

Hydroarylation of Arenes via Reductive Radical-Polar Crossover

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I. General Information

Ia. General Reagent Information

Solvents used in anhydrous reactions were purified by passing over activated alumina and storing under argon. Reagents were purchased from Sigma-Aldrich, Alfa Aesar, Acros Organics, Combi-Blocks, Oakwood Chemicals, Astatech, and TCI America and used as received, unless stated otherwise. n-Butyllithium (n-BuLi) was used as a 1.6 M or 2.5 M solution in hexanes (Aldrich), and stored at 4 °C and titrated prior to use. Organic solutions were concentrated under reduced pressure on a rotary evaporator using a water bath. Chromatographic purification of products was accomplished using forced-flow chromatography on 230–400 mesh silica gel. Preparative HPLC was carried out using an Agilent Technologies 1260 Infinity HPLC with a 21.2 x 250 mm, 7 μ m pore size, ZORBAX Eclipse XDB-C18 Column. Eluents used were unmodified unless otherwise stated. Preparative thin-layer chromatography (PTLC) separations were carried out on 1000 μ m SiliCycle silica gel F-254 plates. Thin-layer chromatography (TLC) was performed on 250 μ m SiliCycle silica gel F-254 plates. Visualization of the developed chromatogram was performed by fluorescence quenching or staining using KMnO₄, p-anisaldehyde, or ninhydrin stains. Solvent was degassed by sonication under mild vacuum for 15 minutes. Photoredox catalysts 3DPAFIPN, 3DPA2FBN, 4CzIPN, 5CzBN, N-POX(Ph₂)₂ were all prepared according to literature procedures^{1,2}

Ib. General Analytical Information

Unless otherwise noted, all yields refer to chromatographically and spectroscopically (¹H NMR) homogenous materials. New compounds were characterized by NMR, IR, HRMS, and melting point (when solid). ¹H and ¹³C NMR spectra were obtained from the Emory University NMR facility and recorded on a Bruker Avance III HD 600 equipped with cryo-probe (600 MHz), INOVA 600 (600 MHz), INOVA 500 (500 MHz), INOVA 400 (400 MHz), VNMR 400 (400 MHz), or Mercury 300 (300 MHz), and are internally referenced to residual protio solvent signals. Data for ¹H NMR are reported as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, dtd = doublet of triplet of doublets, b = broad, etc.), coupling constant (Hz), integration, and assignment, when applicable. Data for decoupled ¹³C NMR are reported in terms of chemical shift and multiplicity when applicable. IR spectra were recorded on a Thermo Fisher DiamondATR and reported in terms of frequency of absorption (cm⁻¹). High resolution mass spectra were obtained through the use of an Agilent 6230 electrospray ionization time-of-flight (ESI-TOF) mass spectrometer. Gas Chromatography Mass Spectrometry (GC-MS) was performed on an Agilent 5977A mass spectrometer with an Agilent 7890A gas chromatography inlet. Liquid Chromatography Mass Spectrometry (LC-MS) was performed on an Agilent 6120 mass spectrometer with an Agilent 1220 Infinity liquid chromatography inlet. Preparative High Pressure Liquid chromatography (Prep-HPLC) was performed on an Agilent 1200 Infinity Series chromatograph using an Agilent Prep-C18 30 x 250 mm 10 μ m column, or an Agilent Prep-C18 21.2 x 100 mm, 5 μ m column.

Ic. Abbreviations

PTFE = polytetrafluoroethylene

DMAP = 4-dimethylaminopyridine

DMSO = dimethyl sulfoxide

DMF = dimethylformamide

DMA = dimethylacetamide

THF = tetrahydrofuran

DCM = dichloromethane

HPLC = high performance liquid chromatography

TLC = thin layer chromatography

DIPEA = diisopropylethylamine

TEA = triethylamine

EtOAc = ethyl acetate

MeCN = acetonitrile

LCMS = liquid chromatography mass spectrometry

GCMS = gas chromatography mass spectrometry

MeOH = methanol

HBTU = *N,N,N',N'*-Tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate

Miyake Phenoxazine = 3,7-Di(4-biphenyl) 1-naphthalene-10-phenoxazine, 3,7-Di([1,1'-biphenyl]-4-yl)-10-(naphthalen-1-yl)-10*H*-phenoxazine

II. General Procedures

IIa. General Procedure A

A 20 mL screw-top test tube was charged with photocatalyst (0.025 mmol, 5 mol%), and substrate (0.5 mmol, 1.0 equiv). The tube was equipped with a stir bar was sealed with a PTFE/silicon septa. The atmosphere was exchanged by applying vacuum and backfilling with nitrogen (this process was conducted a total of three times). Under nitrogen atmosphere, separate degassed solvent was added via syringe (7.5 mL of each MeCN and H₂O to give a 0.03 M solution), followed by DIPEA (3.0 equiv). The resulting mixture was stirred at 1400 RPM for 16 h under irradiation by blue LEDs, unless noted otherwise. The reaction was then extracted with ethyl acetate (3 x), dried with MgSO₄, and concentrated. The residue was purified on silica using the indicated solvent mixture as eluent to afford the title compound.

IIb. General Procedure B

A 20 mL screw-top test tube was charged with photocatalyst (0.025 mmol, 5 mol%), and substrate (0.5 mmol, 1.0 equiv). The tube was equipped with a stir bar was sealed with a PTFE/silicon septa. The atmosphere was exchanged by applying vacuum and backfilling with nitrogen (this process was conducted a total of three times). Under nitrogen atmosphere, separated degassed solvent was added via syringe (7.5 mL of each MeCN and H₂O to give a 0.03 M solution), followed by DIPEA (10.0 equiv). The resulting mixture was stirred at 1400 RPM for 16 h under irradiation by blue LEDs, unless noted otherwise. The reaction was then extracted with ethyl acetate (3 x), dried with MgSO₄, and concentrated. The residue was purified on silica using the indicated solvent mixture as eluent to afford the title compound.

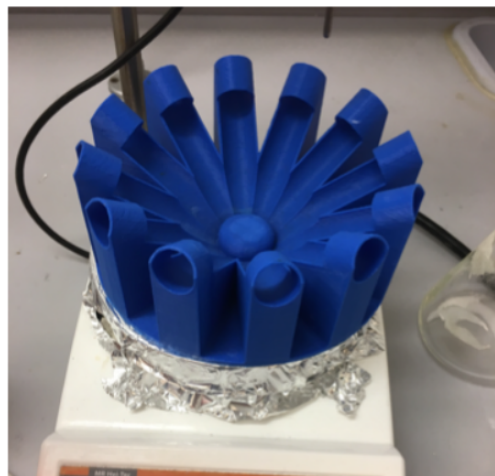
III. Optimization Details

IIIa. Optimization Procedure

An 8 mL screw-top test tube was charged with photocatalyst (0.005 mmol, 5 mol%) and 3-(benzyloxy)-2-bromopyridine (0.1 mmol, 1.0 equiv). The tube was equipped with a stir bar and sealed with a PTFE/silicon septa. The atmosphere was exchanged by applying vacuum and backfilling with nitrogen (this process was conducted a total of three times). Under nitrogen atmosphere, separately degassed solvent was added via syringe, followed by reductant. The resulting mixture was stirred at 800 RPM for 16 h under irradiation by blue LEDs, unless noted otherwise. The reaction was then extracted with ethyl acetate (3 x), washed with brine, dried with MgSO₄, and concentrated. Deutero-chloroform with an internal standard of dibromomethane (7 μL, 0.1 mmol) was added. The sample was analyzed by ¹H NMR (d = 5 s), and the integral values were used to calculate the data given in Table S1.

IIIb. Reaction Setup

All photoredox reactions were set up on the bench top and conducted under nitrogen atmosphere while subject to irradiation from blue LEDs, unless stated otherwise (LED wholesalers PAR38 Indoor Outdoor 16-Watt LED Flood Light Bulb, Blue; or Hydrofarm® PPB1002 PowerPAR LED Bulb-Blue 15W/E27 (available from Amazon). Ambient temperature was maintained by using either a fan or compressed air line. Shown below is a photograph of the reaction setup, where the LED array was positioned approximately 6 inches above the test tubes containing reaction mixture. For convenience, a 3D printed reaction carousel was utilized, where up to 12 reactions could be conducted simultaneously.



Reaction carousel



Positioning of LED array



Reaction setup

Table S1: Optimization of Dearomative Hydroarylation Reaction

BrC1=CC=C(C=C1)OCC2=CC=CC=C2
 $\xrightarrow[\text{solvent, blue LEDs, 16 h}]{\text{PC (5 mol\%) reductant}}$
C1=CC=C(C=C1)C2=CC=CC=C2
OCC3=CC=CC=C3
C1=CC=C(C=C1)C2=CC=CC=C2

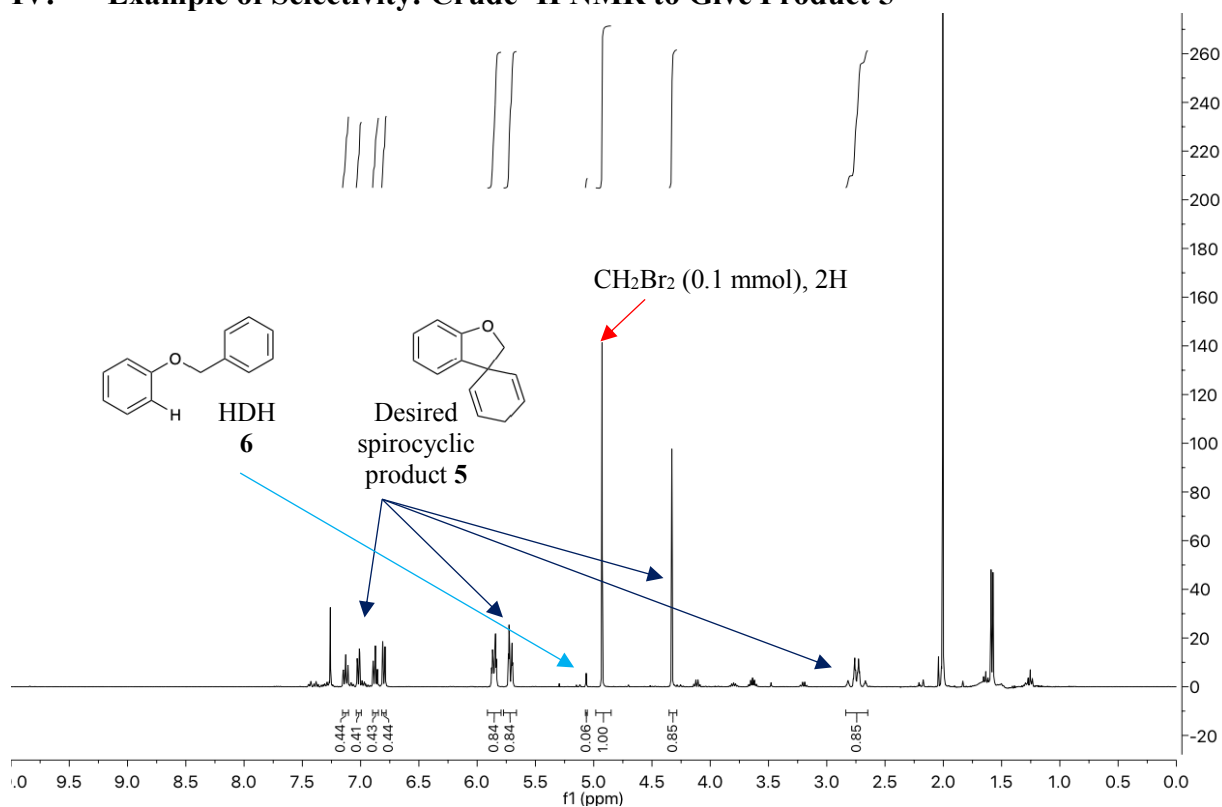
S6
12
HDH
Dimer

(Hydrodehalogenation)

Entry	PC	Reductant (equiv)	% Water	Cosolvent (rxn conc)	S6	12	HDH	Dimer
1	3DPAFIPN	tributylamine (3)	10	DMF (0.1 M)	19	29	27	0
2	3DPAFIPN	tributylamine (3)	10	EtOH (0.1 M)	2	51	20	0
3	3DPAFIPN	tributylamine (3)	10	TFE (0.1 M)	0	57	7	15
4	3DPAFIPN	tributylamine (3)	10	DMSO (0.1 M)	11	43	7	0
5	3DPAFIPN	tributylamine (3)	10	MeCN (0.1 M)	0	60	19	0
6	3DPAFIPN	tributylamine (3)	50	MeCN (0.1 M)	0	71	14	0
7	3DPAFIPN	tributylamine (3)	80	MeCN (0.1M)	0	39	66	0
8	3DPAFIPN	DIPEA (3)	0	MeCN (0.03 M)	6	68	13	8
9	3DPAFIPN	DIPEA (3)	50	MeCN (0.1 M)	0	81	21	0
10	3DPAFIPN	DIPEA (3)	50	MeCN (0.03M)	5	86	6	0
11	4CzIPN	DIPEA (3)	50	MeCN (0.03 M)	46	49	5	0
12	5CzBN	DIPEA (3)	50	MeCN (0.03 M)	36	46	20	0
13	3DPA2FBN	DIPEA (3)	50	MeCN (0.03 M)	0	66	5	9
14	Ir(ppy) ₂ (dtbbpy) PF ₆	DIPEA (3)	50	MeCN (0.03 M)	14	66	15	0
15	Ir(ppy) ₃	DIPEA (3)	50	MeCN (0.03 M)	17	31	8	14
16 ^a	3DPAFIPN	DIPEA (3)	50	MeCN (0.03 M)	49	44	5	0
17	3DPAFIPN	none	50	MeCN (0.03 M)	100	0	0	0
18	none	DIPEA (3)	50	MeCN (0.03 M)	100	0	0	0
19 ^b	3DPAFIPN	DIPEA (3)	50	MeCN (0.03 M)	100	0	0	0

^aReaction conducted open to air (typically conducted after degassing, under N₂). ^bReaction conducted in the dark (tube wrapped in aluminum foil).

IV. Example of Selectivity: Crude ^1H NMR to Give Product 5



1-(benzyloxy)-2-iodobenzene (0.1 mmol) was subjected to General Conditions A. The reaction was then extracted with ethyl acetate (3 x), dried with MgSO_4 , and concentrated. Deutero-chloroform with an internal standard of dibromomethane (7 μL , 0.1 mmol) was added. The sample was analyzed by ^1H NMR ($d = 5$ s), and the integral values are shown in the crude NMR above. NMR was compared to (and was consistent with) reported literature values: *J. Org. Chem.* **2008**, 73 (18), 7145–7152.

V. Fluorescence Quenching and Stern-Volmer Plots

All fluorescence measurements were recorded using a Horiba Scientific Dual-FL Fluorometer. Quenching studies were conducted in MeCN at 20 ± 0.5 °C (Peltier temperature controller) with a photocatalyst (3DPAFIPN) concentration of 9.01×10^{-6} M. Samples were prepared in Starna quartz cuvettes (3-Q-10-GL14-S) with septum seal caps. Dry N₂ was bubbled through the prepared sample for 4 minutes before analysis. Raw fluorescence intensity was measured at $\lambda = 542$ nm after excitation at $\lambda = 380$ nm in the quartz cuvettes with a path length of 1 cm and 0.1 second integration. Measurements of the quenchers shown were plotted using Igor Pro 8; data points were fit with a linear trend line.

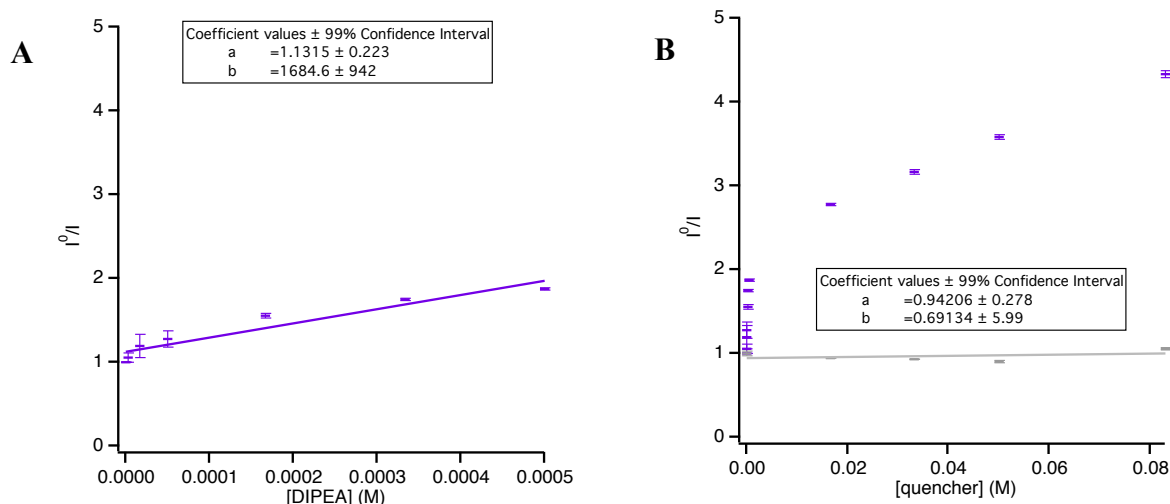


Figure S1: Stern-Volmer plots for (A) DIPEA at low concentrations and (B) DIPEA and 3-(benzyloxy)-2-bromopyridine up to $\sim 10,000$ equivalents with respect to photocatalyst 3DPAFIPN.

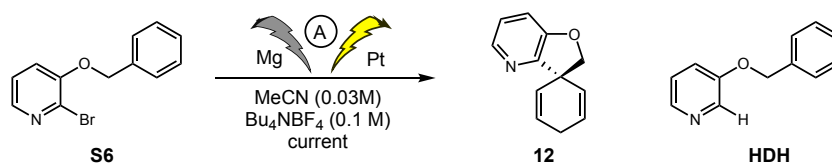
Table S2: Fluorescence Quenching Data

Compound (Quencher)	[Quencher] (M)	I^0/I	Equiv vs PC	Coefficients
Diisopropylethylamine	0	1	0	$y = a + bx$
Diisopropylethylamine	3.3×10^{-6}	1.06	0.4	$a = 1.1 \pm 0.2$
Diisopropylethylamine	1.67×10^{-5}	1.20	1.9	$b = 1684 \pm 942$
Diisopropylethylamine	5.0×10^{-5}	1.27	5.6	
Diisopropylethylamine	1.67×10^{-4}	1.56	19	$\pm 99\% \text{ CI}$
Diisopropylethylamine	3.33×10^{-4}	1.76	37	
Diisopropylethylamine	5.0×10^{-4}	1.88	55	
Diisopropylethylamine	1.67×10^{-2}	2.77	1854	
Diisopropylethylamine	3.33×10^{-2}	3.16	3696	
Diisopropylethylamine	5.0×10^{-2}	3.59	5549	
Diisopropylethylamine	8.3×10^{-2}	4.33	9212	
3-(benzyloxy)-2-bromopyridine	0	1	0	$y = a + bx$
3-(benzyloxy)-2-bromopyridine	1.67×10^{-2}	0.94	1854	$a = 0.94 \pm 0.28$
3-(benzyloxy)-2-bromopyridine	3.33×10^{-2}	0.94	3696	$b = 0.69 \pm 5.99$
3-(benzyloxy)-2-bromopyridine	5.0×10^{-2}	0.91	5549	
3-(benzyloxy)-2-bromopyridine	8.3×10^{-2}	1.06	9212	$\pm 99\% \text{ CI}$

VI. Evaluation of Electrochemical Hydroarylation

To an ElectraSyn vial charged with stir bar was added 3-(benzyloxy)-2-bromopyridine (0.2 mmol, 1 equiv), electrolyte (to make the indicated concentration), and solvent (6 mL) An IKA Mg (anode) and Pt (cathode) plate electrodes were connected to an ElectraSyn vial cap. The ElectraSyn was setup as follows: New exp. > constant current > **X** mA (current)> no ref. electrode > total charge > 0.2 mmol, 3 F/mol > no alternating polarity > start. The reaction was allowed to run with stirring until the ElectraSyn had measured 3 F/mol input. The reaction was then concentrated. Deutero-chloroform with an internal standard of dibromomethane (7 μ L, 0.1 mmol) was added. The sample was analyzed by ^1H NMR (d = 5 s), and the integral values were used to calculate the data given in Table S3.

Table S3: Results from Hydroarylation Under Electrochemical Conditions



entry	current	S6	12	HDH
1	2 mA	100	0	0
2	5 mA	71	0	30
3	10 mA	28	3	60
4	50 mA	29	8	63

VII. Unsuccessful Substrates in Dearomatization

Shown below are substrate classes that did not afford the desired spirocyclic products under standard conditions. The most pronounced limitation here involves electron-deficient aromatics, which are highlighted in gray. In these specific cases, linker fragmentation was the dominant pathway where the observed products arise from arene radical anion formation followed by mesolytic cleavage. In addition, the secondary amide and ester based substrates did not undergo cyclization. Rather, the primary reaction outcome here was hydrodehalogenation, presumably the result of energetic preferences for the linear conformation.

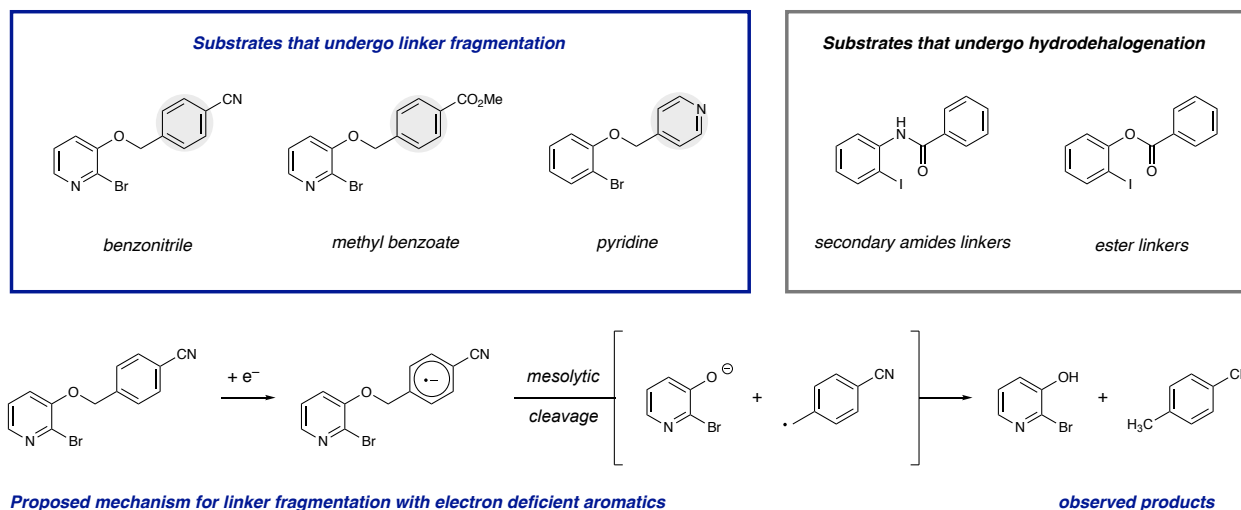
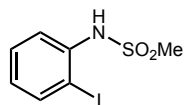


Figure S2. Unsuccessful Dearomatization Substrate Classes

VIII. Preparation of Starting Materials



***N*-(2-iodophenyl)methanesulfonamide (S1)**

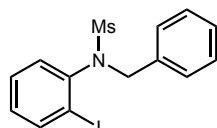
To a solution of 2-iodoaniline (572 mg, 2.6 mmol, 1 equiv) in dichloromethane (25 mL) was added methanesulfonyl chloride (250 μ L, 3.2 mmol, 1.2 equiv) dropwise via syringe, followed by pyridine (250 μ L, 2.8 mmol, 1.1 equiv). The resulting mixture was stirred at room temperature for 4 h and concentrated. The resulting residue was purified on silica gel (20–50% eluent) to afford the title compound as a white solid (770 mg, >99%).

¹H NMR (399 MHz, CDCl₃) δ 7.80 (dd, J = 8.0, 1.5 Hz, 1H), 7.61 (dd, J = 8.2, 1.5 Hz, 1H), 7.35 (tdd, J = 8.0, 1.5, 0.5 Hz, 1H), 6.91 (ddd, J = 8.0, 7.4, 1.5 Hz, 1H), 6.67 (bs, 1H), 2.99 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 139.4, 137.6, 129.9, 127.3, 122.6, 92.3, 40.2.

LRMS (APCI) m/z : [M-H]⁻ calc'd. for C₇H₇INO₂S, 295.9; found 295.8

¹H NMR spectrum is consistent with reported values³



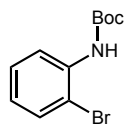
***N*-benzyl-*N*-(2-iodophenyl)methanesulfonamide (S2)**

A 20 mL screw-top vial was charged with *N*-(2-iodophenyl)methanesulfonamide (S1), (459 mg, 1.6 mmol, 1.0 equiv) and K₂CO₃ (365 mg, 2.6 mmol, 1.6 equiv). DMF was added (15 mL) followed by benzyl bromide (450 μ L, 3.7 mmol, 2.3 equiv). The reaction was stirred overnight (ca. 16 h) at room temperature, then heated to 60 °C and heated until starting material was consumed (as determined by LCMS). The reaction was cooled to room temperature and then partitioned between EtOAc and water. The organic layer was washed with brine 3x, dried with MgSO₄ and purified on silica gel (10-50% eluent) to afford the title compound as a colorless oil (394 mg, 66%).

¹H NMR (399 MHz, CDCl₃) δ 7.89 (d, J = 7.9 Hz, 1H), 7.25 (s, 6H), 7.03 (d, J = 7.9 Hz, 1H), 6.99 (t, J = 7.6 Hz, 1H), 5.05 (d, J = 14.6 Hz, 1H), 4.54 (d, J = 14.6 Hz, 1H), 3.04 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 140.7, 140.4, 135.4, 133.1, 130.2, 129.7, 129.0, 128.5, 128.2, 101.0, 54.9, 41.8.

LRMS (APCI) m/z : [M+H]⁺ calc'd. for C₁₄H₁₅INO₂S, 387.9; found 387.7

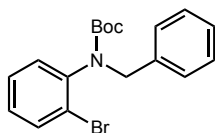


***tert*-butyl (2-bromophenyl)carbamate (S3):** In a round bottom flask, 2-bromoaniline (15 g, 88 mmol, 1.0 equiv) was dissolved in DCM (800 mL) and cooled to 0 °C. Di-*tert*-butyl decarbonate (43 g, 195 mmol, 2.2 equiv) was added slowly to the reaction over the course of 30 minutes. Dimethylaminopyridine (1.8 g, 15 mmol, 0.2 equiv) was then added slowly to the reaction mixture (caution: on this large scale significant exotherm and evolution of CO₂ is possible.). The resulting mixture was stirred until consumption of the starting material was detected by TLC. The reaction was then poured onto water, washed with NaHCO₃, and extracted with EtOAc x3. The combined organic layers were dried with MgSO₄. The crude oil was identified as the di-boc

product by ^1H NMR. One Boc was removed by stirring the crude oil in a dilute solution of TFA in DCM at 0 °C. This reaction was monitored carefully by TLC until the complete removal of one boc was detected. The reaction was then basified, poured onto water and extracted with EtOAc x3. The crude oil was purified on silica (10-30% EtOAc/Hex eluent) to afford the title product as a colorless oil (19 g, 80% over 2 steps).

^1H NMR (400 MHz, CDCl_3) δ 8.13 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 8.0, 1.7 Hz, 1H), 7.32 – 7.16 (m, 1H), 6.97 (bs, 1H), 6.88 (t, J = 7.7 Hz, 1H), 1.52 (s, 9H).

^1H NMR spectrum is consistent with reported values⁴

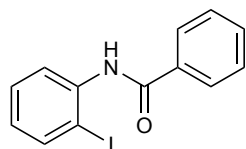


tert-butyl benzyl(2-bromophenyl)carbamate (S4): In a round bottom flask under nitrogen, sodium hydride as a 60% dispersion in mineral oil (180 mg, 4.5 mmol, 1.3 equiv) was suspended in DMF (20 mL) and cooled to 0 °C. **S3** as a solution in DMF (976 mg, 3.6 mmol, 1.0 equiv in about 10 mL DMF) was added dropwise to the sodium hydride suspension and stirred for 30 minutes before the addition of benzyl bromide (513 μL , 4.3 mmol, 1.2 equiv). The reaction was removed from the ice bath, and after reacting for 4.5 h was quenched with methanol then water at 0 °C. The resulting mixture was diluted with ethyl acetate and washed with brine 3x. The organic layer was dried with MgSO_4 , concentrated *in vacuo*, and purified on silica gel (5% EtOAc/Hex eluent) to afford the title compound as a colorless oil (238 mg, >99%).

^1H NMR (500 MHz, CDCl_3 , 60 °C) δ 7.59 (bd, J = 7.9 Hz, 1H), 7.26 (bm, 5H), 7.10 (bm, 2H), 6.84 (bs, 1H), 5.21 (s, 1H), 4.23 (d, J = 14.9 Hz, 1H), 1.44 (bm, J = 61.2 Hz, 9H).

^{13}C NMR (151 MHz, CDCl_3 , 60 °C) δ 154.4, 141.2, 137.9, 133.1, 130.9, 128.9, 128.4, 128.2, 127.6, 127.3, 123.8, 80.5, 52.7, 28.2.

LRMS (APCI) m/z: $[\text{M}-\text{C}_4\text{H}_9\text{H} + \text{H}]^+$ calc'd. for $\text{C}_{14}\text{H}_{12}\text{BrNO}_2$, 305.0; found 305.8.

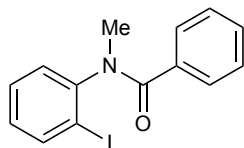


N-(2-iodophenyl)benzamide (S5): To a solution of 2-iodoaniline (641 mg, 2.9 mmol, 1.0 equiv) in DCM (30 mL) was added benzoyl chloride (375 μL , 3.2 mmol, 1.1 equiv) dropwise via syringe, followed by triethylamine (500 μL , 3.6 mmol, 1.2 equiv). The resulting mixture was stirred at room temperature for 4 h, quenched with methanol, and concentrated. The resulting solid was purified on silica gel (10–20% eluent) to afford the title compound as a white solid. (945 mg, >99 %).

^1H NMR (399 MHz, CDCl_3) δ 8.42 (dd, J = 8.2, 1.6 Hz, 1H), 8.30 (bs, 1H), 8.01 – 7.88 (m, 2H), 7.79 (dd, J = 8.0, 1.5 Hz, 1H), 7.61 – 7.45 (m, 3H), 7.37 (ddd, J = 8.1, 7.4, 1.5 Hz, 1H), 6.86 (td, J = 7.7, 1.6 Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 165.3, 138.8, 138.3, 134.5, 132.2, 129.4, 128.9, 127.2, 126.1, 121.9, 90.4.

LRMS (APCI) m/z: $[\text{M}+\text{H}]^+$ calc'd. for $\text{C}_{13}\text{H}_{11}\text{INO}$, 323.9; found 323.7



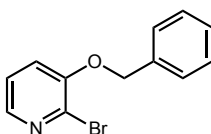
***N*-(2-iodophenyl)-*N*-methylbenzamide (S6):** In a vial under nitrogen, sodium hydride as a 60% dispersion in mineral oil (120 mg, 3.0 mmol, 2.0 equiv) was suspended in DMF (15 mL) and cooled to 0 °C. **S5** as a solution in DMF (476 mg, 1.5 mmol, 1.0 equiv in about 5 mL DMF) was added to the sodium hydride suspension and stirred for 30 minutes before the addition of methyl iodide (140 μ L, 2.2 mmol, 1.5 equiv). The reaction was removed from the ice bath, and after reacting for 1.5 h was quenched with methanol then water at 0 °C. The resulting mixture was diluted with ethyl acetate and washed with brine 3x. The organic layer was dried with MgSO₄, concentrated *in vacuo*, and purified on silica gel (10-25% EtOAc/Hex eluent) to afford the title compound as a white solid (312 mg, 62%).

¹H NMR (399 MHz, CDCl₃) δ 7.75 (dd, J = 8.0, 1.4 Hz, 1H), 7.43 – 7.27 (m, 2H), 7.20 – 7.01 (m, 5H), 6.85 (td, J = 7.6, 1.7 Hz, 1H), 3.35 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 170.8, 146.9, 140.1, 135.6, 130.1, 129.8, 129.3, 129.1, 128.3, 127.6, 99.1, 37.5.

LRMS (APCI) m/z : [M+H]⁺ calc'd. for C₁₄H₁₃INO, 338.0; found 337.7

¹H NMR spectrum is consistent with reported values⁵

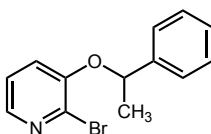


3-(benzyloxy)-2-bromopyridine (S7): A round bottom flask was charged with 2-bromo-3-hydroxypyridine (5.0 g, 29 mmol, 1.0 equiv) and K₂CO₃ (8.0 g, 58 mmol, 2.0 equiv). DMF (100 mL) was added, followed by benzyl bromide (3.7 mL, 31 mmol, 1.1 equiv). The reaction was heated to 80 °C and stirred for 16 h. The reaction was cooled to room temperature and then partitioned between EtOAc and water. The organic layer was washed with brine 3x, dried with MgSO₄ and purified on silica gel (20–50% EtOAc/hexanes eluent) to afford the title compound as a white solid (7.5 g, 99%).

¹H NMR (400 MHz, CDCl₃) δ 7.96 (dd, J = 3.8, 2.4 Hz, 1H), 7.47 – 7.27 (m, 5H), 7.18 – 7.09 (m, 2H), 5.15 (s, 2H).

¹³C NMR (126 MHz, CDCl₃) δ 152.0, 141.6, 135.5, 133.3, 128.7, 128.3, 127.0, 123.3, 120.5, 70.9.

LRMS (APCI) m/z : [M+H]⁺ calc'd. for C₁₂H₁₁BrNO, 264.0; found 263.8



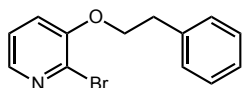
(±) 2-bromo-3-(1-phenylethoxy)pyridine (S8): A round bottom flask was charged with 2-bromo-3-hydroxypyridine (522 mg, 3.0 mmol, 1.0 equiv) and K₂CO₃ (829 mg, 6.0 mmol, 2.0 equiv). MeCN (15 mL) was added, followed by (1-bromoethyl)benzene (0.41 mL, 3.0 mmol, 1.0 equiv). The reaction was heated to 60 °C and stirred for 18 h. The reaction was cooled to room temperature, diluted with water, and extracted with EtOAc 3x. The organic layer was washed

with brine, dried with MgSO₄, and concentrated *in vacuo* to afford the title compound as a colorless oil (834 mg, >99%).

¹H NMR (600 MHz, CDCl₃) δ 7.90 (dt, *J* = 4.6, 1.3 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.35 (tt, *J* = 6.5, 1.0 Hz, 2H), 7.31 – 7.24 (m, 1H), 7.01 (ddt, *J* = 8.2, 4.6, 1.2 Hz, 1H), 6.99 – 6.95 (m, 1H), 5.35 (q, *J* = 6.4 Hz, 1H), 1.72 (dd, *J* = 6.4, 1.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 151.4, 141.5, 141.3, 133.8, 128.9, 128.0, 125.6, 123.2, 121.9, 77.8, 24.4.

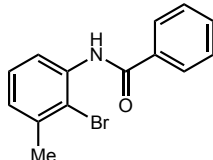
LRMS (APCI) *m/z*: [M+H]⁺ calc'd. for C₁₃H₁₃BrNO, 278.0; found 277.8.



2-bromo-3-phenethoxy pyridine (S9): A 20mL screw-top vial was charged with 2-bromo-3-hydroxypyridine (452 mg, 2.6 mmol, 1.0 equiv) and K₂CO₃ (716 mg, 5.1 mmol, 2.0 equiv). DMF (15 mL) was added, followed by 2(bromoethyl)benzene (380 μL, 2.9 mmol, 1.1 equiv). The reaction was heated to 80 °C and stirred for 16 h. The reaction was cooled to room temperature and then partitioned between EtOAc and water. The organic layer was washed with brine 3x, dried with MgSO₄ and purified on silica gel (20–60% EtOAc/hexanes eluent) to afford the title compound as a white solid (378 mg, 52%).

¹H NMR (399 MHz, CDCl₃) δ 7.93 (dd, *J* = 4.6, 1.6 Hz, 1H), 7.34 – 7.31 (m, 4H), 7.27 – 7.22 (m, 1H), 7.14 (dd, *J* = 8.1, 4.6 Hz, 1H), 7.04 (dd, *J* = 8.2, 1.5 Hz, 1H), 4.18 (t, *J* = 6.8 Hz, 2H), 3.15 (t, *J* = 6.8 Hz, 2H).

¹H NMR spectrum is consistent with reported values⁶

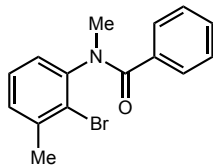


***N*-(2-bromo-3-methylphenyl)benzamide (S10):** To a solution of 2-bromo-3-methylaniline (0.41 mL, 3.3 mmol, 1.1 equiv) in DCM (30 mL) was added benzoyl chloride (0.35 mL, 3.0 mmol, 1.0 equiv) dropwise via syringe, followed by triethylamine (0.46 mL, 3.3 mmol, 1.1 equiv). The resulting mixture was stirred at room temperature for 22 h, washed with 1M HCl (aq), dried over MgSO₄, and concentrated *in vacuo* to afford the title compound as a white solid. (732 mg, 84%).

¹H NMR (400 MHz, CDCl₃) δ 8.60 (s, 1H), 8.43 – 8.37 (m, 1H), 7.99 – 7.91 (m, 2H), 7.64 – 7.56 (m, 1H), 7.56 – 7.49 (m, 2H), 7.29 (d, *J* = 7.8 Hz, 1H), 7.05 (ddd, *J* = 7.5, 1.7, 0.8 Hz, 1H), 2.46 (s, 3H) ppm.

¹³C NMR (151 MHz, CDCl₃) δ 165.5, 138.7, 136.1, 135.0, 132.3, 129.1, 127.9, 127.3, 126.4, 119.3, 116.7, 24.0 ppm.

LRMS (APCI) *m/z*: [M+H]⁺ calc'd. for C₁₄H₁₃BrNO, 290.0; found 289.7

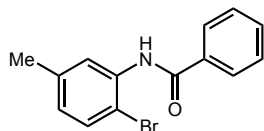


***N*-(2-bromo-3-methylphenyl)-*N*-methylbenzamide (S11):** In a vial under nitrogen, sodium hydride as a 60% dispersion in mineral oil (120 mg, 3.0 mmol, 1.5 equiv) was suspended in DMF (15 mL) and cooled to 0 °C. **S10** (580 mg, 2.0 mmol, 1.0 equiv) as a solution in DMF (6 mL) was added dropwise to the sodium hydride suspension and stirred for 30 minutes before the addition of methyl iodide (0.15 mL, 2.4 mmol, 1.2 equiv). The reaction was removed from the ice bath, and after reacting for 1.5 h was quenched water. The resulting mixture was diluted with ethyl acetate and washed with brine 3x. The organic layer was dried with MgSO₄ and concentrated *in vacuo* to afford the title compound as a light pink solid (573 mg, 94%).

¹H NMR (400 MHz, CDCl₃) δ 7.35 (dt, J = 7.0, 1.4 Hz, 2H), 7.26 – 7.17 (m, 1H), 7.14 (tt, J = 6.7, 1.7 Hz, 2H), 7.09 – 7.01 (m, 2H), 6.91 (dd, J = 7.5, 2.1 Hz, 1H), 3.38 (s, 3H), 2.39 (s, 3H) ppm.

¹³C NMR (151 MHz, CDCl₃) δ 171.2, 144.1, 140.4, 136.1, 129.9, 129.8, 128.2, 127.8, 127.7, 125.5, 37.3, 23.9 ppm.

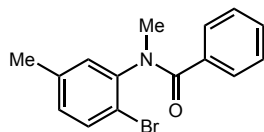
LRMS (APCI) m/z: [M+H]⁺ calc'd. for C₁₅H₁₅BrNO, 304.0; found 303.7



***N*-(2-bromo-5-methylphenyl)benzamide (S12):** To a solution of 2-bromo-5-methylaniline (614 mg, 3.3 mmol, 1.1 equiv) in DCM (30 mL) was added benzoyl chloride (0.35 mL, 3.0 mmol, 1.0 equiv) dropwise via syringe, followed by triethylamine (0.46 mL, 3.3 mmol, 1.1 equiv). The resulting mixture was stirred at room temperature for 16 h, quenched with sat. aq. NH₄Cl, and extracted with DCM 3x. The combined organic layers were washed with 1M HCl (aq) and brine, dried over MgSO₄, and concentrated *in vacuo* to afford the title compound as an off-white solid (839 mg, 96%).

¹H NMR (400 MHz, CDCl₃) δ 8.46 – 8.37 (m, 2H), 7.92 (d, J = 7.0 Hz, 1H), 7.57 (t, J = 7.3 Hz, 1H), 7.51 (t, J = 7.3 Hz, 2H), 7.43 (d, J = 8.2 Hz, 1H), 6.83 (dd, J = 8.2, 2.1 Hz, 1H), 2.35 (s, 3H) ppm.

¹H NMR spectrum is consistent with reported values⁷

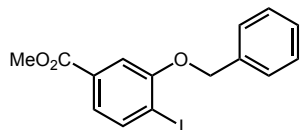


***N*-(2-bromo-5-methylphenyl)-*N*-methylbenzamide (S13):** In a vial under nitrogen, sodium hydride as a 60% dispersion in mineral oil (120 mg, 3.0 mmol, 1.5 equiv) was suspended in DMF (20 mL) and cooled to 0 °C. **S12** as a solution in DMF (580 mg, 2.0 mmol, 1.0 equiv in about 6 mL DMF) was added dropwise to the sodium hydride suspension and stirred for 30 minutes before the addition of methyl iodide (0.15 mL, 2.4 mmol, 1.2 equiv). The reaction was removed from the ice bath, and after reacting for 1 h was quenched with water and extracted with EtOAc 3x. The combined organic layers were washed with water and brine, dried with MgSO₄, and concentrated *in vacuo* to afford the title compound as a light yellow solid (577 mg, 95%).

¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.32 (m, 4H), 7.27 – 7.18 (m, 1H), 7.15 (t, J = 7.5 Hz, 2H), 6.92 – 6.83 (m, 2H), 3.37 (s, 3H), 2.17 (s, 3H) ppm.

¹³C NMR (126 MHz, CDCl₃) δ 171.0, 143.5, 138.8, 135.9, 133.4, 131.3, 130.0, 129.8, 128.2, 127.7, 119.3, 37.2, 20.8 ppm.

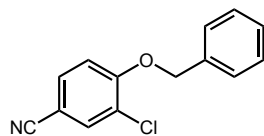
LRMS (APCI) m/z: [M+H]⁺ calc'd. for C₁₅H₁₅BrNO, 304.0; found 303.7



Methyl 3-(benzyloxy)-4-iodobenzoate (S14): A round bottom flask was charged with methyl 3-hydroxy-4-iodobenzoate (417 mg, 1.5 mmol, 1.0 equiv) and K₂CO₃ (415 mg, 1.5 mmol, 1.0 equiv). MeCN (10 mL) was added, followed by benzyl bromide (0.18 mL, 3.0 mmol, 2.0 equiv). The reaction was heated to 60 °C and stirred for 18 h. The reaction was cooled to room temperature, diluted with water, and extracted with EtOAc 3x. The combined organic layers were washed with brine, dried over MgSO₄, and concentrated *in vacuo* to afford the title compound as a white solid (535 mg, 97%).

¹H NMR (500 MHz, CDCl₃) δ 7.88 (d, J = 8.1 Hz, 1H), 7.56 – 7.50 (m, 3H), 7.44 – 7.37 (m, 3H), 7.34 (t, J = 7.3 Hz, 1H), 5.21 (s, 2H), 3.91 (s, 3H) ppm.

¹H NMR spectra are consistent with reported values⁸

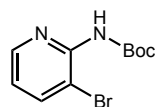


4-(benzyloxy)-3-chlorobenzonitrile (S15): A round bottom flask was charged with 3-chloro-4-hydroxybenzonitrile (461 mg, 3.0 mmol, 1.0 equiv) and K₂CO₃ (829 mg, 6.0 mmol, 2.0 equiv). MeCN (15 mL) was added, followed by benzyl bromide (0.36 mL, 3.0 mmol, 1.0 equiv). The reaction was heated to 60 °C and stirred for 16 h. The reaction was cooled to room temperature, diluted with water, and extracted with EtOAc 3x. The combined organic layers were washed with brine, dried over MgSO₄, and purified on silica gel (5–10% EtOAc/hexanes eluent) to afford the title compound as a white solid (303 mg, 41%).

¹H NMR (400 MHz, CDCl₃) δ 7.68 (d, J = 2.0 Hz, 1H), 7.51 (ddd, J = 8.6, 2.1, 0.3 Hz, 1H), 7.47 – 7.31 (m, 5H), 7.01 (d, J = 8.6 Hz, 1H), 5.23 (s, 2H) ppm.

¹³C NMR (151 MHz, CDCl₃) δ 157.9, 135.3, 133.9, 132.5, 129.0, 128.7, 127.2, 124.4, 118.1, 113.9, 105.2, 71.2 ppm.

LRMS (EI) m/z: [M]⁺ calc'd. for C₁₄H₁₀ClNO, 243.0; found 243.1



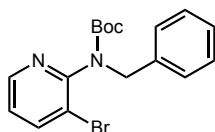
tert-butyl (3-bromopyridin-2-yl)carbamate (S16): To a solution of 2-amino-3-bromopyridine (692 mg, 4.0 mmol, 1.0 equiv) in THF (40 mL) was added triethylamine (1.3 mL, 9.6 mmol, 2.4 equiv), di-*tert*-butyl decarbonate (1.92 g, 8.8 mmol, 2.2 equiv), and DMAP (49 mg, 0.4 mmol, 0.1 equiv). The resulting solution was stirred for 19 h, quenched with sat. aq. NH₄Cl, and extracted with EtOAc 3x. The combined organic layers were dried over MgSO₄ and concentrated *in vacuo*. The resulting solid was dissolved in DCM (40 mL) and cooled to 0 °C. Trifluoroacetic

acid was added dropwise, and the resulting solution was stirred for 5.5 h, quenched with sat. aq. NaHCO₃, extracted with DCM 3x, dried over MgSO₄, and concentrated *in vacuo* to afford the title compound as a light yellow solid (997 mg, 91%).

¹H NMR (400 MHz, CDCl₃) δ 8.41 (dd, J = 4.8, 1.6 Hz, 2H), 7.82 (dd, J = 7.9, 1.7 Hz, 2H), 7.30 (s, 1H), 6.89 (dd, J = 7.9, 4.7 Hz, 2H), 1.55 (s, 17H) ppm.

¹³C NMR (151 MHz, CDCl₃) δ 150.7, 148.8, 147.5, 141.0, 119.8, 109.4, 81.6, 28.3 ppm.

LRMS (APCI) m/z: [M+H]⁺ calc'd. for C₁₀H₁₄BrN₂O₂, 273.0; found 272.7

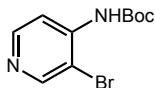


tert-butyl benzyl(3-bromopyridin-2-yl)carbamate (S17): In a round bottom flask under nitrogen, sodium hydride as a 60% dispersion in mineral oil (180 mg, 4.5 mmol, 1.5 equiv) was suspended in DMF (30 mL) and cooled to 0 °C. **S16** as a solution in DMF (819 mg, 3.0 mmol, 1.0 equiv in about 8 mL DMF) was added dropwise to the sodium hydride suspension and stirred for 30 minutes before the addition of benzyl bromide (0.43 mL, 3.6 mmol, 1.2 equiv). The reaction was removed from the ice bath, and after reacting for 1.5 h was quenched with water and extracted with EtOAc 3x. The combined organic layers were washed with brine, dried over MgSO₄, concentrated *in vacuo*, and purified on silica gel (10-20% EtOAc/Hex eluent) to afford the title compound as a white solid (830 mg, 76%).

¹H NMR (400 MHz, CDCl₃) δ 8.41 (d, J = 3.4 Hz, 1H), 7.85 (d, J = 7.9 Hz, 1H), 7.32 (s, 2H), 7.25 – 7.16 (m, 3H), 7.03 (dd, J = 7.9, 4.7 Hz, 1H), 5.00 (s, 1H), 4.89 (s, 1H), 1.41 (s, 9H) ppm.

¹³C NMR (100 MHz, CDCl₃, 50 °C) δ 153.7, 153.6, 147.5, 142.0, 137.9, 128.3, 127.3, 123.2, 120.8, 81.4, 52.4, 28.4 ppm.

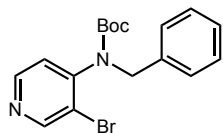
LRMS (APCI) m/z: [M+H]⁺ calc'd. for C₁₇H₂₀BrN₂O₂, 363.1; found 362.8



tert-butyl (3-bromopyridin-4-yl)carbamate (S18): To a solution of 3-bromo-4-pyridinamine (692 mg, 4.0 mmol, 1.0 equiv) in THF (20 mL) was added triethylamine (1.3 mL, 9.6 mmol, 2.4 equiv), di-*tert*-butyl decarbonate (1.92 g, 8.8 mmol, 2.2 equiv), and DMAP (49 mg, 0.4 mmol, 0.1 equiv). After stirring for 2.5 h, 1M aq. HCl (20 mL) was added, and the resulting solution was stirred for 17 h. The reaction was neutralized with 1M aq. NaOH (20 mL), extracted with EtOAc 3x, dried over MgSO₄, concentrated *in vacuo*, and purified on silica gel (30% EtOAc/Hex eluent) to afford the title compound as a white solid (807 mg, 74%).

¹H NMR (400 MHz, CDCl₃) δ 8.58 (d, J = 0.4 Hz, 1H), 8.37 (dd, J = 5.7, 0.6 Hz, 1H), 8.15 (d, J = 5.7 Hz, 1H), 7.17 (s, 1H), 1.54 (s, 9H) ppm.

¹H NMR spectrum is consistent with reported values⁹

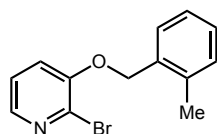


tert-butyl benzyl(3-bromopyridin-4-yl)carbamate (S19): In a round bottom flask under nitrogen, sodium hydride as a 60% dispersion in mineral oil (120 mg, 3.0 mmol, 1.5 equiv) was suspended in DMF (20 mL) and cooled to 0 °C. **S18** (546 mg, 2.0 mmol, 1.0 equiv) as a solution in DMF (5 mL) was added dropwise to the sodium hydride suspension and stirred for 30 minutes before the addition of benzyl bromide (0.29 mL, 2.4 mmol, 1.2 equiv). The reaction was removed from the ice bath, and after reacting for 4 h was quenched with water and extracted with EtOAc 3x. The combined organic layers were washed with water and brine, dried with MgSO₄, concentrated *in vacuo*, and purified on silica gel (10-20% EtOAc/Hex eluent) to afford the title compound as a yellow oil (488 mg, 67%).

¹H NMR (500 MHz, CDCl₃) δ 8.75 (s, 1H), 8.37 (d, J = 5.1 Hz, 1H), 7.30 – 7.26 (m, 3H), 7.21 (dd, J = 7.5, 2.0 Hz, 2H), 6.86 (s, 1H), 5.12 (s, 1H), 4.43 (s, 1H), 1.42 (s, 9H) ppm.

¹³C NMR (151 MHz, CDCl₃, 50 °C) δ 153.5, 153.4, 149.3, 148.8, 137.2, 128.7, 127.9, 125.3, 122.0, 81.7, 65.4, 52.7, 28.3 ppm.

LRMS (APCI) m/z: [M+H]⁺ calc'd. for C₁₇H₂₀BrN₂O₂, 363.0; found 362.8

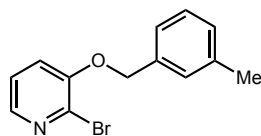


2-bromo-3-((2-methylbenzyl)oxy)pyridine (S20): A round bottom flask was charged with 2-bromo-3-hydroxypyridine (522 mg, 3.0 mmol, 1.0 equiv) and K₂CO₃ (829 mg, 6.0 mmol, 2.0 equiv). MeCN (15 mL) was added, followed by 2-methylbenzyl bromide (0.40 mL, 3.0 mmol, 1.0 equiv). The reaction was heated to 60 °C and stirred for 16 h. The reaction was cooled to room temperature, diluted with water, and extracted with EtOAc 3x. The combined organic layers were washed with brine, dried over MgSO₄, and purified on silica gel (20% EtOAc/hexanes eluent) to afford the title compound as a white solid (677 mg, 81%).

¹H NMR (400 MHz, CDCl₃) δ 8.00 (t, J = 3.1 Hz, 1H), 7.47 – 7.41 (m, 1H), 7.32 – 7.22 (m, 4H), 7.20 (d, J = 3.1 Hz, 1H), 5.14 (s, 2H), 2.41 (s, 3H) ppm.

¹³C NMR (151 MHz, CDCl₃) δ 152.3, 141.7, 136.7, 133.6, 133.5, 130.7, 128.8, 128.5, 126.3, 123.5, 120.4, 69.8, 19.2 ppm.

LRMS (APCI) m/z: [M+H]⁺ calc'd. for C₁₃H₁₃BrNO, 278.0; found 277.8

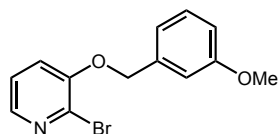


2-bromo-3-((3-methylbenzyl)oxy)pyridine (S21): A round bottom flask was charged with 2-bromo-3-hydroxypyridine (522 mg, 3.0 mmol, 1.0 equiv) and K₂CO₃ (829 mg, 6.0 mmol, 2.0 equiv). MeCN (15 mL) was added, followed by 1-(bromomethyl)-3-methylbenzene (0.41 mL, 3.0 mmol, 1.0 equiv). The reaction was heated to 60 °C and stirred for 15.5 h. The reaction was cooled to room temperature, diluted with water, and extracted with EtOAc 3x. The combined organic layers were washed with brine, dried over MgSO₄, and concentrated *in vacuo* to afford the title compound as a light brown solid (826 mg, 99%).

¹H NMR (400 MHz, CDCl₃) δ 7.99 (dd, *J* = 4.1, 2.1 Hz, 1H), 7.32 – 7.22 (m, 3H), 7.19 – 7.11 (m, 3H), 5.15 (s, 2H), 2.38 (s, 3H) ppm.

¹³C NMR (151 MHz, CDCl₃) δ 152.3, 141.7, 138.7, 135.6, 133.6, 129.3, 128.8, 127.9, 124.3, 123.5, 120.7, 71.2, 21.6 ppm.

LRMS (APCI) *m/z*: [M+H]⁺ calc'd. for C₁₃H₁₃BrNO, 278.0; found 277.8

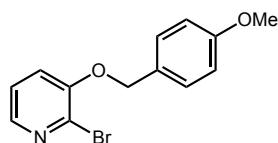


2-bromo-3-((3-methoxybenzyl)oxy)pyridine (S22): A round bottom flask was charged with 2-bromo-3-hydroxypyridine (522 mg, 3.0 mmol, 1.0 equiv) and K₂CO₃ (829 mg, 6.0 mmol, 2.0 equiv). MeCN (15 mL) was added, followed by 3-methoxybenzyl bromide (0.42 mL, 3.0 mmol, 1.0 equiv). The reaction was heated to 60 °C and stirred for 15 h. The reaction was cooled to room temperature, diluted with water, and extracted with EtOAc 3x. The combined organic layers were washed with brine, dried over MgSO₄, and concentrated *in vacuo* to afford the title compound as a white solid (733 mg, 83%).

¹H NMR (600 MHz, CDCl₃) δ 7.99 (dd, *J* = 4.2, 2.0 Hz, 1H), 7.36 – 7.29 (m, 1H), 7.21 – 7.14 (m, 2H), 7.07 – 6.98 (m, 2H), 6.88 (ddd, *J* = 8.3, 2.6, 0.9 Hz, 1H), 5.17 (s, 2H), 3.83 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 156.0, 152.0, 141.6, 137.1, 133.3, 129.8, 123.4, 120.5, 119.1, 113.8, 112.4, 70.7, 55.3.

LRMS (APCI) *m/z*: [M+H]⁺ calc'd. for C₁₃H₁₃BrNO₂, 294.0; found 293.8.

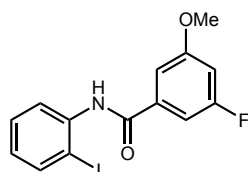


2-bromo-3-((4-methoxybenzyl)oxy)pyridine (S23): A round bottom flask was charged with 2-bromo-3-hydroxypyridine (522 mg, 3.0 mmol, 1.0 equiv) and K₂CO₃ (829 mg, 6.0 mmol, 2.0 equiv). MeCN (15 mL) was added, followed by 4-methoxybenzyl bromide (0.49 mL, 3.6 mmol, 1.2 equiv). The reaction was heated to 60 °C and stirred for 22 h. The reaction was cooled to room temperature, diluted with water, and extracted with EtOAc 3x. The combined organic layers were washed with brine, dried over MgSO₄, and purified on silica gel (10-40% EtOAc/hexanes eluent) to afford the title compound as a white solid (699 mg, 79%).

¹H NMR (400 MHz, CDCl₃) δ 7.99 (dd, *J* = 3.7, 2.5 Hz, 1H), 7.38 (dt, *J* = 8.8, 0.6 Hz, 2H), 7.19 – 7.14 (m, 2H), 6.93 (d, *J* = 8.7 Hz, 2H), 5.11 (s, 2H), 3.82 (s, 3H) ppm.

¹³C NMR (151 MHz, CDCl₃) δ 159.9, 152.3, 141.7, 133.7, 129.0, 127.7, 123.5, 120.8, 114.3, 71.1, 55.5 ppm.

LRMS (APCI) *m/z*: [M+H]⁺ calc'd. for C₁₃H₁₃BrNO₂, 294.0; found 293.8



3-fluoro-N-(2-iodophenyl)-5-methoxybenzamide (S24): To a solution of 3-fluoro-5-methoxybenzoic acid (510 mg, 3.0 mmol, 1.0 equiv) in DMF (12 mL) was added HBTU (1.25 g,

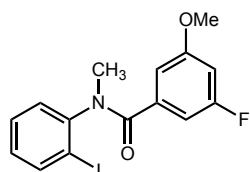
3.3 mmol, 1.1 equiv), 2-iodoaniline (723 mg, 3.3 mmol, 1.1 equiv), and diisopropylethylamine (1.04 mL, 6.0 mmol, 2.0 equiv). After heating at 80 °C for 16.5 h, the reaction was quenched with sat. aq. NH₄Cl and extracted with EtOAc 3x. The combined organic layers were washed with water, 1M aq HCl, and brine, dried over MgSO₄, and purified on silica gel (5% EtOAc/hexanes eluent) to afford the title compound as a light yellow solid (334 mg, 30%).

¹H NMR (400 MHz, CDCl₃) δ 8.42 (dd, J = 8.3, 1.6 Hz, 1H), 8.20 (s, 1H), 7.83 (dd, J = 8.0, 1.4 Hz, 1H), 7.46 – 7.37 (m, 1H), 7.30 (t, J = 1.9 Hz, 1H), 7.23 (dt, J = 8.6, 1.9 Hz, 1H), 6.91 (td, J = 7.7, 1.6 Hz, 1H), 6.83 (dt, J = 10.2, 2.3 Hz, 1H), 3.89 (s, 3H) ppm.

¹³C NMR (125 MHz, CDCl₃) δ 164.2 (d, ⁴J_{C-F} = 3.2 Hz), 163.7 (d, ¹J_{C-F} = 247.5 Hz), 161.5 (d, ³J_{C-F} = 11.1 Hz), 139.0, 138.1, 137.4 (d, ³J_{C-F} = 8.6 Hz), 129.6, 126.5, 122.0, 109.0 (d, ⁴J_{C-F} = 2.6 Hz), 106.6 (d, ²J_{C-F} = 23.5 Hz), 105.6 (d, ²J_{C-F} = 25.1 Hz), 90.5, 56.0 ppm.

¹⁹F NMR (376 MHz, CDCl₃) δ -109.6 (dd, J = 10.0, 8.5 Hz) ppm.

LRMS (APCI) m/z: [M+H]⁺ calc'd. for C₁₄H₁₂FINO₂, 372.0; found 371.6



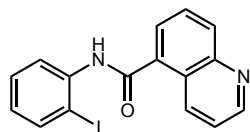
3-fluoro-N-(2-iodophenyl)-5-methoxy-N-methylbenzamide (S25): In a vial under nitrogen, sodium hydride as a 60% dispersion in mineral oil (48 mg, 1.2 mmol, 1.5 equiv) was suspended in DMF (10 mL) and cooled to 0 °C. **S24** (297 mg, 0.80 mmol, 1.0 equiv) as a solution in DMF (3 mL) was added dropwise to the sodium hydride suspension and stirred for 30 minutes before the addition of methyl iodide (60 μL, 0.96 mmol, 1.5 equiv). The reaction was removed from the ice bath, and after reacting for 1 h was quenched with water and extracted with EtOAc 3x. The combined organic layers were washed with water and brine, dried with MgSO₄, and concentrated *in vacuo* to afford the title compound as a yellow solid (287 mg, 93%).

