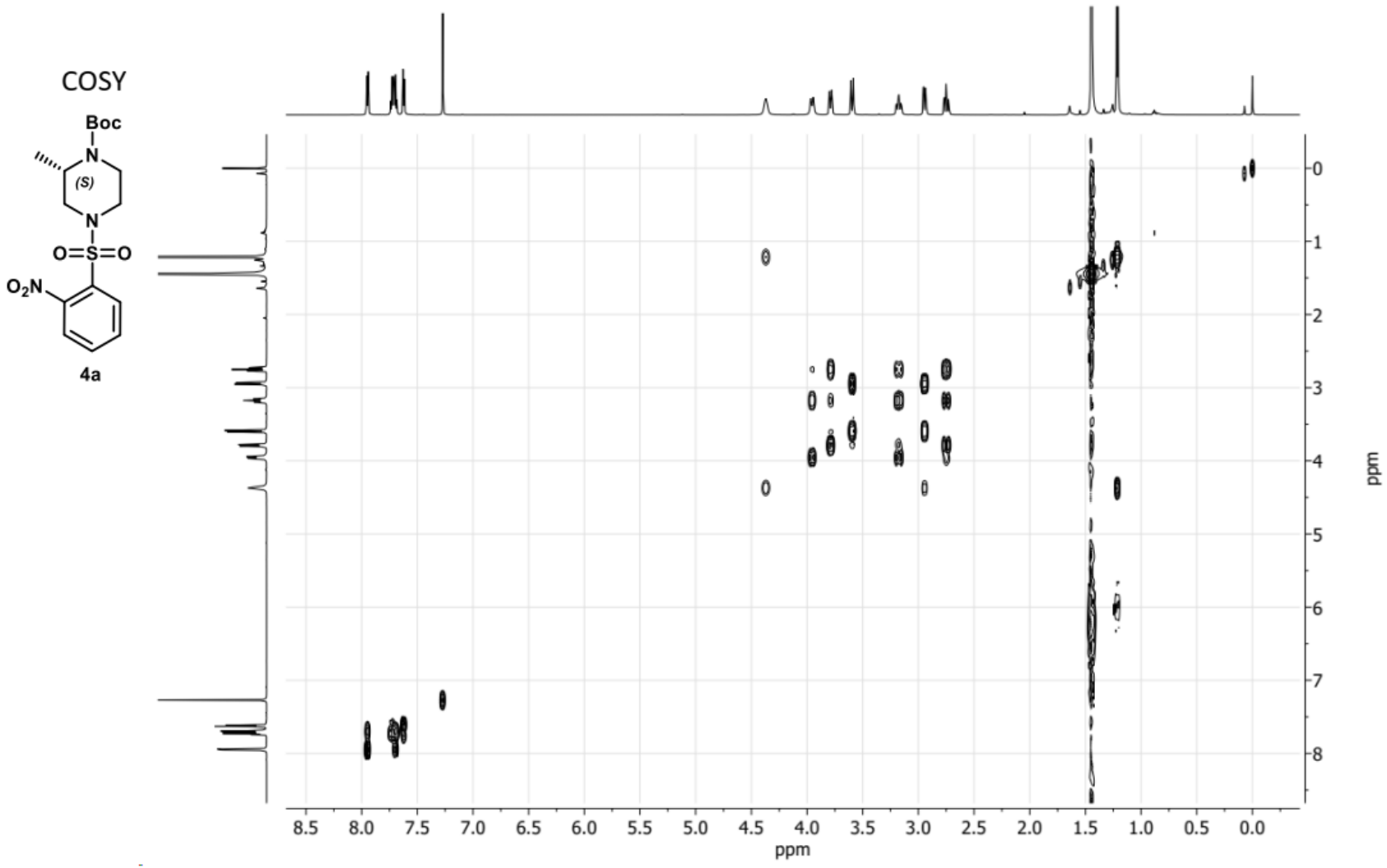
131.5
131.1
131.0
124.1
80.4
50.2
45.9
28.4
14.9
Boc
N
(S)
N
O=S=O
O2N
4a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


COSY
Boc
N
(S)
N
O=S=O
O2N
4a
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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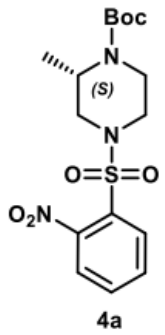
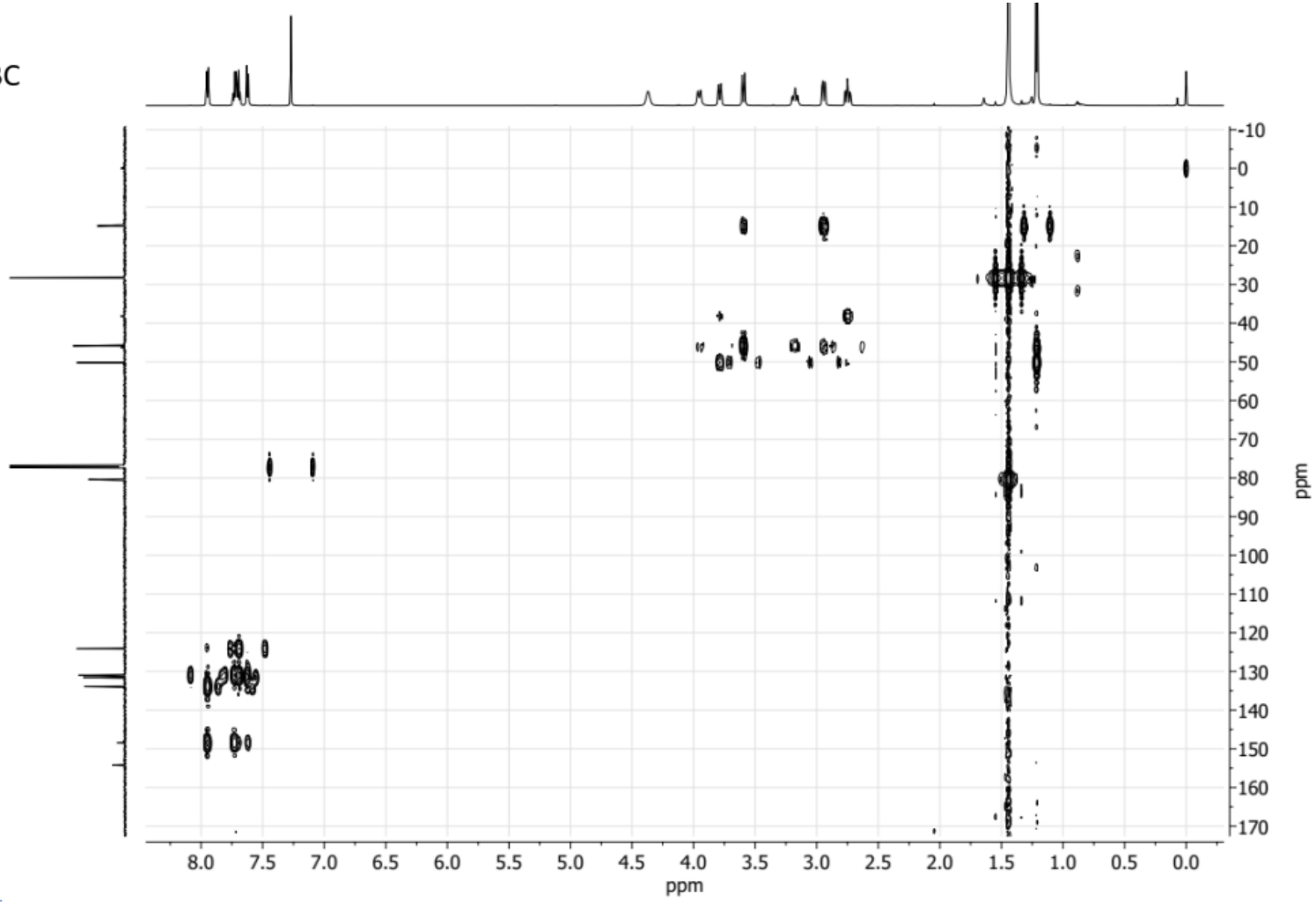
ppm
0
1
2
3
4
5
6
7
8
ppm

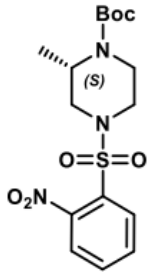
^{1}H, ^{13}C-HMBC



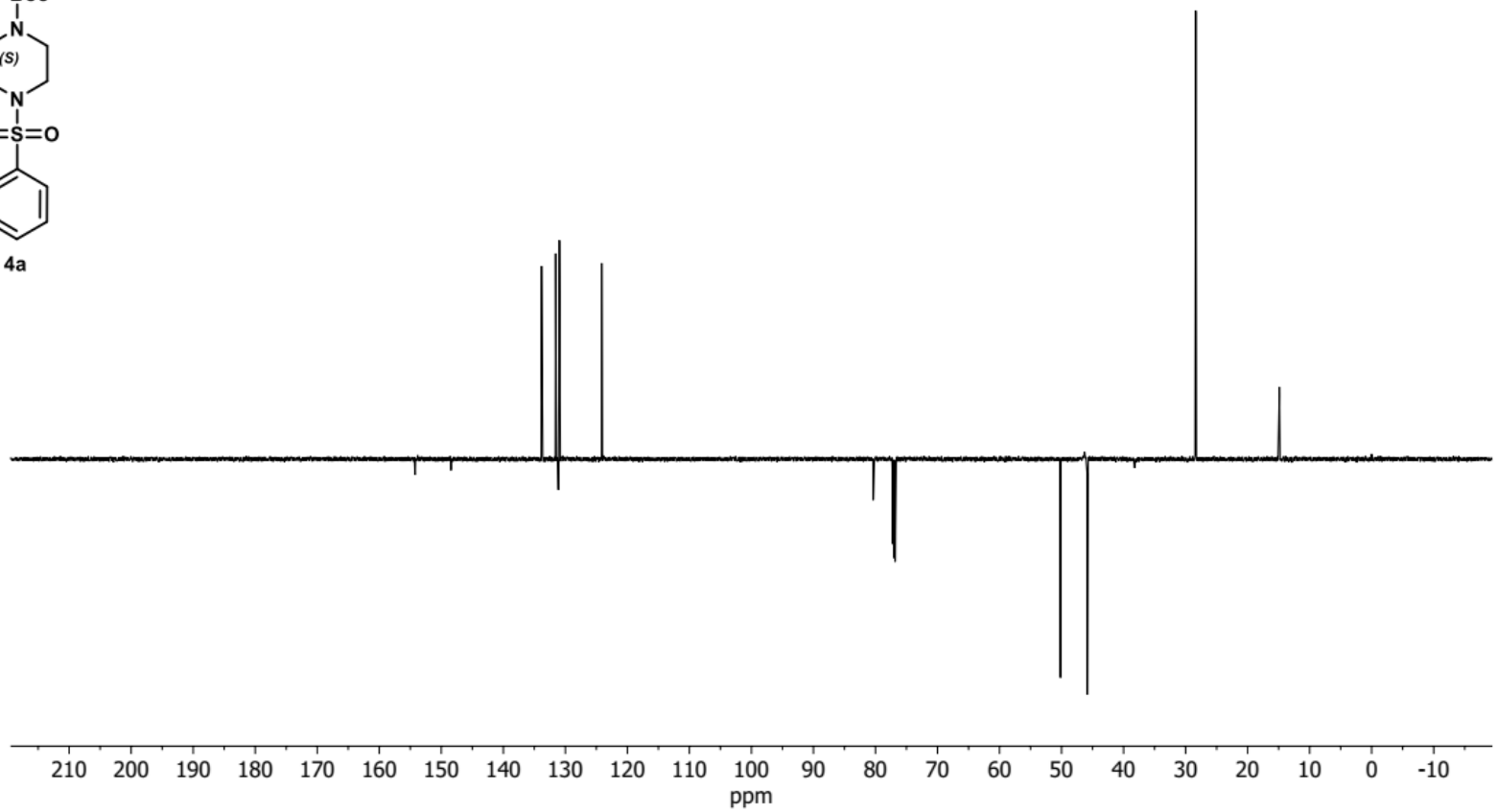
4a



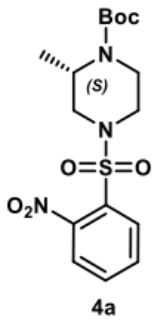
DEPTQ-135


Boc
N
(S)
N
O=S=O
O2N

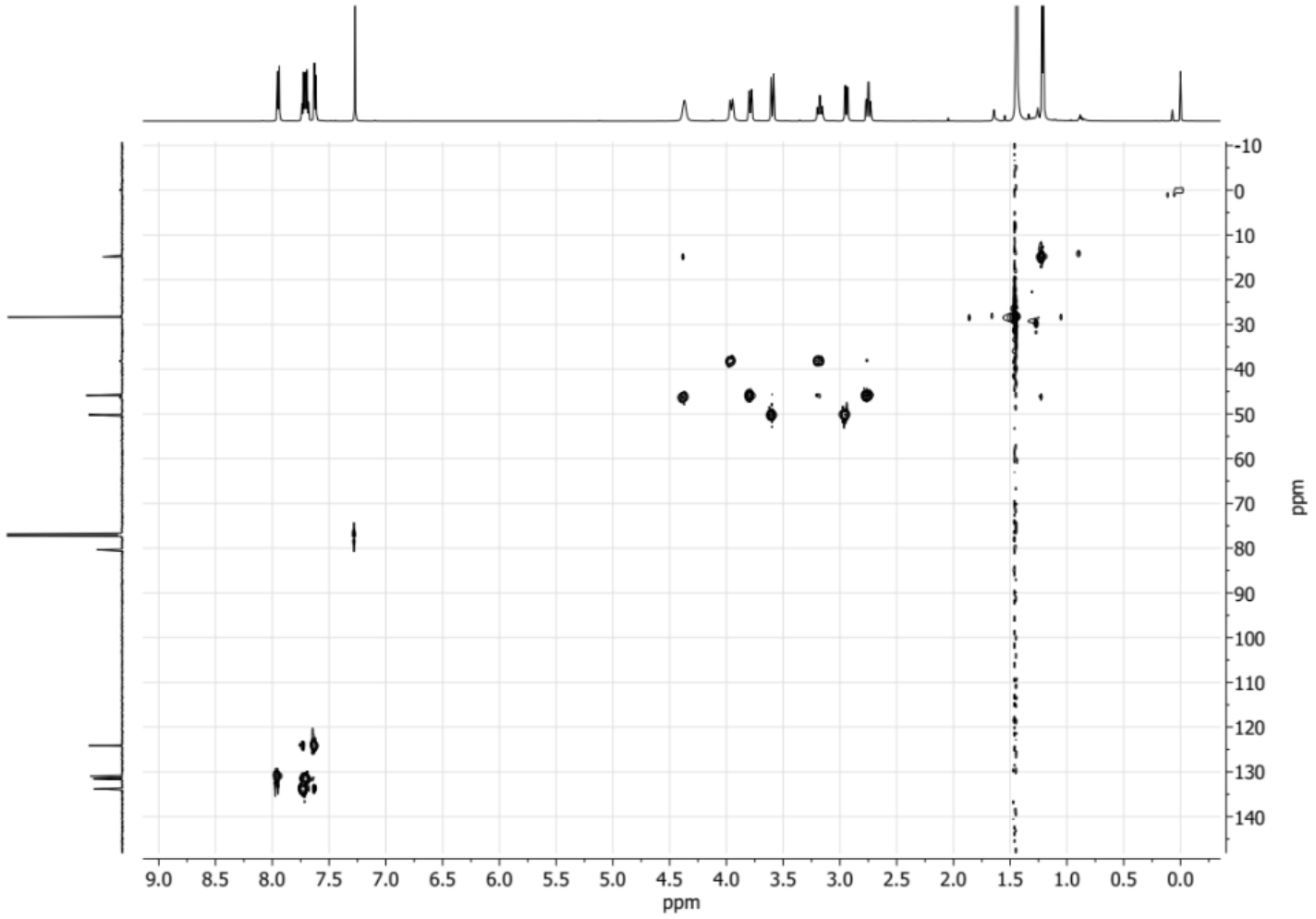
4a

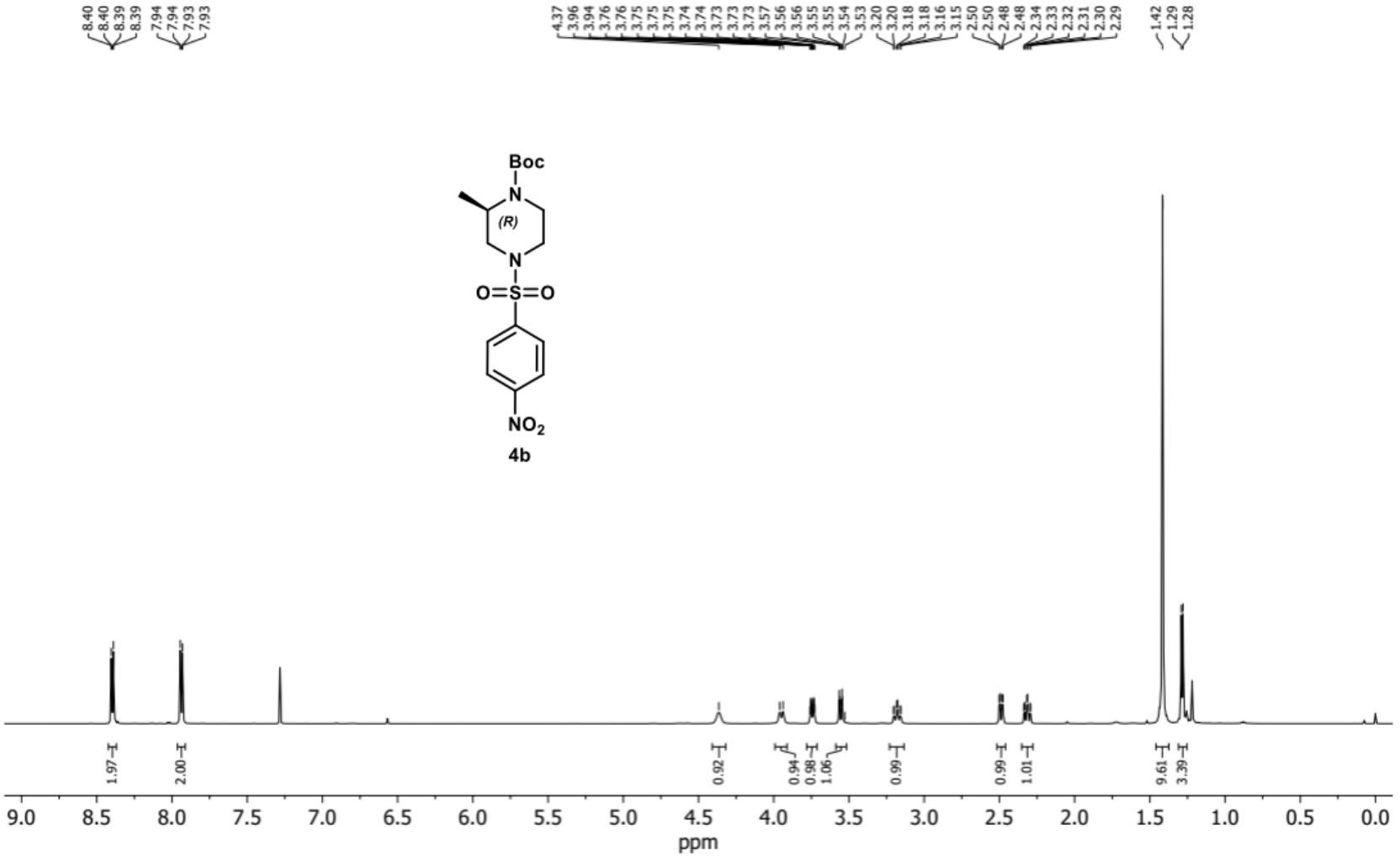

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm

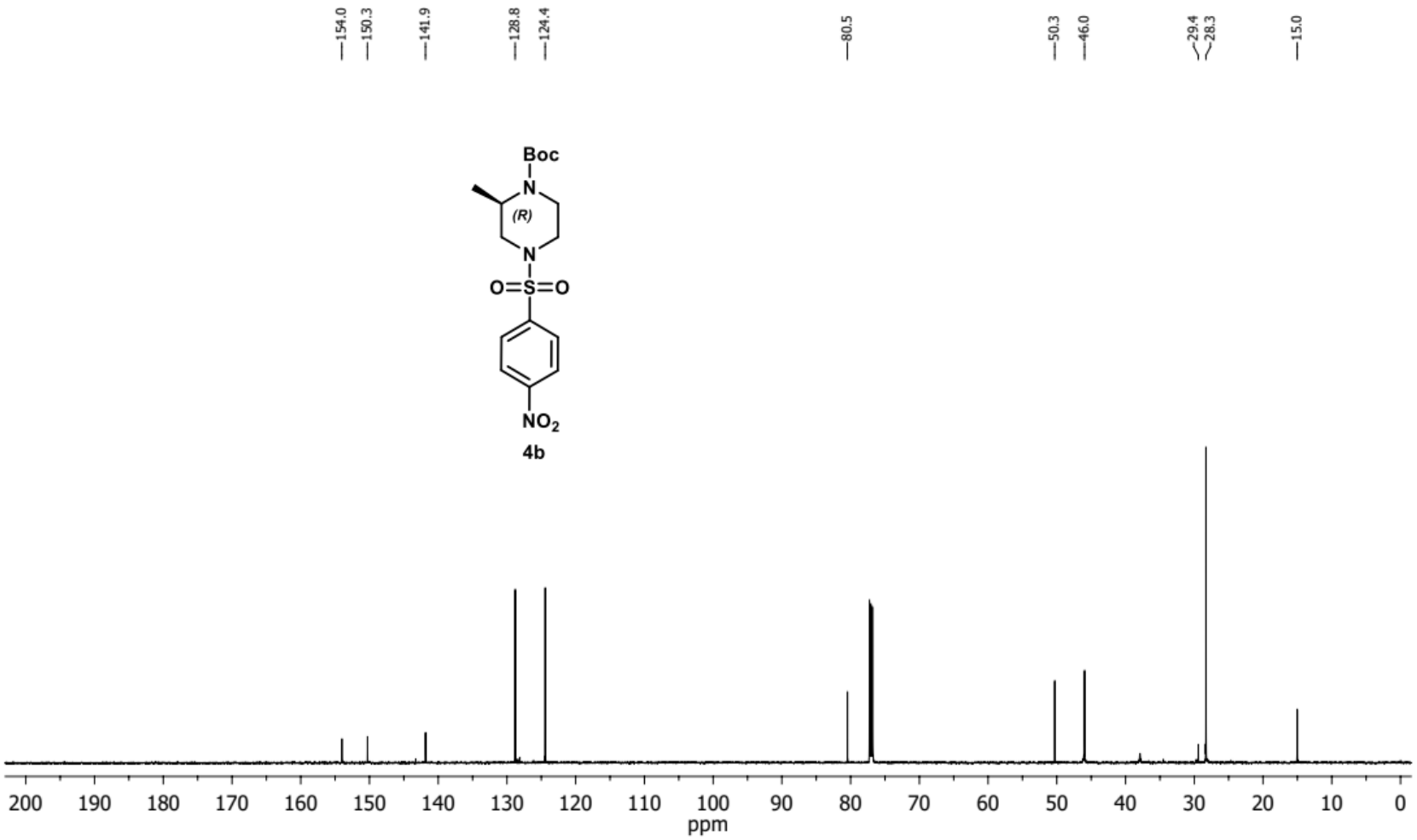
^{1}H, ^{13}C-HSQC

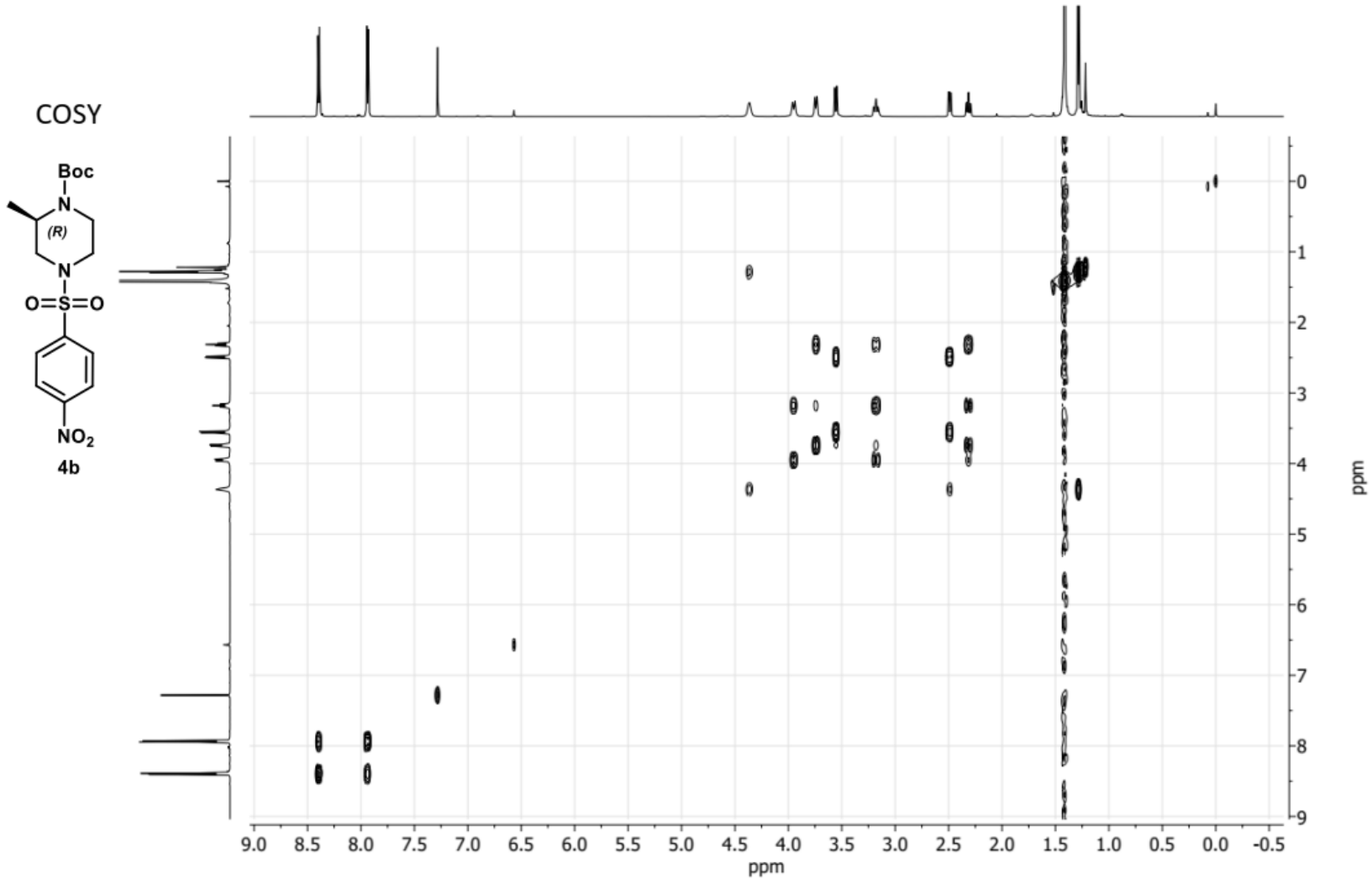


4a

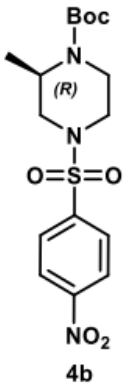



8.40
8.40
8.39
8.39
7.94
7.94
7.93
7.93
4.37
3.96
3.94
3.76
3.76
3.75
3.75
3.75
3.74
3.74
3.73
3.73
3.73
3.57
3.56
3.56
3.55
3.55
3.54
3.53
3.20
3.20
3.18
3.18
3.16
3.15
2.50
2.50
2.48
2.48
2.34
2.33
2.32
2.31
2.30
2.29
1.42
1.29
1.28
Boc
N
(R)
N
O=S=O
NO2
4b
1.97
2.00
0.92
0.94
0.98
1.06
0.99
0.99
1.01
9.61
3.39
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

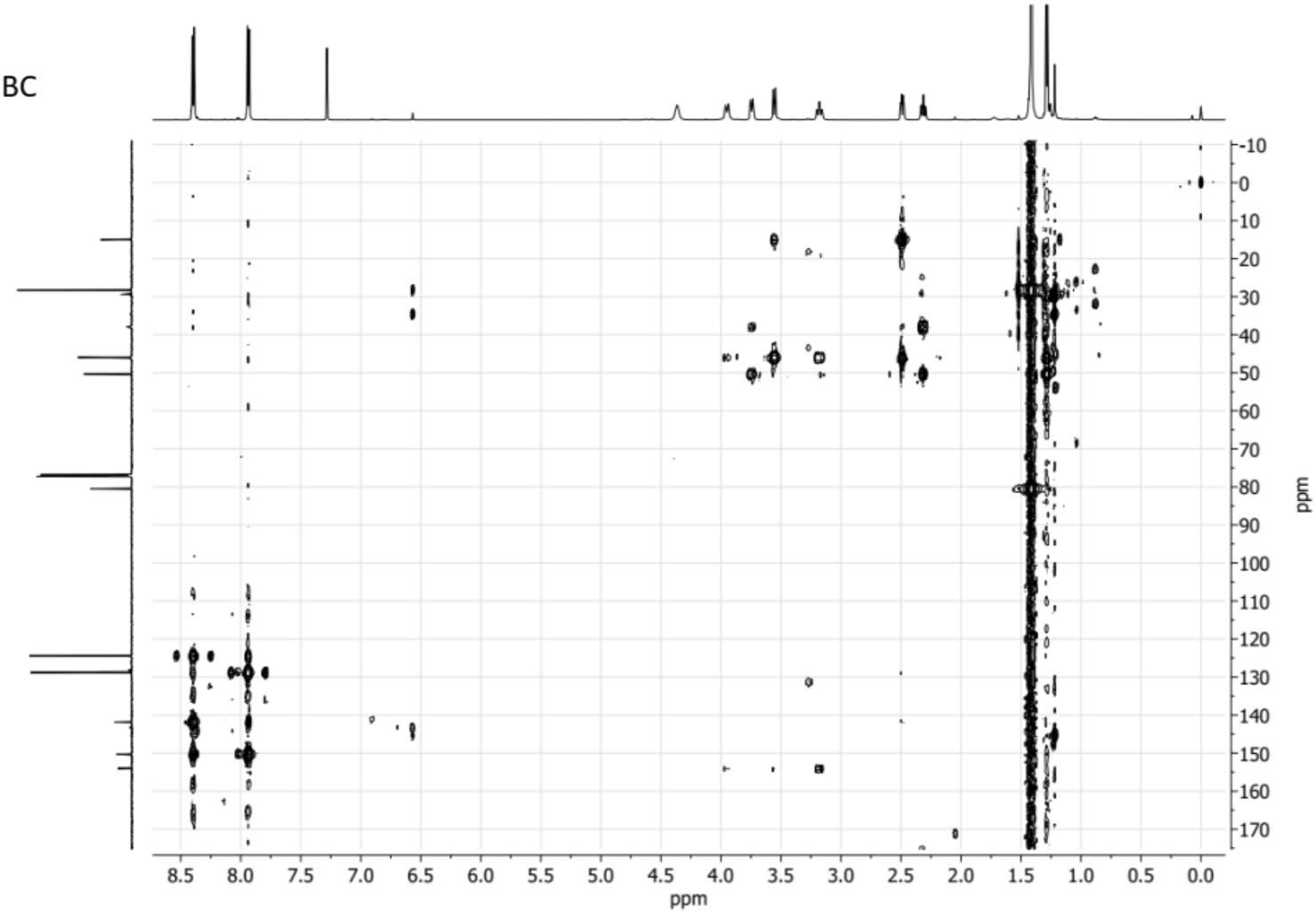

154.0
150.3
141.9
128.8
124.4
80.5
50.3
46.0
29.4
28.3
15.0
Boc
N
(R)
N
O=S=O
NO2
4b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


COSY
Boc
N
(R)
N
O=S=O
NO2
4b
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm
0 1 2 3 4 5 6 7 8 9
ppm

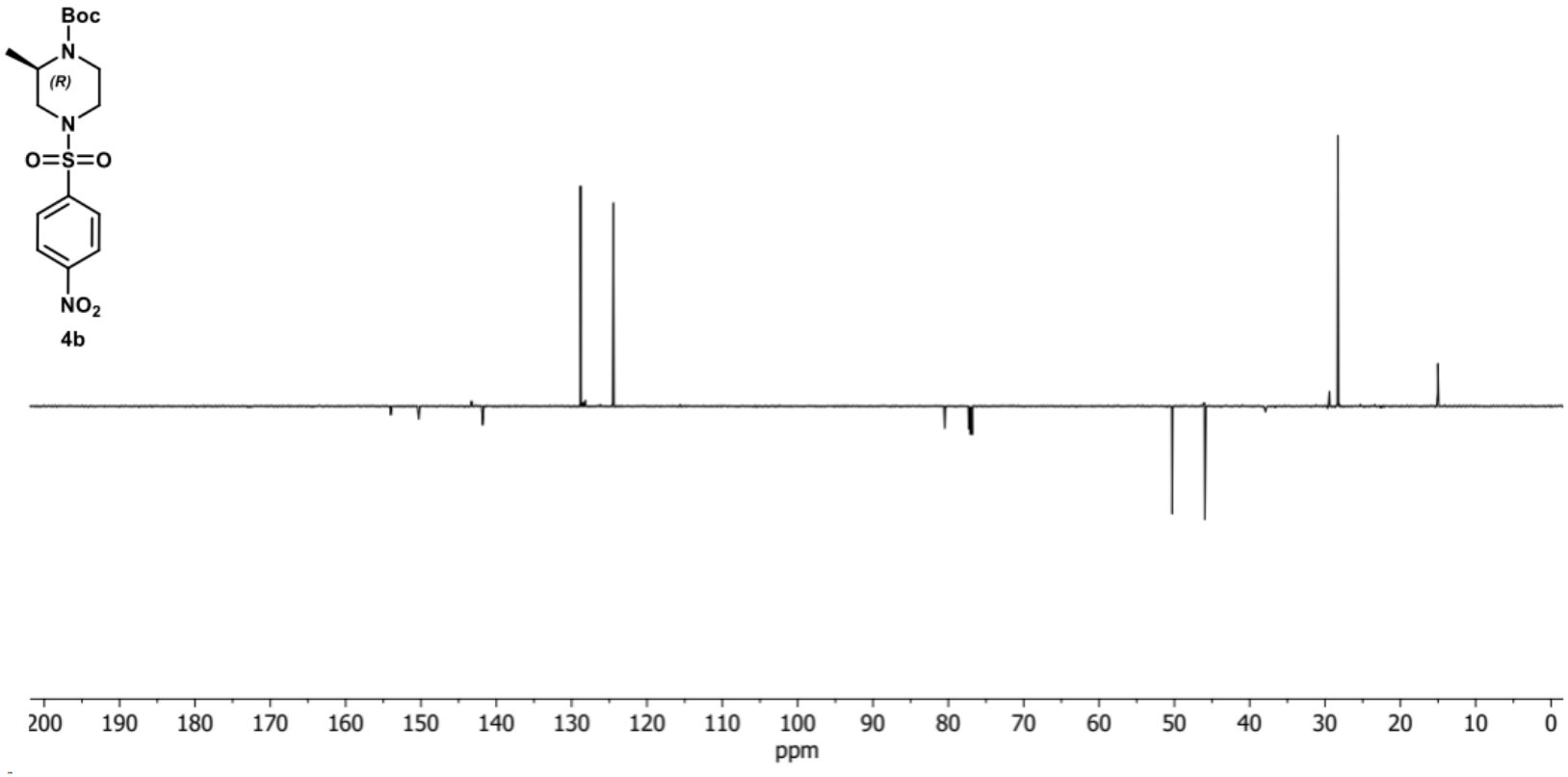
^{1}H, ^{13}C-HMBC



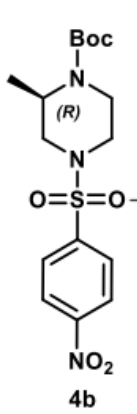
4b



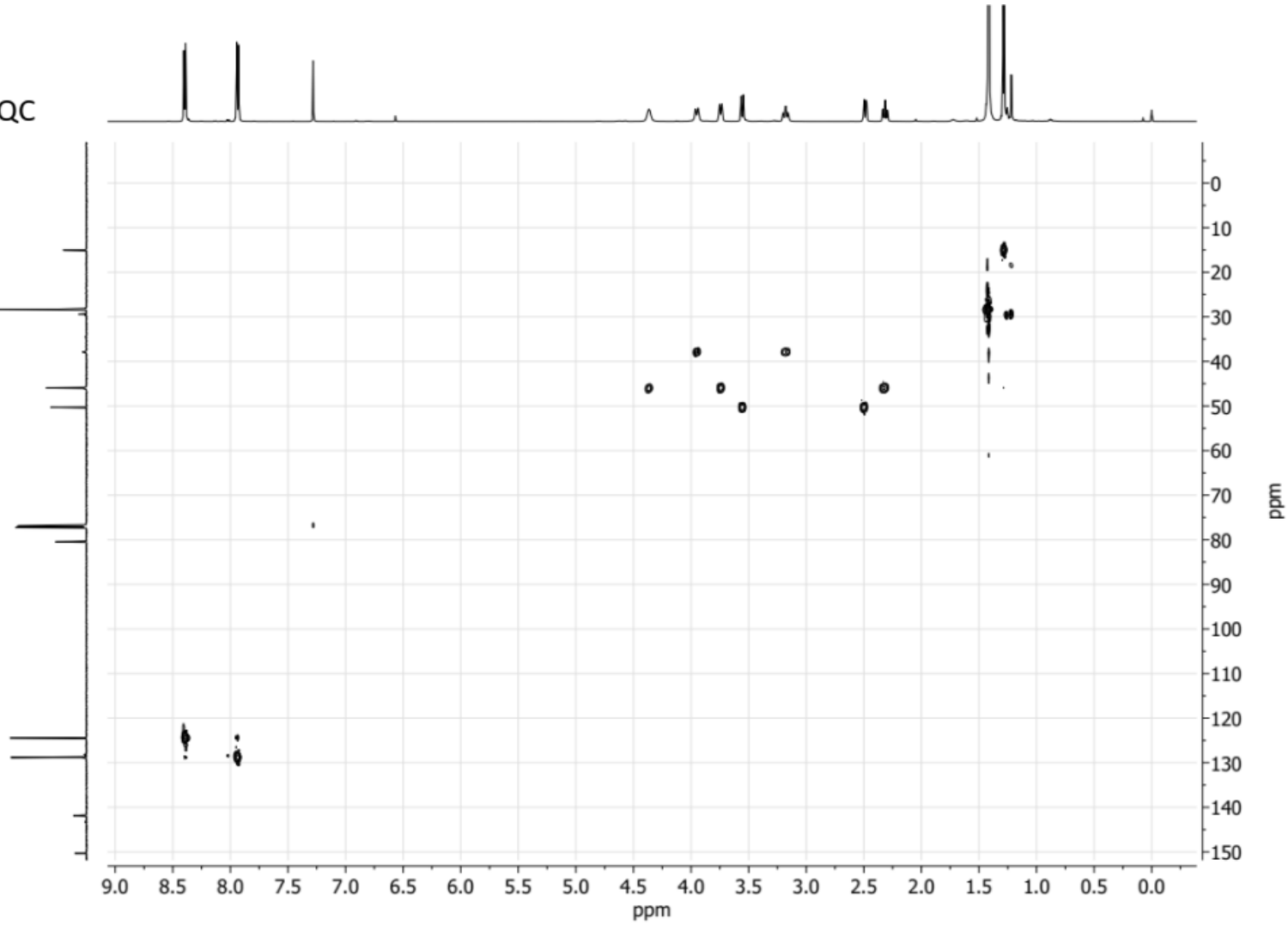
DEPTQ-135

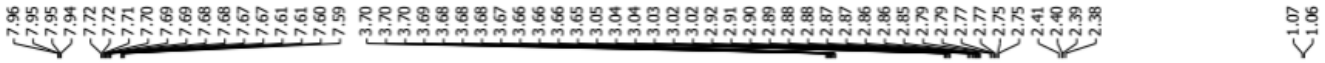

Boc
N
(R)
N
O=S=O
NO2
4b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

^{1}H, ^{13}C-HSQC



4b




7.96
7.95
7.95
7.94
7.72
7.72
7.71
7.70
7.69
7.69
7.68
7.68
7.67
7.67
7.61
7.60
7.59
3.70
3.70
3.70
3.69
3.68
3.68
3.68
3.67
3.66
3.66
3.66
3.65
3.05
3.04
3.04
3.03
3.02
3.02
2.92
2.91
2.90
2.89
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2.87
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2.86
2.86
2.85
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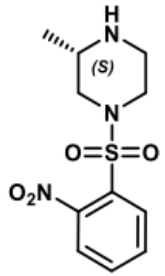
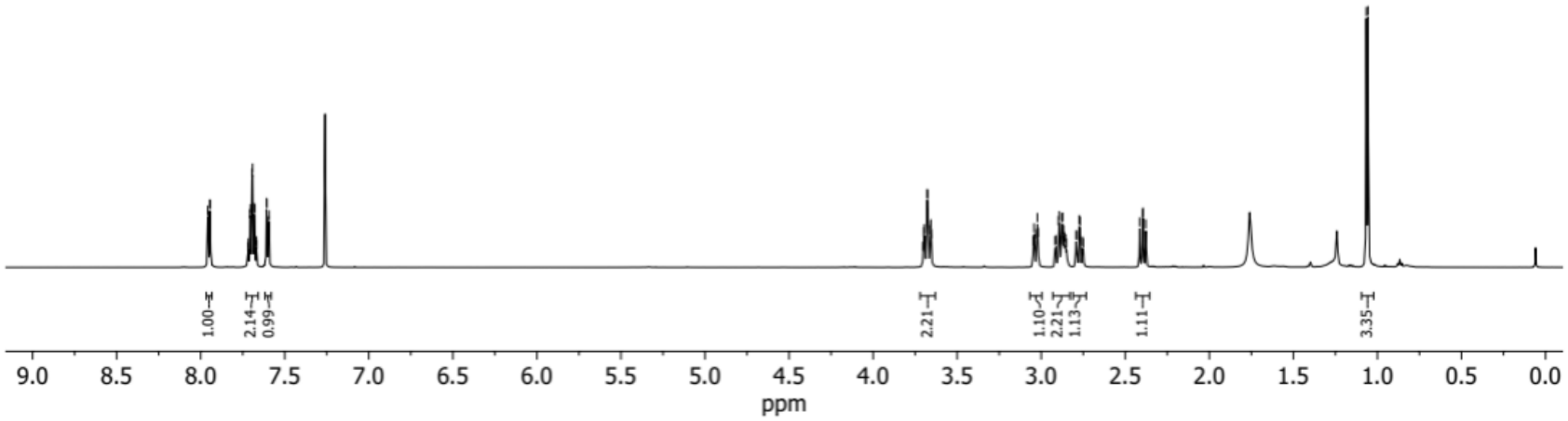
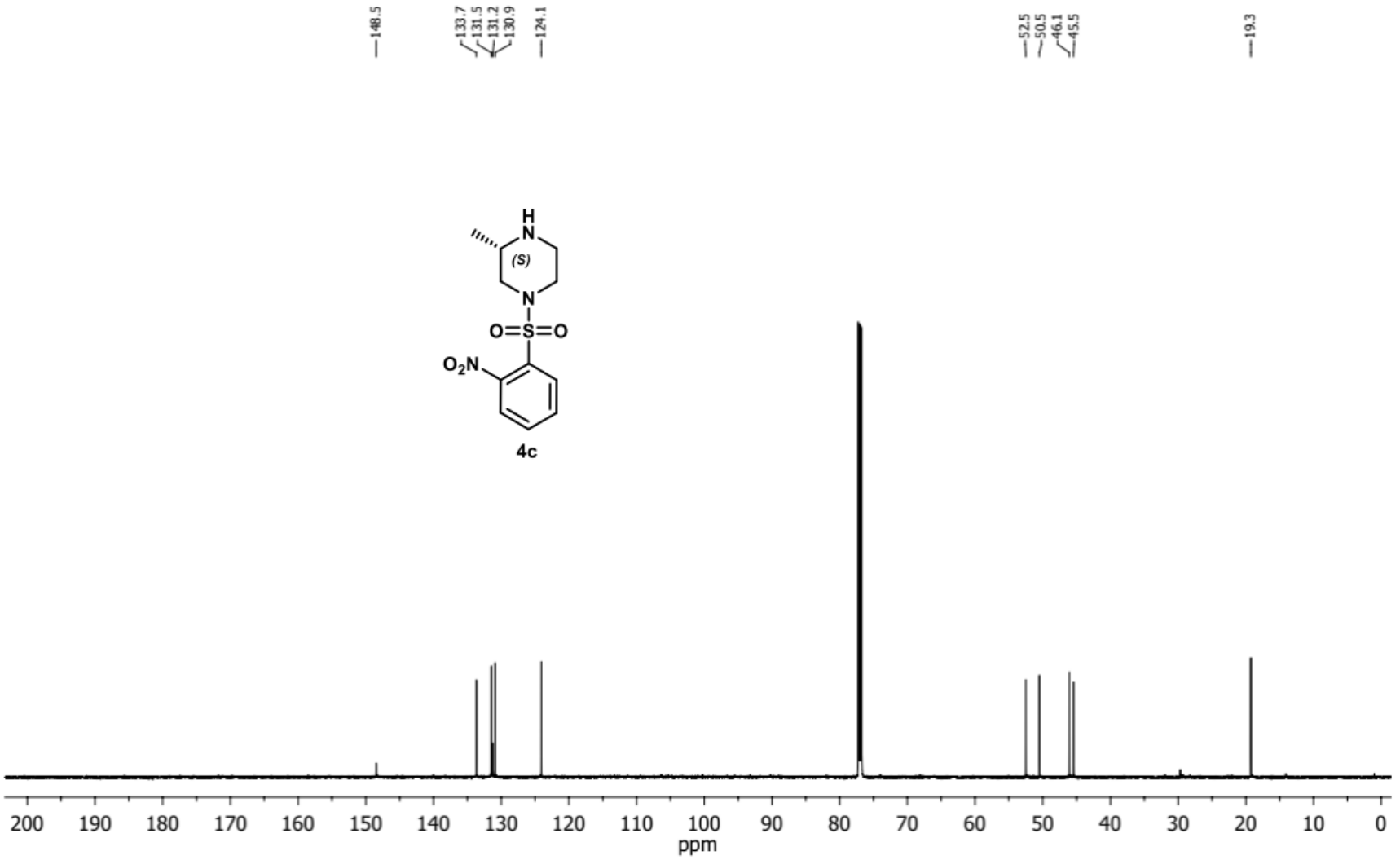
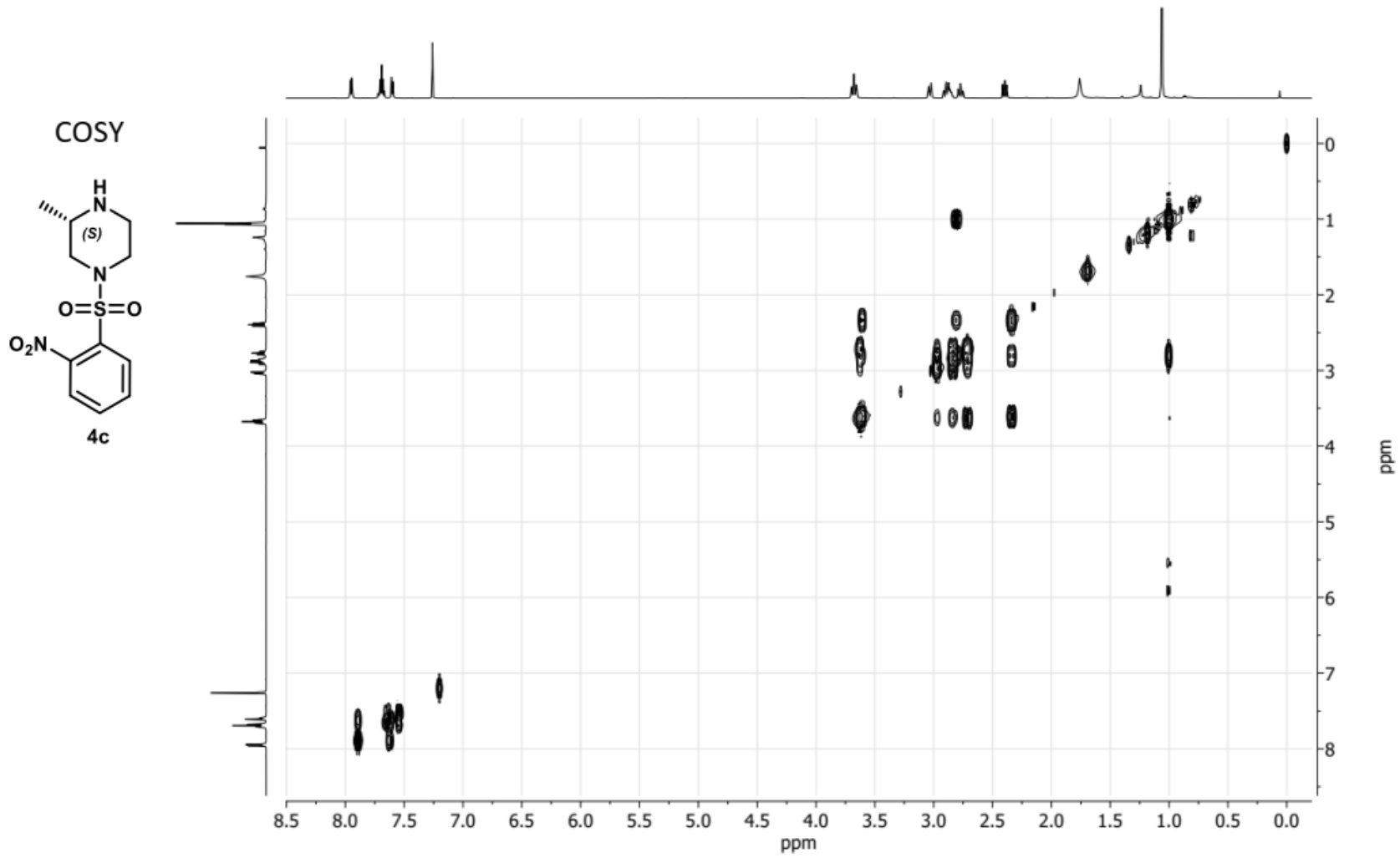
2.41
2.40
2.39
2.38
1.07
1.06


