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Metal-Free Oxidative Cross Coupling of Indoles with Electron-Rich (Hetero)arenes.

Paola Caramenti,[§ a] Raj Kumar Nandi,[§ a] and Jerome Waser[*a]

Abstract: Herein, we report a new method for the synthesis of bi-heteroaryls, based on the Umpolung of indoles with benziodoxol(on)e hypervalent iodine reagents (IndoleBX). The oxidative coupling of IndoleBX with an equimolar amount of electron-rich benzenes, indoles, pyrroles and thiophenes proceeded under mild transition-metal free conditions. Functionalized non-symmetrical bi-indolyl heterocycles were accessed efficiently. Introduction of a new type of C2-substituted indole benziodoxole reagents further allowed extending the scope of the reaction to NH unprotected and C3-alkylated indoles. The obtained bi-heterocycles are important building blocks in synthetic and medicinal chemistry, and could be easily transformed into more complex heterocyclic systems.

Bi- and oligo- (hetero)aryl indoles are important building blocks in synthetic and medicinal chemistry.[1] They are usually accessed via multi-step ring-forming processes.[2] Since 2007, more efficient approaches based on metal-catalyzed direct C-H coupling of two (hetero)arenes have been intensively studied, especially for the coupling of indoles with electron-neutral or -poor (hetero)-arenes.[3-5] However, the direct coupling of indoles with electron-rich heterocycles was successful only in the case of homo-coupling to form symmetrical bi-indolyl compounds.[6] This is an important limitation, as non symmetrical derivatives can be found in natural products like Asteropusazole A (**1**),[7] synthetic bioactive molecules like anti-estrogen **2**,[8] hole transport materials like indole trimer **3**,[9] and transition metal ligands like indole phosphine **4**.[10]

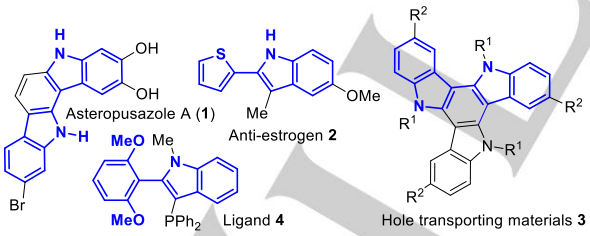
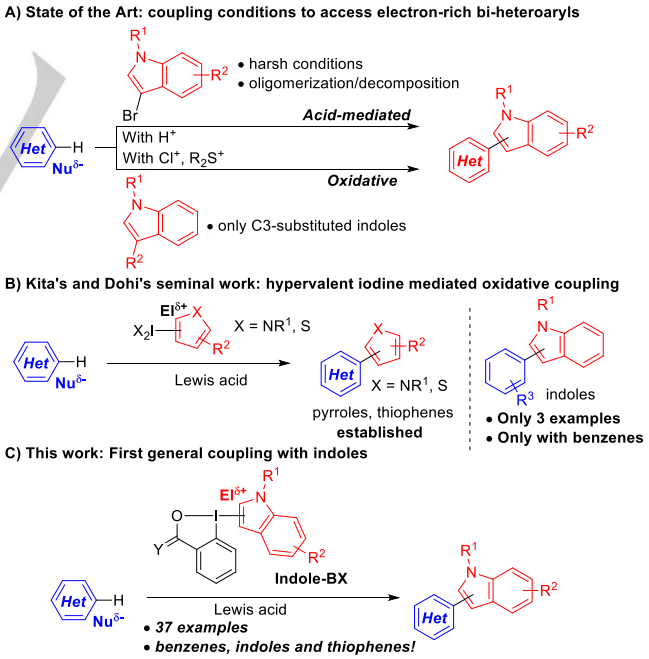


Figure 1. Selected reported compounds containing bi-heteroaryls.

To access non-symmetrical electron-rich bi-heteroaryls, cyclization methods[11] or cross coupling reactions requiring pre-functionalization of both partners[12] remain most often used.[13] The Umpolung of the reactivity of the indole ring to enable selective cross-coupling with electron-rich heterocycles is an attractive alternative approach (Scheme 1).[14] The protonation of 3-bromo indole followed by Friedel-Crafts reaction and elimination has been reported, but required the use of strong acids (Scheme 1A).[15] This led to multiple arylation and oligomerization, and therefore to a limited scope. Oxidative methods based on activation with hypochlorite[16] or sulfonium reagents[17] have been successful only for 3-substituted indoles. Kita and co-workers have been highly successful in the Umpolung of electron-rich benzene rings,[18] pyrroles[19] and thiophenes[20] through the use of hypervalent iodine reagents activated by Lewis acids without the need for any transition metal catalyst (Scheme 1B).[21] However, only very few examples of the Umpolung of indoles were reported.[22] In particular, the synthesis of hetero bi-indolyl compounds has never been reported. Therefore, there is currently no general method for the Umpolung of indoles allowing for reaction with electron-rich heterocycles under mild conditions.



Scheme 1. Umpolung of indoles for accessing non-symmetrical bi-heteroaryls.

The availability of stable isolable indole-based iodonium salts would allow oxidative coupling under more controlled conditions. However, these compounds are often not easily accessible, unstable or substituted with de-activating electron-withdrawing substituents.[23] Our group and Yoshikai and co-workers have introduced more stable indole- and pyrrole

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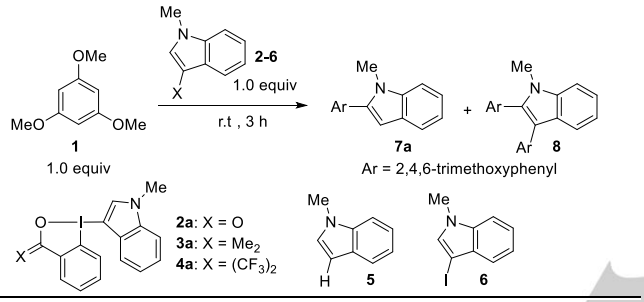
benziodoxol(on)es (BX).[24]. Herein, we report the first use of these reagents for the oxidative coupling of indoles with electron-rich heteroarenes under mild, transition metal free conditions, resulting in the first general coupling method for accessing hetero bi-indolyl compounds (Scheme 1C).

As benchmark reagent for the optimization process we chose 1,3,5-trimethoxy benzene (**1**) as nucleophile. Using Kita's conditions (hexafluoroisopropanol (HFIP) as solvent and trimethylsilylbromide as Lewis acid),[19c] but with indoleBX **2a**, we obtained product **7a** in 41% yield (Table 1, entry 1). Bis-arylated byproduct **8** was also observed in 17% yield. Interestingly, only C2 functionalized indole **7a** was obtained starting from C3-substituted indoleBX **2a**, whereas C3-substituted products were formed when using transition metal catalysis.[24a-c]

Table 1. Optimization of the (hetero)arylation on electrophilic heterocycles.

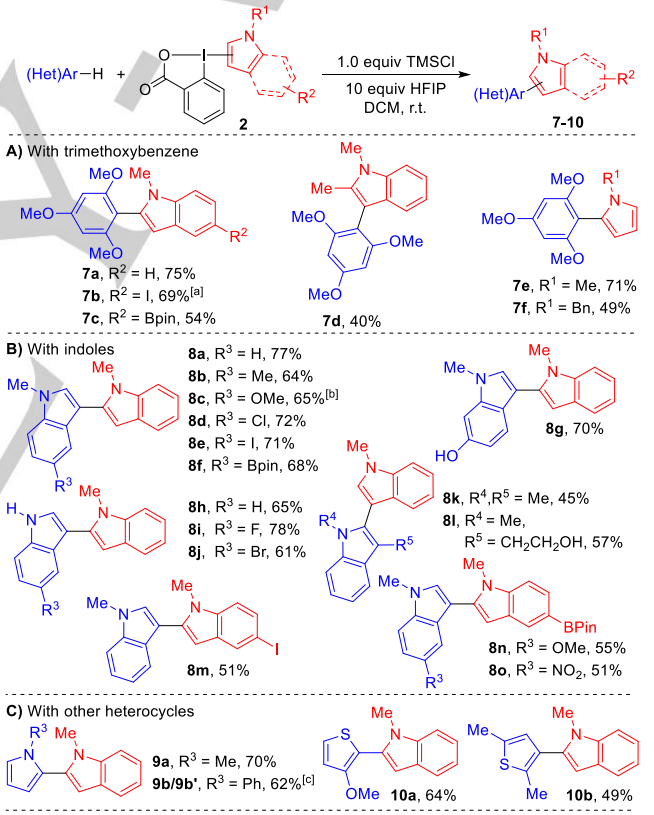


Entry	Reagent	Reaction Conditions[a]	Yield[b] 7a/8
1	**2a**	1.5 equiv **2a**, 2.0 equiv TMSBr, HFIP 0.1 M	41%/17%
2	**2a**	1.0 equiv TMSBr, HFIP 0.1 M	44%/12%
3	**2a**	1.0 equiv TMSCl, HFIP 0.1 M	68%/-%
4	**2a**	0.5 equiv TMSCl, HFIP 0.1 M	10%/-%
5	**2a**	1.5 equiv **2a**, 2.0 equiv HCl, HFIP 0.1 M	-
6	**2a**	no HFIP or no TMSCl	-
7	**2a**	**1.0 equiv TMSCl, 10 equiv HFIP, DCM 0.1 M**	**76%/-%**
8	**3a**	1.0 equiv TMSCl, 10 equiv HFIP, DCM 0.1 M	22%/
9	**4a**	1.0 equiv TMSCl, 10 equiv HFIP, DCM 0.1 M	traces
10	**5**	1.5 equiv 4-F-PIDA, 2.0 equiv TMSCl, HFIP 0.1 M	16%[c]
11	**6**	1.5 equiv **6**, 2.0 equiv. TMSBr, HFIP 0.1 M	-

[a] Reaction performed at 0.10 mmol scale at r.t. using 1.0 equiv indole reagent **2-6** unless stated otherwise. [b] Isolated yield after purification by column chromatography. [c] Yield of **7a** given. Oligomers, bis-indoles and indole-indolines were also detected.

Importantly, using equimolar amounts of TMSBr and reagent **2a** did not change the outcome of the reaction (Table 1, entry 2). Switching from TMSBr to the milder TMSCl improved the yield of the mono-arylated product **7a**, and suppressed the formation of **8** (Table 1, entry 3). A sub-stoichiometric amount of TMSCl led to a lower yield (Table 1, entry 4). Replacing TMSCl with HCl didn't work and both Lewis acid and HFIP were necessary for the reaction to proceed (Table 1, entries 5-6). The latter is probably needed to stabilize cationic aromatic and iodine(III) species.[25] When running the reaction in dichloromethane (DCM), 10 equivalents of HFIP were enough to give indole **7a** in 76% yield (Table 1, entry 7). Only very low yields were obtained with benziodoxole reagents **3a** and **4a** (Table 1, entries 8-9). Using 4-fluorophenyl iodobenzene diacetate (4-F-PIDA) as oxidant together with *N*-methylindole (**5**) as reported by Kita and co-workers,[19c] afforded **7a** in only 16% yield (Table 1, entry 10). Oligomers, bis-indoles and indole-indolines resulting from homocoupling were also detected in the reaction mixture. A control experiment with C3-iodoindole **6** confirmed the necessity of iodine(III) as activator (Table 1, entry 11).

The reaction of different benziodoxolone reagents with trimethoxybenzene as nucleophile was then examined (Scheme 2A). Products **7b** and **7c** bearing an iodine and a boronic esters substituent were obtained in 69 and 54% yield respectively. The method is therefore orthogonal to transition-metal catalyzed cross-couplings, allowing access to useful functionalities. Reagents with a NH-free indole were not successful. Starting from C2-methylated indoleBX, C3-arylated indole **7d** was accessed in 40% yield. Arylated pyrroles **7e-f** were obtained in yield comparable to those reported by Kita and Dohi.[19c]



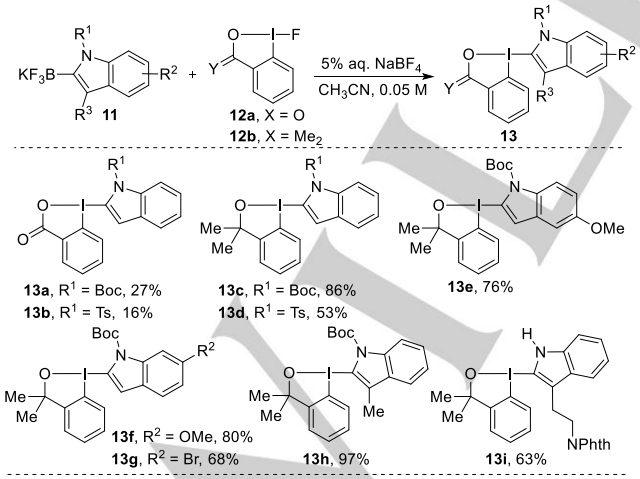
Scheme 2. Scope of the Lewis acid promoted (hetero)arylation of indoles and pyrroles. Reaction conditions; 0.30 mmol nucleophile, 0.30 mmol indole/pyrroleBX **2**, 0.30 mmol TMSCl, 3.0 mmol HFIP, DCM 0.2 M, r.t. [a] As a 9:1 mixture of mono-/bi- arylation products. [b] As a 12:1 mixture of C3:C7 heteroarylation products. [c] As a 1:1 mixture of C2:C3 heteroarylation products.

With indoles as nucleophiles, we were delighted to obtain 3',2 mixed bi-indoles in moderate to good yields, with only minor formation of de-aromatization, oligomerization and homo-coupling side products (Scheme 2B). In addition to homocoupling product **8a**, mixed bi-indolyls **8b-f** bearing electron-donating groups, halogens or boronic esters were obtained in 64-72% yield. When C6-OBn-methylindole was used, benzyl deprotected

product **8g** was formed. *N*-Unprotected indoles afforded products **8h-j** in 61-78% yield. When C3-substituted indoles were used as nucleophiles, 2',3 connected bi-indolyl **8k-l** were obtained in 45-57% yield. Using substituted IndoleBX's allowed to introduce functionalities on the other indole ring (products **8m-o**). For example, bi-indolyls **8e** and **8m** differ only by the position of the iodine atom. This could not have been achieved selectively with any previously reported method. Finally, preliminary results with pyrroles and thiophenes were also obtained (products **9a-b** and **10a-b** respectively, Scheme 1C).

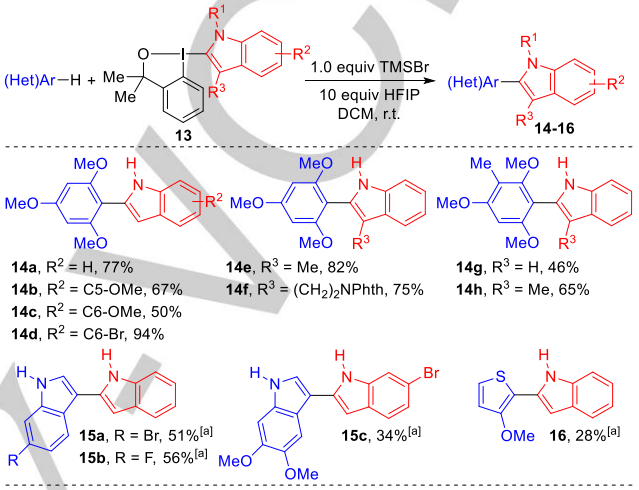
The synthesis of IndoleBXs developed in our group[24a] did not allow access to indoles bearing easily removable nitrogen protecting groups or C3 substituents. We therefore developed a new synthetic approach for IndoleBXs bearing the iodine atom on the C2 position. After intensive screening of indole precursors and conditions,[26] we accessed the desired reagents **13** by reacting indole trifluoroborate salts **11**[27] with fluoro benziodoxol(on)e **12** (Scheme 3).[28] Benziodoxolone reagents **13a-b** were obtained in low yield. IndoleDBX (dimethylbenziodoxole) **13c-d** were isolated in 86% and 53% yield respectively (the procedure was scalable up to two grams for the former). Substituents in C5, C6 and C3, including ethers, halogens and protected amines, were well tolerated, affording benziodoxoles **13e-i** in 63-97% yield.[29]

Best results in the heteroarylation of trimethoxybenzene (**1**) were obtained with *N*-Boc protected IndoleDBX reagents using TMSBr (Scheme 4). Under these conditions, the Boc group was removed, giving NH free indoles **14a-d** in 50-94% yield.[30] It was now possible to obtain C2-arylated-C3-alkylated indoles **14e** and **14f** in 82% and 75% yield respectively. The use of indoles as nucleophiles required milder TMSCl as Lewis acid and gave access to NH unprotected heterodimers **15a-c** in 34-56% yield. Thiophene-indole heteroaryl **16** was obtained in 28% yield.



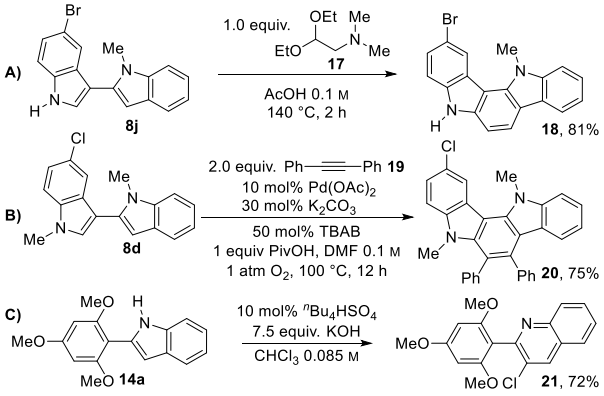
Scheme 3. Synthesis of C2-substituted IndoleBX reagents.

At this stage, it is difficult to propose a reaction mechanism rationalizing the observed regioselectivity. Either a nucleophilic (vicarious) aromatic substitution pathway or a single electron transfer (SET) from a charge-transfer complex could be considered.[18-21] In both cases, Lewis acid activation of the hypervalent iodine reagent would initiate the reaction.[31] The obtained products could be easily modified (Scheme 5). Cyclization of **8j** with acetal **17** gave indole-carbazole **18** in 81% yield (Scheme 5A).[32] Palladium catalysed oxidative cyclization of **8d** led to the formation of carbazole **20** (Scheme 5B).[33] Indole-carbazoles are important sub-structures in optoelectronic materials.[9,34] Finally, a Ciamician-Dennstedt rearrangement converted indole **14a** into quinoline **21** (Scheme 5C).[35]



Scheme 4. Scope of the oxidative heteroarylation using C2-IndoleDBX reagents **13**. Reaction conditions; 0.22 mmol nucleophile, 0.20 mmol indoleDBX, 0.40 mmol TMSBr, 2.0 mmol HFIP, DCM 0.2 M, r.t. [a] TMSCl was used instead of TMSBr.

In conclusion, we have reported a straightforward approach for the selective synthesis of mixed bi-(hetero)arenes. Electrophilic hypervalent iodine reagents (IndoleBX) were combined with equimolar amounts of functionalized indole, pyrrole and thiophene nucleophiles in a metal-free protocol. Selectively functionalized bi-indolyl heterocycles were obtained with high efficiency. New C2-IndoleDBXs reagents were synthesized, increasing significantly the scope of accessible bi-heterocycles. Further investigations are ongoing on the use of benziodoxol(on)e reagents in the Umpolung of electron-rich heterocycles.



Scheme 5. Product derivatizations.

Acknowledgements

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Authors Contribution

[§]P. Caramenti and [§]Dr. R.K. Nandi contributed equally to this work.

Keywords: Indoles • Hypervalent Iodine • Umpolung • C-H Functionalization • Heterocycles

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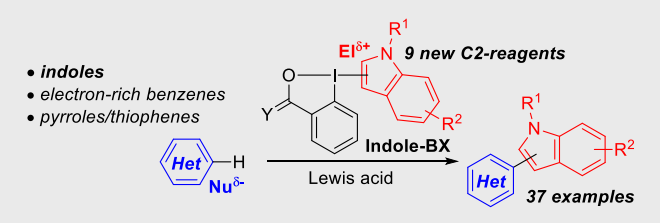

Smooth Umpolung: The use of stable Indole-BenziodoXol(on)e (IndoleBX) hypervalent iodine reagents allows oxidative coupling of electron-rich (hetero)arenes under mild metal-free conditions to access hetero-bi-heterocycles in high yields. High functional group tolerance set the stage for easy and regioselective post-functionalization to access more complex heterocyclic systems.

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Supporting Information

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1. Materials and Methods.

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography, technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et_2O, CH_3CN, toluene, hexane and CH_2Cl_2 were dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 10 ppm, *Karl-Fischer* titration). The solvents were degassed through Freeze-Pump-Thaw method when mentioned. All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Aplichem, or Merck and used as such unless otherwise stated. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, with the solvents indicated as eluent under 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F_{254} TLC glass plates or aluminium plates and visualized with UV light, permanganate stain, CAN stain, or Anisaldehyde stain. Melting points were measured on a Büchi B-540 melting point apparatus using open glass capillaries, the data is uncorrected. ^{1}H-NMR spectra were recorded on a Brucker DPX-400 400 MHz spectrometer in $CDCl_3$, DMSO-d_6 CD_3OD, C_6D_6 and CD_2Cl_2, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal DMSO signal at 2.50 ppm the internal methanol signal at 3.30 ppm, the internal dichloromethane signal at 5.30 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation).^{13}C-NMR spectra were recorded with ^{1}H-decoupling on a Brucker DPX-400 100 MHz spectrometer in $CDCl_3$, DMSO-d_6, CD_3OD or CD_2Cl_2, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm, the internal DMSO signal at 39.5 ppm, the internal methanol signal at 49.0 ppm and the internal dichloromethane signal at 54.0 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S 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. Preparation of IndoleBXs.

The synthesis of the precursors for HeterocyclicBX reagents **2a-2f'**, **3a**, **4a**, **13a-13i** and their starting materials had been already described before.[1,2] The procedures here reported are taken from the cited publications to facilitate reproduction of the results by having all the data in the same file. Compound **12b** is commercially available.

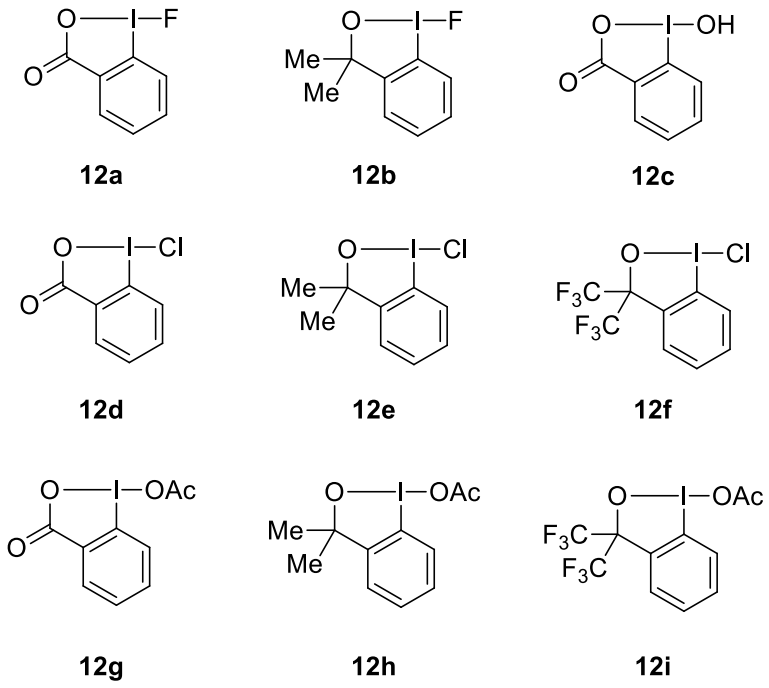
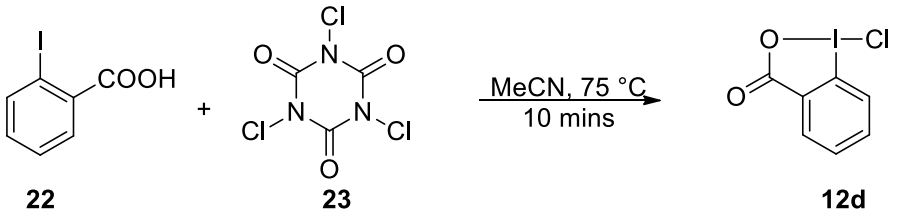


Figure 2.1: Heterocyclic hypervalent iodine reagents precursor.

2.1 Preparation of Hypervalent Iodine Precursors.

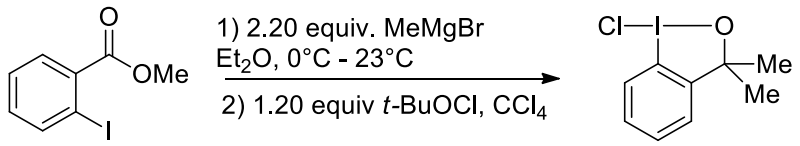
1-Chloro-1,2-benziodoxol 3(1*H*)-one (12d):



Following a slightly modified procedure,[3] commercially available 2- iodobenzoic acid **22** (4.00 g, 16.1 mmol, 1 equiv.) was dissolved in anhydrous MeCN (30 mL). The resulting stirred suspension was heated to 75 °C in an oil bath. The dropping funnel was charged with a solution of trichloroisocyanuric acid **23** (1.41 g, 6.07 mmol, 1.02 Cl^+ equiv.) in 10 mL of anhydrous MeCN by syringe. The solution of trichloroisocyanuric acid **23** was dropped into the vigorously stirred reaction mixture within 5 min. After addition was complete, the reaction mixture was refluxed for an additional 5 min. The reaction mixture was vacuum-filtered over a preheated,

sintered-glass funnel with a tightly packed pad of Celite (1 cm thick), and the filter cake was rinsed with additional hot MeCN (20-50 mL). The combined filtrates were evaporated to near-dryness, and the resulting yellow solid was filtered over a sintered-glass funnel and washed with a small amount of cold MeCN. The mother liquor from filtration was partially concentrated on vacuum, giving a second crop of solids. The combined crops were dried under high vacuum to obtain 1-Chloro-1,2-benziodoxol 3(1*H*)-one **12d** (3.16 g, 11.2 mmol, 69% yield) as light yellow solid. **^{1}H NMR** (400 MHz, *Acetone-d6*) δ 8.34 – 8.24 (m, 1H), 8.16 (ddd, *J* = 7.8, 6.5, 1.8 Hz, 2H), 7.96 – 7.85 (m, 1H). The NMR values correspond to the reported ones.[3]

1-Chloro-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (**12e**)

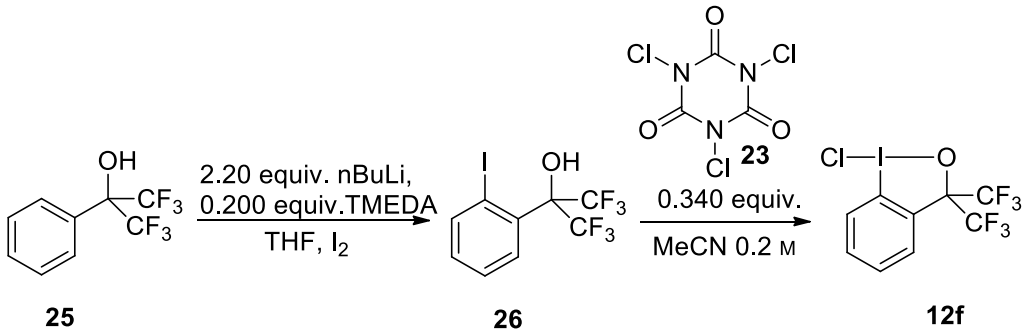


24 **12e**

Following a reported procedure,[3] commercially available methyl 2-iodobenzoate **24** (12.0 mL, 76.0 mmol) was dissolved under N_2 atmosphere in dry diethyl ether (400 mL) and then the solution was cooled to 0 °C with an ice bath. Methylmagnesium bromide (56.0 mL, 0.168 mol, 2.20 equiv.) was added dropwise and the reaction was stirred for 30 min at 0 °C. The reaction mixture was then allowed to warm to room temperature and it was further stirred for 2 h. The reaction was quenched with NH_4Cl in an iced bath. The organic layer was separated and extracted with Et_2O (3 x 100 mL), washed with water (2 x 200 mL), brine (1 x 100 mL) then dried over $MgSO_4$. The solvent was removed *in vacuo*.

With no further purification the crude mixture was dissolved in CCl_4 (7 mL) and *tert*-butyl hypochlorite (100 mL, 92.0 mmol, 1.20 equiv.) and the reaction mixture was stirred at room temperature. After one hour a yellow precipitate was collected by filtration and washed with hexane (60 mL) to afford compound **12e** (7.70 g, 26.0 mmol, 34% yield) as a yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 (dd, 1 H, *J* = 8.1, 1.1 Hz, C*H*Ar), 7.55 (m, 2 H, C*H*Ar), 7.17 (dd, 1 H, *J* = 7.3, 1.7 Hz, C*H*Ar), 1.55 (s, 6 H, (CH_3)$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.5, 131.0, 130.5, 128.4, 126.1, 114.7, 85.2, 29.2. **IR** ν 3729 (w), 3626 (w), 2972 (w), 2924 (w), 2362 (w), 2055 (w), 2018 (w), 1742 (w), 1564 (w), 1464 (w), 1439 (w), 1379 (w), 1378 (w), 1366 (w), 1277 (w), 1276 (w), 1256 (w), 1181 (w), 1154 (m), 1112 (w), 1048 (w), 1003 (w), 982 (w), 943 (m), 866 (m), 808 (w), 790 (w), 789 (w), 762 (s), 745 (w), 724 (w), 718 (w). The characterization data is in accordance with reported literature values.[4]

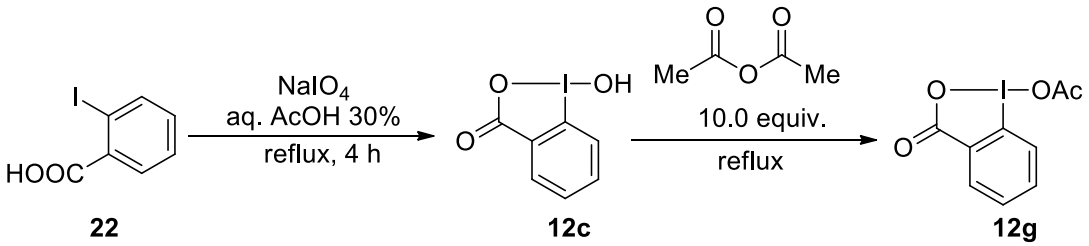
1-Chloro-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole (12f)



25 **26** **12f**

Following a reported procedure, TMEDA (distilled over KOH) (1.26 mL, 8.20 mmol, 0.200 equiv) was added to a solution of *n*BuLi (2.5 M in hexanes, 36.6 mL, 91.6 mmol, 2.20 equiv). After 15 min, the cloudy solution was cooled to 0 °C and **25** (7.00 mL, 42.0 mmol, 1 equiv) in THF (6 mL) was added dropwise. The reaction was stirred 30 min at 0 °C and then at RT overnight. I_2 (11.2 g, 44.0 mmol, 1.06 equiv) was then added portionwise at 0 °C and the mixture stirred at 0 °C for 30 min and 4 h at RT. The reaction was quenched with saturated NH_4Cl. Et_2O (100 mL) was added and the layers were separated. The aqueous layer was then extracted twice with Et_2O (3 x 50 mL). The organic layers were combined, washed twice with saturated NaS_2O_3 (2 x 50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford 15.6 g of crude **26** as an brown oil which was used without further purification. The crude oil was dissolved in MeCN (40 mL) in the dark under air. Trichloroisocyanuric acid **23** (3.42 g, 14.3 mmol, 0.340 equiv.) was then added portionwise at r.t. After 30 min, the resulting suspension was filtered to afford **12f** (7.30 g, 18.1 mmol, 43%) as a yellow solid. The mother liquors were carefully reduced to one third and filtered to afford more **xx** (8.85 g, 21.9 mmol, 52.1% yield) as a yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (d, 1 H, *J* = 8.4 Hz, Ar*H*), 7.85 (m, 1 H, Ar*H*), 7.73 (m, 2 H, Ar*H*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 133.8, 132.1, 131.6, 129.7, 128.5, 122.8 (q, 289 Hz), 113.4, 84.8. The melting point and the ^{1}H NMR correspond to the reported values.[5]

Synthesis of 1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one (12g)

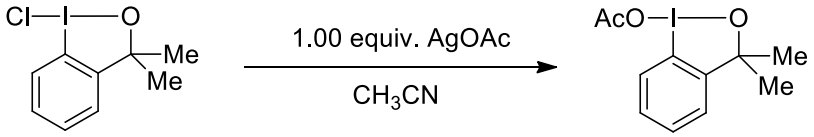


22 **12c** **12g**

Following a reported procedure,[1] $NaIO_4$ (7.24 g, 33.8 mmol, 1.05 equiv) and 2-iodobenzoic acid **22** (8.00 g, 32.2 mmol, 1.00 equiv) were suspended in 30% (v/v) aq. AcOH (48 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (180 mL) and allowed to cool to room temperature, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 20 mL) and acetone (3 x 20 mL), and air-dried in the dark to give the pure hydroxylated intermediate **12c**.

Following a reported procedure,[3] hydroxylated intermediate **12c** (39.1 mmol, 1.00 equiv.) was suspended in acetic anhydride (35 mL) and heated to reflux for 5 minutes, up to dissolution of the starting material. The resulting clear, slightly yellow solution was slowly let to cool down to room temperature and then cooled to 0 °C for 30 minutes. The white suspension was filtered and the filtrate was again cooled to 0 °C for 30 minutes. The suspension was once again filtered and the combined two batches of solid product were washed with hexane (2 x 20 mL) and dried *in vacuo* to afford product **12g**. 1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one **12g** (10.8 g, 35.3 mmol, 90%) as a white solid. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.24 (dd, *J* = 7.6, 1.6 Hz, 1H, Ar*H*), 8.00 (dd, *J* = 8.3, 1.0 Hz, 1H, Ar*H*), 7.92 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1H, Ar*H*), 7.71 (td, *J* = 7.3, 1.1 Hz, 1H, Ar*H*), 2.25 (s, 3 H, COC*H*$_3$). **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 176.5, 168.2, 136.2, 133.3, 131.4, 129.4, 129.1, 118.4, 20.4. NMR values are in accordance with the data reported in literature.[6]

1-Acetoxy-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (12h)

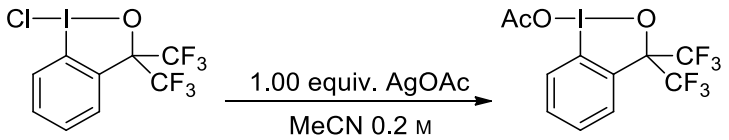


12d **12h**

Following a reported procedure,[3] 1-chloro-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole **12d** (2.60 g, 8.77 mmol) was dissolved in dry acetonitrile (25 mL) under N_2 atmosphere. The reaction flask was covered with aluminum foils and protected from light. Silver acetate (1.46 g, 8.77 mmol, 1.00 equiv.) was then added in one portion. The reaction mixture was stirred in the dark at room temperature for 16 h. Filtration over a Celite plug and evaporation of the solvent yielded compound **12h** (2.6 g, 8.8 mmol, 93%) as a brownish solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (dd, 1 H, *J* = 8.0, 1.3 Hz, C*H*Ar), 7.47 (m, 2H, C*H*Ar), 7.18 (dd, 1 H, *J* = 7.2, 1.7 Hz, C*H*Ar), 2.11 (s, 3 H, COC*H*$_3$), 1.52 (s, 6 H, (C*H*$_3$)$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$)

δ 177.4, 149.4, 130.4, 130.0, 129.9, 126.2, 115.7, 84.6, 29.2, 21.5. **IR** ν 3099 (w), 3057 (w), 2975 (w), 2930 (w), 2930 (w), 2865 (w), 1740 (w), 1640 (s), 1588 (w), 1566 (w), 1462 (w), 1438 (m), 1363 (s), 1294 (s), 1259 (m), 1158 (m), 1114 (w), 1047 (w), 1033 (w), 1009 (w), 949 (m), 926 (w), 866 (w), 761 (s), 723 (w). The characterization data is in accordance with reported literature values.[3]

1-Acetoxy-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole (12i)



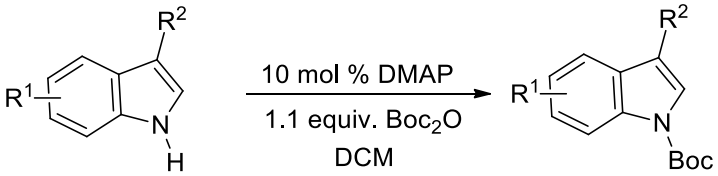
12f **12i**

1-Chloro-1,3,-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole **12f** (8.85 g, 21.9 mmol) and AgOAc (3.65 g, 21.9 mmol, 1.00 equiv.) were suspended in MeCN (109 mL, 0.2 M). After being stirred overnight in the dark, AgCl precipitated and was filtered off. The residue was washed with MeCN. The solvent was removed in vacuo to give **12i** (9.37 g, 21.9 mmol, 100%) as a white solid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.61–7.79 (m, 3H, Ar*H*), 2.18 (s, 3H, *CH_3*). The NMR values correspond to the reported ones.[6]

2.2 Preparation of N-carbamoylated and -tosylated indoles and their trifluoroborate salts.

In this section, only the synthesis of non-commercially available indole compounds is reported. The synthesis of the precursors for HeterocyclicBX reagents **13a-13i** had been already described by our group before. The procedures reported here are taken from the cited publications to facilitate reproduction of the results by having all the data in the same file.[7,8]

General Procedure GP1 for the N-Carbamoylation of Indoles.



Following a reported procedure,[9] to a solution of commercially available *1H*-indoles (10.0 mmol, 1.00 equiv.) and *N*,*N*-dimethylaminopyridine (122 mg, 1.00 mmol, 0.100 equiv) in 0.5 M CH_2Cl_2, di-*tert*-butyl dicarbonate (2.40 g, 11.0 mmol, 1.10 equiv.) was added under vigorous stirring at 0 °C. The reaction was then allowed to stir at room temperature overnight. Brine (50 mL) and CH_2Cl_2 (30 mL) were added to the reaction mixture and the organic layer extracted. The aqueous layer was further extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers were dried over $MgSO_4$ concentrated in vacuum and the crude was directly submitted to short-path flash chromatography (Pentane: EtOAc: 95:5) to afford the desired *N*-Boc indole derivatives **27a-27e**.

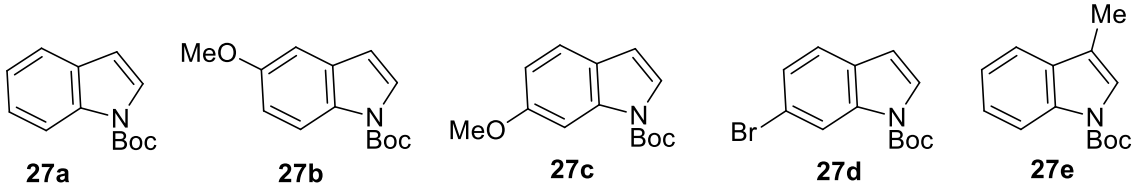
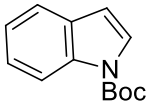


Figure 2.2 N-carbamoylated indoles.

Tert-butyl 1*H*-indole-1-carboxylate (27a)

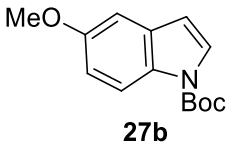


27a

Following the general procedure **GP1** (*synthesis of tert-butyl 1H-indole-1-carboxylate was scaled up to 20.0 mmol without reoptimization of the protocol*.), starting from commercially available 1*H*-indole (2.34 g, 20.0 mmol, 1.00 equiv.), after 16 hours *tert*-butyl 1*H*-indole-1-carboxylate **27a** was obtained as colorless oil (3. 90 g, 17.9 mmol, 90% yield). $\mathbf{R_f}$: 0.8 (Pentane: EtOAc 9:1) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.74 (d, *J* = 3.8 Hz, 1H, Ar*H*), 7.69 (dt, *J* = 7.7, 1.0 Hz, 1H, Ar*H*), 7.47 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1H, Ar*H*), 7.37 (td, *J* = 7.5, 1.1 Hz, 1H, Ar*H*), 6.68 (d, *J* = 3.8 Hz,

1H, Ar*H*), 1.79 (s, 9H, C(CH_3)$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.5, 135.0, 130.3, 125.6, 123.9, 122.4, 120.7, 114.9, 107.1, 83.2, 27.9. The NMR values correspond to the reported ones.[9]

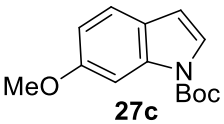
***Tert*-butyl 5-methoxy-1*H*-indole-1-carboxylate (27b)**



27b

Following general procedure **GP1**, starting from commercially available 5-methoxy-1*H*-indole (1.47 g, 10.0 mmol), after 14 hours *tert*-butyl 5-methoxy-1*H*-indole-1-carboxylate **27b** (1.92 g, 7.80 mmol, 78% yield) was obtained as a colorless solid. **R$_f$**: 0.8 (Pentane: EtOAc 95:5). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 9.1 Hz, 1H, Ar*H*), 7.59 (d, *J* = 3.6 Hz, 1H, Ar*H*), 7.04 (d, *J* = 2.6 Hz, 1H, Ar*H*), 6.96 (dd, *J* = 9.0, 2.6 Hz, 1H, Ar*H*), 6.51 (d, *J* = 3.7 Hz, 1H, Ar*H*), 3.86 (s, 3H, OCH_3), 1.68 (s, 9H, C(CH_3)$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.7, 149.6, 131.3, 129.8, 126.4, 115.7, 112.9, 107.1, 103.4, 83.4, 55.5, 28.1. The NMR values correspond to the reported ones.[10]

***Tert*-butyl 6-methoxy-1*H*-indole-1-carboxylate (27c)**



27c

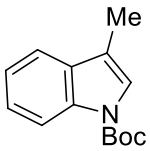
Following general procedure **GP1**, starting from commercially available 6-methoxy-1*H*-indole (1.47 g, 10.0 mmol), after 12 hours *tert*-butyl 6-methoxy-1*H*-indole-1-carboxylate **27c** (2.23 g, 9.02 mmol, 90% yield) was obtained as a colorless solid. **R$_f$**: 0.8 (Pentane: EtOAc 9:1).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (s, 1H, Ar*H*), 7.47 (d, *J* = 3.7 Hz, 1H, Ar*H*), 7.42 (d, *J* = 8.6 Hz, 1H, Ar*H*), 6.87 (dd, *J* = 8.5, 2.4 Hz, 1H, Ar*H*), 6.49 (dd, *J* = 3.7, 0.8 Hz, 1H, Ar*H*), 3.88 (s, 3H, OCH_3), 1.67 (s, 9H, C(CH_3)$_3$).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.6, 149.8, 136.1, 124.5, 124.2, 121.2, 112.1, 107.1, 99.2, 83.4, 55.6, 28.8. NMR values correspond to the reported ones.[11]

***Tert*-butyl 6-bromo-1*H*-indole-1-carboxylate (27d)**

27d

Following general procedure **GP1**, starting from commercially available 6-bromo-1H-indole (2.00 g, 10.2 mmol), after 16 hours *tert*-butyl 6-bromo-1*H*-indole-1-carboxylate **27d** (2.94 g, 9.93 mmol, 97% yield) was obtained as a white solid. **R$_f$**: 0.7 (Pentane: EtOAc 9:1) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.37 (s, 1H, Ar*H*), 7.56 (d, *J* = 3.7 Hz, 1H, Ar*H*), 7.41 (d, *J* = 8.3 Hz, 1H, Ar*H*), 7.34 (dd, *J* = 8.3, 1.8 Hz, 1H, Ar*H*), 6.56 – 6.50 (m, 1H, Ar*H*), 1.68 (s, 9H, C(CH_3)$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.3, 135.8, 129.2, 126.2, 125.8, 121.9, 118.3, 117.8, 106.9, 84.1, 28.1. NMR values correspond to the reported ones.[12]

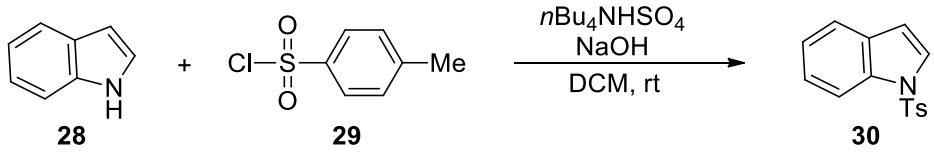
***Tert*-butyl 3-methyl-1*H*-indole-1-carboxylate (27e)**



27e

Following general procedure **GP1**, starting from commercially available 3-methyl-1*H*-indole (1.31 g, 9.99 mmol), after 16 hours *tert*-butyl 6-bromo-1*H*-indole-1-carboxylate **27e** (2.00 g, 8.65 mmol, 87% yield) was obtained as a colorless liquid. **R_f**: 0.9 (Pentane: EtOAc 95:5). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.16 (br-s, 1H, Ar*H*), 7.53 (d, *J* = 7.6 Hz, 1H, , Ar*H*), 7.39 (s, 1H, Ar*H*), 7.35 (ddd, *J* = 8.3, 7.2, 1.4 Hz, 1H, Ar*H*), 7.31 – 7.24 (m, 1H, Ar*H*), 2.31 (s, 3H, *CH*$_3$), 1.70 (s, 9H, C(*CH*$_3$)$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.5, 135.3, 131.2, 123.9, 122.5, 122.1, 118.6, 116.0, 114.9, 82.7, 27.9, 9.3. NMR values correspond to the reported ones.[13]

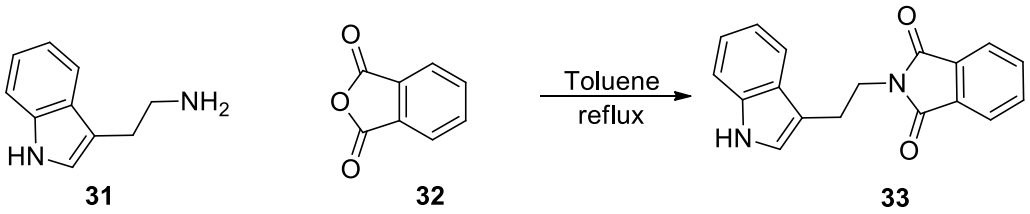
Synthesis of 1-Tosyl-1*H*-indole (30)



28 **29** **30**

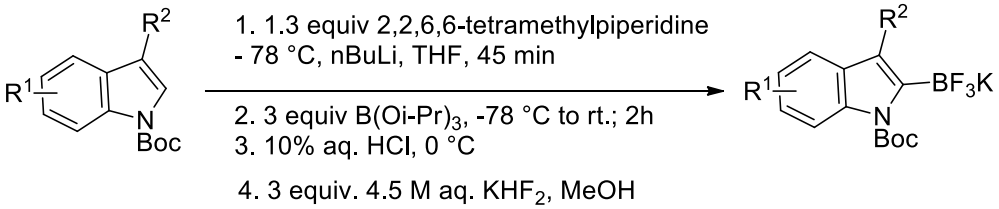
Following a reported procedure[14] to a solution of the commercially available NH-indole **28** (3.52 g, 30.0 mmol, 1.00 equiv.) in anhydrous DCM (0.10 M, 300 mL) was added *n*Bu_4NHSO_4 (1.02 g, 3.00 mmol, 0.100 equiv.) followed by addition of freshly powdered NaOH (4.81 g, 120 mmol, 4.00 equiv.). The resultant solution was allowed to stir at room temperature for 10 minutes before addition of 4-methylbenzene-1-sulfonyl chloride **29** (11.4 g, 60.0 mmol, 2.00 equiv.) and then allowed to stir at room temperature. After 3 hours, the reaction was quenched with H_2O (equal amount to reaction solvent volume), the organic layer was collected, and the aqueous layer was extracted three times with CH_2Cl_2 (equal to reaction volume). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was then purified via flash column chromatography and 1-tosyl-1*H*-indole **30** (6.20 g, 22.8 mmol, 76% yield) was obtained as a colorless solid. **R_f**: 0.6 (Pentane: EtOAc 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.3, 0.9 Hz, 1H, Ar*H*), 7.83 – 7.75 (m, 2H, Ar*H*), 7.58 (d, *J* = 3.6 Hz, 1H, Ar*H*), 7.53 (dt, *J* = 7.8, 1.0 Hz, 1H, Ar*H*), 7.32 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H, Ar*H*), 7.24 (dd, *J* = 7.8, 1.0 Hz, 1H, Ar*H*), 7.22 – 7.16 (m, 2H, Ar*H*), 6.66 (dd, *J* = 3.7, 0.8 Hz, 1H, Ar*H*), 2.32 (s, 3H, *CH*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.8, 135.2, 134.7, 130.6, 129.8, 126.7, 126.2, 124.4, 123.2, 121.3, 113.4, 108.9, 21.4. The NMR values correspond to the reported ones.[14]

Synthesis of 2-(2-(1*H*-Indol-3-yl)ethyl)isoindoline-1,3-dione (33)



Following the reported procedure,[15] a mixture of commercially available tryptamine **31** (1.00 g, 6.24 mmol) and phthalic anhydride **32** (1.02 g, 6.80 mmol) in toluene (25 mL) was refluxed overnight (the reaction was completed as judged by TLC (Pentane: EtOAc 3:2)). The reaction mixture was cooled to room temperature and the solution was concentrated under vacuum. The crude product was purified by column chromatography on silica gel to get 2-(2-(1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione **33** (1.60 g, 5.50 mmol, 88% yield) as a yellow solid. **R_f:** 0.6 (Pentane: EtOAc 2:3). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (br-s, 1H, N*H*), 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H, Ar*H*), 7.77 – 7.66 (m, 3H, Ar*H*), 7.35 (d, *J* = 8.1 Hz, 1H, Ar*H*), 7.22 – 7.03 (m, 3H, Ar*H*), 4.07 – 3.96 (m, 2H, N*CH*$_2$), 3.16 (dd, *J* = 8.9, 6.7 Hz, 2H, C-*CH*$_2$).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.3, 136.2, 133.8, 132.1, 127.3, 123.1, 122.1, 122.0, 119.5, 118.8, 112.3, 111.1, 38.5, 24.4. The NMR values correspond to the reported ones.[16]

General Procedure GP2 for the Borylation of N-Boc-Indoles.



With a slight modification of the reported procedure,[17] 2,2,6,6-tetramethylpiperidine (1.30 equiv.) in anhydrous THF (0.40 M) was cooled to -78 °C under an atmosphere of argon and treated dropwise with *n*-BuLi in Hexane (1.50 equiv.). The mixture was stirred at -78 °C for 10 min, then a solution of the corresponding 1-(*tert*-butoxycarbonyl)-1*H*-indole **27a-27e** (1.00 equiv.) in THF (1.00 M) was added dropwise. The mixture was stirred at -78 °C for 45 min. B(O*i*-Pr)$_3$ (3.00 equiv.) was added dropwise, and the reaction mixture was stirred for 30 min at -78 °C before being warmed to r.t. The reaction mixture was quenched with H_2O (30 mL), slowly acidified with 10% HCl at 0 °C (pH: 6), and extracted with EtOAc (3 times). The combined organic layers were washed with brine, dried over $MgSO_4$, and the solvent was removed under vacuum. In the next step, without further purification, the crude product was

dissolved in MeOH (0.20 M) and cooled at 0° C. Then a 4.5 M aqueous solution of KHF_2 (3.00 equiv.) was slowly added and the reaction mixture was stirred for 4 hours until the clear solution turned to a thick suspension. The solid was then filtered and washed with a minimum of cold MeOH (2 mL). The solid was dried on a high-vacuum line to afford the corresponding trifluoro borate salts **11a-11e**.

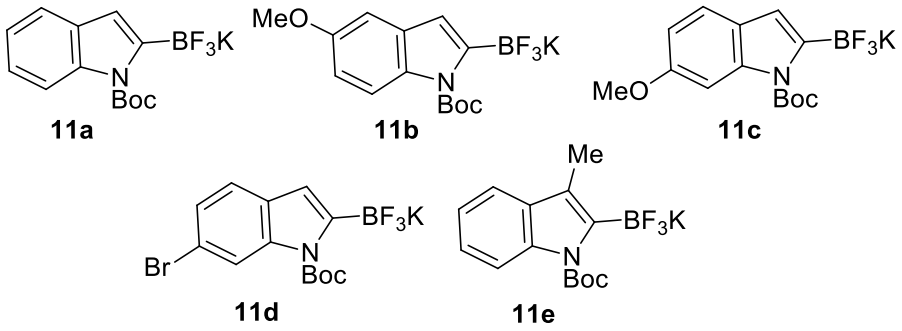
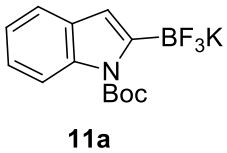


Figure 2.3 Indole-C2-trifluoroborate potassium salts.

Potassium trifluoro(1-*tert*-butoxycarbonyl-*1H*-indol-2-yl)borate (11a)

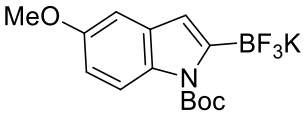


11a

Following general procedure **GP2**, starting from synthesized 1-(*tert*-butoxycarbonyl)-1*H*-indole **27a** (4.50 g, 20.7 mmol., 1.00 equiv.) with commercially available 2,2,6,6-tetramethylpiperidine (4.60 mL, 27.0 mmol. 1.30 equiv.), 2.5 M *n*-BuLi in hexane (12.4 mL, 31.1 mmol, 1.50 equiv.), triisopropyl borate (14.3 mL, 62.1 mmol, 3.00 equiv.) and 4.5 M aqueous solution of KHF_2 (13.8 mL, 62.0 mmol, 3.00 equiv.) Potassium trifluoro(1-*tert*-butoxycarbonyl-1*H*-indol-2-yl)borate (5.20 g, 16.1 mmol, 78% yield) **11a** was obtained as colorless solid. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.02 (dq, *J* = 8.3, 0.9 Hz, 1H, Ar*H*), 7.47 – 7.31 (m, 1H, Ar*H*), 7.22 – 7.03 (m, 2H, Ar*H*), 6.46 (s, 1H, Ar*H*), 1.59 (s, 9H, C(CH_3)$_3$). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 151.3, 137.4, 130.7, 121.7, 121.3, 119.3, 114.6, 111.7, 81.5, 27.7. The NMR values correspond to the reported ones.[17] *NB: the Carbon-Boron bond is not observed as reported in literature.*[18]

Potassium trifluoro(1-(*tert*-butoxycarbonyl)-5-methoxy-*1H*-indol-2-yl)borate (11b)

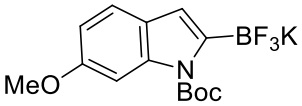
Following general procedure **GP2**, starting from synthesized *tert*-butyl 5-methoxy-1*H*-indole-1-carboxylate **27b** (1.50 g, 6.00 mmol, 1.00 equiv.), with commercially available 2,2,6,6-tetramethylpiperidine (1.33 mL, 7.89 mmol. 1.30 equiv.), 1.6 M *n*-BuLi in hexane (5.70 mL, 9.10 mmol, 1.50 equiv.) triisopropyl borate (4.20 mL, 18.2 mmol, 3.00 equiv.) and 4.5 M aqueous solution of KHF_2 (4.02 mL, 18.1 mmol, 3.00 equiv.) Potassium trifluoro(1-(*tert*-



11b

butoxycarbonyl)-5-methoxy-*1H*-indol-2-yl)borate **11b** (1.18 g, 3.34 mmol, 55% yield). **^{1}H NMR** (400 MHz, CD_3CN) δ 7.56 (d, *J* = 9.0 Hz, 1H, Ar*H*), 6.64 (d, *J* = 2.6 Hz, 1H, Ar*H*), 6.44 (dd, *J* = 9.0, 2.6 Hz, 1H, Ar*H*), 6.30 – 6.16 (m, 1H, Ar*H*), 3.47 (s, 3H, O*CH*$_3$), 1.33 (s, 9H, C(*CH*$_3$)$_3$). **^{13}C NMR** (101 MHz, CD_3CN) δ 156.1, 152.2, 133.2, 132.9, 116.7, 113.7, 111.4, 103.1, 83.2, 55.8, 28.2. The NMR values correspond to the reported ones.[11] *NB: the Carbon-Boron bond is not observed as reported in literature.*[18]

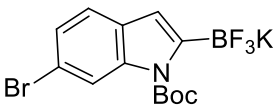
Potassium trifluoro(1-(tert-butoxycarbonyl)-6-methoxy-*1H*-indol-2-yl)borate (11c)



11c

Following general procedure **GP2**, starting from synthesized *tert*-butyl 6-methoxy-1*H*-indole-1-carboxylate **27c** (650 mg, 2.63 mmol, 1.00 equiv.), with commercially available 2,2,6,6-tetramethylpiperidine (582 µL, 3.42 mmol. 1.30 equiv.), 2.5 M *n*-BuLi in hexane (1.58 mL, 3.94 mmol, 1.50 equiv.), triisopropyl borate (1.82 mL, 7.89 mmol, 3.00 equiv.) and 4.5 M aqueous solution of KHF_2 (1.75 mL, 7.89 mmol, 3.00 equiv.). Potassium trifluoro(1-(*tert*-butoxycarbonyl)-6-methoxy-*1H*-indol-2-yl)borate **11c** (813 mg, 2.30 mmol, 88% yield) was obtained as colorless solid. **M.p.** 185 °C, decomposition). **^{1}H NMR** (400 MHz, Acetone-d_6) δ 7.65 (d, *J* = 2.3 Hz, 1H, Ar*H*), 7.25 (d, *J* = 8.4 Hz, 1H, Ar*H*), 6.72 (dd, *J* = 8.4, 2.3 Hz, 1H, Ar*H*), 6.54 (s, 1H, Ar*H*), 3.79 (s, 3H, O*CH*$_3$), 1.68 (s, 9H, C(*CH*$_3$)$_3$). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 157.2, 152.4, 139.4, 126.4, 120.4, 113.5, 111.0, 101.2, 82.8, 55.6, 28.4. **IR** ν 2976 (w), 1730 (m), 1699 (m), 1619 (w), 1484 (m), 1440 (w), 1368 (s), 1222 (m), 1200 (s), 1147 (s), 1092 (s), 1004 (s), 920 (s), 843 (s), 778 (m). **HR-ESI-MS**: calcd for $C_{14}H_{16}BF_3NO_3^+$ 314.1175 $[M - K]^+$; found 314.1187. *NB: the Carbon-Boron bond is not observed as reported in literature.*[18]

Potassium trifluoro(1-(*tert*-butoxycarbonyl)-6-bromo-*1H*-indol-2-yl)borate (11d)

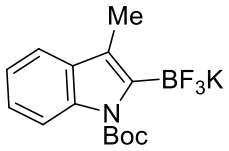


11d

Following general procedure **GP2**, starting from synthesized *tert*-butyl 6-bromo-1*H*-indole-1-carboxylate **27d** (1.50 g, 5.06 mmol, 1.00 equiv.), with commercially available 2,2,6,6-tetramethylpiperidine (1.12 mL, 6.58 mmol. 1.30 equiv.), 2.5 M *n*-BuLi in hexane (3.04 mL, 7.60 mmol, 1.50 equiv.) triisopropyl borate (3.51 mL, 15.2 mmol, 3.00 equiv.) and 4.5 M aqueous solution of KHF_2 (3.38 mL, 15.2 mmol, 3.00 equiv.). Potassium trifluoro(1-(*tert*-butoxycarbonyl)-6-bromo-*1H*-indol-2-yl)borate **11d** (0.830 g, 2.06 mmol, 41% yield) was obtained as colorless solid. **M.p**:

200 °C, decomposition. **^{1}H NMR** (400 MHz, Acetone-d_6) δ 8.26 (d, *J* = 1.9 Hz, 1H, Ar*H*), 7.36 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.23 (dd, *J* = 8.2, 1.8 Hz, 1H, Ar*H*), 6.63 (d, *J* = 0.8 Hz, 1H, Ar*H*), 1.69 (s, 9H, C(*CH*$_3$)$_3$). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 152.0, 139.4, 131.4, 125.1, 121.6, 119.0, 115.7, 113.2, 83.5, 28.2 **IR** ν 1737 (w), 1709 (w), 1448 (w), 1357 (m), 1325 (s), 1247 (w), 1211 (w), 1126 (s), 987 (s), 837 (w). **HR-ESI-MS**: calcd for $C_{13}H_{13}B^{79}BrF_3NO_2^+$ 362.0175 $[M - K]^+$; found 362.0180. *NB: the Carbon-Boron bond is not observed as reported in literature.*[18]

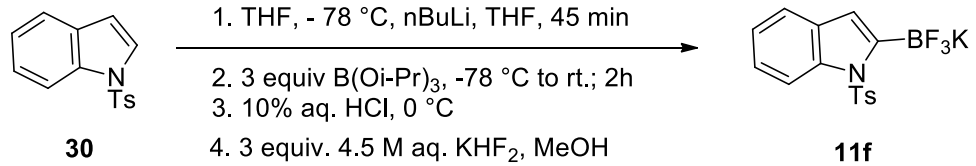
Potassium trifluoro(1-(*tert*-butoxycarbonyl)-3-methyl-*1H*-indol-2-yl)borate (11e)



11e

Following general procedure **GP2**, starting from synthesized *tert*-butyl 6-methoxy-1*H*-indole-1-carboxylate **27e** (2.00 g, 8.65 mmol, 1.00 equiv.), with commercially available 2,2,6,6-tetramethylpiperidine (1.91 mL, 11.2 mmol. 1.30 equiv.), 2.5 M *n*-BuLi in hexane (5.20 mL, 12.9 mmol, 1.50 equiv.), triisopropyl borate (6.00 mL, 25.9 mmol, 3.00 equiv.) and 4.5 M aqueous solution of KHF_2 (5.80 mL, 25.9 mmol, 3.00 equiv.). Potassium trifluoro(1-(*tert*-butoxycarbonyl)-3-methyl-*1H*-indol-2-yl)borate **11e** (2.50 g, 7.40 mmol, 86% yield) was obtained as colorless solid, (Mp: 205 °C). **^{1}H NMR** (400 MHz, Acetone-d_6) δ 7.96 – 7.86 (m, 1H, Ar*H*), 7.48 – 7.34 (m, 1H, Ar*H*), 7.19 – 6.99 (m, 2H, Ar*H*), 2.34 (s, 3H, *CH*$_3$), 1.66 (s, 9H, C(*CH*$_3$)$_3$). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 152.4, 137.8, 133.8, 122.9, 121.8, 121.1, 118.3, 115.5, 82.6, 28.3, 10.3.**IR** ν 2977 (w), 1726 (s), 1454 (w), 1374 (m), 1327 (s), 1238 (m), 1135 (s), 956 (s), 874 (m), 740 (s). **HR-ESI-MS**: calcd for $C_{14}H_{16}BF_3NO_2^+$ 298.1226 $[M - K]^+$; found 298.1230. *NB: the Carbon-Boron bond is not observed as reported in literature.*[18]

Synthesis of potassium trifluoro(1-(tosyl)-*1H*-indol-2-yl)borate (11f)

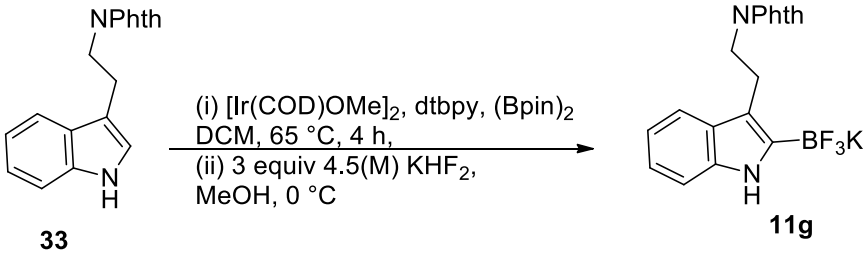


30 **11f**

Following a reported procedure,[19] 1.6 M *n*BuLi in hexane (9.38 mL, 15.0 mmol, 1.5 equiv.) was added dropwise to a solution of *N*-tosyl-1*H*-indole **30** (2.71 g, 10.0 mmol, 1.00 equiv) 50 mL of tetrahydrofuran at -78 °C. The reaction mixture was heated to room temperature and stirred for an additional 20 minutes. After cooling to -78 °C., triisopropyl borate (3.92 mL 17.0 mmol, 1.70 equiv) was added. After 10 minutes of addition, the reaction was allowed to warm

to room temperature and stirred overnight. The reaction mixture was quenched with H_2O (30 mL), slowly acidified with 10% HCl at 0 °C (pH:6), and extracted with EtOAc (3 x 50 mL). The combined organic layers were dried over magnesium sulfate and evaporated under reduced pressure to give 3.15 g of a green oil. The crude product was used without further purification in the next reaction. The crude product was dissolved in MeOH (100 mL) and cooled to 0 °C. A 4.5 M solution of KHF_2 in H_2O (6.6 mL, 30 mmol, 3 equiv.) was slowly added and the resulting pink thick suspension was stirred at r.t. for 4 hours. The solid was filtered and dried under reduced pressure and washed with a minimum of cold MeOH (3 mL). The solid was dried on a high-vacuum line to afford the corresponding trifluoro borate salt potassium trifluoro(1-(tosyl)-*1H*-indol-2-yl)borate **11f** (1.65 g, 4.40 mmol, 44% yield) as colorless solid. **M.p**. 235 °C. **^{1}H NMR** (400 MHz, Acetone-d_6) δ 8.07 (dd, *J* = 8.8, 3.1 Hz, 3H, Ar*H*), 7.39 – 7.25 (m, 1H, Ar*H*), 7.14 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.11 – 6.99 (m, 2H, Ar*H*), 6.45 (d, *J* = 0.8 Hz, 1H, Ar*H*), 2.22 (s, 3H, *CH*$_3$). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 144.2, 138.9, 138.4, 132.7, 129.8, 128.3, 122.9, 122.8, 120.6, 116.8, 115.2, 21.3. **IR** ν 2040 (w), 1834 (w), 1417 (s), 1217 (s), 853 (w). **HR-ESI-MS**: calcd for: Calcd for $C_{15}H_{12}BF_3NO_2S^+$ 338.0634[M - K]$^+$; Found 338.0626. *NB: the Carbon-Boron bond is not observed las reported in literature.*[18]

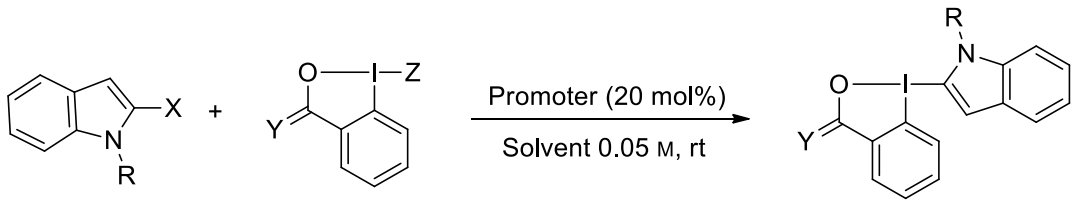
Synthesis and characterization of tryptamine trifluoroborates (11g)

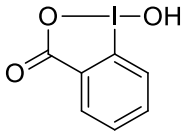


Following a reported procedure,[20] a flame dried 20-mL pressure flask was charged with (1,5-cyclooctadiene)(methoxy)iridium(I) dimer (17.0 mg, 30.0 µmol, 1.50 mol%), 4,4'-di-tert-butyl-2,2'-dipyridyl (14.0 mg, 50.0 µmol, 3.00 mol%), bis(pinacolato)diboron (868 mg, 3.42 mmol, 2.00 equiv.), *N*,*N*-phthaloyltryptamine **33** (500 mg, 1.72 mmol), and a stirring bar and sealed with a septum under an atmosphere of argon. Anhydrous dichloromethane (11 mL) was added via syringe to give a colorless suspension. The septum was replaced with the pressure flask's Teflon seal and the entire mixture was heated in an oil bath set to 65 °C. After completion of reaction (checked by TLC; Pentane: EtOAc 7:3), the reaction mixture is filtered through a small silica path and evaporate to dryness. The crude reaction mixture was used for the next step. The crude product was dissolved in 10 mL MeOH, and cooled at 0 °C, then a 4.5 M solution of

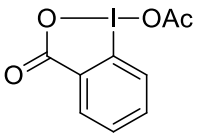
KHF_2 (1.20 mL, 5.20 mmol) was slowly added, and the reaction mixture was stirred for 4 hours until the clear solution turned thick. The solid was filtered and dried under reduced pressure and washed with a minimum of cold MeOH. The solid was dried on a high-vacuum line to afford as potassium trifluoro(2-(2-(1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione) borate **11g** (523 mg, 1.32 mmol, 77%) as yellow solid. **M.p**. 210 °C, decomposition. ^{1}**H NMR** (400 MHz, DMSO-d_6) δ 9.90 (s, 1H, *NH*), 7.90 – 7.74 (m, 4H, Ar*H*), 7.46 (d, *J* = 7.6 Hz, 1H, Ar*H*), 7.23 (d, *J* = 7.7 Hz, 1H, Ar*H*), 6.81 (dt, *J* = 20.5, 7.1 Hz, 2H, Ar*H*), 3.74 (q, *J* = 9.0, 8.3 Hz, 2H, N*CH*$_2$), 3.04 (t, *J* = 7.8 Hz, 2H, NCH$_2$-*CH*$_2$-). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 167.9, 136.5, 134.1, 131.8, 129.1, 122.8, 118.3, 116.8, 116.7, 111.0, 110.6, 39.1, 24.6. **IR** ν 3431 (w), 1705 (m), 1616 (m), 1399 (w), 1325 (m), 1137 (s), 959 (s), 742 (s). **HR-ESI-MS:** calcd for $C_{18}H_{13}BF_3K_0N_2O_2^+$ 357.1022 [M - K]$^+$; found 357.1028. *NB: the Carbon-Boron bond is not observed as reported in literature.*[18]

2.3 Optimization of the synthesis of C2-IndoleBX.





12c



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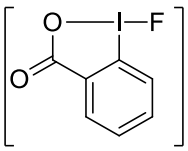
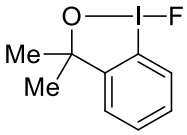
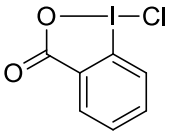


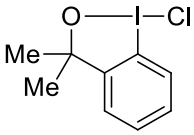
12a



12b



12d



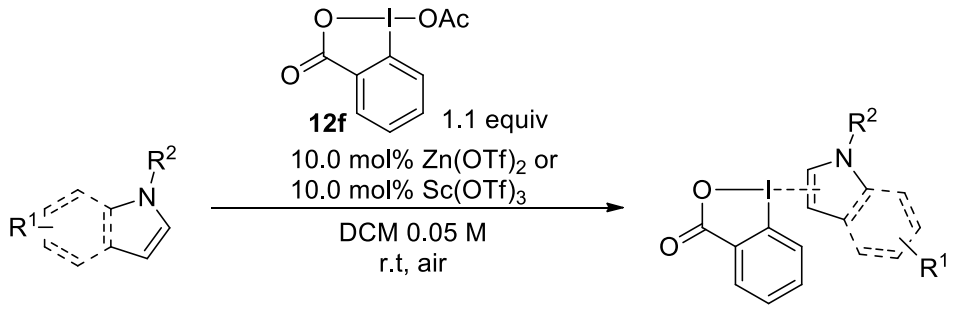
12e

Entry	X	R	Hypervalent reagent (Y,Z)	Promoter (mol%)	Solvents	Yield[a]
1	BF_3K	Boc	**12c**	$Zn(OTf)_2$	DCM	-[b]
2	BF_3K	Boc	**12f**	$Zn(OTf)_2$	DCM	-[b]
3	BF_3K	Boc	**12c**	ZnF_2	DCM	-
4	BF_3K	Boc	**12f**	ZnF_2	DCM	-
5	BF_3K	Boc	**12c**	TfOH	DCM	-[b]
6	BF_3K	Boc	**12f**	TfOH	DCM	-[b]
7	$SiMe_3$	H	**12c**	TMSOTf	MeCN	-
8	BF_3K	Boc	**12a**[c]	$NaBF_4$	MeCN	27%[d,e]
9	BF_3K	Boc	**12e**	$NaBF_4$	MeCN	86%[d,e]
10	$SiMe_3$	Me	**12e**	$NaBF_4$	MeCN,	-[e,f]
11	BF_3K	Boc	**12e**	$AgBF_4$	MeCN,	-[b,f]
12	BF_3K	Boc	**12d**	$AgBF_4$	MeCN	-[b,f]

a) Substrate (0.25 mmol), hypervalent iodine reagent **12a-12d**, **12g-12h** (0.25 mmol), Promoter (20 mol%.) and solvent (0.05 M) at 25 °C. all reactions are carried out overnight (except entry 8: carried out for 30 h; entry 9: best yield was observed only in 2 hours) b) Degradation of reagent, no expected product was observed. c) This reagent was prepared *in situ* d) Isolated yield after flash chromatography is given. e) Entries 8-10, reactions were quenched with 5% aqueous $NaBF_4$ solution. f) Entries 10-12, the reaction initially run at room temperature, no consumption of starting material was observed after 6 h then reactions were allowed to refluxing temperature for additional 12 h

2.4 Preparation of PyrroleBX and IndoleBX Reagents.

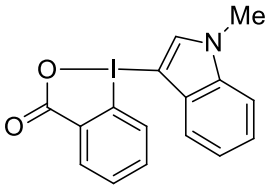
General Procedure GP3 for the Synthesis of C3-Heterocyclic-BX Reagents 2a-2f.



Note: prior to the reaction, the glassware requires to be carefully cleaned with aqua regia to remove all metal traces; the commercially available heterocyclic starting material were purified through a short plug of silica prior to being used.

GP3*: for 1.00 mmol*: in an open air flask, the corresponding heterocycle (1.00 mmol, 1.00 equiv.), freshly prepared acetoxy-benziodoxolone **12f** (1.10 mmol, 1.10 equiv.) and Zinc(II) trifluoromethanesulfonate (72.7 mg, 0.200 mmol, 20 mol%.) were dissolved in DCM (20 mL, 0.05 M). The reaction was stirred while being monitored by TLC (Pentane:EtOAc 9:1 for the starting materials, DCM:MeOH 9:1 for the products). Upon consumption of the starting material, the crude product was directly submitted to short-path flash chromatography (DCM:MeOH 10:1) to afford the desired Heterocyclic-BX compounds **2a-2f.**

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



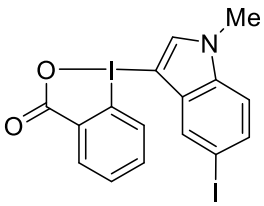
2a

The synthesis of 1-(3-1-methyl-1*H*-indole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one ***2a*** *was scaled up to 10 mmol without reoptimization of the protocol.*

Following procedure **GP3**: starting from commercially available 1-methyl-1-H-indole **5** (1.35 g, 10.0 mmol), after 16 hours 1-(3-1-methyl-1*H*-indole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one **2a** (3.28 g, 8.70 mmol, 87% yield) was obtained as a brown foam. **Rf:** 0.4 (DCM:MeOH 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.40 (dd, *J* = 7.5, 1.7 Hz, 1H, Ar*H*), 7.82 (s, 1H, N*CH*Cl), 7.55 – 7.48 (m, 2H, Ar*H*), 7.39 – 7.35 (m, 2H, Ar*H*), 7.34 – 7.23 (m, 2H, Ar*H* + $CDCl_3$), 6.84 (d, *J* = 8.3 Hz, 1H, Ar*H*), 4.02 (s, 3H, N*CH*$_3$). **^{13}C NMR** (101 MHz, CDCl3) δ 166.8, 138.6, 137.6, 133.4, 133.3, 132.5, 130.5, 129.3, 125.2, 124.3, 122.6, 119.9, 116.1, 110.7, 78.9, 33.9. **IR** ν 3107 (w), 3059 (w), 2948 (w), 1599 (s), 1552 (m),

1506 (m), 1454 (w), 1392 (m), 1277 (s), 1245 (s), 1225 (s), 1166 (s), 1131 (m), 1031 (s), 1004 (w), 842 (w). **HR-ESI-MS** calcd for $C_{16}H_{13}INO_2^+$ $[M+H]^+$ 377.9986, found 377.9990.

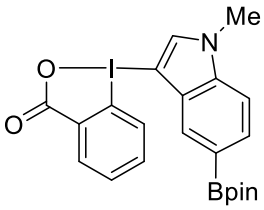
1-(3-5-Iodo-1-methyl-1*H*-indole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one (2b)



2b

Following procedure **GP3**: starting from 5-iodo-1-methyl-1*H*-indole **34d** (257 mg, 1.00 mmol), after 16 hours 1-(3-5-iodo-1-methyl-1*H*-indole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one **2b** (380 mg, 0.755 mmol, 76% yield) was obtained as a yellow amorphous solid. ***NB: the reagent is unstable in acidic deuterated solvents and it decompose in short time, we recommend the immediate use after the synthesis. The proton NMR presents about 21% of the open protonated form***. **Rf:** 0.3 (DCM:MeOH 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.24 (m, 1H, Ar*H*), 7.83 (s, 1H, NCHCI), 7.58 – 7.47 (m, 2H, Ar*H*), 7.26 (m, 1H, Ar*H* + $CDCl_3$), 7.21 - 7.18 (m, 2H, Ar*H*), 6.67 (d, *J* = 8.1 Hz, 1H, Ar*H*), 3.87 (s, 3H, *CH*$_3$N). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.6, 140.5, 136.8, 133.7, 132.6, 132.3, 131.4, 130.3, 128.1, 126.0, 122.3, 119.1, 115.7, 112.9, 86.1, 34.0. **IR** ν 3092 (w), 3061 (w), 1600 (s), 1584 (m), 1557 (m), 1503 (m), 1436 (w), 1422 (w), 1371 (m), 1265 (s), 1245 (s), 1225 (m), 1163 (m), 1113 (w), 1031 (s), 1004 (w), 836 (w). **HR-ESI-MS** calcd for $C_{16}H_{12}I_2NO_2^+$ $[M+H]^+$ 503.8952; found 503.8952.

1-(3-1-Methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole)-1*H*-1λ_3 –benzo [*b*]iodo-3(2*H*)-one (2c)

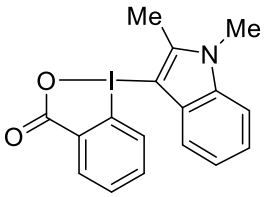


2c

Following procedure **GP3**: starting from commercially available 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (149 mg, 1.00 mmol), after 16 hours 1-(3-1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one **2c** (276 mg, 0.549 mmol, 54% yield) was obtained as an orange amorphous solid. **Rf:** 0.46 (DCM:MeOH 9:1). **^{1}H NMR** (400 MHz, CD_2Cl_2) δ 8.32 (dd, *J* = 7.5, 1.7 Hz, 1H, Ar*H*), 7.93 (s, 1H, N*CH*CI), 7.81 (dd, *J* = 8.4, 1.1 Hz, 1H, Ar*H*), 7.74 (s, 1H, C*CH*CBPin), 7.59 – 7.48 (m, 2H, Ar*H*), 7.31 (ddd, *J* = 8.6, 7.1, 1.7 Hz, 1H, Ar*H*), 6.85 (dd, *J* = 8.3, 0.9 Hz, 1H, Ar*H*), 3.99 (s, 3H, N*CH*$_3$), 1.30 (s, 12H, C*BPin*). **^{13}C NMR** (101 MHz, CD_2Cl_2) δ 167.0, 140.1, 139.6, 134.1, 133.8, 132.6, 131.0, 130.5, 129.5, 127.6, 126.0, 117.1, 110.7, 84.5, 80.3, 34.4, 25.2. *NB: the Carbon-Boron bond is not observed as reported in literature.*[18] **IR** ν 3095 (w), 2979 (w), 1611 (s), 1558 (w), 1507 (w), 1436 (w), 1360 (s), 1303

(w), 1263 (w), 1142 (s), 1114 (w), 1074 (w), 970 (w), 861 (w). **HR-ESI-MS** calcd for $C_{22}H_{24}BINO_4^+$ $[M+H]^+$ 504.0838; found 504.0835.

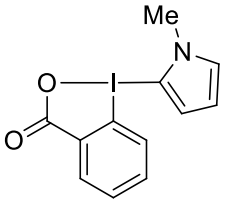
1-(3-1,2-Dimethyl-1*H*-indole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one (2d)



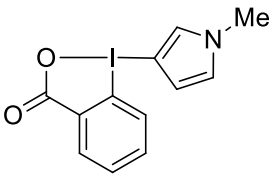
2d

Following procedure **GP3**: starting from 2-methyl-1-methyl-1*H*-indole **34a** (145 mg, 1.00 mmol), after 16 hours 1-(3-1,2-dimethyl-1*H*-indole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one **2d** (364 mg, 0.930 mmol, 93% yield) was obtained as a dark violet foam. **Rf:** 0.43 (DCM:MeOH 9:1).). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.42 (dd, *J* = 7.3, 1.7 Hz, 1H, Ar*H*), 7.52 (td, *J* = 7.3, 0.9 Hz, 1H, Ar*H*), 7.44 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.35 (m, 2H, Ar*H*), 7.28 (m, 1H, Ar*H*), 7.23 (ddd, *J* = 8.2, 6.9, 1.0 Hz, 1H, Ar*H*), 6.77 (m, 1H, Ar*H*), 3.91 (s, 3H, *CH*$_3$N), 2.65 (s, 3H, ICH=CH*CH*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.8, 145.3, 137.9, 133.7, 133.2, 132.7, 130.5, 128.9, 124.7, 123.6, 122.4, 119.2, 115.5, 110.4, 80.1, 31.1, 13.2. **IR** ν 3055 (w), 2987 (w), 2948 (w), 1717 (w), 1605 (s), 1584 (m), 1553 (m), 1516 (w), 1472 (w), 1437 (w), 1395 (m), 1378 (m), 1268 (m), 1154 (w), 1032 (w), 1011 (w), 829 (w). **HR-ESI-MS** calcd for $C_{17}H_{15}INO_2^+$ $[M+H]^+$ 392.0142; found 392.0146.

1-(2-1-Methyl-1*H*-pyrrole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one (2e) and 1-(3-1-methyl-1*H*-pyrrole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one (2e').

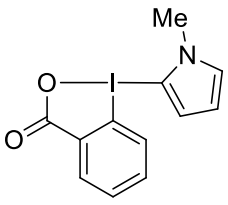


2e



2e'

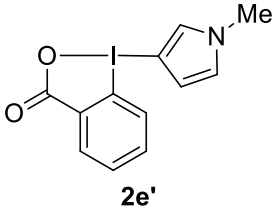
Following procedure **GP3:** starting from commercially available 1-methyl-1*H*-pyrrole (0.890 ml, 1.00 mmol), after 12 hours 1-(2-1-methyl-1*H*-pyrrole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one **2e** and 1-(3-1-methyl-1*H*-pyrrole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one **2e'** were obtained as a 1:1 mixture (310 mg, 0.948 mmol, overall yield 95%) as an off-white, sticky amorphous solid. Rf: 0.5 (DCM:MeOH 9:1). The two compounds were separated by slow flash column chromatography (EtOAc:MeOH 9:1).



2e

1-(2-1-methyl-1*H*-pyrrole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one **2e** (152 mg, 0.465 mmol, 47% yield; off-white, sticky amorphous solid) **Rf:** 0.3 (EtOAc:MeOH 9:1). **^{1}H NMR** (400 MHz, CD_3OD) δ 8.24 (dd, *J* = 7.5, 1.6 Hz, 1H, Ar*H*), 7.65 (td, *J* = 7.4, 1.0 Hz, 1H, Ar*H*), 7.55 (m, 1H, Ar*H*), 7.27 (t, *J* = 2.1 Hz, 1H, Ar*H*), 7.01 (dd, *J* = 3.9, 1.6 Hz, 1H, Ar*H*), 6.72 (dd, *J* = 8.3, 1.0 Hz, 1H, Ar*H*), 6.43 (dd, *J* = 3.9, 2.1 Hz, 1H, Ar*H*), 3.78 (s, 1H, N*CH*$_3$). **^{13}C NMR** (101 MHz, CD_3OD) δ 170.1, 135.5, 134.2, 133.2, 131.9, 131.4, 127.7, 126.6, 119.4, 112.9, 96.0,

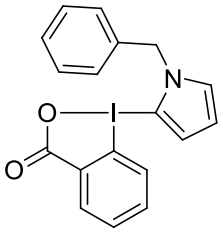
37.4. **IR** ν 3415 (w), 3105 (w), 3049 (w), 2950 (w), 1604 (s), 1584 (m), 1558 (w), 1508 (w), 1437 (w), 1346 (m), 1288 (m), 1223 (w), 1149 (w), 1091 (w), 1047 (w), 1005 (w), 829 (m). **HR-ESI-MS** calcd for $C_{12}H_{11}INO_2^+$ $[M+H]^+$ 327.9829; found 327.9842.



