

Cu-Mediated Direct Regioselective C-2 Chlorination of Indoles

Jing Zhao,^a Xiuzhi Cheng,^a Jun Le,^a Wei Yang,^c Fengtian Xue,^c Xuan Zhang^b and Chao Jiang^{a*}

^a. Department of Pharmaceutical Engineering, School of Chemical Engineering, Nanjing University of Science and Technology, Nanjing, Jiangsu, 210094, China,

E-mail: chaojiang@njust.edu.cn

^b. Jiangsu Key Laboratory of Chemical Pollution Control and Resources Reuse, Nanjing University of Science & Technology, Nanjing, Jiangsu, 210094, China

^c. Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, 20 Penn Street, Baltimore, Maryland 21201, United States

Supporting Information

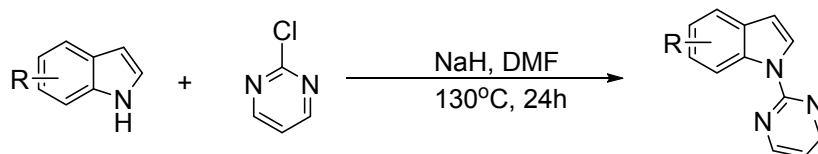
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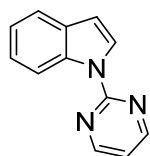
1. General information

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 an TSQ Quantum-LC/MS/MS of Finnigan using Electrospray ionization (ESI) techniques. ¹H and ¹³C NMR spectra were recorded with a Bruker AV-300 and AV-400 spectrometer operating at 300MHz/400MHz and 75MHz/101MHz, respectively, with chemical shift values being reported in ppm relative to chloroform ($\delta=7.26$ ppm) for ¹H NMR, and chloroform ($\delta=77.16$ ppm) for ¹³C NMR.

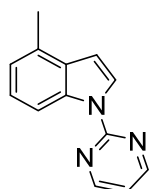
2. General procedure for synthesis of the starting materials



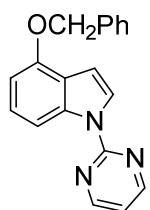
NaH (60% dispersion in mineral oil, 300 mg, 7.5 mmol) was added in portions at 0 °C to a stirred solution of indole (5.0 mmol) in DMF (5 mL). After stirring for 30 min at 0 °C, 2-chloropyrimidine (687.18 g, 6.0 mmol) was added and the mixture was stirred at 130 °C for 24 h. Then, the reaction mixture was cooled to ambient temperature, poured into H₂O (50 mL) and extracted with EtOAc (4×30 mL). The combined organic phase was dried over Na₂SO₄. 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 literature¹.



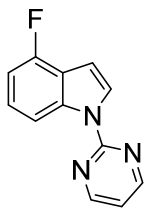
1-(Pyrimidin-2-yl)-1H-indole (1a): white solid. ¹H NMR (300 MHz, CDCl₃) δ 8.83 (d, J = 8.3 Hz, 1H), 8.70 (d, J = 4.8 Hz, 2H), 8.29 (d, J = 3.7 Hz, 1H), 7.64 (d, J = 7.7 Hz, 1H), 7.42 – 7.31 (m, 1H), 7.30 – 7.22 (m, 1H), 7.04 (t, J = 4.8 Hz, 1H), 6.72 (d, J = 3.6 Hz, 1H).



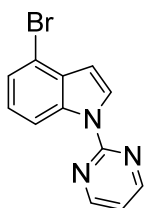
4-Methyl-1-(pyrimidin-2-yl)-1H-indole (1b): white solid. ¹H NMR (300 MHz, CDCl₃) δ 8.70 (d, J = 4.7 Hz, 2H), 8.65 (d, J = 8.4 Hz, 1H), 8.27 (d, J = 3.7 Hz, 1H), 7.26 (d, J = 15.6 Hz, 1H), 7.05 (dd, J = 7.9, 2.6 Hz, 2H), 6.75 (d, J = 3.7 Hz, 1H), 2.58 (s, 3H).



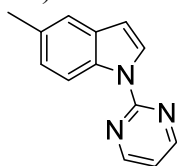
2-Chloro-1-(pyrimidin-2-yl)-1H-indole (1c): light purple solid. ¹H NMR (300 MHz, CDCl₃) δ 8.70 (d, J = 4.8 Hz, 2H), 8.43 (d, J = 8.4 Hz, 1H), 8.20 (d, J = 3.7 Hz, 1H), 7.53 (d, J = 7.3 Hz, 2H), 7.46 – 7.31 (m, 3H), 7.25 (t, J = 8.2 Hz, 1H), 7.05 (t, J = 4.8 Hz, 1H), 6.90 (dd, J = 3.6, 0.5 Hz, 1H), 6.76 (d, J = 7.9 Hz, 1H), 5.25 (s, 2H).



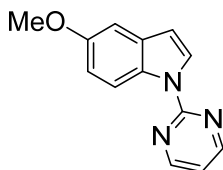
4-Fluoro-1-(pyrimidin-2-yl)-1H-indole (1d): white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.72 (d, $J = 4.8$ Hz, 2H), 8.60 (d, $J = 8.4$ Hz, 1H), 8.26 (d, $J = 3.7$ Hz, 1H), 7.32 – 7.22 (m, 1H), 7.09 (t, $J = 4.8$ Hz, 1H), 6.93 (dd, $J = 9.4, 8.3$ Hz, 1H), 6.85 – 6.77 (d, 1H).



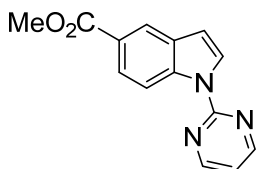
4-Bromo-1-(pyrimidin-2-yl)-1H-indole (1e): white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.78 (s, 1H), 8.67 (d, $J = 4.8$ Hz, 2H), 8.32 (d, $J = 3.7$ Hz, 1H), 7.41 (dd, $J = 7.7, 0.6$ Hz, 1H), 7.20 (t, $J = 8.1$ Hz, 1H), 7.05 (t, $J = 4.8$ Hz, 1H), 6.81 – 6.72 (m, 1H).



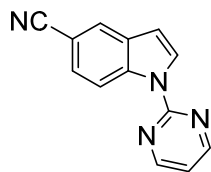
5-Methyl-1-(pyrimidin-2-yl)-1H-indole (1f): orange solid. ^1H NMR (300 MHz, CDCl_3) δ 8.68 (t, $J = 6.6$ Hz, 3H), 8.23 (d, $J = 3.6$ Hz, 1H), 7.41 (s, 1H), 7.16 (d, $J = 8.4$ Hz, 1H), 7.03 (t, $J = 4.7$ Hz, 1H), 6.63 (d, $J = 3.6$ Hz, 1H), 2.48 (s, 3H).



