A pyrone remodeling strategy to access diverse heterocycles: Application to the synthesis of fascaplysin natural products

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Supporting Information

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1 General Considerations

Unless otherwise noted, all reactions were performed in flame or oven-dried glassware fitted with rubber septa under a positive pressure of nitrogen using standard Schlenk techniques. Air- and moisture-sensitive liquids were transferred via syringe or stainless-steel cannula through rubber septa. Solids were added under inert gas or were dissolved in appropriate solvents. Low temperature reactions were carried out in a Dewar vessel filled with a cooling agent: acetone/dry ice (−78 °C), H_2O/ice (0 °C). Reaction temperatures above 23 °C were conducted in an oil bath or in a heated metal block (reactions conducted in tightly capped vials sealed with teflon tape). Reaction mixtures were magnetically stirred and monitored by NMR spectroscopy, liquid chromatography–mass spectrometry (LC-MS) or analytical thin-layer chromatography (TLC), using glass plates precoated with silica gel (Silicycle Siliaplates, glass backed, extra hard layer, 60 Å, 250 µm thickness, F254 indicator). TLC plates were visualized by exposure to ultraviolet light (254 nm), or were stained by submersion in aqueous potassium permanganate solution ($KMnO_4$) and developed by heating with a heat gun. Flash-column chromatography was performed as described by Still et al.,[1] employing silica gel (Silicycle silica gel, 40–63 µm particle size). Organic solutions were concentrated under reduced pressure on a Heidolph temperature-controlled rotary evaporator equipped with a dry ice/isopropanol cold finger. Yields refer to chromatographically and spectroscopically (^{1}H and ^{13}C NMR) pure material.

1.1 Materials

Unless noted below, commercial reagents were purchased from Sigma Aldrich, Acros Organics, Chem-Impex, Oakwood Chemical, Combi-blocks, TCI, and/or Alfa Aesar, and used without additional purification. Solvents were purchased from Fisher Scientific, Acros Organics, Alfa Aesar, or Sigma Aldrich. Tetrahydrofuran (THF), diethyl ether (Et_2O), acetonitrile (CH_3CN), benzene, toluene (PhMe), methanol (MeOH), and triethylamine (Et_3N) were sparged with argon and dried by passing through alumina columns using argon in a Glass Contour solvent purification system. Dichloromethane (CH_2Cl_2, DCM) was freshly distilled over calcium hydride under a N_2 atmosphere prior to each use.

1.2 NMR spectroscopy

NMR spectral data were obtained using deuterated solvents, obtained from Cambridge Isotope Laboratories, Inc. ^{1}H NMR and ^{13}C NMR data were recorded on Bruker AVB-400, AVQ-400, AV-500, AV-600 or AV-700 spectrometers operating at 400 MHz, 400 MHz, 500 MHz, 500 MHz, 600 MHz, 700 MHz for proton nuclei (100 MHz, 100 MHz, 125 MHz, 125 MHz, 150 MHz, 175 MHz for carbon nuclei), respectively. Proton chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to residual protium in the NMR solvent ($CHCl_3$: δ 7.26). Carbon chemical shifts are expressed in parts per million (δ scale, assigned carbon atom) and are referenced to the carbon resonance of the NMR solvent ($CDCl_3$: δ 77.16). ^{19}F NMR spectra were acquired on the AVQ-400 spectrometer and internally referenced to $CFCl_3$ (δ 0.00). ^{11}B NMR spectra were acquired on the AV-600 spectrometer. When ^{13}C signals appeared too weak and/or broad (such as all carbons directly bonded to boron, due to quadrupole relaxation), HSQC spectra were acquired to confirm signal authenticity. ^{1}H NMR spectroscopic data are reported as follows: Chemical shift in ppm (multiplicity, coupling constants *J* (Hz), integration) (e.g., "5.21 (t, ^3J = 7.3 Hz, 1H)"). The multiplicities are abbreviated with s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quartet), p (pentet), se (sextet), h (heptet), m (multiplet) and app (apparent multiplicity). In case of combined multiplicities, the multiplicity with the larger coupling constant is stated first. Except for multiplets, the chemical shift of all signals, as well as for centrosymmetric multiplets, is reported as the center of the resonance range. Data for ^{13}C, ^{19}F and ^{11}B NMR spectroscopy are reported in terms of chemical shift (δ

ppm). In addition to 1D NMR experiments, 2D NMR techniques such as homonuclear correlation spectroscopy (COSY), heteronuclear single quantum coherence (HSQC), heteronuclear multiple bond coherence (HMBC) and nuclear Overhauser enhancement spectroscopy (NOESY) were used to assist structure elucidation. All raw FID files were processed, and the spectra analyzed using the program *MestReNOVA 11.0* from *Mestrelab Research S. L*.

Note: Instruments in the Berkeley College of Chemistry NMR facility are supported in part by NIH S10OD024998.

1.3 Mass spectrometry

Mass spectral data were obtained at the Lawrence Berkeley National Laboratory (LBNL) Catalysis Facility at the University of California, Berkeley, on a PerkinElmer AxION 2 UHPLC-TOF system (ESI). Data acquisition and processing were performed using the "TOF MF Driver" software.

1.4 IR spectroscopy

IR spectral data were obtained from the LBNL Catalysis Facility at the University of California, Berkeley, on a Bruker Vertex80 FT-IR spectrophotometer using a diamond attenuated total reflectance (ATR) accessory. As necessary, analytes were dissolved in dichloromethane prior to direct application on the ATR unit. Data are represented as follows: frequency of absorption (cm^{-1}), and intensity of absorption (s = strong, m = medium, w = weak, br = broad).

Note: Both HRMS and IR instruments were supported by the U.S. Department of Energy (DOE), Office of Science, Basic Energy Sciences, under Contract No. DE-AC02-05CH11231.

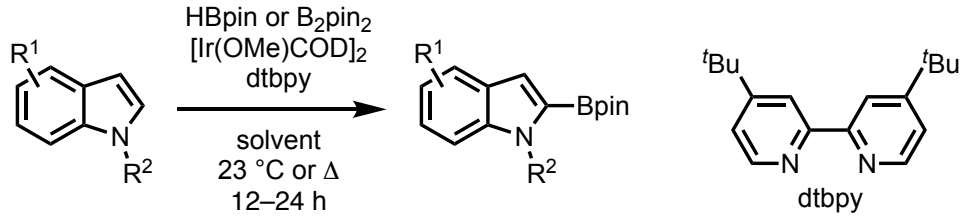
1.5 X-ray analysis

Single-crystal X-ray diffraction experiments were performed at the UC Berkeley CHEXRAY crystallographic facility. Measurements for all compounds were performed on a Rigaku XtaLAB P200 diffractometer equipped with a MicroMax 007HF rotating anode and a Pilatus 200K hybrid pixel array detector. Data were collected using either Mo Kα (λ = 0.71073 A) or Cu Kα (λ = 1.5406 A) radiation. Crystals were kept at 100(2) K throughout the collection. Data collection was performed with CrysAlis^{Pro}.[2] Data processing was conducted with CrysAlis^{Pro} and included a multi-scan absorption correction applied using the SCALE3 ABSPACK scaling algorithm within CrysAlis^{Pro}. All structures were solved with SHELXT.[3] Structures were refined with SHELXL.[4] All non-hydrogen atoms were refined anisotropically, and hydrogen atoms were either included at the geometrically calculated positions and refined using a riding model or located as Q peaks in the Fourier difference map.

2 General Experimental Details

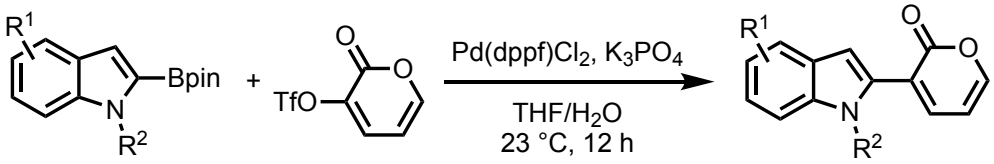
2.1 General Procedure A–E

A. General Procedure A: Preparation of indole boronate esters



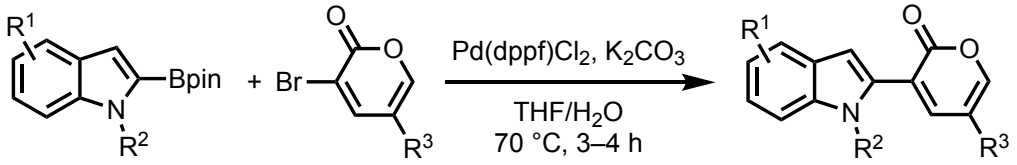
On the basis of the procedure developed by Hartwig et al.,[5] an oven-dried vial was charged with a magnetic stirring bar, (1,5-cyclooctadiene)(methoxy)iridium(I) dimer (1.5 mol%) and 4,4'-di-*tert*-butyl-2,2'-dipyridyl (3 mol%). The vial was flushed with nitrogen and sealed with a septum cap. Anhydrous solvent (0.2 M), pinacolborane (1.1 equiv) or bis(pinacolato)diboron (2 equiv), and indole (1 equiv) were added sequentially and the resulting mixture was stirred at 23 °C or heated in a preheated (indicated temperature) heating block. Stirring was continued at the same temperature until either TLC (for most substrates) or LC-MS analysis indicated complete consumption of starting material. The reaction mixture was then cooled to 23 °C, filtered through a celite plug eluting with ethyl acetate, and the filtrate was concentrated *in vacuo*. The crude residue was either purified by flash column chromatography on silica gel or used directly in the next step without further purification.

B. General Procedure B: Preparation of indole–pyrone adducts from 3-triflyloxy-2-pyrone



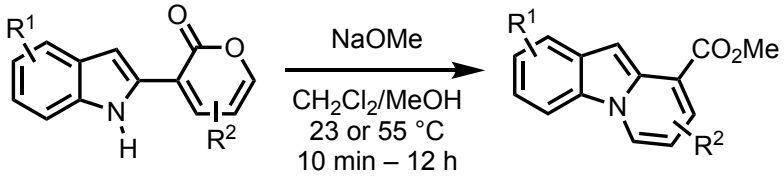
On the basis of the procedure developed by Maulide et al.,[6] an oven-dried vial was charged with a magnetic stirring bar, indole boronate ester (1.1 equiv), 3-triflyloxy-2-pyrone[6] (1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (10 mol%), and tripotassium phosphate (3 equiv). The vial was flushed with nitrogen and sealed with a septum cap. Tetrahydrofuran (0.1 M) and water (0.01 M) were added sequentially and the resulting mixture was stirred at 23 °C. After 12 h, the mixture was diluted with saturated aqueous ammonium chloride solution. The layers were separated, the aqueous layer was extracted with ethyl acetate and the combined organic extracts were washed with saturated aqueous sodium chloride solution. The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel to provide the indole–pyrone adduct.

C. General Procedure C: Preparation of indole–pyrone adducts from 3-bromo-2-pyrone



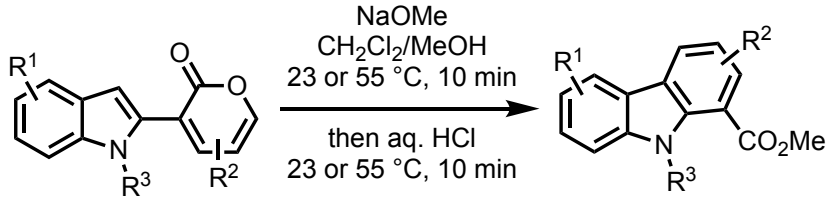
An oven-dried vial was charged with a magnetic stirring bar, indole boronate ester (1.1 equiv), 3-bromo-2-pyrone (1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (10 mol%), and potassium carbonate (2 equiv). The vial was flushed with nitrogen and sealed with a septum cap. Tetrahydrofuran (0.1 M) and water (0.01 M) were added sequentially and the vial was placed in a preheated (70 °C) heating block. Stirring was continued at this temperature until TLC analysis indicated complete consumption of the 3-bromo-2-pyrone starting material. The mixture was then cooled to 23 °C, and diluted with saturated aqueous ammonium chloride solution. The layers were separated, the aqueous layer was extracted with ethyl acetate and the combined organic extracts were washed with saturated aqueous sodium chloride solution. The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel to provide the indole–pyrone adduct.

D. General Procedure D: Preparation of pyrido[1,2-*a*]indoles



A vial was charged with a magnetic stirring bar and indole–pyrone adduct (1 equiv). Dichloromethane (0.1 M) and methanol (0.1 M) were added sequentially and the resulting solution was treated with a solution of sodium methoxide (25 wt% in MeOH, 1.2 equiv) at 23 °C. The resulting mixture was stirred at 23 °C or heated in a preheated (55 °C) heating block with stirring for the indicated time (typically until TLC analysis indicated complete consumption of the starting material). The mixture was then cooled to 23 °C, and diluted with saturated aqueous ammonium chloride solution. The layers were separated, the aqueous layer was extracted with dichloromethane and the combined organic extracts were washed with saturated aqueous sodium chloride solution. The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel to provide the pyrido[1,2-*a*]indole product.

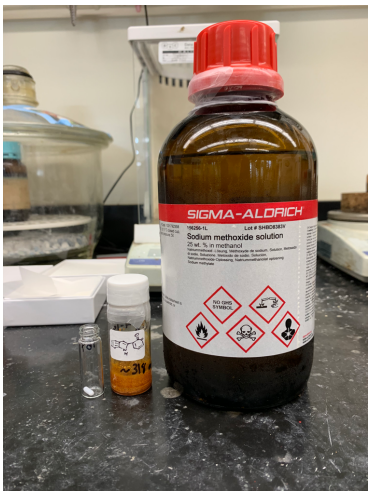
E. General Procedure E: Preparation of carbazoles



A vial was charged with a magnetic stirring bar and indole–pyrone adduct (1 equiv). Dichloromethane (0.1 M) and methanol (0.1 M) were added sequentially and the resulting solution was treated with a solution of sodium methoxide (25 wt% in MeOH, 1.2 equiv) at 23 °C. The resulting mixture was stirred at 23 °C or heated in a preheated (55 °C) heating block with stirring for the indicated time (typically until TLC analysis indicated complete consumption of the starting material). The mixture was then cooled to 23 °C, and was treated with an aqueous hydrogen chloride solution (1 M, 3 equiv) and stirring of the resulting biphasic mixture was continued at 23 °C or heated in a preheated (55 °C) heating block with stirring for the indicated time (typically until TLC analysis indicated complete consumption of the starting material). The mixture was then cooled to 23 °C, and diluted with saturated aqueous ammonium chloride solution. The layers were separated, the aqueous layer was extracted with dichloromethane and the combined organic extracts were washed with saturated aqueous sodium chloride solution. The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel to provide the carbazole product.

2.2 Photographic Guide for the Pyrido[1,2-*a*]indole formation

Illustrated below is the reaction setup and General Procedure D (entry 8 of Table 1, main manuscript or entry 12, Table S1)



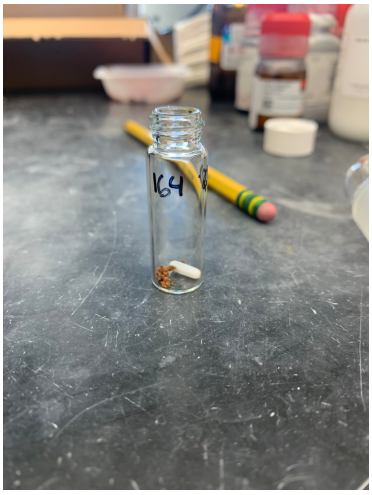


Figure S1. Reagents used in the reaction. From left to right: indole–pyrone adduct and NaOMe solution. On a bench top, a vial is charged with a magnetic stirring bar and indole–pyrone adduct.

Figure S2. Solution of indole–pyrone adduct in dichloromethane and methanol.

Figure S3. Reaction mixture after addition of a NaOMe solution.

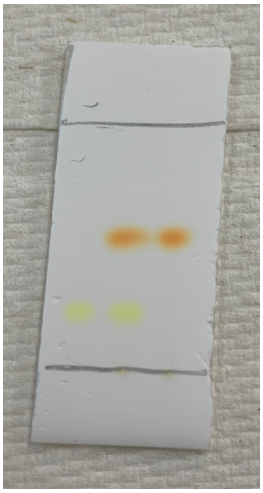


Figure S4. TLC analysis (before and after $KMnO_4$ stained) after stirring at 23 °C for 10 min.

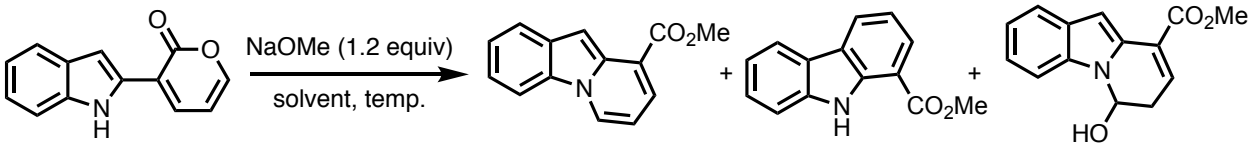
2.3 Reaction Development and Optimization Table

The development and subsequent optimization attempts of this annulative reaction were carried out under varying solvent conditions and temperatures, which have been outlined in Table S1. The general procedures for our optimization studies were as follows:

Entries 1–11: A flame-dried vial was charged with a magnetic stirring bar and indole–pyrone adduct (0.1 mmol, 1 equiv). The vial was taken into a N_2-filled glovebox where sodium methoxide (1.2 equiv) was added. The vial was sealed with a septum cap, taken out of the glovebox, and placed under N_2. Anhydrous solvent (0.05 M) was then added and the resulting mixture was stirred (temperature and times as indicated below). The reaction mixture was filtered through a silica plug eluting with ethyl acetate, the filtrate was concetrated *in vacuo*, and the crude residue was analyzed by quantitative NMR spectroscopy.

Entry 12: The same procedure as above was followed except non-anhydrous conditions (i.e. non-anhydrous solvent, non-flame-dried vial, open-to-air setup, and stirred under air) were employed.

Table S1. Optimization of the annulative reaction.



7a **8a** **9** **10**

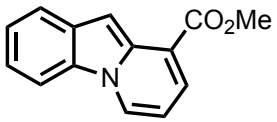
Entry	Conditions	% NMR yield (8a:9:10)[a]
1	MeCN, 23→50 °C	10 : 13 : 16
2	1,4-dioxane, 23 °C	0 : 15 : 21
3[b]	cyclohexane/PhMe (1:1), 23→100 °C	trace : 0 : 0
4[c]	pyridine, 23 °C	0 : trace : trace
5	DMF, 23 °C	decomp.
6[d]	DMSO, 23 °C	decomp.
7[e]	HFIP, 23→50 °C	unreacted **7a**
8	MeOH, 23 °C	45 (53 brsm) : 0 : 0
9	THF/MeOH (1:1), 23 °C	36 : 7 : 10
10	DCE/MeOH, 23 °C	45 : 0 : 0
11	CH_2Cl_2/MeOH (1:1), 23 °C	61 : 0 : 0
12[f]	CH_2Cl_2/MeOH (1:1), 23 °C, open vial	59 : 0 : 0

All reactions (unless otherwise noted): under N_2, anhydrous, 0.1 mmol **7a**, 0.05 M (based on mmol **7a**), 25 min; [a]qNMR yields calculated using 1,2,3-trimethoxybenzene as internal standard; [b]4.5 h; [c]40 min; [d]1 h 10 min; [e]1.5 h; [f]not anhydrous

We initially observed formation of pyrido[1,2-*a*]indole **8a** using MeCN as the solvent, albeit in a low 10% yield, along with formation of carbazole **9** and hemiaminal **10** (entry 1). A mixture of products was also observed with 1,4-dioxane as solvent (entry 2). However, only carbazole **9** and hemiaminal **10** were observed as the sole products. Using cyclohexane with toluene as a co-solvent (entry 3), we only observed trace formation of **8a**. At this point, we decided to investigate whether polar solvents would be beneficial toward selectivity. A survey of polar solvents (i.e., pyridine, DMSO, DMF; entries 4–6) only offered trace **9** and **10** (entry 4) or decomposition of **7a** (entries 5 and 6). Hexafluoroisopropanol (HFIP) at slightly elevated temperatures (50 °C) and prolonged reaction time (1.5 h) only returned the starting indole–pyrone adduct **7a** (entry 7). We then turned toward exploring polar aprotic solvents. To our advantage, employing methanol as the solvent (entry 8) yielded solely the desired **8a** in 45% yield. However, we realized indole–pyrone **7a** is not very soluble in methanol and we presumed that enhancing the solubility could increase

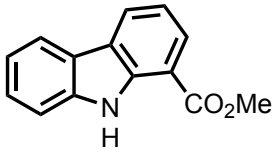
the final yield of **8a**. We then began investigating various co-solvents with methanol to improve the solubility of **7a**. Employing THF as the co-solvent led to diminished yield of **8a** (entry 9) and additionally, also resulted in the formation of carbazole **9** and hemiaminal **10**. Eventually, we turned our attention to chlorinated solvents, and found that a mixture of DCE and MeOH gave **8a** as the exclusive product (entry 10) but did not improve the yield. Gratifyingly, switiching from DCE/MeOH to DCM/MeOH (entry 11) resulted in an increase in yield (45% → 61%) of **8a**. Using the optimal solvent conditions from entry 11, but under open flask/non-anhydrous conditions (entry 12), no significant drop in yield was observed. For this reason, ***the entire scope of this project was developed under non-anhydrous conditions, and for substrates that required more forcing conditions, the reaction vial was tightly capped with Teflon tape and placed in a preheated (55 °C) heating block.***

The characterization data of pyrido[1,2-*a*]indole **8a**, carbazole **9**, and hemiaminal **10** are given below.



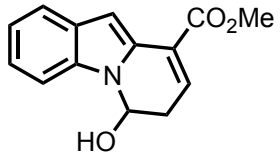
8a

TLC (5:1, hexanes:ethyl acetate): R_f = 0.46 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 6.9 Hz, 1H), 7.91 – 7.81 (m, 3H), 7.46 – 7.40 (m, 1H), 7.37 (br s, 1H), 7.36 – 7.30 (m, 1H), 6.51 (t, *J* = 6.9 Hz, 1H), and 4.01 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.0, 133.1, 130.1, 129.5, 129.2, 128.9, 123.8, 121.2, 120.5, 120.4, 110.3, 106.1, 94.7, and 52.2.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3103 (w), 3052 (w), 2949 (m), 1713 (s), 1607 (w), 1519 (w), 1462 (m), 1345 (w), 1270 (s), 1202 (s), 1129 (m), 1060 (w), 774 (w), and 743 (m).
HRMS (ESI): calcd for ([M+H], $C_{14}H_{12}NO_2)^+$: 226.0863, found: 226.0866.
mp: 95–97 °C (red solid)



9

TLC (3:1, hexanes:ethyl acetate): R_f = 0.73 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 9.93 (br s, 1H), 8.27 (d, *J* = 7.6 Hz, 1H), 8.12 – 8.07 (m, 2H), 7.54 – 7.51 (m, 1H), 7.50 – 7.46 (m, 1H), 7.31 – 7.24 (m, 2H), and 4.03 (s, 3H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 168.0, 140.2, 139.8, 127.5, 126.7, 125.6, 124.8, 122.6, 120.5, 120.1, 118.6, 111.7, 111.2, and 52.1.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3440 (s), 3061 (w), 3038 (w), 2951 (m), 2924 (w), 2850 (w), 1692 (s), 1603 (w), 1494 (m), 1435 (m), 1300 (m), 1267 (s), 1223 (s), 1195 (m), and 1069 (w).
HRMS (ESI): calcd for ([M+H], $C_{14}H_{12}NO_2)^+$: 226.0863, found: 226.0864.
mp: 133–135 °C (off-white solid)

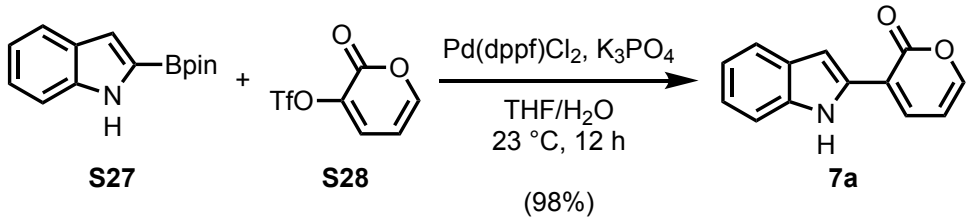


10

TLC (3:1, hexanes:ethyl acetate): R_f = 0.20 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.9 Hz, 1H), 7.42 (d, *J* = 8.2 Hz, 1H), 7.29 – 7.25 (m, 1H), 7.18 (s, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.09 – 7.05 (m, 1H), 6.20 – 6.16 (m, 1H), 3.91 (s, 3H), 3.00 – 2.97 (m, 2H), and 2.37 – 2.32 (m, 1H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 164.9, 135.8, 131.3, 129.4, 129.3, 124.9, 123.4, 121.9, 121.1, 108.8, 104.6, 72.5, 52.2, and 32.9.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3414 (s), 3054 (w), 2950 (m), 2925 (m), 2852 (w), 1718 (s), 1438 (m), 1344 (m), 1271 (s), 1204 (m), 1133 (m), 1073 (m), 1046 (m), 805 (m), and 738 (m).
HRMS (ESI): calcd for ([M+H], $C_{14}H_{14}NO_3$)$^+$: 244.0968, found: 244.0968.
Physical state: yellow oil.

3 Synthesis of Indole–Pyrone Adducts

3.1 Synthesis of indole–pyrone 7a

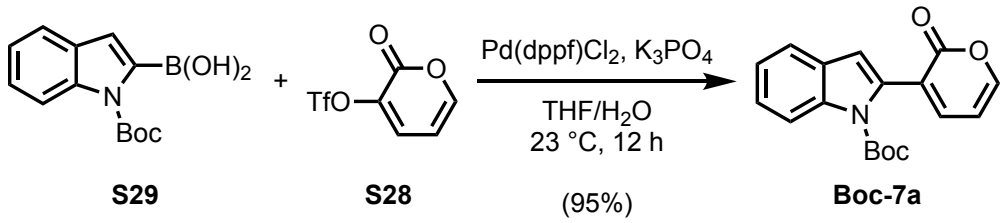


S27 **S28** **7a**

Following General Procedure B, a mixture of indole boronate ester **S27**[7] (1.13 g, 4.65 mmol, 1.1 equiv), 3-triflyloxy-2-pyrone **S28**[6] (1.03 g, 4.22 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (317 mg, 0.43 mmol, 10 mol%), and tripotassium phosphate (2.70 g, 12.7 mmol, 3 equiv) in tetrahydrofuran (40 mL) and water (4 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (12:1→1:1 hexanes:ethyl acetate) to provide indole–pyrone **7a** (873 mg, 4.14 mmol, 98%) as a yellow solid.

TLC (1:1, hexanes:ethyl acetate): R_f = 0.65 (UV/$KMnO_4$)
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.39 (br s, 1H), 7.87 (dd, *J* = 6.9, 1.9 Hz, 1H), 7.64 – 7.59 (m, 1H), 7.53 (dd, *J* = 5.0, 1.9 Hz, 1H), 7.46 – 7.41 (m, 1H), 7.24 – 7.19 (m, 1H), 7.14 – 7.09 (m, 1H), 6.96 – 6.92 (m, 1H), and 6.45 (dd, *J* = 6.9, 5.0 Hz, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 161.8, 149.8, 136.5, 135.7, 131.7, 128.0, 123.2, 120.6, 120.5, 119.9, 111.8, 107.6, and 100.6.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3369 (s), 3055 (w), 2979 (m), 2942 (w), 1696 (s), 1621 (w), 1369 (w), 1324 (w), 1238 (w), 1108 (m), 949 (w), 794 (w), 753 (w), and 691 (m).
HRMS (ESI): calcd for ([M+H], $C_{13}H_{10}NO_2)^+$: 212.0706, found: 212.0717.
mp: 170–177 °C.

3.2 Synthesis of indole–pyrone Boc-7a

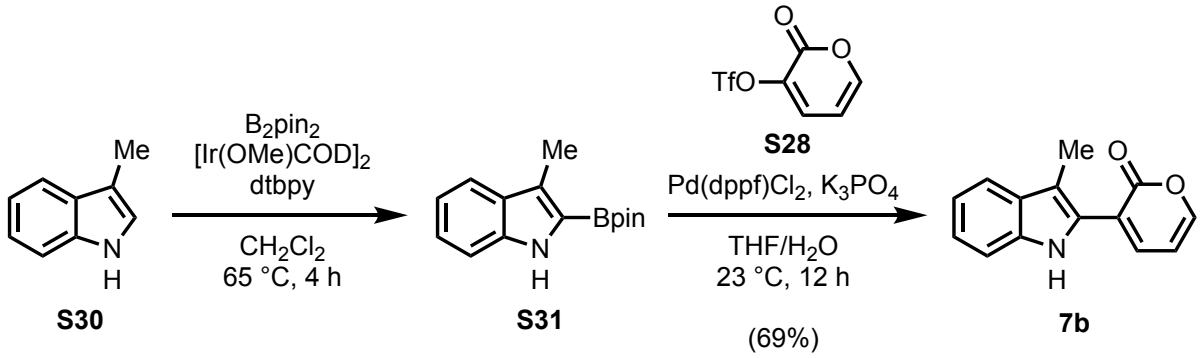


S29 **S28** (95%) **Boc-7a**

Following General Procedure B, a mixture of indole boronic acid **S29** (144 mg, 0.55 mmol, 1.1 equiv), 3-triflyloxy-2-pyrone **S28**[6] (122 mg, 0.50 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (37.0 mg, 0.05 mmol, 10 mol%), and tripotassium phosphate (315 mg, 1.50 mmol, 3 equiv) in tetrahydrofuran (5 mL) and water (0.5 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (3:1 hexanes:ethyl acetate) to provide indole–pyrone **Boc-7a** (148 mg, 0.48 mmol, 95%) as a yellow solid.

TLC (1:1, hexanes:ethyl acetate): R_f = 0.70 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.4 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.38 – 7.32 (m, 2H), 7.23 (t, *J* = 7.5 Hz, 1H), 6.61 (s, 1H), 6.30 (t, *J* = 5.9 Hz, 1H), and 1.54 (s, 9H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 161.0, 151.1, 149.8, 138.3, 137.3, 133.8, 128.7, 125.2, 125.1, 123.0, 120.8, 115.7, 111.2, 106.3, 84.2, and 28.0.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3105 (w), 3053 (w), 2980 (m), 2934 (w), 1717 (s), 1453 (w), 1367 (w), 1324 (s), 1223 (m), 1158 (m), 1133 (m), 1097 (m), 1072 (m), 767 (w), and 730 (m).
HRMS (ESI): calcd for ([M+H], $C_{18}H_{18}NO_4)^+$: 312.1230, found: 312.1233.
mp: 118–121 °C.

3.3 Synthesis of indole–pyrone 7b

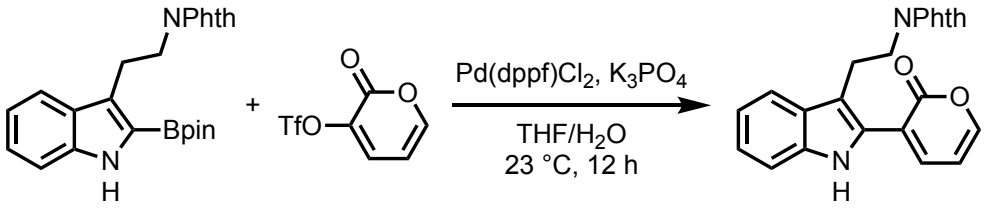


Following General Procedure A, a mixture of indole **S30** (224 mg, 1.70 mmol, 1 equiv), bis(pinacolato)diboron (670 mg, 2.64 mmol, 2 equiv), (1,5-cyclooctadiene)(methoxy)iridium(I) dimer (17 mg, 0.03 mmol, 1.5 mol%), and 4,4'-di-*tert*-butyl-2,2'-dipyridyl (14 mg, 0.05 mmol, 3 mol%) in dichloromethane (10 mL) was heated at 65 °C with stirring for 4 h. The crude residue was purified by flash-column chromatography on silica gel (30:1 hexanes:ethyl acetate) to provide an inseparable mixture (270 mg) of indole boronate ester **S31** (~ 0.89 mmol) and unreacted indole **S30** as a pale yellow oil in a ratio of 6:1, which was directly used in the next step without further purification. The characterization data for **S31** were in full agreement with values previously reported.[8]

Following General Procedure B, a mixture of crude indole boronate ester **S31** (assuming 0.89 mmol, 1.1 equiv), 3-triflyloxy-2-pyrone **S28**[6] (195 mg, 0.80 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (51.0 mg, 0.07 mmol, 10 mol%), and tripotassium phosphate (510 mg, 2.40 mmol, 3 equiv) in tetrahydrofuran (8 mL) and water (0.8 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (2:1 hexanes:ethyl acetate) to provide indole–pyrone **7b** (125 mg, 0.56 mmol, 69%) as a yellow solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.29 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.17 (br s, 1H), 7.73 (dd, *J* = 7.0, 1.9 Hz, 1H), 7.64 – 7.57 (m, 1H), 7.51 (dd, *J* = 5.0, 1.9 Hz, 1H), 7.44 – 7.37 (m, 1H), 7.26 – 7.20 (m, 1H), 7.17 – 7.10 (m, 1H), 6.47 (dd, *J* = 7.0, 5.0 Hz, 1H), and 2.54 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 162.3, 149.1, 137.1, 135.4, 128.9, 127.3, 123.5, 120.7, 119.6, 118.9, 112.0, 111.5, 107.4, and 11.5.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3369 (s), 3056 (w), 2966 (w), 2921 (w), 2866 (w), 1687 (s), 1617 (m), 1385 (w), 1335 (w), 1239 (m), 1115 (w), 1090 (w), 779 (w), 749 (m), 729 (m), and 695 (w).
HRMS (ESI): calcd for ([M+H], $C_{14}H_{12}NO_2$)$^+$: 226.0863, found: 226.0868.
mp: 175–178 °C.

3.4 Synthesis of indole–pyrone 7c

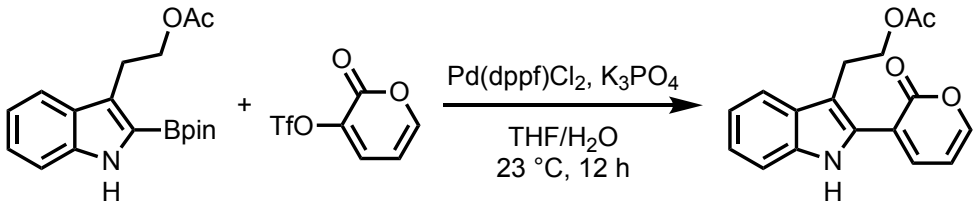


S32 **S28** **7c**

Following General Procedure B, a mixture of indole boronate ester **S32**[9] (260 mg, 0.63 mmol, 1.1 equiv), 3-triflyloxy-2-pyrone **S28**[6] (136 mg, 0.56 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (40.0 mg, 0.05 mmol, 10 mol%), and tripotassium phosphate (357 mg, 1.70 mmol, 3 equiv) in tetrahydrofuran (5.5 mL) and water (0.5 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (2:1→1:1, hexanes:ethyl acetate) to provide indole–pyrone **7c** (104 mg, 0.27 mmol, 49%) as a yellow solid.

TLC (1:1, hexanes:ethyl acetate): R_f = 0.46 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 10.26 (br s, 1H), 8.20 – 8.14 (m, 1H), 7.92 – 7.85 (m, 2H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.77 – 7.71 (m, 2H), 7.57 – 7.52 (m, 1H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.28 – 7.23 (m, 1H), 7.18 (t, *J* = 7.4 Hz, 1H), 6.66 – 6.61 (m, 1H), 3.99 – 3.92 (m, 2H), and 3.32 – 3.25 (m, 2H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 168.5, 162.2, 149.7, 138.5, 135.3, 134.2, 132.3, 128.3, 128.2, 123.7, 123.4, 120.2, 119.8, 118.8, 111.72, 111.65, 107.8, 37.5, and 25.0.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3367 (s), 2919 (m), 2850 (m), 1704 (s), 1618 (w), 1399 (m), 1359 (w), 1242 (w), 1030 (w), 775 (w), 718 (w), and 691 (w).
HRMS (ESI): calcd for ([M+H], $C_{23}H_{17}N_2O_4$)$^+$: 385.1183, found: 379.1179.
mp: 219–221 °C.

3.5 Synthesis of indole–pyrone 7e

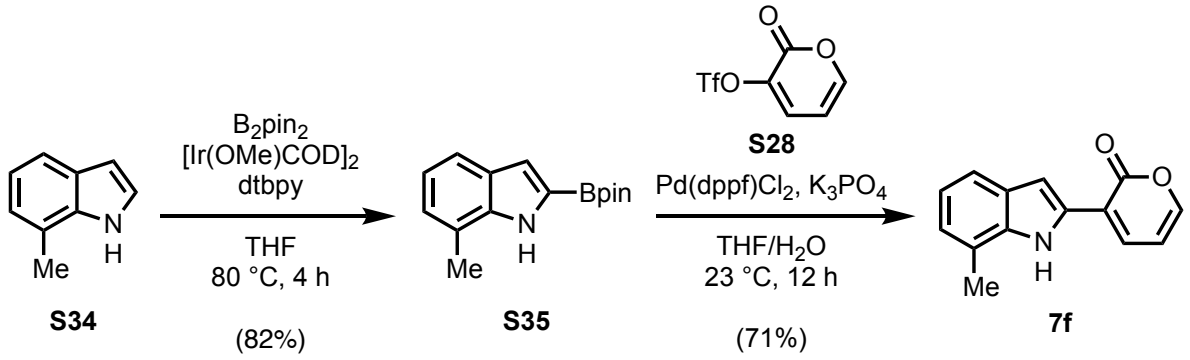


S33 **S28** **7e**

Following General Procedure B, a mixture of indole boronate ester **S33**[10] (90 mg, 0.27 mmol, 1.1 equiv), 3-triflyloxy-2-pyrone **S28**[6] (62 mg, 0.25 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (19.0 mg, 0.03 mmol, 10 mol%), and tripotassium phosphate (160 mg, 0.75 mmol, 3 equiv) in tetrahydrofuran (2.5 mL) and water (0.25 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (2:1 hexanes:ethyl acetate) to provide indole–pyrone **7e** (70 mg, 0.24 mmol, 93%) as a yellow solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.13 (UV/$KMnO_4$)
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.18 (br s, 1H), 8.01 (dd, *J* = 7.0, 1.9 Hz, 1H), 7.67 – 7.61 (m, 1H), 7.54 (dd, *J* = 5.0, 1.8 Hz, 1H), 7.43 – 7.39 (m, 1H), 7.27 – 7.23 (m, 1H), 7.17 – 7.12 (m, 1H), 6.51 (dd, *J* = 7.0, 5.0 Hz, 1H), 4.38 – 4.31 (m, 2H), 3.32 – 3.25 (m, 2H), and 2.08 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 162.2, 149.8, 138.2, 135.4, 128.5, 128.4, 123.6, 120.1, 119.9, 118.7, 111.7, 111.0, 107.6, 63.7, 25.1, and 21.2.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3385 (s), 3104 (w), 3058 (w), 2978 (w), 1705 (s), 1621 (m), 1438 (w), 1366 (w), 1309 (w), 1237 (s), 1106 (w), 1043 (m), 977 (w), 781 (m), and 745 (m).
HRMS (ESI): calcd for ([M+Na], $C_{17}H_{15}NNaO_4$)$^+$: 320.0893, found: 320.0886.
mp: 127–132 °C.

3.6 Synthesis of indole–pyrone 7f

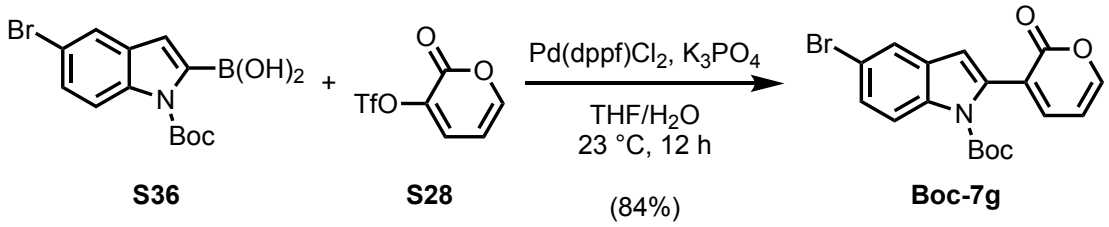


Following General Procedure A, a mixture of indole **S34** (137 mg, 1.04 mmol, 1 equiv), bis(pinacolato)diboron (305 mg, 1.20 mmol, 1.2 equiv), (1,5-cyclooctadiene)(methoxy)iridium(I) dimer (11 mg, 0.02 mmol, 1.5 mol%), and 4,4'-di-*tert*-butyl-2,2'-dipyridyl (9 mg, 0.03 mmol, 3 mol%) in tetrahydrofuran (6 mL) was heated at 80 °C with stirring for 4 h. The crude residue was purified by flash-column chromatography on silica gel (8:1 hexanes:ethyl acetate) to provide indole boronate ester **S35** (220 mg, 0.85 mmol, 82%) as a white foam. The characterization data for **S35** were in full agreement with values previously reported.[8]

Following General Procedure B, a mixture of indole boronate ester **S35** (220 mg, 0.85 mmol, 1.1 equiv), 3-triflyloxy-2-pyrone **S28**[6] (192 mg, 0.79 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (57.0 mg, 0.08 mmol, 10 mol%), and tripotassium phosphate (510 mg, 2.40 mmol, 3 equiv) in tetrahydrofuran (8 mL) and water (0.8 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (5:1→3:1, hexanes:ethyl acetate) to provide indole–pyrone **7f** (125 mg, 0.56 mmol, 71%) as a yellow solid.

TLC (1:1, hexanes:ethyl acetate): R_f = 0.70 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 10.33 (br s, 1H), 7.85 (dd, *J* = 6.9, 1.9 Hz, 1H), 7.51 (dd, *J* = 5.0, 1.9 Hz, 1H), 7.47 (d, *J* = 7.7 Hz, 1H), 7.07 – 7.00 (m, 2H), 6.94 (d, *J* = 2.2 Hz, 1H), 6.43 (dd, *J* = 6.9, 5.0 Hz, 1H), and 2.56 (s, 3H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 161.9, 149.7, 136.2, 135.5, 131.4, 127.6, 123.6, 121.1, 120.7, 119.9, 118.3, 107.5, 101.1, and 16.9.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3412 (s), 3101 (w), 3053 (w), 2919 (w), 2859 (w), 1699 (s), 1619 (m), 1427 (w), 1313 (m), 1237 (w), 1112 (w), 1093 (w), 800 (m), 770 (w), and 745 (m).
HRMS (ESI): calcd for ([M+H], $C_{14}H_{12}NO_2)^+$: 226.0863, found: 226.0867.
mp: 198–201 °C.

3.7 Synthesis of indole–pyrone Boc-7g

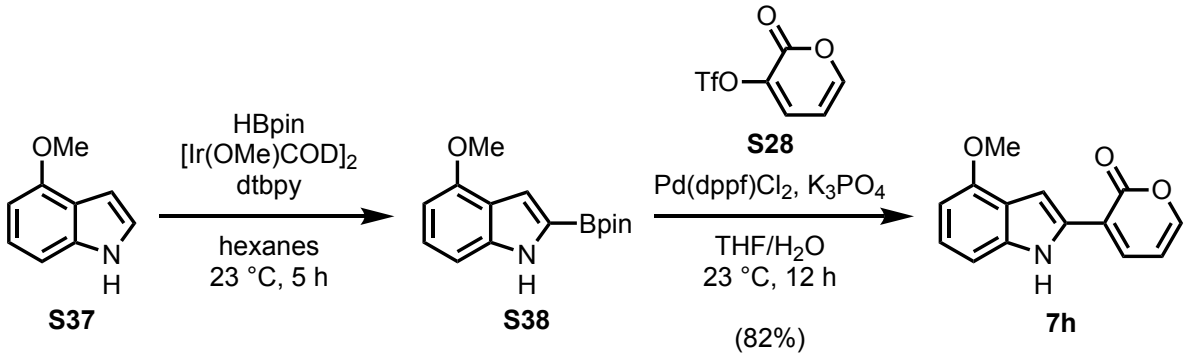


S36 **S28** **Boc-7g**

Following General Procedure B, a mixture of indole boronic acid **S36** (170 mg, 0.5 mmol, 1.1 equiv), 3-triflyloxy-2-pyrone **S28**[6] (111 mg, 0.45 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (35.5 mg, 0.05 mmol, 10 mol%), and tripotassium phosphate (289 mg, 1.36 mmol, 3 equiv) in tetrahydrofuran (4.5 mL) and water (0.5 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (5:1, hexanes:ethyl acetate) to provide indole–pyrone **Boc-7g** (163 mg, 0.42 mmol, 84%) as a yellow solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.22 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.9 Hz, 1H), 7.66 (d, *J* = 2.0 Hz, 1H), 7.54 (dd, *J* = 5.3, 2.1 Hz, 1H), 7.42 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.36 (dd, *J* = 6.5, 2.1 Hz, 1H), 6.53 (s, 1H), 6.31 (dd, *J* = 6.5, 5.2 Hz, 1H), 1.52 (s, 9H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 160.80, 151.35, 149.45, 138.72, 135.98, 134.89, 130.34, 127.94, 124.62, 123.36, 117.13, 116.18, 110.14, 106.30, 84.67, 27.92.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3105 (w), 3056 (w), 2980 (m), 2934 (w), 1719 (s), 1539 (w), 1446 (m), 1338 (s), 1314 (m), 1271 (w), 1221 (m), 1157 (s), 1137 (s), 1098 (m), 1072 (m), 1058 (m), 803 (w), and 734 (m).
HRMS (ESI): calcd for ([M+H], $C_{18}H_{17}BrNO_4$)$^+$: 390.0335, found: 390.0339.
mp: 62–71 °C.

3.8 Synthesis of indole–pyrone 7h

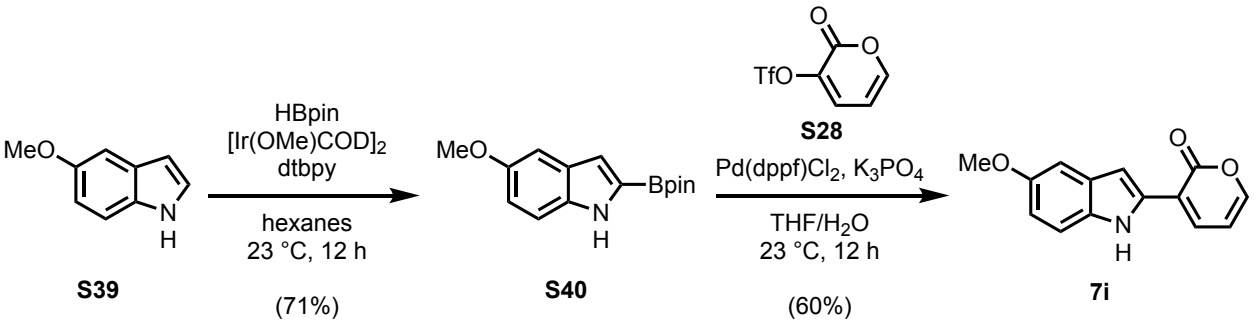


Following General Procedure A, a mixture of indole **S37** (147 mg, 1.00 mmol, 1 equiv), pinacolborane (0.16 mL, 1.1 mmol, 1.1 equiv), (1,5-cyclooctadiene)(methoxy)iridium(I) dimer (10 mg, 0.015 mmol, 1.5 mol%), and 4,4'-di-*tert*-butyl-2,2'-dipyridyl (9 mg, 0.032 mmol, 3 mol%) in hexanes (5 mL) was stirred at 23 °C for 5 h. The crude residue (~0.72 mmol of **S38**) was directly used in the next step without further purification. *Note: The amount of **S38** in the crude residue was determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard.*

Following General Procedure B, a mixture of crude indole boronate ester **S38** (assuming 0.72 mmol, 1.1 equiv), 3-triflyloxy-2-pyrone **S28**[6] (160 mg, 0.66 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (48.0 mg, 0.07 mmol, 10 mol%), and tripotassium phosphate (421 mg, 2.00 mmol, 3 equiv) in tetrahydrofuran (6 mL) and water (0.6 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (3:1→2:1, hexanes:ethyl acetate) to provide indole–pyrone **7h** (130 mg, 0.54 mmol, 82%) as a yellow solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.22 (UV/$KMnO_4$)
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.40 (br s, 1H), 7.86 – 7.80 (m, 1H), 7.52 – 7.47 (m, 1H), 7.17 – 7.11 (m, 1H), 7.08 – 7.02 (m, 2H), 6.51 (d, *J* = 7.7 Hz, 1H), 6.44 – 6.39 (m, 1H), and 3.97 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 161.9, 153.3, 149.5, 137.8, 135.2, 130.4, 124.0, 120.0, 119.3, 107.6, 105.1, 99.7, 98.1, and 55.4.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3295 (s), 3095 (m), 2999 (w), 2957 (w), 2934 (w), 2837 (w), 1686 (s), 1614 (m), 1587 (m), 1510 (m), 1360 (m), 1238 (m), 1186 (w), 1109 (m), 1002 (w), 761 (s), 729 (m), and 522 (w).
HRMS (ESI): calcd for ([M+H], $C_{14}H_{12}NO_3$)$^+$: 242.0812, found: 242.0804.
mp: 175–177 °C.

3.9 Synthesis of indole–pyrone 7i

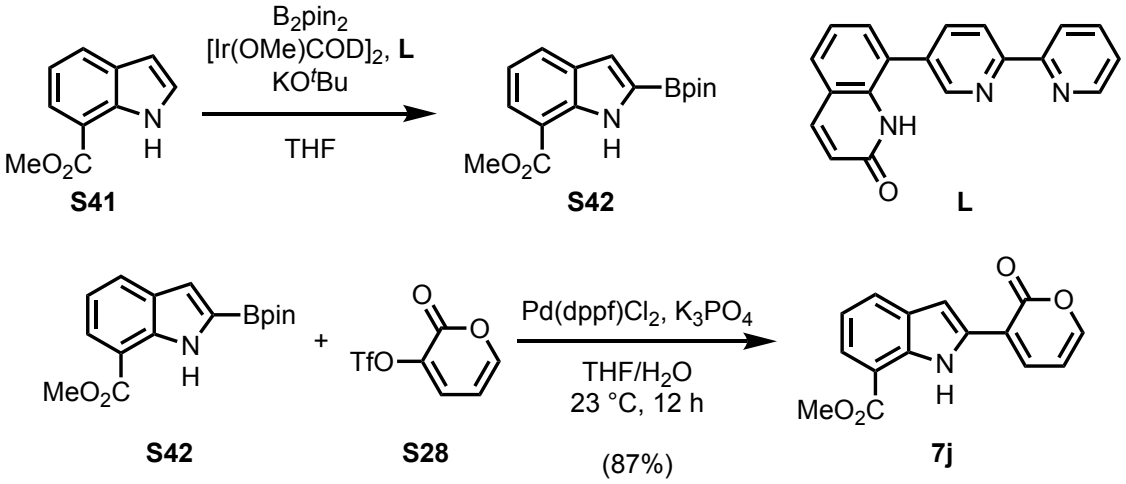


Following General Procedure A, a mixture of indole **S39** (153 mg, 1.04 mmol, 1 equiv), pinacolborane (0.16 mL, 1.10 mmol, 1.1 equiv), (1,5-cyclooctadiene)(methoxy)iridium(I) dimer (12 mg, 0.02 mmol, 1.5 mol%), and 4,4'-di-*tert*-butyl-2,2'-dipyridyl (10 mg, 0.04 mmol, 3 mol%) in hexanes (5 mL) was stirred at 23 °C for 4 h. The crude residue was purified by flash-column chromatography on silica gel (8:1 hexanes:ethyl acetate) to provide indole boronate ester **S40** (203 mg, 0.74 mmol, 71%) as a white foam. The characterization data for **S40** were in full agreement with values previously reported.[8]

Following General Procedure B, a mixture of indole boronate ester **S40** (250 mg, 0.92 mmol, 1.3 equiv), 3-triflyloxy-2-pyrone **S28**[6] (175 mg, 0.72 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (52 mg, 0.07 mmol, 10 mol%), and tripotassium phosphate (446 mg, 2.10 mmol, 3 equiv) in tetrahydrofuran (7 mL) and water (0.7 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (3:1, hexanes:ethyl acetate) to provide indole–pyrone **7i** (104 mg, 0.43 mmol, 60%) as a yellow solid.

TLC (2:1, hexanes:ethyl acetate): R_f = 0.39 (UV/$KMnO_4$)
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.31 (br s, 1H), 7.83 (dd, *J* = 6.9, 1.9 Hz, 1H), 7.51 (dd, *J* = 5.0, 1.9 Hz, 1H), 7.32 (d, *J* = 8.9 Hz, 1H), 7.03 (d, *J* = 2.5 Hz, 1H), 6.89 (dd, *J* = 8.9, 2.4 Hz, 1H), 6.86 (s, 1H), 6.44 (dd, *J* = 6.9, 5.0 Hz, 1H), and, 3.86 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 161.8, 154.7, 149.6, 135.4, 132.2, 131.9, 128.5, 119.9, 114.2, 112.6, 107.6, 101.5, 100.2, and 55.9.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3363 (s), 2955 (w), 2921 (w), 2851 (w), 1698 (s), 1620 (w), 1453 (w), 1220 (m), 1156 (w), 1111 (w), 1034 (w), 806 (w), and 771 (w).
HRMS (ESI): calcd for ([M+H], $C_{14}H_{12}NO_3$)$^+$: 242.0812, found: 242.0810.
mp: 182–186 °C.

3.10 Synthesis of indole–pyrone 7j

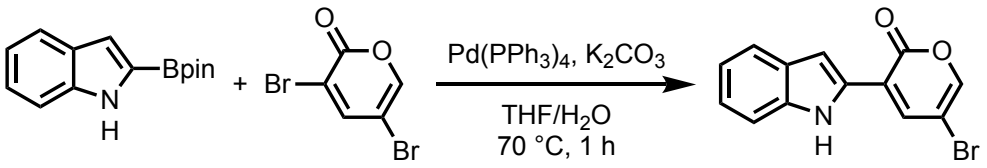


On the basis of the procedure developed by Chattopadhyay et al.,[11] an oven-dried vial was charged with bis(pinacolato)diboron (163 mg, 0.64 mmol, 1.1 equiv), (1,5-cyclooctadiene)(methoxy)iridium(I) dimer (11 mg, 0.02 mmol, 3.0 mol%), ligand **L**[11] (12 mg, 0.04 mmol, 7 mol%), potassium *tert*-butoxide (6 mg, 0.05 mmol, 9 mol%). Tetrahydrofuran (3 mL) and indole **S41** (100 mg, 0.57 mmol, 1.0 equiv) were added sequentially and the resulting mixture was heated in a preheated (80 °C) heating block. After 20 h, the reaction mixture was cooled to 23 °C, filtered through a siliga gel plug eluting with ethyl acetate (5 mL), and the filtrate was concentrated *in vacuo*. The crude residue (~0.13 mmol of **S42**) was used directly in the next step without further purification. *Note: The amount of **S42** in the crude residue was determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard.*

Following General Procedure B, a mixture of crude indole boronate ester **S42** (assuming 0.13 mmol, 1.2 equiv), 3-triflyloxy-2-pyrone **S28**[6] (26 mg, 0.11 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (7.6 mg, 0.01 mmol, 10 mol%), and tripotassium phosphate (69 mg, 0.33 mmol, 3 equiv) in tetrahydrofuran (1 mL) and water (0.1 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (2:1, hexanes:ethyl acetate) to provide indole–pyrone **7j** (25 mg, 0.09 mmol, 87%) as a yellow solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.17 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 11.38 (br s, 1H), 7.91 (d, *J* = 7.4 Hz, 1H), 7.83 – 7.78 (m, 2H), 7.53 – 7.48 (m, 1H), 7.18 – 7.12 (m, 1H), 7.00 – 6.95 (m, 1H), 6.42 – 6.37 (m, 1H), and 4.03 (s, 3H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 167.4, 161.1, 150.3, 136.1, 135.9, 132.7, 129.3, 126.2, 125.6, 119.8, 119.4, 113.2, 107.2, 101.0, and 52.2.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3415 (s), 3105 (w), 3026 (w), 2952 (w), 2850 (w), 1701 (s), 1620 (w), 1587 (w), 1437 (w), 1358 (w), 1276 (s), 1202 (m), 1141 (m), 1109 (w), 1089 (w), 787 (w), and 752 (w).
HRMS (ESI): calcd for ([M+H], $C_{15}H_{12}NO_4$)$^+$: 270.0761, found: 270.0759.
mp: 142–145 °C.

3.11 Synthesis of indole–pyrone 7k

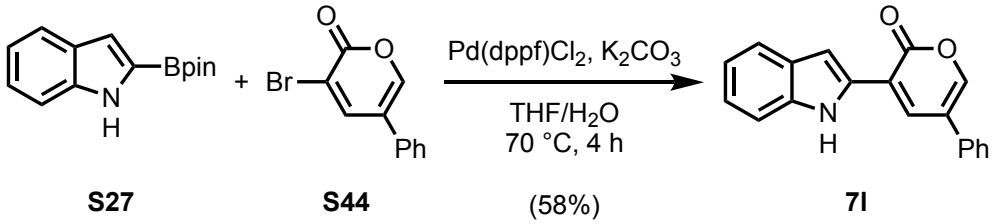


S27 **S43** (46%) **7k**

An oven-dried vial was charged with a magnetic stirring bar, indole boronate ester **S27**[7] (26 mg, 0.11 mmol, 1.1 equiv), 3,5-dibromo-2-pyrone **S43**[12] (25 mg, 0.10 mmol, 1.0 equiv), tetrakis(triphenylphosphine)palladium(0) (12 mg, 0.01 mmol, 10 mol%), and potassium carbonate (27 mg, 0.2 mmol, 2 equiv). The vial was flushed with nitrogen and sealed with a septum cap. Tetrahydrofuran (1 mL) and water (0.1 mL) were added sequentially and the vial was placed in a preheated (70 °C) heating block. After 1 h, the mixture was cooled to 23 °C, and diluted with saturated aqueous ammonium chloride solution (2 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (3×2 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (5 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (12:1, hexanes:ethyl acetate) to provide indole–pyrone **7k** (13 mg, 0.05 mmol, 46%) as a yellow solid.

TLC (8:1, hexanes:ethyl acetate): R_f = 0.23 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.30 (br s, 1H), 7.86 (d, *J* = 2.4 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 2.4 Hz, 1H), 7.43 (d, *J* = 8.3 Hz, 1H), 7.23 (t, *J* = 7.9 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), and 7.01 – 6.96 (m, 1H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 160.1, 147.0, 138.0, 136.8, 130.2, 127.9, 123.9, 120.9, 120.8, 120.4, 111.9, 102.3, and 102.1.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3369 (s), 2923 (w), 2852 (w), 1701 (s), 1605 (w), 1532 (w), 1422 (w), 1322 (w), 1233 (w), 1191 (w), 1069 (w), 784 (m), 747 (m), 728 (m), and 662 (m).
HRMS (ESI): calcd for ([M+H], $C_{13}H_9BrNO_2)^+$: 289.9811, found: 289.9811.
mp: 169–174 °C.

3.12 Synthesis of indole–pyrone 7l

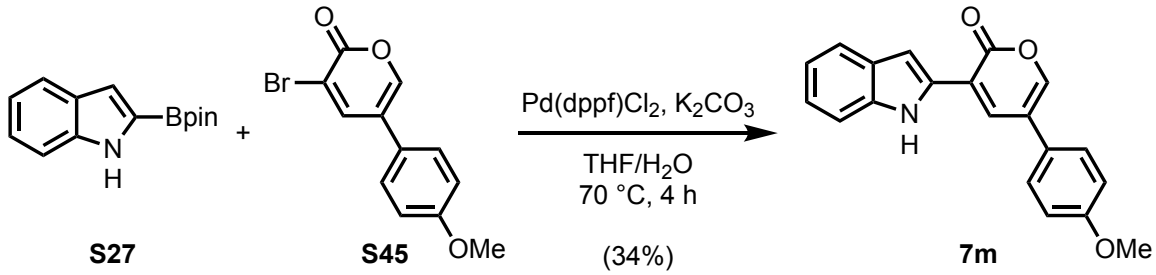


S27 **S44** (58%) **7l**

Following General Procedure C, a mixture of indole boronate ester **S27**[7] (27 mg, 0.11 mmol, 1.1 equiv), 3-bromo-2-pyrone **S44**[13] (24 mg, 0.10 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (7.5 mg, 0.01 mmol, 10 mol%), and potassium carbonate (28 mg, 0.20 mmol, 2 equiv) in tetrahydrofuran (1 mL) and water (0.1 mL) was stirred at 70 °C for 4 h. The crude residue was purified by flash-column chromatography on silica gel (15:1→8:1, hexanes:ethyl acetate) to provide indole–pyrone **7l** (16 mg, 0.06 mmol, 58%) as a yellow solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.32 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, $CDCl_3$) δ 10.44 (br s, 1H), 8.13 (d, *J* = 2.5 Hz, 1H), 7.69 (d, *J* = 2.5 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.52 – 7.42 (m, 6H), 7.25 – 7.21 (m, 1H), 7.15 – 7.11 (m, 1H), and 7.04 – 7.01 (m, 1H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.4, 146.1, 136.7, 136.6, 133.7, 131.7, 129.5, 128.8, 128.1, 126.4, 123.3, 122.3, 120.7, 120.6, 119.2, 111.8, and 101.0.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3405 (s), 3059 (m), 2925 (w), 2857 (w), 1704 (s), 1663 (m), 1629 (w), 1313 (w), 1101 (w), 761 (w), 750 (w), and 697 (w).
HRMS (ESI): calcd for ([M+H], $C_{19}H_{14}NO_2)^+$: 288.1019, found: 288.1017.
mp: 180–183 °C.

3.13 Synthesis of indole–pyrone 7m

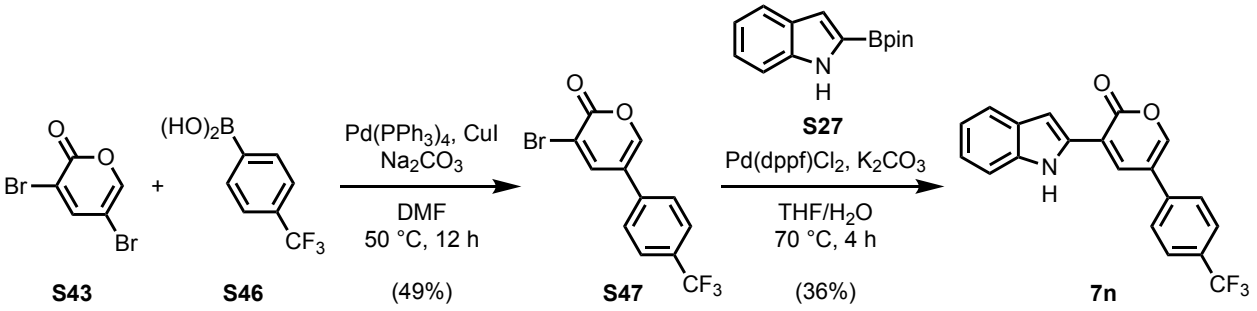


S27 **S45** **7m**

Following General Procedure C, a mixture of indole boronate ester **S27**[7] (152 mg, 0.63 mmol, 1.1 equiv), 3-bromo-2-pyrone **S45**[13] (155 mg, 0.55 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (41 mg, 0.06 mmol, 10 mol%), and potassium carbonate (157 mg, 1.13 mmol, 2 equiv) in tetrahydrofuran (5 mL) and water (0.5 mL) was stirred at 70 °C for 4 h. The crude residue was purified by flash-column chromatography on silica gel (8:1, hexanes:ethyl acetate) to provide indole–pyrone **7m** (60 mg, 0.19 mmol, 34%) as a yellow solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.50 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, $CDCl_3$) δ 10.46 (br s, 1H), 8.12 (d, *J* = 2.4 Hz, 1H), 7.65 (d, *J* = 2.4 Hz, 1H), 7.64 – 7.61 (m, 1H), 7.47 – 7.43 (m, 1H), 7.41 – 7.38 (m, 2H), 7.25 – 7.20 (m, 1H), 7.15 – 7.10 (m, 1H), 7.04 – 7.00 (m, 3H), and 3.87 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.5, 160.2, 145.4, 137.0, 136.6, 131.8, 128.1, 127.7, 126.0, 123.3, 122.0, 120.7, 120.6, 119.1, 114.9, 111.9, 100.8, and 55.6.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3386 (s), 3067 (w), 2927 (m), 2847 (w), 1700 (s), 1626 (w), 1514 (s), 1311 (w), 1249 (m), 1177 (m), 1100 (w), 1025 (w), 827 (w), 793 (w), and 670 (w).
HRMS (ESI): calcd for ([M], $C_{20}H_{15}NO_3$)$^+$: 317.1046, found: 317.1040.
mp: 198–203 °C.

3.14 Synthesis of indole–pyrone 7n



Procedure for 3-bromo-2-pyrone S47 synthesis

An oven-dried vial was charged with a magnetic stirring bar, 3,5-dibromo-2-pyrone **S43**[12] (100 mg, 0.39 mmol, 1.0 equiv), boronic acid **S46** (90 mg, 0.47 mmol, 1.2 equiv), tetrakis(triphenylphosphine)palladium(0) (46 mg, 0.04 mmol, 10 mol%), copper(I) iodide (75 mg, 0.39 mmol, 1.0 equiv), and sodium carbonate (84 mg, 0.79 mmol, 2 equiv). The vial was flushed with nitrogen and sealed with a septum cap. *N*,*N*-dimethylformamide (4 mL) was added and the vial was placed in a preheated (50 °C) heating block. After 12 h, the mixture was cooled to 23 °C, and diluted with saturated aqueous ammonium chloride solution. The layers were separated, the aqueous layer was extracted with ethyl acetate and the combined organic extracts were washed with saturated aqueous sodium chloride solution. The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (8:1, hexanes:ethyl acetate) to provide 3-bromo-2-pyrone **S47** (61 mg, 0.19 mmol, 49%) as an off-white solid.

Procedure for indole–pyrone 7n synthesis

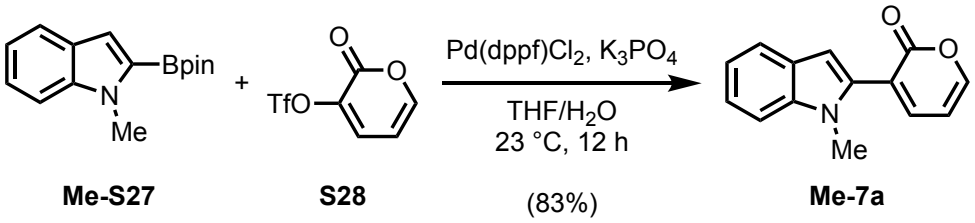
Following General Procedure C, a mixture of indole boronate ester **S27**[7] (86 mg, 0.35 mmol, 1.1 equiv), 3-bromo-2-pyrone **S47** (100 mg, 0.31 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (24 mg, 0.03 mmol, 10 mol%), and potassium carbonate (89 mg, 0.65 mmol, 2 equiv) in tetrahydrofuran (3 mL) and water (0.3 mL) was stirred at 70 °C for 4 h. The crude residue was purified by flash-column chromatography on silica gel (12:1, hexanes:ethyl acetate) to provide indole–pyrone **7n** (40 mg, 0.11 mmol, 36%) as a yellow solid.

Data for 3-bromo-2-pyrone **S47**:

TLC (5:1, hexanes:ethyl acetate): R_f = 0.30 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (d, *J* = 2.4 Hz, 1H), 7.75 (d, *J* = 2.4 Hz, 1H), 7.72 (d, *J* = 8.2 Hz, 2H), and 7.51 (d, *J* = 8.8 Hz, 2H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 157.5, 148.0, 144.4, 136.1, 131.1 (q, *J* = 32.6 Hz), 126.6, 126.5 (q, *J* = 3.6 Hz), 123.9 (q, *J* = 272.6 Hz), 120.5, and 113.3.
^{19}F NMR (376 MHz, $CDCl_3$) δ -61.94.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3074 (w), 2928 (w), 2855 (w), 1738 (s), 1617 (w), 1322 (s), 1275 (w), 1165 (m), 1112 (s), 1069 (s), 1010 (w), 973 (w), 859 (w), 837 (m), and 753 (w).
HRMS (ESI): calcd for ([M+H], $C_{12}H_7BrF_3O_2$)$^+$: 318.9576, found: 318.9573.
mp: 40–44 °C.
Data for indole–pyrone **7n**:

TLC (5:1, hexanes:ethyl acetate): R_f = 0.37 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 10.41 (br s, 1H), 8.11 (d, *J* = 2.5 Hz, 1H), 7.78 – 7.73 (m, 3H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.26 – 7.23 (m, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), and 7.06 – 7.04 (m, 1H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 161.04, 146.57, 137.31, 136.74, 135.58, 131.28, 131.0 (q, *J* = 32.6 Hz), 128.03, 126.78, 126.5 (q, *J* = 3.9 Hz), 124.0 (q, *J* = 272.4 Hz), 123.60, 121.15, 120.80, 120.73, 119.65, 111.89, and 101.36.
^{19}F NMR (376 MHz, $CDCl_3$) δ -61.85.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3415 (s), 3056 (w), 2978 (m), 2928 (w), 1710 (m), 1542 (m), 1458 (w), 1376 (m), 1314 (s), 1265 (m), 1139 (s), 854 (w), and 742 (s).
HRMS (ESI): calcd for ([M], $C_{20}H_{12}F_3NO_2)^+$: 355.0815, found: 355.0816.
mp: 230–235 °C.

3.15 Synthesis of indole–pyrone Me-7a

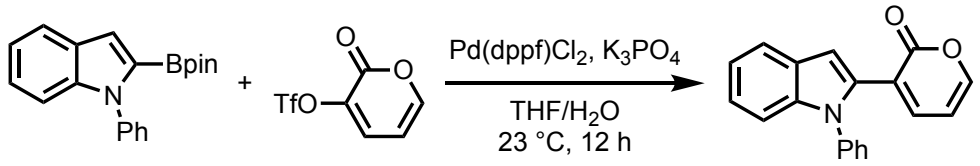


Me-S27 **S28** (83%) **Me-7a**

Following General Procedure B, a mixture of indole boronate ester **Me-S27**[14] (268 mg, 1.04 mmol, 1.1 equiv), 3-triflyloxy-2-pyrone **S28**[6] (230 mg, 0.94 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (70 mg, 0.10 mmol, 10 mol%), and tripotassium phosphate (600 mg, 2.83 mmol, 3 equiv) in tetrahydrofuran (9 mL) and water (1 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (3:1, hexanes:ethyl acetate) to provide indole–pyrone **Me-7a** (177 mg, 0.79 mmol, 83%) as a yellow solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.25 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 7.64 – 7.61 (m, 1H), 7.60 – 7.58 (m, 1H), 7.48 – 7.46 (m, 1H), 7.37 – 7.34 (m, 1H), 7.29 – 7.25 (m, 1H), 7.15 – 7.11 (m, 1H), 6.63 (s, 1H), 6.39 – 6.35 (m, 1H), and 3.71 (s, 3H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 160.9, 152.0, 142.6, 138.7, 134.8, 127.6, 122.7, 121.8, 121.0, 120.0, 109.8, 106.6, 104.2, and 31.6.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3099 (w), 3055 (w), 2942 (w), 1711 (s), 1624 (w), 1466 (m), 1338 (w), 1236 (w), 1101 (m), 1080 (w), 972 (w), 775 (m), and 750 (m).
HRMS (ESI): calcd for ([M+H], $C_{14}H_{12}NO_2)^+$: 226.0863, found: 226.0863.
mp: 127–130 °C.

3.16 Synthesis of indole–pyrone Ph-7a

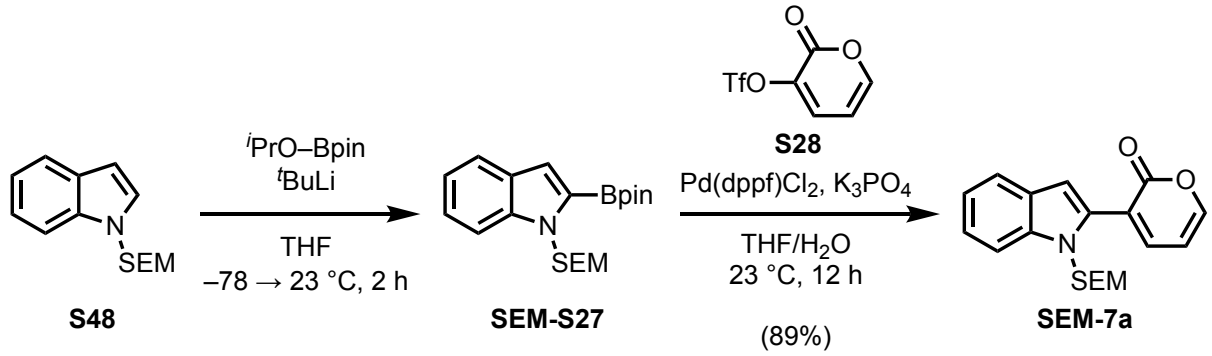


Ph-S27 **S28** (95%) **Ph-7a**

Following General Procedure B, a mixture of indole boronate ester **Ph-S27**[14] (200 mg, 0.63 mmol, 1.2 equiv), 3-triflyloxy-2-pyrone **S28**[6] (125 mg, 0.51 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (37 mg, 0.05 mmol, 10 mol%), and tripotassium phosphate (320 mg, 1.50 mmol, 3 equiv) in tetrahydrofuran (5 mL) and water (0.5 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (5:1, hexanes:ethyl acetate) to provide indole–pyrone **Ph-7a** (140 mg, 0.49 mmol, 95%) as a yellow solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.30 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 7.72 – 7.68 (m, 1H), 7.51 – 7.46 (m, 2H), 7.42 – 7.36 (m, 2H), 7.35 – 7.30 (m, 2H), 7.28 – 7.24 (m, 1H), 7.23 – 7.16 (m, 3H), 7.00 (dd, *J* = 6.9, 2.1 Hz, 1H), and 6.10 (dd, *J* = 6.8, 5.0 Hz, 1H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 160.4, 150.6, 140.5, 139.4, 138.4, 133.0, 129.7, 127.9, 127.74, 127.72, 123.5, 121.4, 121.0, 120.6, 110.6, 107.7, and 106.2.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3099 (w), 3057 (w), 1720 (s), 1625 (w), 1595 (w), 1497 (m), 1452 (w), 1388 (w), 1336 (w), 1235 (w), 1114 (w), 1092 (w), 761 (m), and 699 (w).
HRMS (ESI): calcd for ([M+H], $C_{19}H_{14}NO_2)^+$: 288.1025, found: 288.1021.
mp: 140–143 °C.

3.17 Synthesis of indole–pyrone SEM-7a

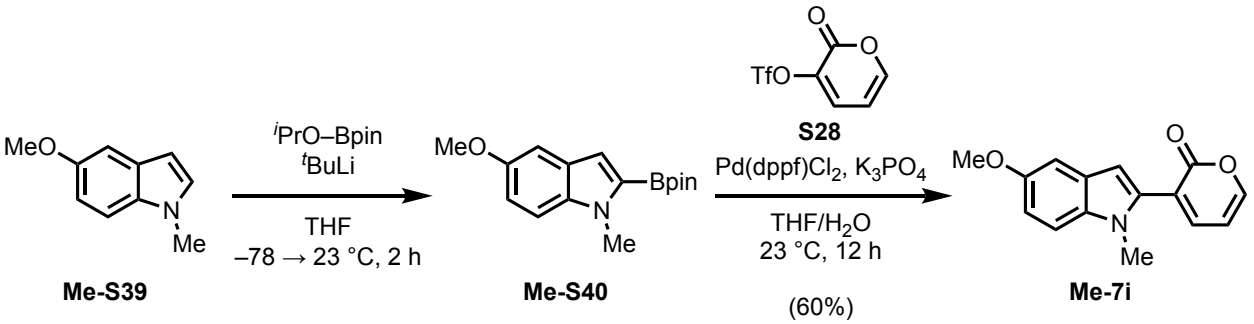


An oven-dried flask was charged with a magnetic stirring bar and indole **S48** (1.0 g, 4.05 mmol, 1.0 equiv). The flask was flushed with nitrogen and sealed with a septum. Tetrahydrofuran (8 mL) was added and the resulting solution was cooled to –78 °C. To the reaction mixture was added dropwise *tert*-butyllithium solution (1.6 M in pentane, 2.8 mL, 4.48 mmol, 1.1 equiv) and the resulting solution was stirred at –78 °C. After 30 min, the mixture was allowed to gradually warm to 23 °C. After 2 h at 23 °C, the reaction mixture was cooled back to –78 °C, and 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1 mL, 4.90 mmol, 1.2 equiv) was added dropwise. After stirring at –78 °C for 30 min, the mixture was allowed to gradually warm to 23 °C. After 2 h at 23 °C, the reaction mixture was diluted with water (6 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (3×5 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (5 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue (~0.91 mmol of **SEM-S27**) was used directly in the next step without further purification. *Note: The amount of **SEM-S27** in the crude residue was determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard.*

Following General Procedure B, a mixture of crude indole boronate ester **SEM-S27** (assuming 0.91 mmol, 1.2 equiv), 3-triflyloxy-2-pyrone **S28**[6] (187 mg, 0.77 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (56 mg, 0.08 mmol, 10 mol%), and tripotassium phosphate (488 mg, 2.30 mmol, 3 equiv) in tetrahydrofuran (7 mL) and water (0.7 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (5:1, hexanes:ethyl acetate) to provide indole–pyrone **SEM-7a** (232 mg, 0.68 mmol, 89%) as a yellow solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.48 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 6.7, 2.2 Hz, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.56 (dd, *J* = 5.1, 2.2 Hz, 1H), 7.49 (d, *J* = 8.3 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.18 – 7.14 (m, 1H), 6.86 (s, 1H), 6.37 (dd, *J* = 6.7, 5.1 Hz, 1H), 5.47 (s, 2H), 3.52 – 3.46 (m, 2H), 0.89 – 0.83 (m, 2H), and -0.06 (s, 9H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 160.9, 151.4, 141.8, 138.8, 133.9, 128.0, 123.3, 121.3, 120.8, 110.3, 106.8, 106.6, 73.7, 66.2, 18.0, and -1.3. (*Missing one carbon signal*)
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3097 (w), 3056 (w), 2952 (m), 2894 (m), 1715 (s), 1625 (w), 1459 (w), 1336 (w), 1311 (w), 1248 (m), 1165 (w), 1071 (s), 858 (m), 835 (s), and 739 (m).
HRMS (ESI): calcd for ([M+H], $C_{19}H_{24}NO_3Si)^+$: 342.1525, found: 342.1531.
mp: 59–62 °C.

3.18 Synthesis of indole–pyrone Me-7i

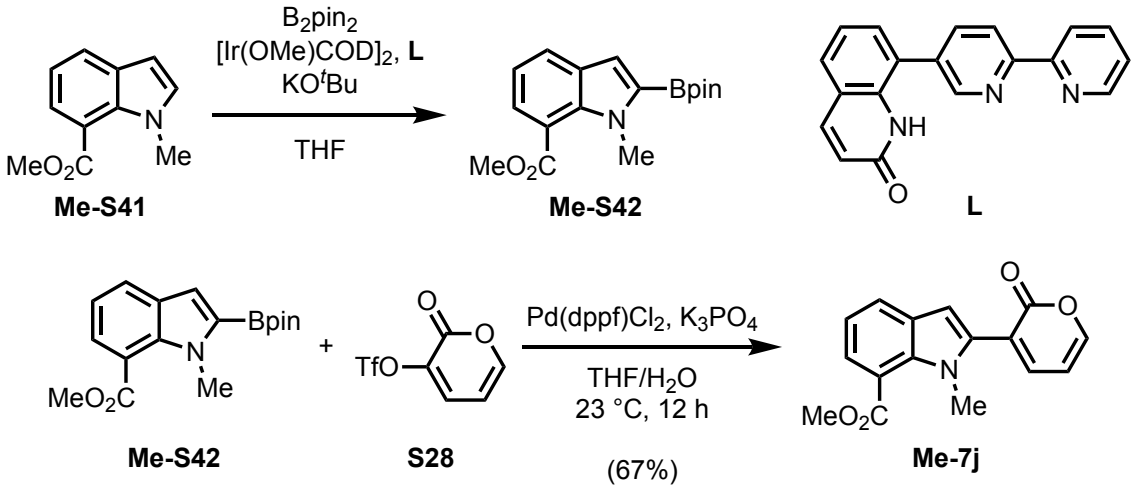


An oven-dried flask was charged with a magnetic stirring bar and indole **Me-S39** (50 mg, 0.30 mmol, 1.0 equiv). The flask was flushed with nitrogen and sealed with a septum. Tetrahydrofuran (0.6 mL) was added and the resulting solution was cooled to –78 °C. To the reaction mixture was added dropwise *tert*-butyllithium solution (1.6 M in pentane, 0.22 mL, 0.35 mmol, 1.1 equiv) and the resulting solution was stirred at –78 °C. After 30 min, the mixture was allowed to gradually warm to 23 °C. After 2 h, the reaction mixture was cooled back to –78 °C, and 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (76 μL, 0.37 mmol, 1.2 equiv) was added dropwise. After stirring at –78 °C for 30 min, the mixture was allowed to gradually warm to 23 °C. After 2 h, the reaction mixture was diluted with water (1 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (3×1 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (2 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue (~0.14 mmol of **Me-S40**) was directly used in the next step without further purification. *Note: The amount of **Me-S40** in the crude residue was determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard.*

Following General Procedure B, a mixture of crude indole boronate ester **Me-S40** (assuming 0.14 mmol, 1.3 equiv), 3-triflyloxy-2-pyrone **S28**[6] (27 mg, 0.11 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (8.3 mg, 0.01 mmol, 10 mol%), and tripotassium phosphate (72 mg, 0.34 mmol, 3 equiv) in tetrahydrofuran (1.1 mL) and water (0.11 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (3:1, hexanes:ethyl acetate) to provide indole–pyrone **Me-7i** (17 mg, 0.07 mmol, 60%) as a yellow solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.12 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 5.2, 2.1 Hz, 1H), 7.45 (dd, *J* = 6.7, 2.1 Hz, 1H), 7.24 (d, *J* = 9.0 Hz, 1H), 7.06 (d, *J* = 2.4 Hz, 1H), 6.92 (dd, *J* = 8.9, 2.5 Hz, 1H), 6.55 (s, 1H), 6.37 (dd, *J* = 6.6, 5.1 Hz, 1H), 3.85 (s, 3H), and 3.68 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 160.8, 154.5, 151.9, 142.3, 135.2, 134.3, 127.9, 121.9, 113.3, 110.6, 106.6, 103.9, 102.4, 56.1, and 31.8.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3102 (w), 2932 (m), 2834 (w), 1718 (s), 1622 (m), 1519 (w), 1482 (m), 1453 (w), 1218 (s), 1140 (m), 1102 (m), 1032 (w), and 778 (m).
HRMS (ESI): calcd for ([M+H], $C_{15}H_{14}NO_3$)$^+$: 256.0968, found: 256.0967.
mp: 134–140 °C.

3.19 Synthesis of indole–pyrone Me-7j

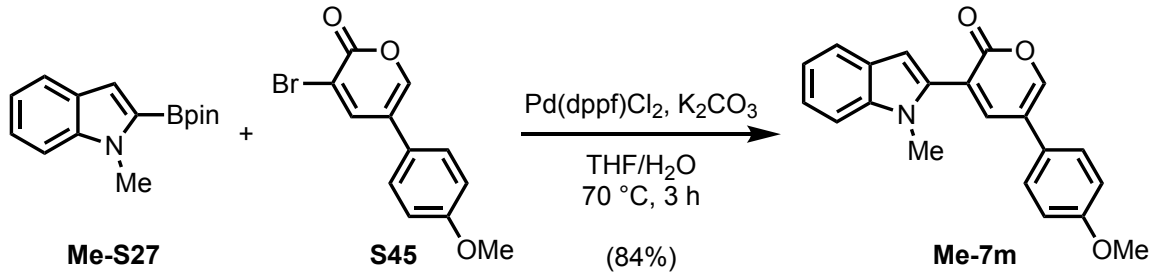


On the basis of the procedure developed by Chattopadhyay et al.,[11] an oven-dried vial was charged with bis(pinacolato)diboron (81 mg, 0.32 mmol, 1.0 equiv), (1,5-cyclooctadiene)(methoxy)iridium(I) dimer (9.0 mg, 0.01 mmol, 3.0 mol%), ligand **L**[11] (7.0 mg, 0.02 mmol, 7 mol%), potassium *tert*-butoxide (4.0 mg, 0.03 mmol, 9 mol%). A solution of indole **Me-S41** (58 mg, 0.31 mmol, 1.0 equiv) in tetrahydrofuran (1.5 mL) was added and the resulting mixture was heated in a preheated (80 °C) heating block. After 18 h, the reaction mixture was cooled to 23 °C, filtered through a silica gel plug eluting with ethyl acetate (5 mL), and the filtrate was concentrated *in vacuo*. The crude residue (~0.25 mmol of **Me-S42**) was used directly in the next step without further purification. *Note: The amount of **Me-S42** in the crude residue was determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard.*

Following General Procedure B, a mixture of crude indole boronate ester **Me-S42** (assuming 0.25 mmol, 1.2 equiv), 3-triflyloxy-2-pyrone **S28**[6] (46 mg, 0.19 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (15 mg, 0.02 mmol, 10 mol%), and tripotassium phosphate (128 mg, 0.60 mmol, 3 equiv) in tetrahydrofuran (2 mL) and water (0.2 mL) was stirred at 23 °C for 12 h. The crude residue was purified by flash-column chromatography on silica gel (2:1, hexanes:ethyl acetate) to provide indole–pyrone **Me-7j** (36 mg, 0.13 mmol, 67%) as a yellow solid.

TLC (1:1, hexanes:ethyl acetate): R_f = 0.37 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 – 7.75 (m, 1H), 7.71 – 7.67 (m, 1H), 7.59 (dd, *J* = 5.1, 2.2 Hz, 1H), 7.47 (dd, *J* = 6.6, 2.2 Hz, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.82 (s, 1H), 6.39 (dd, *J* = 6.6, 5.1 Hz, 1H), 3.98 (s, 3H), and 3.67 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.2, 160.6, 152.0, 142.4, 137.2, 136.6, 130.0, 126.1, 125.5, 121.2, 119.4, 116.6, 106.5, 105.7, 52.3, and 35.7.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3415 (s), 3105 (w), 3026 (w), 2952 (w), 2850 (w), 1701 (s), 1620 (w), 1587 (w), 1437 (w), 1358 (w), 1276 (s), 1202 (m), 1141 (m), 1109 (w), 1089 (w), 787 (w), and 752 (w).
HRMS (ESI): calcd for ([M+H], $C_{16}H_{14}NO_4$)$^+$: 284.0923, found: 284.0925.
mp: 154–158 °C.

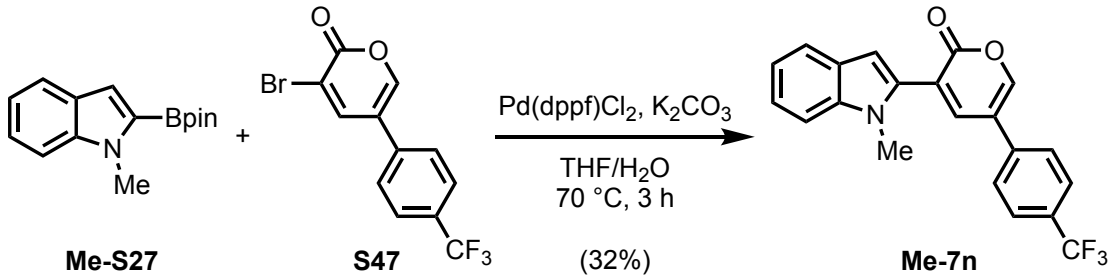
3.20 Synthesis of indole–pyrone Me-7m



Following General Procedure C, a mixture of indole boronate ester **Me-S27**[14] (88 mg, 0.34 mmol, 1.2 equiv), 3-bromo-2-pyrone **S45**[13] (80 mg, 0.29 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (22 mg, 0.03 mmol, 10 mol%), and potassium carbonate (79 mg, 0.57 mmol, 2 equiv) in tetrahydrofuran (3 mL) and water (0.3 mL) was stirred at 70 °C for 3 h. The crude residue was purified by flash-column chromatography on silica gel (8:1, hexanes:ethyl acetate) to provide indole–pyrone **Me-7m** (79 mg, 0.24 mmol, 84%) as a yellow solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.32 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 2.7 Hz, 1H), 7.73 (d, *J* = 2.6 Hz, 1H), 7.65 – 7.61 (m, 1H), 7.39 – 7.34 (m, 3H), 7.30 – 7.26 (m, 1H), 7.16 – 7.12 (m, 1H), 7.01 – 6.97 (m, 2H), 6.69 (s, 1H), 3.85 (s, 3H), 3.76 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 160.5, 160.1, 147.4, 143.8, 138.8, 134.8, 127.6, 127.4, 125.8, 122.8, 121.2, 121.02, 120.99, 120.1, 114.9, 109.8, 104.5, 55.6, and 31.7.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3054 (w), 2933 (w), 2838 (w), 1715 (s), 1610 (w), 1514 (m), 1465 (w), 1284 (w), 1250 (m), 1177 (m), 830 (w), and 750 (w).
HRMS (ESI): calcd for ([M+H], $C_{21}H_{18}NO_3$)$^+$: 332.1281, found: 332.1284.
mp: 105–110 °C.

