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Rhodium-catalyzed C–H functionalization of heteroarenes using indoleBX hypervalent iodine reagents

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Letter

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Abstract

The C–H indolation of heteroarenes was realized using the benziodoxolone hypervalent iodine reagents indoleBXs. Functionalization of the C–H bond in bipyridinones and quinoline *N*-oxides catalyzed by a rhodium complex allowed to incorporate indole rings into aza-heteroaromatic compounds. These new transformations displayed complete regioselectivity for the C-6 position of bipyridinones and the C-8 position of quinoline *N*-oxides and tolerated a broad range of functionalities, such as halogens, ethers, or trifluoromethyl groups.

Introduction

Nitrogen-containing heteroaromatic compounds have valuable properties in medicinal chemistry, pharmacology and functional materials. Among those, pyridinone, sometimes called pyridone, is a key structural motif of well-known active compounds and natural products (Figure 1) [1]. For example, the 2-pyridinone ring is present in milrinone (**1**), used to treat heart failure, while a 4-pyridinone is part of mimosine (**2**), an alkaloid isolated from *Mimosa pudica*. A benzene-fused pyridinone – a quinolone – can be found in brexpiprazole (**3**), a drug used against schizophrenia. In addition, the indole core is also omnipresent in bioactive compounds [2]. It can be directly bound to other heterocycles, such as a dihydropyrazidinone in hamacanthine A (**4**) (Figure 1) [3]. Due to their occurrence in biologically active compounds, it is therefore attractive to develop new methods to functionalize pyridinones. The introduction of further heterocyclic rings, such as indoles, is particularly attractive.

Most of the methods for indolylpyridinone synthesis involve a condensation cascade process to generate the pyridinone ring [4-6]. These methods usually require an electron-withdrawing group (nitrile, nitro, carbonyl), which ends up on the pyridi-

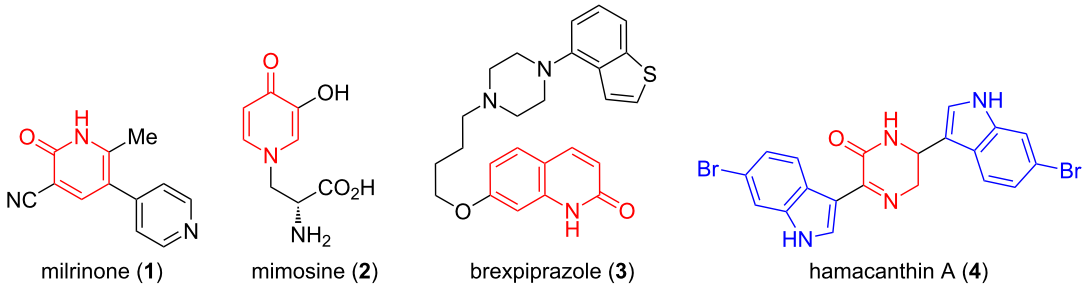
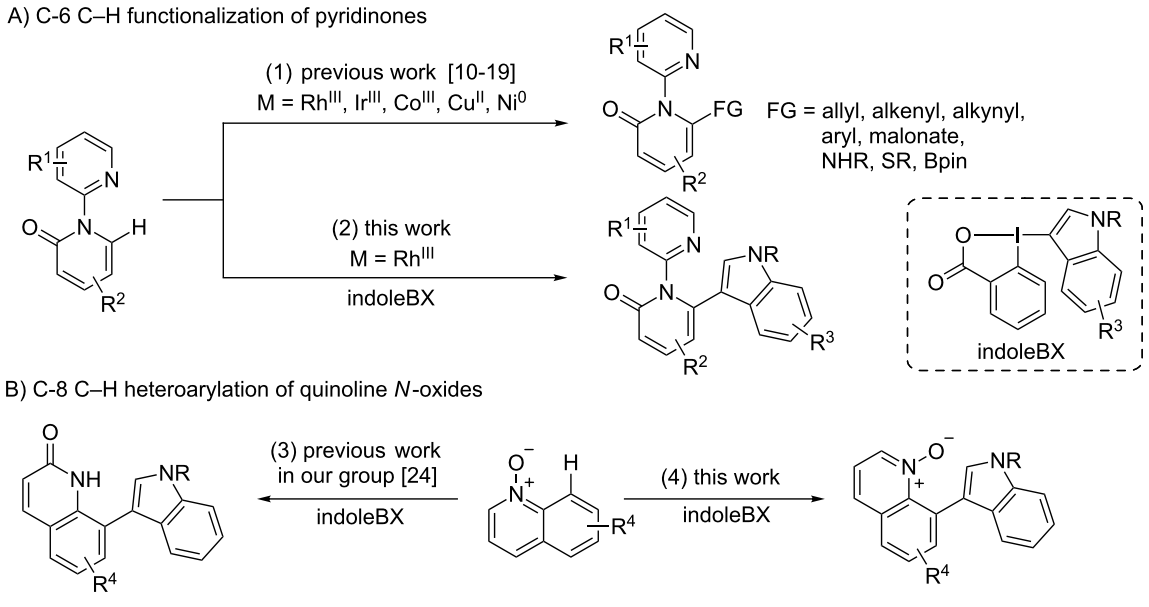


Figure 1: Bioactive compounds with pyridinone, quinolone and indole cores.

none ring. As alternative, a Suzuki–Miyaura coupling between 3-halogenoindoles and (2-methoxypyridyl)boronic acids followed by a deprotection of the methoxy group [7,8] or transition-metal-catalyzed annulation methods [9] have also been reported.

In contrast, several procedures have been described for the modification of pyridinones to introduce other substituents, especially based on highly efficient C–H functionalization methods [10]. Very recently, several research groups have selectively functionalized the C-6 C–H bond by using a 2-pyridyl directing group on the nitrogen and a transition metal catalyst (reaction 1, Scheme 1A) [11-19]. In particular, Li and co-workers have used ethynylbenziodoxolone (EBX) hypervalent iodine reagents to achieve a regiodivergent alkynylation of the pyridinone core employing either a gold(I) or a rhodium(III) catalyst for C-5 and C-6 functionalization, respectively [13]. Hypervalent iodine reagents in general [20], and benziodoxole derivatives in particular [21], have found broad application in synthetic chemistry. Aryl iodonium salts have been used successfully in transition-metal-catalyzed transformations [22], but only one application of indole iodonium salts in copper catalysis by You and co-workers had been reported until 2017 [23]. In this context, indole-based benziodoxole hypervalent iodine reagents, recently introduced by Yoshikai's and our group [24-27], appeared ideal partners to develop a new C–H heteroarylation of pyridinones.

Herein, we report the selective C–H heteroarylation of the C-6 position of bipyridinones by a rhodium-catalyzed reaction with indoleBX (reaction 2, Scheme 1A). In addition, we demonstrate that the mild conditions developed allow the heteroarylation of the C-8 position of quinoline *N*-oxides, whereas formation of the quinolinone had been observed in our previous work (Scheme 1B). The obtained products combine up to three classes of privileged heterocycles in medicinal chemistry in a



Scheme 1: C–H functionalization of pyridinones and quinoline *N*-oxides.

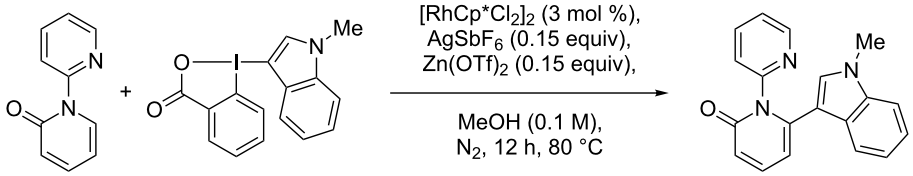
single compound, and are therefore expected to be highly useful building blocks in the search for new bioactive compounds.

Results and Discussion

We started the studies on C–H indolation with the optimization of the reactions conditions (Table 1) for the coupling of [1,2'-bipyridin]-2-one (**5a**) with Me-indoleBX **6a**, easily obtained from commercially available 1-methylindole and 2-iodobenzoic acid [24]. While the reaction conditions previously developed in our group for the C–H functionalization of 2-phenylpyridine [24] failed for the coupling of **5a** with **6a** (Table 1, entry 1), we were pleased to see that addition of 0.15 equiv $Zn(OTf)_2$ allowed a full conversion to the desired product **7a** in 86% yield (Table 1, entry 2). The Lewis acid is supposed to weaken the O–I bond by coordination of the carboxy group in **6a**. No base was required in this case. The reaction was completely selective for the C-6 position of the pyridinone ring. Control experiments pointed out that both Lewis acid (Table 1, entry 3) and $AgSbF_6$ as additive (Table 1, entry 4) were necessary for an efficient reaction. The transformation was tolerant to air (Table 1, entry 5). However, more byproducts were observed. Decreasing the temperature (Table 1, entry 6) or the catalyst loading (Table 1, entry 7) resulted in lower yields. Finally, three control experiments with 1-methylindole (**8**, Table 1, entry 8), 3-iodo-1-methylindole (**9**, Table 1, entry 9) and the poorly stable (1*H*-indol-3-yl)(phenyl)iodonium tetrafluoroborate [23] (**10**, Table 1, entry 10) did not lead to the formation of **7a**, highlighting the unique reactivity of the benziodoxolone hypervalent iodine reagent.

The scope and limitations of the reaction were then studied (Scheme 2). The diversification of the directing group was examined first. The unsubstituted pyridine group led to the formation of product **7a** in 86% yield. The electron-rich 5-methoxypyridine and the electron-poor 5-trifluoromethylpyridine directing groups gave products **7b** and **7c** in 82% and 72% yield, respectively. When a nitro group was present on the pyridine (**5d**), the product was not observed, probably due to a weaker coordination of the nitrogen on the pyridine. Pyrimidine could not be used as directing group (**5e**), confirming what has already been reported by others authors [13]. Quinoline **7f** was obtained in 79% yield. Concerning the pyridinone core, both an electron-donating methyl group and electron-withdrawing trifluoromethyl and fluoro groups (**7g–i**) were well tolerated in the C-3 position. However, the strong electron-withdrawing CF_3 group resulted in a lower 65% yield (**7h**). This observation is also true for the C-4 position. Indeed, products **7j–l** were synthesized in 78% yield for a methyl, 66% yield for a trifluoromethyl and 84% yield for a benzyloxy substituent. As previously reported [13], 5-substituted pyridinone **5m** could not

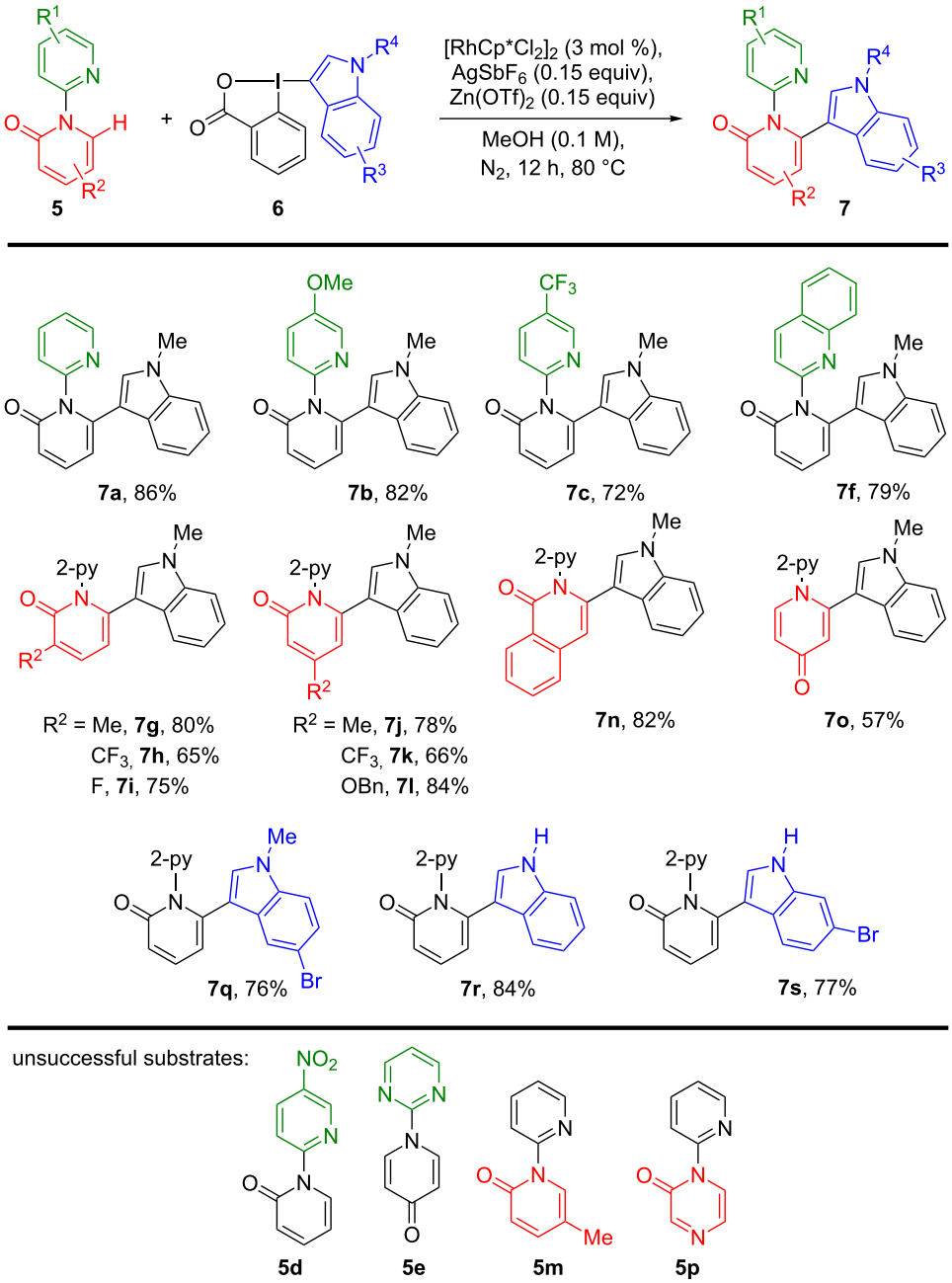
Table 1: Optimization of the C–H heteroarylation[a,b].



5a **6a** **7a**

Entry	Changes from conditions	Yield (%)
1	$[RhCp^*Cl_2]_2$ (2.5 mol %), $AgSbF_6$ (0.10 equiv), NaOPiv (0.10 equiv), DCE, 12 h, 50 °C	no reaction
2	–	86
3	without $Zn(OTf)_2$	no reaction
4	without $AgSbF_6$	60
5	under air atmosphere	80
6	60 °C	48
7	1 mol % of $[RhCp^*Cl_2]_2$	75
8	1-methylindole (**8**)	no reaction
9	3-iodo-1-methylindole (**9**)	0[c]
10	iodonium salt **10**	0[c]

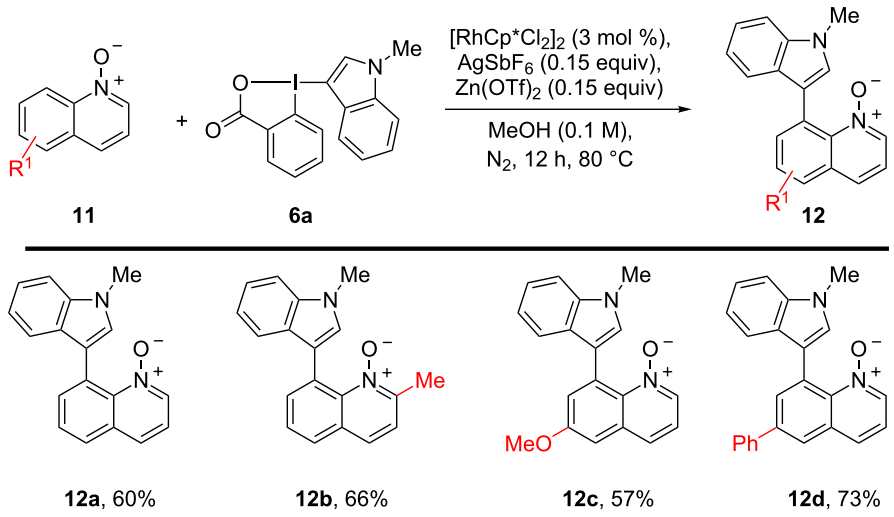
[a]Reactions conditions: **5** (0.20 mmol), **6** (0.20 mmol), $[RhCp^*Cl_2]_2$ (3.7 mg, 6.0 μmol, 3 mol %), $AgSbF_6$ (10.3 mg, 30.0 μmol, 0.15 equiv), $Zn(OTf)_2$ (10.9 mg, 30.0 μmol, 0.15 equiv), methanol (2.0 mL) at 80 °C for 12 h. [b]Isolated yield after preparative TLC. [c]Decomposition.



Scheme 2: Scope and limitations of the Rh-catalyzed C–H activation of [1,2'-bipyridin]-2-one.

be functionalized. Isoquinolone **7n** was prepared in 82% yield. The methodology could also be applied to 4-pyridone in a moderate 57% yield for product **7o**. Unfortunately, pyrazin-2-one **5p** could not be functionalized. Modification of the hypervalent iodine reagent was then investigated with three selected compounds only. A bromo substituent on the benzene ring was well tolerated (**7q**). The coupling could be also performed with N–H unprotected indoleBX reagents to afford products **7r** and **7s** in 84% and 77% yield, respectively.

We also applied these conditions to different quinoline *N*-oxides (Scheme 3). This class of substrates had also been used for C–H alkynylation using EBX reagents [28]. During our previous work, we had attempted the C8-heteroarylation of quinoline *N*-oxide with Me-indoleBX **6a**. However, the transformation required a temperature of 100 °C, leading to the formation of the corresponding isoquinolone in only 38% yield [24]. By employing the milder conditions developed for pyridinones, we were pleased to see that the *N*-oxide group could be preserved and



Scheme 3: Scope of the Rh-catalyzed *peri* C–H activation of quinoline *N*-oxides.

product **12a** was obtained in 60% yield. A methyl substitution in C-2 position gave the product **12b** in 66% yield. In C-6 position both a methoxy and a phenyl group were well tolerated giving 57% and 73% yield of products **12c** and **12d**.

The pyridine directing group could be cleaved by alkylation of the pyridine nitrogen using methyl triflate followed by reduction with sodium cyanoborohydride to deliver the N–H unprotected pyridinone **13** in 74% yield (Scheme 4) [29]. A rearrangement of the *N*-oxide furnished the corresponding isoquinolone **14** in 62% yield.

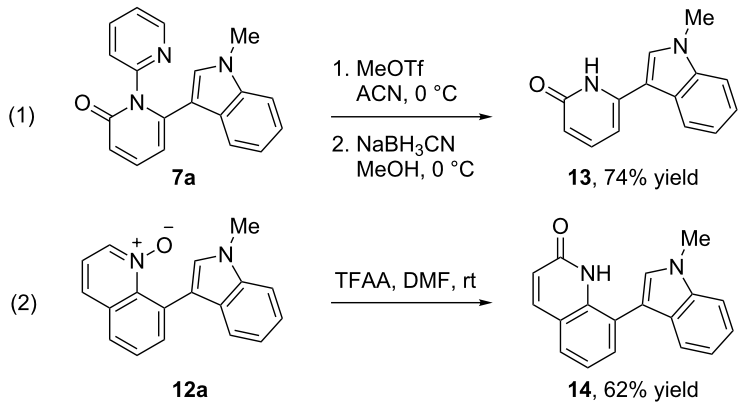
Conclusion

In summary, we have developed the C-6 selective C–H heteroarylation of pyridin-2-ones using indoleBXs as coupling partners, $[RhCp^*Cl_2]_2$ as catalyst, $AgSbF_6$ as co-catalyst and $Zn(OTf)_2$ as Lewis acid. The reaction could also be applied to functionalize one pyridin-4-one in C-6 position, one isoquinolinone in C-3 position and quinoline *N*-oxides in C-8 position. After cleavage of the directing group or rearrangement of the *N*-oxide function, we were able to access 6-(indol-3-yl)pyridinone and 8-(indol-3-yl)quinolone. The developed transformations give access to important heterocyclic building blocks for synthetic and medicinal chemistry and set the stages for the development of other C–H heteroarylation processes based on indoleBX reagents.

Experimental

General procedure for C–H heteroarylation

In a sealed tube, $[RhCp^*Cl_2]_2$ (3.7 mg, 6.0 µmol, 3 mol %), $AgSbF_6$ (10.3 mg, 30.0 µmol, 0.15 equiv), $Zn(OTf)_2$ (10.9 mg, 30.0 µmol, 0.15 equiv), the corresponding pyridinone or quino-



Scheme 4: Product modifications.

line *N*-oxide (0.20 mmol, 1.00 equiv) and the corresponding hypervalent iodine reagent (0.20 mmol, 1.00 equiv) were solubilized in dry MeOH (2.0 mL, 0.1 M) under N_2 atmosphere. The mixture was stirred at 80 °C for 12 h. The mixture was then diluted with DCM (5 mL) and quenched with a saturated aqueous solution of $NaHCO_3$ (5 mL). The two layers were separated and the aqueous layer was extracted twice with DCM (5 mL). The organic layers were combined, dried over magnesium sulfate dehydrate, filtered and concentrated under reduced pressure. The crude residue was purified by preparative TLC using DCM/MeOH to afford the pure desired compound.

Supporting Information

Supporting Information File 1

Detailed experimental procedures, analytical data for all compounds and copies of the NMR spectra of new compounds.
[https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-14-102-S1.pdf]

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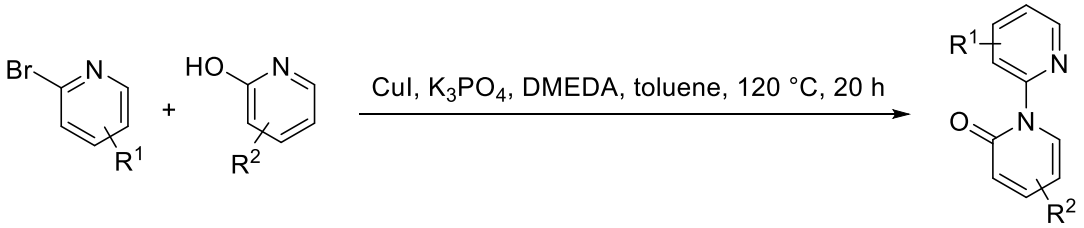
Contents

1. General methods

All reagents and solvents were purchased from commercial sources ABCR, Acros, Sigma Aldrich, Fluka, VWR, Aplichem or Merck and used as such unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å. TLC was performed on Merck silica gel 60 F254 TLC glass plates and visualized with UV light, permanganate stain or phosphomolybdic acid stain. Melting points were measured on a calibrated Büchi B-540 melting point apparatus using open glass capillaries. ^{1}H-NMR spectra were recorded on a Bruker DPX-400 400 MHz spectrometer in $CDCl_3$, CD_2Cl_2 or DMSO-d6; all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal CD_2Cl_2 signal at 5.32 ppm or the internal DMSO signal at 2.50 ppm as standard. The data is being reported as (s = singlet d = doublet t = triplet q = quadruplet quint = quintet m = multiplet or unresolved bs = broad signal, coupling constant(s) in Hz, integration, interpretation). 19F-NMR spectra were recorded on a Bruker DPX-400 376 MHz spectrometer in $CDCl_3$. ^{13}C-NMR spectra were recorded with 1H-decoupling on a Bruker DPX-400 101 MHz spectrometer in $CDCl_3$, CD_2Cl_2 or DMSO-d6; all signals are reported in ppm with the internal chloroform signal at 77.2 ppm, the internal CD_2Cl_2 signal at 53.8 ppm or the internal DMSO signal at 39.5 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 with an ATR device and a ZnSe prisma and are reported as cm^{-1} (w = weak, m = medium, s = strong, br = broad). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API.

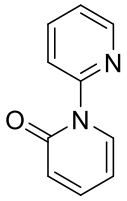
2. Syntheses of starting materials

2. 1. General procedure A for the synthesis of pyridinones



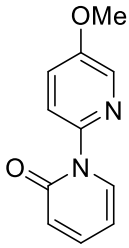
Following a reported procedure,[1] copper iodide (5 mol %), potassium phosphate tribasic (2.00 equiv), the corresponding 2-hydroxypyridine (1.00 equiv) and the corresponding 2-bromopyridine (2.00 equiv) were suspended in toluene [0.4 M] under N_2. *N*,*N*'-dimethylethylenediamine (0.10 equiv) was added and the resulting mixture was stirred 20 h at 120 °C. The resulting mixture was allowed to cool to rt and then quenched with water. A small amount of *N*,*N*'-dimethylethylenediamine was added to dissolve the residual copper salts into the aqueous phase. The layers were separated and the aqueous layer was extracted three times with EtOAc (20 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated under reduced pressure. A purification by flash chromatography (eluent DCM/EtOAc 1:1 with 4%vv of NEt_3) affordeded the desired product.

2*H*-[1,2'-Bipyridin]-2-one (5a)



Following general procedure **A** and starting from commercially available 2-hydroxypyridine (1.43 g, 15.0 mmol) and 2-bromopyridine (2.86 mL, 30.0 mmol), **5a** (2.46 g, 14.3 mmol, 95%) (CAS number 3480-65-7) was obtained as a pale yellow solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 4.7 Hz, 1H, $\underline{H}_{Ar}$), 7.94 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$), 7.85 (ddd, *J* = 13.9, 7.4, 4.0 Hz, 2H, $\underline{H}_{Ar}$), 7.38 (ddd, *J* = 8.9, 6.5, 2.0 Hz, 1H, $\underline{H}_{Ar}$), 7.33-7.29 (m, 1H, $\underline{H}_{Ar}$), 6.64 (d, *J* = 9.2 Hz, 1H, $\underline{H}_{Ar}$), 6.29 (t, *J* = 6.8 Hz, 1H, $\underline{H}_{Ar}$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 152.0, 149.0, 140.3, 137.9, 136.2, 123.3, 122.2, 121.6, 106.4. Spectra data matched with the values reported in literature.[2]
HRMS calculated for $C_{10}H_8N_2NaO^+$ $[M+Na]^+$ 195.0529; found 195.0535.

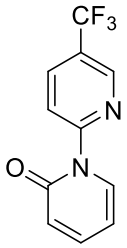
5'-Methoxy-2*H*-[1,2'-bipyridin]-2-one (5b)



Following general procedure **A** and starting from commercially available 2-hydroxypyridine (143 mg, 1.50 mmol) and 2-bromo-5-methoxypyridine (564 mg, 3.00 mmol), **5b** (231 mg, 1.14 mmol, 76%) (CAS number 10201-69-1) was obtained as a white solid.[3]
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 3.0 Hz, 1H, $\underline{H}_{Ar}$), 7.80 (d, *J* = 8.9 Hz, 1H, $\underline{H}_{Ar}$), 7.76 (dd, *J* = 7.0, 1.9 Hz, 1H, $\underline{H}_{Ar}$), 7.40-7.29 (m, 2H, $\underline{H}_{Ar}$), 6.61 (d, *J* = 9.2 Hz, 1H, $\underline{H}_{Ar}$), 6.26 (td, *J* = 6.9, 1.2 Hz, 1H, $\underline{H}_{Ar}$), 3.88 (s, 3H, $OC\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 155.4, 145.0, 140.1, 136.5, 135.8, 122.4, 122.0, 121.9, 106.2, 56.1.
HRMS calculated for $C_{11}H_{11}N_2O_2^+$ $[M+H]^+$ 203.0815; Found 203.0810.

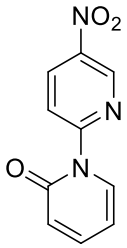
[1] Odani, R.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem. Int. Ed.* **2014**, *53*, 10784–10788.
[2] Londregan, A. T.; Jennings, S.; Wei, L. *Org. Lett.* **2011**, *13*, 1840–1843.
[3] Pyridones **5b-d**, **5e-m** and **5p** are known compounds, however no characterization has been reported. See Ref 1.

5'-(Trifluoromethyl)-2*H*-[1,2'-bipyridin]-2-one (5c)



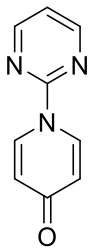
Following general procedure **A** and starting from commercially available 2-hydroxypyridine (143 mg, 1.50 mmol) and 2-bromo-5-(trifluoromethyl)pyridine (678 mg, 3.00 mmol), **5c** (245 mg, 1.02 mmol, 68%) (CAS number 1845694-34-9) was obtained as a white solid.[3]
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H, $\underline{H}_{Ar}$), 8.21 (d, *J* = 8.6 Hz, 1H, $\underline{H}_{Ar}$), 8.05 (dd, *J* = 8.6, 2.2 Hz, 1H, $\underline{H}_{Ar}$), 7.96 (dd, *J* = 7.2, 1.5 Hz, 1H, $\underline{H}_{Ar}$), 7.40 (ddd, *J* = 8.7, 6.5, 2.1 Hz, 1H, $\underline{H}_{Ar}$), 6.64 (d, *J* = 9.3 Hz, 1H, $\underline{H}_{Ar}$), 6.32 (td, *J* = 7.2, 1.3 Hz, 1H, $\underline{H}_{Ar}$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -62.3.
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 154.3, 146.0 (q, *J* = 4.2 Hz), 140.7, 135.3, 135.2 (q, *J* = 3.3 Hz), 125.9 (q, *J* = 33.5 Hz), 123.2 (q, *J* = 272.3 Hz), 122.5, 121.2, 106.9.
HRMS calculated for $C_{11}H_8F_3N_2O^+$ $[M+H]^+$ 241.0583; Found 241.0581.

5'-Nitro-2*H*-[1,2'-bipyridin]-2-one (5d)



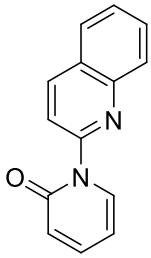
Following general procedure **A** and starting from commercially available 2-hydroxypyridine (143 mg, 1.50 mmol) and 2-bromo-5-nitropyridine (609 mg, 3.00 mmol), **5d** (189 mg, 0.87 mmol, 58%) (CAS number 10201-88-4) was obtained as yellow solid.[3]
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.38 (d, *J* = 2.6 Hz, 1H, $\underline{H}_{Ar}$), 8.60 (dd, *J* = 9.0, 2.7 Hz, 1H, $\underline{H}_{Ar}$), 8.40 (d, *J* = 9.0 Hz, 1H, $\underline{H}_{Ar}$), 8.07 (dd, *J* = 7.3, 1.5 Hz, 1H, $\underline{H}_{Ar}$), 7.43 (ddd, *J* = 8.7, 6.5, 2.0 Hz, 1H, $\underline{H}_{Ar}$), 6.67 (d, *J* = 9.3 Hz, 1H, $\underline{H}_{Ar}$), 6.38-6.34 (m, 1H, $\underline{H}_{Ar}$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 155.3, 144.5, 142.9, 140.8, 134.9, 133.1, 122.6, 121.2, 107.2.
HRMS calculated for $C_{10}H_8N_3O_3^+$ $[M+H]^+$ 218.0560; Found 218.0559.

1-(Pyrimidin-2-yl)pyridin-4(1*H*)-one (5e)



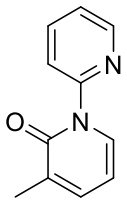
2-chloropyrimidine (172 mg, 1.50 mmol), 4-hydroxypyridine (285 mg, 3.00 mmol), K_2CO_3 (415 mg, 3.00 mmol) were solubilized in water (2 mL) and heated at 90 °C for 30 min. After cooling at rt, the precipitate was filtered off and dried under vacuum to give **5e** (159 mg, 0.918 mmol, 61%) (CAS number 29049-26-1) as a white solid.
^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.83 (d, *J* = 8.2 Hz, 2H), 8.73 (d, *J* = 4.8 Hz, 2H), 7.26 (t, *J* = 4.8 Hz, 1H), 6.36 (d, *J* = 8.2 Hz, 2H).
^{13}C NMR (101 MHz, CD_2Cl_2) δ 180.5, 159.2, 156.0, 134.9, 119.1, 118.7.
HRMS calculated for $C_9H_8N_3O^+$ $[M+H]^+$ 174.0662; Found 174.0661.

1-(Quinolin-2-yl)pyridin-2(1H)-one (5f)



Following general procedure **A** and starting from commercially available 2-hydroxypyridine (152 mg, 1.60 mmol) and 2-bromoquinoline (666 mg, 3.20 mmol), **5f** (342 mg, 1.54 mmol, 96%) (CAS number 10168-48-6) was obtained as a white solid.[3]
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.7 Hz, 1H, $\underline{H}_{Ar}$), 8.08 (d, *J* = 8.4 Hz, 1H, $\underline{H}_{Ar}$), 8.01 (t, *J* = 8.1 Hz, 2H, $\underline{H}_{Ar}$), 7.89 (d, *J* = 8.1 Hz, 1H, $\underline{H}_{Ar}$), 7.76 (t, *J* = 7.7 Hz, 1H, $\underline{H}_{Ar}$), 7.61 (t, *J* = 7.5 Hz, 1H, $\underline{H}_{Ar}$), 7.44 (ddd, *J* = 8.9, 6.5, 1.9 Hz, 1H, $\underline{H}_{Ar}$), 6.69 (d, *J* = 9.3 Hz, 1H, $\underline{H}_{Ar}$), 6.36 (t, *J* = 6.8 Hz, 1H, $\underline{H}_{Ar}$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 152.0, 147.3, 140.6, 137.9, 136.5, 130.2, 129.1, 127.7, 127.7, 127.4, 122.4, 119.6, 106.7.
HRMS calculated for $C_{14}H_{11}N_2O^+$ $[M+H]^+$ 223.0866; found 223.0872.

3-Methyl-2*H*-[1,2'-bipyridin]-2-one (5g)



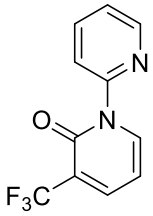
Following general procedure **A** and starting from commercially available 2-hydroxy-3-methylpyridine (458 mg, 4.20 mmol) and 2-bromopyridine (0.80 mL, 8.4 mmol), **5g** (678 mg, 3.64 mmol, 87%) (CAS number 1644063-32-0) was obtained as a colorless oil.[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59-8.54 (m, 1H, $\underline{H}_{Ar}$), 7.95-7.91 (m, 1H, $\underline{H}_{Ar}$), 7.85-7.79 (m, 1H, $\underline{H}_{Ar}$), 7.73 (d, *J* = 7.1 Hz, 1H, $\underline{H}_{Ar}$), 7.33-7.26 (m, 2H, $\underline{H}_{Ar}$), 6.22 (t, *J* = 6.9 Hz, 1H, $\underline{H}_{Ar}$), 2.19 (s, 3H, $C\underline{H}_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 152.4, 148.9, 137.7, 137.3, 133.6, 130.9, 123.1, 121.7, 106.1, 17.4.

HRMS calculated for $C_{11}H_{11}N_2O^+$ $[M+H]^+$ 187.0866; found 187.0866.

3-(Trifluoromethyl)-2*H*-[1,2'-bipyridin]-2-one (5h)



Following general procedure **A** and starting from commercially available 2-hydroxy-3-(trifluoromethyl)-pyridine (326 mg, 2.00 mmol) and 2-bromopyridine (0.38 mL, 4.0 mmol), **5h** (252 mg, 1.05 mmol, 52%) (CAS number 1644063-33-1) was obtained as a white solid.[3]

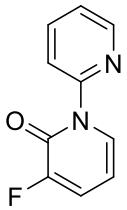
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 4.9, 1.7 Hz, 1H), 8.12 (dd, *J* = 7.1, 1.9 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.88-7.79 (m, 2H), 7.35 (ddd, *J* = 7.4, 4.9, 0.9 Hz, 1H), 6.37 (t, *J* = 7.0 Hz, 1H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -66.0.

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 150.7, 149.0, 140.2, 139.7 (q, *J* = 4.9 Hz), 137.9, 123.8, 122.6 (q, *J* = 271.8 Hz), 121.8 (q, *J* = 30.9 Hz), 121.5, 104.4.

HRMS calculated for $C_{11}H_8F_3N_2O^+$ $[M+H]^+$ 241.0583; Found 241.0584.

