Supporting Information

Palladium-Catalysed Direct C-2 Methylation of Indoles

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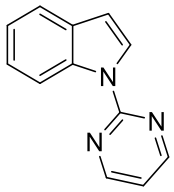
1. General Information

All reagents and metal catalysts were obtained from commercial sources without further purification. Analytical thin layer chromatography (TLC) was performed on precoated silica plates. Yields of the products refer to purification by silica-gel column chromatography. Silica gel 60H (200-300 mesh) manufactured by Qingdao Haiyang Chemical Group Co. (China) was used for general chromatography. IR spectra were recorded on a Nicolet IS-10 Fourier transform infrared spectrometer. Mass spectra were recorded with a TSQ Quantum-LC/MS/MS of Finnigan using Electrospray ionization (ESI) techniques. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AV-300 and AV-500 spectrometer operating at 300MHz/500MHz and75MHz/125MHz, respectively, with chemical shift values being reported in ppm relative to chloroform (δ=7.26 ppm) for ^{1}H NMR, and chloroform (δ=77.16 ppm) for ^{13}C NMR.

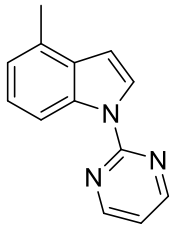
2. Preparation of Starting Materials

General procedure for synthesis of the starting materials

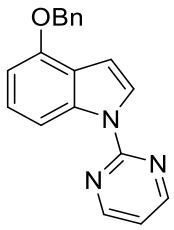
NaH (60 % dispersion in mineral oil, 300 mg, 7.5 mmol) was added in portions at 0 ℃ to a stirred solution of indole (585 mg, 5.0 mmol) in DMF (15 mL). After stirring for 30 min at 0 ℃, 2-chloropyrimidine (687 mg, 6.0 mmol) was added and the mixture was stirred at 130℃ for 24 h. Then, the reaction mixture was cooled to ambient temperature, poured into EtOAc (50 mL) and extracted with H_2O (3 × 50 mL). The combined organic phase was dried over Na_2SO_4. After filtration and evaporation of the solvents under reduced pressure, the crude product was purified by column chromatography on silica gel to get the corresponding product. The spectral data of the starting materials were in accordance with those reported in the literature[1].



1-(Pyrimidin-2-yl)-1H-indole (1a): white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.83(d, J = 8.3 Hz, 1H), 8.70 (d, J = 4.8 Hz, 2H), 8.29 (d, J = 3.7 Hz, 1H), 7.64 (d, J = 7.7Hz, 1H), 7.42-7.31 (m, 1H), 7.30-7.22 (m, 1H), 7.04 (t, J = 4.8 Hz, 1H), 6.72 (d, J= 3.6 Hz, 1H).

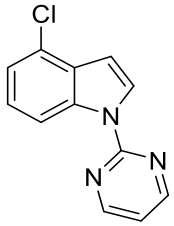


4-Methyl-1-(pyrimidin-2-yl)-1H-indole (1b): white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (d, *J* = 4.7 Hz, 2H), 8.65 (d, *J* = 8.4 Hz, 1H), 8.27 (d, *J* = 3.7 Hz, 1H), 7.26 (d, *J* = 15.6 Hz, 1H), 7.05 (dd, *J* = 7.9, 2.6 Hz, 2H), 6.75 (d, *J* = 3.7 Hz, 1H), 2.58 (s, 3H).

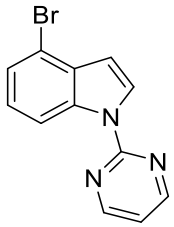


4-(Benzyloxy)-1-(pyrimidin-2-yl)-1H-indole (1c): purple solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (d, *J* = 4.8 Hz, 2H), 8.43 (d, *J* = 8.4 Hz, 1H), 8.20 (d, *J* = 3.7 Hz, 1H), 7.53 (d, *J* = 7.3 Hz, 2H), 7.46 – 7.31 (m, 3H), 7.25 (t, *J* = 8.2 Hz, 1H), 7.05 (t, *J* = 4.8

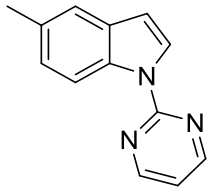
Hz, 1H), 6.90 (dd, *J* = 3.6, 0.5 Hz, 1H), 6.76 (d, *J* = 7.9 Hz, 1H), 5.25 (s, 2H).



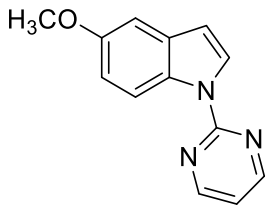
4-Chloro-1-(pyrimidin-2-yl)-1H-indole (1d): white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.79 – 8.67 (m, 3H), 8.33 (d, *J* = 3.7 Hz, 1H), 7.31 – 7.22 (m, 3H), 7.10 (t, *J* = 4.8 Hz, 1H), 6.83 (d, *J* = 3.7 Hz, 1H).



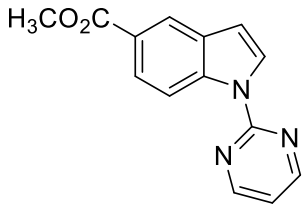
4-Bromo-1-(pyrimidin-2-yl)-1H-indole (1e): white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.67 (d, *J* = 4.8 Hz, 2H), 8.32 (d, *J* = 3.7 Hz, 1H), 7.41 (dd, *J* = 7.7, 0.6 Hz, 1H), 7.20 (t, *J* = 8.1 Hz, 1H), 7.05 (t, *J* = 4.8 Hz, 1H), 6.81 – 6.72 (m, 1H).



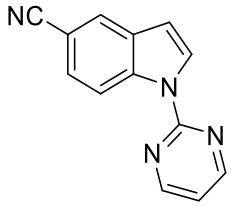
5-Methyl-1-(pyrimidin-2-yl)-1H-indole (1f): orange solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.68 (t, *J* = 6.6 Hz, 3H), 8.23 (d, *J* = 3.6 Hz, 1H), 7.41 (s, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 7.03 (t, *J* = 4.7 Hz, 1H), 6.63 (d, *J* = 3.6 Hz, 1H), 2.48 (s, 3H).



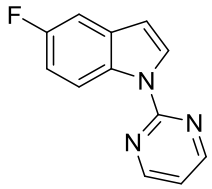
5-Methoxy-1-(pyrimidin-2-yl)-1H-indole (1g): yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.69 (t, *J* = 6.5 Hz, 3H), 8.25 (d, *J* = 3.6 Hz, 1H), 7.10 (d, *J* = 2.5 Hz, 1H), 7.03 (t, *J* = 4.8 Hz, 1H), 7.00 – 6.93 (m, 1H), 6.64 (d, *J* = 3.6 Hz, 1H), 3.89 (s, 3H).



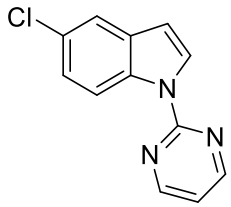
Methyl 1-(pyrimidin-2-yl)-1H-indole-5-carboxylate (1h): white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.85 (d, *J* = 8.8 Hz, 1H), 8.75 (d, *J* = 4.8 Hz, 2H), 8.36 (dd, *J* = 5.8, 2.4 Hz, 2H), 8.04 (dd, *J* = 8.8, 1.7 Hz, 1H), 7.12 (t, *J* = 4.8 Hz, 1H), 6.78 (d, *J* = 3.2 Hz, 1H), 3.96 (s, 3H).



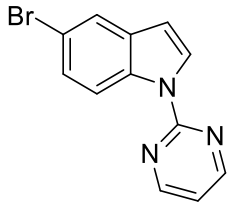
1-(Pyrimidin-2-yl)-1H-indole-5-carbonitrile (1i): yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.93 (d, *J* = 8.8 Hz, 1H), 8.76 (d, *J* = 4.8 Hz, 2H), 8.41 (d, *J* = 3.7 Hz, 1H), 7.97 (d, *J* = 0.9 Hz, 1H), 7.58 (dd, *J* = 8.7, 1.5 Hz, 1H), 7.16 (t, *J* = 4.8 Hz, 1H), 6.77 (d, *J* = 3.7 Hz, 1H).



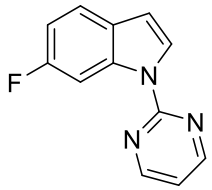
5-Fluoro-1-(pyrimidin-2-yl)-1H-indole (1j): white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.79 – 8.70 (m, 3H), 8.32 (d, *J* = 3.6 Hz, 1H), 7.27 (dd, *J* = 8.3, 3.1 Hz, 1H), 7.07 (dd, *J* = 6.5, 3.0 Hz, 2H), 6.66 (d, *J* = 3.6 Hz, 1H).



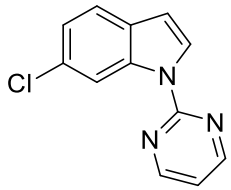
5-Chloro-1-(pyrimidin-2-yl)-1H-indole (1k): white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (dd, *J* = 11.5, 6.8 Hz, 3H), 8.30 (d, *J* = 3.6 Hz, 1H), 7.59 (d, *J* = 2.0 Hz, 1H), 7.38 – 7.26 (m, 1H), 7.08 (t, *J* = 4.8 Hz, 1H), 6.64 (d, *J* = 3.6 Hz, 1H).



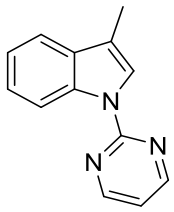
5-Bromo-1-(pyrimidin-2-yl)-1H-indole (1l): white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.71 – 8.68 (m, 3H), 8.28 (d, *J* = 3.7 Hz, 1H), 7.74 (d, *J* = 1.9 Hz, 1H), 7.42 (dd, *J* = 8.9, 1.9 Hz, 1H), 7.08 (t, *J* = 4.8 Hz, 1H), 6.63 (d, *J* = 3.7 Hz, 1H).



6-Fluoro-1-(pyrimidin-2-yl)-1H-indole (1m):white solid.^{1}H NMR (300 MHz, $CDCl_3$) δ 8.72 (d, *J* = 4.8 Hz, 2H), 8.59 (dd, *J* = 11.1, 2.3 Hz, 1H), 8.26 (d, *J* = 3.7 Hz, 1H), 7.53 (dd, *J* = 8.6, 5.6 Hz, 1H), 7.08 (t, *J* = 4.8 Hz, 1H), 7.01 (d, *J* = 2.3 Hz, 1H), 6.68(d, *J* = 3.5 Hz, 1H).



6-Chloro-1-(pyrimidin-2-yl)-1H-indole (1n):orange solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.89 (d, *J* = 1.5 Hz, 1H), 8.72 (d, *J* = 4.8 Hz, 2H), 8.27 (d, *J* = 3.7 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.22 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.09 (t, *J* = 4.8 Hz, 1H), 6.67 (d, *J* = 3.7 Hz, 1H).

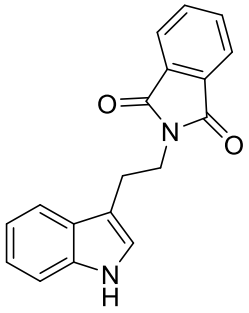


3-Methyl-1-(pyrimidin-2-yl)-1H-indole (1o):white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.77 (d, *J* = 8.2 Hz, 1H), 8.68 (d, *J* = 4.8 Hz, 2H), 8.05 (s, 1H), 7.56 (d, *J* = 7.7 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 2H), 7.01 (t, *J* = 4.8 Hz, 1H), 2.36 (s, 3H).

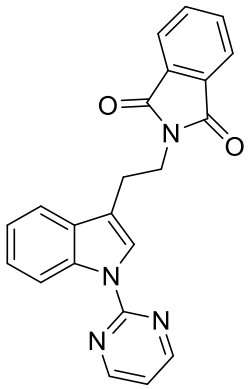
Synthesis of Compound 1p

A mixture of tryptamine (0.48 g, 3 mmol) and phthalic anhydride (0.488 g, 3.3 mmol) in toluene (10 mL) was refluxed overnight (the reaction was completed as judged by

TLC).The reaction mixturewas allowed to cool to ambient temperature, the solution was concentrated under vacuum. The crude product was purified by column chromatography on silica gel (EA : PE = 1:1) to get the yellow solid product **1p'**(0.8 g, 92 %). Next, compound **1p** was synthesized with the general procedure for synthesis of the starting materials.



1p'

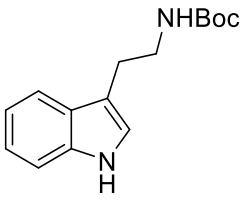


1p

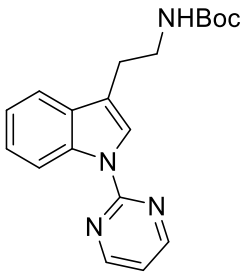
2-(2-(1-(Pyrimidin-2-yl)-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (1p): yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.78 (d, *J* = 8.2 Hz, 1H), 8.66 (d, *J* = 4.6 Hz, 2H), 8.18 (s, 1H), 7.90 – 7.79 (m, 2H), 7.79 – 7.68 (m, 3H), 7.33 (dd, *J* = 16.5, 8.6 Hz, 2H), 7.00 (t, *J* = 4.6 Hz, 1H), 4.09– 4.03 (m, 2H), 3.19 – 3.14 (m, 2H).

Synthesis of Compound 1q

To a yellow suspension of tryptamine (1.00 g, 6.24 mmol) in 1,4-dioxane (5 mL) was added Et_3N (1.80 mL, 12.9 mmol). A solution of $(Boc)_2O$ (1.50 g, 6.87 mmol) in 1,4-dioxane (5 mL) then was cannulated into the reaction mixture. This mixture was stirred for 1 h and the resulting yellow solution was concentrated to dryness under reduced pressure. The crude residue was purified by flash chromatography on silica gel (PE / EA=1 : 2) to give the desired *N*-Boc amine intermediate as white solid (**1q'**) (1.58 g, 98 %). Next, compound **1q** was synthesized with the general procedure for synthesis of the starting materials.



1q'



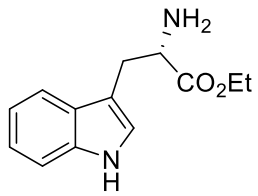
1q

Tert-butyl (2-(1-(pyrimidin-2-yl)-1H-indol-3-yl)ethyl)carbamate (1q): yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.79 (d, *J* = 8.3 Hz, 1H), 8.69 (d, *J* = 4.8 Hz, 2H),

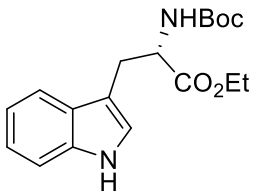
8.12 (s, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.36 (dd, *J* = 11.4, 4.1 Hz, 1H), 7.27 (dd, *J* = 10.3, 4.5 Hz, 1H), 7.03 (t, *J* = 4.8 Hz, 1H), 3.53 (t, *J* = 6.5 Hz, 2H), 3.00 (d, *J* = 6.8 Hz, 2H), 1.45 (s, 9H).

Synthesis of Compound 1r

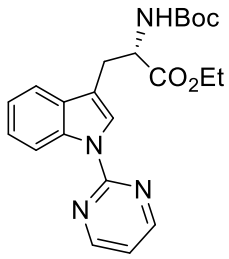
L-tryptophan (2.04 g, 10 mmol) was dissolved in ethanol (30 mL) with a 100 mL round-bottom flask followed by dropwise addition of thionyl chloride (7.1 mL, 100 mmol) through syringe at 0 ^{o}C with ice bath. The reaction mixture was stirred for overnight. After monitored by TLC till full conversion, it was allowed to cool to ambient temperature. Removing the solvent and thionyl chloride directly under reduced pressure to afford the dryness intermediate **1r'** (2.48 g, 93 %). Without further purification, this compound (0.8 g, 3 mmol) was dissolved in 1,4-dioxane (5 mL) was added Et_3N (1.66 mL,12 mmol). A solution of $(Boc)_2O$ (0.78 g, 3.6 mmol) in 1,4-dioxane (5 mL) then was cannulated into the reaction mixture. This mixture was stirred for 4h at ambient temperature, and the resulting yellow solution was concentrated to dryness under reduced pressure. The crude residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate =1 : 2) to give the desired *N*-Boc amine intermediate**1r"** as an amorphous pale yellow solid (0.97 g, quantitative yield). Next, compound **1r** was synthesized with the general procedure for synthesis of the starting materials.



1r'



1r''



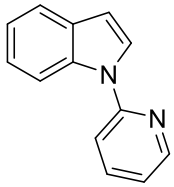
1r

Ethyl N-(tert-butoxycarbonyl)-1-(pyrimidin-2-yl)-L-tryptophanate(1r): white solid.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (d, *J* = 8.2 Hz, 1H), 8.67 (d, *J* = 4.8 Hz, 2H), 8.10 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 7.02 (t, *J* = 4.8 Hz, 1H), 4.43 (q, *J* = 7.1 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.43 – 3.21 (m, 2H), 1.43 (s, 9H), 1.21 (t, *J* = 7.2 Hz, 3H).

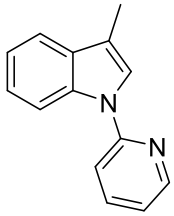
Synthesis of Compound 1s, 1t, 1u, 1v

A 50 mL round flask was charged with corresponding indole, 3-methyl-1H-indole, 4-bromo-1H-indole, 5-methoxy-1H-indole (5 mmol), KOH (12.5 mmol, 0.7 g), 2-bromopyridine (7.5 mmol, 0.72 mL), and dry DMSO (5 mL) under nitrogen

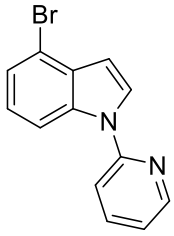
atmosphere. The resulting mixture was stirred in an oil bath at 120 °C until the end of the reaction. The mixture wae quenched with a saturated solution of NH_4Cl and extracted with ethyl acetate (3 × 50 mL). The organic phase was dried over Na_2SO_4, followed by evaporation under reduced presure to remove the solvent. The product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate 4:1).



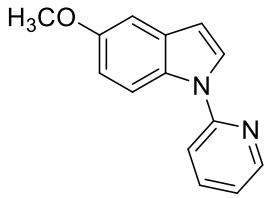
1-(pyridin-2-yl)-1H-indole (1s): yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (d, *J* = 3.3 Hz, 1H), 8.22 (d, *J* = 8.4 Hz, 1H), 7.92 – 7.78 (m, 1H), 7.71 (dd, *J* = 17.3, 5.6 Hz, 2H), 7.51 (d, *J* = 8.2 Hz, 1H), 7.32 (t, *J* = 8.3 Hz, 1H), 7.26 – 7.13 (m, 2H), 6.73 (d, *J* = 3.4 Hz, 1H).



3-methyl-1-(pyridin-2-yl)-1H-indole (1t): colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.6 Hz, 1H), 8.25 (d, *J* = 8.2 Hz, 1H), 7.85 – 7.73 (m, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.53 (s, 1H), 7.45 (d, *J* = 8.3 Hz, 1H), 7.32 (dd, *J* = 11.3, 4.0 Hz, 1H), 7.25 (dd, *J* = 10.3, 4.3 Hz, 1H), 7.12 (dd, *J* = 7.0, 5.2 Hz, 1H), 2.40 (s, 3H).



4-bromo-1-(pyridin-2-yl)-1H-indole (1u): yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 – 8.50 (m, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.84 (td, *J* = 8.0, 1.9 Hz, 1H), 7.75 (d, *J* = 3.5 Hz, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.25 – 7.10 (m, 2H), 6.79 (d, *J* = 3.5 Hz, 1H).

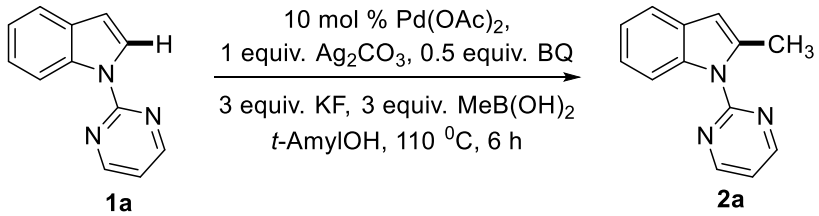


5-methoxy-1-(pyridin-2-yl)-1H-indole (1v): yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.6 Hz, 1H), 8.18 (d, *J* = 9.1 Hz, 1H), 7.90 – 7.75 (m, 1H), 7.70 (d, *J* = 3.4 Hz, 1H), 7.45 (d, *J* = 8.3 Hz, 1H), 7.14 (dd, *J* = 7.6, 3.9 Hz, 2H), 6.95 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.65 (d, *J* = 3.4 Hz, 1H), 3.88 (s, 3H).

3. Detailed Optimization Studies of Reaction Conditions

1a (0.2 mmol), catalyst, oxidant, additives, base, methyl source and solvent were combined under air in a high pressure tube. After sealing the tube, the mixture was stirred at the required temperature for 6 h. The reaction was cooled to room temperature, filtered through a pad of silica gel and washed with 100 mL EtOAc: petroleum ether(1:1). The solvents were removed under reduced pressure and the crude yield of the products are calculated using 1,3,5-trimethoxybenzene as the internal standard measured by ^{1}H-NMR. Full details of the control reactions are listed below (Tables S1-S6).

Table S1. Full details of catalysts effect[a]

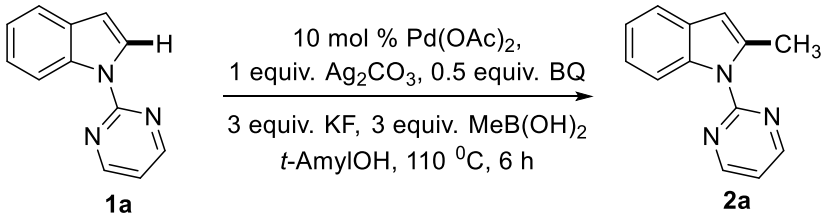


1a **2a**

change from above conditions	Convertion (%)	Yield (%)
None	56	55
$PdCl_2$ instead of $Pd(OAc)_2$	47	45
$Pd(PPh_3)_4$ instead of $Pd(OAc)_2$	46	42
$Pd(TFA)_2$ instead of $Pd(OAc)_2$	43	35
$Pd(CH_3CN)_2Cl_2$ instead of $Pd(OAc)_2$	45	40
50%mmol instead of 10%mmol $Pd(OAc)_2$	80	76

[a]All yields were determined by ^{1}H-NMR using 1,3,5-trimethoxybenzene as the internal standard.

Table S2. Selected silver salts effect[a]:

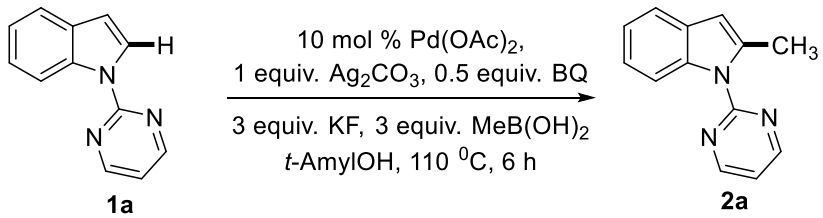


1a **2a**

change from above conditions	recovery yield of 1a(%)	Yield (%)
None	43	55
Ag_2O instead of Ag_2CO_3	46	50
$AgNO_3$ instead of Ag_2CO_3	50	46
AgOAc instead of Ag_2CO_3	42	52
AgF instead of Ag_2CO_3	57	39
$AgSbF_6$ instead of Ag_2CO_3	54	40

[a]All yields were determined by ^{1}H-NMR using 1,3,5-trimethoxybenzene as the internal standard.

Table S3. The oxidants and equivalent effect[a]:

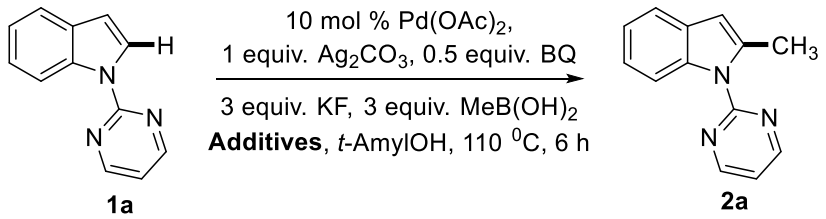


1a **2a**

change from above conditions	Yield (%)
None	55
$K_2S_2O_8$ instead of BQ	<5
PIDA instead of BQ	12
$NaIO_3$ instead of BQ	<5
CAN instead of BQ	trace
1equiv BQ instead of 0.5 equiv BQ	48
12h instead of 6h	56
24h instead of 6h	56

[a]All yields were determined by ^{1}H-NMR using 1,3,5-trimethoxybenzene as the internal standard. PIDA=$PhI(OAc)_2$, CAN=Ceric ammonium nitrate.

Table S4. The acid and base effect[a]:

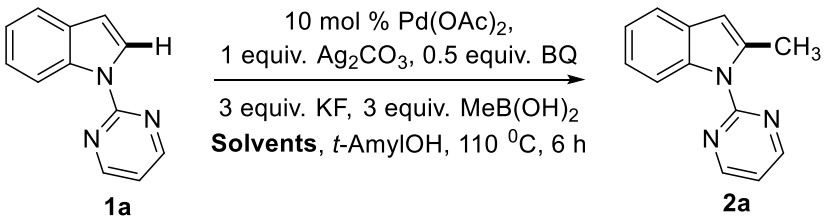


1a **2a**

Additives	Yield (%)
None	55
1 equiv PivOH	25
1 equiv $(BnO)_2PO_2H$	23
1 equiv Na_2CO_3	53
1 equiv K_2CO_3	51
1 equiv KOH	45

[a]All yields were determined by ^{1}H-NMR using 1,3,5-trimethoxybenzene as the internal standard.

Table S5.Selected solvent effect[a]:

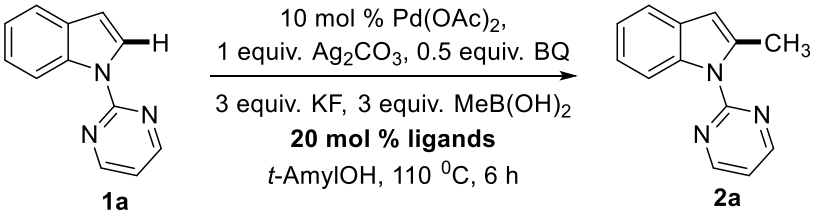


1a **2a**

Solvent	recovery yield of 1a(%)	Yield (%)
t-AmylOH	43	55
CH_3CN	46	trace
Toluene	50	46
DMF	42	19
Dioxane	57	39
HFIP	98	trace
DCE	58	30

[a]All yields were determined by ^{1}H-NMR using 1,3,5-trimethoxybenzene as the internal standard. HFIP=Hexafluoroisopropanol

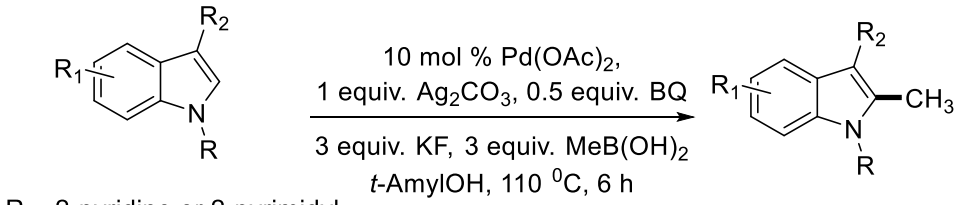
Table S6. The selected ligands effect[a]:



ligands	Yield(%)
Boc-Thr(t-Bu)-OH	46
N-Boc-L-leucine	48
Boc-L-Phe-OH	45
Norbornene	nr
2-Methylpyridine	34
2,6-Lutidine	39

[a]All yields were determined by ^{1}H-NMR using 1,3,5-trimethoxybenzene as the internal standard.

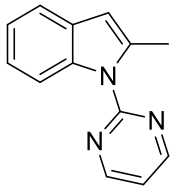
4. General Procedure for the C-H Methylation of Indoles



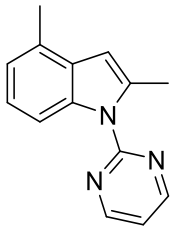
R = 2-pyridine or 2-pyrimidyl

1 **2**

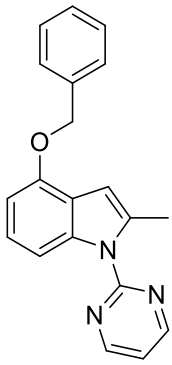
The mixture of $Pd(OAc)_2$ (4.48 mg, 0.02 mmol), Ag_2CO_3 (55 mg, 0.2 mmol), BQ (10.8 mg, 0.1 mmol),KF (34.8 mg, 0.6 mmol), Methylboronic acid (36 mg, 0.6 mmol), substrate **1** (0.2 mmol) and *t*-AmylOH (1 mL) were added under air to a high pressure tube (35 mL). After sealing the tube, the mixture was stirred at 110 ºC for 6 h. After cooling to room temperature, the mixture was evaporated under reduced pressure to remove the solvents and then purified directly *via* chromatography on silica gel with(DCM: petroleum ether = 1:1) to provide the corresponding product **2**. Furthermore, some were purified by preparative thin-layer chromatography.



