Iridium- and Rhodium-Catalyzed Directed C-H Heteroarylation of Benzaldehydes with Benziodoxolone Hypervalent Iodine Reagents

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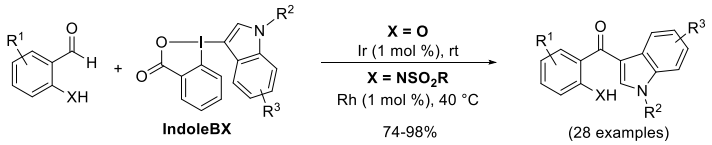
Supporting Information Placeholder



ABSTRACT: The C-H heteroarylation of benzaldehydes with indoles and pyrroles was realized using the benziodoxolone hypervalent iodine reagents Indole- and Pyrrole- BX. Functionalization of the aldehyde C-H bond using either an ortho-hydroxy or amino directing group and catalyzed by an iridium or a rhodium complex allowed the synthesis of salicyloylindoles and (2-sulfonamino)benzoylindoles, respectively with good to excellent yields (74 to 98%). This new transformation could be carried out under mild conditions (rt to 40 °C) and tolerated a broad range of functionalities, such as ethers, halogens, carbonyls or nitro groups.

Indoles and pyrroles are ubiquitous in medicinal chemistry and natural products.[1] Aryl indolyl ketones have attracted strong interest due to their interesting biological activities, in particular through interactions with the cannabinoid receptor.[2] Among them, the subclass in which the aryl moiety wears a hydroxy or an amino group in *ortho* position to the carbonylshowed in addition diverse biological activities (Figure 1). Polymethoxylated indole derivatives **1** were cytotoxic against KB, MKN45, MCF-7 and colon HT-29 cells.[3] 3-(2-Aminobenzoyl)indole **2** led to VEGFR-2 inhibition.[4] Furthermore, the salicoyl pyrrole core is present in bhimamycins **3**, antibiotic natural products isolated from the bacteria *Streptomyces sp.*[5]

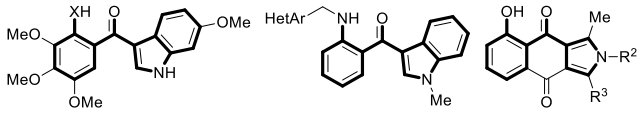
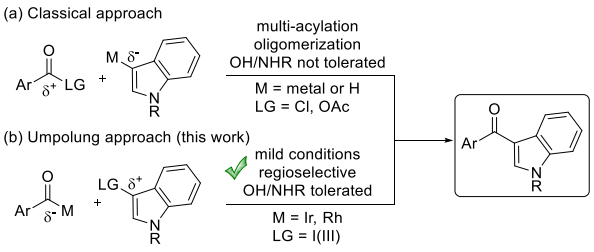


Figure 1. Synthetic and natural bioactive compounds with a 2-hydroxy or 2-amino benzoyl indole or pyrrole core

Due to their occurrence in biologically active compounds, the efficient synthesis of 3-benzoyl-indoles or -pyrroles is important. The most straightforward approach is based on the innate reactivity of the heterocycles as nucleophiles combined with an electrophilic acylation reagent (Scheme 1a). However, Friedel-Crafts acylation of indoles under standard conditions usually leads to a complex mixture of mono-, di-acylated and oligomerization products due to their high electron density.[1a] This issue can be partially resolved by the introduction of electron-withdrawing protecting groups, the use of milder Lewis acids (Et_2AlCl[6a-b], imidazolium chloroaluminate[6c] or $ZrCl_4$[6d]), reaction with nitrilium salts[7] or the use of hexafluoroisopropanol as solvent.[8] Furthermore, the nucleophilicity of the heterocycles can be enhanced by conversion into Grignard or other organometallic reagents, which can then be added directly to electrophiles or used in metal-catalyzed cross-couplings.[9] Recently, direct C-H acylation catalyzed by transition metals has also been reported.[10] The synthesis of 3-salicyloyl indoles was either not reported in these works, or required the protection/deprotection of the hydroxy group. Therefore, developing a more direct access to these compounds would be highly desirable. In this respect, only limited success has been achieved by the ring-opening of chromones,[11,12] 1,3-dipolar cycloaddition, followed by decarboxylation,[13] and alkylation of indoles with nitroolefins, followed by oxidative C-C bond cleavage.[14]

Scheme 1. Classical *vs* Umpolung approaches for the synthesis of 3-arylcarbonyl indoles



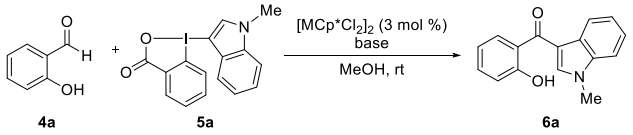
As an alternative strategy, we envisaged an Umpolung pathway involving a nucleophilic acyl metal intermediate generated

via C_{sp2}-H activation of an aldehyde[15] and an electrophilic indole (Scheme 1b). Concerning the nucleophilic partners, benzaldehydes substituted with oxygen or nitrogen heteroatoms in *ortho* position are privileged substrates, as the directing group is necessary for C-H activation under mild conditions.[15a] As electrophilic partners, we considered hypervalent iodine(III) reagents, which have been extensively used as Umpolung reagents in numerous transformations.[16] In fact, both aryl iodoniums and ethynylbenziodoxolones (EBX) have been used to introduce phenyl or alkyne derivatives via cross-coupling on salicylaldehydes.[17] However, there are only few methods for the synthesis of indole-and pyrrole-based iodonium salts.[18] Furthermore, due to their limited stability, these compounds have found only very limited use in transition metal catalysis. Recently, our's and Yoshikai's group reported the synthesis of bench-stable indole- and pyrrole-benziodoxolones (indoleBX and pyrroleBX).[19] We further demonstrated that the new indole- and pyrrole- BX reagents could be used for directed C-H functionalization with rhodium or ruthenium catalysts, whereas iodonium salts were not successful.[19a] Herein, we report the C-H functionalization of 2-hydroxy and 2-amino benzaldehydes derivatives with Indole- and Pyrrole-BX reagents using either iridium or rhodium catalysts to give access to important indole and pyrrole building blocks.

We initiated the studies on C-H indolation with the optimization of the reaction conditions for the coupling of salicylaldehyde **4a** with Me-indoleBX **5a** (Table 1). While $[RhCp^*Cl_2]_2$ as catalyst gave only traces of the desired product **6a** (Table 1, entry 1), we were pleased to see that the use of $[IrCp^*Cl_2]_2$ led to formation of **6a** in excellent 91% yield in the presence of cesium acetate at room temperature (Table 1, entry 2). This is the first example of the use of an iridium catalyst with IndoleBX reagents. Furthermore, the reaction did not require any particular precautions concerning the presence of water or oxygen. Complete conversion was reached after 10 minutes at room temperature. Cheaper potassium acetate could also be used to give 90% yield of the ketone product **6a** (Table 1, entry 3). Variation of the amount of KOAc revealed that a superstoichiometric amount was not necessary (Table 1, entry 4). However, the yield decreased when the base was used in a substoichiometric quantity (Table 1, entry 5) and without base only 56% yield was obtained, even if full conversion was still observed (Table 1, entry 6). Finally, we were able to reduce the catalyst loading to 1 mol % without significant change in yield, demonstrating the robustness of the catalyst (Table 1, entry 7). A scale-up to 1.20 mmol allowed us to decrease the iridium catalyst loading to 0.5 mol %, giving 93% yield of **6a** in the same reaction time (Table 1, entry 8). Control experiments indicated that the transition metal complex is essential for the reaction.[20] When 3-bromo-1-methylindole and 3-iodo-1-methylindole were used as reagents, the desired compounds were obtained in 59% and 53% yield respectively, but only after heating over night at 80 °C.[20] This result further highlights the exceptional reactivity of IndoleBX reagents.

The scope of the reaction was then studied (Scheme 2). The effect of substituents in the *para* position to the hydroxy group was examined first (**6a-i**). In terms of electronic effect, both electron-donating alkyl and ether groups (**6b** and **6c**) and electron-withdrawing halogens, aldehyde and nitro groups (**6d-i**) were well tolerated. The exclusive formation of product **6h** starting from a bis-formylated benzene confirmed the requirement of a directing group for C-H activation.[21] In term of substitution pattern of the benzene ring, a methoxy group was tolerated also in all other positions (**6j-l**).

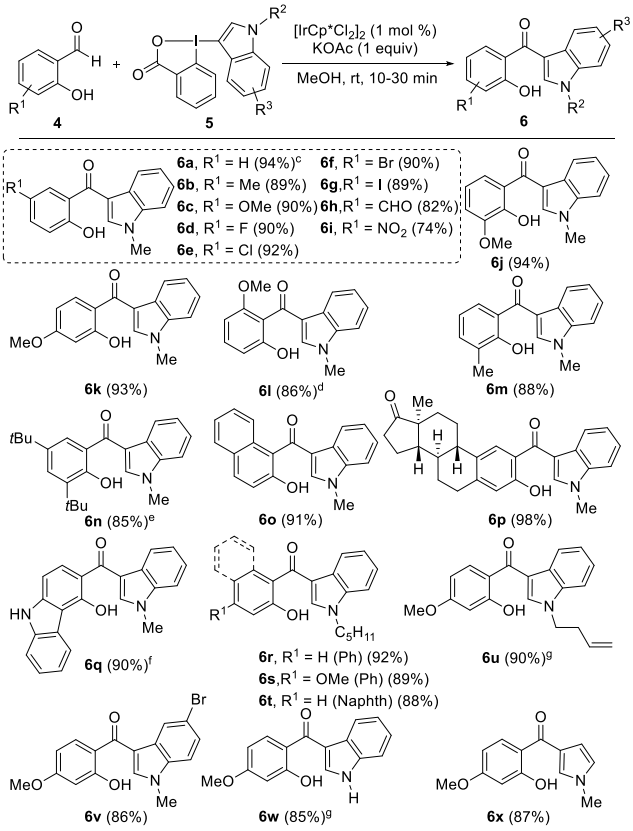
Table 1. Optimization studies[a]



entry	catalyst	base (equiv)	yield (%)[b]
1	$[RhCp^*Cl_2]_2$	CsOAc (1.2)	traces[c]
2	$[IrCp^*Cl_2]_2$	CsOAc (1.2)	91
3	$[IrCp^*Cl_2]_2$	KOAc (1.2)	90
4	$[IrCp^*Cl_2]_2$	KOAc (1.0)	90
5	$[IrCp^*Cl_2]_2$	KOAc (0.5)	86
6	$[IrCp^*Cl_2]_2$	-	56
7	$[IrCp^*Cl_2]_2$	KOAc (1.0)	94[d]
8	$[IrCp^*Cl_2]_2$	KOAc (1.0)	93[e]

[a]Reactions conditions: **4a** (0.05 mmol), **5a** (0.05 mmol), $[IrCp^*Cl_2]_2$ (3 mol %), base, methanol (0.5 mL) at rt for 10 min. [b]Isolated yield after column chromatography. [c]Reaction performed at 80 °C. [d]$[IrCp^*Cl_2]_2$ (1 mol %). [e]Yield at a 1.20 mmol scale with 0.5 mol % $[IrCp^*Cl_2]_2$.

Scheme 2. Ir(III)-catalyzed C-H indolation of 2-hydroxybenzaldehydes.[a,b]



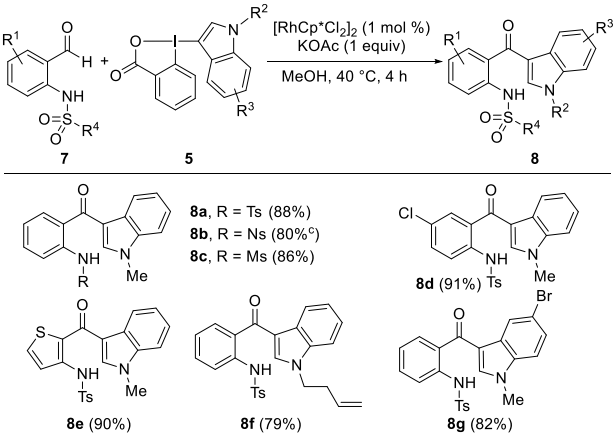
[a]Reactions conditions: **4** (0.15 mmol), **5** (0.15 mmol), $[IrCp^*Cl_2]_2$ (1 mol %), KOAc (0.15 mmol), methanol (1.5 mL) at rt for 10 min. [b]Isolated yield after column chromatography. [c]93%

yield for a reaction at 1.20 mmol scale. [d]30 min. [e]1 h. [f]Reaction performed at 50 °C for 2 h. [g]Reaction performed at 70 °C for 2 h.

A longer reaction time of 30 minutes was observed only in case of 2-hydroxy-6-methoxybenzaldehyde **4l** to give **6l** in 86% yield. Alkyl-substituted products **6m** and **6n** were also obtained in good yields. Naphthalene and estrone-derivatives **6o** and **6p** were isolated in excellent 91% and 98% yields respectively. Pentacyclic compound **6q** wearing a carbazole heterocycle was obtained in 90% yield. Modification of the hypervalent iodine reagent was then investigated. Changing the *N*-substitution from methyl to pentyl or butenyl delivered indoles **6r-u**. The corresponding *O*-methylated compounds are reported synthetic cannabinoids.[22] A bromo substituent on the benzene ring was well tolerated (**6v**).The *N*-H free compound **6w** could be also obtained with complete regioselectivity in 85% yield. For products **6u** and **6w**, it was necessary to perform the reaction at 70 °C to reach full conversion. Importantly, the method could be extended to the synthesis of pyrrole **6x** using a PyrroleBX as reagent.

We then turned to the use of nitrogen-based directing groups for the activation of the aldehyde C-H bond. In the case of 2-aminobenzaldehyde **7a** bearing a *N*-tosyl directing group a Rh(III) dimer catalyst proved to be as effective as the Ir(III) catalyst (Scheme 3), in contrast to what had been observed with salicylaldehyde **4a** (Table 1). The reaction was best run in MeOH at 40 °C during 4 h.[20] Several *N*-sulfonyl groups (tosyl, *para*-nosyl and mesyl) could be used to direct the C-H functionalization, giving products **8a-c** in 80-88% yield. In contrast, a *N*-boc directing group was inefficient for this transformation (result not shown). The reaction could be perform in the presence of a chlorine atom on the phenyl ring affording the product **8d** with 91% yield. The thiophene-derivatived compound **8e** was isolated in an excellent 90% yield. This rhodium-catalyzed reaction also tolerated a *N*-butenyl substituent or a bromo group on the indole benzene ring, giving the desired products **8f** and **8g** in 79% and 82% yields, respectively.

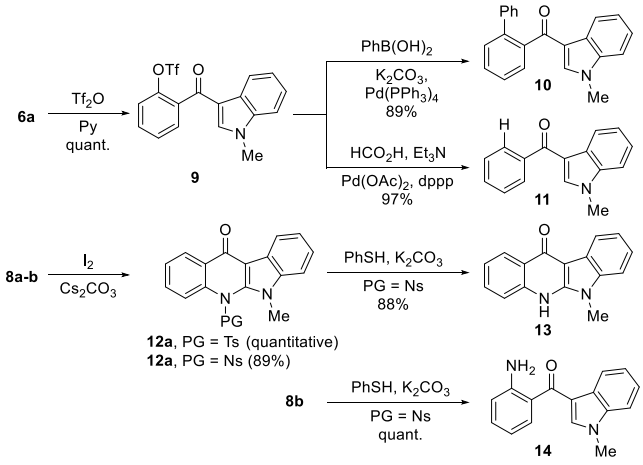
Scheme 3. Rh(III)-catalyzed C-H indolation of 2-sulfonylaminobenzaldehydes.[a,b]



[a]Reactions conditions: **7** (0.15 mmol), **5** (0.15 mmol), $[RhCp^*Cl_2]_2$ (1 mol %), KOAc (0.15 mmol), methanol (1.5 mL) at 40 °C for 4 h. [b]Isolated yield after column chromatography. [c]80% yield for a reaction at 0.80 mmol scale.

The directing groups were not only useful for allowing C-H functionalization under mild conditions (see Supporting Information for a mechanism proposal),[15a,17c] they also served as handles for further modifications (Scheme 4). For example, phenol **6a** was quantitatively transformed into the corresponding triflate **9** by reaction with triflic anhydride. Suzuki-Miyaura cross-coupling with phenyl boronic acid gave then biphenyl derivative **10** in 89% yield over 2 steps. Alternatively, the directing group could be fully removed by a palladium-catalyzed reduction of the triflate to furnish 3-benzoylindole **11**. From *N*-sulfonylphenyl substituted ketones **8a** and **8b**, an iodine-mediated oxidative C-2 amination generated tetracyclic indolo-[2,3*b*]quinolinone **12a** and **12b** in quantitative yield for tosyl **8a** and 89% yield for nosyl **8b**.[22] The nosyl protecting group was synthetically especially useful, as it could be removed in presence of thiophenol, either on the cyclized product **12b** or the indolation product **8b** to give the *N*-H free heterocycles **13** and **14**.

Scheme 4. Product modifications



In summary, we have reported the first example of aldehyde C-H heteroarylation giving highly useful indole and pyrrole building blocks. The reaction proceeded under mild, neutral conditions using either an alcohol or a sulfonylamide directing group with an iridium or a rhodium catalyst, respectively and the cyclic hypervalent iodine reagents Indole- and PyrroleBX. This represented also the first use of an iridium catalyst with Indole- and PyrroleBX as reagents. As the reaction tolerated a broad range of functional groups and the obtained versatile indole and pyrrole building blocks could be easily further modified, the method is expected to be highly useful in synthetic and medicinal chemistry.

ASSOCIATED CONTENT

Supporting Information

Detailed optimization tables, experimental procedures, analytical data for all compounds and copies of the NMR spectra for new compounds are available free of charge on the ACS Publications website.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

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[23] For an example of iodine mediated C2 amination of indoles, see: Li, Y.-X.; Wang, H.-X.; Ali, S.; Xia, X.-F.; Liang, Y.-M. *Chem. Commun.* **2012**, *48*, 2343. In our work, this methodology is applied for the first time to the synthesis of quinolinones.

Supporting Information

72 pages

Iridium- and Rhodium-Catalyzed Directed C-H Heteroarylation of Benzaldehydes with Benziodoxolone Hypervalent Iodine Reagents

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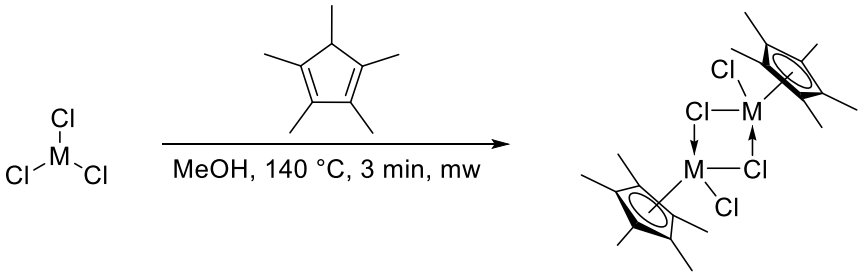
Contents

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, DMSO-d6, CD_3OD; all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal CD2Cl2 signal at 5.32 ppm, the internal DMSO signal at 2.50 ppm or the internal methanol signal at 3.30 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, DMSO-d6, CD_3OD; all signals are reported in ppm with the internal chloroform signal at 77.2 ppm, the internal CD2Cl2 signal at 54.0 ppm, the internal DMSO signal at 39.5 ppm or the internal methanol signal at 49.0 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 or a Brucer Alpha-P spectrophotometer 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.

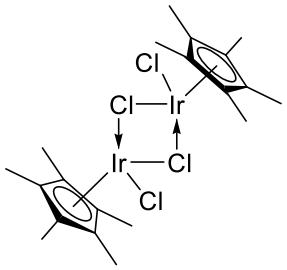
2. Syntheses of starting materials

2. 1. General procedure A for the synthesis of iridium and rhodium complexes



Following a reported procedure,[1] the metal trichloride hydrate (1.00 equiv) and 1,2,3,4,5-pentamethylcyclopenta-1,3-diene (1.50 equiv) were solubilized in MeOH [0.2 M]. The mixture was stirred at 140 °C for 3 min under microwave irradiation. The mixture was washed three times with pentane (same volume as MeOH). Et_2O (same volume as MeOH) was added, the precipitate was isolated, washed twice with Et_2O and dried under reduced pressure to afford the title compound.

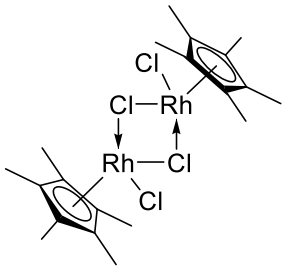
Pentamethylcyclopentadienyliridium (III) dichloride dimer [IRCp*Cl$_2$]$_2$



Following general procedure A and starting from commercially available iridium (III) chloride hydrate (245 mg, 0.820 mmol), pentamethylcyclopentadienyl-iridium (III) dichloride dimer (264 mg, 0.320 mmol, 39% yield) (CAS number 12354-84-6) was obtained as an orange solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62 (s, 30H).[2]

Pentamethylcyclopentadienylrhodium (III) chloride dimer [RhCp*Cl$_2$]$_2$



Following general procedure A and starting from commercially available rhodium (III) chloride hydrate (385 mg, 1.84 mmol), pentamethylcyclopenta-dienylrhodium (III) dichloride dimer (382 mg, 0.590 mmol, 67% yield) (CAS number 12354-85-7) was obtained as a red solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.59 (s, 30H).

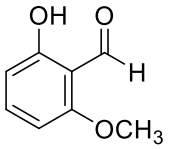
[1] Tönnemann, *J*.; Risse, *J*.; Grote, Z.; Scopelliti, R.; Severin, K. *Eur. JIC* **2013**, 4558−4562.

[2] Vázquez-Villa, H.; Reber, S.; Ariger, M. A.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2011**, *50* , 8979 –8981.

2.2. Procedures for the synthesis of 2-hydroxybenzaldehydes

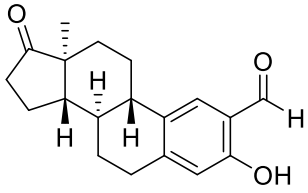
The reagents **4a**-**k**, **4m**, **4n** and **4o** are commercially available.

2-Hydroxy-6-methoxybenzaldehyde (4l)



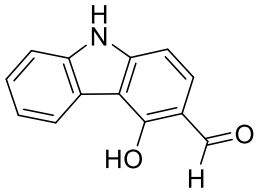
Aluminium trichloride (2.00 g, 15.0 mmol, 3 .00 equiv.) were suspended in dry DCM (20 mL) under Ar. Commercially available 2,6-dimethoxybenzaldehyde (831 mg, 5.00 mmol, 1.00 equiv) was solubilized in dry DCM (20 mL) under Ar and added to the solution at rt. The mixture was stirred 24 h at rt and quenched with aqueous 1 M HCl solution (20 mL). The two layers were separated and the aqueouse layer was extracted three times with DCM (20 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (Pentane/EtOAc 4:1) affording the title compound **4l** (210 mg, 1.38 mmol, 27% yield) as a white solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.98 (s, 1H, O<u>H</u>), 10.33 (s, 1H, C<u>H</u>O), 7.41 (t, *J* = 8.4 Hz, 1H, <u>H</u>$_{Ar}$), 6.52 (d, *J* = 8.5 Hz, 1H, <u>H</u>$_{Ar}$), 6.37 (d, *J* = 8.3 Hz, 1H, <u>H</u>$_{Ar}$), 3.89 (s, 3H, OC<u>H</u>$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.5, 163.8, 162.6, 138.6, 111.0, 110.0, 101.1, 56.0. Spectra data matched with the values reported in literature.[3]

(8*R*,9*S*,13*S*,14*S*)-3-Hydroxy-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta-[*a*]phenanthrene-2-carbaldehyde (4p)



Following a reported procedure,[4] commercially available estrone (243 mg, 0.899 mmol, 1.00 equiv), magnesium chloride (257 mg, 2.70 mmol, 3.00 equiv) and formaldehyde (81.0 mg, 2.70 mmol, 3.00 equiv.) were suspended in dry THF (9 mL) under Ar. Triethylamine (0.50 mL, 3.6 mmol, 4.0 equiv.) was added to the solution and the mixture was stirred 2 h at reflux. The solution was quenched with aqueous 4 M HCl solution (10 mL) and extracted three times with EtOAc (10 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (Pentane/EtOAc 4:1) affording the title compound **4p** (180 mg, 0.602 mmol, 67% yield) as a white solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.77 (s, 1H, O<u>H</u>), 9.79 (s, 1H, C<u>H</u>O), 7.41 (s, 1H, <u>H</u>$_{Ar}$), 6.69 (s, 1H, <u>H</u>$_{Ar}$), 2.97-2.85 (m, 2H, <u>H</u>$_{aliph}$), 2.50 (dd, *J* = 18.9, 8.6 Hz, 1H, <u>H</u>$_{aliph}$), 2.40 (s, 1H, <u>H</u>$_{aliph}$), 2.27-1.96 (m, 5H, <u>H</u>$_{aliph}$), 1.67-1.38 (m, 6H, <u>H</u>$_{aliph}$), 0.91 (s, 3H, C<u>H</u>$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.2, 159.4, 147.8, 132.2, 130.6, 119.1, 117.1, 50.5, 48.0, 43.5, 38.0, 35.9, 31.5, 30.1, 26.2, 25.9, 21.7, 13.9. Spectra data matched with the values reported in literature.[4]

4-Hydroxy-9*H*-carbazole-3-carbaldehyde (4q)



Following a reported procedure,[5] phosphoryl trichloride (0.400 mL, 4.30 mmol, 1.20 equiv.) was slowly added to DMF (2 mL) at 15 °C under Ar. 9*H*-carbazol-4-ol (655 mg, 3.58 mmol, 1.00 equiv.) was solubilized in DMF (4 mL) and slowly added at rt. The mixture was stirred 1 h at 35 °C and poured into crush ice and treated with 1 M NaOH (5 mL). The mixture was extracted three times with EtOAc (10 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (Pentane/EtOAc 7:3) and washed with Et_2O affording the title compound **4q** (430 mg, 2.04 mmol, 57% yield) as a grey solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 12.42 (s, 1H, O<u>H</u>), 9.88 (s, 1H, C<u>H</u>O), 8.39 (bs, 1H, N<u>H</u>), 8.37 (d, *J* = 7.8 Hz, 1H, <u>H</u>$_{Ar}$), 7.50 (d, *J* = 8.4 Hz, 1H, <u>H</u>$_{Ar}$), 7.45 (d, *J* = 3.9 Hz, 2H, <u>H</u>$_{Ar}$), 7.35 (m, 1H, <u>H</u>$_{Ar}$), 7.02 (d, *J* = 8.4 Hz, 1H, <u>H</u>$_{Ar}$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 195.2, 160.4, 145.4, 138.8, 131.5, 126.0, 123.4, 122.9, 121.5, 113.7, 111.5, 110.7, 103.6. Spectra data differs slightly from the values reported in literature.[5]

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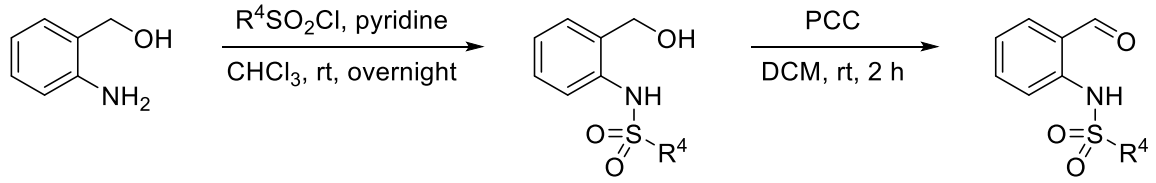
[3] Yoshioka, E.; Kohtani, S.; Miyabe, H. *Org. Lett.* **2010**, *12*, 1956-1959.

[4] Akselsen, Ø. W.; Hansen, T. V. *Tetrahedron* **2011**, *67*, 7738-7742.

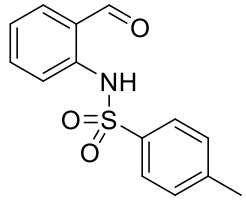
[5] Bhosale, S. M.; Momin, A. A.; Kusurkar, R. S. *Tetrahedron* **2012**, *68*, 6420-6426.

2.3. General procedure B for the synthesis of *N*-(2-formylphenyl)sulfonamides



(2-aminophenyl)methanol (1.00 equiv) and the corresponding sulfonyl chloride (1.10 equiv) were solubilized in $CHCl_3$ [0.4 M]. Pyridine (1.20 equiv) was added to the solution and the mixture was stirred overnight at room temperature. The mixture was concentrated under reduced pressure. The residue was taken up in EtOAc (30 mL) and washed three times with an aqueous 4 M HCl solution (15 mL) and once with a $NaHCO_3$ solution (15 mL). The organic layer was dried over magnesium sulfate dehydrate, filtered and concentrated under reduced pressure. The desired *N*-(2-(hydroxymethyl)phenyl)sulfonamide, obtained without further purification, was solubilized in DCM [0.3 M]. Pyridinium chlorochromate (1.50 equiv) was added in one portion and the mixture was stirred at room temperature for 2 hours. The solution was filtered on a 5 cm pad of silica gel then washed with DCM (100 mL). The filtrate was concentrated under reduced pressure. The residue was purified by recrystallization in EtOH/$CHCl_3$ 4:1 to afford the title compound.

N-(2-Formylphenyl)4-methylbenzenesulfonamide (7a)

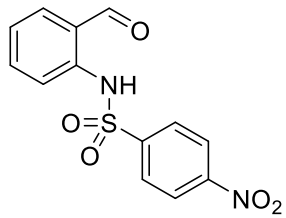


Following general procedure **B** and starting from commercially available (2-aminophenyl)methanol (0.75 g, 6.1 mmol), *N*-(2-formylphenyl)4-methylbenzenesulfonamide **7a** (1.40 g, 5.08 mmol, 83% yield) (CAS number 6590-65-4) was obtained as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.79 (s, 1H, NHTs), 9.83 (s, 1H, CHO), 7.77 (d, J = 8.3 Hz, 2H, H_{tolyl}), 7.69 (d, J = 8.4 Hz, 1H, H_{Ar}), 7.59 (dd, J = 7.7, 1.5 Hz, 1H, H_{Ar}), 7.51 (td, J = 8.6, 8.1, 1.6 Hz, 1H, H_{Ar}), 7.24 (d, J = 8.0 Hz, 2H, H_{tolyl}), 7.16 (td, J = 7.6, 0.9 Hz, 1H, H_{Ar}), 2.37 (s, 3H, CH_3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 195.1, 144.3, 140.1, 136.5, 136.2, 136.0, 129.9, 127.4, 123.1, 122.0, 117.9, 21.7. Spectra data matched with the values reported in literature.[6]

N-(2-Formylphenyl)4-nitrobenzenesulfonamide (7b)



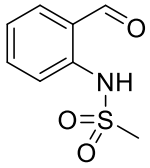
Following general procedure **B** and starting from commercially available (2-aminophenyl)methanol (0.75 g, 6.1 mmol), *N*-(2-formylphenyl)4-nitrobenzenesulfonamide **7b** (1.20 g, 3.92 mmol, 64% yield) (CAS number 601481-97-4) was obtained as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.92 (s, 1H, NHNs), 9.83 (s, 1H, CHO), 8.29 (d, *J* = 8.9 Hz, 2H, H_{nosyl}), 8.06 (d, *J* = 8.9 Hz, 2H, H_{nosyl}), 7.73 (d, *J* = 8.4 Hz, 1H, H_{Ar}), 7.64 (dd, *J* = 7.6, 1.5 Hz, 1H, H_{Ar}), 7.59-7.55 (m, 1H, H_{Ar}), 7.25 (td, *J* = 7.6, 0.8 Hz, 1H, H_{Ar}).

^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 150.5, 145.1, 139.0, 136.5, 136.2, 128.7, 124.6, 124.2, 122.4, 118.3. ^{1}H NMR Spectra data matched with the values reported in literature.[5]

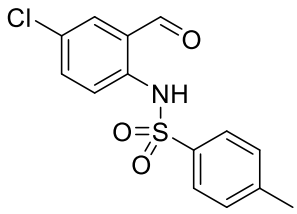
[6] Hechavarría Fonseca, M.; Eibler, E.; Zabelb, M.; König, B. *Tetrahedron: Asymmetry* **2003**, *14*, 1989-1994.

***N*-(2-Formylphenyl)methanesulfonamide (7c)**



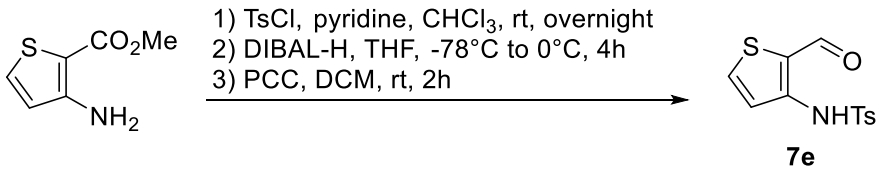
Following general procedure **B** and starting from commercially available (2-aminophenyl)methanol (0.75 g, 6.1 mmol), *N*-(2-formylphenyl)methanesulfonamide **7c** (0.680 g, 3.42 mmol, 56% yield) (CAS number 94532-99-7) was obtained as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.60 (s, 1H, NHMs), 9.92 (s, 1H, CHO), 7.73 (t, *J* = 7.6 Hz, 2H, H_{Ar}), 7.62 (t, *J* = 7.9 Hz, 1H, H_{Ar}), 7.28-7.24 (m, 1H, H_{Ar}), 3.10 (s, 3H, CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 195.2, 140.3, 136.6, 136.3, 123.1, 121.7, 117.1, 40.5. Spectra data matched with the values reported in literature.[7]

***N*-(4-Chloro-2-formylphenyl)-4-methylbenzenesulfonamide (7d)**



Following general procedure **B** and starting from commercially available (2-amino-5-chlorophenyl)methanol (236 mg, 1.50 mmol), *N*-(4-chloro-2-formylphenyl)4-methylbenzenesulfonamide **7d** (416 mg, 1.34 mmol, 89% yield) (CAS number 34159-03-0) was obtained as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.63 (s, 1H, NHTs), 9.77 (s, 1H, CHO), 7.75 (d, J = 8.3 Hz, 2H, H_{tolyl}), 7.68 (d, J = 8.9 Hz, 1H, H_{Ar}), 7.55 (d, J = 2.5 Hz, 1H, H_{Ar}), 7.46 (dd, J = 8.9, 2.5 Hz, 1H, H_{Ar}), 7.25 (d, J = 8.3 Hz, 2H, H_{tolyl}), 2.37 (s, 3H, CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.9, 144.6, 138.6, 136.2, 135.8, 135.3, 130.0, 128.5, 127.4, 122.9, 119.7, 21.7. Spectra data matched with the values reported in literature.[8]

***N*-(2-Formylthiophen-3-yl)-4-methylbenzenesulfonamide (7e)**



7e

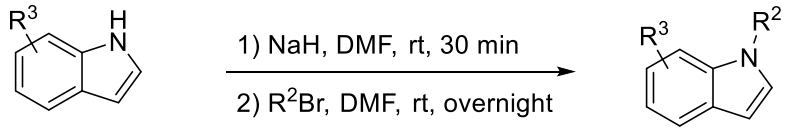
Methyl 3-amino-2-thiophenecarboxylate (1.00 equiv) and tosyl chloride (1.10 equiv) were solubilized in $CHCl_3$ [0.4 M]. Pyridine (1.20 equiv) was added to the solution and the mixture was stirred overnight at room temperature. The mixture was concentrated under reduced pressure. The residue was taken up in EtOAc (30 mL) and washed three times with an aqueous 4 M HCl solution (15 mL) and once with a $NaHCO_3$ solution (15 mL). The organic layer was dried over magnesium sulfate dehydrate, filtered and concentrated under reduced pressure. In a flame-dried flask, the methyl 3-(4-methylphenylsulfonamido)thiophene-2-carboxylate, obtained without further purification, was solubilized in dry THF [0.2 M] under Ar. DIBAL-H (4.00 equiv.) was added to the solution at -78 °C and the mixture was stirred 4 h until 0 °C. The mixture was quenched with a saturated aqueous solution of Rochelle's salt (10 mL) and filtered over Celite. The layers were separated and the aqueous layer was extracted three times with EtOAc (20 mL). The organic layer was dried over magnesium sulfate dehydrate, filtered and concentrated under reduced pressure. The *N*-(2-(hydroxymethyl)thiophen-3-yl)-4-methylbenzenesulfonamide, obtained without further purification, was solubilized in dry DCM [0.2 M]. Pyridinium chlorochromate (1.50 equiv) was added in one portion and the mixture was stirred at room temperature for 2 hours. The solution was filtered on a 5 cm pad of silica gel then washed with DCM (100 mL). The filtrate was concentrated under reduced pressure to afford the title compound **7e** (60% yield over 3 steps). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.14 (s, 1H, NHTs), 9.59 (s, 1H, CHO), 7.76 (d, *J* = 6.5 Hz, 2H, H_{tolyl}), 7.65-7.58 (m, 1H, $H_{thiophenyl}$), 7.47-7.38 (m, 1H, $H_{thiophenyl}$), 7.27 (d, *J* = 5.7 Hz, 2H, H_{tolyl}), 2.39 (s, 3H, CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 184.0, 144.6, 143.8, 136.4, 136.4, 130.0, 127.2, 121.0, 120.7, 21.7. Spectra data matched with the values reported in literature.[9]

[7] Nemoto, T.; Fukuda, T.; Hamada, Y. *Tetrahedron Letters* **2006**, *47*, 4365-4368.

[8] Theeraladanon, C.; Arisawa, M.; Nishida, A.; Nakagawa, M. *Tetrahedron* **2004**, *60*, 3017-3035.

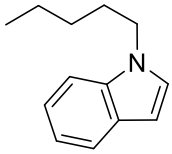
[9] Mu, D.; Wang, X.; Chen, G.; He, G. *J. Org. Chem.* **2017**, *82*, 4497−4503.

2.4. General procedure C for the synthesis of *N*-alkylindoles



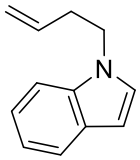
Sodium hydride (60% in mineral oil, 1.10 equiv) was suspended in DMF [0.6 M]. *N*-H-indole (1.00 equiv) was solubilized in DMF [1.0 M] and added to the suspension at 0 °C. The mixture was stirred at rt for 30 min. Bromoalkyl or TMSCl (1.50 equiv) was diluted in DMF [3.0 M] and added to the solution at 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 afford the title compound.

1-Pentyl-1*H*-indole (15b)



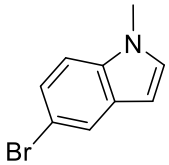
Following general procedure **C** and starting from commercially available indole (1.32 g, 11.3 mmol), **15b** (2.11 g, 11.3 mmol, quantitative yield) (CAS number 59529-21-4) was obtained as a colorless liquid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.9 Hz, 1H, $\underline{H}_{Ar}$), 7.37 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$), 7.23 (t, *J* = 7.6 Hz, 1H, $\underline{H}_{Ar}$), 7.14-7.10 (m, 2H, $\underline{H}_{Ar}$), 6.51 (d, *J* = 3.0 Hz, 1H, $\underline{H}_{Ar}$), 4.13 (t, *J* = 7.2 Hz, 2H, $NC\underline{H}_2$), 1.86 (quint, *J* = 7.2 Hz, 2H, $\underline{H}_{aliph}$), 1.42-1.20 (m, 4H, $\underline{H}_{aliph}$), 0.91 (t, *J* = 6.9 Hz, 3H, $C\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 136.1, 128.7, 127.9, 121.4, 121.0, 119.3, 109.5, 100.9, 46.5, 30.1, 29.3, 22.5, 14.1. Spectra data matched with the values reported in literature.[10]

1-(But-3-en-1-yl)-1H-indole (15c)



Following general procedure **C** and starting from commercially available indole (1.54 g, 13.1 mmol), **15c** (0.39 g, 2.3 mmol, 17%) (CAS number 46169-71-5) was obtained as a colorless liquid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.9 Hz, 1H, $\underline{H}_{Ar}$), 7.36 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$), 7.24-7.20 (m, 1H, $\underline{H}_{Ar}$), 7.13-7.09 (m, 2H, $\underline{H}_{Ar}$), 6.49 (d, *J* = 3.1 Hz, 1H, $\underline{H}_{Ar}$), 5.80 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H, $C\underline{H}{=}CH_2$), 5.11-5.05 (m, 2H, $CH{=}C\underline{H}_2$), 4.20 (t, *J* = 7.2 Hz, 2H, $NC\underline{H}_2$), 2.59 (q, *J* = 6.9 Hz, 2H, $NCH_2C\underline{H}_2$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 136.0, 134.8, 128.7, 127.9, 121.5, 121.1, 119.4, 117.5, 109.5, 101.2, 46.1, 34.7. Spectra data matched with the values reported in literature.[11]

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



Following general procedure **C** and starting from commercially available 5-bromoindole (0.59 mg, 3.0 mmol), **15d** (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.[12]

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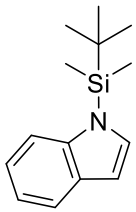
[10] Banister, S. D.; Wilkinson, S. M.; Longworth, M.; Stuart, *J.*; Apetz, N.; English, K.; Brooker, L.; Goebel, C.; Hibbs, D. E.; Glass, M.; Connor, M.; McGregor, I. S.; Kassiou, M. *ACS Chem. Neurosci.* **2013**, *4*, 1081−1092.
[11] Kerchner, H. A.; Montgomery, *J. Org. Lett.* **2016**, *18*, 5760–5763.
[12] Greulich, T.W.; Daniliuc, C.*J.*; Studer, A. *Org. Lett.* **2015**, *17*, 254−257.

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



Following general procedure **C** and starting from commercially available indole (2.34 g, 20.0 mmol), **15e** (4.63 g, 20.0 mmol, quantitative yield) (CAS number 40899-73-8) was obtained as a pale yellow solid.

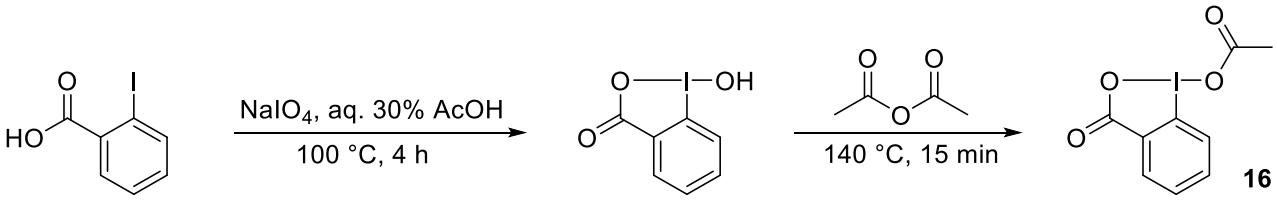
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.2 Hz, 1H, $\underline{H}_{Ar}$), 7.44 (d, *J* = 7.7 Hz, 1H, $\underline{H}_{Ar}$), 7.10 (d, *J* = 3.2 Hz, 1H, $\underline{H}_{Ar}$), 7.09-6.99 (m, 2H, $\underline{H}_{Ar}$), 6.54 (d, *J* = 2.7 Hz, 1H, $\underline{H}_{Ar}$), 0.85 (s, 9H, $C(C\underline{H}_3)_3$), 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.[13]

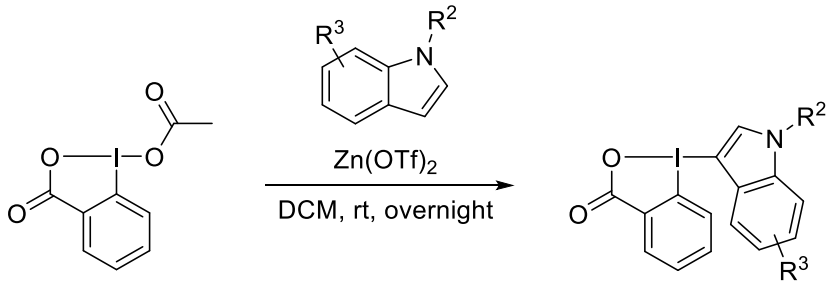
[13] Dhanak, D.; Reese, C. B. *J. Chem. Soc., Perkin Trans. 1* **1986**, 2181–2186

2.5. General procedure D for the synthesis of indoleBX and pyrroleBX reagents

1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one (16)

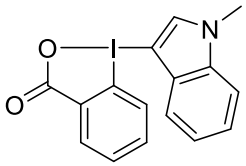


Following a reported procedure[14], sodium periodate (18.1 g, 85.0 mmol, 1.05 equiv) and 2-iodobenzoic acid (20.0 g, 81.0 mmol, 1.00 equiv) were suspended in 30% (v:v) aq. AcOH (160 mL). The mixture was vigorously stirred and refluxed for 4 h and allowed to cool to room temperature, while protecting 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 afford 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 afford 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,[15] 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 afford the pure desired hypervalent iodine reagent.

1-(3-1-Methyl-1*H*-indole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one (5a)



Following general procedure **D**, starting from commercially available 1-methylindole (0.43 mL, 3.4 mmol) and **16**, a purification by column chromatography (DCM/MeOH 19:1) afford the title compound **5a** (0.79 g, 2.1 mmol, 61% yield) (CAS number 2130906-04-4) as an off-white solid.

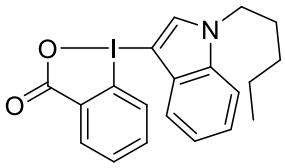
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 7.5 Hz, 1H, $\underline{H}_{Ar}$), 7.77 (s, 1H, C$\underline{H}$-N), 7.56-7.49 (m, 2H, $\underline{H}_{Ar}$), 7.47-7.41 (m, 2H, $\underline{H}_{Ar}$), 7.35-7.26 (m, 2H, $\underline{H}_{Ar}$), 6.85 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$), 4.02 (s, 3H,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

^{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.[12]

[14] Parsons, A. T.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2011**, *50*, 9120–9123

[15] Caramenti, P.; Nicolai, S.; Waser, *J. Chem. Eur. J.* **2017**, *23*,14702–14706

1-(3-1-Pentyl-1*H*-indole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one (5b)



Following general procedure **D**, starting from **15b** (257 mg, 1.37 mmol) and **16**, a purification by column chromatography (DCM/MeOH 19:1) afford the title compound **5b** (357 mg, 0.820 mmol, 60% yield) as an off-white solid. **mp** 194-196 °C. **Rf** 0.37 (DCM/MeOH 19:1).

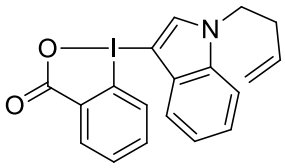
^{1}H NMR (400 MHz, MeOD) δ 8.26 (d, *J* = 6.6 Hz, 1H, $\underline{H}_{Ar}$), 8.15 (s, 1H, C$\underline{H}$-N), 7.70 (d, *J* = 8.3 Hz, 1H, $\underline{H}_{Ar}$), 7.60 (t, *J* = 7.3 Hz, 1H, $\underline{H}_{Ar}$), 7.48 (d, *J* = 8.0 Hz, 1H, $\underline{H}_{Ar}$), 7.44-7.37 (m, 2H, $\underline{H}_{Ar}$), 7.29 (t, *J* = 7.5 Hz, 1H, $\underline{H}_{Ar}$), 6.87 (d, *J* = 8.3 Hz, 1H, $\underline{H}_{Ar}$), 4.42 (t, *J* = 7.0 Hz, 2H, NC$\underline{H}_2$), 2.03-1.90 (m, 2H, $\underline{H}_{aliph}$), 1.47-1.24 (m, 4H, $\underline{H}_{aliph}$), 0.91 (t, *J* = 6.9 Hz, 3H, C$\underline{H}_3$).

^{13}C NMR (101 MHz, MeOD) δ 170.3, 140.2, 138.5, 135.0, 134.5, 133.2, 131.7, 130.6, 127.7, 125.1, 123.5, 120.6, 116.8, 112.4, 77.9, 48.3, 30.8, 30.1, 23.3, 14.3.

IR ν_{max} 2927 (w), 1596 (s), 1555 (s), 1435 (m), 1340 (s), 1292 (m), 826 (s), 744 (s), 583 (s).

HRMS calculated for $C_{20}H_{21}INO_2^+$ $[M+H]^+$ 434.0612; found 434.0622.

1-(3-1-(But-3-en-1-yl)-1*H*-indole)-1*H*-1λ3 -benzo[*b*]iodo-3(2*H*)-one (5c)

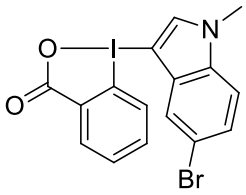


Following general procedure **D**, starting from **15c** (390 mg, 2.28 mmol) and **16**, a purification by column chromatography (DCM/MeOH 32:1) afford the title compound **5c** (501 mg, 1.16 mmol, 53% yield) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 7.3 Hz, 1H, $\underline{H}_{Ar}$), 7.73-7.68 (m, 1H, $\underline{H}_{Ar}$), 7.57-7.51 (m, 2H, C$\underline{H}$-N + $\underline{H}_{Ar}$), 7.48-7.42 (m, 2H, $\underline{H}_{Ar}$), 7.33-7.28 (m, 2H, $\underline{H}_{Ar}$), 6.77 (d, *J* = 8.3 Hz, 1H, $\underline{H}_{Ar}$), 5.80 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H, C$\underline{H}$=CH_2), 5.11-5.04 (m, 2H, CH=C$\underline{H}_2$), 4.39 (t, *J* = 6.8 Hz, 2H, NC$\underline{H}_2$), 2.71 (q, *J* = 6.8 Hz, 2H, $NCH_2C\underline{H}_2$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 137.6, 137.5, 136.9, 133.6, 133.6, 133.4, 132.8, 130.8, 129.6, 125.3, 124.5, 122.8, 120.3, 118.9, 116.4, 111.0, 79.7, 47.1, 34.3. Spectra data matched with the values reported in literature.[12]

1-(3-5-Bromo-1-methyl-1*H*-indole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one (5d)



Following general procedure **D**, starting from **15d** (406 mg, 1.93 mmol) and **16**, a purification by column chromatography (DCM/MeOH 19:1) afford the title compound **5d** (470 mg, 1.03 mmol, 53% yield) as an off-white solid. **mp** 223-225 °C. **Rf** 0.21 (DCM/MeOH 19:1).

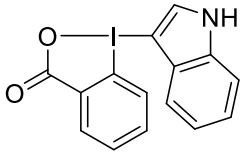
^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.33 (d, *J* = 7.4 Hz, 1H, $\underline{H}_{Ar}$), 7.70 (s, 1H, C$\underline{H}$-N), 7.63 (s, 1H, $\underline{H}_{Ar}$), 7.57 (t, *J* = 7.3 Hz, 1H, $\underline{H}_{Ar}$), 7.52 (dd, *J* = 8.8, 1.6 Hz, 1H, $\underline{H}_{Ar}$), 7.44 (d, *J* = 8.8 Hz, 1H, $\underline{H}_{Ar}$), 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.

IR ν_{max} 3075 (m), 1601 (s), 1495 (s), 1347 (s), 740 (s), 685 (m).

HRMS calculated for $C_{16}H_{12}{}^{79}BrINO_2^+$ $[M+H]^+$ 455.9091; found 455.9093.

1-(3-1*H*-Indole)-1*H*-1λ*3* -benzo[*b*]iodo-3(2*H*)-one (5e)

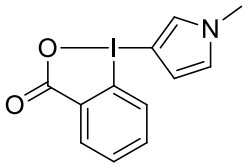


Following general procedure **D** and remplacing $Zn(OTf)_2$ by $Sc(OTf)_3$, starting from **15e** (579 mg, 2.50 mmol) and **16**, a purification by column chromatography (DCM/MeOH 5:1) afforded the title compound **5e** (527 mg, 1.45 mmol, 58% yield) as a pale beige solid.

^{1}H NMR (400 MHz, DMSO-d6) δ 12.36 (s, 1H, NH), 8.26 (s, 1H, CH-N), 8.12 (d, *J* = 7.3 Hz, 1H, H_{Ar}), 7.64 (d, *J* = 8.2 Hz, 1H, H_{Ar}), 7.56 (t, *J* = 7.3 Hz, 1H, H_{Ar}), 7.49 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.41 (t, *J* = 7.6 Hz, 1H, H_{Ar}), 7.31 (t, *J* = 7.6 Hz, 1H, H_{Ar}), 7.20 (t, *J* = 7.5 Hz, 1H, H_{Ar}), 6.76 (d, *J* = 8.2 Hz, 1H, 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.[12]

1-(3-1-Methyl-1*H*-pyrrole)-1*H*-1λ$_3$ -benzo[*b*]iodo-3(2*H*)-one (5f)



Following general procedure **D,** starting from 1-methylpyrrole (0.37 mL, 4.2 mmol) and **16**, a purification by column chromatography (EtOAc/MeOH 9:1) afford the title compound **5f** (763 mg, 2.33 mmol, 56% yield) (CAS number 2130906-17-9**)** as a off-white solid and 1-(2-1-methyl-1*H*-pyrrole)-1*H*-1λ$_3$-benzo[*b*]iodo-3(2*H*)-one (525 mg, 1.64 mmol, 39% yield) (CAS number 2130906-18-0) as a pale brown solid.