H
N
(S)
N
O=S=O
O2N

4c


1.00
2.14
0.99
2.21
1.10
2.21
1.13
1.11
3.35
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


148.5
133.7
131.5
131.2
130.9
124.1
52.5
50.5
46.1
45.5
19.3
H
N
(S)
N
O=S=O
O2N
4c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


COSY
(S)
O_2N
4c
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
0 1 2 3 4 5 6 7 8
ppm

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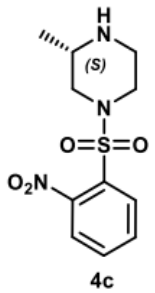
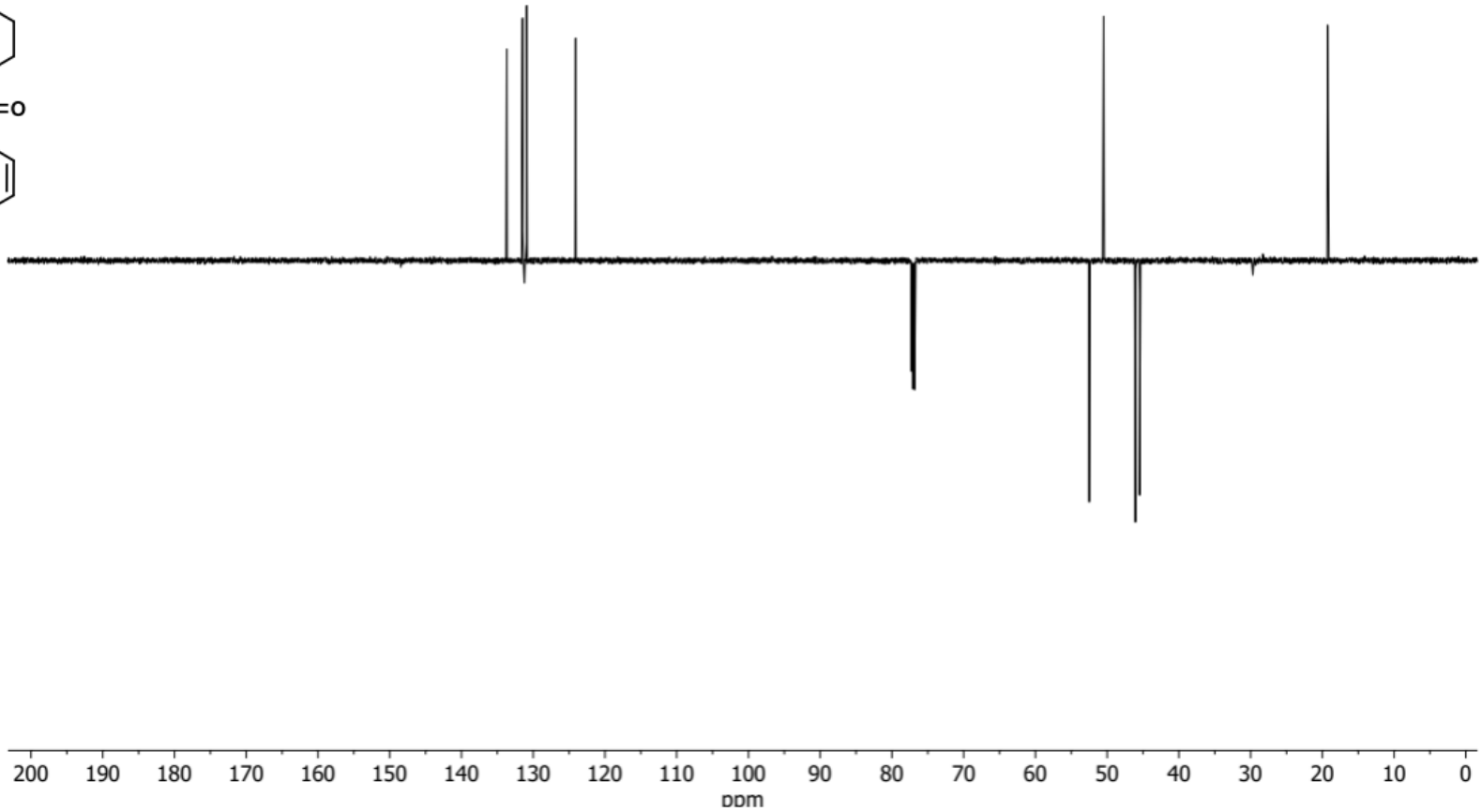
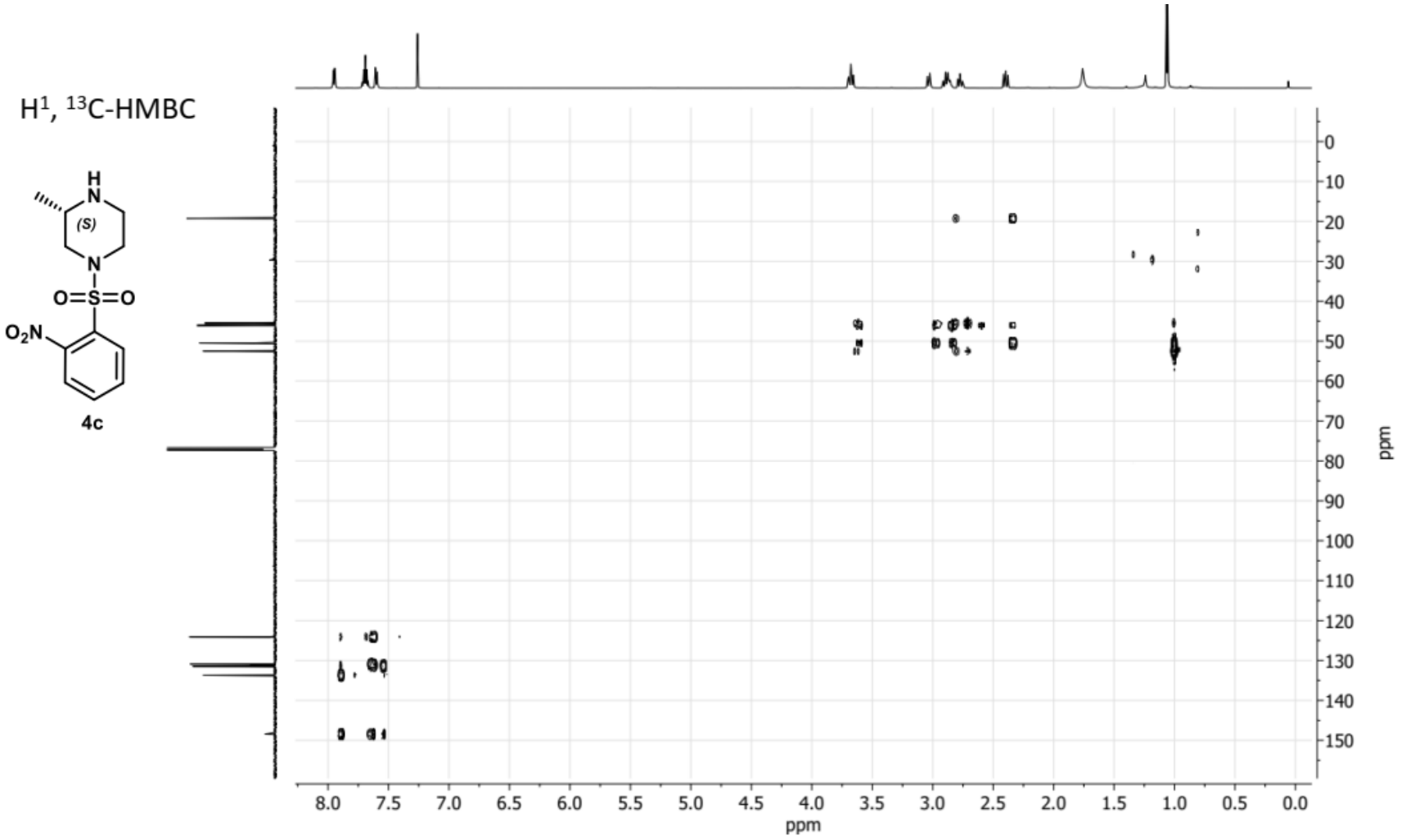
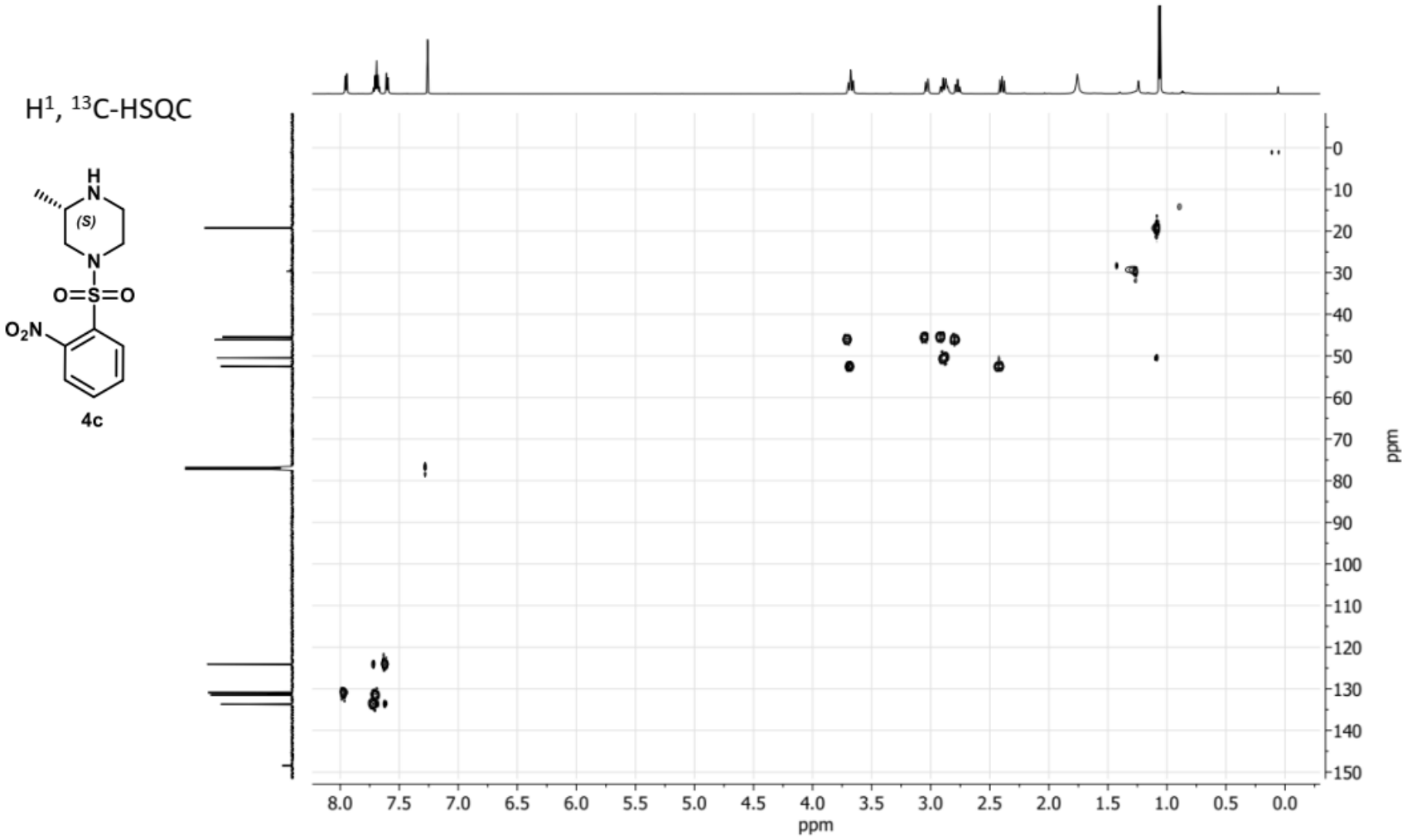

H
N
(S)
N
O=S=O
O2N

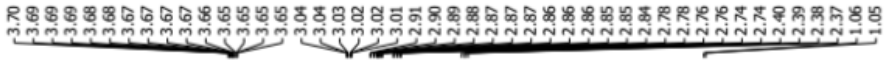
4c


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


H1, 13C-HMBC
(S)
O=S=O
O2N
4c
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
ppm


H1, 13C-HSQC
(S)
O=S=O
O2N
4c
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
ppm


7.95
7.95
7.95
7.94
7.94
7.71
7.70
7.70
7.69
7.69
7.68
7.68
7.67
7.66
7.60
7.60
7.59
7.59
7.59


3.70
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3.69
3.69
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3.68
3.67
3.67
3.67
3.67
3.66
3.65
3.65
3.65
3.65
3.04
3.04
3.03
3.02
3.02
3.01
2.91
2.90
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2.87
2.87
2.87
2.86
2.86
2.86
2.85
2.85
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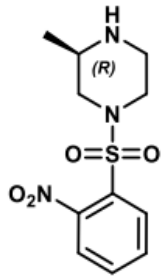
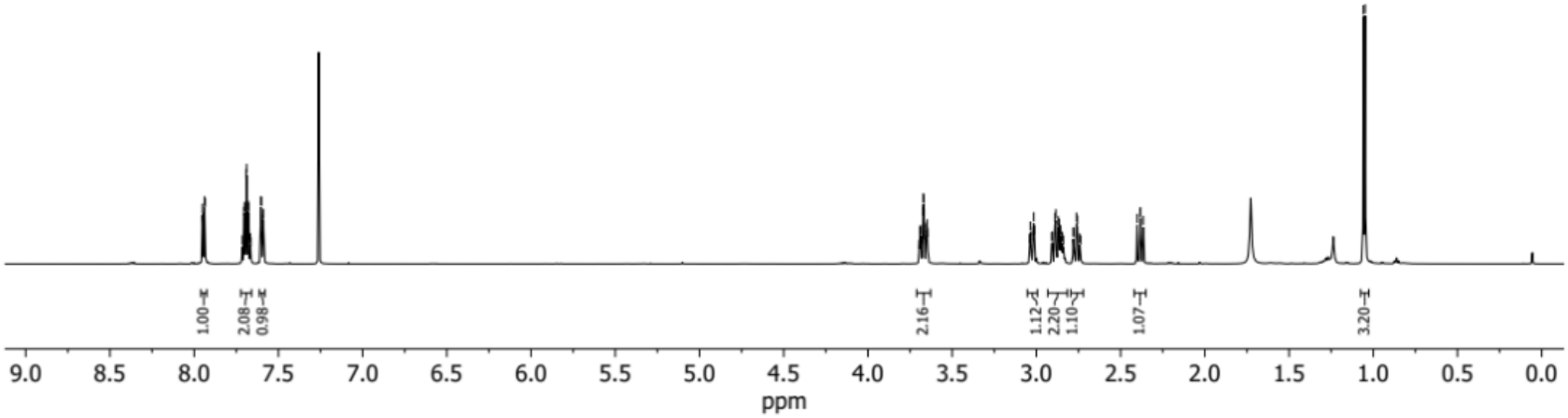
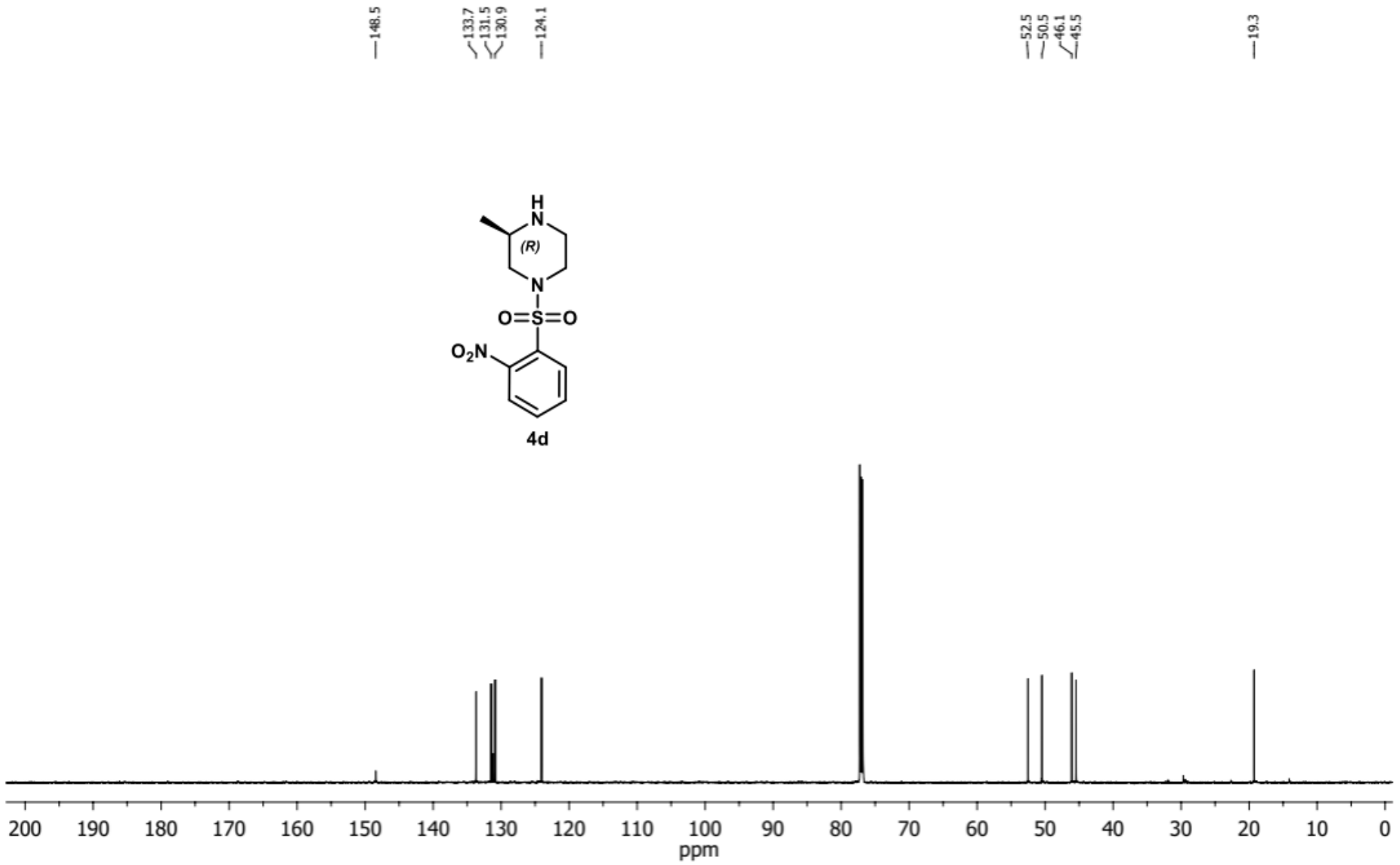
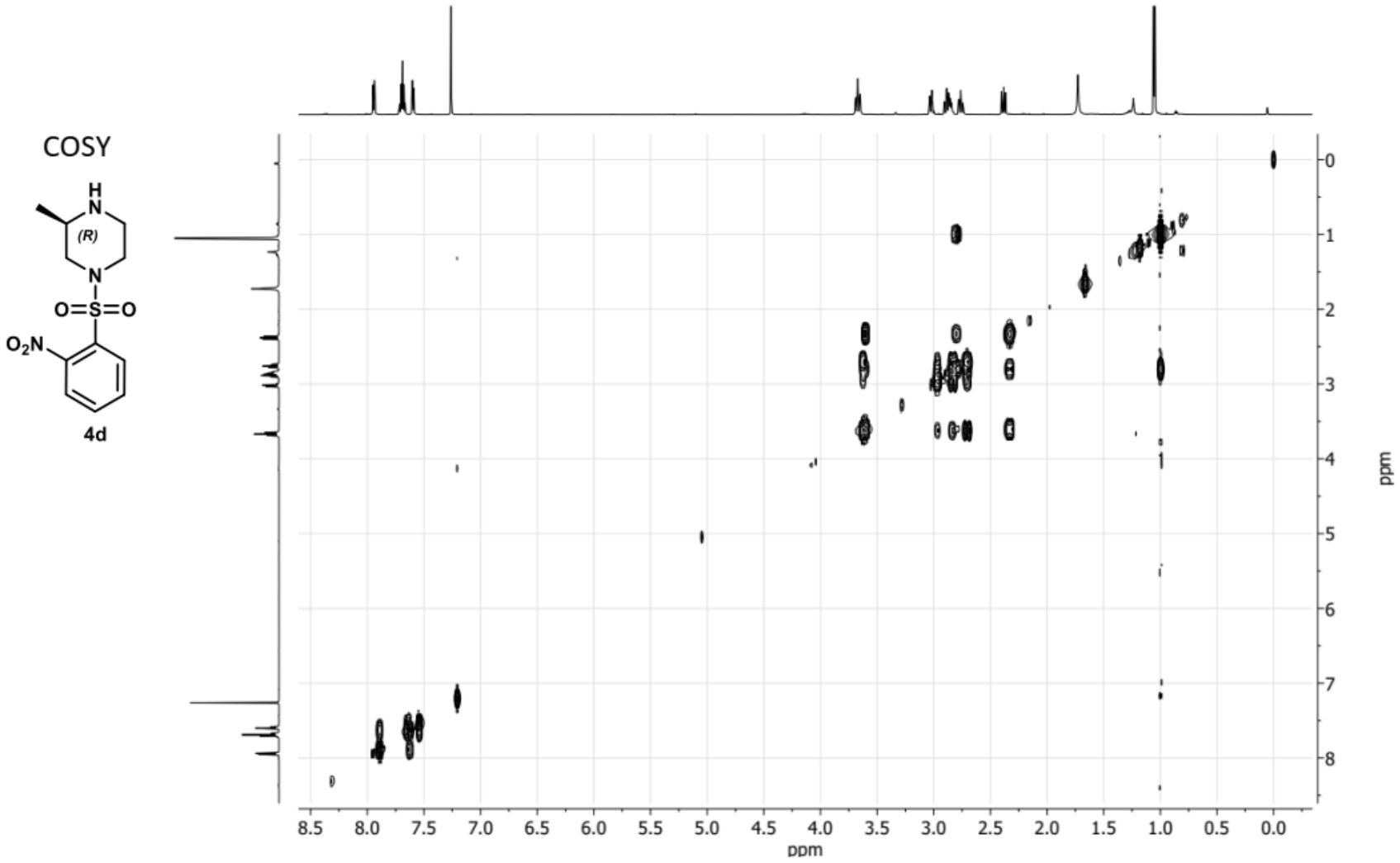
2.40
2.39
2.38
2.37
1.06
1.05

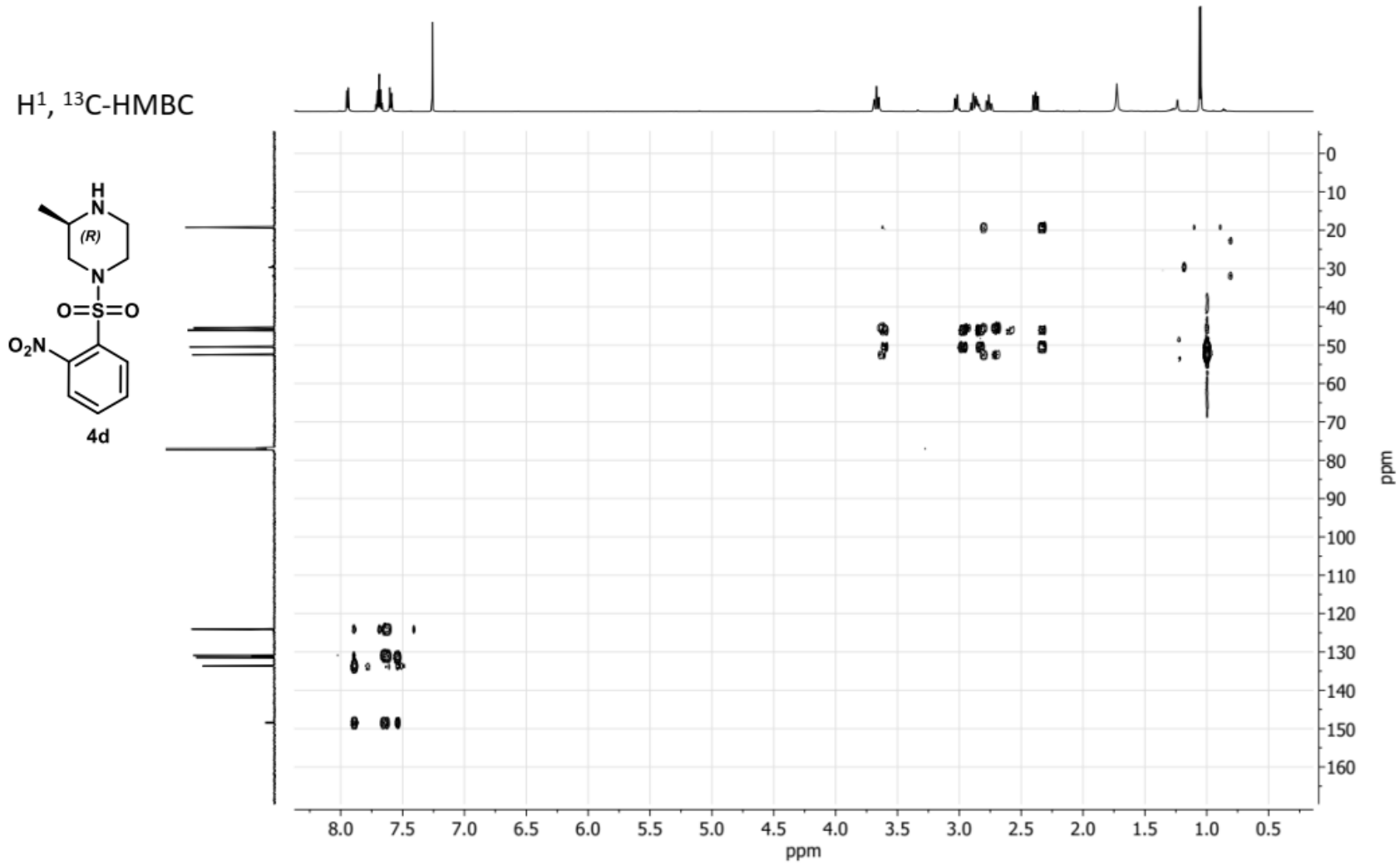

H
N
(R)
N
O=S=O
O2N

4d


1.00
2.08
0.98
2.16
1.12
2.20
1.10
1.07
3.20
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


148.5
133.7
131.5
130.9
124.1
52.5
50.5
46.1
45.5
19.3
H
N
(R)
N
O=S=O
O2N
4d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


COSY
(R)
4d
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
0 1 2 3 4 5 6 7 8
ppm


H1, 13C-HMBC
(R)
O=S=O
O2N
4d
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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50
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80
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100
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120
130
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150
160
ppm

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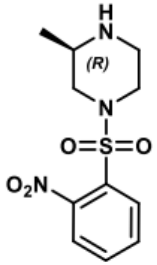
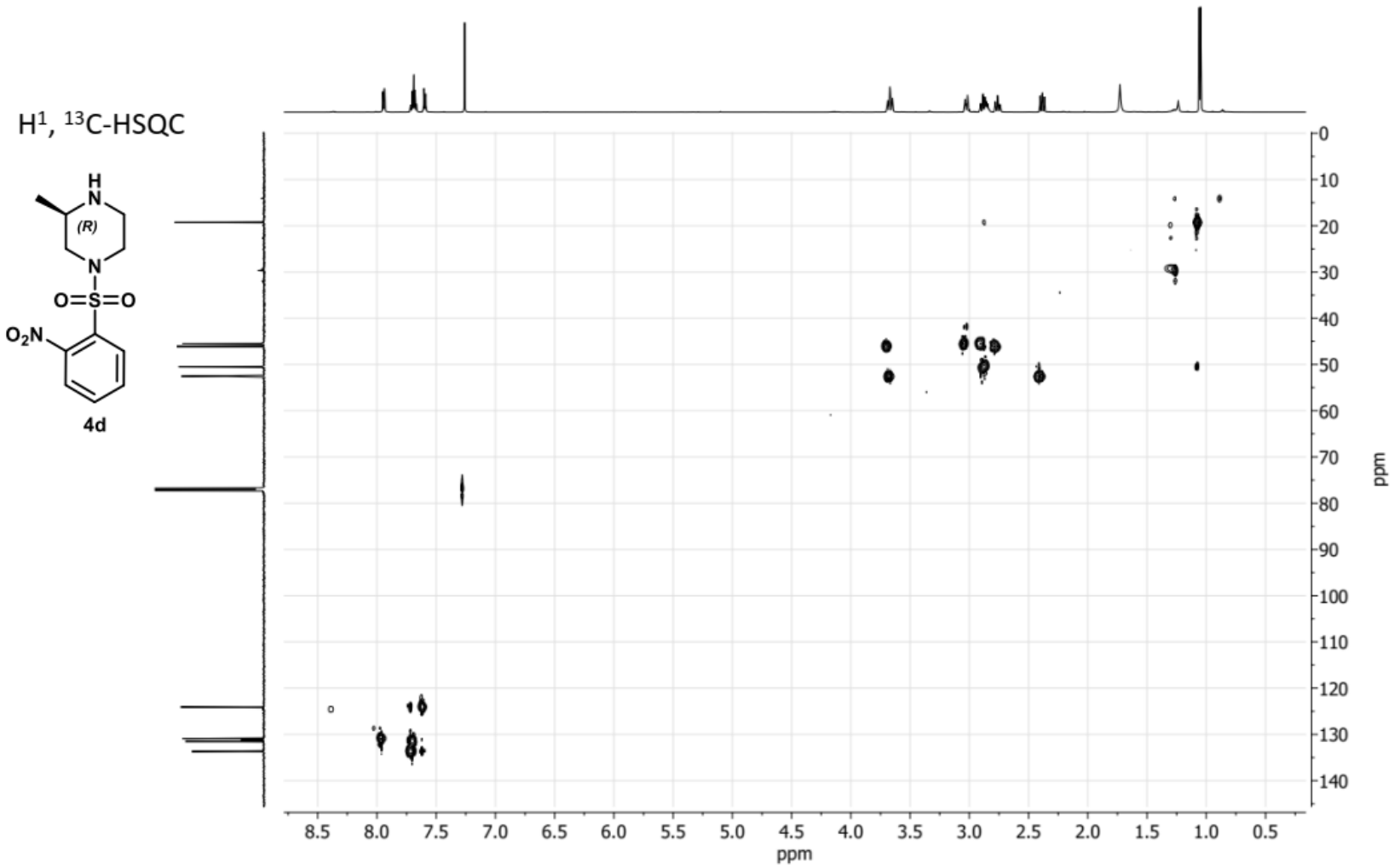
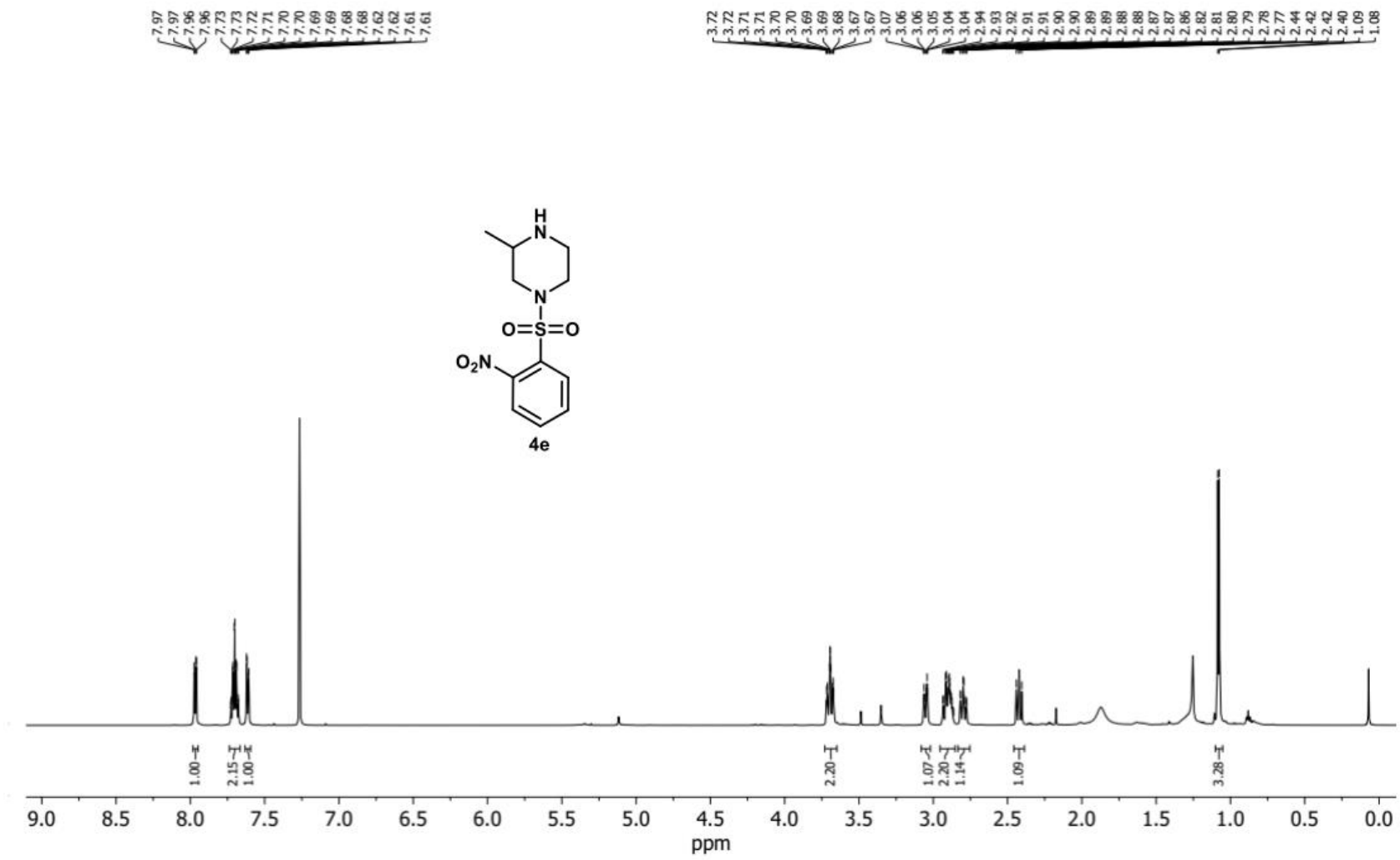

H
N
(R)
N
O=S=O
O_2N

4d

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


H1, 13C-HSQC
(R)
O=S=O
O2N
4d
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140
ppm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7.97
7.96
7.96
7.73
7.73
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7.71
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7.70
7.69
7.69
7.68
7.68
7.62
7.61
7.61
3.72
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2.81
2.80
2.79
2.78
2.77
2.44
2.42
2.42
2.40
1.09
1.08
H
N
N
O=S=O
O2N
4e
1.00
2.15
1.00
2.20
1.07
2.20
1.14
1.09
3.28
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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5.0
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4.0
3.5
3.0
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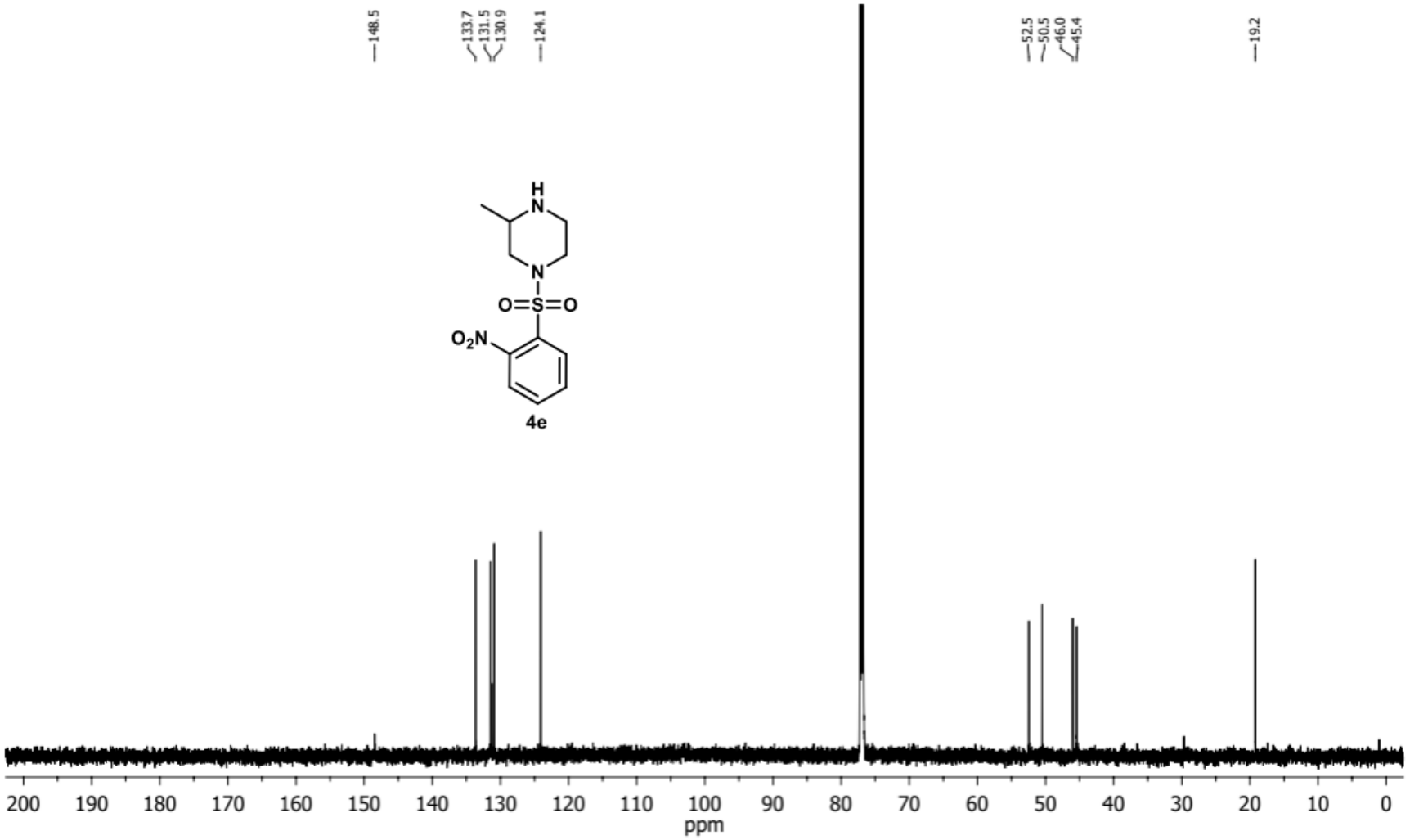
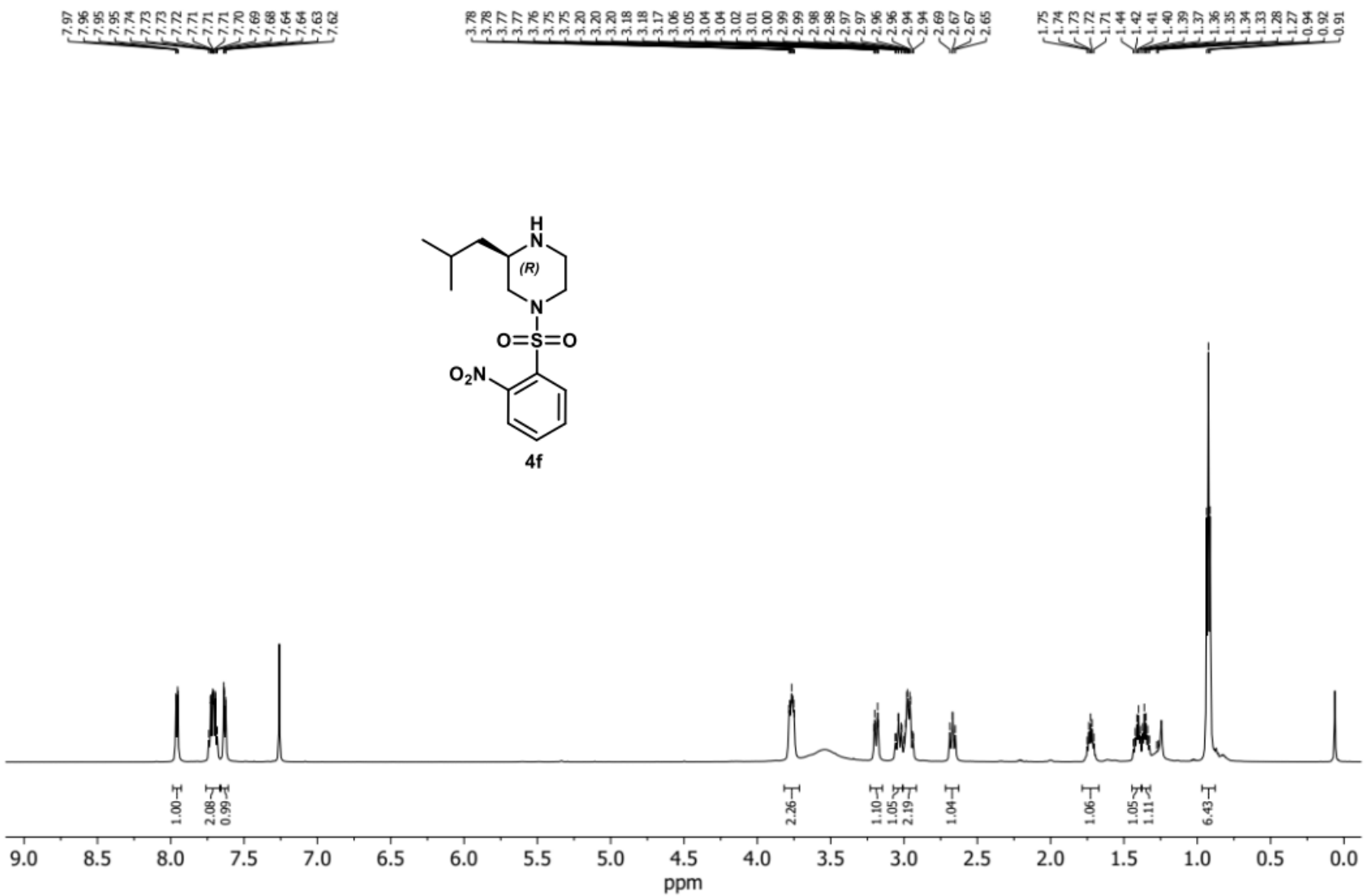
2.0
1.5
1.0
0.5
0.0
ppm