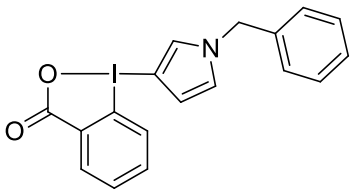
2e'

1-(3-1-methyl-1*H*-pyrrole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one **2e'** (158 mg, 0.483 mmol, 48% yield; off-white, sticky amorphous solid). **Rf:** 0.25 (EtOAc:MeOH 9:1). **^{1}H NMR** (400 MHz, CD_3OD) δ 8.15 (dd, *J* = 7.5, 1.7 Hz, 1H, Ar*H*), 7.53 (td, *J* = 7.3, 1.1 Hz, 1H, Ar*H*), 7.49 – 7.40 (m, 2H, Ar*H*), 7.04 – 6.98 (m, 2H, Ar*H*), 6.58 (d, *J* = 1.2 Hz, 1H, Ar*H*), 3.85 (s, 3H, N*Me*). **^{13}C NMR** (101 MHz, CD_3OD) δ 170.0, 134.9, 134.2, 133.4, 132.8, 131.5, 127.9, 127.7, 117.4, 116.6, 82.8, 37.1. **IR** ν 3447 (w), 3106 (w), 2947 (w), 2863 (w), 1603 (s), 1591 (m), 1558 (m), 1512 (m), 1437 (w), 1354 (m), 1294 (w), 1110 (m), 1083 (w), 1007 (w), 829 (m). **HR-ESI-MS** calcd for $C_{12}H_{11}INO_2^+$ $[M+H]^+$ 327.9829; found 327.9842.

1-(2-1-benzyl-1*H*-pyrrole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one (2f) and 1-(3-1-benzyl-1*H*-pyrrole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one (2f')

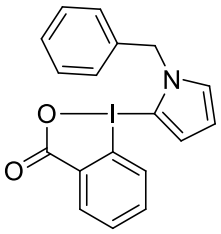


2f



2f'

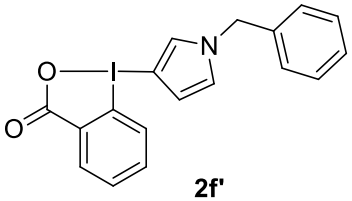
Following procedure **GP3**: starting from commercially available 1-benzyl-1*H*-pyrrole (0.890 ml, 1.00 mmol), after 12 hours 1-(2-1-benzyl-1*H*-pyrrole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one **2f** and 1-(3-1-benzyl-1*H*-pyrrole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one **2f'** were obtained in 3:1 mixture (345 mg, 0.856 mmol, overall yield 86%), as a colorless amorphous solid. **Rf**: 0.7 (DCM:MeOH 9:1). The two compounds were separated by slow flash column chromatography (EtOAc:MeOH 9:1).



2f'

1-(2-1-benzyl-1*H*-pyrrole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one **2f** (85.0 mg, 0.211 mmol, 21% yield); colorless foam. **Rf:** 0.5 (EtOAc:MeOH 9:1). **^{1}H NMR** (400 MHz, *2:1 mixture CD_3OD:C_6D_6, refererred to CD_3OD*) δ 8.18 (dd, *J* = 7.5, 1.6 Hz, 1H, Ar*H*), 7.28 (t, *J* = 7.4 Hz, 1H, Ar*H*), 7.10 (t, *J* = 2.2 Hz, 1H, Ar*H*), 6.92 (m, *J* = 7.6, 2.9 Hz, 6H, Ar*H* + C_6D_6), 6.71 (dd, *J* = 3.9, 1.7 Hz, 1H, Ar*H*), 6.35 (t, *J* = 3.4 Hz, 1H, Ar*H*), 6.23 (d, *J* = 8.3 Hz, 1H, Ar*H*), 4.90 (s, 2H, NCH_2Ph). **^{13}C NMR** (101 MHz, *2:1 mixture CD_3OD:C_6D_6, refererred to CD_3OD*) δ 169.8, 136.9, 134.6, 132.7, 131.2, 131.1, 129.5, 129.0, 128.5, 127.2, 119.2, 112.9,

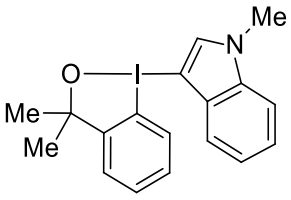
94.8, 54.7 *(two Carbon signals under the deuterated benzene*). **IR** ν 3109 (w), 3064 (w), 2968 (w), 2875 (w), 1609 (s), 1585 (m), 1558 (w), 1503 (w), 1456 (w), 1440 (w), 1357 (m), 1277 (w), 1103 (m), 1079 (w), 1032 (w), 1031 (w), 830 (w). **HR-ESI-MS** calcd for $C_{18}H_{15}INO_2^+$ $[M+H]^+$ 404.0142; found 404.0140.



2f'

1-(3-1-benzyl-1*H*-pyrrole)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one **2f'** (260 mg, 0.645 mmol, 65% yield); colorless foam. **Rf:** 0.46 (EtOAc:MeOH 9:1). **^{1}H NMR** (400 MHz, *2:1 mixture CD_3OD:C_6D_6, refered to CD_3OD*) δ 8.29 (dd, *J* = 7.5, 1.7 Hz, 1H, Ar*H*), 7.36 (t, *J* = 7.3 Hz, 1H, Ar*H*), 7.30 – 7.20 (m, 3H Ar*H* + C_6D_6), 7.18 – 7.08 (m, 3H, Ar*H*), 6.97 (d, *J* = 2.0 Hz, 1H, Ar*H*), 6.83 – 6.78 (m, 2H, Ar*H*), 6.30 (dd, *J* = 3.0, 1.7 Hz, 1H, Ar*H*), 4.93 (s, 2H, N*CH*$_2$Ph). **^{13}C NMR** (101 MHz, *2:1 mixture CD_3OD:C_6D_6, refered to CD_3OD*) δ 168.7, 136.8, 133.5, 133.0, 131.8, 130.9, 130.3, 128.8, 128.1, 127.4, 126.2, 125.5, 116.3, 115.3, 82.4, 53.5. **IR** ν 3409 (w), 3114 (w), 2971 (w), 1609 (s), 1585 (m), 1558 (w), 1456 (w), 1438 (w), 1365 (m), 1277 (s), 1160 (w), 1079 (w), 1032 (m), 835 (w). **HR-ESI-MS** calcd for $C_{18}H_{15}INO_2^+$ $[M+H]^+$ 404.0142; found 404.0140.

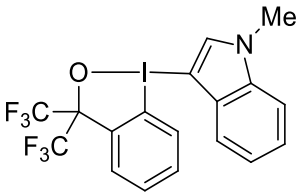
1-(3-1-Methyl-1*H*-indole)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodoxole (3a)



3a

Following procedure **GP3** (on 0.100 mmol scale): starting from commercially available 1-methyl-1-H-indole **5** (26.2 mg, 0.100 mmol) and 3,3-dimethyl-1λ_3-benzo[*d*][1,2]iodoxol-1(3*H*)-yl acetate **12e** (70.4 mg, 0.220 mmol, 1.10 equiv.), after 16 hours 1-(3-1-methyl-1*H*-indole)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodoxole **3a** (40.1 mg, 0.102 mmol, 51% yield) was obtained as a brown foam. **Rf:** 0.7 (DCM:MeOH 9:1). **IR** ν 3115 (w), 3050 (w), 2986 (w), 1509 (w), 1455 (w), 1372 (w), 1284 (s), 1247 (s), 1225 (m), 1166 (m), 1110 (w), 1031 (s), 992 (w).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (s, 1H, N*CH*Cl), 7.54 (m, 1H, Ar*H*), 7.47 (m, 1H, Ar*H*), 7.45 – 7.40 (m, 3H, Ar*H*), 7.34 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1H, Ar*H*), 7.08 (ddd, *J* = 8.7, 5.8, 2.9 Hz, 1H, Ar*H*), 6.87 (m, 1H, Ar*H*), 4.02 (s, 3H, N*CH*$_3$), 1.75 (s, 6H, C(*CH*$_3$)$_2$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 146.3, 140.2, 137.7, 130.9, 130.4, 128.9, 128.7, 127.0, 124.8, 123.3, 119.6, 111.0, 108.9, 74.6, 72.9, 34.2, 30.5. **HR-ESI-MS** calcd for $C_{18}H_{19}INO^+$ $[M+H]^+$ 392.0506; found 392.0510.

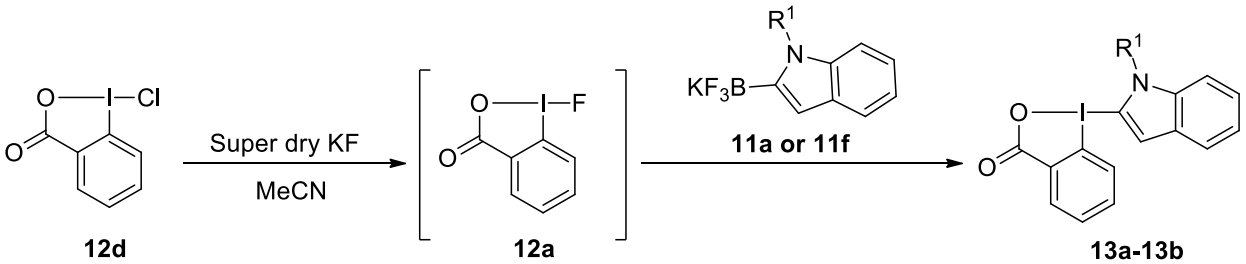
1-(3-1-Methyl-1*H*-indole)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ$_3$-benzo[*d*][1,2]iodaoxole (4a)



4a

Following procedure **GP3** (on 0.100 mmol scale): starting from commercially available 1-methyl-1-H-indole **5** (26.2 mg, 0.100 mmol), 1-acetoxy-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole **12f** (94.0 mg, 0.220 mmol, 1.10 equiv.) and in Et_2O 0.05 M, after 16 hours 1 (3-1-methyl-1*H*-indole)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodaoxole **4a** (56.1 mg, 0.112 mmol, 56% yield) was obtained as a brown foam. **Rf:** 0.7 (DCM:MeOH 9:1). **IR** ν 3069 (w), 2922 (w), 2852 (w), 1732 (w), 1504 (m), 1457 (w), 1263 (s), 1212 (m), 1178 (s), 1157 (s), 1130 (m), 1047 (w), 948 (s). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (m, 1H, Ar*H*), 7.53 (s, 1H, N*CH*Cl), 7.52 – 7.46 (m, 3H, Ar*H*), 7.41 (ddd, *J* = 8.3, 7.0, 1.1 Hz, 1H, Ar*H*), 7.28 (m, 1H, Ar*H*), 7.23 (m, 1H, Ar*H*), 6.95 (d, *J* = 8.3 Hz, 1H, Ar*H*), 3.96 (s, 3H, N*CH*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.5, 137.4, 131.7, 131.4, 130.1, 129.9, 126.9, 123.9, 123.2 (m), 122.1, 120.4, 112.2, 110.3, 84.2, 81.55 (dt, *J* = 57.1, 28.5 Hz), 33.6 *(one aromatic Carbon signal not resolved)*. **HR-ESI-MS** calcd for $C_{18}H_{13}F_6INO^+$ $[M+H]^+$ 499.9941; found 499.9946.

General Procedure GP4 for the Synthesis of C2-IndoleBX Reagents 13a-13b.



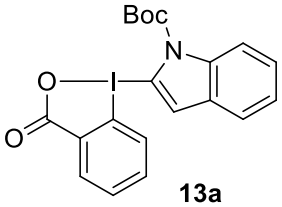
12d **12a** generated *in situ* not isolated **13a-13b**

Note: prior to the reaction, the glassware requires to be carefully cleaned with aqua regia to remove all metal traces; the commercially available heterocyclic starting material were purified through a short plug of silica prior to being used.

Following a reported procedure,[21] commercially available spray-dried KF (581 mg, 10.0 mmol) was dried in a schlenk flask at 150 °C under vacuum over 5 min. After cooling down to r.t., 1-chloro-1,2-benziodoxol-(*1H*)-one **12d** (1.00 equiv.) was added to the vial, followed by anhydrous MeCN (5 mL). The yellow slurry of **12a** was stirred for 2 h at 80 °C. After cooling down to r.t., the suspension was filtered over a sintered glass filter in a dry schlenk flask under inert conditions (*NB: oxygen has to be completely avoided*). A solution of the correspondent

potassium trifluoroborate substrate **11a** or **11f** (2.00 mmol, in 15 mL MeCN, 1.00 equiv.) was added and the resulting solution stirred at r.t. The reaction was monitored in TLC (DCM:MeOH 9:1). After 2 hours the solution slightly changed its color. The reaction was left running overnight, and stopped after 30 h. Then 5% aqueous $NaBF_4$ (60 mL) was added and the reaction mixture was vigorously stirred for 1 additional hour. (The reaction was stopped upon completion checked by TLC). The quenched reaction mixture was extracted using DCM (2x40 mL), the combined organic layers washed with saturated $NaHCO_3$ solution (40 mL) and then the organic layer dried over Na_2SO_4. The solvent was then removed under reduced pressure and the crude product purified via column chromatography (DCM:MeOH 10:1) to afford pure reagents **13a-13b.**

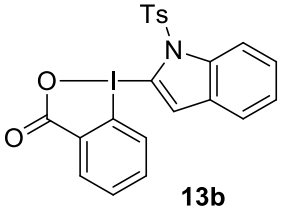
1-(*Tert*-butyl 1*H*-indole-1-carboxylate)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one (13a)



13a

Following general procedure **GP4**, starting from potassium trifluoro(1-*tert*-butoxycarbonyl-1*H*-indol-2-yl)borate **11a** (646 mg, 2.00 mmol, in 15 mL MeCN, 1.00 equiv.) and 1-chloro-1,2-benziodoxol-(*1H*)-one **11a** (565 mg, 2.00 mmol, 1.00 equiv.), 1-(*tert*-butyl 1*H*-indole-1-carboxylate)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one **13a** (250 mg, 0.540 mmol, 27%), was obtained as a brown solid. **M.p.** 150 °C, decomposition. **R_f:** 0.5 (DCM: MeOH 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.41 (dd, *J* = 7.6, 1.7 Hz, 1H, Ar*H*), 8.31 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.74 – 7.59 (m, 2H, Ar*H*), 7.55 – 7.42 (m, 3H, Ar*H*), 7.37 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.00 (d, *J* = 8.4 Hz, 1H, Ar*H*), 1.44 (s, 9H, C(CH_3)$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.7, 148.5, 138.0, 134.0, 132.4, 130.9, 129.5, 127.5, 126.1, 126.0, 124.0, 121.7, 119.6, 116.1, 105.9, 86.8, 27.8. (*One aromatic carbon not resolved).* **IR** ν 1728 (m), 1636 (s), 1567 (s), 1451 (m), 1349 (m), 1227 (m), 1156 (w), 968 (w). **HR-ESI-MS**: calcd for $C_{20}H_{19}INO_4^+$ 464.0353 $[M + H]^+$; found 464.0353.

1-(2-1-(Tosyl)-*1H*-indol-2-yl)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one (13b)

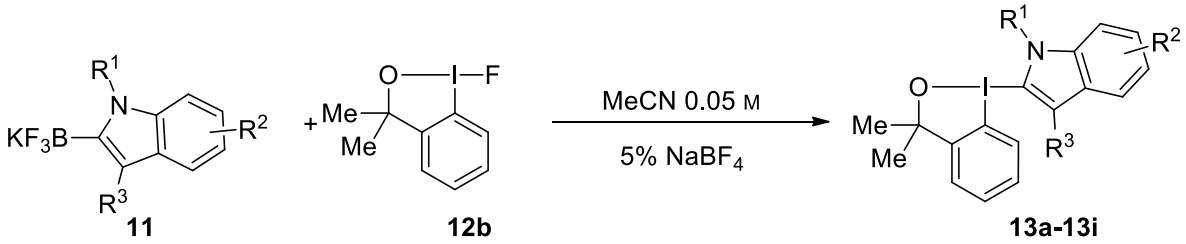


13b

Following general procedure **GP4**, starting from potassium trifluoro(1-(tosyl)-*1H*-indol-2-yl)borate **11f** (943 mg, 2.50 mmol, 1.00 equiv.) and 1-chloro-1,2-benziodoxol-(*1H*)-one **xx** (706 mg, 2.50 mmol, 1.00 equiv.), **1**-(2-1-(tosyl)-*1H*-indol-2-yl)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one **13b** (205 mg, 0.400 mmol, 16% yield) was obtained as colorless solid. **M.p.:** 185 °C. **R_f:** 0.5 (DCM: MeOH 9:1). **^{1}H NMR** (400 MHz, Acetone-d_6) δ 8.22 (d, *J* = 8.5 Hz, 1H, Ar*H*), 8.08 (d, *J* = 7.4 Hz, 1H, Ar*H*), 7.92 – 7.84 (m, 2H, Ar*H*), 7.73 (s, 1H, Ar*H*),

7.67 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.54 (t, *J* = 7.3 Hz, 1H, Ar*H*), 7.47 (ddd, *J* = 8.5, 7.2, 1.3 Hz, 1H, Ar*H*), 7.43 – 7.35 (m, 1H, Ar*H*), 7.35 – 7.27 (m, 1H, Ar*H*), 7.21 (d, *J* = 8.1 Hz, 2H, Ar*H*), 6.82 (d, *J* = 8.4 Hz, 1H, Ar*H*), 2.20 (s, 3H, *CH*$_3$). **^{13}C NMR** (101 MHz, Acetone-d_6) δ 166.9, 147.1, 138.6, 135.4, 134.9, 133.9, 132.2, 131.3, 131.2, 131.1, 128.2, 128.1, 127.9, 127.8, 125.1, 123.1, 120.0, 115.6, 110.1, 21.4. **IR** ν 1646 (w), 1603 (s), 1558 (w), 1370 (m), 1173 (s), 1089 (s), 1007 (w), 827 (w). **HR-ESI-MS**: calcd for $C_{22}H_{16}INNaO_4S^+$ 539.9737 [M + Na]$^+$; found 539.9736.

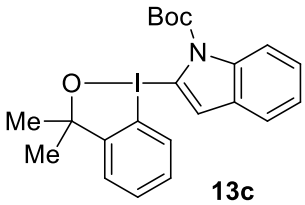
General Procedure GP5 for the Synthesis of C2-IndoleDBX Reagents 13c-13i.



Note: prior to the reaction, the glassware requires to be carefully cleaned with aqua regia to remove all metal traces; the commercially available heterocyclic starting material were purified through a short plug of silica prior to being used.

In a dry round bottom flask, commercially available 1-fluoro-3,3-dimethyl-1,2-benziodoxole **12b** (1.00 equiv.) was dissolved in anhydrous MeCN (0.050 M). Potassium trifluoro indole borate salt **11** (1.00 equiv.) was added, and the mixture was stirred at r.t under inert atmosphere. After 2 hour 5% aqueous $NaBF_4$ (30 mL/mmol, 13.6 equiv.) was added and the reaction mixture was additionally stirred for 1 hour. (The reaction was stopped upon completion, checked by TLC (DCM: MeOH 9:1). The quenched reaction mixture was extracted using DCM (2x20 mL), the combined organic layers were washed with saturated $NaHCO_3$ solution (20 mL), then the organic layer was dried over Na_2SO_4. Then the solvent was removed under reduced pressure. Column chromatrography purification with EtOAc: MeOH (10:1) afforded the desired C2-IndoleDBXs **13c-13i**.

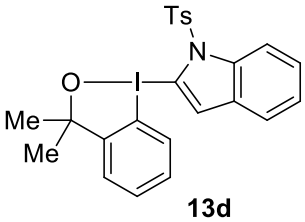
1-(2-*Tert*-butyl 1*H*-indole-1-carboxylate)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodoxol (13c)



13c

Following general procedure **GP5**, starting from potassium trifluoro(1-(*tert*-butoxycarbonyl-1*H*-indol-2-yl)borate **11a** (168 mg, 0.520 mmol, 1.00 equiv.) and commercially available 1-fluoro-3,3-dimethyl-1,2-benziodoxole **12b** (146 mg, 0.520 mmol, 1.00 equiv.), 1-(2-*tert*-butyl 1*H*-indole-1-carboxylate)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo[*d*][1,2] iodoxol **13c** was obtained (215 mg, 0.450 mmol, 86%) as an off-white foam (**M.p**.: 128-133 °C). [*Using same procedure this reaction was scaled up upto 5.00 mmol scale (1.40 g of Indole salt **11a**) and desired product **13c** was obtained (2.02 g, 4.23 mmol, 85% yield) in same efficiency*]. **R$_f$:** 0.6 (DCM: MeOH 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (dd, *J* = 8.5, 1.0 Hz, 1H, Ar*H*), 7.59 (dt, *J* = 7.8, 1.1 Hz, 1H, Ar*H*), 7.46 (td, *J* = 7.3, 1.0 Hz, 1H, Ar*H*), 7.43 – 7.36 (m, 2H, Ar*H*), 7.32 – 7.26 (m, 1H, Ar*H*), 7.20 – 7.16 (m, 1H, Ar*H*), 7.15 (d, *J* = 0.8 Hz, 1H, Ar*H*), 6.84 (dd, *J* = 8.3, 1.0 Hz, 1H, Ar*H*), 1.54 (s, 6H, C(CH_3)$_2$), 1.46 (s, 9H, C(CH_3)$_3$).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.3, 148.3, 137.7, 130.1, 129.9, 128.7, 127.0, 126.8, 125.7, 123.1, 122.3, 120.9, 119.3, 115.8, 113.9, 85.0, 74.8, 32.3, 27.8. **IR** ν 2968 (w), 1729 (s), 1435 (m), 1354 (s), 1325 (s), 1159 (s), 1136 (m), 1032 (m), 970 (m), 801 (m), 746 (s). **HR-ESI-MS**: calcd for $C_{22}H_{25}INO_3^+$ 478.0874 $[M + H]^+$; found 478.0886.

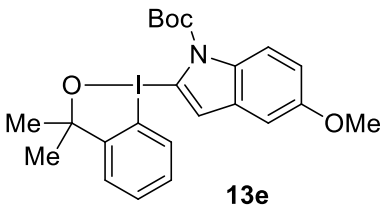
1-(2-1-Tosyl-1*H*-indole)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo[*d*][1,2] iodoxole (13d)



13d

Following general procedure **GP5**, starting from potassium trifluoro(1-(tosyl)-*1H*-indol-2-yl)borate **11f** (566 mg, 1.50 mmol, 1.00 equiv.) and commercially available 1-fluoro-3,3-dimethyl-1,2-benziodoxole **12b** (420 mg, 1.5 mmol, 1.00 equiv.), 1-(2-1-tosyl-1*H*-indole)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo[*d*][1,2] iodoxole **13d** (425 mg, 0.800 mmol, 53% yield) was obtained as colorless solid. **M.p**. 135-138 °C. **R$_f$:** 0.4 (DCM: MeOH 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 8.5, 1.0 Hz, 1H, Ar*H*), 7.81 – 7.74 (m, 2H, Ar*H*), 7.56 (dt, *J* = 7.8, 1.1 Hz, 1H, Ar*H*), 7.47 – 7.32 (m, 3H, Ar*H*), 7.30 (td, *J* = 7.6, 1.0 Hz, 1H, Ar*H*), 7.18 – 7.11 (m, 3H, Ar*H*), 7.07 (ddd, *J* = 8.4, 6.8, 1.7 Hz, 1H), 6.69 (dd, *J* = 8.3, 0.9 Hz, 1H, Ar*H*), 2.31 (s, 3H, CH_3), 1.58 (s, 6H, C(CH_3)$_2$).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.3, 145.2, 137.6, 135.5, 130.6, 129.9, 129.8, 128.9, 127.1, 126.7, 126.4, 126.1, 123.7, 123.6, 121.4, 120.2, 114.7, 114.4, 75.2, 31.5, 21.5. **IR** ν 2963 (w), 1597 (w), 1562 (w), 1430 (m), 1366 (s), 1155 (s), 1090 (s), 951 (m). **HR-ESI-MS**: calcd for $C_{24}H_{23}INO_3S^+$ 532.0438 $[M + H]^+$; found 532.0436.

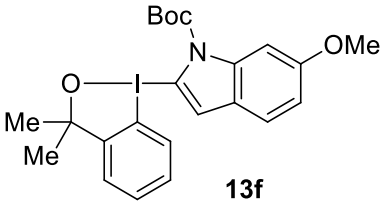
1-(2-5-Methoxy-1-*tert*-butyl-1*H*-indole-1-carboxylate)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo [*d*][1,2]iodoxole (13e)



13e

Following general procedure **GP5**, starting from potassium trifluoro(1-(*tert*-butoxycarbonyl)-5-methoxy-1*H*-indol-2-yl)borate **11b** (706 mg, 2.00 mmol, 1.00 equiv.) and commercially available 1-fluoro-3,3-dimethyl-1,2-benziodoxole **12b** (560 mg, 2.00 mmol, 1.00 equiv.), 1-(2-5-methoxy-1-*tert*-butyl-1*H*-indole-1-carboxylate)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo [*d*][1,2]iodoxole **13e** (775 mg, 1.53 mmol, 76% yield) was obtained as brown solid foam. **M.p.** 72-75 °C. **R$_f$:** 0.5 (DCM: MeOH 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 – 8.06 (m, 1H, Ar*H*), 7.40 – 7.36 (m, 1H, Ar*H*), 7.30 (dd, *J* = 7.6, 1.6 Hz, 1H, Ar*H*), 7.10 (ddd, *J* = 8.4, 7.0, 1.6 Hz, 1H, Ar*H*), 7.01 (s, 1H, Ar*H*), 6.95 (dq, *J* = 5.9, 2.6 Hz, 2H, Ar*H*), 6.76 (dd, *J* = 8.3, 1.0 Hz, 1H, Ar*H*), 3.79 (s, 3H, O*CH$_3$*), 1.46 (s, 6H, C(*CH$_3$*)$_2$), 1.36 (s, 9H, C(*CH$_3$*)$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.1, 149.3, 148.4, 132.5, 130.9, 130.0, 128.9, 127.2, 126.9, 122.3, 119.1, 116.6, 115.1, 114.0, 102.7, 85.0, 74.8, 55.6, 32.4, 27.9. **IR** ν 2965 (w), 1727 (s), 1612 (w), 1434 (w), 1357 (m), 1325 (s), 1253 (m), 1159 (s), 1117 (s), 1026 (s), 844 (m), 756 (s). **HR-ESI-MS**: calcd for $C_{23}H_{27}INO_4^+$ 508.0979 $[M + H]^+$; found 508.0981.

1-(2-6-Methoxy-1-*tert*-butyl-1*H*-indole-1-carboxylate)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo [*d*][1,2]iodoxole (13f)

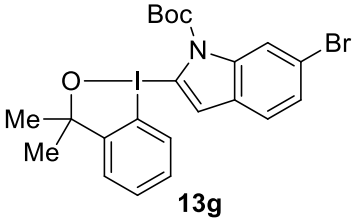


13f

Following general procedure **GP5**, starting from potassium trifluoro(1-(*tert*-butoxycarbonyl)-6-methoxy-1*H*-indol-2-yl)borate **11c** (706 mg, 2.00 mmol, 1.00 equiv.) and commercially available 1-fluoro-3,3-dimethyl-1,2-benziodoxole **12b** (560 mg, 2.00 mmol, 1.00 equiv.), the corresponding indole reagent **13f** (812 mg, 1.60 mmol, 80% yield) was obtained as brown solid foam, (**M.P**.: 70-75 °C). **R$_f$:** 0.6 (DCM: MeOH 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 2.3 Hz, 1H, Ar*H*), 7.41 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.34 (dd, *J* = 7.6, 1.6 Hz, 1H, Ar*H*), 7.14 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H, Ar*H*), 7.05 (s, 1H, Ar*H*), 6.90 (dd, *J* = 8.6, 2.3 Hz, 1H, Ar*H*), 6.85 – 6.80 (m, 1H, Ar*H*), 3.88 (s, 3H, O*CH$_3$*), 1.50 (s, 6H, C(*CH$_3$*)$_2$), 1.41 (s, 9H, C(*CH$_3$*)$_3$).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.8, 149.4, 148.3, 138.8, 129.8, 128.7, 126.9, 126.8, 123.8, 122.6, 121.3, 117.1, 114.1, 113.0, 99.4, 84.9, 74.7, 55.5, 32.4, 27.8. **IR** ν 2963 (w), 1727 (m), 1613

(w), 1487 (w), 1362 (m), 1326 (s), 1155 (s), 1045 (m), 945 (m), 824 (m), 756 (m). **HR-ESI-MS**: calcd for $C_{23}H_{27}INO_4^+$ 508.0979 $[M + H]^+$; found 508.0983.

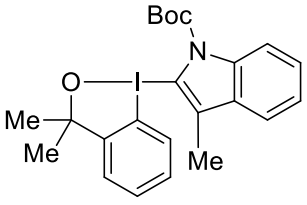
1-(2-5-Bromo-1-*tert*-butyl-1*H*-indole-1-carboxylate)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo [*d*][1,2]iodoxole (13g)



13g

Following general procedure **GP5**, starting from potassium trifluoro(1-(*tert*-butoxycarbonyl)-6-bromo-1*H*-indol-2-yl)borate **11d** (402 mg, 1.00 mmol, 1.00 equiv.) and commercially available 1-fluoro-3,3-dimethyl-1,2-benziodoxole **12b** (280 mg, 1.00 mmol, 1.00 equiv.), 1-(2-5-bromo-1-*tert*-butyl-1*H*-indole-1-carboxylate)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo [*d*][1,2]iodoxole **13g** (377 mg, 0.680 mmol, 68% yield) was obtained as off-white solid foam. **M.p**. 73-78 °C **R_f:** 0.5 (DCM: MeOH 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.54 (dt, *J* = 1.5, 0.7 Hz, 1H, Ar*H*), 7.50 – 7.35 (m, 4H, Ar*H*), 7.18 (ddd, *J* = 8.4, 7.0, 1.6 Hz, 1H, Ar*H*), 7.13 (d, *J* = 0.8 Hz, 1H, Ar*H*), 6.80 (dd, *J* = 8.3, 1.0 Hz, 1H, Ar*H*), 1.54 (s, 6H, C(CH_3)$_2$), 1.45 (s, 9H, C(CH_3)$_3$).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.1, 148.3, 138.3, 130.1, 129.1, 129.0, 127.2, 127.1, 126.6, 122.3, 121.9, 120.0, 119.1, 114.0, 85.9, 75.1, 32.2, 27.8 (one C is not resolved). **IR** ν 2969 (w), 1731 (s), 1352 (s), 1321 (s), 1235 (m), 1157 (s), 1137 (m), 1031 (m), 970 (m), 908 (m), 754 (s). **HR-ESI-MS**: calcd for $C_{22}H_{24}{}^{79}BrINO_3^+$ 555.9979 $[M + H]^+$; found 556.0001

1-(2-3-Methyl-1-*tert*-butyl-1*H*-indole-1-carboxylate)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo [*d*][1,2]iodoxole (13h)

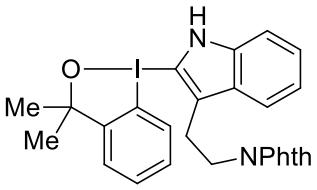


13h

Following general procedure **GP5**, starting from potassium trifluoro(1-(*tert*-butoxycarbonyl)-3-methyl-1*H*-indol-2-yl)borate **11e** (1.69 g, 5.00 mmol, 1.00 equiv.) and commercially available 1-fluoro-3,3-dimethyl-1,2-benziodoxole **12b** (1.41 mg, 5.00 mmol, 1.00 equiv.), 1-(2-3-methyl-1-*tert*-butyl-1*H*-indole-1-carboxylate)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo [*d*][1,2]iodoxole **13h** (2.40 g, 4.88 mmol, 97% yield) was obtained as off-white foam. **M.p**. 128-130 °C. **R_f:** 0.6 (DCM: MeOH 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.53 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.46 – 7.32 (m, 3H, Ar*H*), 7.28 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.12 (t, *J* = 7.6 Hz, 1H, Ar*H*), 6.80 (d, *J* = 8.3 Hz, 1H, Ar*H*), 2.42 (s, 3H, CH_3), 1.54 (s, 6H, C(CH_3)$_2$), 1.45 (s, 9H, C(CH_3)$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.3, 148.4, 137.5, 129.7, 129.6, 128.6, 126.8, 126.4, 125.8, 122.7, 119.3, 117.6, 115.8, 113.3, 84.5, 74.3, 32.3, 27.7, 11.9 (*one aromatic*

carbon signal is not resolved) **IR** ν 1727 (w), 1352 (w), 1325 (m), 1157 (s), 1089 (m), 971 (w), 857 (w), 750 (s). **HR-ESI-MS**: calcd for $C_{23}H_{27}INO_3^+$ 492.1030 $[M + H]^+$; found 492.1038.

1-(2-(1*H*-Indol-3-yl)ethyl)isoindoline-1,3-dione)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo[*d*][1,2] iodoxole (13i)



13i

Following general procedure **GP5**, starting from potassium trifluoro(2-(2-(1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione) borate **11g** (396 mg, 1.00 mmol, 1.00 equiv.) and commercially available 1-fluoro-3,3-dimethyl-1,2-benziodoxole (280 mg, 1.00 mmol, 1.00 equiv.), 1-(2-(1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo[*d*][1,2] iodoxole **13i** (347 mg, 0.630 mmol, 63% yield) was obtained as yellow solid. **M.p**. 132-135 °C. **R$_f$:** 0.4 (DCM: MeOH 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 – 7.58 (m, 5H, Ar*H*), 7.48 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.22 (d, *J* = 7.5 Hz, 3H, Ar*H*), 7.07 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.96 – 6.84 (m, 1H, Ar*H*), 6.66 (d, *J* = 8.3 Hz, 1H, Ar*H*), 3.83 (t, *J* = 7.7 Hz, 2H, N*CH$_2$*), 3.12 (bs, 2H, C-*CH$_2$*), 1.57 (s, 6H, C(*CH$_3$*)$_2$). (N*H was not resolved*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.9, 148.1, 139.5, 133.7, 131.9, 130.0, 129.3, 127.4, 126.9, 126.5, 123.8, 123.0, 121.0, 119.9, 119.1, 112.6, 112.4, 73.8, 38.5, 29.7, 25.6 (*one aromatic Carbon signal is not resolved*). **IR** ν 2965 (w), 1704 (m), 1434 (m), 1356 (w), 1155 (s), 954 (s), 871 (m), 748 (s). **HR-ESI-MS**: calcd for $C_{27}H_{24}IN_2O_3^+$ 551.0826 $[M + H]^+$; found 551.0834.

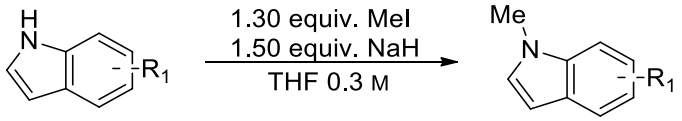
3. Metal Free (Hetero)-Arylation of Indoles.

All commercially available chemicals were purchased from the suppliers quoted in Paragraph 1.0 of Supplementary Informations: these chemicals were purified through a short plug of celite prior to their use in catalysis. The synthesis of non commercial available compounds is presented below.

The synthesis of the starting materials **34a-34f** had been already described before.[1] The procedures here reported are taken from the cited publication to facilitate reproduction of the results by having all the data in the same file.

3.1 Synthesis of Methylated Indoles.

General Procedure GP6 for the N-Methylation of Indoles.



GP6: The corresponding indole (1.00 - 5.00 mmol, 1.00 equiv.) was dissolved in dry THF (0.3 M). Sodium hydride (60% suspension in mineral oil; 1.50 equiv.) was slowly added under N_2 flow at 0 °C. After being stirred at 0 °C for 15 min,the reaction mixture was allowed to warm to r.t for 1.5 h. It was then cooled back to 0 °C and methyl iodide (1.30 equiv.) was added. The mixture was warmed to r.t. and stirred overnight. After cooling again to 0 °C, the reaction was quenched with water (10 mL), extracted with Et_2O (3 x 10 mL), the combined organic layers were dried over $MgSO_4$, and the solvent removed under reduced pressure. The resulting crude product was purified via flash column chromatography (Pentane:EtOAc 9:1-4:1), to give the desired N-methylated indole**.**

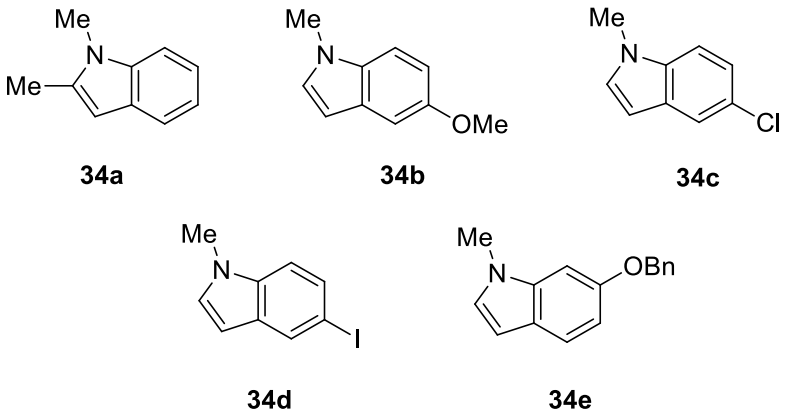
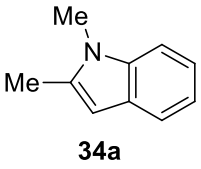


Figure 3.1 Methylated Indole used for IndoleBX's synthesis and Nucleophilic partners

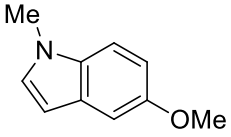
1,2-Dimethyl-1*H*-indole (34a)



34a

Following procedure **GP6**: starting from commercially available 2-methylindole (656 mg, 5.00 mmol), 1,2-dimethyl-1H-indole **34a** (683 mg, 4.70 mmol, 94% yield) was obtained as an off-white solid. **^{1}H NMR** (400 MHz $CDCl_3$) δ 7.69 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.41 (dd, *J* = 8.1, 1.0 Hz, Ar*H*), 7.32 (m, 1H, Ar*H*), 7.24 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H, Ar*H*), 6.42 (s, 1H, NC(CH_3)C*H*), 3.79 (s, 3H, NCH_3), 2.57 (d, *J* = 1.0 Hz, 3H, NCCH_3). **^{13}C NMR** (125 MHz, $CDCl_3$) *δ* 138.1, 136.9, 128.1, 120.6, 119.8, 119.4, 108.8, 99.7, 29.5, 12.9. **IR** ν (neat) 3050 (w), 3020 (w), 2970 (m), 1610 (w), 1400 (s), 1340 (m), 1240 (m), 930 (m), 910 (w), 780 (m), 750 (m), 730 (s). ^{1}H NMR values are in accordance with the data reported in literature.[22]

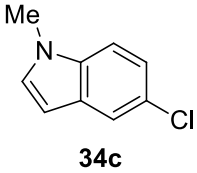
5-Methoxy-1-methyl-1*H*-indole (34b)



34b

Following procedure **GP6**: starting from commercially available 5-methoxy-1*H*-indole (736 mg, 5.00 mmol), 5-methoxy-1-methyl-1*H*-indole **34b** (730 mg, 4.53 mmol, 91% yield) was obtained as a colorless crystalline solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 (d, 1H, *J* = 8.5 Hz, Ar*H*) 7.13 (s, 1H, Ar*H*), 7.05 (s, 1 H, Ar*H*), 6.92 (d, 1H, *J* = 8.8 Hz, Ar*H*), 6.43 (d, 1H, *J* = 1.0 Hz, Ar*H*), 3.90 (s, 3H, N*Me*), 3.80 (s, 3H, O*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.0, 132.2, 129.3, 128.8, 111.9, 109.9, 102.5, 100.4, 55.9, 33.0. **IR** ν 2952 (w), 2918 (w), 2834 (w), 1622 (m), 1608 (w), 1577 (w), 1496 (s), 1459 (w), 1450 (m), 1449 (m), 1421 (s), 1347 (w), 1293 (w), 1243 (s), 1191 (m), 1152 (s), 1102 (w), 1026 (m), 942 (w), 855 (m), 845 (w), 805 (s).

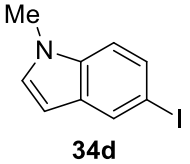
5-Chloro-1-methyl-1*H*-indole (34c)



34c

Following procedure **GP6**: starting from commercially available 5-chloro-1*H*-indole (758 mg, 5.00 mmol), 5-chloro-1-methyl-1*H*-indole **34c** (800 mg, 4.83 mmol, 97% yield) was obtained as a colorless solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 2.1 Hz, 1H, Ar*H*), 7.30 – 7.19 (m, 2H, Ar*H*), 7.10 (d, *J* = 3.1 Hz, 1H, Ar*H*), 6.47 (dd, *J* = 3.1, 0.7 Hz, 1H, Ar*H*), 3.80 (s, 3H, N*CH*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 135.1, 130.1, 130.1, 125.1, 121.8, 120.2, 110.2, 100.6, 33.1. **IR** ν 3102 (w), 2943 (w), 2913 (w), 2881 (w), 2817 (w), 1567 (w), 1513 (m), 1475 (s), 1441 (m), 1421 (s), 1379 (w), 1331 (m), 1278 (s), 1241 (s), 1199 (m), 1146 (m), 1106 (w), 1082 (m), 1063 (s), 1009 (m), 909 (m), 870 (m), 869 (m).

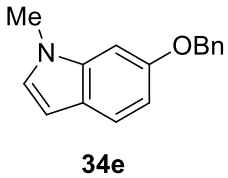
5-Iodo-1*H*-indole (34d)



34d

Following procedure **GP6**: starting from commercially available 5-iodo-1*H*-indole (257 mg, 1.00 mmol), 5-iodo-1-methyl-1*H*-indole **34d** (380 mg, 0.755 mmol, 76% yield) was obtained as a colorless solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (s, 1 H, Ar*H*), 7.49 (d, *J* = 8.6 Hz, 1H, Ar*H*), 7.13 (d, *J* = 8.6 Hz, 1H, Ar*H*), 7.04 (s, 1H, Ar*H*), 6.43 (s, 1H, Ar*H*), 3.80 (s, 3H, N*CH*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 135.8, 131.0, 129.8, 129.7, 129.6, 111.3, 100.3, 82.9, 33.0. **IR** ν 3093 (w), 3053 (w), 2940 (w), 2919 (w), 2886 (w), 2876 (w), 2856 (w), 1557 (m), 1510 (s), 1473 (s), 1432 (m), 1420 (s), 1379 (w), 1329 (m), 1277 (s), 1242 (s), 1193 (w), 1151 (w), 1103 (m), 1079 (m), 1045 (w), 1007 (m), 888 (s), 868 (m).

6-(Benzyloxy)-1-methyl-1*H*-indole (34e)

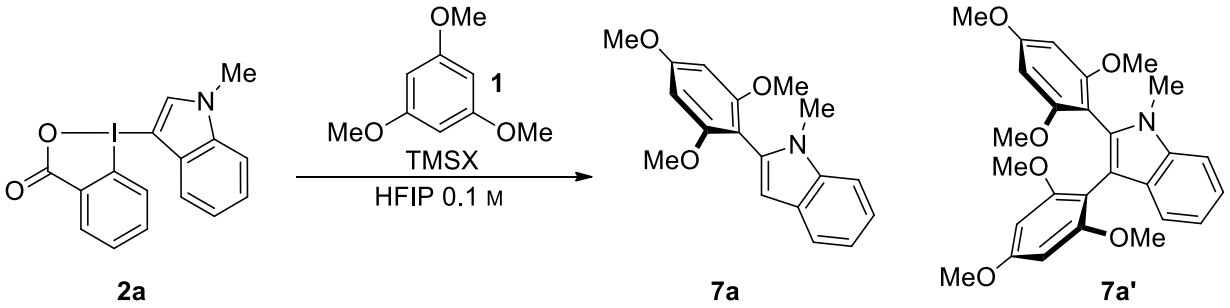


34e

Following procedure **GP6**: starting from commercially available 6-benzyloxyindole (223 mg, 1.00 mmol), 6-(benzyloxy)-1-methyl-1*H*-indole **34e** (237 mg, 1.00 mmol, 100% yield) was obtained as a orange solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 – 7.48 (m, 3H, Ar*H*), 7.43 – 7.38 (m, 2H, Ar*H*), 7.34 (m, 1H, Ar*H*), 6.96 (d, *J* = 3.1 Hz, 1H, Ar*H*), 6.93 – 6.85 (m, 2H, Ar*H*), 6.43 (dd, *J* = 3.1, 0.8 Hz, 1H, Ar*H*), 5.15 (s, 2H, *CH*$_2$), 3.73 (s, 3H, N*Me*). ^{1}H-NMR values are in accordance with the data reported in literature.[23]

3.2 Optimization of the Metal Free (Hetero)-Arylation of Indoles with the C3 Reagent.

Table 3.1: equivalents of 1 and LA screening:

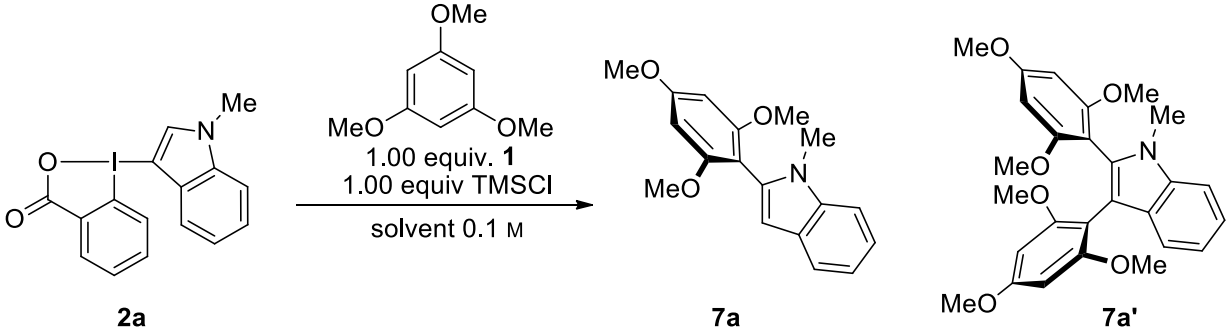


2a **7a** **7a'**

Entry	Equiv. of xx	Lewis Acid (equiv.)	Yield%[a] xx/xx
1	1.5	TMSBr (2)	41.4%/17%
2	1	-	-[b]
3	1	TMSBr (2)	40%/23%
4	1	TMSBr (1)	44%/12%
5	**1**	**TMSCl (1)**	**68%/-**
6	1	TMSI (1)	-[c]

a) Substrate **2a** (0.100 mmol), 1,3,5 trimethoxybenzene **1** (equiv. given in the table), TMSCl-TMSBr-TMSI (x equiv.) and HFIP (0.1 M) at 25 °C. Isolated yield after flash chromatography is given. b) no conversion, reagent **2a** and nucleophile **1** are recovered. c) complete decomposition and polymerization.

Table 3.2: Screening of the solvent:



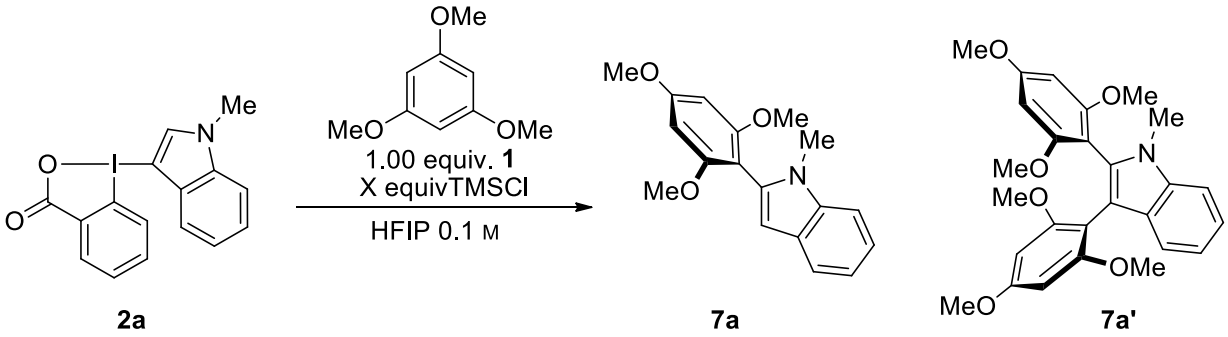
2a **7a** **7a'**

Entry	Solvent	Yield%[a] xx/xx
1	DCM	-[b]
2	DCE	-[b]
3	MeCN	4%/-
4	THF	-[b]

5	Et_2O	traces/-
6	**HFIP**	**68%/-**
7	MeOH	traces/-
8	TFE	20%/-

a) Substrate **2a** (0.100 mmol), 1,3,5 trimethoxybenzene **1** (0.100 mmol), TMSCl (1.00 equiv.) and HFIP (0.1 M) at 25 °C. Isolated yield after flash chromatography is given. b) no conversion, reagent **xx** and nucleophile **xx** are recovered.

Table 3.3: screening of TMSCl equivalents:

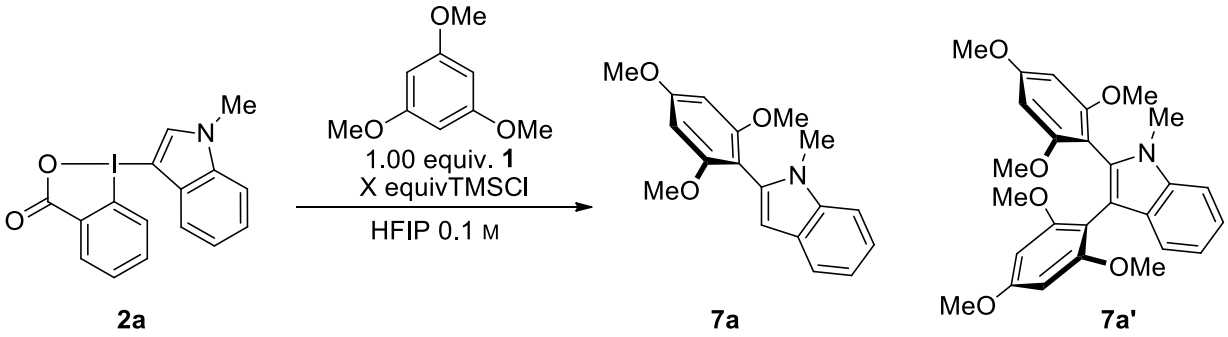


2a **7a** **7a'**

Entry	TMSCl (equiv.)	Yield%[a] xx/xx
1	0.1	-[b]
2	0.2	-[b]
3	0.4	4%/-
4	0.5	10%/-
5	0.8	39%/-
6	**1**	**68%/-**
7	1.2	70%/-
8	2	40%/-[c]

a) Substrate **2a** (0.100 mmol), 1,3,5 trimethoxybenzene **1** (0.100 mmol), TMSCl (X equiv.) and HFIP (0.1 M) at 25 °C. Isolated yield after flash chromatography is given. b) no conversion, reagent **2a** and nucleophile **1** are recovered. c) decomposition and polymerization of both reagent **2a** and nucleophile **1** are detected.

Table 3.4: Screening of substrate's molarity in HFIP:

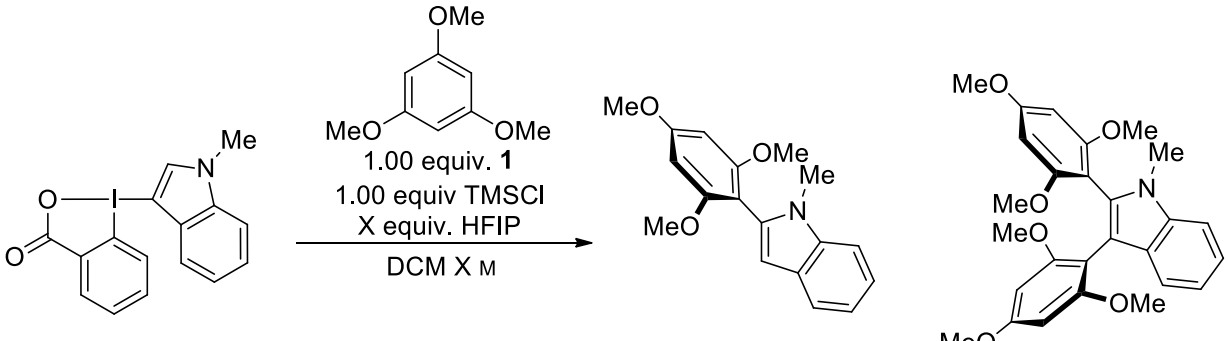


2a **7a** **7a'**

Entry	HFIP (M)	Yield%[a] xx/xx
1	0.012	44%/-[b]
2	0.025	47%/-[b]
3	0.1	68%/-
4	0.25	64%/-[c]
5	**0.5 = 20 equiv.**	**70%/-[c]**

a) Substrate **2a** (0.100 mmol), 1,3,5 trimethoxybenzene **1** (0.100 mmol), TMSCl (1.00 equiv.) and HFIP (X M) at 25 °C. Isolated yield after flash chromatography is given. b) reagent **2a** and nucleophile **1** are recovered. c) solubility problem of reagent **2a**, incomplete reaction.

Table 3.5: Screening of HFIP equivalents and concentration in DCM:



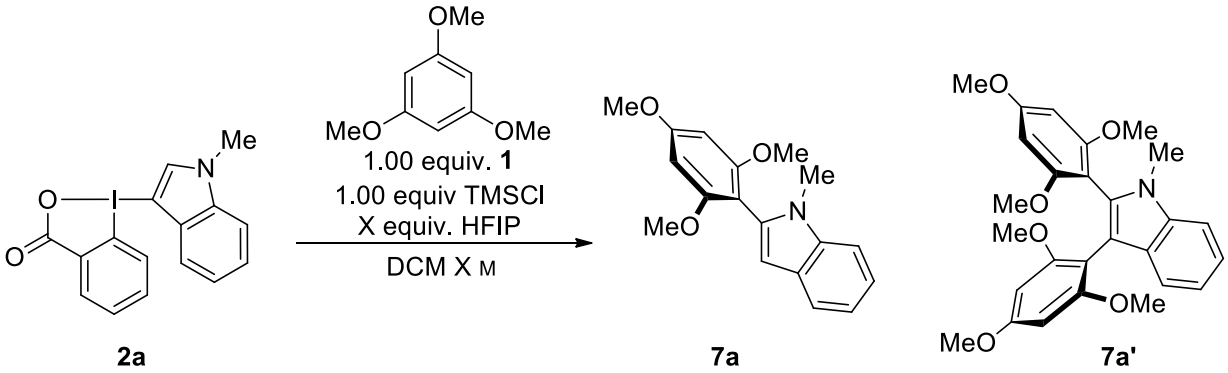
2a **7a** **7a'**

Entry	DCM (M)	HFIP (equiv.)	Yield%[a] xx/xx
1	0.1	20 equiv. = 0.5 M	75%/-
2	0.1	10	68%/-
3	0.1	5	64%/-
4	0.1	2	-[b]
5	0.1	1	-[b]
6	0.2	5	66%/-

7	**0.2**	**10**	**75%/-**
8	0.2	20	75%/-
9	0.25	10	68%/-[c]

a) Substrate **2a** (0.100 mmol), 1,3,5 trimethoxybenzene **1** (0.100 mmol), TMSCl (1.00 equiv.) and HFIP (X equiv.) in DCM (X M) at 25 °C. Isolated yield after flash chromatography is given. b) no conversion, reagent **2a** and nucleophile **1** are recovered. c) decomposition of the reagent **2a** is detected

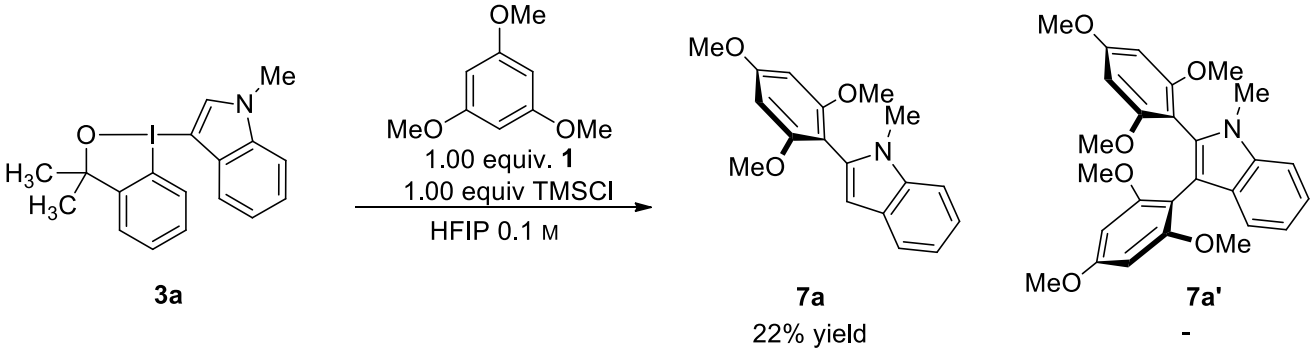
Table 3.6: screening of HFIP equivalents and concentration in DCM at 50 °C:



2a **7a** **7a'**

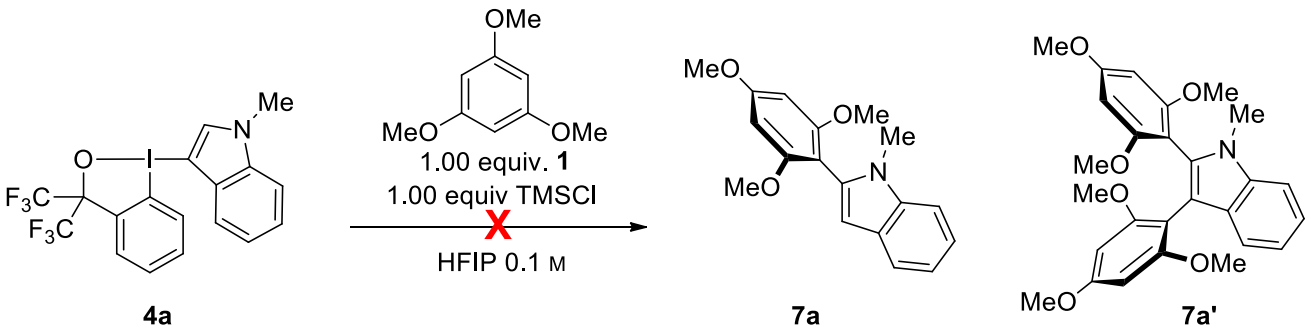
Entry	T (°C)	HFIP (equiv.)	DCM (M)	Yield%[a] xx/xx
1	**25**	**10**	**0.2**	**75%/-**
2	50	10	0.1	74%/-[b]
3	50	5	0.1	70%/-[b]
4	50	2	0.1	68%/-[b]
5	50	1	0.1	23%/-[b]

a) Substrate **2a** (0.100 mmol), 1,3,5 trimethoxybenzene **1** (0.100 mmol), TMSCl (1.00 equiv.) and HFIP (X equiv.) in DCM (X M) at 25 °C. Isolated yield after flash chromatography is given. b) decomposition of the reagent **2a** is detected



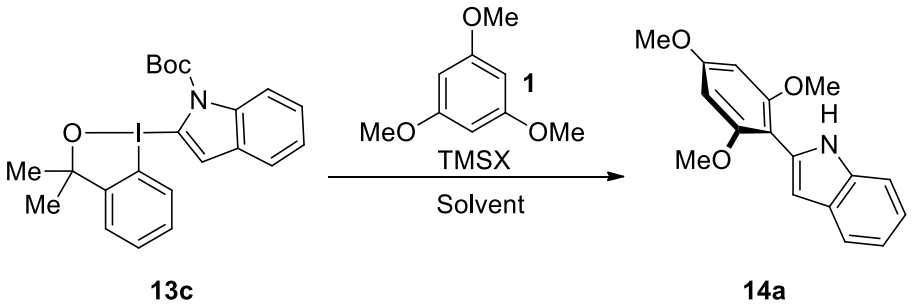
3a **7a** 22% yield **7a'** -

Substrate **3a** (0.100 mmol), 1,3,5 trimethoxybenzene **1** (0.100 mmol), TMSCl (1.00 equiv.) in HFIP (0.1 M) at 25 °C. Isolated yield after flash chromatography is given.



Substrate **4a** (0.100 mmol), 1,3,5 trimethoxybenzene **1** (0.100 mmol), TMSCl (1.00 equiv.) in HFIP (0.1 M) at 25 °C. Isolated yield after flash chromatography is given.

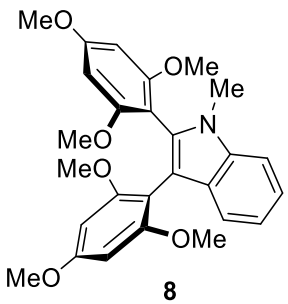
Table 3.7: Optimization for Lewis acid and solvents for Arylation of IndoleDBX



Entry[a]	Lewis Acid (equiv.)	Solvent	Yield%[a]
1	TMSCl (2)	HFIP (0.1 M)	-[b]
2	TMSCl (2)	HFIP (10.0 equiv.)+DCM(0.2 M)	Traces
3	TMSBr (2)	HFIP	60%
4	**TMSBr (1)**	**HFIP (10.0 equiv.)+DCM(0.2 M)**	**77%**
5	TMSI (2)	HFIP (10.0 equiv.)+DCM(0.2 M)	-[c]
6	TMS-1*H*-imidazole (2)	HFIP (10.0 equiv.)+DCM(0.2 M)	-[c]

a) Substrate **13c** (0.100 mmol), 1,3,5 trimethoxybenzene **1** (xx 0.110mmol, 1.10 equiv.), TMSCl-TMSBr-TMSI (2 equiv.) at 25 °C. Isolated yield after flash chromatography is given. b) no conversion, reagent **13c** and nucleophile **1** are recovered. c) complete decomposition and polymerization.

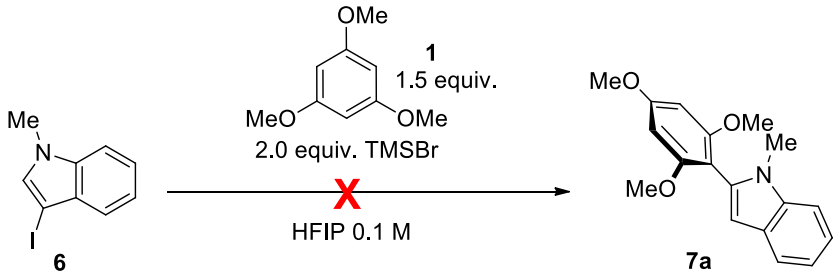
1-Methyl-2,3-bis(2,4,6-trimethoxyphenyl)-1*H*-indole (8).



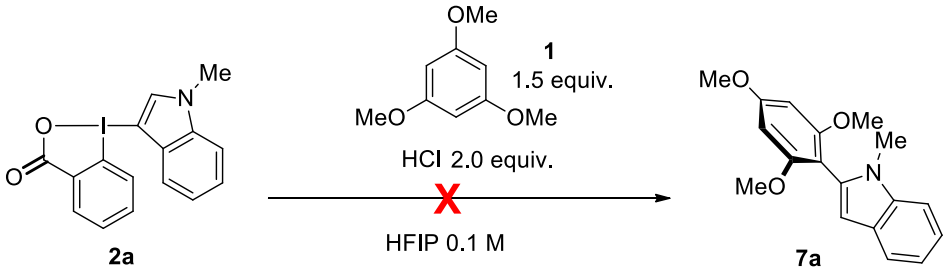
8

White resin. **Rf:** 0.38 (Pentane:EtOAc 1:1) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 2H, Ar*H*), 7.13 (ddd, *J* = 8.3, 7.0, 1.1 Hz, 1H, Ar*H*), 6.99 (ddd, *J* = 7.9, 7.0, 0.9 Hz, 1H, Ar*H*), 6.12 (s, 2H, Ar*H*), 6.11 (s, 2H, Ar*H*), 3.82 (s, 3H, O*Me*), 3.82 (s, 3H, O*Me*), 3.60 (s, 3H, O*Me*), 3.57 (s, 6H, N*Me*), 3.53 (s, 6H, O*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.3, 159.8, 159.5, 159.2, 137.1, 131.8, 127.8, 120.6, 120.3, 118.4, 109.3, 107.2, 106.7, 103.8, 90.5, 90.4, 55.5, 55.5, 55.2, 55.2, 30.7. **IR** ν 3001 (w), 2935 (w), 2836 (w), 1587 (m), 1584 (s), 1464 (m), 1415 (m), 1336 (w), 1226 (s), 1128 (s), 1041 (w), 811 (m), 741 (m). **HR-ESI-MS** calcd for $C_{27}H_{29}NO_6^+$ $[M+H]^+$ 464.1995; found 464.2093.

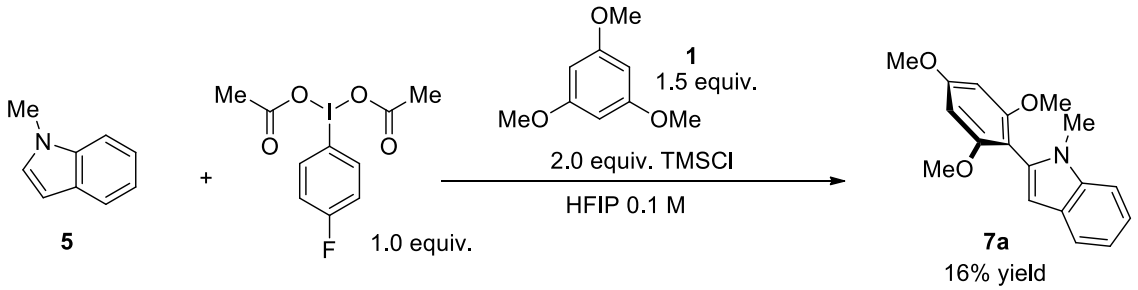
3.3 Control experiments



In an open air vial, commercially available 3-Iodoindole **6** (26.0 mg, 0.100 mmol, 1.00 equiv.), 1,3,5-trimethoxybenzene **1** (25.0 mg, 0.150 mmol, 1.50 equiv.) and TMSBr (26.0 µL, 0.200 mmol, 2.00 equiv.) were dissolved in HFIP (1 mL, 0.1 M). The reaction was stirred for three hours and then quenched with sat. aqueous $NaHCO_3$ (4 mL); the organic layer was extracted with DCM (3x5 mL), then the solvent was removed under reduced pressure. No conversion in the desired product 1-methyl-3-(2,4,6-trimethoxyphenyl)-1H-indole **7a** was detected.



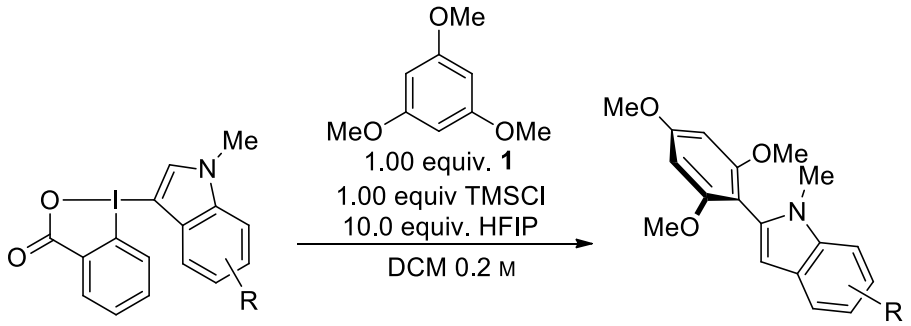
In an open air vial, IndoleBX reagent **2a** (38.0 mg, 0.100 mmol, 1.00 equiv.), 1,3,5-trimethoxybenzene **1** (25.0 mg, 0.150 mmol, 1.50 equiv.) and HCl in EtOH (80.0 µL, 0.200 mmol, 2.00 equiv., 1.25 M in EtOH) were dissolved in HFIP (1 mL, 0.1 M). The reaction was stirred for three hours and then quenched with sat. aqueous $NaHCO_3$ (20 mL); the organic layer was extracted with DCM (3x5 mL), then the solvent was removed under reduced pressure. No conversion in the desired product 1-methyl-3-(2,4,6-trimethoxyphenyl)-1H-indole **7a** was detected.



In an open air vial, commercially available N-methylindole **5** (13 µL, 0.10 mmol, 1.00 equiv.) and commercially available 4F-PIDA (34.0 mg, 1.00 mmol, 1.00 equiv) were left stirring in HFIP (1 mL, 0.1 M) for 30 minutes. Then 1,3,5-trimethoxybenzene **1** (25.0 mg, 0.150 mmol, 1.50 equiv.) and TMSCl (25.5 µL, 0.200 mmol, 2.00 equiv.) were added to the mixture. The reaction mixture was stirred for three hours and then quenched with sat. aqueous $NaHCO_3$ (4 mL); the organic layer was extracted with DCM (3x5 mL), then the solvent was removed under reduced pressure. 1-methyl-3-(2,4,6-trimethoxyphenyl)-1H-indole **7a** was obtained as white resin (4.80 mg, 16.0 µmol, 16% yield). *For full characterization see the scope section.*

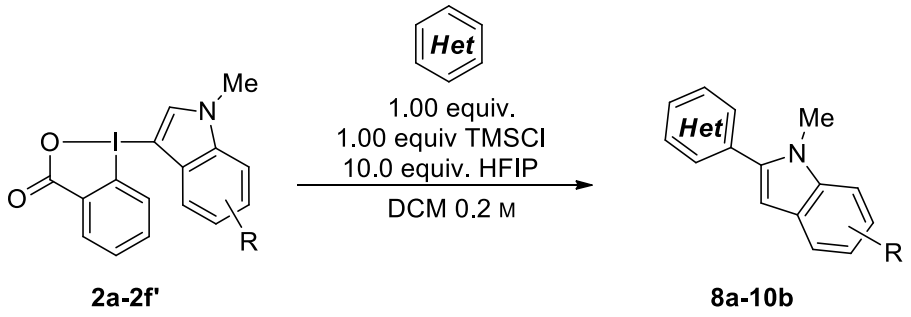
3.4 Scope of the Metal Free (Hetero)-Arylation of Indoles.

General Procedures GP7-GP9 Metal Free (Hetero)-Arylation of Indoles.



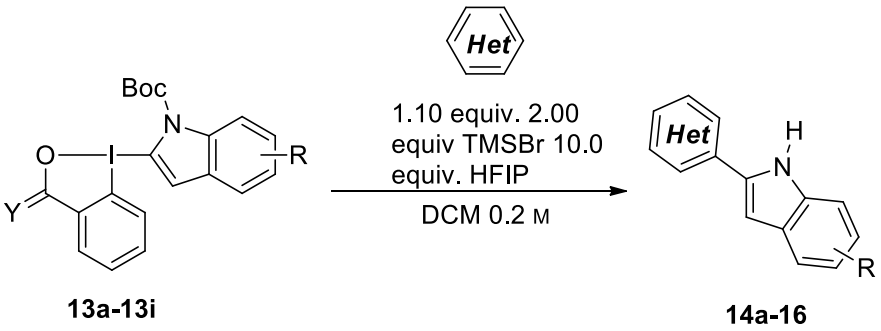
2a-2f' **7a-7f**

GP7: In an open air vial, the corresponding IndoleBX **2a-2f'** (0.300 mmol, 1.00 equiv.), the 1,3,5-trimethoxybenzene **1** (0.300 mmol, 1.00 equiv.), HFIP (315 µL, 3.00 mmol, 10.0 equiv.) and TMSCl (38.0 µL, 0.300 mmol, 1.00 equiv.) were dissolved in DCM (1.50 mL, 0.2 M). The reaction was stirred for three hours and then quenched with sat. aqueous $NaHCO_3$ (4 mL); the organic layer was extracted with DCM (3x5 mL), then the solvent was removed under reduced pressure. Flash column chromatography (Pentane:EtOAc 9:1) afforded the desired products **7a-7f**.



2a-2f' **8a-10b**

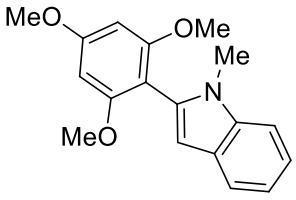
GP8: In an open air vial, IndoleBX **2a-2f'** (0.300 mmol, 1.00 equiv.), the corresponding heterocycle (0.300 mmol, 1.00 equiv.), HFIP (315 µL, 3.00 mmol, 10.0 equiv.) and TMSCl (38.0 µL, 0.300 mmol, 1.00 equiv.) were dissolved in DCM (1.50 mL, 0.2 M). The reaction was stirred for three hours and then quenched with sat. aqueous $NaHCO_3$ (4 mL); the organic layer was extracted with DCM (3x5 mL), then the solvent was removed under reduced pressure. Flash column chromatography (Pentane:DCM 1:1) afforded the desired products **8a-10b**.



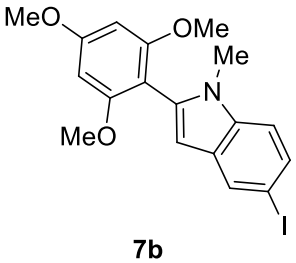
13a-13i **14a-16**

GP9: In an open air vial, the corresponding C2-IndoleDBXs or C2-IndoleBXs **13a-13i** (0.20 mmol, 1.0 equiv.), the 1,3,5-trimethoxybenzene (**1**) or the heterocycle (0.22 mmol, 1.1 equiv.), HFIP (210 µL, 2.00 mmol, 10.0 equiv.) and TMSBr (52.8 µL, 0.400 mmol, 2.00 equiv.) were dissolved in DCM (1.0 mL, 0.20 M). The reaction was stirred for three hours and then quenched with saturated aqueous $NaHCO_3$ (4 mL); the organic layer was extracted with DCM (3x5 mL), then the solvent was removed under reduced pressure. Purification on Preparative TLC (with mixture of EtOAc and Pentane as eluent) afforded the desired products **14a**-**16**.

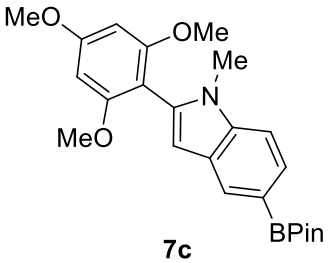
3.4.1: Scope of trimethoxyphenylated-N-protected-Indoles and -Pyrroles



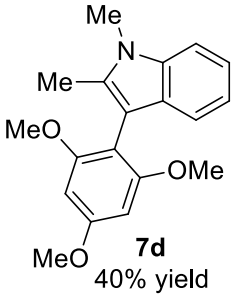
7a
75% yield



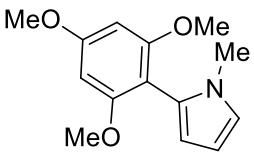
7b
69% yield (9:1)



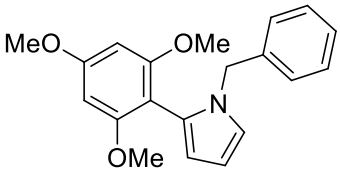
7c
54% yield



7d
40% yield

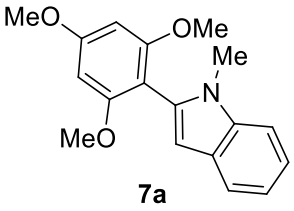


7e
71% yield



7f
59% yield

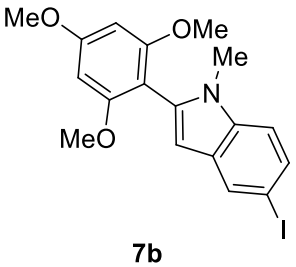
1-Methyl-2-(2,4,6-trimethoxyphenyl)-1*H*-indole (7a)



7a

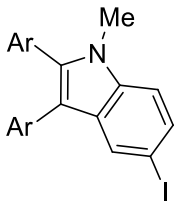
Following procedure **GP7**: using IndoleBX reagent **2a** (113 mg, 0.300 mmol), after 3 hours 1-methyl-2-(2,4,6-trimethoxyphenyl)-1*H*-indole **7a** (64.0 mg, 0.216 mmol, 75% yield) was obtained as a white resin. **Rf:** 0.42 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.33 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.18 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H, Ar*H*), 7.08 (m, 1H, Ar*H*), 6.45 (s, 1H, Ar*H*), 6.24 (s, 2H, Ar*H*), 3.89 (s, 3H, O*Me*), 3.73 (s, 6H, O*Me*), 3.51 (s, 3H, N*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.9, 160.0, 137.1, 133.2, 128.0, 120.5, 120.4, 118.9, 109.2, 103.0, 102.4, 90.7, 55.8, 55.4, 30.1. **IR** ν 2379 (w), 2321 (w), 1627 (s), 1523 (m), 1438 (s), 1362 (m), 1287 (m), 1178 (w), 1106 (s), 1073 (s), 979 (w), 906 (m), 850 (m), 720 (s). **HR-ESI-MS** calcd for $C_{18}H_{20}NO_3^+$ $[M+H]^+$ 298.1438; found 298.1451.

5-Iodo-1-methyl-2-(2,4,6-trimethoxyphenyl)-1*H*-indole (7b) and and 5-iodo-1-methyl-2,3-bis(2,4,6-trimethoxyphenyl)-1*H*-indole (7b')



7b
(mono: major)

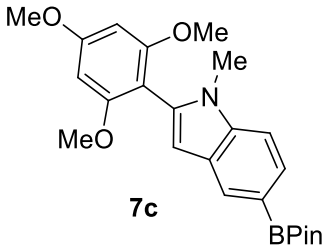
(9:1)



7b'
(di: minor)

Following procedure **GP7**: using IndoleBX reagent **2c** (151 mg, 0.300 mmol), after 3 hours an unseparable mixture of mono-di products 5-Iodo-1-methyl-2-(2,4,6-trimethoxyphenyl)-1*H*-indole **7b** and and 5-iodo-1-methyl-2,3-bis(2,4,6-trimethoxyphenyl)-1*H*-indole **7b'** (88.0 mg, 0.207 mmol, 69% yield, 9:1 *major-mono*:*minor-di*) were obtained as yellow oil. **Rf:** 0.38 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 1.7 Hz, 1H, Ar*H major*), 7.81 (d, *J* = 1.7 Hz, 1H, Ar*H minor*), 7.48 (dd, *J* = 8.6, 1.7 Hz, 1H, Ar*H minor*), 7.42 (dd, *J* = 8.5, 1.7 Hz, 1H, Ar*H major*), 7.11 (d, *J* = 8.6 Hz, 1H, Ar*H major*), 7.07 (d, *J* = 8.8 Hz, 1H, Ar*H minor*), 6.38 (s, 1H, Ar*H major*), 6.24 (s, 2H, Ar*H major*), 6.20 (s, 2H, Ar*H minor*), 3.90 (s, 4.3H, O*Me major* + O*Me minor*), 3.82 (s, 3H, O*Me minor*), 3.73 (s, 6.8H, O*Me major* + 2xO*Me minor*), 3.54 (s, 3H, N*Me minor*), 3.48 (s, 3H, N*Me major*). **^{13}C NMR** (101 MHz, $CDCl_3$) *major* 162.1, 159.9 (2 aromatic carbon signals overlapped), 136.2, 134.2, 130.5, 128.9, 128.7, 111.3, 101.7, 90.6, 82.4, 55.8, 55.4, 30.2. *minor* 162.8, 160.0, 159.4, 156.5, 137.4, 136.4, 132.7, 130.1, 129.6, 111.6, 102.3, 91.5, 90.7, 83.2, 59.7, 56.3, 55.8, 55.5, 31.2 (two aromatic carbon not resolved). **IR** ν 3006 (w), 2937 (w), 2838 (w), 1613 (s), 1587 (m), 1467 (s), 1415 (m), 1229 (m), 1128 (s), 1065 (w), 950 (w), 817 (w), 791 (m). **HR-ESI-MS** *mono*: $C_{18}H_{19}INO_3^+$ $[M+H]^+$ 424.0404; found 424.0412, di not detected.

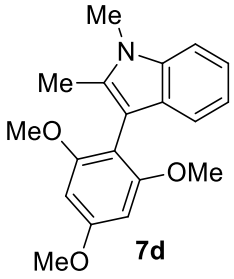
1-Methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(2,4,6-trimethoxyphenyl)-1*H*-indole (7c)



7c

Following procedure **GP7**: using IndoleBX reagent **2d** (151 mg, 0.300 mmol), after 3 hours 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(2,4,6-trimethoxyphenyl)-1*H*-indole **7c** (68.3 mg, 0.161 mmol, 54% yield) was obtained as a yellow oil. **Rf:** 0.40 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15 (s, 1H, Ar*H*), 7.63 (dd, *J* = 8.3, 1.2 Hz, 1H, Ar*H*), 7.32 (d, *J* = 8.3 Hz, 1H, Ar*H*), 6.47 (s, 1H, Ar*H*), 6.23 (s, 2H, Ar*H*), 3.89 (s, 3H, O*Me*), 3.71 (s, 6H, O*Me*), 3.50 (s, 3H, N*Me*), 1.37 (s, 12H, BPin-*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.9, 160.0 (*two aromatic carbon signals overlap*), 139.1, 133.3, 128.3, 127.8, 126.8, 108.6, 103.2, 102.9, 90.7, 83.2, 55.8 (*two methoxy carbon signals overlap*), 55.4, 30.1, 24.9. **IR** ν 2976 (w), 2935 (w), 2840 (w), 1610 (m), 1584 (m), 1354 (s), 1327 (s), 1204 (m), 1125 (s), 1064 (m), 966 (w), 860 (m). **HR-ESI-MS** calcd for $C_{24}H_{31}BNO_5^+$ $[M+H]^+$ 424.2290; found 424.2289.

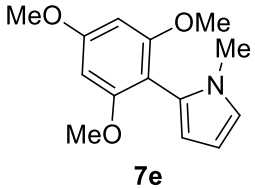
1,2-Dimethyl-3-(2,4,6-trimethoxyphenyl)-1*H*-indole (7d)



7d

Following procedure **GP7**: using IndoleBX reagent **2b** (117 mg, 0.300 mmol), after 3 hours 1,2-dimethyl-3-(2,4,6-trimethoxyphenyl)-1*H*-indole **7d** (37.1 mg, 0.120 mmol, 40% yield) was obtained as a yellow oil. **Rf:** 0.52 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.27 (m, 1H, Ar*H*), 7.21 (dt, *J* = 7.8, 1.0 Hz, 1H, Ar*H*), 7.11 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H, Ar*H*), 7.00 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H, Ar*H*), 6.28 (s, 2H, Ar*H*), 3.90 (s, 3H, O*Me*), 3.71 (s, 9H, O*Me* + N*Me*) 2.25 (s, 3H, NC*CH$_3$*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.3, 159.3, 136.7, 135.2, 127.7, 120.1, 119.7, 118.7, 108.7, 105.2, 104.6, 90.8, 55.7, 55.4, 29.7, 11.6. **IR** ν 3002 (w), 2942 (w), 2837 (w), 1606 (m), 1585 (m), 1469 (m), 1414 (w), 1205 (s), 1126 (s), 1062 (w), 956 (w), 739 (m). **HR-ESI-MS** calcd for $C_{19}H_{22}NO_3^+$ $[M+H]^+$ 312.1594; found 312.1596.

1-Methyl-2-(2,4,6-trimethoxyphenyl)-1*H*-pyrrole (7e)

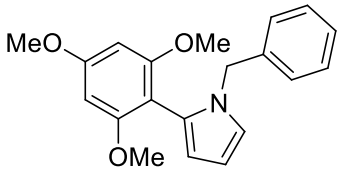


7e

Following procedure **GP7**: using PyrroleBX reagent **2e** or **2e'** (98.0 mg, 0.300 mmol), after 3 hours 1-methyl-2-(2,4,6-trimethoxyphenyl)-1*H*-pyrrole **7e** (52.4 mg, 0.212 mmol, 71% yield) was obtained as a white solid. **Rf:** 0.60 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.72

(dd, *J* = 2.7, 1.8 Hz, 1H, *ArH*), 6.23 (dd, *J* = 3.5, 2.6 Hz, 1H, *ArH*), 6.19 (s, 2H, *ArH*), 6.07 (dd, *J* = 3.5, 1.7 Hz, 1H, *ArH*), 3.86 (s, 3H, CH_3), 3.74 (s, 6H, CH_3), 3.39 (s, 3H, CH_3). ^{1}H-NMR values are in accordance with the data reported in literature.[24]

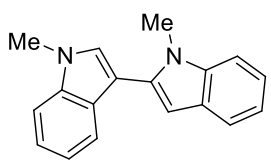
1-Benzyl-2-(2,4,6-trimethoxyphenyl)-1*H*-pyrrole (7f)



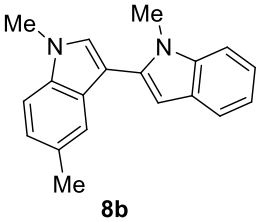
7f

Following procedure **GP7**: using PyrroleBX reagent **2f** or **2f'** (121 mg, 0.300 mmol), after 3 hours 1-benzyl-2-(2,4,6-trimethoxyphenyl)-1*H*-pyrrole **7f** (57.1 mg, 0.177 mmol, 59% yield) was obtained as a white solid. **Rf:** 0.58 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 – 7.15 (m, 3H, *ArH*), 7.04 – 6.98 (m, 2H, *ArH*), 6.73 (dd, *J* = 2.8, 1.8 Hz, 1H, *ArH*), 6.30 (t, *J* = 3.1 Hz, 1H, *ArH*), 6.12 (s, 2H, *ArH*), 6.09 (m, 1H, Ar*H*), 6.11 – 6.06 (m, 2H, ArCH_2), 3.83 (s, 3H, O*Me*), 3.62 (s, 6H, O*Me*). ^{1}H-NMR values are in accordance with the data reported in literature.[24]

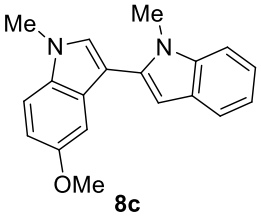
3.4.2: Scope of mixed 3'-2 biindoles.