3-Fluoro-2*H*-[1,2'-bipyridin]-2-one (5i)



Following general procedure **A** and starting from commercially available 3-fluro-2-hydroxypyridine (226 mg, 2.00 mmol) and 2-bromopyridine (0.38 mL, 4.0 mmol), **5i** (281 mg, 1.48 mmol, 74%) (CAS number 1872255-08-7) was obtained as a white solid.[3]

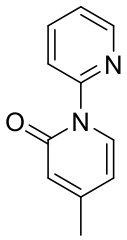
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (ddd, *J* = 4.9, 1.9, 0.8 Hz, 1H, $\underline{H}_{Ar}$), 7.97 (dt, *J* = 8.2, 0.9 Hz, 1H, $\underline{H}_{Ar}$), 7.85 (ddd, *J* = 8.2, 7.5, 1.9 Hz, 1H, $\underline{H}_{Ar}$), 7.74 (dt, *J* = 7.2, 1.7 Hz, 1H, $\underline{H}_{Ar}$), 7.34 (ddd, *J* = 7.4, 4.9, 1.0 Hz, 1H, $\underline{H}_{Ar}$), 7.15 (ddd, *J* = 9.2, 7.4, 1.8 Hz, 1H, $\underline{H}_{Ar}$), 6.22 (td, *J* = 7.3, 4.5 Hz, 1H, $\underline{H}_{Ar}$).

^{19}F NMR (376 MHz, $CDCl_3$) δ -130.1.

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.2 (d, *J* = 26.5 Hz), 152.8 (d, *J* = 249.9 Hz), 151.1, 149.1, 138.1, 131.4 (d, *J* = 5.3 Hz), 123.7, 121.4, 120.4 (d, *J* = 17.3 Hz), 104.1 (d, *J* = 5.9 Hz).

HRMS calculated for $C_{10}H_8FN_2O^+$ $[M+H]^+$ 191.0615; Found 191.0618.

4-Methyl-2*H*-[1,2'-bipyridin]-2-one (5j)



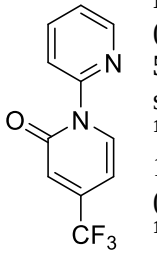
Following general procedure **A** and starting from commercially available 2-hydroxy-4-methylpyridine (458 mg, 4.20 mmol) and 2-bromopyridine (0.80 mL, 8.4 mmol), **5j** (764 mg, 4.10 mmol, 98%) (CAS number 1644063-34-2) was obtained as an off-white solid.[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.9 Hz, 1H, $\underline{H}_{Ar}$), 7.95 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$), 7.84-7.76 (m, 2H, $\underline{H}_{Ar}$), 7.29 (ddd, *J* = 7.3, 4.9, 0.9 Hz, 1H, $\underline{H}_{Ar}$), 6.44 (s, 1H, $\underline{H}_{Ar}$), 6.14 (dd, *J* = 7.2, 1.8 Hz, 1H, $\underline{H}_{Ar}$), 2.22 (s, 3H, $C\underline{H}_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 152.1, 152.0, 148.9, 137.8, 135.0, 123.1, 121.5, 120.2, 109.2, 21.5.

HRMS calculated for $C_{11}H_{11}N_2O^+$ $[M+H]^+$ 187.0866; found 187.0866.

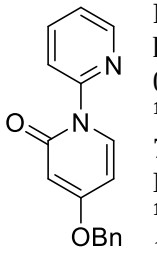
4-(Trifluoromethyl)-2*H*-[1,2'-bipyridin]-2-one (5k)



Following general procedure **A** and starting from commercially available 2-hydroxy-3-(trifluoromethyl)-pyridine (245 mg, 1.50 mmol) and 2-bromopyridine (0.29 mL, 3.0 mmol), **5k** (203 mg, 0.850 mmol, 57%) (CAS number 1644063-35-3) was obtained as a pale yellow solid.[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (ddd, *J* = 4.9, 1.8, 0.8 Hz, 1H, $\underline{H}_{Ar}$), 8.06 (d, *J* = 7.4 Hz, 1H, $\underline{H}_{Ar}$), 7.95 (dt, *J* = 8.2, 0.9 Hz, 1H, $\underline{H}_{Ar}$), 7.85 (ddd, *J* = 8.2, 7.5, 1.9 Hz, 1H, $\underline{H}_{Ar}$), 7.35 (ddd, *J* = 7.4, 4.9, 1.0 Hz, 1H, $\underline{H}_{Ar}$), 6.93-6.91 (m, 1H, $\underline{H}_{Ar}$), 6.41 (dd, *J* = 7.4, 2.0 Hz, 1H, $\underline{H}_{Ar}$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.0.
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 151.0, 149.2, 141.7 (q, *J* = 34.0 Hz), 138.1, 138.0, 123.8, 122.1 (q, *J* = 274.0 Hz), 121.2, 119.9 (q, *J* = 4.4 Hz), 101.6 (q, *J* = 2.4 Hz).
HRMS calculated for $C_{11}H_8F_3N_2O^+$ $[M+H]^+$ 241.0583; Found 241.0582.

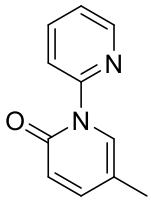
4-(Benzyloxy)-2*H*-[1,2'-bipyridin]-2-one (5l)



Following general procedure **A** and starting from commercially available 4-benzyloxy-2-hydroxypyridine (302 g, 1.50 mmol) and 2-bromopyridine (0.29 mL, 3.0 mmol), **5l** (113 mg, 0.410 mmol, 27%) (CAS number 1644063-36-4) was obtained as a white solid.[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 3.9 Hz, 1H, $\underline{H}_{Ar}$), 7.94 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$), 7.86-7.78 (m, 2H, $\underline{H}_{Ar}$), 7.403-7.33 (m, 5H, $\underline{H}_{Ar}$), 7.30-7.27 (m, 1H, $\underline{H}_{Ar}$), 6.11 (dd, *J* = 7.8, 2.6 Hz, 1H, $\underline{H}_{Ar}$), 6.03 (d, *J* = 2.5 Hz, 1H, $\underline{H}_{Ar}$), 5.05 (s, 2H, $OC\underline{H}_2$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7, 163.7, 151.8, 148.9, 137.8, 136.2, 135.3, 128.9 (2C), 128.7, 127.9 (2C), 122.9, 121.5, 102.2, 98.6, 70.5.
HRMS calculated for $C_{17}H_{14}N_2NaO_2^+$ $[M+Na]^+$ 301.0953; Found 301.0948.

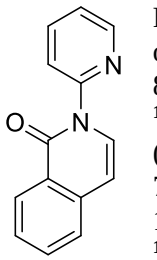
5-Methyl-2*H*-[1,2'-bipyridin]-2-one (5m)



Following general procedure **A** and starting from commercially available 2-hydroxy-4-methylpyridine (458 mg, 4.20 mmol) and 2-bromopyridine (0.80 mL, 8.4 mmol), **5m** (691 mg, 3.71 mmol, 88%) (CAS number 53427-88-6) was obtained as a white solid.[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 3.9 Hz, 1H, $\underline{H}_{Ar}$), 7.93 (d, *J* = 8.1 Hz, 1H, $\underline{H}_{Ar}$), 7.85-7.78 (m, 1H, $\underline{H}_{Ar}$), 7.64 (s, 1H, $\underline{H}_{Ar}$), 7.32-7.22 (m, 2H, $\underline{H}_{Ar}$), 6.58 (d, *J* = 9.3 Hz, 1H, $\underline{H}_{Ar}$), 2.12 (s, 3H, $C\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6, 152.1, 148.9, 143.1, 137.7, 133.2, 123.0, 121.7, 121.6, 115.3, 17.3.
HRMS calculated for $C_{11}H_{11}N_2O^+$ $[M+H]^+$ 187.0866; found 187.0867.

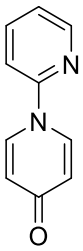
2-(Pyridin-2-yl)isoquinolin-1(2*H*)-one (5n)



Following general procedure **A** and starting from commercially available isoquinolin-1(2*H*)-one (218 mg, 1.50 mmol) and 2-bromopyridine (0.29 mL, 3.0 mmol), **5n** (276 mg, 1.24 mmol, 83%) (CAS number 1532-89-4) was obtained as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.49 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.86 (td, *J* = 7.8, 1.9 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.69 (td, *J* = 8.2, 7.8, 1.3 Hz, 1H), 7.58-7.49 (m, 2H), 7.31 (ddd, *J* = 7.3, 4.9, 0.9 Hz, 1H), 6.63 (d, *J* = 7.6 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 152.4, 148.9, 137.7, 137.2, 133.0, 130.1, 128.5, 127.2, 126.7, 126.1, 122.7, 121.7, 106.9. Spectra data matched with the values reported in literature.[2]
HRMS calculated for $C_{14}H_{10}N_2NaO^+$ $[M+Na]^+$ 245.0685; Found 245.0694.

4*H*-[1,2'-bipyridin]-4-one (5o)



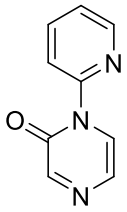
Following general procedure **A** and starting from commercially available 4-hydroxypyridine (143 mg, 1.50 mmol) and 2-bromopyridine (0.29 mL, 3.0 mmol), **5o** (181 mg, 1.05 mmol, 70%) (CAS number 76520-27-9) was obtained as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 4.8 Hz, 1H, $\underline{H}_{Ar}$), 8.18 (d, *J* = 8.0 Hz, 2H, $\underline{H}_{Ar}$), 7.89 (ddd, *J* = 15.7, 8.2, 1.9 Hz, 1H, $\underline{H}_{Ar}$), 7.38 (d, *J* = 8.3 Hz, 1H, $\underline{H}_{Ar}$), 7.30 (dd, *J* = 7.4, 4.8 Hz, 1H, $\underline{H}_{Ar}$), 6.45 (d, *J* = 8.0 Hz, 2H, $\underline{H}_{Ar}$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 180.0, 152.1, 149.2, 139.7, 136.1 (2C), 122.6, 118.9 (2C), 113.0. Spectra data matched with the values reported in literature.[2]

HRMS calculated for $C_{10}H_9N_2O^+$ $[M+H]^+$ 173.0709; Found 173.0713.

1-(Pyridin-2-yl)pyrazin-2(1*H*)-one (5p)



Following general procedure **A** and starting from commercially available 2-hydroxy-4-methylpyridine (192 mg, 2.00 mmol) and 2-bromopyridine (0.38 mL, 4.0 mmol), **5p** (335 mg, 1.93 mmol, 97%) was obtained as a white solid. **mp** 124-126 °C. **Rf** 0.80 (DCM/MeOH 19:1).[3]

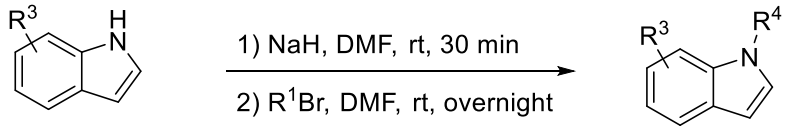
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 4.9, 1.0 Hz, 1H, $\underline{H}_{Ar}$), 8.25 (d, *J* = 0.9 Hz, 1H, $\underline{H}_{Ar}$), 8.16 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$), 7.94 (dd, *J* = 4.7, 1.0 Hz, 1H, $\underline{H}_{Ar}$), 7.87 (td, *J* = 7.9, 1.8 Hz, 1H, $\underline{H}_{Ar}$), 7.42 (d, *J* = 4.7 Hz, 1H, $\underline{H}_{Ar}$), 7.36 (ddd, *J* = 7.4, 4.9, 0.6 Hz, 1H, $\underline{H}_{Ar}$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5, 151.5, 149.9, 149.1, 138.3, 125.3, 123.9, 123.9, 120.4.

IR 2994 (w), 1679 (s), 1587 (s), 1569 (s), 1502 (s), 1470 (m), 1443 (s), 1287 (s), 1264 (s), 1250 (s), 1216 (s), 1156 (m), 1034 (m), 1020 (m), 995 (m), 851 (m), 798 (s), 782 (s), 736 (s).

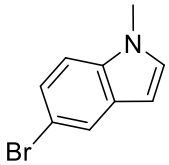
HRMS calculated for $C_9H_8N_3O^+$ $[M+H]^+$ 174.0662; found 174.0662.

2.2. General procedure B for the synthesis of *N*-alkylindoles



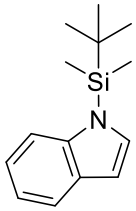
Sodium hydride (60% in mineral oil, 1.10 equiv) was suspended in DMF [0.6 M]. *N*-H-indole (1.00 equiv) was solubilized in DMF [1.0 M] and added to the suspension at 0 °C. The mixture was stirred at rt for 30 min. Bromoalkyl or TMSCl (1.50 equiv) was diluted in DMF [3.0 M] and added to the solution at 0 °C. The mixture was stirred at rt for 1 hour. The solution was quenched with water (20 mL) and extracted three times with EtOAc (10 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated under reduced pressure. The liquid was filtered through a 5 cm pad of silica with 100% pentane or Et_2O to afforded the title compound.

5-Bromo-1-methyl-1*H*-indole (15b)



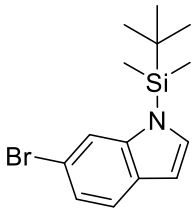
Following general procedure **B** and starting from commercially available 5-bromoindole (0.59 mg, 3.0 mmol), **15b** (630 mg, 3.00 mmol, quantitative yield) (CAS number 10075-52-2) was obtained as a pale yellow solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 1.6 Hz, 1H, $\underline{H}_{Ar}$), 7.30 (dd, *J* = 8.7, 1.8 Hz, 1H, $\underline{H}_{Ar}$), 7.19 (d, *J* = 8.7 Hz, 1H, $\underline{H}_{Ar}$), 7.05 (d, *J* = 3.1 Hz, 1H, $\underline{H}_{Ar}$), 6.43 (d, *J* = 3.1 Hz, 1H, $\underline{H}_{Ar}$), 3.78 (s, 3H, $NC\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 135.5, 130.2, 130.1, 124.4, 123.4, 112.8, 110.8, 100.6, 33.1. Spectra data matched with the values reported in literature.[4]

1-(*Tert*-butyldimethylsilyl)-1*H*-indole (15c)



Following general procedure **B** and starting from commercially available indole (2.34 g, 20.0 mmol), **15c** (4.63 g, 20.0 mmol, quantitative yield) (CAS number 40899-73-8) was obtained as a pale yellow solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.2 Hz, 1H, $\underline{H}_{Ar}$), 7.44 (d, *J* = 7.7 Hz, 1H, $\underline{H}_{Ar}$), 7.10 (d, *J* = 3.2 Hz, 1H, $\underline{H}_{Ar}$), 7.09-6.99 (m, 2H, $\underline{H}_{Ar}$), 6.54 (d, *J* = 2.7 Hz, 1H, $\underline{H}_{Ar}$), 0.85 (s, 9H, $C(C\underline{H}_3)_3$), 0.52 (s, 6H, $Si(C\underline{H}_3)_2$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 141.1, 131.5, 131.1, 121.5, 120.8, 119.9, 114.0, 104.9, 26.5, 19.7, -3.8. Spectra data matched with the values reported in literature.[5]

6-Bromo-1-(*tert*-butyldimethylsilyl)-1*H*-indole (15d)

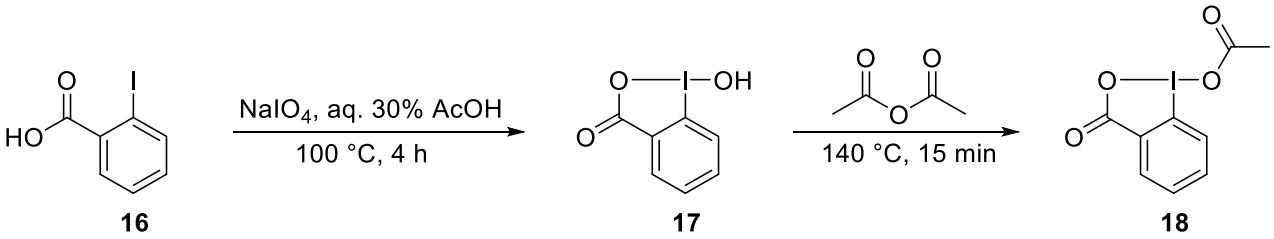


Following general procedure **B** and starting from commercially available indole (2.34 g, 20.0 mmol), **Xd** (4.63 g, 20.0 mmol, quantitative yield) (CAS number 40899-73-8) was obtained as a pale yellow solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H, $\underline{H}_{Ar}$), 7.48 (d, *J* = 8.4 Hz, 1H, $\underline{H}_{Ar}$), 7.21 (dd, *J* = 8.4, 1.7 Hz, 1H, $\underline{H}_{Ar}$), 7.15 (d, *J* = 3.2 Hz, 1H, $\underline{H}_{Ar}$), 6.58 (dd, *J* = 3.2, 0.8 Hz, 1H, $\underline{H}_{Ar}$), 0.93 (s, 9H, $C(C\underline{H}_3)_3$), 0.61 (s, 6H, $Si(C\underline{H}_3)_2$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 142.1, 131.9, 130.4, 123.3, 121.9, 116.9, 115.2, 105.1, 26.5, 19.7, -3.7. Spectra data matched with the values reported in literature.[6]

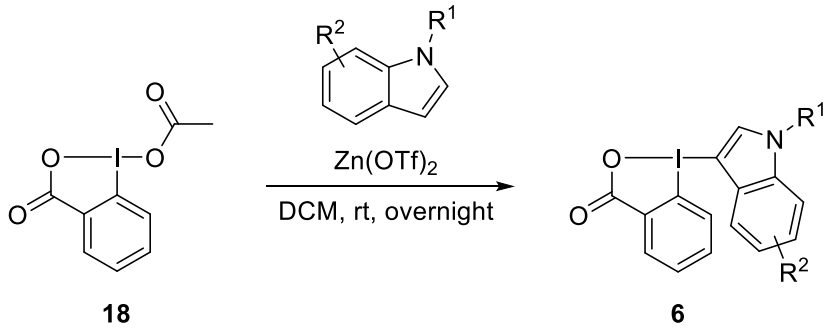
[4] Greulich, T.W.; Daniliuc, C.J.; Studer, A. *Org. Lett.* **2015**, *17*, 254−257.
[5] Dhanak, D.; Reese, C. B. *J. Chem. Soc., Perkin Trans. 1* **1986**, 2181–2186.
[6] Kawasaki, I.; Yamashita, M; Ohta, S. *Chem. Pharm. Bull.* **1996**, *44*, 1831–1839.

2.3. General procedure C for the synthesis of indoleBX reagents

1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one (18)

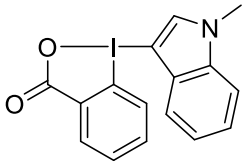


Following a reported procedure[7], sodium periodate (18.1 g, 85.0 mmol, 1.05 equiv) and 2-iodobenzoic acid (20.0 g, 81.0 mmol, 1.00 equiv) were suspended in 30% (v:v) aq. AcOH (160 mL). The mixture was vigorously stirred and refluxed for 4 h and allowed to cool to room temperature, while protecting it from light. After 1 h, the crude product was collected by filtration. The crystals were washed with ice water (3 x 40 mL) followed by acetone (45 mL) and dried under reduced pressure in the dark to afforded 1-hydroxy-1,2-benziodoxol-3-(1*H*)-one (20.8 g, 79.0 mmol, 98%) as a white solid. Following a reported procedure, 1-hydroxy-1,2-benziodoxol-3-(1*H*)-one (20.8 g, 79.0 mmol, 1.00 equiv) was suspended in acetic anhydride (75.0 mL, 788 mmol, 10.0 equiv) and heated to reflux (140 °C) until complete dissolution (about 15 min). The resulting clears solution was slowly let to cool to room temperature and then cooled to 5 °C in the fridge. The white crystals were filtered, washed with pentane (3 x 30 mL) and dried under reduced pressure to afforded 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (22.3 g, 73.0 mmol, 92%) as a white solid.



Following a slightly modified reported procedure,[8] 1-acetoxy-1,2- benziodoxol-3-(1*H*)-one (1.20 equiv), the corresponding azaheterocycle (1.00 equiv) and zinc (II) trifluoromethanesulfonate (0.20 equiv) were dissolved in DCM [0.05 M]. The reaction was stirred overnight at room temperature, directly purified by flash chromatography (eluent DCM/MeOH see ratio thereafter) and triturated in ACN to afforded the pure desired hypervalent iodine reagent.

1-(3-1-Methyl-1*H*-indole)-1*H*-1λ$_3$ -benzo[*b*]iodo-3(2*H*)-one (6a)



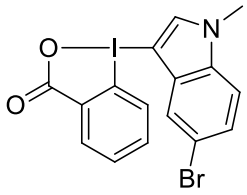
Following general procedure **C**, starting from commercially available 1-methylindole (0.43 mL, 3.4 mmol) and **16**, a purification by column chromatography (DCM/MeOH 19:1) affordeded the title compound **6a** (0.79 g, 2.1 mmol, 61% yield) (CAS number 2130906-04-4) as an off-white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 7.5 Hz, 1H, $\underline{H}_{Ar}$), 7.77 (s, 1H, C$\underline{H}$-N), 7.56-7.49 (m, 2H, $\underline{H}_{Ar}$), 7.47-7.41 (m, 2H, $\underline{H}_{Ar}$), 7.35-7.26 (m, 2H, $\underline{H}_{Ar}$), 6.85 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$), 4.02 (s, 3H, NC$\underline{H}_3$).

[7] Parsons, A. T.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2011**, *50*, 9120–9123.
[8] Caramenti, P.; Nicolai, S.; Waser, *J. Chem. - Eur. J.* **2017**, *23*, 14702–14706.

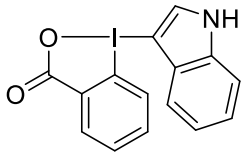
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 138.7, 137.7, 133.6, 133.4, 132.7, 130.7, 129.5, 125.4, 124.5, 122.8, 120.1, 116.3, 110.9, 79.2, 34.1. Spectra data matched with the values reported in literature.[7]

1-(3-5-Bromo-1-methyl-1*H*-indole)-1*H*-1λ$_3$ -benzo[*b*]iodo-3(2*H*)-one (6b)



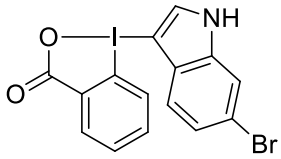
Following general procedure **C**, starting from **15b** (406 mg, 1.93 mmol) and **16**, a purification by column chromatography (DCM/MeOH 19:1) affordeded the title compound **6b** (470 mg, 1.03 mmol, 53% yield) as an off-white solid.
^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.33 (d, *J* = 7.4 Hz, 1H, $\underline{H}_{Ar}$), 7.70 (s, 1H, C$\underline{H}$-N), 7.63 (s, 1H, $\underline{H}_{Ar}$), 7.57 (t, *J* = 7.3 Hz, 1H, $\underline{H}_{Ar}$), 7.52 (dd, *J* = 8.8, 1.6 Hz, 1H, $\underline{H}_{Ar}$), 7.44 (d, *J* = 8.8 Hz, 1H, $\underline{H}_{Ar}$), 7.34 (t, *J* = 7.1 Hz, 1H, $\underline{H}_{Ar}$), 6.84 (d, *J* = 8.3 Hz, 1H, $\underline{H}_{Ar}$), 3.96 (s, 3H, NC$\underline{H}_3$).
^{13}C NMR (101 MHz, CD_2Cl_2) δ 166.6, 139.9, 136.9, 133.9, 133.7, 132.5, 131.5, 131.0, 127.5, 125.7, 123.0, 116.7, 116.2, 112.8, 79.5, 34.4. Spectra data matched with the values reported in literature.[9]

1-(3-1*H*-Indole)-1*H*-1λ3 -benzo[*b*]iodo-3(2*H*)-one (6c)



Following general procedure **C** but replacing $Zn(OTf)_2$ by $Sc(OTf)_3$, starting from **15c** (579 mg, 2.50 mmol) and **16**, a purification by column chromatography (DCM/MeOH 5:1) affordeded the title compound **6c** (527 mg, 1.45 mmol, 58% yield) as a pale beige solid.
^{1}H NMR (400 MHz, DMSO-d6) δ 12.36 (s, 1H, N$\underline{H}$), 8.26 (s, 1H, C$\underline{H}$-N), 8.12 (d, *J* = 7.3 Hz, 1H, $\underline{H}_{Ar}$), 7.64 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$), 7.56 (t, *J* = 7.3 Hz, 1H, $\underline{H}_{Ar}$), 7.49 (d, *J* = 7.9 Hz, 1H, $\underline{H}_{Ar}$), 7.41 (t, *J* = 7.6 Hz, 1H, $\underline{H}_{Ar}$), 7.31 (t, *J* = 7.6 Hz, 1H, $\underline{H}_{Ar}$), 7.20 (t, *J* = 7.5 Hz, 1H, $\underline{H}_{Ar}$), 6.76 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$).
^{13}C NMR (101 MHz, DMSO-d6) δ 165.8, 136.5 (2C), 134.6, 133.1, 131.3, 130.1, 128.6, 126.2, 123.3, 121.6, 119.2, 116.0, 112.9, 80.3. Spectra data matched with the values reported in literature.[7]

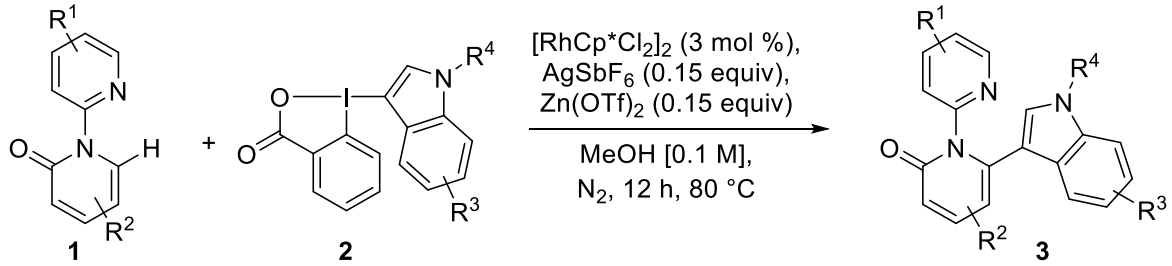
1-(3-(6-Bromo-1*H*-indole))-1*H*-1λ3 -benzo[*b*]iodo-3(2*H*)-one (6d)



Following general procedure **C**, but replacing $Zn(OTf)_2$ by $Sc(OTf)_3$, starting from **15d** (528 mg, 1.70 mmol) and **16**, a purification by column chromatography (DCM/MeOH 19:1) and washing with DCM affordeded the title compound **6d** (563 mg, 1.27 mmol, 75% yield) as a white solid. **mp 194-196** °C. **Rf** 0.58 (DCM/MeOH 9:1).
^{1}H NMR (400 MHz, DMSO-d6) δ 12.46 (bs, 1H, N$\underline{H}$), 8.27 (s, 1H, $\underline{H}_{Ar}$), 8.12 (dd, *J* = 7.5, 1.5 Hz, 1H, $\underline{H}_{Ar}$), 7.86 (d, *J* = 1.5 Hz, 1H, $\underline{H}_{Ar}$), 7.57 (t, *J* = 7.3 Hz, 1H, $\underline{H}_{Ar}$), 7.49 (d, *J* = 8.5 Hz, 1H, $\underline{H}_{Ar}$), 7.42 (td, *J* = 7.3, 1.5 Hz, 1H, $\underline{H}_{Ar}$), 7.32 (dd, *J* = 8.5, 1.7 Hz, 1H, $\underline{H}_{Ar}$), 6.74 (d, *J* = 8.1 Hz, 1H, $\underline{H}_{Ar}$).
^{13}C NMR (101 MHz, DMSO-d6) δ 165.9, 137.5, 137.4, 134.4, 133.3, 131.4, 130.2, 127.7, 126.3, 124.4, 121.2, 116.1, 116.0, 115.4, 80.9.
IR ν_{max} 2606 (br), 1593 (m), 1578 (m), 1549 (m), 1366 (s), 1265 (m), 887 (m), 828 (s), 794 (s), 736 (s).
HRMS calculated for $C_{15}H_{10}{}^{79}BrINO_2^+$ $[M+H]^+$ 441.8934; found 441.8933.

[9] Grenet, E.; Waser, J. *Org. Lett.* **2018**, *20*, 1473-1475.

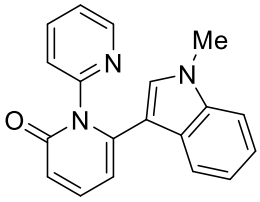
3. General procedure D for the synthesis of 6-(indol-3-yl)-1,2'-bipyridin-2-ones



1 **2** **3**

In a sealed tube, $[RhCp^*Cl_2]_2$ (3.7 mg, 6.0 µmol, 3 mol %), $AgSbF_6$ (10.3 mg, 30.0 µmol, 0.15equiv), $Zn(OTf)_2$ (10.9 mg, 30.0 µmol, 0.15 equiv), the corresponding pyridinone (0.20 mmol, 1.00 equiv) and the corresponding hypervalent iodine reagent (0.20 mmol, 1.00 equiv) were solubilized in dry MeOH (2.0 mL, 0.1 M) under N_2. The mixture was stirred at 80 °C for 12 h. The suspension was diluted with DCM (5 mL) and quenched with a saturated aqueous solution of $NaHCO_3$ (5 mL). The two layers were separated and the aqueous layer was extracted twice with DCM (5 mL). The organic layers were combined, dried over magnesium sulfate dehydrate, filtered and concentrated under reduced pressure. The crude residue was purified by preparative TLC using DCM/MeOH 19:1 as eluent to afforded the pure title compound.

6-(1-Methyl-1*H*-indol-3-yl)-2*H*-[1,2'-bipyridin]-2-one (7a)



Following General Procedure **D**, starting from **5a** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **7a** (51.9 mg, 0.172 mmol, 86% yield) as a white solid. **mp** 231-233 °C. **Rf** 0.51 (DCM/MeOH 19:1).

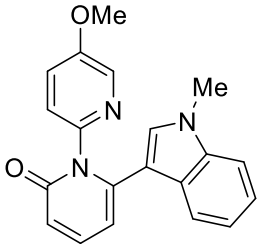
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (ddd, *J* = 4.9, 1.8, 0.7 Hz, 1H, $\underline{H}_{Ar}$), 7.71 (d, *J* = 8.0 Hz, 1H, $\underline{H}_{Ar}$), 7.63 (td, *J* = 7.7, 1.9 Hz, 1H, $\underline{H}_{Ar}$), 7.50 (dd, *J* = 9.2, 7.0 Hz, 1H, $\underline{H}_{Ar}$), 7.25-7.21 (m, 3H, $\underline{H}_{Ar}$), 7.19-7.12 (m, 2H, $\underline{H}_{Ar}$), 6.63 (dd, *J* = 9.2, 1.1 Hz, 1H, $\underline{H}_{Ar}$), 6.50 (dd, *J* = 7.0, 1.1 Hz, 1H, $\underline{H}_{Ar}$), 6.47 (s, 1H, $C2_{indole}\underline{H}$), 3.57 (s, 3H, $NC\underline{H}_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 153.2, 149.2, 143.2, 140.3, 138.4, 136.3, 129.9, 126.7, 124.2, 123.7, 122.6, 120.6, 119.9, 118.7, 109.6, 109.5, 108.0, 33.0.

IR ν_{max} 3080 (w), 1660 (s), 1591 (s), 1580 (s), 1557 (s), 1437 (m), 1391 (m), 1237 (m), 1142 (m), 807 (s), 786 (m), 750 (s).

HRMS calculated for $C_{19}H_{16}N_3O^+$ $[M+H]^+$ 302.1288; Found 302.1291.

5'-Methoxy-6-(1-methyl-1*H*-indol-3-yl)-2*H*-[1,2'-bipyridin]-2-one (7b)



Following General Procedure **D**, starting from **5b** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **7b** (54.3 mg, 0.164 mmol, 82% yield) as a yellow solid. **mp** 225-227 °C. **Rf** 0.51 (DCM/MeOH 19:1).

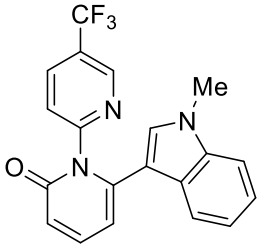
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 2.6 Hz, 1H, $\underline{H}_{Ar}$), 7.61 (d, *J* = 8.0 Hz, 1H, $\underline{H}_{Ar}$), 7.37 (dd, *J* = 9.2, 7.0 Hz, 1H, $\underline{H}_{Ar}$), 7.14 (d, *J* = 3.8 Hz, 2H, $\underline{H}_{Ar}$), 7.09-7.00 (m, 2H, $\underline{H}_{Ar}$), 6.95 (d, *J* = 8.7 Hz, 1H, $\underline{H}_{Ar}$), 6.50 (dd, *J* = 9.2, 1.2 Hz, 1H, $\underline{H}_{Ar}$), 6.41 (s, 1H, $C2_{indole}\underline{H}$), 6.37 (dd, *J* = 7.0, 1.2 Hz, 1H, $\underline{H}_{Ar}$), 3.72 (s, 3H, $OC\underline{H}_3$), 3.50 (s, 3H, $NC\underline{H}_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 155.5, 145.7, 143.6, 140.1, 136.3, 136.2, 130.0, 126.7, 124.2, 122.9, 122.6, 120.6, 119.9, 118.5, 109.6, 109.6, 107.9, 56.0, 33.1.

IR ν_{max} 3080 (w), 1662 (s), 1582 (s), 1543 (s), 1473 (s), 1260 (s), 807 (s), 752 (s), 737 (s).

HRMS calculated for $C_{20}H_{18}N_3O_2^+$ $[M+H]^+$ 332.1394; Found 332.1392.

6-(1-Methyl-1*H*-indol-3-yl)-5'-(trifluoromethyl)-2*H*-[1,2'-bipyridin]-2-one (7c)



Following General Procedure **D**, starting from **5c** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **7c** (53.2 mg, 0.144 mmol, 72% yield) as a yellow solid. **mp** > 300 °C. **Rf** 0.74 (DCM/MeOH 19:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H, $\underline{H}_{Ar}$), 7.88 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$), 7.66 (d, *J* = 8.0 Hz, 1H, $\underline{H}_{Ar}$), 7.54 (dd, *J* = 9.2, 7.0 Hz, 1H, $\underline{H}_{Ar}$), 7.34 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$), 7.29-7.24 (m, 2H, $\underline{H}_{Ar}$), 7.22-7.11 (m, 1H, $\underline{H}_{Ar}$), 6.67 (d, *J* = 9.2 Hz, 1H, $\underline{H}_{Ar}$), 6.54-6.49 (m, 2H, $\underline{H}_{Ar}$ + $C2_{indole}\underline{H}$), 3.63 (s, 1H, $NC\underline{H}_3$).

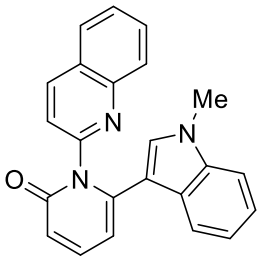
^{19}F NMR (376 MHz, $CDCl_3$) δ -62.3.

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0, 156.1, 146.4 (q, *J* = 3.6 Hz), 142.9, 140.7, 136.4, 135.7 (q, *J* = 3.2 Hz), 129.7, 126.6 (q, *J* = 33.5 Hz), 126.5, 124.4, 123.2 (q, *J* = 272.7 Hz), 122.9, 120.8, 119.7, 118.9, 109.8, 109.3, 108.5, 33.1.

IR ν_{max} 1663 (m), 1583 (m), 1544 (m), 1326 (s), 1128 (s), 1081 (s), 1017 (s), 799 (s), 743 (s).

HRMS calculated for $C_{20}H_{15}F_3N_3O^+$ $[M+H]^+$ 370.1162; Found 370.1160.

6-(1-Methyl-1*H*-indol-3-yl)-1-(quinolin-2-yl)pyridin-2(1*H*)-one (7f)



Following General Procedure **D**, starting from **5f** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **7f** (55.4 mg, 0.158 mmol, 79% yield) as a pale yellow solid. **mp** 231-233 °C. **Rf** 0.58 (DCM/MeOH 19:1).