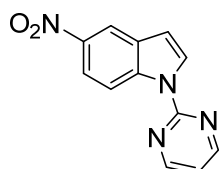
5-Methoxy-1-(pyrimidin-2-yl)-1H-indole (1g): white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.69 (t, $J = 6.5$ Hz, 3H), 8.25 (d, $J = 3.6$ Hz, 1H), 7.10 (d, $J = 2.5$ Hz, 1H), 7.03 (t, $J = 4.8$ Hz, 1H), 7.00 – 6.93 (m, 1H), 6.64 (d, $J = 3.6$ Hz, 1H), 3.89 (s, 3H).



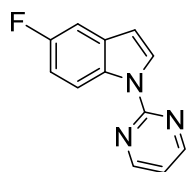
Methyl 1-(pyrimidin-2-yl)-1H-indole-5-carboxylate (1h): white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.85 (d, $J = 8.8$ Hz, 1H), 8.75 (d, $J = 4.8$ Hz, 2H), 8.36 (dd, $J = 5.8, 2.4$ Hz, 2H), 8.04 (dd, $J = 8.8, 1.7$ Hz, 1H), 7.12 (t, $J = 4.8$ Hz, 1H), 6.78 (d, $J = 3.2$ Hz, 1H), 3.96 (s, 3H).



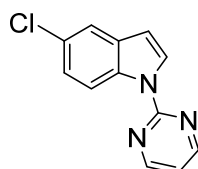
1-(Pyrimidin-2-yl)-1H-indole-5-carbonitrile (1i): white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.93 (d, J = 8.8 Hz, 1H), 8.76 (d, J = 4.8 Hz, 2H), 8.41 (d, J = 3.7 Hz, 1H), 7.97 (d, J = 0.9 Hz, 1H), 7.58 (dd, J = 8.7, 1.5 Hz, 1H), 7.16 (t, J = 4.8 Hz, 1H), 6.77 (d, J = 3.7 Hz, 1H).



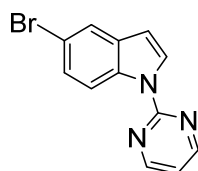
5-Nitro-1-(pyrimidin-2-yl)-1H-indole (1j): yellow solid. ^1H NMR (300 MHz, CDCl_3) δ 8.94 (d, J = 9.2 Hz, 1H), 8.78 (d, J = 4.8 Hz, 2H), 8.56 (d, J = 2.2 Hz, 1H), 8.45 (d, J = 3.7 Hz, 1H), 8.23 (dd, J = 9.2, 2.3 Hz, 1H), 7.19 (t, J = 4.8 Hz, 1H), 6.86 (d, J = 3.6 Hz, 1H).



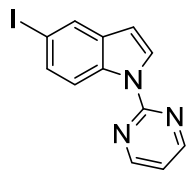
5-Fluoro-1-(pyrimidin-2-yl)-1H-indole (1k): yellow solid. ^1H NMR (300 MHz, CDCl_3) δ 8.83 – 8.61 (m, 3H), 8.32 (d, J = 3.6 Hz, 1H), 7.27 (dd, J = 8.3, 3.1 Hz, 1H), 7.07 (dd, J = 6.5, 3.0 Hz, 2H), 6.66 (d, J = 3.6 Hz, 1H).



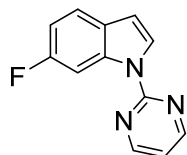
5-Chloro-1-(pyrimidin-2-yl)-1H-indole (1l): white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.73 (dd, J = 11.5, 6.8 Hz, 3H), 8.30 (d, J = 3.6 Hz, 1H), 7.59 (d, J = 2.0 Hz, 1H), 7.38 – 7.26 (m, 1H), 7.08 (t, J = 4.8 Hz, 1H), 6.64 (d, J = 3.6 Hz, 1H).



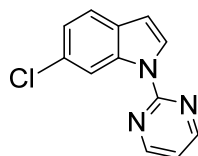
5-Bromo-1-(pyrimidin-2-yl)-1H-indole (1m): white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.76 – 8.61 (m, 3H), 8.28 (d, J = 3.7 Hz, 1H), 7.74 (d, J = 1.9 Hz, 1H), 7.42 (dd, J = 8.9, 1.9 Hz, 1H), 7.08 (t, J = 4.8 Hz, 1H), 6.64 (d, J = 3.7 Hz, 1H).



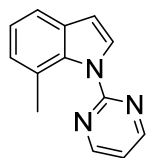
5-Iodo-1-(pyrimidin-2-yl)-1H-indole (1n): brown solid. ^1H NMR (300 MHz, CDCl_3) δ 8.71 (d, J = 4.8 Hz, 2H), 8.59 (d, J = 8.8 Hz, 1H), 8.25 (d, J = 3.6 Hz, 1H), 7.96 (s, 1H), 7.59 (d, J = 10.3 Hz, 1H), 7.09 (t, J = 4.8 Hz, 1H), 6.63 (d, J = 3.5 Hz, 1H).



6-Fluoro-1-(pyrimidin-2-yl)-1H-indole (1o): yellow solid. ^1H 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 (1p): orange solid. ^1H 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).



7-Methyl-1-(pyrimidin-2-yl)-1H-indole (1q): yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 8.76 (d, J = 4.7 Hz, 2H), 7.80 (d, J = 3.5 Hz, 1H), 7.50 (d, J = 7.3 Hz, 1H), 7.22 – 7.06 (m, 3H), 6.72 (d, J = 3.5 Hz, 1H), 2.42 (s, 3H).

3. General procedure for the C-H chlorination reaction and characterizations of products

Optimization studies (Table 1S)

1a (0.2 mmol), catalyst, chloride (bromine or iodide), additives and solvent were combined under air in a high pressure tube. After sealing the tube, the mixture was stirred at the required temperature for 12h. The reaction was cooled to room temperature, filtered through a pad of silica gel and washed with 100mL 50% EtOAc/ petroleum ether. The solvents were removed under reduced pressure and the crude yield was measured by NMR.

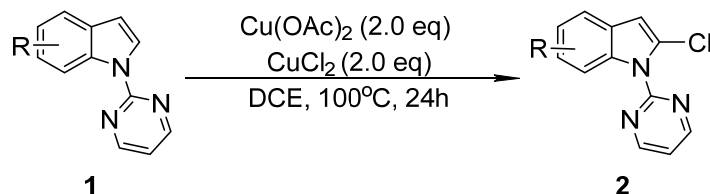
Table 1S. Optimization studies for C-2 chlorination of indole