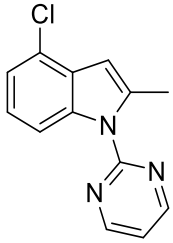
2-Methyl-1-(pyrimidin-2-yl)-1H-indole (2a): Yield: 55%, yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.7 Hz, 2H), 8.36 – 8.23 (m, 1H), 7.52 (dd, *J* = 6.7, 2.1 Hz, 1H), 7.25 – 7.09 (m, 3H), 6.44 (s, 1H), 2.73 (s, 3H). The spectral data of the product was in accordance with that reported in the literature.[2]



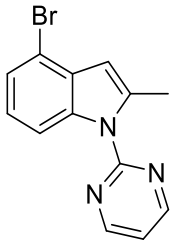
2,4-Dimethyl-1-(pyrimidin-2-yl)-1H-indole(2b): Yield: 62%, yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.8 Hz, 2H), 8.14 (dd, *J* = 8.0, 3.9 Hz, 1H), 7.25 – 7.07 (m, 2H), 7.06 – 6.92 (m, 1H), 6.47 (s, 1H), 2.73 (d, *J* = 2.2 Hz, 3H), 2.53 (d, *J* = 3.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.52, 158.09, 137.17, 136.67, 129.04, 128.81, 122.49, 122.24, 116.95, 111.60, 105.18, 18.65, 16.67. IR (neat): 2918, 2850, 1570, 1557, 1432, 1347, 1316, 1263, 1228, 768, 733. HRMS (ESI) calcd. for $C_{14}H_{14}N_3[M+H]^+$: 224.1188, found: 224.1184.



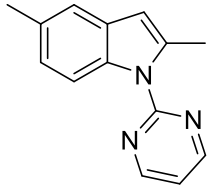
4-(Benzyloxy)-2-methyl-1-(pyrimidin-2-yl)-1H-indole (2c): Yield:56%, yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.7 Hz, 2H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.54 (d, *J* = 7.5 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.36 (t, *J* = 7.3 Hz, 1H), 7.21 – 7.04 (m, 2H), 6.73 (d, *J* = 7.8 Hz, 1H), 6.67 (s, 1H), 5.26 (s, 2H), 2.73 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.52, 158.12, 151.36, 138.31, 137.72, 136.33, 128.55, 127.79, 127.40, 123.06, 120.16, 117.08, 107.72, 103.87, 70.12, 16.60. The spectral data of the product was in accordance with that reported in the literature.[2]



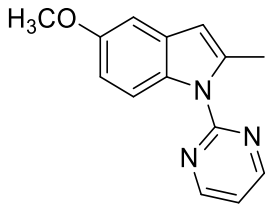
4-Chloro-2-methyl-1-(pyrimidin-2-yl)-1H-indole (2d): Yield: 47%, white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.80 (d, *J* = 4.8 Hz, 2H), 8.18 (d, *J* = 7.9 Hz, 1H), 7.20 – 7.10 (m, 3H), 6.57 (s, 1H), 2.73 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.06 (3C, for three carbons on pyrimidine), 138.60, 137.39, 127.96, 124.56, 122.80, 121.41, 117.31, 112.49, 104.60, 16.52. IR (neat): 2918, 2856, 1543, 1420, 1345, 1325, 1253, 1177, 959, 811, 765, 732. HRMS (ESI) calcd. for $C_{13}H_{11}ClN_3[M+H]^+$: 244.0642, found 244.0648.



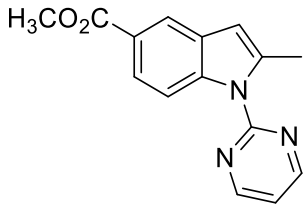
4-Bromo-2-methyl-1-(pyrimidin-2-yl)-1H-indole (2e): Yield:51%, white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.78 (d, *J* = 4.8 Hz, 2H), 8.22 (d, *J* = 8.3 Hz, 1H), 7.34 (d, *J* = 7.7 Hz, 1H), 7.15 (dd, *J* = 6.2, 3.3 Hz, 1H), 7.07 (t, *J* = 8.0 Hz, 1H), 6.52 (s, 1H), 2.72 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.21 (3C), 138.78, 137.13, 129.96, 124.66, 123.26, 117.47, 113.35, 113.14, 106.48, 16.64. IR (neat): 2924, 2850, 1556, 1426, 1253, 1172, 943, 807, 764, 701. HRMS (ESI) calcd. for $C_{13}H_{11}BrN_3[M+H]^+$: 288.0136, found: 288.0131.



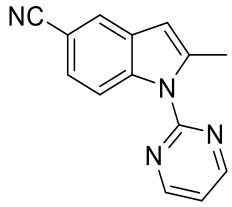
2,5-Dimethyl-1-(pyrimidin-2-yl)-1H-indole (2f): Yield: 85%, yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.8 Hz, 2H), 8.20 (d, *J* = 8.5 Hz, 1H), 7.30 (s, 1H), 7.11 (t, *J* = 4.8 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 6.36 (s, 1H), 2.71 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.36, 157.88, 137.75, 135.02, 131.01, 129.63, 123.64, 119.33, 116.56, 113.78, 106.45, 21.30, 16.76. IR (neat): 2918, 2714, 1581, 1556, 1429, 1259, 1044, 907, 801, 731. HRMS (ESI) calcd. for $C_{14}H_{14}N_3[M+H]^+$: 224.1188, found: 224.1179.



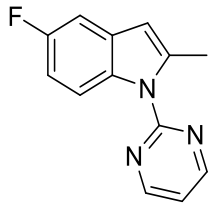
5-Methoxy-2-methyl-1-(pyrimidin-2-yl)-1H-indole (2g): Yield: 56%, yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.8 Hz, 2H), 8.25 (d, *J* = 9.0 Hz, 1H), 7.10 (t, *J* = 4.8 Hz, 1H), 6.99 (d, *J* = 2.4 Hz, 1H), 6.85 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.37 (s, 1H), 3.87 (s, 3H), 2.72 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.31, 157.87, 155.31, 138.48, 131.65, 130.16, 116.51, 115.08, 111.02, 106.67, 102.00, 55.63, 16.91. The spectral data of the product was in accordance with that reported in the literature.[2]



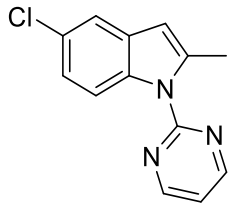
Methyl 2-methyl-1-(pyrimidin-2-yl)-1H-indole-5-carboxylate (2h): Yield: 43%, white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.82 (d, *J* = 6.4 Hz, 2H), 8.26 (d, *J* = 11.8 Hz, 2H), 7.91 (dd, *J* = 11.6, 2.1 Hz, 1H), 7.21 (t, *J* = 6.4 Hz, 1H), 6.51 (s, 1H), 3.94 (s, 3H), 2.72 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.91, 158.12, 157.91, 139.36, 139.20, 128.95, 123.69, 123.50 121.84, 117.48, 113.43, 106.95, 51.78, 16.40. IR (neat):2918, 1717, 1562, 1449, 1427, 1352, 1303, 1262, 1237, 1072, 907, 735. HRMS (ESI) calcd. for $C_{15}H_{14}N_3O_2[M+H]^+$: 268.1086, found: 268.1090.



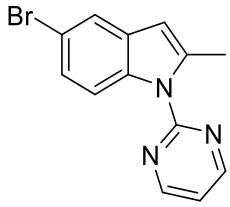
2-Methyl-1-(pyrimidin-2-yl)-1H-indole-5-carbonitrile (2i): Yield:37%, white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (d, *J* = 4.8 Hz, 2H), 8.31 (d, *J* = 8.7 Hz, 1H), 7.83 (s, 1H), 7.44 (dd, *J* = 8.7, 1.3 Hz, 1H), 7.24 (t, *J* = 4.8 Hz, 1H), 6.48 (s, 1H), 2.72 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.36, 157.82, 140.46, 138.60, 129.32, 125.53, 124.42, 120.51, 118.00, 114.75, 106.32, 104.84, 16.50. IR (neat): 2918, 2865, 2218, 1562, 1429, 1260, 1067, 803, 734. HRMS (ESI) calcd. for $C_{14}H_{11}N_4[M+H]^+$: 235.0984, found: 235.0980.



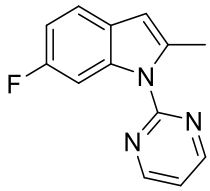
5-Fluoro-2-methyl-1-(pyrimidin-2-yl)-1H-indole (2j): Yield: 55%, white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.78 (d, *J* = 6.2 Hz, 2H), 8.26 (dd, *J* = 11.9, 6.2 Hz, 1H), 7.16 (dd, *J* = 7.8, 4.5 Hz, 2H), 6.93 (td, *J* = 12.2, 3.2 Hz, 1H), 6.39 (s, 1H), 2.72 (s,3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 158.87 (d, *J* = 237.6 Hz), 158.10, 157.95, 139.54, 133.13, 130.11 (d, *J* = 9.6 Hz), 116.95, 115.03 (d, *J* = 8.9Hz), 109.81 (d, *J*= 25.4 Hz), 106.42, 104.60 (d, *J* = 24.8 Hz), 16.78. IR (neat): 1564, 1470, 1427, 1173, 1112, 957, 835, 792, 773, 590, 552. HRMS (ESI) calcd. for $C_{13}H_{11}FN_3[M+H]^+$: 228.0937, found: 228.0932.



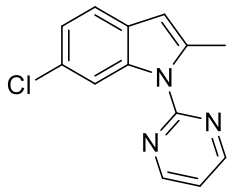
5-Chloro-2-methyl-1-(pyrimidin-2-yl)-1H-indole (2k): Yield: 46%, white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.8 Hz, 2H), 8.24 (d, *J* = 8.9 Hz, 1H), 7.47 (d, *J* = 2.1 Hz, 1H), 7.16 (dt, *J* = 8.9, 3.5 Hz, 2H), 6.38 (s, 1H), 2.72 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.00 (3C), 139.25, 135.07, 130.52, 127.11, 122.25, 118.83, 117.10, 115.14, 105.97, 16.71. IR (neat): 2931, 2571, 1556, 1422, 1261, 1206, 1069, 804, 740. HRMS (ESI) calcd. for $C_{13}H_{11}ClN_3[M+H]^+$: 244.0642, found: 244.0647.



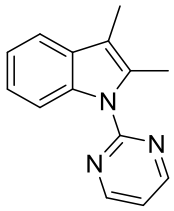
5-Bromo-2-methyl-1-(pyrimidin-2-yl)-1H-indole (2l): Yield: 34%, yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.79 (d, *J* = 3.8 Hz, 2H), 8.18 (d, *J* = 7.1 Hz, 1H), 7.62 (d, *J* = 1.6 Hz, 1H), 7.28 (dd, *J* = 7.1, 1.6 Hz, 1H), 7.17 (t, *J* = 3.8 Hz, 1H), 6.37 (s, 1H), 2.71 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.12 (3C), 139.22, 135.54, 131.22, 125.02, 122.00, 117.22, 115.64, 114.99, 105.97, 16.72. IR (neat): 2930, 2837, 1568, 1556, 1439, 1241, 1203, 801, 726. HRMS (ESI) calcd. for $C_{13}H_{11}BrN_3[M+H]^+$: 288.0136, found: 288.0132.



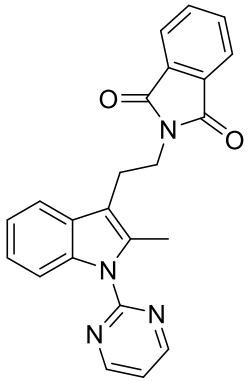
6-Fluoro-2-methyl-1-(pyrimidin-2-yl)-1H-indole (2m): Yield: 56%, white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.8 Hz, 2H), 8.10 (d, *J* = 11.3 Hz, 1H), 7.40 (dd, *J* = 8.2, 5.9 Hz, 1H), 7.16 (t, *J* = 4.8 Hz, 1H), 6.94 (t, *J* = 8.7 Hz, 1H), 6.39 (s, 1H), 2.71 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.91 (d, *J* = 236.4 Hz), 158.12, 157.97, 138.16, 136.74 (d, *J* = 12.7 Hz), 125.66, 119.66 (d, *J* = 9.7 Hz), 117.00, 109.79 (d, *J* = 24.1 Hz), 106.31, 101.47 (d, J = 28.8 Hz), 16.72. IR (neat): 1628, 1599, 1561, 1478, 1432, 1370, 1349, 1324, 1262, 1203, 1133, 979, 800, 725, 629, 575. HRMS (ESI) calcd. for $C_{13}H_{11}FN_3[M+H]^+$: 228.0937, found: 228.0933.



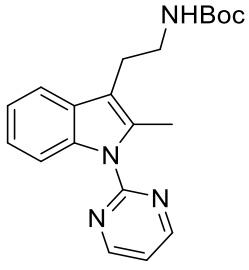
6-Chloro-2-methyl-1-(pyrimidin-2-yl)-1H-indole (2n): Yield: 55%, yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (d, *J* = 4.8 Hz, 2H), 8.35 (d, *J* = 1.2 Hz, 1H), 7.40 (d, *J* = 8.3 Hz, 1H), 7.21 – 7.08 (m, 2H), 6.40 (s, 1H), 2.71 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.15 (3C), 138.67, 137.13, 128.19, 127.96, 122.28, 120.10, 117.25, 114.37, 106.46, 16.75. The spectral data of the product was in accordance with that reported in the literature.[2]



2,3-Dimethyl-1-(pyrimidin-2-yl)-1H-indole (2o): Yield: 95%, yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.7 Hz, 2H), 8.33 – 8.21 (m, 1H), 7.55 – 7.47 (m, 1H), 7.23 (dd, *J* = 6.2, 2.4 Hz, 2H), 7.13 – 7.05 (m, 1H), 2.64 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.34, 157.93, 136.07, 132.94, 130.63, 122.56, 121.47, 117.79, 116.55, 113.68, 112.69, 13.60, 8.91. The spectral data of the product was in accordance with that reported in the literature.[2]

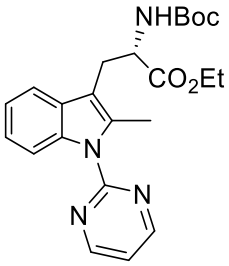


2-(2-(2-Methyl-1-(pyrimidin-2-yl)-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (2p): Yield: 77%, yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.76 (dd, *J* = 4.8, 0.9 Hz, 2H), 8.23 (dd, *J* = 6.1, 3.2 Hz, 1H), 7.89 – 7.79 (m, 2H), 7.75 – 7.64 (m, 3H), 7.25 – 7.17 (m, 2H), 7.11 (td, *J* = 4.8, 1.2 Hz, 1H), 3.94 – 3.89 (m, 2H), 3.15 – 3.09 (m, 2H), 2.70 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 168.21, 158.10, 158.05, 136.02, 134.19, 133.80, 132.11, 129.40, 123.09, 122.66, 121.71, 117.71, 116.85, 113.56, 113.12, 37.71, 23.55, 13.36. IR (neat): 2920, 1775, 1713, 1562, 1462, 1424, 1392, 1266, 1025, 809, 723. HRMS (ESI) calcd. for $C_{23}H_{19}N_4O_2[M+H]^+$:383.1508, found: 383.1513.

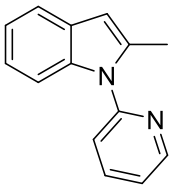


***Tert*-butyl (2-(2-methyl-1-(pyrimidin-2-yl)-1H-indol-3-yl)ethyl)carbamate (2q)**: Yield: 55%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.5 Hz, 2H), 8.65 (d, *J* = 4.7 Hz, 1H), 8.21 (d, *J* = 7.3 Hz, 1H), 7.55 – 7.46 (m, 1H), 7.20 (d, *J* = 6.1 Hz, 1H), 7.12 (t, *J* = 4.8 Hz, 1H), 4.78 (s, 2H), 3.59 – 3.28 (m, 2H), 2.97 (t, *J* = 5.6 Hz, 2H), 2.62 (s, 3H), 1.44 (s, 9H). HRMS (ESI) calcd. for $C_{20}H_{25}N_4O_2[M+H]^+$: 353.1978, found ：

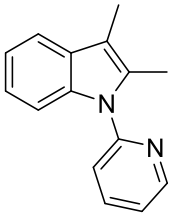
353.1972.



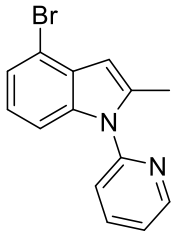
Ethyl(S)-2-((tert-butoxycarbonyl)amino)-3-(2-methyl-1-(pyrimidin-2-yl)-1H-indol-3yl) propanoate (2r): Yield: 35%, yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.4 Hz, 2H), 8.20 (d, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 7.3 Hz, 1H), 7.24 – 7.17 (m, 2H), 7.15 (t, *J* = 4.7 Hz, 1H), 4.21 – 4.06 (m, 2H), 4.08 – 3.98 (m, 1H), 3.28 (d, *J* = 5.6 Hz, 2H), 2.61 (s, 3H), 1.42 (s, 9H), 1.14 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.18, 158.01, 155.02, 135.97, 135.04, 129.78, 122.66, 121.58, 117.82, 116.97, 113.41, 111.38, 79.65, 61.37, 53.90, 28.25, 27.41, 13.84, 13.58. IR (neat):2980, 2937, 1709, 1563, 1462, 1429, 1267, 1163, 1042, 733, 691. HRMS (ESI) calcd. for $C_{23}H_{29}N_4O_4[M+H]^+$: 425.2189, found: 425.2180.



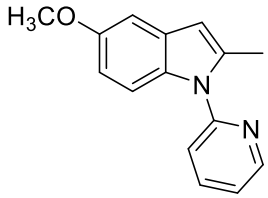
2-methyl-1-(pyridin-2-yl)-1H-indole (2s): Yield: 67%, yellow oil.^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 (dd, *J* = 4.8, 1.0 Hz, 1H), 7.90 (td, *J* = 7.8, 1.8 Hz, 1H), 7.63 – 7.50 (m, 1H), 7.48 – 7.28 (m, 3H), 7.13 (dd, *J* = 6.0, 3.1 Hz, 2H), 6.43 (s, 1H), 2.47 (s, 3H). The spectral data of the product was in accordance with that reported in the literature.[2]



2,3-dimethyl-1-(pyridin-2-yl)-1H-indole (2t): Yield: 85%, brown gel. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.69 (d, *J* = 3.4 Hz, 1H), 7.86 (t, *J* = 6.8 Hz, 1H), 7.61 (dd, *J* = 5.5, 3.2 Hz, 1H), 7.52 – 7.37 (m, 2H), 7.35 – 7.24 (m, 1H), 7.24 – 7.13 (m, 2H), 2.45 (s, 3H), 2.38 (s, 3H). The spectral data of the product was in accordance with that reported in the literature.[3]

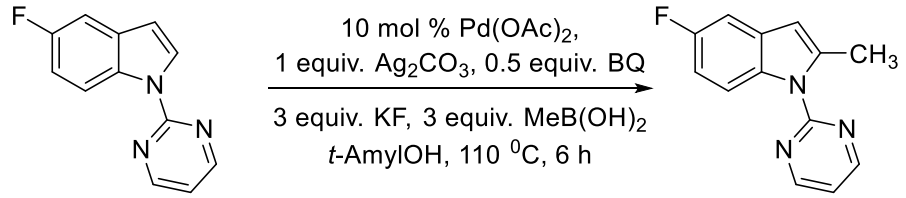


4-bromo-2-methyl-1-(pyridin-2-yl)-1H-indole (2u): Yield: 47%, brown gel. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 (d, *J* = 4.7 Hz, 1H), 7.90 (t, *J* = 7.7 Hz, 1H), 7.42 – 7.34 (m, 2H), 7.29 (d, *J* = 7.8 Hz, 2H), 6.98 (t, *J* = 7.9 Hz, 1H), 6.49 (s, 1H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.98, 149.63, 138.34, 137.66, 137.33, 129.22, 125.13, 123.42, 122.37, 120.87, 113.56, 109.41, 103.23, 13.85. HRMS (ESI) calcd. for $C_{14}H_{12}BrN_2[M+H]^+$: 287.0184, found: 287.0180.



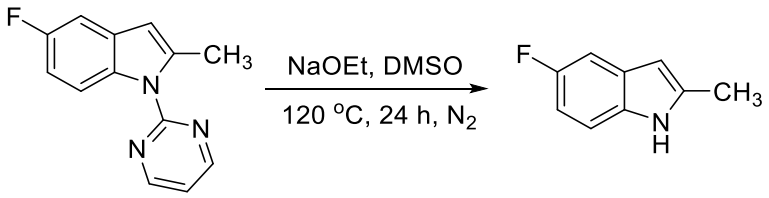
5-methoxy-2-methyl-1-(pyridin-2-yl)-1H-indole (2v): Yield: 62%, brown gel. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (d, *J* = 3.5 Hz, 1H), 7.85 (td, *J* = 7.8, 1.9 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.35 – 7.24 (m, 2H), 7.04 (d, *J* = 2.0 Hz, 1H), 6.79 (dd, *J* = 8.9, 2.1 Hz, 1H), 6.36 (s, 1H), 3.86 (s, 3H), 2.46 (s, 3H).The spectral data of the product was in accordance with that reported in the literature.[2]

5. Scale up Experiment on Gram Scale and Removal of Directing Group



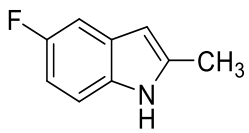
1j **2j**

Substrate **1j**(1.065 g, 5 mmol), $Pd(OAc)_2$(0.112 g, 0.5 mmol), Ag_2CO_3(1.375 g,5 mmol),BQ(0.27 g, 2.5 mmol), KF(0.87 g, 15 mmol), methylboronic acid(0.9 g, 15 mmol) and *t*-AmylOH(25 mL) were combined under air in a 100 mL flask and stirred at 110 ^oC for 6 h. The resulting mixture was cooled to room temperature, filtered through a pad of silica gel and washed with 100 mL 50 % EtOAc/ petroleumether. Then the solvents were evaporated under reduced pressure and then purified directly *via* chromatography on silica gel (DCM : petroleum ether =1:1) to give the5-fluoro-2-methyl-1-(pyrimidin-2-yl)-1*H*-indole **2j** as a white solid (Yield: 40 %).



2j **3j**

The mixture of **2j** (45.4 mg, 0.2 mmol), NaOEt (68.05 mg, 1.0 mmol) and DMSO (1.5 mL) were added under nitrogen atmosphere for 24 h. After sealing the tube,the mixture was stirred at 120 ^oC. After cooling to ambient temperature, the reaction mixture was diluted with EtOAc (50 mL) and washed with H_2O (3 × 40 mL).The aqueous phase was extracted with EtOAc (2 × 40 mL), and the combined organic phase was dried over Na_2SO_4, after filtration and evaporation of the solvents in vacuo, the crude product was purified by column chromatography on silica gel (EtOAc : petroleum ether = 3%) to give the 5-fluoro-2-methyl-1H-indole **3j** (Yield: 86%).



5-Fluoro-2-methyl-1H-indole (3j): Yield: 86%, yellow solid. ^1H NMR (500 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.17 (ddd, *J* = 9.8, 6.0, 3.5 Hz, 2H), 6.85 (td, *J* = 9.1, 2.5 Hz, 1H), 6.19 (s, 1H), 2.44 (s, 3H). The spectral data of the product was in accordance with that reported in the literature.[4]

6. References

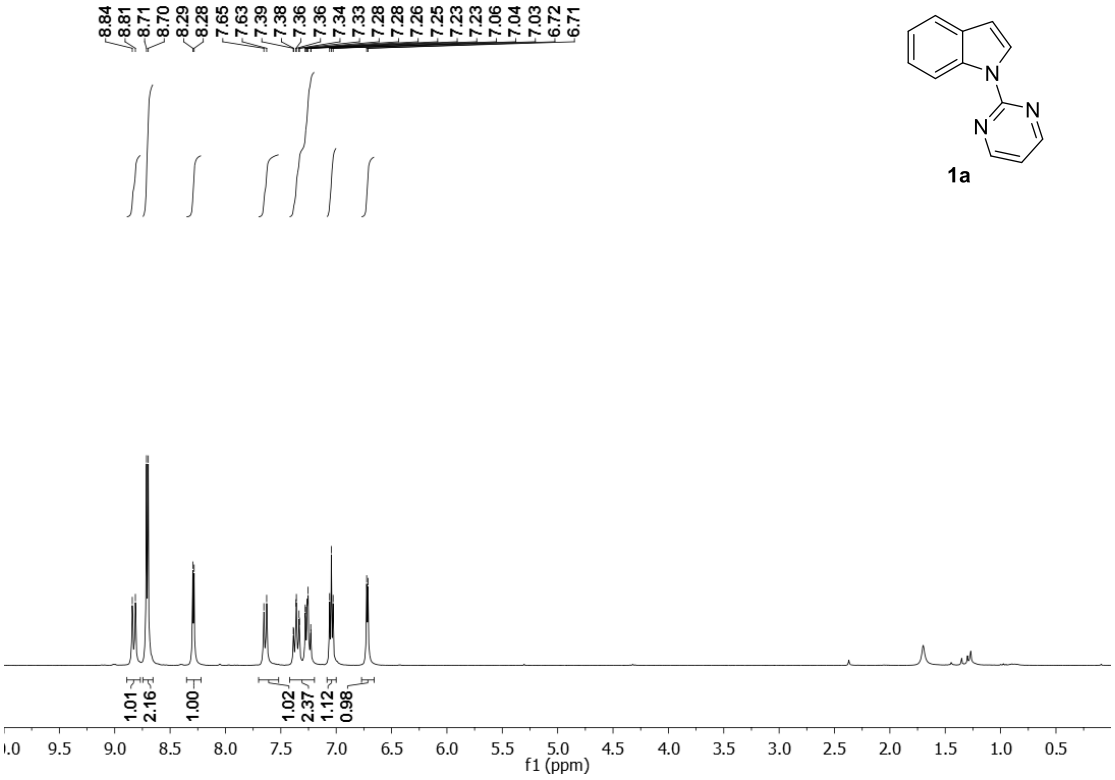
1.(a) J. Zhao, X. Cheng, J. Le, W. Yang, F. Xue, X. Zhang and C. Jiang, *Org. Biomol. Chem.*, 2015, **13**, 9000-9004; (b) L. Ackermann and A. V. Lygin, *Org. Lett.*, 2011, **13**, 3332-3335; (c) Z. Ding and N.Yoshikai, *Angew. Chem. Int. Ed. Engl.*, 2012, **51**, 4698-4701; (d) J. Shi, B. Zhou, Y. Yang and Y. Li, *Org. Biomol. Chem*, 2012, **10**, 8953-8955; (e) S. Xu, X. Huang, X. Hong and B. Xu, *Org. Lett.*, 2012, **14**, 4614-4617; (f) P. Feng, Y. Fan, F. Xue, W. Liu, S. Li and Y. Shi. *Org. Lett.*, 2011, **13**, 5827–5829; (g) K. S. Feldman and P. Ngernmeesri**,** *Org. Lett.*, 2010, **12**, 4502–4505; (h) A. K. Maity and S. Roy, *Adv. Synth. Catal.*, 2014, **356**, 2627-2642; (i) R. Cano, D. J. Ramon and M. Yus, *J. Org. Chem.*, 2011, **76**, 654-660.

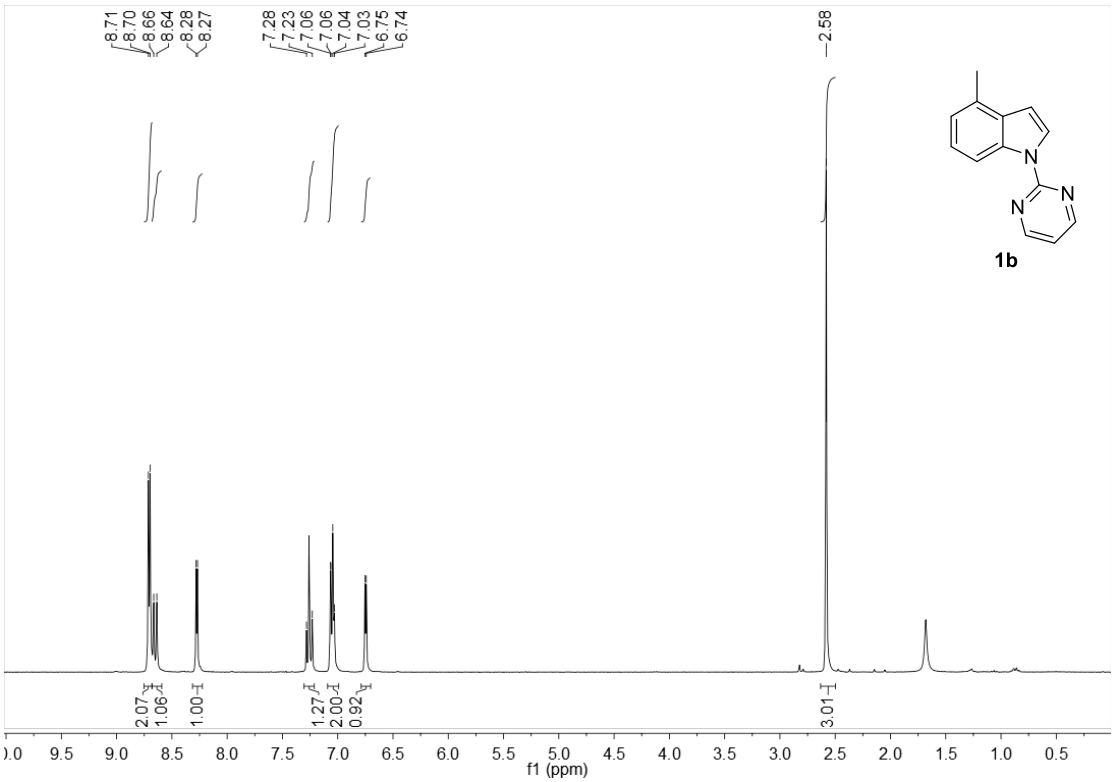
2.H. Wang, S. Yu, Z. Qi and X. Li,*Org. Lett.*, 2015, **17**, 2812−2815.