¹H NMR (400 MHz, CDCl₃) δ 7.83 (dd, J = 7.9, 1.4 Hz, 1H), 7.25 – 7.21 (m, 1H), 7.09 (dd, J = 7.9, 1.6 Hz, 1H), 6.94 (td, J = 7.8, 1.6 Hz, 1H), 6.73 – 6.65 (m, 2H), 6.48 (dt, J = 10.4, 2.4 Hz, 1H), 3.66 (s, 3H), 3.36 (s, 3H) ppm.

¹³C NMR (126 MHz, CDCl₃) δ 169.2 (d, ⁴J_{C-F} = 3.3 Hz), 162.6 (d, ¹J_{C-F} = 246.0 Hz), 160.1 (d, ³J_{C-F} = 10.9 Hz), 146.6, 140.2, 138.0 (d, ³J_{C-F} = 8.3 Hz), 130.0, 129.5, 129.4, 109.2, 107.9 (d, ²J_{C-F} = 23.8 Hz), 103.8 (d, ⁴J_{C-F} = 24.5 Hz), 98.9, 55.6, 37.5 ppm.

¹⁹F NMR (376 MHz, CDCl₃) δ -111.5 (t, J = 9.6 Hz) ppm.

LRMS (APCI) m/z: [M+H]⁺ calc'd. for C₁₅H₁₄FINO₂, 386.0; found 385.6

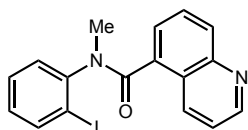


N-(2-iodophenyl)quinoline-5-carboxamide (S26): To a solution of quinoline-5-carboxylic acid (520 mg, 3.0 mmol, 1.0 equiv) in DMF (12 mL) was added HBTU (1.25 g, 3.3 mmol, 1.1 equiv), 2-iodoaniline (723 mg, 3.3 mmol, 1.1 equiv), and diisopropylethylamine (1.04 mL, 6.0 mmol, 2.0 equiv). After heating at 80 °C for 20.5 h, the reaction was quenched with sat. aq. NH₄Cl and extracted with EtOAc 3x. The combined organic layers were washed with water, 1M aq HCl, and brine, dried over MgSO₄, and purified on silica gel (30-50% EtOAc/hexanes eluent) to afford the title compound as an off-white solid (385 mg, 34%).

¹H NMR (500 MHz, CDCl₃) δ 9.01 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.95 (d, *J* = 8.7 Hz, 1H), 8.48 (d, *J* = 7.9 Hz, 1H), 8.33 (d, *J* = 8.5 Hz, 1H), 8.12 (s, 1H), 8.00 (d, *J* = 7.2 Hz, 1H), 7.86 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.82 (t, *J* = 7.8 Hz, 1H), 7.55 (dd, *J* = 8.7, 4.2 Hz, 1H), 7.46 (dd, *J* = 8.5, 7.1 Hz, 1H), 6.97 – 6.92 (m, 1H) ppm.

¹³C NMR (151 MHz, CDCl₃) δ 166.3, 151.3, 148.5, 139.2, 138.4, 134.5, 134.0, 133.3, 129.7, 128.6, 126.8, 126.2, 125.9, 122.5, 122.4, 90.7 ppm.

LRMS (APCI) *m/z*: [M+H]⁺ calc'd. for C₁₆H₁₂IN₂O, 375.0; found 374.6

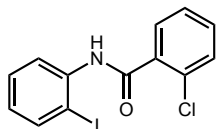


***N*-(2-iodophenyl)-*N*-methylquinoline-5-carboxamide (S27):** In a vial under nitrogen, sodium hydride as a 60% dispersion in mineral oil (48 mg, 1.2 mmol, 1.5 equiv) was suspended in DMF (5 mL) and cooled to 0 °C. **S26** (299 mg, 0.80 mmol, 1.0 equiv) as a solution in DMF (3 mL) was added dropwise to the sodium hydride suspension and stirred for 30 minutes before the addition of methyl iodide (60 μL, 0.96 mmol, 1.5 equiv). The reaction was removed from the ice bath, and after reacting for 1 h was quenched with water and extracted with EtOAc 3x. The combined organic layers were washed with water and brine, dried over MgSO₄, and purified on silica gel (30-50% EtOAc/hexanes eluent) to afford the title compound as a white solid (218 mg, 70%). Appeared as rotameric mixtures in ¹H NMR; no coalescence of peaks in CDCl₃ up to 60 °C; major observed reported.

¹H NMR (400 MHz, CDCl₃) δ 8.92 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.66 – 8.60 (m, 1H), 7.95 (dt, *J* = 8.2, 1.2 Hz, 1H), 7.74 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.53 – 7.37 (m, 3H), 7.04 – 6.92 (m, 2H), 6.80 (ddd, *J* = 7.9, 7.2, 1.8 Hz, 1H), 3.52 (s, 3H) ppm.

¹³C NMR (126 MHz, CDCl₃) δ 169.3, 150.7, 148.1, 146.3, 140.4, 134.5, 133.8, 131.1, 129.5, 129.4, 129.4, 128.0, 126.0, 125.6, 121.7, 98.8, 37.2 ppm.

LRMS (APCI) *m/z*: [M+H]⁺ calc'd. for C₁₇H₁₄IN₂O, 389.0; found 388.6

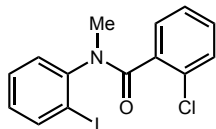


2-chloro-*N*-(2-iodophenyl)benzamide (S28): To a solution of 2-iodoaniline (604 mg, 2.8 mmol, 1.0 equiv) in DCM (30 mL) was added 2-chlorobenzoyl chloride (390 μL, 3.0 mmol, 1.1 equiv) dropwise via syringe, followed by triethylamine (450 μL, 3.2 mmol, 1.1 equiv). The resulting mixture was stirred at room temperature for 4 h, quenched with methanol, and concentrated. The resulting solid was purified on silica gel (10–20% eluent) to afford the title compound as a white solid. (695 mg, 71 %).

¹H NMR (399 MHz, CDCl₃) δ 8.39 (d, *J* = 8.3 Hz, 1H), 8.16 (s, 1H), 7.81 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.76 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.55 – 7.31 (m, 4H), 6.89 (td, *J* = 7.7, 1.6 Hz, 1H).

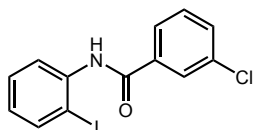
¹³C NMR (100 MHz, CDCl₃) δ 164.6, 139.1, 138.2, 134.9, 131.9, 130.9, 130.6, 130.2, 129.3, 127.3, 126.5, 122.4, 90.1.

LRMS (APCI) *m/z*: [M+H]⁺ calc'd. for C₁₃H₁₀ClINO, 357.9; found 357.6



2-chloro-*N*-(2-iodophenyl)-*N*-methylbenzamide (S29): In a vial under nitrogen, sodium hydride as a 60% dispersion in mineral oil (90 mg, 2.2 mmol, 1.8 equiv) was suspended in DMF (15 mL) and cooled to 0 °C. **S28** as a solution in DMF (441 mg, 1.2 mmol, 1.0 equiv in about 4 mL DMF) was added to the sodium hydride suspension dropwise and stirred for 30 minutes before the addition of methyl iodide (120 μ L, 1.8 mmol, 1.5 equiv). The reaction was removed from the ice bath, and after reacting for 1.5 h was quenched with methanol then water at 0 °C. The resulting mixture was diluted with ethyl acetate and washed with brine 3x. The organic layer was dried with MgSO₄, concentrated *in vacuo*, and purified on silica gel (10-25% EtOAc/Hex eluent) to afford the title compound as a white solid (384 mg, 84%). Appeared as rotameric mixtures in ¹H NMR; no coalescence of peaks in CDCl₃ up to 60 °C; major observed reported. **¹H NMR** (400 MHz, CDCl₃) δ 7.75 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.40 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.35 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.20 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.14 (td, *J* = 7.6, 1.4 Hz, 1H), 7.07 (td, *J* = 7.7, 1.8 Hz, 1H), 7.00 (td, *J* = 7.5, 1.3 Hz, 1H), 6.83 (td, *J* = 7.6, 1.6 Hz, 1H), 3.39 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ 167.9, 145.4, 139.9, 136.0, 130.0, 129.6, 129.4, 129.3, 129.0, 127.9, 127.0, 126.20 98.8, 36.4.

LRMS (APCI) *m/z*: [M+H]⁺ calc'd. for C₁₄H₁₂ClINO, 371.9; found 371.6

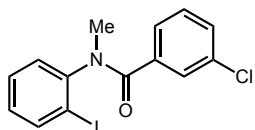


3-chloro-*N*-(2-iodophenyl)benzamide (S30): To a solution of 2-iodoaniline (608 mg, 2.8 mmol, 1.0 equiv) in DCM (30 mL) was added 3-chlorobenzoyl chloride (380 μ L, 3.0 mmol, 1.1 equiv) dropwise via syringe, followed by triethylamine (450 μ L, 3.2 mmol, 1.1 equiv). The resulting mixture was stirred at room temperature for 4 h, quenched with methanol, and concentrated. The resulting solid was purified on silica gel (10–20% eluent) to afford the title compound as a white solid. (767 mg, 77 %).

¹H NMR (399 MHz, CDCl₃) δ 8.39 (dd, *J* = 8.2, 1.6 Hz, 1H), 8.20 (s, 1H), 8.01 – 7.90 (m, 1H), 7.86 – 7.75 (m, 2H), 7.55 (ddd, *J* = 8.0, 2.1, 1.1 Hz, 1H), 7.46 (t, *J* = 7.9 Hz, 1H), 7.40 (m, 1H), 6.89 (ddd, *J* = 8.0, 7.3, 1.6 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 163.9, 138.8, 137.9, 136.3, 135.2, 132.2, 130.2, 129.4, 127.7, 126.4, 125.0, 121.9, 90.4.

LRMS (APCI) *m/z*: [M+H]⁺ calc'd. for C₁₃H₁₀ClINO, 357.9; found 357.6



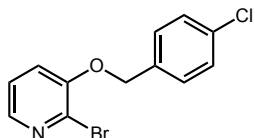
3-chloro-*N*-(2-iodophenyl)-*N*-methylbenzamide (S31): In a vial under nitrogen, sodium hydride as a 60% dispersion in mineral oil (66 mg, 1.7 mmol, 1.9 equiv) was suspended in DMF (15 mL) and cooled to 0 °C. **S30** as a solution in DMF (321 mg, 0.9 mmol, 1.0 equiv in about 3 mL DMF) was added dropwise to the sodium hydride suspension and stirred for 30 minutes before the addition of methyl iodide (90 μ L, 1.4 mmol, 1.6 equiv). The reaction was removed from the ice bath, and after reacting for 1.5 h was quenched with methanol then water at 0 °C.

The resulting mixture was diluted with ethyl acetate and washed with brine 3x. The organic layer was dried with MgSO₄, concentrated *in vacuo*, and purified on silica gel (10-25% EtOAc/Hex eluent) to afford the title compound as a white solid (215 mg, 64%).

¹H NMR (399 MHz, CDCl₃) δ 7.77 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.39 (t, *J* = 1.9 Hz, 1H), 7.24 – 7.19 (m, 1H), 7.16 (dd, *J* = 7.9, 1.9 Hz, 2H), 7.09 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.03 (dd, *J* = 8.4, 7.3 Hz, 1H), 6.90 (td, *J* = 7.7, 1.6 Hz, 1H), 3.34 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 169.2, 146.4, 140.2, 137.3, 133.7, 130.0, 129.9, 129.5, 129.4, 128.9, 128.6, 126.3, 98.9, 37.5.

LRMS (APCI) *m/z*: [M+H]⁺ calc'd. for C₁₄H₁₂ClINO, 372.0; found 371.6

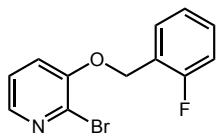


2-bromo-3-((4-chlorobenzyl)oxy)pyridine (S32): A round bottom flask was charged with 2-bromo-3-hydroxypyridine (522 mg, 3.0 mmol, 1.0 equiv) and K₂CO₃ (829 mg, 6.0 mmol, 2.0 equiv). MeCN (15 mL) was added, followed by 4-chlorobenzyl bromide (740 mg, 3.6 mmol, 1.2 equiv). The reaction was heated to 60 °C and stirred for 20 h. The reaction was cooled to room temperature, diluted with water, and extracted with EtOAc 3x. The combined organic layers were washed with brine, dried over MgSO₄, and purified on silica gel (20% EtOAc/hexanes eluent) to afford the title compound as a white solid (771 mg, 86%).

¹H NMR (500 MHz, CDCl₃) δ 8.02 (dd, *J* = 4.6, 1.6 Hz, 1H), 7.44 – 7.34 (m, 4H), 7.19 (dd, *J* = 8.1, 4.6 Hz, 1H), 7.14 (dd, *J* = 8.1, 1.6 Hz, 1H), 5.15 (s, 2H) ppm.

¹³C NMR (151 MHz, CDCl₃) δ 151.9, 141.9, 134.3, 134.1, 133.5, 129.0, 128.5, 123.4, 120.5, 70.3 ppm.

LRMS (APCI) *m/z*: [M+H]⁺ calc'd. for C₁₂H₁₀BrClNO, 298.0; found 297.7



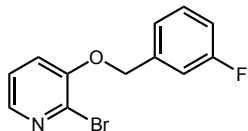
2-bromo-3-((2-fluorobenzyl)oxy)pyridine (S33): A round bottom flask was charged with 2-bromo-3-hydroxypyridine (522 mg, 3.0 mmol, 1.0 equiv) and K₂CO₃ (829 mg, 6.0 mmol, 2.0 equiv). MeCN (15 mL) was added, followed by 2-fluorobenzyl bromide (0.36 mL, 3.0 mmol, 1.0 equiv). The reaction was heated to 60 °C and stirred for 15 h. The reaction was cooled to room temperature, diluted with water, and extracted with EtOAc 3x. The combined organic layers were washed with brine, dried over MgSO₄, and purified on silica gel (10-30% EtOAc/hexanes eluent) to afford the title compound as a white solid (753 mg, 89%).

¹H NMR (400 MHz, CDCl₃) δ 8.02 (dd, *J* = 3.8, 2.4 Hz, 1H), 7.60 (tdd, *J* = 7.5, 1.9, 0.8 Hz, 1H), 7.38 – 7.30 (m, 1H), 7.24 – 7.17 (m, 3H), 7.10 (ddd, *J* = 10.3, 8.2, 1.1 Hz, 1H), 5.25 (s, 3H) ppm.

¹³C NMR (151 MHz, CDCl₃) δ 160.3 (d, ¹J_{C-F} = 246.6 Hz), 152.0, 142.1, 133.6, 130.2 (d, ³J_{C-F} = 8.3 Hz), 129.5 (d, ³J_{C-F} = 3.8 Hz), 124.8 (d, ⁴J_{C-F} = 3.7 Hz), 123.6, 123.0 (d, ²J_{C-F} = 13.9 Hz), 120.5, 115.5 (d, ²J_{C-F} = 21.0 Hz), 64.8 (d, ³J_{C-F} = 4.6 Hz) ppm.

¹⁹F NMR (376 MHz, CDCl₃-d) δ -117.7 – -121.1 (m) ppm.

LRMS (APCI) *m/z*: [M+H]⁺ calc'd. for C₁₂H₁₀BrFNO, 282.0; found 281.8



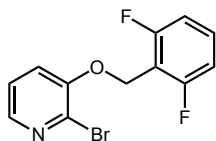
2-bromo-3-((3-fluorobenzyl)oxy)pyridine (S34): A round bottom flask was charged with 2-bromo-3-hydroxypyridine (522 mg, 3.0 mmol, 1.0 equiv) and K_2CO_3 (829 mg, 6.0 mmol, 2.0 equiv). MeCN (15 mL) was added, followed by 3-fluorobenzyl bromide (0.37 mL, 3.0 mmol, 1.0 equiv). The reaction was heated to 60 °C and stirred for 15 h. The reaction was cooled to room temperature, diluted with water, and extracted with EtOAc 3x. The combined organic layers were washed with brine, dried over $MgSO_4$, and purified on silica gel (10-30% EtOAc/hexanes eluent) to afford the title compound as a white solid (765 mg, 90%).

1H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, $J = 4.6, 1.7$ Hz, 1H), 7.37 (td, $J = 7.9, 5.7$ Hz, 1H), 7.25 – 7.17 (m, 3H), 7.14 (dd, $J = 8.1, 1.7$ Hz, 1H), 7.04 (tdd, $J = 8.6, 2.7, 0.9$ Hz, 1H), 5.17 (s, 2H) ppm.

^{13}C NMR (151 MHz, $CDCl_3$) δ 163.2 (d, $^1J_{C-F} = 247.0$ Hz), 152.0, 142.1, 138.3 (d, $^3J_{C-F} = 7.4$ Hz), 133.6, 130.6 (d, $^3J_{C-F} = 8.3$ Hz), 123.5, 122.5 (d, $^4J_{C-F} = 3.0$ Hz), 120.5, 115.4 (d, $^2J_{C-F} = 21.2$ Hz), 114.1 (d, $^2J_{C-F} = 22.6$ Hz), 70.3 (d, $^4J_{C-F} = 2.1$ Hz) ppm.

^{19}F NMR (376 MHz, $CDCl_3$) δ -112.2 (td, $J = 9.1, 5.9$ Hz) ppm.

LRMS (APCI) m/z : $[M+H]^+$ calc'd. for $C_{12}H_{10}BrFNO$, 282.0; found 281.8



2-bromo-3-((2,6-difluorobenzyl)oxy)pyridine (S35): A round bottom flask was charged with 2-bromo-3-hydroxypyridine (522 mg, 3.0 mmol, 1.0 equiv) and K_2CO_3 (829 mg, 6.0 mmol, 2.0 equiv). MeCN (15 mL) was added, followed by 2,6-difluorobenzyl bromide (621 mg, 3.0 mmol, 1.0 equiv). The reaction was heated to 60 °C and stirred for 15 h. The reaction was cooled to room temperature, diluted with water, and extracted with EtOAc 3x. The combined organic layers were washed with brine and dried over $MgSO_4$ to afford the title compound as an off-white solid (868 mg, 96%).

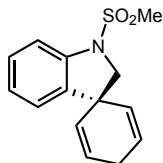
1H NMR (400 MHz, $CDCl_3$) δ 8.04 – 8.00 (m, 1H), 7.41 – 7.31 (m, 2H), 7.25 – 7.21 (m, 1H), 6.96 (dd, $J = 8.3, 7.4$ Hz, 2H), 5.22 (s, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.1 (dd, $^1J_{C-F} = 251.6, ^3J_{C-F} = 7.3$ Hz), 152.2, 142.4, 134.0, 131.5 (t, $^3J_{C-F} = 10.5$ Hz), 123.5, 121.4, 111.8 (dd, $^2J_{C-F} = 21.0, ^4J_{C-F} = 4.8$ Hz), 111.7 (t, $^2J_{C-F} = 18.8$ Hz), 59.6 (t, $^3J_{C-F} = 3.7$ Hz) ppm.

^{19}F NMR (376 MHz, $CDCl_3$) δ -114.1 (t, $J = 6.8$ Hz) ppm.

LRMS (APCI) m/z : $[M+H]^+$ calc'd. for $C_{12}H_9BrF_2NO$, 300.0; found 299.8

IX. Preparation of Products from the Substrate Table

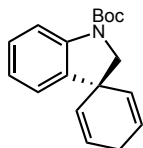


1'-(methylsulfonyl)spiro[cyclohexane-1,3'-indoline]-2,5-diene (9): Prepared according to General Procedure A using *N*-benzyl-*N*-(2-iodophenyl) methanesulfonamide (**S3**) (145 mg, 0.4 mmol, 1.0 equiv), DIPEA (210 μ L, 1.2 mmol, 3 equiv) and 3DPAFIPN (11.8 mg, 5 mol%). After 16 h, the reaction was purified on silica (10 – 30% EtOAc/hexanes) to provide the desired product as a colorless oil (63.3 mg, 65% yield).

¹H NMR (500 MHz, CDCl₃) δ 7.41 (d, J = 8.1, 0.7 Hz, 1H), 7.22 (ddd, J = 8.0, 5.2, 3.5 Hz, 1H), 7.08 – 7.03 (m, 3H), 5.91 (dtt, J = 10.3, 3.4, 1.1 Hz, 3H), 5.69 (app. dp, J = 10.4, 2.3 Hz, 2H), 3.81 (s, 2H), 2.92 (s, 3H), 2.85 – 2.70 (m, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 140.3, 138.1, 128.6, 128.6, 125.5, 124.7, 124.1, 113.3, 63.4, 45.2, 34.5, 25.9.

HRMS (ESI) m/z : [M+H]⁺ calc'd. for C₁₄H₁₆NO₂S, 262.0902, found 262.0884.

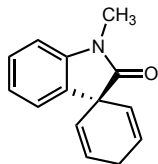


tert-butyl spiro[cyclohexane-1,3'-indoline]-2,5-diene-1'-carboxylate (10): Prepared according to General Procedure A using *tert*-butyl benzyl(2-bromophenyl)carbamate (**S4**) (69 mg, 0.2 mmol, 1 equiv), DIPEA (105 μ L, 0.6 mmol, 3 equiv) and 3DPAFIPN (16.2 mg, 5 mol%). After 16 h, the reaction was purified on silica (0–5% EtOAc/hexanes) to provide the desired product as a light yellow oil (47 mg, 79% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.68 (bs, 1H), 7.20 (ddd, J = 8.3, 7.4, 1.5 Hz, 1H), 7.02 (dd, J = 7.5, 1.3 Hz, 1H), 6.97 (td, J = 7.4, 1.1 Hz, 1H), 5.87 (dt, J = 10.2, 3.4 Hz, 2H), 5.71 (dt, J = 10.3, 2.0 Hz, 2H), 3.87 (s, 2H), 2.81 (dddd, J = 23.1, 5.4, 3.3, 2.1 Hz, 1H), 2.74 (dtt, J = 23.2, 3.5, 2.0 Hz, 1H), 1.60 (s, 9H).

¹³C NMR (151 MHz, CDCl₃) δ 152.4, 141.1, 138.1, 130.0, 128.0, 124.8, 123.4, 122.7, 114.7, 80.9, 61.7, 44.5, 28.5, 25.9.

HRMS (ESI) m/z : [M+H]⁺ calc'd. for C₁₈H₂₂NO₂, 284.1650; found 284.1657



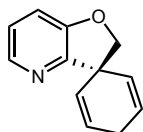
1'-methylspiro[cyclohexane-1,3'-indoline]-2,5-dien-2'-one (11): Prepared according to General Procedure A using *N*-(2-iodophenyl)-*N*-methylbenzamide (**S6**) (165 mg, 0.5 mmol, 1.0 equiv), DIPEA (260 μ L, 1.5 mmol, 3 equiv) and 3DPAFIPN (14 mg, 4 mol%). After 16 h, the reaction was purified on silica (10–20% EtOAc/hexanes) to provide the desired product as a white solid (58 mg, 55% yield).

¹H NMR (500 MHz, CDCl₃) δ 7.29 (tt, *J* = 7.7, 1.2 Hz, 1H), 7.14 – 7.11 (m, 1H), 7.06 (tt, *J* = 7.4, 1.0 Hz, 1H), 6.85 (d, *J* = 7.8, 0.8 Hz, 1H), 6.14 (dtd, *J* = 10.3, 3.4, 0.9 Hz, 2H), 5.39 (dtd, *J* = 10.5, 2.0, 0.9 Hz, 2H), 3.23 (s, 3H), 3.02 – 2.94 (m, 1H), 2.90 – 2.81 (m, 1H).

¹³C NMR (126 MHz, CDCl₃) δ 177.9, 143.0, 134.2, 128.4, 127.3, 124.7, 123.8, 122.9, 108.0, 51.8, 26.6, 25.7.

HRMS (ESI) *m/z*: [M+H]⁺ calc'd. for C₁₄H₁₄NO, 212.1075; found 212.1118.

¹H NMR spectrum is consistent with reported values¹⁰

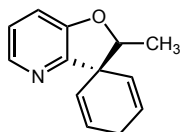


2'H-spiro[cyclohexane-1,3'-furo[3,2-*b*]pyridine]-2,5-diene (12): Prepared according to General Procedure A using 3-(benzyloxy)-2-bromopyridine (**S7**) (128 mg, 0.5 mmol, 1 equiv), DIPEA (270 μL, 1.5 mmol, 3 equiv) and 3DPAFIPN (18 mg, 6 mol %). After 16 h, the reaction was purified on silica (20 – 40% Et₂O/hexanes) to provide the desired product as a colorless oil (65 mg, 72% yield).

¹H NMR (600 MHz, CDCl₃) δ 8.14 (dd, *J* = 4.7, 1.4 Hz, 1H), 7.09 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.05 (dd, *J* = 8.1, 4.7 Hz, 1H), 6.02 (dt, *J* = 10.2, 3.4 Hz, 2H), 5.75 (dt, *J* = 10.3, 2.0 Hz, 2H), 4.46 (s, 2H), 2.93 (dtt, *J* = 23.3, 3.3, 2.1 Hz, 1H), 2.74 (dtt, *J* = 23.4, 3.5, 2.1 Hz, 1H).

¹³C NMR (151 MHz, CDCl₃) δ 155.1, 152.6, 142.8, 127.0, 125.8, 122.8, 116.6, 83.0, 47.6, 26.0

HRMS (ESI) *m/z*: [M+H]⁺ calc'd. for C₁₂H₁₂NO, 186.0918; found 186.1081.

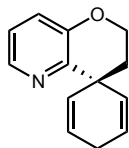


2'-methyl-2'H-spiro[cyclohexane-1,3'-furo[3,2-*b*]pyridine]-2,5-diene (13): Prepared according to General Procedure B using 2-bromo-3-(1-phenylethoxy)pyridine (**S8**) (152 mg, 0.6 mmol, 1 equiv), DIPEA (1.1 mL, 6.2 mmol, 10 equiv) and 3DPAFIPN (17 mg, 4 mol %). After 16 h, the reaction was purified on silica (15– 20% EtOAc/hexanes) to provide the desired product as a yellow oil (54 mg, 50% yield).

¹H NMR (600 MHz, CDCl₃) δ 8.12 (dd, *J* = 4.5, 1.7 Hz, 1H), 7.07 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.04 (dd, *J* = 8.1, 4.5 Hz, 1H), 6.15 (dtd, *J* = 10.0, 3.4, 1.6 Hz, 1H), 5.98 (dtd, *J* = 10.1, 3.4, 1.6 Hz, 1H), 5.67 (dq, *J* = 10.0, 2.1 Hz, 1H), 5.59 (dq, *J* = 10.1, 2.1 Hz, 1H), 4.57 (q, *J* = 6.6 Hz, 1H), 2.91 (dtt, *J* = 23.4, 3.7, 2.0 Hz, 1H), 2.76 (dtt, *J* = 23.3, 3.2, 2.2 Hz, 1H), 1.42 (d, *J* = 6.6 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 156.3, 152.4, 142.7, 127.9, 126.4, 125.9, 124.5, 122.8, 116.4, 88.7, 50.7, 26.3, 15.2.

HRMS (ESI) *m/z*: [M+H]⁺ calc'd. for C₁₃H₁₄NO, 200.1075; found 200.1184

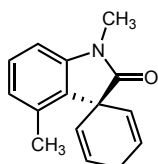


2',3'-dihydrospiro[cyclohexane-1,4'-pyrano[3,2-*b*]pyridine]-2,5-diene (14): Prepared according to General Procedure A using 2-bromo-3-phenethoxy pyridine (**S9**) (59 mg, 0.2 mmol, 1 equiv) DIPEA (105 μ L, 0.6 mmol, 3 equiv) and 3DPAFIPN (6 mg, 5 mol %). After 16 h, the reaction was purified on silica (20 – 30% EtOAc/hexanes) to provide the desired product as a colorless oil (18 mg, 46% yield).

¹H NMR (500 MHz, CDCl₃) δ 8.24 (dd, J = 4.5, 1.5 Hz, 1H), 7.12 (dd, J = 8.2, 1.5 Hz, 1H), 7.05 (dd, J = 8.2, 4.5 Hz, 1H), 5.96 (dt, J = 10.3, 3.4 Hz, 2H), 5.77 (dt, J = 10.4, 2.0 Hz, 2H), 4.35 – 4.19 (m, 2H), 2.92 (dtt, J = 23.0, 3.6, 1.8 Hz, 1H), 2.73 (dddd, J = 23.0, 5.5, 3.1, 2.4 Hz, 1H), 2.11 – 2.01 (m, 2H).

¹³C NMR (151 MHz, CDCl₃) δ 150.4, 148.4, 142.4, 131.0, 124.4, 124.4, 122.8, 77.2, 77.0, 76.8, 62.4, 39.3, 37.4, 26.2.

HRMS (ESI) m/z : [M+H]⁺ calc'd. for C₁₃H₁₄NO, 200.1075, found 200.1247.

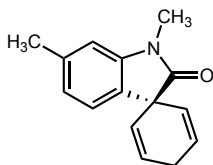


1',4'-dimethylspiro[cyclohexane-1,3'-indoline]-2,5-dien-2'-one (15): Prepared according to General Procedure A using *N*-(2-bromo-3-methylphenyl)-*N*-methylbenzamide (**S11**) (170 mg, 0.6 mmol, 1 equiv), DIPEA (300 μ L, 1.7 mmol, 3 equiv) and 3DPAFIPN (15 mg, 4 mol %). After 16 h, the reaction was purified on silica (20 % EtOAc/hexanes) to provide the desired product as a yellow solid (106 mg, 84% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.22 (t, J = 7.8 Hz, 1H), 6.85 (dt, J = 7.8, 0.8 Hz, 1H), 6.72 (dt, J = 7.7, 0.8 Hz, 1H), 6.17 (dt, J = 10.3, 3.4 Hz, 2H), 5.36 (dt, J = 10.3, 2.0 Hz, 2H), 3.23 (s, 3H), 3.04 (dtt, J = 23.3, 3.4, 2.1 Hz, 1H), 2.82 (dtt, J = 23.2, 3.4, 2.1 Hz, 1H), 2.22 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 177.6, 143.1, 136.0, 130.1, 128.3, 127.7, 125.1, 122.7, 105.7, 51.8, 26.7, 25.8, 16.7.

HRMS (ESI) m/z : [M+H]⁺ calc'd. for C₁₅H₁₆NO, 226.1232; found 226.1323.



1',6'-dimethylspiro[cyclohexane-1,3'-indoline]-2,5-dien-2'-one (16)

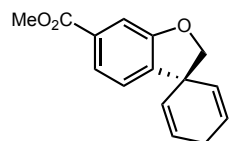
Prepared according to General Procedure A using *N*-(2-bromo-5-methylphenyl)-*N*-methylbenzamide (**S13**) (152 mg, 0.5 mmol, 1 equiv), DIPEA (280 μ L, 1.5 mmol, 3 equiv) and 3DPAFIPN (15 mg, 5 mol%). After 16 h, purification via preparative HPLC on an Agilent 1200 Infinity Series chromatograph using an Agilent PrepC18 30 x 250 mm 10 μ m column, with a linear gradient using water and 0.1% formic acid (FA) (Solvent A) and MeCN and 0.1% FA

(Solvent B); $t=0$ min, 50% B, $t=25$ min, 99% B, with a flow rate 40 mL/min, to provide the desired product as a light yellow solid (80.0 mg, 71% yield).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.00 (d, $J = 7.5$ Hz, 1H), 6.87 (ddd, $J = 7.4, 1.5, 0.8$ Hz, 1H), 6.67 (dd, $J = 1.6, 0.8$ Hz, 1H), 6.16 – 6.07 (m, 2H), 5.37 (dt, $J = 10.3, 2.0$ Hz, 2H), 3.21 (s, 3H), 2.97 (dt, $J = 23.3, 3.3, 2.2$ Hz, 1H), 2.84 (dt, $J = 23.2, 3.6, 2.0$ Hz, 1H), 2.39 (d, $J = 0.7$ Hz, 3H) ppm.

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 178.3, 143.2, 138.8, 131.5, 127.2, 124.6, 124.2, 123.5, 109.1, 51.7, 26.7, 25.9, 21.9 ppm.

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calc'd. for $\text{C}_{15}\text{H}_{16}\text{NO}$, 226.1232; found 226.1303.

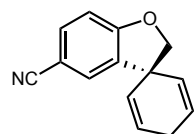


methyl 2H-spiro[benzofuran-3,1'-cyclohexane]-2',5'-diene-6-carboxylate (17): Prepared according to General Procedure A using methyl 3-(benzyloxy)-4-iodobenzoate (**S14**) (156 mg, 0.4 mmol, 1 equiv), DIPEA (260 μL , 1.5 mmol, 3 equiv) and 3DPAFIPN (17 mg, 5 mol %). After 16 h, the reaction was purified on silica (10 – 30% EtOAc/hexanes) to provide the desired product as a yellow oil (66 mg, 64% yield).

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.60 (dd, $J = 7.8, 1.5$ Hz, 1H), 7.44 (d, $J = 1.5$ Hz, 1H), 7.06 (d, $J = 7.7$ Hz, 1H), 5.90 (dt, $J = 10.1, 3.4$ Hz, 2H), 5.70 (dt, $J = 10.2, 2.0$ Hz, 2H), 4.39 (s, 2H), 3.89 (s, 3H), 2.81 (dddd, $J = 23.3, 5.4, 3.2, 2.1$ Hz, 1H), 2.72 (dt, $J = 23.3, 3.5, 2.1$ Hz, 1H).

$^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.9, 159.0, 139.7, 130.8, 128.3, 124.6, 124.6, 123.1, 110.7, 83.7, 77.2, 77.0, 76.8, 52.1, 47.4, 25.9.

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calc'd. for $\text{C}_{15}\text{H}_{15}\text{O}_3$, 243.1021; found 243.1062.

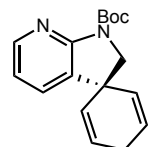


2H-spiro[benzofuran-3,1'-cyclohexane]-2',5'-diene-5-carbonitrile (18): Prepared according to General Procedure B using 4-(benzyloxy)-3-chlorobenzonitrile (**S15**) (119 mg, 0.5 mmol, 1 equiv), DIPEA (900 μL , 5.2 mmol, 10 equiv) and 3DPAFIPN (18 mg, 6 mol %). After 16 h, the reaction was purified on silica (5% EtOAc/hexanes) to provide the desired product as a yellow solid (55 mg, 54% yield).

$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.47 (dd, $J = 8.3, 1.8$ Hz, 1H), 7.31 (d, $J = 1.8$ Hz, 1H), 6.86 (d, $J = 8.3$ Hz, 1H), 5.94 (dt, $J = 10.1, 3.4$ Hz, 2H), 5.69 (dt, $J = 10.2, 2.0$ Hz, 2H), 4.44 (s, 2H), 2.83 (dddd, $J = 23.4, 5.4, 3.4, 2.1$ Hz, 1H), 2.75 (dt, $J = 23.4, 3.7, 2.0$ Hz, 1H).

$^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 162.4, 136.1, 133.8, 129.3, 127.9, 125.1, 119.4, 110.7, 104.3, 84.3, 47.0, 25.8.

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calc'd. for $\text{C}_{14}\text{H}_{12}\text{NO}$, 210.0919; found 210.0954.



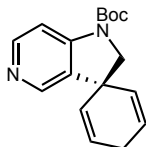
tert-butyl spiro[cyclohexane-1,3'-pyrrolo[2,3-b]pyridine]-2,5-diene-1'(2'H)-carboxylate (19): Prepared according to General Procedure A using *tert*-butyl benzyl(3-bromopyridin-2-

yl)carbamate (**S17**) (182 mg, 0.5 mmol, 1 equiv), DIPEA (260 μ L, 1.5 mmol, 3 equiv) and 3DPAFIPN (16 mg, 5 mol%). After 16 h, the reaction was purified on silica (10 – 30% EtOAc/hexanes) to provide the desired product as a yellow oil (109 mg, 77% yield).

$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.25 (dd, $J = 5.1, 1.7$ Hz, 1H), 7.27 – 7.23 (m, 1H), 6.84 (dd, $J = 7.4, 5.1$ Hz, 1H), 5.88 (dt, $J = 10.2, 3.4$ Hz, 2H), 5.65 (dt, $J = 10.3, 2.0$ Hz, 2H), 3.85 (s, 2H), 2.78 (dt, $J = 23.3, 3.3, 2.1$ Hz, 1H), 2.72 (dt, $J = 23.3, 3.4, 2.1$ Hz, 1H), 1.55 (s, 9H) ppm.

$^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 155.4, 151.0, 148.1, 133.3, 131.7, 129.2, 124.4, 118.1, 81.6, 60.9, 42.5, 28.5, 26.0 ppm.

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calc'd. for $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}_2$, 285.1603; found 285.1752.

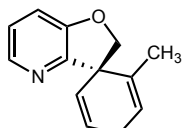


tert-butyl spiro[cyclohexane-1,3'-pyrrolo[3,2-c]pyridine]-2,5-diene-1'(2'H)-carboxylate (20**):** Prepared according to General Procedure A using *tert*-butyl benzyl(3-bromopyridin-4-yl)carbamate (**S19**) (182 mg, 0.5 mmol, 1 equiv), DIPEA (260 μ L, 1.5 mmol, 3 equiv) and 3DPAFIPN (16 mg, 5 mol%). After 16 h, the reaction was purified on silica (20-30% EtOAc/hexanes) to provide the desired product as a yellow oil (127 mg, 89% yield).

$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.35 (d, $J = 5.5$ Hz, 1H), 8.12 (d, $J = 0.8$ Hz, 1H), 7.67 (s, 1H), 5.88 (dt, $J = 10.1, 3.4$ Hz, 2H), 5.67 (dt, $J = 10.3, 2.0$ Hz, 2H), 3.85 (s, 2H), 2.81 (dddd, $J = 23.3, 5.4, 3.3, 2.1$ Hz, 1H), 2.73 (dt, $J = 23.4, 3.8, 2.1$ Hz, 1H), 1.57 (s, 9H) ppm.

$^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 152.0, 149.8, 148.1, 146.7, 133.8, 129.2, 124.3, 109.5, 82.3, 62.2, 43.4, 28.5, 25.9 ppm.

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calc'd. for $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}_2$, 285.1603; found 285.1696

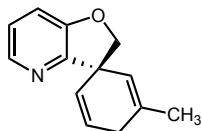


2-methyl-2'H-spiro[cyclohexane-1,3'-furo[3,2-b]pyridine]-2,5-diene (21**):** Prepared according to General Procedure A using 2-bromo-3-((2-methylbenzyl)oxy)pyridine (**S20**) (156 mg, 0.6 mmol, 1 equiv) DIPEA (260 μ L, 1.5 mmol, 3 equiv) and 3DPAFIPN (16 mg, 4 mol%). After 16 h, the reaction was purified on silica (15 – 30% EtOAc/hexanes) to provide the desired product as a yellow oil (97 mg, 87% yield).

$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.14 (dd, $J = 4.7, 1.5$ Hz, 1H), 7.07 (dd, $J = 8.1, 1.6$ Hz, 1H), 7.04 (dd, $J = 8.1, 4.6$ Hz, 1H), 6.00 (dtd, $J = 9.9, 3.4, 1.5$ Hz, 1H), 5.71 – 5.67 (m, 2H), 4.65 (d, $J = 9.3$ Hz, 1H), 4.37 (d, $J = 9.3$ Hz, 1H), 2.91 (dt, $J = 23.3, 3.7, 1.9$ Hz, 1H), 2.73 (dt, $J = 23.3, 3.4, 1.9$ Hz, 1H), 1.53 (q, $J = 1.8$ Hz, 3H).

$^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 154.5, 153.3, 142.8, 132.0, 127.7, 125.6, 122.7, 122.2, 116.6, 81.5, 50.6, 27.0, 19.0.

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calc'd. for $\text{C}_{13}\text{H}_{14}\text{NO}$, 200.1075; found 200.1057.

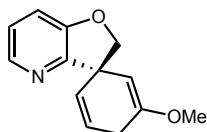


3-methyl-2'*H*-spiro[cyclohexane-1,3'-furo[3,2-*b*]pyridine]-2,5-diene (22): Prepared according to General Procedure A using 2-bromo-3-((3-methylbenzyl)oxy)pyridine (**S21**) (131 mg, 0.5 mmol, 1 equiv), DIPEA (260 μ L, 1.5 mmol, 3 equiv) and 3DPAFIPN (17 mg, 5 mol %). After 16 h, the reaction was purified on silica (20 – 30% EtOAc/hexanes) to provide the desired product as a light yellow solid (94 mg, 72% yield).

¹H NMR (600 MHz, CDCl₃) δ 8.12 (dd, J = 4.8, 1.4 Hz, 1H), 7.07 (dd, J = 8.1, 1.4 Hz, 1H), 7.03 (dd, J = 8.1, 4.8 Hz, 1H), 5.99 (dt, J = 9.9, 3.4 Hz, 1H), 5.72 (dq, J = 9.9, 2.1 Hz, 1H), 5.46 (p, J = 1.7 Hz, 1H), 4.41 (d, J = 1.2 Hz, 2H), 2.82 (d, J = 23.2 Hz, 1H), 2.62 (d, J = 23.5 Hz, 1H), 1.79 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 155.4, 152.6, 142.7, 133.4, 126.9, 125.7, 122.7, 121.8, 116.5, 83.1, 48.8, 30.8, 23.2.

HRMS (ESI) m/z : [M+H]⁺ calc'd. for C₁₃H₁₄NO, 200.1075; found 200.1304

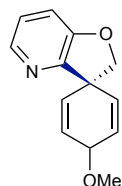


3-methoxy-2'*H*-spiro[cyclohexane-1,3'-furo[3,2-*b*]pyridine]-2,5-diene (23): Prepared according to General Procedure A using 2-bromo-3-((3-methoxybenzyl)oxy)pyridine (**S22**) (145 mg, 0.5 mmol, 1 equiv) DIPEA (260 μ L, 1.5 mmol, 3 equiv) and 3DPAFIPN (16 mg, 5 mol%). After 16 h, the reaction was purified on silica (20 – 30% EtOAc/hexanes) to provide the desired product as an orange solid (89 mg, 84% yield).

¹H NMR (600 MHz, CDCl₃) δ 8.14 (dd, J = 4.8, 1.4 Hz, 1H), 7.09 (dd, J = 8.1, 1.4 Hz, 1H), 7.05 (dd, J = 8.1, 4.7 Hz, 1H), 5.91 (dt, J = 9.9, 3.5 Hz, 1H), 5.71 (dq, J = 9.8, 2.1 Hz, 1H), 4.69 (q, J = 1.3 Hz, 1H), 4.47 (d, J = 8.9 Hz, 1H), 4.42 (d, J = 9.0 Hz, 1H), 3.57 (s, 3H), 2.97 (d, J = 22.0 Hz, 1H), 2.78 (d, J = 22.0 Hz, 1H).

¹³C NMR (151 MHz, CDCl₃) δ 155.6, 154.7, 152.5, 142.8, 127.4, 124.2, 122.7, 116.6, 95.5, 83.7, 54.0, 49.6, 28.6.

HRMS (ESI) m/z : [M+H]⁺ calc'd. for C₁₃H₁₄NO₂, 216.1025; found 216.1049

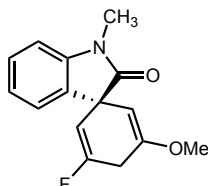


4-methoxy-2'*H*-spiro[cyclohexane-1,3'-furo[3,2-*b*]pyridine]-2,5-diene (24): Prepared according to General Procedure B using 2-bromo-3-((4-methoxybenzyl)oxy)pyridine (**S23**) (159 mg, 0.5 mmol, 1 equiv) DIPEA (900 μ L, 5.2 mmol, 10 equiv) and 3DPAFIPN (19 mg, 5 mol %). After 16 h, the reaction was purified on silica (20 – 50% EtOAc/hexanes) to isolate a single diastereomer as a light yellow oil (72 mg, 62% yield).

¹H NMR (600 MHz, CDCl₃) δ 8.12 (dd, J = 4.8, 1.4 Hz, 1H), 7.13 (dd, J = 8.1, 1.4 Hz, 1H), 7.08 (dd, J = 8.1, 4.8 Hz, 1H), 6.13 (dd, J = 10.2, 3.2 Hz, 2H), 6.02 (dd, J = 10.1, 1.6 Hz, 2H), 4.61 (tt, J = 3.2, 1.6 Hz, 1H), 4.54 (s, 2H), 3.39 (s, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ 153.3, 153.1, 142.8, 130.7, 126.6, 123.2, 117.0, 80.7, 69.2, 54.4, 48.5.

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calc'd. for $\text{C}_{13}\text{H}_{14}\text{NO}_2$, 216.1025; found 216.1081.



3-fluoro-5-methoxy-1'-methylspiro[cyclohexane-1,3'-indoline]-2,5-dien-2'-one (25):

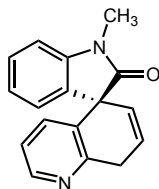
Prepared according to General Procedure A using 3-fluoro-*N*-(2-iodophenyl)-5-methoxy-*N*-methylbenzamide (**S25**) (77 mg, 0.2 mmol, 1 equiv), DIPEA (105 μL , 0.6 mmol, 3 equiv) and 3DPAFIPN (6 mg, 5 mol%). After 16 h, the reaction was purified on silica (10-30% EtOAc/hexanes) to provide the desired product as a yellow oil (35 mg, 68% yield).

^1H NMR (400 MHz, CDCl_3) δ 7.30 (td, $J = 7.6, 1.5$ Hz, 1H), 7.13 (ddd, $J = 7.4, 1.5, 0.6$ Hz, 1H), 7.07 (td, $J = 7.4, 1.0$ Hz, 1H), 6.85 (dt, $J = 7.8, 0.8$ Hz, 1H), 4.98 (dq, $J = 14.7, 1.5$ Hz, 1H), 4.33 (t, $J = 1.6$ Hz, 1H), 3.54 (s, 3H), 3.24 (s, 3H), 3.24 (dt, $J = 20.8, 1.5$ Hz, 1H), 3.09 (dq, $J = 21.0, 1.3$ Hz, 1H) ppm.

^{13}C NMR (126 MHz, CDCl_3) δ 178.2, 158.9 (d, $^1J_{\text{C-F}} = 257.2$ Hz), 154.5 (d, $^3J_{\text{C-F}} = 16.1$ Hz), 142.8, 133.9, 128.7, 124.8, 123.2, 101.6 (d, $^2J_{\text{C-F}} = 18.4$ Hz), 92.9, 54.8, 52.1 (d, $^3J_{\text{C-F}} = 9.2$ Hz), 29.6 (d, $^2J_{\text{C-F}} = 28.2$ Hz), 26.76 ppm.

^{19}F NMR (376 MHz, CDCl_3) δ -103.4 (d, $J = 14.6$ Hz) ppm.

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calc'd. for $\text{C}_{15}\text{H}_{15}\text{FNO}_2$, 260.1087; found 260.1191

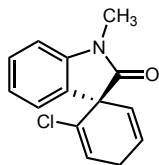


1-methyl-8'*H*-spiro[indoline-3,5'-quinolin]-2-one (26): Prepared according to General Procedure A using *N*-(2-iodophenyl)-*N*-methylquinoline-5-carboxamide (**S27**) (116 mg, 0.3 mmol, 1 equiv), DIPEA (160 μL , 0.9 mmol, 3 equiv) and 3DPAFIPN (10 mg, 5 mol%). After 16 h, the reaction was purified on silica (30-100% EtOAc/hexanes) to provide the desired product as a yellow solid (74 mg, 94% yield).

^1H NMR (400 MHz, CDCl_3) δ 8.47 (dd, $J = 4.7, 1.7$ Hz, 1H), 7.35 (td, $J = 7.7, 1.4$ Hz, 1H), 7.07 (td, $J = 7.5, 1.0$ Hz, 1H), 7.03 – 6.97 (m, 2H), 6.95 (dt, $J = 7.8, 0.8$ Hz, 1H), 6.87 (dd, $J = 7.9, 1.7$ Hz, 1H), 6.37 (ddd, $J = 9.9, 4.1, 3.2$ Hz, 1H), 5.54 (ddd, $J = 9.9, 2.5, 1.8$ Hz, 1H), 3.92 (dt, $J = 22.7, 2.9$ Hz, 1H), 3.74 (ddd, $J = 22.6, 4.0, 1.8$ Hz, 1H), 3.28 (s, 3H) ppm.

^{13}C NMR (126 MHz, CDCl_3) δ 177.5, 154.6, 148.5, 143.5, 134.9, 134.7, 129.9, 128.9, 128.3, 124.7, 124.7, 123.5, 122.0, 108.4, 55.1, 33.0, 26.7 ppm.

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calc'd. for $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}$, 263.1184; found 263.1247.

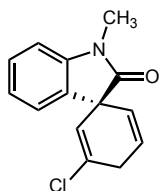


2-chloro-1'-methylspiro[cyclohexane-1,3'-indoline]-2,5-dien-2'-one (27): Prepared according to General Procedure A using 2-chloro-*N*-(2-iodophenyl)-*N*-methylbenzamide (**S29**) (186 mg, 0.5 mmol, 1 equiv), DIPEA (260 μ L, 1.5 mmol, 3 equiv), and 3DPAFIPN (16 mg, 5 mol%). After 16 h, the reaction was purified on silica (10–30% EtOAc/hexanes) to provide the desired product as an off-white solid (86 mg, 70% yield).

¹H NMR (400 MHz, CDCl₃) δ 7.32 (t, J = 7.6 Hz, 1H), 7.14 (d, J = 8.1 Hz, 1H), 7.09 (d, J = 7.3 Hz, 1H), 6.85 (d, J = 7.8 Hz, 1H), 6.23 (t, J = 3.7 Hz, 1H), 6.04 (dt, J = 9.8, 3.4 Hz, 1H), 5.34 (dt, J = 9.8, 2.1 Hz, 1H), 3.25 (s, 3H), 3.16 – 3.05 (m, 1H), 3.05 – 2.95 (m, 1H).

¹³C NMR (126 MHz, CDCl₃) δ 175.4, 143.7, 131.6, 129.1, 128.0, 126.3, 125.5, 124.3, 124.2, 123.1, 108.2, 56.7, 28.3, 26.71.

HRMS (ESI) m/z : [M+H]⁺ calc'd. for C₁₄H₁₃ClNO, 246.0686; found 246.0675

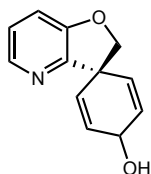


3-chloro-1'-methylspiro[cyclohexane-1,3'-indoline]-2,5-dien-2'-one (28): Prepared according to General Procedure A using 3-chloro-*N*-(2-iodophenyl)-*N*-methylbenzamide (**S31**) (159 mg, 0.4 mmol, 1 equiv), DIPEA (210 μ L, 1.2 mmol, 3 equiv), and 3DPAFIPN (14.0 mg, 5 mol%). After 16 h, the reaction was purified on silica (10–20% EtOAc/hexanes) to provide the desired product as light yellow solid (59.9 mg, 57% yield).

¹H NMR (500 MHz, CDCl₃) δ 7.31 (tt, J = 7.7, 1.3 Hz, 1H), 7.15 – 7.11 (m, 1H), 7.08 (tt, J = 7.4, 1.0 Hz, 1H), 6.88 – 6.82 (m, 1H), 6.06 (dtd, J = 9.8, 3.5, 1.0 Hz, 1H), 5.52 (q, J = 1.7 Hz, 1H), 5.40 – 5.35 (m, 1H), 3.31 – 3.06 (m, 5H).

¹³C NMR (126 MHz, CDCl₃) δ 176.4, 142.9, 133.4, 132.5, 128.9, 126.5, 124.9, 123.4, 123.1, 121.21, 121.20, 54.4, 33.2, 26.7.

HRMS (ESI) m/z : [M+H]⁺ calc'd. for C₁₄H₁₃ClNO, 246.0686; found 246.0770.



2'*H*-spiro[cyclohexane-1,3'-furo[3,2-*b*]pyridine]-2,5-dien-4-ol (**29**): Prepared according to General Procedure A using 2-bromo-3-((4-chlorobenzyl)oxy)pyridine (**S32**) (167 mg, 0.6 mmol, 1 equiv), DIPEA (315 μ L, 1.8 mmol, 3 equiv) and 3DPAFIPN (19 mg, 5 mol %). After 16 h, the reaction was purified on silica (100% EtOAc/hexanes to 10% MeOH/EtOAc) to provide the desired product as a 1.8 : 1 mixture of diastereomers (combined yield 97 mg, 85% yield).

Major Diastereomer:

¹H NMR (600 MHz, CDCl₃) δ 8.08 (dd, *J* = 4.8, 1.3 Hz, 1H), 7.11 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.06 (dd, *J* = 8.1, 4.8 Hz, 1H), 6.20 (dd, *J* = 9.8, 4.2 Hz, 2H), 5.94 (d, *J* = 9.1 Hz, 2H), 4.54 (s, 2H), 4.50 (tt, *J* = 4.1, 0.9 Hz, 1H) ppm.

¹³C NMR (151 MHz, CDCl₃) δ 153.7, 152.1, 142.6, 131.5, 130.2, 123.3, 117.4, 81.7, 60.9, 49.0 ppm.

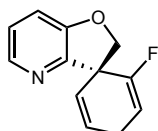
HRMS (ESI) *m/z*: [M+H] calc'd for C₁₂H₁₃NO₂, 202.0868, found 202.0874

Minor Diastereomer:

¹H NMR (600 MHz, CDCl₃) δ 8.06 (dd, *J* = 4.8, 1.3 Hz, 1H), 7.08 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.03 (dd, *J* = 8.1, 4.8 Hz, 1H), 6.09 (dd, *J* = 10.1, 3.2 Hz, 2H), 5.88 (dd, *J* = 10.0, 1.5 Hz, 2H), 4.79 (s, 1H), 4.47 (s, 2H).

¹³C NMR (151 MHz, CDCl₃) δ 153.1, 153.1, 142.9, 129.3, 129.1, 123.2, 117.0, 80.7, 61.7, 48.3.

HRMS (ESI) *m/z*: [M+H] calc'd for C₁₂H₁₂NO₂, 202.0868, found 202.0929



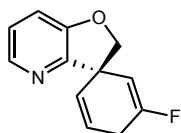
2-fluoro-2'*H*-spiro[cyclohexane-1,3'-furo[3,2-*b*]pyridine]-2,5-diene (30): Prepared according to General Procedure A using 2-bromo-3-((2-fluorobenzyl)oxy)pyridine (**S33**) (144 mg, 0.5 mmol, 1 equiv), DIPEA (280 μL, 1.6 mmol, 3 equiv) and 3DPAFIPN (17 mg, 5 mol %). After 16 h, the reaction was purified on silica (20 – 30% EtOAc/hexanes) to provide the desired product as a yellow solid (86 mg, 83% yield).

¹H NMR (600 MHz, CDCl₃) δ 8.17 (dd, *J* = 3.6, 2.5 Hz, 1H), 7.11 (s, 1H), 7.10 (d, *J* = 1.3 Hz, 1H), 5.95 (dddd, *J* = 10.7, 4.5, 3.4, 1.2 Hz, 1H), 5.69 (tt, *J* = 9.6, 2.0 Hz, 1H), 5.54 (dtd, *J* = 16.7, 3.6, 1.2 Hz, 1H), 4.83 (d, *J* = 9.3 Hz, 1H), 4.45 (d, *J* = 9.3 Hz, 1H), 3.09 (ddtd, *J* = 22.8, 5.4, 3.5, 2.0 Hz, 1H), 2.91 (ddtd, *J* = 22.8, 4.6, 3.5, 2.0 Hz, 1H).

¹³C NMR (151 MHz, CDCl₃) δ 156.2 (d, ¹*J*_{C-F} = 253.6 Hz), 153.6, 151.3, 142.8, 127.1 (d, ³*J*_{C-F} = 5.8 Hz), 125.3 (d, ⁴*J*_{C-F} = 2.4 Hz), 123.5, 116.8, 102.5 (d, ²*J*_{C-F} = 16.5 Hz), 79.3, 49.8 (d, ²*J*_{C-F} = 24.5 Hz), 26.4 (d, ³*J*_{C-F} = 6.7 Hz).

¹⁹F NMR (565 MHz, CDCl₃) δ -117.94 – -118.05 (1F, m).

HRMS (ESI) *m/z*: [M+H]⁺ calc'd for C₁₂H₁₁FNO, 204.0825; found 204.0956.



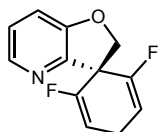
3-fluoro-2'*H*-spiro[cyclohexane-1,3'-furo[3,2-*b*]pyridine]-2,5-diene (31): Prepared according to General Procedure A using 2-bromo-3-((3-fluorobenzyl)oxy)pyridine (**S34**) (152 mg, 0.5 mmol, 1 equiv), DIPEA (300 μL, 1.7 mmol, 3 equiv) and 3DPAFIPN (17 mg, 5 mol %). After 16 h, the reaction was purified on silica (20 – 30% EtOAc/hexanes) to provide the desired product as a colorless oil (91 mg, 83% yield).

¹H NMR (600 MHz, CDCl₃) δ 8.14 (dd, *J* = 4.6, 1.6 Hz, 1H), 7.10 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.07 (dd, *J* = 8.1, 4.6 Hz, 1H), 5.89 (ddt, *J* = 9.8, 7.7, 3.5 Hz, 2H), 5.73 – 5.69 (m, 2H), 5.32 (dq, *J* = 16.3, 1.5 Hz, 1H), 4.47 (dd, *J* = 9.2, 1.4 Hz, 1H), 4.44 (dd, *J* = 9.2, 0.7 Hz, 1H), 3.10 (ddt, *J* = 22.3, 3.1, 1.5 Hz, 2H), 2.92 (ddt, *J* = 22.3, 3.4, 2.1 Hz, 2H).

¹³C NMR (151 MHz, CDCl₃) δ 158.8 (d, ¹J_{C-F} = 258.2 Hz), 153.9 (d, ⁴J_{C-F} = 2.0 Hz), 152.5, 142.9, 127.4 (d, ³J_{C-F} = 2.8 Hz), 123.2, 123.2, 123.1, 116.9, 104.0 (d, ²J_{C-F} = 16.7 Hz), 82.4 (d, ⁴J_{C-F} = 2.8 Hz), 50.0 (d, ³J_{C-F} = 8.1 Hz), 26.8 (d, ²J_{C-F} = 26.1 Hz).

¹⁹F NMR (565 MHz, CDCl₃) δ -103.27 (dd, *J* = 16.9, 7.8 Hz).

HRMS (ESI) *m/z*: [M+H]⁺ calc'd. for C₁₂H₁₁FNO, 204.0825; found 204.1005.



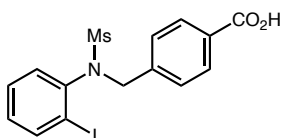
2,6-difluoro-2'*H*-spiro[cyclohexane-1,3'-furo[3,2-*b*]pyridine]-2,5-diene (32): Prepared according to General Procedure A using 2-bromo-3-((2,6-difluorobenzyl)oxy)pyridine (**S35**) (175 mg, 0.6 mmol, 1 equiv), DIPEA (300 μL, 1.5 mmol, 3 equiv) and 3DPAFIPN (16 mg, 4 mol%). After 16 h, the reaction was purified on silica (10 – 30% EtOAc/hexanes) to provide the desired product as a light yellow solid (83 mg, 64% yield).

¹H NMR (600 MHz, CDCl₃) δ 8.20 (dd, *J* = 4.4, 1.7 Hz, 1H), 7.16 (dd, *J* = 8.2, 4.4 Hz, 1H), 7.14 (dd, *J* = 8.2, 1.7 Hz, 1H), 5.58 (ddt, *J* = 10.4, 5.3, 3.7 Hz, 2H), 4.80 (s, 2H), 3.07 (dtt, *J* = 22.2, 5.1, 3.7 Hz, 1H), 2.89 (dtt, *J* = 22.3, 4.9, 3.7 Hz, 1H).

¹³C NMR (151 MHz, CDCl₃) δ 154.4 (dd, ¹J_{C-F} = 254.8, ³J_{C-F} = 12.1 Hz), 154.6, 147.7, 142.8, 124.2, 117.0, 102.3 (d, ²J_{C-F} = 14.4 Hz), 75.5, 52.1 (t, ²J_{C-F} = 27.8 Hz), 22.2 (t, ³J_{C-F} = 8.0 Hz).

¹⁹F NMR (565 MHz, CDCl₃) δ -119.83 (dq, *J* = 10.2, 5.1 Hz).