3.21 Synthesis of indole–pyrone Me-7n



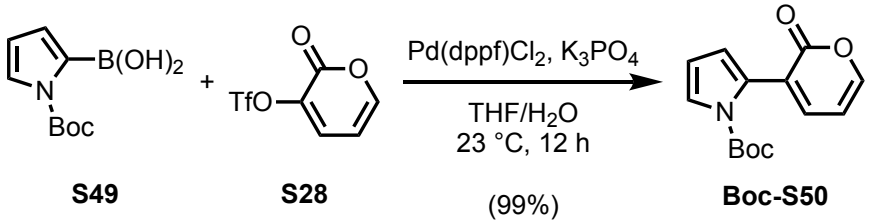
Me-S27 **S47** **Me-7n**

Following General Procedure C, a mixture of indole boronate ester **Me-S27**[14] (46 mg, 0.18 mmol, 1.2 equiv), 3-bromo-2-pyrone **S47** (48 mg, 0.15 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (12 mg, 0.02 mmol, 10 mol%), and potassium carbonate (41 mg, 0.30 mmol, 2 equiv) in tetrahydrofuran (1.5 mL) and water (0.2 mL) was stirred at 70 °C for 3 h. The crude residue was purified by flash-column chromatography on silica gel (12:1, hexanes:ethyl acetate) to provide indole–pyrone **Me-7n** (18 mg, 0.05 mmol, 32%) as a yellow solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.47 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85 (d, *J* = 2.7 Hz, 1H), 7.77 (d, *J* = 2.7 Hz, 1H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.65 – 7.62 (m, 1H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.40 – 7.35 (m, 1H), 7.31 – 7.27 (m, 1H), 7.16 – 7.12 (m, 1H), 6.70 (s, 1H), and 3.76 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 160.0, 148.9, 142.5, 139.0, 137.1, 134.4, 130.9 (q, *J* = 32.6 Hz), 127.6, 126.53, 126.52 (q, *J* = 3.4 Hz), 124.0 (q, *J* = 272.0 Hz), 123.0, 121.8, 121.1, 120.2, 120.2, 109.9, 104.8, and 31.8.
^{19}F NMR (376 MHz, $CDCl_3$) δ -61.87.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3059 (w), 2924 (m), 2851 (w), 1724 (s), 1617 (w), 1466 (w), 1326 (s), 1167 (w), 1120 (m), 1069 (m), and 839 (w).
HRMS (ESI): calcd for ([M+H], $C_{21}H_{15}F_3NO_3$)$^+$: 370.1049, found: 370.1044.
mp: 162–169 °C.

4 Synthesis of other N-Heterocyclic–Pyrone adducts

4.1 Synthesis of pyrrole–pyrone Boc-S50

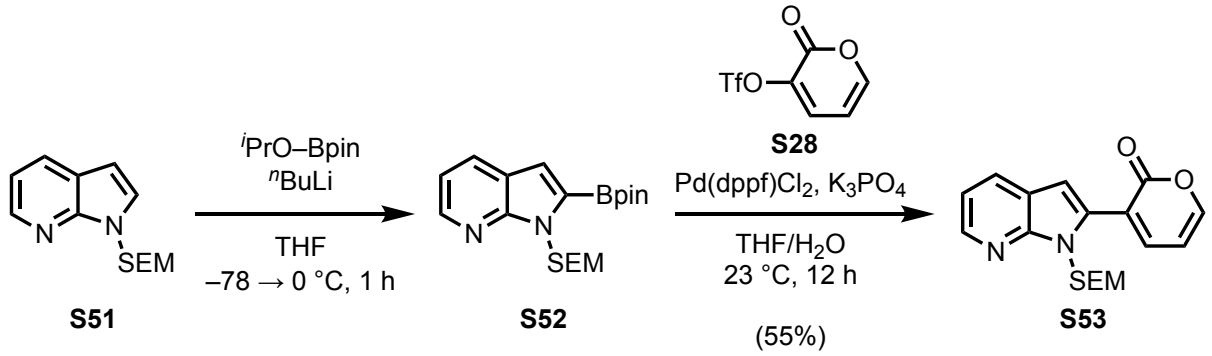


S49 **S28** **Boc-S50**

An oven-dried vial was charged with a magnetic stirring bar, pyrrole boronic acid **S49** (100 mg, 0.47 mmol, 1.2 equiv), 3-triflyloxy-2-pyrone **S28**[6] (100 mg, 0.41 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (31 mg, 0.04 mmol, 10 mol%), and tripotassium phosphate (252 mg, 1.19 mmol, 3 equiv). The vial was flushed with nitrogen and sealed with a septum cap. Tetrahydrofuran (4.5 mL) and water (0.5 mL) were added sequentially and the resulting mixture was stirred at 23 °C. After 12 h, the mixture was diluted with saturated aqueous ammonium chloride solution (5 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (3×5 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (5 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (3:1, hexanes:ethyl acetate) to provide pyrrole–pyrone **Boc-S50** (105 mg, 0.40 mmol, 99%) as a yellow oil.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.40 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 5.1, 2.2 Hz, 1H), 7.38 – 7.35 (m, 1H), 7.25 (dd, *J* = 6.5, 2.2 Hz, 1H), 6.26 – 6.22 (m, 2H), 6.21 – 6.19 (m, 1H), and 1.49 (s, 9H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 161.3, 150.6, 148.9, 138.2, 127.9, 124.5, 123.4, 115.6, 110.6, 106.2, 84.2, and 27.8.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3106 (w), 3058 (w), 2981 (m), 2935 (w), 1719 (s), 1477 (w), 1313 (s), 1147 (s), 1103 (m), 1086 (m), 1062 (w), 847 (w), 769 (w), and 729 (s).
HRMS (ESI): calcd for ([M+H], $C_{14}H_{16}NO_4$)$^+$: 262.1074, found: 262.1076.

4.2 Synthesis of 7-azaindole–pyrone S53

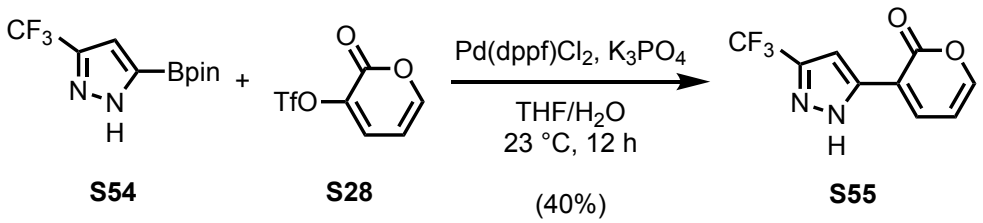


An oven-dried flask was charged with a magnetic stirring bar and 7-azaindole **S51** (515 mg, 2.08 mmol, 1.0 equiv). The flask was flushed with nitrogen and sealed with a septum. Tetrahydrofuran (20 mL) was added and the resulting solution was cooled to –78 °C. To the reaction mixture was added dropwise a *n*-butyllithium solution (2.5 M in hexanes, 1.6 mL, 4.00 mmol, 2.0 equiv) and the resulting solution was allowed to gradually warm to 0 °C. After 30 min, to the mixture was added dropwise 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.8 mL, 4.00 mmol, 2.0 equiv) at 0 °C. After 30 min, the reaction mixture was allowed to warm to 23 °C and diluted with water (20 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (3×15 mL). The combined organic extracts were washed with saturated aqueous sodium chloride solution (30 mL) and the organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue (~1.22 mmol of **S52**) was used directly in the next step without further purification. *Note: The amount of **S52** in the crude residue was determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard.*

An oven-dried vial was charged with a magnetic stirring bar, crude 7-azaindole boronate ester **S52** (assuming 1.22 mmol, 1.2 equiv), 3-triflyloxy-2-pyrone **S28**[6] (240 mg, 0.98 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (73 mg, 0.10 mmol, 10 mol%), and tripotassium phosphate (640 mg, 3.02 mmol, 3 equiv). The vial was flushed with nitrogen and sealed with a septum cap. Tetrahydrofuran (10 mL) and water (1 mL) were added sequentially and the resulting mixture was stirred at 23 °C. After 12 h, the mixture was diluted with saturated aqueous ammonium chloride solution (10 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (3×10 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (10 mL). The combined organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (5:1, hexanes:ethyl acetate) to provide 7-azaindole–pyrone **S53** (185 mg, 0.54 mmol, 55%) as a yellow oil.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.32 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.36 – 8.33 (m, 1H), 7.99 – 7.94 (m, 1H), 7.93 – 7.89 (m, 1H), 7.57 – 7.53 (m, 1H), 7.12 – 7.08 (m, 1H), 6.97 (s, 1H), 6.42 – 6.36 (m, 1H), 5.71 (s, 2H), 3.70 – 3.65 (m, 2H), 0.94 – 0.87 (m, 2H), and -0.07 (s, 9H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 160.7, 151.3, 149.9, 144.2, 141.7, 133.9, 129.1, 120.5, 120.0, 117.2, 106.7, 105.0, 71.1, 66.5, 18.0, and -1.4.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3050 (w), 2952 (m), 2894 (m), 1718 (s), 1626 (w), 1572 (w), 1429 (w), 1318 (w), 1246 (m), 1158 (w), 1073 (s), 859 (m), 835 (s), and 773 (s).
HRMS (ESI): calcd for ([M+H], $C_{18}H_{23}N_2O_3Si)^+$: 343.1472, found: 343.1468.

4.3 Synthesis of pyrazole–pyrone S55

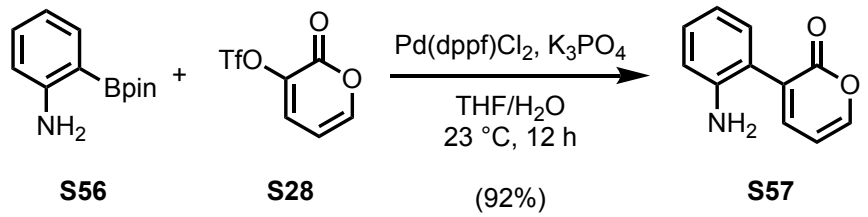


S54 **S28** **S55**

An oven-dried vial was charged with a magnetic stirring bar, pyrazole boronate ester **S54**[5] (90 mg, 0.34 mmol, 1.1 equiv), 3-triflyloxy-2-pyrone **S28**[6] (76 mg, 0.31 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (25 mg, 0.03 mmol, 10 mol%), and tripotassium phosphate (195 mg, 0.92 mmol, 3 equiv). The vial was flushed with nitrogen and sealed with a septum cap. Tetrahydrofuran (3 mL) and water (0.3 mL) were added sequentially and the resulting mixture was stirred at 23 °C. After 12 h, the mixture was diluted with saturated aqueous ammonium chloride solution (3 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (3×3 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (3 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (3:1→1:1, hexanes:ethyl acetate) to provide pyrazole–pyrone **S55** (28 mg, 0.12 mmol, 40%) as an off-white solid.

TLC (1:1, hexanes:ethyl acetate): R_f = 0.43 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 12.18 (br s, 1H), 7.84 – 7.74 (m, 1H), 7.61 (dd, *J* = 5.2, 2.1 Hz, 1H), 6.89 (s, 1H), and 6.56 – 6.45 (m, 1H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 160.9, 151.6, 143.8 (q, *J* = 38.7 Hz), 138.3, 121.3 (q, *J* = 268.7 Hz), 116.4, 107.2, and 101.3 (q, *J* = 2.2 Hz). (*Missing one carbon signal*)
^{19}F NMR (376 MHz, $CDCl_3$) δ -61.46.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3305 (s), 3136 (w), 3048 (w), 2925 (w), 1722 (s), 1566 (w), 1541 (w), 1496 (w), 1389 (w), 1265 (s), 1235 (w), 1159 (s), 1144 (m), 1112 (m), 971 (s), 818 (w), and 769 (m).
HRMS (ESI): calcd for ([M+H], $C_9H_6F_3N_2O_2)^+$: 231.0376, found: 231.0374.
mp: 166–170 °C.

4.4 Synthesis of aniline–pyrone S57



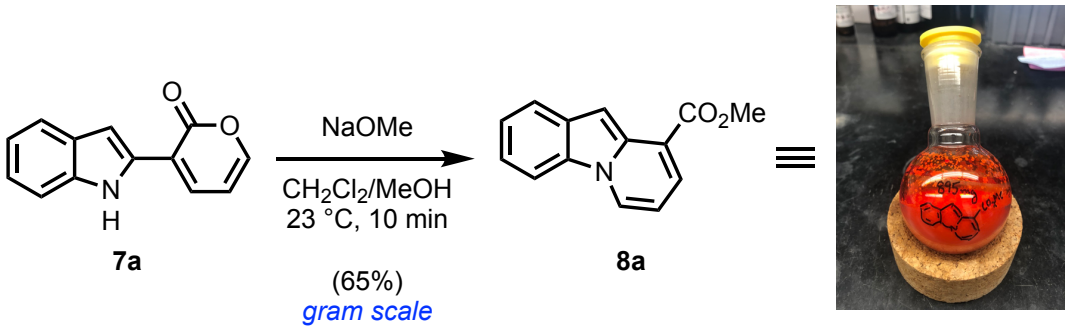
S56 **S28** (92%) **S57**

An oven-dried vial was charged with a magnetic stirring bar, aniline boronate ester **S56**[15] (347 mg, 1.58 mmol, 1.1 equiv), 3-triflyloxy-2-pyrone **S28**[6] (351 mg, 1.44 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (103 mg, 0.14 mmol, 10 mol%), and tripotassium phosphate (920 mg, 4.33 mmol, 3 equiv). The vial was flushed with nitrogen and sealed with a septum cap. Tetrahydrofuran (14 mL) and water (1.4 mL) were added sequentially and the resulting mixture was stirred at 23 °C. After 12 h, the mixture was diluted with saturated aqueous ammonium chloride solution (15 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (3×15 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (20 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (1:1, hexanes:ethyl acetate) to provide aniline–pyrone **S57** (249 mg, 1.33 mmol, 92%) as a yellow solid.

TLC (1:1, hexanes:ethyl acetate): R_f = 0.35 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 5.1, 2.2 Hz, 1H), 7.42 (dd, *J* = 6.7, 2.3 Hz, 1H), 7.23 – 7.17 (m, 1H), 7.12 – 7.05 (m, 1H), 6.85 – 6.80 (m, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 6.41 – 6.32 (m, 1H), and 3.92 (br s, 2H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 161.5, 151.2, 145.2, 142.9, 131.1, 130.1, 128.9, 122.0, 119.2, 117.4, and 106.9.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3425 (s), 3366 (s), 3242 (w), 3098 (w), 3034 (w), 1702 (s), 1624 (m), 1555 (w), 1494 (w), 1453 (w), 1343 (w), 1090 (w), 968 (w), 785 (m), and 753 (m).
HRMS (ESI): calcd for ([M+H], $C_{11}H_{10}NO_2$)$^+$: 188.0706, found: 188.0703.
mp: 145–148 °C.

5 Synthesis of pyrido[1,2-*a*]indoles

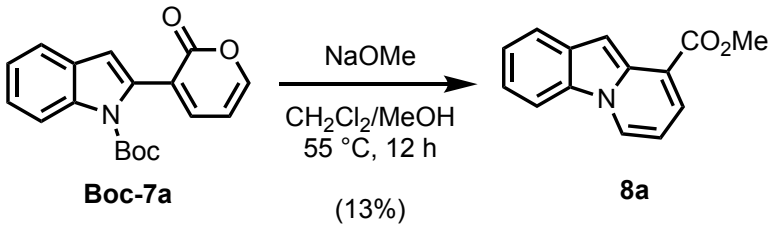
5.1 Synthesis of pyrido[1,2-*a*]indole 8a



Following General Procedure D, a solution of indole–pyrone **7a** (1.3 g, 6.16 mmol, 1.0 equiv) in dichloromethane (60 mL) and methanol (60 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 1.7 mL, 7.43 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was stirred at the same temperature for 10 min. The crude residue was purified by flash column chromatography on silica gel (12:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8a** (895 mg, 3.98 mmol, 65%) as a red solid. The characterization data of **8a** were in full agreement with the values reported in Section 2.3 of the SI.

Recrystallization (ethyl acetate/dichloromethane) of the product gave crystals suitable for X-ray diffraction (see Section 11)

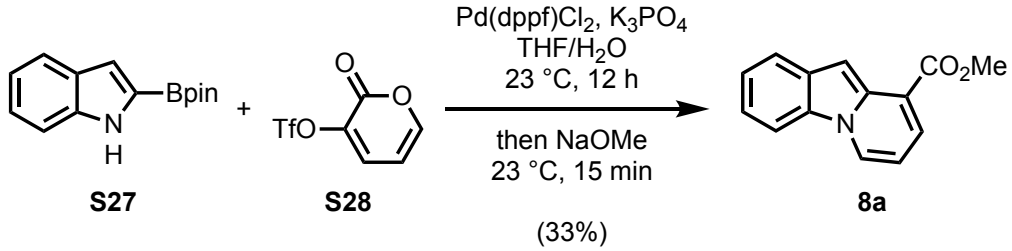
5.2 Synthesis of pyrido[1,2-*a*]indole 8a from indole–pyrone Boc-7a



Boc-7a (13%) **8a**

A vial was charged with a magnetic stirring bar and indole–pyrone **Boc-7a** (32 mg, 0.10 mmol, 1.0 equiv). Dichloromethane (1 mL) and methanol (1 mL) were added sequentially and the resulting solution was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.03 mL, 0.13 mmol, 1.2 equiv) at 23 °C. The resulting mixture was heated in a preheated (55 °C) heating block with stirring for 12 h. The mixture was then cooled to 23 °C, and diluted with saturated aqueous ammonium chloride solution (1 mL). The layers were separated, the aqueous layer was extracted with dichloromethane (3×2 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (2 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (12:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8a** (3.0 mg, 0.01 mmol, 13%) as a red solid. The characterization data of **8a** were in full agreement with the values reported in Section 2.3 of the SI.

5.3 One-pot synthesis of pyrido[1,2-*a*]indole 8a from 3-triflyloxy-2-pyrone S28

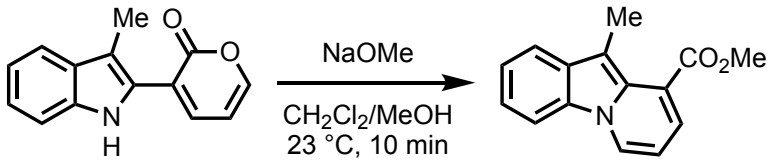


S27 **S28** **8a**

(33%)

An oven-dried vial was charged with a magnetic stirring bar, indole boronate ester **S27**[7] (56 mg, 0.23 mmol, 1.2 equiv), 3-triflyloxy-2-pyrone **S28**[6] (50 mg, 0.21 mmol, 1.0 equiv), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) (15 mg, 0.02 mmol, 10 mol%), and tripotassium phosphate (126 mg, 0.59 mmol, 3 equiv). The vial was flushed with nitrogen and sealed with a septum cap. Tetrahydrofuran (2 mL) and water (0.2 mL) were added sequentially and the resulting mixture was stirred at 23 °C. After 12 h, to the mixture was added a solution of sodium methoxide (25 wt% in MeOH, 0.15 mL, 0.66 mmol, 3.0 equiv) at 23 °C. After 10 min, the reaction mixture was diluted with saturated aqueous ammonium chloride solution (2 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (3×3 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (3 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (15:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8a** (15 mg, 0.07 mmol, 33%) as a red solid. The characterization data of **8a** were in full agreement with the values reported in Section 2.3 of the SI.

5.4 Synthesis of pyrido[1,2-*a*]indole 8b

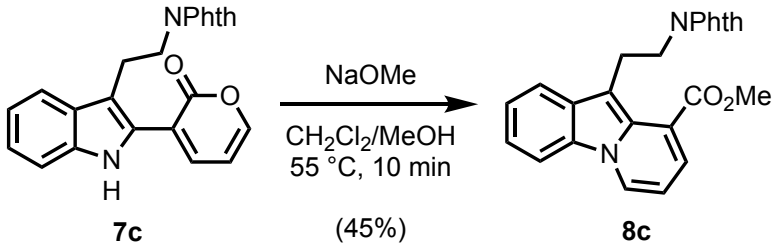


7b (60%) **8b**

Following General Procedure D, a solution of indole–pyrone **7b** (23 mg, 0.10 mmol, 1.0 equiv) in dichloromethane (1 mL) and methanol (1 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.03 mL, 0.13 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was stirred at the same temperature for 10 min. The crude residue was purified by flash column chromatography on silica gel (15:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8b** (15 mg, 0.06 mmol, 60%) as a red solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.52 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (dd, *J* = 7.1, 1.3 Hz, 1H), 7.87 – 7.79 (m, 2H), 7.47 – 7.41 (m, 1H), 7.39 (dd, *J* = 6.7, 1.1 Hz, 1H), 7.37 – 7.31 (m, 1H), 6.39 (t, *J* = 6.8 Hz, 1H), 3.99 (s, 3H), and 2.54 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 167.4, 130.5, 128.9, 128.7, 128.0, 126.7, 123.2, 123.1, 120.7, 119.2, 110.0, 105.1, 101.4, 52.3, and 10.5.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3346 (s), 3057 (w), 2949 (m), 2923 (w), 2867 (w), 1720 (s), 1604 (w), 1527 (w), 1463 (m), 1346 (w), 1269 (s), 1238 (w), 1194 (m), 1144 (w), 1082 (w), and 738 (s).
HRMS (ESI): calcd for ([M], $C_{15}H_{13}NO_2)^+$: 239.0941, found: 239.0941.
mp: 54–57 °C.

5.5 Synthesis of pyrido[1,2-*a*]indole 8c

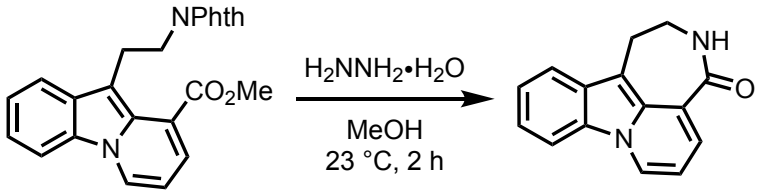


7c **8c**

Following General Procedure D, a solution of indole–pyrone **7c** (28 mg, 0.07 mmol, 1.0 equiv) in dichloromethane (0.75 mL) and methanol (0.75 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.02 mL, 0.09 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was heated at 55 °C with stirring and held at this temperature for 10 min. The crude residue was purified by flash column chromatography on silica gel (3:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8c** (13 mg, 0.04 mmol, 45%) as a red solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.47 (UV/$KMnO_4$)
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (dd, *J* = 7.0, 1.2 Hz, 1H), 8.09 – 8.05 (m, 1H), 7.86 – 7.83 (m, 1H), 7.81 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.69 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.48 (dd, *J* = 6.7, 1.2 Hz, 1H), 7.45 – 7.41 (m, 1H), 7.36 – 7.30 (m, 1H), 6.45 (t, *J* = 6.9 Hz, 1H), 4.12 (s, 3H), 3.99 – 3.92 (m, 2H), and 3.53 – 3.46 (m, 2H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.5, 167.2, 133.9, 132.4, 130.3, 129.2, 129.1, 128.2, 127.9, 123.7, 123.2, 123.0, 121.0, 119.3, 110.1, 105.5, 102.3, 52.9, 38.7, and 24.5.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3094 (w), 3057 (w), 2950 (w), 2929 (w), 2853 (w), 1708 (s), 1528 (w), 1466 (w), 1392 (m), 1349 (w), 1271 (m), 1194 (w), 1115 (w), 741 (m), and 719 (m).
HRMS (ESI): calcd for ([M+H], $C_{24}H_{19}N_2O_4)^+$: 399.1339, found: 399.1338.
mp: 180–182 °C.

5.6 Synthesis of tetracyclic lactam 8d from pyrido[1,2-*a*]indole 8c

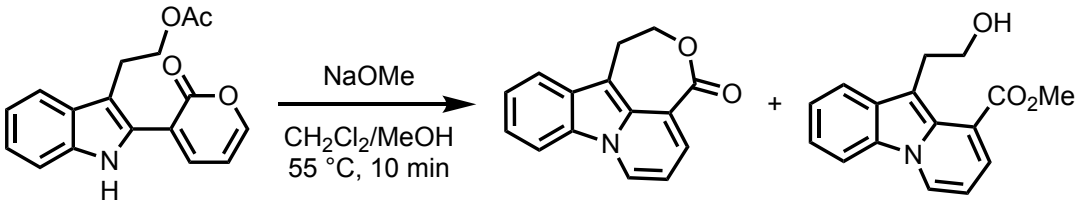


8c (75%) **8d**

An oven-dried vial was charged with a magnetic stirring bar and pyrido[1,2-*a*]indole **8c** (18 mg, 0.045 mmol, 1.0 equiv). The vial was flushed with nitrogen and sealed with a septum cap. Methanol (2 mL) was added and the resulting solution was treated with hydrazine monohydrate (0.01 mL, 0.20 mmol, 4.0 equiv) at 23 °C. After 2 h, the reaction mixture was diluted with saturated aqueous ammonium chloride solution (1 mL) and dichloromethane (2 mL). The layers were separated, the aqueous layer was extracted with dichloromethane (3×2 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (2 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (5% methanol in ethyl acetate) to provide the tetracyclic lactam **8d** (8 mg, 0.03 mmol, 75%) as a carrot orange solid.

TLC (100% ethyl acetate): R_f = 0.46 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 7.1 Hz, 1H), 7.94 – 7.88 (m, 2H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.48 – 7.42 (m, 1H), 7.39 – 7.31 (m, 1H), 6.59 – 6.51 (m, 2H), 3.77 – 3.69 (m, 2H), 3.33 – 3.26 (m, 2H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 169.7, 134.4, 130.0, 129.5, 128.7, 128.3, 128.2, 123.5, 120.6, 118.4, 110.4, 106.6, 104.4, 42.7, and 26.9.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3279 (s), 3203 (s), 3053 (m), 2924 (m), 2851 (w), 1719 (w), 1649 (s), 1613 (w), 1525 (w), 1462 (m), 1397 (w), 1353 (m), 1334 (m), and 739 (m).
HRMS (ESI): calcd for ([M+H], $C_{15}H_{13}N_2O)^+$: 237.1022, found: 237.1024.
mp: 222–225 °C.

5.7 Synthesis of pyrido[1,2-*a*]indoles 8e and 8e'



7e **8e** (42%) **8e'** (19%)

Following General Procedure D, a solution of indole–pyrone **7e** (30 mg, 0.10 mmol, 1.0 equiv) in dichloromethane (1 mL) and methanol (1 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.03 mL, 0.13 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was heated at 55 °C with stirring for 10 min. The crude residue was purified by flash column chromatography on silica gel (8:1→2:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8e** (10 mg, 0.04 mmol, 42%) as a dark red solid and pyrido[1,2-*a*]indole **8e'** (5 mg, 0.02 mmol, 19%) as a red oil, in order of elution.

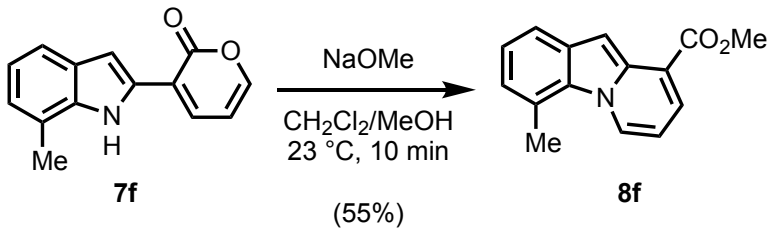
Data for pyrido[1,2-*a*]indole **8e**:

TLC (3:1, hexanes:ethyl acetate): R_f = 0.29 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 6.9 Hz, 1H), 7.95 (d, *J* = 6.9 Hz, 1H), 7.91 (d, *J* = 8.3 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.51 – 7.44 (m, 1H), 7.42 – 7.35 (m, 1H), 6.56 (t, *J* = 6.9 Hz, 1H), 4.80 – 4.73 (m, 2H), and 3.46 – 3.39 (m, 2H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 168.8, 133.0, 129.49, 129.46, 128.9, 128.2, 124.0, 121.0, 120.2, 118.5, 110.5, 106.5, 103.9, 69.1, and 26.4.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3085 (w), 3055 (w), 2924 (s), 2854 (w), 1694 (s), 1604 (w), 1519 (m), 1461 (m), 1412 (w), 1387 (w), 1344 (m), 1274 (w), 1248 (m), 1093 (w), and 738 (w).
HRMS (ESI): calcd for ([M+H], $C_{15}H_{12}NO_2$)$^+$: 238.0863, found: 238.0850.
mp: 171–176 °C.

Data for pyrido[1,2-*a*]indole **8e'**:

TLC (1:1, hexanes:ethyl acetate): R_f = 0.39 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.44 (d, *J* = 7.0 Hz, 1H), 7.88 – 7.83 (m, 2H), 7.48 (d, *J* = 6.6 Hz, 1H), 7.46 – 7.42 (m, 1H), 7.38 – 7.34 (m, 1H), 6.43 (t, *J* = 6.8 Hz, 1H), 3.99 (s, 3H), 3.98 – 3.94 (m, 2H), 3.40 (t, *J* = 6.5 Hz, 2H), and 2.31 (br s, 1H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 167.7, 130.3, 129.4, 129.3, 128.5, 128.2, 123.6, 122.7, 121.1, 119.3, 110.2, 105.4, 102.7, 63.3, 52.7, and 28.2.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3384 (s), 2924 (s), 2854 (m), 1718 (s), 1527 (w), 1464 (m), 1438 (w), 1346 (w), 1268 (s), 1196 (m), 1146 (w), 1085 (w), 1042 (w), and 740 (s).
HRMS (ESI): calcd for ([M+H], $C_{16}H_{16}NO_3$)$^+$: 270.1125, found: 270.1123.

5.8 Synthesis of pyrido[1,2-*a*]indole 8f

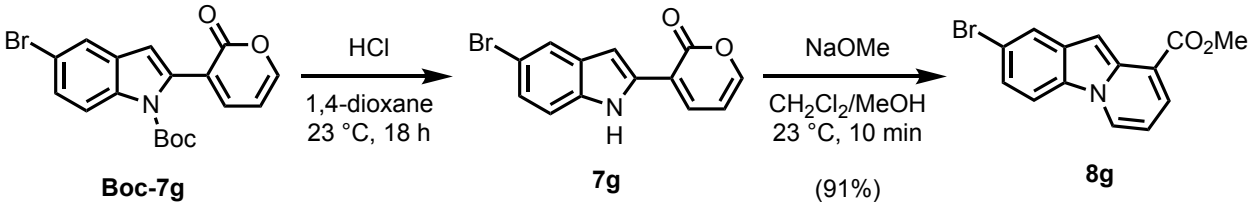


7f (55%) **8f**

Following General Procedure D, a solution of indole–pyrone **7f** (24 mg, 0.11 mmol, 1.0 equiv) in dichloromethane (1 mL) and methanol (1 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.03 mL, 0.13 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was stirred at 23 °C for 10 min. The crude residue was purified by flash column chromatography on silica gel (12:1→8:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8f** (14 mg, 0.06 mmol, 55%) as a red solid.

TLC (8:1, hexanes:ethyl acetate): R_f = 0.50 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.92 (d, *J* = 7.1 Hz, 1H), 7.81 (d, *J* = 6.7 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.44 (br s, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.07 (d, *J* = 7.1 Hz, 1H), 6.47 (t, *J* = 7.0 Hz, 1H), 4.00 (s, 3H), and 2.93 (s, 3H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 166.1, 133.4, 132.0, 130.7, 128.7, 128.5, 123.5, 123.4, 123.1, 120.1, 119.1, 106.0, 95.7, 52.2, and 21.6.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3150 (w), 3049 (w), 2950 (m), 2850 (w), 1710 (s), 1597 (w), 1523 (m), 1436 (w), 1342 (m), 1264 (s), 1205 (s), 1133 (s), 797 (m), and 736 (s).
HRMS (ESI): calcd for ([M+H], $C_{15}H_{14}NO_2)^+$: 240.1019, found: 240.1017.
mp: 115–118 °C.

5.9 Synthesis of pyrido[1,2-*a*]indole 8g



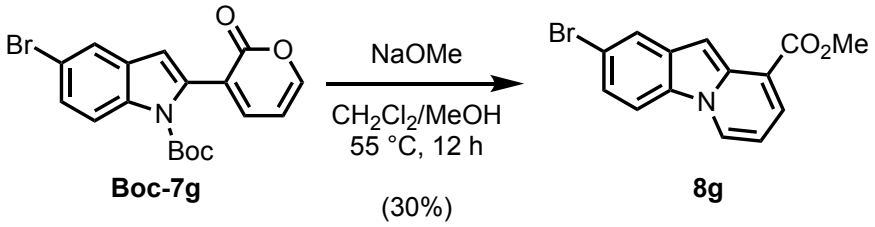
Boc-7g **7g** (91%) **8g**

An oven-dried vial was charged with a magnetic stirring bar and indole–pyrone **Boc-7g** (78 mg, 0.2 mmol, 1.0 equiv). A hydrogen chloride solution (4 M in 1,4-dioxane, 4 mL) was added and stirring of the resulting mixture was continued at 23 °C. After 18 h, the mixture was diluted with saturated aqueous sodium bicarbonate solution (4 mL) and ethyl acetate (2 mL). The layers were separated, the aqueous layer was extracted with dichloromethane (3×3 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (5 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (3:1, hexanes:ethyl acetate) to provide an inseparable mixture of Boc cleaved indole–pyrone **7g** (~0.015 mmol) and unreacted **Boc-7g** in a ratio of 2:1, which was directly used in the next step without further purification.

Following General Procedure D, a solution of indole–pyrone **7g** (assuming 0.015 mmol) in dichloromethane (0.15 mL) and methanol (0.15 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 5 μL, 0.02 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was stirred at 23 °C for 10 min. The crude residue was purified by flash column chromatography on silica gel (12:1→8:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8g** (4 mg, 0.013 mmol, 91%) as a red solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.41 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.44 (d, *J* = 6.9 Hz, 1H), 7.97 (d, *J* = 1.9 Hz, 1H), 7.87 (d, *J* = 6.7 Hz, 1H), 7.73 (d, *J* = 8.7 Hz, 1H), 7.38 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.29 (br s, 1H), 6.57 (t, *J* = 6.9 Hz, 1H), and 4.00 (s, 3H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 165.7, 134.1, 131.5, 129.7, 128.8, 128.1, 123.5, 123.4, 120.5, 117.3, 111.7, 106.9, 94.3, and 52.4.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3091 (w), 2950 (w), 2924 (m), 2853 (w), 1713 (s), 1599 (w), 1516 (w), 1462 (m), 1435 (w), 1345 (w), 1266 (s), 1228 (w), 1200 (m), 1131 (m), 1054 (w), 768 (w), and 639 (w).
HRMS (ESI): calcd for ([M+H], $C_{14}H_{11}BrNO_2)^+$: 303.9968, found: 303.9973.
mp: 118–128 °C.

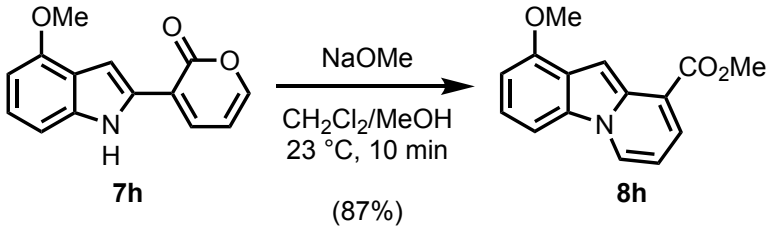
5.10 Synthesis of pyrido[1,2-*a*]indole 8g from indole–pyrone Boc-7g



Boc-7g **8g**

A vial was charged with a magnetic stirring bar and Boc protected indole–pyrone **Boc-7g** (39 mg, 0.10 mmol, 1.0 equiv). Dichloromethane (1 mL) and methanol (1 mL) were added sequentially and the resulting solution was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.03 mL, 0.13 mmol, 1.2 equiv) at 23 °C. The resulting mixture was heated in a preheated (55 °C) heating block with stirring for 12 h. The mixture was then cooled to 23 °C, and diluted with saturated aqueous ammonium chloride solution (1 mL). The layers were separated, the aqueous layer was extracted with dichloromethane (3×2 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (2 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (15:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8g** (9.0 mg, 0.03 mmol, 30%) as a red solid. The characterization data of **8g** were in full agreement with the values reported in Section 5.9.

5.11 Synthesis of pyrido[1,2-*a*]indole 8h

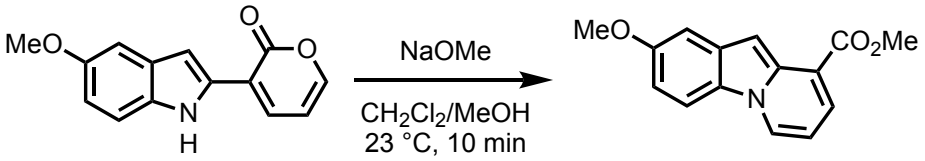


7h (87%) **8h**

Following General Procedure D, a solution of indole–pyrone **7h** (25 mg, 0.1 mmol, 1.0 equiv) in dichloromethane (1 mL) and methanol (1 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.03 mL, 0.13 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was stirred at 23 °C for 10 min. The crude residue was purified by flash column chromatography on silica gel (12:1→8:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8h** (23 mg, 0.09 mmol, 87%) as a red solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.39 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 6.8 Hz, 1H), 7.83 (dd, *J* = 6.8, 1.1 Hz, 1H), 7.49 (d, *J* = 8.3 Hz, 1H), 7.43 (s, 1H), 7.26 (br s, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 6.55 (t, *J* = 7.0 Hz, 1H), 4.04 (s, 3H), and 4.02 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.1, 153.7, 132.0, 130.7, 128.9, 128.6, 121.5, 121.4, 120.9, 106.6, 103.4, 102.5, 92.1, 55.7, and 52.3.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3090 (w), 2997 (w), 2949 (m), 2840 (w), 1712 (s), 1577 (m), 1534 (w), 1498 (m), 1458 (m), 1382 (w), 1258 (s), 1203 (m), 1130 (w), 1054 (w), and 761 (m).
HRMS (ESI): calcd for ([M+H], $C_{15}H_{14}NO_3)^+$: 256.0968, found: 256.0962.
mp: 136–139 °C.

5.12 Synthesis of pyrido[1,2-*a*]indole 8i

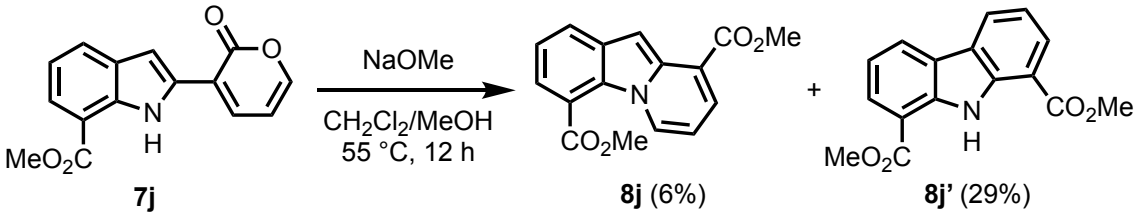


7i (89%) **8i**

Following General Procedure D, a solution of indole–pyrone **7i** (52 mg, 0.22 mmol, 1.0 equiv) in dichloromethane (2 mL) and methanol (2 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.06 mL, 0.26 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was stirred at 23 °C for 10 min. The crude residue was purified by flash column chromatography on silica gel (15:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8i** (49 mg, 0.19 mmol, 89%) as a red solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.22 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.46 (d, *J* = 6.5 Hz, 1H), 7.84 (d, *J* = 6.7 Hz, 1H), 7.78 (d, *J* = 9.0 Hz, 1H), 7.29 (br s, 1H), 7.23 (d, *J* = 2.5 Hz, 1H), 6.99 – 6.94 (m, 1H), 6.53 (t, *J* = 7.1 Hz, 1H), 4.00 (s, 3H), and 3.92 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.1, 157.2, 134.0, 131.1, 131.0, 128.8, 124.8, 119.9, 111.8, 111.3, 106.1, 101.2, 94.4, 55.8, and 52.2.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3426 (w), 3102 (w), 2995 (w), 2950 (m), 2833 (w), 1708 (s), 1610 (s), 1517 (w), 1460 (m), 1436 (m), 1313 (m), 1266 (s), 1221 (m), 1195 (s), 1162 (s), 1143 (s), 1060 (m), and 767 (w).
HRMS (ESI): calcd for ([M+H], $C_{15}H_{14}NO_3$)$^+$: 256.0968, found: 256.0970.
mp: 144–146 °C.

5.13 Synthesis of pyrido[1,2-*a*]indole 8j and carbazole 8j'



7j **8j** (6%) **8j'** (29%)

Following General Procedure D, a solution of indole–pyrone **7j** (25 mg, 0.093 mmol, 1.0 equiv) in dichloromethane (1 mL) and methanol (1 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.03 mL, 0.13 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was heated at 55 °C with stirring for 12 h. The crude residue was purified by preparative thin layer chromatography on silica gel (12:1, hexanes:ethyl acetate) to provide carbazole **8j'** (7.5 mg, 0.026 mmol, 29%) as a pale yellow solid and pyrido[1,2-*a*]indole **8j** (1.5 mg, 0.005 mmol, 6%) as a red solid, in order of elution.

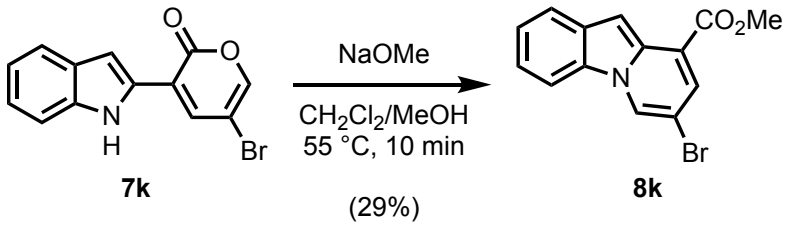
Data for carbazole **8j'**:

TLC (5:1, hexanes:ethyl acetate): R_f = 0.46 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 11.20 (br s, 1H), 8.28 (d, *J* = 7.6 Hz, 2H), 8.14 (dd, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), and 4.07 (s, 6H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 167.4, 134.0, 128.4, 125.7, 124.0, 119.4, 112.6, and 52.3.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3461 (m), 3439 (m), 3002 (w), 2953 (w), 2924 (w), 2850 (w), 1703 (s), 1600 (w), 1495 (w), 1435 (m), 1265 (s), 1207 (s), 1144 (s), 752 (m), and 732 (w).
HRMS (ESI): calcd for ([M+H], $C_{16}H_{14}NO_4$)$^+$: 284.0917, found: 284.0920.
mp: 140–144 °C.

Data for pyrido[1,2-*a*]indole **8j**:

TLC (5:1, hexanes:ethyl acetate): R_f = 0.44 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 9.41 (d, *J* = 7.3 Hz, 1H), 8.08 – 8.05 (m, 1H), 7.90 – 7.85 (m, 2H), 7.57 (br s, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 6.53 (t, *J* = 7.0 Hz, 1H), 4.06 (s, 3H), and 4.00 (s, 3H).
^{13}C NMR (226 MHz, $CDCl_3$) δ 168.5, 165.9, 134.4, 134.0, 131.9, 129.3, 126.6, 126.4, 125.0, 122.4, 120.1, 118.1, 106.4, 96.2, 52.8, and 52.3.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 2951 (w), 2924 (m), 2853 (w), 1712 (s), 1599 (w), 1495 (w), 1435 (m), 1327 (w), 1261 (s), 1207 (s), and 756 (m).
HRMS (ESI): calcd for ([M+H], $C_{16}H_{14}NO_4$)$^+$: 284.0917, found: 284.0914.
mp: 124–128 °C.

5.14 Synthesis of pyrido[1,2-*a*]indole 8k

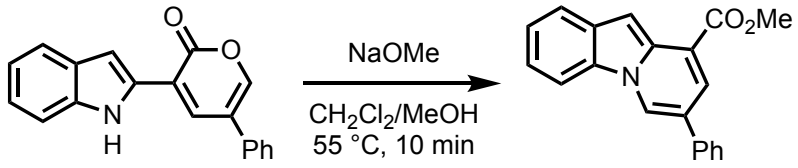


7k (29%) **8k**

Following General Procedure D, a solution of indole–pyrone **7k** (15 mg, 0.05 mmol, 1.0 equiv) in dichloromethane (0.5 mL) and methanol (0.5 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 15 μL, 0.06 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was heated at 55 °C with stirring for 10 min. The crude residue was purified by flash column chromatography on silica gel (30:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8k** (4.5 mg, 0.015 mmol, 29%) as a red solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.54 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.68 – 8.65 (m, 1H), 7.91 – 7.87 (m, 3H), 7.48 – 7.44 (m, 1H), 7.44 (br s, 1H), 7.41 – 7.37 (m, 1H), and 4.04 (s, 3H).
^{13}C NMR (226 MHz, $CDCl_3$) δ 164.9, 131.5, 131.3, 130.0, 129.3, 128.9, 124.2, 121.6, 121.4, 121.2, 110.4, 100.0, 96.0, and 52.6.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3073 (w), 2950 (w), 2922 (m), 2851 (w), 1720 (s), 1511 (w), 1453 (m), 1437 (w), 1411 (w), 1331 (w), 1259 (s), 1201 (s), 1154 (w), 787 (m), and 729 (w).
HRMS (ESI): calcd for ([M+H], $C_{14}H_{11}BrNO_2)^+$: 303.9968, found: 303.9976.
mp: 163–167 °C.

5.15 Synthesis of pyrido[1,2-*a*]indole 8l



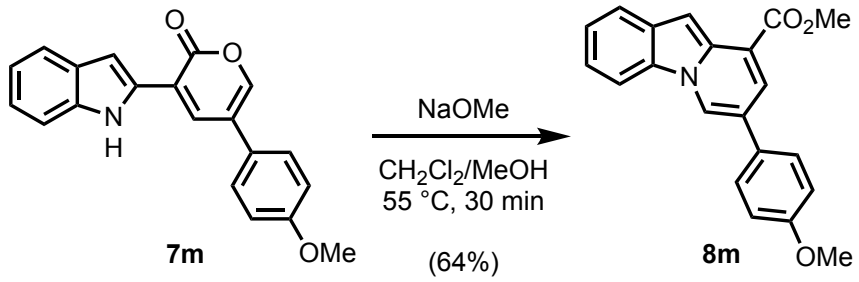
7l **8l**

(66%)

Following General Procedure D, a solution of indole–pyrone **7l** (23 mg, 0.08 mmol, 1.0 equiv) in dichloromethane (0.8 mL) and methanol (0.8 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 25 μL, 0.11 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was heated at 55 °C with stirring for 10 min. The crude residue was purified by flash column chromatography on silica gel (30:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8l** (16 mg, 0.05 mmol, 66%) as a red solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.39 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 – 8.70 (m, 1H), 8.22 – 8.17 (m, 1H), 7.96 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.70 – 7.62 (m, 2H), 7.54 – 7.48 (m, 2H), 7.47 – 7.33 (m, 4H), and 4.04 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 165.9, 137.3, 132.4, 130.5, 129.9, 129.7, 129.3, 127.7, 126.5, 126.0, 124.0, 121.4, 120.7, 120.6, 120.5, 110.5, 94.8, and 52.4.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3055 (w), 3033 (w), 2949 (w), 2925 (w), 2852 (w), 1713 (s), 1605 (w), 1456 (m), 1411 (w), 1336 (w), 1283 (m), 1245 (s), 1132 (w), 1060 (w), 789 (m), 732 (m), and 695 (m).
HRMS (ESI): calcd for ([M+H], $C_{20}H_{16}NO_2$)$^+$: 302.1176, found: 302.1171.
mp: 160–163 °C.

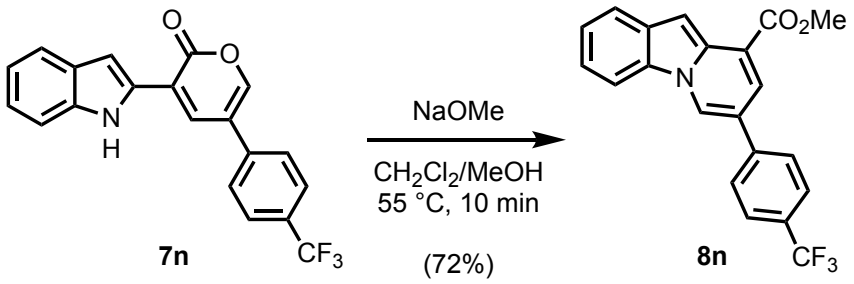
5.16 Synthesis of pyrido[1,2-*a*]indole 8m



Following General Procedure D, a solution of indole–pyrone **7m** (23 mg, 0.07 mmol, 1.0 equiv) in dichloromethane (0.7 mL) and methanol (0.7 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 20 μL, 0.09 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was heated at 55 °C with stirring for 30 min. The crude residue was purified by flash column chromatography on silica gel (10:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8m** (15 mg, 0.05 mmol, 64%) as a red solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.35 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.15 – 8.12 (m, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 8.6 Hz, 2H), 7.45 – 7.40 (m, 1H), 7.39 – 7.31 (m, 2H), 7.03 (d, *J* = 8.6 Hz, 2H), 4.04 (s, 3H), and 3.88 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.0, 159.5, 132.4, 130.4, 129.9, 129.8, 127.7, 125.3, 123.9, 121.4, 120.64, 120.57, 120.4, 114.8, 110.5, 94.6, 55.6, and 52.4. *(Missing one carbon signal)*
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3051 (w), 2999 (w), 2950 (m), 2908 (w), 2836 (w), 1712 (s), 1607 (w), 1505 (m), 1455 (m), 1333 (w), 1279 (w), 1245 (s), 1179 (m), 1132 (w), 1052 (w), 827 (m), 787 (m), and 747 (w).
HRMS (ESI): calcd for ([M+H], $C_{21}H_{18}NO_3)^+$: 332.1281, found: 332.1266.
mp: 141–145 °C.

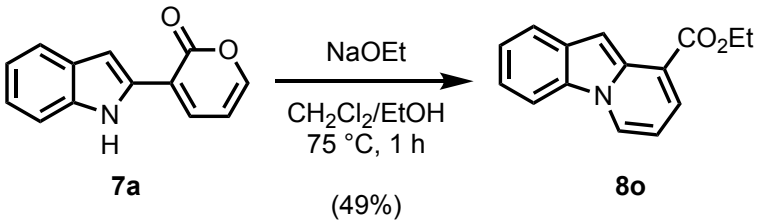
5.17 Synthesis of pyrido[1,2-*a*]indole 8n



Following General Procedure D, a solution of indole–pyrone **7n** (6 mg, 0.017 mmol, 1.0 equiv) in dichloromethane (0.35 mL) and methanol (0.35 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 5 μL, 0.022 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was heated at 55 °C with stirring for 10 min. The crude residue was purified by flash column chromatography on silica gel (30:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8n** (4.5 mg, 0.012 mmol, 72%) as a red solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.57 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.67 (d, *J* = 1.7 Hz, 1H), 8.10 (d, *J* = 1.7 Hz, 1H), 7.91 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.77 – 7.69 (m, 4H), 7.46 – 7.42 (m, 1H), 7.40 – 7.33 (m, 2H), and 4.03 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 165.7, 140.8, 132.2, 130.6, 130.0, 129.7 (q, *J* = 32.6 Hz), 128.7, 126.6, 126.5, 126.3 (q, *J* = 3.9 Hz), 124.31 (q, *J* = 272.0 Hz), 124.26, 121.5, 121.1, 120.8, 119.0, 110.4, 95.5, and 52.5.
^{19}F NMR (376 MHz, $CDCl_3$) δ -61.61.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3055 (w), 2952 (w), 2927 (w), 2852 (w), 1714 (s), 1614 (m), 1456 (m), 1433 (w), 1323 (s), 1248 (s), 1203 (m), 1165 (m), 1113 (s), 1072 (m), 836 (m), 789 (m), and 733 (m).
HRMS (ESI): calcd for ([M+H], $C_{21}H_{15}F_3NO_2)^+$: 370.1049, found: 370.1048.
mp: 165–169 °C.

5.18 Synthesis of pyrido[1,2-*a*]indole 8o

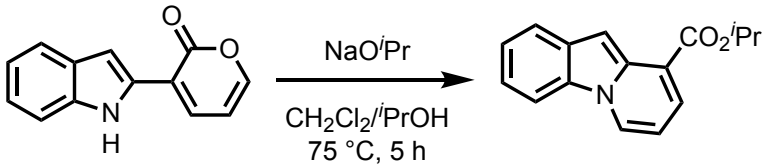


7a (49%) **8o**

A vial was charged with a magnetic stirring bar and indole–pyrone **7a** (20 mg, 0.10 mmol, 1.0 equiv). Dichloromethane (1 mL) and ethanol (1 mL) were added sequentially and the resulting solution was treated with sodium ethoxide (34 mg, 0.50 mmol, 5.0 equiv) at 23 °C. The resulting mixture was heated in a preheated (75 °C) heating block with stirring for 1 h. The mixture was then cooled to 23 °C, and diluted with saturated aqueous ammonium chloride solution (1 mL). The layers were separated, the aqueous layer was extracted with dichloromethane (3×2 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (2 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (8:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8o** (11 mg, 0.05 mmol, 49%) as a red solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.57 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.52 (d, *J* = 7.1 Hz, 1H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.88 – 7.85 (m, 2H), 7.44 – 7.40 (m, 1H), 7.37 (br s, 1H), 7.35 – 7.31 (m, 1H), 6.55 (t, *J* = 6.8 Hz, 1H), 4.48 (q, *J* = 7.2 Hz, 2H), and 1.48 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 165.5, 133.5, 130.1, 129.6, 129.3, 129.0, 123.9, 121.3, 120.9, 120.6, 110.4, 106.4, 94.4, 61.3, and 14.6.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3053 (w), 2980 (w), 2926 (w), 2854 (w), 1707 (s), 1607 (w), 1519 (w), 1461 (m), 1343 (w), 1263 (s), 1198 (s), 1145 (m), 1128 (m), 1058 (m), 773 (m), and 742 (m).
HRMS (ESI): calcd for ([M+H], $C_{15}H_{14}NO_2$)$^+$: 240.1019, found: 240.1035.
mp: 64–66 °C.

5.19 Synthesis of pyrido[1,2-*a*]indole 8p



7a **8p**

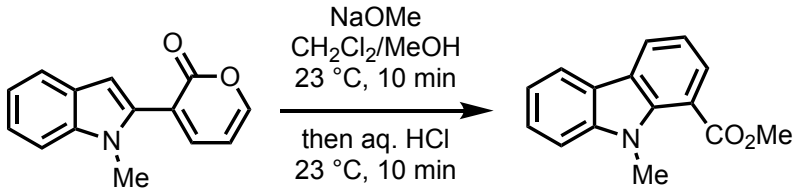
(12%, 18% brsm)

A vial was charged with a magnetic stirring bar and indole–pyrone **7a** (21 mg, 0.10 mmol, 1.0 equiv). Dichloromethane (1 mL) and isopropanol (1 mL) were added sequentially and the resulting solution was treated with sodium isopropoxide (41 mg, 0.50 mmol, 5.0 equiv) at 23 °C. The resulting mixture was heated in a preheated (75 °C) heating block with stirring for 5 h. The mixture was then cooled to 23 °C, and diluted with saturated aqueous ammonium chloride solution (1 mL). The layers were separated, the aqueous layer was extracted with dichloromethane (3×2 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (2 mL). The washed organic layer was dried over sodium sulfate. The dried solution was filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (8:1→3:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole **8p** (3 mg, 0.01 mmol, 12%, 18% brsm) as a red solid and unreacted indole–pyrone **7a** (7.5 mg, 0.04 mmol) as a yellow solid, in order of elution.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.52 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.52 (d, *J* = 6.9 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.88 – 7.84 (m, 2H), 7.44 – 7.40 (m, 1H), 7.36 (br s, 1H), 7.35 – 7.31 (m, 1H), 6.55 (t, *J* = 6.8 Hz, 1H), 5.36 (hept, *J* = 6.4 Hz, 1H), and 1.46 (d, *J* = 6.3 Hz, 6H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 165.1, 133.4, 132.2, 130.1, 129.5, 129.1, 128.8, 123.8, 121.2, 120.54, 120.47, 110.4, 106.3, 94.7, 68.8, and 22.2.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3054 (w), 2979 (m), 2925 (w), 2852 (w), 1708 (s), 1606 (w), 1520 (w), 1462 (m), 1339 (w), 1263 (s), 1200 (m), 1107 (m), 1054 (w), 774 (w), and 743 (m).
HRMS (ESI): calcd for ([M+H], $C_{16}H_{16}NO_2$)$^+$: 254.1176, found: 254.1173.
mp: 76–81 °C.

6 Synthesis of carbazoles

6.1 Synthesis of carbazole 15a

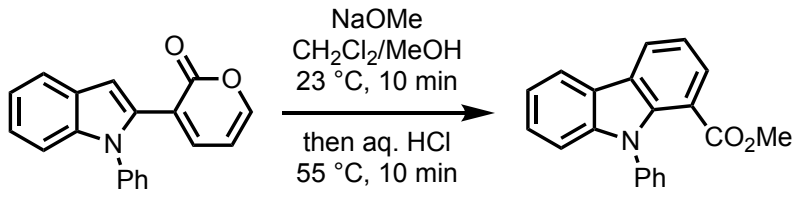


Me-7a (78%) **15a**

Following General Procedure E, a solution of indole–pyrone **Me-7a** (24 mg, 0.11 mmol, 1.0 equiv) in dichloromethane (1 mL) and methanol (1 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.03 mL, 0.13 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was stirred at 23 °C for 10 min. Subsequently, aqueous hydrogen chloride solution (1 M, 0.3 mL, 0.3 mmol, 3.0 equiv) was added and stirring of the biphasic mixture was continued at 23 °C for 10 min. The crude residue was purified by flash column chromatography on silica gel (12:1, hexanes:ethyl acetate) to provide carbazole **15a** (20 mg, 0.08 mmol, 78%) as a white solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.57 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.25 (dd, *J* = 7.6, 1.4 Hz, 1H), 8.12 – 8.08 (m, 1H), 7.90 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.55 – 7.51 (m, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.25 (t, *J* = 7.6 Hz, 1H), 4.03 (s, 3H), and 3.91 (s, 3H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 168.3, 142.7, 139.2, 128.5, 126.6, 125.5, 124.1, 122.5, 120.1, 119.9, 118.3, 115.3, 109.5, 52.4, and 33.5.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3053 (w), 2990 (w), 2949 (m), 2841 (w), 1714 (s), 1577 (w), 1487 (m), 1465 (m), 1440 (m), 1410 (m), 1312 (w), 1261 (s), 1202 (s), 1139 (s), 1068 (m), and 748 (s).
HRMS (ESI): calcd for ([M+H], $C_{15}H_{14}NO_2$)$^+$: 240.1025, found: 240.1029.
mp: 49–52 °C.

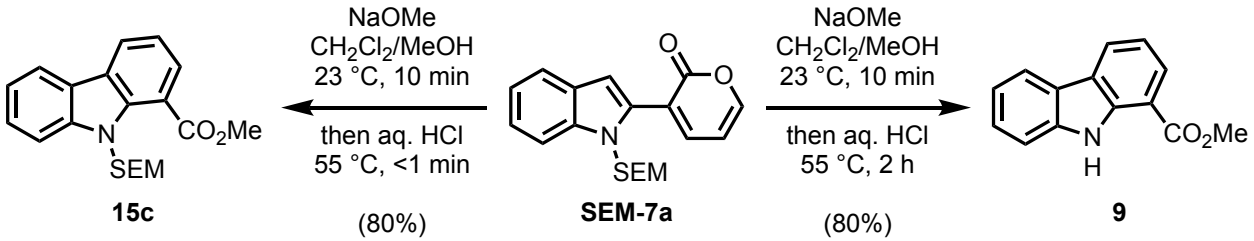
6.2 Synthesis of carbazole 15b



Following General Procedure E, a solution of indole–pyrone **Ph-7a** (30 mg, 0.10 mmol, 1.0 equiv) in dichloromethane (1 mL) and methanol (1 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.03 mL, 0.13 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was stirred at 23 °C for 10 min. Subsequently, aqueous hydrogen chloride solution (1 M, 0.3 mL, 0.3 mmol, 3.0 equiv) was added and the biphasic mixture was heated at 55 °C with stirring for 10 min. The crude residue was purified by flash column chromatography on silica gel (15:1, hexanes:ethyl acetate) to provide carbazole **15b** (26 mg, 0.086 mmol, 83%) as a white solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.61 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 7.7, 1.4 Hz, 1H), 8.15 (d, *J* = 7.7 Hz, 1H), 7.78 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.60 – 7.55 (m, 2H), 7.46 – 7.40 (m, 4H), 7.37 – 7.31 (m, 3H), and 3.20 (s, 3H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 168.1, 142.6, 140.1, 138.2, 129.9, 128.0, 127.6, 126.8, 126.6, 125.8, 123.8, 123.0, 120.9, 120.2, 119.6, 116.6, 110.5, and 51.6.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3058 (w), 2948 (w), 2926 (w), 2853 (w), 1718 (s), 1595 (w), 1500 (m), 1453 (m), 1422 (s), 1280 (s), 1224 (w), 1205 (m), 1135 (s), 750 (s), and 699 (w).
HRMS (ESI): calcd for ([M+H], $C_{20}H_{16}NO_2)^+$: 302.1181, found: 302.1181.
mp: 111–114 °C.

6.3 Synthesis of carbazoles 15c and 9



Procedure for the synthesis of carbazole 15c

Following General Procedure E, a solution of indole–pyrone **SEM-7a** (24 mg, 0.07 mmol, 1.0 equiv) in dichloromethane (0.7 mL) and methanol (0.7 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.02 mL, 0.09 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was stirred at 23 °C for 10 min. Subsequently, aqueous hydrogen chloride solution (1 M, 0.2 mL, 0.2 mmol, 3.0 equiv) was added and the biphasic mixture was heated at 55 °C with stirring for <1 min. The crude residue was purified by flash column chromatography on silica gel (15:1, hexanes:ethyl acetate) to provide carbazole **15c** (20 mg, 0.056 mmol, 80%) as a pale yellow oil.

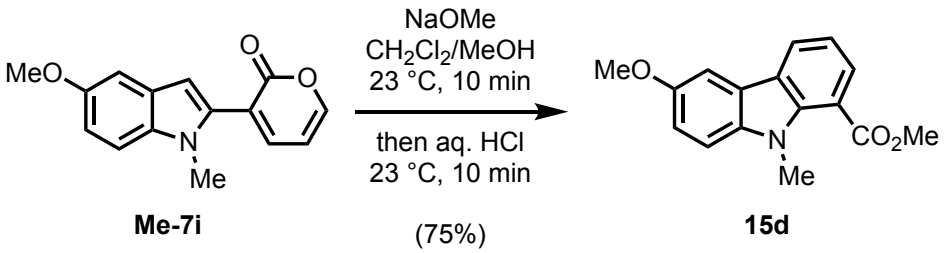
TLC (5:1, hexanes:ethyl acetate): R_f = 0.50 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.24 (dd, *J* = 7.7, 1.4 Hz, 1H), 8.09 (d, *J* = 7.6 Hz, 1H), 7.84 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.52 – 7.48 (m, 1H), 7.32 – 7.27 (m, 2H), 5.95 (s, 2H), 4.01 (s, 3H), 3.16 – 3.12 (m, 2H), 0.76 – 0.70 (m, 2H), and -0.18 (s, 9H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 168.4, 142.1, 136.9, 128.1, 126.7, 126.1, 123.8, 123.0, 120.5, 120.2, 119.3, 117.4, 110.0, 73.9, 65.3, 52.6, 17.6, and -1.5.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3056 (w), 2951 (m), 2896 (w), 1718 (s), 1456 (w), 1305 (w), 1261 (m), 1200 (s), 1141 (m), 1079 (s), 835 (m), and 749 (s).
HRMS (ESI): calcd for ([M+Na], $C_{20}H_{25}NNaO_3Si)^+$: 378.1501, found: 378.1501.

Procedure for the synthesis of carbazole 9

Following General Procedure E, a solution of indole–pyrone **SEM-7a** (20 mg, 0.06 mmol, 1.0 equiv) in dichloromethane (0.6 mL) and methanol (0.6 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 15 μL, 0.07 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was stirred at 23 °C for 10 min. Subsequently, aqueous hydrogen chloride solution (1 M, 0.2 mL, 0.2 mmol, 3.0 equiv) was added and the biphasic mixture was heated at 55 °C with stirring for 2 h. The crude residue was purified by flash column chromatography on silica gel (12:1, hexanes:ethyl acetate) to provide carbazole **9** (10.5 mg, 0.05 mmol, 80%) as an off-white solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.73 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 9.93 (br s, 1H), 8.27 (d, *J* = 7.6 Hz, 1H), 8.12 – 8.06 (m, 2H), 7.53 (d, *J* = 8.1 Hz, 1H), 7.50 – 7.46 (m, 1H), 7.31 – 7.24 (m, 2H), and 4.03 (s, 3H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 168.0, 140.2, 139.8, 127.5, 126.7, 125.6, 124.8, 122.6, 120.5, 120.1, 118.6, 111.7, 111.2, and 52.1.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3440 (s), 3061 (w), 3038 (w), 2951 (w), 2924 (w), 2850 (w), 1692 (s), 1603 (w), 1494 (m), 1435 (m), 1300 (m), 1267 (s), and 1223 (s).
HRMS (ESI): calcd for ([M+H], $C_{14}H_{12}NO_2)^+$: 226.0863, found: 226.0864.
mp: 133–135 °C.

6.4 Synthesis of carbazole 15d

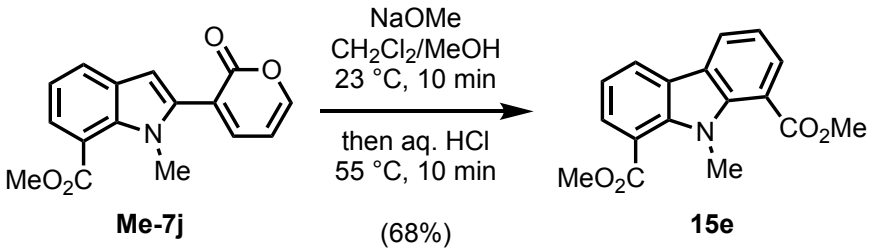


Me-7i (75%) **15d**

Following General Procedure E, a solution of indole–pyrone **Me-7i** (15 mg, 0.06 mmol, 1.0 equiv) in dichloromethane (0.6 mL) and methanol (0.6 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 20 μL, 0.09 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was stirred at 23 °C for 10 min. Subsequently, aqueous hydrogen chloride solution (1 M, 0.2 mL, 0.2 mmol, 3.0 equiv) was added and the biphasic mixture was continued to stir at 23 °C for 10 min. The crude residue was purified by flash column chromatography on silica gel (15:1, hexanes:ethyl acetate) to provide carbazole **15d** (12 mg, 0.04 mmol, 75%) as a white solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.29 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.87 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.56 (d, *J* = 2.5 Hz, 1H), 7.36 (d, *J* = 8.8 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.16 (dd, *J* = 8.8, 2.6 Hz, 1H), 4.01 (s, 3H), 3.94 (s, 3H), and 3.88 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.3, 154.4, 139.8, 137.8, 128.6, 125.4, 124.2, 122.9, 117.8, 115.7, 115.3, 110.3, 103.0, 56.2, 52.3, and 33.6.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 2994 (w), 2949 (m), 2832 (w), 1714 (s), 1493 (m), 1436 (w), 1261 (m), 1197 (s), 1138 (s), 1067 (w), and 744 (w).
HRMS (ESI): calcd for ([M+H], $C_{16}H_{16}NO_3$)$^+$: 270.1125, found: 270.1123.
mp: 108–111 °C.

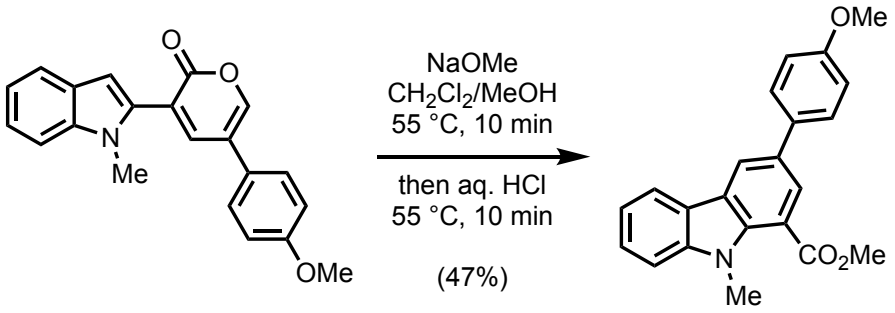
6.5 Synthesis of carbazole 15e



Following General Procedure E, a solution of indole–pyrone **Me-7j** (26 mg, 0.09 mmol, 1.0 equiv) in dichloromethane (1 mL) and methanol (1 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.03 mL, 0.13 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was stirred at 23 °C for 10 min. Subsequently, aqueous hydrogen chloride solution (1 M, 0.3 mL, 0.3 mmol, 3.0 equiv) was added and the biphasic mixture was heated at 55 °C with stirring for 10 min. The crude residue was purified by flash column chromatography on silica gel (5:1, hexanes:ethyl acetate) to provide carbazole **15e** (19 mg, 0.06 mmol, 68%) as a white solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.63 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21 (dd, *J* = 7.7, 1.3 Hz, 2H), 7.95 (dd, *J* = 7.6, 1.3 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 4.03 (s, 6H), and 3.71 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 167.8, 142.2, 129.5, 125.3, 124.1, 119.7, 116.2, 52.4, and 39.5.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3004 (w), 2960 (w), 2931 (w), 1721 (s), 1584 (w), 1489 (w), 1428 (m), 1263 (s), 1202 (m), 1147 (m), 1087 (m), and 738 (m).
HRMS (ESI): calcd for ([M+H], $C_{17}H_{16}NO_4$)$^+$: 298.1074, found: 298.1077.
mp: 163–166 °C.

6.6 Synthesis of carbazole 15f

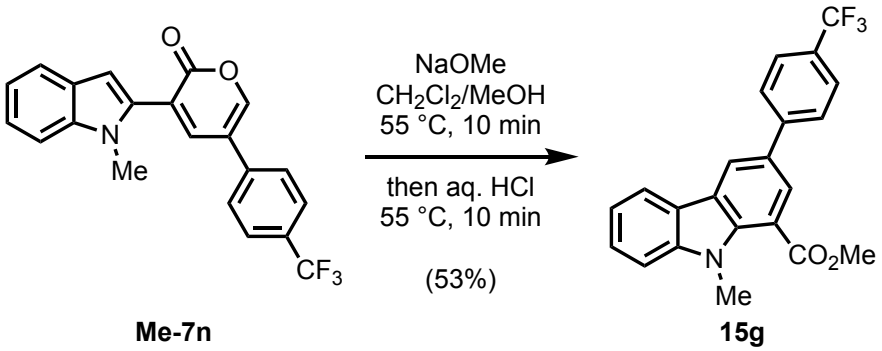


Me-7m **15f**

Following General Procedure E, a solution of indole–pyrone **Me-7m** (16 mg, 0.05 mmol, 1.0 equiv) in dichloromethane (0.5 mL) and methanol (0.5 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 15 μL, 0.07 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was heated at 55 °C with stirring for 10 min. Subsequently, aqueous hydrogen chloride solution (1 M, 0.15 mL, 0.15 mmol, 3.0 equiv) was added and the biphasic mixture was heated at 55 °C with stirring for 10 min. The crude residue was purified by flash column chromatography on silica gel (8:1, hexanes:ethyl acetate) to provide carbazole **15f** (8 mg, 0.02 mmol, 47%) as a white solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.39 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.41 – 8.38 (m, 1H), 8.13 (d, *J* = 7.7 Hz, 1H), 8.10 – 8.08 (m, 1H), 7.67 – 7.63 (m, 2H), 7.55 – 7.51 (m, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.05 – 7.00 (m, 2H), 4.04 (s, 3H), 3.93 (s, 3H), and 3.88 (s, 3H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 168.3, 159.0, 143.1, 138.4, 133.7, 131.6, 128.4, 127.5, 126.8, 126.2, 122.7, 122.0, 120.2, 120.0, 115.5, 114.4, 109.6, 55.6, 52.5, and 33.5.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 2996 (w), 2949 (m), 2836 (w), 1715 (s), 1518 (w), 1482 (m), 1463 (m), 1436 (w), 1253 (s), 1221 (w), 1200 (m), 1182 (w), 1069 (w), 830 (w), and 748 (w).
HRMS (ESI): calcd for ([M+H], $C_{22}H_{20}NO_3$)$^+$: 346.1443, found: 346.1442.
mp: 95–104 °C.

6.7 Synthesis of carbazole 15g



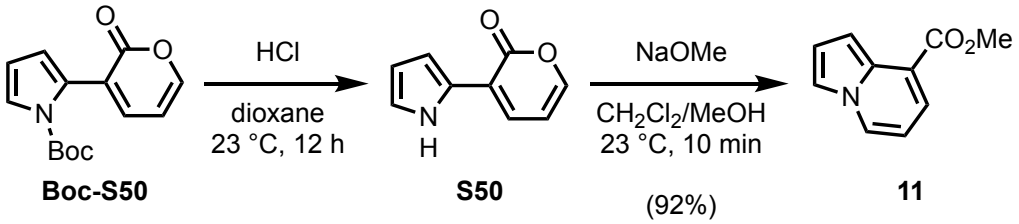
Me-7n **15g**

Following General Procedure E, a solution of indole–pyrone **Me-7n** (20 mg, 0.05 mmol, 1.0 equiv) in dichloromethane (0.5 mL) and methanol (0.5 mL) was treated with a solution of sodium methoxide (25 wt% in MeOH, 15 μL, 0.07 mmol, 1.2 equiv) at 23 °C, and the resulting mixture was heated at 55 °C with stirring for 10 min. Subsequently, aqueous hydrogen chloride solution (1 M, 0.15 mL, 0.15 mmol, 3.0 equiv) was added and the biphasic mixture was heated at 55 °C with stirring for 10 min. The crude residue was purified by flash column chromatography on silica gel (15:1, hexanes:ethyl acetate) to provide carbazole **15g** (11 mg, 0.03 mmol, 53%) as a white solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.34 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 2.0 Hz, 1H), 8.17 – 8.10 (m, 2H), 7.83 (d, *J* = 7.9 Hz, 2H), 7.73 (d, *J* = 8.8 Hz, 2H), 7.59 – 7.53 (m, 1H), 7.51 – 7.47 (m, 1H), 7.35 – 7.29 (m, 1H), 4.06 (s, 3H), and 3.95 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.0, 144.6, 143.2, 139.1, 130.2, 129.1 (q, *J* = 32.6 Hz), 127.7, 127.5, 127.1, 126.4, 126.0 (q, *J* = 3.9 Hz), 124.5 (q, *J* = 272.0 Hz), 122.6, 122.5, 120.34, 120.27, 115.8, 109.8, 52.6, and 33.6.
^{19}F NMR (376 MHz, $CDCl_3$) δ -61.47.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3054 (w), 2952 (m), 2926 (m), 2853 (w), 1719 (s), 1616 (w), 1483 (w), 1324 (s), 1253 (m), 1201 (m), 1164 (m), 1121 (s), 1068 (m), 838 (w), 784 (w), and 748 (w).
HRMS (ESI): calcd for ([M+H], $C_{22}H_{17}F_3NO_2)^+$: 384.1206, found: 384.1206.
mp: 117–120 °C.

7 Synthesis of other *N*-heterocyclic cores

7.1 Synthesis of indolizine 11

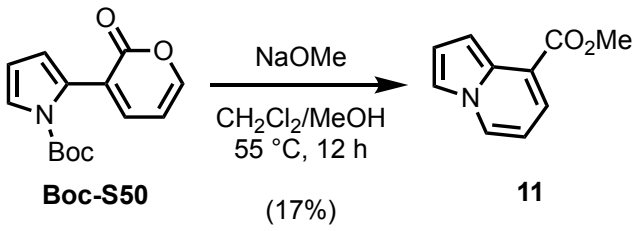


An oven-dried vial was charged with a magnetic stirring bar and pyrrole–pyrone **Boc-S50** (70 mg, 0.27 mmol, 1.0 equiv). A hydrogen chloride solution (4 M in 1,4-dioxane, 4 mL) was added and the resulting mixture was stirred at 23 °C. After 12 h, the mixture was diluted with saturated aqueous sodium bicarbonate solution (4 mL) and ethyl acetate (2 mL). The layers were separated, the aqueous layer was extracted with dichloromethane (3×3 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (5 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (5:1, hexanes:ethyl acetate) to provide an inseparable mixture of Boc cleaved pyrrole–pyrone **S50** (~0.075 mmol) and unreacted **Boc-S50** in a ratio of 11:1, which was used directly in the next step without further purification.

A vial was charged with a magnetic stirring bar and pyrrole–pyrone **S50** (assuming 0.075 mmol, 1.0 equiv). Dichloromethane (0.75 mL) and methanol (0.75 mL) were added sequentially and the resulting solution was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.02 mL, 0.09 mmol, 1.2 equiv) at 23 °C. After 10 min, the mixture was diluted with saturated aqueous ammonium chloride solution (0.5 mL). The layers were separated, the aqueous layer was extracted with dichloromethane (3×2 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (2 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (15:1, hexanes:ethyl acetate) to provide indolizine **11** (12 mg, 0.07 mmol, 92%) as a bright yellow oil.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.57 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.07 (m, 1H), 7.60 – 7.55 (m, 1H), 7.41 – 7.36 (m, 1H), 7.12 – 7.07 (m, 1H), 6.93 – 6.88 (m, 1H), 6.53 (t, *J* = 6.9 Hz, 1H), and 3.97 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.3, 129.9, 129.7, 123.5, 120.9, 115.2, 113.4, 108.9, 101.7, and 52.1.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3131 (w), 3102 (w), 2997 (w), 2950 (m), 2847 (w), 1709 (s), 1543 (w), 1435 (w), 1352 (w), 1308 (m), 1283 (s), 1196 (s), 1050 (w), and 746 (m).
HRMS (ESI): calcd for ([M+H], $C_{10}H_{10}NO_2$)$^+$: 176.0706, found: 176.0704.

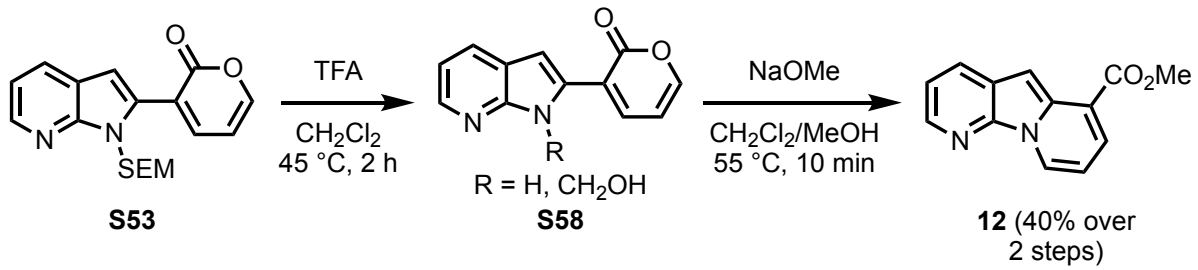
7.2 Synthesis of indolizine 11 from pyrrole–pyrone Boc-S50



Boc-S50 (17%) **11**

A vial was charged with a magnetic stirring bar and pyrrole–pyrone **Boc-S50** (14 mg, 0.05 mmol, 1.0 equiv). Dichloromethane (0.5 mL) and methanol (0.5 mL) were added sequentially and the resulting solution was treated with a solution of sodium methoxide (25 wt% in MeOH, 15 μL, 0.07 mmol, 1.2 equiv) at 23 °C. The resulting mixture was heated in a preheated (55 °C) heating block with stirring for 12 h. The mixture was then cooled to 23 °C, and diluted with saturated aqueous ammonium chloride solution (0.5 mL). The layers were separated, the aqueous layer was extracted with dichloromethane (3×1 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (1 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (8:1, hexanes:ethyl acetate) to provide indolizine **11** (1.5 mg, 0.01 mmol, 17%) as a bright yellow oil. The characterization data of **11** were in full agreement with the values reported in Section 7.1.

7.3 Synthesis of pyrido[3,2-*b*]indolizine 12

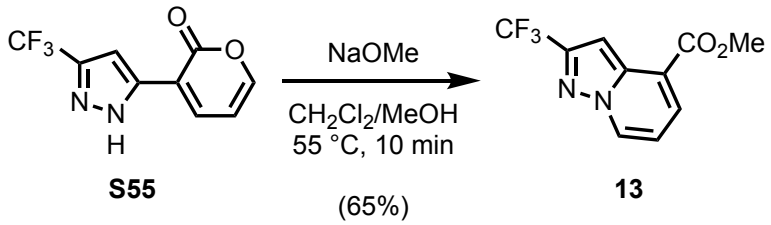


A vial was charged with a magnetic stirring bar and SEM protected 7-azaindole–pyrone **S53** (35 mg, 0.1 mmol, 1.0 equiv). Dichloromethane (2 mL) was subsequently added and the resulting solution was treated with trifluoroacetic acid (0.08 mL, 1.0 mmol, 10 equiv) at 23 °C. The resulting mixture was heated in a preheated (45 °C) heating block with stirring for 2 h. The mixture was then cooled to 23 °C, and diluted with saturated aqueous sodium bicarbonate solution (2 mL). The layers were separated, the aqueous layer was extracted with dichloromethane (3×2 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (2 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. NMR analysis of the crude residue indicated the presence of both hemiaminal and free (NH)-7-azaindole–pyrone **S58**, which was used directly in the next step without further purification.

A vial was charged with a magnetic stirring bar and crude 7-azaindole–pyrone **S58** (assuming 0.1 mmol). Dichloromethane (1 mL) and methanol (1 mL) were added sequentially and the resulting solution was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.03 mL, 0.13 mmol, 1.2 equiv) at 23 °C. The resulting mixture was heated in a preheated (55 °C) heating block with stirring for 10 min. The mixture was then cooled to 23 °C, and diluted with saturated aqueous ammonium chloride solution (1 mL). The layers were separated, the aqueous layer was extracted with dichloromethane (3×2 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (2 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (5:1, hexanes:ethyl acetate) to provide pyrido[3,2-*b*]indolizine **12** (9 mg, 0.04 mmol, 40% over 2 steps) as a red solid.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.35 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 9.01 – 8.96 (m, 1H), 8.47 – 8.43 (m, 1H), 8.17 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.94 (dd, *J* = 6.8, 1.3 Hz, 1H), 7.39 (dd, *J* = 8.0, 4.5 Hz, 1H), 7.29 (s, 1H), 6.62 (t, *J* = 6.9 Hz, 1H), and 4.01 (s, 3H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 165.8, 141.5, 141.1, 132.9, 131.0, 129.2, 128.4, 122.4, 120.3, 120.0, 106.9, 92.2, and 52.3.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3097 (w), 2950 (w), 2926 (w), 2852 (w), 1715 (s), 1571 (w), 1534 (w), 1514 (w), 1437 (m), 1406 (m), 1314 (w), 1271 (s), 1201 (s), 799 (w), and 760 (m).
HRMS (ESI): calcd for ([M+H], $C_{13}H_{11}N_2O_2)^+$: 227.0815, found: 227.0810.
mp: 108–110 °C.

7.4 Synthesis of 3-azaindolizine 13

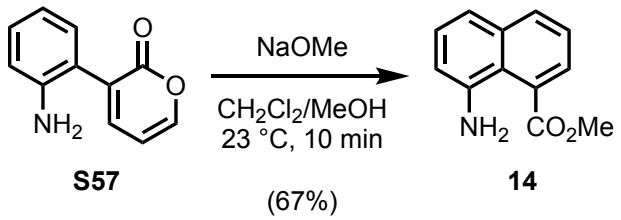


S55 (65%) **13**

A vial was charged with a magnetic stirring bar and pyrazole–pyrone **S55** (13 mg, 0.06 mmol, 1.0 equiv). Dichloromethane (0.6 mL) and methanol (0.6 mL) were added sequentially and the resulting solution was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.02 mL, 0.09 mmol, 1.2 equiv) at 23 °C. The resulting mixture was heated in a preheated (55 °C) heating block with stirring for 10 min. The mixture was then cooled to 23 °C, and diluted with saturated aqueous ammonium chloride solution (1 mL). The layers were separated, the aqueous layer was extracted with dichloromethane (3×2 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (2 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (3:1, hexanes:ethyl acetate) to provide 3-azaindolizine **13** (9 mg, 0.04 mmol, 65%) as a white solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.30 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 6.9 Hz, 1H), 8.08 (d, *J* = 7.2 Hz, 1H), 7.40 (s, 1H), 7.02 (t, *J* = 7.1 Hz, 1H), and 4.02 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 145.8 (q, *J* = 38.1 Hz), 139.2, 133.1, 129.8, 121.9, 121.5 (q, *J* = 269.8 Hz), 112.9, 98.3 (q, *J* = 2.8 Hz), and 52.8.
^{19}F NMR (376 MHz, $CDCl_3$) δ -61.16.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3178 (w), 3099 (w), 3038 (w), 2956 (w), 2850 (w), 1721 (s), 1552 (w), 1503 (w), 1438 (w), 1416 (w), 1290 (m), 1227 (m), 1165 (s), 1125 (s), 793 (w), and 754 (w).
HRMS (ESI): calcd for ([M+H], $C_{10}H_8F_3N_2O_2$)$^+$: 245.0532, found: 245.0539.
mp: 108–110 °C.

7.5 Synthesis of 1-naphthylamine 14



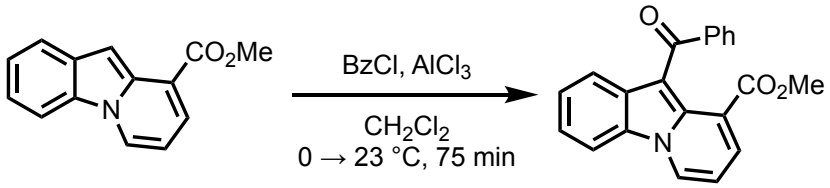
S57 (67%) **14**

A vial was charged with a magnetic stirring bar and aniline–pyrone **S57** (19 mg, 0.1 mmol, 1.0 equiv). Dichloromethane (1 mL) and methanol (1 mL) were added sequentially and the resulting solution was treated with a solution of sodium methoxide (25 wt% in MeOH, 0.03 mL, 0.13 mmol, 1.2 equiv) at 23 °C. After 10 min, the reaction mixture was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (2:1, hexanes:ethyl acetate) to provide 1-naphthylamine **14** (13.5 mg, 0.07 mmol, 67%) as a yellow oil. *Note: 1-Naphthylamine **14** decomposes quickly both upon concentration and exposure to acidic conditions.*

TLC (1:1, hexanes:ethyl acetate): R_f = 0.52 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.65 (m, 2H), 7.43 – 7.39 (m, 2H), 7.26 – 7.21 (m, 1H), 6.91 (t, *J* = 7.3 Hz, 1H), 3.82 (s, 3H), and 2.60 (br s, 2H).
^{1}H NMR (600 MHz, C_6D_6) δ 7.85 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.55 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.14 – 7.09 (m, 2H), 7.00 – 6.97 (m, 1H), 6.57 – 6.53 (m, 1H), 3.36 (s, 3H), and 1.80 (br s, 2H).
^{13}C NMR (151 MHz, C_6D_6) δ 166.5, 153.7, 148.5, 133.3, 132.0, 130.9, 128.4, 128.0, 126.6, 126.5, 123.9, and 51.6.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3359 (s), 3060 (w), 3027 (w), 3002 (w), 2952 (m), 2851 (w), 1716 (s), 1604 (w), 1484 (w), 1436 (w), 1253 (s), 1024 (w), and 758 (m).
HRMS (ESI): calcd for ([M+H], $C_{12}H_{12}NO_2)^+$: 202.0863, found: 202.0862.