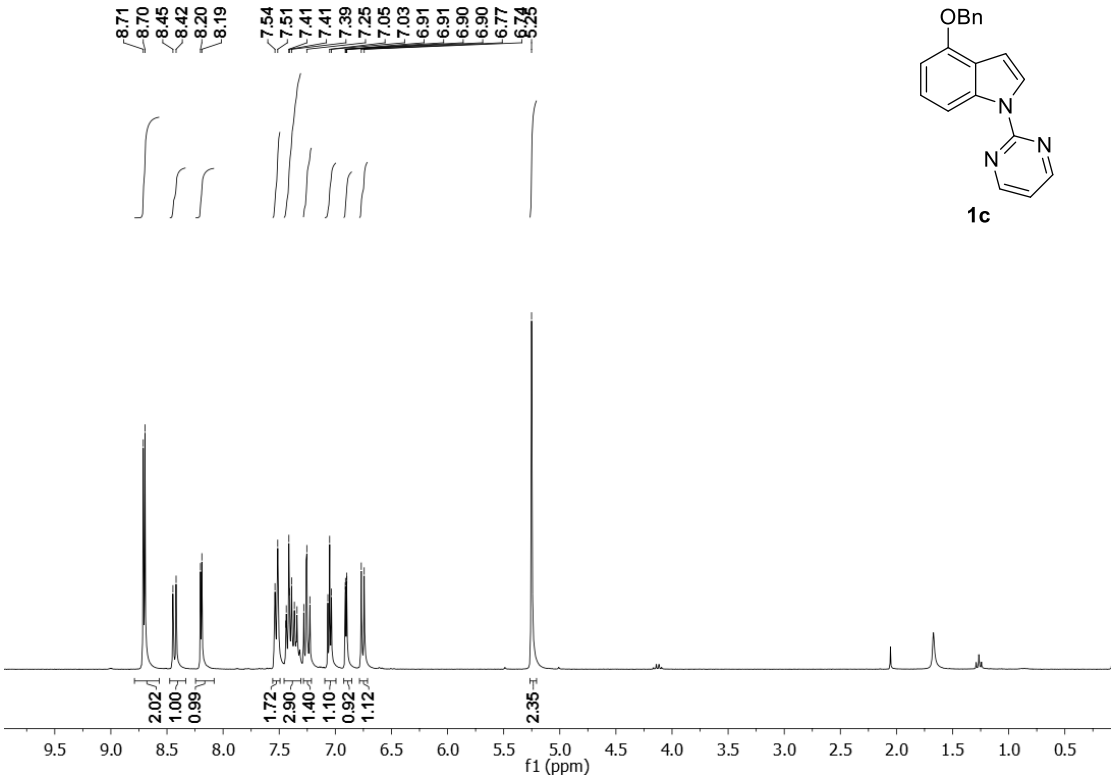
3. G. S. Kumar and M. Kapur, *Org. Lett.*, 2016, **18**, 1112-1115

4.V. Ramella, Z. He, C. G. Daniliuc and A. Studer, *Org. Lett.* 2015, **17**, 664−667.

7. ^{1}H and ^{13}C NMR spectra of starting materials and products



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8.70
8.45
8.42
8.20
8.19
7.54
7.51
7.41
7.41
7.39
7.25
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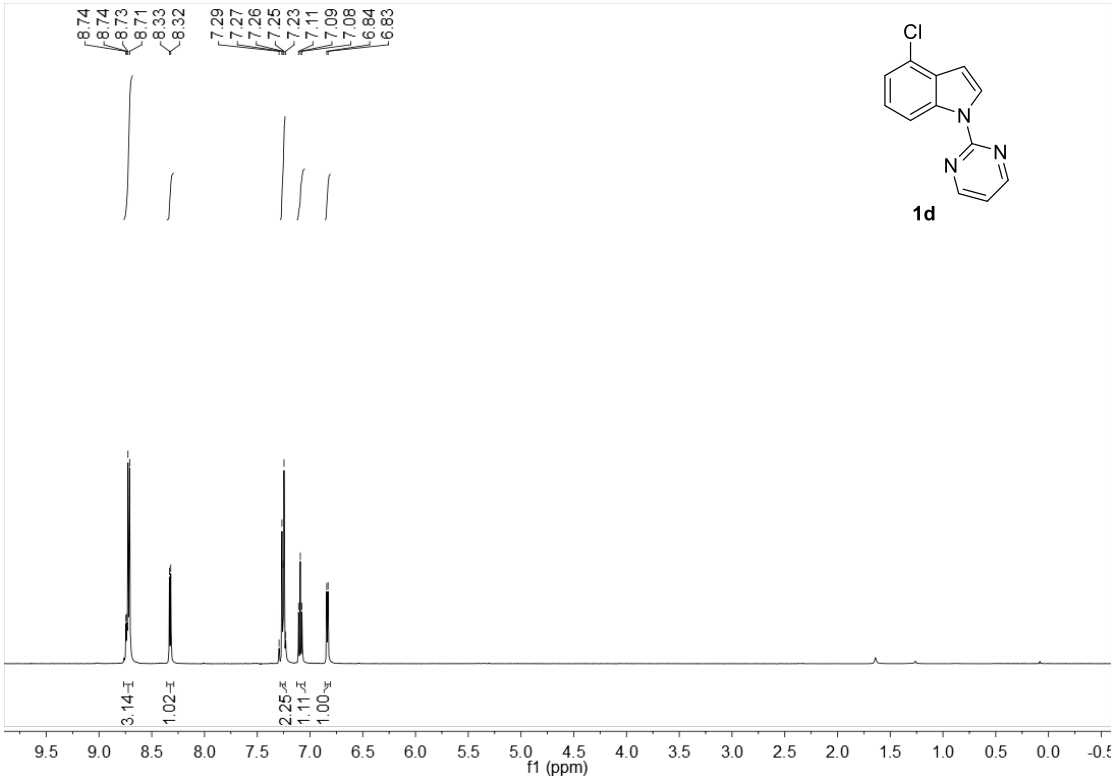
7.03
6.91
6.91
6.90
6.90
6.77
6.74
5.25
OBn
N
N
N
1c
2.02
1.00
0.99
1.72
2.90
1.40
1.10
0.92
1.12
2.35
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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8.74
8.73
8.71
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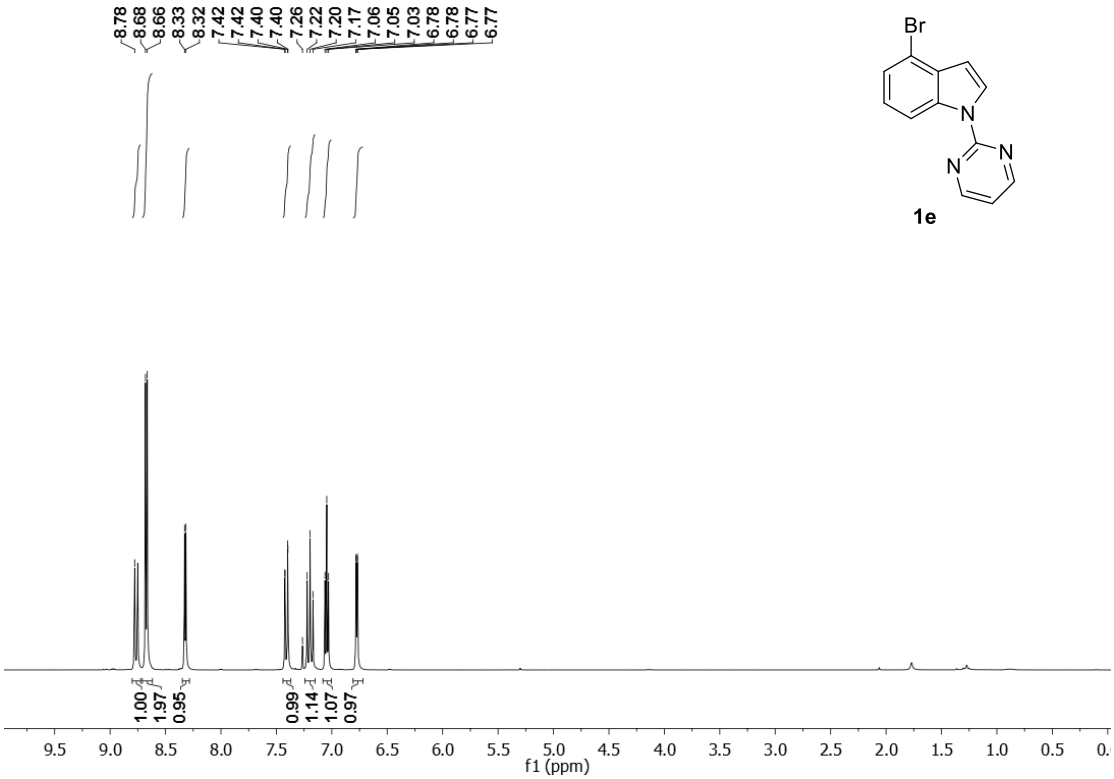
8.32
7.29
7.27
7.26
7.25
7.23
7.11
7.09
7.08
6.84
6.83
Cl
N
N
N
1d
3.14
1.02
2.25
1.11
1.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


8.78
8.68
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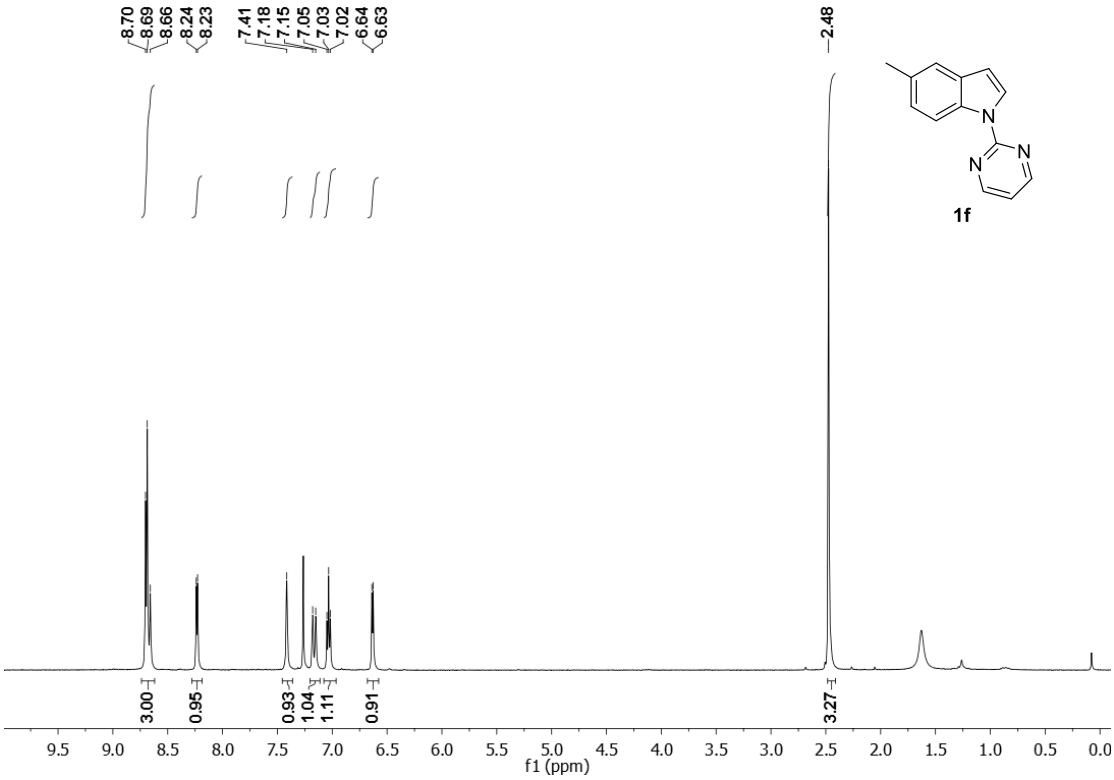
8.32
7.42
7.42
7.40
7.40
7.26
7.22
7.20
7.17
7.06
7.05
7.03
6.78
6.78
6.77
6.77
Br
N
N
N
1e
1.00
1.97
0.95
0.99
1.14
1.07
0.97
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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7.18
7.15
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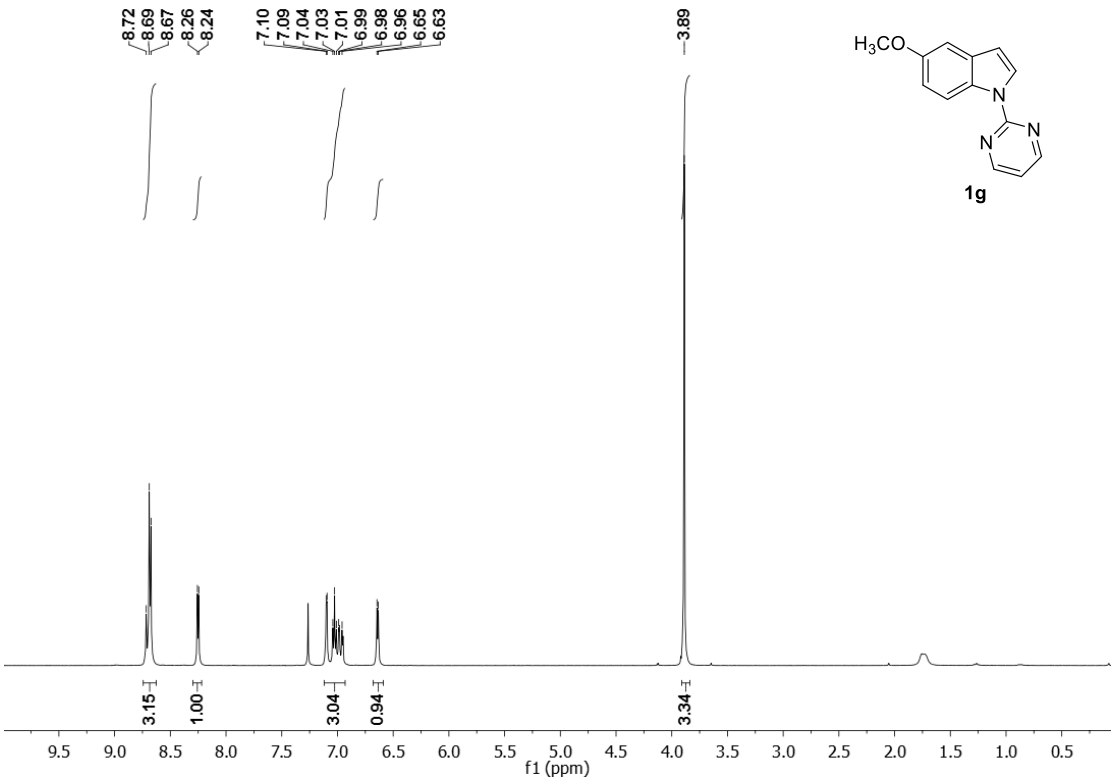
7.03
7.02
6.64
6.63
2.48
N
N
N
1f
3.00
0.95
0.93
1.04
1.11
0.91
3.27
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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7.03
7.01
6.99
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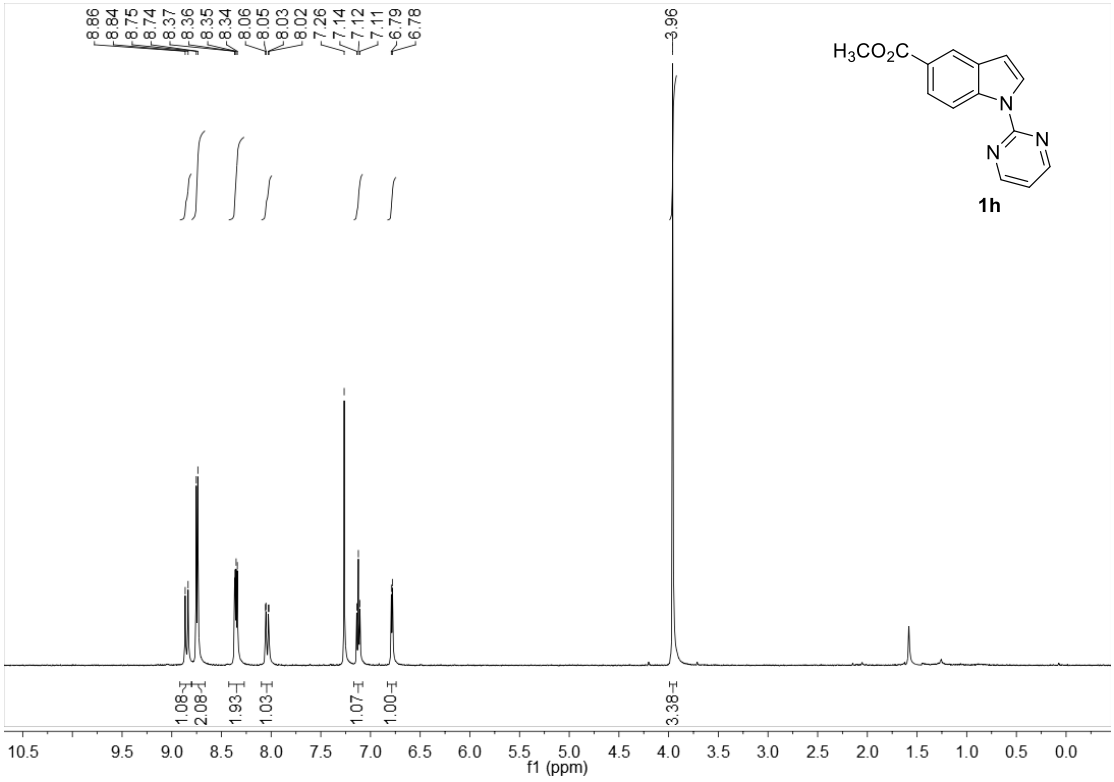
6.96
6.65
6.63
3.89
H3CO
N
N
N
1g
3.15
1.00
3.04
0.94
3.34
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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8.84
8.75
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8.35
8.34
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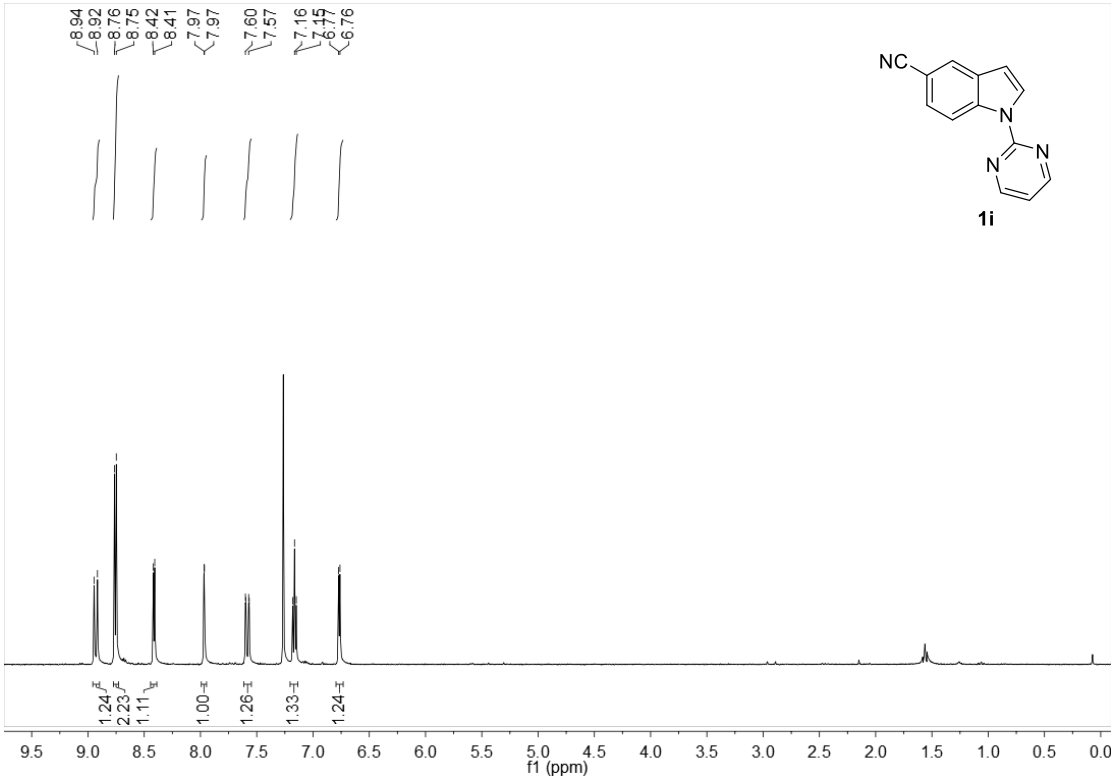
8.05
8.03
8.02
7.26
7.14
7.12
7.11
6.79
6.78
3.96
H3CO2C
N
N
N
1h
1.08
2.08
1.93
1.03
1.07
1.00
3.38
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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8.92
8.76
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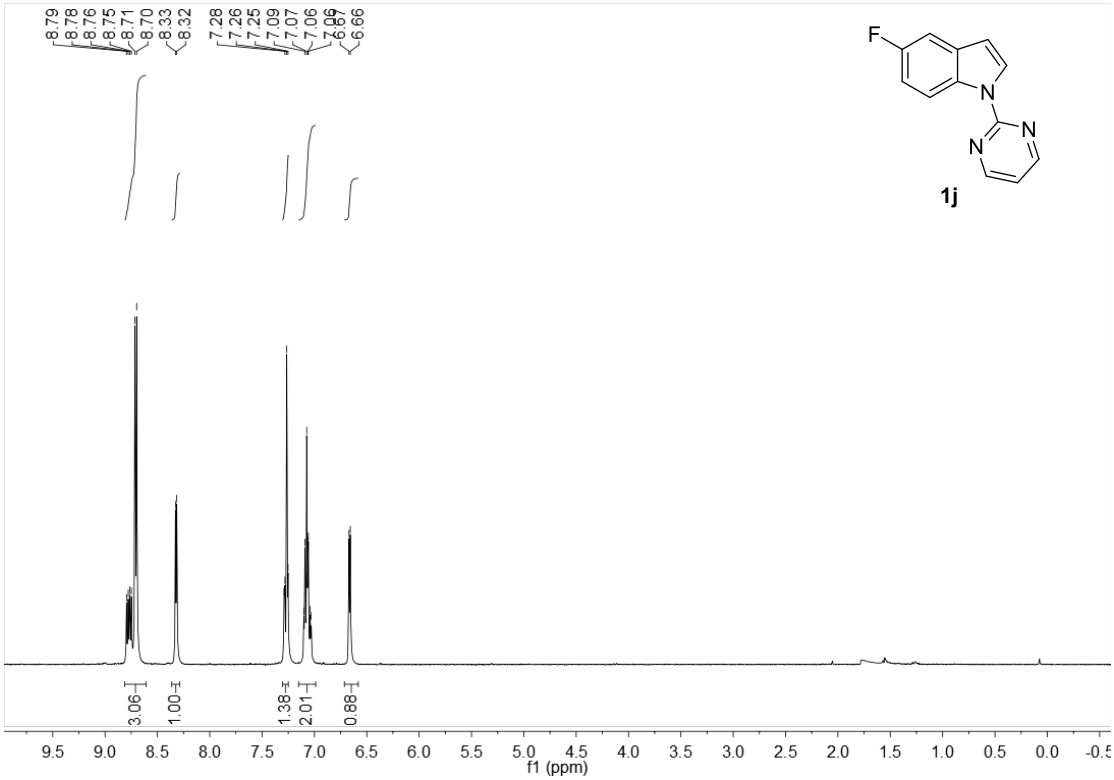
8.41
7.97
7.97
7.60
7.57
7.16
7.15
6.77
6.76
NC
N
N
N
1i
1.24
2.23
1.11
1.00
1.26
1.33
1.24
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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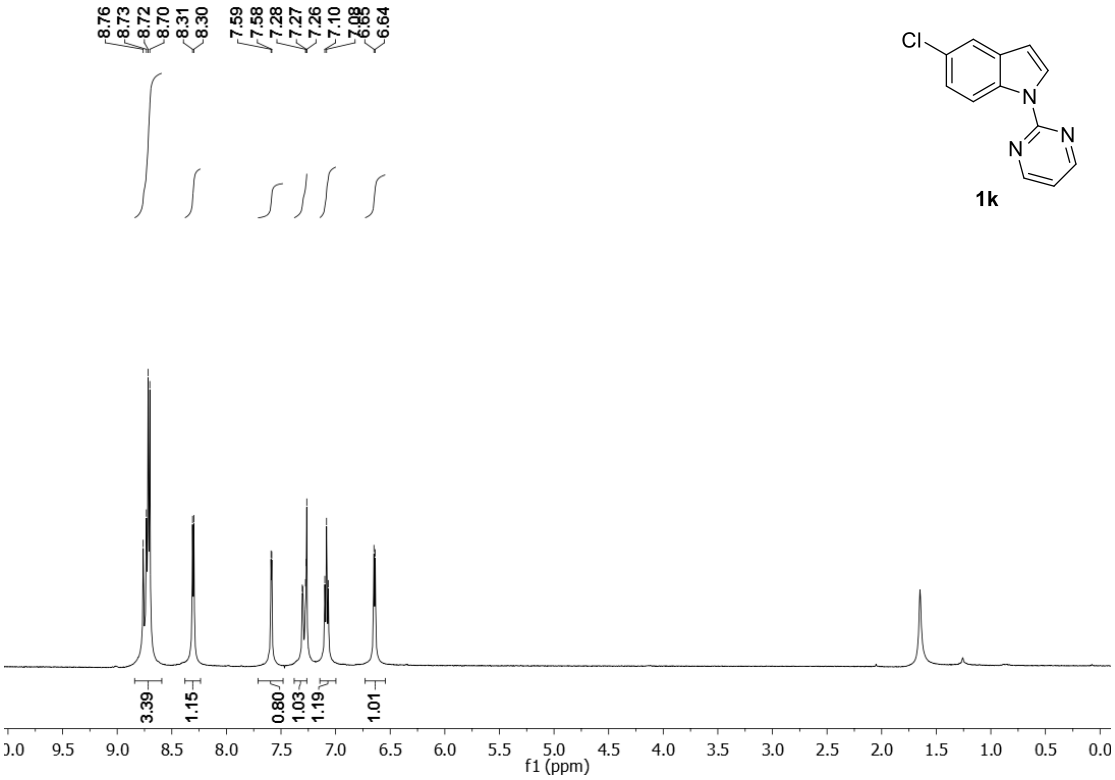
8.70
8.33
8.32
7.28
7.26
7.25
7.09
7.07
7.06
6.67
6.66
F
N
N
N
1j
3.06
1.00
1.38
2.01
0.88
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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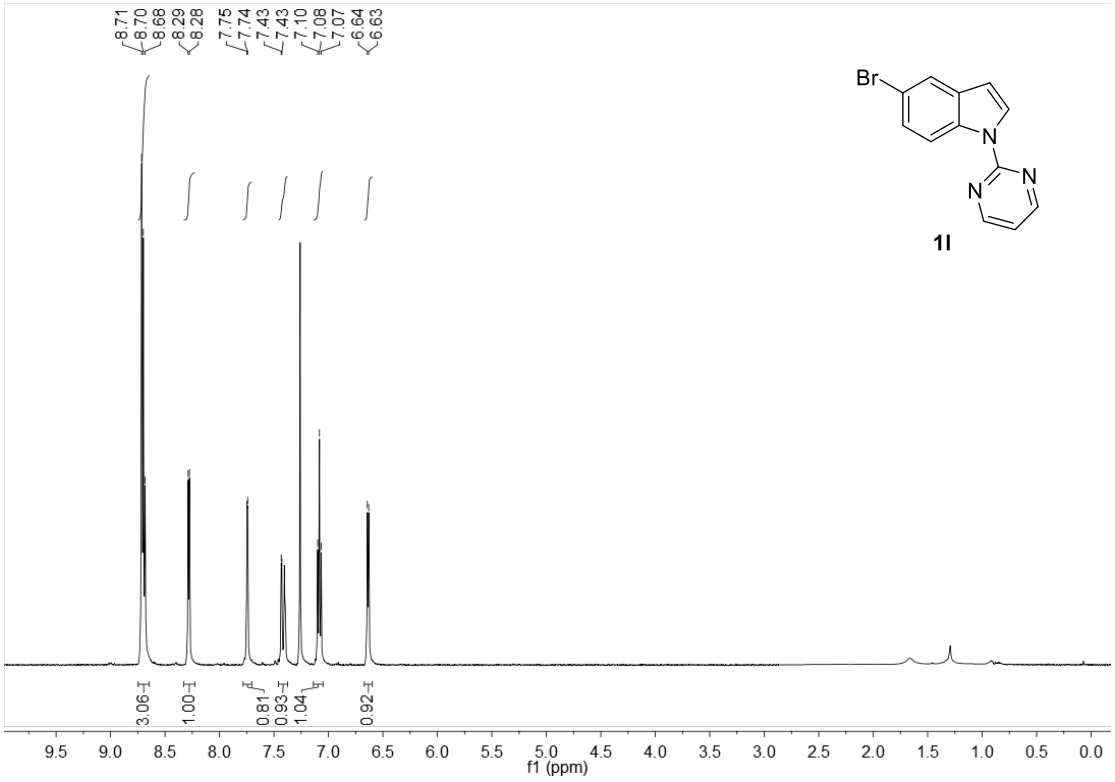
8.73
8.72
8.70
8.31
8.30
7.59
7.58
7.28
7.27
7.26
7.10
6.64
Cl
N
N
N
1k
3.39
1.15
0.80
1.03
1.19
1.01
f1 (ppm)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8.70
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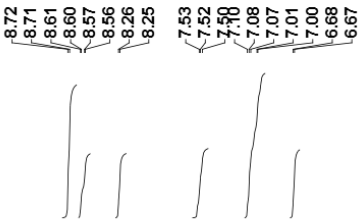
8.29
8.28
7.75
7.74
7.43
7.43
7.10
7.08
7.07
6.64
6.63
Br
N
N
N
1l
3.06
1.00
0.81
0.93
1.04
0.92
f1 (ppm)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8.61
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8.56
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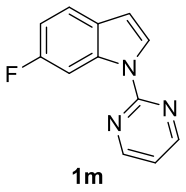
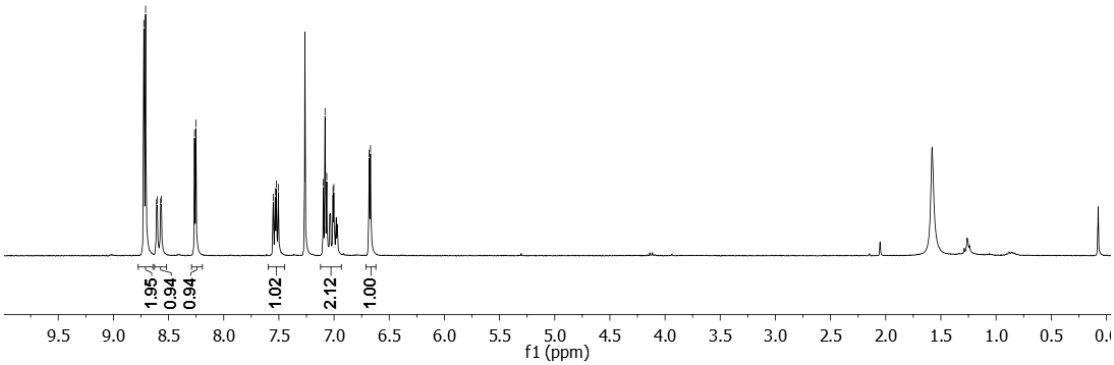
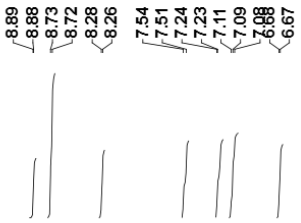
7.52
7.10
7.08
7.07
7.01
7.00
6.68
6.67