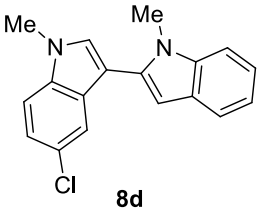
8a



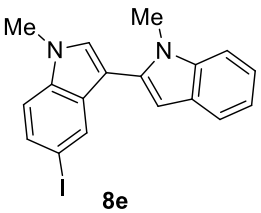
8b



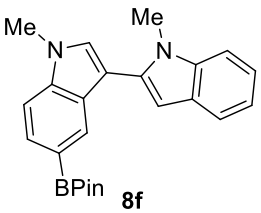
8c



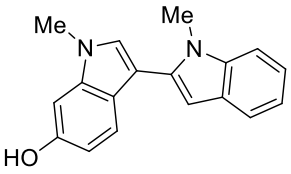
8d



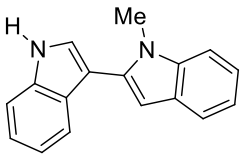
8e



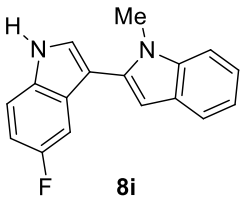
8f



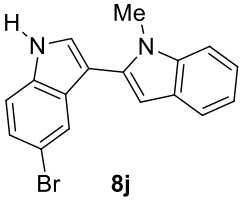
8g



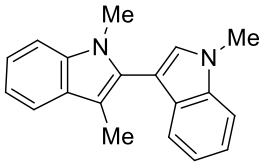
8h



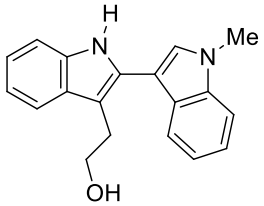
8i



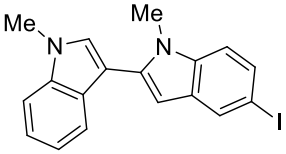
8j



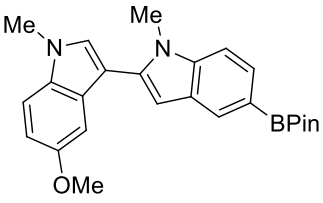
8k



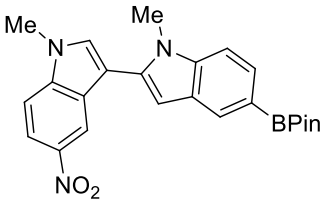
8l



8m

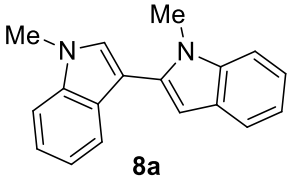


8n



8o

1,1'-Dimethyl-1*H*,1'*H*-2,3'-biindole (8a)

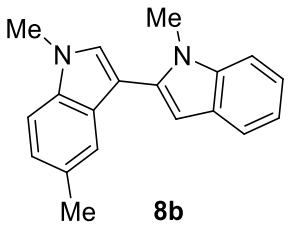


8a

Following procedure **GP8**: using commercially available N-Methyl-Indole **5** (113 mg, 0.300 mmol), after 3 hours 1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole **8a** (61.2 mg, 0.230 mmol, 77% yield) was obtained as a white solid. **Rf:** 0.40 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.76 (d, *J* = 7.7 Hz, 1H, *ArH*), 7.50 – 7.46

(m, 2H, *ArH*), 7.42 (t, *J* = 7.6 Hz, 1H, *ArH*), 7.37 – 7.22 (m, 4H, *ArH*), 6.74 (s, 1H, *ArH*), 3.93 (s, 3H, N*Me*), 3.84 (s, 3H, N*Me*). ^{1}H-NMR values are in accordance with the data reported in literature.[25]

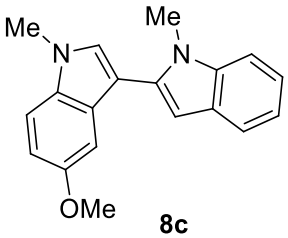
1,1',5'-Trimethyl-1*H*,1'*H*-2,3'-biindole (8b)



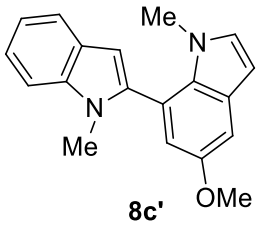
8b

Following procedure **GP8**: using commercially available 1,5-dimethyl-1H-indole (43.6 mg, 0.300 mmol), after 3 hours ,1',5'-trimethyl-1*H*,1'*H*-2,3'-biindole **8b** (52.6 mg, 0.192 mmol, 64% yield) was obtained as a yellow oil. **Rf:** 0.44 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 (dt, *J* = 7.8, 1.0 Hz, 1H, Ar*H*), 7.51 (dt, *J* = 1.8, 0.9 Hz, 1H, Ar*H*), 7.40 (m, 1H, Ar*H*), 7.31 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.25 (m, 1H, Ar*H*), 7.22 – 7.12 (m, 3H, Ar*H*), 6.63 (s, 1H, Ar*H*), 3.86 (s, 3H, N*Me*), 3.77 (s, 3H, N*Me*), 2.49 (s, 3H, *CH_3*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.9, 135.3, 129.6, 128.5, 128.3, 127.9, 123.9, 120.9, 120.0, 119.9, 119.9, 119.5, 109.3, 109.2, 106.6, 101.2, 33.0, 31.0, 21.5. **IR** ν 3050 (w), 2916 (w), 1592 (w), 1467 (s), 1336 (m), 1249 (m), 1151 (w), 1015 (w), 788 (m), 749 (s). **HR-ESI-MS** calcd for $C_{19}H_{19}N_2^+$ $[M+H]^+$ 275.1543; found 275.1539.

5'-Methoxy-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole (8c) and 5'-methoxy-1,1'-dimethyl-1*H*,1'*H*-2,7'-biindole (8c')



8c

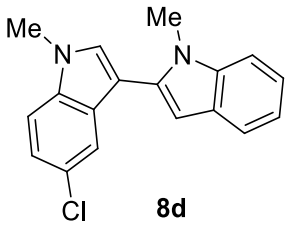


8c'

Following procedure **GP8**: using 5-methoxy-1-methyl-1*H*-indole **34b** (48.4 mg, 0.300 mmol), after 3 hours, 5'-methoxy-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole **8c** and 5'-methoxy-1,1'-dimethyl-1*H*,1'*H*-2,7'-biindole **8c'** (57.1 mg, 0.197 mmol, 65% yield, *ratio major* **8c**: *minor* **8c'** 12:1) were obtained as an unseparable mixture of yellow oil. **Rf:** 0.60 (Pentane:DCM 1:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 – 7.68 (m, 1H, Ar*H minor*), 7.65 (dd, *J* = 7.8, 1.0 Hz, 1H, Ar*H major*), 7.52 (s, 1H, Ar*H minor*), 7.39 (d, *J* = 8.3 Hz, 1H Ar*H major* + 1H Ar*H minor*), 7.29 (d, *J* = 8.8 Hz, 1H Ar*H major* + 2H Ar*H minor*), 7.25 – 7.22 (m, 1H Ar*H major* + 1H Ar*H minor*), 7.18 (br s, 1H, Ar*H major*), 7.15 (td, *J* = 7.5, 7.1, 1.0 Hz, 1H, Ar*H major*), 7.12 (d, *J* = 2.4 Hz, 1H, Ar*H major*), 6.97 (dd, *J* = 8.9, 2.5 Hz, 1H, Ar*H major*), 6.92 (d, *J* = 2.4 Hz, 1H, Ar*H minor*), 6.60 (br s, 1H, Ar*H major – fast exchange with $CDCl_3$*), 3.89 (s, 3H, *CH_3 minor*), 3.87 (s, 3H, *CH_3 major*), 3.82 (s, 3H, *CH_3 major*), 3.80 (s, 3H, *CH_3 minor*), 3.76 (s, 3H, *CH_3 major*), 3.69 (s, 3H, *CH_3 minor*).**^{13}C NMR** (101 MHz, $CDCl_3$) δ *major:* 154.8, 137.9, 132.2, 129.0, 129.0, 128.3, 128.1,

121.0, 120.0, 119.6, 112.9, 110.4, 109.3, 106.8, 101.6, 55.9, 33.2, 31.0 (*one aromatic carbon signal not resolved - minor not resolved).* **IR** ν 3004 (w), 2950 (w), 2828 (w), 1668 (w), 1623 (m), 1542 (m), 1489 (s), 1421 (w), 1288 (m), 1220 (m), 1140 (m), 1025 (w), 901 (m), 798 (s). **HR-ESI-MS** calcd for $C_{19}H_{19}N_2O^+$ $[M+H]^+$ 291.1492; found 291.1486.

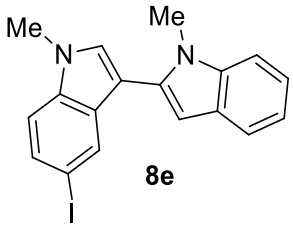
5'-Chloro-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole (8d)



8d

Following procedure **GP8**: using 5-chloro-1-methyl-1*H*-indole **34d** (49.7 mg, 0.300 mmol), after 3 hours 5'-chloro-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole **8d** (63.4 mg, 0.215 mmol, 72% yield) was obtained as a yellow oil. **Rf:** 0.38 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 2.0, 0.7 Hz, 1H, Ar*H*), 7.64 (dt, *J* = 7.9, 1.1 Hz, 1H, Ar*H*), 7.35 (dd, *J* = 8.2, 0.9 Hz, 1H, Ar*H*), 7.27 (dd, *J* = 8.8, 0.7 Hz, 1H, Ar*H*), 7.26 – 7.21 (m, 2H, Ar*H*), 7.17 – 7.12 (m, 2H, Ar*H*), 6.60 (s, 1H, Ar*H*), 3.82 (s, 3H, N*Me*), 3.71 (s, 3H, N*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) 137.9, 135.3, 134.1, 129.4, 128.6, 128.2, 126.2, 122.6, 121.2, 120.1, 119.6, 119.6, 110.6, 109.3, 107.0, 101.6, 33.2, 30.9. δ. **IR** ν 3054 (w), 2942 (w), 2885 (w), 1590 (m), 1586 (m), 1466 (s), 1369 (m), 1271 (s), 1244 (m), 1145 (m), 1092 (m), 795 (s). **HR-ESI-MS** calcd for $C_{18}H_{16}ClN_2^+$ $[M+H]^+$ 295.0997; found 295.0995.

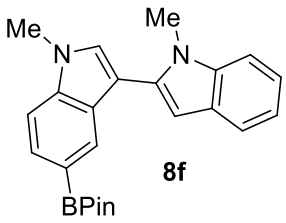
5'-Iodo-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole (8e).



8e

Following procedure **GP8**: using 5-iodo-1*H*-indole **34e** (77.0 mg, 0.300 mmol), after 3 hours 5'-iodo-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole **8e** (82.5 mg, 0.214 mmol, 71% yield) was obtained as a yellow oil. **Rf:** 0.40 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 1.7, 0.5 Hz, 1H, Ar*H*), 7.56 (dt, *J* = 7.8, 1.1 Hz, 1H, Ar*H*), 7.45 (dd, *J* = 8.6, 1.7 Hz, 1H, Ar*H*), 7.28 (m, 1H, Ar*H*), 7.16 (m, 1H, Ar*H*), 7.09 – 7.04 (m, 2H, Ar*H*), 7.03 (s, 1H, Ar*H*), 6.51 (d, *J* = 0.8 Hz, 1H, Ar*H*), 3.74 (s, 3H, N*Me*), 3.63 (s, 3H, N*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.9, 136.0, 134.0, 130.6, 130.1, 129.0, 128.9, 128.2, 121.2, 120.1, 119.7, 111.5, 109.4, 106.7, 101.7, 83.8, 33.1, 30.9. **IR** ν 2931 (m), 2855 (m), 1828 (w), 1730 (s), 1655 (w), 1524 (w), 1436 (s), 1333 (m), 1278 (s), 1199 (s), 1058 (m), 992 (m), 897 (m), 762 (w). **HR-ESI-MS** calcd for $C_{18}H_{16}IN_2^+$ $[M+H]^+$ 387.0353; found 387.0355.

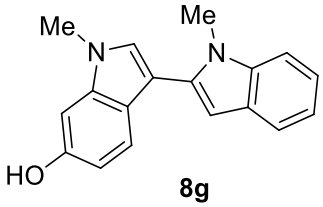
1,1'-Dimethyl-5'-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*,1'*H*-2,3'-biindole (8f)



8f

Following procedure **GP8**: using commercially available 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (77.0 mg, 0.300 mmol), after 3 hours 1,1'-dimethyl-5'-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*,1'*H*-2,3'-biindole **8f** (79.2 mg, 0.205 mmol, 68% yield) was obtained as a yellow oil. **Rf:** 0.38 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.19 (s, 1H, Ar*H*), 7.78 (dd, *J* = 8.3, 1.1 Hz, 1H, Ar*H*), 7.68 (dt, *J* = 7.8, 1.0 Hz, 1H, Ar*H*), 7.41 (dd, *J* = 4.8, 0.9 Hz, 1H, Ar*H*), 7.39 (dd, *J* = 4.7, 0.9 Hz, 1H, Ar*H*), 7.25 (m, 1H, Ar*H*), 7.18 (s, 1H, Ar*H*), 7.15 (m, 1H, Ar*H*), 6.66 (d, *J* = 0.8 Hz, 1H, Ar*H*), 3.88 (s, 3H, N*Me*), 3.75 (s, 3H, N*Me*), 1.36 (s, 12H, BPin-*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.8, 137.9, 134.7, 128.5, 128.4, 128.3, 128.0, 127.5, 121.0, 120.0, 119.5, 109.3, 108.8, 108.0, 101.8, 83.5, 60.4, 33.0, 30.9, 24.8. *NB: the Carbon-Boron bond is not observed as reported in literature.*[18] **IR** ν 3050 (w), 2978 (w), 2927 (w), 1614 (w), 1466 (m), 1352 (s), 1311 (m), 1143 (s), 1095 (m), 968 (w), 866 (m), 737 (s). **HR-ESI-MS** calcd for $C_{24}H_{28}BN_2O_2^+$ $[M+H]^+$ 387.2238; found 387.2244.

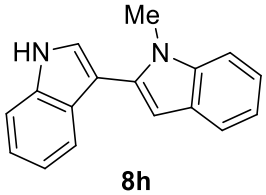
1,1'-Dimethyl-1*H*,1'*H*-[2,3'-biindol]-6'-ol (8g)



8g

Following procedure **GP8**: using 6-(benzyloxy)-1-methyl-1*H*-indole **34e** (77.0 mg, 0.300 mmol), after 3 hours 1,1'-dimethyl-1*H*,1'*H*-[2,3'-biindol]-6'-ol **8g** (57.8 mg, 0.209 mmol, 70% yield) was obtained as a yellow oil. **Rf:** 0.28 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.54 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.37 (m, 1H, Ar*H*), 7.24 (m, 1H, Ar*H*), 7.15 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H, Ar*H*), 7.07 (s, 1H, Ar*H*), 6.83 (d, *J* = 2.3 Hz, 1H, Ar*H*), 6.74 (dd, *J* = 8.5, 2.3 Hz, 1H, Ar*H*), 6.61 (s, 1H, Ar*H*), 4.97 (br s, 1H, OH), 3.77 (s, 3H, N*Me*), 3.76 (s, 3H, N*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.3, 137.9, 137.8, 135.1, 128.3, 127.3, 122.2, 121.1, 120.9, 119.9, 119.5, 110.2, 109.3, 107.4, 101.2, 95.3, 33.0, 30.9. **IR** ν 3369 (w), 2941 (w), 2900 (w), 1627 (s), 1593 (s), 1463 (m), 1395 (m), 1320 (m), 1234 (m), 1183 (m), 1171 (m), 1081 (m), 966 (s), 780 (s). **HR-ESI-MS** calcd for calcd for $C_{18}H_{17}N_2O^+$ $[M+H]^+$ 277.1335; found 277.1344.

1-Methyl-1*H*,1'*H*-2,3'-biindole (8h)

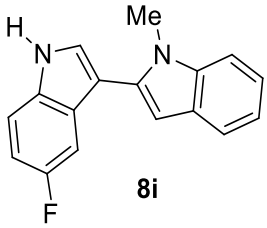


8h

Following procedure **GP8**: using commercially available 1*H*-indole (35.1 mg, 0.300 mmol), after 3 hours 1-methyl-1*H*,1'*H*-2,3'-biindole **8h** (48.3 mg, 0.196 mmol, 65% yield) was obtained as a yellow oil. **Rf:** 0.50 (Pentane:EtOAc 1:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.38 (br s, 1H,

N*H*), 7.72 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.66 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.48 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.43 – 7.33 (m, 2H, Ar*H*), 7.33 – 7.10 (m, 4H, Ar*H*), 6.66 (s, 1H, Ar*H*), 3.71 (s, 3H, N*Me*) *(NB: the product is highly unstable under atmosphere – presence of grease in the proton NMR).* **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.1, 136.1, 135.1, 128.4, 127.3, 124.0, 122.9, 121.2, 120.8, 120.3, 120.2, 119.7, 111.5, 109.5, 109.0, 101.7, 31.1. **IR** ν 3402 (m), 3058 (w), 2926 (w), 2846 (w), 1593 (w), 1458 (m), 1329 (w), 1242 (m), 1097 (m), 1011 (w), 784 (m), 747 (s). **HR-ESI-MS** calcd for $C_{17}H_{15}N_2^+$ $[M+H]^+$ 247.1230; found 247.1226.

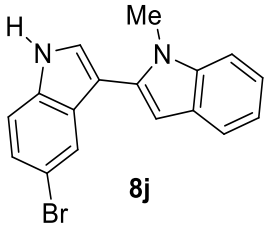
5'-Fluoro-1-methyl-1H,1'H-2,3'-biindole (8i)



8i

Following procedure **GP8**: using commercially available 5-fluoro-1*H*-indole (40.5 mg, 0.300 mmol), after 3 hours 5'-fluoro-1-methyl-1H,1'H-2,3'-biindole **8i** (62.0 mg, 0.235 mmol, 78% yield) was obtained as a yellow resin. **Rf:** 0.42 (Pentane:EtOAc 1:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (br s, 1H), 7.67 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.42 – 7.32 (m, 4H, Ar*H*), 7.26 (m, 1H, Ar*H*), 7.17 (t, *J* = 7.4 Hz, 1H, Ar*H*), 7.04 (td, *J* = 9.0, 2.5 Hz, 1H, Ar*H*), 6.64 (s, 1H, Ar*H*), 3.75 (s, 3H, N*Me*) *(NB: the product is highly unstable under atmosphere – presence of grease in the proton NMR).* **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.51 (d, *J* = 236.2 Hz), 137.9, 134.3, 132.5, 128.6, 128.2, 127.63 (d, *J* = 8.5 Hz), 127.0, 125.4, 121.2, 119.90 (d, *J* = 46.8 Hz), 112.05 (d, *J* = 7.3 Hz), 111.31 (d, *J* = 26.3 Hz), 105.10 (d, *J* = 24.2 Hz), 101.6, 30.9. **IR** ν 3433 (w), 3400 (m), 3050 (w), 1583 (m), 1486 (s), 1467 (s), 1387 (w), 1281 (m), 1243 (m), 1163 (m), 930 (m), 744 (s). **HR-ESI-MS** calcd for $C_{17}H_{14}FN_2^+$ $[M+H]^+$ 265.1136; found 265.1137.

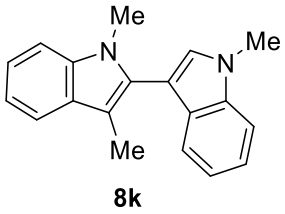
5'-Bromo-1-methyl-1H,1'H-2,3'-biindole (8j)



8j

Following procedure **GP8**: using commercially available 5-bromo-1*H*-indole (58.8 mg, 0.300 mmol), after 3 hours 5'-bromo-1-methyl-1H,1'H-2,3'-biindole **8j** (60.8 mg, 0.187 mmol, 62% yield) was obtained as a yellow resin. **Rf:** 0.40 (Pentane:EtOAc 1:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (br s, 1H, N*H*), 7.81 (d, *J* = 1.8 Hz, 1H, Ar*H*), 7.65 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.35 (m, 2H, Ar*H*), 7.28 (s, 1H, Ar*H*), , 7.28 – 7.22 (m, 2H, Ar*H*), 7.15 (td, *J* = 7.5, 1.1 Hz, 1H, Ar*H*), 6.62 (s, 1H, Ar*H*), 3.70 (s, 3H, N*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.9, 134.6, 133.9, 128.9, 128.2, 125.7, 124.8, 122.7, 121.3, 120.2, 119.7, 114.0, 112.8, 109.4, 108.6, 101.9, 30.9. **IR** ν 3399 (w), 3157 (w), 2987 (w), 2888 (w), 1621 (w), 1535 (w), 1477 (m), 1429 (m), 1267 (s), 1224 (s), 1090 (s), 1024 (s), 885 (m), 761 (m). **HR-ESI-MS** calcd for $C_{17}H_{14}{}^{79}BrN_2^+$ $[M+H]^+$ 325.0335; found 325.0329.

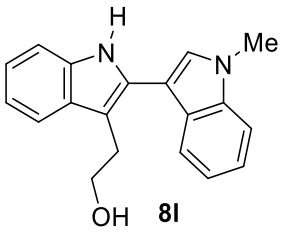
1,1',3-Trimethyl-1*H*,1'*H*-2,3'-biindole (8k)



8k

Following procedure **GP8**: using commercially available 1,3-dimethyl-1*H*-indole (43.6 mg, 0.300 mmol), after 3 hours 1,1',3-trimethyl-1*H*,1'*H*-2,3'-biindole **8k** (36.9 mg, 0.134 mmol, 45% yield) was obtained as a yellow oil. **Rf:** 0.44 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (dt, *J* = 7.9, 1.0 Hz, 1H, Ar*H*), 7.46 (dt, *J* = 7.2, 0.7 Hz, 1H, Ar*H*), 7.44 (m, 1H, Ar*H*), 7.36 (dt, *J* = 8.0, 0.9 Hz, 1H, Ar*H*), 7.32 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H, Ar*H*), 7.17 (m, 2H, Ar*H*), 7.15 (m, 2H, Ar*H*), 3.92 (s, 3H, N*Me*), 3.63 (s, 3H, N*Me*), 2.29 (s, 3H, *CH*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.3, 136.9, 131.5, 129.4, 128.6, 128.2, 122.0, 121.1, 120.5, 119.9, 118.7, 118.5, 109.5, 109.1, 109.0, 106.1, 33.0, 30.8, 9.7. **IR** ν 3422 (s), 1592 (m), 1493 (w), 1442 (w), 1360 (w), 1287 (w), 1222 (w), 1144 (w), 1025 (m). **HR-ESI-MS** calcd for $C_{19}H_{19}N_2^+$ $[M+H]^+$ 275.1543; found 275.1542.

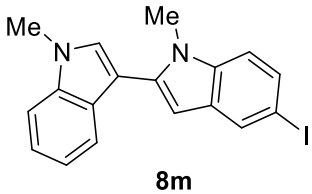
2-(1'-Methyl-1*H*,1'*H*-[2,3'-biindol]-3-yl)ethanol (8l)



8l

Following procedure **GP8**: using commercially available 2-(1*H*-indol-3-yl)ethanol (48.4 mg, 0.300 mmol), after 3 hours 2-(1'-methyl-1*H*,1'*H*-[2,3'-biindol]-3-yl)ethanol **8l** (49.8 mg, 0.172 mmol, 57% yield) was obtained as a yellow oil. **Rf:** 0.60 (Pentane:EtOAc 1:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.23 (br s, 1H, N*H*), 7.78 (dt, *J* = 7.9, 1.0 Hz, 1H, Ar*H*), 7.68 – 7.59 (m, 1H, Ar*H*), 7.46 (s, 1H, Ar*H*), 7.41 (m, 2H, Ar*H*), 7.32 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H, Ar*H*), 7.21 (m, 2H, Ar*H*), 7.16 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H, Ar*H*), 3.95 (t, *J* = 6.4 Hz, 2H, *CH*$_2$), 3.86 (s, 3H, N*Me*), 3.15 (t, *J* = 6.4 Hz, 2H, *CH*$_2$), 1.55 (s, 1H, *OH*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.0, 135.9, 131.3, 128.9, 128.5, 126.8, 122.4, 121.6, 120.2, 119.6, 119.5, 118.4, 110.7, 109.7, 107.7, 106.8, 62.9, 33.0, 28.3. **IR** ν 2926 (w), 2866 (w), 1550 (s), 1528 (s), 1507 (s), 1475 (s), 1325 (s), 1276 (s), 1263 (s), 1193 (s), 1159 (s), 1116 (m), 1068 (m), 1003 (m), 930 (s), 886 (m), 811 (m). **HR-ESI-MS** calcd for $C_{19}H_{18}N_2NaO^+$ $[M+Na]^+$ 313.1311; found 313.1314.

5-Iodo-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole (8m)

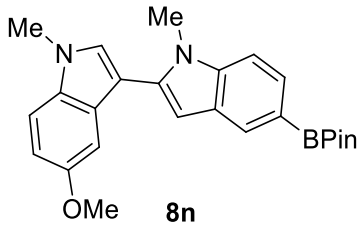


8m

Following procedure **GP8**: using commercially available methylindole **5** (39.4 mg, 0.300 mmol) and IndoleBX **2c** (151 mg, 0.300 mmol), after 3 hours 5-iodo-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole **8m** (58.9 mg, 0.152 mmol, 51% yield) was obtained as a

yellow oil. **Rf:** 0.35 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 1.6 Hz, 1H, Ar*H*), 7.69 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.48 (dd, *J* = 8.6, 1.7 Hz, 1H, Ar*H*), 7.42 (d, *J* = 8.3 Hz, 1H, Ar*H*), 7.34 (m, 1H, Ar*H*), 7.23 (m, 1H, Ar*H*), 7.20 (s, 1H, Ar*H*), 7.15 (d, *J* = 8.5 Hz, 1H, Ar*H*), 6.55 (s, 1H, Ar*H*), 3.89 (s, 3H, N*Me*), 3.73 (s, 3H, N*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.0, 136.9, 136.0, 130.9, 129.1, 128.6, 128.5, 127.5, 122.4, 120.4, 120.2, 111.3, 109.6, 106.7, 100.5, 83.0, 33.1, 31.1. **IR** ν 048 (w), 2928 (w), 1734 (w), 1618 (m), 1589 (m), 1467 (m), 1392 (m), 1372 (m), 1265 (m), 1248 (m), 1133 (w), 1089 (w), 1044 (w), 951 (w), 897 (w), 871 (w), 787 (m), 741 (s). **HR-ESI-MS**) calcd for $C_{18}H_{16}IN_2^+$ $[M+H]^+$ 387.0353; found 387.0356.

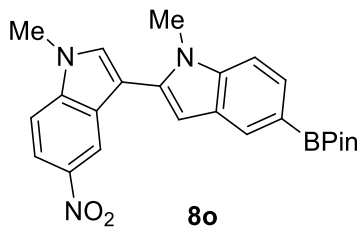
5'-Methoxy-1,1'-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*,1'*H*-2,3'-biindole (8n).



8n

Following procedure **GP8**: using 5-methoxy-1-methyl-1*H*-indole **34b** (48.4 mg, 0.300 mmol) and IndoleBX **2d** (151 mg, 0.300 mmol), after 3 hours 5'-methoxy-1,1'-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*,1'*H*-2,3'-biindole **8n** (69.0 mg, 0.166 mmol, 55% yield) was obtained as a yellow oil. **Rf:** 0.15 (Pentane:DCM 1:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 (s, 1H, Ar*H*), 7.68 (dd, *J* = 8.2, 1.2 Hz, 1H, Ar*H*), 7.37 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.29 (d, *J* = 8.9 Hz, 1H, Ar*H*), 7.17 (s, 1H, Ar*H*), 7.09 (d, *J* = 2.5 Hz, 1H, Ar*H*), 6.96 (dd, *J* = 8.9, 2.5 Hz, 1H, Ar*H*), 6.62 (s, 1H, Ar*H*), 3.86 (s, 3H, N*Me*), 3.81 (s, 3H, N*Me*), 3.75 (s, 3H, N*Me*), 1.38 (s, 12H, *BPin*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.8, 139.8, 135.3, 132.2, 128.9, 128.1, 128.1, 127.9, 127.2, 112.9, 110.4, 108.7, 106.7, 101.8, 101.4, 83.4, 55.9, 33.2, 30.9, 24.9. *NB: the Carbon-Boron bond is not observed as reported in literature.*[18] **IR** ν 2996 (m), 2867 (w), 2837 (w), 1521 (m), 1431 (m), 1361 (w), 1288 (m), 1148 (w), 991 (s), 862 (s). **HR-ESI-MS** calcd for $C_{25}H_{29}BN_2O_3^+$ [M+] 416.2094; found 416.2286.

5'-Nitro-1,1'-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*,1'*H*-2,3'-biindole (8o)



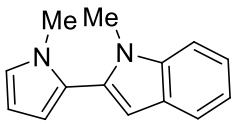
8o

Following procedure **GP8**: using commercially available 1-methyl-5-nitro-1*H*-indole (53.0 mg, 0.300 mmol) and IndoleBX **2d** (151 mg, 0.300 mmol), after 3 hours 5'-nitro-1,1'-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*,1'*H*-2,3'-biindole **8o** (65.4 mg, 0.152 mmol, 51% yield) was obtained as

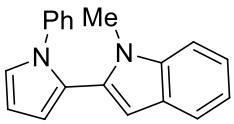
an orange oil. **Rf:** 0.20 (Pentane:EtOAc 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.62 (s, 1H, Ar*H*), 8.25 – 8.15 (m, 2H, Ar*H*), 7.72 (m, 1H, Ar*H*), 7.44 – 7.35 (m, 2H, Ar*H*), 7.34 (d, *J* = 1.3 Hz, 1H, Ar*H*), 6.66 (s, 1H, Ar*H*), 3.94 (s, 3H, N*Me*), 3.75 (s, 3H, N*Me*), 1.39 (s, 12H, BPin-*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.3, 140.0, 139.5, 132.8, 131.1, 128.2, 127.8 (*2 aromatic carbon signals overlapped*), 127.0, 118.0, 117.6, 110.1, 109.6, 108.9, 103.0, 83.4, 33.5, 31.0, 24.9. *NB: the Carbon- bound to Boron is not observed as reported in literature.*[18] **IR** ν 3482 (w), 3333 (w), 3090 (w), 1519 (s), 1330 (s), 1282 (m), 1149 (m), 995 (m), 931 (s), 856 (s), 833 (s). **HR-ESI-MS** calcd for $C_{24}H_{26}BN_3NaO_4^+$ $[M+Na]^+$ 454.1909; found 454.1914.

3.4.3: Scope of pyrrole- and thiophene-2-methylindoles.

Pyrroles

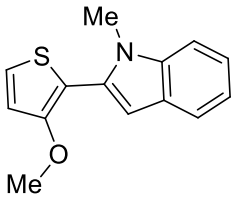


9a

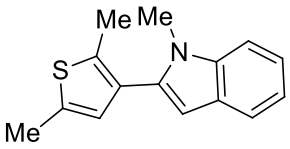


9b-9b'

Thiophenes

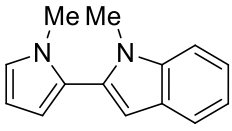


10a



10b

1-Methyl-2-(1-methyl-1*H*-pyrrol-2-yl)-1*H*-indole (9a)

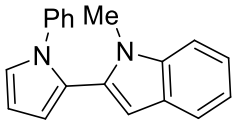


9a

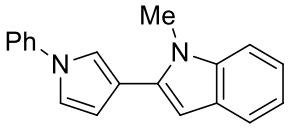
Following procedure **GP8**: using commercially available 1-methyl-1*H*-pyrrole (27.0 µL, 0.300 mmol), after 3 hours 1-methyl-2-(1-methyl-1*H*-pyrrol-2-yl)-1*H*-indole **9a** (44.3 mg, 0.211 mmol, 70% yield) was obtained as a yellow oil. **Rf:** 0.70 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.36 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.26 (m, 1H, Ar*H*), 7.15 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H, Ar*H*), 6.81 (dd, *J* = 2.7, 1.8 Hz, 1H, Ar*H*), 6.53 (s, 1H, Ar*H*), 6.30 (dd, *J* = 3.6, 1.7 Hz, 1H, Ar*H*), 6.27 (dd, *J* = 3.6, 2.6 Hz, 1H, Ar*H*), 3.66 (s, 3H, N*Me*), 3.60 (s, 3H, N*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.5, 132.2, 127.6, 124.5, 123.6, 121.7, 120.4, 119.7, 111.4, 109.5, 107.8, 103.2, 34.7, 30.6. **IR** ν 3050 (w), 2984 (w), 2887 (w), 1614

(w), 1471 (w), 1384 (w), 1259 (m), 1047 (m), 959 (s), 785 (m). **HR-ESI-MS** calcd for $C_{14}H_{15}N_2^+$ $[M+H]^+$ 211.1230; found 211.1227.

1-Methyl-2-(1-phenyl-1*H*-pyrrol-2-yl)-1*H*-indole 9b and 1-methyl-2-(1-phenyl-1*H*-pyrrol-3-yl)-1*H*-indole (9b')



9b



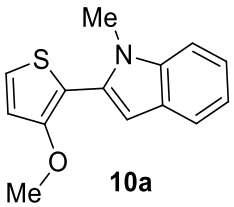
9b'

Following procedure **GP8**: using commercially available 1-phenyl-1*H*-pyrrole (43.0 µL, 0.300 mmol), after 3 hours a separable mixture of 1-methyl-2-(1-phenyl-1*H*-pyrrol-2-yl)-1*H*-indole **9b** (26.2 mg, 96.0 µmol, 32% yield) and 1-methyl-2-(1-phenyl-1*H*-pyrrol-3-yl)-1*H*-indole **9b'** (24.1 mg, 88.0 µmol, 30% yield) was obtained as a yellow oil.

9b Rf: 0.40 (Pentane:EtOAc 9:1) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.29 – 7.13 (m, 7H, Ar*H*), 7.13 – 7.06 (m, 2H, Ar*H*), 6.50 (dd, *J* = 3.5, 1.8 Hz, 1H, Ar*H*), 6.44 (t, *J* = 3.2 Hz, 1H, Ar*H*), 6.42 (s, 1H, Ar*H*), 3.34 (s, 3H, N*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.2, 137.4, 132.6, 129.1, 127.8, 126.4, 124.3, 124.2, 123.7, 121.5, 120.4, 119.5, 114.0, 109.4 (*2 aromatic carbon signals overlapped*), 103.5, 30.5. **IR** ν 3106 (w), 2978 (w), 2901 (w), 1558 (s), 1489 (s), 1371 (s), 1292 (s), 1218 (s), 1054 (m), 818 (s). **HR-ESI-MS** calcd for $C_{19}H_{17}N_2^+$ $[M+H]^+$ 273.1386; found 273.1379.

9b' Rf: 0.38 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.30 – 7.18 (m, 7H, Ar*H*), 7.07 (ddd, *J* = 8.0, 6.9, 1.2 Hz, 1H, Ar*H*), 6.96 (dd, *J* = 2.9, 1.8 Hz, 1H, Ar*H*), 6.51 (m, 1H, Ar*H*), 6.49 (s, 1H, Ar*H*), 6.42 (dd, *J* = 3.5, 2.8 Hz, 1H, Ar*H*), 3.66 (s, 3H, N*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.8, 136.5, 128.7, 127.4, 127.3, 127.1, 126.4, 125.7, 122.6, 121.7, 120.4, 119.5, 109.9, 109.1, 109.0, 107.7, 32.7. **IR** ν 3106 (w), 3045 (w), 1599 (m), 1499 (s), 1426 (w), 1366 (m), 1321 (m), 1254 (w), 1103 (w), 912 (w), 743 (s). **HR-ESI-MS** calcd for $C_{19}H_{17}N_2^+$ $[M+H]^+$ 273.1386; found 273.1386.

2-(3-Methoxythiophen-2-yl)-1-methyl-1*H*-indole (10a)

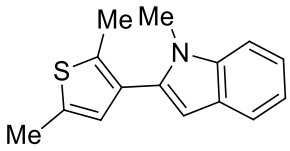


10a

Following procedure **GP8**: using commercially available 3-methoxythiophen (30.0 mg, 0.300 mmol), after 3 hours 2-(3-methoxythiophen-2-yl)-1-methyl-1*H*-indole **10a** (46.8 mg, 0.192 mmol, 64% yield) was obtained as a yellow oil. **Rf:** 0.80 (Pentane:EtOAc 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.36 (m, 1H, Ar*H*), 7.31 (d, *J* = 5.5

Hz, 1H, Ar*H*), 7.24 (m, 1H, Ar*H*), 7.12 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H, Ar*H*), 6.96 (d, *J* = 5.5 Hz, 1H, Ar*H*), 6.62 (s, 1H, Ar*H*), 3.85 (s, 3H, N*Me*), 3.73 (s, 3H, O*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.8, 137.9, 131.5, 127.8, 124.7, 121.7, 120.4, 119.6, 116.7, 110.4, 109.4, 103.5, 58.7, 30.8. **IR** ν 3108 (w), 2935 (w), 2851 (w), 1583 (w), 1465 (m), 1378 (s), 1337 (m), 1252 (s), 1103 (w), 1070 (s), 929 (w), 780 (m), 750 (s). **HR-ESI-MS** calcd for $C_{14}H_{14}NOS^+$ $[M+H]^+$ 244.0791; found 244.0787.

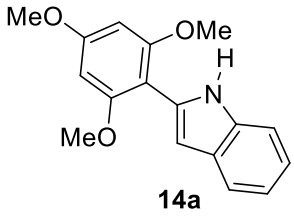
2-(2,5-Dimethylthiophen-3-yl)-1-methyl-1*H*-indole (10b)



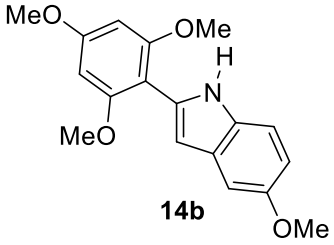
10b

Following procedure **GP8**: using commercially available 2,5-dimethylthiophene (34.0 mg, 0.300 mmol), after 3 hours 2-(2,5-dimethylthiophen-3-yl)-1-methyl-1*H*-indole **10b** (35.2 mg, 0.146 mmol, 49% yield) was obtained as a yellow oil. **Rf:** 0.85 (Pentane:EtOAc 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.35 (m, 1H, Ar*H*), 7.29 – 7.24 (m, 1H, Ar*H*), 7.14 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H, Ar*H*), 7.03 (s, 1H, Ar*H*), 6.85 (d, *J* = 1.3 Hz, 1H, Ar*H*), 3.84 (s, 3H, N*Me*), 2.48 (s, 3H, CH_3), 2.43 (s, 3H, CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 136.7, 135.2, 131.2, 130.9, 127.6, 127.3, 127.1, 121.7, 120.3, 119.3, 111.4, 109.2, 32.8, 15.3, 14.2. **IR** ν 3499 (w), 2919 (s), 2854 (m), 1685 (w), 1484 (m), 1332 (w), 1218 (m), 1137 (s), 1015 (m), 815 (m). **HR-APPI-MS** calcd for $C_{15}H_{15}NS$ [M+] 241.0920; found 241.0926.

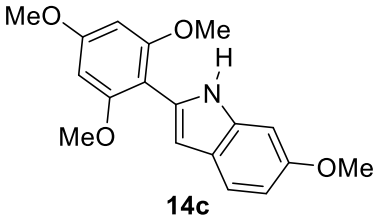
3.4.4: Scope of trimethoxy(methyl)phenylated-N*H*-indoles.



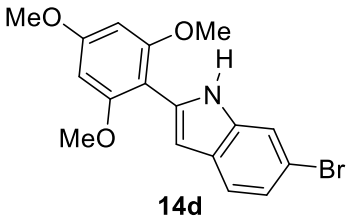
14a



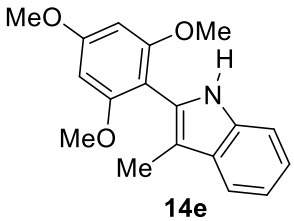
14b



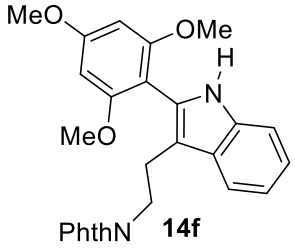
14c



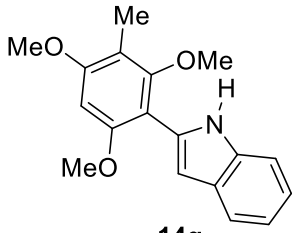
14d



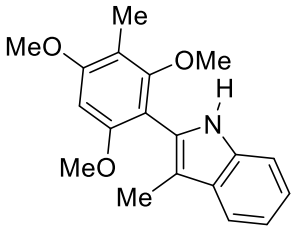
14e



14f

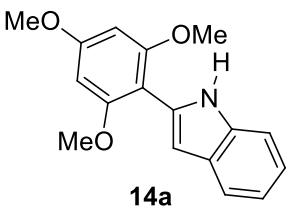


14g



14h

2-(2,4,6-Trimethoxyphenyl)-1*H*-indole (14a)



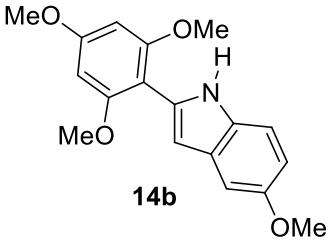
14a

Following procedure **GP9**: starting from C2-IndoleDBX **13c** (95.5 mg, 0.200 mmol, 1.00 equiv.), after 3 hours 2-(2,4,6-trimethoxyphenyl)-1*H*-indole **14a** (43.4 mg, 0.150 mmol, 77% yield) was obtained as a grey solid. **M.p.** 132-137 °C. **R_f:** 0.55 (Pentane:EtOAc 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.47 (s, 1H, N*H*), 7.64 (dt, *J* = 7.8, 1.0 Hz, 1H, Ar*H*), 7.39 (dd, *J* = 8.0, 1.2 Hz, 1H, Ar*H*), 7.16 (ddd, *J* = 8.1, 7.0, 1.3 Hz, 1H, Ar*H*), 7.11 – 7.07 (m, 2H, Ar*H*), 6.29 (s, 2H, Ar*H*), 3.93 (s, 6H, *o*-O*CH*$_3$), 3.88 (s, 3H, *p*-O*CH*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.1, 158.7, 135.0, 131.2, 128.2, 121.1, 120.0, 119.1, 110.3, 103.7, 103.6, 91.5, 56.0, 55.3. **IR** ν 3434 (w), 2938 (w), 2837 (w), 1605 (m), 1583 (m), 1486 (w), 1455 (s), 1414 (m), 1330 (m), 1204 (m), 1122 (s) **HR-ESI-MS**: calcd for $C_{17}H_{18}NO_3^+$ 284.1281 $[M + H]^+$; found 284.1284.

*NB: when C2-IndoleBX **13a** was used, the desired compound **14a** was obtained in 67% yield.*

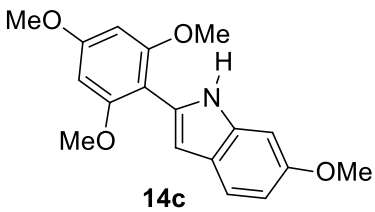
5-Methoxy-2-(2,4,6-trimethoxyphenyl)-1*H*-indole (14b)

Following procedure **GP9**: starting from C2-IndoleDBX **13e** (101 mg, 0.200 mmol), after 3 hours 5-methoxy-2-(2,4,6-trimethoxyphenyl)-1*H*-indole **14b** (41.7 mg, 0.130 mmol, 67% yield) was obtained as a green solid. **M.p.** 115-120 °C. **R_f:** 0.45 (Pentane:EtOAc 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.38 (s, 1H, N*H*), 7.27 (d, *J* = 8.6 Hz, 1H, Ar*H*), 7.11 (d, *J* = 2.4 Hz, 1H, Ar*H*), 7.00 (s, 1H, Ar*H*), 6.82 (dd, *J* = 8.7, 2.4 Hz, 1H, Ar*H*), 6.28 (s, 2H, Ar*H*), 3.92 (s, 6H, *o*-O*CH*$_3$), 3.87 (s, 6H, *p*-O*CH*$_3$,and *5*-O*CH*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.1, 158.6, 153.8, 131.9, 130.3, 128.5, 128.4, 111.5, 111.0, 103.6, 101.7, 91.5, 56.0, 55.8, 55.3. **IR** ν 3431 (w), 2937 (w), 2841 (w), 1604 (m), 1580 (m), 1459 (m), 1204 (s), 1120 (s), 1034 (m), 799 (s). **HR-ESI-MS**: calcd for $C_{18}H_{20}NO_4^+$ 314.1387[M + H]$^+$; found 314.1391.



14b

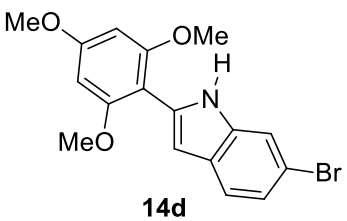
6-Methoxy-2-(2,4,6-trimethoxyphenyl)-1*H*-indole (14c)



14c

Following procedure **GP9**: starting from C2-IndoleDBX **13f** (101 mg, 0.200 mmol), after 3 hours 6-methoxy-2-(2,4,6-trimethoxyphenyl)-1*H*-indole **14c** (31.1 mg, 0.100 mmol, 50% yield) was obtained as a green solid. **M.p** 165-168 °C. **Rf:** 0.51 (Pentane:EtOAc 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.38 (s, 1H, N*H*), 7.49 (d, *J* = 8.6 Hz, 1H, Ar*H*), 6.99 (dd, *J* = 2.1, 0.9 Hz, 1H, Ar*H*), 6.90 (d, *J* = 2.3 Hz, 1H, Ar*H*), 6.76 (dd, *J* = 8.6, 2.3 Hz, 1H, Ar*H*), 6.28 (s, 2H, Ar*H*), 3.92 (s, 6H, *o*-O*CH*$_3$), 3.87 (s, 3H, O*CH*$_3$), 3.86 (s, 3H, O*CH*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.8, 158.4, 155.9, 135.6, 130.0, 122.6, 120.7, 109.2, 103.8, 103.6, 93.9, 91.5, 56.0, 55.6, 55.3. **IR** ν 3442 (s), 1604 (s), 1479 (s), 1329 (s), 1303 (s), 1234 (s), 1116 (w). **HR-ESI-MS**: calcd for $C_{18}H_{20}NO_4^+$ 314.1387[M + H]$^+$; found 314.1389.

6-Bromo-2-(2,4,6-trimethoxyphenyl)-1*H*-indole (14d)

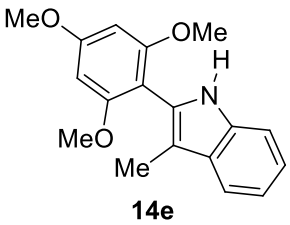


14d

Following procedure **GP9**: starting from C2-IndoleDBX **13g** (111 mg, 0.200 mmol), after 3 hours 6-bromo-2-(2,4,6-trimethoxyphenyl)-1*H*-indole **14d** (68.0 mg, 0.190 mmol, 94% yield) was obtained as a colorless solid. **M.p**. 133-138 °C. **R_f:** 0.49 (Pentane:EtOAc 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.52 (s, 1H, N*H*), 7.53 (d, *J* = 1.8 Hz, 1H, Ar*H*), 7.47 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.16 (dd, *J* = 8.4, 1.7 Hz, 1H, Ar*H*), 7.03 (s, 1H, Ar*H*), 6.28 (s, 2H, Ar*H*), 3.93 (s, 6H, *o*-O*CH*$_3$), 3.87 (s, 3H, *p*-O*CH*$_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 158.7, 135.7, 132.2, 127.1, 122.4, 121.2, 114.4, 113.2, 103.7, 102.9, 91.5, 56.0, 55.3. **IR** ν 3444 (w), 1605 (w), 1581 (w), 1454 (w), 1329 (w), 1205 (w), 1115 (s), 1067 (m). **HR-ESI-MS**: calcd for $C_{17}H_{17}Br^{79}NO_3^+$ 362.0386 $[M + H]^+$; found 362.0388.

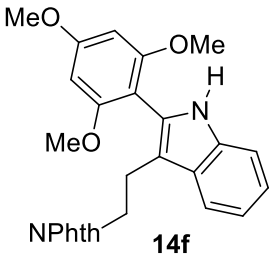
3-Methyl-2-(2,4,6-trimethoxyphenyl)-1*H*-indole (14e)



14e

Following procedure **GP9**: starting from C2-IndoleDBX **13h** (98.0 mg, 0.200 mmol), after 3 hours 3-methyl-2-(2,4,6-trimethoxyphenyl)-1*H*-indole **14e** (49.0 mg, 0.160 mmol, 82% yield) was obtained as a pale yellow solid. **M.p.** 128-131 °C. **R_f:** 0.46 (Pentane:EtOAc 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15 (s, 1H, N*H*), 7.68 (ddt, *J* = 7.5, 1.6, 0.8 Hz, 1H, Ar*H*), 7.41 (dt, *J* = 8.0, 1.0 Hz, 1H, Ar*H*), 7.21 (dddd, *J* = 21.2, 8.2, 7.1, 1.2 Hz, 2H, Ar*H*), 6.34 (s, 2H, Ar*H*), 3.98 (s, 3H, *p*-O*CH*$_3$), 3.85 (s, 6H, *o*-O*CH*$_3$), 2.28 (s, 3H, *CH*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.5, 159.4, 135.9, 128.9, 127.1, 121.1, 118.5, 118.5, 110.8, 110.4, 103.1, 90.7, 55.7, 55.3, 9.7. **IR** ν 3395 (w), 2939 (w), 2840 (w), 1609 (m), 1581 (m), 1456 (m), 1412 (m), 1224 (m), 1126 (s), 1033 (m), 941 (m), 816 (w). **HR-ESI-MS**: calcd for $C_{18}H_{20}NO_3^+$ 298.1438 $[M + H]^+$; found 298.1440.

2-(2-(2-(2,4,6-Trimethoxyphenyl)-1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione (14f)

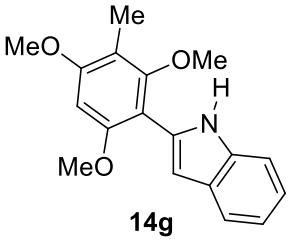


14f

Following procedure **GP9**: starting from C2-IndoleDBX **13i** (110 mg, 0.200 mmol), after 3 hours 2-(2-(2-(2,4,6-trimethoxyphenyl)-1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione **14f** (68.1 mg, 0.150 mmol, 75% yield) was obtained as an orange solid. **M.p.** 195-200 °C. **R_f:** 0.68 (Pentane:EtOAc 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (s, 1H, N*H*), 7.90 (dd, *J* = 6.5, 2.3 Hz, 1H, Ar*H*), 7.79 (dt, *J* = 7.0, 3.5 Hz, 2H, Ar*H*), 7.68 (dd, *J* = 5.5, 3.0 Hz, 2H, Ar*H*), 7.35 (dt, *J* = 7.3, 2.1 Hz, 1H, Ar*H*), 7.20 – 7.09 (m, 2H, Ar*H*), 6.18 (s, 2H, Ar*H*), 4.01 – 3.99 (m, 2H, CH_2), 3.87 (s, 3H, *p*-O*CH*$_3$), 3.75 (s, 6H, *o*-O*CH*$_3$), 3.03 – 2.99 (m, 2H, CH_2). **^{13}C NMR (**101 MHz, $CDCl_3$) δ 168.2, 161.6, 159.4, 135.9, 133.5, 132.3, 128.1, 128.0, 122.9, 121.3, 119.0, 118.8, 111.1, 110.6, 102.4, 90.5, 55.7, 55.3, 37.7, 24.7. **IR** ν 3392 (w), 1770 (w), 1704 (s), 1395 (s), 1359 (m), 1127 (m), 1042 (w). **HR-ESI-MS**: calcd for $C_{27}H_{25}N_2O_5^+$ 457.1758 $[M + H]^+$; found 457.1766.

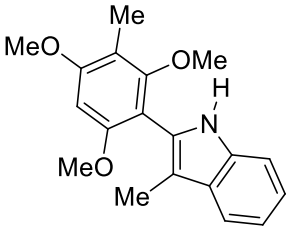
2-(2,4,6-trimethoxy-3-methylphenyl)-1*H*-indole (14g)

Following procedure **GP9**: starting from C2-IndoleDBX **13c** (95.5 mg, 0.200 mmol), after 3 hours 2-(2,4,6-trimethoxy-3-methylphenyl)-1*H*-indole **14g** (27.1 mg, 90.0 µmol, 46% yield) was obtained as a white solid. **M.p**. 135-138 °C. **Rf:** 0.62 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.46 (s, 1H, N*H*), 7.64 (dd, *J* = 7.8, 1.3 Hz, 1H, Ar*H*), 7.40 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.16 (ddd, *J* = 8.1, 7.0, 1.3 Hz, 1H, Ar*H*), 7.09 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 2H, Ar*H*), 6.41 (s, 1H, Ar*H*), 3.92 (s, 3H, O*CH*$_3$), 3.90 (s, 3H, O*CH*$_3$), 3.53 (s, 3H, O*CH*$_3$), 2.17 (s, 3H, *CH*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.2, 157.4, 156.3, 135.3, 131.1, 128.4, 121.3, 120.2, 119.3, 112.8, 110.4, 107.6, 103.7, 92.3, 60.2, 56.2, 55.6, 8.4. **IR** ν 3325 (w), 2960 (w), 1611 (m), 1452 (m), 1201 (m), 1110 (s), 797 (m). **HR-ESI-MS**: calcd for $C_{18}H_{20}NO_3^+$ 298.1438[M + H]$^+$; found 298.1443.



14g

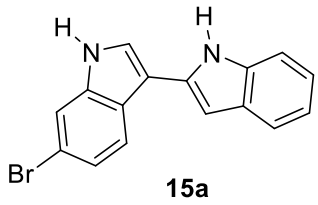
3-Methyl-2-(2,4,6-trimethoxy-3-methylphenyl)-1*H*-indole (14h)



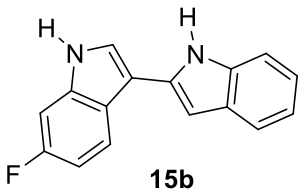
14h

Following procedure **GP9**: starting from C2-IndoleDBX **13h** (98.0 mg, 0.200 mmol), after 3 hours 3-methyl-2-(2,4,6-trimethoxy-3-methylphenyl)-1*H*-indole **14h** (40.6 mg, 0.130 mmol, 65% yield) was obtained as a brown solid. **M.p**. 164-166 °C. **R$_f$:** 0.58 (Pentane:EtOAc 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 (s, 1H, N*H*), 7.63 – 7.61 (m, 1H, Ar*H*), 7.35 (dt, *J* = 8.1, 1.0 Hz, 1H, Ar*H*), 7.15 (dddd, *J* = 21.4, 8.1, 7.1, 1.2 Hz, 2H, Ar*H*), 6.39 (s, 1H, Ar*H*), 3.92 (s, 3H, O*CH*$_3$), 3.79 (s, 3H, O*CH*$_3$), 3.30 (s, 3H, O*CH*$_3$), 2.24 (s, 3H, *CH*$_3$), 2.15 (s, 3H, *CH*$_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.1, 158.3, 156.9, 136.0, 128.9, 127.4, 121.3, 118.6, 118.5, 111.9, 110.8, 110.4, 107.4, 91.5, 60.0, 55.9, 55.6, 9.7, 8.4. **IR** ν 3353 (w), 2935 (w), 1606 (w), 1449 (m), 1434 (m), 1326 (m), 1185 (m), 1111 (s), 1006 (w), 806 (m), 736 (s). **HR-ESI-MS**: calcd for $C_{19}H_{22}NO_3^+$ 312.1594 [M + H]$^+$; found 312.1593.

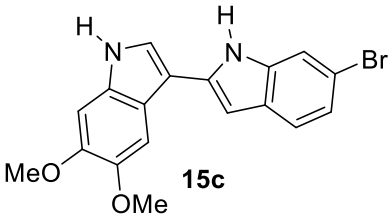
3.4.5: Scope of mixed 3'-2-N*H*-biindoles.



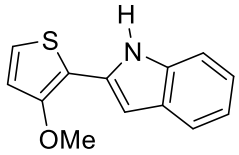
15a



15b

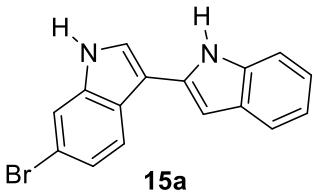


15c



16

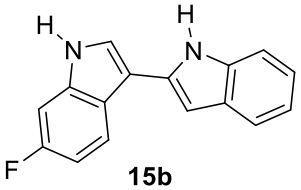
6'-Bromo-1*H*,1'*H*-2,3'-biindole (15a)



15a

Following procedure **GP9** *and using TMSCl as promoter*: starting from commercially available 6-bromo-1H indole (43.1 mg, 0.200 mmol), after 3 hours 6'-bromo-1*H*,1'*H*-2,3'-biindole **15a** (32.0 mg, 0.103 mmol, 51% yield). was obtained as a brown resin. $\mathbf{R_f}$: 0.41 (Pentane:EtOAc 7:3). **^{1}H NMR** (400 MHz, CD_3CN) δ 9.64 (s, 1H, N*H*), 9.54 (s, 1H, N*H*), 7.91 (dd, *J* = 8.5, 0.6 Hz, 1H, Ar*H*), 7.70 (dd, *J* = 1.8, 0.6 Hz, 1H, Ar*H*), 7.65 (d, *J* = 2.7 Hz, 1H, Ar*H*), 7.59 – 7.52 (m, 1H, Ar*H*), 7.41 (dd, *J* = 8.0, 1.0 Hz, 1H, Ar*H*), 7.31 (dd, *J* = 8.5, 1.8 Hz, 1H, Ar*H*), 7.11 (ddd, *J* = 8.1, 7.1, 1.3 Hz, 1H, Ar*H*), 7.04 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H, Ar*H*), 6.76 (dd, *J* = 2.2, 0.9 Hz, 1H, Ar*H*). **^{13}C NMR** (101 MHz, CD_3CN) δ 138.6, 137.3, 134.1, 130.4, 125.0, 124.4, 124.1, 122.2, 122.1, 120.5, 120.4, 116.2, 115.6, 111.5, 110.3, 99.1. **IR ν** 3413 (w), 3395 (w), 1615 (m), 1595 (m), 1454 (s), 1308 (s), 1230 (m), 1103 (m), 894 (s). **HR-ESI-MS**: calcd for $C_{16}H_{12}Br^{79}N_2^+$ 311.0178 $[M + H]^+$; found 311.0173.

6'-Fluoro-1*H*,1'*H*-2,3'-biindole (15b)

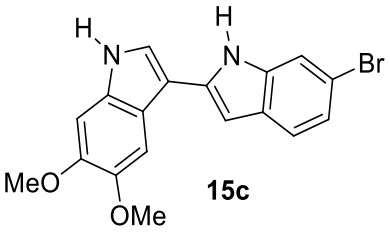


15b

Following procedure **GP9** *and using TMSCl as promoter*: starting from commercially available 6-fluoro-1H indole (30.0 mg, 0.200 mmol), after 3 hours 6'-fluoro-1*H*,1'*H*-2,3'-biindole **15b** (28.0 mg, 0.112 mmol, 56% yield) was obtained as a brown oil. $\mathbf{R_f}$: 0.42 (Pentane:EtOAc 7:3). **^{1}H NMR** (400 MHz, Acetone-d_6) δ 10.63 (s, 1H, N*H*), 10.43 (s, 1H, N*H*), 8.04 (dd, *J* = 8.8, 5.3 Hz, 1H, Ar*H*), 7.85 (d, *J* = 2.5 Hz, 1H, Ar*H*), 7.55 (dd, *J* = 7.5, 1.3 Hz, 1H, Ar*H*), 7.37 (dd, *J* = 7.9, 1.3 Hz, 1H, Ar*H*), 7.25 (dd, *J* = 9.8, 2.4 Hz, 1H, Ar*H*), 7.13 – 6.93

(m, 3H, Ar*H*), 6.86 – 6.71 (m, 1H, Ar*H*) (*^{13}C could not recorded due to unstable nature of this compound in solution).* **HR-ESI-MS** calcd for $C_{16}H_{11}FN_2^+$ 250.0901 $[M]^+$ found 250.0903.

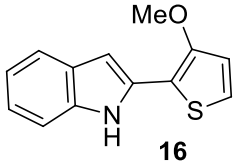
6-Bromo-5',6'-dimethoxy-1*H*,1'*H*-2,3'-biindole (15c)



15c

Following procedure **GP9**: using commercially available 5,6-dimethoxy-1*H*-indole (53.2 mg, 0.200 mmol), after 3 hours 6-bromo-5',6'-dimethoxy-1*H*,1'*H*-2,3'-biindole **15c** (38.1 mg, 0.103 mmol, 34% yield) was obtained as a yellow oil. **Rf:** 0.35 (Pentane:EtOAc 1:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.21 (br s, 1H, N*H*), 8.16 (br s, 1H, N*H*), 7.53 (s, 1H, Ar*H*), 7.49 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.35 (s, 1H, Ar*H*), 7.32 (d, *J* = 2.6 Hz, 1H, Ar*H*), 7.22 (dd, *J* = 8.3, 1.7 Hz, 1H, Ar*H*), 6.94 (s, 1H, Ar*H*), 6.70 (dd, *J* = 2.0, 0.9 Hz, 1H, Ar*H*), 3.99 (s, 3H, O*Me*), 3.94 (s, 3H, O*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.8, 146.0, 136.8, 134.2, 130.8, 128.5, 123.2, 121.0, 119.8, 118.1, 114.6, 113.3, 109.8, 101.4, 99.0, 94.6, 56.5, 56.2 (*the compound spontaneously decompose in acidic deuterated solvents, it presents about 9% of decomposed products – grease signal not purified*). **IR** ν 2873 (m), 1691 (m), 1349 (m), 1277 (w), 1046 (s), 970 (m), 850 (s), 766 (w), 749 (w). **HR-ESI-MS** calcd for $C_{18}H_{15}{}^{79}BrN_2NaO_2^+$ $[M+Na]^+$ 393.0209; found 393.0201.

2-(3-Methoxythiophen-2-yl)-1*H*-indole (16)

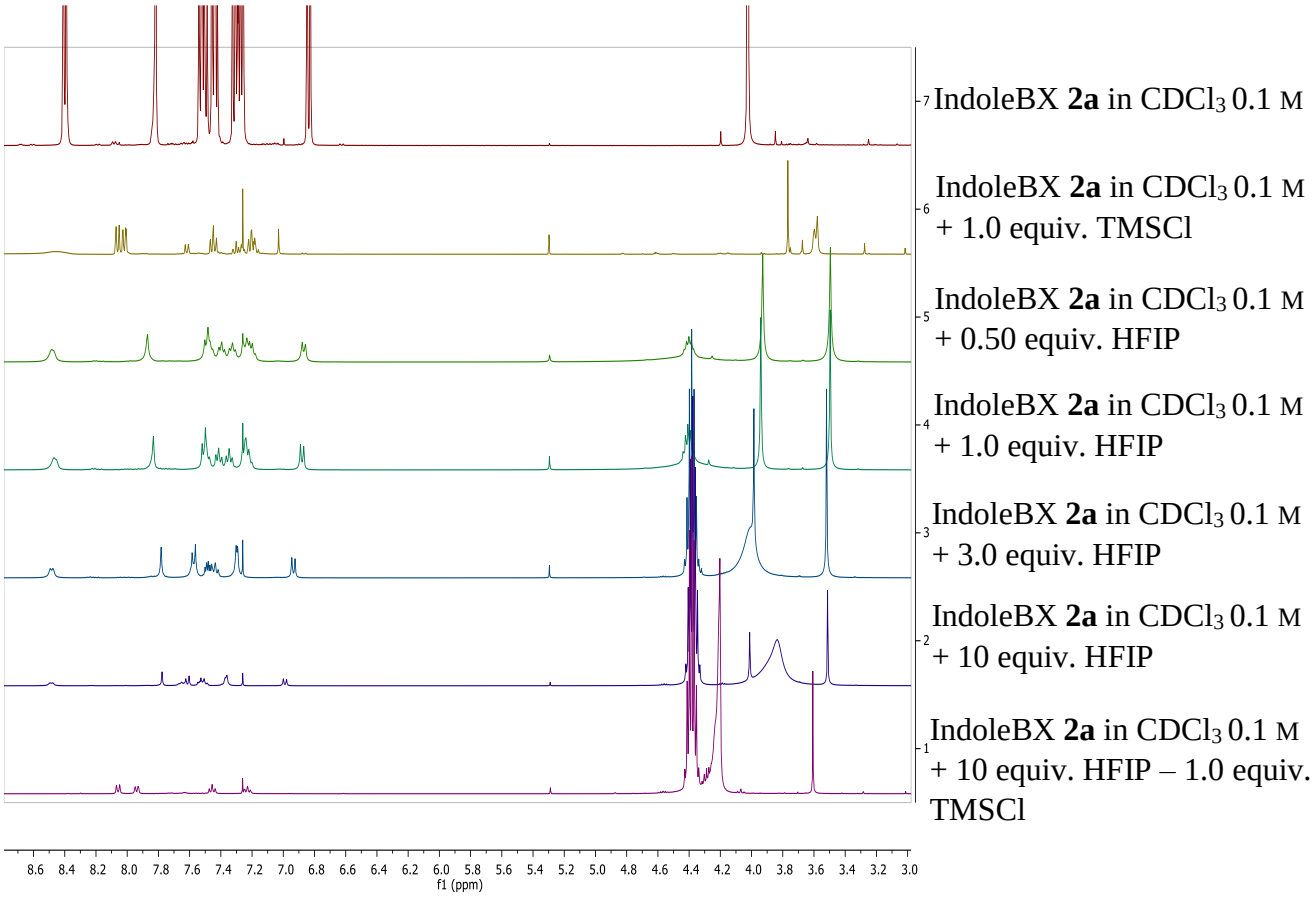


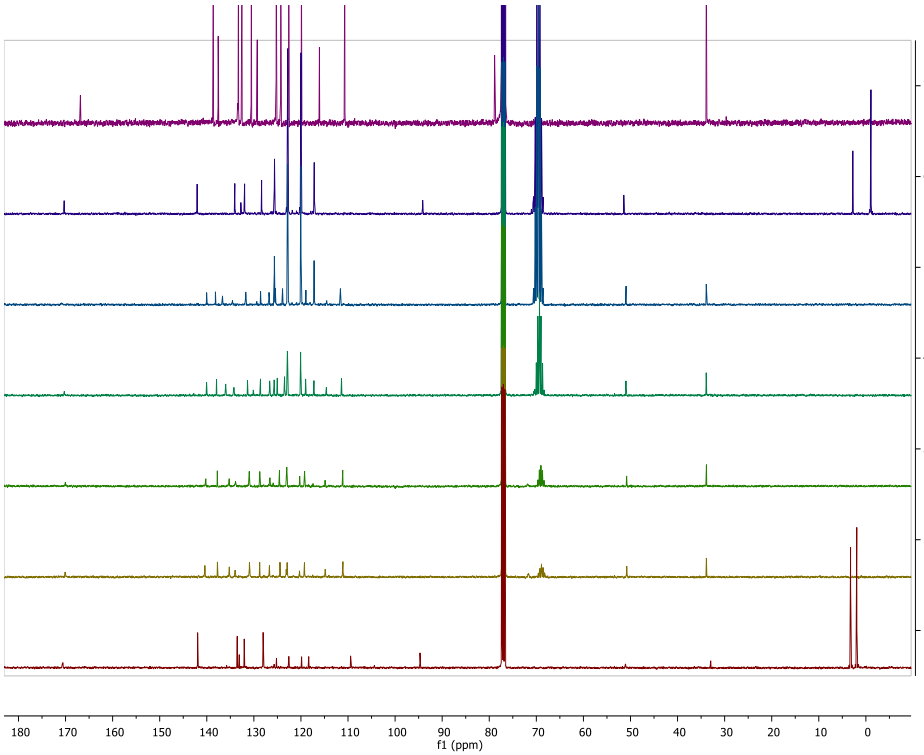
16

Following procedure **GP9**: using commercially available 3-methoxythiophen (22.8 mg, 0.200 mmol), after 3 hours 2-(3-methoxythiophen-2-yl)-1*H*-indole **16** (13.0 mg, 60.0 µmol, 28% yield) was obtained as a green oil. **R$_f$:** 0.6 (Pentane:EtOAc 9:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.30 (s, 1H, N*H*), 7.56 (dq, *J* = 7.7, 1.0 Hz, 1H, Ar*H*), 7.38 (dt, *J* = 8.0, 1.0 Hz, 1H, Ar*H*), 7.19 – 7.04 (m, 3H, Ar*H*), 6.90 (d, *J* = 5.5 Hz, 1H, Ar*H*), 6.60 (dd, *J* = 2.1, 0.9 Hz, 1H, Ar*H*), 4.04 (s, 3H, O*CH$_3$*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.5, 135.8, 131.8, 128.3, 122.3, 121.6, 119.9, 119.9, 116.3, 112.8, 110.5, 97.9, 58.9. **IR** ν 3440 (w), 1706 (w), 1588 (w), 1516 (w), 1457 (w), 1380 (m), 1293 (m), 1069 (s), 776 (s), 747 (s). **HR-ESI-MS**: calcd for $C_{13}H_{12}NOS^+$ 230.0634$[M + H]^+$; found 230.0637.

4. Working model for the reaction mechanism.

In order to establish the role of both promoter and fluorinated solvent we performed several NMR experiments in deuterated $CDCl_3$ (solvent of characterization) and CD_2Cl_2 (solvent of reaction).We screened different equivalents of HFIP and TMSCl. As we've seen in the control experiment, the presence of TMSCl as promoter is essential. When we added 1.0 equiv. of TMSCl to reagent **2a** in deuterated solvent, we immediately observed decomposition of the reagent in its constituents. The observed aromatic peaks corresponds to the ones of iodo-benzoic acid.[26] In the carbon it is possible to observe that the hypervalent character of C-I bond is lost, as it shift from 78 ppm to 94 ppm. HFIP alone doesn't promote immediate decomposition but shift of peaks; it is possible that it coordinates with the reagent via hydrogen bond-type interactions. However, HFIP plays an important role in stabilizing the intermediate form, as the sole Lewis Acid would immediately decompose the hypervalent iodine reagent. When we mixed both fluorinated solvent and TMSCl we observed decomposition in absence of a suitable nucleophile.





IndoleBX **2a** in $CDCl_3$ 0.1 M

IndoleBX **2a** in $CDCl_3$ 0.1 M + 1.0 equiv. TMSCl

IndoleBX **2a** in $CDCl_3$ 0.1 M + 0.50 equiv. HFIP

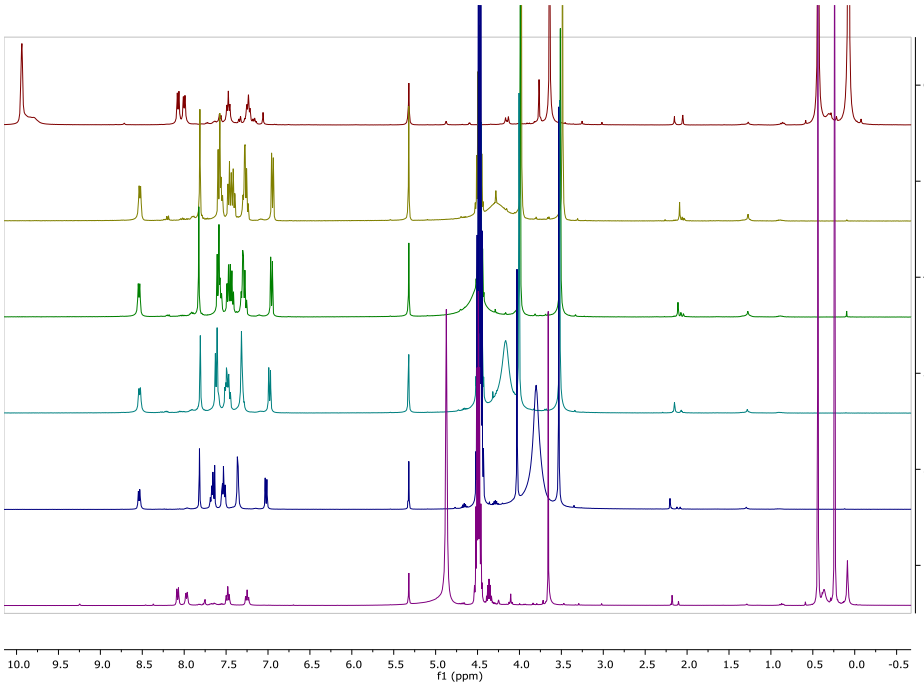
IndoleBX **2a** in $CDCl_3$ 0.1 M + 1.0 equiv. HFIP

IndoleBX **2a** in $CDCl_3$ 0.1 M + 3.0 equiv. HFIP

IndoleBX **2a** in $CDCl_3$ 0.1 M + 10 equiv. HFIP

IndoleBX **2a** in $CDCl_3$ 0.1 M + 10 equiv. HFIP – 1.0 equiv. TMSCl

NMR analysis in CD_2Cl_2 showed the same reactivity pattern as in $CDCl_3$



IndoleBX **2a** in CD_2Cl_2 0.1 M + 1.0 equiv. TMSCl

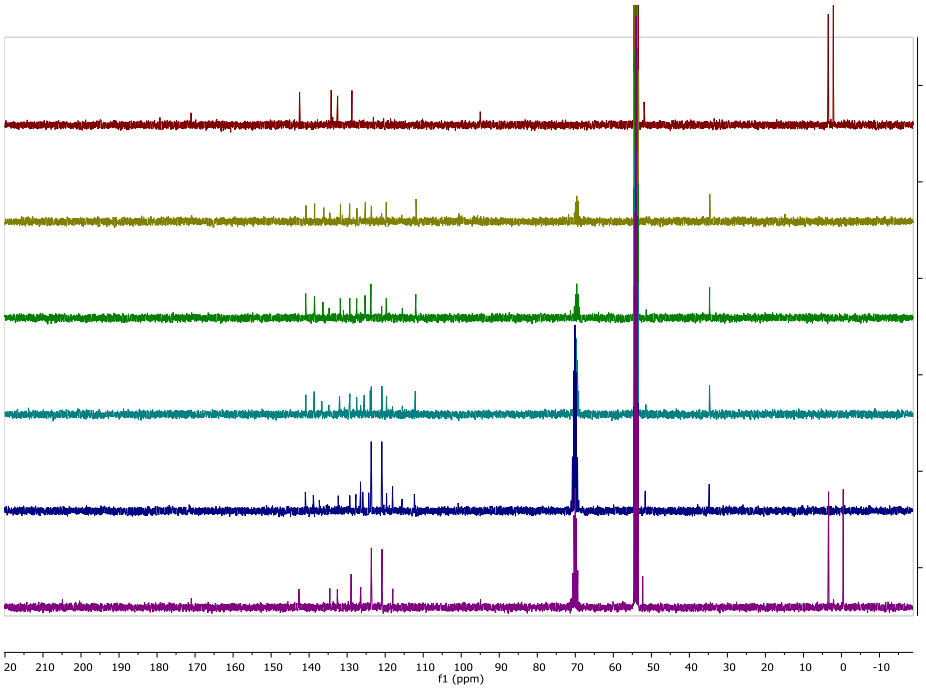
IndoleBX **2a** in CD_2Cl_2 0.1 M + 0.50 equiv. HFIP

IndoleBX **2a** in CD_2Cl_2 0.1 M + 1.0 equiv. HFIP

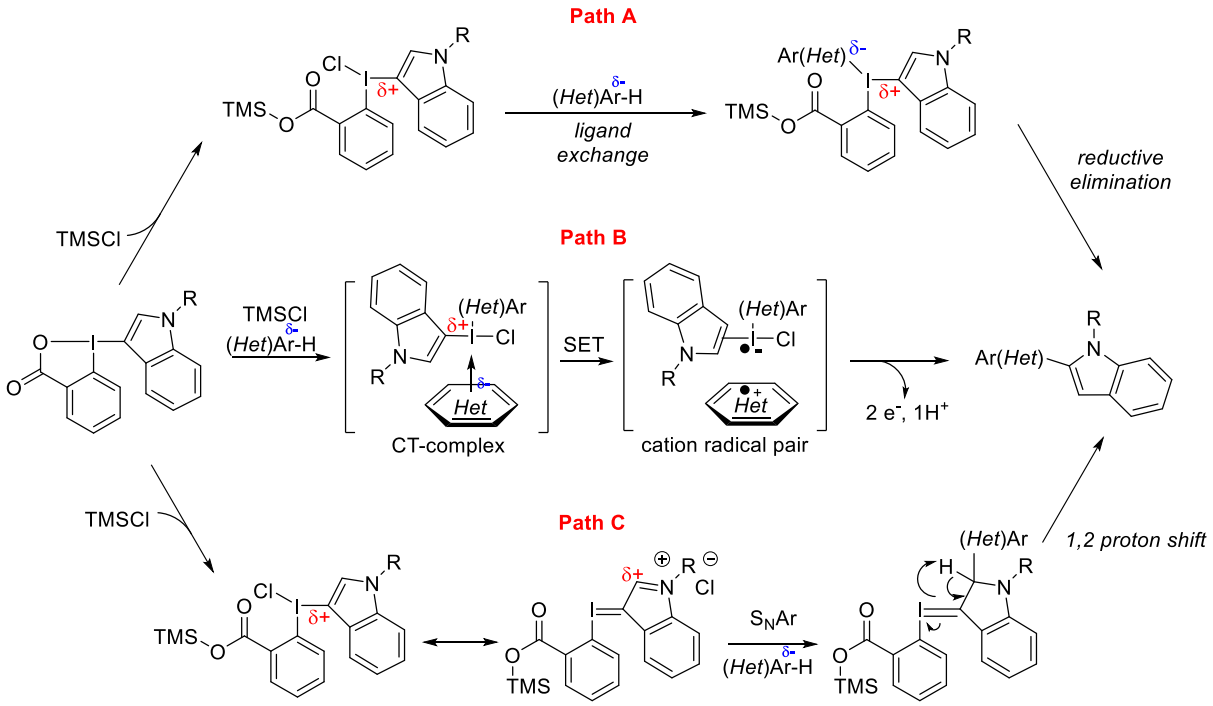
IndoleBX **2a** in CD_2Cl_2 0.1 M + 3.0 equiv. HFIP

IndoleBX **2a** in CD_2Cl_2 0.1 M + 10 equiv. HFIP

IndoleBX **2a** in CD_2Cl_2 0.1 M + 10 equiv. HFIP – 1.0 equiv. TMSCl

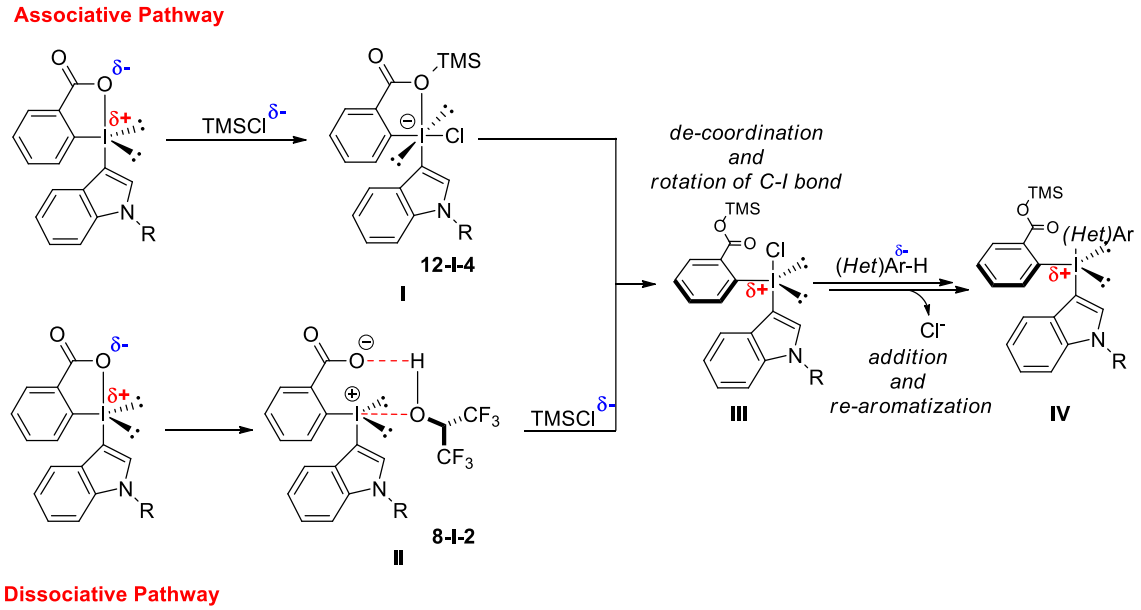


We currently hypothetize three possible mechanisms for this transformation, a *Path A* would involve ligand exchange with the nucleophile and reductive elimination to afford the product. *Path B* envisages a SET pathway and *Path C* a S_NAr pathway, in which a iodonium carbene resonance structure may play a role (*Scheme S1*).



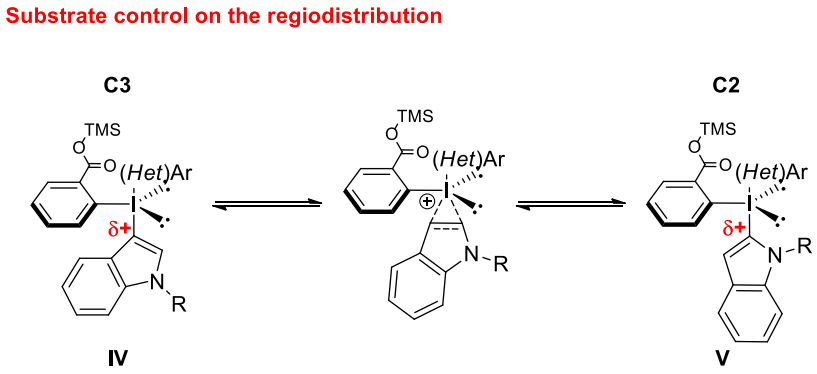
Scheme S1: Three mechanistical hypotheses for the hypervalent iodine-mediated oxidative coupling.

As already reported,[27] heteroatom-ligands of the $I^{(III)}$ can exchange with different nucleophiles. For *Path A*, two pathways could be considered: associative and dissociative (*Scheme S2*). In the associative pathway we speculate that the Cl^- derived from TMSCl rapidly add to the C-I σ* orbital and form a *trans* tetracoordinated [12-I-4] iodate **I** with a square-planar arrangement. Rapid isomerization and elimination of the carboxylate form a λ3 -iodane **III**. The addition-elimination sequence proceed at a low-energy barrier and is generally reversible. Conversely, the dissociative pathway would involve a high-energy dicoordinated [8-I-2] iodonium species, possibly stabilized by ionic or hydrogen interaction with the protic fluorinated solvent on apical sites to arrive at **II**. Addition of Cl^- would lead to intermediate **III.** For addition of (*hetero*)aryl-H the same mechanisms are considered, but a rearomatization of the nucleophile has also to be accounted to get intermediate **IV**.



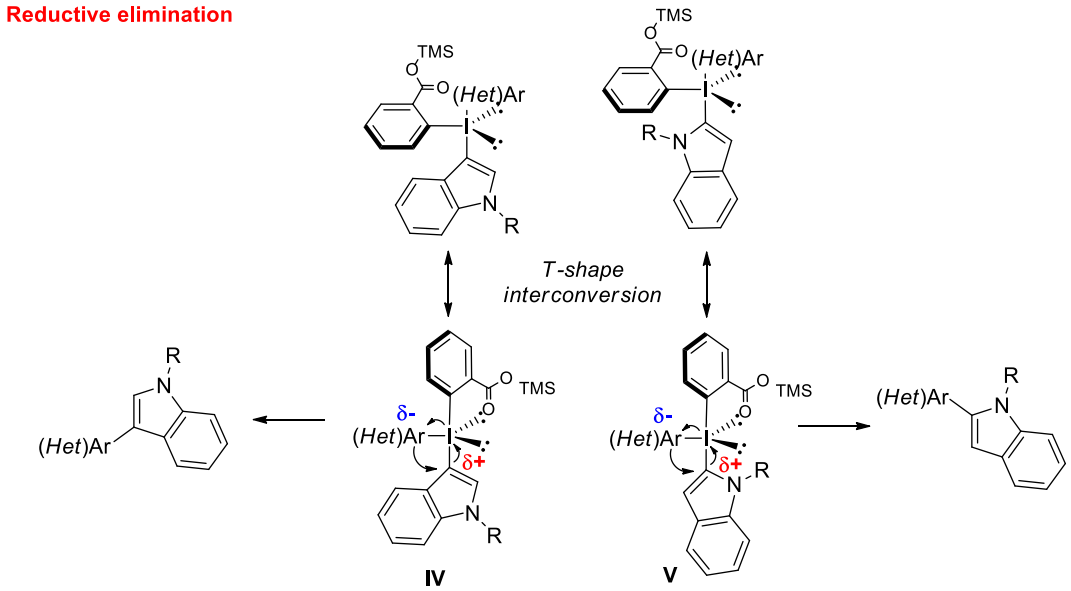
Scheme S2: Associative and Dissociative pathways for the formation of **III** and **IV**.