8 Pyrido[1,2-*a*]indole Derivatization

8.1 Synthesis of benzoyl pyrido[1,2-*a*]indole 16

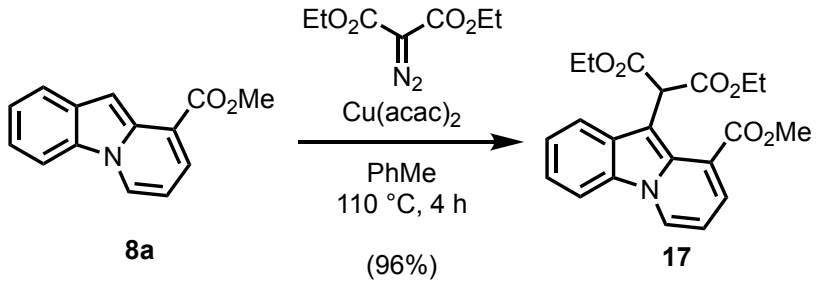


8a (61%) **16**

A flame-dried microwave vial was charged with a magnetic stirring bar and taken into a N_2-filled glovebox where aluminum chloride (27 mg, 0.20 mmol, 2.0 equiv) was added. The vial was sealed with a septum cap, taken out of the glovebox, and anhydrous dichloromethane (1 mL) was added under N_2. The resulting mixture was cooled to 0 °C, and benzoyl chloride (14 μL, 0.12 mmol, 1.2 equiv) followed by a solution of pyrido[1,2-*a*]indole **8a** (23 mg, 0.10 mmol, 1.0 equiv) in dichloromethane (1 mL) were added at 0 °C, and the resulting mixture was gradually warmed to 23 °C. After 75 min, the reaction mixture was diluted with water (2 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (3×2 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (3 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by Yamazen automated flash column chromatography on silica gel (3:1→1:3, hexanes:ethyl acetate) to provide benzoyl pyrido[1,2-*a*]indole **16** (20 mg, 0.06 mmol, 61%) as a yellow oil.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.30 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.62 (dd, *J* = 7.0, 1.2 Hz, 1H), 7.95 – 7.90 (m, 1H), 7.90 – 7.86 (m, 2H), 7.69 (dd, *J* = 6.9, 1.2 Hz, 1H), 7.67 – 7.62 (m, 1H), 7.58 – 7.54 (m, 1H), 7.49 – 7.44 (m, 2H), 7.41 – 7.36 (m, 2H), 6.84 (t, *J* = 6.9 Hz, 1H), and 3.58 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 191.8, 166.6, 140.6, 134.9, 132.2, 130.2, 129.8, 129.4, 129.3, 128.7, 127.7, 125.5, 124.7, 122.1, 121.4, 110.4, 109.4, 106.7, and 52.2.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3057 (w), 3029 (m), 2950 (m), 2849 (w), 1724 (s), 1623 (m), 1499 (s), 1464 (s), 1403 (w), 1337 (w), 1275 (s), 1224 (s), 1199 (m), 1146 (w), 1090 (w), 760 (m), 745 (m), and 707 (m).
HRMS (ESI): calcd for ([M+H], $C_{21}H_{16}NO_3$)$^+$: 330.1125, found: 330.1126.

8.2 Synthesis of pyrido[1,2-*a*]indole malonate 17

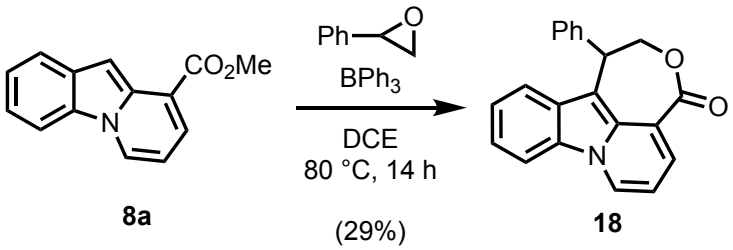


8a **17**

An oven-dried vial was charged with a magnetic stirring bar and pyrido[1,2-*a*]indole **8a** (11 mg, 0.05 mmol, 1.0 equiv). The vial was flushed with nitrogen and sealed with a septum cap. A solution of diethyl 2-diazomalonate (12 mg, 0.06 mmol, 1.2 equiv) in toluene (1.5 mL) was subsequently added and the resulting solution was treated with copper(II) acetylacetonate (0.7 mg, 0.003 mmol, 5 mol%) at 23 °C. The resulting mixture was then heated to 110 °C and held at this temperature. After 4 h, the reaction mixture was cooled to 23 °C and was directly poured onto a pre-packed silica gel column and the mixture was purified by flash column chromatography (3:1, hexanes:ethyl acetate) to provide pyrido[1,2-*a*]indole malonate **17** (18 mg, 0.05 mmol, 96%) as a red solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.13 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.46 (d, *J* = 7.0 Hz, 1H), 7.89 (d, *J* = 8.3 Hz, 1H), 7.83 (d, *J* = 8.3 Hz, 1H), 7.64 (d, *J* = 6.9 Hz, 1H), 7.43 – 7.38 (m, 1H), 7.35 – 7.31 (m, 1H), 6.49 (t, *J* = 6.9 Hz, 1H), 5.78 (s, 1H), 4.27 – 4.17 (m, 4H), 3.97 (s, 3H), and 1.23 (t, *J* = 7.1 Hz, 6H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 169.5, 167.1, 130.4, 130.0, 129.6, 129.2, 128.6, 124.0, 122.0, 121.3, 121.1, 110.1, 106.0, 98.2, 61.6, 52.8, 50.3, and 14.2.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3095 (w), 2982 (m), 2956 (w), 2933 (w), 2854 (w), 1718 (s), 1526 (w), 1465 (w), 1305 (w), 1266 (s), 1193 (m), 1180 (s), 1032 (w), and 743 (m).
HRMS (ESI): calcd for ([M+H], $C_{21}H_{22}NO_6$)$^+$: 384.1442, found: 384.1436.
mp: 91–95 °C.

8.3 Synthesis of tetracyclic lactone 18

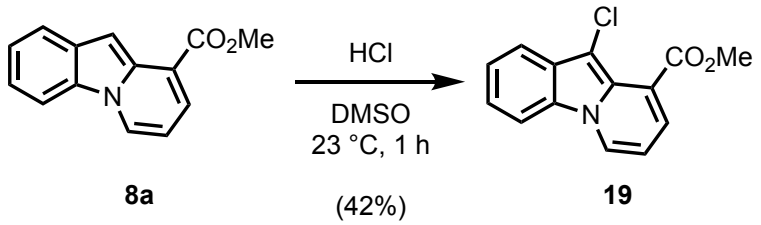


A flame-dried vial was charged with a magnetic stirring bar, pyrido[1,2-*a*]indole **8a** (24 mg, 0.11 mmol, 1.0 equiv), and styrene oxide (36 μL, 0.32 mmol, 3.0 equiv). The vial was taken into a N_2-filled glovebox where triphenyl borane (26 mg, 0.11 mmol, 1.0 equiv) and N_2-sparged (30 min) 1,2-dichloroethane (0.5 mL) were added sequentially at 23 °C. The resulting mixture was heated at 80 °C with stirring. After 14 h, the reaction mixture was cooled to 23 °C and filtered through a silica plug eluting with ethyl acetate and concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (5:1→3:1, hexanes:ethyl acetate) followed by preparative thin layer chromatography on silica gel (5:1, dichloromethane:ethyl acetate) to provide tetracyclic lactone **18** (9.7 mg mg, 0.03 mmol, 29%) as a dark red solid.

Recrystallization (ethyl acetate/hexanes) of the product gave crystals suitable for X-ray diffraction (see Section 11)

TLC (3:1, hexanes:ethyl acetate): R_f = 0.20 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, Acetone) δ 9.05 (dd, *J* = 7.0, 1.0 Hz, 1H), 8.23 (d, *J* = 8.2 Hz, 1H), 7.99 (dd, *J* = 6.9, 1.1 Hz, 1H), 7.40 – 7.21 (m, 8H), 6.77 (t, *J* = 6.9 Hz, 1H), 4.98 – 4.91 (m, 2H), and 4.86 – 4.82 (m, 1H).
^{13}C NMR (151 MHz, Acetone) δ 168.1, 142.1, 134.1, 131.5, 130.9, 130.5, 129.4, 129.3, 128.9, 127.7, 124.6, 121.8, 120.8, 119.6, 112.0, 107.4, 106.7, 73.4, and 44.1.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3059 (w), 3028 (w), 2927 (w), 2853 (w), 1700 (s), 1520 (m), 1460 (m), 1343 (m), 1255 (m), 1100 (w), and 742 (m).
HRMS (ESI): calcd for ([M+Na], $C_{21}H_{15}NNaO_2)^+$: 336.0995, found: 336.0999.
mp: 180–182 °C.

8.4 Synthesis of chloro pyrido[1,2-*a*]indole 19



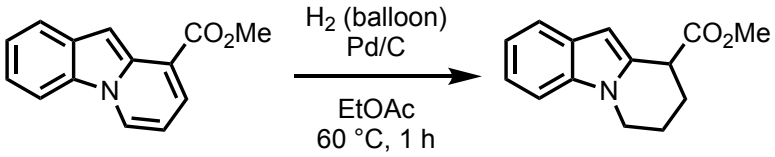
8a (42%) **19**

An oven-dried vial was charged with a magnetic stirring bar and pyrido[1,2-*a*]indole **8a** (23 mg, 0.10 mmol, 1.0 equiv). The vial was flushed with nitrogen and sealed with a septum cap. Dimethyl sulfoxide (1 mL) was subsequently added and the resulting solution was treated with an aqueous hydrogen chloride solution (12 M, 0.4 mL) at 23 °C. After 1 h, the reaction mixture was diluted with saturated aqueous sodium bicarbonate solution (1 mL) and diethyl ether (2 mL). The layers were separated, the aqueous layer was extracted with diethyl ether (3×2 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (3 mL). The washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (5:1→3:1, hexanes:ethyl acetate) to provide chloro pyrido[1,2-*a*]indole **19** (11 mg, 0.042 mmol, 42%) as a red solid.

Recrystallization (ethyl acetate/hexanes) of the product gave crystals suitable for X-ray diffraction (see Section 11)

TLC (5:1, hexanes:ethyl acetate): R_f = 0.26 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, $CDCl_3$) δ 8.40 (dd, *J* = 7.1, 1.0 Hz, 1H), 7.86 (dd, *J* = 8.3, 3.6 Hz, 2H), 7.52 – 7.47 (m, 1H), 7.41 – 7.36 (m, 2H), 6.52 (t, *J* = 6.9 Hz, 1H), and 4.03 (s, 3H).
^{13}C NMR (176 MHz, $CDCl_3$) δ 166.7, 128.2, 127.6, 127.4, 127.3, 126.9, 124.3, 122.9, 121.9, 118.7, 110.2, 106.5, 95.8, and 52.6.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3054 (w), 2949 (m), 2925 (w), 2852 (w), 1724 (s), 1519 (w), 1461 (m), 1435 (w), 1345 (m), 1277 (s), 1232 (m), 1196 (m), 1180 (m), and 738 (s).
HRMS (ESI): calcd for ([M+H], $C_{14}H_{11}ClNO_2)^+$: 260.0473, found: 260.0476.
mp: 67–70 °C.

8.5 Synthesis of tricyclic indole 20

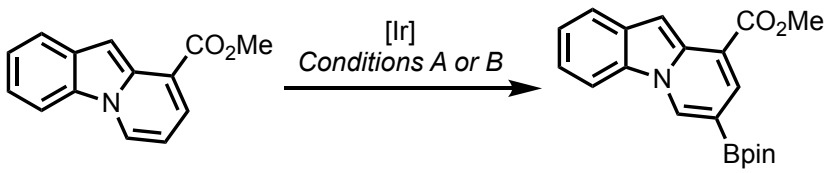


8a (78%) **20**

A flame-dried vial was charged with a magnetic stirring bar, pyrido[1,2-*a*]indole **8a** (23 mg, 0.1 mmol, 1.0 equiv), and palladium on carbon (10 wt.%, 11 mg, 0.01 mmol, 0.1 equiv). The vial was flushed with nitrogen and sealed with a septum cap. Anhydrous ethyl acetate (2 mL) was subsequently added and the resulting mixture was sparged with hydrogen gas for 5 min. The reaction mixture was then heated at 60 °C under H_2 atmosphere while stirring. After 1 h, the reaction mixture was cooled to 23 °C and was filtered through a Celite® plug eluting with ethyl acetate (5 mL), and the filtrate was concetrated *in vacuo*. The crude residue was purified by Yamazen automated flash column chromatography on silica gel (20:1→3:1, hexanes:ethyl acetate) to provide tricyclic indole **20** (18 mg, 0.08 mmol, 78%) as a yellow oil.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.50 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 – 7.53 (m, 1H), 7.30 – 7.27 (m, 1H), 7.19 – 7.15 (m, 1H), 7.12 – 7.07 (m, 1H), 6.41 – 6.39 (m, 1H), 4.10 – 4.05 (m, 3H), 3.78 (s, 3H), 2.34 – 2.27 (m, 1H), 2.26 – 2.19 (m, 1H), 2.17 – 2.11 (m, 1H), and 2.08 – 2.00 (m, 1H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 173.1, 136.4, 132.8, 128.0, 121.2, 120.3, 120.1, 109.0, 99.7, 52.5, 42.1, 40.9, 24.4, and 21.3.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3050 (w), 3023 (w), 2950 (m), 2869 (w), 1733 (s), 1456 (m), 1366 (w), 1313 (m), 1261 (w), 1207 (m), 1164 (s), 1026 (w), and 748 (m).
HRMS (ESI): calcd for ([M+H], $C_{24}H_{16}NO_2)^+$: 230.1176, found: 230.1178.

8.6 Synthesis of boronate ester 21



8a **21**

Table S2. Optimization of C–H borylation of pyrido[1,2-*a*]indole **8a**.

Entry	mmol 8a	Conditions A or B, Temp.	8a:21 (% qNMR yield 21)
1	0.0479	A, 23→80 °C	2.79 : 1.00
2	0.0444	B, 23→80 °C	1.00 : 3.15 (20%), not very clean
3	0.0453	A, 100 °C	1.00 : 1.55 (33%)
4	0.0462	B, 60 °C	no SM (52%), fairly clean
5	0.102	B, 60 °C	40% isolated (see below for details)

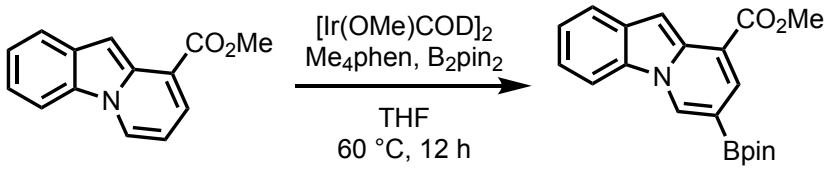
qNMR yields (entries 2–4) were determined by using 1,2,3-trimethoxybenzene as an internal standard.

Condition A[7]: In a N_2-filled glovebox, a flame-dried vial was charged with a magnetic stirring bar, (1,5-cyclooctadiene)(methoxy)iridium(I) dimer (4.0 mol%), 4,4'-di-*tert*-butyl-2,2'-dipyridyl (8.0 mol%), N_2-sparged (30 min) tetrahydrofuran (0.25 mL), and pinacolborane (1.1 equiv). The resulting mixture was brought out of the glovebox and was stirred at 23 °C for 10 min. A solution of pyrido[1,2-*a*]indole **8a** (1.0 equiv) in tetrahydrofuran (0.25 mL) was subsequently added and the resulting mixture was heated in a preheated (indicated temperature) heating block. After 16 h, the reaction mixture was cooled to 23 °C and was filtered through a Celite® plug eluting with ethyl acetate, and the filtrate was concetrated *in vacuo*. The crude residue was analyzed by quantitative NMR spectroscopy.

Condition B[5]: A flame-dried vial was charged with a magnetic stirring bar and bis(pinacolato)diboron (1.0 equiv) and taken into a N_2-filled glovebox. An aliquot (0.2 mL) of a stock solution (3 mg [Ir]/2 mL of THF) of (1,5-cyclooctadiene)(methoxy)iridium(I) dimer (1.0 mol%) and 3,4,7,8-tetramethyl-1,10-phenanthroline (2.0 mol%) in tetrahydrofuran was added and the resulting mixture was heated at 80 °C with stirring for 1 h. The resulting mixture was then transferred to a separate flame-dried vial charged with a magnetic stirring bar and pyrido[1,2-*a*]indole **8a** (1.0 equiv) at 23 °C. The catalyst vial was rinsed with additional tetrahydrofuran (0.2 mL) and the resulting mixture was heated in a preheated (indicated temperature) heating block. After 16 h, the reaction mixture was cooled to 23 °C and was filtered through a Celite® plug eluting with ethyl acetate, and the filtrate was concetrated *in vacuo*. The crude residue was analyzed by quantitative NMR spectroscopy.

During our optimization efforts for the borylation of pyrido[1,2-*a*]indole **8a**, we focused mainly on screening conditions A and B at various temperatures. Both conditions A and B did not provide any product at lower temperatures (23 °C) and required heating to achieve conversion. Heating to 80 °C (entries 1 and 2, Table S2) provided a complex mixture of unreacted starting material, boronate ester **21**, and unidentified side products. Employing condition A at 100 °C (entry 3) further improved conversion compared to entry 1 and provided **21** in moderate yield (33% qNMR yield). We then found that utilizing condition B at moderately elevated temperatures (60 °C, entry 4) provided an overall cleaner reaction (as judged by TLC and crude NMR) with full conversion and good yield (52% qNMR yield). This optimal set of conditions scaled well to 0.1 mmol of **8a** (entry 5), once again providing full conversion and a moderate isolated yield (40%).

Procedure for the synthesis of boronate ester **21**:

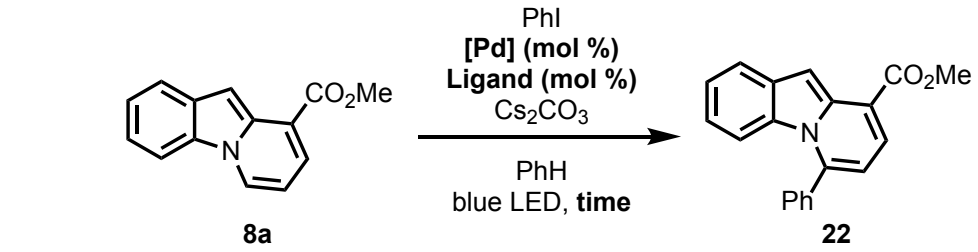


8a (40%) **21**

A flame-dried vial was charged with a magnetic stirring bar and bis(pinacolato)diboron (25 mg, 0.10 mmol, 1.0 equiv). The vial was flushed with nitrogen and sealed with a septum cap. An aliquot (0.5 mL) of a stock solution (3 mg [Ir]/2.5 mL of THF) of (1,5-cyclooctadiene)(methoxy)iridium(I) dimer (1.0 mol%) and 3,4,7,8-tetramethyl-1,10-phenanthroline (2.0 mol%) in tetrahydrofuran was subsequently added and the resulting mixture was heated at 80 °C with stirring for 1 h. The resulting complex was then transferred to a separate flame-dried vial charged with a magnetic stirring bar and pyrido[1,2-*a*]indole **8a** (23 mg, 0.10 mmol, 1.0 equiv) at 23 °C. The vial that contained the complex was rinsed with additional tetrahydrofuran (0.5 mL) and the resulting mixture was heated in a preheated (60 °C) heating block. After 12 h, the reaction mixture was cooled to 23 °C and was directly poured onto a pre-packed silica gel column and the mixture was purified by flash column chromatography (8:1, hexanes:ethyl acetate) to provide boronate ester **21** (14 mg, 0.04 mmol, 40%) as an orange solid. *Note: Slow decomposition of **21** is observed upon prolonged exposure to acidic conditions*.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.60 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.94 (d, *J* = 1.1 Hz, 1H), 8.11 (d, *J* = 1.1 Hz, 1H), 8.01 – 7.98 (m, 1H), 7.85 – 7.81 (m, 1H), 7.45 – 7.41 (m, 1H), 7.37 (br s, 1H), 7.35 – 7.31 (m, 1H), 3.99 (s, 3H), 1.39 (s, 12H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.0, 136.8, 133.4, 133.2, 130.7, 129.9, 124.3, 121.1, 120.8, 119.4, 110.8, 95.7, 84.3, 52.1, and 25.0. (*Missing the carbon signal directly bonded to boron, due to quadrupole relaxation*)
^{11}B NMR (193 MHz, $CDCl_3$) δ 30.5
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3054 (w), 2978 (m), 2950 (w), 2927 (w), 2855 (w), 1715 (s), 1606 (m), 1460 (w), 1390 (s), 1339 (m), 1311 (s), 1259 (s), 1201 (s), 1141 (s), 793 (w), and 671 (w).
HRMS (ESI): calcd for ([M+H], $C_{20}H_{23}BNO_4$)$^+$: 352.1715, found: 352.1717.
mp: 184–189 °C.

8.7 Synthesis of biaryl compound 22



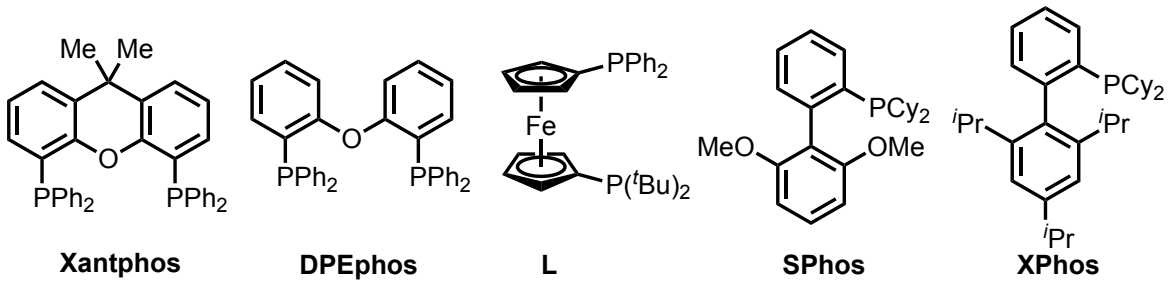


Table S3. Optimization of Heck coupling.

Entry	[Pd] (mol %)	Ligand (mol %)	Modification	Time	8a:22 (% NMR yield, % brsm)[a]
1	$Pd(PCy_3)_2$ (10 mol %)	None	1,4-dioxane, 100 °C, no light	16 h	Mostly **8a**, trace **22**
2	$Pd(OAc)_2$ (20 mol %)	Xantphos (40 mol %)	–	19 h	4.67 : 1.00 (15%, 44% brsm)
3	$Pd(OAc)_2$ (20 mol %)	Xantphos (40 mol %)	–	48 h	2.06 : 1.00 (19%, 34% brsm)
4	$Pd(OAc)_2$ (50 mol %)	Xantphos (100 mol %)	–	15.5 h	3.40 : 1.00 (20%, 60% brsm)
5	$Pd(OAc)_2$ (100 mol %)	Xantphos (200 mol %)	–	15.5 h	3.22 : 1.00 (22%, 77% brsm)
6	$Pd(OAc)_2$ (2 mol %)	Xantphos (4 mol %)	–	19 h	Mostly **8a**, trace **22**
7[b]	$Pd(OAc)_2$ (60 mol %)	Xantphos (120 mol %)	–	3 d	1.97 : 1.00 (29%, 66% brsm)
8	$Pd(OAc)_2$ (50 mol %)	Xantphos (100 mol %)	80 °C, no light	16.5 h	Only unreacted **8a**
9	$Pd(OAc)_2$ (50 mol %)	Xantphos (100 mol %)	2 LED lamps	24 h	3.90 : 1.00 (18%, 59% brsm)
10	$Pd(OAc)_2$ (20 mol %)	DPEphos (40 mol %)	–	20 h	6.08 : 1.00 (12%, 43% brsm)
11	$Pd(OAc)_2$ (20 mol %)	L (40 mol %)	–	20 h	6.10 : 1.00 (11%, 34% brsm)
12	$Pd(OAc)_2$ (20 mol %)	SPhos (40 mol %)	–	19 h	Mostly **8a**, trace **22**
13	$Pd(OAc)_2$ (20 mol %)	XPhos (40 mol %)	–	19 h	8.32 : 1.00 (7%)
14[b]	$Pd(OAc)_2$ (60 mol %)	Xantphos (120 mol %)	0.1 mmol scale	3 d	23% isolated (91% brsm)

The reaction conditions of the initial attempts to access biaryl compound (**22**) and subsequent optimization attempts of this cross-coupling are summarized in Table S3. All of the optimization attempts (entries 1–13, Table S3) were conducted on approximately 0.04 mmol scale following the procedure outlined below.

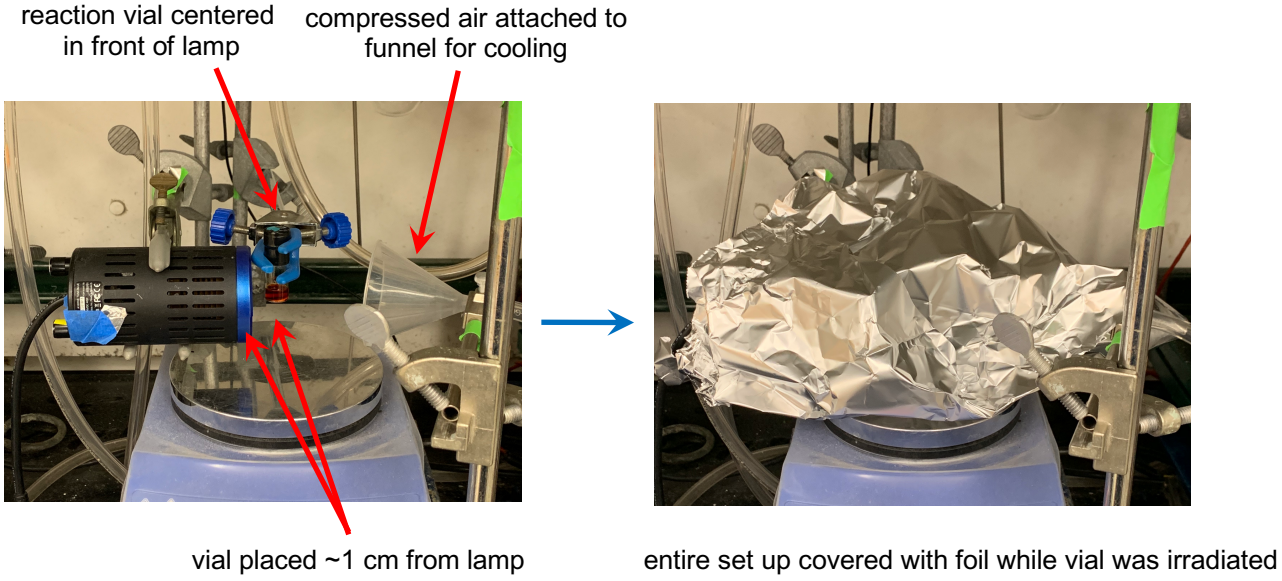
General procedure followed for conducting the optimization attempts:

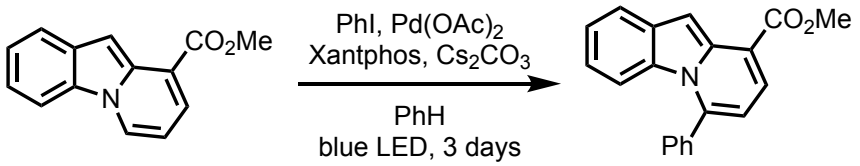
A flame-dried vial was charged with a magnetic stirring bar, pyrido[1,2-*a*]indole **8a** (1.0 equiv), ligand (Note: DPEPhos, L, and XPhos were all stored and added in a glovebox), and Pd-catalyst (Note: $Pd(PCy_3)_2$ was stored and added in a glovebox). The vial was sealed and taken into a N_2-filled glvoebox where cesium carbonate (3.0 equiv), benzene (freeze-pump-thawed 5 cycles, 0.18 M), and iodobenzene were added sequentially. The vial was sealed, taken out of the glovebox, and the reaction mixture was stirred while either being heated (using a preheated heating block) or irradiated with one or two Kessil A160WE Tuna Blue LED lamp(s) [Note: for reactions that were irradiated, compressed air was used for cooling to maintain a temperature of 23 °C, the vial was placed 1 cm away from the lamp(s), and the entire setup was covered with foil (see Figure S5 for details)]. After the indicated period of time (Table S3), the reaction mixture was filtered through a Celite® plug eluting with ethyl acetate, the filtrate was concetrated *in vacuo*, and the crude residue was analyzed by NMR spectroscopy.

Our screening efforts for this reaction began by testing standard Heck coupling conditions between pyrido[1,2-*a*]indole **8a** and iodobenzene with a Pd(0) catalyst ($Pd(PCy_3)_2$) in dioxane (sparged with N_2) at 100 °C (entry 1, Table S3). After 16 h, we mostly recovered the starting pyrido[1,2-*a*]indole **8a** with trace amounts of a coupled product that was later identified as biaryl compound **22**. On this basis, we next turned our attention toward investigating photo-mediated Heck-type couplings.[16] We first began by testing a $Pd(OAc)_2$ (20 mol %)/Xantphos (40 mol %) catalyst system with blue LED irradtion (entry 2), which formed biaryl coupound **22** in 15% yield (44% brsm). We observed that the yield only slightly improved (15%→19%) when the mixture was irradiated for 48 h instead (entry 3). Next, we investigated catalyst loading (entries 4–6) and found that as the catalyst loading increased, the yield mildly improved; however, we were only able to obtain 22% yield of **22** with stoichiometric quantities of $Pd(OAc)_2$ (entry 5). Low catalyst loading (entry 6) only provided trace amounts of **22**. In an attempt to further improve conversion, we performed three iterative additions of 20 mol % of catalyst over the course of three days (entry 7), which provided the highest yield thus far (29%, 66% brsm). A control experiment (entry 8) was performed where the mixture was heated, but not irradiated with light, which only returned the starting material and no product. This result confirmed the necessity of light for this process. Intrigued by the necessity for blue LED irradiation, we next irradiated the reaction mixture with two lamps instead of one, but this unfortunately did not improve conversion or yield (entry 9). Finally, we investigated the effect of other bidentate (entries 10 and 11) and monodentate (entries 12 and 13) phosphine ligands on this cross-coupling; however, all of the ligands we screened did not improve the yield. From these studies, we concluded that entry 7 (iterative addition of catalyst over three days) was the most effective set of conditions, and we performed this reaction on 0.1 mmol scale (discussed in detail below), which furnished the desired cross-coupled product (**22**) in 23% (91% brsm) isolated yield.

Reaction Set Up:

Figure S5. Reaction set up for photo-mediated Heck coupling to access **22.**





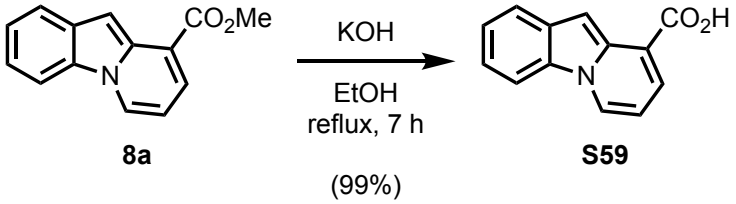
8a (23%, 91% brsm) **22**

A flame-dried vial was charged with a magnetic stirring bar, pyrido[1,2-*a*]indole **8a** (24 mg, 0.11 mmol, 1.0 equiv), Xantphos (24 mg, 0.04 mmol, 0.4 equiv) and palladium(II) acetate (5 mg, 0.02 mmol, 0.2 equiv). The vial was then taken into a N_2-filled glovebox where cesium carbonate (104 mg, 0.32 mmol, 3.0 equiv), benzene (freeze-pump-thawed 5 cycles, 0.6 mL), and iodobenzene (18 μL, 0.16 mmol, 1.5 equiv) were added sequentially. The vial was sealed, taken out of the glovebox, and the reaction mixture was irradiated with a Kessil A160WE Tuna Blue LED lamp. The temperature of the reaction system was maintained at 23 °C by cooling with a compressed air set up, and the vial distance from the lamp was about 1 cm. After 24 h, the reaction mixture was treated with a second portion of Xantphos (24 mg, 0.04 mmol, 0.4 equiv), palladium(II) acetate (5 mg, 0.02 mmol, 0.2 equiv), and benzene (0.1 mL), and the stirring was continued under irradiation. After an additional 24 h, the mixture was once again treated with a third portion of Xantphos (24 mg, 0.04 mmol, 0.4 equiv), palladium(II) acetate (5 mg, 0.02 mmol, 0.2 equiv), and benzene (0.1 mL), and stirring was continued under the same conditions. After a total of 3 d, the reaction mixture was filtered through a Celite® plug eluting with ethyl acetate (5 mL), and the filtrate was concetrated *in vacuo*. The crude residue was purified by preparative thin layer chromatography on silica gel (3:1, hexanes:ethyl acetate) to provide biaryl compound **22** (7.4 mg, 0.02 mmol, 23%; 91% brsm) as a red oil and unreacted **8a** (18 mg, 0.08 mmol, 75%) as a red solid, in order of elution.

TLC (3:1, hexanes:ethyl acetate): R_f = 0.60 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 – 7.87 (m, 1H), 7.84 – 7.80 (m, 1H), 7.64 – 7.56 (m, 4H), 7.54 – 7.50 (m, 2H), 7.30 – 7.26 (m, 1H), 6.90 – 6.85 (m, 1H), 6.54 – 6.50 (m, 1H), 6.37 – 6.34 (m, 1H), and 4.03 (s, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.1, 145.4, 136.1, 135.0, 131.0, 130.5, 130.0, 129.3, 128.9, 128.7, 123.2, 120.9, 119.8, 119.2, 115.3, 109.3, 96.1, and 52.3.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3058 (w), 2950 (m), 2925 (m), 2853 (w), 1714 (s), 1543 (w), 1446 (w), 1274 (w), 1246 (s), 1204 (m), 1129 (m), 791 (w), 768 (w), and 702 (w).
HRMS (ESI): calcd for ([M+H], $C_{20}H_{16}NO_2)^+$: 302.1176, found: 302.1180.

9 Formal Synthesis of Fascaplysin Congeners

9.1 Synthesis of carboxylic acid S59

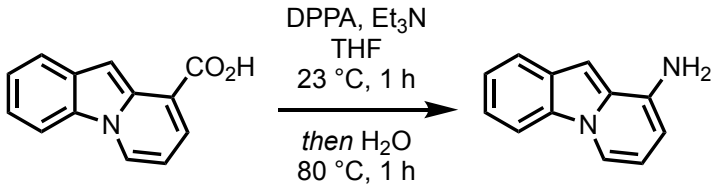


8a **S59**

A round-bottomed flask was charged with a magnetic stirring bar and pyrido[1,2-*a*]indole **8a** (589 mg, 2.62 mmol, 1.0 equiv). A solution of potassium hydroxide (3 g, 53.5 mmol, 20 equiv) in ethanol (26 mL) was added and the resulting mixture was heated at 80 °C. After 7 h, the reaction mixture was cooled to 23 °C, and diluted with water (20 mL) and diethyl ether (30 mL). The layers were separated and the organic layer was washed with water (2×20 mL). The combined aqueous layers were acidified with glacial acetic acid (1.5 mL) and the resulting mixture was extracted with ethyl acetate (3×20 mL). The combined organic extracts were washed with saturated aqueous sodium chloride solution (50 mL) and the washed organic layer was dried over sodium sulfate, filtered, and the filtrate was concentrated *in vacuo* to provide carboxylic acid **S59** (546 mg, 2.60 mmol, 99%) as a red solid.

TLC (100% ethyl acetate): R_f = 0.57 (UV/$KMnO_4$)
^{1}H NMR (400 MHz, DMSO) δ 13.12 (br s, 1H), 9.16 – 9.11 (m, 1H), 8.31 – 8.25 (m, 1H), 7.86 – 7.79 (m, 2H), 7.42 – 7.35 (m, 1H), 7.33 – 7.28 (m, 1H), 7.26 (br s, 1H) and 6.70 (t, *J* = 6.9 Hz, 1H).
^{13}C NMR (151 MHz, DMSO) δ 166.2, 132.8, 130.3, 129.3, 129.14, 129.07, 123.5, 120.4, 120.0, 111.5, 107.8, 106.4, and 93.7.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3054 (s), 2923 (s), 2852 (m), 2607 (m), 1671 (s), 1615 (w), 1519 (w), 1445 (w), 1296 (m), 1207 (w), 907 (w), 768 (m), and 743 (m).
HRMS (ESI): calcd for ([M+H], $C_{13}H_{10}NO_2)^+$: 212.0706, found: 212.0697.
mp: Decomposed at 236 °C.

9.2 Synthesis of amine 23



S59 **23**

(94%)

An oven-dried vial was charged with a magnetic stirring bar and carboxylic acid **S59** (74 mg, 0.35 mmol, 1.0 equiv). Tetrahydrofuran (3.5 mL) was subsequently added and the resulting solution was treated with triethylamine (0.12 mL) and diphenylphosphoryl azide (0.08 mL, 0.37 mmol, 1.05 equiv) in a sequential fashion, at 23 °C. After 1 h, water (0.6 mL) was added and the resulting mixture was heated at 80 °C. After an additional 1 h, the reaction mixture was cooled to 23 °C and was diluted with saturated aqueous sodium carbonate solution (3 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (3×3 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (3 mL). The washed organic layer was dried over sodium sulfate. The dried solution was filtered, and the filtrate was concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (5:1, hexanes:ethyl acetate) to provide amine **23** (60 mg, 0.33 mmol, 94%) as a yellow solid.

TLC (5:1, hexanes:ethyl acetate): R_f = 0.17 (UV/$KMnO_4$)
^{1}H NMR (700 MHz, Acetone) δ 8.09 (d, *J* = 6.9 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.29 – 7.24 (m, 1H), 7.22 – 7.18 (m, 1H), 6.77 (br s, 1H), 6.45 (t, *J* = 7.0 Hz, 1H), 6.15 (d, *J* = 7.0 Hz, 1H), and 5.14 (br s, 2H).
^{13}C NMR (176 MHz, Acetone) δ 139.2, 132.6, 131.3, 129.5, 123.0, 121.2, 120.1, 114.9, 111.6, 110.2, 99.2, and 88.9.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3456 (s), 3375 (s), 3217 (m), 3104 (w), 3045 (m), 2924 (m), 2853 (w), 1615 (m), 1544 (s), 1513 (w), 1465 (w), 1320 (m), 1228 (w), 760 (m), and 732 (s).
HRMS (ESI): calcd for ([M+H], $C_{12}H_{11}N_2$)$^+$: 183.0917, found: 183.0915.
mp: 138–143 °C.

9.3 Synthesis of 12*H*-pyrido[1,2-*a*:3,4-*b'*]diindole 24

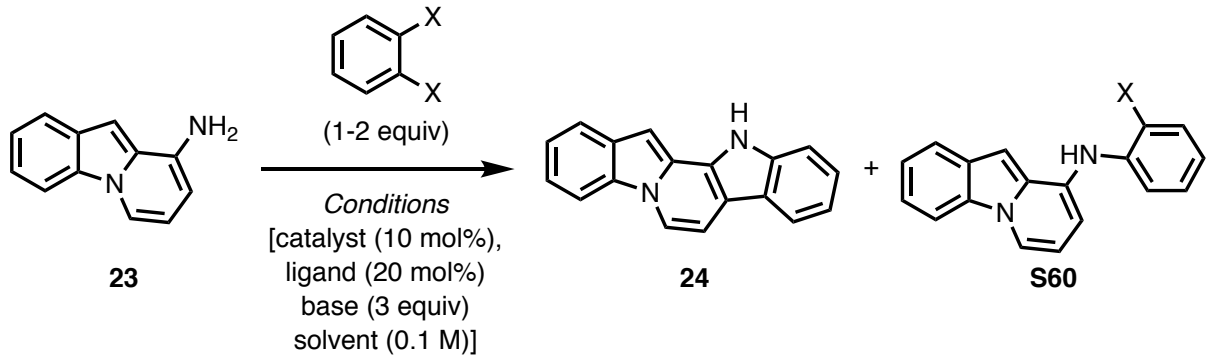


Table S4. Initial discovery and optimization of the domino reaction.

Entry	Conditions	Modification	Comments
1	**X = Cl**, $Pd(OAc)_2$, PCy_3, K_3PO_4, NMP, RT to 110 °C, 12 h	polar-solvent	negligible **24**, very messy
2	**X = Cl**, $Pd(OAc)_2$, PCy_3, NaO^tBu, PhMe, RT to 110 °C, 15 h	non-polar solvent	16% **24** + complex mix (**S60**)
3	**X = Cl**, $Pd(OAc)_2$, PCy_3, NaO^tBu, PhMe, 110 °C, 8 h	shorter rxn time	15% **24**, same as above
4	**X = Br**, $Pd(OAc)_2$, PCy_3, NaO^tBu, PhMe, 100 °C, 20 h	X = Br	7% **24** (14% brsm), 49% conv.[a]
5	**X = I**, $Pd(OAc)_2$, PCy_3, NaO^tBu, PhMe, 100 °C, 20 h	X = I	21% **24** (31% brsm), 67% conv.[a]
6	**X = Cl**, $Pd(OAc)_2$, PCy_3, Cs_2CO_3, PhMe, 100 °C, 8 h	Base = Cs_2CO_3	recovered ~50% **23**
7	**X = I**, $Pd(OAc)_2$, XPhos, NaO^tBu, PhMe, 100 °C, 16 h	Ligand = Xphos	6% **24** + complex mix (**S60**)[a]
8	**X = I**, $Pd(OAc)_2$, DavePhos, NaO^tBu, PhMe, 100 °C, 16 h	Ligand = DavePhos	15% **24** + complex mix (**S60**)[a]
9	**X = I**, $Pd(OAc)_2$, RuPhos, NaO^tBu, PhMe, 100 °C, 16 h	Ligand = RuPhos	14% **24** + complex mix (**S60**)[a]
10	**X = I**, $Pd(OAc)_2$, SPhos, NaO^tBu, PhMe, 100 °C, 16 h	Ligand = SPhos	13% **24** + complex mix (**S60**)[a]
11	**X = I**, $Pd(OAc)_2$, PPh_3, NaO^tBu, PhMe, 100 °C, 16 h	Ligand = PPh_3	4% **24** + 61% **23** + complex mix (**S60**)[a]
12	**X = I**, $Pd(OAc)_2$, P^tBu_3, NaO^tBu, PhMe, 100 °C, 16 h	Ligand = P^tBu_3	5% **24** + 65% **23** + complex mix (**S60**)[a]
13	**X = I**, $PdCl_2$dppf, dppf, NaO^tBu, PhMe, 100 °C, 12 h	bidentate ligand	10% **24**, 28% **S60** (much cleaner)[a]
14	**X = I**, $PdCl_2$dppf, dppf, NaO^tBu, THF, 100 °C, 15 h	THF	15% **24**, 39% **S60**[a]
15	**X = Cl**, $PdCl_2$dppf, dppf, NaO^tBu, PhMe, 100 °C, 15 h	dppf + X = Cl	99% **S60**[a]
16	**X = Br**, $PdCl_2$dppf, dppf, NaO^tBu, PhMe, 100 °C, 15 h	dppf + X = Br	12% **24**, 51% **S60**[a]
17	**X = Cl**, $PdCl_2$dppf, dppf, NaO^tBu, PhMe, 100 °C, 24 h	excess cat. + ligand	4% **24**, 92% **S60**
18	**X = Cl**, $Pd(OAc)_2$, dppf, NaO^tBu, PhMe, 100 °C, 18 h	$Pd(OAc)_2$+dppf	44% **24**, 31% **S60**
19	**X = Cl**, $Pd(OAc)_2$, dppf, NaO^tBu, PhMe, 100 °C, 24 h	longer rxn time	18% **24** + complex mix (**S60**)
20	**X = Br**, $Pd(OAc)_2$, dppf, NaO^tBu, PhMe, 100 °C, 24 h	X = Br	56% **24**, 26% **S60**
21	**X = Br**, $Pd(OAc)_2$, dppf, PivOH, Cs_2CO_3, PhMe, 100 °C, 18 h	PivOH + Cs_2CO_3	25% **24**, 52% **S60**
22	**X = Br**, $Pd(OAc)_2$, dppf, NaO^tBu, PhMe, H_2O, 100 °C, 24 h	PhMe/H_2O	30% **24**, 17% **S60**
23	**X = I**, $Pd(OAc)_2$, dppf, NaO^tBu, PhMe, 100 °C, 24 h	X = I	33% **24**
24	**X = Br**, $Pd(OAc)_2$, dppe, NaO^tBu, PhMe, 100 °C, 18 h	dppe	11% **24** + complex mix (**S60**)
25	**X = Br**, $Pd(OAc)_2$, dppp, NaO^tBu, PhMe, 100 °C, 19 h	dppp	13% **24** + 32% **S60**
26	**X = Br**, $Pd(OAc)_2$, dppb, NaO^tBu, PhMe, 100 °C, 18 h	dppb	6% **24** + complex mix (**S60**)
27	**X = Br**, $Pd(OAc)_2$, dppm, NaO^tBu, PhMe, 100 °C, 19 h	dppm	no reaction
28	**X = Br**, $Pd(OAc)_2$, dppBz, NaO^tBu, PhMe, 100 °C, 19 h	dppBz	no reaction
29	**X = Br**, $Pd(OAc)_2$, (*R*)-BINAP, NaO^tBu, PhMe, 100 °C, 20 h	BINAP	10% **24** + complex mix (**S60**)
30	**X = Br**, $Pd(OAc)_2$, dppf, NaO^tBu, PhMe, 100 °C, 24 h	0.1 mmol scale	55% **24**, 12% **S60**

[a]Yield determined by ^{1}H NMR analysis using 1,1,2,2-tetrachloroethane as an internal standard.

The reaction conditions of the initial attempts to access the pentacyclic 12*H*-pyrido[1,2-*a*:3,4-*b'*]diindole (**24**) and subsequent optimization of this domino reaction are summarized in Table S4. All the optimization attempts (except for entry 30) were conducted on a 0.04 mmol scale following the procedure given below.

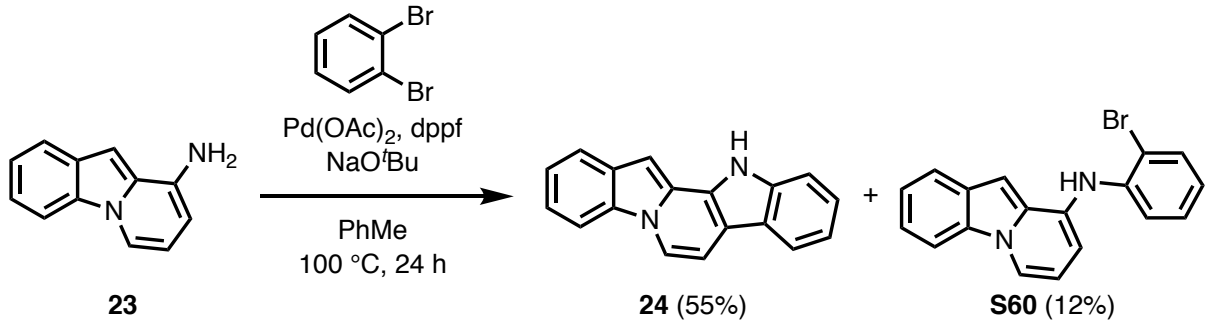
General optimization procedure for the synthesis of 24:

An oven-dried vial was charged with a magnetic stirring bar, amine **23** (1.0 equiv), catalyst (10 mol%), ligand (20 mol%), and base (3.0 equiv). The vial was flushed with nitrogen and sealed with a septum cap. A solution of 1,2-dihalobenzene (1–2 equiv) in anhydrous solvent (0.1 M) was subsequently added and the resulting mixture was heated in a preheated (indicated temperature) heating block with stirring for 8–24 h. The reaction mixture was then cooled to 23 °C, and was filtered through a Celite® plug eluting with ethyl acetate, and the filtrate was concetrated *in vacuo*. The crude residue was either analyzed by NMR spectroscopy or purified by flash column chromatography on silica gel to obtain an isolated yield of **24**.

We commenced our investigation on the basis of the work reported by Ackermann and co-workers,[17] describing a domino reaction between aniline derivatives and 1,2-dihalobenzene to construct a wide variety of carbazole heterocyclic cores. While attempting our envisioned transformation under the previously reported reaction conditions, we found that the polarity of the solvent played a major role in the outcome of the desired domino N–H/C–H activation process; we identified non-polar solvents such as toluene to give the desired product **24** in 16% yield whereas we observed negligible formation of **24** when the reaction was conducted in polar solvents like NMP (entries 1–2). Hence, we decided to proceed with our optimization using toluene as the solvent. We next surveyed other alternative 1,2-dihalobenzene coupling partners and also explored other basic conditions (entries 3–6). A slightly better result was observed with 1,2-diiodobenzene in the presence of sodium *tert*-butoxide as the base (entry 5). These two variables were kept constant for the next set of attempted conditions. Next, a variety of monodentate ligands were screened, but unfortunately, none proved to enhance the yield (entries 7–12).

Interestingly, when the reaction was carried out in the presence of a bidentate catalyst system, Pd(dppf)Cl_2 + dppf, the formation of other undesired side-products were significantly minimized, which was validated by ^{1}H NMR analysis (entry 13). While the net yield of the desired product **24** was still unimproved, the yield of the initial C–N bond forming event was significantly enhanced, which was observed when 1,2-dichlorobenzene (DCB) was used as the coupling partner (entry 15). Although we did not observe the presence of desired pentacyclic compound **24**, the intermediate biaryl amine **S60** was formed almost quantitatively (entry 15), thereby supporting the hypothesis of dppf facilitating the initial C–N bond forming event. We then explored several variations, such as increasing catalyst loading, prolonging reaction time, and screening other 1,2-dihalobenzenes (14–17); however, these all proved unfruitful in improving the yield of **24**. As the second step of the domino reaction involves C–H functionalization to construct the final C–C bond to complete the pentacyclic framework of **24**, we presumed this proceeds through a Concerted Metalation-Deprotonation (CMD) type mechanism. Assuming the advantageous role of dppf in promoting the initial amination process, we chose to combine this ligand with a suitable precatalyst that could favor the subsequent C–H functionalization event. Hence, we chose to return to $Pd(OAc)_2$, which is typically employed as a precatalyst to faciliate CMD-type processes.[18] To our benefit, when the reaction was conducted with a combination of Pd(OAc)2 + dppf catalyst system, the pentacyclic compound (**24**) was isolated in 44% yield (entry 18) and we observed a further elevation in the yield when 1,2-dibromobenzene was used as the coupling partner (entry 20). With this promising result, other variants such as different solvent conditions, alternate bases, and other bidendate ligands were explored (entries 21–29). To our dismay, no attempted variations proved to be beneficial. Hence, we adopted the best yielding reaction conditions (entry 20), and repeated the domino reaction on a 0.1 mmol scale, which gave **24** in 55% yield (entry 30, see below for procedure).

Synthesis of 12*H*-pyrido[1,2-*a*:3,4-*b'*]diindole **24**:



23 **24** (55%) **S60** (12%)

An oven-dried vial was charged with a magnetic stirring bar, amine **23** (18 mg, 0.10 mmol, 1.0 equiv), catalyst (2.5 mg, 0.01 mmol, 10 mol%), ligand (12 mg, 0.02 mmol, 20 mol%), and base (29 mg, 0.30 mmol, 3.0 equiv). The vial was flushed with nitrogen and sealed with a septum cap. A solution of 1,2-dibromobenzene (50 mg, 0.21 mmol, 2.0 equiv) in toluene (1 mL) was subsequently added and the resulting mixture was heated in a preheated (100 °C) heating block. After 24 h, the reaction mixture was cooled to 23 °C and was directly poured onto a pre-packed silica gel column, and the mixture was purified by flash column chromatography on silica gel (30:1→8:1, hexanes:ethyl acetate) to provide aryl amine **S60** (4 mg, 0.01 mmol, 12%) as a bright yellow oil and 12*H*-pyrido[1,2-*a*:3,4-*b'*]diindole **24** (14 mg, 0.06 mmol, 55%) as a yellow solid, in order of elution.

Data for aryl amine **S60**:

TLC (5:1, hexanes:ethyl acetate): R_f = 0.52 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, DMSO) δ 8.45 (d, *J* = 6.9 Hz, 1H), 8.17 (d, *J* = 8.3 Hz, 1H), 7.77 – 7.73 (m, 1H), 7.72 – 7.65 (m, 2H), 7.36 – 7.28 (m, 2H), 7.26 – 7.20 (m, 2H), 7.06 – 7.01 (m, 1H), 6.77 (s, 1H), 6.52 (t, *J* = 7.0 Hz, 1H), and 6.20 (d, *J* = 7.0 Hz, 1H).
^{13}C NMR (151 MHz, DMSO) δ 140.4, 134.2, 133.2, 131.6, 130.0, 128.5, 127.9, 124.6, 124.3, 122.6, 120.3, 119.6, 118.0, 117.3, 111.4, 108.3, 103.6, and 89.5.
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3388 (s), 3055 (m), 2955 (w), 2924 (w), 2853 (w), 1591 (m), 1543 (s), 1505 (m), 1463 (m), 1322 (m), and 734 (s).
HRMS (ESI): calcd for ([M+H], $C_{18}H_{14}BrN_2$)$^+$: 337.0335, found: 337.0334.

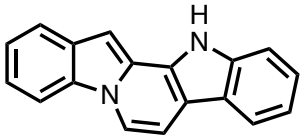
Data for 12*H*-pyrido[1,2-*a*:3,4-*b'*]diindole **24**:

TLC (5:1, hexanes:ethyl acetate): R_f = 0.37 (UV/$KMnO_4$)
^{1}H NMR (600 MHz, DMSO) δ 12.19 (s, 1H), 8.60 (dd, *J* = 7.2, 1.8 Hz, 1H), 8.24 (d, *J* = 8.3 Hz, 1H), 8.03 (d, *J* = 7.9 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 7.38 – 7.31 (m, 3H), 7.30 – 7.25 (m, 1H), 7.24 – 7.19 (m, 1H), and 6.99 (s, 1H).
^{13}C NMR (151 MHz, DMSO) δ 138.2, 130.8, 128.4, 128.3, 123.8, 123.3, 122.3, 120.1, 119.7, 119.6, 119.5, 117.9, 111.6, 111.4, 111.1, 102.8, and 88.7. (*Missing one carbon signal*)
IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: = 3413 (s), 3391 (s), 3054 (w), 2956 (w), 2923 (s), 2853 (m), 1708 (w), 1543 (w), 1518 (w), 1479 (w), 1462 (w), 1439 (m), 1358 (w), 1320 (m), 1221 (w), and 738 (s).
HRMS (ESI): calcd for ([M+H], $C_{18}H_{13}N_2$)$^+$: 257.1073, found: 257.1071.
mp: 227–229 °C.

10 ^{1}H and ^{13}C NMR comparison of 12*H*-pyrido[1,2-*a*:3,4-*b'*]diindole 24 with reported values

10.1 ^{1}H NMR comparison of 12*H*-pyrido[1,2-*a*:3,4-*b'*]diindole 24 with reported values

^{1}H NMR comparison in DMSO-d_6 of our synthetic 12*H*-pyrido[1,2-*a*:3,4-*b'*]diindole (**24**) with Gribble's data[19]

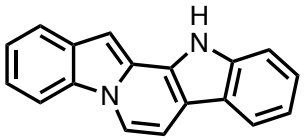


24

Gribble's data[19] (DMSO-d_6)	**Our synthetic data (600 MHz, DMSO-d_6)**	**$\Delta\delta$ (ppm)**
12.20 (s, 1H)	12.19 (s, 1H)	0.01
8.60 (d, 1H)	8.60 (dd, *J* = 7.2, 1.8 Hz, 1H)	0
8.23 (d, 1H)	8.24 (d, *J* = 8.3 Hz, 1H)	0.01
8.03 (d, 1H)	8.03 (d, *J* = 7.9 Hz, 1H)	0
7.83 (d, 1H)	7.83 (d, *J* = 8.0 Hz, 1H)	0
7.59 (d, 1H)	7.60 (d, *J* = 8.1 Hz, 1H)	0.01
7.38–7.17 (m, 5H)	7.38 – 7.31 (m, 3H) 7.30 – 7.25 (m, 1H) 7.24 – 7.19 (m, 1H)	-
6.99 (s, 1H)	6.99 (s, 1H)	0

10.2 ^{1}H NMR comparison of 12*H*-pyrido[1,2-*a*:3,4-*b'*]diindole 24 with reported values

^{13}C NMR comparison in DMSO-d_6 of our synthetic 12*H*-pyrido[1,2-*a*:3,4-*b'*]diindole (**24**) with Gribble's data.[19] Similar to the previously reported data, we also observed a missing carbon signal.



24

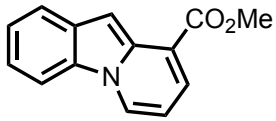
Gribble's data[19] (DMSO-d_6)	Our synthetic data (151 MHz, DMSO-d_6)	$\Delta\delta$ (ppm)
138.2	138.2	0
130.8	130.8	0
128.4	128.4	0
128.3	128.3	0
123.8	123.8	0
123.3	123.3	0
122.3	122.3	0
120.1	120.1	0
119.7	119.7	0
119.6	119.6	0
119.5	119.5	0
117.9	117.9	0
111.6	111.6	0
111.4	111.4	0
111.1	111.1	0
102.8	102.8	0
88.8	88.7	0.1

11 X-Ray Crystallographic Data

X-ray crystallographic data for pyrido[1,2-*a*]indole **8a**, tetracyclic lactone **18**, and chloro pyrido[1,2-*a*]indole **19** (along with their .cif files) are provided along with this supporting information. The X-ray structures in the main manuscript and shown below were visualized using CYLview.[20]

	pyrido[1,2-*a*]indole **8a**	tetracyclic lactone **18**	chloro pyrido[1,2-*a*]indole **19**
Chemical formula	$C_{14}H_{11}NO_2$	$C_{21}H_{15}NO_2$	$C_{14}H_{10}ClNO_2$
Formula weight	225.24	313.34	259.68
Temperature (K)	100(2)	100(2)	100(2)
Wavelength (Å)	1.54184	1.54184	1.54184
Crystal system	Monoclinic	Triclinic	Monoclinic
Space group	P 21/n	P -1	P 21/n
a (Å)	5.04510(10)	10.1840(3)	8.64150(10)
b (Å)	13.6147(3)	11.0563(3)	14.2584(3)
c (Å)	15.6358(3)	14.3733(3)	9.2288(2)
α (°)	90	69.266(2)	90
β (°)	93.956(2)	87.583(2)	97.831(2)
γ (°)	90	89.765(2)	90
V (Å^3)	1071.43(4)	1512.13(7)	1126.51(4)
Z	4	4	4
Densitiy (Mg m^{-3})	1.396	1.376	1.531
Absorption coefficient (mm^{-1})	0.764	0.709	2.942
F(000)	472	656	536
Crystal size (mm^3)	0.240 x 0.190 x 0.170	0.170 x 0.150 x 0.090	0.140 x 0.080 x 0.050
Theta range for data collection (°)	4.310 to 74.502	3.291 to 74.475	5.749 to 74.442
Index ranges	-6<=h<=6, -16<=k<=17, -18<=l<=19	-12<=h<=12, -13<=k<=13, -17<=l<=17	-10<=h<=10, -17<=k<=17, 11<=l<=8
Reflections collected	12038	59212	12636
Independent reflections	2171 [R(int) = 0.1153]	6158 [R(int) = 0.0499]	2301 [R(int) = 0.0436]
Completeness to theta = 74.0°	99.1 %	99.7 %	99.8 %
Absorption correction	Semi-empirical from equivalents	Semi-empirical from equivalents	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.78460	1.00000 and 0.88354	1.00000 and 0.60173
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	2171 / 0 / 156	6158 / 0 / 433	2301 / 0 / 164
Goodness-of-fit on F^2	1.071	1.038	1.064
Final R indices [I>2sigma(I)]	R1 = 0.0561, wR2 = 0.1650	R1 = 0.0366, wR2 = 0.0924	R1 = 0.0350, wR2 = 0.0951
R indices (all data)	R1 = 0.0573, wR2 = 0.1667	R1 = 0.0390, wR2 = 0.0941	R1 = 0.0379, wR2 = 0.0971
Extinction coefficient	0.012(3)	n/a	n/a
Largest diff. Peak and hole (e.Å^{-3})	0.304 and -0.345	0.234 and -0.238	0.240 and -0.363

a) pyrido[1,2-*a*]indole **8a**



8a

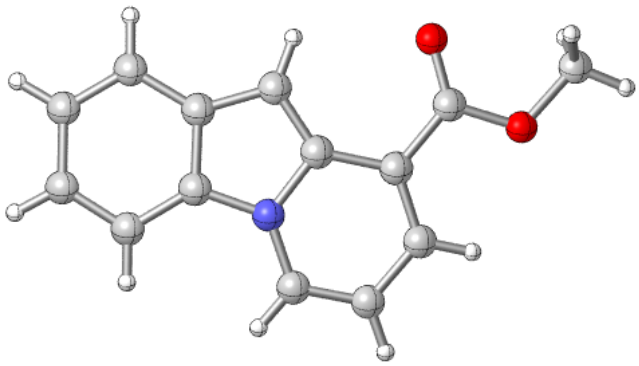
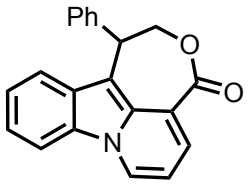


Figure S6. CYLview rendering of pyrido[1,2-*a*]indole **8a**

This crystal structure has been deposited at the Cambridge Crystallographic Data Center under **CCDC 2034052**.

b) tetracyclic lactone **18**



18

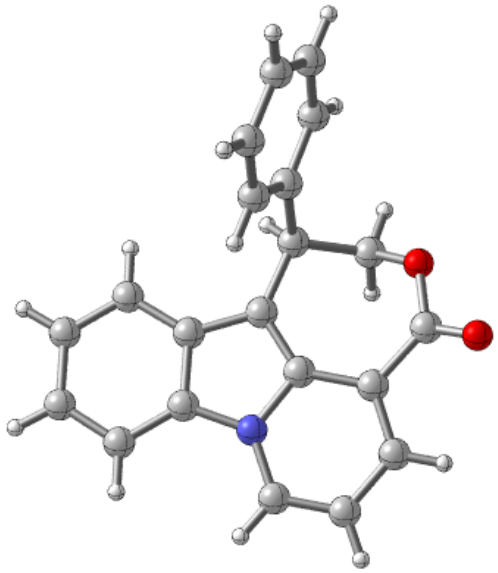
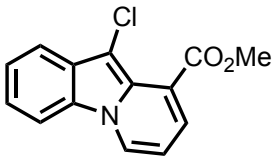


Figure S7. CYLview rendering of tetracyclic lactone **18**

This crystal structure has been deposited at the Cambridge Crystallographic Data Center under **CCDC 2034054**.

a) chloro pyrido[1,2-*a*]indole **19**



19

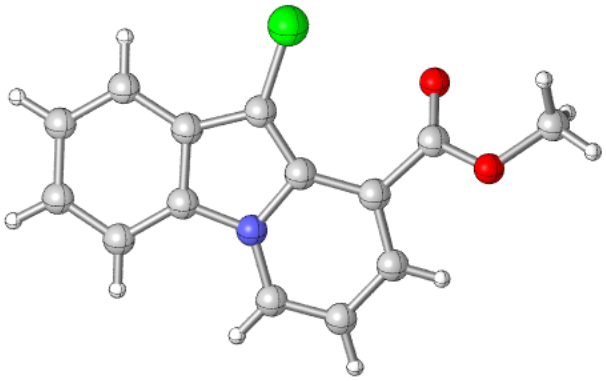
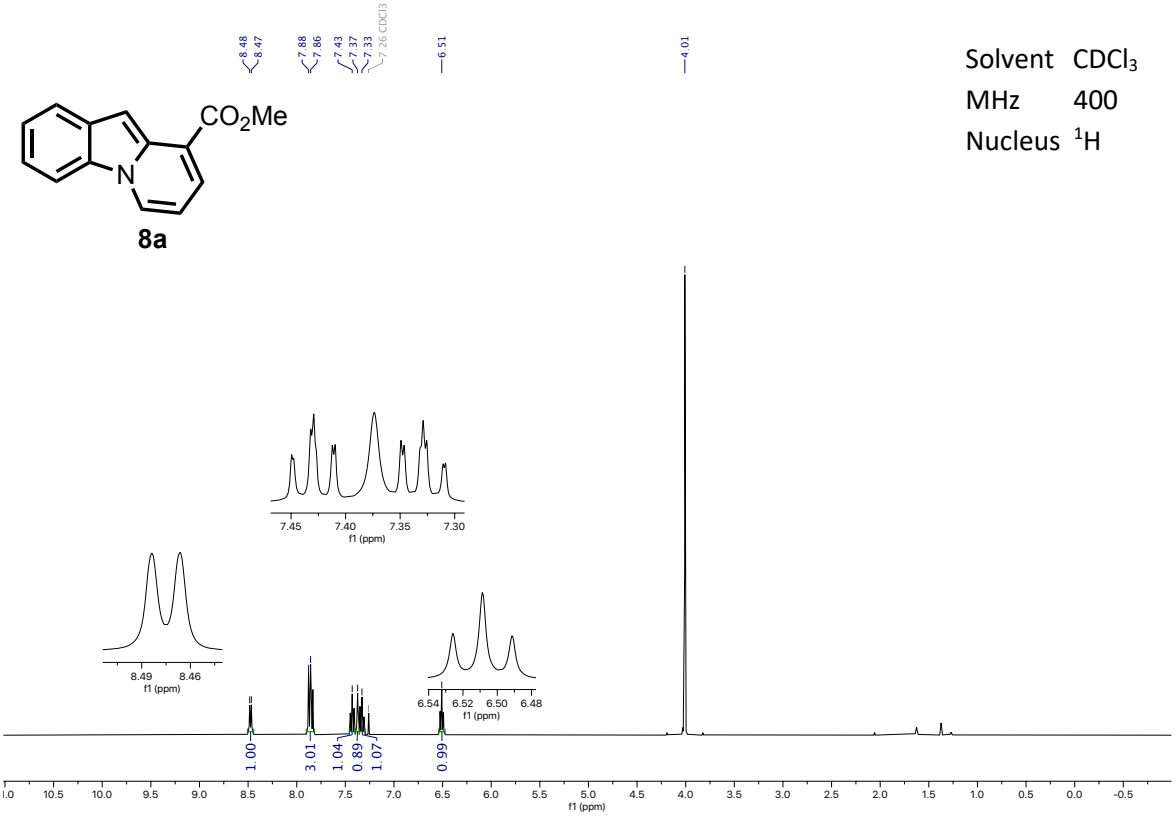
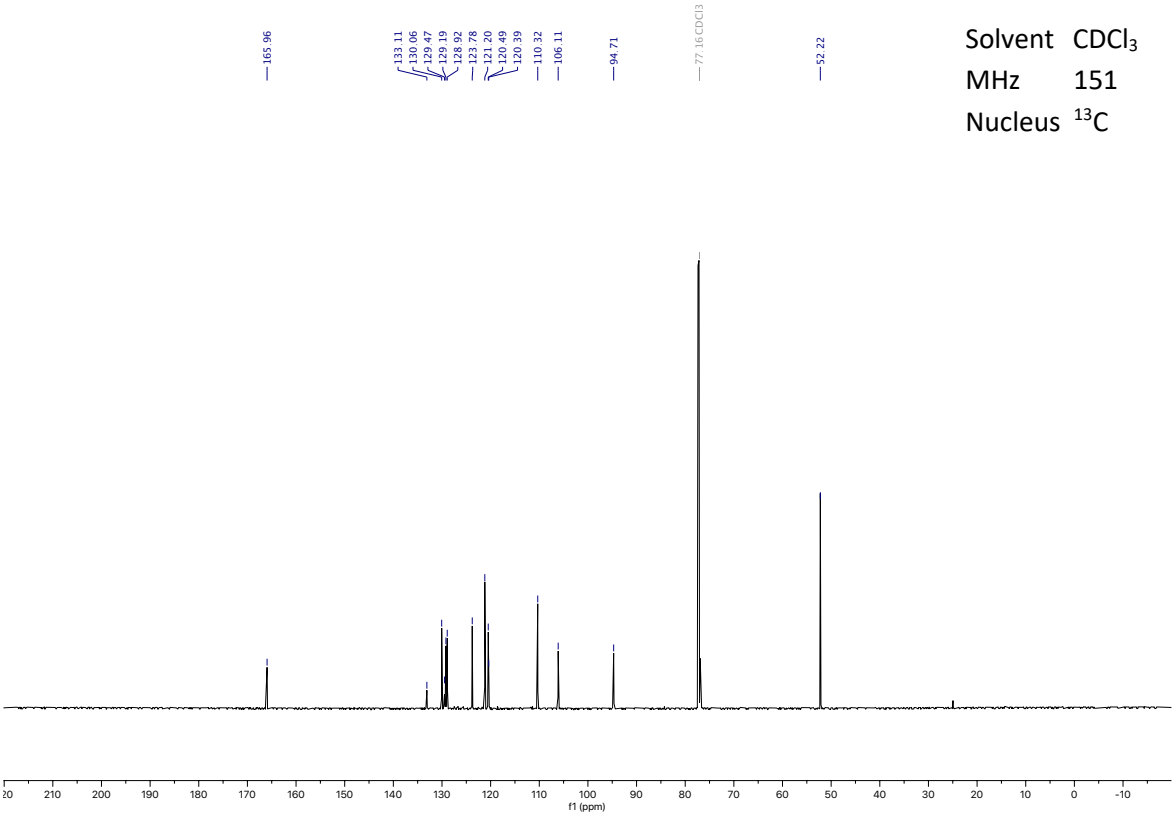


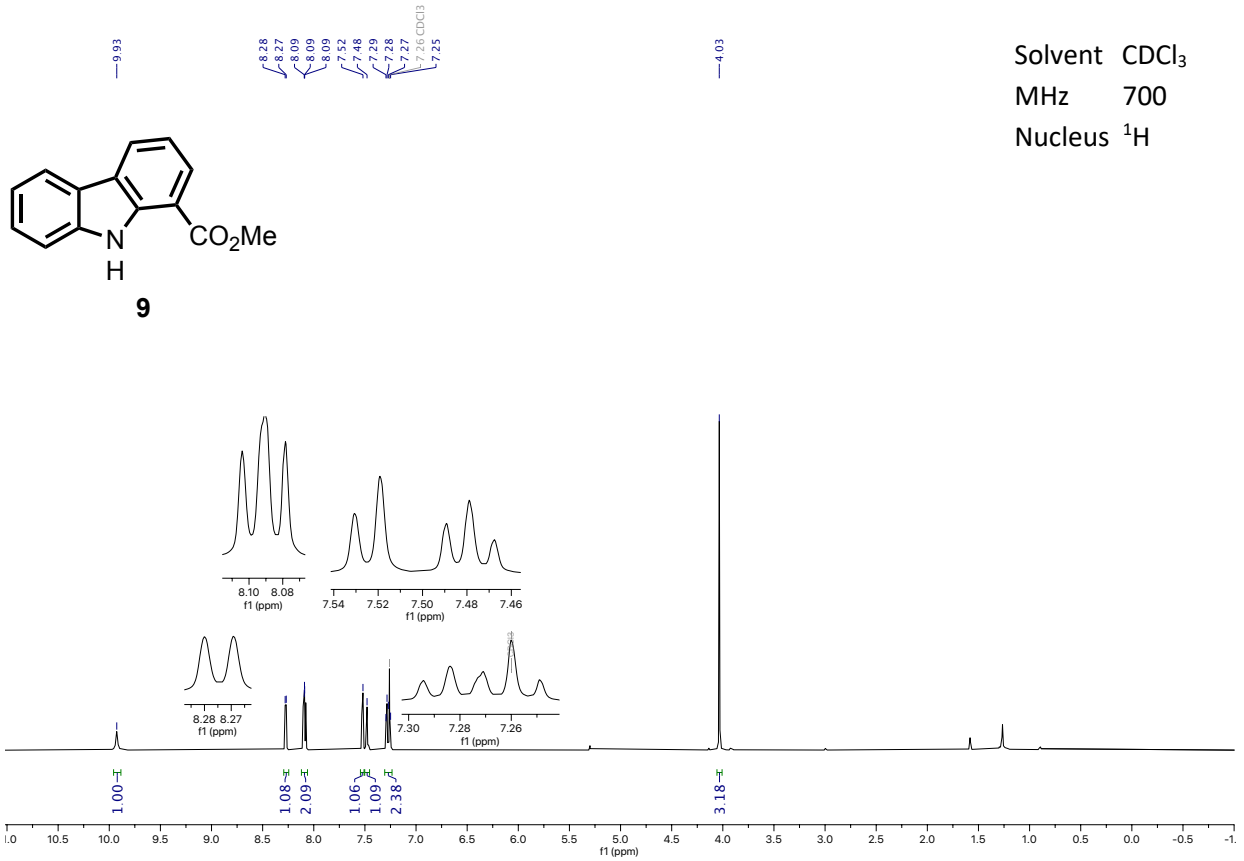
Figure S8. CYLview rendering of chloro pyrido[1,2-*a*]indole **19**

This crystal structure has been deposited at the Cambridge Crystallographic Data Center under **CCDC 2034053**.

12 ^{1}H and ^{13}C NMR Spectra

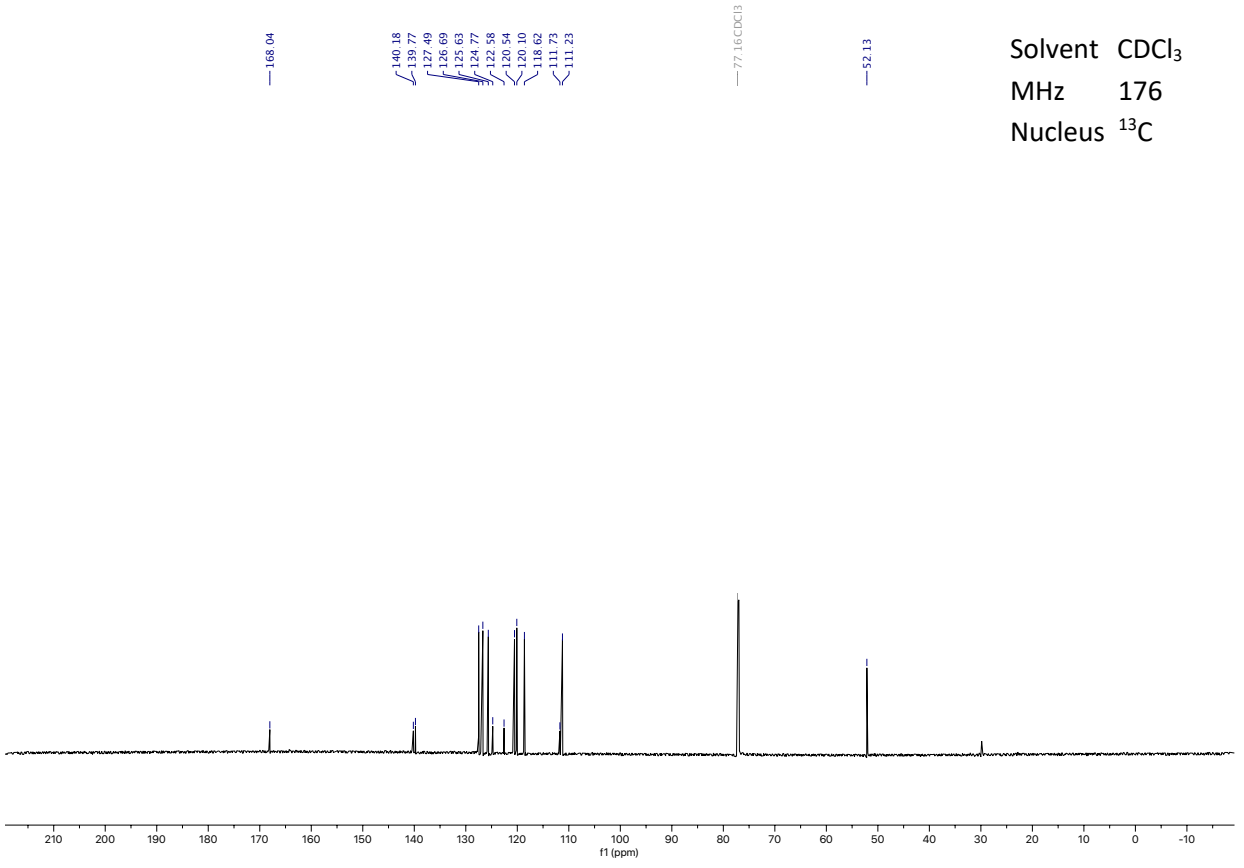




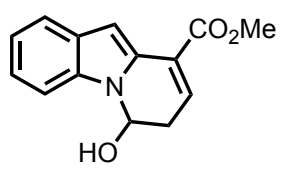


Solvent $CDCl_3$
MHz 700
Nucleus ^{1}H

9



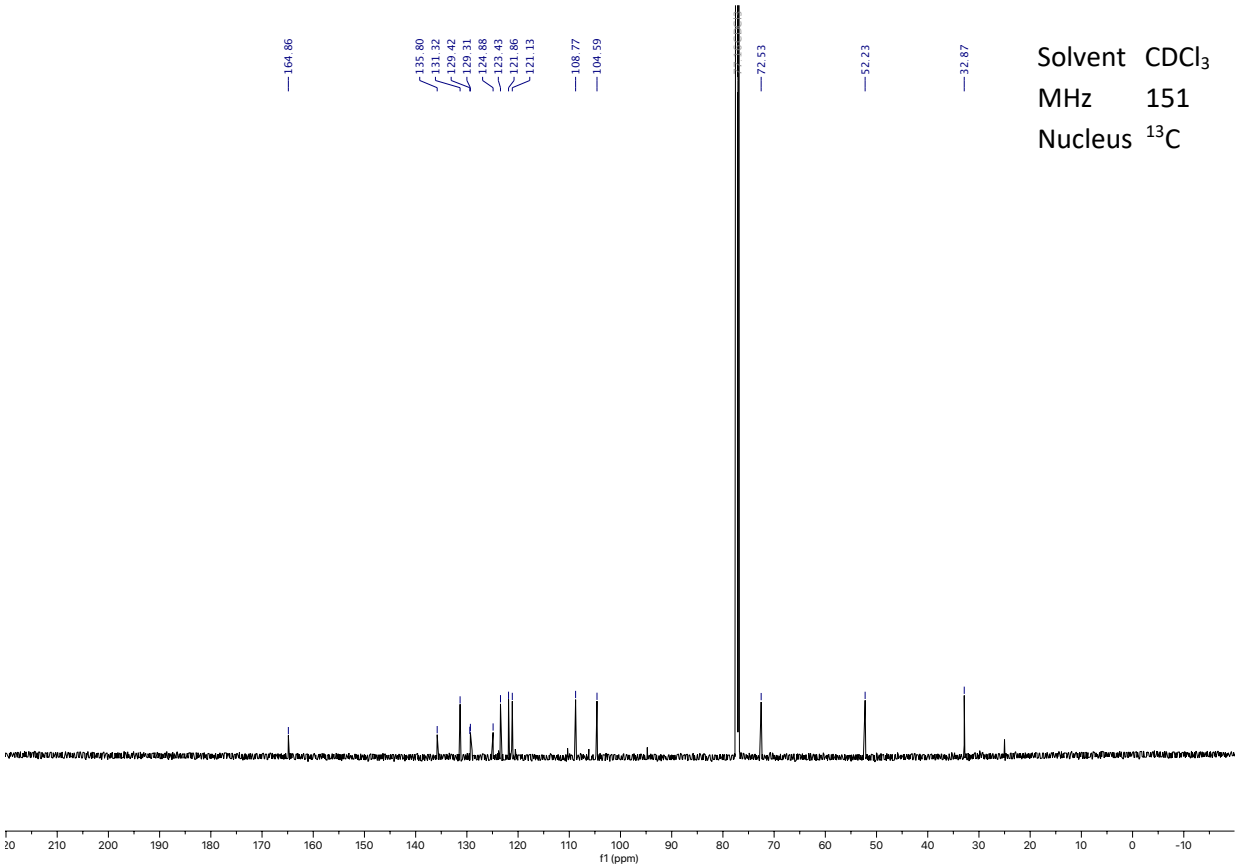
Solvent $CDCl_3$
MHz 176
Nucleus ^{13}C

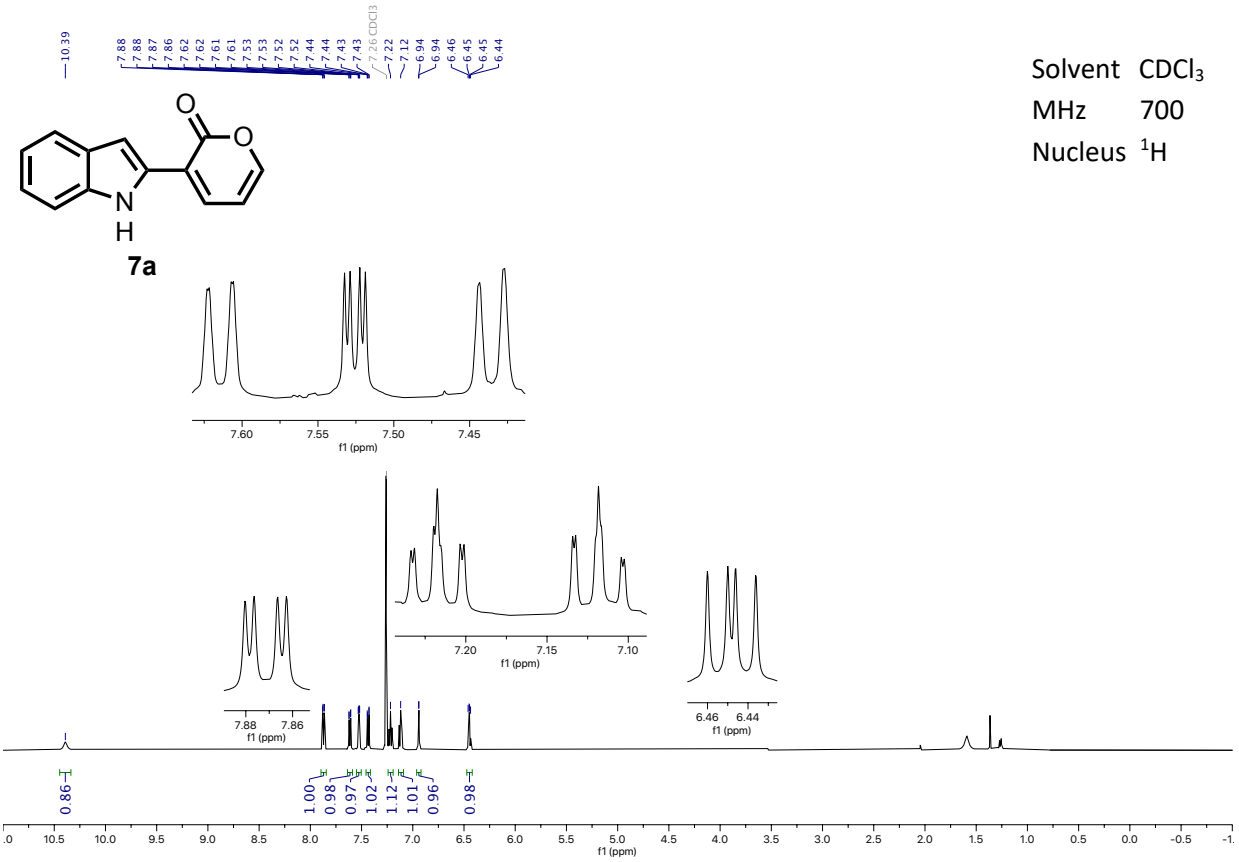


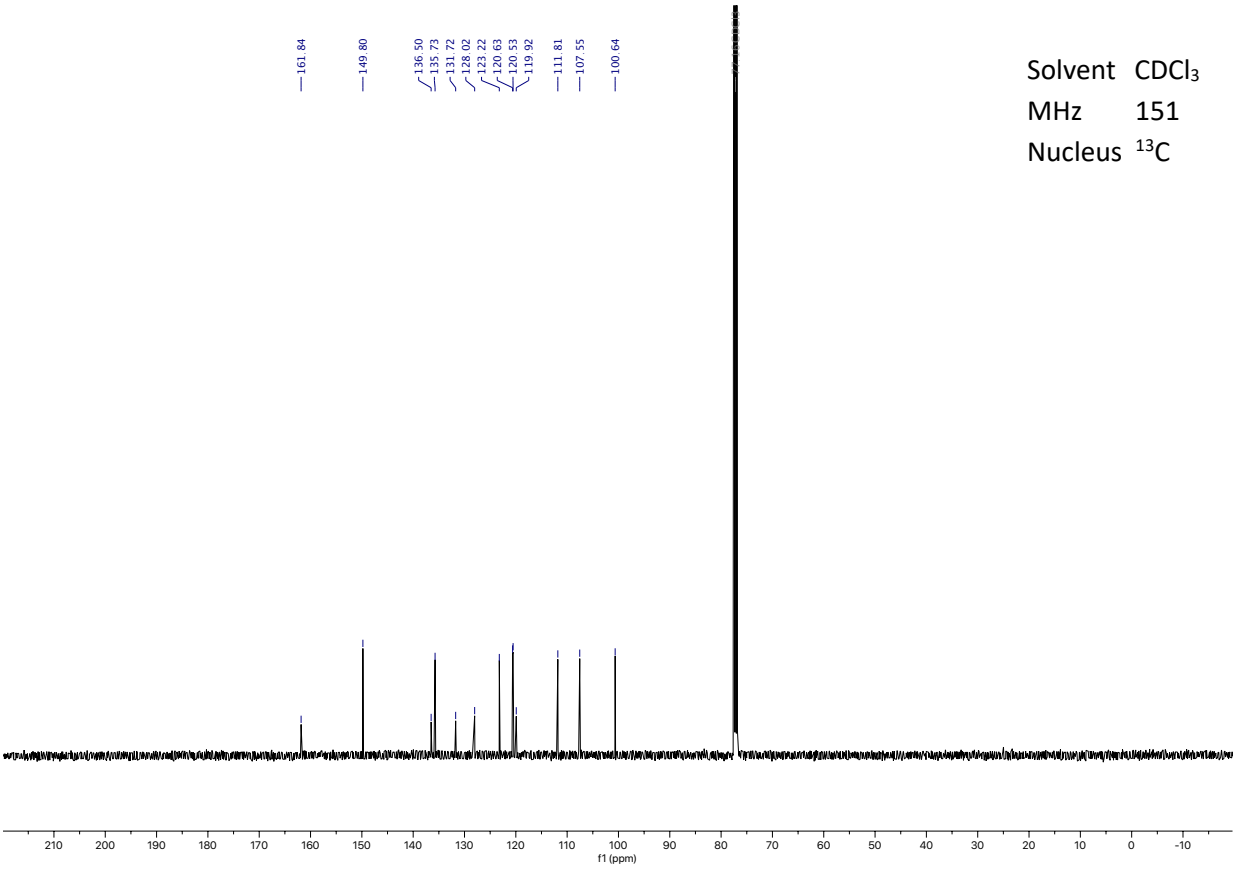
10

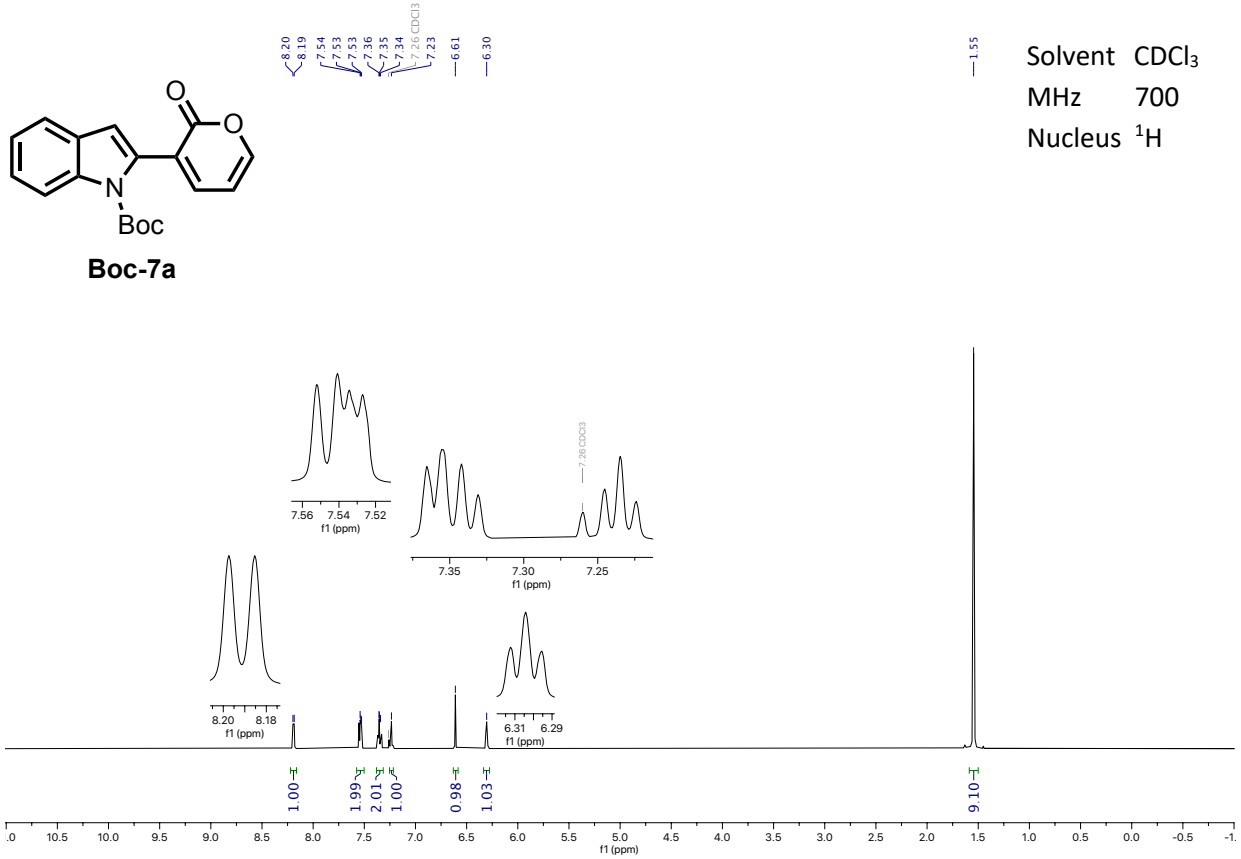
Solvent $CDCl_3$
MHz 700
Nucleus ^{1}H

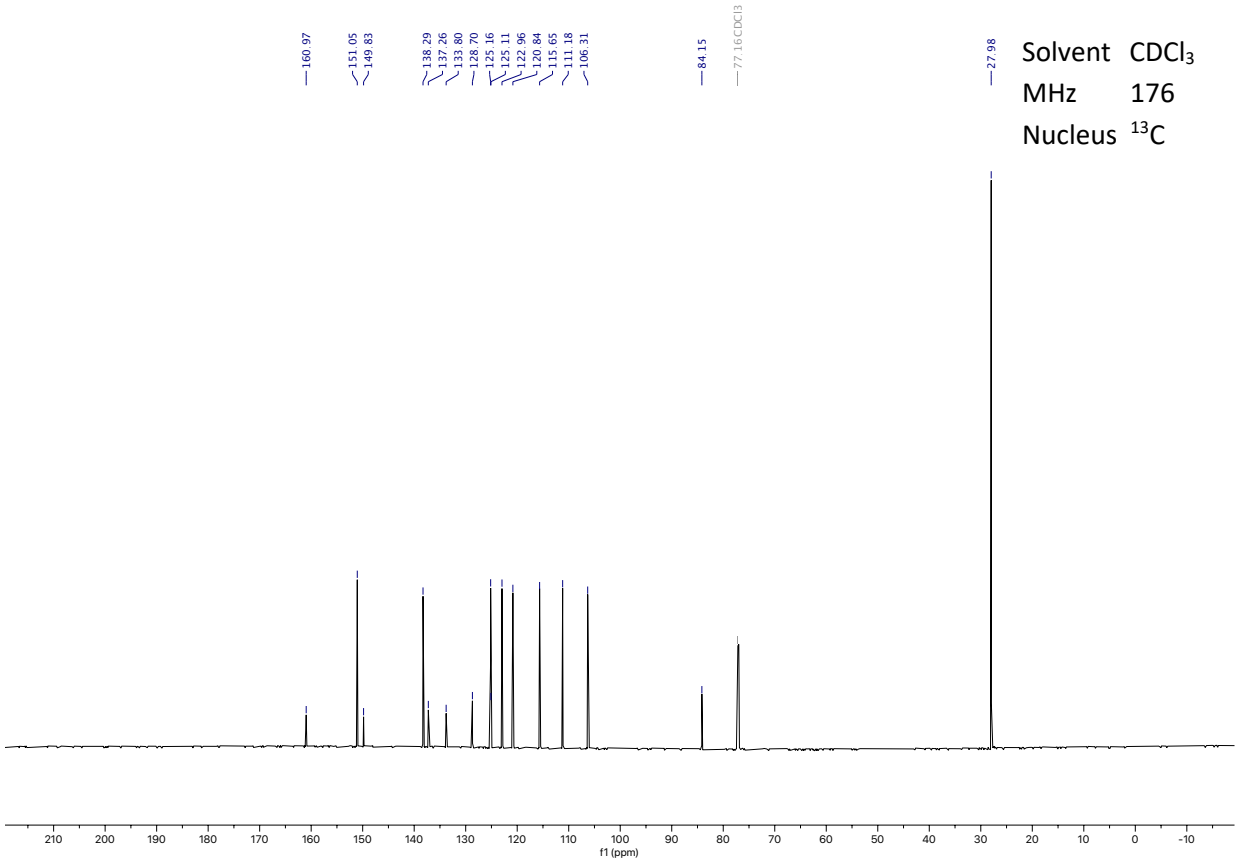
Solvent $CDCl_3$
MHz 151
Nucleus ^{13}C

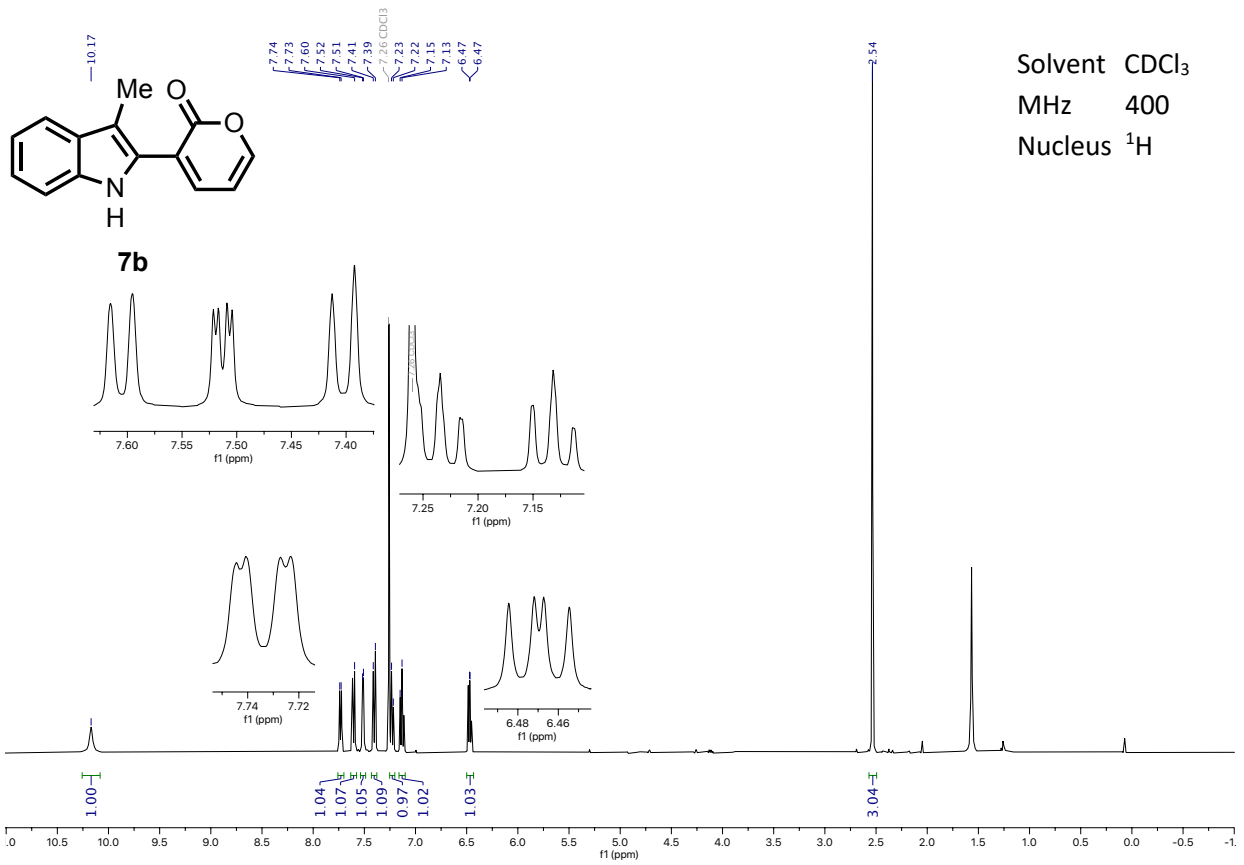


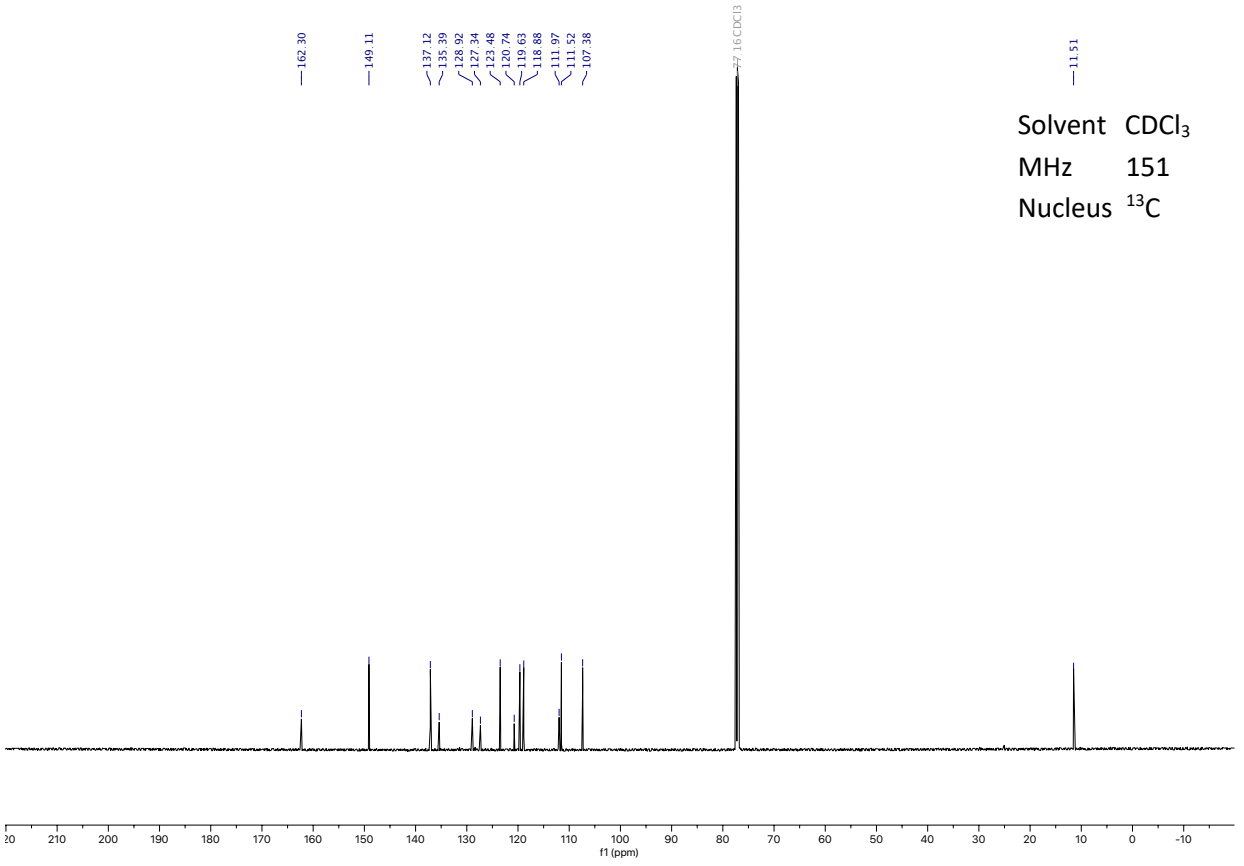

10.39
7.88
7.88
7.87
7.86
7.62
7.62
7.61
7.61
7.53
7.53
7.52
7.52
7.44
7.44
7.43
7.43
7.26 CDCl3
7.22
7.12
6.94
6.94
6.46
6.45
6.45
6.44
O
O
N
H
7a
Solvent CDCl3
MHz 700
Nucleus 1H
f1 (ppm)
0.86
1.00
0.98
0.97
1.02
1.12
1.01
0.96
0.98