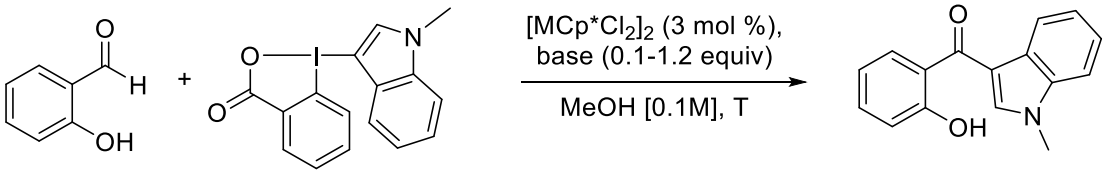
^{1}H NMR (400 MHz, MeOD) δ 8.25 (dd, *J* = 7.5, 1.6 Hz, 1H, H_{Ar}), 7.64 (t, *J* = 7.3 Hz, 1H, H_{Ar}), 7.55 (td, *J* = 7.8, 7.3, 1.7 Hz, 1H, H_{Ar}), 7.48-7.45 (m, 1H, H_{Ar}), 7.12 (d, *J* = 8.2 Hz, 1H, H_{Ar}), 7.06-7.02 (m, 1H, H_{Ar}), 6.62 (dd, *J* = 2.8, 1.7 Hz, 1H, H_{Ar}), 3.87 (s, 3H, NCH_3).

^{13}C NMR (101 MHz, MeOD) δ 170.3, 135.3, 133.8, 133.5, 133.0, 131.7, 128.1, 127.8, 117.4, 116.7, 82.4, 37.1. Spectra data matched with the values reported in literature.[11]

3. Optimization of the transition metal-catalyzed C-H activation

4a (9.8 mg, 80 µmol, 1.0 equiv.), **5a** (30.3 mg, 80.0 µmol, 1.00 equiv.), metal catalyst (2.0 mg, 2.5 µmol, 3 mol %) and base (see Table 1 below) were solubilized in dry MeOH [0.1 M]. The mixture was stirred at room temperature for 10 minutes. 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 column chromatography on silica gel using Pentane/EtOAc 85:15 as eluent to afford the pure title compound.

Table 1: Optimization for the iridium-catalyzed 3-acylation with salicylaldehyde **4a** and Me-indoleBX **5a**

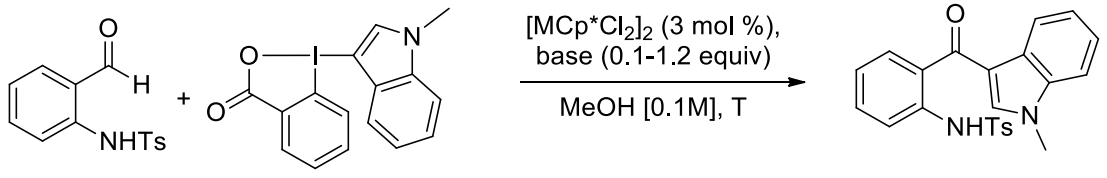


4a **5a** **6a**

Catalyst	Temperature (°C)	Base	Isolated yield (%)
-	80	CsOAc (1.2 equiv)	NR
$[RhCp^*Cl_2]_2$	80	CsOAc (1.2 equiv)	< 20
$[IrCp^*Cl_2]_2$	rt	CsOAc (1.2 equiv)	91
$[IrCp^*Cl_2]_2$	rt	NaOAc (1.2 equiv)	90
$[IrCp^*Cl_2]_2$	rt	KOAc (1.2 equiv)	90
$[IrCp^*Cl_2]_2$	rt	KOAc (1.0 equiv)	90
$[IrCp^*Cl_2]_2$	rt	KOAc (0.5 equiv)	86[a]
$[IrCp^*Cl_2]_2$	rt	-	56[a]
$[IrCp^*Cl_2]_2$ (1 mol%)	rt	KOAc (1.0 equiv)	94
$[IrCp^*Cl_2]_2$ (1 mol%)	80	KOAc (1.0 equiv)	53[b]
$[IrCp^*Cl_2]_2$ (1 mol%)	80	KOAc (1.0 equiv)	59[c]
$[IrCp^*Cl_2]_2$	80	KOAc (1.0 equiv)	decomposition[d,e]
$[IrCp^*Cl_2]_2$	50	KOAc (1.0 equiv)	decomposition[f,e]
$[IrCp^*Cl_2]_2$	50	KOAc (1.0 equiv)	decomposition[g,e]

[a]by-products were observed. [b]3-Iodo-1-methylindole was used instead of **5a**. [c]3-Bromo-1-methylindole was used instead of **5a**. [d]Benzaldehyde was used instead of **4a**. [e]No conversion at rt. [f]o-Anisaldehyde was used instead of **4a**. [g]2-Acetoxybenzaldehyde was used instead of **4a**.

Table 2: Optimization for the rhodium-catalyzed 3-acylation with *N*-(2-formylphenyl)-4-methylbenzenesulfonamide **7a** and Me-indoleBX **5a**

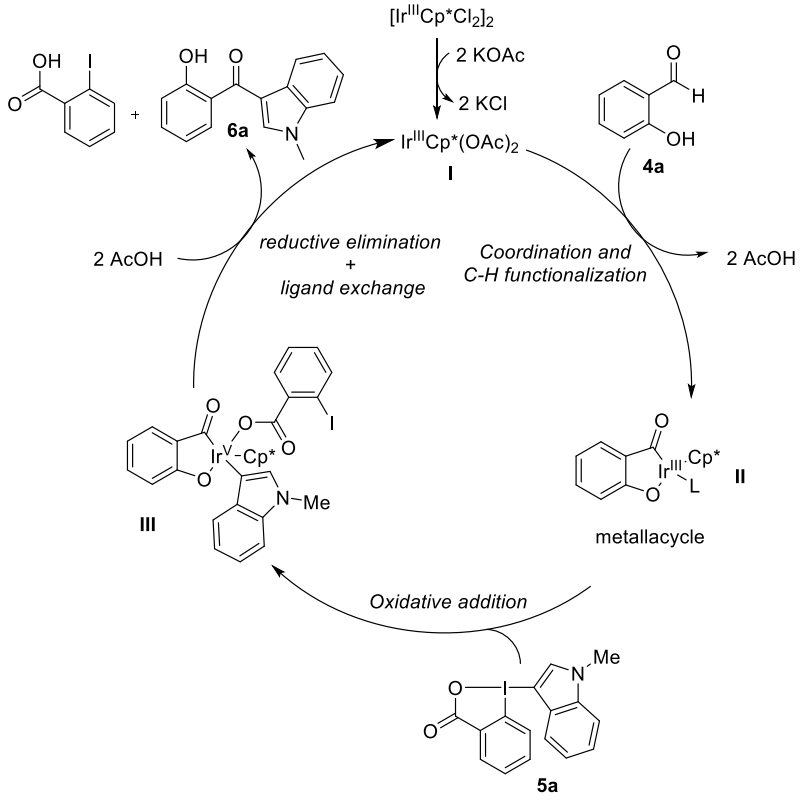


7a **5a** **8a**

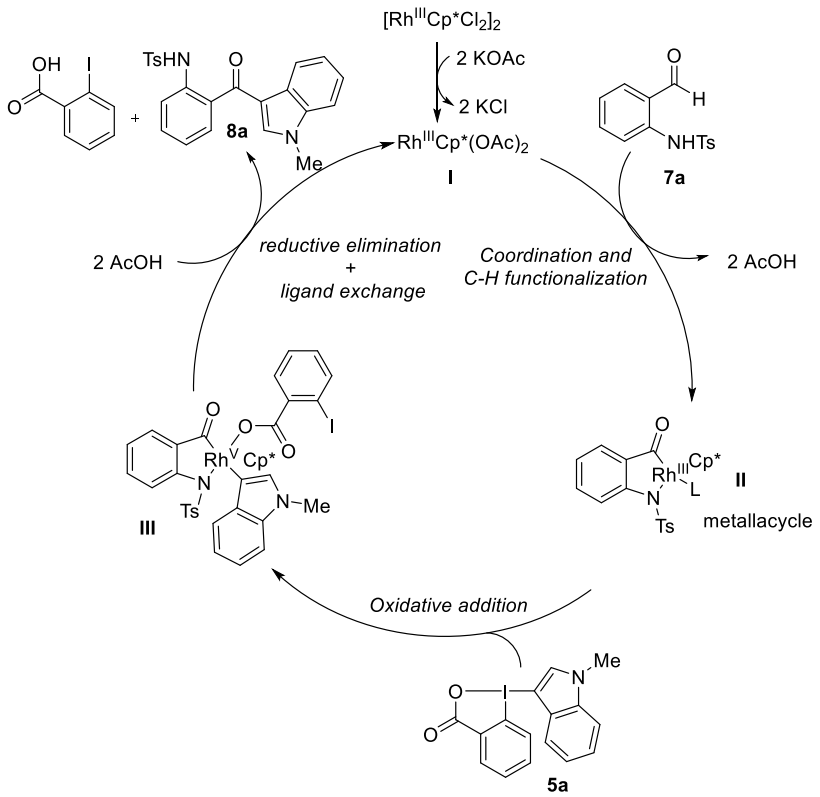
Catalyst	Temperature (°C)	Solvent	Isolated yield (%)
-	80	DCE	NR
$[IrCp^*Cl_2]_2$	rt	DCE	75
$[RhCp^*Cl_2]_2$	rt	DCE	78
$[RhCp^*Cl_2]_2$	rt	MeOH	82
$[RhCp^*Cl_2]_2$	40	MeOH	86
$[RhCp^*Cl_2]_2$ (1 mol%)	40	MeOH	89

4. Mechanism proposal

Scheme S1: Plausible mechanism of the iridium-catalyzed C-H functionalization for salicylaldehyde **4a** and Me-indoleBX **5a**



Scheme S2: Plausible mechanism of the rhodium-catalyzed C-H functionalization for *N*-(2-formylphenyl)-4-methylbenzenesulfonamide **7a** and Me-indoleBX **5a**

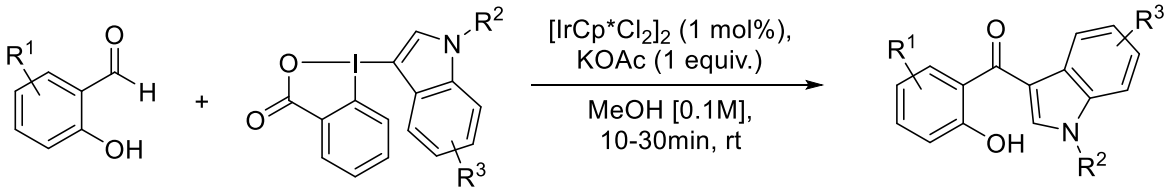


Discussion: A very similar catalytic cycle can be proposed for both the iridium and rhodium catalyst. Ligand exchange with potassium acetate first gives the active catalyst, which reacts than with either **4a** or **7a** via coordination and C-H activation to form metallacycle **II** and two equivalents of acetic acid. In fact, metallacycle **II** bearing a rhodium center and L = pyridine or MeCN could be isolated in excellent yields using similar reaction conditions.[16] In the second step, oxidative addition of hypervalent iodine reagent **5a** onto metallacycle **II** gives high valent metal intermediate **III**. Finally, reductive elimination and ligand exchange regenerate the metal acetate complex. This mechanism is in accordance with what was proposed for alkynylation.[16] Further work will be done to fully elucidate the mechanism of this transformation.

[16] Wang, H.; Xie, F.; Qi, Z.; Li, X. *Org. Lett.* **2015**, *17*, 920.

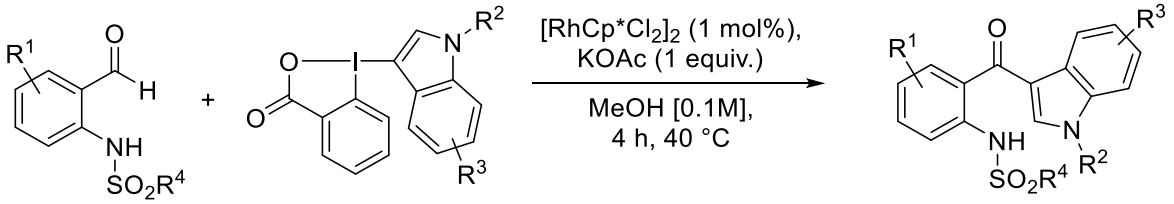
5. Scope

5.1. General procedure E1 for the synthesis of 3-salicyloylindoles



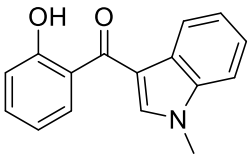
$[IrCp^*Cl_2]_2$ (1.2 mg, 1.5 µmol, 1 mol %), potassium acetate (14.8 mg, 0.150 mmol, 1.00 equiv), corresponding salicylaldehyde (0.15 mmol, 1.00 equiv) and the corresponding hypervalent iodine reagent (0.15 mmol, 1.00 equiv) were solubilized in dry MeOH (1.5 mL, 0.1 M). The mixture was stirred at room temperature for 10 minutes. 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 column chromatography on silica gel using the indicated solvents to afford the pure title compound.

5.2 General procedure E2 for the synthesis of 3-(2-sulfonamino)benzoylindoles



$[RhCp^*Cl_2]_2$ (0.93 mg, 1.5 µmol, 1 mol %), potassium acetate (14.8 mg, 0.150 mmol, 1.00 equiv), corresponding salicylaldehyde (0.15 mmol, 1.00 equiv) and corresponding hypervalent iodine reagent (0.15 mmol, 1.00 equiv) were solubilized in dry MeOH (1.5 mL, 0.1 M). The mixture was stirred at 40 °C for 4 hours. 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 column chromatography on silica gel using the indicated solvents to afford the pure title compound.

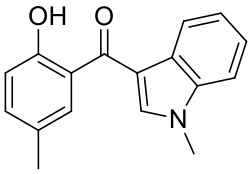
(2-Hydroxyphenyl)(1-methyl-1*H*-indol-3-yl)methanone (6a)



Following General Procedure **E1**, starting from commercially available salicylaldehyde and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 85:15) afford the title compound **6a** (35.4 mg, 0.140 mmol, 94% yield) or (281 mg, 1.12 mmol, 93% yield) as a yellow solid. **mp** 128-130 °C. **Rf** 0.46 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.06 (bs, 1H, O<u>H</u>), 8.33-8.28 (m, 1H, <u>H</u>$_{Ar}$), 7.84 (dd, *J* = 7.9, 1.6 Hz, 1H, <u>H</u>$_{Ar}$), 7.62 (s, 1H, C<u>H</u>-N), 7.46 (ddd, *J* = 8.6, 7.4, 1.6 Hz, 1H, <u>H</u>$_{Ar}$), 7.40-7.32 (m, 3H, <u>H</u>$_{Ar}$), 7.06 (d, *J* = 8.3 Hz, 1H, <u>H</u>$_{Ar}$), 6.92 (t, *J* = 8.0 Hz, 1H, <u>H</u>$_{Ar}$), 3.86 (s, 3H, NC<u>H</u>$_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 162.0, 137.4, 137.0, 134.7, 131.5, 127.3, 123.9, 122.8, 122.4, 121.4, 118.7, 118.2, 114.7, 109.9, 33.8.
IR ν_{max} 1586 (s), 1521 (s), 1463 (s), 1370 (s), 1330 (m), 1276 (m), 1236 (s), 1200 (s), 1154 (s), 1128 (s), 1099 (s), 887 (s), 743 (s), 663 (s).
HRMS calculated for $C_{16}H_{13}NO_2^+$ $[M+H]^+$ 252.1019; found 252.1022.

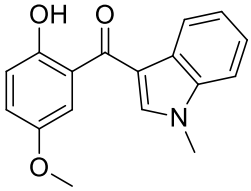
(2-Hydroxy-5-methylphenyl)(1-methyl-1*H*-indol-3-yl)methanone (6b)



Following General Procedure **E1**, starting from commercially available 2-hydroxy-5-methylbenzaldehyde and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 85:15) afford the title compound **6b** (35.4 mg, 0.134 mmol, 89% yield) as a yellow solid. **mp** 170-172 °C. **Rf** 0.40 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.82 (bs, 1H, O<u>H</u>), 8.30-8.26 (m, 1H, <u>H</u>$_{Ar}$), 7.63 (d, *J* = 1.4 Hz, 1H, <u>H</u>$_{Ar}$), 7.61 (s, 1H, C<u>H</u>-N), 7.39-7.31 (m, 3H, <u>H</u>$_{Ar}$), 7.27 (dd, *J* = 8.7, 2.0 Hz, 1H, <u>H</u>$_{Ar}$), 6.96 (d, *J* = 8.4 Hz, 1H, <u>H</u>$_{Ar}$), 3.87 (s, 3H, NC<u>H</u>$_3$), 2.33 (s, 3H, C<u>H</u>$_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 193.6, 159.8, 137.4, 136.8, 135.6, 131.4, 127.7, 127.4, 123.8, 122.7, 122.5, 121.2, 117.9, 114.8, 109.9, 33.7, 20.7.
IR ν_{max} 2913 (w), 1564 (s), 1521 (s), 1469 (s), 1343 (s), 1219 (s), 1109 (s), 823 (s), 748 (s).
HRMS calculated for $C_{17}H_{16}NO_2^+$ $[M+H]^+$ 266.1176; found 266.1177.

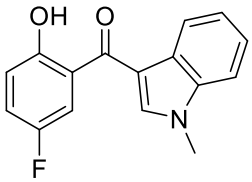
(2-Hydroxy-5-methoxyphenyl)(1-methyl-1*H*-indol-3-yl)methanone (6c)



Following General Procedure **E1**, starting from commercially available 2-hydroxy-5-methoxybenzaldehyde and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 7:3) afford the title compound **6c** (38.0 mg, 0.135 mmol, 90% yield) as a yellow solid. **mp** 147-149 °C. **Rf** 0.24 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.45 (bs, 1H, O<u>H</u>), 8.31-8.27 (m, 1H, <u>H</u>$_{Ar}$), 7.68 (s, 1H, C<u>H</u>-N), 7.41-7.33 (m, 4H, <u>H</u>$_{Ar}$), 7.10 (dd, *J* = 9.0, 3.1 Hz, 1H, <u>H</u>$_{Ar}$), 7.01 (d, *J* = 9.0 Hz, 1H, <u>H</u>$_{Ar}$), 3.88 (s, 3H, OC<u>H</u>$_3$), 3.79 (s, 3H, NC<u>H</u>$_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 155.9, 151.7, 137.5, 136.8, 127.3, 123.9, 122.9, 122.5, 121.4, 121.2, 118.8, 115.9, 114.9, 110.0, 56.2, 33.8.
IR ν_{max} 3102 (w), 2927 (m), 2852 (w), 1562 (s), 1520 (s), 1484 (s), 1460 (s), 1221 (s), 1101 (s), 1035 (s), 828 (s), 742 (s), 670 (s).
HRMS calculated for $C_{17}H_{16}NO_3^+$ $[M+H]^+$ 282.1125; found 282.1128.

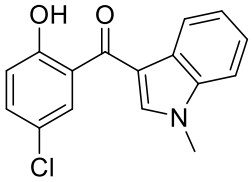
(5-Fluro-2-hydroxyphenyl)(1-methyl-1*H*-indol-3-yl)methanone (6d)



Following General Procedure **E1**, starting from commercially available 5-fluoro-2-hydroxybenzaldehyde and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 85:15) afford the title compound **6d** (36.3 mg, 0.135 mmol, 90% yield) as a yellow solid. **mp** 160-162 °C. **Rf** 0.51 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.71 (s, 1H, O$\underline{H}$), 8.32-8.29 (m, 1H, $\underline{H}_{Ar}$), 7.65 (s, 1H, C$\underline{H}$-N), 7.54 (dd, *J* = 9.0, 3.1 Hz, 1H, $\underline{H}_{Ar}$), 7.42-7.34 (m, 3H, $\underline{H}_{Ar}$), 7.23-7.17 (m, 1H, $\underline{H}_{Ar}$), 7.01 (dd, *J* = 9.1, 4.6 Hz, 1H, $\underline{H}_{Ar}$), 3.89 (s, 3H, NC$\underline{H}_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -124.7.
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.2 (d, *J* = 2.2 Hz), 158.0 (d, *J* = 1.5 Hz), 155.0 (d, *J* = 237.5 Hz), 137.5, 136.9, 127.2, 124.1, 123.1, 122.5, 121.7 (d, *J* = 23.4 Hz), 121.1 (d, *J* = 6.1 Hz), 119.3 (d, *J* = 7.3 Hz), 116.7 (d, *J* = 23.7 Hz), 114.4, 110.0, 33.9.
IR ν_{max} 2927 (w), 1571 (m), 1525 (s), 1464 (s), 1423 (m), 1341 (s), 1222 (s), 1125 (s), 1099 (s), 829 (s), 791 (s), 750 (s), 676 (s).
HRMS calculated for $C_{16}H_{13}FNO_2^+$ $[M+H]^+$ 270.0925; found 270.0930.

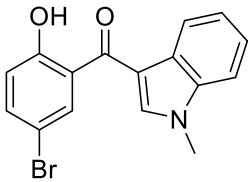
(5-Chloro-2-hydroxyphenyl)(1-methyl-1*H*-indol-3-yl)methanone (6e)



Following General Procedure **E1**, starting from commercially available 5-chloro-2-hydroxybenzaldehyde and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 85:15) afford the title compound **6e** (39.3 mg, 0.138 mmol, 92% yield) as a yellow solid. **mp** 187-189 °C. **Rf** 0.58 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.90 (s, 1H, O$\underline{H}$), 8.29 (dd, *J* = 5.9, 2.4 Hz, 1H, $\underline{H}_{Ar}$), 7.82 (d, *J* = 2.5 Hz, 1H, $\underline{H}_{Ar}$), 7.66 (s, 1H, C$\underline{H}$-N), 7.43-7.34 (m, 4H, $\underline{H}_{Ar}$), 7.01 (d, *J* = 8.8 Hz, 1H, $\underline{H}_{Ar}$), 3.92 (s, 3H, NC$\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.1, 160.5, 137.6, 137.0, 134.4, 130.5, 127.3, 124.2, 123.4, 123.2, 122.5, 122.2, 119.8, 114.5, 110.1, 33.9.
IR ν_{max} 1563 (m), 1521 (s), 1470 (s), 1335 (s), 1276 (s), 1217 (s), 1128 (m), 812 (s), 748 (s), 723 (s).
HRMS calculated for $C_{16}H_{13}ClNO_2^+$ $[M+H]^+$ 286.0629; found 286.0636.

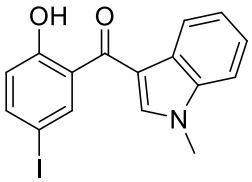
(5-Bromo-2-hydroxyphenyl)(1-methyl-1*H*-indol-3-yl)methanone (6f)



Following General Procedure **E1**, starting from commercially available 5-bromo-2-hydroxybenzaldehyde and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 85:15) afford the title compound **6f** (44.4 mg, 0.135 mmol, 90% yield) as a yellow solid. **mp** 171-173 °C. **Rf** 0.58 (Pentane/EtOAc 4:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.93 (s, 1H, O$\underline{H}$), 8.32-8.25 (m, 1H, $\underline{H}_{Ar}$), 7.96 (d, *J* = 2.5 Hz, 1H, $\underline{H}_{Ar}$), 7.65 (s, 1H, C$\underline{H}$-N), 7.54 (dd, *J* = 8.8, 2.5 Hz, 1H, $\underline{H}_{Ar}$), 7.43-7.34 (m, 3H, $\underline{H}_{Ar}$), 6.96 (d, *J* = 8.8 Hz, 1H, $\underline{H}_{Ar}$), 3.91 (s, 3H, NC$\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.0, 160.9, 137.6, 137.2, 137.0, 133.5, 127.2, 124.2, 123.2, 122.8, 122.5, 120.2, 114.4, 110.4, 110.1, 34.0.
IR ν_{max} 2913 (w), 1565 (m), 1523 (s), 1463 (s), 1337 (s), 1274 (m), 1215 (s), 812 (m), 746 (s).
HRMS calculated for $C_{16}H_{13}{}^{79}BrNO_2^+$ $[M+H]^+$ 330.0124; found 330.0129.

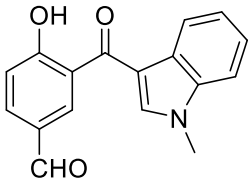
(2-Hydroxy-5-iodophenyl)(1-methyl-1*H*-indol-3-yl)methanone (6g)



Following General Procedure **E1**, starting from commercially available 5-iodo-2-hydroxybenzaldehyde and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 85:15) afford the title compound **6g** (50.1 mg, 0.133 mmol, 89% yield) as a yellow solid. **mp** 181-183 °C. **Rf** 0.61 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.94 (s, 1H, O<u>H</u>), 8.29-8.25 (m, 1H, <u>H</u>$_{Ar}$), 8.13 (d, *J* = 2.2 Hz, 1H, <u>H</u>$_{Ar}$), 7.70 (dd, *J* = 8.7, 2.2 Hz, 1H, <u>H</u>$_{Ar}$), 7.63 (s, 1H, C<u>H</u>-N), 7.43-7.34 (m, 3H, <u>H</u>$_{Ar}$), 6.85 (d, *J* = 8.7 Hz, 1H, <u>H</u>$_{Ar}$), 3.92 (s, 3H, NC<u>H</u>$_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.9, 161.6, 142.9, 139.5, 137.6, 137.0, 127.2, 124.2, 123.7, 123.2, 122.5, 120.7, 114.5, 110.1, 79.7, 34.0.
IR ν_{max} 1570 (s), 1554 (s), 1520 (s), 1461 (s), 1337 (s), 1272 (s), 1213 (s), 1108 (s), 888 (s), 808 (s), 755 (s), 736 (s).
HRMS calculated for $C_{16}H_{13}INO_2^+$ $[M+H]^+$ 377.9986; found 377.9984.

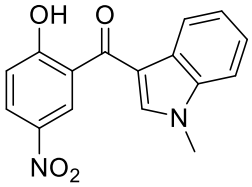
4-Hydroxy-3-(1-methyl-1*H*-indole-3-carbonyl)benzaldehyde (6h)



Following General Procedure **E1**, starting from commercially available 4-hydroxyisophthalaldehyde and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 3:2) afford the title compound **6h** (34.3 mg, 0.123 mmol, 82% yield) as a yellow solid. **mp** 203-205 °C. **Rf** 0.50 (Pentane/EtOAc 1:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.84 (s, 1H, O<u>H</u>), 9.90 (s, 1H, C<u>H</u>O), 8.43 (d, *J* = 2.0 Hz, 1H, <u>H</u>$_{Ar}$), 8.32-8.27 (m, 1H, <u>H</u>$_{Ar}$), 7.98 (dd, *J* = 8.6, 2.1 Hz, 1H, <u>H</u>$_{Ar}$), 7.71 (s, 1H, C<u>H</u>-N), 7.44-7.35 (m, 3H, <u>H</u>$_{Ar}$), 7.17 (d, *J* = 8.6 Hz, 1H, <u>H</u>$_{Ar}$), 3.93 (s, 3H, NC<u>H</u>$_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.6, 190.3, 167.5, 137.6, 137.2, 135.9, 133.6, 128.1, 127.3, 124.4, 123.3, 122.5, 121.3, 119.2, 114.4, 110.1, 34.0.
IR ν_{max} 3115 (w), 2921 (m), 1693 (s), 1609 (s), 1562 (s), 1525 (s), 1469 (s), 1354 (s), 1229 (s), 1102 (s), 834 (s), 741 (s), 725 (s).
HRMS calculated for $C_{17}H_{14}NO_3^+$ $[M+H]^+$ 280.0968; found 280.0966.

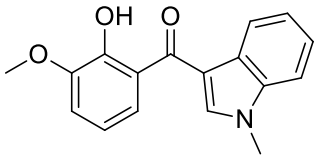
(2-Hydroxy-5-nitrophenyl)(1-methyl-1*H*-indol-3-yl)methanone (6i)



Following General Procedure **E1**, starting from commercially available 2-hydroxy-5-nitrobenzaldehyde and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/DCM 1:1) afford the title compound **6i** (32.9 mg, 0.111 mmol, 74% yield) as a yellow solid. **mp** 227-229 °C. **Rf** 0.44 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.97 (s, 1H, O<u>H</u>), 8.86 (d, *J* = 2.7 Hz, 1H, <u>H</u>$_{Ar}$), 8.35 (dd, *J* = 9.2, 2.7 Hz, 1H, <u>H</u>$_{Ar}$), 8.33-8.29 (m, 1H, <u>H</u>$_{Ar}$), 7.75 (s, 1H, C<u>H</u>-N), 7.47-7.37 (m, 3H, <u>H</u>$_{Ar}$), 7.14 (d, *J* = 9.2 Hz, 1H, <u>H</u>$_{Ar}$), 3.96 (s, 3H, NC<u>H</u>$_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.6, 167.6, 139.7, 137.8, 137.4, 129.7, 127.6, 127.3, 124.7, 123.7, 122.7, 120.4, 119.3, 114.2, 110.4, 34.3.
IR ν_{max} 1581 (m), 1522 (s), 1458 (m), 1341 (s), 1286 (s), 1224 (s), 1095 (m), 832 (s), 735 (s), 722 (s).
HRMS calculated for $C_{16}H_{13}N_2O_4^+$ $[M+H]^+$ 297.0870; found 297.0874.

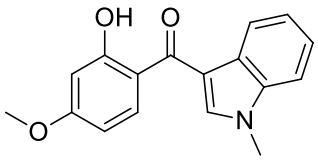
(2-Hydroxy-3-methoxyphenyl)(1-methyl-1*H*-indol-3-yl)methanone (6j)



Following General Procedure **E1**, starting from commercially available 2-hydroxy-3-methoxybenzaldehyde and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 7:3) afford the title compound **6j** (39.6 mg, 0.141 mmol, 94% yield) as a yellow solid. **mp** 134-136 °C. **Rf** 0.56 (Pentane/EtOAc 1:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.22 (bs, 1H, O<u>H</u>), 8.32-8.28 (m, 1H, <u>H</u>$_{Ar}$), 7.61 (s, 1H, C<u>H</u>-N), 7.42 (dd, *J* = 8.0, 1.4 Hz, 1H, <u>H</u>$_{Ar}$), 7.36-7.30 (m, 3H, <u>H</u>$_{Ar}$), 7.05 (dd, *J* = 8.0, 1.3 Hz, 1H, <u>H</u>$_{Ar}$), 6.86 (t, *J* = 8.0 Hz, 1H, <u>H</u>$_{Ar}$), 3.92 (s, 3H, OC<u>H</u>$_3$), 3.84 (s, 3H, NC<u>H</u>$_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 152.0, 148.9, 137.4, 137.3, 127.3, 123.9, 122.9, 122.8, 122.5, 121.6, 118.1, 115.6, 114.8, 109.9, 56.3, 33.7.
IR ν_{max} 2933 (w), 1563 (s), 1524 (s), 1461 (s), 1350 (s), 1239 (s), 1088 (m), 931 (m), 743 (s).
HRMS calculated for $C_{17}H_{16}NO_3^+$ $[M+H]^+$ 282.1125; found 282.1132.

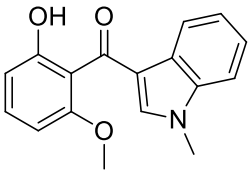
(2-Hydroxy-4-methoxyphenyl)(1-methyl-1*H*-indol-3-yl)methanone (6k)



Following General Procedure **E1**, starting from commercially available 2-hydroxy-4-methoxybenzaldehyde and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 4:1) afford the title compound **6k** (39.2 mg, 0.140 mmol, 93% yield) as a yellow solid. **mp** 133-135 °C. **Rf** 0.40 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.88 (s, 1H, O<u>H</u>), 8.24-8.20 (m, 1H, <u>H</u>$_{Ar}$), 7.79 (d, *J* = 8.8 Hz, 1H, <u>H</u>$_{Ar}$), 7.58 (s, 1H, C<u>H</u>-N), 7.38-7.29 (m, 3H, <u>H</u>$_{Ar}$), 6.52 (d, *J* = 2.5 Hz, 1H, <u>H</u>$_{Ar}$), 6.45 (dd, *J* = 8.9, 2.5 Hz, 1H, <u>H</u>$_{Ar}$), 3.85 (s, 6H, OC<u>H</u>$_3$+ NC<u>H</u>$_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.7, 165.2, 165.1, 137.3, 135.8, 133.3, 127.3, 123.6, 122.5, 122.3, 114.9, 114.7, 109.9, 106.8, 101.3, 55.6, 33.6.
IR ν_{max} 2920 (w), 2839 (w), 1618 (s), 1560 (s), 1505 (s), 1459 (s), 1369 (s), 1340 (s), 1299 (s), 1267 (s), 1241 (s), 1221 (s), 1145 (s), 1107 (s), 852 (s), 751 (s).
HRMS calculated for $C_{17}H_{16}NO_3^+$ $[M+H]^+$ 282.1125; found 282.1127.

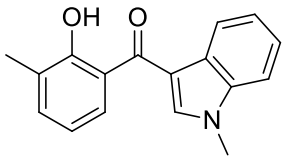
(2-Hydroxy-6-methoxyphenyl)(1-methyl-1*H*-indol-3-yl)methanone (6l)



Following General Procedure **E1** (30 minutes), starting from 2-hydroxy-6-methoxybenzaldehyde **13** and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 7:3) afford the title compound **6l** (36.1 mg, 0.128 mmol, 86% yield) as a off-white solid. **mp** 250-252 °C. **Rf** 0.54 (Pentane/EtOAc 1:1).

^{1}H NMR (400 MHz, DMSO-d6) δ 9.49 (s, 1H, O<u>H</u>), 8.09 (d, *J* = 7.6 Hz, 1H, <u>H</u>$_{Ar}$), 7.60 (s, 1H, C<u>H</u>-N), 7.52 (d, *J* = 8.0 Hz, 1H, <u>H</u>$_{Ar}$), 7.26 (dtd, *J* = 21.1, 7.2, 1.2 Hz, 2H, <u>H</u>$_{Ar}$), 7.18 (t, *J* = 8.3 Hz, 1H, <u>H</u>$_{Ar}$), 6.55 (dd, *J* = 8.2, 4.3 Hz, 2H, <u>H</u>$_{Ar}$), 3.80 (s, 3H, NC<u>H</u>$_3$), 3.63 (s, 3H, OC<u>H</u>$_3$).
^{13}C NMR (101 MHz, DMSO-d6) δ 188.0, 157.2, 154.9, 138.9, 137.5, 129.6, 125.7, 122.8, 122.1, 121.2, 188.6, 116.9, 110.7, 108.7, 102.1, 55.4, 33.0.
IR ν_{max} 3150 (br), 1596 (s), 1573 (s), 1527 (s), 1459 (s), 1371 (s), 1227 (s), 1078 (s), 876 (s), 757 (s), 741 (s), 712 (s).
HRMS calculated for $C_{17}H_{16}NO_3^+$ $[M+H]^+$ 282.1125; found 282.1124.

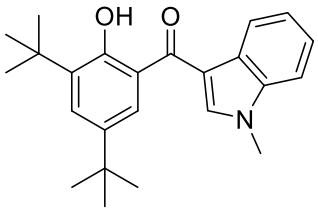
(2-Hydroxy-3-methylphenyl)(1-methyl-1*H*-indol-3-yl)methanone (6m)



Following General Procedure **E1**, starting from commercially available 2-hydroxy-3-methylbenzaldehyde and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 85:15) afforded the title compound **6m** (34.9 mg, 0.132 mmol, 88% yield) as a yellow solid. **mp** 110-112 °C. **Rf** 0.45 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.31 (bs, 1H, O<u>H</u>), 8.31-8.28 (m, 1H, <u>H</u>$_{Ar}$), 7.70 (dd, *J* = 7.9, 1.2 Hz, 1H, <u>H</u>$_{Ar}$), 7.61 (s, 1H, C<u>H</u>-N), 7.39-7.32 (m, 4H, <u>H</u>$_{Ar}$), 6.83 (t, *J* = 7.6 Hz, 1H, <u>H</u>$_{Ar}$), 3.86 (s, 3H, NC<u>H</u>$_3$), 2.34 (s, 3H, C<u>H</u>$_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 194.0, 160.4, 137.4, 136.9, 135.6, 129.2, 127.4, 127.1, 123.8, 122.7, 122.5, 120.7, 118.0, 114.9, 109.9, 33.7, 15.9.
IR ν_{max} 2906 (w), 1599 (m), 1562 (m), 1517 (s), 1471 (m), 1425 (m), 1339 (s), 1238 (s), 1078 (s), 741 (s).
HRMS calculated for $C_{17}H_{16}NO_2^+$ $[M+H]^+$ 266.1176; found 266.1179.

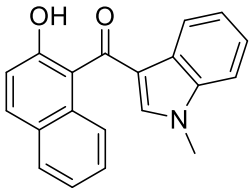
(3,5-Di-tert-butyl-2-hydroxyphenyl)(1-methyl-1*H*-indol-3-yl)methanone (6n)



Following General Procedure **E1** (60 minutes), starting from commercially available 3,5-di-tert-butyl-2-hydroxybenzaldehyde and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/Et_2O 9:1) afforded the title compound **6n** (30.8 mg, 0.085 mmol, 85% yield) as a yellow solid. **mp** 210-212 °C. **Rf** 0.78 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.49 (s, 1H, O<u>H</u>), 8.24 (dd, *J* = 6.8, 1.4 Hz, 1H, <u>H</u>$_{Ar}$), 7.73 (d, *J* = 2.5 Hz, 1H, <u>H</u>$_{Ar}$), 7.61 (s, 1H, C<u>H</u>-N), 7.56 (d, *J* = 2.4 Hz, 1H, <u>H</u>$_{Ar}$), 7.42-7.31 (m, 3H, <u>H</u>$_{Ar}$), 3.89 (s, 3H, NC<u>H</u>$_3$), 1.50 (s, 9H, C(C<u>H</u>$_3$)$_3$), 1.32 (s, 9H, C(C<u>H</u>$_3$)$_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 194.8, 159.0, 139.5, 137.4, 137.3, 136.5, 129.3, 127.3, 126.2, 123.6, 122.5 (2C), 120.5, 115.5, 109.8, 35.2, 34.3, 33.6, 31.5, 29.5.
IR ν_{max} 2947 (m), 2866 (m), 1567 (s), 1518 (s), 1459 (s), 1429 (s), 1361 (s), 1217 (s), 1125 (s), 1078 (s), 799 (s), 750 (s), 731 (s).
HRMS calculated for $C_{24}H_{30}NO_2^+$ $[M+H]^+$ 364.2271; found 364.2280.

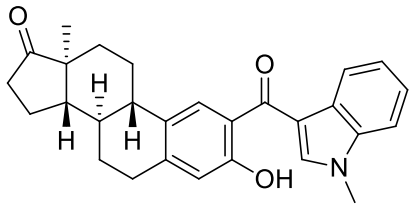
(2-Hydroxynaphthalen-1-yl)(1-methyl-1*H*-indol-3-yl)methanone (6o)



Following General Procedure **E1**, starting from commercially available 2-hydroxy-1-naphthaldehyde and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 7:3) afforded the title compound **6o** (44.1 mg, 0.136 mmol, 91% yield) as a white solid. **mp** 261-263 °C. **Rf** 0.65 (Pentane/EtOAc 1:1).

^{1}H NMR (400 MHz, DMSO-d6) δ 9.84 (s, 1H, O<u>H</u>), 8.21 (bs, 1H, <u>H</u>$_{Ar}$), 7.87 (t, *J* = 8.1 Hz, 2H, <u>H</u>$_{Ar}$), 7.59 (s, 1H, C<u>H</u>-N), 7.54 (d, *J* = 7.4 Hz, 1H, <u>H</u>$_{Ar}$), 7.45 (d, *J* = 8.2 Hz, 1H, <u>H</u>$_{Ar}$), 7.36-7.26 (m, 5H, <u>H</u>$_{Ar}$), 3.76 (s, 3H, NC<u>H</u>$_3$).
^{13}C NMR (101 MHz, DMSO-d6) δ 190.4, 151.3, 139.6, 137.6, 131.9, 129.7, 128.0, 127.5, 126.6, 125.8, 123.6, 123.0, 122.8, 122.3, 122.0, 121.3, 118.5, 117.0, 110.8, 33.0.
IR ν_{max} 3109 (br), 1594 (s), 1524 (s), 1459 (m), 1368 (m), 1347 (m), 1242 (m), 1212 (s), 1090 (m), 819 (m), 754 (s).
HRMS calculated for $C_{20}H_{15}NNaO_2^+$ $[M+Na]^+$ 324.0995; found 324.0991.

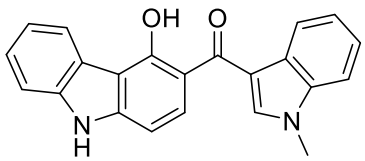
(8*R*,9*S*,13*S*,14*S*)-3-Hydroxy-13-methyl-2-(1-methyl-1*H*-indole-3-carbonyl)-7,8,9,11,12,13,15,16-octahydro-6*H*-cyclopenta[*a*]phenanthren-17(14*H*)-one (6p)



Following General Procedure **E1**, starting from 2-formyl estrone **13** and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 3:2) afforded the title compound **6p** (63.0 mg, 0.147 mmol, 98% yield) as a yellow solid. **mp** 135-137 °C. **Rf** 0.62 (Pentane/EtOAc 1:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.85 (bs, 1H, O$\underline{H}$), 8.23 (d, *J* = 7.2 Hz, 1H, $\underline{H}_{Ar}$), 7.76 (s, 1H, $\underline{H}_{Ar}$), 7.61 (s, 1H, C$\underline{H}$-N), 7.40-7.30 (m, 3H, $\underline{H}_{Ar}$), 6.78 (s, 1H, $\underline{H}_{Ar}$), 3.90 (s, 3H, NC$\underline{H}_3$), 3.00-2.92 (m, 2H, $\underline{H}_{aliph}$), 2.52 (dd, *J* = 18.6, 8.7 Hz, 1H, $\underline{H}_{aliph}$), 2.32-2.22 (m, 2H, $\underline{H}_{aliph}$), 2.20-2.00 (m, 3H, $\underline{H}_{aliph}$), 1.96-1.89 (m, 1H, $\underline{H}_{aliph}$), 1.70-1.40 (m, 6H, $\underline{H}_{aliph}$), 0.93 (s, 3H, C$\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 220.8, 193.6, 159.8, 144.8, 137.5, 136.2, 130.4, 128.6, 127.3, 123.9, 122.7, 122.5, 119.5, 117.6, 115.1, 109.9, 50.5, 48.1, 43.9, 38.4, 36.0, 33.9, 31.6, 29.9, 26.4, 26.1, 21.7, 14.0.
IR ν_{max} 2927 (m), 2852 (w), 1736 (s), 1566 (m), 1521 (s), 1463 (s), 1363 (s), 1221 (s), 847 (s), 737 (s).
HRMS calculated for $C_{28}H_{29}NNaO_3^+$ $[M+Na]^+$ 450.2040; found 450.2041.

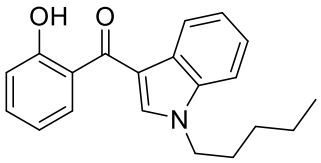
(4-Hydroxy-9*H*-carbazol-3-yl)(1-methyl-1*H*-indol-3-yl)methanone (6q)



Following General Procedure **E1**, starting from 4-hydroxy-9*H*-carbazole-3-carbaldehyde **4q** and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 1:1) afford the title compound **6q** (45.9 mg, 0.135 mmol, 90% yield) as a ochre solid. **mp** 238-240 °C. **Rf** 0.36 (Pentane/EtOAc 1:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 13.84 (s, 1H, O$\underline{H}$), 8.46 (d, *J* = 7.7 Hz, 1H, $\underline{H}_{Ar}$), 8.28-8.23 (m, 2H, N$\underline{H}$ + $\underline{H}_{Ar}$), 7.93 (d, *J* = 8.6 Hz, 1H, $\underline{H}_{Ar}$), 7.65 (s, 1H, C$\underline{H}$-N), 7.46-7.29 (m, 6H, $\underline{H}_{Ar}$), 6.92 (d, *J* = 8.6 Hz, 1H, $\underline{H}_{Ar}$), 3.89 (s, 3H, NC$\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 161.4, 144.3, 138.8, 137.4, 135.7, 130.2, 127.5, 125.5, 123.6, 123.5, 123.4, 122.5, 122.4, 121.0, 115.3, 113.2, 112.1, 110.4, 109.9, 101.9, 33.7.
IR ν_{max} 3672 (w), 2982 (s), 2902 (s), 1590 (m), 1524 (m), 1459 (m), 1393 (s), 1382 (s), 1368 (s), 1263 (s), 1240 (s), 1230 (s), 1075 (s), 1045 (s), 740 (s), 720 (s).
HRMS calculated for $C_{22}H_{17}N_2O_2^+$ $[M+H]^+$ 341.1285; found 341.1288.

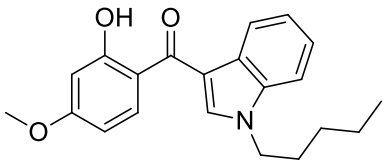
(2-Hydroxyphenyl)(1-pentyl-1*H*-indol-3-yl)methanone (6r)



Following General Procedure **E1**, starting from commercially available salicylaldehyde and Pe-indoleBX **5b**, a purification by column chromatography on silica gel (Pentane/EtOAc 19:1) afford the title compound **6r** (42.5 mg, 0.138 mmol, 92% yield) as a yellow solid. **mp** 76-78 °C. **Rf** 0.85 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.07 (bs, 1H, O$\underline{H}$), 8.34-8.29 (m, 1H, $\underline{H}_{Ar}$), 7.86 (dd, *J* = 7.9, 1.6 Hz, 1H, $\underline{H}_{Ar}$), 7.68 (s, 1H, C$\underline{H}$-N), 7.48 (ddd, *J* = 8.8, 7.3, 1.7 Hz, 1H, $\underline{H}_{Ar}$), 7.44-7.40 (m, 1H, $\underline{H}_{Ar}$), 7.38-7.32 (m, 2H, $\underline{H}_{Ar}$), 7.07 (d, *J* = 8.3 Hz, 1H, $\underline{H}_{Ar}$), 6.94 (t, *J* = 7.6 Hz, 1H, $\underline{H}_{Ar}$), 4.19 (t, *J* = 7.2 Hz, 2H, NC$\underline{H}_2$), 1.90 (p, *J* = 7.3 Hz, 2H, $\underline{H}_{aliph}$), 1.43-1.30 (m, 4H, $\underline{H}_{aliph}$), 0.91 (t, *J* = 6.9 Hz, 3H, C$\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 193.6, 162.0, 136.8, 136.1, 134.6, 131.5, 127.5, 123.8, 122.8, 122.6, 121.5, 118.7, 118.2, 114.7, 110.2, 47.4, 29.7, 29.1, 22.3, 14.0.
IR ν_{max} 2927 (m), 2859 (m), 1564 (m), 1517 (s), 1482 (s), 1463 (s), 1388 (s), 1347 (m), 1216 (m), 1194 (s), 1131 (s), 887 (m), 765 (s), 736 (s), 671 (s).
HRMS calculated for $C_{20}H_{22}NO_2^+$ $[M+H]^+$ 308.1645; found 308.1648.

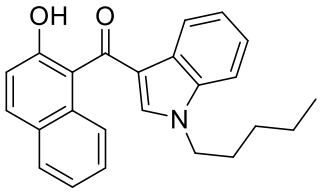
(2-Hydroxy-4-methoxyphenyl)(1-pentyl-1*H*-indol-3-yl)methanone (6s)



Following General Procedure **E1**, starting from commercially available 2-hydroxy-4-methoxybenzaldehyde and Pe-indoleBX **5b**, a purification by column chromatography on silica gel (Pentane/EtOAc 9:1) afforded the title compound **6s** (45.0 mg, 0.133 mmol, 89% yield) as a yellow solid. **mp** 87-89 °C. **Rf** 0.75 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.85 (bs, 1H, O$\underline{H}$), 8.25-8.21 (m, 1H, $\underline{H}_{Ar}$), 7.80 (d, *J* = 8.8 Hz, 1H, $\underline{H}_{Ar}$), 7.65 (s, 1H, C$\underline{H}$-N), 7.43-7.38 (m, 1H, $\underline{H}_{Ar}$), 7.35-7.28 (m, 2H, $\underline{H}_{Ar}$), 6.54 (d, *J* = 2.5 Hz, 1H, $\underline{H}_{Ar}$), 6.47 (dd, *J* = 8.8, 2.5 Hz, 1H, $\underline{H}_{Ar}$), 4.19 (t, *J* = 7.2 Hz, 2H, NC$\underline{H}_2$), 3.86 (s, 3H, OC$\underline{H}_3$), 1.90 (p, *J* = 7.4 Hz, 2H, $\underline{H}_{aliph}$), 1.42-1.30 (m, 4H, $\underline{H}_{aliph}$), 0.91 (t, *J* = 6.9 Hz, 3H, C$\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.8, 165.2, 165.1, 136.7, 134.9, 133.3, 127.5, 123.5, 122.4, 122.4, 115.0, 114.7, 110.1, 106.9, 101.3, 55.6, 47.3, 29.7, 29.1, 22.4, 14.0.
IR ν_{max} 2954 (m), 2927 (m), 2859 (m), 1625 (m), 1563 (s), 1517 (s), 1498 (s), 1461 (s), 1387 (s), 1267 (s), 1233 (s), 1165 (s), 1112 (s), 850 (s), 779 (s), 739 (s).
HRMS calculated for $C_{21}H_{24}NO_3^+$ $[M+H]^+$ 338.1751; found 338.1753.

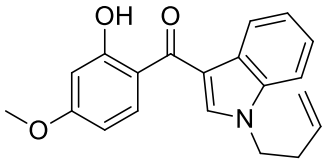
(2-Hydroxynaphthalen-1-yl)(1-pentyl-1*H*-indol-3-yl)methanone (6t)



Following General Procedure **E1**, starting from commercially available 2-hydroxy-1-naphthaldehyde and Pe-indoleBX **5b**, a purification by column chromatography on silica gel (Pentane/EtOAc 6:1) afforded the title compound **6t** (47.2 mg, 0.132 mmol, 88% yield) as an off-white solid. **mp** 154-156 °C. **Rf** 0.48 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (bs, 1H, O$\underline{H}$), 8.37-8.33 (m, 1H, $\underline{H}_{Ar}$), 7.95 (d, *J* = 8.5 Hz, 1H, $\underline{H}_{Ar}$), 7.89 (d, *J* = 8.9 Hz, 1H, $\underline{H}_{Ar}$), 7.78 (d, *J* = 8.1 Hz, 1H, $\underline{H}_{Ar}$), 7.41-7.20 (m, 7H, C$\underline{H}$-N + $\underline{H}_{Ar}$), 4.02 (t, *J* = 7.0 Hz, 2H, NC$\underline{H}_2$), 1.76 (p, *J* = 7.1 Hz, 2H), 1.33-1.17 (m, 4H), 0.86 (t, *J* = 7.1 Hz, 3H, C$\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.3, 157.4, 138.5, 137.0, 133.7, 132.7, 128.9, 128.4, 127.0, 126.3 (2C), 123.8, 123.7, 123.3, 122.9, 119.2, 117.9, 117.5, 110.4, 47.4, 29.7, 29.0, 22.4, 14.1.
IR ν_{max} 3265 (br), 2947 (m), 1588 (s), 1513 (s), 1462 (m), 1384 (s), 1177 (s), 1131 (s), 751 (s).
HRMS calculated for $C_{24}H_{24}NO_2^+$ $[M+H]^+$ 358.1802; found 358.1808.

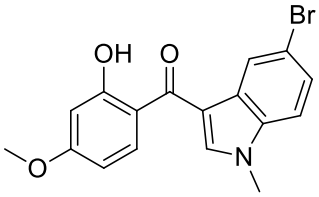
(1-(But-3-en-1-yl)-1*H*-indol-3-yl)(2-hydroxy-4-methoxyphenyl)methanone (6u)



Following General Procedure E1, but performing the reaction at 70 °C, starting from commercially available 2-hydroxy-4-methoxybenzaldehyde and butenyl-indoleBX **5c**, a purification by column chromatography on silica gel (Pentane/EtOAc 9:1) afford the title compound **6u** (43.4 mg, 0.135 mmol, 90% yield) as a yellow oil. **Rf** 0.56 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.83 (bs, 1H, O$\underline{H}$), 8.24-8.22 (m, 1H, $\underline{H}_{Ar}$), 7.79 (d, *J* = 8.8 Hz, 1H, $\underline{H}_{Ar}$), 7.64 (s, 1H, C$\underline{H}$-N), 7.43-7.40 (m, 1H, $\underline{H}_{Ar}$), 7.36-7.29 (m, 2H, $\underline{H}_{Ar}$), 6.54 (d, *J* = 2.5 Hz, 1H, $\underline{H}_{Ar}$), 6.47 (dd, *J* = 8.9, 2.5 Hz, 1H, $\underline{H}_{Ar}$), 5.80 (ddt, *J* = 17.1, 10.3, 6.9 Hz, 1H, $\underline{H}_{Ar}$), 5.13-5.06 (m, 2H, $\underline{H}_{Ar}$), 4.26 (t, *J* = 7.0 Hz, 2H, NC$\underline{H}_2$), 3.87 (s, 3H, OC$\underline{H}_3$), 2.65 (q, *J* = 7.0 Hz, 2H, NCH$_2$C$\underline{H}_2$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.8, 165.2, 165.2, 136.5, 135.0, 133.8, 133.3, 127.5, 123.6, 122.5, 118.5, 115.0, 114.8, 110.0, 106.9, 101.3, 55.6, 46.7, 34.2.
IR ν_{max} 2927 (w), 2852 (w), 1619 (s), 1582 (s), 1517 (s), 1461 (s), 1388 (s), 1365 (s), 1259 (s), 1231 (s), 1202 (s), 1160 (s), 1107 (s), 868 (s), 837 (s), 741 (s).
HRMS calculated for $C_{20}H_{20}NO_3^+$ $[M+H]^+$ 322.1438; found 322.1435.