HRMS (ESI) *m/z*: [M+H]⁺ calc'd. for C₁₂H₁₀F₂NO, 222.0730; found 222.0972



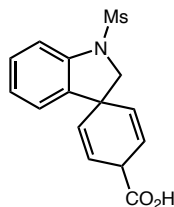
4-((*N*-(2-iodophenyl)methylsulfonamido)methyl)benzoic acid (33)

A 100 mL round bottom flask was charged with *N*-(2-iodophenyl)methanesulfonamide (**S1**), (414 mg, 1.4 mmol, 1.0 equiv) and K₂CO₃ (480 mg, 3.5 mmol, 2.2 equiv). DMF was added (50 mL), followed by benzyl bromide (350 μL, 2.4 mmol, 2.3 equiv). The reaction was stirred overnight (ca. 16 h) at 50 °C. The reaction was cooled to room temperature and then partitioned between EtOAc and water. The organic layer was washed with brine 3x, dried with MgSO₄ and concentrated. The crude oil was dissolved in THF/H₂O (1:1 v/v) and lithium hydroxide (excess, ca 10 equiv) was added. The reaction was stirred at 50 °C until reaction completion as determined by TLC. The reaction was then cooled to room temperature and partitioned between EtOAc and water. The organic layer was washed 3x with 1M NaOH. The organic layer was then discarded. EtOAc was added and the aqueous layer was re-acidified with HCl. The aqueous layer was extracted 3x with EtOAc. The combined organic layers were dried with Na₂SO₄ and concentrated. The desired product was purified by trituration with a minimal amount of EtOAc and was collected by filtration as a white solid (371 mg, 62% over 2 steps).

¹H NMR (400 MHz, CDCl₃) δ 8.04 (d, *J* = 8.3 Hz, 1H), 7.94 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.40 (d, *J* = 8.3 Hz, 2H), 7.26 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.09 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.05 (td, *J* = 7.5, 1.6 Hz, 1H), 5.16 (d, *J* = 14.9 Hz, 1H), 4.66 (d, *J* = 14.9 Hz, 1H), 3.13 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 171.2, 141.6, 140.6, 140.2, 134.3, 130.4, 129.7, 129.2, 129.0, 126.6, 101.8, 55.2, 40.4.

LRMS (APCI) *m/z*: [M+H]⁺ calc'd. for C₁₅H₁₅INO₄S 432.0, found 431.6.



1'-(methylsulfonyl)spiro[cyclohexane-1,3'-indoline]-2,5-diene-4-carboxylic acid (34)

Prepared according to General Procedure A using 4-((*N*-(2-iodophenyl) methylsulfonylamido) methyl) benzoic acid **33** (120 mg, 0.28 mmol, 1.0 equiv), DIPEA (244 μ L, 1.4 mmol, 5.0 equiv) and 3DPAFIPN (10.1 mg, 5 mol%). After 16 h, the reaction mixture was partitioned between EtOAc and water. The aqueous layer was acidified with 1N HCl and extracted 5x. The combined organic layers were washed with brine, dried with Na₂SO₄, filtered, and concentrated. ¹H NMR analysis of the crude reaction mixture indicated a 1:1 diastereomeric ratio. Purification of the residue by silica gel chromatography (EtOAc (containing 1% v/v AcOH):Hex, 30–100% gradient) afforded three fractions: the leading fraction contained a single diastereomer (f1: 30.8 mg), followed by two fractions that were enriched in either diastereomer (f2: 176.9 mg, 1.6:1 dr; f3 210.7 mg, 1:2 dr), combined yield: 418.4 mg (95%).

Diastereomer 1 (f1):

¹H NMR (400 MHz, CDCl₃) δ 6.04 (dd, *J* = 10.1, 3.6 Hz, 1H), 5.91 (dd, *J* = 10.2, 2.1 Hz, 1H), 3.89 (m, 1H), 3.87 (s, 2H), 2.95 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 177.2, 141.1, 136.2, 130.9, 129.1, 125.8, 124.4, 121.7, 113.3, 62.3, 45.3, 41.8, 34.7.

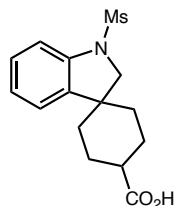
Diastereomer 2 (characteristic peaks):

¹H NMR (400 MHz, CDCl₃) δ 6.08 (dd, *J* = 10.1, 3.4 Hz, 1H), 5.92 (dd, *J* = 10.1, 2.2 Hz, 1H), 3.95 – 3.91 (m, 1H)

For the mixture of diastereomers (f2)

¹³C NMR (151 MHz, CDCl₃) δ 177.9, 176.3, 141.9, 136.4, 136.2, 131.0, 130.9, 129.2, 129.1, 125.8, 125.3, 124.4, 124.2, 122.5, 121.7, 113.5, 113.3, 62.3, 62.3, 45.3, 42.4, 41.5, 35.9, 34.7, 32.6.

LRMS (APCI) m/z: [M-H]⁻ calc'd for C₁₅H₁₄NO₄S 304.1, found 304.1

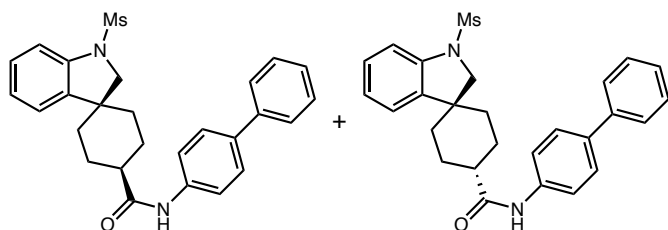


1'-(methylsulfonyl)spiro[cyclohexane-1,3'-indoline]-4-carboxylic acid (S36)

A 4 mL vial was charged with 1'-(methylsulfonyl)spiro[cyclohexane-1,3'-indoline]-2,5-diene-4-carboxylic acid (**S37**, from f2 (1.6:1 dr; 15.4 mg, 0.05 mmol), 5 mg 5% Pd/C (wet basis), and a stir bar. To the vial was added 2 mL of 200 proof ethanol and the vial was placed in Parr high-pressure reactor. The reactor was sealed, evacuated, and backfilled with hydrogen at 1 PSI. This was repeated for a total of 5 times. The reactor was then pressurized to 40 PSI with hydrogen and

stirred for 72 hours. Upon reaction completion, the reactor was depressurized and dismantled. 0.5 mL of water was added to the reaction vial then the reaction mixture was filtered through celite. The filtrate was concentrated then azeotroped with 10 mL of MeCN to remove the remaining water. Quantitative conversion to the hydrogenated product was detected by ^1H NMR and LRMS. The crude residue was used in the next step without further purification.

LRMS (APCI) m/z : $[\text{M}-\text{H}]^-$ calc'd for $\text{C}_{15}\text{H}_{18}\text{NO}_4\text{S}$ 308.1, found 308.1



***N*-([1,1'-biphenyl]-4-yl)-1'-(methylsulfonyl)spiro[cyclohexane-1,3'-indoline]-4-carboxamide (35)**

In an 8mL reaction tube equipped with a stir bar, 1'-(methylsulfonyl)spiro[cyclohexane-1,3'-indoline]-4-carboxylic acid (**35**) (15.4 mg, 0.05 mmol, 1.0 equiv) was dissolved in EtOAc to make a 0.1 M solution. 4-aminobiphenyl 10 mg, 0.06 mmol, 1.2 equiv) was added, followed by DIPEA 35 μL , 0.2 mmol, 4.0 equiv). Propanephosphonic acid anhydride (as a 50% w/w solution in EtOAc) 55 μL , 0.08 mmol, 1.6 equiv) was then added in one portion. The reaction mixture was allowed to stir for 3 h before being partitioned between water and EtOAc. The organic layer was washed with 1M HCl 3x then brine 3x. The organic layer was then dried with Na_2SO_4 , filtered, and concentrated. The crude residue was purified by preparatory TLC in 50% EtOAc/Hex eluent to separate both diastereomers and afford the desired products as white solids: diastereomer 1 (R_f 0.47, 50% EtOAc/Hex): 12.0 mg; diastereomer 2 (R_f 0.35, 50% EtOAc/Hex): 5.8 mg; Combined yield: 17.8 mg, 82% over 2-steps).

Diastereomer 1 (R_f 0.47):

^1H NMR (600 MHz, CDCl_3) δ 7.61 (d, J = 8.5 Hz, 2H), 7.57 (d, J = 8.3 Hz, 4H), 7.46 – 7.39 (m, 3H), 7.37 – 7.31 (m, 1H), 7.27 – 7.21 (m, 2H), 7.15 (d, J = 7.6 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 3.87 (s, 2H), 2.92 (s, 3H), 2.43 – 2.32 (m, 1H), 2.08 (d, J = 11.4 Hz, 2H), 1.91 (d, J = 11.0 Hz, 2H), 1.83 – 1.71 (m, 4H).

^{13}C NMR (151 MHz, CDCl_3) δ 173.0, 141.4, 140.5, 139.0, 137.8, 137.1, 129.3, 128.3, 127.7, 127.2, 126.9, 123.7, 122.9, 120.7, 115.5, 58.4, 45.8, 44.8, 43.9, 35.9, 34.7, 29.7, 26.2.

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calc'd. for $\text{C}_{27}\text{H}_{29}\text{N}_2\text{O}_3\text{S}$, 461.1821, found 461.1875

Diastereomer 2 (R_f 0.35):

^1H NMR (600 MHz, CDCl_3) δ 7.63 (d, J = 8.6 Hz, 2H), 7.61 – 7.56 (m, 4H), 7.48 – 7.38 (m, 4H), 7.36 – 7.31 (m, 1H), 7.29 (s, 1H), 7.23 (ddd, J = 8.1, 7.5, 1.3 Hz, 1H), 7.06 (td, J = 7.5, 1.1 Hz, 1H), 3.76 (s, 2H), 2.91 (s, 3H), 2.62 – 2.52 (m, 1H), 2.25 – 2.12 (m, 4H), 1.94 – 1.86 (m, 2H), 1.69 – 1.62 (m, 2H).

^{13}C NMR (151 MHz, CDCl_3) δ 173.1, 141.1, 140.5, 139.1, 137.7, 137.1, 128.8, 128.5, 127.7, 127.2, 126.9, 124.9, 123.7, 120.1, 115.3, 61.7, 45.8, 43.3, 42.1, 34.3, 34.1, 30.2, 25.8.

HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calc'd. for $\text{C}_{27}\text{H}_{29}\text{N}_2\text{O}_3\text{S}$, 461.1821, found 461.1874.

X. Computational Details

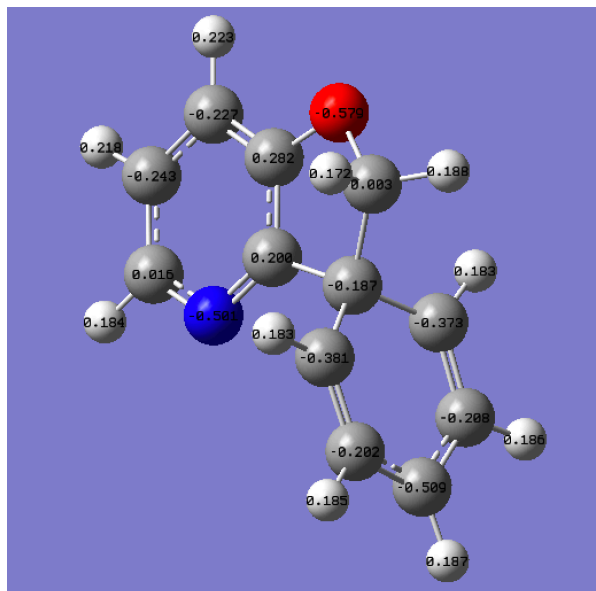
All DFT calculations were carried out using the Gaussian 16 software package¹¹ at the uM06¹² level of theory with the 6-311+G(d,p)¹³ basis set. The CPCM formalism for the Self Consistent Reaction Field (SCRF) model of solvation was employed in calculations to account for solvation in MeCN, and the default parameters as implemented in Gaussian were used. NBO charges were obtained using NBO Version 3.1 in Gaussian 16.¹⁴ Orbitals were visualized using Avagadro version 1.2.0¹⁵ or GaussView 6.¹¹

Reduction potentials were calculated using a modified procedure as described by Nicewicz and coworkers.¹⁶ Geometry optimizations were carried out for the reduced and neutral forms of each molecule, and frequency calculations were performed on the minimized structures to ensure no imaginary frequencies existed. Gibbs free energies (G_{298}) were obtained from the calculation and employed in the following equation:

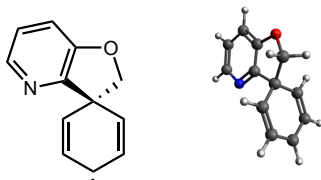
$$E_{1/2}^{0,calc} = -\frac{(G_{298}[reduced] - G_{298}[oxidized])}{n_e \mathcal{F}} - E_{1/2}^{0,SHE} + E_{1/2}^{0,SCE}$$

Where n_e is the number of electrons transferred ($n_e = 1$ for all calculations here), \mathcal{F} is the Faraday constant (value 23.061 kcal mol⁻¹ V⁻¹), $E_{1/2}^{0,SHE}$ is the absolute value for the standard hydrogen electrode (SHE, value = 4.281 V) and $E_{1/2}^{0,SCE}$ is the potential of the saturated calomel electrode (SCE) relative to the SHE in MeCN (value = -0.141V)¹⁷, and $G_{298}[oxidized]$ and $G_{298}[reduced]$ are the Gibbs free energies in DMSO obtained from DFT calculations.

NBO coefficients for the cyclohexadienyl anion shown in Figure 3 are shown below. These values suggest that the diallyl anion is the dominant resonance contributor.



Molecular coordinates of optimized structures:



Charge: 0

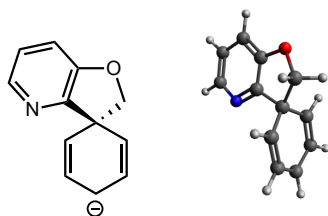
Multiplicity: 2

Number of Imaginary Frequencies: 0

Solvation: MeCN

G₂₉₈: -592.774968 Hartree

C	2.1359520	-1.8896820	-0.0496070
C	3.1861070	-0.9987020	0.1321480
C	2.9431520	0.3713730	0.1841100
C	1.6254950	0.7551680	0.0419870
C	0.6391270	-0.2082310	-0.1308360
N	0.8577230	-1.5059140	-0.1734550
H	3.7393170	1.0946780	0.3238200
H	2.3295360	-2.9585960	-0.0925660
H	4.1976640	-1.3776000	0.2302670
O	1.1400950	2.0143860	0.0668640
C	-0.2220040	1.9418370	-0.4049320
H	-0.2233980	2.1681040	-1.4787000
H	-0.8062050	2.6922400	0.1295300
C	-0.7197230	0.4922050	-0.1623780
C	-1.5940820	-0.0037460	-1.2661860
C	-1.3538670	0.3427030	1.1893470
C	-2.7817220	-0.6228760	-1.0343270
H	-1.2186370	0.1187960	-2.2800550
C	-2.5460480	-0.2838250	1.3700900
H	-0.7962480	0.7415160	2.0352210
C	-3.2796340	-0.7941480	0.2761670
H	-3.3647350	-0.9882490	-1.8752470
H	-2.9500320	-0.3834420	2.3738660
H	-4.2286040	-1.2935920	0.4396380



Charge: -1
 Multiplicity: 1
 Number of Imaginary Frequencies: 0
 Solvation: MeCN
 G₂₉₈: -592.888245 Hartree

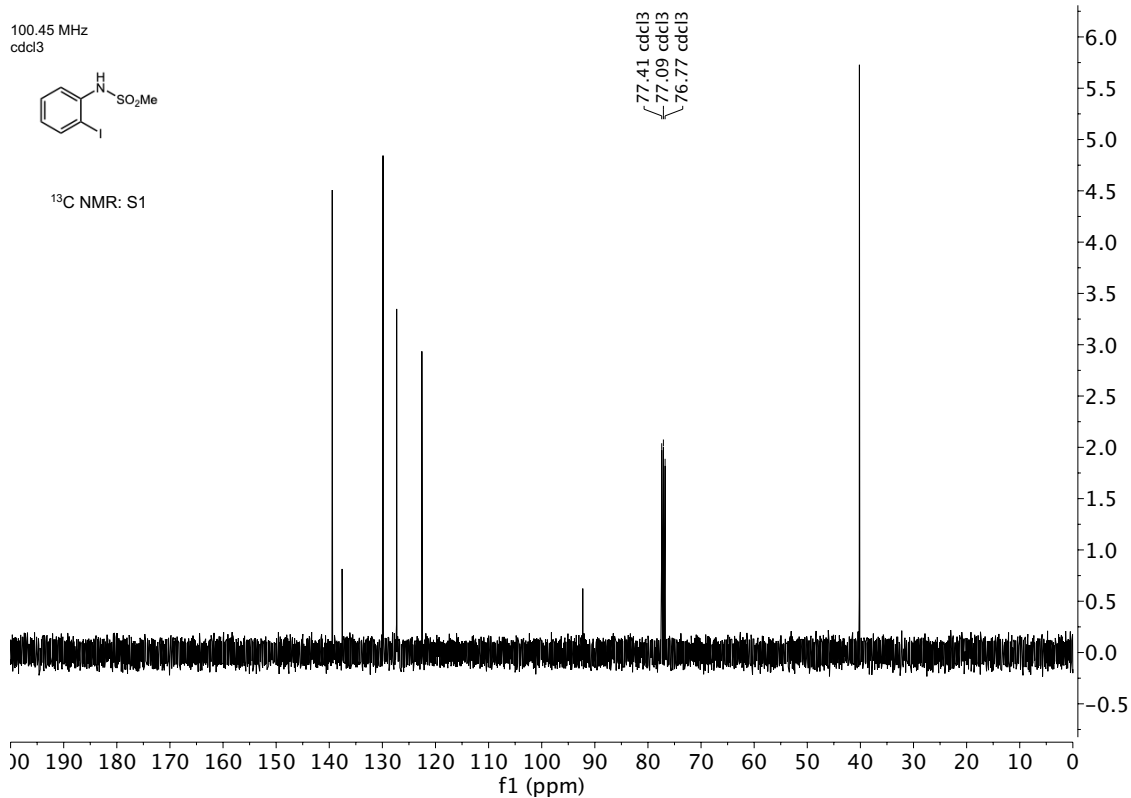
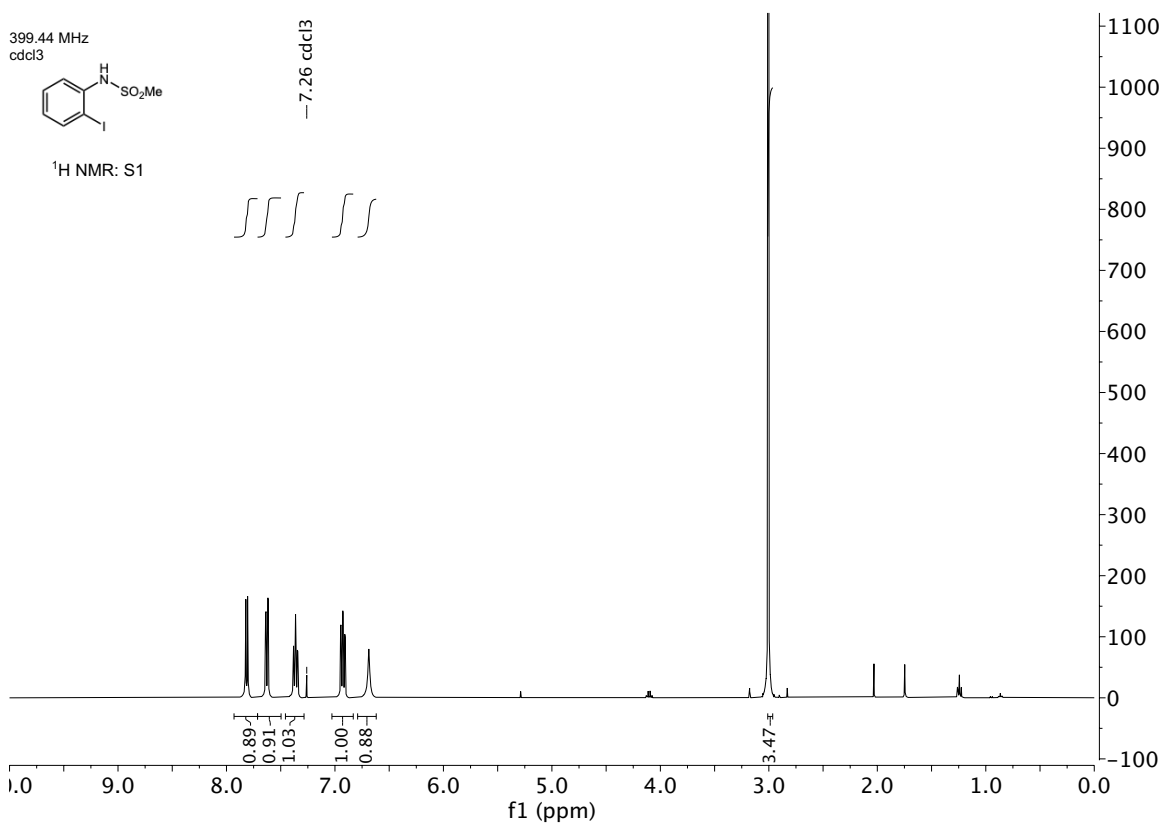
C	2.076487	-1.923675	-0.112260
C	3.153155	-1.081021	0.121502
C	2.951311	0.296572	0.212533
C	1.650719	0.725897	0.059913
C	0.621043	-0.189039	-0.156695
N	0.812151	-1.493178	-0.247670
H	3.769359	0.989395	0.383874
H	2.235740	-2.997189	-0.193741
H	4.149697	-1.497808	0.224187
O	1.220503	2.653200	0.102935
C	-0.155812	1.989316	-0.358778
H	-0.152963	2.265084	-1.423647
H	-0.708878	2.739142	0.211695
C	-0.710632	0.558718	-0.164365
C	-1.671897	0.164641	-1.256064
C	-1.383810	0.481000	1.186441
C	-2.795092	-0.578860	-1.972200
H	-1.389390	0.419182	-2.278172
C	-2.512029	-0.354137	1.356645
H	-0.879557	0.854767	2.040930
C	-3.227819	-0.932789	0.286072
H	-3.399656	-0.881098	-1.867266
H	-2.895207	-0.471807	2.372384
H	-4.151973	-1.478266	0.448639

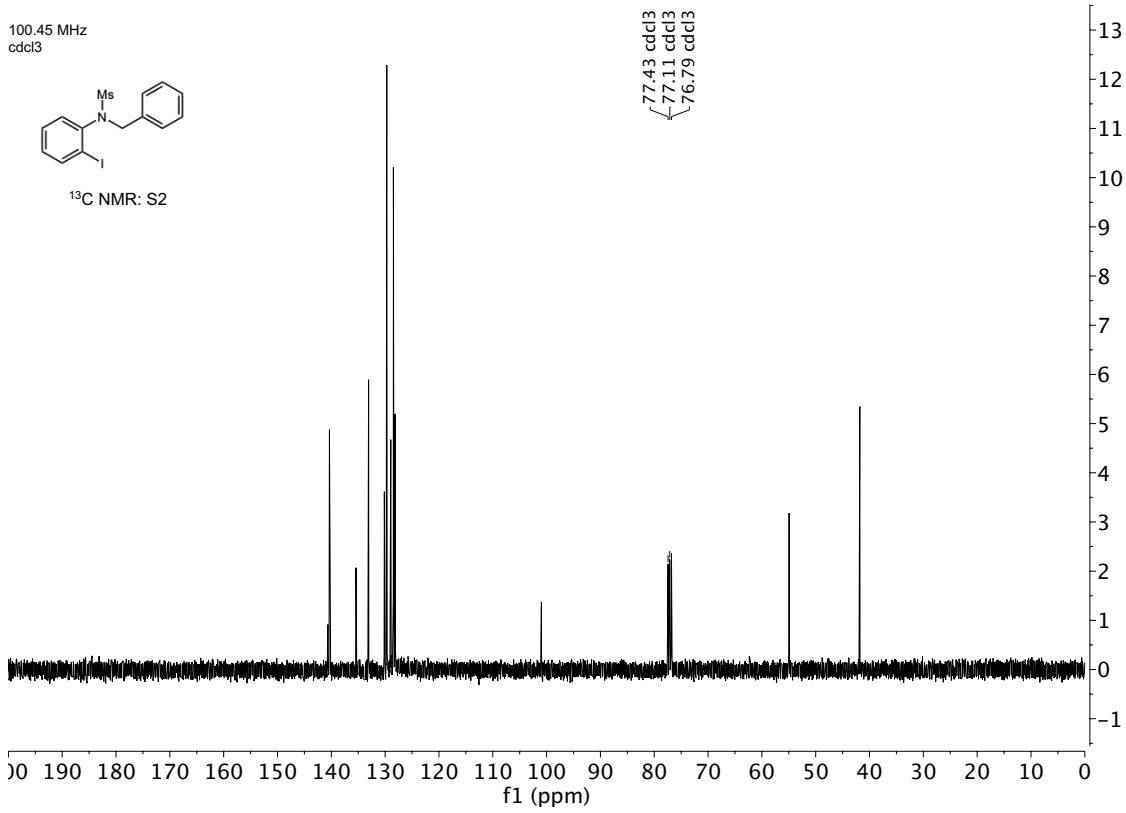
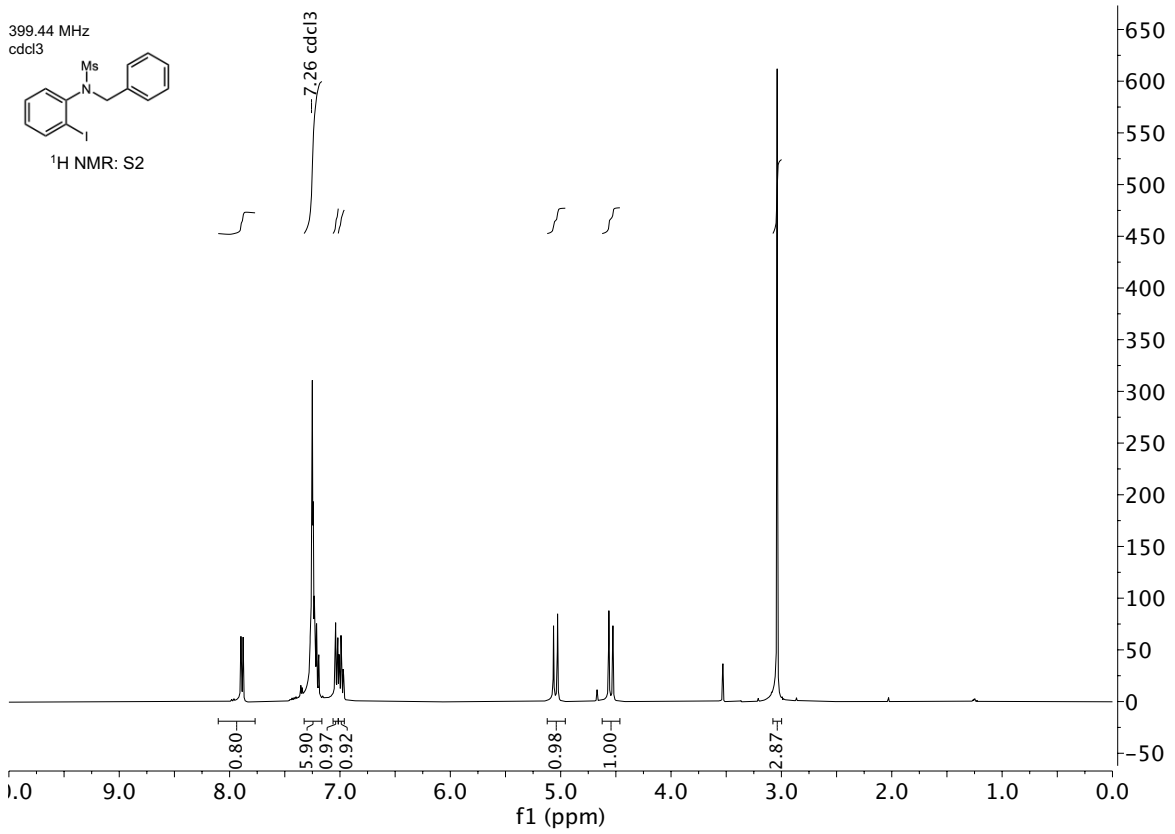
XI. References

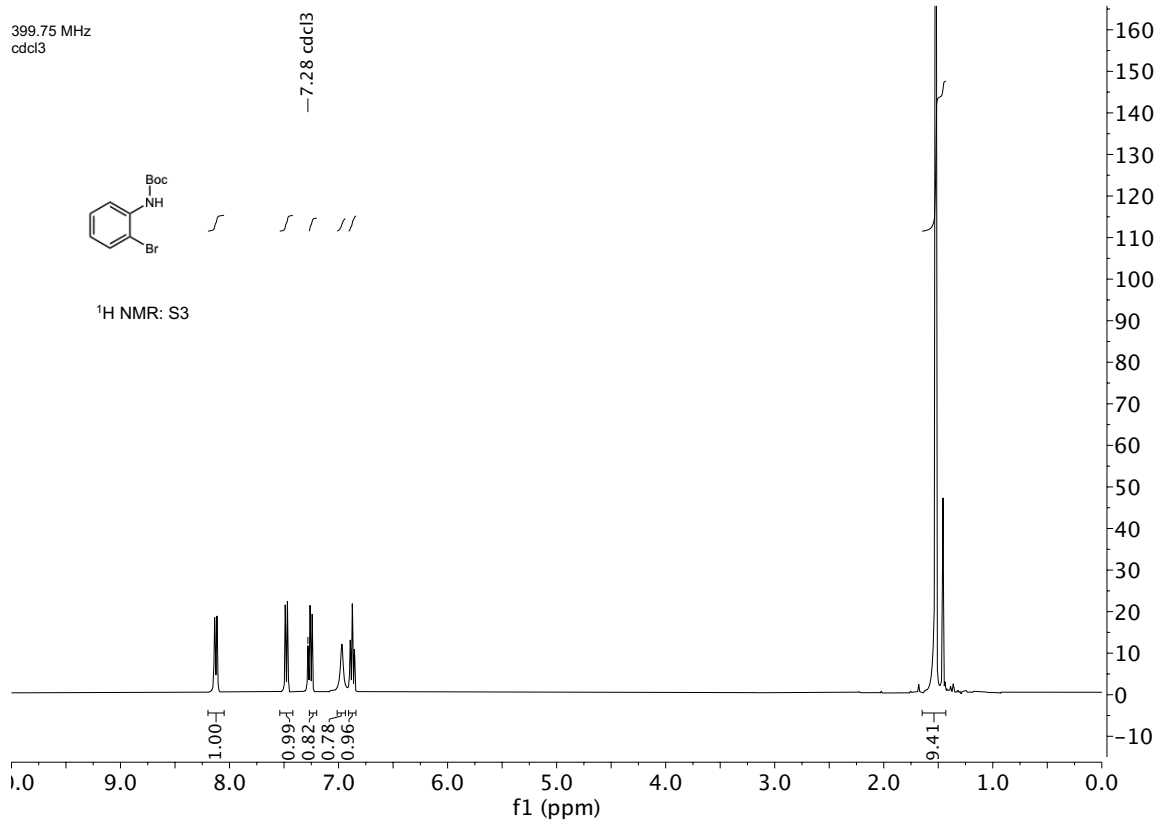
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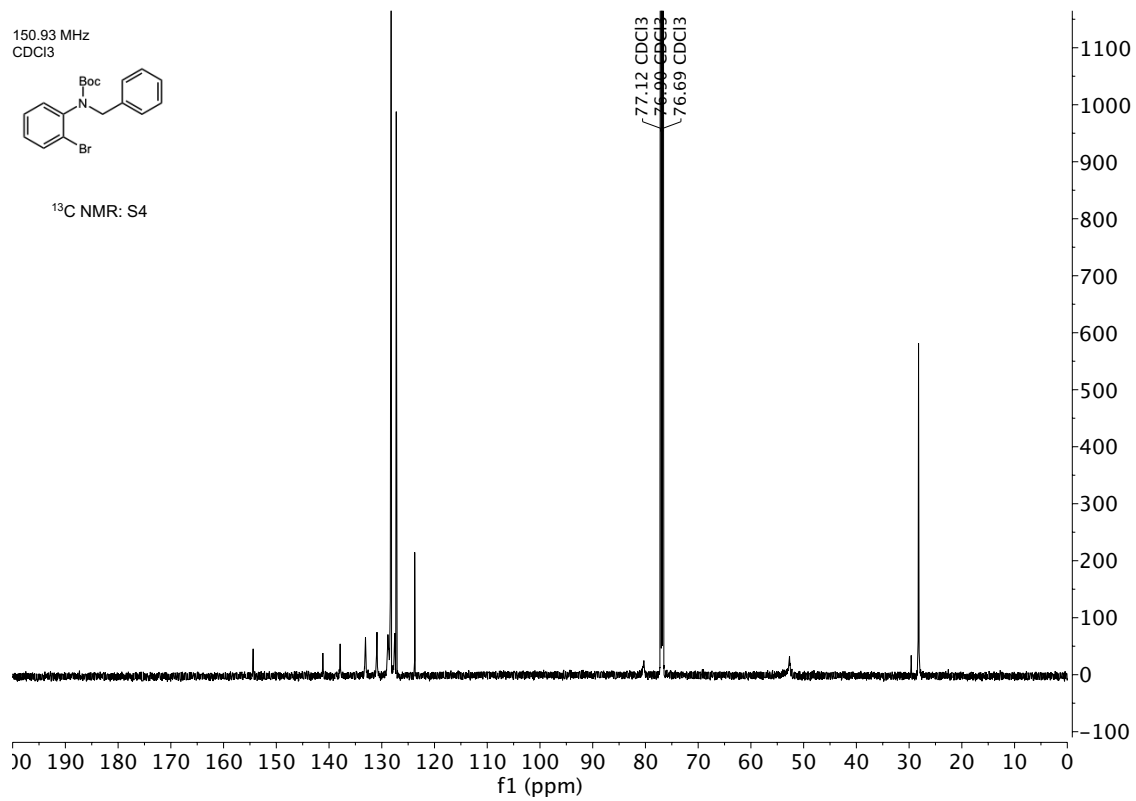
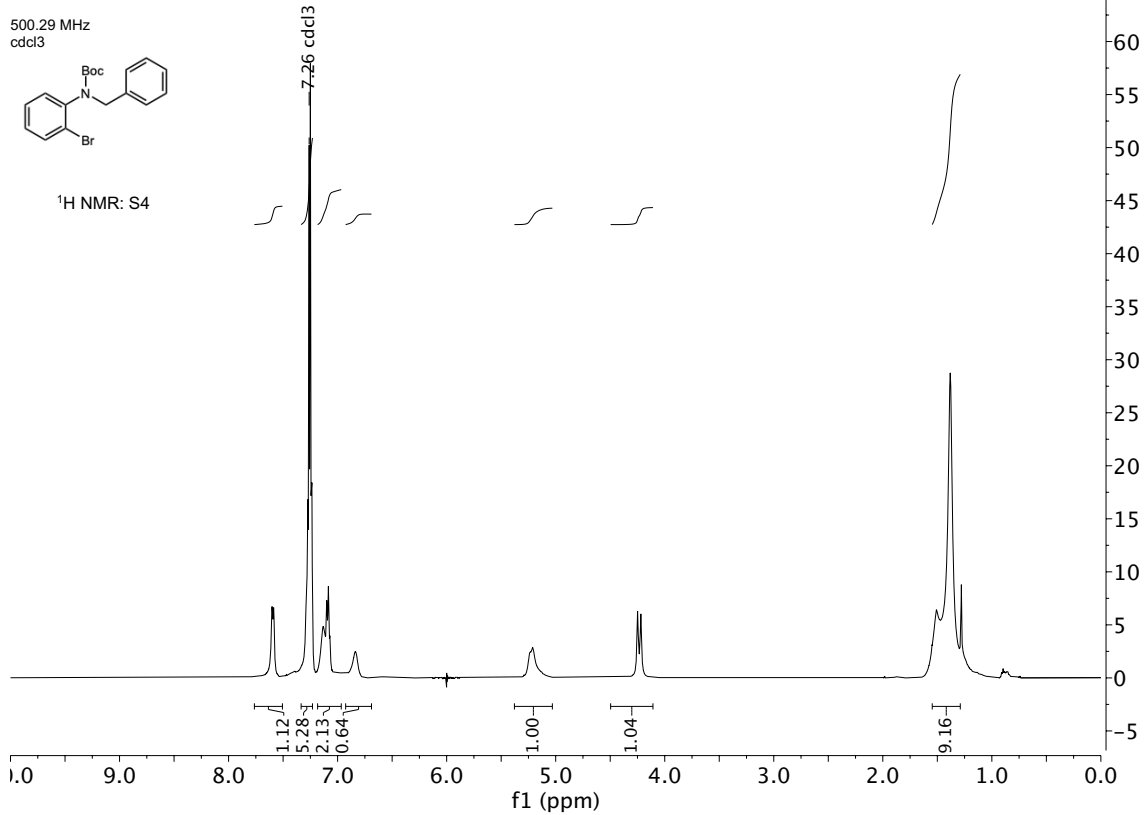
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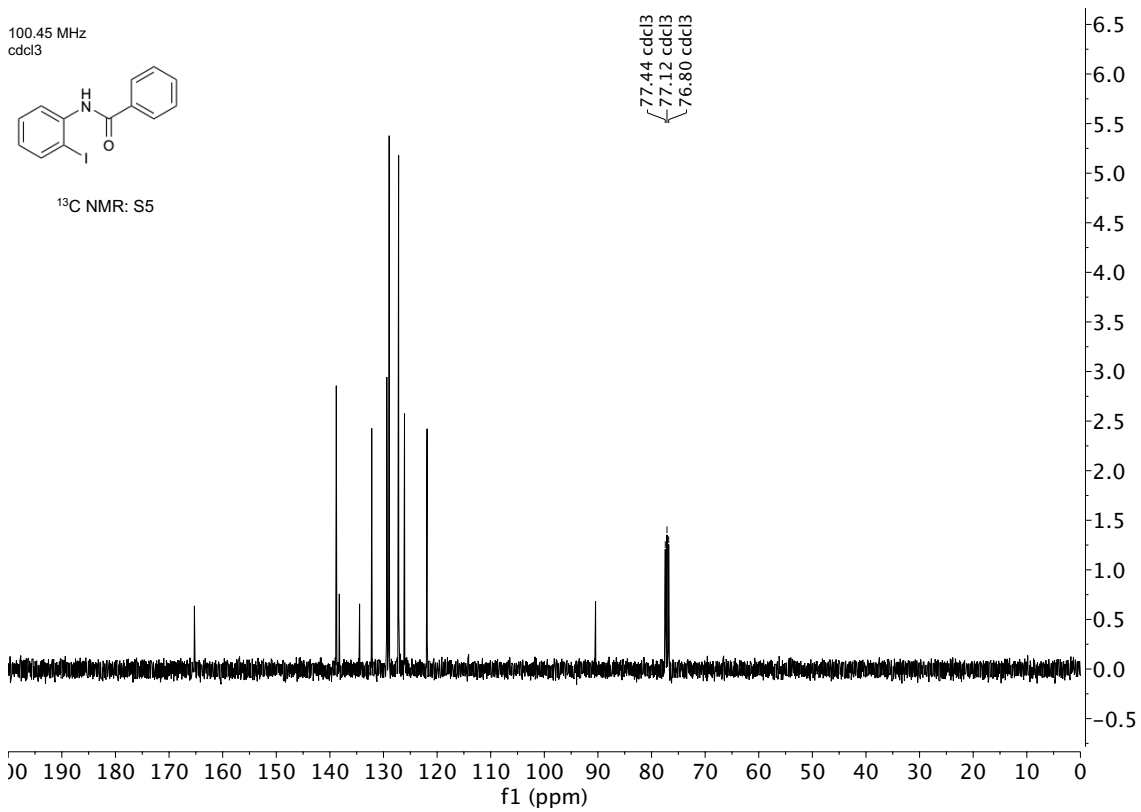
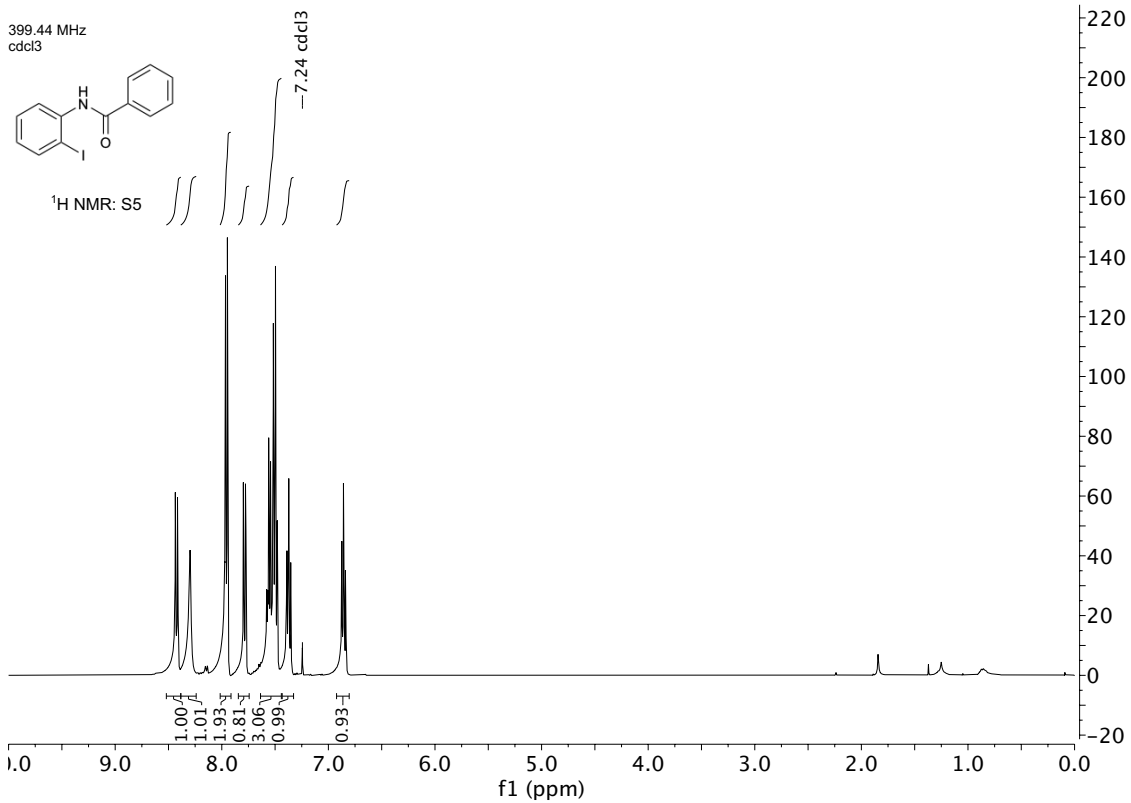
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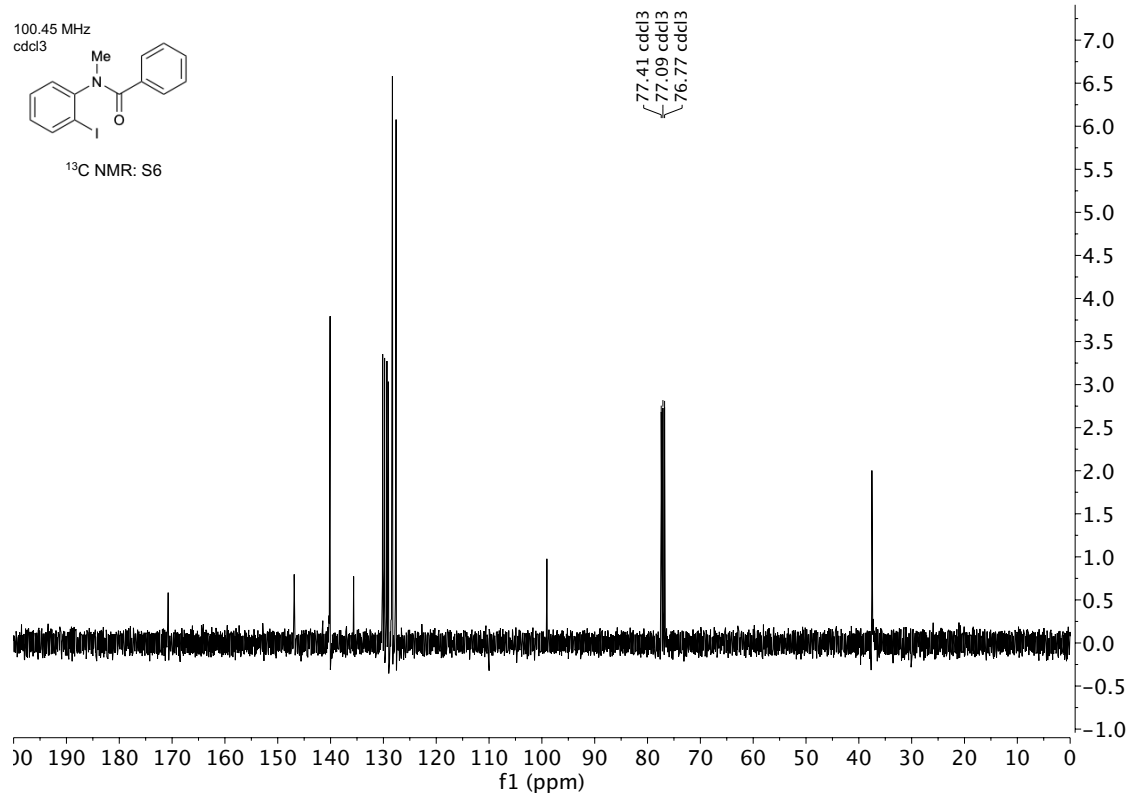
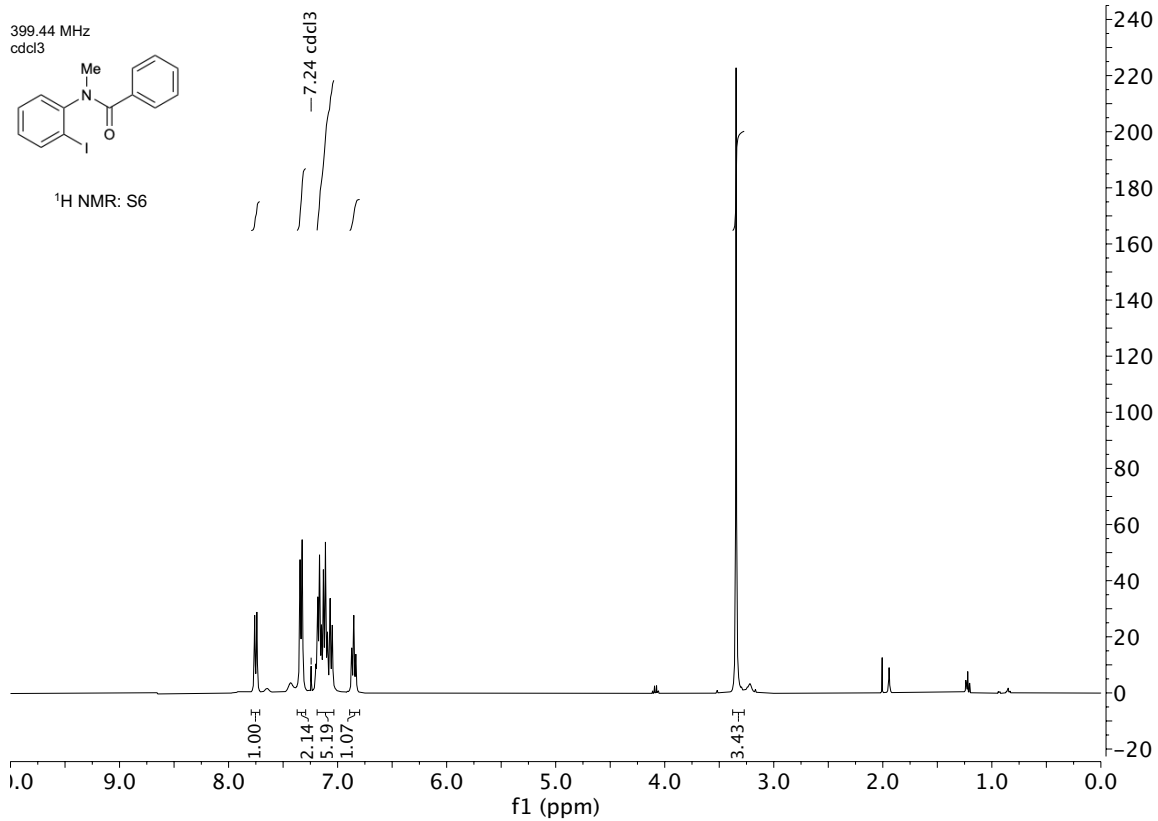


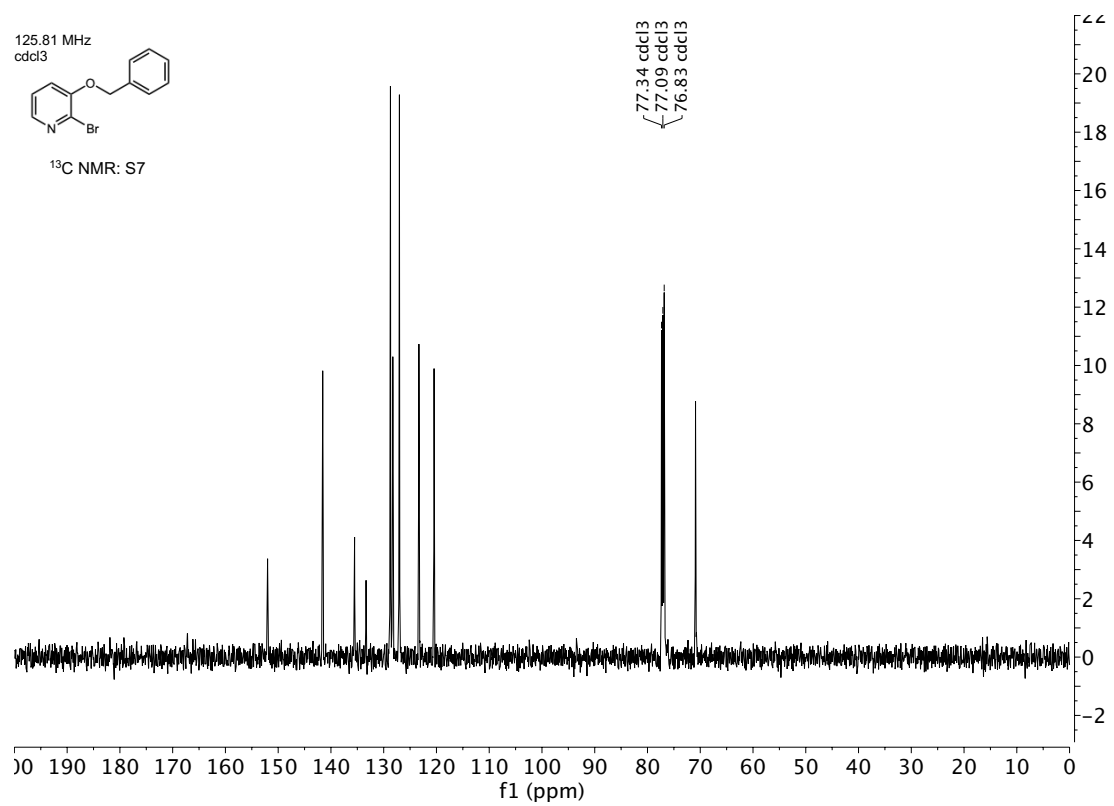
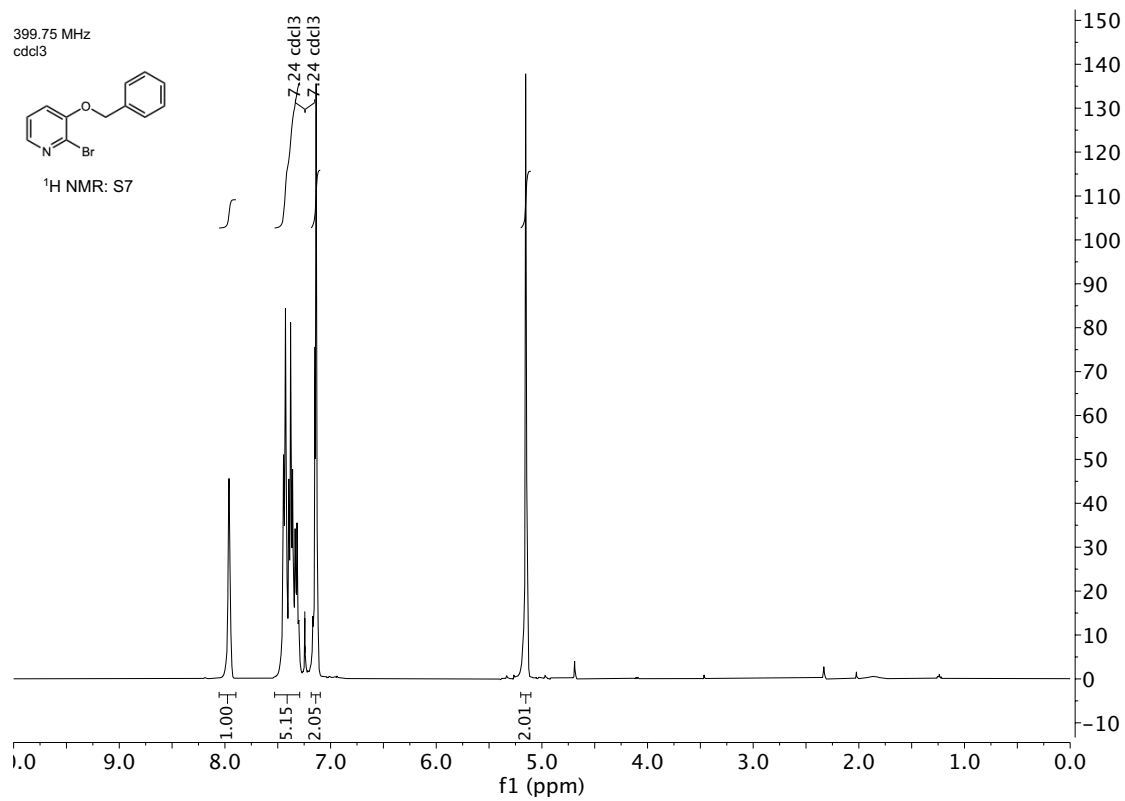


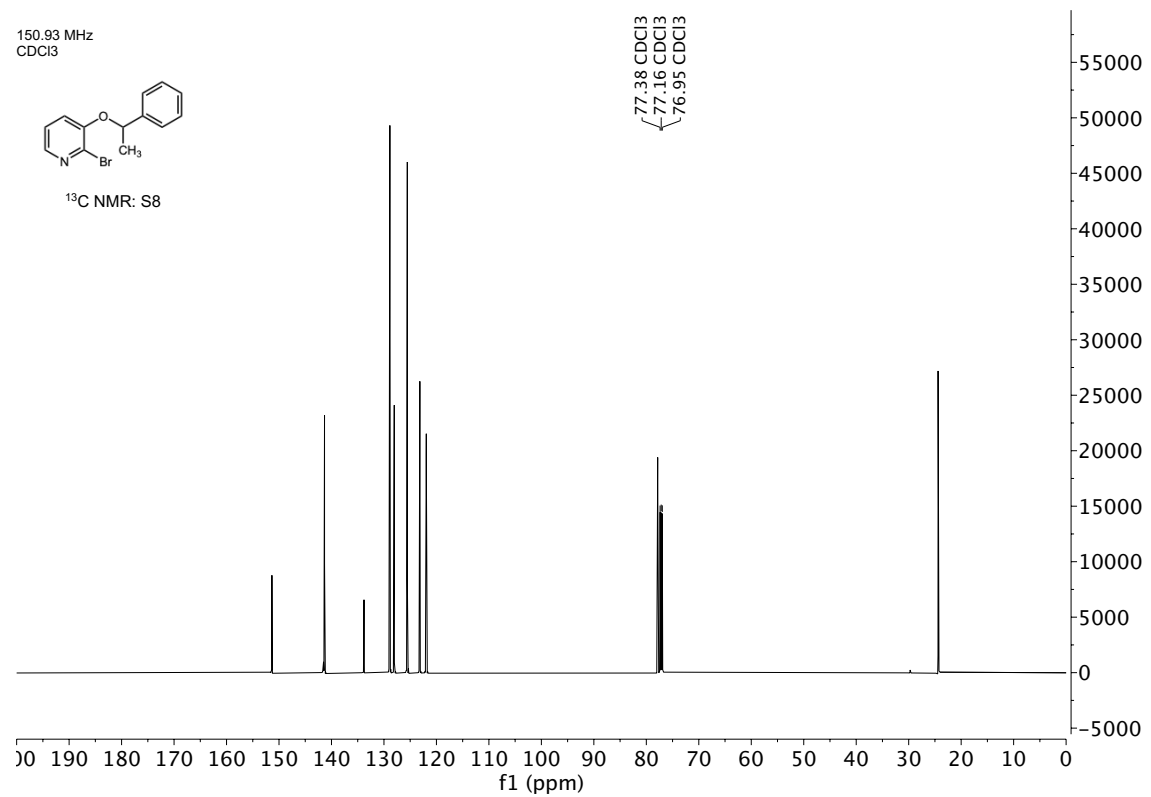
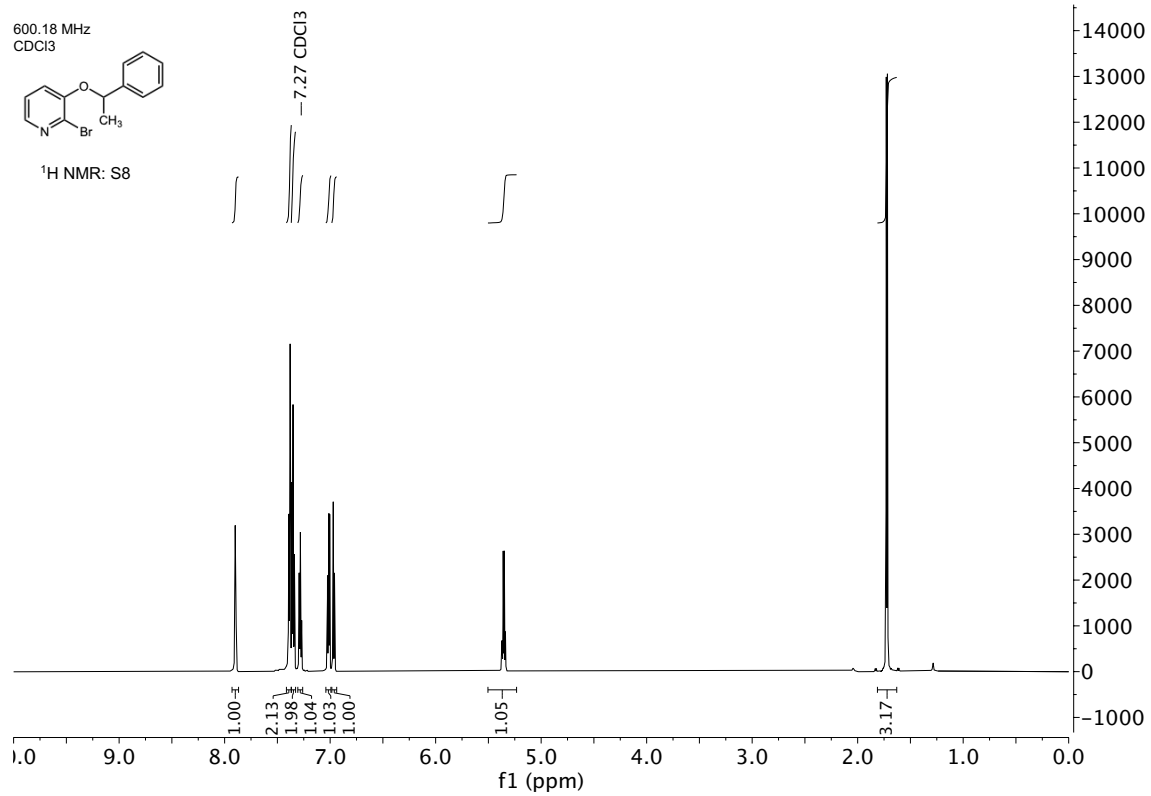