148.5
133.7
131.5
130.9
124.1
52.5
50.5
46.0
45.4
19.2
H
N
N
O=S=O
O2N
4e
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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7.96
7.95
7.95
7.74
7.73
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7.72
7.71
7.71
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7.70
7.69
7.68
7.64
7.64
7.63
7.62
3.78
3.78
3.77
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3.76
3.75
3.75
3.20
3.20
3.20
3.18
3.18
3.17
3.06
3.05
3.04
3.04
3.02
3.01
3.00
2.99
2.99
2.98
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2.96
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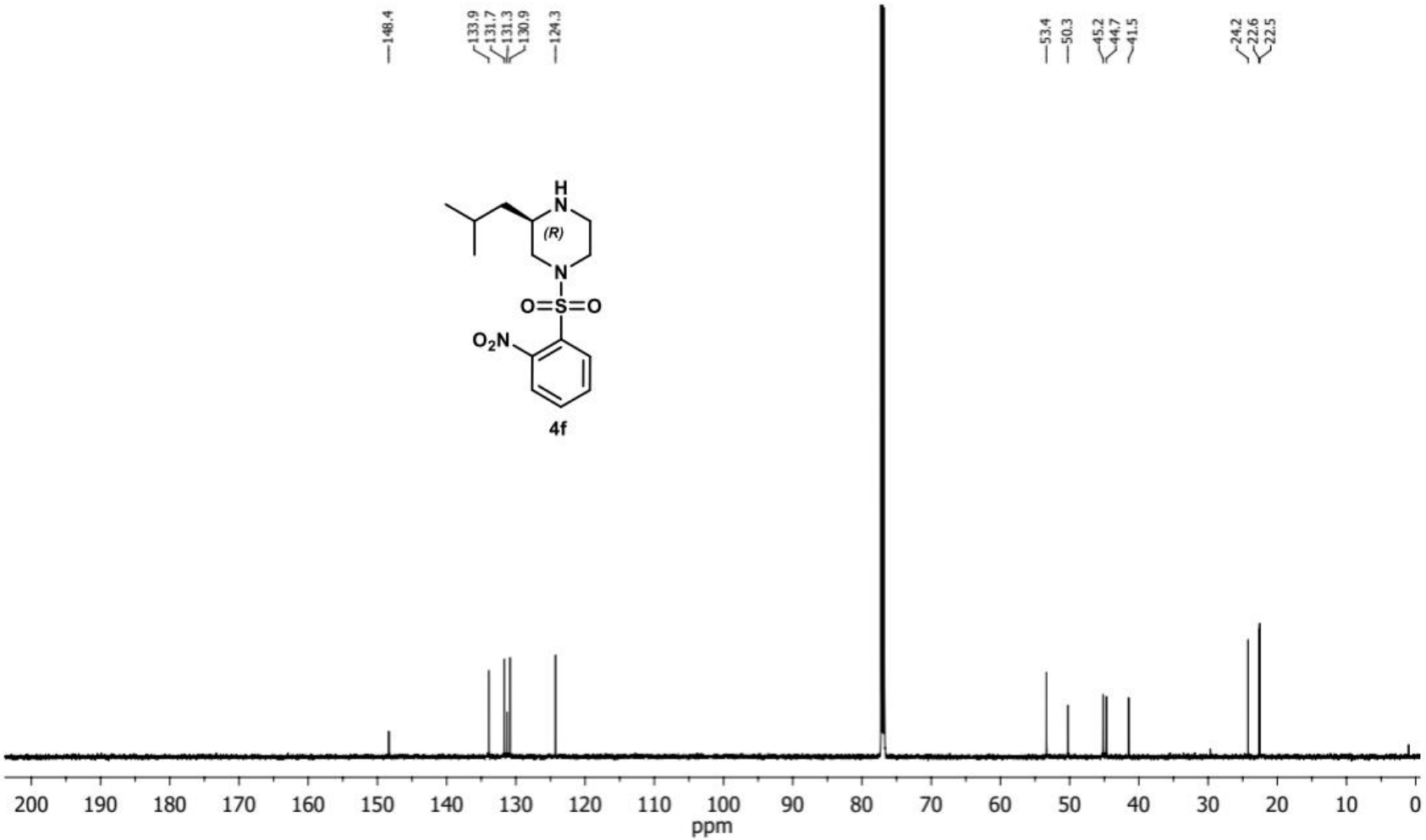
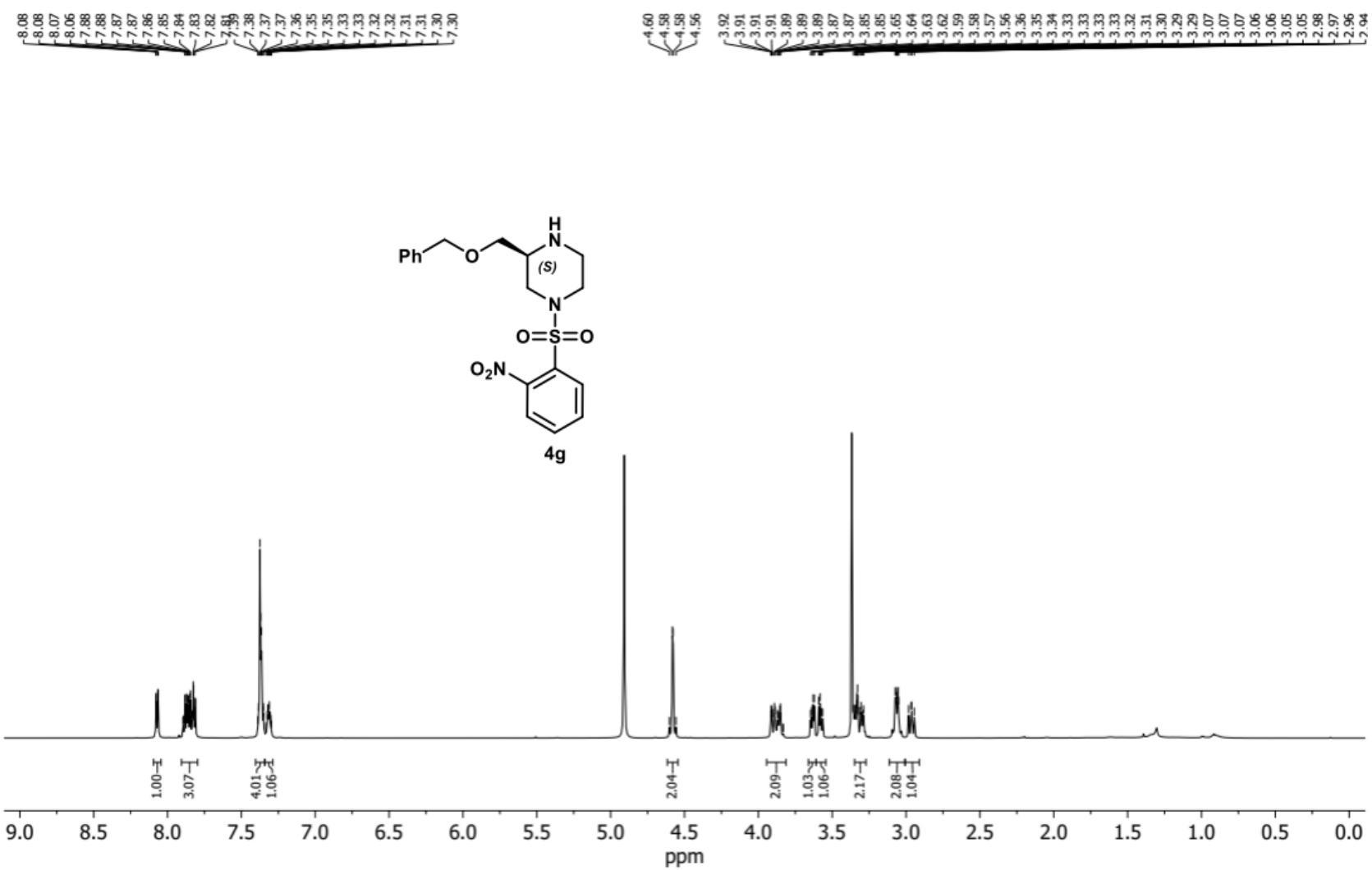
1.73
1.72
1.71
1.44
1.42
1.41
1.40
1.39
1.37
1.36
1.35
1.34
1.33
1.28
1.27
0.94
0.92
0.91
H
N
(R)
N
O=S=O
O2N
4f
1.00
2.08
0.99
2.26
1.10
1.05
2.19
1.04
1.06
1.05
1.11
6.43
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


148.4
133.9
131.7
131.3
130.9
124.3
53.4
50.3
45.2
44.7
41.5
24.2
22.6
22.5
H
N
(R)
N
O=S=O
O2N
4f
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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8.08
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7.88
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7.85
7.84
7.83
7.82
7.81
7.39
7.38
7.37
7.37
7.36
7.35
7.35
7.33
7.33
7.32
7.32
7.31
7.31
7.30
7.30
4.60
4.58
4.58
4.56
3.92
3.91
3.91
3.91
3.89
3.89
3.89
3.87
3.87
3.85
3.85
3.65
3.64
3.63
3.62
3.59
3.58
3.57
3.56
3.36
3.35
3.34
3.33
3.33
3.33
3.32
3.31
3.30
3.29
3.29
3.07
3.07
3.07
3.06
3.06
3.05
3.05
2.98
2.97
2.96
2.94
Ph
O
H
N
(S)
N
O=S=O
O2N
4g
1.00
3.07
4.01
1.06
2.04
2.09
1.03
1.06
2.17
2.08
1.04
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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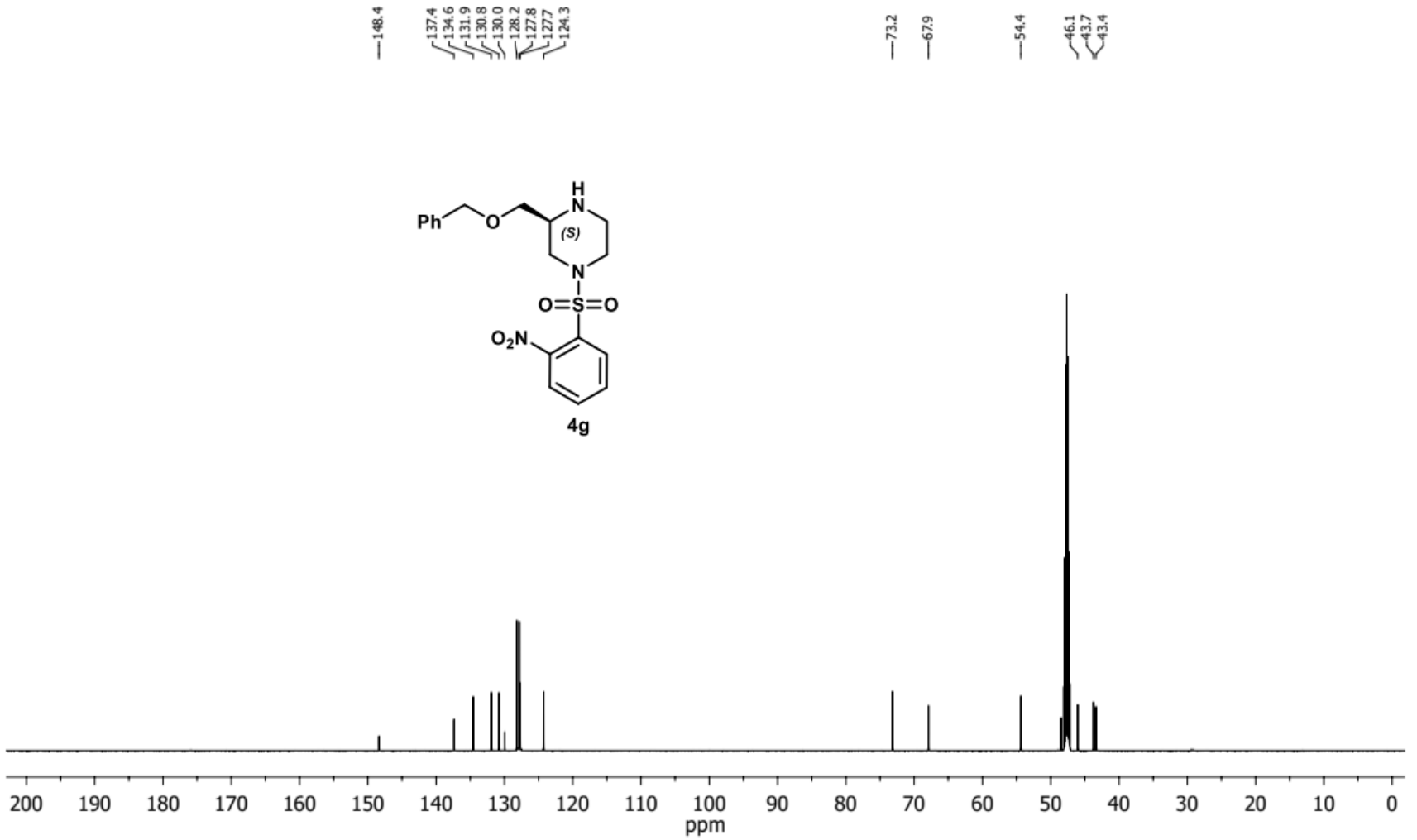
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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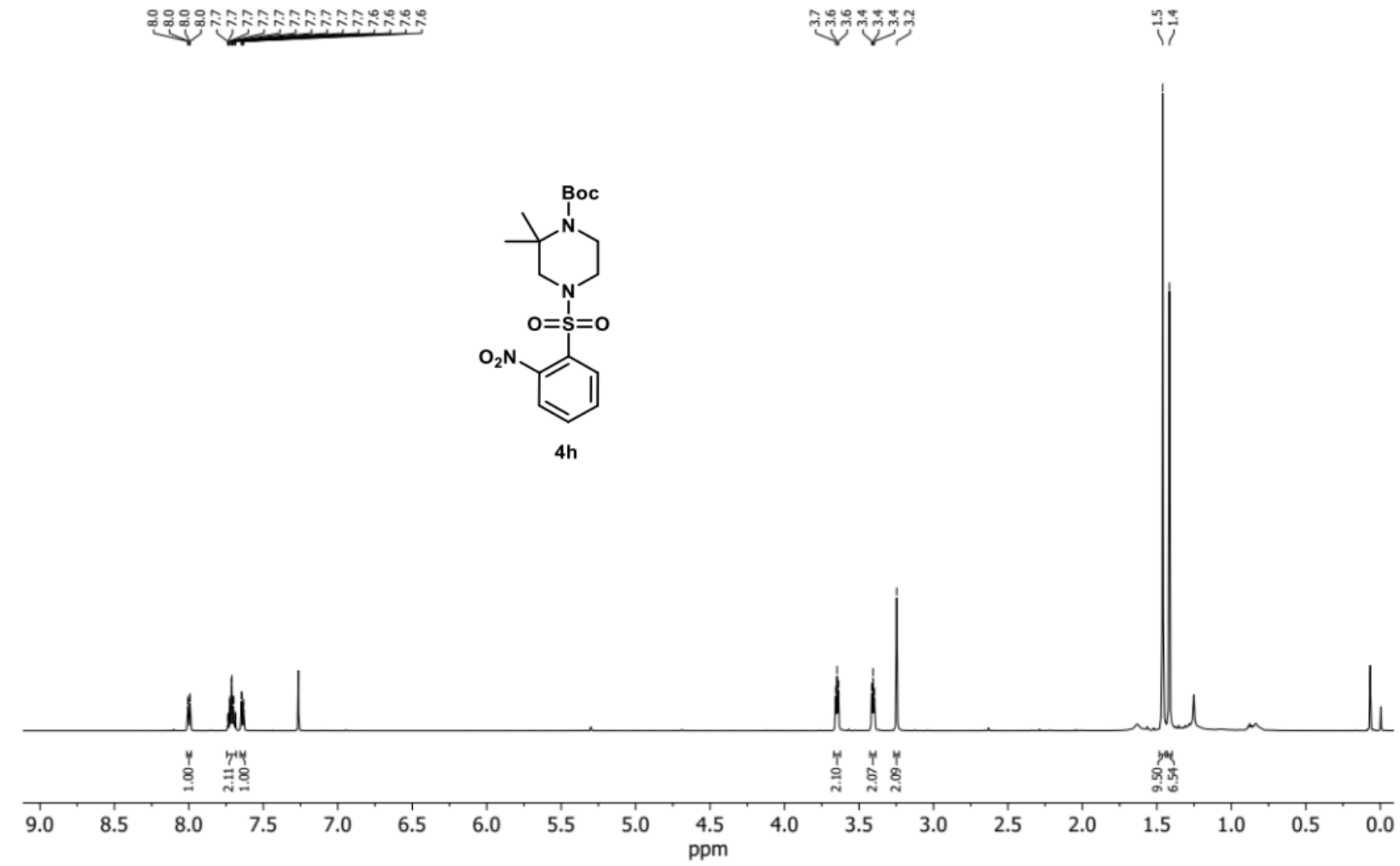
137.4
134.6
131.9
130.8
130.0
128.2
127.8
127.7
124.3
73.2
67.9
54.4
46.1
43.7
43.4
Ph
O
H
N
(S)
N
O=S=O
O2N
4g
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


8.0
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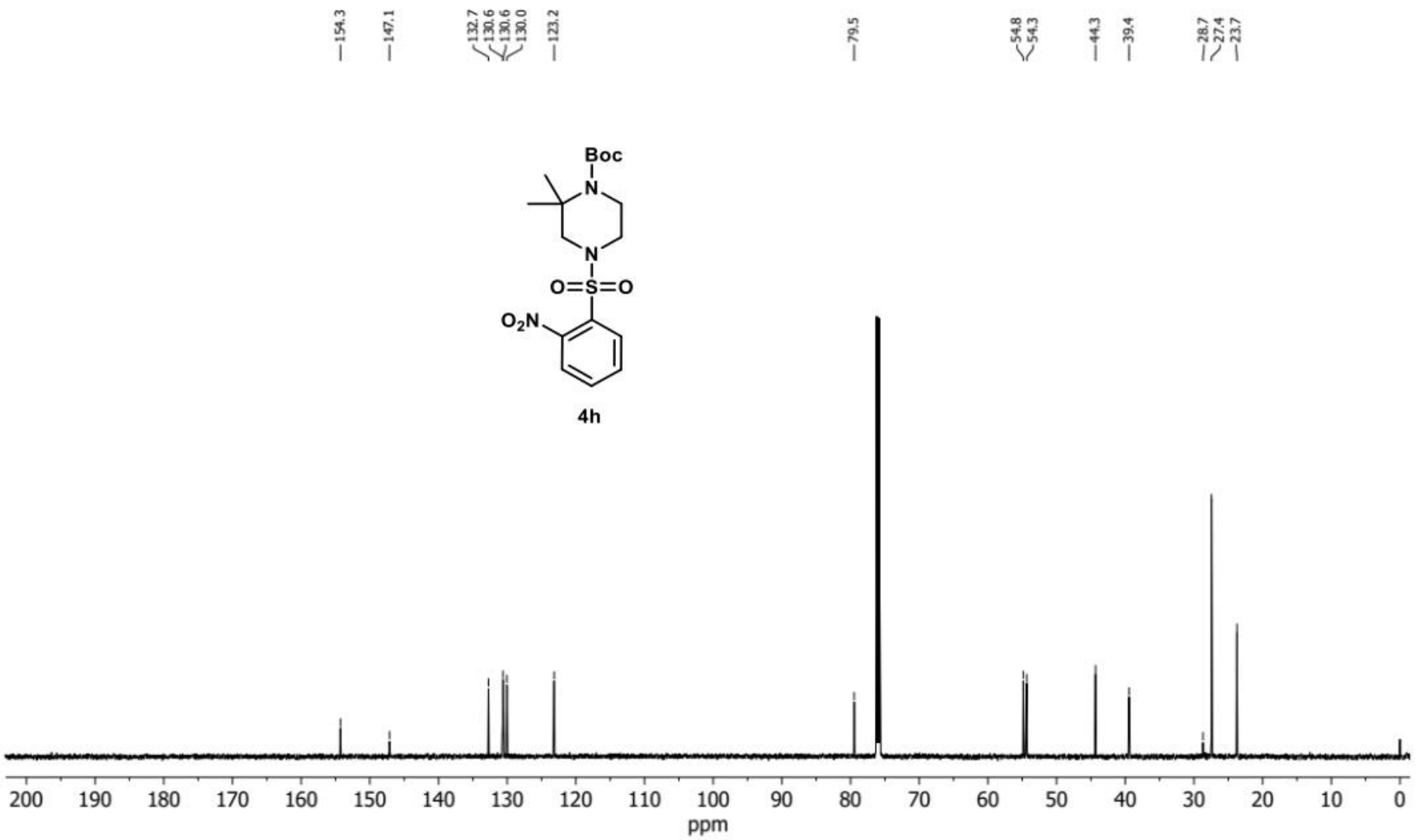
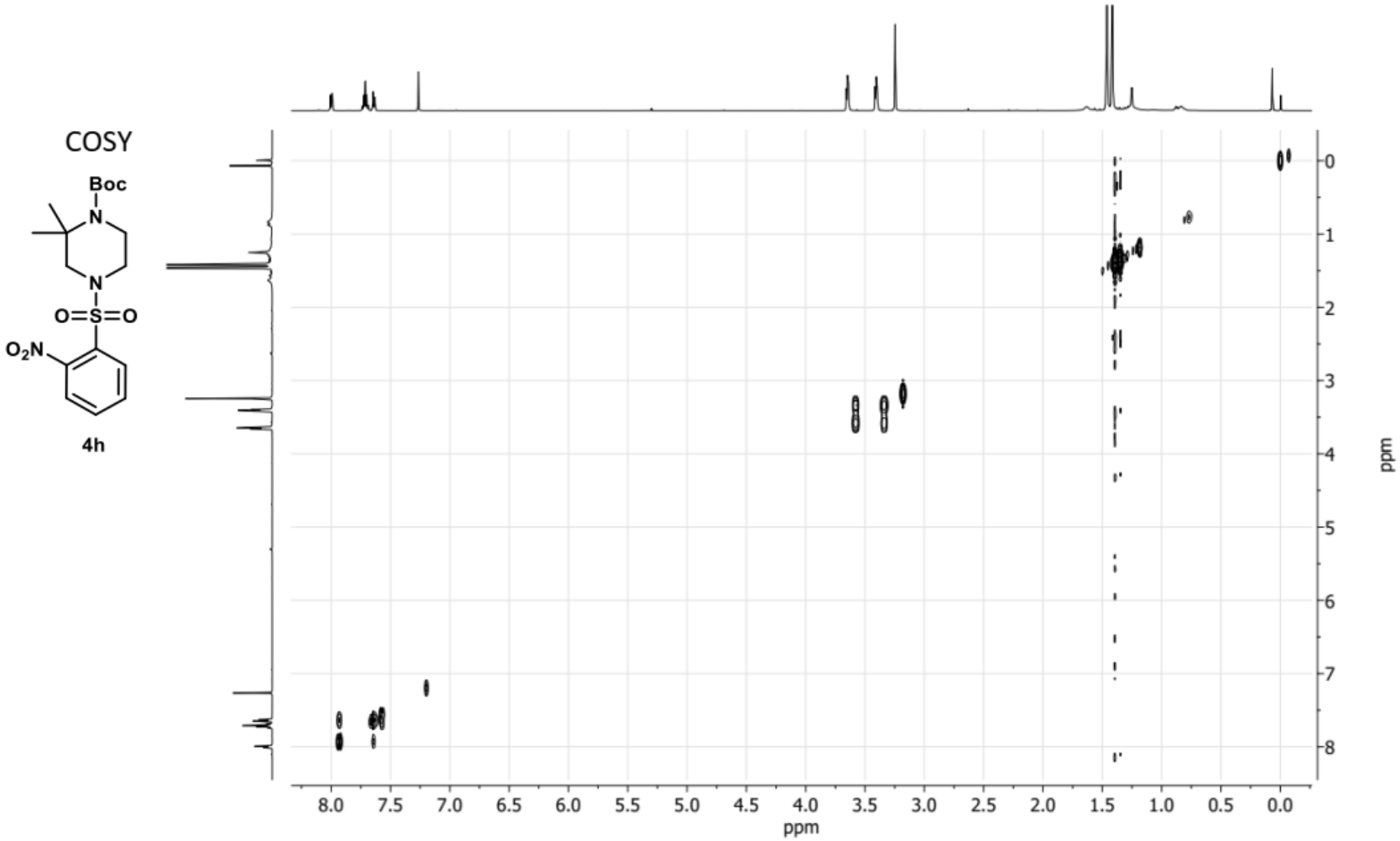
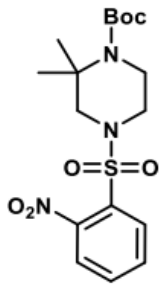
8.0
8.0
7.7
7.7
7.7
7.7
7.7
7.7
7.7
7.7
7.7
7.7
7.6
7.6
7.6
7.6
3.7
3.6
3.6
3.4
3.4
3.4
3.2
1.5
1.4
Boc
N
N
O=S=O
O2N
4h
1.00
2.11
1.00
2.10
2.07
2.09
9.50
6.54
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

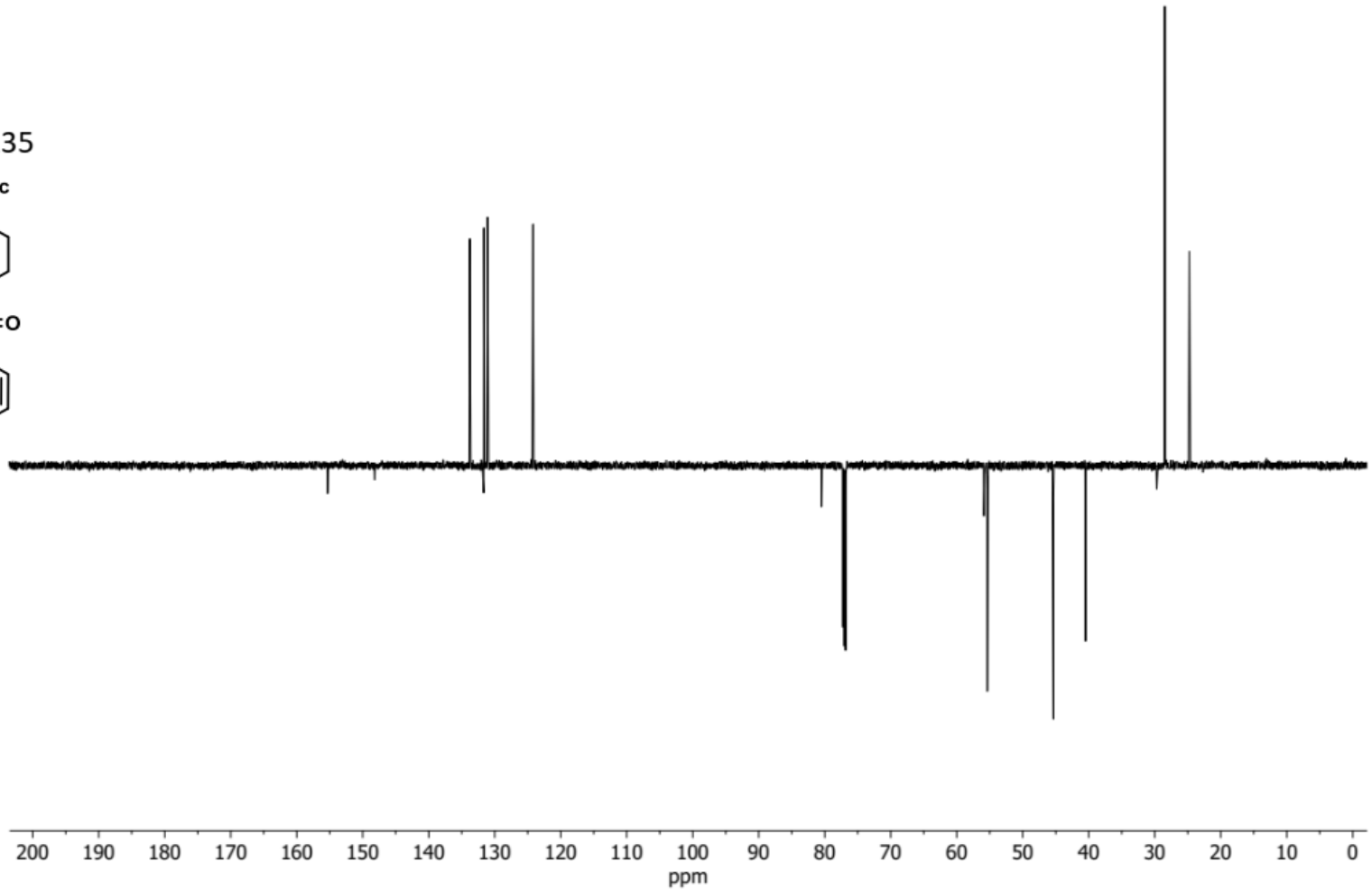

154.3
147.1
132.7
130.6
130.6
130.0
123.2
79.5
54.8
54.3
44.3
39.4
28.7
27.4
23.7
Boc
N
N
O=S=O
O2N
4h
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

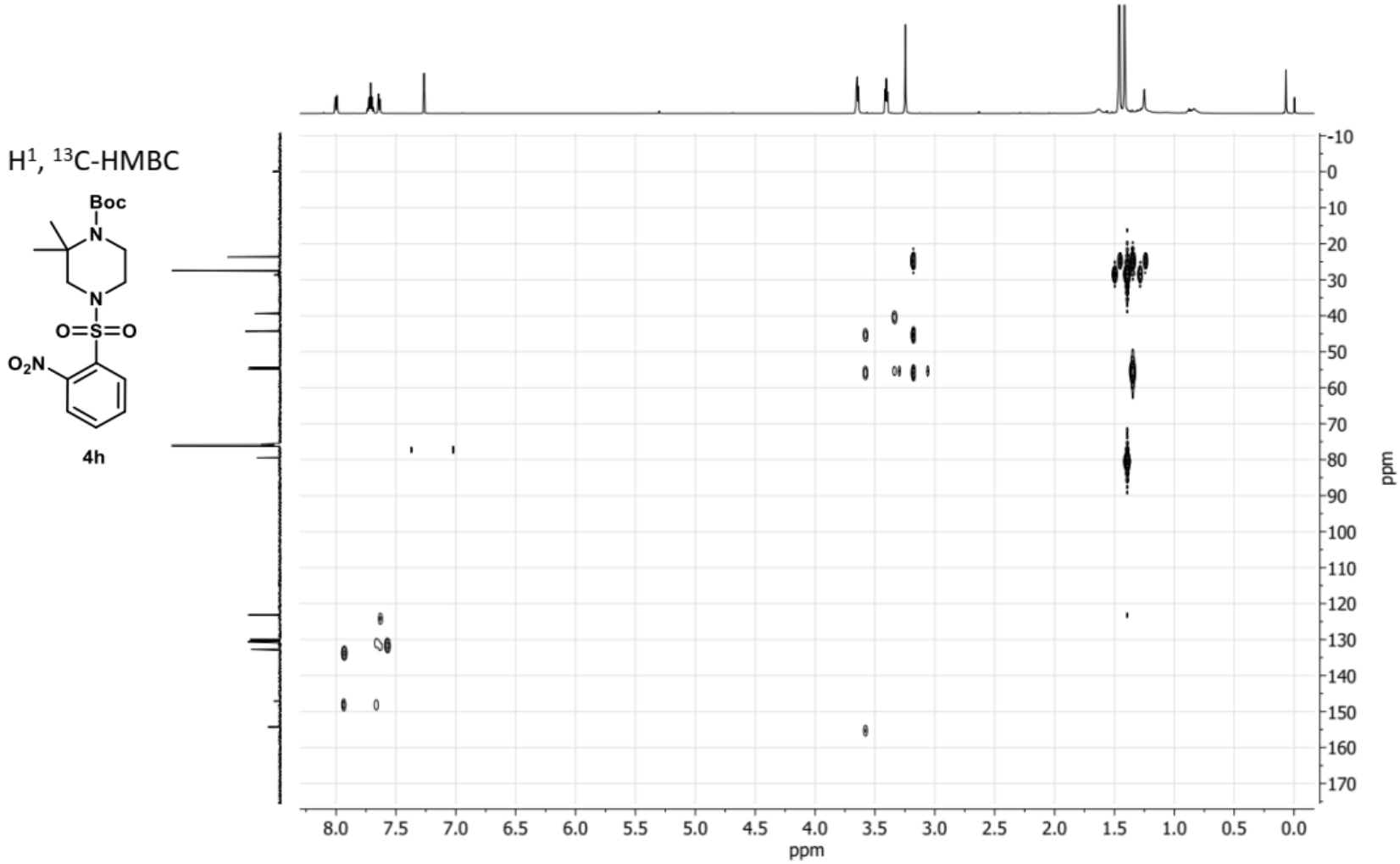

COSY
Boc
N
N
O=S=O
O2N
4h
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0
1
2
3
4
5
6
7
8
ppm

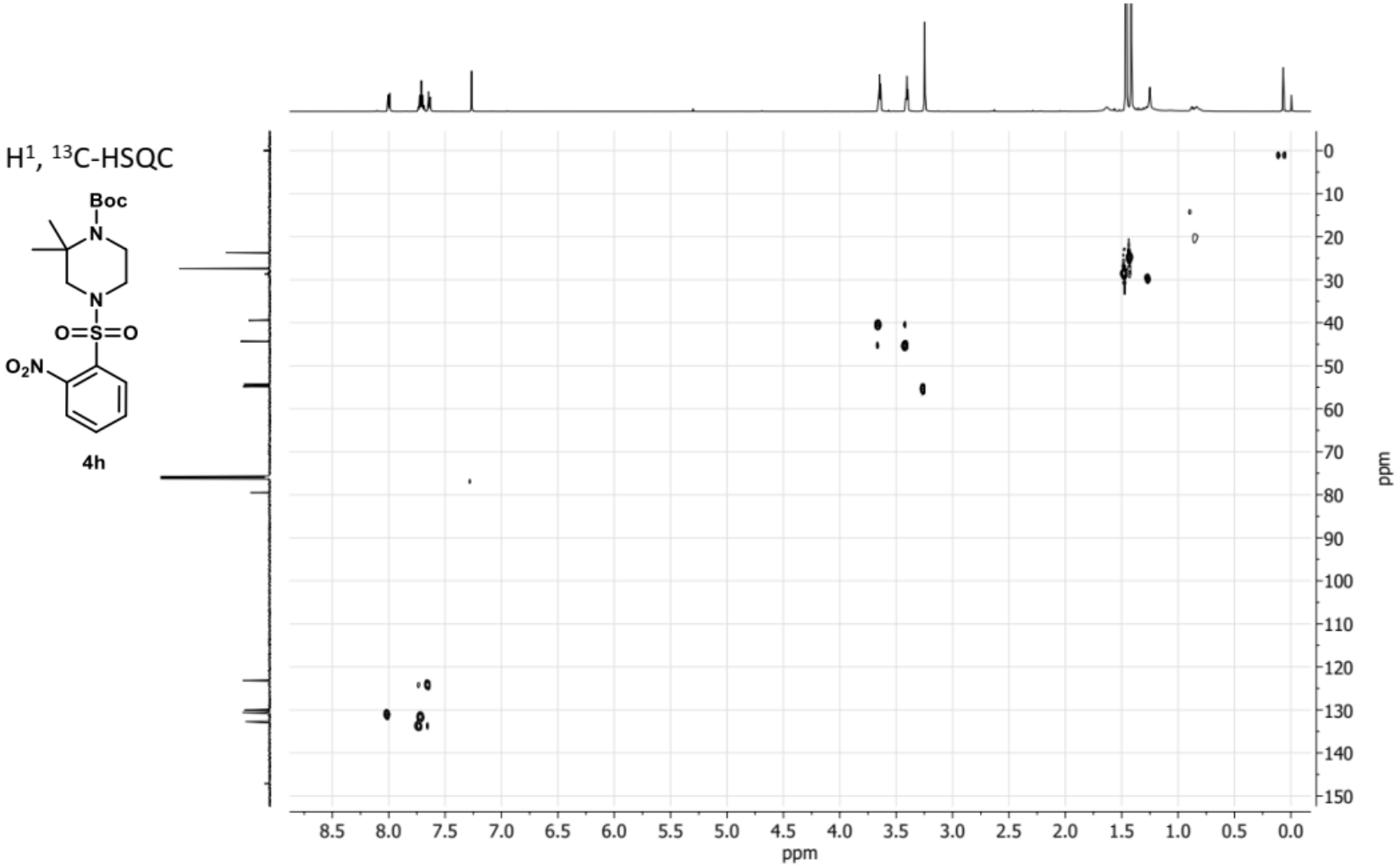
DEPTQ-135

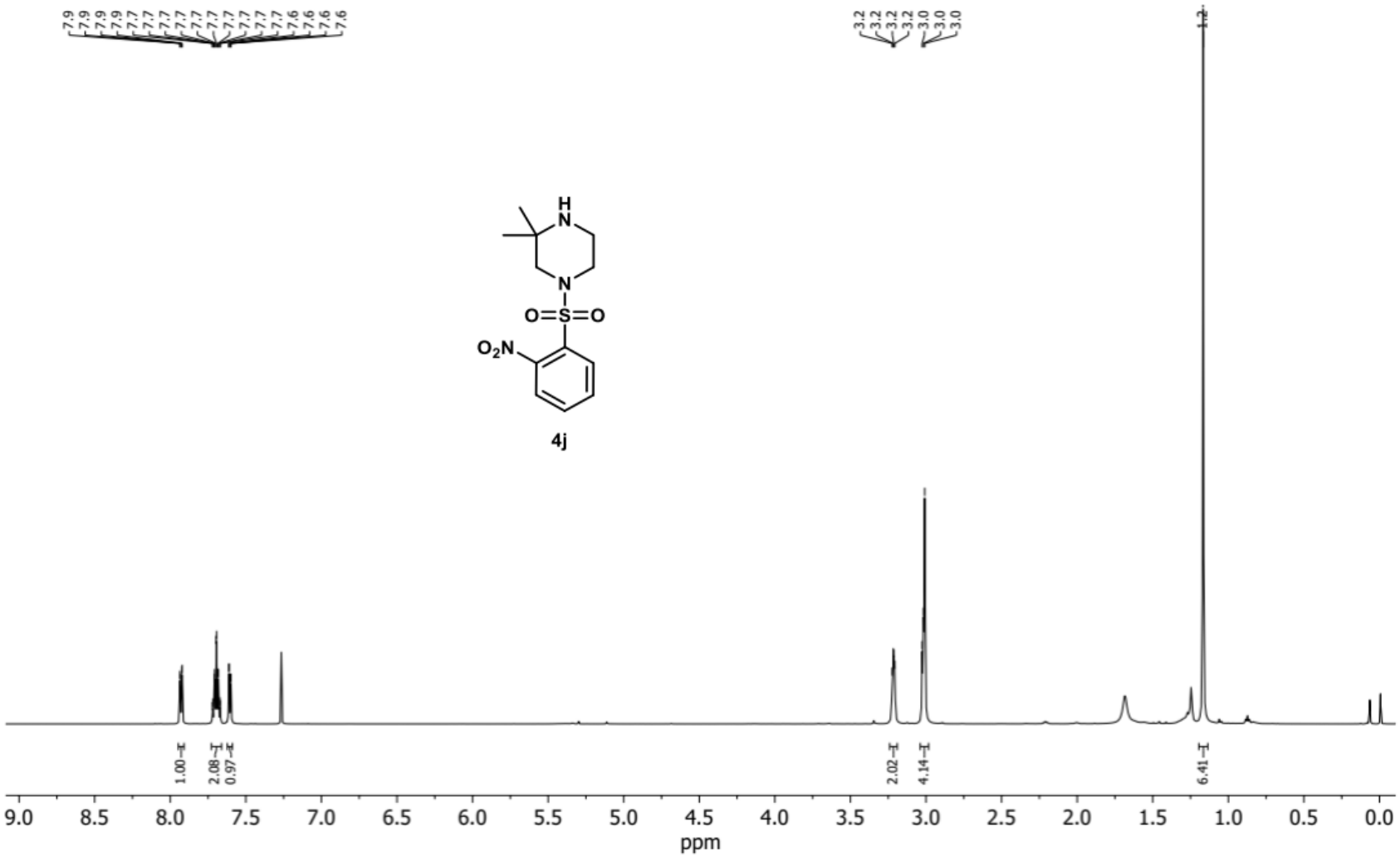

Boc
N
N
O=S=O
O2N

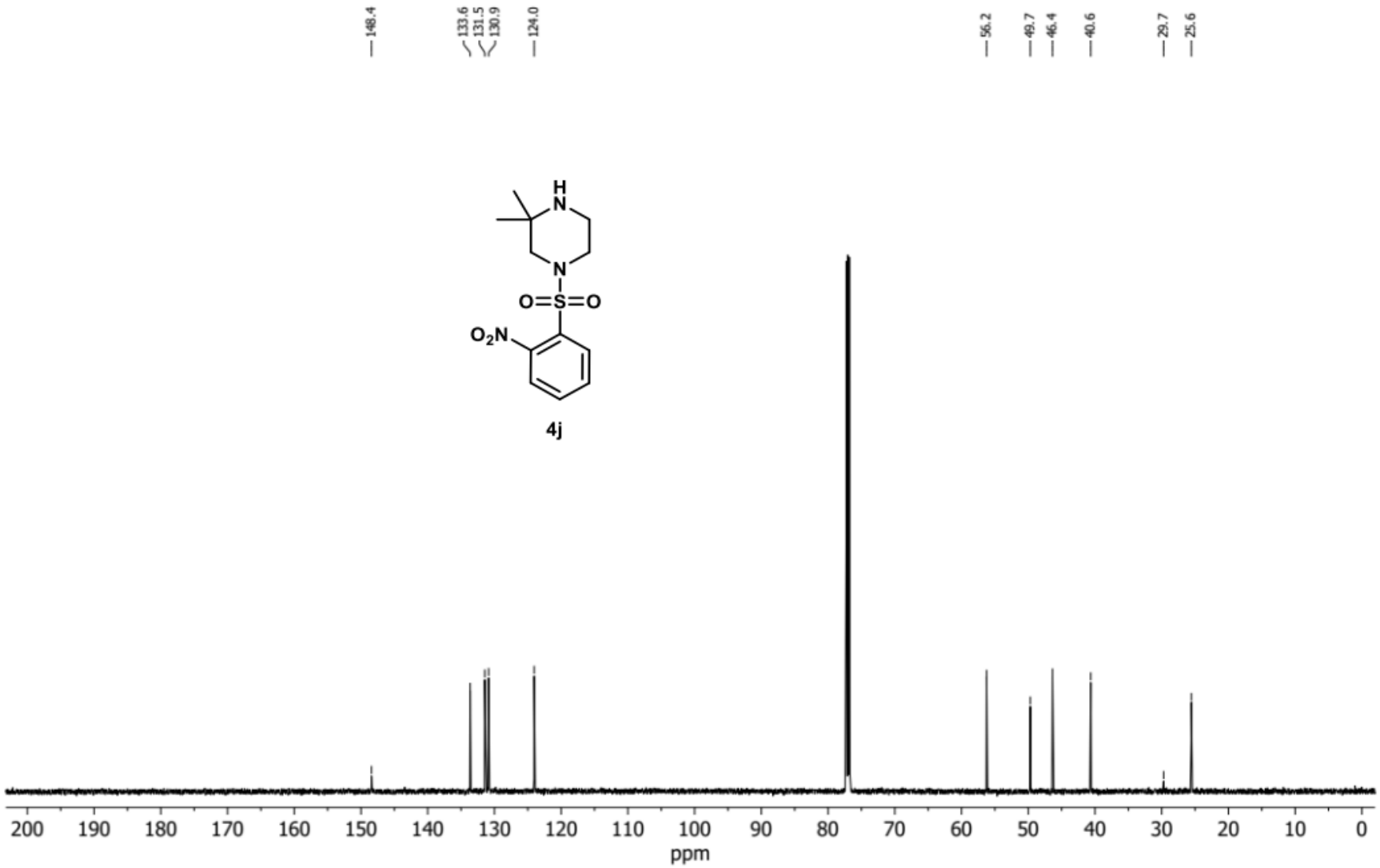
4h

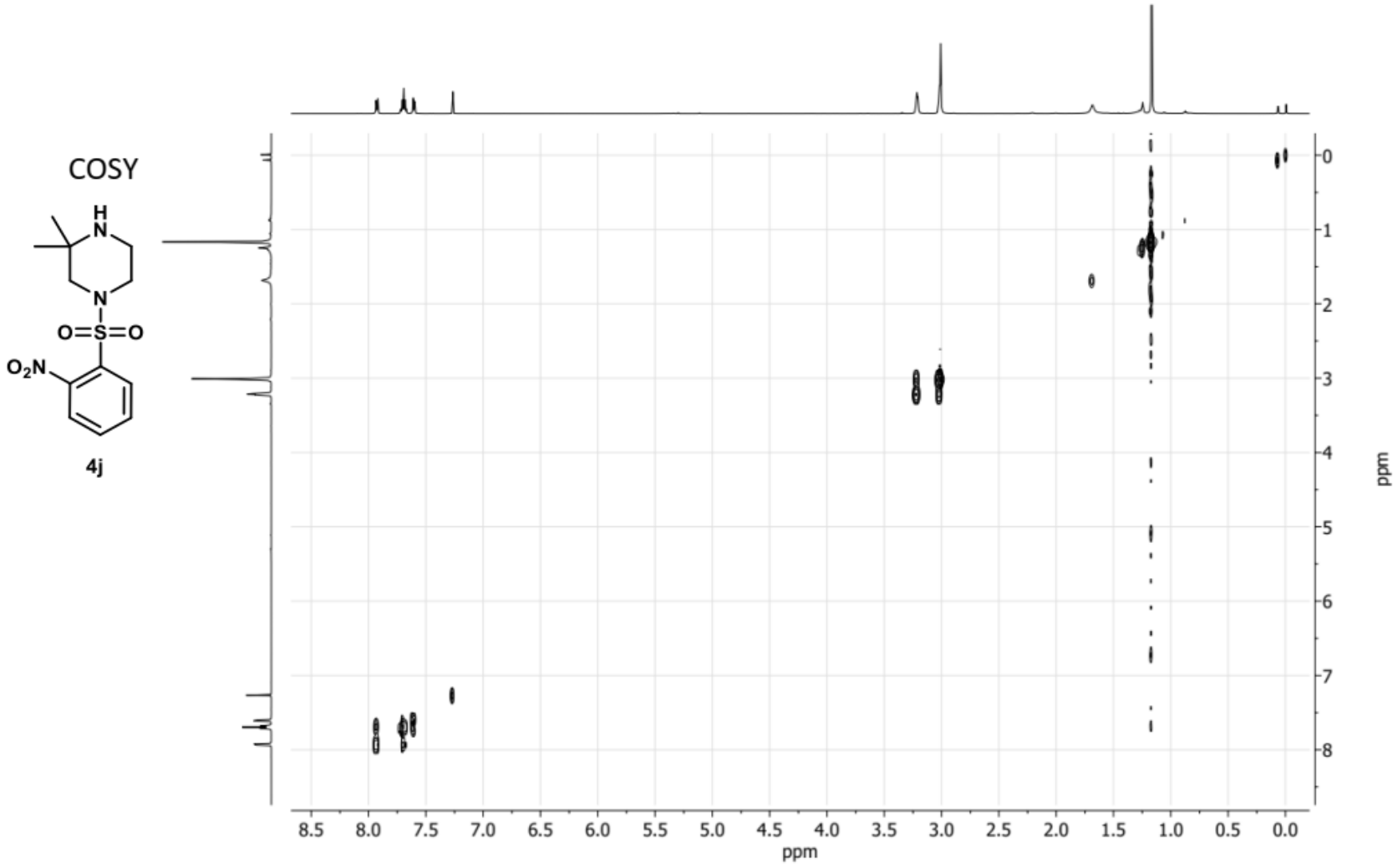

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


H1, 13C-HMBC
Boc
N
N
O=S=O
O2N
4h
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
-10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170
ppm

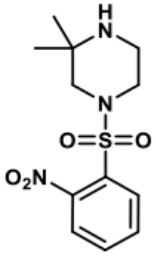

H1, 13C-HSQC
Boc
N
N
O=S=O
O2N
4h
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
ppm


7.9
7.9
7.9
7.9
7.7
7.7
7.7
7.7
7.7
7.7
7.7
7.7
7.7
7.6
7.6
7.6
3.2
3.2
3.2
3.2
3.0
3.0
3.0
1.2
H
N
N
O=S=O
O2N
4j
1.00
2.08
0.97
2.02
4.14
6.41
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


148.4
133.6
131.5
130.9
124.0
56.2
49.7
46.4
40.6
29.7
25.6
H
N
N
O=S=O
O2N
4j
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

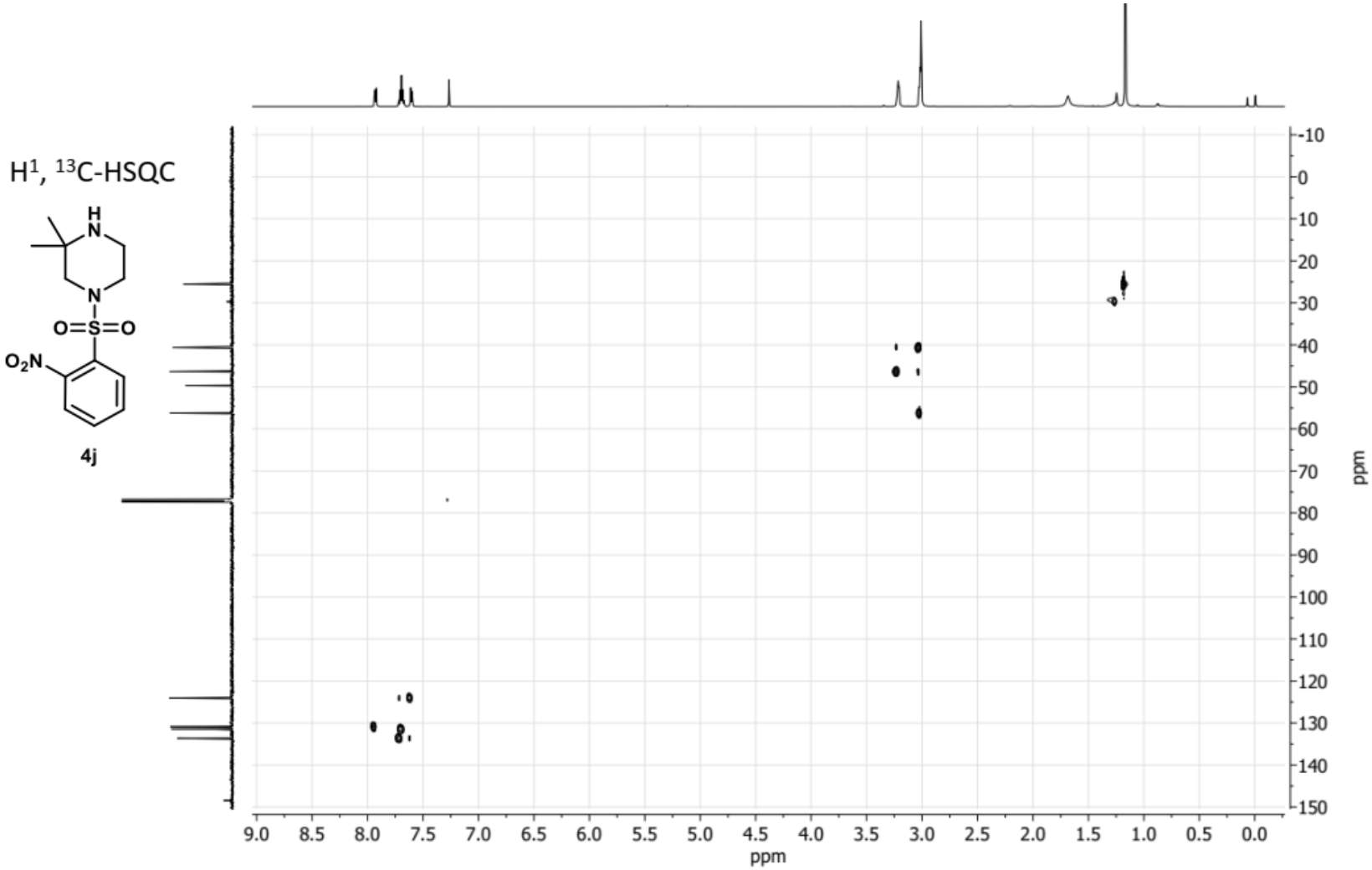

COSY
4j
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
0 1 2 3 4 5 6 7 8
ppm