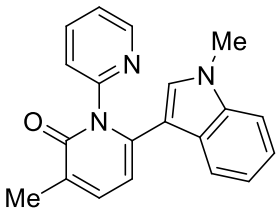
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.6 Hz, 1H, $\underline{H}_{Ar}$), 8.08 (d, *J* = 8.6 Hz, 1H, $\underline{H}_{Ar}$), 7.80-7.71 (m, 3H, $\underline{H}_{Ar}$), 7.59-7.52 (m, 2H, $\underline{H}_{Ar}$), 7.23-7.13 (m, 4H, $\underline{H}_{Ar}$), 6.66 (dd, *J* = 9.2, 1.2 Hz, 1H, $\underline{H}_{Ar}$), 6.55-6.52 (m, 2H, $\underline{H}_{Ar}$ + $C2_{indole}\underline{H}$), 3.39 (s, 3H, $NC\underline{H}_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 152.5, 147.1, 143.1, 140.4, 138.8, 136.2, 130.4, 130.1, 129.5, 127.8, 127.7, 127.5, 126.9, 122.6, 121.6, 120.7, 119.8, 118.8, 109.6, 109.2, 108.1, 32.9.

IR ν_{max} 3062 (w), 1669 (s), 1586 (s), 1544 (s), 1504 (m), 1398 (m), 1236 (m), 815 (s), 803 (s), 768 (s), 745 (s).

HRMS calculated for $C_{23}H_{17}N_3NaO^+$ $[M+Na]^+$ 374.1264; found 374.1271.

3-Methyl-6-(1-methyl-1*H*-indol-3-yl)-2*H*-[1,2'-bipyridin]-2-one (7g)



Following General Procedure **D**, starting from **5g** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **7g** (50.5 mg, 0.160 mmol, 80% yield) as a pale yellow solid. **mp** 228-230 °C. **Rf** 0.51 (DCM/MeOH 19:1).

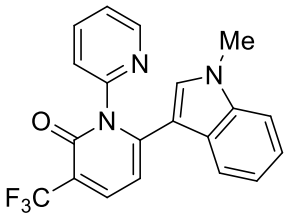
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 4.9, 1.1 Hz, 1H, $\underline{H}_{Ar}$), 7.70 (d, *J* = 8.0 Hz, 1H, $\underline{H}_{Ar}$), 7.61 (td, *J* = 7.7, 1.9 Hz, 1H, $\underline{H}_{Ar}$), 7.38 (dd, *J* = 7.0, 1.1 Hz, 1H, $\underline{H}_{Ar}$), 7.24-7.19 (m, 3H, $\underline{H}_{Ar}$), 7.18-7.10 (m, 2H, $\underline{H}_{Ar}$), 6.46 (s, 1H, $C2_{indole}\underline{H}$), 6.43 (d, *J* = 7.0 Hz, 1H, $\underline{H}_{Ar}$), 3.57 (s, 3H, $NC\underline{H}_3$), 2.22 (d, *J* = 0.8 Hz, 3H, $C\underline{H}_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.4, 153.6, 149.1, 140.2, 138.2, 137.5, 136.3, 129.6, 127.7, 126.8, 124.2, 123.5, 122.5, 120.4, 119.9, 109.8, 109.5, 107.7, 32.9, 17.1.

IR ν_{max} 3087 (w), 2926 (w), 1650 (s), 1603 (m), 1556 (s), 1469 (m), 1243 (m), 1133 (m), 809 (m), 792 (s), 746 (s).

HRMS calculated for $C_{20}H_{18}N_3O^+$ $[M+H]^+$ 316.1444; Found 316.1448.

6-(1-Methyl-1*H*-indol-3-yl)-3-(trifluoromethyl)-2*H*-[1,2'-bipyridin]-2-one (7h)



Following General Procedure **D**, starting from **5h** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **7h** (48.0 mg, 0.130 mmol, 65% yield) as an off-white solid. **mp** 265-267 °C. **Rf** 0.71 (DCM/MeOH 19:1).

^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.59 (d, *J* = 3.5 Hz, 1H, $\underline{H}_{Ar}$), 7.89 (d, *J* = 7.5 Hz, 1H, $\underline{H}_{Ar}$), 7.73 (d, *J* = 7.3 Hz, 2H, $\underline{H}_{Ar}$), 7.39-7.09 (m, 5H, $\underline{H}_{Ar}$), 6.60 (d, *J* = 7.5 Hz, 1H, $\underline{H}_{Ar}$), 6.46 (s, 1H, $C2_{indole}\underline{H}$), 3.57 (s, 3H, $NC\underline{H}_3$).

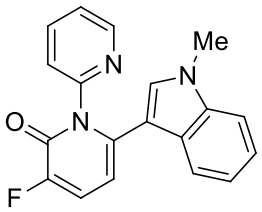
^{19}F NMR (376 MHz, $CDCl_3$) δ -63.6.

^{13}C NMR (101 MHz, CD_2Cl_2) δ 160.1, 152.6, 149.7, 148.6, 139.8 (q, *J* = 4.8 Hz), 138.9, 136.8, 131.2, 126.6, 124.6, 124.4, 123.7 (q, *J* = 270.8 Hz), 123.2, 121.4, 119.8, 117.0 (q, *J* = 30.7 Hz), 110.3, 108.7, 105.9, 33.4.

IR ν_{max} 3105 (w), 1672 (m), 1555 (s), 1416 (m), 1318 (s), 1142 (s), 1117 (s), 1104 (s), 1057 (s), 1038 (s), 739 (s).

HRMS calculated for $C_{20}H_{14}F_3N_3NaO^+$ $[M+Na]^+$ 392.0981; Found 392.0984.

3-Fluoro-6-(1-methyl-1*H*-indol-3-yl)-2*H*-[1,2'-bipyridin]-2-one (7i)



Following General Procedure **D**, starting from **5i** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **7i** (47.9 mg, 0.150 mmol, 75% yield) as an off-white solid. **mp** 204-206 °C. **Rf** 0.58 (DCM/MeOH 19:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 4.9, 1.2 Hz, 1H, $\underline{H}_{Ar}$), 7.67-7.62 (m, 2H, $\underline{H}_{Ar}$), 7.30-7.24 (m, 2H, $\underline{H}_{Ar}$), 7.24-7.21 (m, 2H, $\underline{H}_{Ar}$), 7.18-7.11 (m, 2H, $\underline{H}_{Ar}$), 6.50 (s, 1H, $C2_{indole}\underline{H}$), 6.38 (dd, *J* = 7.8, 4.4 Hz, 1H, $\underline{H}_{Ar}$), 3.59 (s, 3H, $NC\underline{H}_3$).

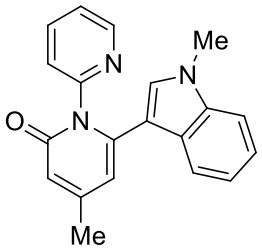
^{19}F NMR (376 MHz, $CDCl_3$) δ -133.9.

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.5 (d, *J* = 26.0 Hz), 152.1 (d, *J* = 1.3 Hz), 151.0 (d, *J* = 248.5 Hz), 149.3, 138.7 (d, *J* = 5.4 Hz), 138.5, 136.2, 129.7, 126.6, 124.0, 123.9, 122.6, 120.9 (d, *J* = 16.5 Hz), 120.6, 119.6, 109.6, 108.9, 105.5 (d, *J* = 5.1 Hz), 33.0.

IR ν_{max} 3056 (w), 1673 (s), 1617 (s), 1570 (m), 1278 (s), 1239 (s), 1223 (m), 1137 (m), 819 (m), 784 (m), 753 (s), 745 (s).

HRMS calculated for $C_{19}H_{15}FN_3O^+$ $[M+H]^+$ 320.1194; Found 320.1192.

4-Methyl-6-(1-methyl-1*H*-indol-3-yl)-2*H*-[1,2'-bipyridin]-2-one (7j)



Following General Procedure **D**, starting from **5j** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **7j** (49.2 mg, 0.156 mmol, 78% yield) as an off-white solid. **mp** 186-188 °C. **Rf** 0.41 (DCM/MeOH 19:1).

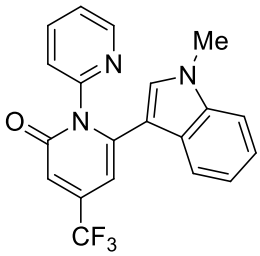
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (dd, *J* = 4.6, 1.4 Hz, 1H, $\underline{H}_{Ar}$), 7.70 (d, *J* = 8.0 Hz, 1H, $\underline{H}_{Ar}$), 7.60 (td, *J* = 7.7, 1.9 Hz, 1H, $\underline{H}_{Ar}$), 7.24-7.09 (m, 5H, $\underline{H}_{Ar}$), 6.49 (s, 1H, $C2_{indole}\underline{H}$), 6.44 (s, 1H, $C(O)C\underline{H}$), 6.34 (d, *J* = 1.6 Hz, 1H), 3.57 (s, 3H, $NC\underline{H}_3$), 2.28 (s, 3H, $C\underline{H}_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 153.2, 151.7, 149.1, 141.8, 138.2, 136.3, 129.9, 126.6, 124.3, 123.5, 122.5, 120.5, 119.8, 117.2, 110.6, 109.6, 109.5, 33.0, 21.7.

IR ν_{max} 2970 (m), 2902 (m), 1657 (s), 1599 (s), 1588 (s), 1549 (s), 1470 (s), 1435 (m), 1396 (s), 1339 (m), 1261 (m), 1239 (m), 1070 (s), 1051 (s), 1011 (s), 826 (m), 786 (m), 732 (s).

HRMS calculated for $C_{20}H_{18}N_3O^+$ $[M+H]^+$ 316.1444; Found 316.1446.

6-(1-Methyl-1*H*-indol-3-yl)-4-(trifluoromethyl)-2*H*-[1,2'-bipyridin]-2-one (7k)



Following General Procedure **D**, starting from **5k** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **7k** (48.7 mg, 0.132 mmol, 66% yield) as a pale yellow solid. **mp** 200-202 °C. **Rf** 0.65 (DCM/MeOH 19:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 3.7 Hz, 1H, $\underline{H}_{Ar}$), 7.68 (ddd, *J* = 12.2, 6.4, 2.3 Hz, 2H, $\underline{H}_{Ar}$), 7.33-7.13 (m, 5H, $\underline{H}_{Ar}$), 6.88 (s, 1H, C(O)C$\underline{H}$), 6.63 (d, *J* = 1.5 Hz, 1H, $\underline{H}_{Ar}$), 6.51 (s, 1H, C2$_{indole}\underline{H}$), 3.59 (s, 3H, NC$\underline{H}_3$).

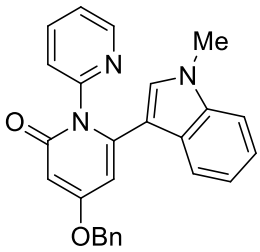
^{19}F NMR (376 MHz, $CDCl_3$) δ -66.8.

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 152.5, 149.5, 145.4, 141.8 (q, *J* = 33.5 Hz), 138.7, 136.4, 130.4, 126.3, 124.2, 124.0, 123.1, 122.6 (q, *J* = 274.2 Hz), 121.2, 119.6, 115.7 (q, *J* = 4.0 Hz), 109.8, 108.8, 102.7 (q, *J* = 2.1 Hz), 33.1.

IR ν_{max} 3099 (w), 3062 (w), 2926 (w), 1675 (m), 1610 (m), 1552 (s), 1282 (s), 1170 (s), 1133 (s), 1079 (m), 1006 (m), 932 (m), 857 (s), 734 (s).

HRMS calculated for $C_{20}H_{14}F_3N_3NaO^+$ $[M+Na]^+$ 392.0981; Found 392.0990.

4-(Benzyloxy)-6-(1-methyl-1*H*-indol-3-yl)-2*H*-[1,2'-bipyridin]-2-one (7l)



Following General Procedure **D**, starting from **5l** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **7l** (68.4 mg, 0.168 mmol, 84% yield) as an off-white solid. **mp** 162-164 °C. **Rf** 0.37 (DCM/MeOH 19:1).

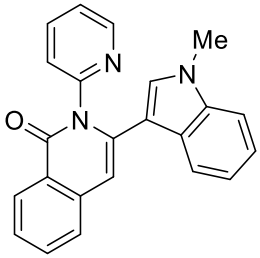
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, *J* = 4.8 Hz, 1H, $\underline{H}_{Ar}$), 7.71 (d, *J* = 8.0 Hz, 1H, $\underline{H}_{Ar}$), 7.62 (td, *J* = 7.7, 1.8 Hz, 1H, $\underline{H}_{Ar}$), 7.48-7.33 (m, 5H, $\underline{H}_{Ar}$), 7.25-7.19 (m, 3H, $\underline{H}_{Ar}$), 7.18-7.12 (m, 2H, $\underline{H}_{Ar}$), 6.47 (s, 1H, C2$_{indole}\underline{H}$), 6.33 (d, *J* = 2.5 Hz, 1H, $\underline{H}_{Ar}$), 6.12 (d, *J* = 2.5 Hz, 1H, $\underline{H}_{Ar}$), 5.11 (s, 2H, OC$\underline{H}_2$), 3.56 (s, 3H, NC$\underline{H}_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 165.8, 152.9, 149.1, 143.0, 138.3, 136.3, 135.6, 129.9, 128.8 (2C), 128.5, 127.9 (2C), 126.5, 124.6, 123.6, 122.6, 120.6, 119.9, 109.6, 109.1, 102.8, 96.4, 70.3, 33.0.

IR ν_{max} 2982 (m), 2902 (m), 1660 (m), 1637 (m), 1552 (m), 1431 (m), 1398 (m), 1371 (m), 1344 (m), 1244 (m), 1197 (m), 1073 (m), 745 (s).

HRMS calculated for $C_{26}H_{22}N_3O_2^+$ $[M+H]^+$ 408.1707; Found 408.1701.

3-(1-Methyl-1*H*-indol-3-yl)-2-(pyridin-2-yl)isoquinolin-1(2*H*)-one (7n)



Following General Procedure **D**, starting from **5n** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **7n** (57.6 mg, 0.164 mmol, 82% yield) as a pale yellow solid. **mp** 173-175 °C. **Rf** 0.60 (DCM/MeOH 19:1).

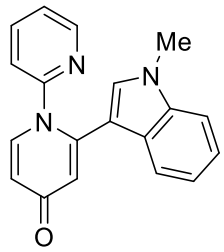
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (ddd, *J* = 4.9, 1.8, 0.7 Hz, 1H, $\underline{H}_{Ar}$), 8.42 (d, *J* = 8.1 Hz, 1H, $\underline{H}_{Ar}$), 7.72 (d, *J* = 8.0 Hz, 1H, $\underline{H}_{Ar}$), 7.65 (ddd, *J* = 8.3, 7.2, 1.3 Hz, 1H, $\underline{H}_{Ar}$), 7.58 (td, *J* = 7.8, 1.9 Hz, 1H, $\underline{H}_{Ar}$), 7.53 (d, *J* = 7.8 Hz, 1H, $\underline{H}_{Ar}$), 7.45 (ddd, *J* = 8.2, 7.2, 1.2 Hz, 1H, $\underline{H}_{Ar}$), 7.22-7.09 (m, 5H, $\underline{H}_{Ar}$), 6.77 (s, 1H, $\underline{H}_{Ar}$), 6.56 (s, 1H, C2$_{indole}\underline{H}$), 3.57 (s, 1H, NC$\underline{H}_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.9, 153.4, 149.1, 138.1, 137.5, 136.5, 136.3, 132.9, 129.7, 128.3, 127.0, 126.5, 126.0, 125.2, 124.6, 123.4, 122.4, 120.3, 120.0, 110.1, 109.5, 108.1, 32.9.

IR ν_{max} 2976 (w), 2902 (w), 1655 (m), 1618 (m), 1588 (m), 1563 (m), 1471 (m), 1394 (m), 1376 (m), 1334 (m), 1244 (m), 1130 (m), 1064 (m), 788 (m), 752 (m), 742 (s).

HRMS calculated for $C_{23}H_{18}N_3O^+$ $[M+H]^+$ 352.1444; Found 352.1451.

2-(1-Methyl-1*H*-indol-3-yl)-4*H*-[1,2'-bipyridin]-4-one (7o)



Following General Procedure **D**, starting from **5o** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **7o** (34.4 mg, 0.114 mmol, 57% yield) as an off-white solid. **mp** 150-152 °C. **Rf** 0.34 (DCM/MeOH 19:1).

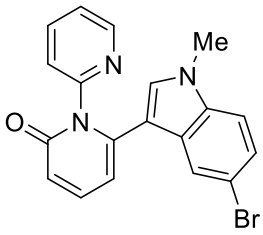
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 3.9 Hz, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.43-7.33 (m, 2H), 7.24 (d, *J* = 8.6 Hz, 1H), 7.20-7.13 (m, 2H), 7.02 (t, *J* = 7.4 Hz, 1H), 6.81 (d, *J* = 8.1 Hz, 1H), 6.77 (s, 1H), 6.64 (d, *J* = 2.5 Hz, 1H), 6.50 (dd, *J* = 7.8, 2.5 Hz, 1H), 3.68 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.9, 154.0, 149.2, 144.5, 140.8, 137.8, 136.6, 129.6, 125.8, 123.2, 122.7, 121.5, 120.9, 119.9, 119.6, 117.6, 109.7, 109.3, 33.2.

IR ν_{max} 3056 (w), 2933 (w), 1625 (s), 1566 (s), 1547 (s), 1466 (s), 1447 (s), 1430 (s), 1277 (s), 1246 (s), 790 (m), 740 (s).

HRMS calculated for $C_{19}H_{16}N_3O^+$ $[M+H]^+$ 302.1288; Found 302.1284.

6-(5-Bromo-1-methyl-1*H*-indol-3-yl)-2*H*-[1,2'-bipyridin]-2-one (7q)



Following General Procedure **D**, starting from **5a** and **6b**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **7q** (58.0 mg, 0.156 mmol, 76% yield) as a white solid. **mp** 215-217 °C. **Rf** 0.39 (DCM/MeOH 19:1).

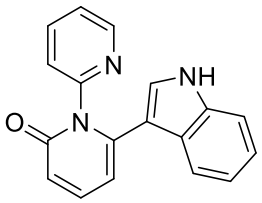
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 3.7 Hz, 1H, $\underline{H}_{Ar}$), 7.79 (d, *J* = 1.7 Hz, 1H, $\underline{H}_{Ar}$), 7.64 (d, *J* = 1.9 Hz, 1H, $\underline{H}_{Ar}$), 7.49 (dd, *J* = 9.2, 6.9 Hz, 1H, $\underline{H}_{Ar}$), 7.28 (dd, *J* = 8.7, 1.8 Hz, 1H, $\underline{H}_{Ar}$), 7.22 (ddd, *J* = 7.5, 4.9, 0.9 Hz, 1H, $\underline{H}_{Ar}$), 7.14 (d, *J* = 7.9 Hz, 1H, $\underline{H}_{Ar}$), 7.07 (d, *J* = 8.7 Hz, 1H, $\underline{H}_{Ar}$), 6.62 (dd, *J* = 9.2, 1.1 Hz, 1H, $\underline{H}_{Ar}$), 6.50 (s, 1H, $C2_{indole}\underline{H}$), 6.42 (dd, *J* = 6.9, 1.2 Hz, 1H, $\underline{H}_{Ar}$), 3.55 (s, 3H, $NC\underline{H}_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0, 152.9, 149.2, 142.4, 140.2, 138.4, 134.9, 130.8, 128.1, 125.5, 124.1, 123.8, 122.3, 119.2, 114.1, 111.1, 109.2, 108.0, 33.2.

IR ν_{max} 3093 (w), 2920 (w), 1661 (s), 1588 (s), 1548 (s), 1467 (s), 1434 (m), 1142 (m), 799 (s), 785 (s), 746 (m), 730 (m).

HRMS calculated for $C_{19}H_{14}{}^{79}BrN_3NaO^+$ $[M+Na]^+$ 402.0212; found 402.0210.

6-(1*H*-Indol-3-yl)-2*H*-[1,2'-bipyridin]-2-one (7r)



Following General Procedure **D**, starting from **5a** and **6c**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **7r** (48.2 mg, 0.168 mmol, 84% yield) as a pale brown solid. **mp** 175-177 °C. **Rf** 0.35 (DCM/MeOH 19:1).

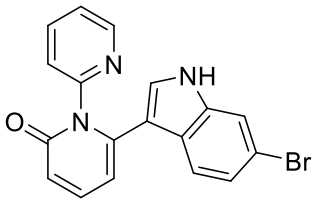
^{1}H NMR (400 MHz, MeOD) δ 8.47 (ddd, *J* = 4.9, 1.7, 0.6 Hz, 1H, $\underline{H}_{Ar}$), 7.78 (td, *J* = 7.8, 1.9 Hz, 1H, $\underline{H}_{Ar}$), 7.73 (dd, *J* = 9.1, 7.1 Hz, 1H, $\underline{H}_{Ar}$), 7.62 (d, *J* = 7.6 Hz, 1H, $\underline{H}_{Ar}$), 7.36 (ddd, *J* = 7.5, 5.0, 0.9 Hz, 1H, $\underline{H}_{Ar}$), 7.30-7.27 (m, 2H, $\underline{H}_{Ar}$), 7.14-7.05 (m, 2H, $\underline{H}_{Ar}$), 6.72-6.67 (m, 2H, $\underline{H}_{Ar}$), 6.62 (dd, *J* = 9.1, 1.0 Hz, 1H, $\underline{H}_{Ar}$). N$\underline{H}$ is not resolved in MeOD but could be observed at 10.45 ppm as a broad singlet in acetone-d6.

^{13}C NMR (101 MHz, MeOD) δ 166.2, 153.7, 149.9, 145.8, 143.1, 140.3, 137.2, 127.3, 127.2, 125.6, 125.5, 123.5, 121.4, 120.0, 118.2, 112.6, 110.6, 110.5.

IR ν_{max} 3124 (br), 1641 (s), 1545 (s), 1510 (m), 1461 (m), 1431 (s), 1389 (s), 1144 (m), 1016 (m), 801 (s), 794 (s), 739 (s).

HRMS calculated for $C_{18}H_{14}N_3O^+$ $[M+H]^+$ 288.1131; found 288.1132.

6-(6-Bromo-1*H*-indol-3-yl)-2*H*-[1,2'-bipyridin]-2-one (7s)



Following General Procedure **D**, starting from **5a** and **6d**, a purification by preparative TLC (DCM/MeOH 24:1) afforded the title compound **7s** (56.2 mg, 0.153 mmol, 77% yield) as a pale brown solid. **mp** 213-215 °C. **Rf** 0.28 (DCM/MeOH 19:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (bs, 1H, NH), 8.44 (dd, *J* = 4.8, 1.1 Hz, 1H, H_{Ar}), 7.61-7.50 (m, 2H, H_{Ar}), 7.47 (d, *J* = 8.6 Hz, 1H, H_{Ar}), 7.31 (d, *J* = 1.5 Hz, 1H, H_{Ar}), 7.18 (dd, *J* = 8.6, 1.7 Hz, 1H, H_{Ar}), 7.16-7.08 (m, 1H, H_{Ar}), 7.06 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 6.60 (dd, *J* = 9.2, 1.0 Hz, 1H, H_{Ar}), 6.53 (d, *J* = 2.7 Hz, 1H, H_{Ar}), 6.48 (dd, *J* = 7.0, 1.0 Hz, 1H, H_{Ar}).

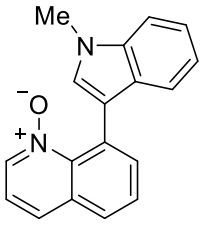
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.4, 152.7, 149.2, 143.2, 140.8, 138.6, 136.4, 126.5, 124.9, 124.0, 123.9, 123.8, 120.5, 118.7, 116.1, 114.8, 110.2, 108.7.

IR ν_{max} 3253 (br), 1665 (s), 1585 (m), 1546 (s), 1467 (m), 1441 (m), 1104 (m), 803 (s), 788 (m).

HRMS calculated for $C_{18}H_{12}{}^{79}BrN_3NaO^+$ $[M+Na]^+$ 388.0056; found 388.0054.

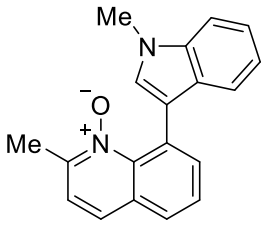
4. Same general procedure D for the synthesis of 8-(indol-3-yl)-quinoline *N*-oxides

8-(1-Methyl-1*H*-indol-3-yl)quinoline 1-oxide (12a)



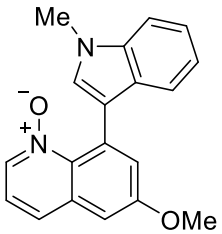
Following General Procedure **D**, starting from quinoline *N*-oxide **11a** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **12a** (32.8 mg, 0.120 mmol, 60% yield) as a yellow oil. **Rf** 0.80 (DCM/MeOH 19:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (dd, *J* = 6.0, 1.2 Hz, 1H, $\underline{H}_{Ar}$), 7.83 (dd, *J* = 8.1, 1.6 Hz, 1H, $\underline{H}_{Ar}$), 7.73 (dd, *J* = 8.5, 1.1 Hz, 1H, $\underline{H}_{Ar}$), 7.67 (dd, *J* = 7.2, 1.6 Hz, 1H, $\underline{H}_{Ar}$), 7.59 (dd, *J* = 8.0, 7.3 Hz, 1H, $\underline{H}_{Ar}$), 7.41-7.32 (m, 2H, $\underline{H}_{Ar}$), 7.29-7.17 (m, 2H, $\underline{H}_{Ar}$), 7.12 (s, 1H, $C2_{indole}\underline{H}$), 7.09 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H, $\underline{H}_{Ar}$), 3.86 (s, 3H, $NC\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 140.9, 137.2, 136.3, 135.5, 132.6, 129.3, 129.2, 127.9, 127.9, 127.3, 125.6, 121.5, 121.0, 120.1, 119.6, 117.0, 109.3, 33.0.
IR ν_{max} 3051 (w), 2930 (w), 1707 (m), 1613 (w), 1570 (m), 1476 (m), 1418 (m), 1366 (m), 1302 (m), 1245 (s), 1160 (w), 1058 (w), 1021 (w), 902 (w), 824 (m).
HRMS calculated for $C_{18}H_{15}N_2O^+$ $[M+H]^+$ 275.1179; found 275.1188.

2-Methyl-8-(1-methyl-1*H*-indol-3-yl)quinoline 1-oxide (12b)



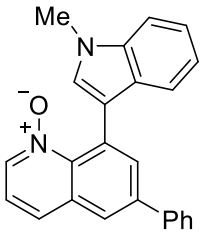
Following General Procedure **D**, starting from 2-methylquinoline *N*-oxide **11b** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **12b** (38.2 mg, 0.132 mmol, 66% yield) as a yellow oil. **Rf** 0.85 (DCM/MeOH 19:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 8.0, 1.6 Hz, 1H, $\underline{H}_{Ar}$), 7.66-7.62 (m, 2H, $\underline{H}_{Ar}$), 7.54 (dd, *J* = 8.0, 7.3 Hz, 1H, $\underline{H}_{Ar}$), 7.34 (m, 1H, $\underline{H}_{Ar}$), 7.30 (m, 2H, $\underline{H}_{Ar}$), 7.22 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H, $\underline{H}_{Ar}$), 7.14 (s, 1H, $C2_{indole}\underline{H}$), 7.05 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H, $\underline{H}_{Ar}$), 3.86 (s, 3H, $NC\underline{H}_3$), 2.56 (s, 3H, $C\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 146.8, 140.9, 136.3, 135.6, 131.3, 129.4, 128.8, 127.9, 126.9, 126.9, 124.5, 123.0, 121.5, 120.1, 119.3, 117.8, 109.3, 33.0, 19.4.
IR ν_{max} 3048 (w), 2936 (w), 2837 (w), 1665 (s), 1548 (s), 1466 (s), 1436 (m), 1362 (m), 1339 (m), 1228 (m), 1159 (m), 1125 (m), 1033 (m), 846 (m), 804 (s), 737 (m).
HRMS calculated for $C_{19}H_{17}N_2O^+$ $[M+H]^+$ 289.1335; found 289.1346.

6-Methoxy-8-(1-methyl-1*H*-indol-3-yl)quinoline 1-oxide (12c)



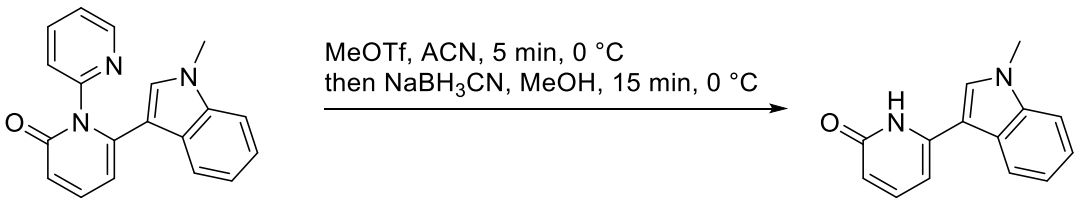
Following General Procedure **D**, starting from 6-methoxyquinoline *N*-oxide **11c** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **12c** (34.9 mg, 0.115 mmol, 57% yield) as a yellow oil. **Rf** 0.78 (DCM/MeOH 19:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 6.0, 1.2 Hz, 1H, $\underline{H}_{Ar}$), 7.61 (dd, *J* = 8.4, 1.2 Hz, 1H, $\underline{H}_{Ar}$), 7.39 (dt, *J* = 7.9, 1.0 Hz, 1H, $\underline{H}_{Ar}$), 7.34 (dt, *J* = 8.4, 0.9 Hz, 1H, $\underline{H}_{Ar}$), 7.31 (d, *J* = 2.9 Hz, 1H, $\underline{H}_{Ar}$), 7.25-7.17 (m, 2H, $\underline{H}_{Ar}$), 7.12 (s, 1H, $C2_{indole}\underline{H}$), 7.12-7.05 (m, 2H, $\underline{H}_{Ar}$), 3.94 (s, 3H, $OC\underline{H}_3$), 3.85 (s, 3H, $NC\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 136.8, 136.3, 135.4, 134.1, 131.1, 129.2, 127.4, 126.8, 124.7, 121.6, 121.5, 120.1, 119.7, 116.7, 109.3, 106.0, 55.7, 33.0.
IR ν_{max} 3051 (w), 2985 (w), 1665 (m), 1609 (w), 1584 (m), 1552 (w), 1465 (w), 1436 (w), 1362 (w), 1266 (s), 1230 (w), 1159 (w), 1126 (w), 1030 (w), 805 (w).
HRMS calculated for $C_{19}H_{17}N_2O_2^+$ $[M+H]^+$ 305.1285; found 305.1287.

8-(1-methyl-1*H*-indol-3-yl)-6-phenylquinoline 1-oxide (12d)



Following General Procedure **D**, starting from 6-phenylquinoline *N*-oxide **11d** and **6a**, a purification by preparative TLC (DCM/MeOH 19:1) afforded the title compound **12d** (51.3 mg, 0.146 mmol, 73% yield) as a yellow oil. **Rf** 0.58 (DCM/MeOH 19:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, *J* = 6.0, 1.2 Hz, 1H, $\underline{H}_{Ar}$), 7.98 (d, *J* = 2.1 Hz, 1H, $\underline{H}_{Ar}$), 7.93 (d, *J* = 2.1 Hz, 1H, $\underline{H}_{Ar}$), 7.75 (dd, *J* = 8.4, 1.1 Hz, 1H, $\underline{H}_{Ar}$), 7.73-7.65 (m, 2H, $\underline{H}_{Ar}$), 7.46 (t, *J* = 7.4 Hz, 2H, $\underline{H}_{Ar}$), 7.41 (dd, *J* = 8.5, 7.3 Hz, 2H, $\underline{H}_{Ar}$), 7.34 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$), 7.25-7.19 (m, 2H, $\underline{H}_{Ar}$), 7.16 (s, 1H, $C2_{indole}\underline{H}$), 7.12-7.05 (m, 1H, $\underline{H}_{Ar}$), 3.84 (s, 3H, $NC\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 140.2, 139.9, 138.9, 136.9, 136.2, 134.8, 132.8, 129.6, 129.1, 129.0, 128.2, 127.4, 127.3, 125.8, 125.1, 121.4, 121.2, 120.0, 119.5, 116.7, 109.2, 32.8.
IR ν_{max} 3050 (w), 2975 (m), 2932 (m), 2873 (m), 1576 (m), 1478 (m), 1363 (m), 1332 (m), 1288 (m), 1250 (m), 1231 (m), 1170 (m), 1133 (m), 1116 (m), 1060 (m), 846 (m), 797 (m), 762 (s), 736 (s).
HRMS calculated for $C_{24}H_{19}N_2O^+$ $[M+H]^+$ 351.1492; found 351.1490.

5. Product modifications



7a **13**

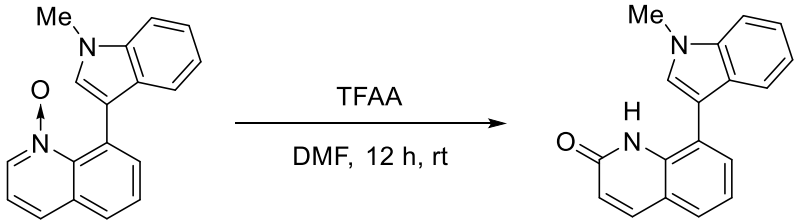
Following a modified reported procedure,[10] **7a** (90 mg, 0.30 mmol, 1.0 equiv) was solubilized in dry ACN (0.6 mL) under N_2. MeOTf (0.10 mL, 0.90 mmol, 3.0 equiv) was added to the mixture at 0 °C. The mixture was stirred 5 min at 0 °C and MeOH (3 mL) was added. $NaBH_3CN$ (94 mg, 1.5 mmol, 5.0 equiv) was added portionwise to the solution at 0 °C. The mixture was stirred 15 min at 0 °C and then quenched with H_2O (2 mL). The mixture was diluted with EtOAc (5 mL) and the layers were separated. The aqueous layer was extracted three times with EtOAc (5 mL). The organic layers were combined, dried over magnesium sulfate dehydrate, filtered and concentrated under reduced pressure. The crude residue was purified by preparative TLC using DCM/MeOH 19:1 as eluent to afforded **13** (50 mg, 0.22, 74%) as an off-white solid. **mp** 217-219 °C. **Rf** 0.53 (DCM/MeOH 19:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.08 (s, 1H, NH), 7.96 (s, 1H, H_{Ar}), 7.89 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.49 (dd, *J* = 8.9, 7.2 Hz, 1H, H_{Ar}), 7.38 (d, *J* = 8.1 Hz, 1H, H_{Ar}), 7.31 (t, *J* = 7.4 Hz, 1H, H_{Ar}), 7.23 (t, *J* = 7.3 Hz, 1H, H_{Ar}), 6.66 (d, *J* = 7.0 Hz, 1H, H_{Ar}), 6.39 (d, *J* = 8.9 Hz, 1H, H_{Ar}), 3.87 (s, 3H, NCH_3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 143.0, 142.1, 137.8, 130.0, 125.3, 122.8, 121.2, 119.9, 115.9, 110.2, 109.1, 104.1, 33.5.

IR ν_{max} 3104 (m), 3043 (w), 2944 (br), 1650 (s), 1601 (s), 1570 (m), 1532 (m), 1460 (s), 1367 (s), 1256 (m), 1238 (m), 1137 (m), 1101 (s), 980 (m), 894 (s), 777 (s), 736 (s), 713 (s).

HRMS calculated for $C_{14}H_{13}N_2O^+$ $[M+H]^+$ 225.1022; found 225.1027.