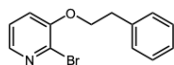




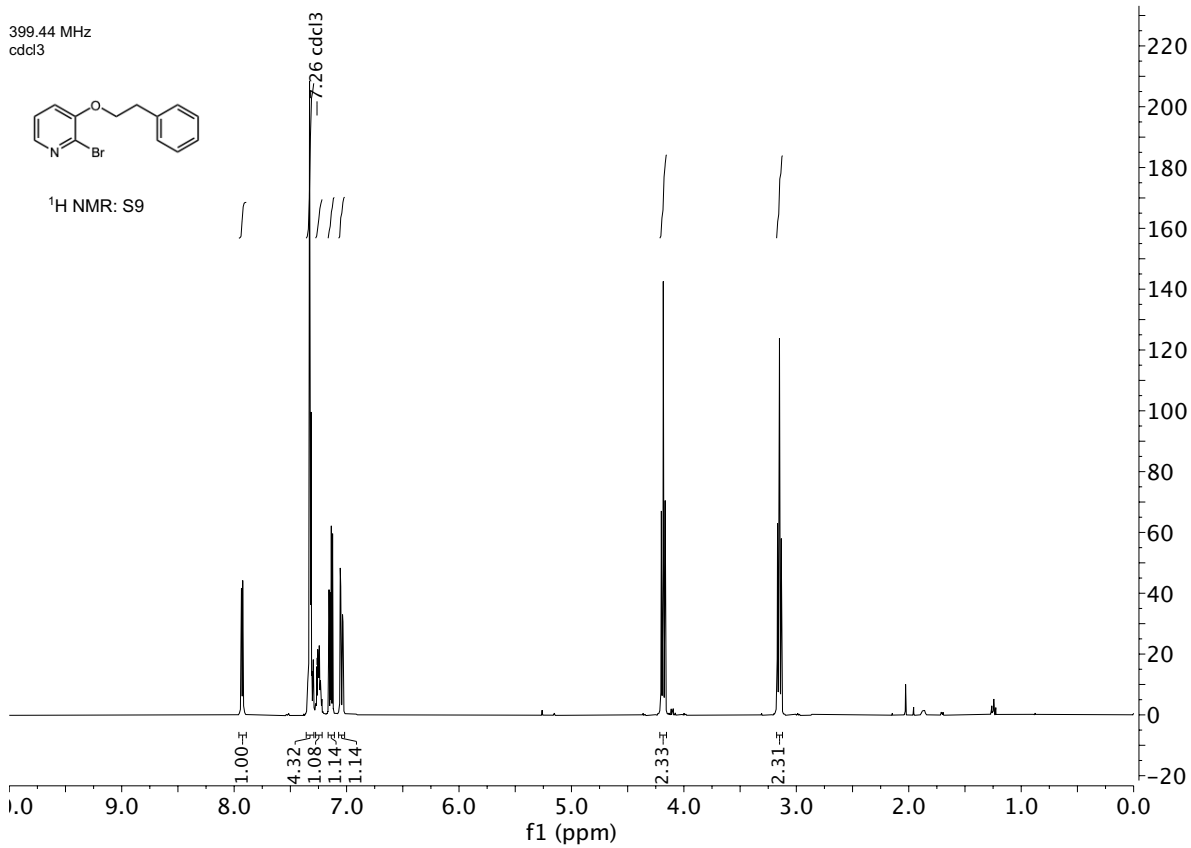


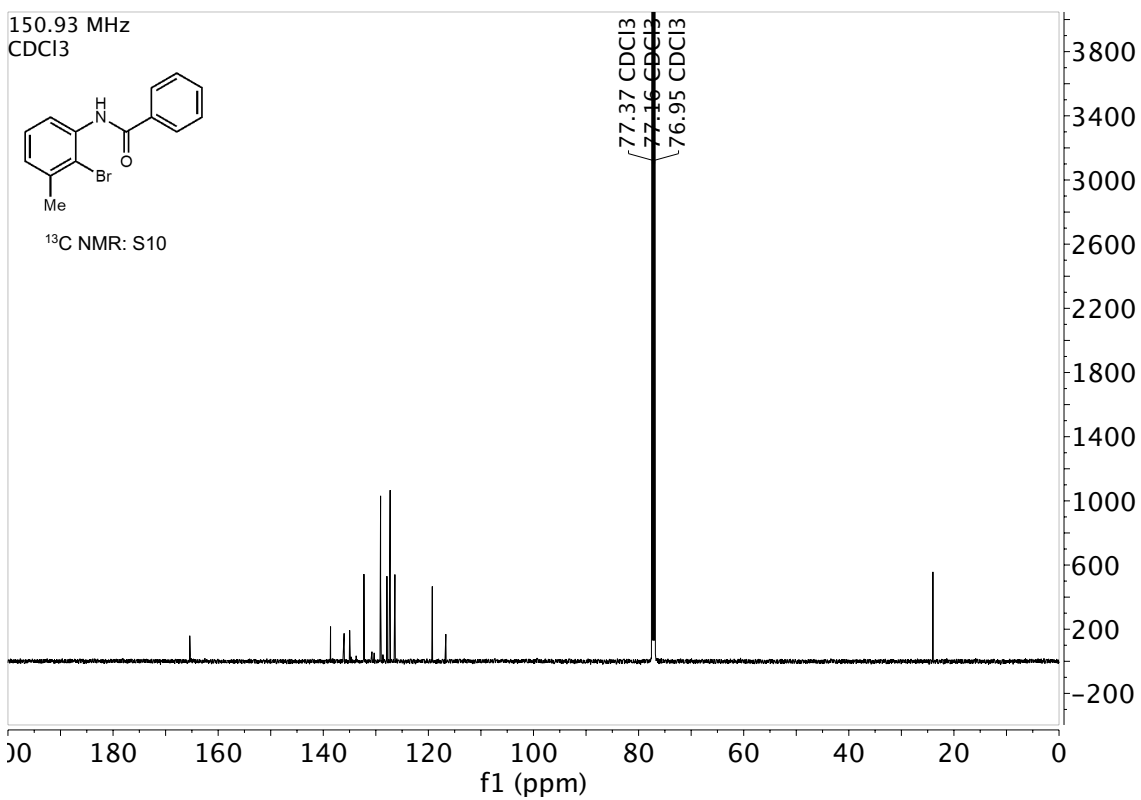
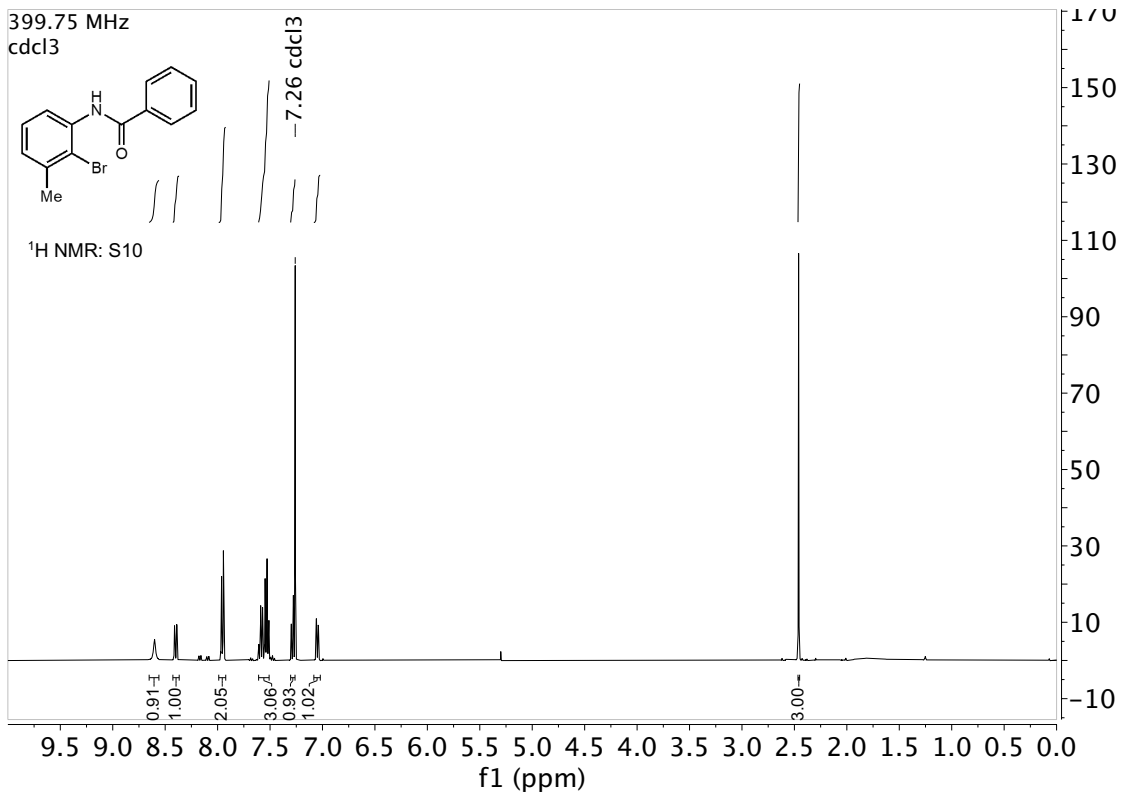


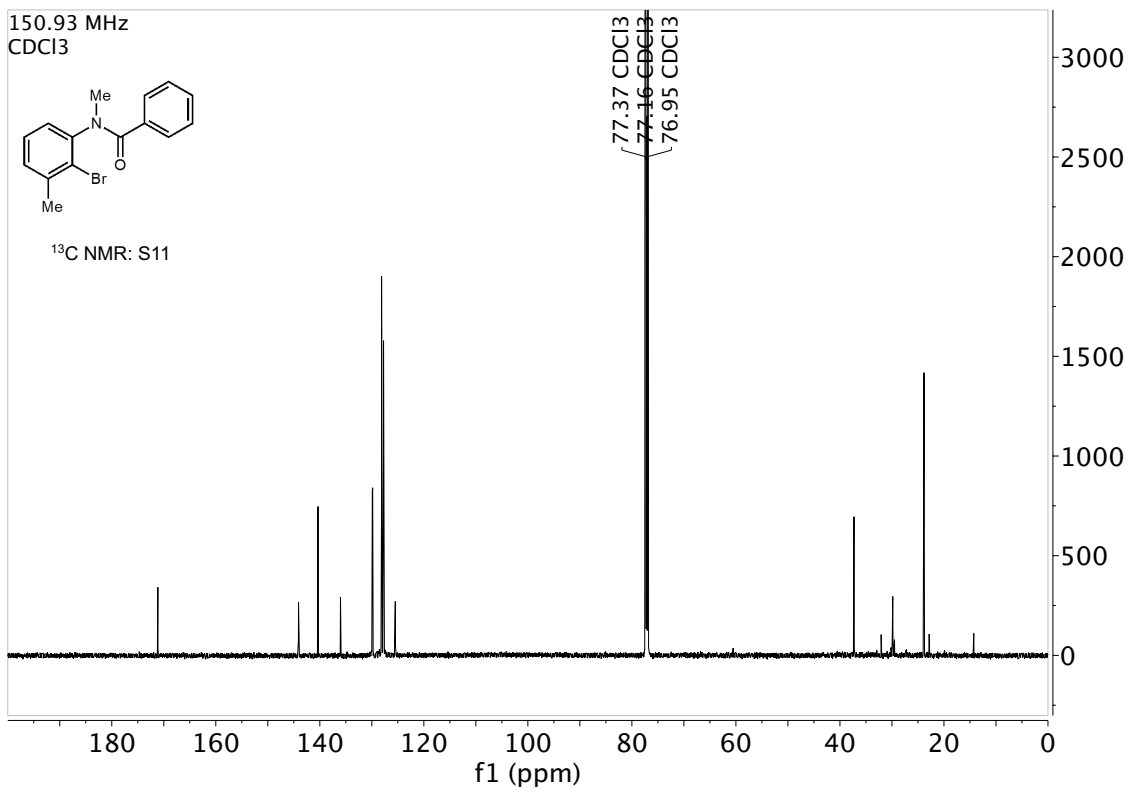
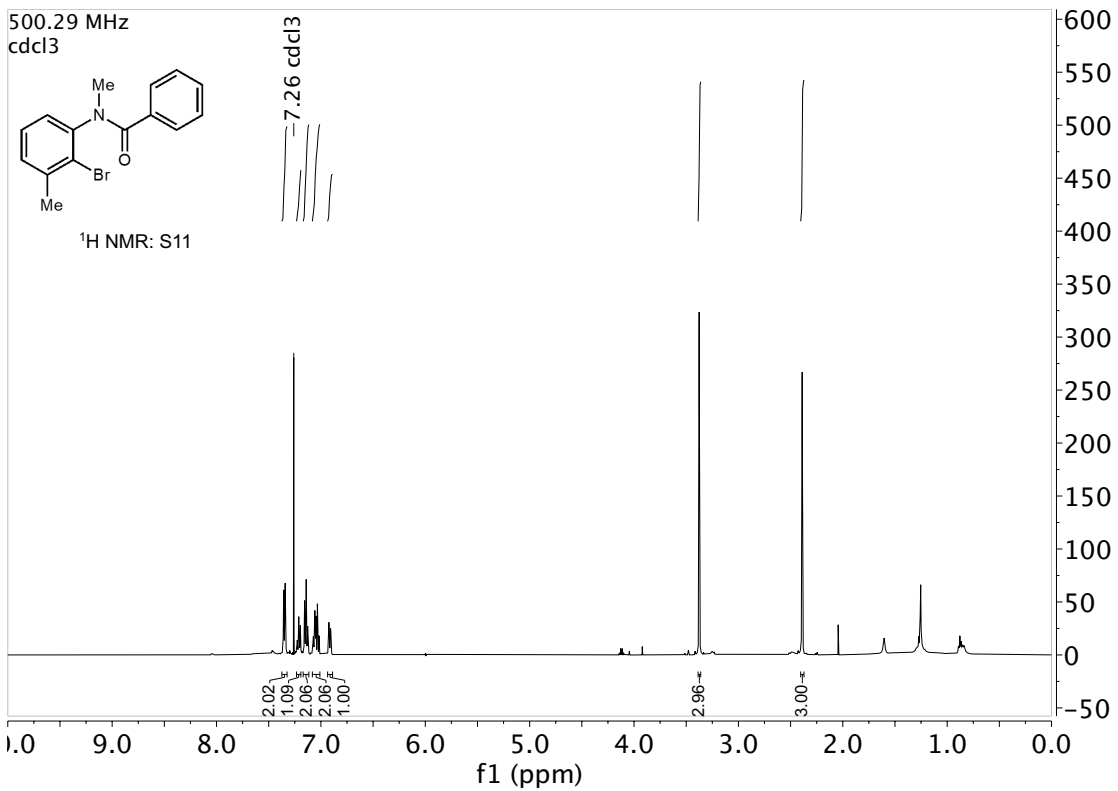
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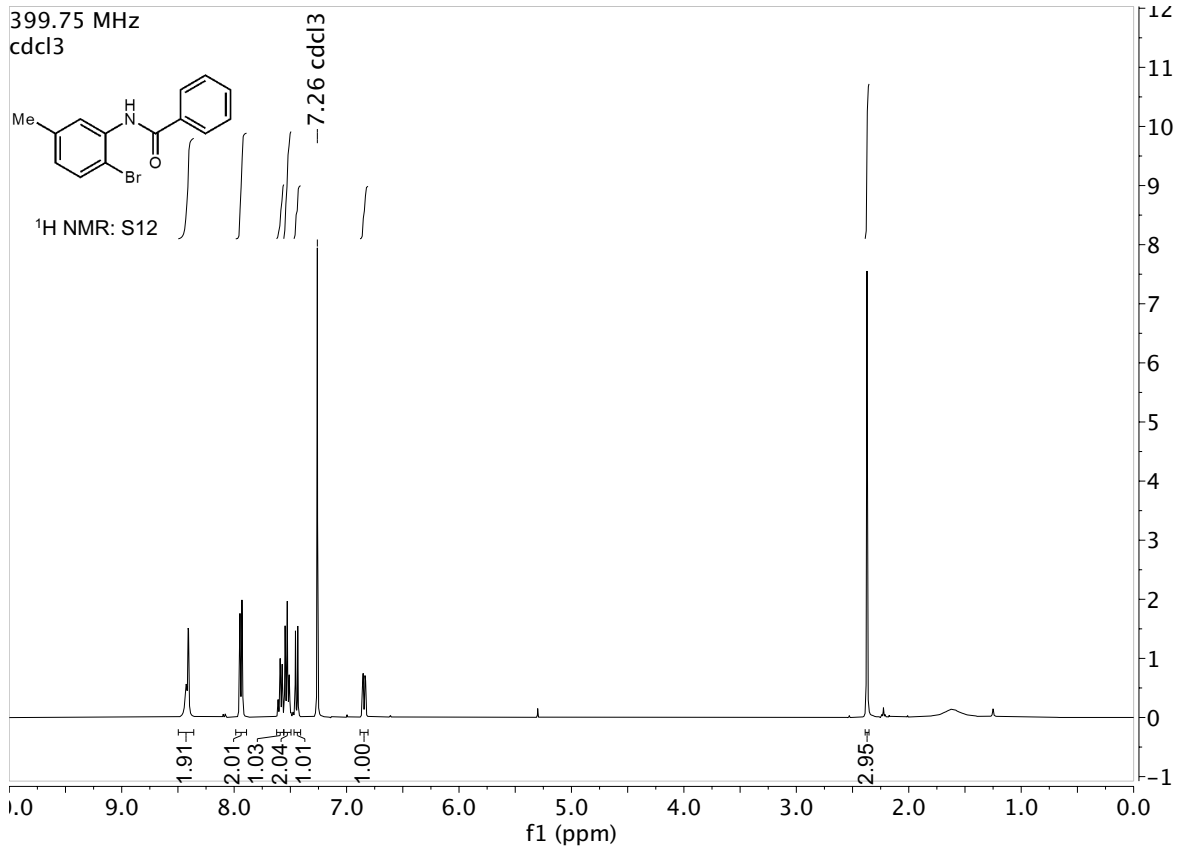


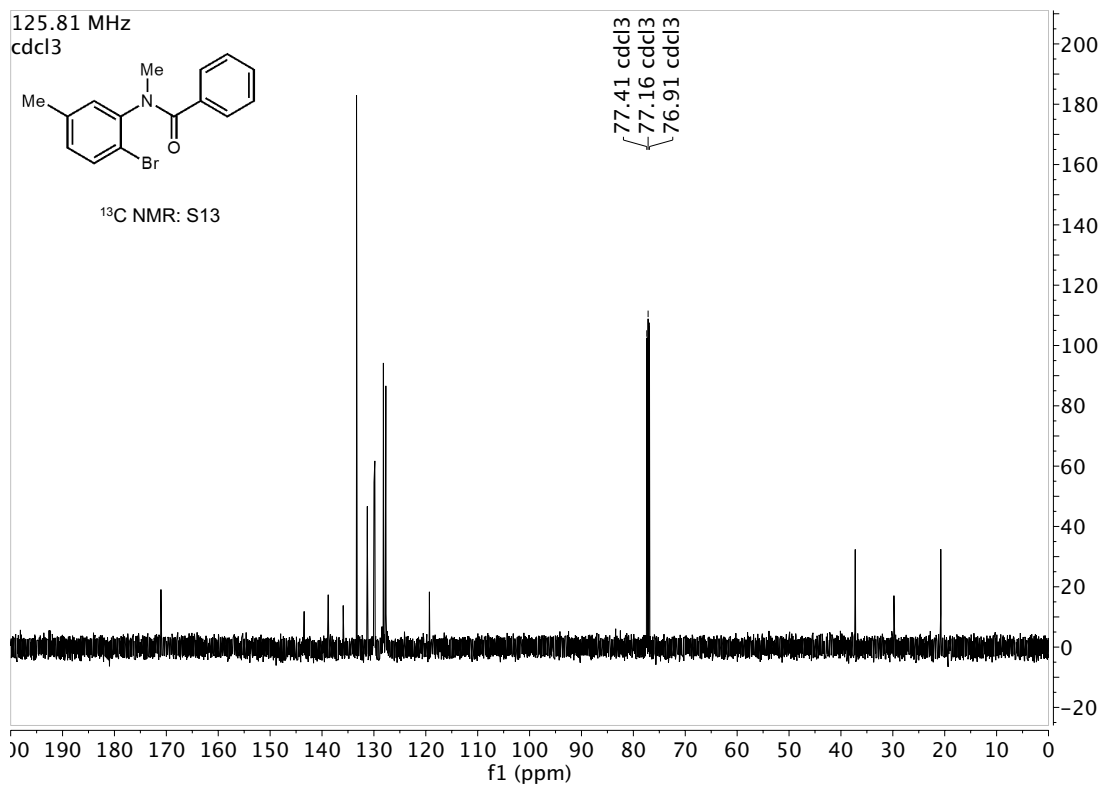
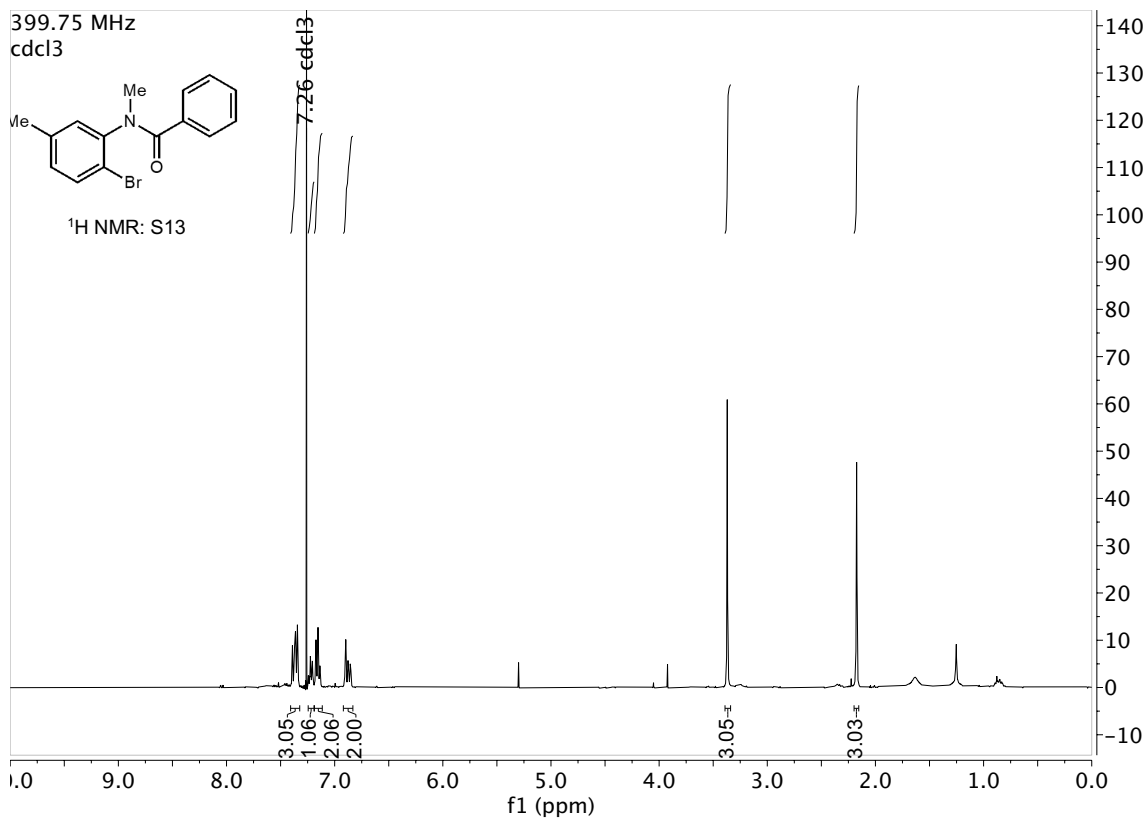
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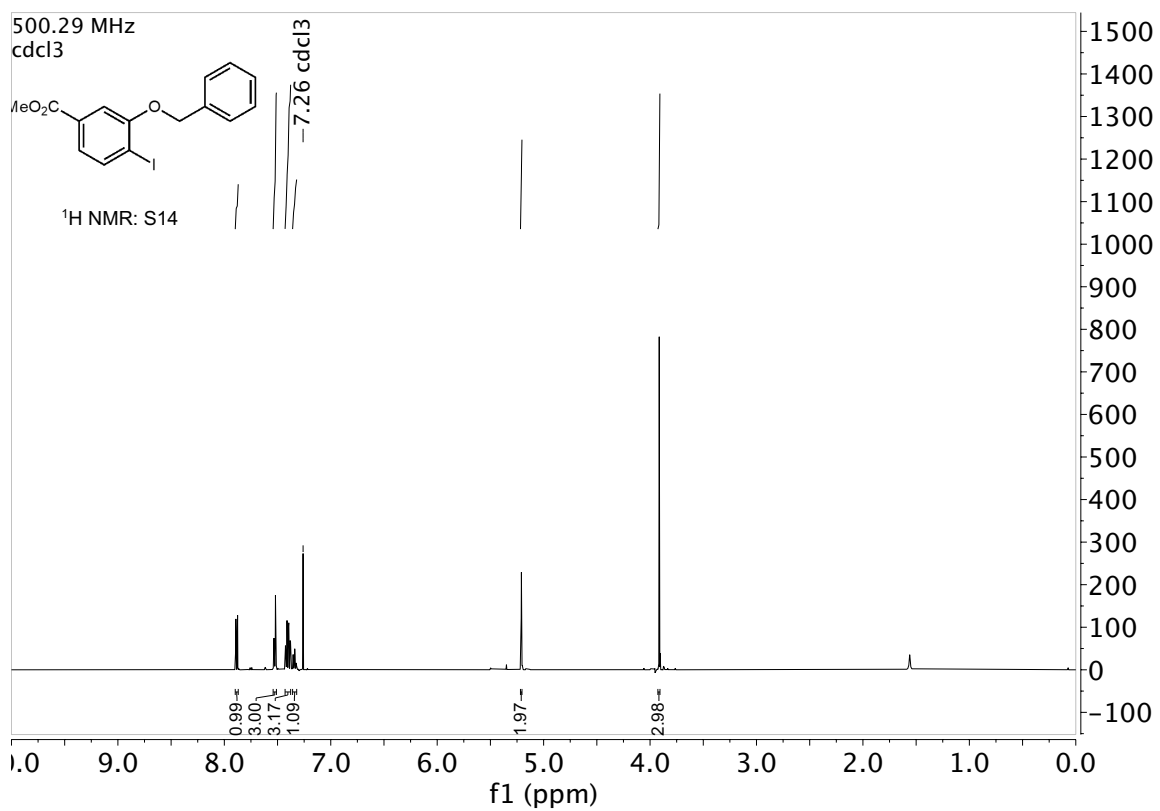


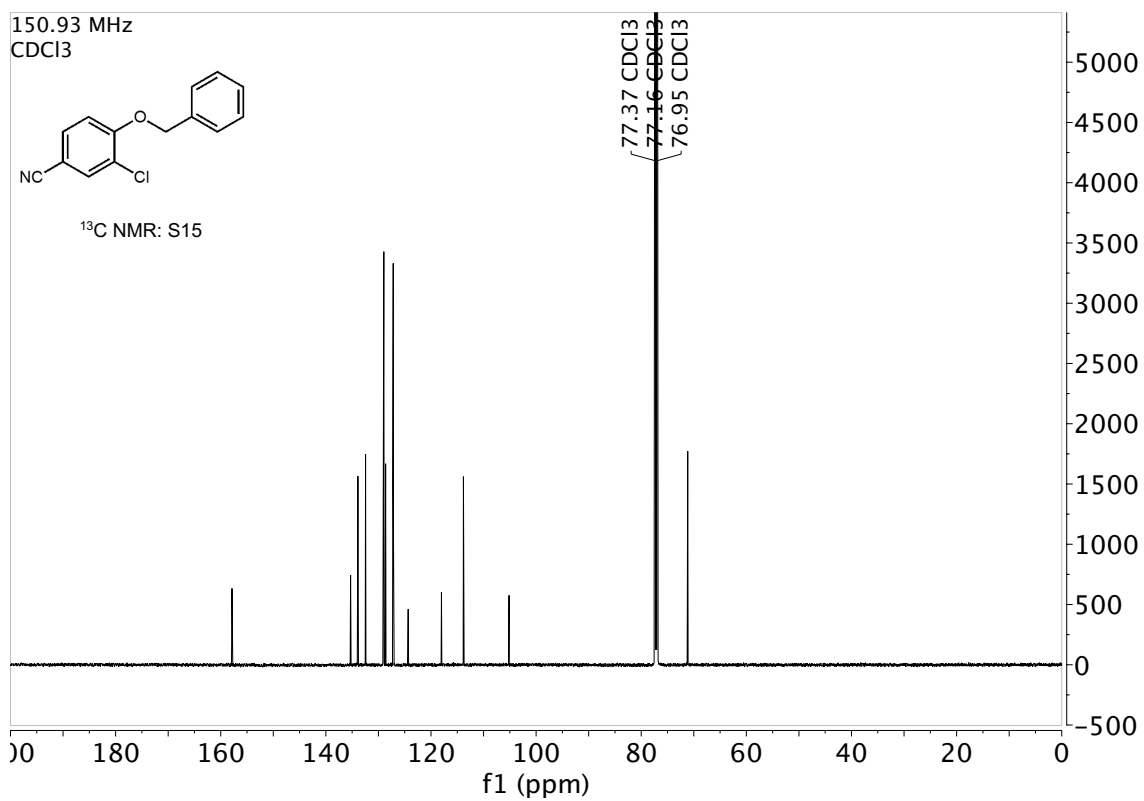
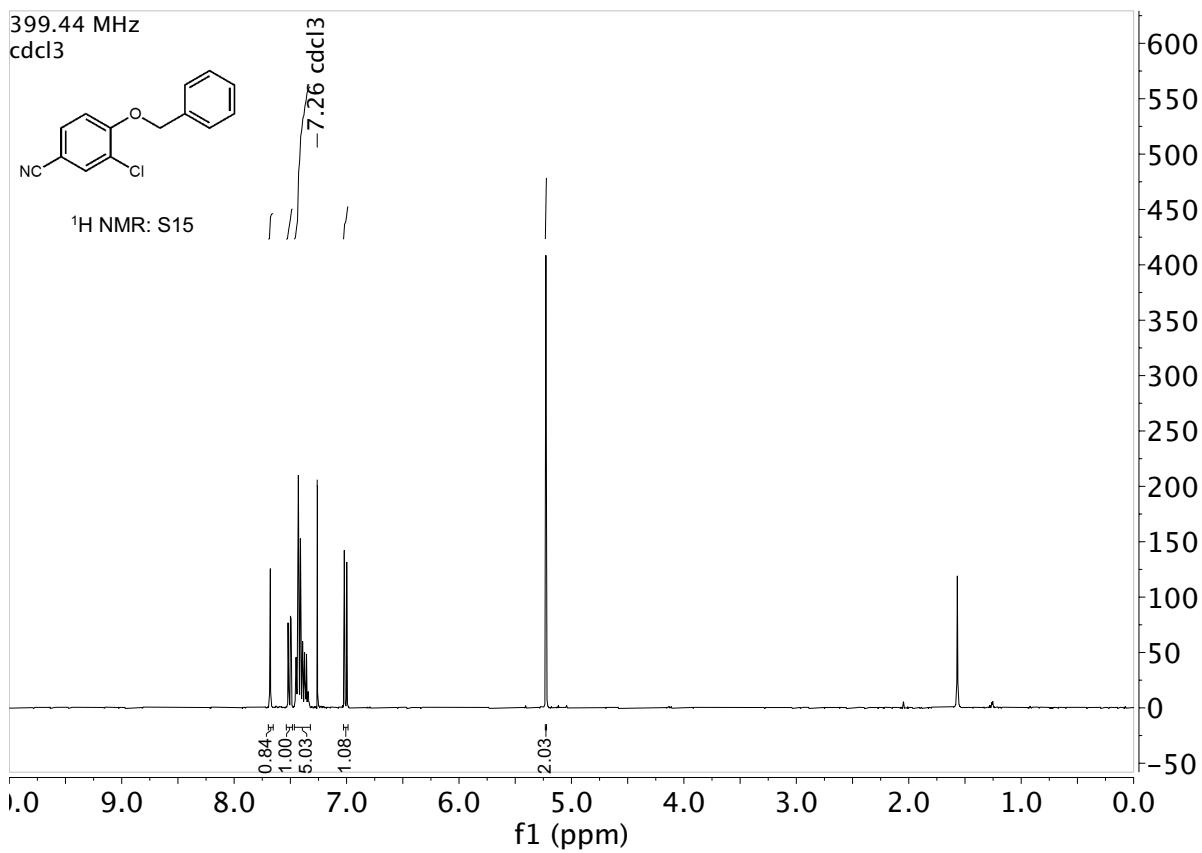


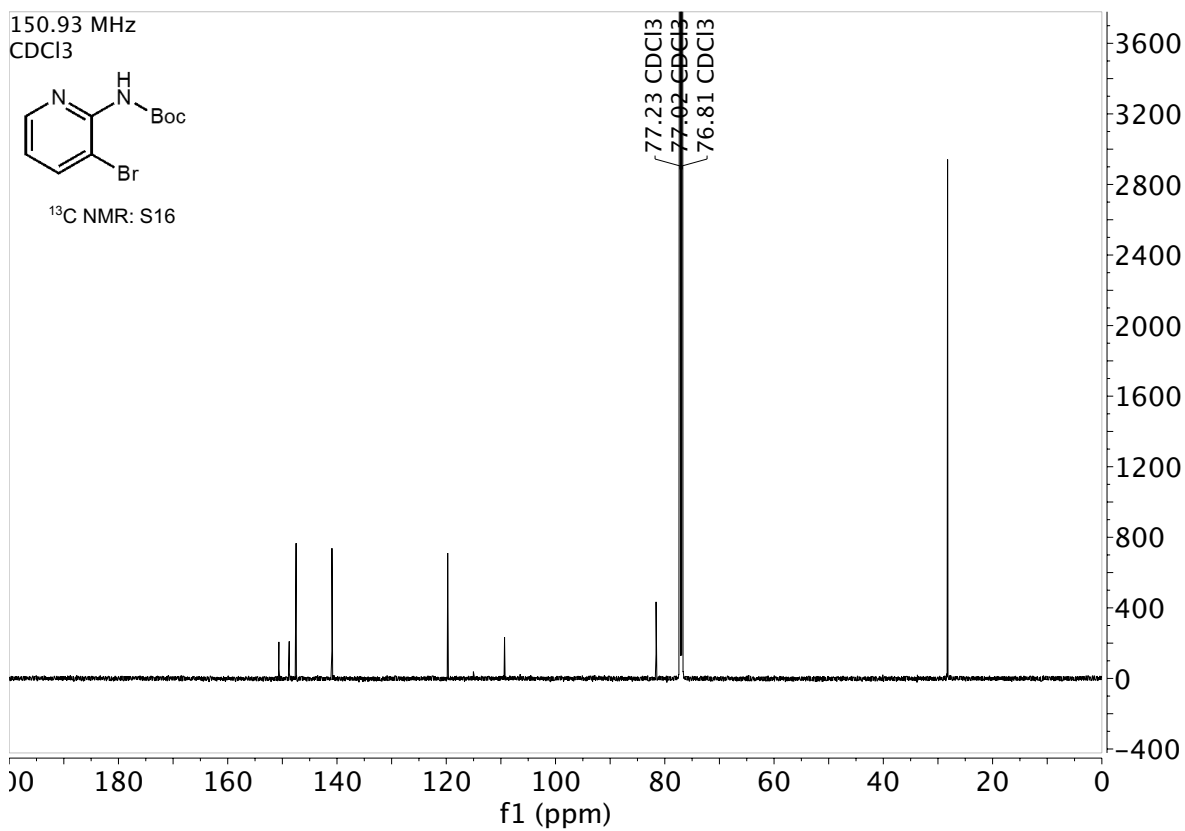
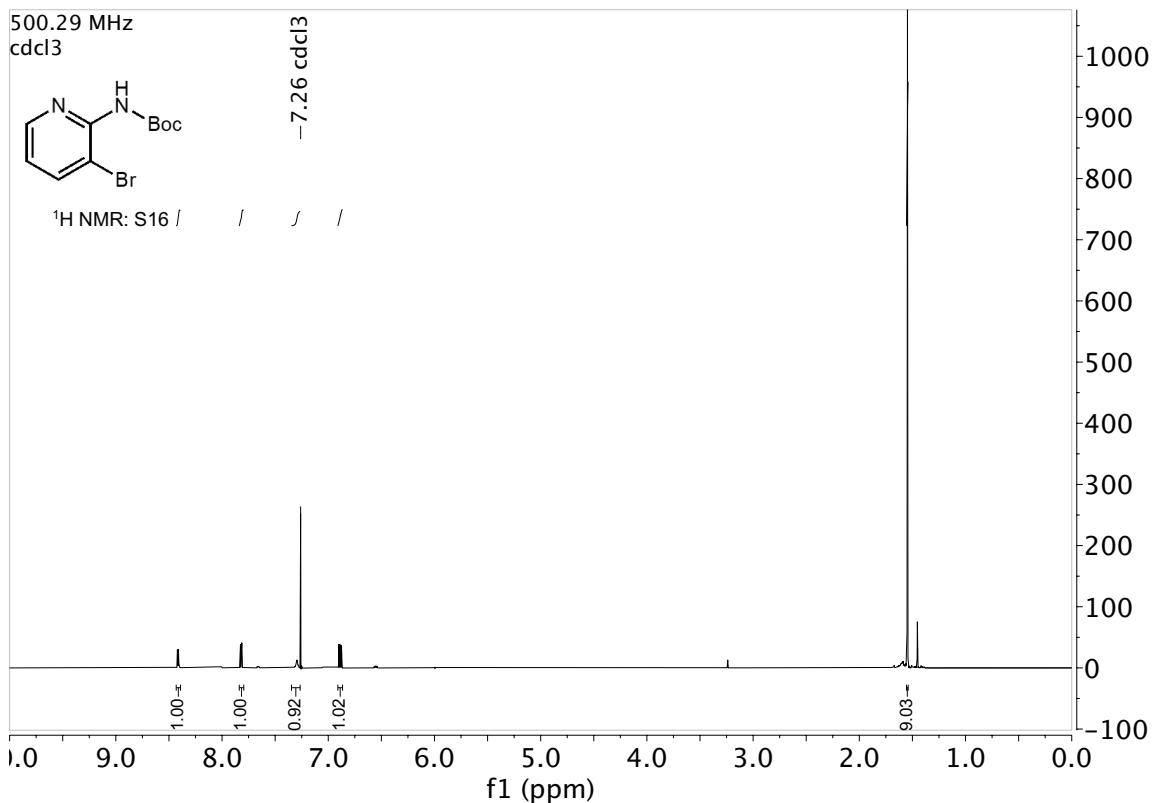


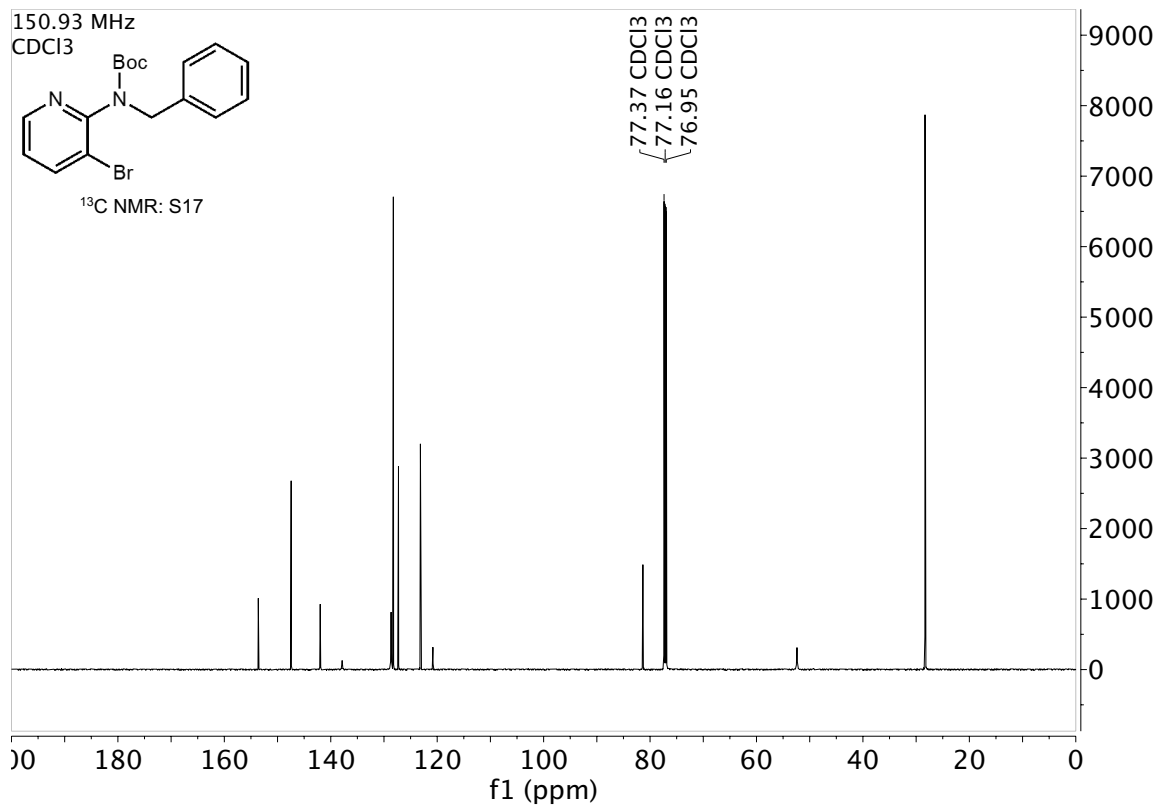
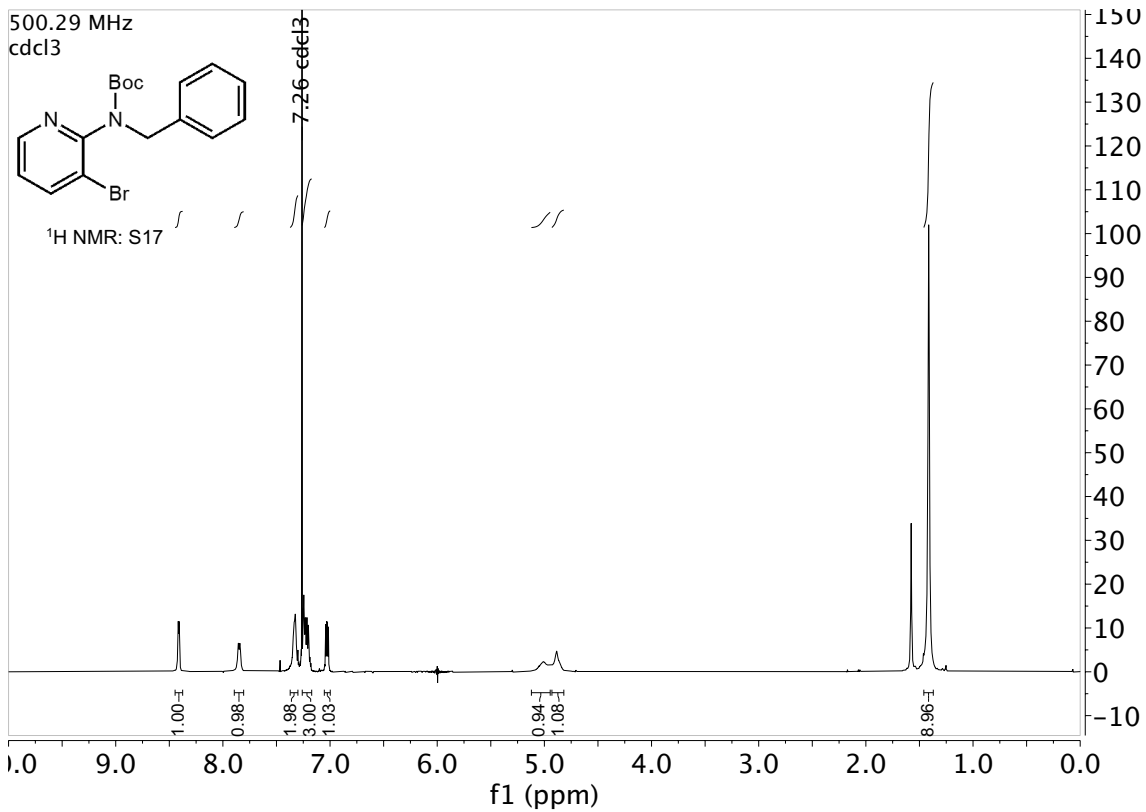


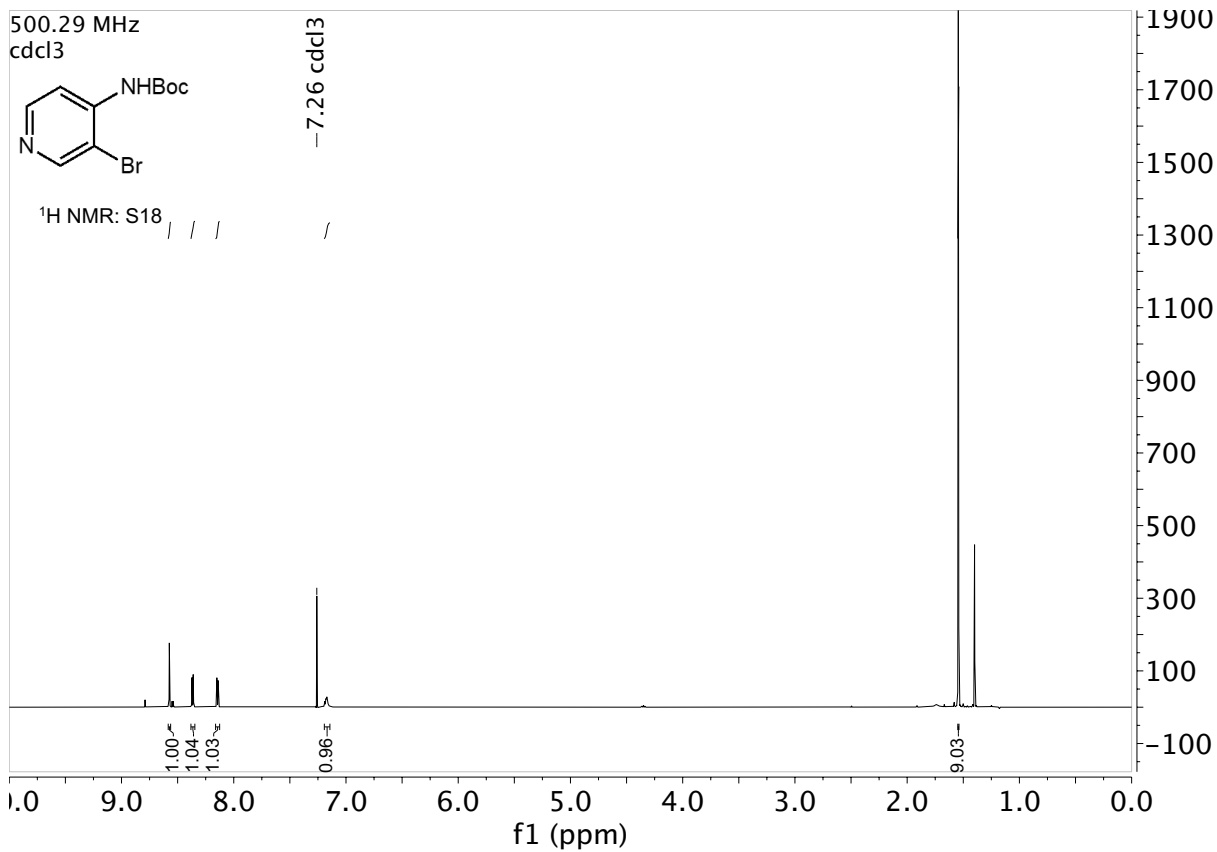


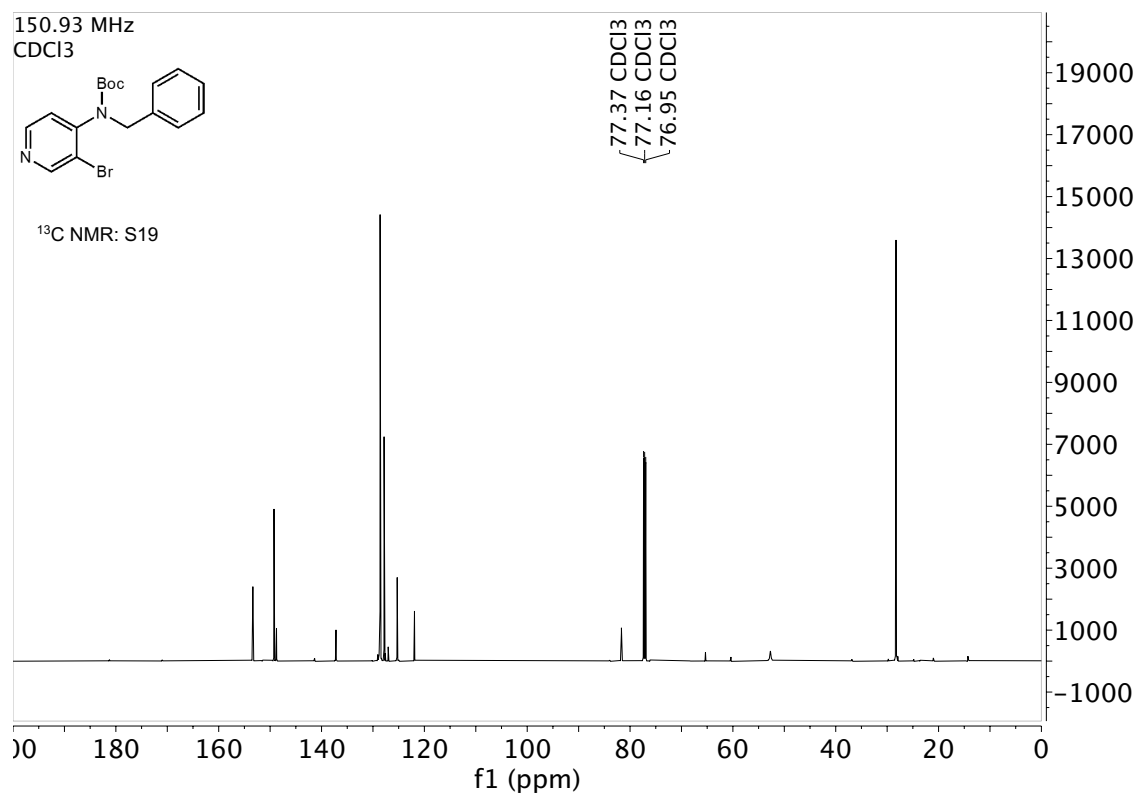
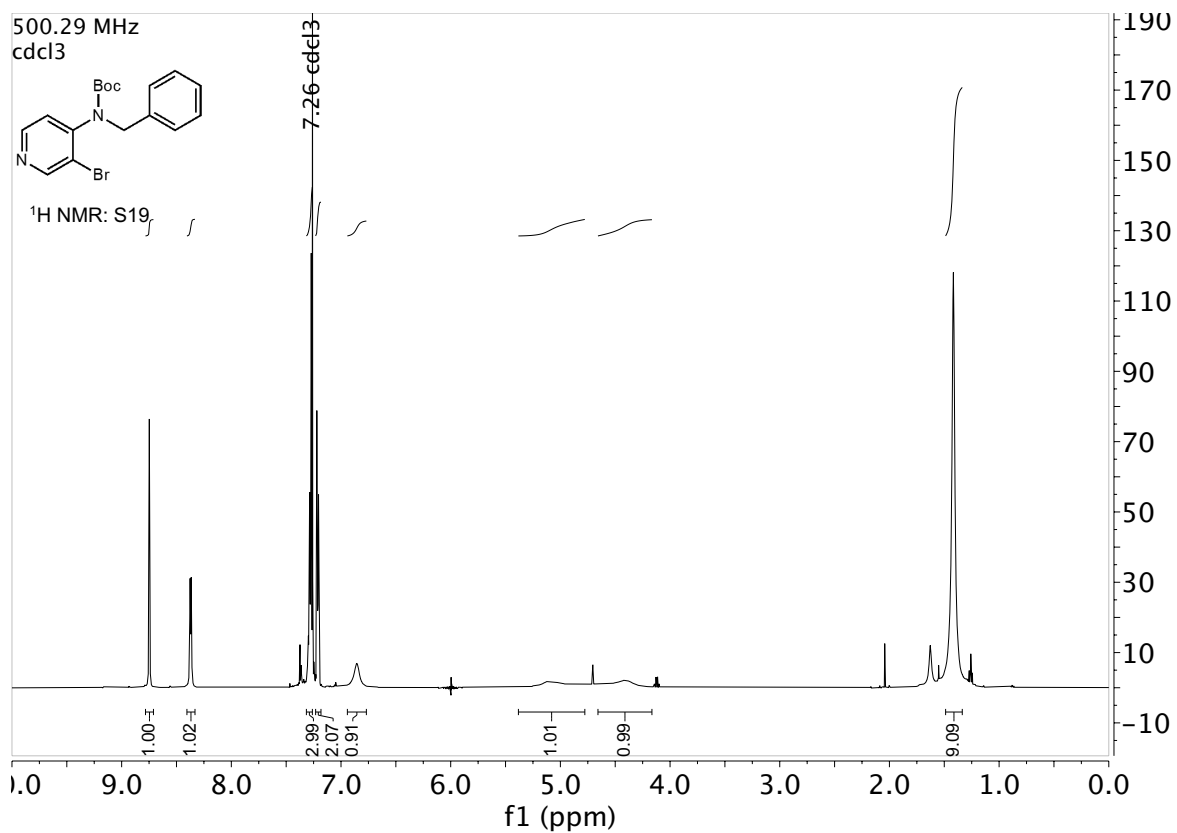


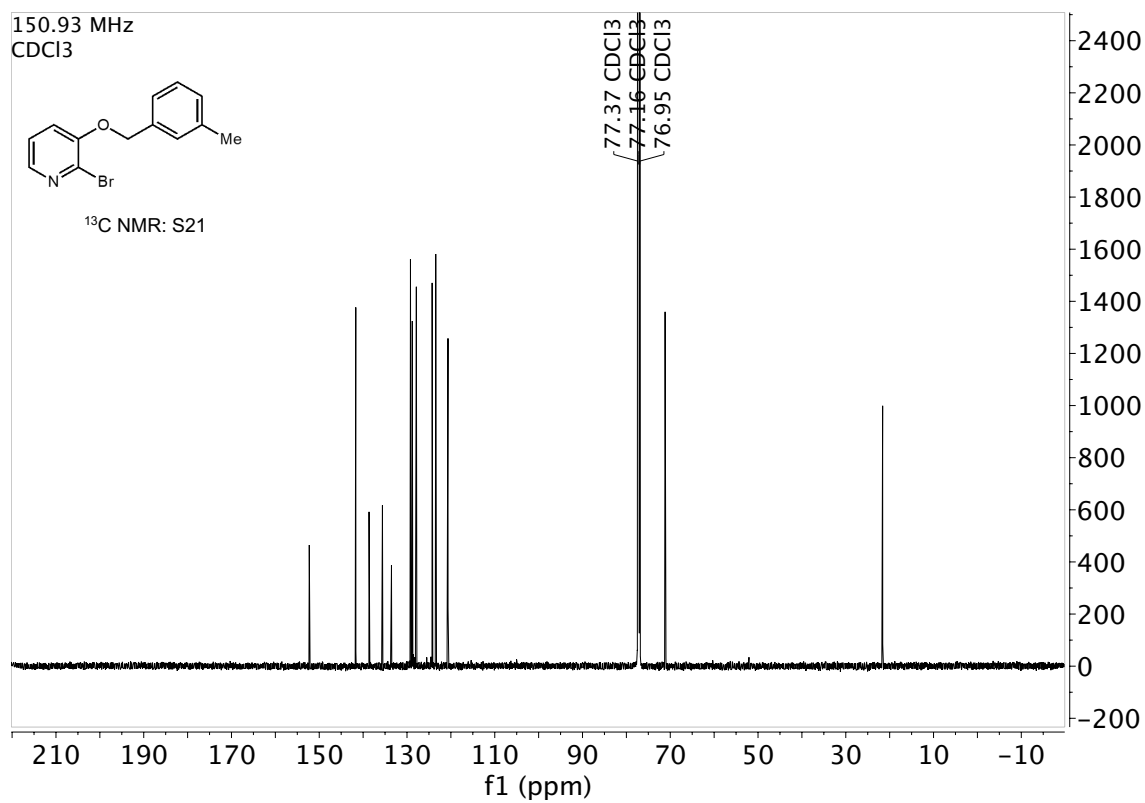
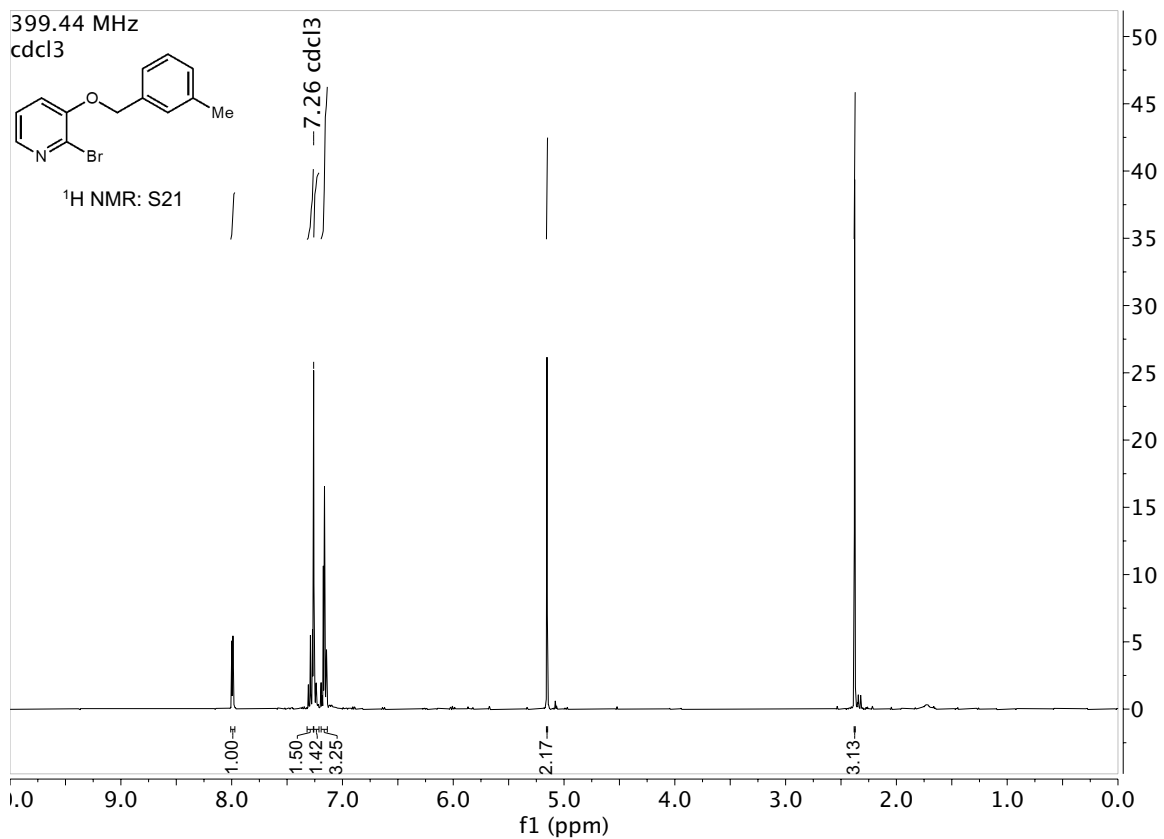