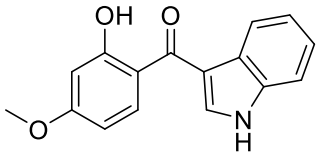
(5-Bromo-1-methyl-1*H*-indol-3-yl)(2-hydroxy-4-methoxyphenyl)methanone (6v)



Following General Procedure **E1**, starting from commercially available 2-hydroxy-4-methoxybenzaldehyde and Me-bromoindoleBX **5d**, a purification by column chromatography on silica gel (Pentane/EtOAc 4:1) afforded the title compound **6v** (46.5 mg, 0.129 mmol, 86% yield) as a yellow solid. **mp** 186-188 °C. **Rf** 0.53 (Pentane/EtOAc 1:1).

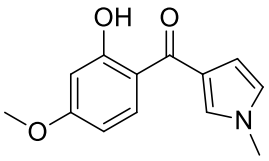
^{1}H NMR (400 MHz, $CDCl_3$) δ 12.75 (s, 1H, O<u>H</u>), 8.37 (d, *J* = 1.8 Hz, 1H, <u>H</u>$_{Ar}$), 7.73 (d, *J* = 8.8 Hz, 1H, <u>H</u>$_{Ar}$), 7.55 (s, 1H, C<u>H</u>-N), 7.39 (dd, *J* = 8.7, 1.9 Hz, 1H, <u>H</u>$_{Ar}$), 7.20 (d, *J* = 8.7 Hz, 1H, <u>H</u>$_{Ar}$), 6.50 (d, *J* = 2.5 Hz, 1H, <u>H</u>$_{Ar}$), 6.45 (dd, *J* = 8.8, 2.5 Hz, 1H, <u>H</u>$_{Ar}$), 3.86 (s, 3H, OC<u>H</u>$_3$), 3.85 (s, 3H, NC<u>H</u>$_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.2, 165.4, 165.4, 136.5, 136.1, 133.1, 129.0, 126.8, 125.1, 116.3, 114.7, 114.3, 111.4, 107.2, 101.5, 55.8, 34.0.
IR ν_{max} 2920 (m), 2852 (m), 1628 (m), 1574 (s), 1504 (s), 1460 (s), 1338 (s), 1291 (s), 1233 (s), 1137 (s), 1113 (s), 1020 (s), 796 (s), 764 (s).
HRMS calculated for $C_{17}H_{15}{}^{79}BrNO_3^+$ $[M+H]^+$ 360.0230; found 360.0232.

(2-Hydroxy-4-methoxyphenyl)(1*H*-indol-3-yl)methanone (6w)



Following General Procedure **E1**, but performing the reaction at 70 °C, starting from commercially available 2-hydroxy-4-methoxybenzaldehyde and NH-indoleBX **5e**, a purification by column chromatography on silica gel (Pentane/EtOAc 4:1) afforded the title compound **6w** (34.1 mg, 0.128 mmol, 85% yield) as a yellow solid. **mp** 175-177 °C. **Rf** 0.63 (Pentane/EtOAc 1:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 12.85 (bs, 1H, O<u>H</u>), 8.73 (s, 1H, N<u>H</u>), 8.24-8.15 (m, 1H, <u>H</u>$_{Ar}$), 7.81 (d, *J* = 8.9 Hz, 1H, <u>H</u>$_{Ar}$), 7.72 (d, *J* = 2.9 Hz, 1H, <u>H</u>$_{Ar}$), 7.48-7.40 (m, 1H, <u>H</u>$_{Ar}$), 7.34-7.28 (m, 2H, <u>H</u>$_{Ar}$), 6.54 (d, *J* = 2.4 Hz, 1H, <u>H</u>$_{Ar}$), 6.46 (dd, *J* = 8.9, 2.5 Hz, 1H, <u>H</u>$_{Ar}$), 3.87 (s, 3H, OC<u>H</u>$_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 193.4, 165.4 (2C), 136.2, 133.5, 131.3, 126.5, 124.1, 122.6, 122.2, 116.5, 114.9, 111.6, 107.1, 101.4, 55.7.
IR ν_{max} 3244 (br), 1615 (m), 1567 (s), 1500 (s), 1425 (s), 1358 (s), 1195 (s), 1109 (s), 871 (s), 835 (s), 741 (s).
HRMS calculated for $C_{16}H_{14}NO_3^+$ $[M+H]^+$ 268.0968; found 268.0980.

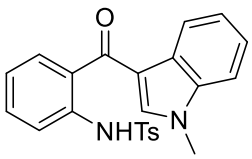
(2-Hydroxy-4-methoxyphenyl)(1-methyl-1*H*-pyrrol-3-yl)methanone (6x)



Following General Procedure **E1**, starting from commercially available 2-hydroxy-4-methoxybenzaldehyde and Me-pyrroleBX **5f**, a purification by column chromatography on silica gel (Pentane/EtOAc 4:1) afforded the title compound **6x** (30.3 mg, 0.131 mmol, 87% yield) as a pale yellow oil. **Rf** 0.31 (Pentane/EtOAc 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.99 (s, 1H, O<u>H</u>), 7.88 (d, *J* = 8.9 Hz, 1H, <u>H</u>$_{Ar}$), 7.23 (s, 1H, C<u>H</u>-N), 6.64 (t, *J* = 1.9 Hz, 2H, <u>H</u>$_{Ar}$), 6.48 (d, *J* = 2.5 Hz, 1H, <u>H</u>$_{Ar}$), 6.44 (dd, *J* = 8.9, 2.5 Hz, 1H, <u>H</u>$_{Ar}$), 3.84 (s, 3H, OC<u>H</u>$_3$), 3.72 (s, 3H, NC<u>H</u>$_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.7, 165.6, 165.2, 133.6, 127.7, 123.8, 123.2, 114.3, 111.2, 106.9, 101.2, 55.6, 36.8.
IR ν_{max} 2927 (w), 1608 (s), 1584 (s), 1524 (s), 1500 (s), 1443 (s), 1353 (s), 1236 (s), 1212 (s), 1149 (s), 1110 (s), 961 (s), 856 (s), 829 (s), 766 (s).
HRMS calculated for $C_{13}H_{14}NO_3^+$ $[M+H]^+$ 232.0968; found 232.0971.

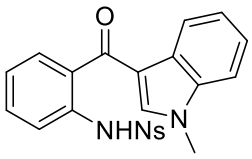
4-Methyl-*N*-(2-(1-methyl-1*H*-indole-3-carbonyl)phenyl)benzenesulfonamide (8a)



Following General Procedure **E2**, starting from *N*-(2-formylphenyl)4-methylbenzenesulfonamide **7a** and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 7:3) afforded the title compound **8a** (53.3 mg, 0.132 mmol, 88% yield) as a white solid. **mp** 75-77 °C. **Rf** 0.47 (Pentane/EtOAc 1:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61 (s, 1H, NHTs), 8.19 (d, *J* = 7.3 Hz, 1H, H_{Ar}), 7.72 (d, *J* = 8.2, 0.8 Hz, 2H, H_{Ar}), 7.53 (dd, *J* = 7.7, 1.5 Hz, 1H, H_{Ar}), 7.51-7.43 (m, 3H, H_{tolyl} + H_{Ar}), 7.38-7.31 (m, 3H, H_{Ar}), 7.15 (td, *J* = 7.6, 1.1 Hz, 1H, H_{Ar}), 7.09 (s, 1H, CH-N), 6.79 (d, *J* = 8.0 Hz, 2H, H_{tolyl}), 3.81 (s, 3H, NCH_3), 2.05 (s, 3H, CH_3).
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8, 143.1, 138.5, 137.4, 137.2, 136.2, 132.1, 130.6, 130.3, 129.2, 127.4, 127.0, 124.1, 124.0, 123.9, 123.1, 122.7, 115.8, 109.8, 33.7, 21.4.
IR ν_{max} 3216 (w), 2920 (w), 1595 (m), 1521 (s), 1487 (m), 1466 (s), 1396 (m), 1365 (s), 1334 (s), 1233 (s), 1159 (s), 1126 (m), 1092 (m), 1073 (m), 925 (m), 869 (s), 814 (m), 747 (s).
HRMS calculated for $C_{23}H_{20}N_2NaO_3S^+$ $[M+Na]^+$ 427.1087; found 427.1095.

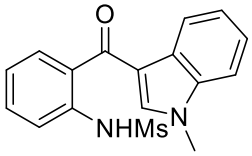
***N*-(2-(1-Methyl-1*H*-indole-3-carbonyl)phenyl)-4-nitrobenzenesulfonamide (8b)**



Following General Procedure **E2**, starting from *N*-(2-formylphenyl)4-nitrobenzenesulfonamide **7b** and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc/DCM 6:3:1) afforded the title compound **8b** (52.0 mg, 0.119 mmol, 80% yield) or (280 mg, 0.643 mmol, 80% yield) as a yellow solid. **mp** 212-214 °C. **Rf** 0.67 (Pentane/EtOAc 1:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.46 (s, 1H, NHNs), 8.17 (d, *J* = 7.1 Hz, 1H, H_{Ar}), 7.77 (d, *J* = 8.1 Hz, 1H, H_{Ar}), 7.68 (d, *J* = 8.9 Hz, 2H, H_{nosyl}), 7.60 (d, *J* = 8.9 Hz, 2H, H_{nosyl}), 7.58-7.51 (m, 2H, H_{Ar}), 7.43-7.34 (m, 2H, H_{Ar}), 7.33-7.27 (m, 2H, H_{Ar}), 6.97 (s, 1H, CH-N), 3.73 (s, 3H, NCH_3).
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.0, 149.2, 144.7, 138.3, 137.2, 135.5, 132.2, 132.1, 129.8, 128.7, 126.8, 126.6, 125.8, 124.6, 123.7, 123.5, 122.6, 115.6, 110.2, 33.6.
IR ν_{max} 3105 (w), 2933 (w), 1737 (w), 1608 (m), 1595 (m), 1527 (s), 1466 (m), 1404 (m), 1367 (s), 1349 (s), 1232 (m), 1164 (s), 874 (m), 856 (m), 763 (s), 757 (m), 739 (s), 712 (m).
HRMS calculated for $C_{22}H_{17}N_3NaO_5S^+$ $[M+Na]^+$ 458.0781; found 458.0780.

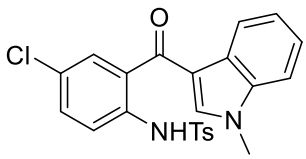
***N*-(2-(1-Methyl-1*H*-indole-3-carbonyl)phenyl)methanesulfonamide (8c)**



Following General Procedure **E2**, starting from *N*-(2-formylphenyl)4-methylsulfonamide **7c** and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 7:3) afforded the title compound **8c** (42.6 mg, 0.130 mmol, 86% yield) as a white solid. **mp** 132-134 °C. **Rf** 0.41 (Pentane/EtOAc 1:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H, NHMs), 8.37-8.31 (m, 1H, H_{Ar}), 7.79-7.75 (m, 2H, H_{Ar}), 7.55-7.51 (m, 2H, CH-N + H_{Ar}), 7.41-7.34 (m, 3H, H_{Ar}), 7.22 (t, *J* = 7.6 Hz, 1H, H_{Ar}), 3.87 (s, 3H, NCH_3), 2.97 (s, 3H, CH_3).
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.3, 138.6, 138.2, 137.8, 132.8, 131.6, 128.2, 127.2, 124.3, 123.5, 123.4, 122.7, 121.0, 116.0, 110.2, 40.1, 34.0.
IR ν_{max} 3216 (br), 2933 (w), 1608 (m), 1521 (s), 1488 (s), 1464 (s), 1363 (s), 1327 (s), 1233 (s), 1149 (s), 1127 (s), 1104 (m), 1074 (m), 969 (s), 924 (m), 868 (s), 744 (s).
HRMS calculated for $C_{17}H_{16}N_2NaO_3S^+$ $[M+Na]^+$ 351.0774; found 351.0770.

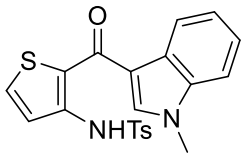
***N*-(4-Chloro-2-(1-methyl-1H-indole-3-carbonyl)phenyl)-4-methylbenzenesulfonamide (8d)**



Following General Procedure **E2**, starting from *N*-(4-chloro-2-formylphenyl)4-methylbenzenesulfonamide **7d** and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 7:3) afforded the title compound **8d** (59.9 mg, 0.136 mmol, 91% yield) as a white solid. **mp** 193-195 °C. **Rf** 0.68 (Pentane/EtOAc 1:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.36 (s, 1H, NHTs), 8.21-8.18 (m, 1H, H_{Ar}), 7.68 (d, *J* = 8.7 Hz, 1H, H_{Ar}), 7.50-7.46 (m, 3H, H_{tolyl} + H_{Ar}), 7.43 (dd, *J* = 8.7, 2.4 Hz, 1H, H_{Ar}), 7.40-7.33 (m, 3H, H_{Ar}), 7.08 (s, 1H, CH-N), 6.79 (d, *J* = 8.1 Hz, 2H, H_{tolyl}), 3.83 (s, 3H, NCH_3), 2.05 (s, 3H, CH_3).
^{13}C NMR (101 MHz, $CDCl_3$) δ 189.0, 143.3, 138.4, 137.5, 136.0, 135.6, 131.9, 131.8, 130.0, 129.8, 129.3, 127.4, 126.9, 125.8, 124.3, 123.5, 122.7, 115.5, 109.9, 33.9, 21.4.
IR ν_{max} 3228 (m), 1608 (m), 1594 (m), 1523 (s), 1469 (m), 1396 (m), 1385 (m), 1362 (s), 1328 (s), 1233 (m), 1160 (s), 1129 (m), 1090 (s), 878 (s), 814 (s), 750 (s), 715 (s).
HRMS calculated for $C_{23}H_{19}ClN_2NaO_3S^+$ $[M+Na]^+$ 461.0697; found 461.0701.

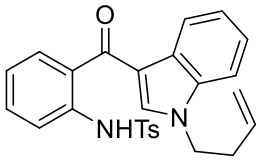
4-Methyl-N-(2-(1-methyl-1H-indole-3-carbonyl)thiophen-3-yl)benzenesulfonamide (8e)



Following General Procedure **E2**, starting from *N*-(2-formylthiophen-3-yl)-4-methylbenzenesulfonamide **7e** and Me-indoleBX **5a**, a purification by column chromatography on silica gel (Pentane/EtOAc 3:2) afforded the title compound **8e** (55.5 mg, 0.135 mmol, 90% yield) as a yellow solid. **mp** 158-160 °C. **Rf** 0.50 (Pentane/EtOAc 1:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.32 (s, 1H, NHTs), 8.36 (d, *J* = 5.9 Hz, 1H, H_{Ar}), 7.87 (s, 1H, CH-N), 7.78 (d, *J* = 7.8 Hz, 2H, H_{tolyl}), 7.47 (d, *J* = 5.4 Hz, 1H, H_{Ar}), 7.38 (d, *J* = 5.4 Hz, 1H, H_{Ar}), 7.34-7.29 (m, 3H, H_{Ar}), 7.20 (d, *J* = 7.8 Hz, 2H, H_{tolyl}), 3.84 (s, 3H, NCH_3), 2.32 (s, 3H, CH_3).
^{13}C NMR (101 MHz, $CDCl_3$) δ 182.9, 143.9, 137.3, 136.9, 135.0, 130.8, 129.8, 127.4, 127.2, 124.0, 122.9, 122.7, 121.3, 119.2, 115.8, 109.9, 33.8, 21.6. One aromatic C is not resolved.
IR ν_{max} 3117 (w), 3087 (w), 1554 (s), 1515 (s), 1463 (s), 1399 (s), 1370 (s), 1344 (s), 1227 (s), 1152 (s), 1087 (s), 862 (s), 815 (s), 748 (s).
HRMS calculated for $C_{21}H_{19}N_2O_3S_2^+$ $[M+H]^+$ 411.0832; found 411.0832.

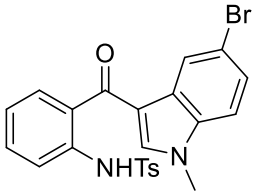
***N*-(2-(1-(But-3-en-1-yl)-1*H*-indole-3-carbonyl)phenyl)-4-methylbenzenesulfonamide (8f)**



Following General Procedure **E2**, starting from *N*-(2-formylphenyl)4-methylbenzenesulfonamide **7a** and butenyl-indoleBX **5d**, a purification by column chromatography on silica gel (Pentane/EtOAc 7:3) afforded the title compound **8d** (52.7 mg, 0.119 mmol, 79% yield) as a pale yellow solid. **mp** 50-52 °C. **Rf** 0.80 (Pentane/EtOAc 1:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H, NHTs), 8.18 (d, *J* = 7.0 Hz, 1H, H_{Ar}), 7.73 (d, *J* = 8.2 Hz, 1H, H_{Ar}), 7.57-7.53 (m, 3H, H_{tolyl} + H_{Ar}), 7.46 (td, *J* = 8.1, 1.5 Hz, 1H, H_{Ar}), 7.41-7.30 (m, 3H, H_{Ar}), 7.21 (s, 1H, CH-N), 7.14 (td, *J* = 7.6, 1.1 Hz, 1H, H_{Ar}), 6.87 (d, *J* = 8.0 Hz, 2H, H_{tolyl}), 5.76 (ddt, *J* = 17.1, 10.3, 6.9 Hz, 1H, $CH=CH_2$), 5.15-5.05 (m, 2H, $CH=CH_2$), 4.19 (t, *J* = 7.1 Hz, 2H, NCH_2), 2.60 (q, *J* = 7.0 Hz, 2H, NCH_2CH_2), 2.08 (s, 3H, CH_3).
^{13}C NMR (101 MHz, $CDCl_3$) δ 191.1, 143.3, 137.6, 137.6, 136.7, 136.5, 133.7, 132.3, 130.9, 129.8, 129.4, 127.5, 127.3, 124.1, 123.9, 123.3, 123.2, 123.0, 118.8, 116.0, 110.1, 46.8, 34.3, 21.5.
IR ν_{max} 3672 (w), 3222 (br), 2976 (m), 2914 (m), 1607 (m), 1599 (m), 1520 (s), 1486 (m), 1466 (m), 1394 (s), 1377 (s), 1335 (m), 1158 (s), 1090 (s), 1048 (m), 922 (m), 868 (s), 735 (s).
HRMS calculated for $C_{26}H_{25}N_2O_3S^+$ $[M+H]^+$ 445.1580; found 445.1576.

***N*-(2-(5-Bromo-1-methyl-1*H*-indole-3-carbonyl)phenyl)-4-methylbenzenesulfonamide (8g)**

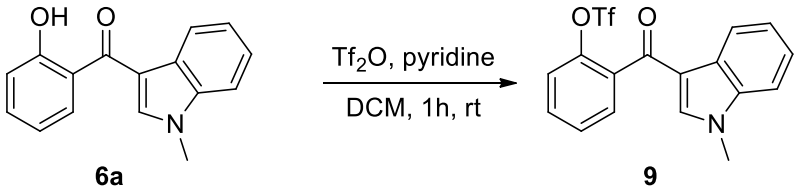


Following General Procedure **E2**, starting from *N*-(2-formylphenyl)4-methylbenzenesulfonamide **7a** and Me-bromoindoleBX **5b**, a purification by column chromatography on silica gel (Pentane/EtOAc 1:1) afforded the title compound **8e** (59.3 mg, 0.123 mmol, 82% yield) as an off-white solid. **mp** 186-188 °C. **Rf** 0.27 (Pentane/EtOAc 1:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55 (s, 1H, NHTs), 8.30 (d, *J* = 1.6 Hz, 1H, H_{Ar}), 7.72 (dd, *J* = 8.2, 0.8 Hz, 1H, H_{Ar}), 7.53-7.43 (m, 5H, H_{tolyl} + H_{Ar}), 7.22 (d, *J* = 8.5 Hz, 1H, H_{Ar}), 7.16 (td, *J* = 7.6, 1.1 Hz, 1H, H_{Ar}), 7.12 (s, 1H, CH-N), 6.85 (d, *J* = 8.0 Hz, 2H, H_{tolyl}), 3.80 (s, 3H, NCH_3), 2.07 (s, 3H, CH_3).
^{13}C NMR (101 MHz, $CDCl_3$) δ 190.6, 143.2, 138.8, 137.3, 136.3, 136.1, 132.4, 130.5, 129.8, 129.3, 128.5, 127.4, 127.1, 125.3, 124.1, 124.0, 116.9, 115.3, 111.3, 33.9, 21.4.
IR ν_{max} 3222 (br), 2933 (m), 1607 (m), 1596 (s), 1525 (s), 1486 (m), 1460 (s), 1450 (m), 1390 (m), 1366 (s), 1332 (s), 1232 (s), 1163 (s), 1090 (m), 877 (m), 803 (s), 763 (s), 719 (s).
HRMS calculated for $C_{23}H_{20}{}^{79}BrN_2O_3S^+$ $[M+H]^+$ 483.0373; found 483.0372.

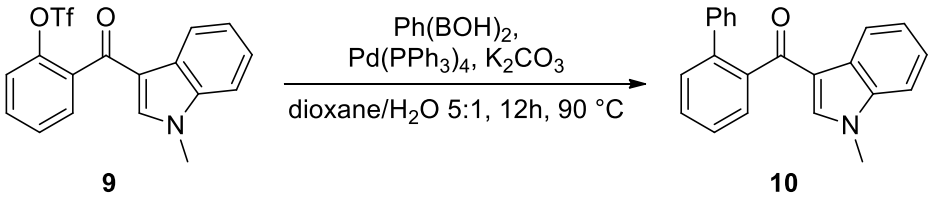
6. Product modifications

2-(1-Methyl-1*H*-indole-3-carbonyl)phenyl trifluoromethanesulfonate (9)



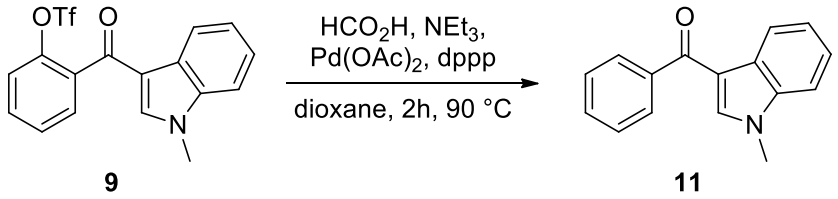
6a (126 mg, 0.500 mmol, 1.00 equiv.) and pyridine (80 µL, 1.0 mmol, 2.0 equiv.) were solubilized in DCM (2.5 mL). Triflic anhydride (100 µL, 0.600 mmol, 1.20 equiv.) was added at 0 °C. The mixture was stirred 1 h at rt and then quenched with H_2O. The layers were separated and the aqueous layer was extracted three times with DCM (10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. A purification by column chromatography on silica gel (Pentane/EtOAc 7:3) afford the title compound **9** (192 mg, 0.500 mmol, 100% yield) as a white solid. **mp** 148-150 °C. **Rf** 0.66 (Pentane/EtOAc 1:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40-8.33 (m, 1H, $\underline{H}_{Ar}$), 7.64 (dd, *J* = 7.5, 1.8 Hz, 1H, $\underline{H}_{Ar}$), 7.61-7.55 (m, 1H, $\underline{H}_{Ar}$), 7.50-7.45 (m, 1H, $\underline{H}_{Ar}$), 7.42 (d, *J* = 8.3 Hz, 1H, $\underline{H}_{Ar}$), 7.38-7.33 (m, 4H, C$\underline{H}$-N + $\underline{H}_{Ar}$), 3.83 (s, 3H, NC$\underline{H}_3$). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -73.6. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 185.7, 146.5, 138.7, 137.9, 135.0, 131.6, 130.6, 128.2, 126.7, 124.1, 123.3, 122.8, 122.5, 118.6 (q, *J* = 320 Hz), 116.4, 109.9, 33.8. **IR** ν_{max} 1620 (s), 1525 (m), 1466 (m), 1422 (s), 1369 (m), 1237 (m), 1215 (s), 1206 (s), 1144 (s), 1096 (m), 1073 (m), 907 (s), 881 (m), 853 (s), 772 (s), 759 (s), 732 (m). **HRMS** calculated for $C_{17}H_{13}F_3NO_4S^+$ $[M+H]^+$ 384.0512; found 384.0507.

[1,1'-Biphenyl]-2-yl(1-methyl-1*H*-indol-3-yl)methanone (10)



9 (90.0 mg, 0.235 mmol, 1.00 equiv.), $PhB(OH)_2$ (29.0 mg, 0.238 mmol, 1.00 equiv.), K_2CO_3 (64.9 mg, 0.470 mmol, 2.00 equiv.) and $Pd(PPh_3)_4$ (8.1 mg, 7.0 µmol, 3 mol %) were solubilized in dioxane (1.0 mL)/ water (0.2 mL) previously degazed by bubbling N_2. The mixture was stirred 12 h at 90 °C and then quenched with H_2O. The layers were separated and the aqueous layer was extracted three times with EtOAc (10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. A purification by column chromatography on silica gel (Pentane/EtOAc 4:1) afforded the title compound **10** (65.2 mg, 0.209 mmol, 89% yield) as a white solid. **mp** 174-176 °C. **Rf** 0.80 (Pentane/EtOAc 1:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$), 7.57-7.48 (m, 3H, $\underline{H}_{Ar}$), 7.45-7.37 (m, 3H, $\underline{H}_{Ar}$), 7.33-7.13 (m, 7H, C$\underline{H}$-N + $\underline{H}_{Ar}$), 3.70 (s, 3H, NC$\underline{H}_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.5, 141.2, 140.7, 140.3, 138.6, 137.6, 130.4, 129.7, 128.9, 128.5, 128.4, 127.3, 127.0, 126.7, 123.5, 122.7 (2C), 117.2, 109.6, 33.5. **IR** ν_{max} 3105 (w), 3050 (w), 3031 (w), 1620 (s), 1524 (s), 1463 (m), 1369 (s), 1228 (s), 1124 (m), 1073 (m), 887 (m), 870 (m), 743 (s). **HRMS** calculated for $C_{22}H_{18}NO^+$ $[M+H]^+$ 312.1383; found 312.1386.

(1-Methyl-1*H*-indol-3-yl)(phenyl)methanone (11)

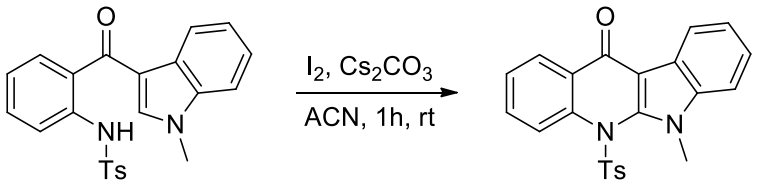


9 **11**

9 (38.3 mg, 0.100 mmol, 1.00 equiv.), $Pd(OAc)_2$ (2.2 mg, 10 µmol, 0.10 equiv) and dppp (12.4 mg, 30.0 µmol, 0.300 equiv) were solubilized in dioxane (1.0 mL) previously degazed by bubbling N_2. Formic acid (15 µL, 0.40 mmol, 4.0 equiv.) and triethylamine (55 µL, 0.40 mmol, 4.0 equiv.) were added to the solution. The mixture was stirred 2 h at 90 °C and then quenched with H_2O. The layers were separated and the aqueous layer was extracted three times with EtOAc (10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. A purification by column chromatography on silica gel (Pentane/EtOAc 4:1) afforded the title compound **11** (22.9 mg, 97.0 µmol, 97% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.48-8.41 (m, 1H, $\underline{H}_{Ar}$), 7.81 (d, *J* = 7.0 Hz, 2H, $\underline{H}_{Ar}$), 7.59-7.44 (m, 4H, $\underline{H}_{Ar}$), 7.39-7.32 (m, 3H, $\underline{H}_{Ar}$), 3.83 (s, 3H, $NC\underline{H}_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.0, 141.0, 138.0, 137.6, 131.2, 128.8, 128.4, 127.3, 123.7, 122.8, 122.8, 115.7, 109.7, 33.7. Spectra data matched with the values reported in literature.[17]

[17] Taylor, *J.* E.; *J*ones, M. D.; Williams, *J*. M. *J*.; Bull, S. D. *Org. Lett.* **2010**, *12*, 5740–5743.

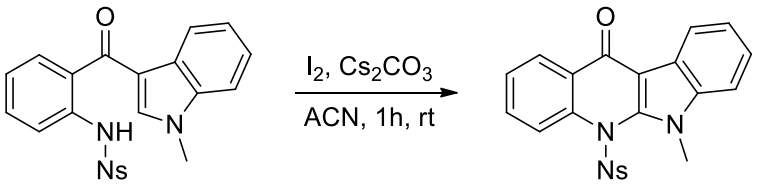
6-Methyl-5-((4-methylphenyl)sulfonyl)-5,6-dihydro-11*H*-indolo[2,3*b*]quinolin-11-one (12a)



8a **12a**

Following a reported procedure,[18] **8a** (36.4 mg, 90.0 µmol, 1.00 equiv.) and Cs_2CO_3 (58.7 mg, 180 µmol, 2.00 equiv.) were suspended in ACN (9 mL). I_2 (45.7 mg, 180 µmol, 2.00 equiv.) was added, the mixture was stirred 1 h at rt and then quenched with a saturated aqueous $Na_2S_2O_3$ solution. The layers were separated and the aqueous layer was extracted three times with EtOAc (10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. A purification by column chromatography on silica gel (Pentane/EtOAc 4:1) afforded the title compound **12a** (36.2 mg, 90.0 µmol, 100% yield) as a white solid. **mp** 161-163 °C. **Rf** 0.85 (Pentane/EtOAc 1:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 7.7 Hz, 1H, $\underline{H}_{Ar}$), 8.17 (d, *J* = 8.2 Hz, 1H, $\underline{H}_{Ar}$), 7.99 (dd, *J* = 7.8, 1.5 Hz, 1H, $\underline{H}_{Ar}$), 7.60 (td, *J* = 8.3, 7.9, 1.6 Hz, 1H, $\underline{H}_{Ar}$), 7.50 (d, *J* = 8.0 Hz, 1H, $\underline{H}_{Ar}$), 7.48-7.36 (m, 3H, $\underline{H}_{Ar}$), 6.91 (d, *J* = 8.2 Hz, 2H, $\underline{H}_{Ar}$), 6.81 (d, *J* = 8.4 Hz, 2H, $\underline{H}_{Ar}$), 4.10 (s, 3H, NC$\underline{H}_3$), 2.26 (s, 3H, C$\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 175.9, 146.0, 144.4, 139.2, 136.7, 131.1, 129.2, 128.9, 128.2, 127.6, 126.4, 125.8, 124.6, 123.2, 122.6, 121.9, 110.3, 109.2, 33.3, 21.8. One carbon atom is not resolved.
IR ν_{max} 3056 (w), 1640 (m), 1596 (w), 1524 (w), 1486 (m), 1461 (m), 1448 (w), 1417 (w), 1370 (m), 1263 (m), 1169 (m), 780 (m), 736 (s).
HRMS calculated for $C_{23}H_{19}N_2O_3S^+$ $[M+H]^+$ 403.1111; found 403.1112.

6-Methyl-5-((4-nitrophenyl)sulfonyl)-5,6-dihydro-11*H*-indolo[2,3*b*]quinolin-11-one (12b)

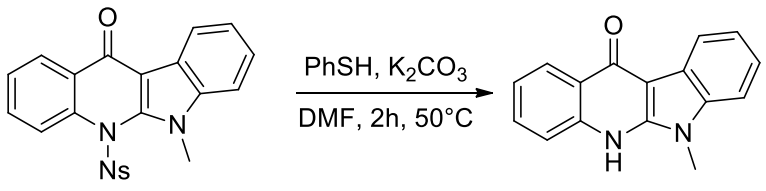


8b **12b**

Following the same procedure as described for **12a**, starting from **8b** (87.0 mg, 0.200 mmol, 1.00 equiv.), Cs_2CO_3 (130 mg, 0.400 mmol, 2.00 equiv.) and I_2 (101 mg, 0.400 mmol, 2.00 equiv.). A purification by column chromatography on silica gel (Pentane/EtOAc 4:1) afforded the title compound **12b** (77.0 mg, 0.178 mmol, 89% yield) as a yellow solid. **mp** 187-189 °C. **Rf** 0.89 (Pentane/EtOAc 1:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 7.8 Hz, 1H, $\underline{H}_{Ar}$), 8.17 (d, *J* = 7.9 Hz, 1H, $\underline{H}_{Ar}$), 8.00 (dd, *J* = 7.8, 1.6 Hz, 1H, $\underline{H}_{Ar}$), 7.99-7.95 (m, 2H, $\underline{H}_{Ar}$), 7.66 (td, *J* = 8.1, 1.6 Hz, 1H, $\underline{H}_{Ar}$), 7.54-7.45 (m, 3H, $\underline{H}_{Ar}$), 7.42 (td, *J* = 7.6, 1.3 Hz, 1H, $\underline{H}_{Ar}$), 7.15-7.09 (m, 2H, $\underline{H}_{Ar}$), 4.11 (s, 3H, NC$\underline{H}_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 175.4, 151.0, 143.3, 138.3, 137.2, 136.7, 131.6, 131.1, 129.6, 128.4, 126.9, 125.9, 125.2, 123.7, 123.6, 122.4, 122.1, 110.5, 109.3, 33.3.
IR ν_{max} 3105 (w), 3062 (w), 1646 (s), 1601 (m), 1532 (s), 1491 (s), 1461 (s), 1379 (m), 1350 (s), 1186 (s), 1171 (s), 784 (s), 738 (s).
HRMS calculated for $C_{22}H_{15}N_3NaO_5S^+$ $[M+Na]^+$ 456.0625; found 456.0630.

[18] Li, Y.-X.; Wang, H.-X.; Ali, S.; Xia, X.-F.; Liang, Y.-M. *Chem. Commun.* **2012**, *48*, 2343–2345.

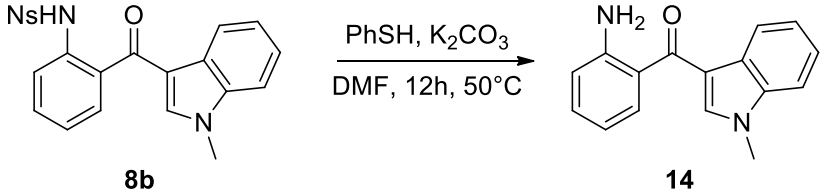
6-Methyl-5,6-dihydro-11*H*-indolo[2,3*b*]quinolin-11-one (13)



12b **13**

12b (65.0 mg, 0.150 mmol, 1.00 equiv.), K_2CO_3 (124 mg, 0.900 mmol, 6.00 equiv.) and benzenethiol (61 µL, 0.60 mmol, 4.0 equiv.) were solubilized in DMF (1.5 mL). The mixture was stirred 2 h at 50 °C and then filtered over Celite with MeOH (20 mL). A purification by column chromatography on silica gel (DCM 100% to DCM/MeOH 4:1) afforded the title compound **13** (32.7 mg, 0.132 mmol, 88% yield) as a white solid. **mp** > 350 °C. **Rf** 0.34 (DCM/MeOH 19:1).
^{1}H NMR (400 MHz, DMSO-d6) δ 12.33 (s, 1H, NH), 8.28 (d, *J* = 7.3 Hz, 1H, H_{Ar}), 8.21 (d, *J* = 7.4 Hz, 1H, H_{Ar}), 7.82 (d, *J* = 8.2 Hz, 1H, H_{Ar}), 7.66 (t, *J* = 7.0 Hz, 1H, H_{Ar}), 7.53 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.37-7.28 (m, 2H, H_{Ar}), 7.24 (t, *J* = 7.2 Hz, 1H, H_{Ar}), 3.95 (s, 3H, NCH_3).
^{13}C NMR (101 MHz, DMSO-d6) δ 172.0, 145.9, 138.5, 136.2, 130.8, 125.3, 123.6, 123.3, 122.6, 121.7, 121.2, 120.0, 117.7, 109.1, 101.2, 29.3.
IR ν_{max} 2994 (br), 1639 (s), 1583 (s), 1535 (s), 1482 (s), 1465 (s), 740 (s).
HRMS calculated for $C_{16}H_{13}N_2O^+$ $[M+H]^+$ 249.1022; found 249.1024.

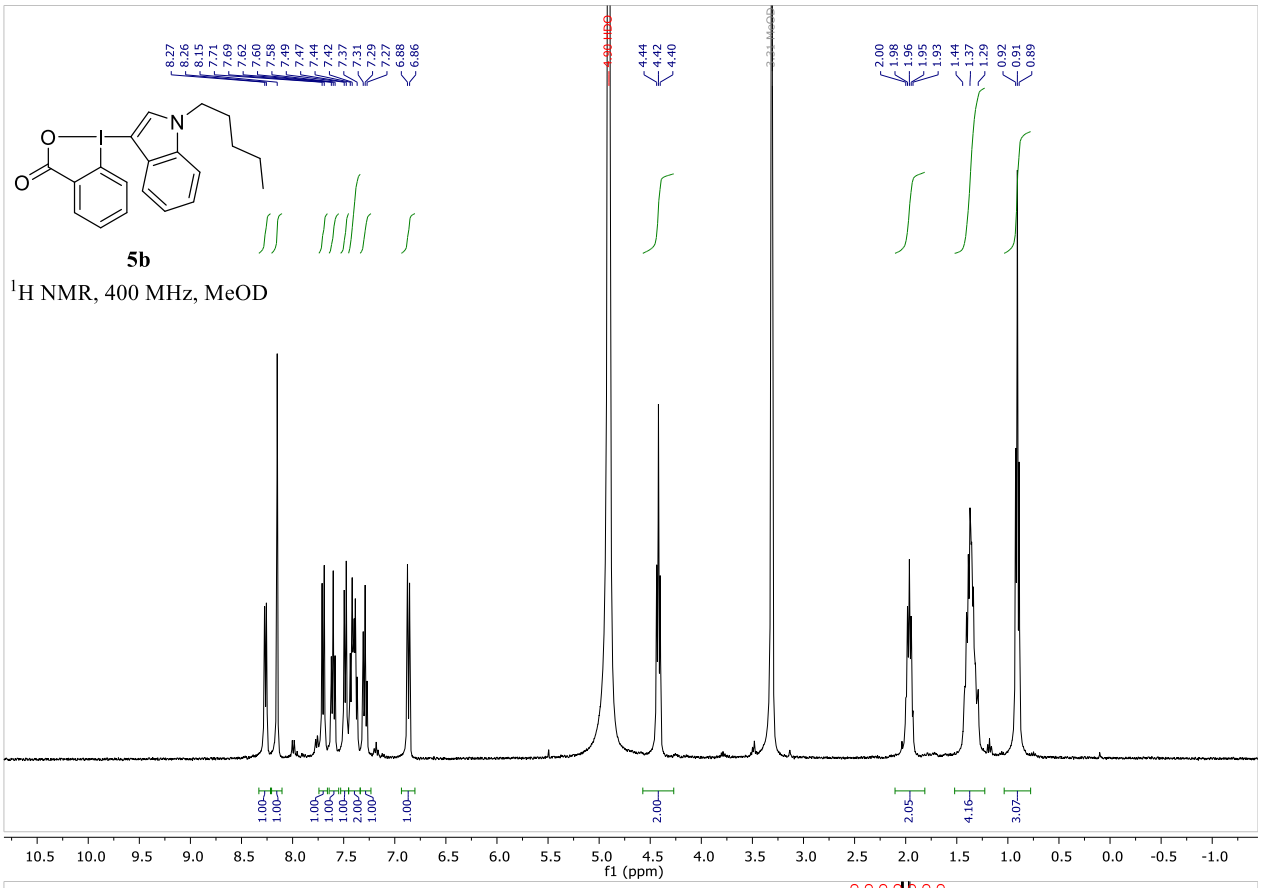
(2-Aminophenyl)(1-methyl-1*H*-indol-3-yl)methanone (14)



8b **14**

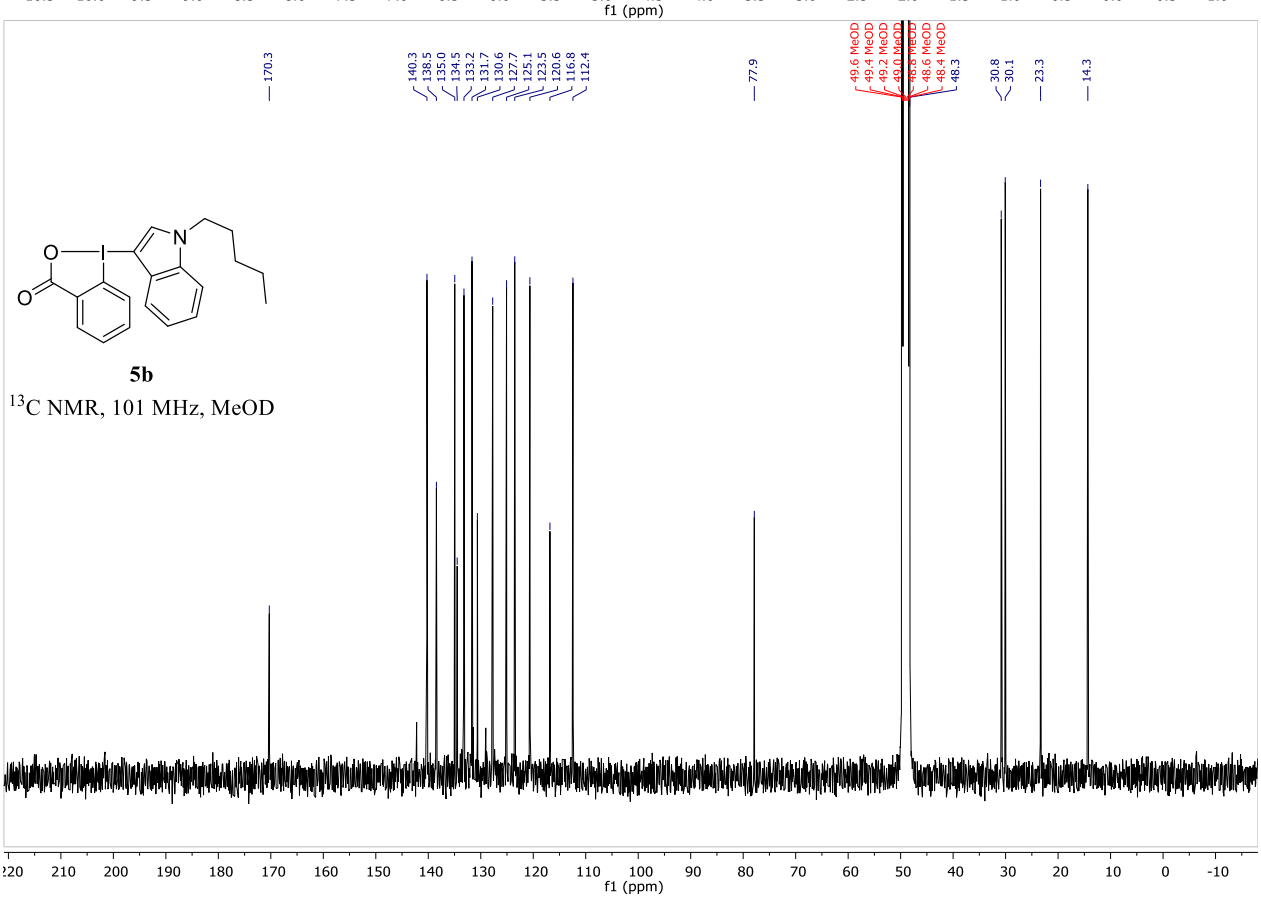
8b (87.0 mg, 0.200 mmol, 1.00 equiv.), K_2CO_3 (166 mg, 1.20 mmol, 6.00 equiv.) and benzenethiol (82 µL, 0.80 mmol, 4.00 equiv.) were solubilized in DMF (2 mL). The mixture was stirred overnight at 50 °C. The mixture was diluted with water (10 mL). The layers were separated and the aqueous layer was extracted three times with EtOAc (10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. A purification by column chromatography on silica gel (Pentane/EtOAc 4:1) afforded the title compound **14** (50 mg, 0.20 mmol, 100% yield) as a yellow solid. **mp** 183-185 °C. **Rf** 0.72 (Pentane/EtOAc 1:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37-8.31 (m, 1H, H_{Ar}), 7.64 (dd, *J* = 7.8, 1.5 Hz, 1H, H_{Ar}), 7.48 (s, 1H, CH-N), 7.39-7.31 (m, 3H, H_{Ar}), 7.30-7.24 (m, 1H, H_{Ar}), 6.76-6.68 (m, 2H, H_{Ar}), 5.45 (s, 2H, NH_2), 3.81 (s, 3H, NCH_3).
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.4, 148.8, 137.5, 137.2, 132.5, 132.1, 127.4, 127.1, 123.5, 122.5, 122.5, 116.8, 116.5, 116.1, 109.7, 33.5.
IR ν_{max} 3672 (br), 3475 (w), 3364 (w), 2976 (s), 2902 (s), 1610 (s), 1577 (m), 1521 (s), 1462 (m), 1394 (s), 1367 (s), 1230 (s), 1075 (s), 1053 (s), 888 (s), 744 (s).
HRMS calculated for $C_{16}H_{14}N_2NaO^+$ $[M+Na]^+$ 273.0998; found 273.0999.

