Iridium-Catalyzed Synthesis of Saturated N-Heterocycles from Aldehydes and SnAP Reagents with Continuous Flow Photochemistry

Supporting Information

Chalupat Jindakun, Sheng-Ying Hsieh and Jeffrey W. Bode*

Laboratorium für Organische Chemie, Department of Chemistry and Applied Biosciences ETH Zürich, Zürich 8093, Switzerland

bode@org.chem.ethz.ch

Table of contents

General information

All reactions were performed in oven-dried glassware under a dry N_2 atmosphere. Reaction mixtures were mechanically stirred with a magnetic stir bar unless otherwise indicated and monitored by thin layer chromatography (TLC) on Merck precoated glass-backed silica gel 60 F-254 0.25 mm plates with visualization by fluorescence quenching at 254 nm. TLC plates were stained using potassium permanganate or ninhydrin solutions. Chromatographic purification of products (flash column chromatography) was performed on high-purity grade (7734) silica gel (pore size 60 Å, 70–230 mesh) from Sigma-Aldrich using an air-pressured flow of eluent at 0.3–0.5 bar. Concentration of reaction product solutions and chromatographic fractions under reduced pressure was performed by rotary evaporation at 40 °C at the appropriate pressure and then at r.t., ca. 0.1 mmHg (vacuum pump) unless otherwise indicated.

Materials

All chemicals were purchased from Acros, Aldrich, Fluka, Merck, ABCR, Maybridge, Fluorochem, TCI, Alfa Aesar or Strem and used as such unless stated otherwise. Commercial grade reagents and solvents were used without further purification except as indicated below. *N*,*N*-Dimethylformamide (DMF), acetonitrile (CH_3CN), toluene, tetrahydrofuran (THF) and dichloromethane (CH_2Cl_2) were purified by pressure filtration through activated alumina. 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP), 2,2,2-trifluoroethanol (TFE) and methanol (MeOH) were used as purchased. MS 4A was dried at 110 °C under high vacuum (ca. 0.1 mmHg) for 2 h and stored in desiccator for weeks. Photoredox catalysts $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (**1**)[1] and 2CzIPN (**3**)[2] were synthesized according to literature procedures. Adamantane-1-carboxaldehyde was obtained from oxidation of adamantylmethanol with pyridinium chlorochromate according to Gary procedure[3]. Yields given refer to chromatographically purified and spectroscopically pure compounds unless otherwise stated.

Instrumentation

Infrared (IR) spectra were recorded on a JASCO FT:IR-4100 spectrophotometer and reported as wavenumber (cm^{-1}) of the absorption maxima for the range between 4000 cm^{-1} and 750 cm^{-1} with only major peaks reported. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance spectrometers (400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR). ^1H NMR chemical shifts are expressed in parts per million (δ) downfield from tetramethylsilane (with the $CHCl_3$ peak at 7.26 ppm used as a standard). ^{13}C NMR chemical shifts are expressed in parts per million (δ) downfield from tetramethylsilane (with the central peak of $CDCl_3$ at 77.16 ppm used as a standard). All ^{13}C spectra were measured with complete proton decoupling. NMR coupling constants (J) are reported in Hertz (Hz), and splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; dd, doublet of doublet; ddd, double of doublet of doublet; dt, doublet of triplet; t, triplet; q, quartet; quint, quintet; sext, sextet; m, multiplet. High-resolution mass spectrometric measurements (HRMS) were performed by the mass spectrometry service of the LOC at the ETHZ on Agilent 1200 (LC-MS), Bruker maXis for ESI-Q-TOF or Waters Micromass AutoSpec Ultima MassLynx 4.0 (GC-MS). Melting points were measured on an Electrothermal Mel-Temp melting point apparatus and are

uncorrected. UV-Vis spectra were recorded on a Thermo Scientific™ NanoDrop 2000c with a 10-mm-path-length quartz cuvette and reported in a wavelength region 200 – 700 nm.

Photocatalytic reaction

Batch condition

Nichia LumiFlex LED strip (blue light, λ_{max} = 467 nm, 6 W for 30 LEDs) were purchased from Lumitronix® LED-Technik (http://www.leds.de/) and assembled in a 15×12×12 cm^3 metal case with total 150 blue LEDs (**maximum power: 30 W**). The case was also equipped with a cooling fan (12×12 cm^2) to maintain the temperature at room temperature. Detailed specification of the blue LEDs can be found in this webpage: http://www.leds.de/en/LED-strips-modules-oxid-oxid-oxid/Flexible-LED-strips/LumiFlex-LED-Leiste-30- LEDs-50cm-24V-blue.html.

Photocatalytic reactions were carried out in closed glass vials (sizes depended on reaction scales), neither degassed beforehand nor conducted under dry conditions. The vials were exposed next to the blue LEDs as shown in Figure S1.

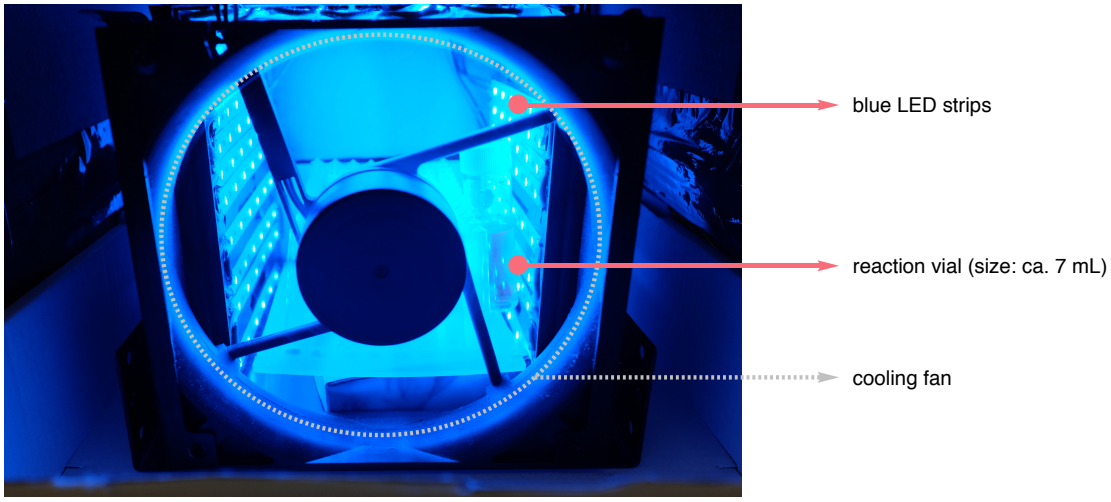


Figure S1. Blue light reactor/reaction setup. We thank Dr. Benedikt Wanner from ETH Zürich for the construction of this blue reactor.

Flow condition

A self-built photo-flow reactor was used. The reaction mixture was passed through a glass chip (channel size = 1.00 mm, volume = 1.7 mL) via a syringe pump at a given flow rate, illuminated by a Luxeonstar LXML-PR02-A900 Royal Blue (λ_{max} = 460 nm, I = 700 mA) and collected in a glass vial or an Erlenmeyer flask. The distance between the LED and the glass chip was 2.0 cm. The reaction mixture was homogenized by sonication or stirring before injecting into the reactor. The top of the reactor was covered with aluminum foil. Cooling-fan was also equipped to maintain room temperature during the reaction (Figure S2).

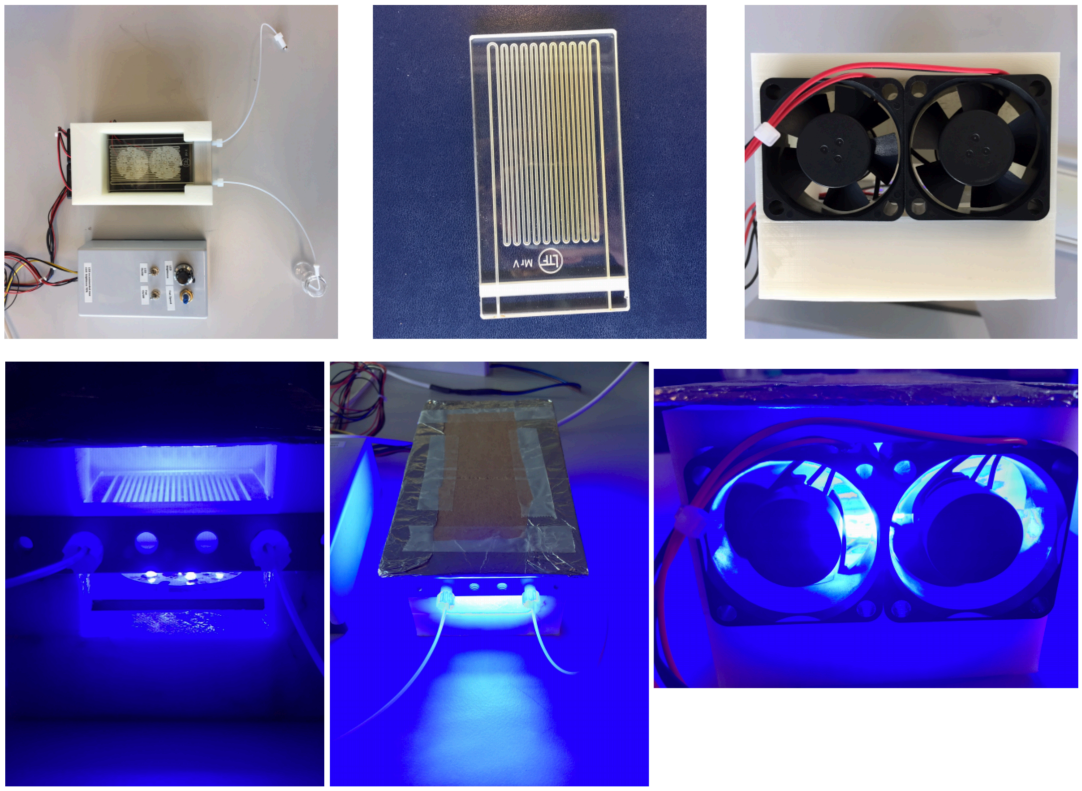
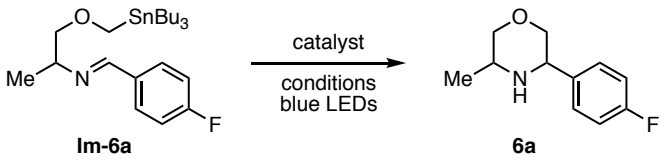


Figure S2. Blue-light-flow reactor/reaction setup. We thank Dr. Benedikt Wanner from ETH Zürich and Dr. Anastasios Polyzos from University of Melbourne for the construction of this flow reactor.

Photocatalytic synthesis of N-heterocycles from SnAP reagents

Initial experiments

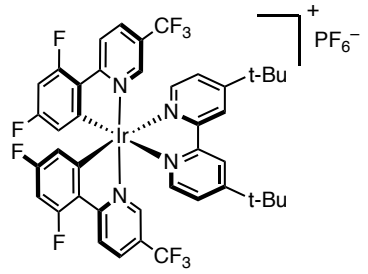
Batch condition[a]



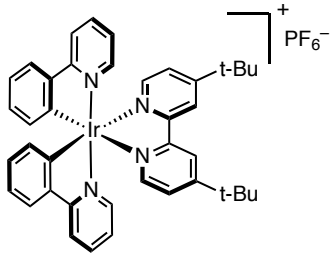
Im-6a **6a**

Entry	Catalyst	Solvent	conv (%)[b]	NMR yield (%)[b]
1	1 mol % **1**	4:1 CH_3CN/MeOH	92	58
2	2.5 mol % **2**	4:1 CH_3CN/MeOH	14	14
3	5 mol % **3**	4:1 CH_3CN/MeOH	100	51
4	5 mol % **3**[c]	15:4:1 CH_3CN/MeOH/DMF	0	0
5	5 mol % **4**	9:1 toluene/HFIP	0	0
6	1 mol % **1**	4:1 CH_2Cl_2/MeOH	76	61
7	1 mol % **1**	4:1 toluene/MeOH	41	40
8	1 mol % **1**	4:1 THF/ MeOH	33	42
9	1 mol % **1**	4:1 CH_3CN/TFE	92	59
10	1 mol % **1**	4:1 CH_3CN/HFIP	97	47

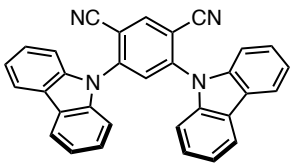
[a]The reaction was carried out in 0.2 mmol scale in 0.05 mM concentration at rt for 16 h.
[b]Conv (conversion) and yield were measured from ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as an internal standard.
[c]a solution of **3** in degassed DMF was used.



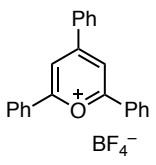
$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (**1**)



$Ir(ppy)_2(dtbbpy)PF_6$ (**2**)

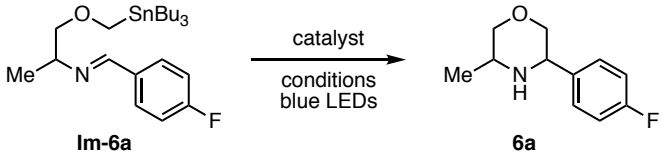


2CzIPN (**3**)



Triphenylpyrylium (**4**)

Flow condition[a]



Entry	Catalyst	Solvent	Flow rate (mL/min)	conv (%)[b]	NMR yield (%)[b]
1	1 mol % **1**	4:1 CH_3CN/MeOH	0.13	72	50
2	1 mol % **1**	4:1 CH_3CN/MeOH	0.06[c]	74	52
3	2 mol % **1**	4:1 CH_3CN/MeOH	0.13	75	70
4	2.5 mol % **1**	4:1 CH_3CN/MeOH	0.13	82	69
5	2.5 mol % **1**	4:1 CH_3CN/*i*-PrOH	0.13	85	64
6	2.5 mol % **1**	4:1 CH_3CN/TFE	0.13	92	58
7	2.5 mol % **1**	4:1 CH_3CN/HFIP	0.13	91	55
8	2.5 mol % **1**	4:1 CH_3CN/TFE	0.13	89	58
9	2.5 mol % **1**	4:1 CH_3CN/TFE	0.20	91	67
10	2.5 mol % **1**	4:1 CH_3CN/TFE	0.25	85	69
11	2.5 mol % **1**	1:1 CH_3CN/TFE	0.25	93	65
12	2.5 mol % **1**	1:1 CH_3CN/TFE	0.38	86	58
13	2.5 mol % **1**	1:1 CH_3CN/MeOH	0.25	89	58
14	2.5 mol % **1**	1:1 CH_2Cl_2/TFE	0.25	90	65

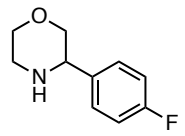
[a]The reaction was carried out in 0.2 mmol scale in 0.05 mM concentration at rt.
[b]Conv (conversion) and yield were measured from ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as an internal standard.
[c]the lowest flow rate of our flow reactor.

General procedure

To a solution of the amino tributylstannane (SnAP reagent 0.50 mmol, 1.00 equiv) in CH_2Cl_2 (1.00 mL) was added the corresponding aldehyde (0.50 mmol, 1.00 equiv) and MS 4A (ca. 100 mg) at rt. The reaction mixture was stirred at rt for 2–12 h (depending on the aldehyde) and filtered through a short layer of Celite (CH_2Cl_2 rinse). The filtrate was concentrated under reduced pressure to afford the pure imine.

The photoredox catalyst **1** (14.0 mg, 12.5 μmol, 2.50 mol %) was added to a solution of imine in a 1:1 mixture of MeCN/TFE (10.0 mL, 0.05 mM) at rt under ambient atmosphere and then sonicated or stirred to homogenize the reaction mixture before injecting into the photo-flow reactor with a given flow rate. The resulting mixture was concentrated *in vacuo* and purified with column chromatography with appropriate eluents with 0.1% NEt_3 v/v.

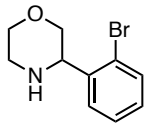
Substrate scope



5a

3-(4-Fluorophenyl)morpholine 5a: Prepared according to the general procedure with SnAP M (182 mg, 0.50 mmol, 1.00 equiv) and 4-fluorobenzaldehyde (62.2 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.20 mL/min. The desired product was obtained by flash column chromatography (50% EtOAc/CH_2Cl_2) as a yellowish oil (43 mg, 46%).

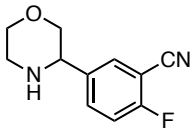
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 2H), 7.04 – 6.96 (m, 2H), 3.93 – 3.83 (m, 2H), 3.78 (dd, *J* = 11.1, 3.2 Hz, 1H), 3.65 (td, *J* = 11.3, 2.7 Hz, 1H), 3.36 (dd, *J* = 11.2, 10.1 Hz, 1H), 3.10 (td, *J* = 11.6, 3.3 Hz, 1H), 3.01 – 2.95 (m, 1H), 2.75 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5 (d, $^1J_{CF}$ = 250 Hz), 136.0 (d, $^4J_{CF}$ = 3.0 Hz), 128.9 (d, $^3J_{CF}$ = 8.1 Hz), 115.5 (d, $^2J_{CF}$ = 21.2 Hz), 73.5, 73.5, 67.1, 59.8, 46.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ –114.4;
The spectroscopic characteristics were identical to the previous report[3]



5b

3-(2-Bromophenyl)morpholine 5b: Prepared according to the general procedure with SnAP M (182 mg, 0.50 mmol, 1.00 equiv) and 2-bromobenzaldehyde (93.5 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.20 mL/min. The desired product was obtained by flash column chromatography (20% EtOAc/CH_2Cl_2 to 50% EtOAc/CH_2Cl_2) as a yellowish oil (69 mg, 57%).

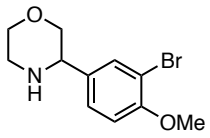
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.52 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.29 (td, *J* = 7.6, 1.3 Hz, 1H), 7.11 (ddd, *J* = 7.9, 7.3, 1.8 Hz, 1H), 4.34 (dd, *J* = 9.7, 3.1 Hz, 1H), 3.95 (dd, *J* = 11.0, 3.1 Hz, 1H), 3.90 – 3.83 (m, 1H), 3.65 (td, *J* = 11.2, 2.6 Hz, 1H), 3.27 (dd, *J* = 11.0, 9.6 Hz, 1H), 3.15 (td, *J* = 11.5, 3.3 Hz, 1H), 3.03 – 2.96 (m, 1H), 2.36 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 132.9, 129.1, 128.8, 127.8, 123.6, 71.8, 67.2, 59.1, 46.5. ESI-HRMS calcd for $C_{10}H_{12}BrNO$ $[M+H]^+$ = 244.0155 and 242.0175, found 244.0158 and 242.0178. IR (thin film): ν 2957, 2911, 2850, 1604, 1509, 1490, 1473, 1456, 1223, 110, 833 cm^{-1}.



5c

2-Fluoro-5-(morpholin-3-yl)benzonitrile 5c: Prepared according to the general procedure with SnAP M (182 mg, 0.50 mmol, 1.00 equiv) and 2-fluoro-5-formylbenzonitrile (74.7 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.20 mL/min. The desired product was obtained by flash column chromatography (20% EtOAc/CH_2Cl_2 to 50% EtOAc/CH_2Cl_2) as a yellowish oil (50 mg, 48%).

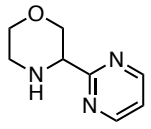
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 6.1, 2.3 Hz, 1H), 7.66 – 7.59 (m, 1H), 7.16 (t, *J* = 8.7 Hz, 1H), 3.93 (dd, *J* = 10.0, 3.3 Hz, 1H), 3.89 – 3.82 (m, 1H), 3.75 (dd, *J* = 11.1, 3.2 Hz, 1H), 3.62 (td, *J* = 11.2, 2.7 Hz, 1H), 3.28 (dd, *J* = 11.1, 10.0 Hz, 1H), 3.10 (td, *J* = 11.5, 3.3 Hz, 1H), 2.99 (dt, *J* = 11.8, 2.0 Hz, 1H), 2.23 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6 (d, $^1J_{CF}$ = 260 Hz), 137.9 (d, $^4J_{CF}$ = 3 Hz), 134.1 (d, $^3J_{CF}$ = 7 Hz), 132.2, 116.6 (d, $^2J_{CF}$ = 20 Hz), 113.9, 101.6 (d, $^3J_{CF}$ = 15 Hz), 73.3, 73.3, 67.2, 59.0, 46.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ –108.0. ESI-HRMS calcd for $C_{11}H_{12}FN_2O$ $[M+H]^+$ = 207.0928, found 207.0928; IR (thin film): ν 3320, 2957, 2913, 2852, 2236, 1674, 1612, 1498, 1451, 1332, 1267, 1252, 1106, 834, 730 cm^{-1}.



5d

3-(3-Bromo-4-methoxyphenyl)morpholine 5d: Prepared according to the general procedure with SnAP M (182 mg, 0.50 mmol, 1.00 equiv) and 3-bromo-4-methoxybenzaldehyde (107 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.20 mL/min. The desired product was obtained by flash column chromatography (20% EtOAc/CH_2Cl_2 to 50% EtOAc/CH_2Cl_2) as a yellowish solid (65 mg, 48%).

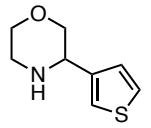
m.p.: 166–168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.58 (m, 1H), 7.29 – 7.25 (m, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 3.87 (s, 3H), 3.86 – 3.81 (m, 2H), 3.62 (td, *J* = 11.2, 2.7 Hz, 1H), 3.32 (dd, *J* = 11.0, 10.0 Hz, 1H), 3.10 (td, *J* = 11.5, 3.3 Hz, 1H), 3.00 – 2.95 (m, 1H), 1.89 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.5, 134.4, 132.1, 127.3, 111.9, 111.8, 73.7, 67.3, 59.5, 56.4, 46.6. ESI-HRMS calcd for $C_{11}H_{15}BrNO_2$ $[M+H]^+$ = 272.0281 and 274.0261, found 272.0280 and 274.0261. IR (thin film): ν 3318, 2955, 2905, 2843, 1603, 1498, 1453, 1441, 1329, 1288, 1256, 1104, 1052, 1019, 812, 676, 613 cm^{-1}.



5e

3-(Pyrimidin-2-yl)morpholine 5e: Prepared according to the general procedure with SnAP M (182 mg, 0.50 mmol, 1.00 equiv) and pyrimidine-2-carboxaldehyde (54.3 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.20 mL/min. The desired product was obtained by flash column chromatography (CH_2Cl_2 to 7% MeOH/CH_2Cl_2) as a yellowish oil (32 mg, 39%).

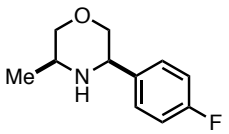
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 4.9 Hz, 2H), 7.21 (td, *J* = 4.9, 0.6 Hz, 1H), 4.34 (dd, *J* = 11.2, 3.4 Hz, 1H), 4.27 (dd, *J* = 8.8, 3.4 Hz, 1H), 3.92 (dt, *J* = 11.4, 3.1 Hz, 1H), 3.79 – 3.63 (m, 2H), 3.17 (dd, *J* = 6.8, 3.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 157.2, 119.8, 71.0, 67.3, 59.8, 45.3; ESI-HRMS calcd for $C_{17}H_{25}N_4O_2$ $[M+H]^+$ = 166.0975, found 166.0974. IR (thin film): ν 2959, 2922, 2856, 1653, 1567, 1423, 1104, cm^{-1}.



5f

3-(Thiophen-3-yl)morpholine 5f: Prepared according to the general procedure with SnAP M (182 mg, 0.50 mmol, 1.00 equiv) and thiophen-3-carboxaldehyde (56.5 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.15 mL/min. The desired product was obtained by flash column chromatography (20% EtOAc/CH_2Cl_2 to 50% EtOAc/CH_2Cl_2) as a yellowish oil (28 mg, 33%).

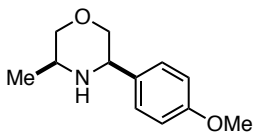
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.24 – 7.20 (m, 1H), 7.06 (dd, *J* = 5.0, 1.3 Hz, 1H), 4.04 (dd, *J* = 9.9, 3.2 Hz, 1H), 3.92 – 3.81 (m, 2H), 3.62 (td, *J* = 11.2, 2.7 Hz, 1H), 3.40 (dd, *J* = 11.1, 10.0 Hz, 1H), 3.09 (td, *J* = 12.0, 3.3 Hz, 1H), 3.01 – 2.93 (m, 1H), 1.92 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 126.4, 125.9, 121.4, 73.2, 67.4, 56.3, 46.6.
The spectroscopic characteristics were identical to the previous report[4]



6a

***cis*-3-(4-Fluorophenyl)-5-methylmorpholine 5a:** Prepared according to the general procedure with SnAP 3-M M (189 mg, 0.50 mmol, 1.00 equiv) and 4-fluorobenzaldehyde (62.2 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (30% EtOAc/hexanes) as a yellowish oil (69 mg, 57%).

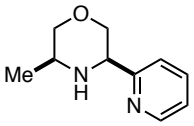
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 2H), 7.04 – 6.96 (m, 2H), 3.96 (dd, *J* = 10.3, 3.2 Hz, 1H), 3.81 – 3.73 (m, 2H), 3.24 (dd, *J* = 11.1, 10.2 Hz, 1H), 3.19 – 3.05 (m, 2H), 1.96 (br s, 1H), 1.02 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4 (d, $^1J_{CF}$ = 300 Hz), 136.3, 128.8 (d, $^3J_{CF}$ = 10 Hz), 115.4 (d, $^2J_{CF}$ = 26 Hz), 73.2, 73.1, 73.1, 60.1, 51.0, 17.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ –114.8. ESI-HRMS calcd for $C_{11}H_{15}FNO_2$ $[M+H]^+$ = 196.1132, found 196.1135. IR (thin film): ν 3303, 3052, 2963, 2846, 1605, 1509, 1454, 1378, 1327, 1224, 1106, 1047, 974, 927, 888, 834, 790 cm^{-1}.



6b

***cis*-3-(4-Methoxyphenyl)-5-methylmorpholine 6b:** Prepared according to the general procedure with SnAP 3-M M (189 mg, 0.50 mmol, 1.00 equiv) and 4-methoxybenzaldehyde (68.1 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (30% EtOAc/hexanes) as a yellowish oil (52 mg, 50%).

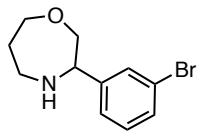
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 2H), 6.88 – 6.83 (m, 2H), 3.92 (dd, *J* = 10.3, 3.2 Hz, 1H), 3.78 (s, 3H), 3.78 (d, *J* = 2.3 Hz, 1H), 3.75 (d, *J* = 2.7 Hz, 1H), 3.27 (dd, *J* = 11.0, 10.3 Hz, 1H), 3.18 – 3.04 (m, 2H), 1.90 (br s, 1H), 1.02 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 132.7, 128.4, 113.9, 73.2, 60.2, 55.3, 51.1, 17.9. ESI-HRMS calcd for $C_{12}H_{18}NO_2$ $[M+H]^+$ = 208.1332, found 208.1335. IR (thin film): ν 3304, 2996, 2959, 2840, 1611, 1584, 1461 1412, 1250, 1159, 774, 727 cm^{-1}.



6c

***cis*-3-(Pyridine-2-yl)-5-methylmorpholine 5c:** Prepared according to the general procedure with SnAP 3-M M (189 mg, 0.50 mmol, 1.00 equiv) and picolinaldehyde (54.0 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (50% EtOAc/hexanes to 70% EtOAc/hexanes) as a yellowish oil (45 mg, 51%).

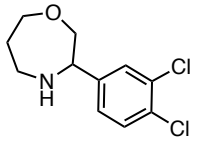
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1H), 7.61 (td, *J* = 7.7, 1.8 Hz, 1H), 7.29 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.14 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 4.10 (dd, *J* = 10.4, 3.3 Hz, 1H), 3.98 (ddd, *J* = 10.9, 3.4, 0.6 Hz, 1H), 3.82 – 3.75 (m, 1H), 3.33 (t, *J* = 10.7 Hz, 1H), 3.15 – 3.04 (m, 2H), 2.15 (br s, 1H), 1.02 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 149.4, 136.7, 122.6, 121.7, 73.4, 71.8, 60.8, 50.4, 17.7. ESI-HRMS calcd for $C_{10}H_{15}N_2O$ $[M+H]^+$ = 179.1179, found 179.1181; IR (thin film): ν 3299, 3055, 2961, 2845, 1591, 1571, 1508, 1472, 1456, 1326, 1100, 773, 749 cm^{-1}.



9a

3-(2-Bromophenyl)-1,4-oxazepane 9a: Prepared according to the general procedure with SnAP OA (189 mg, 0.50 mmol, 1.00 equiv) and 3-bromobenzaldehyde (95.2 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.20 mL/min. The desired product was obtained by flash column chromatography (20% EtOAc/CH_2Cl_2 to 50% EtOAc/CH_2Cl_2) as a yellowish oil (65 mg, 51%).