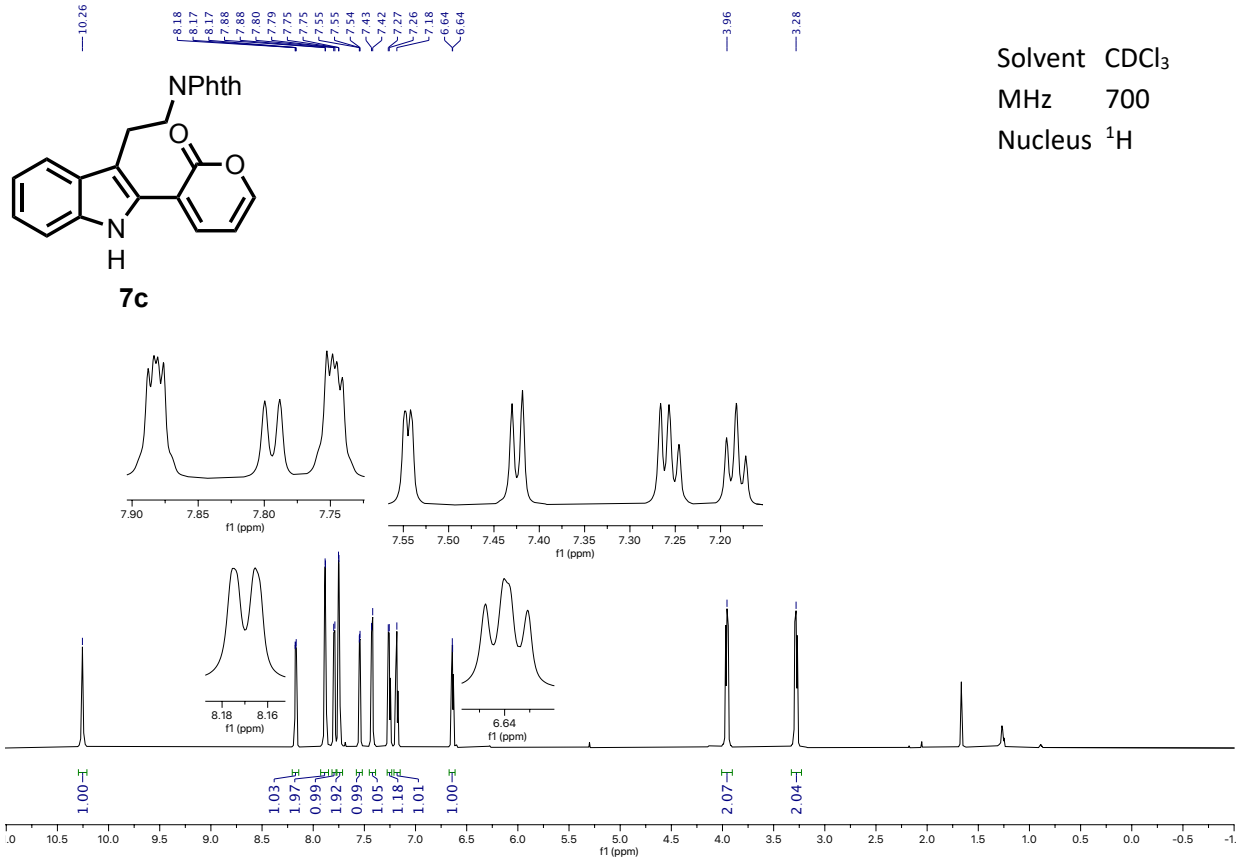

161.84
149.80
136.50
135.73
131.72
128.02
123.22
120.63
120.53
119.92
111.81
107.55
100.64
Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)


Boc
Boc-7a
Solvent CDCl3
MHz 700
Nucleus 1H
f1 (ppm)

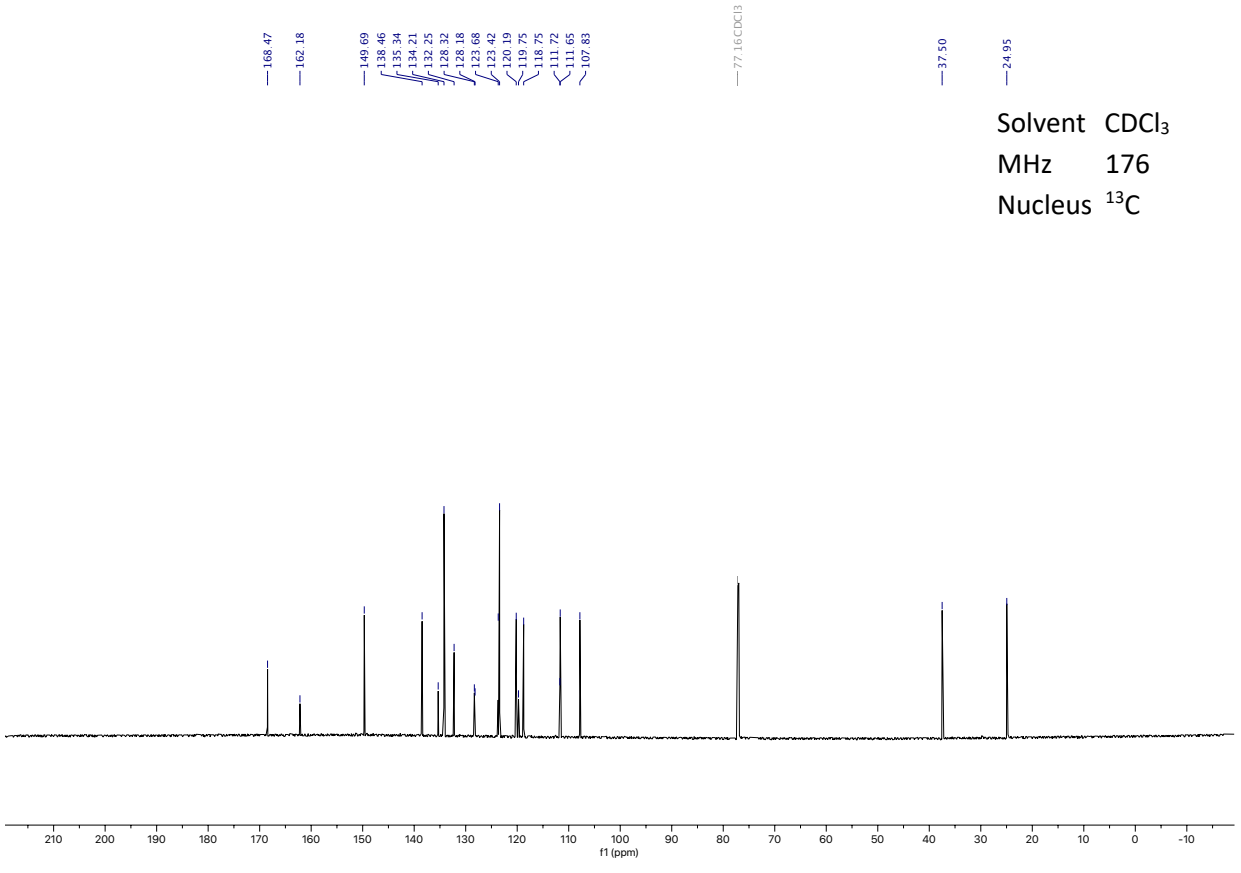

Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)


Me
O
O
N
H
7b
Solvent CDCl3
MHz 400
Nucleus 1H
f1 (ppm)

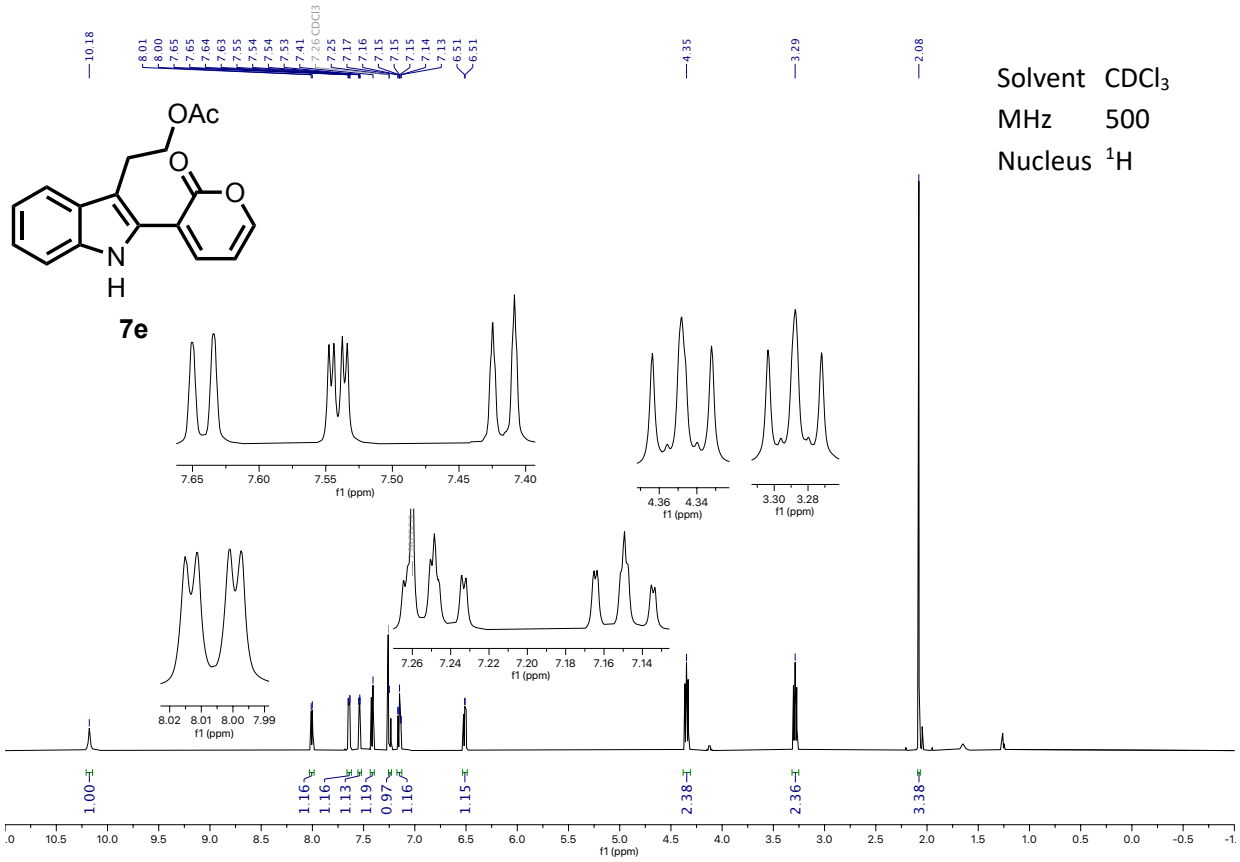

Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)

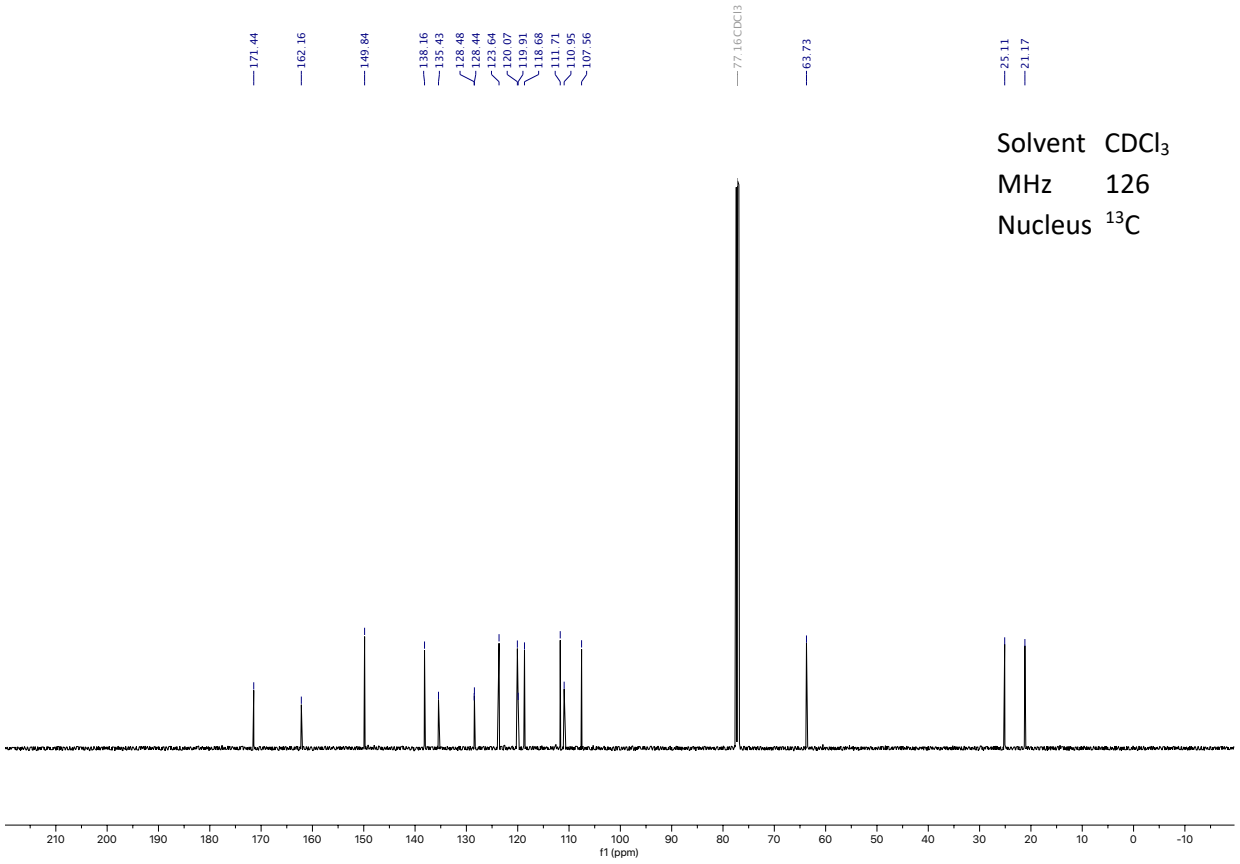


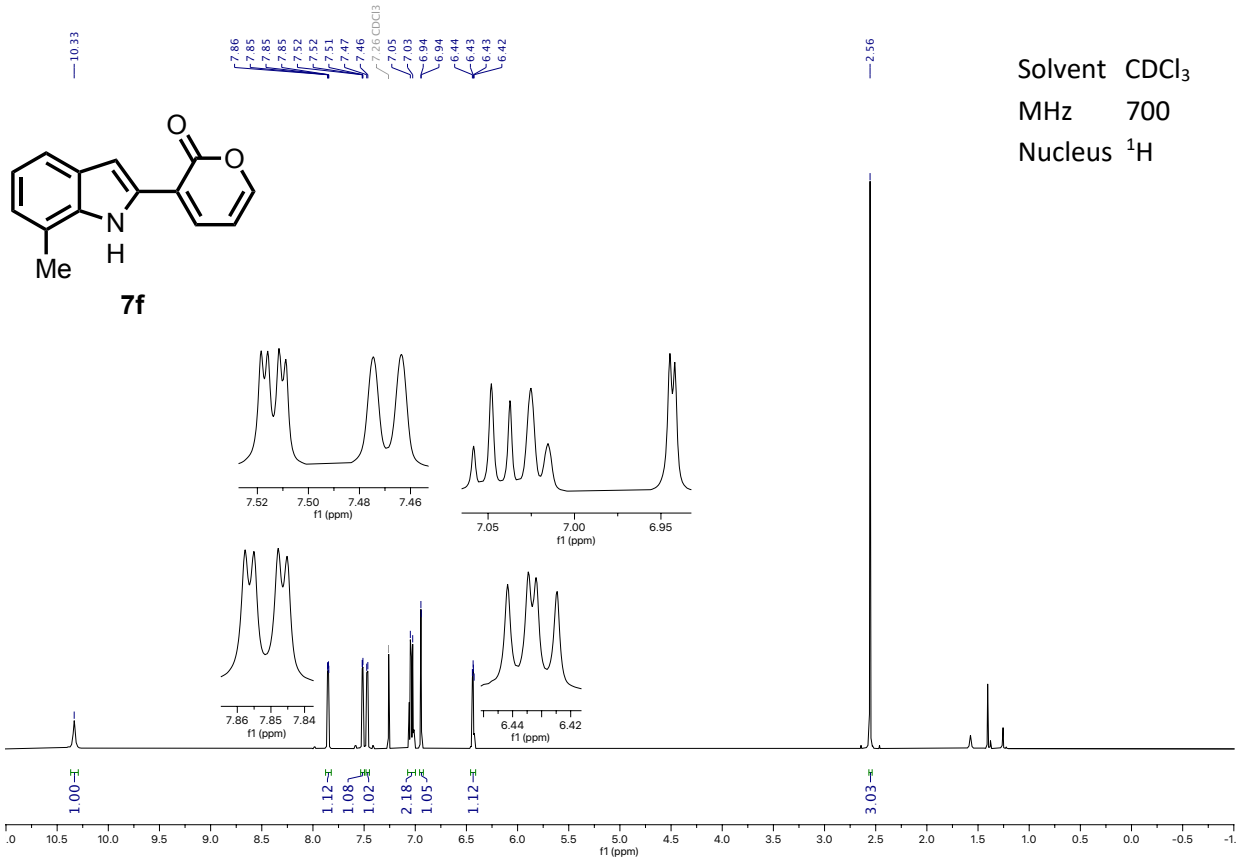
Solvent $CDCl_3$
MHz 700
Nucleus ^{1}H



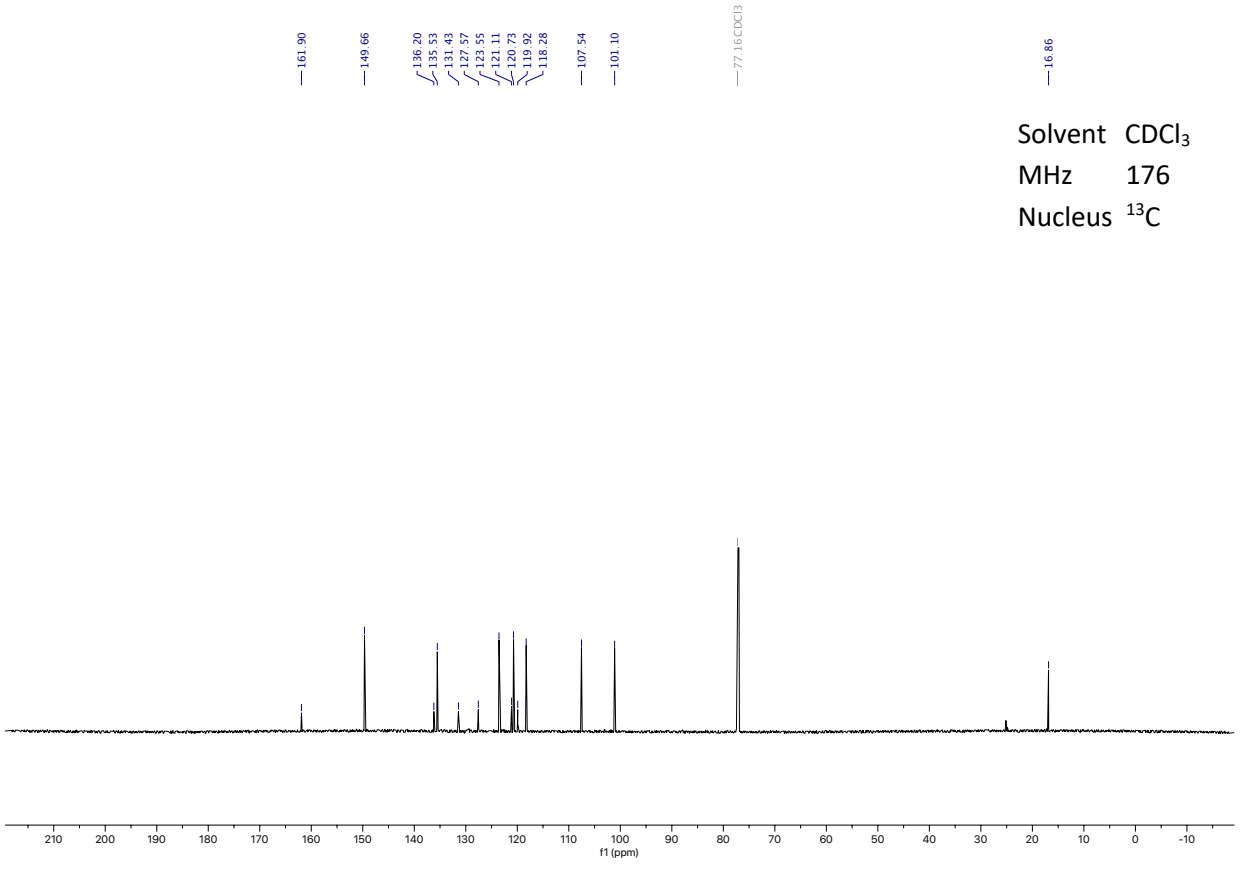
Solvent $CDCl_3$
MHz 176
Nucleus ^{13}C


Solvent CDCl3
MHz 500
Nucleus 1H
7e

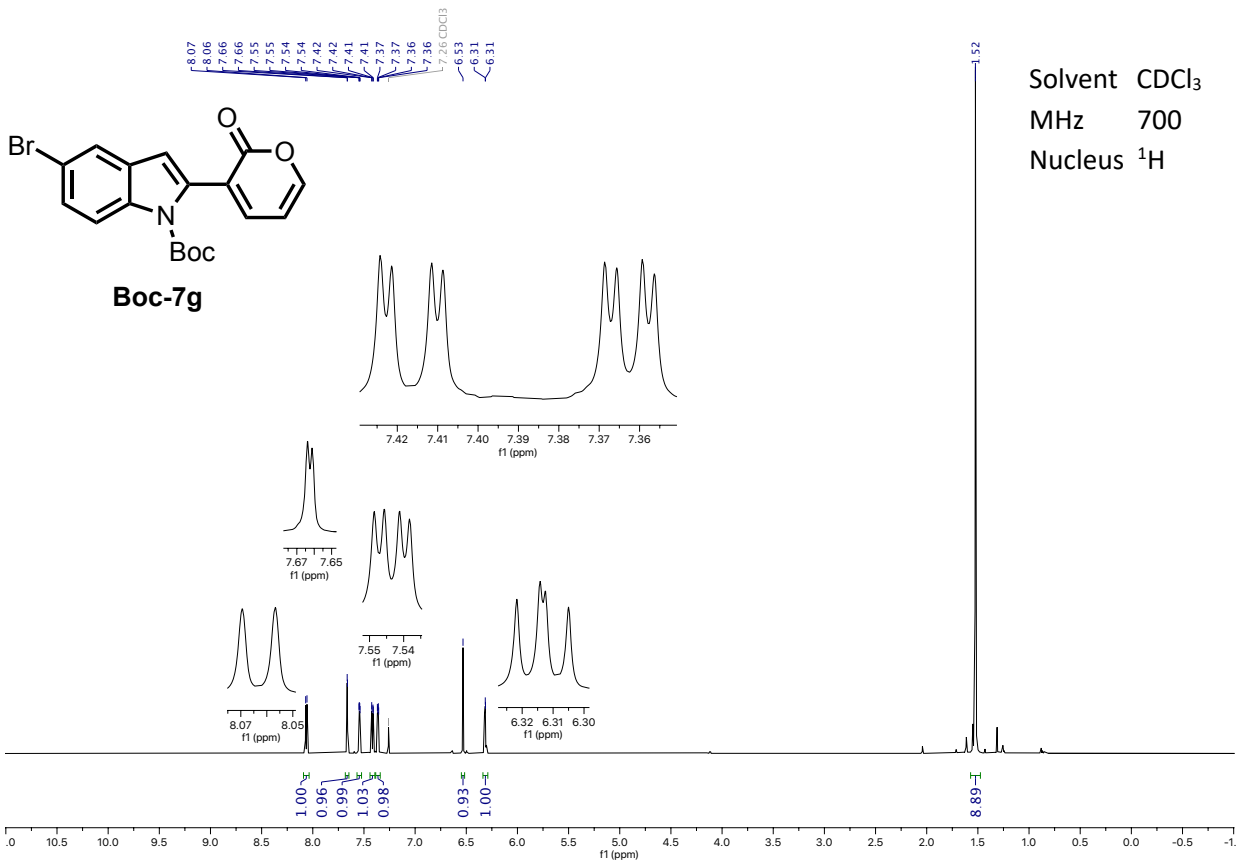

Solvent CDCl3
MHz 126
Nucleus 13C

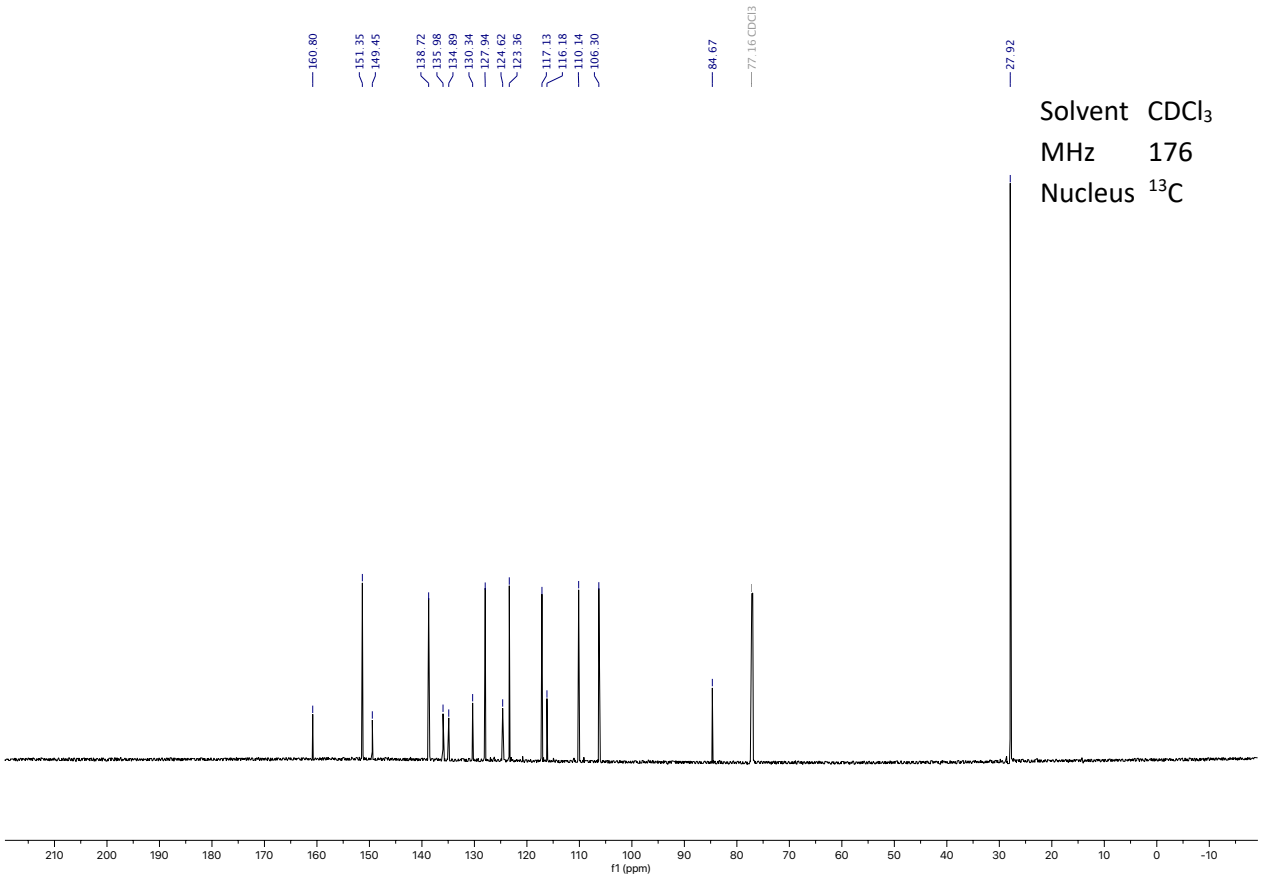


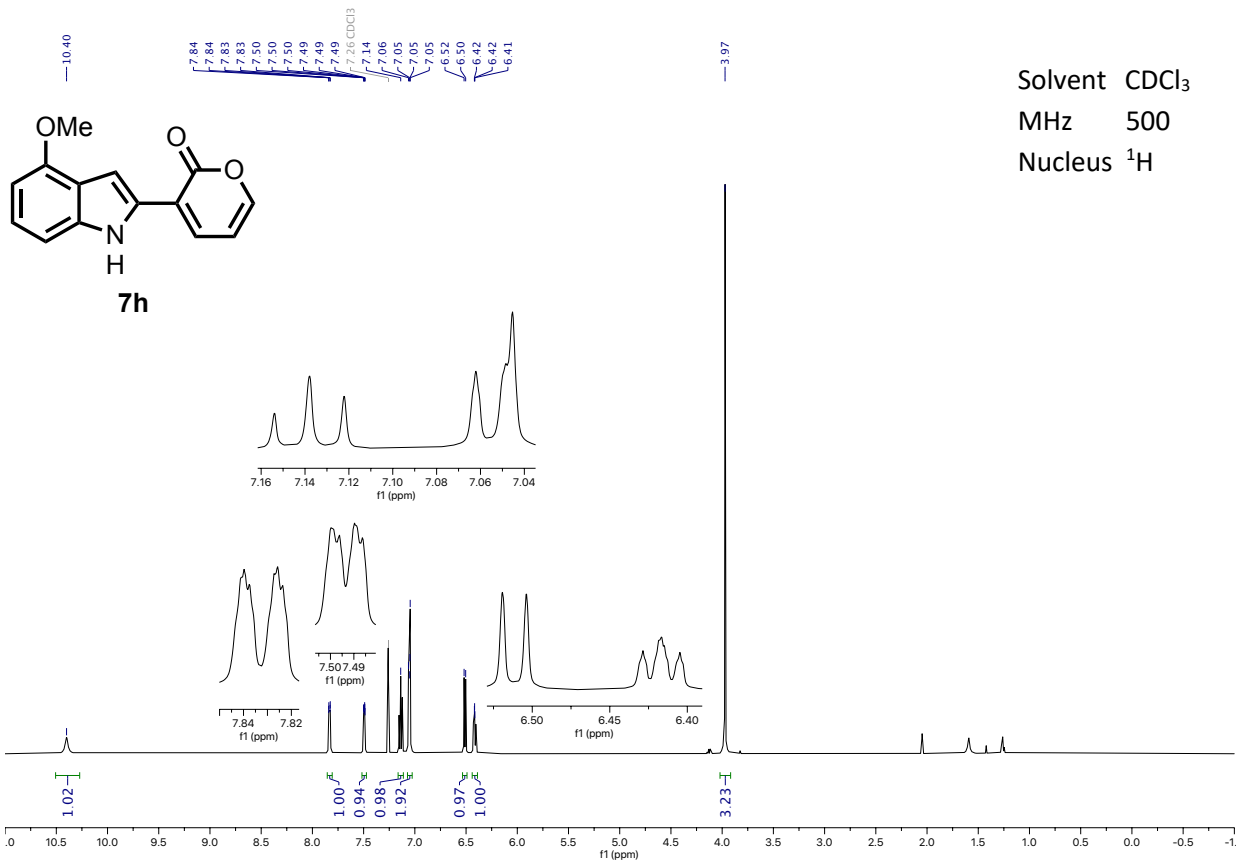
Solvent $CDCl_3$
MHz 700
Nucleus ^{1}H

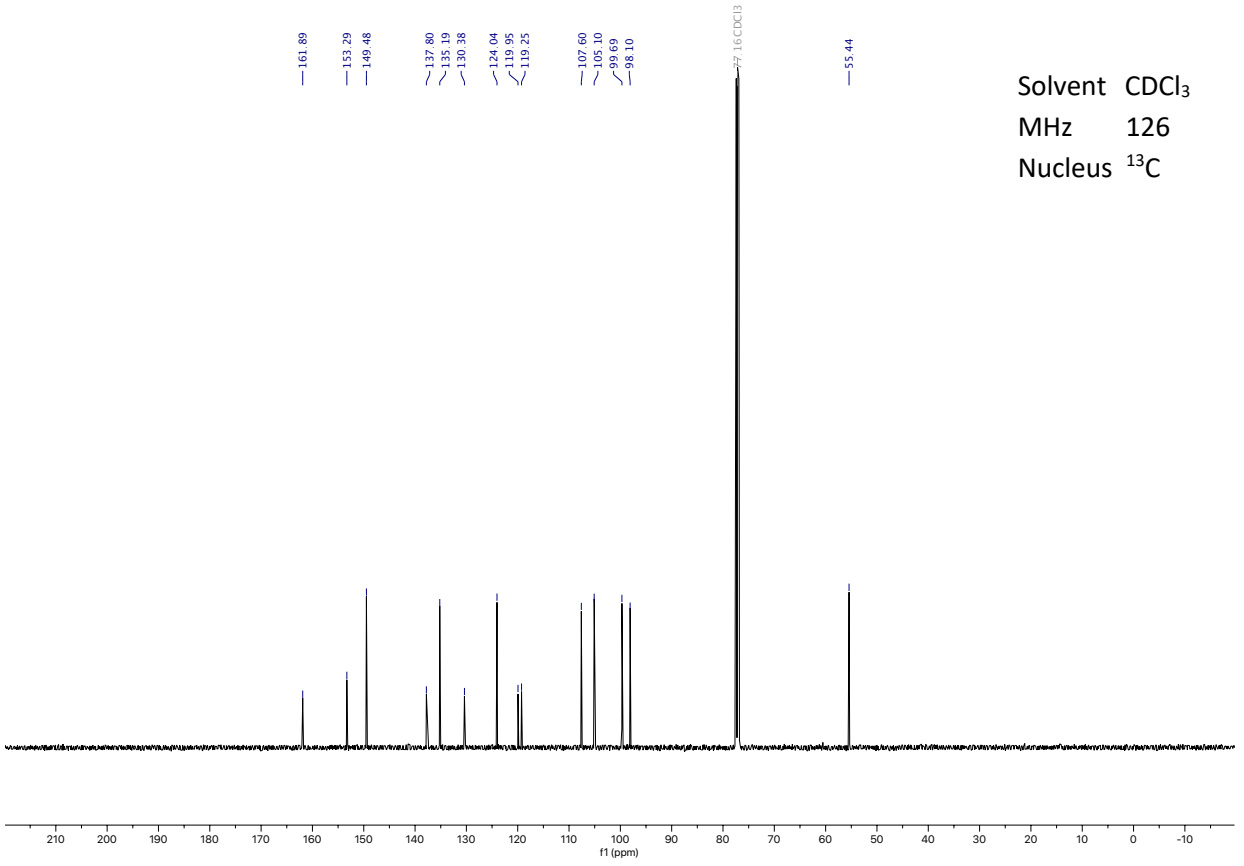


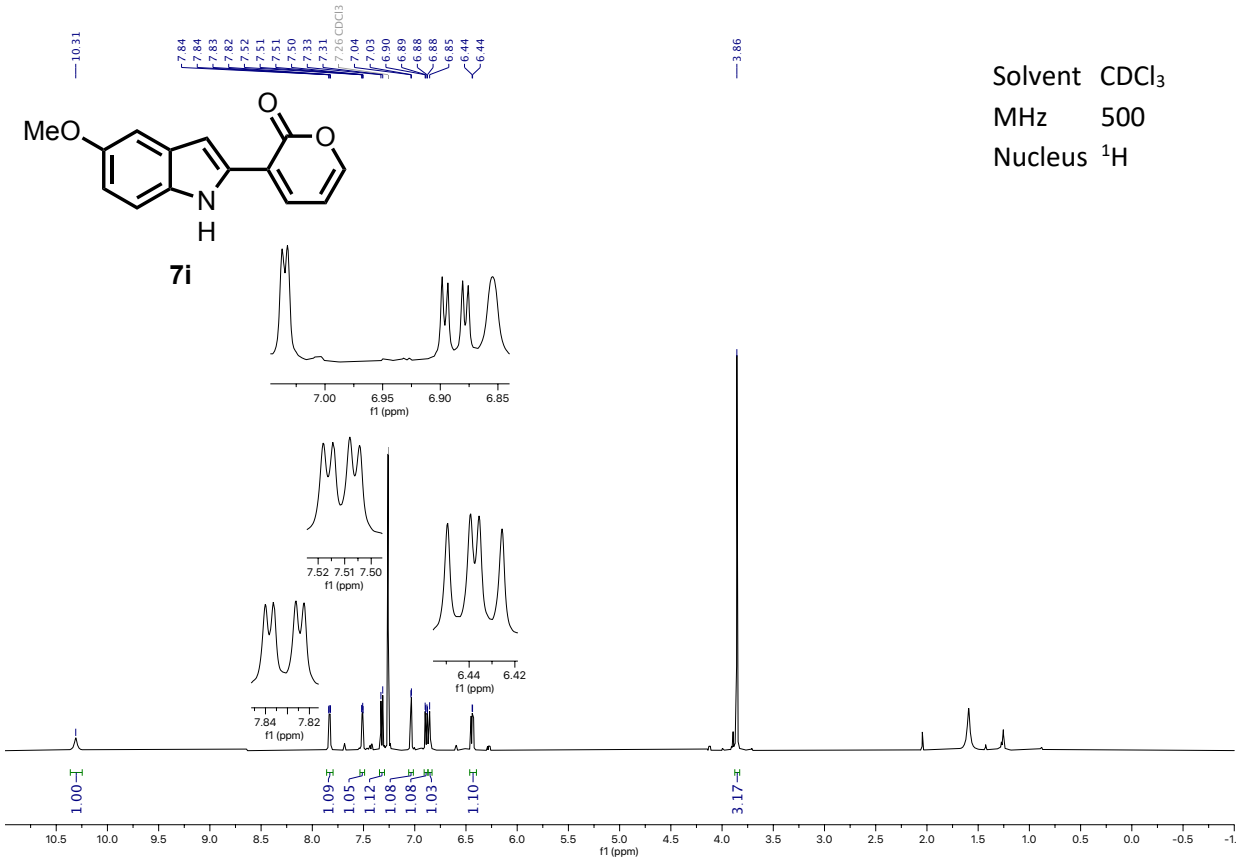
Solvent $CDCl_3$
MHz 176
Nucleus ^{13}C

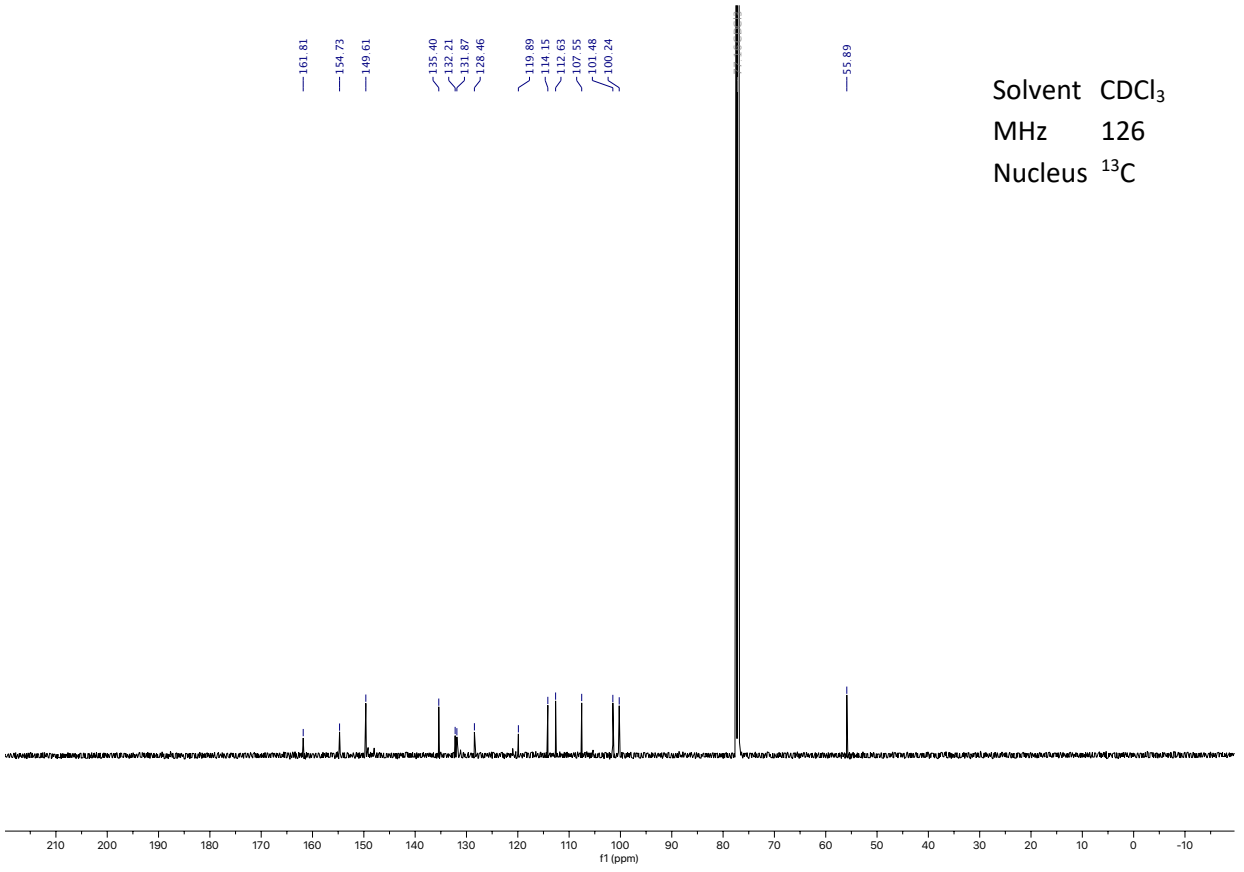

Br
O
O
N
Boc
Boc-7g
Solvent CDCl3
MHz 700
Nucleus 1H
f1 (ppm)

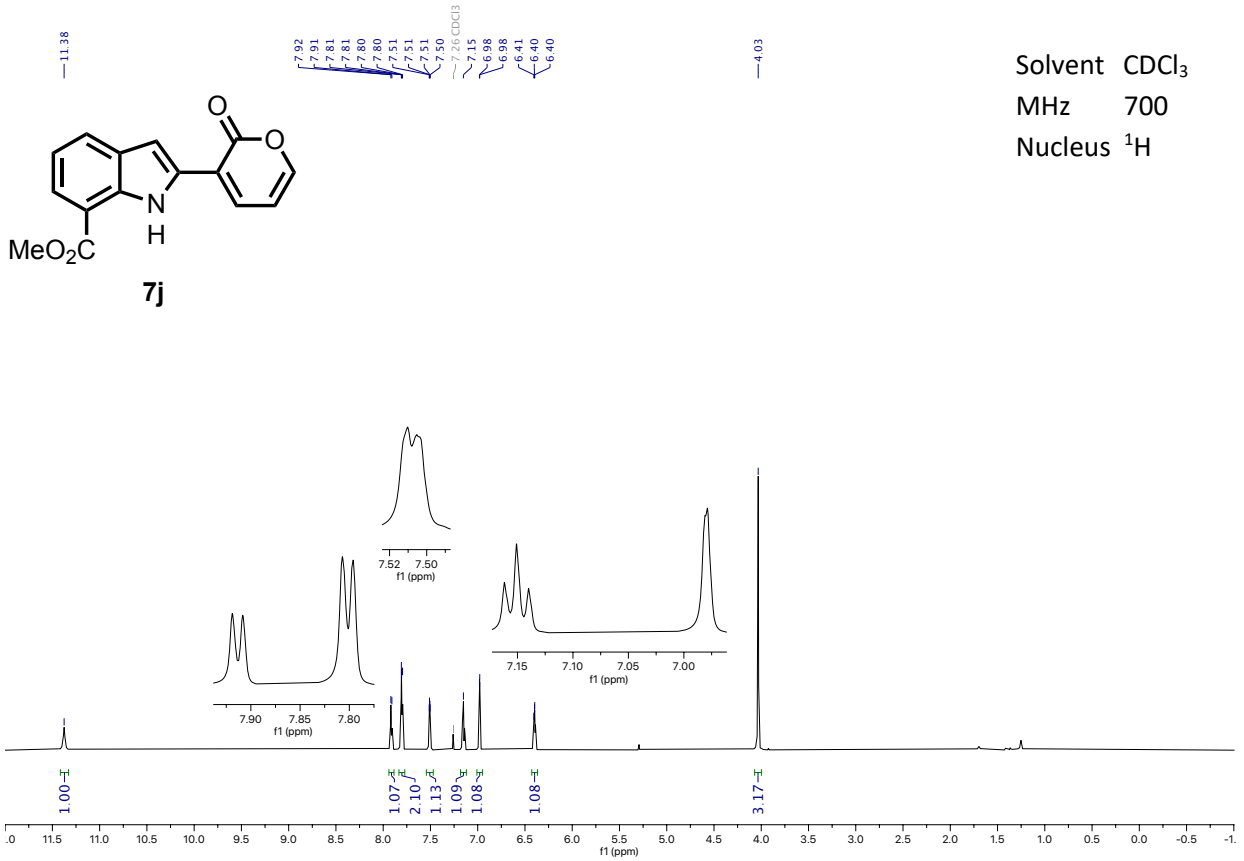

Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)

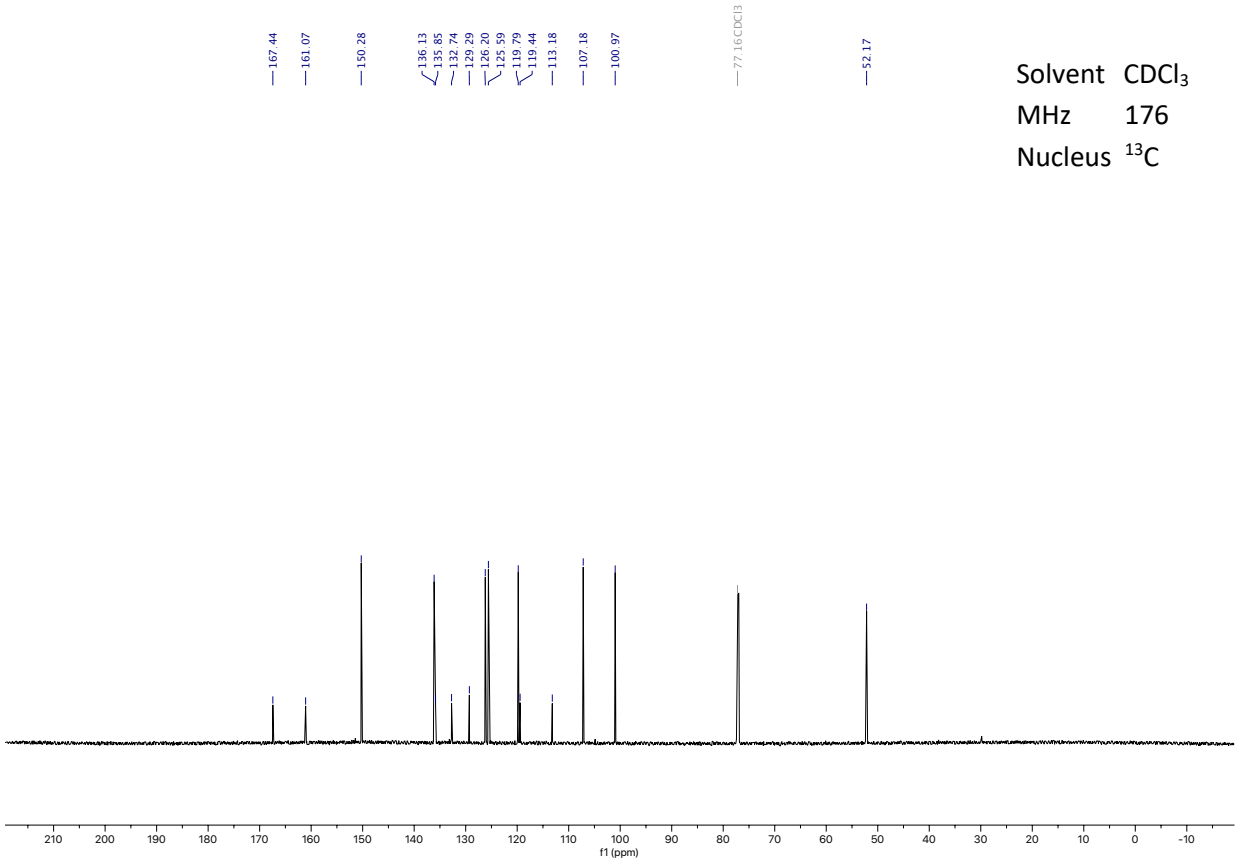

Solvent CDCl3
MHz 500
Nucleus 1H
OMe
O
O
N
H
7h
f1 (ppm)

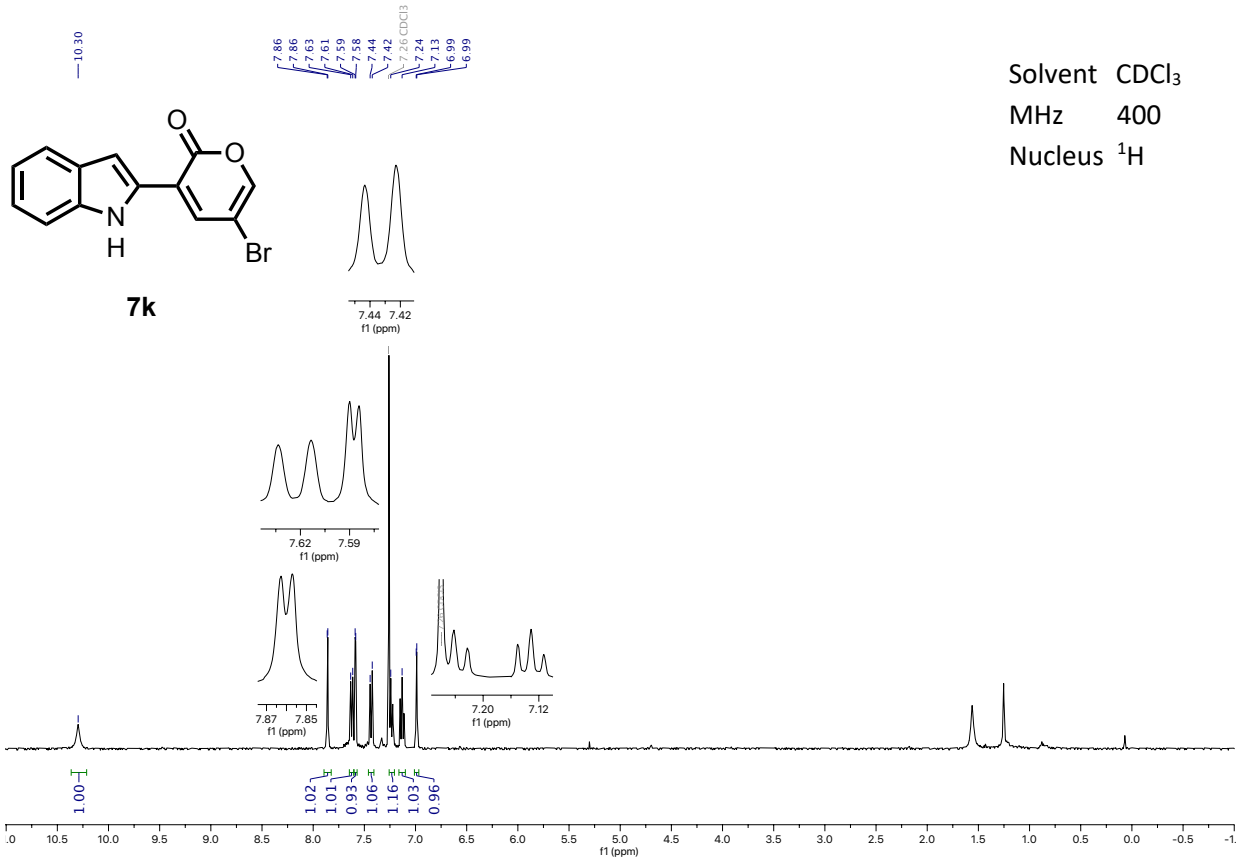

Solvent CDCl3
MHz 126
Nucleus 13C
f1 (ppm)


10.31
7.84
7.84
7.83
7.82
7.52
7.51
7.51
7.50
7.33
7.31
7.26 CDCl3
7.04
7.03
6.90
6.89
6.88
6.88
6.85
6.44
6.44
3.86
MeO
O
O
N
H
7i
7.00
6.95
6.90
6.85
f1 (ppm)
7.52 7.51 7.50
f1 (ppm)
6.44
6.42
f1 (ppm)
7.84
7.82
f1 (ppm)
1.00
1.09
1.05
1.12
1.08
1.08
1.03
1.10
3.17
f1 (ppm)
Solvent CDCl3
MHz 500
Nucleus 1H

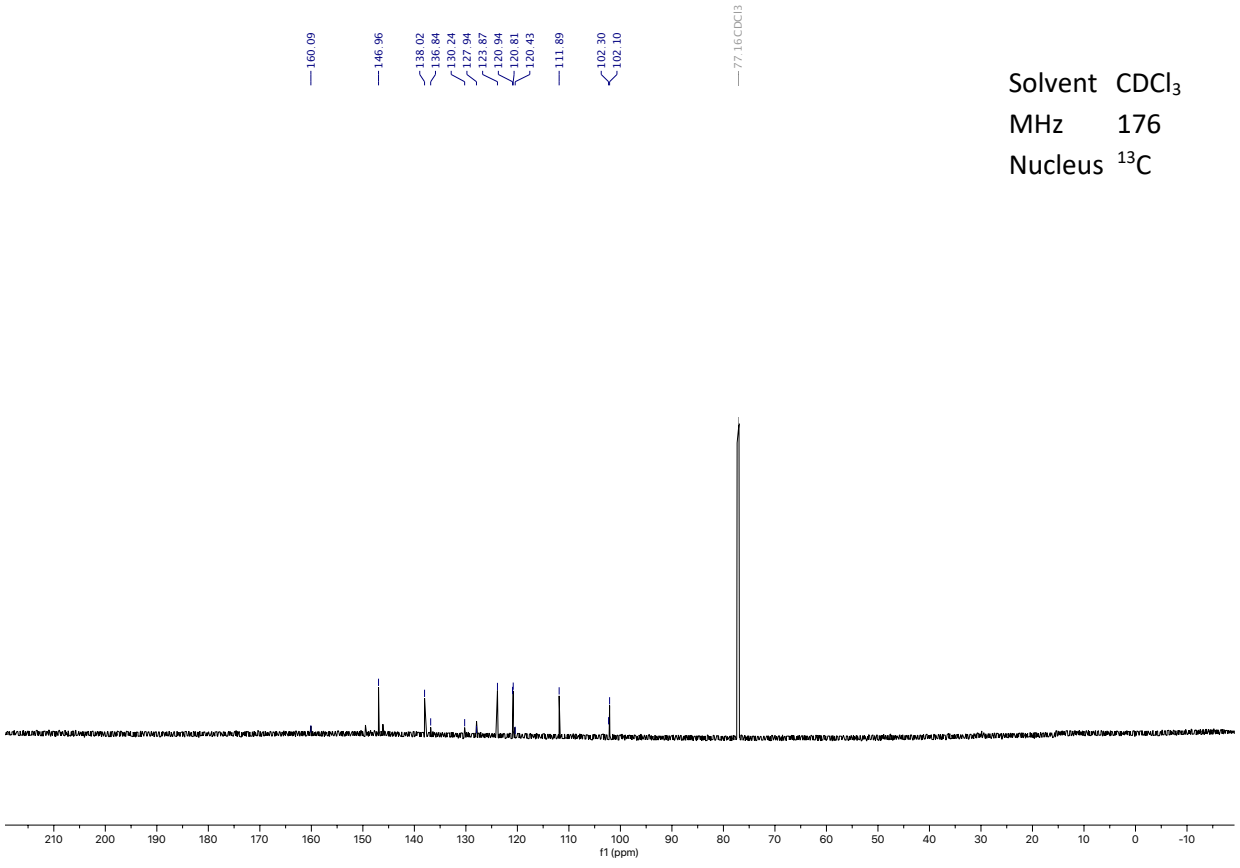

161.81
154.73
149.61
135.40
132.21
131.87
128.46
119.89
114.15
112.63
107.55
101.48
100.24
55.89
f1 (ppm)
Solvent CDCl3
MHz 126
Nucleus 13C


11.38
7.92
7.91
7.81
7.81
7.80
7.80
7.51
7.51
7.51
7.50
7.26 CDCl3
7.15
6.98
6.98
6.41
6.40
6.40
4.03
O
O
N
H
MeO2C
7j
Solvent CDCl3
MHz 700
Nucleus 1H
7.52 7.50
f1 (ppm)
7.15 7.10 7.05 7.00
f1 (ppm)
7.90 7.85 7.80
f1 (ppm)
1.00
1.07
2.10
1.13
1.09
1.08
1.08
3.17
f1 (ppm)

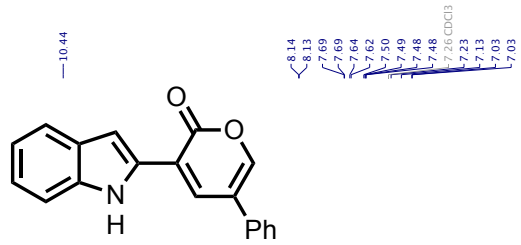

167.44
161.07
150.28
136.13
135.85
132.74
129.29
126.20
125.59
119.79
119.44
113.18
107.18
100.97
77.16 CDCl3
52.17
Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)



Solvent $CDCl_3$
MHz 400
Nucleus ^{1}H

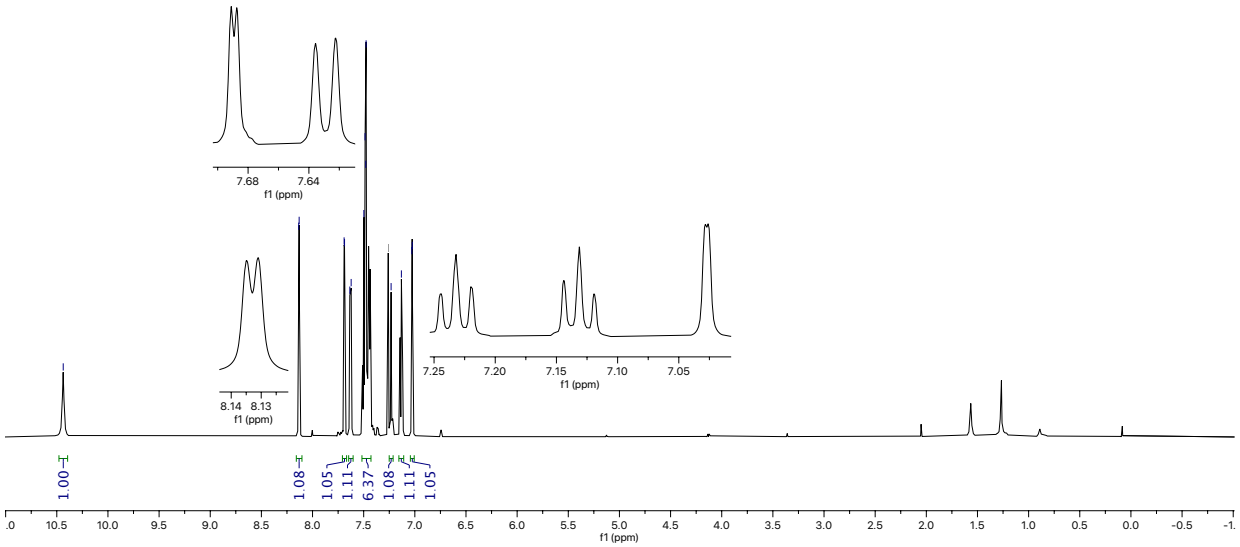


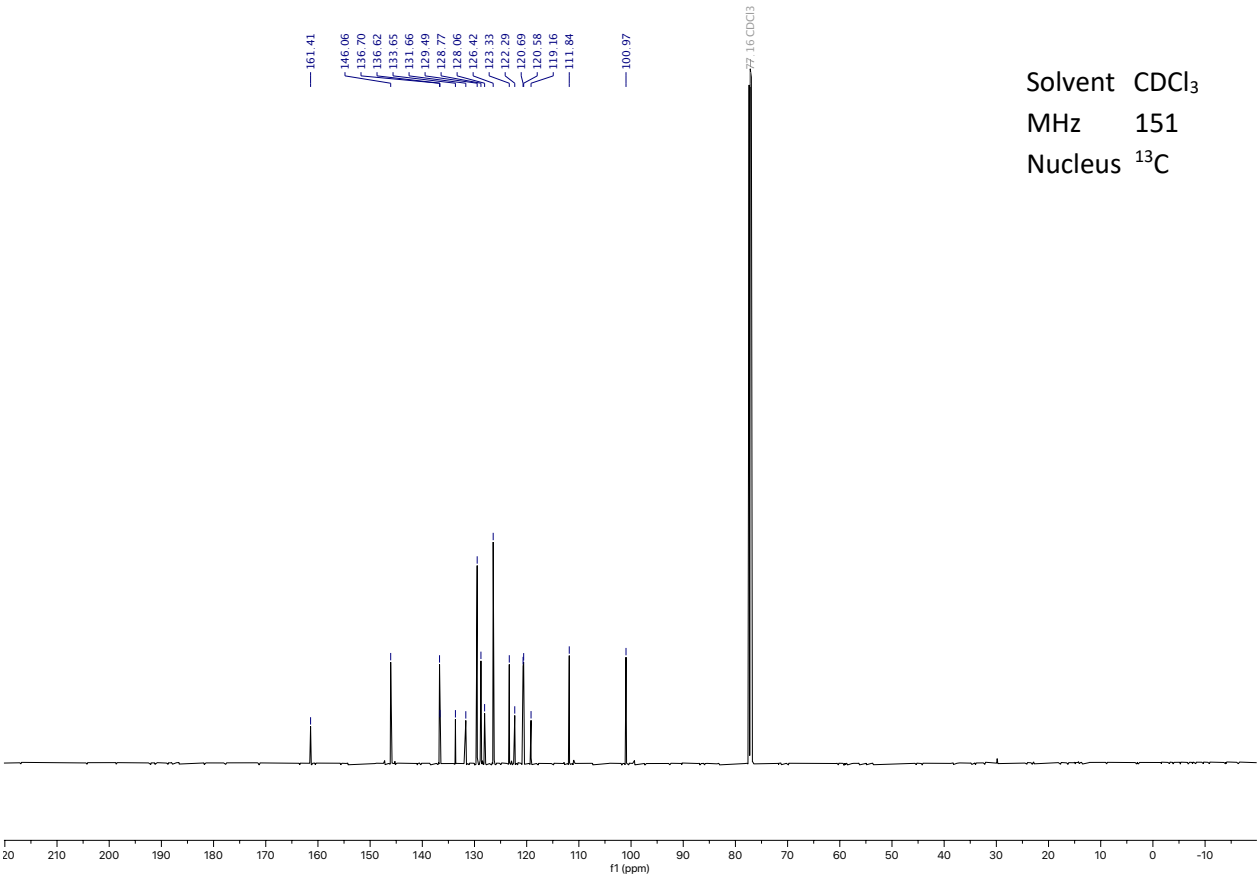
Solvent $CDCl_3$
MHz 176
Nucleus ^{13}C



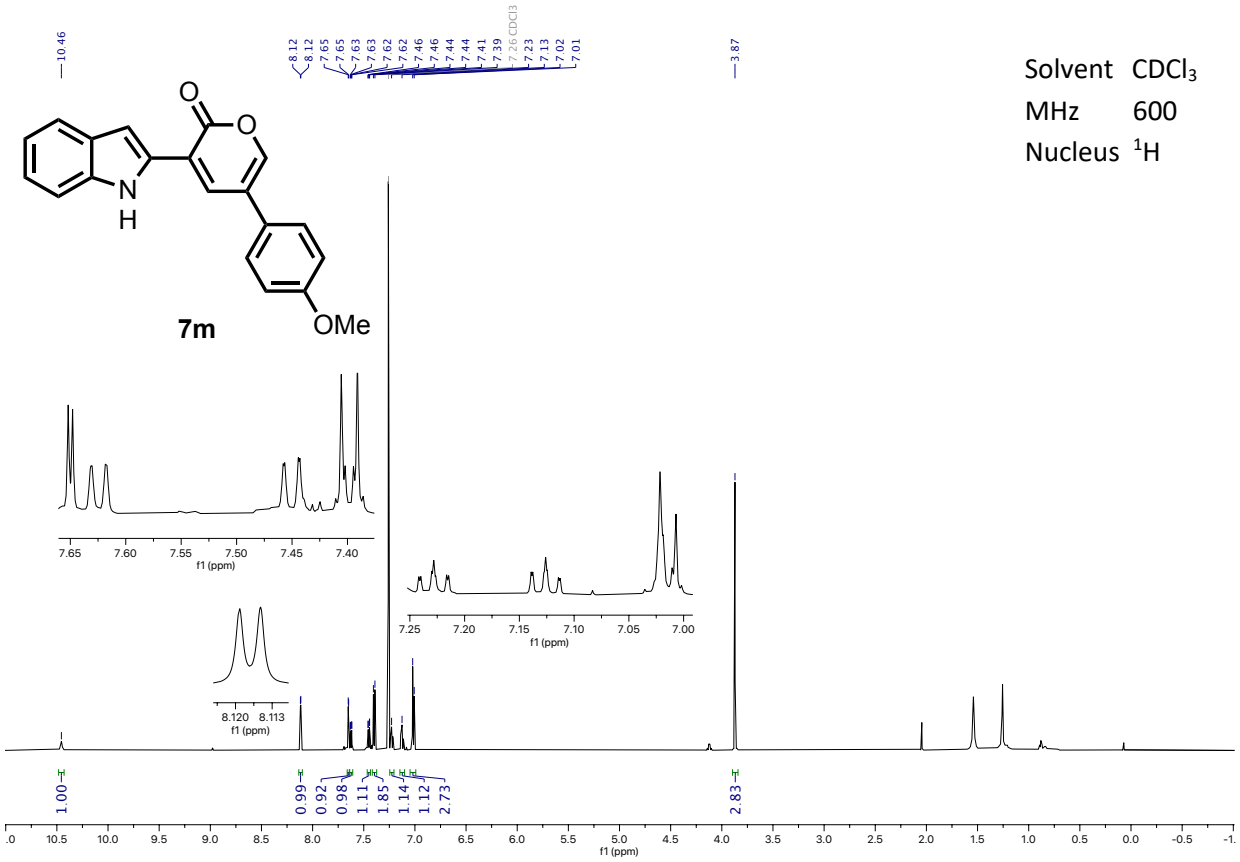
7l

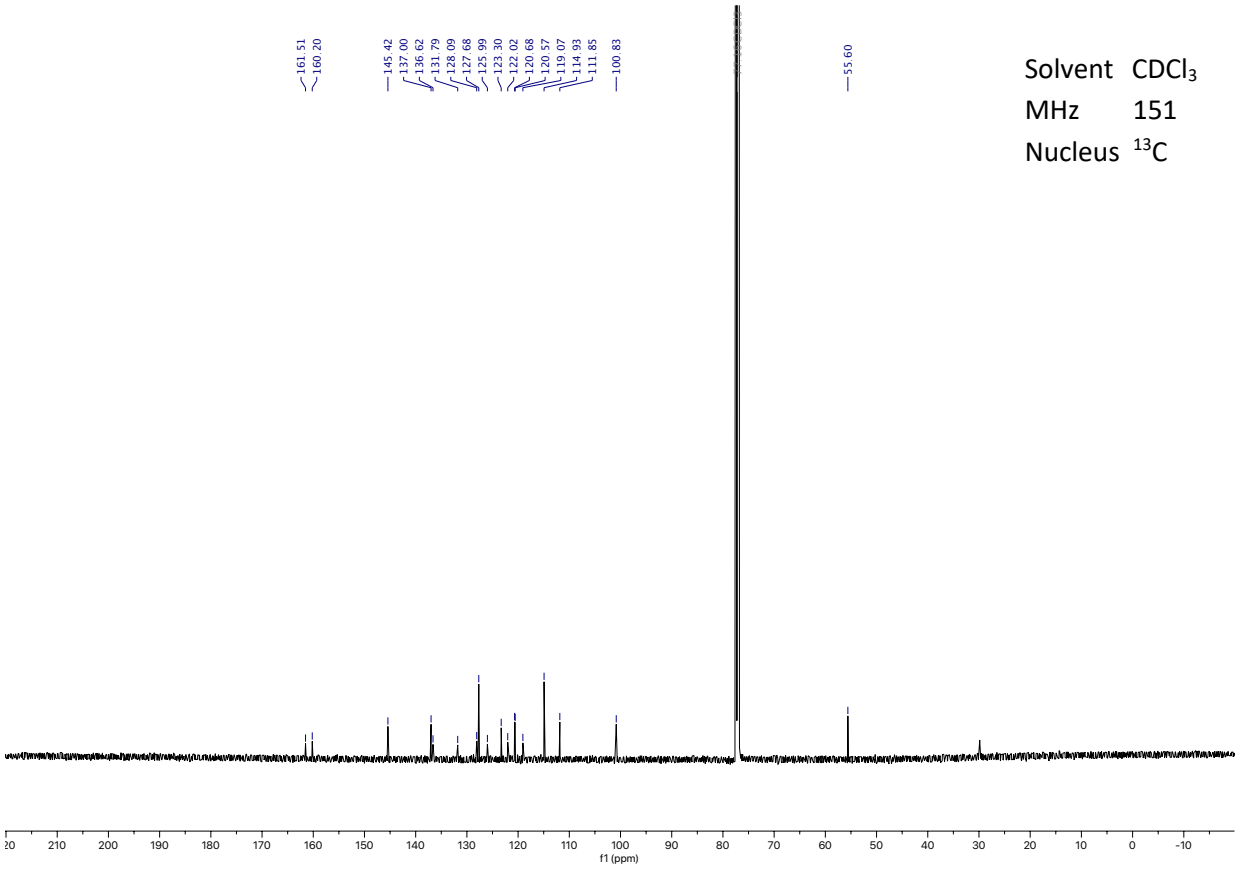
Solvent $CDCl_3$
MHz 600
Nucleus ^{1}H

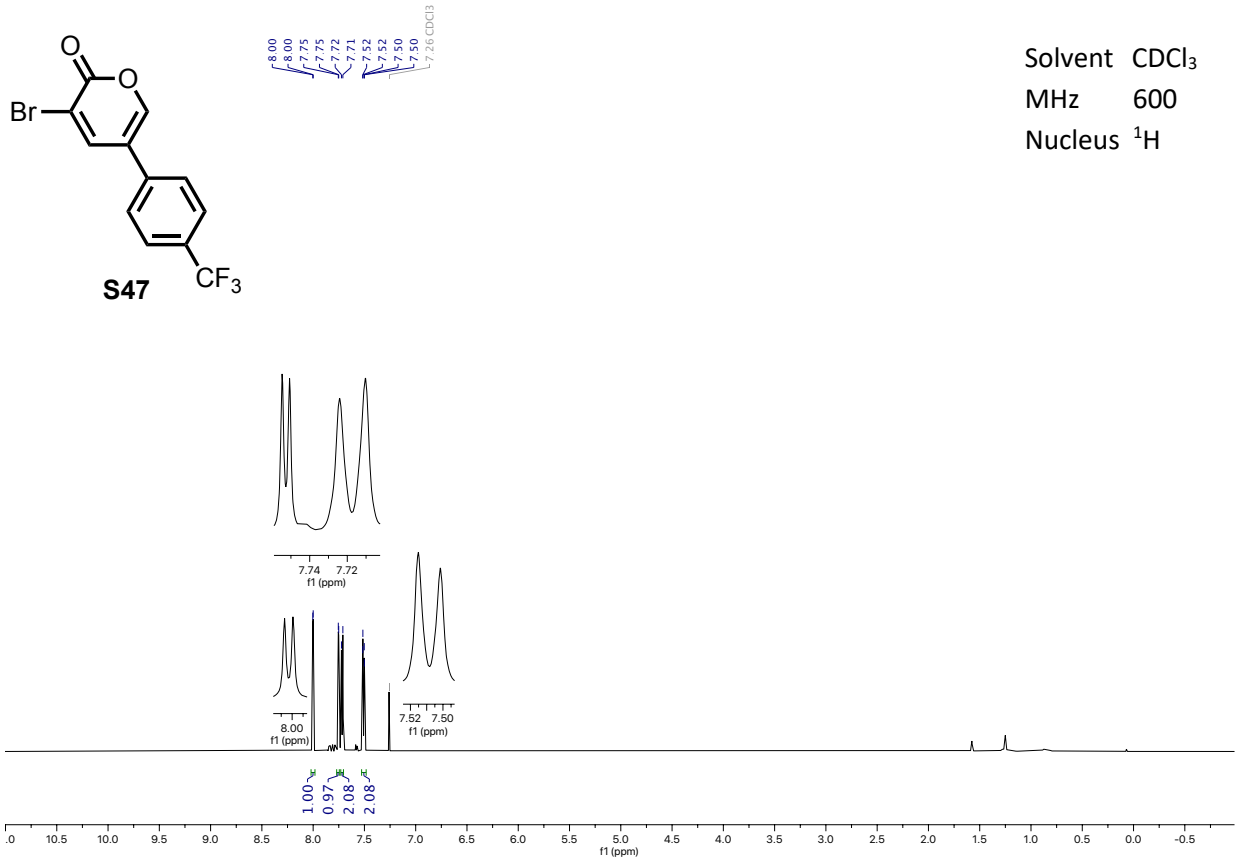




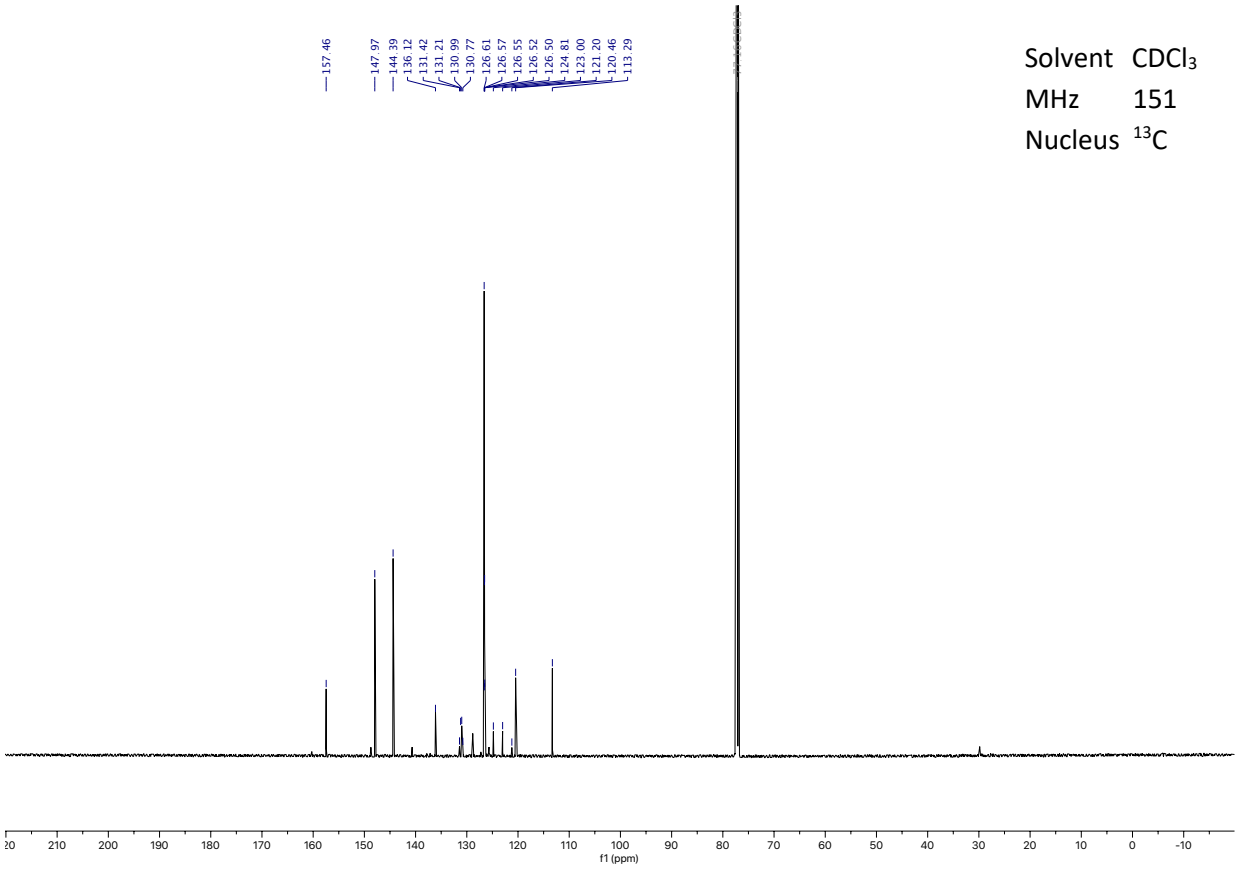
Solvent $CDCl_3$
MHz 151
Nucleus ^{13}C


10.46
8.12
8.12
7.65
7.65
7.63
7.63
7.62
7.62
7.46
7.46
7.44
7.44
7.41
7.39
7.26 CDCl3
7.23
7.13
7.02
7.01
3.87
O
O
N
H
7m
OMe
Solvent CDCl3
MHz 600
Nucleus 1H
1.00
0.99
0.92
0.98
1.11
1.85
1.14
1.12
2.73
2.83
f1 (ppm)