7. Spectra of new compounds



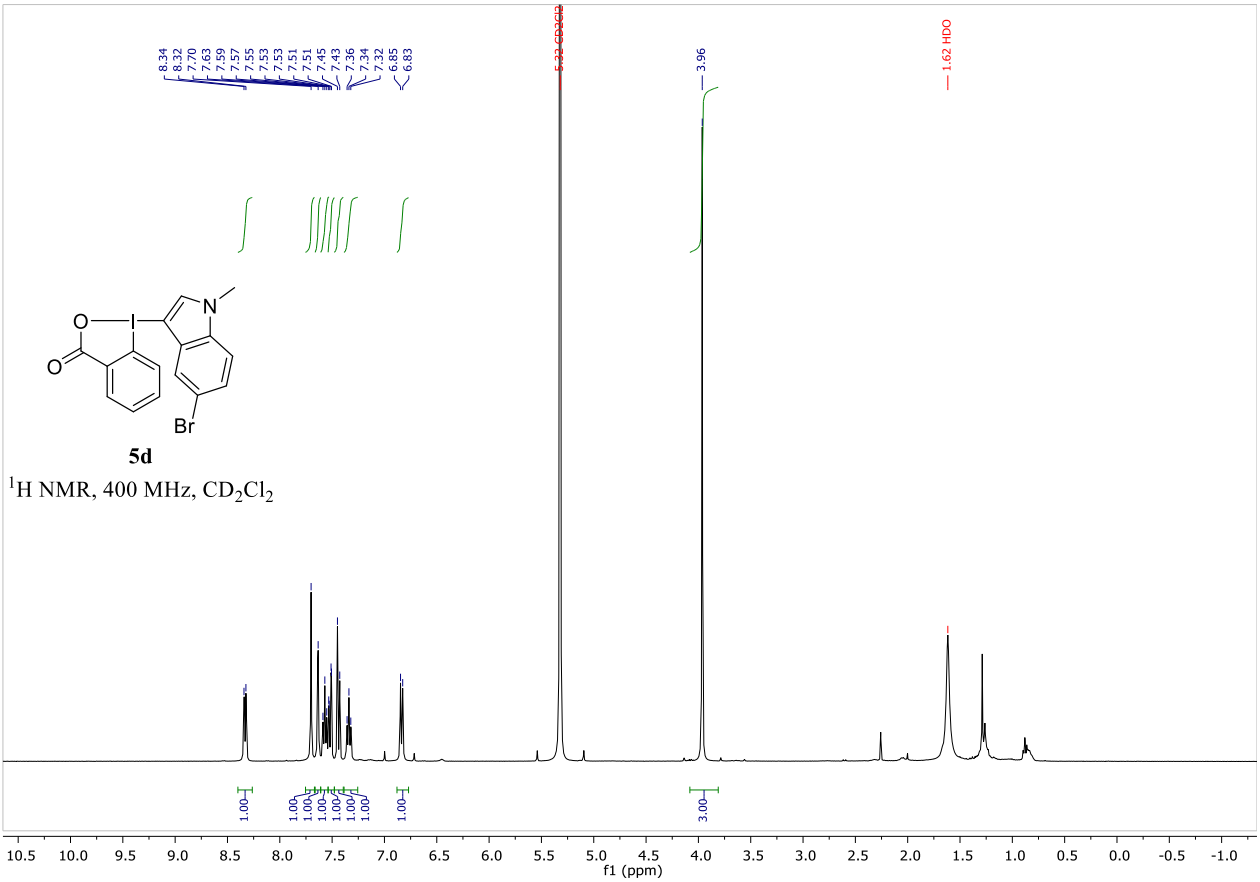
5b

^{1}H NMR, 400 MHz, MeOD



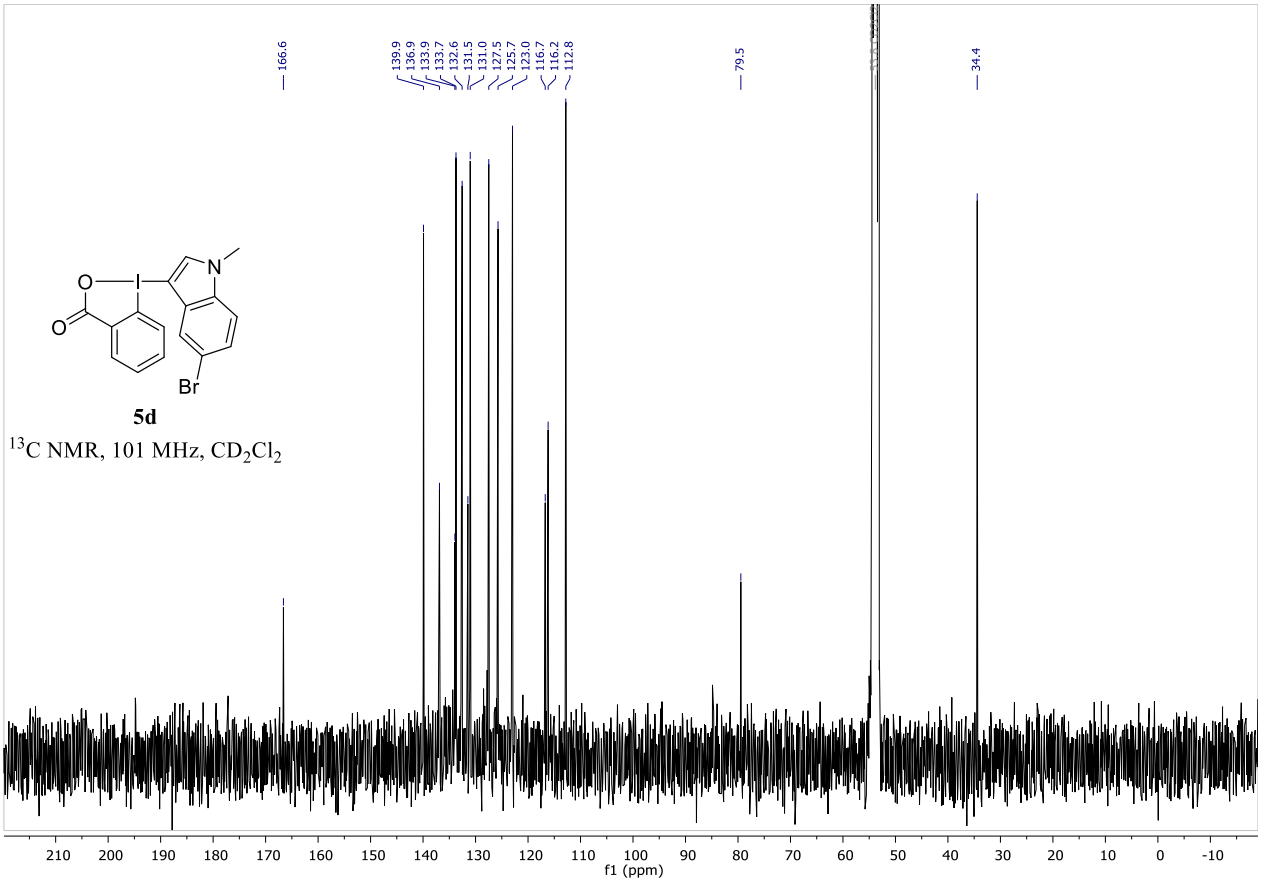
5b

^{13}C NMR, 101 MHz, MeOD



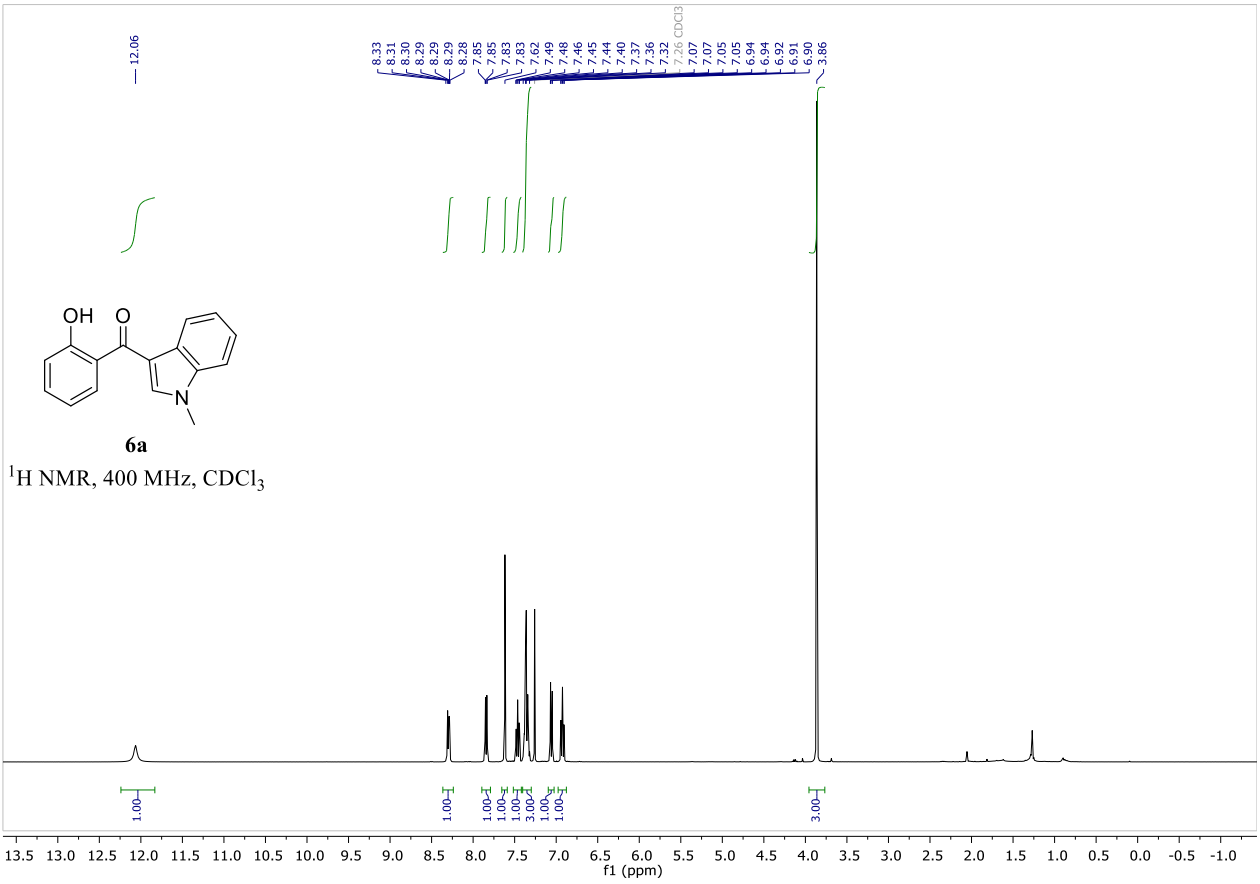
5d

^{1}H NMR, 400 MHz, CD_2Cl_2



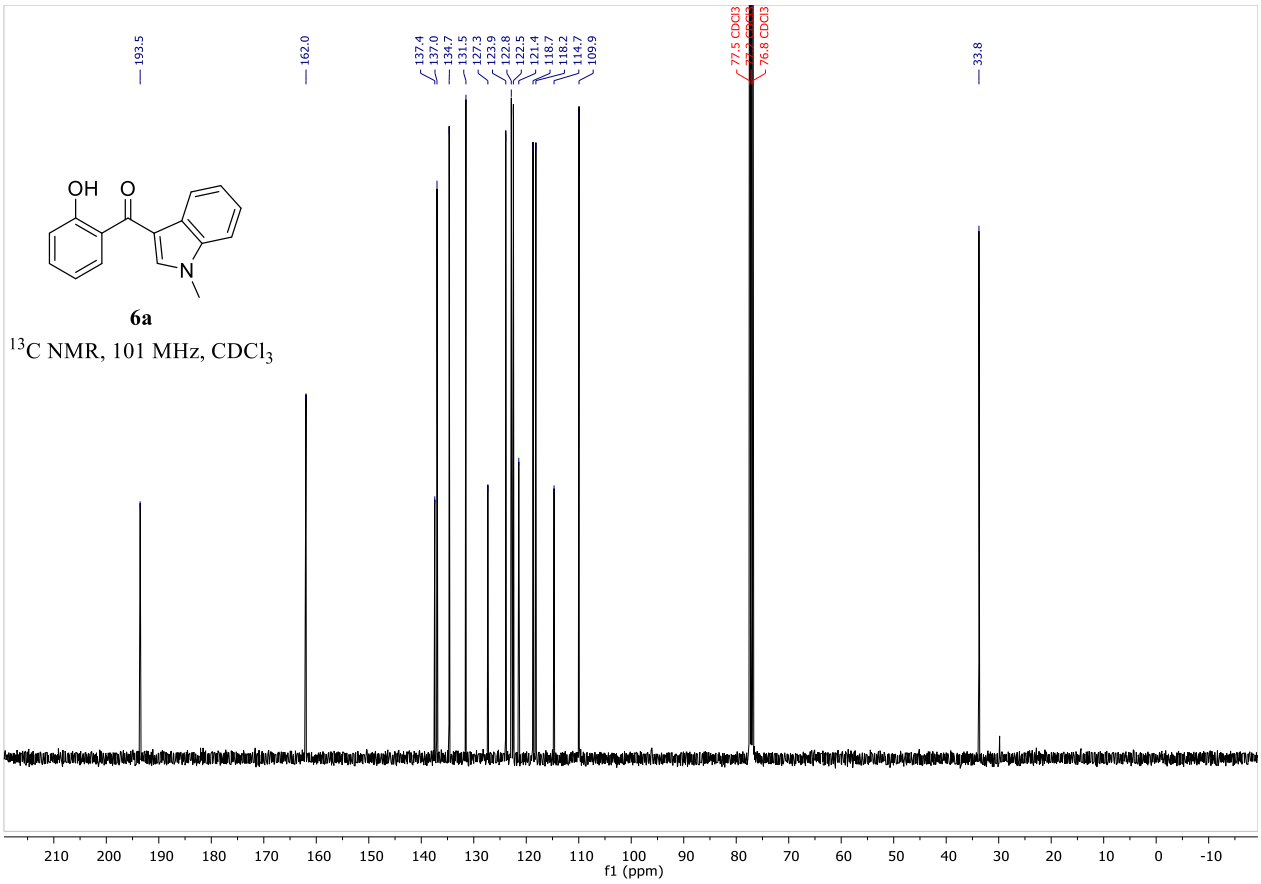
5d

^{13}C NMR, 101 MHz, CD_2Cl_2



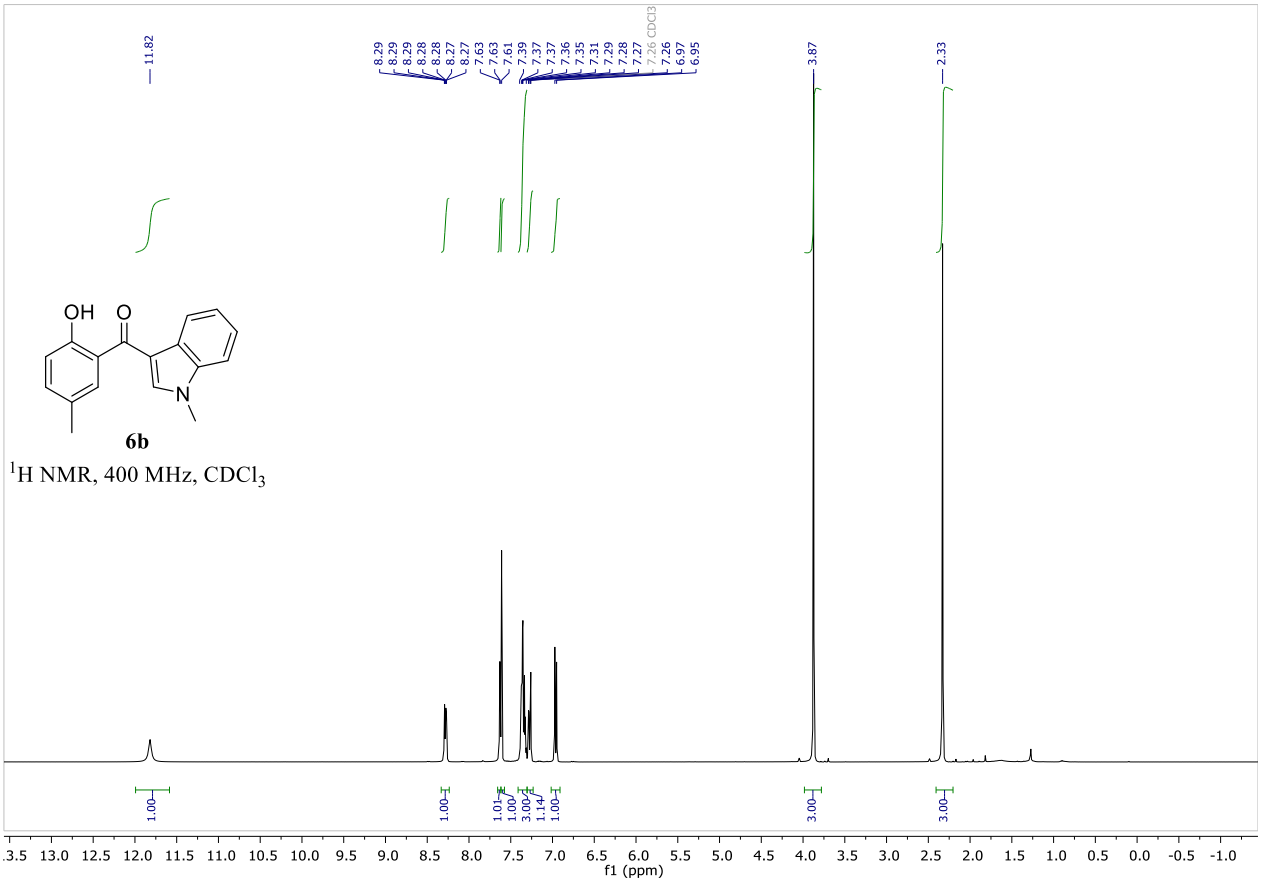
6a

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



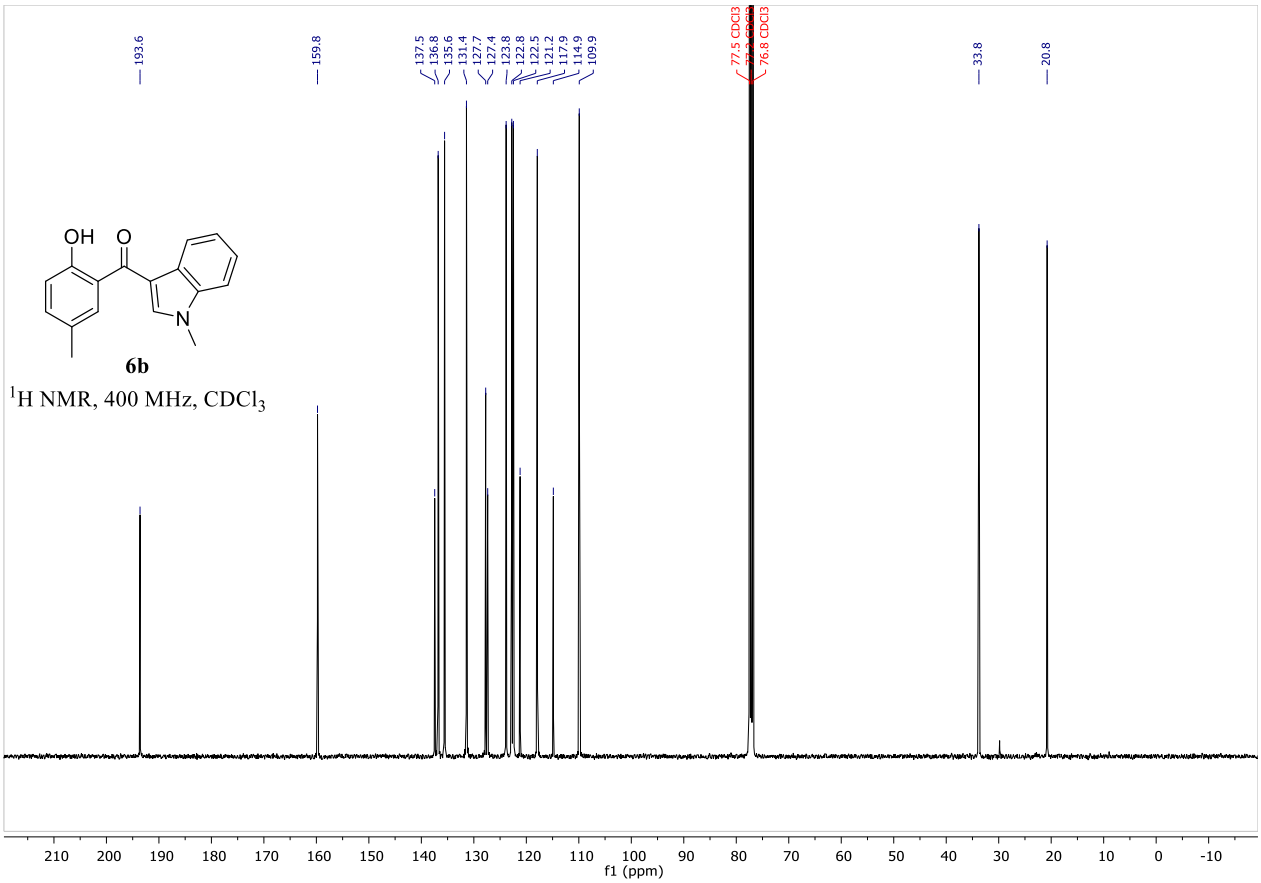
6a

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



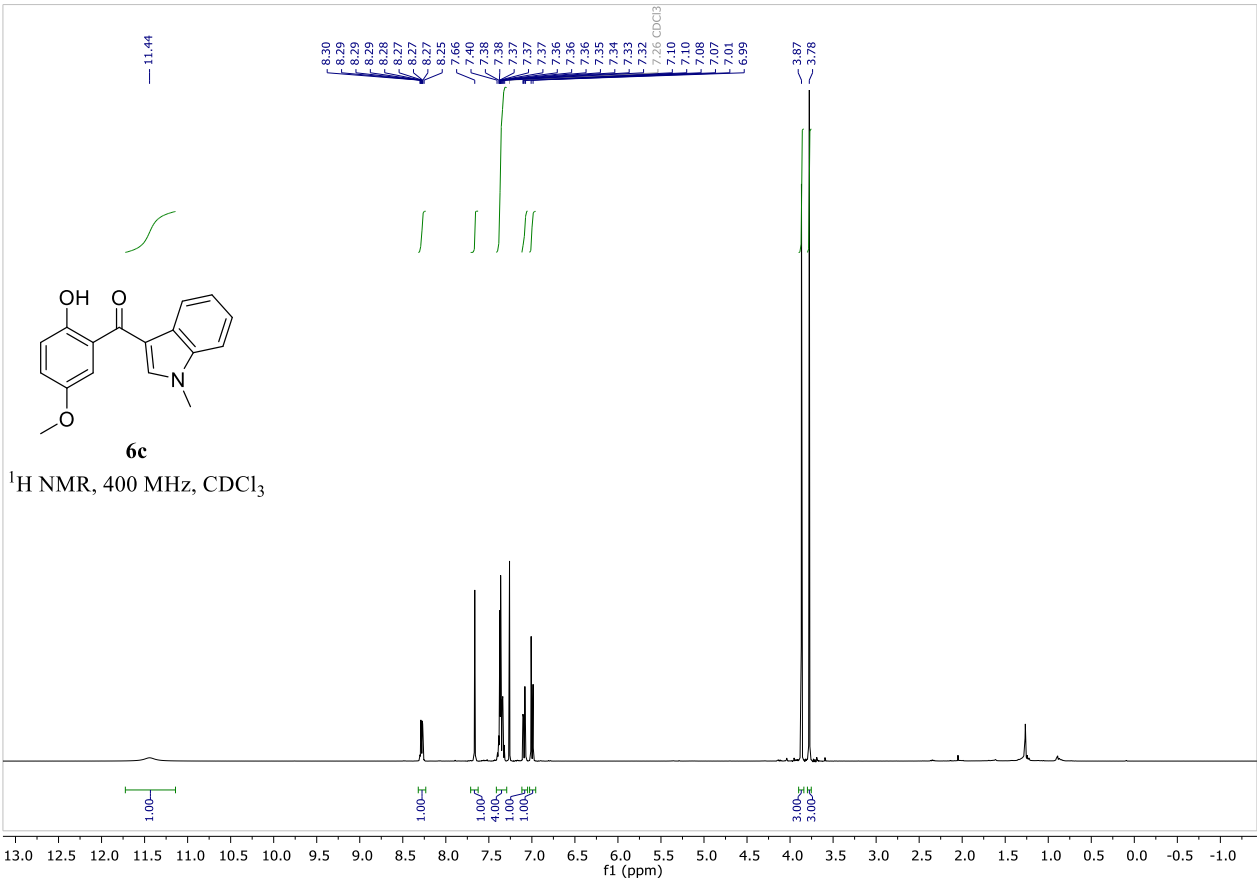
6b

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



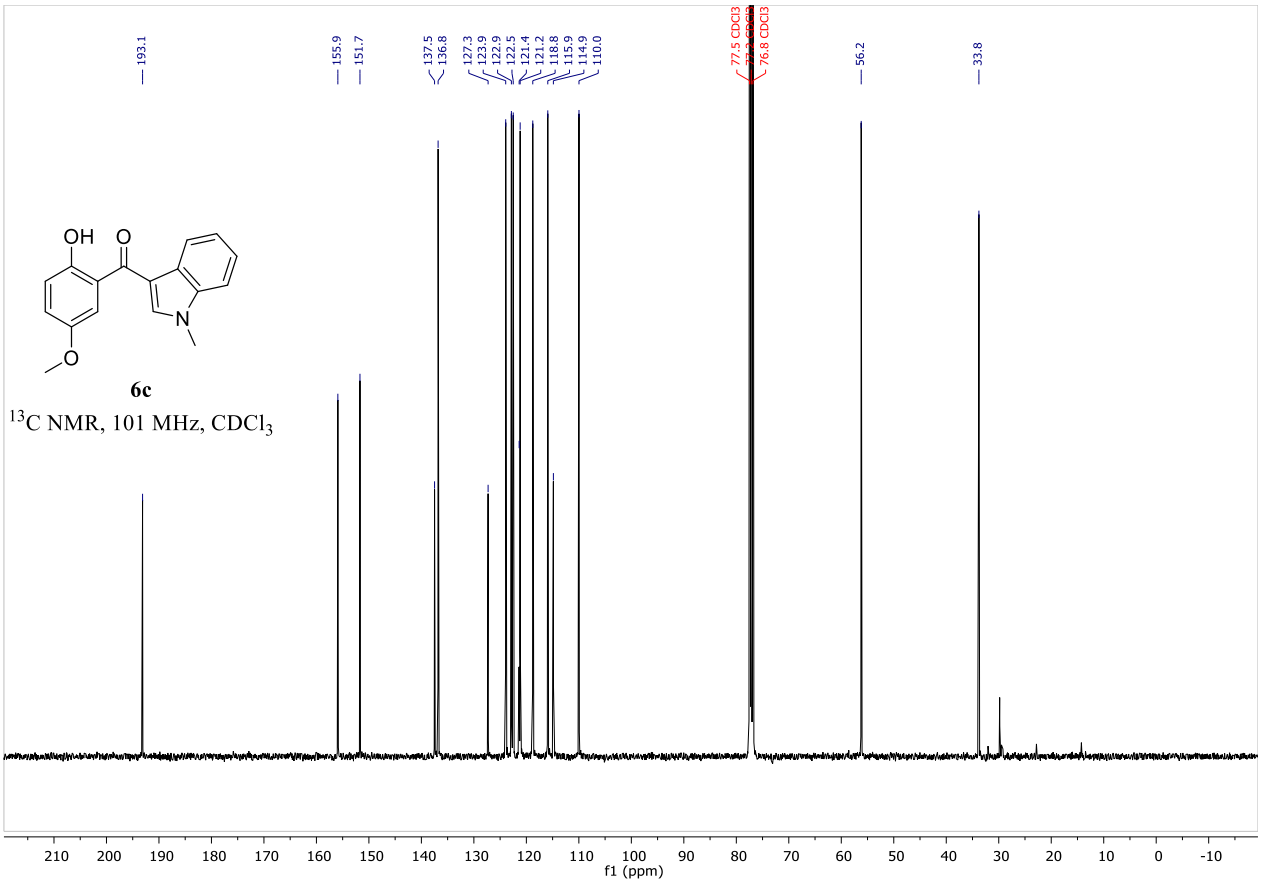
6b

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



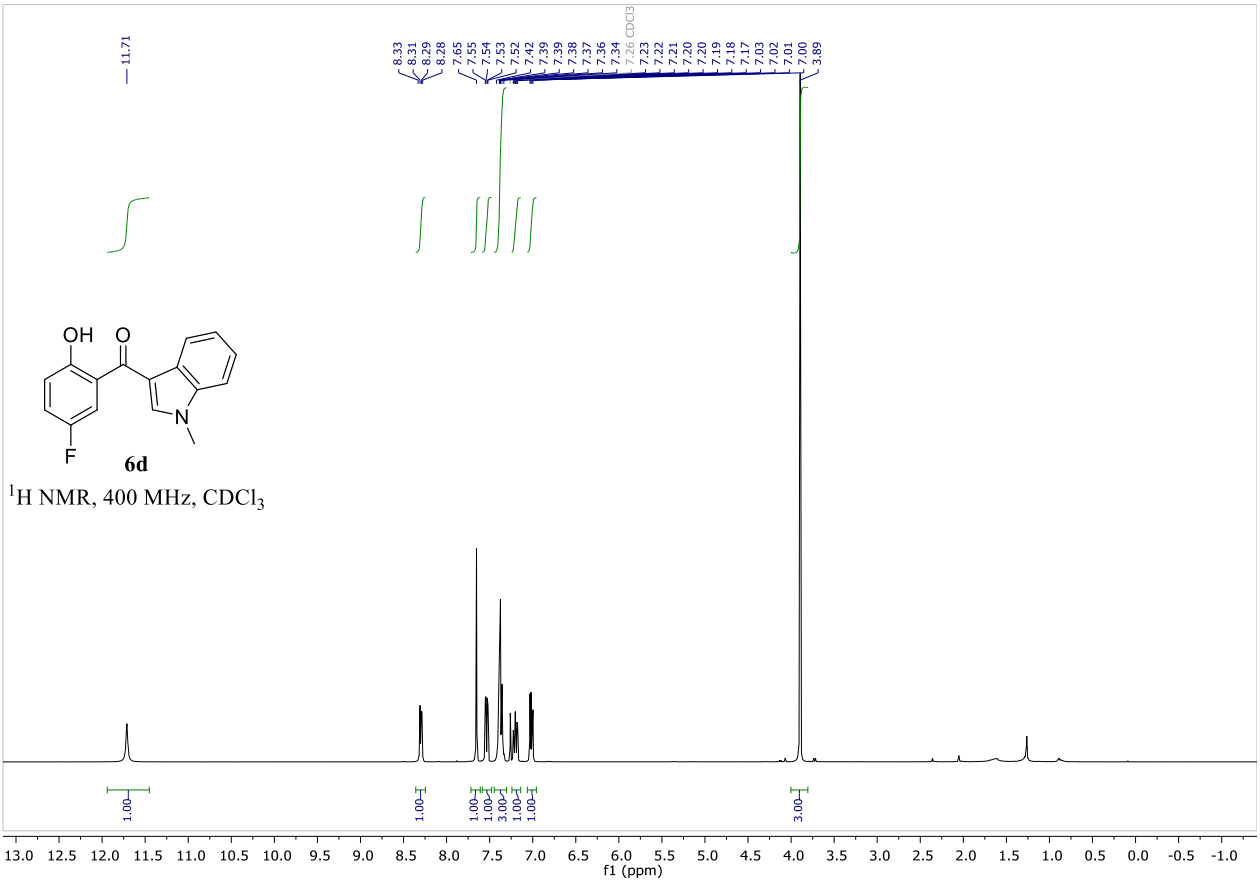
6c

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



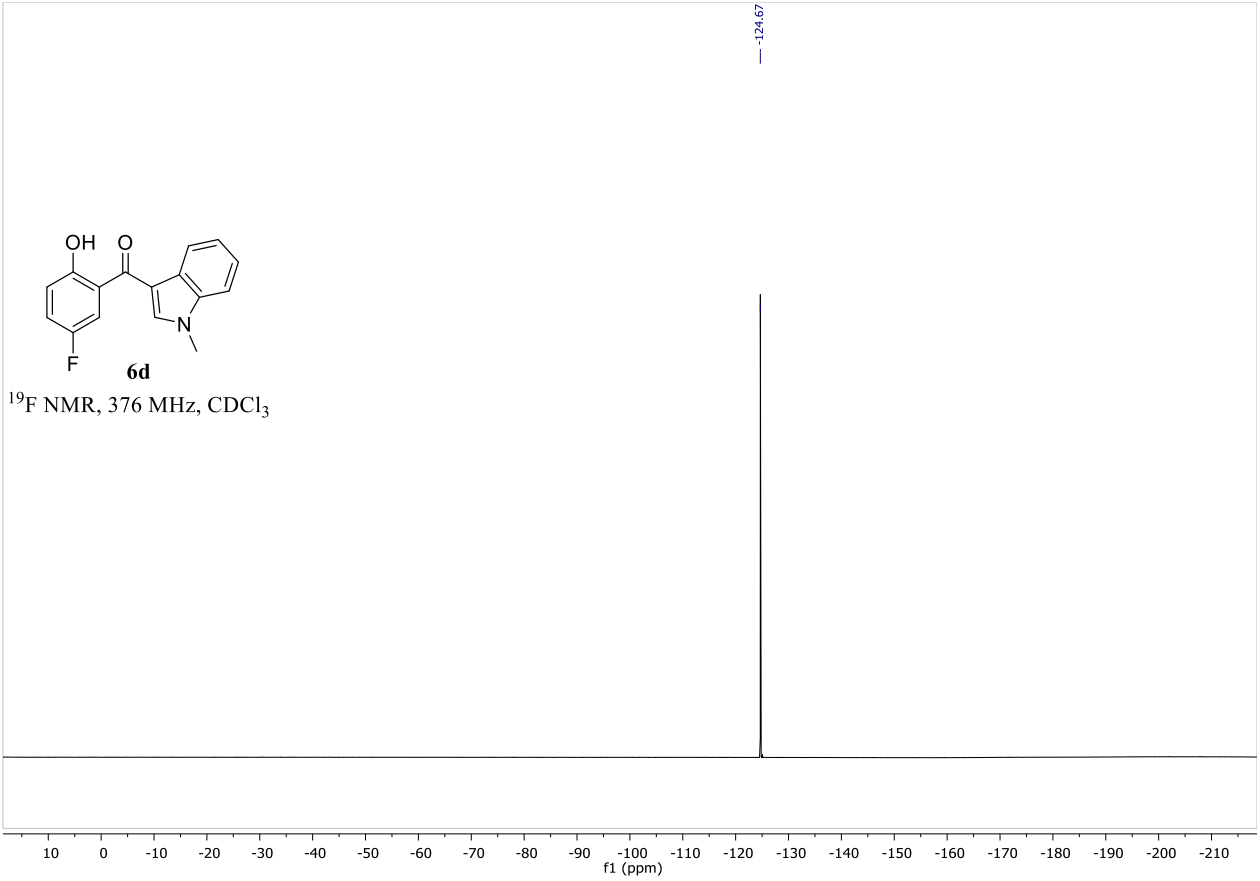
6c

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



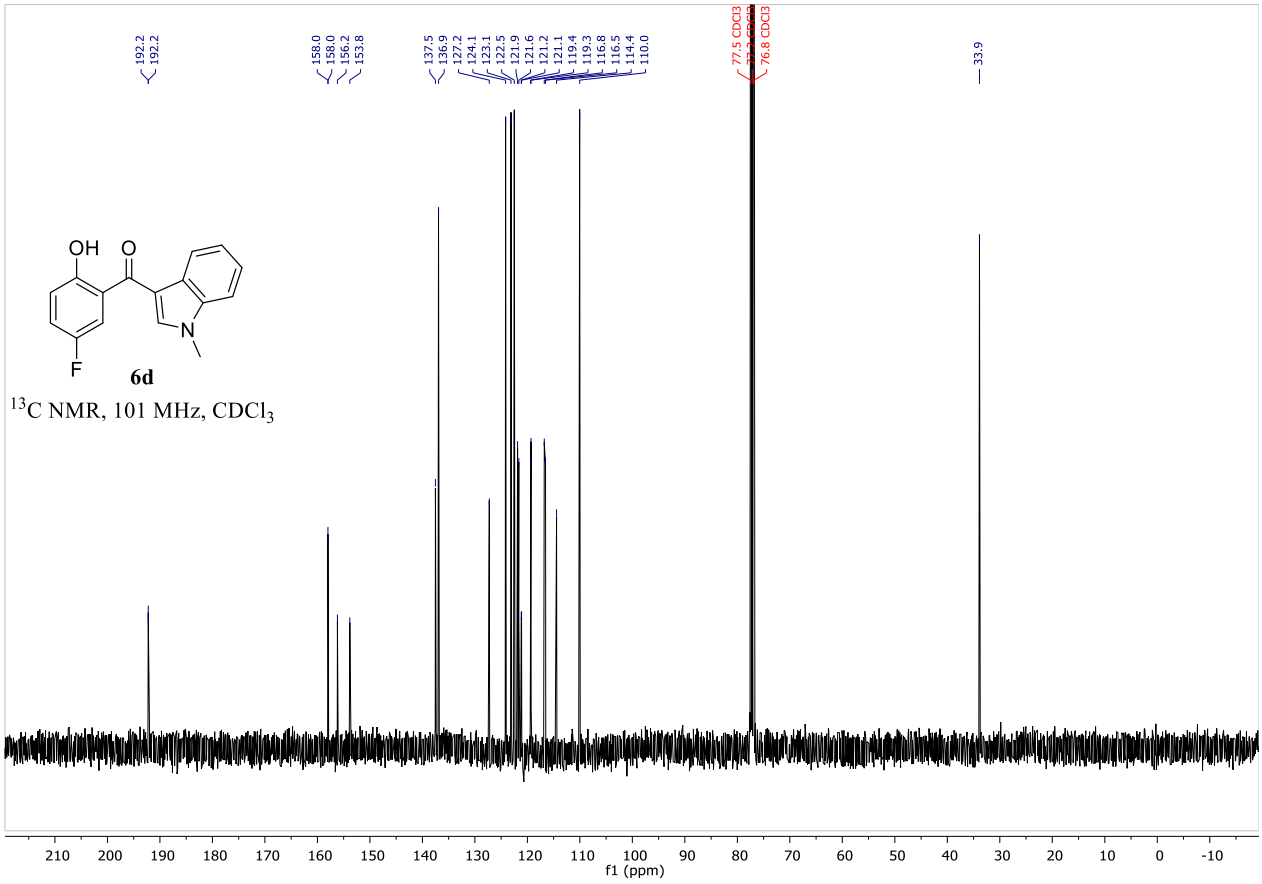
6d

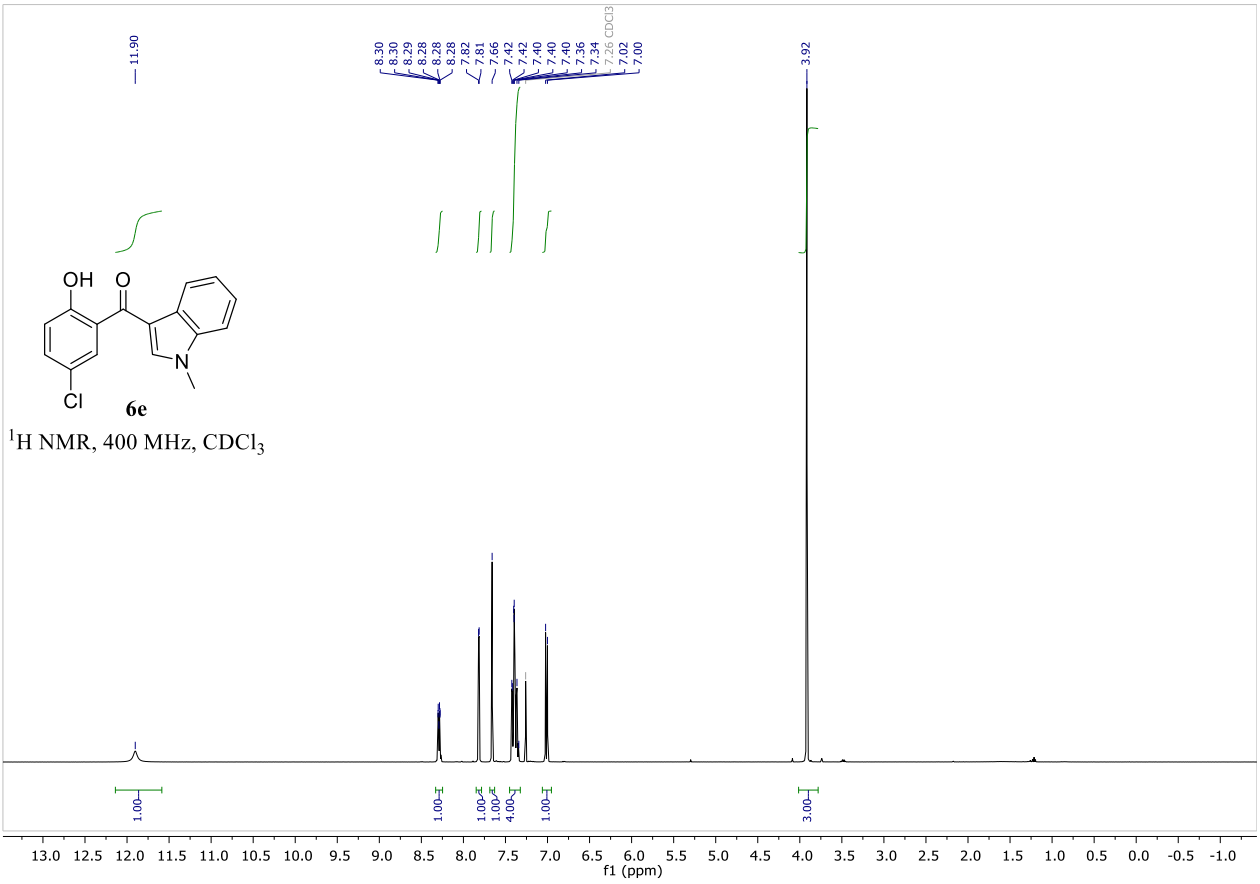
^{1}H NMR, 400 MHz, $CDCl_3$



6d

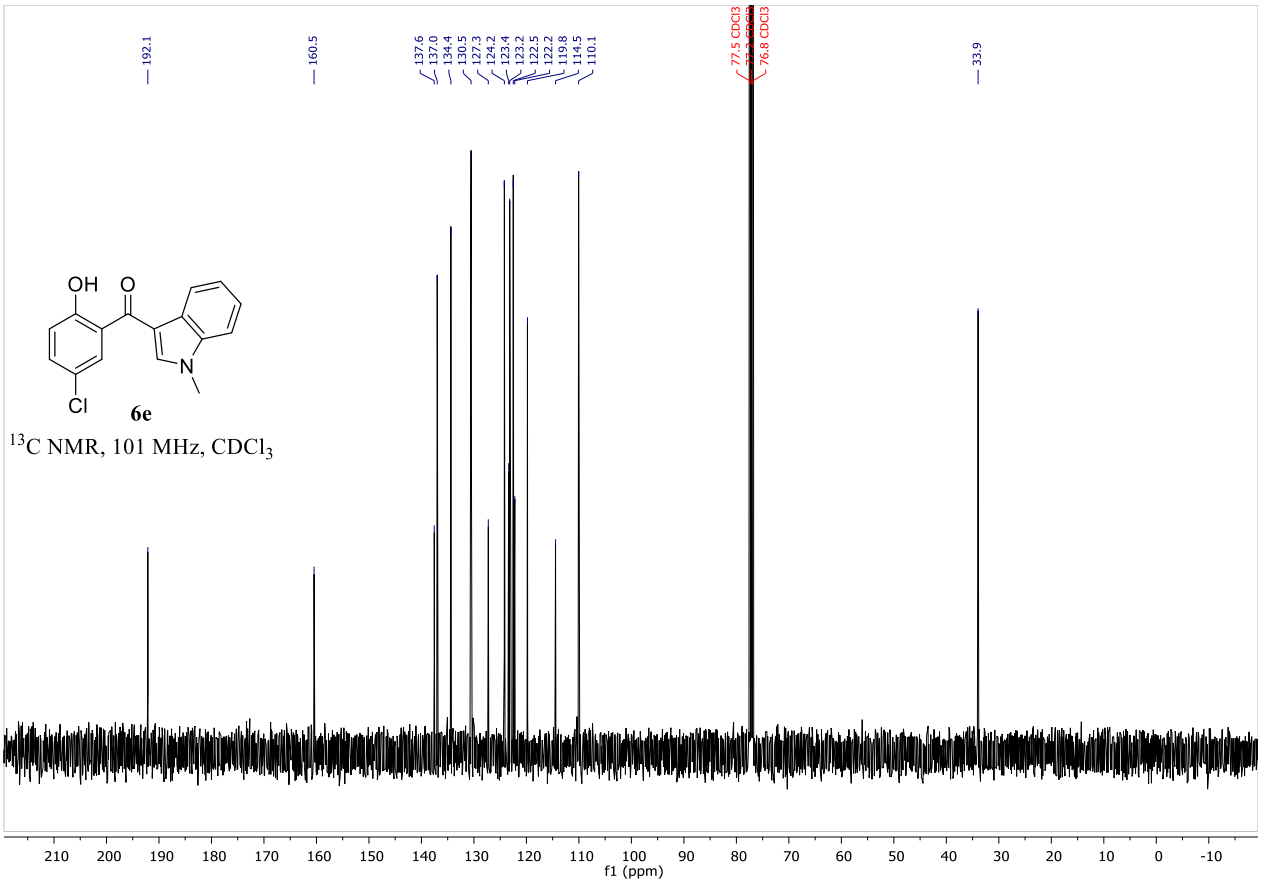
^{19}F NMR, 376 MHz, $CDCl_3$


192.2
192.2
158.0
158.0
156.2
153.8
137.5
136.9
127.2
124.1
123.1
122.5
121.9
121.6
121.2
121.1
119.4
119.3
116.8
116.5
114.4
110.0
77.5 CDCl3
76.8 CDCl3
33.9
OH
O
N
F
6d
13C NMR, 101 MHz, CDCl3
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)