F
N
N
N

1m


1.95
0.94
0.94
1.02
2.12
1.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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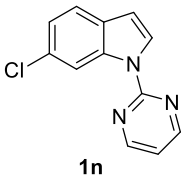
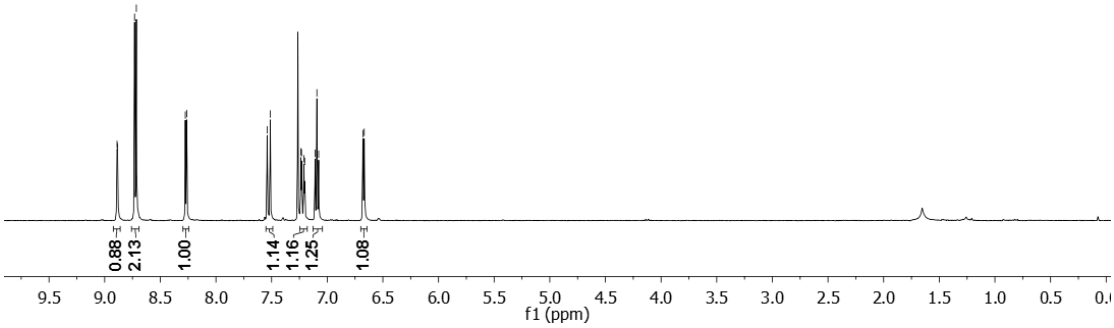
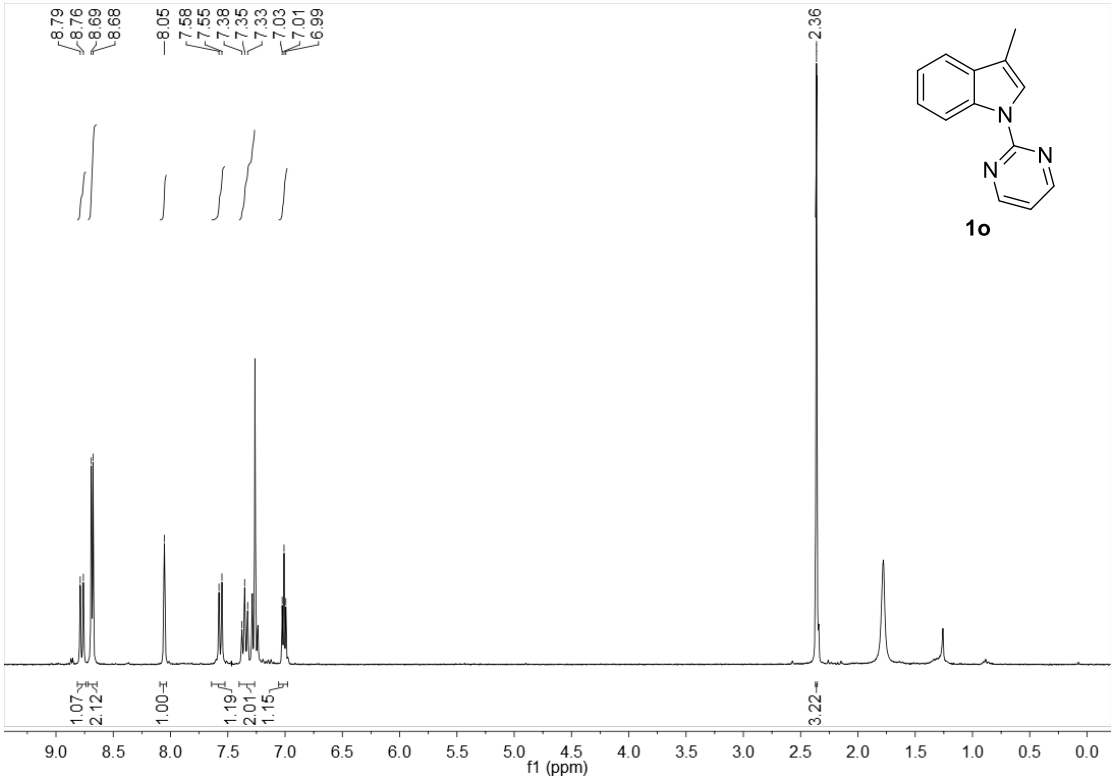
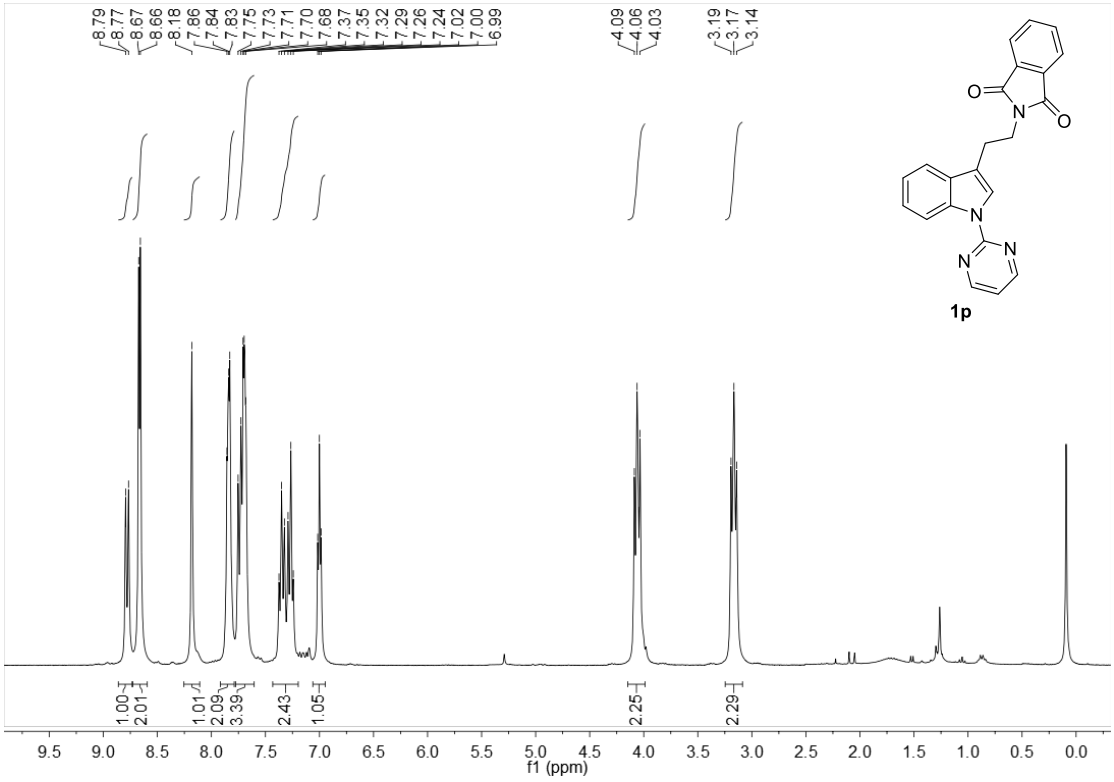
8.88
8.73
8.72
8.28
8.26
7.54
7.51
7.24
7.23
7.11
7.09
6.68
6.67

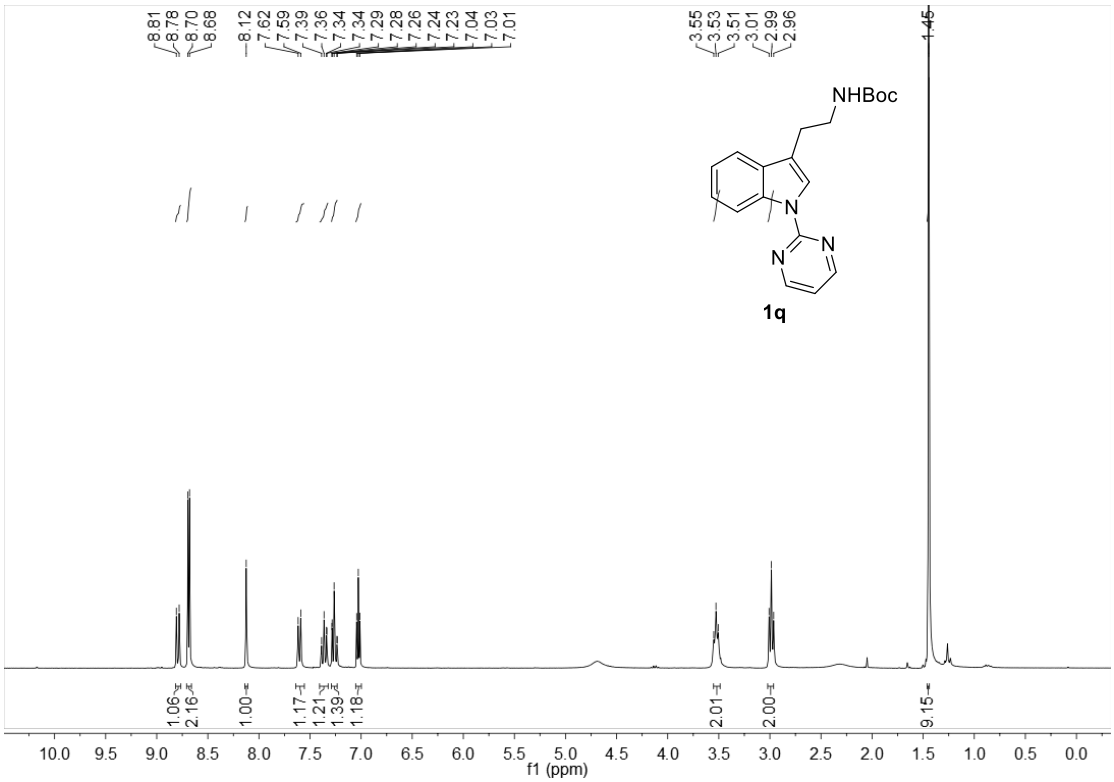

Cl
N
N
N

1n


0.88
2.13
1.00
1.14
1.16
1.25
1.08
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


8.79
8.76
8.69
8.68
8.05
7.58
7.55
7.38
7.35
7.33
7.03
7.01
6.99
2.36
1.07
2.12
1.00
1.19
2.01
1.15
3.22
f1 (ppm)
1o


8.79
8.77
8.67
8.66
8.18
7.86
7.84
7.83
7.75
7.73
7.71
7.70
7.68
7.37
7.35
7.32
7.29
7.26
7.24
7.02
7.00
6.99
4.09
4.06
4.03
3.19
3.17
3.14
1.00
2.01
1.01
2.09
3.39
2.43
1.05
2.25
2.29
f1 (ppm)
1p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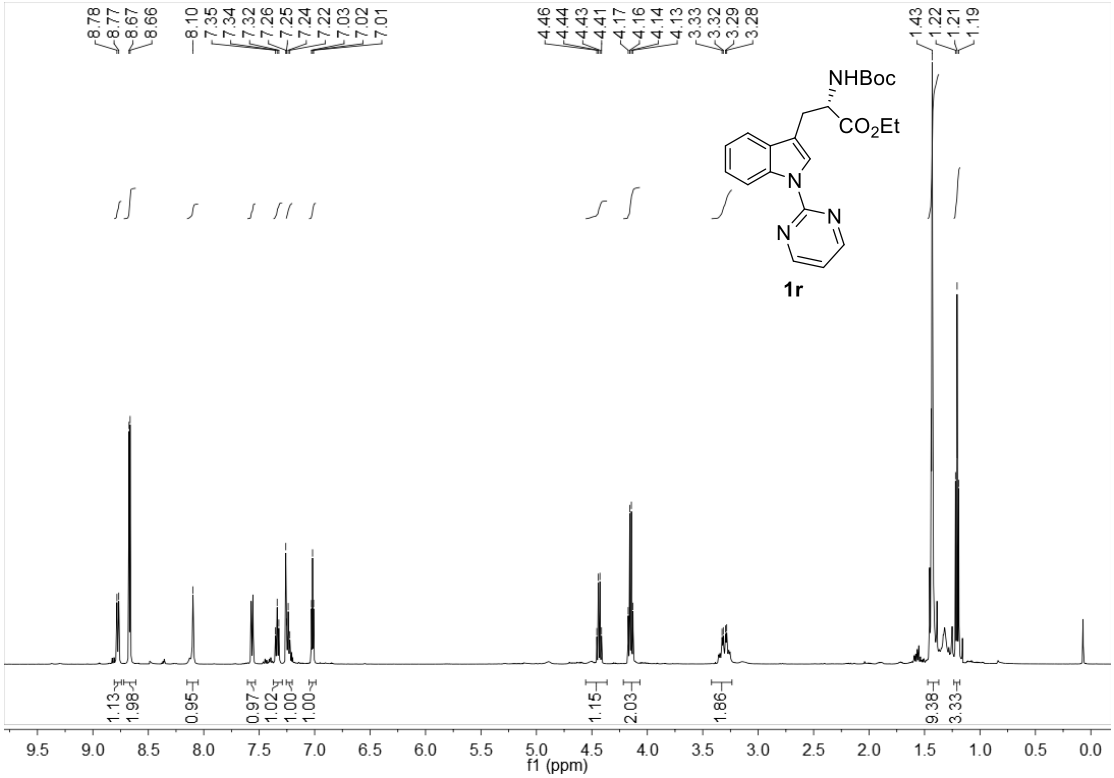
8.70
8.68
8.12
7.62
7.59
7.39
7.36
7.34
7.34
7.29
7.28
7.26
7.24
7.23
7.04
7.03
7.01
3.55
3.53
3.51
3.01
2.99
2.96
1.45
NHBoc
N
N
N
1q
1.06
2.16
1.00
1.17
1.21
1.39
1.18
2.01
2.00
9.15
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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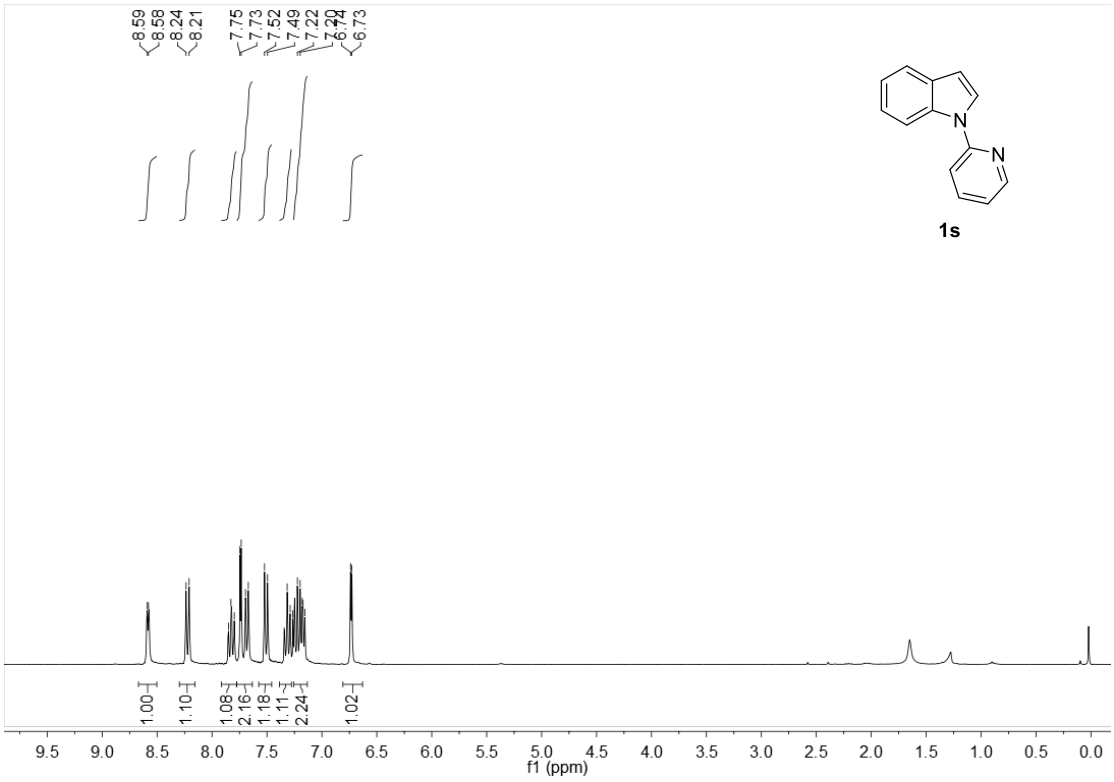
8.77
8.67
8.66
8.10
7.35
7.34
7.32
7.26
7.25
7.24
7.22
7.03
7.02
7.01
4.46
4.44
4.43
4.41
4.17
4.16
4.14
4.13
3.33
3.32
3.29
3.28
1.43
1.22
1.21
1.19
NHBoc
CO2Et
N
N
N
1r
1.13
1.98
0.95
0.97
1.02
1.00
1.00
1.15
2.03
1.86
9.38
3.33
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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8.58
8.24
8.21
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7.73
7.52
7.49
7.22
6.73
1s
1.00
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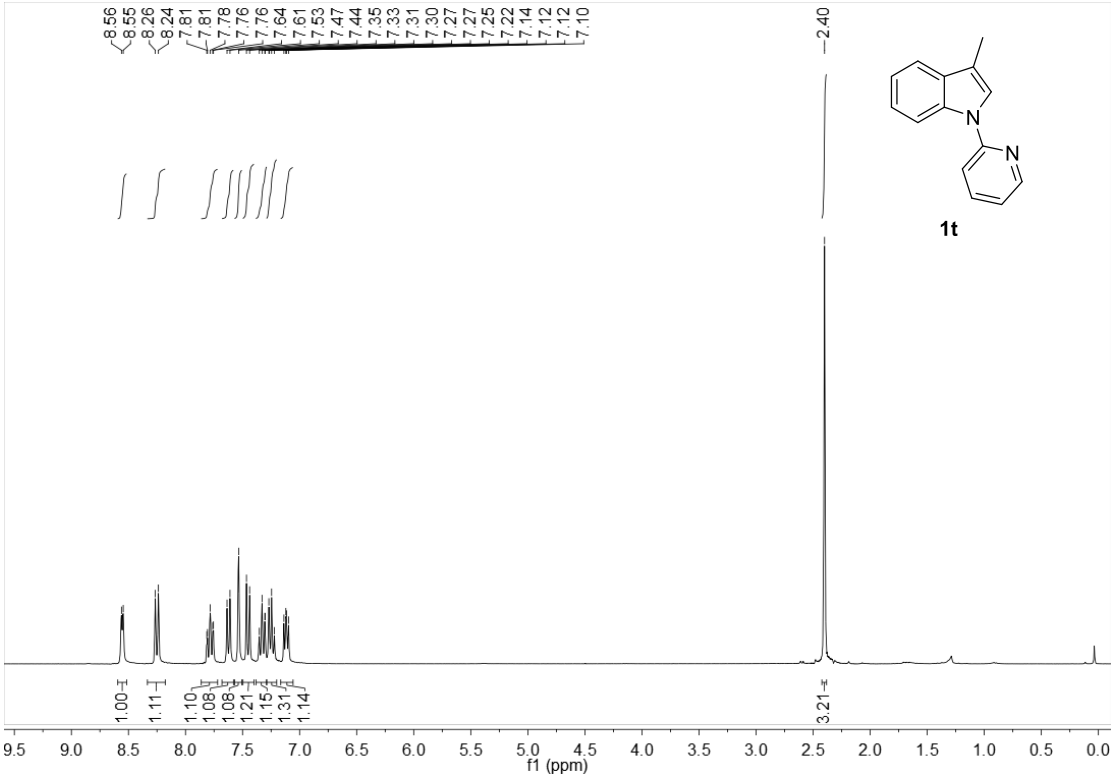
1.18
1.11
2.24
1.02
f1 (ppm)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8.26
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7.81
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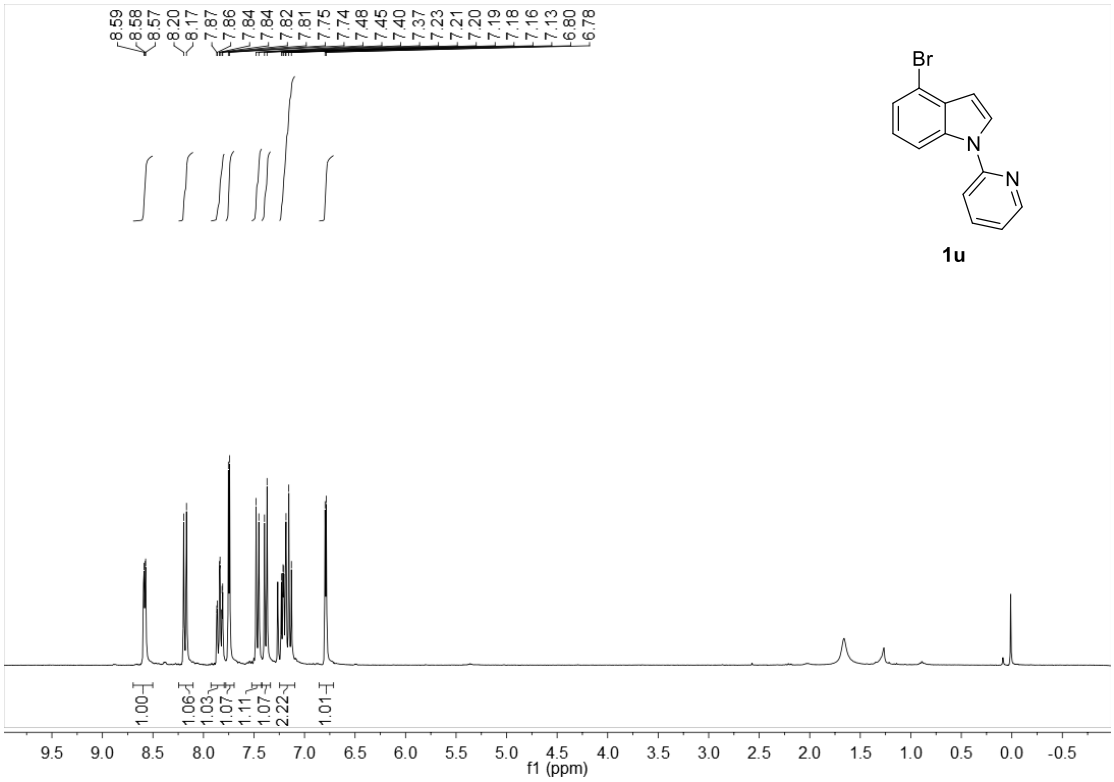
7.76
7.76
7.64
7.61
7.53
7.47
7.44
7.35
7.33
7.31
7.30
7.27
7.27
7.25
7.22
7.14
7.12
7.12
7.10
2.40
1t
1.00
1.11
1.10
1.08
1.08
1.21
1.15
1.31
1.14
3.21
f1 (ppm)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8.58
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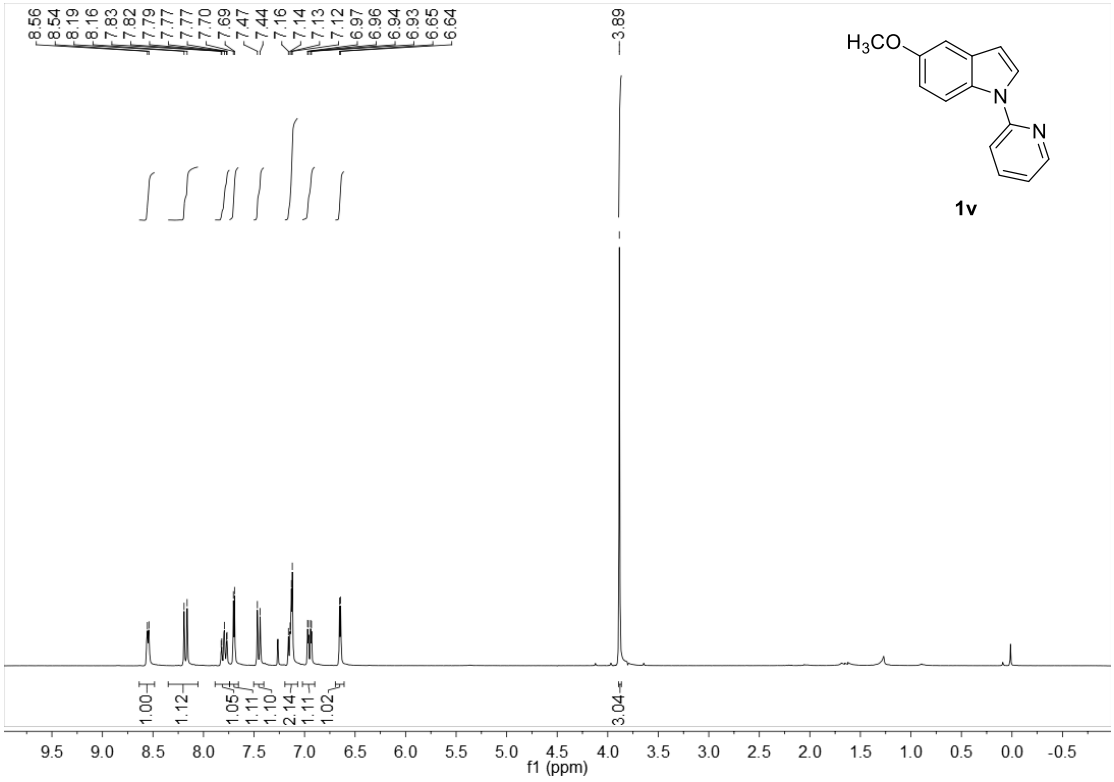
7.87
7.86
7.84
7.84
7.82
7.81
7.75
7.74
7.48
7.45
7.40
7.37
7.23
7.21
7.20
7.19
7.18
7.16
7.13
6.80
6.78
Br
N
N
1u
1.00
1.06
1.03
1.07
1.11
1.07
2.22
1.01
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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8.16
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7.82
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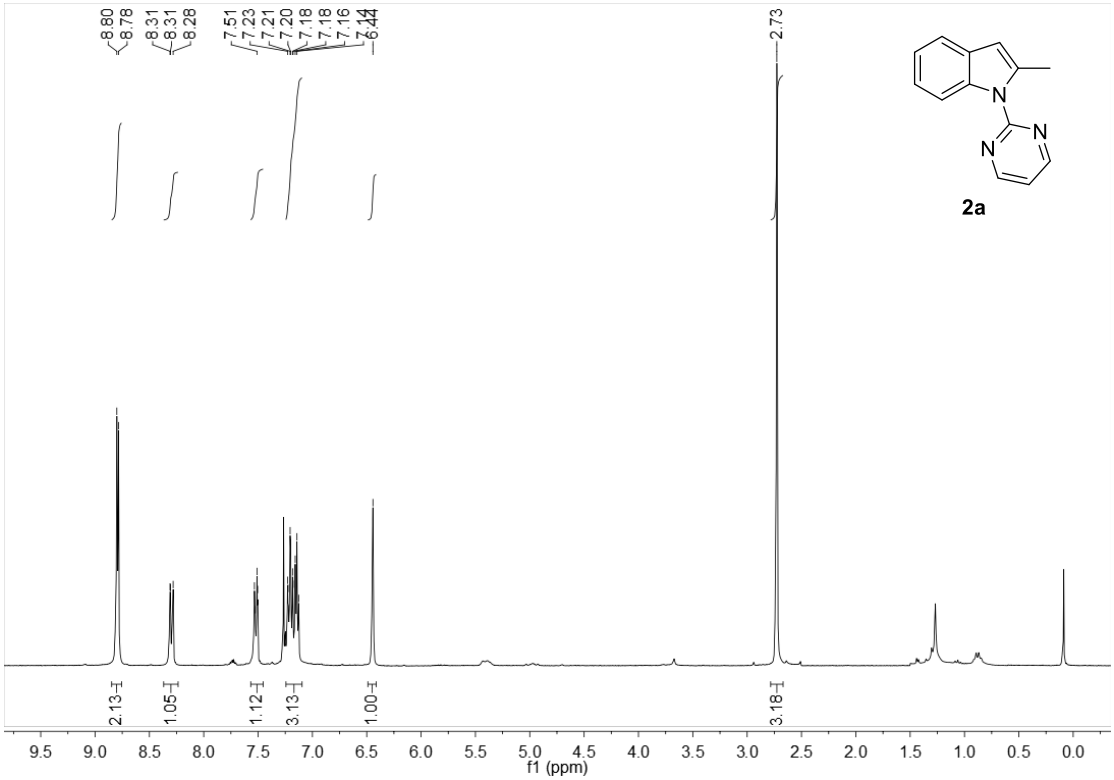
7.77
7.77
7.70
7.69
7.47
7.44
7.16
7.14
7.13
7.12
6.97
6.96
6.94
6.93
6.65
6.64
3.89
H3CO
N
N
1v
1.00
1.12
1.05
1.11
1.10
2.14
1.11
1.02
3.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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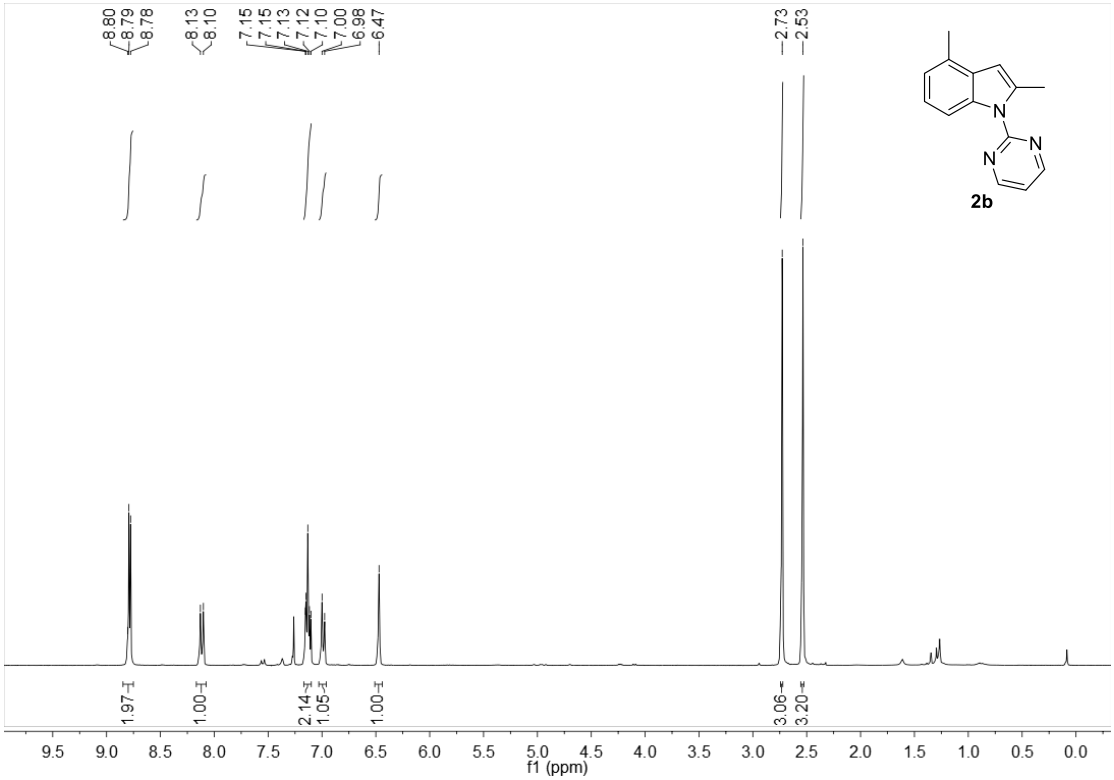
8.78
8.31
8.31
8.28
7.51
7.23
7.21
7.20
7.18
7.18
7.16
7.14
6.44
2.73
2.13
1.05
1.12
3.13
1.00
3.18
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
N
N
N
2a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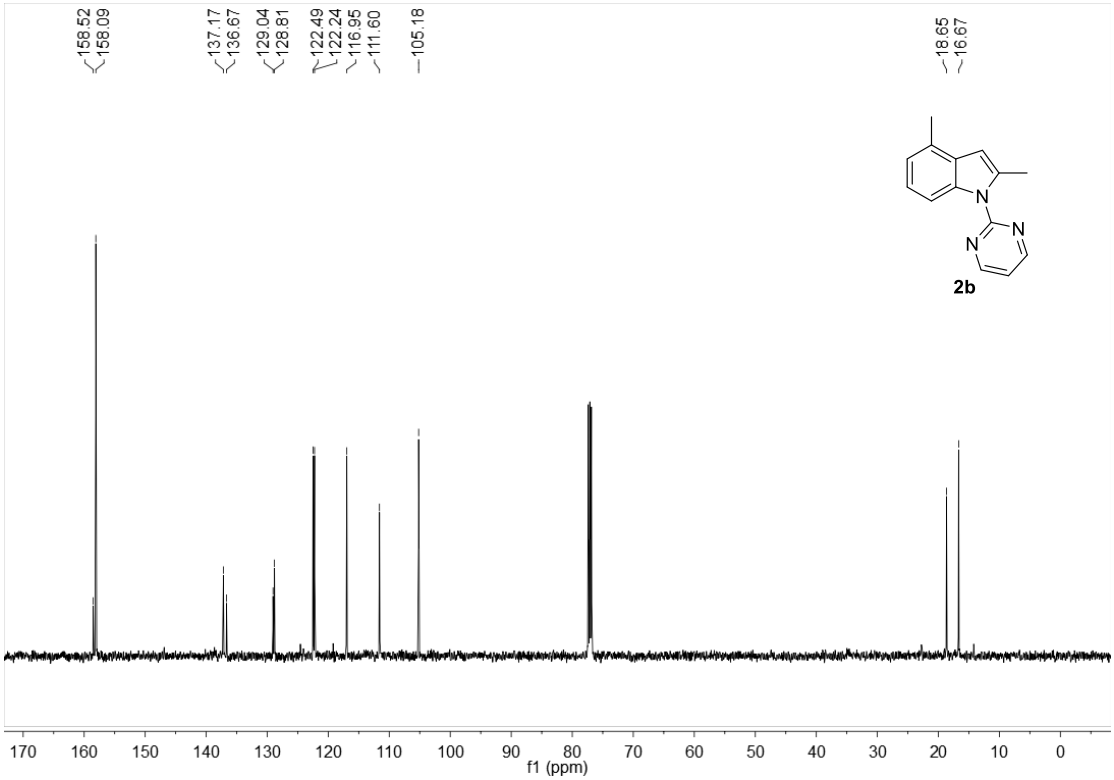
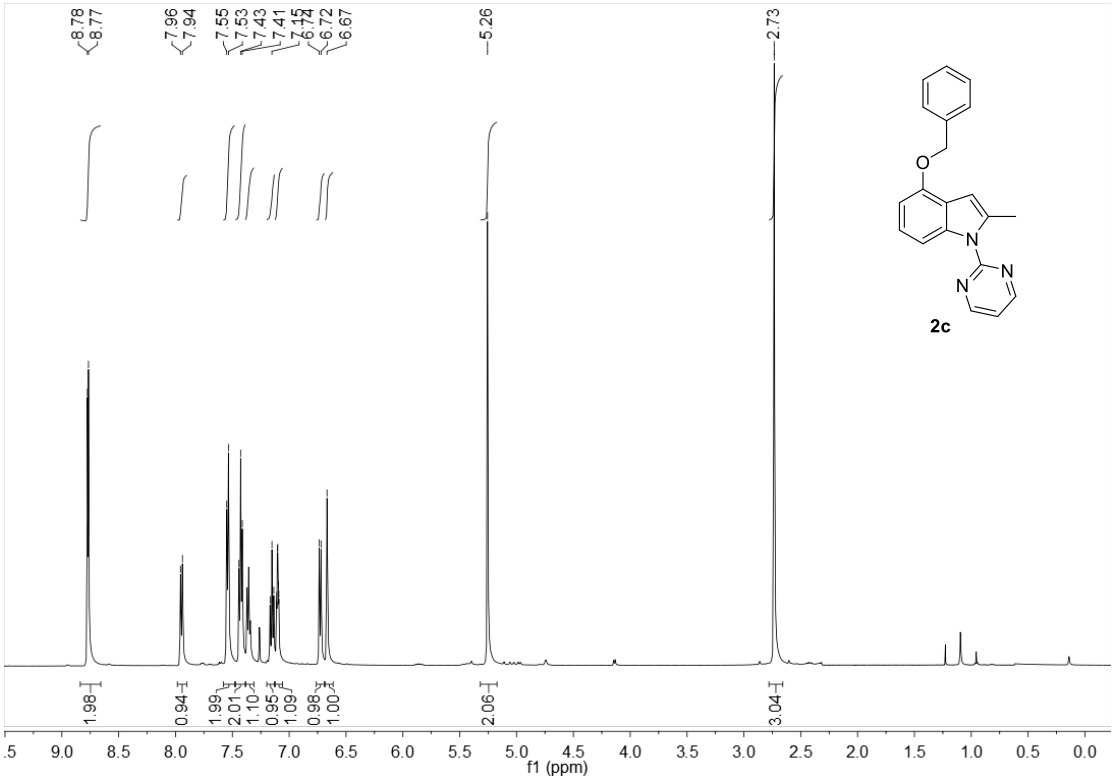
8.79
8.78
8.13
8.10
7.15
7.15
7.13
7.12
7.10
7.00
6.98
6.47
2.73
2.53
1.97
1.00
2.14
1.05
1.00
3.06
3.20
f1 (ppm)