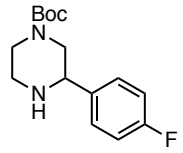
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (t, *J* = 1.8 Hz, 1H), 7.40 – 7.36 (m, 1H), 7.30 – 7.26 (m, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 4.00 – 3.87 (m, 3H), 3.86 – 3.78 (m, 1H), 3.50 (td, *J* = 11.2, 3.0 Hz, 1H), 3.20 (dt, *J* = 13.5, 4.9 Hz, 1H), 3.04 – 2.95 (m, 2H), 2.07 – 1.93 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 130.8, 130.4, 130.2, 126.1, 122.8, 77.8, 70.0, 65.8, 46.1, 32.3.
The spectroscopic characteristics were identical to the previous report[5]



9b

3-(3,4-Dichlorophenyl)-1,4-oxazepane 9a: Prepared according to the general procedure with SnAP OA (189 mg, 0.50 mmol, 1.00 equiv) and 3,4-dichlorobenzaldehyde (87.7 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.20 mL/min *except a 1:1 mixture of CH_2Cl_2/TFE was used for the reaction solvent*. The desired product was obtained by flash column chromatography (20% EtOAc/CH_2Cl_2 to 50% EtOAc/CH_2Cl_2) as an off-white solid (54 mg, 44%).

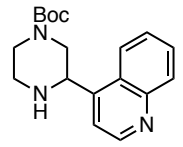
m.p.: decomposed >180 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 2.0 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.19 (dd, *J* = 8.3, 2.1 Hz, 1H), 3.99 – 3.85 (m, 3H), 3.80 (m, 1H), 3.46 (dd, *J* = 12.4, 9.2 Hz, 1H), 3.18 (dt, *J* = 13.4, 4.9 Hz, 1H), 2.99 (m, 1H), 2.42 (br s, 1H), 2.04 – 1.93 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 132.7, 131.5, 130.6, 129.3, 126.7, 77.8, 70.2, 65.2, 46.0, 32.6. ESI-HRMS calcd for $C_{11}H_{12}Cl_2NO$ $[M+H]^+$ = 246.0447 and 248.0417, found 246.0449 and 248.0421. IR (thin film): ν 3321, 3090, 3059, 2939, 2853, 1464, 1394, 1335, 1132, 1029, 822, 673 cm^{-1}.



7a

***tert*-Butyl 3-(4-fluorophenyl)piperazine-1-carboxylate 7a:** Prepared according to the general procedure with SnAP Pip (232 mg, 0.50 mmol, 1.00 equiv) and 4-fluorobenzaldehyde (62.2 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (20% EtOAc/CH_2Cl_2 to 50% EtOAc/CH_2Cl_2) as an off-white solid (77 mg, 55%).

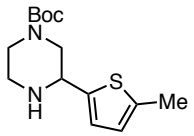
m.p.: 98–102 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 8.6, 5.5 Hz, 2H), 7.05 (t, *J* = 8.7 Hz, 2H), 4.06 (br s, 2H), 3.72 (dd, *J* = 10.7, 3.1 Hz, 1H), 3.13 – 3.04 (m, 1H), 2.90 (dd, *J* = 12.9, 10.3 Hz, 2H), 2.74 (br s, 1H), 1.49 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4 (d, $^1J_{CF}$ = 240 Hz), 154.80, 137.4 (d, $^4J_{CF}$ = 3 Hz), 128.7 (d, $^3J_{CF}$ = 8 Hz), 115.4 (d, $^2J_{CF}$ = 21 Hz), 79.87, 59.6, 54.3, 51.5, 50.2, 46.1, 44.2, 43.8, 28.5. ^{19}F NMR (377 MHz, $CDCl_3$) δ –114.60. ESI-HRMS calcd for $C_{15}H_{22}FN_2O_2$ $[M+H]^+$ = 281.1660, found 281.1659. IR (thin film): ν 3320, 3004, 2976, 2931, 2857, 1693, 1605, 1510, 1477, 1454, 1418, 1366, 1267, 1247, 1227, 1124, 836, 770 cm^{-1}.



7b

***tert*-Butyl 3-(quinolin-4-nyl)piperazine-1-carboxylate 7b:** Prepared according to the general procedure with SnAP Pip (232 mg, 0.50 mmol, 1.00 equiv) and quinoline-4-carboxaldehyde (79.1 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (1:5:4 MeOH/EtOAc/hexanes) as a yellowish oil (74 mg, 47%).

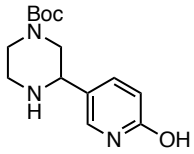
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (d, *J* = 4.5 Hz, 1H), 8.19 (d, *J* = 8.5 Hz, 1H), 8.13 (d, *J* = 8.3 Hz, 1H), 7.71 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.65 (dd, *J* = 4.5, 0.8 Hz, 1H), 7.59 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 4.48 (dd, *J* = 10.3, 2.8 Hz, 1H), 4.35 (br s, 1H), 4.14 (br s, 1H), 3.18 (d, *J* = 8.4 Hz, 1H), 3.07 – 2.94 (m, 2H), 2.74 (br s, 1H), 2.18 (br s, 1H), 1.50 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 150.6, 148.4, 146.7, 130.6, 129.30, 126.9, 126.2, 122.7, 118.2, 80.2, 77.5, 55.8, 51.4, 46.3, 44.0, 28.6, 28.5. ESI-HRMS calcd for $C_{18}H_{24}N_3O_2$ $[M+H]^+$ = 314.1863, found 314.1864. IR (thin film): ν 3315, 3003, 2975, 2930, 1693, 1602, 1591, 1509, 1476, 1456, 1416, 1365, 1273, 1250, 1163, 858, 758 cm^{-1}.



7c

***tert*-Butyl 3-(5-methylthiophen-2-nyl)piperazine-1-carboxylate 7c:** Prepared according to the general procedure with SnAP Pip (232 mg, 0.50 mmol, 1.00 equiv) and 5-methylthiophene-2-carboxaldehyde (63.7 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (30% EtOAc/CH_2Cl_2) as a yellowish oil (51 mg, 36%).

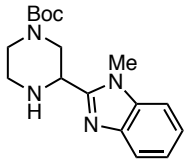
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77 (d, *J* = 3.4 Hz, 1H), 6.59 (dd, *J* = 3.5, 1.3 Hz, 1H), 3.97 (br s, 1H), 3.93 (dd, *J* = 10.1, 3.2 Hz, 1H), 3.06 – 2.98 (m, 1H), 2.98 – 2.89 (m, 1H), 2.84 (td, *J* = 11.1, 2.7 Hz, 2H), 2.44 (d, *J* = 1.1 Hz, 3H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 142.5, 138.9, 124.7, 124.0, 79.9, 55.8, 52.3, 45.8, 44.9, 28.6, 15.4. ESI-HRMS calcd for $C_{14}H_{23}N_2O_2S$ $[M+H]^+$ = 283.1475, found 283.1476. IR (thin film): ν 3326, 3005, 2975, 2921, 2859, 1692, 1475, 1455, 1418, 1365, 1268, 1248, 1168, 1124, 861, 799, 765 cm^{-1}.



7d

***tert*-Butyl 3-(6-hydroxypyridin-3-nyl)piperazine-1-carboxylate 7d:** Prepared according to the general procedure with SnAP Pip (232 mg, 0.50 mmol, 1.00 equiv) and 6-hydroxynicotinaldehyde (61.4 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (5% MeOH/EtOAc) as a yellowish oil (77 mg, 55%).

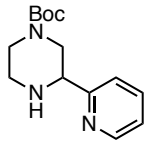
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 9.4, 2.5 Hz, 1H), 7.42 (d, *J* = 2.5 Hz, 1H), 6.56 (d, *J* = 9.4 Hz, 1H), 3.99 (br s, 2H), 3.49 (dd, *J* = 10.5, 3.1 Hz, 1H), 3.02 (d, *J* = 9.1 Hz, 1H), 2.83 (d, *J* = 10.7 Hz, 2H), 2.63 (br s, 1H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 154.8, 141.4, 132.7, 120.7, 120.4, 80.1, 56.6, 50.6, 45.9, 43.8, 28.6. ESI-HRMS calcd for $C_{14}H_{22}N_3O_3$ $[M+H]^+$ = 280.1656, found 280.1661. IR (thin film): ν 3282, 3126, 2975, 2930, 2900, 1683, 1662, 1619, 1548, 1476, 1455, 1422, 1366, 1269, 1250, 1171, 1125, 863, 835, 769, 735 cm^{-1}.



7e

***tert*-Butyl 3-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)piperazine-1-carboxylate 7d:** Prepared according to the general procedure with SnAP Pip (232 mg, 0.50 mmol, 1.00 equiv) and 1-methyl-2-formylbenzimidazole (80.1 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (5% MeOH/CH_2Cl_2) as a yellowish solid (77 mg, 48%).

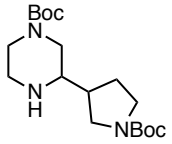
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.69 (m, 1H), 7.40 – 7.20 (m, 4H), 4.32 (d, *J* = 13.3 Hz, 1H), 4.08 (dd, *J* = 10.7, 3.3 Hz, 2H), 3.85 (br s, 3H), 3.24 – 2.98 (m, 2H), 2.92 (dd, *J* = 13.4, 10.9 Hz, 2H), 1.92 (br s, 2H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 152.8, 142.2, 135.8, 122.8, 122.2, 119.7, 109.3, 80.1, 77.4, 77.2, 77.0, 76.7, 52.32, 48.4, 45.4 30.0, 28.5.
The spectroscopic characteristics were identical to the previous report[4]



7f

***tert*-Butyl 3-(pyridin-2-nyl)piperazine-1-carboxylate 7f:** Prepared according to the general procedure with SnAP Pip (232 mg, 0.50 mmol, 1.00 equiv) and picolinaldehyde (54.0 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (5% MeOH/EtOAc) as a yellowish oil (56 mg, 43%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.8 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.30 (d, *J* = 6.8 Hz, 1H), 7.18 – 7.11 (m, 1H), 4.16 (br s, 1H), 3.97 (br s, 1H), 3.82 (dd, *J* = 10.4, 3.3 Hz, 1H), 3.05 (d, *J* = 6.5 Hz, 1H), 2.87 (t, *J* = 7.1 Hz, 3H), 2.21 (br s, 1H), 1.43 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 149.4, 136.7, 122.6, 121.5, 79.8, 60.2, 49.5, 45.4, 43.8, 28.5.
The spectroscopic characteristics were identical to the previous report[4]

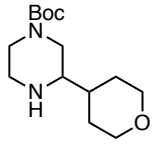


7g

***tert*-Butyl 3-(1-(*tert*-butoxycarbonyl)pyrrolidin-3-yl)piperazine-1-carboxylate 7g:** Prepared according to the general procedure with SnAP PIP (232 mg, 0.50 mmol, 1.00 equiv) and *tert*-butyl 3-formylpyrrolidine-1-carboxylate (100 mg, 0.50 mmol, 1.00 equiv) with a flow

rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (5% MeOH/EtOAc) as a yellowish oil (30 mg, 17%).

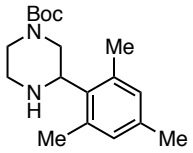
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.89 (d, *J* = 13.6 Hz, 2H), 3.66 – 3.43 (m, 2H), 3.31 – 3.19 (m, 1H), 3.07 – 2.95 (m, 2H), 2.95 – 2.81 (m, 1H), 2.80 – 2.69 (m, 1H), 2.66 – 2.46 (m, 2H), 2.18 – 1.99 (m, 2H), 1.60 (m, 1H), 1.46 (s, 18H), 1.38 – 1.19 (m, 2 H), 0.97 – 0.79 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 154.6, 80.0, 79.4, 58.3, 48.5, 48.2, 45.9, 45.6, 44.8, 41.5, 29.8, 29.5, 29.1, 28.7, 28.5, 13.8. ESI-HRMS calcd for $C_{18}H_{34}N_3O_4$ $[M+H]^+$ = 356.2544, found 356.2546. IR (thin film): ν 3444, 3004, 2959, 2929, 1675, 1478, 1455, 1416, 1365, 1251, 1171, 1133, 874, 770 cm^{-1}.



7h

***tert*-Butyl 3-(tetrahydro-2*H*-pyran)pyrrolidin-4-yl)piperazine-1-carboxylate 7h:** Prepared according to the general procedure with SnAP PIP (232 mg, 0.50 mmol, 1.00 equiv) and tetrahydro-2*H*-pyrancarboxaldehyde (57.1 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (EtOAc to 5% MeOH/EtOAc) as a yellowish oil (38 mg, 28%).

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 4.02 – 3.93 (m, 2H), 3.88 (d, *J* = 13.0 Hz, 1H), 3.34 (m, 2H), 2.97 (dt, *J* = 11.7, 2.8 Hz, 1H), 2.85 (m, 1H), 2.70 (td, *J* = 11.5, 3.2 Hz, 1H), 2.54 (br s, 1H), 2.38 (dt, *J* = 5.9, 2.9 Hz, 1H), 1.70 – 1.56 (m, 2H), 1.55 – 1.47 (m, 1H), 1.44 (s, 9H), 1.41 – 1.26 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 79.9, 68.0, 67.9, 59.3, 47.4, 46.8, 45.5, 44.7, 44.0, 38.1, 29.2, 29.2, 28.5. ESI-HRMS calcd for $C_{14}H_{27}N_2O_3$ $[M+H]^+$ = 271.2016, found 271.2015. IR (thin film): ν 2932, 2844, 1693, 1455, 1422, 1365, 1250, 1172, 1137, 1119, 1094, 861, 770 cm^{-1}.

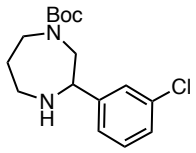


7i

***tert*-Butyl 3-mesitylpiperazine-1-carboxylate 7i:** Prepared according to the general procedure with SnAP Pip (232 mg, 0.50 mmol, 1.00 equiv) and mesitaldehyde (74.4 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (20% EtOAc/hexanes) as a yellowish oil (44 mg, 32%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (s, 2H), 4.10 (dd, *J* = 11.0, 3.3 Hz, 1H), 4.06 (br s, 1H), 3.96 – 3.77 (m, 1H), 3.22 – 3.04 (m, 2H), 2.99 – 2.78 (m, 2H), 2.51 (s, 6H), 2.25 (s, 3H), 1.65 (br s, 1H), 1.47 (s, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 137.4, 136.8, 133.8, 130.4, 79.6, 58.1, 47.4, 47.1, 43.7, 28.6, 21.6, 20.8. ESI-HRMS calcd for $C_{18}H_{29}N_2O_2$ $[M+H]^+$ = 305.2224, found

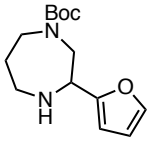
305.2225. IR (thin film): ν 3324, 3005, 2973, 2925, 1696, 1611, 1476, 1452, 1416, 1365, 1266, 1251, 1173, 851, 768 cm^{-1}.



10a

***tert*-Butyl 3-(3-chlorophenyl)-1,4-diazepane-1-carboxylate 10a:** Prepared according to the general procedure with SnAP DA (239 mg, 0.50 mmol, 1.00 equiv) and 3-chlorobenzaldehyde (70.4 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.20 mL/min. The desired product was obtained by flash column chromatography (20% EtOAc/CH_2Cl_2 to 40% EtOAc/CH_2Cl_2) as a yellowish oil (54 mg, 34%).

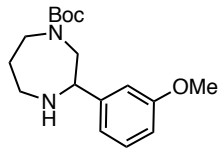
(rotamer 1:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 18.5 Hz, 2H), 7.31 – 7.20 (m, 6H), 4.06 (dd, *J* = 13.8, 3.3 Hz, 1H), 3.98 – 3.78 (m, 5H), 3.29 – 3.12 (m, 4H), 2.98 – 2.77 (m, 2H), 2.77 – 2.65 (m, 2H), 2.32 (br s, 2H), 2.11 – 1.90 (m, 3H), 1.90 – 1.80 (m, 2H), 1.49 (d, *J* = 3.7 Hz, 19H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 155.5, 144.4, 144.0, 134.6, 134.5, 130.0, 129.9, 127.8, 127.2, 127.1, 125.4, 125.1, 79.8, 79.7, 64.6, 64.5, 56.5, 56.4, 47.0, 46.7, 46.2, 45.6, 29.8, 29.8, 28.7, 28.6. ESI-HRMS calcd for $C_{16}H_{24}ClN_2O_2$ $[M+H]^+$ = 311.1521 and 313.1496, found 311.1523 and 313.1498. IR (thin film): ν 3328, 3062, 2975, 2932, 1691, 1597, 1573, 1477, 1413, 1365, 1245, 1170, 924, 784, 695 cm^{-1}.



10b

***tert*-Butyl 3-(furan-2-yl)-1,4-diazepane-1-carboxylate 10c:** Prepared according to the general procedure with SnAP DA (239 mg, 0.50 mmol, 1.00 equiv) and furan-2-carboxaldehyde (48.8 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.20 mL/min. The desired product was obtained by flash column chromatography (20% EtOAc/hexanes) as a yellowish oil (37 mg, 28%).

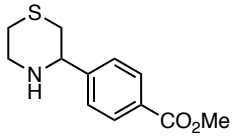
(rotamer 1:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 6.7 Hz, 2H), 6.35 – 6.26 (m, 2H), 6.20 – 6.15 (m, 2H), 4.18 (dd, *J* = 13.9, 3.7 Hz, 1H), 4.08 – 3.97 (m, 3H), 3.96 – 3.88 (m, 1H), 3.83 – 3.76 (m, 1H), 3.24 – 3.04 (m, 6H), 2.78 – 2.66 (m, 2H), 2.03 – 1.94 (m, 1H, 2NH), 1.91 – 1.84 (m, 1H), 1.82 – 1.72 (m, 2H), 1.47 (s, 9H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 155.4, 155.2, 154.8, 141.9, 110.2, 110.2, 105.7, 105.4, 79.7, 79.6, 57.5, 57.4, 53.5, 53.3, 46.6, 46.3, 46.2, 45.9, 30.3, 28.6. ESI-HRMS calcd for $C_{14}H_{23}N_2O_3$ $[M+H]^+$ = 267.1703, found 267.1702. IR (thin film): ν 3339, 2974, 2932, 1691, 1601, 1504, 1478, 1456, 1415, 1366, 1249, 1170, 884, 770, 737 cm^{-1}.



10c

***tert*-Butyl 3-(3-methoxyphenyl)-1,4-diazepane-1-carboxylate 10c:** Prepared according to the general procedure with SnAP DA (239 mg, 0.50 mmol, 1.00 equiv) and 3-chlorobenzaldehyde (68.3 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.20 mL/min. The desired product was obtained by flash column chromatography (20% EtOAc/CH_2Cl_2 to 50% EtOAc/CH_2Cl_2) as a yellowish oil (52 mg, 34%).

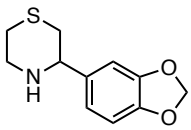
(rotamer 1:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.18 (m, 2H), 7.00 – 6.91 (m, 4H), 6.83 – 6.76 (m, 2H), 4.07 (dd, *J* = 13.9, 3.4 Hz, 1H), 3.98 – 3.80 (m, 5H), 3.79 (s, 3H) , 3.78 (s, 3H), 3.29 – 3.13 (m, 4H), 3.00 – 2.82 (m, 2H), 2.78 – 2.60 (m, 4H), 2.09 – 1.99 (m, 1H), 1.99 – 1.80 (m, 3H), 1.49 (s, 9H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 159.9, 155.7, 155.5, 143.6, 143.4, 129.7, 129.6, 119.4, 119.2, 113.5, 113.1, 112.4, 112.2, 79.7, 79.5, 65.4, 65.2, 56.5, 56.5, 55.4, 47.1, 46.9, 46.1, 45.4, 29.6, 29.5, 28.7, 28.6. ESI-HRMS calcd for $C_{17}H_{27}N_2O_3$ $[M+H]^+$ = 307.2016, found 307.2019. IR (thin film): ν 3330, 3052, 2972, 2934, 2835, 1692, 1602, 1585, 1479, 1456, 1435, 1412, 1365, 1332, 1252, 1167, 1040, 777, 701 cm^{-1}.



8a

Methyl 4-(thiomorpholin-3-yl)benzoate 8a: Prepared according to the general procedure with SnAP TM (190 mg, 0.50 mmol, 1.00 equiv) and methyl 4-formylbenzoate (82.3 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (EtOAc to 2% MeOH/EtOAc) as a yellowish oil (47 mg, 39%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.92 (m, 2H), 7.48 – 7.40 (m, 2H), 3.98 (dd, *J* = 10.6, 2.3 Hz, 1H), 3.88 (s, 3H), 3.47 – 3.40 (m, 1H), 3.14 (td, *J* = 11.9, 2.3 Hz, 1H), 2.95 – 2.85 (m, 1H), 2.85 – 2.76 (m, 1H), 2.53 – 2.39 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 148.8, 130.1, 129.7, 126.7, 62.7, 52.2, 48.9, 34.7, 27.4.
The spectroscopic characteristics were identical to the previous report.[6]

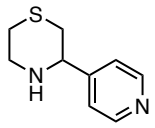


8b

3-(Benzo[*d*][1,3]dioxol-5-yl)thiomorpholine 8b: Prepared according to the general procedure with SnAP TM (190 mg, 0.50 mmol, 1.00 equiv) and piperonal (75.2 mg, 0.50

mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (EtOAc to 2% MeOH/EtOAc) as a yellowish oil (54 mg, 49%).

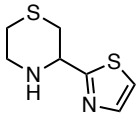
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (d, *J* = 1.7 Hz, 1H), 6.80 (ddd, *J* = 7.9, 1.7, 0.5 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 5.91 (s, 2H), 3.82 (dd, *J* = 10.6, 2.2 Hz, 1H), 3.40 (ddd, *J* = 12.0, 4.3, 1.9 Hz, 1H), 3.12 (td, *J* = 11.9, 2.3 Hz, 1H), 2.87 (ddd, *J* = 13.3, 11.7, 2.9 Hz, 1H), 2.82 – 2.74 (m, 1H), 2.46 – 2.35 (m, 2H), 2.28 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 147.0, 138.2, 119.9, 108.3, 107.1, 101.1, 62.8, 49.2, 35.0, 27.4. ESI-HRMS calcd for $C_{11}H_{14}NO_2S$ $[M+H]^+$ = 224.0740, found 224.0746. IR (thin film): ν 3301, 2904, 2817, 1502, 1485, 1440, 1247, 1038, 930, 813 cm^{-1}.



8c

3-(pyridin-4-yl)thiomorpholine 8c: Prepared according to the general procedure with SnAP TM (190 mg, 0.50 mmol, 1.00 equiv) and isopicolinaldehyde (53.5 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (7% MeOH/CH_2Cl_2) as a yellowish solid (47 mg, 52%).

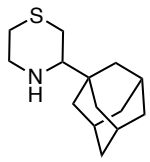
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 – 8.49 (m, 2H), 7.39 – 7.17 (m, 2H), 3.95 (dd, *J* = 10.5, 2.3 Hz, 1H), 3.54 – 3.40 (m, 1H), 3.16 (td, *J* = 11.9, 2.3 Hz, 1H), 2.89 (ddd, *J* = 13.1, 11.7, 3.0 Hz, 1H), 2.76 (dd, *J* = 13.1, 10.5 Hz, 1H), 2.47 (ddt, *J* = 16.4, 13.1, 2.4 Hz, 2H), 1.92 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.5, 150.3, 121.7, 61.7, 48.7, 34.6, 27.5.
The spectroscopic characteristics were identical to the previous report.[3–4,6]



8d

3-(Thiazol-2-yl)thiomorpholine 8c: Prepared according to the general procedure with SnAP TM (190 mg, 0.50 mmol, 1.00 equiv) and thiazol-2-carboxaldehyde (56.7 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.25 mL/min. The desired product was obtained by flash column chromatography (50% EtOAc/CH_2Cl_2 to 70% EtOAc/CH_2Cl_2) as a yellowish oil (35 mg, 37%).

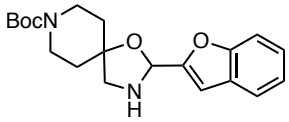
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 3.3 Hz, 1H), 7.26 (d, *J* = 3.3 Hz, 1H), 4.36 (dd, *J* = 9.6, 3.1 Hz, 1H), 3.44 (dt, *J* = 12.7, 3.3 Hz, 1H), 3.21 – 3.12 (m, 1H), 2.93 – 2.75 (m, 3H), 2.47 – 2.40 (m, 1H), 2.28 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 142.5, 118.9, 59.1, 48.0, 33.6, 27.6. ESI-HRMS calcd for $C_7H_{11}N_2S_2$ $[M+H]^+$ = 187.0358, found 187.0361. IR (thin film): ν 3270, 3075, 2908, 2835, 1670, 1499, 1456, 1416, 1310, 1290, 1189, 1134, 1017, 764, 729 cm^{-1}.



8e

3-(Adamantan-1-yl)thiomorpholine 8c: Prepared according to the general procedure with SnAP TM (190 mg, 0.50 mmol, 1.00 equiv) and adamantine-1-carboxaldehyde (82.2 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.15 mL/min. The desired product was obtained by flash column chromatography (20% EtOAc/hexanes) as a yellowish oil (16 mg, 14%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.50 (d, *J* = 12.1 Hz, 1H), 3.01 (td, *J* = 12.2, 2.4 Hz, 1H), 2.85 (t, *J* = 12.4 Hz, 1H), 2.70 – 2.56 (m, 1H), 2.56 – 2.47 (m, 1H), 2.47 – 2.40 (m, 1H), 2.39 – 2.30 (m, 1H), 2.03 – 1.96 (m, 3H), 1.76 – 1.53 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 67.8, 49.6, 38.7, 37.2, 36.3, 28.5, 27.6, 27.5. ESI-HRMS calcd for $C_{14}H_{24}NS$ $[M+H]^+$ = 238.1624, found 238.1627; IR (thin film): ν 2902, 2846, 1448, 1313, 1107, 787, 768 cm^{-1}.

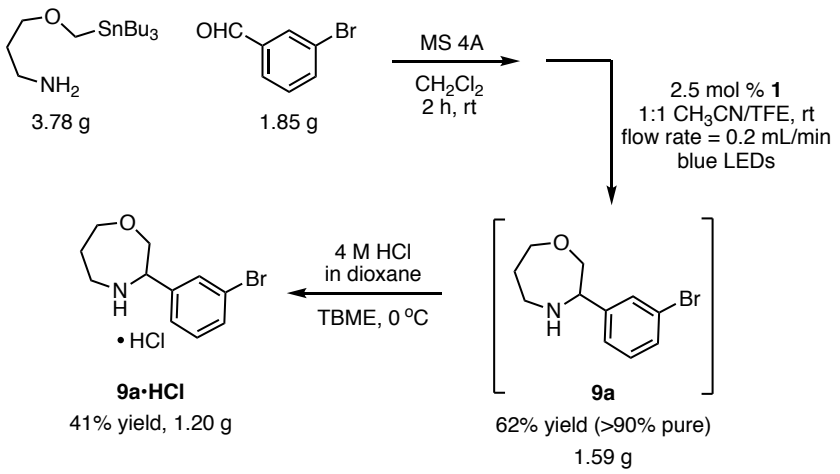


11

***tert*-Butyl 2-(benzofuran-2-yl)-1-oxa-3,8-diazaspiro[4.5]decane-8-carboxylate 11:** Prepared according to the general procedure with SnAP-2-Spiro-(4-Pip) M (267 mg, 0.50 mmol, 1.00 equiv) and benzofurane-2-carboxaldehyde (73.6 mg, 0.50 mmol, 1.00 equiv) with a flow rate of 0.15 mL/min and a 4:1 mixture of HFIP/MeCN was used for a reaction solvent instead. The cyclization product was obtained by flash column chromatography (50% EtOAc/CH_2Cl_2 to 70% EtOAc/CH_2Cl_2) as an off-white solid (87 mg, 48%).

m.p.: 140–144 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.48 – 7.40 (m, 1H), 7.32 – 7.14 (m, 2H), 6.63 (d, *J* = 11.9 Hz, 1H), 4.13 (dd, *J* = 9.3, 3.4 Hz, 1H), 3.99 (dd, *J* = 11.4, 3.7 Hz, 1H), 3.86 (ddd, *J* = 25.9, 11.5, 9.0 Hz, 1H), 3.75 – 3.25 (m, 4H), 2.99 (d, *J* = 8.1 Hz, 2H), 2.46 – 1.78 (m, 3H), 1.46 (d, *J* = 2.1 Hz, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 154.8, 154.7, 154.6, 128.1, 124.3, 122.9, 121.0, 111.3, 103.5, 103.4, 80.4, 79.5, 66.3, 66.1, 65.6, 55.3, 54.8, 53.5, 53.2, 52.1, 51.8, 51.6, 51.5, 50.8, 44.7, 44.2, 44.1, 43.7, 35.7, 35.0, 31.9, 31.2, 28.7, 28.6. ESI-HRMS calcd for $C_{20}H_{26}N_2O_4$ $[M+H]^+$ = 359.1965, found 359.1971; IR (thin film): ν 3317, 3063, 2975, 1692, 1602, 1476, 1454, 1164, 1092, 910, 883, 751 cm^{-1}.