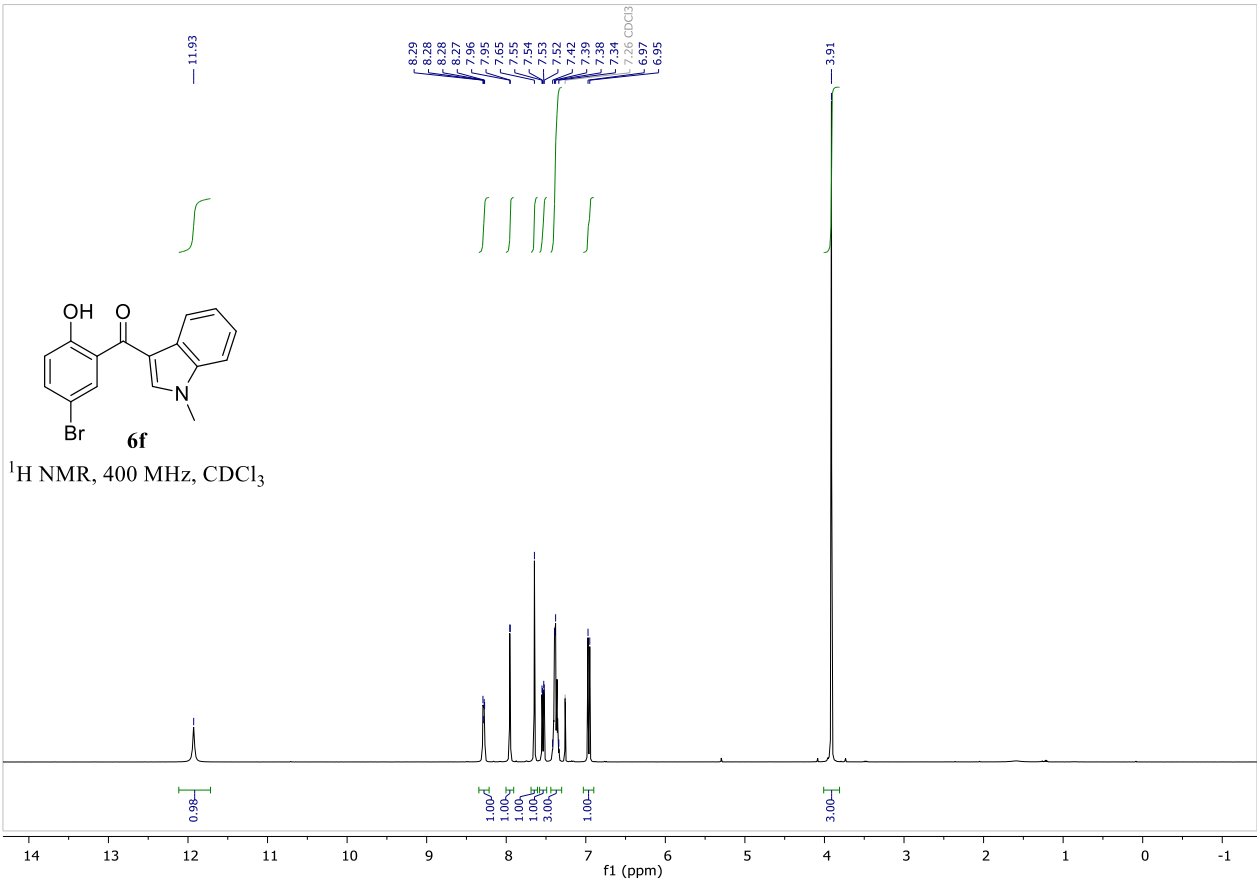
6e

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

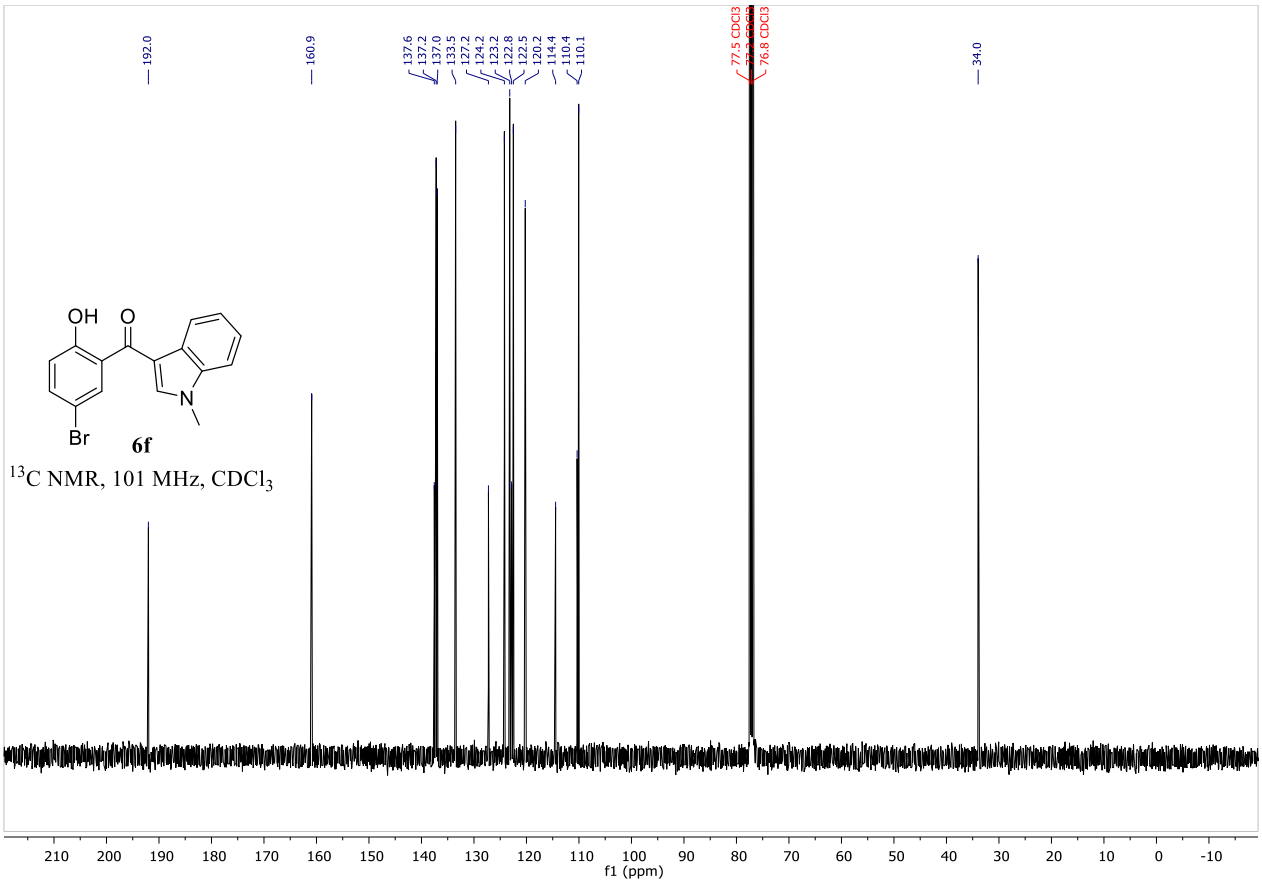


6e

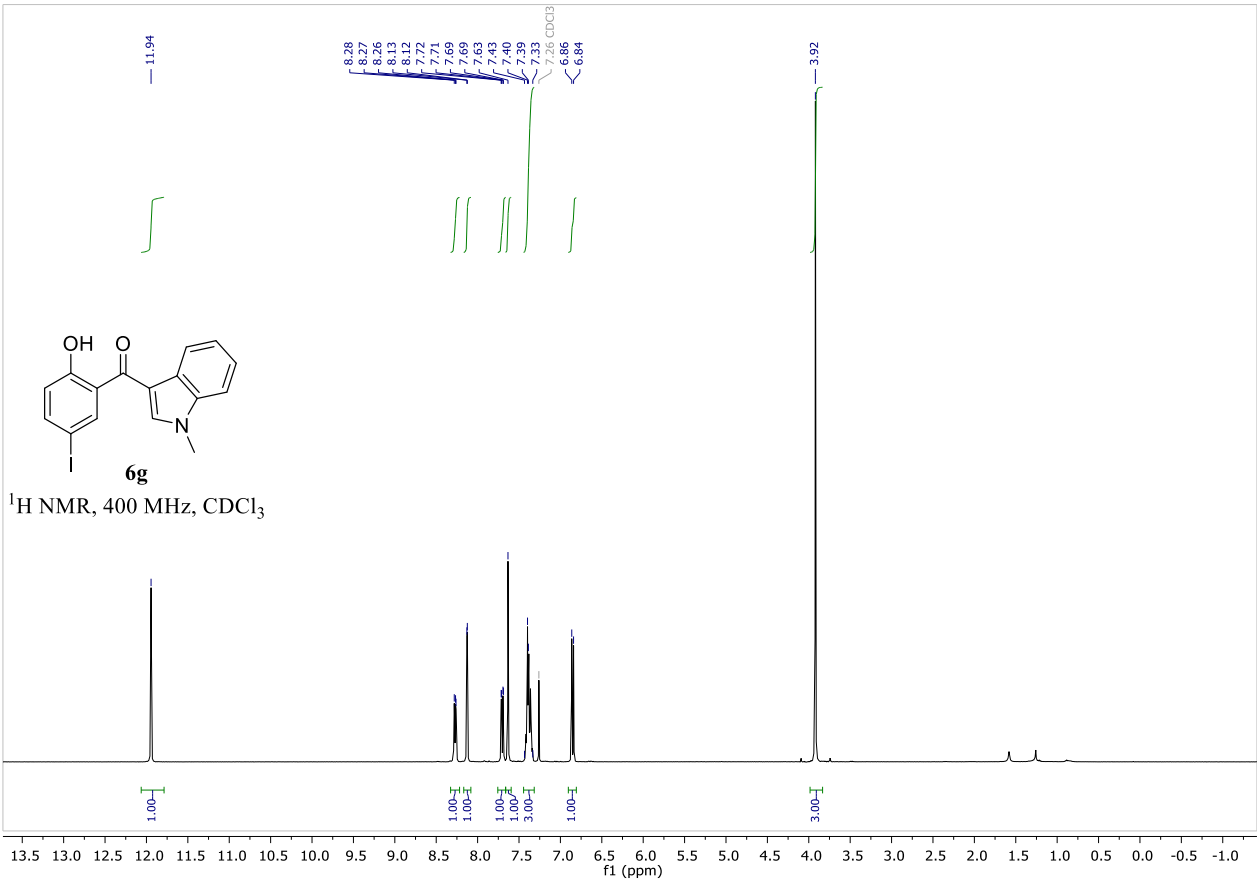
^{13}C NMR, 101 MHz, $CDCl_3$



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

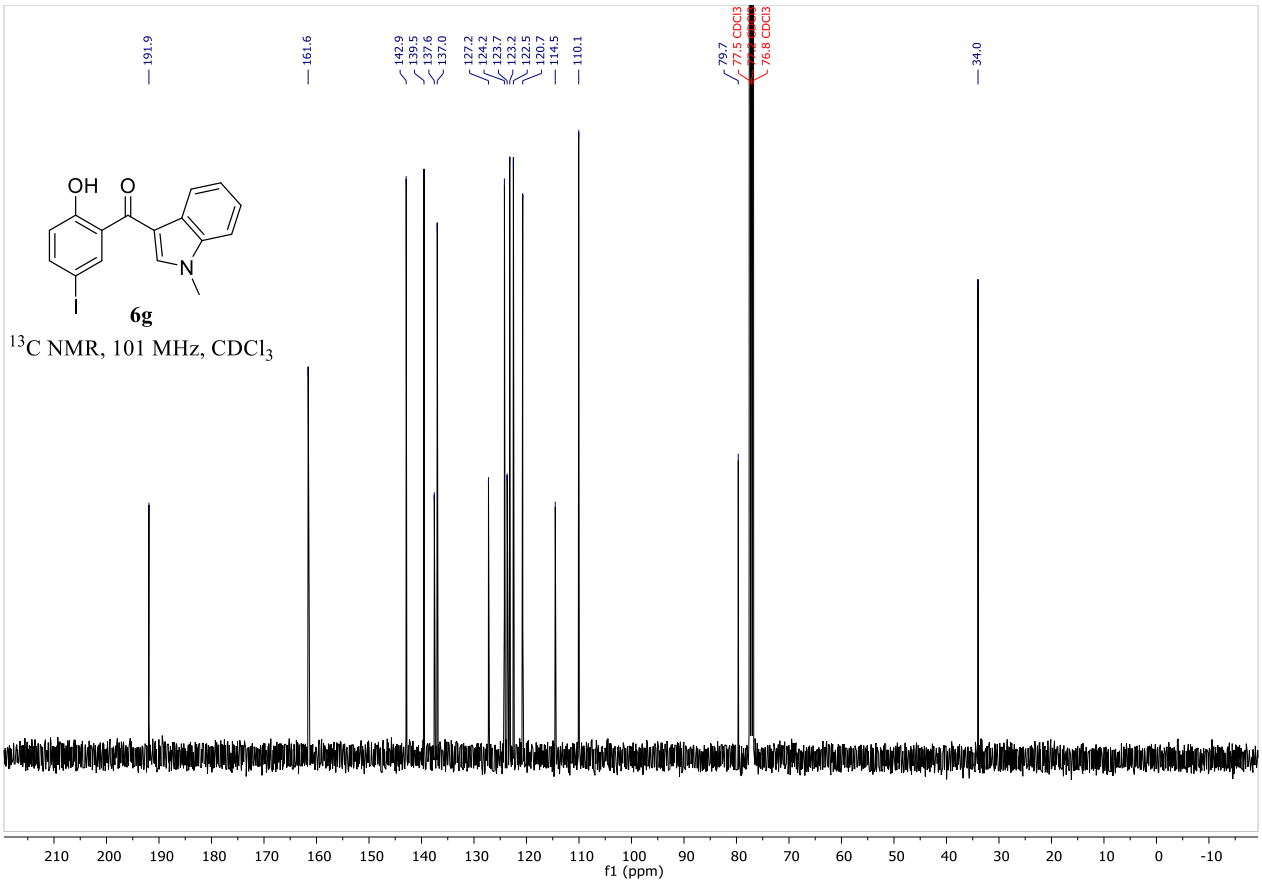


^{13}C NMR, 101 MHz, $CDCl_3$



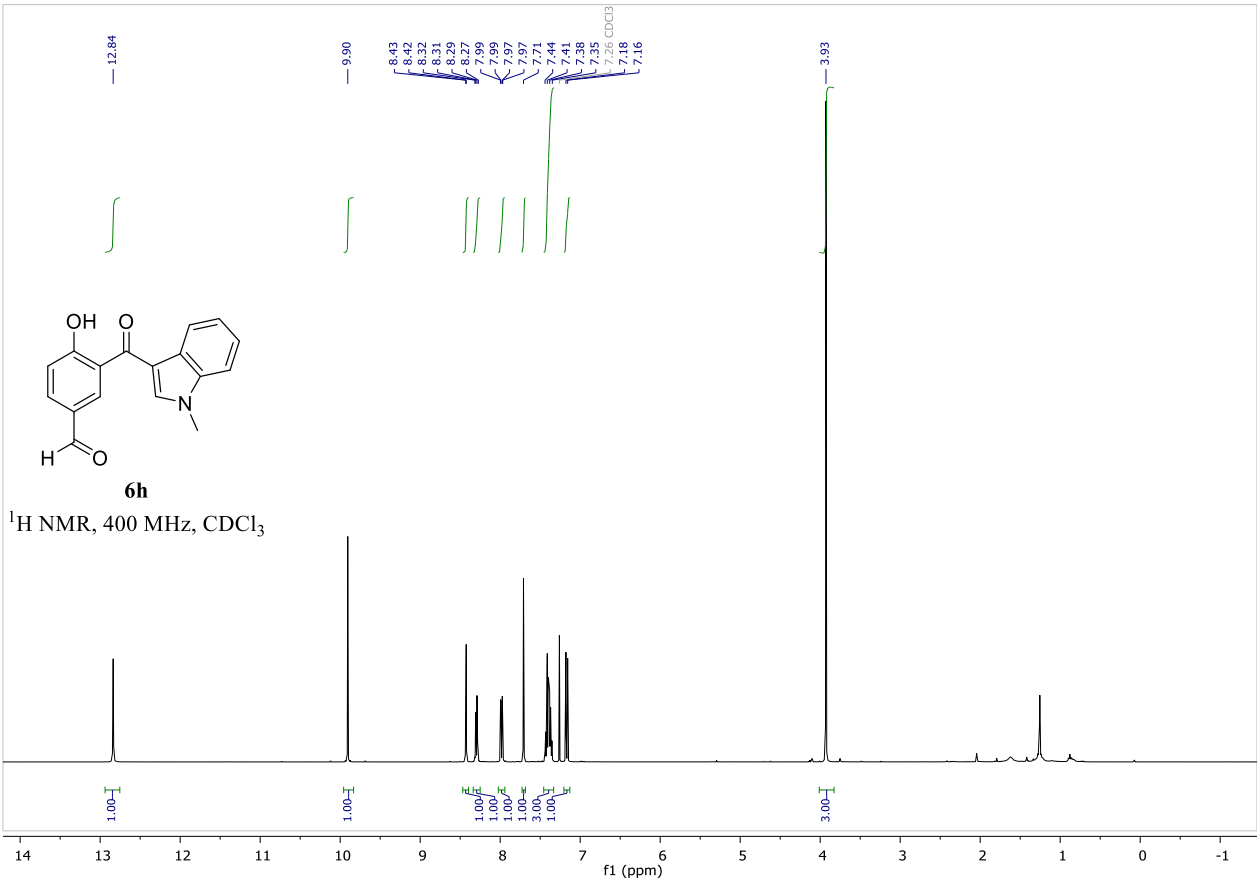
6g

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



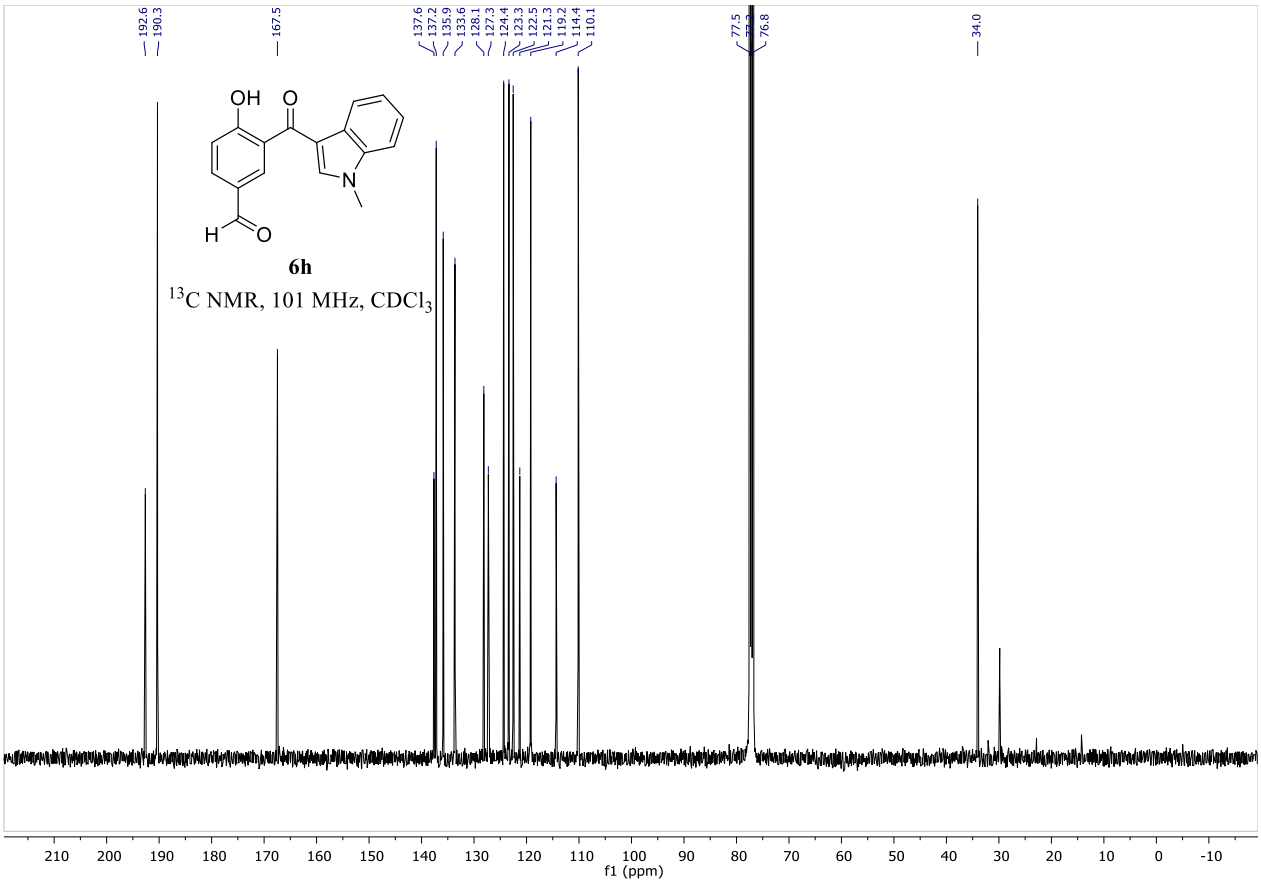
6g

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



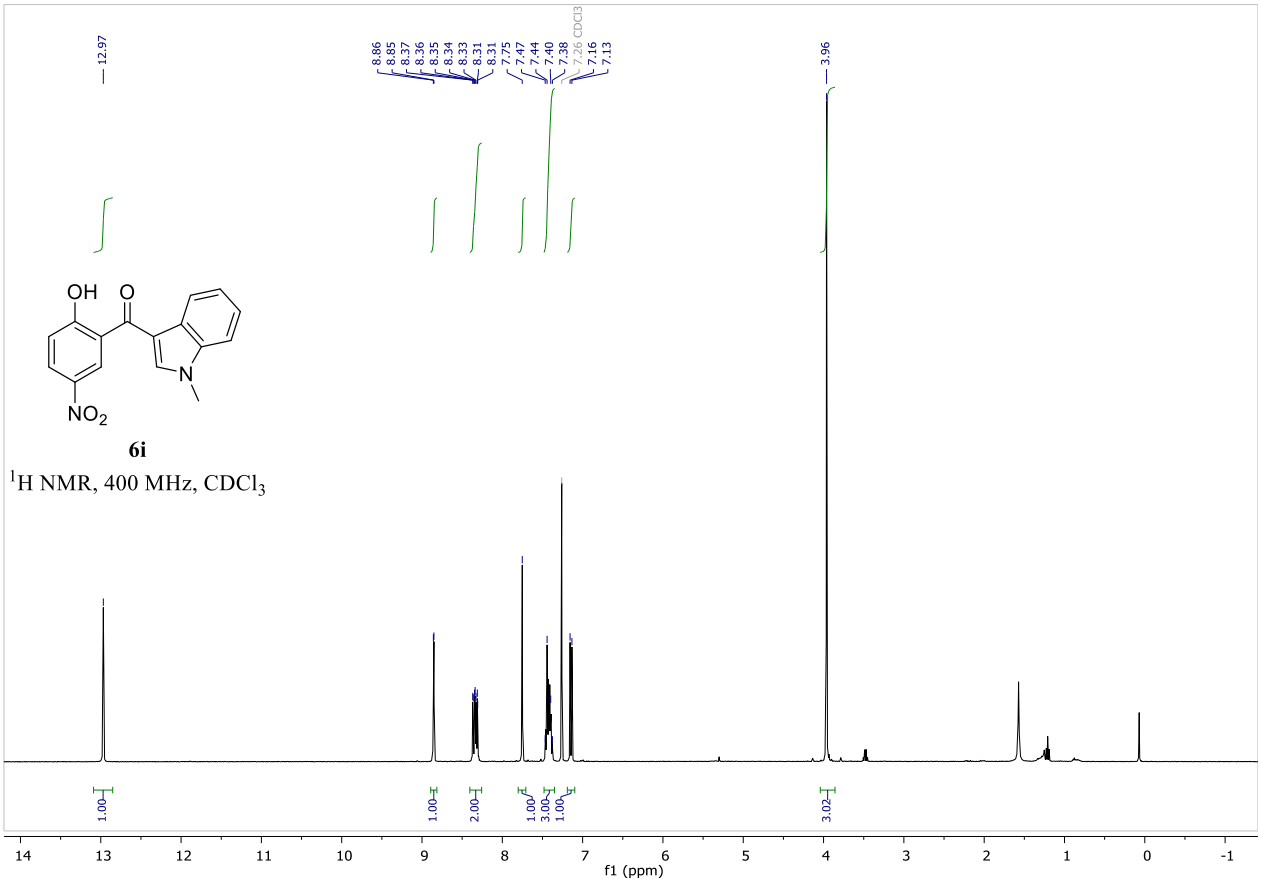
6h

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



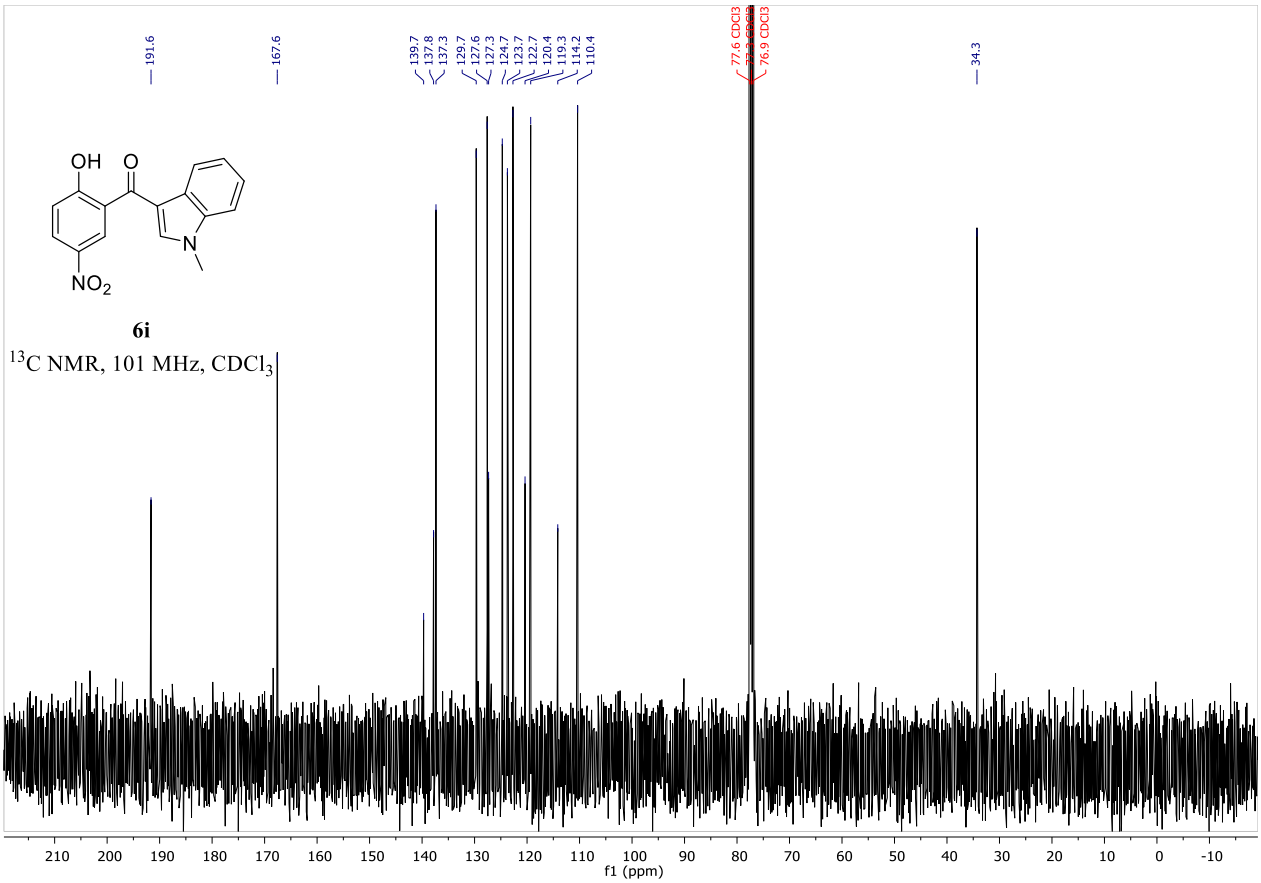
6h

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



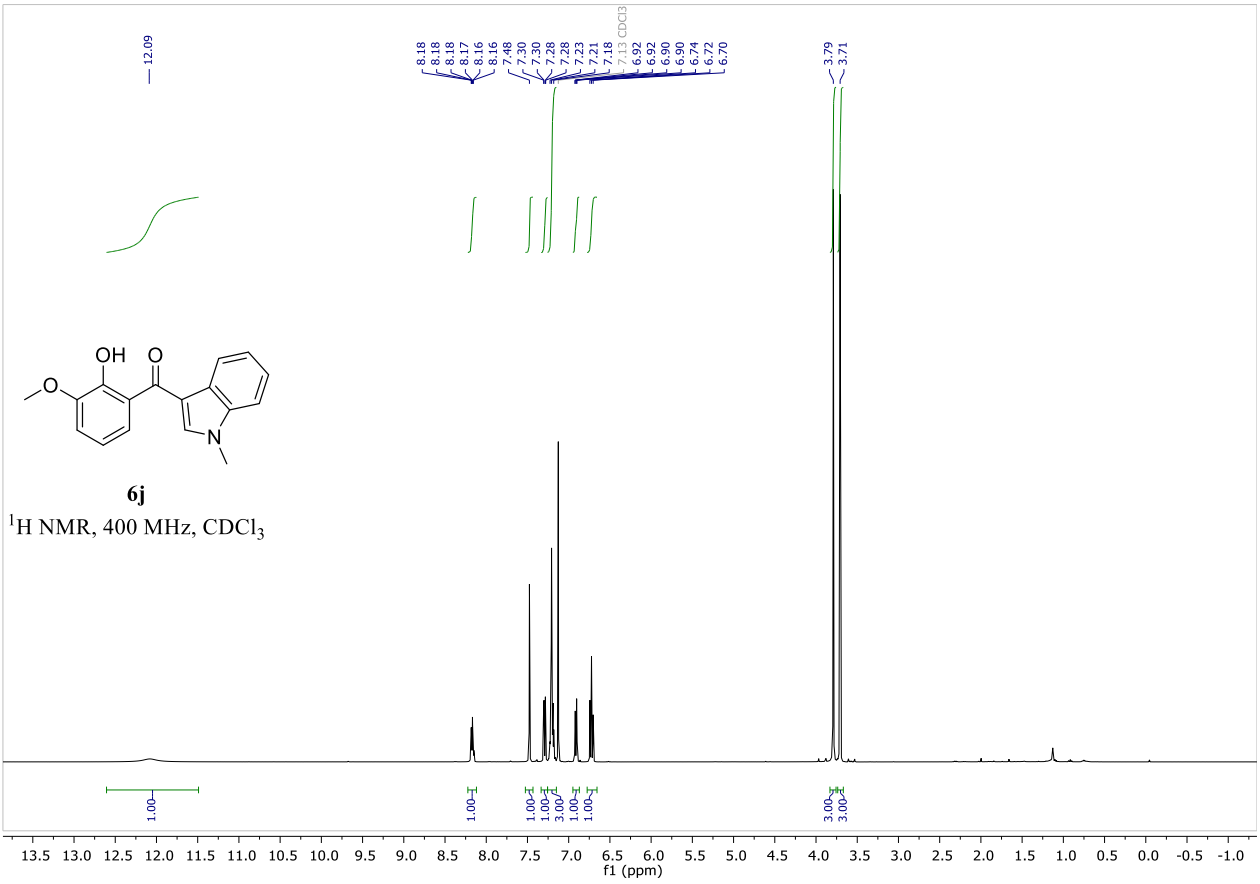
6i

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



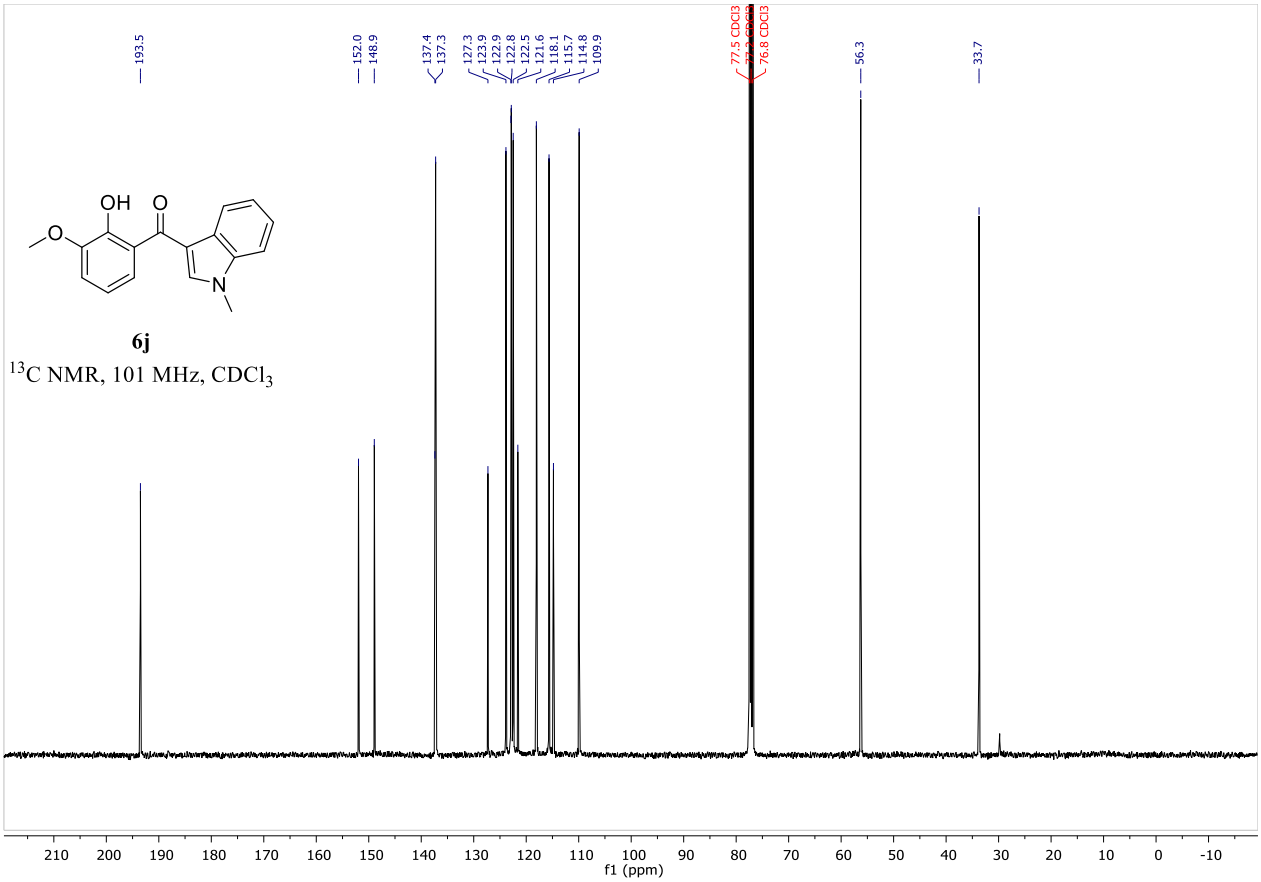
6i

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



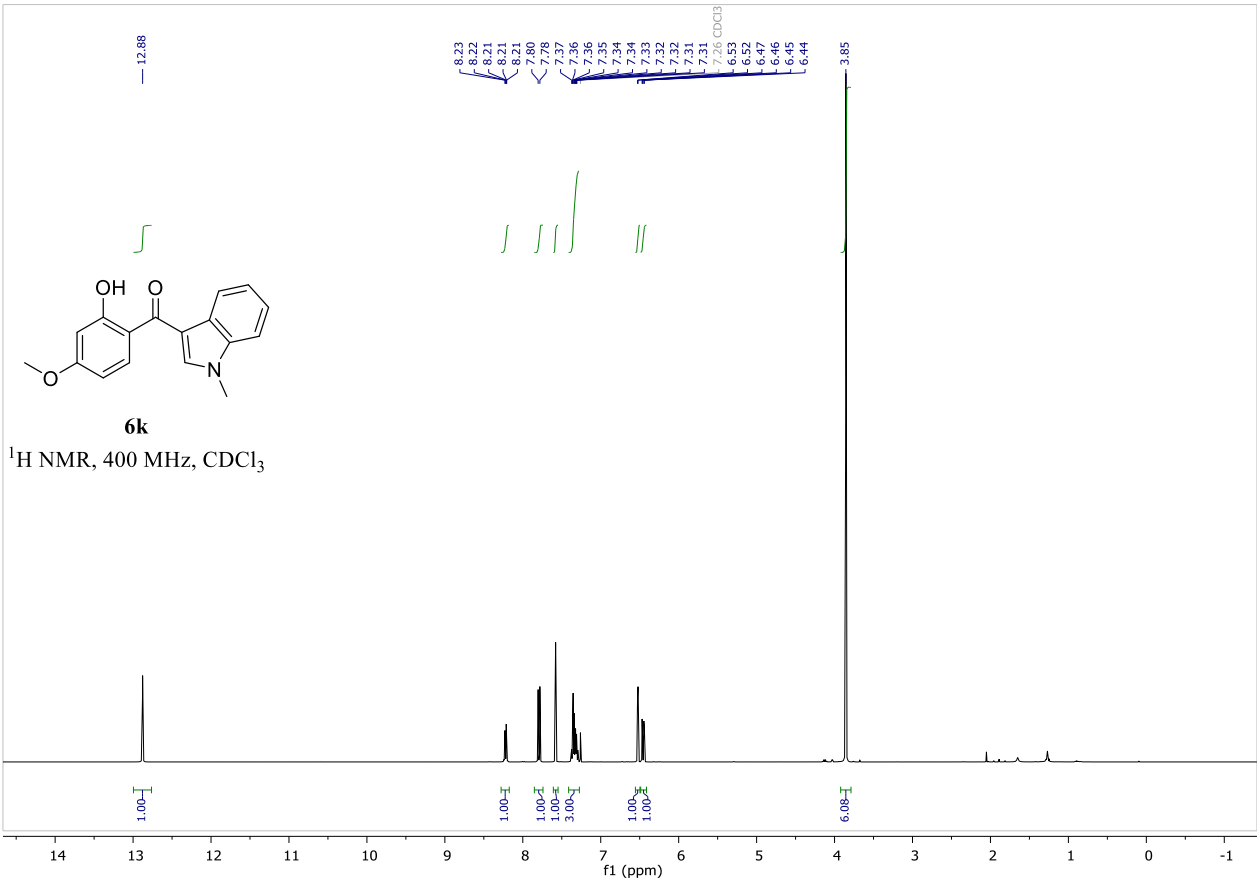
6j

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



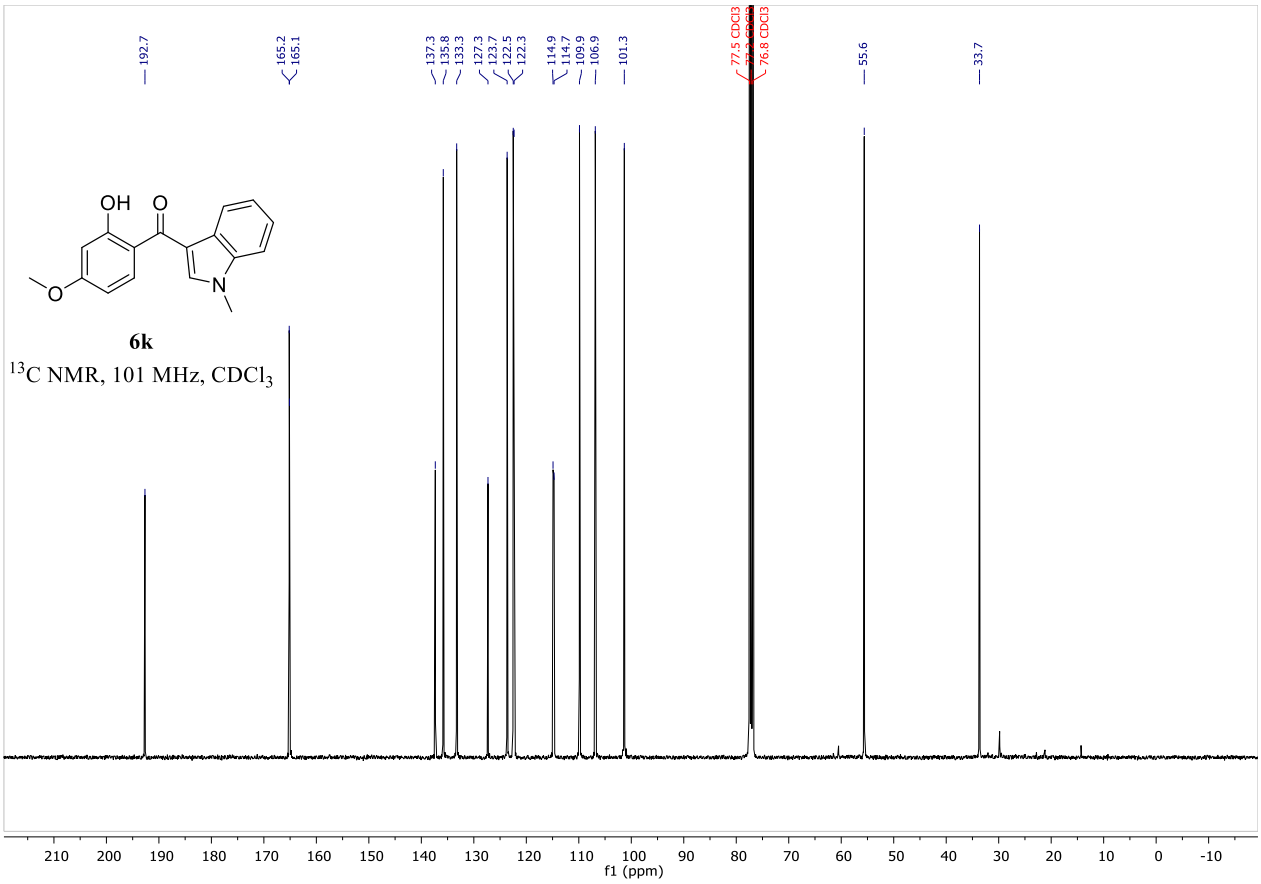
6j

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



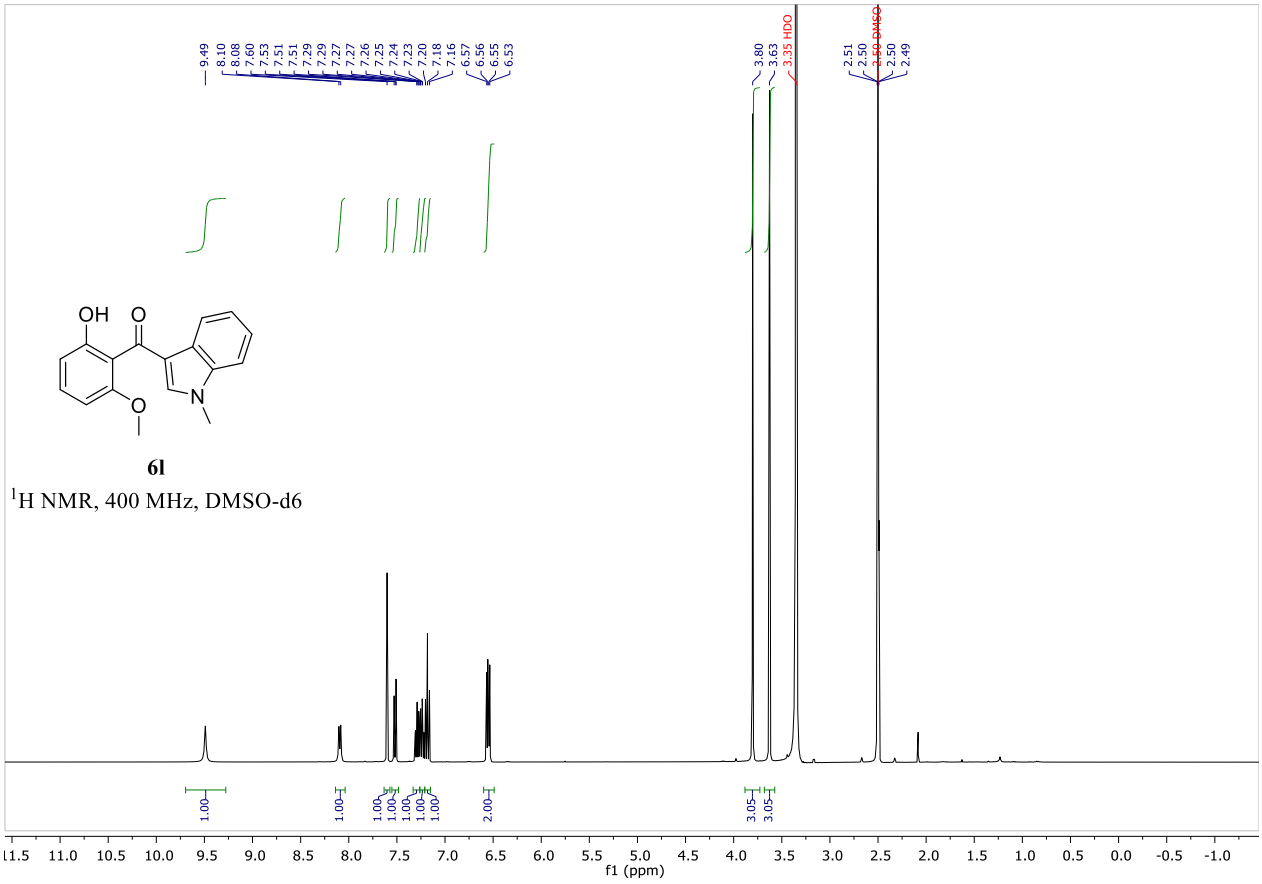
6k

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



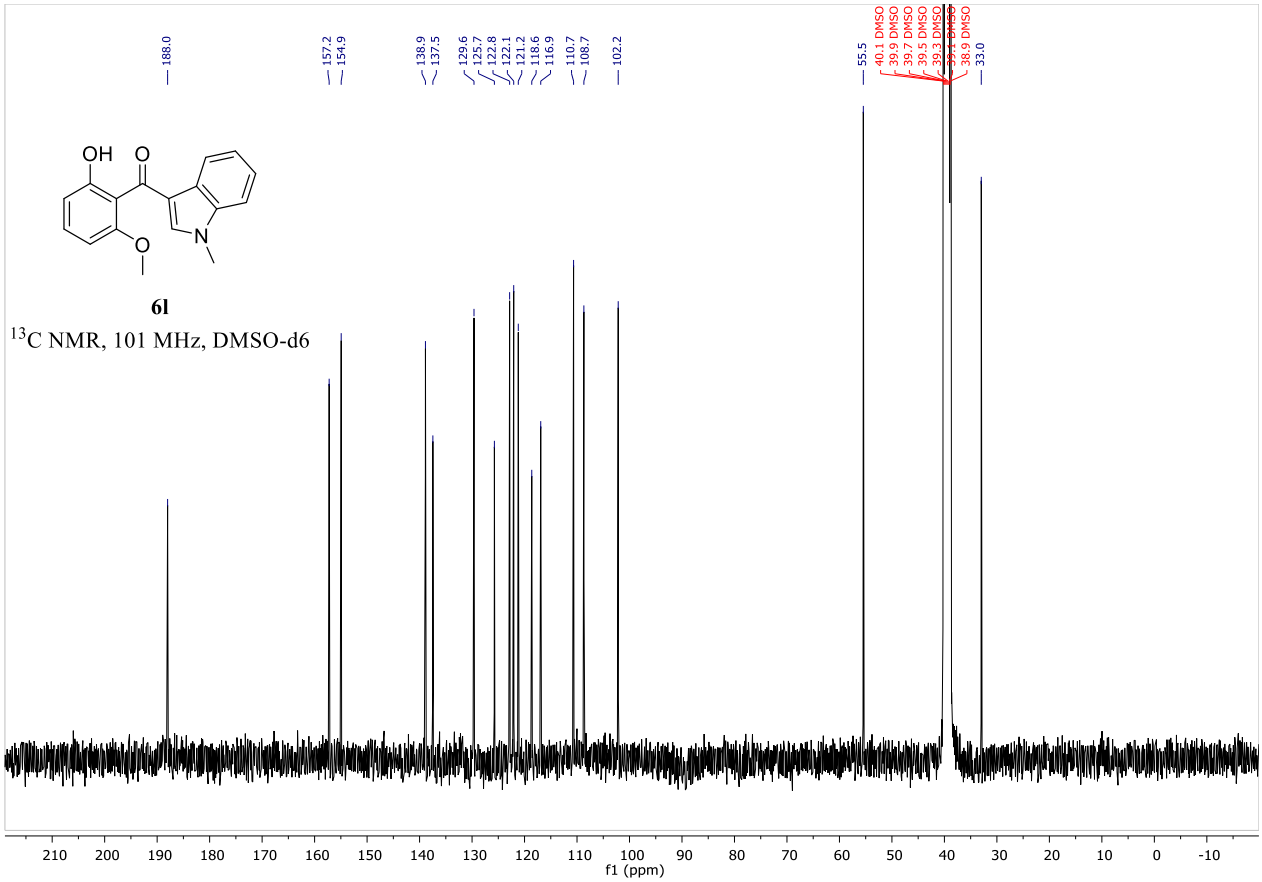
6k

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