Entry	Conditions ^a	Yield(%) ^b of 2a/3a/4a
1	Pd(OAc) ₂ (5 %), NCS (1.1 eq), AcOH, 120°C	0/3/92
2	Pd(OAc) ₂ (10 %), NCS (1.1 eq), DCE, 100°C	0/12/75
3	Pd(OAc) ₂ (10 %), NCS (1.1 eq), MeCN, 100°C	0/7/77
4	Pd(OAc) ₂ (10 %), LiCl (2 eq), K ₂ S ₂ O ₈ (2 eq), AcOH, 120°C	0/15/0
5	Pd(OAc) ₂ (10 %), LiCl (2 eq), NaIO ₃ (2 eq), AcOH, 120°C	0/5/14
6	Pd(OAc) ₂ (10 %), LiCl (2 eq), PIDA (2 eq), AcOH, 120°C	0/8/25
7	Pd(OAc) ₂ (10 %), CuCl ₂ (2 eq), Cu(OAc) ₂ (2 eq), DCE, 100°C	70/12/0
8	CuCl₂ (2 eq), Cu(OAc)₂ (2 eq), DCE, 100°C	79/10/0
9	CuCl ₂ (2 eq), DCE, 100°C	0/18/46
10	NaCl (2 eq), Cu(OAc) ₂ (2 eq), DCE, 100°C	n.r.
11	KCl (2 eq), Cu(OAc) ₂ (2 eq), DCE, 100°C	n.r.
12	CsCl (2 eq), Cu(OAc) ₂ (2 eq), DCE, 100°C	n.r.
13	NH ₄ Cl (2 eq), Cu(OAc) ₂ (2 eq), DCE, 100°C	21/0/0
14	Bu ₄ NCl (2 eq), Cu(OAc) ₂ (2 eq), DCE, 100°C	36/0/0
15	CuCl ₂ (2 eq), Cu(OAc) ₂ (1.5 eq), DCE, 100°C	73/14/0
16	CuCl ₂ (2 eq), Cu(OAc) ₂ (1 eq), DCE, 100°C	62/23/0
17	CuCl ₂ (1.5 eq), Cu(OAc) ₂ (2 eq), DCE, 100°C	65/7/0
18	CuCl ₂ (1 eq), Cu(OAc) ₂ (2 eq), DCE, 100°C	53/6/0
19	Cu(OAc) ₂ (2 eq), CuCl ₂ (2 eq), toluene, 120°C	69/12/0
20	Cu(OAc) ₂ (2 eq), CuCl ₂ (2 eq), HOAc, 120°C	42/0/0
21	Cu(OAc) ₂ (2 eq), CuCl ₂ (2 eq), MeCN, 100°C	56/0/0
22	Cu(OAc) ₂ (2 eq), CuCl ₂ (2 eq), HOAc(1 eq), DCE, 100°C	69/13/0

23	Cu(OAc) ₂ (2 eq), LiCl (4 eq), DCE, 100°C	24/0/0
24	Cu(OAc) ₂ (2 eq), LiCl (2 eq), HOAc, 120°C	trace//trace/0
25	Cu(NO ₃) ₂ • 3H ₂ O (2 eq), LiCl (3 eq), HOAc, 120°C	trace//trace/0
26	Cu(OAc) ₂ (2 eq), CuCl ₂ (2 eq), DCE, 80°C	78/10/0
27	Cu(OAc) ₂ (2 eq), CuBr ₂ (2 eq), DCE, 100°C	0/28/57
28	Cu(OAc) ₂ (2 eq), CuBr ₂ (1.5 eq), DCE, 100°C	0/16/42
29	Cu(OAc) ₂ (2 eq), CuI (2 eq), DCE, 100°C	n.r.
30	Cu(OAc) ₂ (2 eq), I ₂ (2 eq), DCE, 100°C	0/24/58
31	Cu(OAc) ₂ (2 eq), LiBr (2 eq), DCE, 100°C	0/8/35
32	Cu(OAc) ₂ (2 eq), KF (2 eq), DCE, 100°C	n.r.
33	Cu(OAc) ₂ (2 eq), AgF (2 eq), DCE, 100°C	n.r.

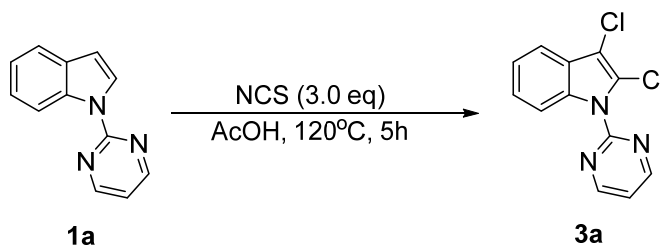
[a] Reaction conditions: **1a** (0.2 mmol), catalyst, chloride (bromine or iodide) source and additives as specified, solvent (0.4M), 12h. [b] Determined by ¹H NMR spectroscopy. n.r. = no reaction.

General procedure for C-2 chlorination of indoles:



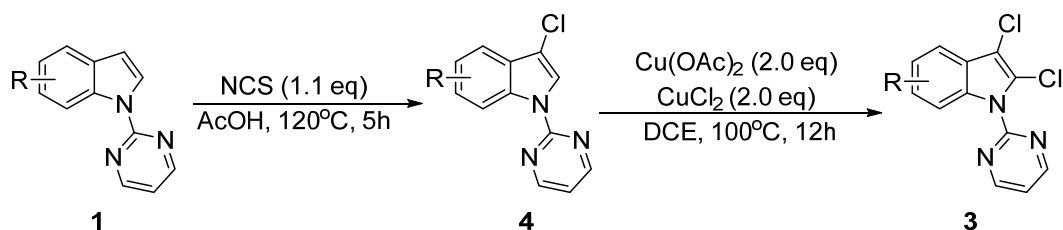
The mixture of Cu(OAc)₂ (72.65 mg, 0.4 mmol), CuCl₂ (53.78 mg, 0.4 mmol), substrate **1** (0.2 mmol) and DCE (1 mL) were added under air to a high pressure tube (35 mL). After sealing the tube, the mixture was stirred at 100 °C for 24 h. After cooling to room temperature, the mixture was evaporated under reduced pressure to remove the solvents and then purified directly via chromatography on silica gel with 3% EtOAc/ petroleum ether to provide the corresponding product **2**. Furthermore, Some were purified by preparative thin-layer chromatography.

Synthesis 2,3-dichloroindole using excess NCS:



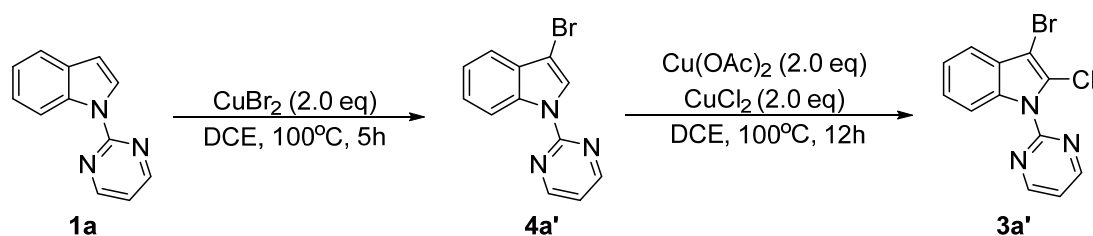
Substrate **1a** (0.1 mmol), NCS (40.10 mg, 0.3 mmol) and AcOH (1 mL) were combined under air to a high pressure tube. After sealing the tube, the mixture was stirred at 120 °C for 5 h. After cooling to ambient temperature, the reaction mixture was washed with NaHCO₃ (80 mL) and extracted with EtOAc (2×40 mL). Then the combined organic phase was dried over Na₂SO₄. After filtration and evaporation of the solvents under reduced pressure, the crude product was purified by silica gel column (3% EtOAc/ petroleum ether) to give the product **3a** (Yield: 47%).