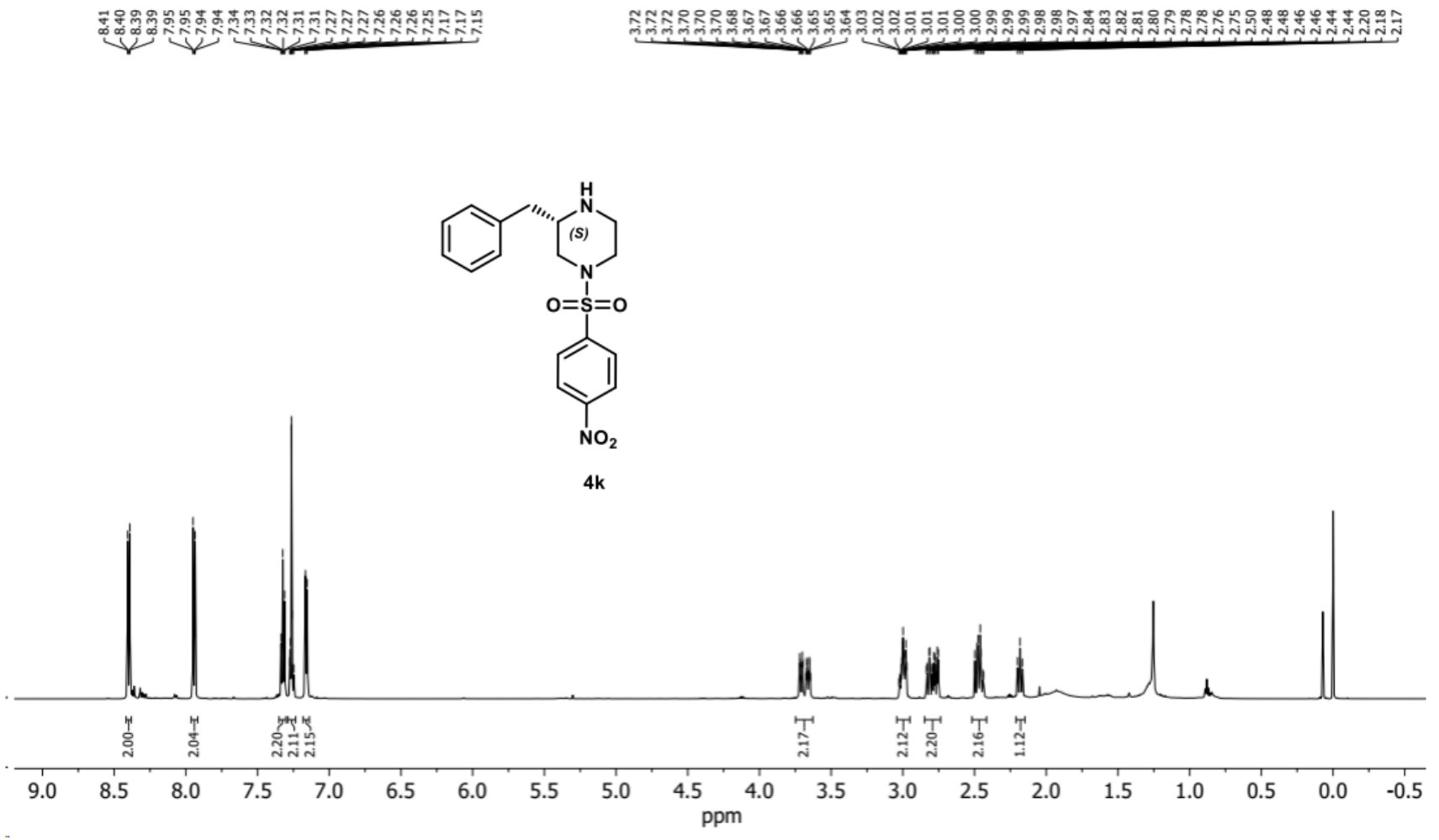
DEPTQ-135

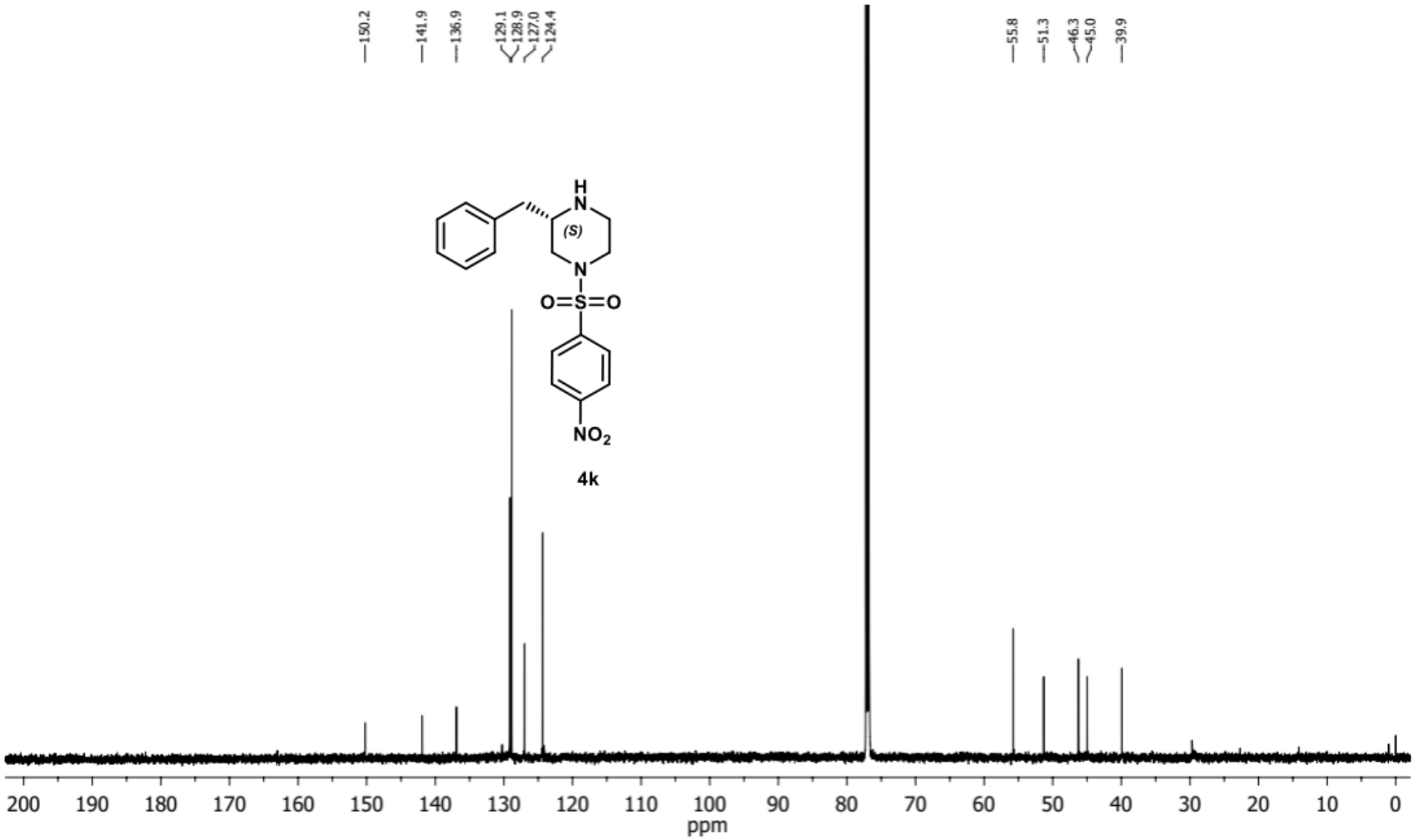

H
N
N
O=S=O
O2N

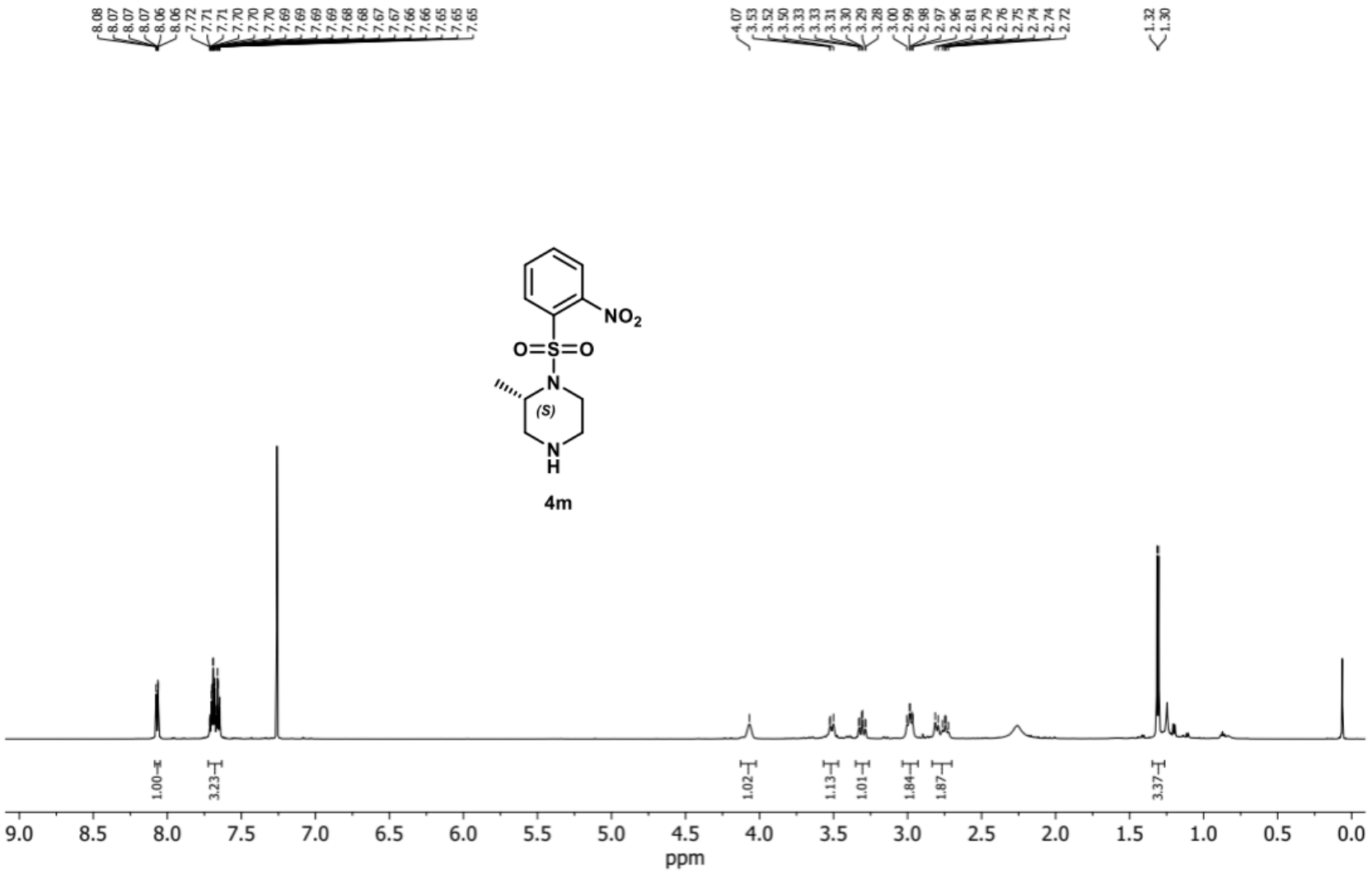
4j

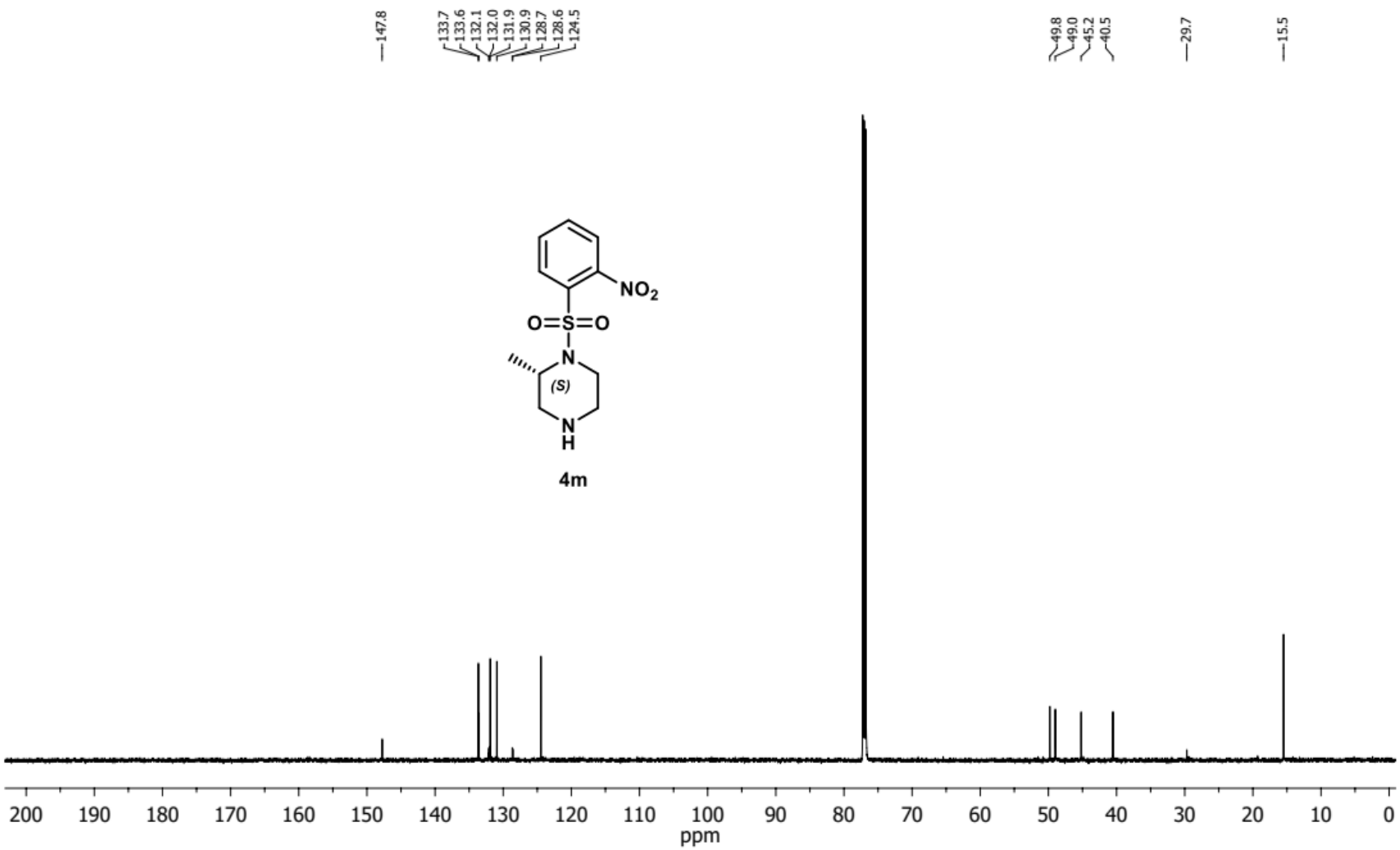
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

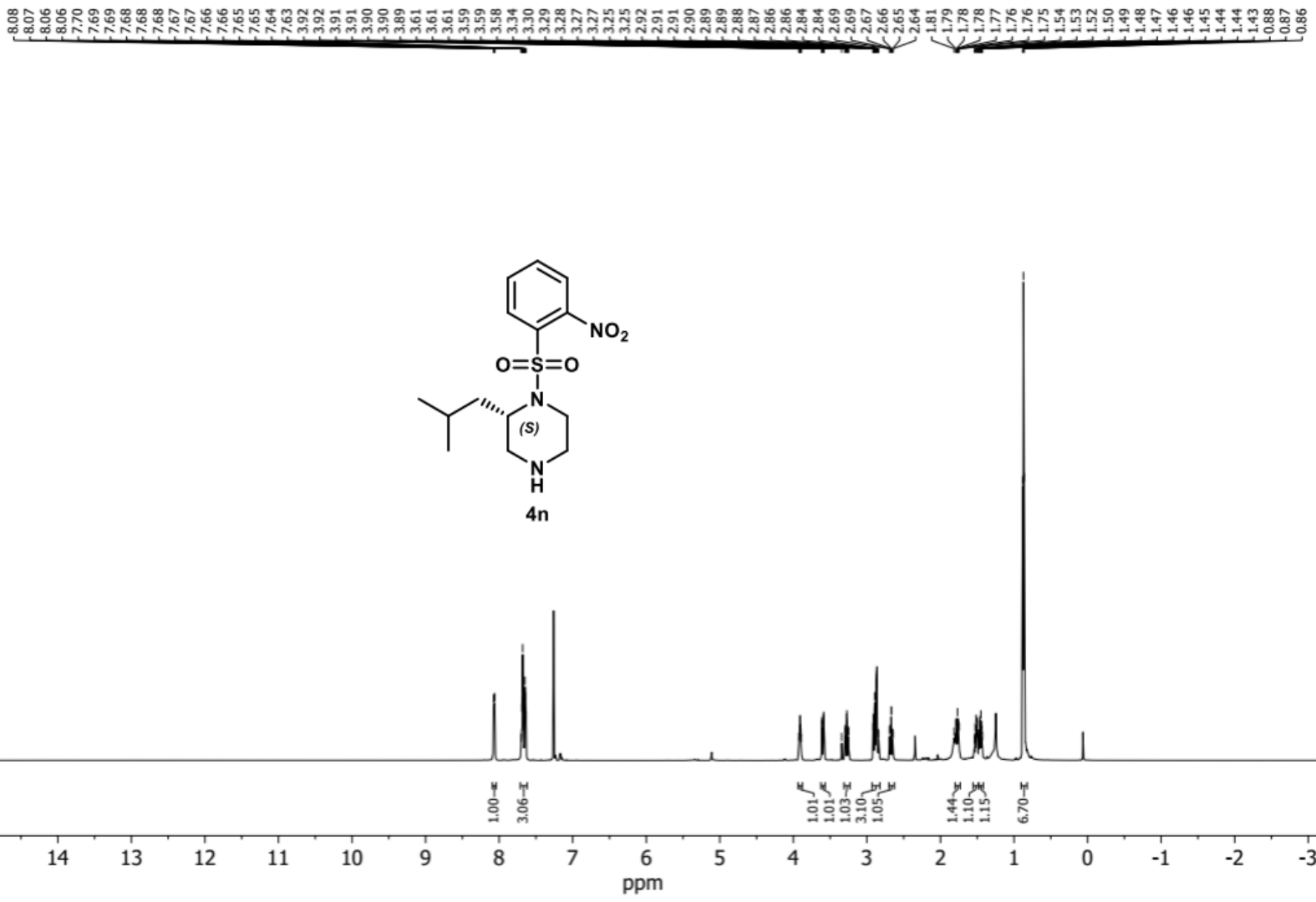

H1, 13C-HSQC
4j
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
-10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
ppm

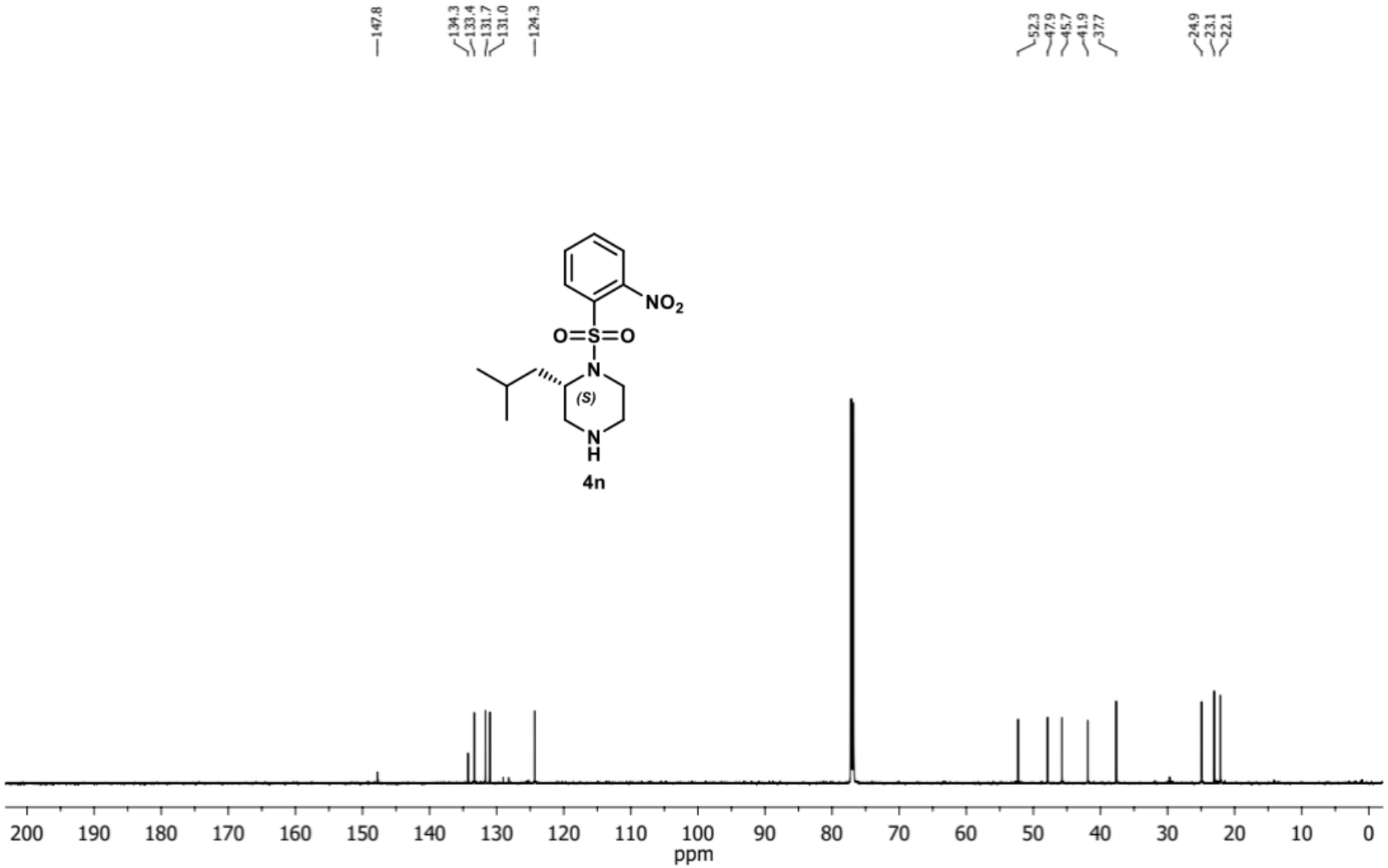

8.41 8.40 8.39 8.39 7.95 7.95 7.94 7.94 7.34 7.33 7.32 7.32 7.31 7.31 7.27 7.27 7.27 7.26 7.26 7.26 7.25 7.17 7.17 7.15
3.72 3.72 3.72 3.70 3.70 3.70 3.68 3.67 3.67 3.66 3.66 3.65 3.65 3.64 3.03 3.02 3.02 3.01 3.01 3.01 3.00 3.00 2.99 2.99 2.99 2.98 2.98 2.97 2.84 2.83 2.82 2.81 2.80 2.79 2.78 2.78 2.76 2.75 2.50 2.48 2.48 2.46 2.46 2.44 2.44 2.20 2.18 2.17
H
N
(S)
N
O=S=O
NO2
4k
2.00 2.04 2.20 2.11 2.15 2.17 2.12 2.20 2.16 1.12
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

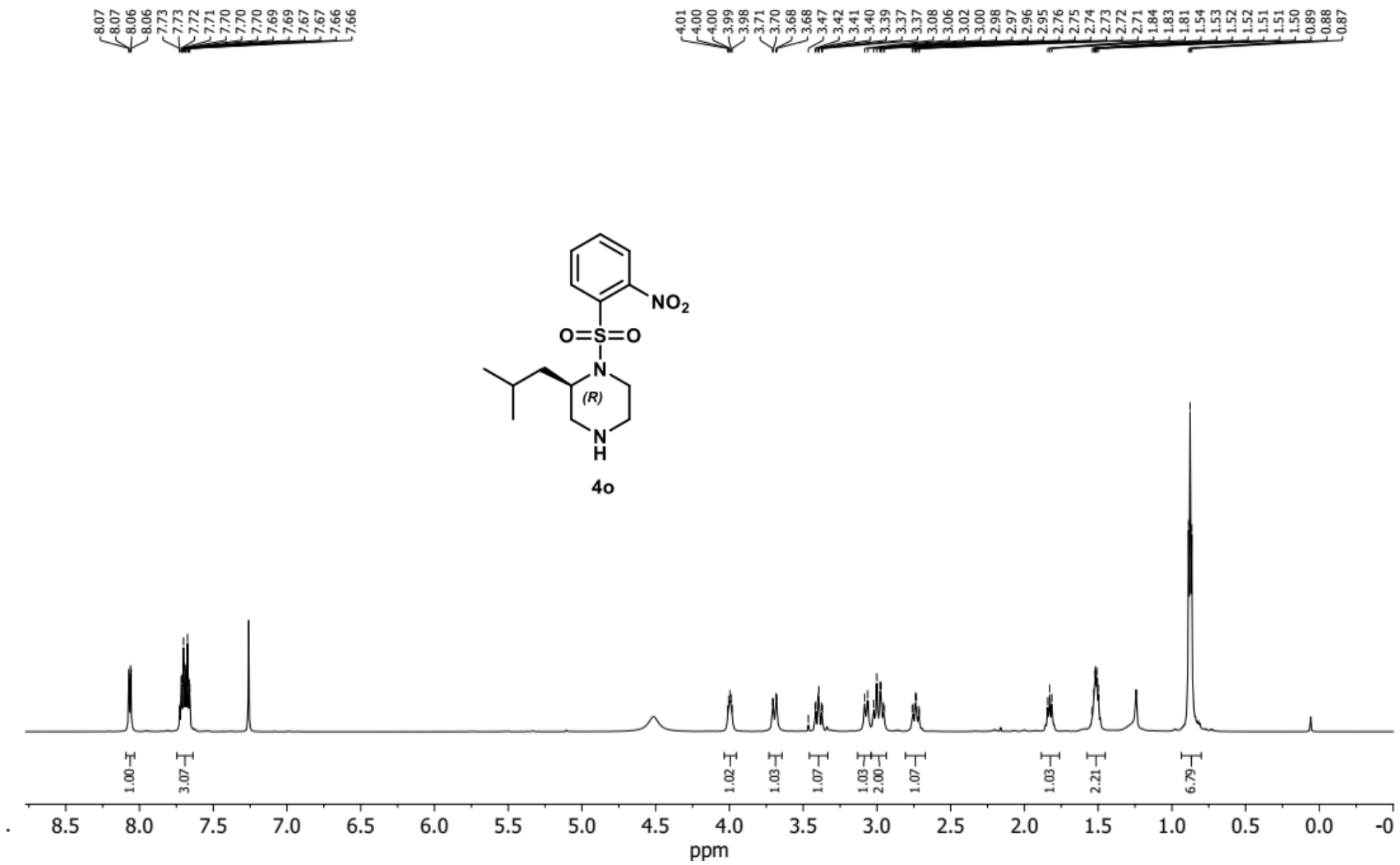

150.2
141.9
136.9
129.1
128.9
127.0
124.4
55.8
51.3
46.3
45.0
39.9
H
N
(S)
N
O=S=O
NO2
4k
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


8.08
8.07
8.07
8.07
8.06
8.06
7.72
7.71
7.71
7.70
7.70
7.70
7.69
7.69
7.69
7.69
7.68
7.68
7.67
7.67
7.66
7.66
7.65
7.65
7.65
4.07
3.53
3.52
3.50
3.33
3.33
3.31
3.30
3.29
3.28
3.00
2.99
2.98
2.97
2.96
2.81
2.79
2.76
2.75
2.74
2.74
2.72
1.32
1.30
NO2
O=S=O
N
(S)
N
H
4m
1.00
3.23
1.02
1.13
1.01
1.84
1.87
3.37
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


147.8
133.7
133.6
132.1
132.0
131.9
130.9
128.7
128.6
124.5
49.8
49.0
45.2
40.5
29.7
15.5
NO2
O=S=O
N
(S)
N
H
4m
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


8.08 8.07 8.06 8.06 7.70 7.69 7.69 7.68 7.68 7.68 7.67 7.67 7.66 7.66 7.65 7.65 7.64 7.63 3.92 3.92 3.91 3.91 3.90 3.90 3.89 3.61 3.61 3.61 3.59 3.59 3.58 3.34 3.30 3.29 3.28 3.27 3.27 3.25 2.92 2.91 2.91 2.90 2.89 2.89 2.88 2.87 2.86 2.86 2.84 2.84 2.69 2.69 2.67 2.66 2.65 2.64 1.81 1.79 1.78 1.78 1.77 1.76 1.76 1.75 1.54 1.53 1.52 1.50 1.49 1.48 1.47 1.46 1.46 1.45 1.44 1.44 1.43 0.88 0.87 0.86
NO2
O=S=O
N
(S)
N
H
4n
1.00
3.06
1.01
1.01
1.03
3.10
1.05
1.44
1.10
1.15
6.70
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
ppm


147.8
134.3
133.4
131.7
131.0
124.3
52.3
47.9
45.7
41.9
37.7
24.9
23.1
22.1
NO2
O=S=O
N
(S)
N
H
4n
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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8.07
8.06
8.06
7.73
7.73
7.72
7.71
7.70
7.70
7.70
7.69
7.69
7.67
7.67
7.66
7.66
4.01
4.00
4.00
3.99
3.98
3.71
3.70
3.68
3.68
3.47
3.42
3.41
3.40
3.39
3.37
3.37
3.08
3.06
3.02
3.00
2.98
2.97
2.96
2.95
2.76
2.75
2.74
2.73
2.72
2.71
1.84
1.83
1.81
1.54
1.53
1.52
1.52
1.51
1.51
1.50
0.89
0.88
0.87
NO2
O=S=O
N
(R)
N
H
4o
1.00
3.07
1.02
1.03
1.07
1.03
2.00
1.07
1.03
2.21
6.79
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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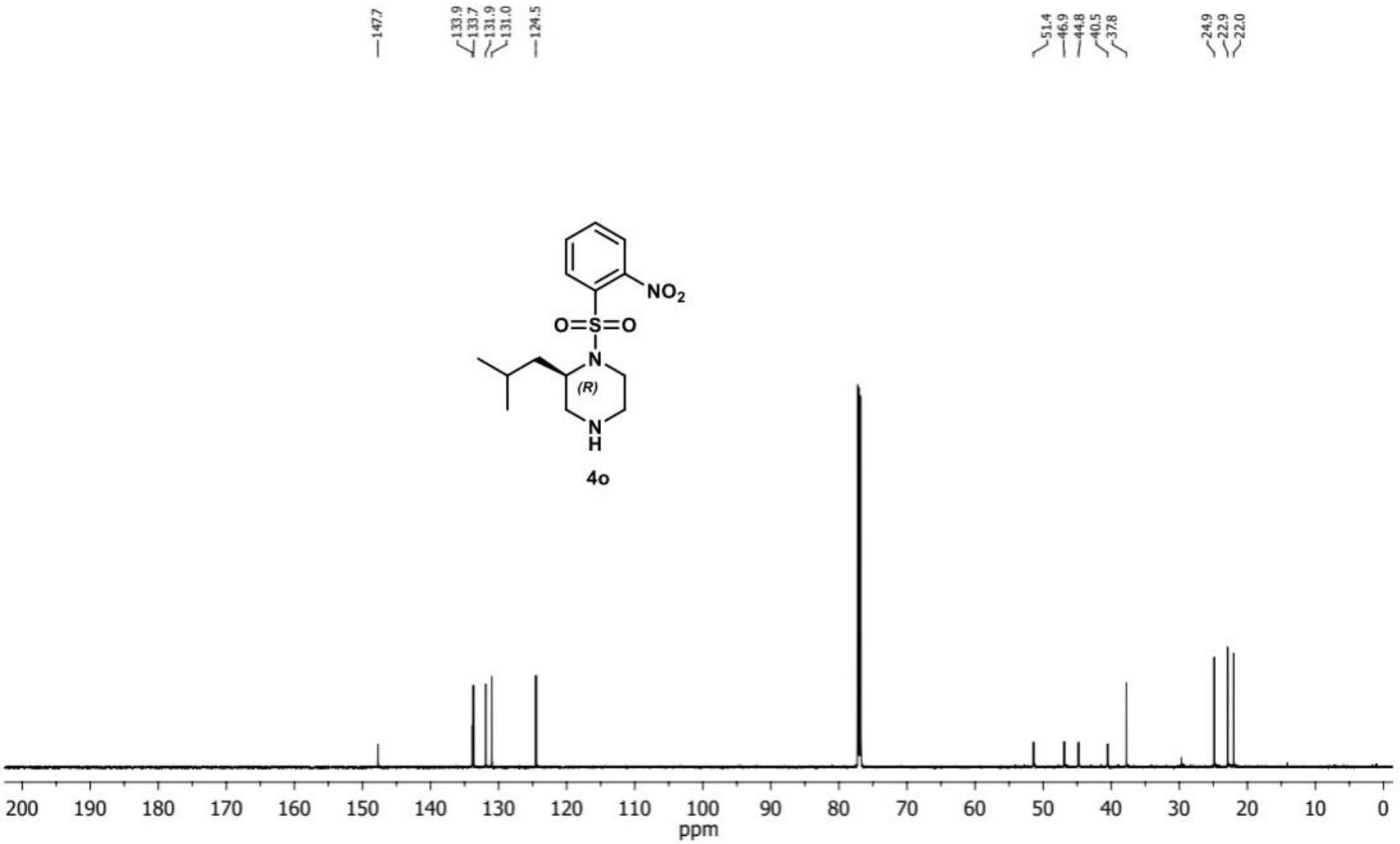
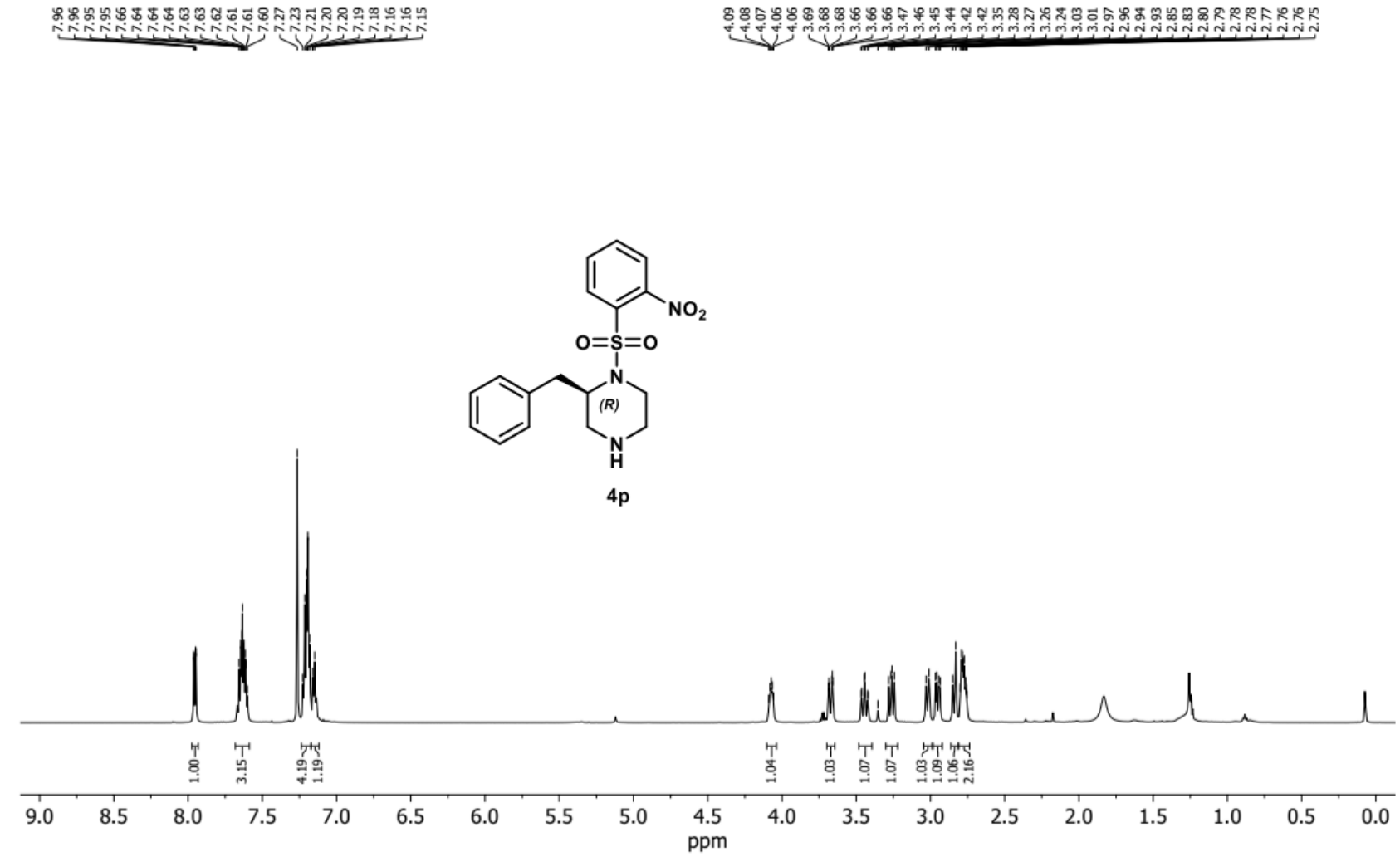
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
ppm