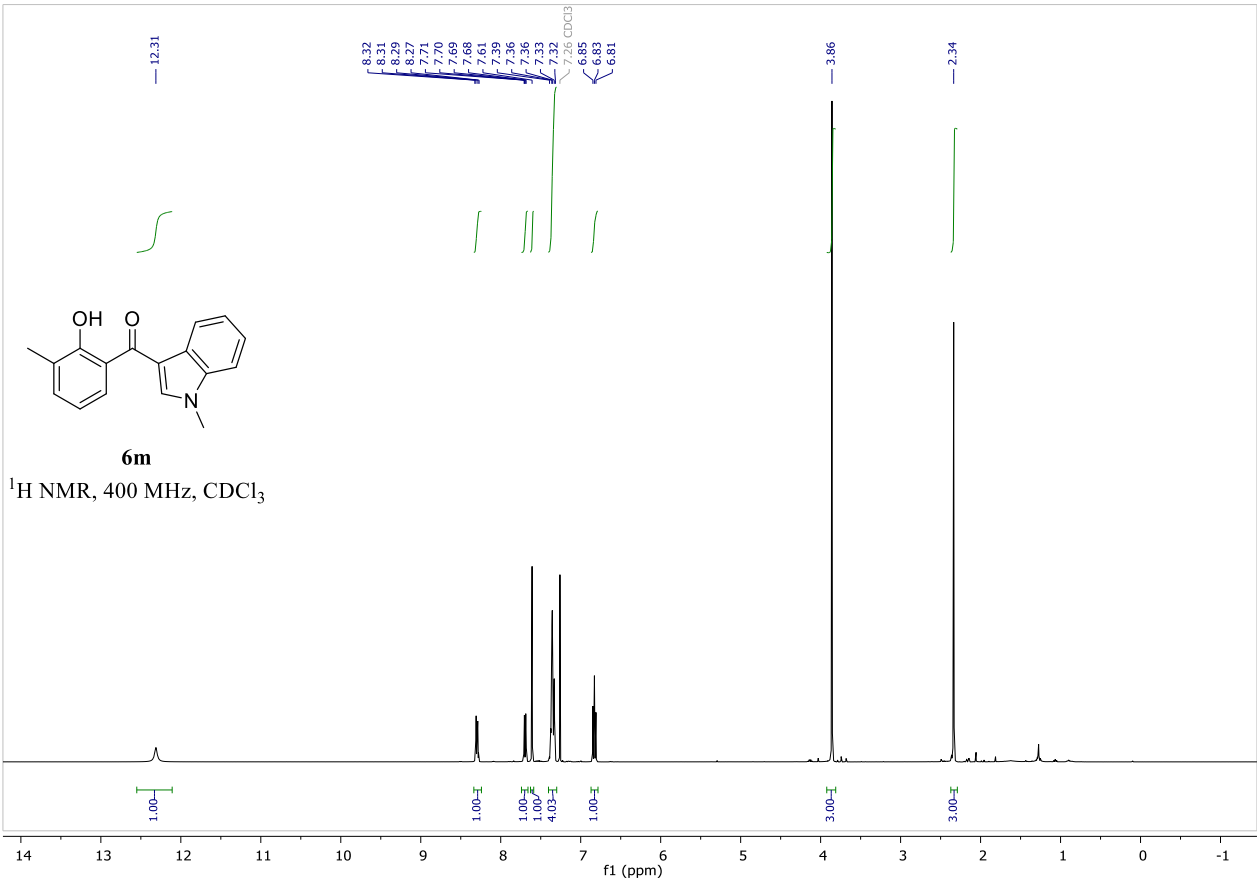
6l

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



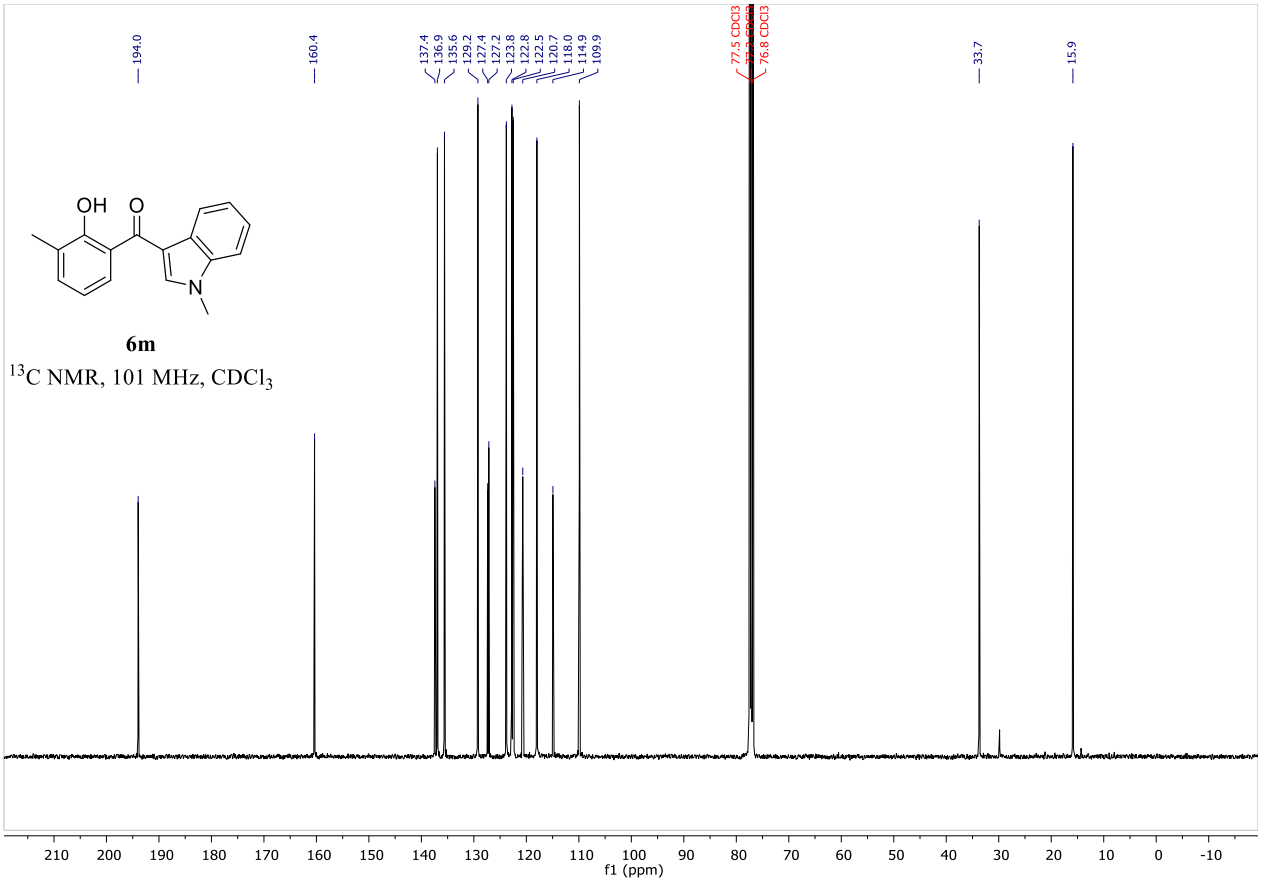
6l

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



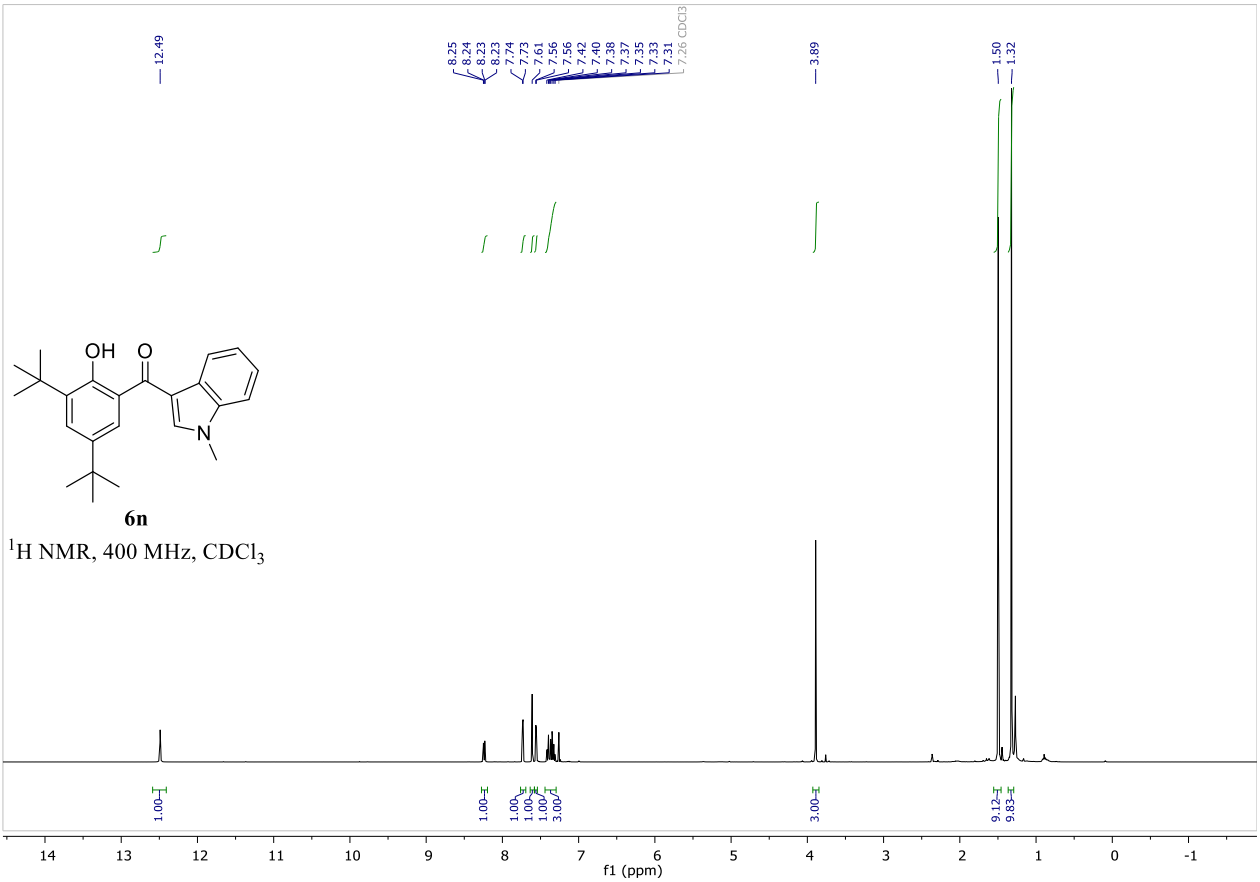
6m

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



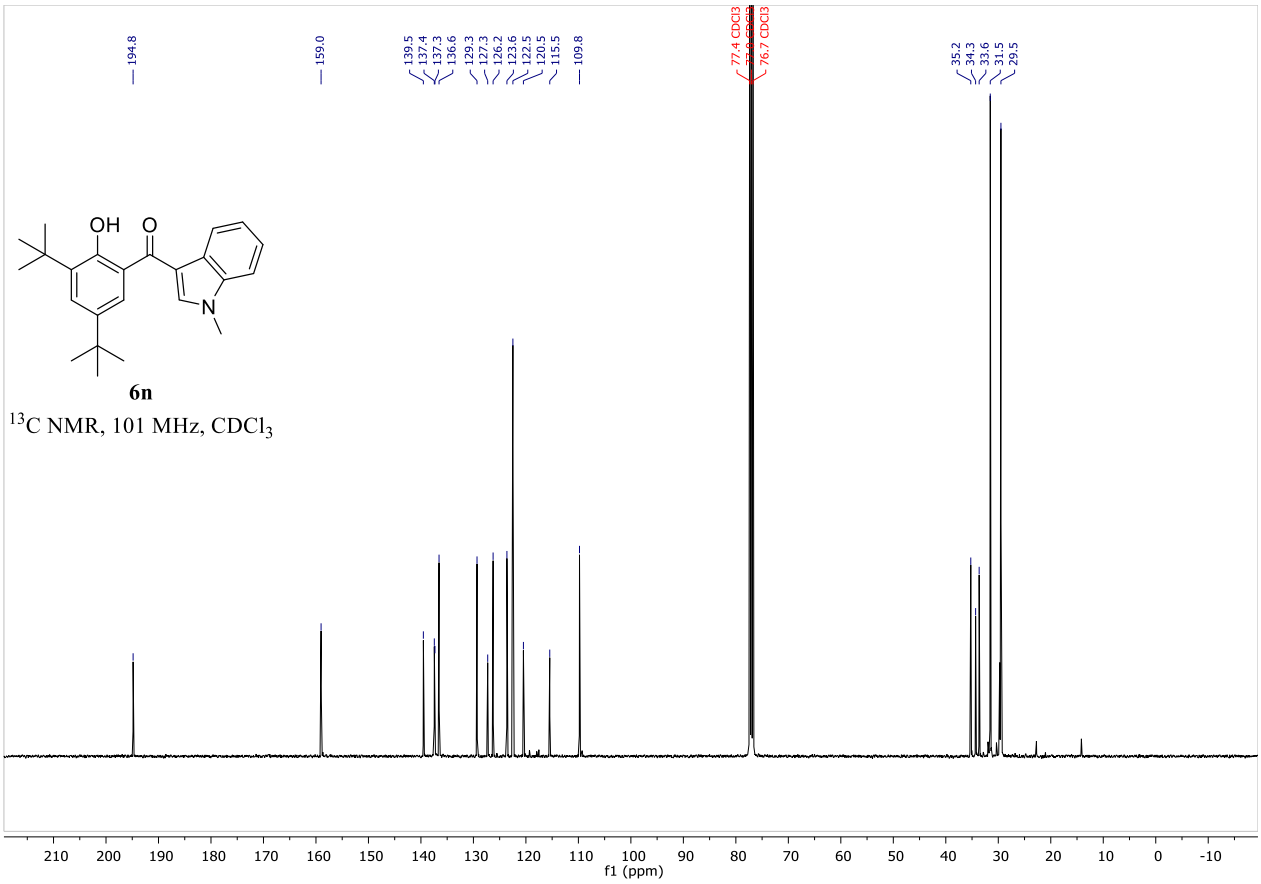
6m

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



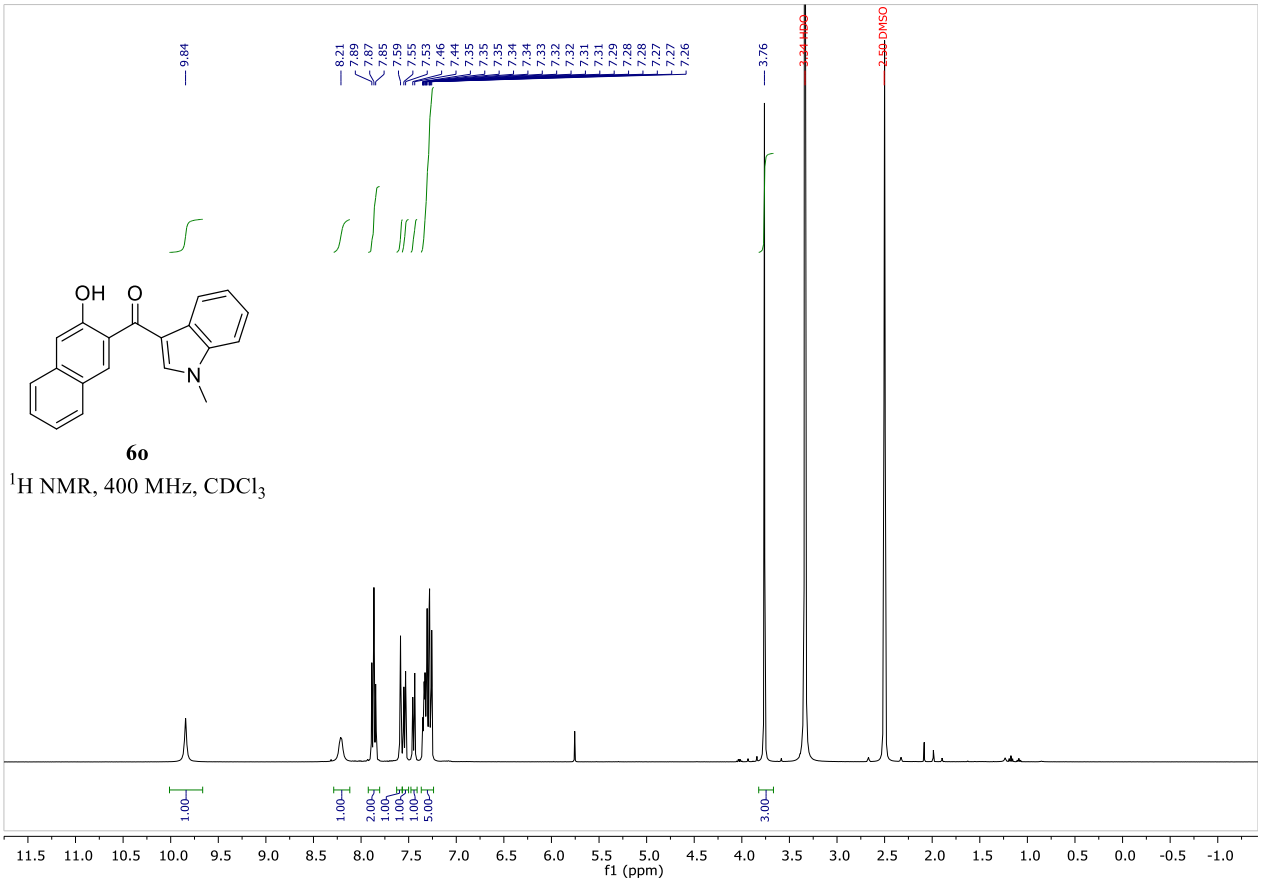
6n

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



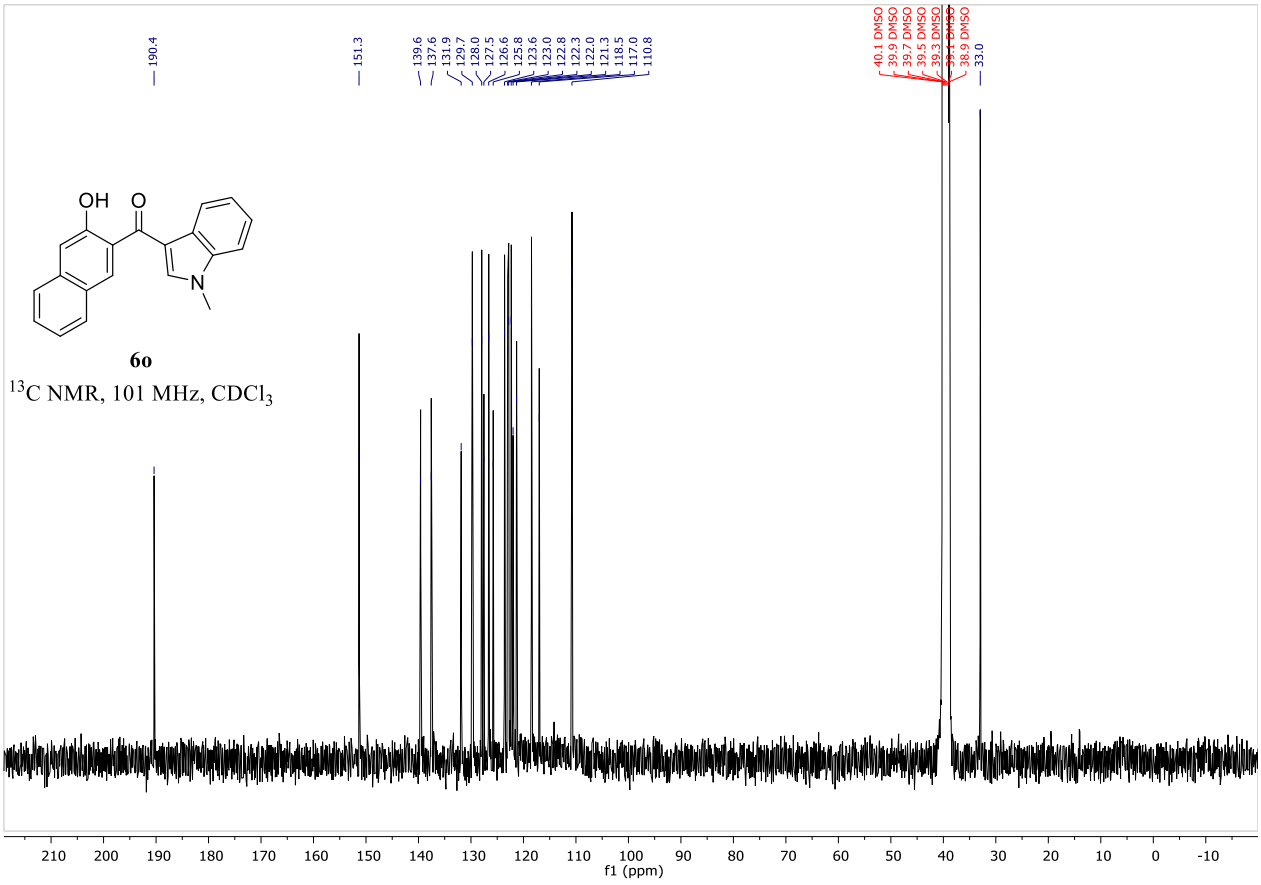
6n

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



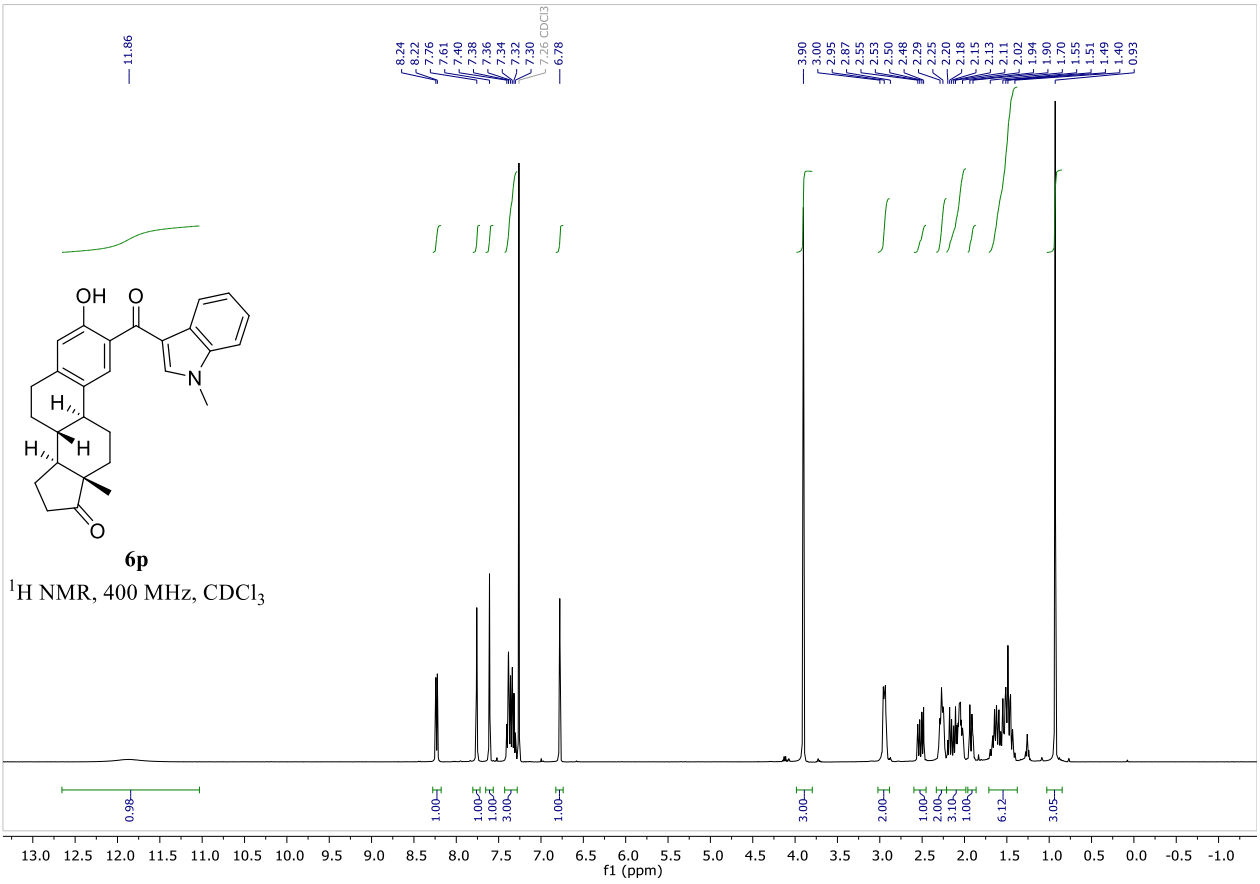
6o

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



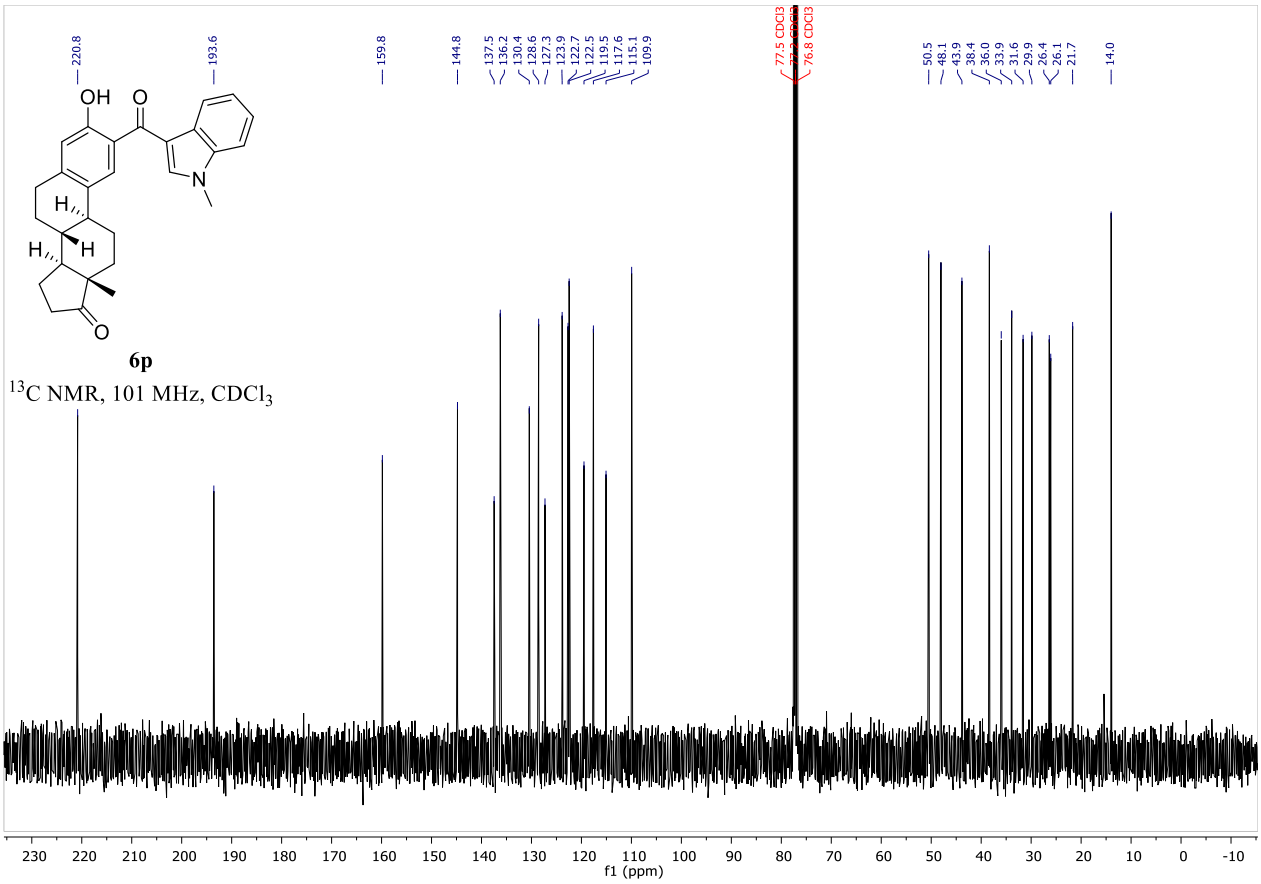
6o

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



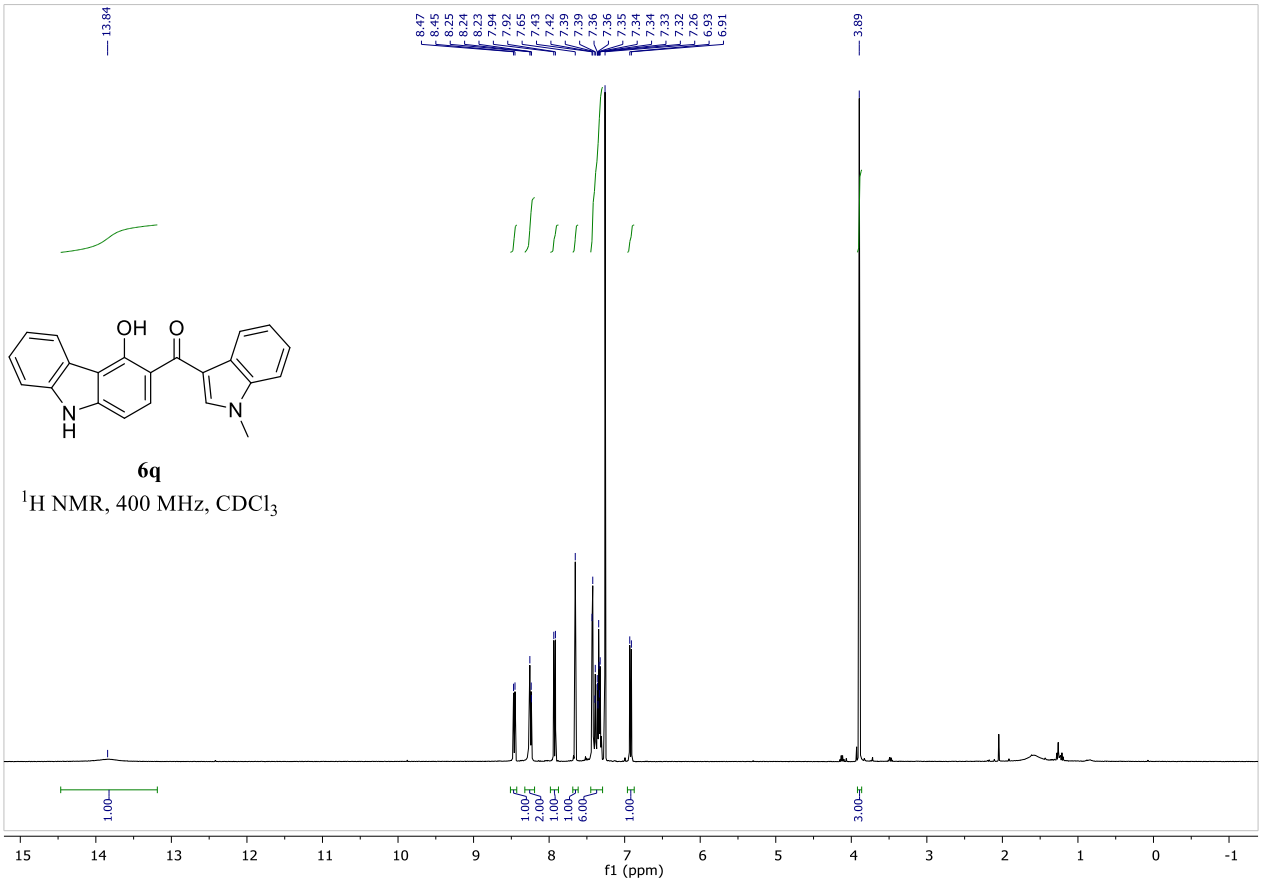
6p

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



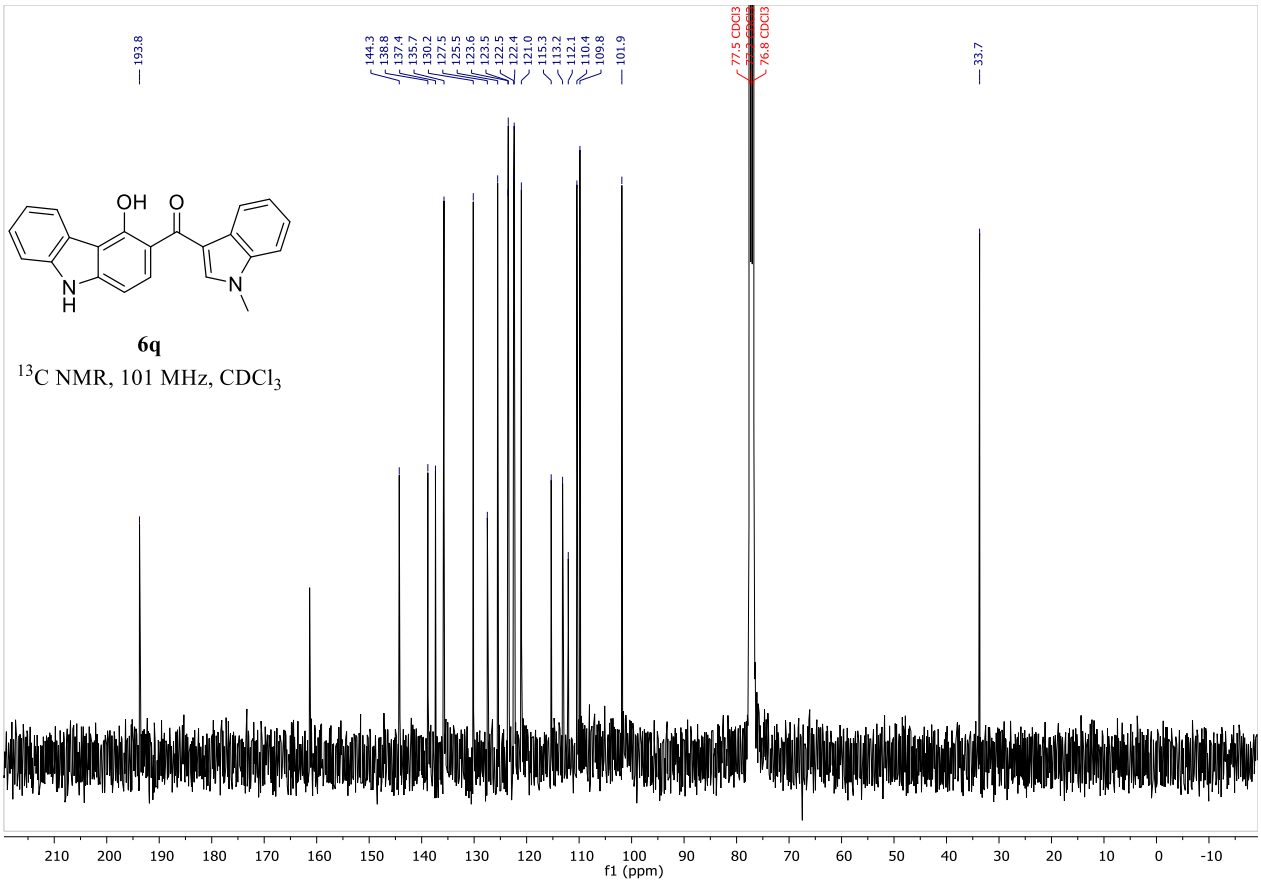
6p

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



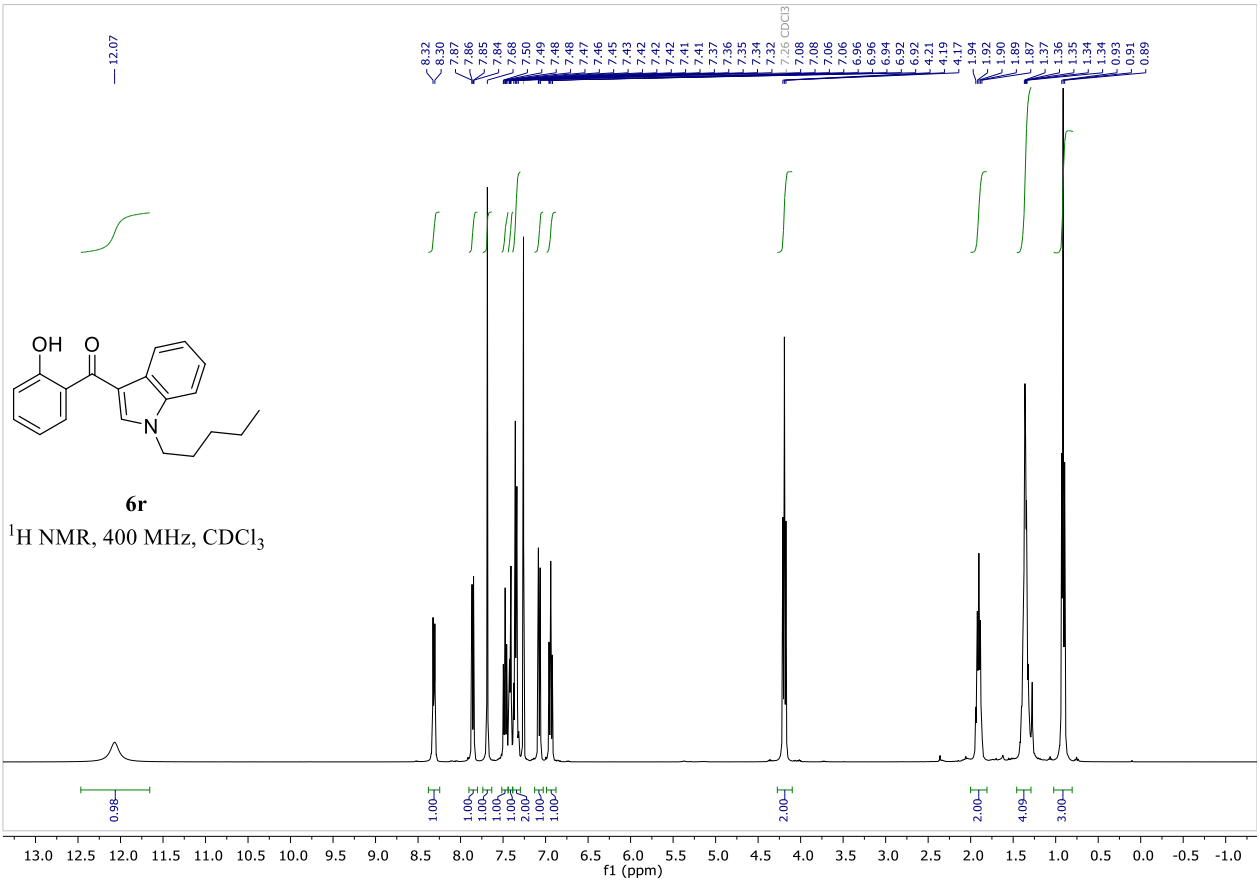
6q

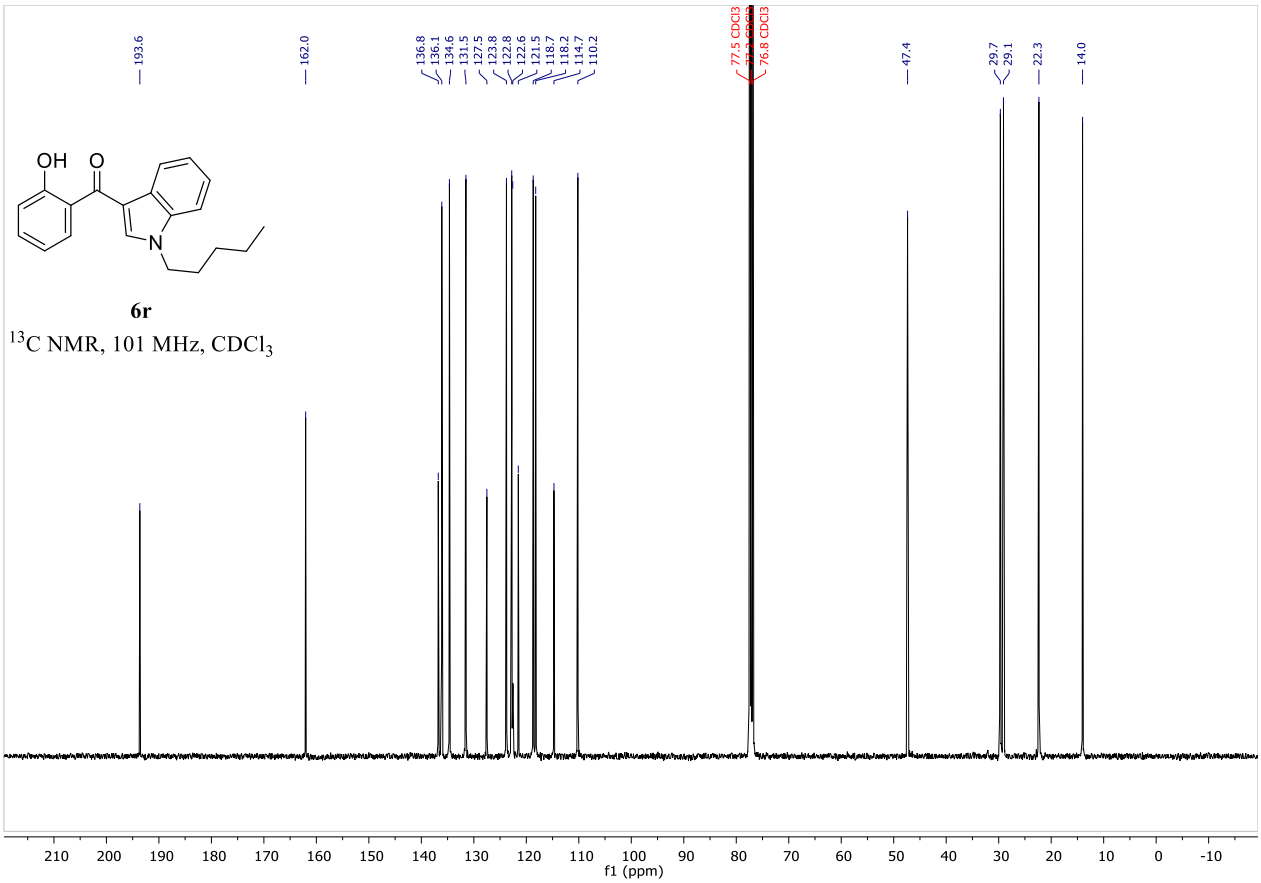
^{1}H NMR, 400 MHz, $CDCl_3$

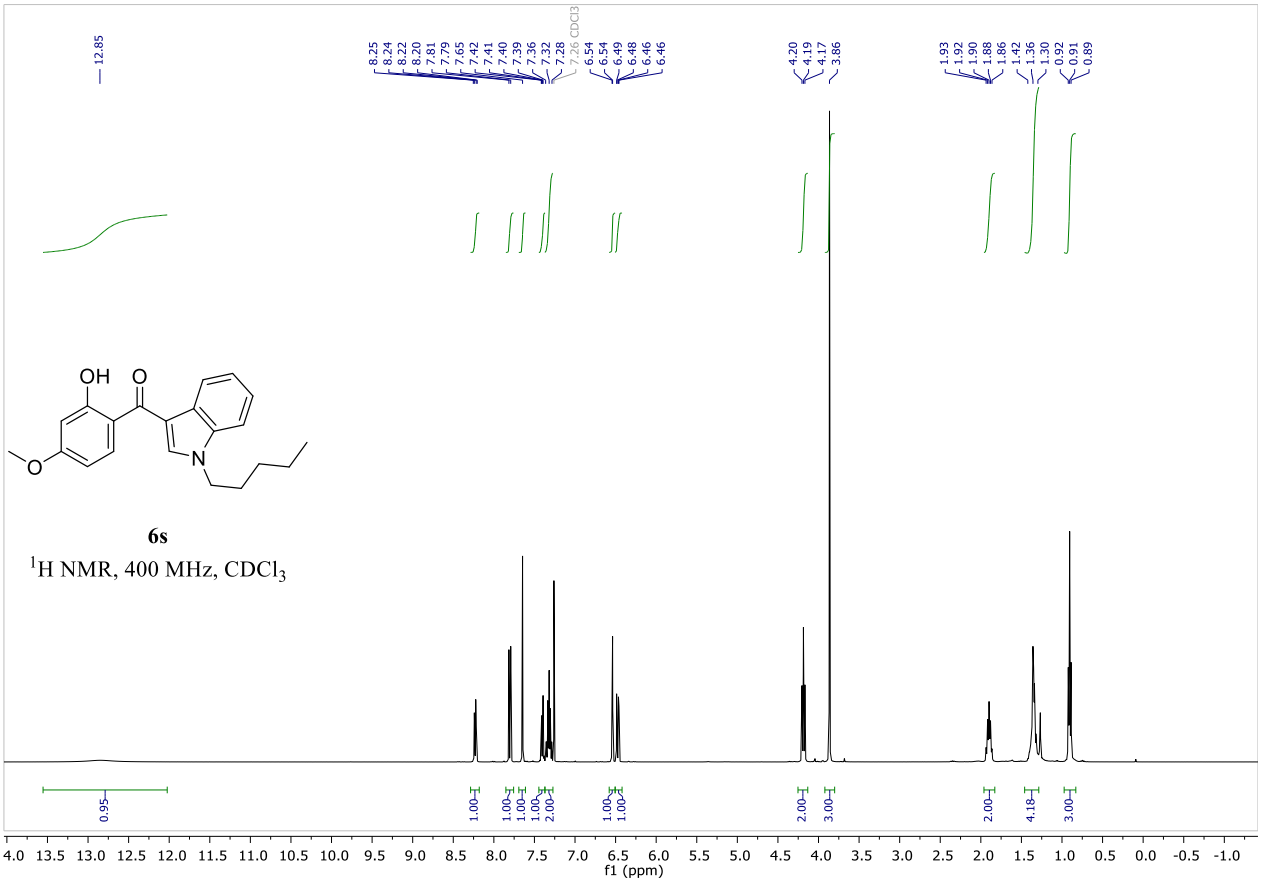


6q

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

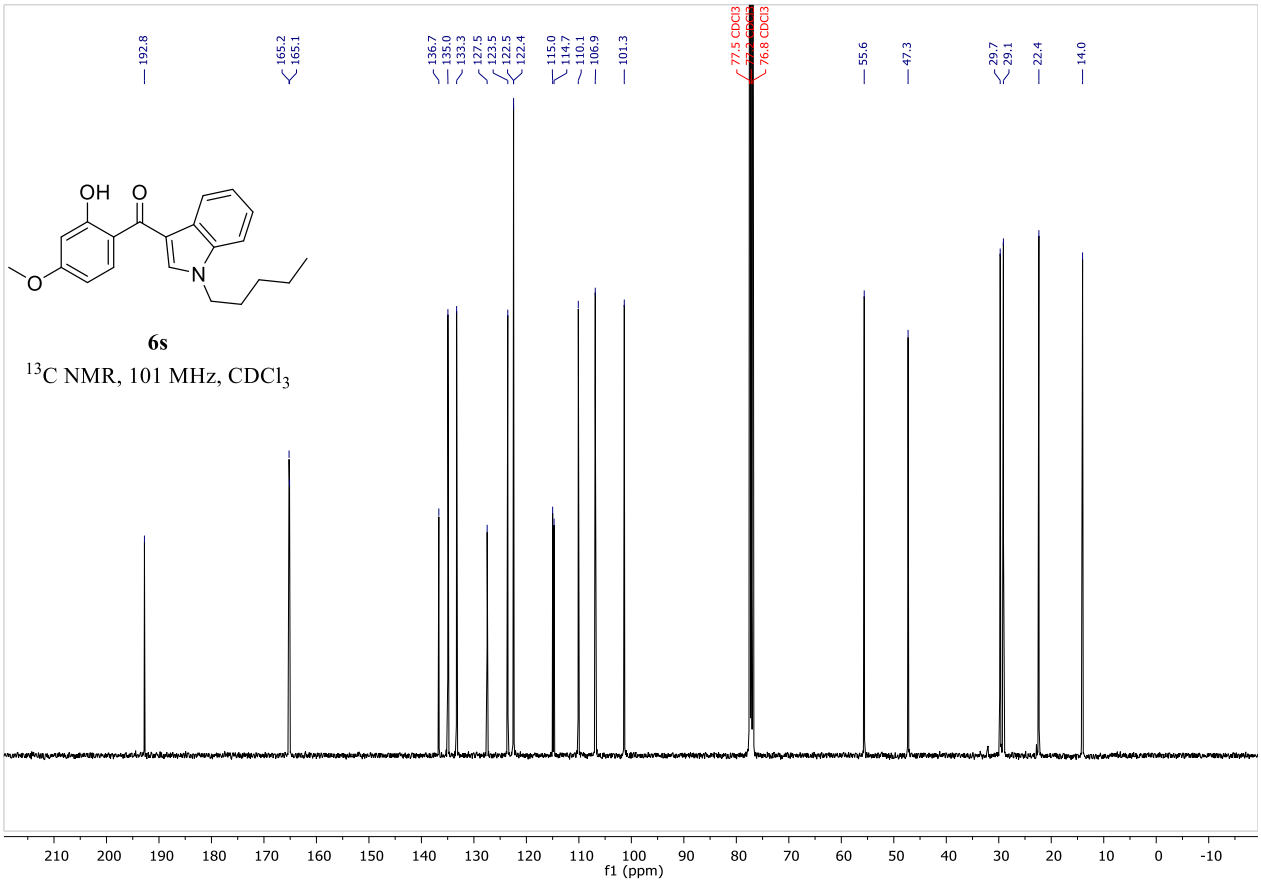

OH
O
N
6r
^{1}H NMR, 400 MHz, $CDCl_3$
f1 (ppm)


OH
O
N
6r
^{13}C NMR, 101 MHz, $CDCl_3$
f1 (ppm)