The two step synthesis of 2,3-chloroindoles:



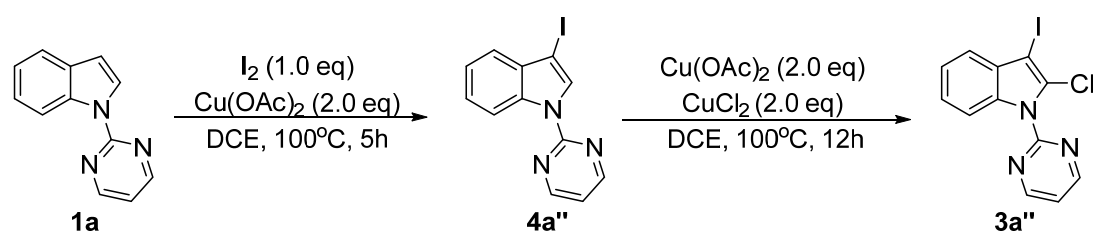
The mixture of NCS (58.75 mg, 0.44 mmol), substrate **1** (0.4 mmol) and AcOH (2 mL) were added under air to a high pressure tube. After sealing the tube, the mixture was stirred at 120 °C for 5h. The resulting mixture was cooled to room temperature, evaporated under reduced pressure to remove the solvents and then silica gel column directly (3% EtOAc/ petroleum ether) to give the product **4**. Then, the general procedure for C–2 chlorination of indoles was followed to give the desired product **3**.

Synthesis of 3-bromo-2-chloroindoles:

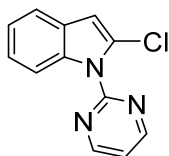


Substrate **1a** (78.0 mg, 0.4 mmol), CuBr₂ (178.68 mg, 0.8 mmol) and DCE (2 mL) were combined under air in a high pressure tube. Then sealing the tube and the mixture were stirred at 100°C for 5 h. After cooling to ambient temperature and evaporation, the mixture was purified directly by silica gel column (3% EtOAc/ petroleum ether) to give the product **4a'** (Yield: 53%). Then, following the general procedure for C–2 chlorination of indoles to give the desired product **3a'** (Yield: 94%).

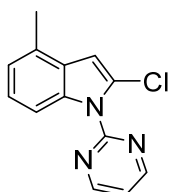
Synthesis of 2-chloro-3-iodoindoles:



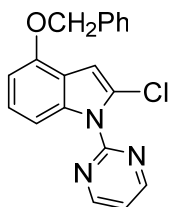
Substrate **1a** (78.0 mg, 0.4 mmol), I₂ (101.52 mg, 0.4 mmol), Cu(OAc)₂ (145.3 mg, 0.8 mmol) and DCE (2 mL) were combined under air in a high pressure tube. Then sealing the tube and the mixture were stirred at 100°C for 5 h. After cooling to ambient temperature and evaporation, the mixture was purified directly by silica gel column (3% EtOAc/ petroleum ether) to give the product **4a''** (Yield: 42%). Then, following the general procedure for C–2 chlorination of indoles to give the desired product **3a''** (Yield: 98%).



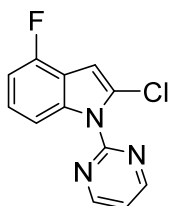
2-Chloro-1-(pyrimidin-2-yl)-1H-indole (2a): 12h, Yield 80%, white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.89 (d, J = 4.8 Hz, 2H), 7.98 (d, J = 7.9 Hz, 1H), 7.55 (dd, J = 7.3, 1.0 Hz, 1H), 7.33 – 7.17 (m, 3H), 6.70 (d, J = 0.4 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.11, 156.15, 135.77, 127.39, 124.33, 123.11, 121.97, 119.51, 118.08, 112.30, 106.09. IR (neat): 2917, 1562, 1522, 1446, 1415, 1342, 1308, 1207, 790, 744, 627. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_8\text{ClN}_3$: 229.0407. Found: 229.0403.



2-Chloro-4-methyl-1-(pyrimidin-2-yl)-1H-indole (2b): Yield 73%, pale yellow solid. ^1H NMR (300 MHz, CDCl_3) δ 8.89 (d, J = 4.8 Hz, 2H), 7.80 (d, J = 8.4 Hz, 1H), 7.28 (t, J = 4.9 Hz, 1H), 7.20 – 7.13 (m, 1H), 7.02 (d, J = 7.3 Hz, 1H), 6.73 (s, 1H), 2.53 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.10, 156.23, 135.54, 128.93, 127.11, 123.62, 123.17, 122.25, 118.05, 109.78, 104.67, 18.18. IR (neat): 2920, 1562, 1523, 1412, 1341, 1311, 1221, 1158, 1076, 818, 765, 732, 626. HRMS (ESI) calcd. for $\text{C}_{13}\text{H}_{10}\text{ClN}_3$: 243.0563. Found: 243.0567.

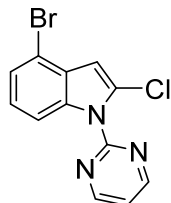


4-Benzyloxy-2-chloro-1-(pyrimidin-2-yl)-1H-indole (2c): Yield 70%, white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.89 (d, J = 4.8 Hz, 2H), 7.58 (d, J = 8.4 Hz, 1H), 7.50 (d, J = 7.2 Hz, 2H), 7.46 – 7.33 (m, 3H), 7.30 (t, J = 4.9 Hz, 1H), 7.16 (t, J = 8.2 Hz, 1H), 6.88 (s, 1H), 6.71 (d, J = 7.9 Hz, 1H), 5.22 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.10, 156.27, 150.91, 137.06, 136.83, 128.15, 127.48, 126.94, 123.83, 122.57, 118.37, 118.11, 105.72, 103.59, 103.53, 69.69. IR (neat): 2925, 1564, 1488, 1434, 1378, 1349, 1272, 1223, 1072, 1013, 766, 736, 696. HRMS (ESI) calcd. for $\text{C}_{19}\text{H}_{14}\text{ClNO}$: 335.0825. Found: 335.0828.

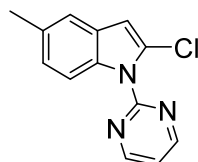


2-Chloro-4-fluoro-1-(pyrimidin-2-yl)-1H-indole (2d): Yield 98%, white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.88 (d, J = 4.8 Hz, 2H), 7.73 (d, J = 8.4 Hz, 1H), 7.29 (t,

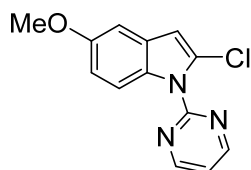
$J = 4.8$ Hz, 1H), 7.17 (dd, $J = 13.6, 8.1$ Hz, 1H), 6.90 (t, $J = 8.9$ Hz, 1H), 6.79 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.19, 156.27, 156.03, 152.99, 137.86, 137.72, 124.44, 123.64, 123.54, 118.46, 116.66, 116.35, 108.42, 107.11, 106.86, 101.63. IR (neat): 1567, 1529, 1490, 1436, 1343, 1218, 1044, 996, 869, 817, 759, 734, 624, 595. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_7\text{ClFN}_3$: 247.0313. Found: 247.0317.