12a **14**

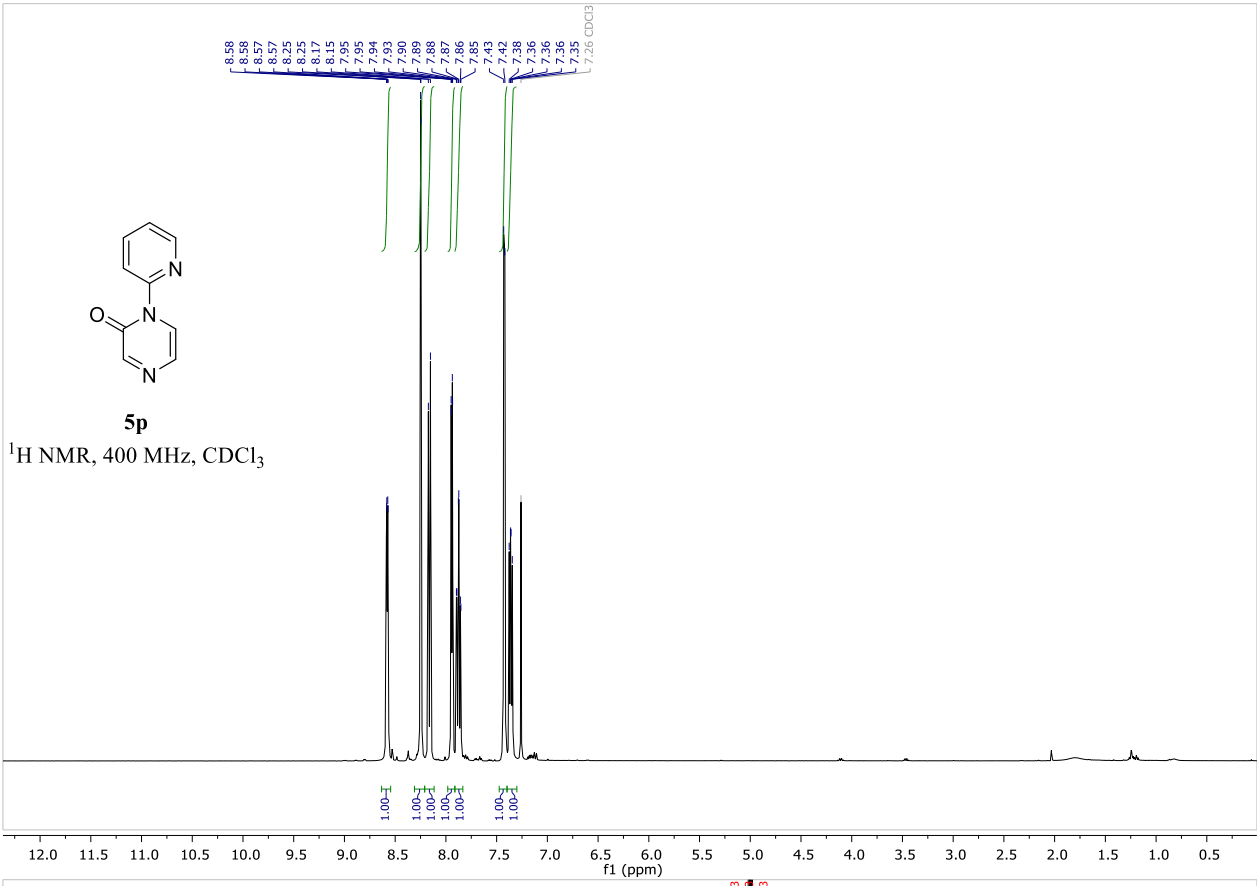
Following a reported procedure,[11] **12a** (27.4 mg, 0.100 mmol, 1.00 equiv) was solubilized in dry DMF (3 mL). TFAA (140 µL, 1.00 mmol, 10.0 equiv) was added to the mixture at rt. The mixture was stirred overnight and the TFAA excess was eliminated under reduced pressure. The mixture was poured into H_2O (30 mL) and extracted three times with EtOAc (10 mL). The organic layers were combined, washed twice with brine (5 mL), dried over magnesium sulfate dehydrate, filtered and concentrated under reduced pressure. The crude residue was purified by preparative TLC using DCM/MeOH 24:1 as eluent to afforded **14** (17.0 mg, 0.062 mmol, 62%) as a pale brown solid. **mp** 192-194 °C. **Rf** 0.92 (DCM/MeOH 19:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1H, NH), 7.83 (d, *J* = 9.5 Hz, 1H, H_{Ar}), 7.61-7.54 (m, 2H, H_{Ar}), 7.45 (t, *J* = 7.4 Hz, 2H, H_{Ar}), 7.36-7.31 (m, 1H, H_{Ar}), 7.30 (d, *J* = 7.7 Hz, 1H, H_{Ar}), 7.23 (s, 1H, $C2_{indole}H$), 7.20-7.15 (m, 1H, H_{Ar}), 6.66 (d, *J* = 9.5 Hz, 1H, H_{Ar}), 3.91 (s, 3H, NCH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.6, 141.2, 137.4, 136.4, 132.4, 127.9, 127.0, 126.8, 123.0, 122.5, 122.0, 121.8, 120.7, 120.1, 119.5, 110.0, 109.5, 33.3. Spectra data matched with the values reported in literature.[7]

[10] Smout, V.; Peschiulli, A.; Verbeeck, S.; Mitchell, E. A.; Herrebout, W.; Bultinck, P.; Vande Velde, C. M. L.; Berthelot, D.; Meerpoel, L.; Maes, B. U. W. *J. Org. Chem.* **2013**, *78*, 9803–9814.

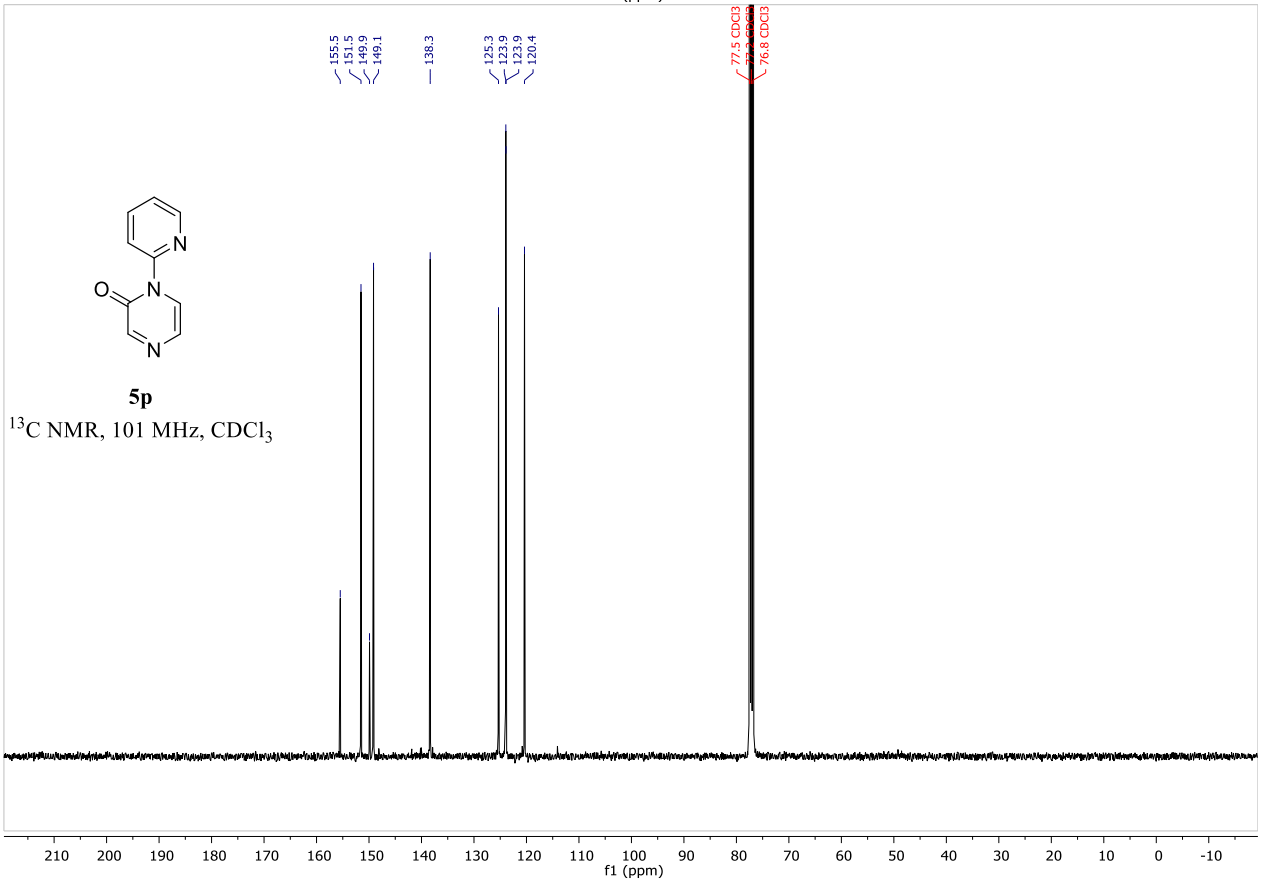
[11] Konno, K.; Hashimoto, K.; Shirahama, H.; Matsumoto, T. Heterocycles 1986, 24, 2169–2172.

6. Spectra of new compounds



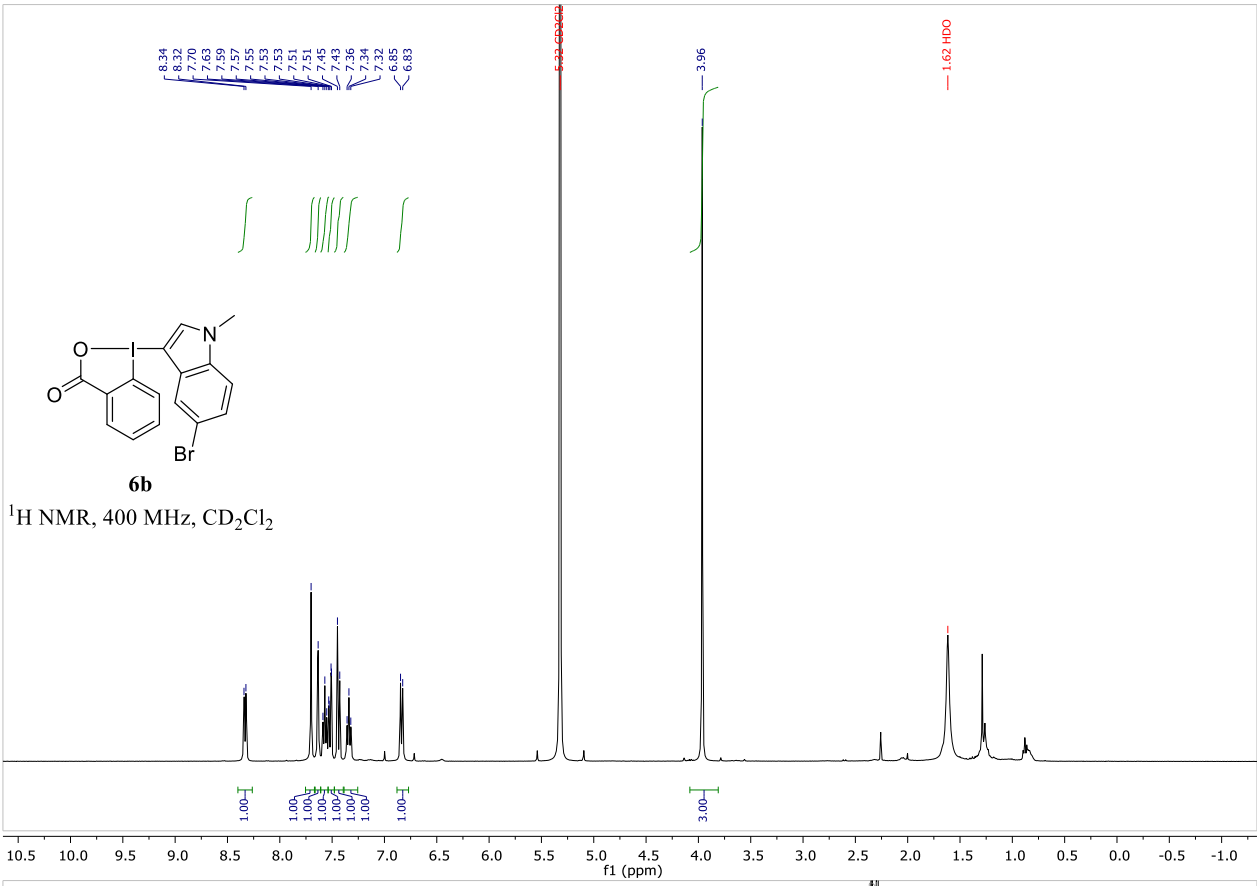
5p

^{1}H NMR, 400 MHz, $CDCl_3$



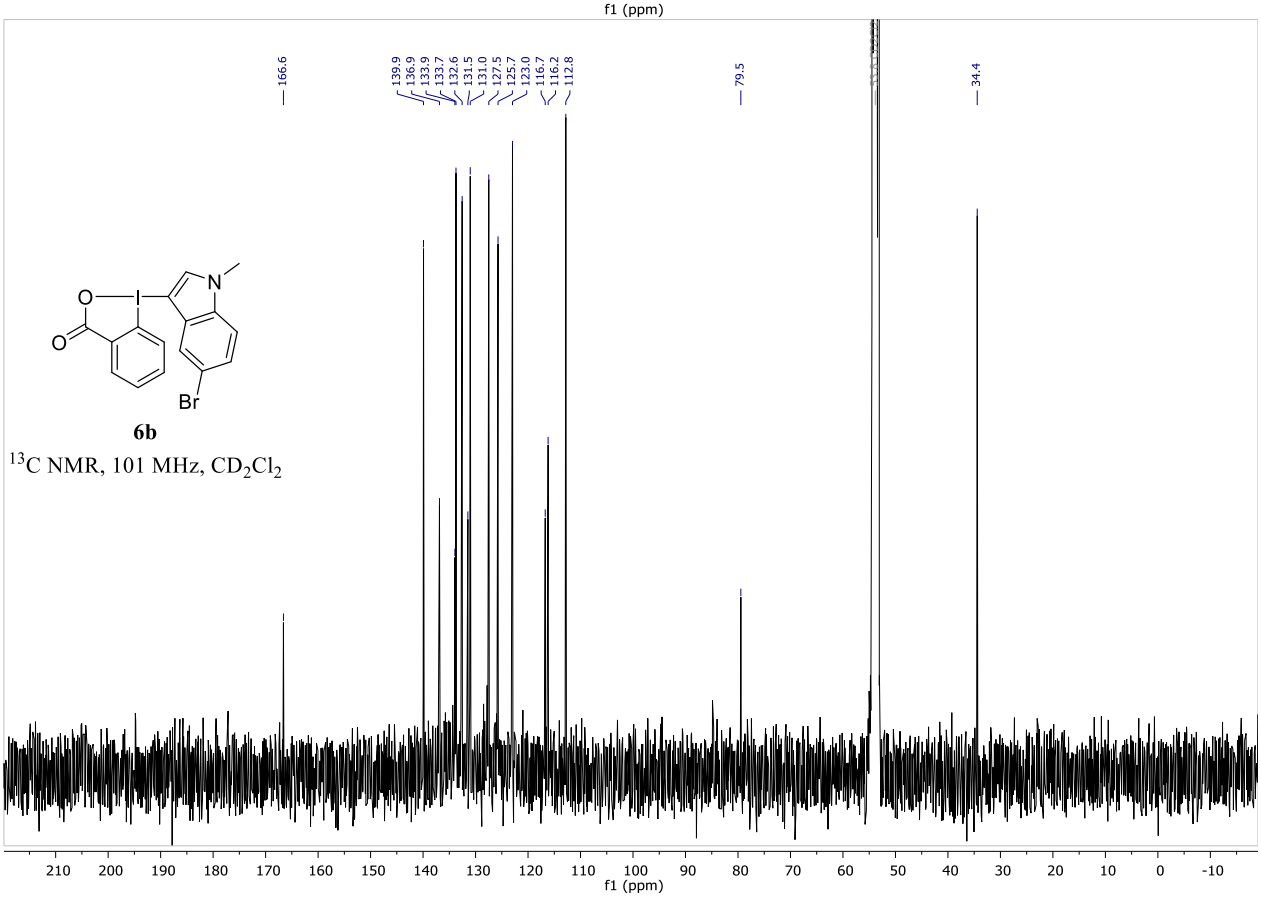
5p

^{13}C NMR, 101 MHz, $CDCl_3$



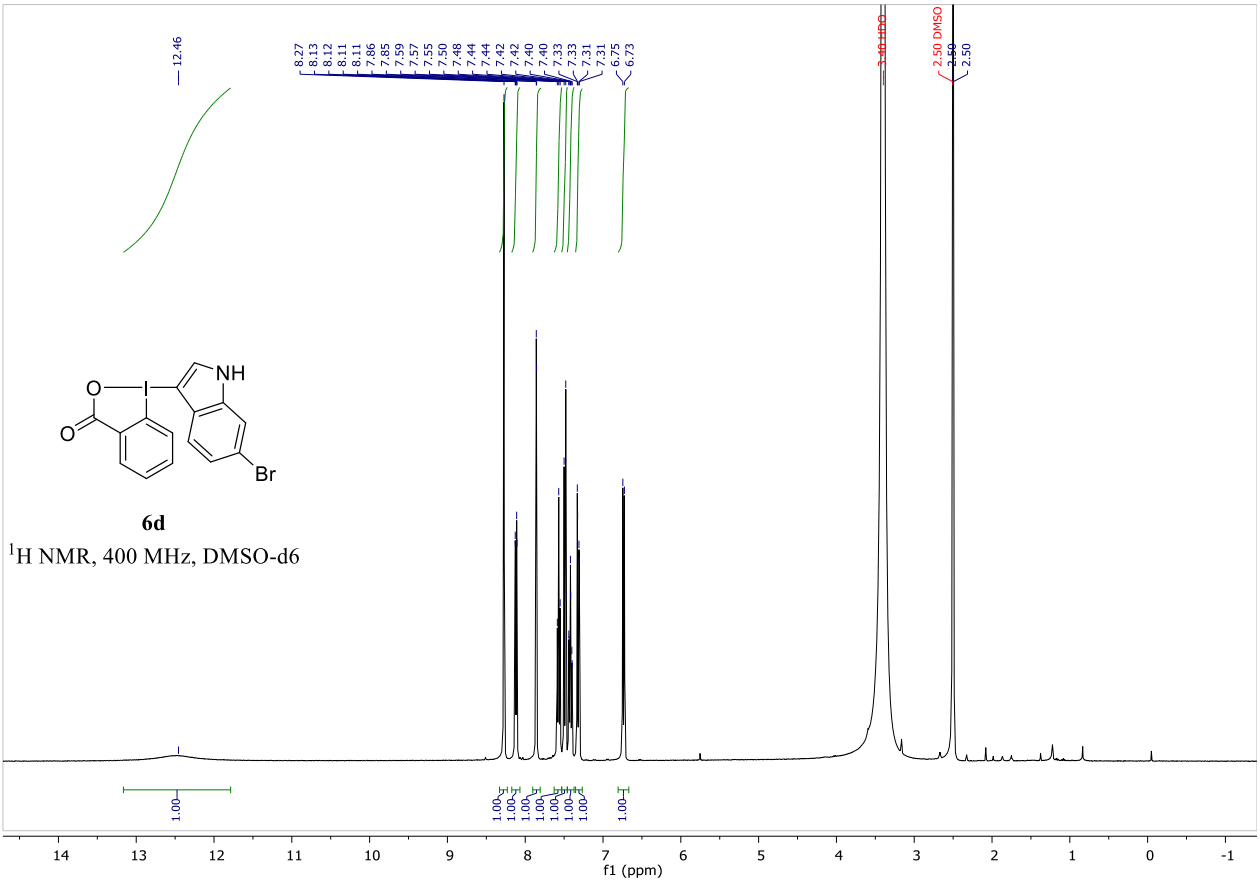
6b

^{1}H NMR, 400 MHz, CD_2Cl_2



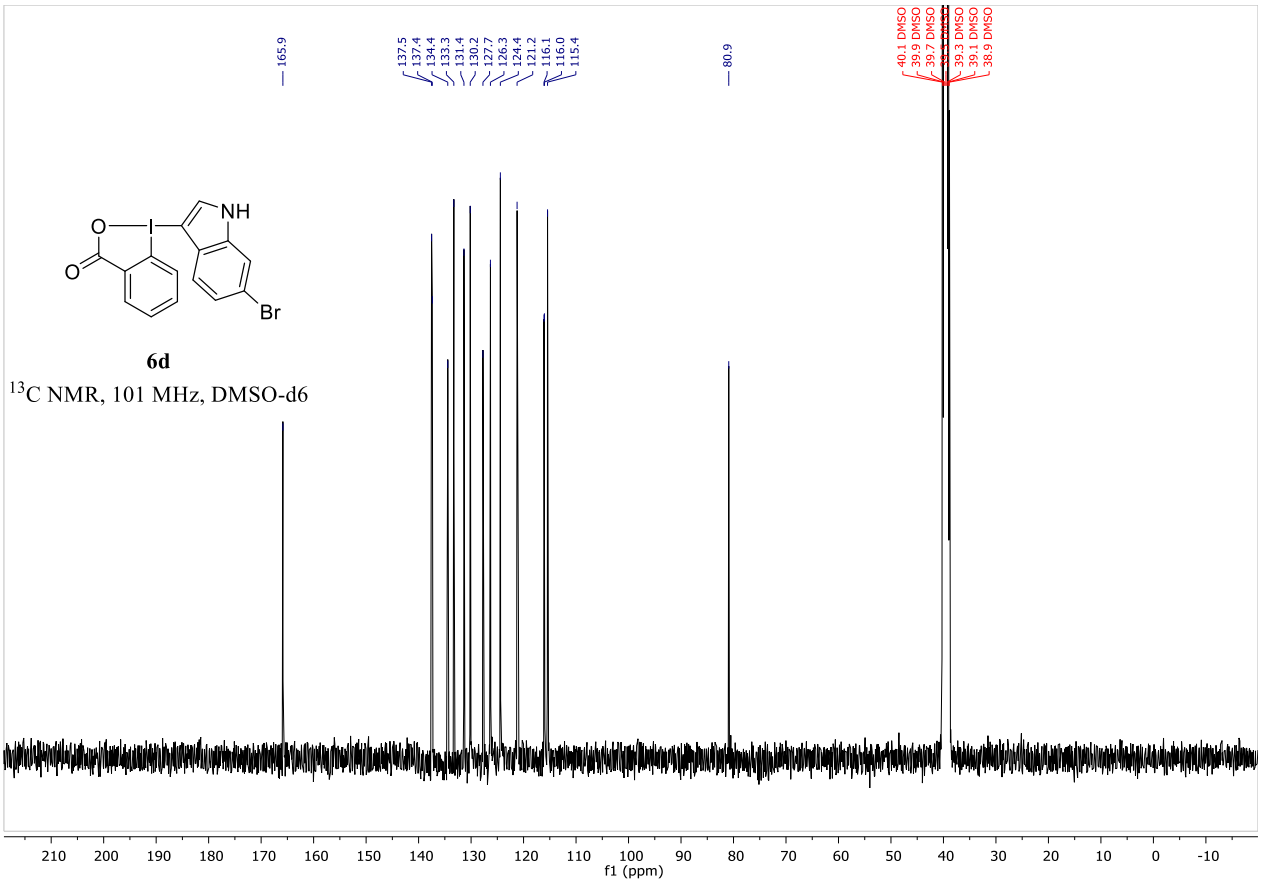
6b

^{13}C NMR, 101 MHz, CD_2Cl_2



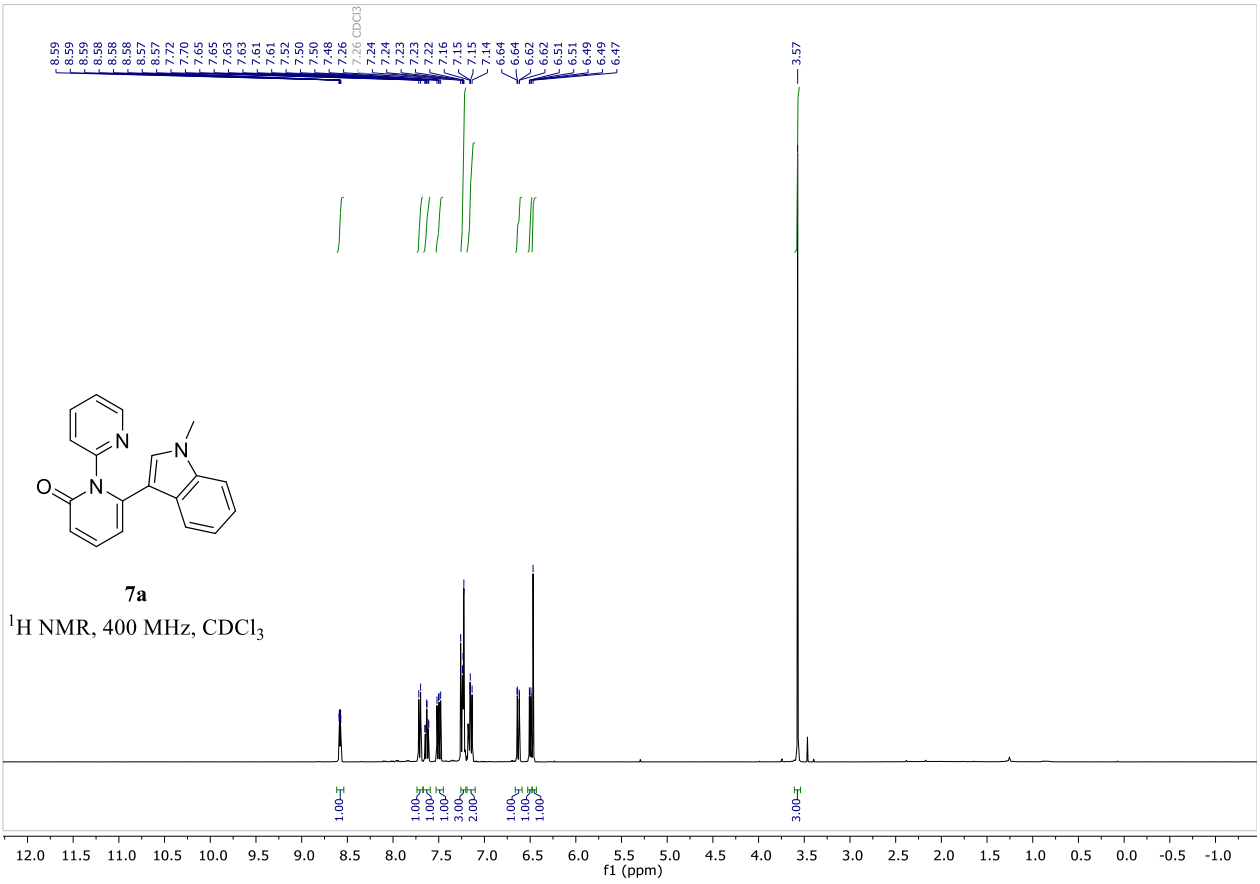
6d

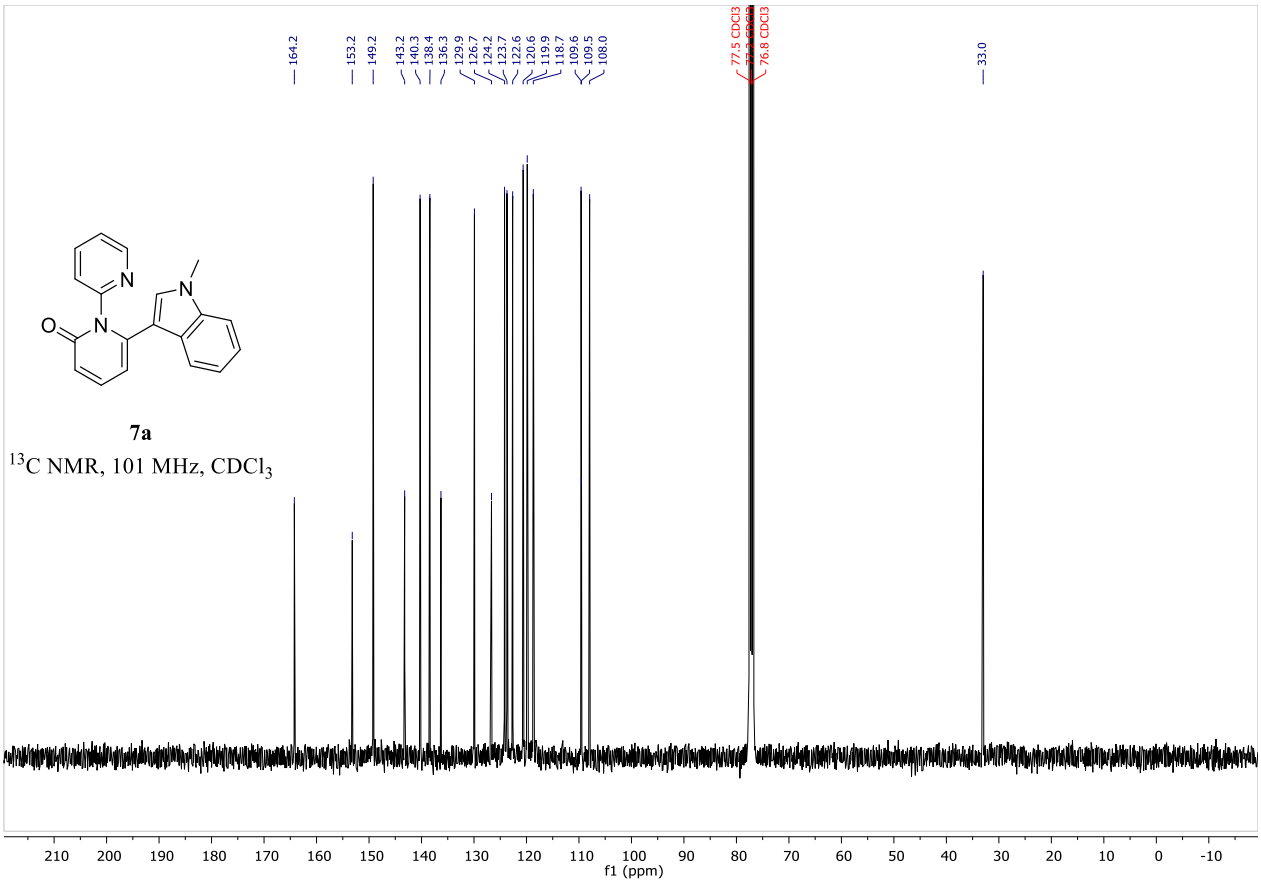
^{1}H NMR, 400 MHz, DMSO-d6

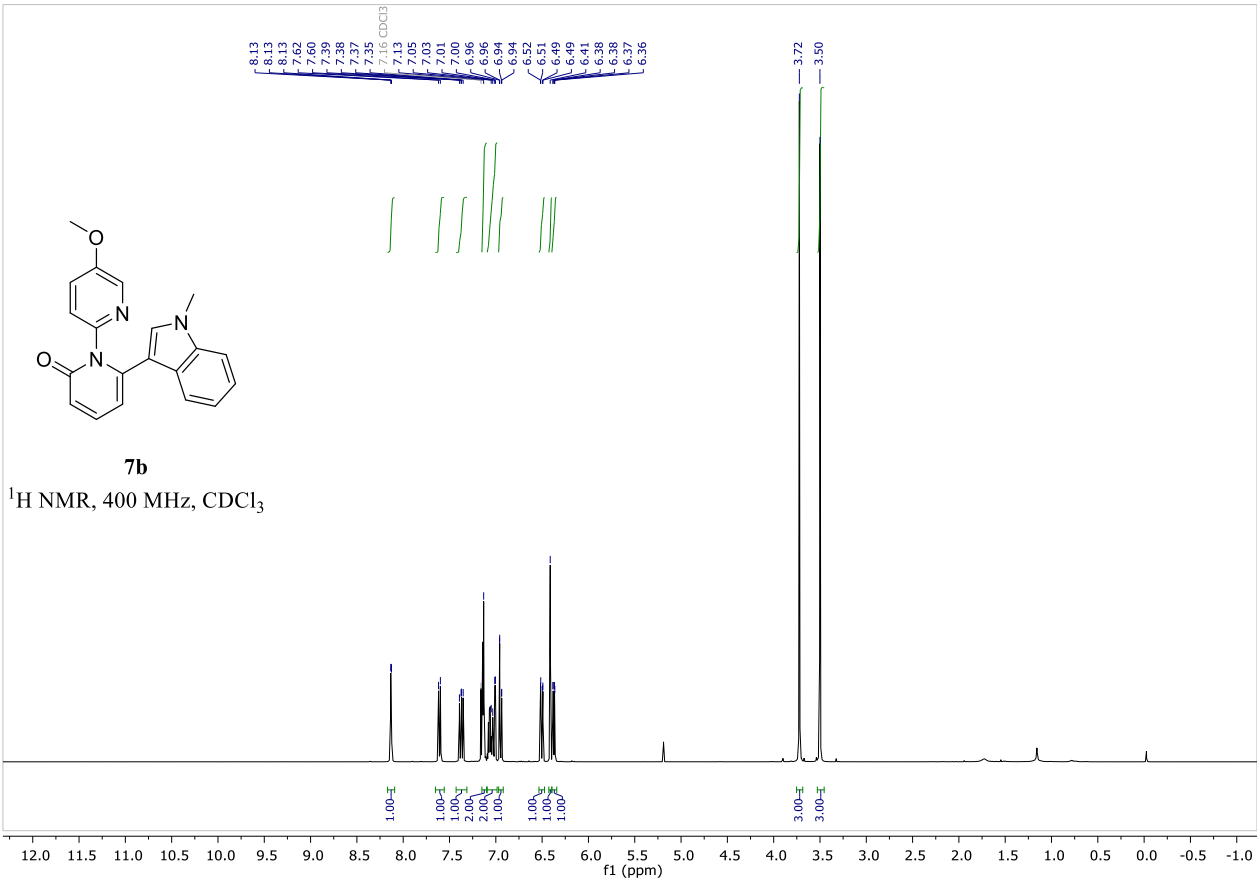


6d

^{13}C NMR, 101 MHz, DMSO-d6

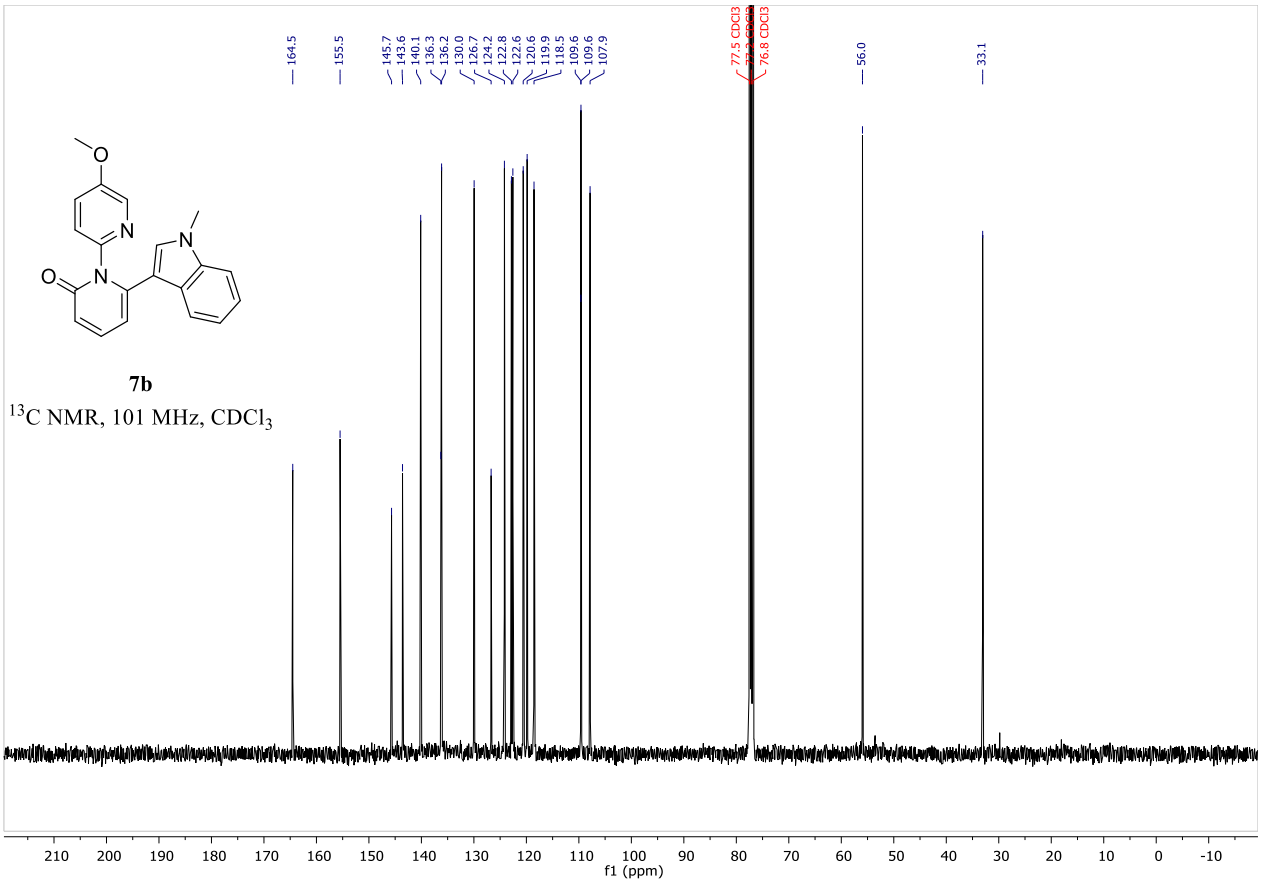

7a
1H NMR, 400 MHz, CDCl3
f1 (ppm)