To explain the regio-distribution of the product, we hypothetize that **IV**, the C3 regiosisomer would exist in equilibrium with **V**, the C2 one (*Scheme S3*). When a C3-alkylated indole is used as nucleophile, the equilibrium should be shifted towards intermediate **IV** due to sterical hindrance.



Scheme S3: Equilibrium of two regioisomers IV and V.

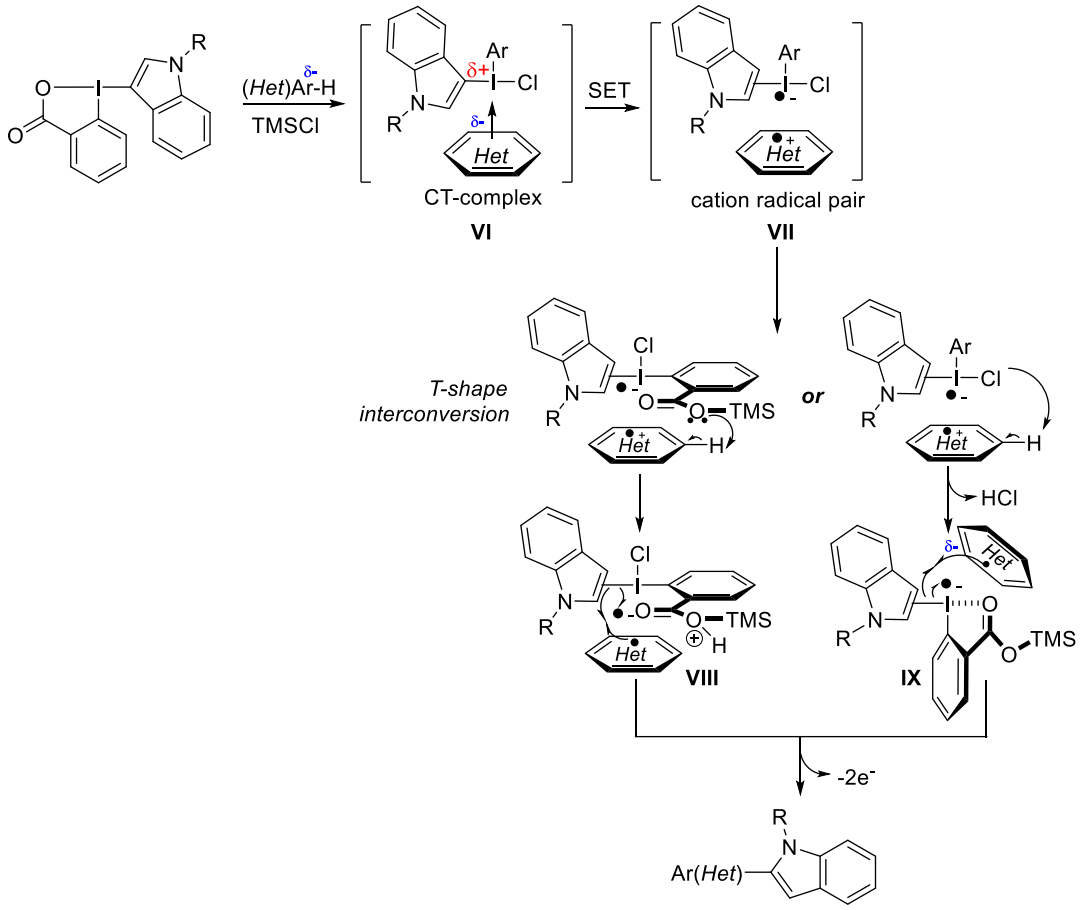
Finally, the hypervalent λ3 -iodanes **IV** or **V** would undergo reductive elimination to afford the coupled product and iodo-benzoic acid as monovalent iodide. The process if facile because the hypervalent iodine is a hypernucleofuge (hypervalent leaving group better than a super-ion as $^-$OTf). The process is most probably concerted, (as shown in *Scheme S4)* and require therefore isomerization of the reagent to have the two desired aryl groups in cis relationship. In this step, elimination to form the more sterically hindered product may be more difficult, allowing also to rationalize the regioselectivity based on kinetics instead of thermodynamics. A stepwise, mechanism involving high energy carbo-cation and –anion intermediates is less probable. A weak point of pathway A is that it is difficult to rationalize the high selectivity observed for bi-heteroaryl formation: In fact, at least some reductive elimination to give undesired cross-products with iodobenzoic acid would have been expected.



Scheme S4: Reductive elimination

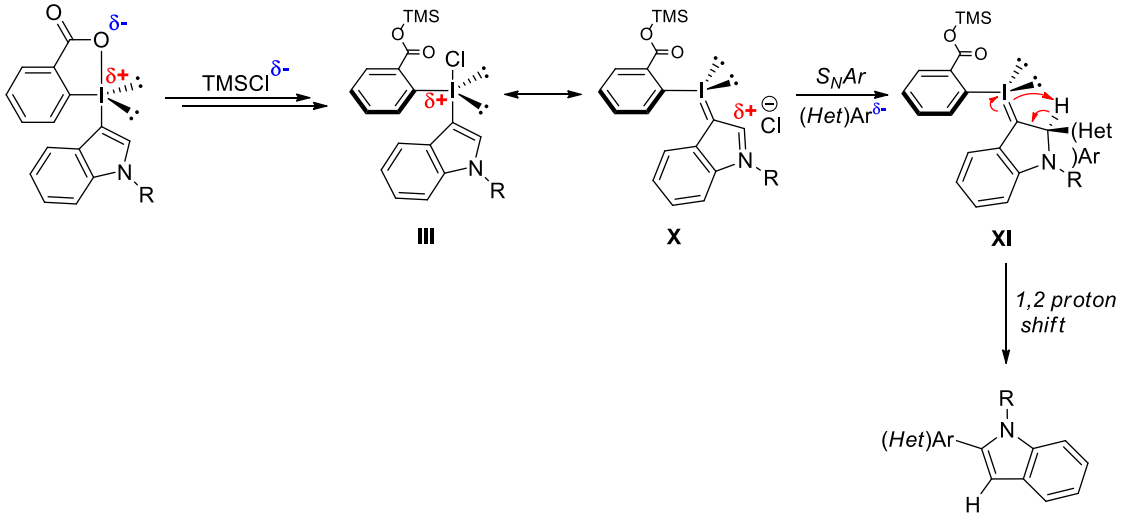
Another proposal involves, as theorized by Kita for the oxidative coupling of arenes and heterocycles,[28,29] a radical mechanism. This would be a viable alternative to the ligand

exchange proposed in *Path A*. The TMSCl should induce the formation of Charge-Transfer complex **VI** (CT-complex) between the (hetero)arene and the electrophilic hypervalent iodine (*Scheme S5*). A SET would form the oxidized cationic radical (hetero)arene and transfer one electron on the electrophilic iodane. The aromatic cation radical intermediate **VII** could be stabilized by the enamine bond of the indole, with the iodane shifting between the C2-C3 carbons. Intramolecular deprotonation by either the chlorine moiety or the carboxylate the would afford intermediates **VIII** and **IX**. Final SET recombination would afford the corresponding mixed bi-(hetero)arenes. Alternatively, recombination on iodine would lead back to intermediate **IV** and **V**, which could then undergo reductive elimination.



Scheme S5: SET pathway

Finally, *Path C* takes into account the donating effect of the N-lone pair in stabilizing **III** via its resonance form **X**. S_NAr attack of the nucleophile would form intermediate **XI**. Finally, 1,2-proton shift of the C2-proton on the C3-iodo-carbene would afford the desired product (*Scheme S6*).

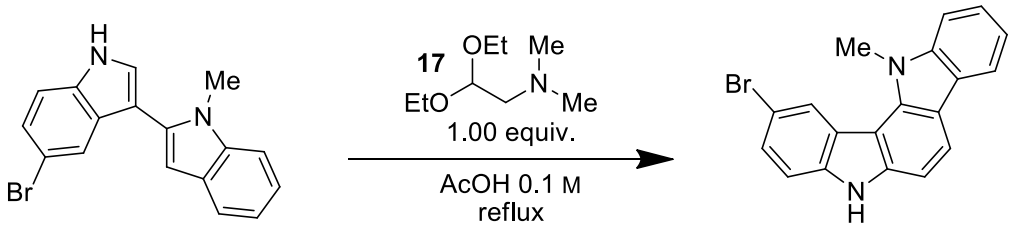


Scheme S6: Vicarious nucleophilic aromatic substitution.

5. Further Modifications of the (Hetero)-Arylated Indoles.

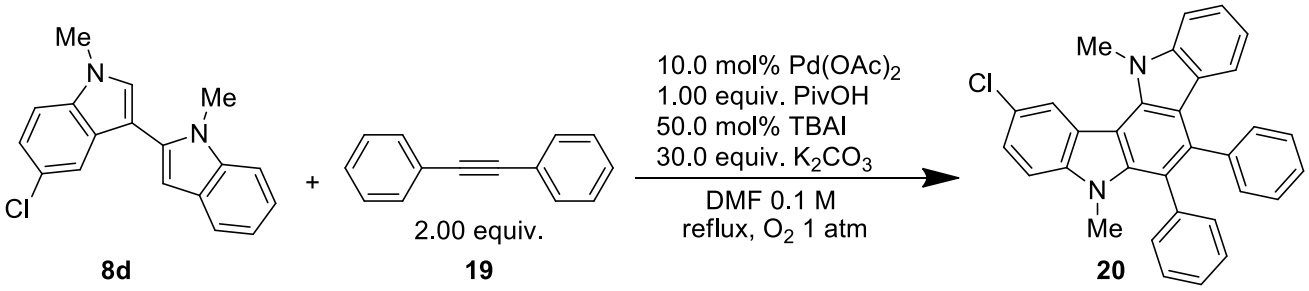
All commercially available chemicals were purchased from the suppliers quoted in Paragraph 1.0 of Supplementary Informations: these chemicals were purified through a short plug of celite prior to their use in catalysis.

Synthesis of 2-bromo-12-methyl-5,12-dihydroindolo[3,2-a]carbazole (18)



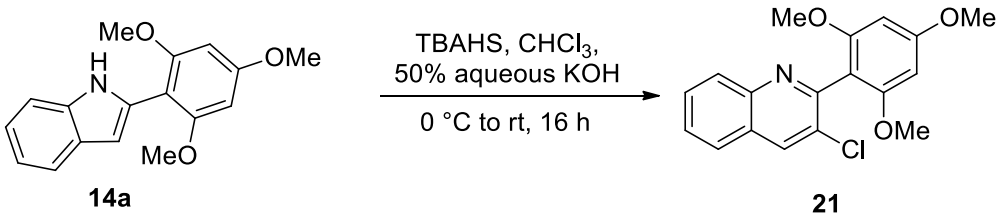
Following a reported procedure,[30] in a flame dried vial under nitrogen atmosphere, 5'-bromo-1-methyl-1*H*,1'*H*-2,3'-biindole **8j** (32.5 mg, 1.00 mmol, 1.00 equiv.) was dissolved in AcOH (1 mL, 0.1 M); commercially available 2,2-diethoxy-*N*,*N*-dimethylethanamine (20.0 µL, 1.00 mmol, 1.00 equiv.) **17** was added under vigorous stirring. The reaction mixture was heated up to reflux (135 °C) and monitored via TLC (1:1 Pentane/EtOAc). Upon complete consumption of the starting material (1 hour), the reaction was cooled to room temperature and the solvent removed under reduced pressure. The crude product was purified via flash chromatography (gradient 5:1-1:2 Pentane:EtOAc) to afford 2-bromo-12-methyl-5,12-dihydroindolo[3,2-a]carbazole **18** (28.3 mg, 81.0 µmol, 81% yield) as a yellow oil. **Rf** 0.4 (Pentane:EtOAc 1:1) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 1.7 Hz, 1H, Ar*H*), 8.37 (s, 1H, N*H*), 8.13 (d, *J* = 8.4 Hz, 1H, Ar*H*), 8.09 (dt, *J* = 7.7, 0.9 Hz, 1H, Ar*H*), 7.54 – 7.43 (m, 3H, Ar*H*), 7.37 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.33 – 7.26 (m, 2H, Ar*H*), 4.48 (s, 3H, N*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.8, 140.4, 137.5, 137.2, 127.1, 125.2, 124.1, 124.1, 123.5, 119.7, 119.6, 118.9, 116.6, 112.3, 112.1, 108.9, 107.0, 103.5, 34.7. **IR** ν 3053 (w), 2939 (w), 1619 (w), 1589 (w), 1466 (s), 1369 (m), 1339 (m), 1272 (m), 1244 (m), 1145 (m), 1092 (w), 830 (m), 790 (s), 748 (a). No high resolution mass spectrum could be obtained for this compound due to insufficient ionization.

Synthesis of 2-chloro-5,12-dimethyl-6,7-diphenyl-5,12-dihydroindolo[3,2-*a*]carbazole (20)



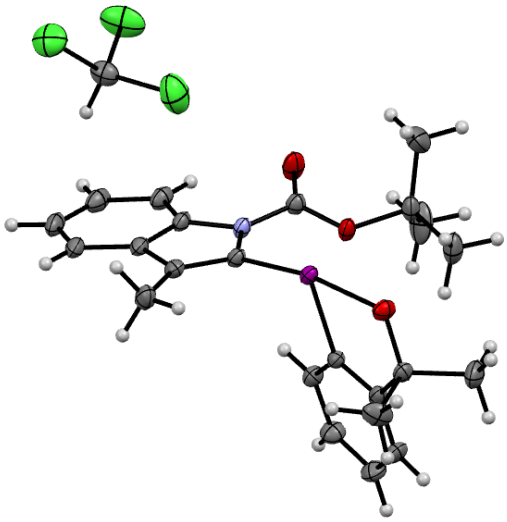
Following a reported procedure,[31] $Pd(OAc)_2$ (2.25 mg, 10.0 µmol, 10.0 mol%), K_2CO_3 (4.15 mg, 30.0 µmol, 30 mol%), TBAB (16.0 mg, 50.0 µmol, 0.5 equiv.), PivOH (10.2 mg, 0.100 mmol, 1.00 equiv.), 5'-chloro-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole **8d** (29.5 mg, 0.100 mmol) and commercially available diphenylacetylene **19** (35.6 mg, 0.200 mmol, 2.00 equiv.) were added to a flame dried vial under nitrogen atmosphere. The tube was purged with O_2 three times before DMF (1.0 mL, 0.1 M) was added. The reaction mixture was stirred at 100 °C under O_2 (1 atm) for 12 h and was monitored by TLC (Pentane:EtOAc 4:1). The solution was then cooled to RT, diluted with ethyl acetate (10 mL), washed with H_2O (3x10 mL), dried over $MgSO_4$, filtered, and dried under vaccum. The crude product was purified by column chromatography on silica gel (gradient 10:1 to 4:1 Pentane:EtOAc) to afford 2-chloro-5,12-dimethyl-6,7-diphenyl-5,12-dihydroindolo[3,2-a]carbazole **20** (35.1 mg, 75.0 µmol, 75% yield). **Rf** 0.7 (Pentane:EtOAc 4:1) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 1.9 Hz, 1H, Ar*H*), 7.49 (d, *J* = 8.1 Hz, 1H, Ar*H*), 7.43 (dd, *J* = 8.7, 2.0 Hz, 1H, Ar*H*), 7.37 (d, *J* = 7.5 Hz, 1H, Ar*H*), 7.35 – 7.17 (m, 11H, Ar*H*), 6.92 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.51 (d, *J* = 7.9 Hz, 1H, Ar*H*), 4.50 (s, 3H, N*Me*), 3.26 (s, 3H, N*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.2, 140.1, 139.8, 139.7, 138.4, 136.7, 136.5, 132.2, 130.2, 127.9, 127.3, 126.7, 124.5, 124.3, 124.3, 124.0, 122.1, 121.9, 121.1, 119.5, 118.3, 115.2, 110.0, 108.9, 106.5, 35.5, 33.1 (*one aromatic Carbon not resolved*). **IR** ν 2975 (w), 2943 (w), 2903 (w), 1722 (w), 1613 (w), 1468 (s), 1422 (m), 1369 (m), 1338 (m), 1271 (m), 1247 (m), 1208 (w), 1087 (m), 1045 (m), 880 (w), 787 (m), 750 (s). **HR-ESI-MS** calcd for $C_{32}H_{24}ClN_2^+$ $[M+H]^+$ 471.1623; found 471.1616.

Synthesis of 3-Chloro-2-(2,4,6-trimethoxyphenyl)quinolone (21)

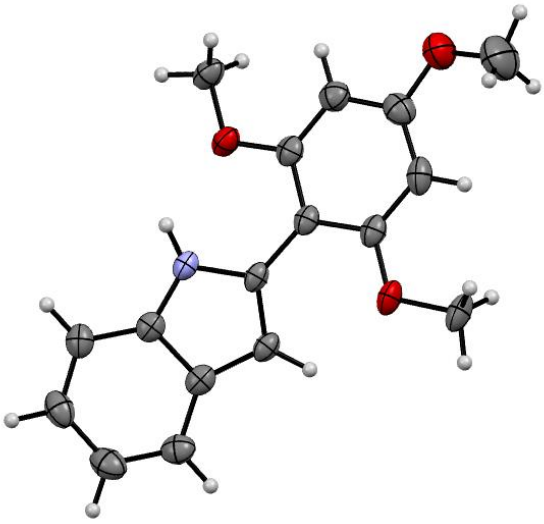


With slight modification of a reported procedure[32,33] 50% aqueous KOH (72.0 μL, 0.635 mmol, 7.50 equiv.) was added to a vigorously stirred solution of 2-(2,4,6-trimethoxyphenyl)-1*H*-indole **14a** (24.0 mg, 85.0 μmol, 1.00 equiv.) and $^{n}Bu_4NHSO_4$ (2.88 mg, 8.47 μmol, 0.100 equiv.) in chloroform (1.10 mL) under ice-cooling bath. The reaction mixture was stirred at 0 °C for 2 h and left overnight at room temperature. After 16 h The aqueous layer was separated and extracted with chloroform. The organic layers were dried over $MgSO_4$. After filtration and evaporation, the crude was purified by PTLC,and 3-chloro-2-(2,4,6-trimethoxyphenyl)quinoline **21** (20.0 mg, 60.0 μmol, 72% yield) was obtained as brown crystalline solid. **M.p.** 158-162 °C **R_f**: 0.35 (25% EtOAc in Pentane). **^{1}H NMR** (400 MHz, *Acetone-d6*) δ 8.44 (s, 1H, Ar*H*), 8.09 – 8.02 (m, 1H, Ar*H*), 7.97 (dd, *J* = 8.1, 1.5 Hz, 1H, Ar*H*), 7.81 – 7.73 (m, 1H, Ar*H*), 7.65 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H, Ar*H*), 6.37 (s, 2H, Ar*H*), 3.90 (s, 3H, *p*-O*CH*$_3$), 3.70 (s, 6H, *o*-O*CH*$_3$). **^{13}C NMR** (101 MHz, *Acetone-d6*) δ 163.1, 159.8, 154.8, 147.1, 135.4, 131.2, 130.3, 129.8, 128.9, 128.1, 127.8, 110.5, 91.5, 56.1, 55.7. **IR** ν 2256 (w), 1728 (m), 1704 (s), 1611 (w), 1340 (w), 1249 (s), 1158 (w), 1131 (w), 1035 (w), 971 (w). **HR-ESI-MS**: calcd for $C_{18}H_{17}ClNO_3^+$ 330.0891[M + H]$^+$; found 330.0895.

6. Crystal Structures.



A single crystal was grown by slow diffusion of the solution of **13h** in $CDCl_3$. Supplementary crystallographic data for this compound have been deposited at Cambridge Crystallographic Data Centre (**1824408**) and can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

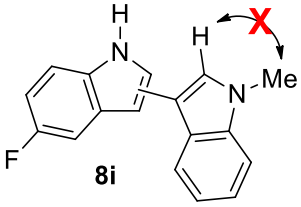


A single crystal was grown by removal of reaction solvent from **14a** by evaporation. Supplementary crystallographic data for this compound have been deposited at Cambridge Crystallographic Data Centre (**1824407**) and can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

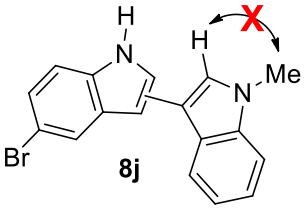
7. Determination of the regio-distribution.

Given the all-aromatic nature of the mixed bi-indole frameworks, NMR studies were required to assign the correct regiodistribution of the products. NMR-analysis of bis-methylated bi-indoles **8a**-**8h** already shown a 3'-2/2'-3 connectivity between the two heterocyclic core. We then decide to procede in steps, focusing our attention on mixed bi-indole obtained when a NH-indole was used as nucleophile in the reaction.

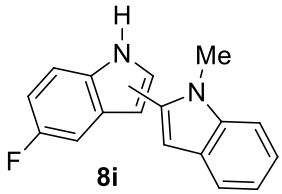
In *Figure 7.1* all four possible regioisomers **I-IV** are reported: in order to determine the correct structure we performed bidimensional NMR analysis of product **8i**-**8j** and their derivatives **35**-**36**. We concentrated our attention to the H-signal at about 6.6 ppm: given the shift we postulated its belonging to either C2-C3 carbons of one of the two indoles. HMBC analysis of products **8i**-**8j** didn't show correlation between the N*CH*$_3$-carbon and the H-signal at about 6.6 ppm. For this reason we were able to exclude



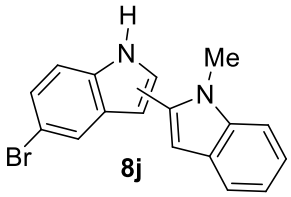
8i



8j

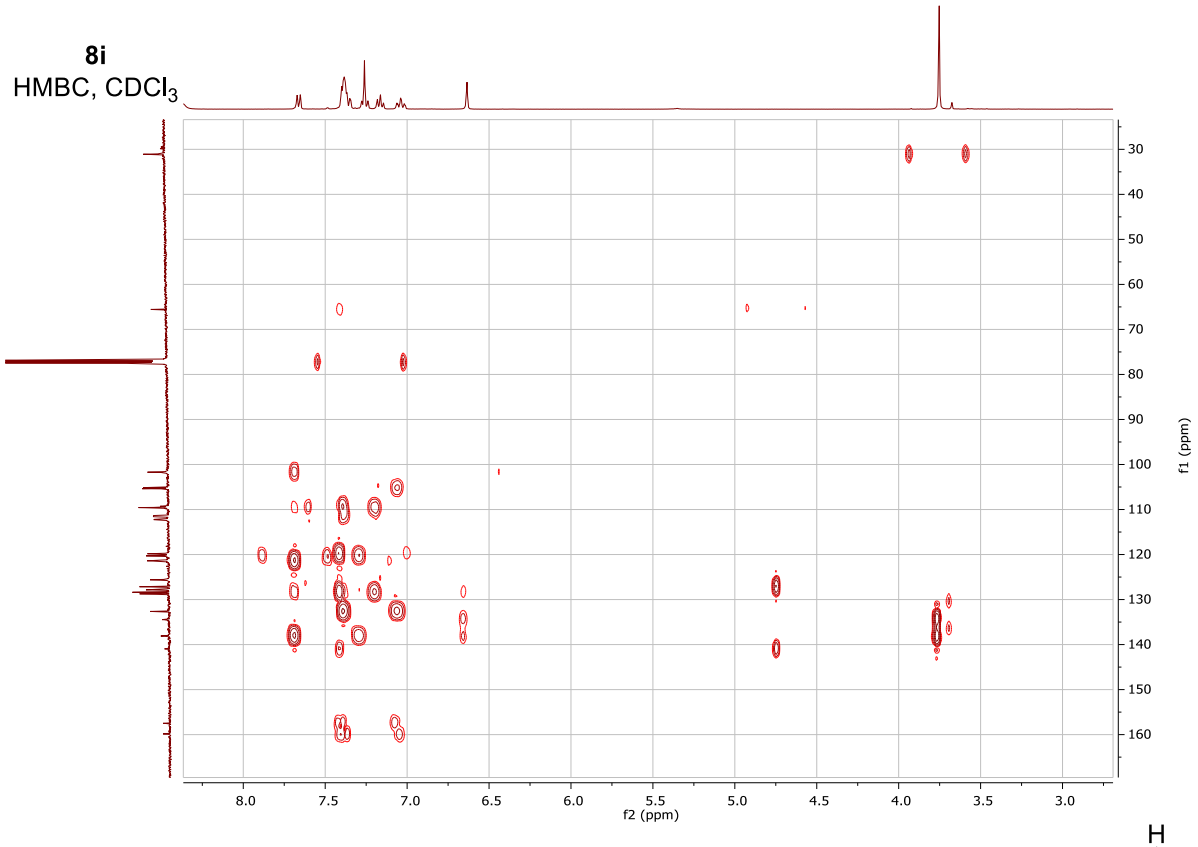


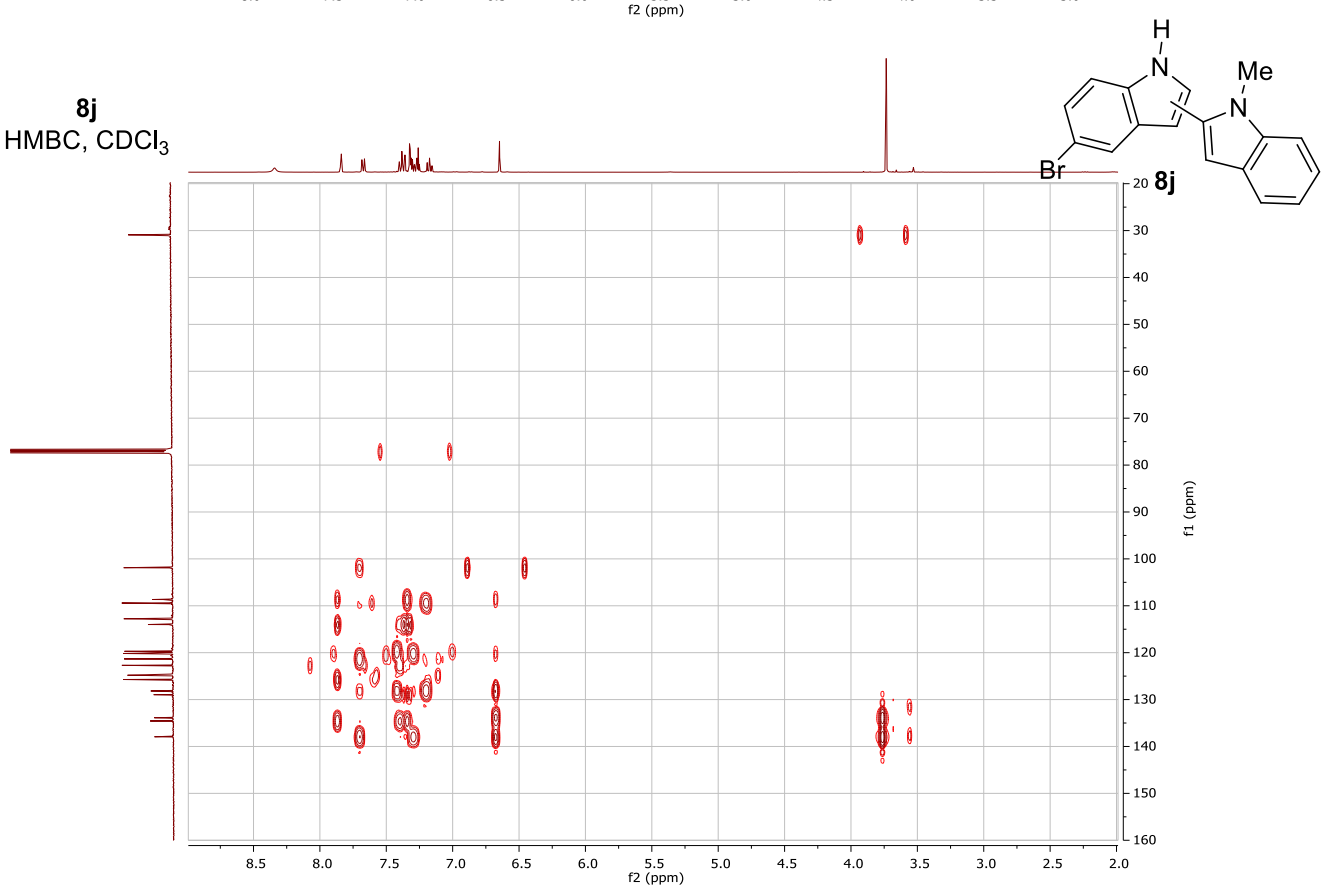
8i



8j

regioisomers of classes **I** and **II** and assign the singlet to a C3-carbon.

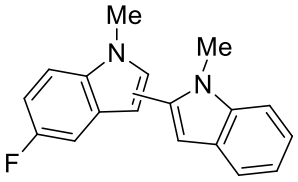




To distinguish between the remaining two regioisomers **III** and **IV**, it was not possible to use COSY correlation between the NH bond and the C2-H, as the signal was too weak, independently of the substitution pattern. We therefore methylated **8i**-**8j** to obtain **35**-**36**.

Following general procedure GP6: the corresponding biindoles **8i-8j** (0.100 mmol, 1.00 equiv.) were dissolved in dry THF (1.00 mL, 0.1 M). Sodium hydride (4.00 mg, 1.00 mmol, 1.00 equiv. 60% suspension in mineral oil) was slowly added under N_2 flow at 0 °C. After being stirred at 0 °C for 15 min,the reaction mixture was allowed to warm to r.t for 1.5 h. It was then cooled back to 0 °C and methyl iodide (11.0 µL, 1.00 mmol, 1.00 equiv.) was added. The mixture was warmed to r.t. and stirred overnight. After cooling again to 0 °C, the reaction was quenched with water (10 mL), extracted with Et_2O (3 x 10 mL), the combined organic layers were dried over $MgSO_4$, and the solvent removed under reduced pressure. The resulting crude product was purified via flash column chromatography (Pentane:EtOAc 4:1) to give methylated bi-indoles **35**-**36**.

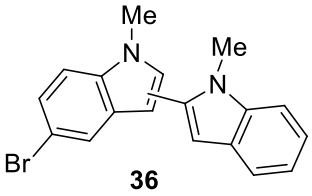
5'-Fluoro-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole (35).



35

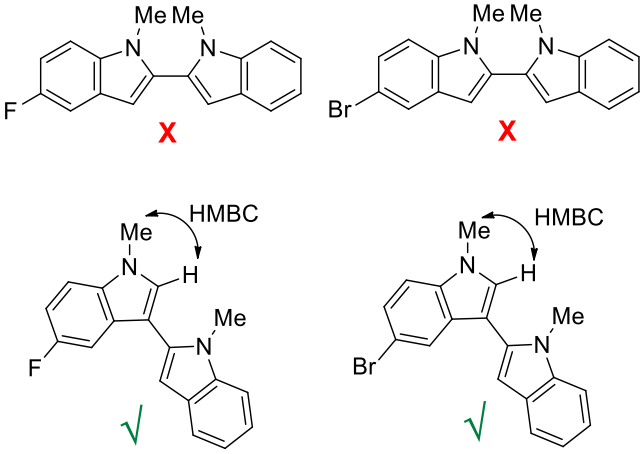
Following general procedure GP6 *on a 0.1 mmol scale and using 1.0 equiv. of NaH and MeI*: starting from 5'-fluoro-1-methyl-1*H*,1'*H*-2,3'-biindole **8i** (26.4 mg, 0.100 mmol, 1.00 equiv.), 5'-fluoro-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole **xx** (21.3 mg, 77.0 µmol, 77% yield) as a yellow oil. **Rf** 0.4 (Pentane:EtOAc 4:1) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.36 (ddd, *J* = 11.9, 8.9, 1.7 Hz, 2H, Ar*H*), 7.31 (dd, *J* = 8.9, 4.2 Hz, 1H, Ar*H*), 7.26 – 7.22 (m, 2H, Ar*H*), 7.15 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H, Ar*H*), 7.06 (td, *J* = 9.0, 2.5 Hz, 1H, Ar*H*), 6.60 (d, *J* = 0.9 Hz, 1H, Ar*H*), 3.89 (s, 3H, N*Me*), 3.75 (s, 3H, N*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.5 (d, *J* = 235.7 Hz), 137.9, 134.4, 133.6, 129.8, 128.3, 128.0 (d, *J* = 10.1 Hz), 121.1, 120.0, 119.6, 110.8 (d, *J* = 26.6 Hz), 110.2 (d, *J* = 9.8 Hz), 109.3, 107.3 (d, *J* = 4.6 Hz), 105.2 (d, *J* = 24.2 Hz), 101.4, 33.3, 30.9. **IR** ν 3054 (w), 2929 (w), 2854 (w), 1626 (w), 1592 (w), 1489 (m), 1467 (w), 1280 (m), 1241 (w), 1194 (w), 1119 (w), 1013 (w), 913 (m), 748 (s). **HR-ESI-MS** calcd for $C_{18}H_{16}FN_2^+$ $[M+H]^+$ 279.1292; found 279.1287.

5'-Bromo-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole (36).



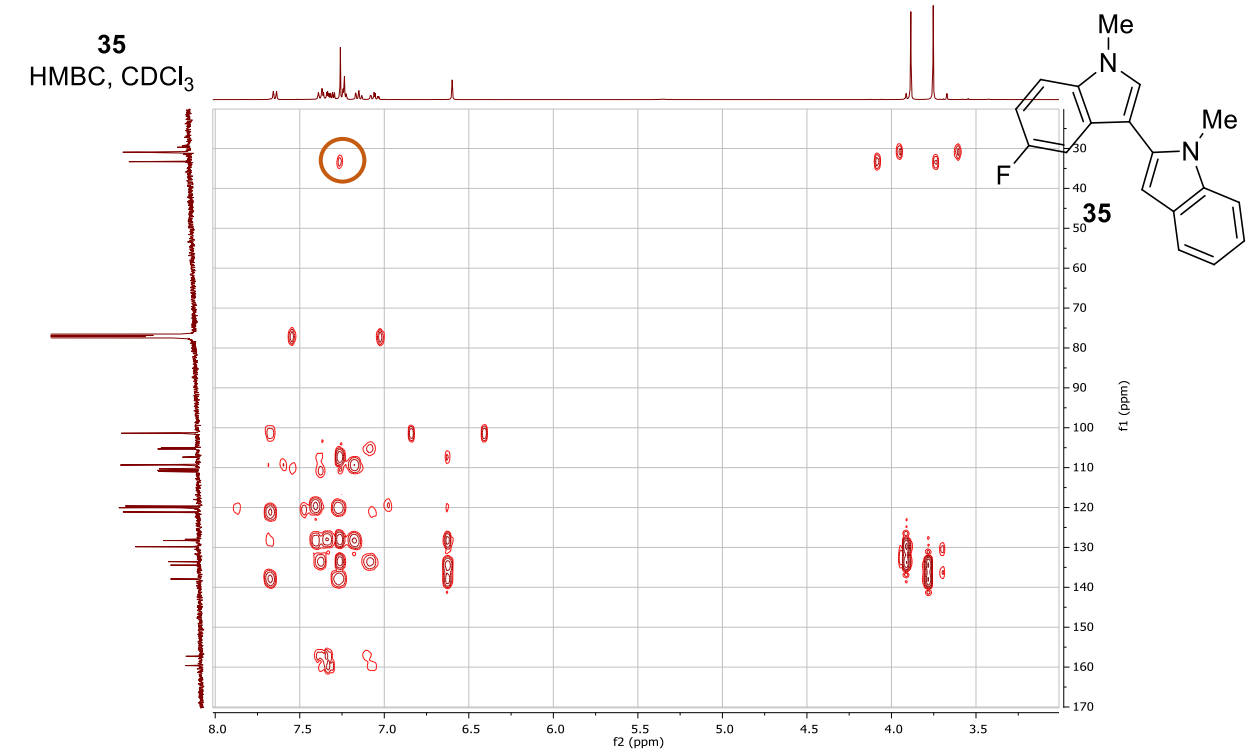
36

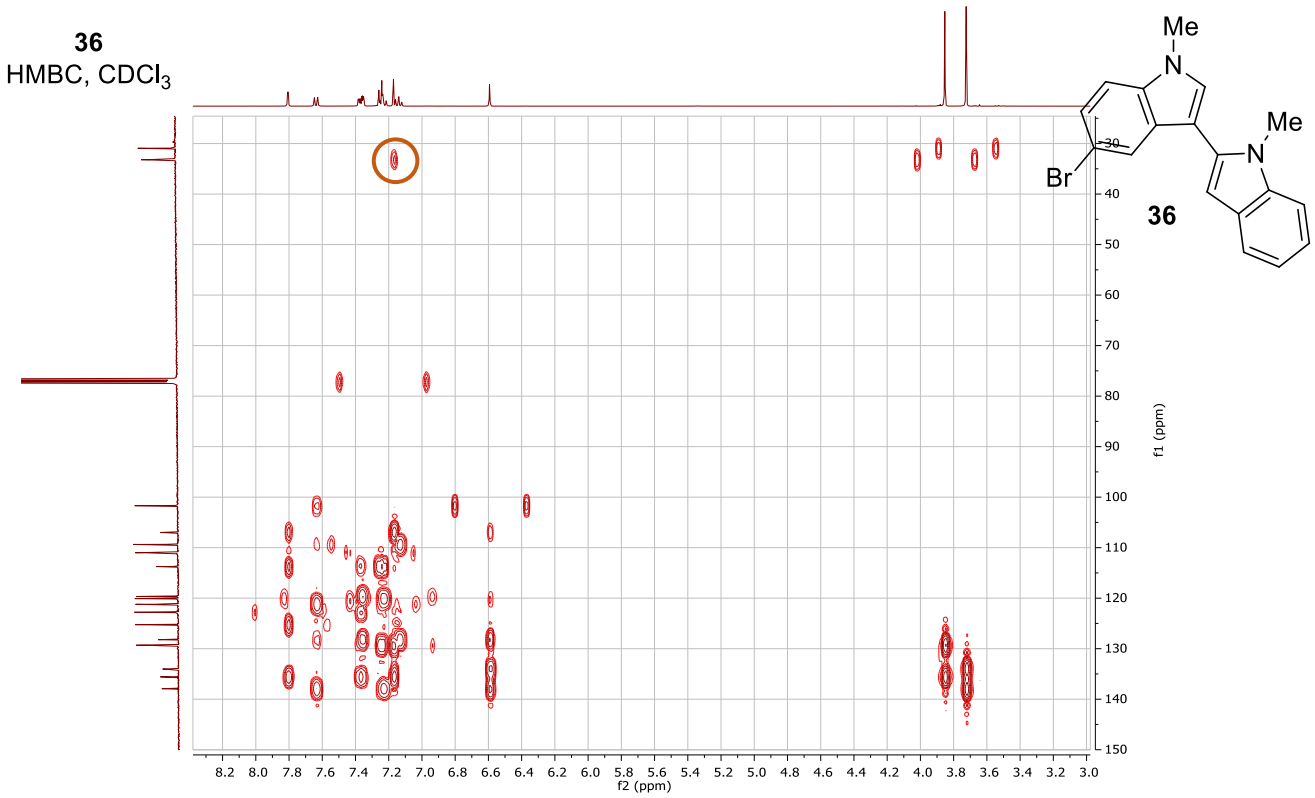
Following general procedure GP6 *on a 0.1 mmol scale and using 1.0 equiv. of NaH and MeI*: starting from 5'-bromo-1-methyl-1*H*,1'*H*-2,3'-biindole **8j** (32.5 mg, 0.100 mmol, 1.00 equiv.) 5'-bromo-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole **36** (27.9 mg, 82.0 µmol, 82% yield) was obtained as yellow oil. **Rf** 0.75 (Pentane:EtOAc 4:1) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 1.9, 0.5 Hz, 1H, Ar*H*), 7.64 (m, 1H, Ar*H*), 7.38 (dd, *J* = 4.1, 1.4 Hz, 1H, Ar*H*), 7.36 (dd, *J* = 3.6, 1.4 Hz, 1H, Ar*H*), 7.25 – 7.21 (m, 2H, Ar*H*), 7.17 (s, 1H, Ar*H*), 7.14 (ddd, *J* = 8.0, 7.1, 1.1 Hz, 1H, Ar*H*), 6.59 (s, 1H, Ar*H*), 3.85 (s, 3H, N*Me*), 3.72 (s, 3H, N*Me*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.9, 135.6, 134.0, 129.3, 129.3, 128.2, 125.2, 122.8, 121.2, 120.1, 119.7, 113.7, 111.0, 109.4, 107.0, 101.7, 33.2, 30.9. **IR** ν 2957 (w), 2932 (w), 2869 (w), 1718 (s), 1610 (w), 1537 (w), 1452 (w), 1436 (w), 1385 (m), 1255 (m), 1214 (m), 1162 (m), 1060 (w), 1035 (w), 880 (w), 803 (w), 721 (m). **HR-ESI-MS** calcd for $C_{18}H_{16}{}^{79}BrN_2^+$ $[M+H]^+$ 339.0491; found 339.0485.



The HMBC analysis showed interaction between the H-singlet at 7.25 (**35**) and 7.16 (**36**) and the newly installed NCH_3, thereby excluding the 2'-2 connection and allowing to assign the structure. As expected we obtained the 3'-2 connection. The structure of the other bi-indoles obtained in the scope was assigned by analogy, except for compounds **8l-8m**. The latter compounds were obtained with a C3-alkylated indole as nucleophile and the steric

hindrance played an important role in reversing the regio-distribution. An insight on the mechanism is given in SI-Par.4.



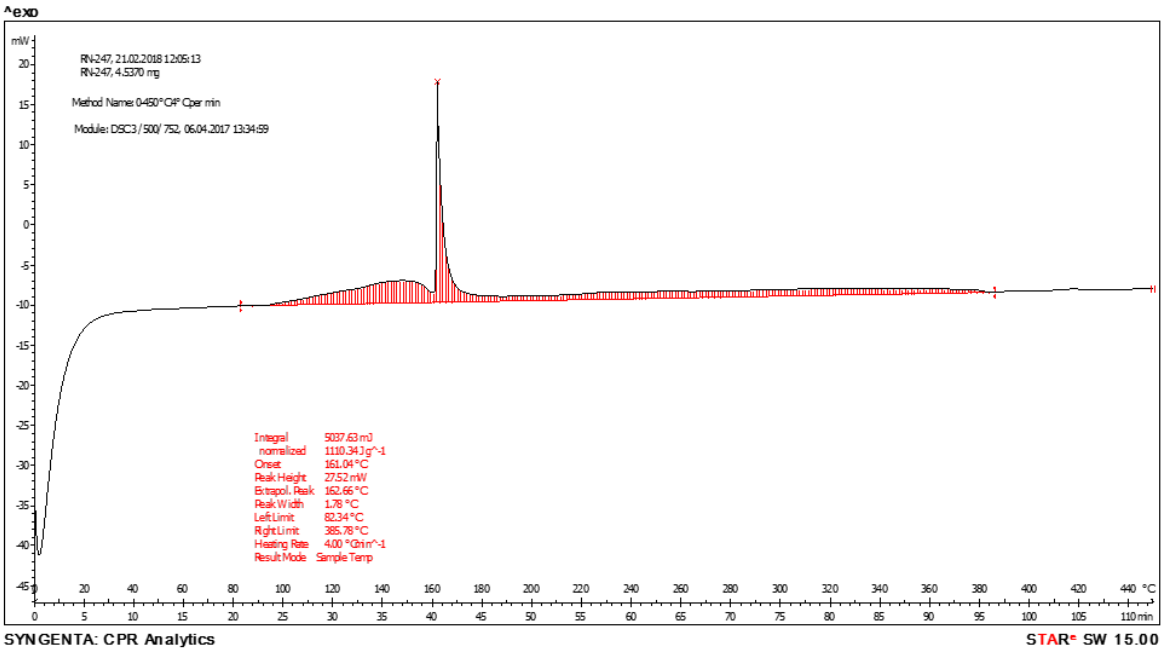


6. DSC studies.

DSC analysis of C2-NBoc-IndoleDBX (13a)

Measured by: Marylène Stempien

Weight after analysis: 4.205mg



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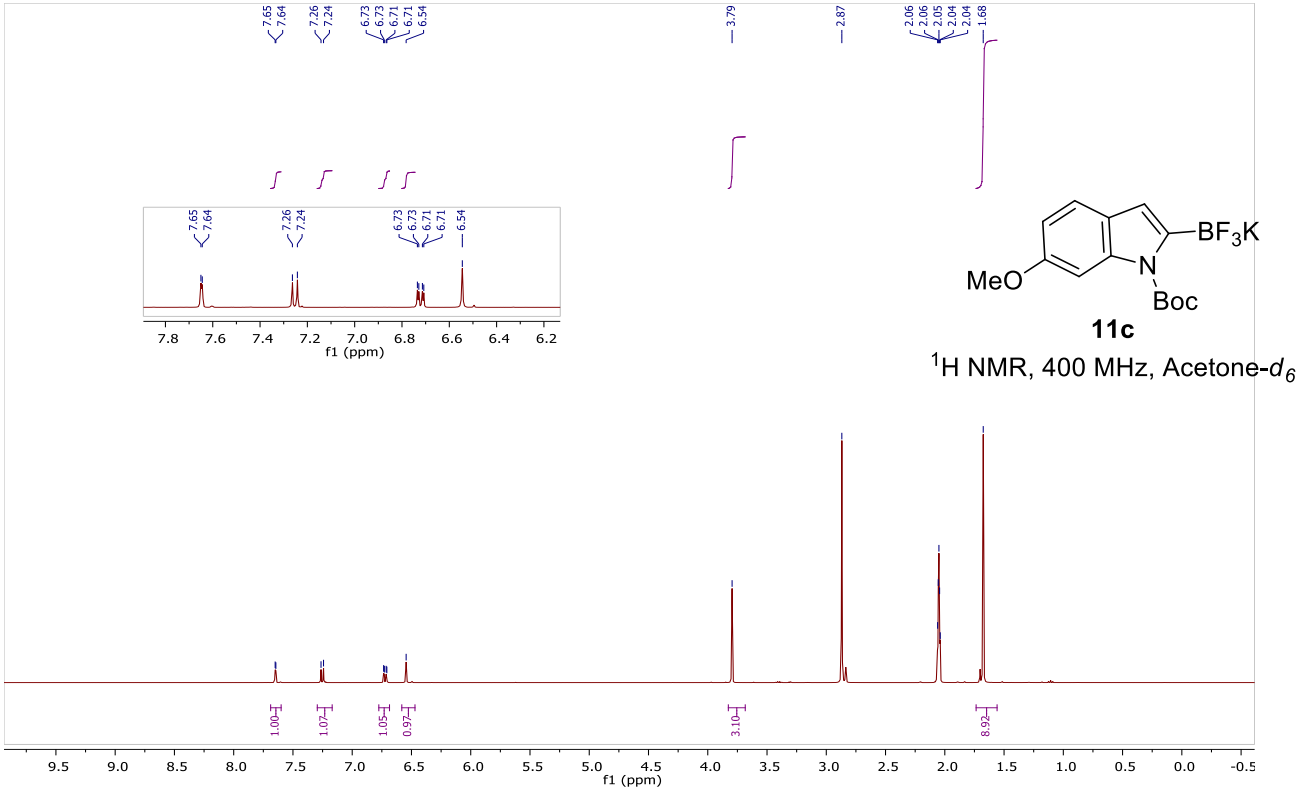
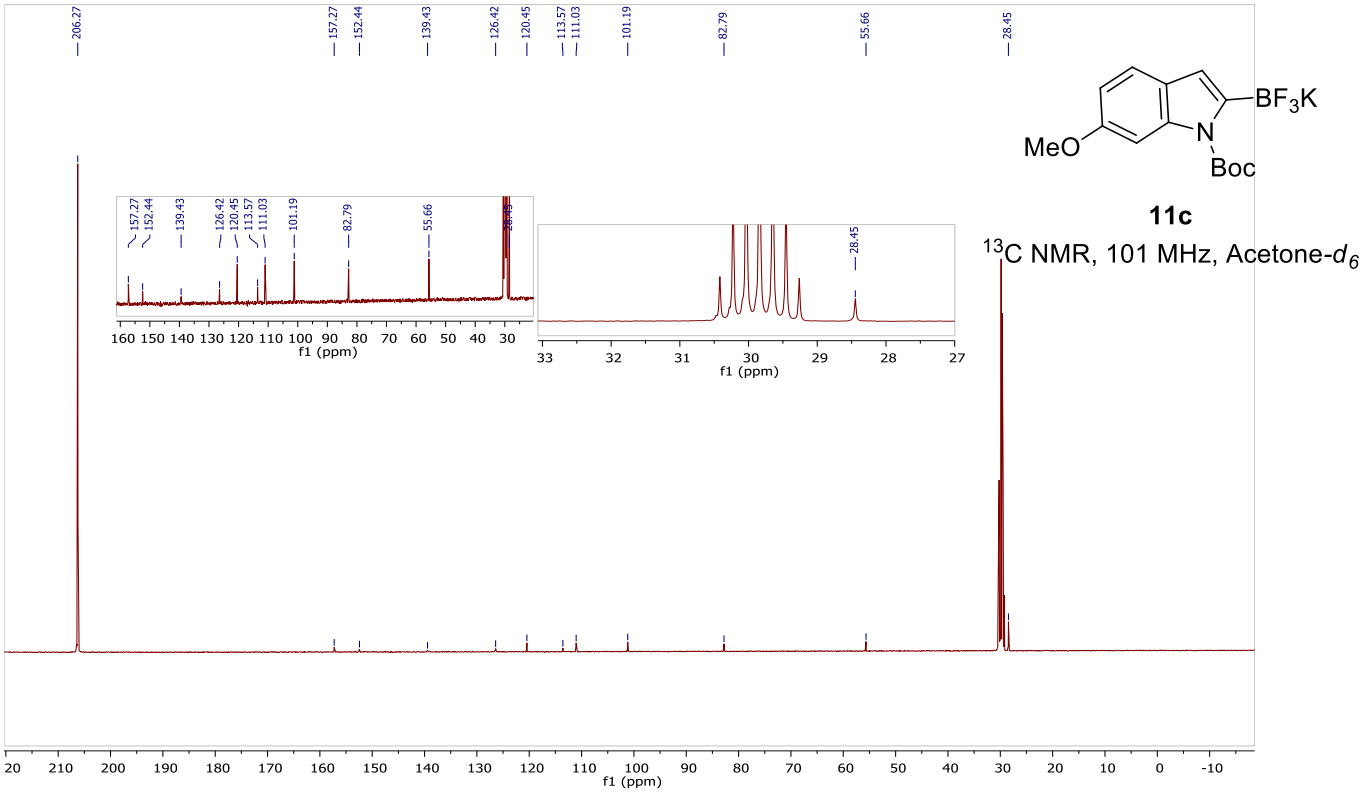
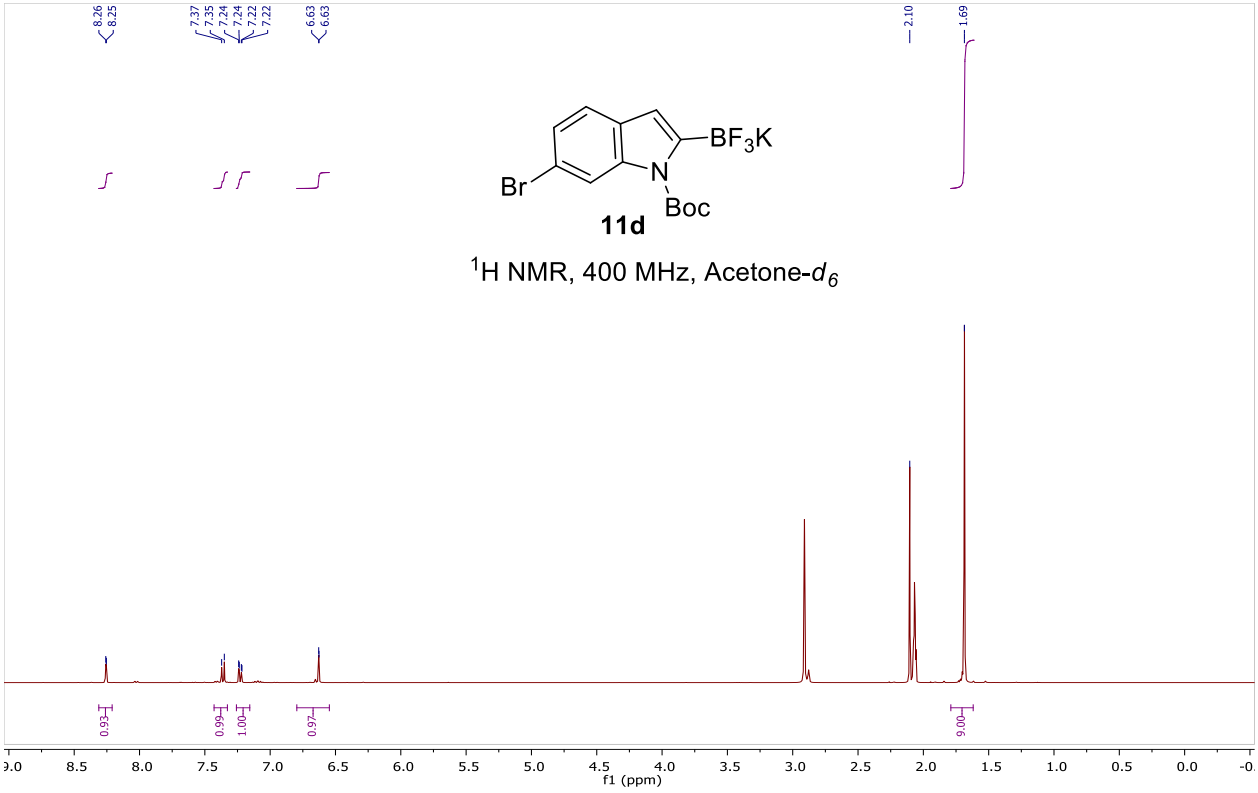
8. Spectra of new compounds

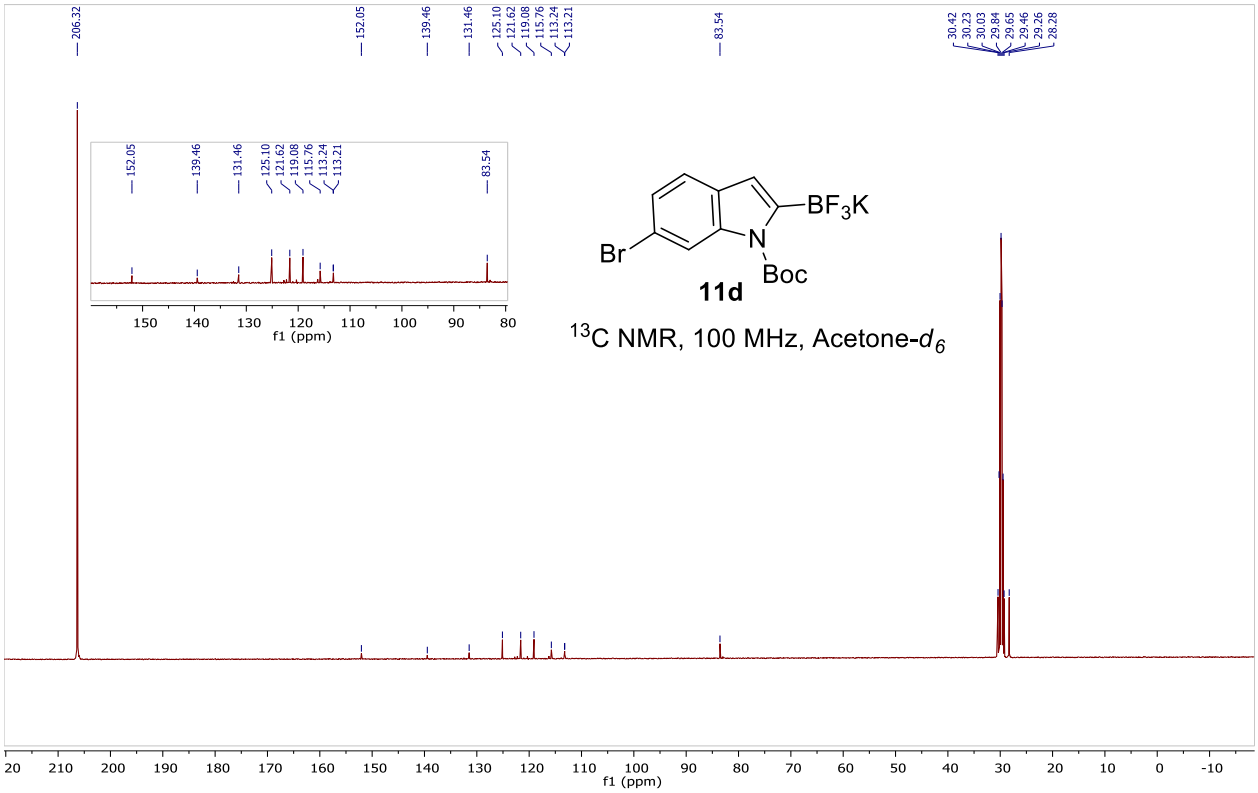
Potassium trifluoro(1-(*tert*-butoxycarbonyl)-6-methoxy-*1H*-indol-2-yl)borate (11c)



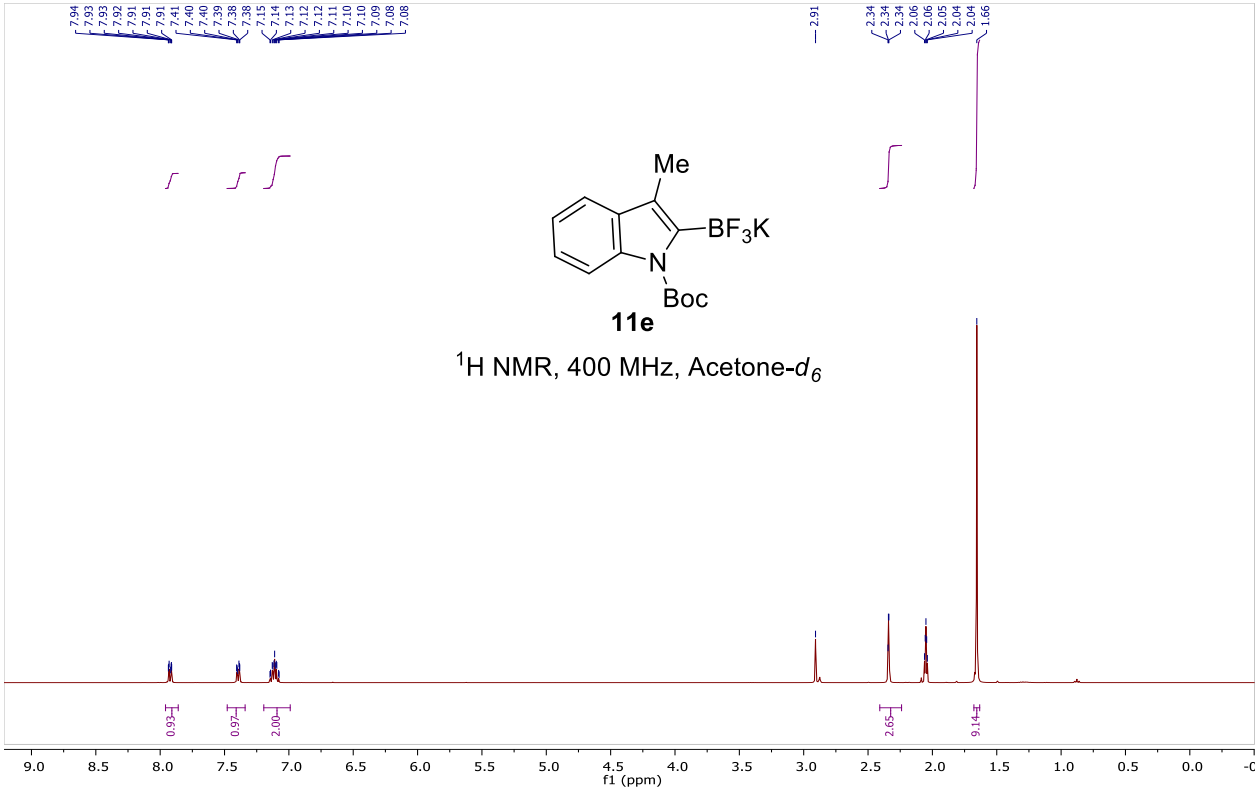


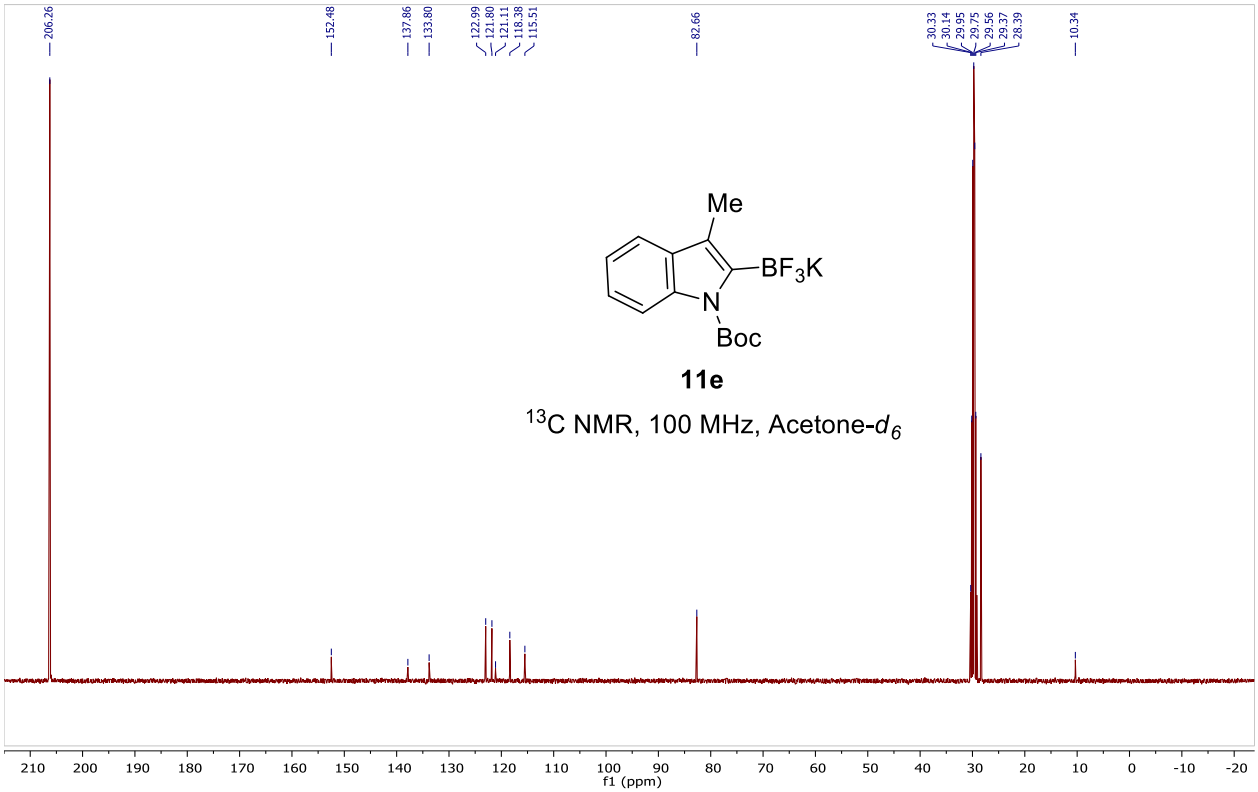
Potassium trifluoro(1-(*tert*-butoxycarbonyl)-6-bromo-*1H*-indol-2-yl)borate (11d):



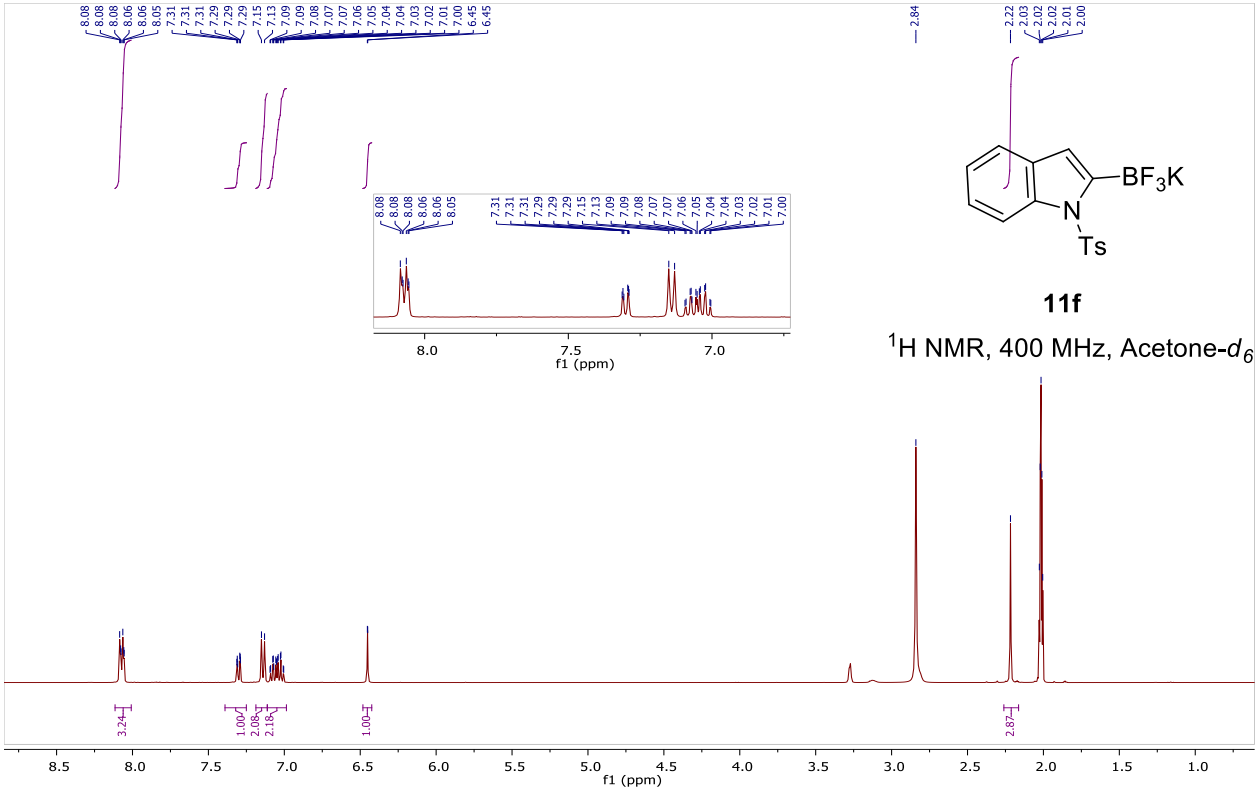


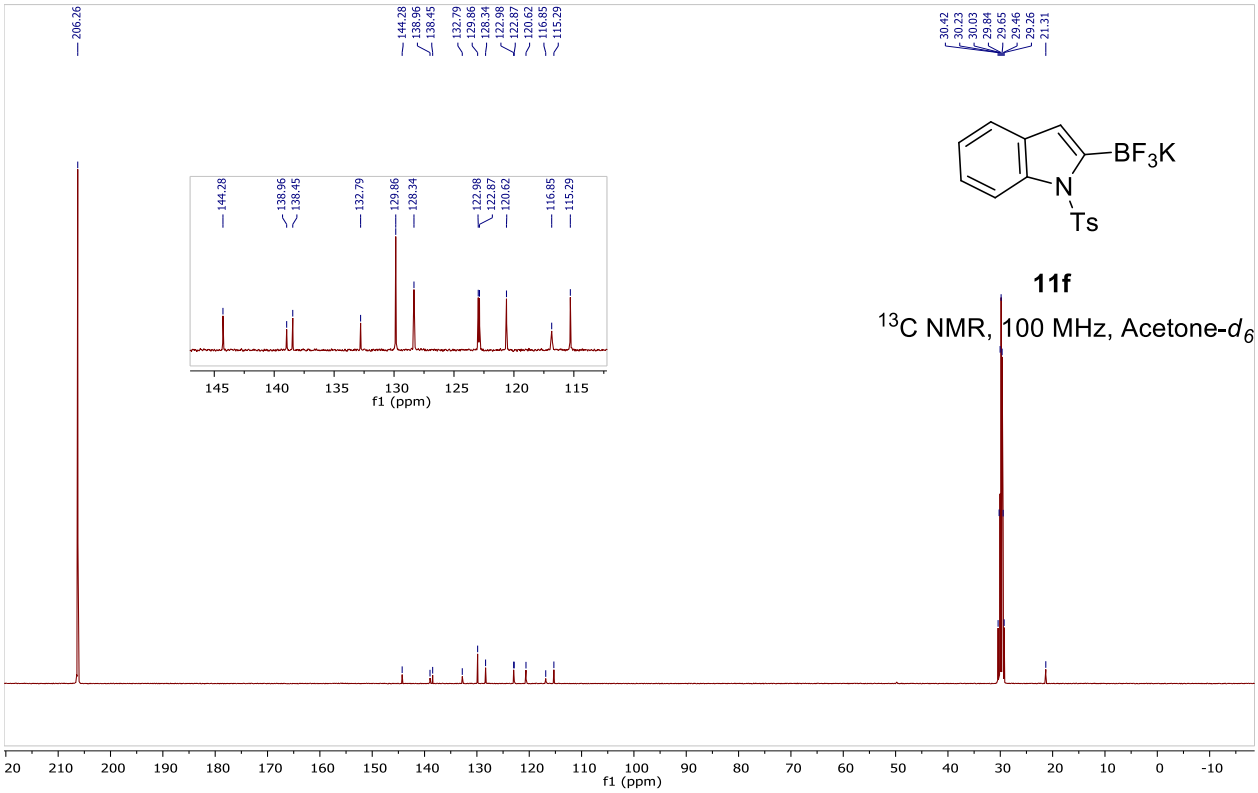
Potassium trifluoro(1-(*tert*-butoxycarbonyl)-3-methyl-*1H*-indol-2-yl)borate (11e):



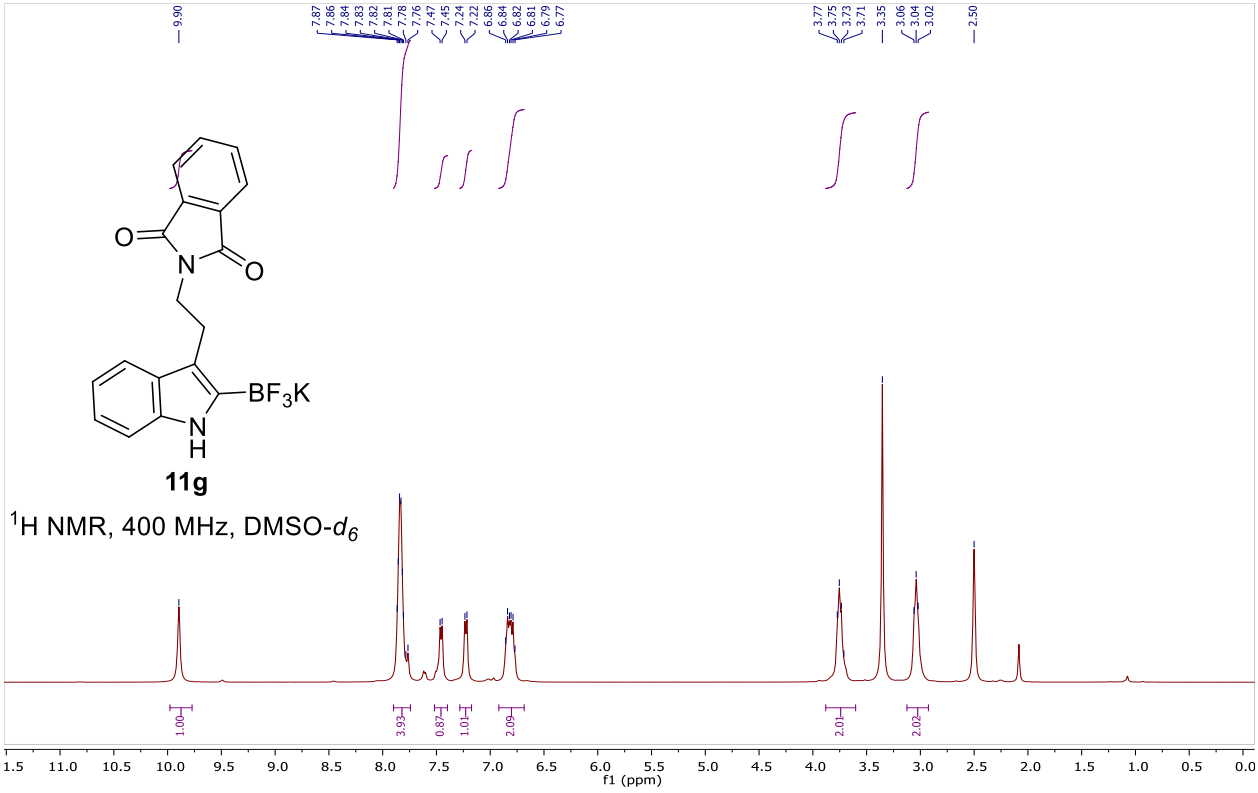


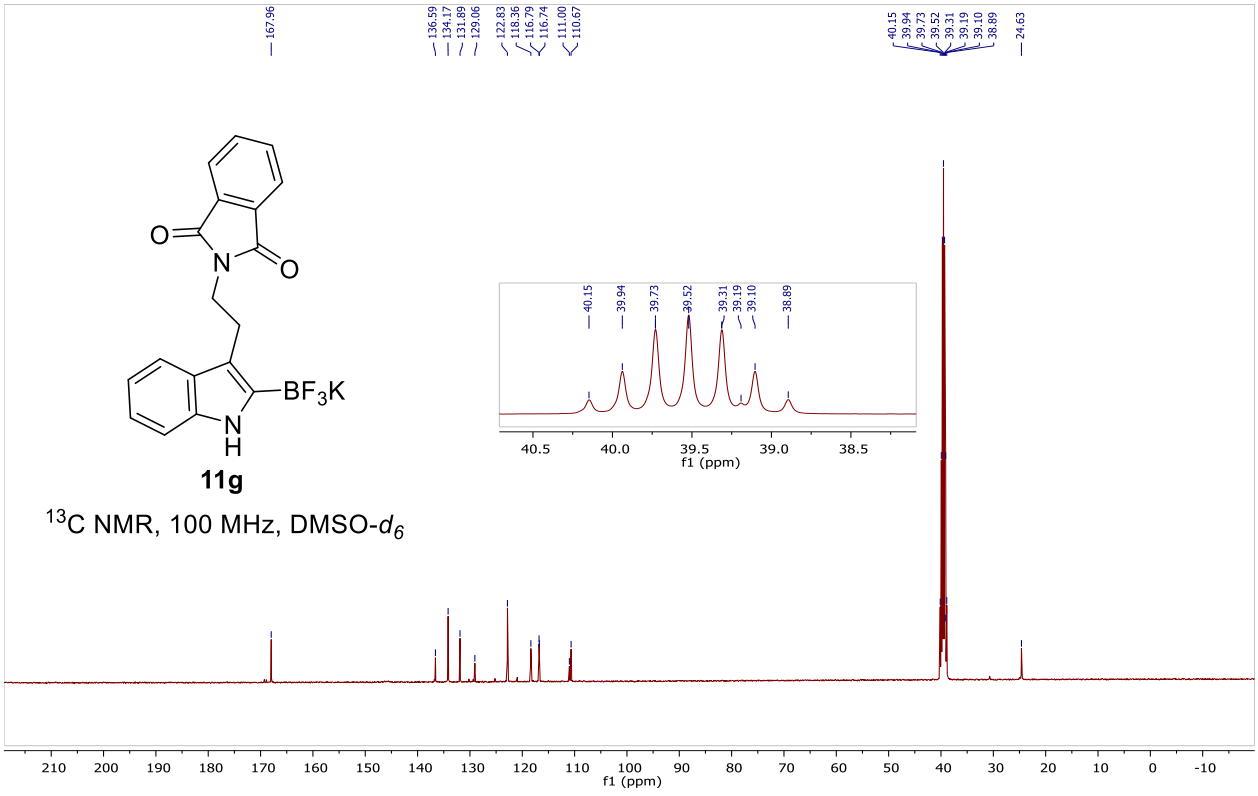
Potassium trifluoro(1-(tosyl)-*1H*-indol-2-yl)borate (11f):



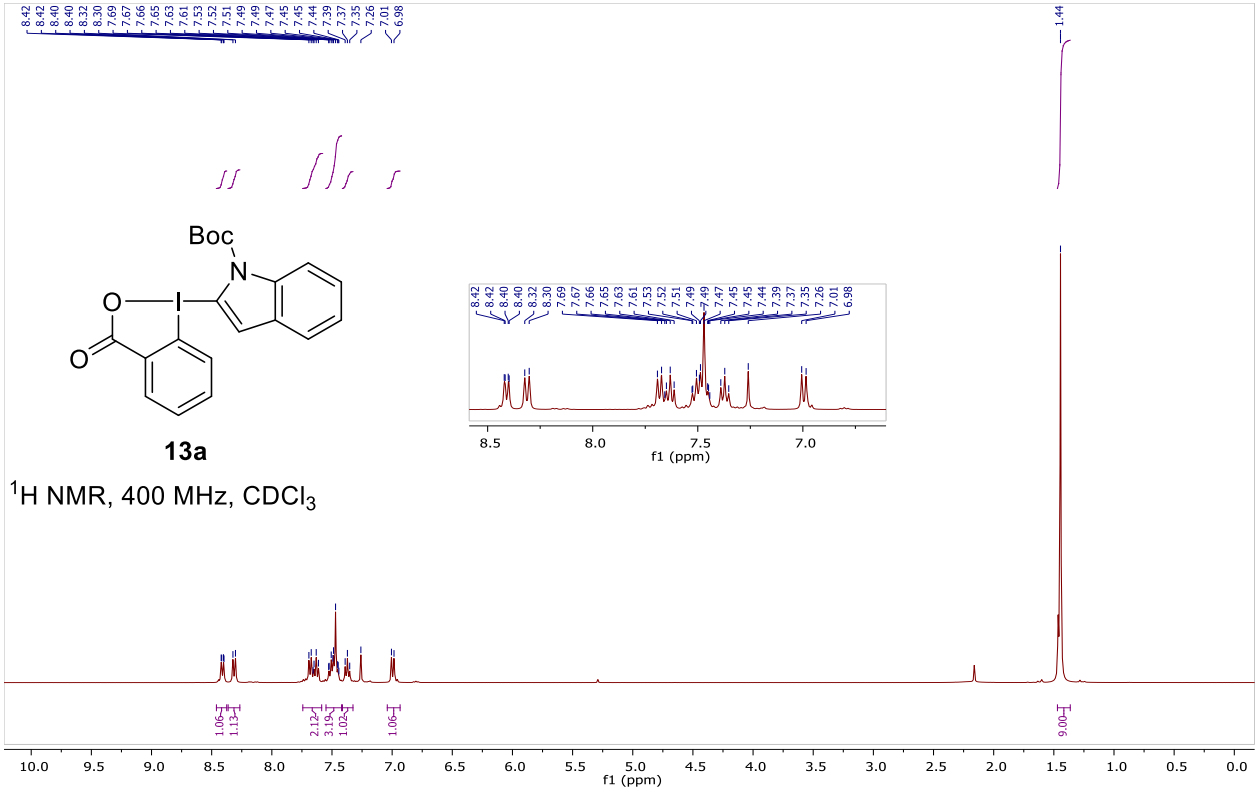


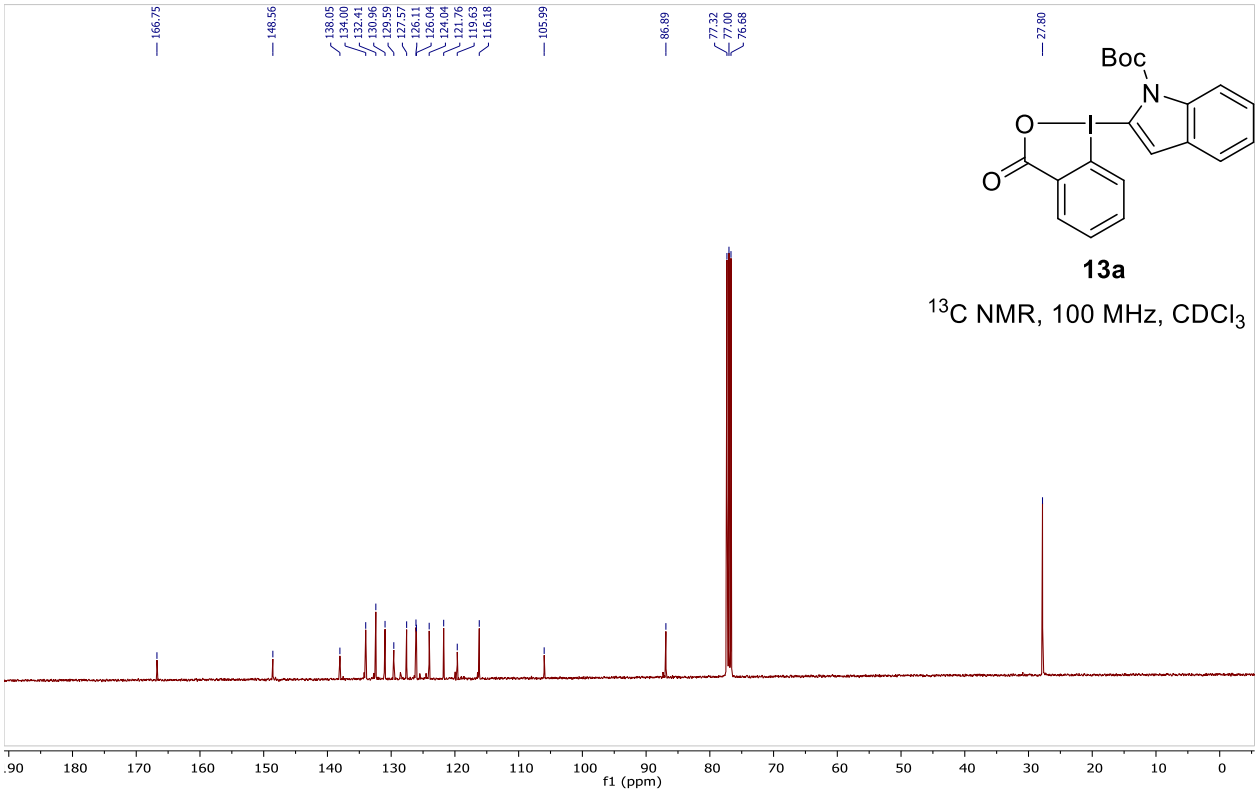
Potassium trifluoro(2-(2-(1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione)borate (11g):