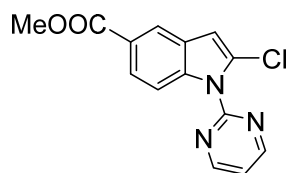
4-Bromo-2-chloro-1-(pyrimidin-2-yl)-1H-indole (2e): Yield 99%, pale yellow solid. ^1H NMR (300 MHz, CDCl_3) δ 8.90 (d, $J = 4.8$ Hz, 2H), 7.90 (d, $J = 8.4$ Hz, 1H), 7.38 (d, $J = 7.7$ Hz, 1H), 7.33 (t, $J = 4.8$ Hz, 1H), 7.12 (t, $J = 8.1$ Hz, 1H), 6.78 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.21, 155.91, 135.88, 128.12, 125.32, 124.82, 123.95, 118.51, 113.10, 111.50, 105.91. IR (neat): 2922, 1569, 1525, 1417, 1337, 1314, 1233, 1165, 1076, 926, 804, 756, 686, 636, 599, 570. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_7\text{BrClN}_3$: 306.9512. Found: 306.9516.



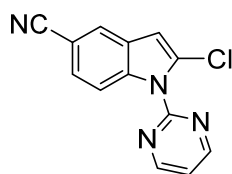
2-Chloro-5-methyl-1-(pyrimidin-2-yl)-1H-indole (2f): Yield 76%, white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.87 (d, $J = 4.8$ Hz, 2H), 7.88 (d, $J = 8.5$ Hz, 1H), 7.33 (s, 1H), 7.26 (d, $J = 9.6$ Hz, 1H), 7.08 (d, $J = 8.5$ Hz, 1H), 6.63 (s, 1H), 2.44 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.06, 156.26, 134.03, 131.38, 127.58, 124.52, 124.10, 119.30, 117.85, 112.09, 105.96, 20.99. IR (neat): 2971, 1561, 1455, 1471, 1334, 1215, 1161, 1077, 801, 631, 589, 565. HRMS (ESI) calcd. for $\text{C}_{13}\text{H}_{10}\text{ClN}_3$: 243.0563. Found: 243.0567.



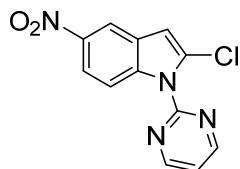
2-Chloro-5-methoxy-1-(pyrimidin-2-yl)-1H-indole (2g): Yield 76%, pale yellow solid. ^1H NMR (300 MHz, CDCl_3) δ 8.86 (d, $J = 4.8$ Hz, 2H), 7.93 (d, $J = 9.1$ Hz, 1H), 7.26 (d, $J = 9.7$ Hz, 1H), 7.00 (d, $J = 2.4$ Hz, 1H), 6.89 (dd, $J = 9.1, 2.5$ Hz, 1H), 6.63 (s, 1H), 3.86 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.05, 156.22, 155.28, 130.62, 128.07, 124.48, 117.83, 113.51, 112.36, 106.16, 101.62, 55.31. IR (neat): 2927, 1561, 1414, 1334, 1249, 1191, 1163, 1114, 1031, 795, 728, 631, 598, 568. HRMS (ESI) calcd. for $\text{C}_{13}\text{H}_{10}\text{ClN}_3\text{O}$: 259.0512. Found: 259.0516.



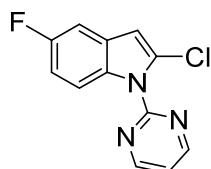
Methyl 2-chloro-1-(pyrimidin-2-yl)-1H-indole-5-carboxylate (2h): Yield 99%, white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.92 (d, $J = 4.8$ Hz, 2H), 8.29 (s, 1H), 7.96 (d, $J = 1.1$ Hz, 2H), 7.36 (t, $J = 4.8$ Hz, 1H), 6.78 (s, 1H), 3.94 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 167.15, 158.27, 155.72, 138.14, 126.90, 125.82, 124.33, 123.85, 121.97, 118.64, 112.03, 106.46, 51.67. IR (neat): 2922, 1709, 1562, 1537, 1423, 1322, 1267, 1231, 1199, 1094, 982, 895, 807, 758, 630, 596. HRMS (ESI) calcd. for $\text{C}_{14}\text{H}_{10}\text{ClN}_3\text{O}_2$: 287.0462. Found: 287.0466.



2-Chloro-1-(pyrimidin-2-yl)-1H-indole-5-carbonitrile (2i): Yield 51%, white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.93 (d, $J = 4.8$ Hz, 2H), 8.02 (d, $J = 8.7$ Hz, 1H), 7.90 (s, 1H), 7.50 (d, $J = 8.7$ Hz, 1H), 7.40 (d, $J = 4.8$ Hz, 1H), 6.77 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.39, 155.52, 137.26, 127.19, 126.05, 124.48, 119.50, 119.00, 113.28, 105.67, 105.28. IR (neat): 2970, 2223, 1561, 1459, 1420, 1323, 1215, 1155, 1080, 883, 795, 716, 633, 695, 550. HRMS (ESI) calcd. for $\text{C}_{13}\text{H}_7\text{ClN}_4$: 254.0359. Found: 254.0363.

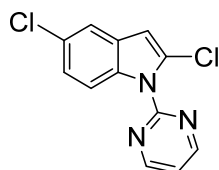


2-Chloro-5-nitro-1-(pyrimidin-2-yl)-1H-indole (2j): Yield 57%, yellow solid. ^1H NMR (300 MHz, CDCl_3) δ 8.95 (d, $J = 4.8$ Hz, 2H), 8.50 (d, $J = 2.0$ Hz, 1H), 8.16 (dd, $J = 9.2, 2.2$ Hz, 1H), 8.01 (d, $J = 9.2$ Hz, 1H), 7.41 (t, $J = 4.8$ Hz, 1H), 6.86 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.43, 155.46, 143.04, 138.46, 127.88, 126.80, 119.16, 118.33, 116.04, 112.60, 106.67. IR (neat): 3135, 2987, 1568, 1510, 1450, 1418, 1338, 1313, 1205, 1070, 878, 810, 746, 629, 605. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_7\text{ClN}_4\text{O}_2$: 274.0258. Found: 274.0262.