7a
13C NMR, 101 MHz, CDCl3
f1 (ppm)



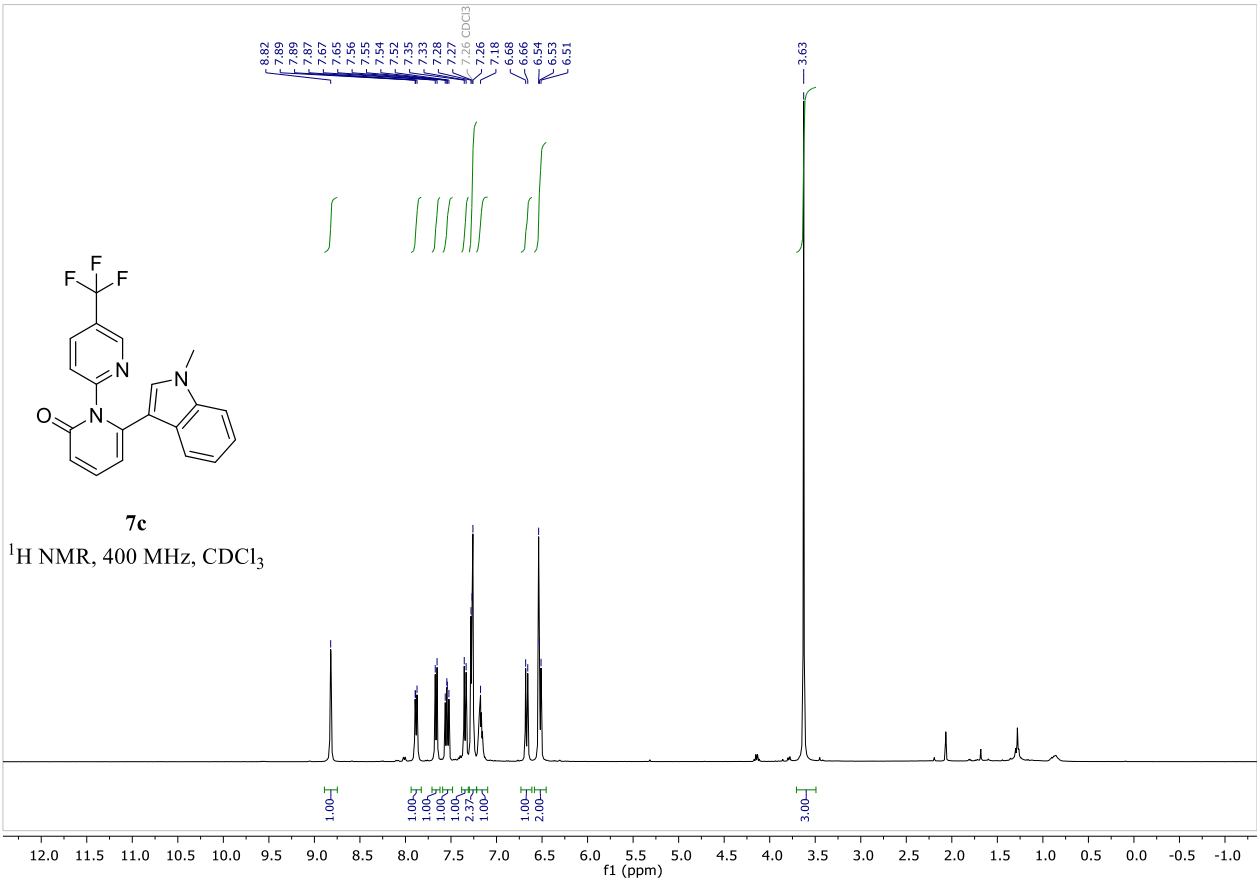
7b

^{1}H NMR, 400 MHz, $CDCl_3$



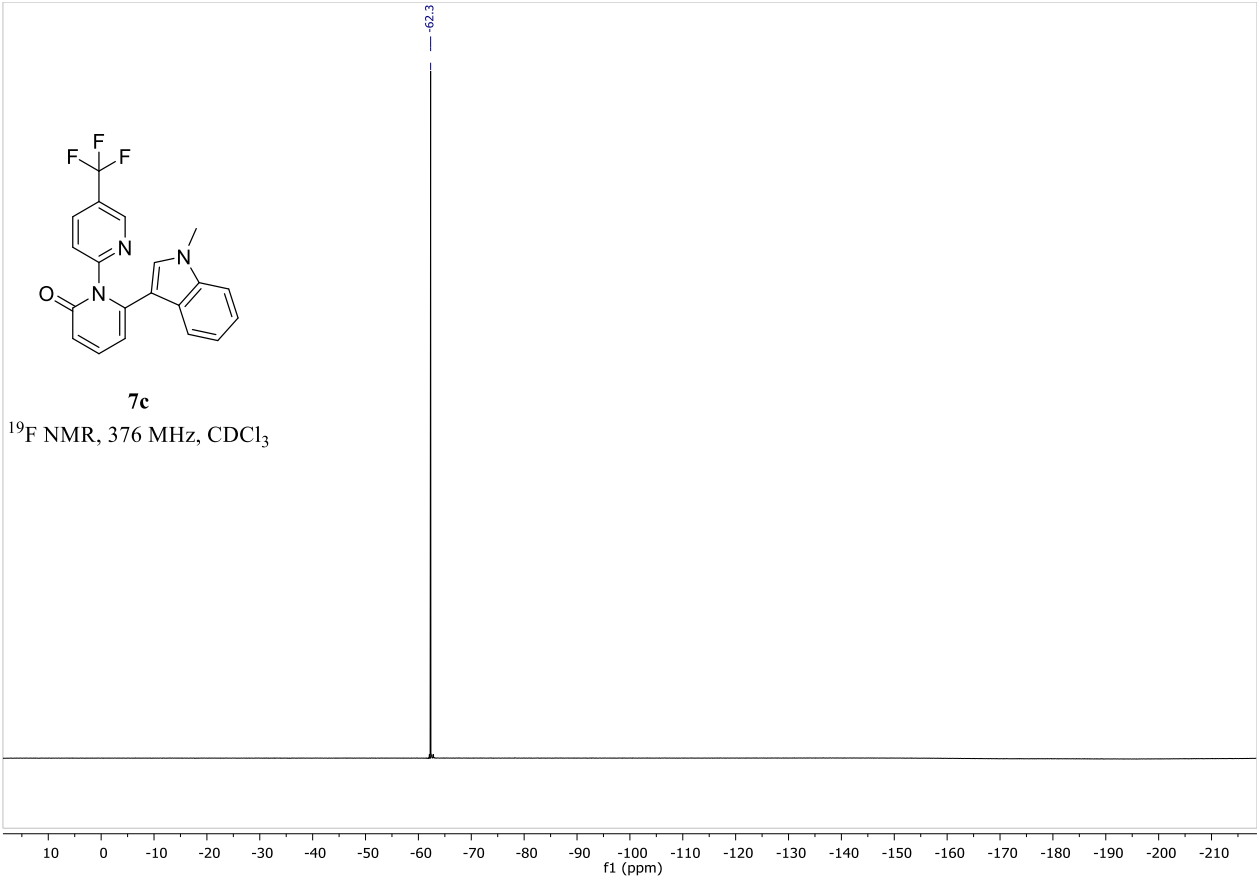
7b

^{13}C NMR, 101 MHz, $CDCl_3$



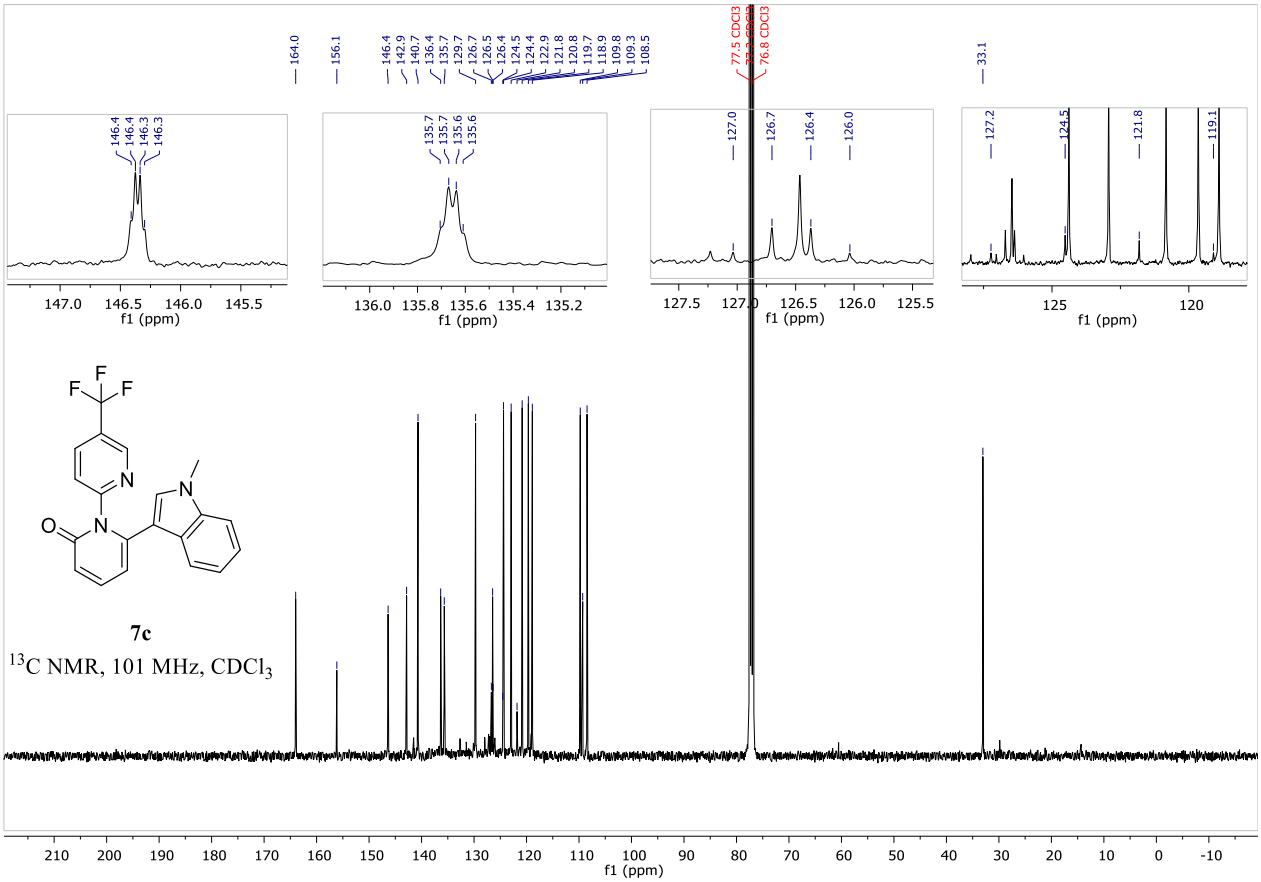
7c

^{1}H NMR, 400 MHz, $CDCl_3$



7c

^{19}F NMR, 376 MHz, $CDCl_3$


164.0
156.1
146.4
142.9
140.7
136.4
135.7
129.7
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126.4
124.5
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122.9
121.8
120.8
119.7
118.9
109.8
109.3
108.5
77.5 CDCl3
76.8 CDCl3
33.1
146.4
146.4
146.3
146.3
135.7
135.7
135.6
135.6
127.0
126.7
126.4
126.0
127.2
124.5
121.8
119.1
f1 (ppm)
F
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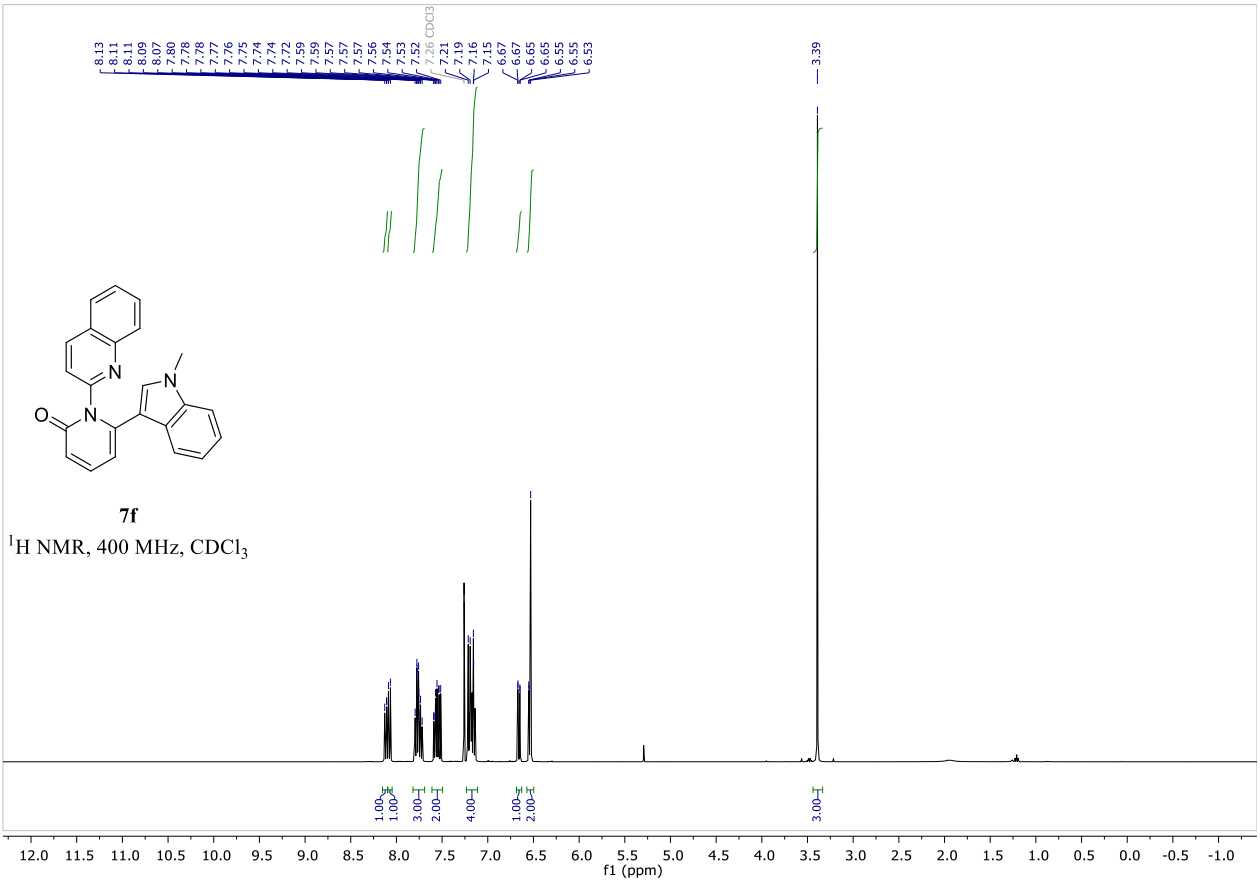
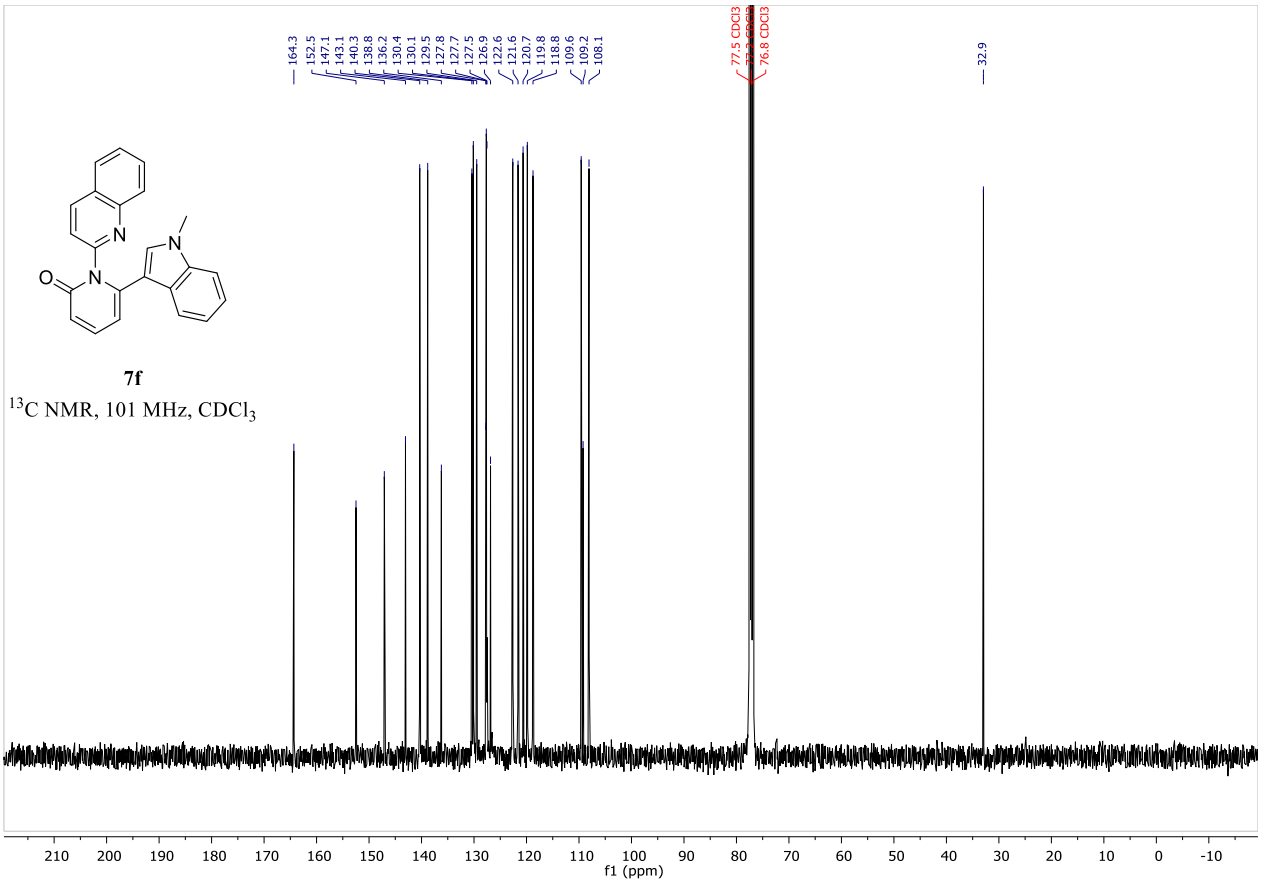
F
N
O
N
N
7c
13C NMR, 101 MHz, CDCl3