147.7
133.9
133.7
131.9
131.0
124.5
51.4
46.9
44.8
40.5
37.8
24.9
22.9
22.0
NO2
O=S=O
N
(R)
N
H
4o
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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7.95
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7.64
7.63
7.63
7.62
7.61
7.61
7.60
7.27
7.23
7.21
7.20
7.20
7.19
7.18
7.16
7.16
7.15
4.09
4.08
4.07
4.06
4.06
3.69
3.68
3.68
3.66
3.66
3.66
3.47
3.46
3.45
3.44
3.42
3.42
3.35
3.28
3.27
3.26
3.24
3.03
3.01
2.97
2.96
2.94
2.93
2.85
2.83
2.80
2.79
2.78
2.78
2.77
2.76
2.76
2.75
NO2
O=S=O
N
(R)
N
H
4p
1.00
3.15
4.19
1.19
1.04
1.03
1.07
1.07
1.03
1.09
1.06
2.16
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
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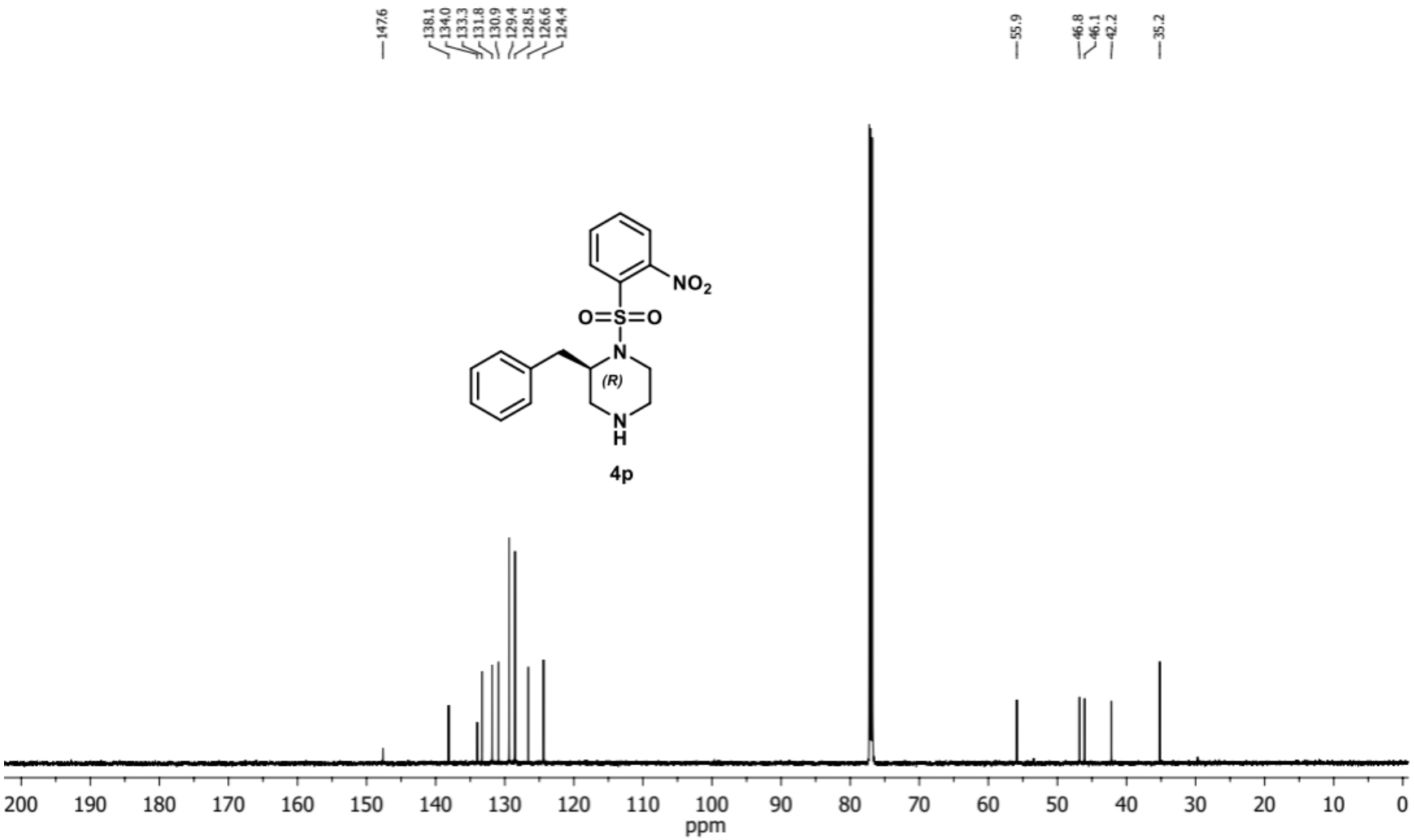
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134.0
133.3
131.8
130.9
129.4
128.5
126.6
124.4
55.9
46.8
46.1
42.2
35.2
NO2
O=S=O
N
(R)
N
H
4p
200
190
180
170
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150
140
130
120
110
100
90
80
70
60
50
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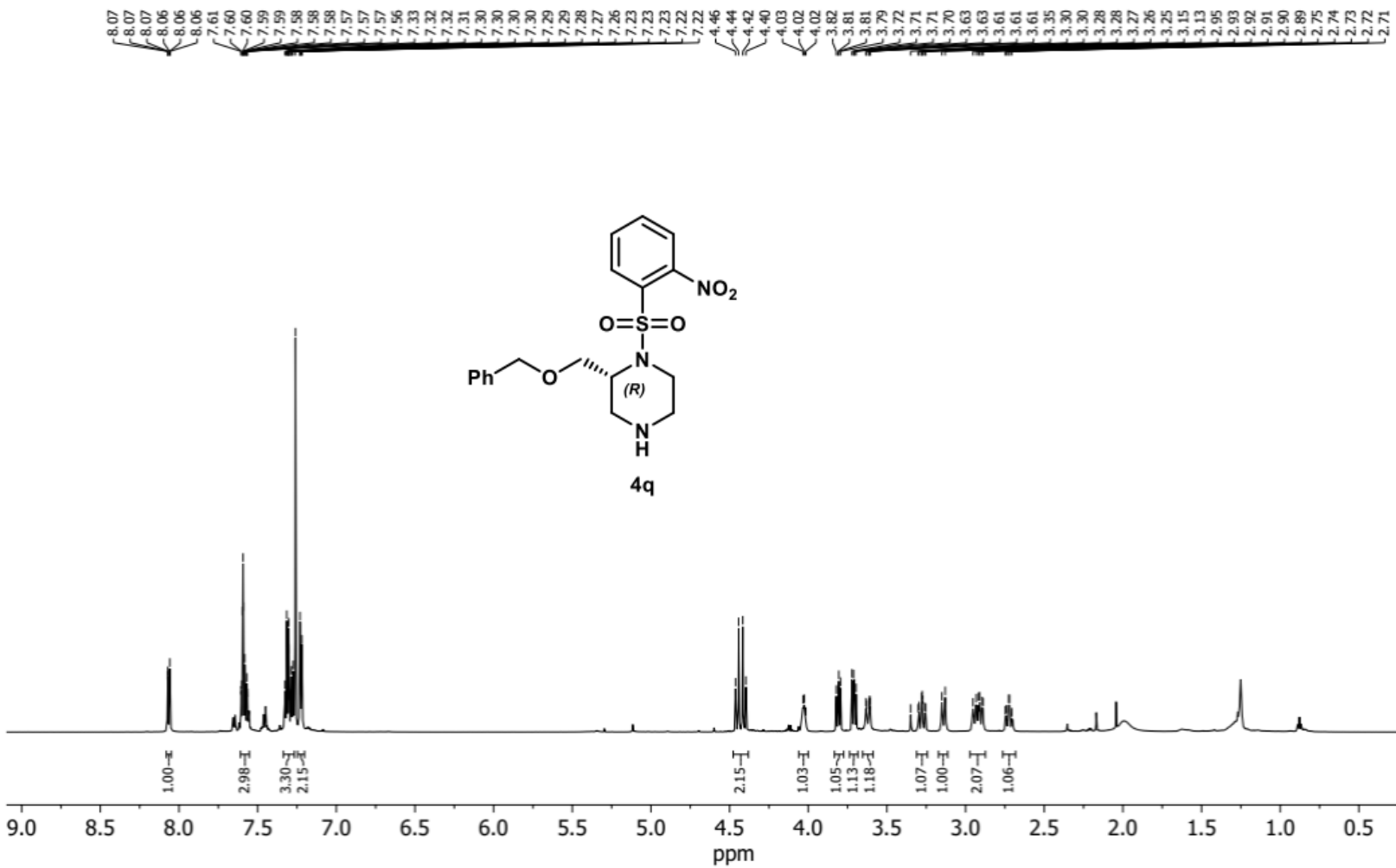
30
20
10
0
ppm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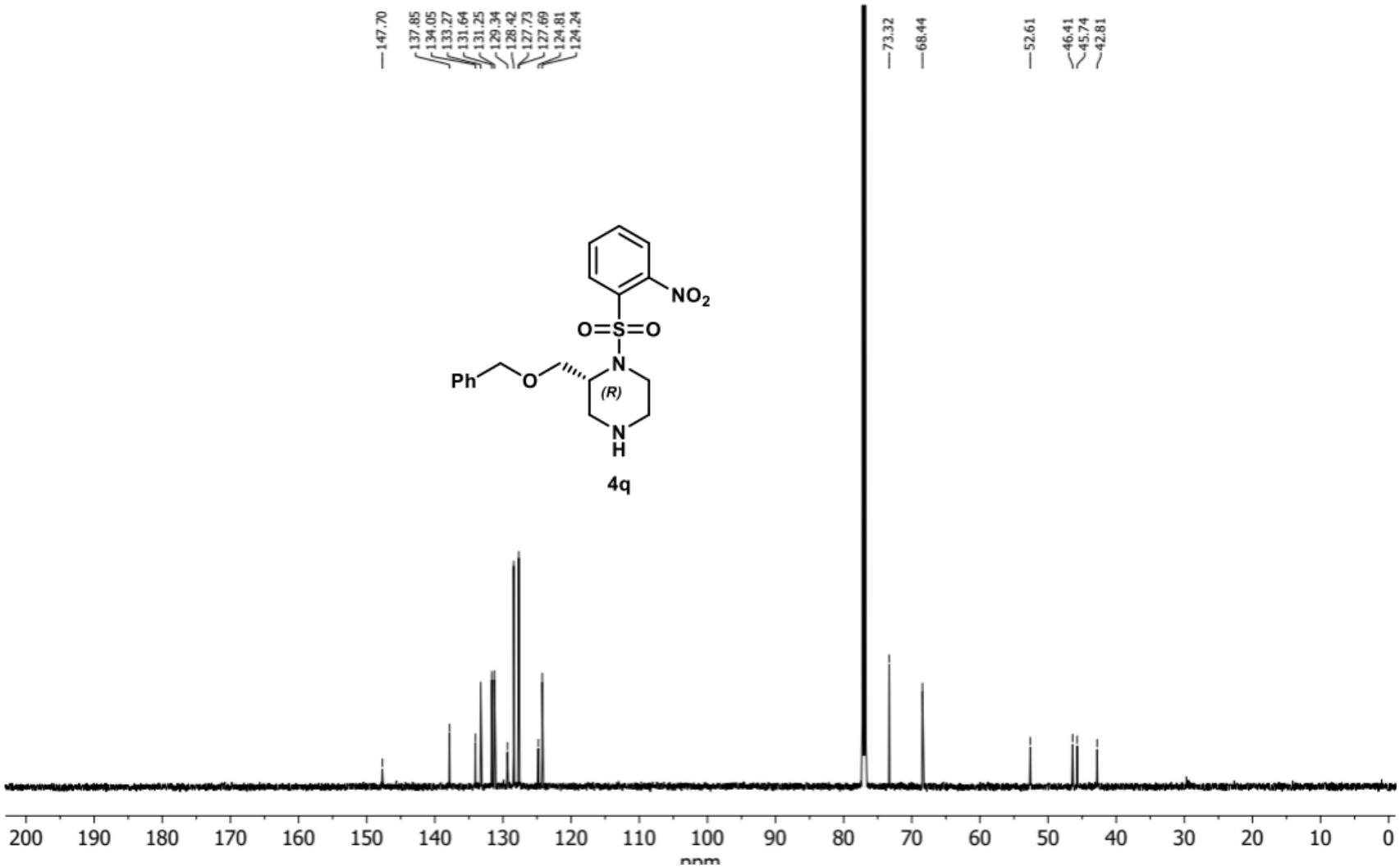
NO2
O=S=O
N
Ph
O
(R)
N
H
4q
1.00 2.98 3.30 2.15 2.15 1.03 1.05 1.13 1.18 1.07 1.00 2.07 1.06
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm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131.25
129.34
128.42
127.73
127.69
124.81
124.24
73.32
68.44
52.61
46.41
45.74
42.81
NO2
O=S=O
N
Ph
O
(R)
N
H
4q
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
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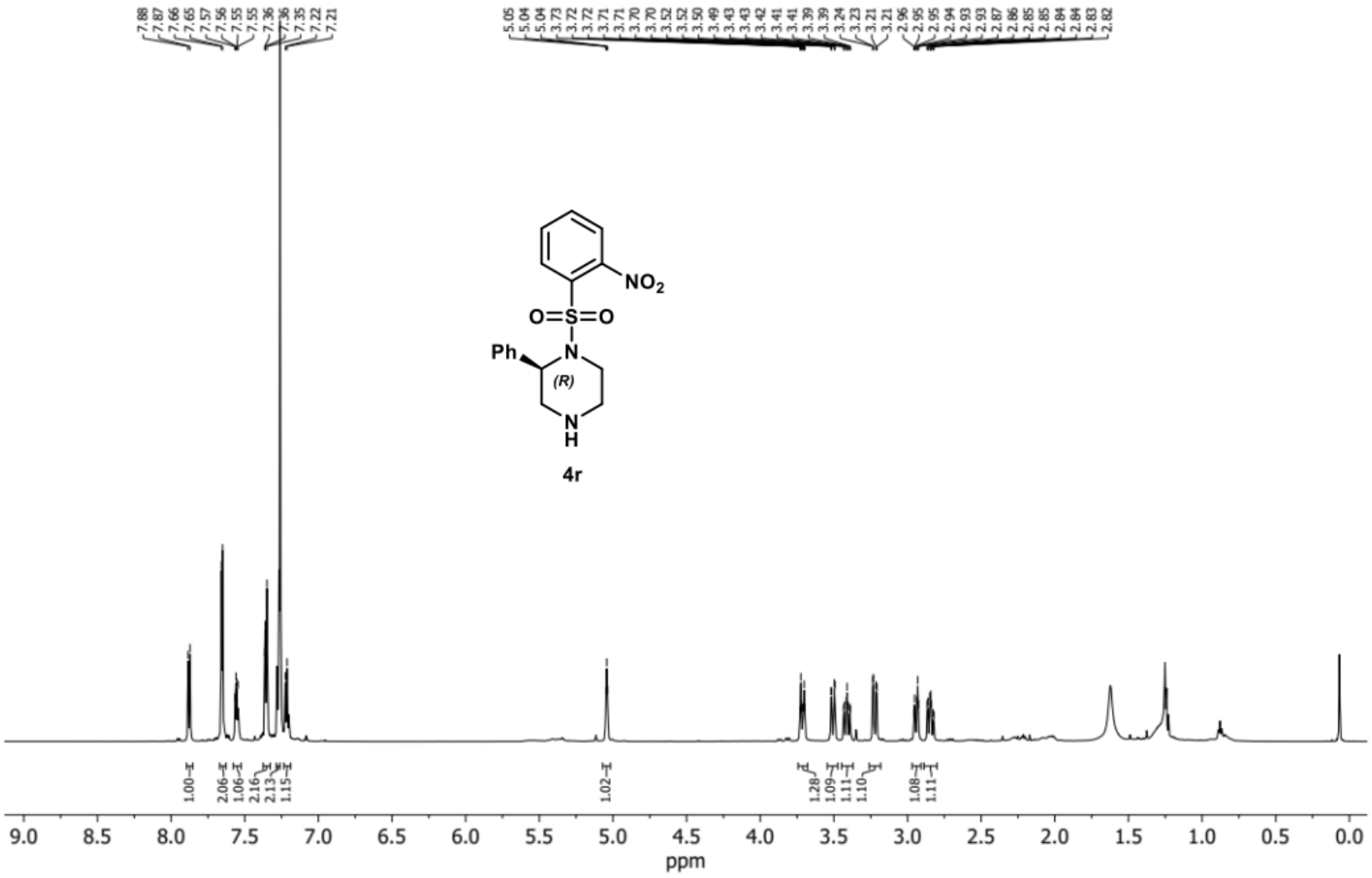
30
20
10
0
ppm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7.87
7.66
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7.56
7.55
7.55
7.36
7.36
7.35
7.22
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5.05
5.04
5.04
3.73
3.72
3.72
3.71
3.71
3.70
3.70
3.52
3.52
3.50
3.49
3.43
3.43
3.42
3.41
3.41
3.39
3.39
3.24
3.23
3.21
3.21
2.96
2.95
2.95
2.94
2.93
2.93
2.87
2.86
2.85
2.85
2.84
2.84
2.83
2.82
NO2
O=S=O
Ph
N
(R)
N
H
4r
1.00
2.06
1.06
2.16
2.13
1.15
1.02
1.28
1.09
1.11
1.10
1.08
1.11
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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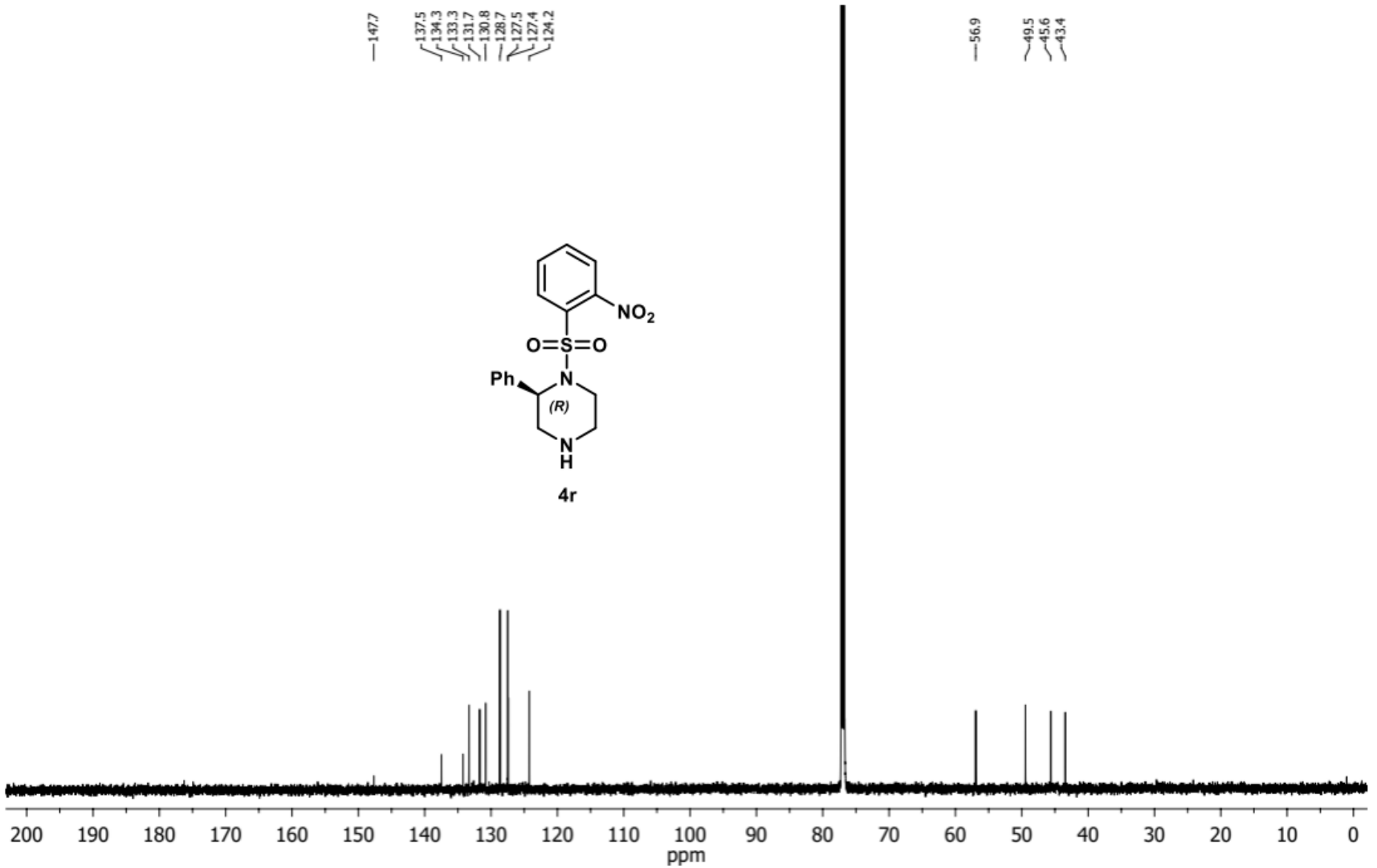
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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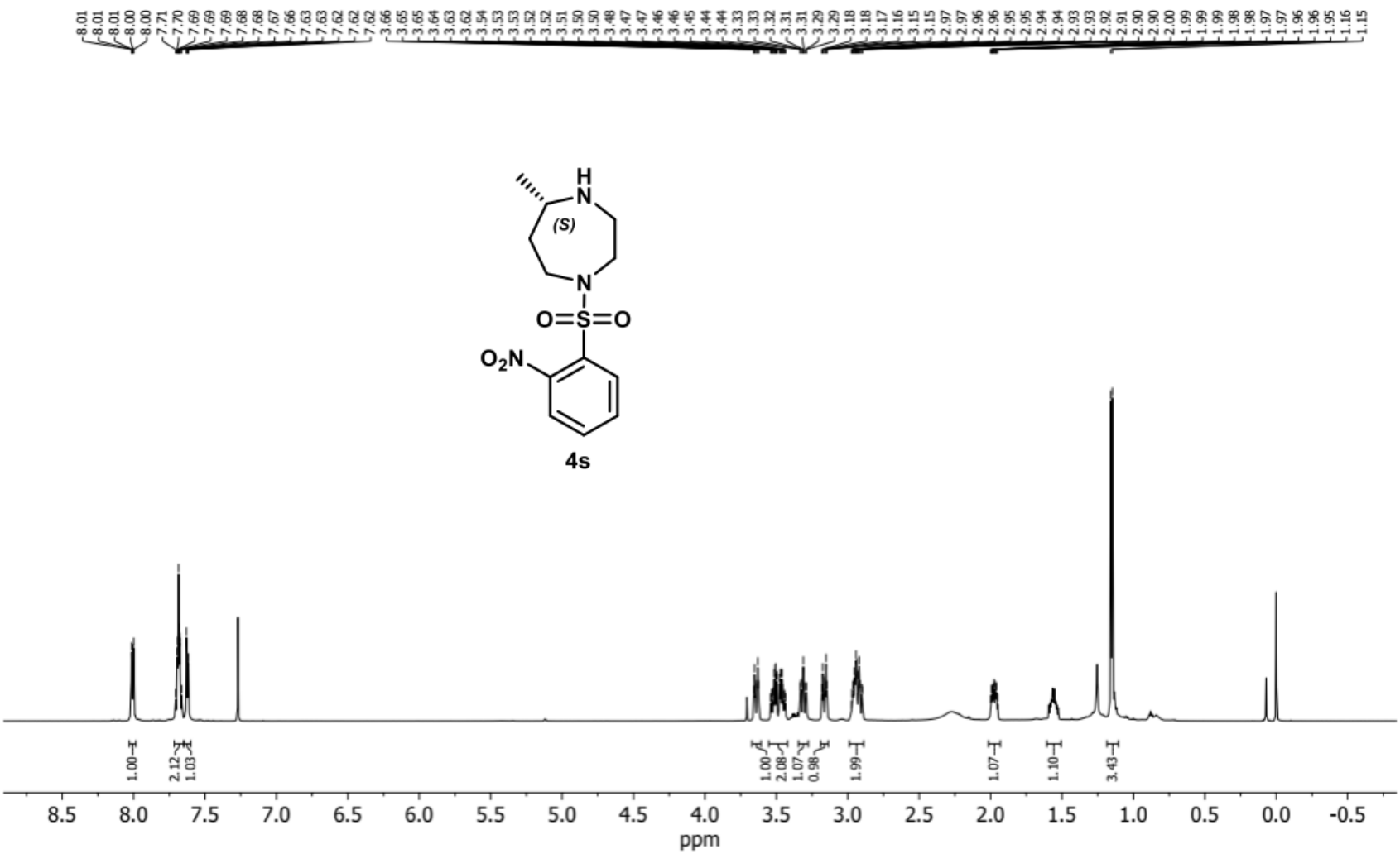
134.3
133.3
131.7
130.8
128.7
127.5
127.4
124.2
56.9
49.5
45.6
43.4
NO2
O=S=O
Ph
N
(R)
N
H
4r
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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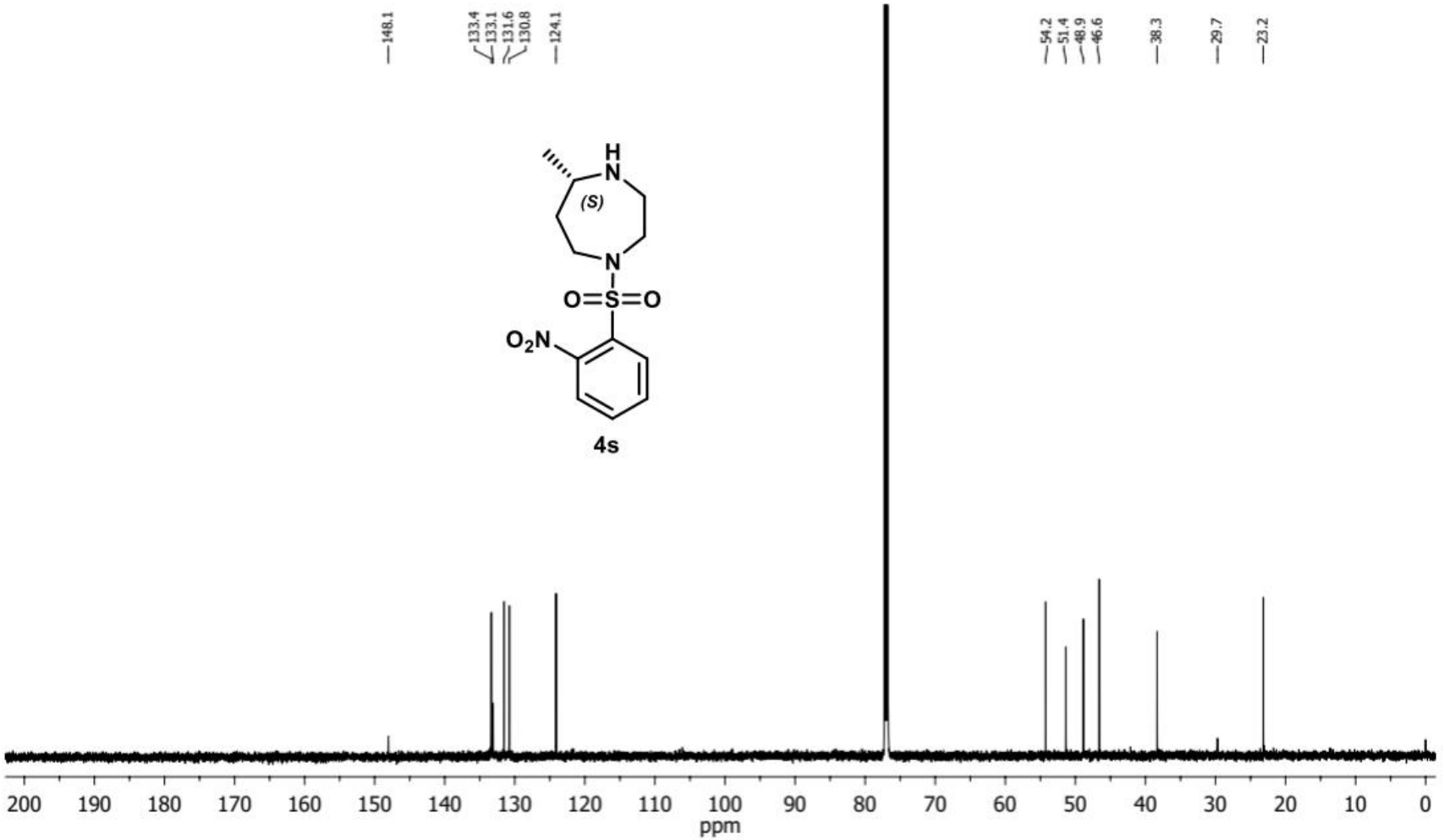
H
N
(S)
N
O=S=O
O2N
4s
1.00
2.12
1.03
1.00
2.08
1.07
0.98
1.99
1.07
1.10
3.43
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm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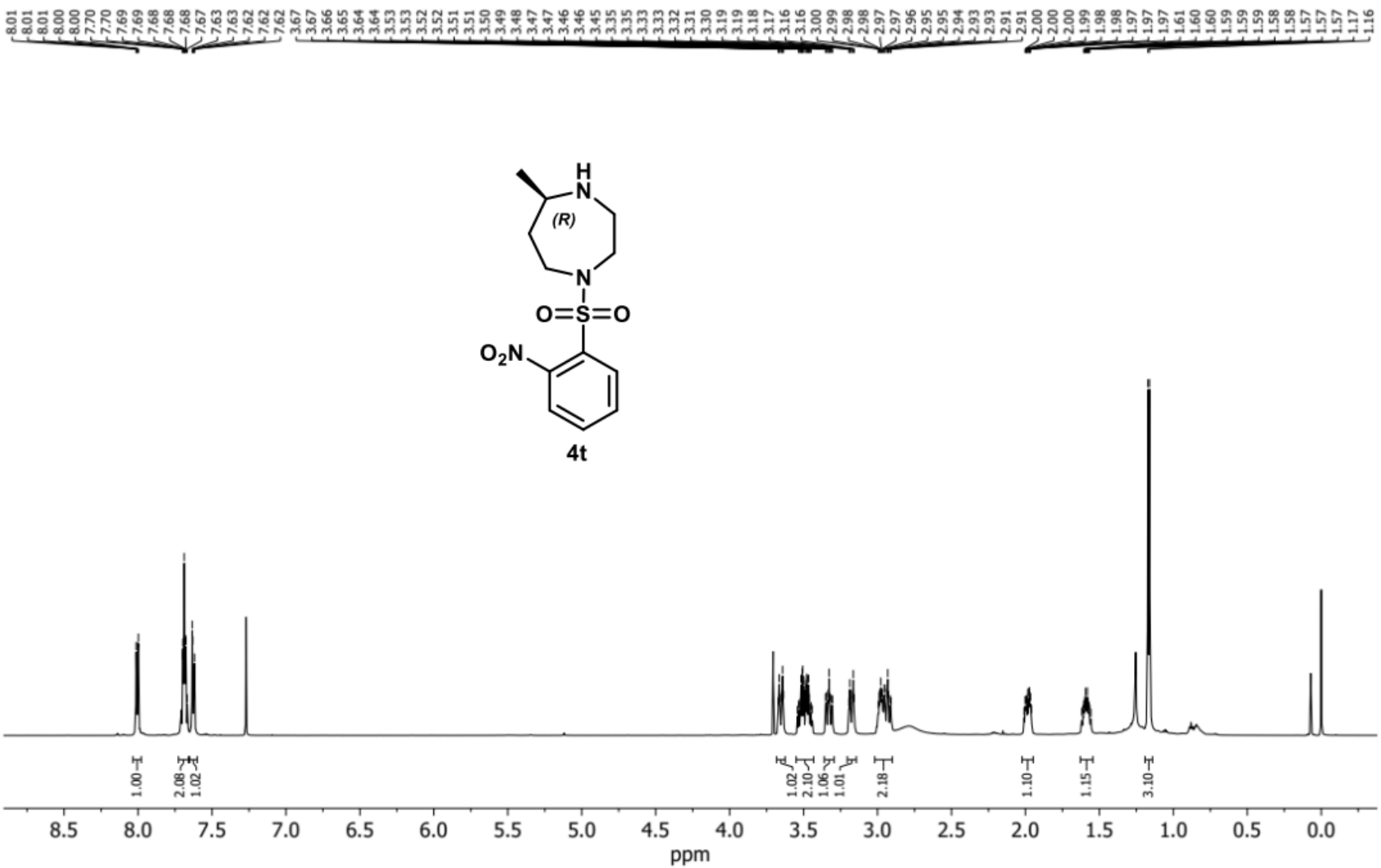
133.4
133.1
131.6
130.8
124.1
54.2
51.4
48.9
46.6
38.3
29.7
23.2
H
N
(S)
N
O=S=O
O2N
4s
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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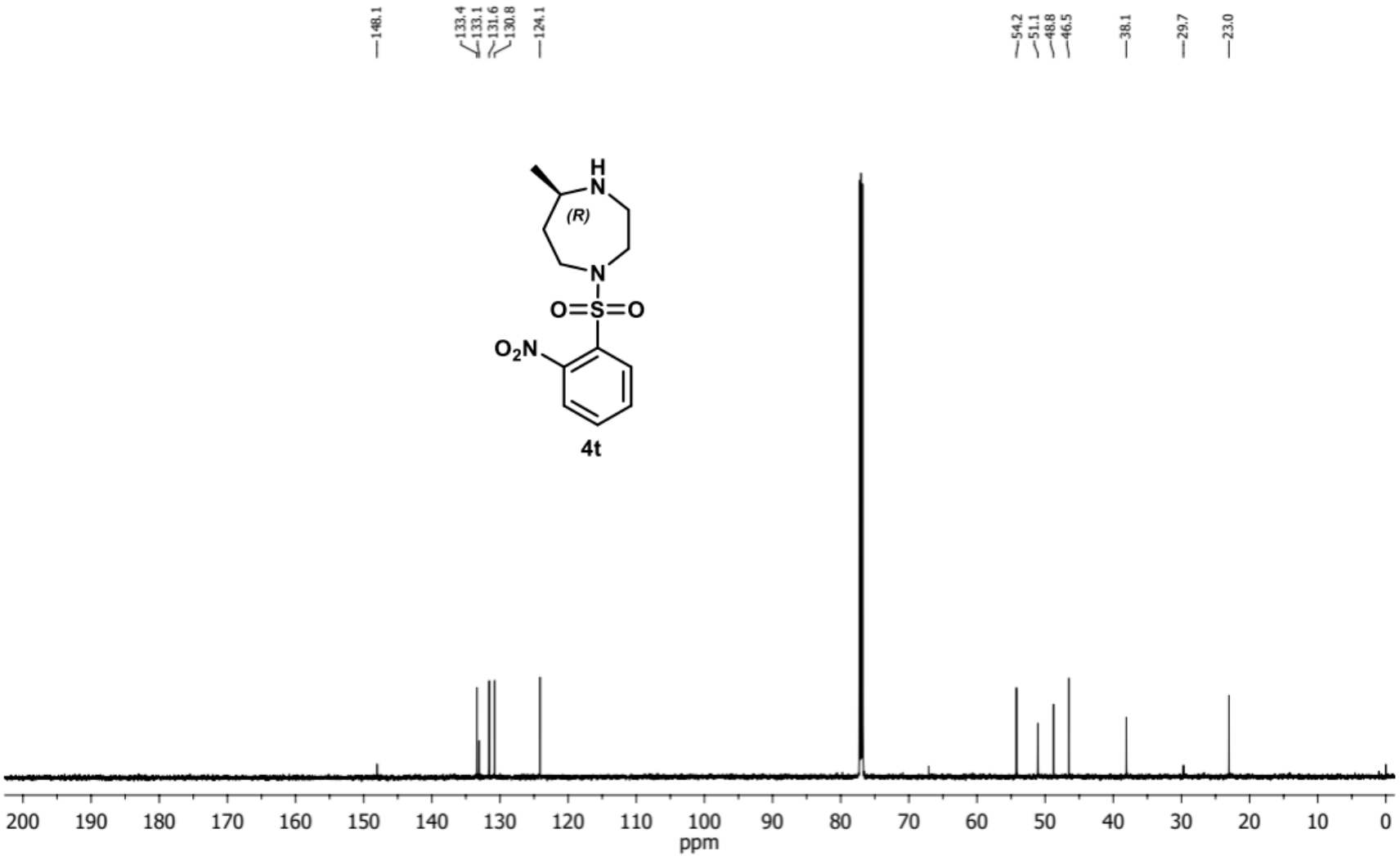
2.00 2.00 2.00 1.99 1.98 1.98 1.97 1.97 1.97 1.61 1.60 1.60 1.59 1.59 1.59 1.58 1.58 1.57 1.57 1.57 1.17 1.16
H
N
(R)
N
O=S=O
O2N
4t
1.00
2.08
1.02
1.02
2.10
1.06
1.01
2.18
1.10
1.15
3.10
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm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133.4
133.1
131.6
130.8
124.1
54.2
51.1
48.8
46.5
38.1
29.7
23.0
H
N
(R)
N
O=S=O
O2N
4t
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.95
7.95
7.94
7.94
7.93
7.73
7.73
7.72
7.72
7.72
7.71
7.71
7.70
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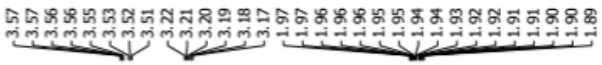
7.68
7.67
7.65
7.64
7.63
7.63


3.57
3.57
3.56
3.56
3.55
3.53
3.52
3.51
3.22
3.21
3.20
3.19
3.18
3.17
1.97
1.97
1.96
1.96
1.96
1.96
1.95
1.95
1.94
1.94
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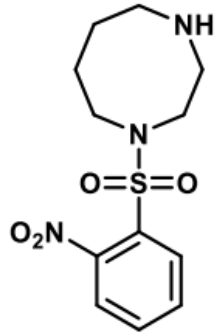
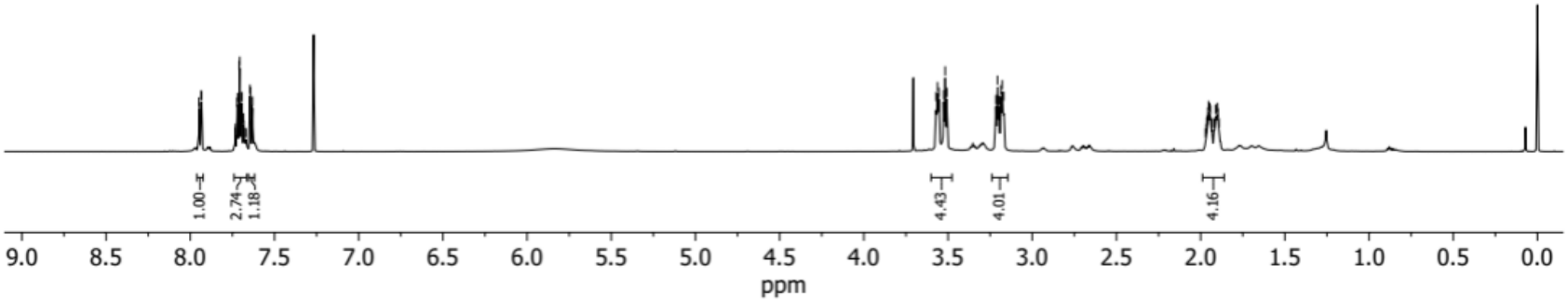
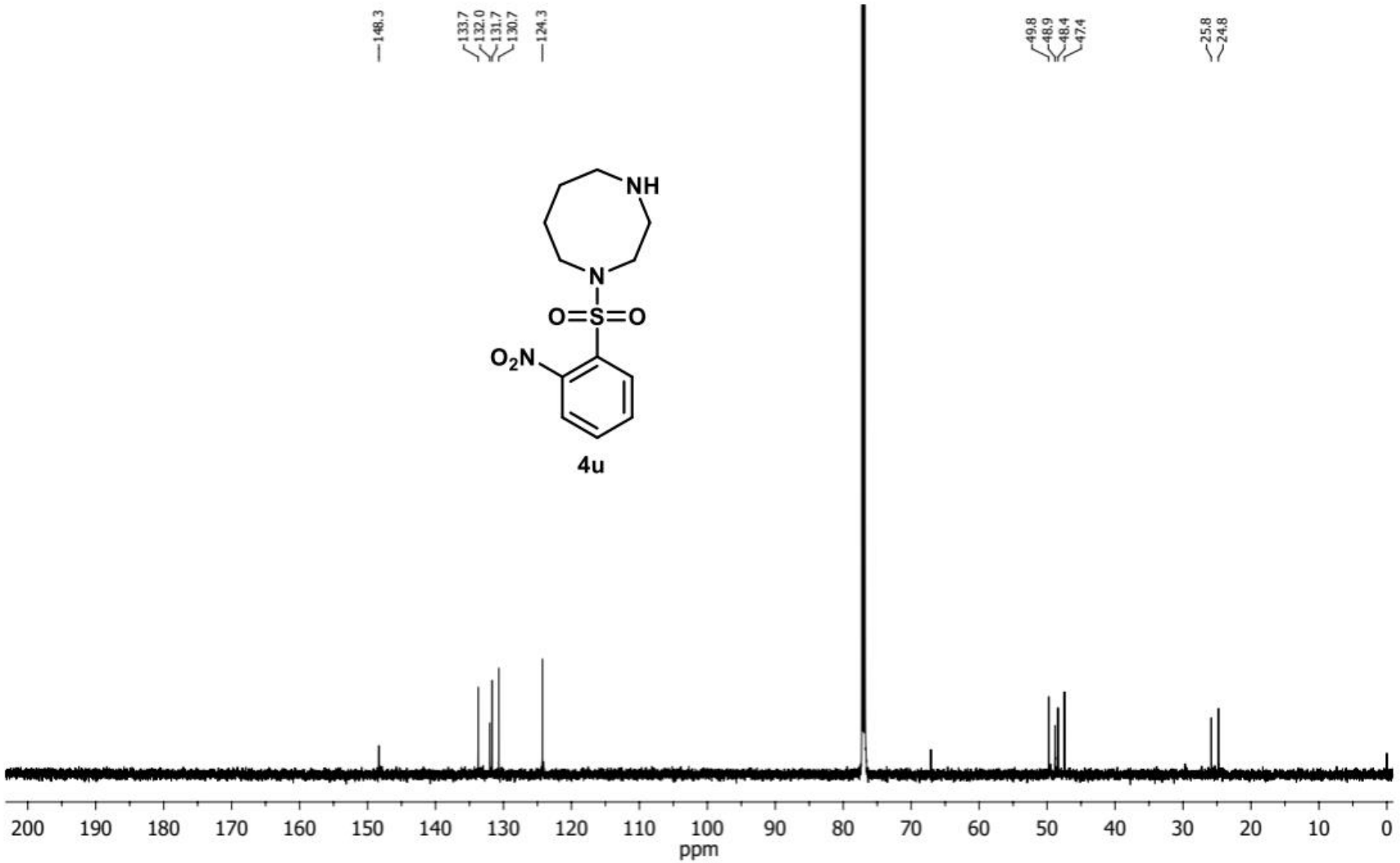
1.92
1.91
1.91
1.90
1.90
1.89


NH
N
O=S=O
O2N

4u


1.00
2.74
1.18
4.43
4.01
4.16
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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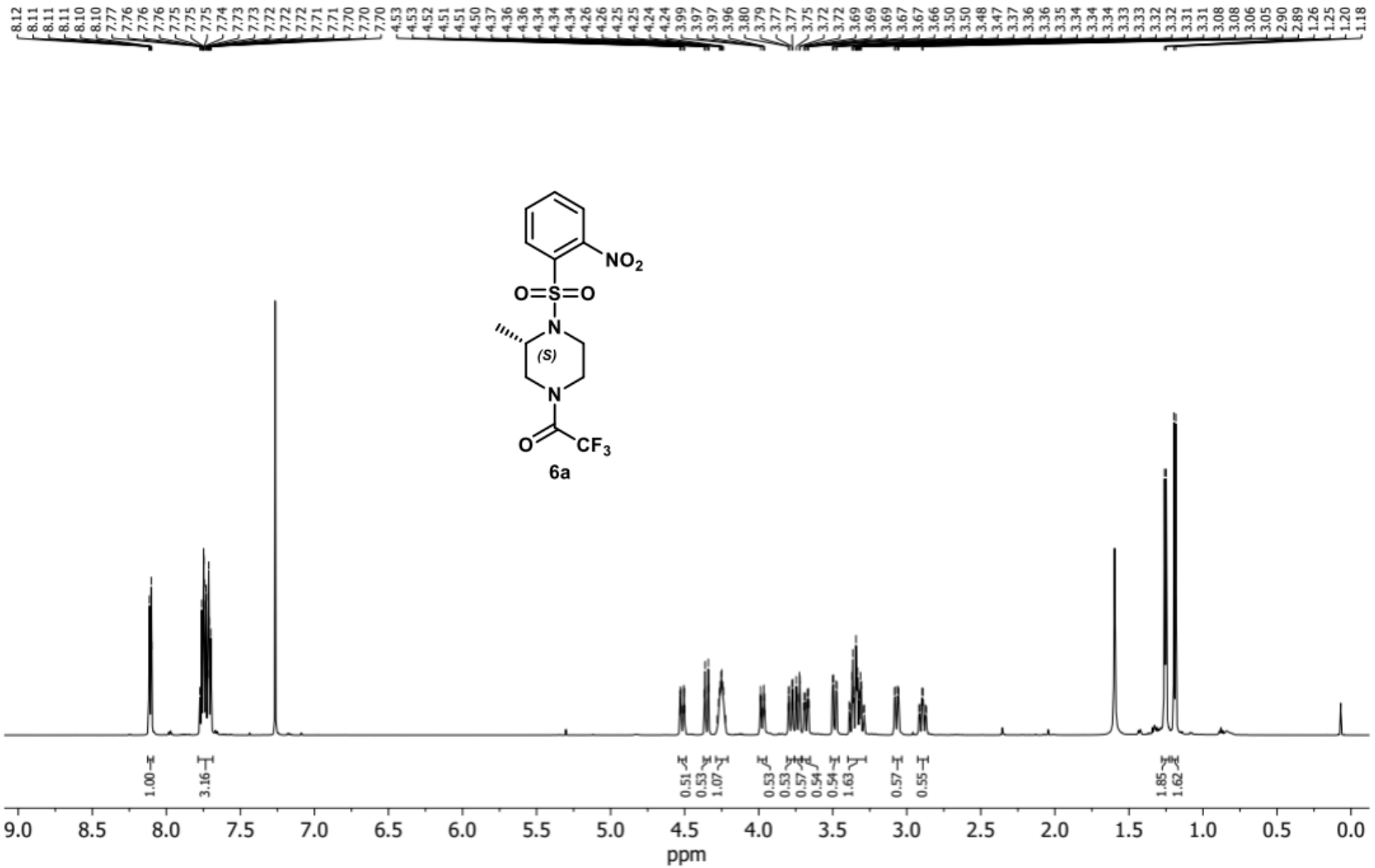
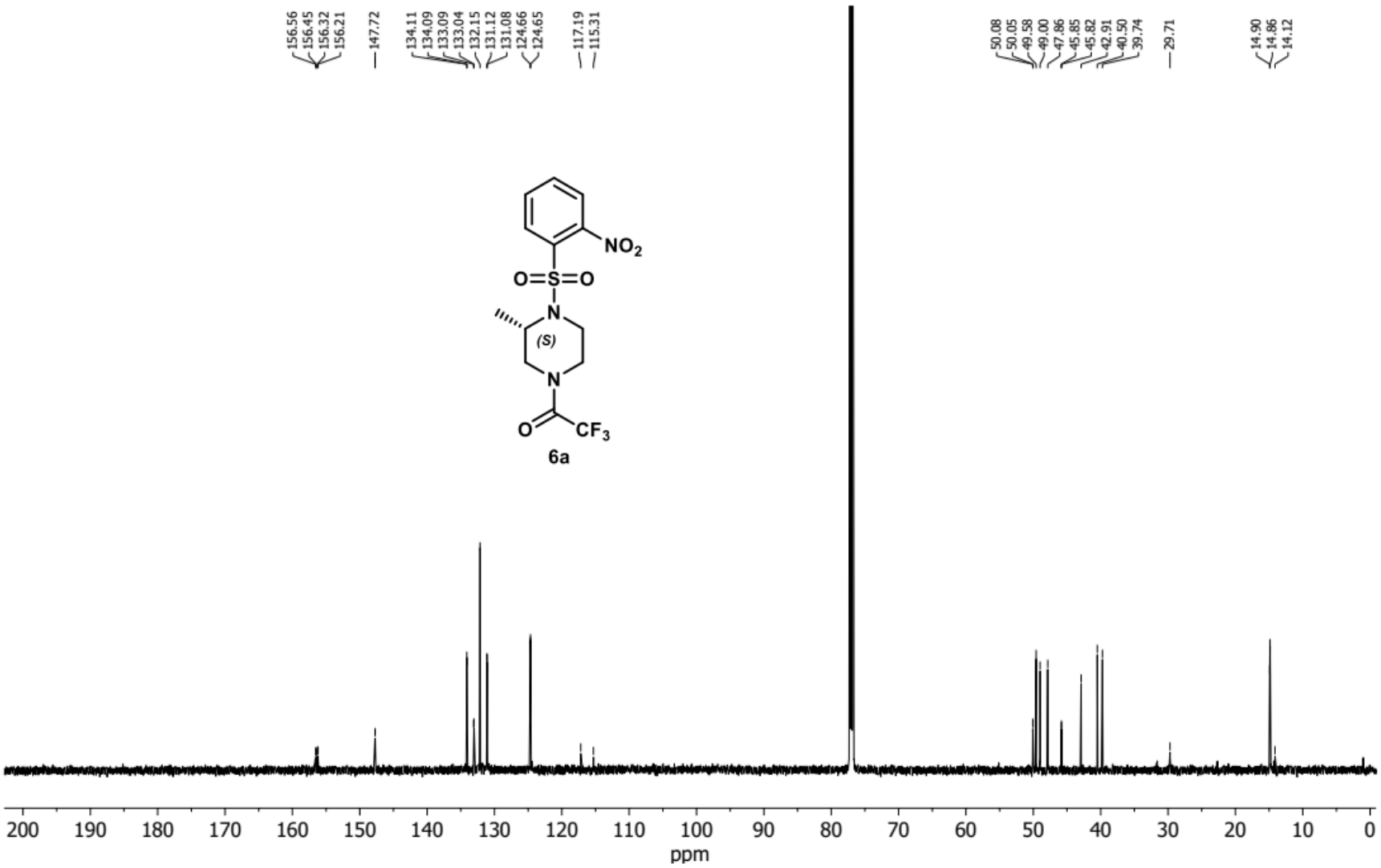
133.7
132.0
131.7
130.7
124.3
49.8
48.9
48.4
47.4
25.8
24.8
NH
N
O=S=O
O2N
4u
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


8.12 8.11 8.11 8.11 8.10 8.10 7.77 7.76 7.76 7.76 7.75 7.75 7.75 7.74 7.73 7.73 7.72 7.72 7.72 7.71 7.71 7.70 7.70 7.70
4.53 4.53 4.52 4.51 4.51 4.50 4.37 4.36 4.36 4.34 4.34 4.34 4.26 4.26 4.25 4.25 4.24 4.24 3.99 3.97 3.97 3.96 3.80 3.79 3.77 3.77 3.75 3.72 3.72 3.69 3.69 3.69 3.67 3.67 3.66 3.50 3.50 3.48 3.47 3.37 3.36 3.36 3.35 3.34 3.34 3.34 3.33 3.33 3.32 3.32 3.31 3.31 3.08 3.08 3.06 3.05 2.90 2.89 1.26 1.25 1.20 1.18
NO2
O=S=O
N
(S)
N
O
CF3
6a
1.00
3.16
0.51
0.53
1.07
0.53
0.53
0.57
0.54
0.54
1.63
0.57
0.55
1.85
1.62
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm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156.32
156.21
147.72
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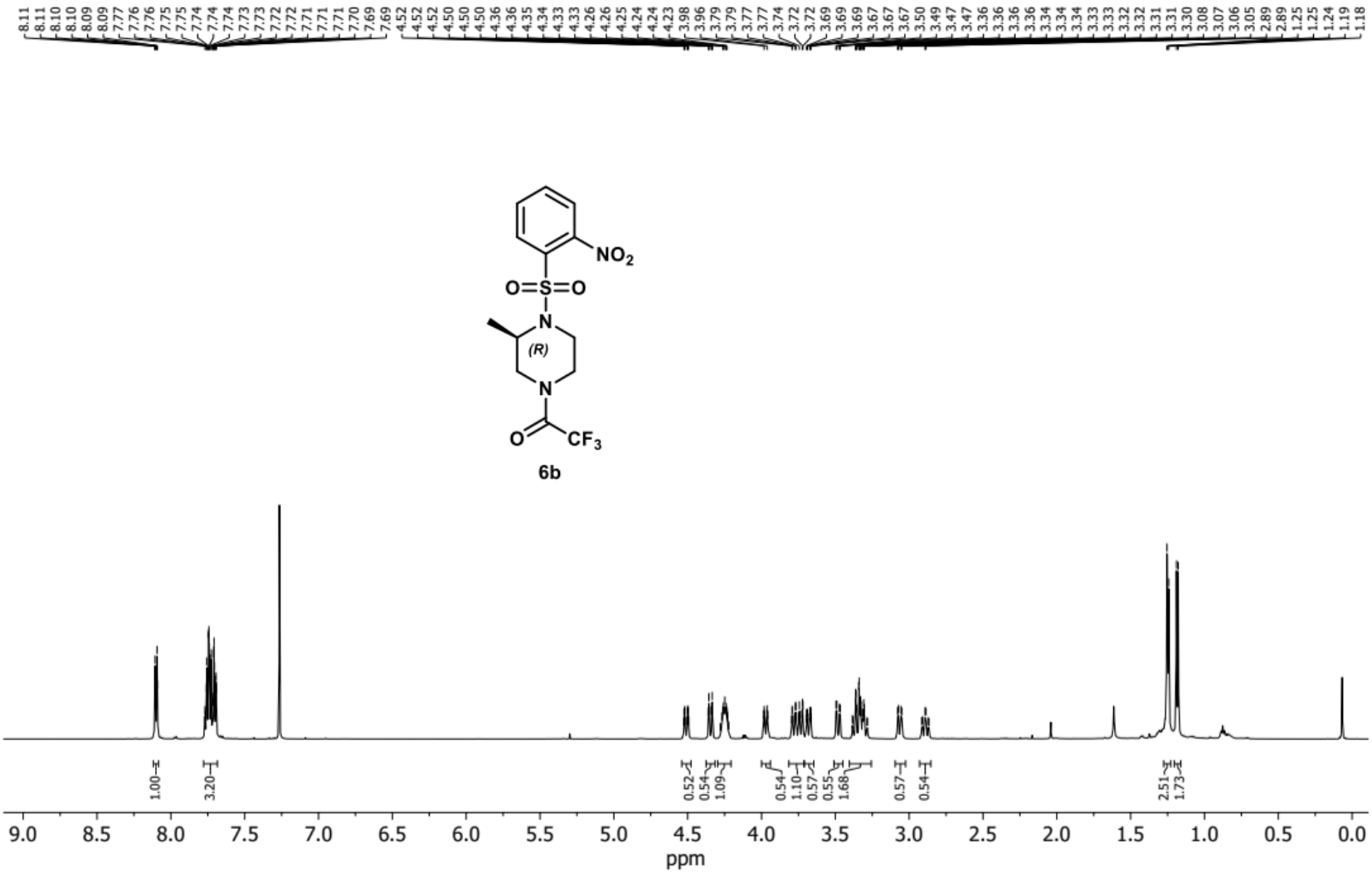
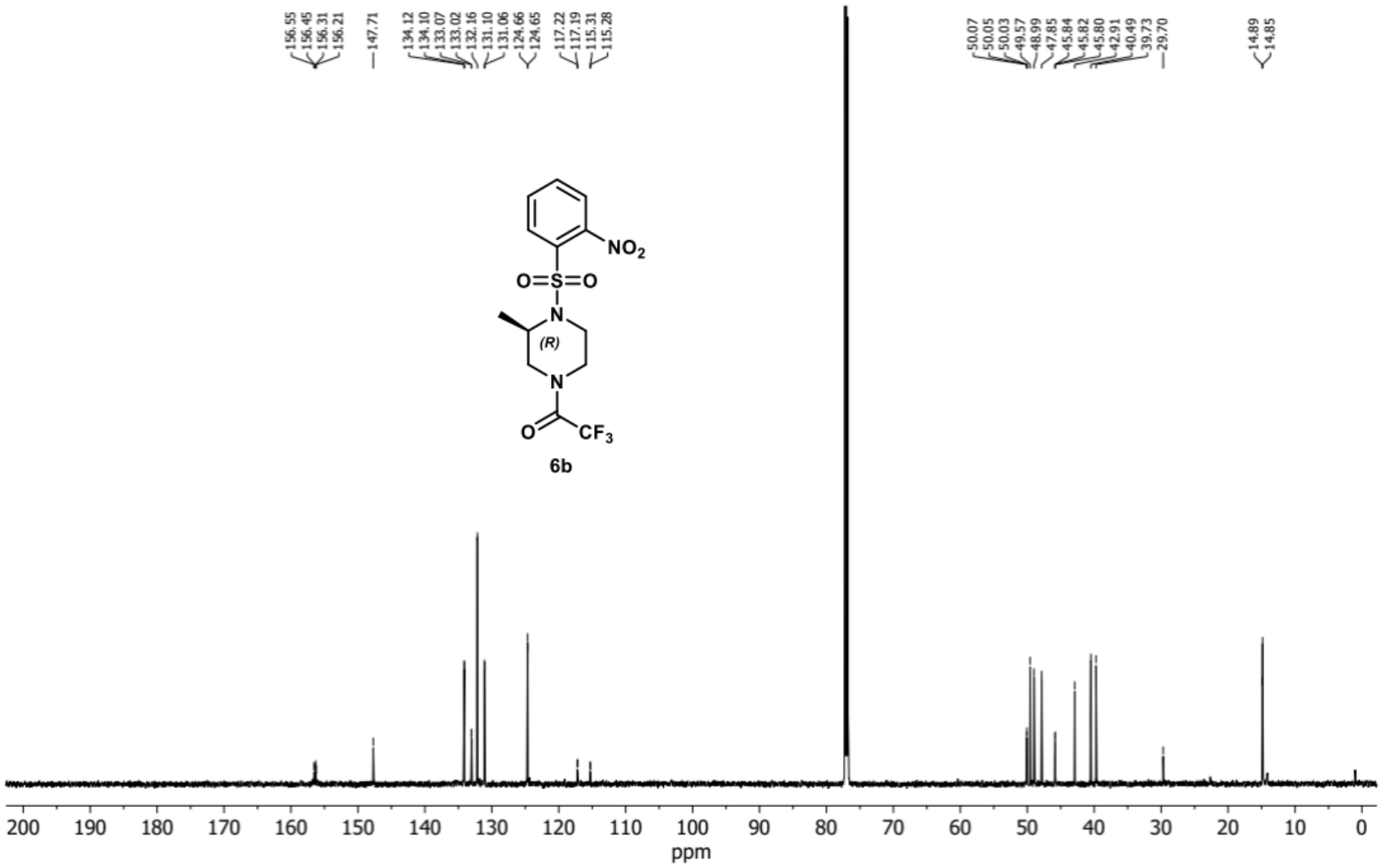
134.09
133.09
133.04
132.15
131.12
131.08
124.66
124.65
117.19
115.31
50.08
50.05
49.58
49.00
47.86
45.85
45.82
42.91
40.50
39.74
29.71
14.90
14.86
14.12
NO2
O=S=O
N
(S)
N
O
CF3
6a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