Gram-scale synthesis of 3-(2-Bromophenyl)-1,4-oxazepane



The oxazepane was prepared according to the general procedure with SnAP OA (3.78 g, 10.0 mmol, 1.00 equiv), 3-bromobenzaldehyde (1.85 g, 10.0 mmol, 1.00 equiv), and Ir catalyst **1** (140 mg, 0.125 mmol, 2.50 mol %) in 200 mL of a 1:1 mixture of MeCN/TFE with a flow rate of 0.20 mL/min, which gives a total time of 17 h. After concentration, the crude residue was diluted with Et_2O (100 mL) and washed with 1 N HCl (3 x 50 mL). The combined aqueous layer was washed with Et_2O (2 x 50 mL) and basified with K_2CO_3 until pH ≥ 10. The heterocycle product was extracted with CH_2Cl_2 (5 x 70 mL). The organic layer was dried with anhydrous Na_2SO_4, filtered, and then concentrated *in vacuo* to give the crude oxazepane was further purified though salt formation with HCl.

The crude residue was dissolved in TBME (10 mL) and cooled in ice bath. 4 M HCl in dioxane (3 mL) was slowly dropped into the solution over 10 min. After addition, the suspension was gradually warmed to rt before volatile substances were removed *in vacuo*. The resulting residue was suspended in TBME (20 mL) and filtered over sintered glass funnel to provide **9a·HCl** salt (1.20 g, 41%) as an off-white solid.[4]

UV-Vis spectra of naphthylimine and photocatalyst 1

A 1.00 μM solution of naphthylimine of SnAP Pip in a 1:1 mixture of CH_3CN/TFE and a 10.0 μM solution of the photocatalyst **1** in the same solvent were prepared and measured UV-Vis spectra.

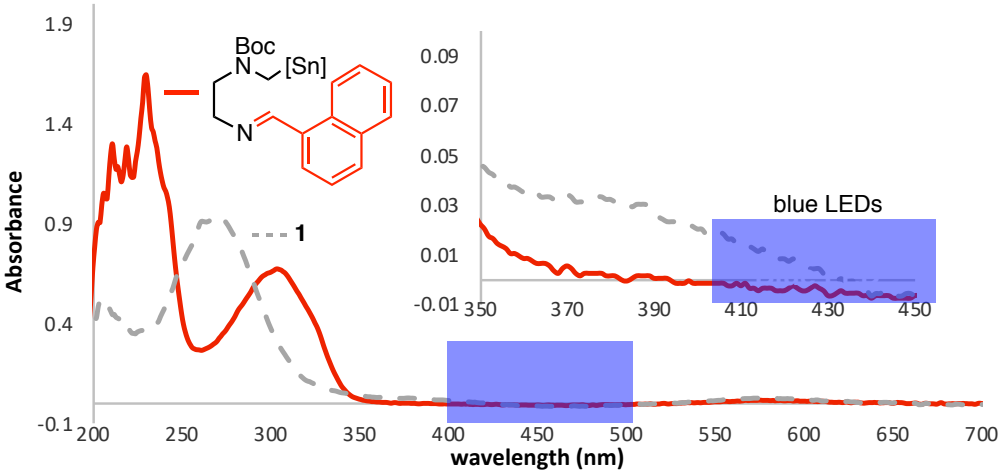
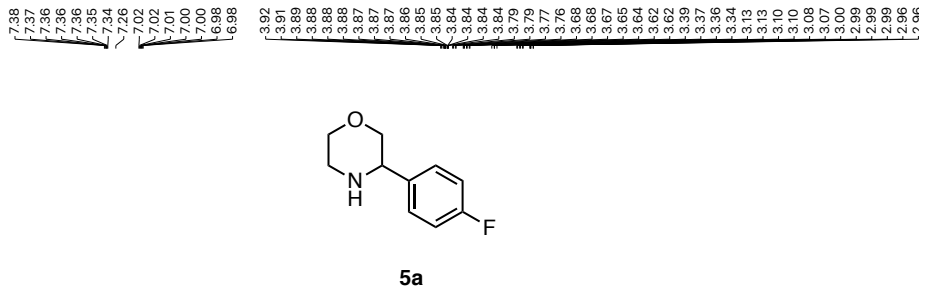


Figure S3. The UV-Vis spectra of unsuccessfully cyclized naphthylimine and the photocatalyst **1** in a 1:1 mixture of CH_3CN/TFE. The blue box showed the emission wavelength region of our blue LEDs.

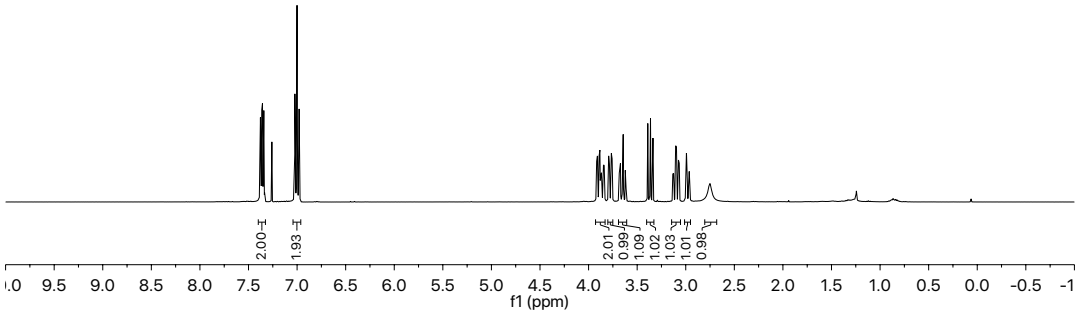
References

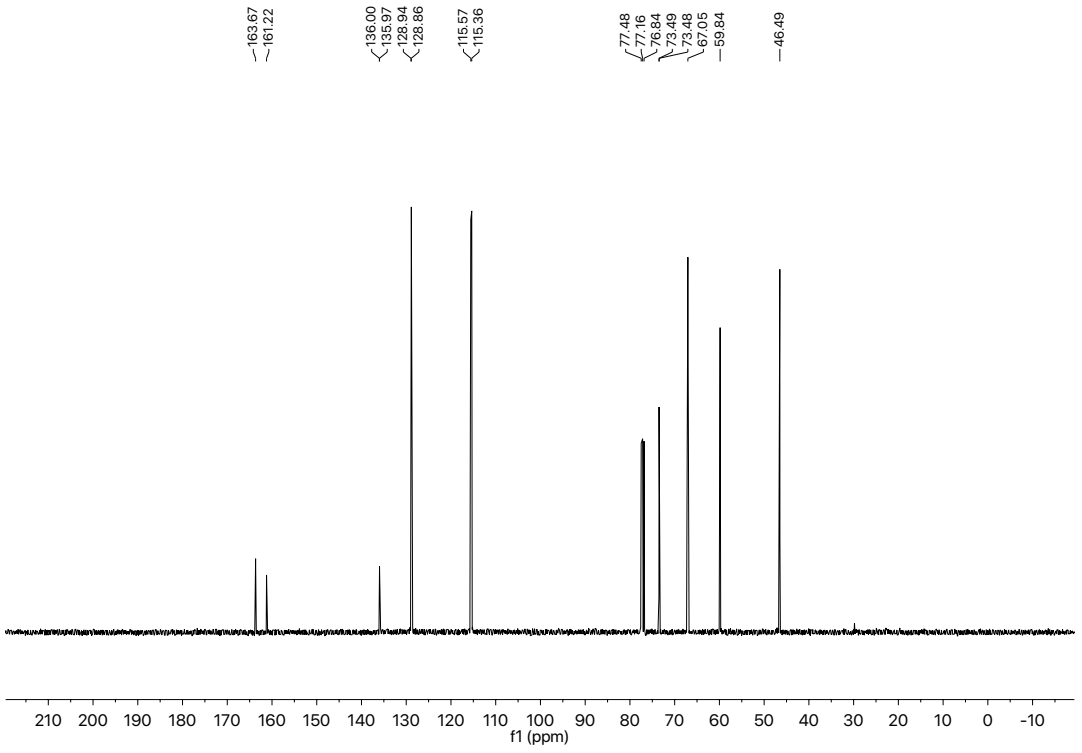
1. Singh, A.; Teegardin, K.; Kelly, M.; Prasad, K; Krishnan, S.; Weaver, J. D. *J. Organomet. Chem.* **2015**, *776*, 51–59.
2. Luo, J.; Zhang, J. *ACS Catal.* **2016**, *6*, 873–877.
3. Hsieh, S-.Y.; Bode, J. W. *ACS Cent. Sci.* **2017**, *3*, 66–72.
4. Luescher, M. U.; Bode, J. W. *Angew. Chem. Int. Ed.*. **2015**, *54*, 10884–10888.
5. Vo, C.-V.; Luescher, M. U.; Bode, J. W. *Nat. Chem.* **2014**, *6*, 310–314.
6. Vo, C.-V.; Mikutis, G.; Bode, J. W *Angew. Chem. Int. Ed.* **2013**, *52*, 1705–1708.

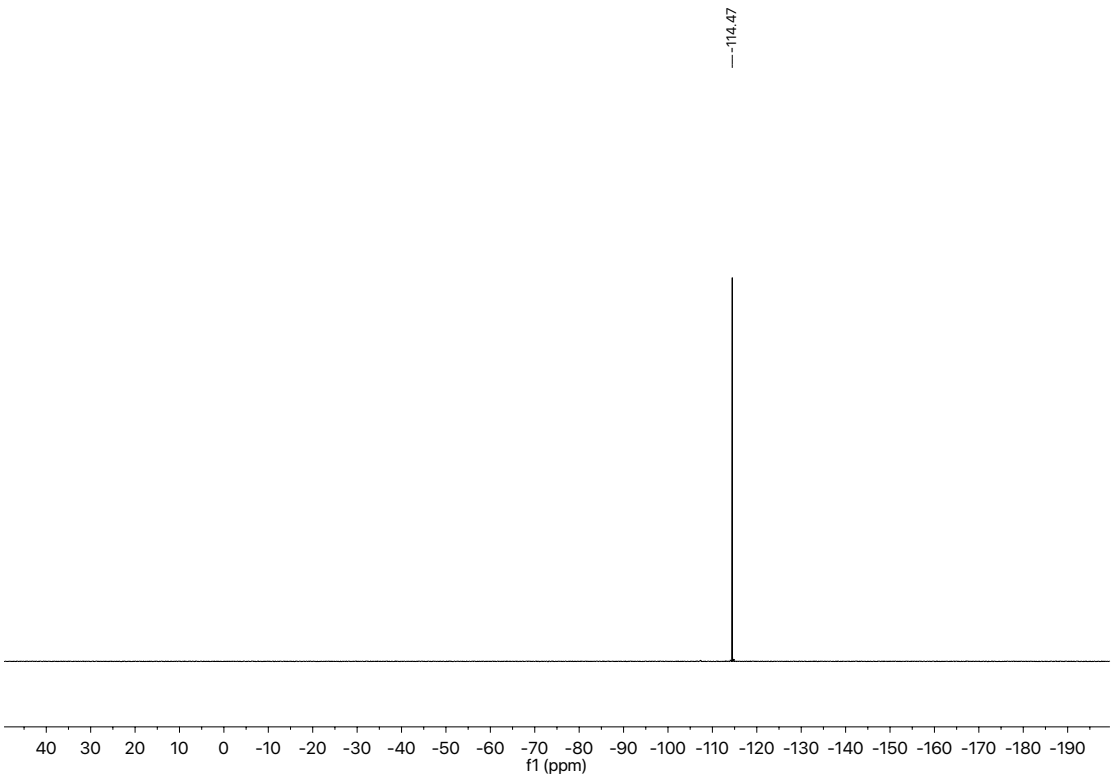
^{1}H and ^{13}C NMR Spectra

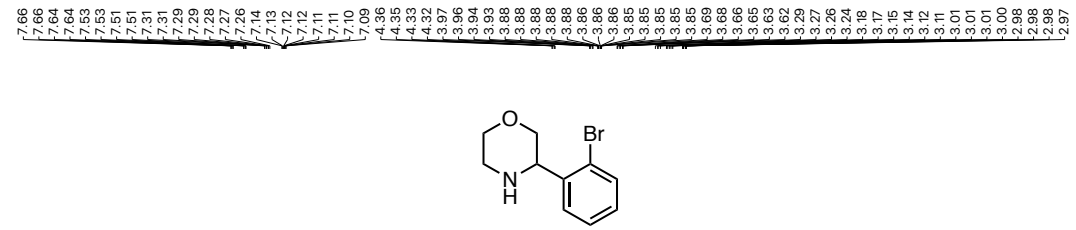


5a



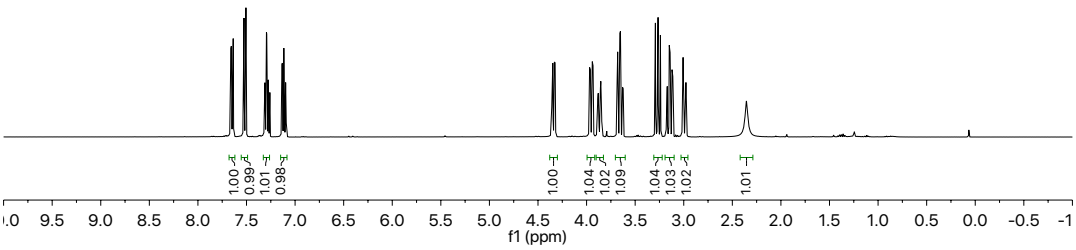


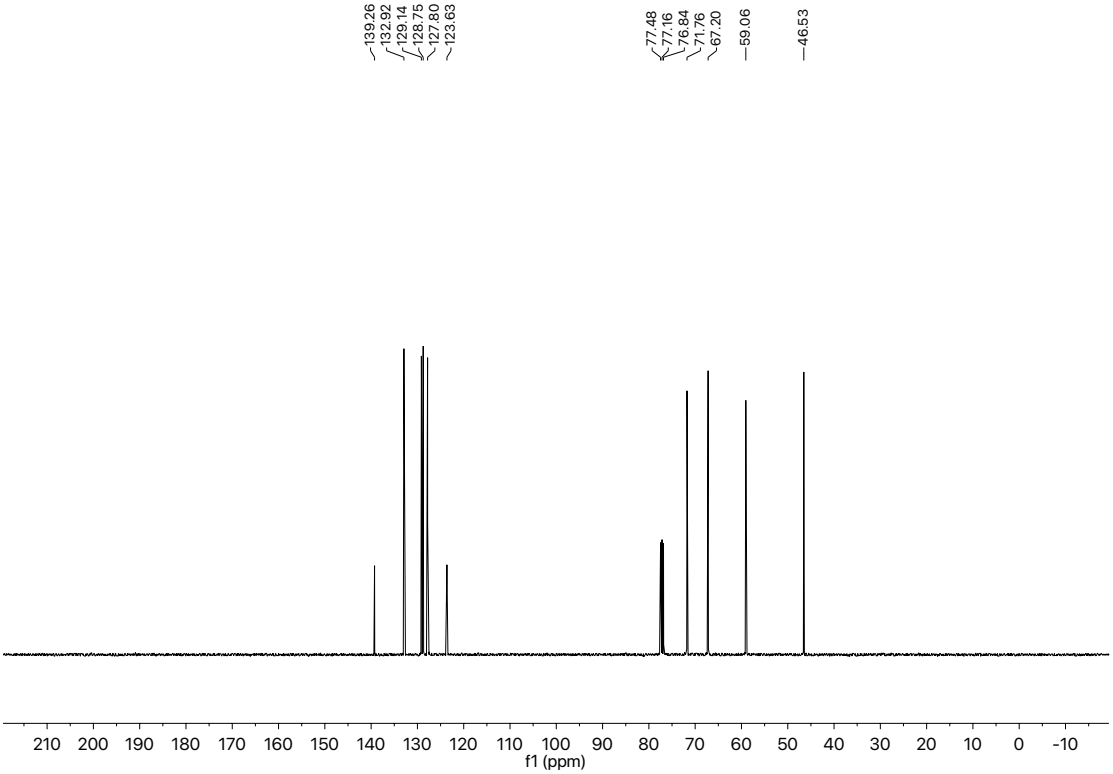

-114.47
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

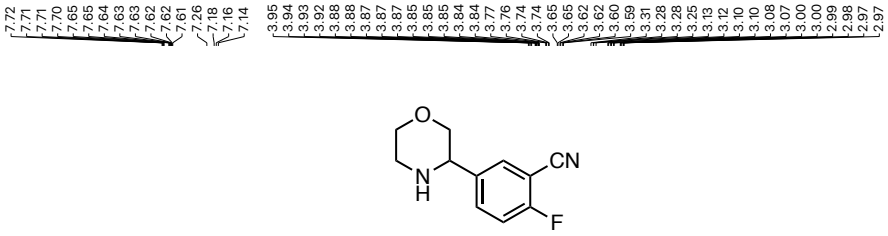

7.66
7.66
7.64
7.64
7.53
7.53
7.51
7.51
7.31
7.29
7.29
7.28
7.27
7.26
7.14
7.13
7.12
7.12
7.11
7.11
7.10
7.09
4.36
4.35
4.33
4.32
3.97
3.96
3.94
3.93
3.88
3.88
3.88
3.88
3.88
3.86
3.86
3.86
3.85
3.85
3.85
3.85
3.85
3.69
3.68
3.66
3.65
3.63
3.62
3.29
3.27
3.26
3.24
3.18
3.17
3.15
3.14
3.12
3.11
3.01
3.01
3.01
3.00
2.98
2.98
2.98
2.97

O
Br
N
H

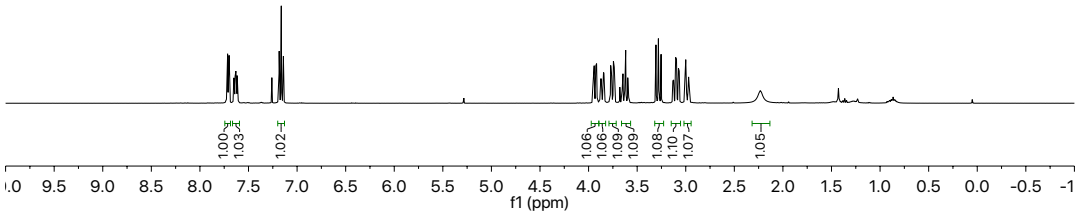
5b

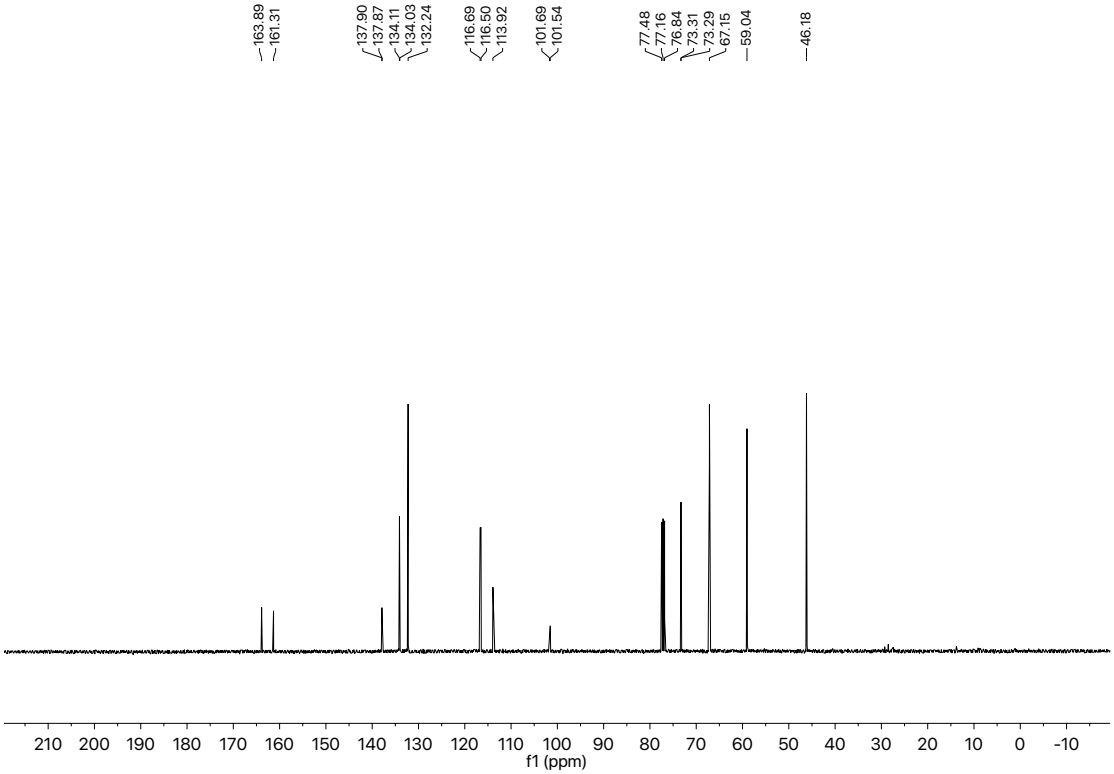

1.00
0.99
1.01
0.98
1.00
1.04
1.02
1.09
1.04
1.03
1.02
1.01
f1 (ppm)

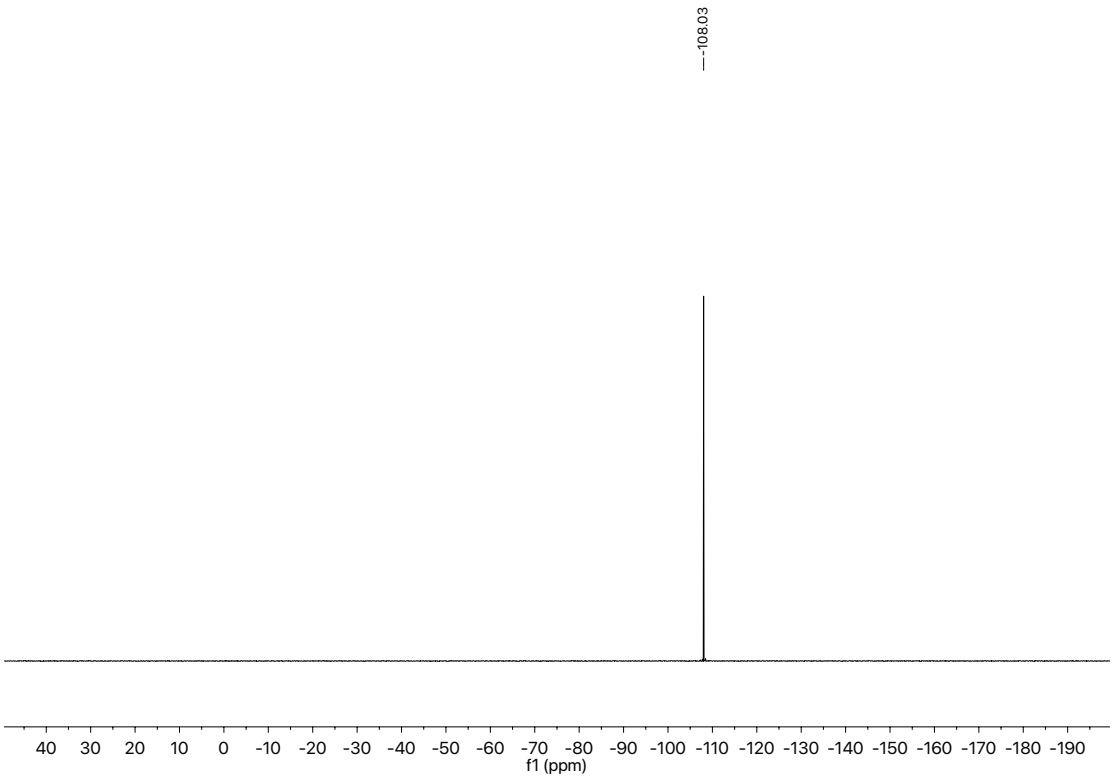

139.26
132.92
129.14
128.75
127.80
123.63
77.48
77.16
76.84
71.76
67.20
59.06
46.53
f1 (ppm)

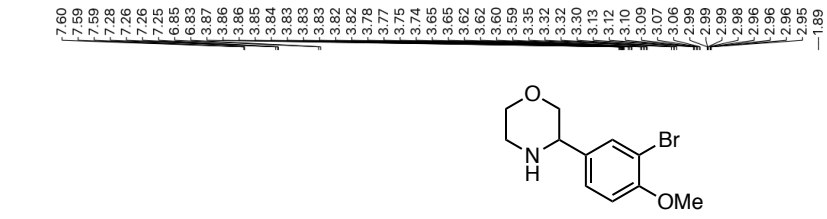

7.72
7.71
7.71
7.70
7.65
7.65
7.64
7.63
7.63
7.62
7.62
7.61
7.26
7.18
7.16
7.14
3.95
3.94
3.93
3.92
3.88
3.88
3.87
3.87
3.87
3.85
3.85
3.85
3.84
3.84
3.77
3.76
3.74
3.74
3.65
3.65
3.62
3.62
3.60
3.59
3.31
3.28
3.28
3.25
3.13
3.12
3.10
3.10
3.08
3.07
3.00
3.00
2.99
2.98
2.97
2.97
O
N
H
CN
F

5c


1.00
1.03
1.02
1.06
1.06
1.09
1.09
1.08
1.10
1.07
1.05
f1 (ppm)

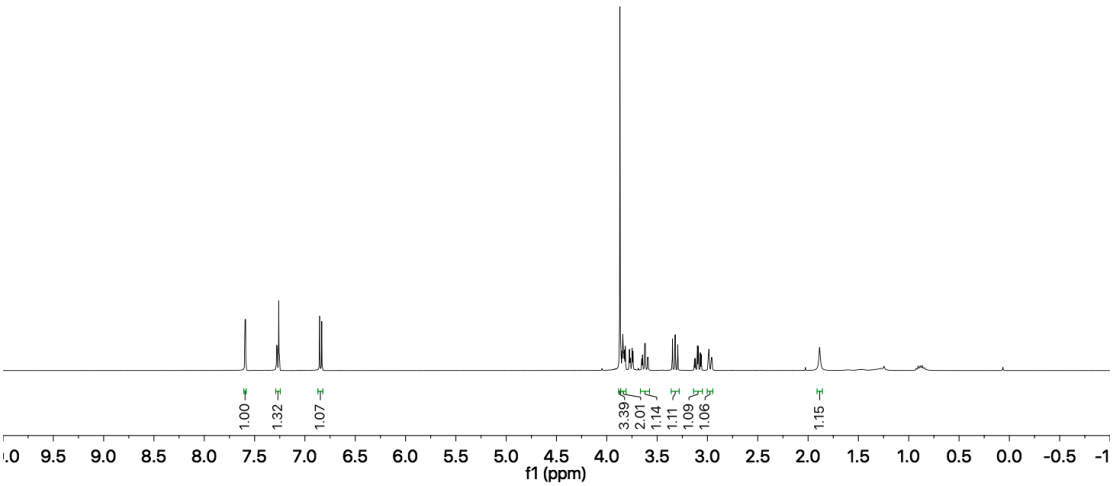

163.89
161.31
137.90
137.87
134.11
134.03
132.24
116.69
116.50
113.92
101.69
101.54
77.48
77.16
76.84
73.31
73.29
67.15
59.04
46.18
f1 (ppm)