2b


158.52
158.09
137.17
136.67
129.04
128.81
122.49
122.24
116.95
111.60
105.18
18.65
16.67
f1 (ppm)

2b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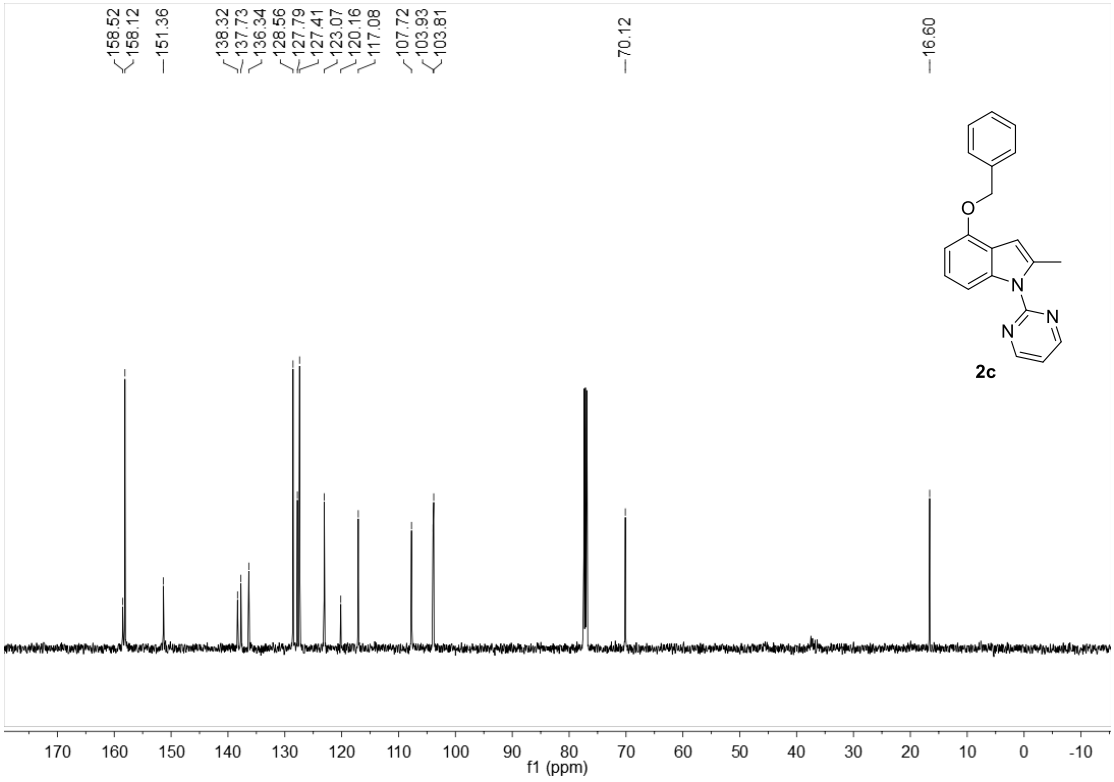
8.77
7.96
7.94
7.55
7.53
7.43
7.41
6.72
6.67
5.26
2.73
1.98
0.94
1.99
2.01
1.10
0.95
1.09
0.98
1.00
2.06
3.04
f1 (ppm)
2c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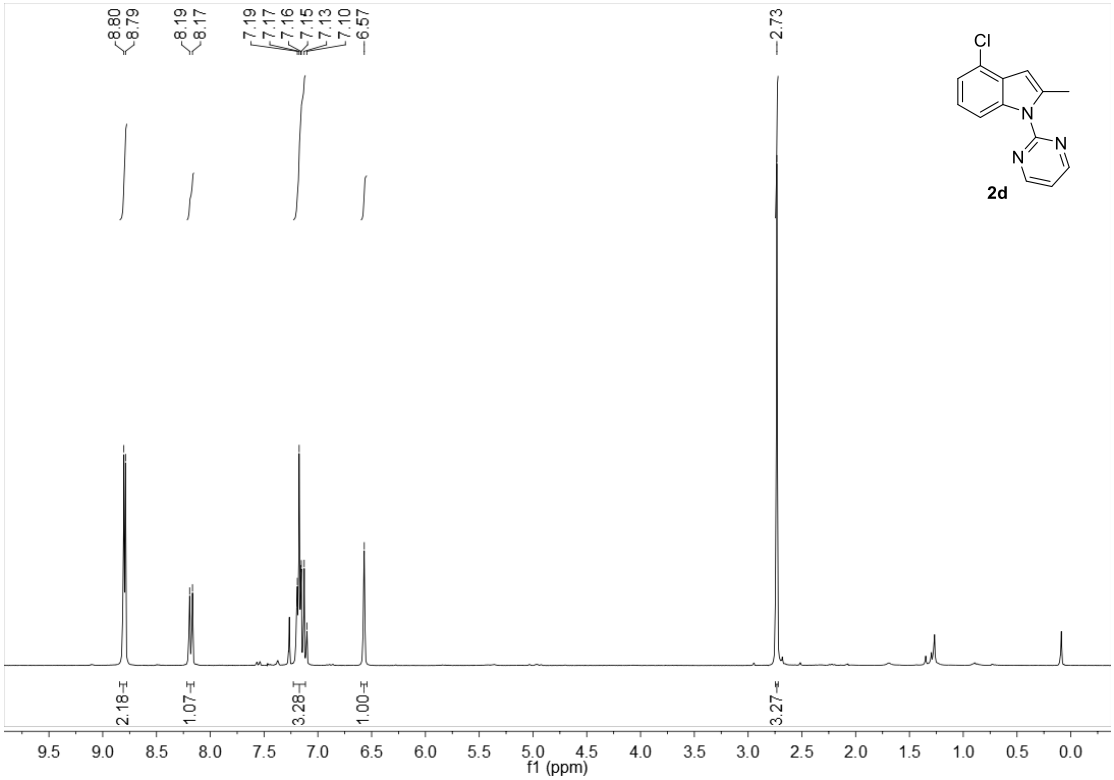
158.12
151.36
138.32
137.73
136.34
128.56
127.79
127.41
123.07
120.16
117.08
107.72
103.93
103.81
70.12
16.60
f1 (ppm)
2c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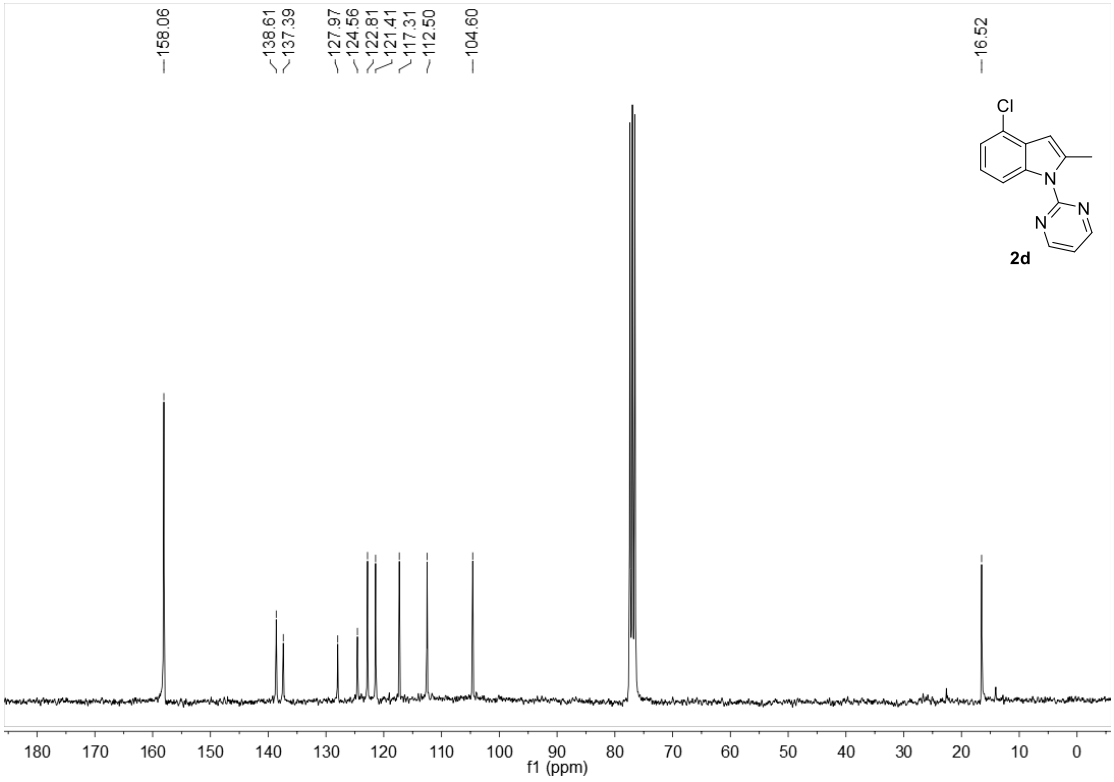
8.79
8.19
8.17
7.19
7.17
7.16
7.15
7.13
7.10
6.57
2.73
Cl
N
N
N
2d
2.18
1.07
3.28
1.00
3.27
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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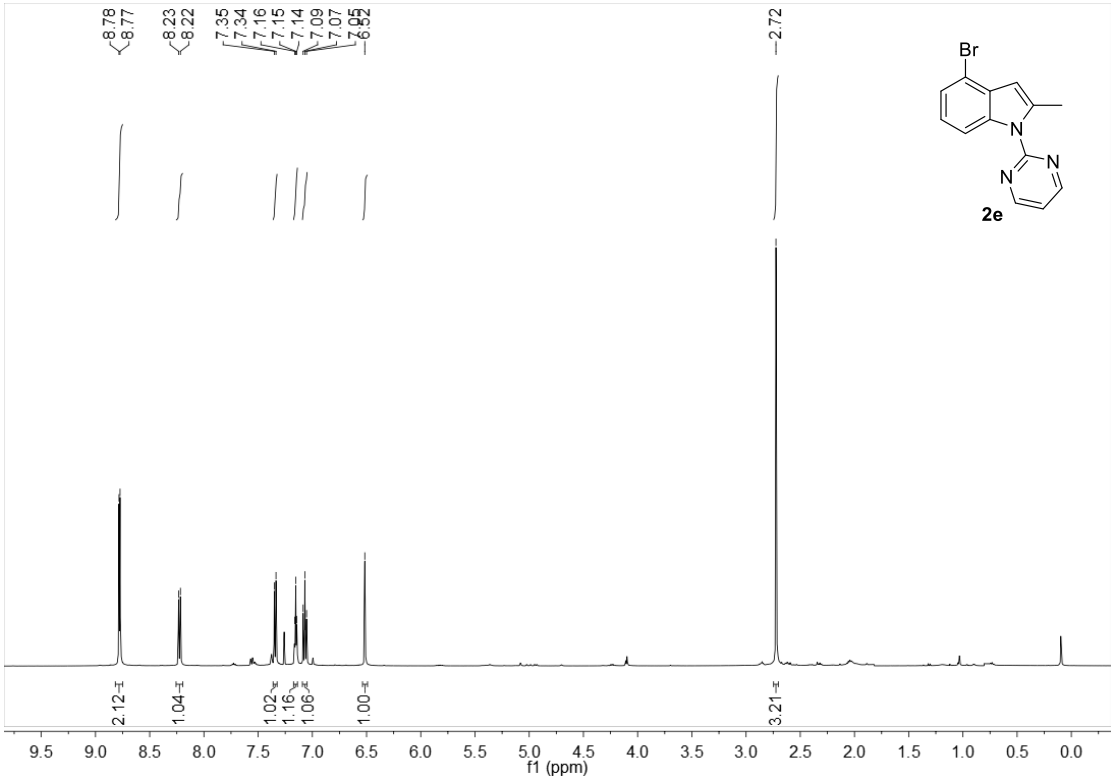
138.61
137.39
127.97
124.56
122.81
121.41
117.31
112.50
104.60
16.52
Cl
N
N
N
2d
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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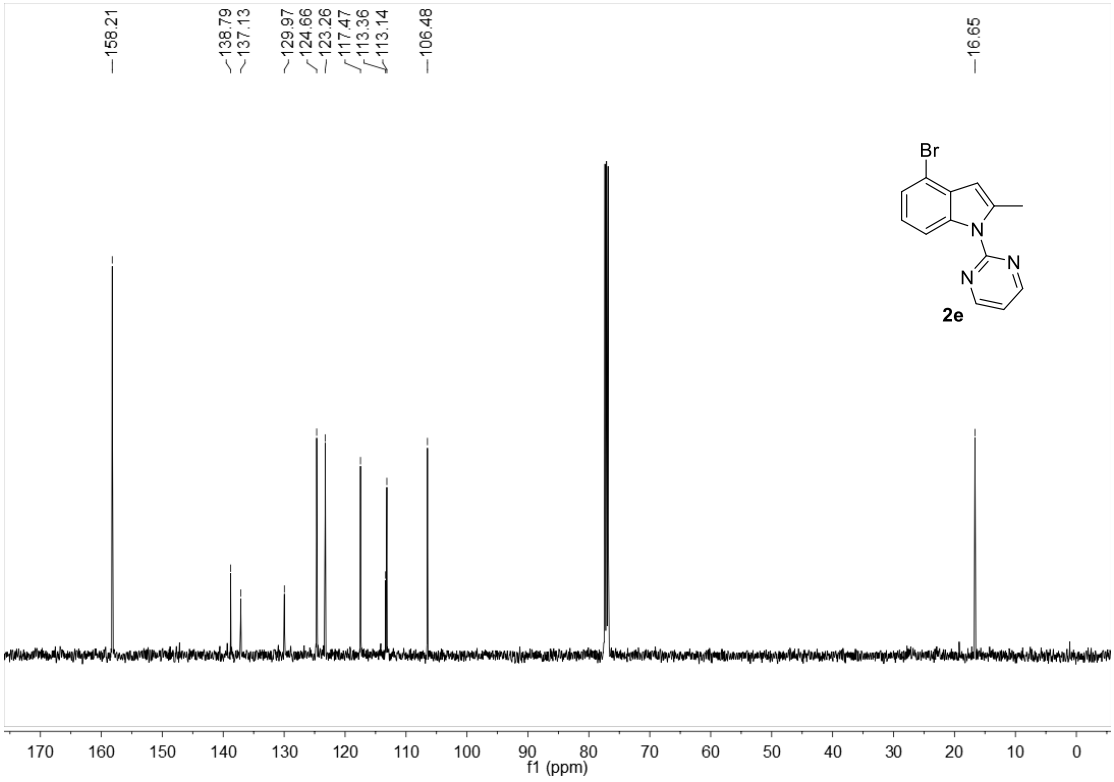
8.77
8.23
8.22
7.35
7.34
7.16
7.15
7.14
7.09
7.07
2.72
Br
N
N
N
2e
2.12
1.04
1.02
1.16
1.06
1.00
3.21
f1 (ppm)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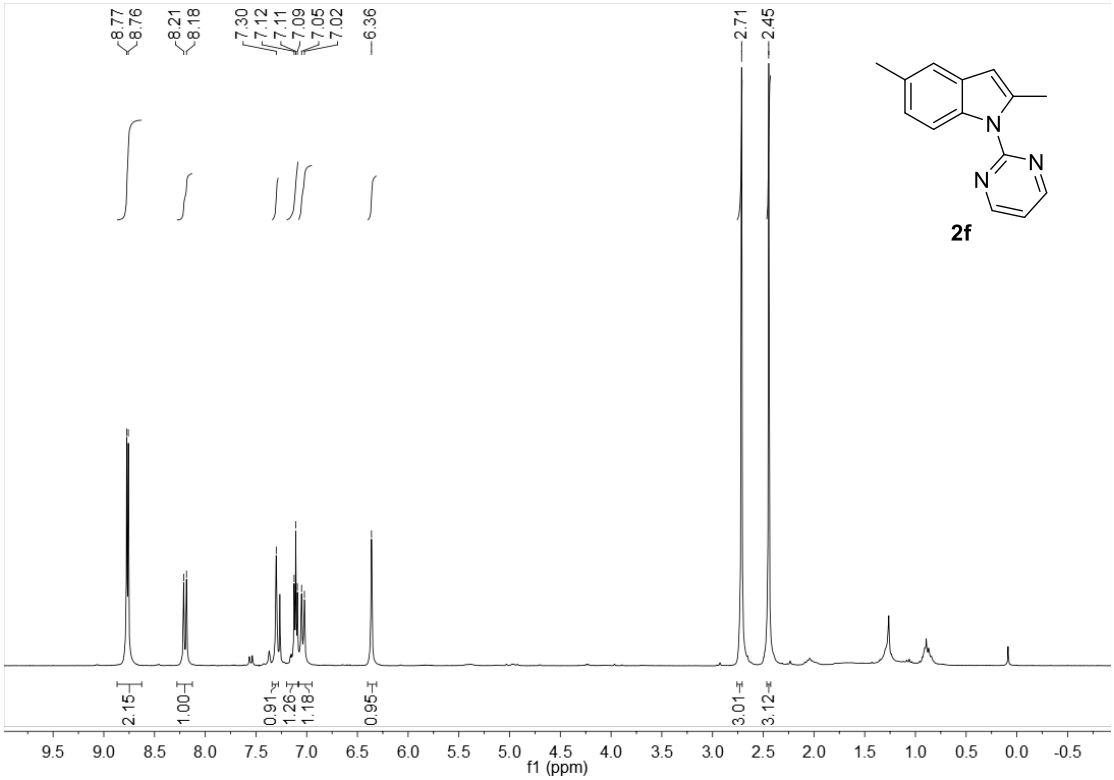
123.26
117.47
113.36
113.14
106.48
16.65
Br
N
N
N
2e
f1 (ppm)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8.76
8.21
8.18
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7.12
7.11
7.09
7.05
7.02
6.36
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2.45
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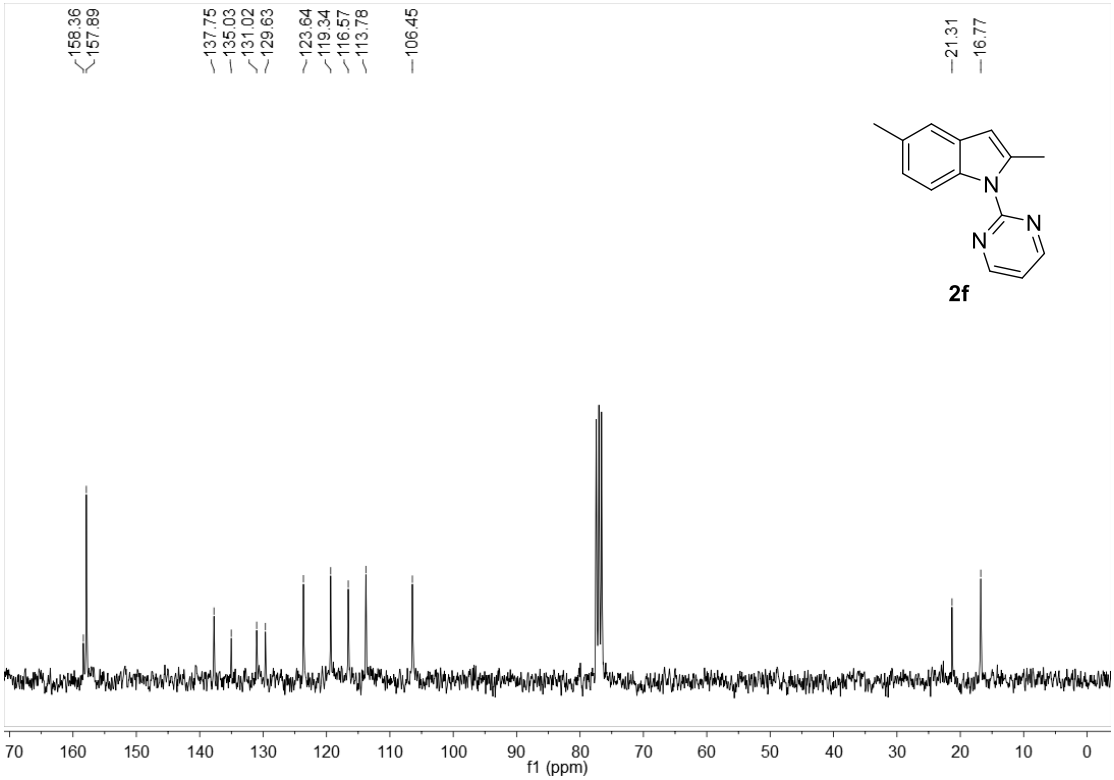
1.00
0.91
1.26
1.18
0.95
3.01
3.12
f1 (ppm)
2f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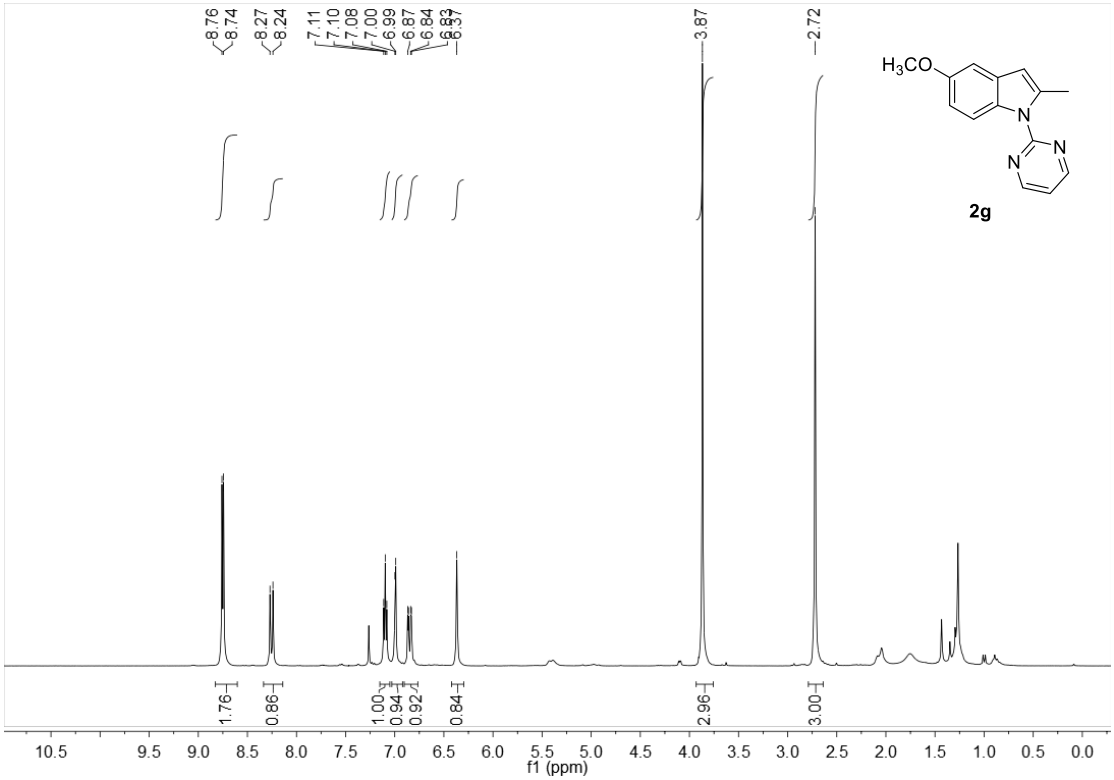
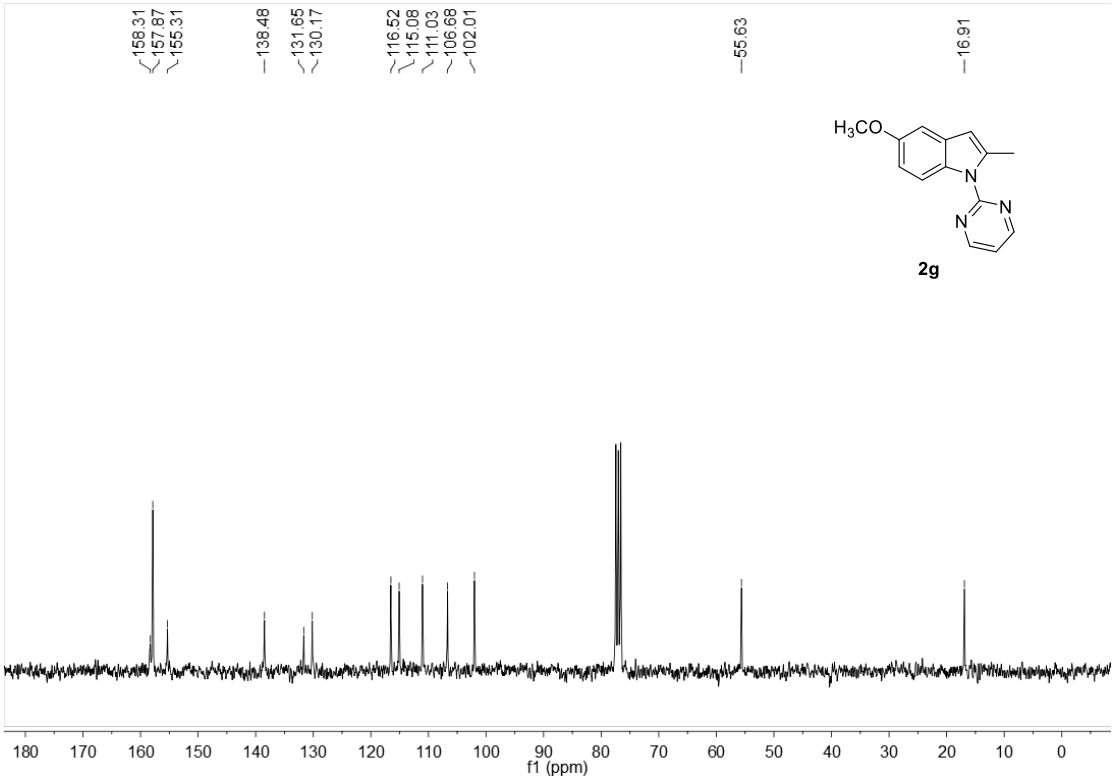
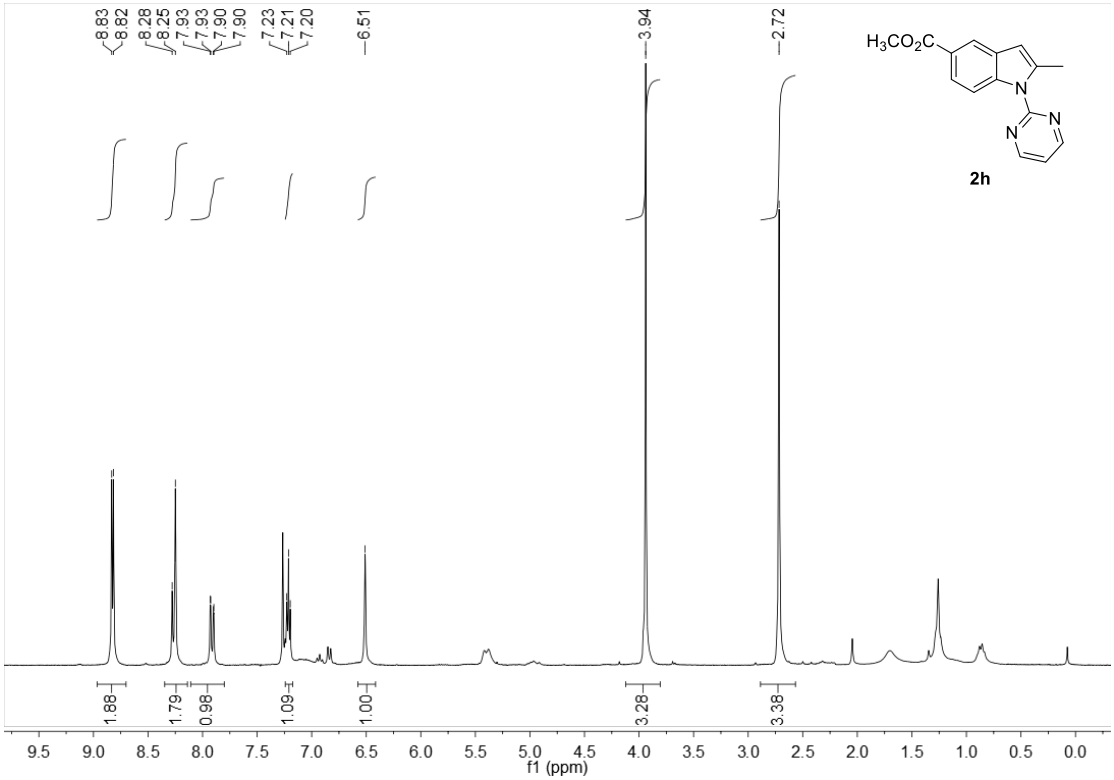
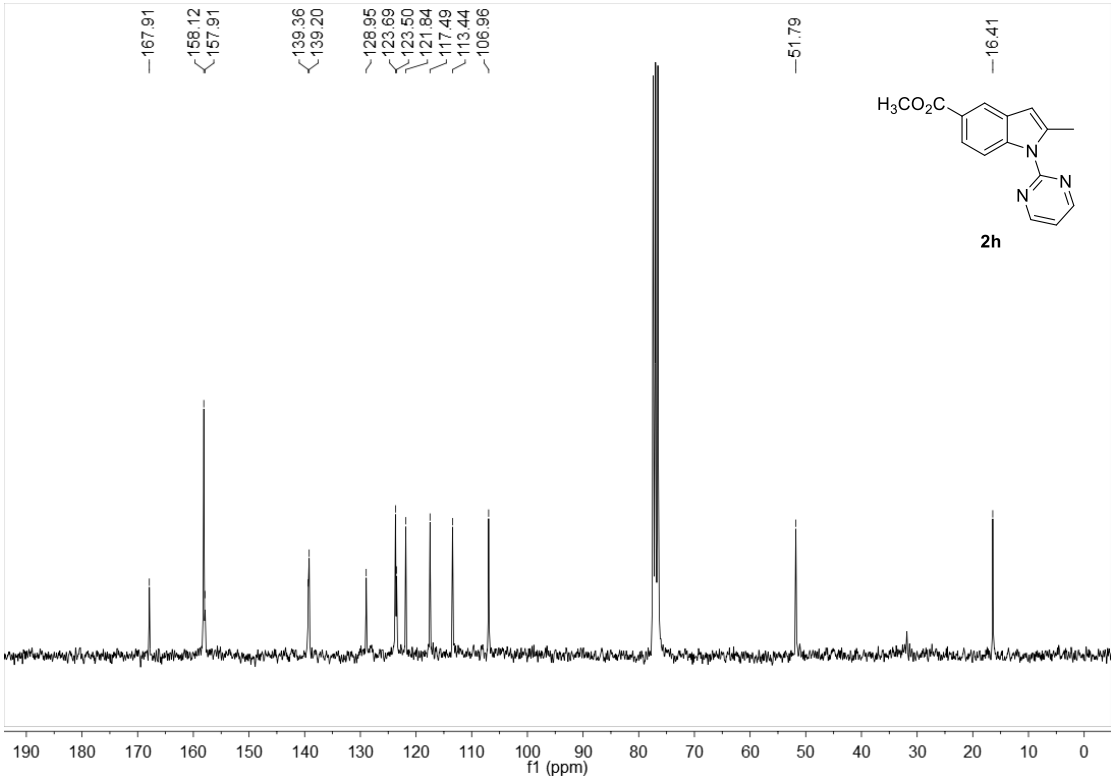
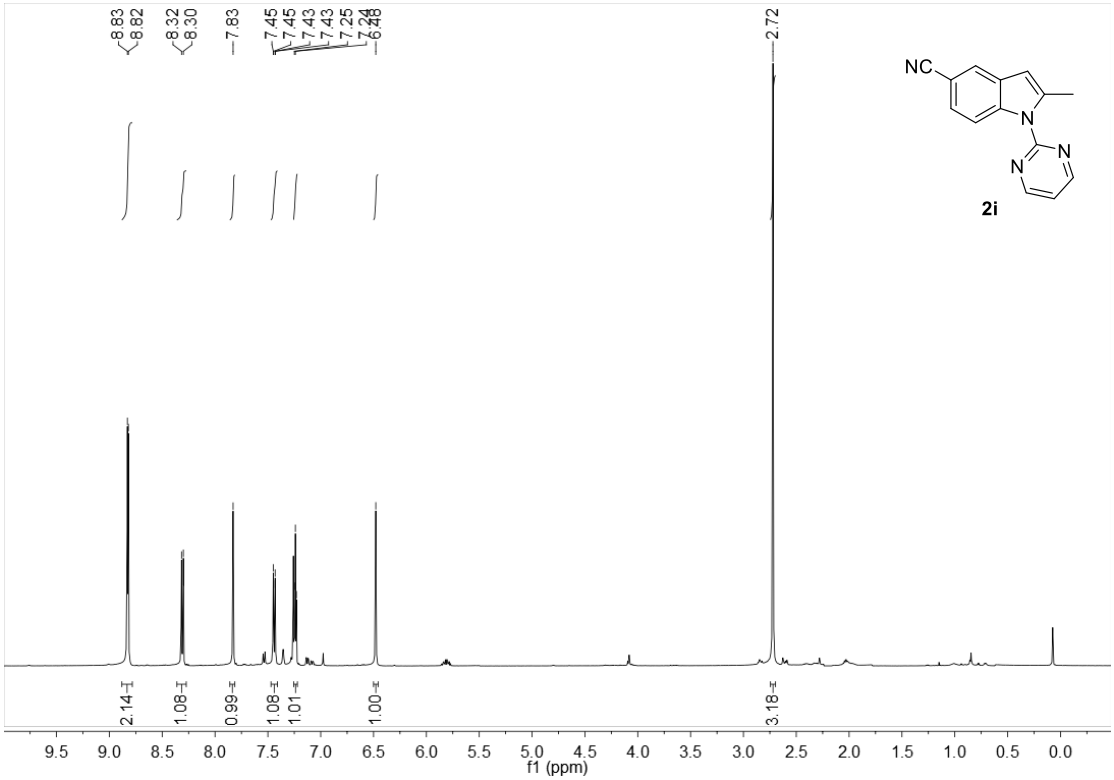
135.03
131.02
129.63
123.64
119.34
116.57
113.78
106.45
21.31
16.77
f1 (ppm)
2f