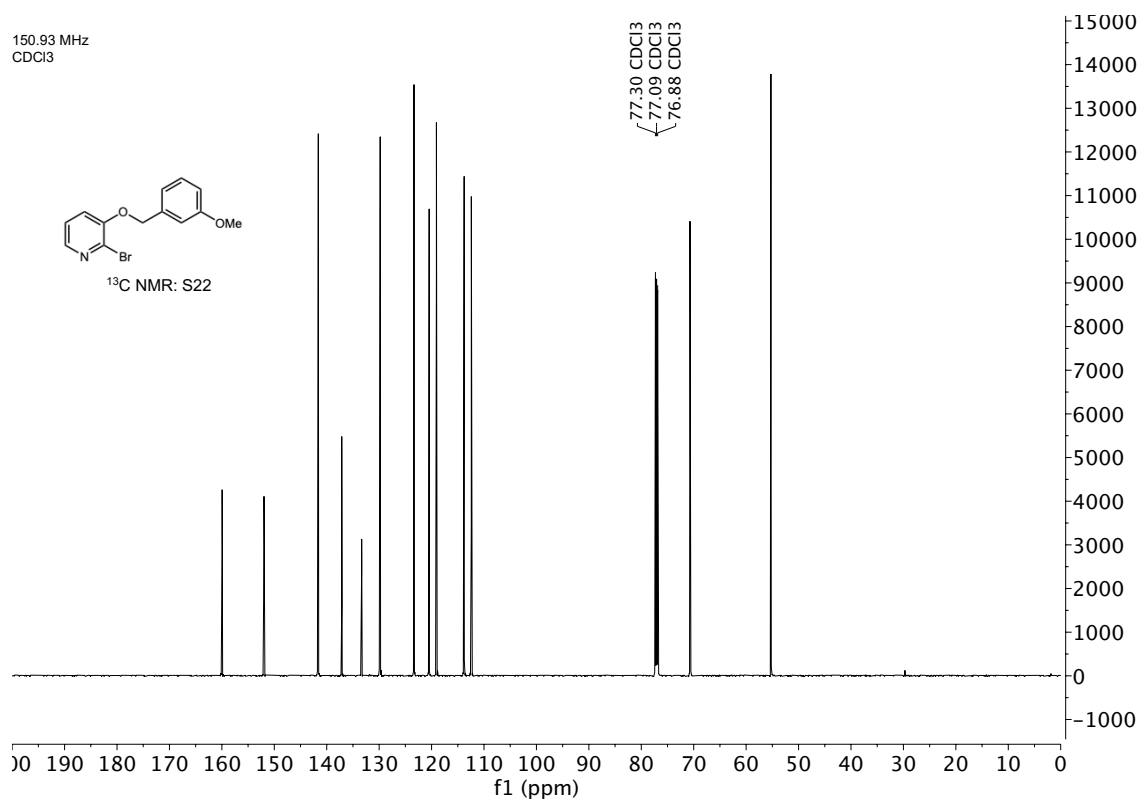
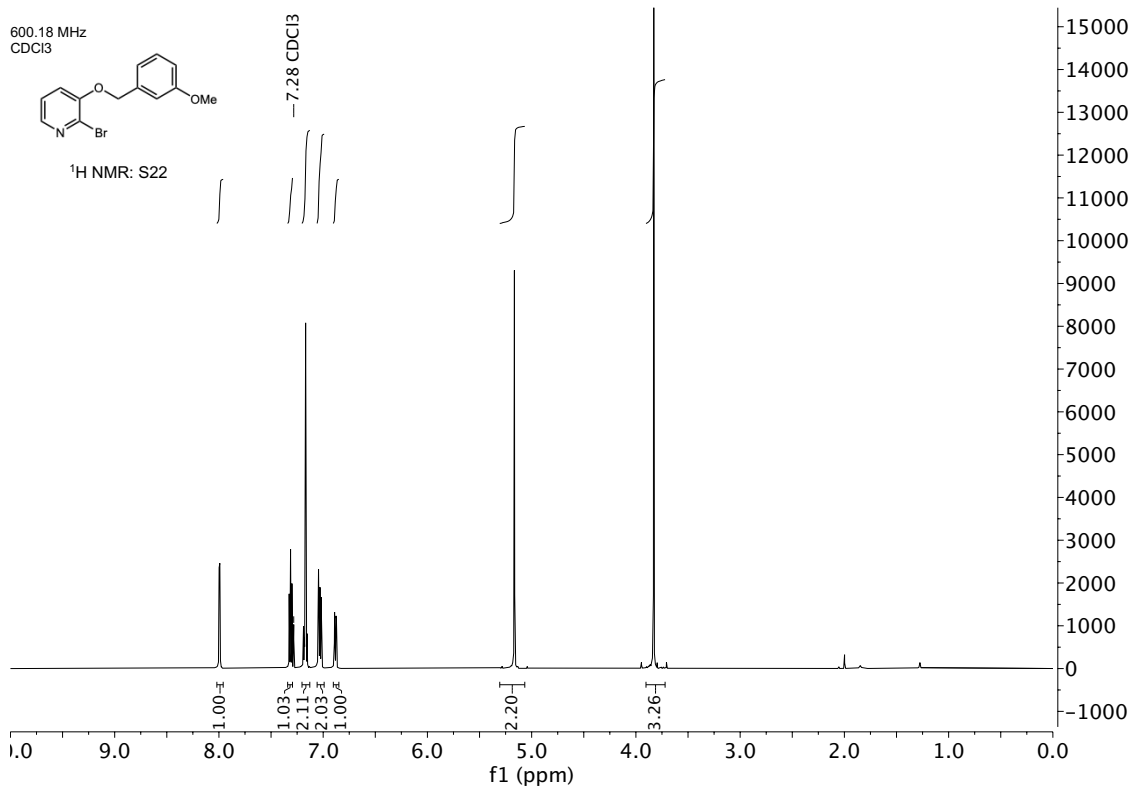


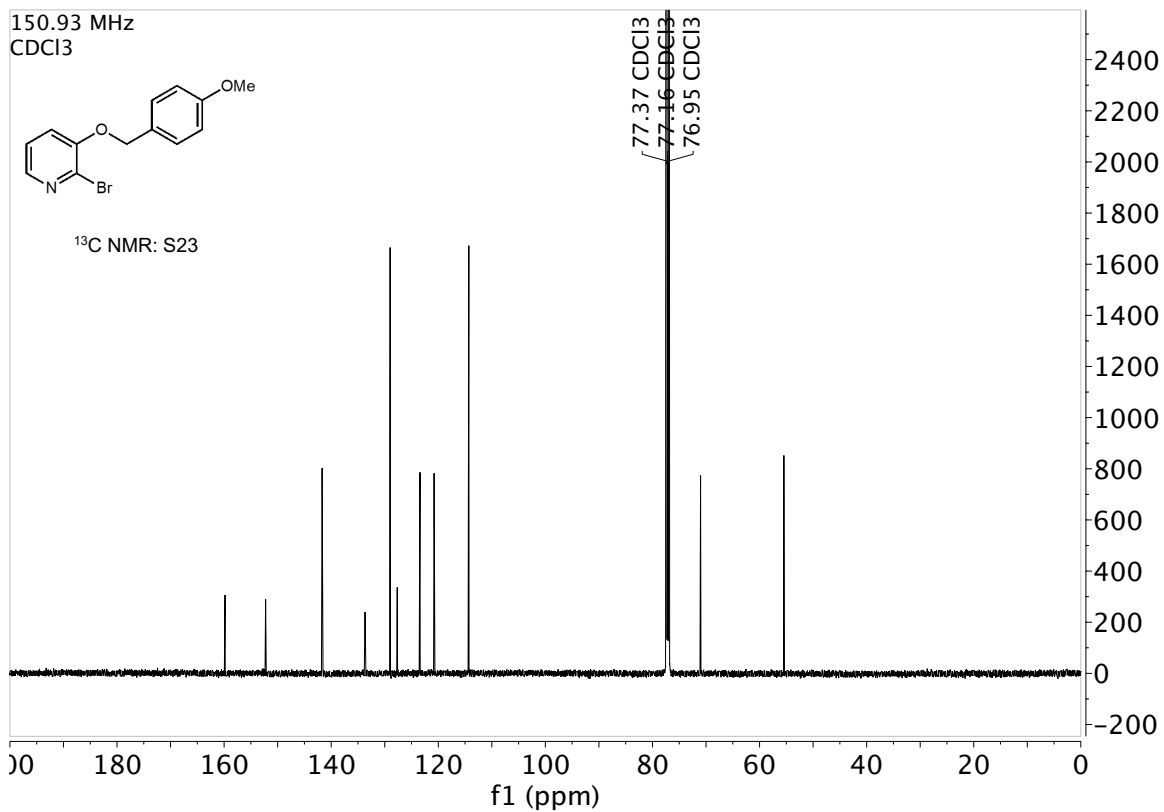
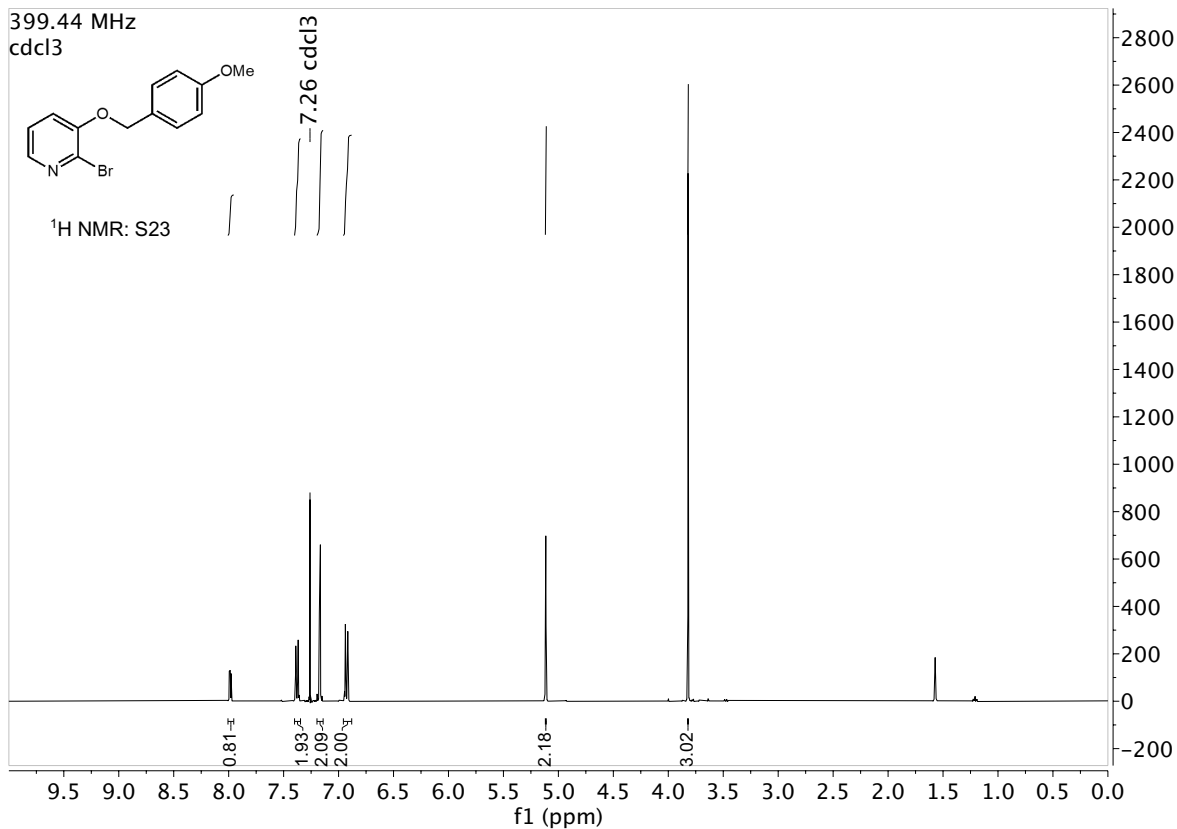


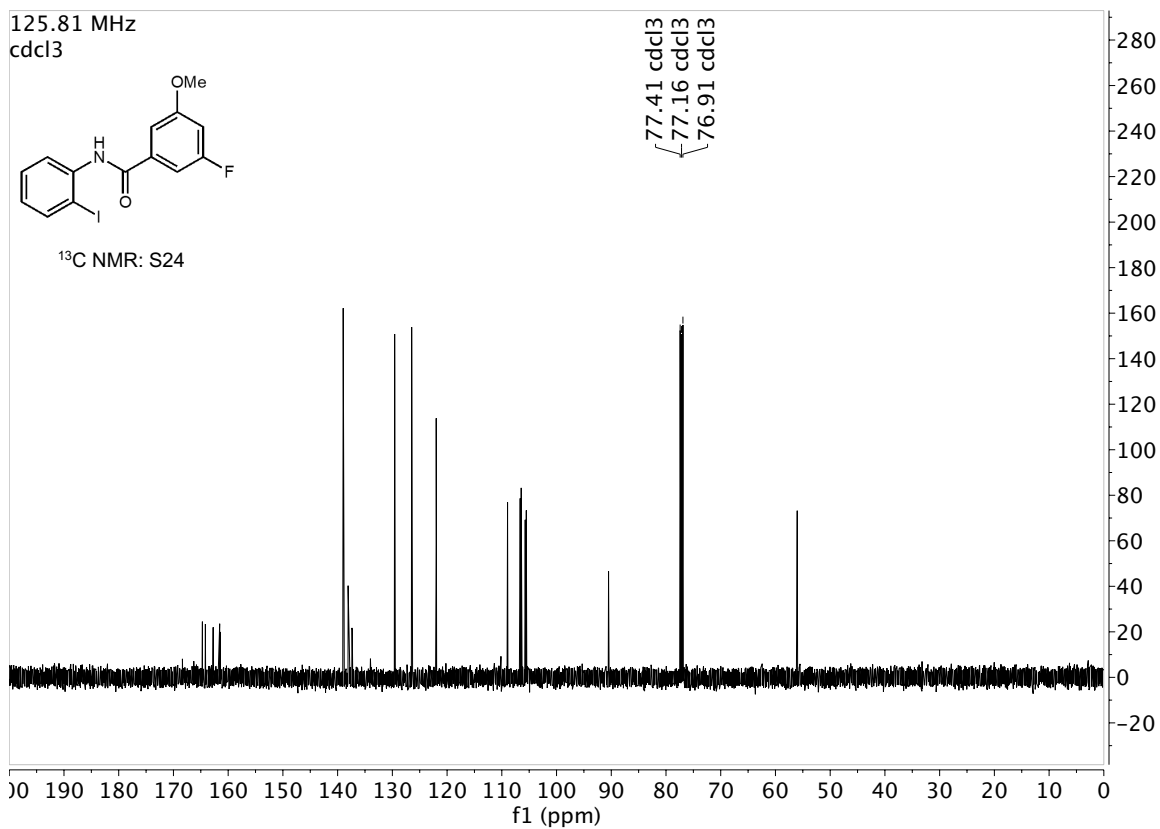
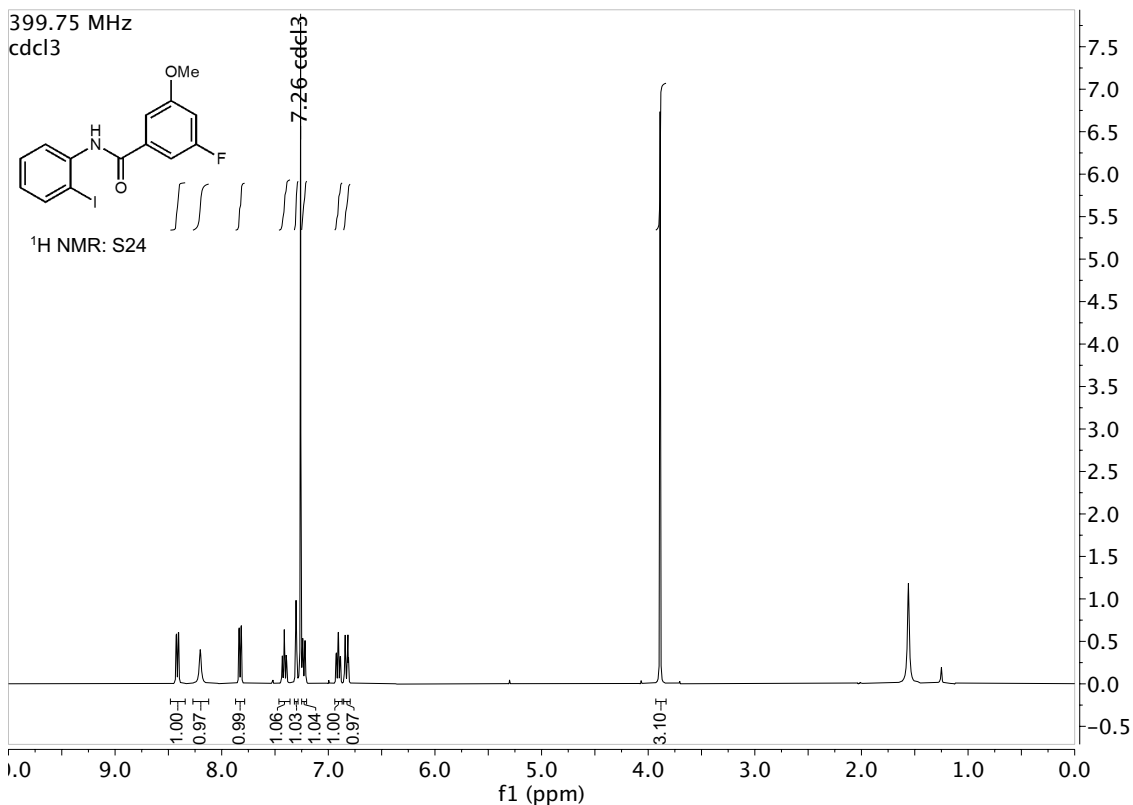


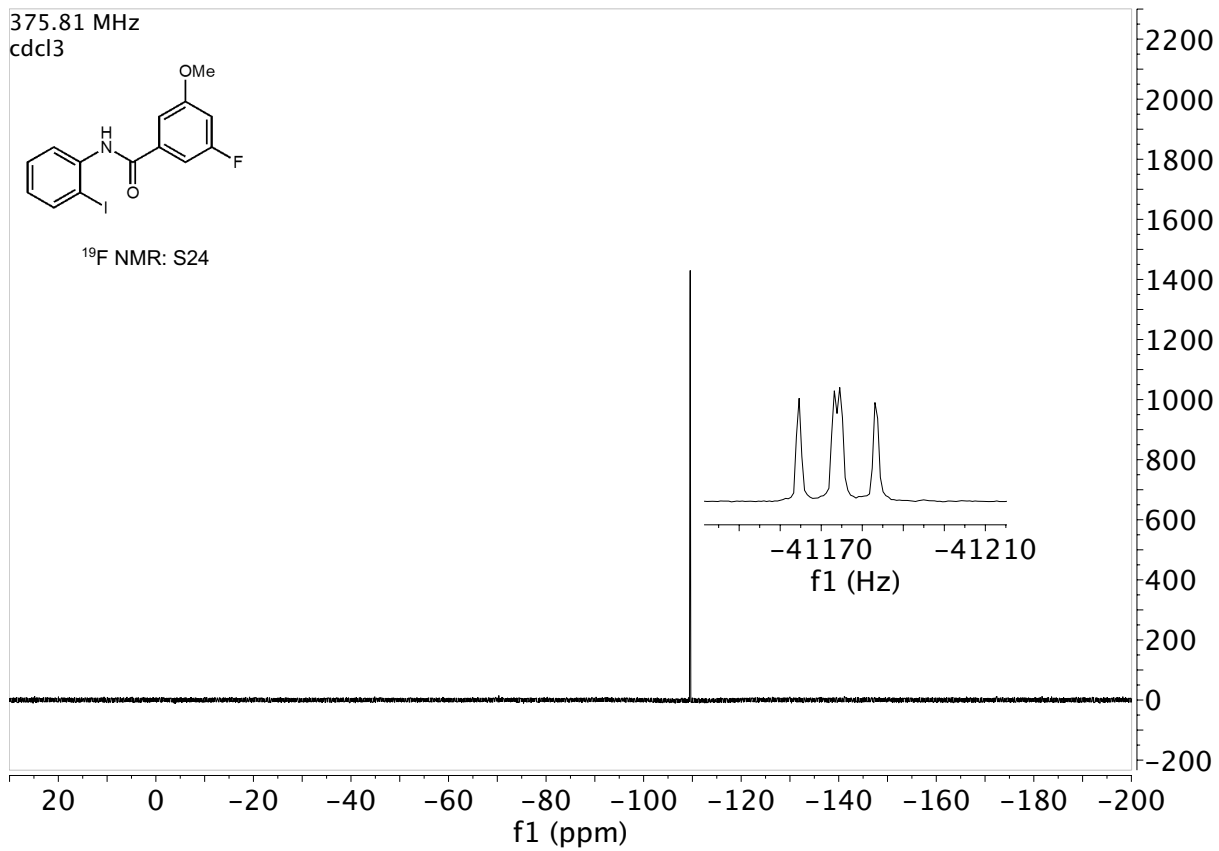


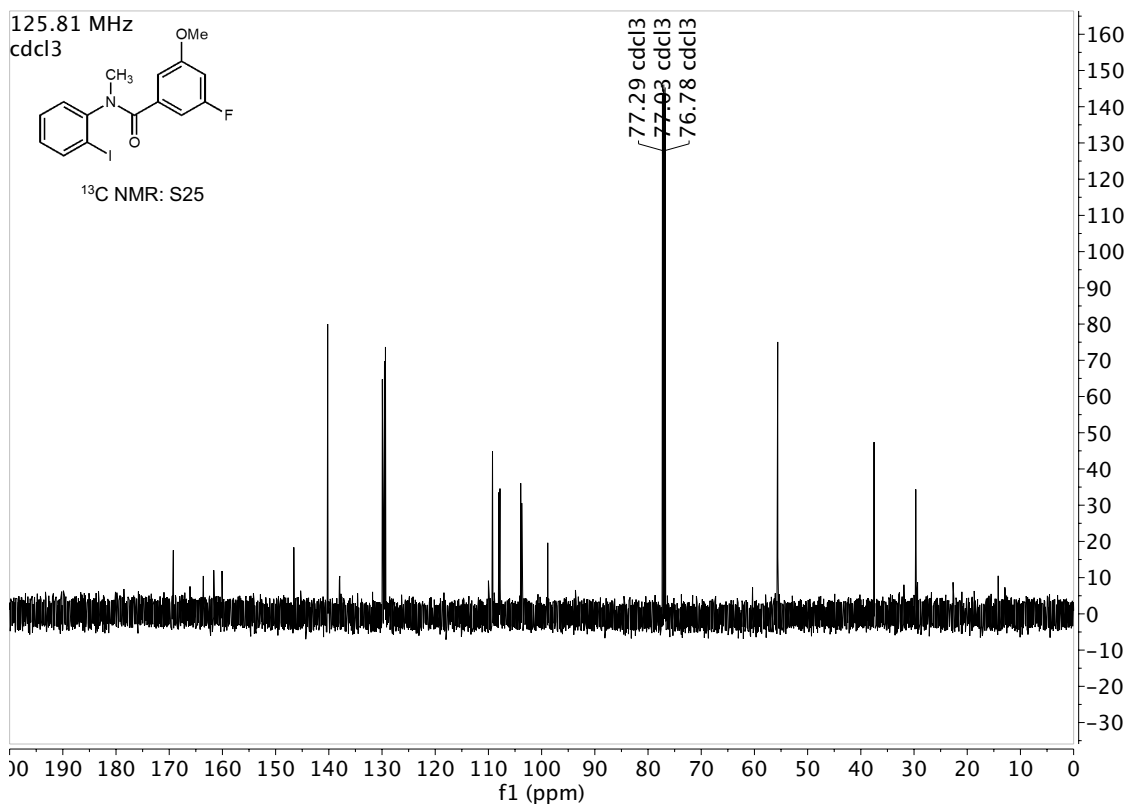
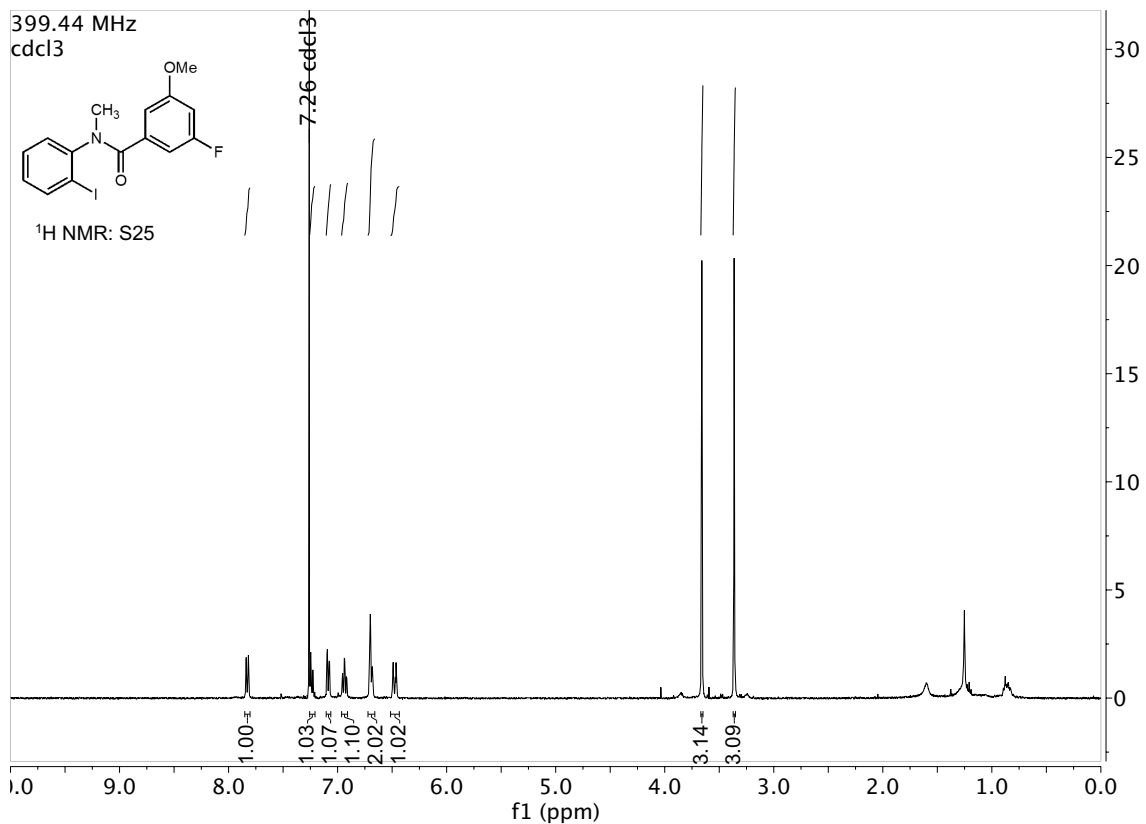


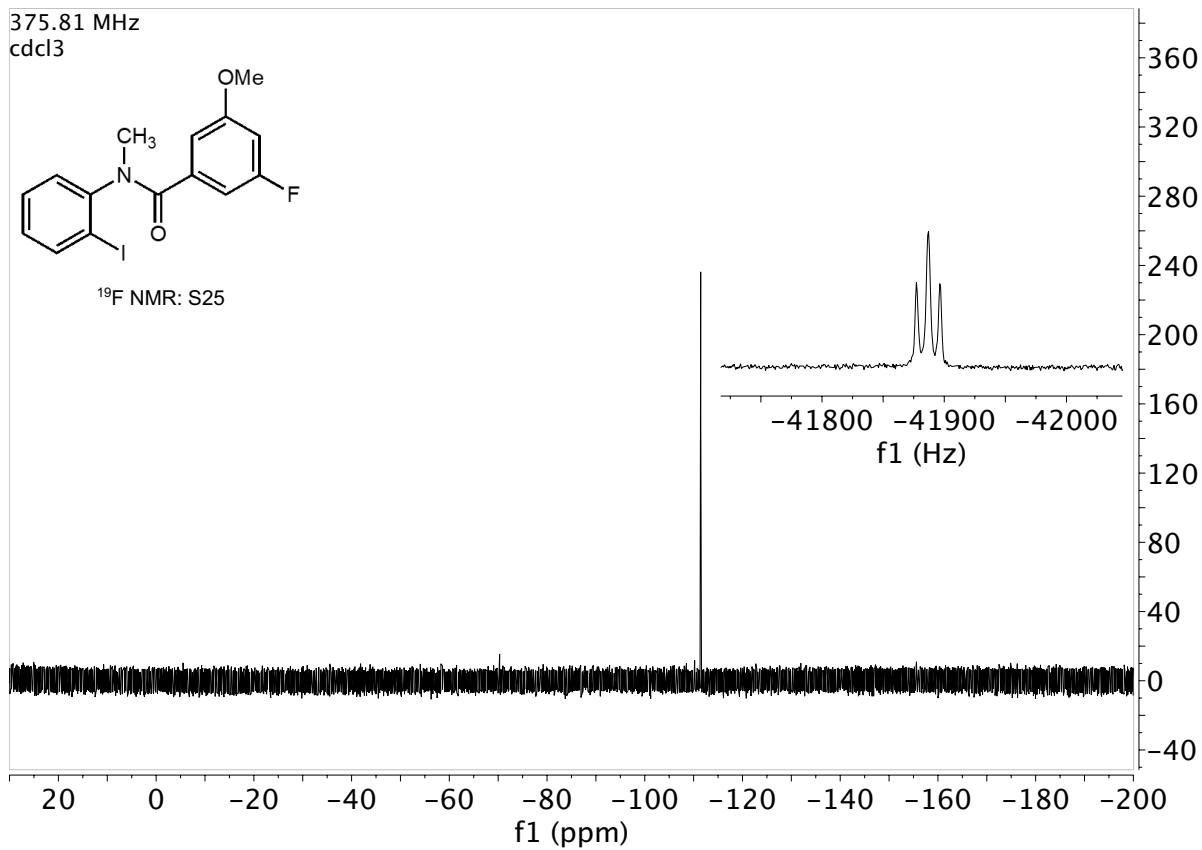


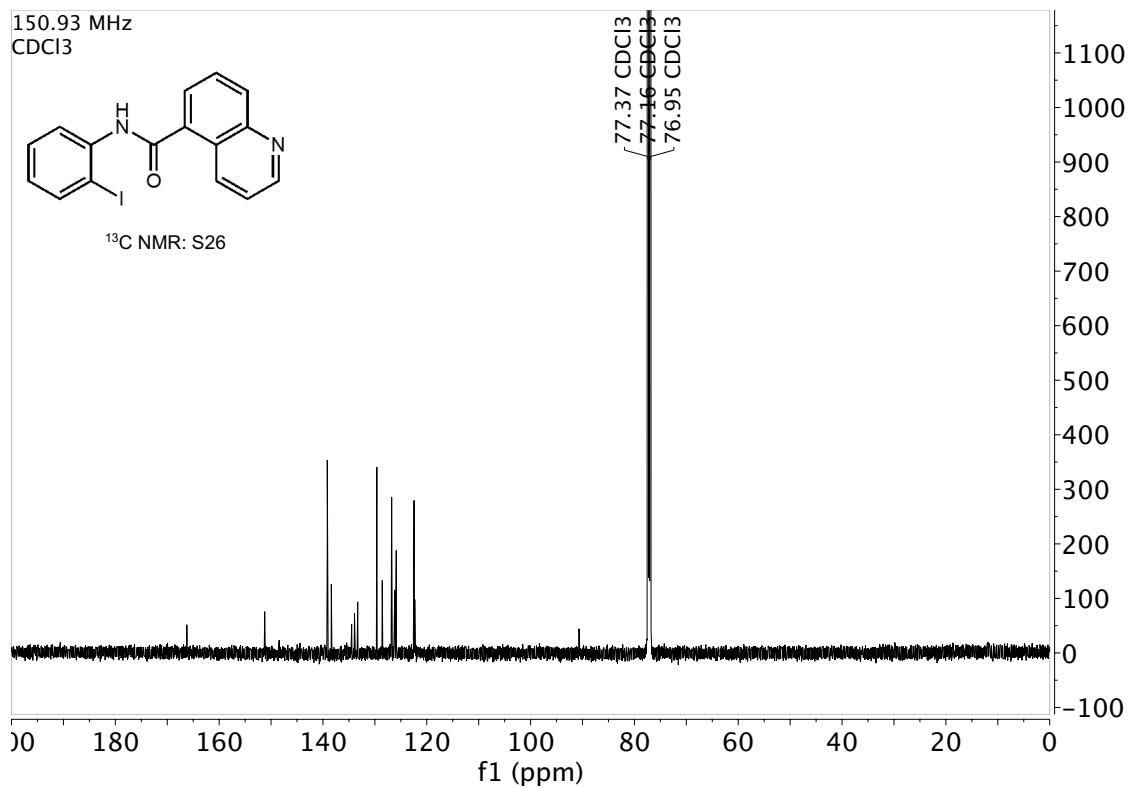
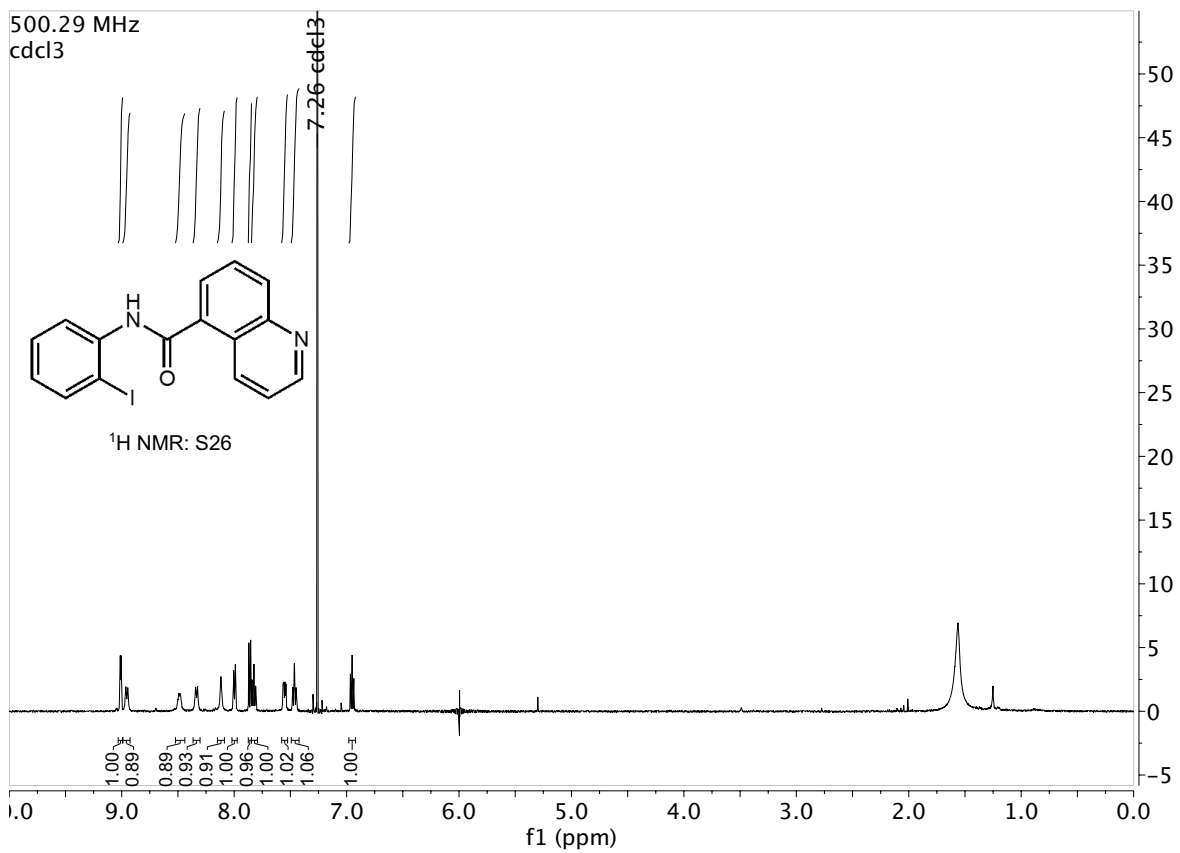


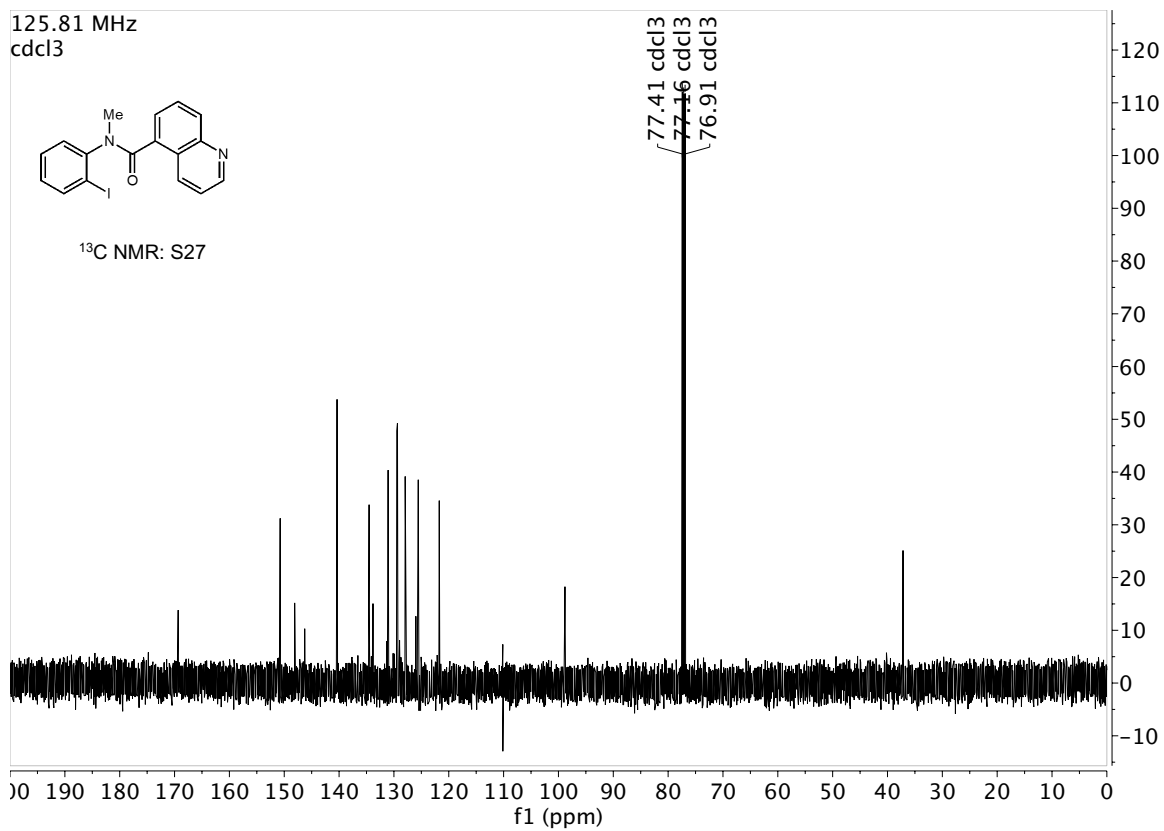
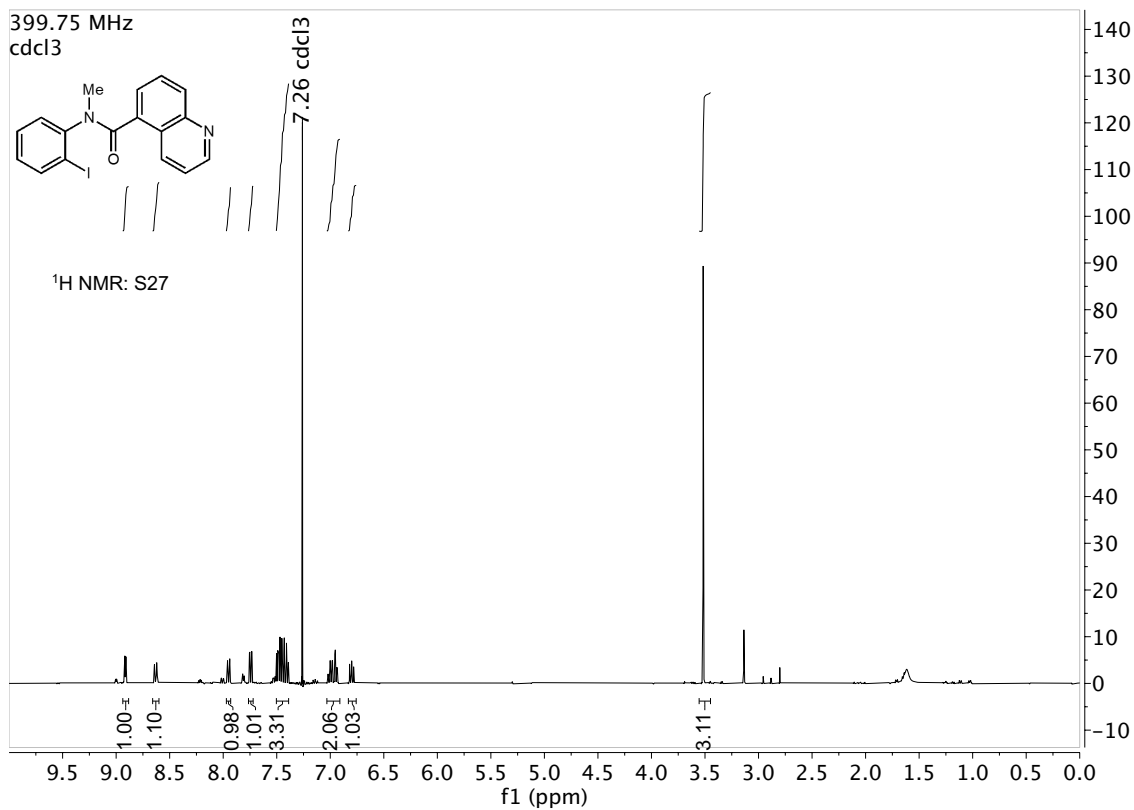


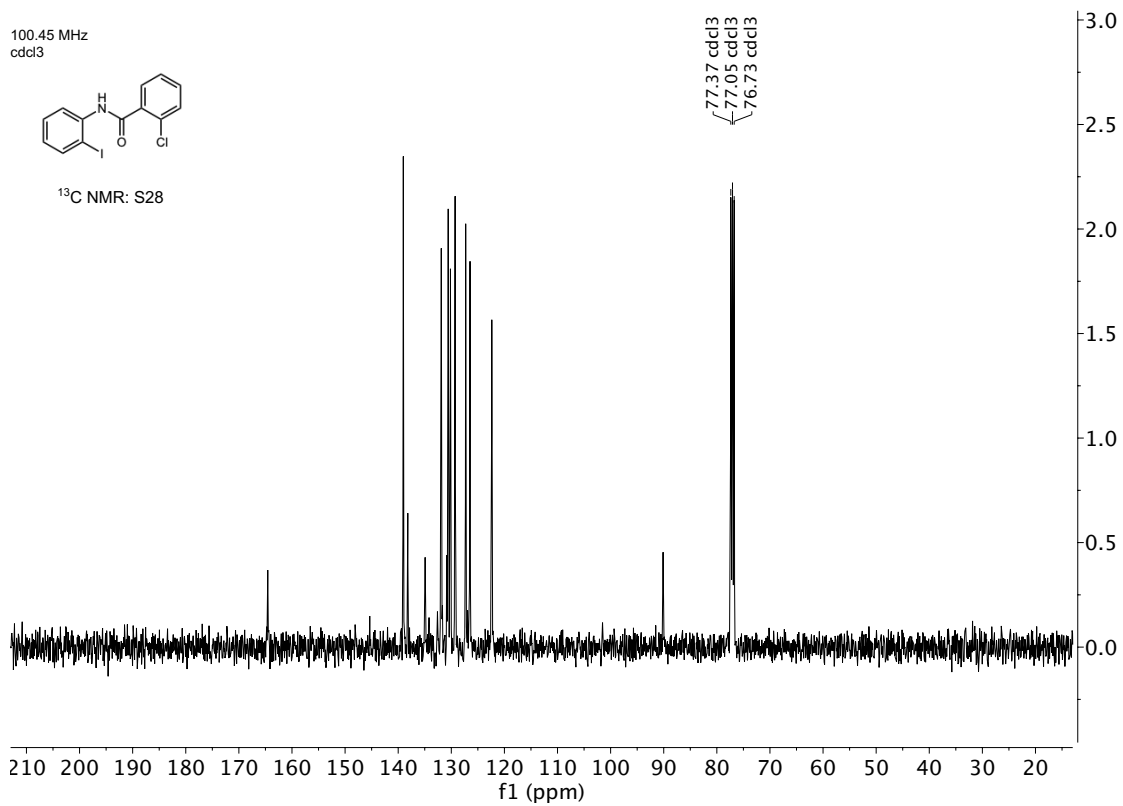
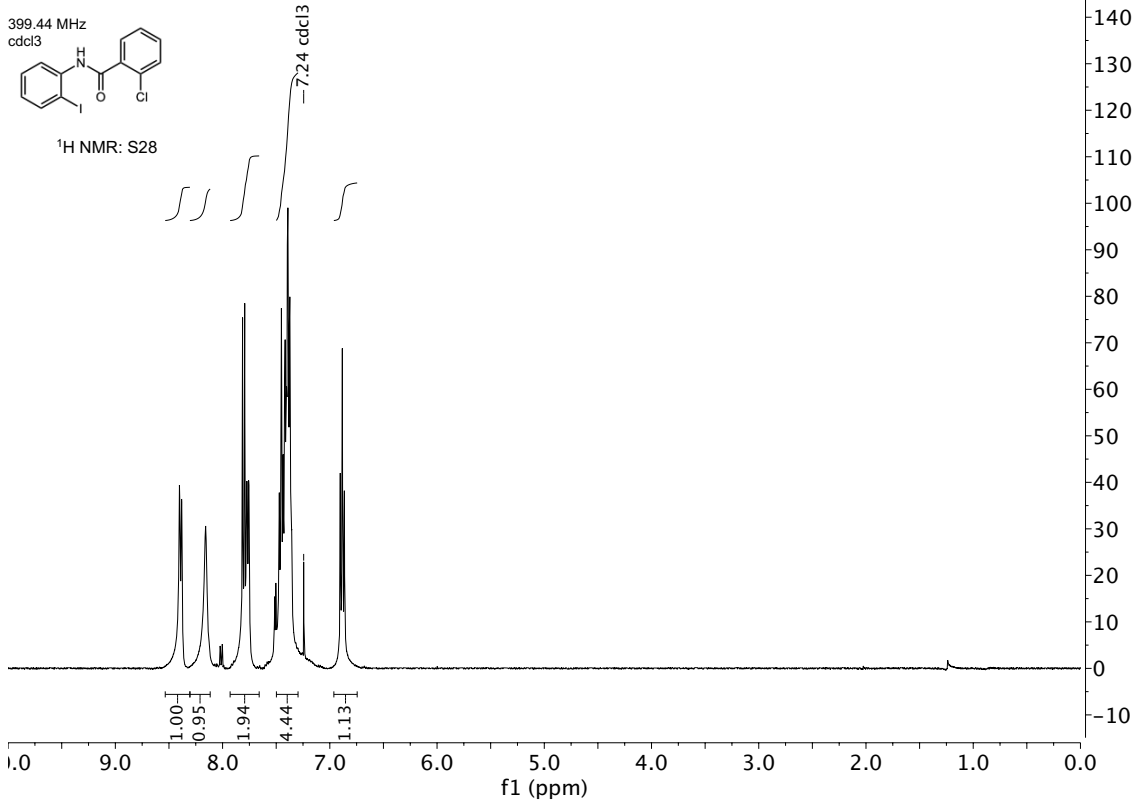


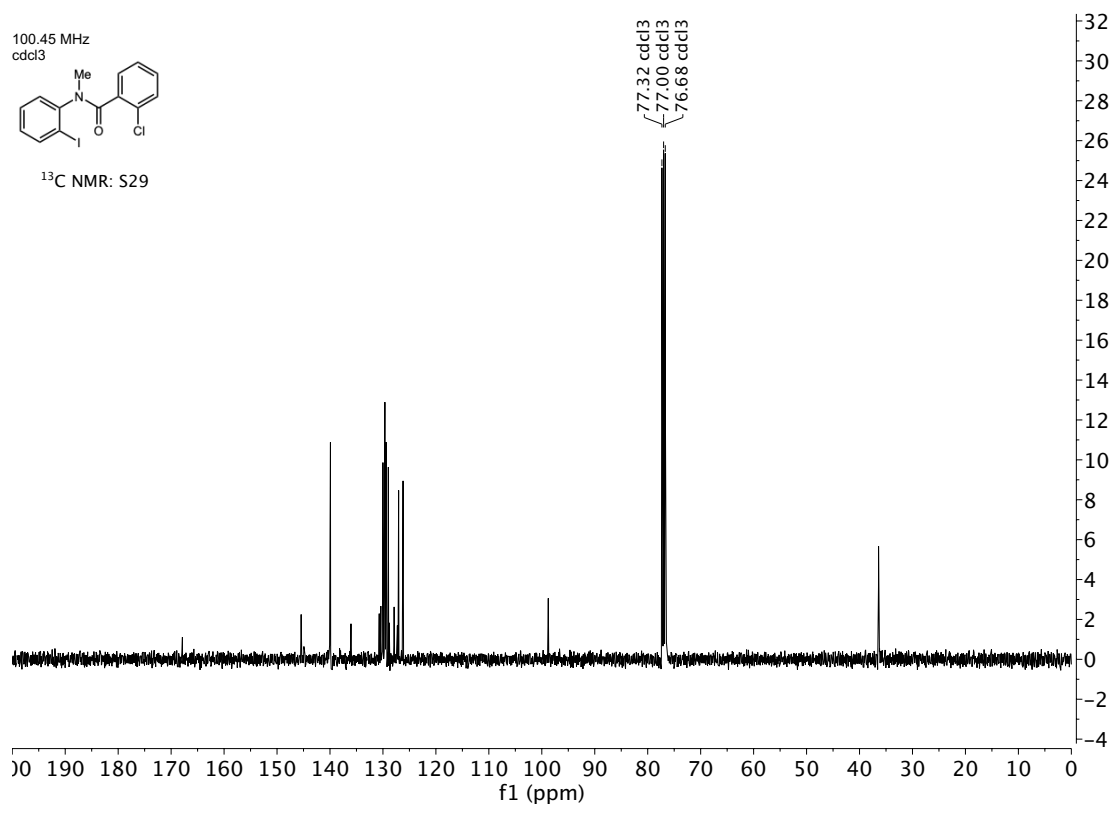
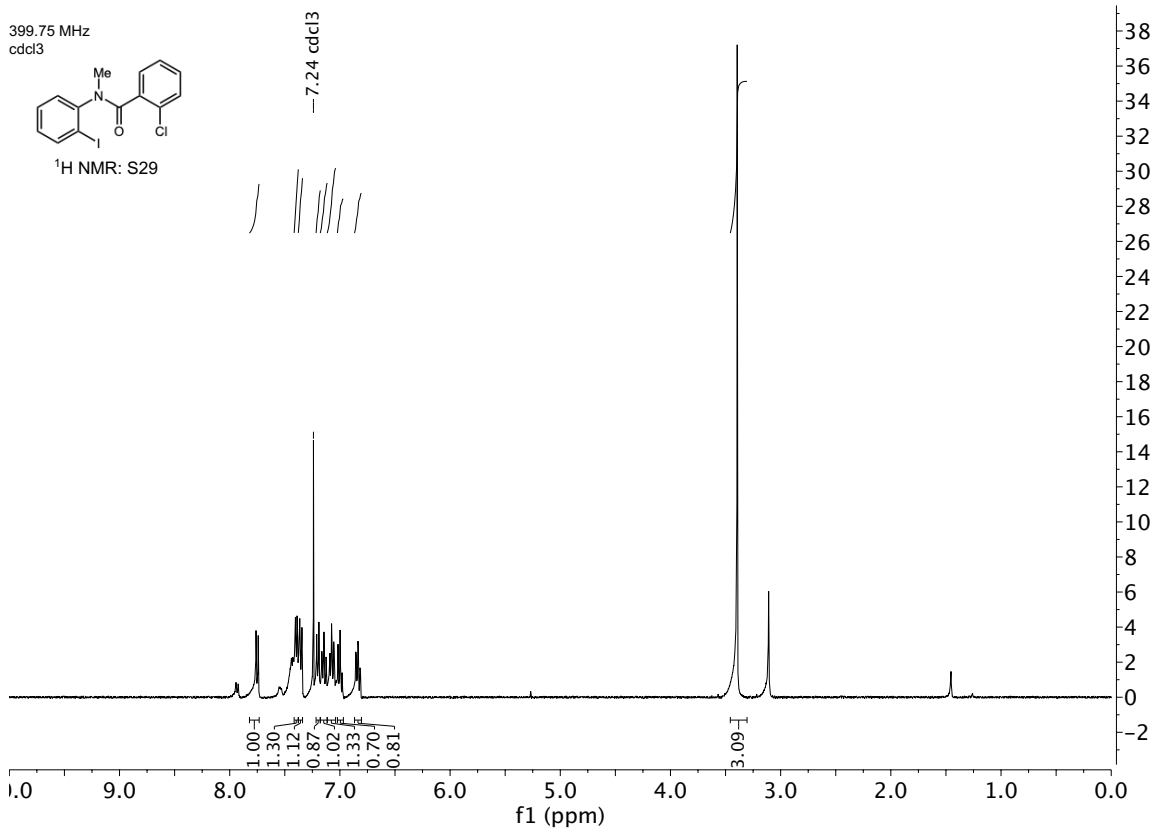


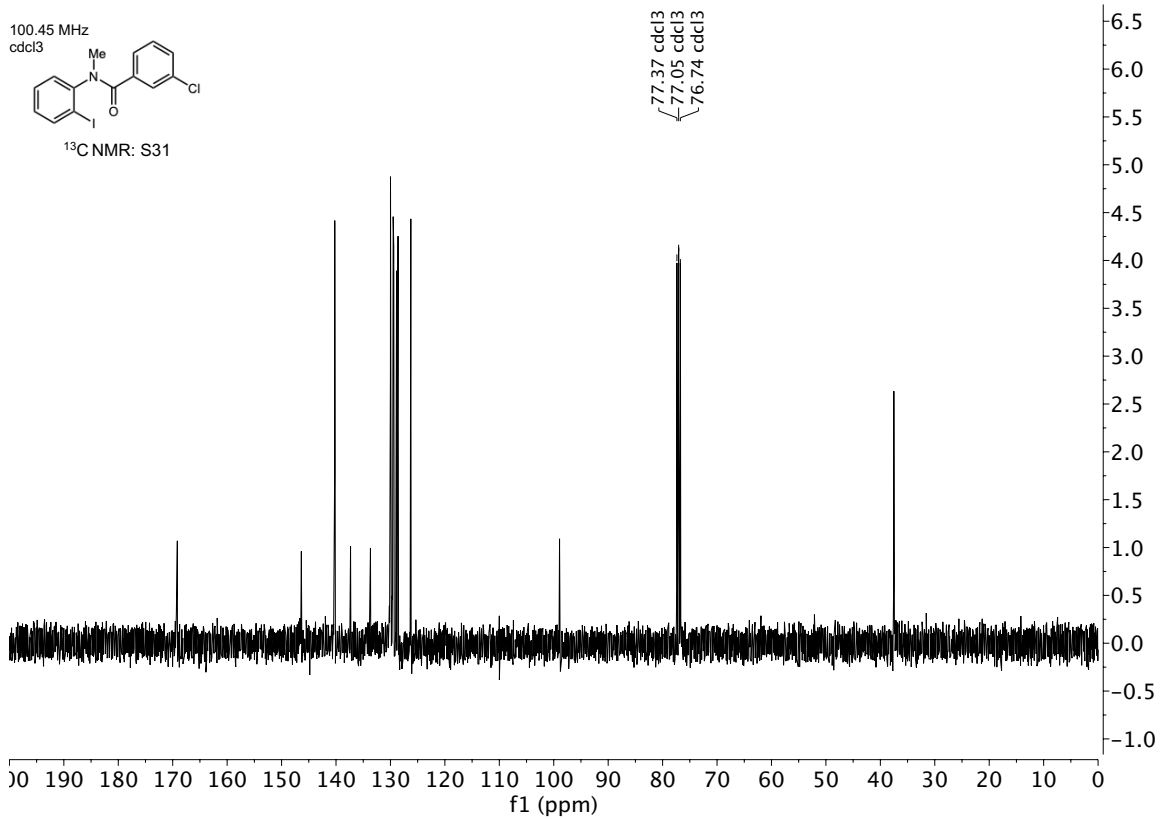
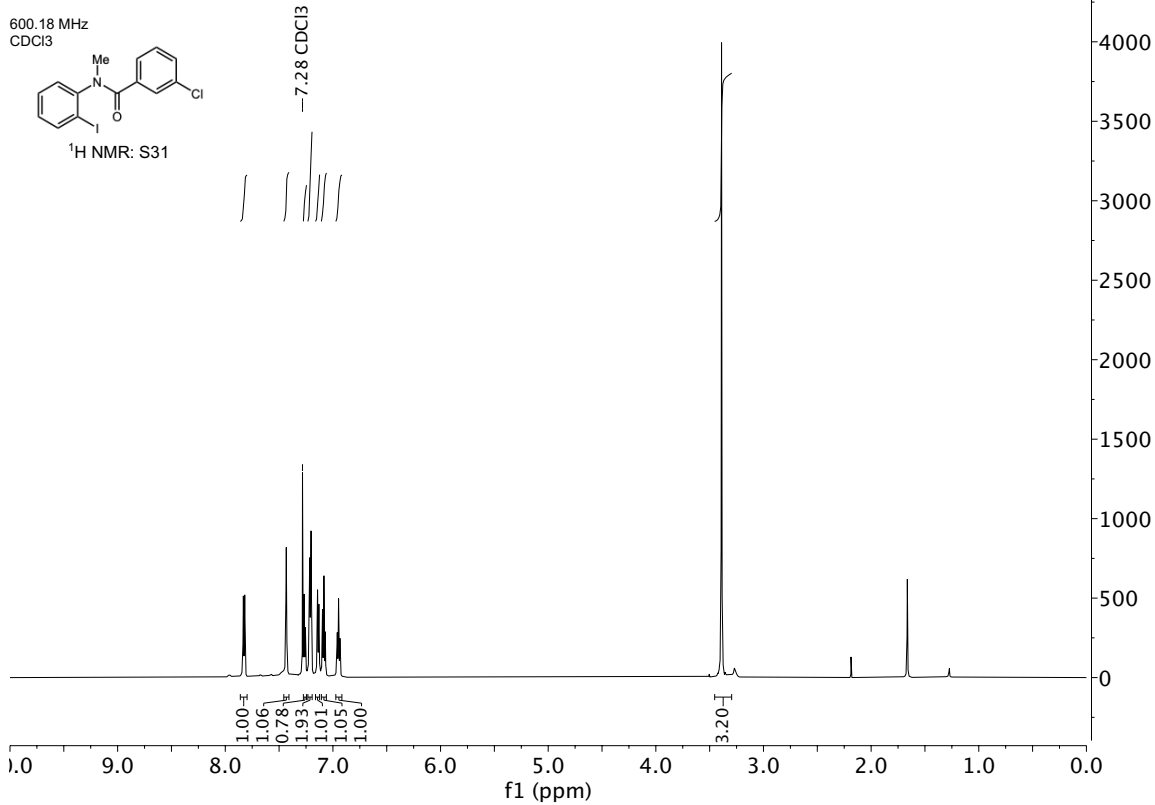


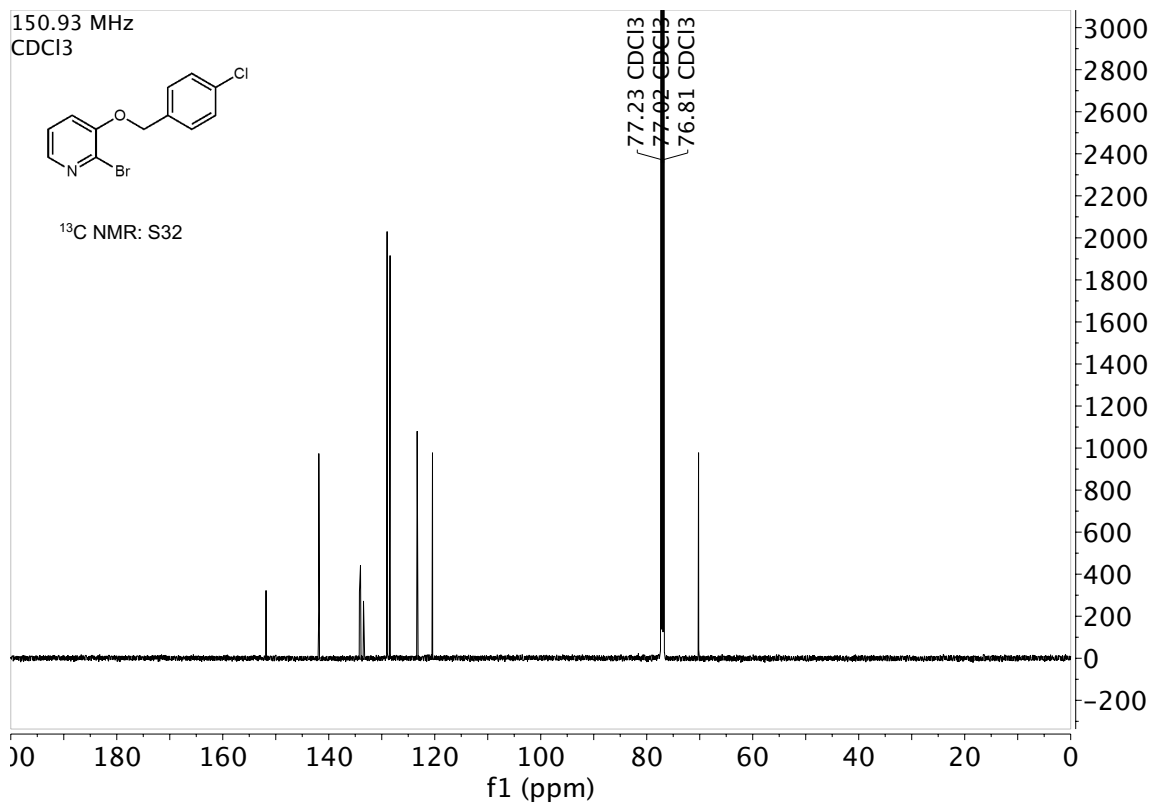
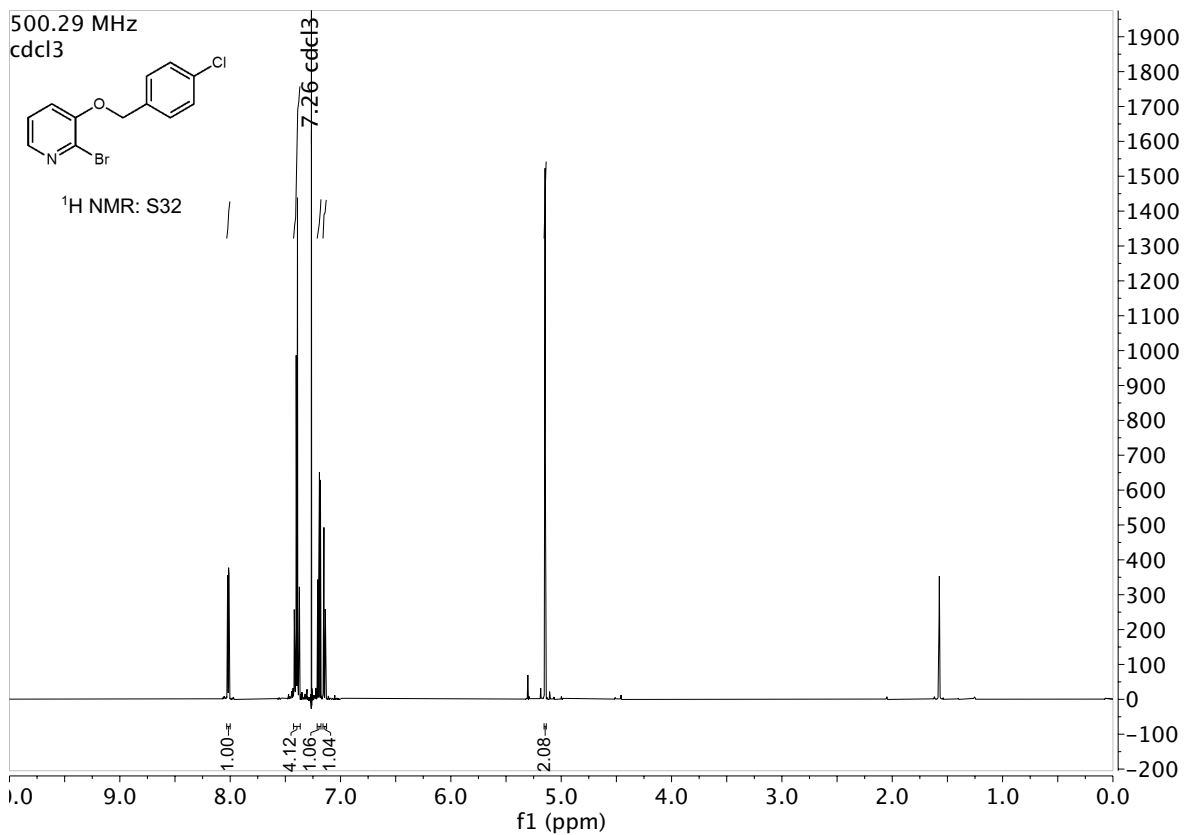