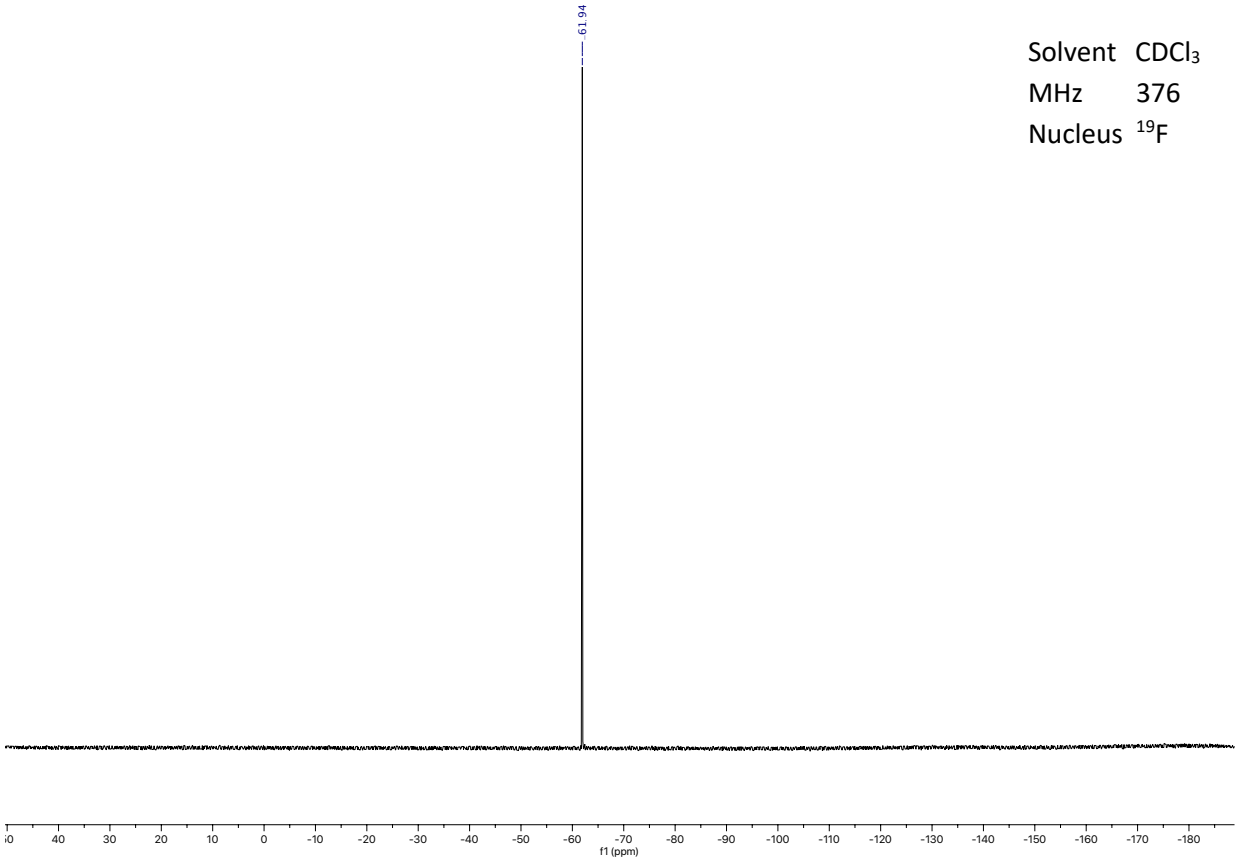

161.51
160.20
145.42
137.00
136.62
131.79
128.09
127.68
125.99
123.30
122.02
120.68
120.57
119.07
114.93
111.85
100.83
55.60
Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)

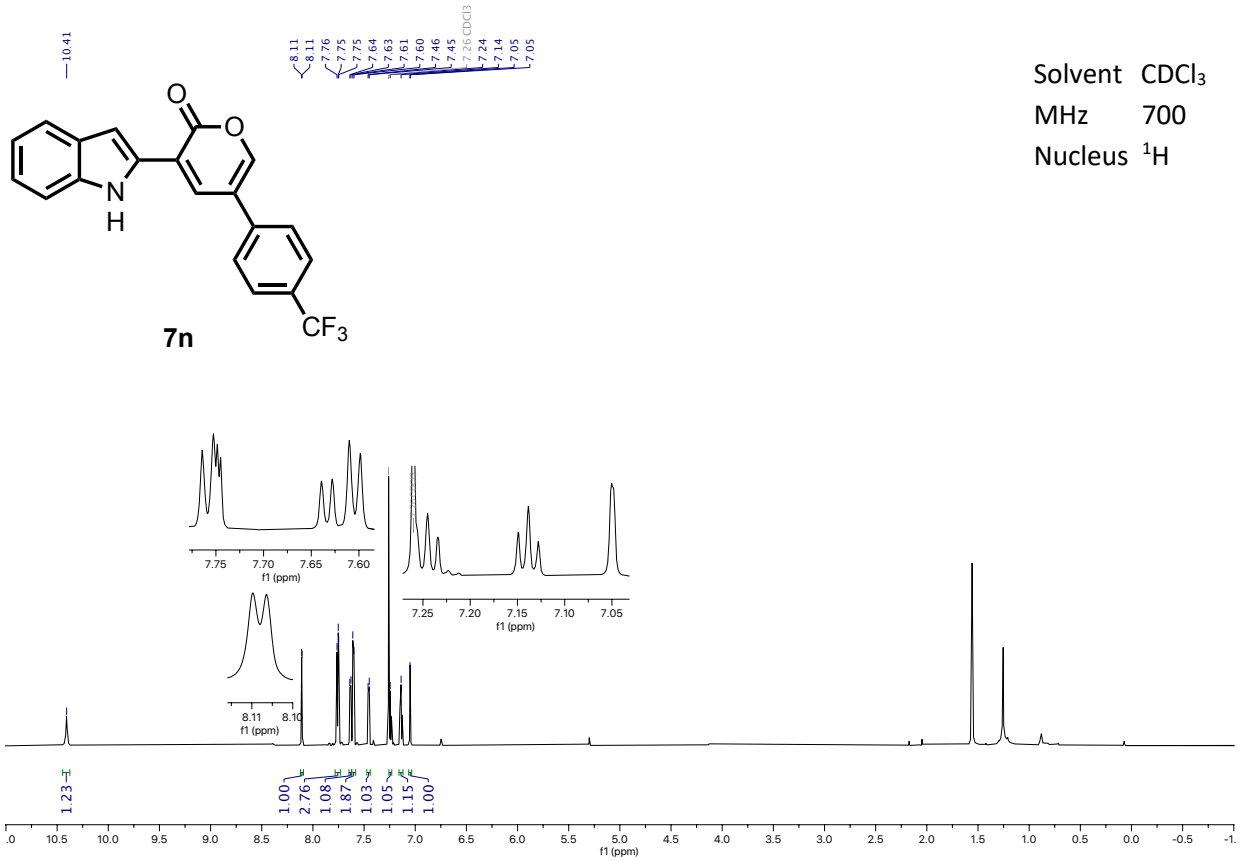


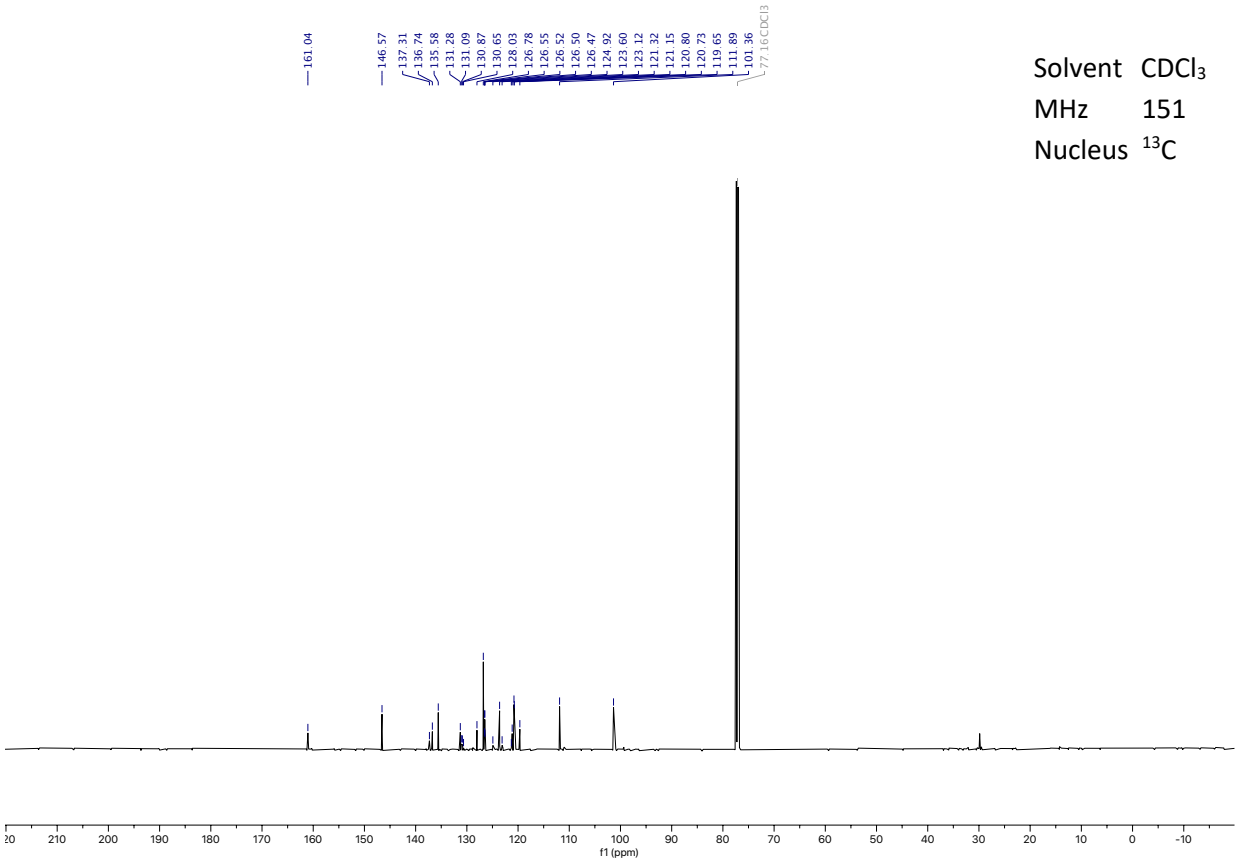
Solvent $CDCl_3$
MHz 600
Nucleus ^{1}H

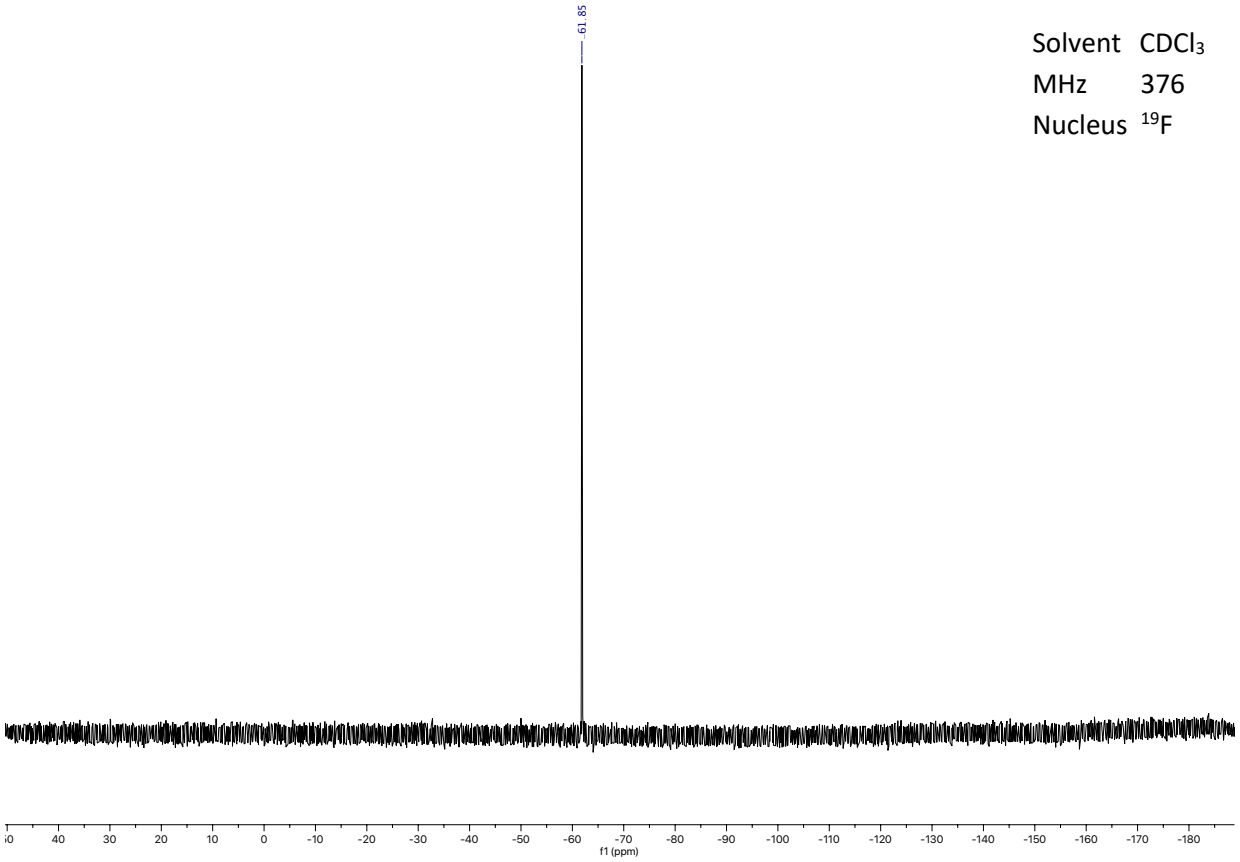


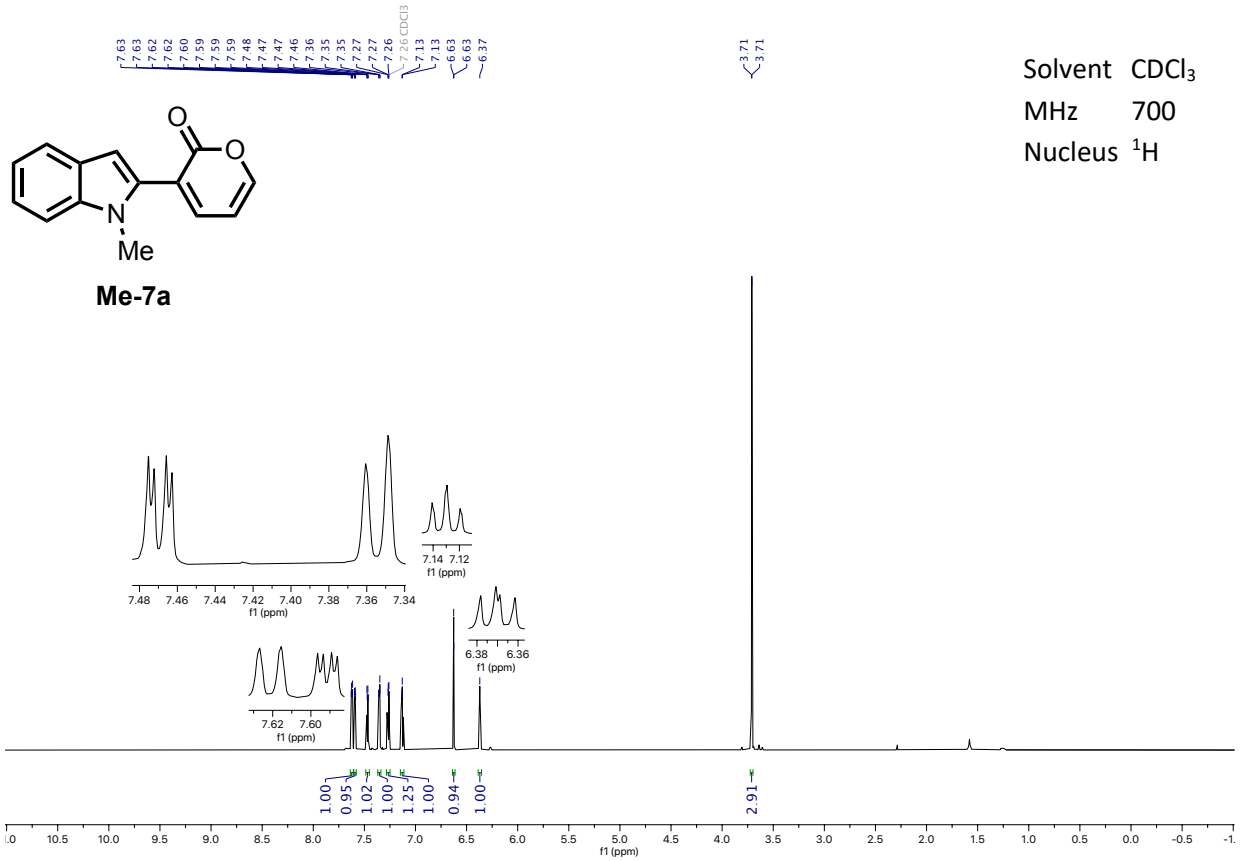
Solvent $CDCl_3$
MHz 151
Nucleus ^{13}C

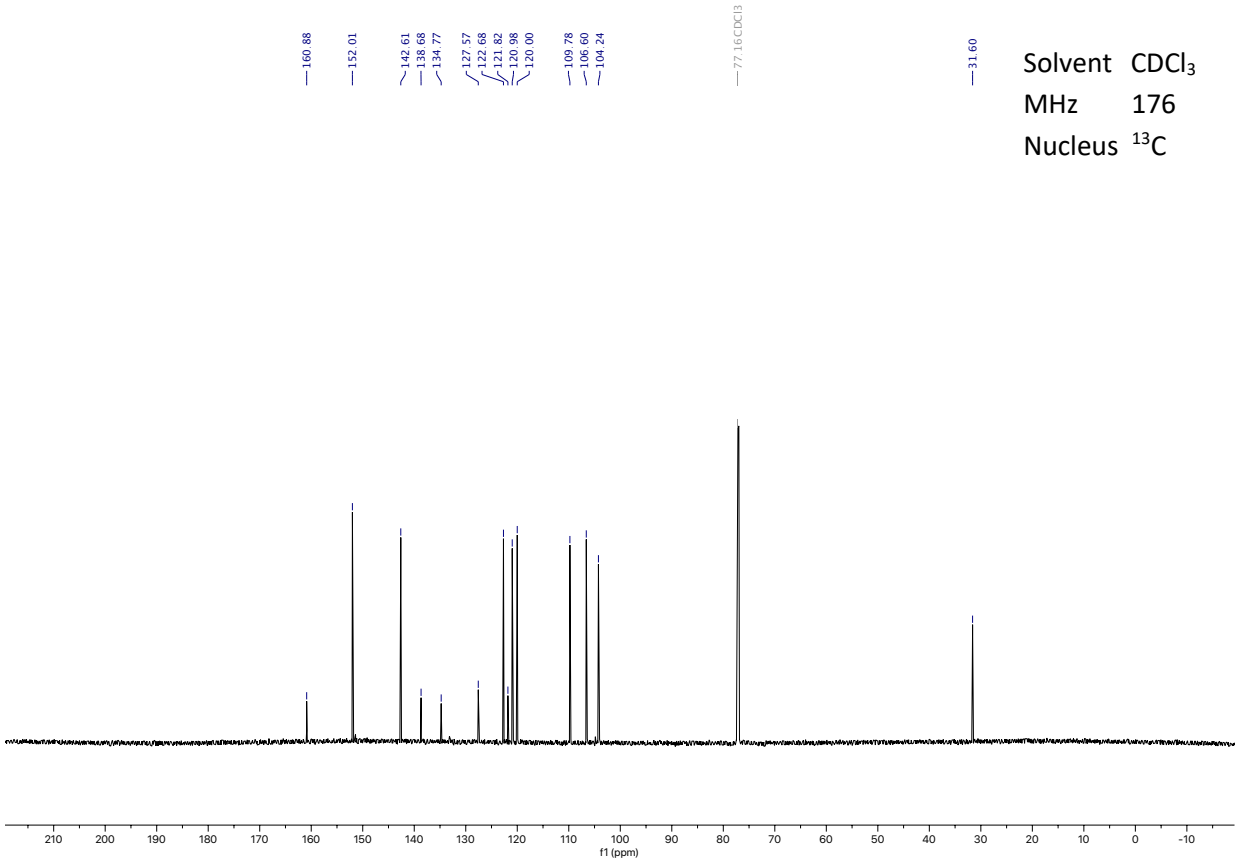

61.94
Solvent CDCl3
MHz 376
Nucleus 19F
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
f1 (ppm)

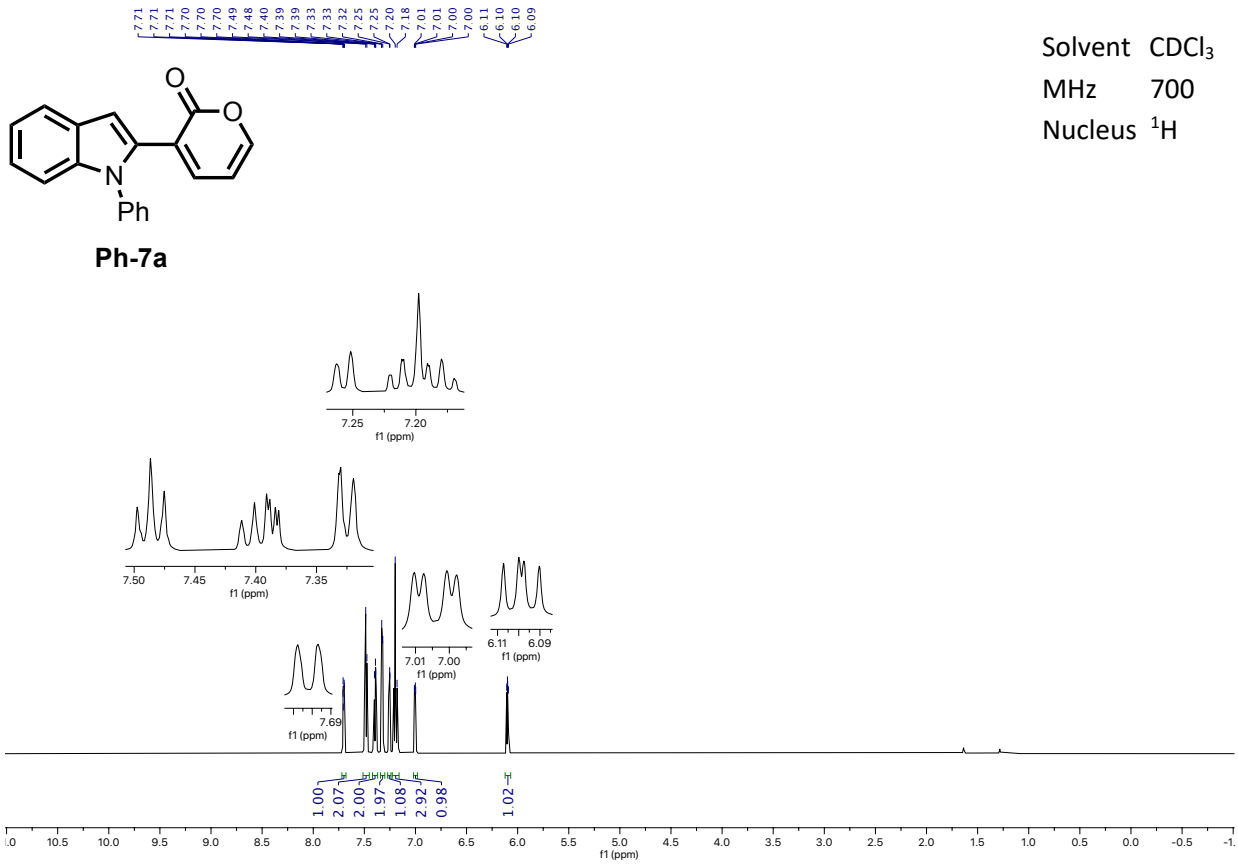

10.41
8.11
8.11
7.76
7.75
7.75
7.64
7.63
7.61
7.60
7.46
7.45
7.26 CDCl3
7.24
7.14
7.05
7.05
O
O
N
H
CF3
7n
Solvent CDCl3
MHz 700
Nucleus 1H
7.75 7.70 7.65 7.60
f1 (ppm)
7.25 7.20 7.15 7.10 7.05
f1 (ppm)
8.11 8.10
f1 (ppm)
1.23
1.00
2.76
1.08
1.87
1.03
1.05
1.15
1.00
f1 (ppm)


161.04
146.57
137.31
136.74
135.58
131.28
131.09
130.87
130.65
128.03
126.78
126.55
126.52
126.50
126.47
124.92
123.60
123.12
121.32
121.15
120.80
120.73
119.65
111.89
101.36
77.16 CDCl3
Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)


61.85
Solvent CDCl3
MHz 376
Nucleus 19F
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180
f1 (ppm)

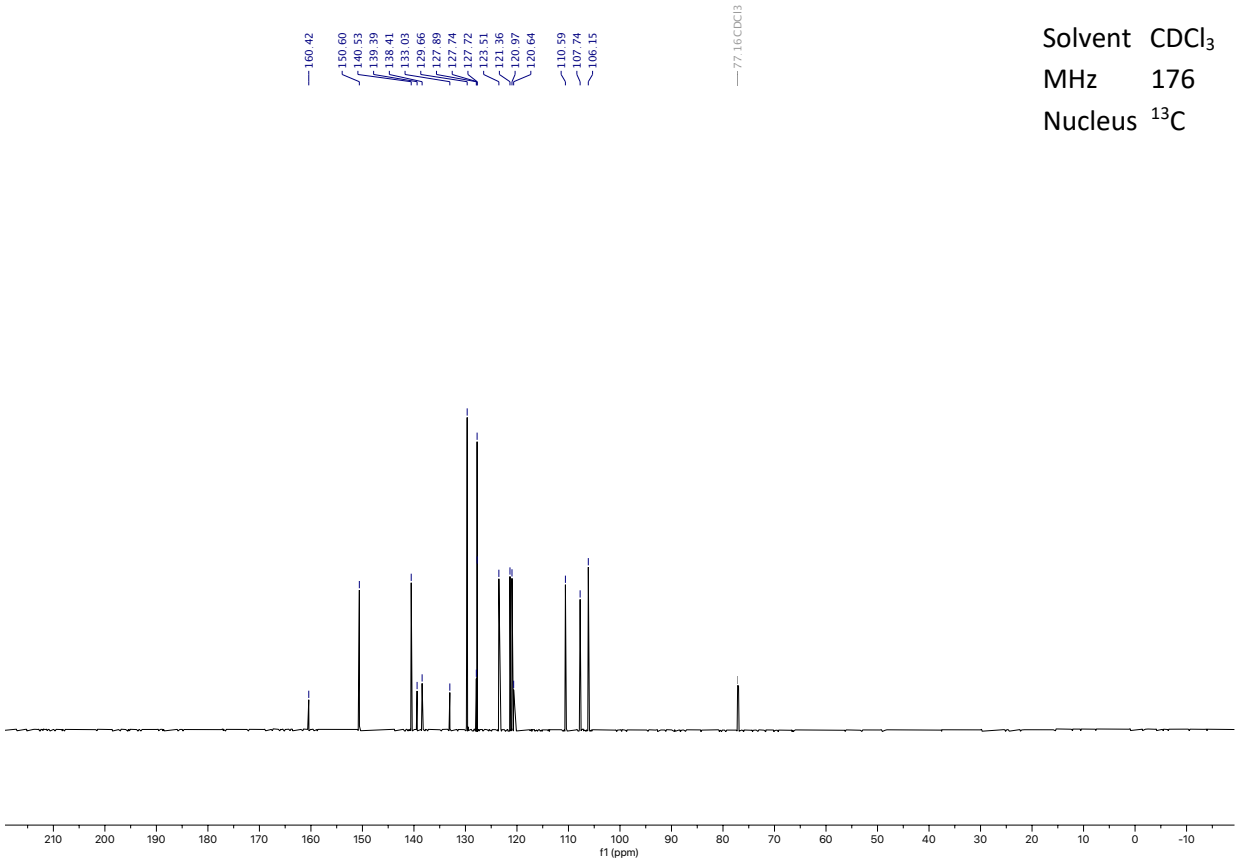

Me
Me-7a
Solvent CDCl3
MHz 700
Nucleus 1H
f1 (ppm)


Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)

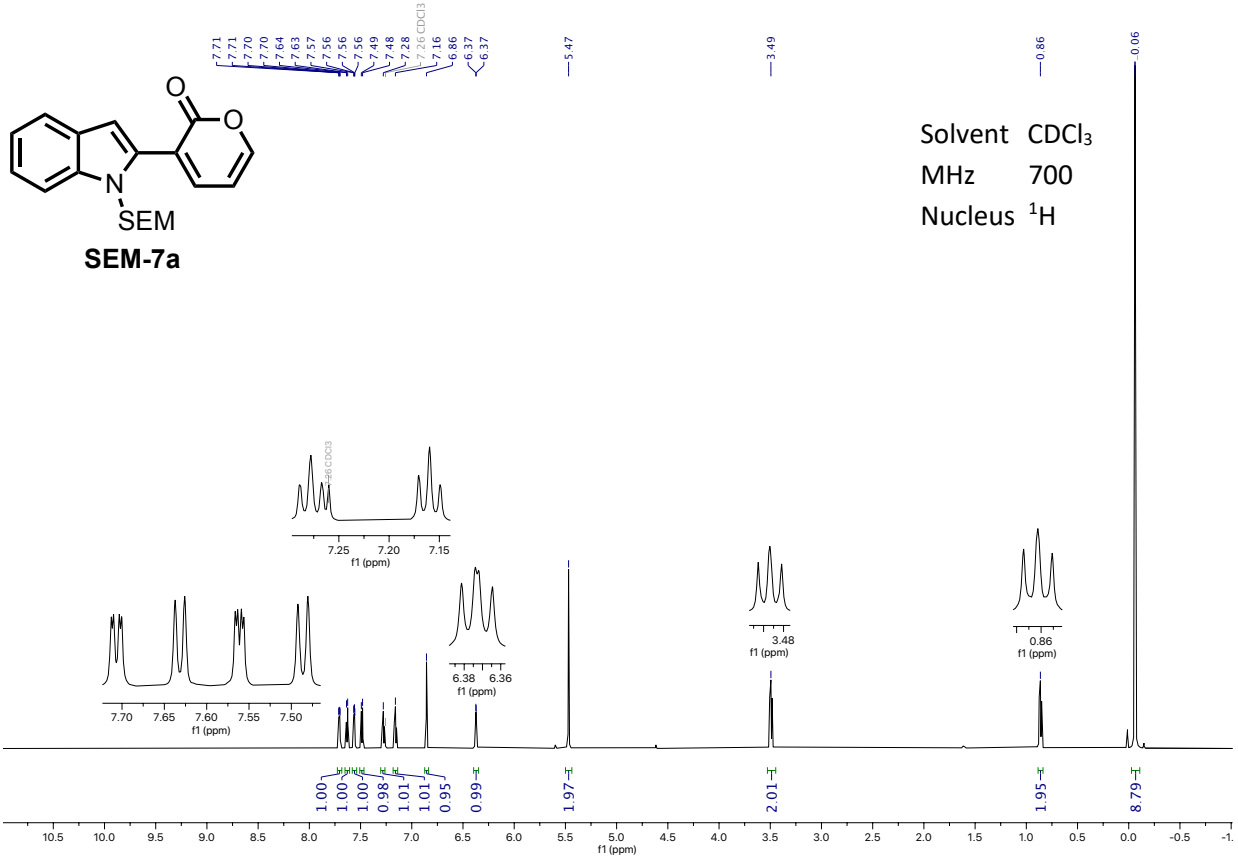


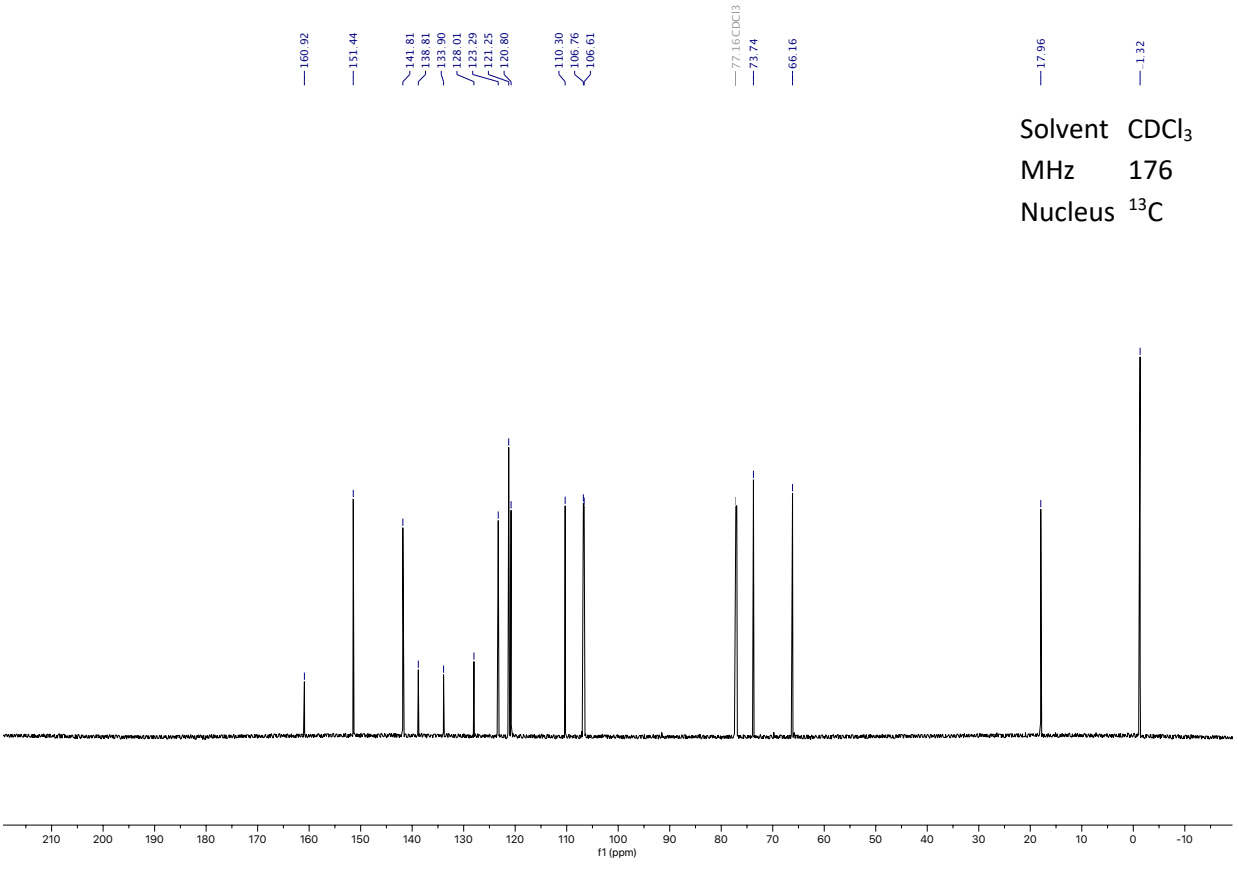
Ph-7a

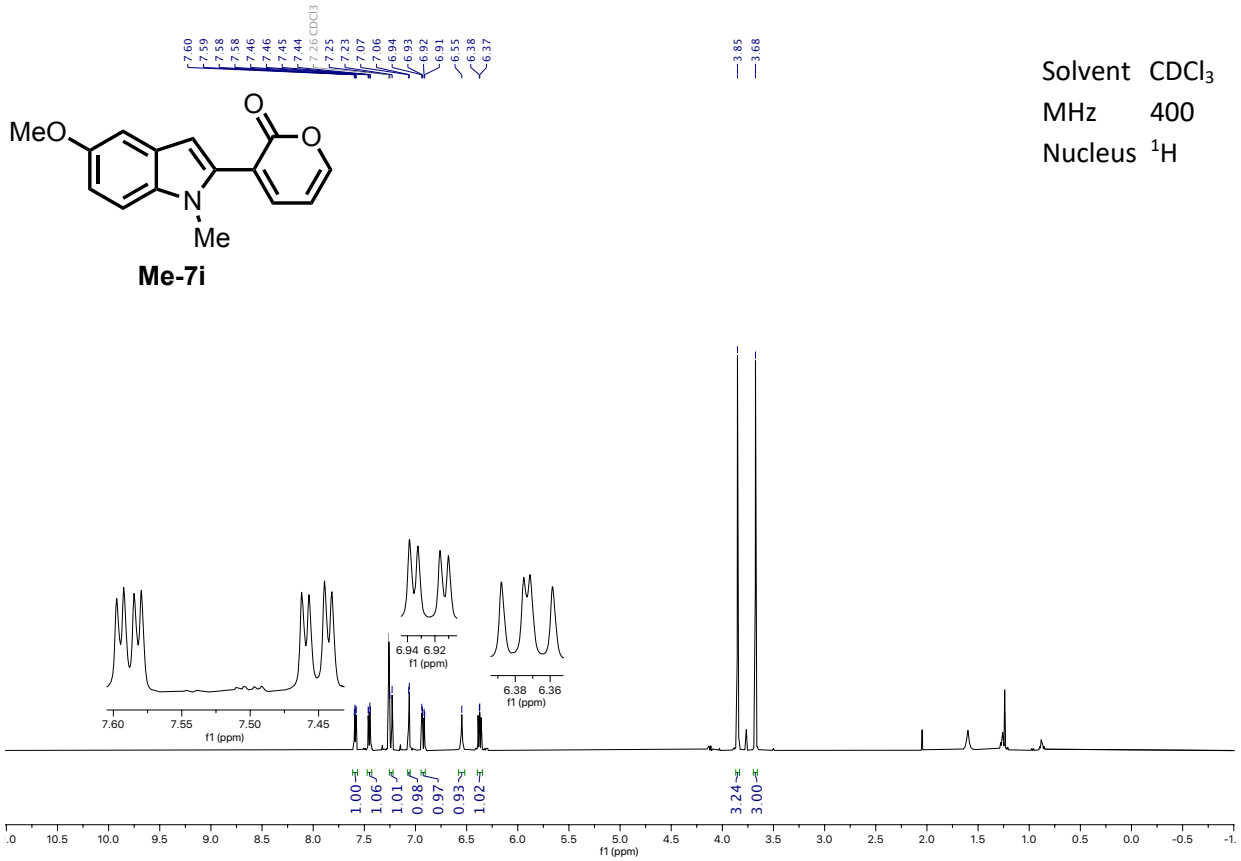
Solvent $CDCl_3$
MHz 700
Nucleus ^{1}H

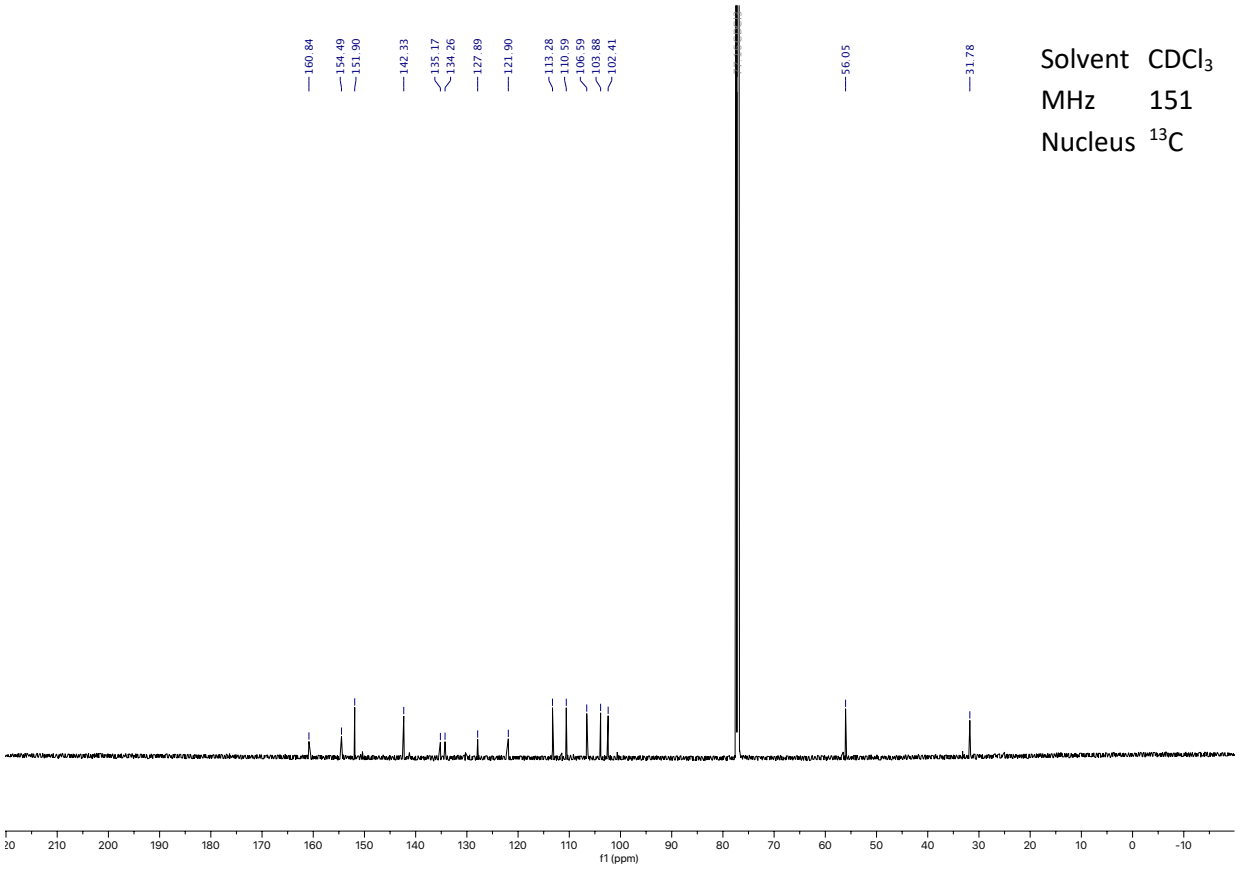


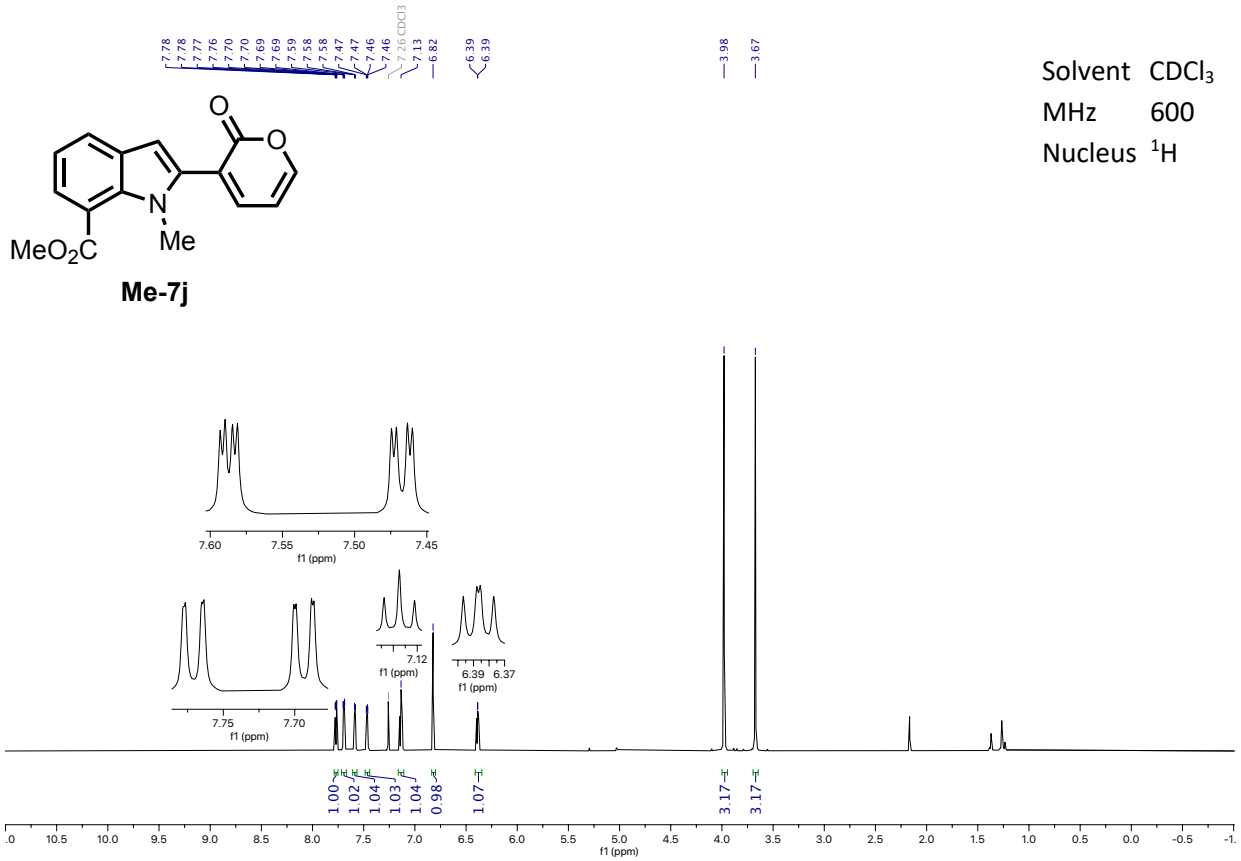
Solvent $CDCl_3$
MHz 176
Nucleus ^{13}C

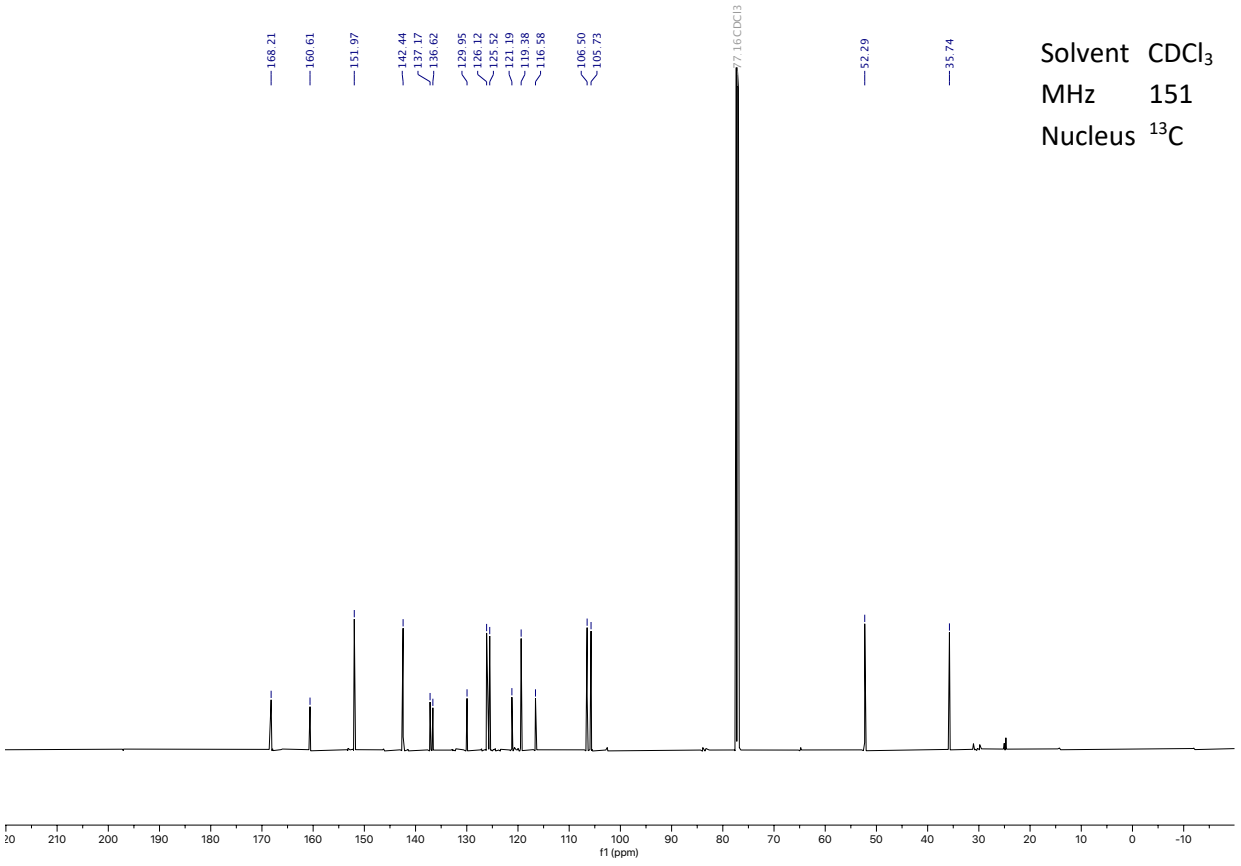

SEM
SEM-7a
Solvent CDCl3
MHz 700
Nucleus 1H

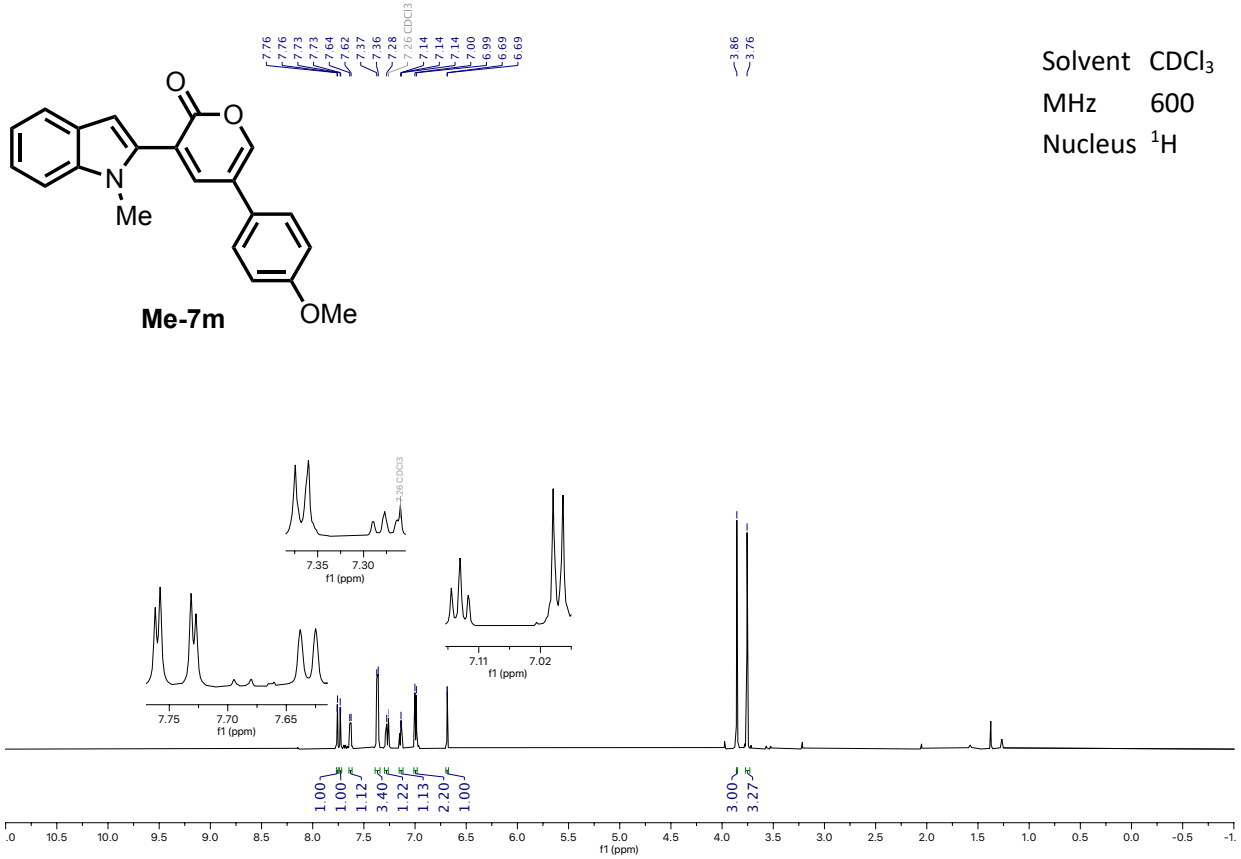

Solvent CDCl3
MHz 176
Nucleus 13C

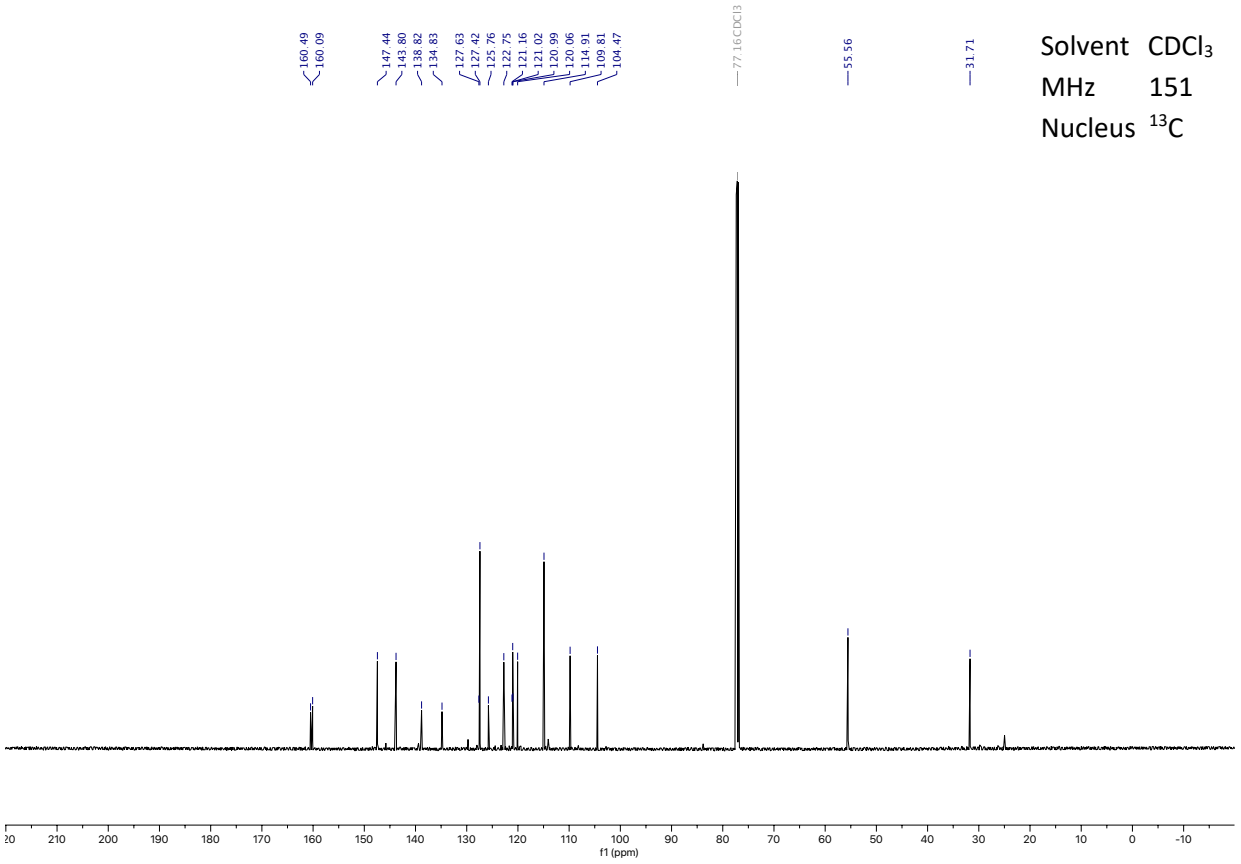

MeO
O
O
N
Me
Me-7i
Solvent CDCl3
MHz 400
Nucleus 1H
f1 (ppm)

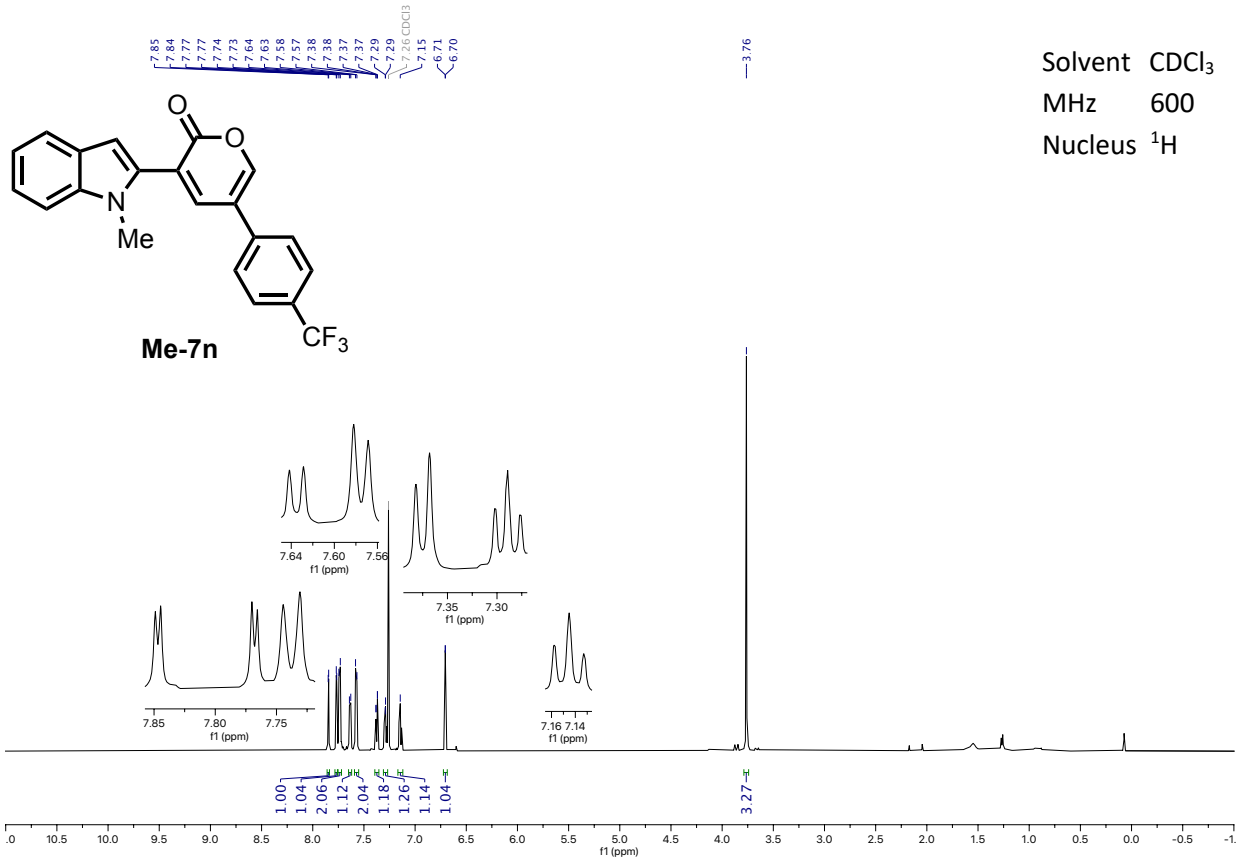

Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)

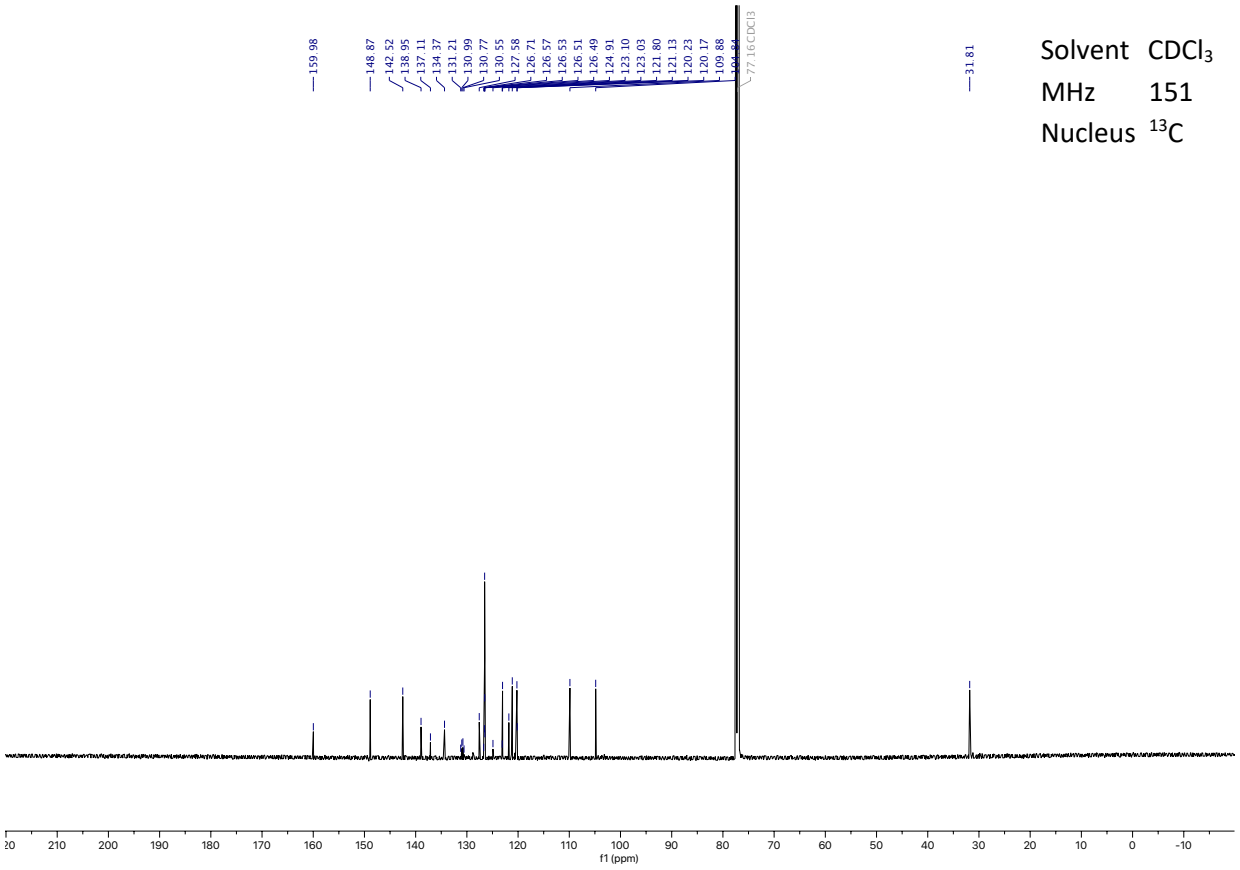

Solvent CDCl3
MHz 600
Nucleus 1H
Me-7j

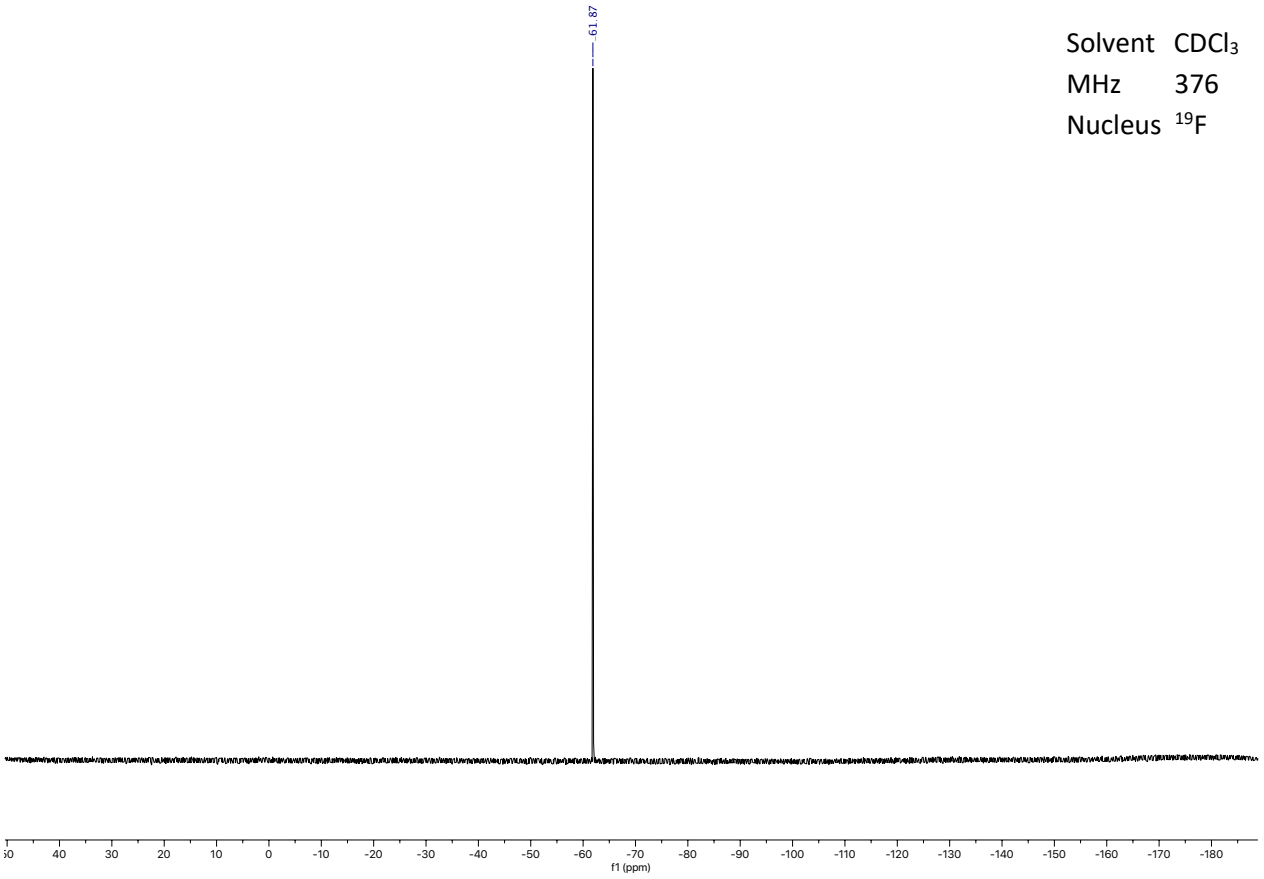

Solvent CDCl3
MHz 151
Nucleus 13C

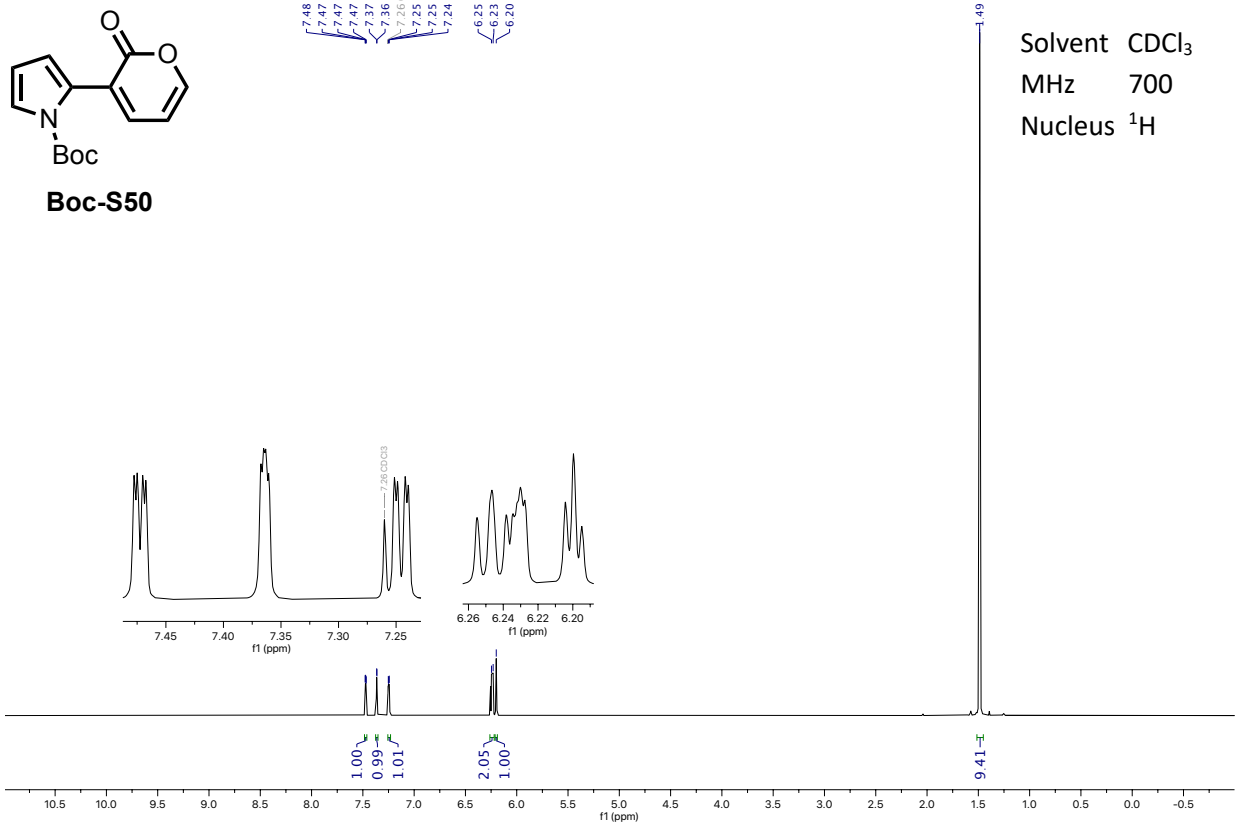

Me-7m
OMe
Solvent CDCl3
MHz 600
Nucleus 1H

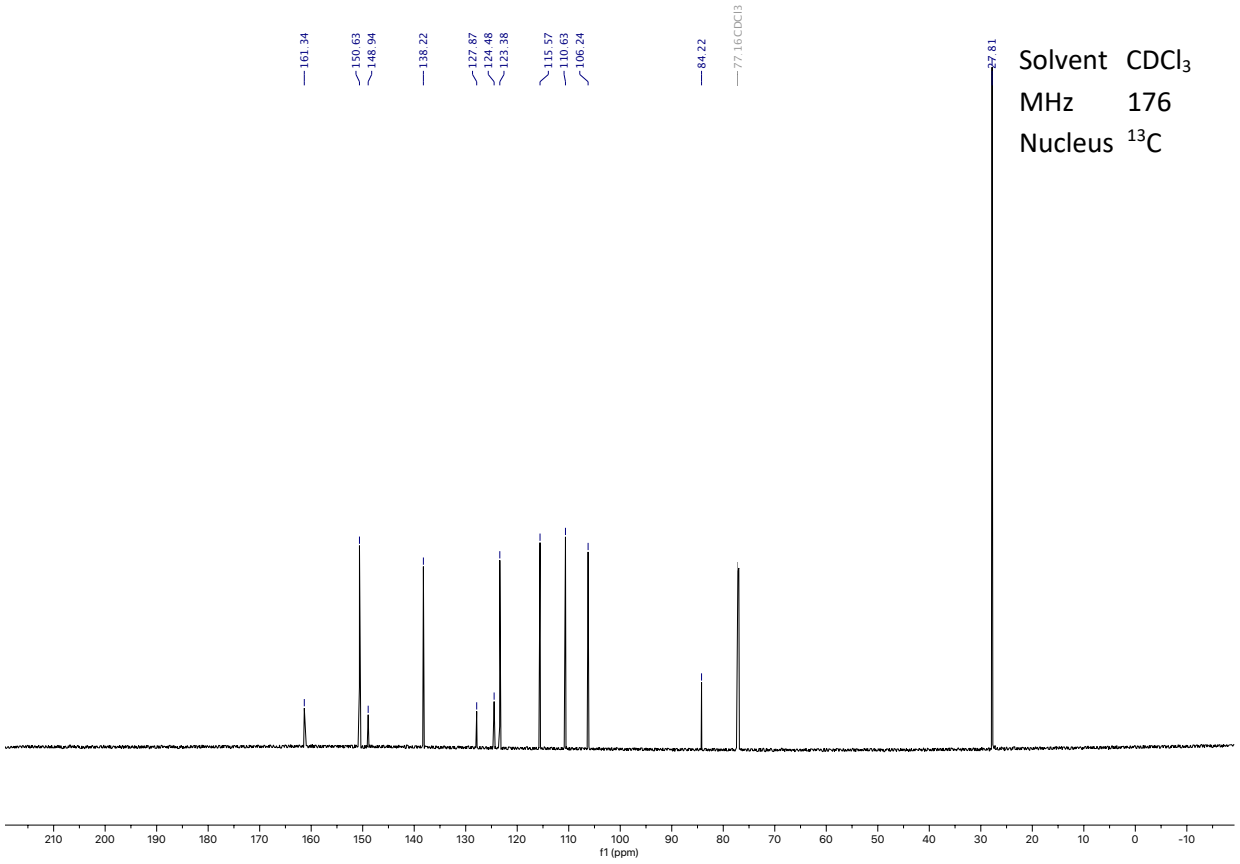

Solvent CDCl3
MHz 151
Nucleus 13C

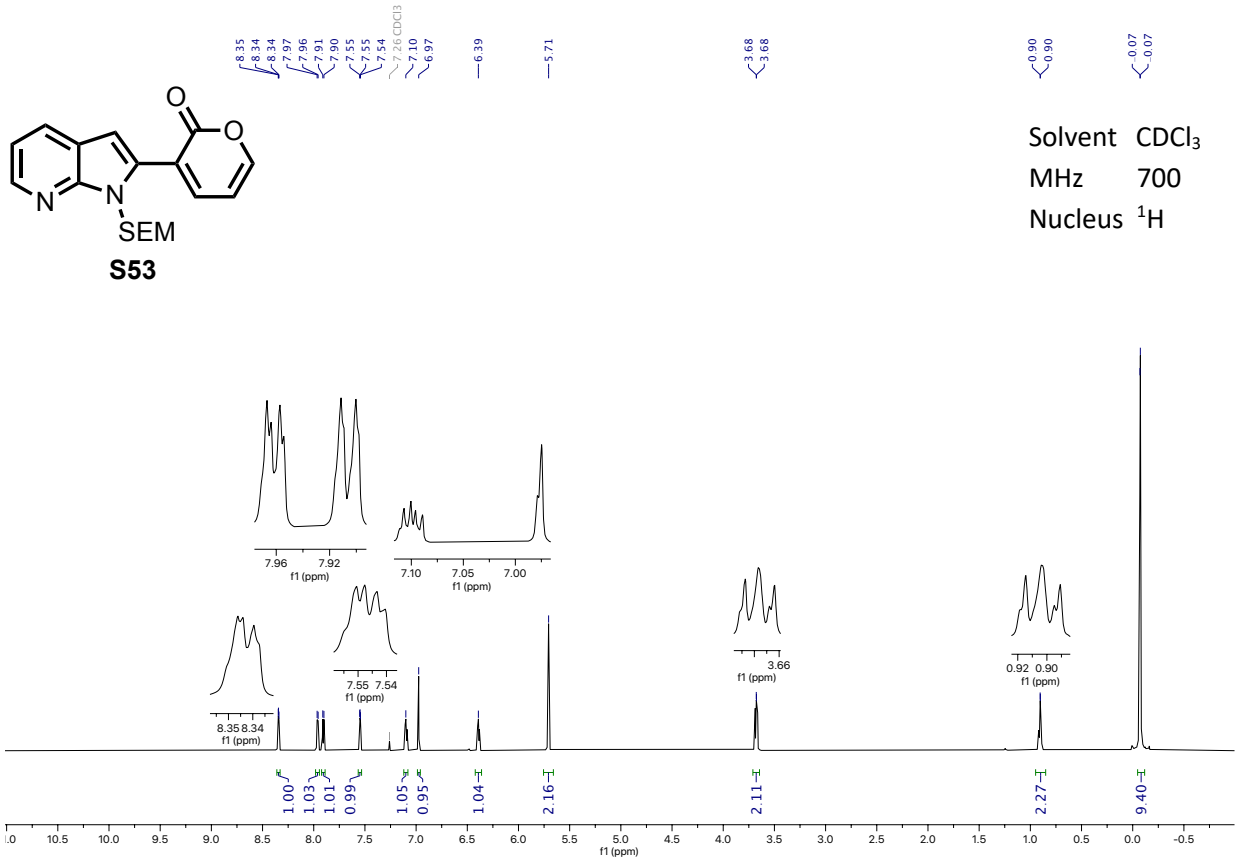

Me-7n
Solvent CDCl3
MHz 600
Nucleus 1H
f1 (ppm)

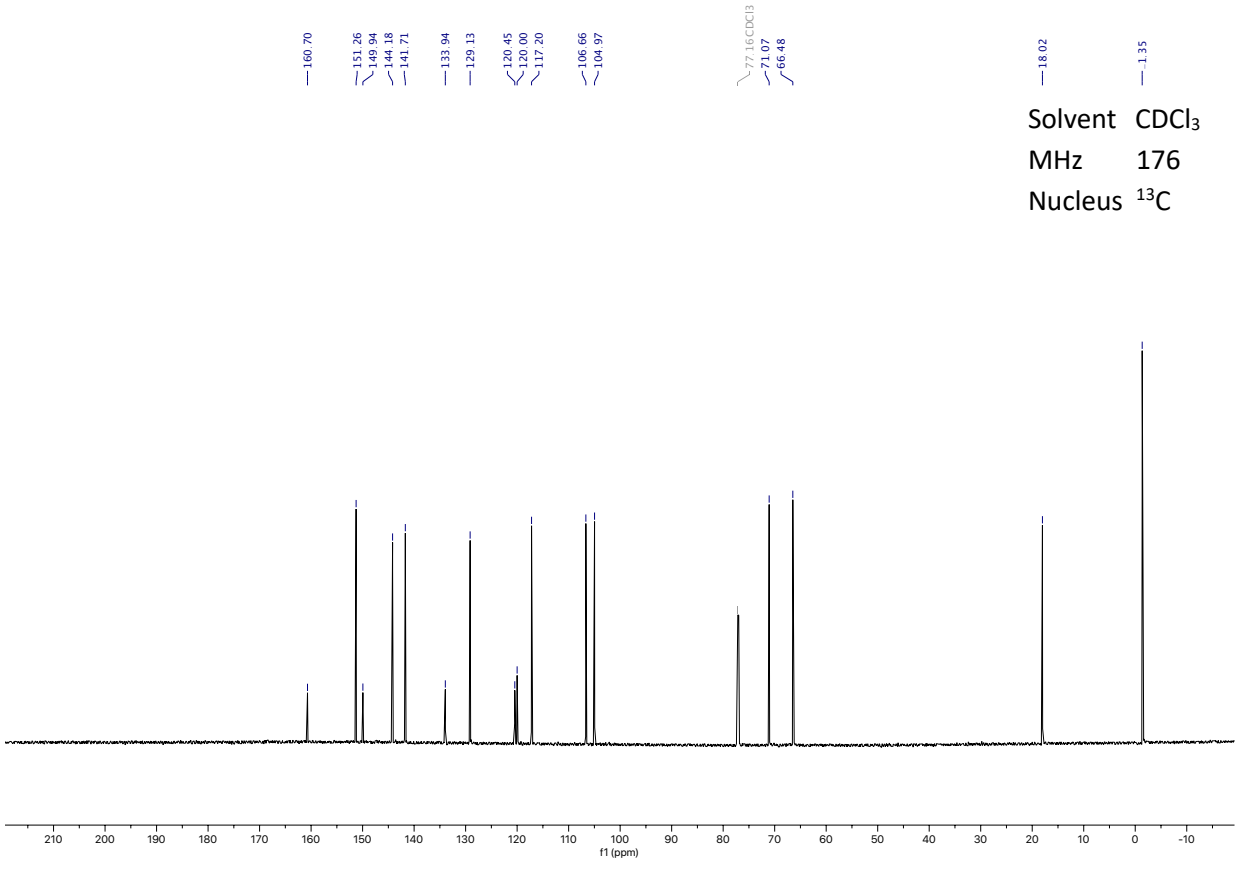

Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)


61.87
Solvent CDCl3
MHz 376
Nucleus 19F
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180
f1 (ppm)

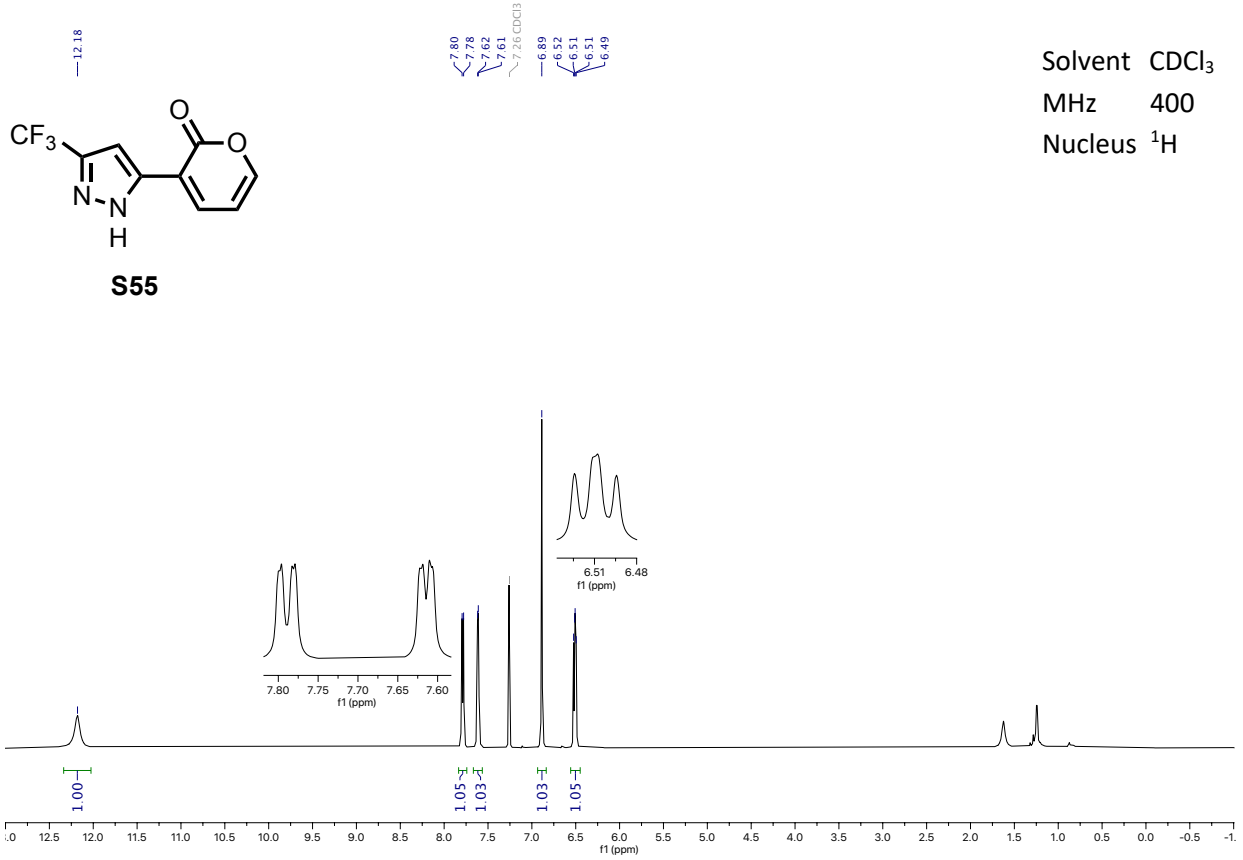

Boc
Boc-S50
Solvent CDCl3
MHz 700
Nucleus 1H
f1 (ppm)

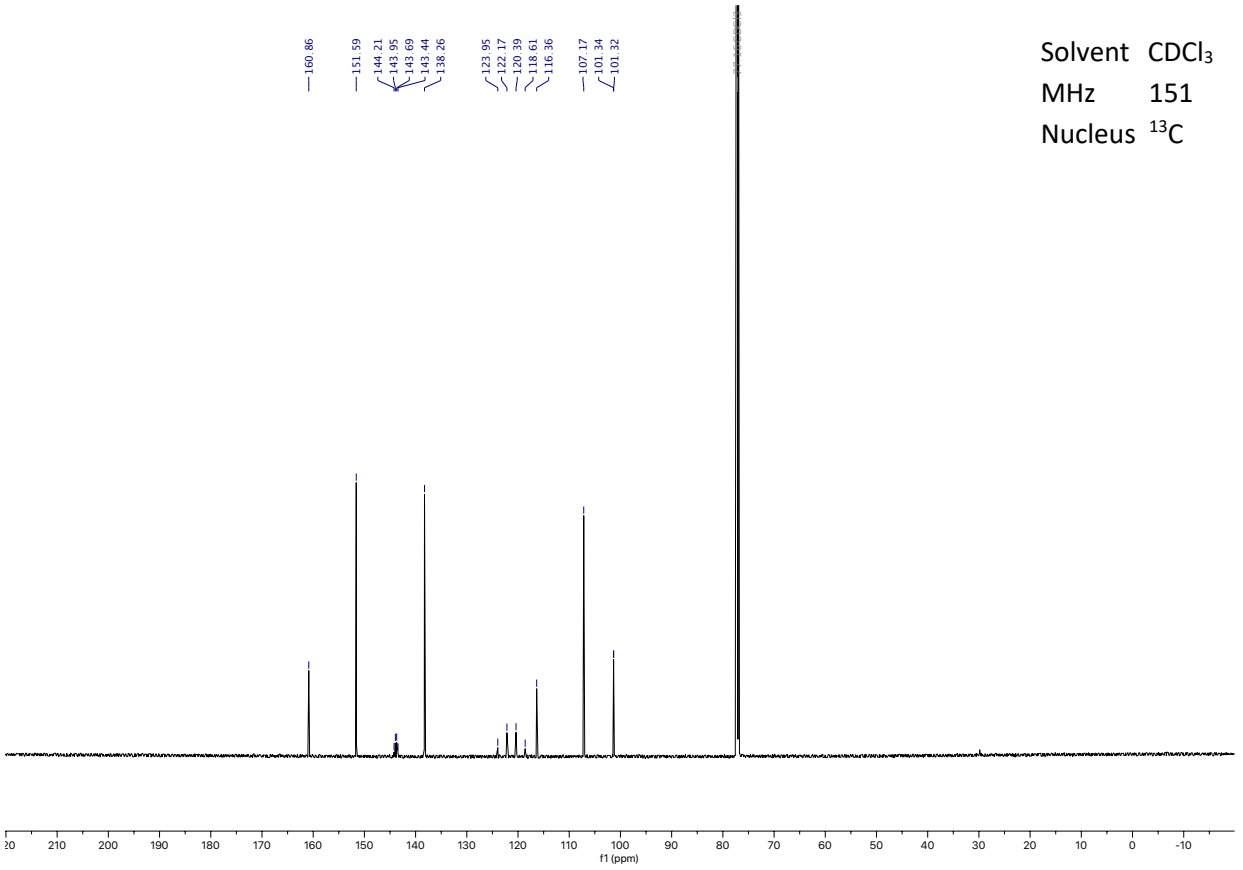

Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)

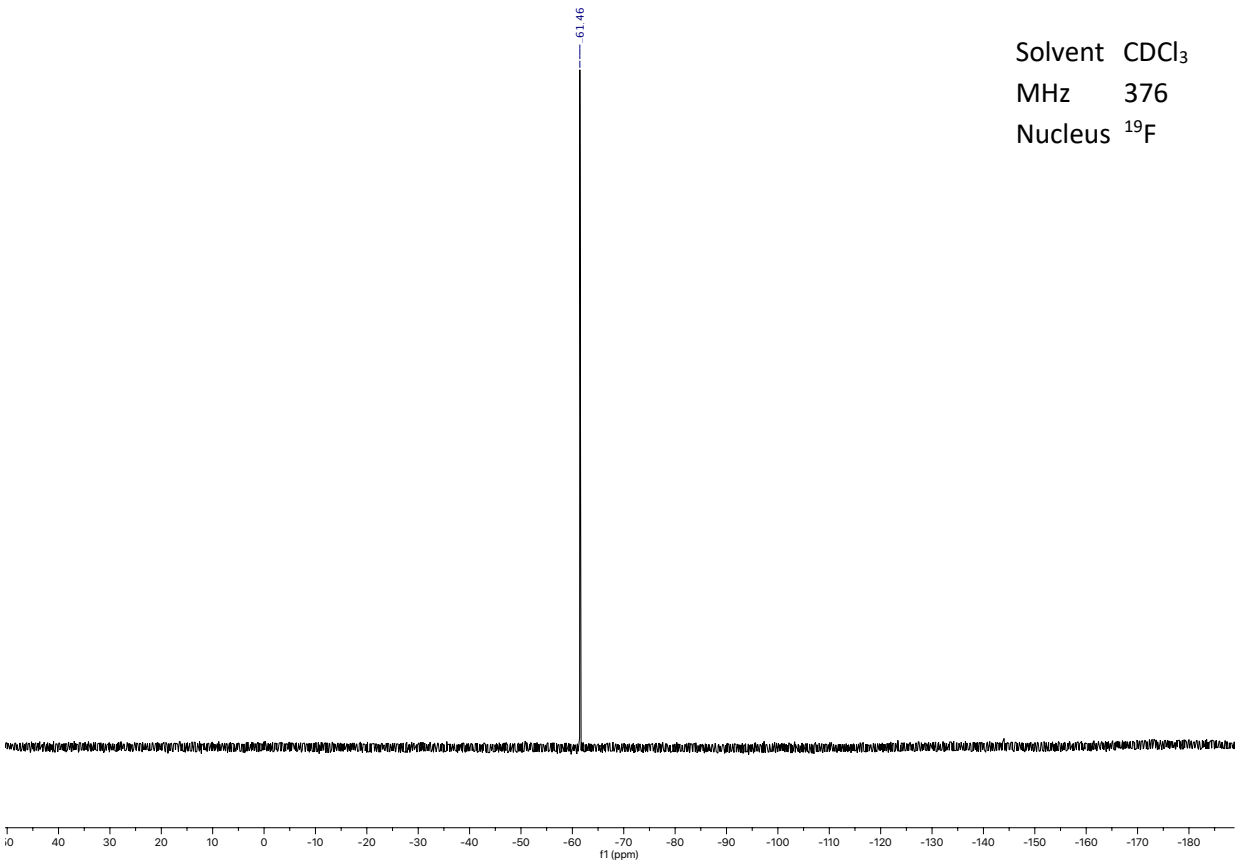

8.35
8.34
8.34
7.97
7.96
7.91
7.90
7.55
7.55
7.54
7.26 CDCl3
7.10
6.97
6.39
5.71
3.68
3.68
0.90
0.90
0.07
-0.07
O
O
N
N
SEM
Solvent CDCl3
MHz 700
Nucleus 1H
7.96 7.92
f1 (ppm)
7.10 7.05 7.00
f1 (ppm)
7.55 7.54
f1 (ppm)
8.35 8.34
f1 (ppm)
3.66
f1 (ppm)
0.92 0.90
f1 (ppm)
1.00
1.03
1.01
0.99
1.05
0.95
1.04
2.16
2.11
2.27
9.40
f1 (ppm)