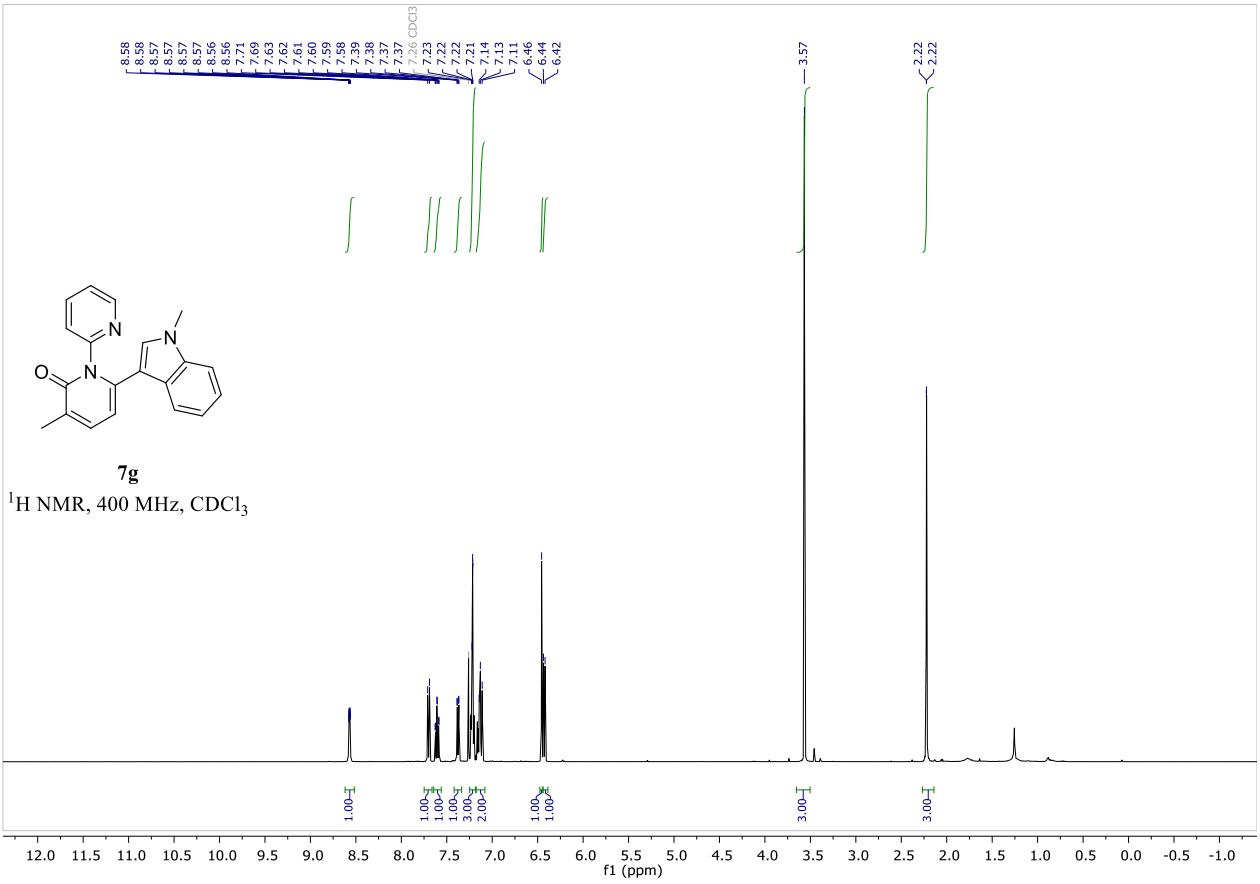
7f

^{1}H NMR, 400 MHz, $CDCl_3$



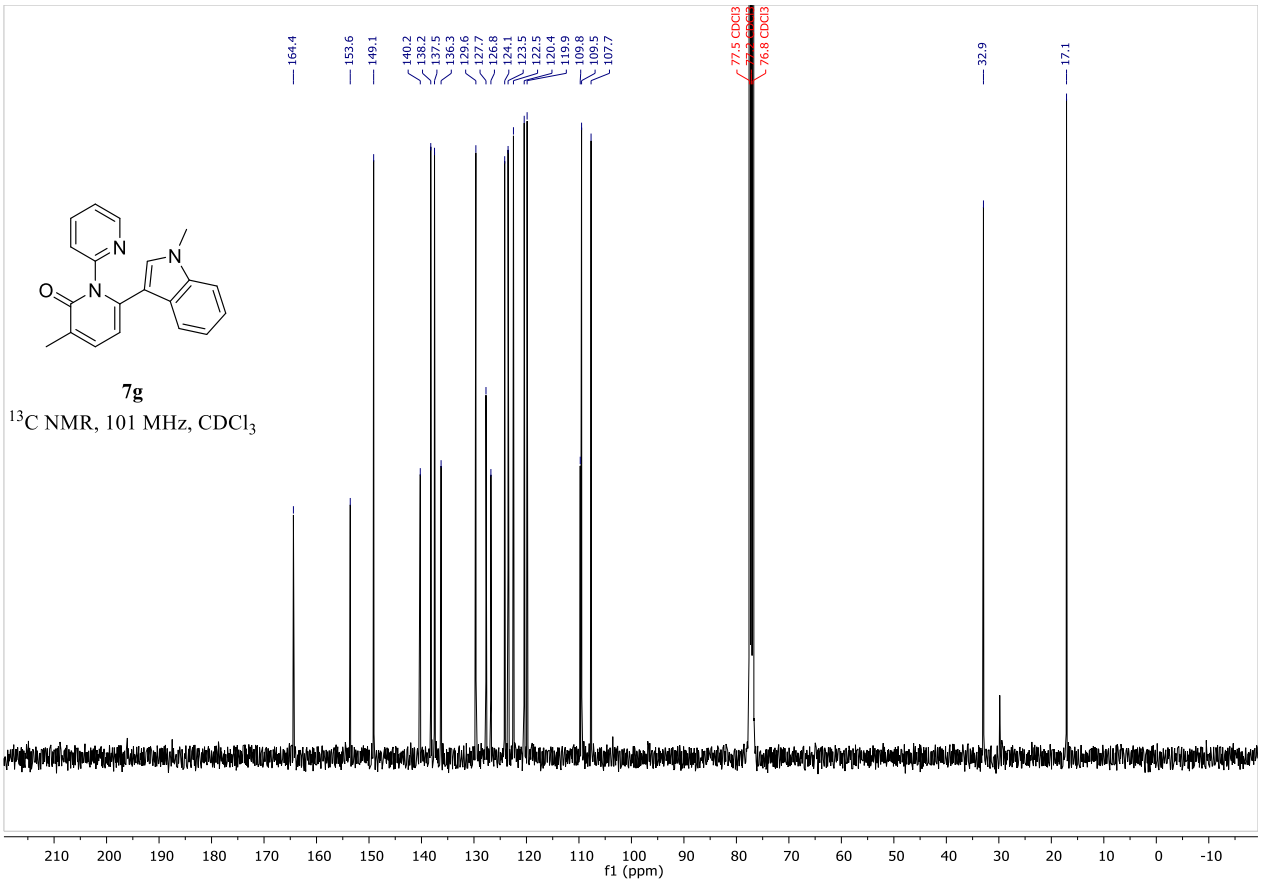
7f

^{13}C NMR, 101 MHz, $CDCl_3$



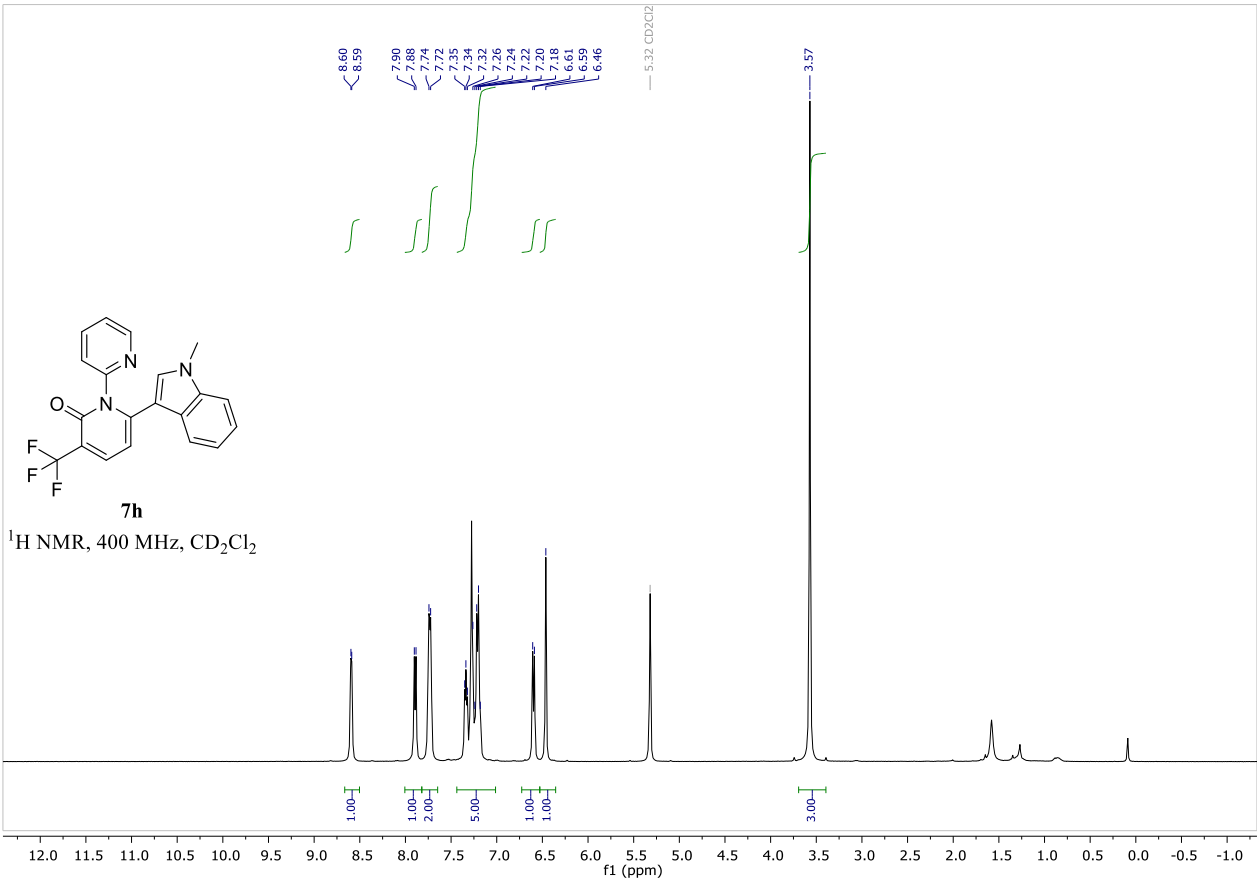
7g

^{1}H NMR, 400 MHz, $CDCl_3$



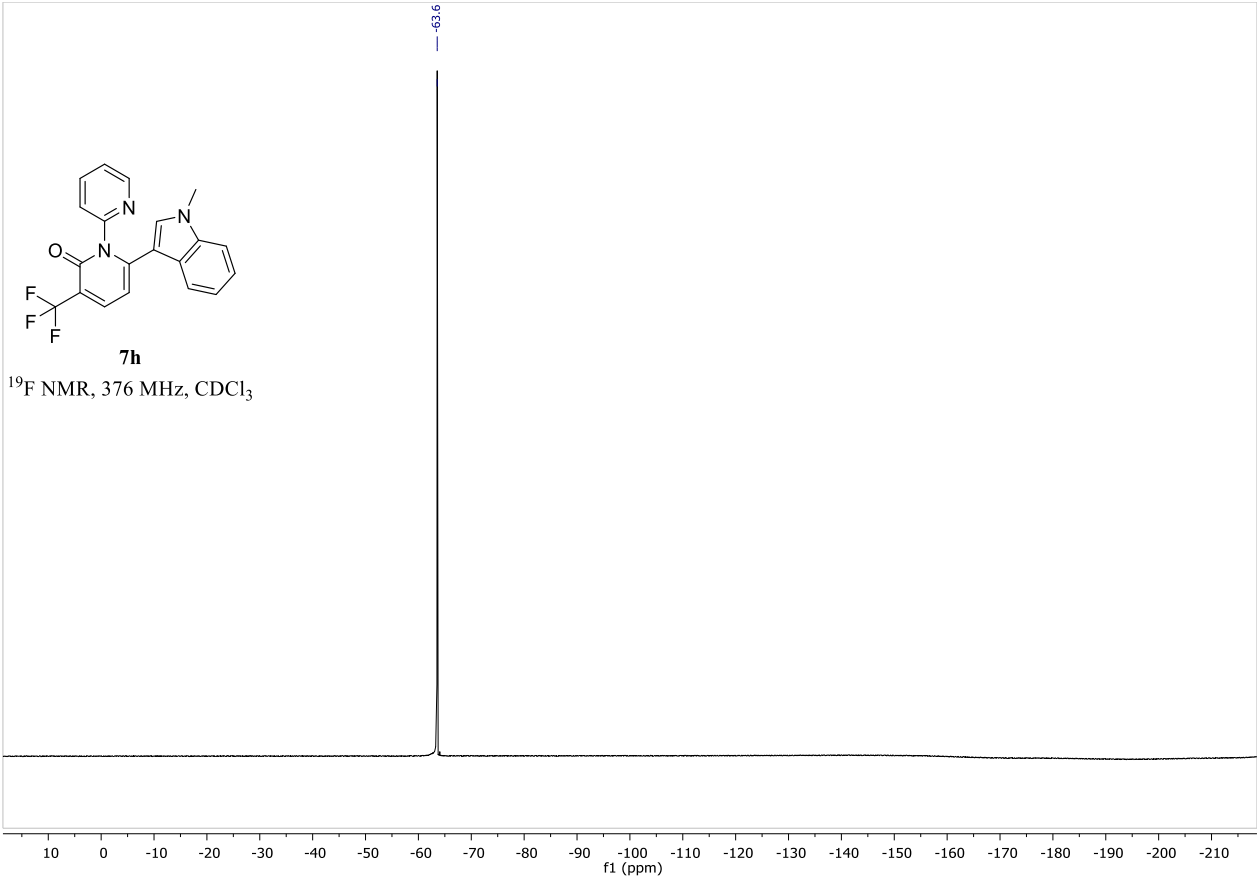
7g

^{13}C NMR, 101 MHz, $CDCl_3$



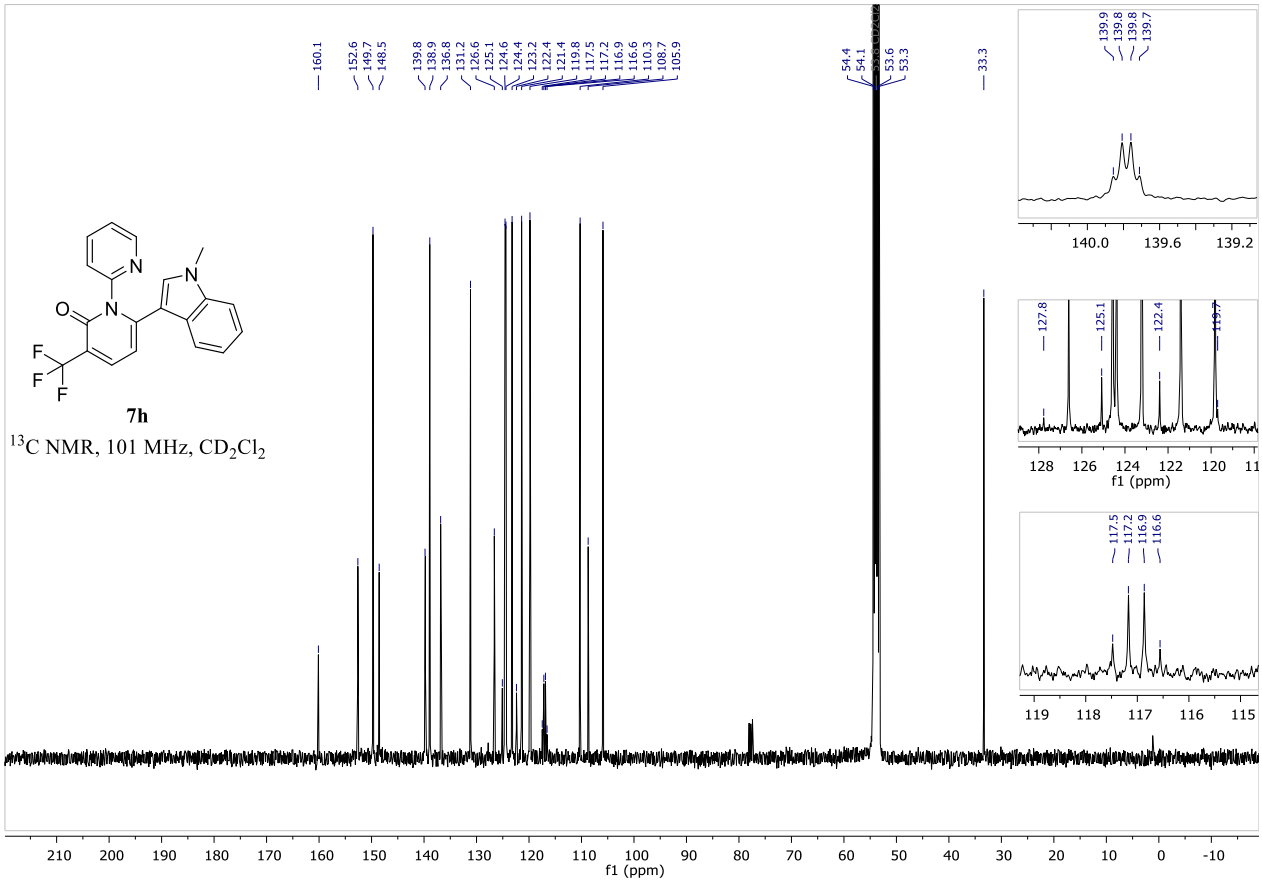
7h

^{1}H NMR, 400 MHz, CD_2Cl_2



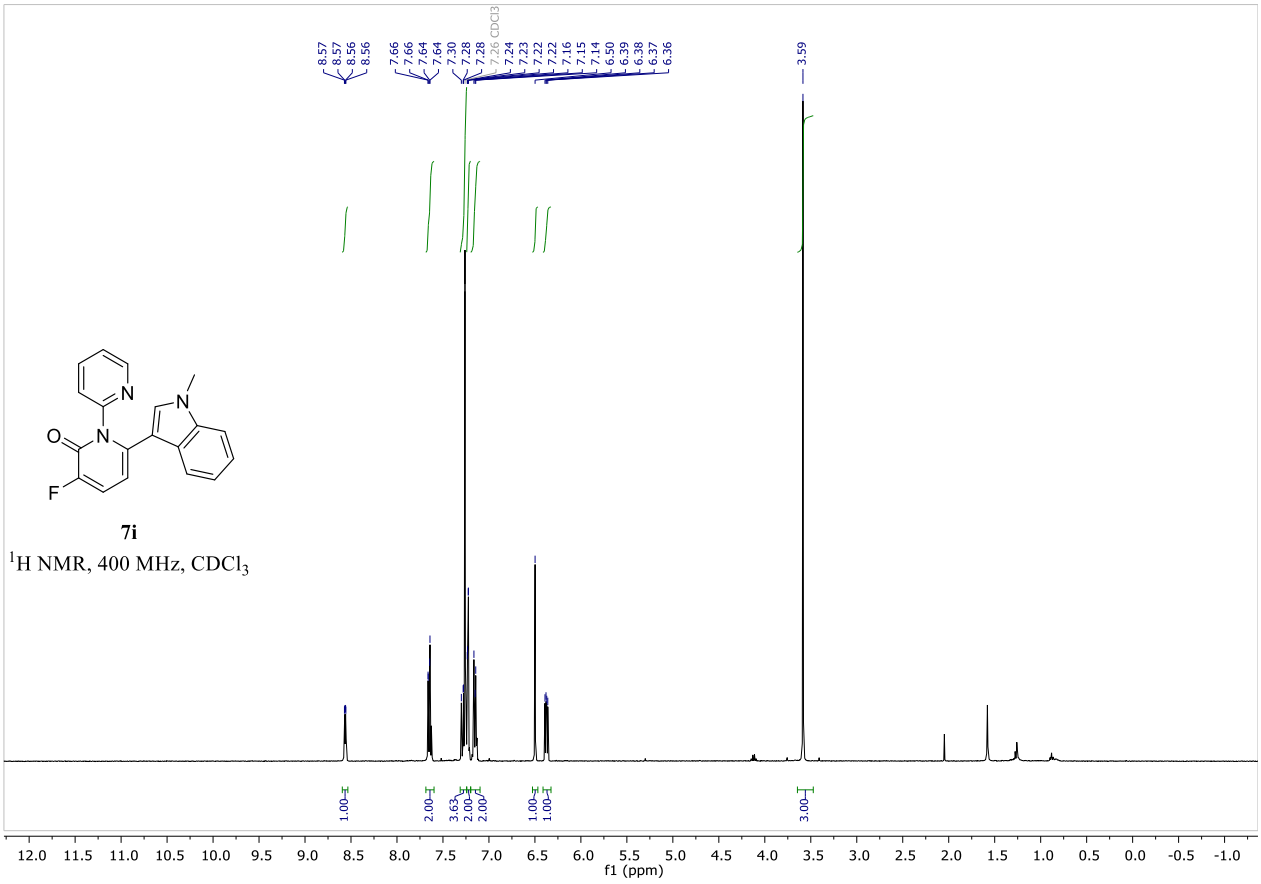
7h

^{19}F NMR, 376 MHz, $CDCl_3$



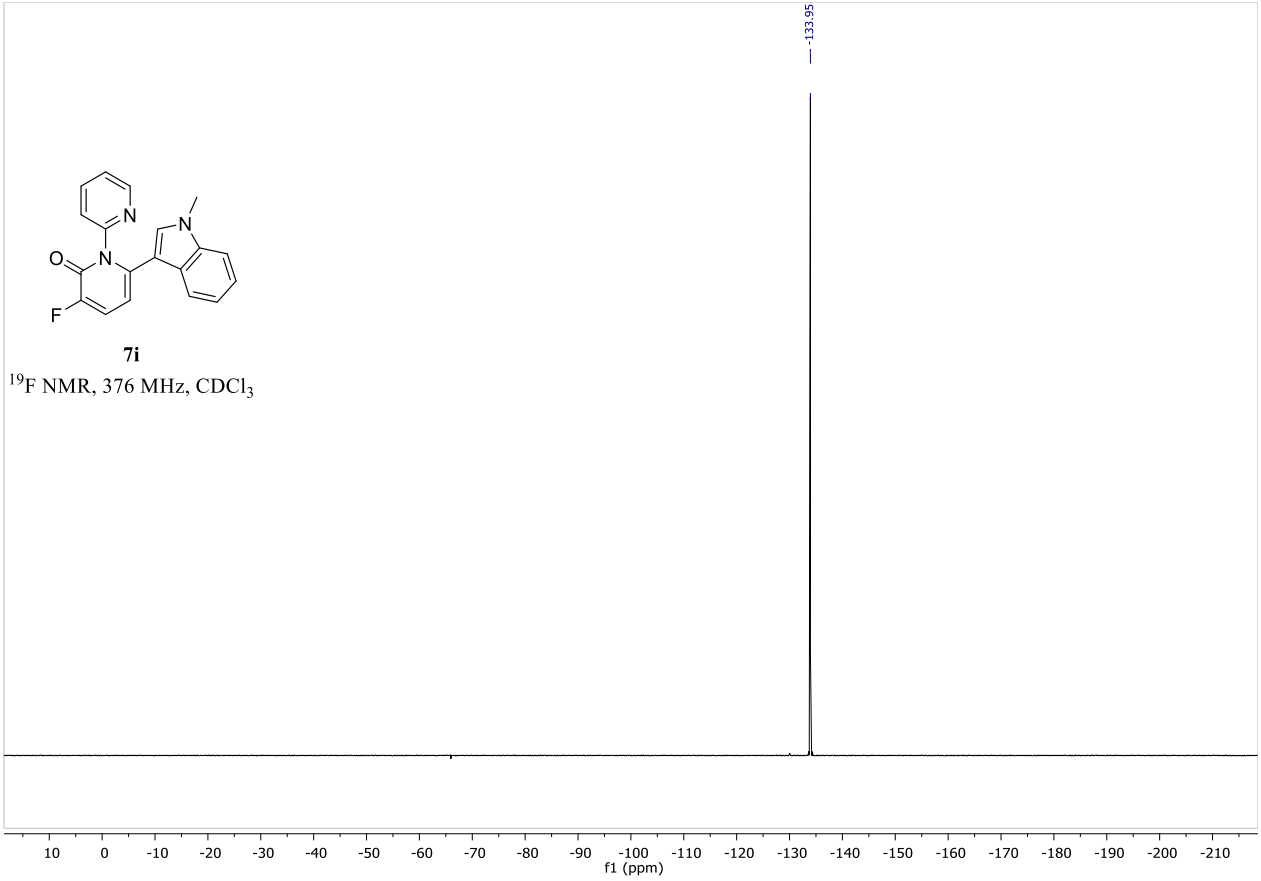
7h

^{13}C NMR, 101 MHz, CD_2Cl_2



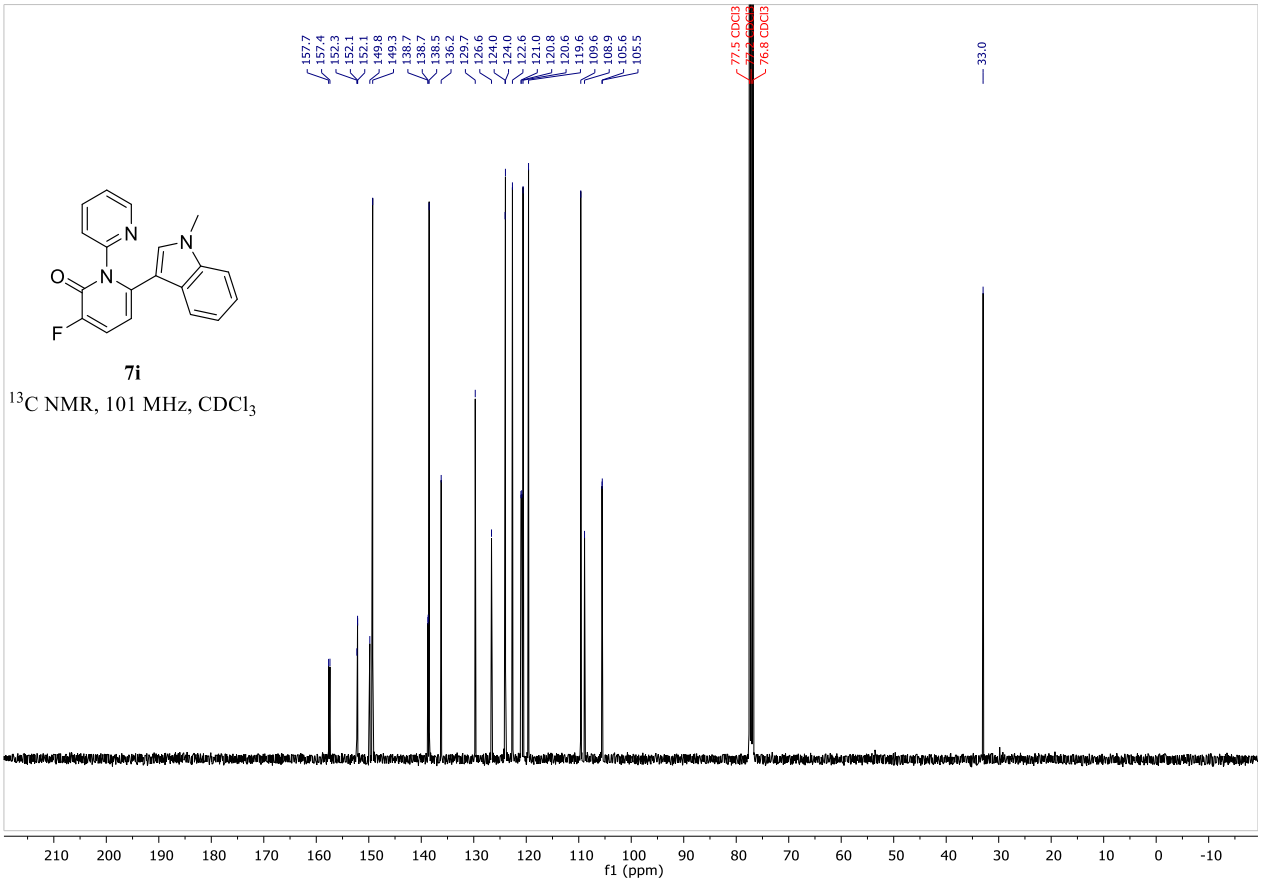
7i

^{1}H NMR, 400 MHz, $CDCl_3$



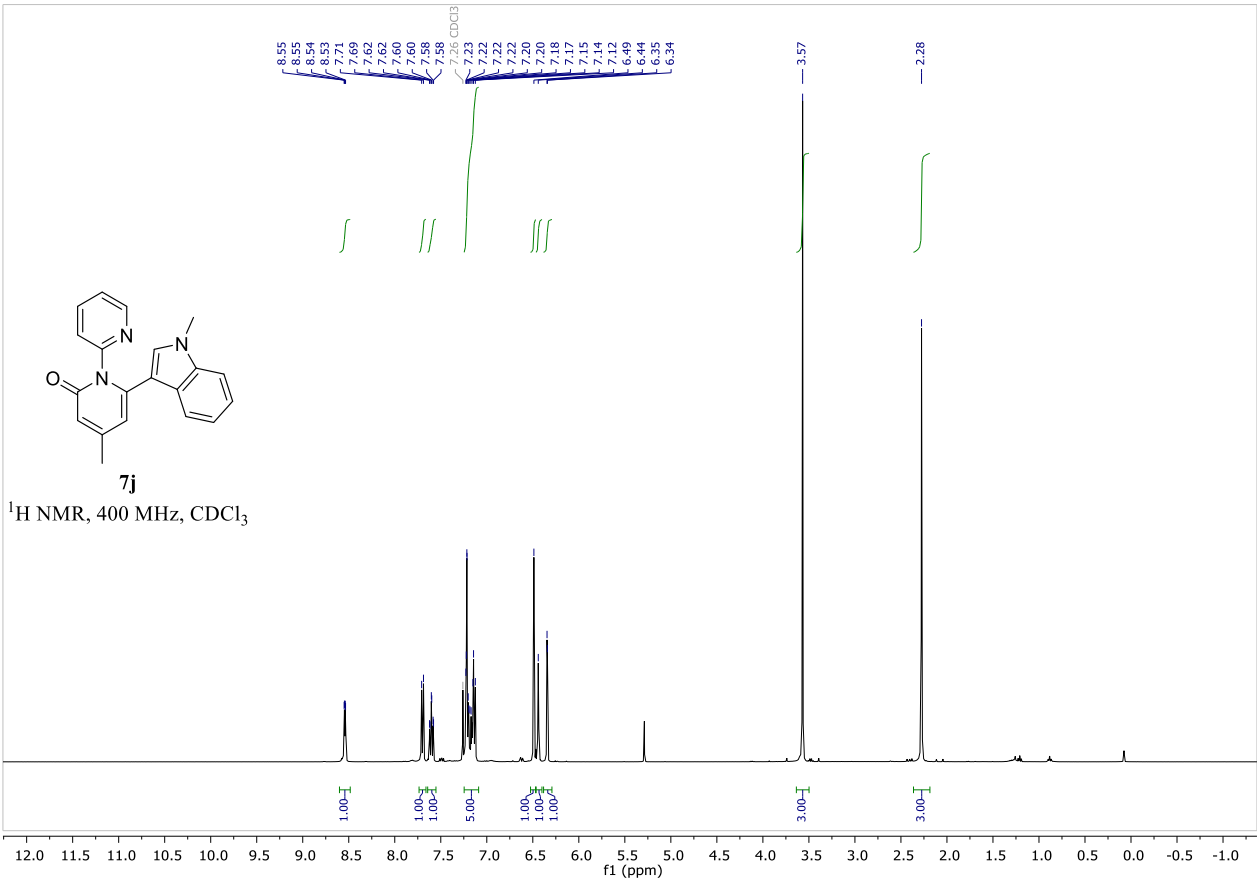
7i

^{19}F NMR, 376 MHz, $CDCl_3$



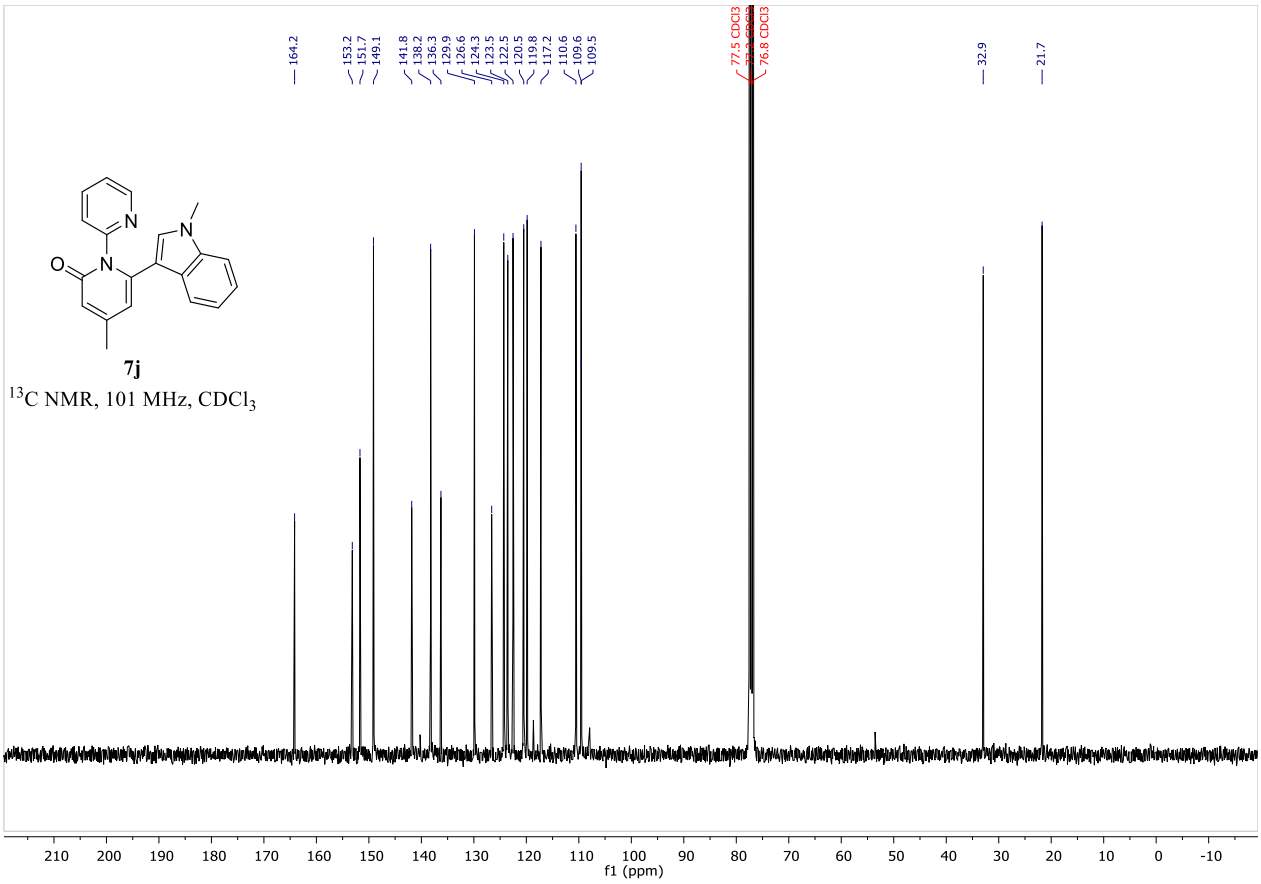
7i

^{13}C NMR, 101 MHz, $CDCl_3$



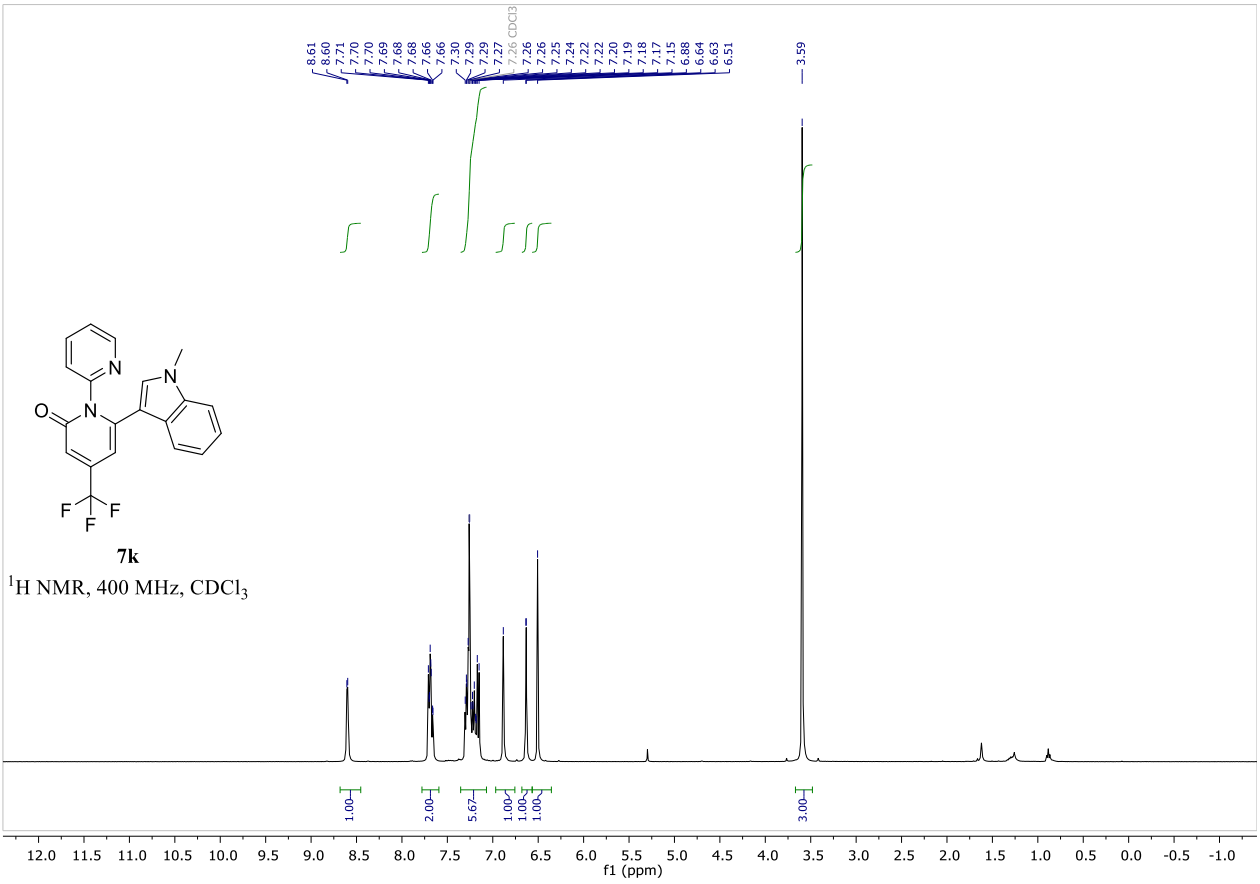
7j

^{1}H NMR, 400 MHz, $CDCl_3$



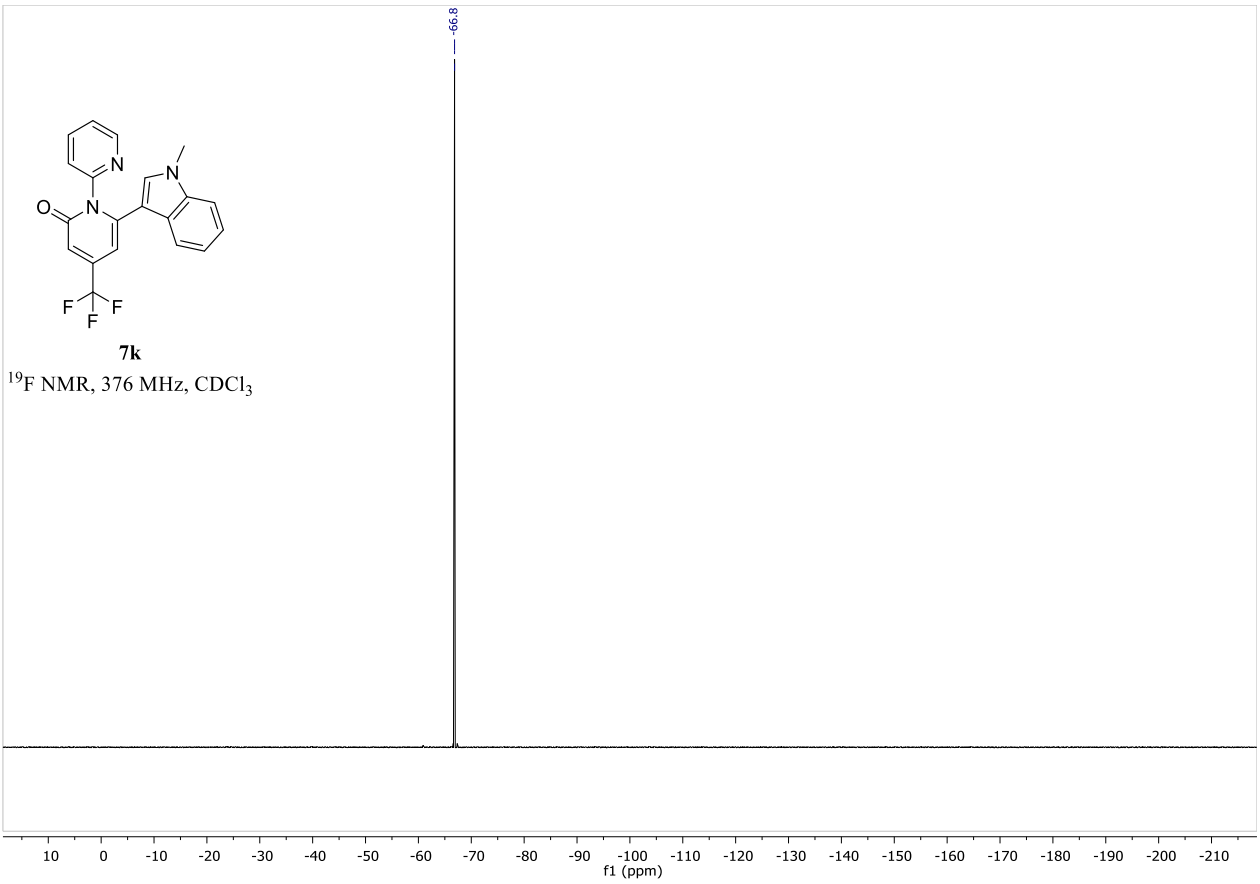
7j

^{13}C NMR, 101 MHz, $CDCl_3$



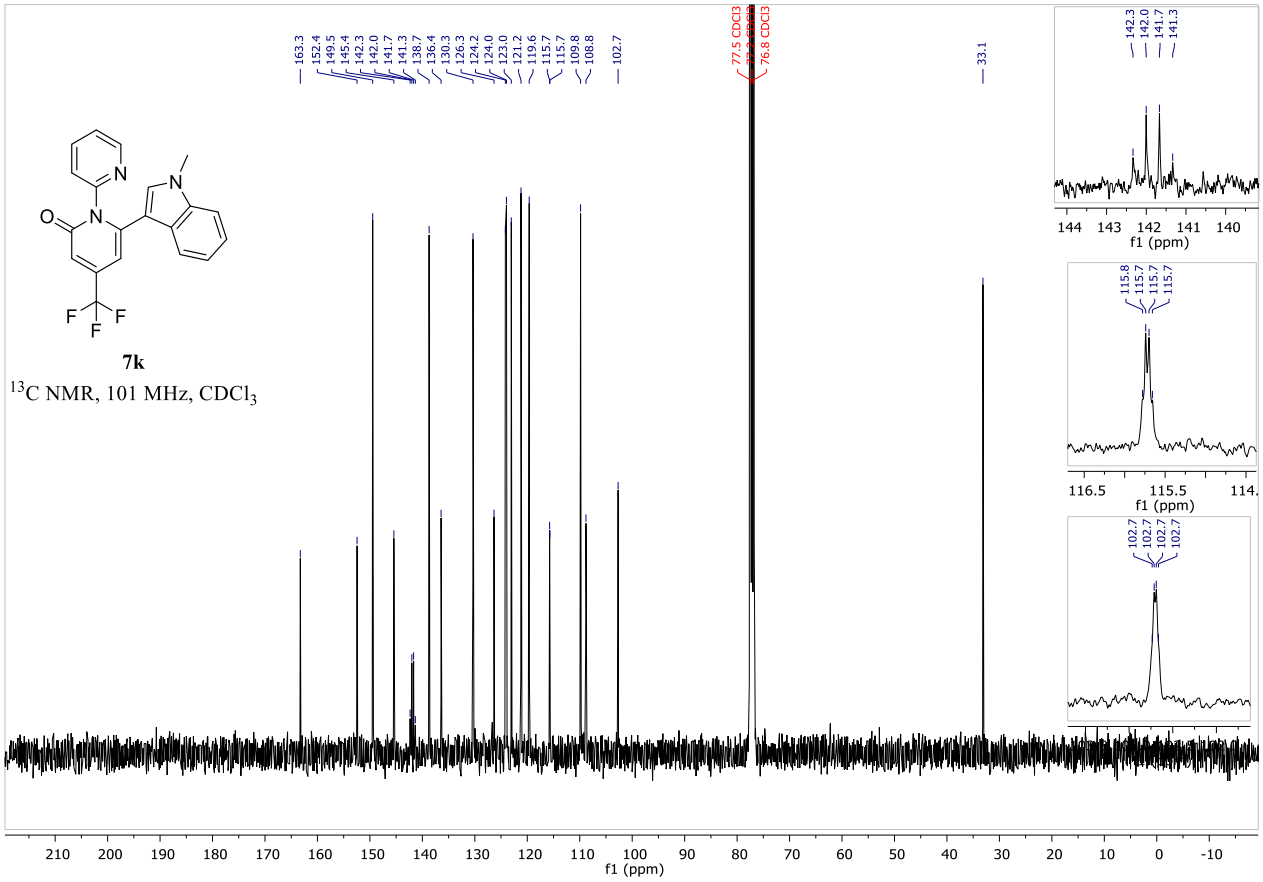
7k

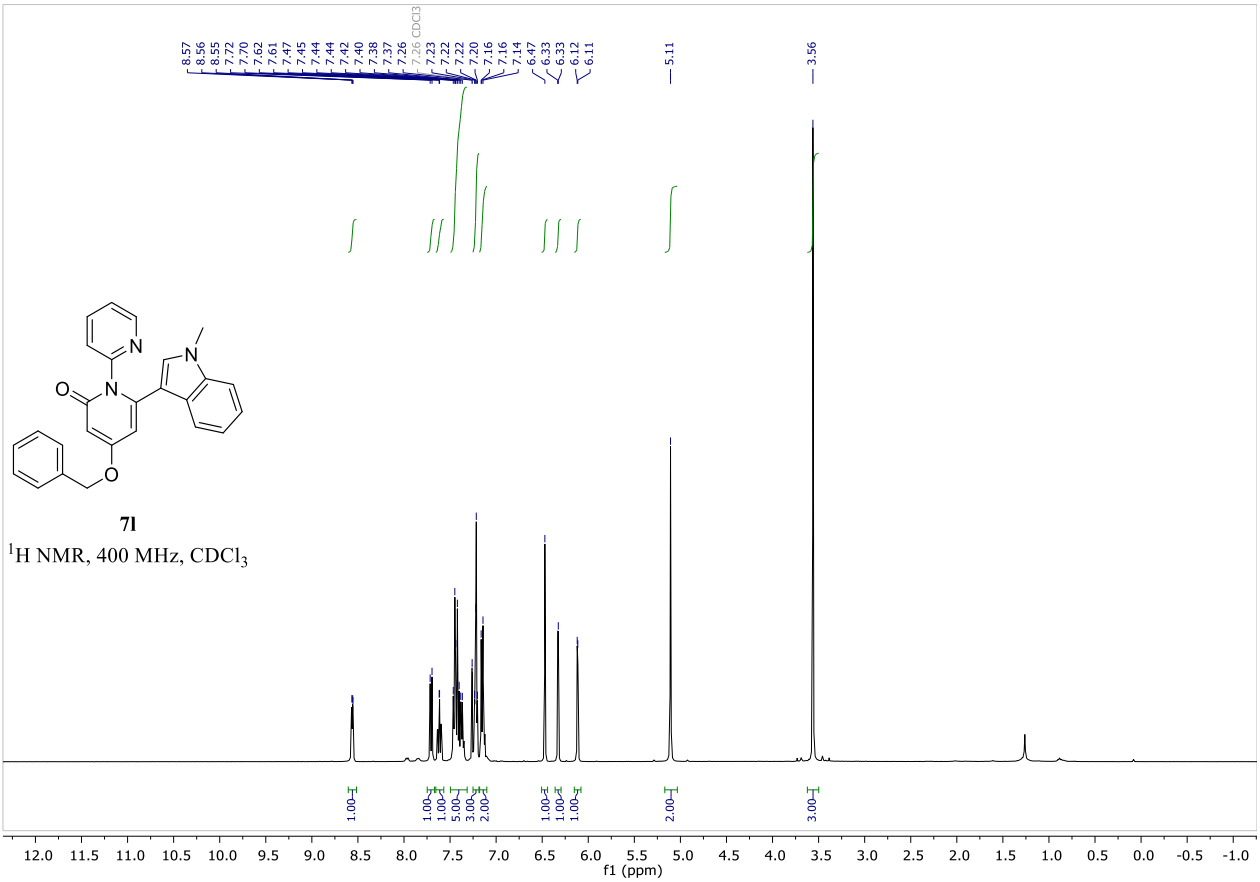
^{1}H NMR, 400 MHz, $CDCl_3$



7k

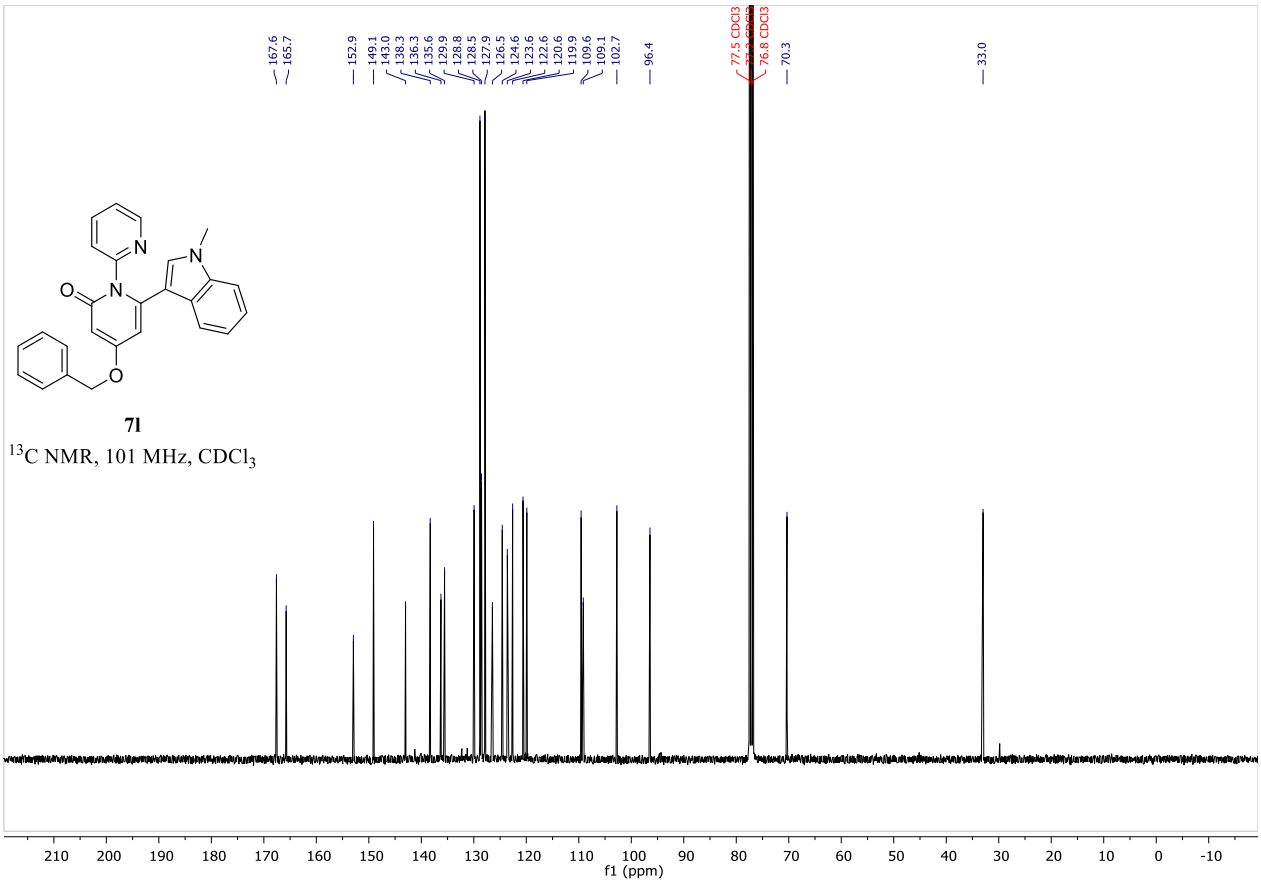
^{19}F NMR, 376 MHz, $CDCl_3$


7k
13C NMR, 101 MHz, CDCl3
163.3
152.4
149.5
145.4
142.3
142.0
141.7
141.3
138.7
136.4
130.3
126.3
124.2
124.0
123.0
121.2
119.6
115.7
115.7
109.8
108.8
102.7
77.5 CDCl3
76.8 CDCl3
33.1
142.3
142.0
141.7
141.3
144 143 142 141 140
f1 (ppm)
115.8
115.7
115.7
115.7
116.5 115.5
f1 (ppm)
102.7
102.7
102.7
102.7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