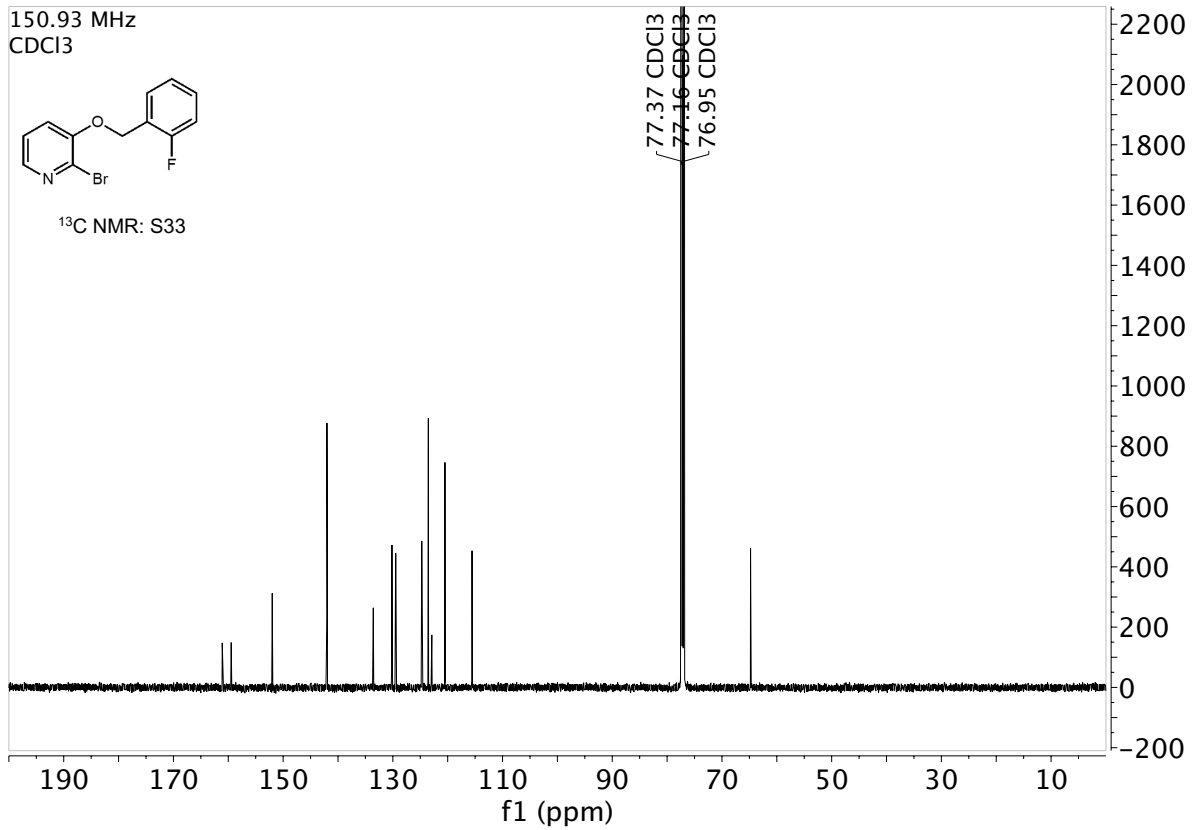
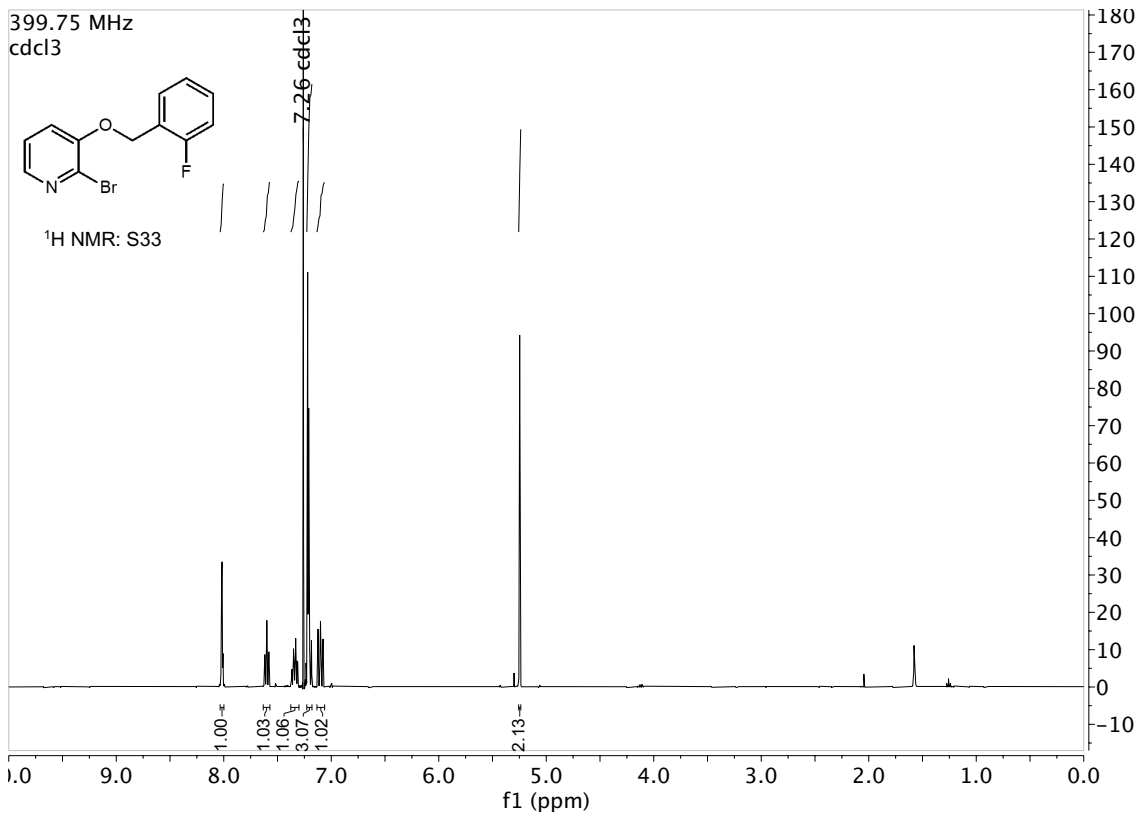


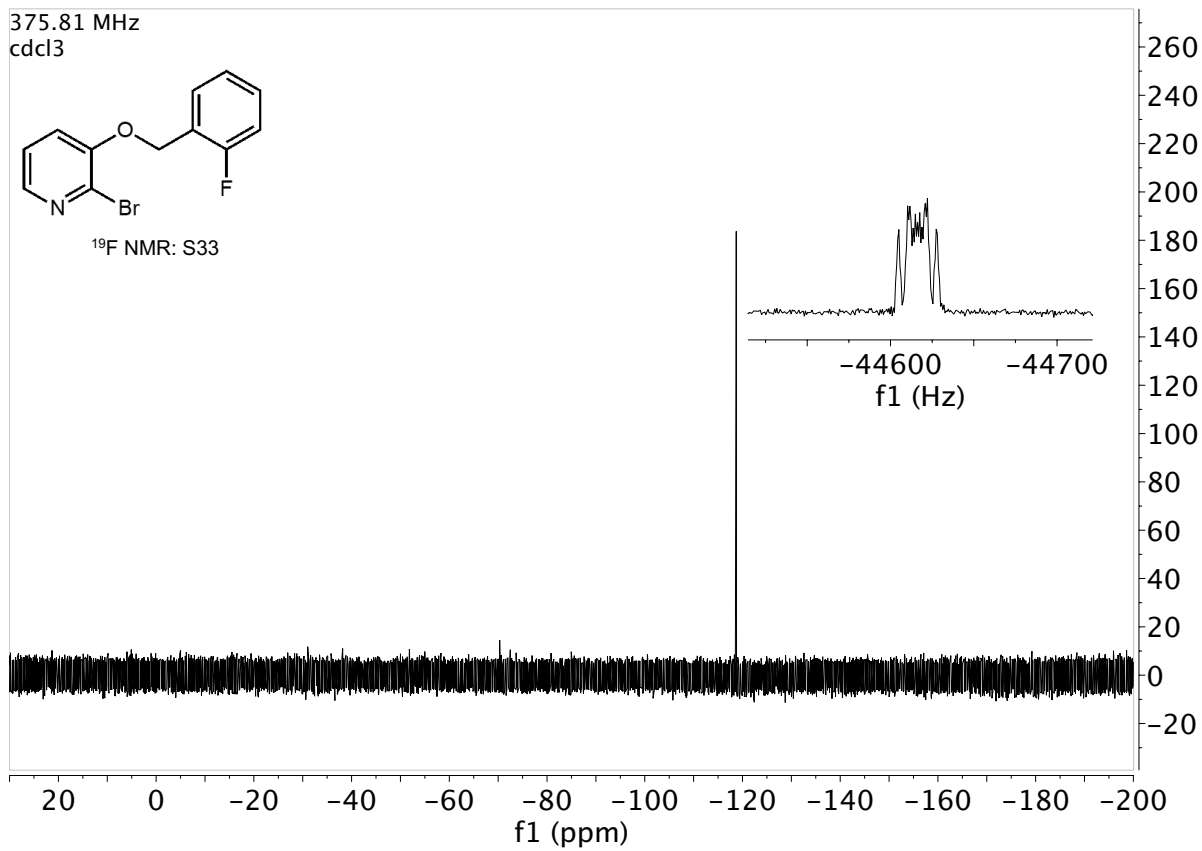


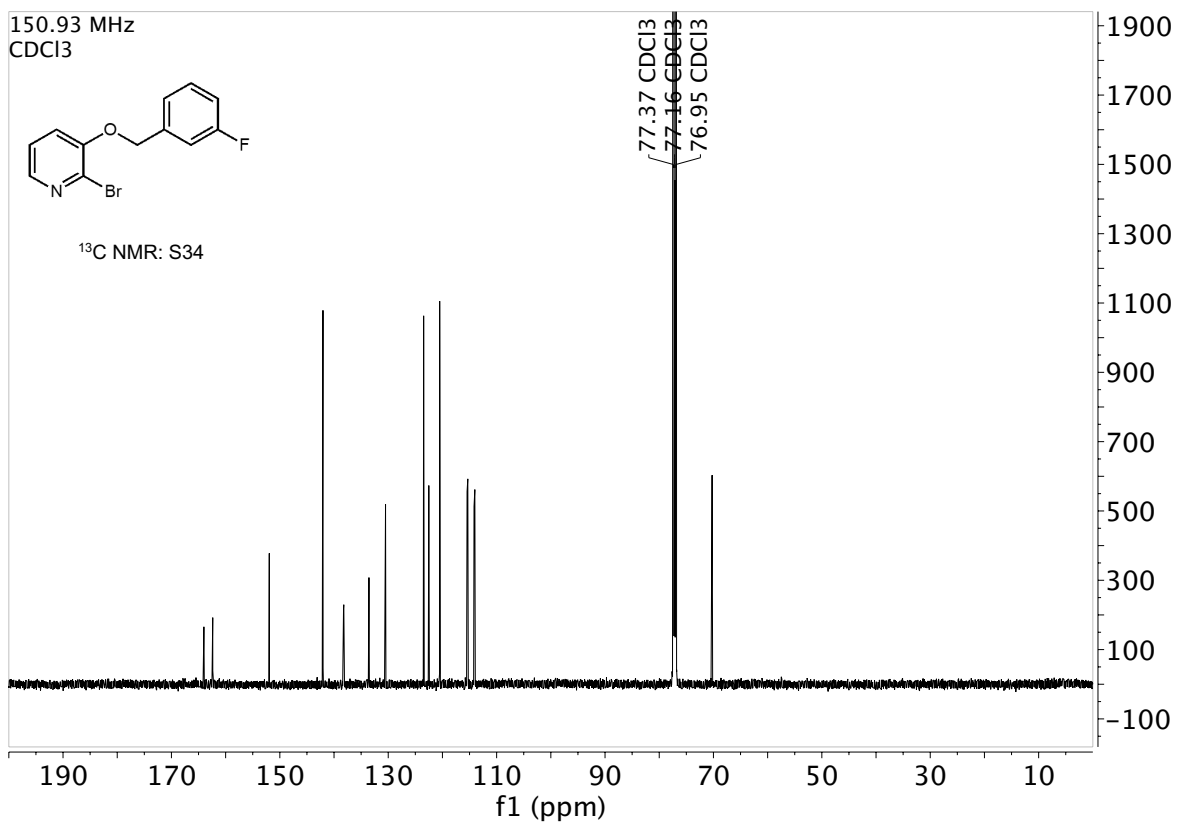
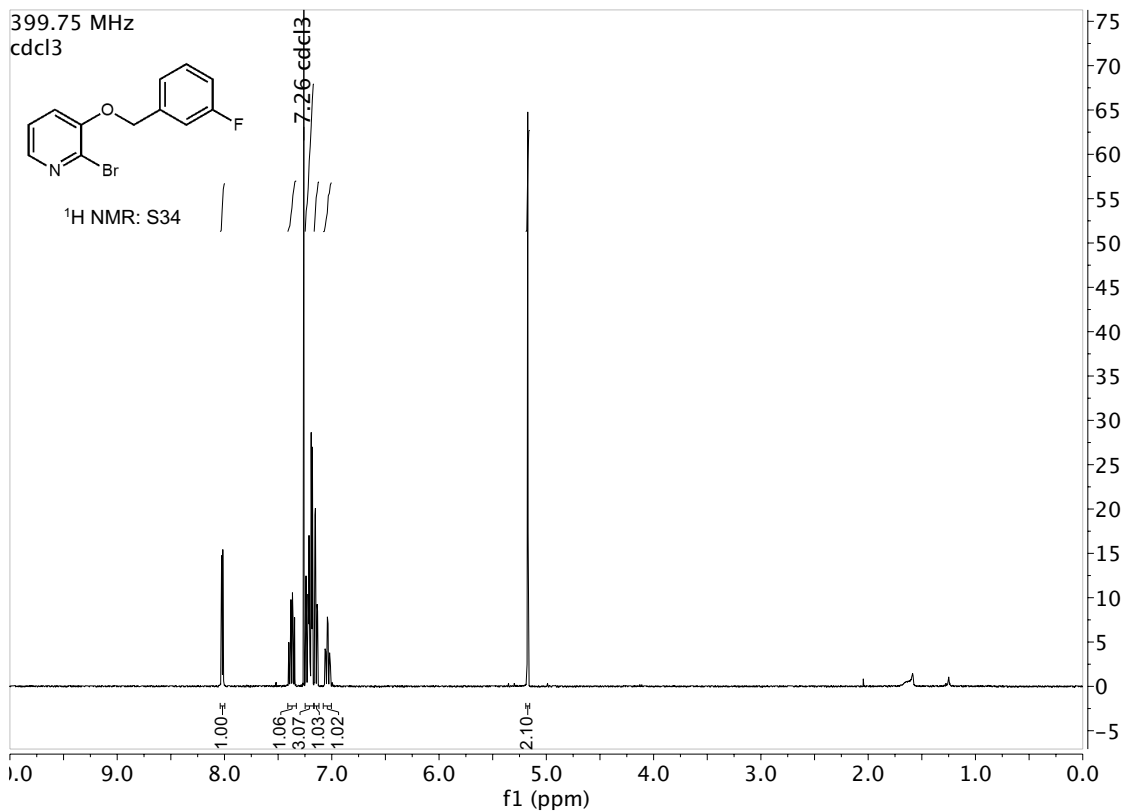


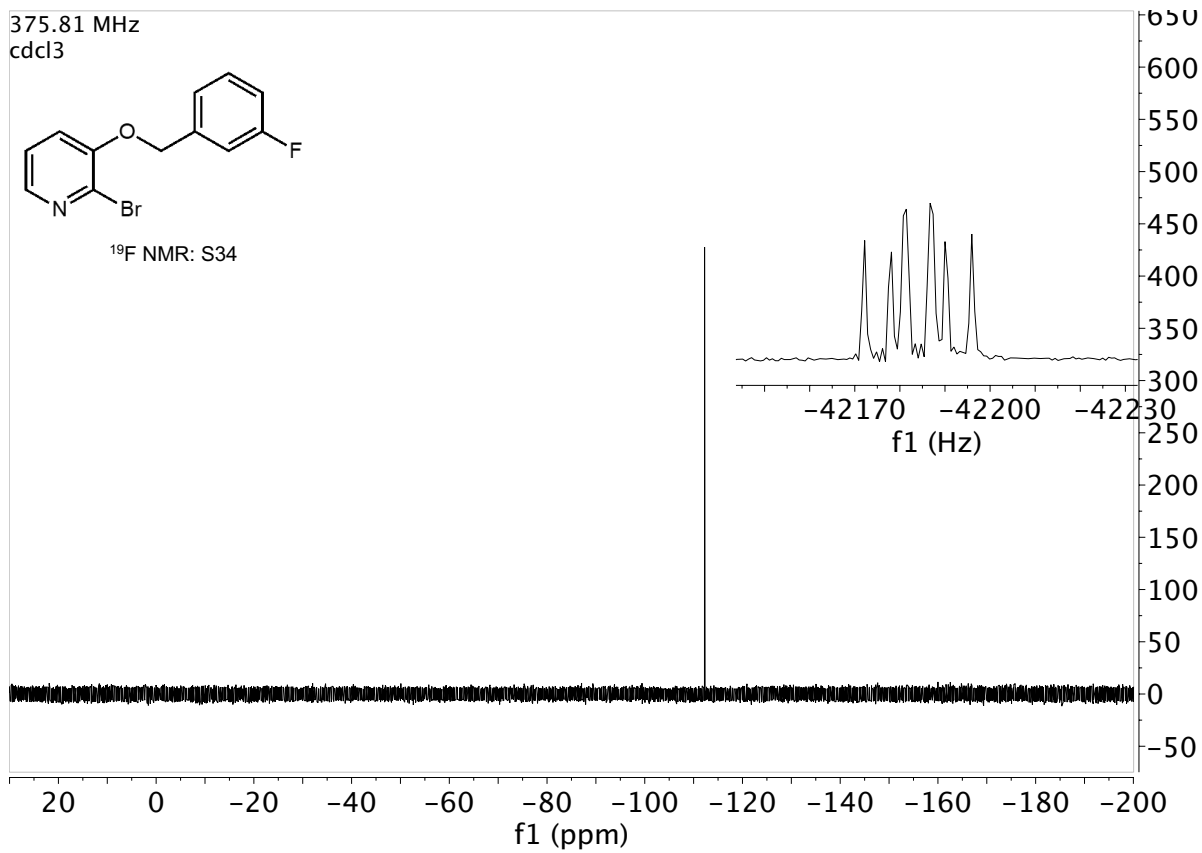


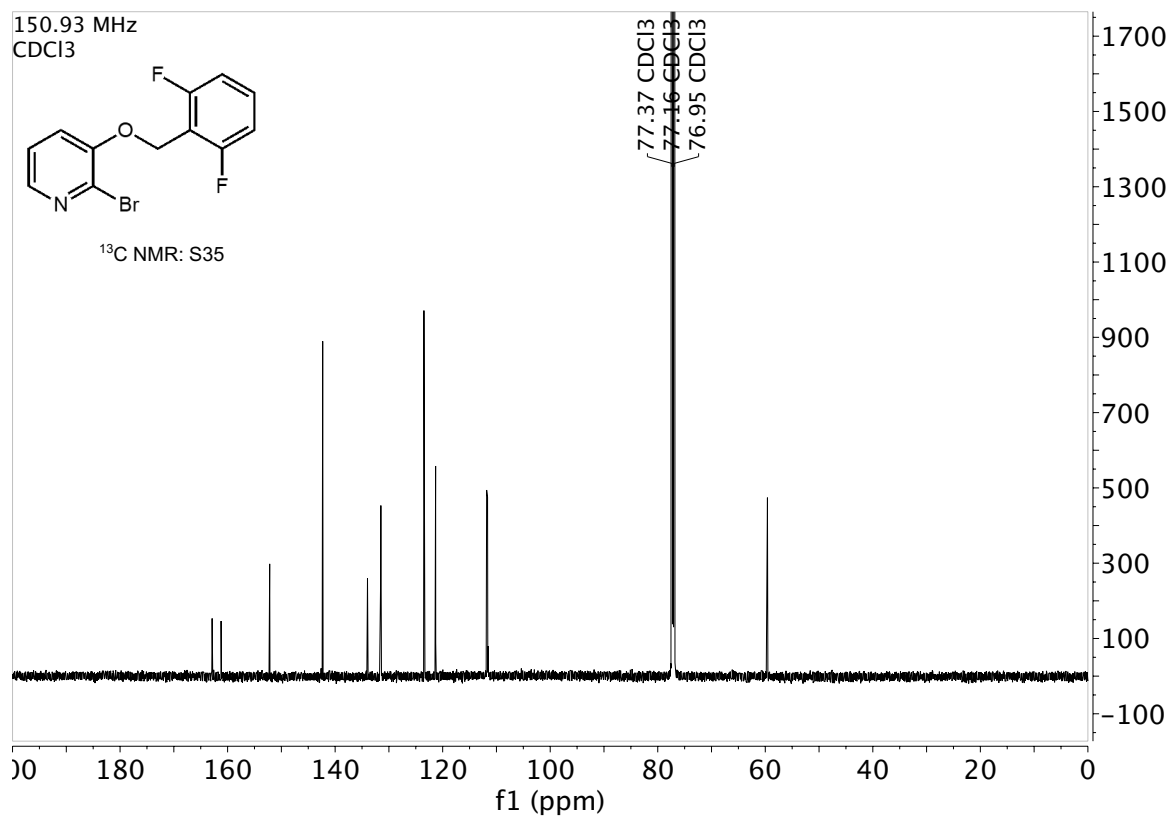
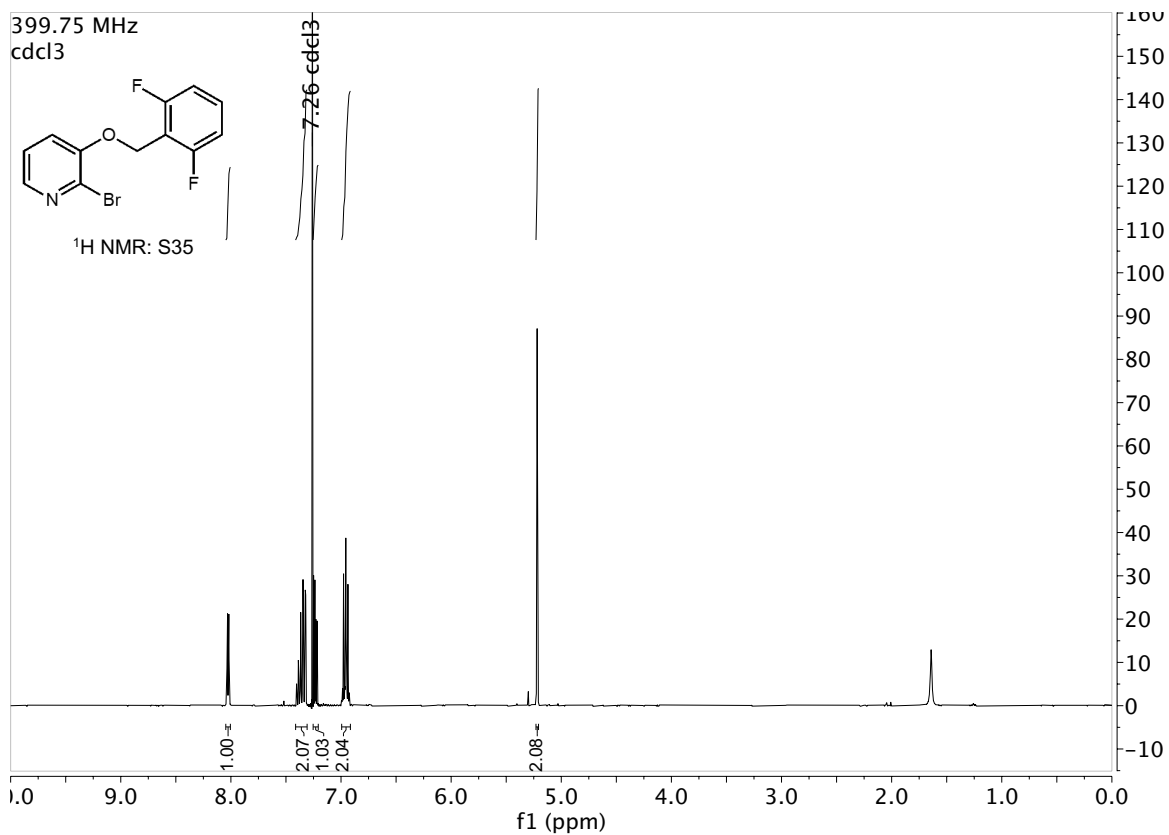




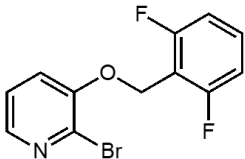




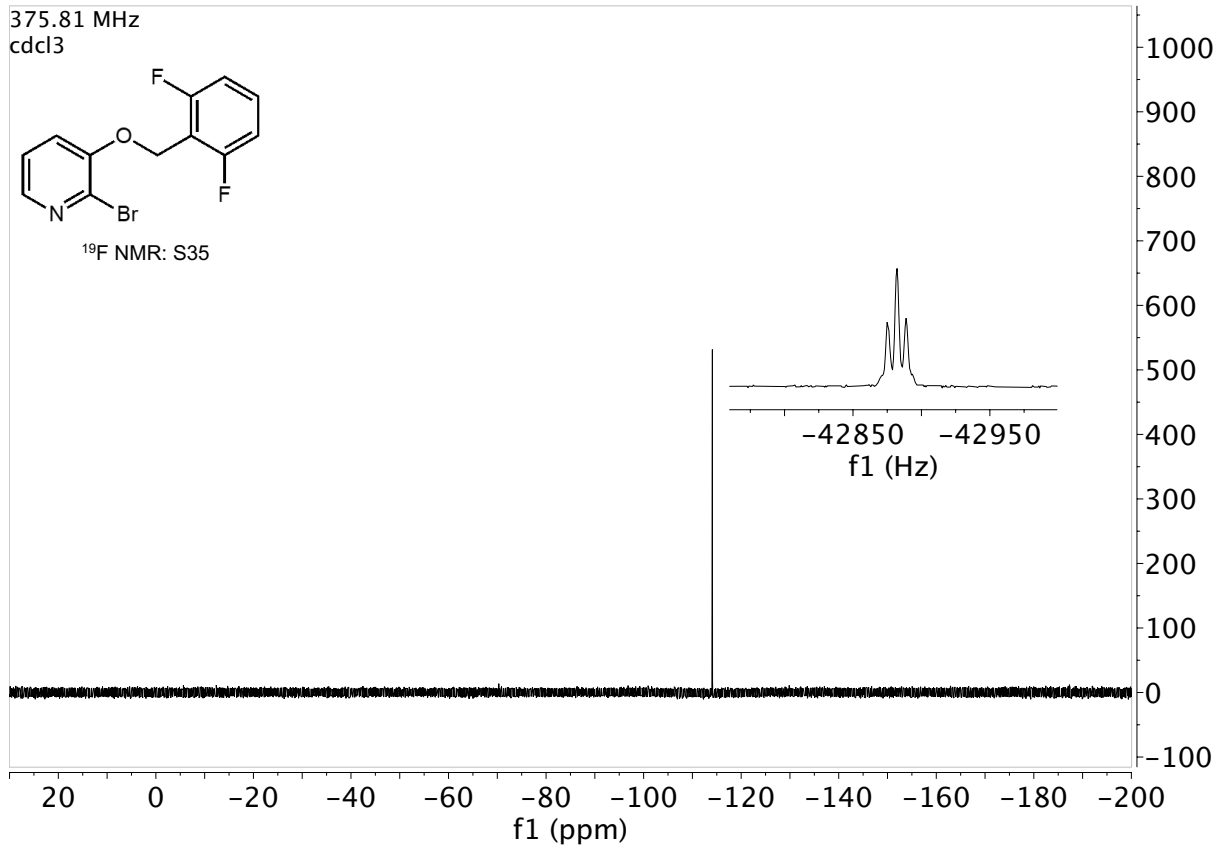


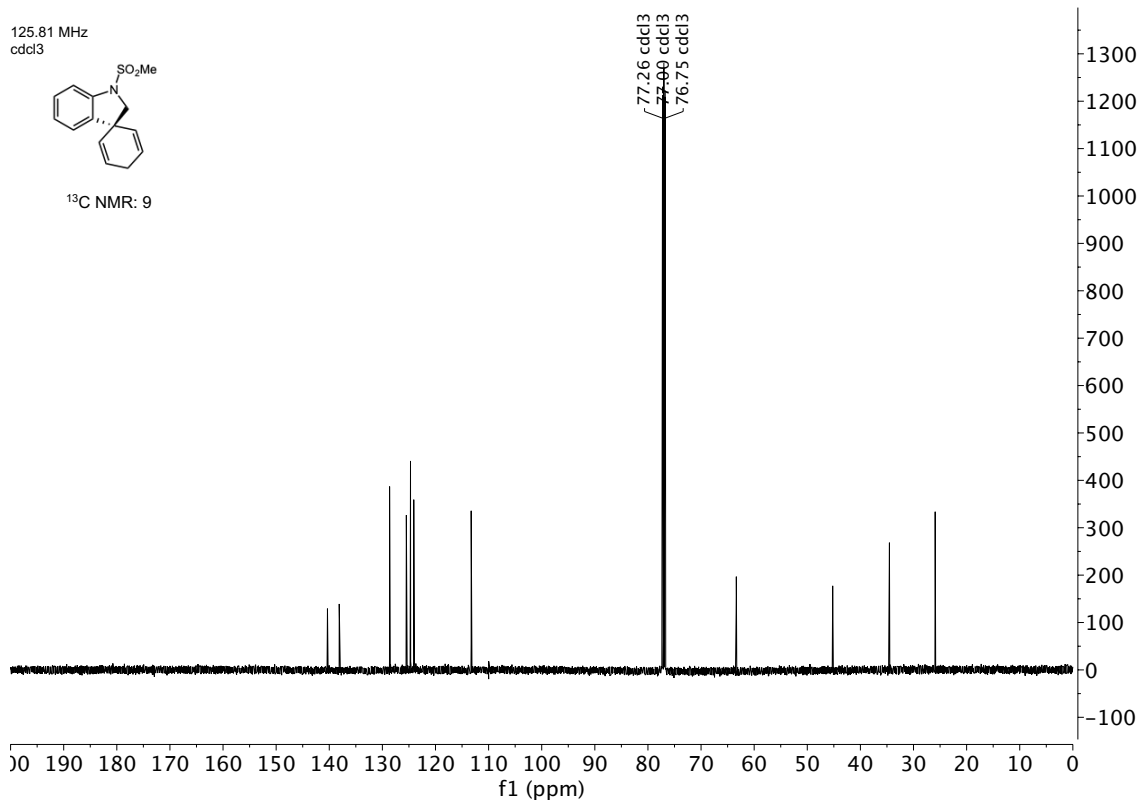
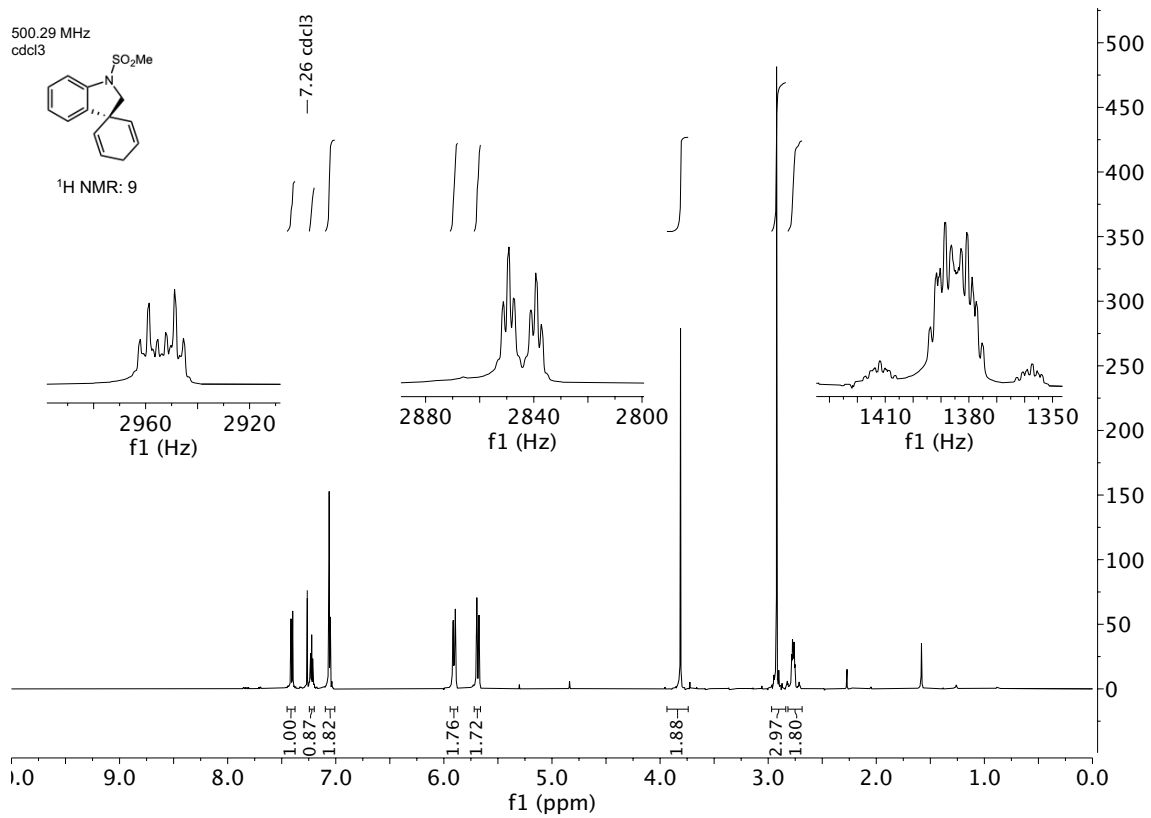


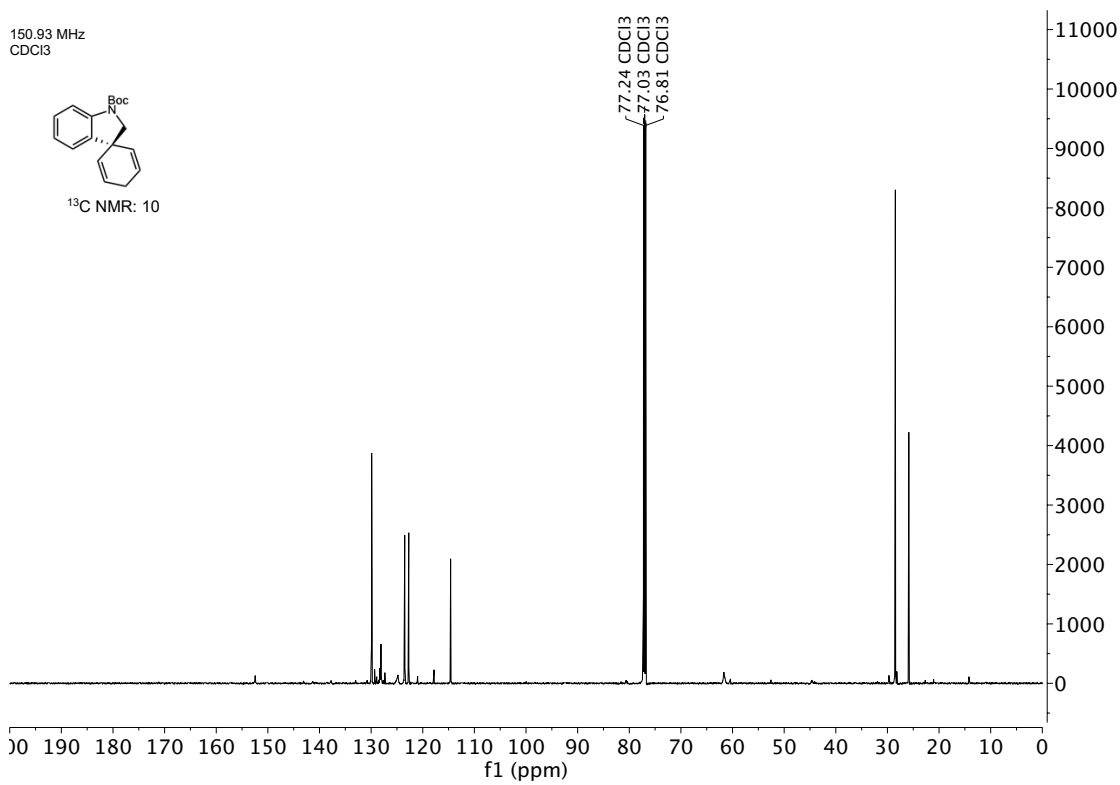
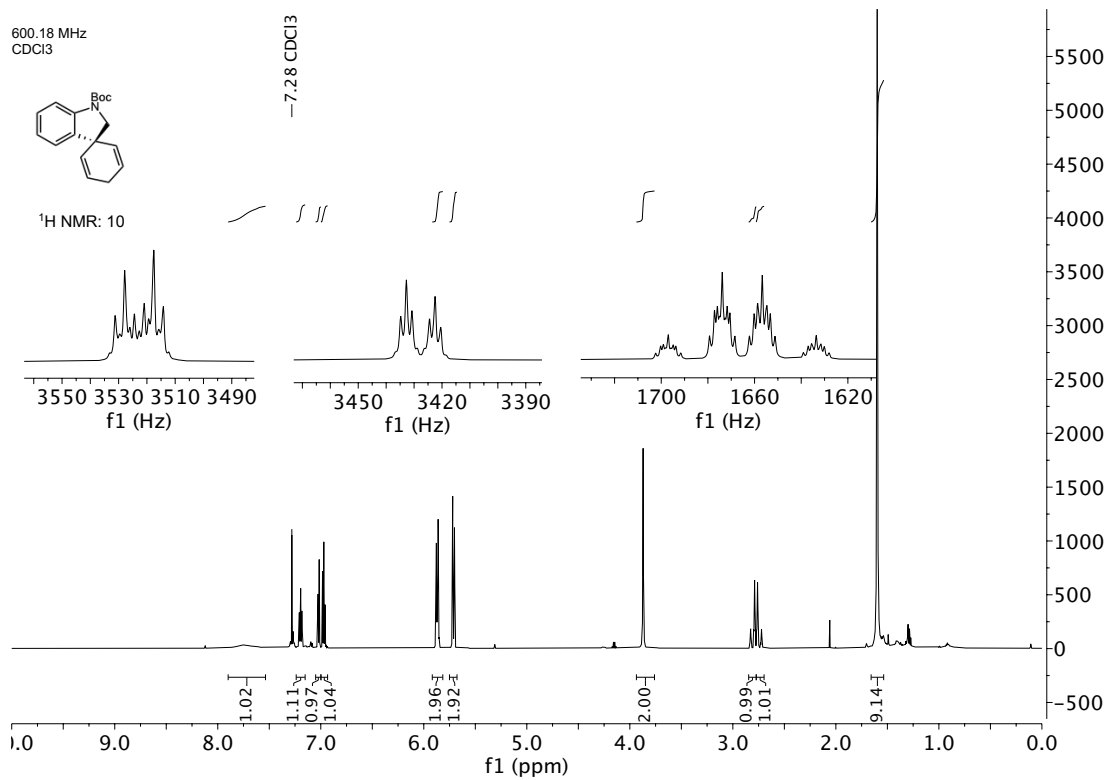
375.81 MHz
cdcl3

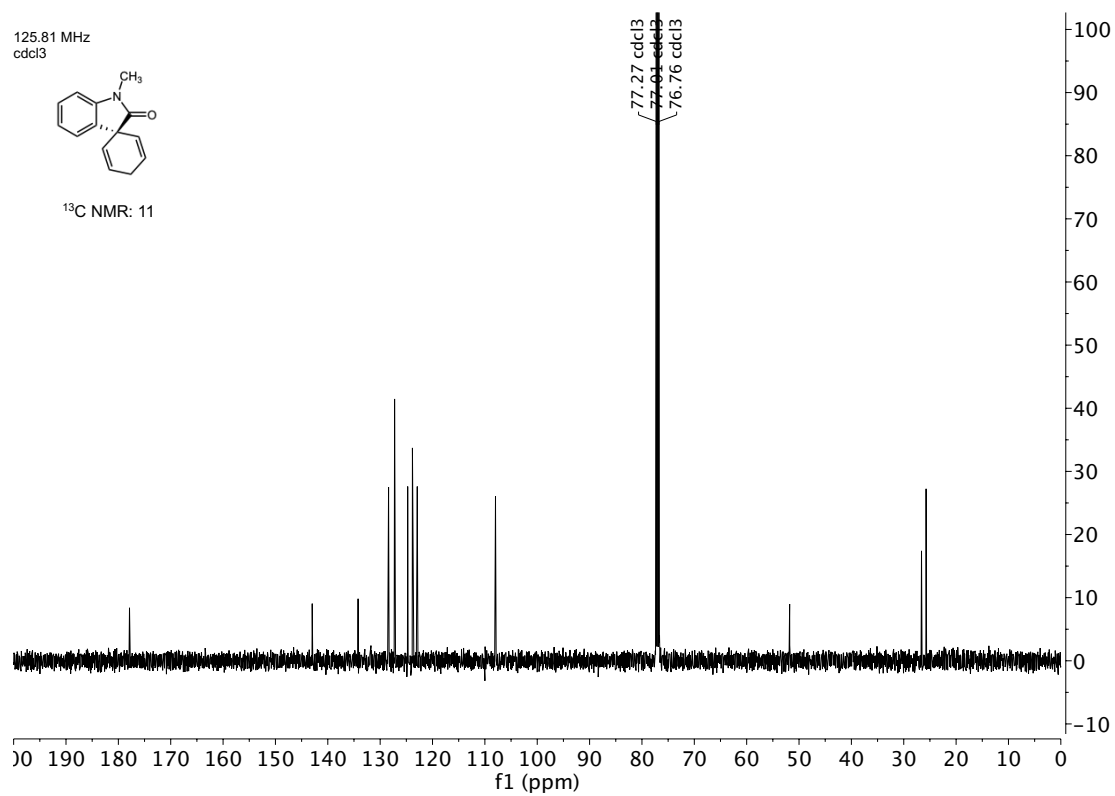
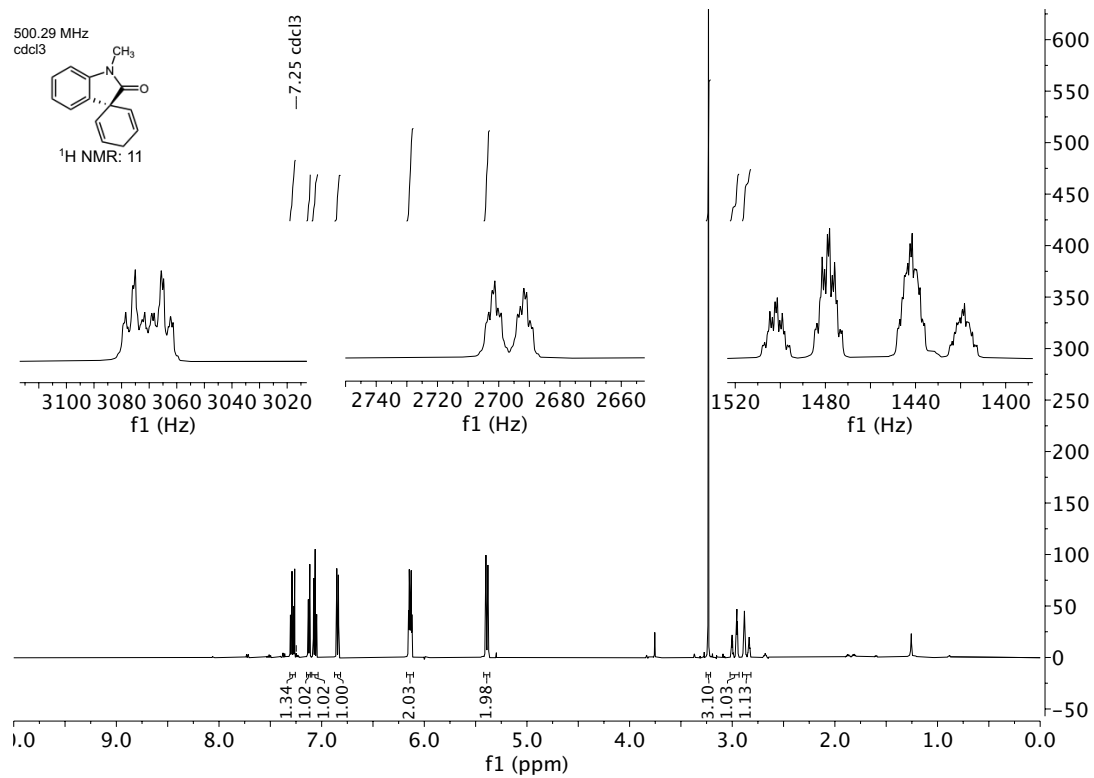


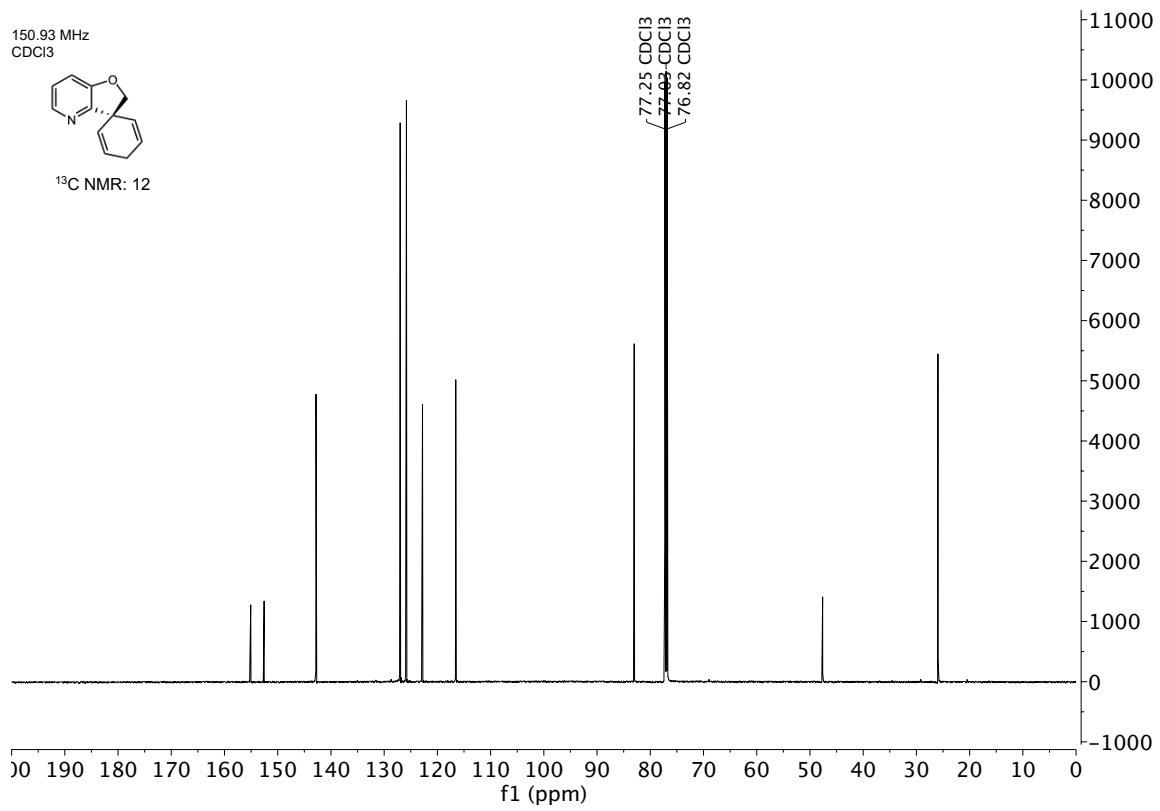
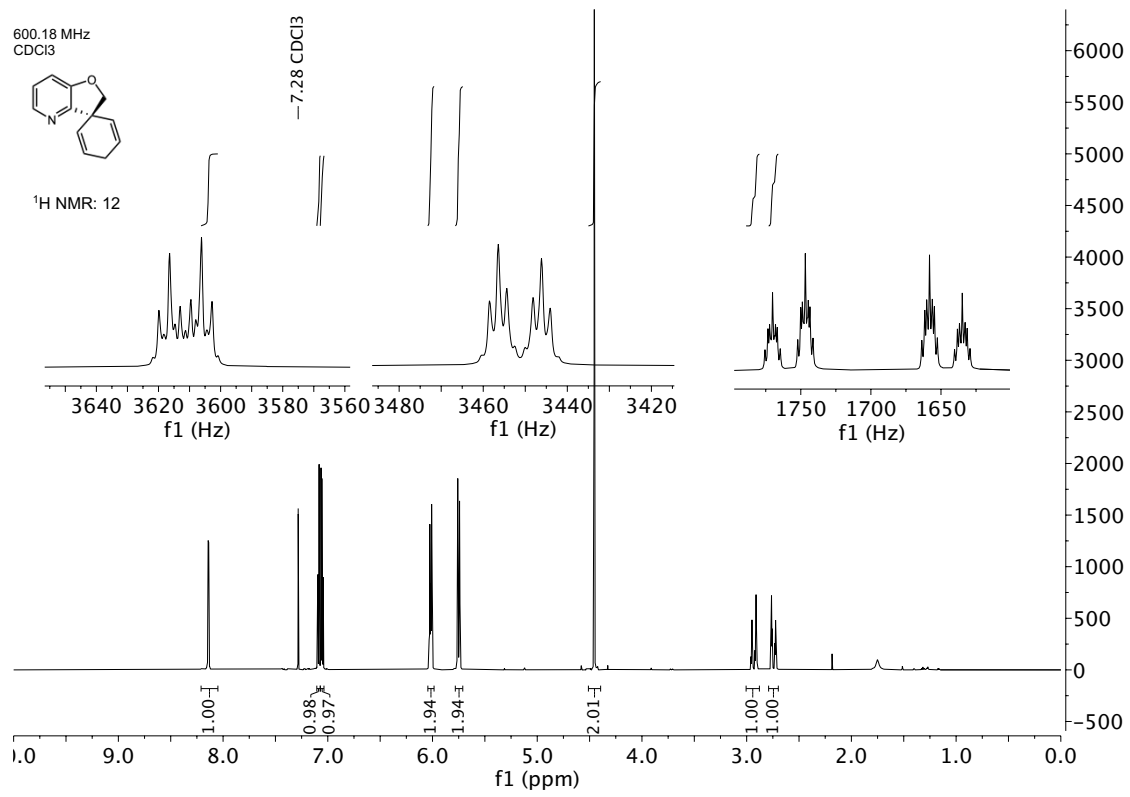
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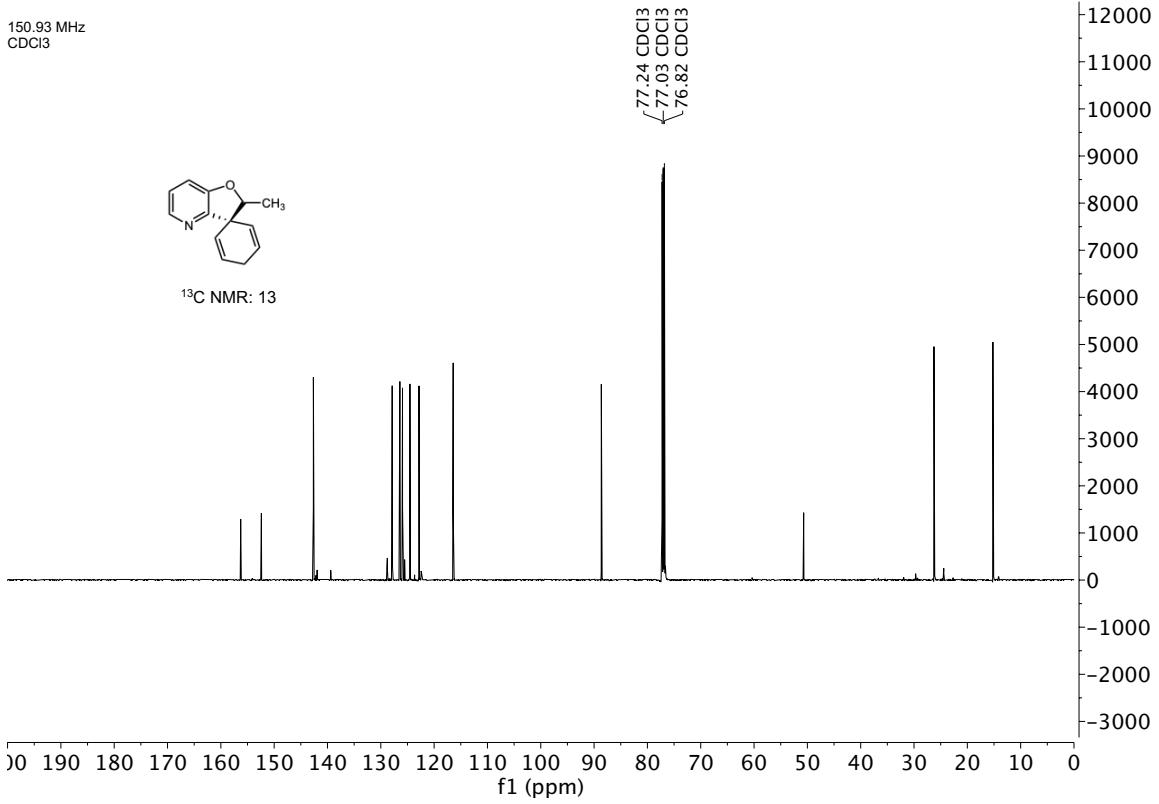
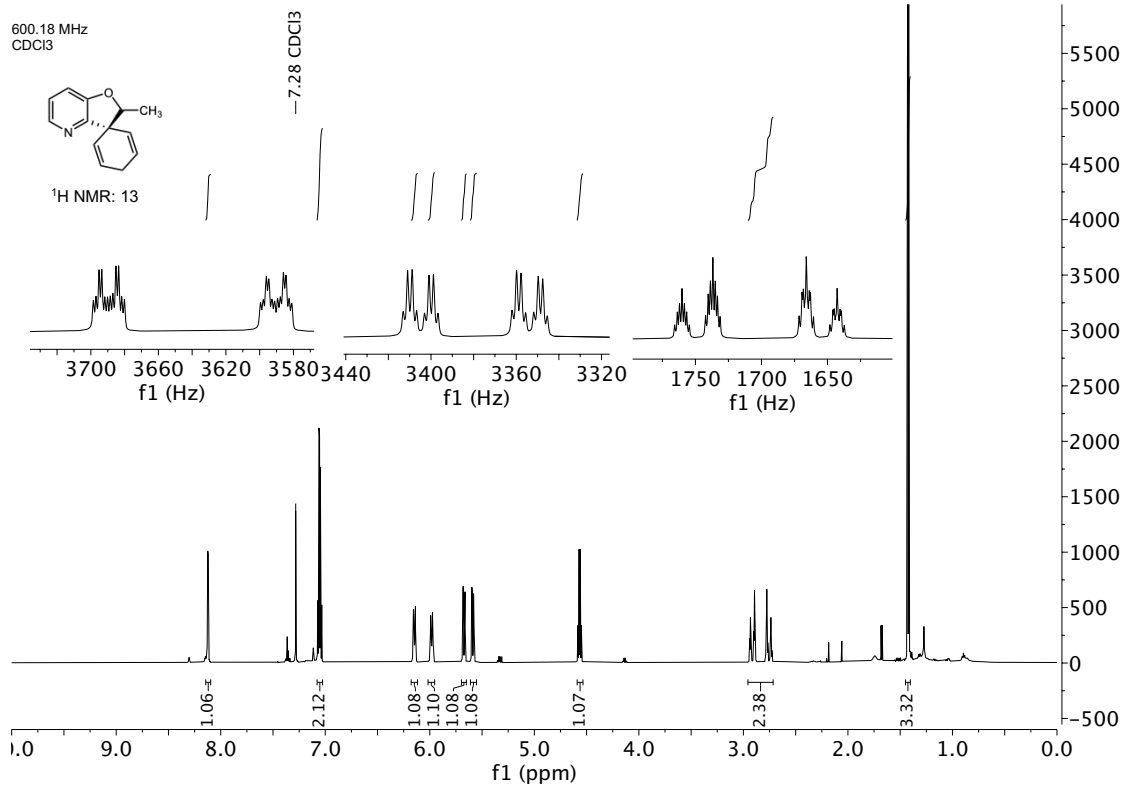