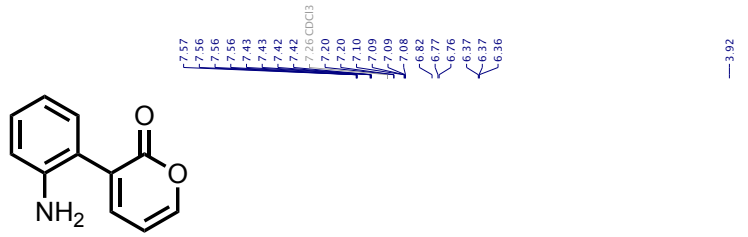

160.70
151.26
149.94
144.18
141.71
133.94
129.13
120.45
120.00
117.20
106.66
104.97
77.16 CDCl3
71.07
66.48
18.02
1.35
Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)

S53


12.18
7.80
7.78
7.62
7.61
7.26 CDCl3
6.89
6.52
6.51
6.51
6.49
Solvent CDCl3
MHz 400
Nucleus 1H
CF3
O
O
N
N
H
S55
1.00
1.05
1.03
1.03
1.05
f1 (ppm)

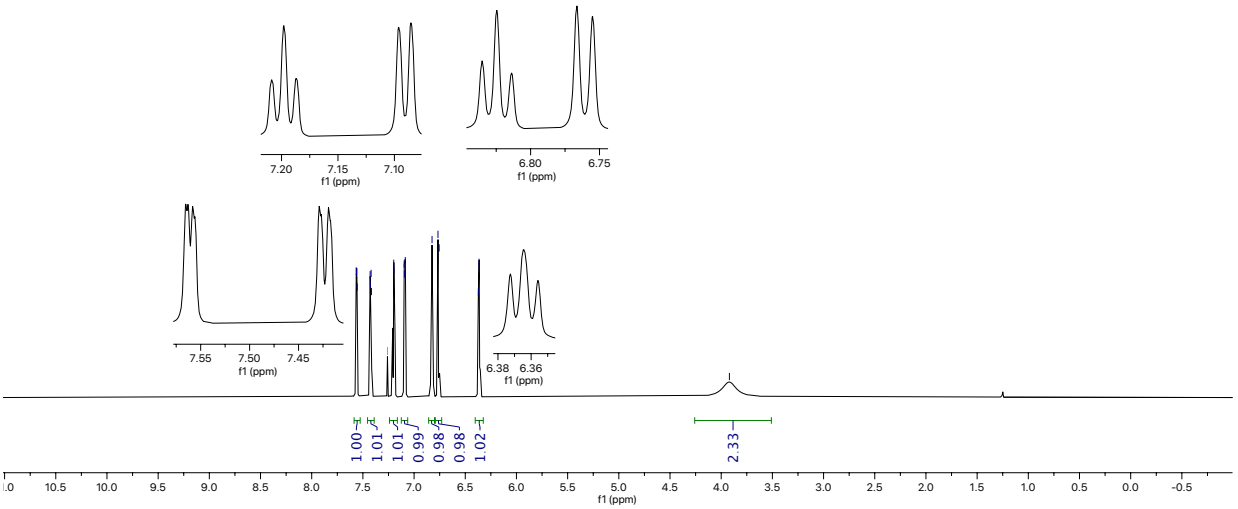

160.86
151.59
144.21
143.95
143.69
143.44
138.26
123.95
122.17
120.39
118.61
116.36
107.17
101.34
101.32
Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)


-61.46
Solvent CDCl3
MHz 376
Nucleus 19F
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
f1 (ppm)

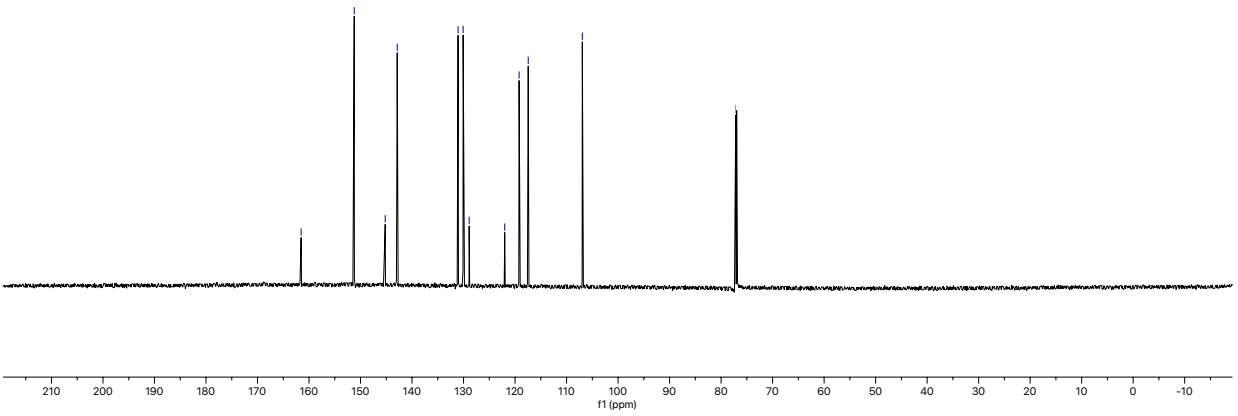


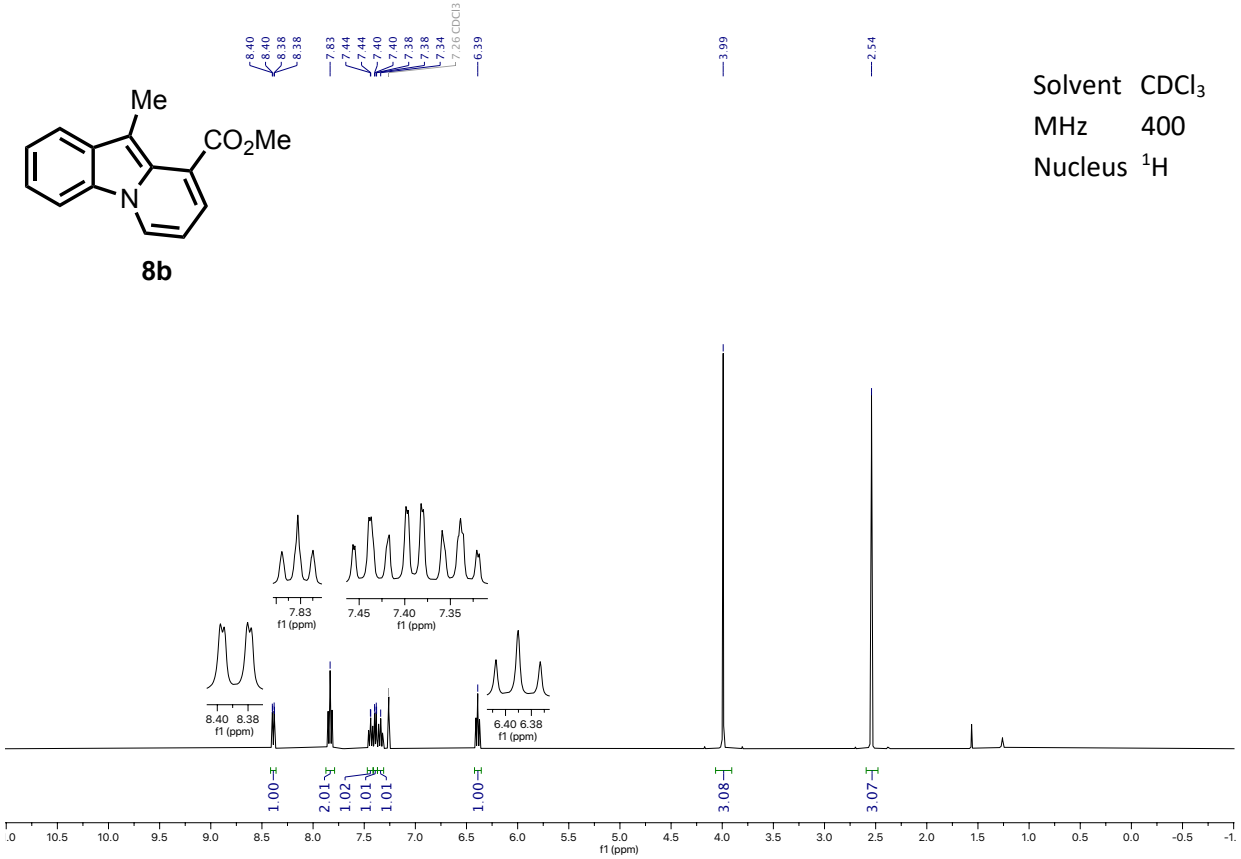
S57

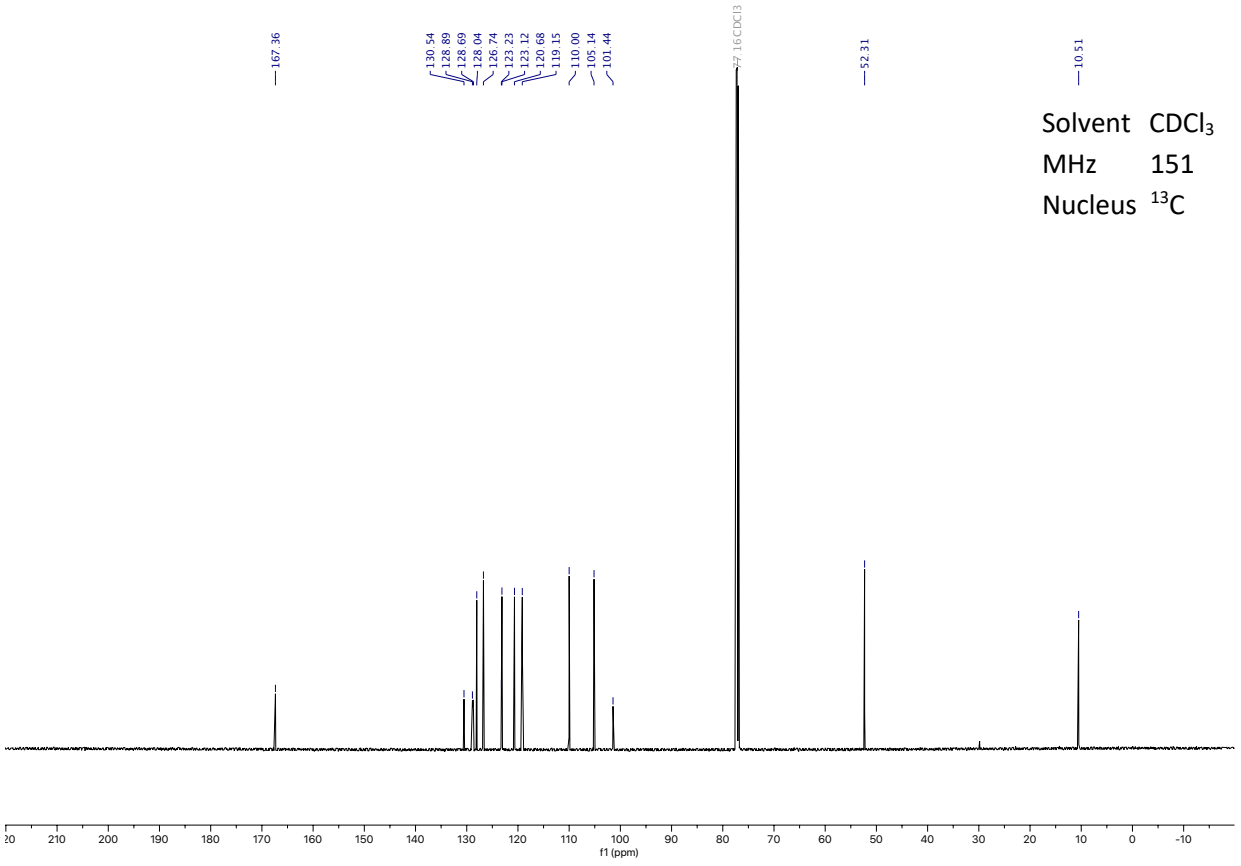
Solvent $CDCl_3$
MHz 700
Nucleus ^{1}H

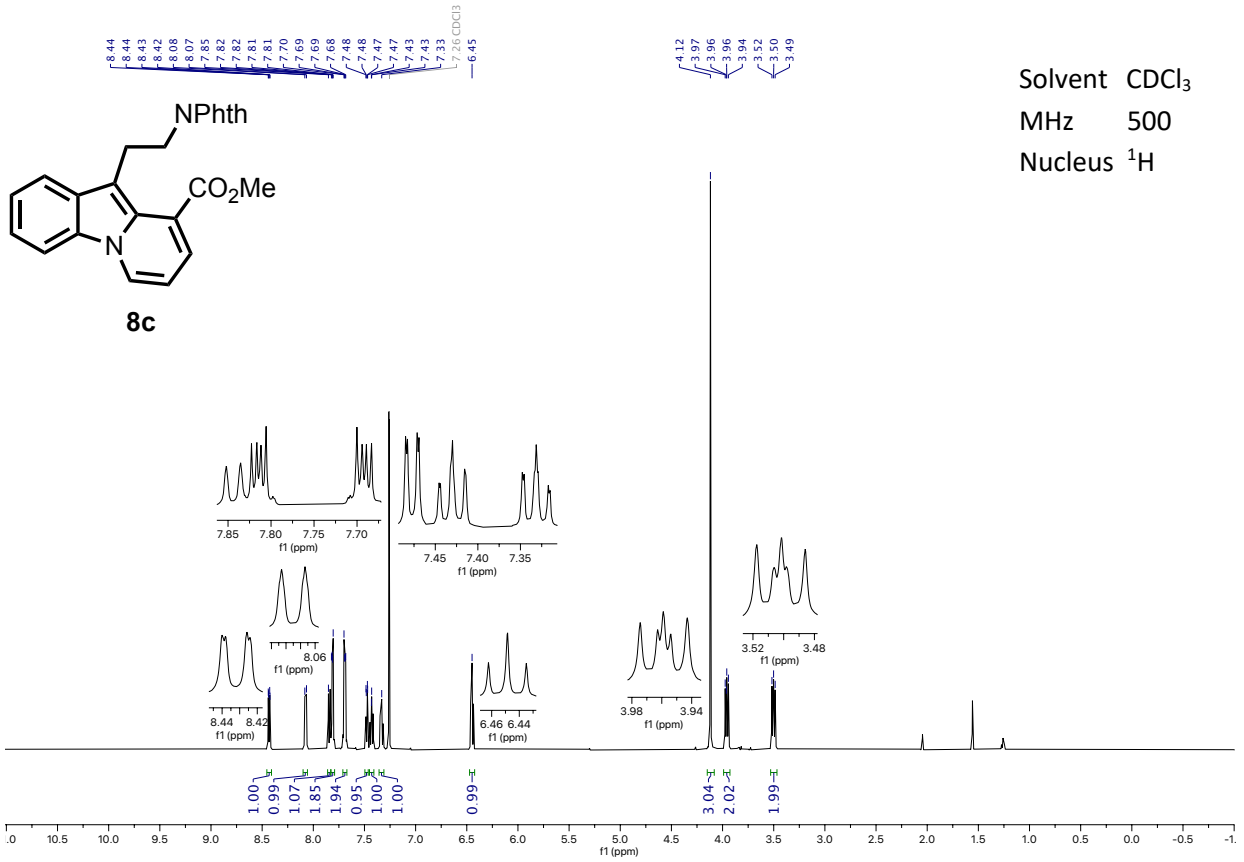


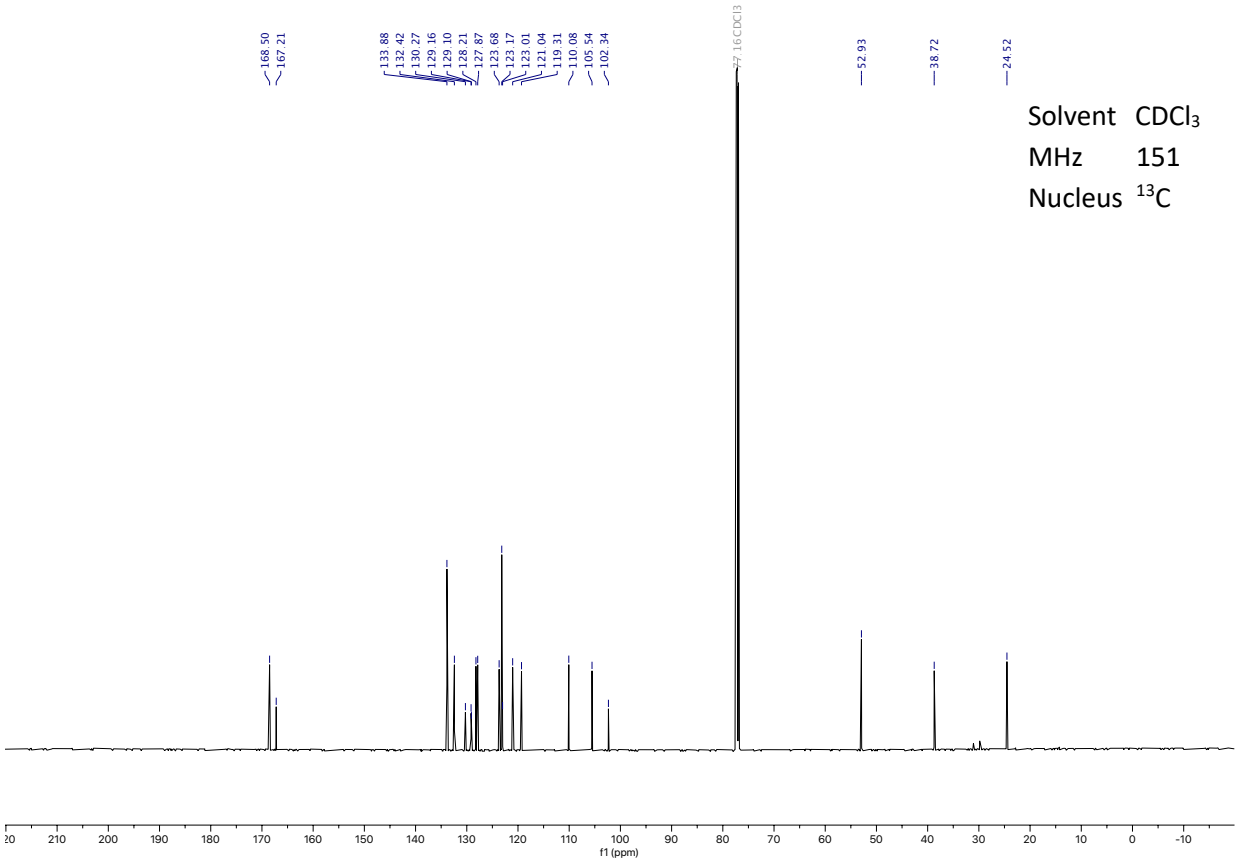
Solvent $CDCl_3$
MHz 176
Nucleus ^{13}C

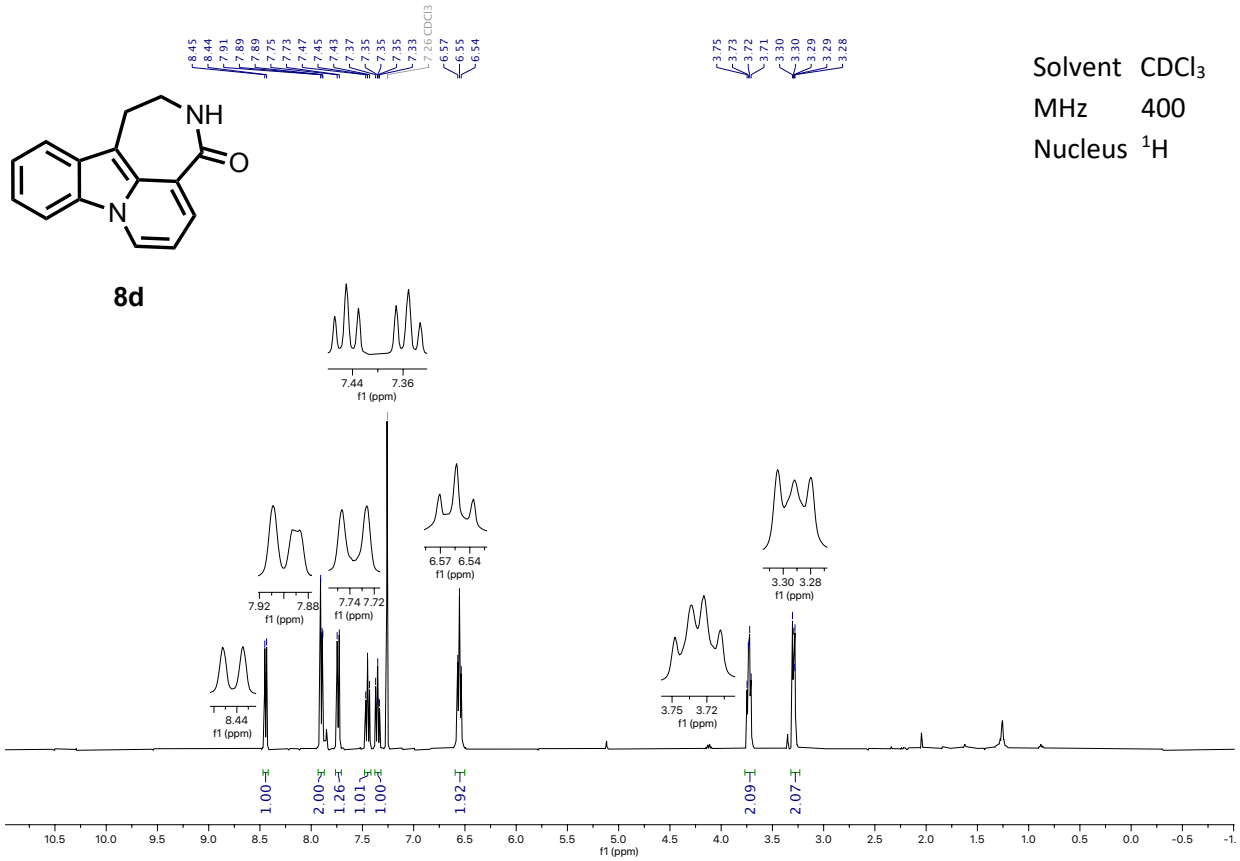



Me
CO2Me
N
8b
Solvent CDCl3
MHz 400
Nucleus 1H
f1 (ppm)

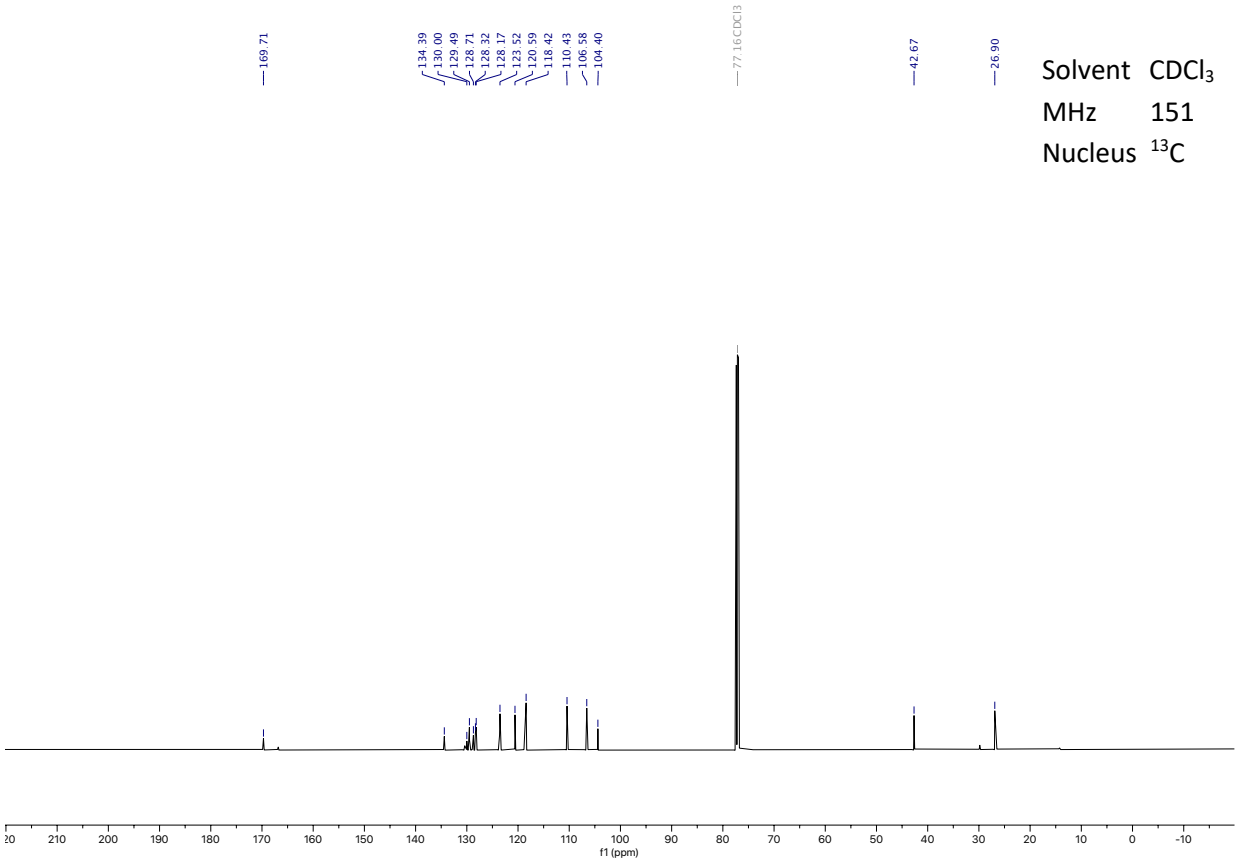

Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)


NPhth
CO2Me
N
8c
Solvent CDCl3
MHz 500
Nucleus 1H
f1 (ppm)

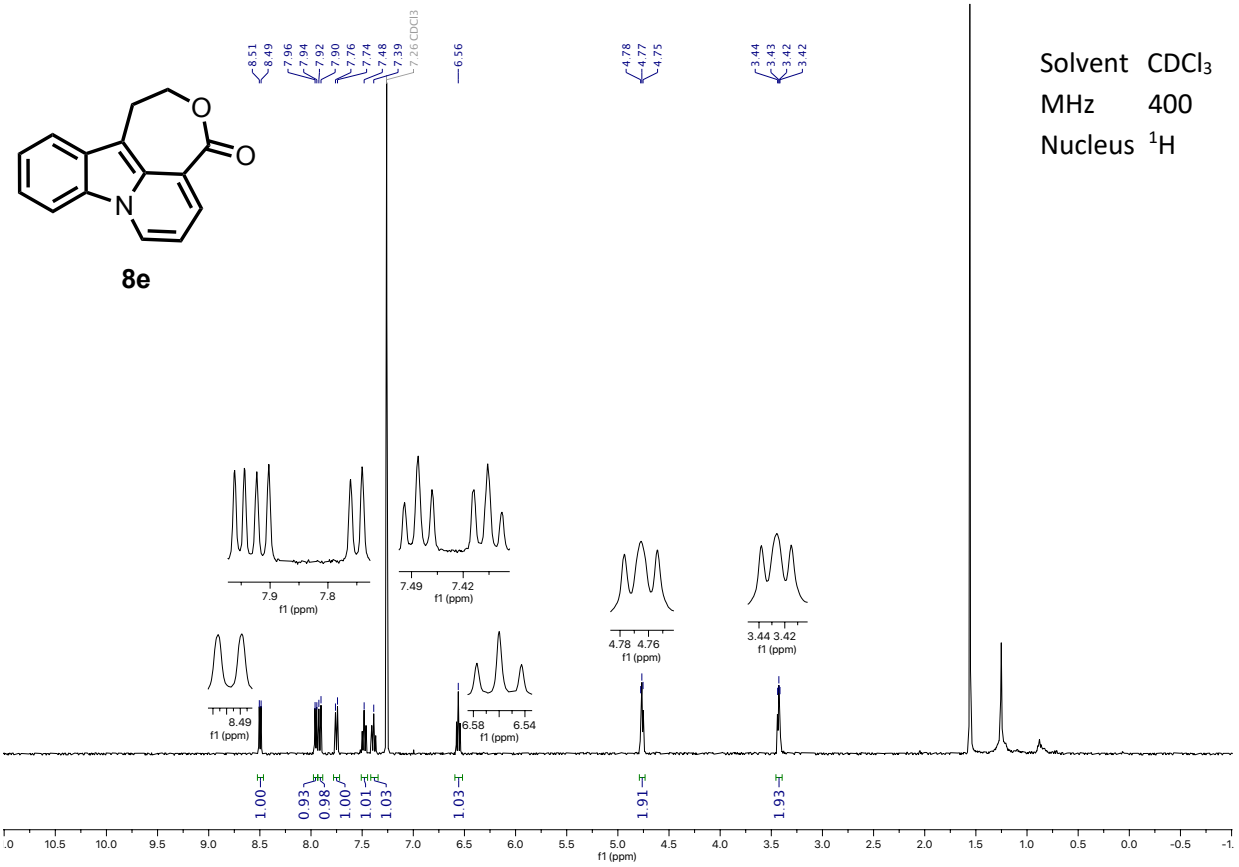

Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)

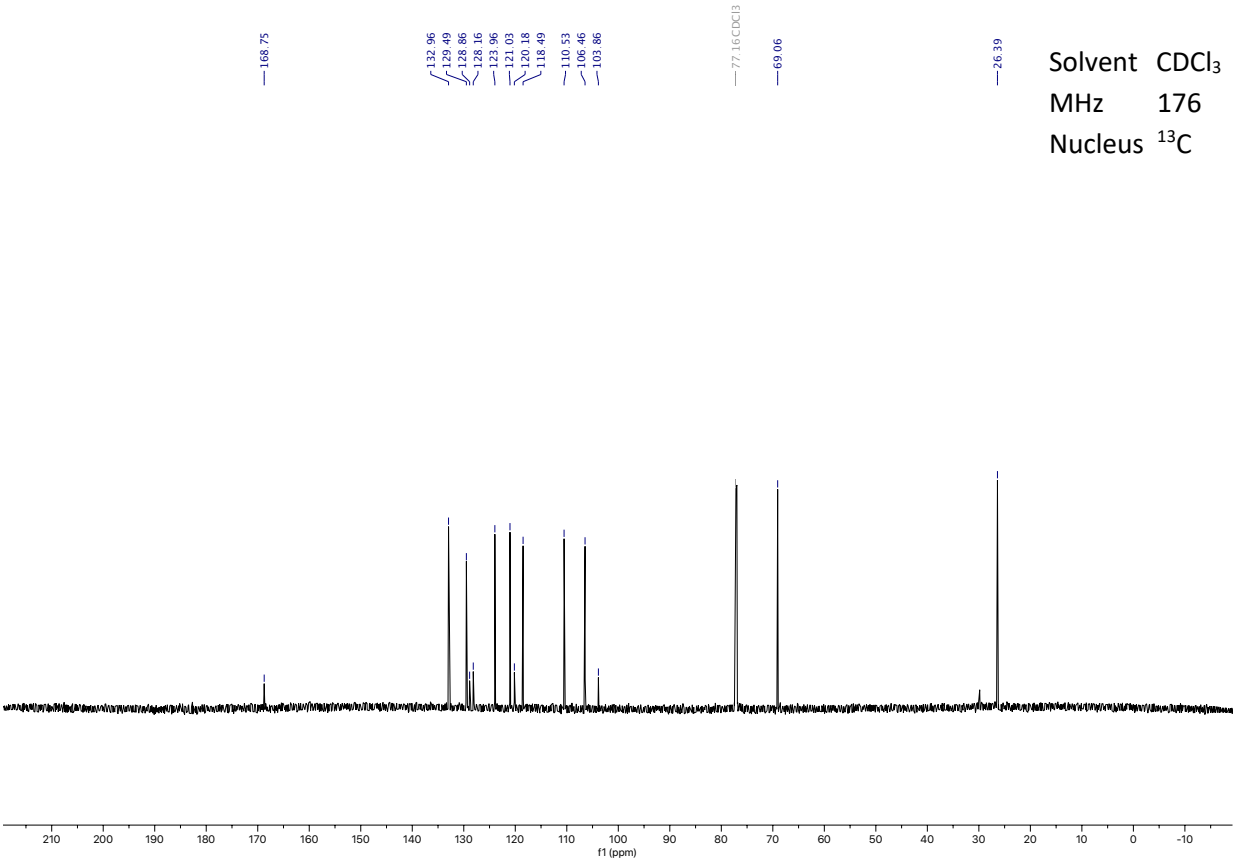


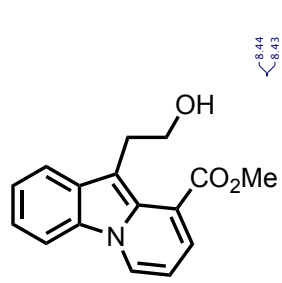
Solvent $CDCl_3$
MHz 400
Nucleus ^{1}H



Solvent $CDCl_3$
MHz 151
Nucleus ^{13}C

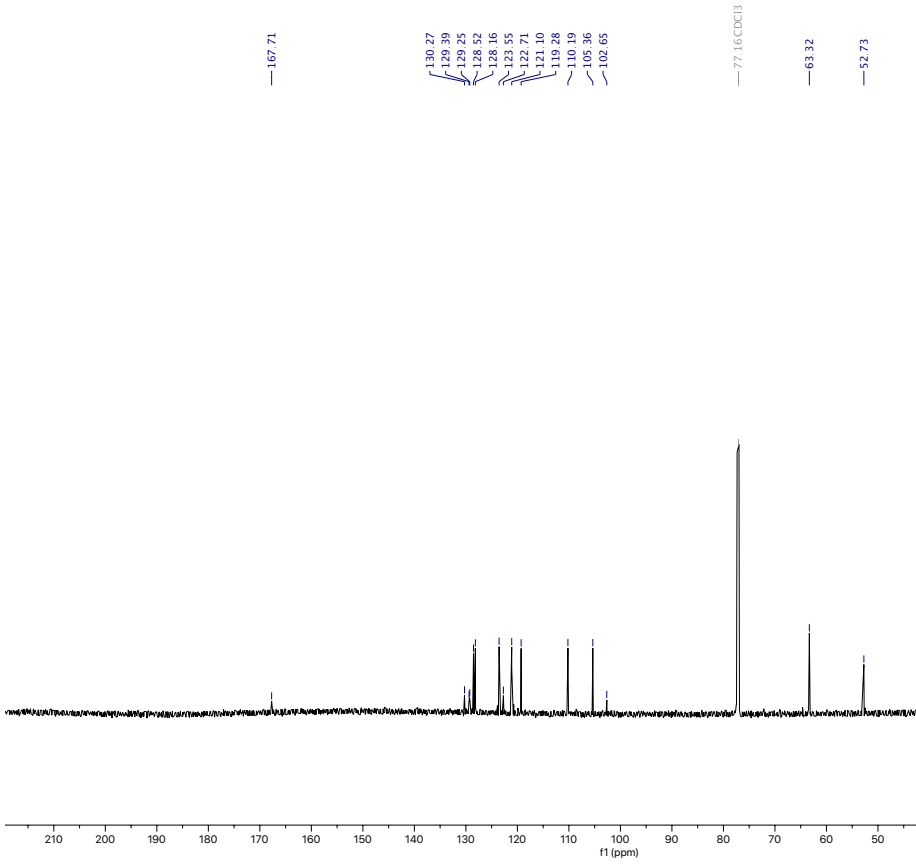

8.51
8.49
7.96
7.94
7.92
7.90
7.76
7.74
7.48
7.39
7.26 CDCl3
6.56
4.78
4.77
4.75
3.44
3.43
3.42
3.42
Solvent CDCl3
MHz 400
Nucleus 1H
8e
7.9
7.8
f1 (ppm)
7.49
7.42
f1 (ppm)
4.78 4.76
f1 (ppm)
3.44 3.42
f1 (ppm)
8.49
f1 (ppm)
6.58
6.54
f1 (ppm)
1.00
0.93
0.98
1.00
1.01
1.03
1.03
1.91
1.93
f1 (ppm)


168.75
132.96
129.49
128.86
128.16
123.96
121.03
120.18
118.49
110.53
106.46
103.86
77.16 CDCl3
69.06
26.39
Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)

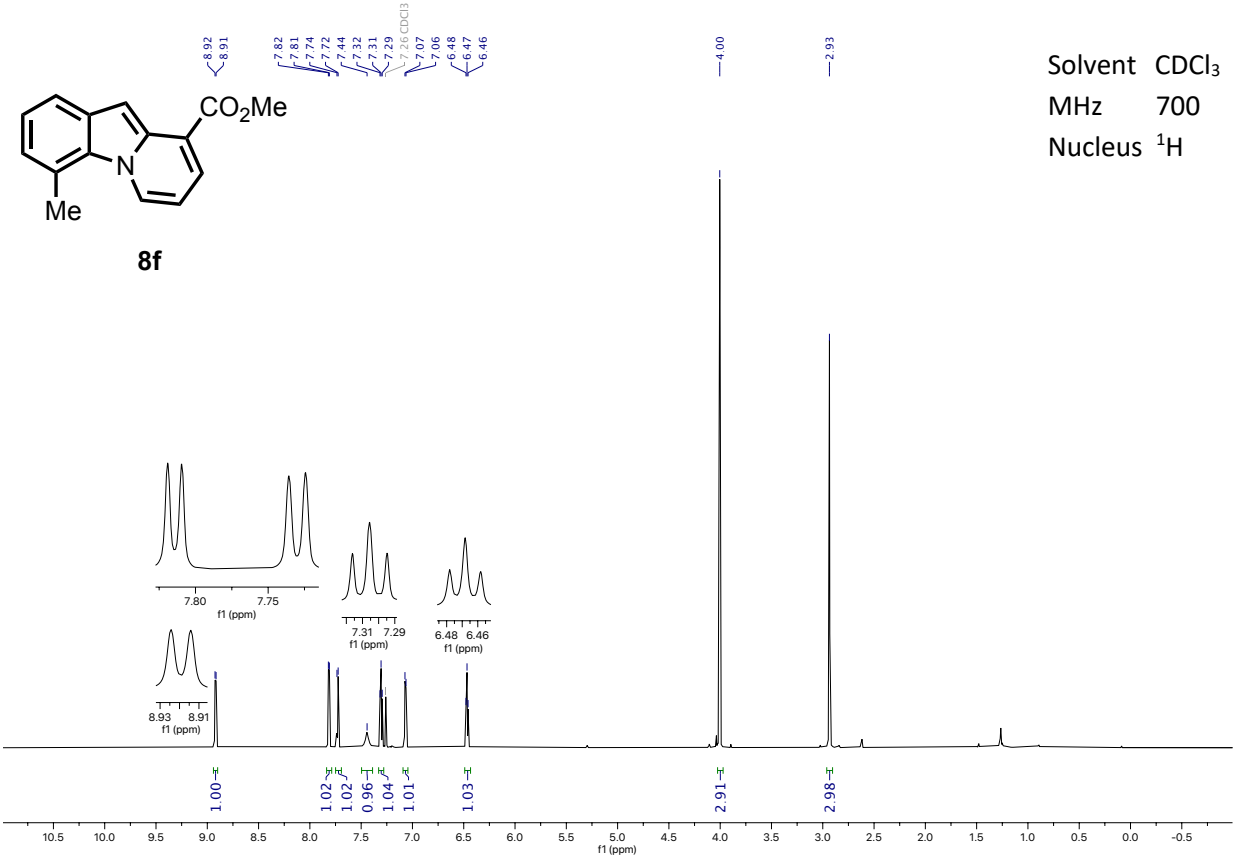


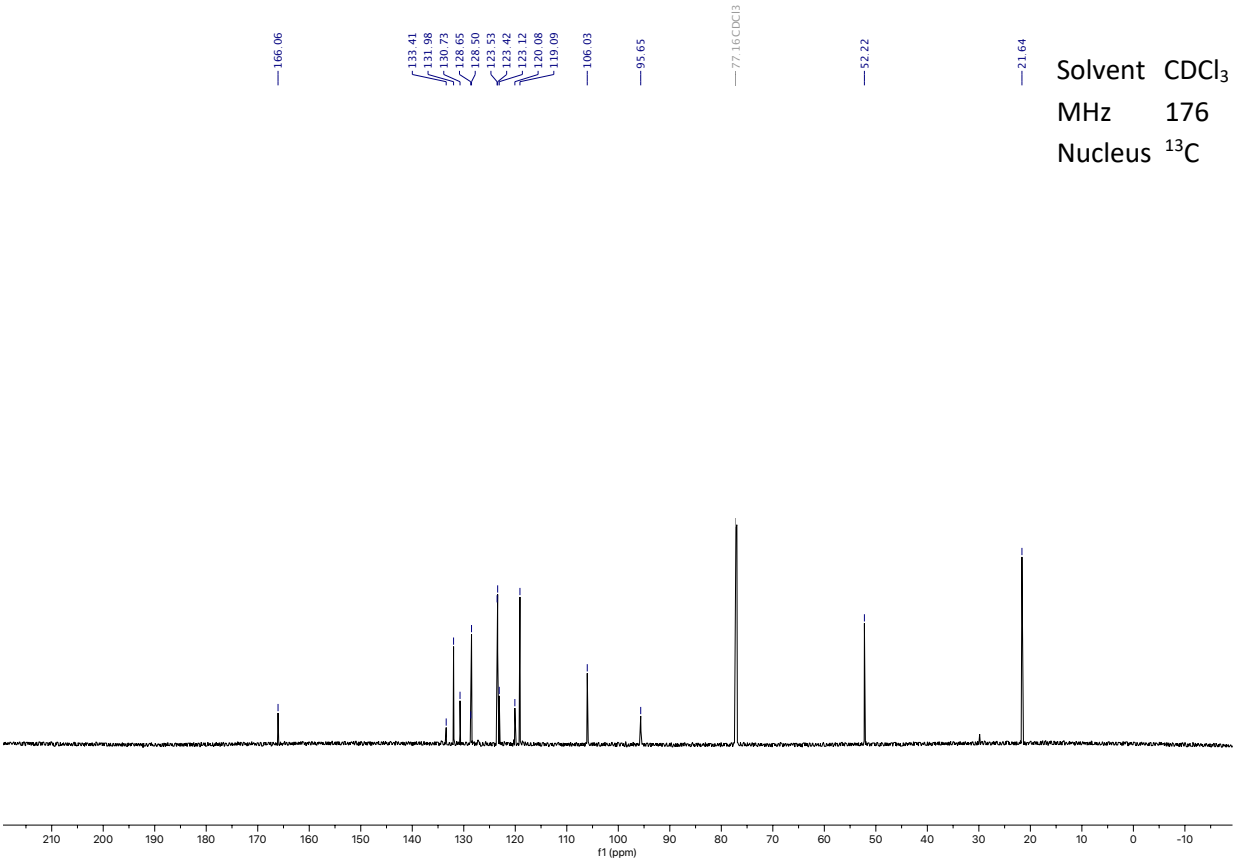
8e'

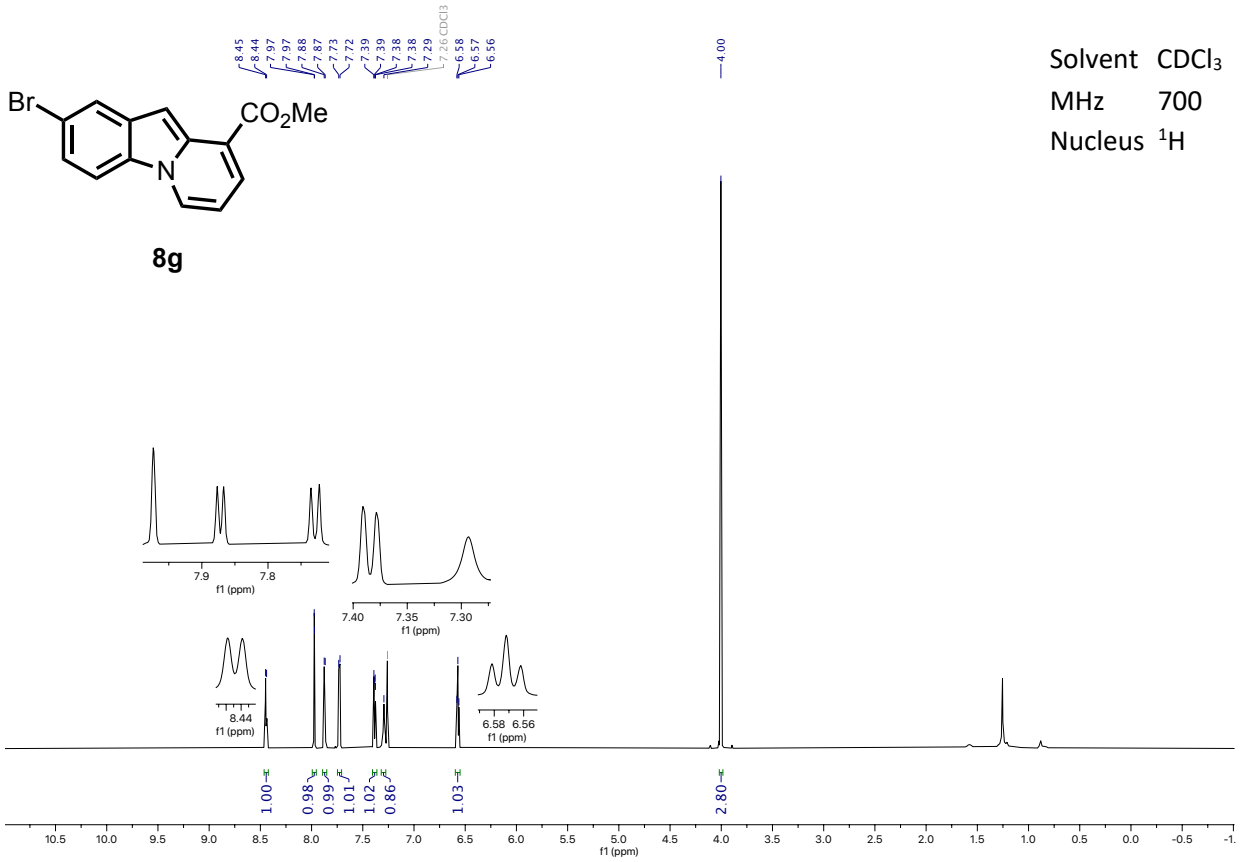
Solvent $CDCl_3$
MHz 700
Nucleus ^{1}H

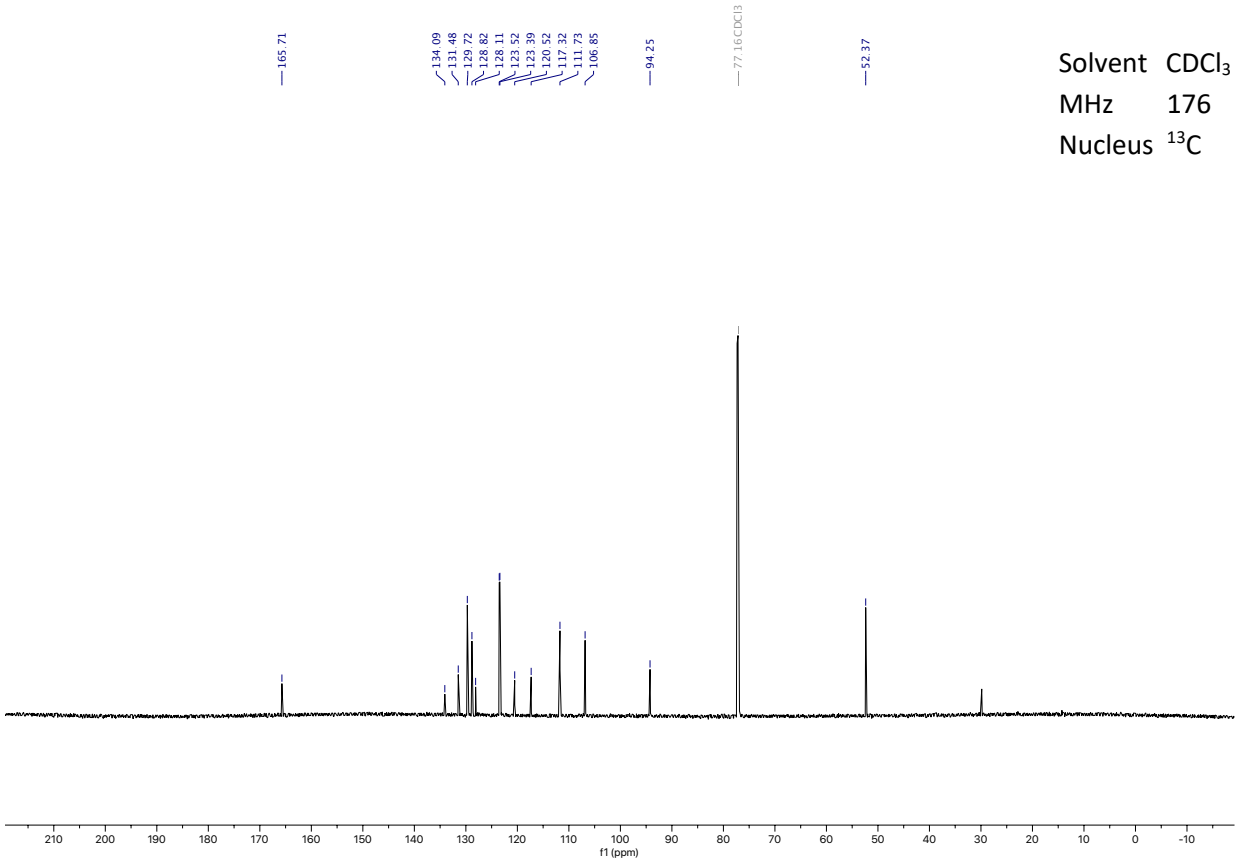


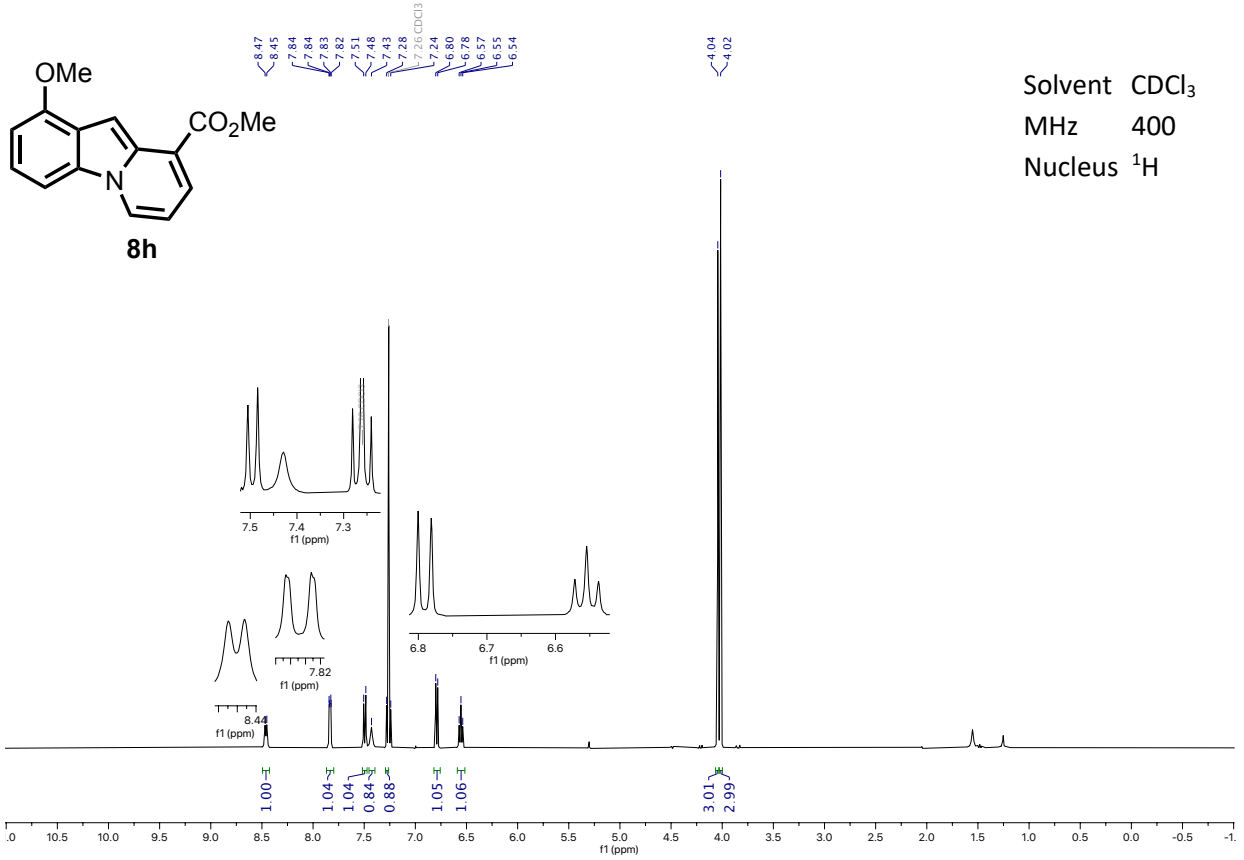
Solvent $CDCl_3$
MHz 176
Nucleus ^{13}C

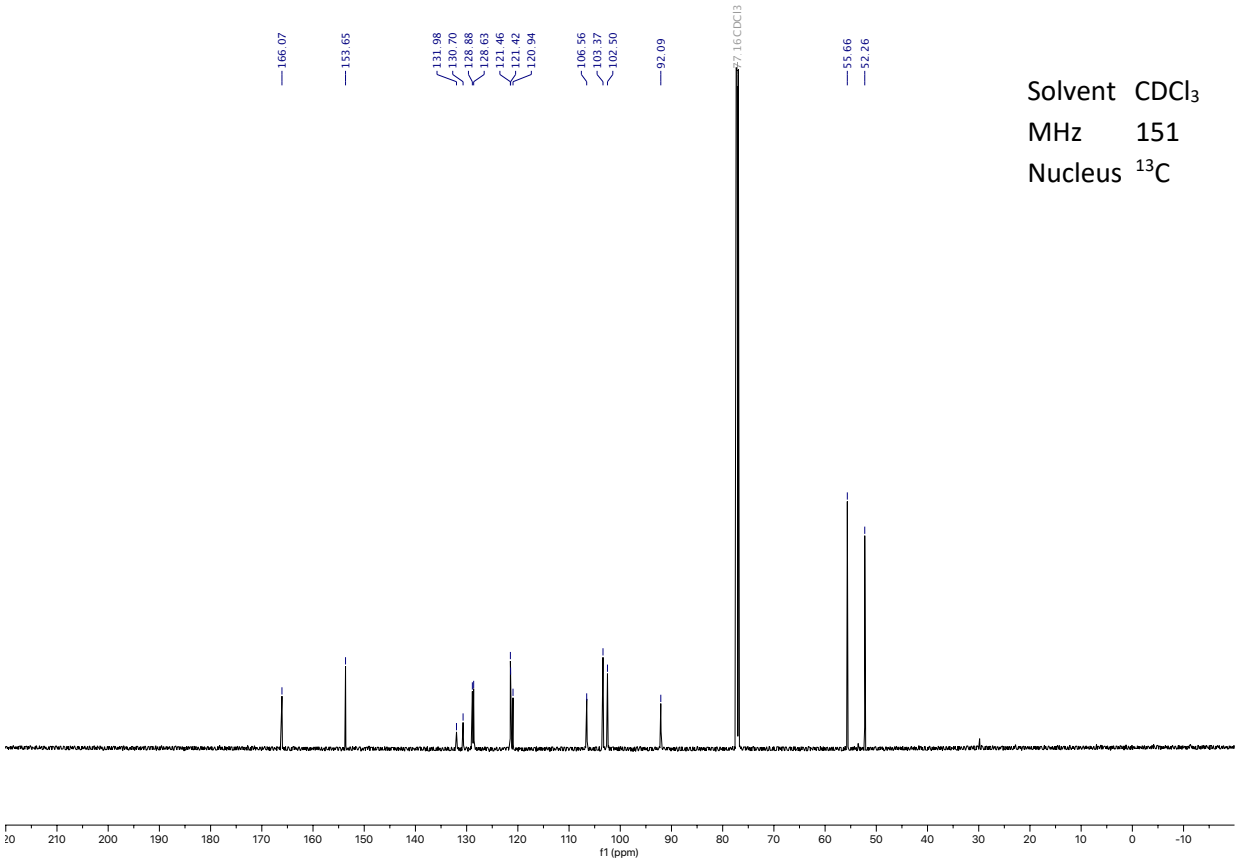

8.92
8.91
7.82
7.81
7.74
7.72
7.44
7.32
7.31
7.29
7.26 CDCl3
7.07
7.06
6.48
6.47
6.46
4.00
2.93
CO2Me
N
Me
8f
Solvent CDCl3
MHz 700
Nucleus 1H
7.80 7.75
f1 (ppm)
7.31 7.29
f1 (ppm)
6.48 6.46
f1 (ppm)
8.93 8.91
f1 (ppm)
1.00
1.02
1.02
0.96
1.04
1.01
1.03
2.91
2.98
f1 (ppm)

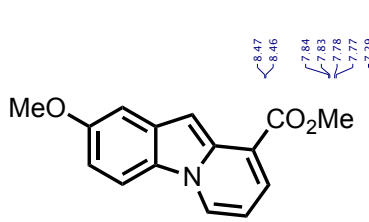

166.06
133.41
131.98
130.73
128.65
128.50
123.53
123.42
123.12
120.08
119.09
106.03
95.65
77.16 CDCl3
52.22
21.64
Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)


Br
CO2Me
N
8g
Solvent CDCl3
MHz 700
Nucleus 1H
f1 (ppm)


Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)


OMe
CO2Me
N
8h
Solvent CDCl3
MHz 400
Nucleus 1H
f1 (ppm)

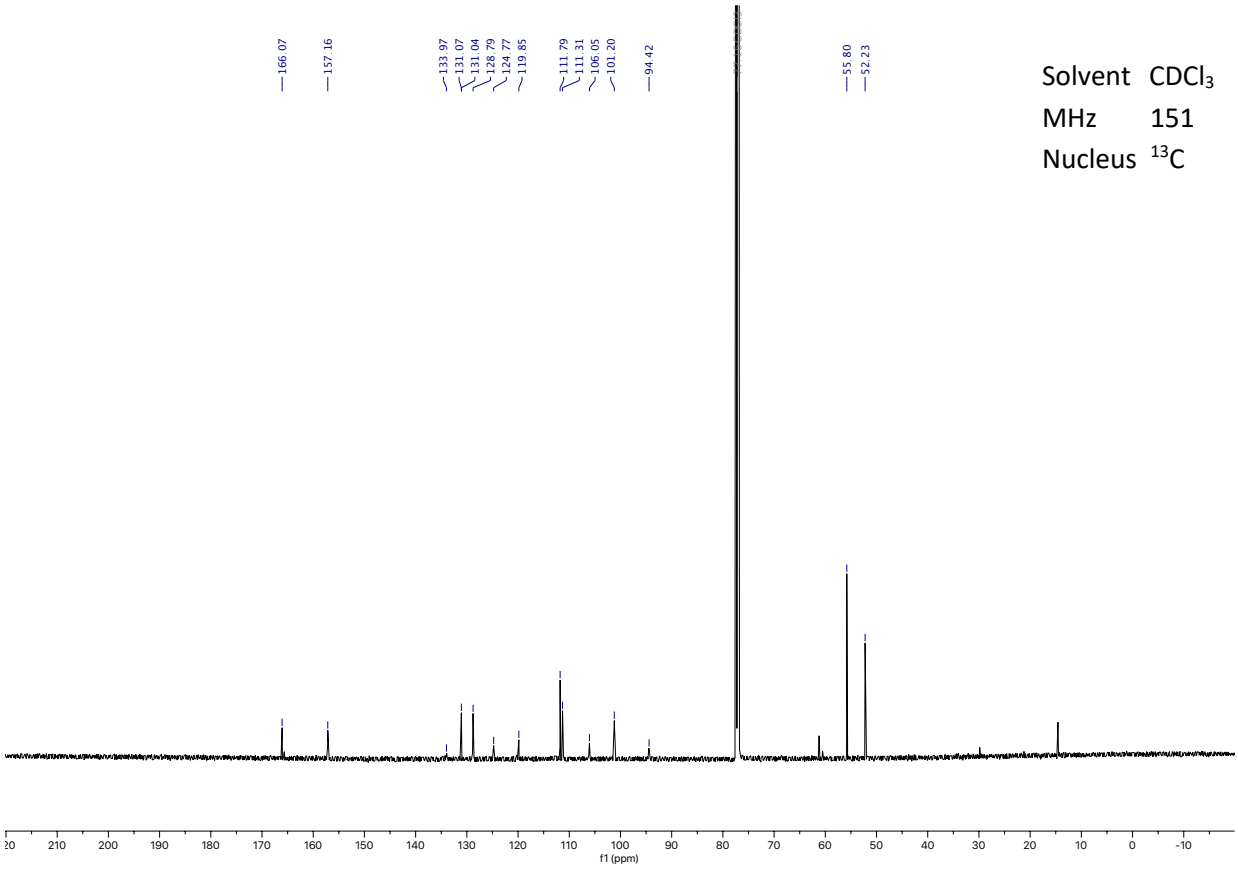

Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)

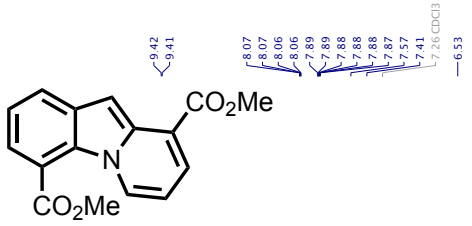


8i

Solvent $CDCl_3$
MHz 600
Nucleus ^{1}H

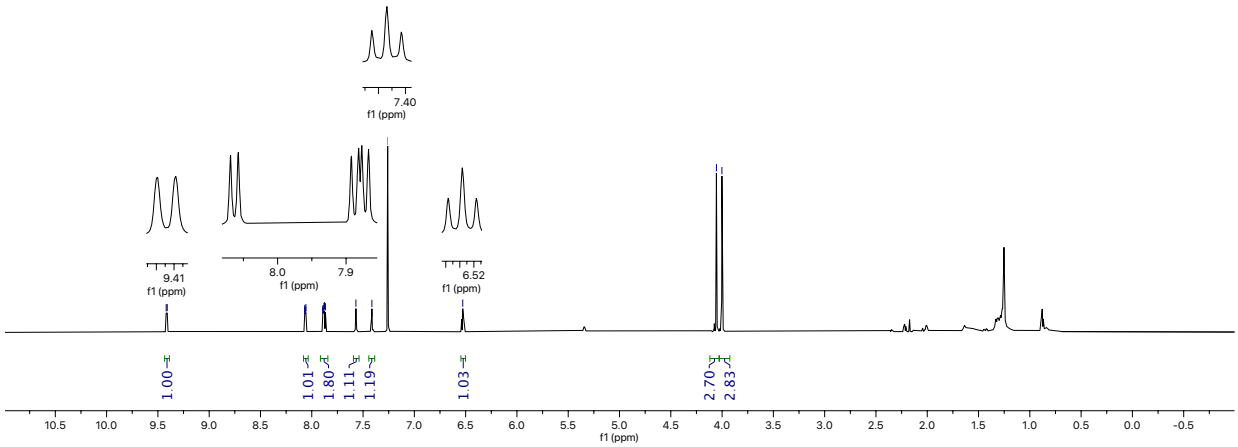
Solvent $CDCl_3$
MHz 151
Nucleus ^{13}C

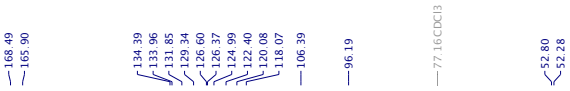




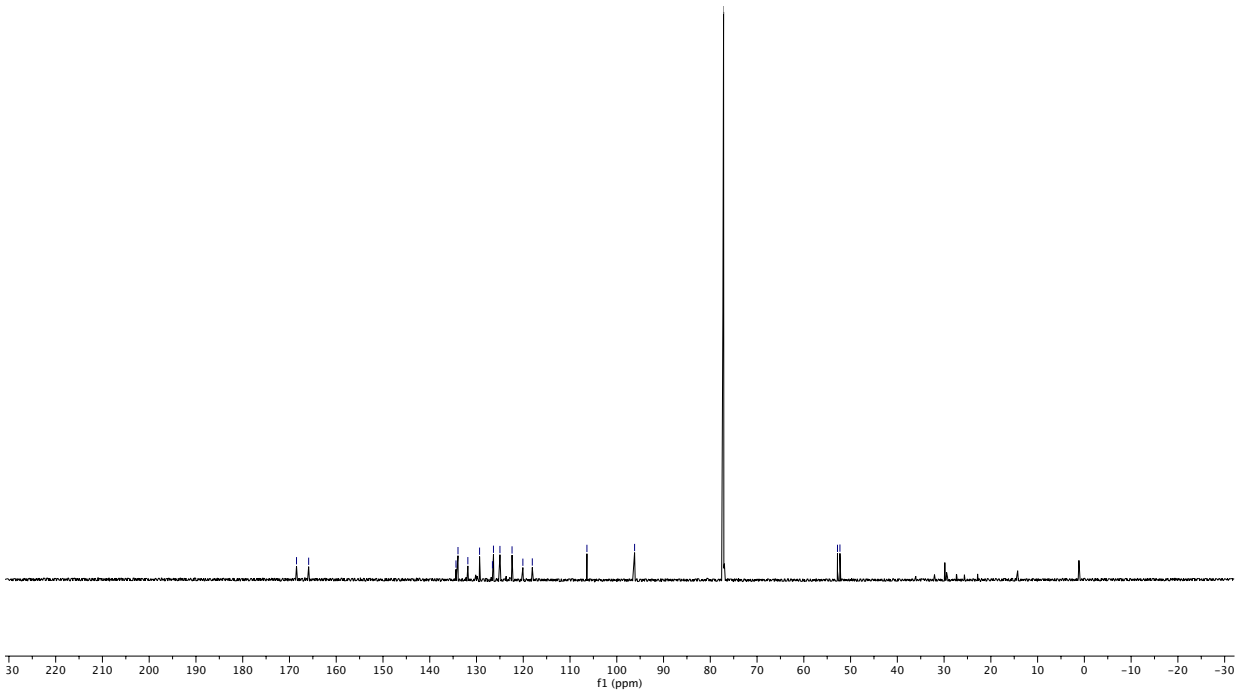
8j

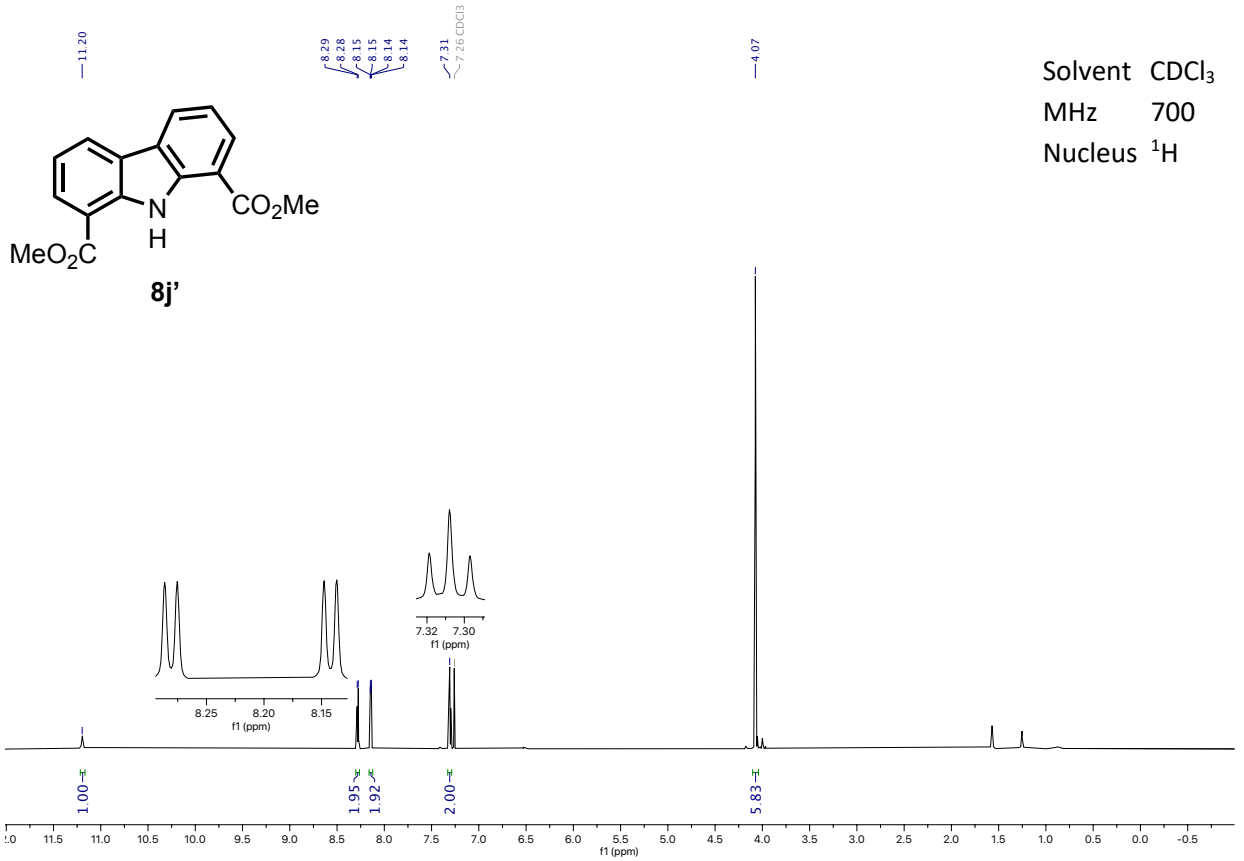
Solvent $CDCl_3$
MHz 700
Nucleus ^{1}H

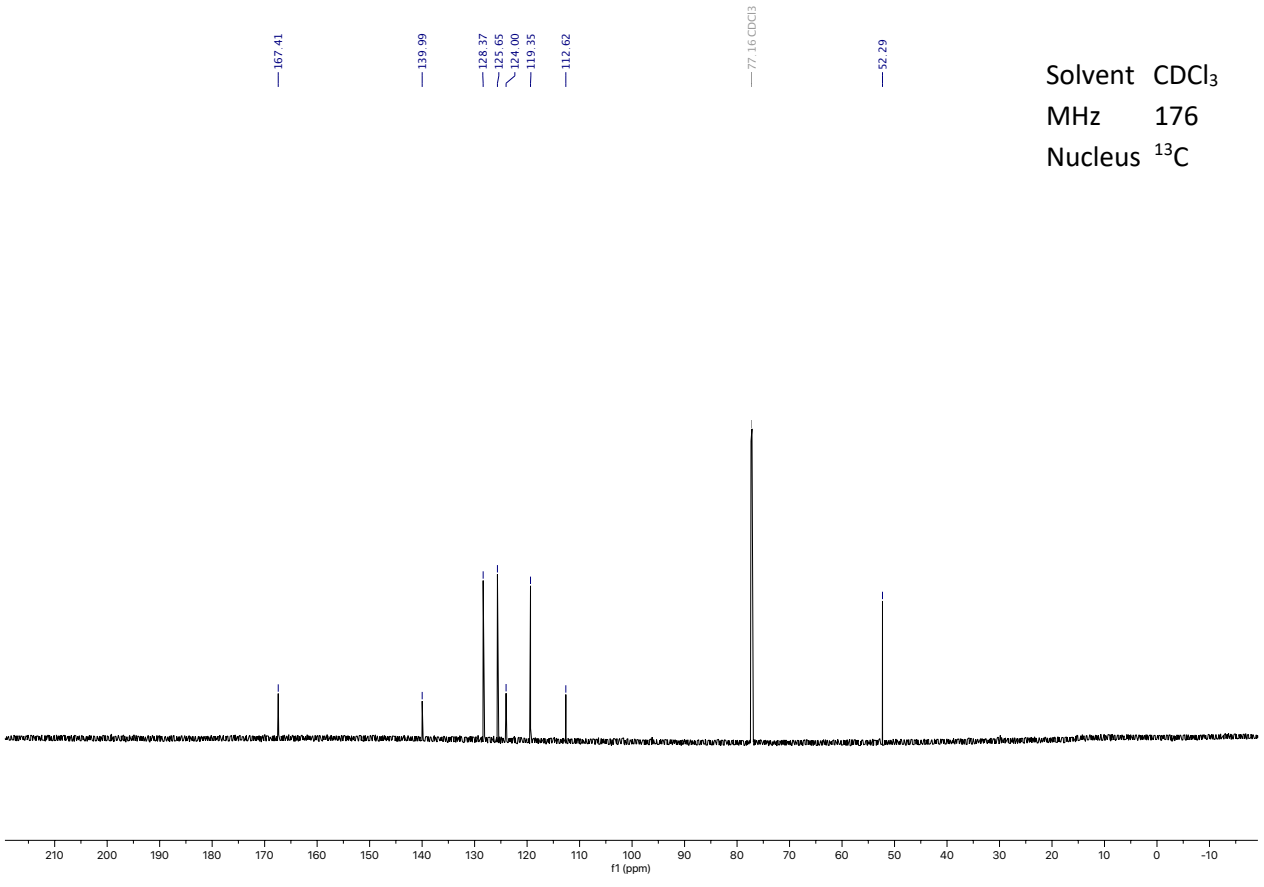


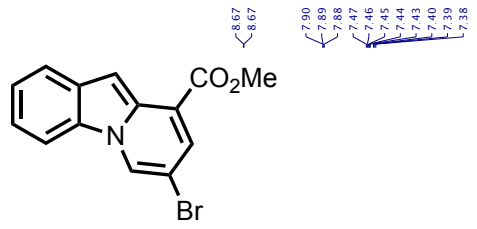


Solvent $CDCl_3$
MHz 226
Nucleus ^{13}C



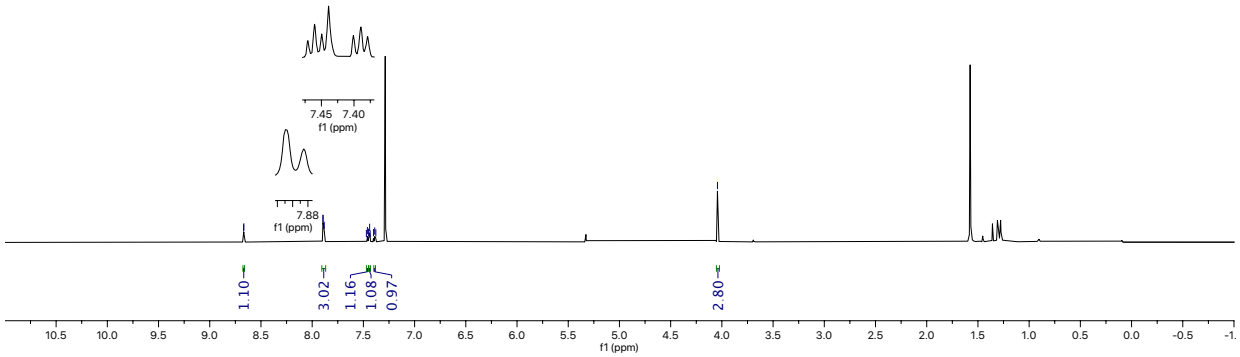

11.20
8.29
8.28
8.15
8.15
8.14
8.14
7.31
7.26 CDCl3
4.07
Solvent CDCl3
MHz 700
Nucleus 1H
N
H
CO2Me
MeO2C
8j'
7.32
7.30
f1 (ppm)
8.25
8.20
8.15
f1 (ppm)
1.00
1.95
1.92
2.00
5.83
f1 (ppm)


167.41
139.99
128.37
125.65
124.00
119.35
112.62
77.16 CDCl3
52.29
Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)

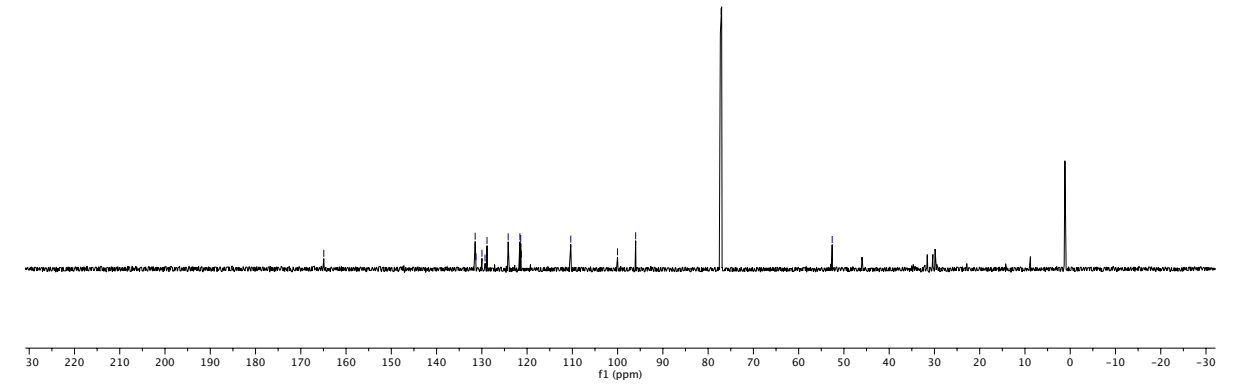


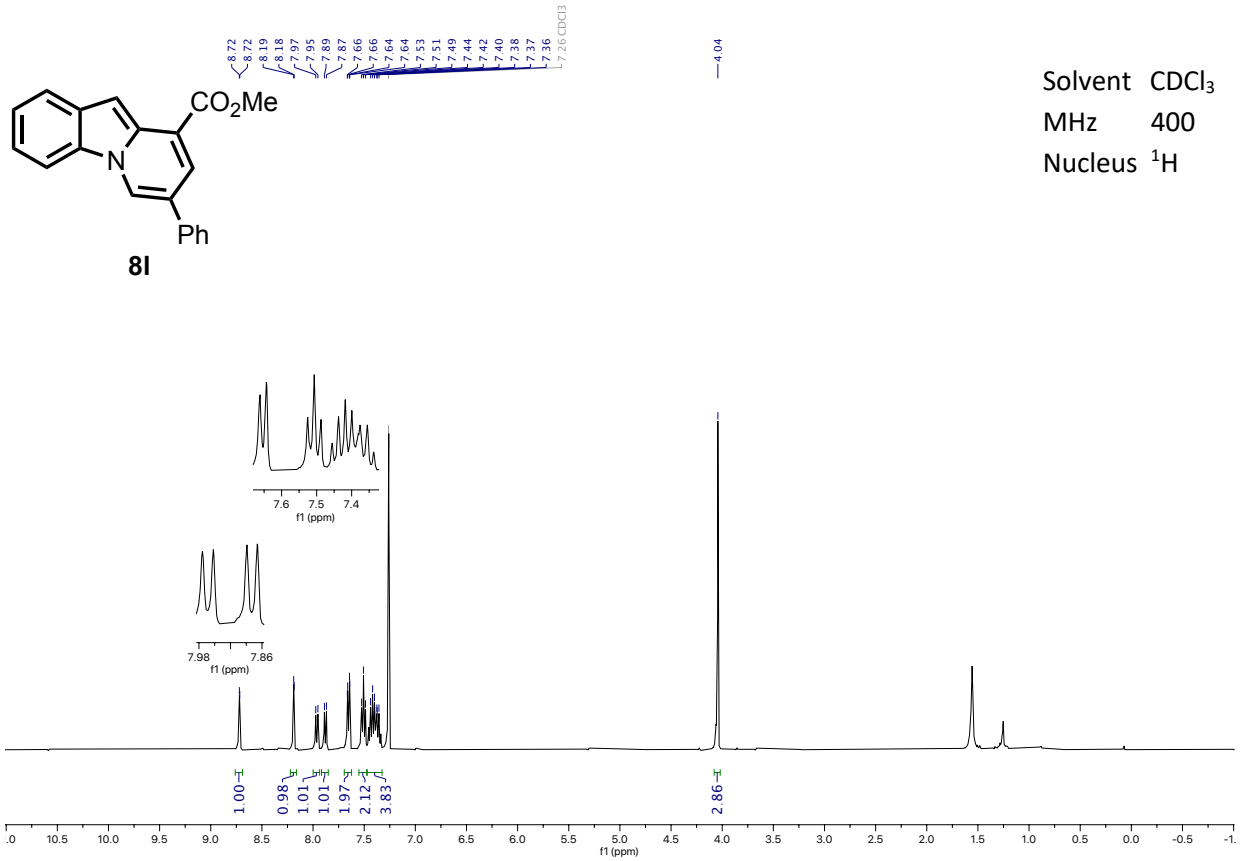
8k

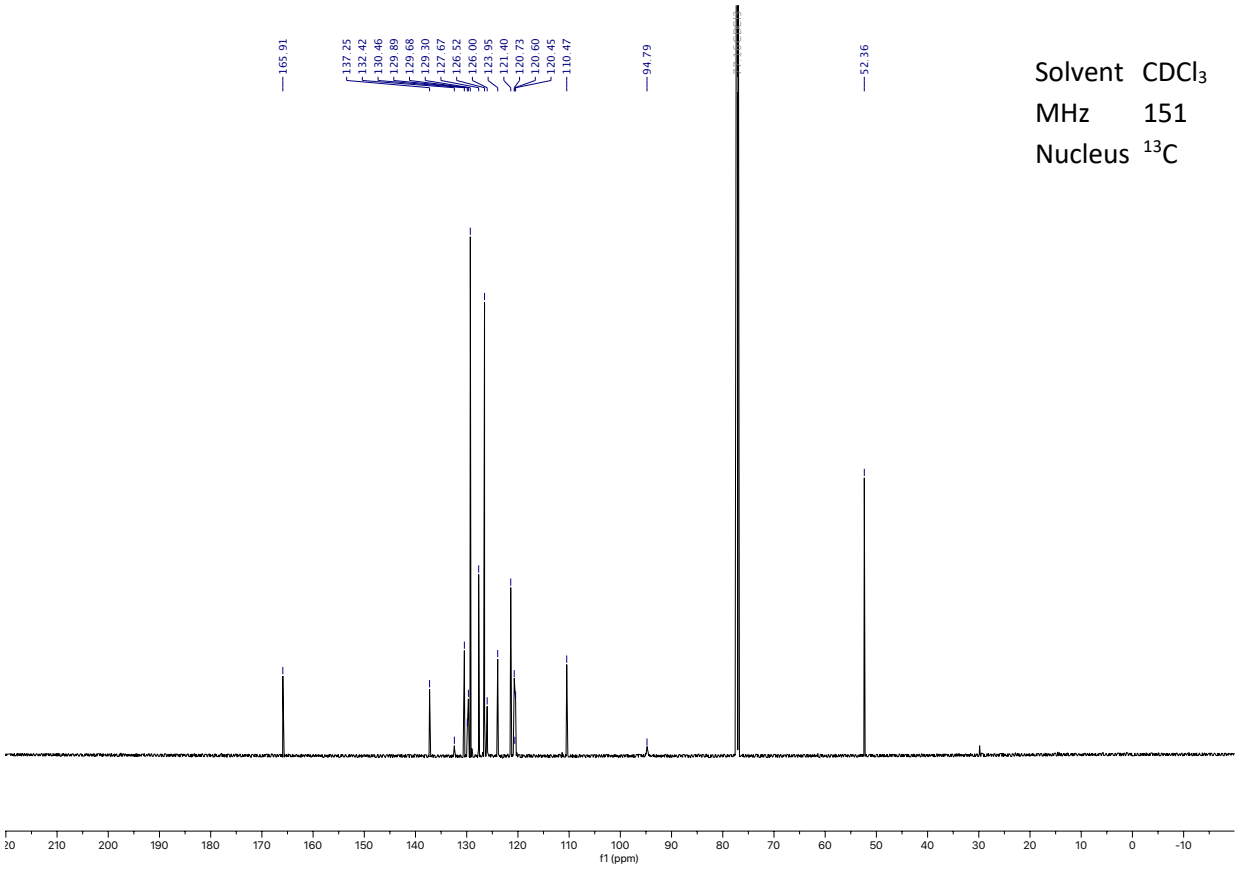
Solvent $CDCl_3$
MHz 700
Nucleus ^{1}H

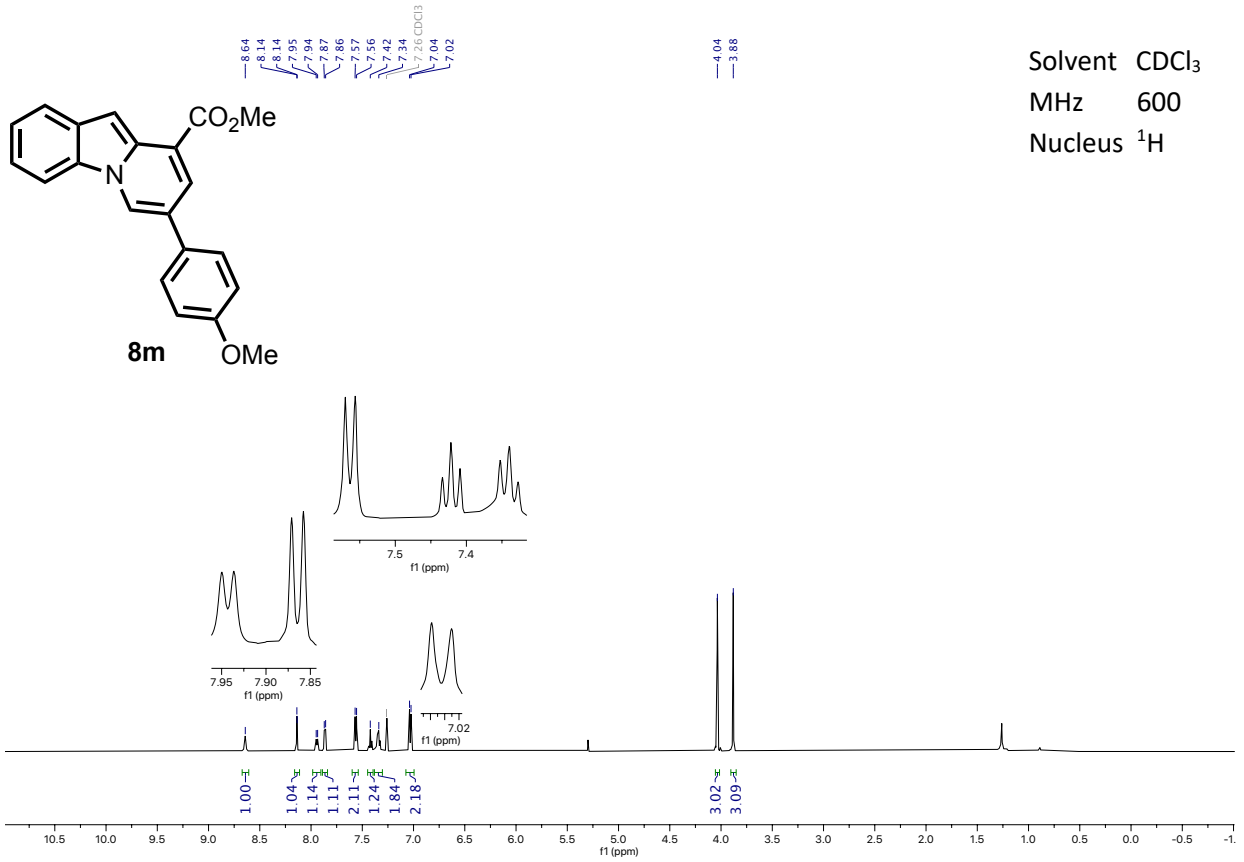


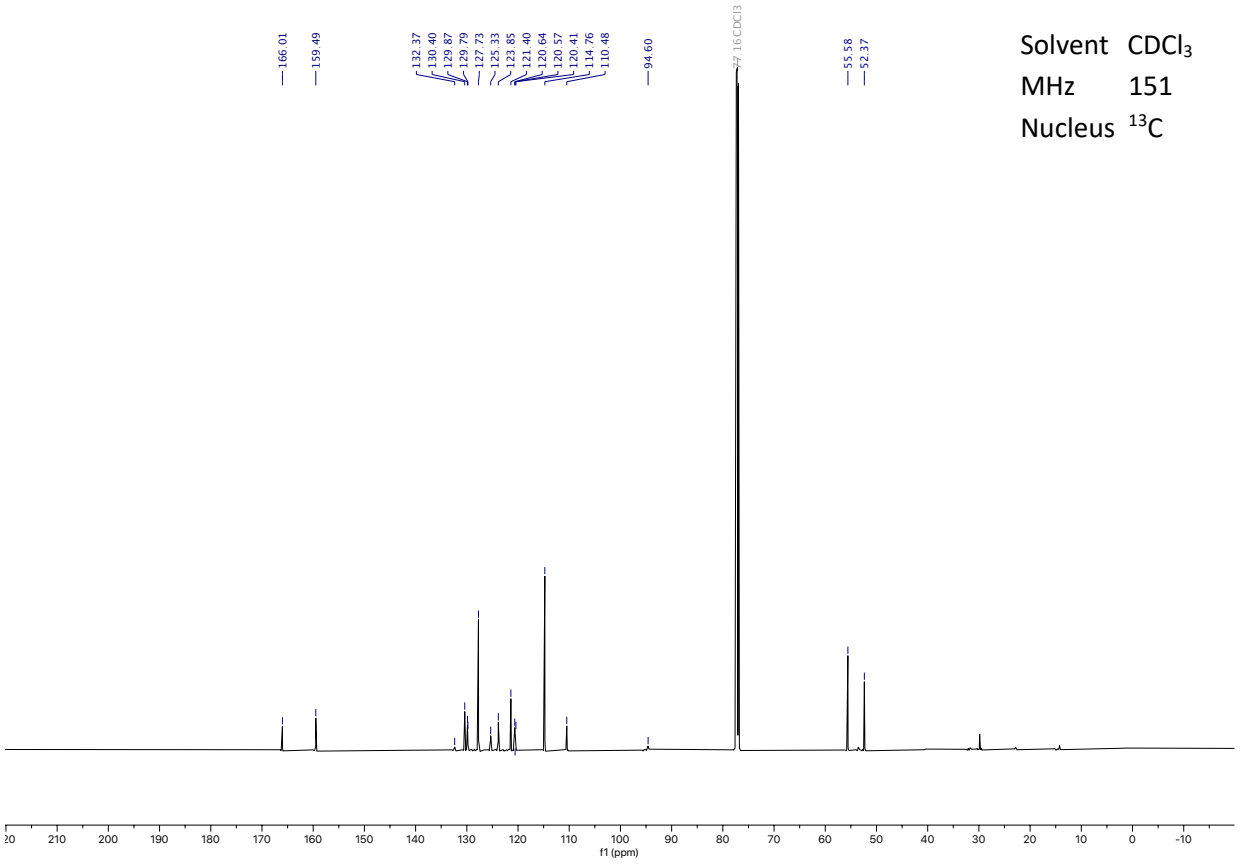
Solvent $CDCl_3$
MHz 226
Nucleus ^{13}C

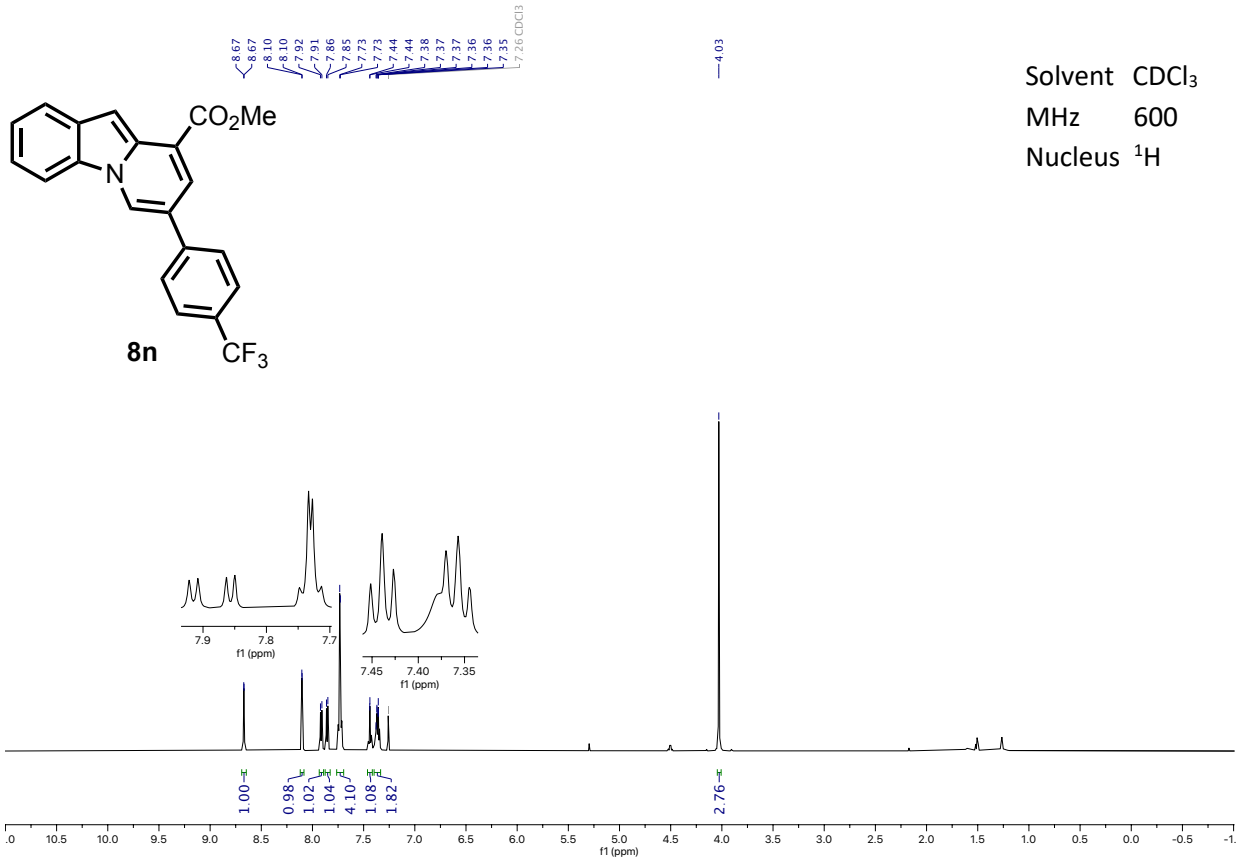



CO2Me
N
Ph
8I
Solvent CDCl3
MHz 400
Nucleus 1H
f1 (ppm)