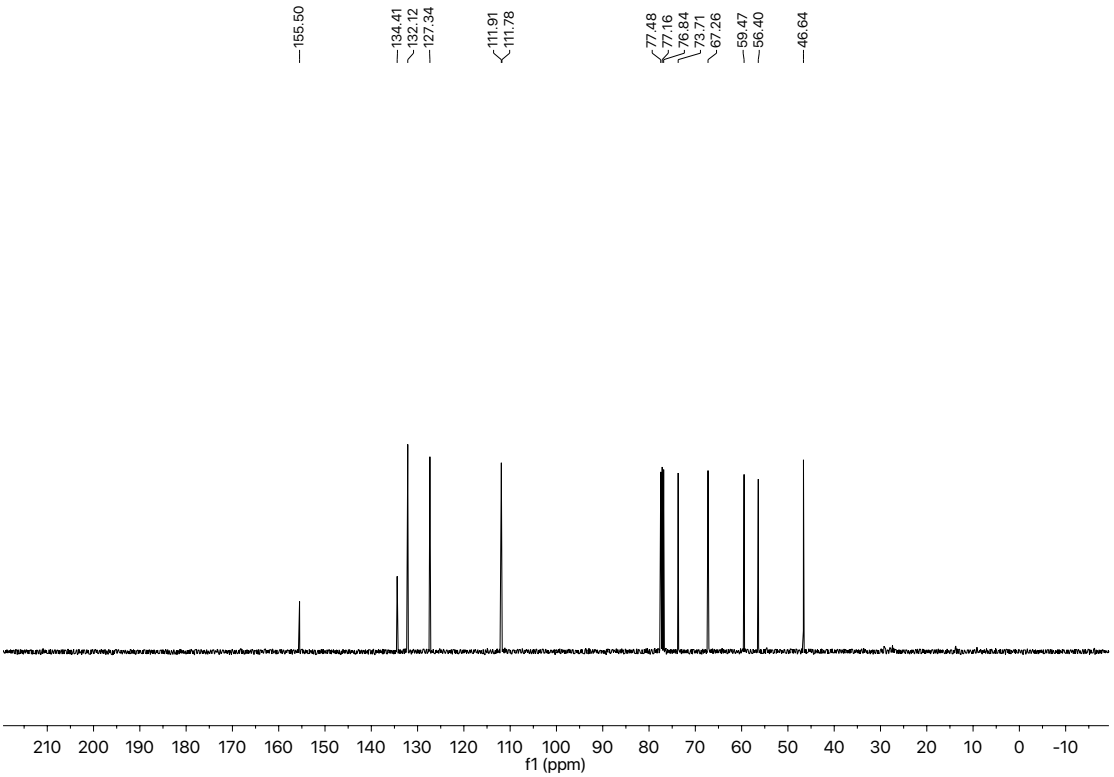

-108.03
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

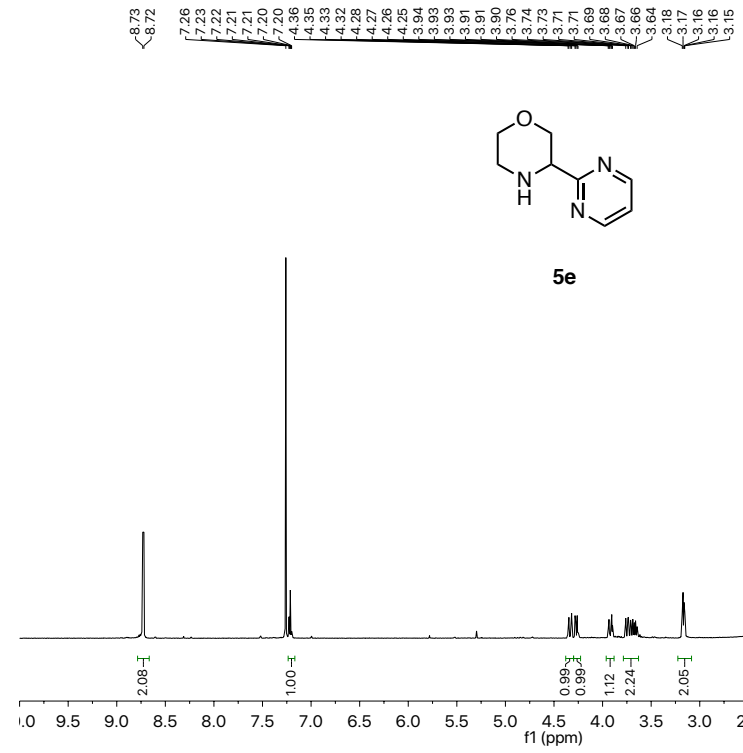

7.60
7.59
7.59
7.28
7.26
7.26
7.25
6.85
6.83
3.87
3.86
3.86
3.85
3.84
3.83
3.83
3.83
3.82
3.82
3.78
3.77
3.75
3.74
3.65
3.65
3.62
3.62
3.60
3.59
3.35
3.32
3.32
3.30
3.13
3.12
3.10
3.09
3.07
3.06
2.99
2.99
2.99
2.98
2.96
2.96
2.96
2.95
1.89

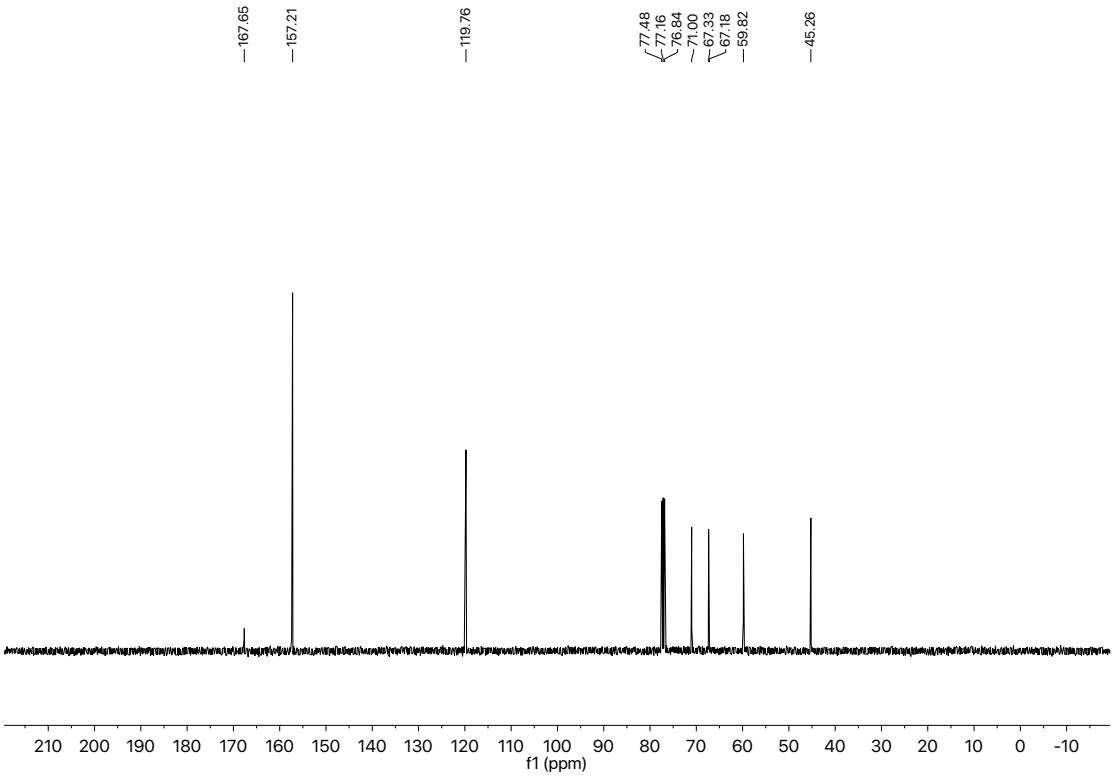
O
N
H
Br
OMe

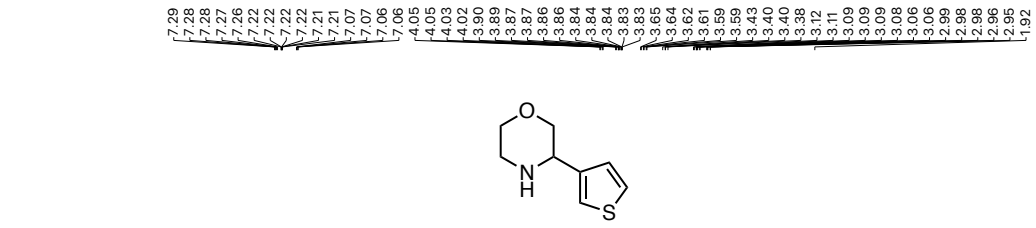
5d


1.00
1.32
1.07
3.39
2.01
1.14
1.11
1.09
1.06
1.15
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
f1 (ppm)

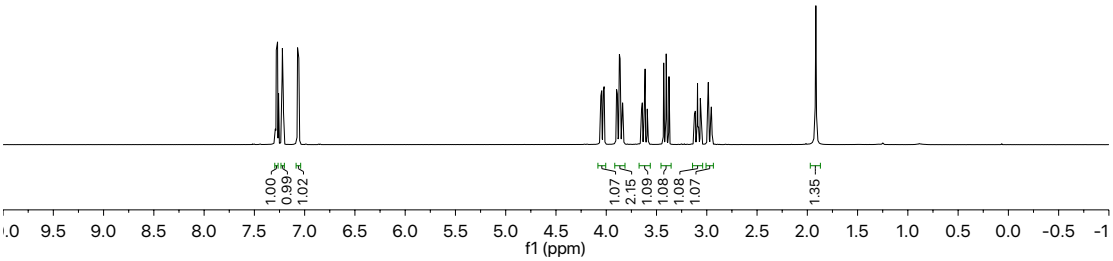

155.50
134.41
132.12
127.34
111.91
111.78
77.48
77.16
76.84
73.71
67.26
59.47
56.40
46.64
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

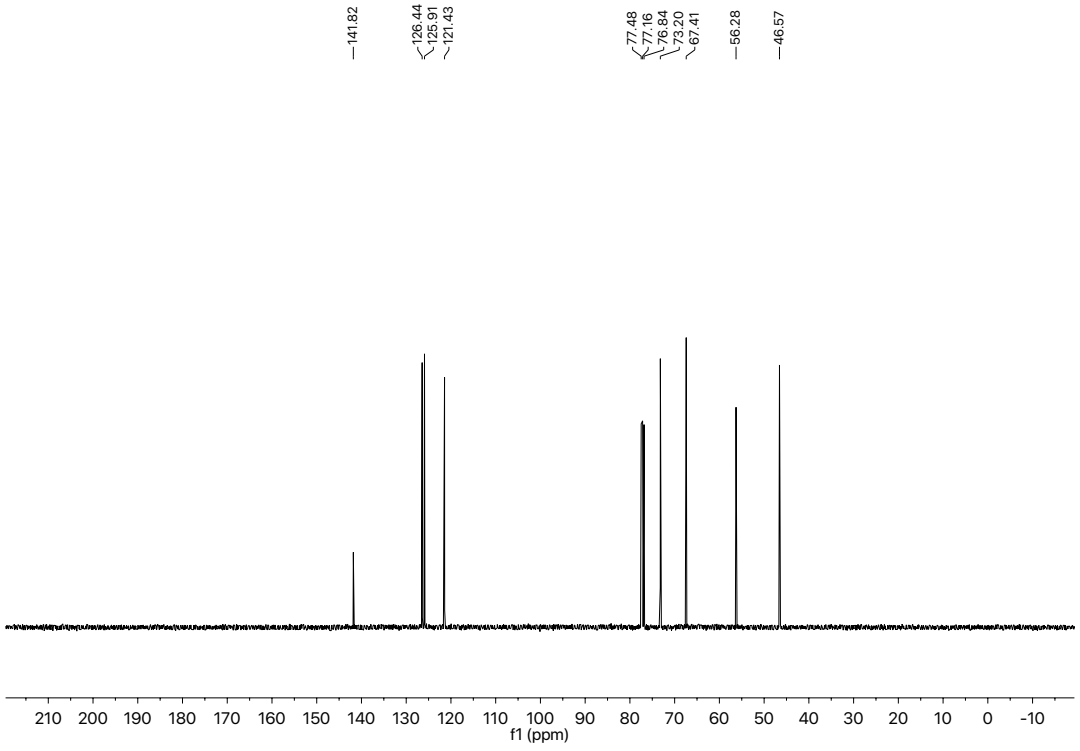

8.73
8.72
7.26
7.23
7.22
7.21
7.21
7.20
7.20
4.36
4.35
4.33
4.32
4.28
4.27
4.26
4.25
3.94
3.93
3.93
3.91
3.91
3.90
3.76
3.74
3.73
3.71
3.71
3.69
3.68
3.67
3.66
3.64
3.18
3.17
3.16
3.16
3.15
O
N
H
N
N
5e
2.08
1.00
0.99
0.99
1.12
2.24
2.05
f1 (ppm)

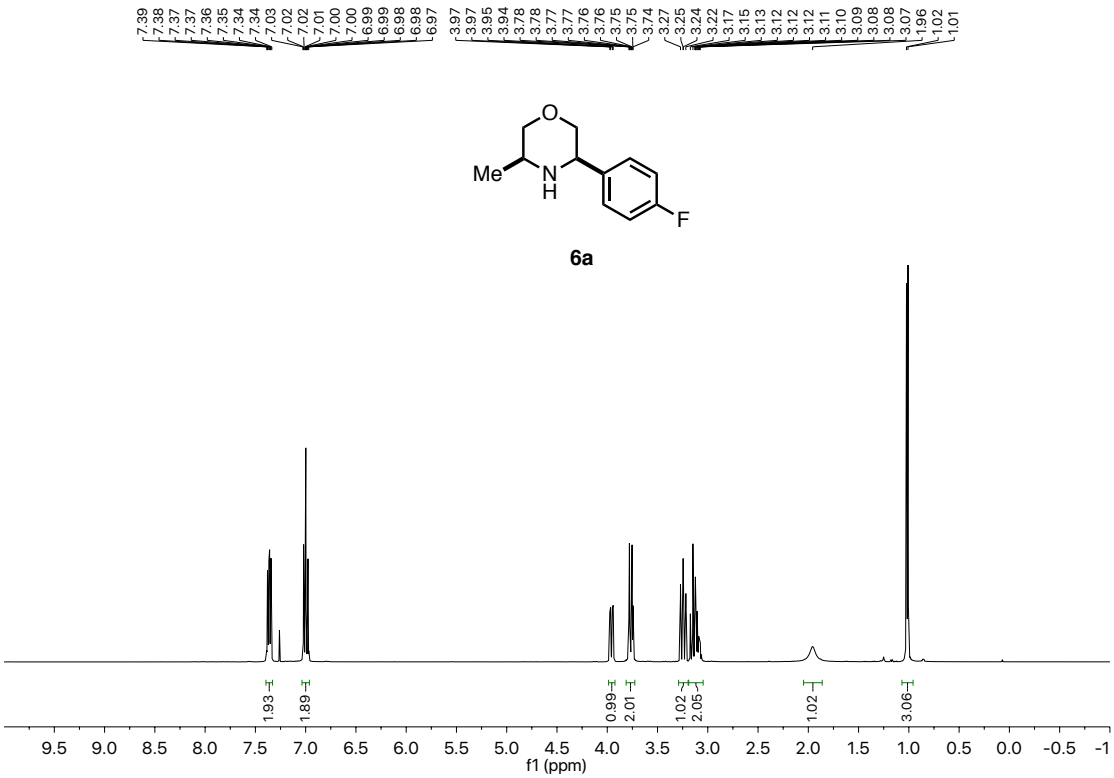

167.65
157.21
119.76
77.48
77.16
76.84
71.00
67.33
67.18
59.82
45.26
f1 (ppm)

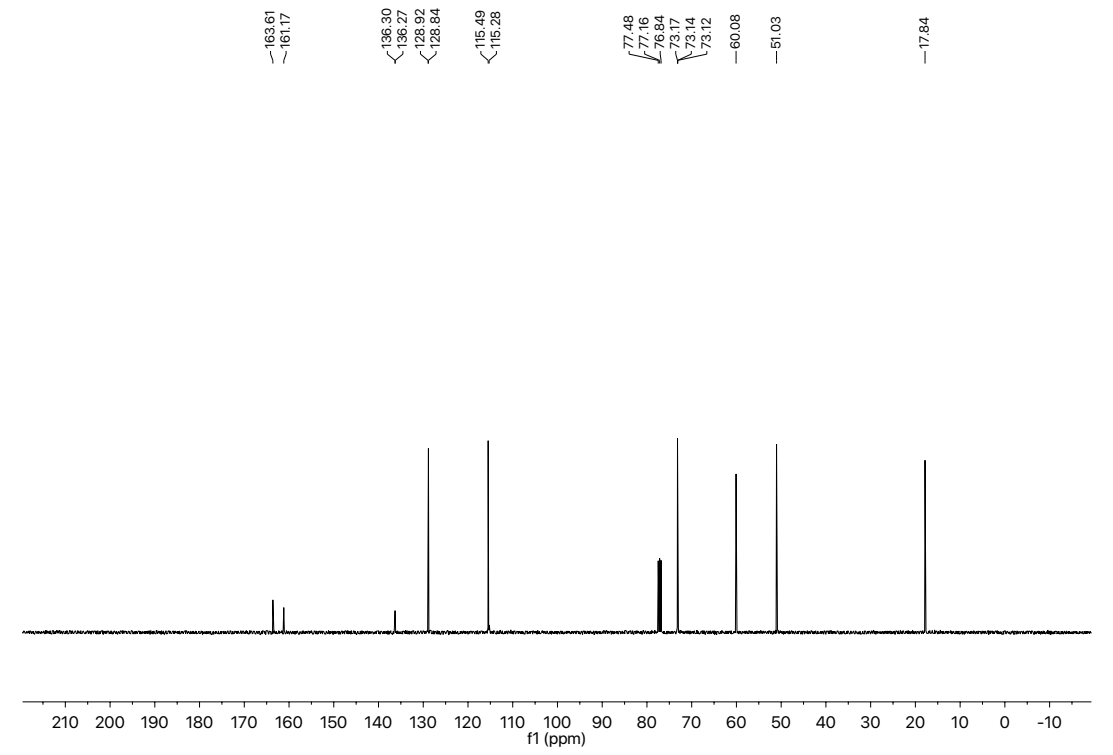

7.29
7.28
7.28
7.27
7.26
7.22
7.22
7.22
7.22
7.21
7.21
7.07
7.07
7.06
7.06
4.05
4.05
4.03
4.02
3.90
3.89
3.87
3.87
3.86
3.86
3.84
3.84
3.84
3.83
3.83
3.65
3.64
3.62
3.61
3.59
3.59
3.43
3.40
3.40
3.38
3.12
3.11
3.09
3.09
3.09
3.08
3.06
3.06
2.99
2.98
2.98
2.96
2.95
1.92
O
N
H
S

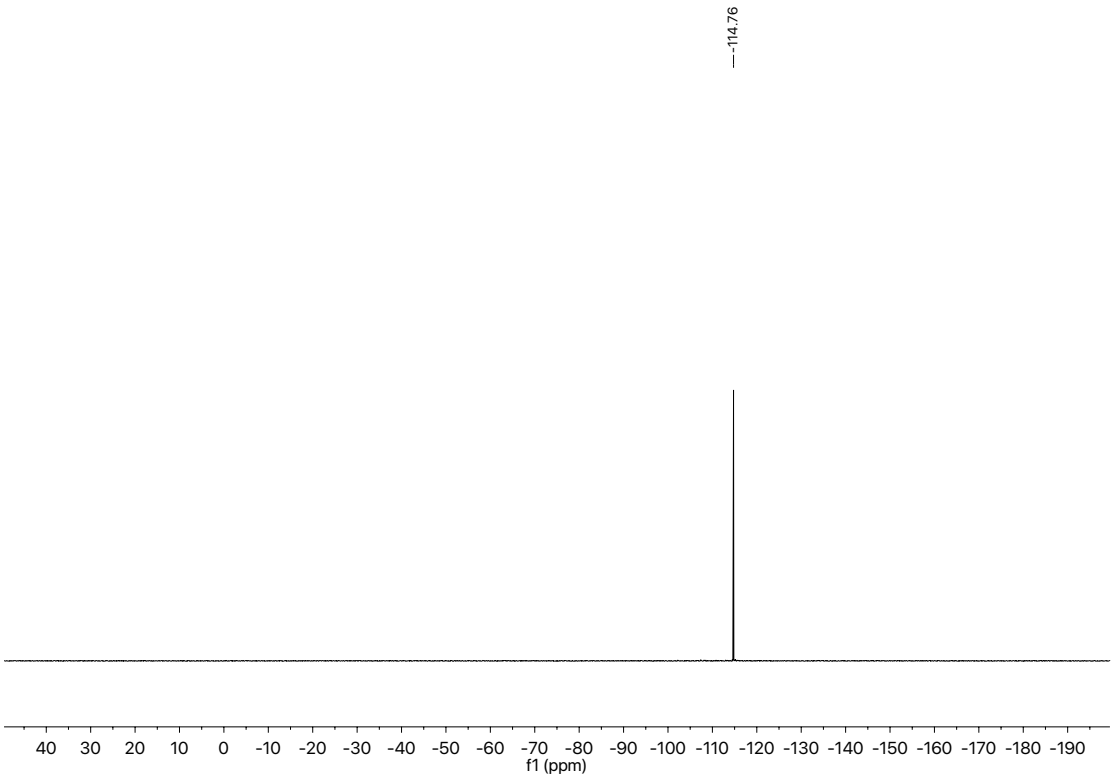
5f

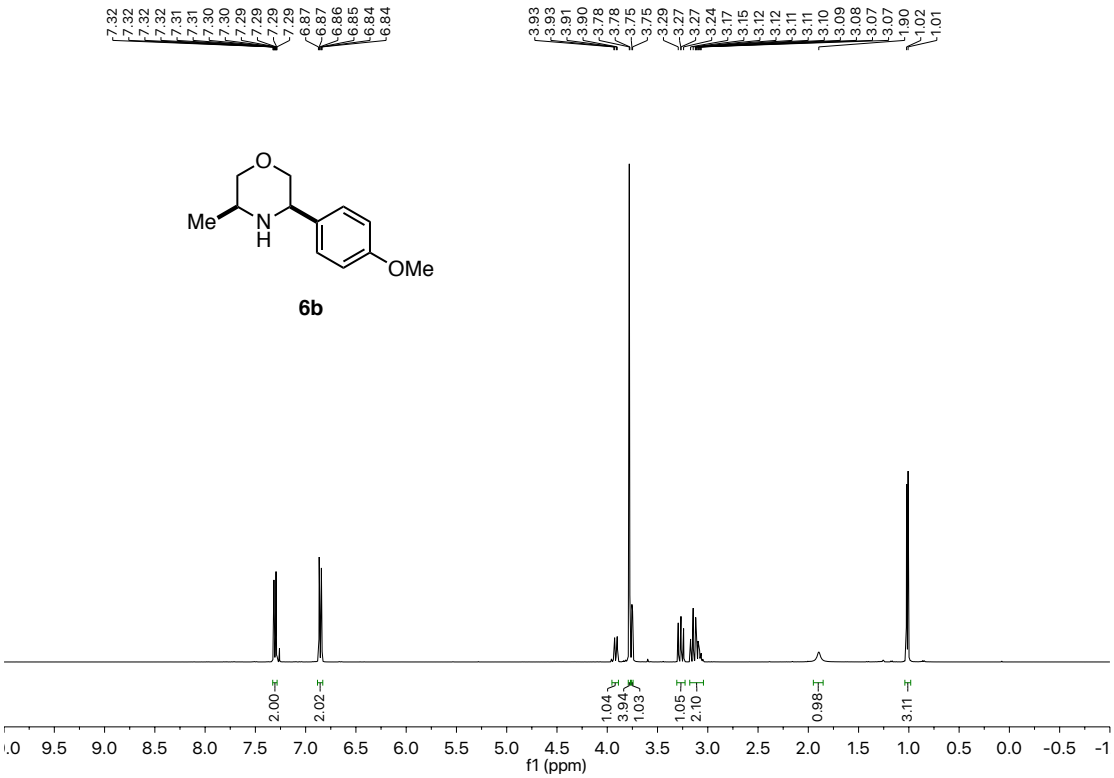

1.00
0.99
1.02
1.07
2.15
1.09
1.08
1.08
1.07
1.35
f1 (ppm)

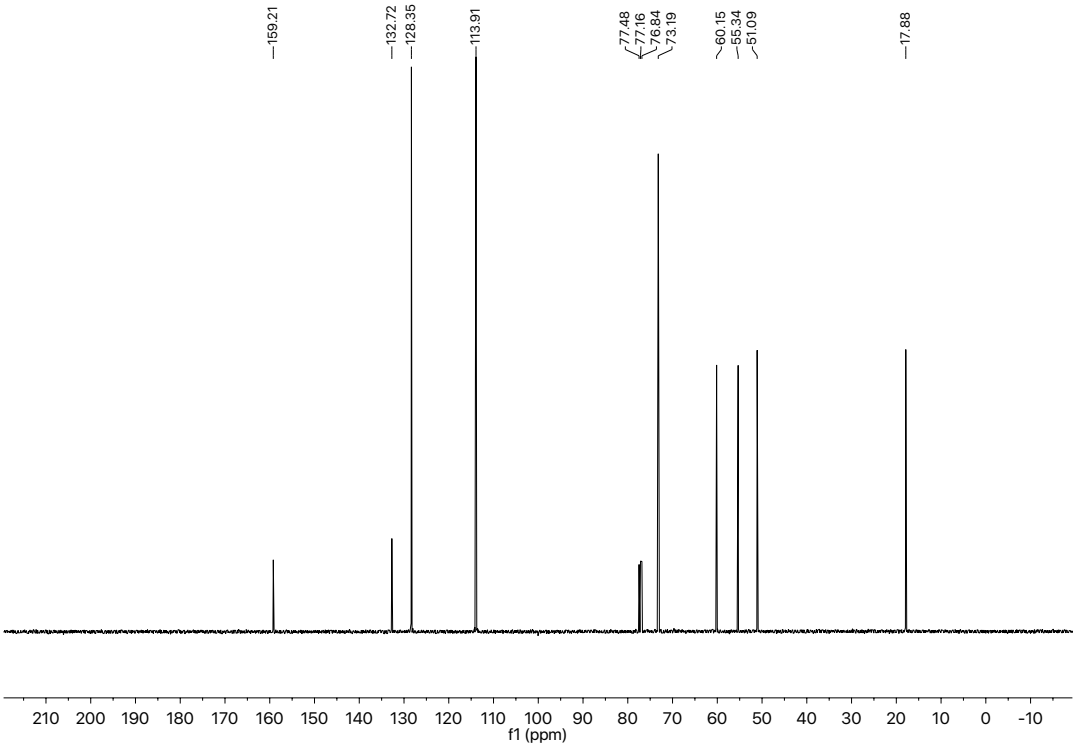

141.82
126.44
125.91
121.43
77.48
77.16
76.84
73.20
67.41
56.28
46.57
f1 (ppm)

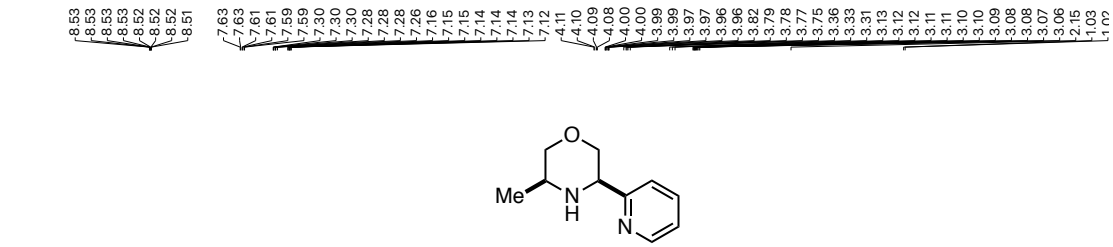

7.39
7.38
7.37
7.37
7.36
7.35
7.34
7.34
7.03
7.02
7.02
7.01
7.00
7.00
6.99
6.99
6.98
6.98
6.97
3.97
3.97
3.95
3.94
3.78
3.78
3.77
3.77
3.76
3.76
3.75
3.75
3.74
3.27
3.25
3.24
3.22
3.17
3.15
3.13
3.12
3.12
3.12
3.11
3.10
3.09
3.08
3.08
3.07
1.96
1.02
1.01
O
Me
N
H
F
6a
1.93
1.89
0.99
2.01
1.02
2.05
1.02
3.06
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
f1 (ppm)


163.61
161.17
136.30
136.27
128.92
128.84
115.49
115.28
77.48
77.16
76.84
73.17
73.14
73.12
60.08
51.03
17.84
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-114.76
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

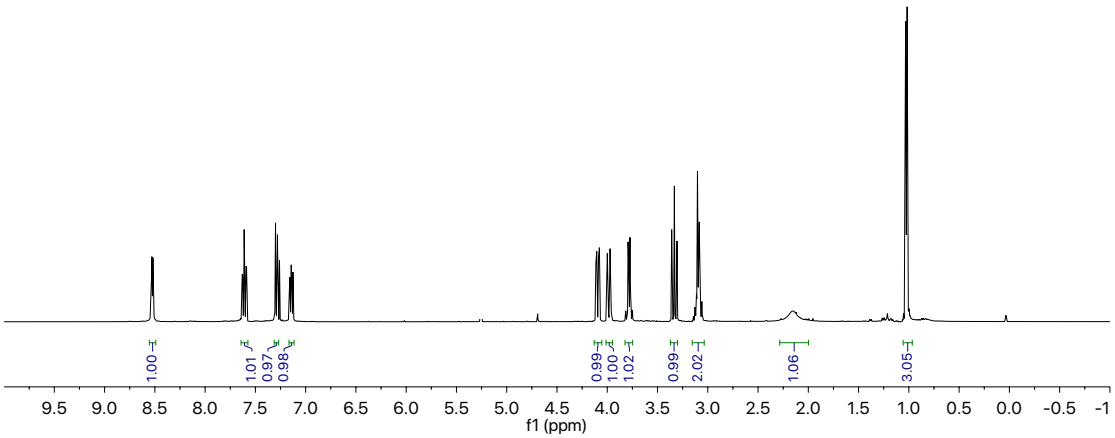

7.32
7.32
7.32
7.32
7.31
7.31
7.30
7.30
7.29
7.29
7.29
7.29
6.87
6.87
6.86
6.85
6.84
6.84
3.93
3.93
3.91
3.90
3.78
3.78
3.75
3.75
3.29
3.27
3.27
3.24
3.17
3.15
3.12
3.12
3.11
3.11
3.10
3.09
3.08
3.07
3.07
1.90
1.02
1.01
O
Me
N
H
OMe
6b
2.00
2.02
1.04
3.94
1.03
1.05
2.10
0.98
3.11
f1 (ppm)