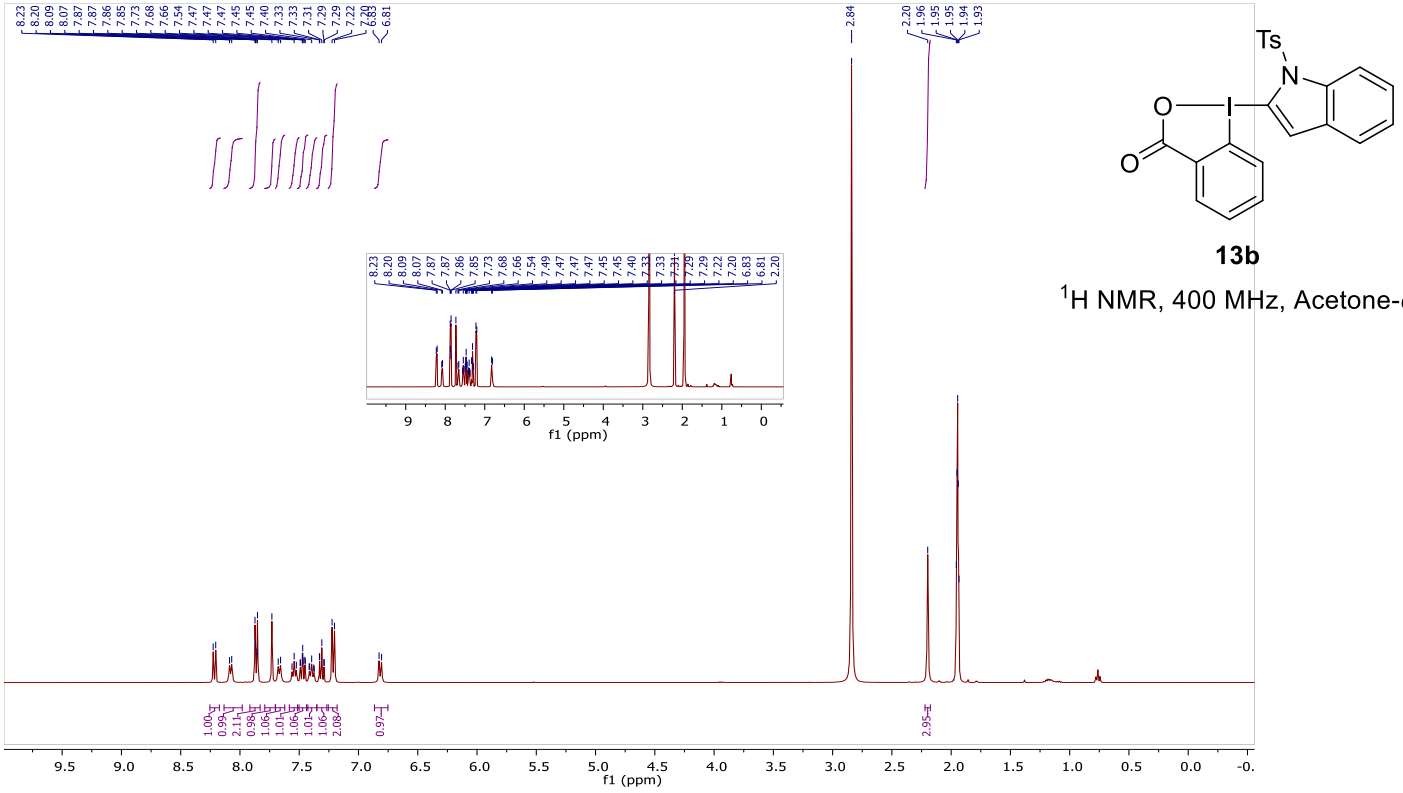


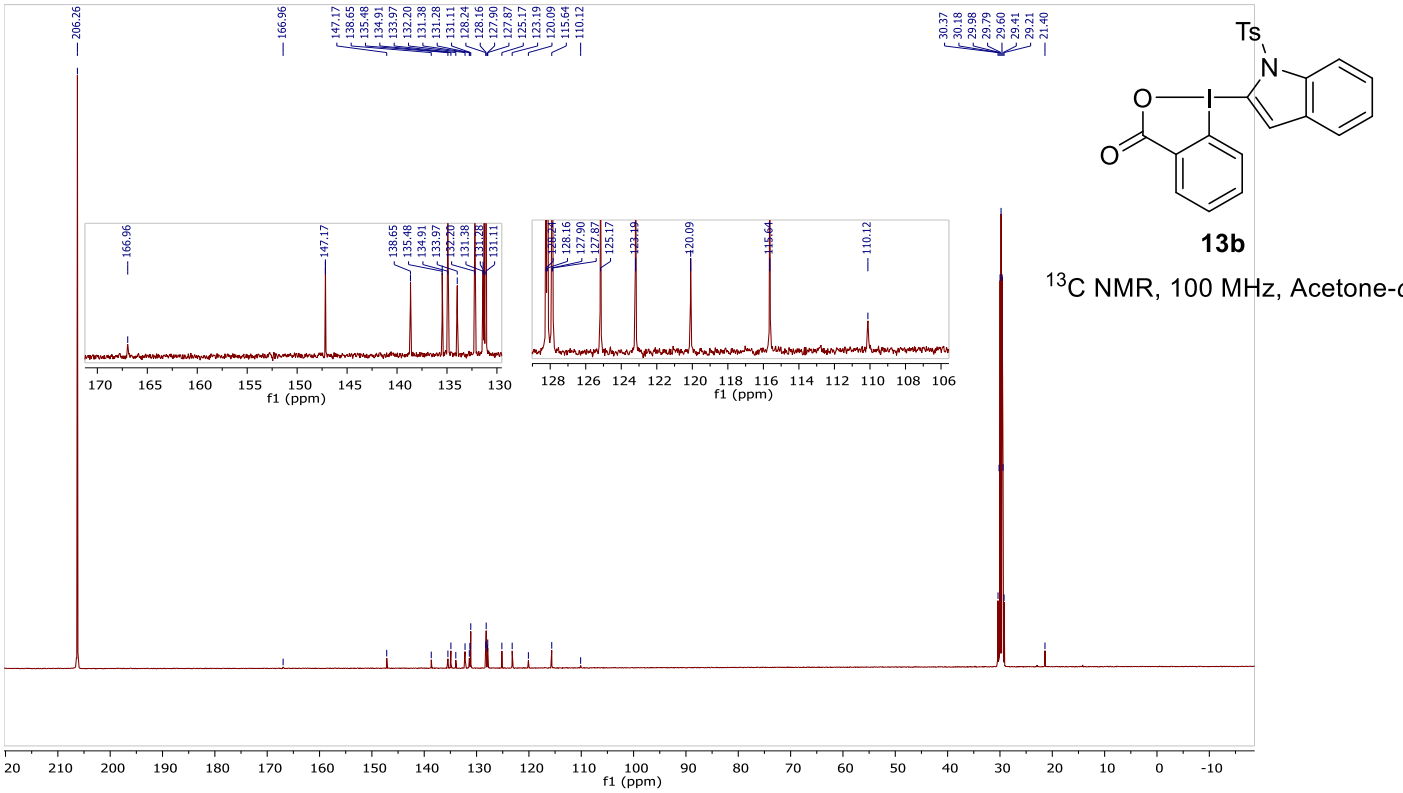
1-(*Tert*-butyl 1*H*-indole-1-carboxylate)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one (13a):



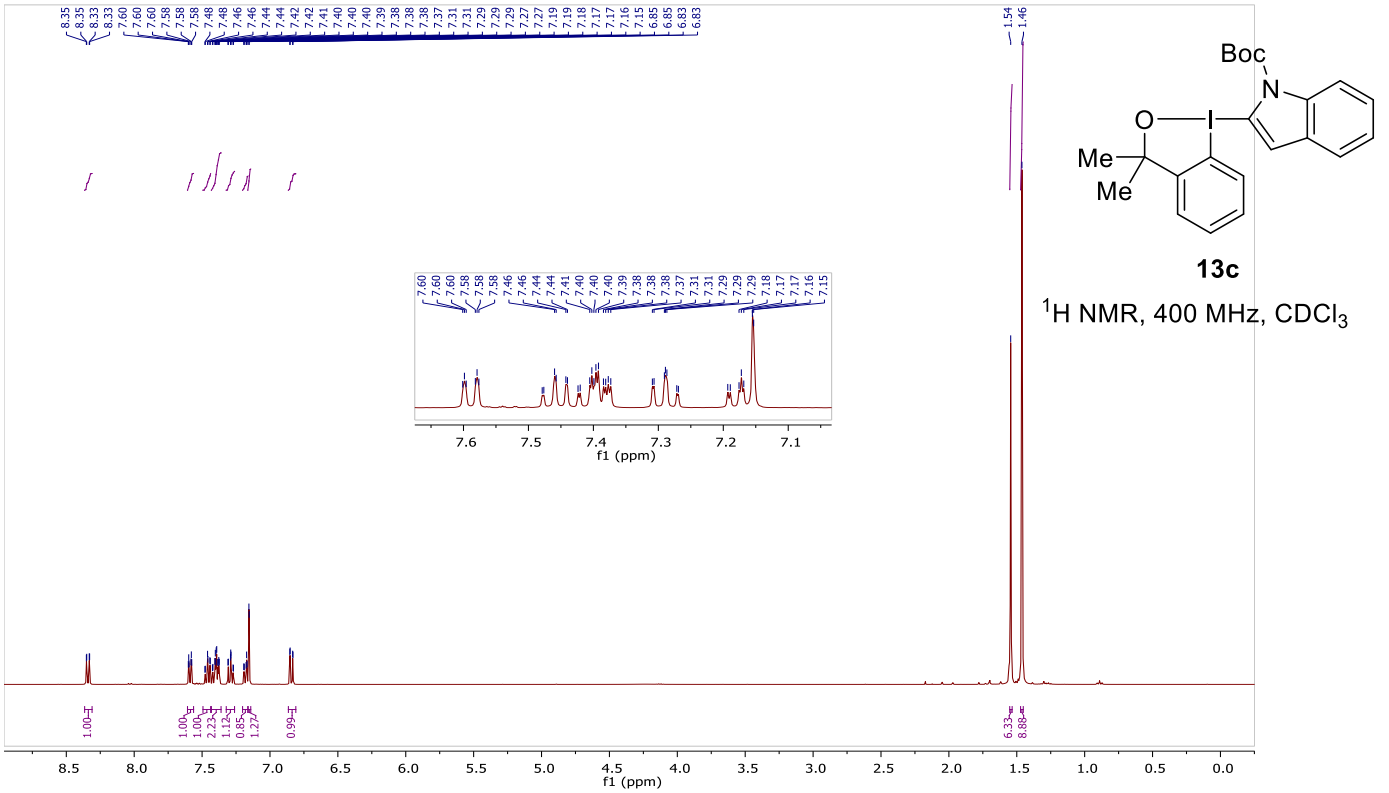


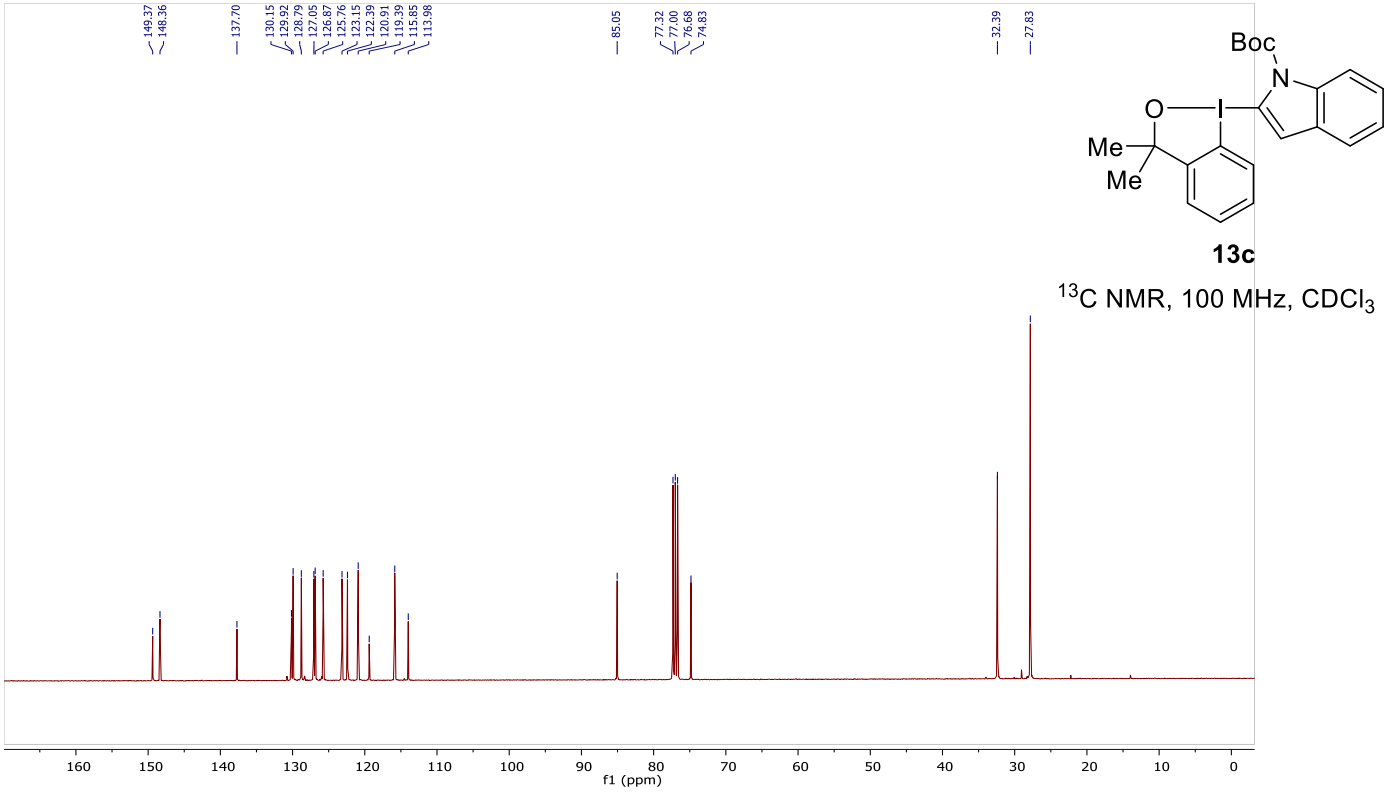
1-(2-1-(Tosyl)-*1H*-indol-2-yl)-1*H*-1λ_3 -benzo[*b*]iodo-3(2*H*)-one (13b):



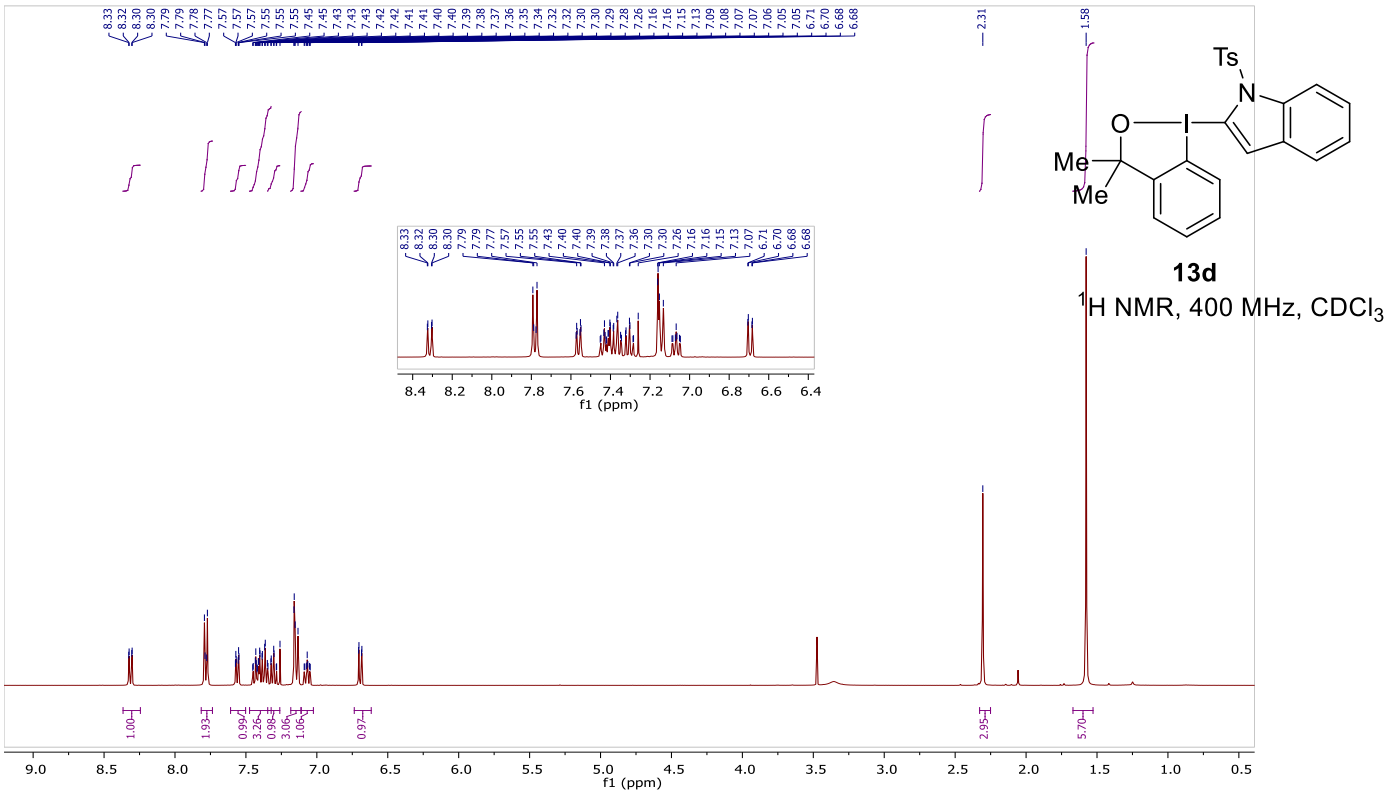


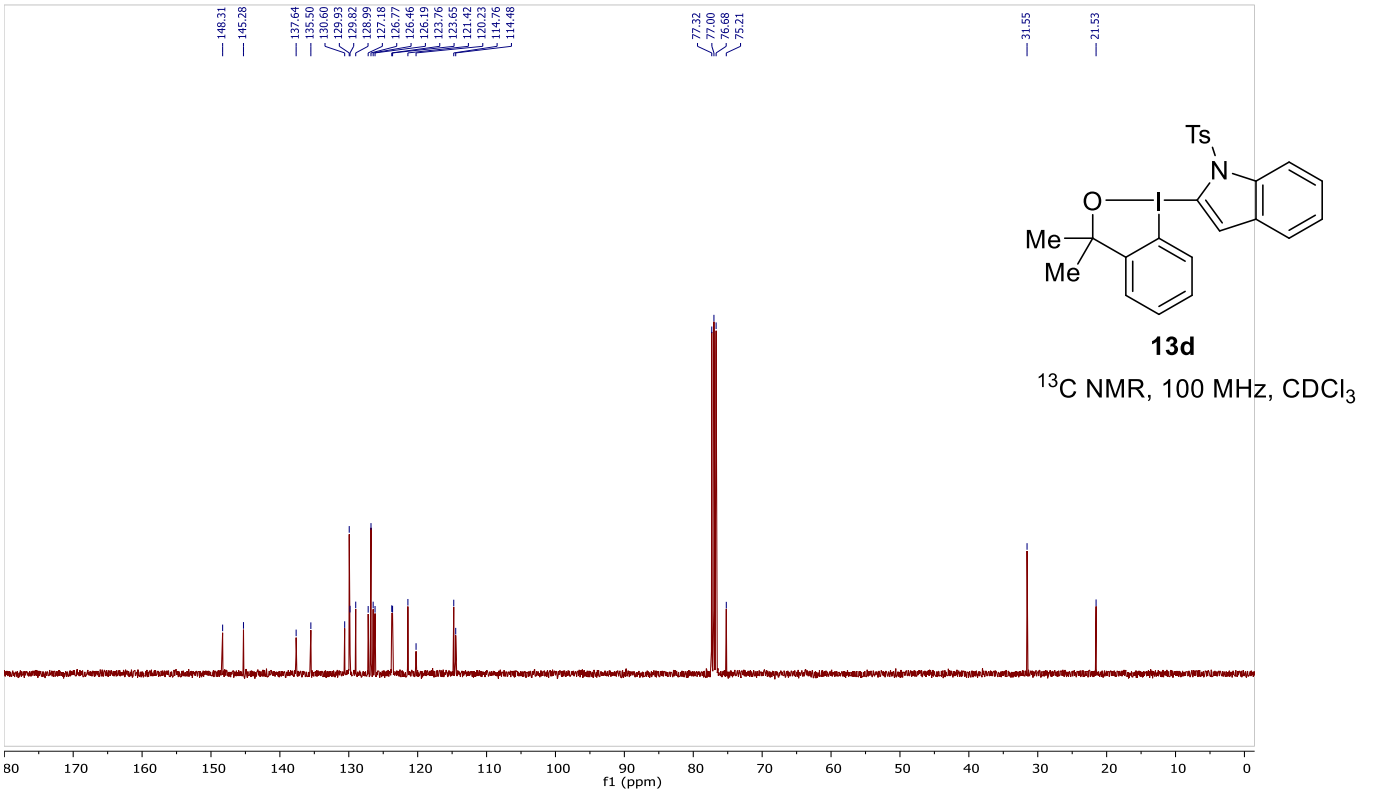
1-(2-*Tert*-butyl 1*H*-indole-1-carboxylate)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodoxol (13c):



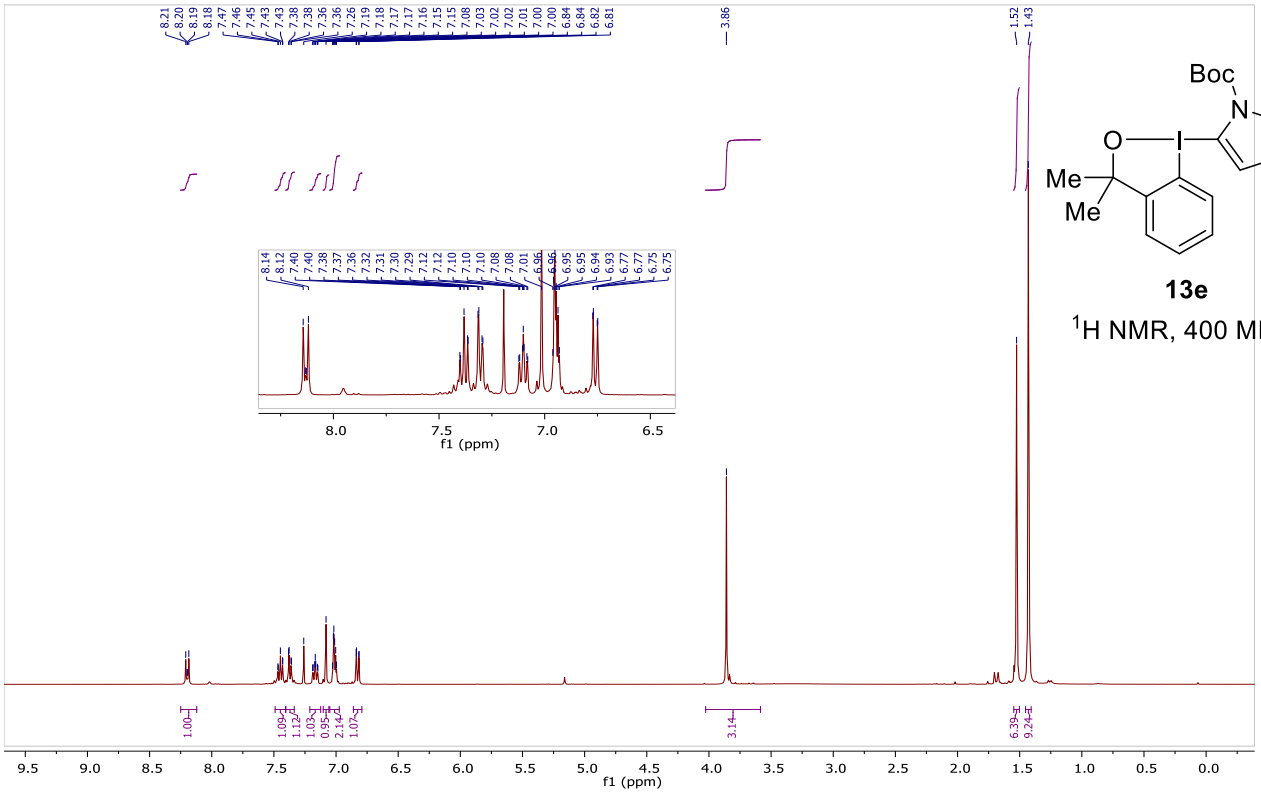


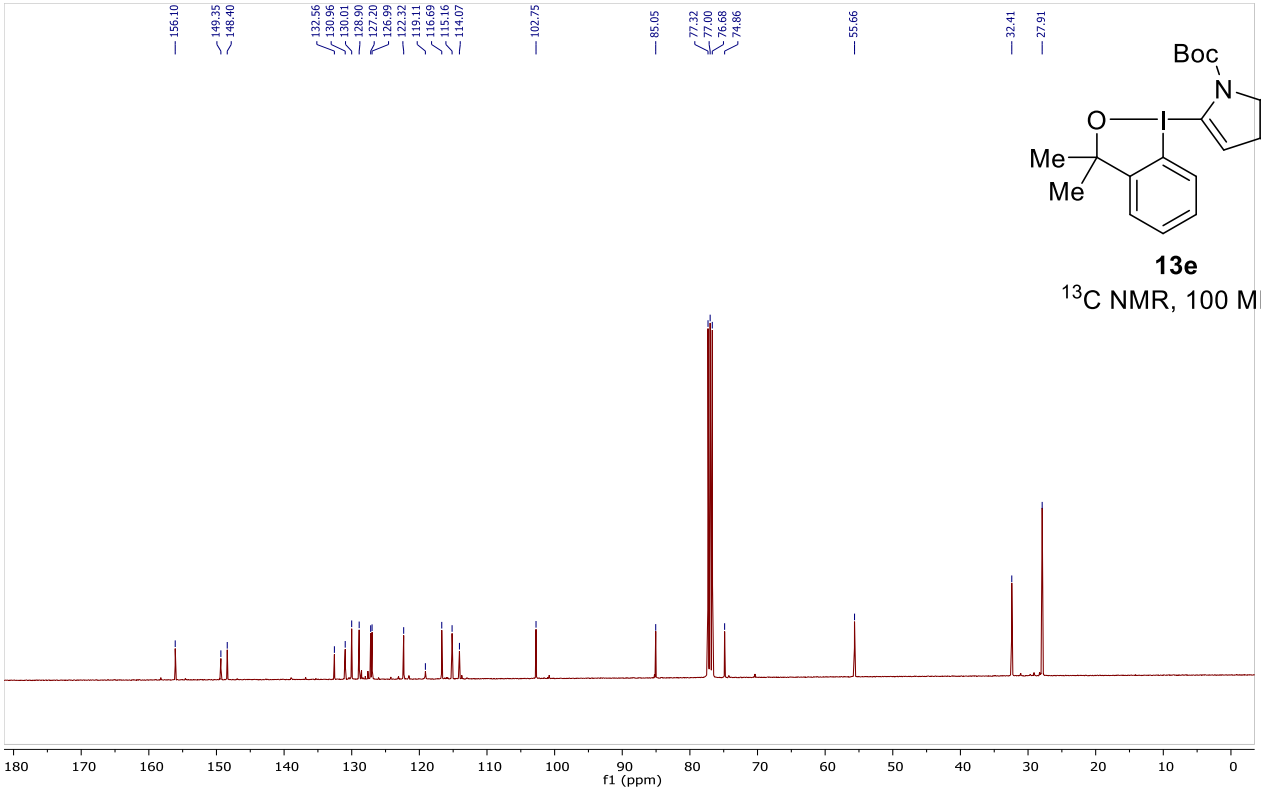
1-(2-1-Tosyl-1*H*-indole)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo[*d*][1,2] iodoxole (13d):



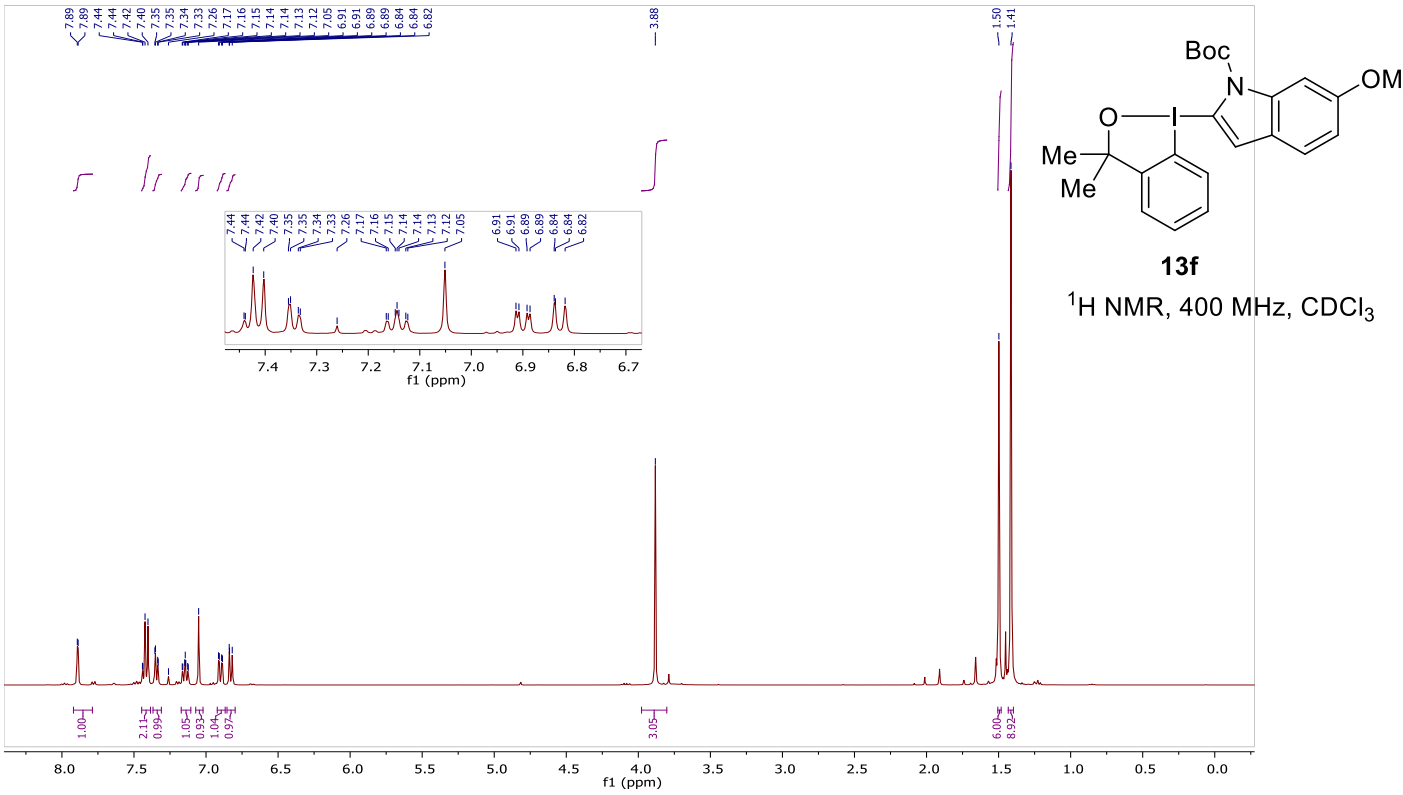


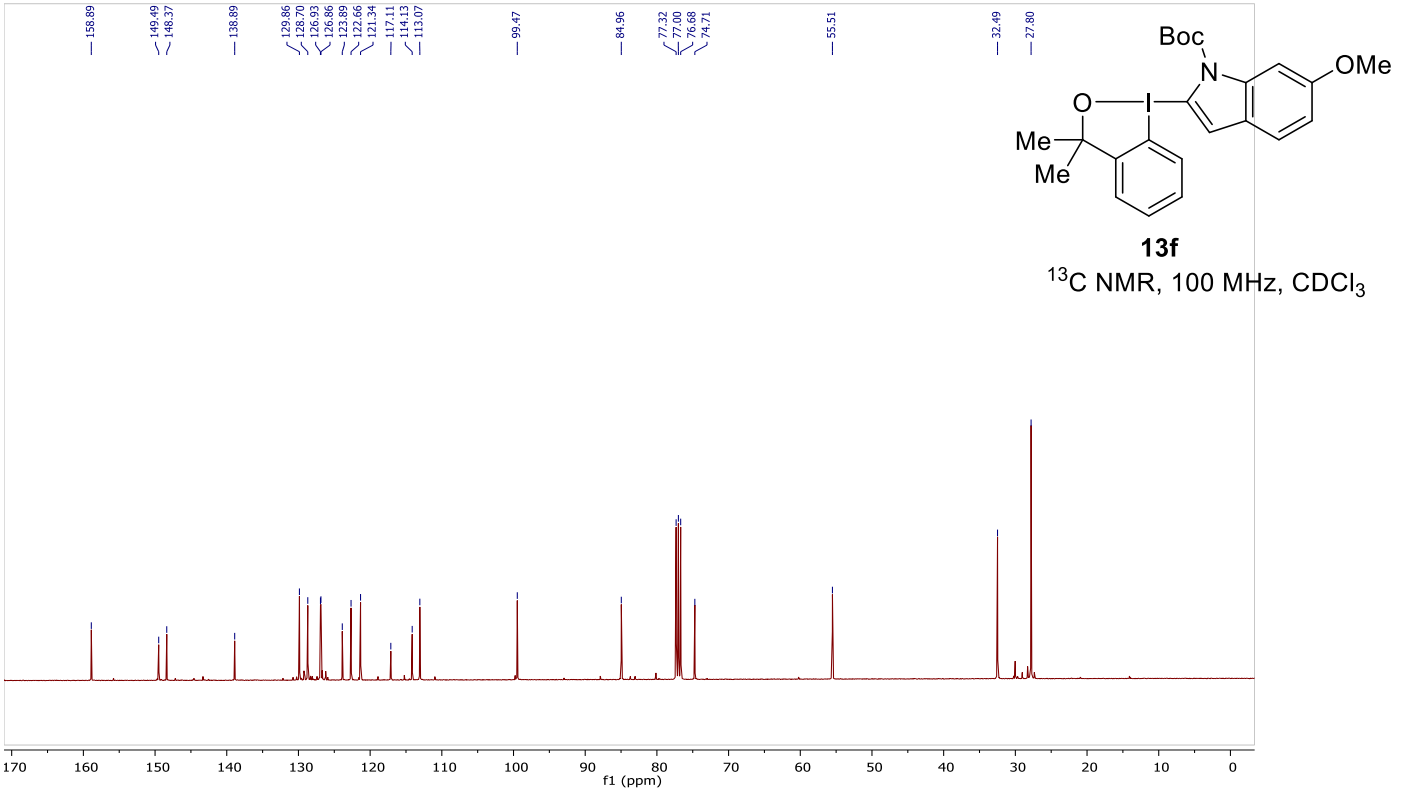
1-(2-5-Methoxy-1-*tert*-butyl-1*H*-indole-1-carboxylate)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo [*d*][1,2]iodoxole (13e):



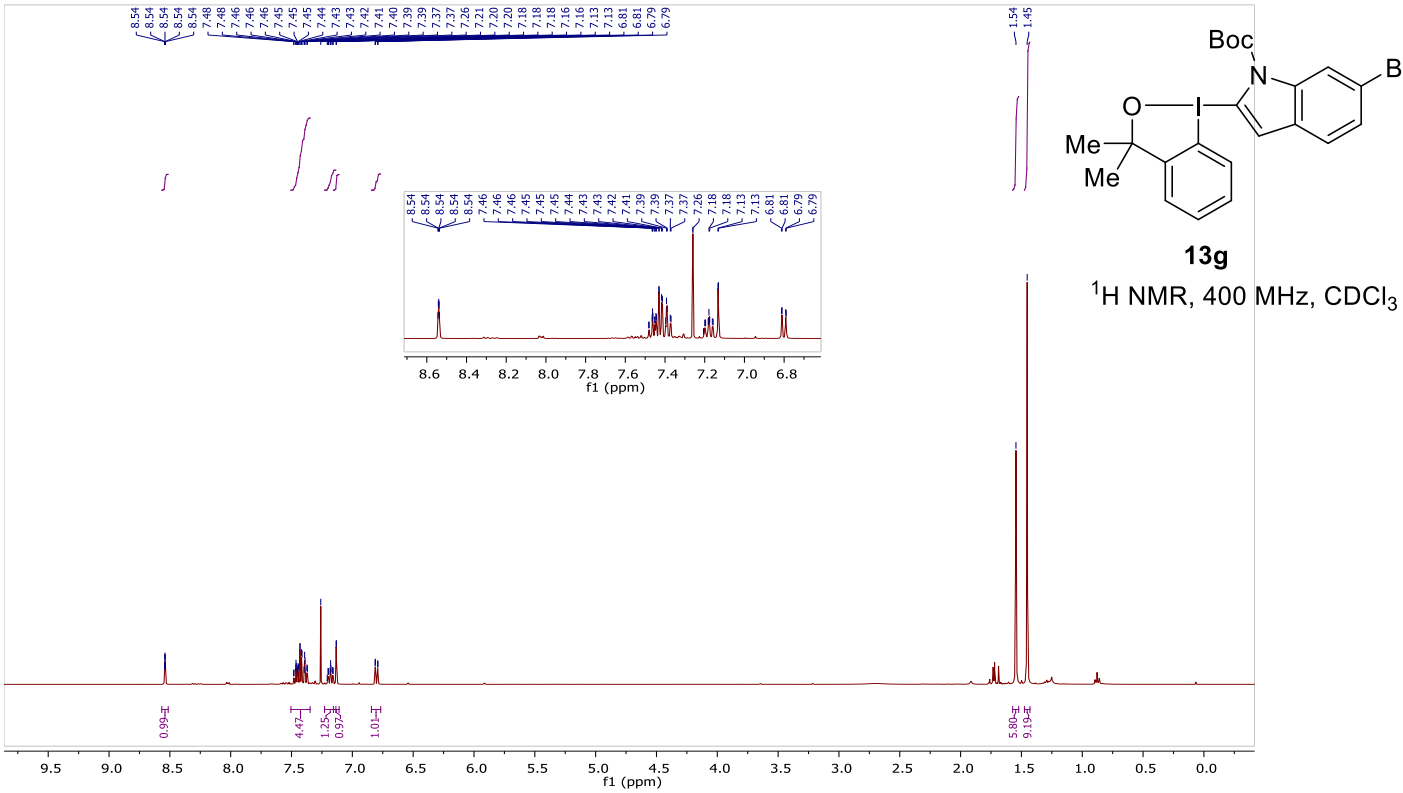


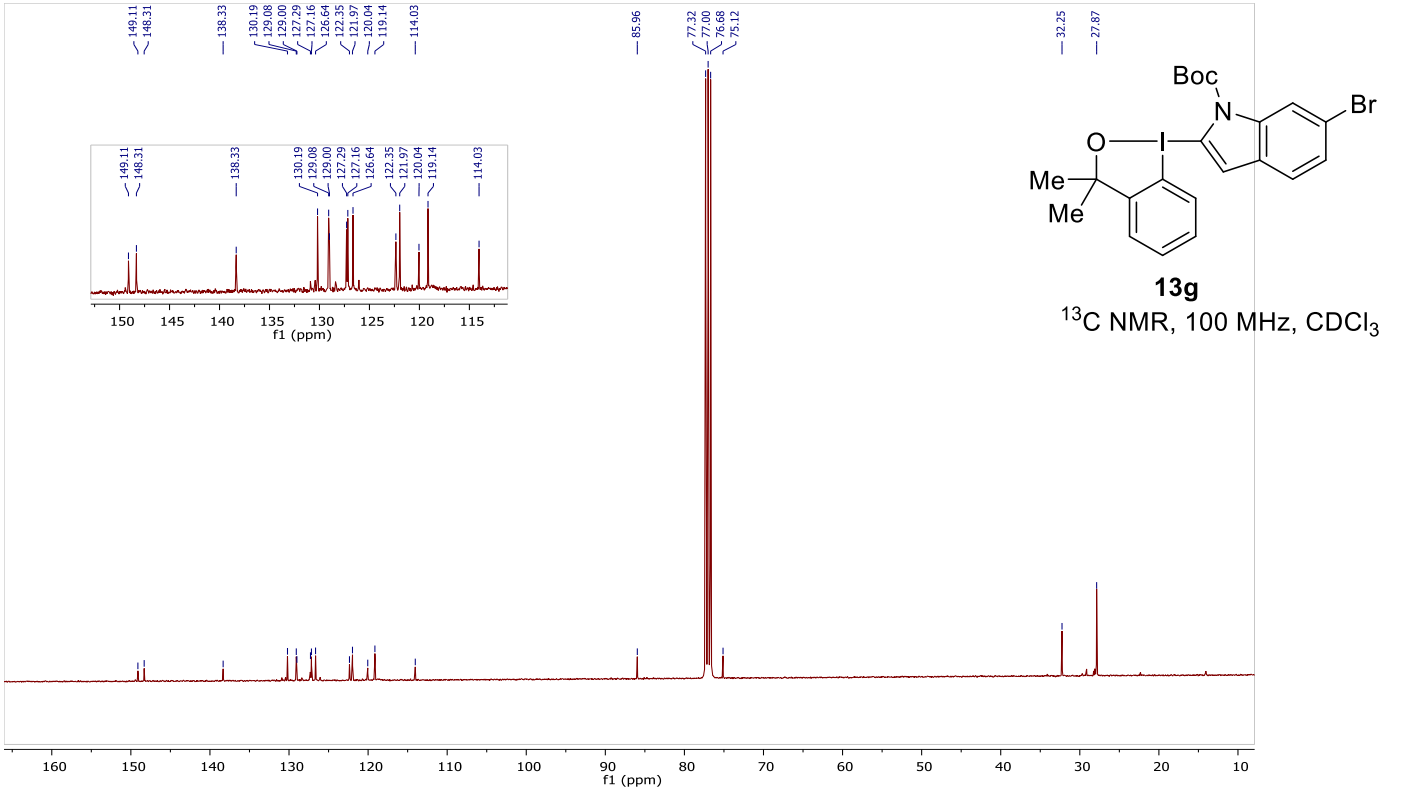
1-(2-6-Methoxy-1-*tert*-butyl-1*H*-indole-1-carboxylate)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo [*d*][1,2]iodoxole (13f):



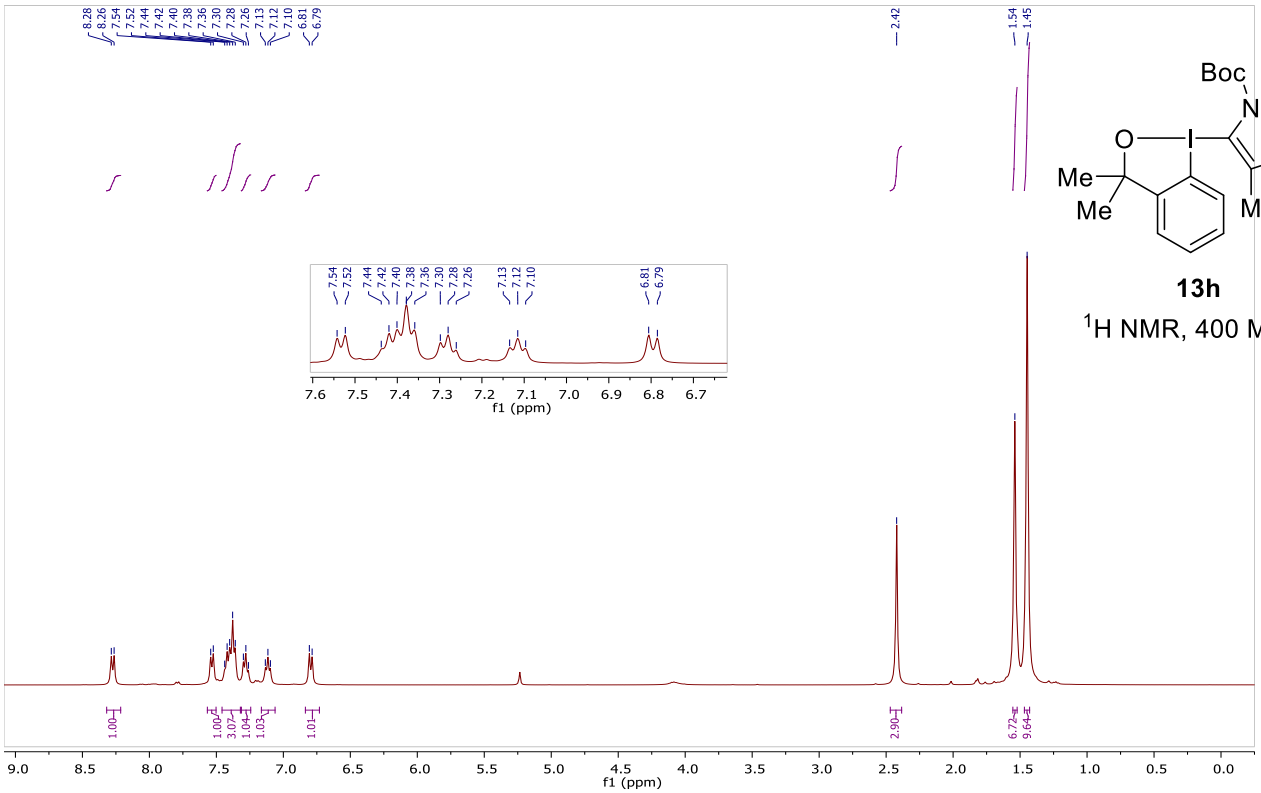


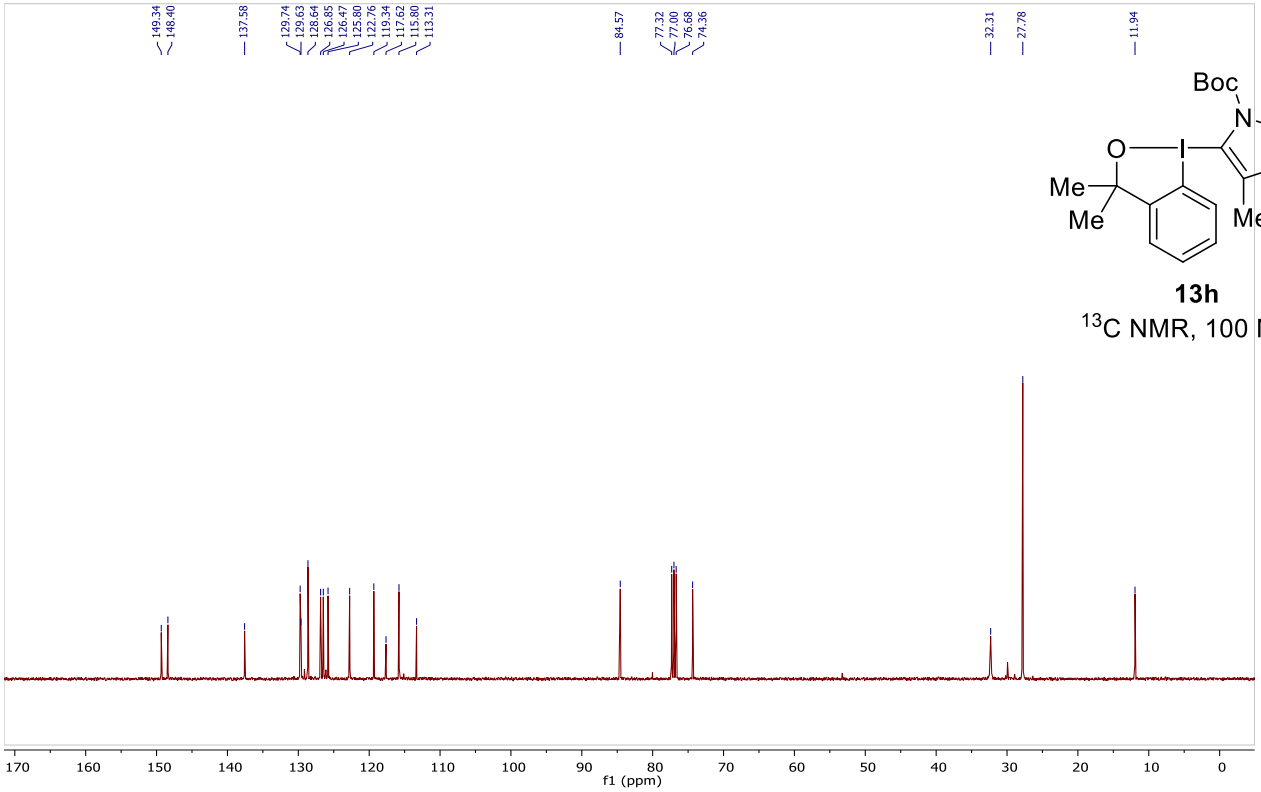
1-(2-5-Bromo-1-*tert*-butyl-1*H*-indole-1-carboxylate)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo [*d*][1,2]iodoxole (13g):



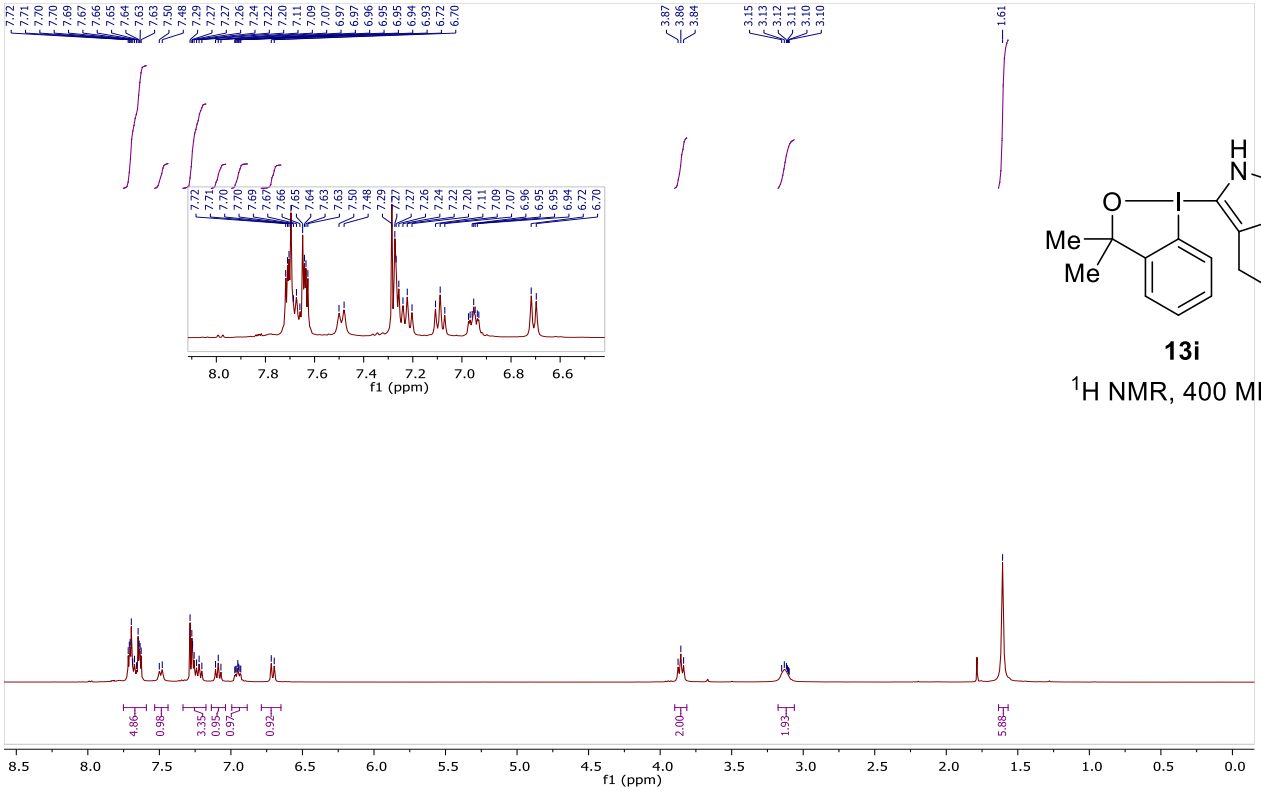


1-(2-3-Methyl-1-*tert*-butyl-1*H*-indole-1-carboxylate)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo [*d*][1,2]iodoxole (13h):



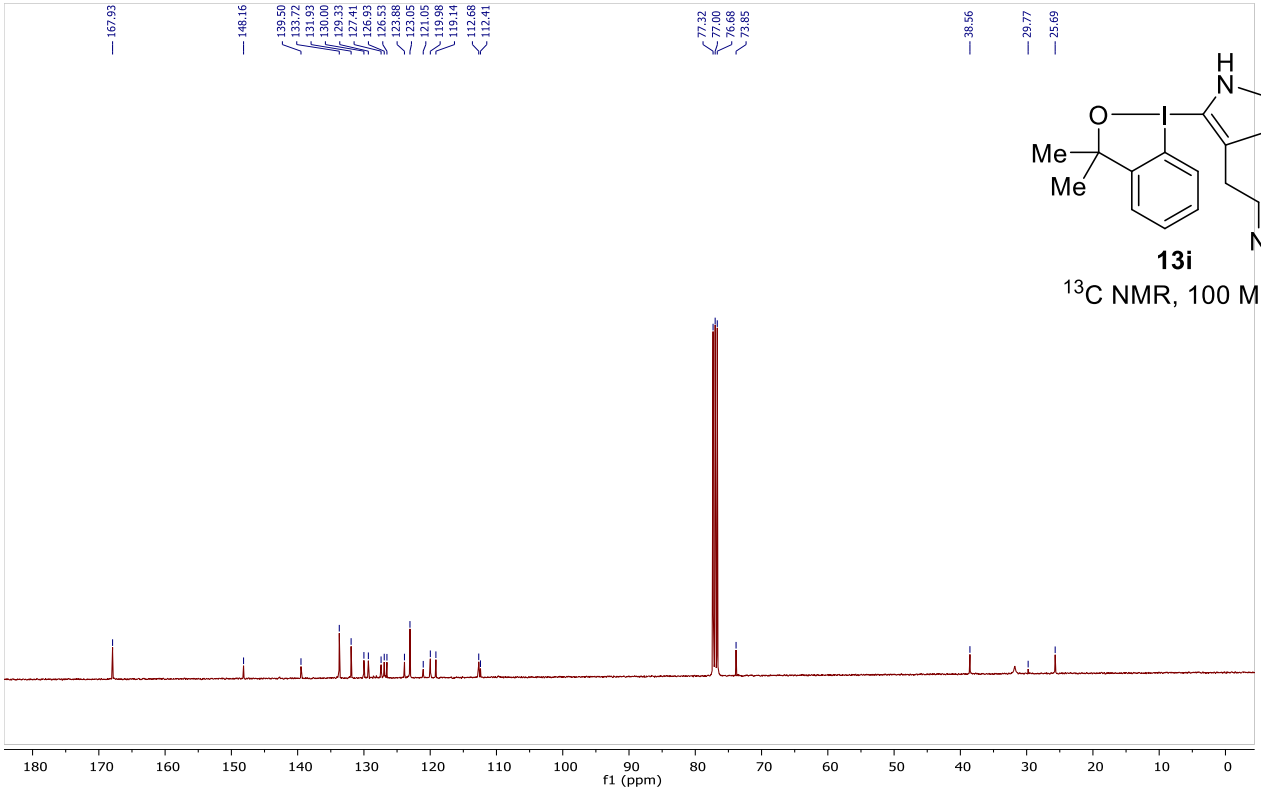


1-(2-(1*H*-Indol-3-yl)ethyl)isoindoline-1,3-dione)-3,3-dimethyl-1,3-dihydro-1λ^3-benzo[*d*][1,2] iodoxole (13i):



13i

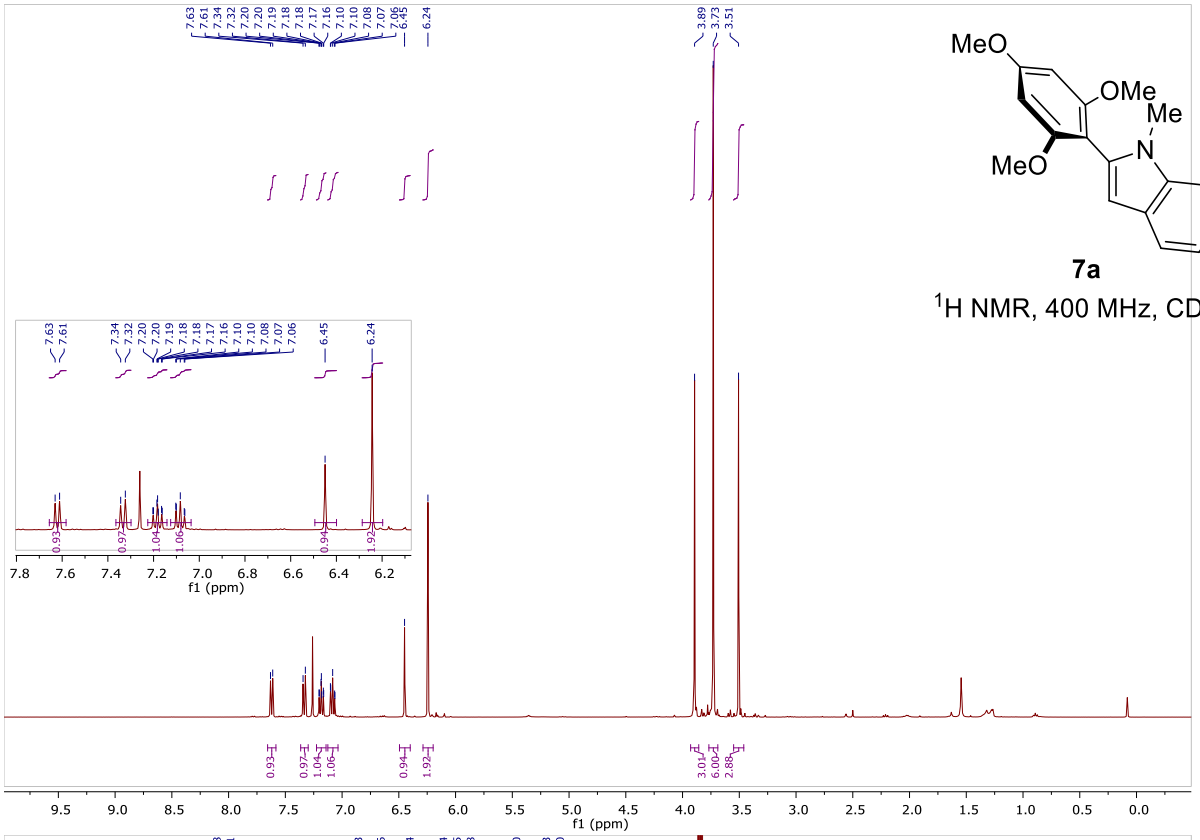
^{1}H NMR, 400 MHz, $CDCl_3$

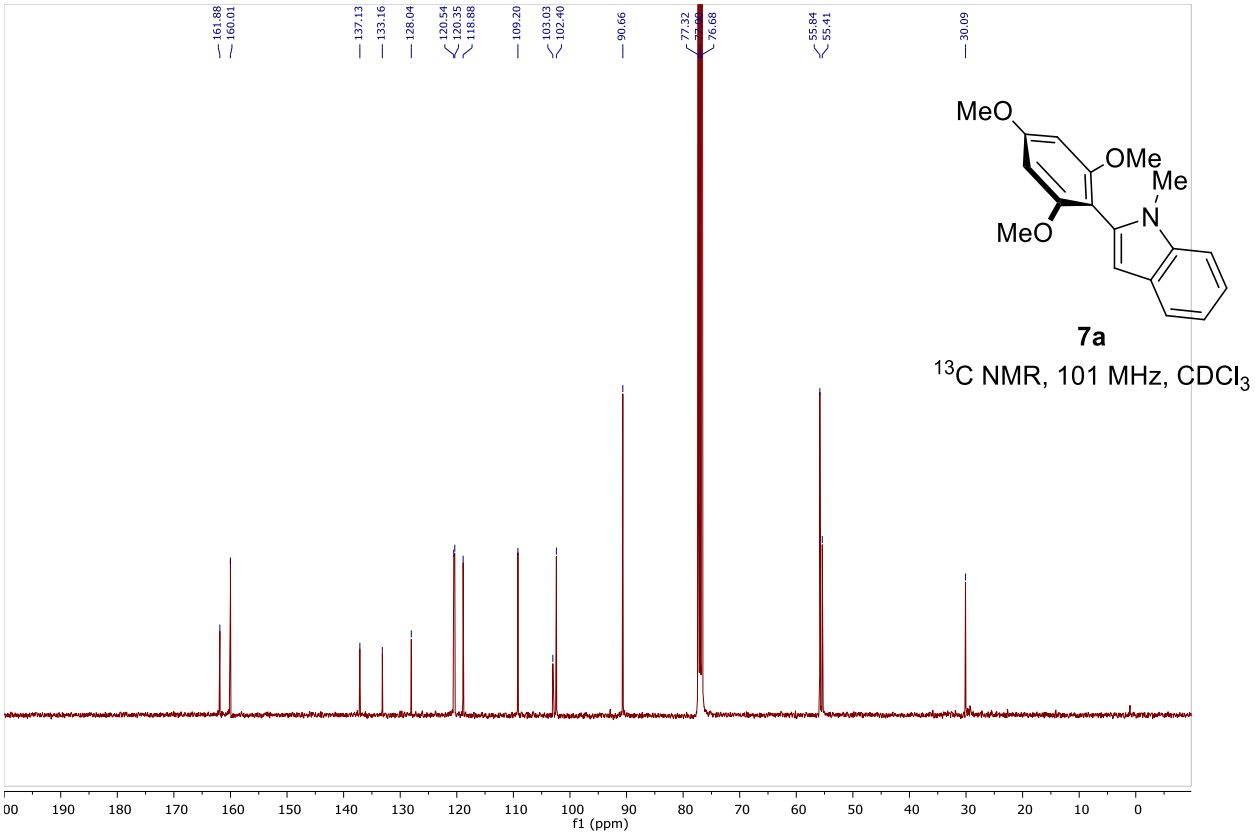


13i

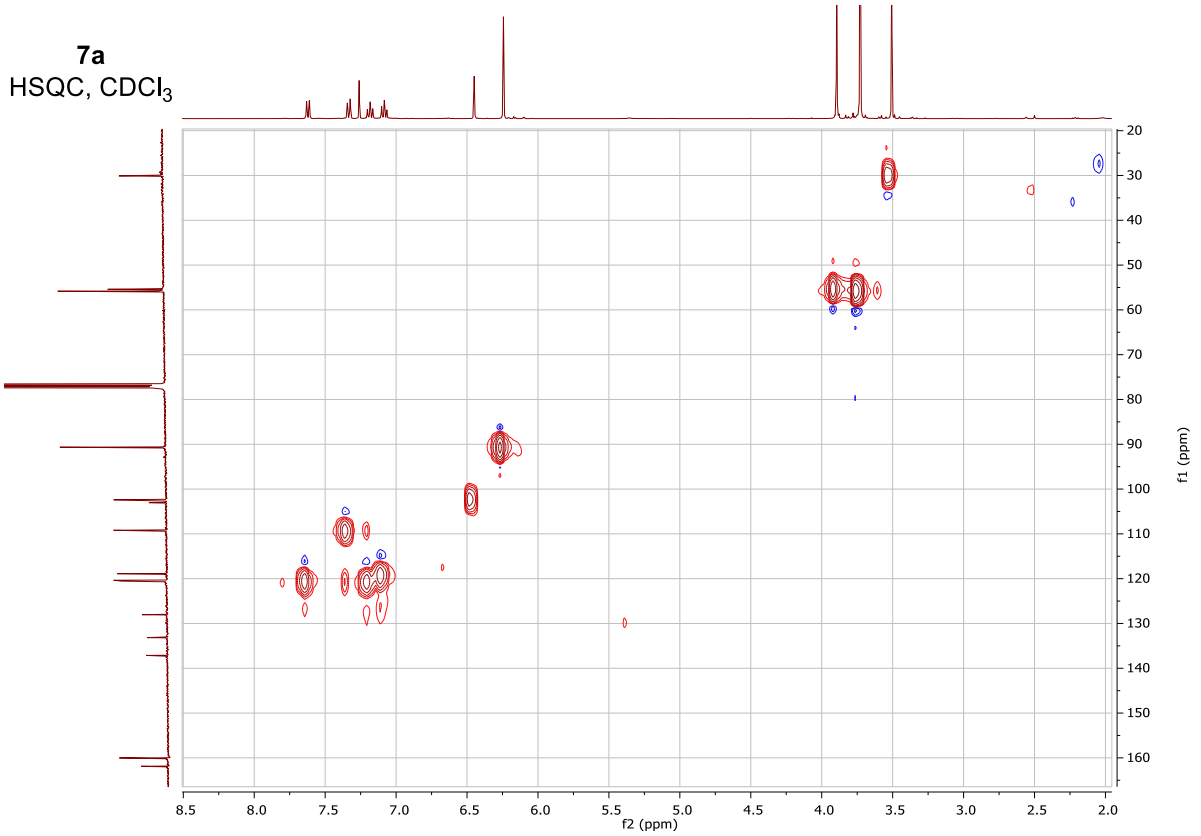
^{13}C NMR, 100 MHz, $CDCl_3$

1-Methyl-2-(2,4,6-trimethoxyphenyl)-1*H*-indole (7a)

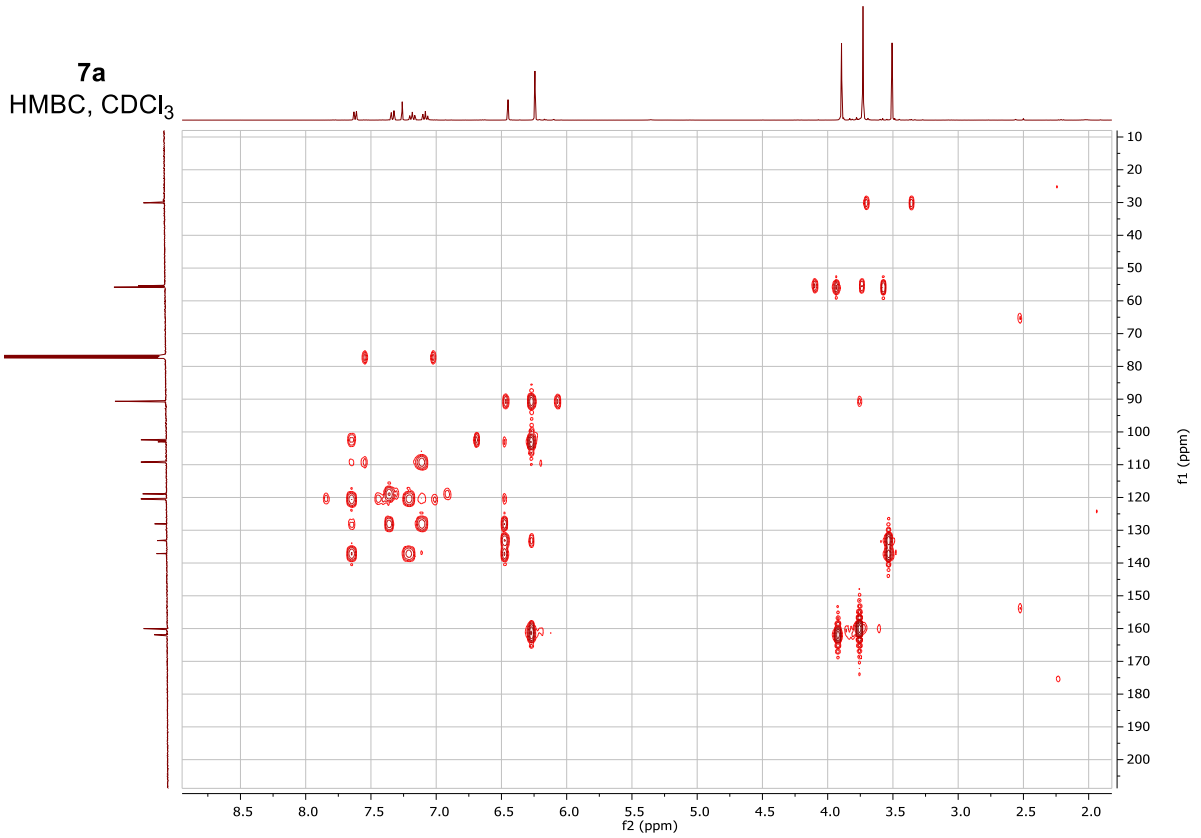




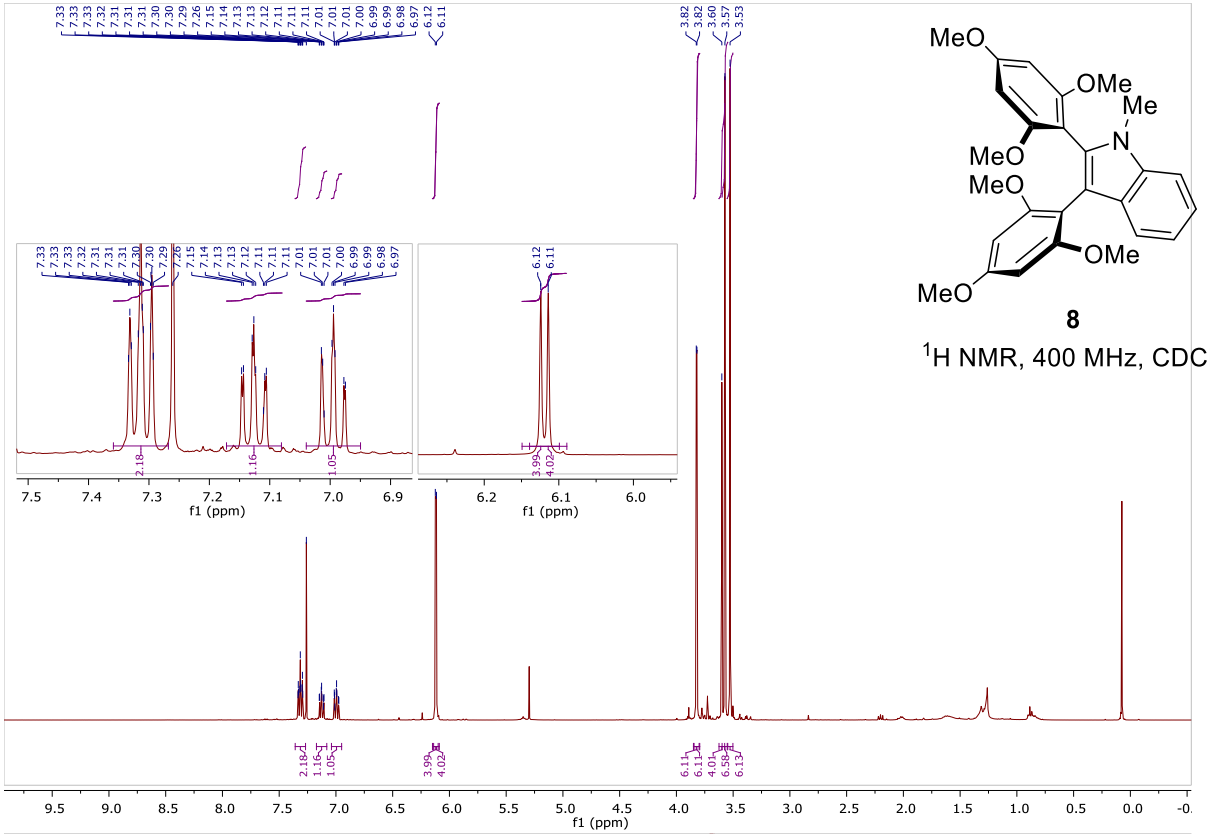
7a
HSQC, $CDCl_3$

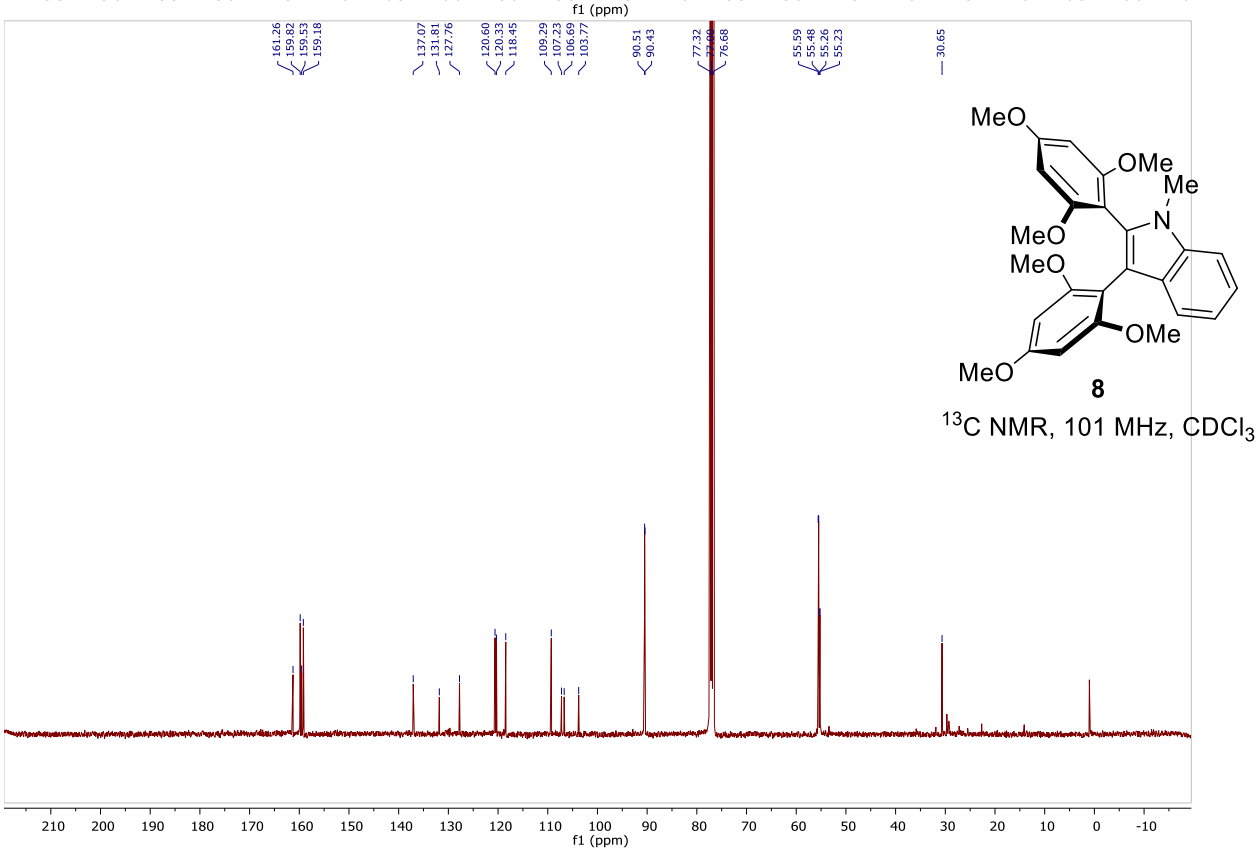


7a
HMBC, $CDCl_3$

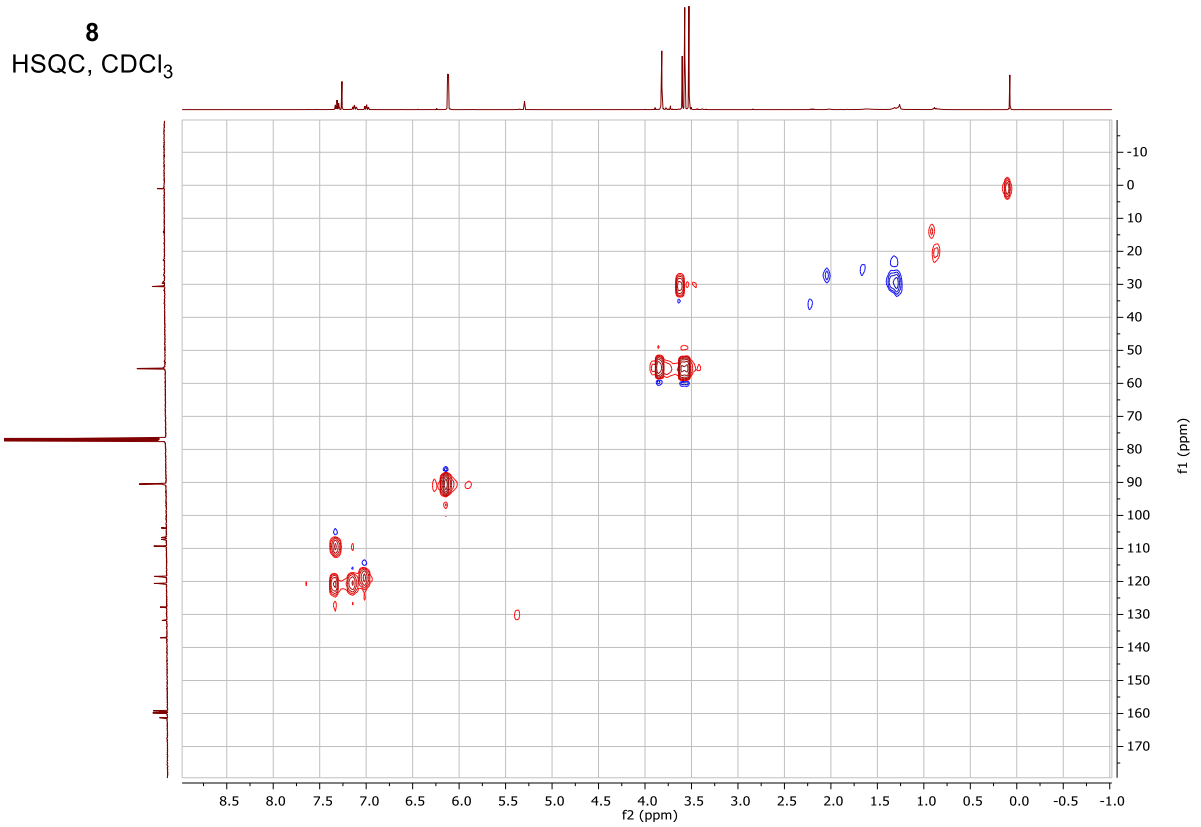


1-Methyl-2,3-bis(2,4,6-trimethoxyphenyl)-1*H*-indole (8).