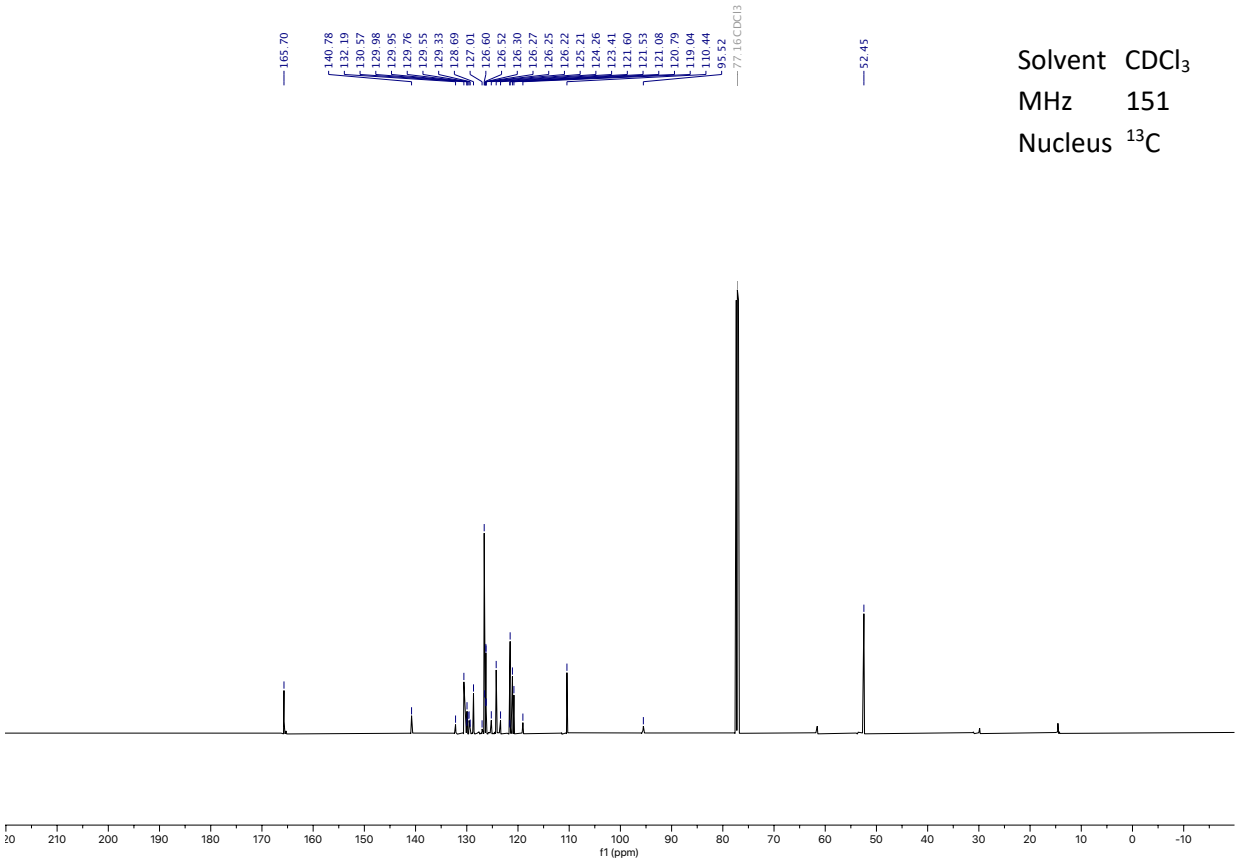

Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)


8.64
8.14
8.14
7.95
7.94
7.87
7.86
7.57
7.56
7.42
7.34
7.26 CDCl3
7.04
7.02
4.04
3.88
CO2Me
N
OMe
8m
Solvent CDCl3
MHz 600
Nucleus 1H
7.5
7.4
f1 (ppm)
7.95
7.90
7.85
f1 (ppm)
7.02
f1 (ppm)
1.00
1.04
1.14
1.11
2.11
1.24
1.84
2.18
3.02
3.09
f1 (ppm)

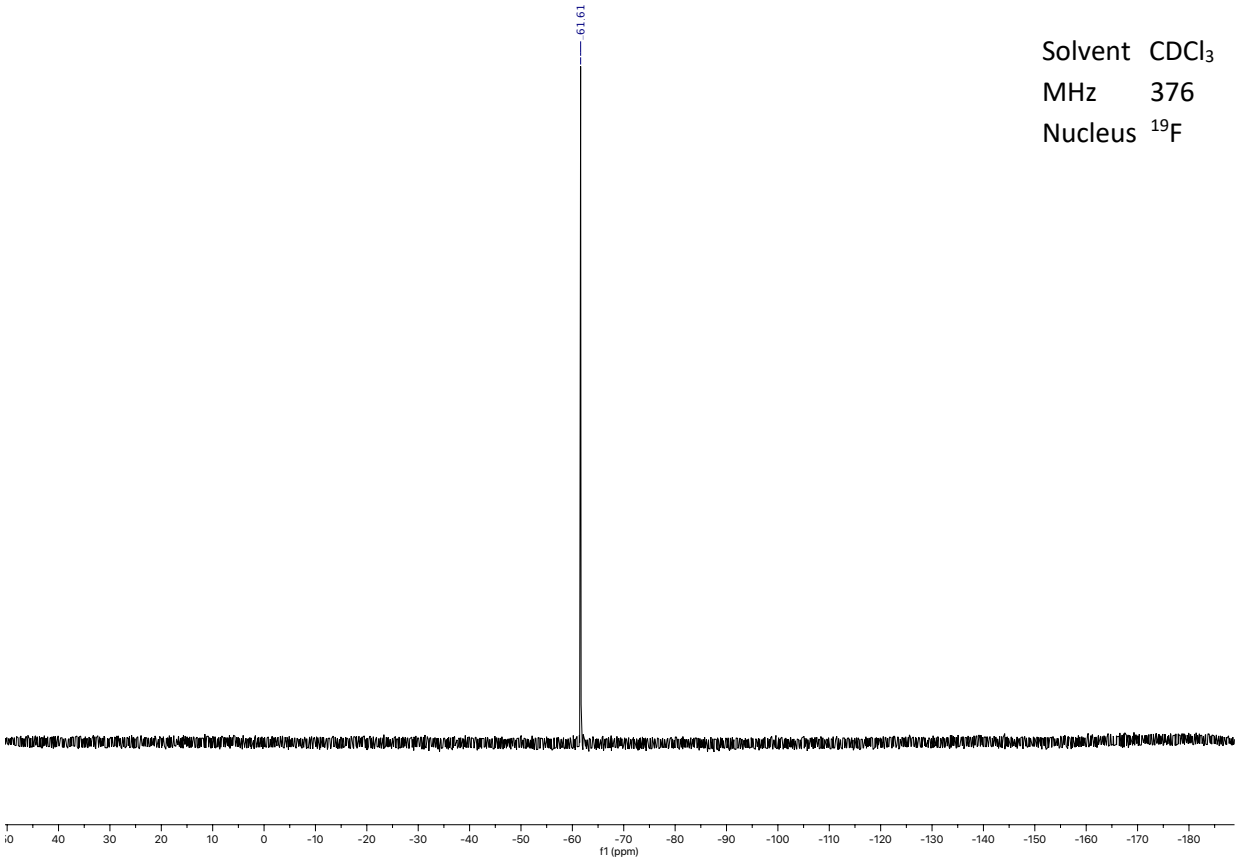

166.01
159.49
132.37
130.40
129.87
129.79
127.73
125.33
123.85
121.40
120.64
120.57
120.41
114.76
110.48
94.60
77.16 CDCl3
55.58
52.37
Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)

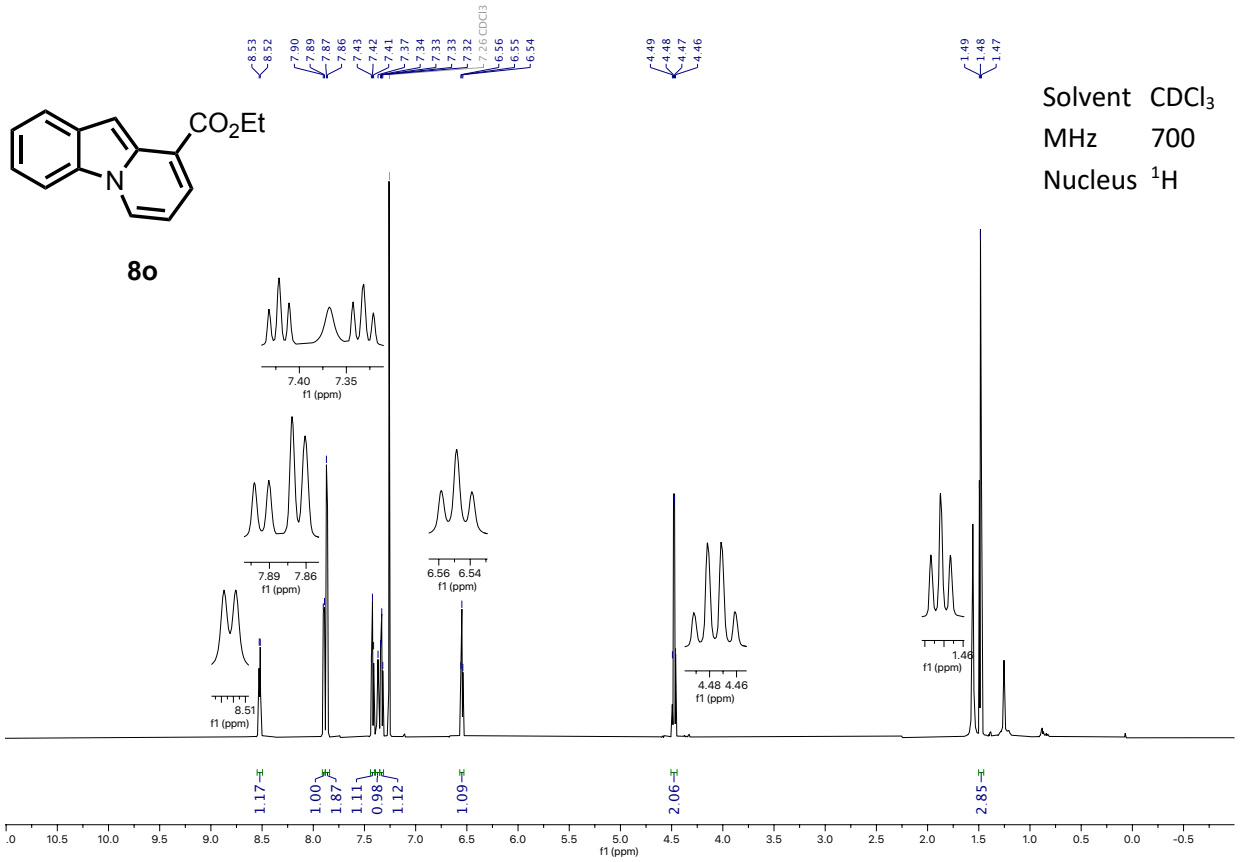


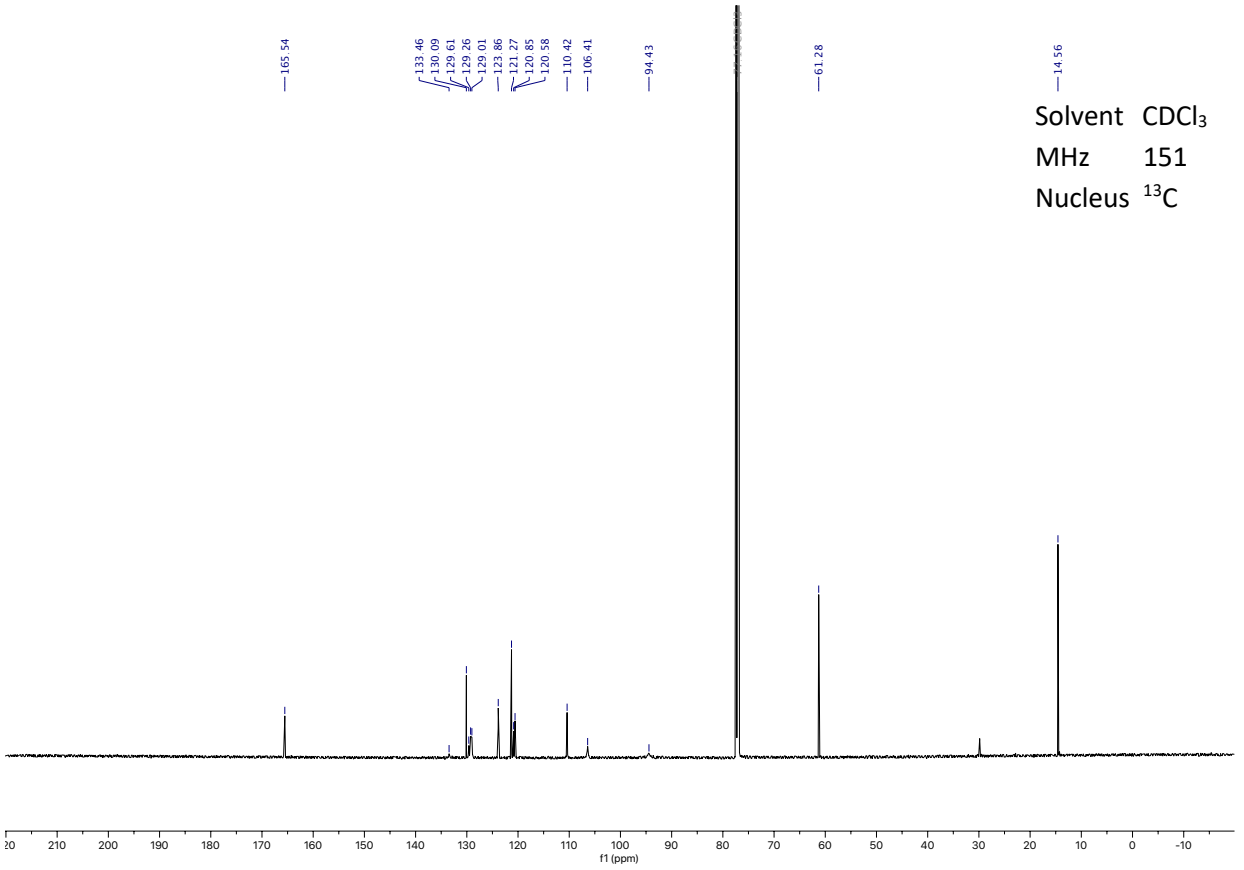
Solvent $CDCl_3$
MHz 600
Nucleus ^{1}H

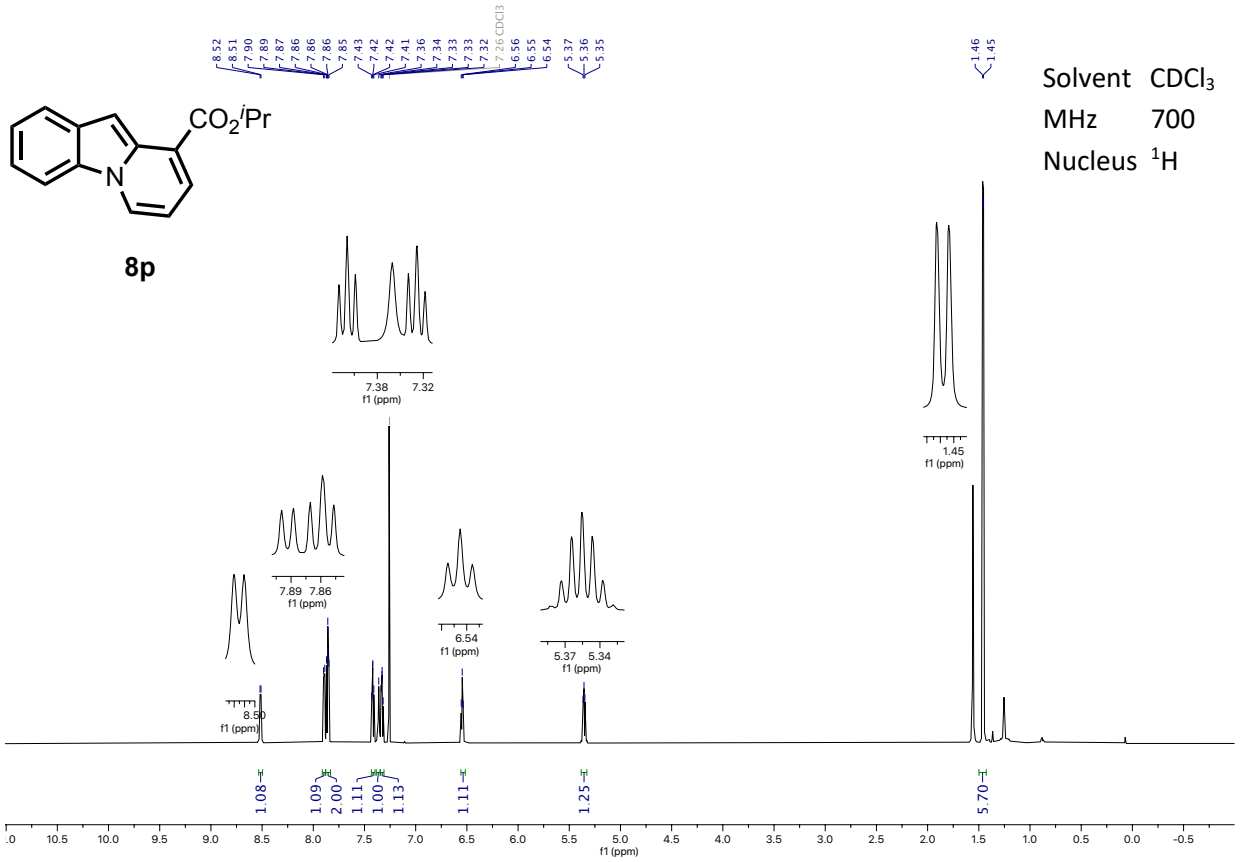


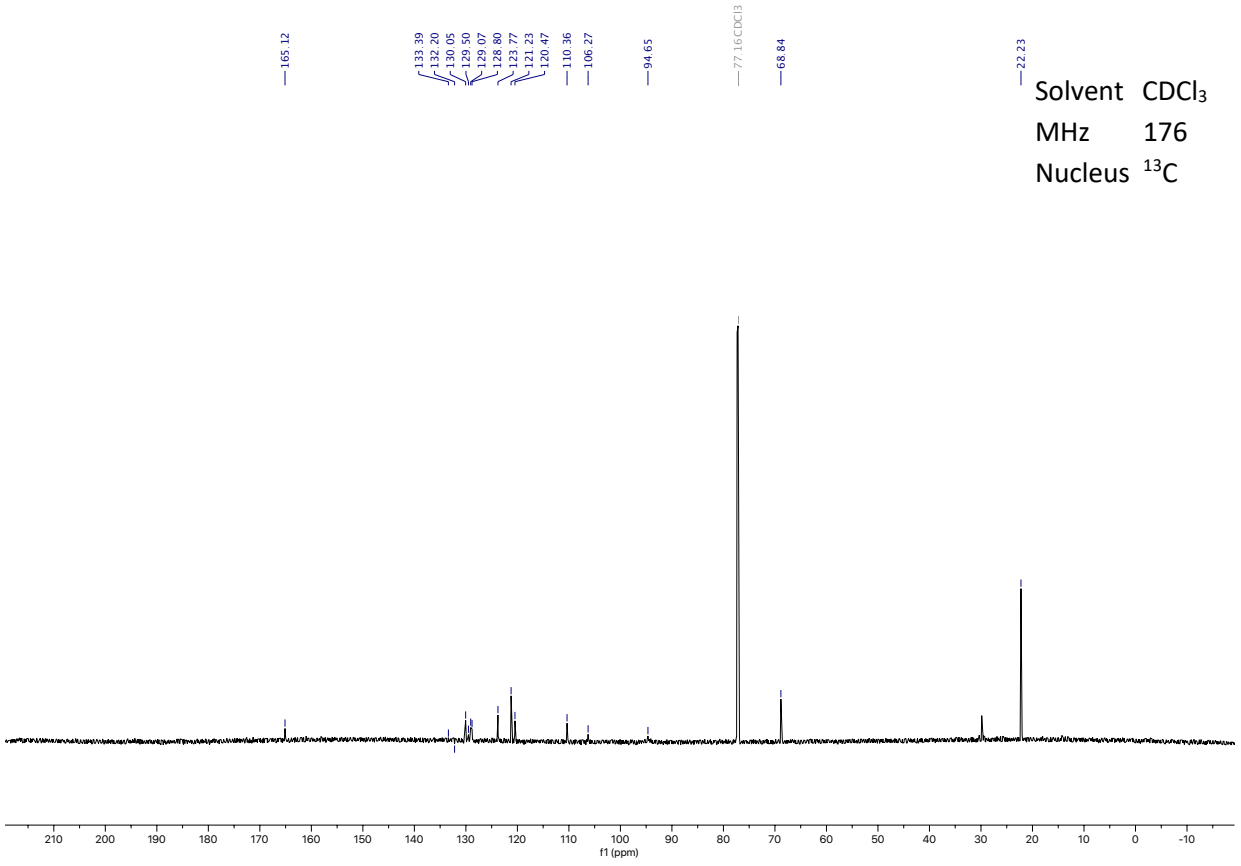
Solvent $CDCl_3$
MHz 151
Nucleus ^{13}C

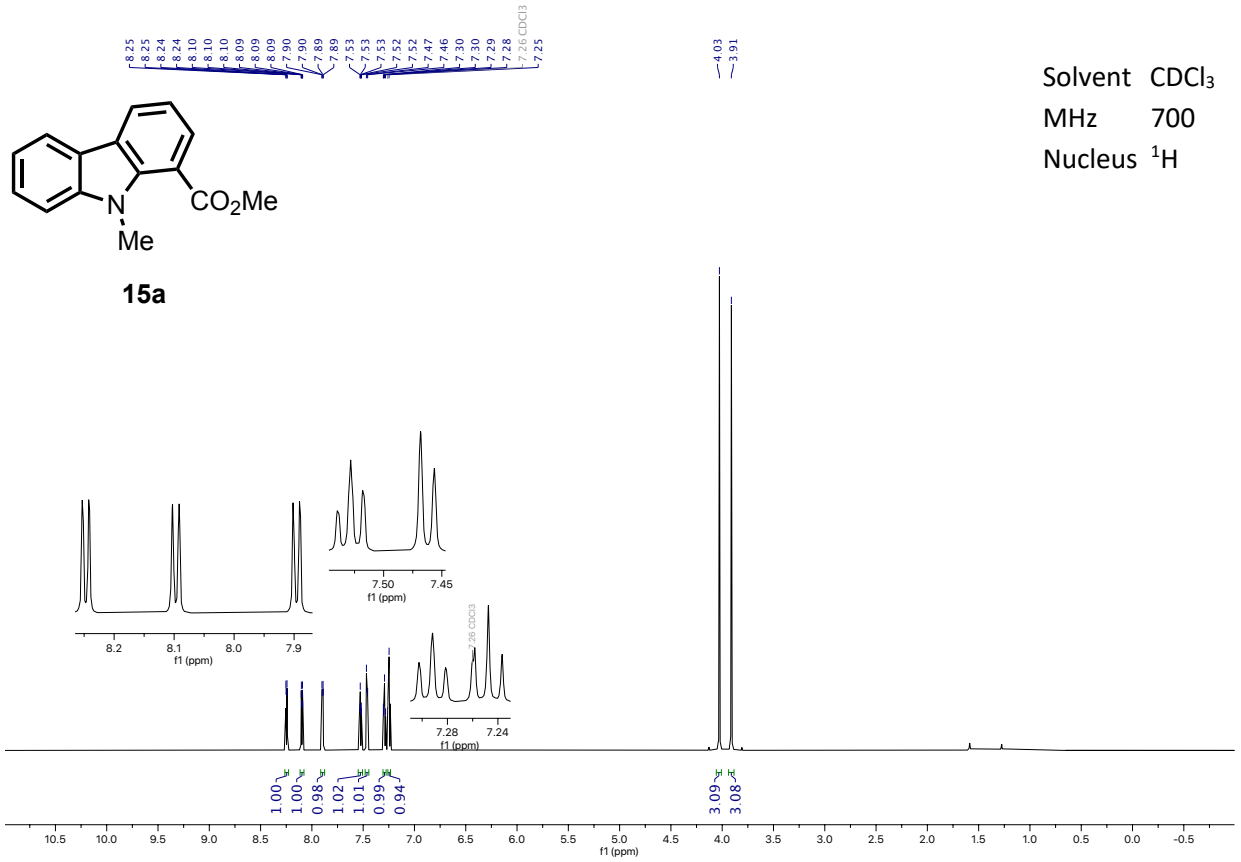

-61.61
Solvent CDCl3
MHz 376
Nucleus 19F
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
f1 (ppm)

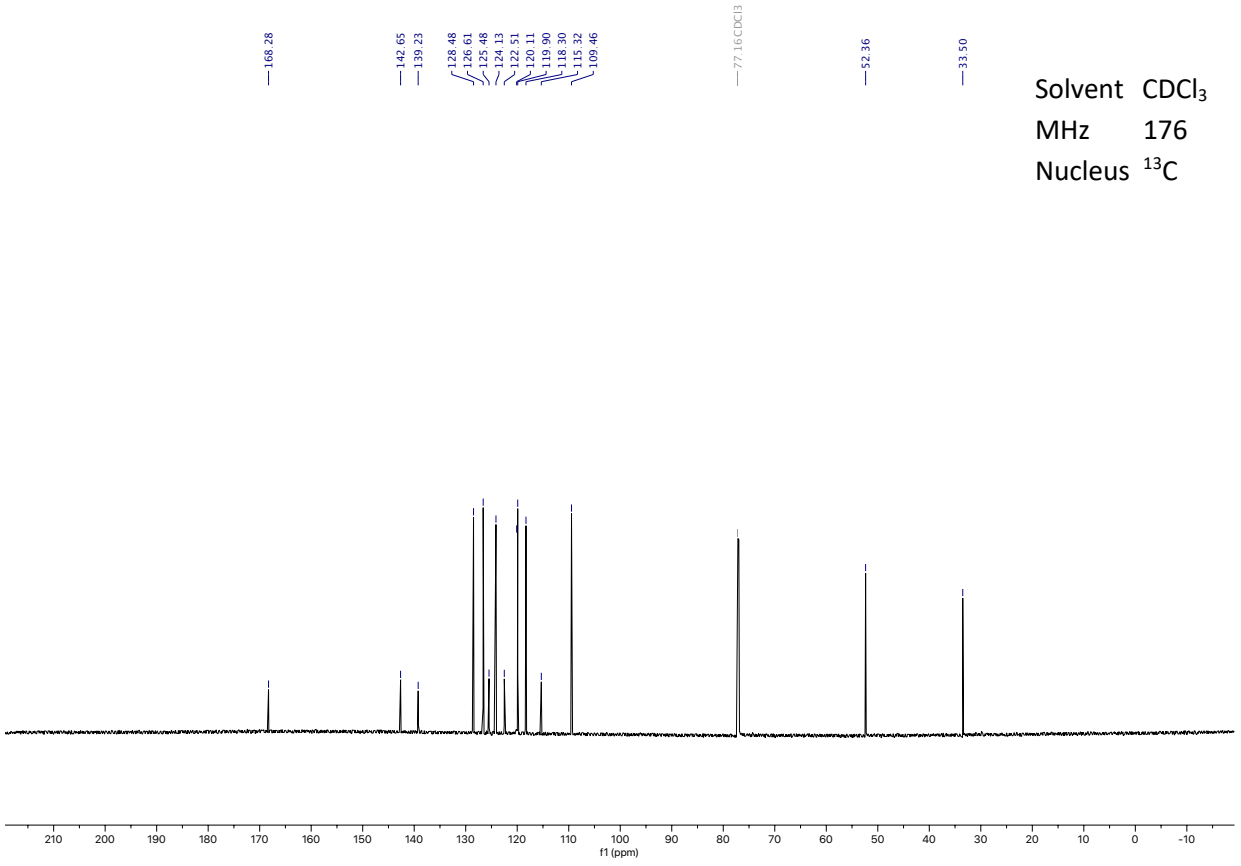

CO2Et
N
8o
Solvent CDCl3
MHz 700
Nucleus 1H
f1 (ppm)

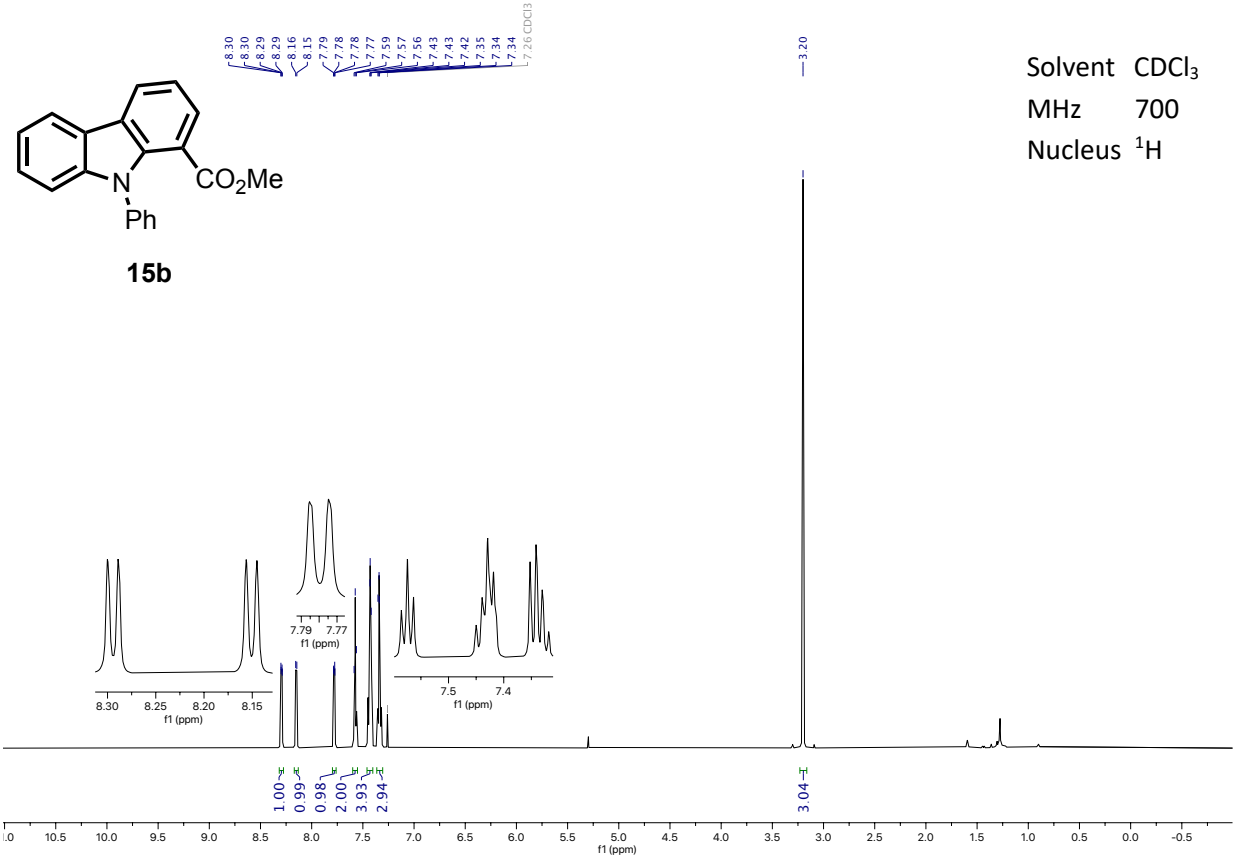

Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)

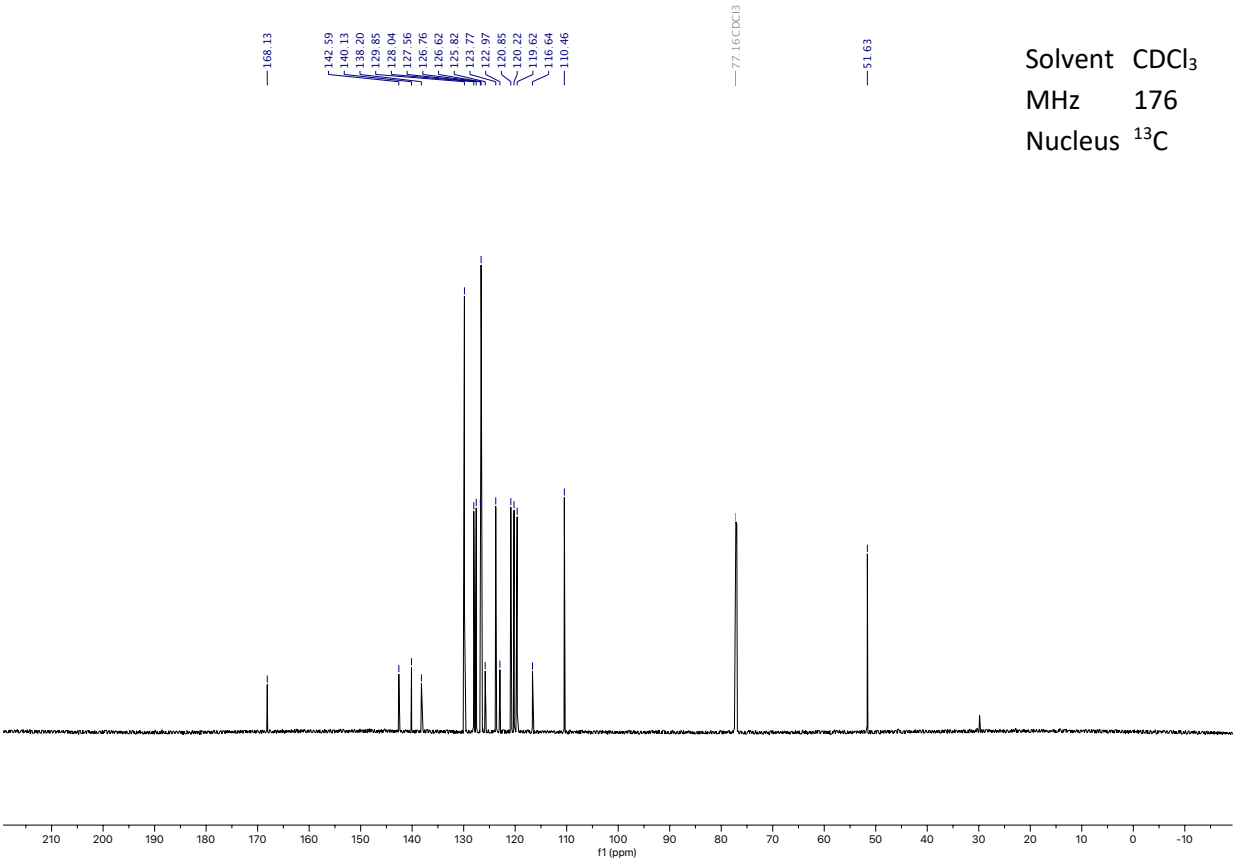

8.52
8.51
7.90
7.89
7.87
7.86
7.86
7.86
7.85
7.43
7.42
7.42
7.41
7.36
7.34
7.33
7.33
7.32
7.26 CDCl3
6.56
6.55
6.54
5.37
5.36
5.35
1.46
1.45
CO2iPr
N
8p
Solvent CDCl3
MHz 700
Nucleus 1H
7.38
7.32
f1 (ppm)
7.89
7.86
f1 (ppm)
6.54
f1 (ppm)
5.37
5.34
f1 (ppm)
8.50
f1 (ppm)
1.45
f1 (ppm)
1.08
1.09
2.00
1.11
1.00
1.13
1.11
1.25
5.70
f1 (ppm)

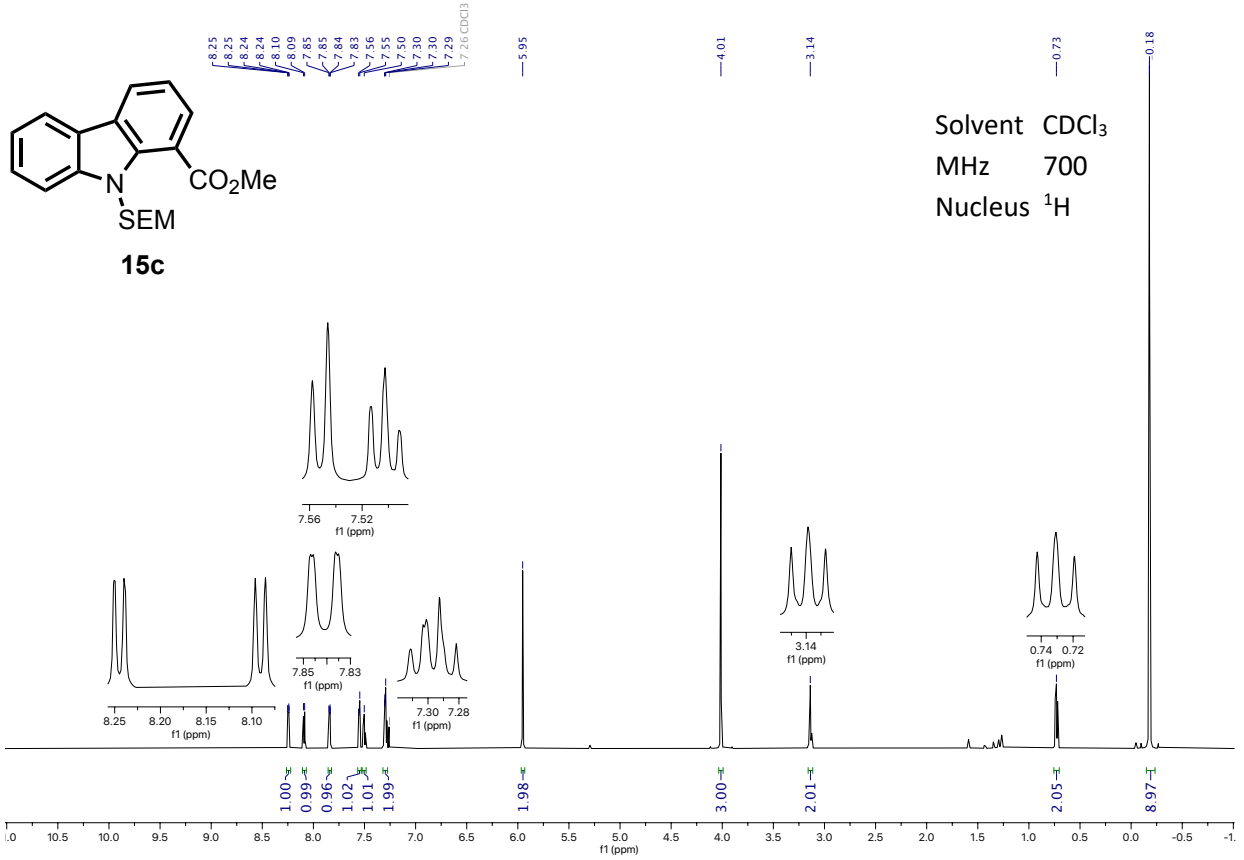

165.12
133.39
132.20
130.05
129.50
129.07
128.80
123.77
121.23
120.47
110.36
106.27
94.65
77.16 CDCl3
68.84
22.23
Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)

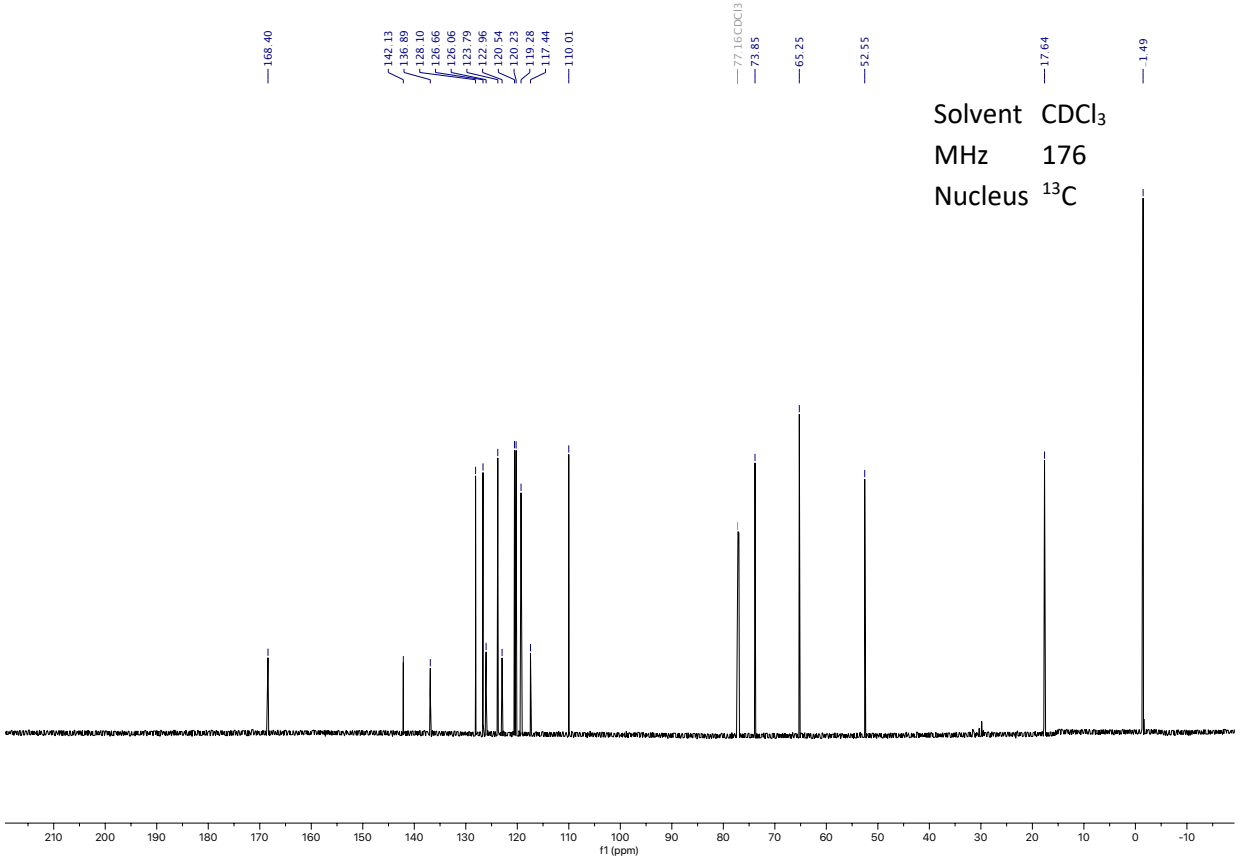

8.25
8.25
8.24
8.24
8.10
8.10
8.09
8.09
8.09
7.90
7.90
7.89
7.89
7.53
7.53
7.53
7.52
7.52
7.47
7.46
7.30
7.30
7.29
7.28
7.26 CDCl3
7.25
4.03
3.91
CO2Me
N
Me
15a
Solvent CDCl3
MHz 700
Nucleus 1H
7.50
7.45
f1 (ppm)
8.2
8.1
8.0
7.9
f1 (ppm)
7.28
7.24
f1 (ppm)
1.00
1.00
0.98
1.02
1.01
0.99
0.94
3.09
3.08
f1 (ppm)

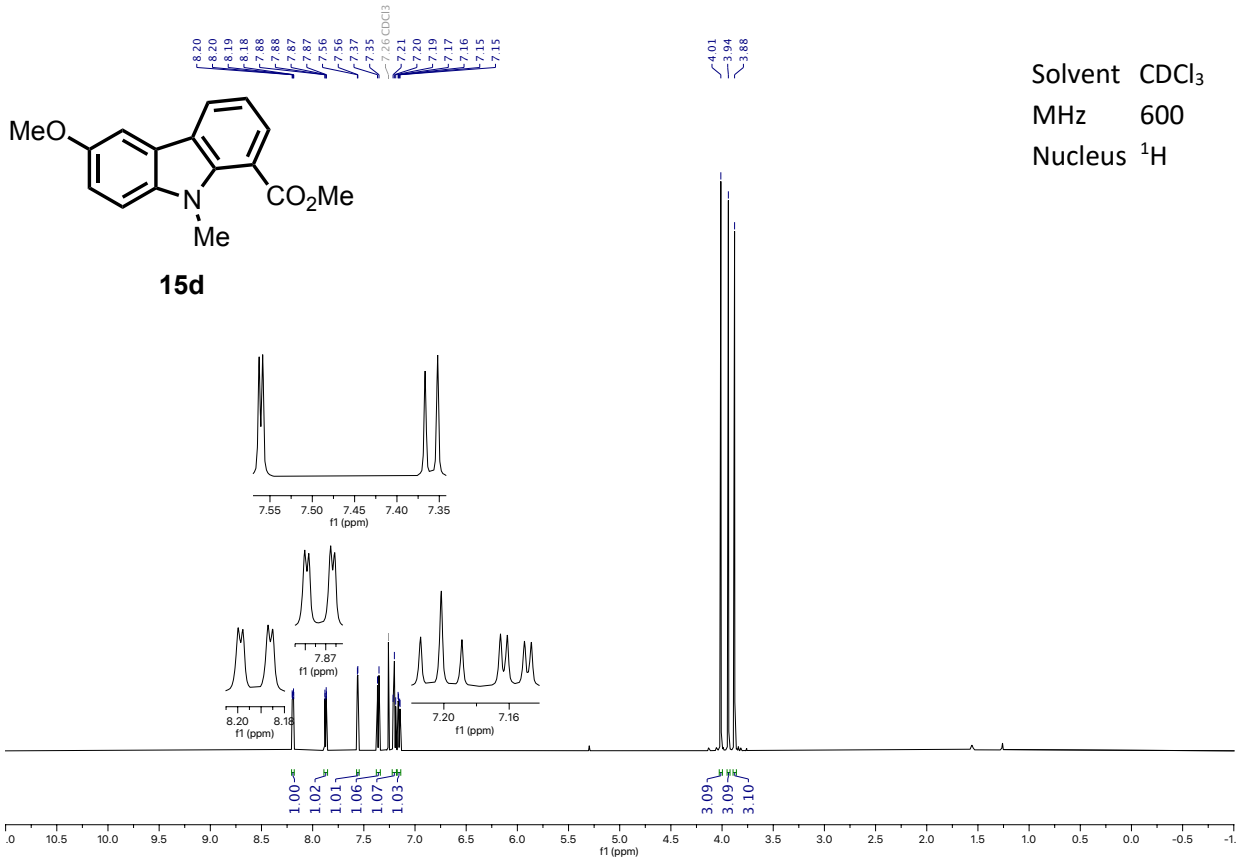

168.28
142.65
139.23
128.48
126.61
125.48
124.13
122.51
120.11
119.90
118.30
115.32
109.46
77.16 CDCl3
52.36
33.50
Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)

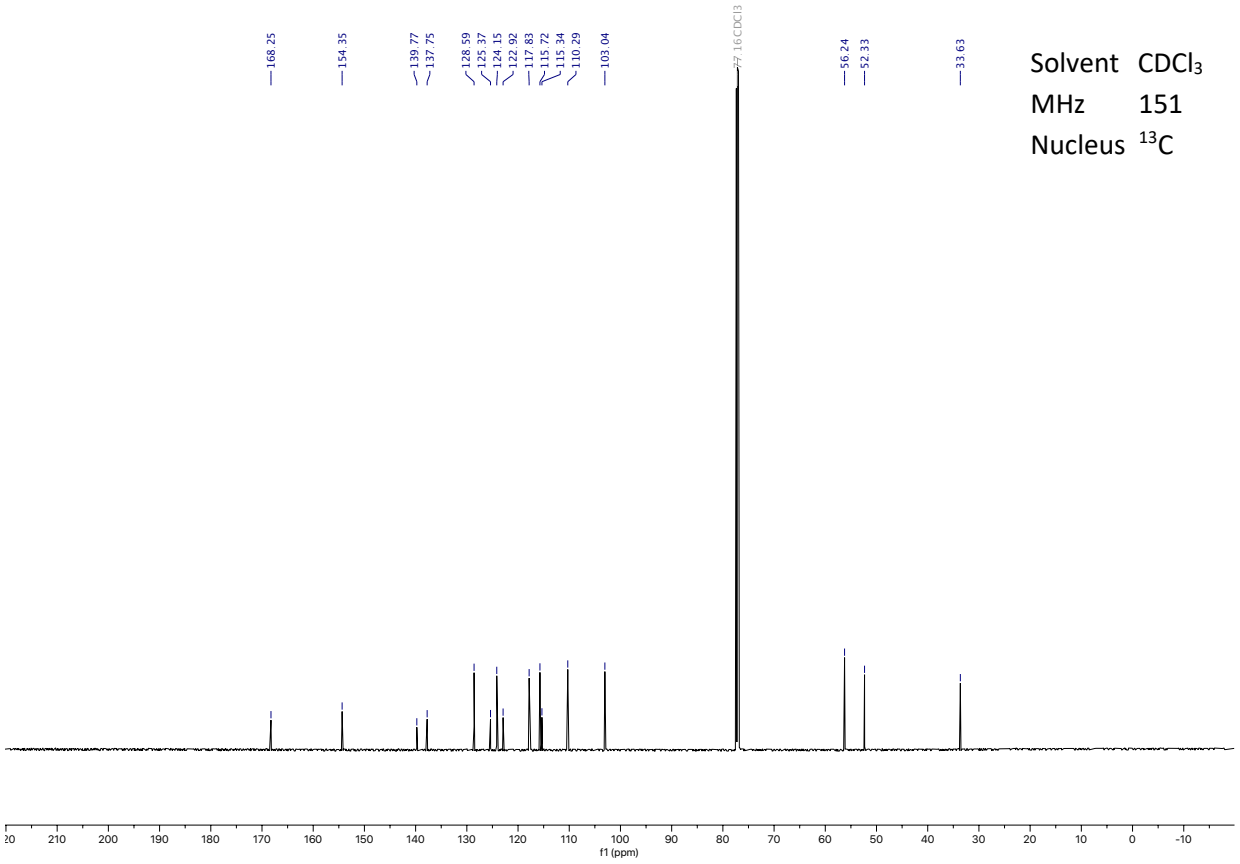

8.30
8.30
8.29
8.29
8.16
8.15
7.79
7.78
7.78
7.77
7.77
7.59
7.57
7.56
7.43
7.42
7.35
7.34
7.34
7.26 CDCl3
3.20
N
CO2Me
Ph
15b
Solvent CDCl3
MHz 700
Nucleus 1H
7.79 7.77
f1 (ppm)
8.30 8.25 8.20 8.15
f1 (ppm)
7.5 7.4
f1 (ppm)
1.00
0.99
0.98
2.00
3.93
2.94
3.04
f1 (ppm)

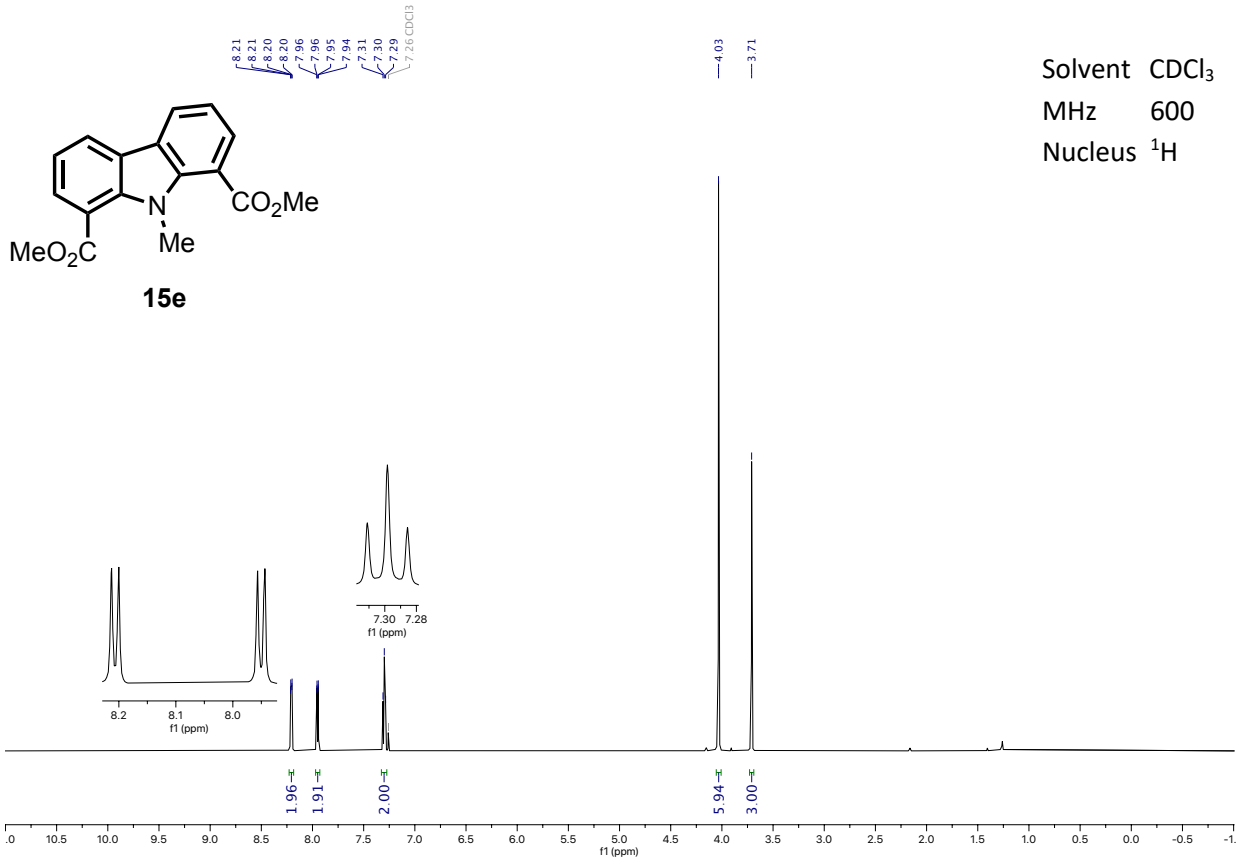

168.13
142.59
140.13
138.20
129.85
128.04
127.56
126.76
126.62
125.82
123.77
122.97
120.85
120.22
119.62
116.64
110.46
77.16 CDCl3
51.63
Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)

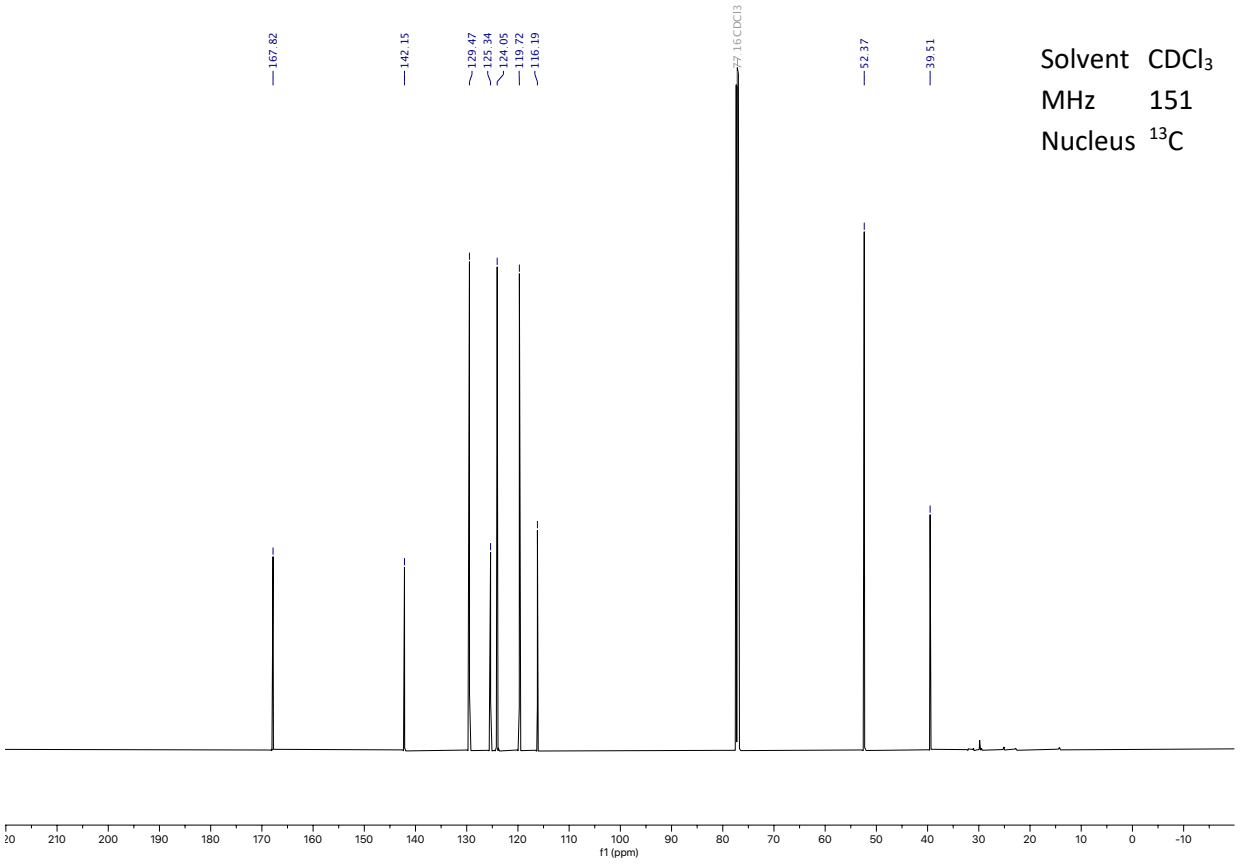

Solvent CDCl3
MHz 700
Nucleus 1H
CO2Me
N
SEM
15c

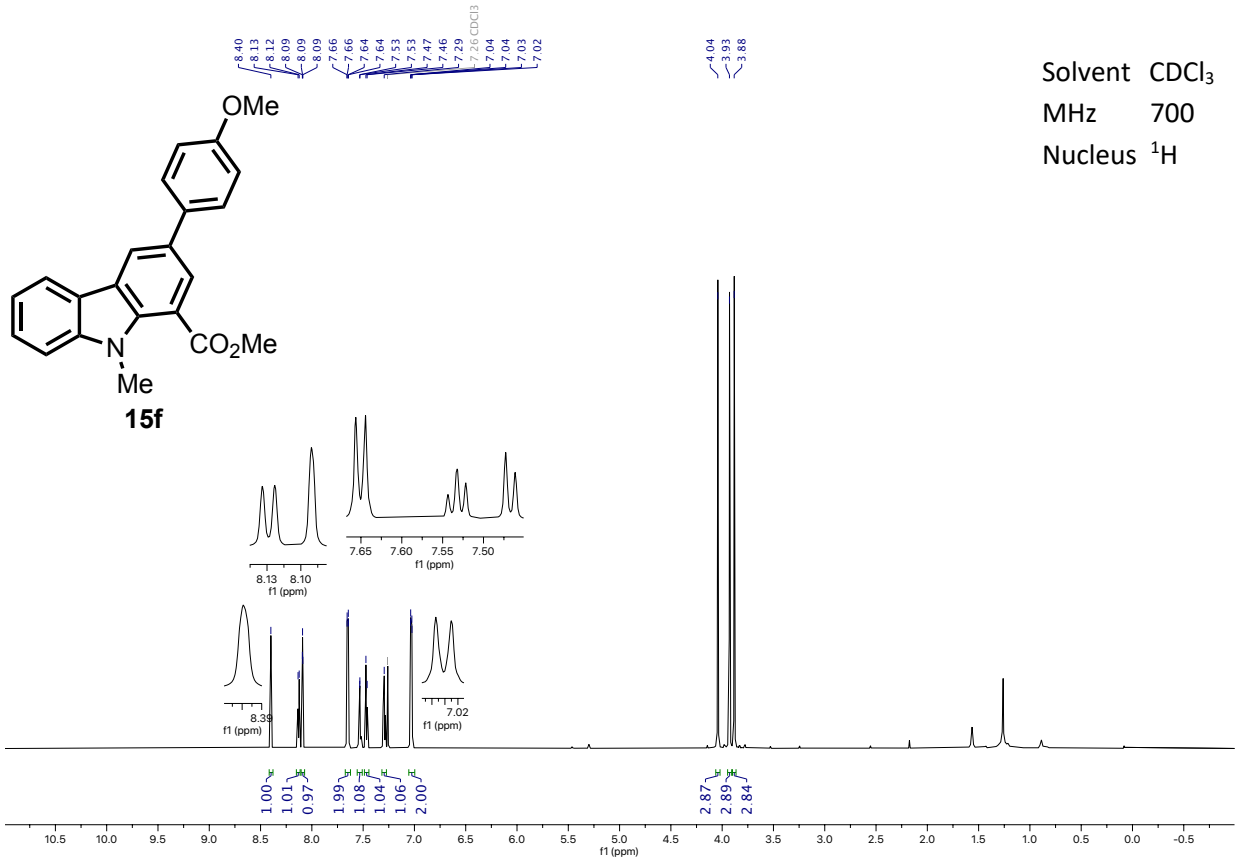

Solvent CDCl3
MHz 176
Nucleus 13C

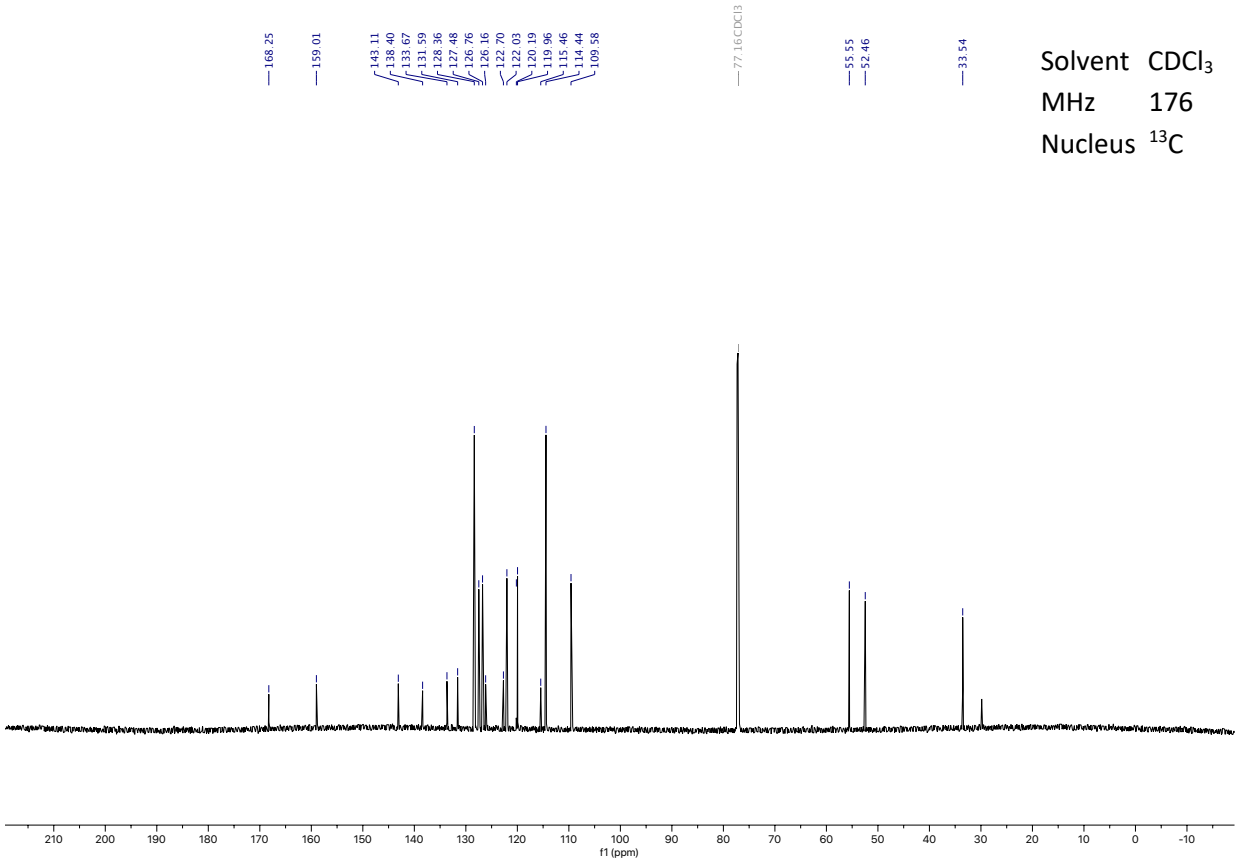

MeO
N
Me
CO2Me
15d
Solvent CDCl3
MHz 600
Nucleus 1H
f1 (ppm)

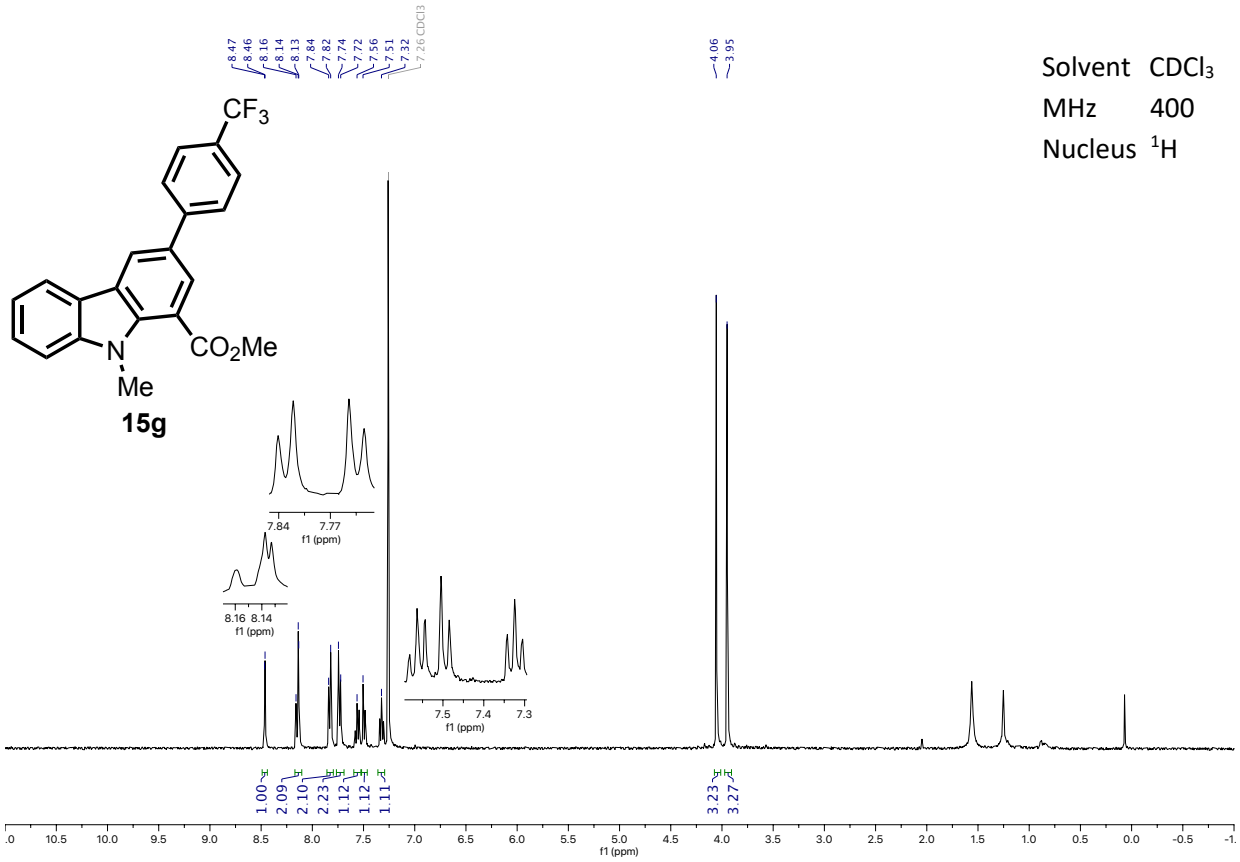

Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)

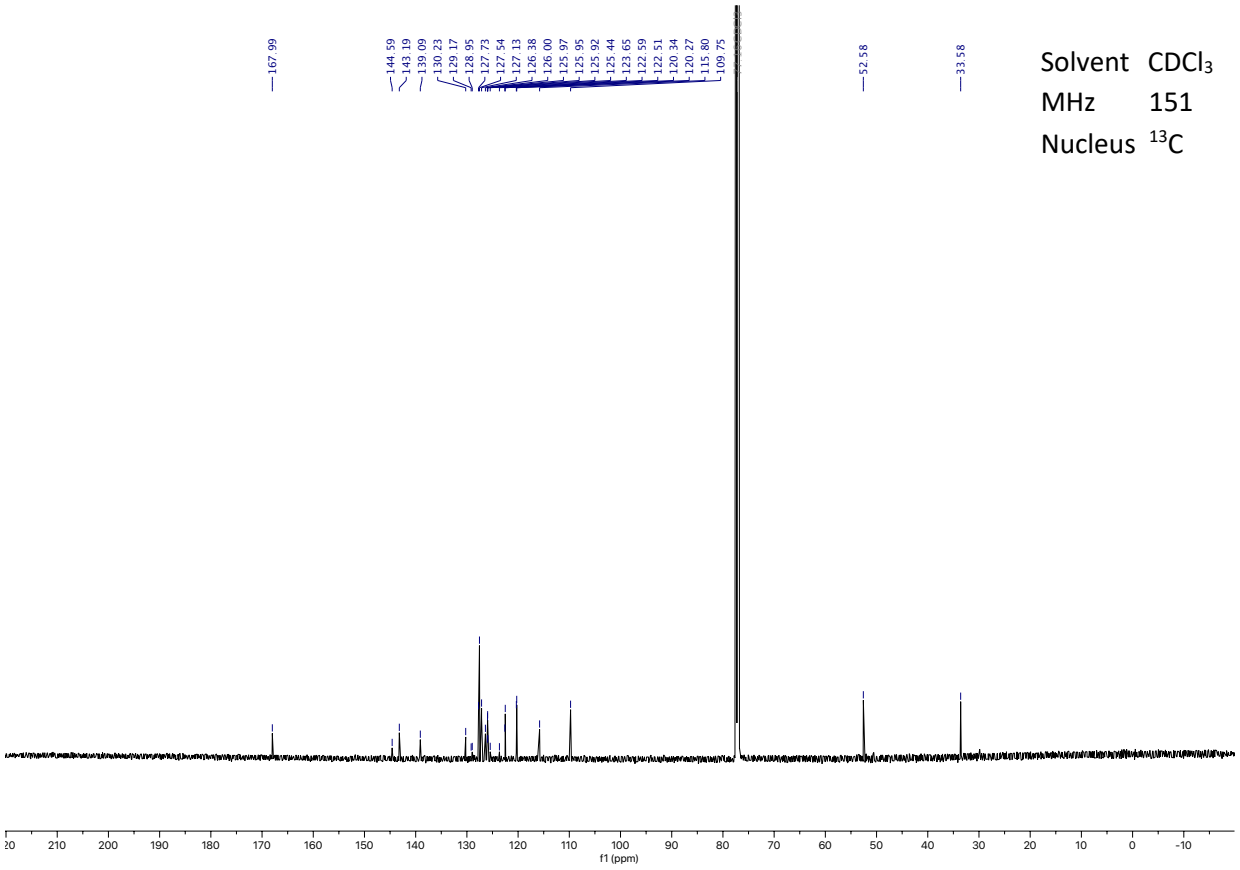

8.21
8.21
8.20
8.20
7.96
7.96
7.95
7.94
7.31
7.30
7.29
7.26 CDCl3
4.03
3.71
Solvent CDCl3
MHz 600
Nucleus 1H
CO2Me
N
Me
MeO2C
15e
7.30 7.28
f1 (ppm)
8.2 8.1 8.0
f1 (ppm)
1.96
1.91
2.00
5.94
3.00
f1 (ppm)

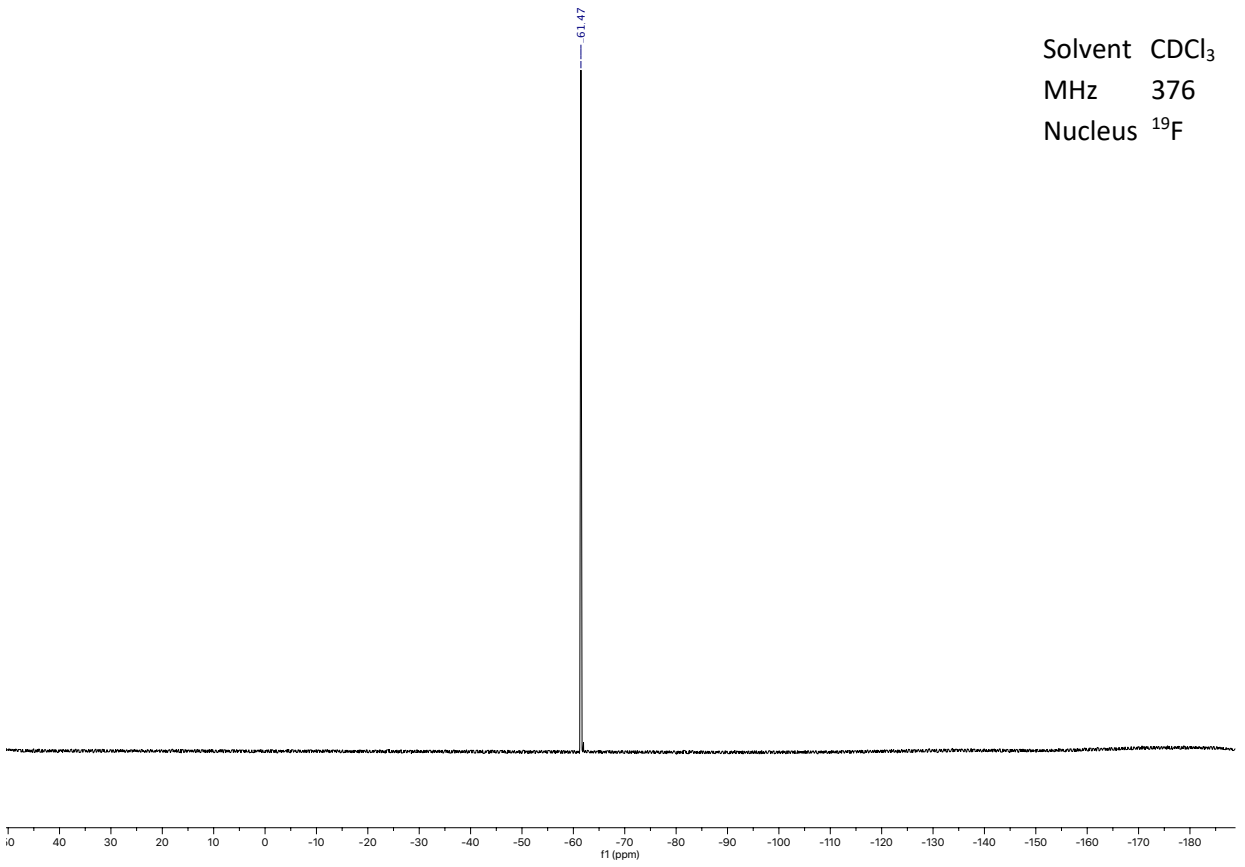

167.82
142.15
129.47
125.34
124.05
119.72
116.19
77.16 CDCl3
52.37
39.51
Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)

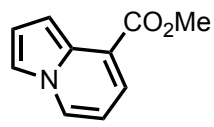

OMe
CO2Me
N
Me
15f
Solvent CDCl3
MHz 700
Nucleus 1H
f1 (ppm)


Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)


Solvent CDCl3
MHz 400
Nucleus 1H
CF3
CO2Me
N
Me
15g


Solvent CDCl3
MHz 151
Nucleus 13C

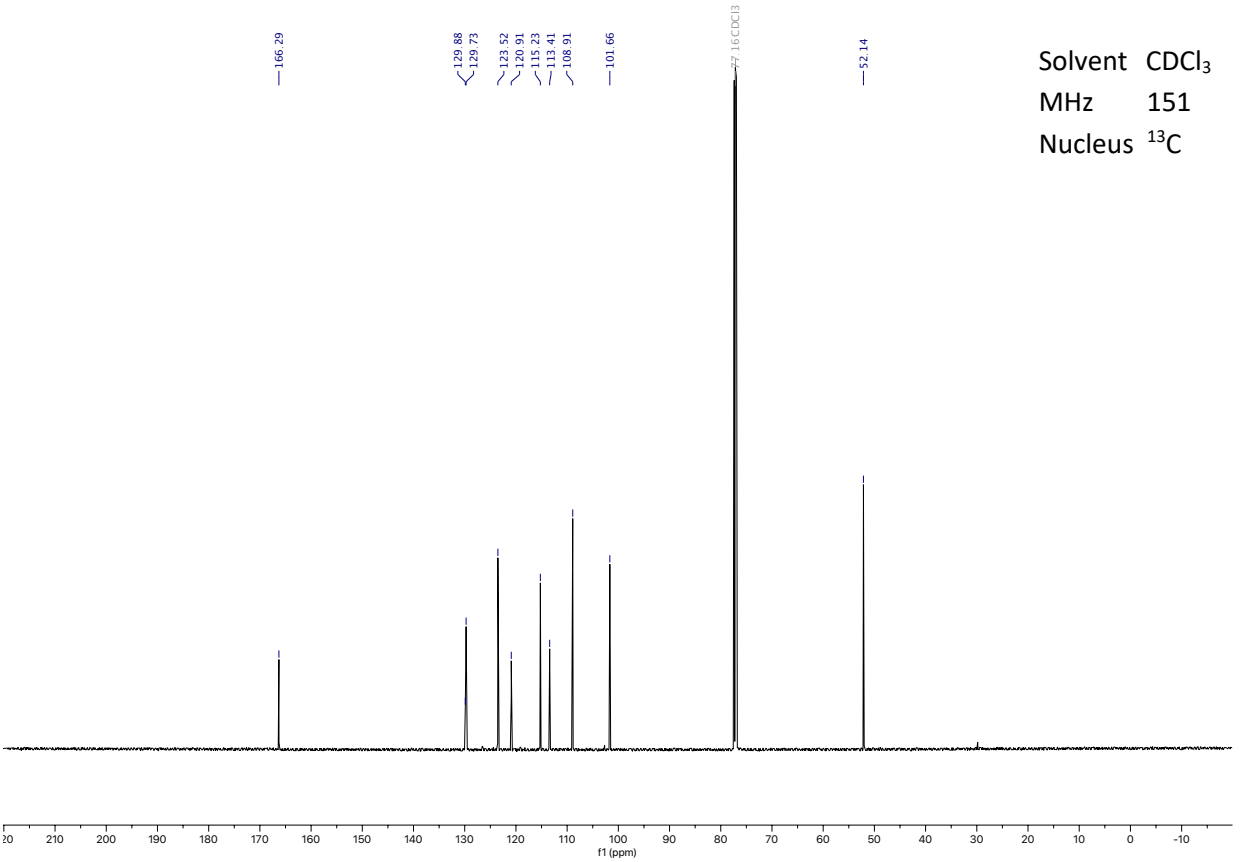

-61.47
Solvent CDCl3
MHz 376
Nucleus 19F
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180
f1 (ppm)