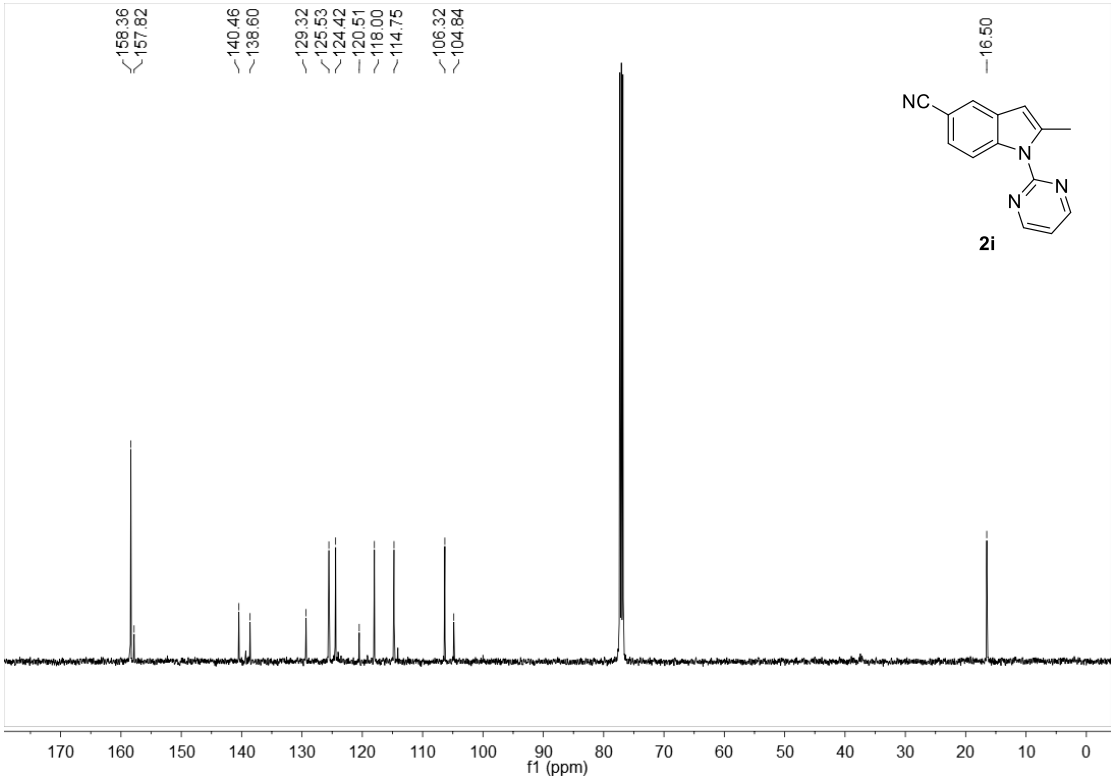

8.76
8.74
8.27
8.24
7.11
7.10
7.08
7.00
6.99
6.87
6.84
6.83
6.81
3.87
2.72
1.76
0.86
1.00
0.94
0.92
0.84
2.96
3.00
f1 (ppm)
2g


158.31
157.87
155.31
138.48
131.65
130.17
116.52
115.08
111.03
106.68
102.01
55.63
16.91
f1 (ppm)
2g


8.83
8.82
8.28
8.25
7.93
7.93
7.90
7.90
7.23
7.21
7.20
6.51
3.94
2.72
1.88
1.79
0.98
1.09
1.00
3.28
3.38
f1 (ppm)
2h


167.91
158.12
157.91
139.36
139.20
128.95
123.69
123.50
121.84
117.49
113.44
106.96
51.79
16.41
f1 (ppm)
2h


8.83
8.82
8.32
8.30
7.83
7.45
7.45
7.43
7.43
7.25
7.24
6.48
2.72
NC
N
N
N
2i
2.14
1.08
0.99
1.08
1.01
1.00
3.18
f1 (ppm)


158.36
157.82
140.46
138.60
129.32
125.53
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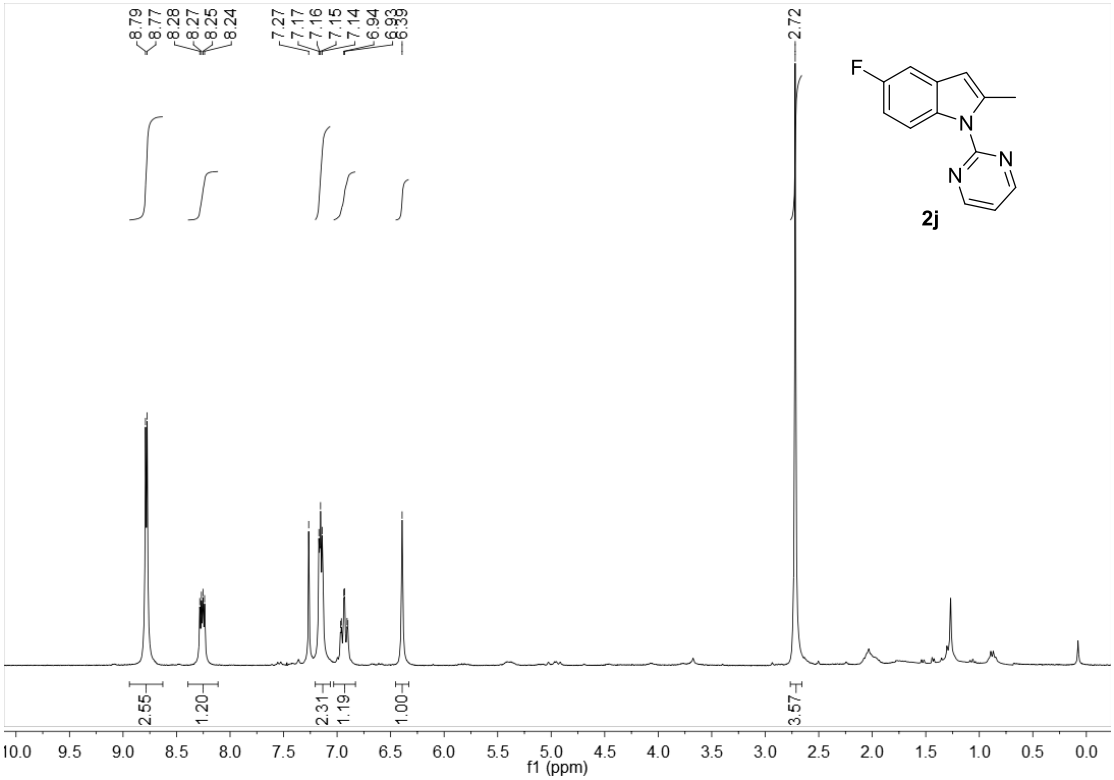
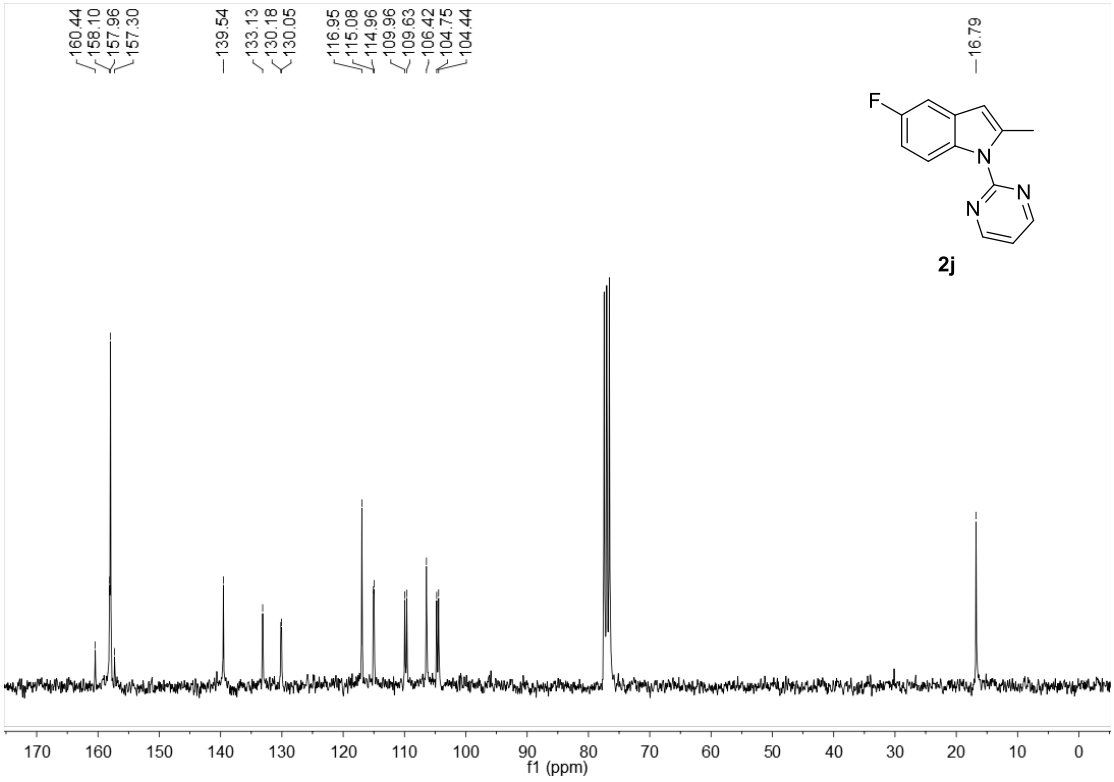
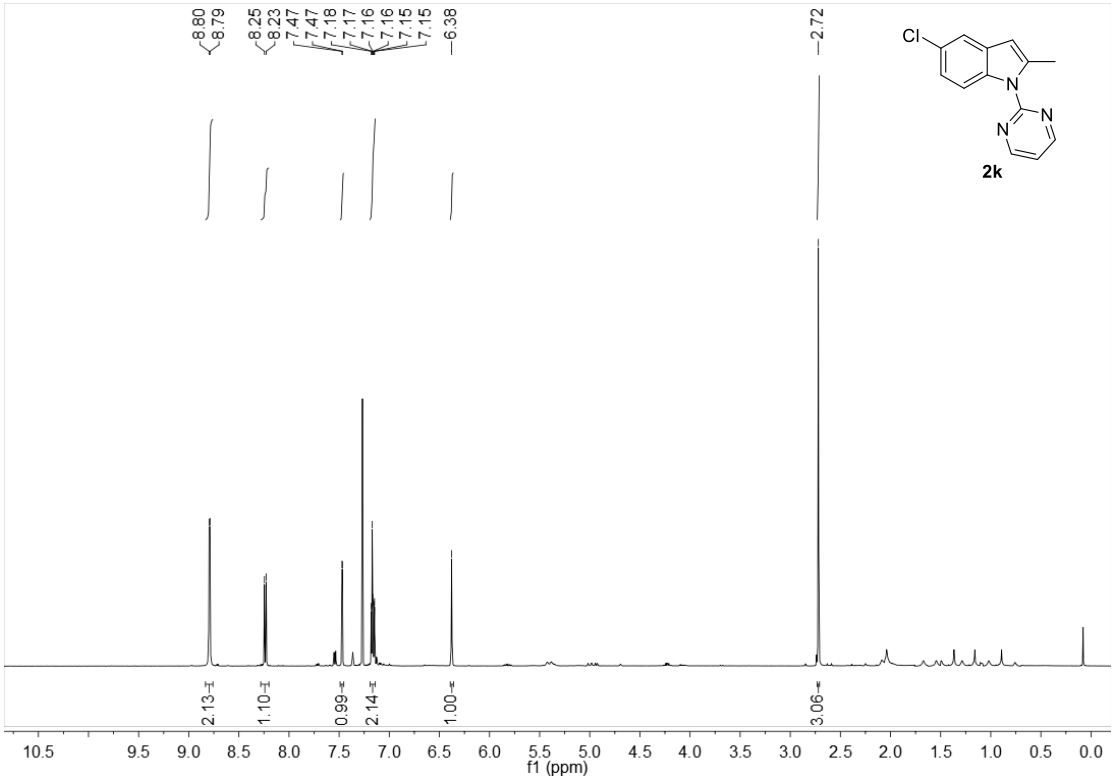
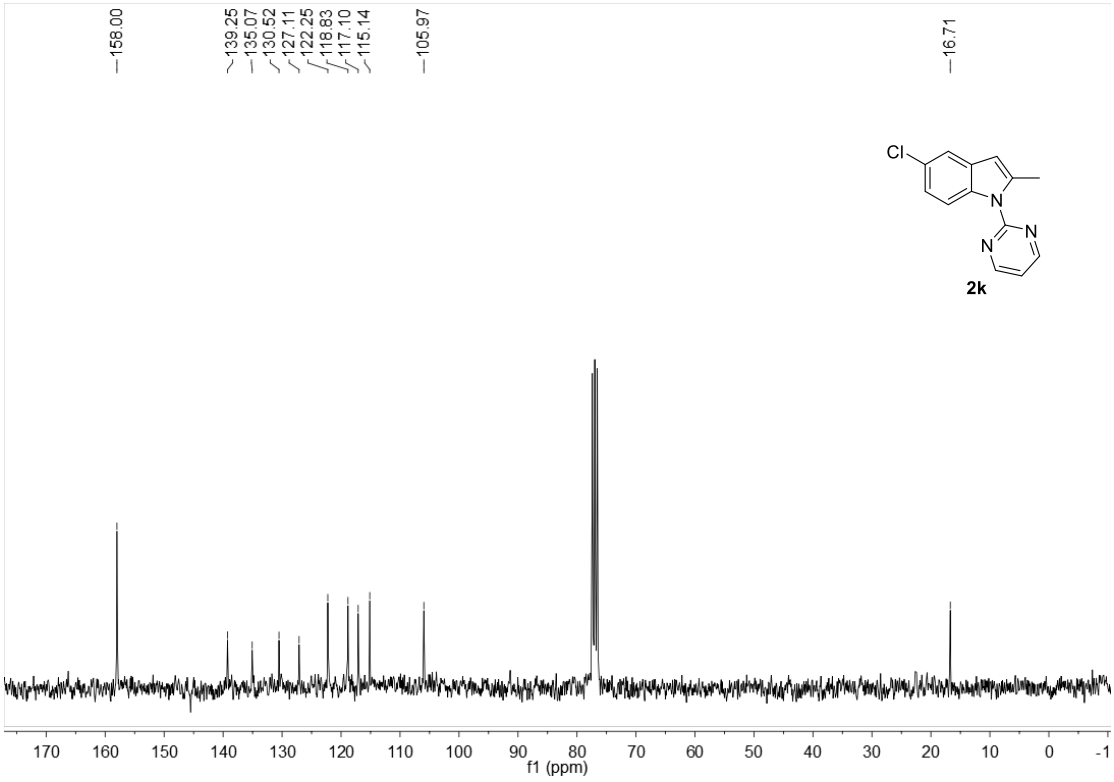
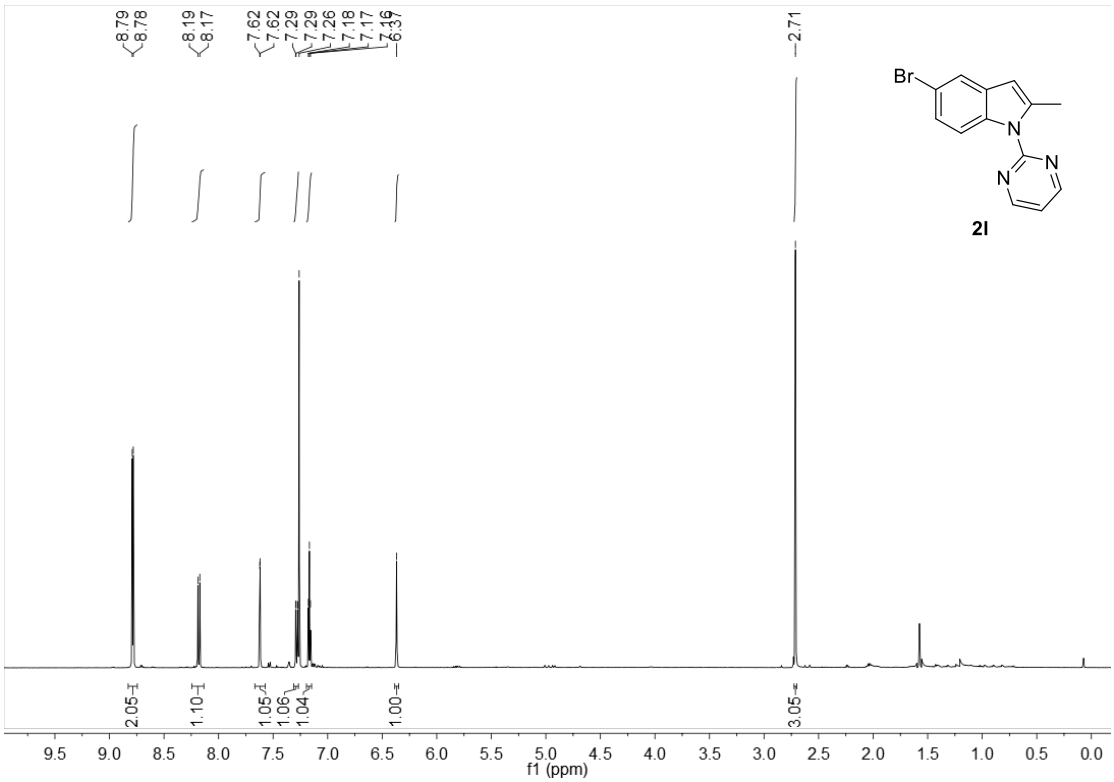
120.51
118.00
114.75
106.32
104.84
16.50
NC
N
N
N
2i
f1 (ppm)