8.11 8.11 8.10 8.10 8.09 8.09 7.77 7.76 7.76 7.75 7.75 7.74 7.74 7.74 7.73 7.73 7.72 7.72 7.71 7.71 7.71 7.70 7.69 7.69
4.52 4.52 4.50 4.50 4.50 4.36 4.36 4.35 4.34 4.33 4.26 4.25 4.24 4.24 4.23 3.98 3.96 3.79 3.79 3.77 3.74 3.72 3.72 3.69 3.69 3.69 3.67 3.67 3.67 3.50 3.49 3.47 3.47 3.36 3.36 3.36 3.34 3.34 3.34 3.33 3.33 3.32 3.32 3.31 3.31 3.30 3.08 3.07 3.06 3.05 2.89 2.89 1.25 1.25 1.24 1.19 1.18
NO2
O=S=O
N
(R)
N
O
CF3
6b
1.00
3.20
0.52
0.54
1.09
0.54
1.10
0.57
0.55
1.68
0.57
0.54
2.51
1.73
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm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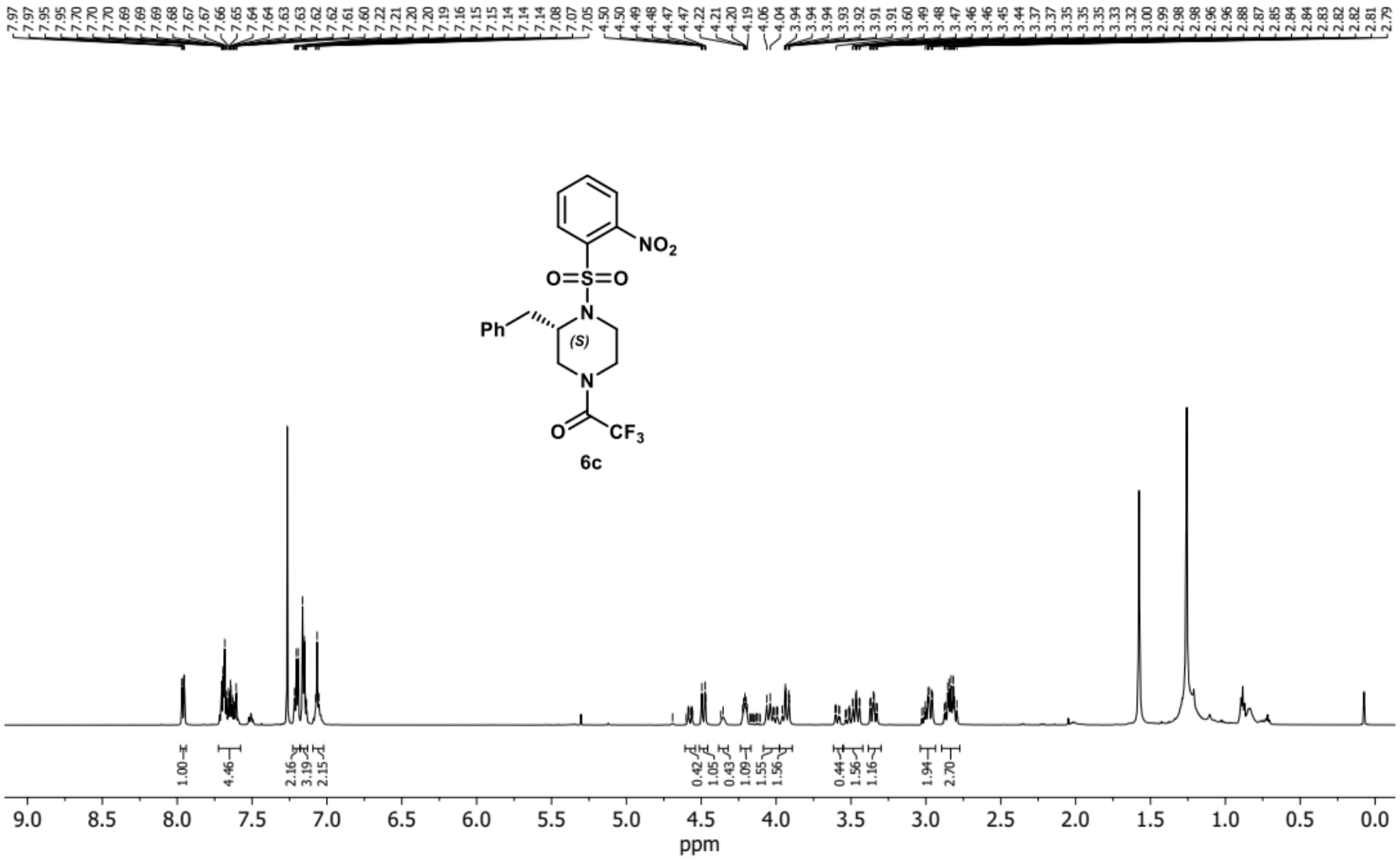
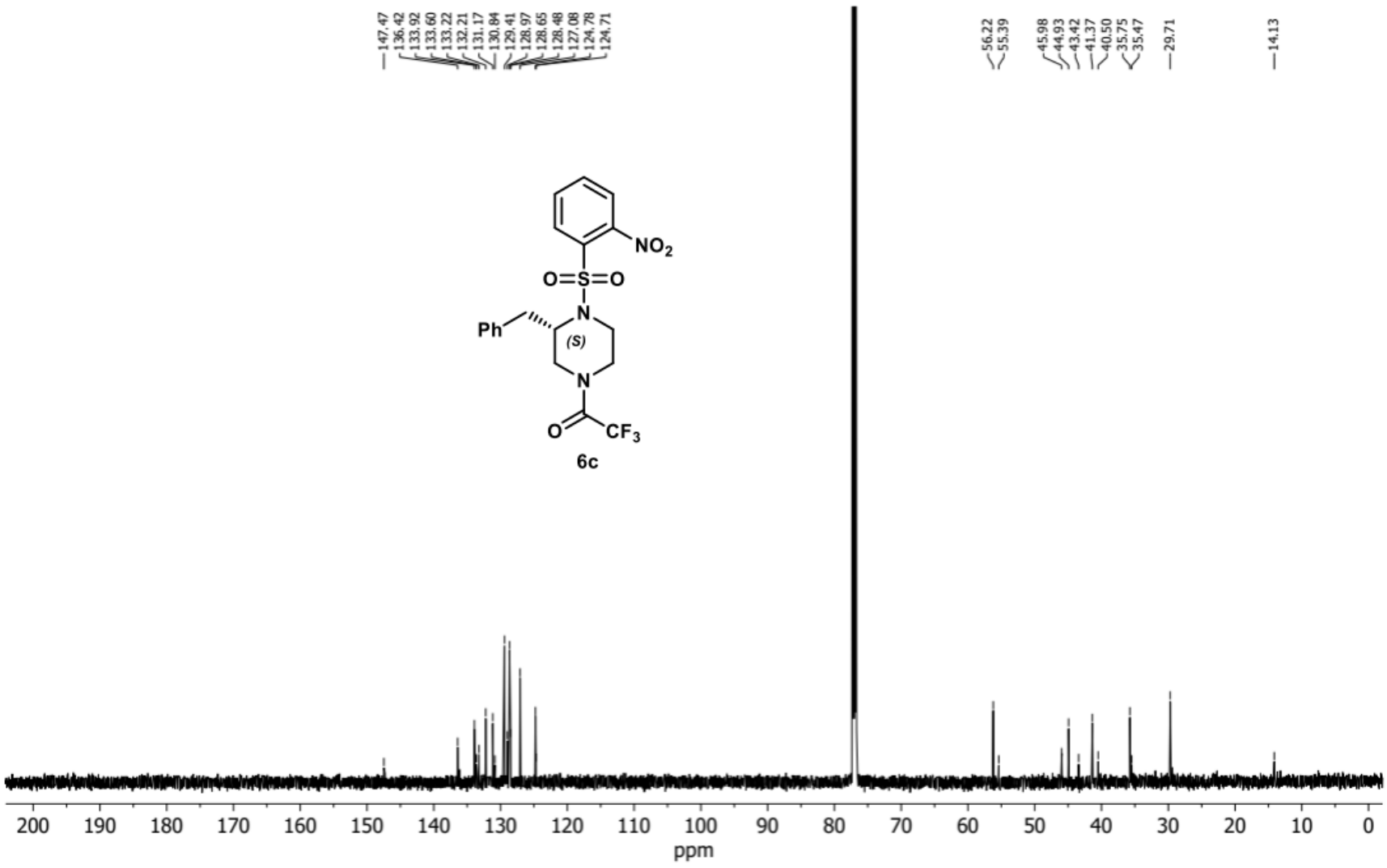
134.12
134.10
133.07
133.02
132.16
131.10
131.06
124.66
124.65
117.22
117.19
115.31
115.28
50.07
50.05
50.03
49.57
48.99
47.85
45.84
45.82
45.80
42.91
40.49
39.73
29.70
14.89
14.85
NO2
O=S=O
N
(R)
N
O
CF3
6b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.97 7.97 7.95 7.95 7.70 7.70 7.70 7.69 7.69 7.69 7.68 7.67 7.67 7.66 7.65 7.64 7.64 7.63 7.63 7.62 7.62 7.61 7.60 7.22 7.21 7.20 7.20 7.19 7.16 7.15 7.15 7.14 7.14 7.14 7.08 7.07 7.05
4.50 4.50 4.49 4.48 4.47 4.47 4.22 4.21 4.20 4.19 4.06 4.04 3.94 3.94 3.94 3.93 3.92 3.91 3.91 3.60 3.49 3.48 3.47 3.46 3.46 3.45 3.44 3.37 3.37 3.35 3.35 3.35 3.33 3.32 3.00 2.99 2.98 2.98 2.96 2.96 2.88 2.87 2.85 2.84 2.84 2.83 2.82 2.82 2.81 2.79
NO2
O=S=O
N
Ph
(S)
N
O
CF3
6c
1.00 4.46 2.16 3.19 2.15 0.42 1.05 0.43 1.09 1.55 1.56 0.44 1.56 1.16 1.94 2.70
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm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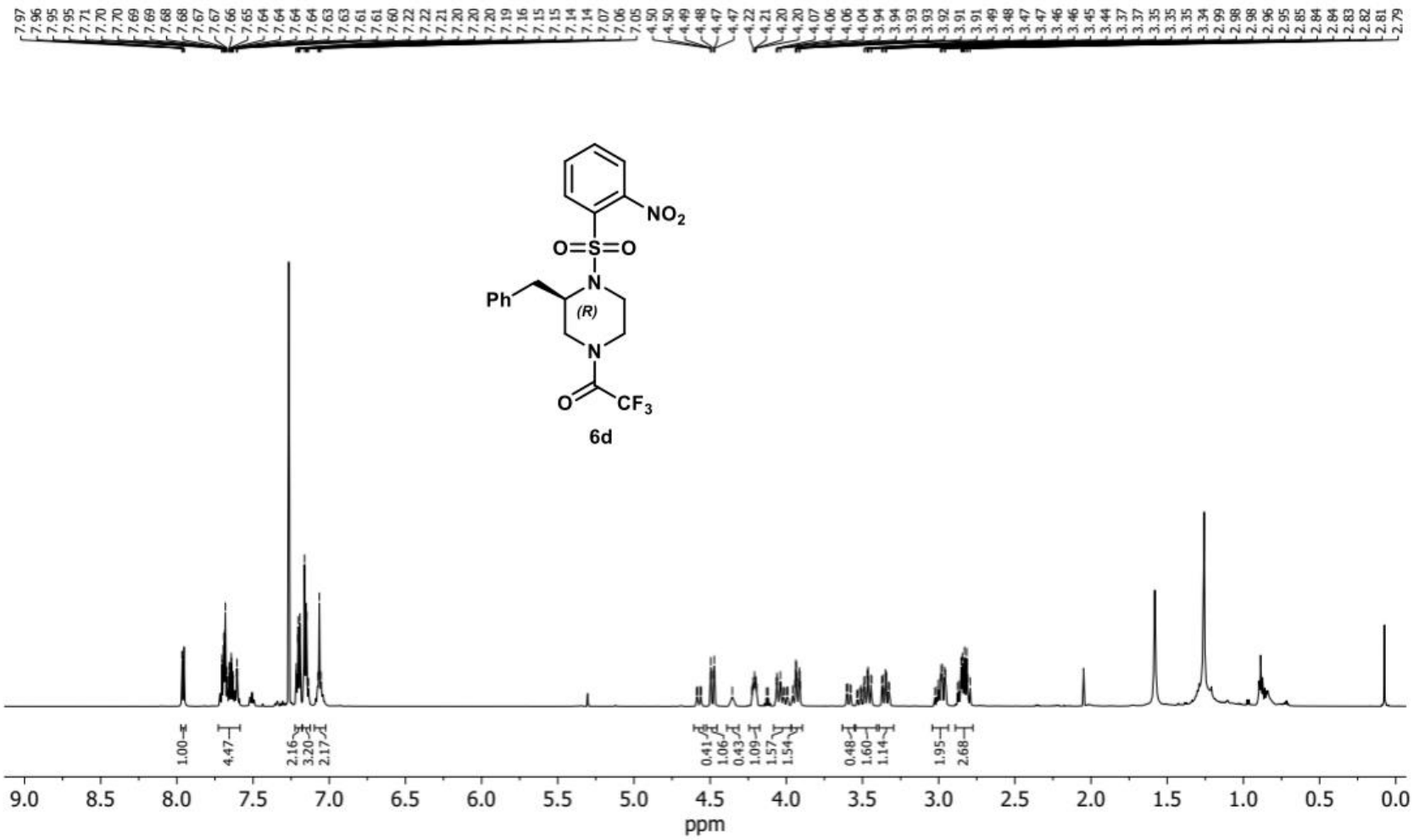
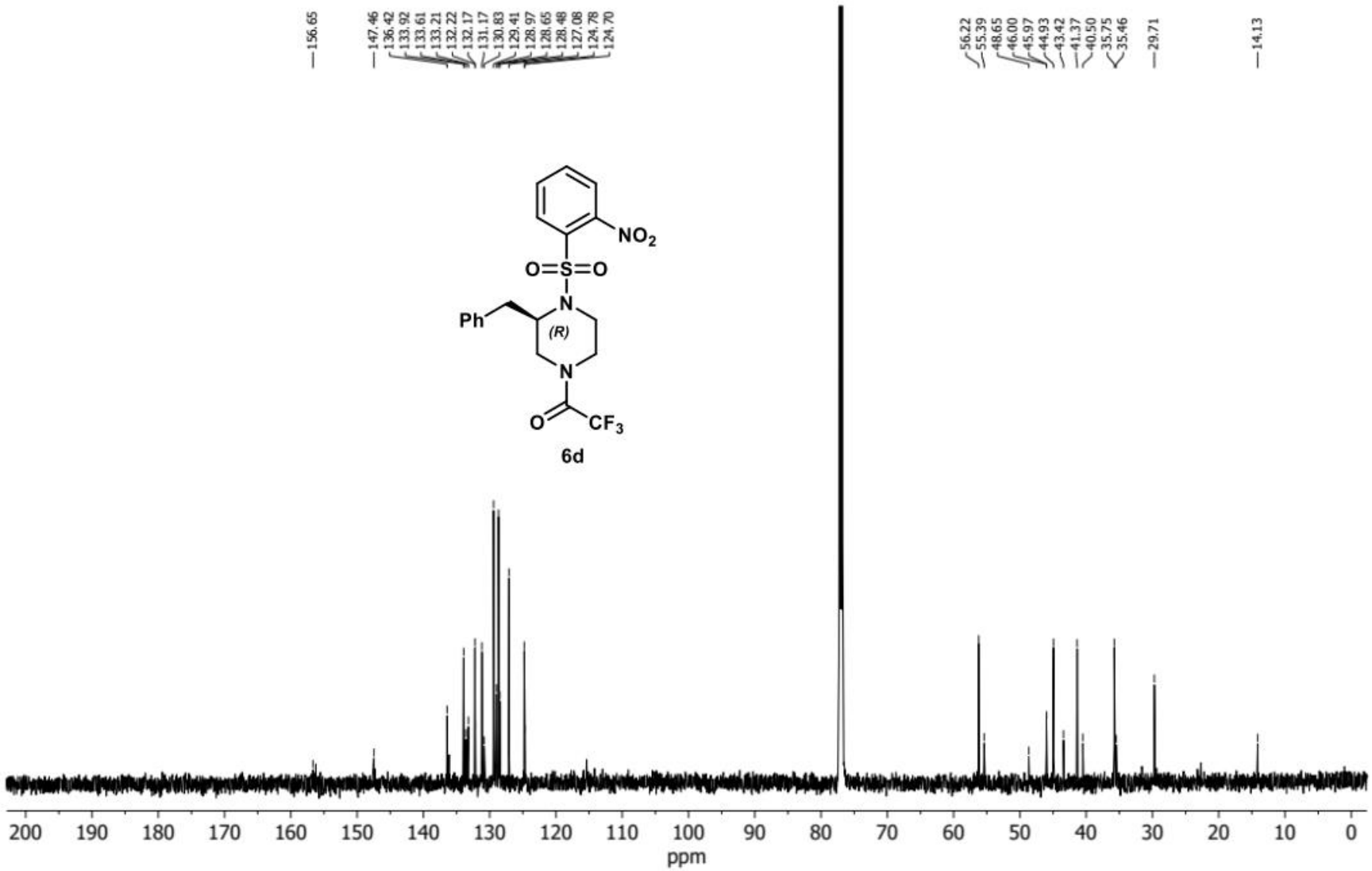
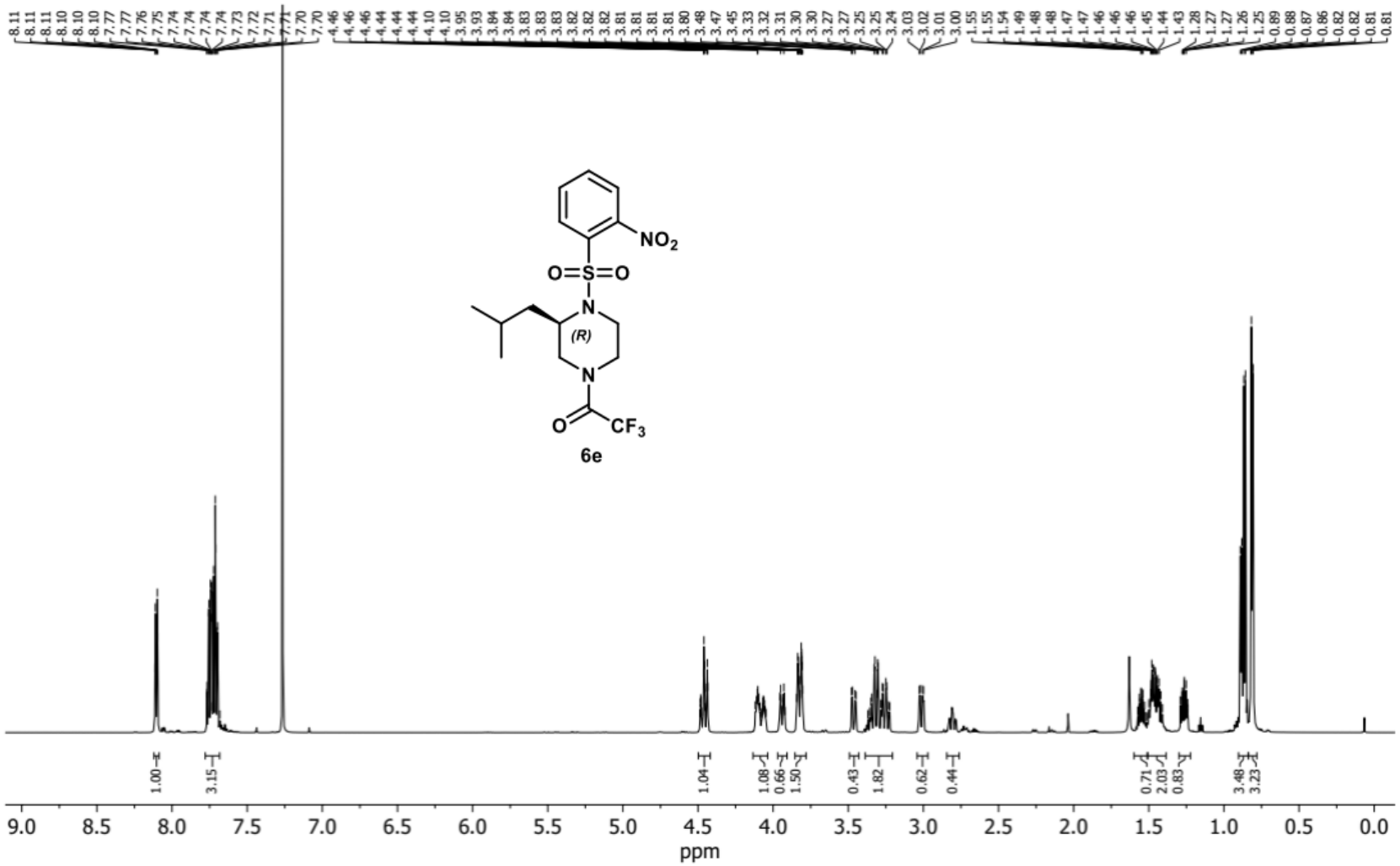
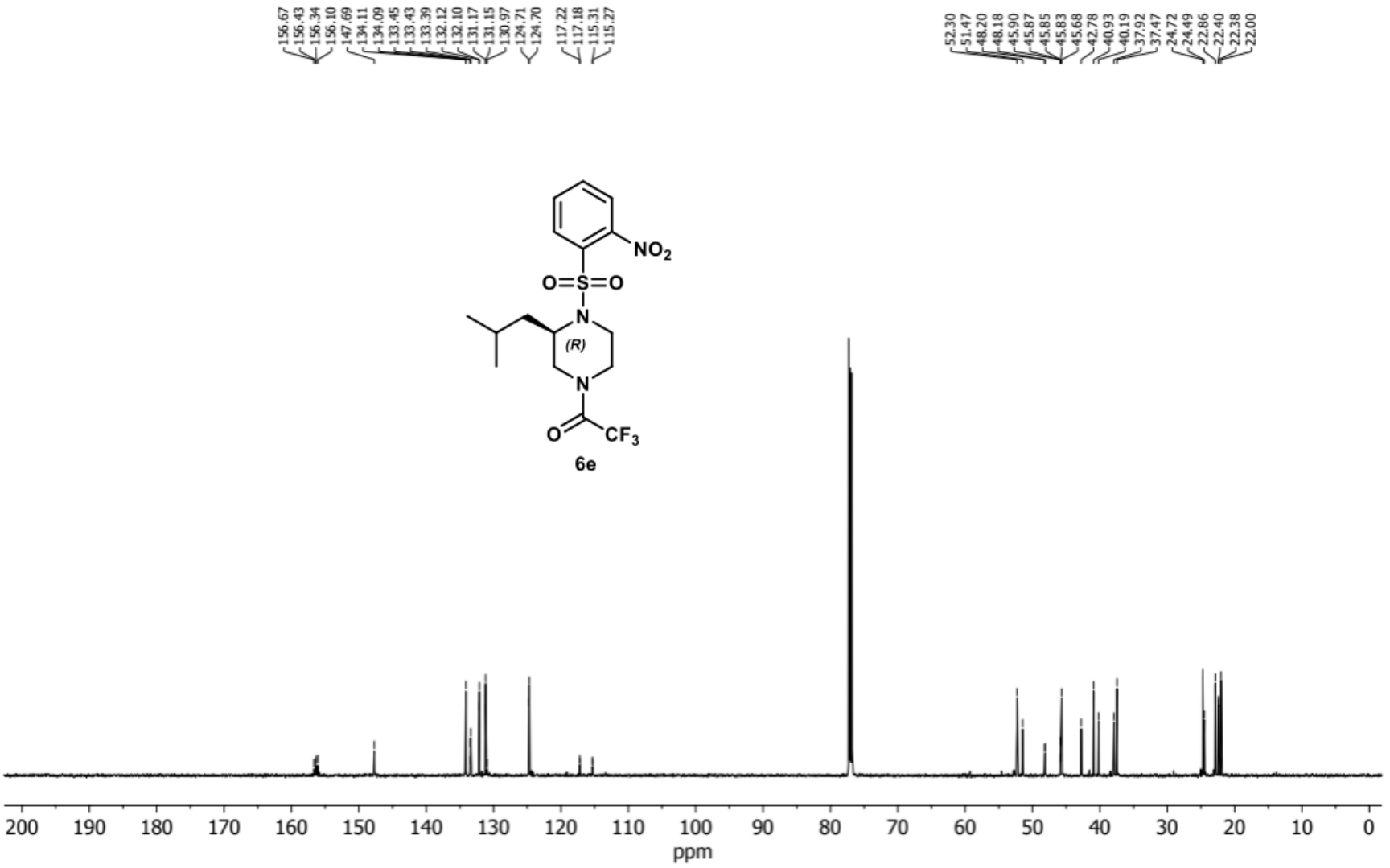
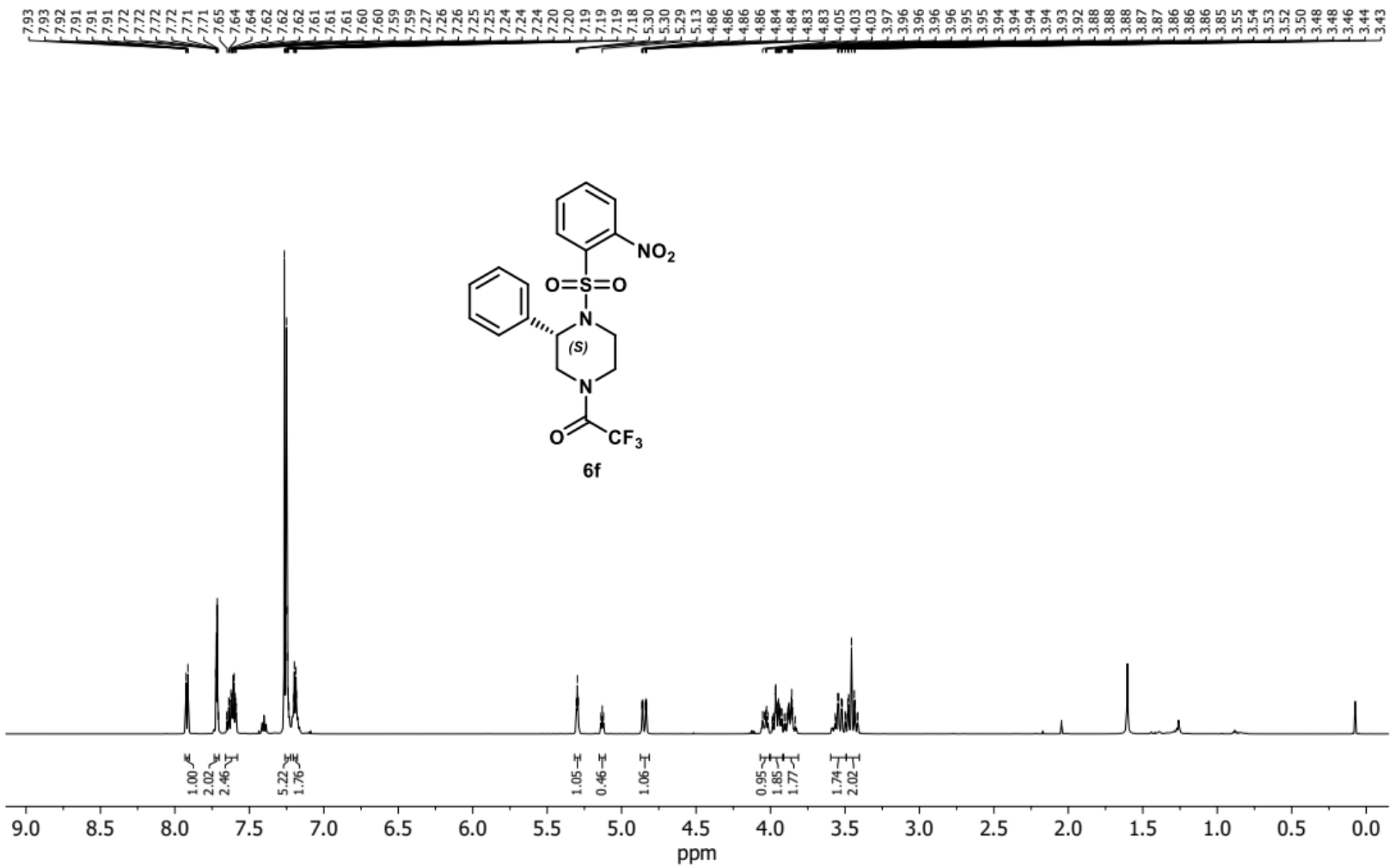
132.21
131.17
130.84
129.41
128.97
128.65
128.48
127.08
124.78
124.71
56.22
55.39
45.98
44.93
43.42
41.37
40.50
35.75
35.47
29.71
14.13
NO2
O=S=O
N
Ph
(S)
N
O
CF3
6c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

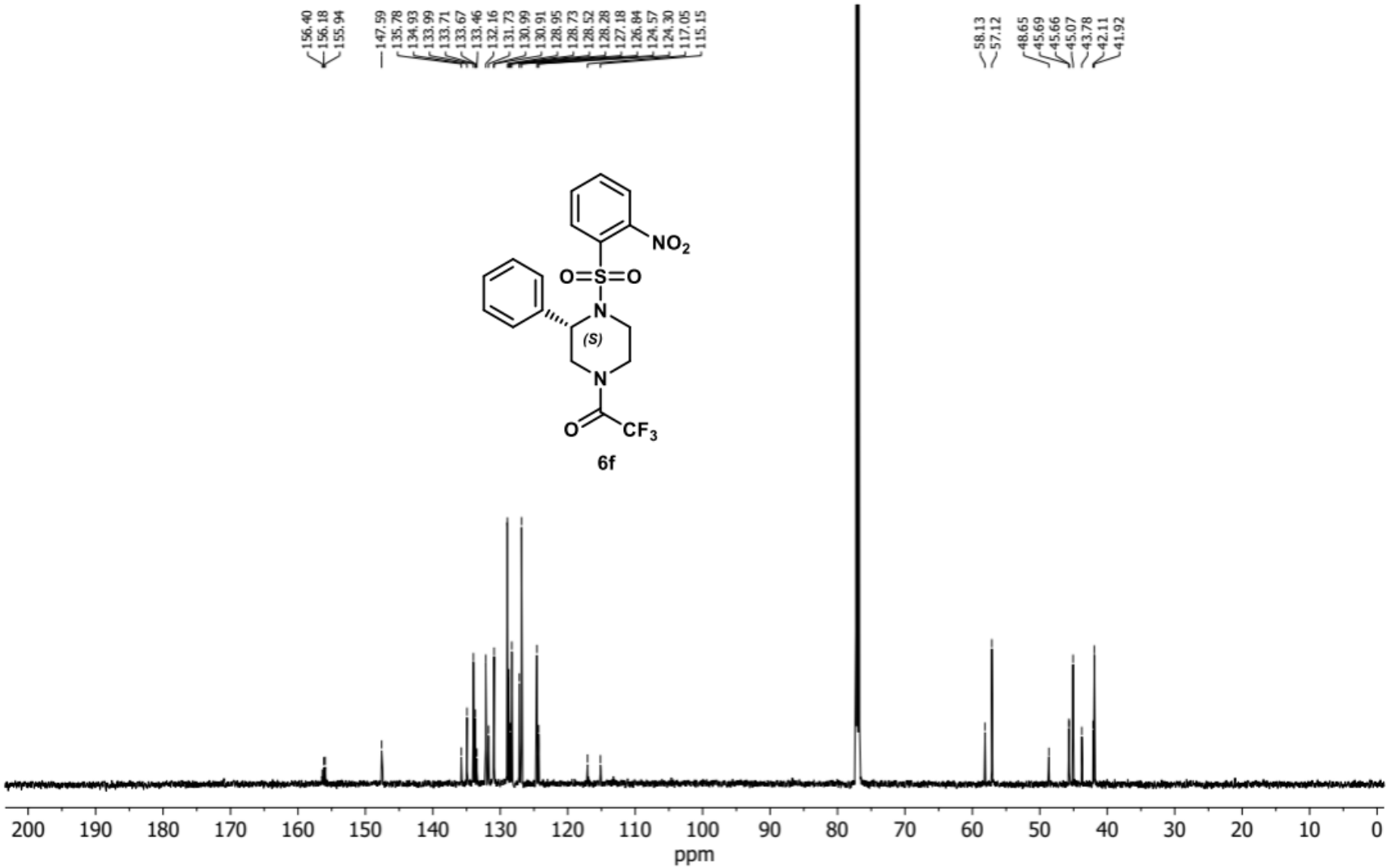

NO2
O=S=O
N
Ph
(R)
N
O
CF3
6d
1.00
4.47
2.16
3.20
2.17
0.41
1.06
0.43
1.09
1.57
1.54
0.48
1.60
1.14
1.95
2.68
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

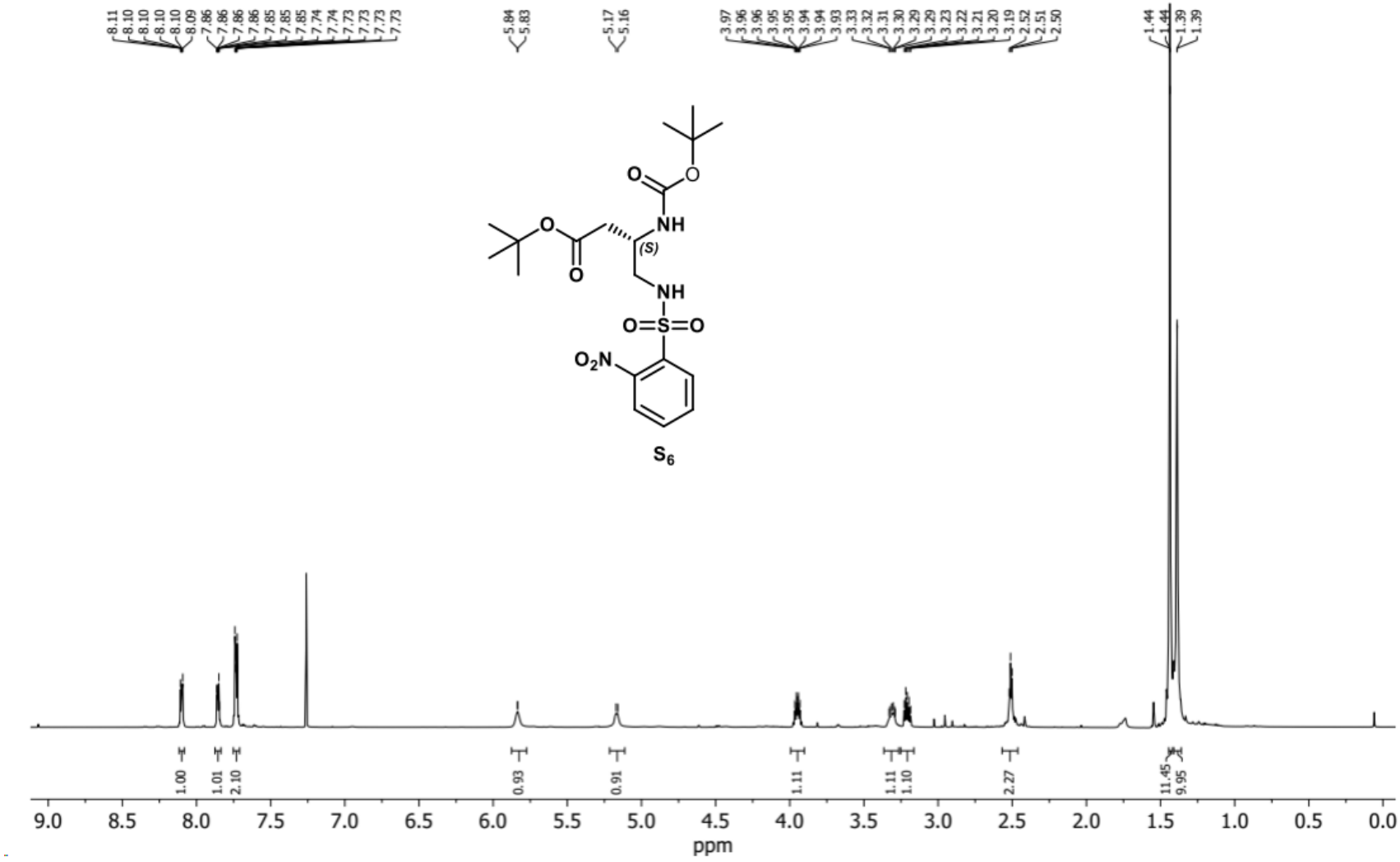

156.65
147.46
136.42
133.92
133.61
133.21
132.22
132.17
131.17
130.83
129.41
128.97
128.65
128.48
127.08
124.78
124.70
56.22
55.39
48.65
46.00
45.97
44.93
43.42
41.37
40.50
35.75
35.46
29.71
14.13
NO2
O=S=O
N
Ph
(R)
N
O
CF3
6d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

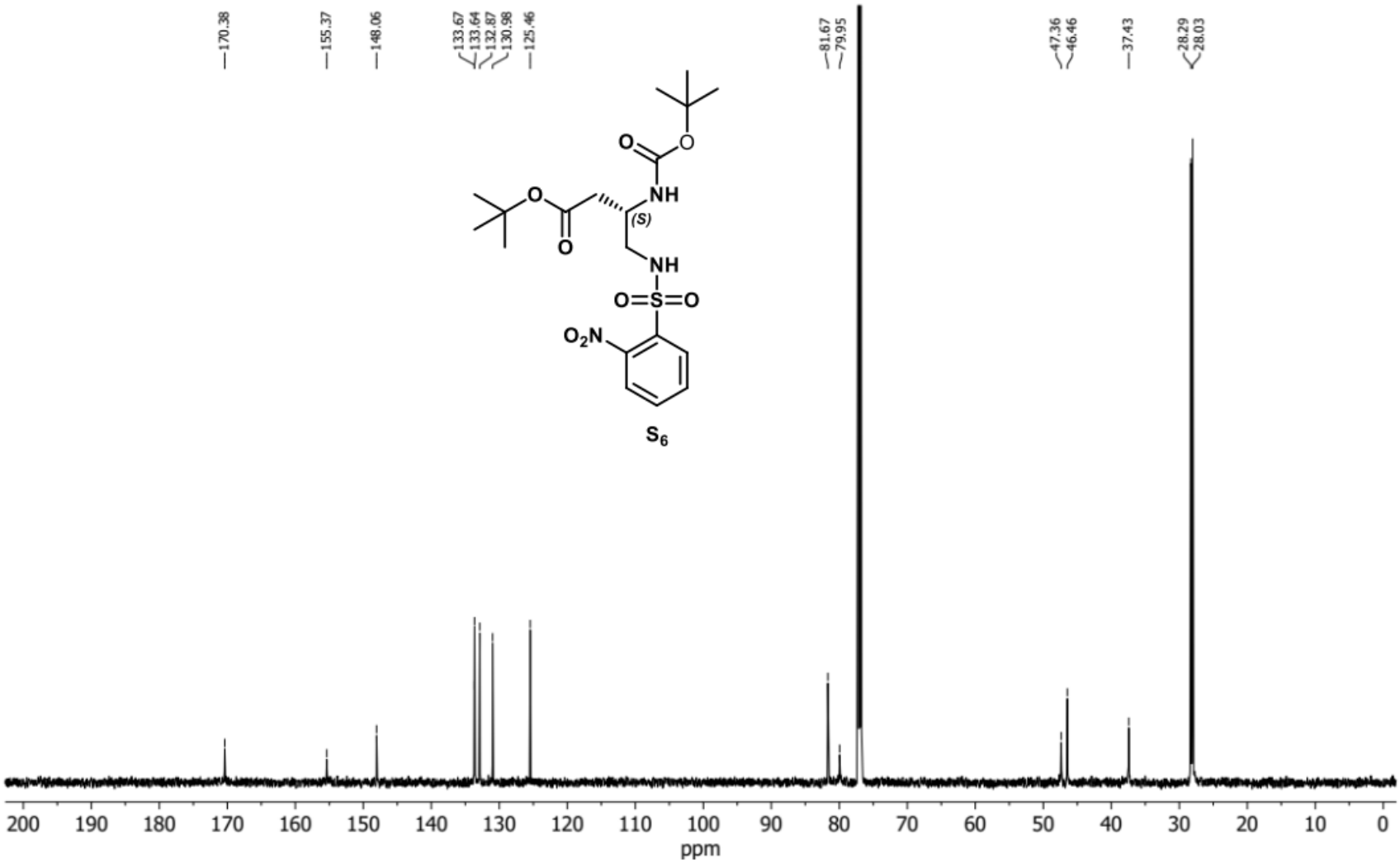

NO2
O=S=O
N
(R)
N
O
CF3
6e
ppm


156.67
156.43
156.34
156.10
147.69
134.11
134.09
133.45
133.43
133.39
132.12
132.10
131.17
131.15
130.97
124.71
124.70
117.22
117.18
115.31
115.27
52.30
51.47
48.20
48.18
45.90
45.87
45.85
45.83
45.68
42.78
40.93
40.19
37.92
37.47
24.72
24.49
22.86
22.40
22.38
22.00
NO2
O=S=O
N
(R)
N
O
CF3
6e
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

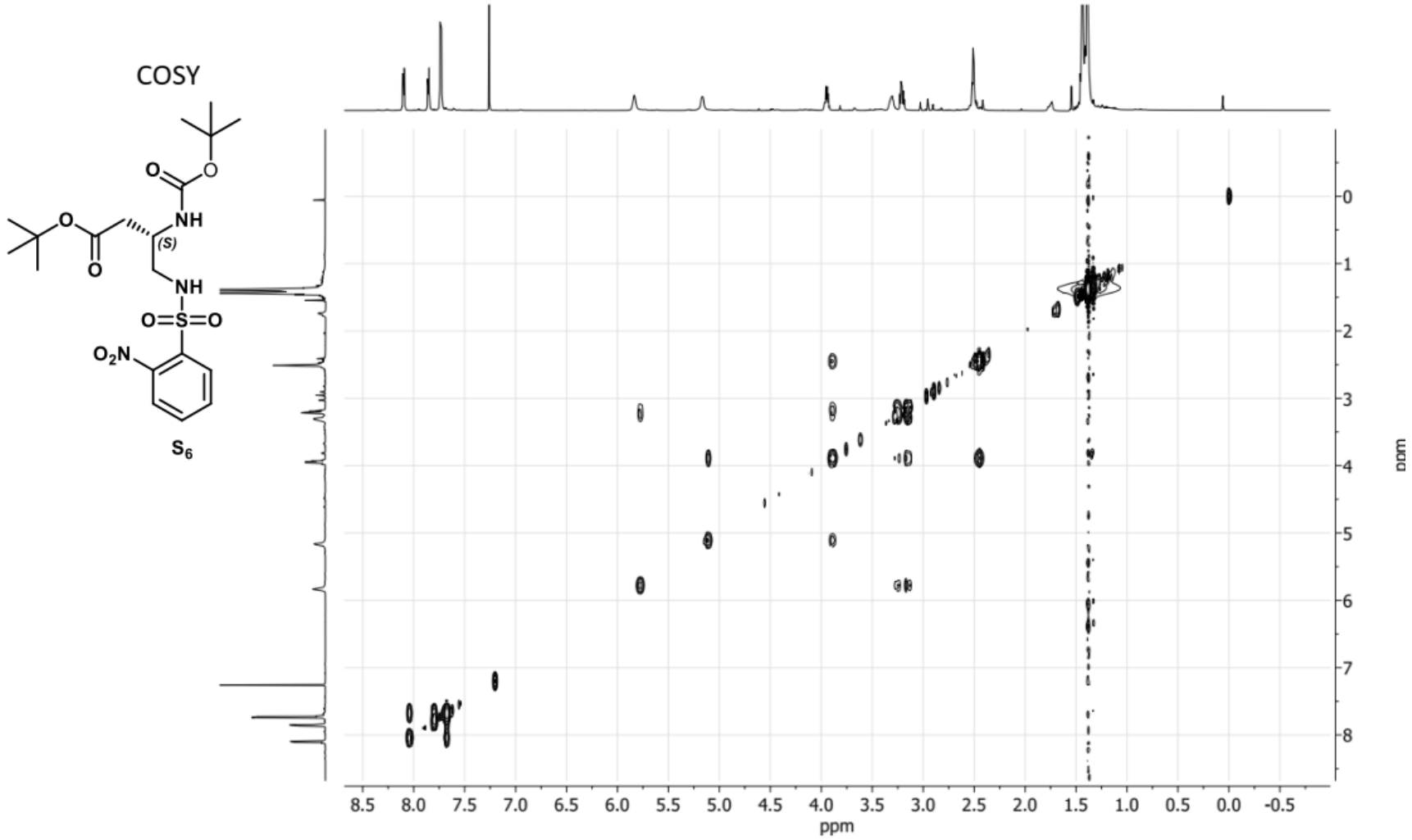

7.93 7.93 7.92 7.91 7.91 7.91 7.72 7.72 7.72 7.72 7.71 7.71 7.65 7.64 7.64 7.62 7.62 7.62 7.61 7.61 7.61 7.60 7.60 7.59 7.59 7.27 7.26 7.26 7.25 7.25 7.24 7.24 7.24 7.20 7.20 7.19 7.19 7.19 7.18 5.30 5.30 5.29 5.13 4.86 4.86 4.86 4.86 4.84 4.84 4.83 4.05 4.03 4.03 3.97 3.96 3.96 3.96 3.96 3.95 3.95 3.94 3.94 3.94 3.94 3.93 3.92 3.88 3.88 3.88 3.87 3.87 3.86 3.86 3.86 3.85 3.55 3.54 3.53 3.52 3.50 3.48 3.48 3.46 3.44 3.43
NO2
O=S=O
N
(S)
N
O
CF3
6f
1.00 2.02 2.46 5.22 1.76 1.05 0.46 1.06 0.95 1.85 1.77 1.74 2.02
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