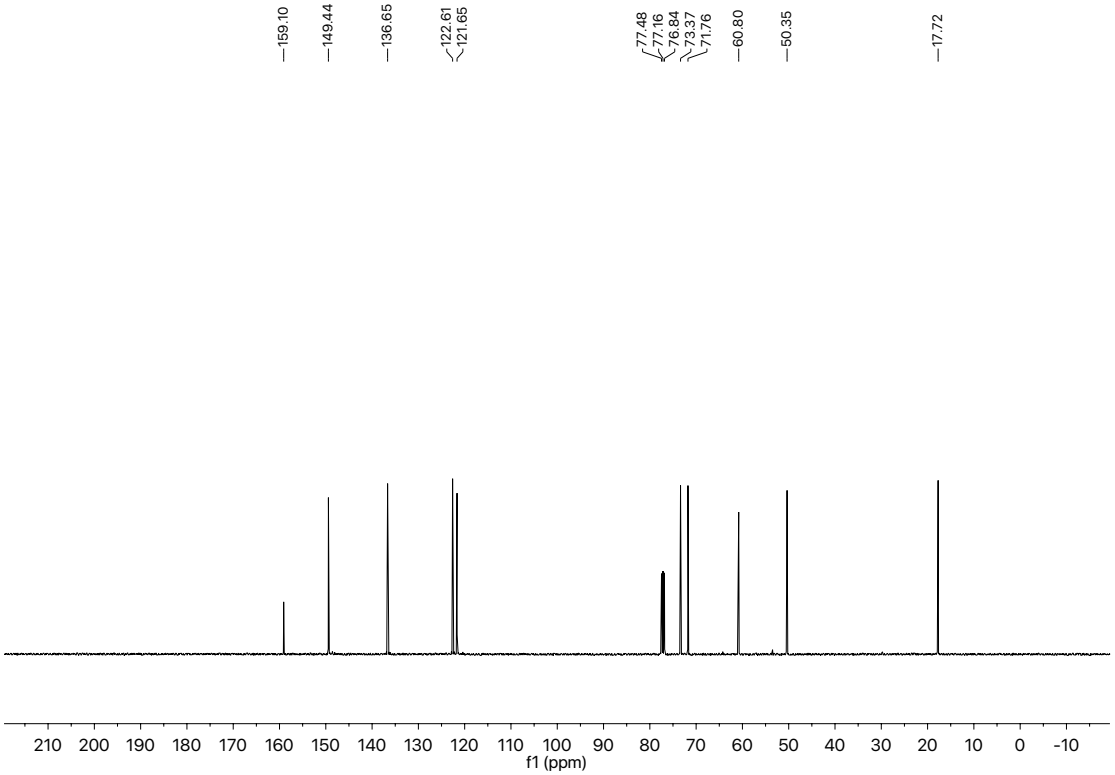

159.21
132.72
128.35
113.91
77.48
77.16
76.84
73.19
60.15
55.34
51.09
17.88
f1 (ppm)

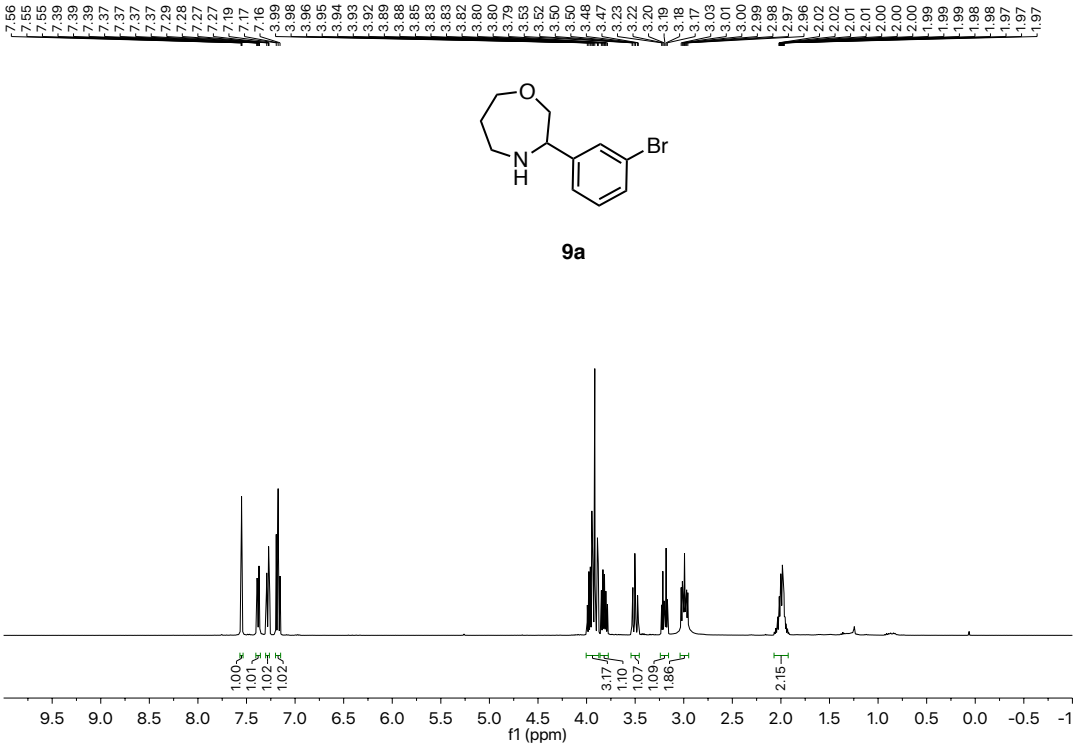


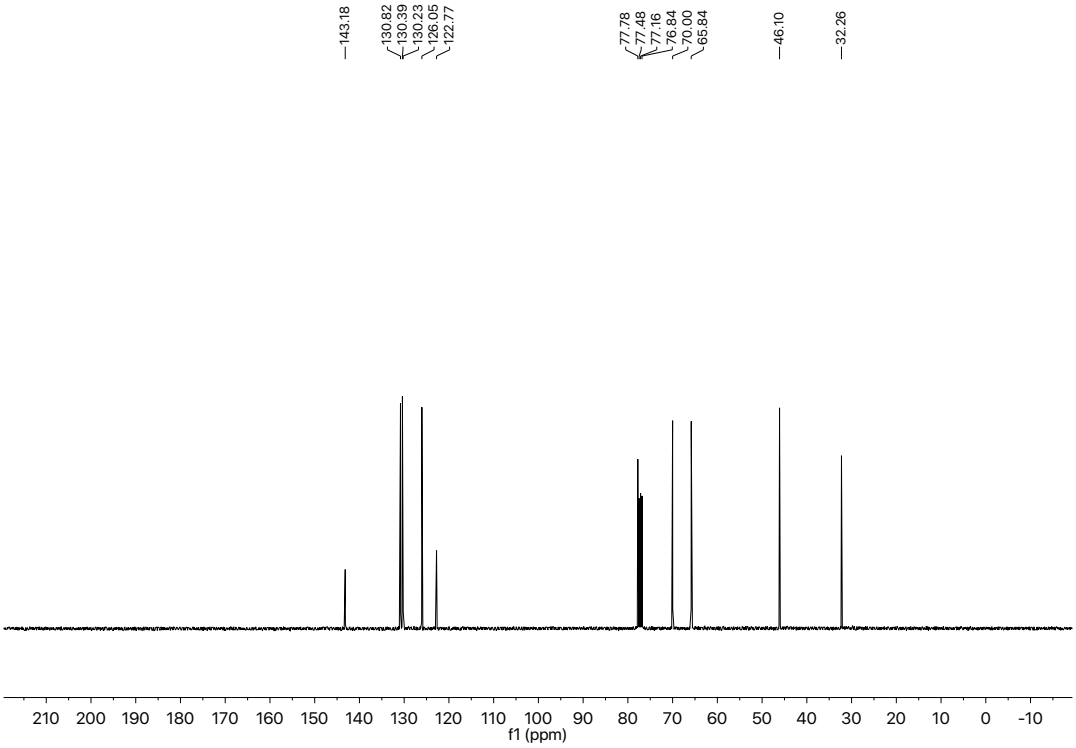
O
Me
N
H
N

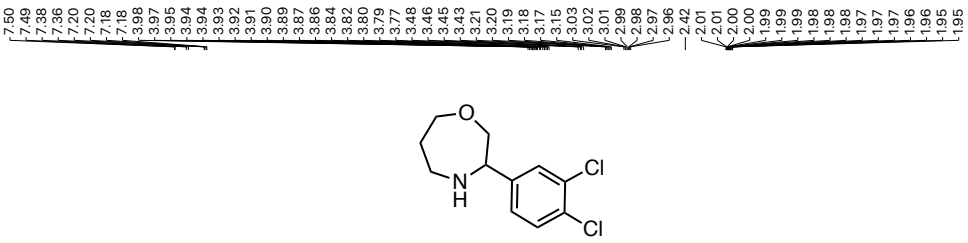
6c


1.00
1.01
0.97
0.98
0.99
1.00
1.02
0.99
2.02
1.06
3.05
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
f1 (ppm)


159.10
149.44
136.65
122.61
121.65
77.48
77.16
76.84
73.37
71.76
60.80
50.35
17.72
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

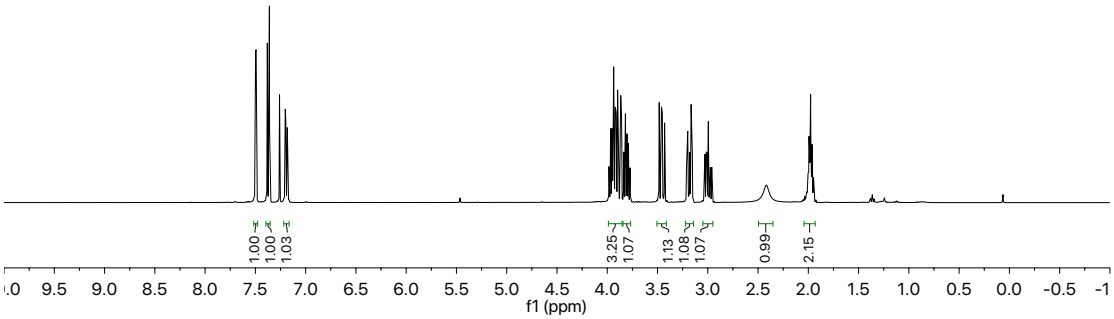

7.56
7.55
7.55
7.39
7.39
7.39
7.37
7.37
7.37
7.37
7.29
7.28
7.27
7.27
7.19
7.17
7.16
3.99
3.98
3.96
3.95
3.94
3.93
3.92
3.89
3.88
3.85
3.83
3.83
3.82
3.80
3.80
3.79
3.53
3.52
3.50
3.50
3.48
3.47
3.23
3.22
3.20
3.19
3.18
3.17
3.03
3.01
3.00
2.99
2.98
2.97
2.96
2.02
2.02
2.01
2.00
2.00
1.99
1.99
1.99
1.98
1.98
1.97
1.97
1.97
O
N
H
Br
9a
1.00
1.01
1.02
1.02
3.17
1.10
1.07
1.09
1.86
2.15
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
f1 (ppm)

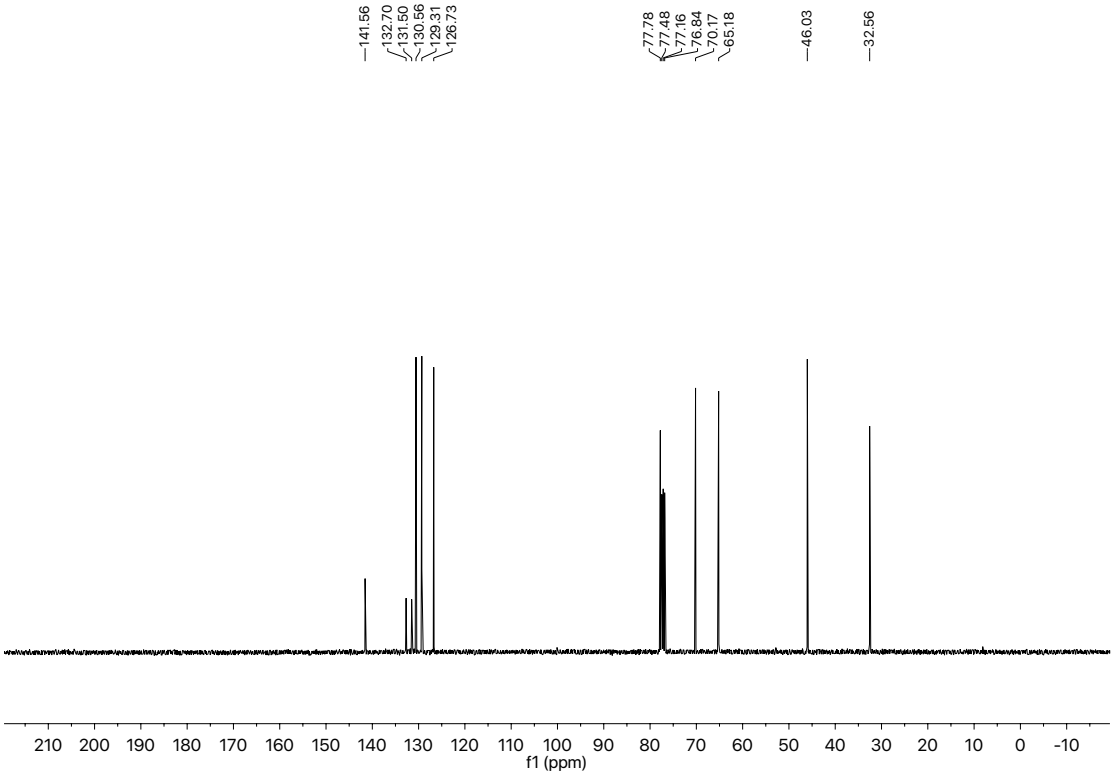

143.18
130.82
130.39
130.23
126.05
122.77
77.78
77.48
77.16
76.84
70.00
65.84
46.10
32.26
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

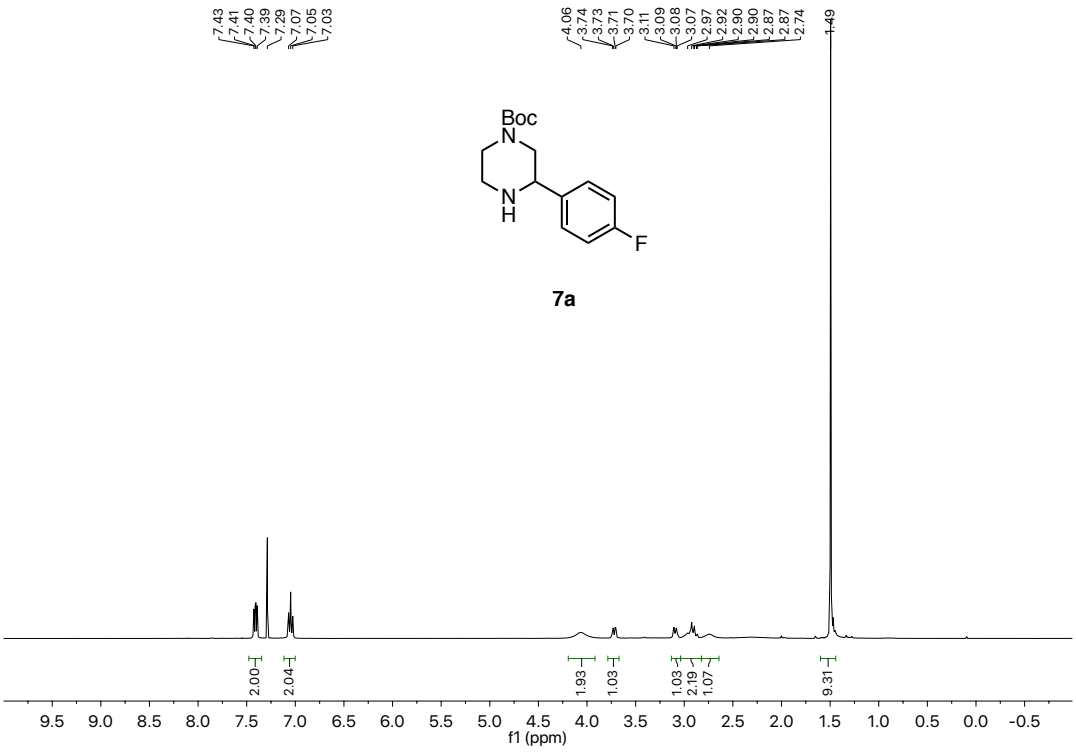

7.50
7.49
7.38
7.36
7.20
7.20
7.18
7.18
3.98
3.97
3.95
3.94
3.94
3.93
3.92
3.91
3.90
3.89
3.87
3.86
3.84
3.82
3.80
3.79
3.77
3.48
3.46
3.45
3.43
3.21
3.20
3.19
3.18
3.17
3.15
3.03
3.02
3.01
2.99
2.98
2.97
2.96
2.42
2.01
2.01
2.00
2.00
1.99
1.99
1.98
1.98
1.98
1.97
1.97
1.96
1.96
1.95
1.95

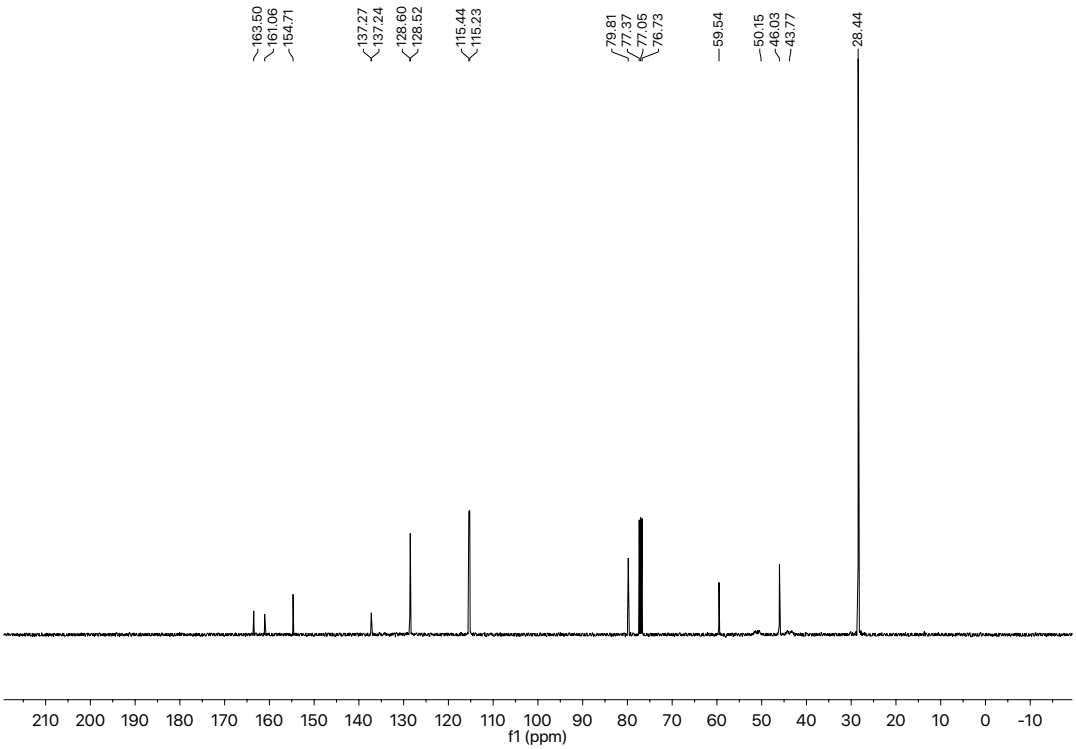
O
N
H
Cl
Cl

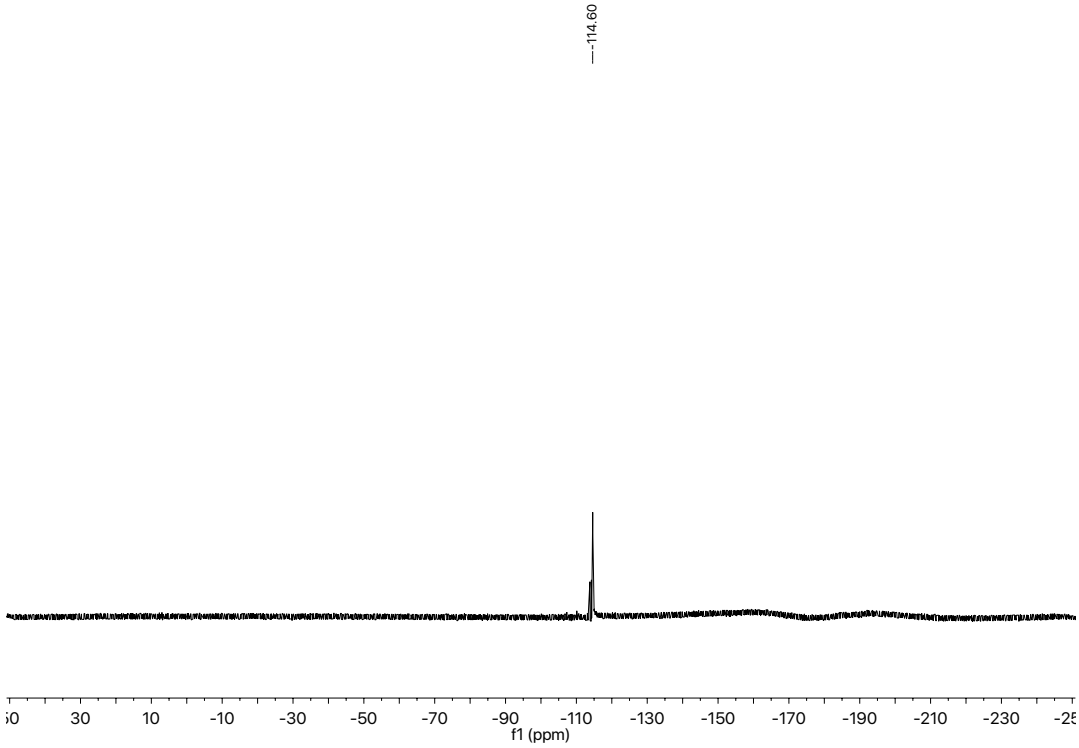
9b

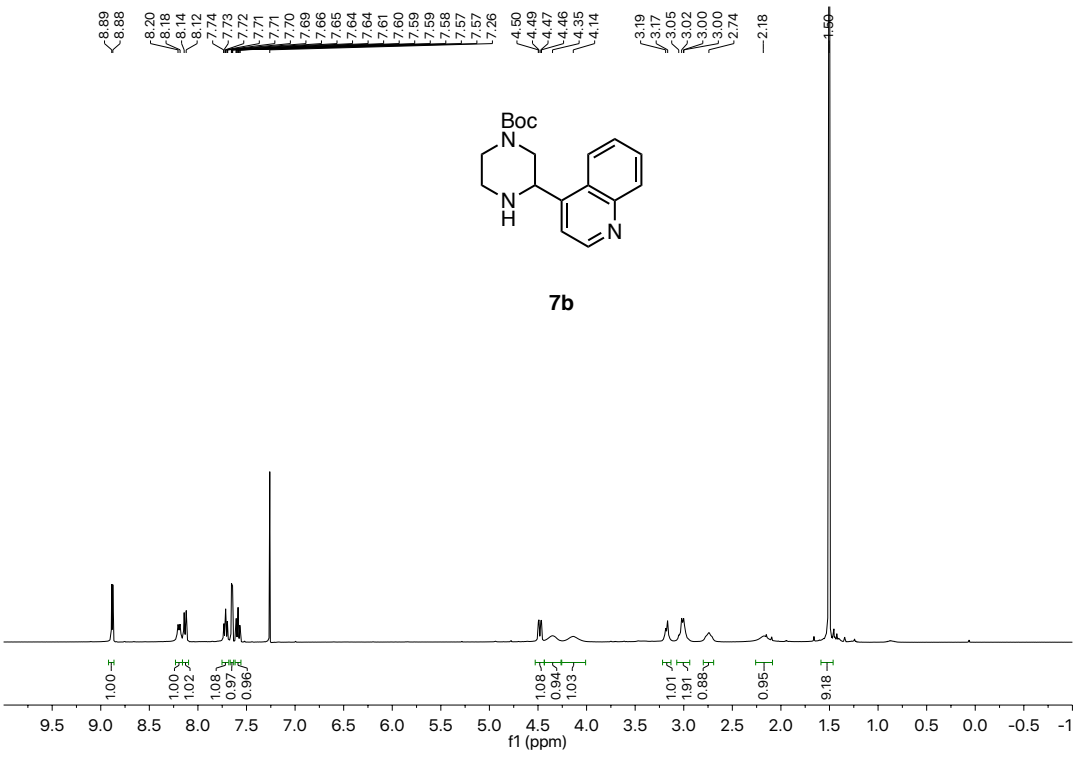

1.00
1.00
1.03
3.25
1.07
1.13
1.08
1.07
0.99
2.15
f1 (ppm)

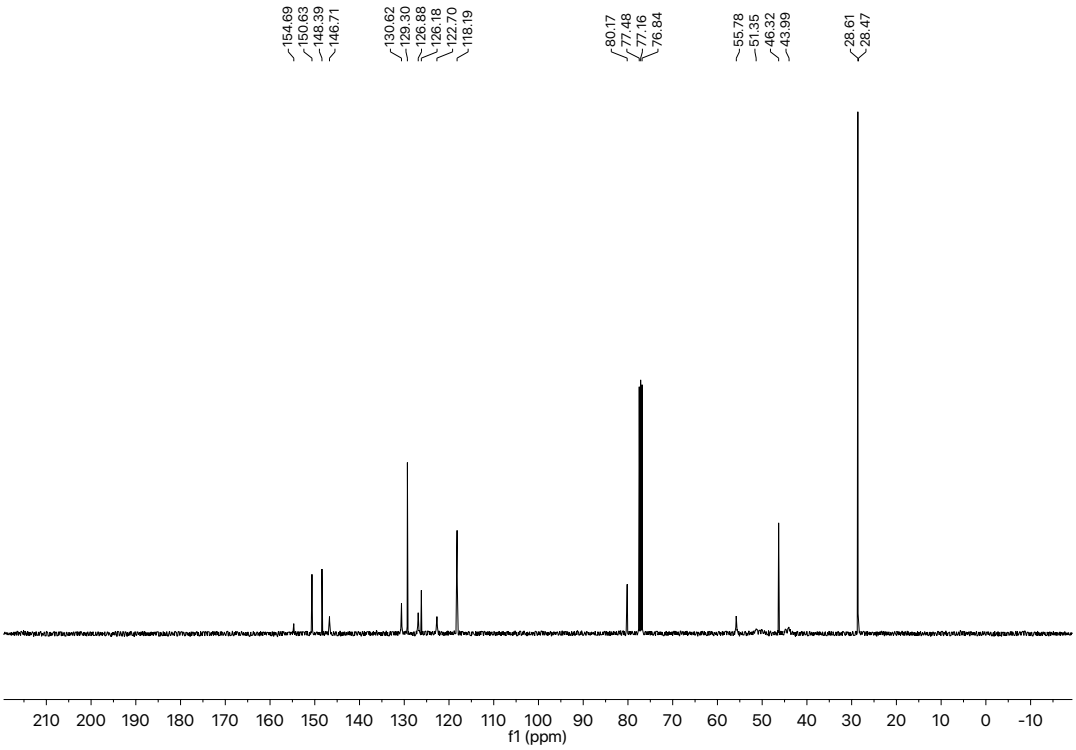

141.56
132.70
131.50
130.56
129.31
126.73
77.78
77.48
77.16
76.84
70.17
65.18
46.03
32.56
f1 (ppm)

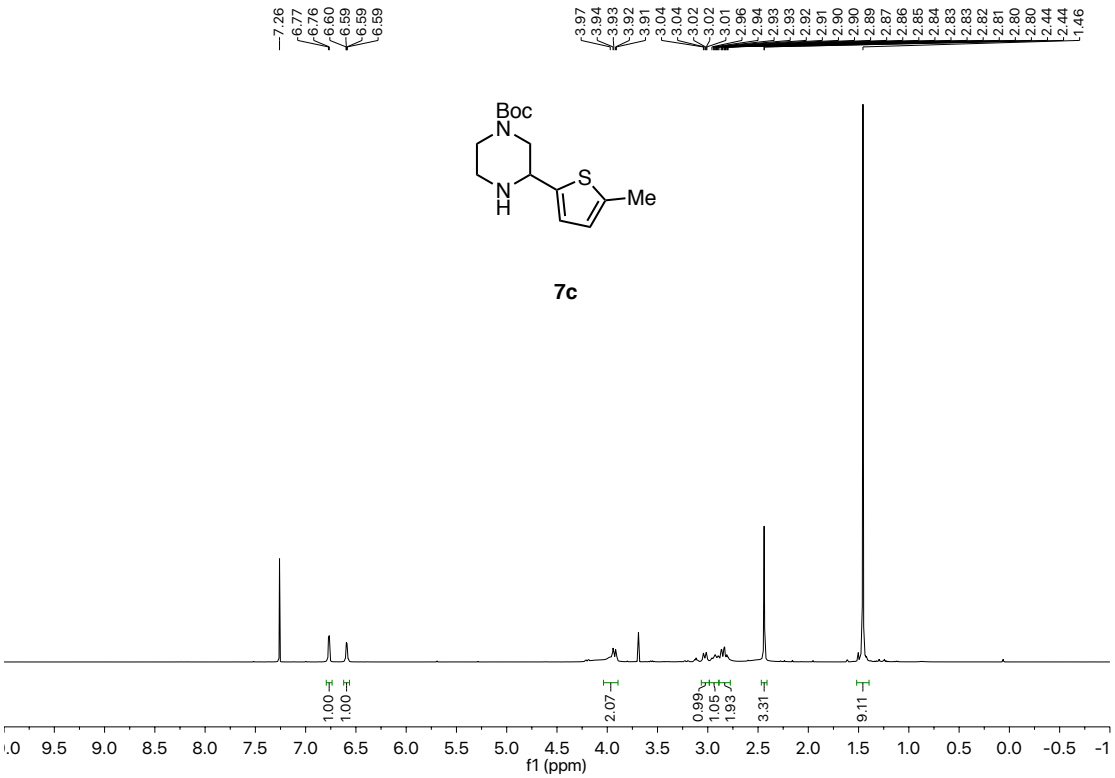

7.43
7.41
7.40
7.39
7.29
7.07
7.05
7.03
4.06
3.74
3.73
3.71
3.70
3.11
3.09
3.08
3.07
2.97
2.92
2.90
2.90
2.87
2.87
2.74
1.49
Boc
N
N
H
F
7a
2.00
2.04
1.93
1.03
1.03
2.19
1.07
9.31
f1 (ppm)