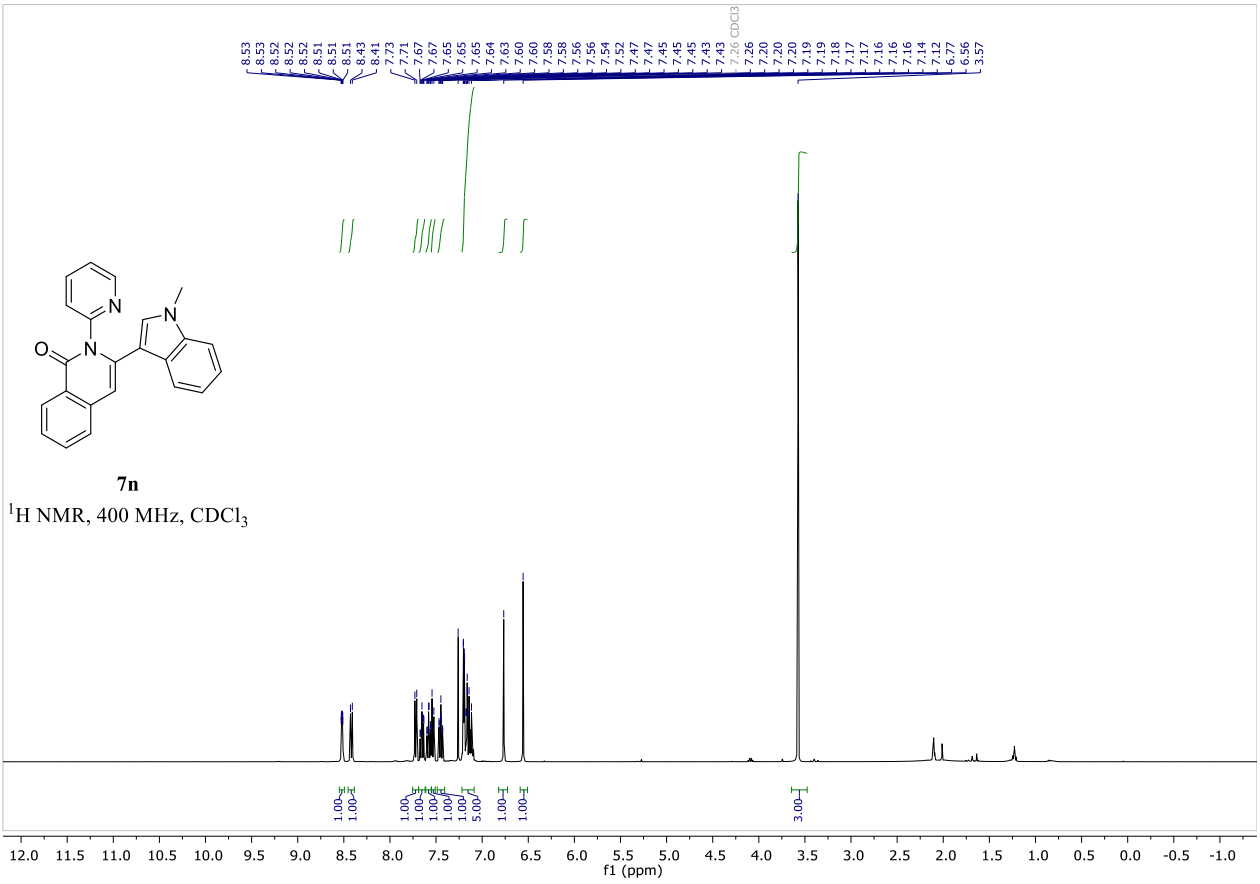
7l

^{1}H NMR, 400 MHz, $CDCl_3$



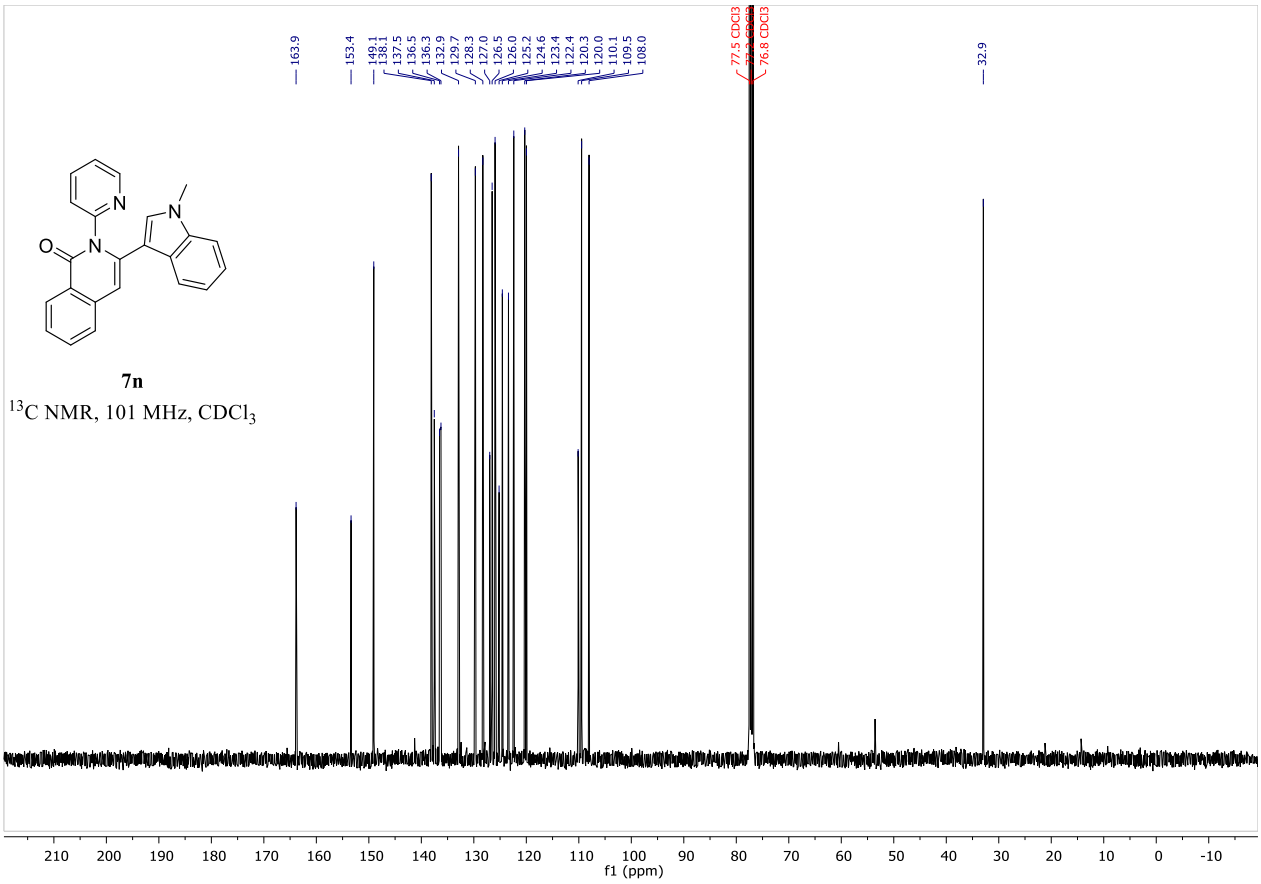
7l

^{13}C NMR, 101 MHz, $CDCl_3$



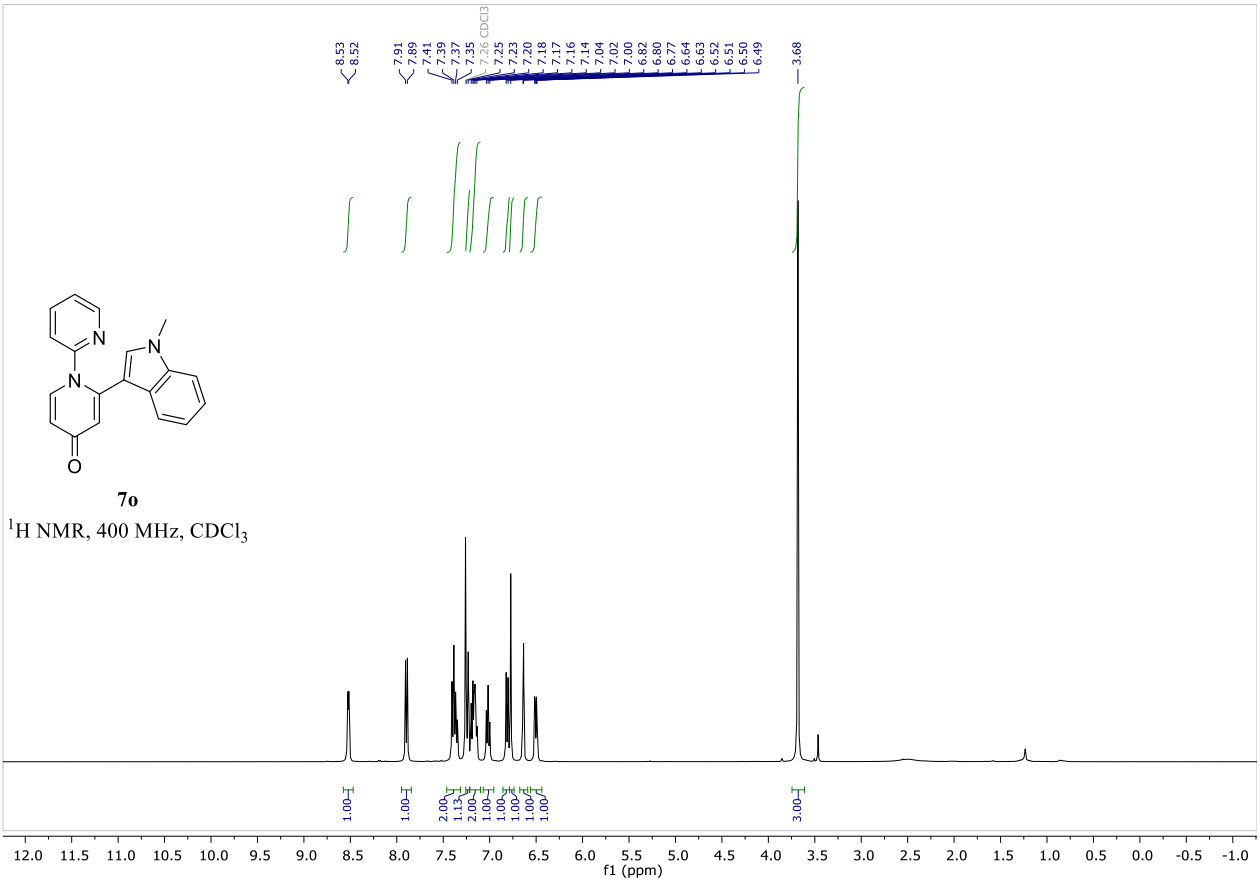
7n

^{1}H NMR, 400 MHz, $CDCl_3$



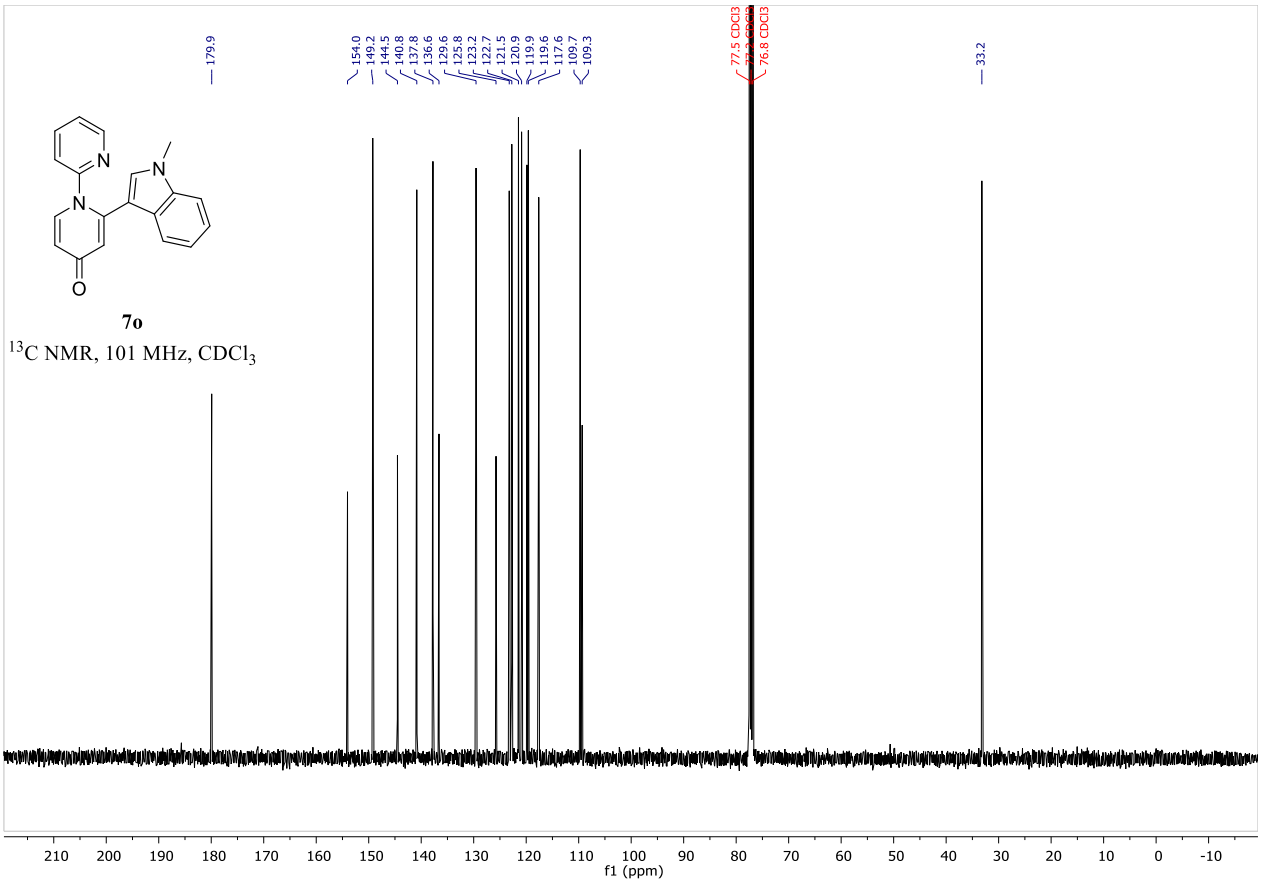
7n

^{13}C NMR, 101 MHz, $CDCl_3$



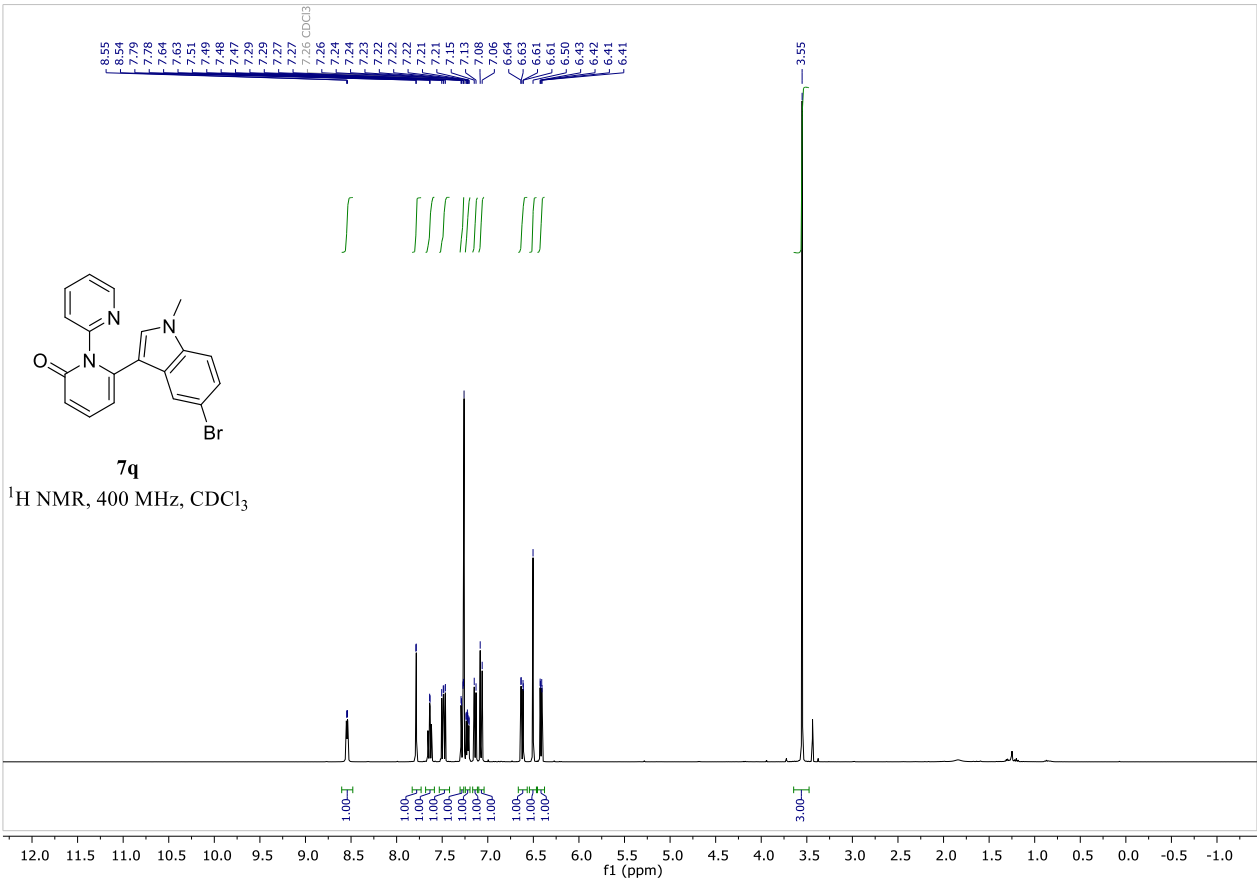
7o

^{1}H NMR, 400 MHz, $CDCl_3$



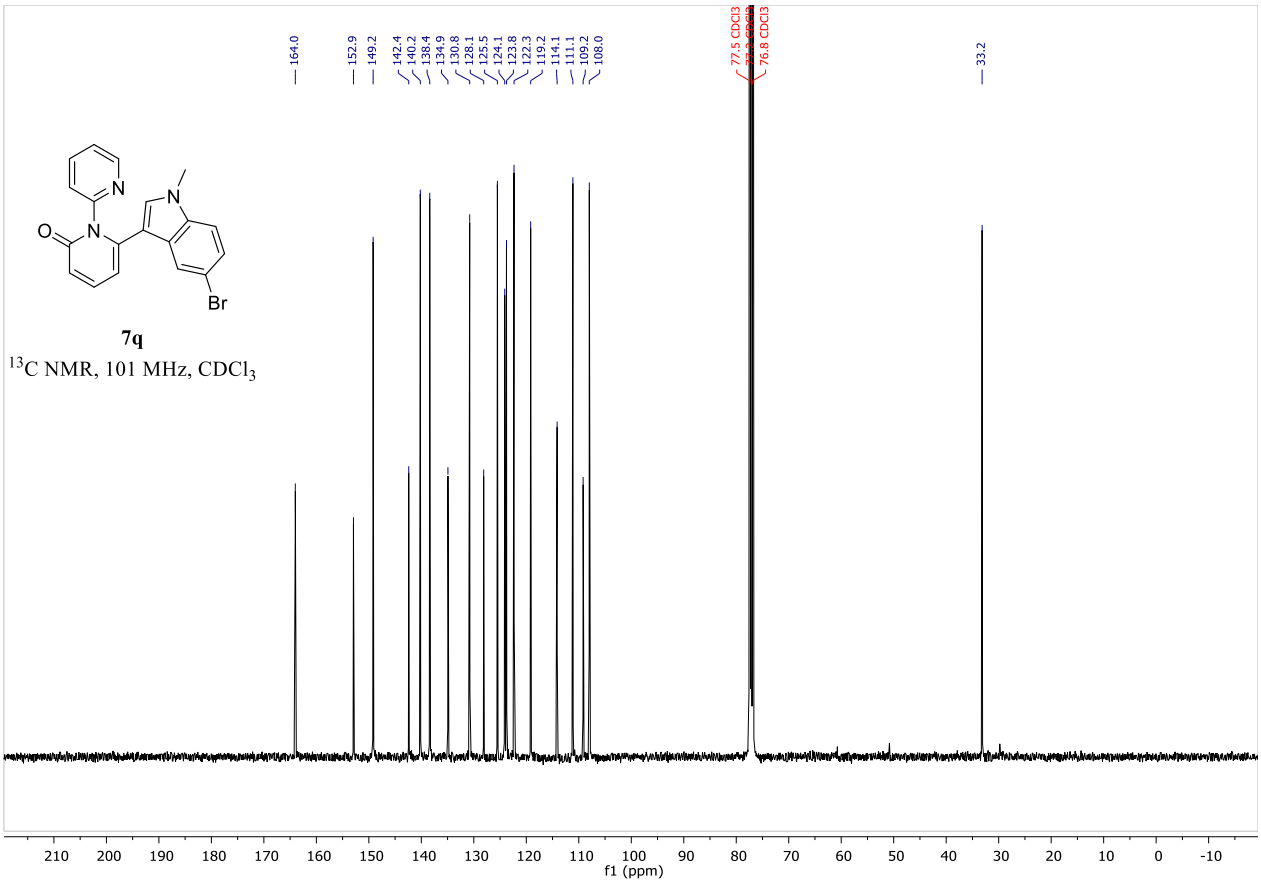
7o

^{13}C NMR, 101 MHz, $CDCl_3$



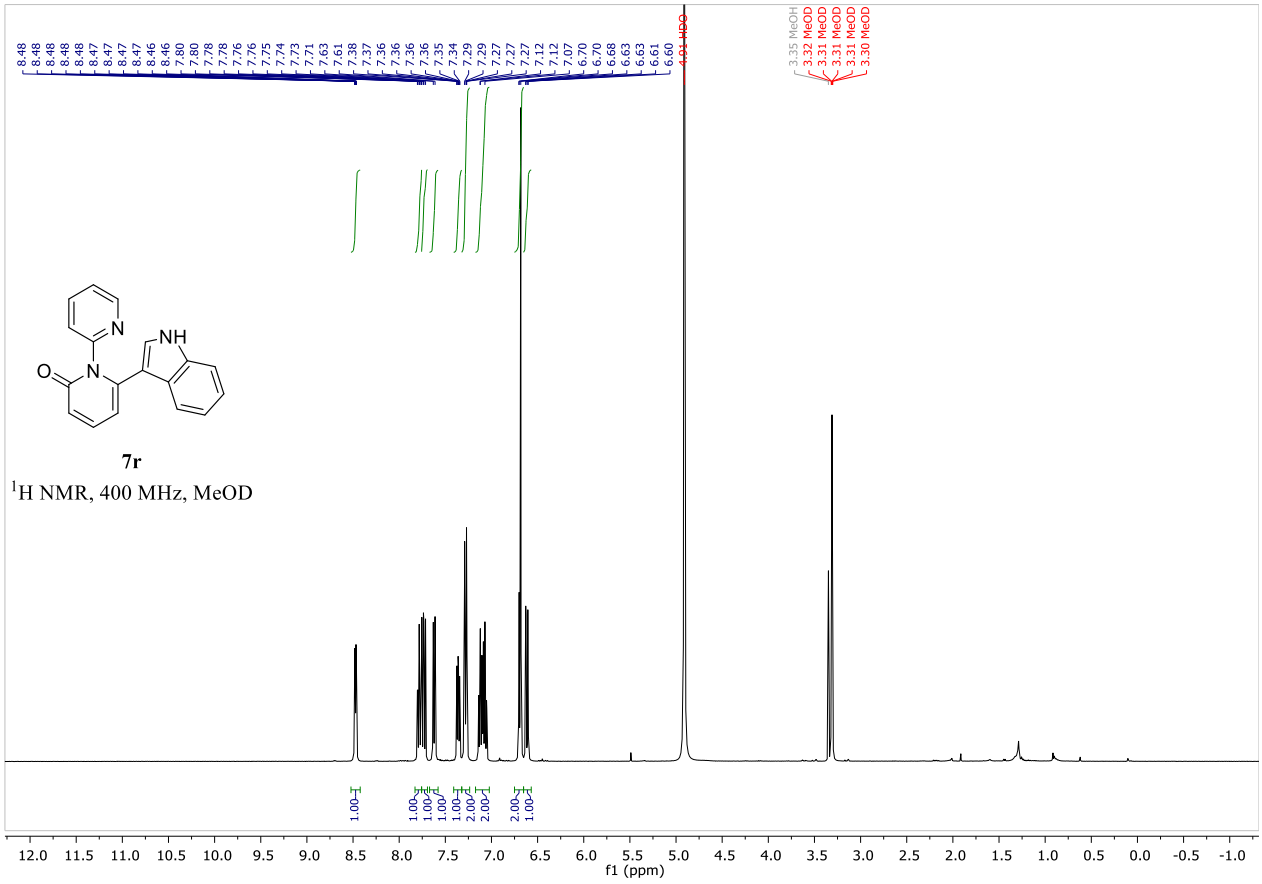
7q

^{1}H NMR, 400 MHz, $CDCl_3$



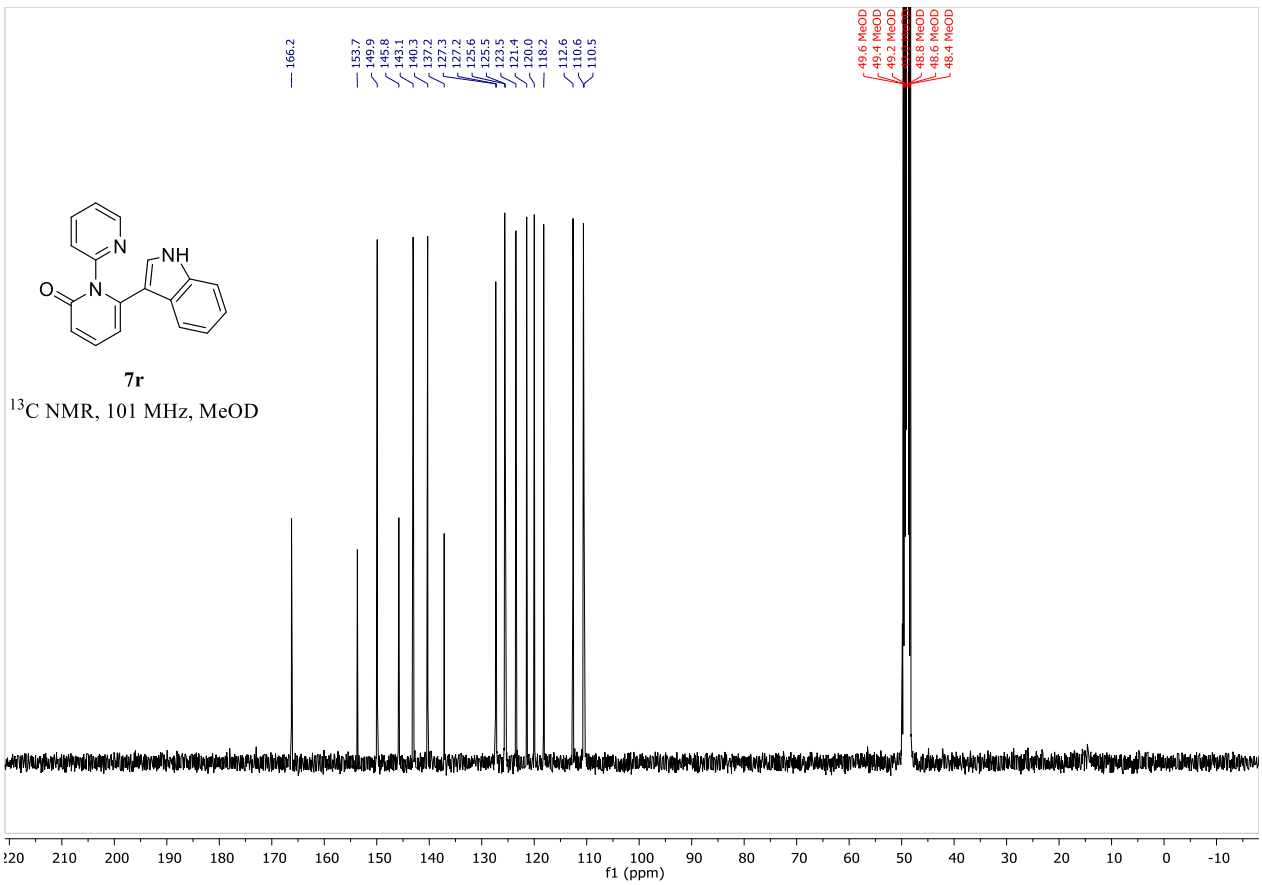
7q

^{13}C NMR, 101 MHz, $CDCl_3$



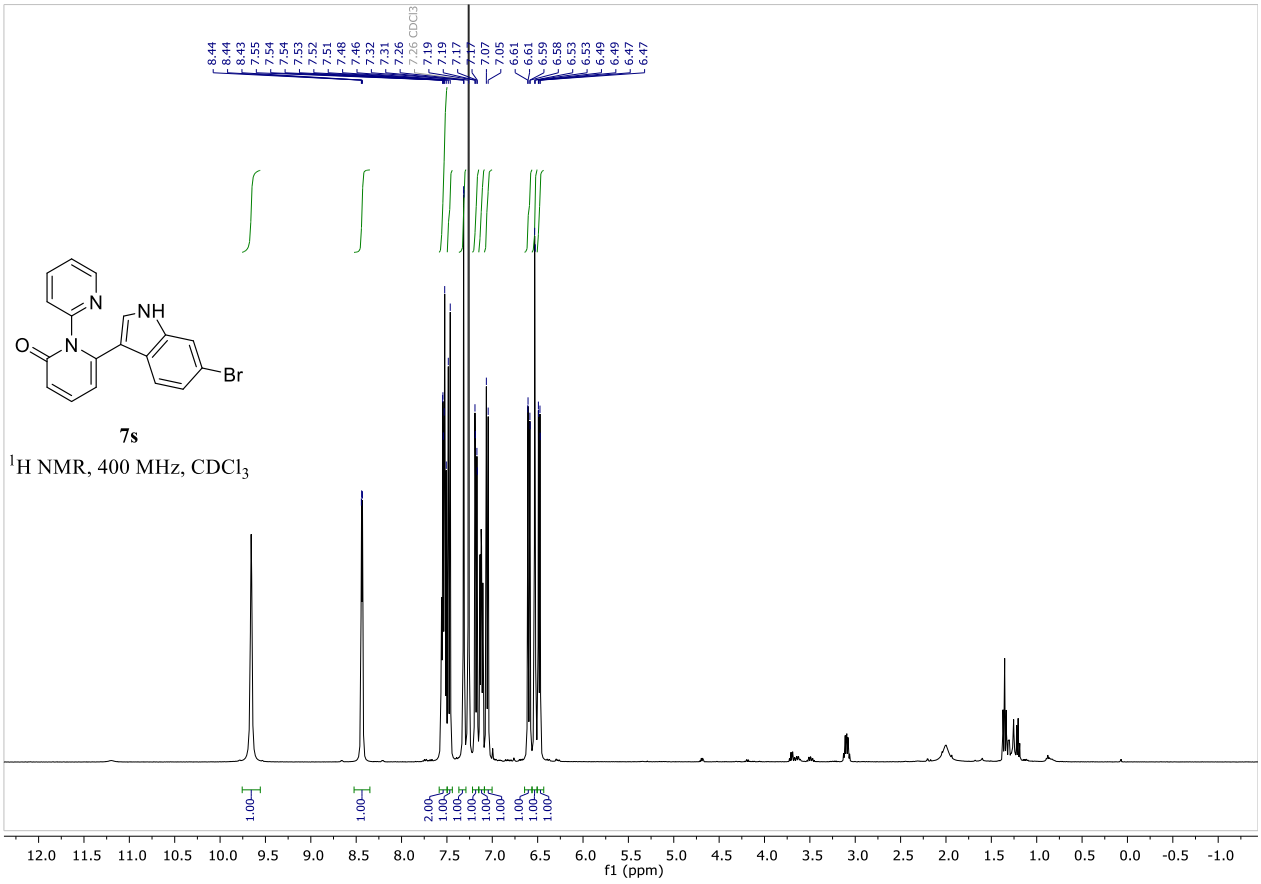
7r

^{1}H NMR, 400 MHz, MeOD



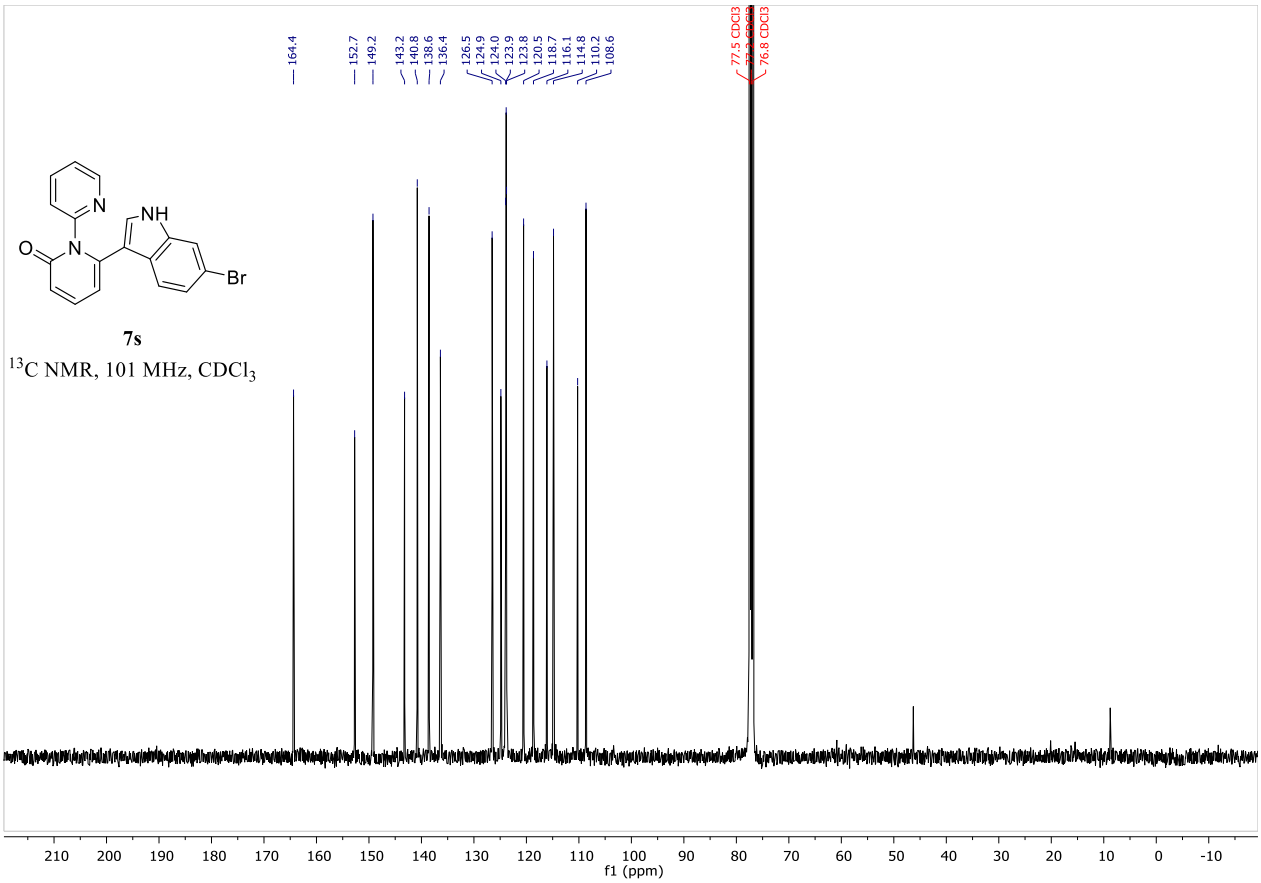
7r

^{13}C NMR, 101 MHz, MeOD



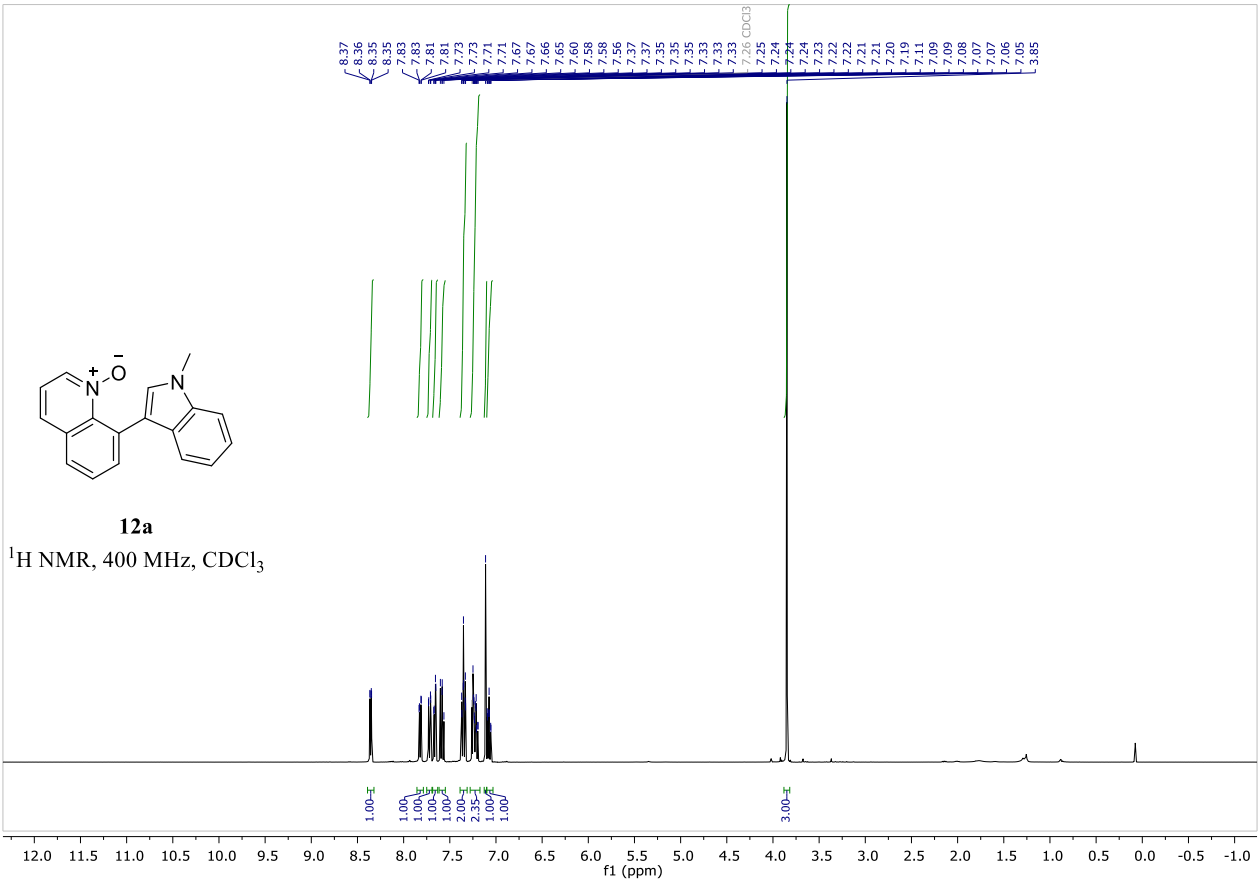