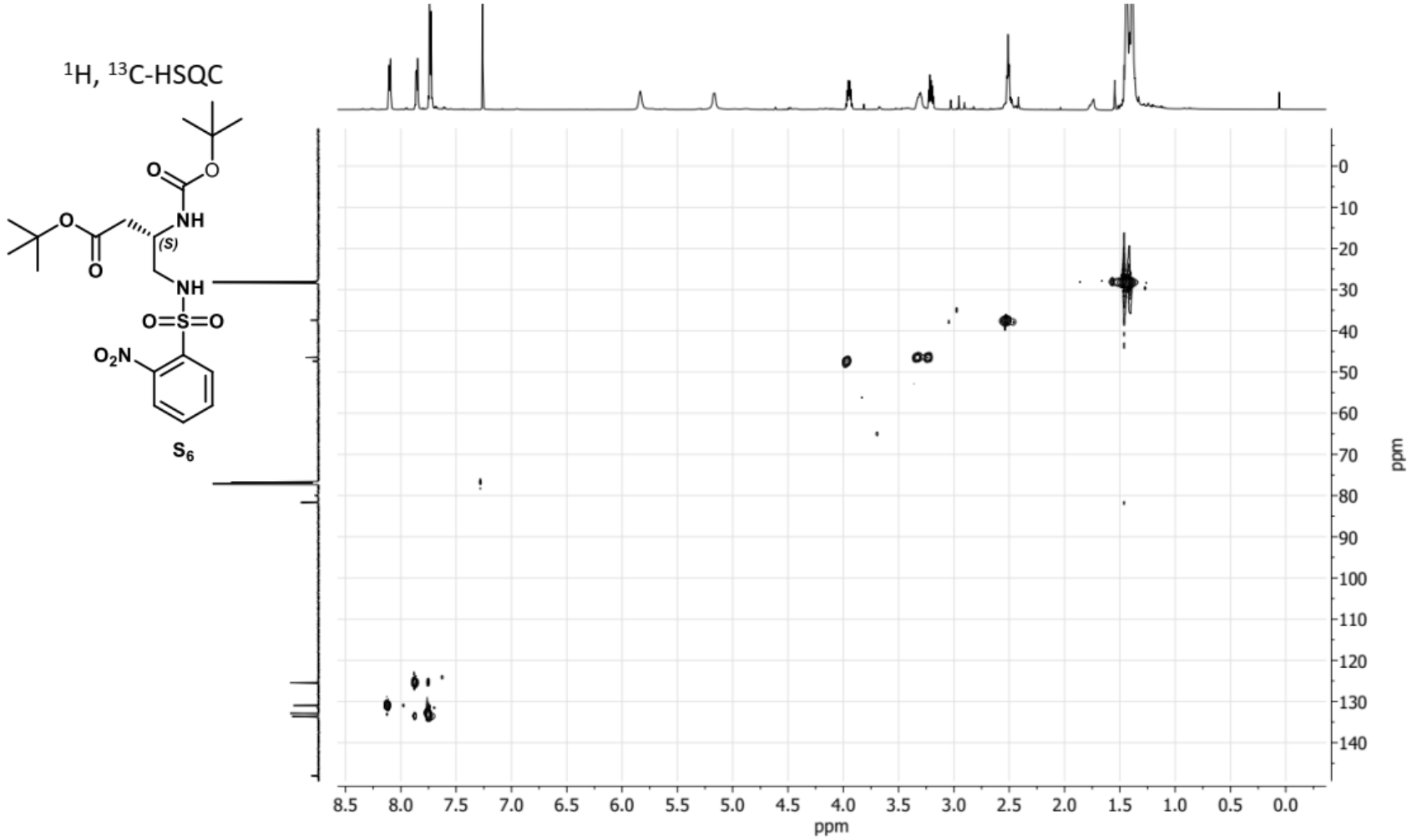

156.40
156.18
155.94
147.59
135.78
134.93
133.99
133.71
133.67
133.46
132.16
131.73
130.99
130.91
128.95
128.73
128.52
128.28
127.18
126.84
124.57
124.30
117.05
115.15
58.13
57.12
48.65
45.69
45.66
45.07
43.78
42.11
41.92
NO2
O=S=O
N
(S)
N
O
CF3
6f
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

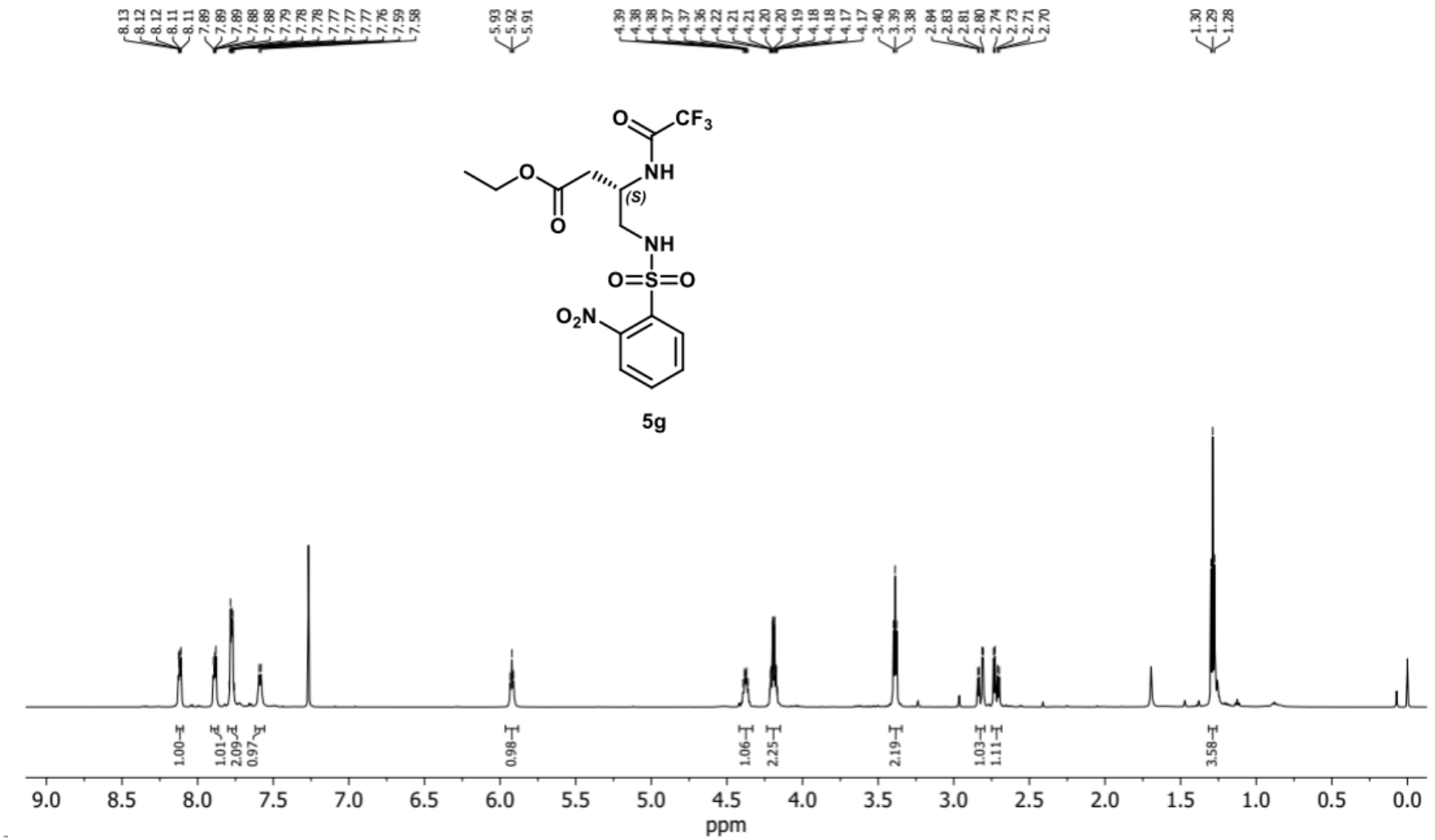

8.11 8.10 8.10 8.10 8.10 8.09 7.86 7.86 7.86 7.86 7.85 7.85 7.85 7.74 7.74 7.73 7.73 7.73 7.73
5.84 5.83
5.17 5.16
3.97 3.96 3.96 3.95 3.95 3.94 3.94 3.93 3.33 3.32 3.31 3.30 3.29 3.29 3.23 3.22 3.21 3.20 3.19 2.52 2.51 2.50
1.44 1.44 1.39 1.39
O
O
NH
(S)
O
O
NH
O=S=O
O2N
S6
1.00 1.01 2.10 0.93 0.91 1.11 1.11 1.10 2.27 11.45 9.95
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

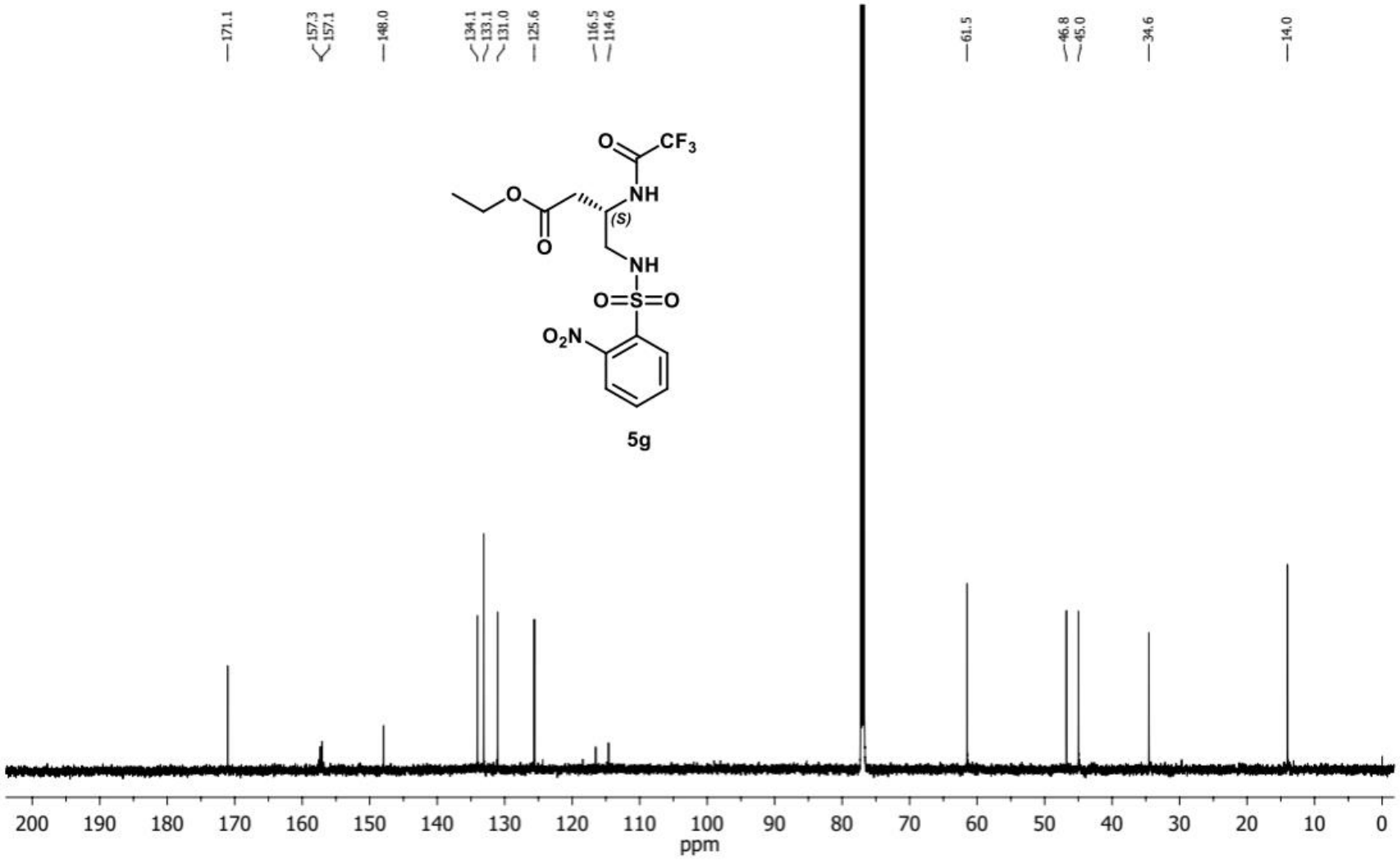

170.38
155.37
148.06
133.67
133.64
132.87
130.98
125.46
81.67
79.95
47.36
46.46
37.43
28.29
28.03
O
O
NH
(S)
O
O
NH
O=S=O
O2N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

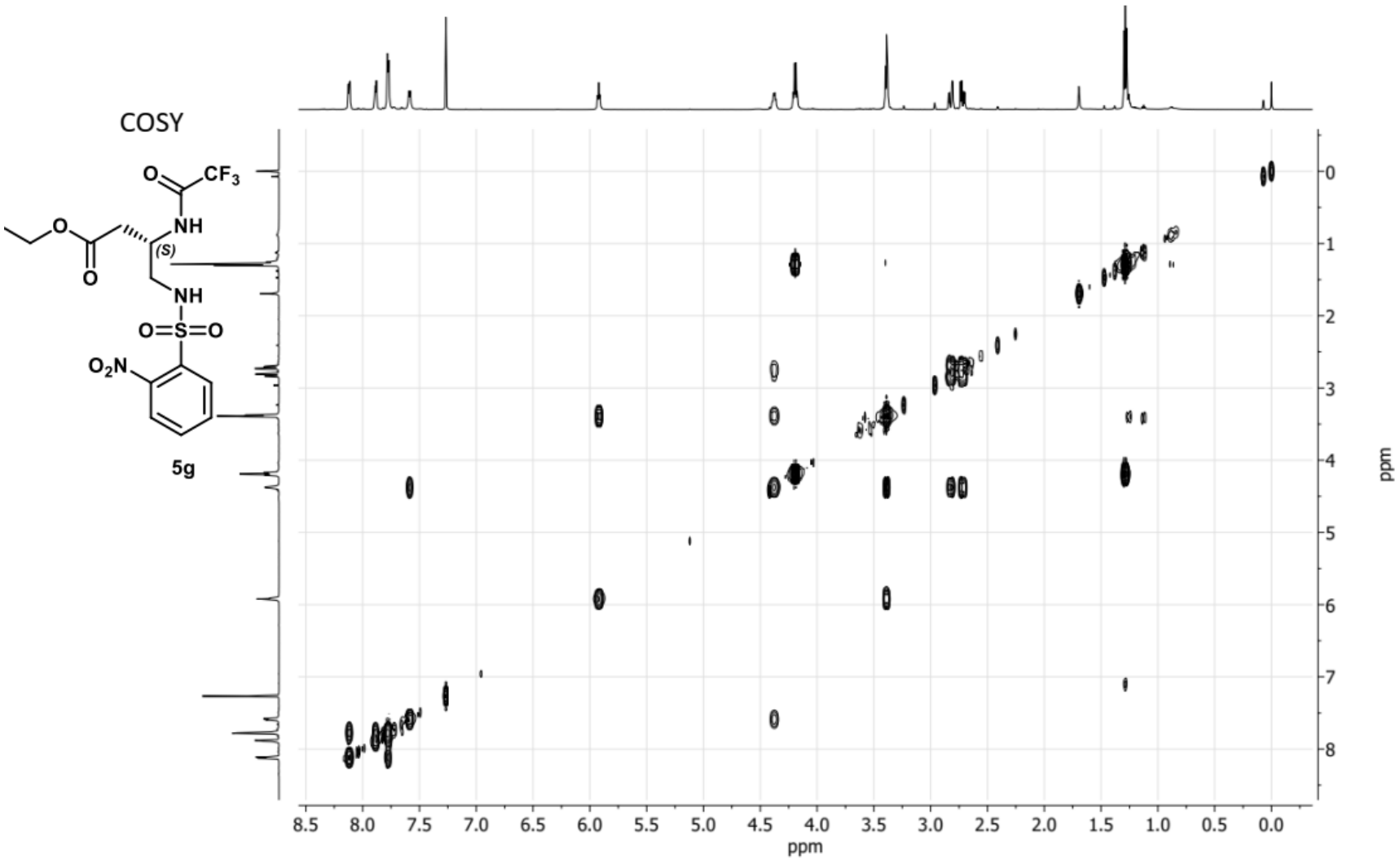
S_6

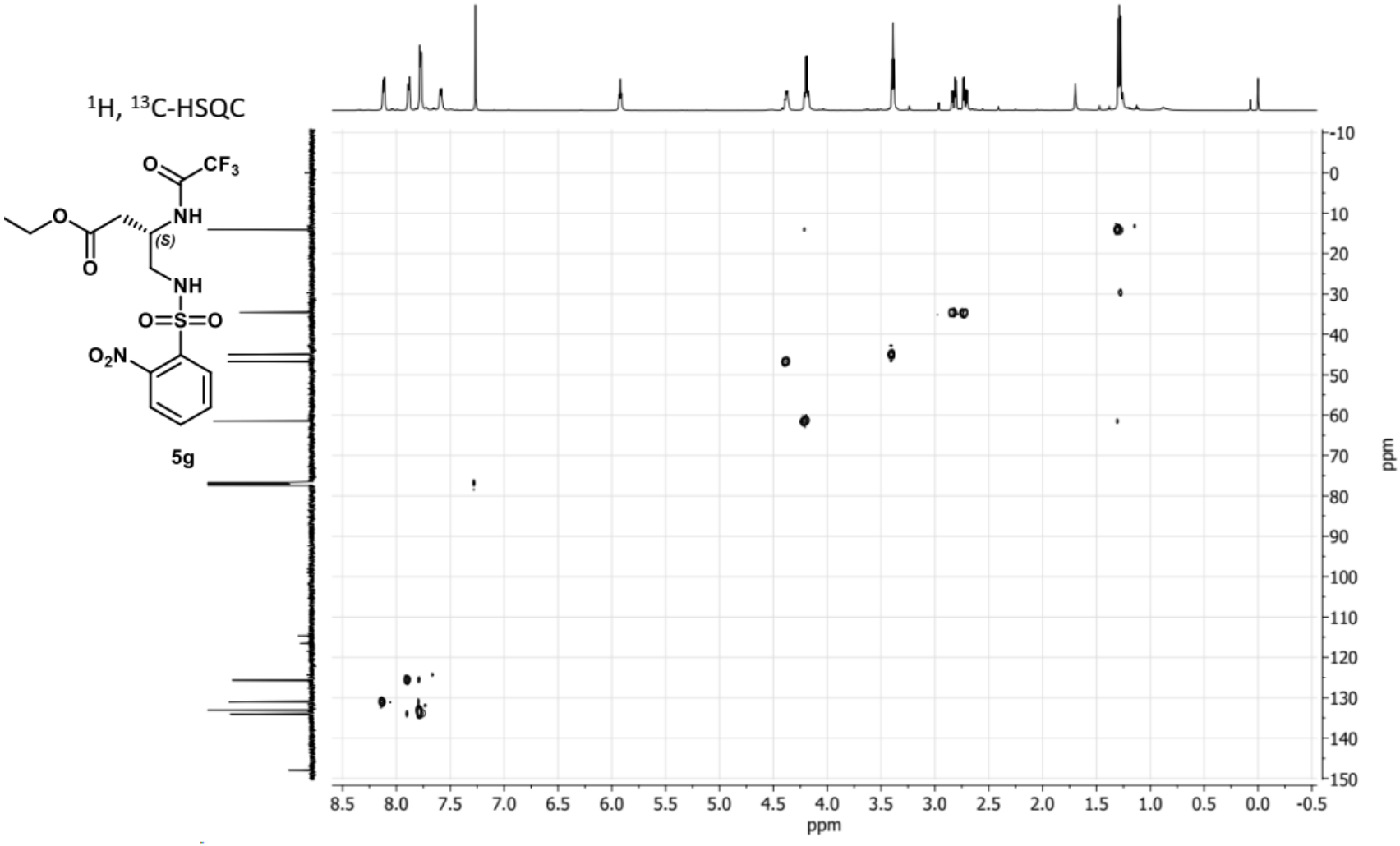

COSY
O
O
NH
(S)
O
O
NH
O=S=O
O2N
S6
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm
0
1
2
3
4
5
6
7
8
ppm

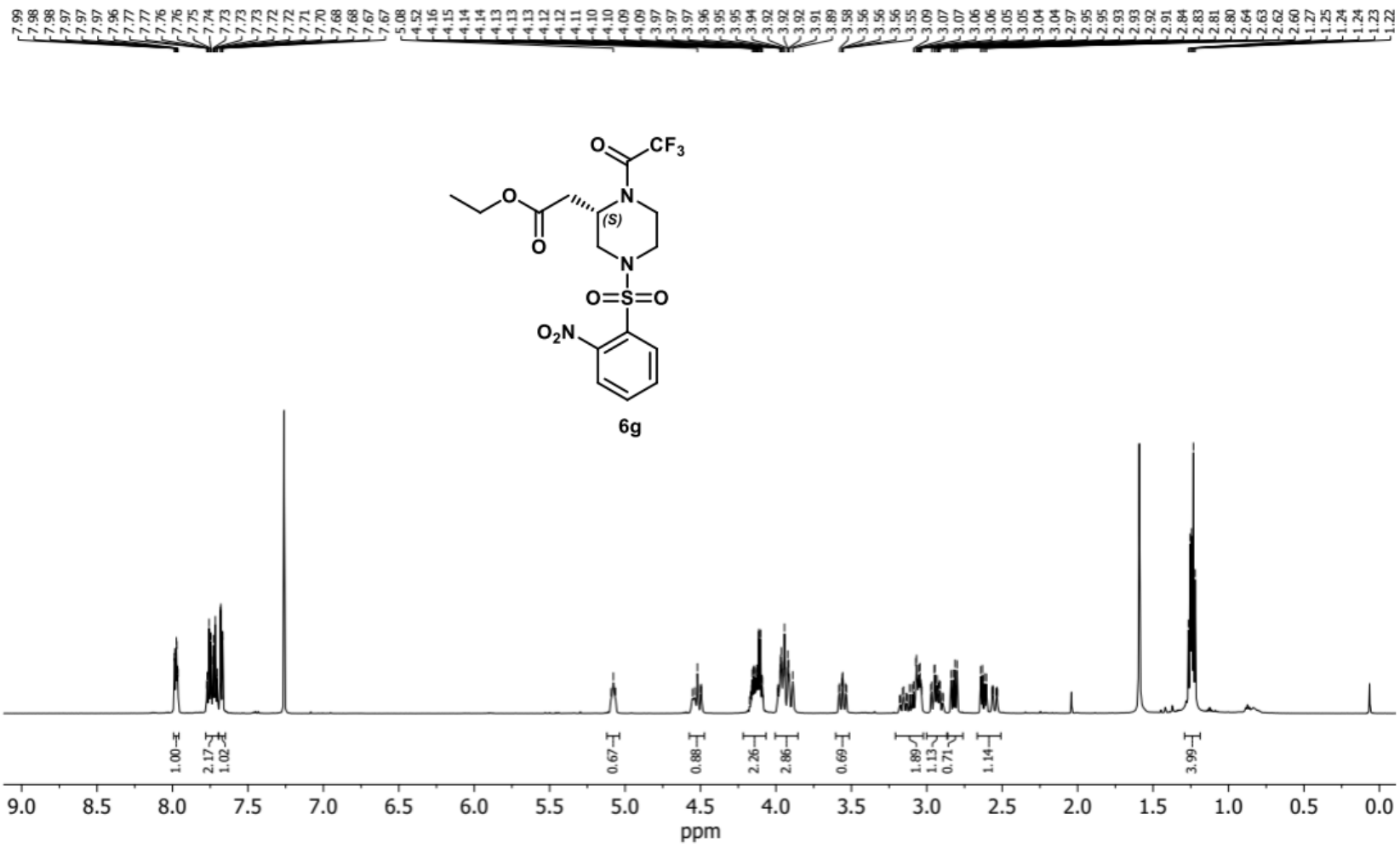

^{1}H, ^{13}C-HSQC
S$_6$
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140
ppm

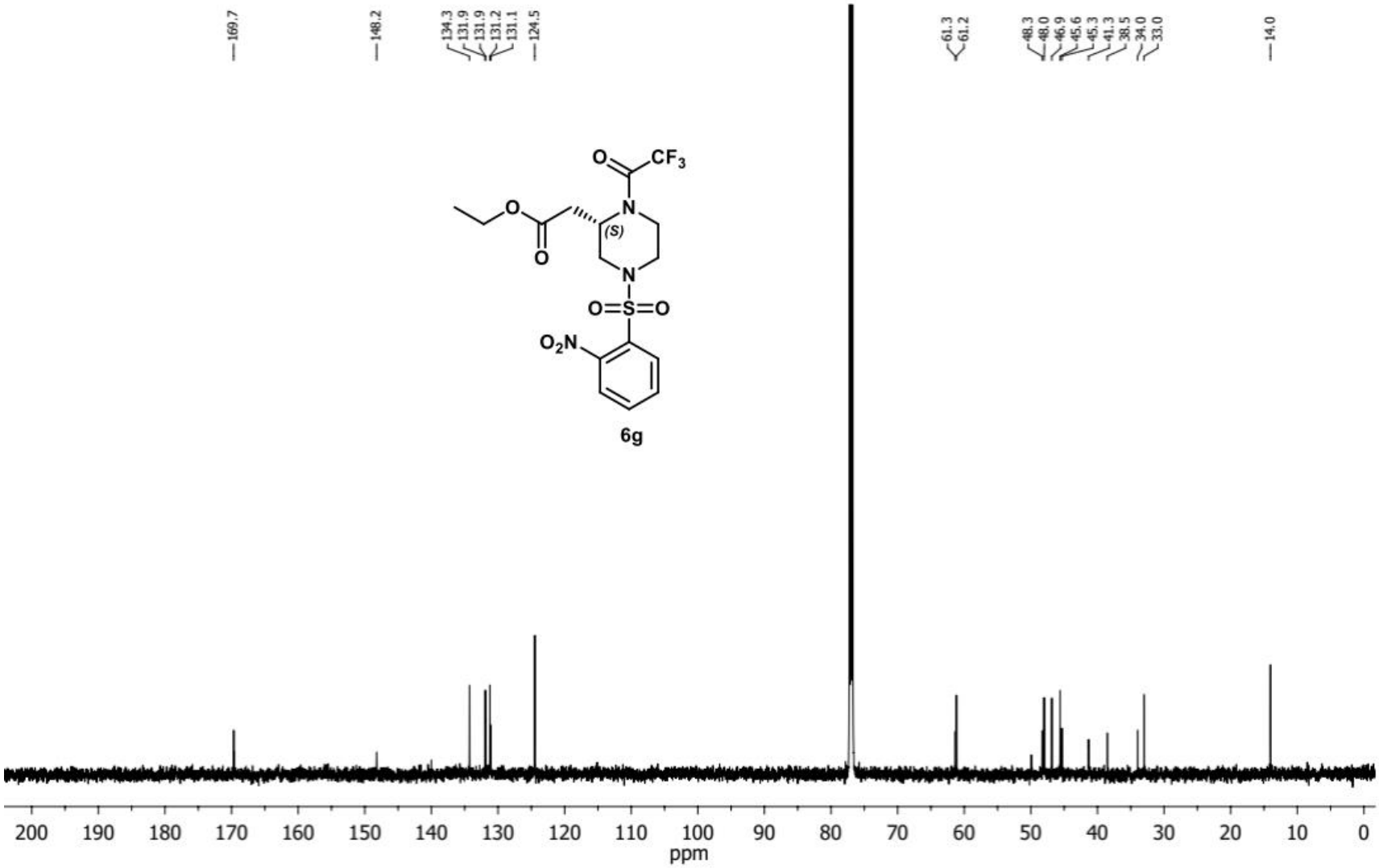

8.13 8.12 8.12 8.11 8.11 7.89 7.89 7.89 7.88 7.88 7.79 7.78 7.78 7.77 7.77 7.77 7.76 7.59 7.58
5.93 5.92 5.91
4.39 4.38 4.38 4.37 4.37 4.36 4.22 4.21 4.21 4.20 4.20 4.19 4.18 4.18 4.17 4.17 3.40 3.39 3.38
2.84 2.83 2.81 2.80 2.74 2.73 2.71 2.70
1.30 1.29 1.28
O
CF3
NH
O
(S)
O
NH
O=S=O
O2N
5g
1.00 1.01 2.09 0.97 0.98 1.06 2.25 2.19 1.03 1.11 3.58
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

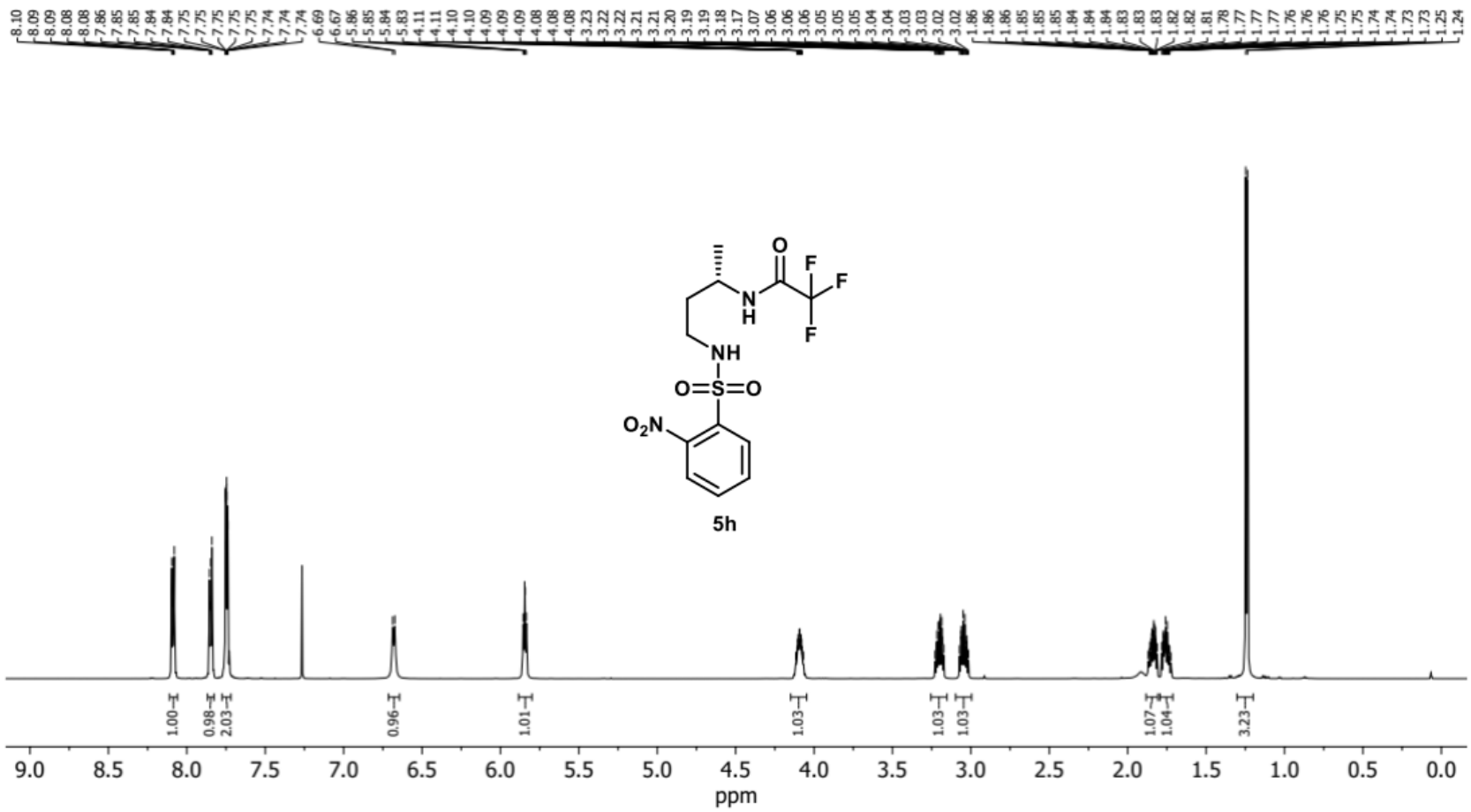

171.1
157.3
157.1
148.0
134.1
133.1
131.0
125.6
116.5
114.6
61.5
46.8
45.0
34.6
14.0
O
CF3
NH
(S)
O
O
NH
O=S=O
O2N
5g
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

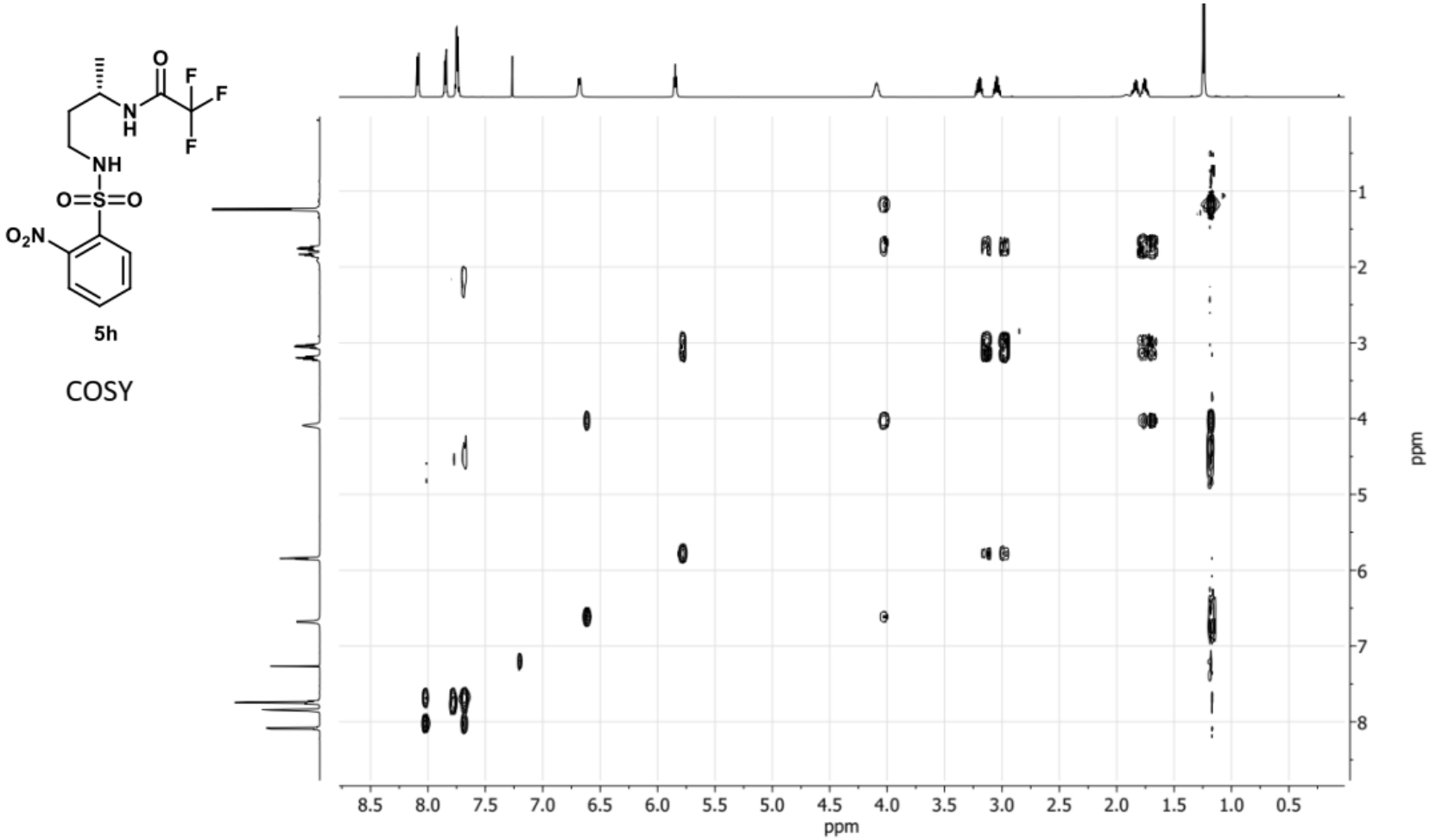

COSY
5g
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
0 1 2 3 4 5 6 7 8
ppm

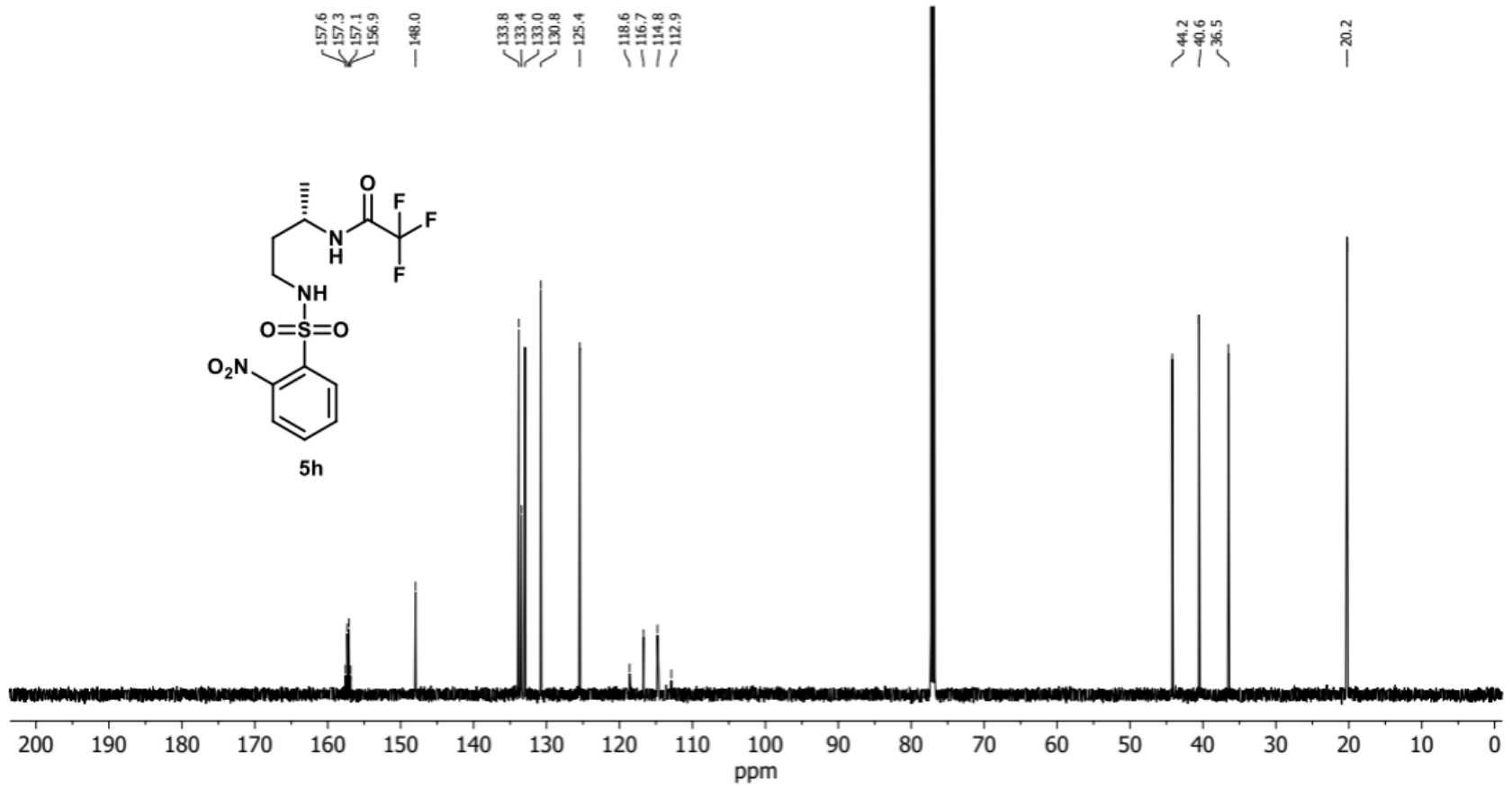

^{1}H, ^{13}C-HSQC
O
CF3
NH
(S)
O
O
NH
O=S=O
O2N
5g
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm
-10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
ppm

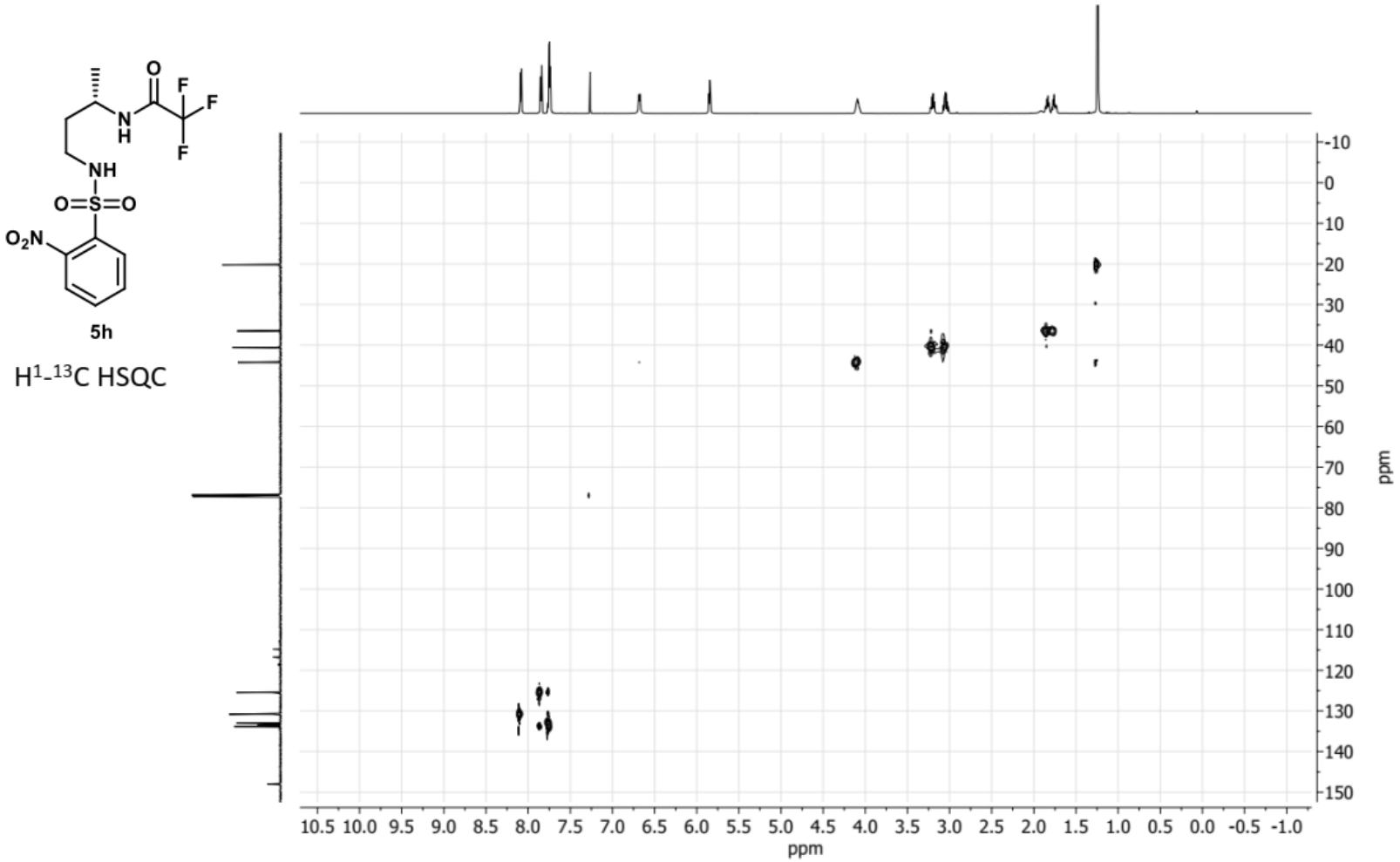

6g
ppm

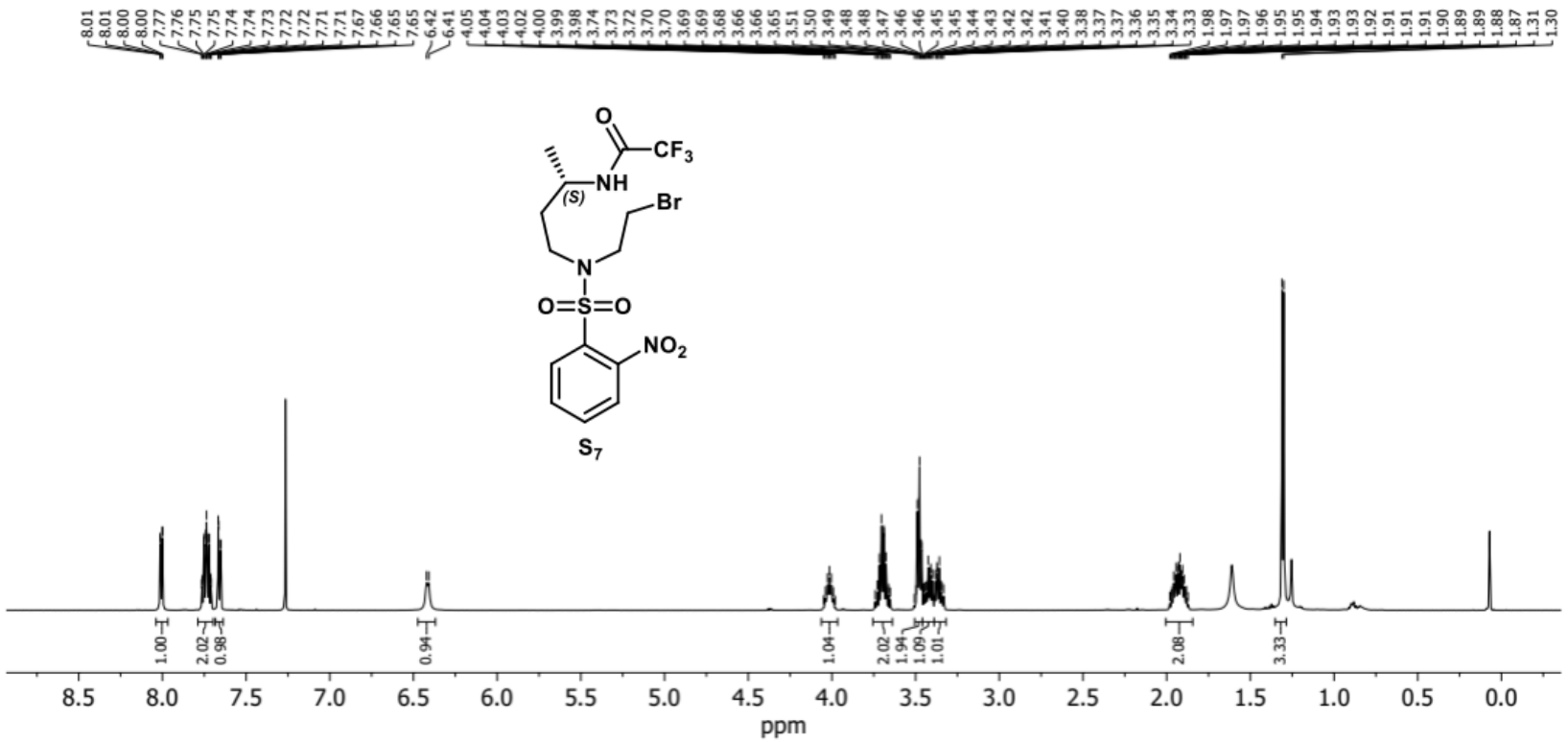

169.7
148.2
134.3
131.9
131.9
131.2
131.1
124.5
61.3
61.2
48.3
48.0
46.9
45.6
45.3
41.3
38.5
34.0
33.0
14.0
O
CF3
N
O
(S)
O
N
O=S=O
O2N
6g
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