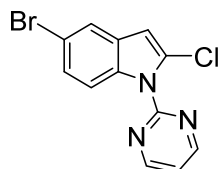


2-Chloro-5-fluoro-1-(pyrimidin-2-yl)-1H-indole (2k): Yield 99%, pale pink solid. ^1H NMR (300 MHz, CDCl_3) δ 8.88 (d, $J = 4.8$ Hz, 2H), 7.95 (dd, $J = 9.1, 4.5$ Hz, 1H), 7.30 (t, $J = 4.8$ Hz, 1H), 7.20 (dd, $J = 8.9, 2.5$ Hz, 1H), 6.99 (td, $J = 9.2, 2.6$ Hz, 1H), 6.66 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.67 (d, $J = 238.0$ Hz), 158.16, 155.99,

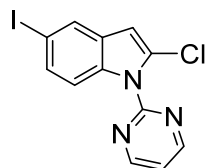
132.10, 127.96 (d, $J = 10.3$ Hz), 125.78, 118.24, 113.56 (d, $J = 9.0$ Hz), 111.03 (d, $J = 25.4$ Hz), 105.91, 104.79 (d, $J = 24.1$ Hz). IR (neat): 2987, 1565, 1425, 1319, 1245, 1204, 1160, 1111, 949, 844, 805, 787, 631, 595, 561. HRMS (ESI) calcd. for $C_{12}H_7ClFN_3$: 247.0313. Found: 247.0317.



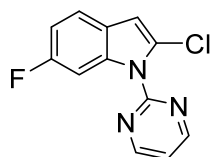
2, 5-Chloro-1-(pyrimidin-2-yl)-1H-indole (2l): Yield 99%, pink solid. 1H NMR (300 MHz, $CDCl_3$) δ 8.89 (d, $J = 4.8$ Hz, 2H), 7.92 (d, $J = 8.9$ Hz, 1H), 7.51 (d, $J = 2.1$ Hz, 1H), 7.31 (t, $J = 4.8$ Hz, 1H), 7.21 (dd, $J = 8.9, 2.1$ Hz, 1H), 6.64 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.16, 155.91, 134.04, 128.40, 127.53, 125.76, 123.24, 118.93, 118.33, 113.65, 105.46. IR (neat): 3109, 2987, 1565, 1522, 1424, 1337, 1314, 1263, 1202, 1064, 918, 854, 787, 629, 582. HRMS (ESI) calcd. for $C_{12}H_7Cl_2N_3$: 263.0017. Found: 263.0021.



5-Bromo-2-chloro-1-(pyrimidin-2-yl)-1H-indole (2m): Yield 94%, white solid. 1H NMR (300 MHz, $CDCl_3$) δ 8.89 (d, $J = 4.9$ Hz, 2H), 7.87 (d, $J = 8.9$ Hz, 1H), 7.67 (d, $J = 1.9$ Hz, 1H), 7.38 – 7.29 (m, 2H), 6.64 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.16, 155.89, 134.36, 128.96, 125.86, 125.66, 121.97, 118.35, 115.16, 114.02, 105.31. IR (neat): 2922, 1561, 1522, 1438, 1414, 1332, 1310, 1202, 1057, 912, 864, 800, 749, 628. HRMS (ESI) calcd. for $C_{12}H_7BrClN_3$: 306.9512. Found: 306.9516.

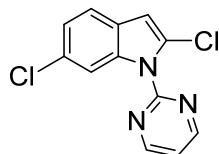


5-Iodo-2-chloro-1-(pyrimidin-2-yl)-1H-indole (2n): Yield 93%, pale pink solid. 1H NMR (300 MHz, $CDCl_3$) δ 8.88 (d, $J = 4.8$ Hz, 2H), 7.88 (d, $J = 1.3$ Hz, 1H), 7.76 (d, $J = 8.8$ Hz, 1H), 7.51 (dd, $J = 8.8, 1.6$ Hz, 1H), 7.31 (t, $J = 4.8$ Hz, 1H), 6.62 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.16, 155.87, 134.89, 131.43, 129.60, 128.15, 125.33, 118.35, 114.42, 105.00, 85.72. IR (neat): 2923, 1560, 1519, 1411, 1329, 1306, 1200, 1013, 907, 865, 792, 747, 628, 604, 578. HRMS (ESI) calcd. for $C_{12}H_7ClIN_3$: 354.9373. Found: 354.9376.

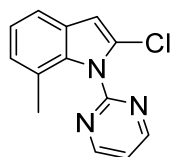


2-Chloro-6-fluoro-1-(pyrimidin-2-yl)-1H-indole (2o): Yield 97%, pale yellow solid.

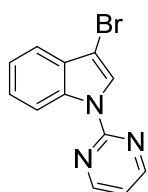
^1H NMR (300 MHz, CDCl_3) δ 8.89 (d, J = 4.8 Hz, 2H), 7.76 (dd, J = 10.4, 2.2 Hz, 1H), 7.45 (dd, J = 8.6, 5.4 Hz, 1H), 7.30 (t, J = 4.8 Hz, 1H), 7.05 – 6.90 (m, 1H), 6.67 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 160.13 (d, J = 239.1 Hz), 158.15, 156.01, 135.73 (d, J = 12.6 Hz), 124.23, 123.72, 120.20 (d, J = 9.7 Hz), 118.22, 110.42 (d, J = 24.4 Hz), 106.01, 99.83 (d, J = 28.7 Hz). IR (neat): 2987, 1564, 1533, 1484, 1425, 1349, 1314, 1264, 1202, 1143, 1108, 1075, 836, 789, 732, 632, 583. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_7\text{ClFN}_3$: 247.0313. Found: 247.0317.



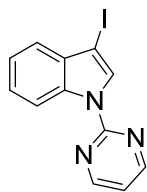
2, 6-Chloro-1-(pyrimidin-2-yl)-1H-indole (2p): Yield 94%, yellow solid. ^1H NMR (300 MHz, CDCl_3) δ 8.90 (d, J = 4.8 Hz, 2H), 8.03 (d, J = 1.6 Hz, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.32 (t, J = 4.8 Hz, 1H), 7.19 (dd, J = 8.4, 1.9 Hz, 1H), 6.67 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.21, 155.89, 135.93, 129.08, 125.87, 125.02, 122.61, 120.27, 118.34, 112.66, 105.95. IR (neat): 2922, 1563, 1523, 1417, 1339, 1308, 1229, 1066, 810, 695, 630. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_7\text{Cl}_2\text{N}_3$: 263.0017. Found: 263.0021.



2-Chloro-7-methyl-1-(pyrimidin-2-yl)-1H-indole (2q): Yield 43%, yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 8.93 (d, J = 4.8 Hz, 2H), 7.46 – 7.39 (m, 2H), 7.10 (t, J = 7.6 Hz, 1H), 6.98 (d, J = 7.3 Hz, 1H), 6.63 (s, 1H), 1.89 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.21, 157.35, 135.47, 127.86, 125.41, 125.15, 121.40, 121.01, 119.92, 117.63, 103.18, 18.73. IR (neat): 2964, 1560, 1529, 1457, 1413, 1342, 1318, 1251, 1077, 790, 739, 714, 613, 581. HRMS (ESI) calcd. for $\text{C}_{13}\text{H}_{10}\text{ClN}_3$: 243.0563. Found: 243.0567.