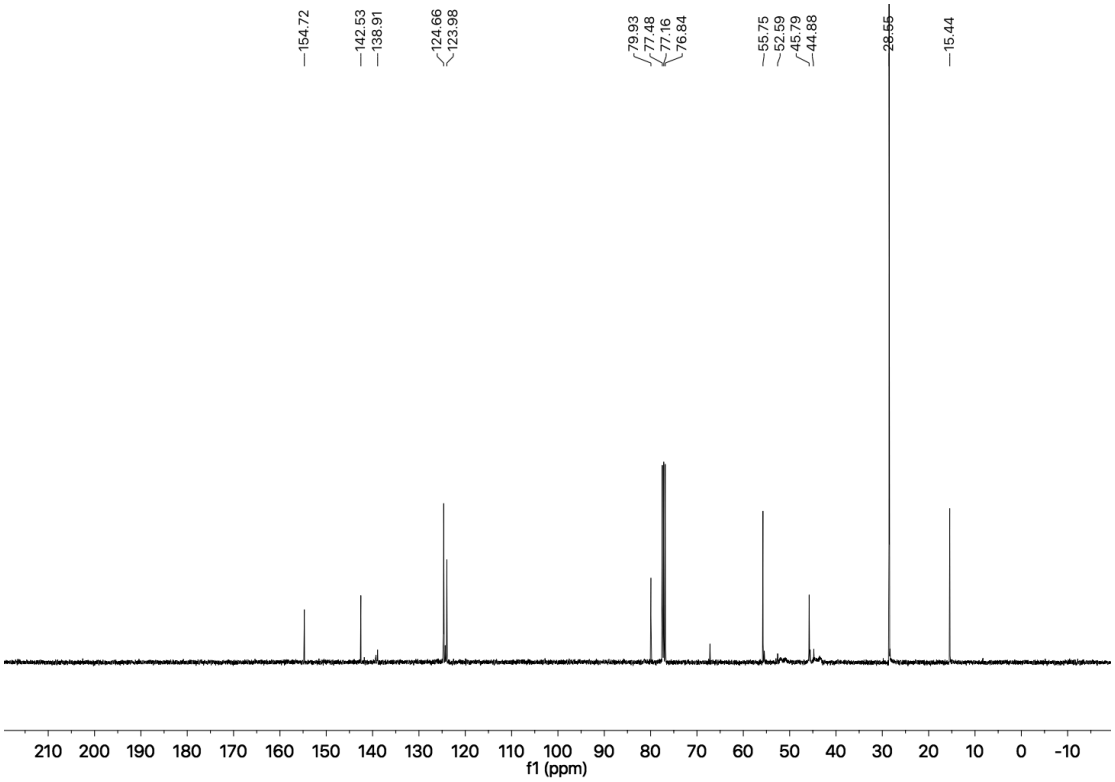

163.50
161.06
154.71
137.27
137.24
128.60
128.52
115.44
115.23
79.81
77.37
77.05
76.73
59.54
50.15
46.03
43.77
28.44
f1 (ppm)

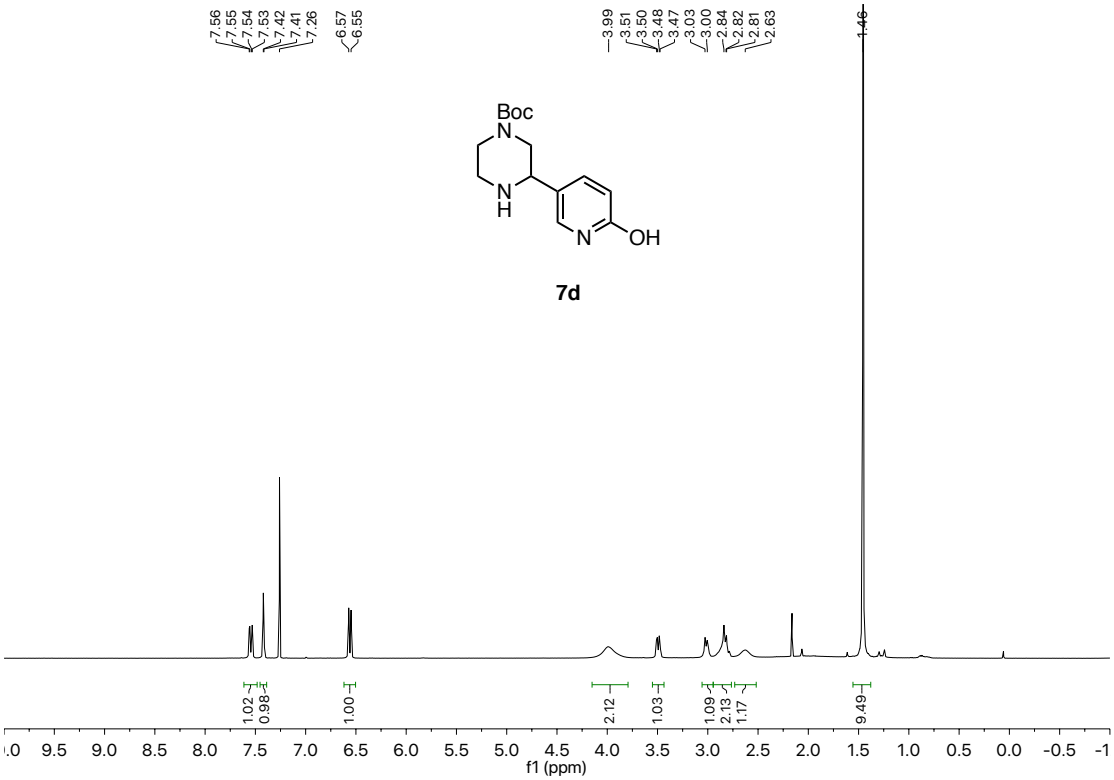

-114.60
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
-230
f1 (ppm)


8.89
8.88
8.20
8.18
8.14
8.12
7.74
7.73
7.72
7.71
7.71
7.70
7.69
7.66
7.65
7.64
7.64
7.61
7.60
7.59
7.59
7.58
7.57
7.57
7.26
4.50
4.49
4.47
4.46
4.35
4.14
3.19
3.17
3.05
3.02
3.00
3.00
2.74
2.18
1.60
Boc
N
N
H
N
7b
1.00
1.00
1.02
1.08
0.97
0.96
1.08
0.94
1.03
1.01
1.91
0.88
0.95
9.18
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
f1 (ppm)

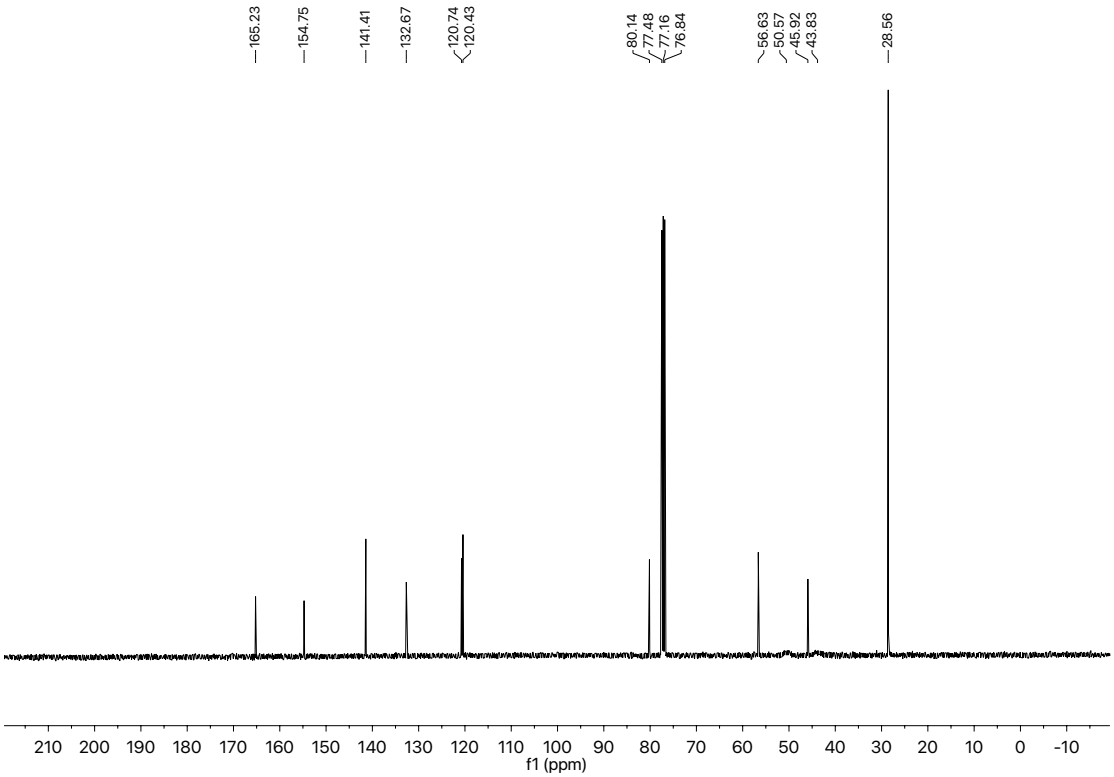

154.69
150.63
148.39
146.71
130.62
129.30
126.88
126.18
122.70
118.19
80.17
77.48
77.16
76.84
55.78
51.35
46.32
43.99
28.61
28.47
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

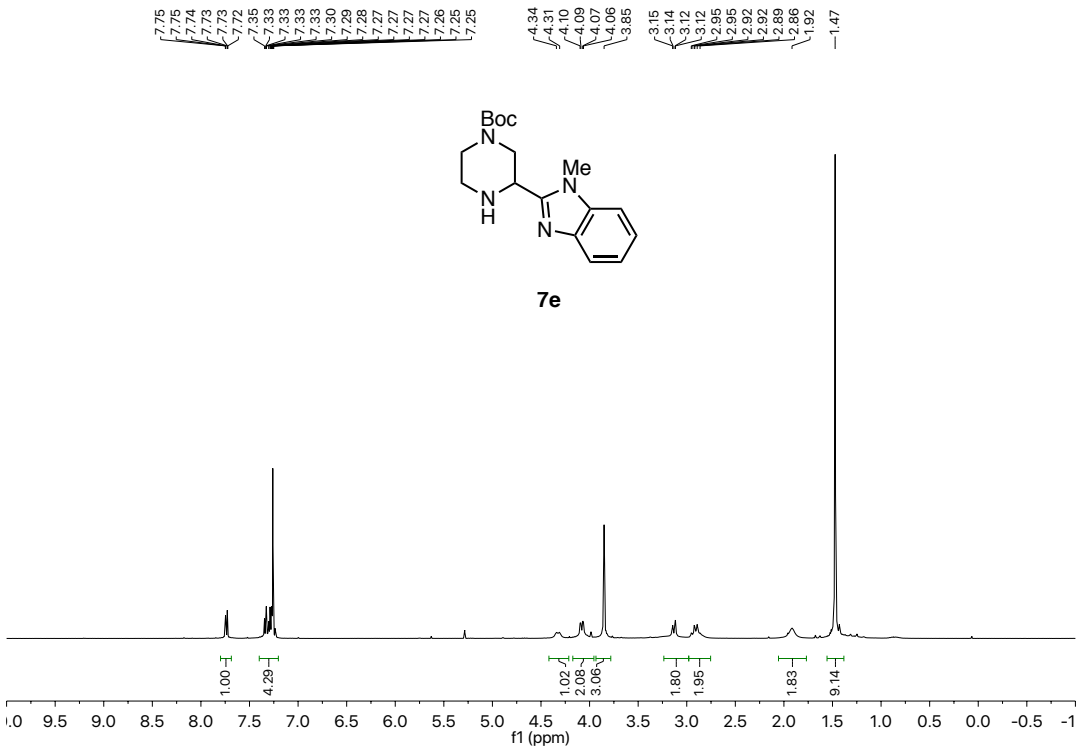

7.26
6.77
6.76
6.60
6.59
6.59
6.59
3.97
3.94
3.93
3.92
3.91
3.04
3.04
3.02
3.02
3.01
2.96
2.94
2.93
2.93
2.92
2.91
2.90
2.90
2.89
2.87
2.86
2.85
2.84
2.83
2.83
2.82
2.81
2.80
2.80
2.44
2.44
1.46
Boc
N
N
H
S
Me
7c
1.00
1.00
2.07
0.99
1.05
1.93
3.31
9.11
f1 (ppm)

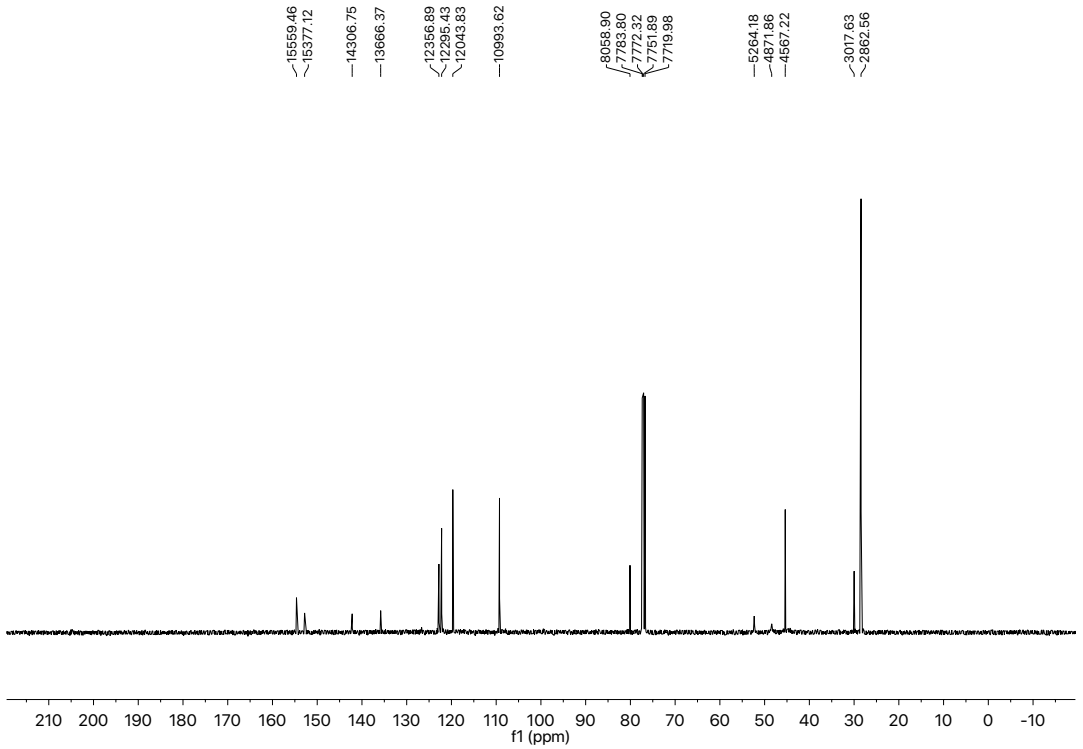

154.72
142.53
138.91
124.66
123.98
79.93
77.48
77.16
76.84
55.75
52.59
45.79
44.88
28.55
15.44
f1 (ppm)

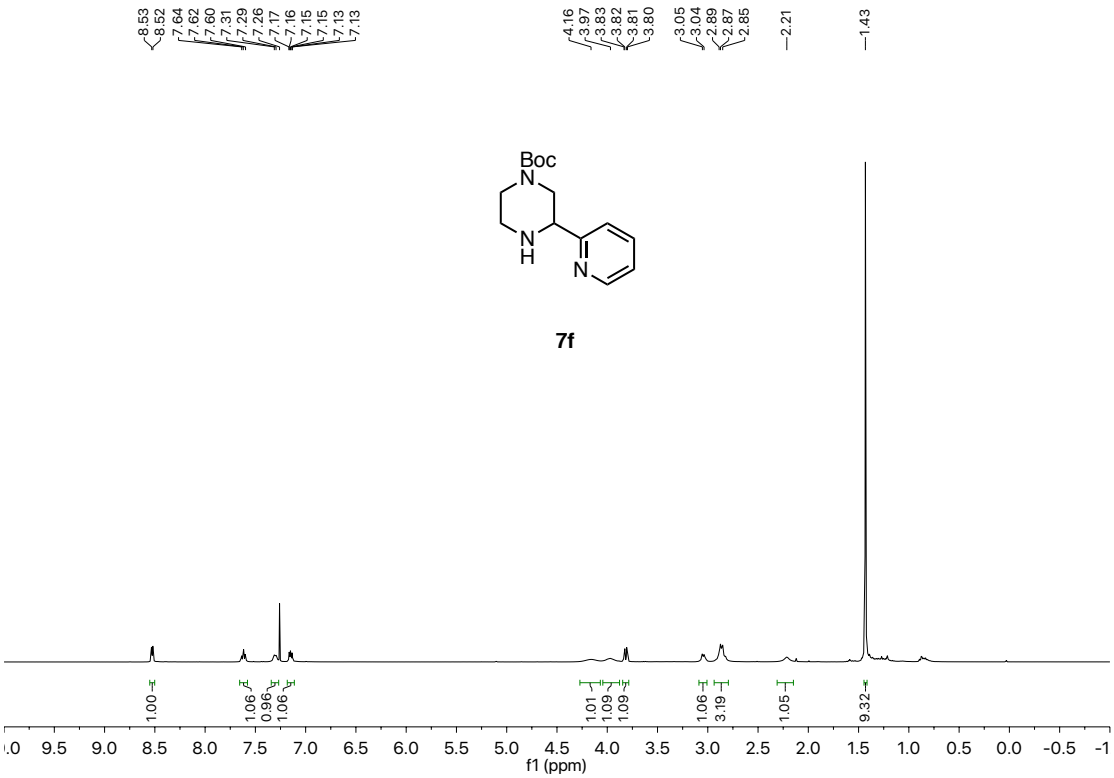

7.56
7.55
7.54
7.53
7.42
7.41
7.26
6.57
6.55
3.99
3.51
3.50
3.48
3.47
3.03
3.00
2.84
2.82
2.81
2.63
1.46
Boc
N
N
H
N
OH
1.02
0.98
1.00
2.12
1.03
1.09
2.13
1.17
9.49
f1 (ppm)

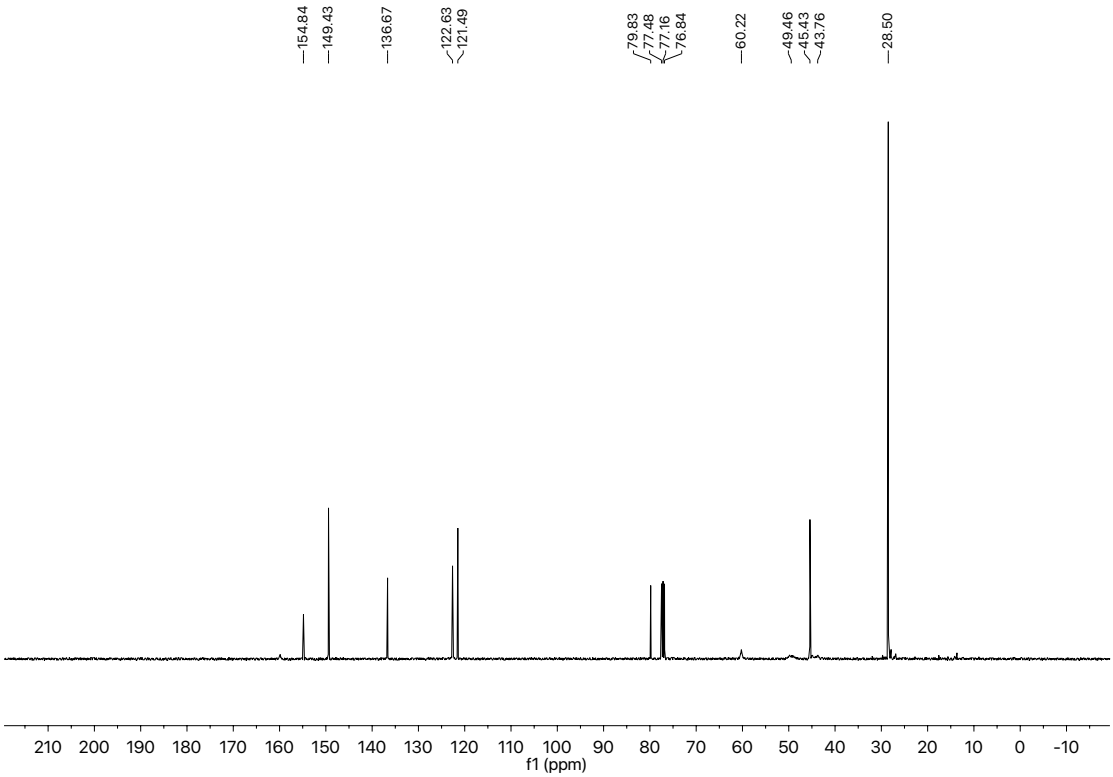
7d

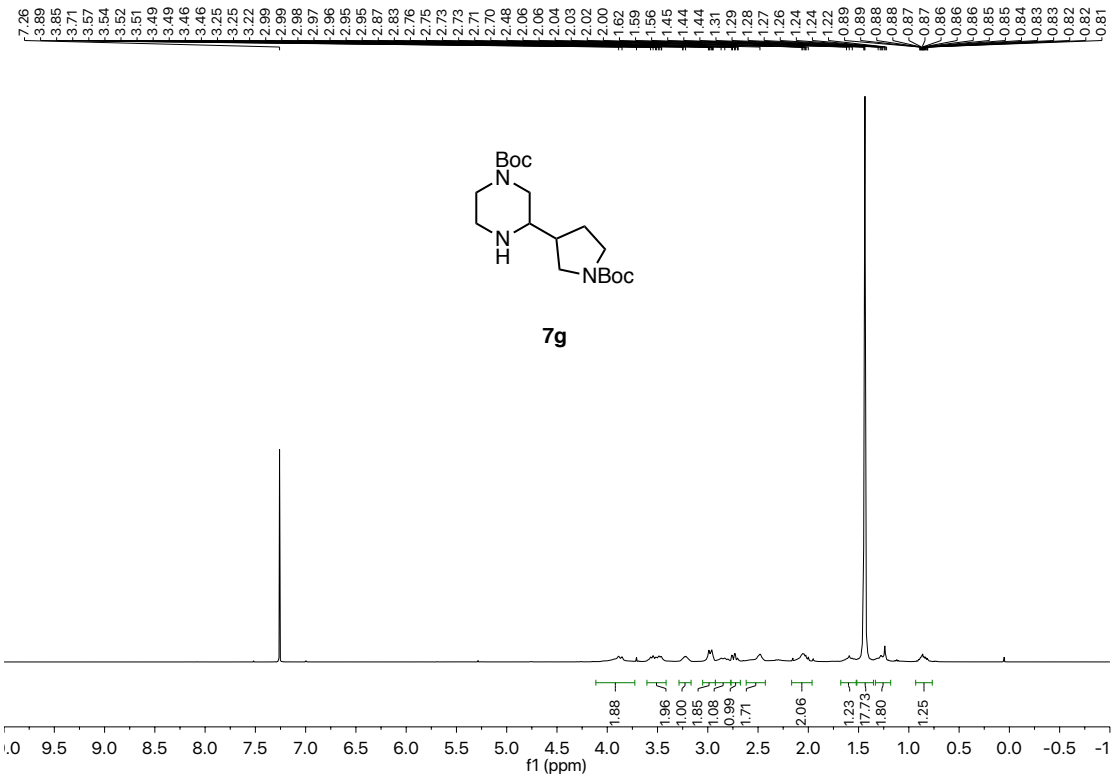

165.23
154.75
141.41
132.67
120.74
120.43
80.14
77.48
77.16
76.84
56.63
50.57
45.92
43.83
28.56
f1 (ppm)

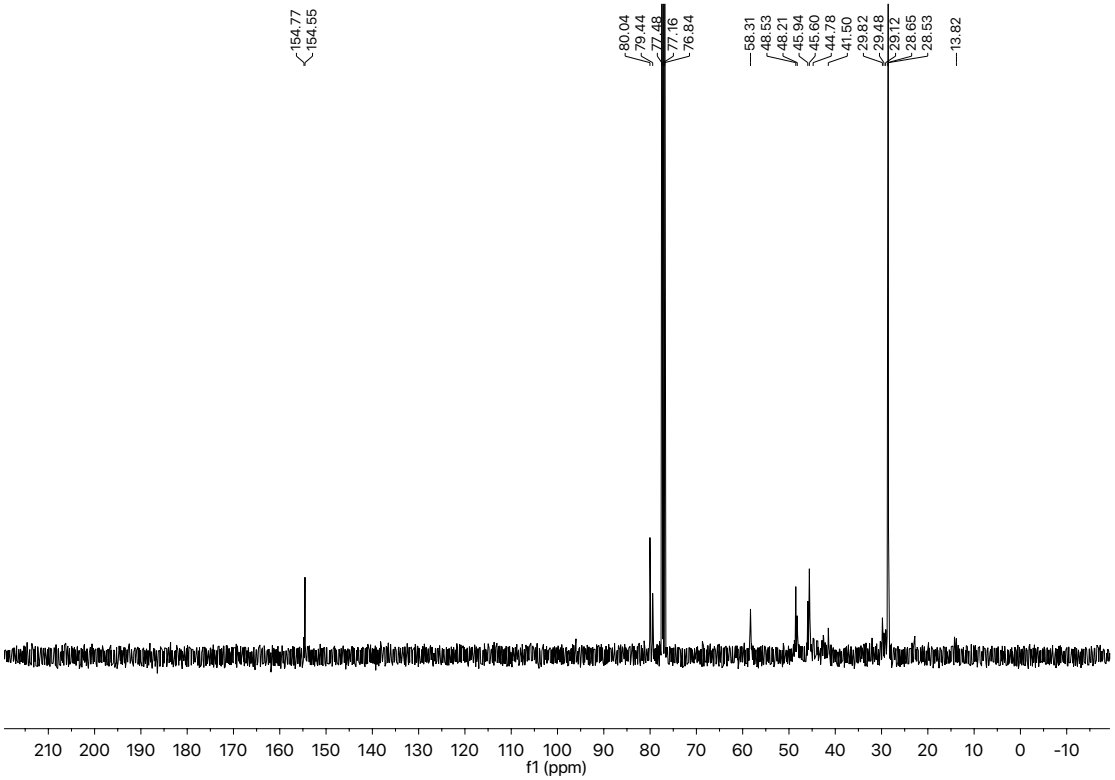

7.75
7.75
7.74
7.73
7.73
7.72
7.35
7.33
7.33
7.33
7.30
7.29
7.28
7.27
7.27
7.27
7.27
7.26
7.25
7.25
4.34
4.31
4.10
4.09
4.07
4.06
3.85
3.15
3.14
3.12
3.12
2.95
2.95
2.92
2.92
2.89
2.86
1.92
1.47
Boc
N
N
H
Me
N
N
7e
1.00
4.29
1.02
2.08
3.06
1.80
1.95
1.83
9.14
f1 (ppm)

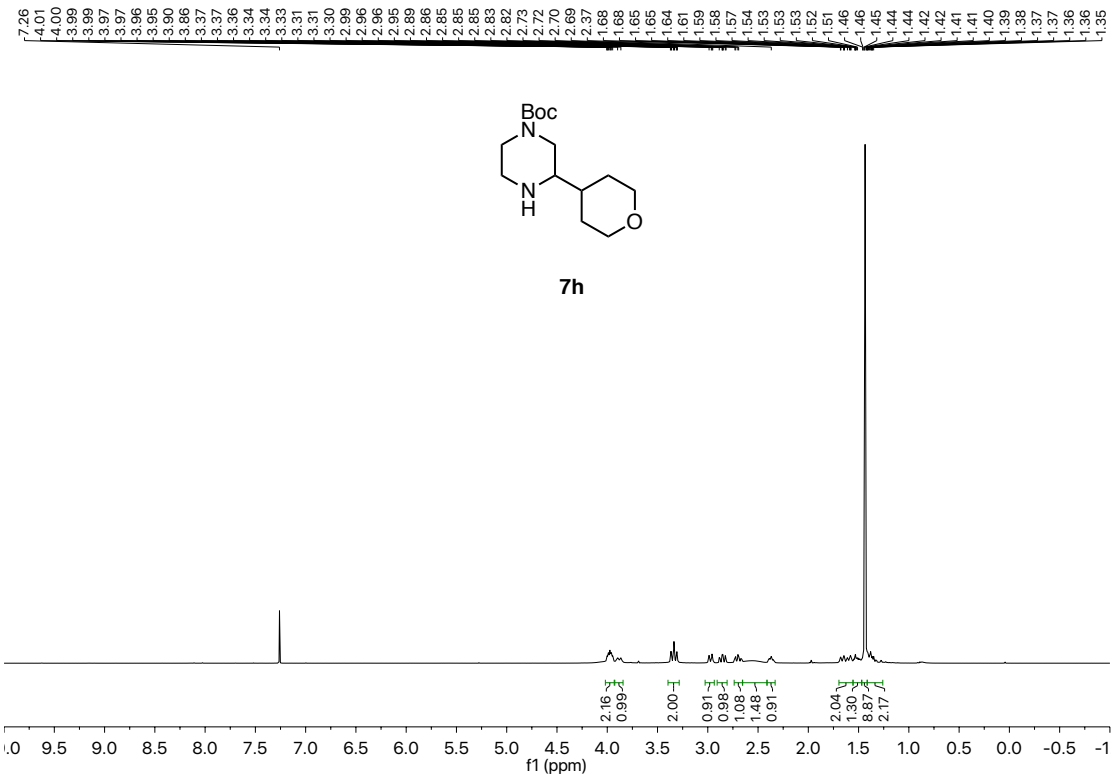

15559.46
15377.12
14306.75
13666.37
12356.89
12295.43
12043.83
10993.62
8058.90
7783.80
7772.32
7751.89
7719.98
5264.18
4871.86
4567.22
3017.63
2862.56
f1 (ppm)