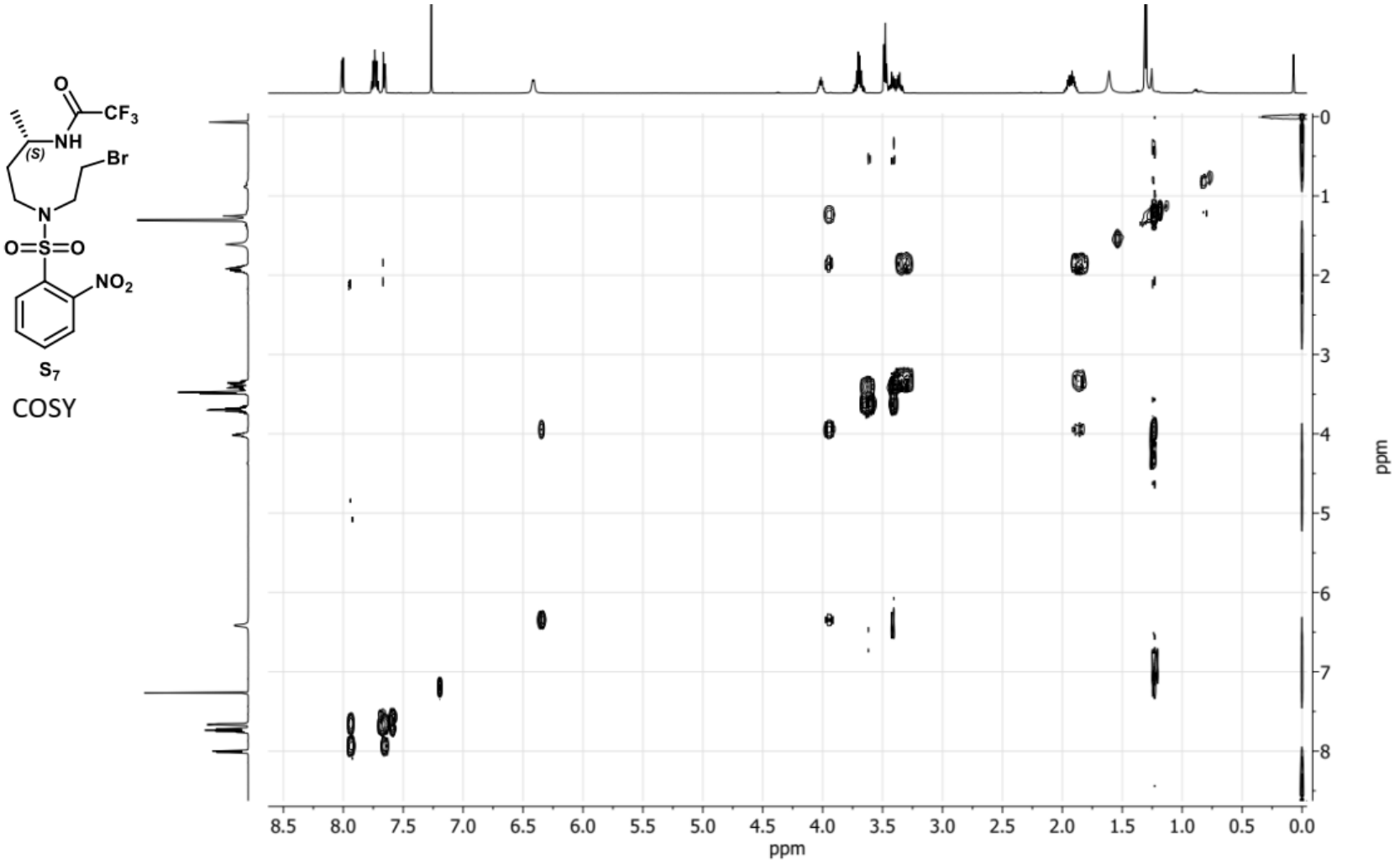

8.10 8.09 8.09 8.08 8.08 7.86 7.85 7.85 7.84 7.84 7.75 7.75 7.75 7.75 7.74 7.74 7.74
6.69 6.67 5.86 5.85 5.84 5.83 4.11 4.11 4.10 4.10 4.09 4.09 4.09 4.08 4.08 4.08 3.23 3.22 3.21 3.21 3.20 3.19 3.19 3.18 3.17 3.07 3.06 3.06 3.06 3.05 3.05 3.05 3.04 3.04 3.03 3.03 3.02 3.02 3.02
1.86 1.86 1.86 1.85 1.85 1.85 1.84 1.84 1.84 1.83 1.83 1.83 1.82 1.82 1.81 1.78 1.77 1.77 1.77 1.76 1.76 1.76 1.75 1.75 1.74 1.74 1.73 1.73 1.25 1.24
O
F
F
F
N
H
NH
O=S=O
O2N
5h
1.00
0.98
2.03
0.96
1.01
1.03
1.03
1.03
1.07
1.04
3.23
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

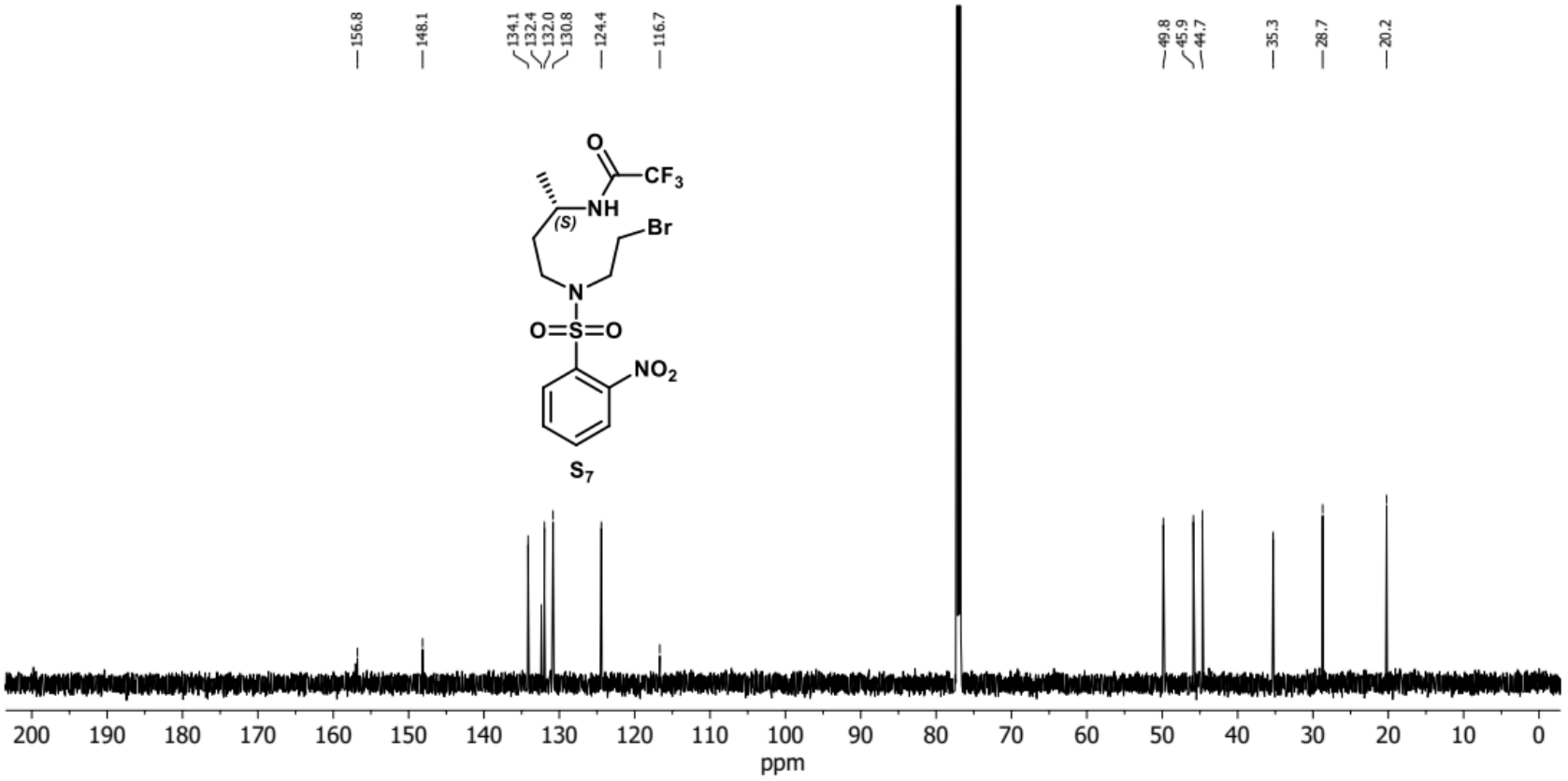

O
F
F
F
N
H
NH
O=S=O
O2N
5h
COSY
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1
2
3
4
5
6
7
8
ppm

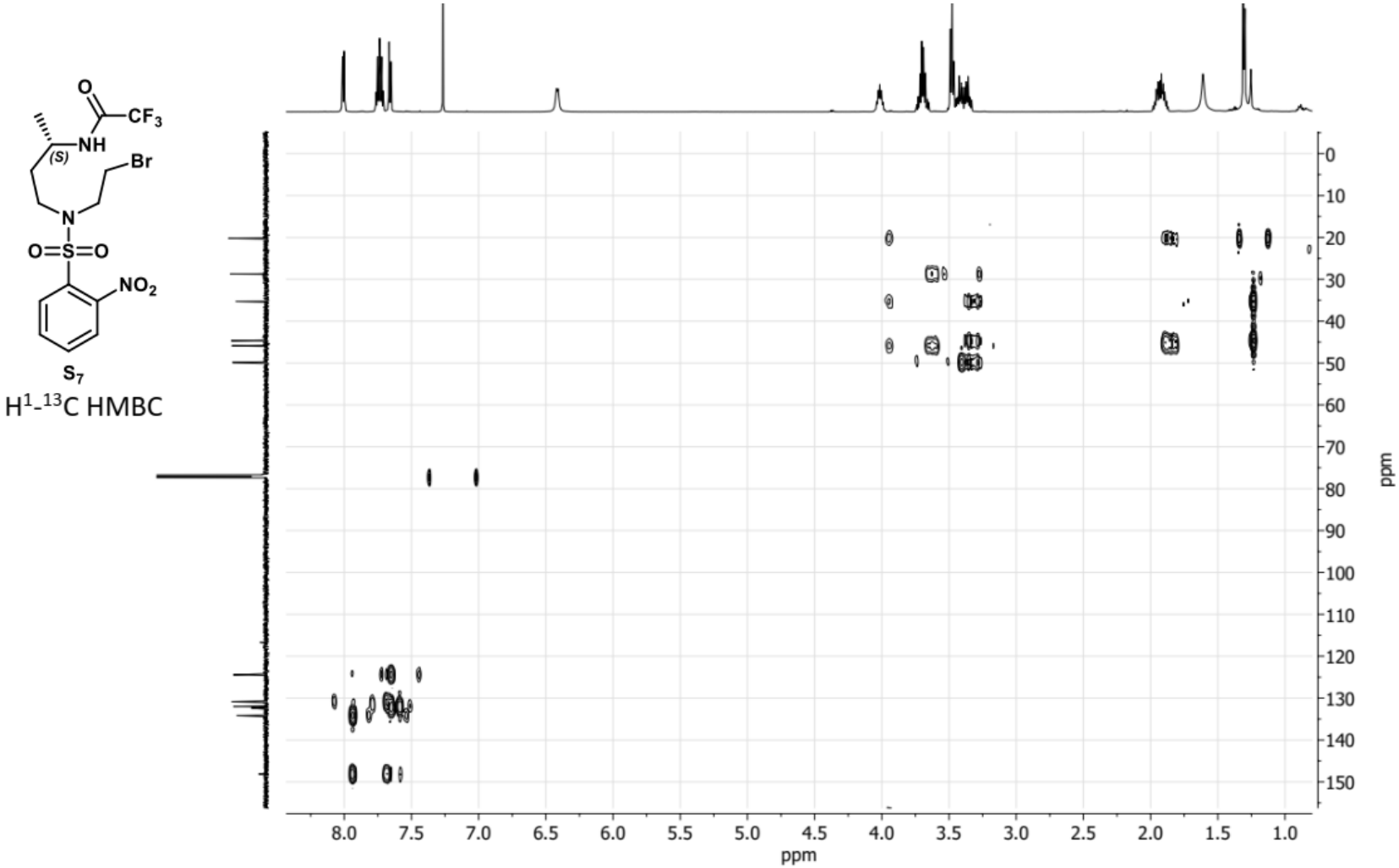

157.6
157.3
157.1
156.9
148.0
133.8
133.4
133.0
130.8
125.4
118.6
116.7
114.8
112.9
44.2
40.6
36.5
20.2
O
F
F
F
N
H
NH
O=S=O
O2N
5h
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

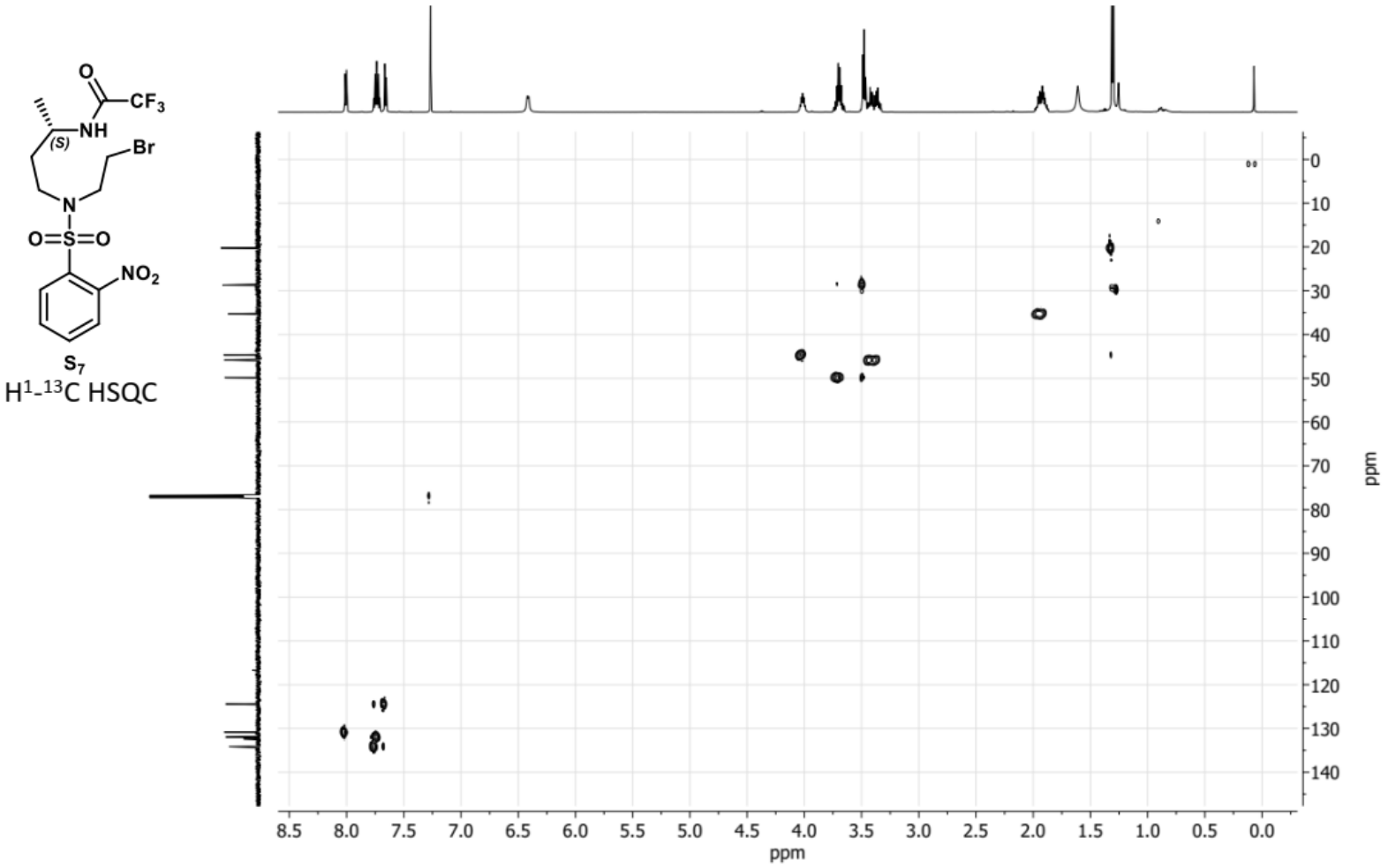

5h
H1-13C HSQC
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
ppm
-10 0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150
ppm

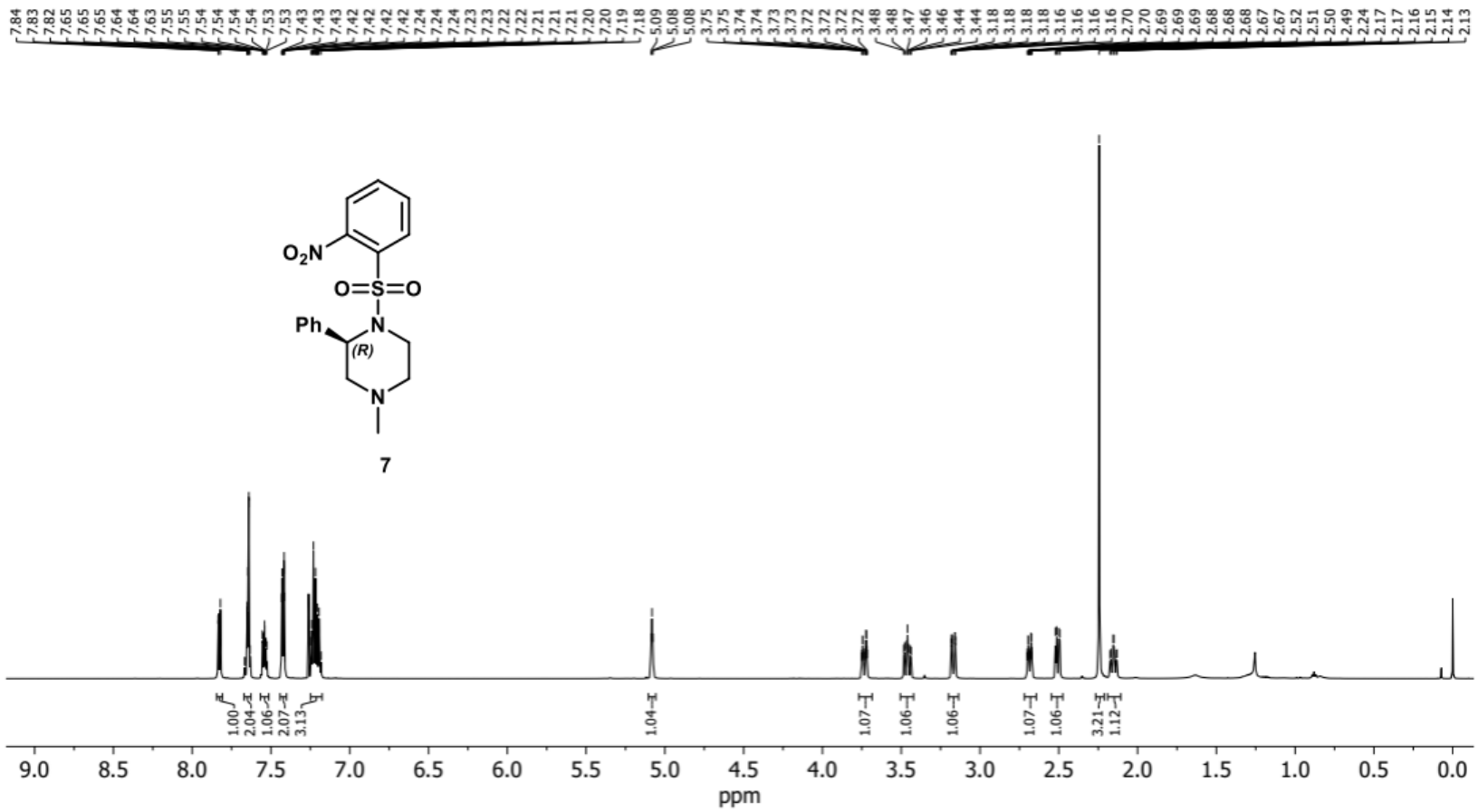

8.01 8.01 8.00 8.00 7.77 7.76 7.75 7.75 7.74 7.74 7.73 7.72 7.72 7.71 7.71 7.67 7.66 7.65 7.65 6.42 6.41 4.05 4.04 4.03 4.02 4.00 3.99 3.98 3.74 3.73 3.72 3.70 3.70 3.69 3.69 3.68 3.66 3.66 3.65 3.51 3.50 3.49 3.48 3.48 3.47 3.46 3.46 3.45 3.45 3.44 3.43 3.42 3.42 3.41 3.40 3.38 3.37 3.37 3.36 3.35 3.34 3.33 1.98 1.97 1.97 1.96 1.95 1.95 1.94 1.93 1.93 1.92 1.91 1.91 1.91 1.90 1.89 1.89 1.88 1.87 1.31 1.30
O
CF3
NH
(S)
Br
N
O=S=O
NO2
S7
1.00
2.02
0.98
0.94
1.04
2.02
1.94
1.09
1.01
2.08
3.33
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

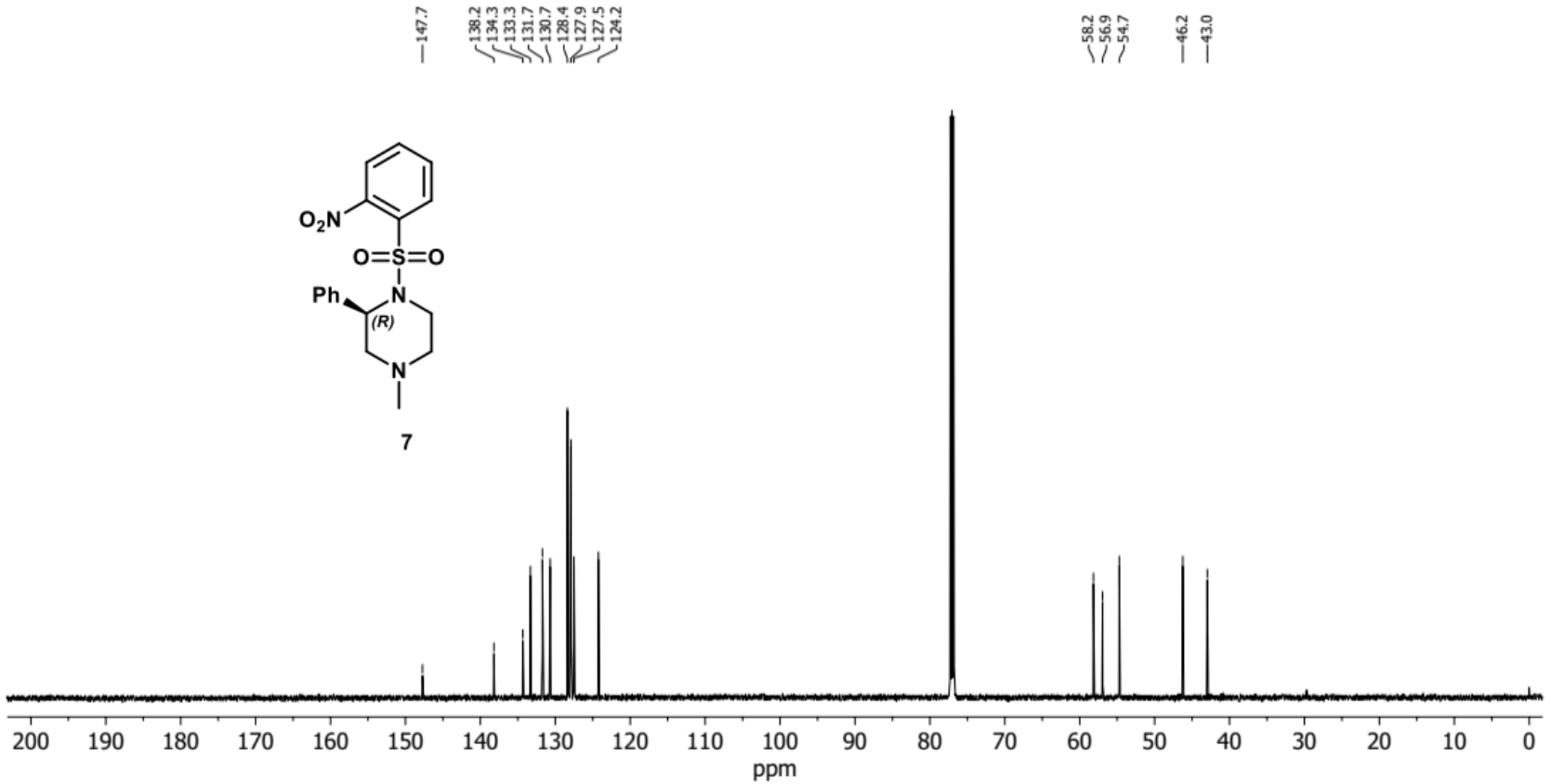

O
CF3
NH
(S)
Br
N
O=S=O
NO2
S7
COSY
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0
1
2
3
4
5
6
7
8
ppm

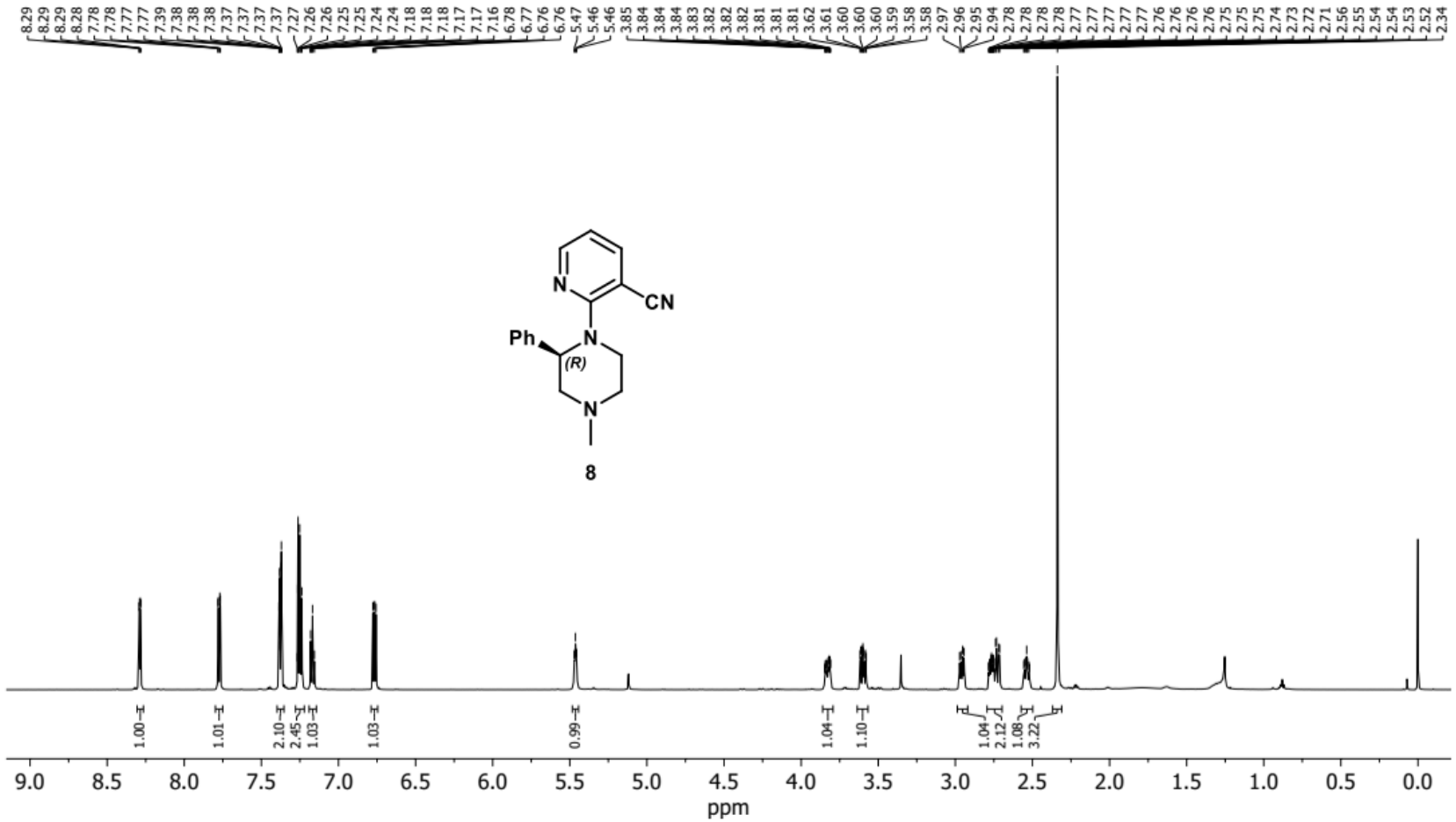

156.8
148.1
134.1
132.4
132.0
130.8
124.4
116.7
49.8
45.9
44.7
35.3
28.7
20.2
O
CF3
NH
(S)
Br
N
O=S=O
NO2
S7
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

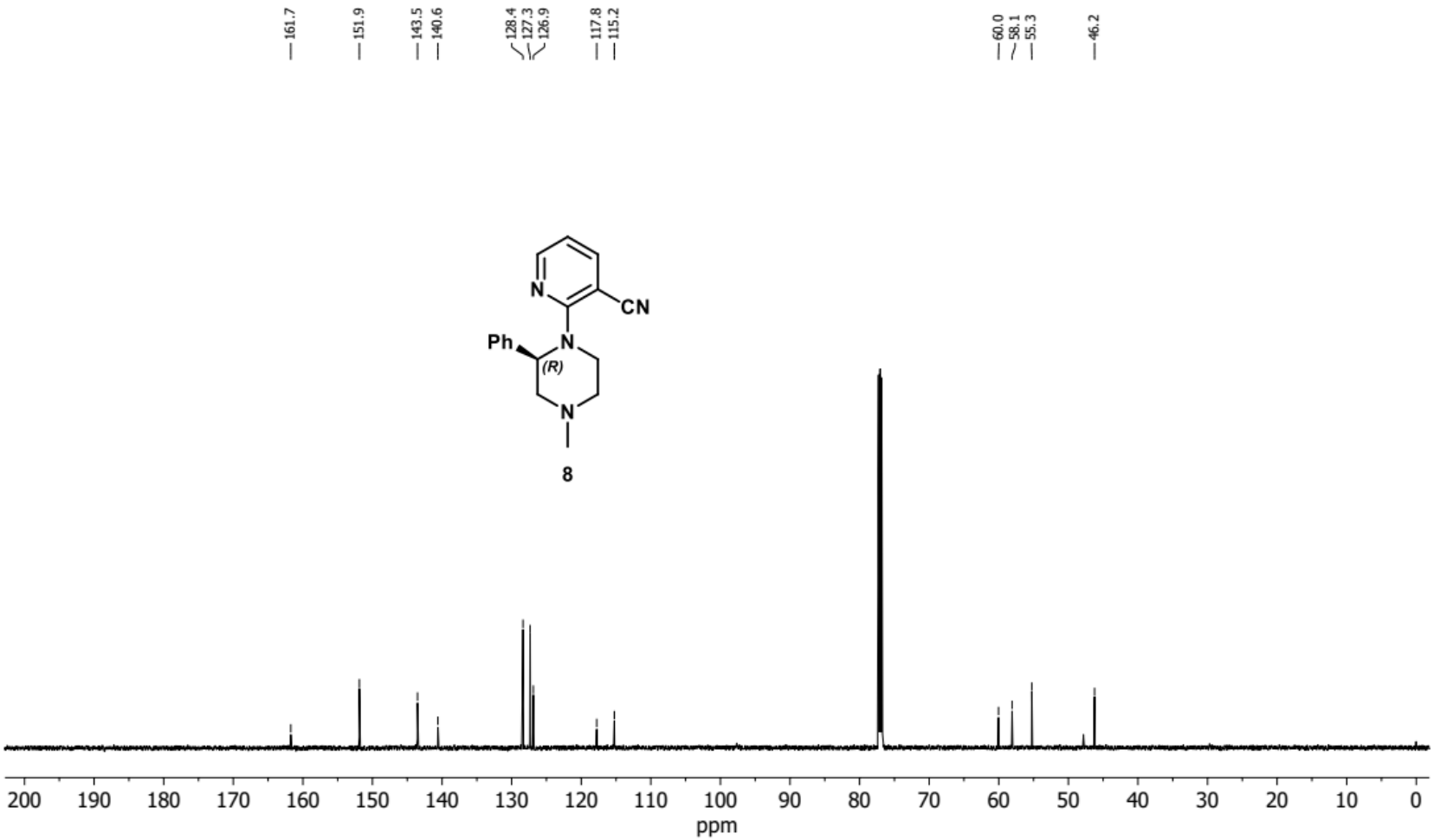

O
CF3
NH
(S)
Br
N
O=S=O
NO2
S7
H1-13C HMBC
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
ppm


O
CF3
NH
(S)
Br
N
O=S=O
NO2
S7
H1-13C HSQC
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140
ppm

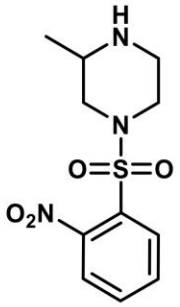

7.84 7.83 7.82 7.65 7.65 7.65 7.64 7.64 7.63 7.55 7.55 7.54 7.54 7.54 7.54 7.53 7.53 7.43 7.43 7.43 7.42 7.42 7.42 7.42 7.24 7.24 7.24 7.23 7.23 7.22 7.22 7.21 7.21 7.21 7.20 7.20 7.19 7.18 5.09 5.08 5.08 3.75 3.75 3.74 3.74 3.73 3.73 3.72 3.72 3.72 3.72 3.48 3.48 3.47 3.47 3.46 3.46 3.44 3.44 3.18 3.18 3.18 3.18 3.16 3.16 3.16 3.16 2.70 2.70 2.69 2.69 2.69 2.68 2.68 2.68 2.67 2.67 2.52 2.51 2.50 2.49 2.24 2.17 2.17 2.16 2.15 2.14 2.13
O2N
O=S=O
Ph
(R)
N
N
7
1.00 2.04 1.06 2.07 3.13 1.04 1.07 1.06 1.06 1.07 1.06 3.21 1.12
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm


147.7
138.2
134.3
133.3
131.7
130.7
128.4
127.9
127.5
124.2
58.2
56.9
54.7
46.2
43.0
O2N
O=S=O
Ph
N
(R)
N
7
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm


8.29 8.29 8.29 8.28 7.78 7.78 7.77 7.77 7.39 7.38 7.38 7.37 7.37 7.37 7.37 7.27 7.26 7.26 7.25 7.25 7.24 7.24 7.18 7.18 7.18 7.17 7.17 7.16 6.78 6.77 6.76 6.76 5.47 5.46 5.46 3.85 3.84 3.84 3.84 3.83 3.82 3.82 3.82 3.81 3.81 3.81 3.62 3.61 3.60 3.60 3.60 3.59 3.58 3.58 2.97 2.96 2.95 2.94 2.78 2.78 2.78 2.77 2.77 2.77 2.77 2.77 2.76 2.76 2.76 2.76 2.75 2.75 2.75 2.74 2.74 2.73 2.72 2.71 2.56 2.55 2.54 2.54 2.53 2.52 2.34
N
CN
Ph
N
(R)
N
8
1.00
1.01
2.10
2.45
1.03
1.03
0.99
1.04
1.10
1.04
2.12
1.08
3.22
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm


161.7
151.9
143.5
140.6
128.4
127.3
126.9
117.8
115.2
60.0
58.1
55.3
46.2
N
CN
Ph
N
(R)
N
8
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

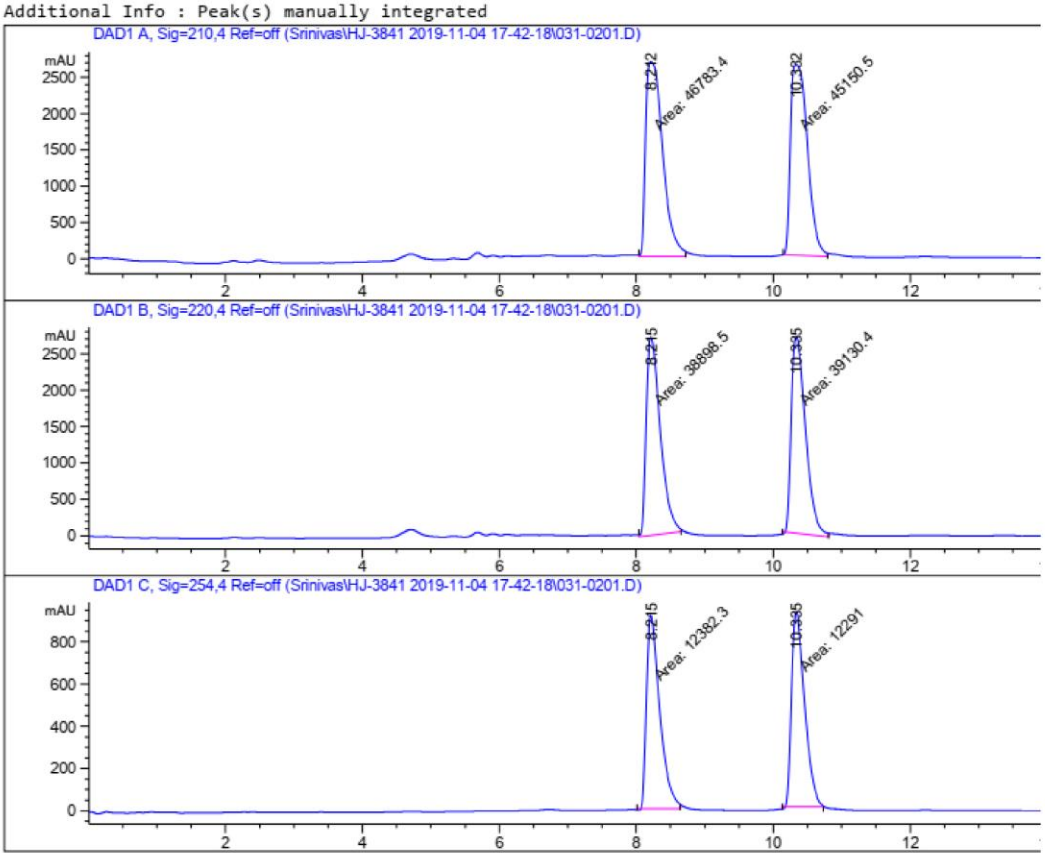
Chiral HPLC



4e

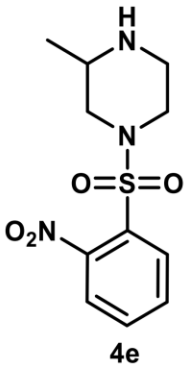
```
======================================================================
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : CHIRAL                         Location :   31
Injection Date  : 11/4/2019 6:00:28 PM               Inj :   1
                                                Inj Volume : 5.000 µl
Different Inj Volume from Sample Entry!  Actual Inj Volume : 10.000 µl
Method          : C:\Chem32\1\Data\Srinivas\HJ-3841 2019-11-04 17-42-18\FAST_Chiral_Scout_IA_
                  nHep_Ethanol.M (Sequence Method)
Last changed    : 11/4/2019 5:42:18 PM by SYSTEM
Method Info     : Scouting method for normal phase chiral separations ChiralPak IA with n-
                  Heptane and Ethanol

Additional Info : Peak(s) manually integrated
```




```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs
```



4e

Signal 1: DAD1 A, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.212	MM	0.2906	4.67834e4	2683.20776	50.8881
2	10.332	MM	0.2869	4.51505e4	2623.08179	49.1119
Totals :				9.19339e4	5306.28955	

Signal 2: DAD1 B, Sig=220,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.215	MM	0.2389	3.88985e4	2714.01636	49.8514
2	10.335	MM	0.2425	3.91304e4	2689.41455	50.1486
Totals :				7.80289e4	5403.43091	

Signal 3: DAD1 C, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.215	MM	0.2257	1.23823e4	914.21948	50.1849
2	10.335	MM	0.2222	1.22910e4	922.11060	49.8151
Totals :				2.46734e4	1836.33008	

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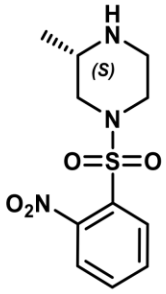
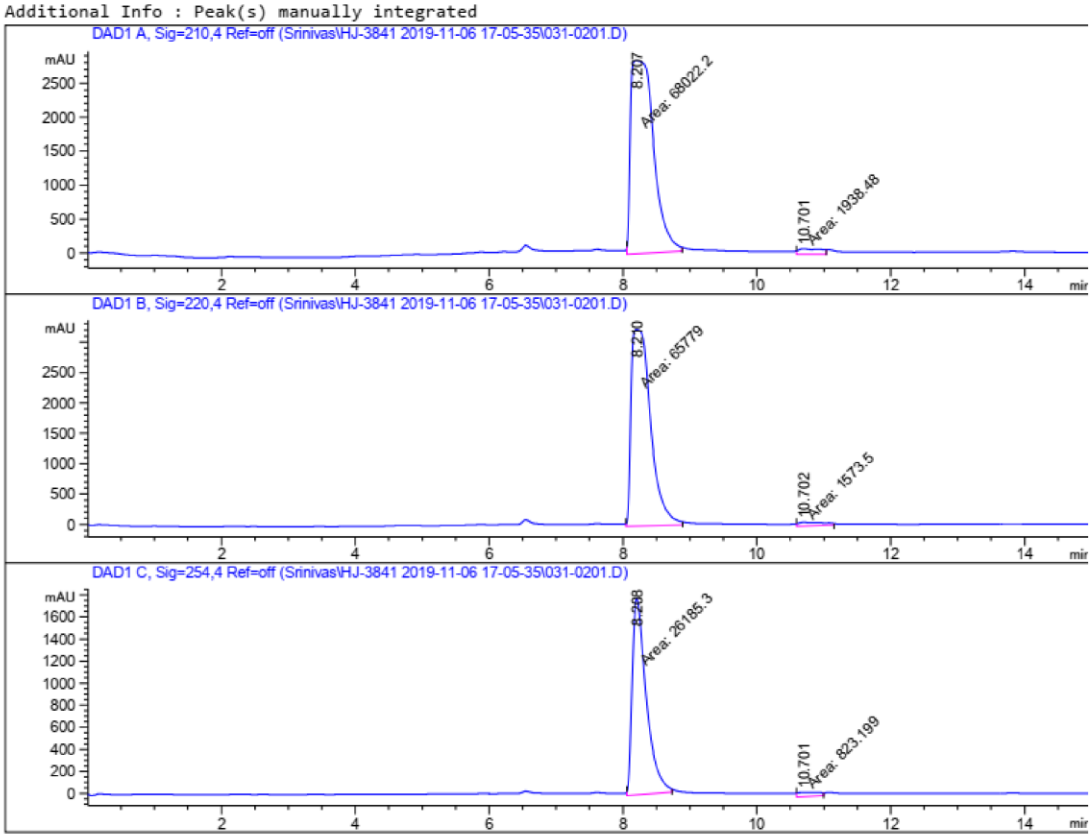
*** End of Report ***



4c

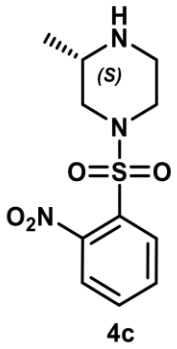
```
==================================================================
Acq. Operator   : SYSTEM                        Seq. Line :   2
Acq. Instrument : CHIRAL                         Location :   31
Injection Date  : 11/6/2019 5:23:51 PM               Inj :   1
                                               Inj Volume : 5.000 µl
Different Inj Volume from Sample Entry!  Actual Inj Volume : 10.000 µl
Method          : C:\Chem32\1\Data\Srinivas\HJ-3841 2019-11-06 17-05-35\FAST_Chiral_Scout_IA_
                  nHep_Ethanol.M (Sequence Method)
Last changed    : 11/6/2019 5:05:35 PM by SYSTEM
Method Info     : Scouting method for normal phase chiral separations ChiralPak IA with n-
                  Heptane and Ethanol

Additional Info : Peak(s) manually integrated
```




```
==================================================================
                        Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs
```



4c

Signal 1: DAD1 A, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.207	MM	0.3490	6.80222e4	2839.32886	97.2292
2	10.701	MM	0.3876	1938.47900	83.35078	2.7708
Totals :				6.99607e4	2922.67964	

Signal 2: DAD1 B, Sig=220,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.210	MM	0.3389	6.57790e4	3234.55884	97.6638
2	10.702	MM	0.4054	1573.49976	64.69689	2.3362
Totals :				6.73525e4	3299.25573	

Signal 3: DAD1 C, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.208	MM	0.2450	2.61853e4	1780.98474	96.9521
2	10.701	MM	0.3381	823.19885	40.57403	3.0479
Totals :				2.70085e4	1821.55877	

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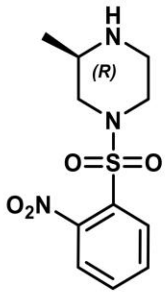
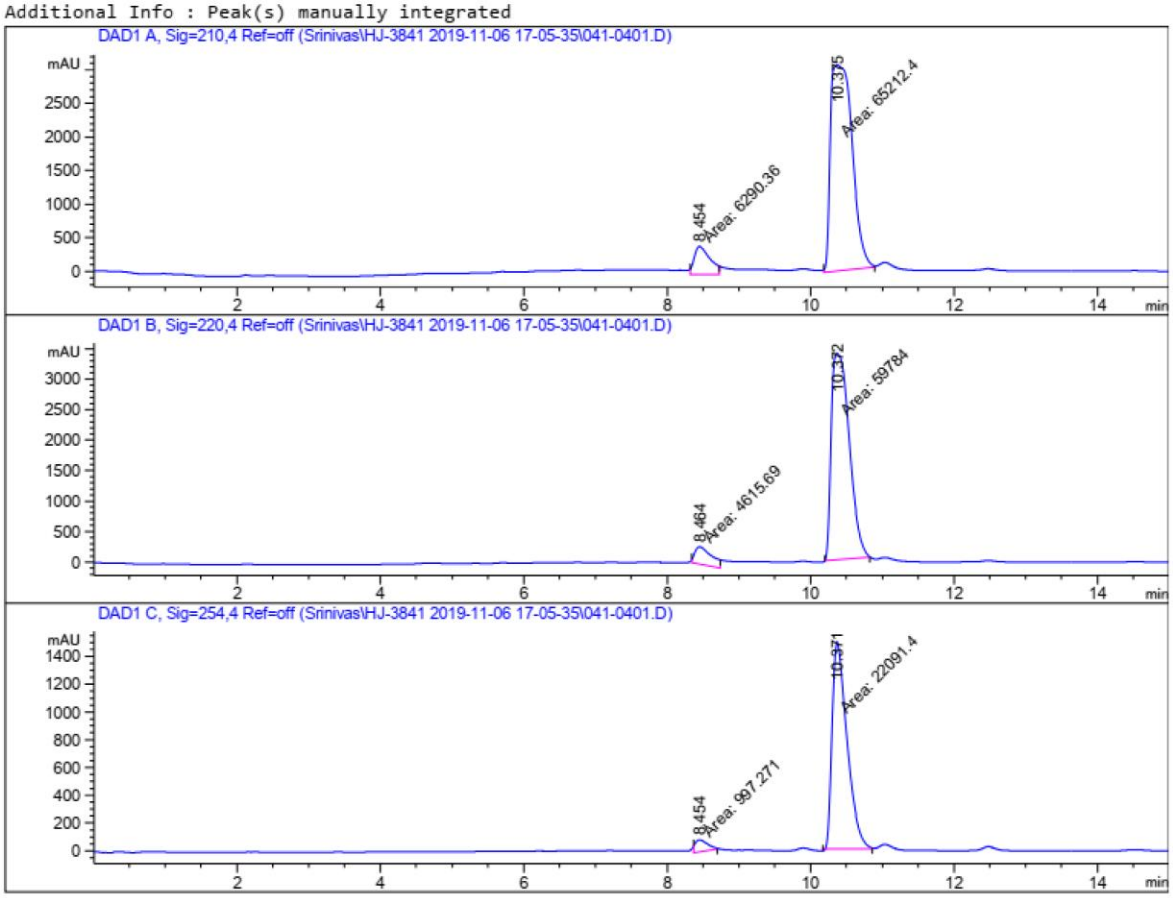
*** End of Report ***



4d

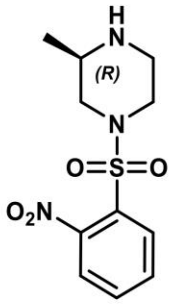
```
======================================================================
Acq. Operator   : SYSTEM                        Seq. Line :   4
Acq. Instrument : CHIRAL                         Location :   41
Injection Date  : 11/6/2019 5:56:14 PM               Inj :   1
                                              Inj Volume : 5.000 µl
Different Inj Volume from Sample Entry!  Actual Inj Volume : 10.000 µl
Method          : C:\Chem32\1\Data\Srinivas\HJ-3841 2019-11-06 17-05-35\FAST_Chiral_Scout_IA_
                  nHep_Ethanol.M (Sequence Method)
Last changed    : 11/6/2019 5:05:35 PM by SYSTEM
Method Info     : Scouting method for normal phase chiral separations ChiralPak IA with n-
                  Heptane and Ethanol

Additional Info : Peak(s) manually integrated
```




```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs
```



4d

Signal 1: DAD1 A, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.454	MM	0.2533	6290.36230	413.85803	8.7974
2	10.375	MM	0.3541	6.52124e4	3069.39160	91.2026
Totals :				7.15028e4	3483.24963	

Signal 2: DAD1 B, Sig=220,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.464	MM	0.2715	4615.68848	283.35751	7.1673
2	10.372	MM	0.2943	5.97840e4	3385.49194	92.8327
Totals :				6.43996e4	3668.84946	

Signal 3: DAD1 C, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.454	MM	0.1935	997.27118	85.90546	4.3193
2	10.371	MM	0.2462	2.20914e4	1495.26611	95.6807
Totals :				2.30886e4	1581.17157	

*** End of Report ***