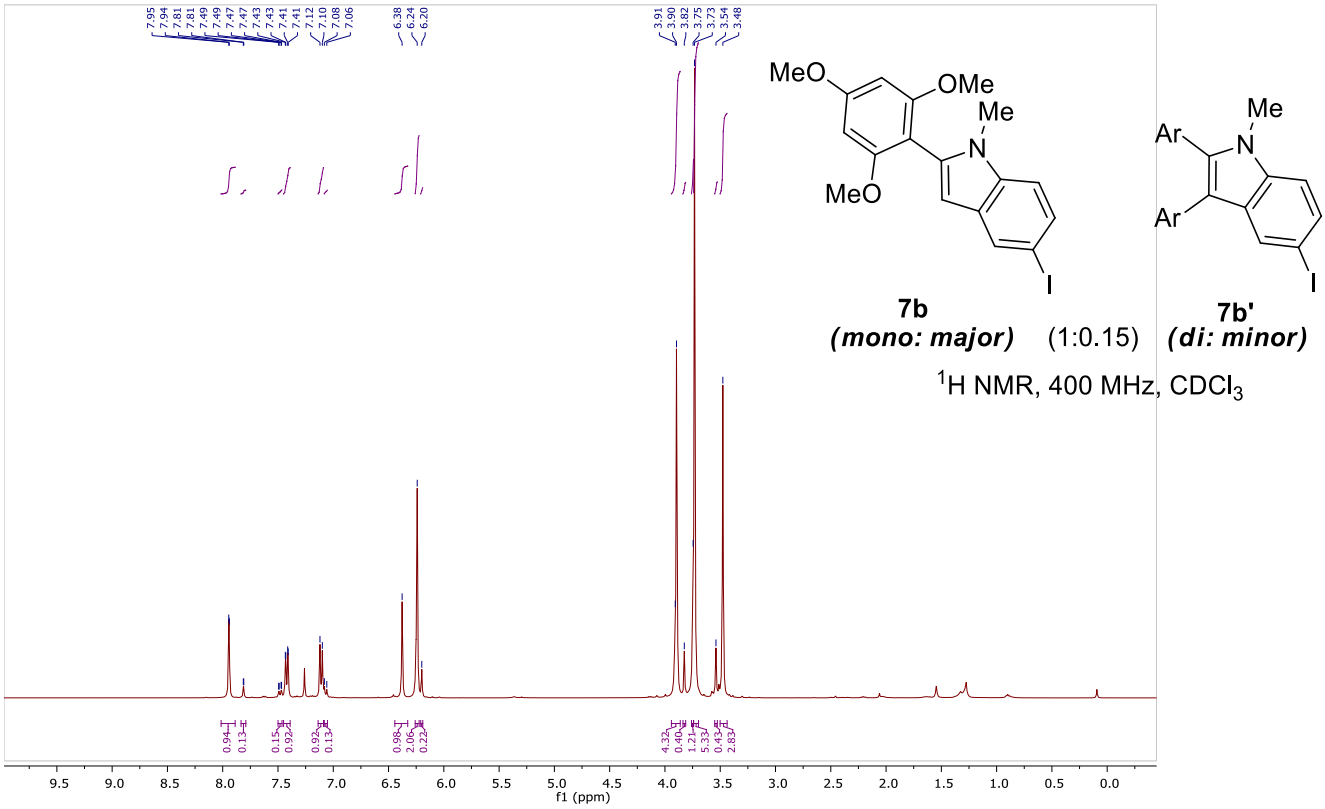


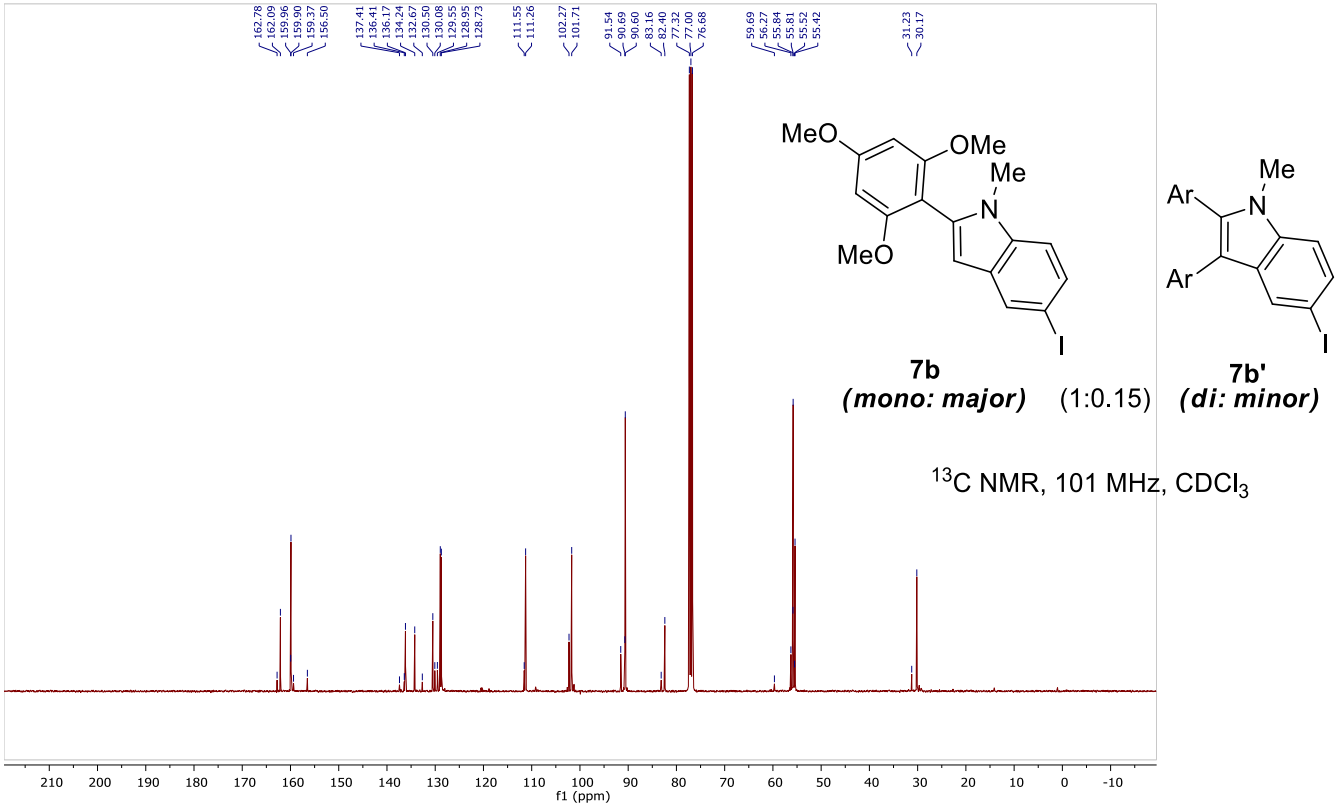
8
HSQC, $CDCl_3$



8
HMBC, $CDCl_3$

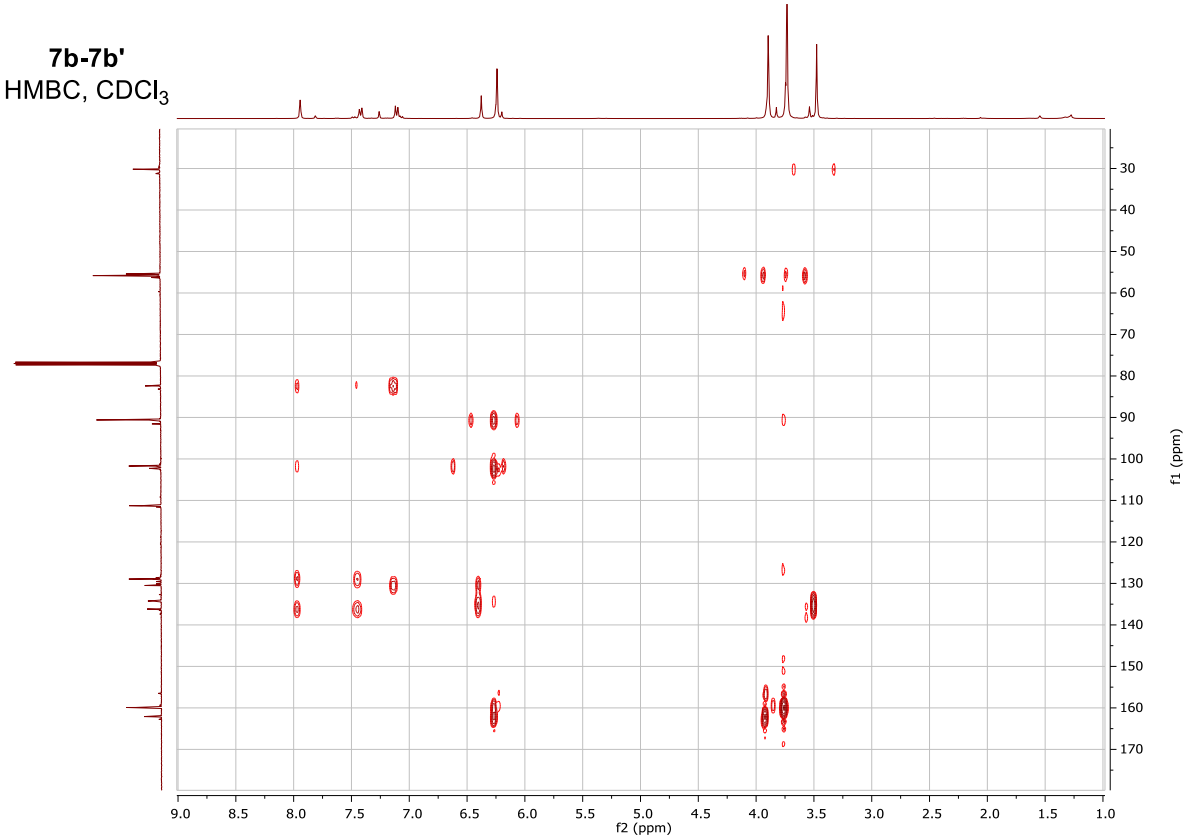
5-Iodo-1-methyl-2-(2,4,6-trimethoxyphenyl)-1*H*-indole (7b) and and 5-iodo-1-methyl-2,3-bis(2,4,6-trimethoxyphenyl)-1*H*-indole (7b')



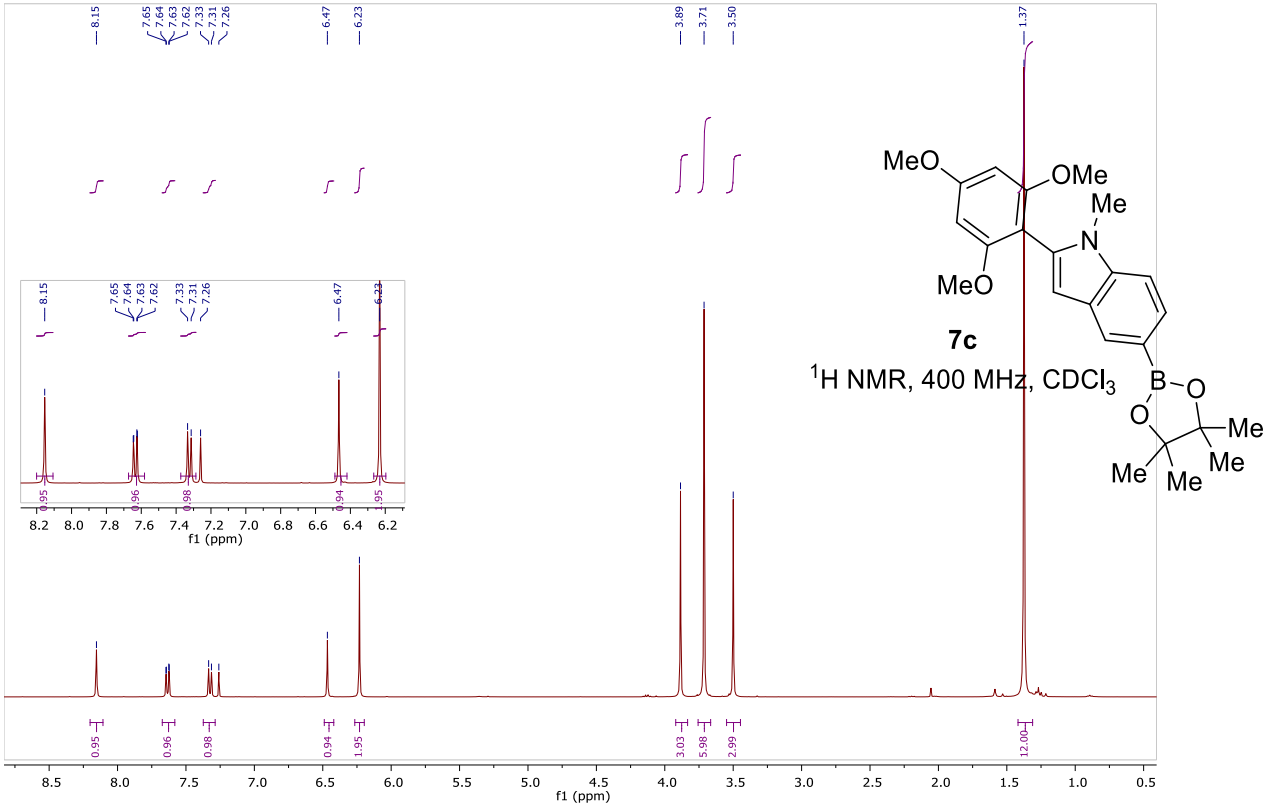


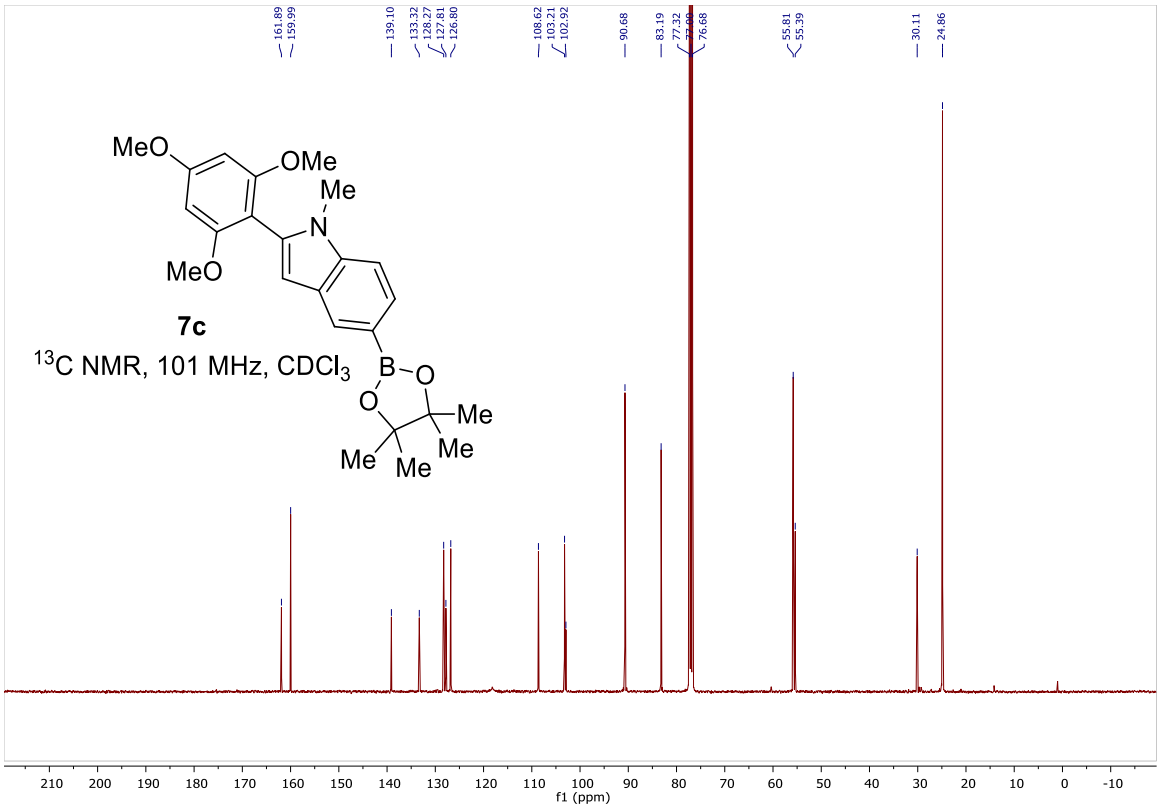
7b-7b'
HSQC, $CDCl_3$

7b-7b'
HMBC, $CDCl_3$

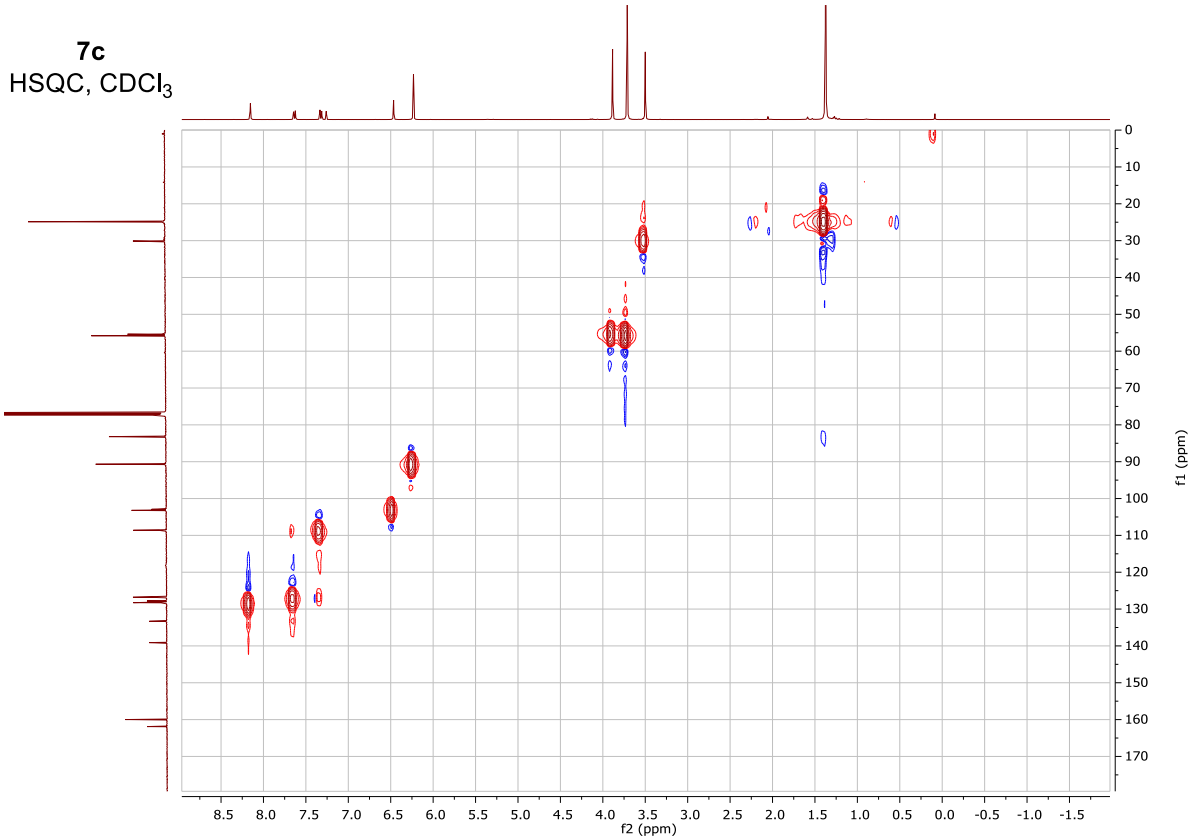


1-Methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(2,4,6-trimethoxyphenyl)-1*H*-indole (7c)

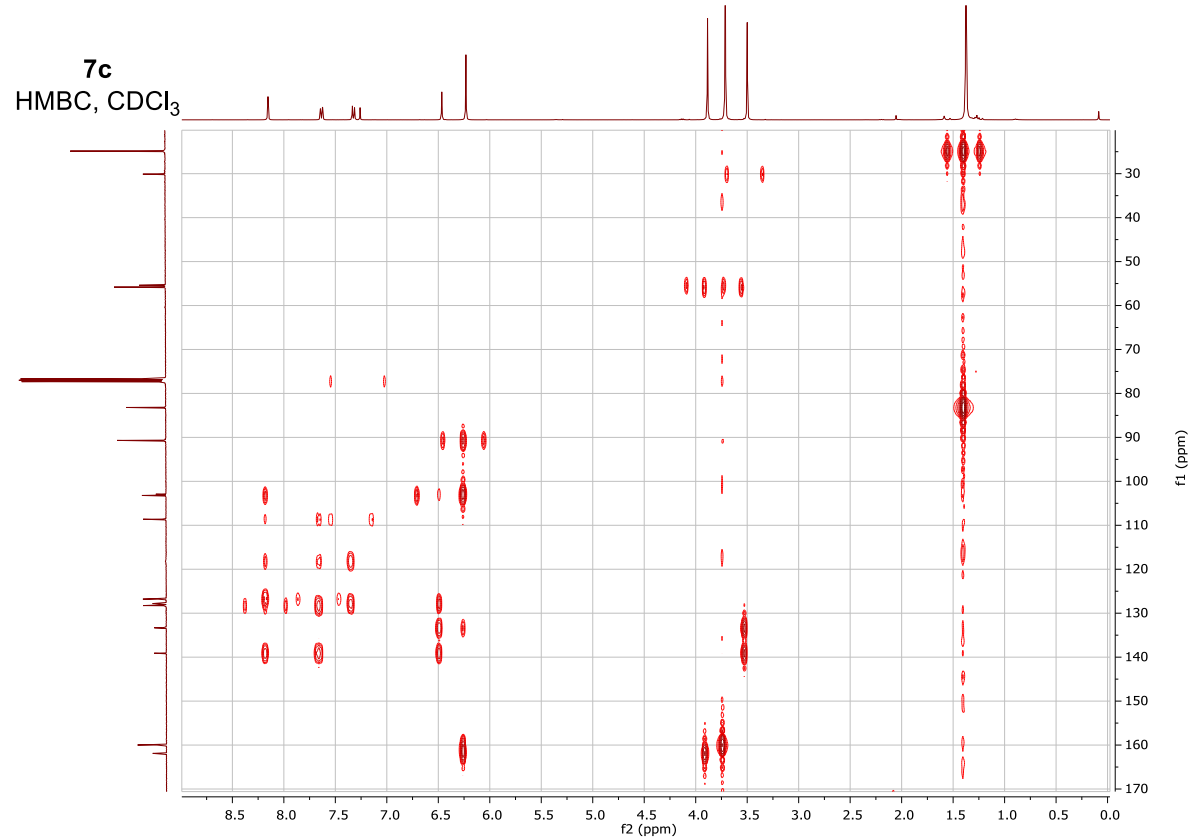




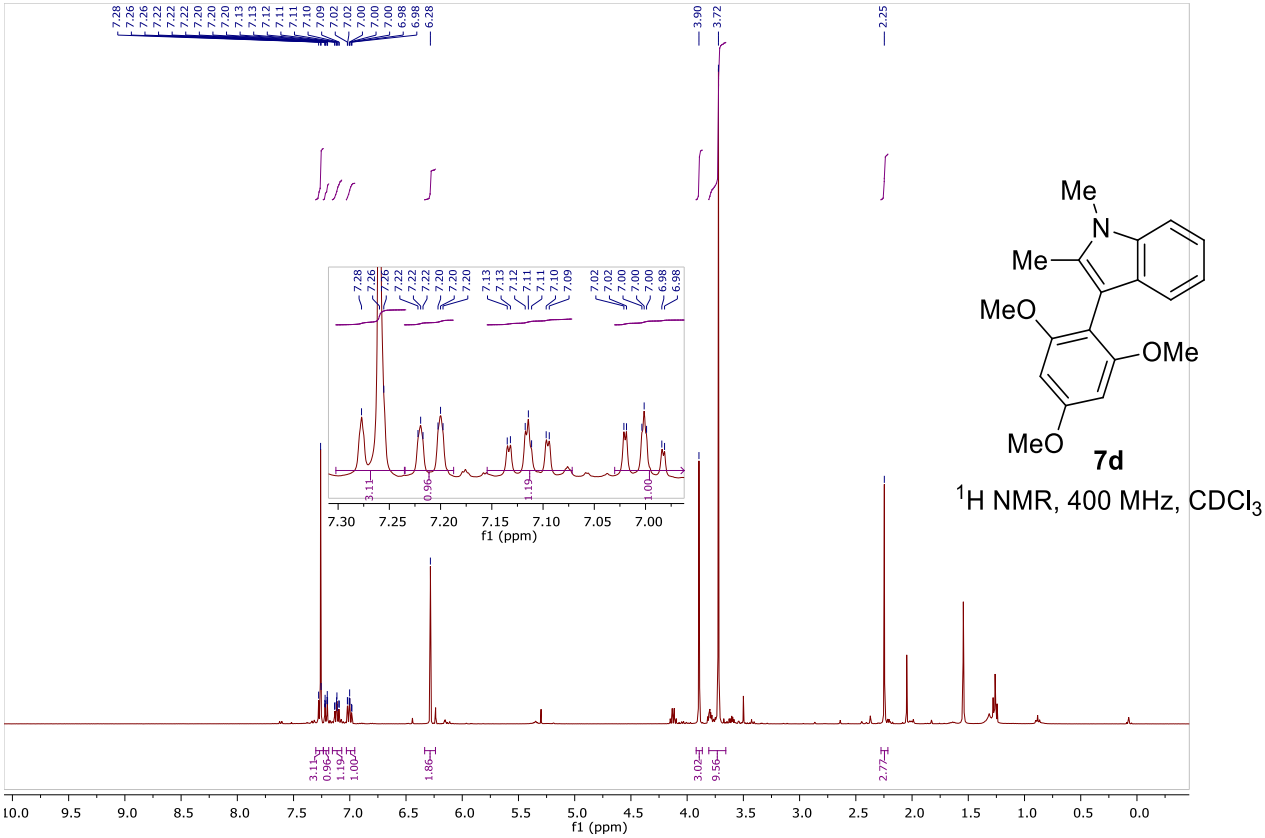
7c
HSQC, $CDCl_3$

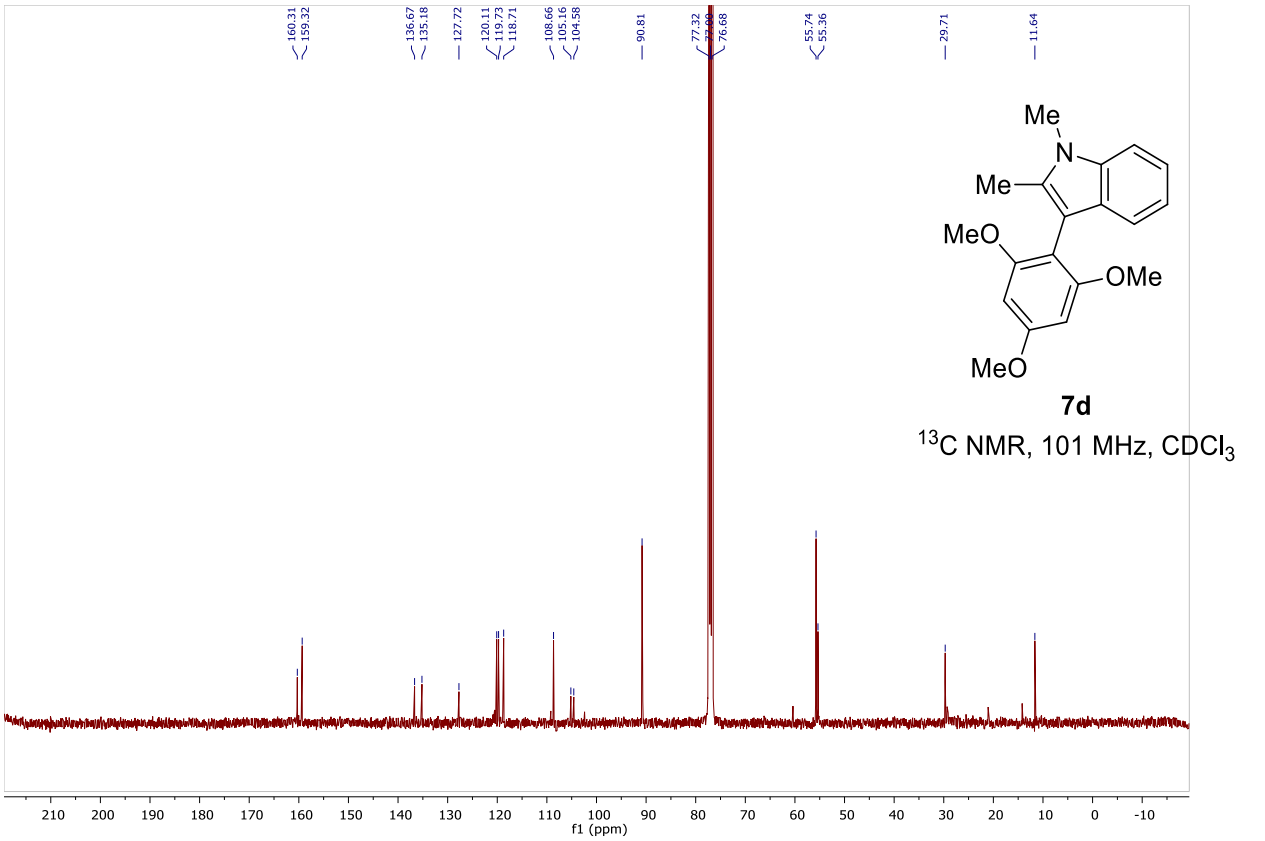


7c
HMBC, $CDCl_3$

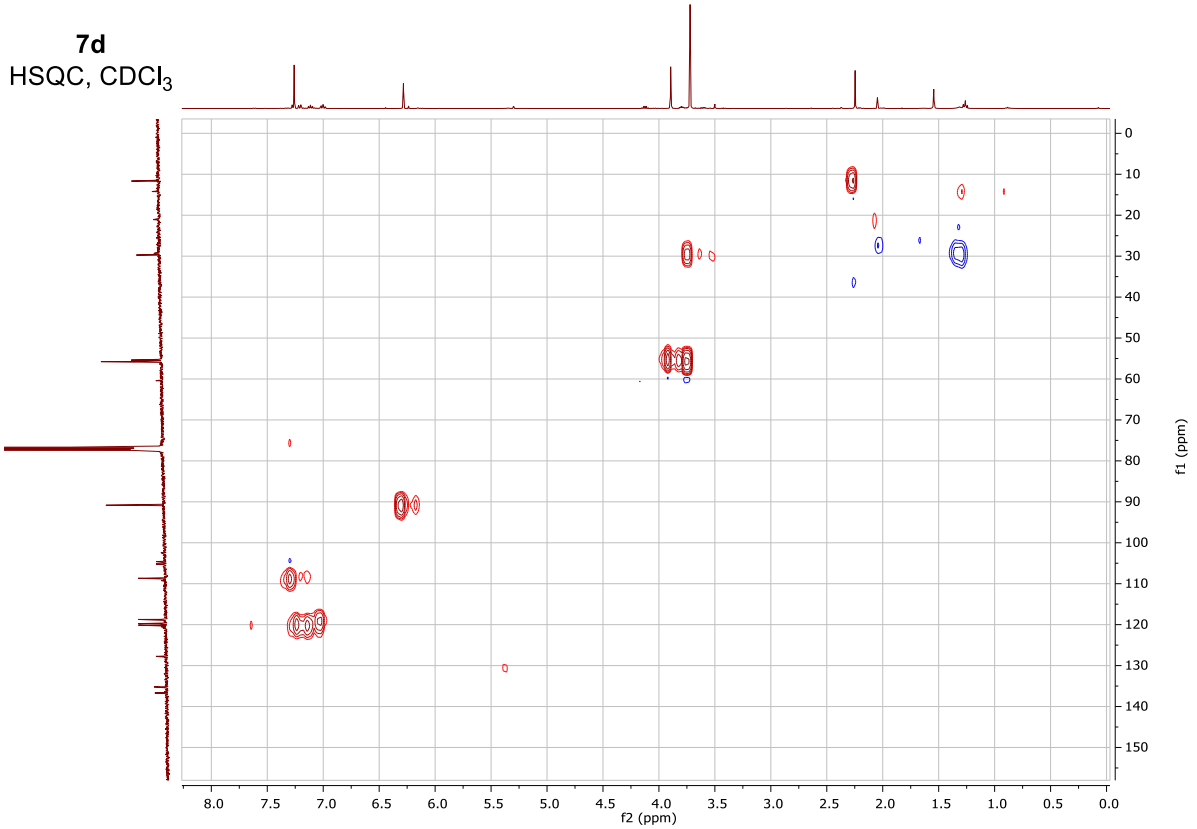


1,2-Dimethyl-3-(2,4,6-trimethoxyphenyl)-1*H*-indole (7d)

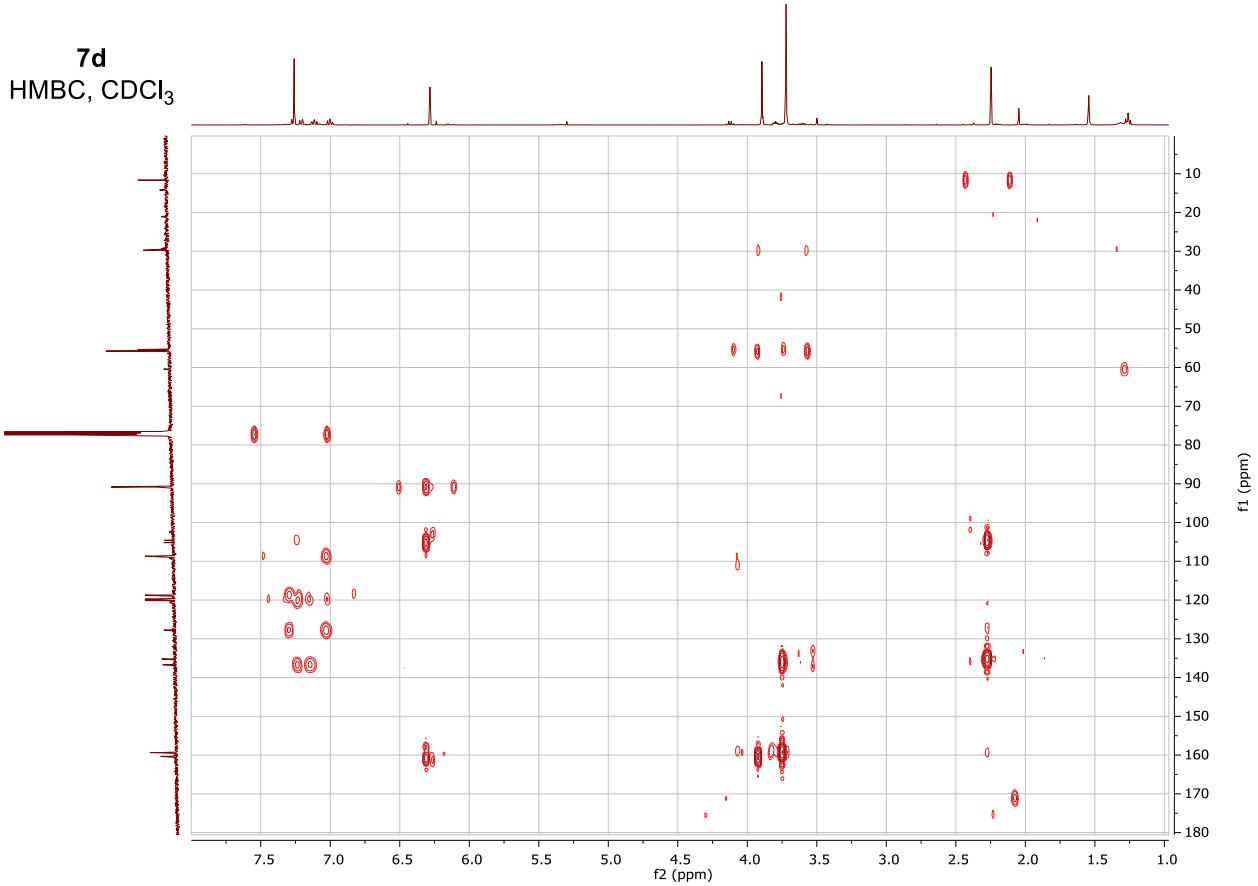




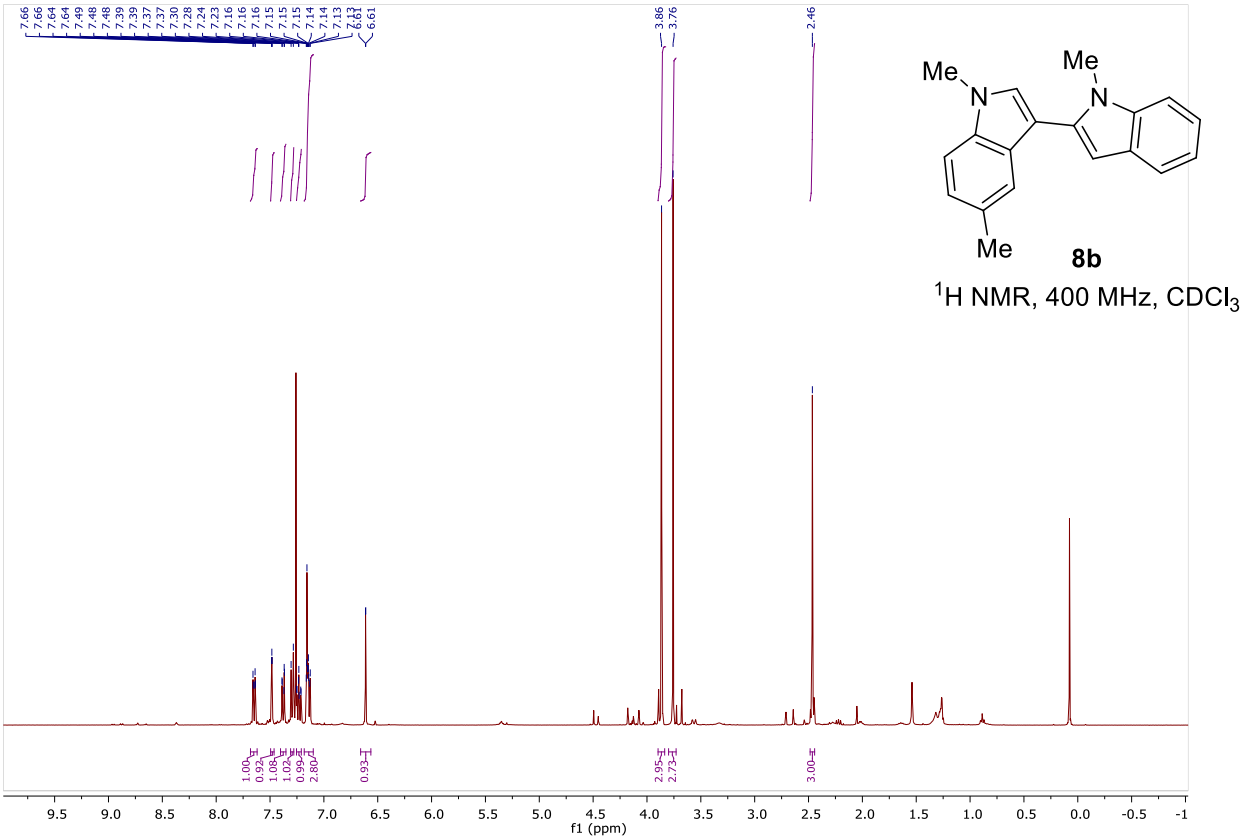
7d
HSQC, $CDCl_3$

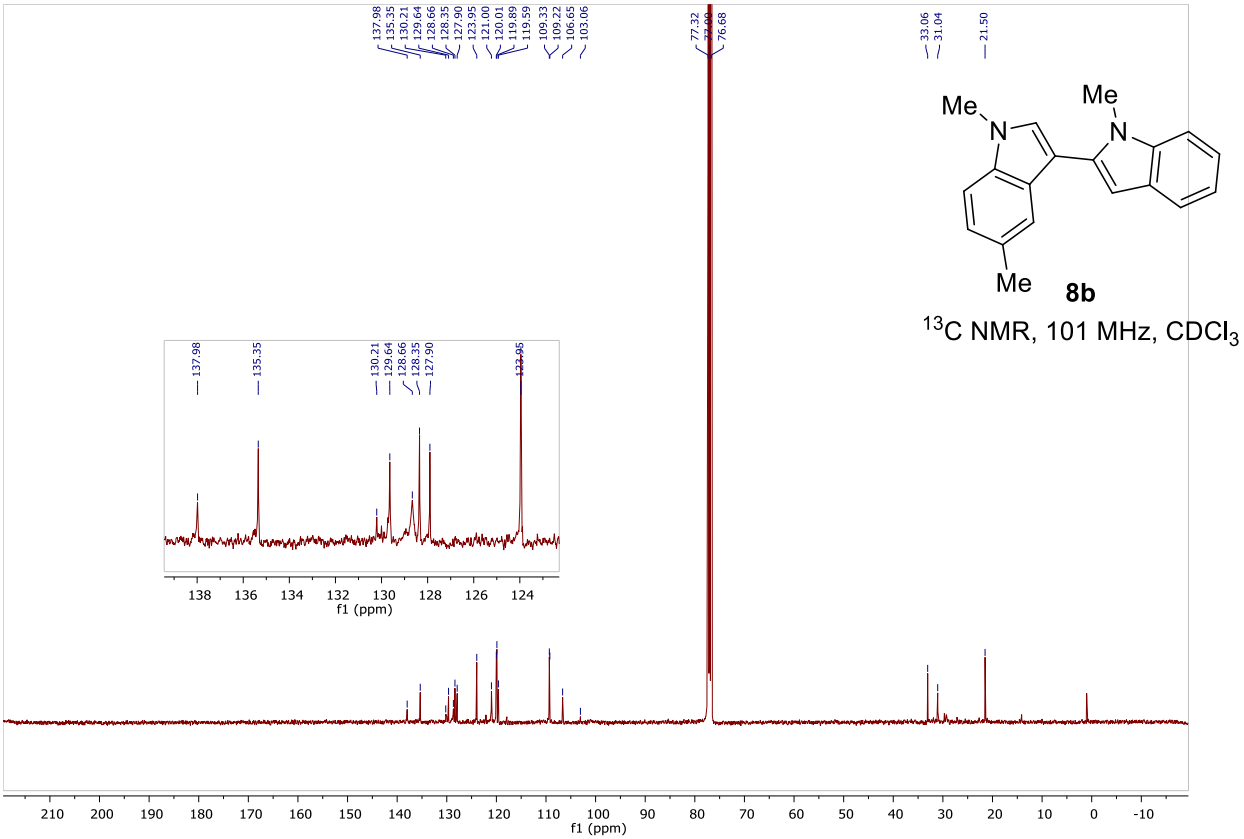


7d
HMBC, $CDCl_3$

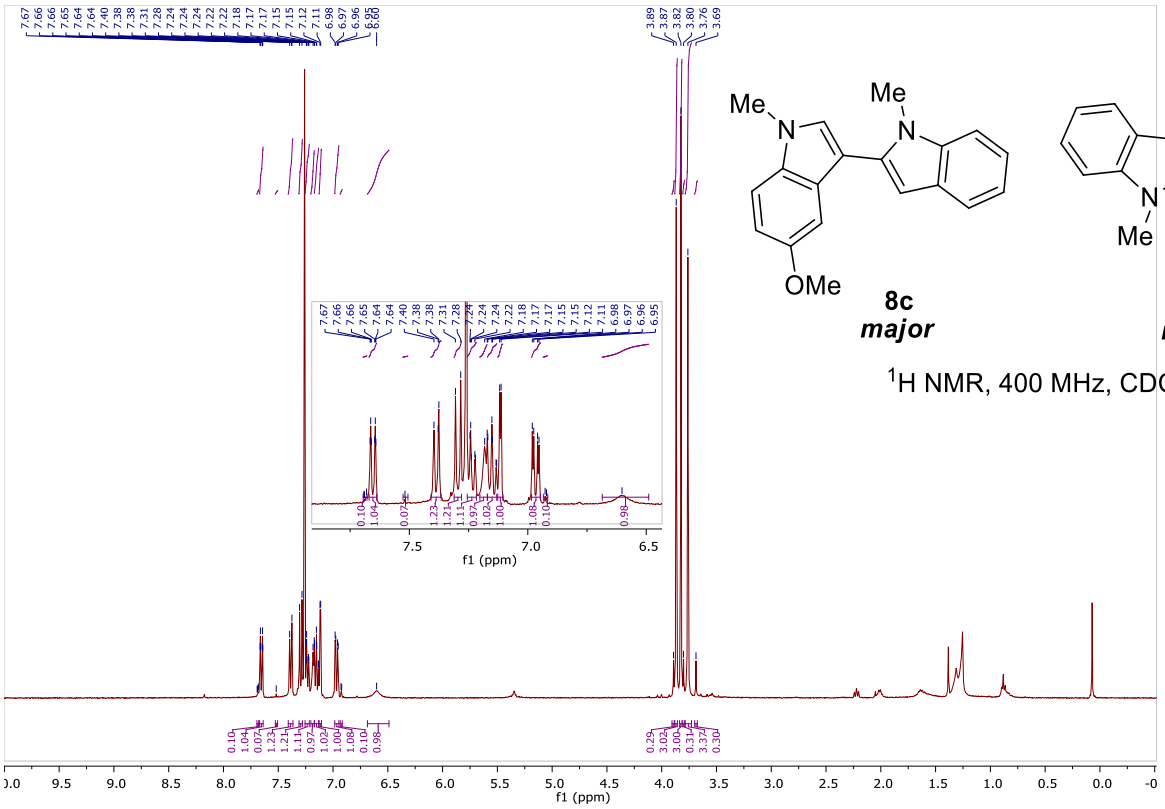


1,1'-Dimethyl-1*H*,1'*H*-2,3'-biindole (8b)

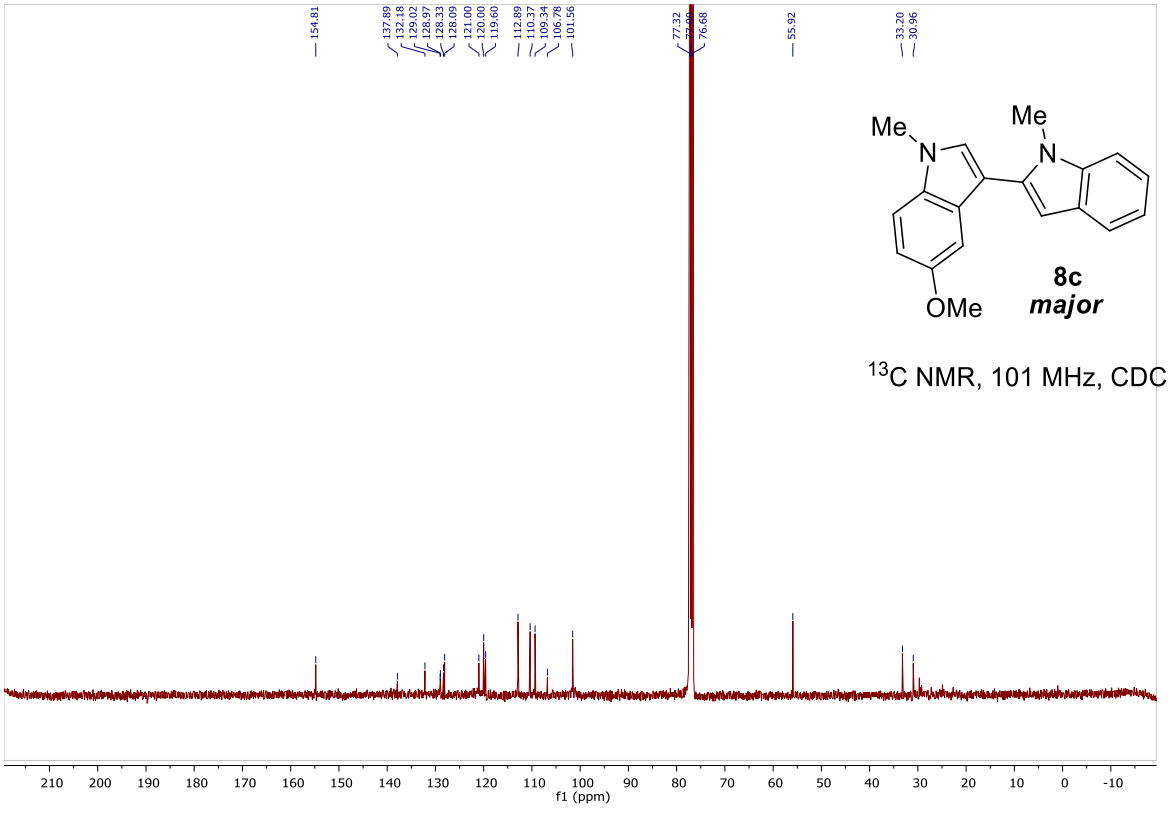




5'-Methoxy-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole (8c) and 5'-methoxy-1,1'-dimethyl-1*H*,1'*H*-2,7'-biindole (8c')

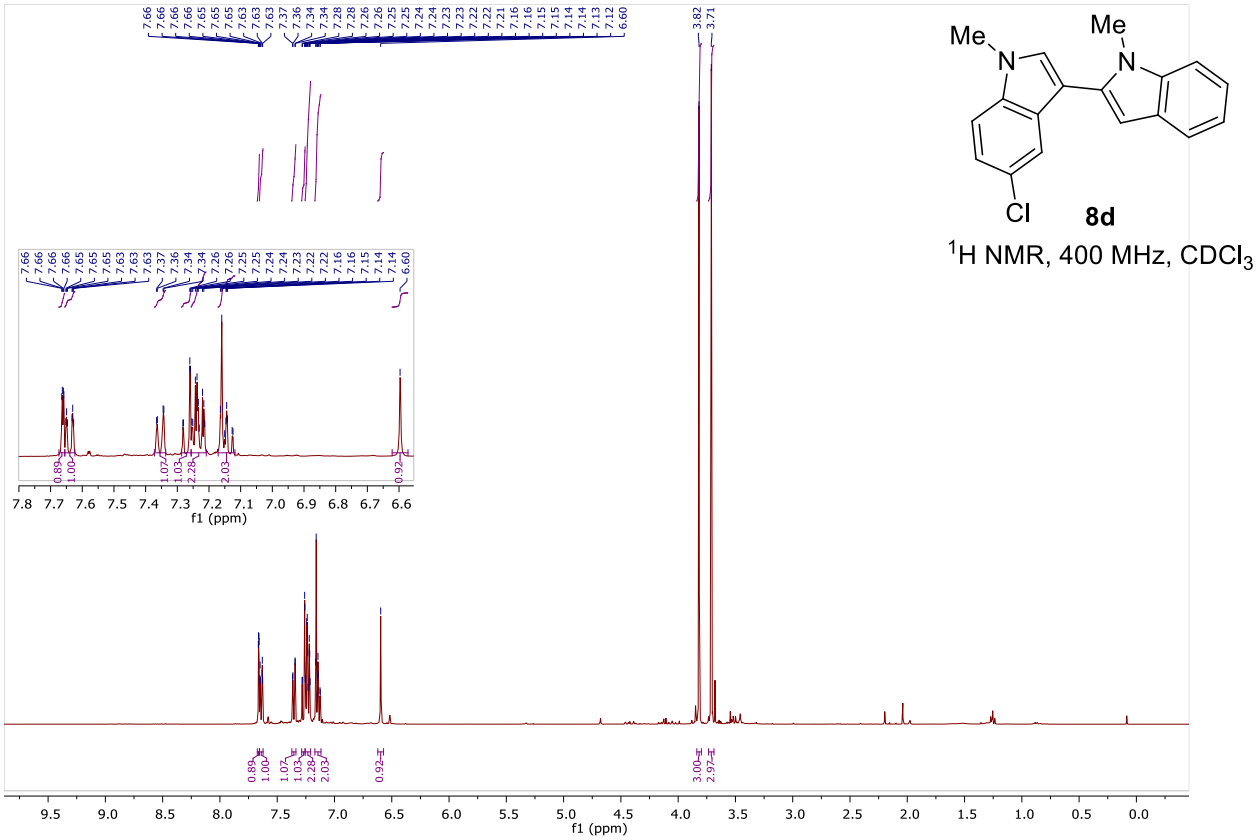


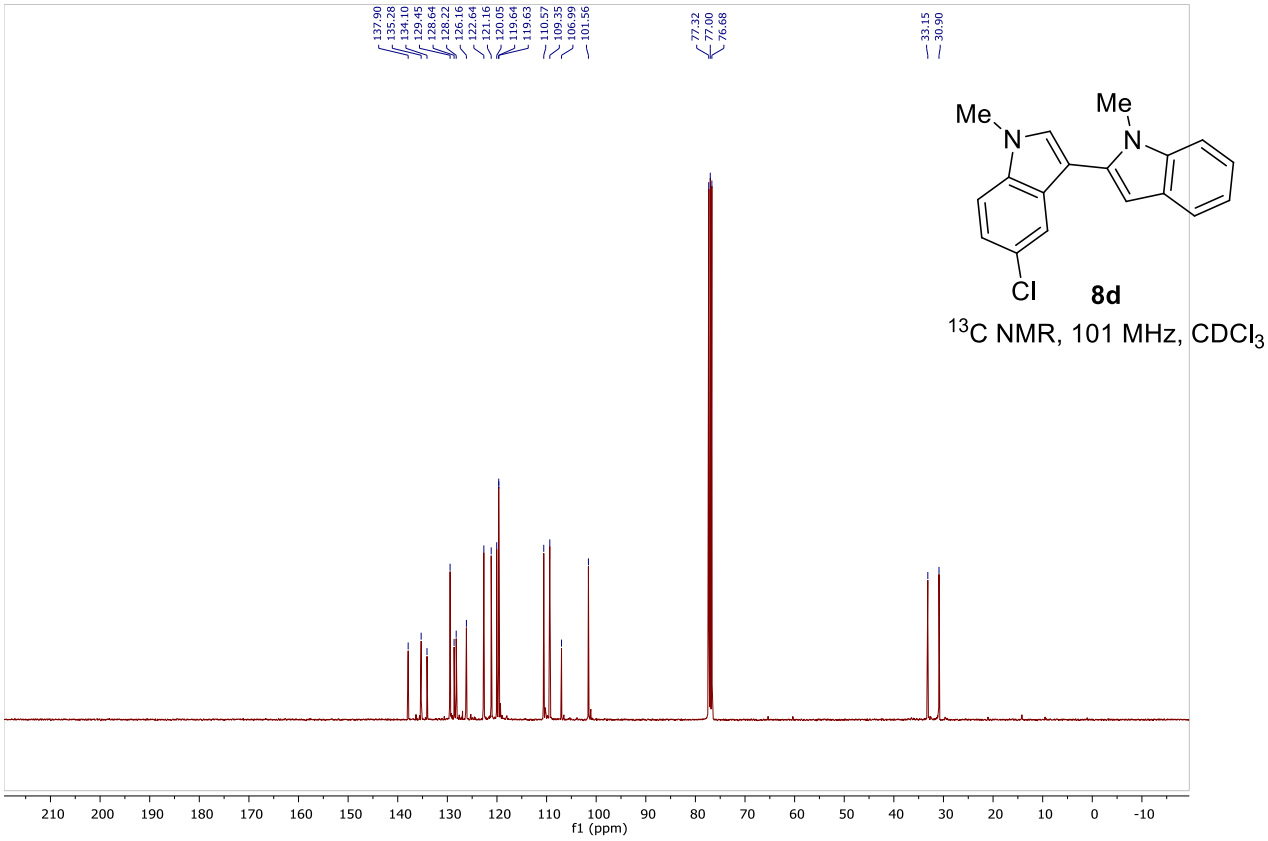
^{1}H NMR, 400 MHz, $CDCl_3$



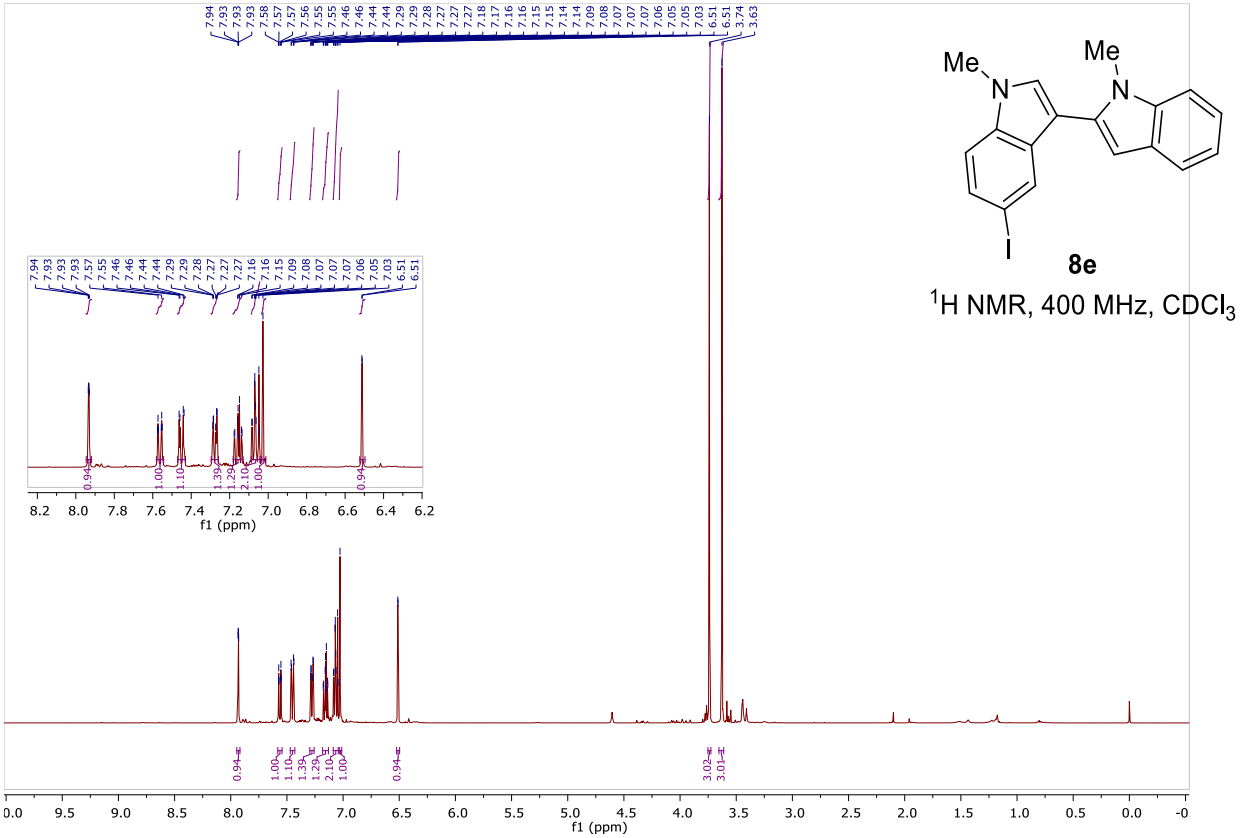
^{13}C NMR, 101 MHz, $CDCl_3$

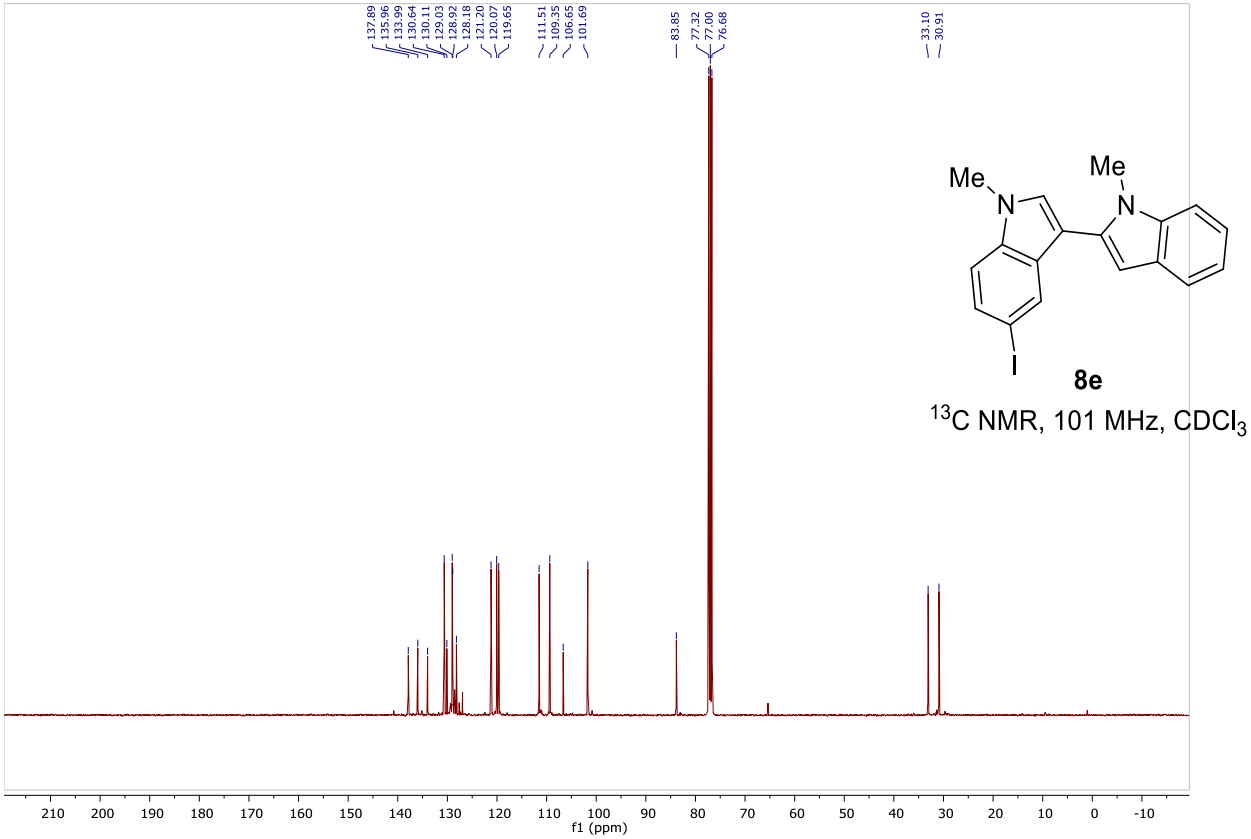
5'-Chloro-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole (8d)



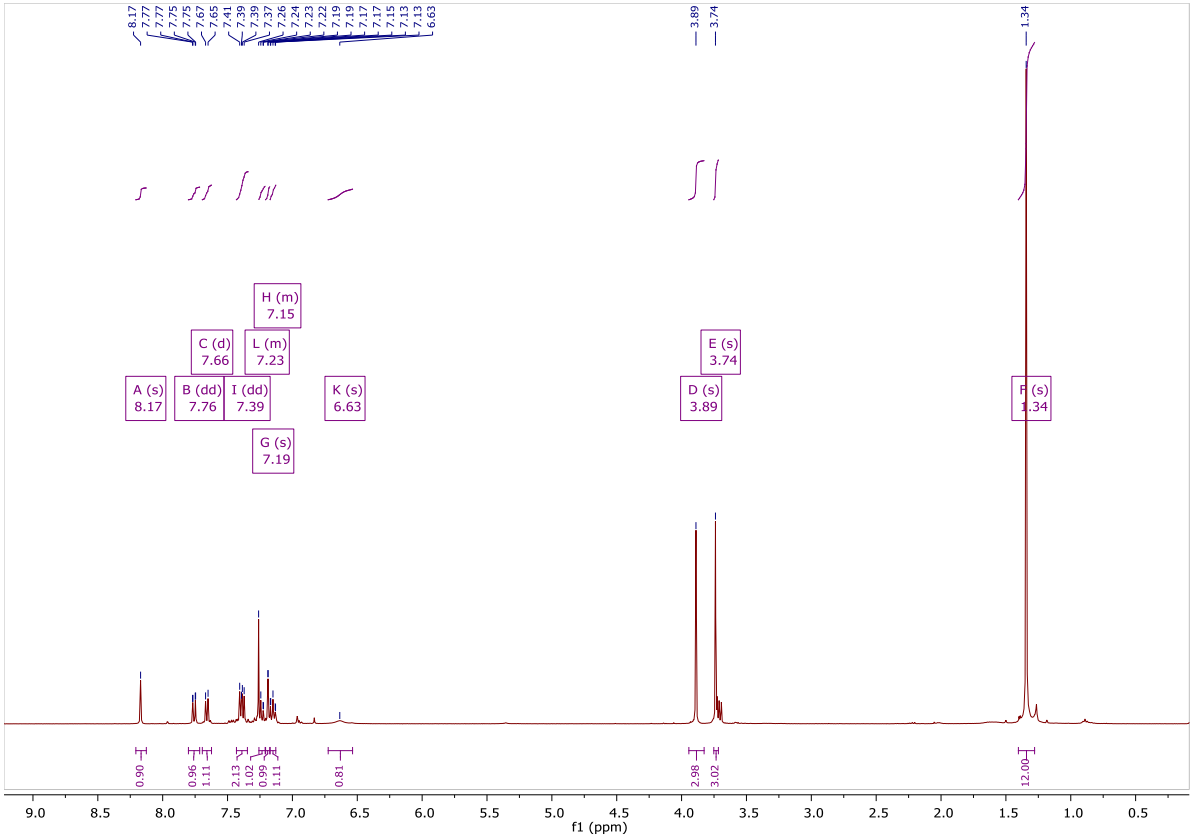


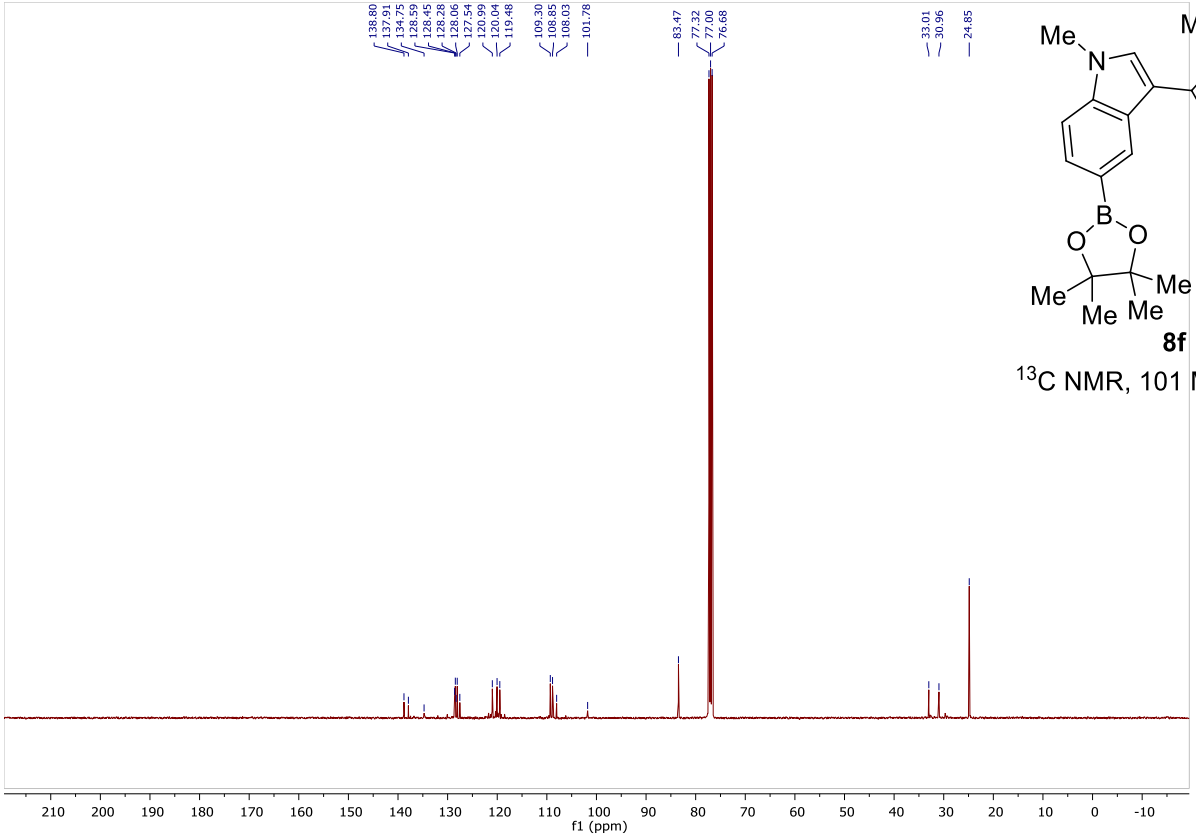
5'-Iodo-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole (8e)





1,1'-Dimethyl-5'-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*,1'*H*-2,3'-biindole (8f)

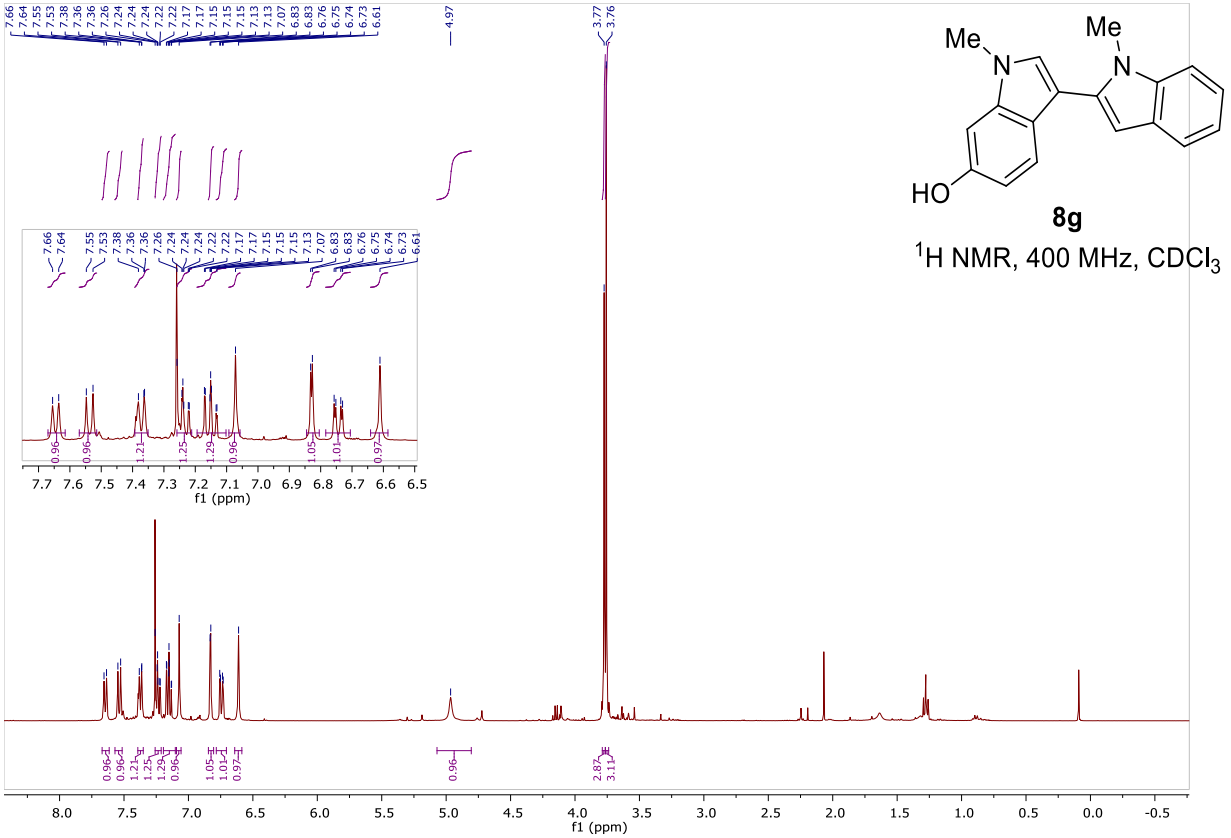


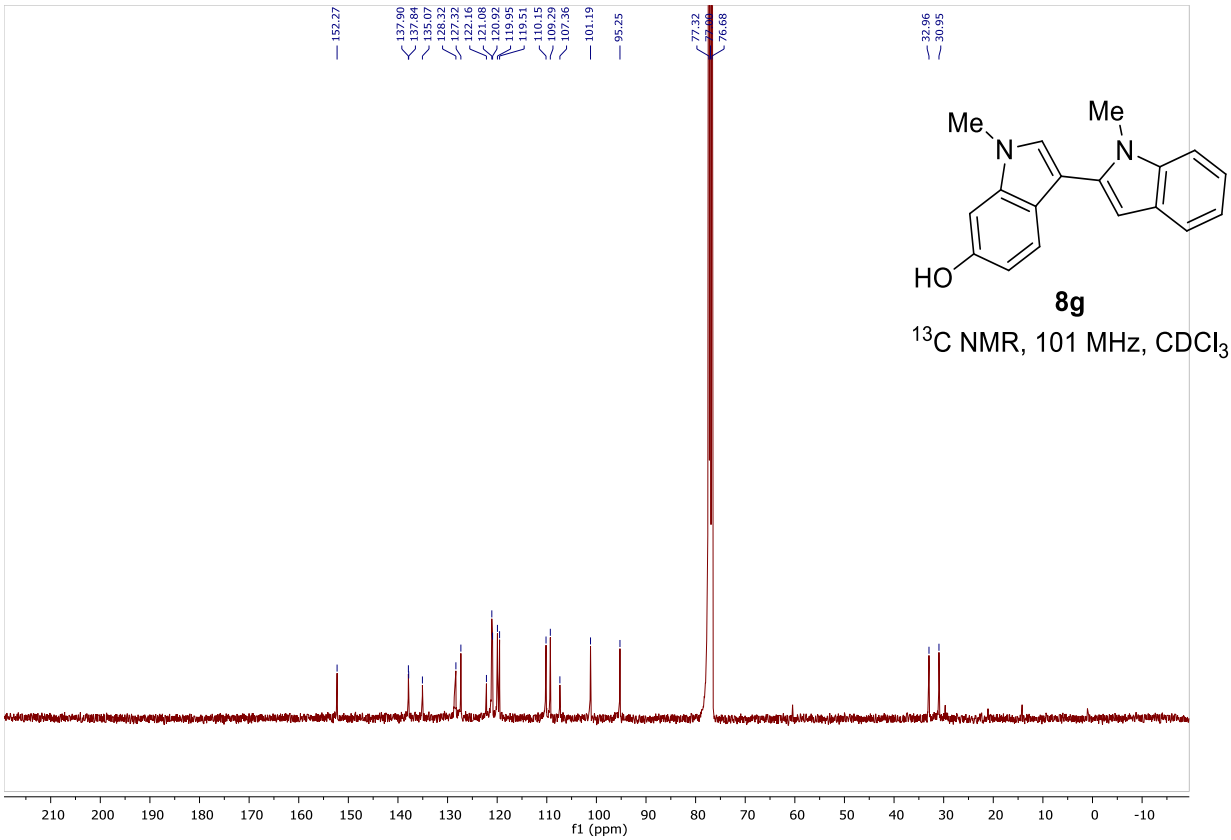


8f

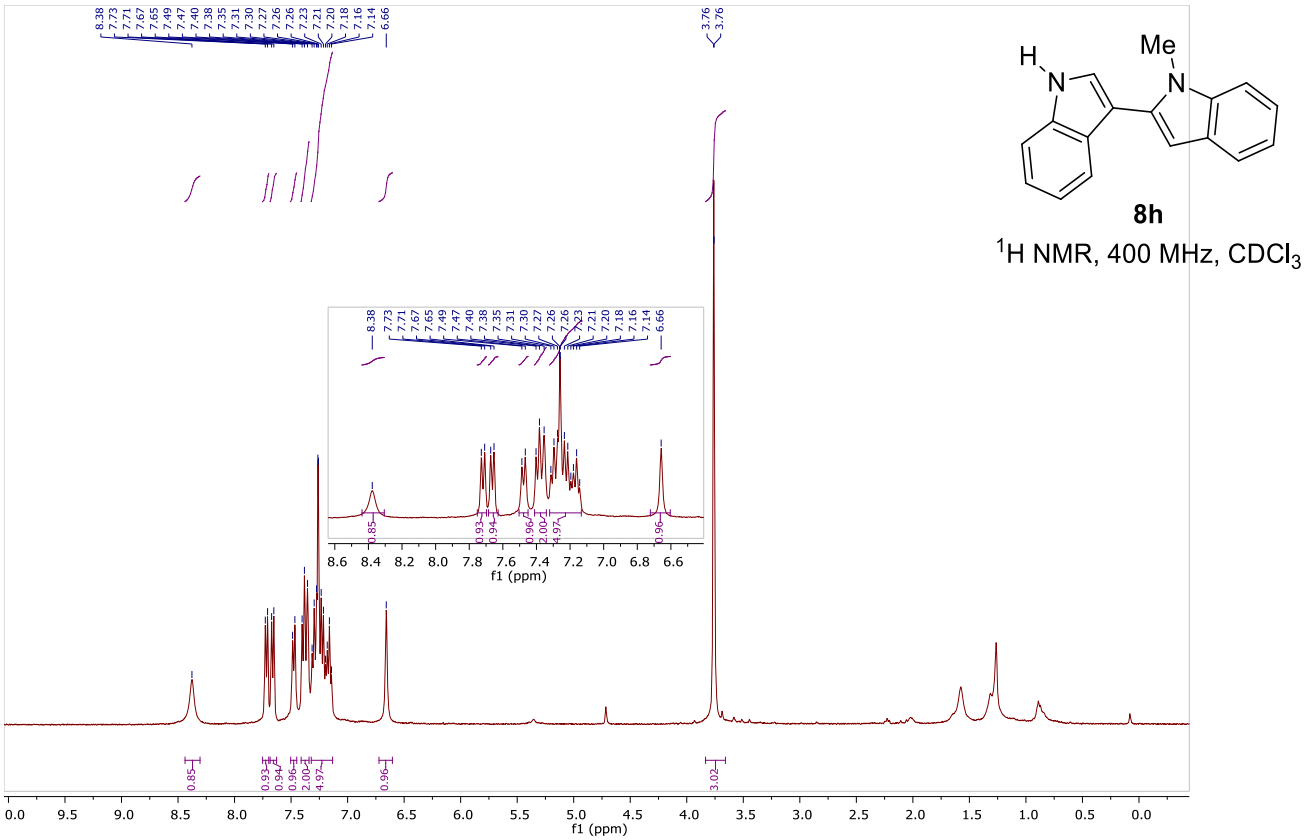
^{13}C NMR, 101 MHz, $CDCl_3$

1,1'-Dimethyl-1*H*,1'*H*-[2,3'-biindol]-6'-ol (8g)



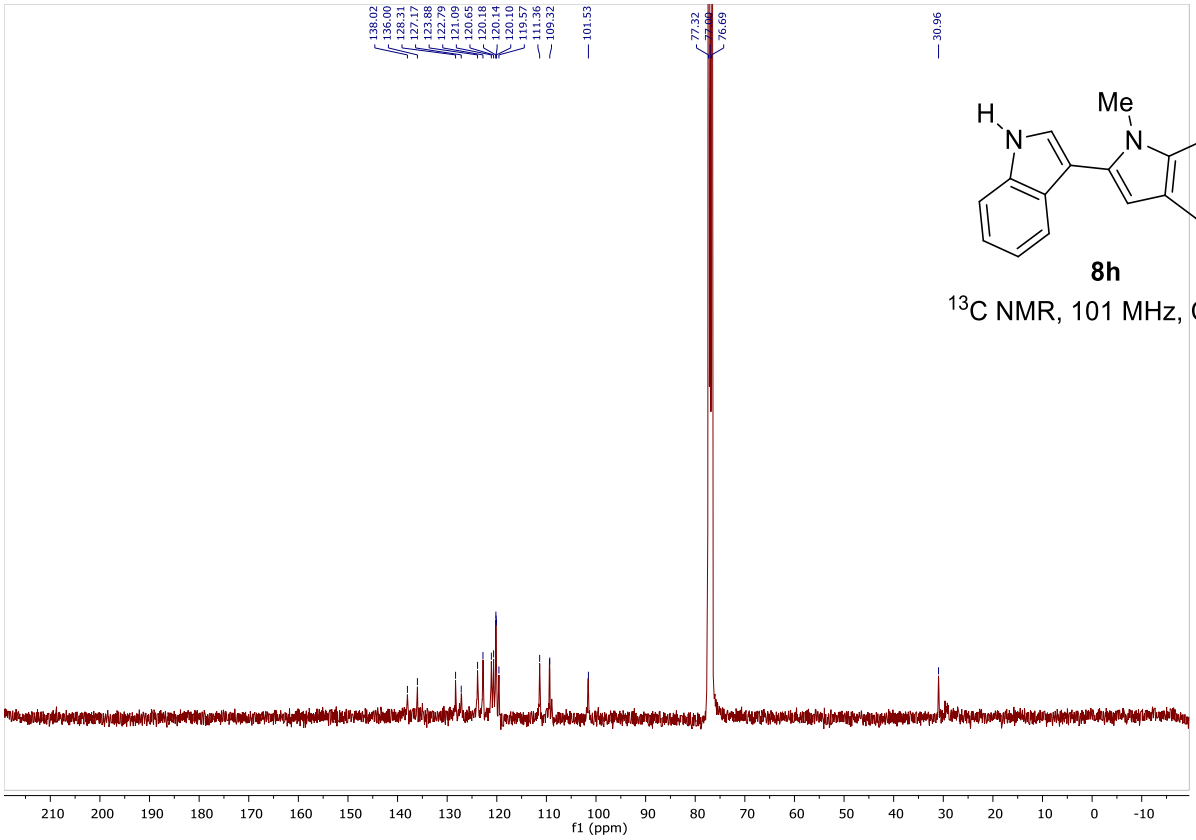


1-Methyl-1*H*,1'*H*-2,3'-biindole (8h)



8h

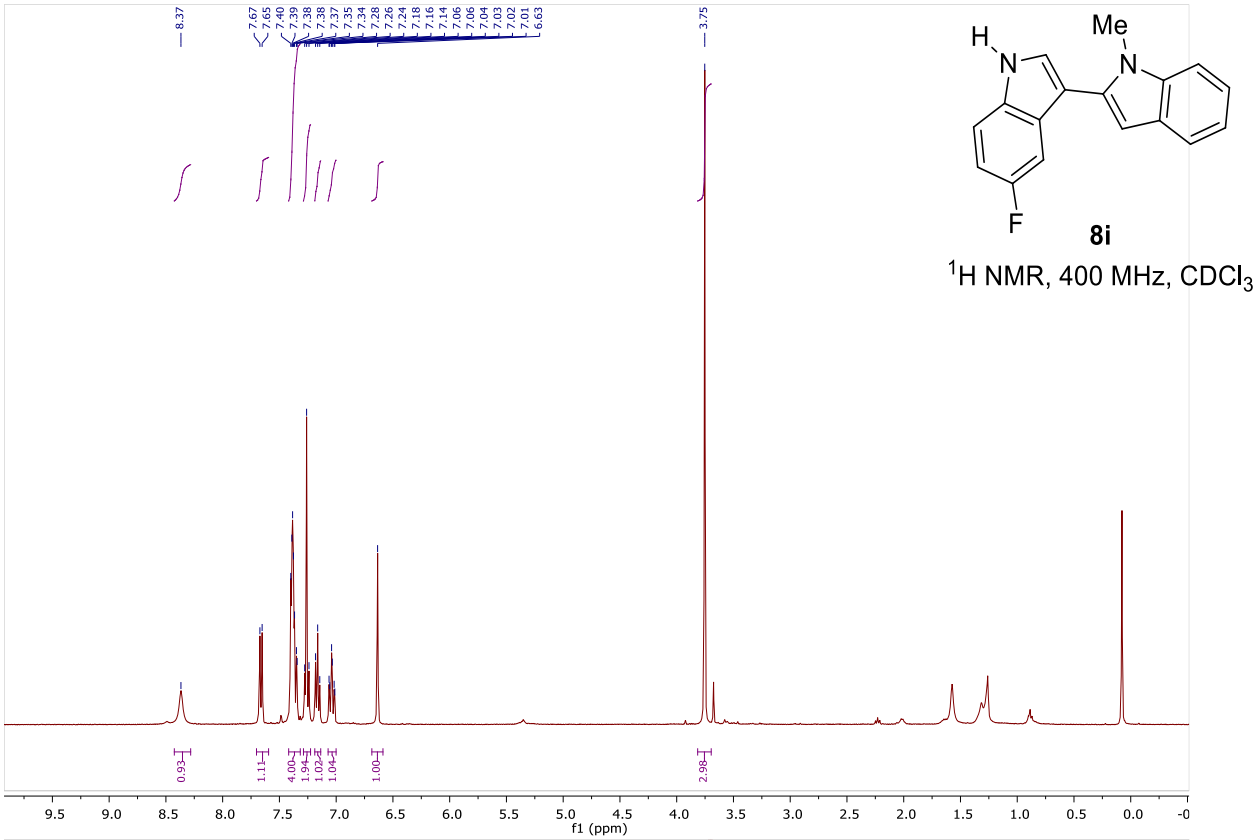
^{1}H NMR, 400 MHz, $CDCl_3$

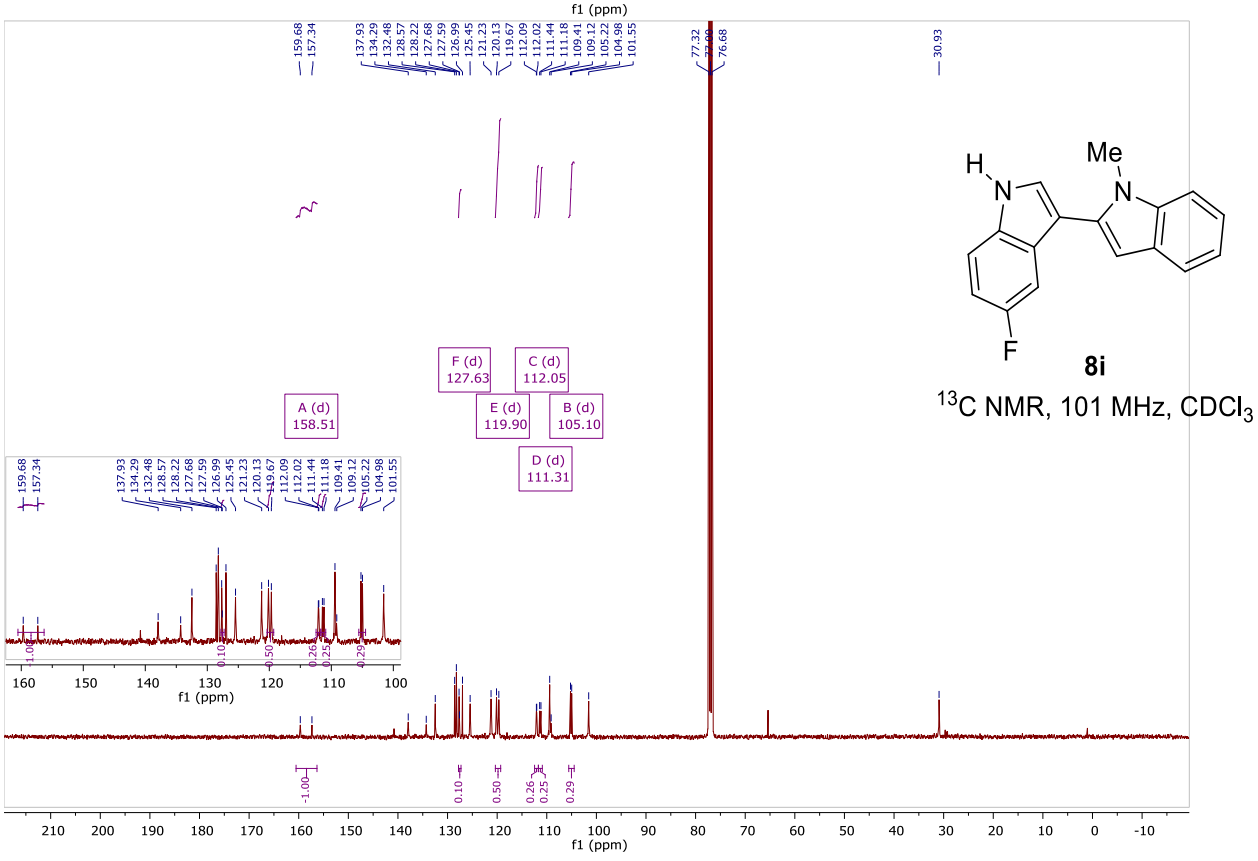


8h

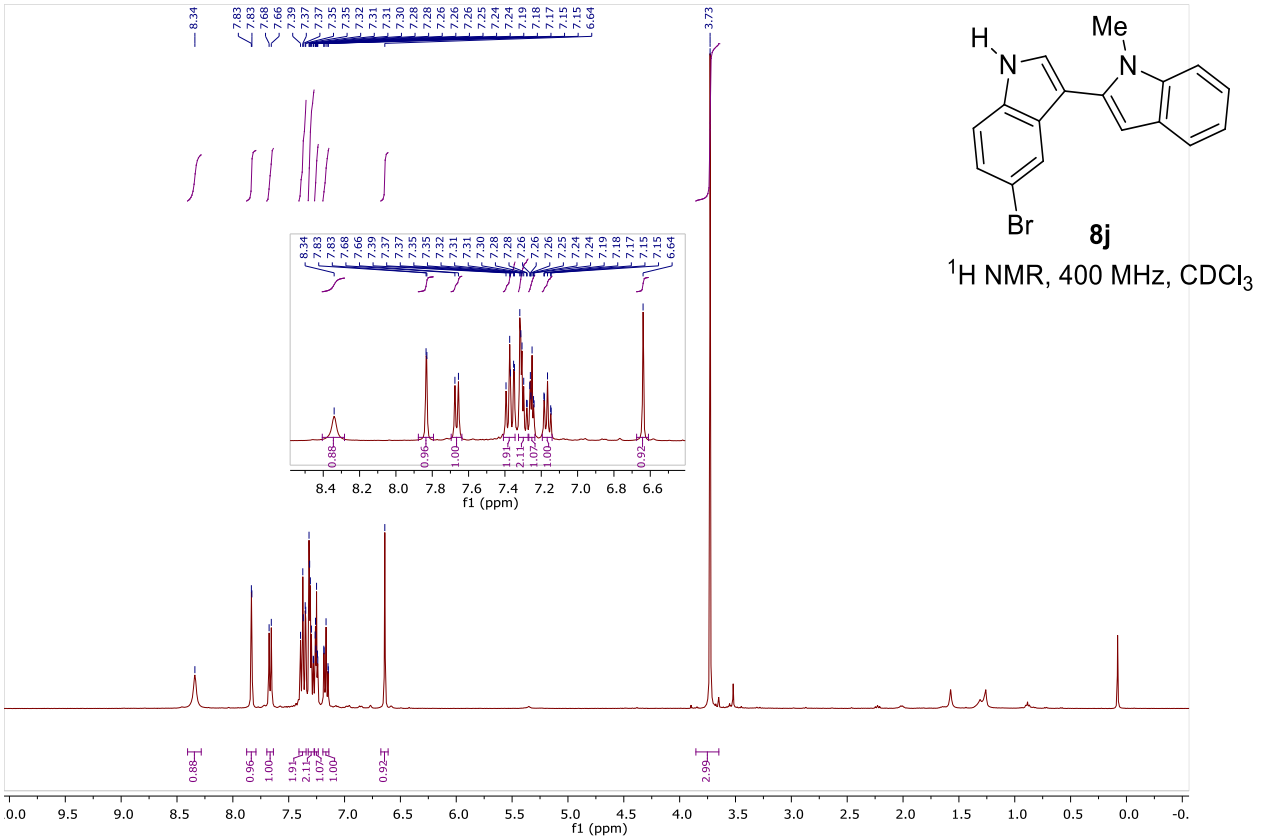
^{13}C NMR, 101 MHz, $CDCl_3$

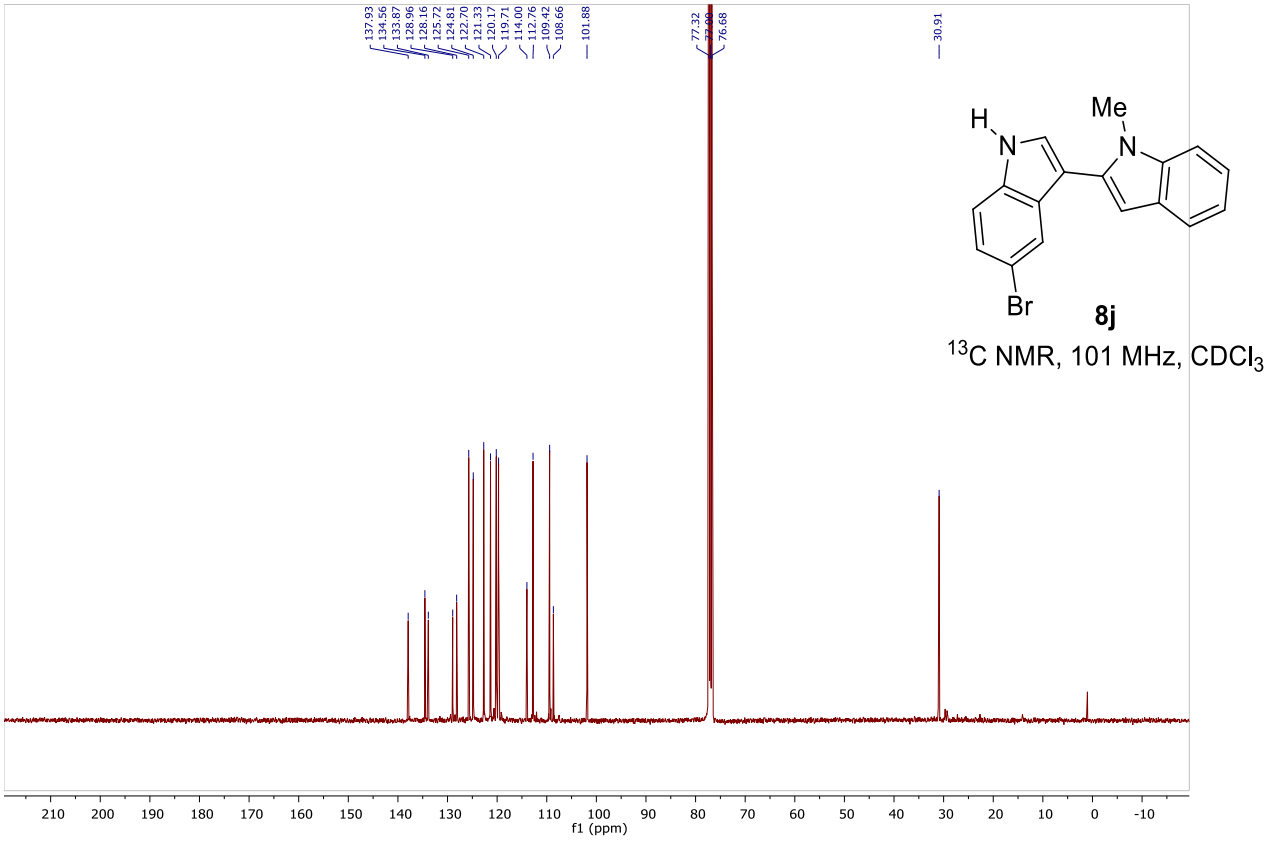
5'-Fluoro-1-methyl-1H,1'H-2,3'-biindole (8i)