7s

^{1}H NMR, 400 MHz, $CDCl_3$



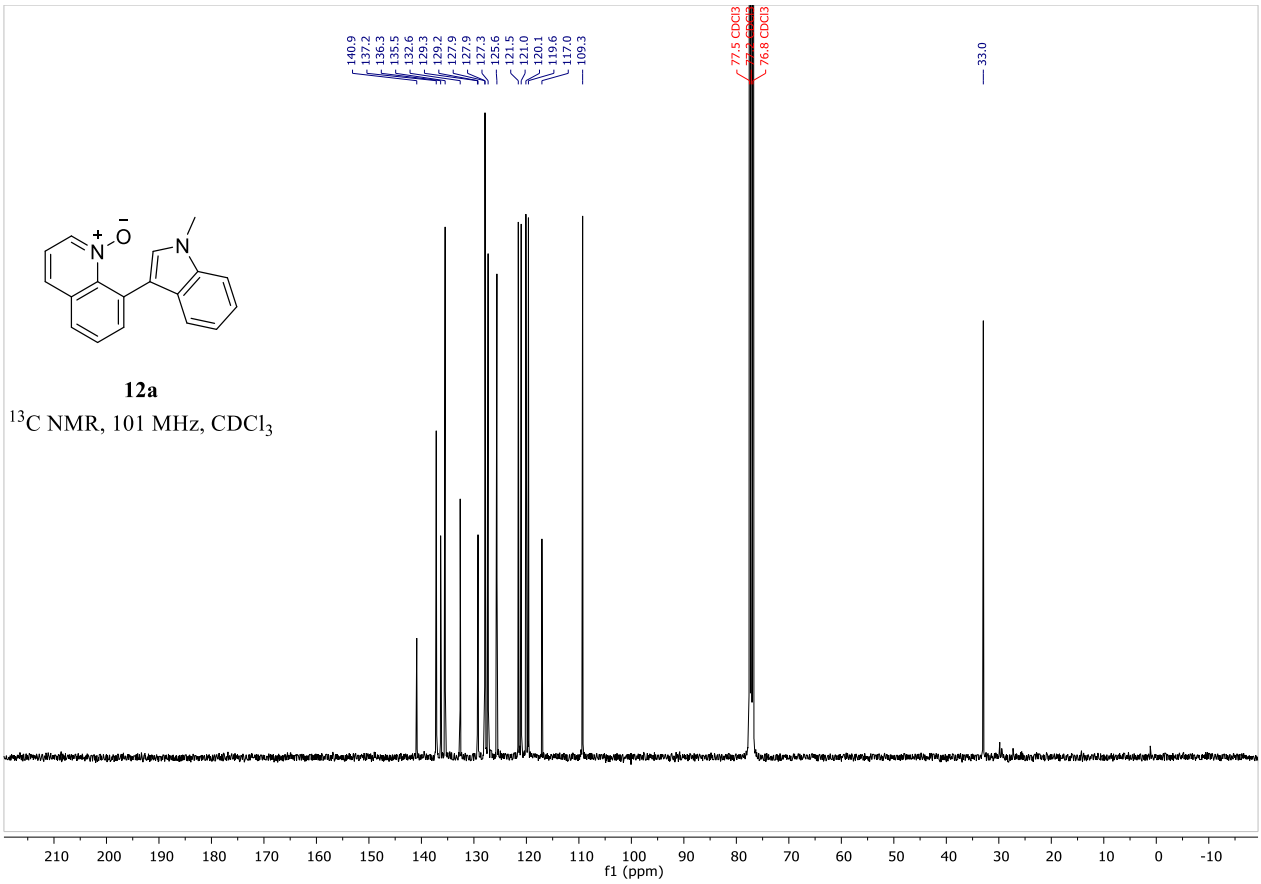
7s

^{13}C NMR, 101 MHz, $CDCl_3$



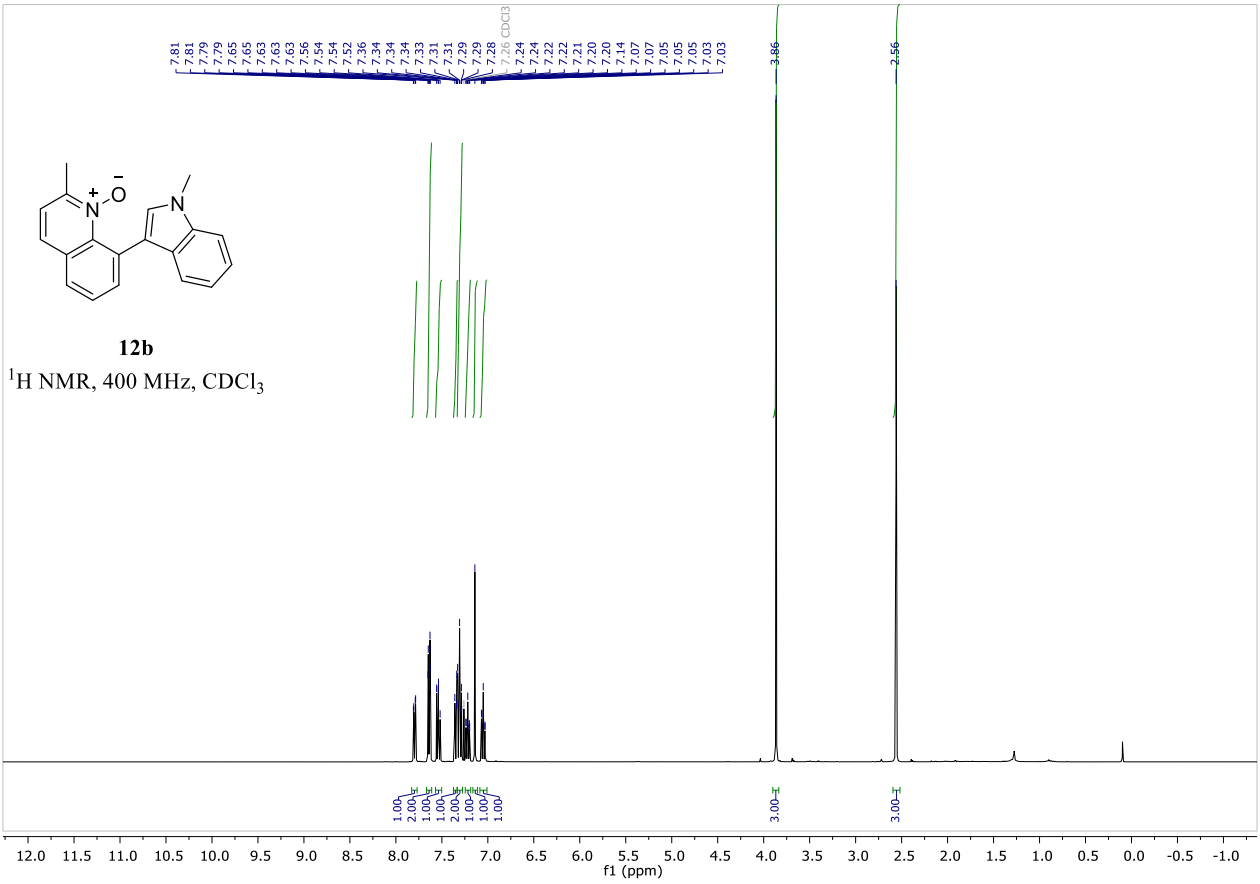
12a

^{1}H NMR, 400 MHz, $CDCl_3$



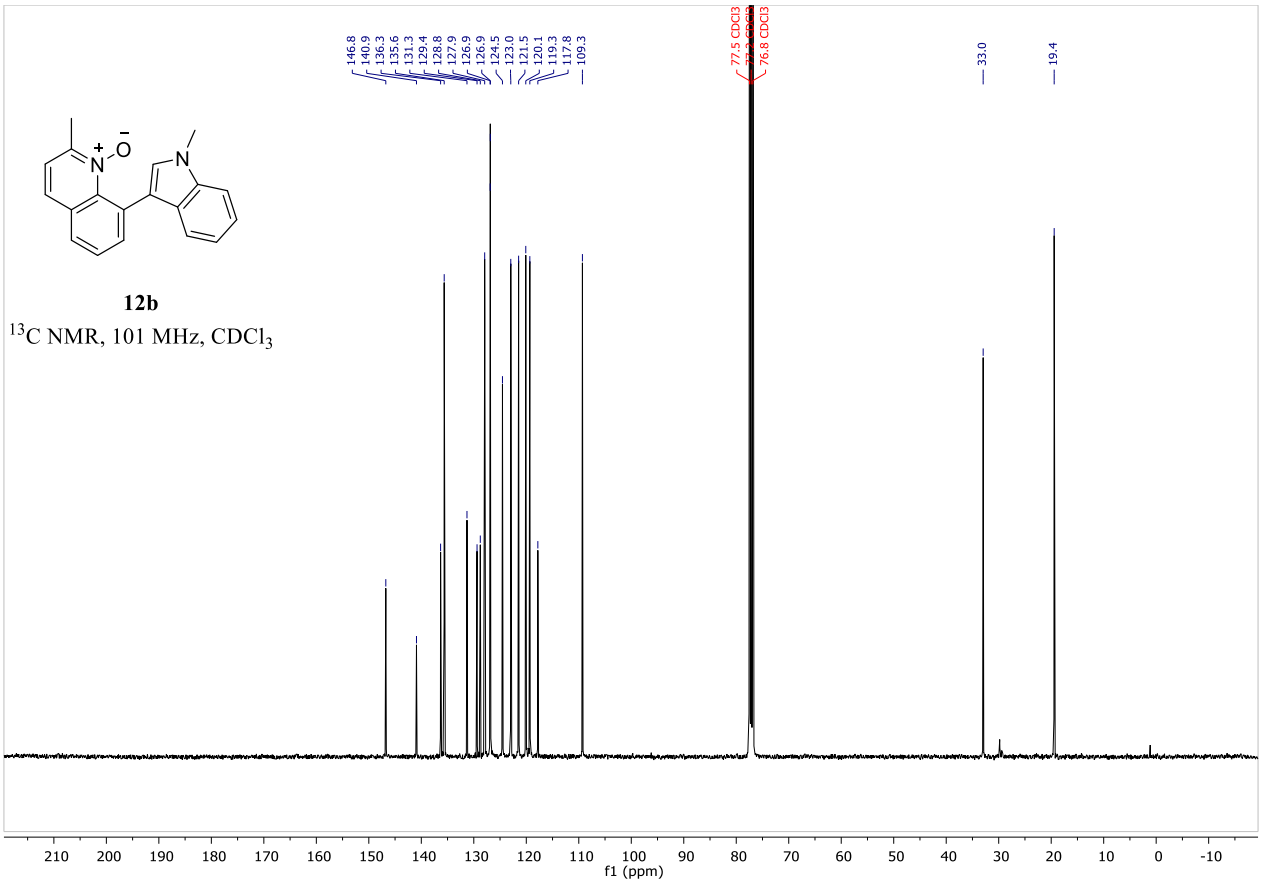
12a

^{13}C NMR, 101 MHz, $CDCl_3$



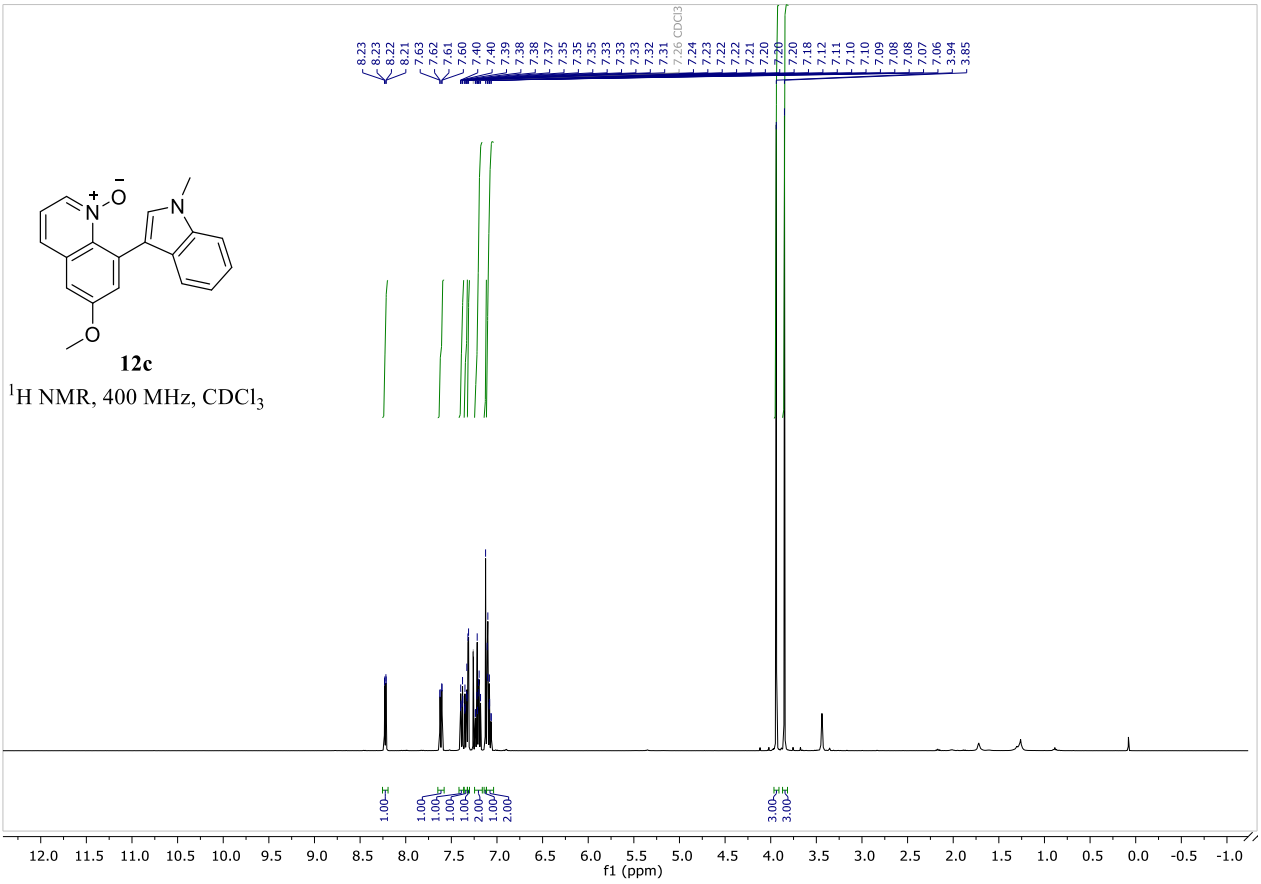
12b

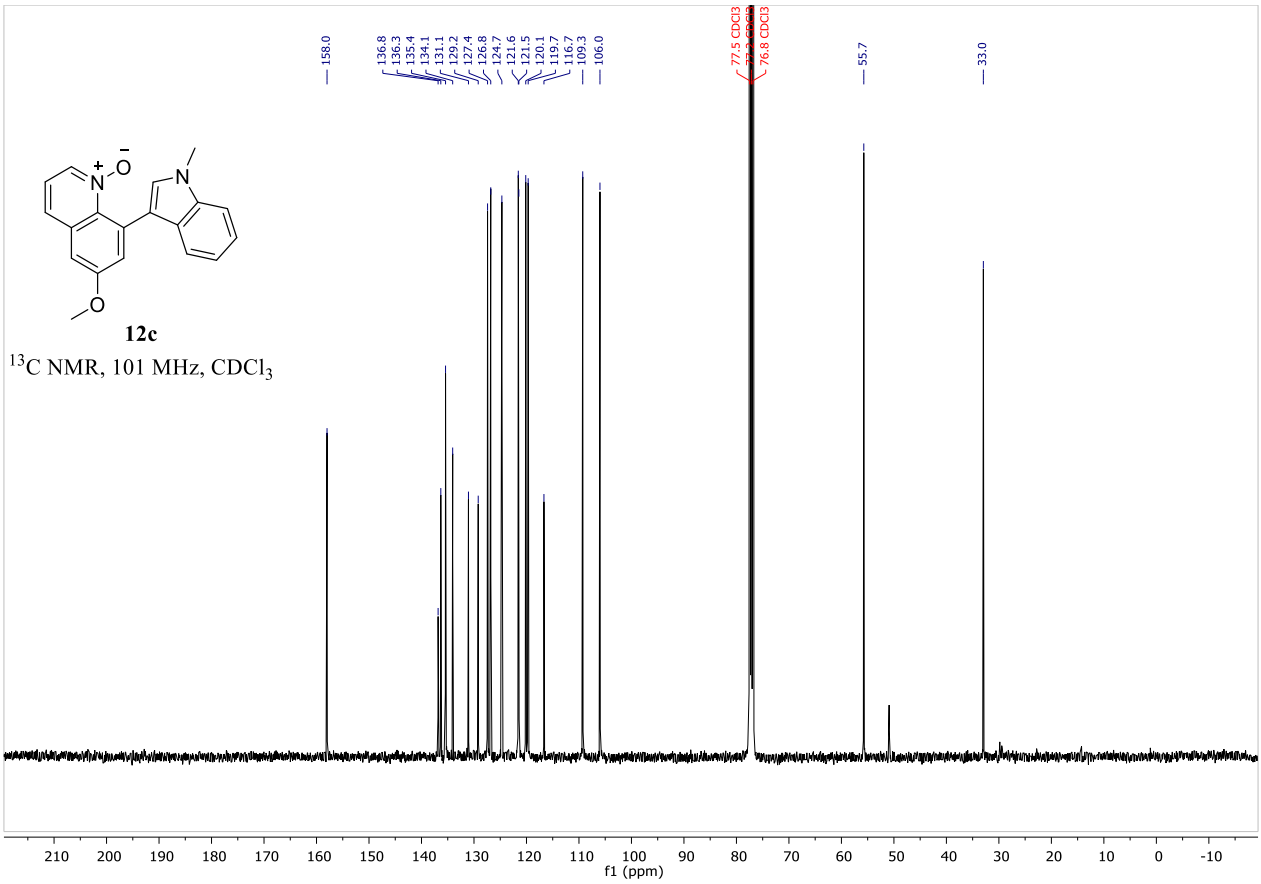
^{1}H NMR, 400 MHz, $CDCl_3$

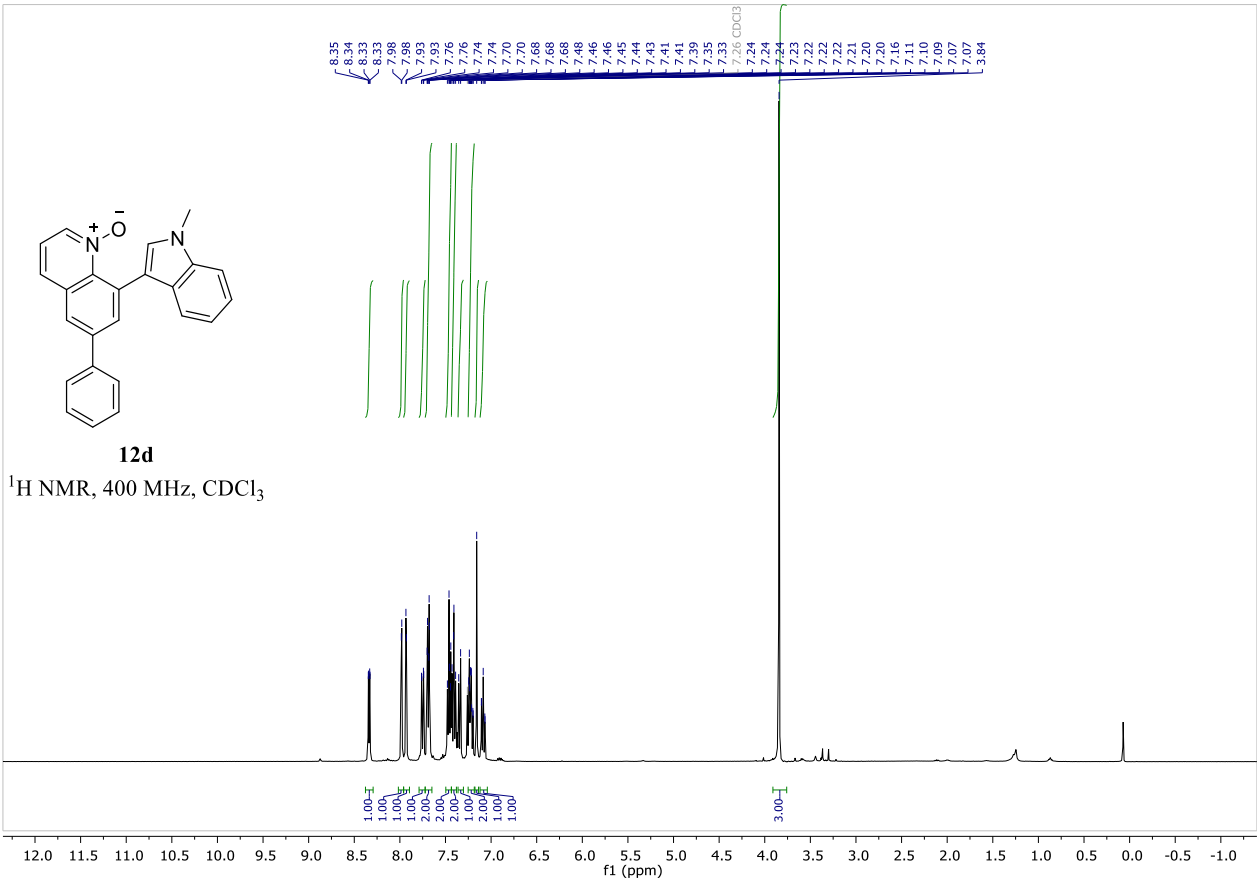


12b

^{13}C NMR, 101 MHz, $CDCl_3$

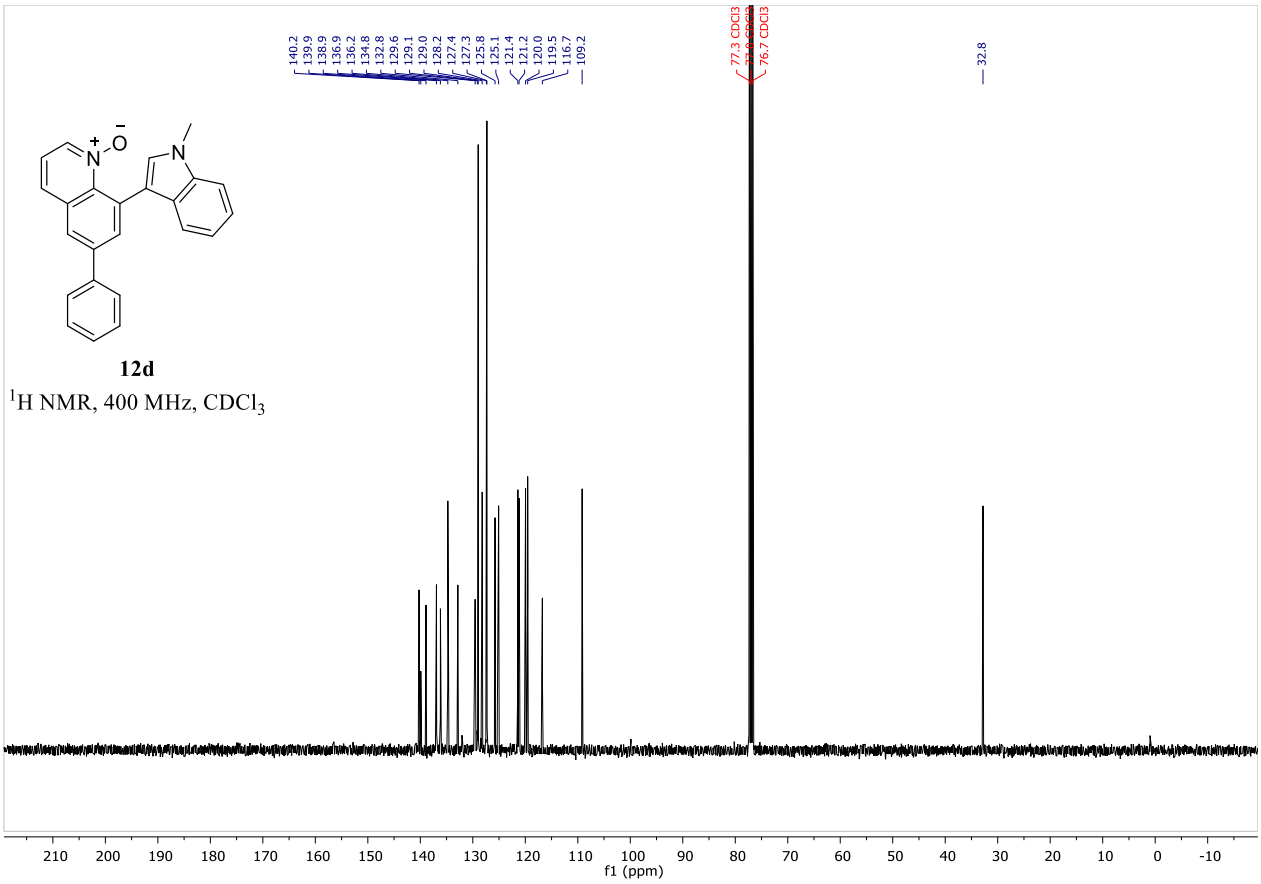

12c
1H NMR, 400 MHz, CDCl3
f1 (ppm)


12c
13C NMR, 101 MHz, CDCl3
f1 (ppm)



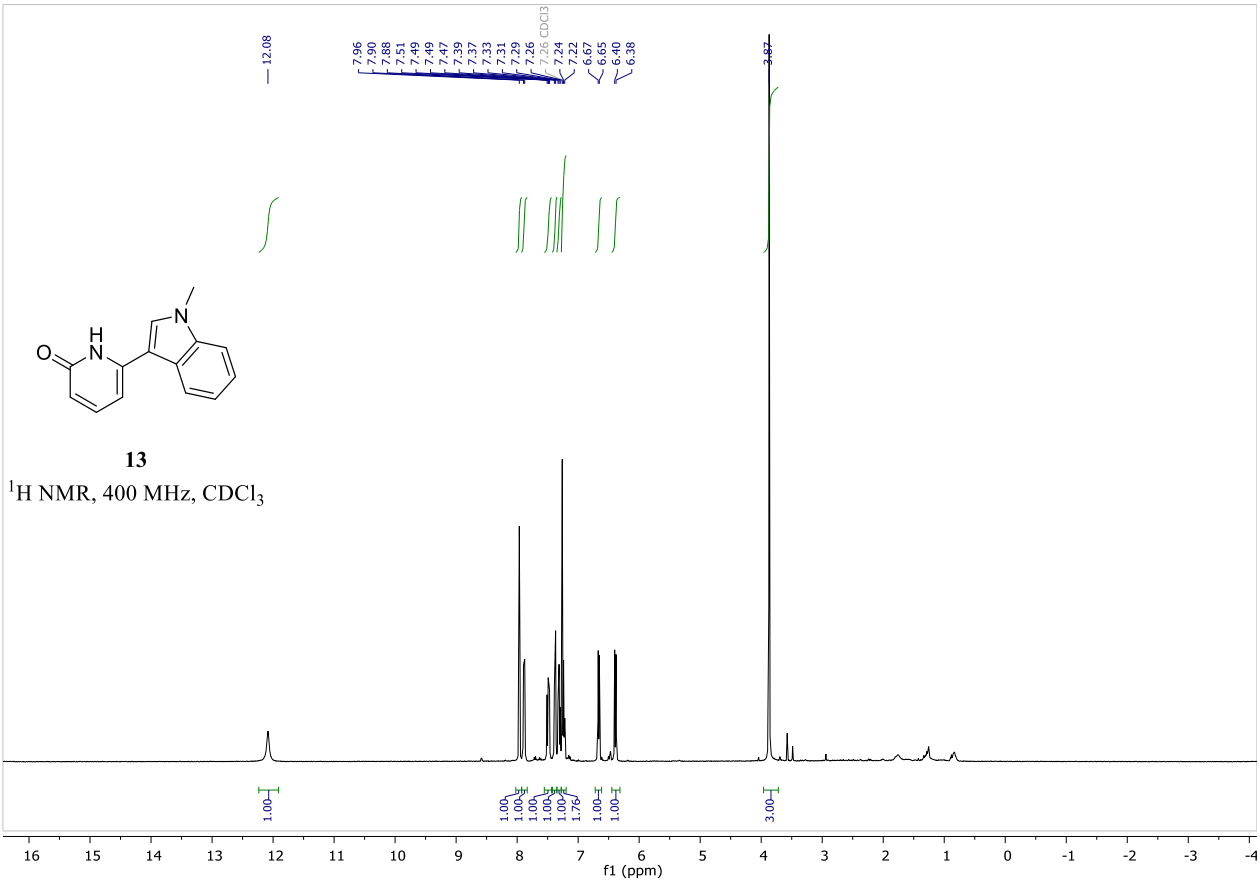
12d

^{1}H NMR, 400 MHz, $CDCl_3$



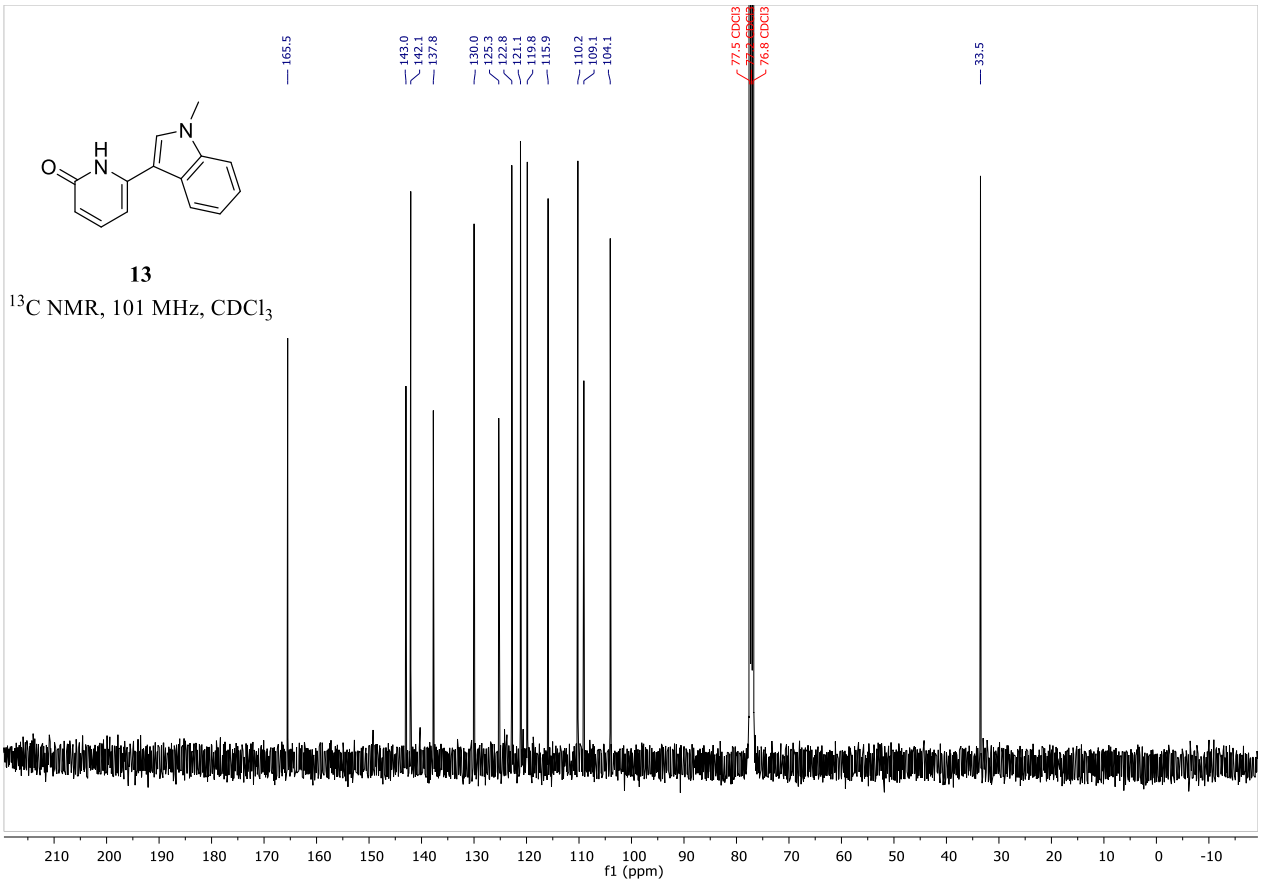
12d

^{1}H NMR, 400 MHz, $CDCl_3$



13

^{1}H NMR, 400 MHz, $CDCl_3$



13

^{13}C NMR, 101 MHz, $CDCl_3$