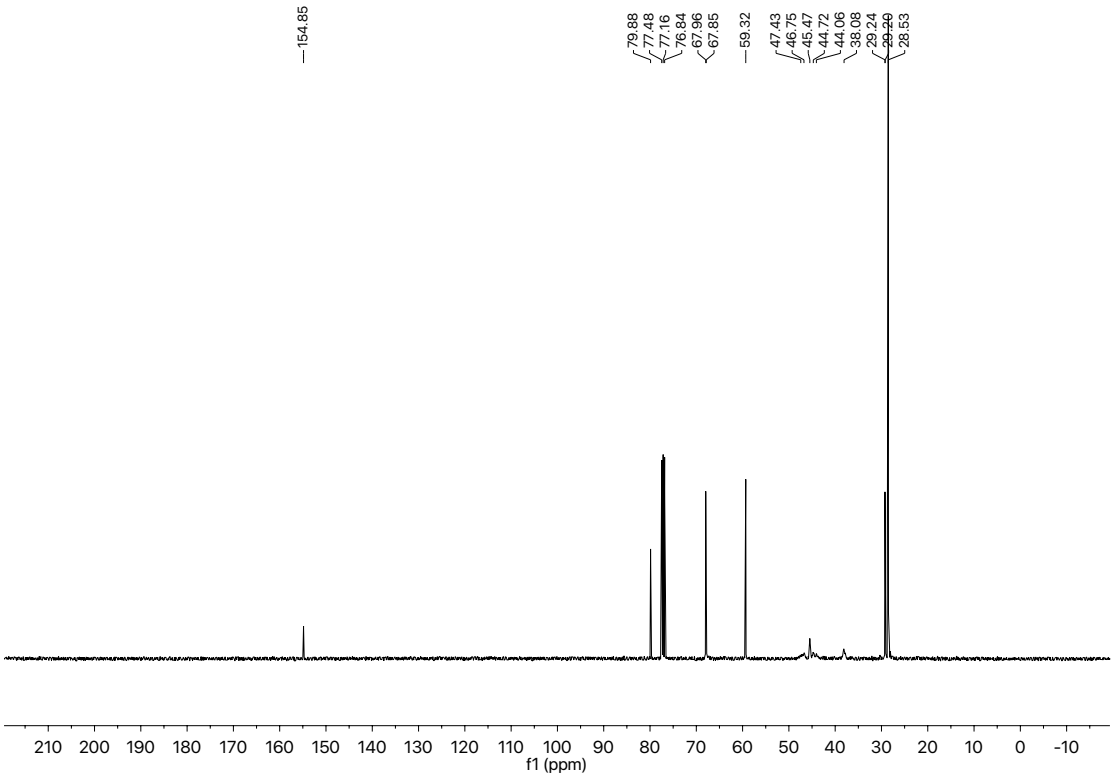

8.53
8.52
7.64
7.62
7.60
7.31
7.29
7.26
7.17
7.16
7.15
7.15
7.13
7.13
4.16
3.97
3.83
3.82
3.81
3.80
3.05
3.04
2.89
2.87
2.85
2.21
1.43
Boc
N
N
H
N
7f
1.00
1.06
0.96
1.06
1.01
1.09
1.09
1.06
3.19
1.05
9.32
f1 (ppm)

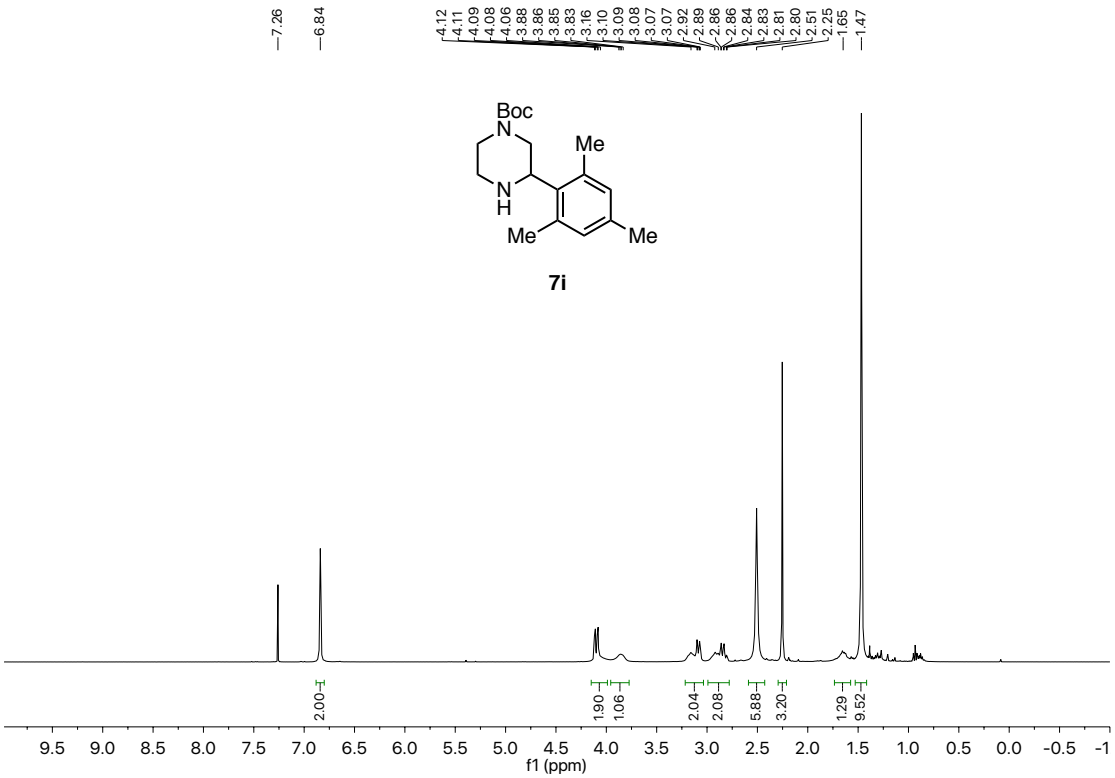

154.84
149.43
136.67
122.63
121.49
79.83
77.48
77.16
76.84
60.22
49.46
45.43
43.76
28.50
f1 (ppm)


Boc
N
N
H
NBoc
7g
1.88
1.96
1.00
1.85
1.08
0.99
1.71
2.06
1.23
17.73
1.80
1.25
f1 (ppm)

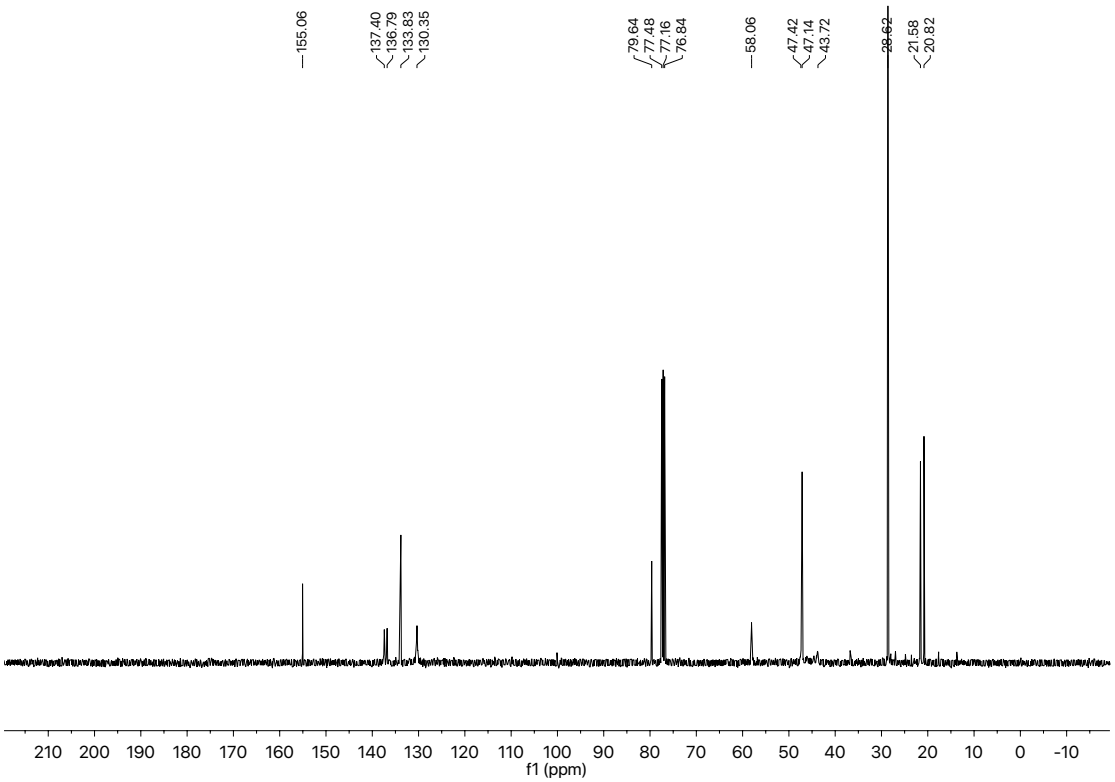

154.77
154.55
80.04
79.44
77.48
77.16
76.84
58.31
48.53
48.21
45.94
45.60
44.78
41.50
29.82
29.48
29.12
28.65
28.53
13.82
f1 (ppm)

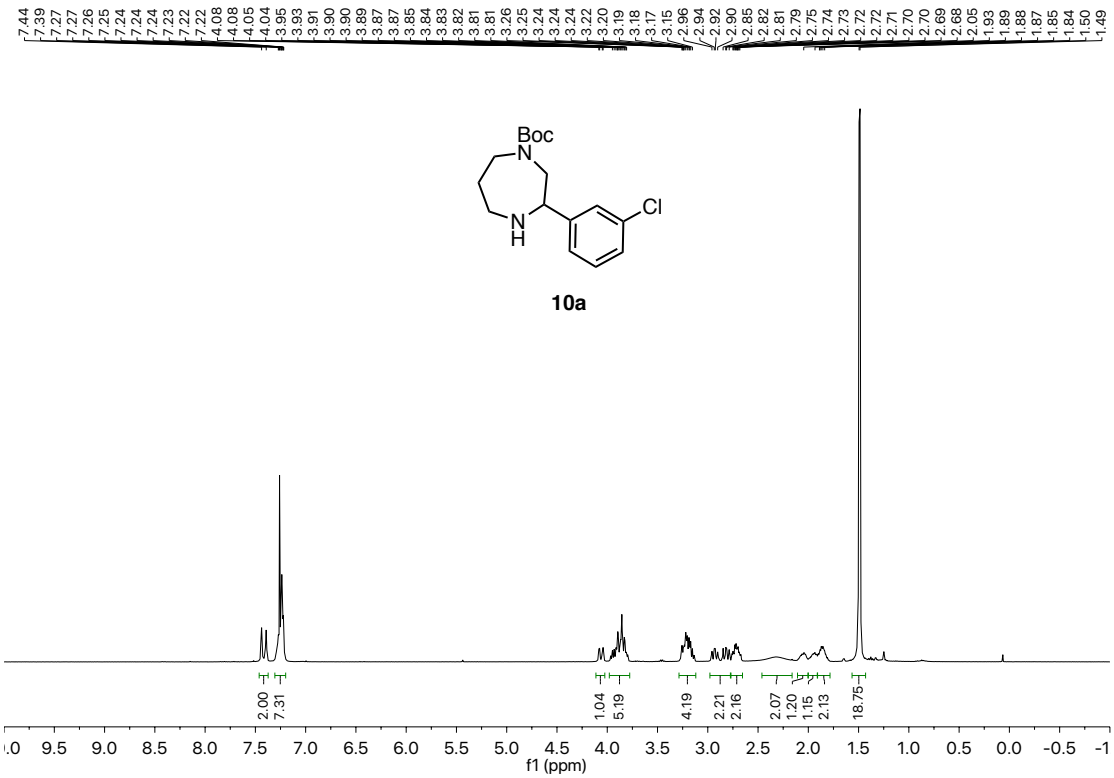

Boc
N
N
H
O
7h
f1 (ppm)

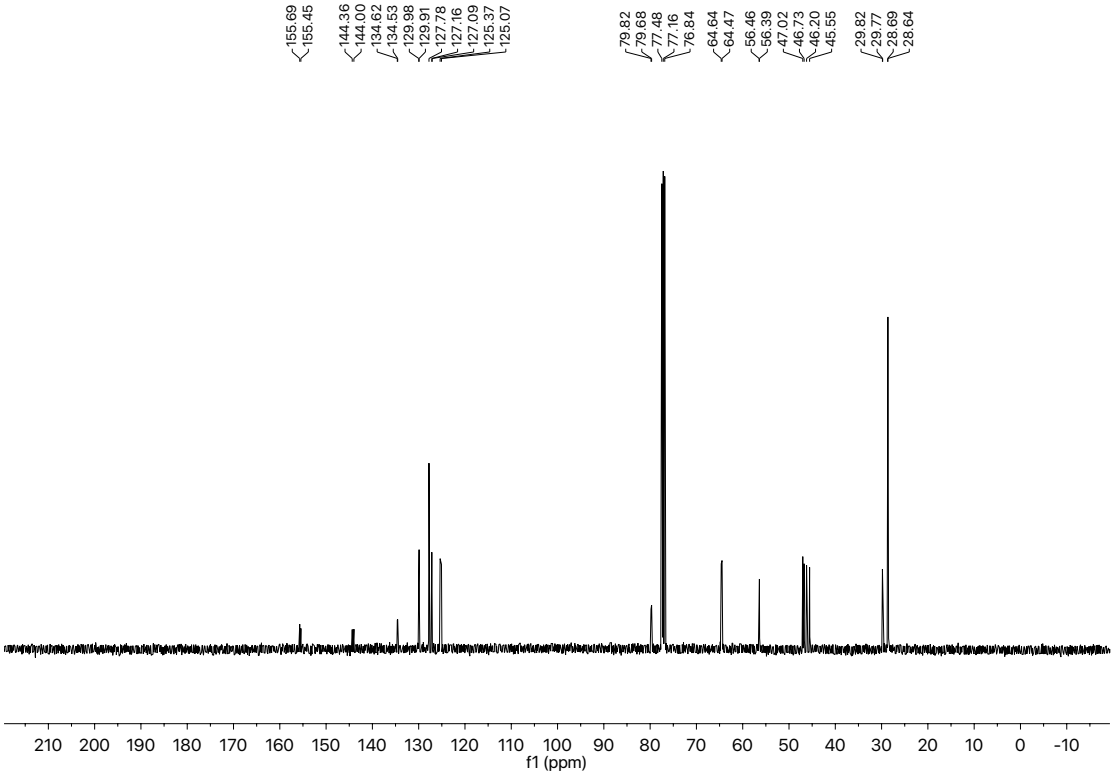

f1 (ppm)

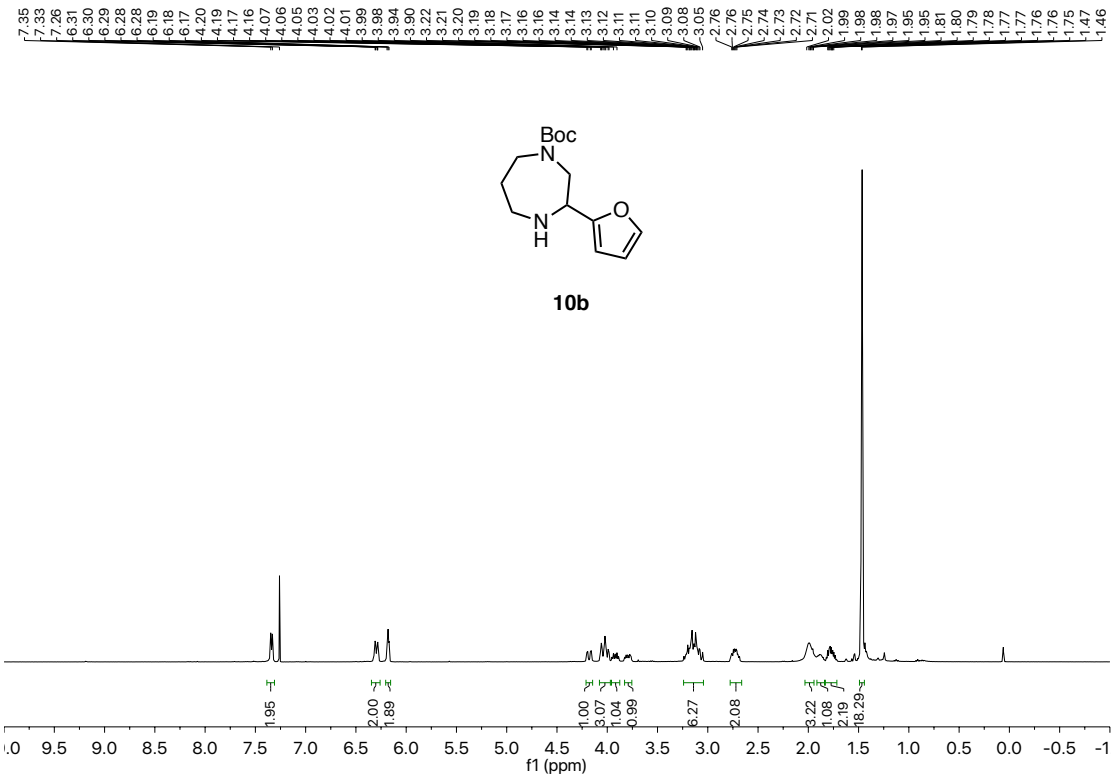

7.26
6.84
4.12
4.11
4.09
4.08
4.06
3.88
3.86
3.85
3.83
3.16
3.10
3.09
3.08
3.07
3.07
2.92
2.89
2.86
2.86
2.84
2.83
2.81
2.80
2.51
2.25
1.65
1.47
Boc
N
N
H
Me
Me
Me
2.00
1.90
1.06
2.04
2.08
5.88
3.20
1.29
9.52
f1 (ppm)

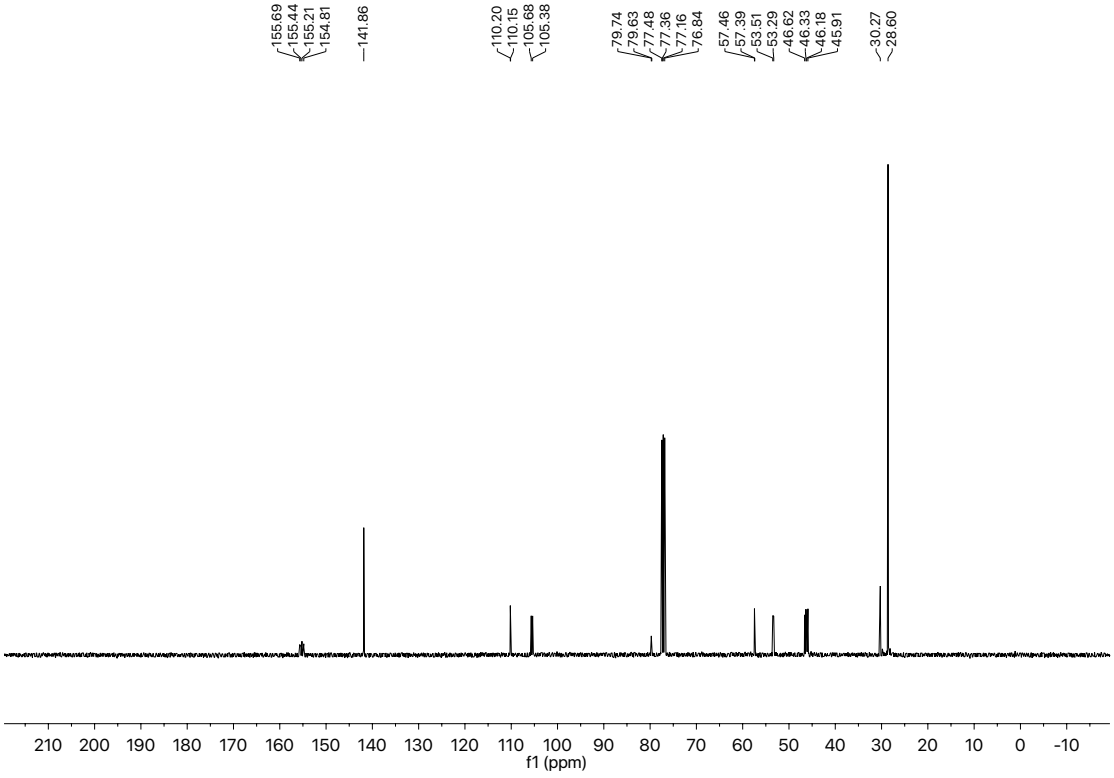
7i

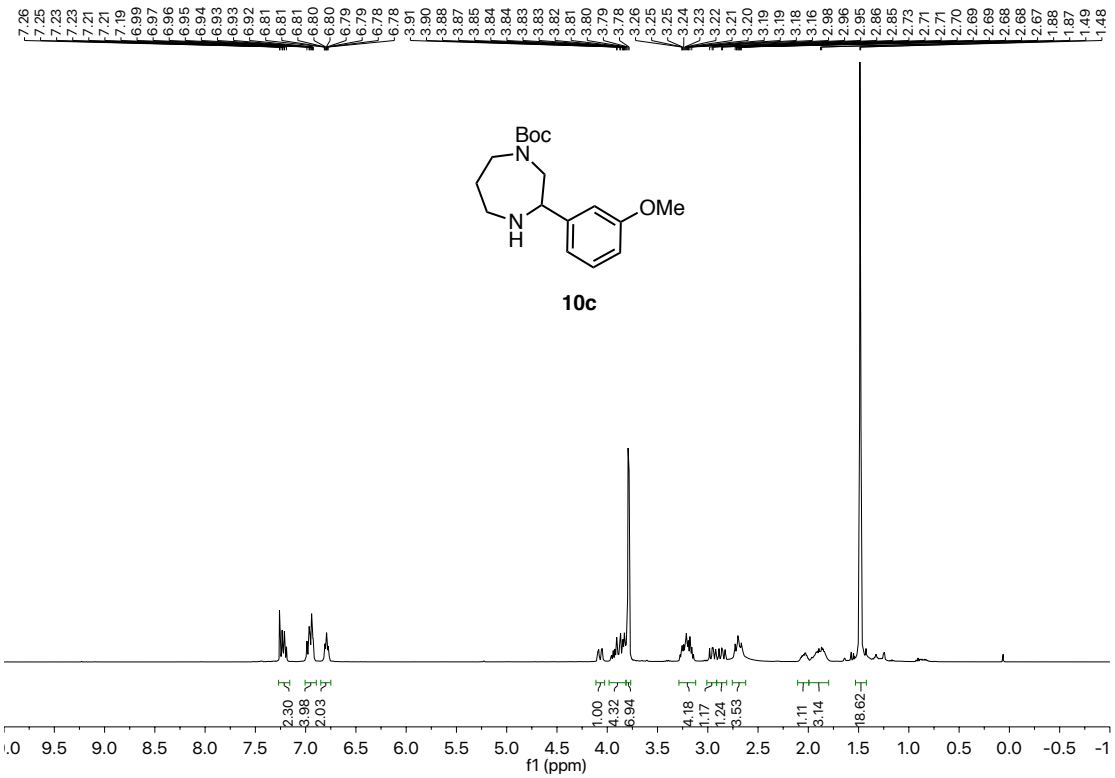

155.06
137.40
136.79
133.83
130.35
79.64
77.48
77.16
76.84
58.06
47.42
47.14
43.72
28.62
21.58
20.82
f1 (ppm)

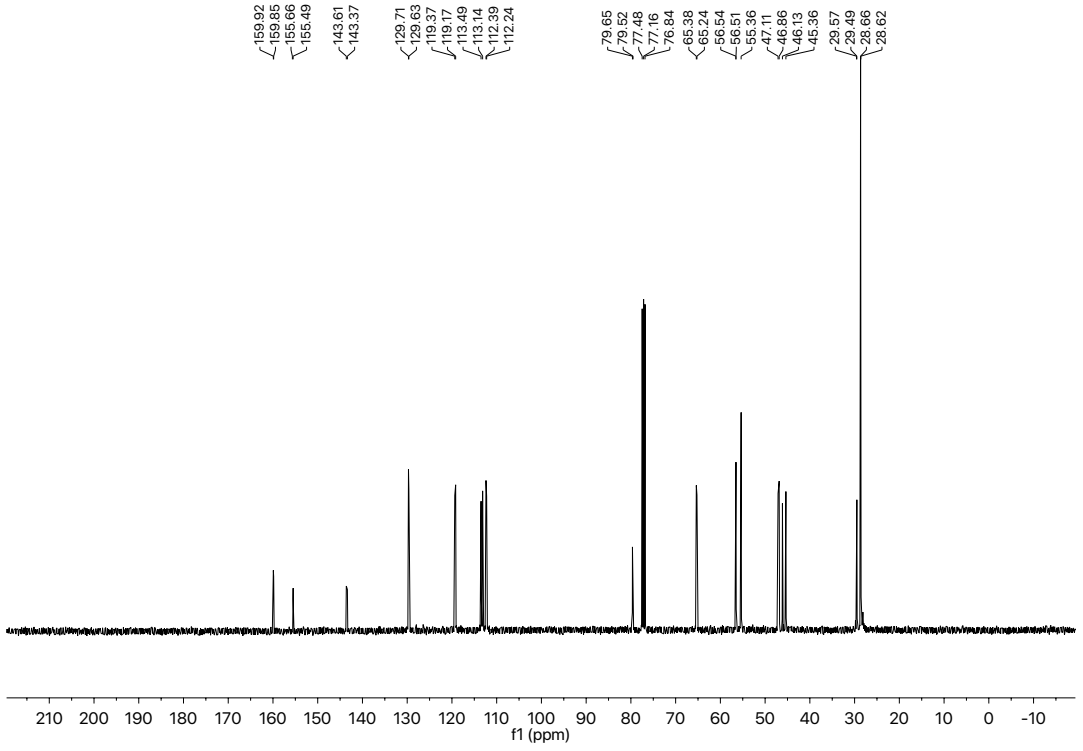

Boc
N
N
H
Cl
10a
2.00
7.31
1.04
5.19
4.19
2.21
2.16
2.07
1.20
1.15
2.13
18.75
f1 (ppm)

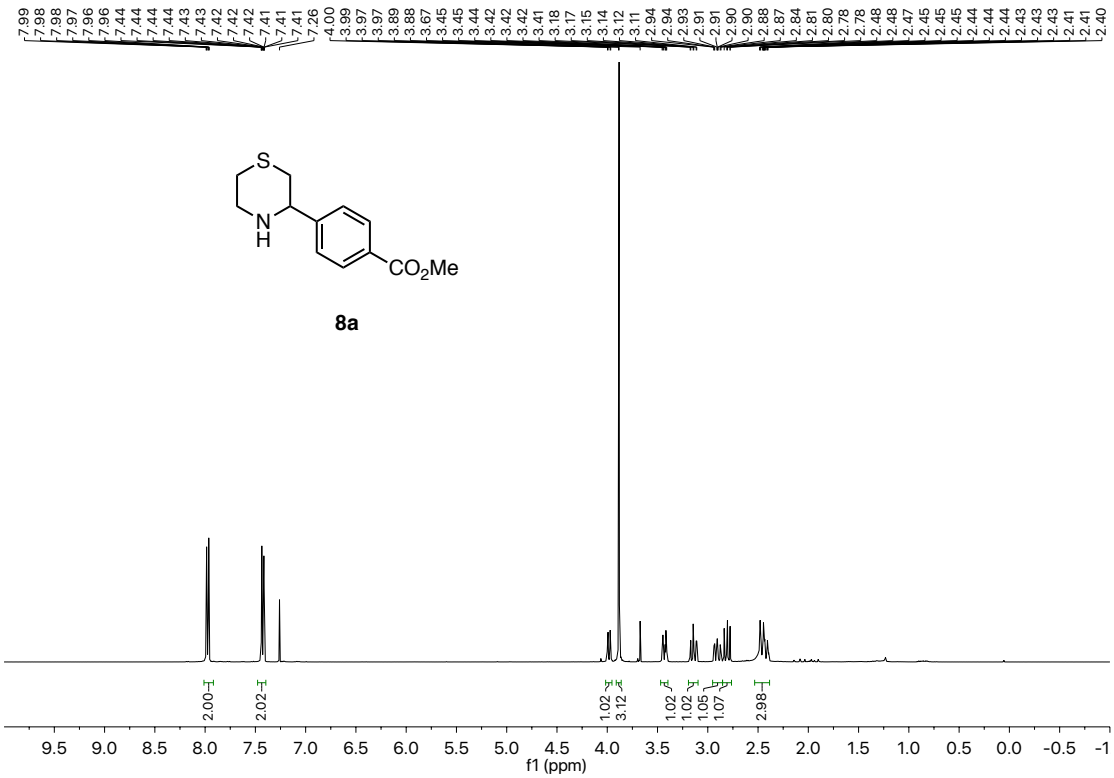

f1 (ppm)