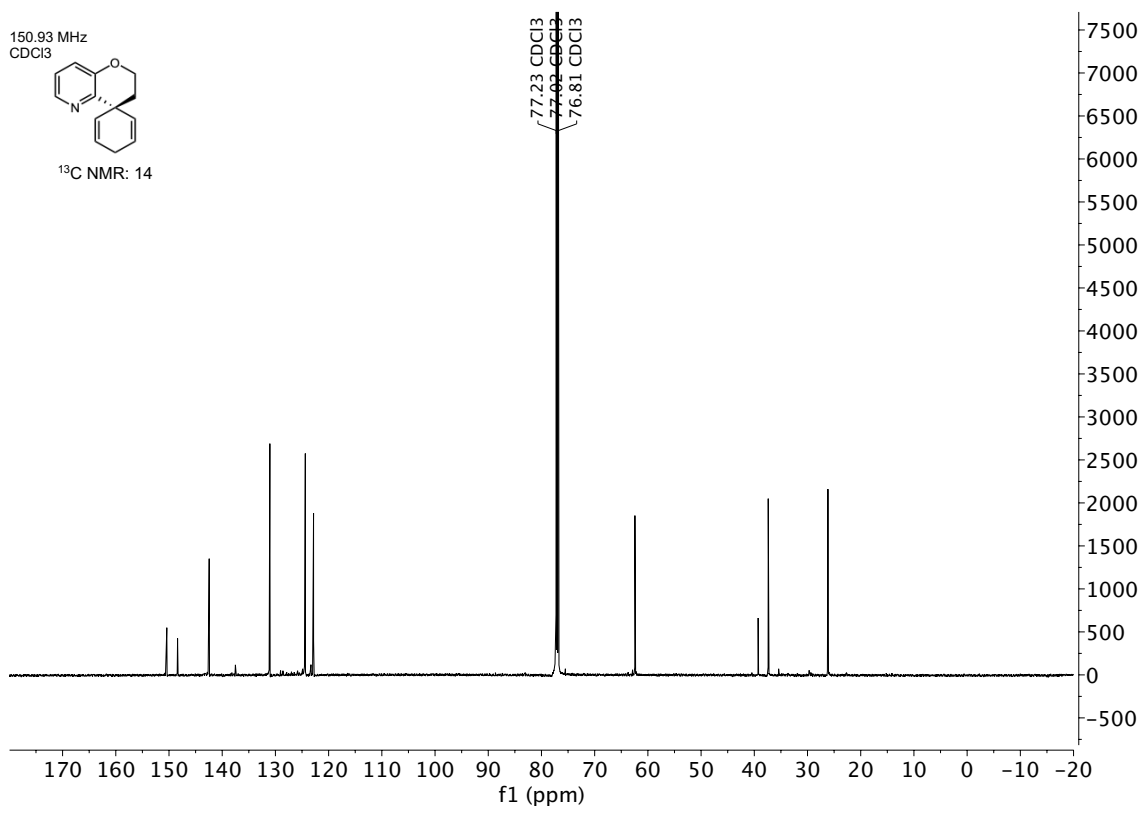
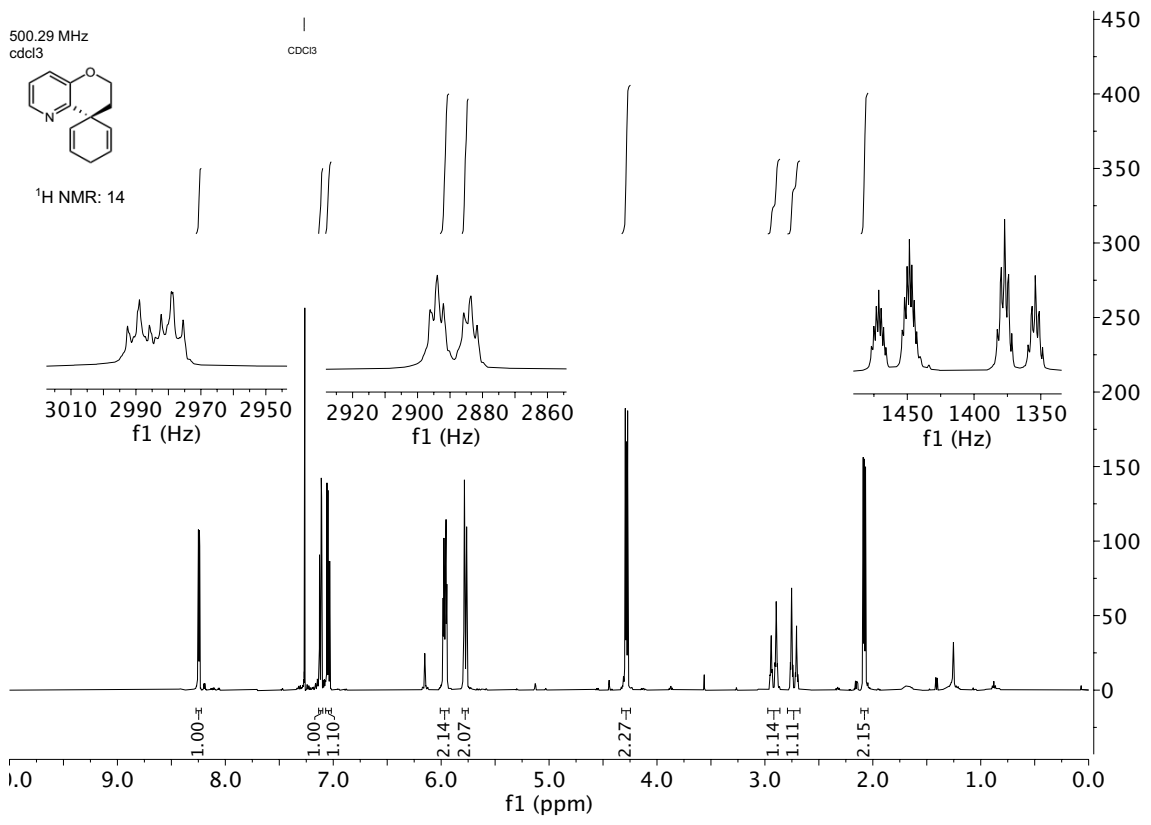


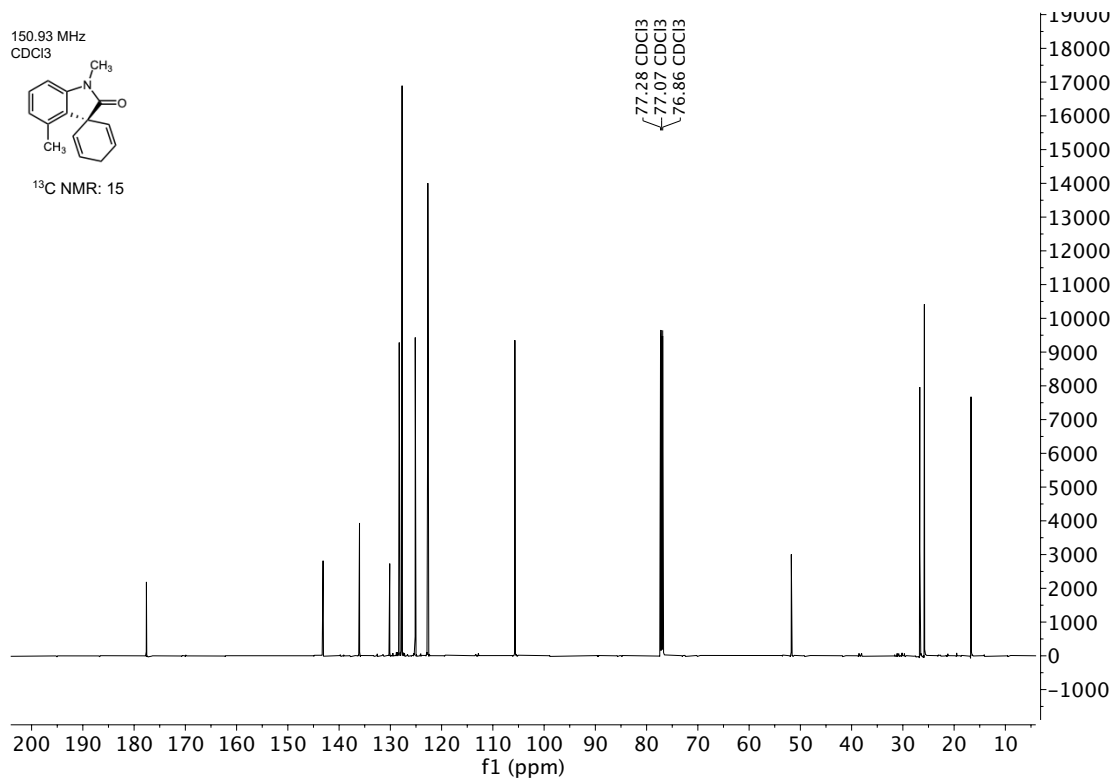
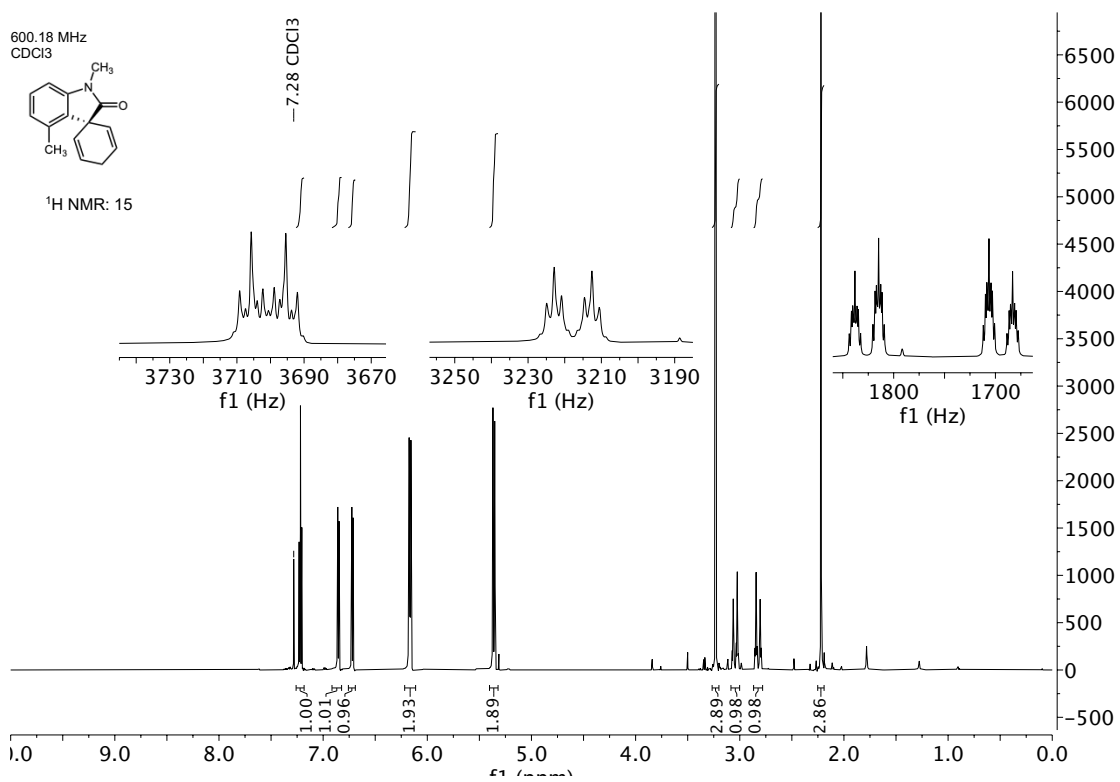


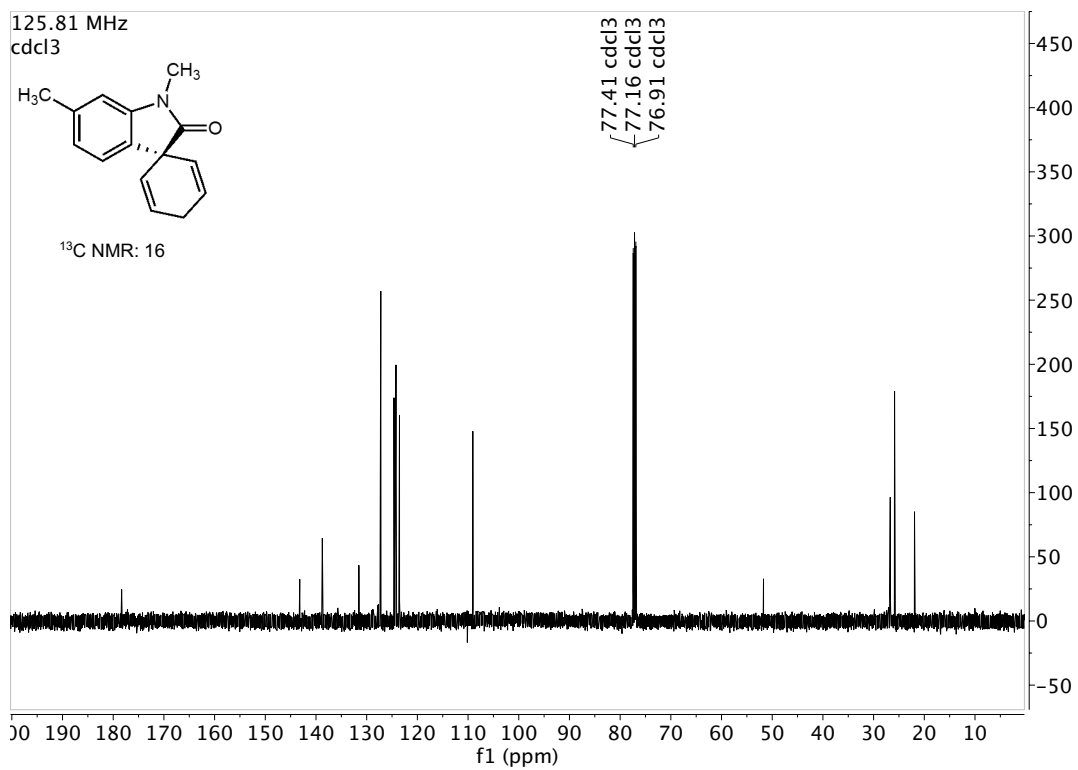
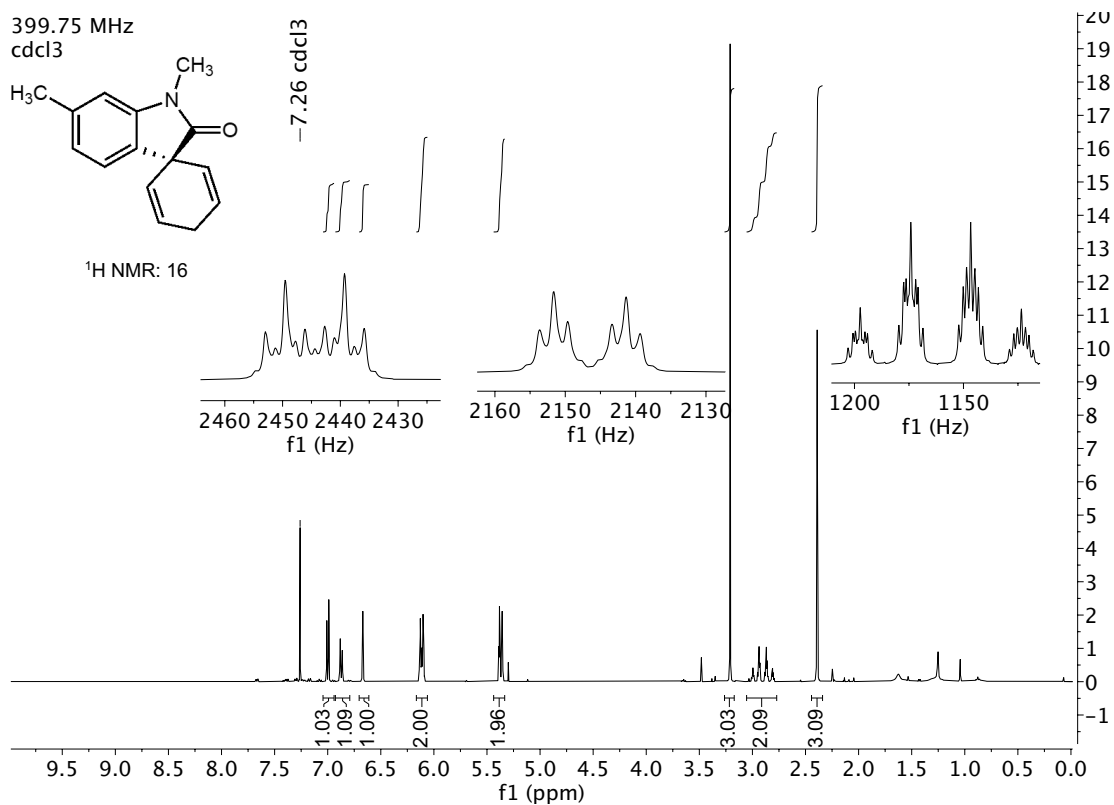


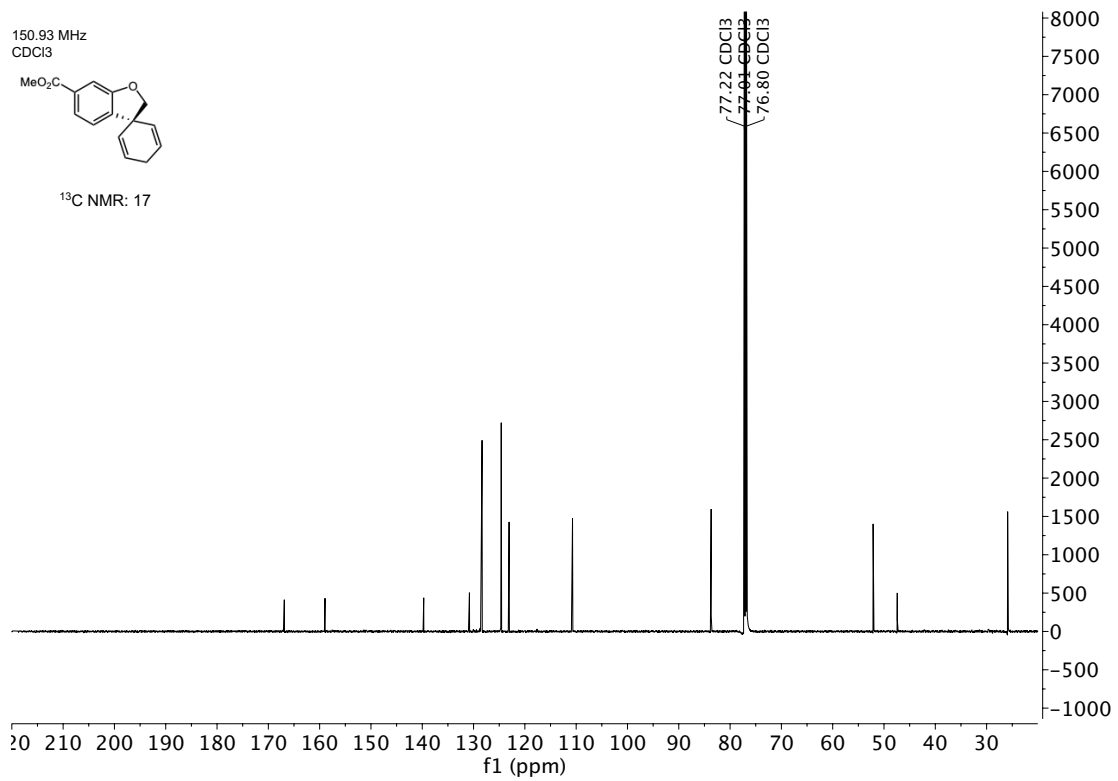
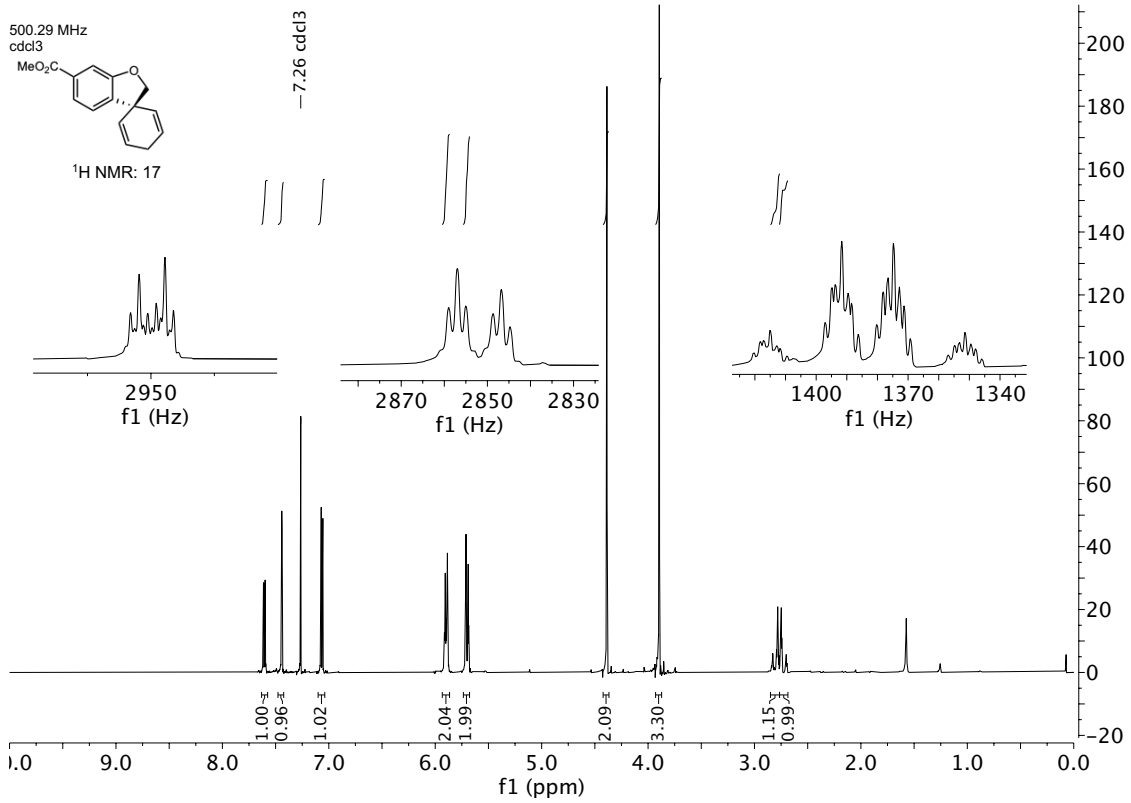


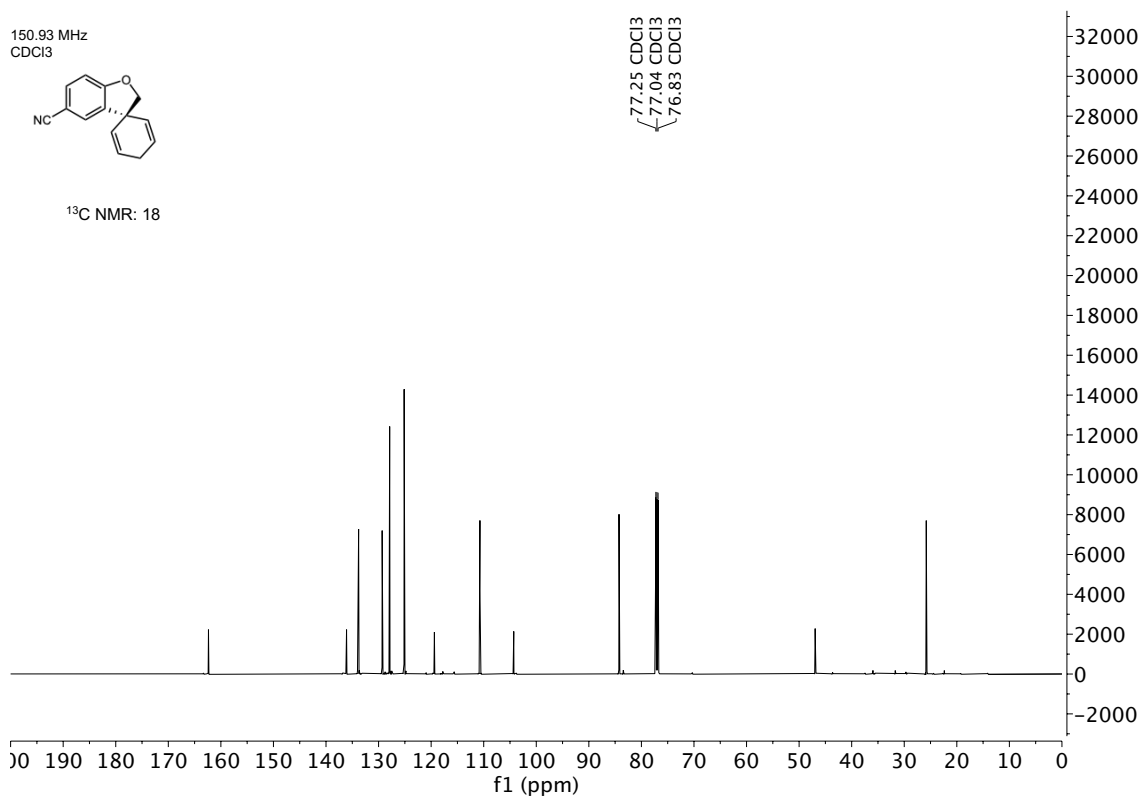
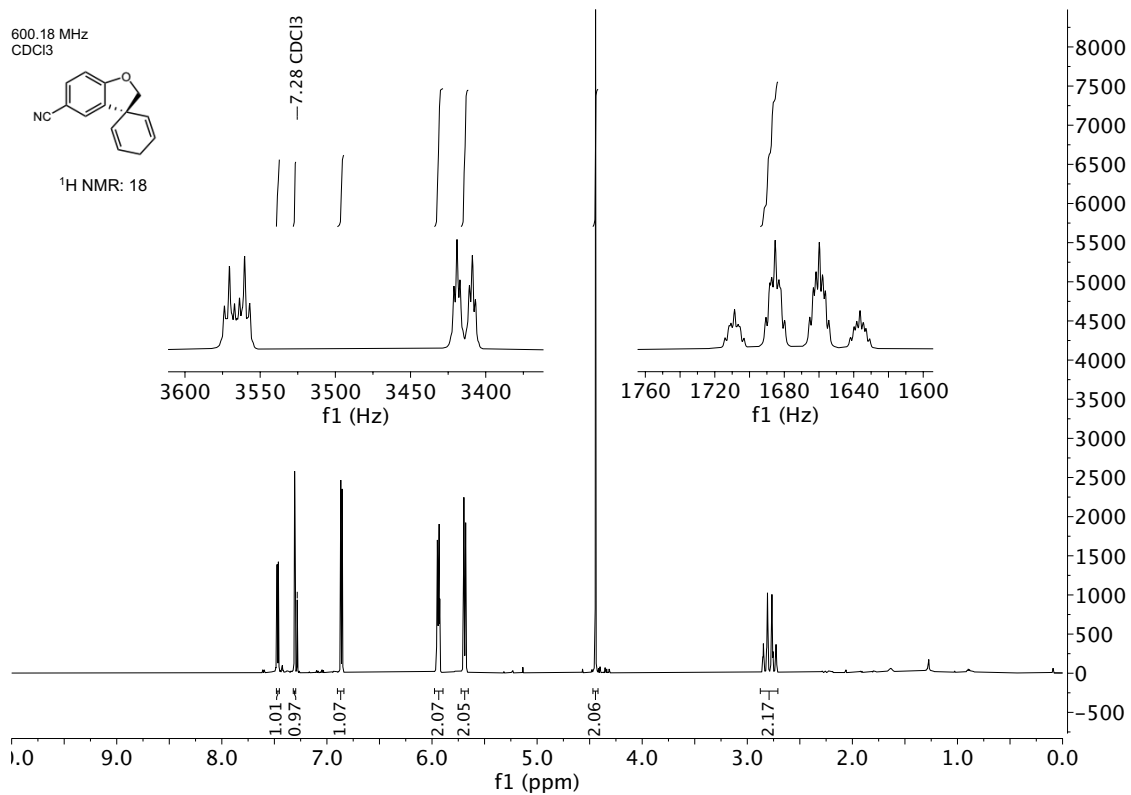


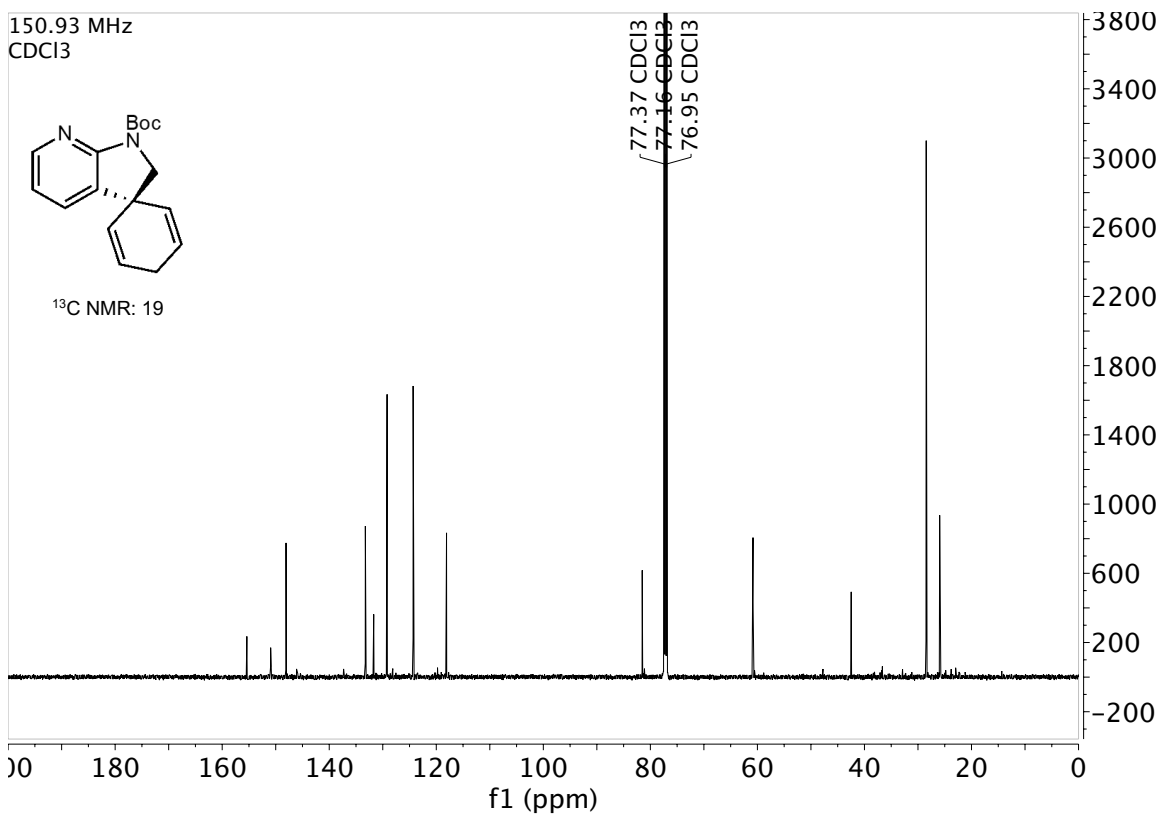
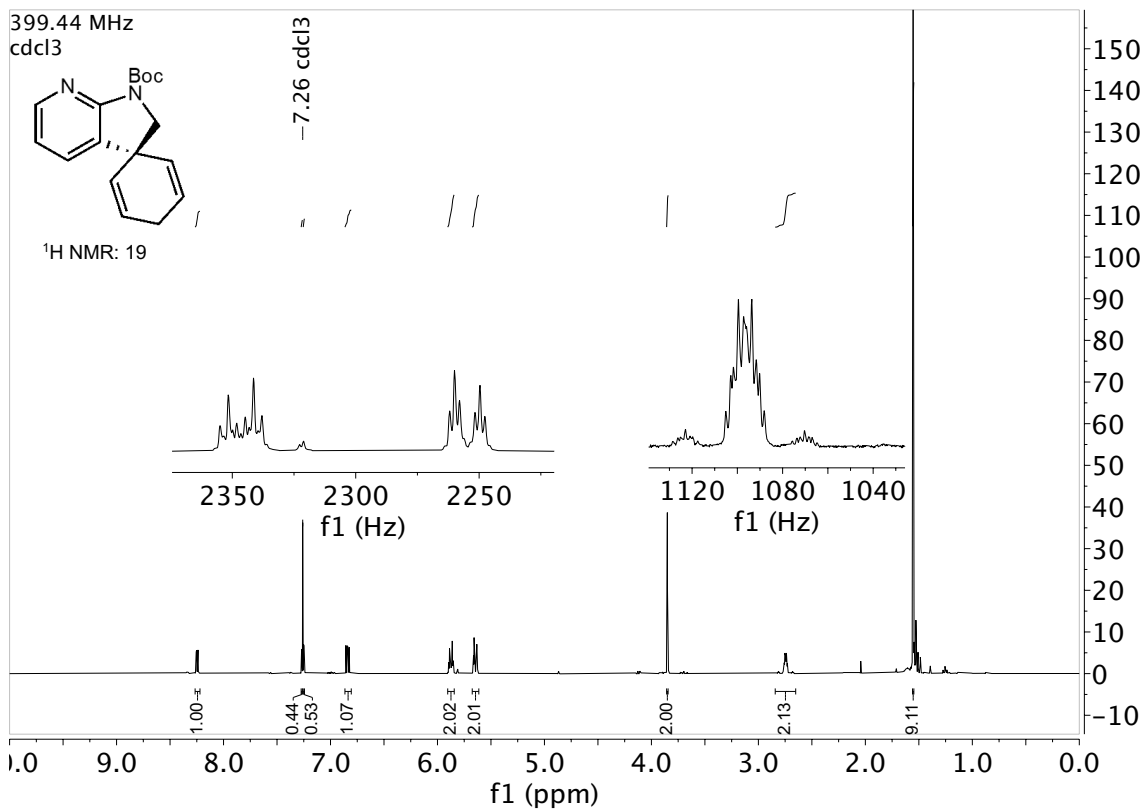


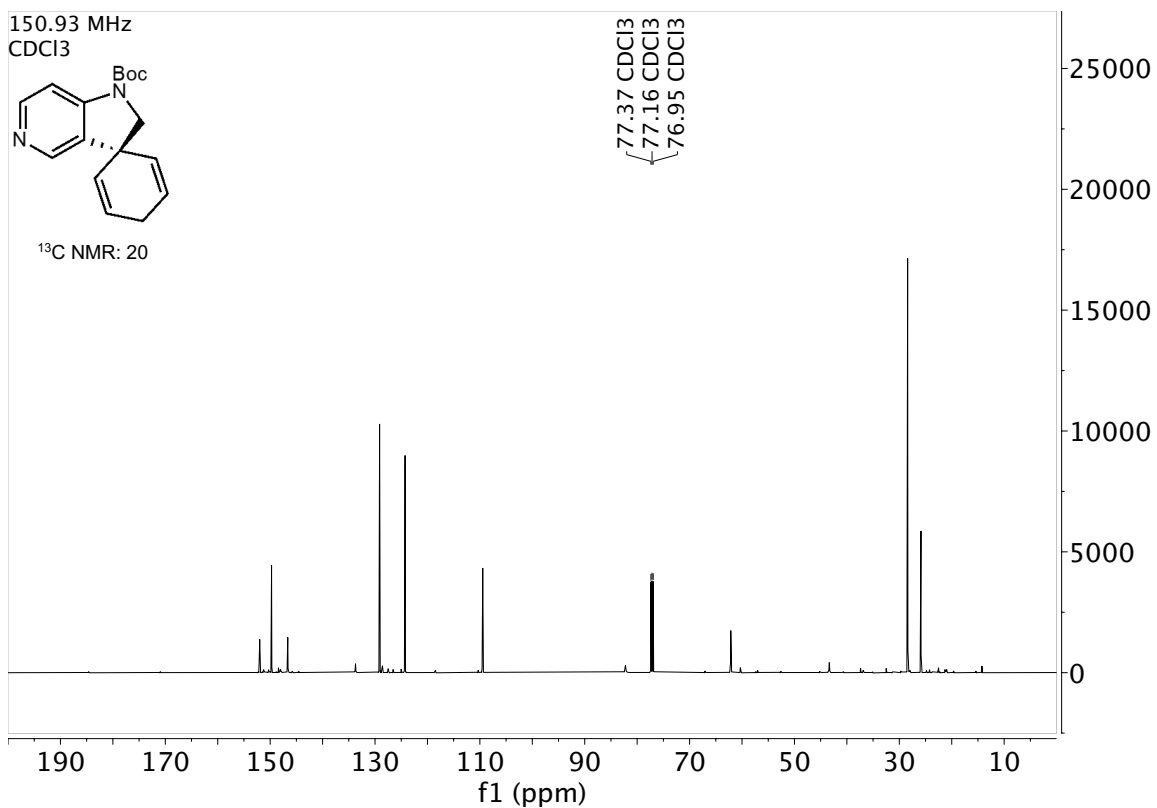
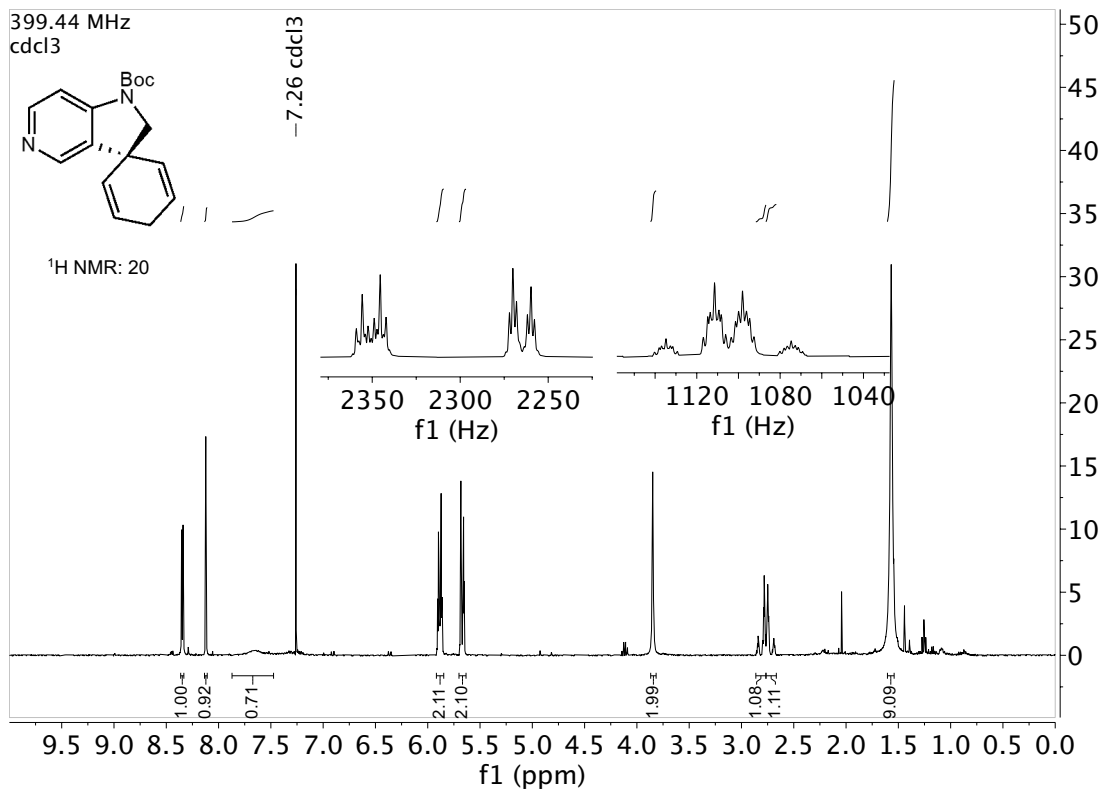


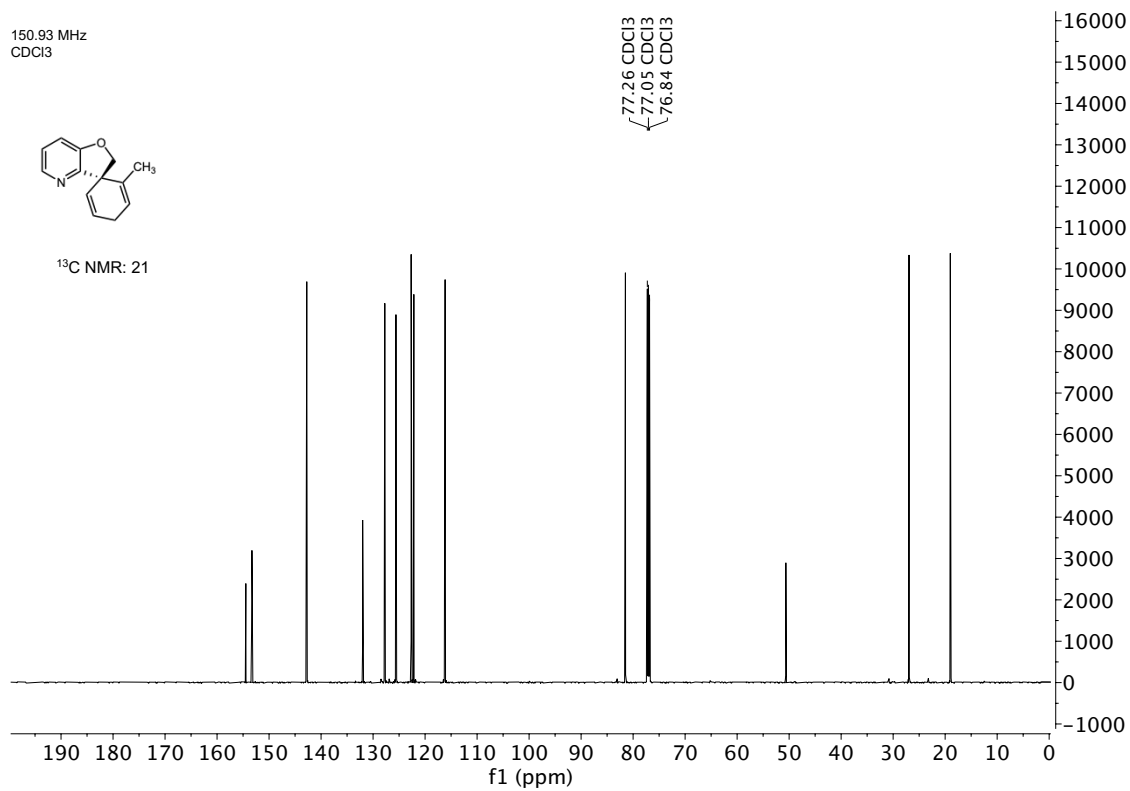
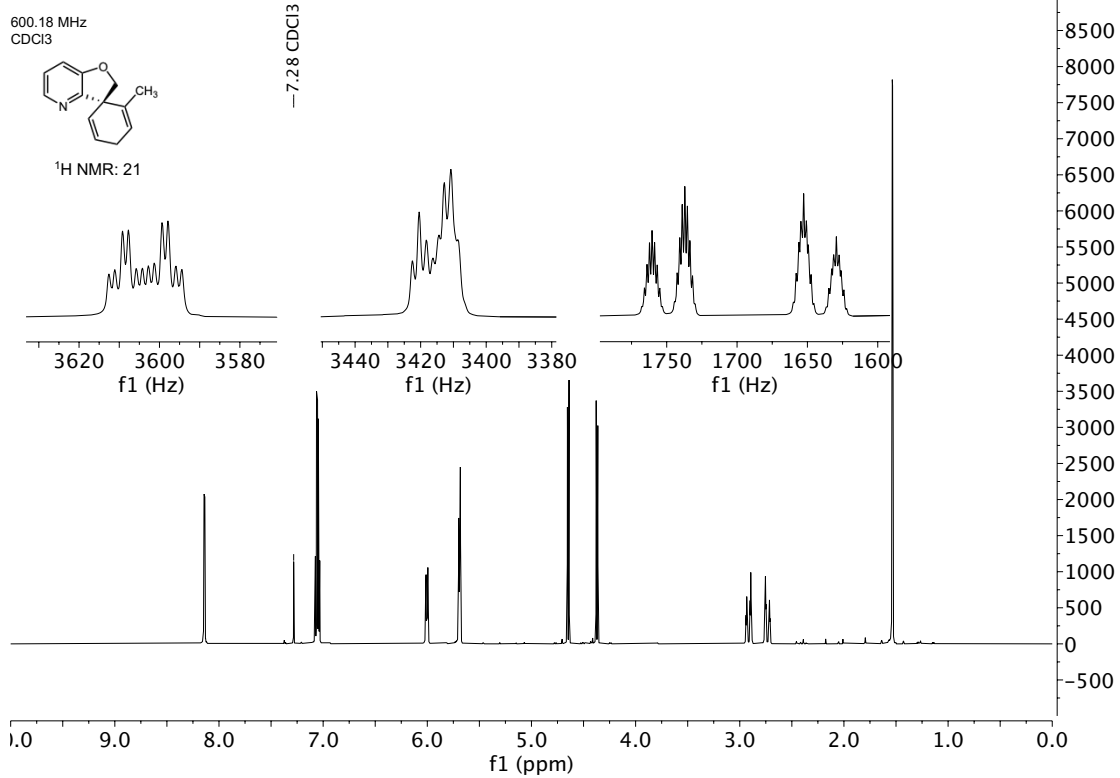


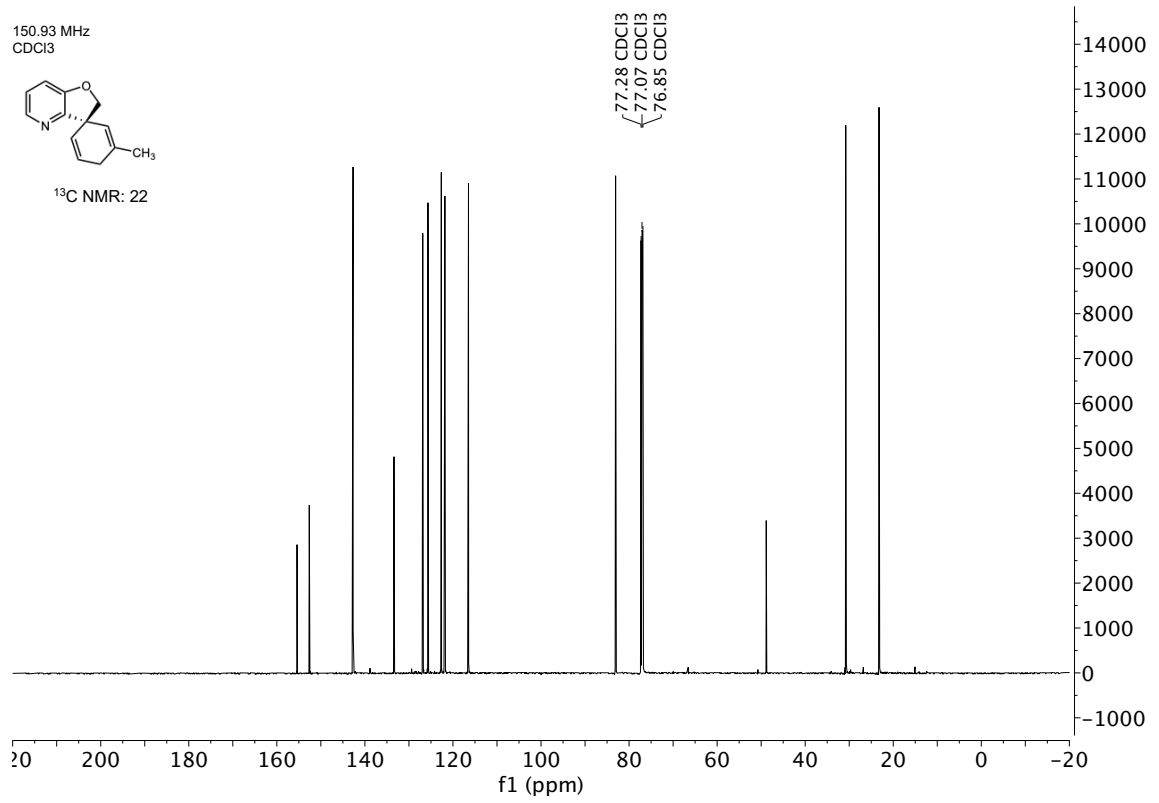
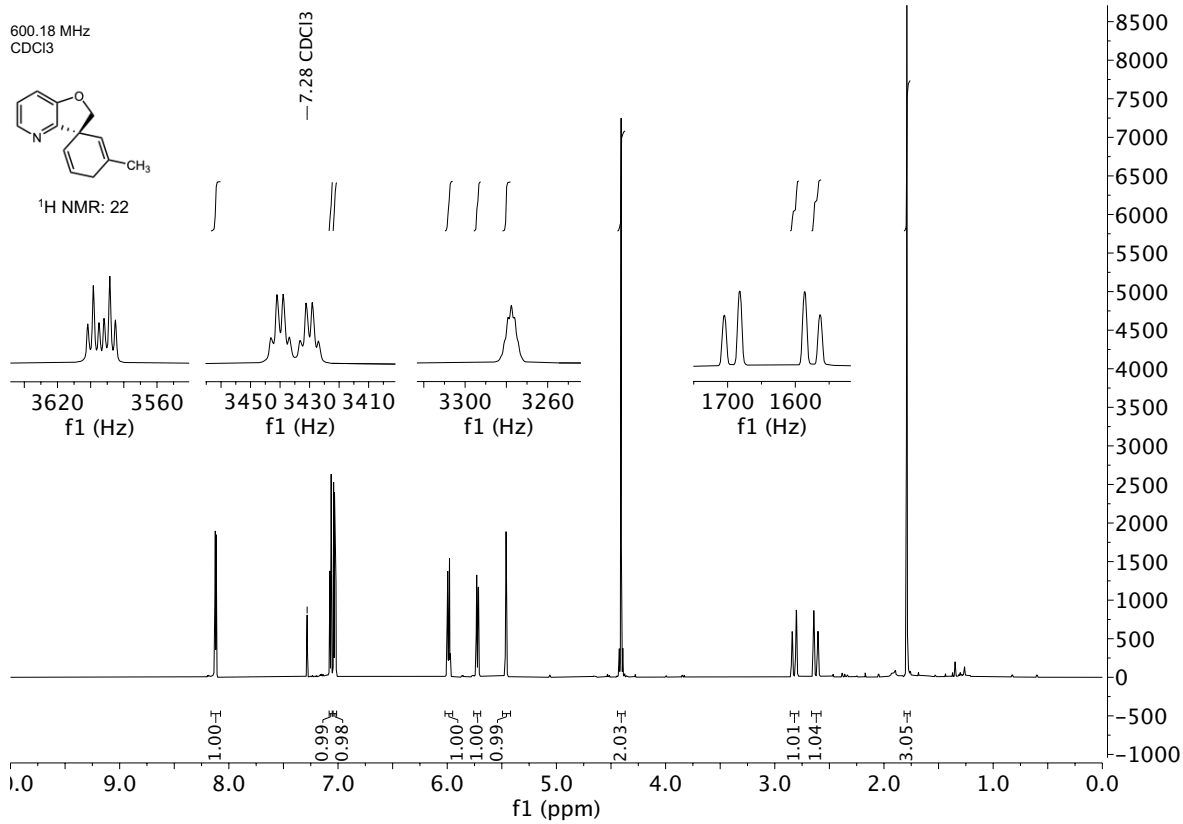


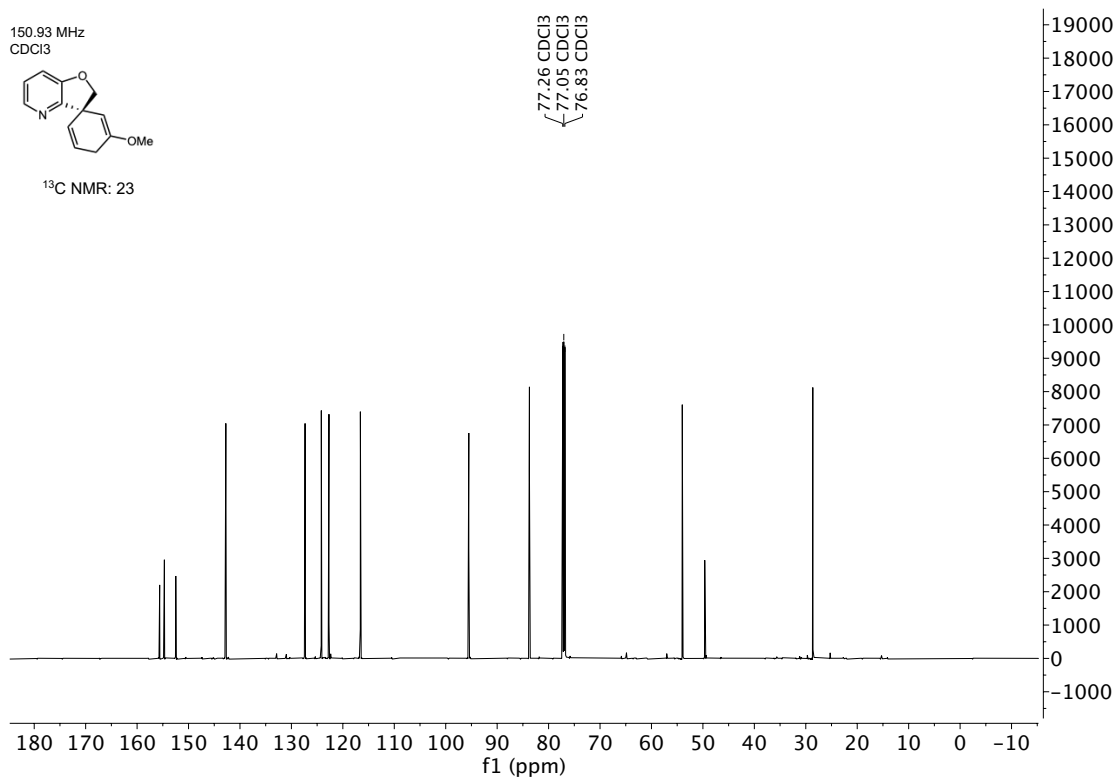
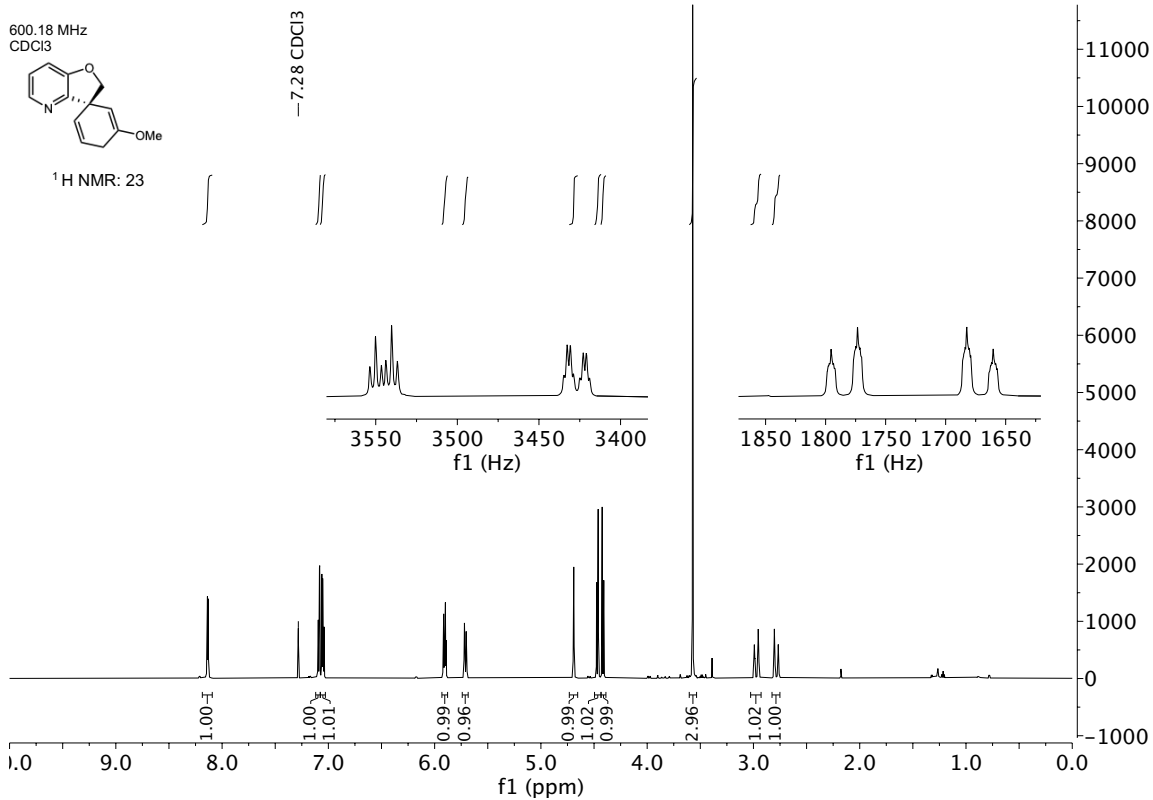


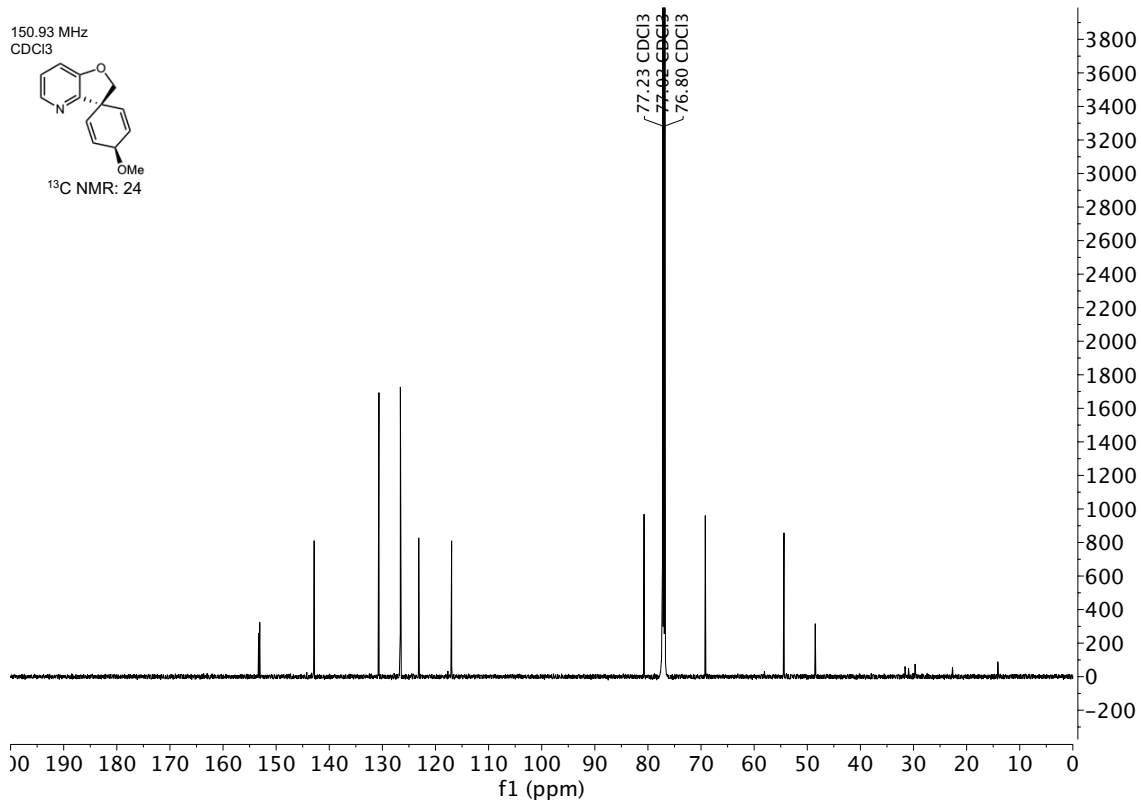
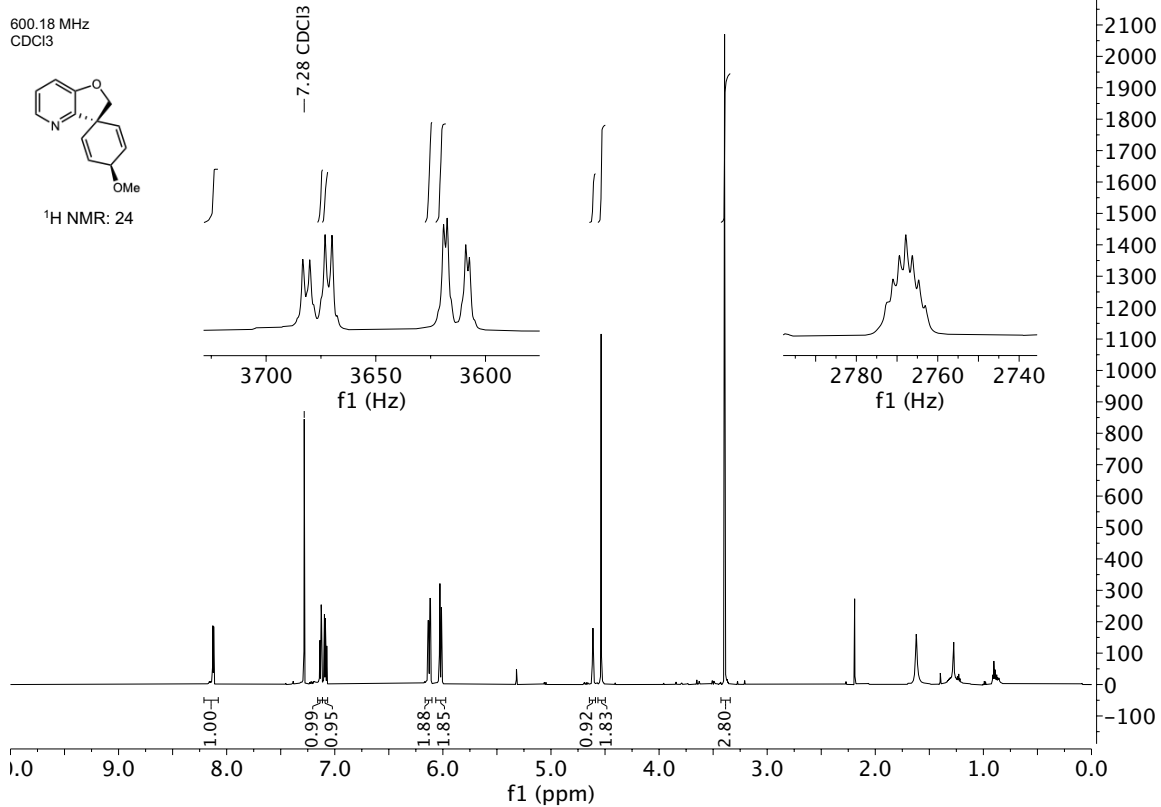