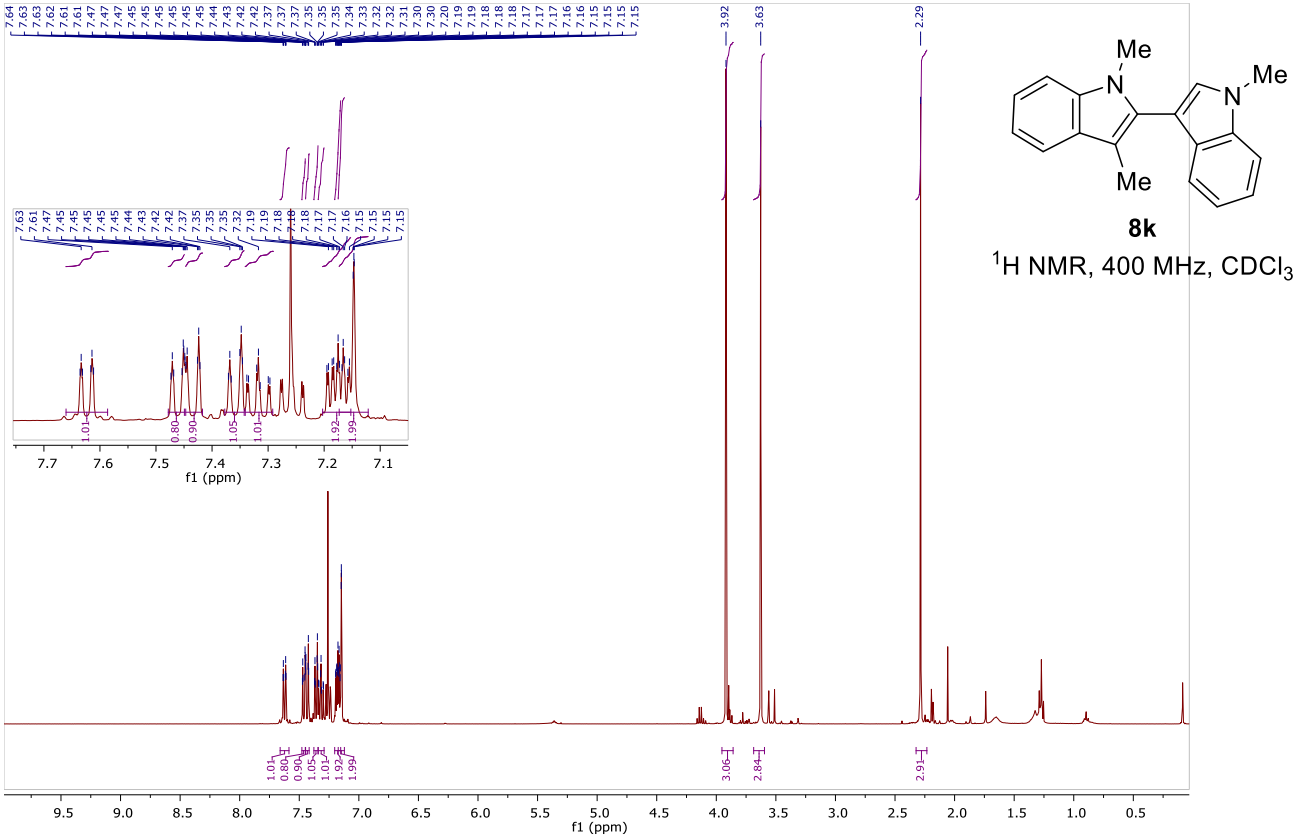


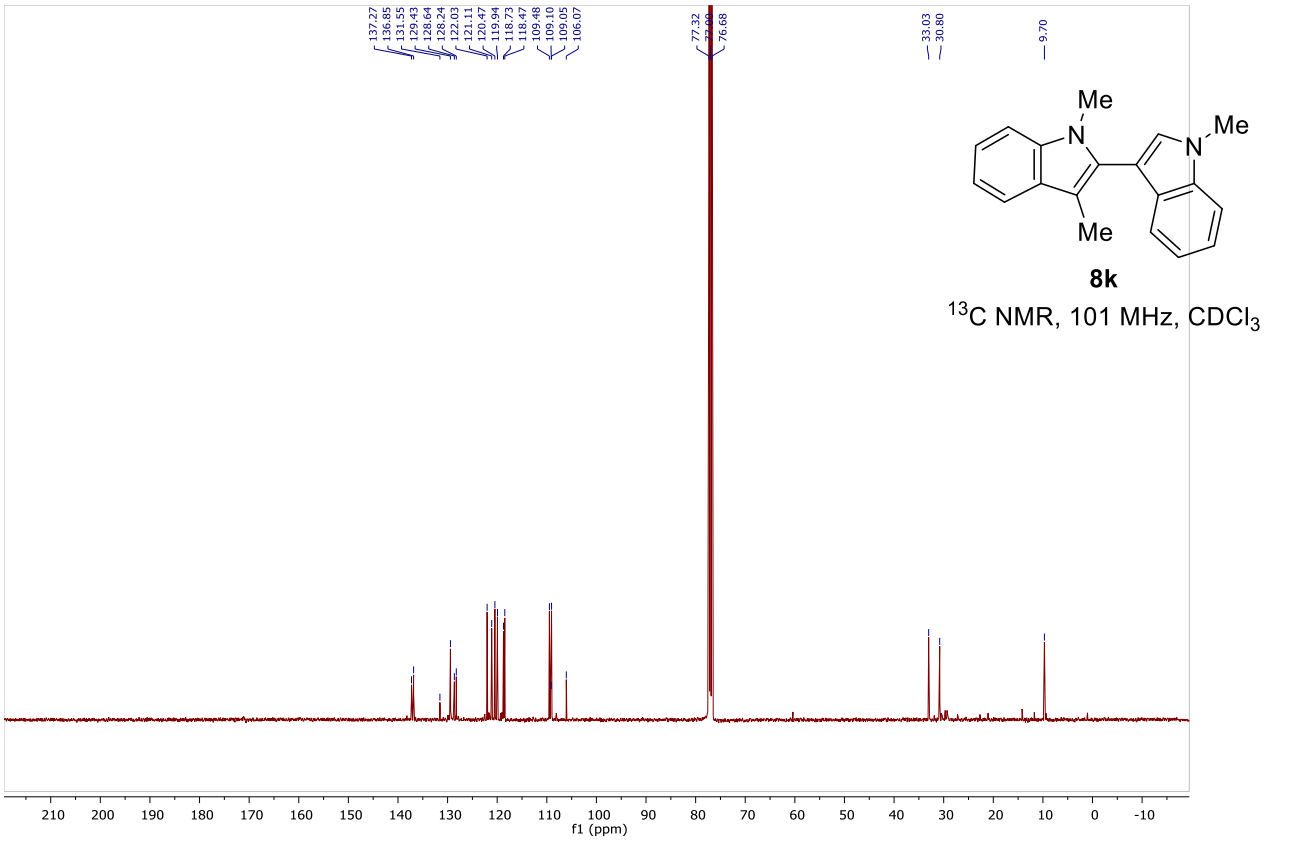
5'-Bromo-1-methyl-1H,1'H-2,3'-biindole (8j)



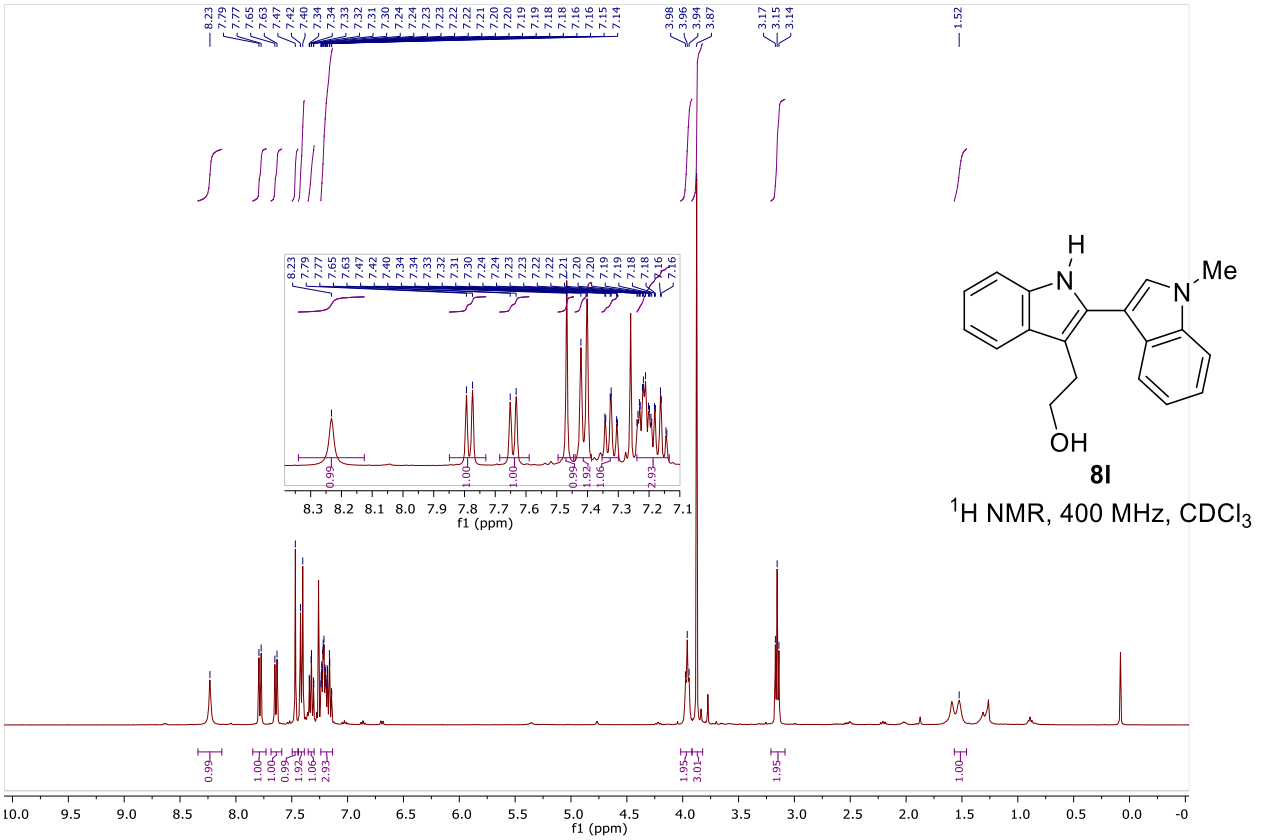


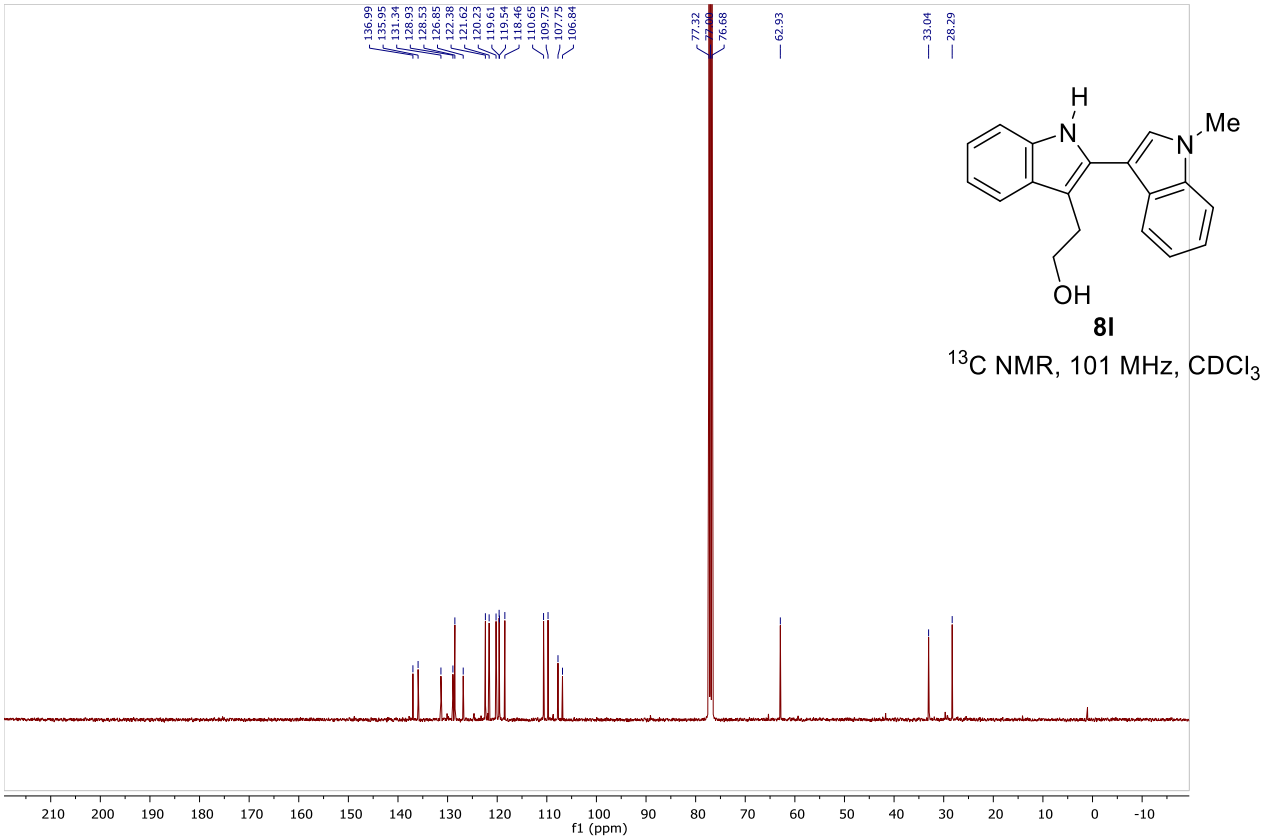
1,1',3-Trimethyl-1*H*,1'*H*-2,3'-biindole (8k)



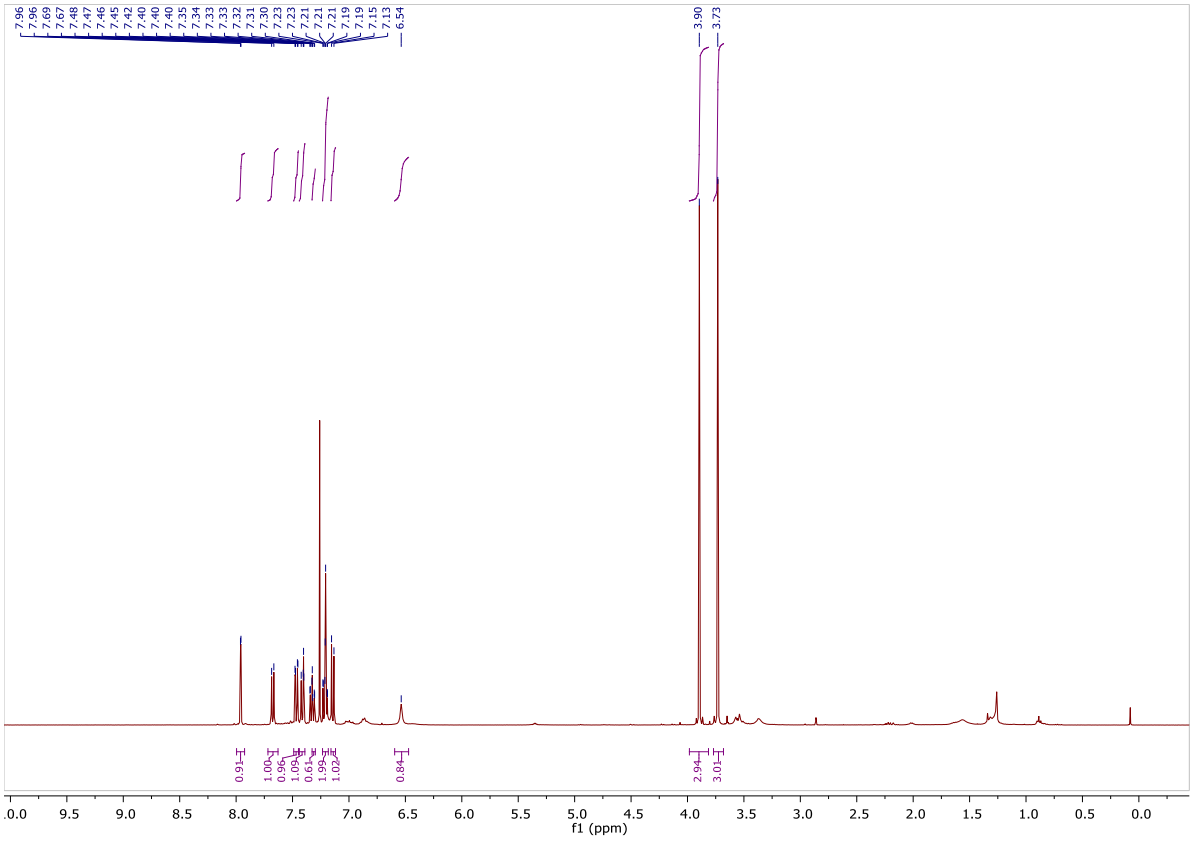


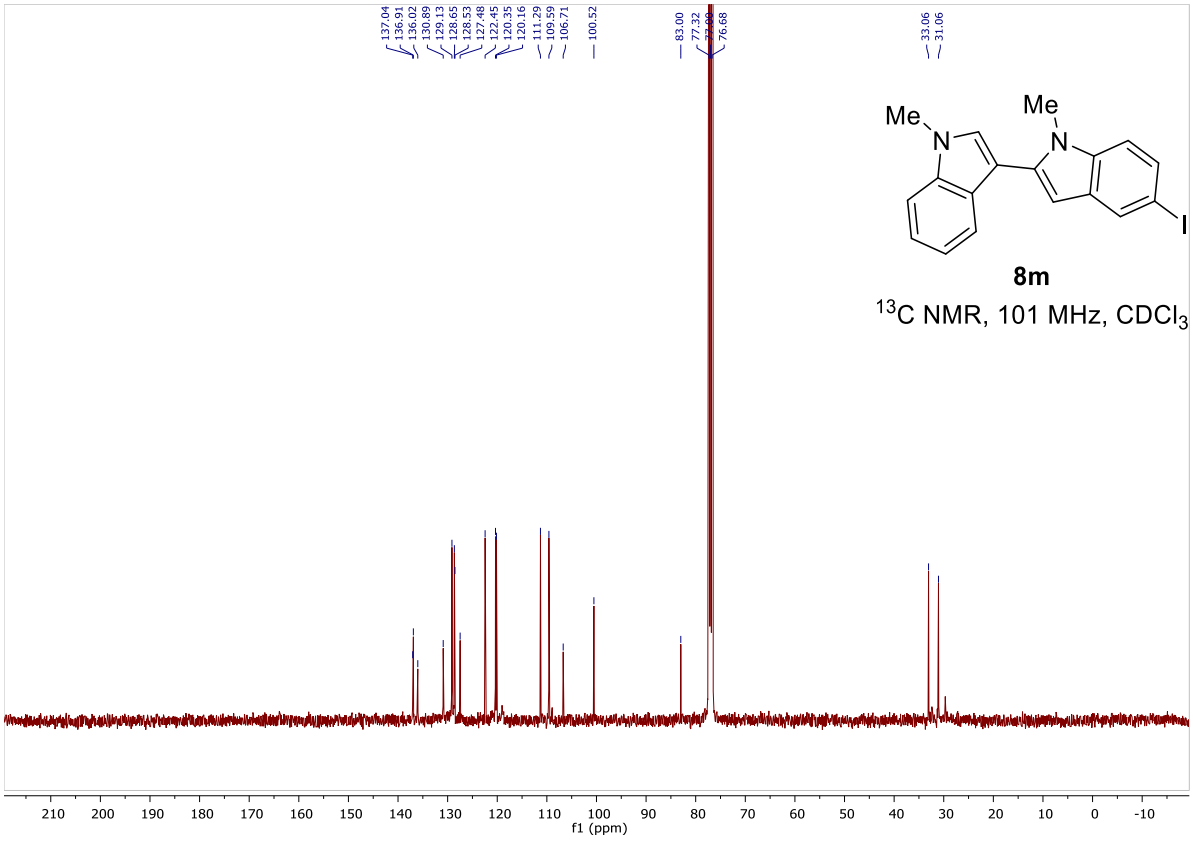
2-(1'-Methyl-1*H*,1'*H*-[2,3'-biindol]-3-yl)ethanol (8l)



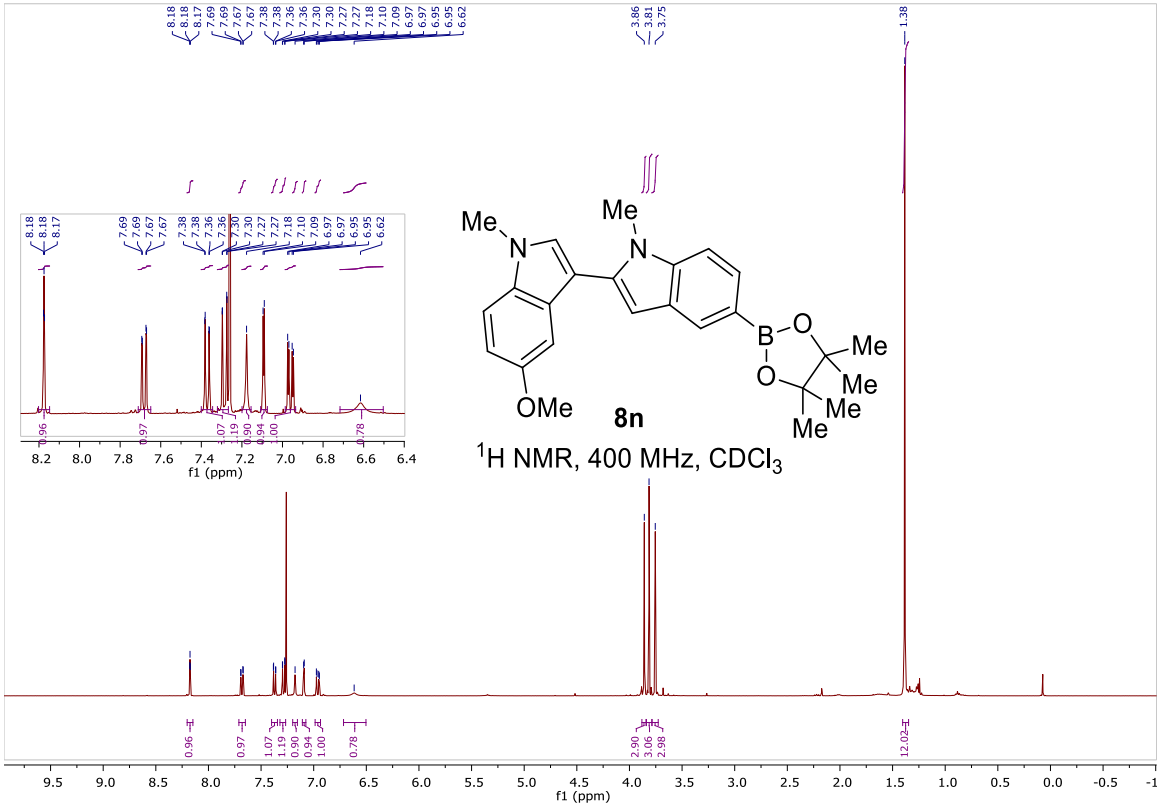


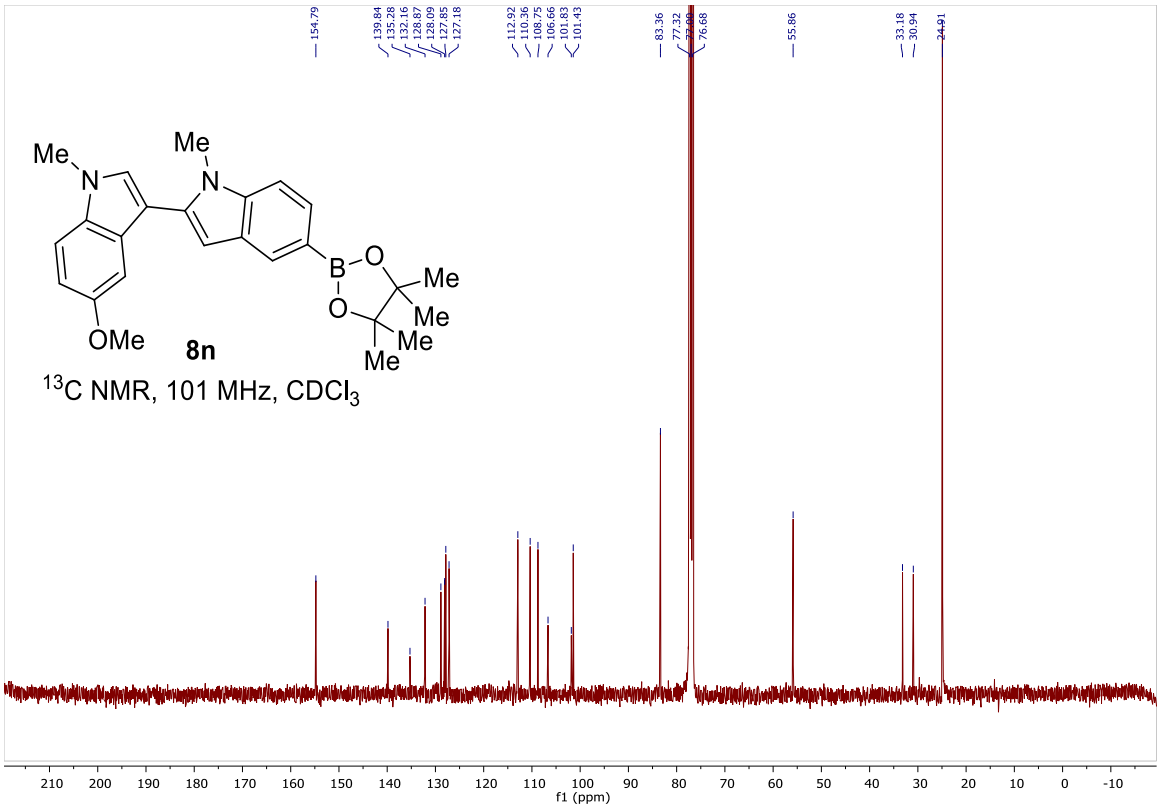
5-Iodo-1,1'-dimethyl-1H,1'H-2,3'-biindole (8m)



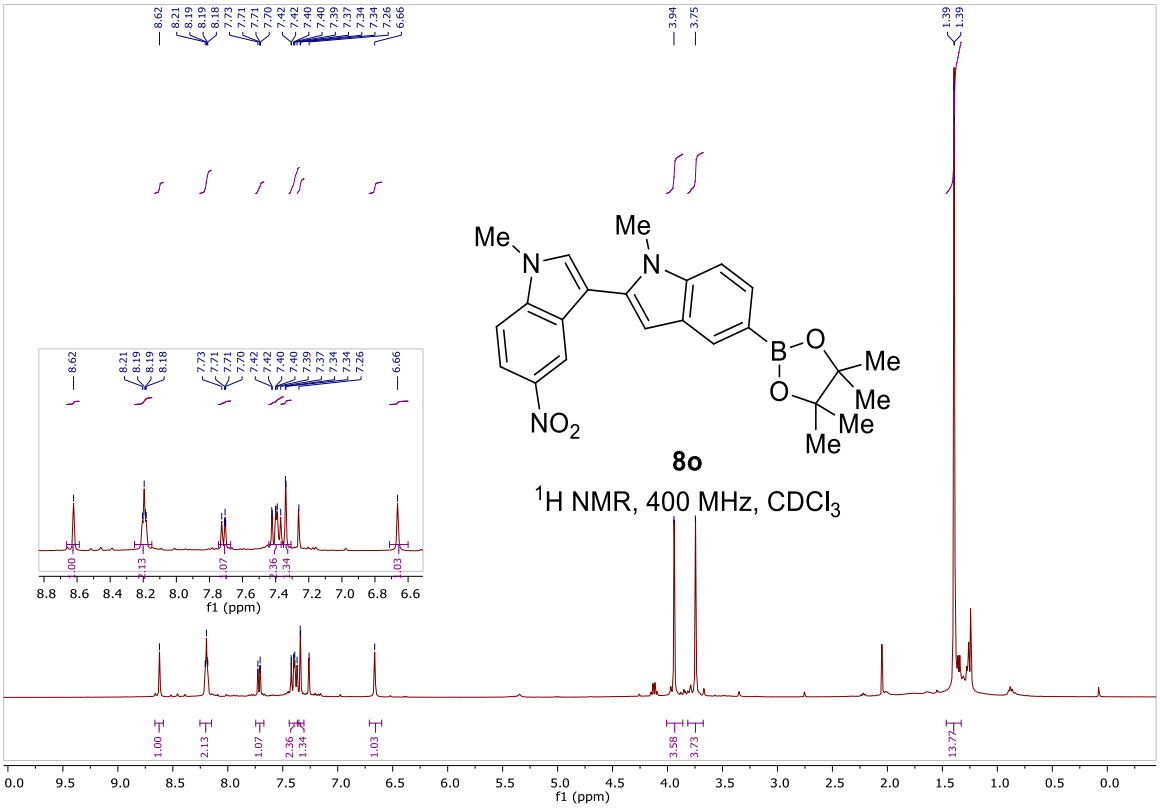


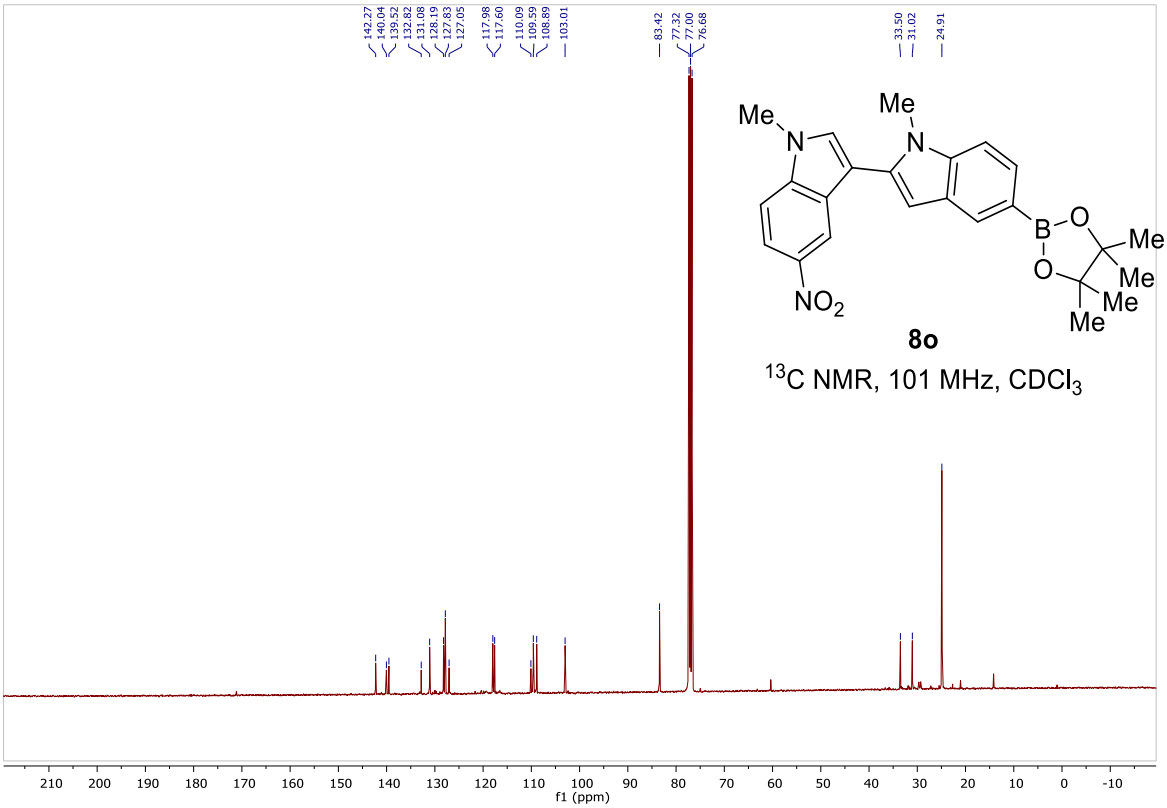
5'-Methoxy-1,1'-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*,1'*H*-2,3'-biindole (8n).



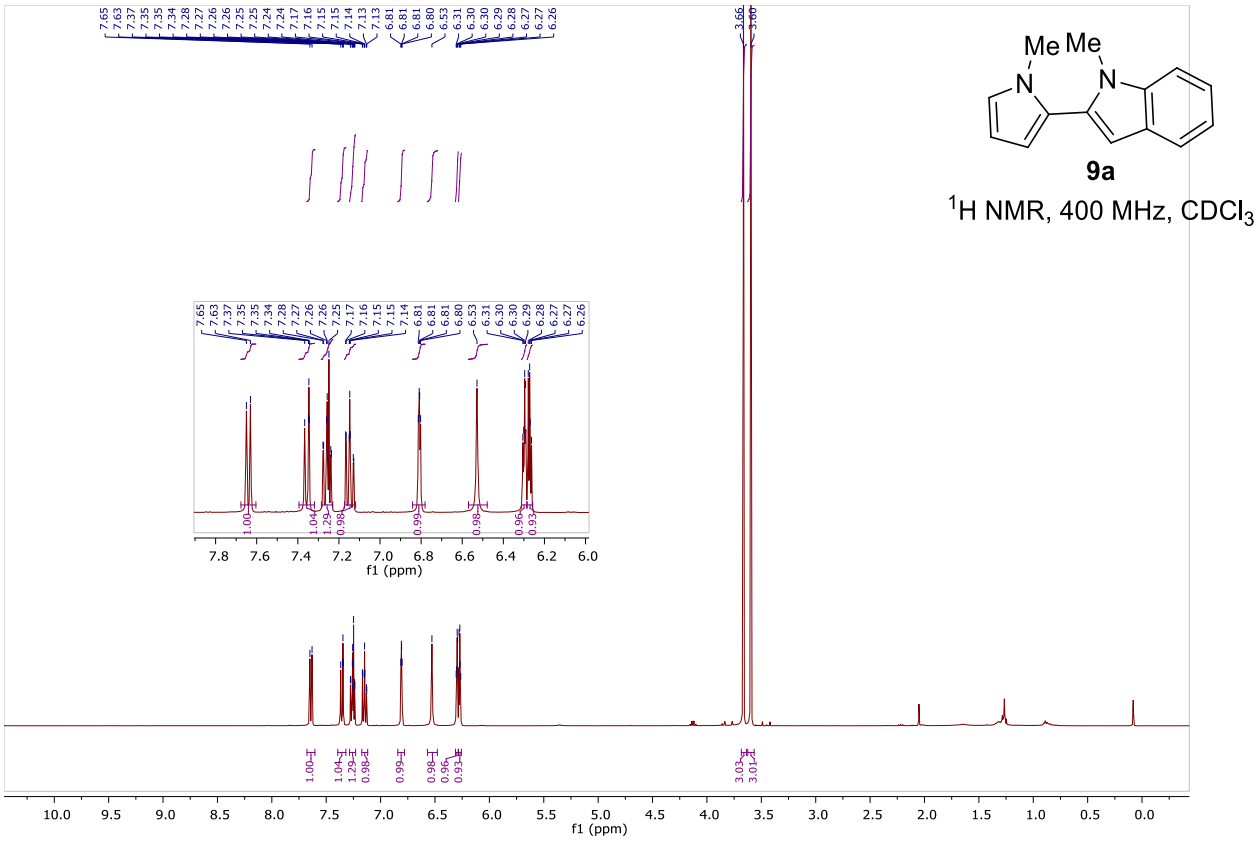


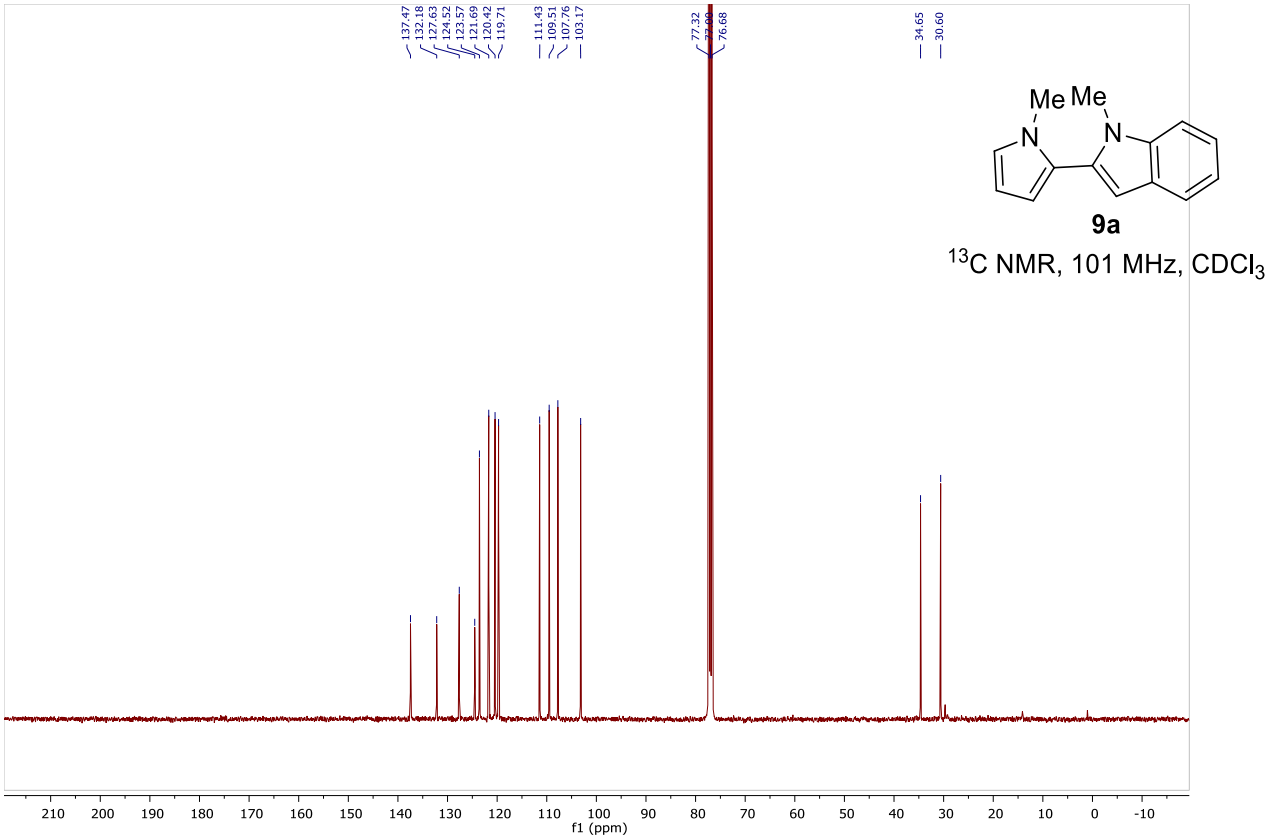
5'-Nitro-1,1'-dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*,1'*H*-2,3'-biindole (8o)



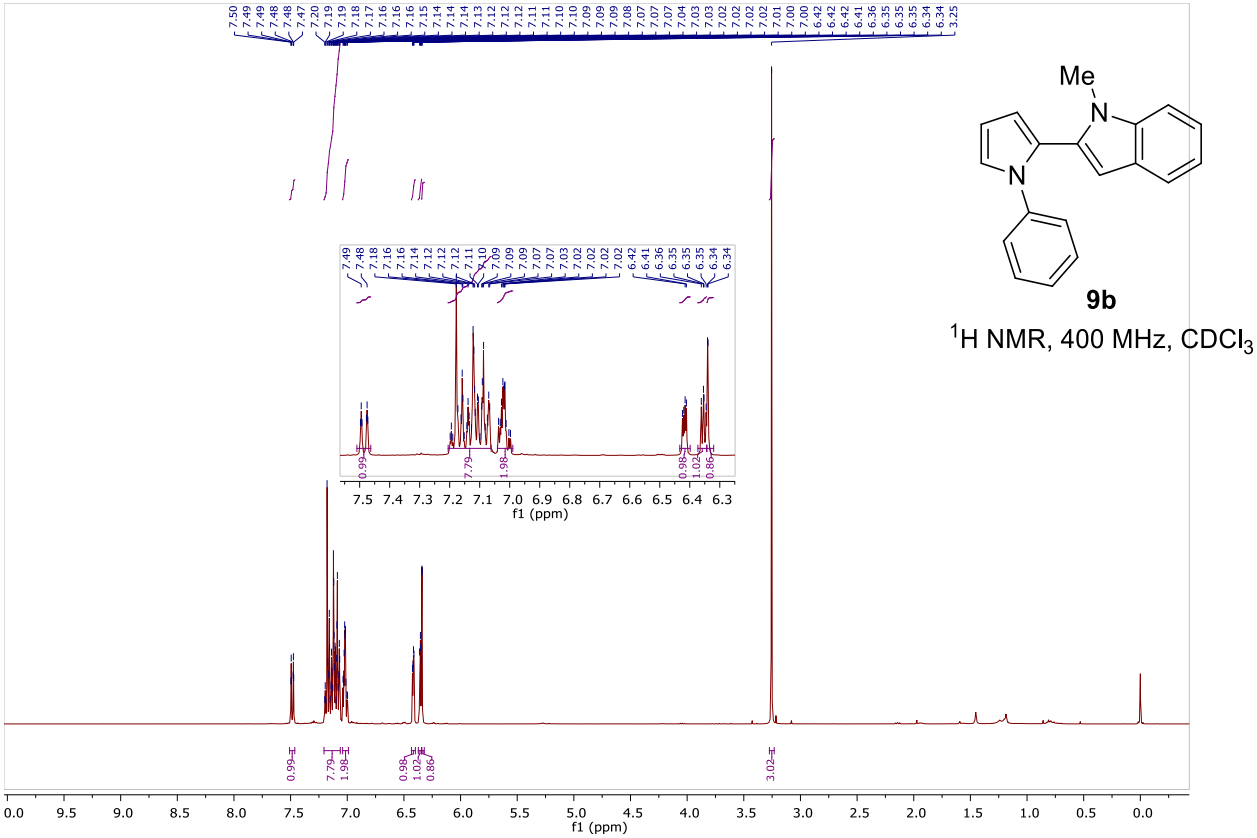


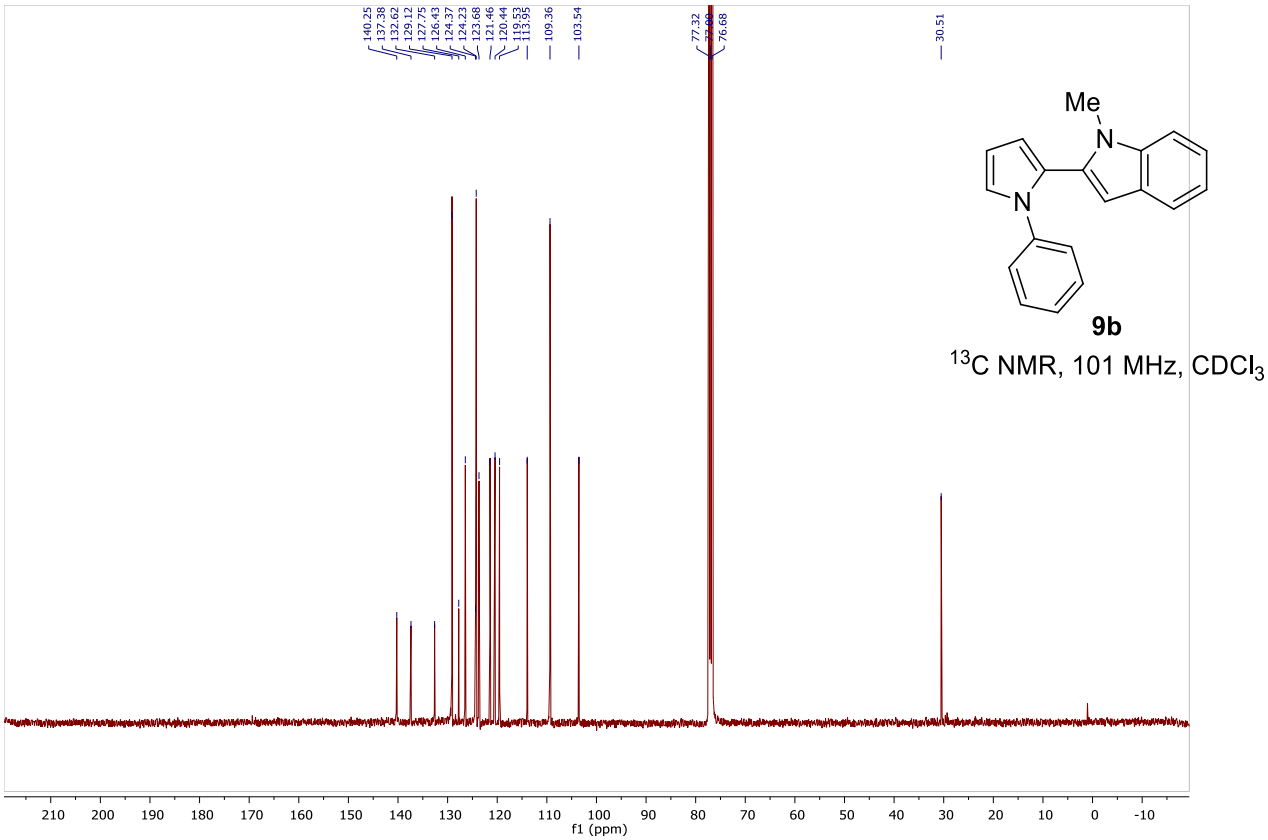
1-Methyl-2-(1-methyl-1*H*-pyrrol-2-yl)-1*H*-indole (9a)


Me Me
N
N
9a
1H NMR, 400 MHz, CDCl3
f1 (ppm)

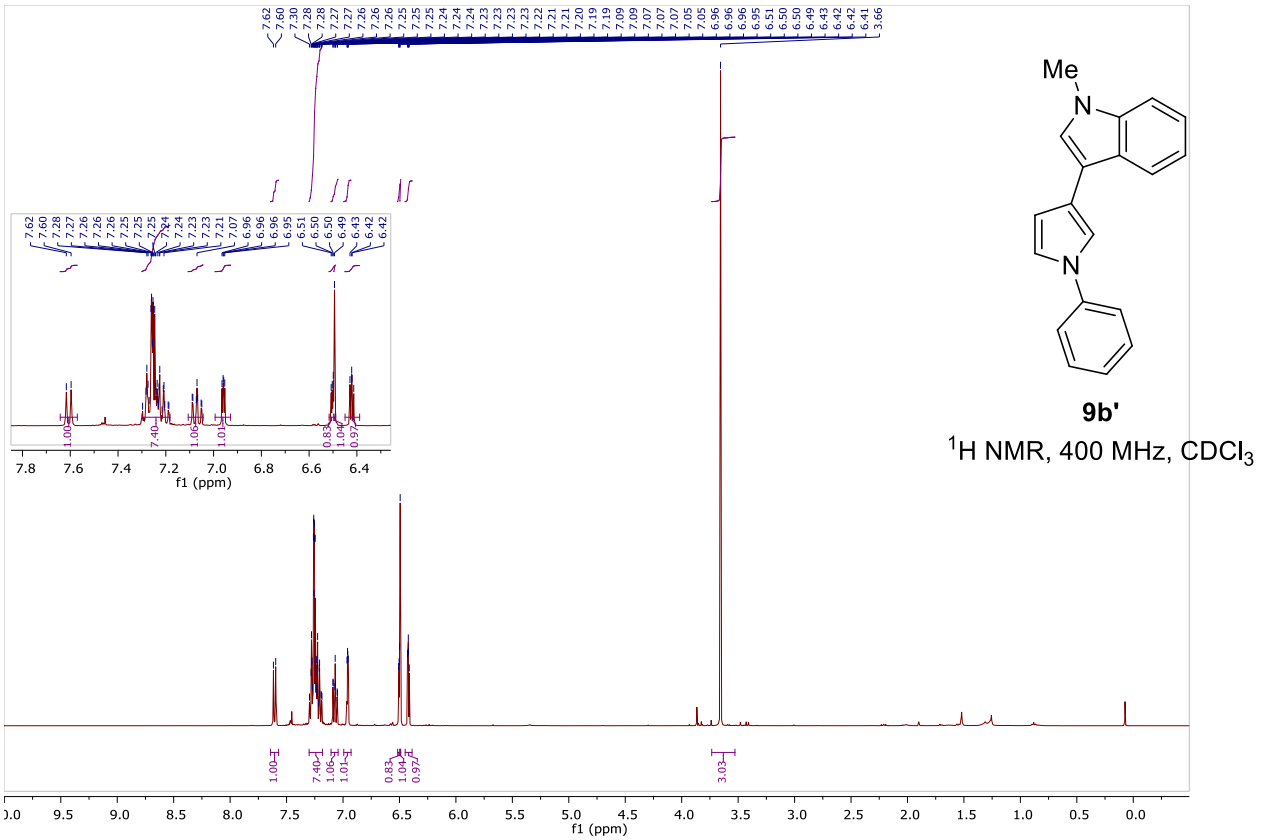

Me Me
N
N
9a
13C NMR, 101 MHz, CDCl3
f1 (ppm)

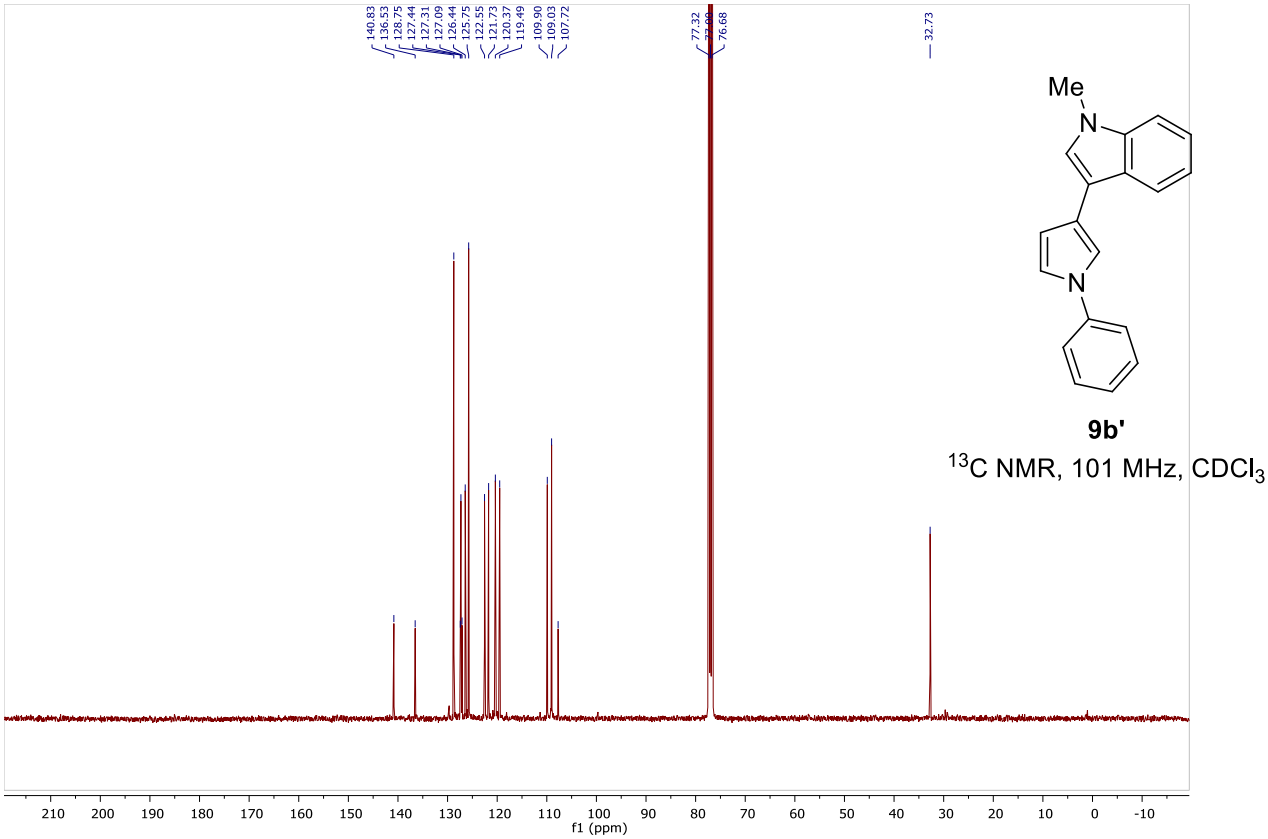
1-Methyl-2-(1-phenyl-1*H*-pyrrol-2-yl)-1*H*-indole (9b)



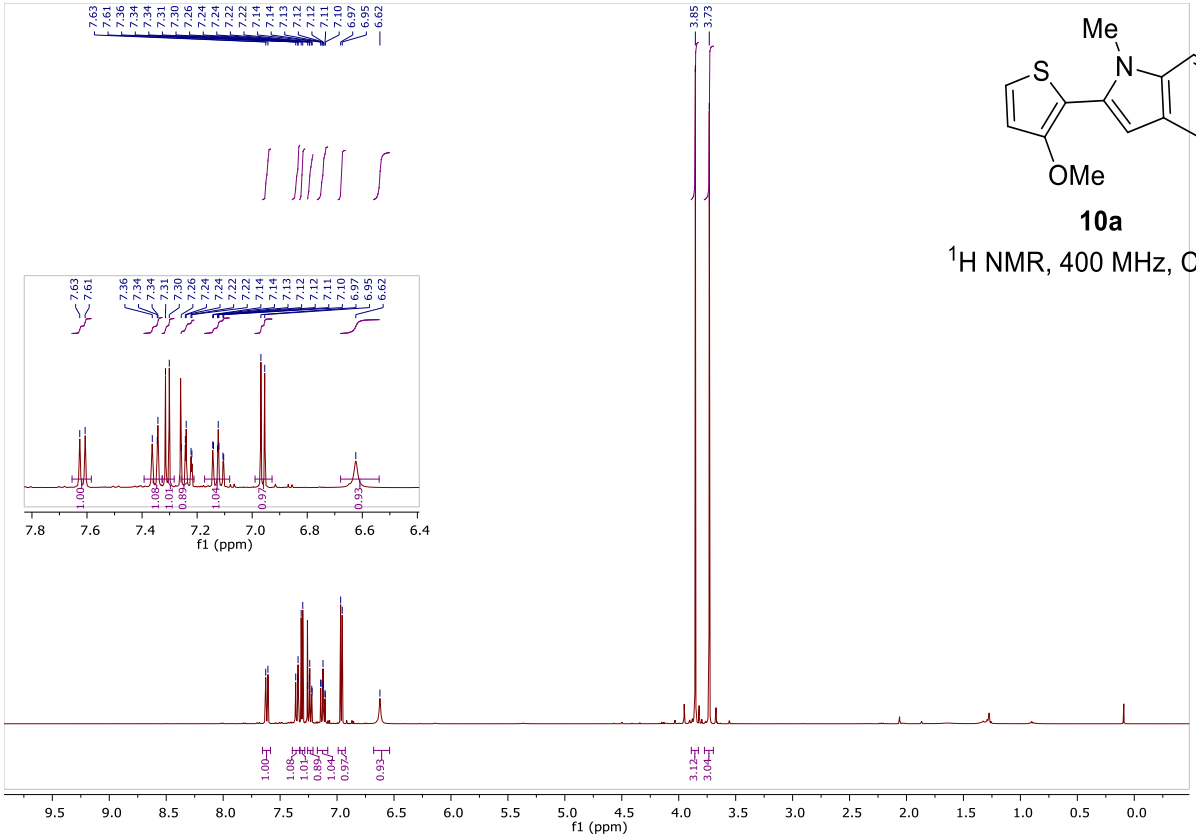


1-methyl-2-(1-phenyl-1*H*-pyrrol-3-yl)-1*H*-indole (9b')



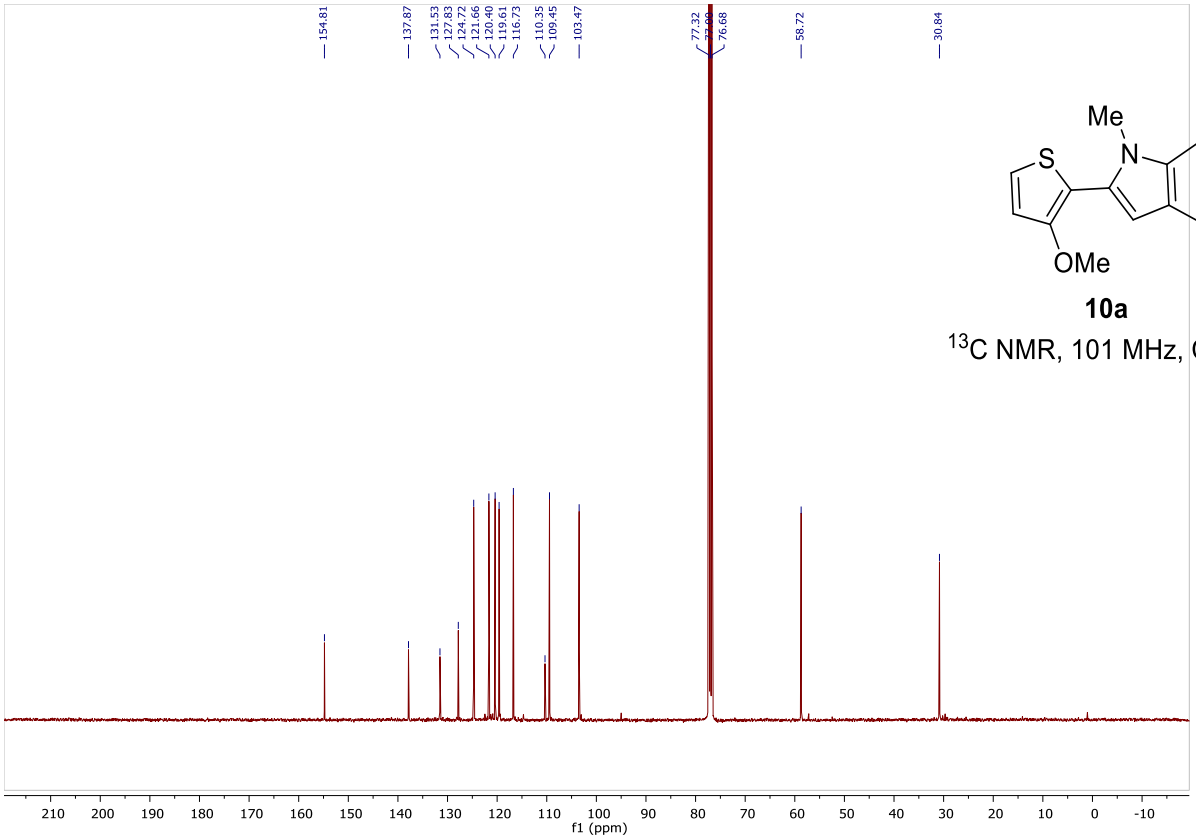


2-(3-Methoxythiophen-2-yl)-1-methyl-1*H*-indole (10a)



10a

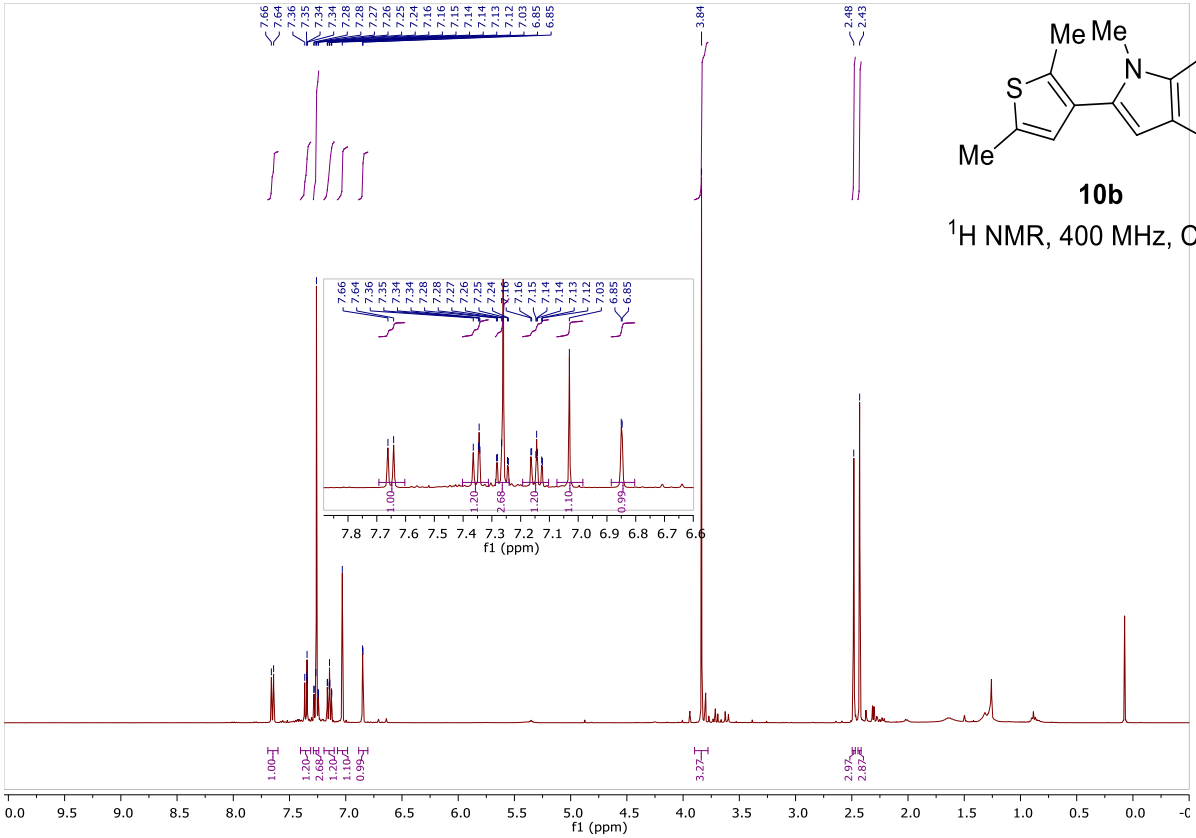
^{1}H NMR, 400 MHz, $CDCl_3$

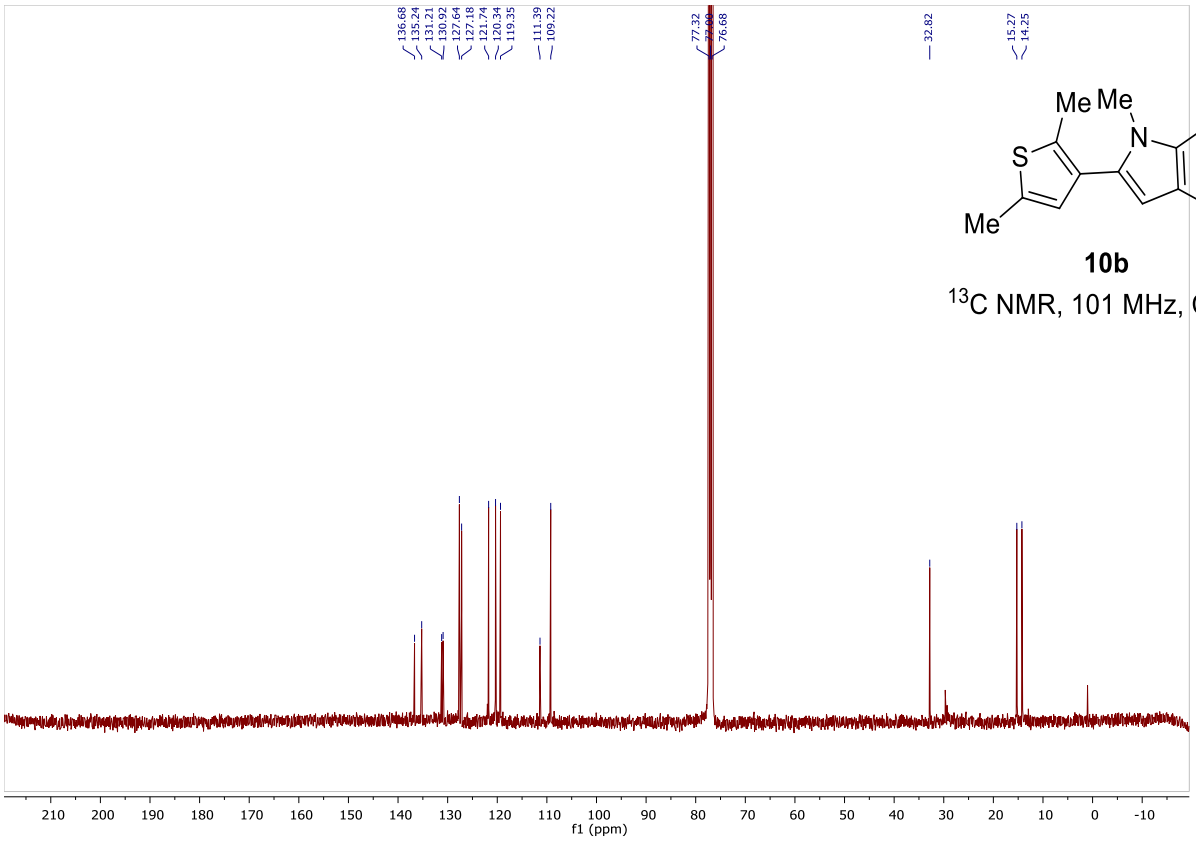


10a

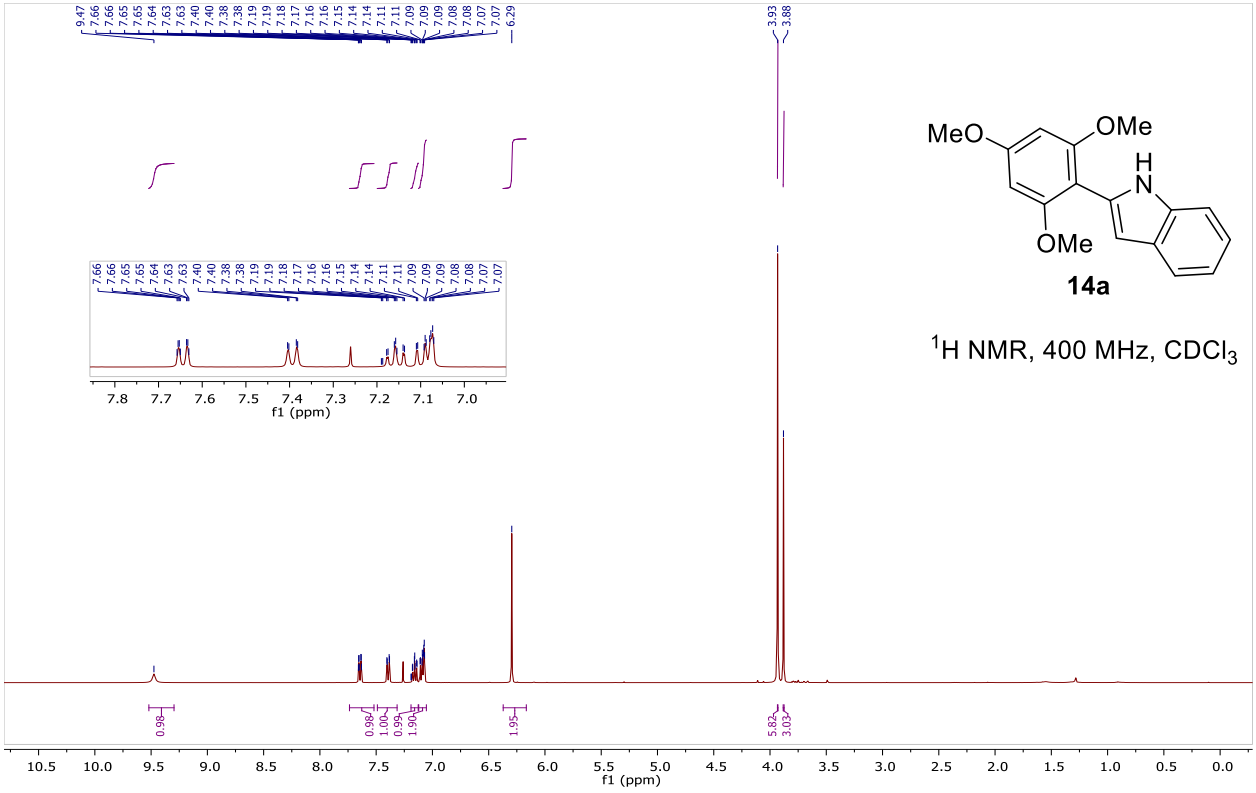
^{13}C NMR, 101 MHz, $CDCl_3$

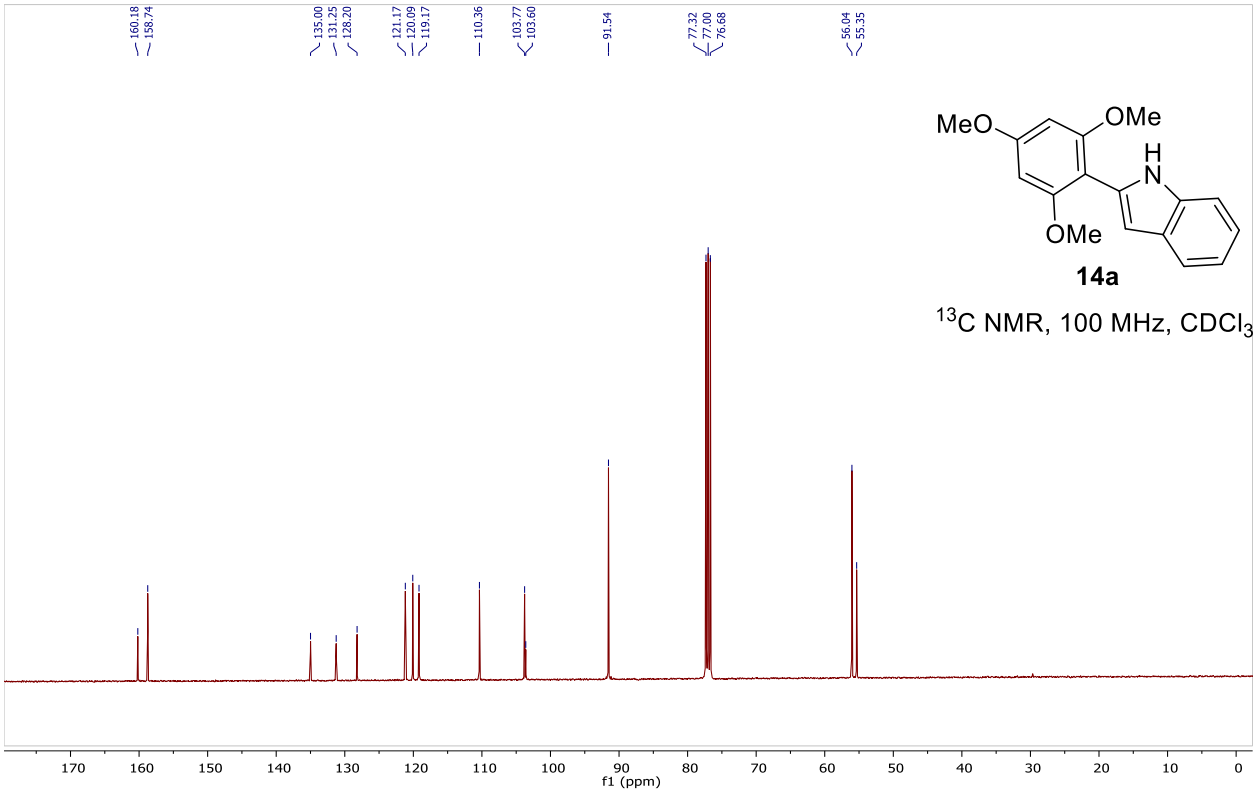
2-(2,5-Dimethylthiophen-3-yl)-1-methyl-1*H*-indole (10b)



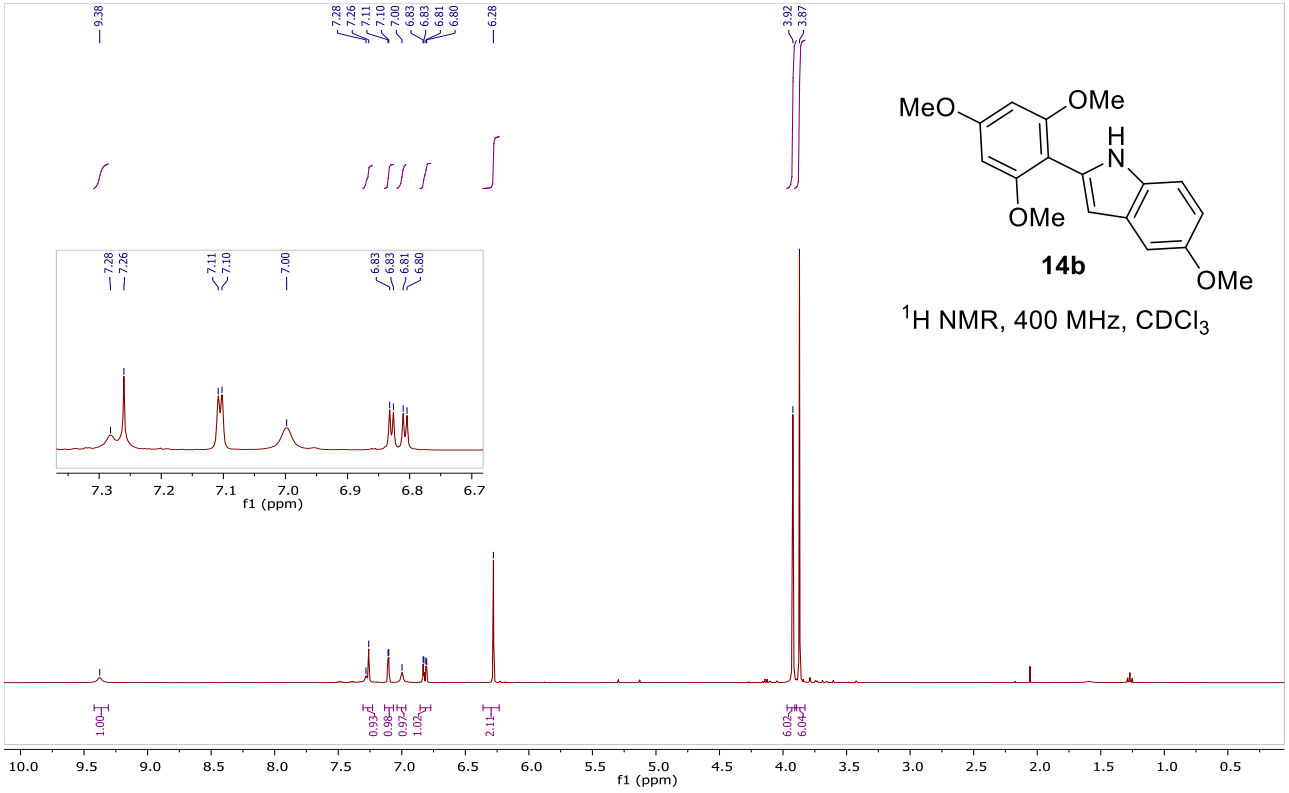


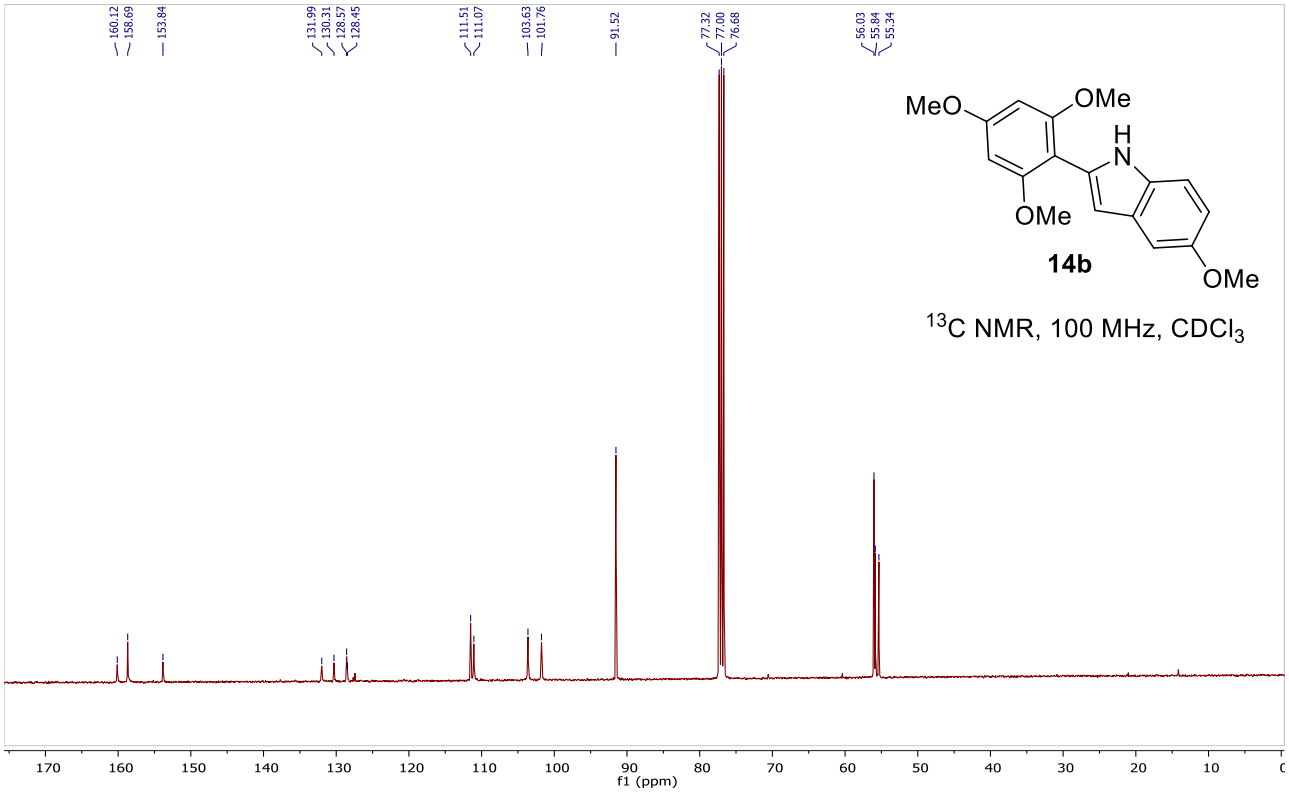
2-(2,4,6-Trimethoxyphenyl)-1*H*-indole (14a)



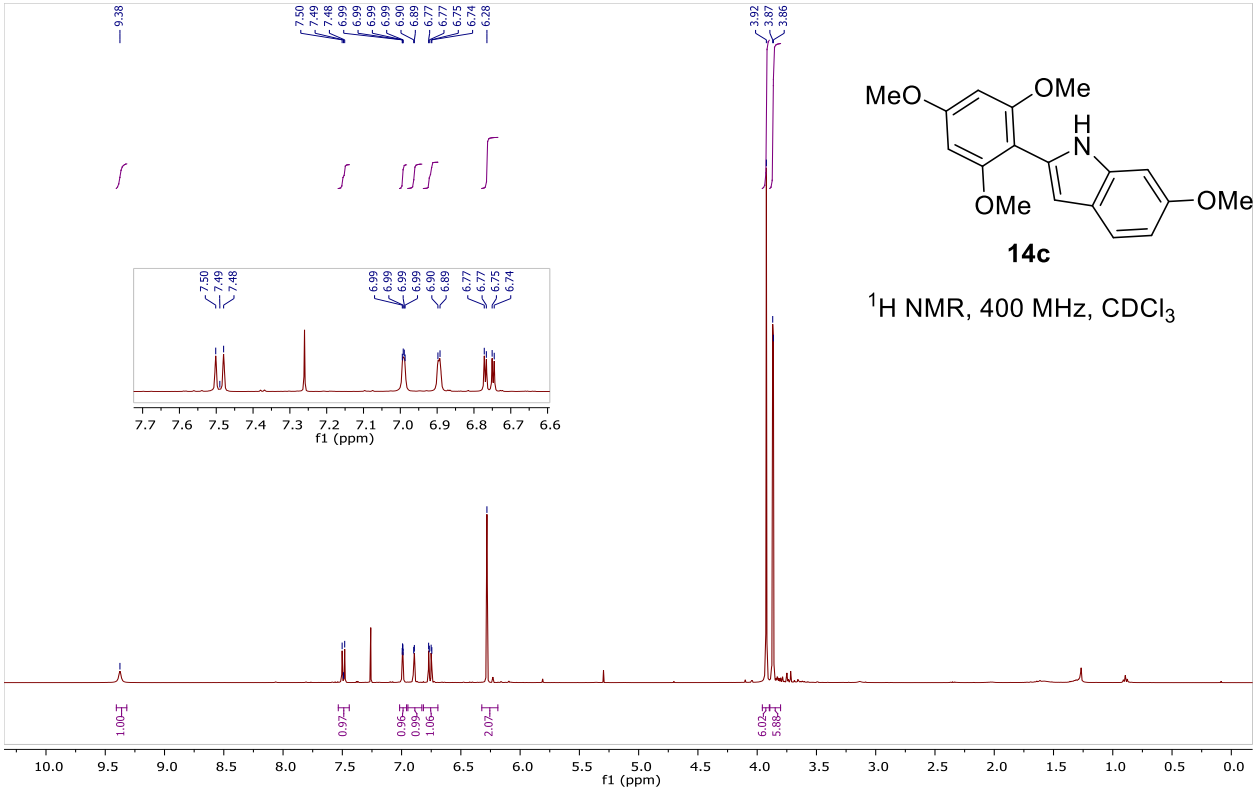


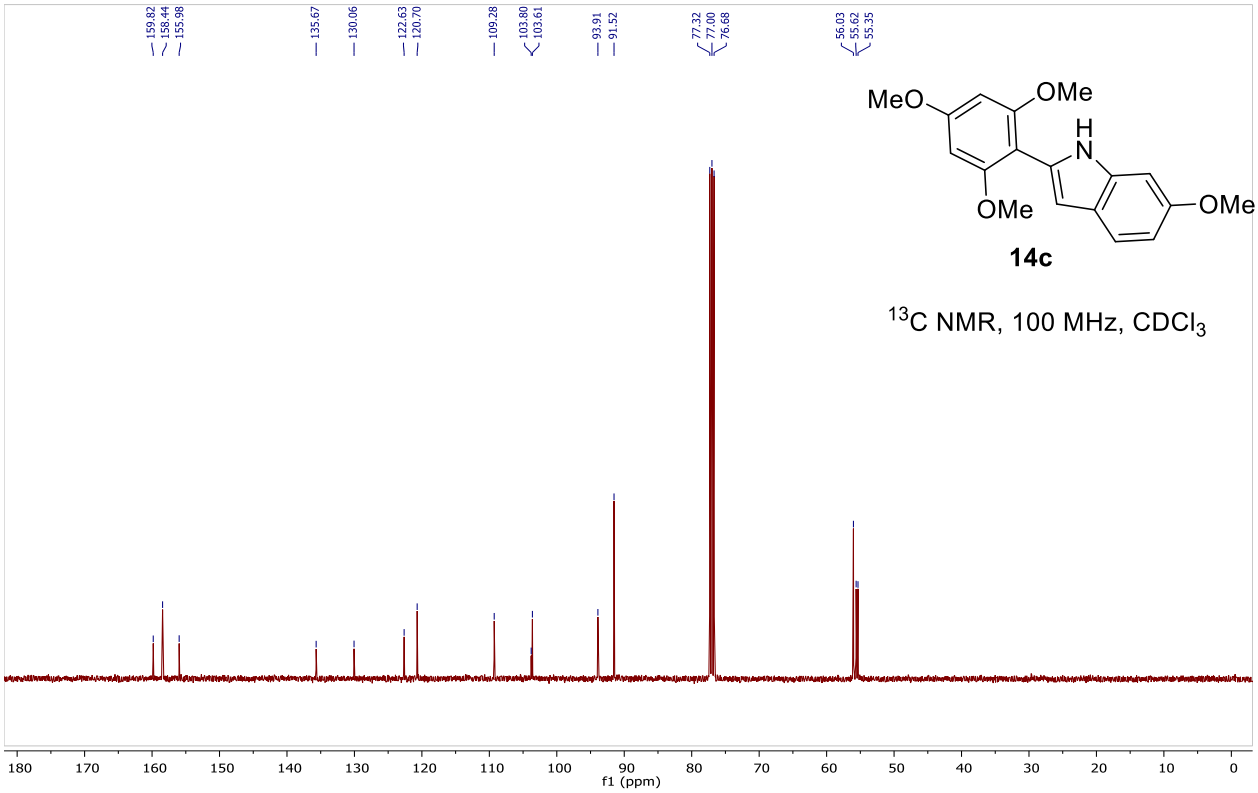
5-Methoxy-2-(2,4,6-trimethoxyphenyl)-1*H*-indole (14b)