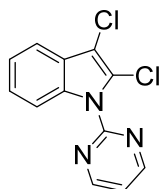


3-Bromo-1-(pyrimidin-2-yl)-1H-indole (4a'): white solid. ^1H NMR (400 MHz, CDCl_3) δ 8.82 (d, J = 8.4 Hz, 1H), 8.71 (d, J = 4.8 Hz, 2H), 8.37 (s, 1H), 7.64 – 7.58 (m, 1H), 7.46 – 7.39 (m, 1H), 7.38 – 7.32 (m, 1H), 7.09 (t, J = 4.8 Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 158.20, 157.19, 134.79, 130.00, 124.88, 124.79, 122.72, 119.38, 116.52, 116.35, 97.47. IR (neat): 2918.02, 1576.45, 1449.92, 1422.87, 1348.27, 1317.82, 1204.43, 1075.11, 802.26, 790.42, 747.18. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_8\text{BrN}_3$: 272.9902. Found: 272.9906.

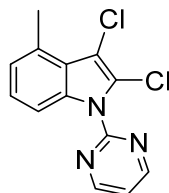


3-Iodo-1-(pyrimidin-2-yl)-1H-indole (4a''): white solid. ^1H NMR (400 MHz, CDCl_3) δ 8.77 (d, J = 8.3 Hz, 1H), 8.69 (d, J = 4.7 Hz, 2H), 8.43 (s, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.41 (dd, J = 11.2, 4.1 Hz, 1H), 7.33 (t, J = 7.4 Hz, 1H), 7.06 (t, J = 4.7 Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 158.20, 157.02, 135.08, 132.80, 130.14, 124.76, 122.83, 121.37, 116.63, 116.25, 64.70. IR (neat): 2914.93, 1574.76, 1449.55, 1423.74, 1345.91, 1314.25, 1236.42, 1201.19, 801.50, 747.75. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_8\text{IN}_3$: 320.9763. Found: 320.9769.

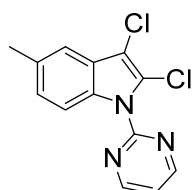
For the following products **3** except **3m**, the yields from **4** to **3** were given.



2,3-Dichloro-1-(pyrimidin-2-yl)-1H-indole (3a): Yield 98%, white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.85 (d, J = 4.8 Hz, 2H), 8.06 (dd, J = 6.6, 2.1 Hz, 1H), 7.60 (dd, J = 6.1, 2.6 Hz, 1H), 7.39 – 7.23 (m, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.14, 155.95, 134.14, 125.27, 124.41, 122.51, 121.31, 118.24, 117.48, 112.73, 109.54. IR (neat): 1564, 1446, 1412, 1341, 1313, 1212, 1160, 950, 814, 741, 677, 625. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_7\text{Cl}_2\text{N}_3$: 263.0017. Found: 263.0012.

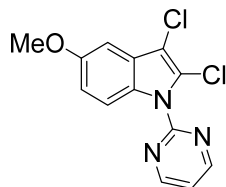


2,3-Dichloro-4-methyl-1-(pyrimidin-2-yl)-1H-indole (3b): Yield 99%, white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.87 (d, J = 4.8 Hz, 2H), 7.83 (d, J = 8.4 Hz, 1H), 7.29 (t, J = 4.8 Hz, 1H), 7.17 (dd, J = 8.2, 7.6 Hz, 1H), 6.99 (dd, J = 7.3, 0.6 Hz, 1H), 2.80 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.16, 155.88, 134.47, 129.78, 124.16, 124.04, 122.98, 121.34, 118.35, 110.13, 109.46, 18.83. IR (neat): 2923, 1565, 1417, 1263, 1225, 1079, 969, 816, 740, 657, 629. HRMS (ESI) calcd. for $\text{C}_{13}\text{H}_9\text{Cl}_2\text{N}_3$: 277.0174. Found: 277.0170.

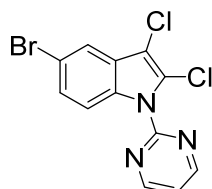


2,3-Dichloro-5-methyl-1-(pyrimidin-2-yl)-1H-indole (3f): Yield 98%, white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.83 (d, J = 4.8 Hz, 2H), 7.95 (d, J = 8.6 Hz, 1H), 7.38

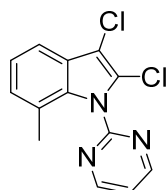
(s, 1H), 7.24 (t, J = 4.8 Hz, 1H), 7.14 (dd, J = 8.6, 1.2 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.06, 156.06, 132.45, 132.16, 125.86, 125.40, 121.06, 118.00, 117.16, 112.60, 109.34, 20.97. IR (neat): 2919, 1560, 1411, 1326, 1292, 1212, 1173, 799, 736, 687, 634, 585. HRMS (ESI) calcd. for $\text{C}_{13}\text{H}_9\text{Cl}_2\text{N}_3$: 277.0174. Found: 277.0170.



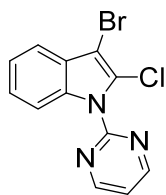
2,3-Dichloro-5-methoxy-1-(pyrimidin-2-yl)-1H-indole (3g): Yield 93%, white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.83 (d, J = 4.7 Hz, 2H), 8.00 (d, J = 9.1 Hz, 1H), 7.23 (t, J = 4.8 Hz, 1H), 7.02 (d, J = 2.5 Hz, 1H), 6.94 (dd, J = 9.1, 2.6 Hz, 1H), 3.89 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.04, 156.03, 155.81, 128.86, 125.97, 121.36, 117.97, 114.22, 114.04, 109.39, 99.16, 55.34. IR (neat): 1561, 1479, 1415, 1331, 1289, 1209, 1172, 1031, 803, 692, 634. HRMS (ESI) calcd. for $\text{C}_{13}\text{H}_9\text{Cl}_2\text{N}_3\text{O}$: 293.0123. Found: 293.0128.



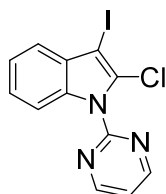
5-Bromo-2,3-dichloro-1-(pyrimidin-2-yl)-1H-indole (3f): Yield 93%, white solid. ^1H NMR (300 MHz, CDCl_3) δ 8.86 (d, J = 4.8 Hz, 2H), 7.94 (d, J = 8.9 Hz, 1H), 7.72 (d, J = 1.7 Hz, 1H), 7.39 (dd, J = 8.9, 1.7 Hz, 1H), 7.30 (t, J = 4.8 Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.19, 155.70, 132.72, 127.22, 126.79, 122.63, 120.07, 118.48, 115.80, 114.54, 108.65. IR (neat): 1563, 1425, 1329, 1209, 1066, 975, 857, 791, 692, 633. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_6\text{BrCl}_2\text{N}_3$: 340.9122. Found: 304.9126.



2,3-Dichloro-7-methyl-1-(pyrimidin-2-yl)-1H-indole (3m): Yield 22% (table 2), yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 8.91 (d, J = 4.8 Hz, 2H), 7.49 (d, J = 7.8 Hz, 1H), 7.40 (t, J = 4.9 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.05 (d, J = 7.3 Hz, 1H), 1.91 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 158.36, 156.93, 133.79, 126.42, 125.68, 122.41, 121.96, 121.56, 120.17, 115.60, 106.52, 18.70. IR (neat): 1560, 1409, 1338, 1289, 1224, 1097, 805, 774, 737, 669, 636. HRMS (ESI) calcd. for $\text{C}_{13}\text{H}_9\text{Cl}_2\text{N}_3$: 277.0174. Found: 277.0179.