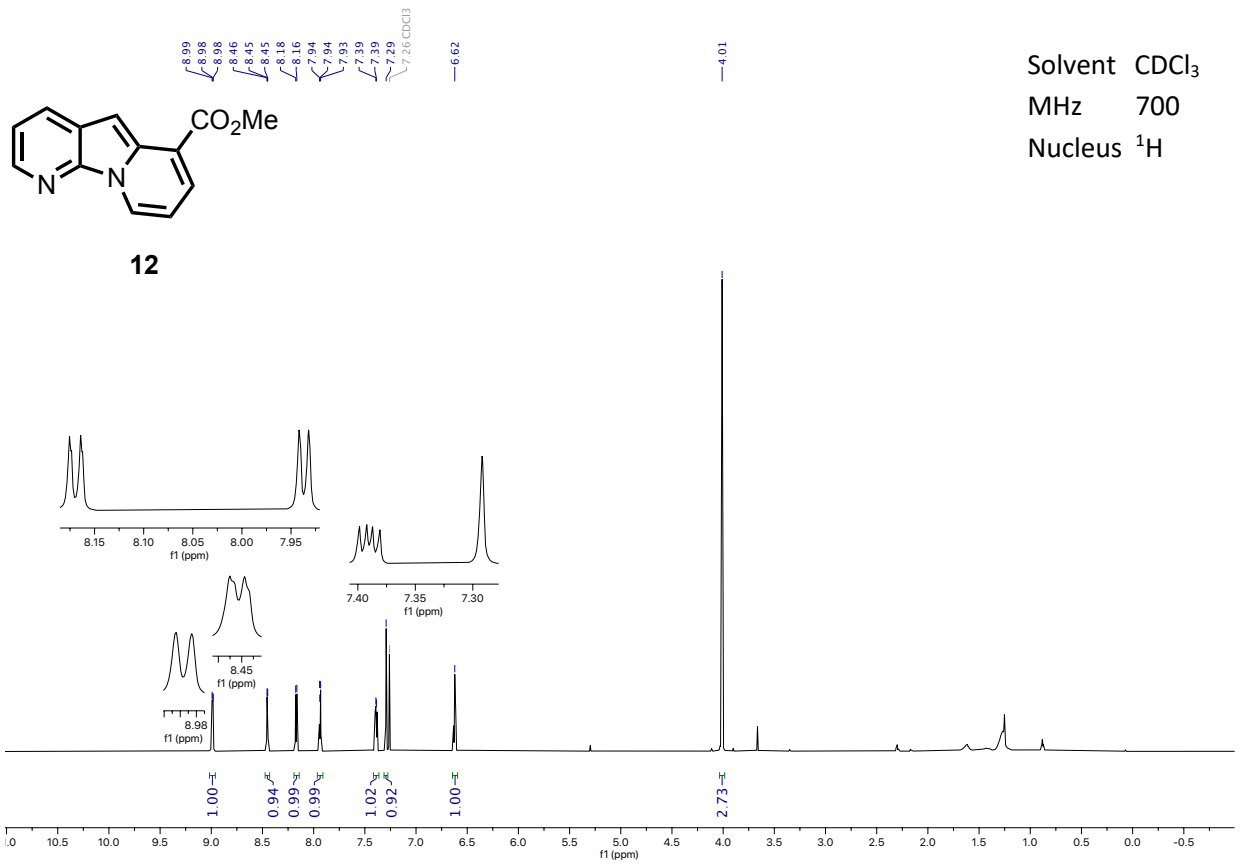


11

Solvent $CDCl_3$
MHz 400
Nucleus ^{1}H

Solvent $CDCl_3$
MHz 151
Nucleus ^{13}C

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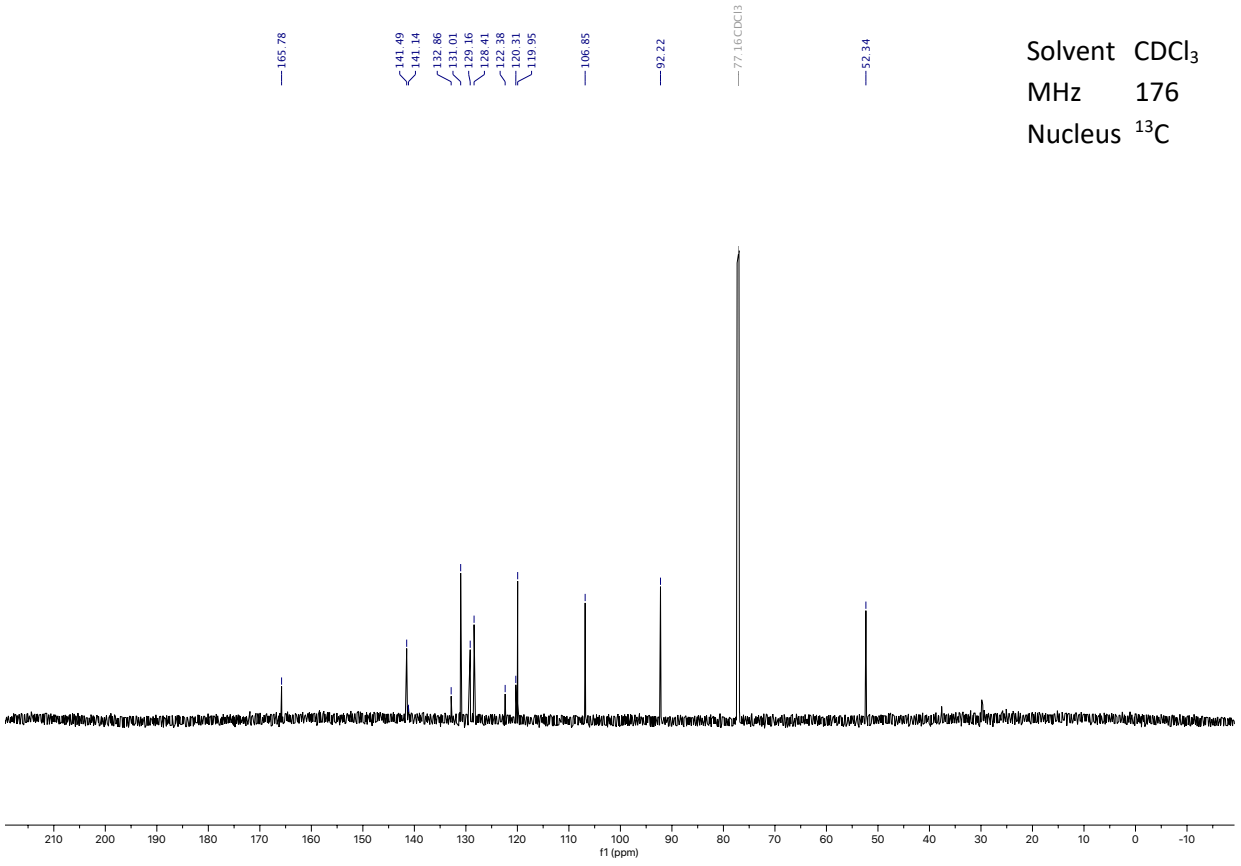
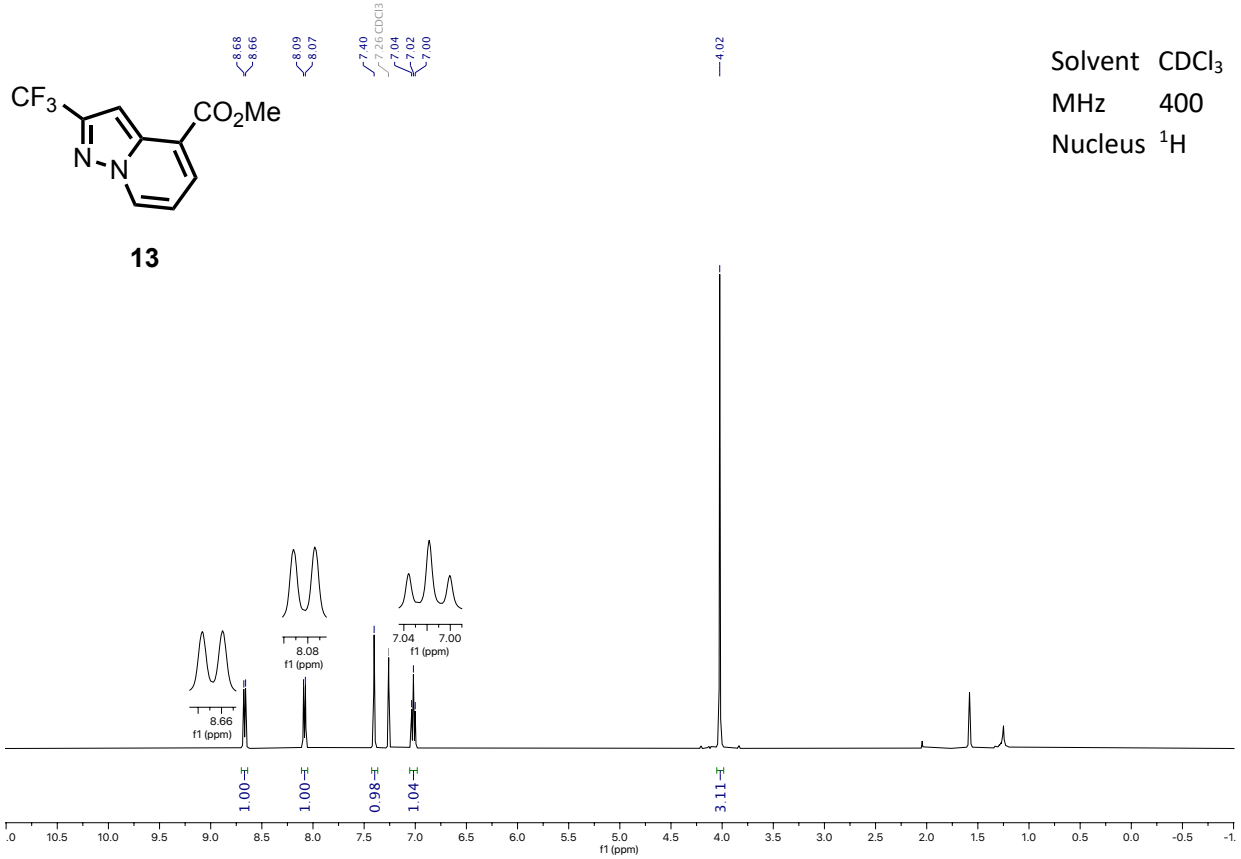
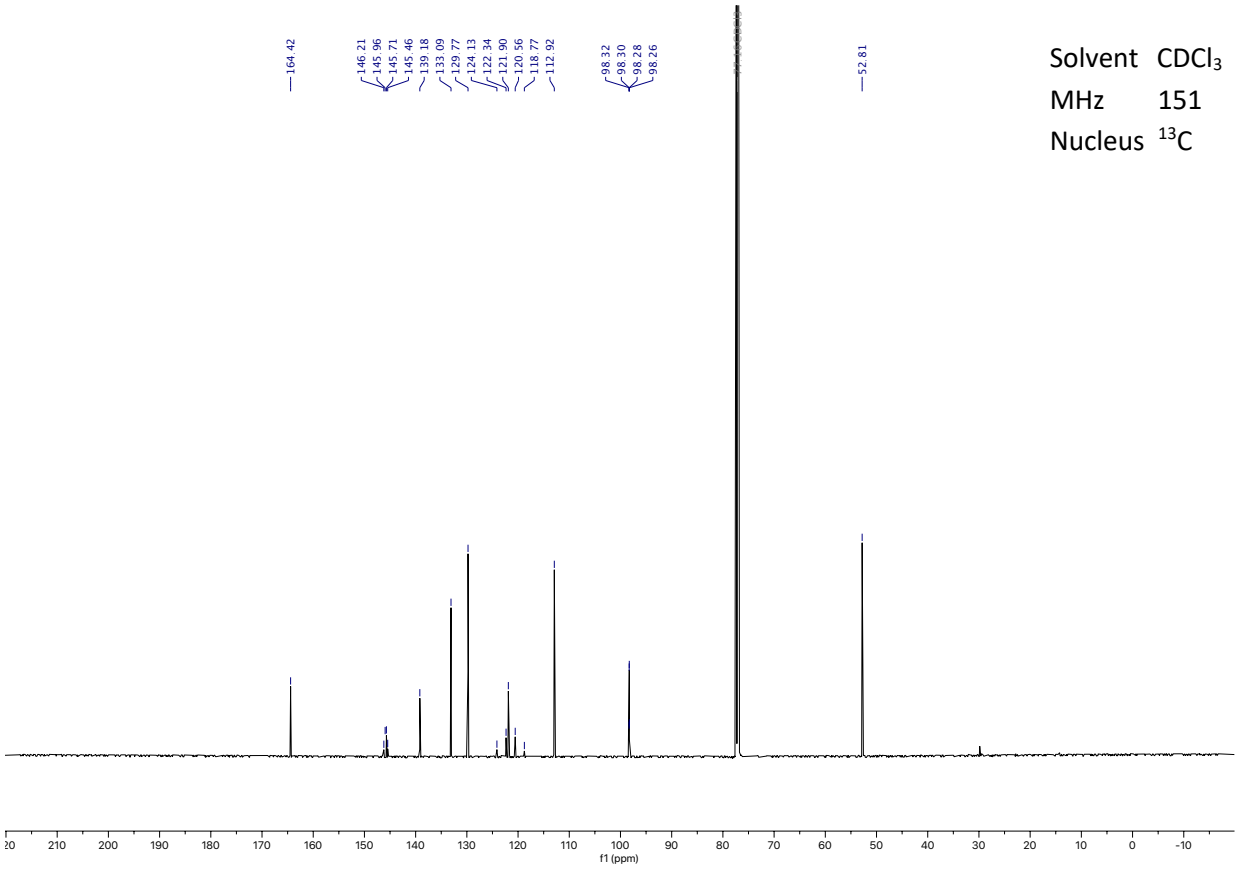
8.98
8.98
8.46
8.45
8.45
8.18
8.16
7.94
7.94
7.93
7.39
7.39
7.29
7.26 CDCl3
6.62
4.01
CO2Me
N
N
12
Solvent CDCl3
MHz 700
Nucleus 1H
8.15
8.10
8.05
8.00
7.95
f1 (ppm)
7.40
7.35
7.30
f1 (ppm)
8.45
f1 (ppm)
8.98
f1 (ppm)
1.00
0.94
0.99
0.99
1.02
0.92
1.00
2.73
f1 (ppm)


165.78
141.49
141.14
132.86
131.01
129.16
128.41
122.38
120.31
119.95
106.85
92.22
77.16 CDCl3
52.34
Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)

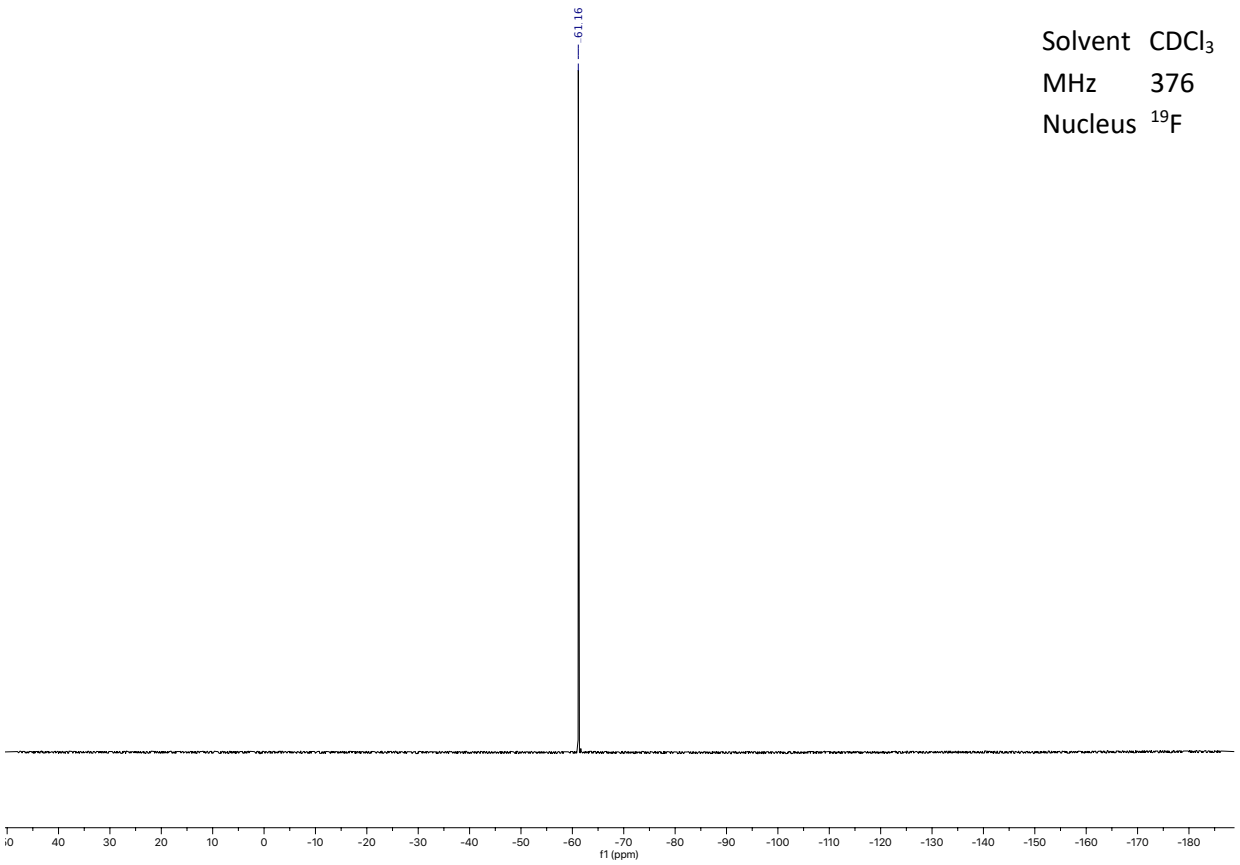


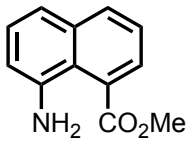
13

Solvent $CDCl_3$
MHz 400
Nucleus ^{1}H



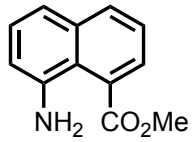
Solvent $CDCl_3$
MHz 151
Nucleus ^{13}C


-61.16
Solvent CDCl3
MHz 376
Nucleus 19F
40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180
f1 (ppm)


NH2
CO2Me

14

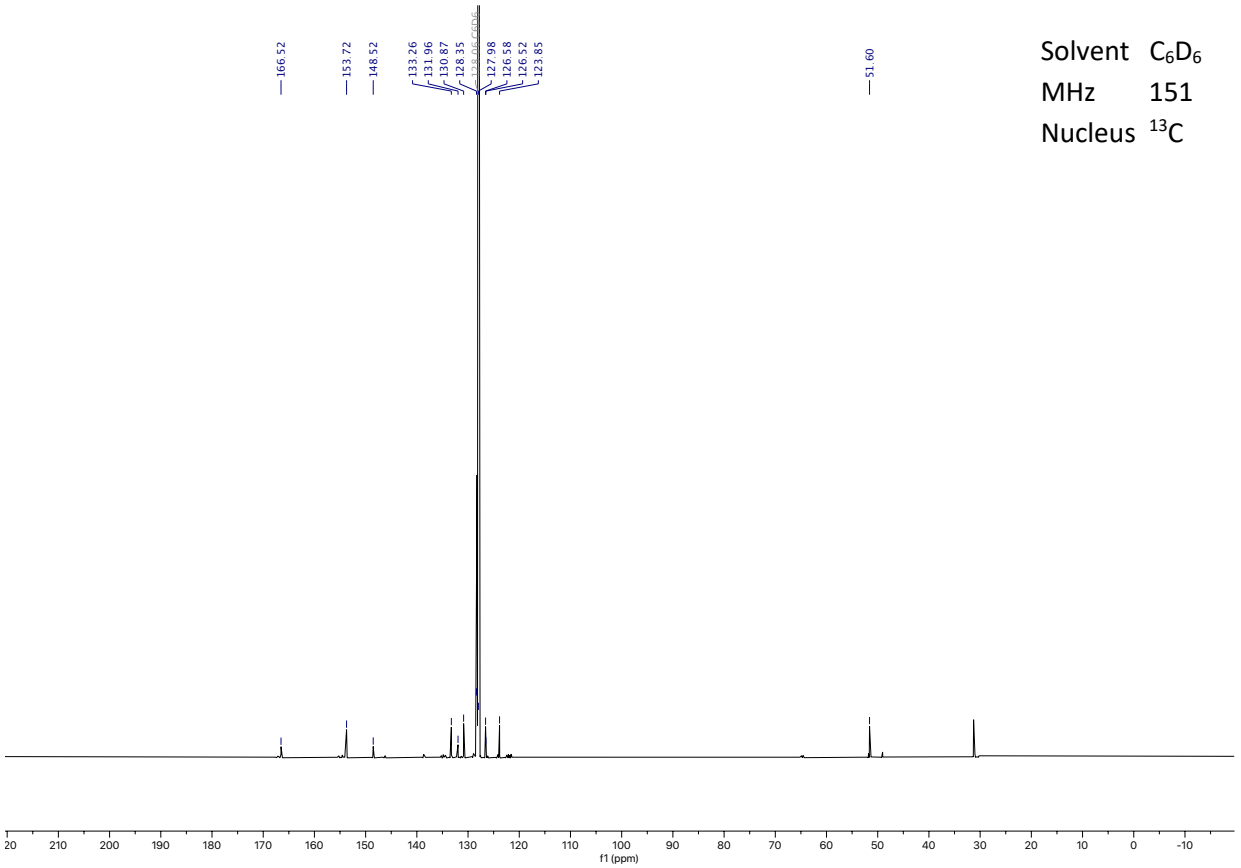
7.72
7.70
7.70
7.69
7.67
7.42
7.41
7.26 CDCl3
7.24
7.23
6.93
6.91
6.89
3.82
2.60
Solvent CDCl3
MHz 400
Nucleus 1H
7.26 7.23
f1 (ppm)
7.71 7.68
f1 (ppm)
6.92 6.90
f1 (ppm)
2.02
1.89
1.19
1.00
3.03
1.99
f1 (ppm)

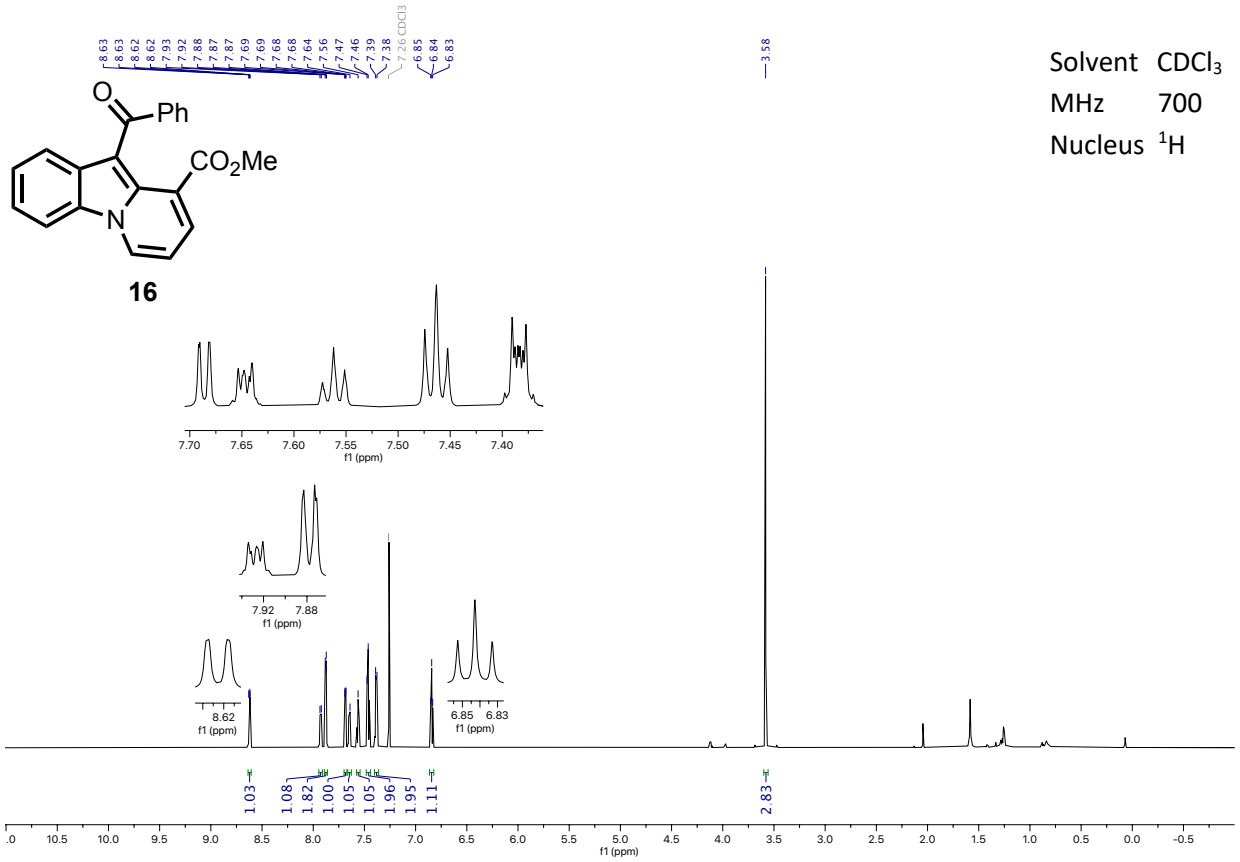


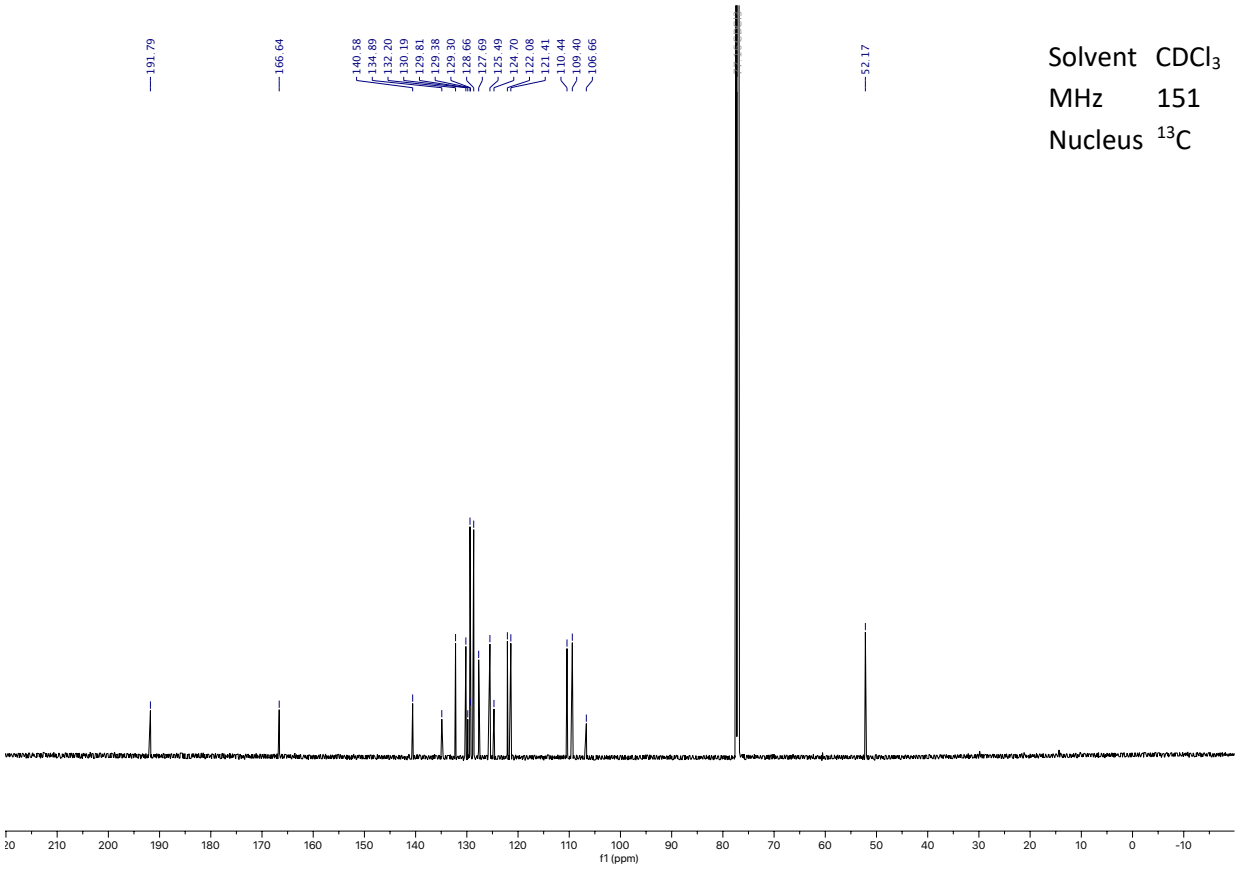
14

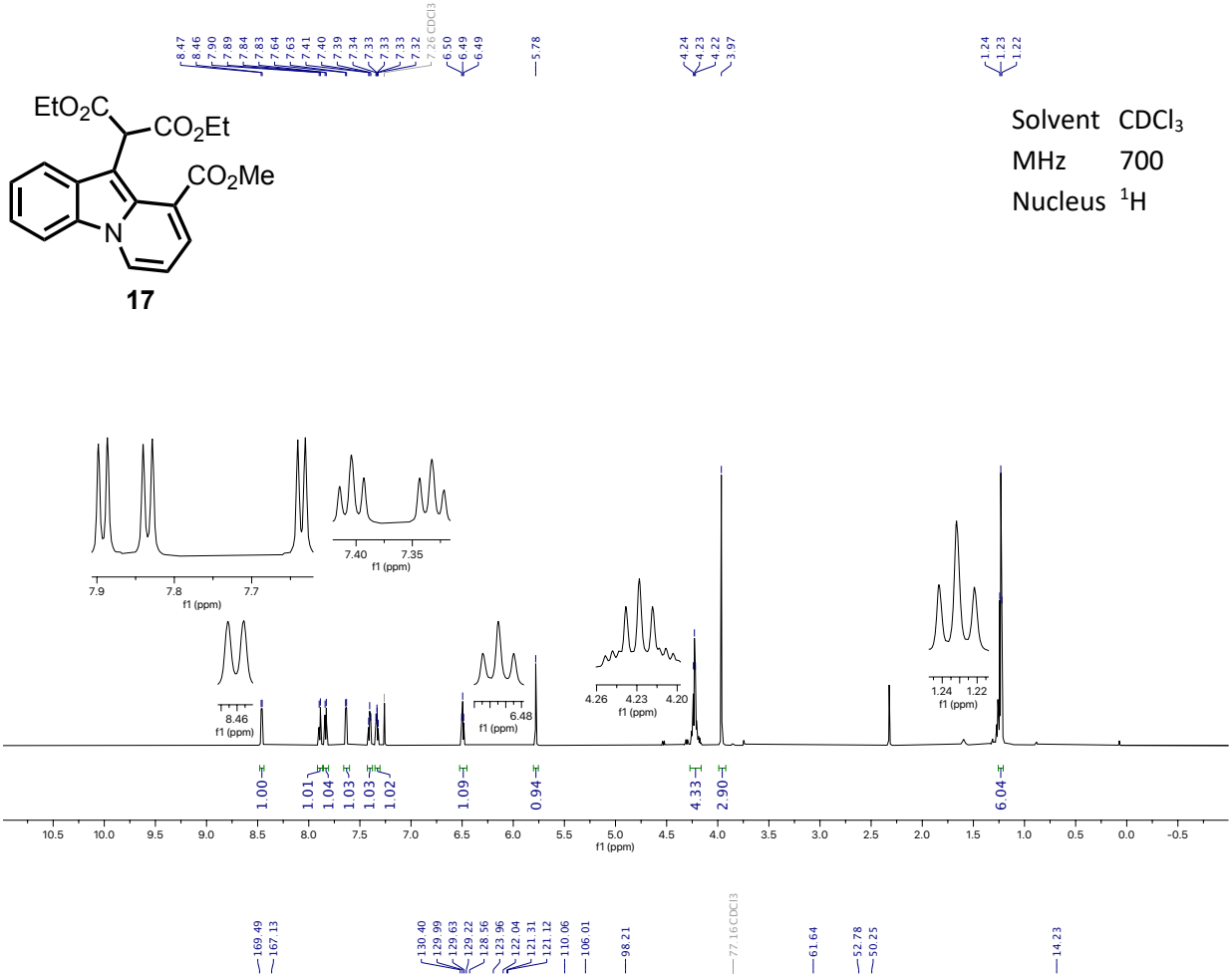
Solvent C_6D_6
MHz 600
Nucleus ^{1}H

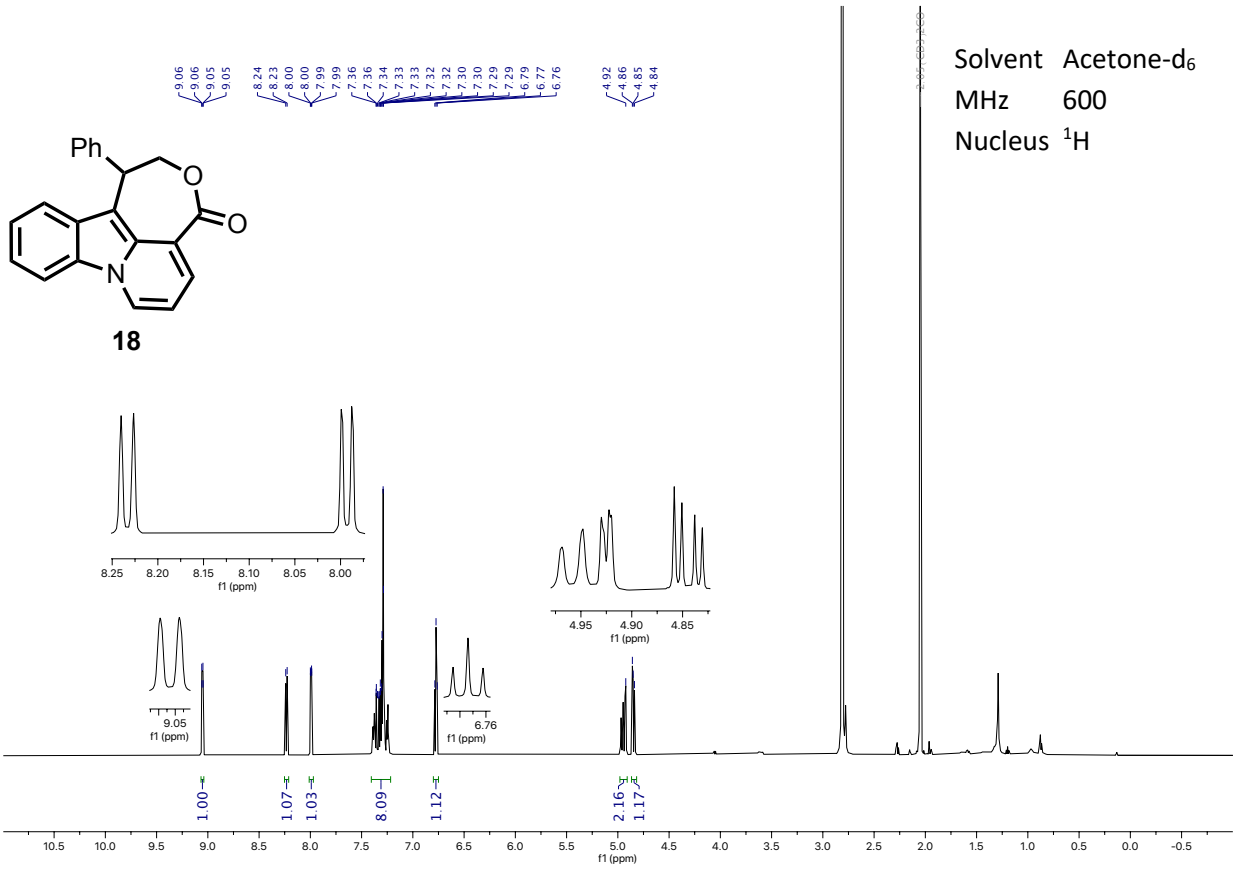
Solvent C_6D_6
MHz 151
Nucleus ^{13}C

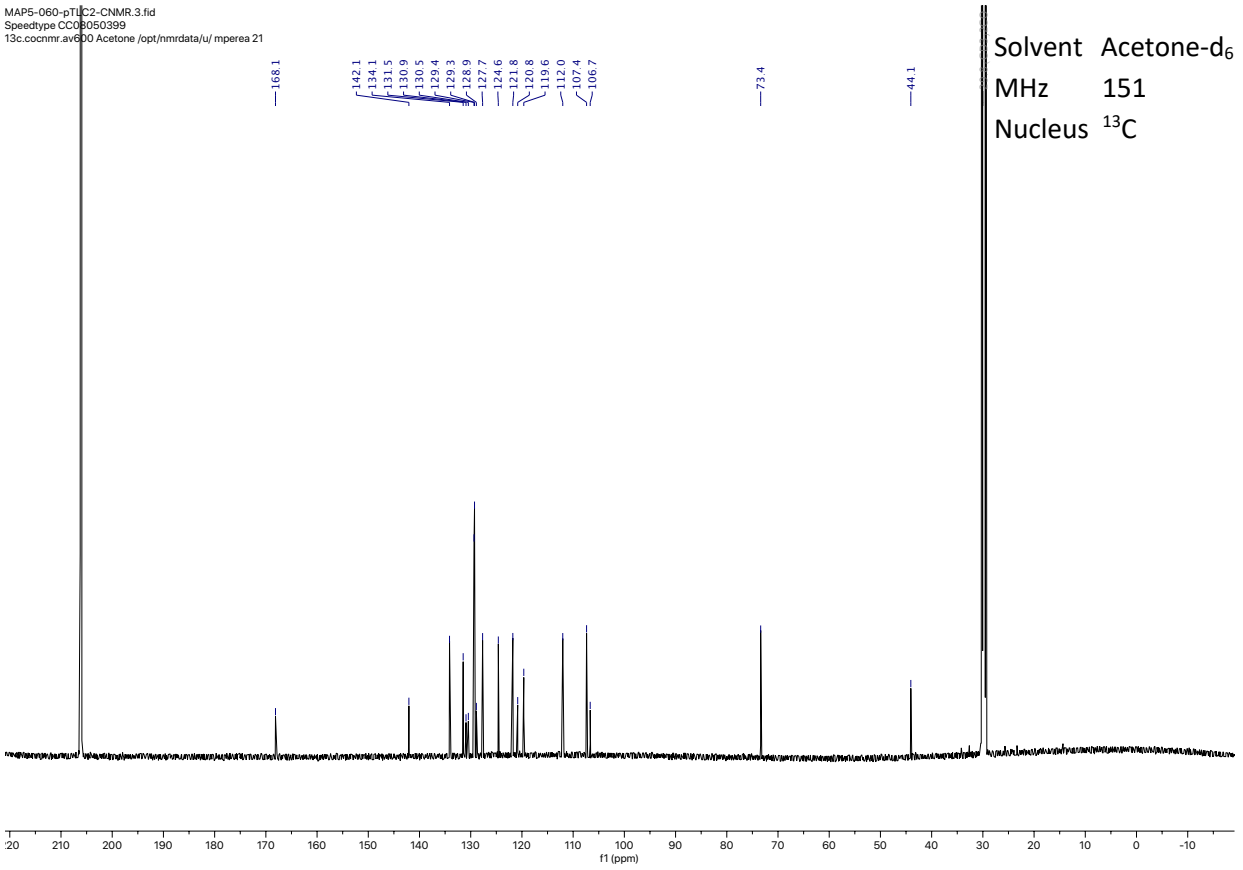


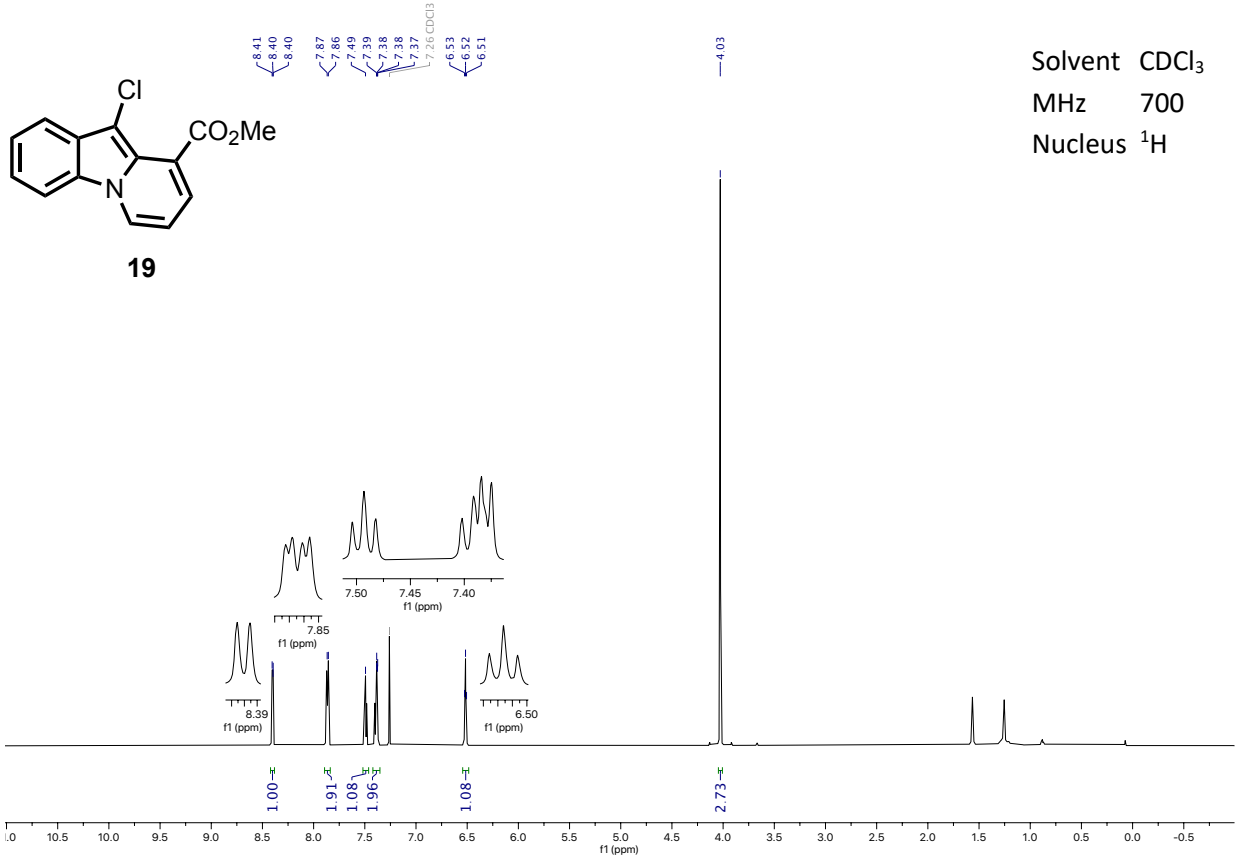

Solvent CDCl3
MHz 700
Nucleus 1H
16
f1 (ppm)

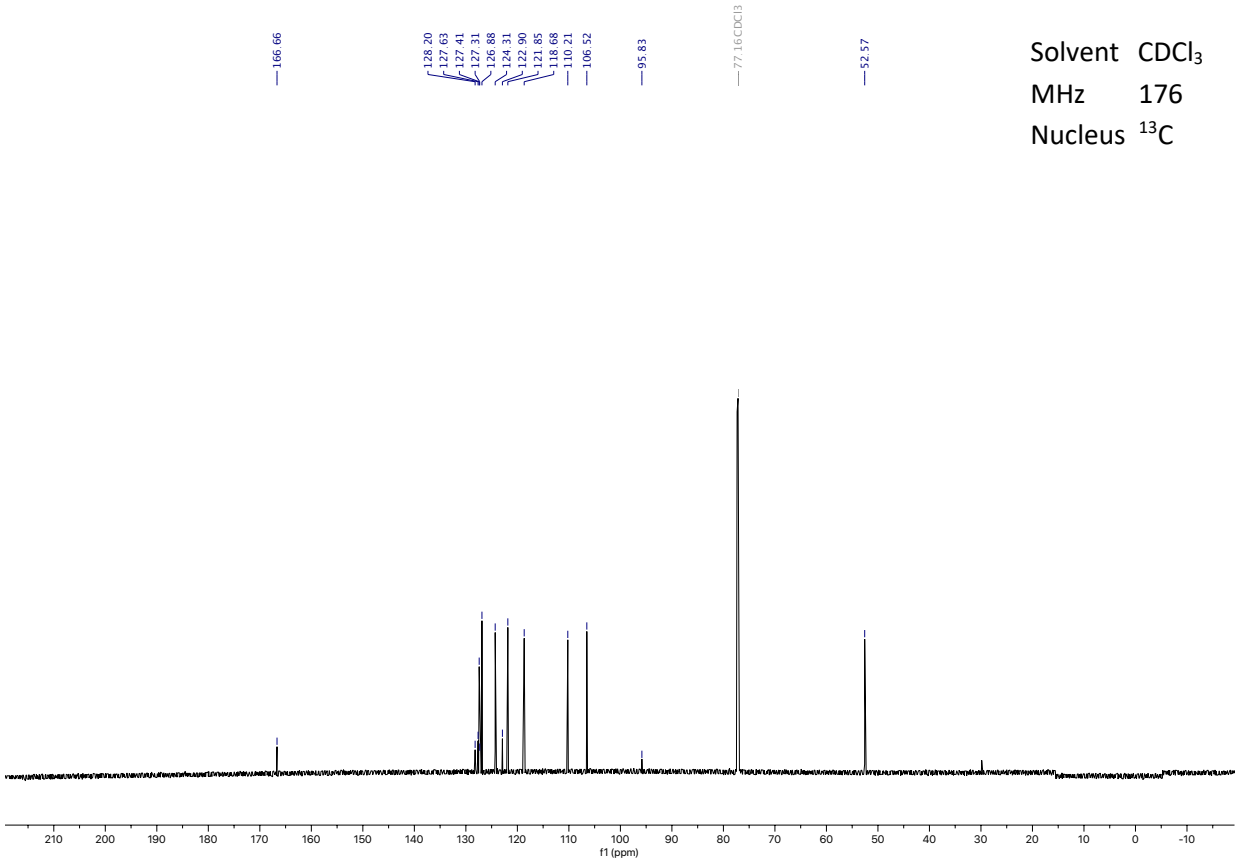

Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)

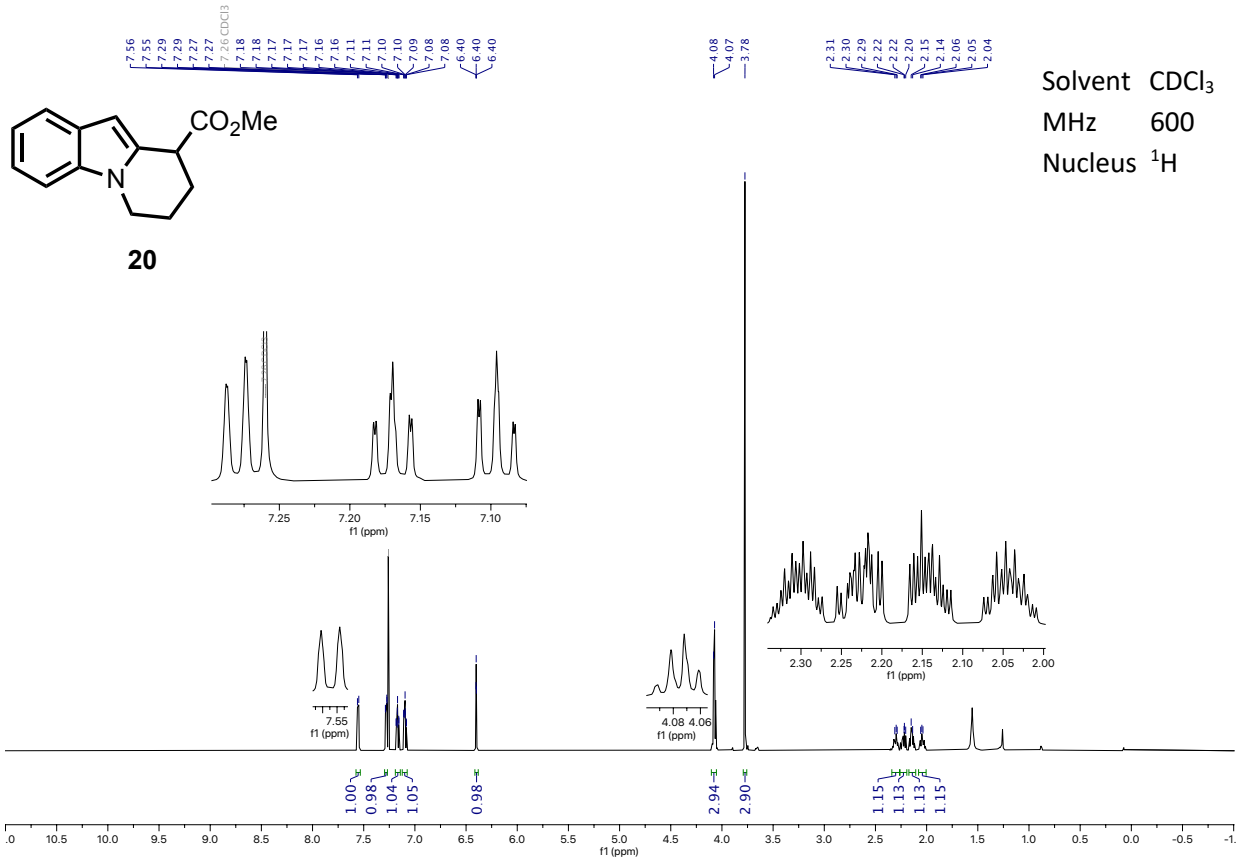

8.47
8.46
7.90
7.89
7.84
7.83
7.64
7.63
7.41
7.40
7.39
7.34
7.33
7.33
7.33
7.32
7.26 CDCl3
6.50
6.49
6.49
5.78
4.24
4.23
4.22
3.97
1.24
1.23
1.22
EtO2C
CO2Et
CO2Me
N
17
Solvent CDCl3
MHz 700
Nucleus 1H
7.9
7.8
7.7
f1 (ppm)
7.40
7.35
f1 (ppm)
8.46
f1 (ppm)
6.48
f1 (ppm)
4.26
4.23
4.20
f1 (ppm)
1.24
1.22
f1 (ppm)
1.00
1.01
1.04
1.03
1.03
1.02
1.09
0.94
4.33
2.90
6.04
f1 (ppm)
169.49
167.13
130.40
129.99
129.63
129.22
128.56
123.96
122.04
121.31
121.12
110.06
106.01
98.21
77.16 CDCl3
61.64
52.78
50.25
14.23
Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)

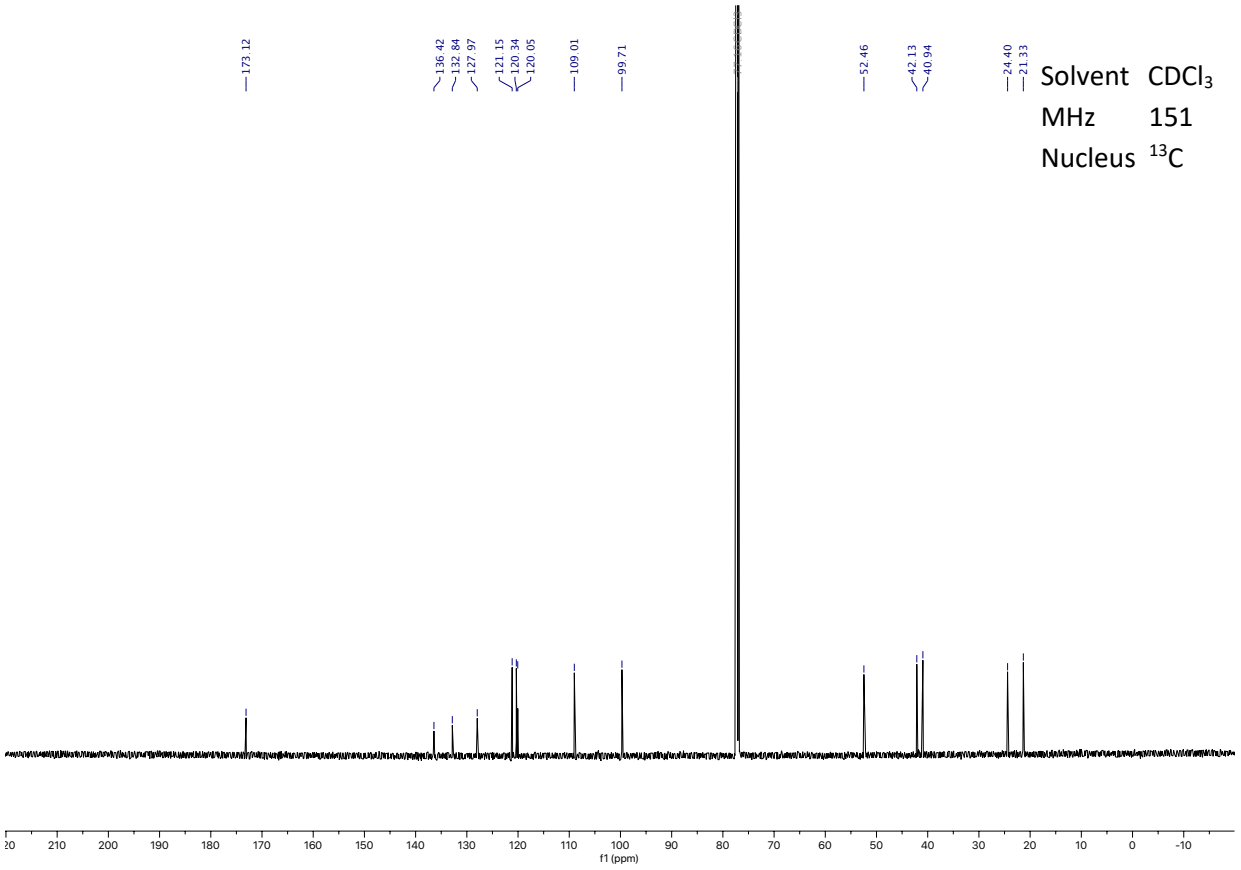

Solvent Acetone-d6
MHz 600
Nucleus 1H
Ph
O
O
N
18
f1 (ppm)

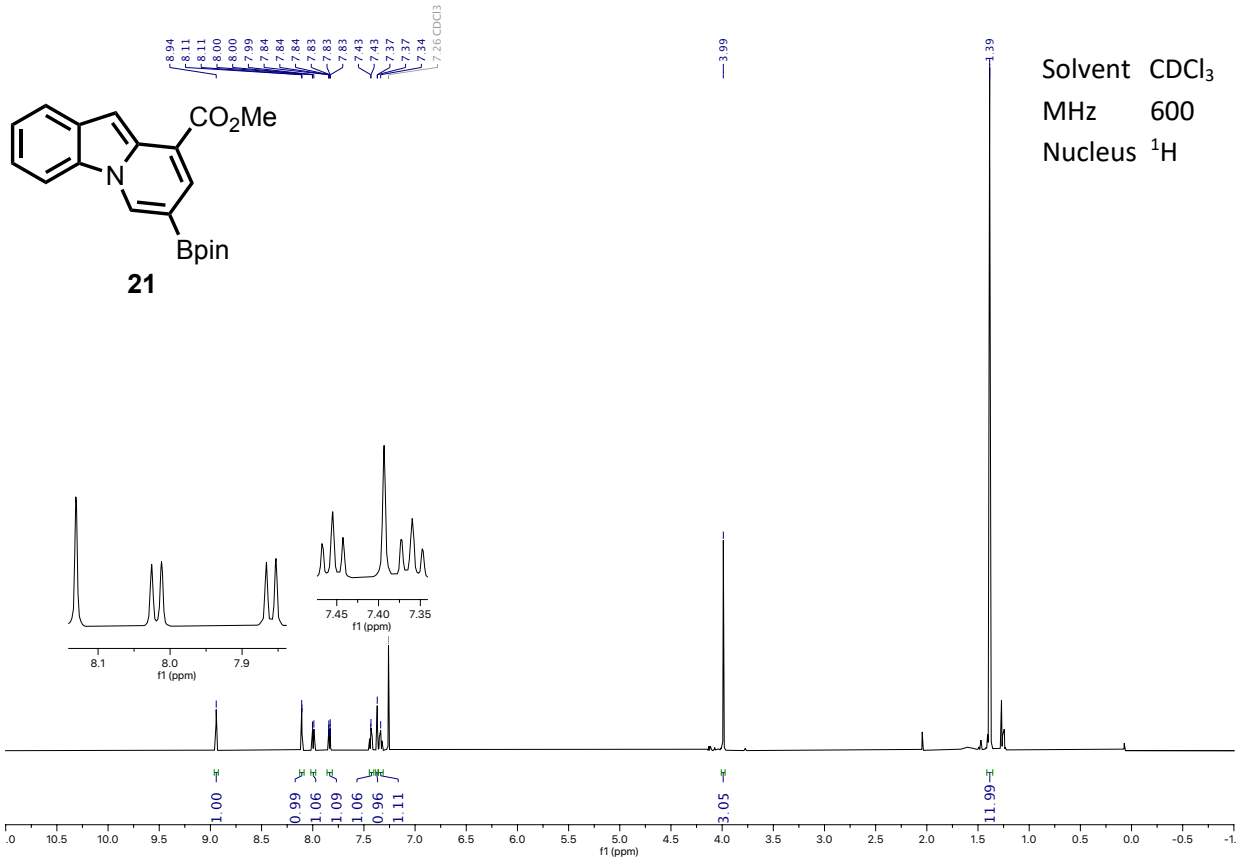

Solvent Acetone-d6
MHz 151
Nucleus 13C
f1 (ppm)

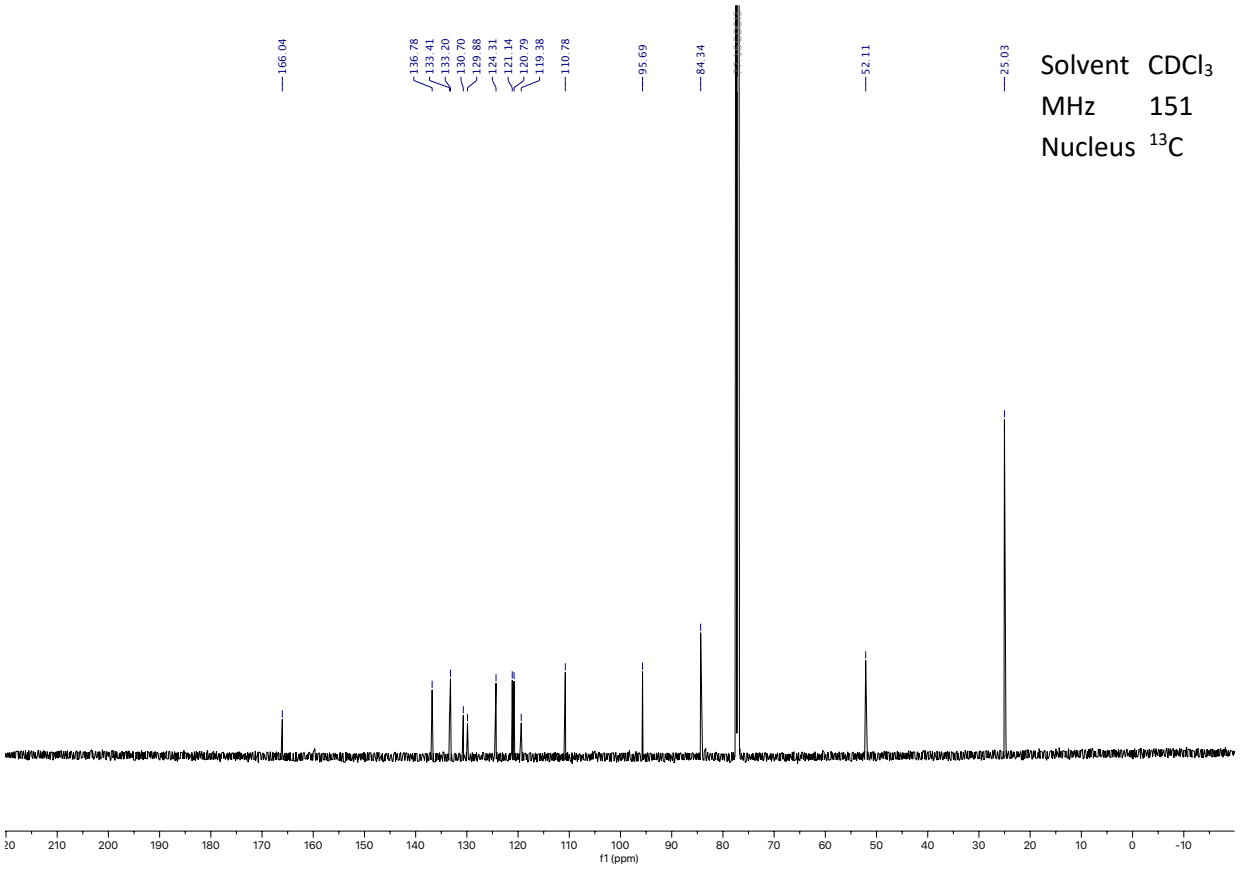

Cl
CO2Me
N
19
Solvent CDCl3
MHz 700
Nucleus 1H
f1 (ppm)

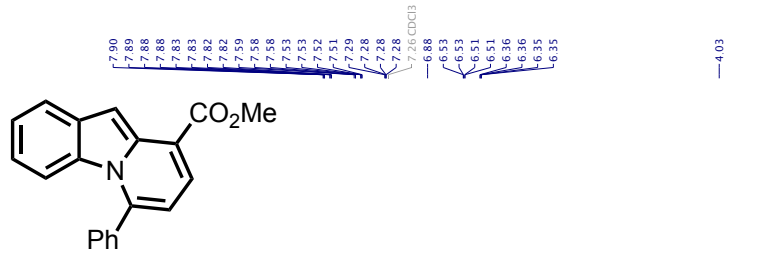

Solvent CDCl3
MHz 176
Nucleus 13C
f1 (ppm)


CO2Me
N
20
Solvent CDCl3
MHz 600
Nucleus 1H
f1 (ppm)


Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)

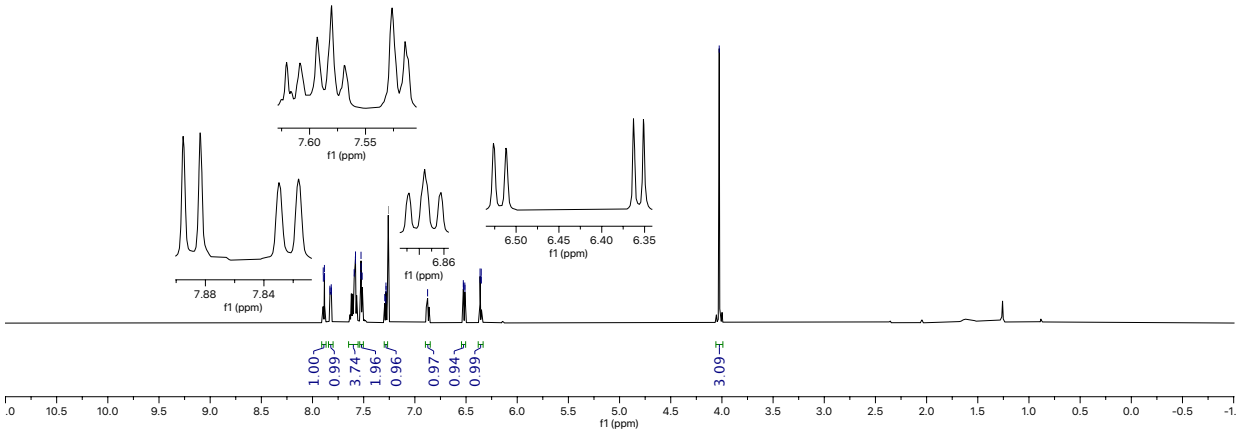

CO2Me
N
Bpin
21
Solvent CDCl3
MHz 600
Nucleus 1H
f1 (ppm)

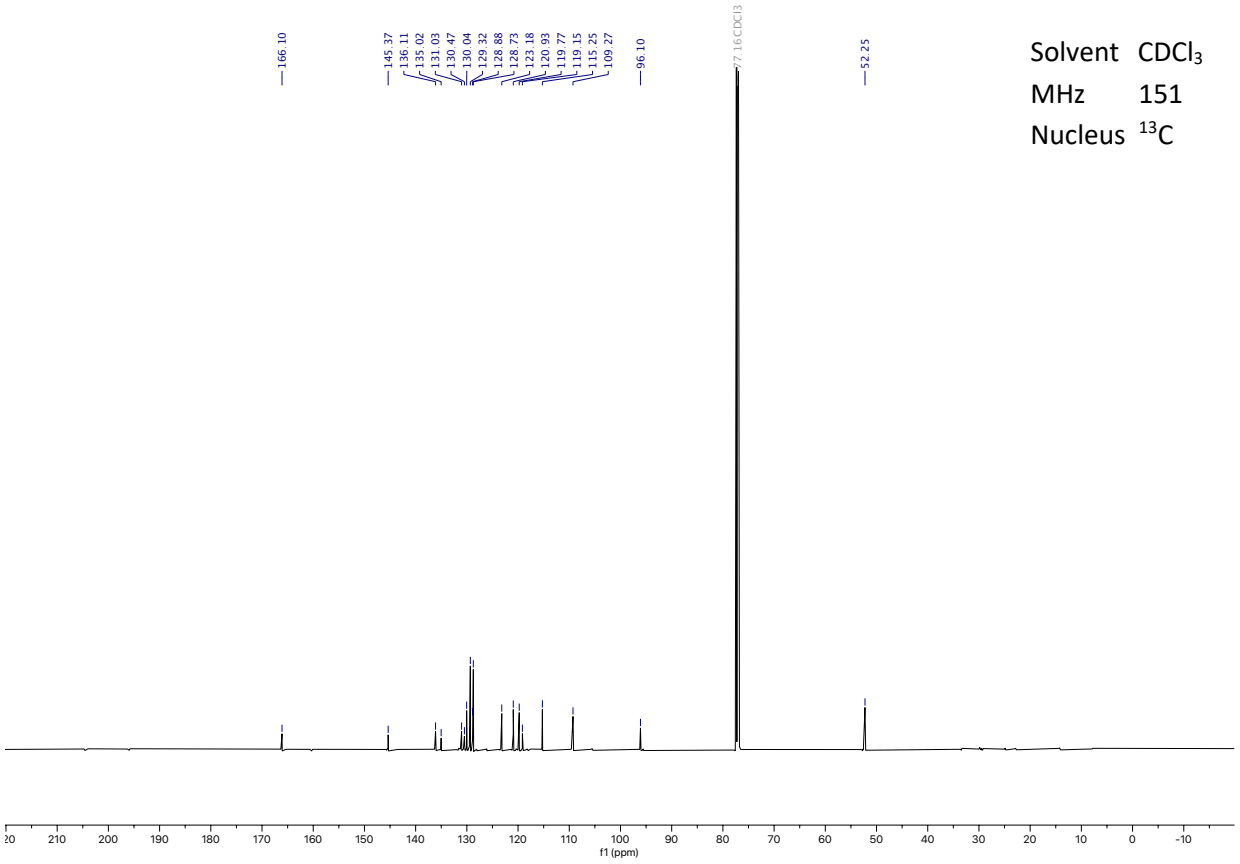

Solvent CDCl3
MHz 151
Nucleus 13C
f1 (ppm)



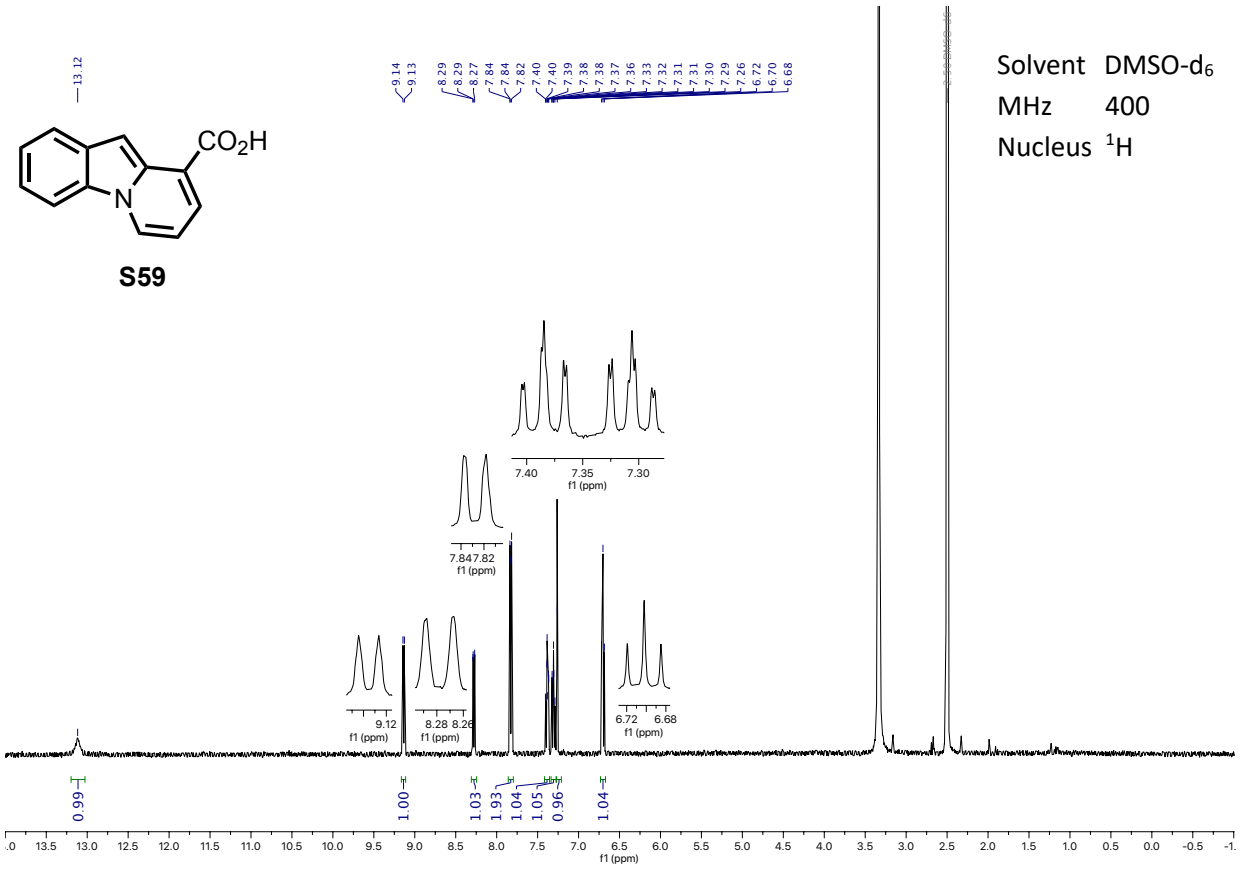
22

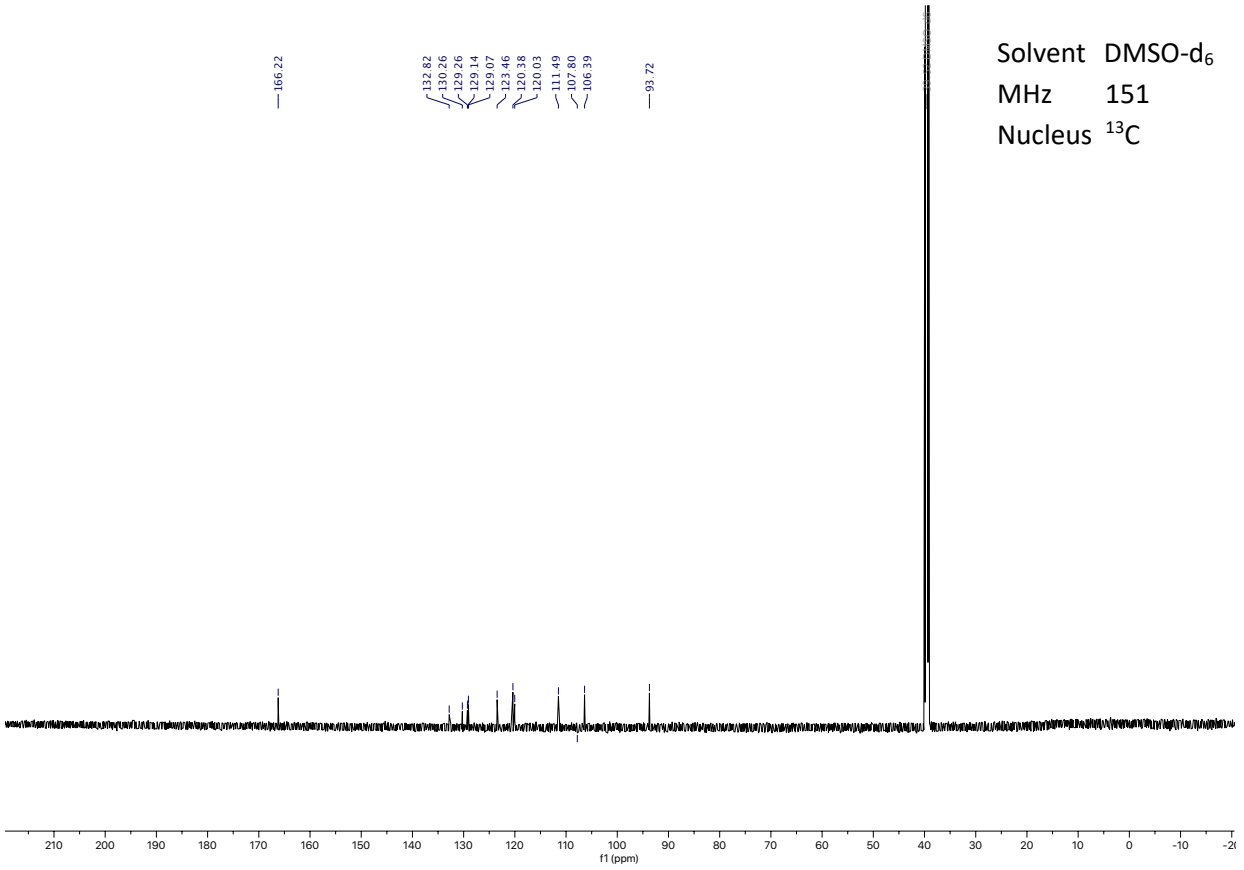
Solvent $CDCl_3$
MHz 600
Nucleus ^{1}H

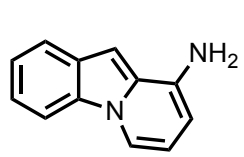




Solvent $CDCl_3$
MHz 151
Nucleus ^{13}C

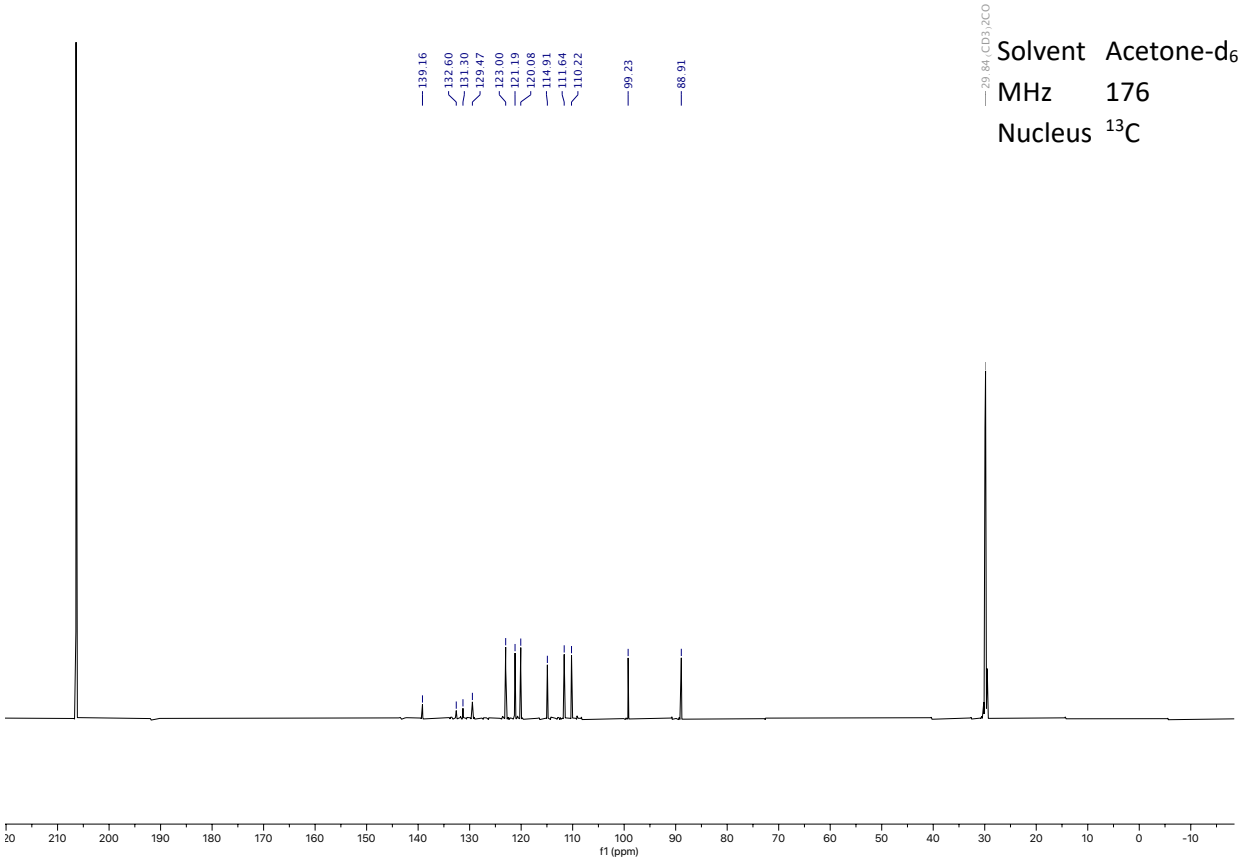

CO2H
N
S59
Solvent DMSO-d6
MHz 400
Nucleus 1H
f1 (ppm)

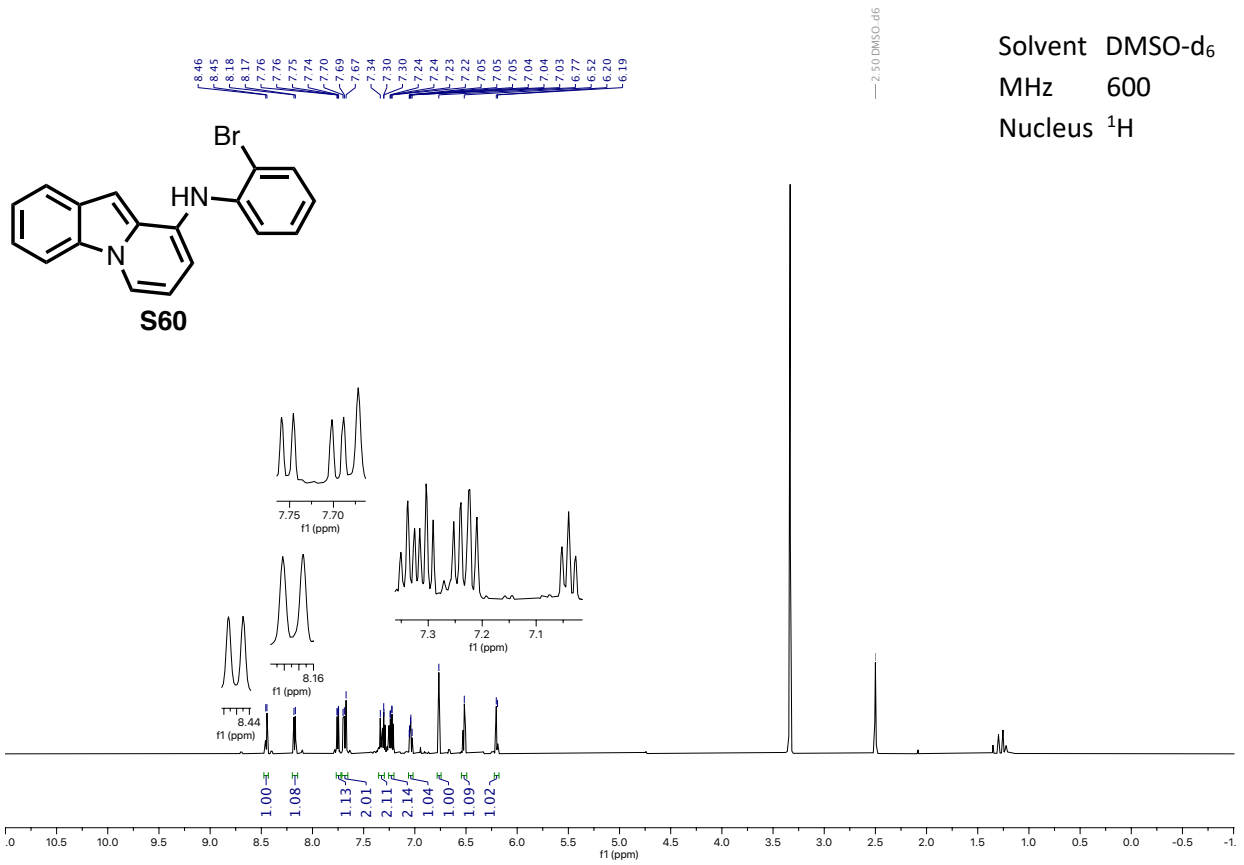

Solvent DMSO-d6
MHz 151
Nucleus 13C
f1 (ppm)

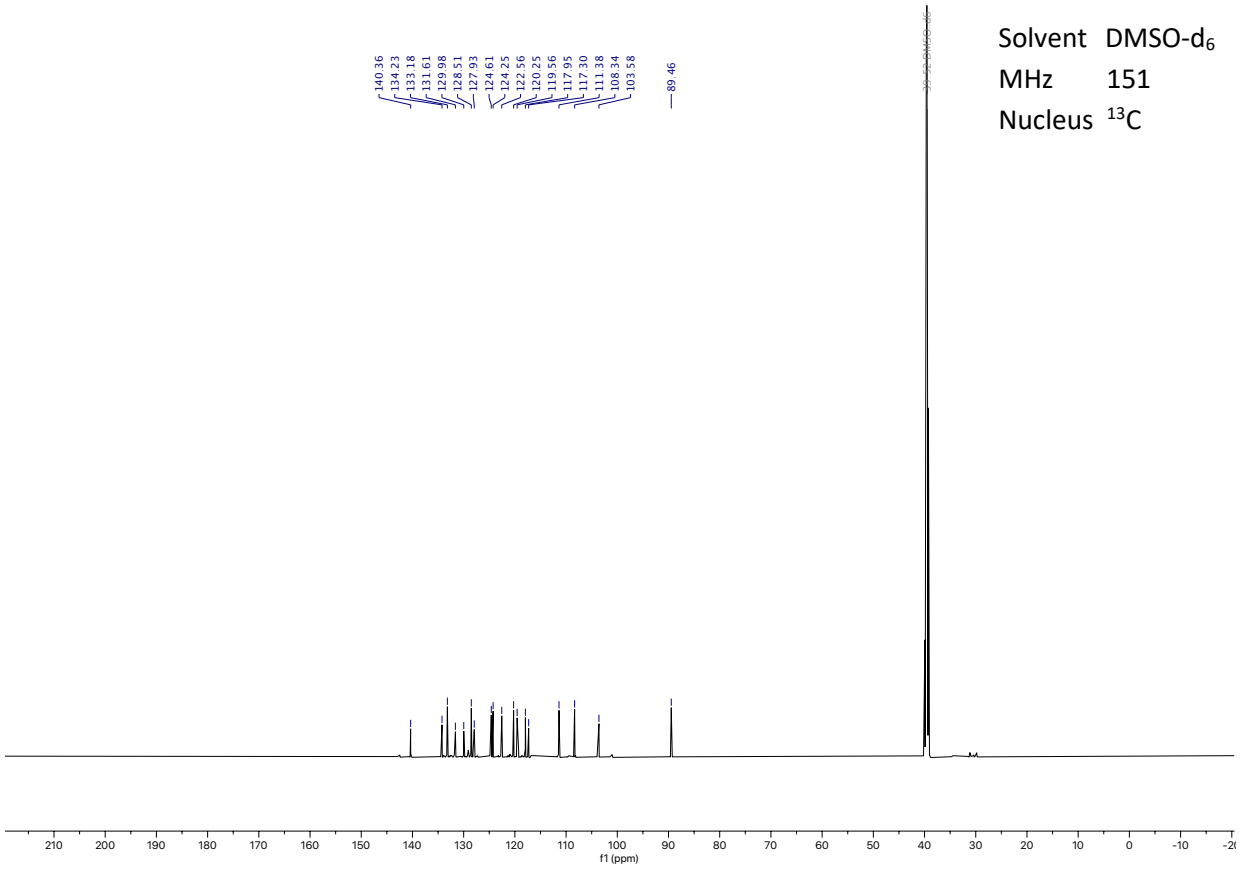

NH2
N

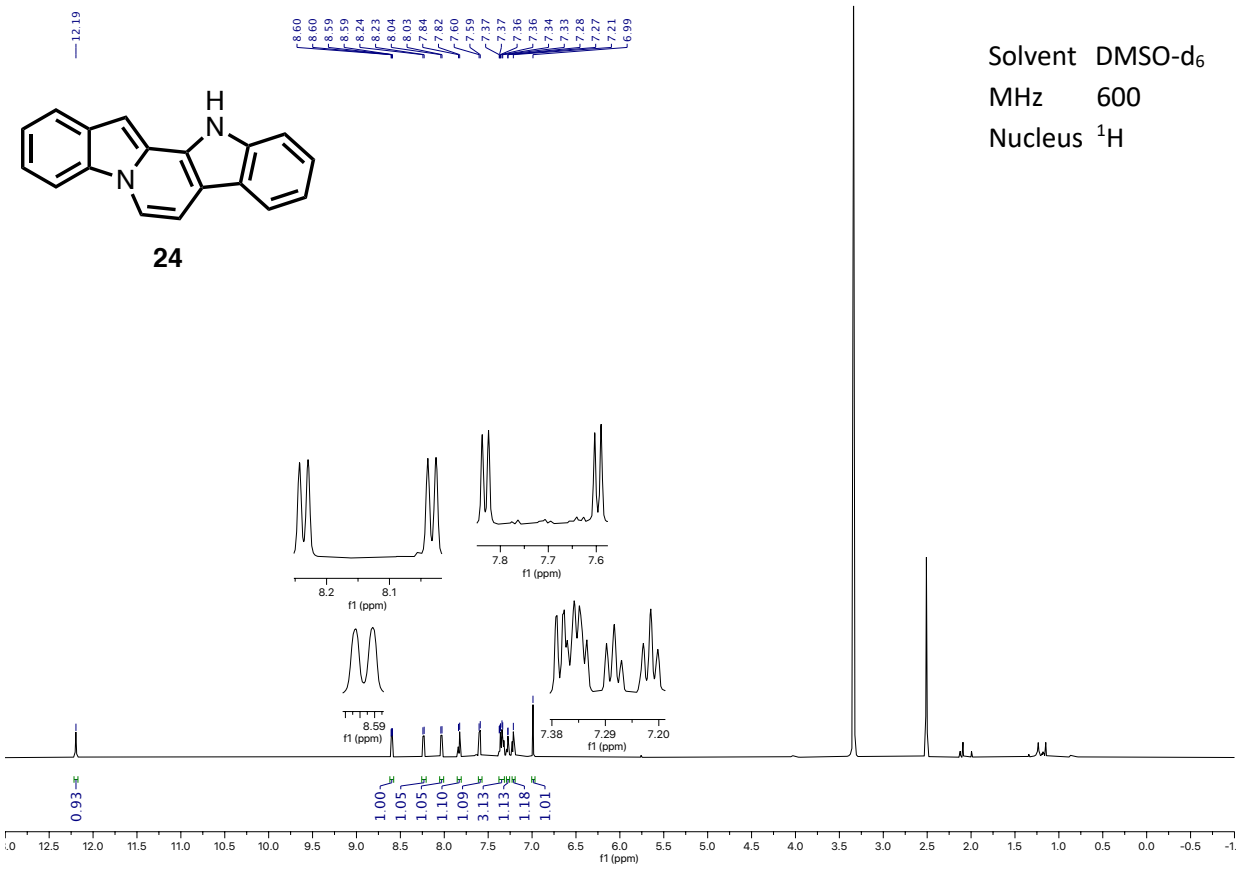
23

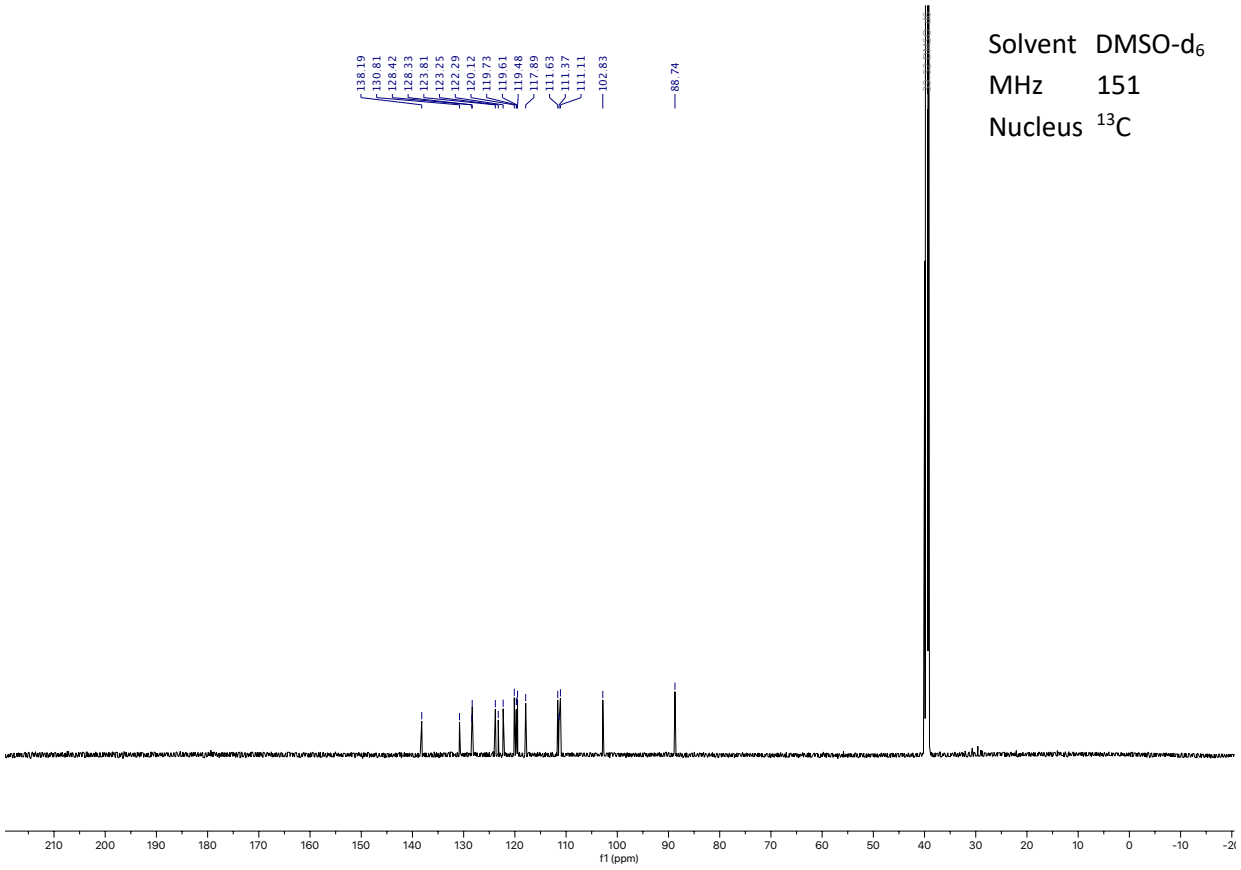
8.09
8.08
8.01
7.99
7.74
7.73
7.27
7.20
6.77
6.45
6.15
6.14
5.14
2.05, CD3,2CO
Solvent Acetone-d6
MHz 700
Nucleus 1H
1.03
0.97
1.00
1.03
0.99
0.93
0.94
0.97
1.90
f1 (ppm)


139.16
132.60
131.30
129.47
123.00
121.19
120.08
114.91
111.64
110.22
99.23
88.91
29.84, CD3,2CO
Solvent Acetone-d6
MHz 176
Nucleus 13C
f1 (ppm)


Solvent DMSO-d6
MHz 600
Nucleus 1H
Br
HN
N
S60


Solvent DMSO-d6
MHz 151
Nucleus 13C


12.19
8.60
8.60
8.59
8.59
8.24
8.23
8.04
8.03
7.84
7.82
7.60
7.59
7.37
7.37
7.36
7.36
7.34
7.33
7.28
7.27
7.21
6.99
H
N
N
24
Solvent DMSO-d6
MHz 600
Nucleus 1H
8.2
8.1
f1 (ppm)
7.8
7.7
7.6
f1 (ppm)
8.59
f1 (ppm)
7.38
7.29
7.20
f1 (ppm)
0.93
1.00
1.05
1.05
1.10
1.09
3.13
1.13
1.18
1.01
f1 (ppm)


138.19
130.81
128.42
128.33
123.81
123.25
122.29
120.12
119.73
119.61
119.48
117.89
111.63
111.37
111.11
102.83
88.74
Solvent DMSO-d6
MHz 151
Nucleus 13C
f1 (ppm)

13 References

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