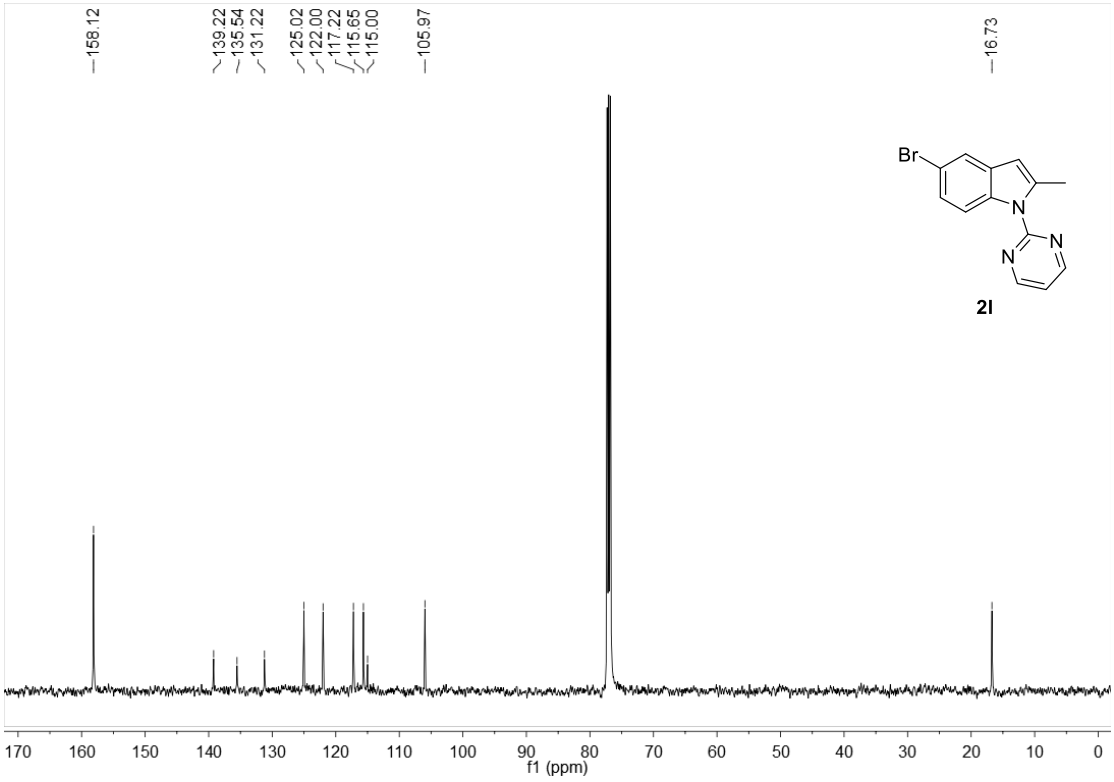

8.79
8.77
8.28
8.27
8.25
8.24
7.27
7.17
7.16
7.15
7.14
6.94
6.93
6.93
2.72
F
N
N
N
2j
2.55
1.20
2.31
1.19
1.00
3.57
f1 (ppm)

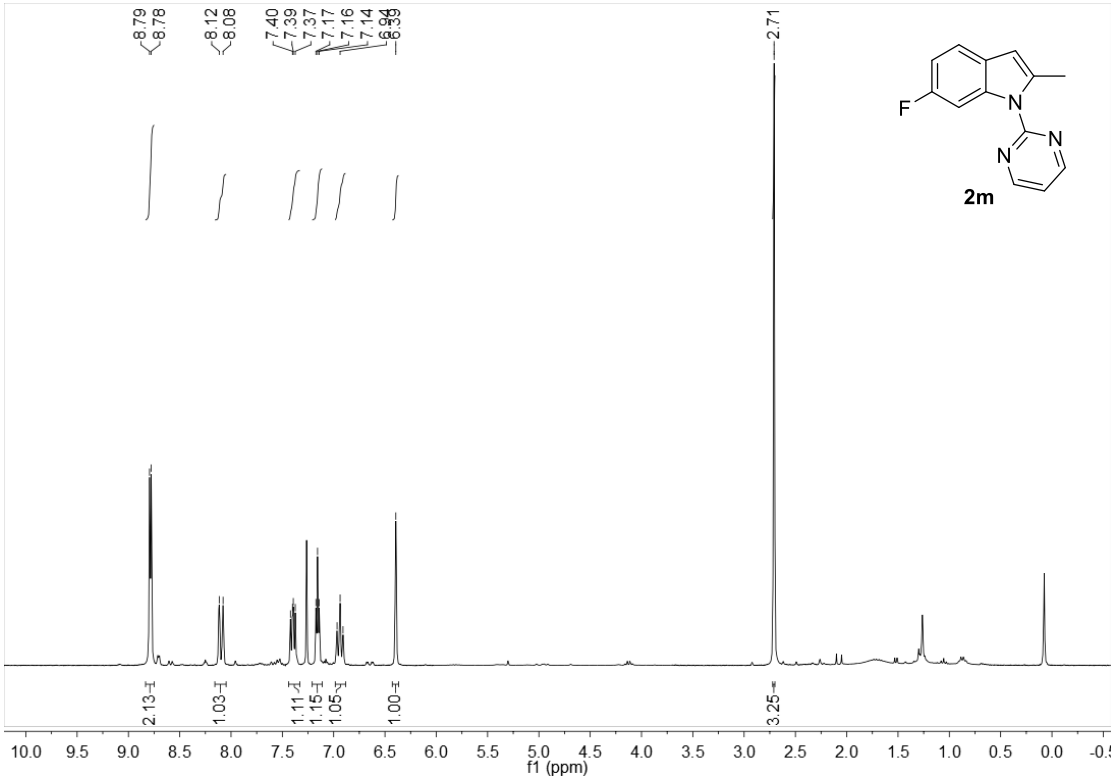

160.44
158.10
157.96
157.30
139.54
133.13
130.18
130.05
116.95
115.08
114.96
109.96
109.63
106.42
104.75
104.44
16.79
F
N
N
N
2j
f1 (ppm)

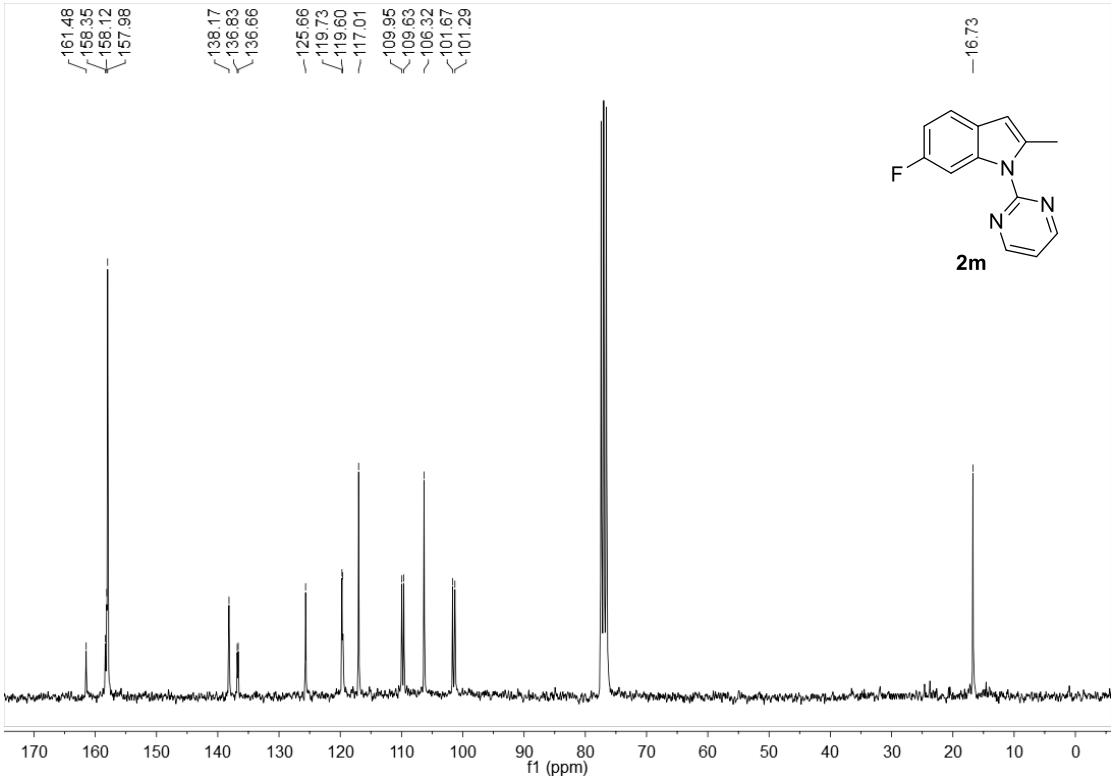

8.80
8.79
8.25
8.23
7.47
7.47
7.18
7.17
7.16
7.16
7.15
7.15
6.38
2.72
Cl
N
N
N
2k
2.13
1.10
0.99
2.14
1.00
3.06
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

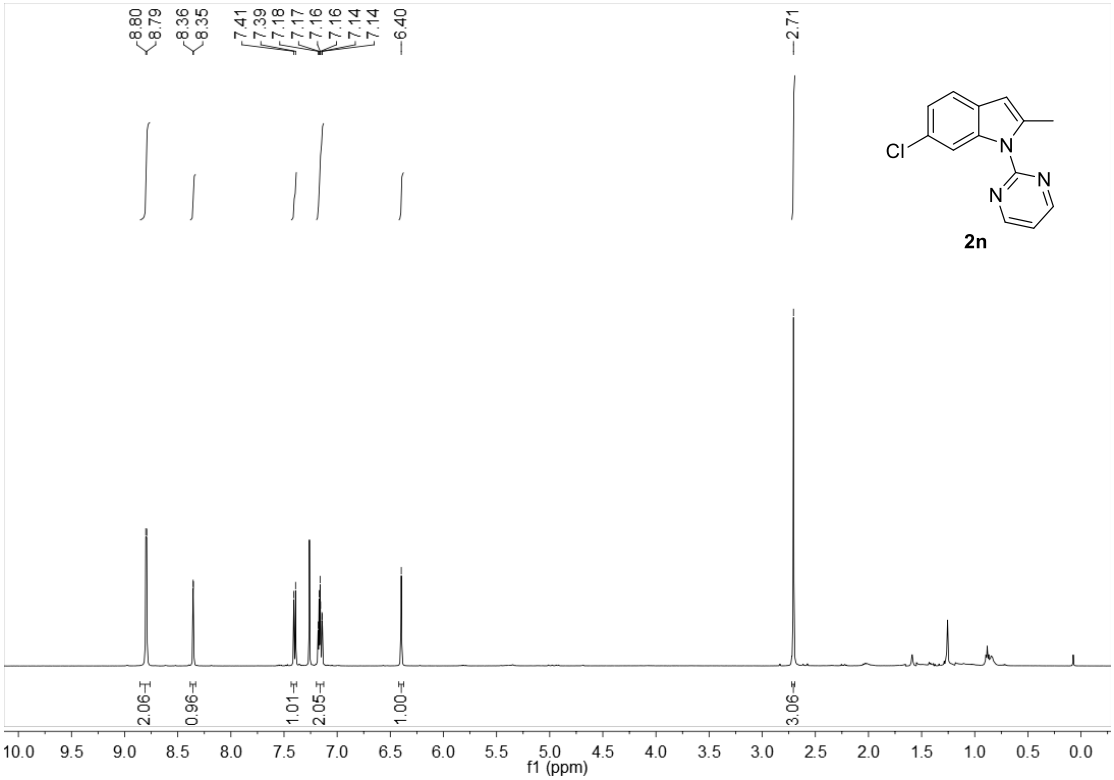

158.00
139.25
135.07
130.52
127.11
122.25
118.83
117.10
115.14
105.97
16.71
Cl
N
N
N
2k
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

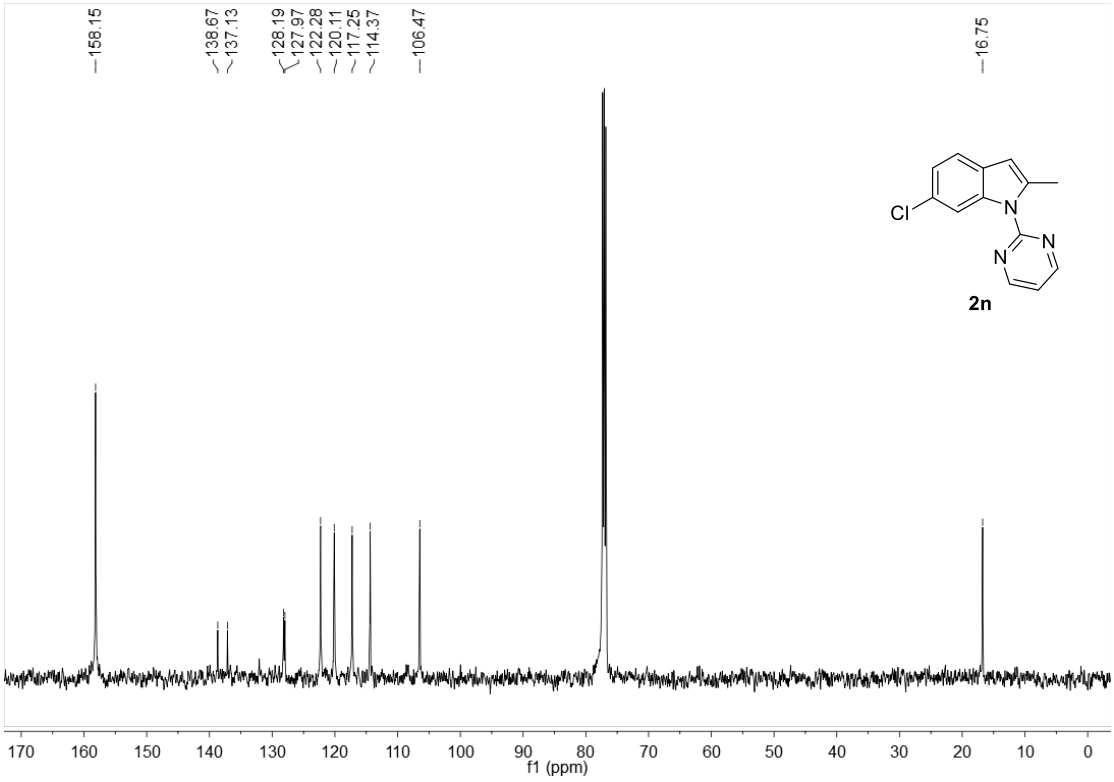

8.79
8.78
8.19
8.17
7.62
7.62
7.29
7.29
7.26
7.18
7.17
7.16
6.37
2.71
Br
N
N
N
2l
2.05
1.10
1.05
1.06
1.04
1.00
3.05
f1 (ppm)

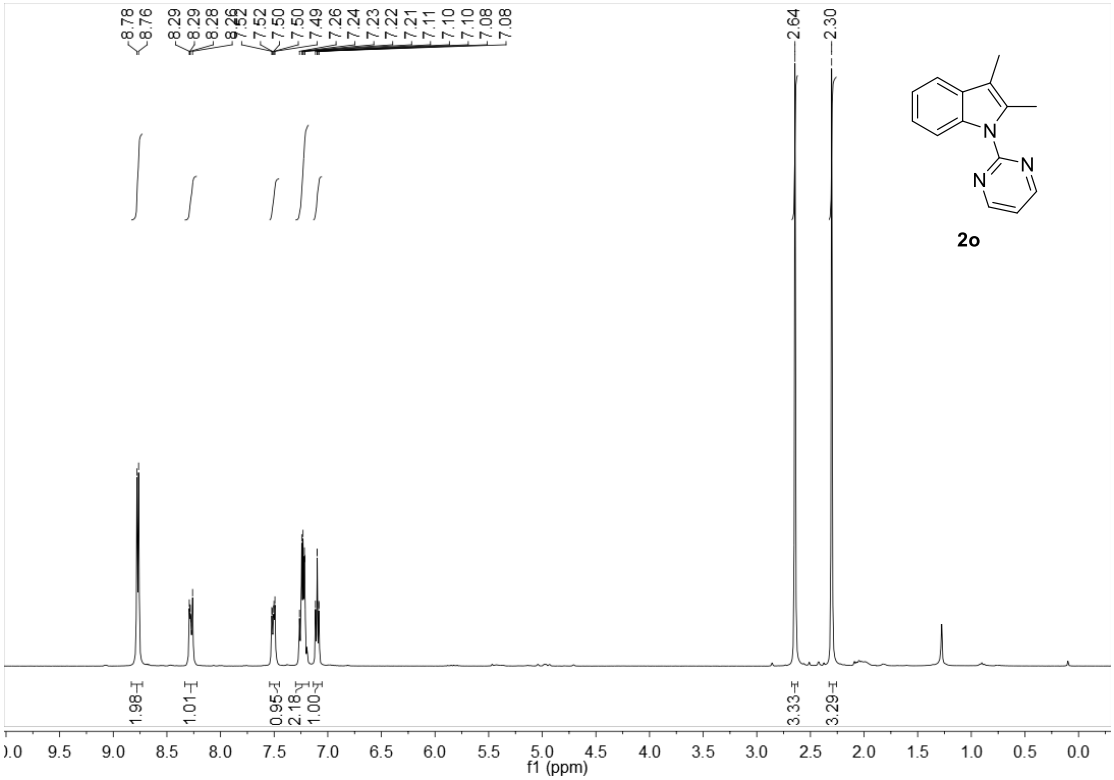

158.12
139.22
135.54
131.22
125.02
122.00
117.22
115.65
115.00
105.97
16.73
Br
N
N
N
2l
f1 (ppm)

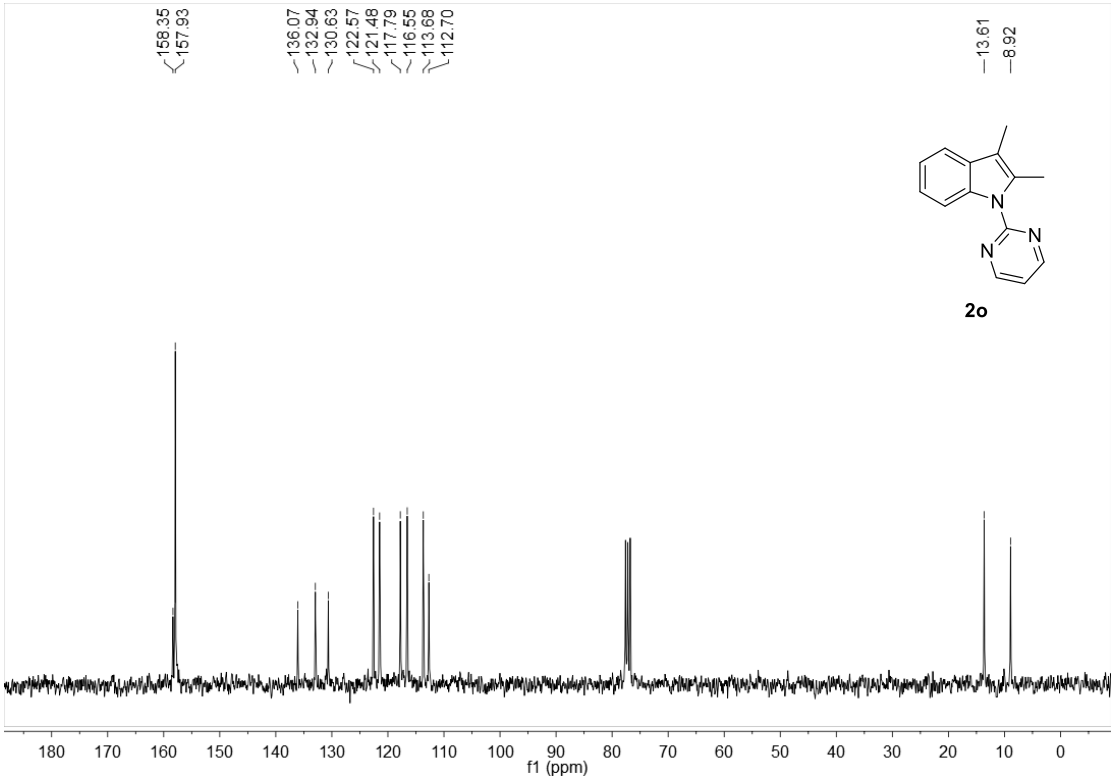

8.79
8.78
8.12
8.08
7.40
7.39
7.37
7.17
7.16
7.14
6.94
6.93
2.71
F
N
N
N
2m
2.13
1.03
1.11
1.15
1.05
1.00
3.25
f1 (ppm)

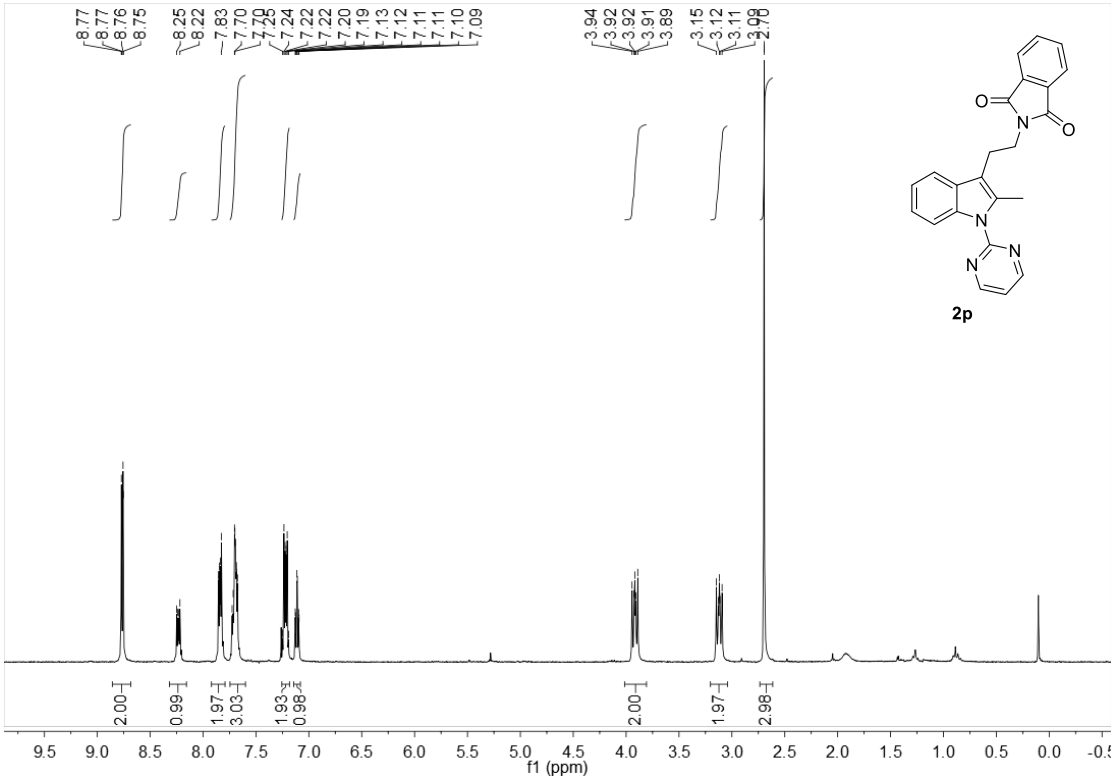

161.48
158.35
158.12
157.98
138.17
136.83
136.66
125.66
119.73
119.60
117.01
109.95
109.63
106.32
101.67
101.29
16.73
F
N
N
N
2m
f1 (ppm)

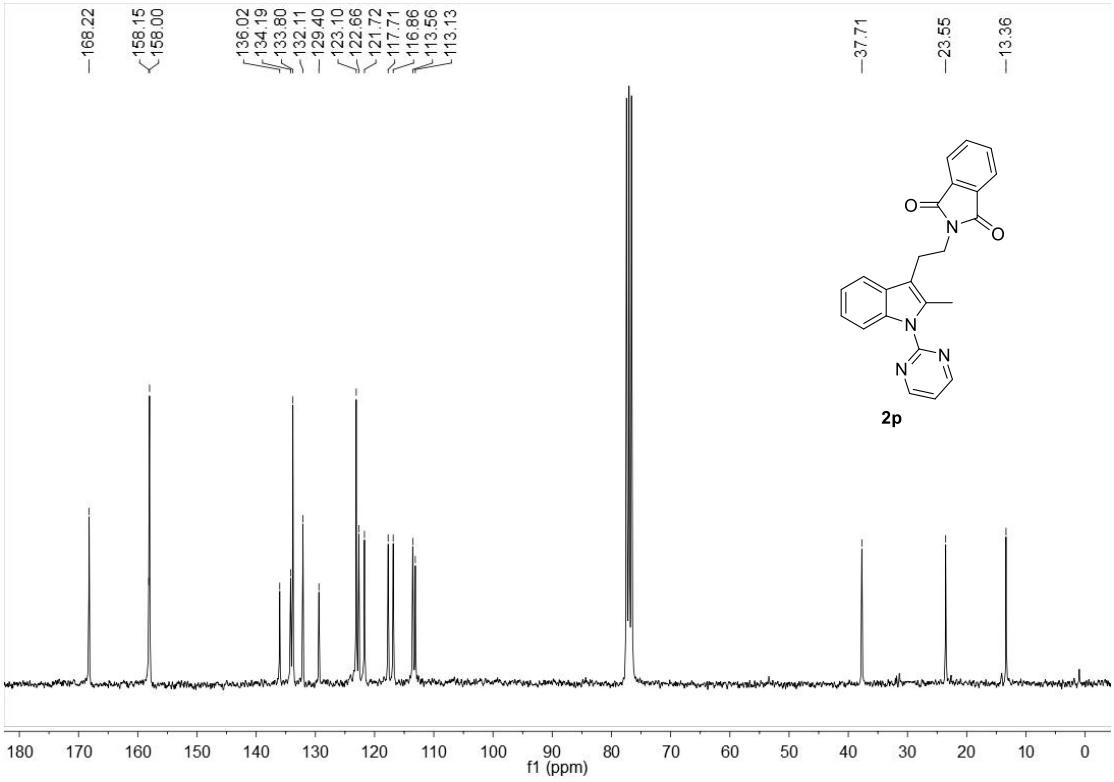

8.80
8.79
8.36
8.35
7.41
7.39
7.18
7.17
7.16
7.16
7.14
7.14
6.40
2.71
Cl
N
N
N
2n
2.06
0.96
1.01
2.05
1.00
3.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