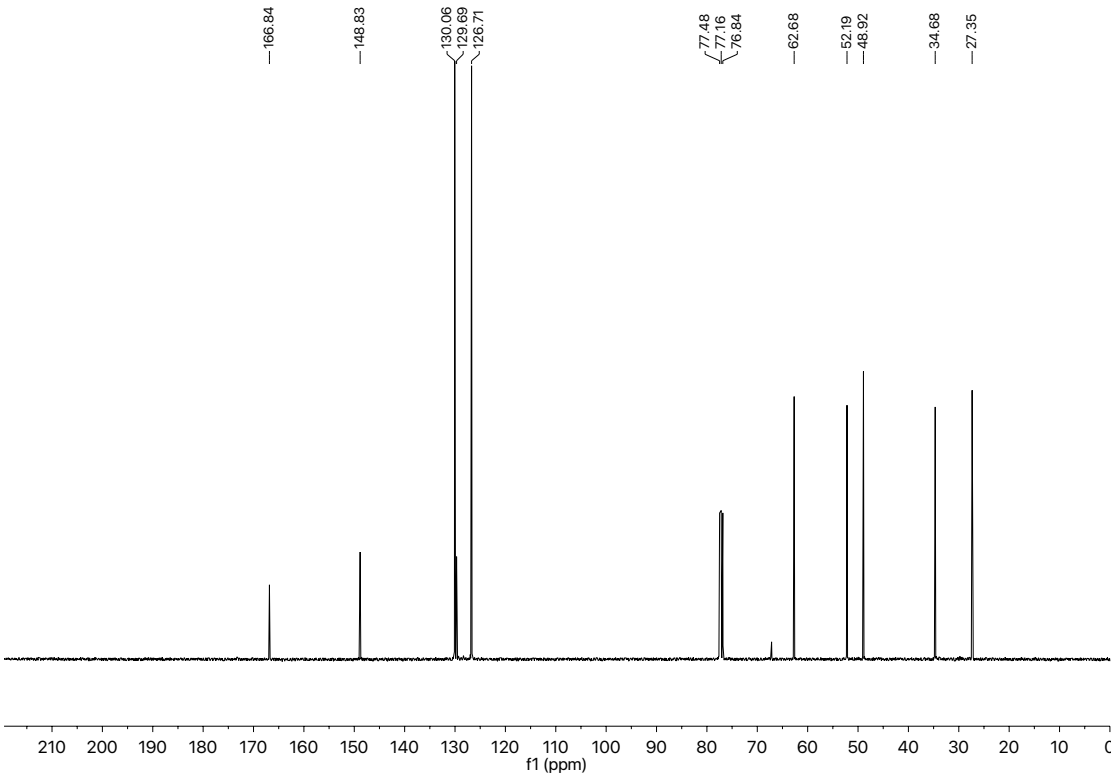

Boc
N
N
H
O
10b
f1 (ppm)

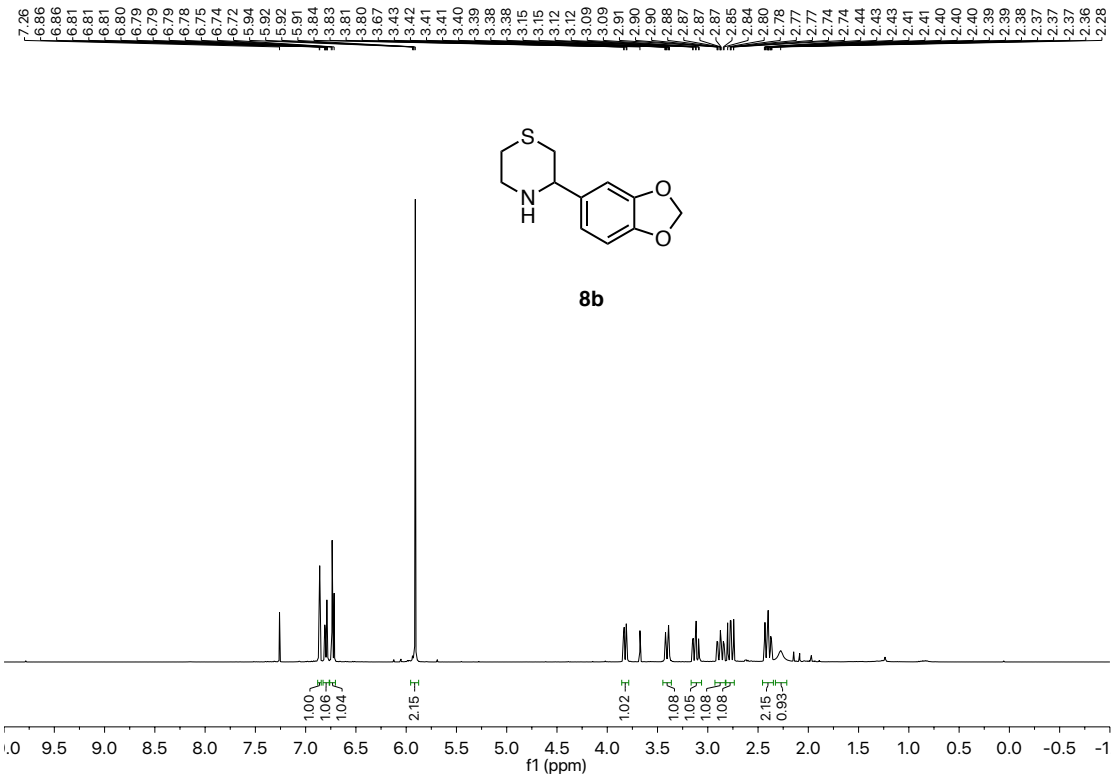

f1 (ppm)

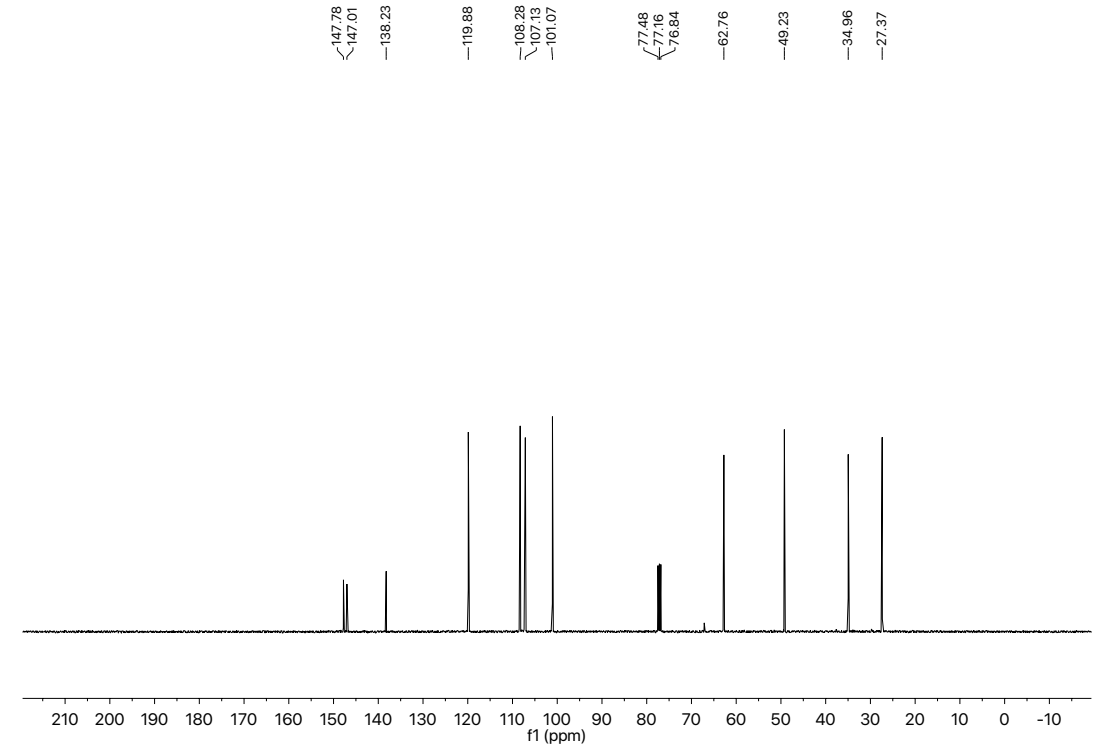

Boc
N
N
H
OMe
10c
f1 (ppm)

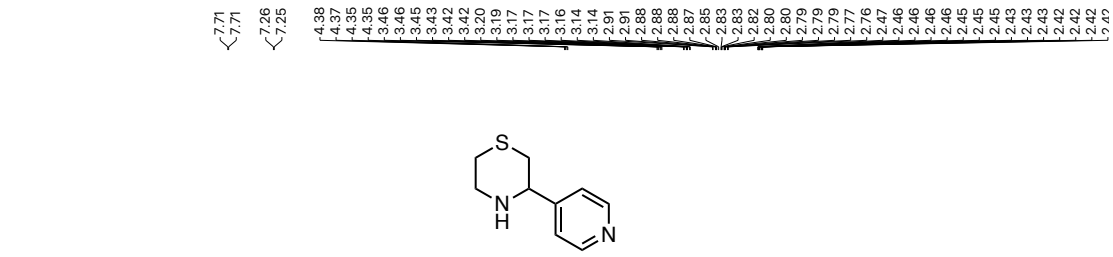

f1 (ppm)


7.99
7.98
7.98
7.97
7.96
7.96
7.44
7.44
7.44
7.44
7.43
7.43
7.42
7.42
7.42
7.41
7.41
7.41
7.26
4.00
3.99
3.97
3.97
3.89
3.88
3.67
3.45
3.45
3.44
3.42
3.42
3.42
3.41
3.18
3.17
3.15
3.14
3.12
3.11
2.94
2.94
2.93
2.91
2.91
2.90
2.90
2.88
2.87
2.84
2.81
2.80
2.78
2.48
2.48
2.47
2.45
2.45
2.44
2.44
2.44
2.43
2.43
2.41
2.41
2.40
S
N
H
CO2Me
8a
2.00
2.02
1.02
3.12
1.02
1.02
1.05
1.07
2.98
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
f1 (ppm)

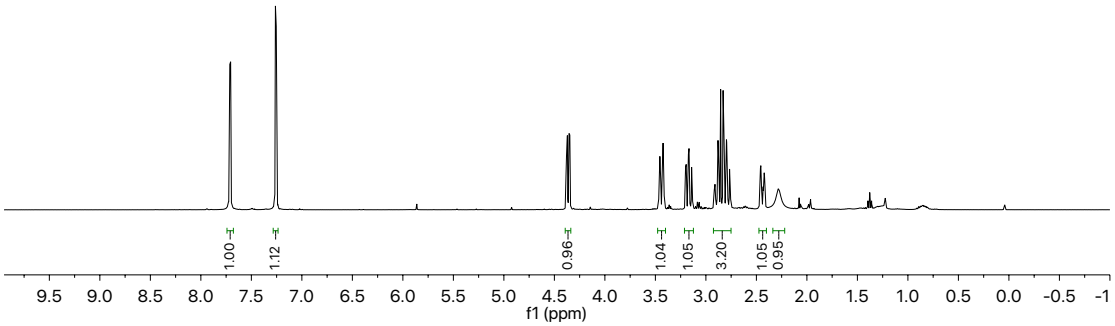

166.84
148.83
130.06
129.69
126.71
77.48
77.16
76.84
62.68
52.19
48.92
34.68
27.35
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

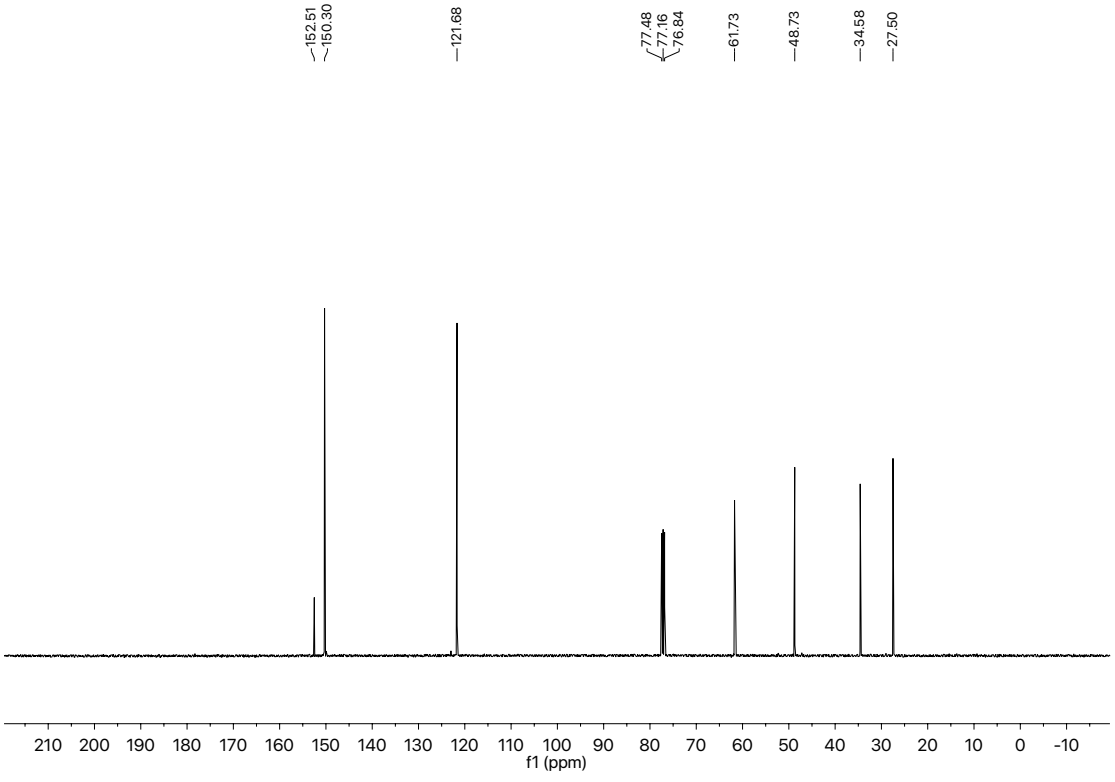

7.26
6.86
6.86
6.81
6.81
6.81
6.80
6.79
6.79
6.79
6.78
6.75
6.74
6.72
5.94
5.92
5.92
5.91
3.84
3.83
3.81
3.80
3.67
3.43
3.42
3.41
3.41
3.40
3.39
3.38
3.38
3.15
3.15
3.12
3.12
3.09
3.09
3.09
2.91
2.90
2.90
2.88
2.87
2.87
2.87
2.85
2.84
2.80
2.78
2.77
2.74
2.74
2.44
2.43
2.43
2.41
2.41
2.40
2.40
2.40
2.39
2.39
2.38
2.37
2.37
2.36
2.28
S
N
H
O
O
8b
1.00
1.06
1.04
2.15
1.02
1.08
1.05
1.08
1.08
2.15
0.93
f1 (ppm)

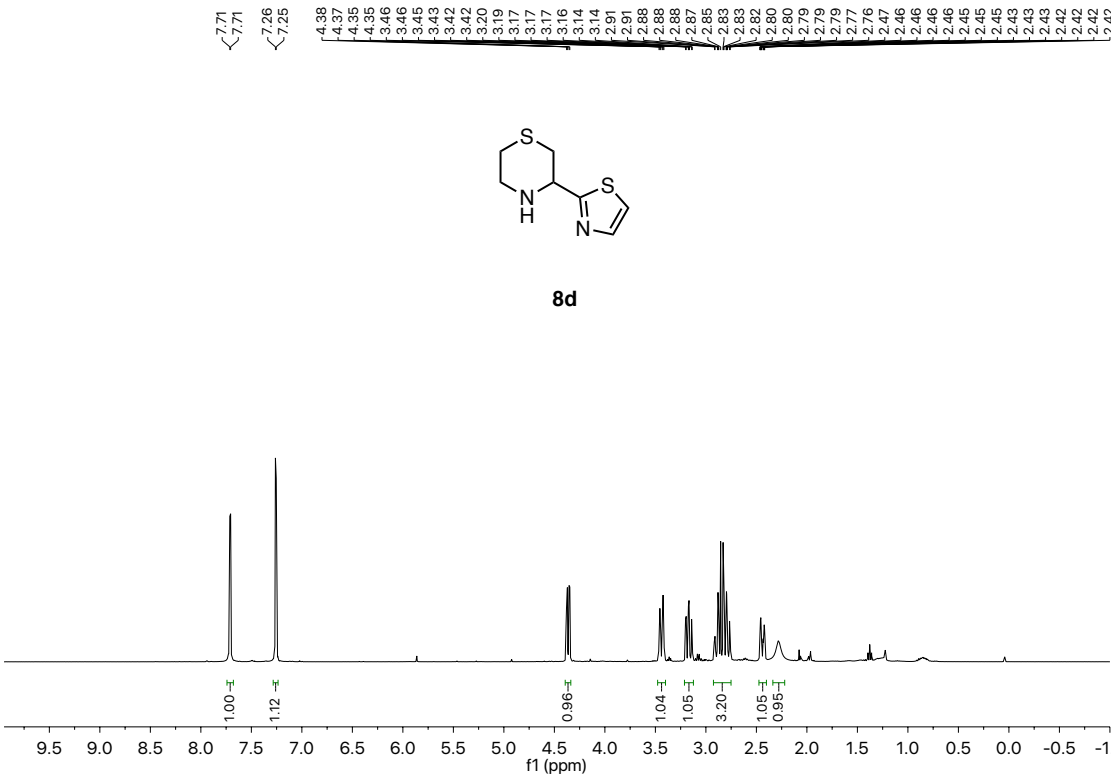

147.78
147.01
138.23
119.88
108.28
107.13
101.07
77.48
77.16
76.84
62.76
49.23
34.96
27.37
f1 (ppm)

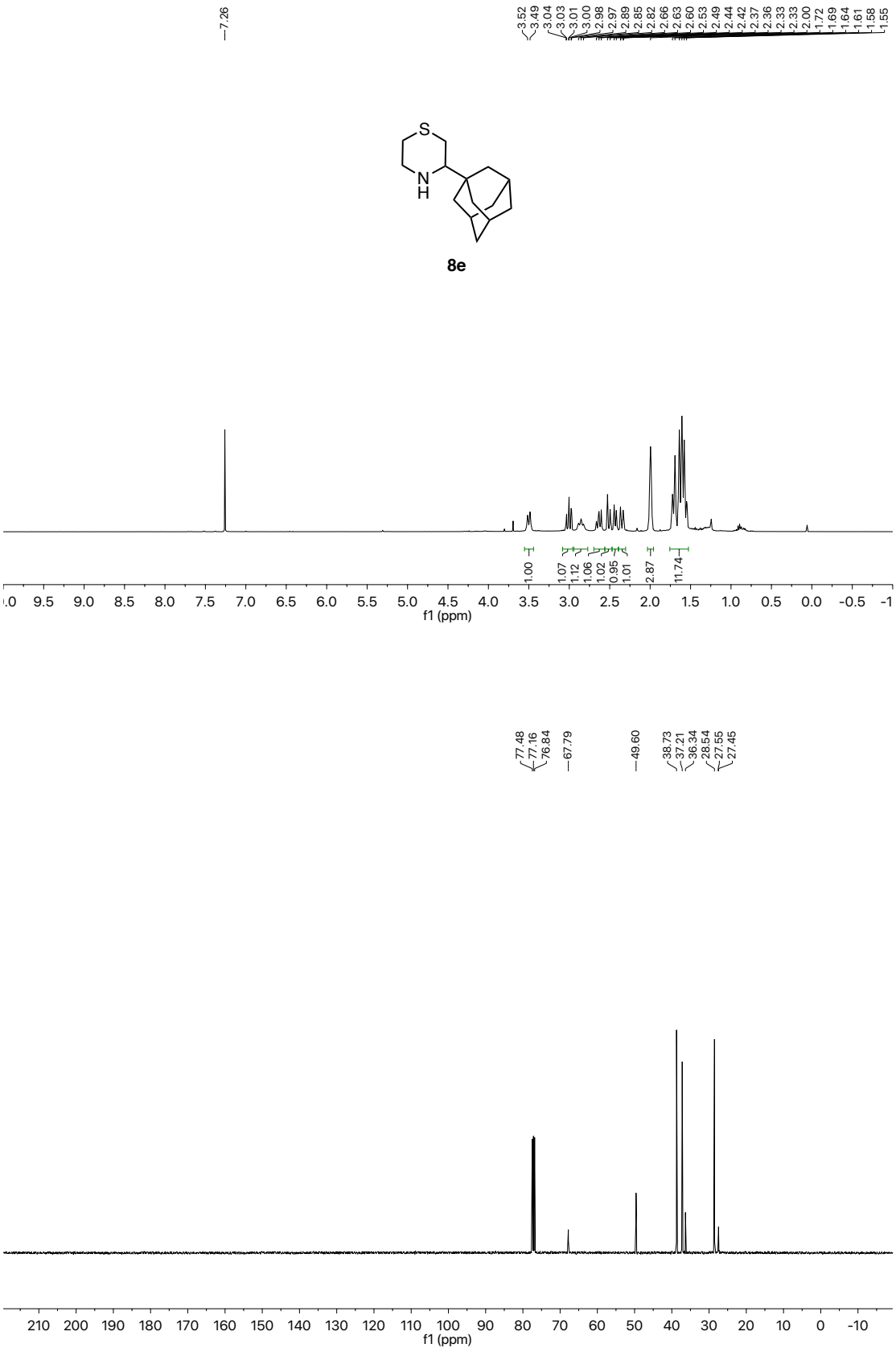


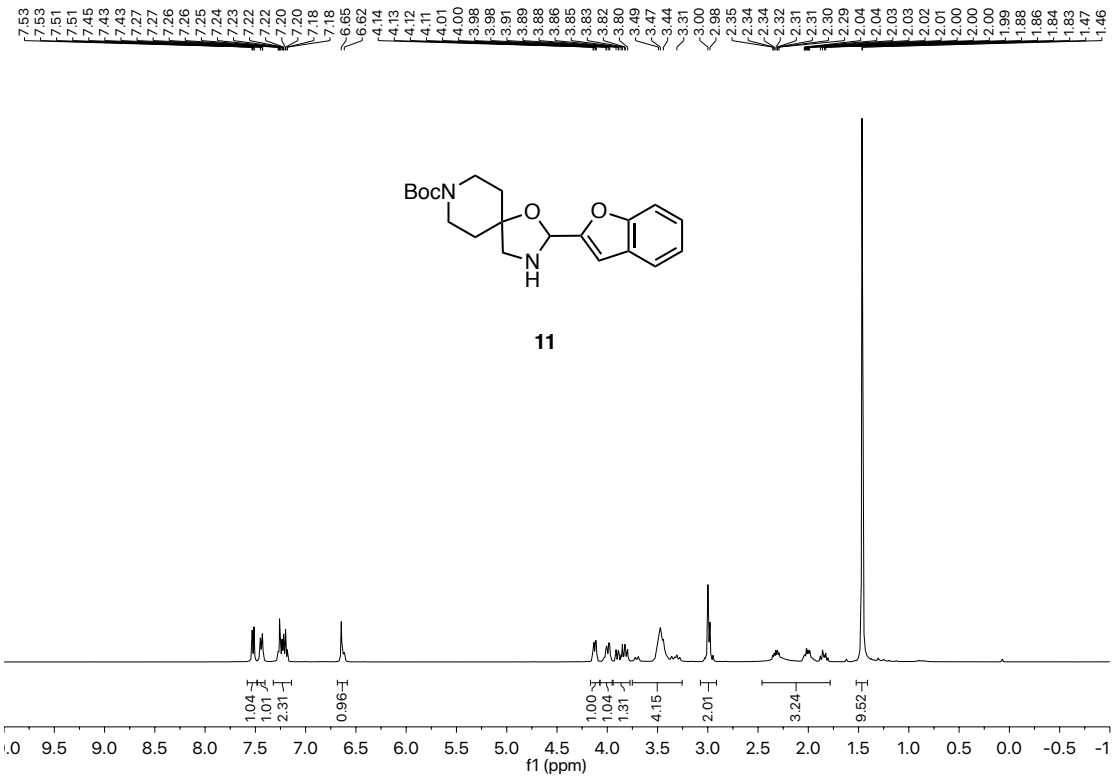
8c

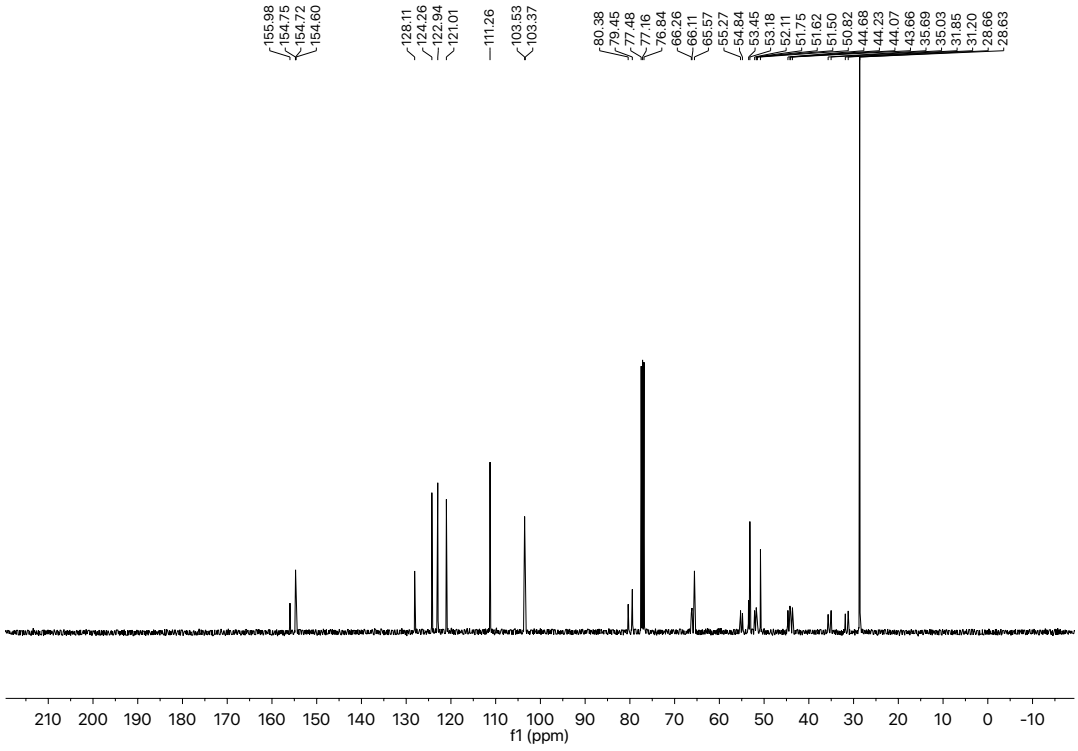

1.00
1.12
0.96
1.04
1.05
3.20
1.05
0.95
f1 (ppm)


152.51
150.30
121.68
77.48
77.16
76.84
61.73
48.73
34.58
27.50
f1 (ppm)


7.71
7.71
7.26
7.25
4.38
4.37
4.35
4.35
3.46
3.46
3.45
3.43
3.42
3.42
3.20
3.19
3.17
3.17
3.17
3.16
3.14
3.14
2.91
2.91
2.88
2.88
2.88
2.87
2.85
2.83
2.83
2.82
2.80
2.80
2.79
2.79
2.79
2.77
2.76
2.47
2.46
2.46
2.46
2.46
2.45
2.45
2.45
2.43
2.43
2.43
2.42
2.42
2.42
S
N
H
S
N
8d
1.00
1.12
0.96
1.04
1.05
3.20
1.05
0.95
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
f1 (ppm)
173.01
142.52
118.91
77.48
77.16
76.84
59.12
47.95
33.57
27.60
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.26
3.52
3.49
3.04
3.03
3.01
3.00
2.98
2.97
2.89
2.85
2.82
2.66
2.63
2.60
2.53
2.49
2.44
2.42
2.37
2.36
2.33
2.33
2.00
1.72
1.69
1.64
1.61
1.58
1.55
S
N
H
8e
1.00
1.07
1.12
1.06
1.02
0.95
1.01
2.87
11.74
f1 (ppm)
77.48
77.16
76.84
67.79
49.60
38.73
37.21
36.34
28.54
27.55
27.45
f1 (ppm)


BocN
O
O
N
H
11
f1 (ppm)


f1 (ppm)