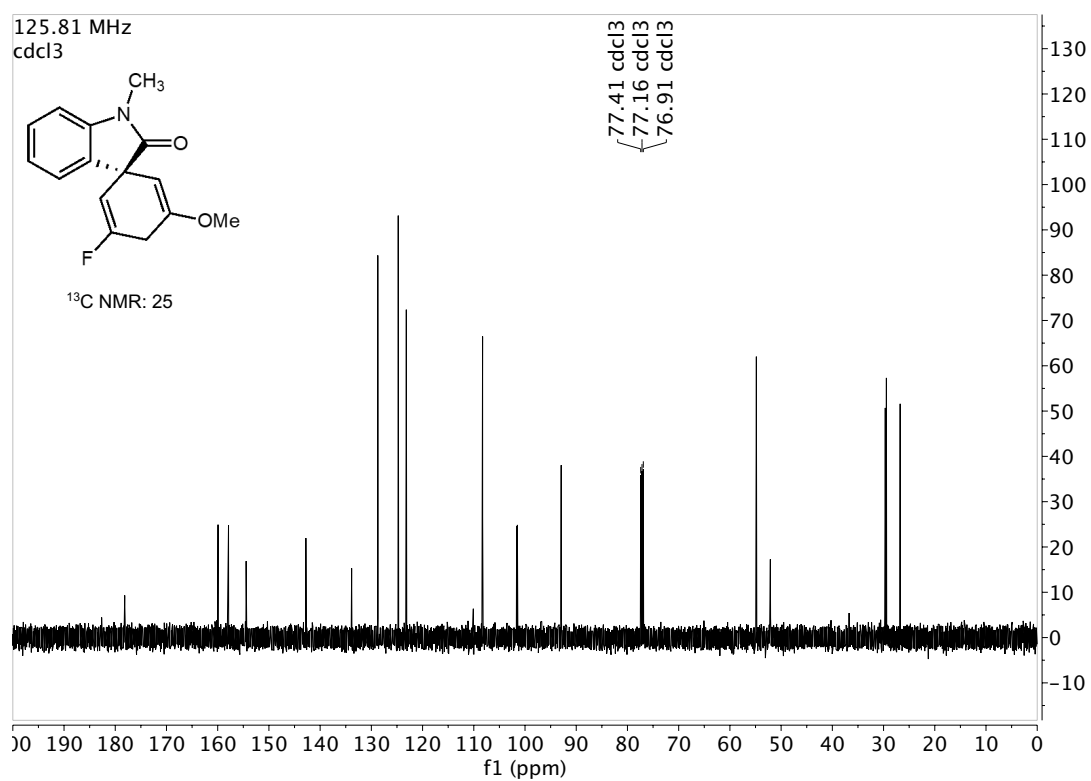
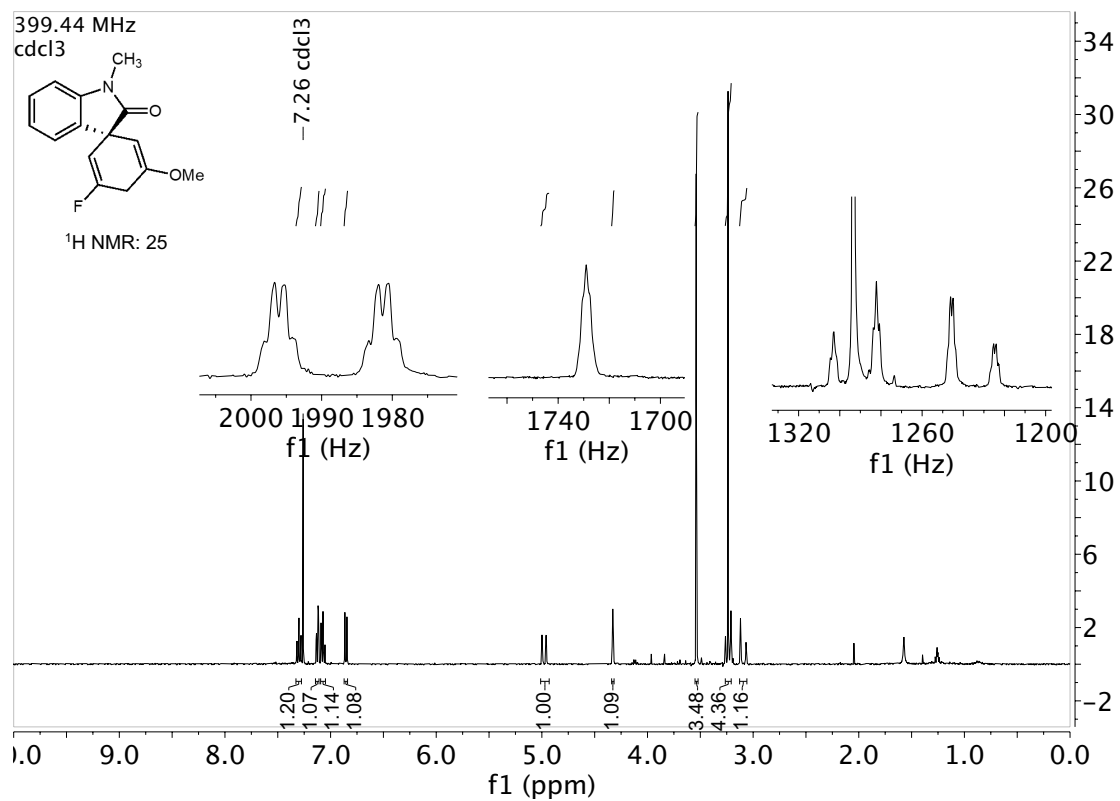


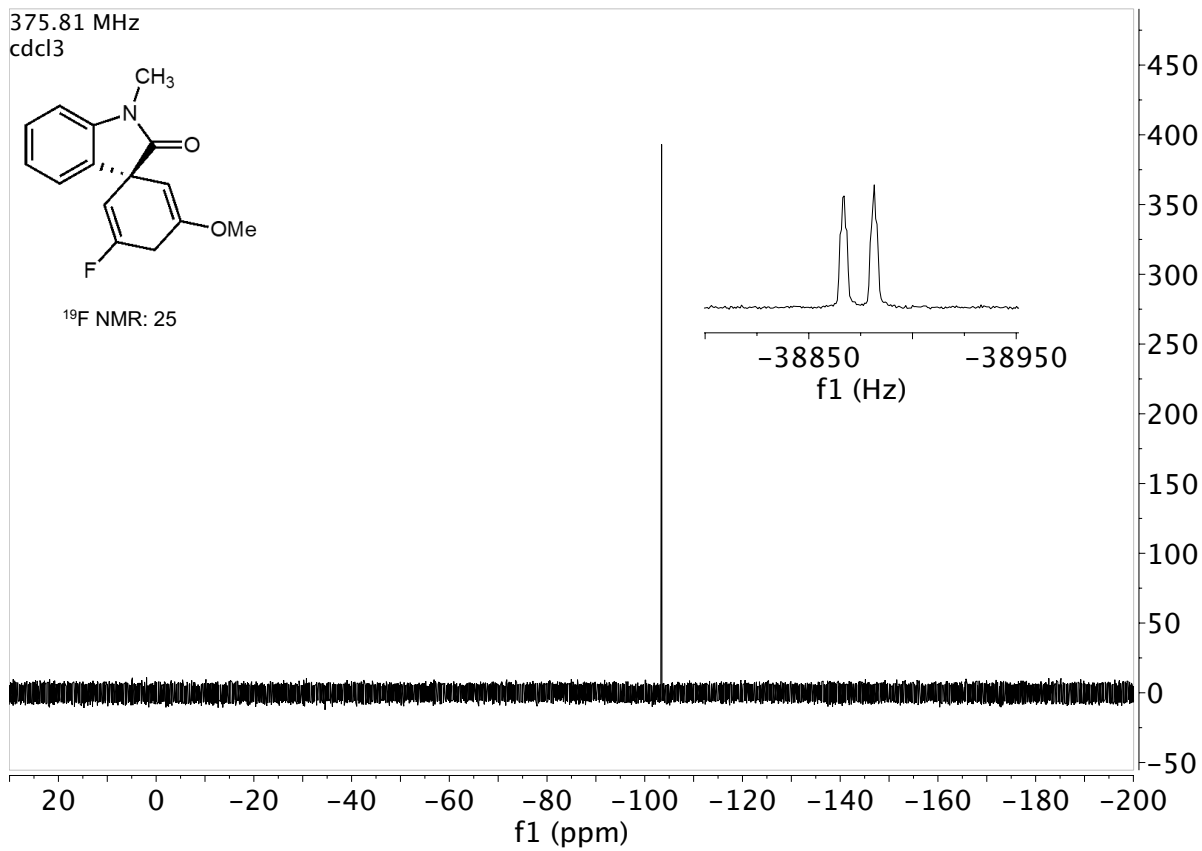


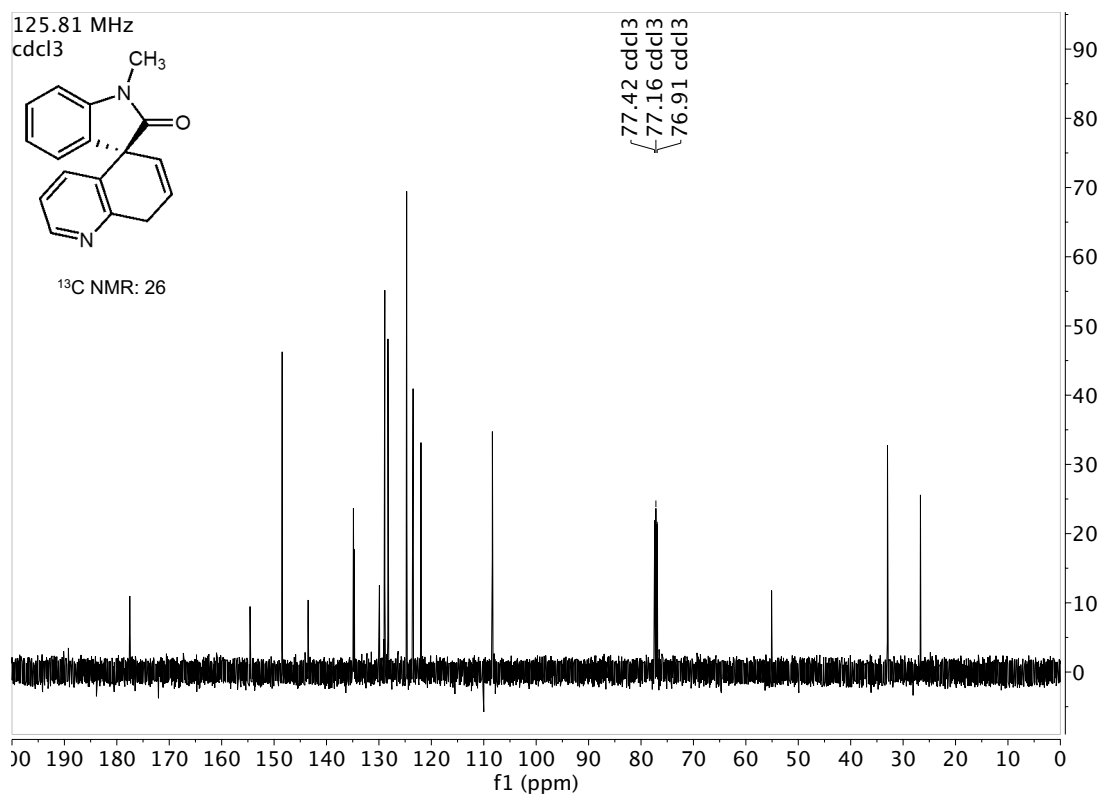
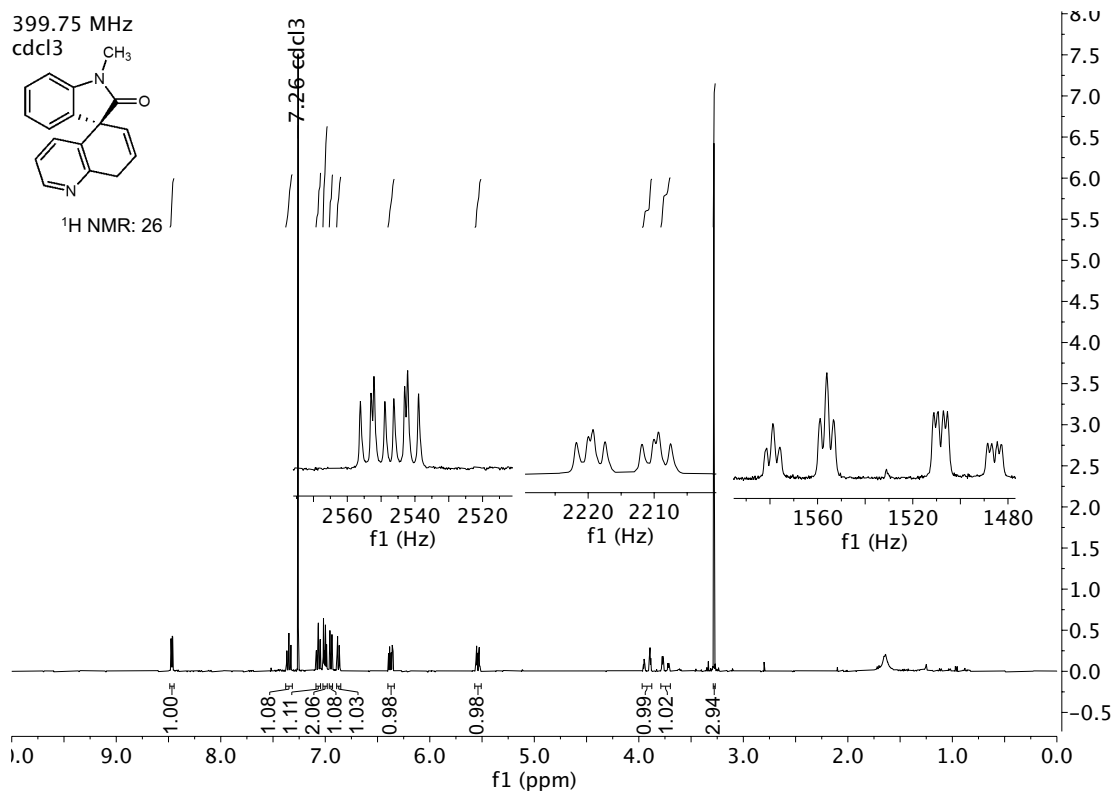


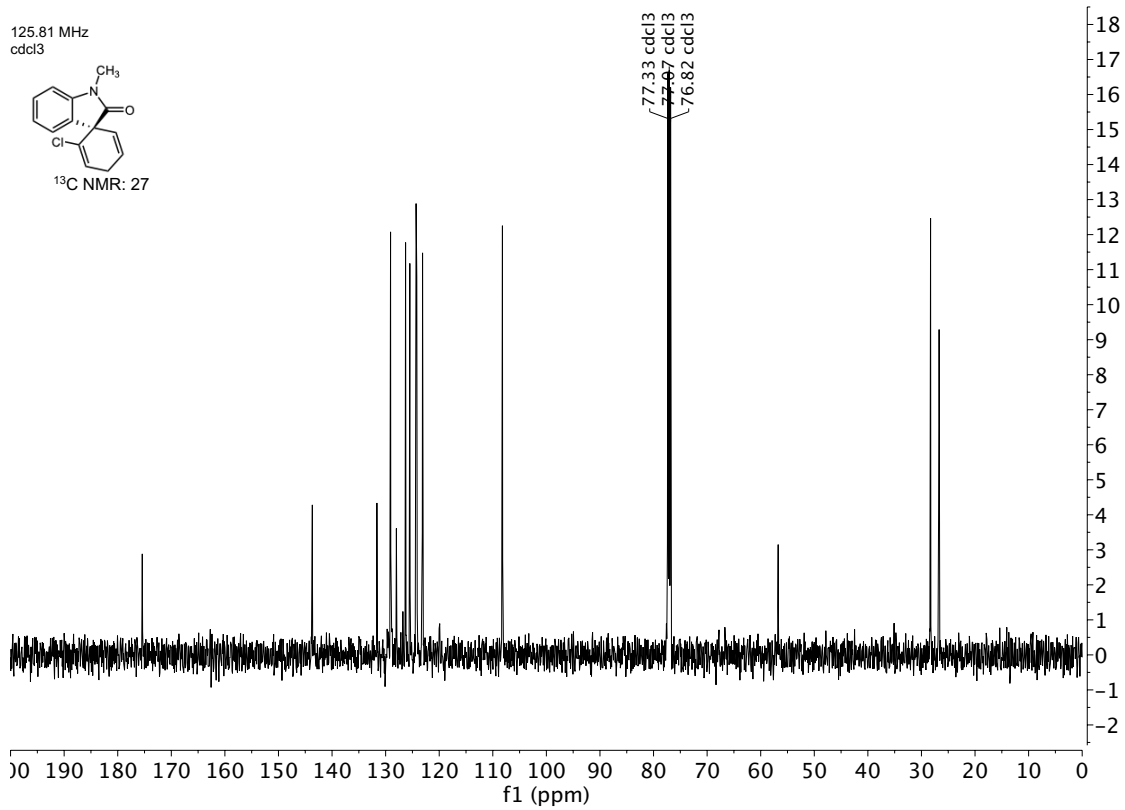
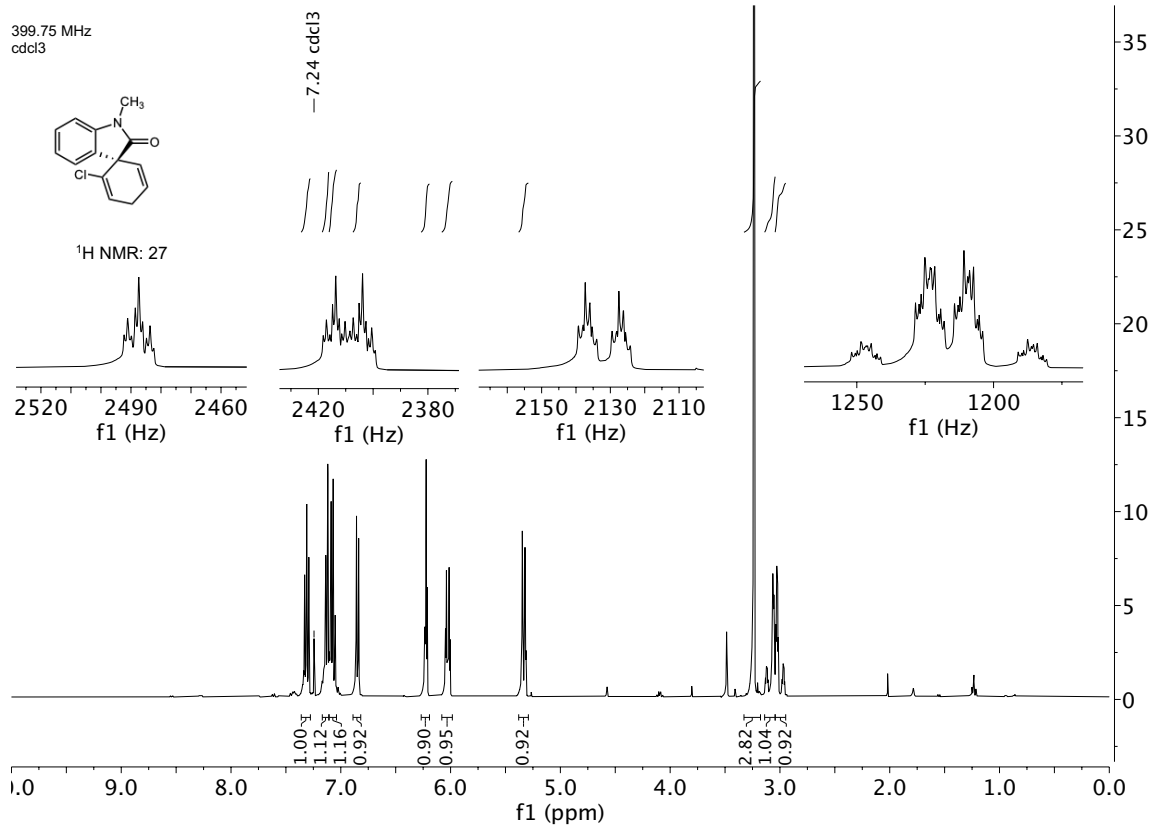


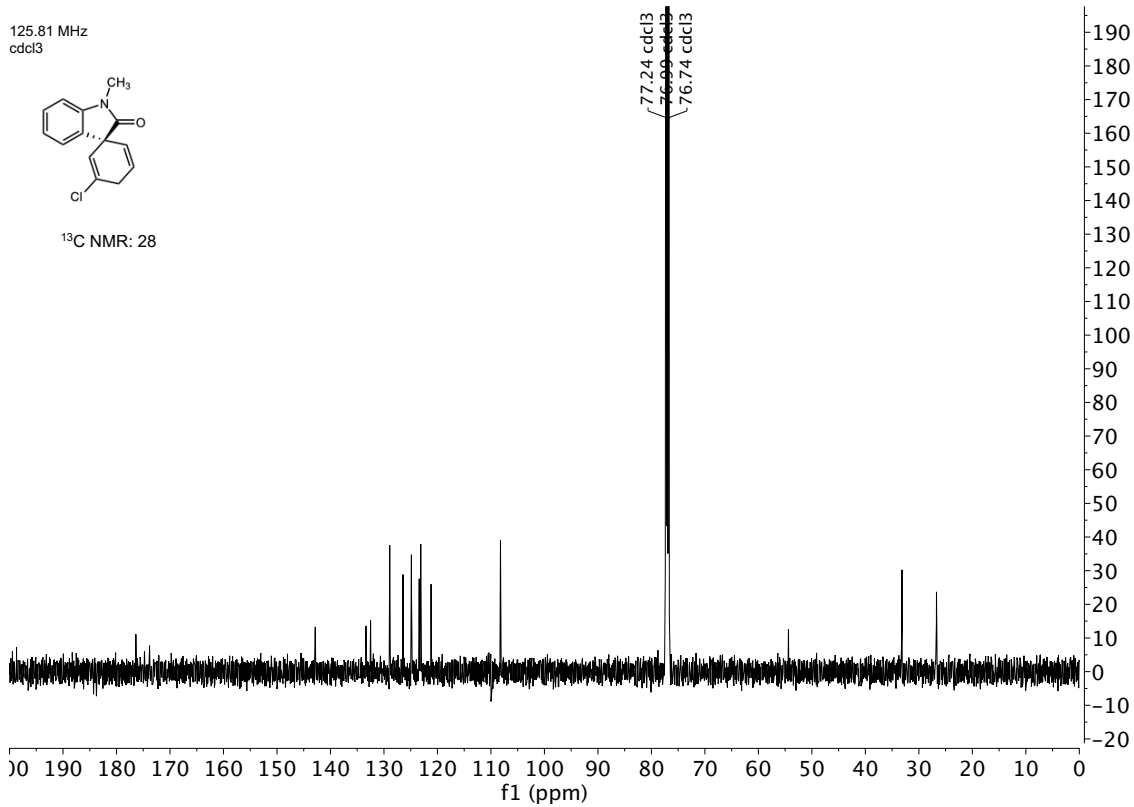
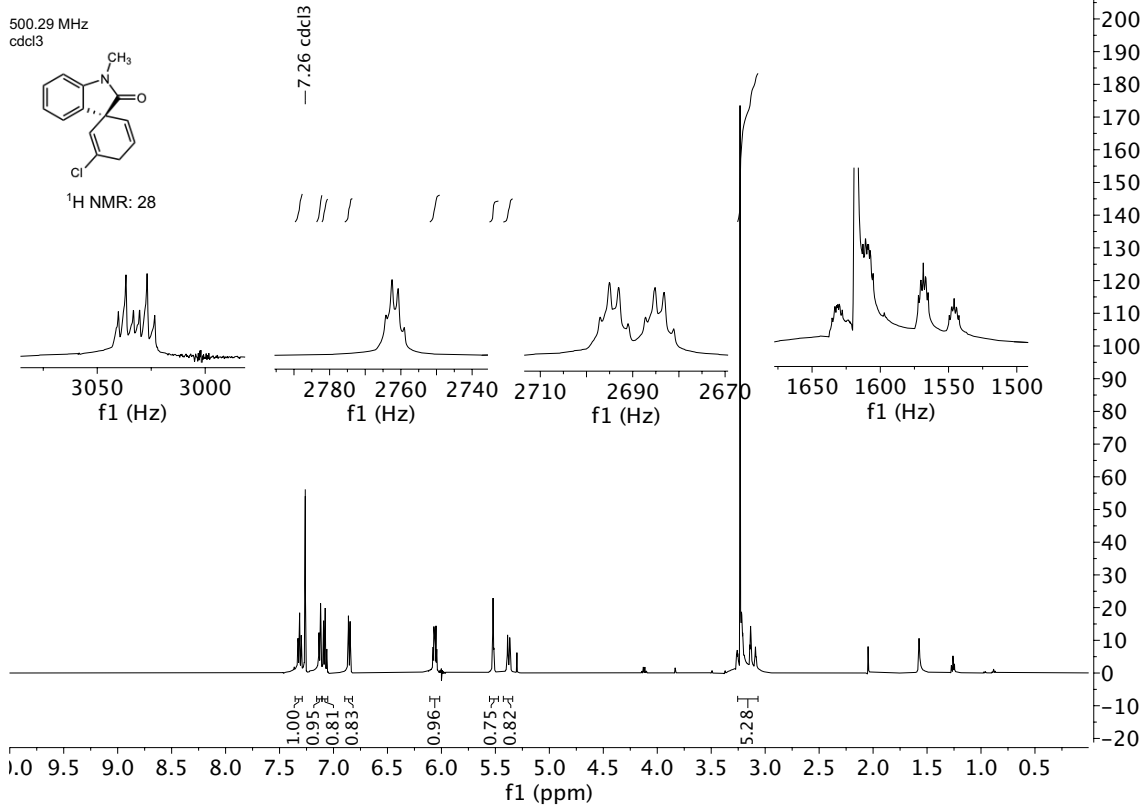


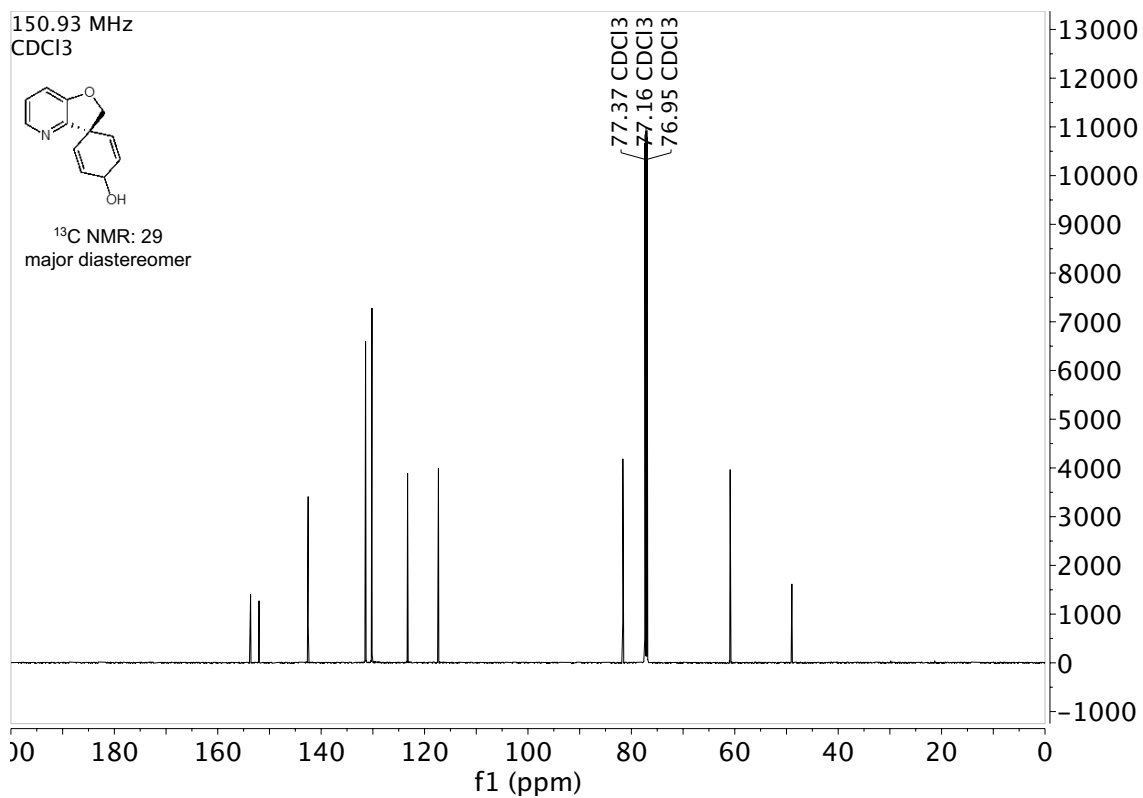
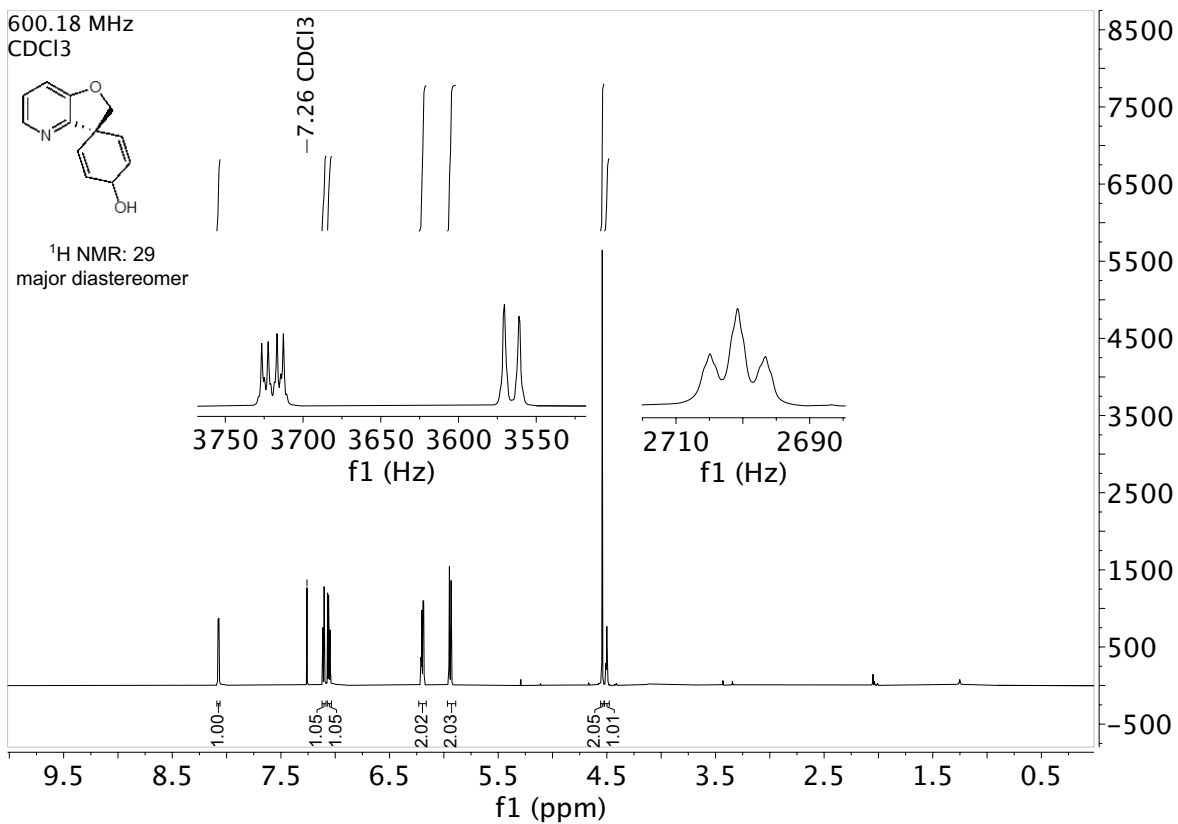


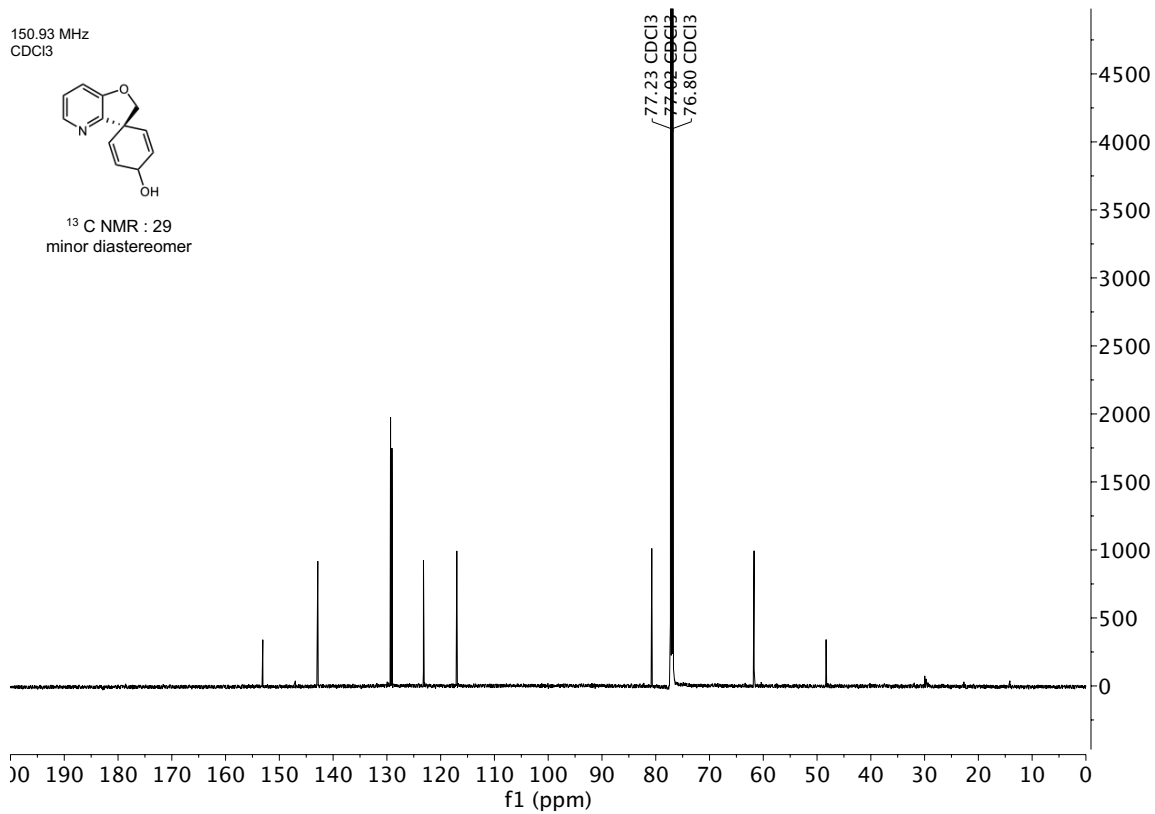
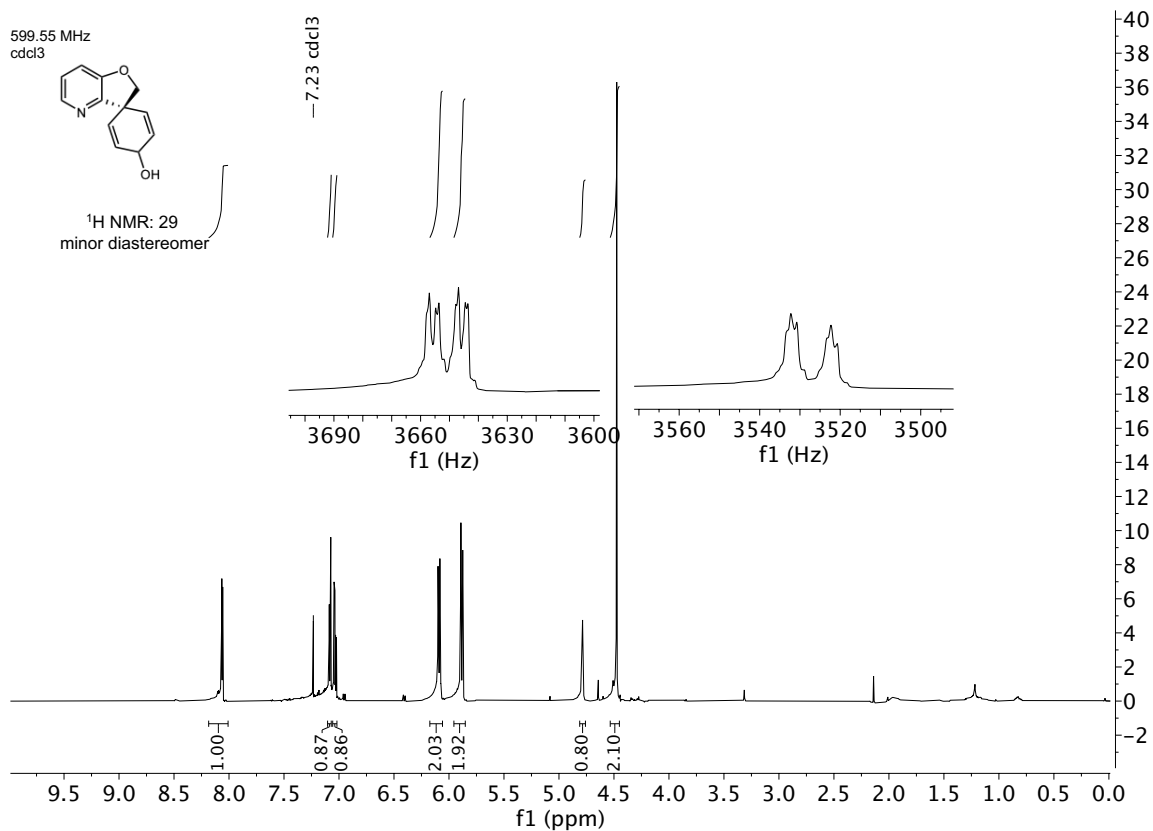


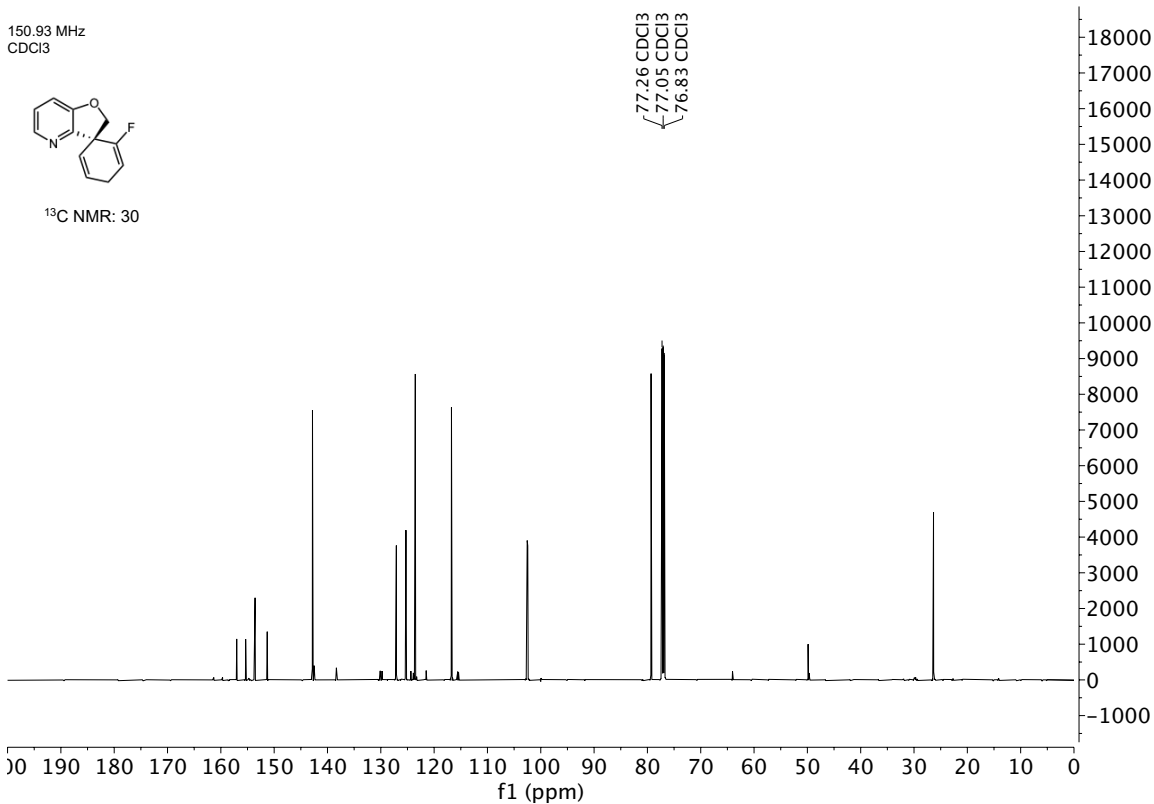
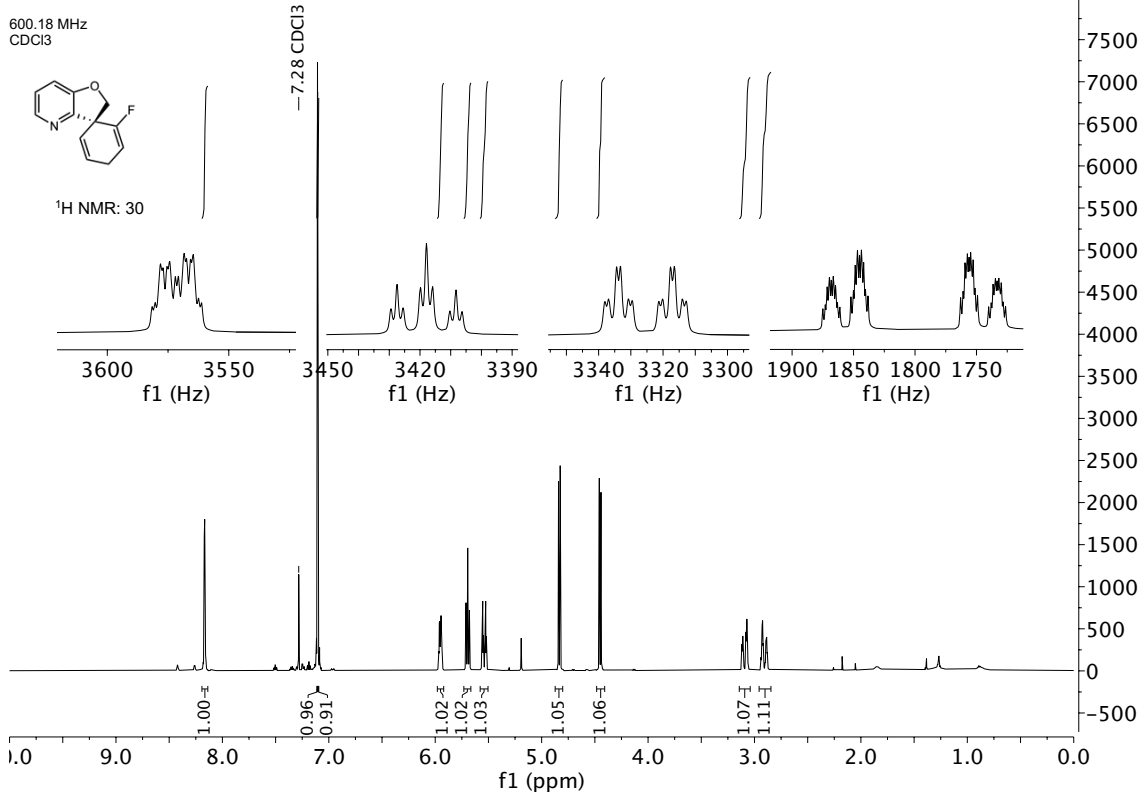




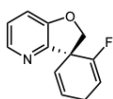




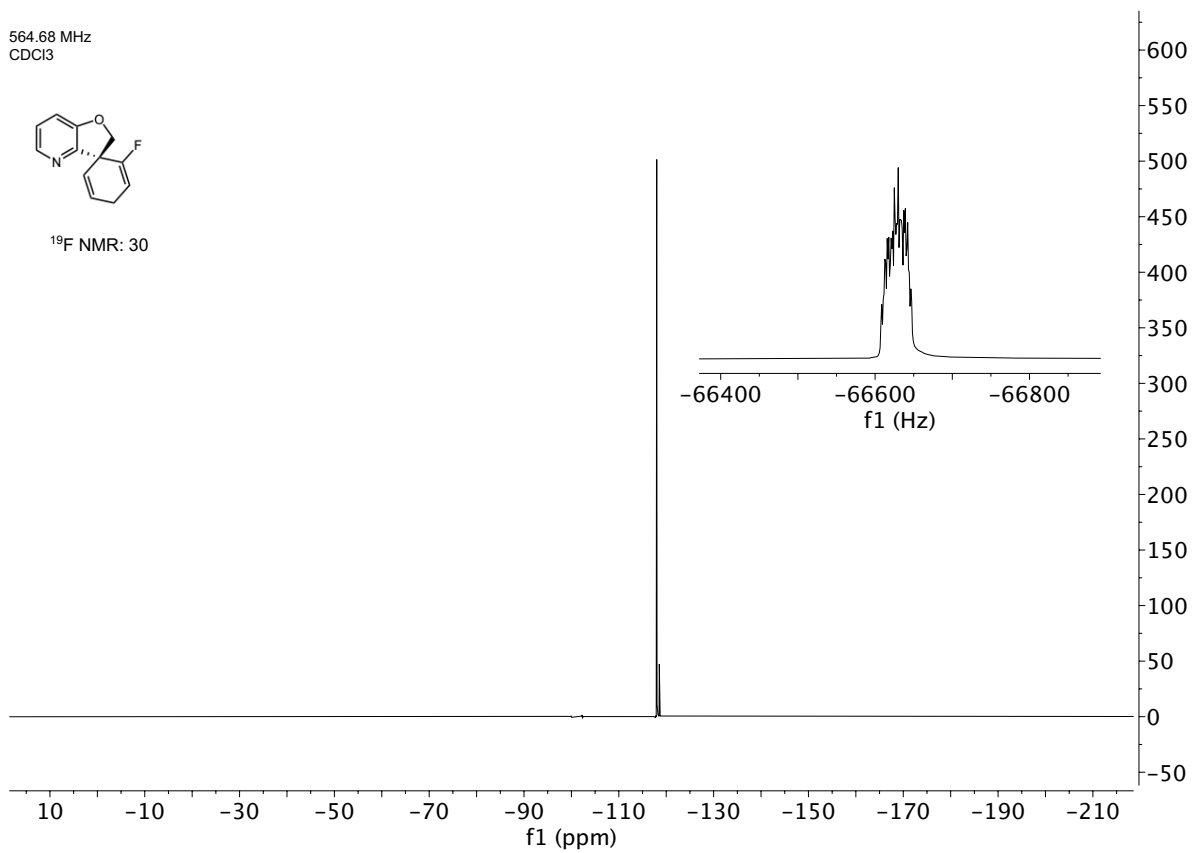


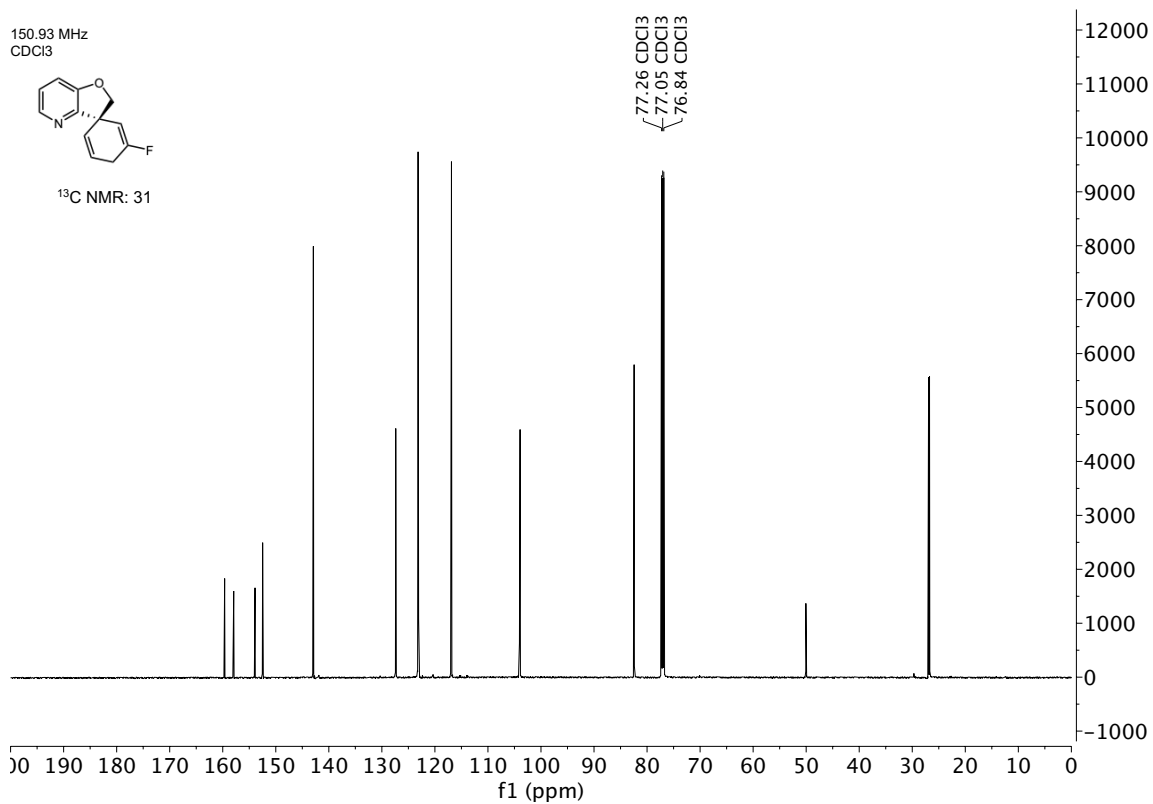
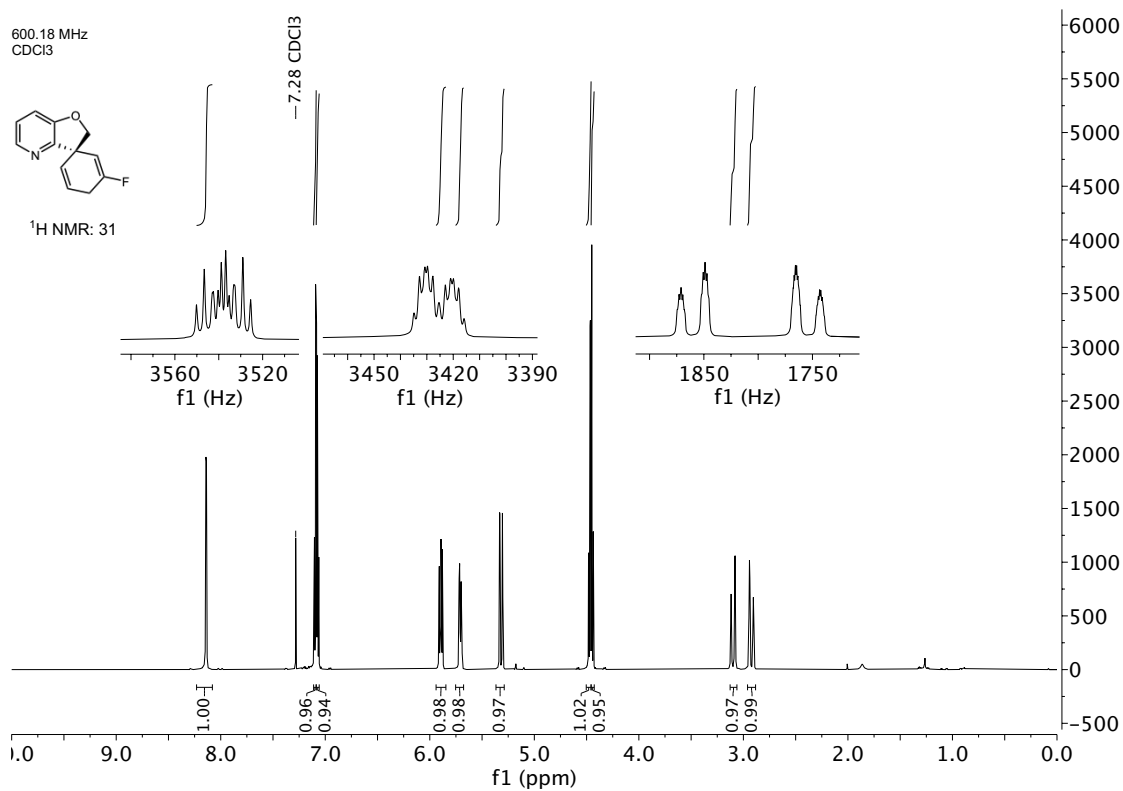


564.68 MHz
CDCl₃

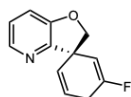


¹⁹F NMR: 30

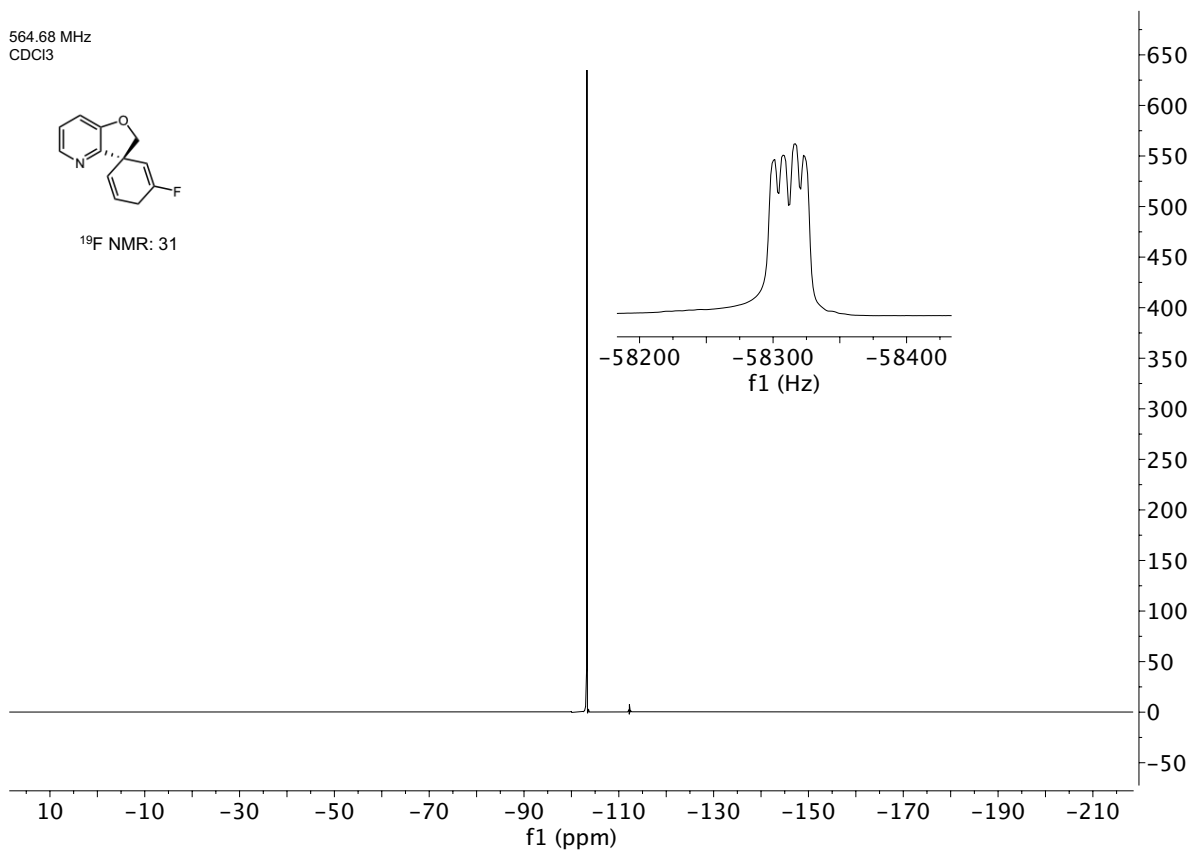




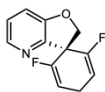
564.68 MHz
CDCl₃



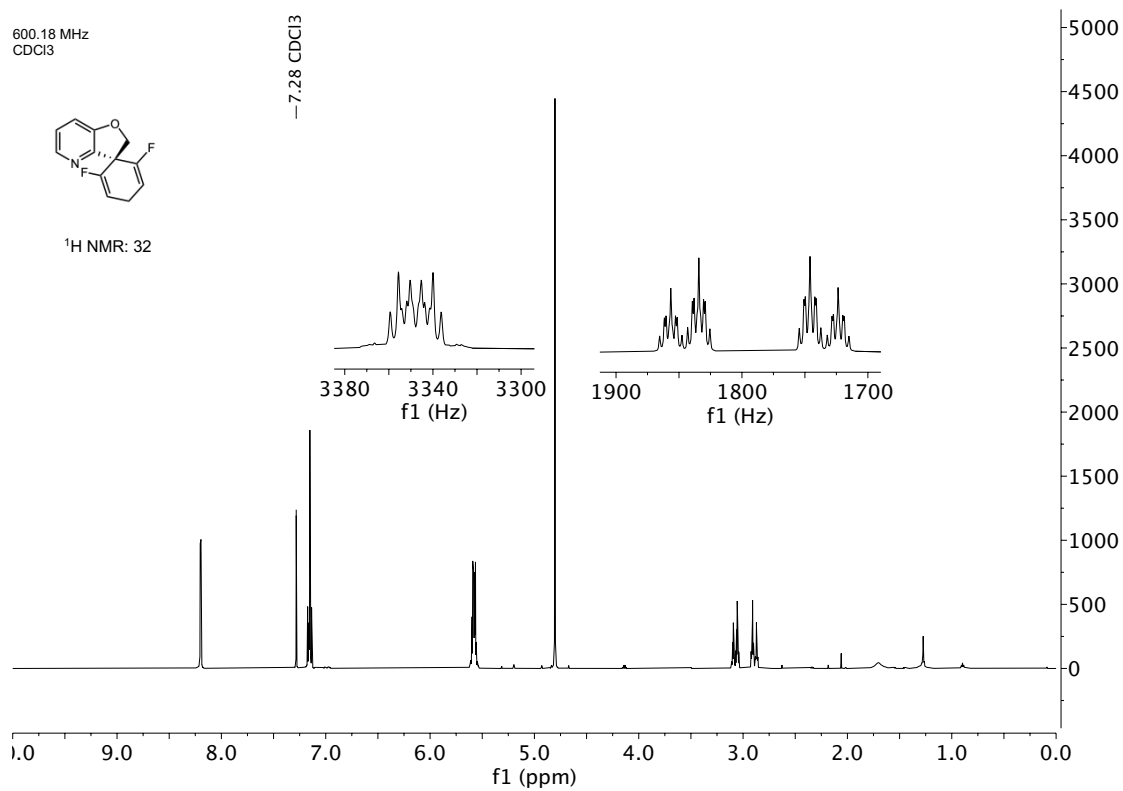
¹⁹F NMR: 31



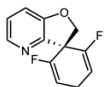
600.18 MHz
CDCl₃



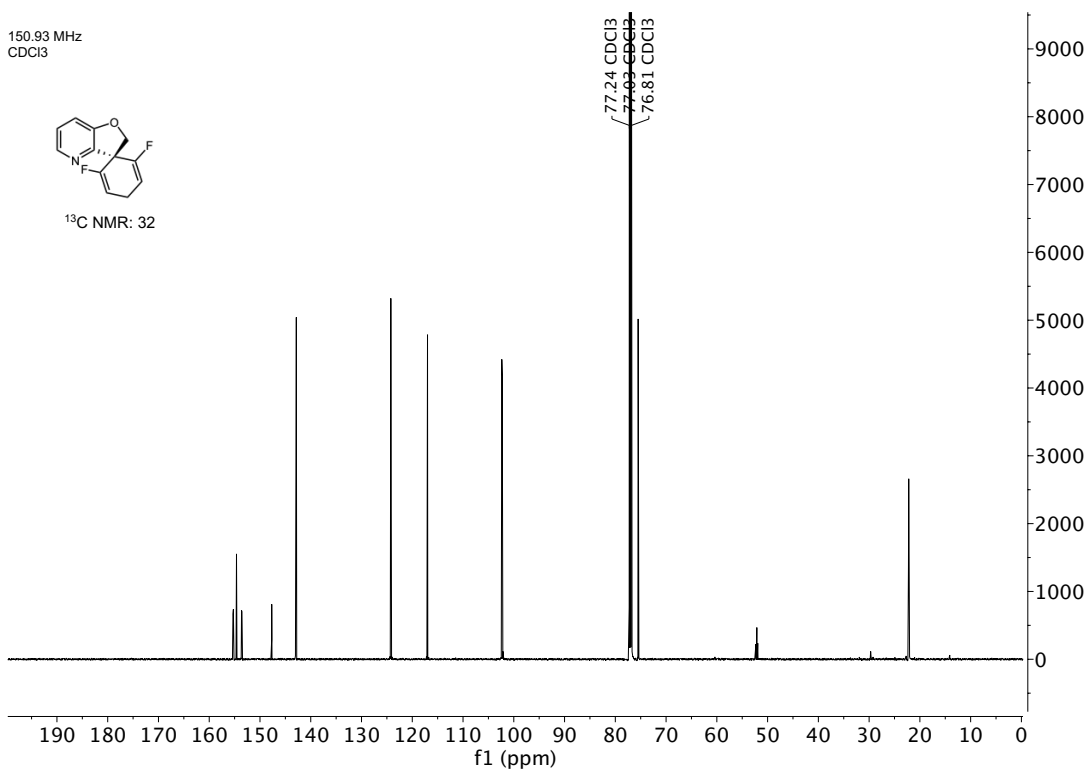
¹H NMR: 32



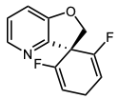
150.93 MHz
CDCl₃



¹³C NMR: 32



564.68 MHz
CDCl₃



¹⁹F NMR: 32