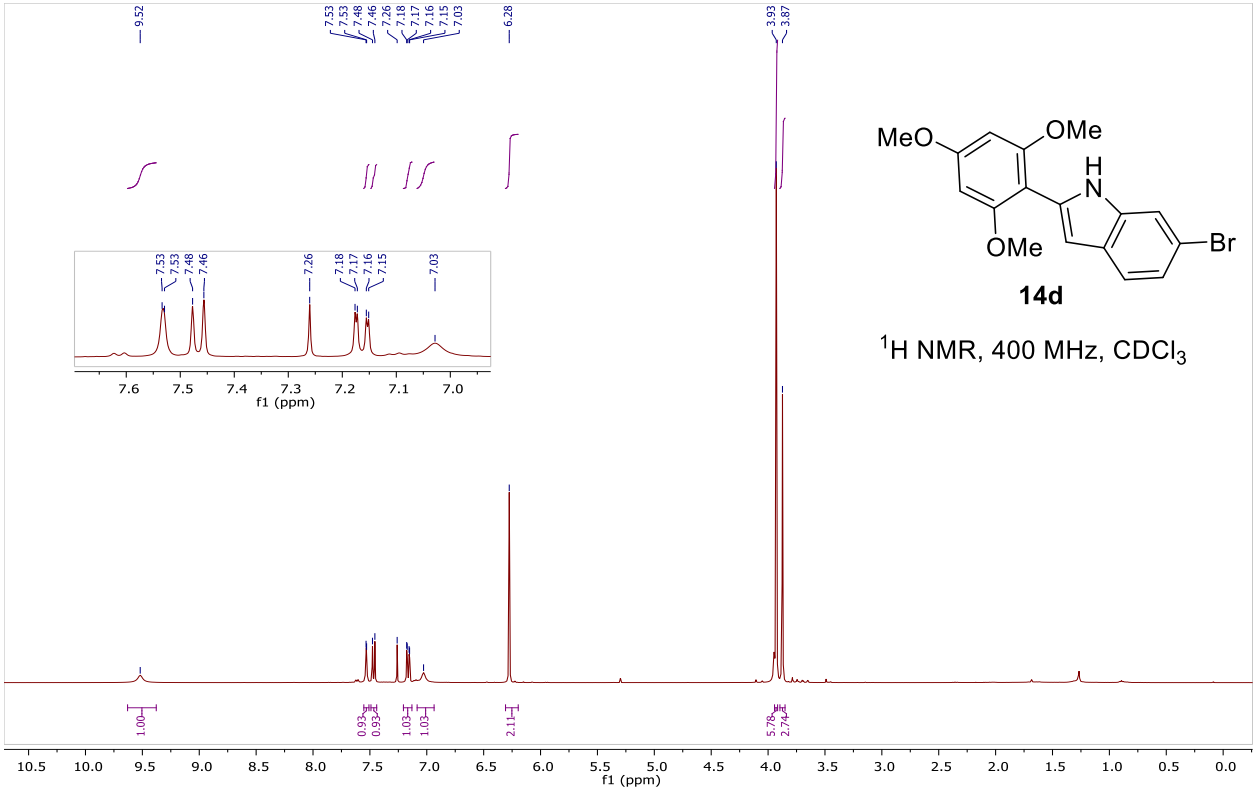


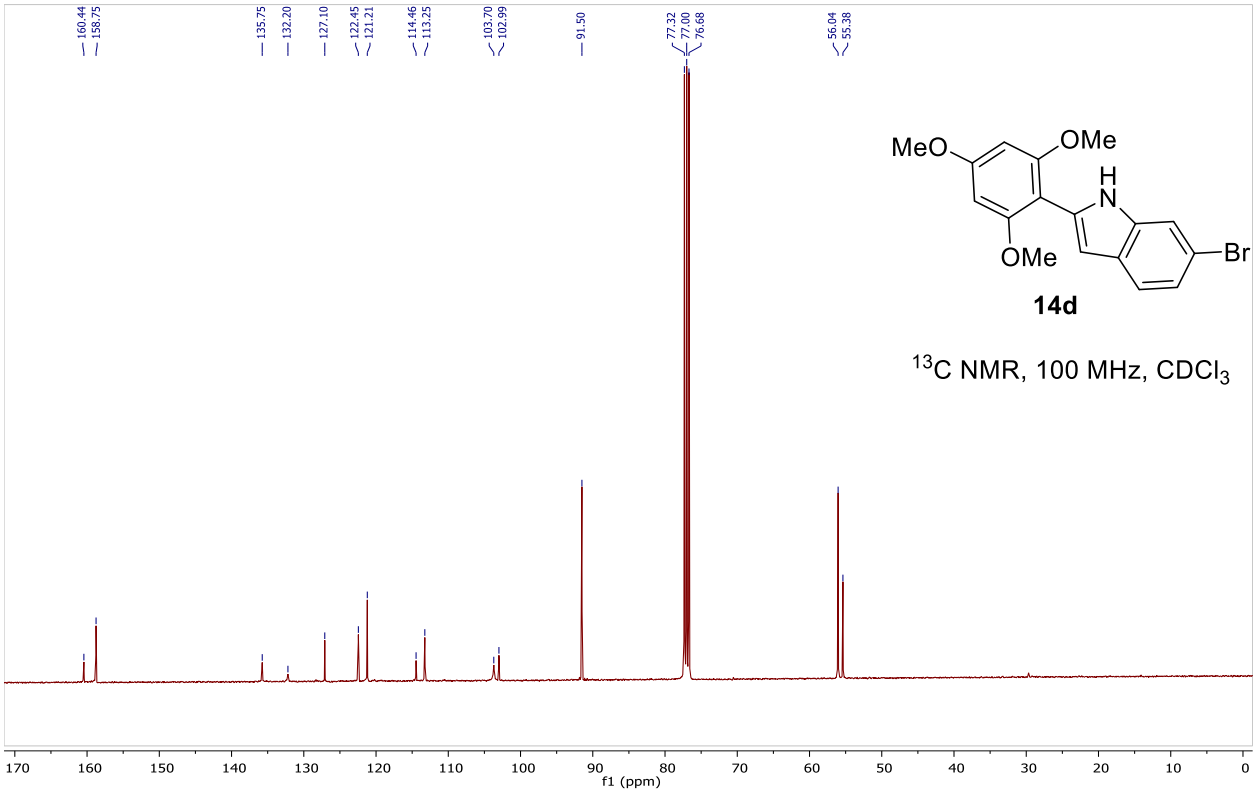
6-Methoxy-2-(2,4,6-trimethoxyphenyl)-1*H*-indole (14c)



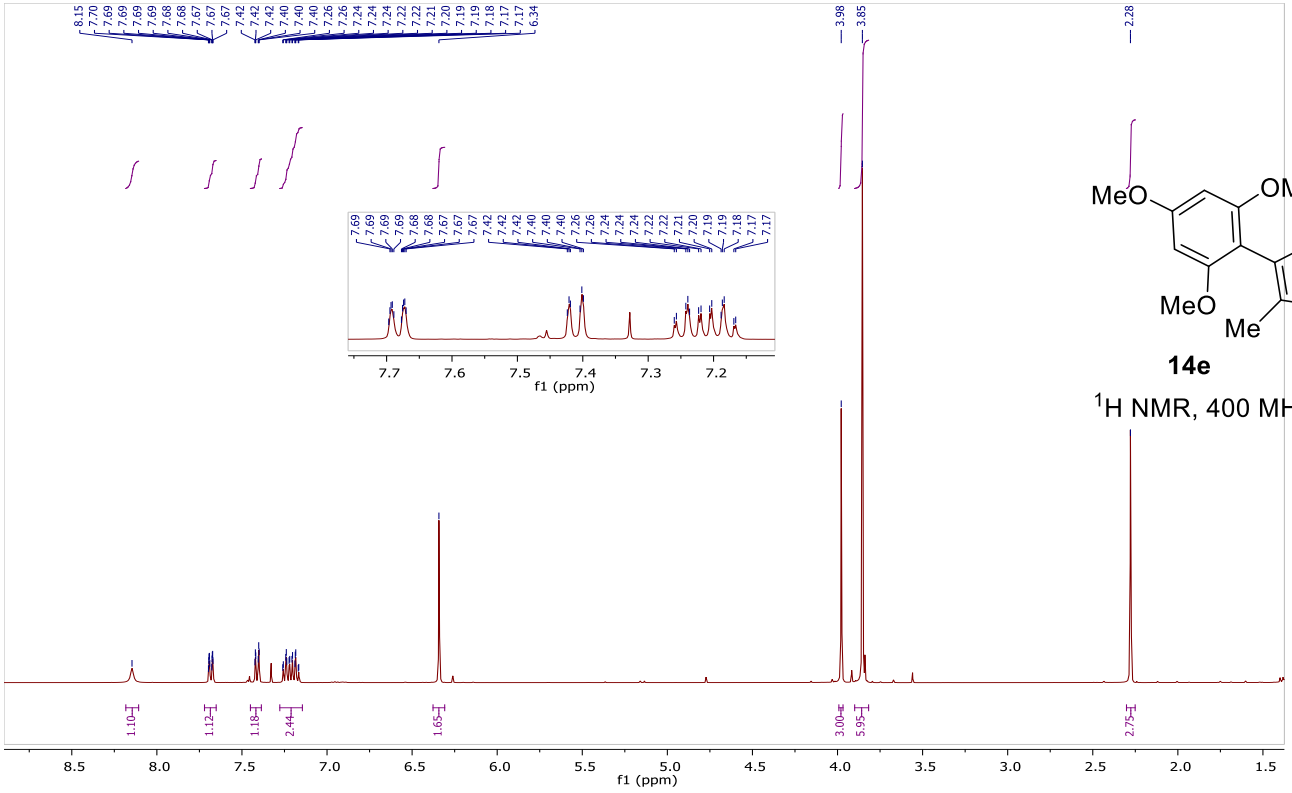


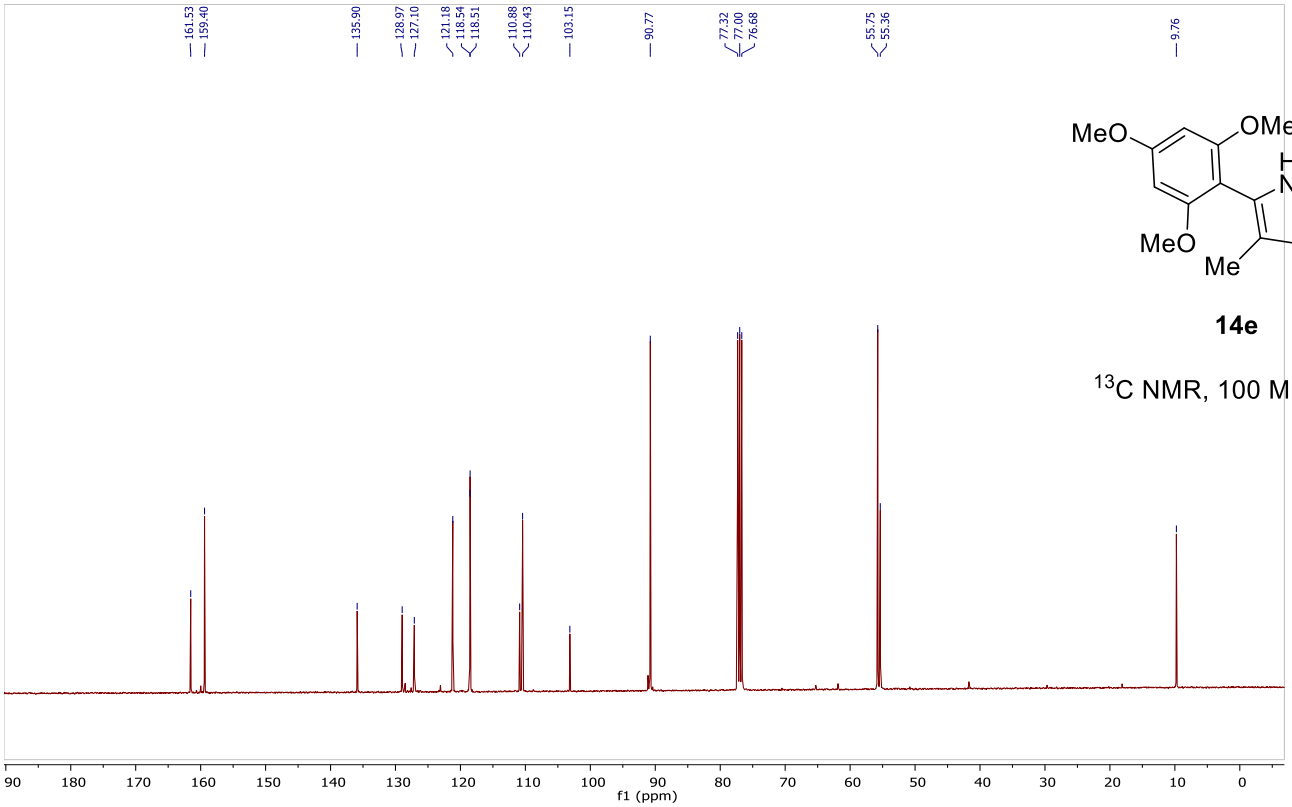
6-Bromo-2-(2,4,6-trimethoxyphenyl)-1*H*-indole (14d)



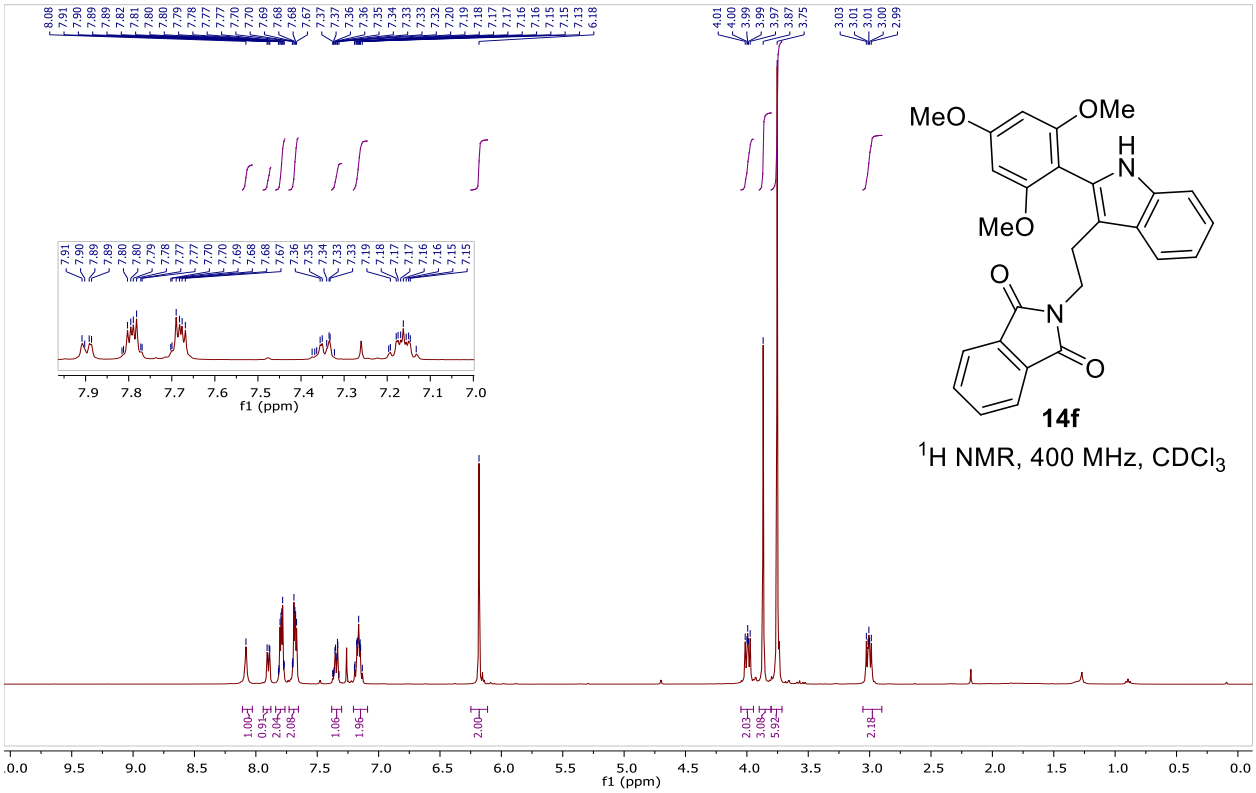


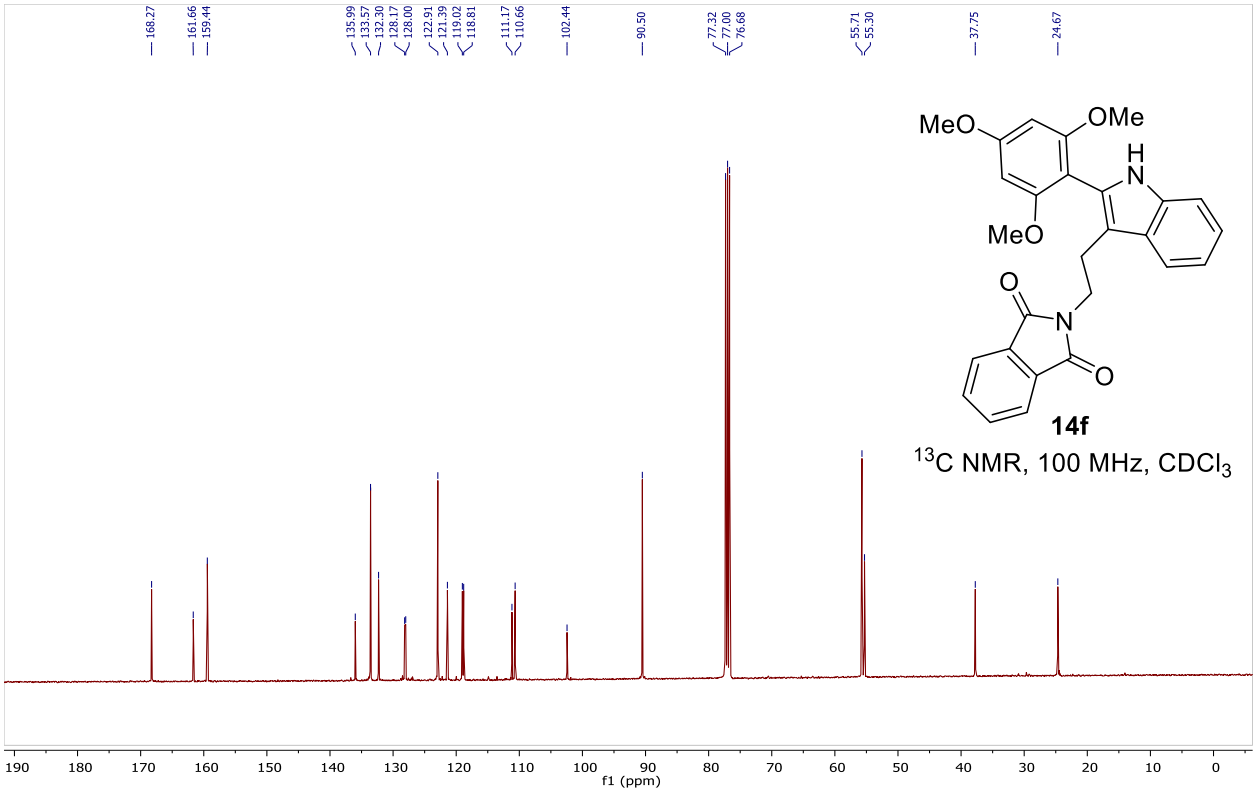
3-Methyl-2-(2,4,6-trimethoxyphenyl)-1*H*-indole (14e)



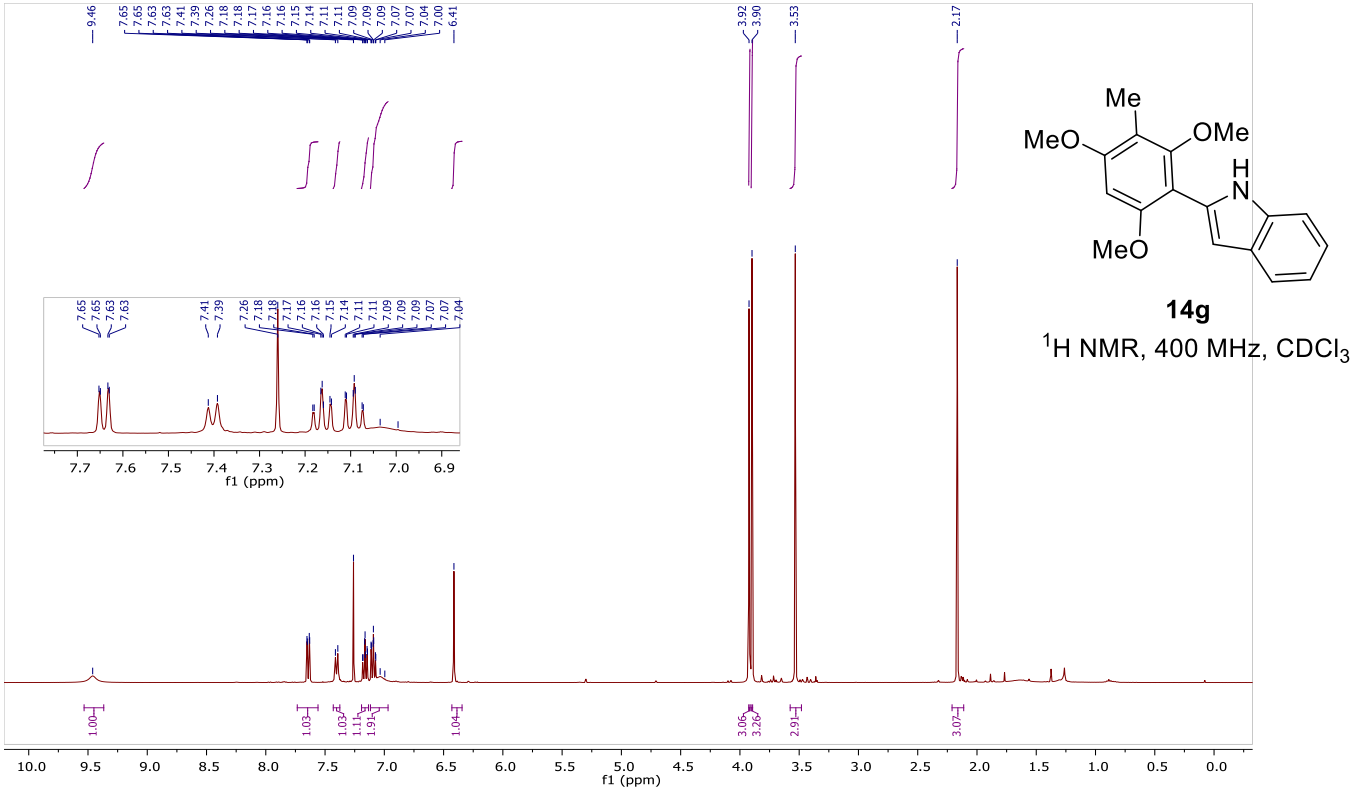


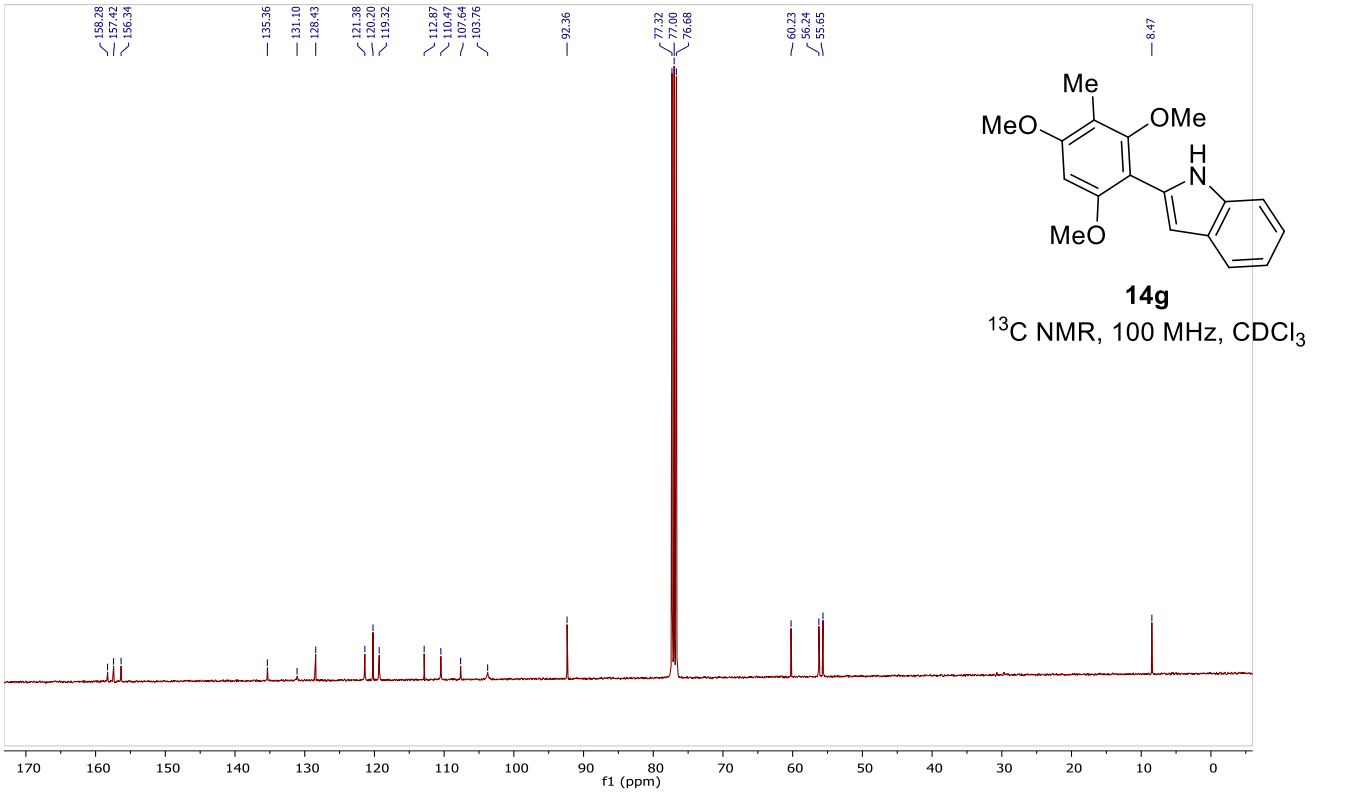
2-(2-(2-(2,4,6-Trimethoxyphenyl)-1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione (14f)



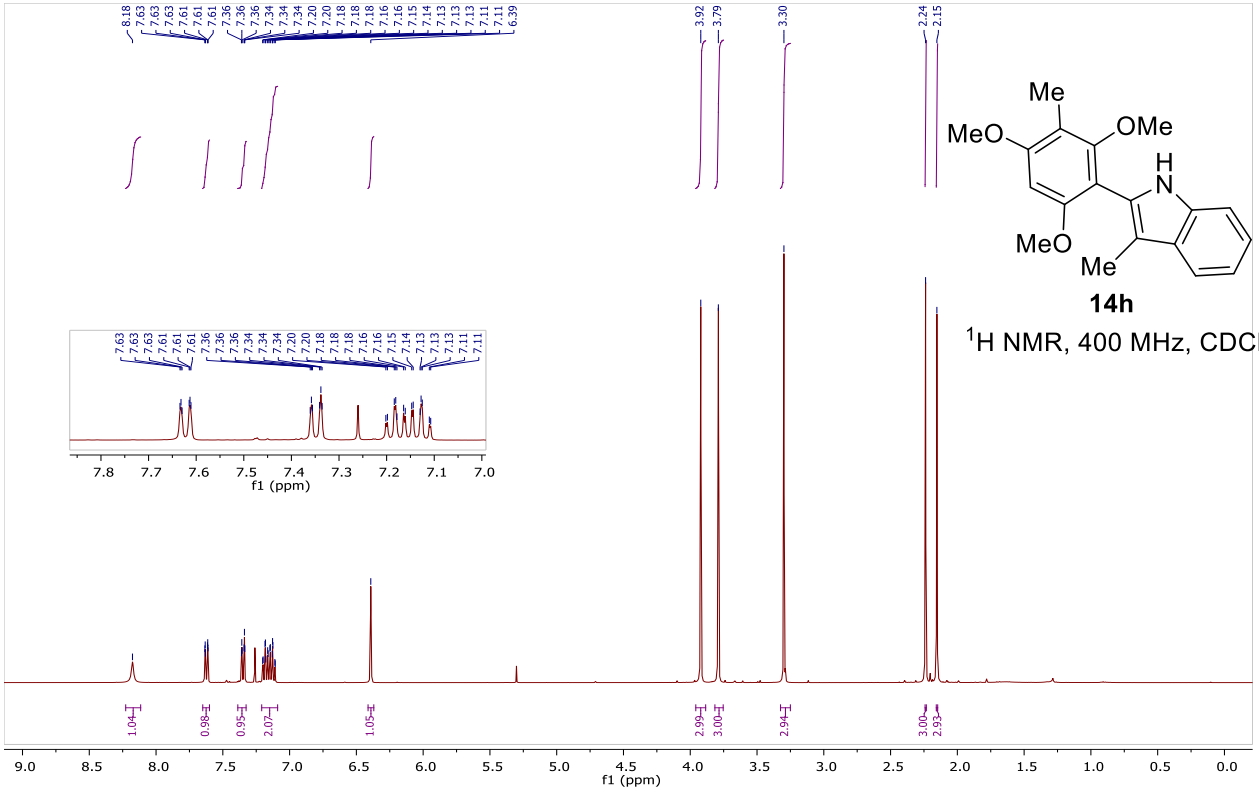


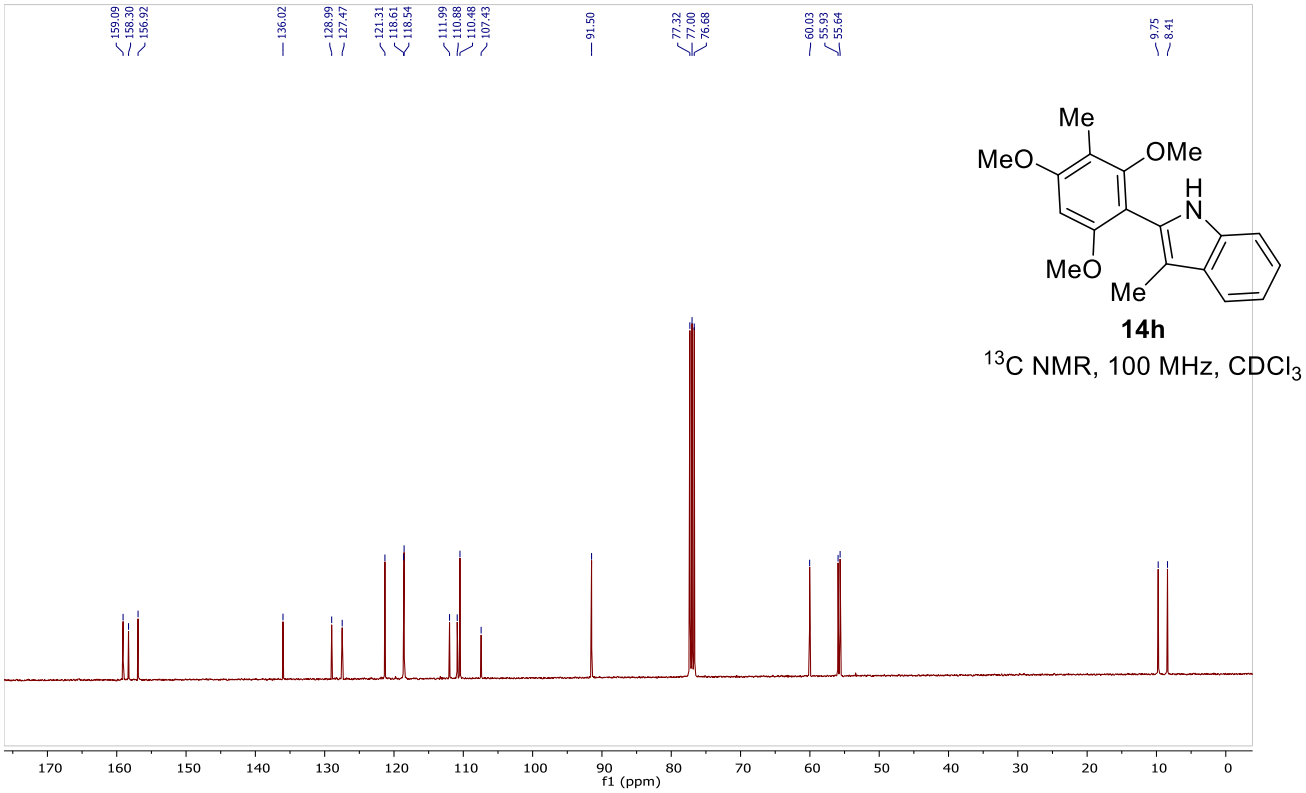
2-(2,4,6-Trimethoxy-3-methylphenyl)-1*H*-indole (14g)



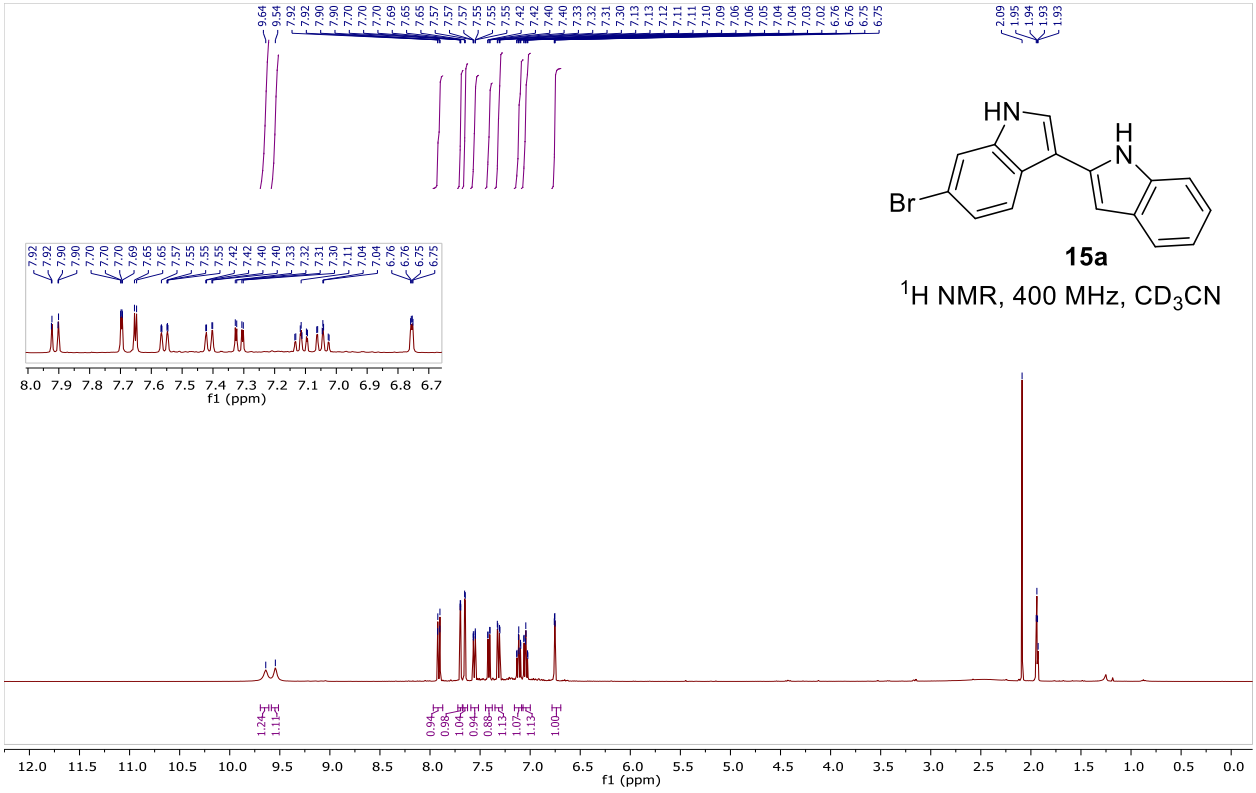


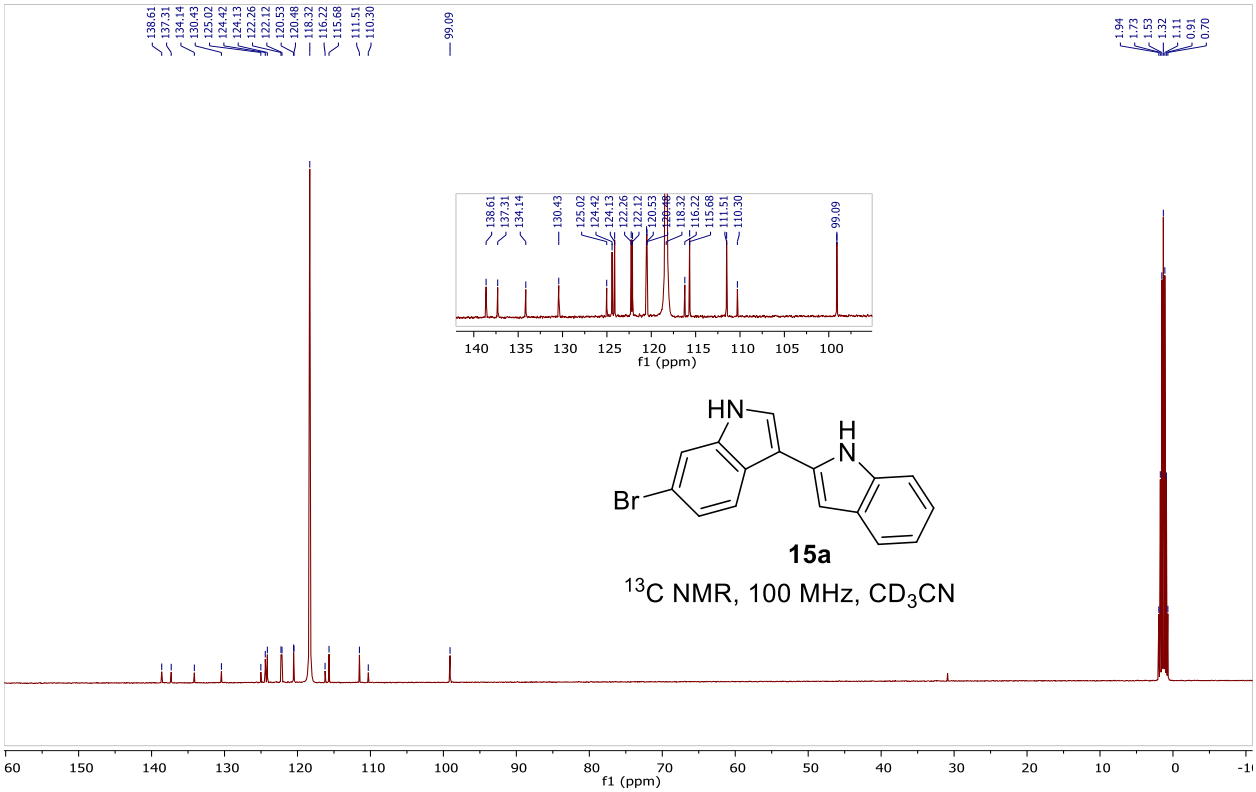
3-Methyl-2-(2,4,6-trimethoxy-3-methylphenyl)-1*H*-indole (14h)



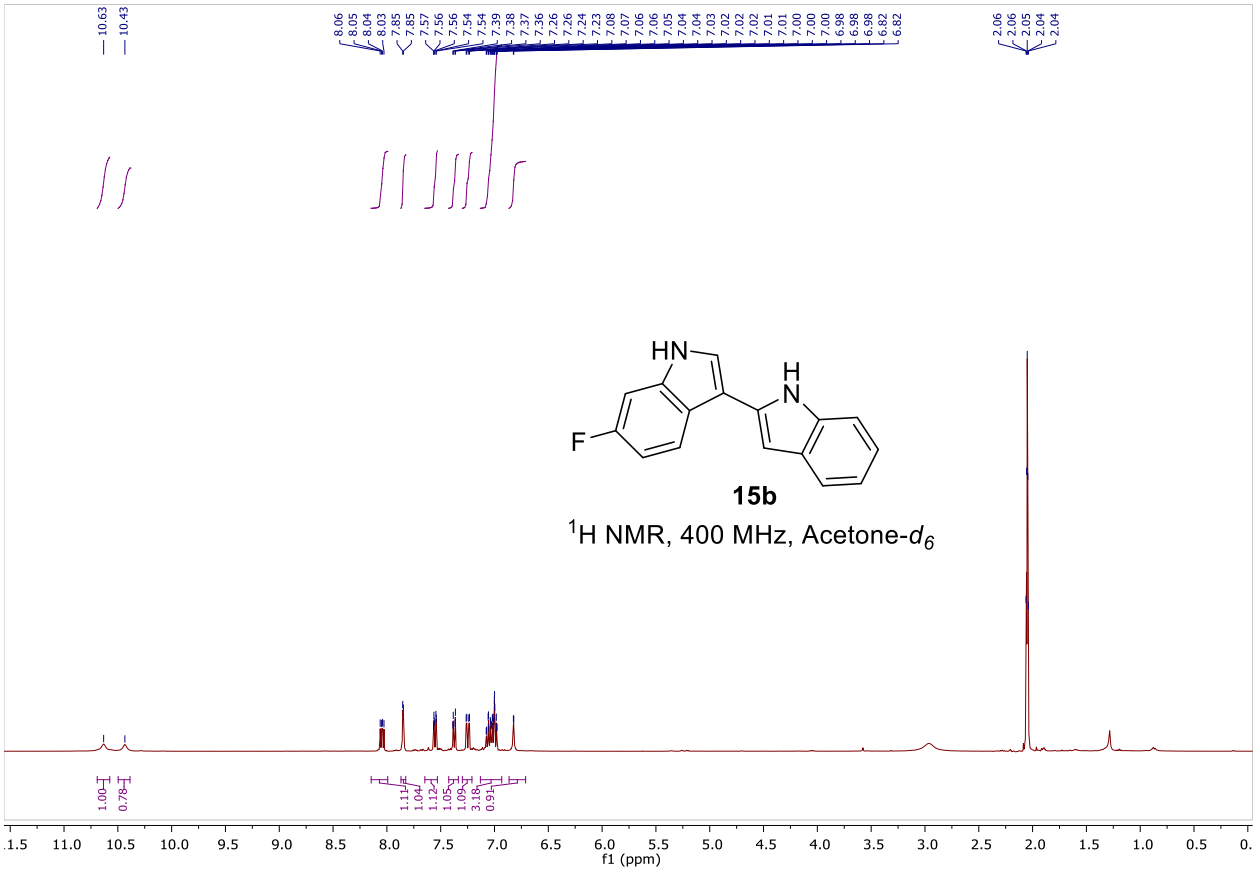


6'-Bromo-1*H*,1'*H*-2,3'-biindole (15a)

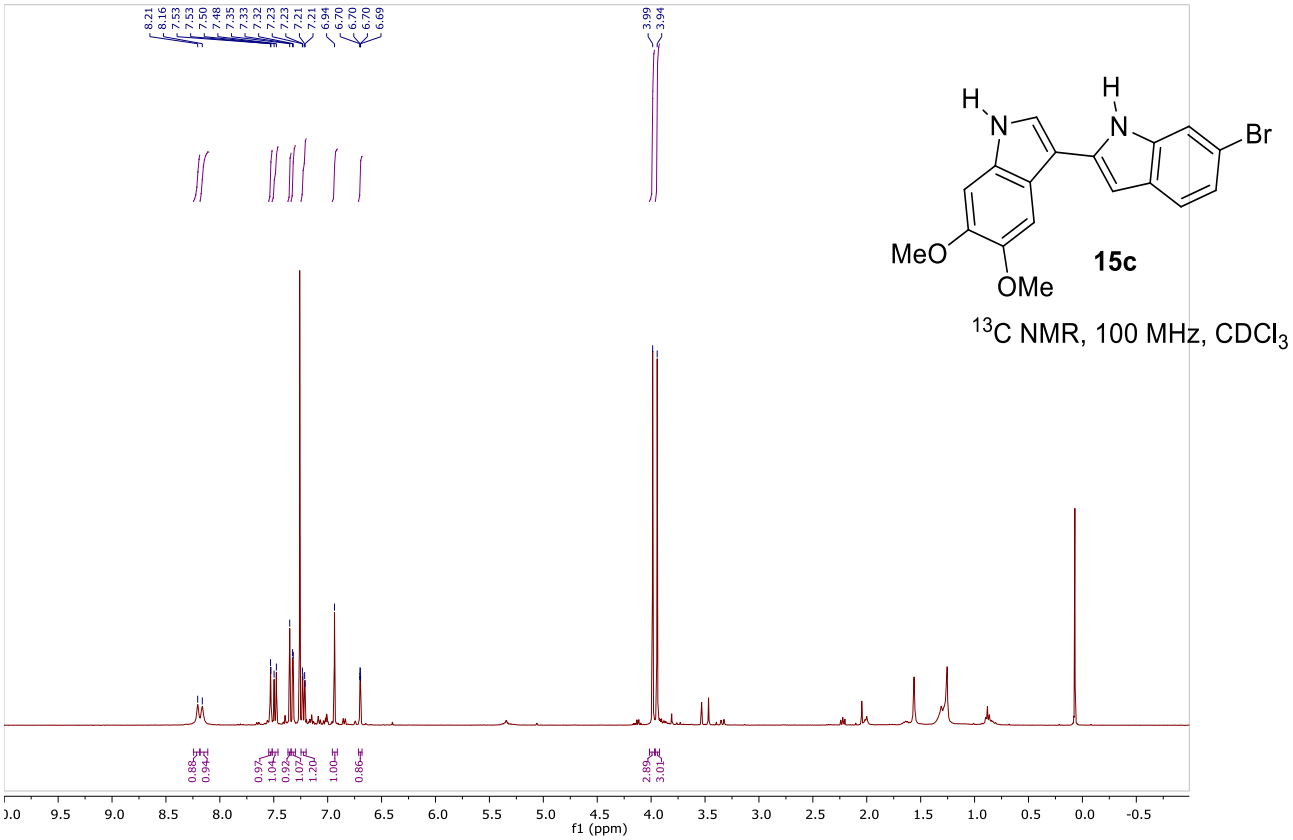


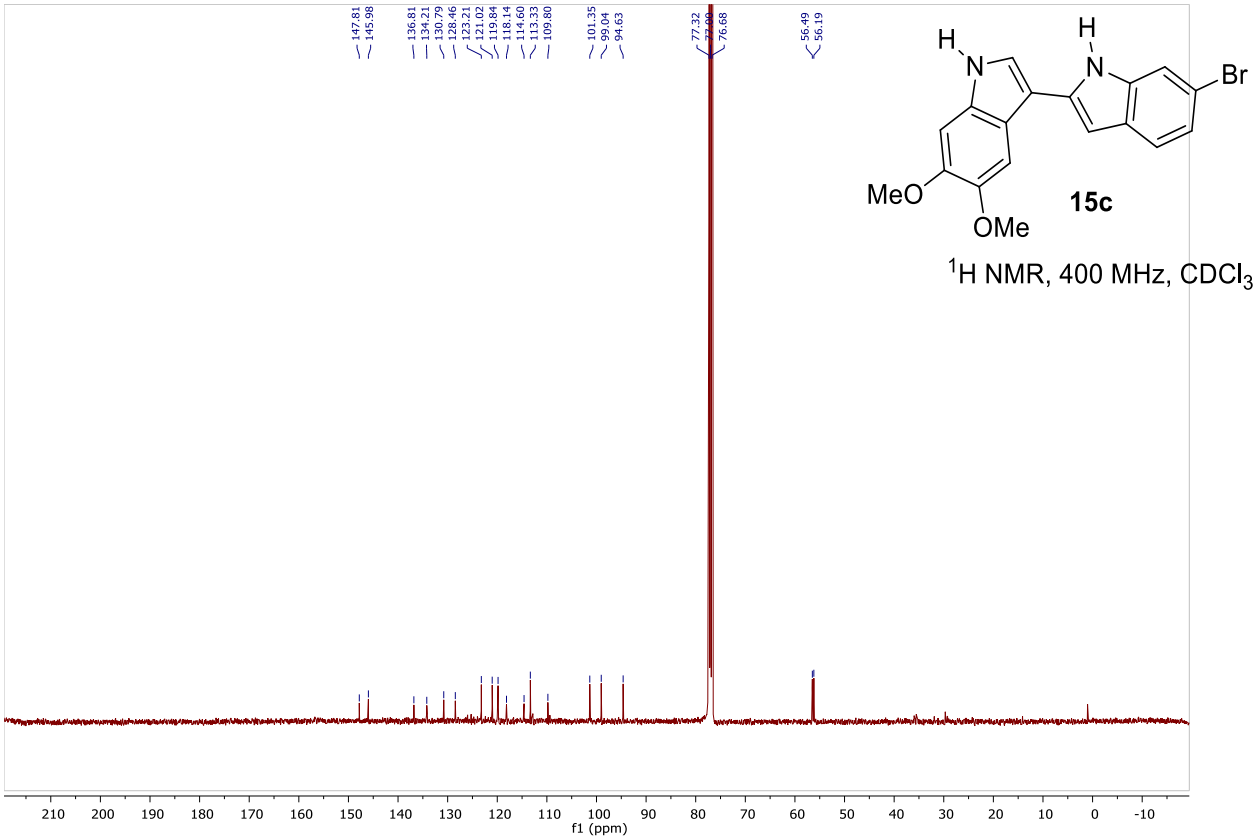


6'-Fluoro-1*H*,1'*H*-2,3'-biindole (15b)

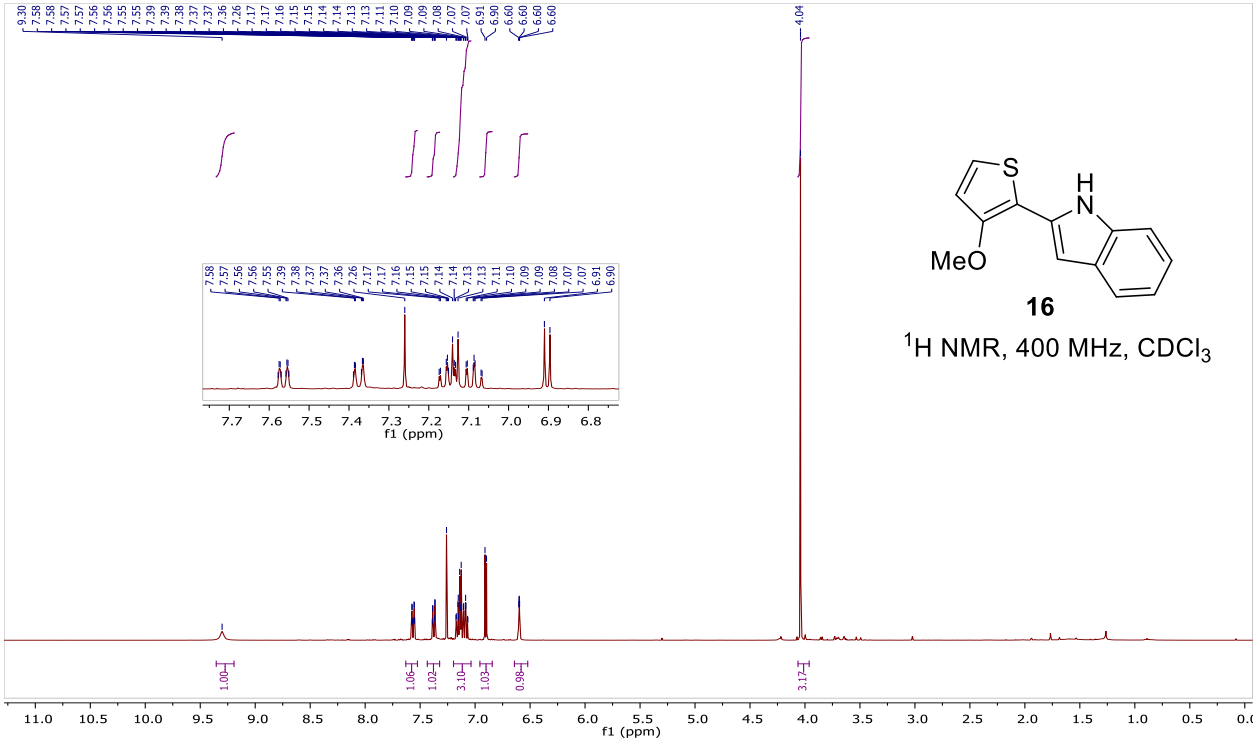


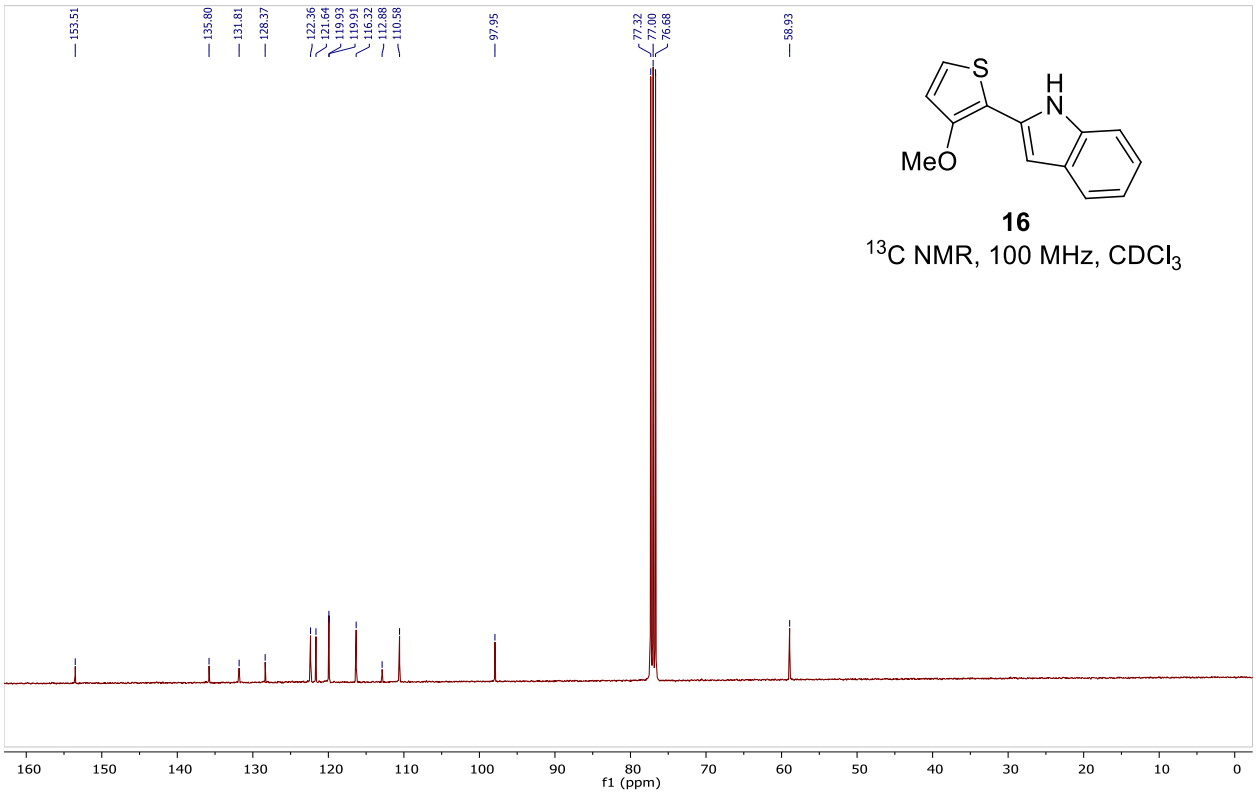
6-Bromo-5',6'-dimethoxy-1*H*,1'*H*-2,3'-biindole (15c)



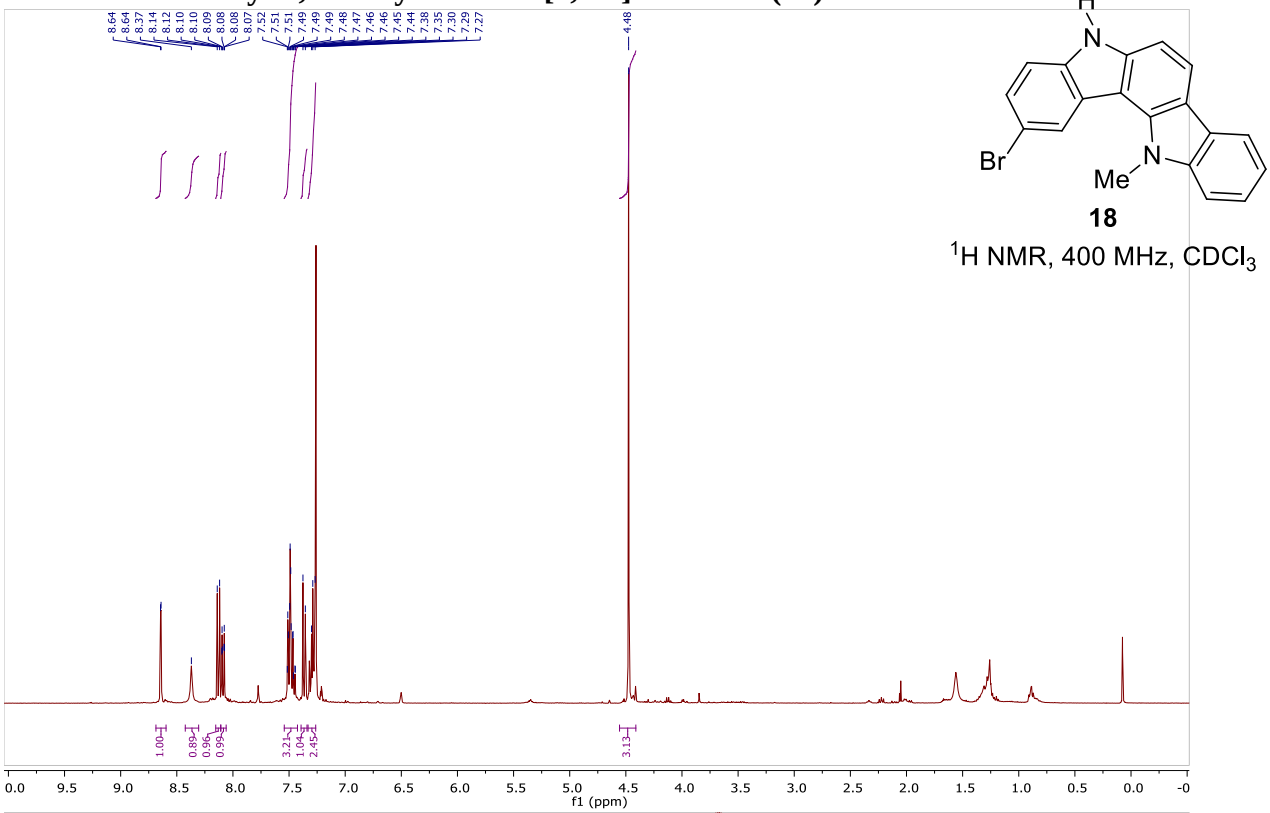


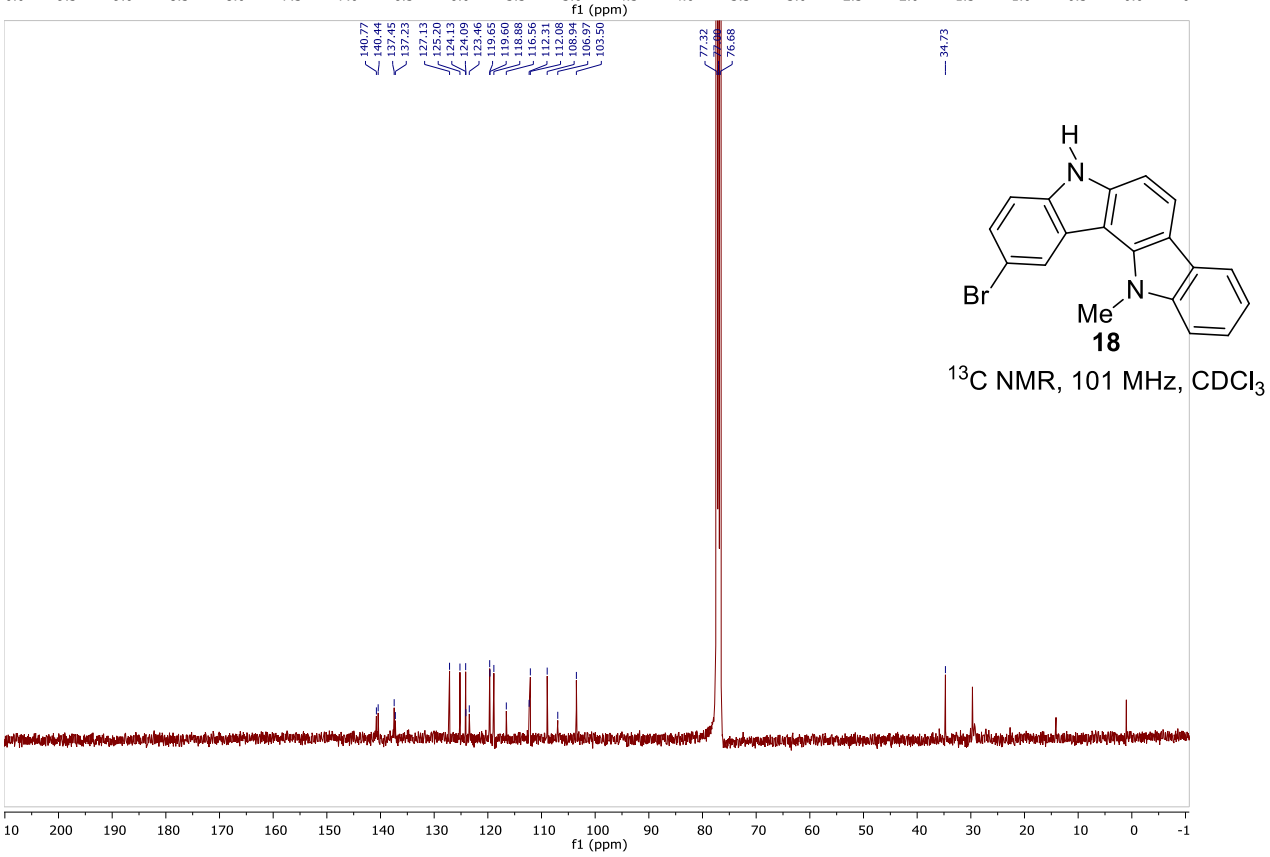
2-(3-Methoxythiophen-2-yl)-1*H*-indole (16)



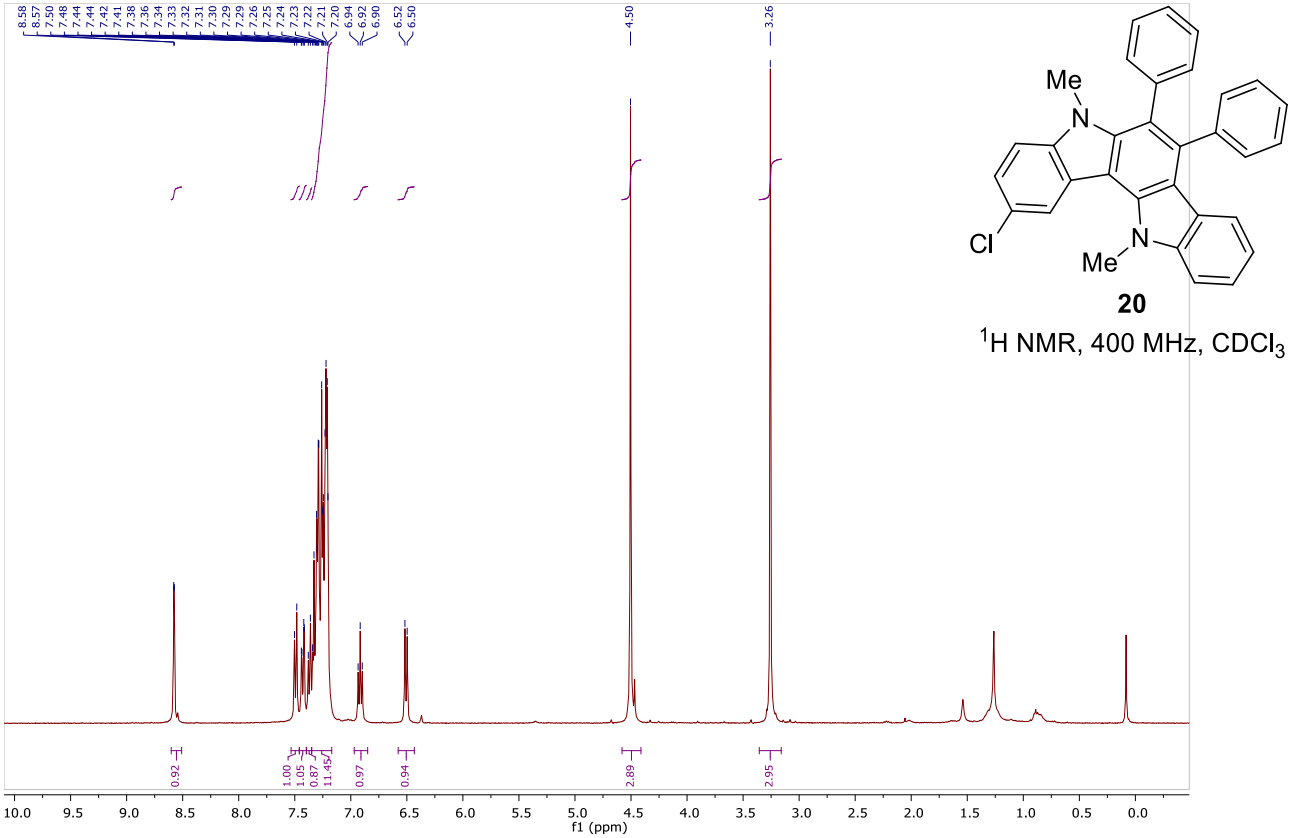


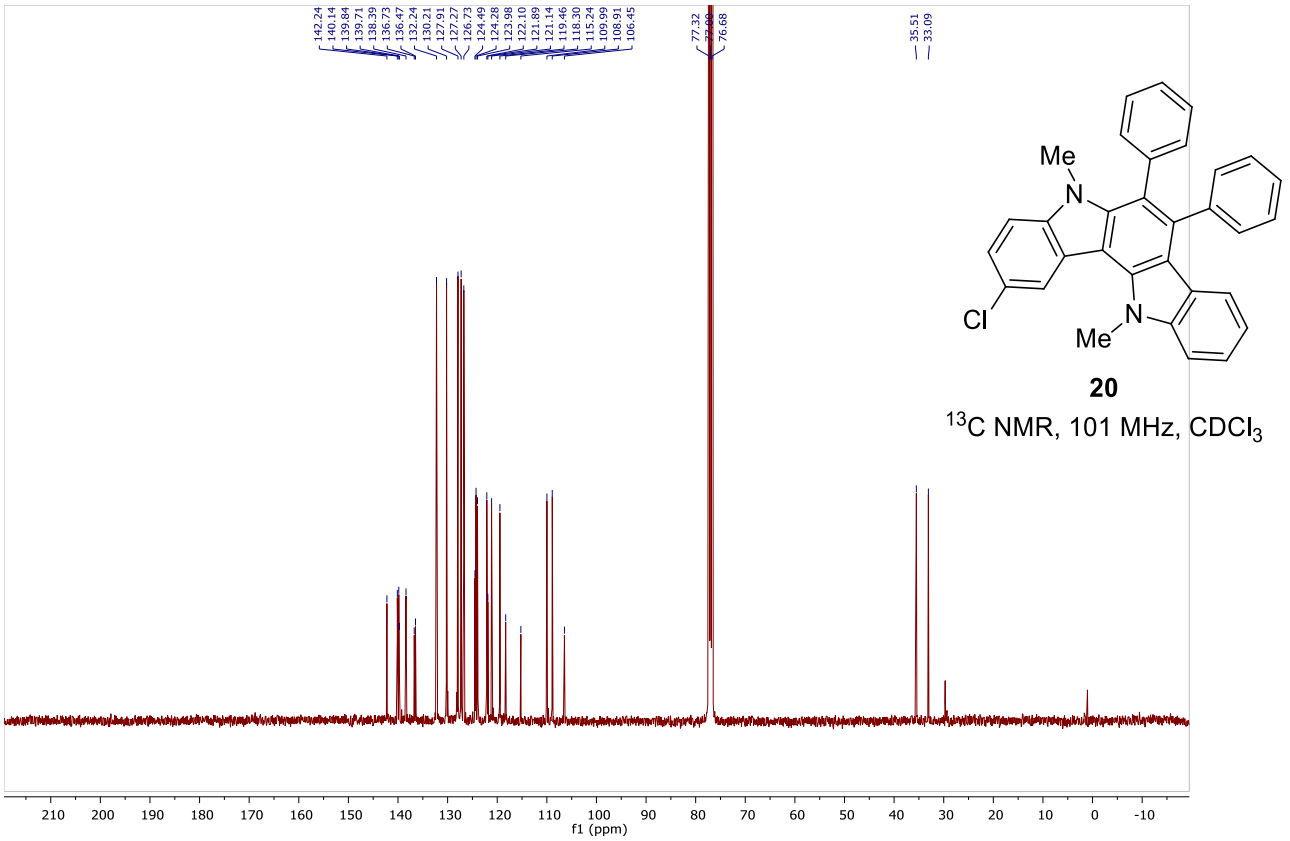
2-Bromo-12-methyl-5,12-dihydroindolo[3,2-a]carbazole (18)



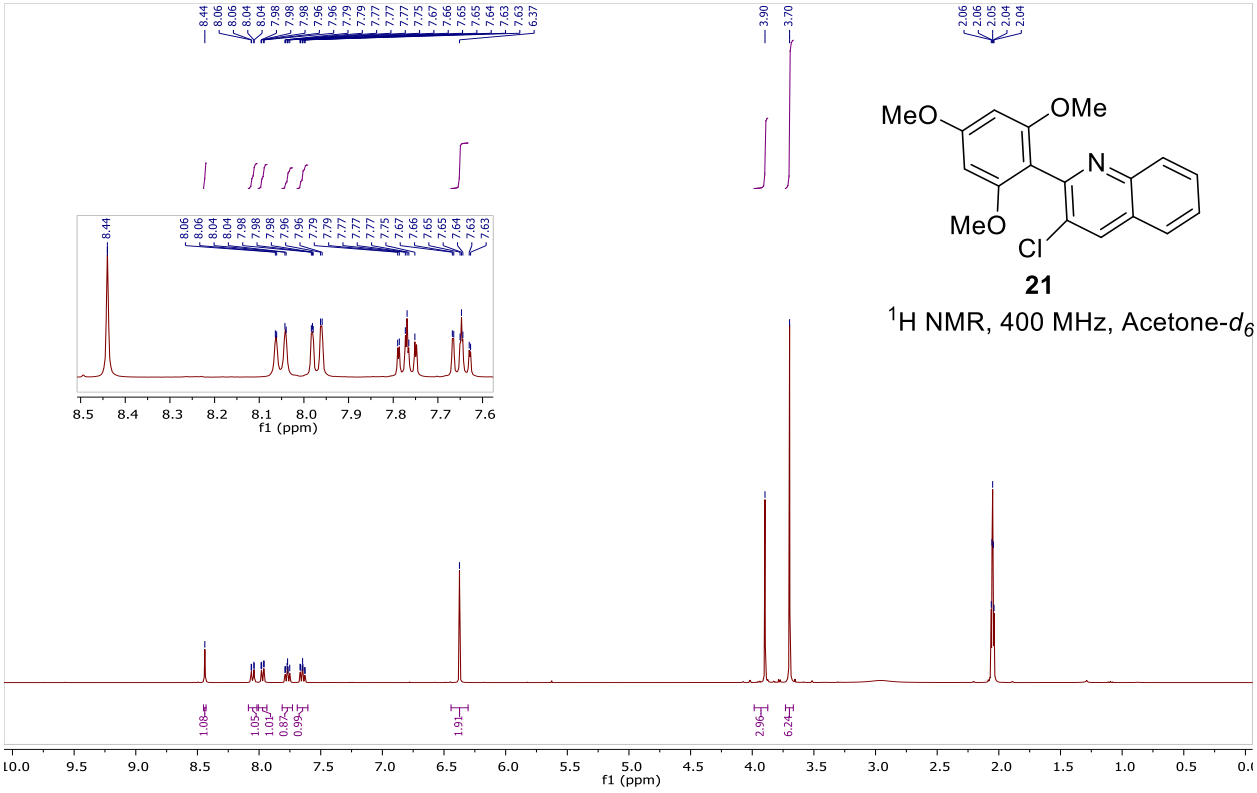


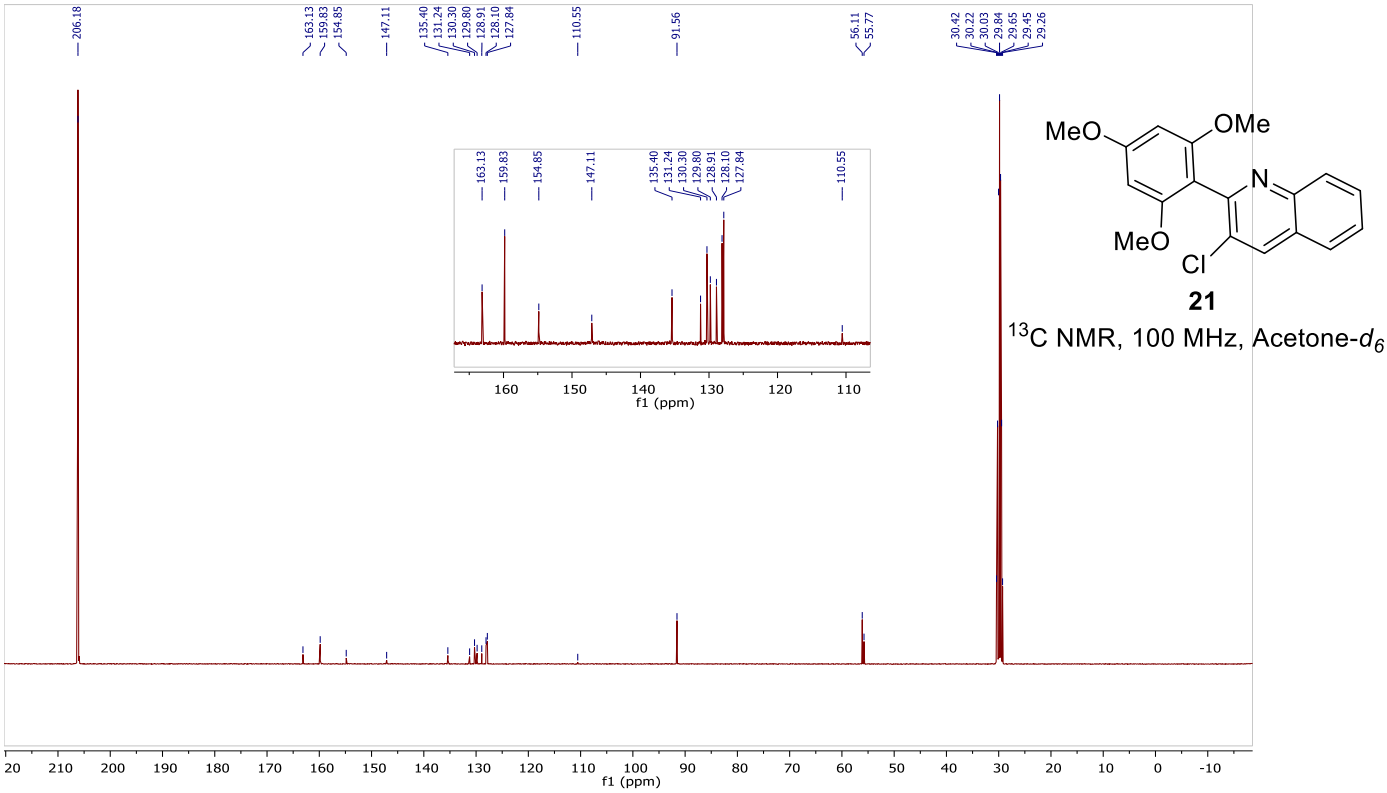
2-Chloro-5,12-dimethyl-6,7-diphenyl-5,12-dihydroindolo[3,2-*a*]carbazole (20)



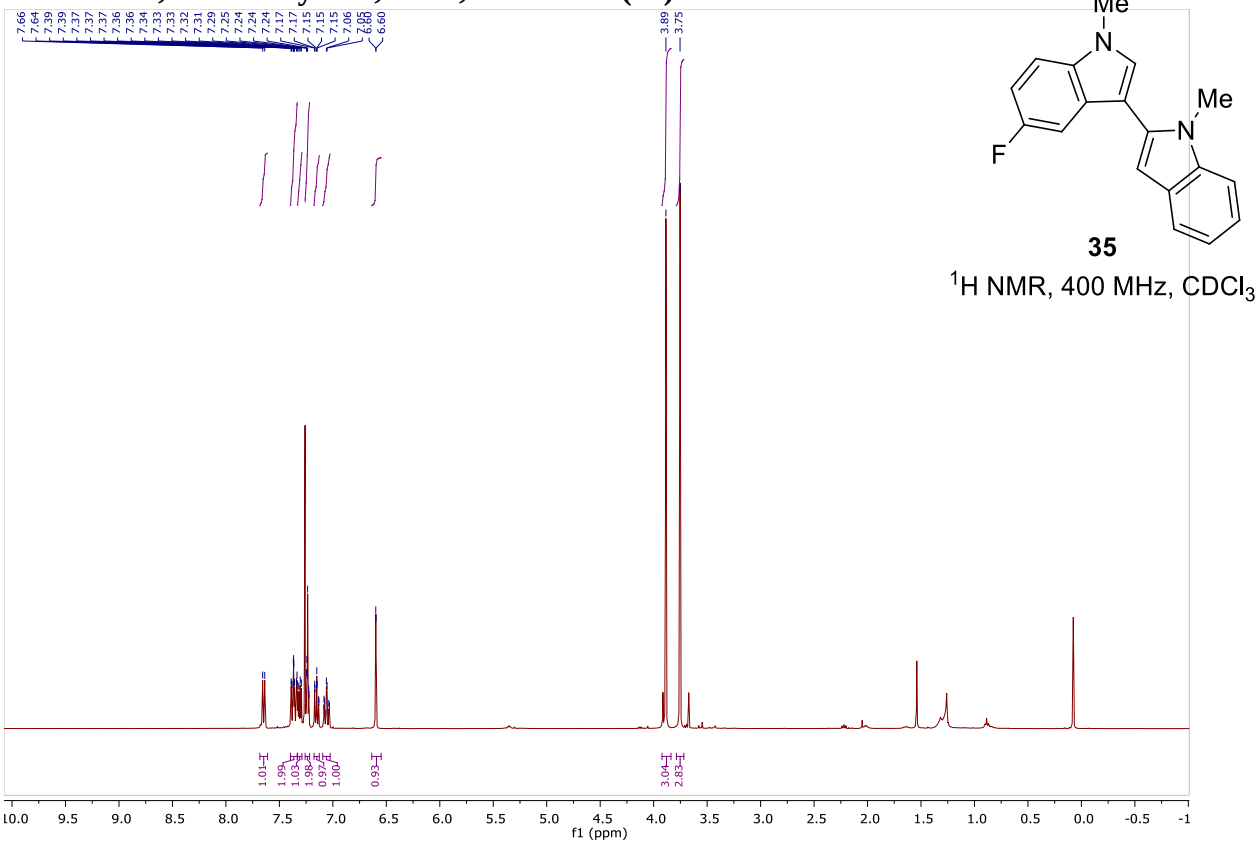


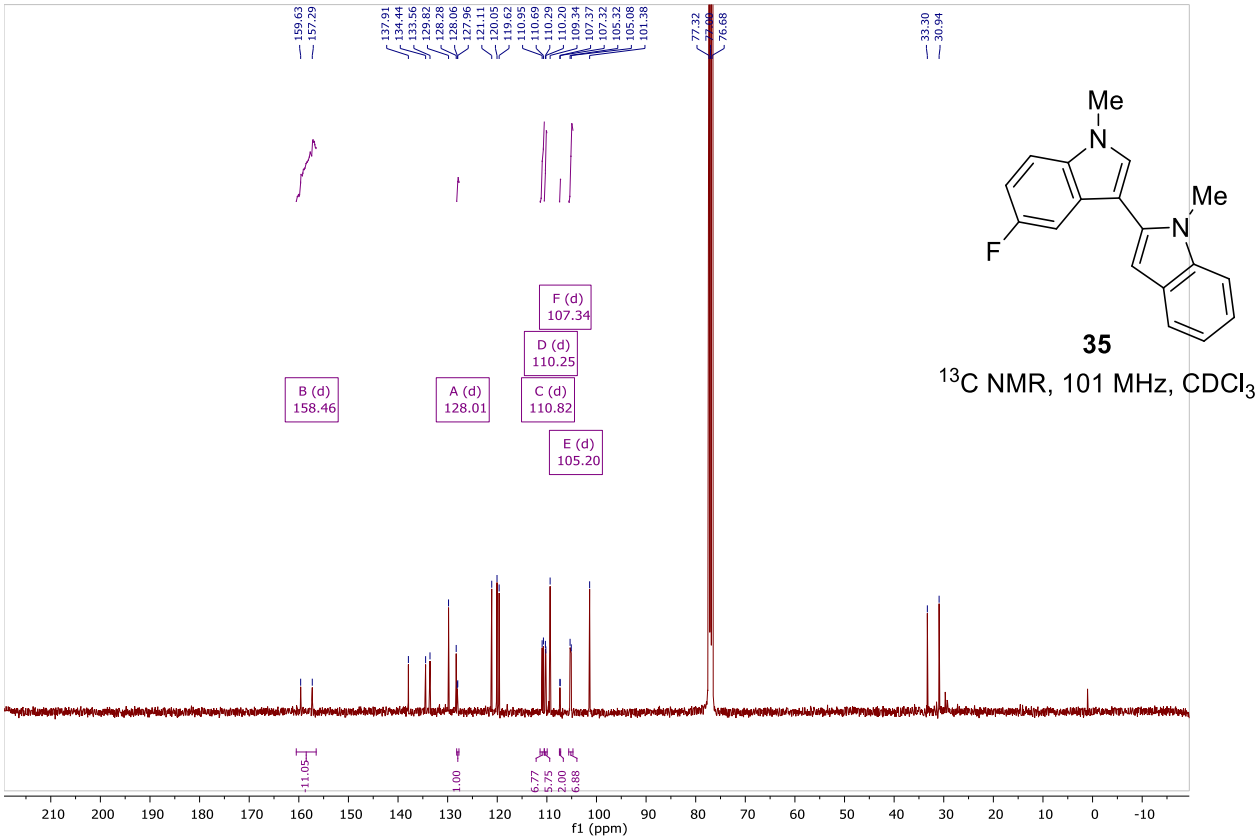
3-Chloro-2-(2,4,6-trimethoxyphenyl)quinolone (21)





5'-Fluoro-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole (35)





5'-Bromo-1,1'-dimethyl-1*H*,1'*H*-2,3'-biindole (36)