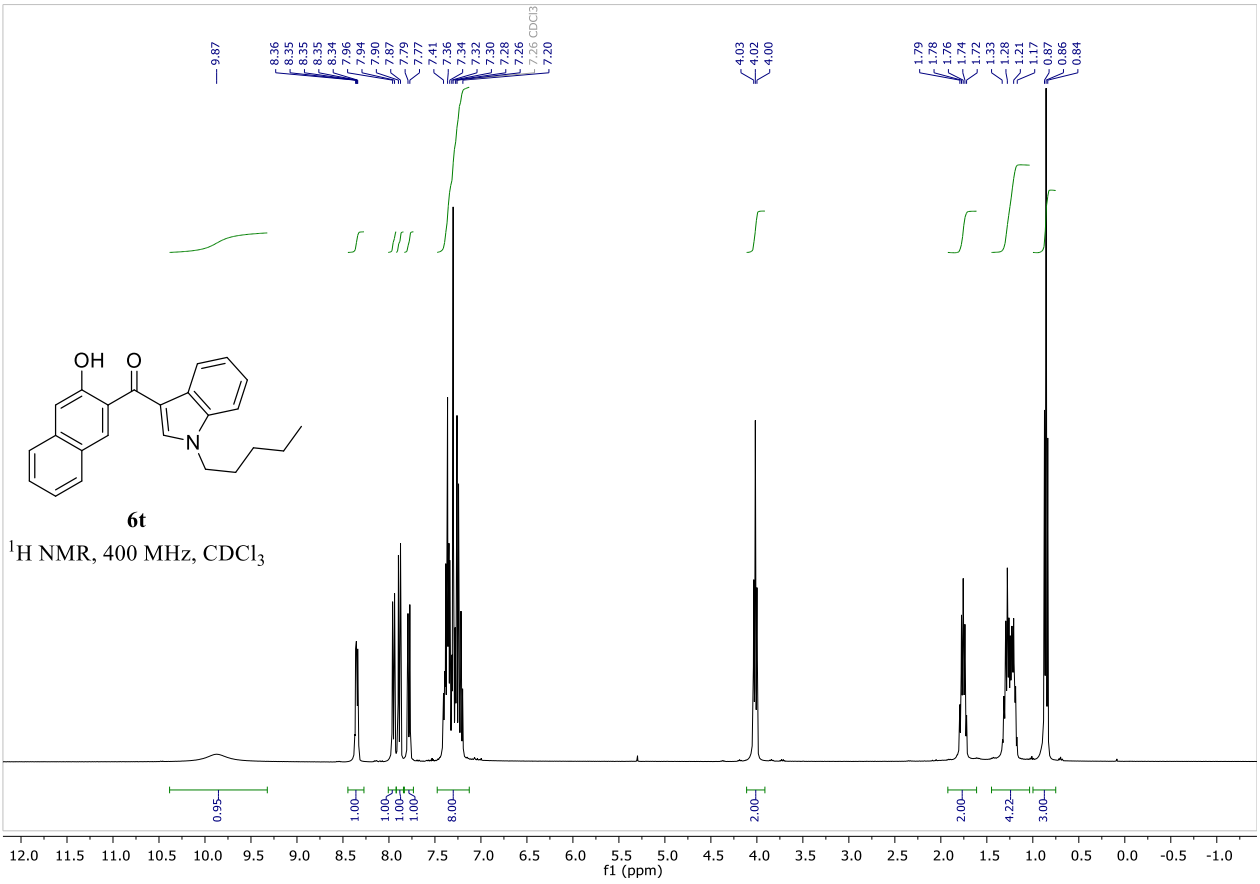
6s

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



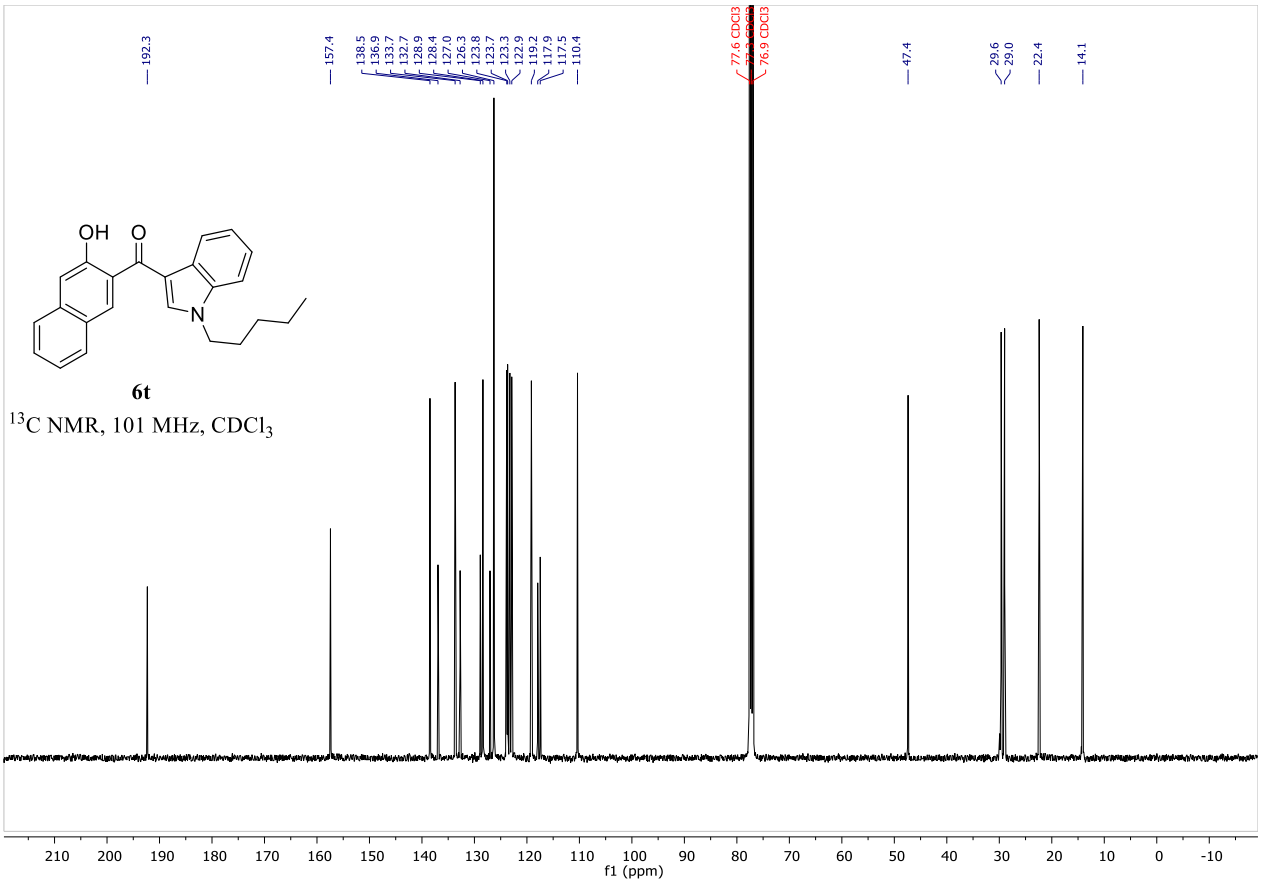
6s

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



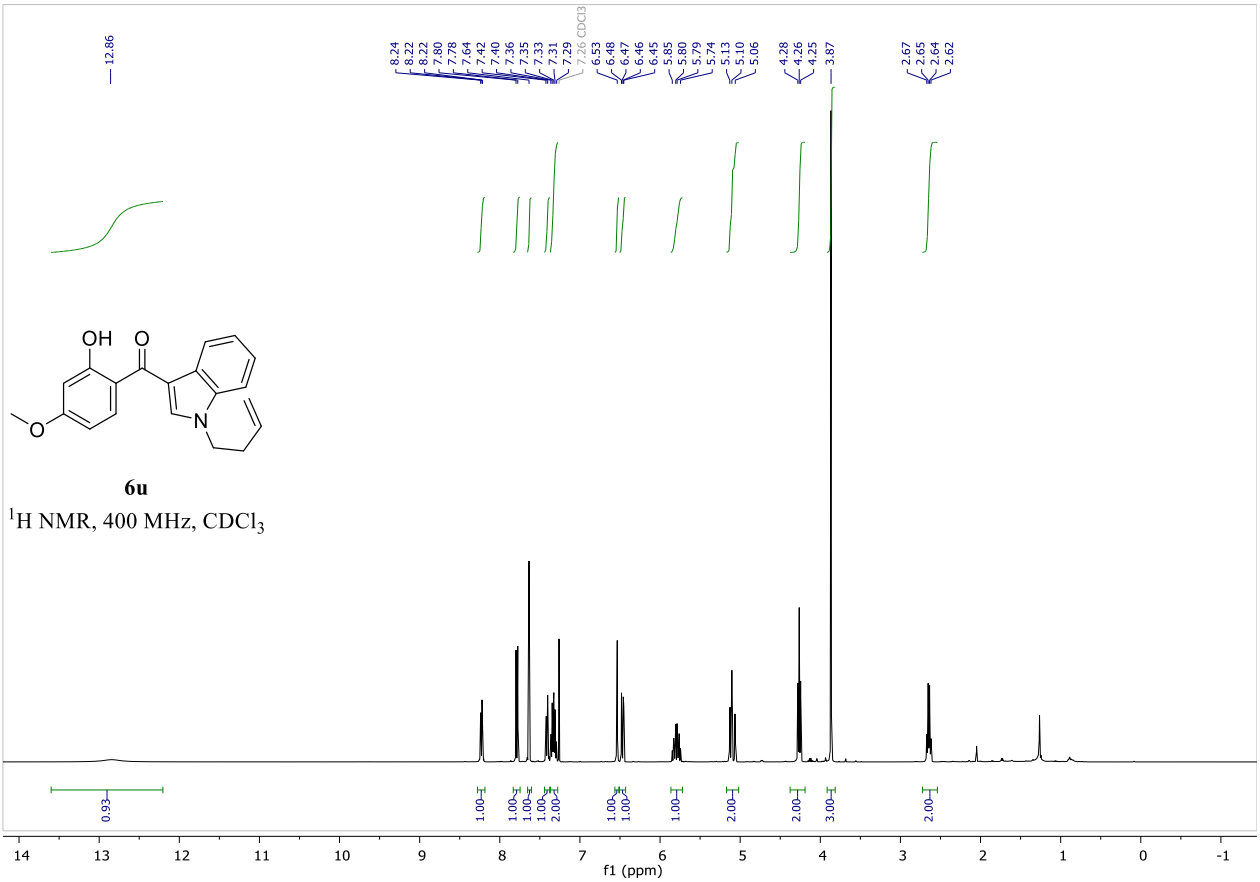
6t

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



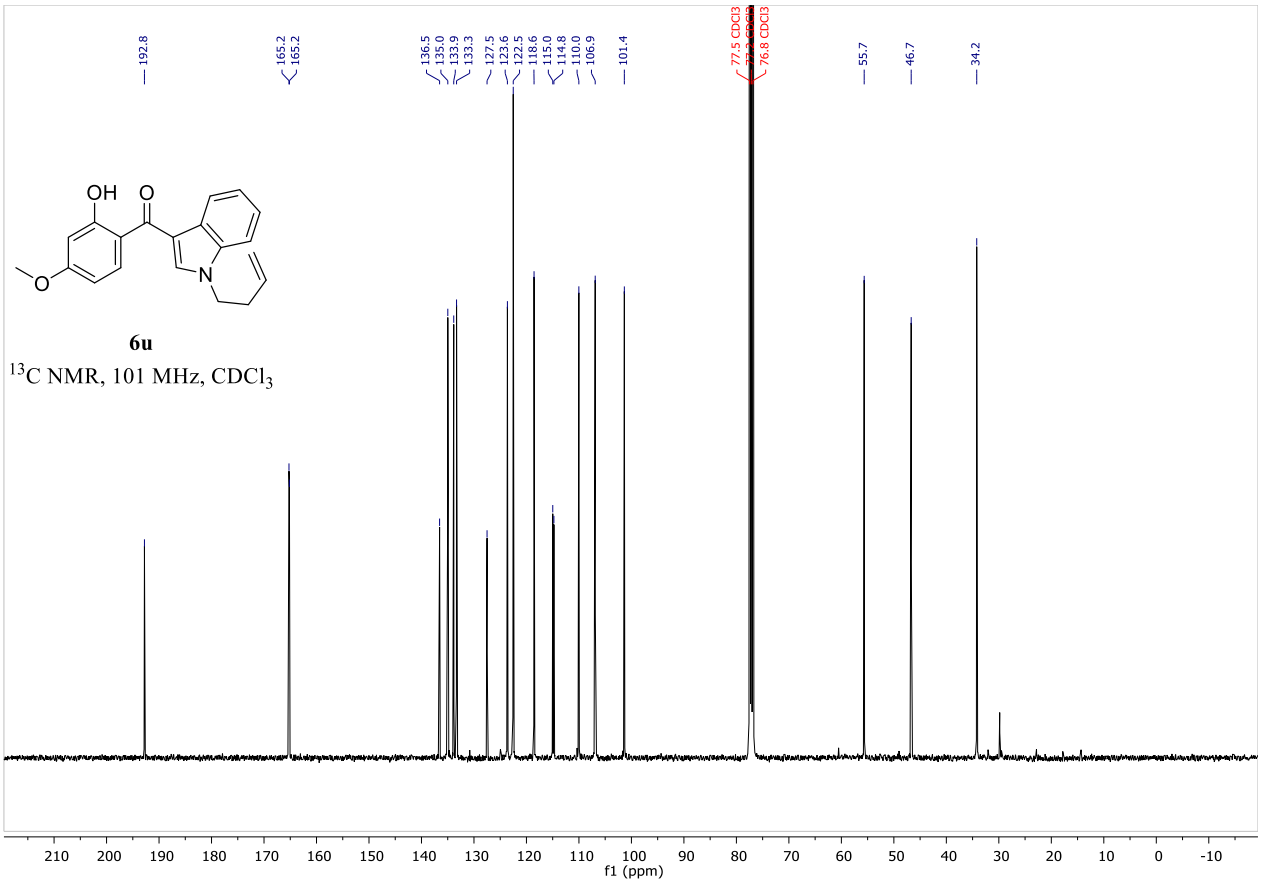
6t

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



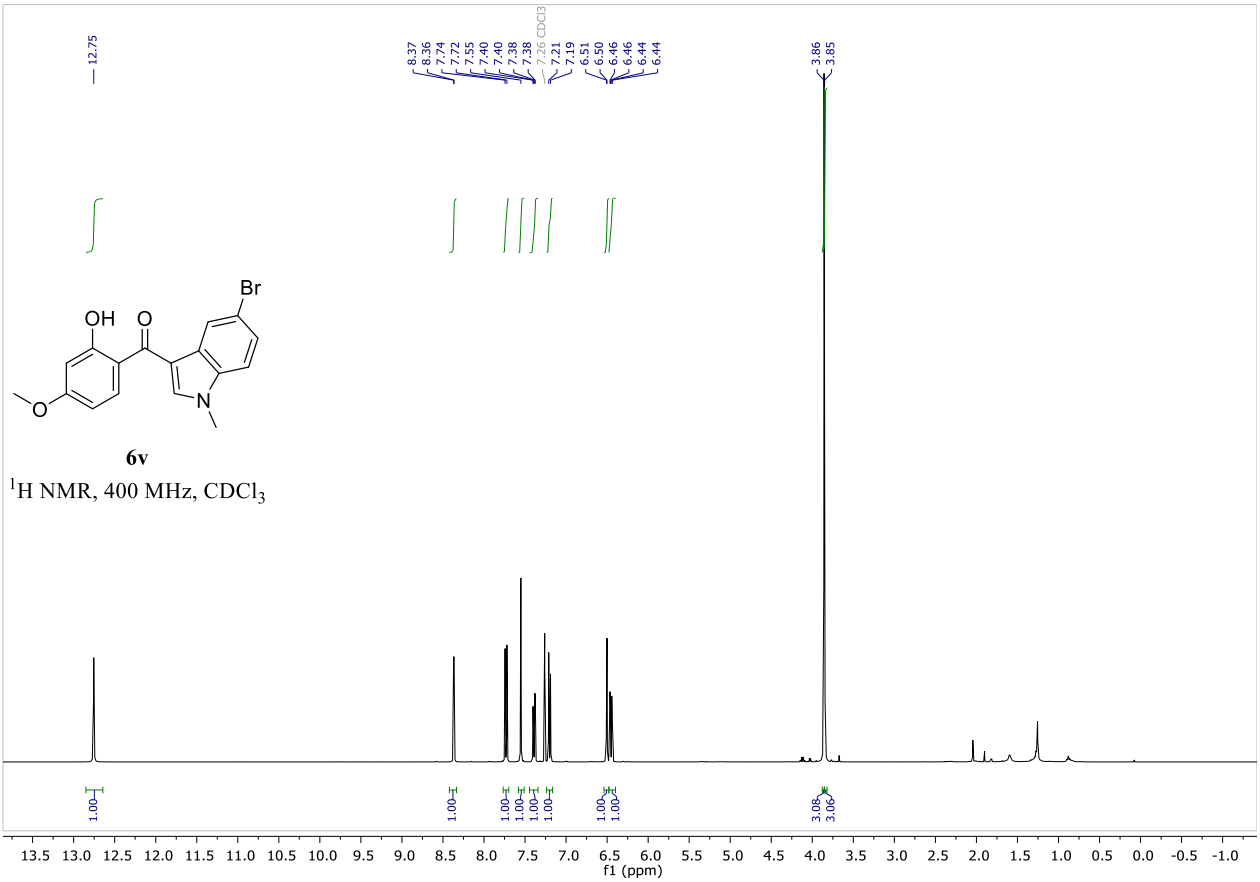
6u

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



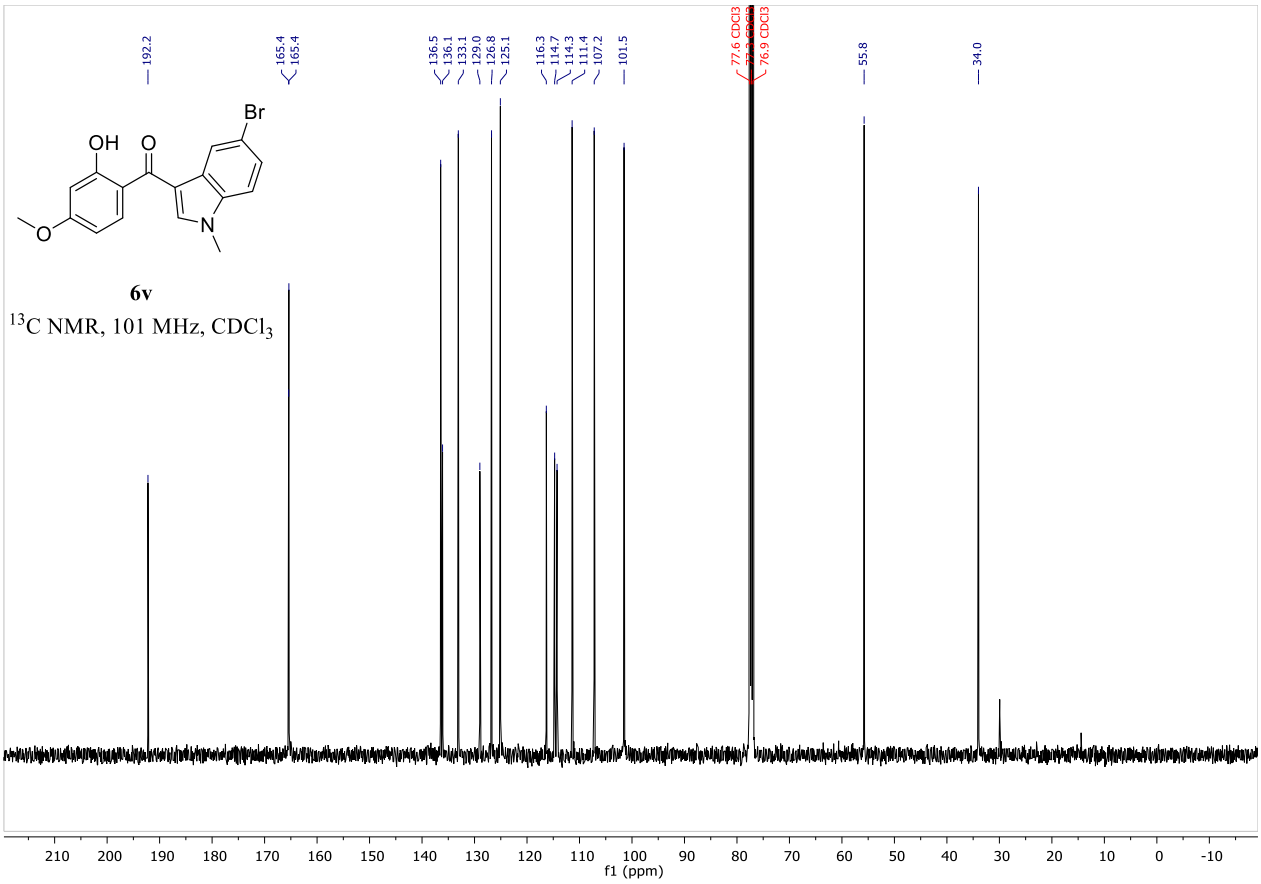
6u

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



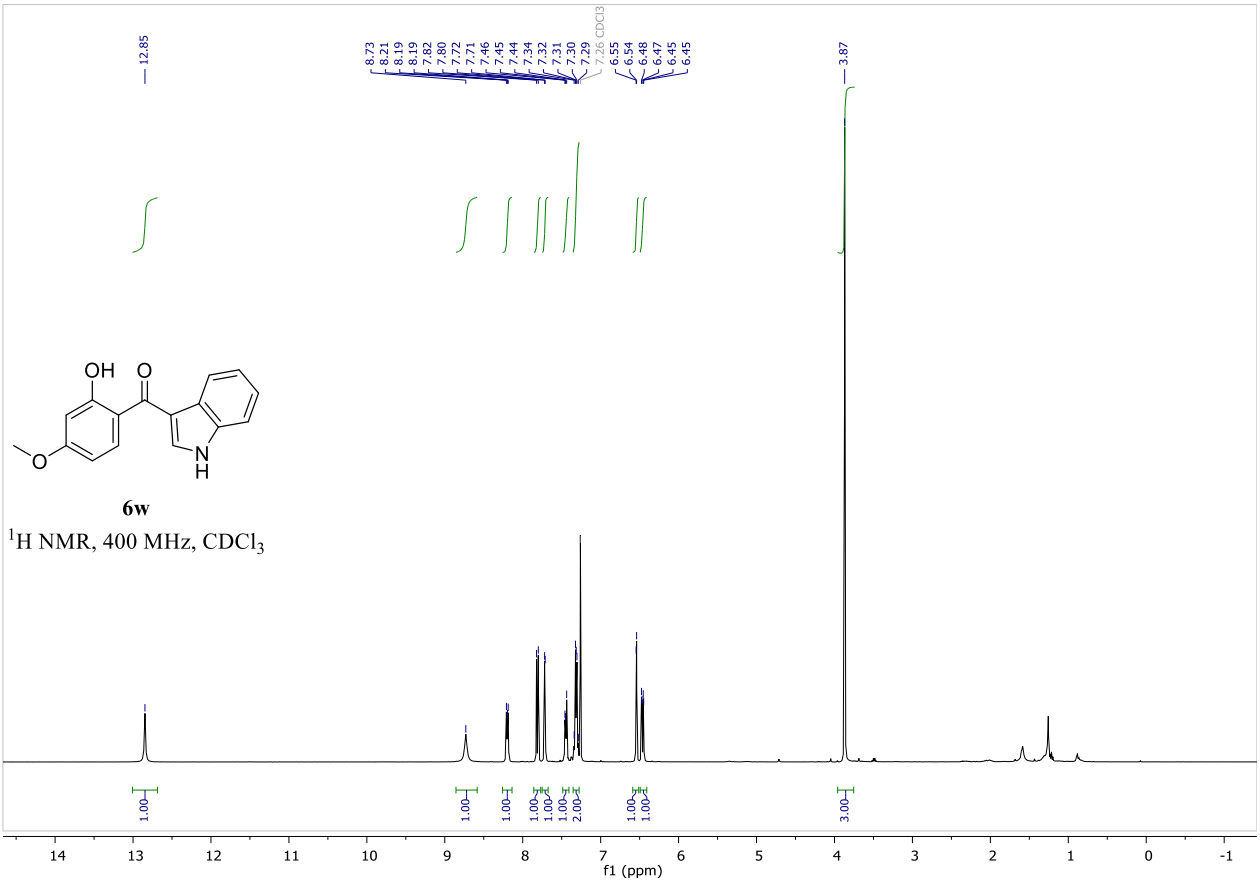
6v

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



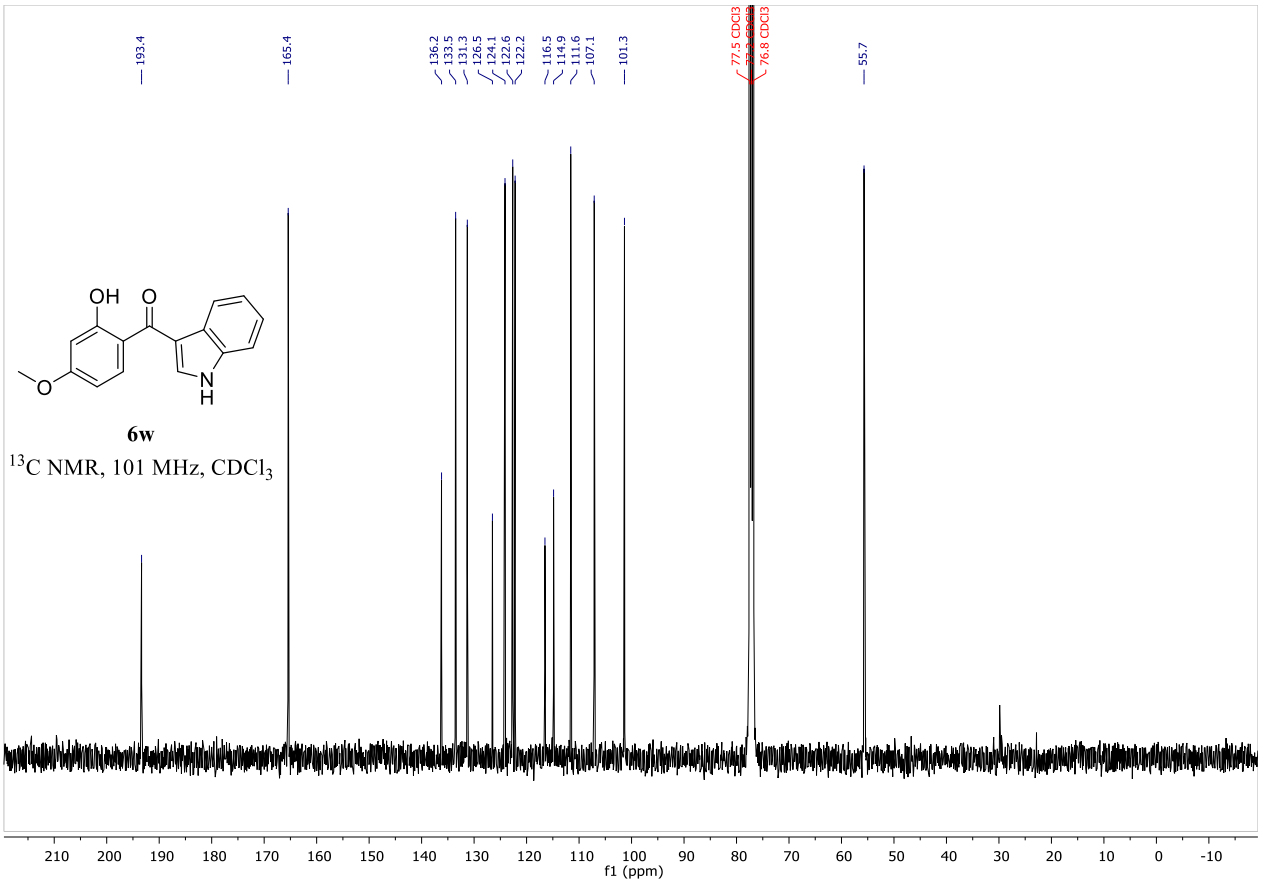
6v

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



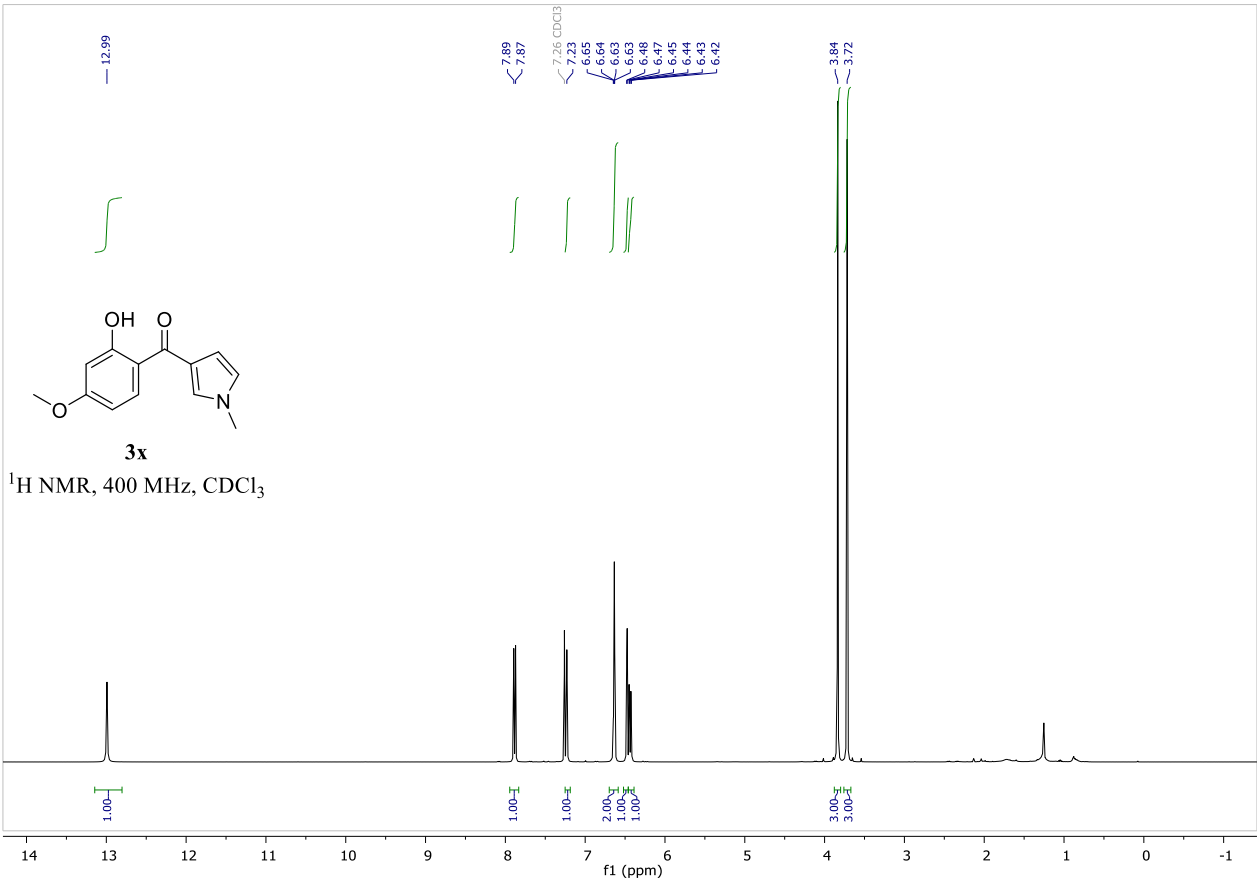
6w

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



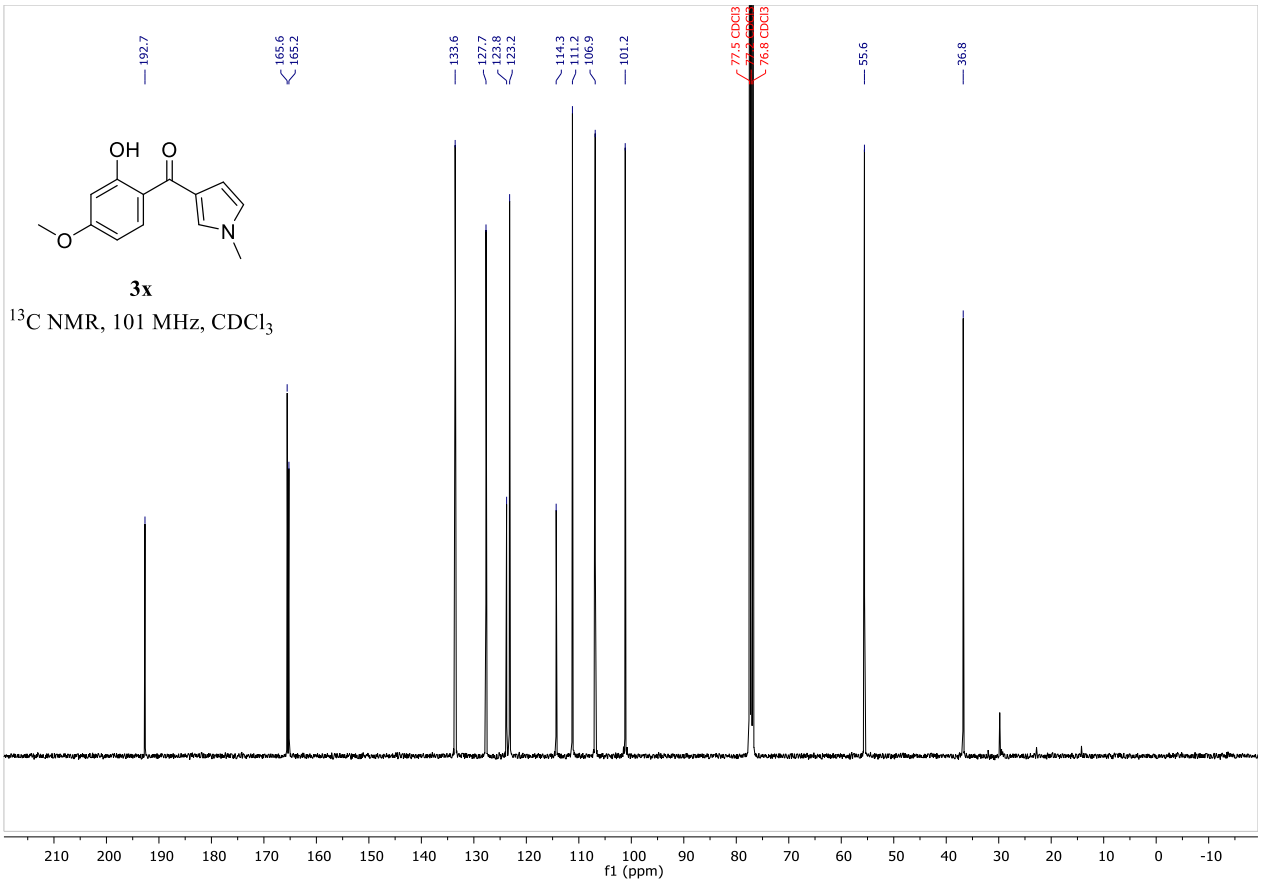
6w

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



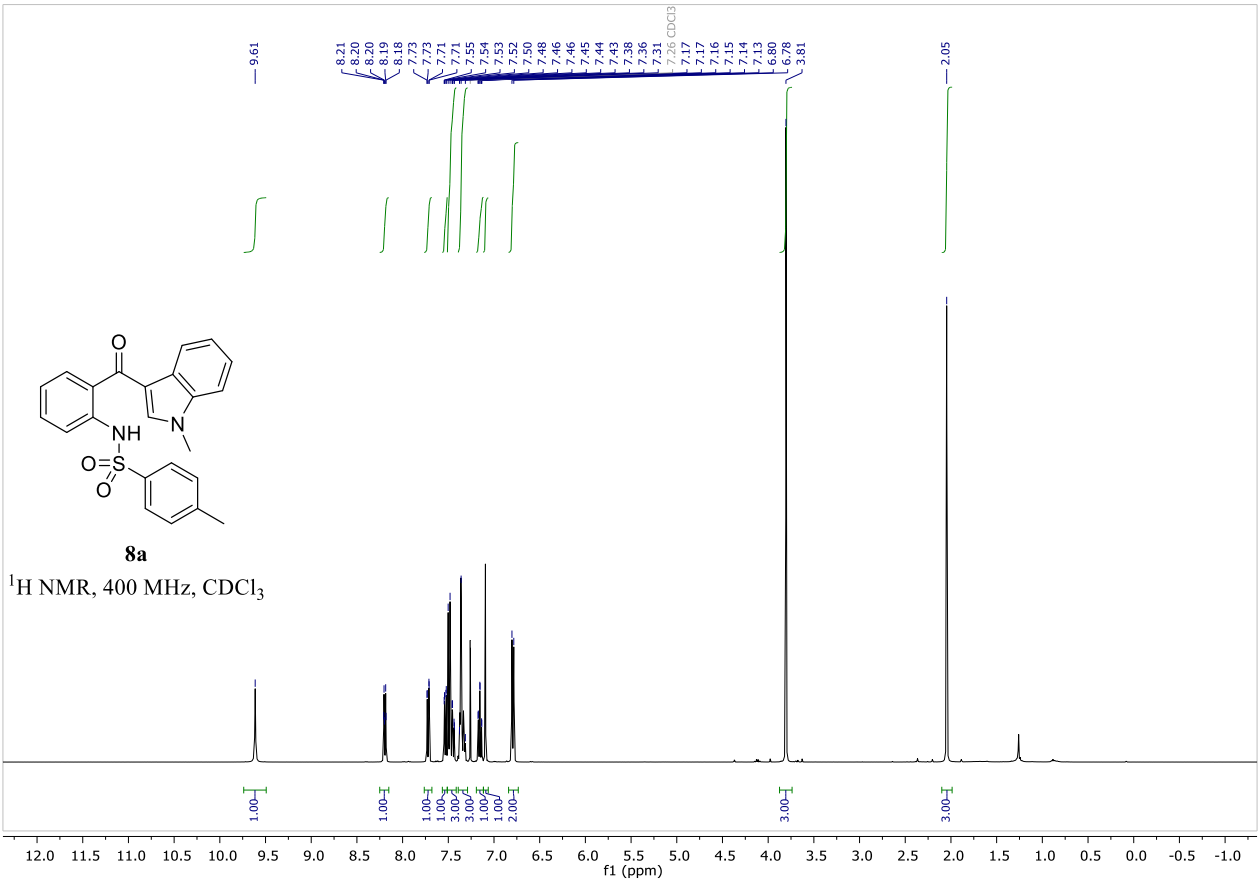
3x

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



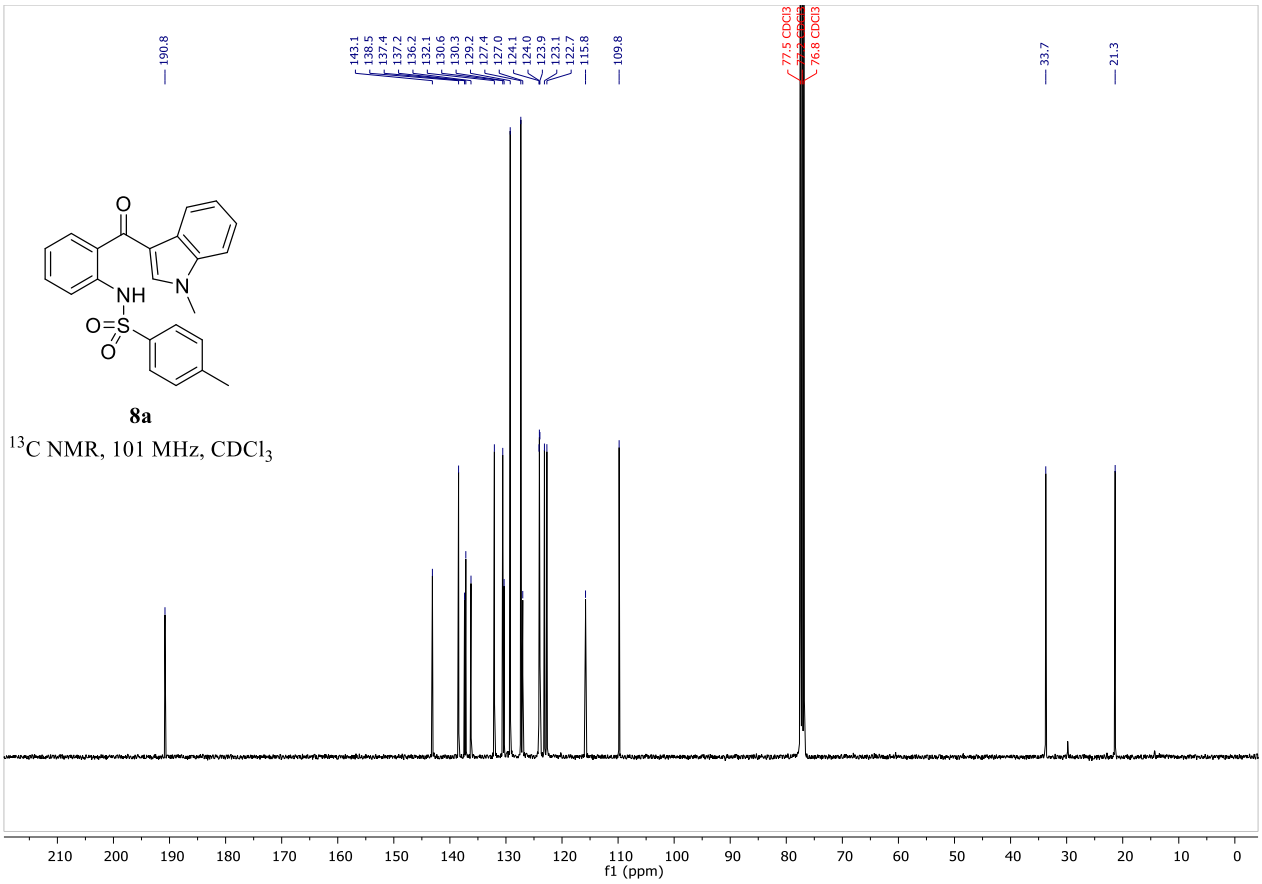
3x

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



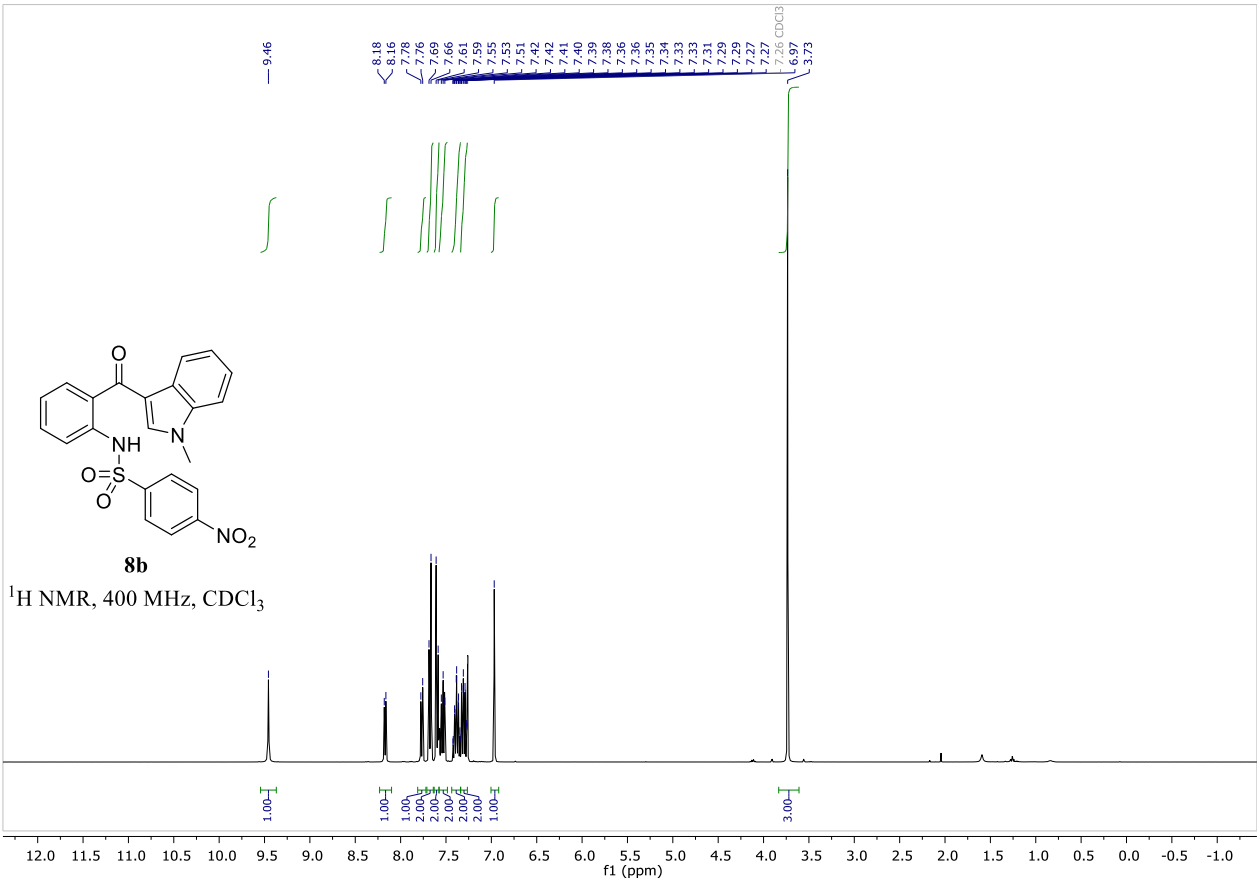
8a

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



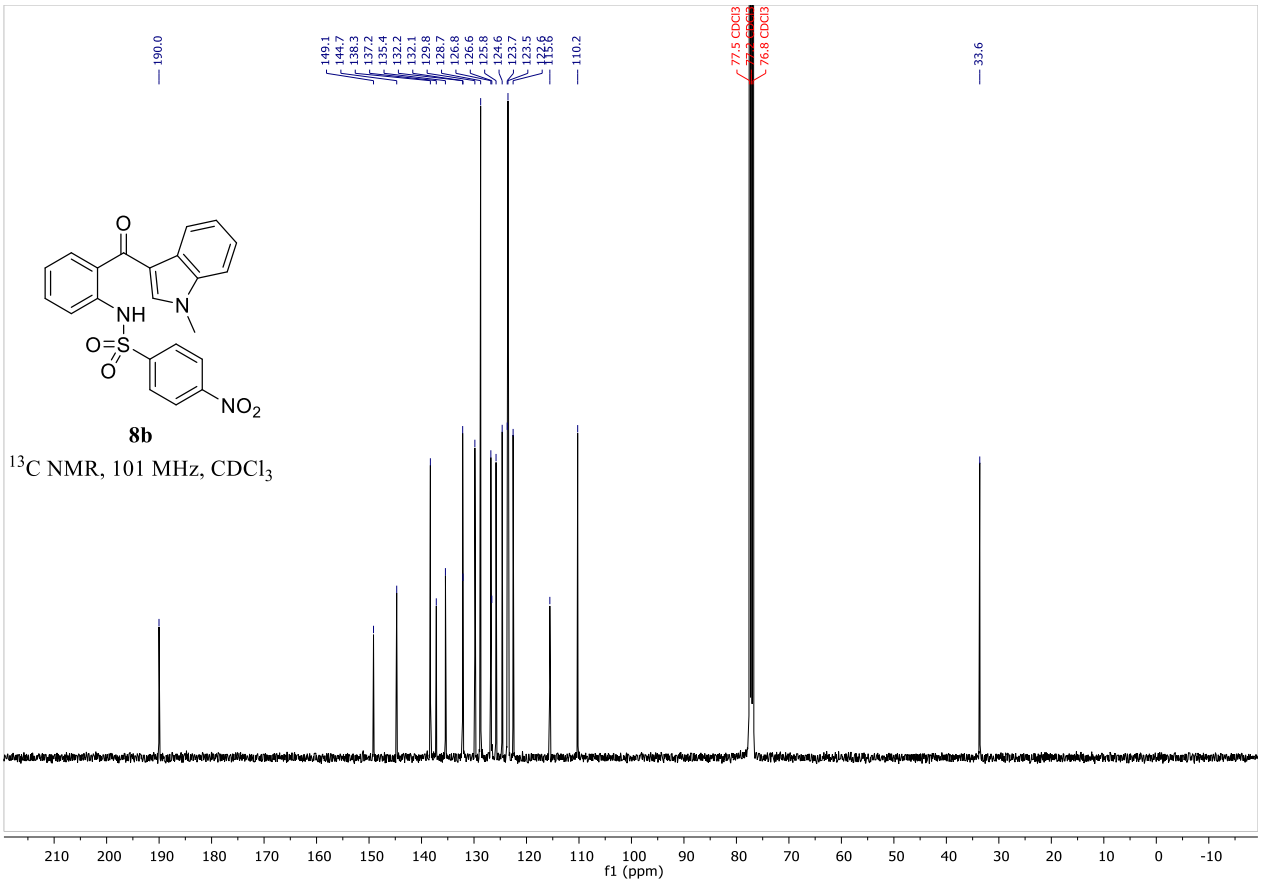
8a

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



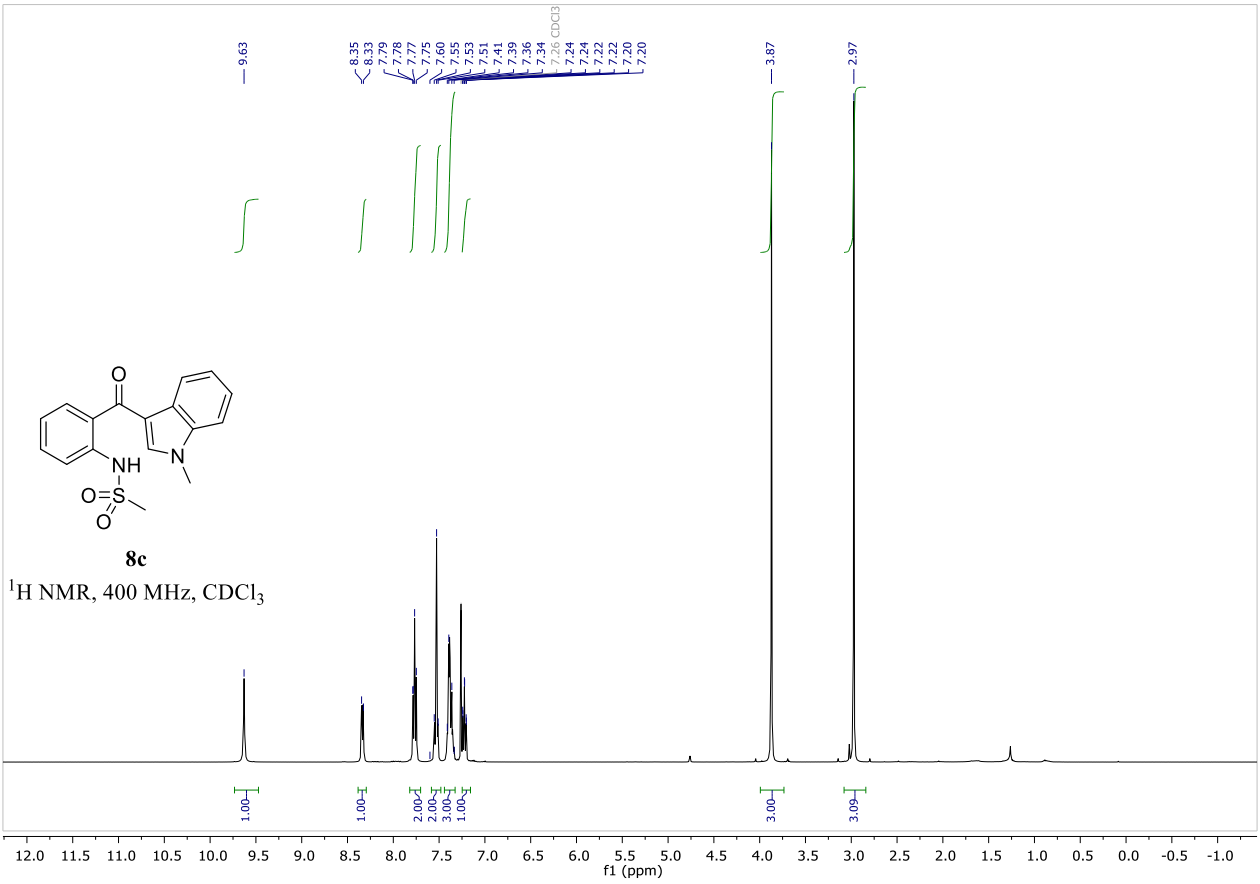
8b

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



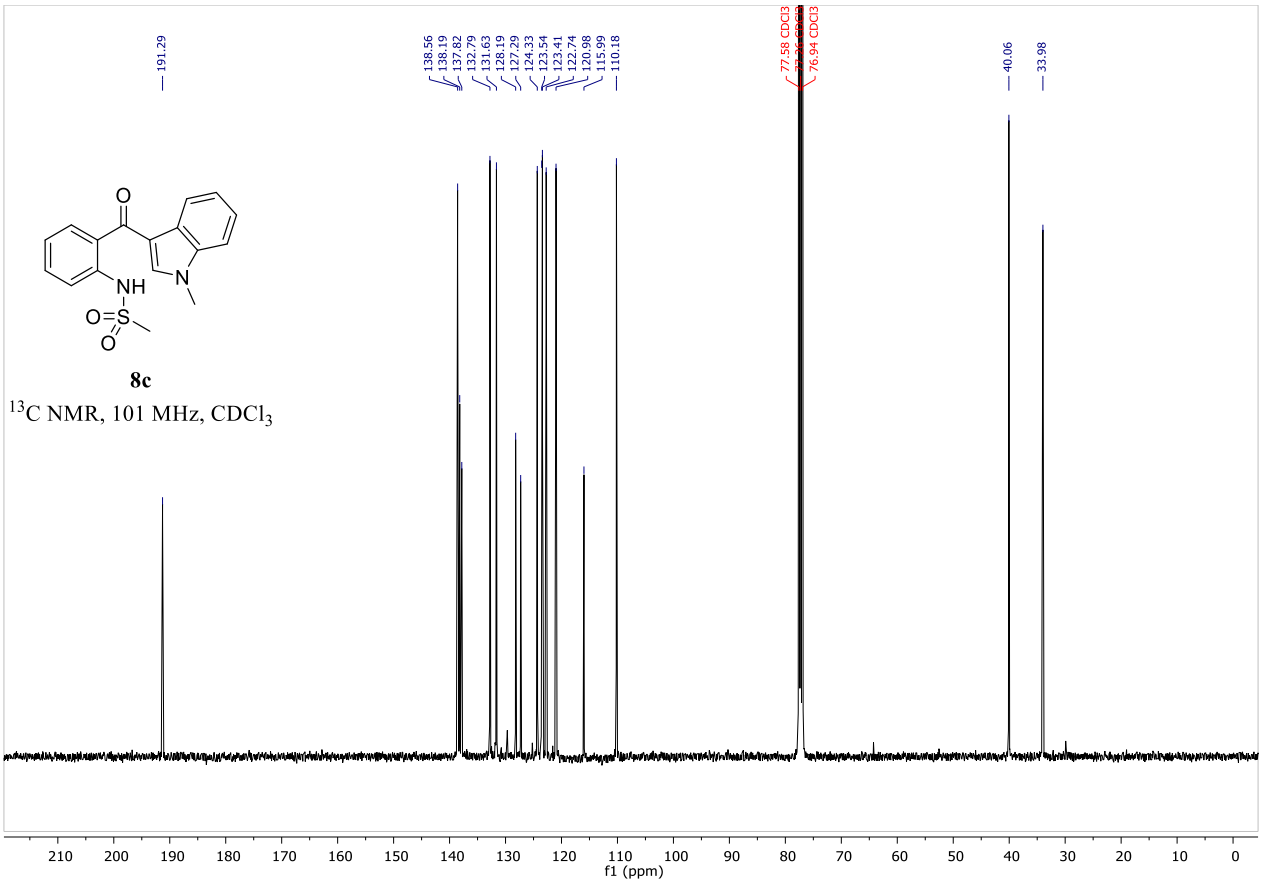
8b

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



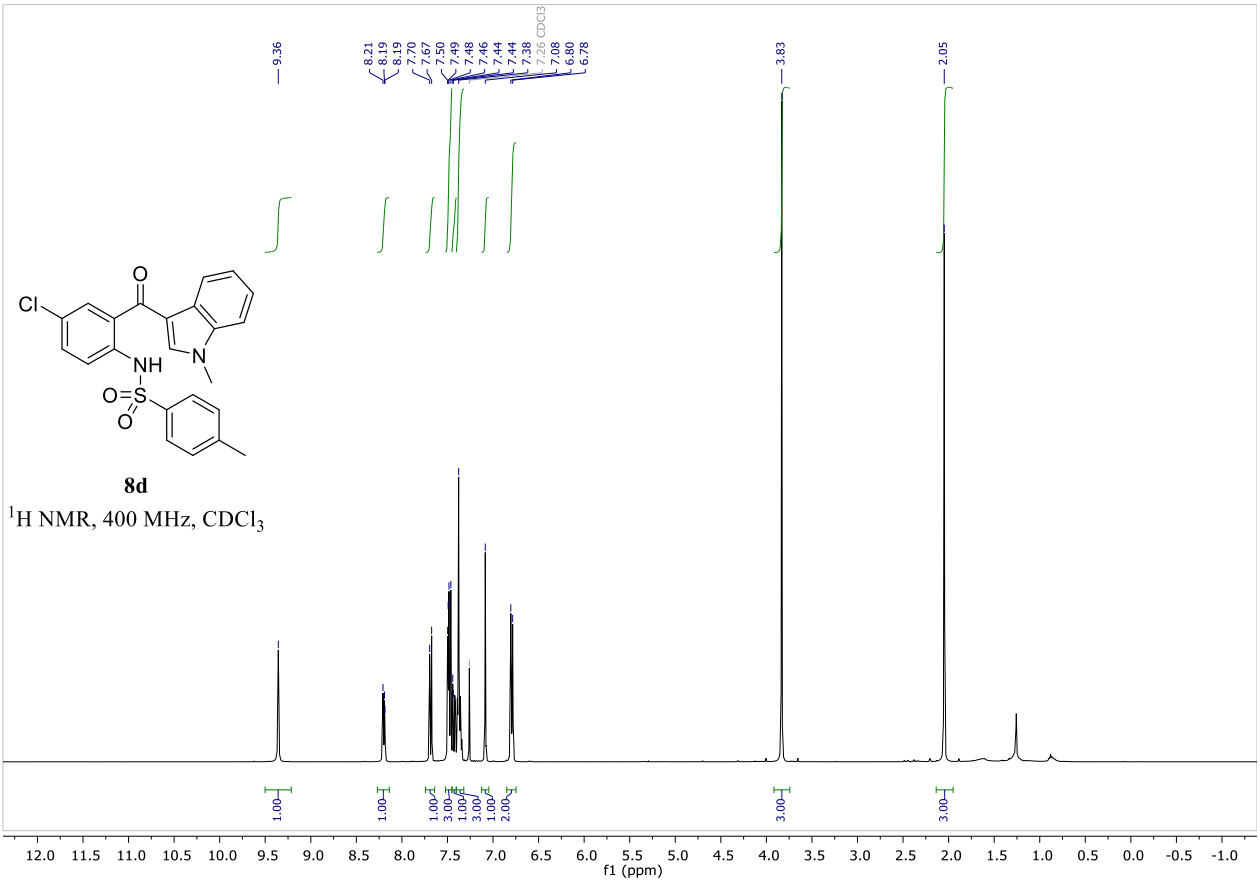
8c

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



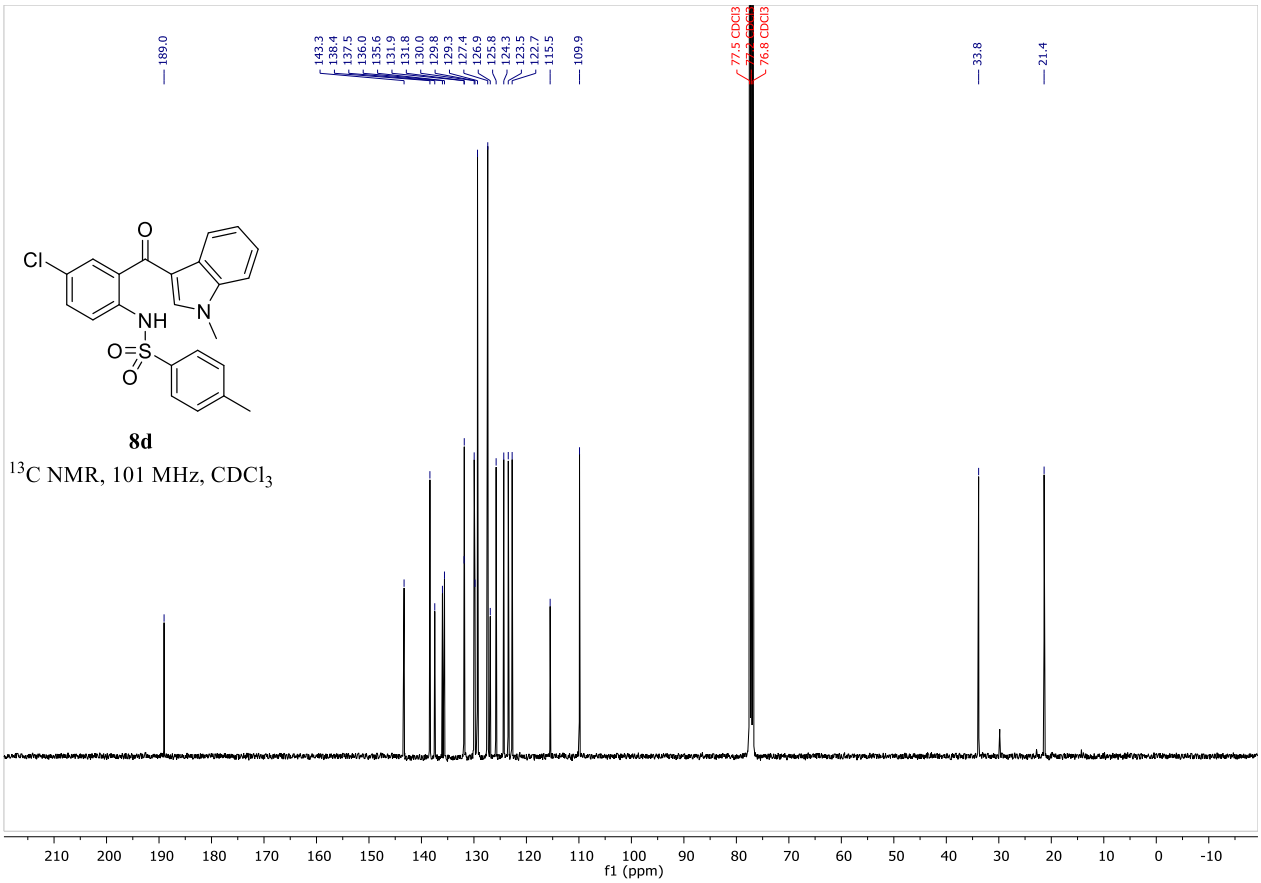
8c

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



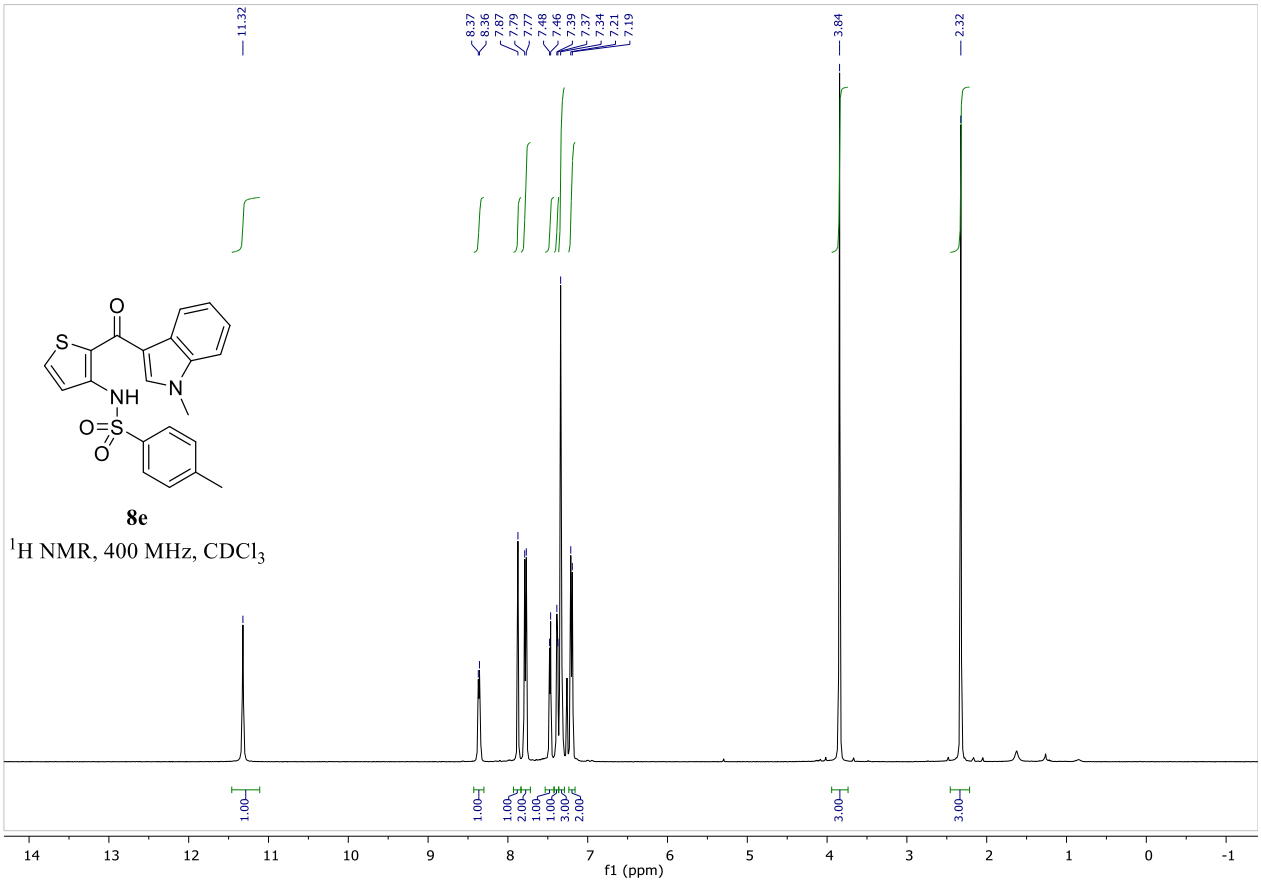
8d

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