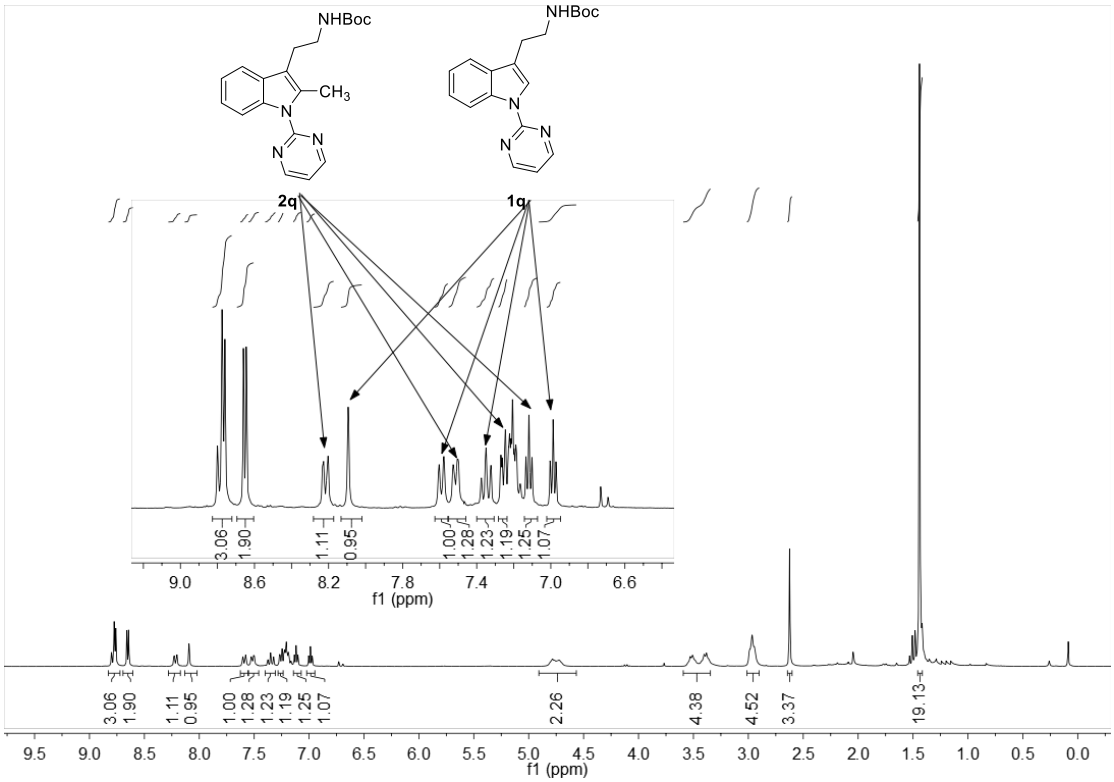

158.15
138.67
137.13
128.19
127.97
122.28
120.11
117.25
114.37
106.47
16.75
Cl
N
N
N
2n
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

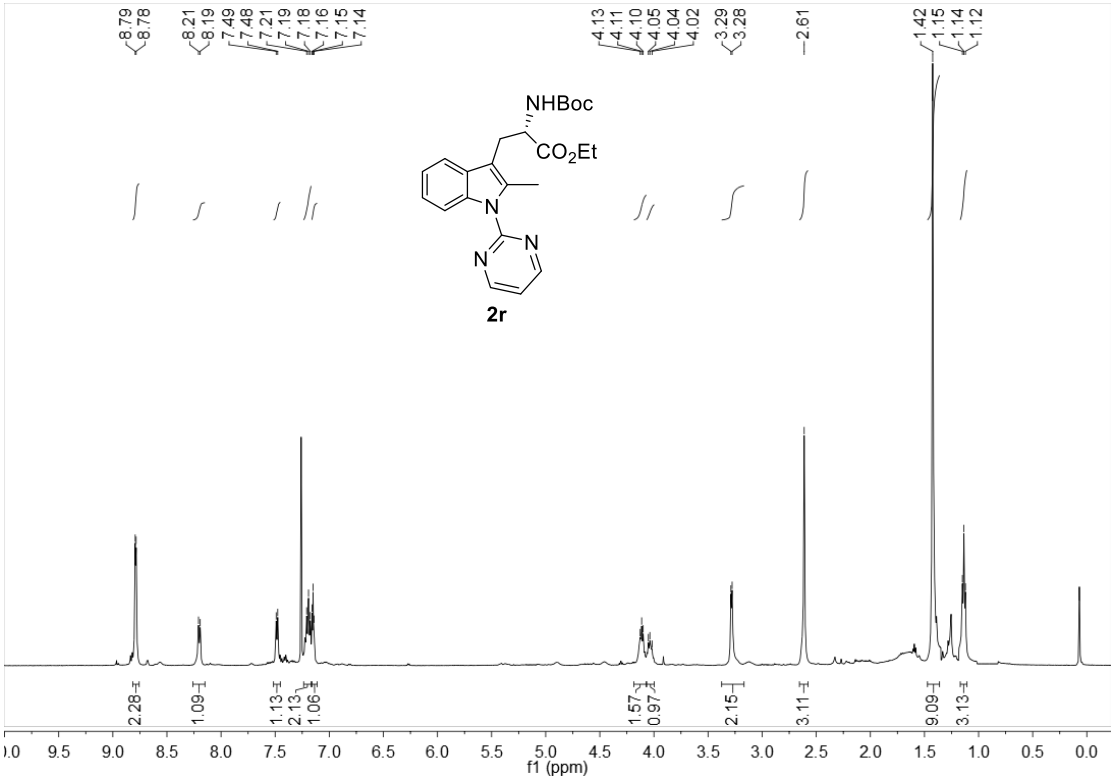

8.78
8.76
8.29
8.29
8.28
7.52
7.50
7.50
7.49
7.26
7.24
7.23
7.22
7.21
7.11
7.10
7.10
7.08
7.08
2.64
2.30
1.98
1.01
0.95
2.18
1.00
3.33
3.29
f1 (ppm)
2o

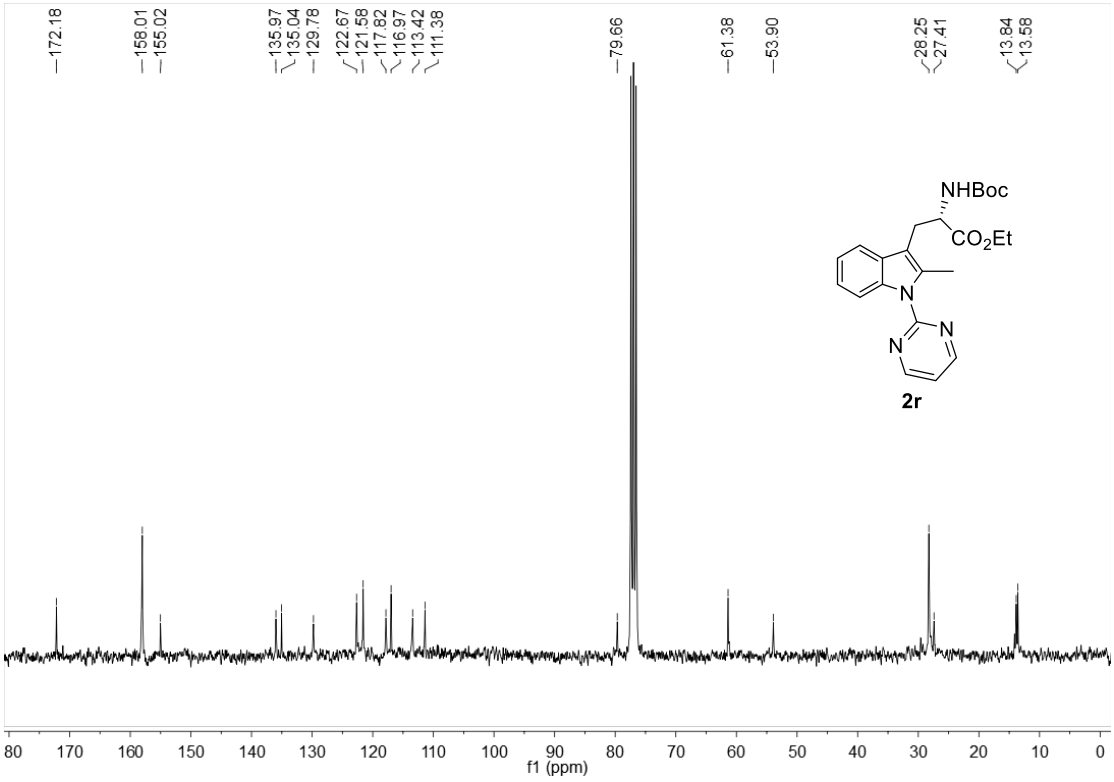

158.35
157.93
136.07
132.94
130.63
122.57
121.48
117.79
116.55
113.68
112.70
13.61
8.92
f1 (ppm)
2o


8.77
8.77
8.76
8.75
8.25
8.22
7.83
7.70
7.25
7.24
7.22
7.22
7.20
7.19
7.13
7.12
7.11
7.11
7.10
7.09
3.94
3.92
3.92
3.91
3.89
3.15
3.12
3.11
2.98
2.00
0.99
1.97
3.03
1.93
0.98
2.00
1.97
2.98
f1 (ppm)
2p


168.22
158.15
158.00
136.02
134.19
133.80
132.11
129.40
123.10
122.66
121.72
117.71
116.86
113.56
113.13
37.71
23.55
13.36
f1 (ppm)
2p


NHBoc
CH3
N
N
N
2q
NHBoc
N
N
N
1q
3.06
1.90
1.11
0.95
1.00
1.28
1.23
1.19
1.25
1.07
9.0
8.6
8.2
7.8
7.4
7.0
6.6
f1 (ppm)
3.06
1.90
1.11
0.95
1.00
1.28
1.23
1.19
1.25
1.07
2.26
4.38
4.52
3.37
19.13
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


8.79
8.78
8.21
8.19
7.49
7.48
7.21
7.19
7.18
7.16
7.15
7.14
4.13
4.11
4.10
4.05
4.04
4.02
3.29
3.28
2.61
1.42
1.15
1.14
1.12
NHBoc
CO2Et
N
N
N
2r
2.28
1.09
1.13
2.13
1.06
1.57
0.97
2.15
3.11
9.09
3.13
f1 (ppm)


172.18
158.01
155.02
135.97
135.04
129.78
122.67
121.58
117.82
116.97
113.42
111.38
79.66
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27.41
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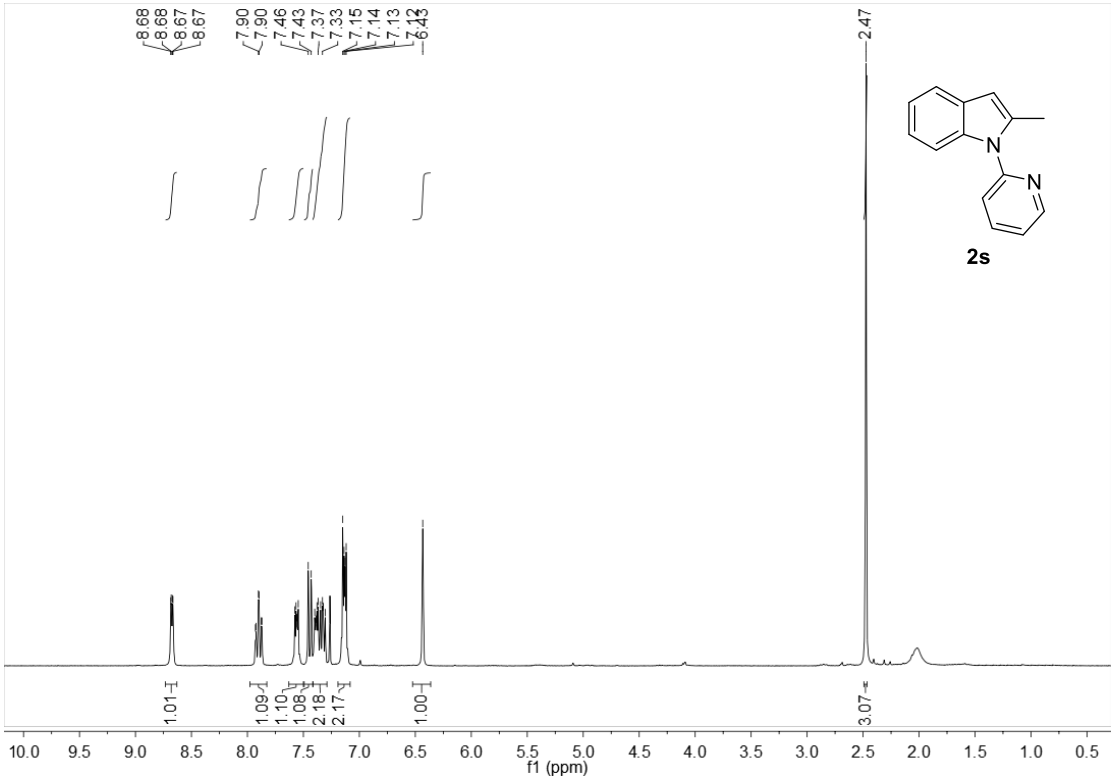
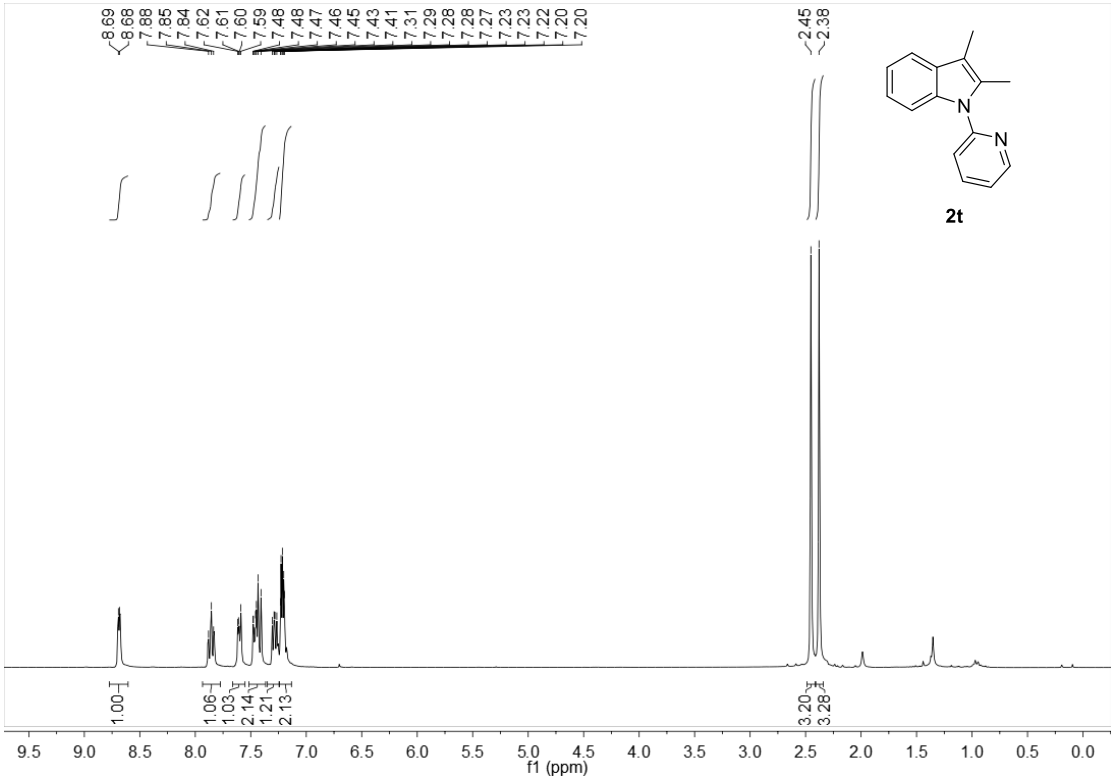
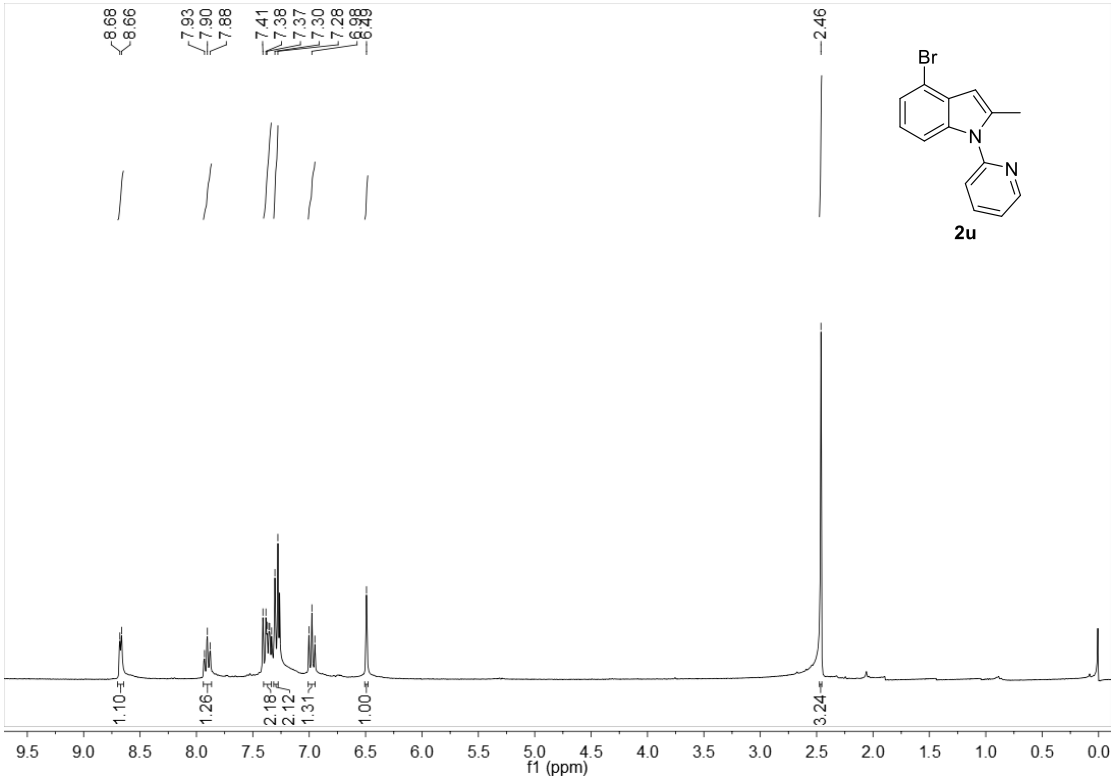
13.58
NHBoc
CO2Et
N
N
N
2r
f1 (ppm)

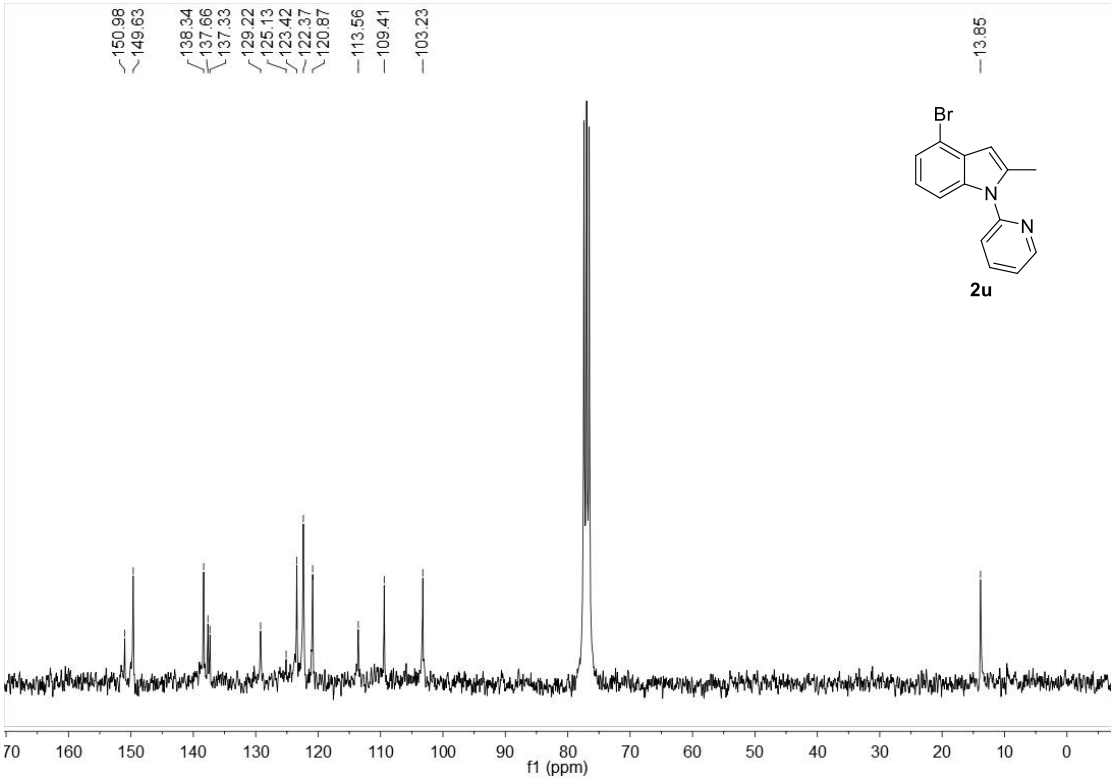

8.68
8.68
8.67
8.67
7.90
7.90
7.46
7.43
7.37
7.33
7.15
7.14
7.13
6.43
2.47
1.01
1.09
1.10
1.08
2.18
2.17
1.00
3.07
f1 (ppm)

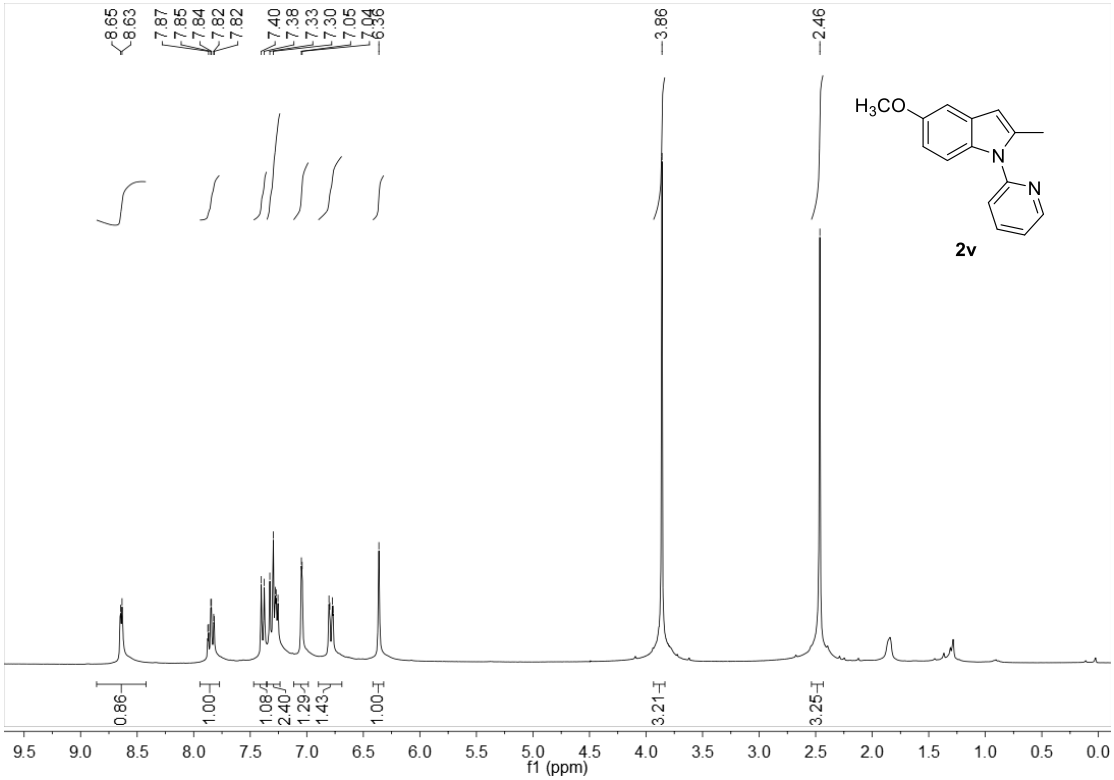
2s

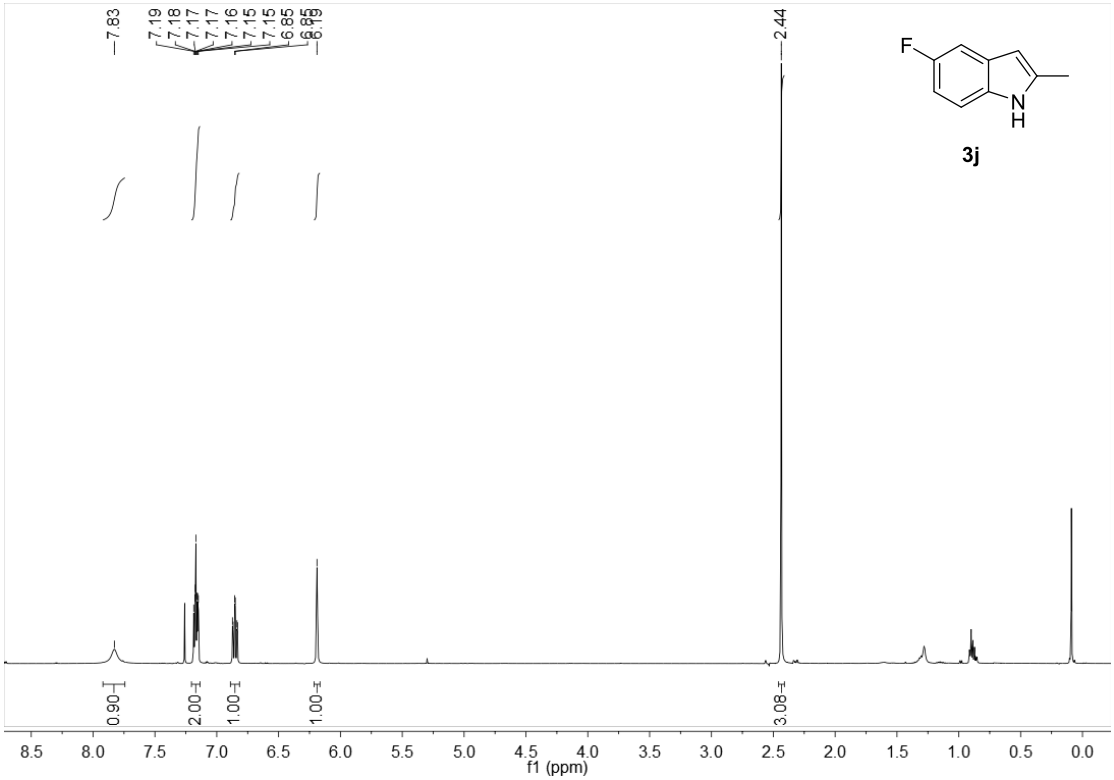

8.69
8.68
7.88
7.85
7.84
7.62
7.61
7.60
7.59
7.48
7.48
7.47
7.46
7.45
7.43
7.41
7.31
7.29
7.28
7.28
7.27
7.23
7.23
7.22
7.20
7.20
2.45
2.38
1.00
1.06
1.03
2.14
1.21
2.13
3.20
3.28
f1 (ppm)

2t


8.68
8.66
7.93
7.90
7.88
7.41
7.38
7.37
7.30
7.28
6.98
6.49
2.46
Br
N
N
2u
1.10
1.26
2.18
2.12
1.31
1.00
3.24
f1 (ppm)


150.98
149.63
138.34
137.66
137.33
129.22
125.13
123.42
122.37
120.87
113.56
109.41
103.23
13.85
Br
N
N
2u
f1 (ppm)


8.65
8.63
7.87
7.85
7.84
7.82
7.82
7.40
7.38
7.33
7.30
7.05
7.04
6.36
3.86
2.46
H3CO
N
N
2v
0.86
1.00
1.08
2.40
1.29
1.43
1.00
3.21
3.25
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


7.83
7.19
7.18
7.17
7.17
7.16
7.15
7.15
6.85
6.85
6.84
2.44
F
N
H
3j
0.90
2.00
1.00
1.00
3.08
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)