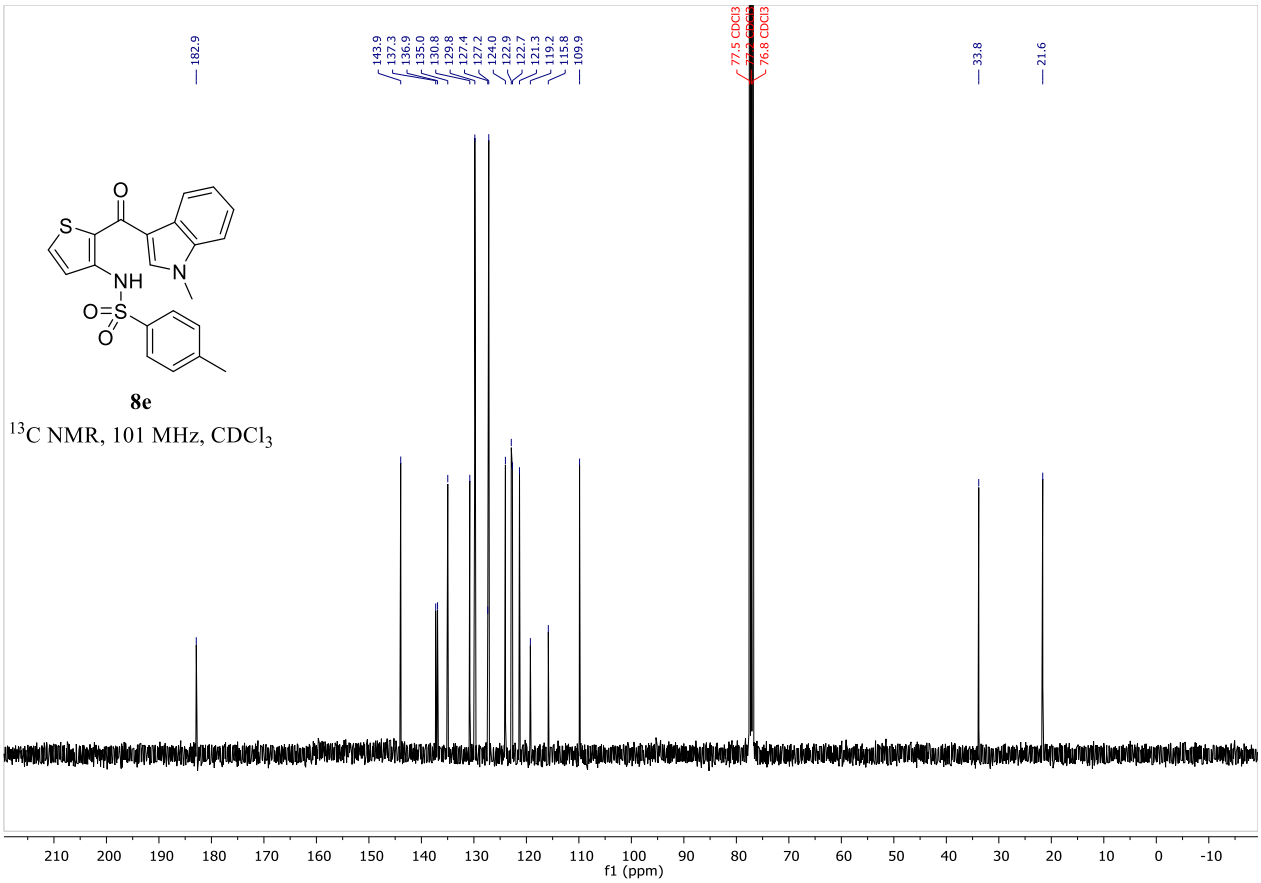
8d

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



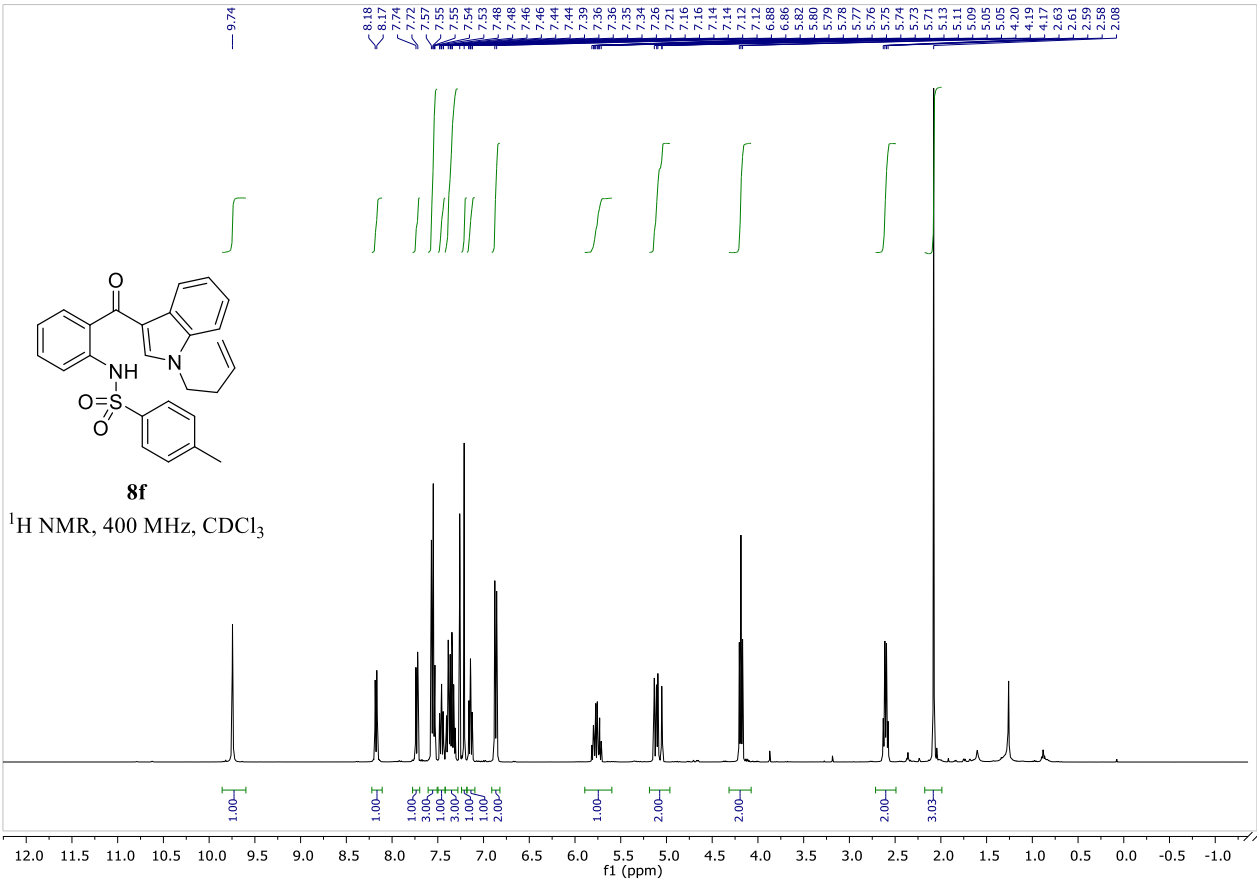
8e

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



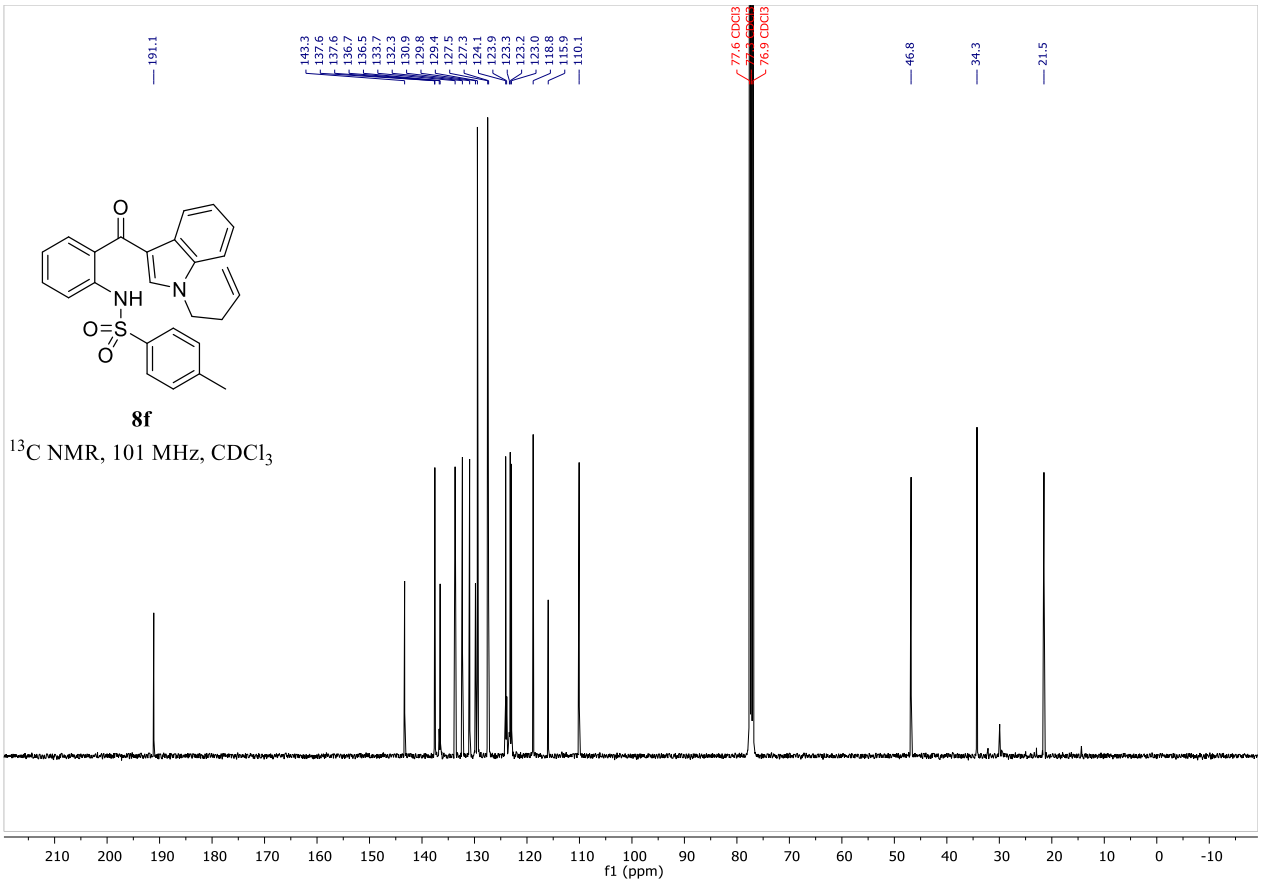
8e

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



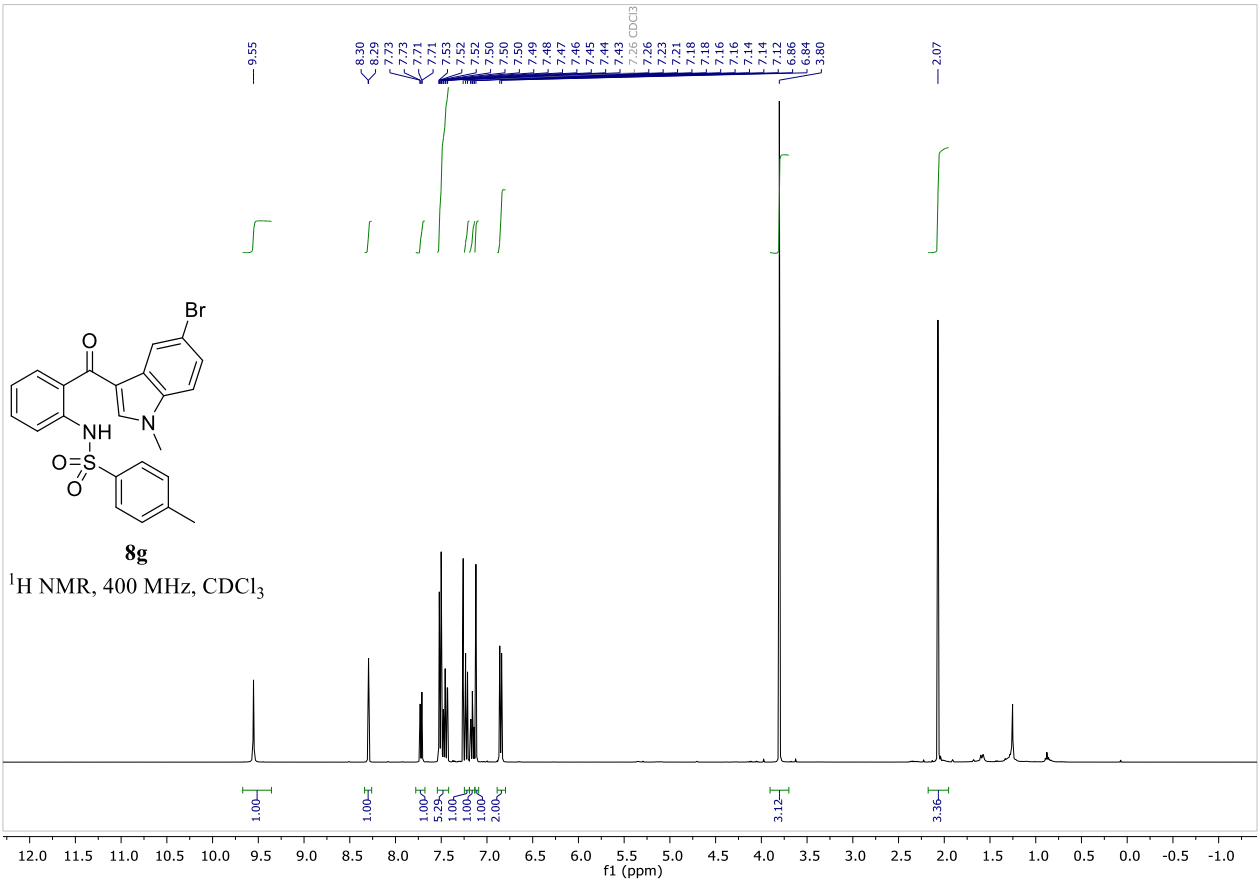
8f

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



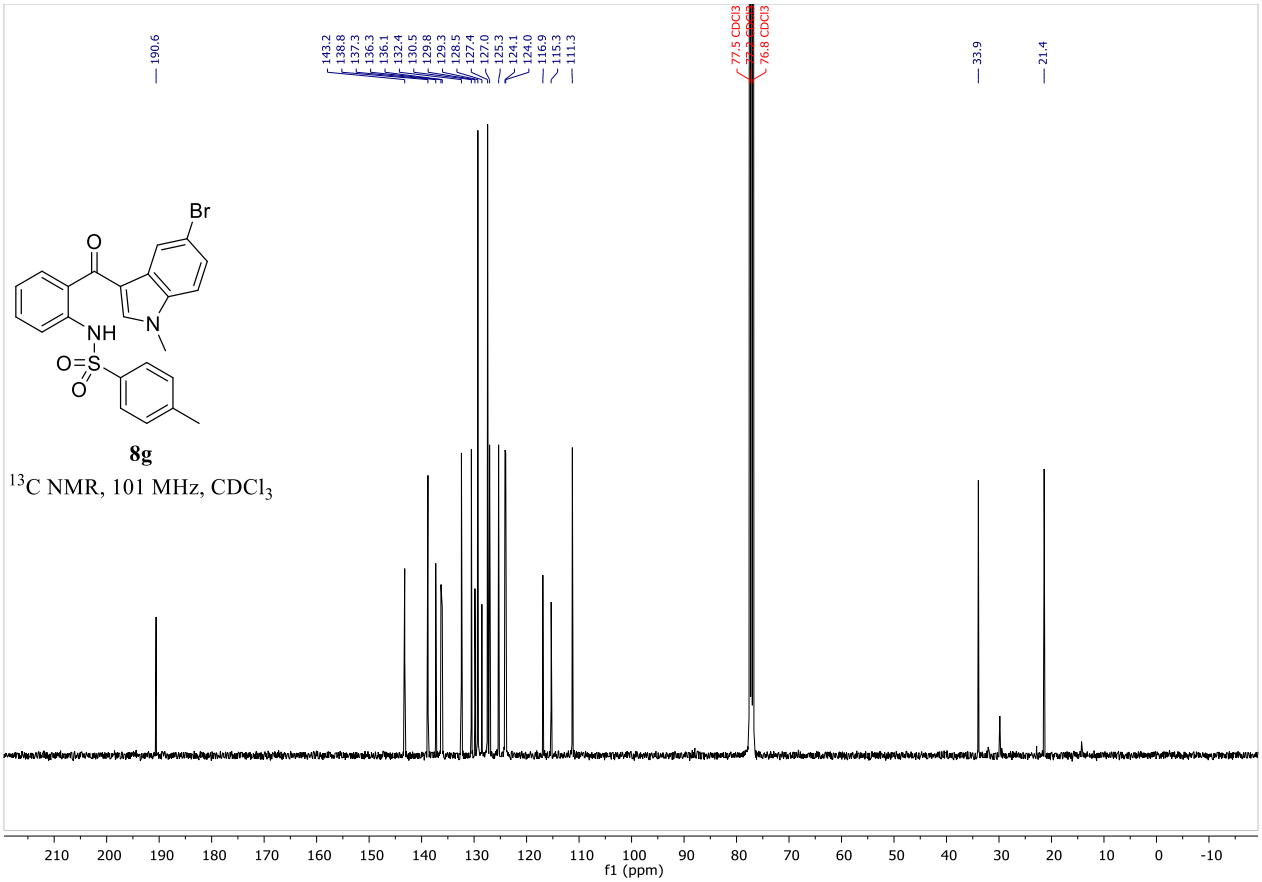
8f

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



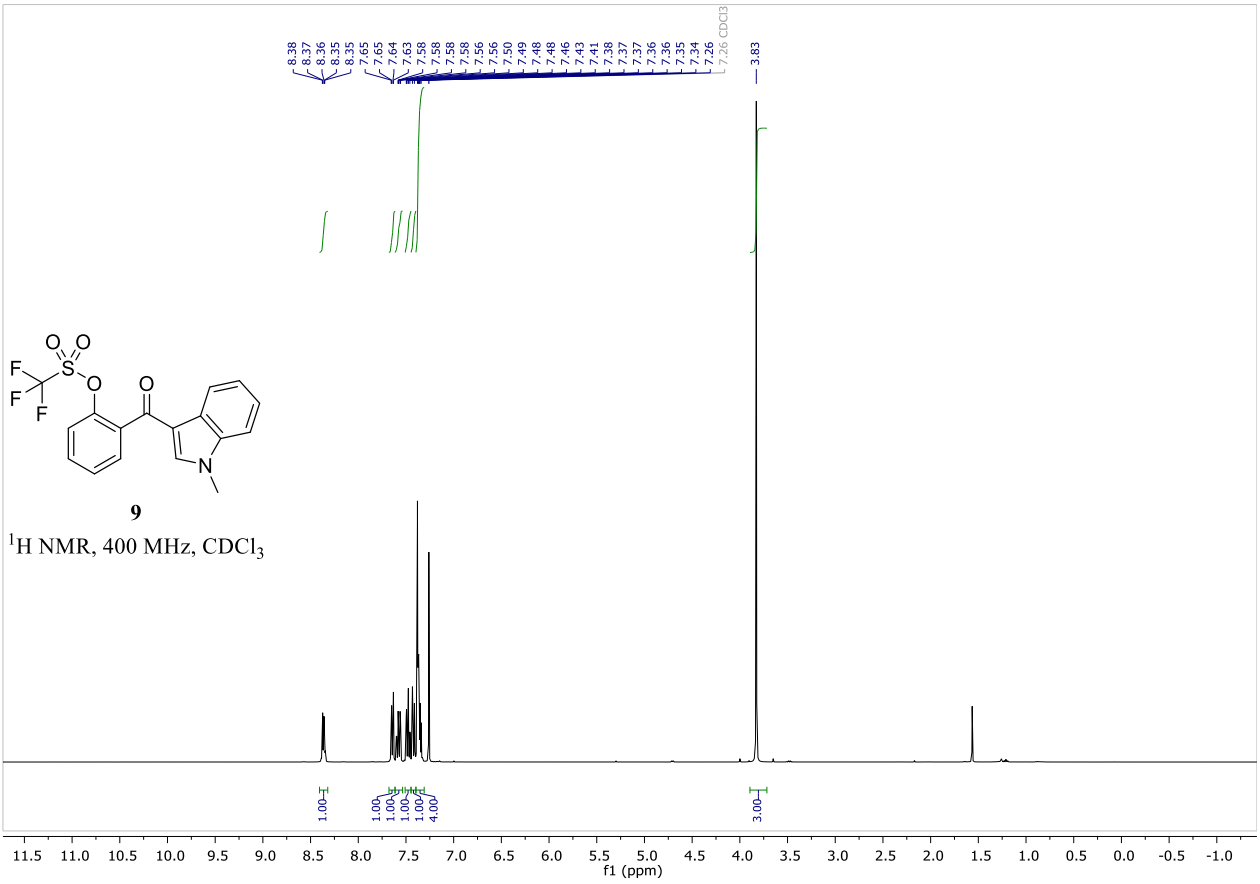
8g

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



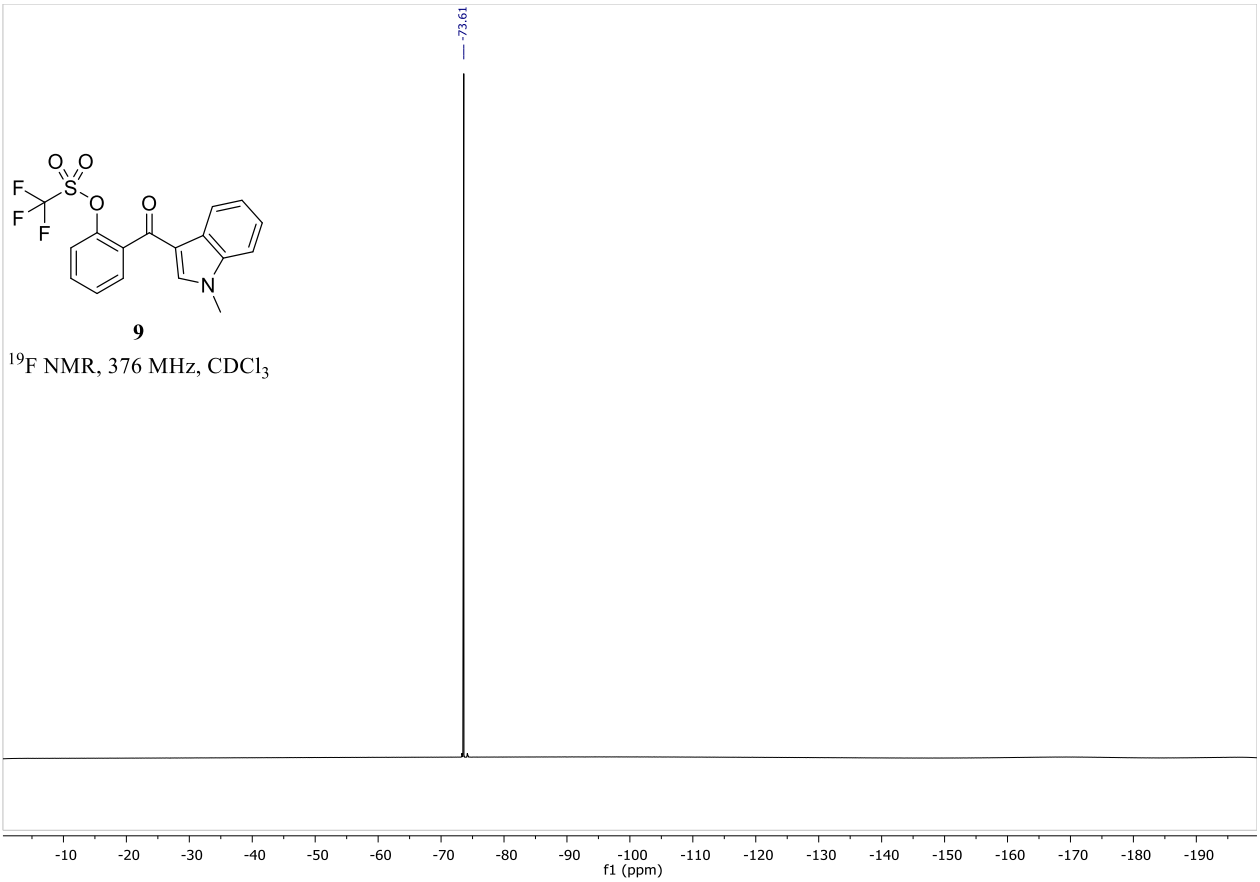
8g

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



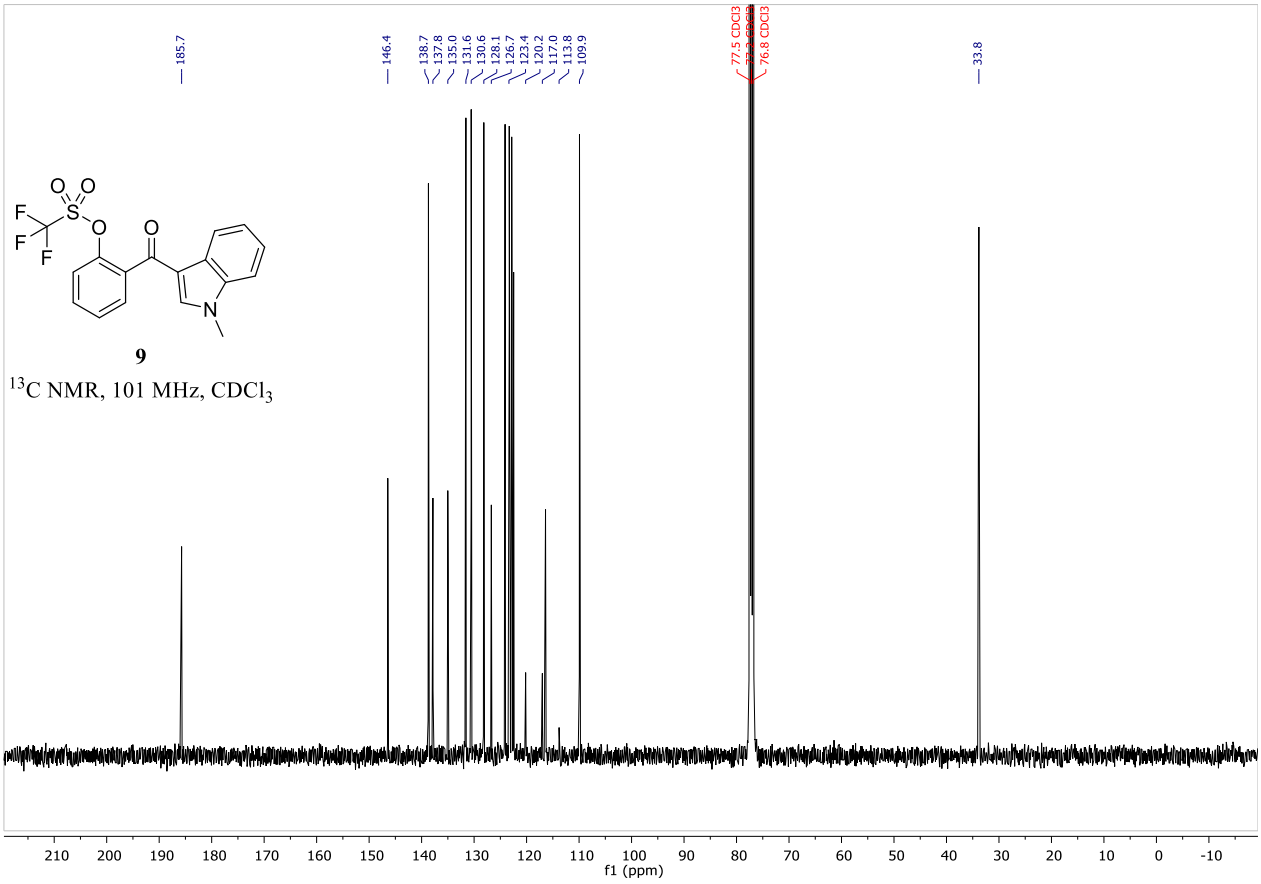
9

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



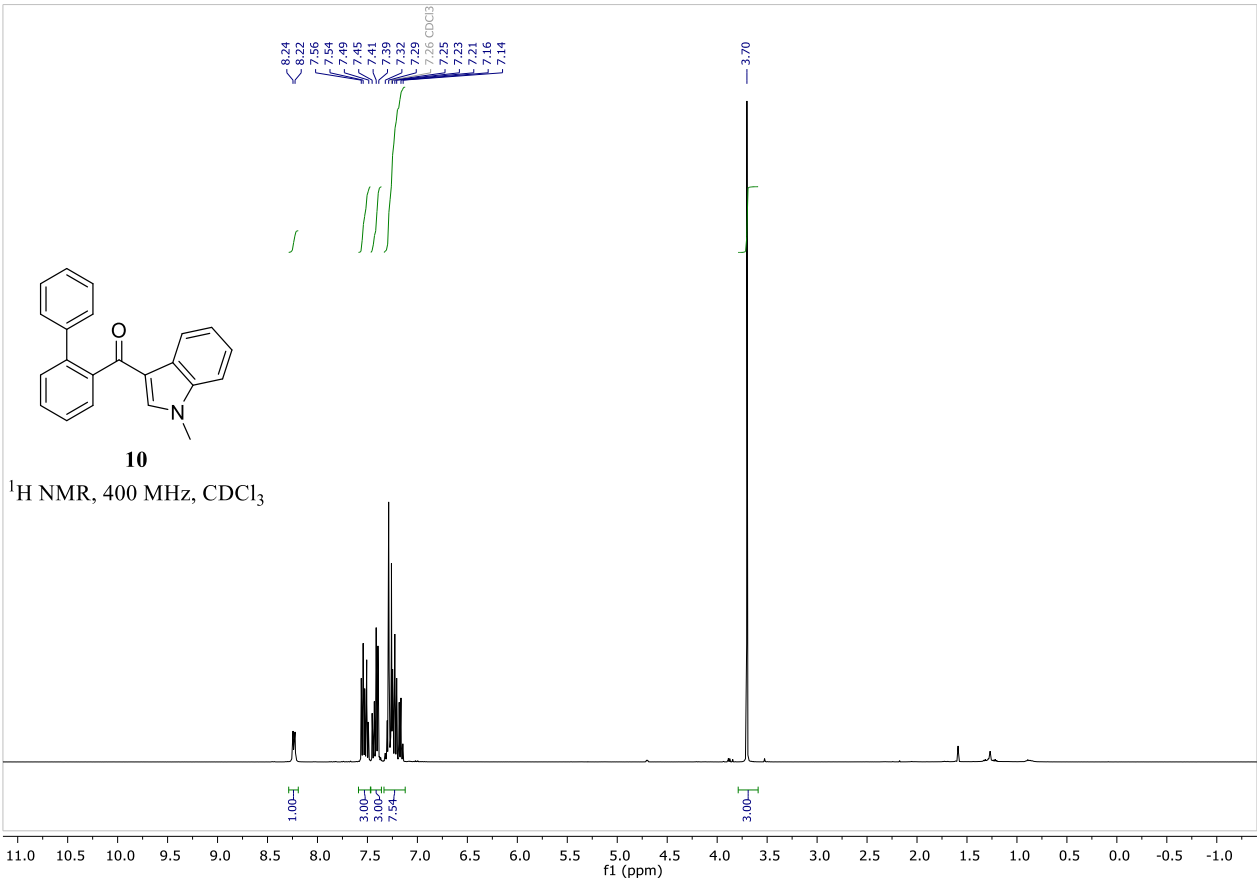
9

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



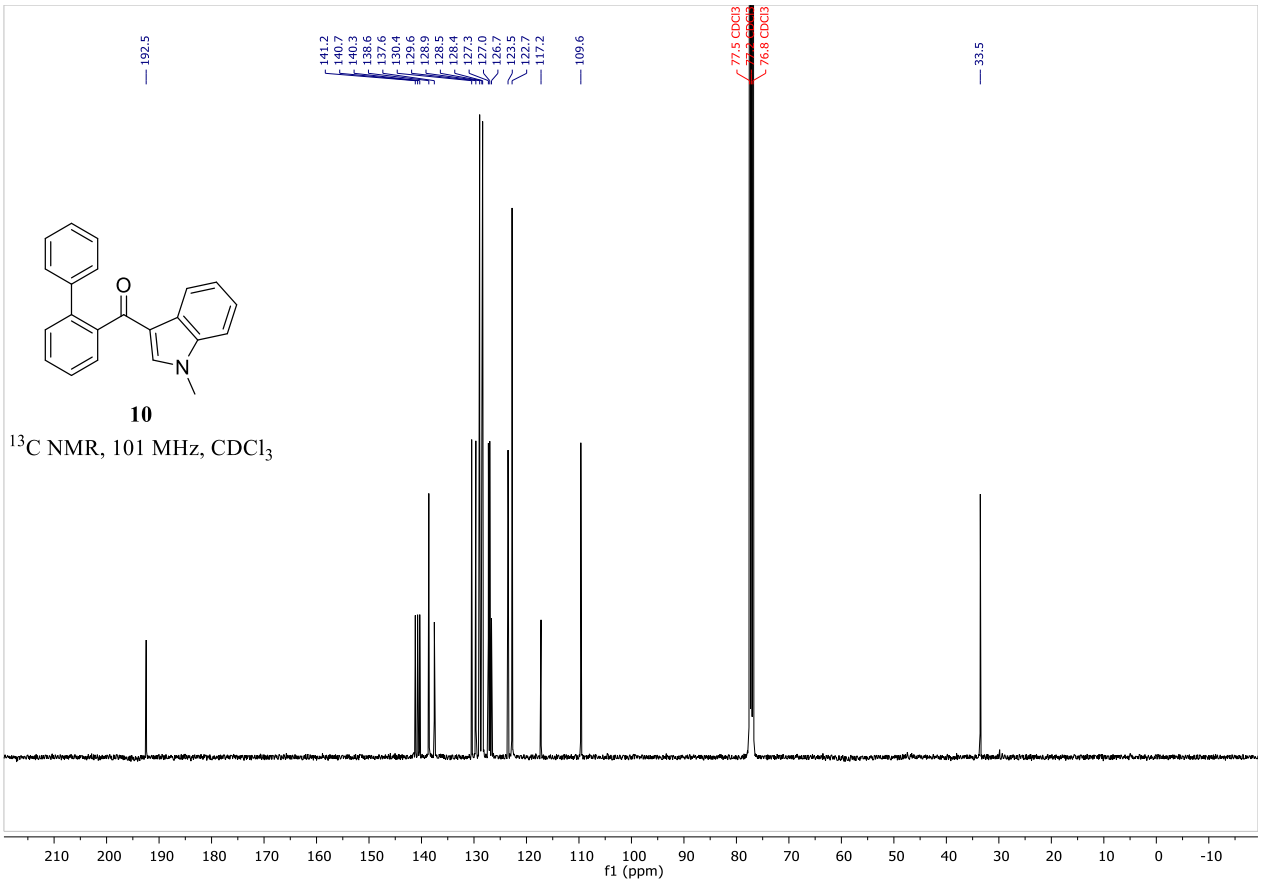
9

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



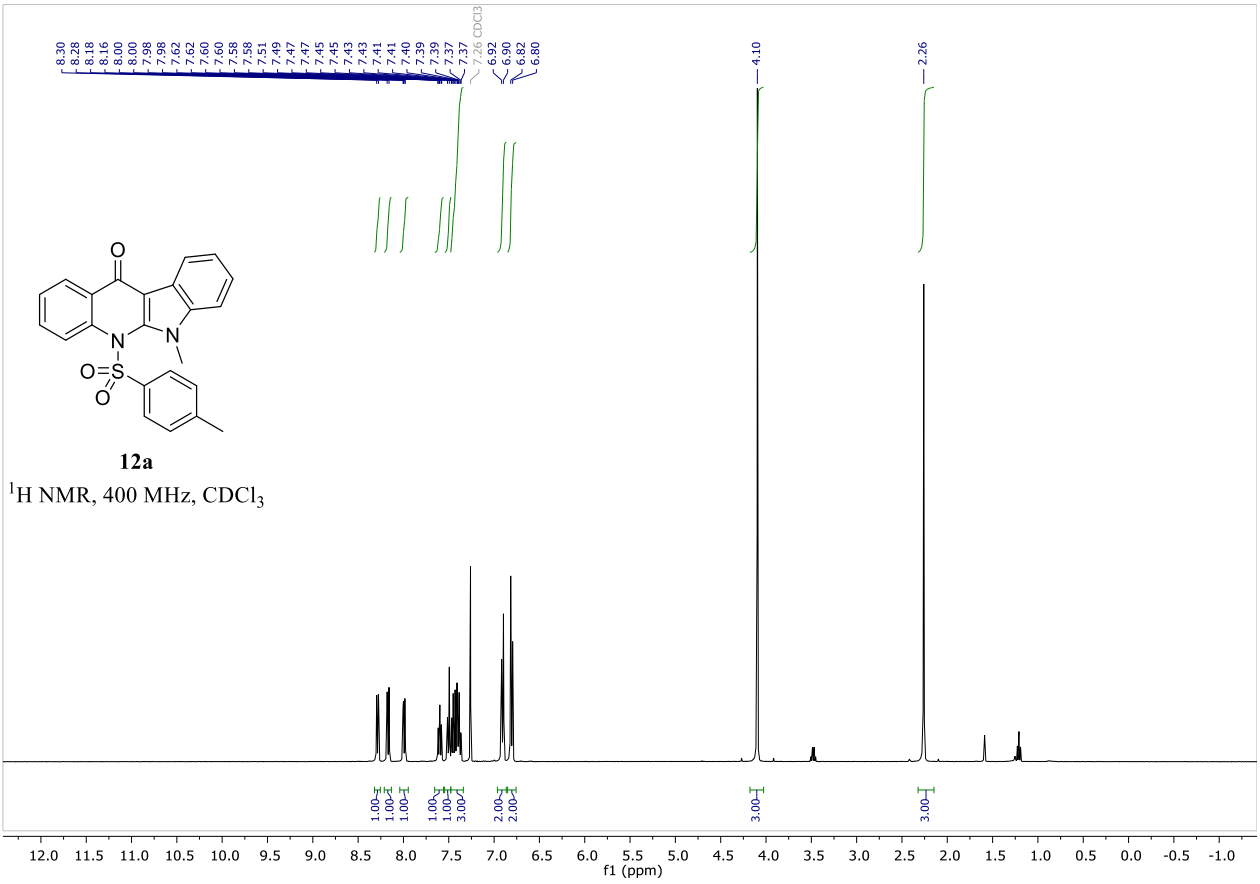
10

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



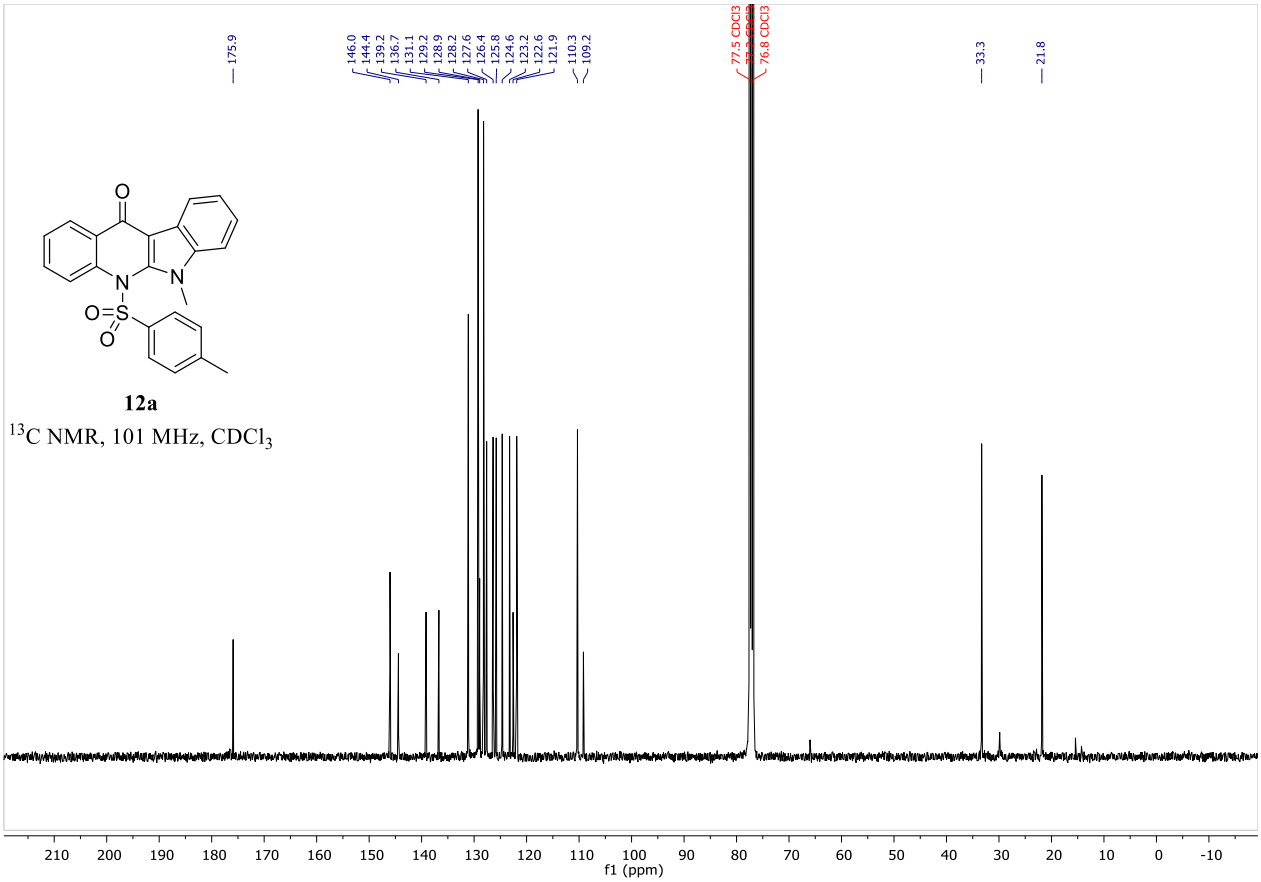
10

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



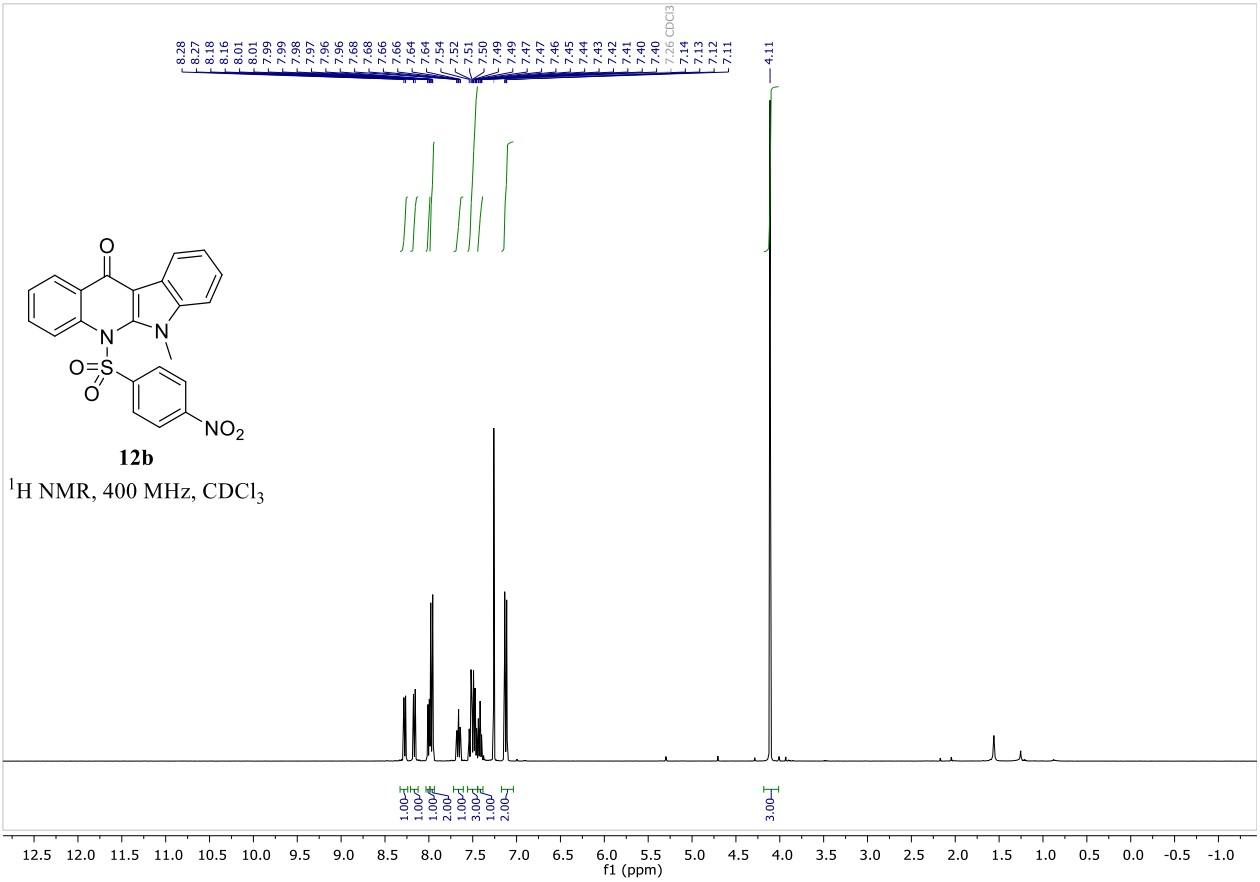
12a

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



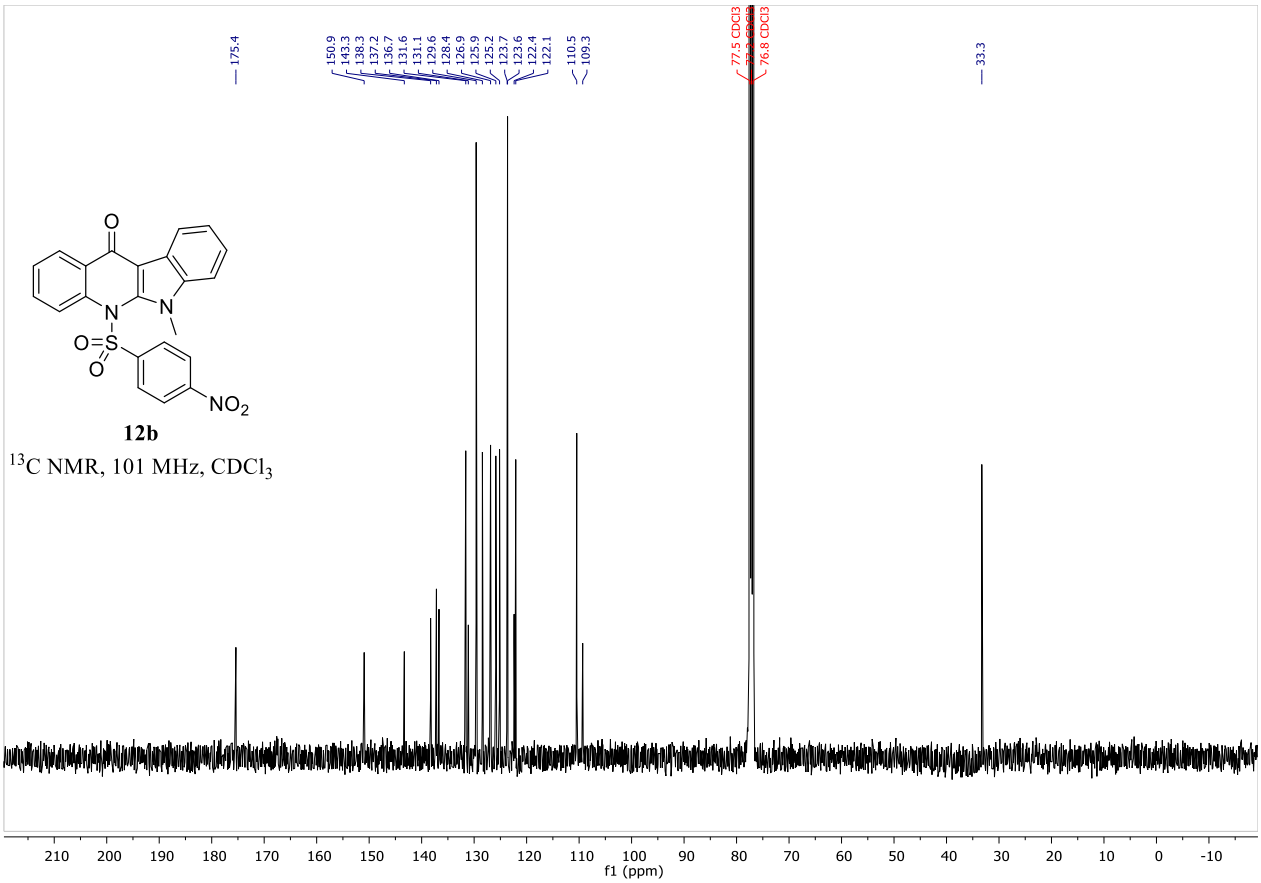
12a

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



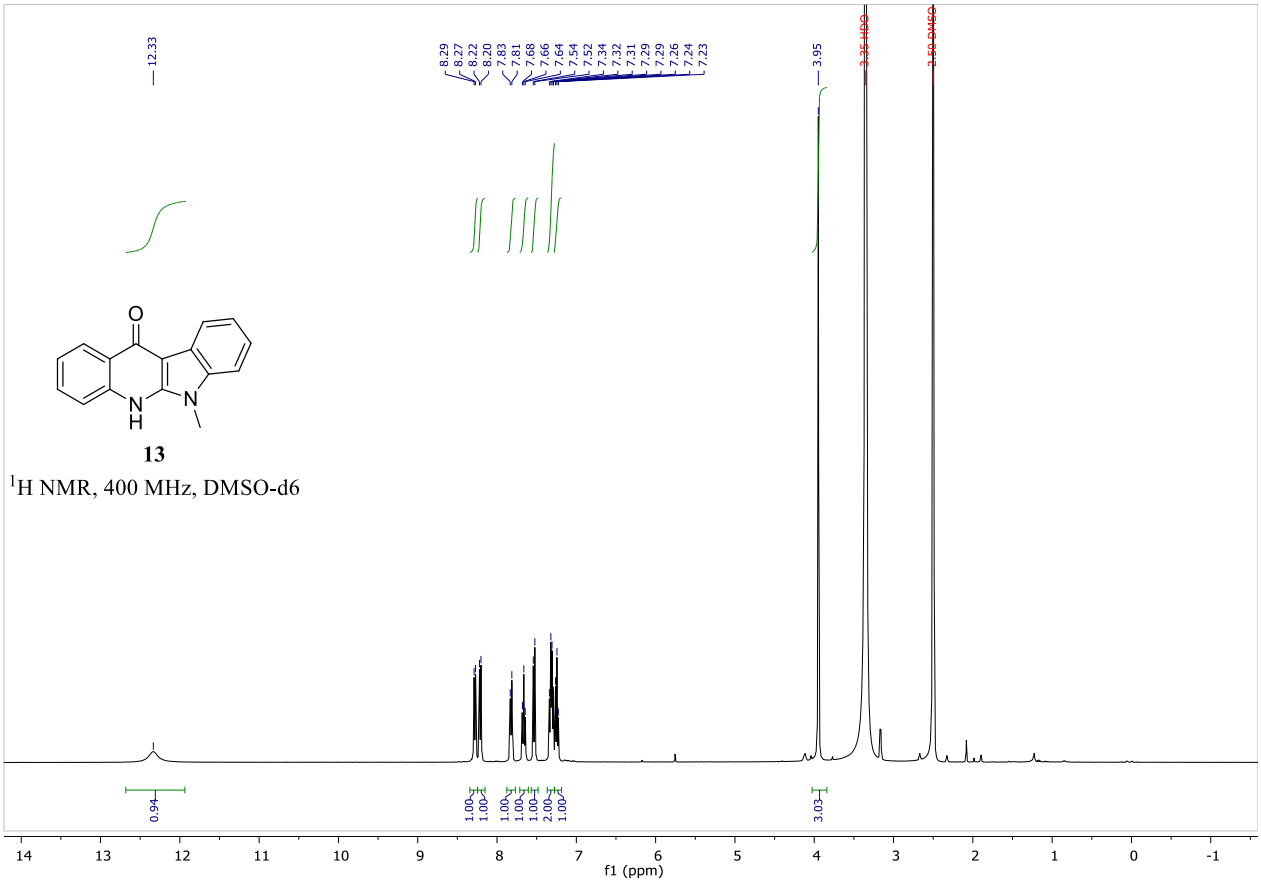
12b

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



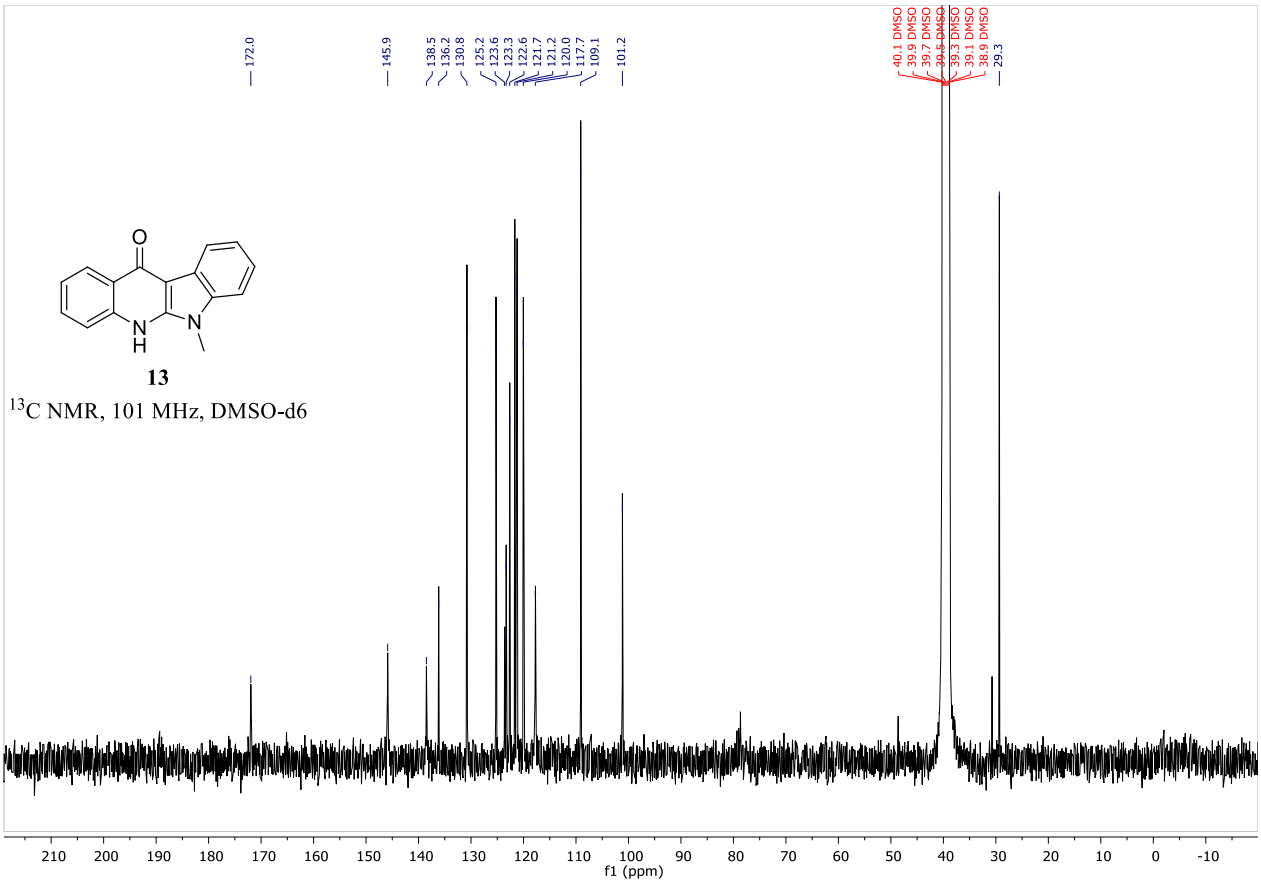
12b

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



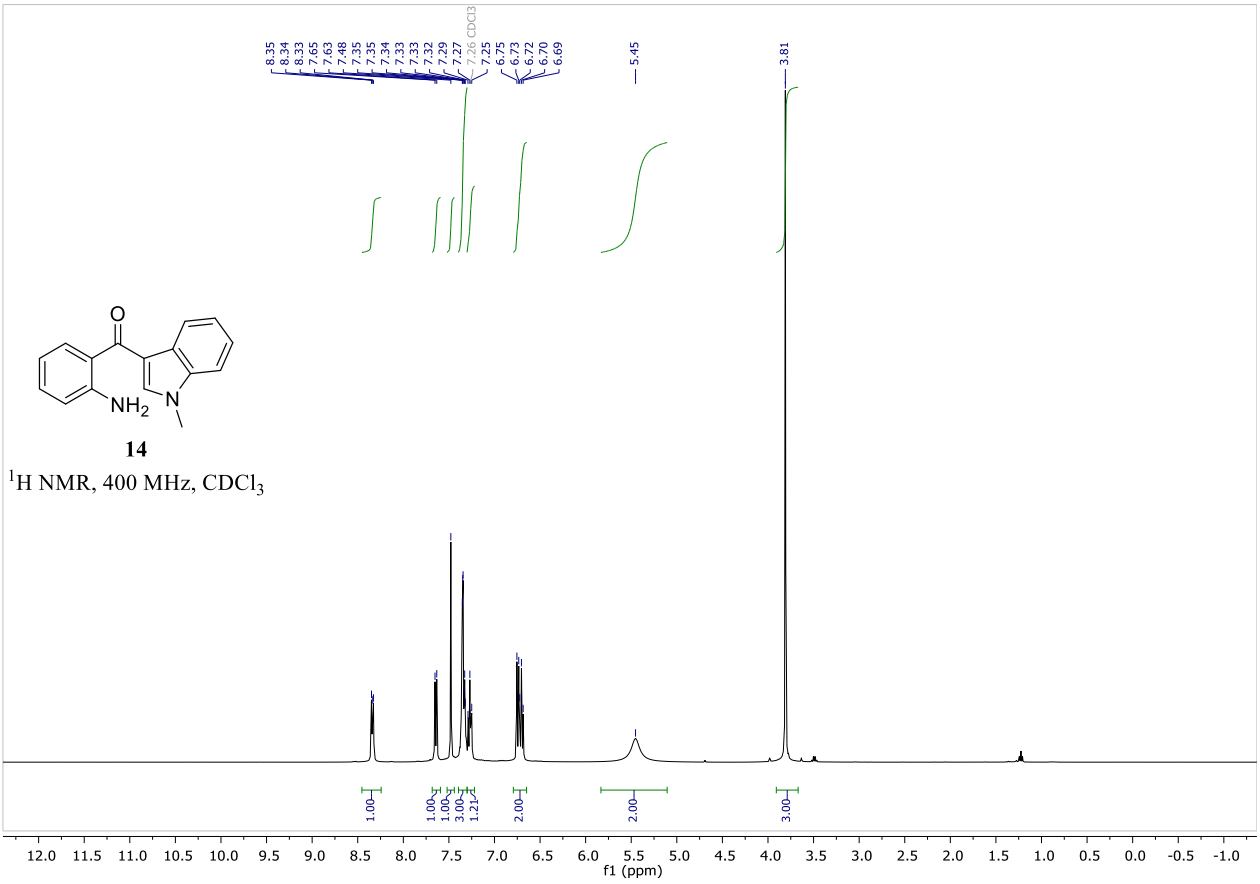
13

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



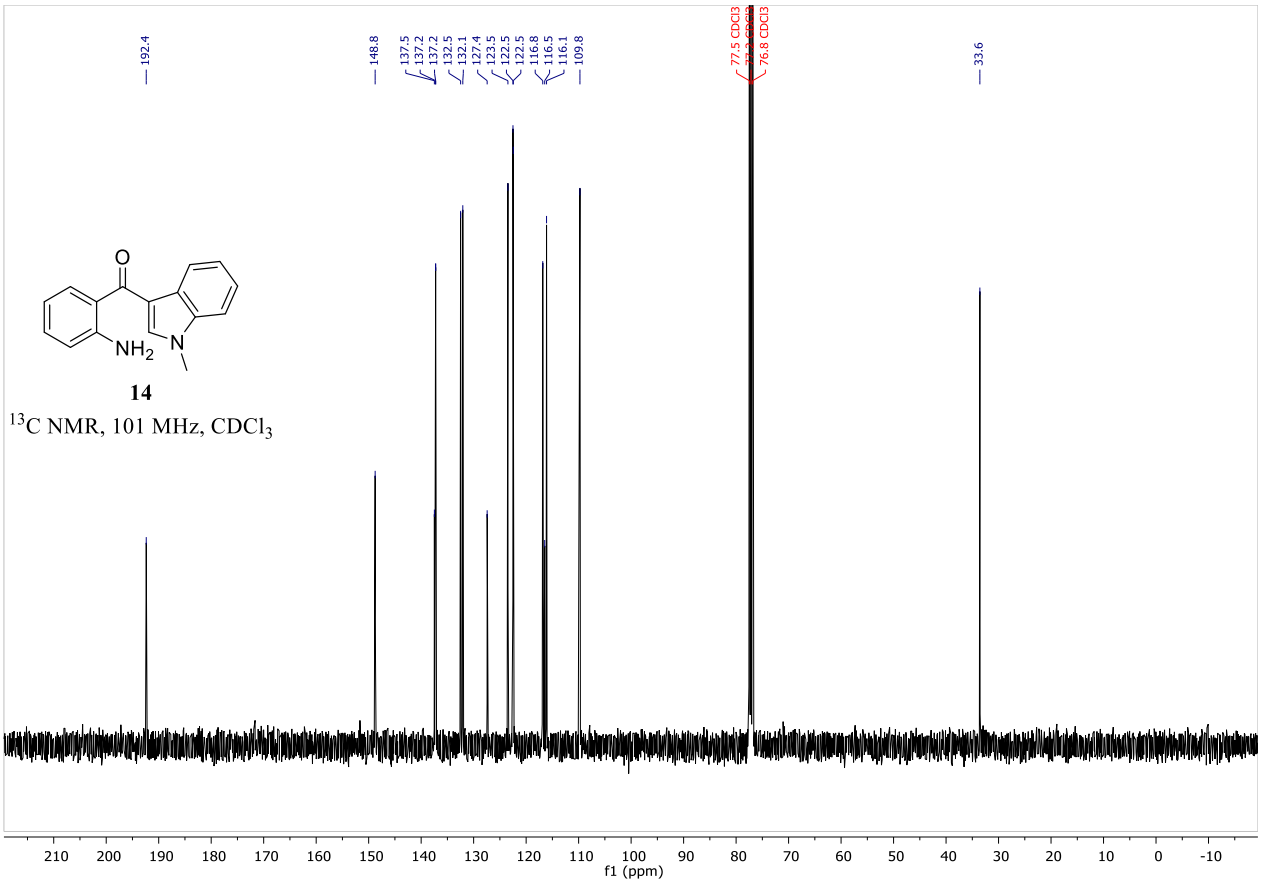
13

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



14

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



14

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