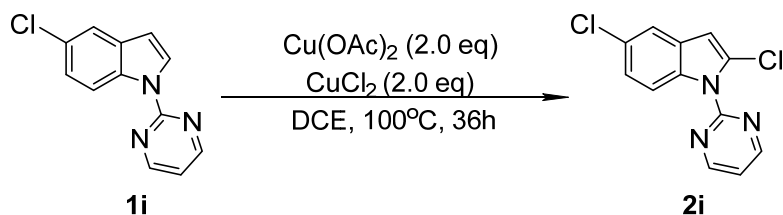


3-Bromo-2-chloro-1-(pyrimidin-2-yl)-1H-indole (3a'): Yield 94%, yellow solid. ^1H NMR (400 MHz, CDCl_3) δ 8.87 (d, J = 4.8 Hz, 2H), 8.05 – 7.97 (m, 1H), 7.59 – 7.51 (m, 1H), 7.31 (ddd, J = 12.5, 6.7, 3.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 158.57, 156.35, 135.12, 127.19, 124.75, 123.86, 122.97, 118.97, 118.73, 112.96, 97.40. IR (neat): 2918.02, 1562.57, 1449.89, 1411.46, 1337.63, 1310.43, 1209.64, 807.08, 741.78, 661.00, 626.83. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_7\text{BrClN}_3$: 306.9512. Found: 306.9516.

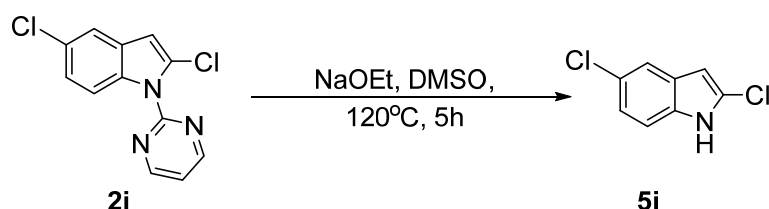


2-Chloro-3-iodo-1-(pyrimidin-2-yl)-1H-indole (3a''): Yield 98%, yellow solid. ^1H NMR (400 MHz, CDCl_3) δ 8.88 (d, J = 4.3 Hz, 2H), 7.94 (d, J = 8.6 Hz, 1H), 7.44 (dd, J = 5.9, 3.0 Hz, 1H), 7.30 (dd, J = 9.4, 5.5 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 158.62, 156.34, 135.97, 130.16, 128.09, 124.73, 123.07, 121.11, 118.88, 112.89, 67.77. IR (neat): 2921.11, 1562.31, 1444.12, 1412.51, 1335.84, 1307.77, 1207.78, 806.54, 741.89, 626.34. HRMS (ESI) calcd. for $\text{C}_{12}\text{H}_7\text{ClIN}_3$: 354.9373. Found: 354.9379.

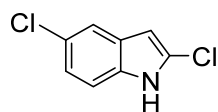
4. General procedure for gram scale experiment and deprotection



Substrate **1i** (1.15 g, 5 mmol), $\text{Cu}(\text{OAc})_2$ (1.82 g, 10 mmol), CuCl_2 (1.34 mg, 10 mmol) and DCE (25 mL) were combined under air in a 100 mL flask and stirred at 100°C for 36 h with an air balloon. The resulting mixture was cooled to room temperature, filtered through a pad of silica gel and washed with 100 mL 50% EtOAc/ petroleum ether. Then the solvents were evaporated under reduced pressure to give the 2,5-dichloro-1-(pyrimidin-2-yl)-1H-indole **2i** as a pink solid (Yield 99%).



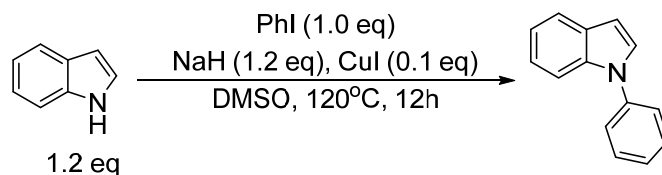
The mixture of chlorinated product **2i** (0.2 mmol), NaOEt (68.05 mg, 1.0 mmol) and DMSO (0.8 mL) were added under air to a high pressure tube. After sealing the tube, the mixture was stirred at 120°C for 5h. After cooling to ambient temperature, the reaction mixture was diluted with EtOAc (80 mL) and washed with H_2O (2×40 mL). The aqueous phase was extracted with EtOAc (2×40 mL), and the combined organic phase was dried over Na_2SO_4 , filtered and concentrated to give the 2,5-dichloro-1H-indole **5i** (Yield 99%).



2,5-Dichloro-1H-indole (5i): brown solid. ^1H NMR (300 MHz, CDCl_3) δ 8.11 (s, 1H), 7.49 (s, 1H), 7.16 (dt, $J = 8.6, 5.2$ Hz, 2H), 6.37 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 132.92, 128.70, 125.83, 124.35, 122.11, 118.87, 111.08, 100.03. IR (neat): 3407, 1694, 1570, 1440, 1327, 1192, 1062, 1013, 914, 865, 775, 689, 620, 587. HRMS (ESI) calcd. for $\text{C}_8\text{H}_5\text{Cl}_2\text{N}$: 184.9799. Found: 184.9794.

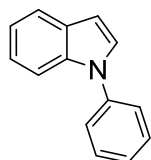
5. General procedure for control experiments with 1-H and 1-phenyl indoles

Synthesis of 1-Phenyl-1H-indole²:

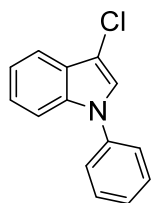


NaH (0.6 mmol), indole (0.6 mmol) and DMSO (1 mL) were added to a high pressure tube. The mixture was stirred for 0.5 h under ambient temperature, CuI (0.1 mmol) and PhI (0.5 mmol) were added. The mixture was heated in an oil bath at 120°C and the process was monitored by TLC. When the reaction completed, the resulting mixture was cooled to room temperature and diluted by 10 mL water. The product was extracted by ethyl acetate (10 mL×3). The combined extracts were dried over Na₂SO₄, evaporated under reduced pressure and further purified by column chromatography to afford the yellow-oil product (Yield 72%).

The control experiments with 1-H and 1-phenyl indoles followed the general procedure for C-2 chlorination of indoles. Under the optimized conditions for C-2 chlorination, 1-phenylindole turned into 3-chloro-1-phenylindole in 60% yield and 1H-indole turned into something on the baseline of TLC that we couldn't identify.



1-Phenyl-1H-indole: yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.70 (d, *J* = 7.5 Hz, 1H), 7.61 – 7.56 (m, 1H), 7.55 – 7.49 (m, 4H), 7.40 – 7.34 (m, 2H), 7.26 – 7.15 (m, 2H), 6.70 (d, *J* = 3.2 Hz, 1H). The spectral data of the starting material was in accordance with that reported in the literature².

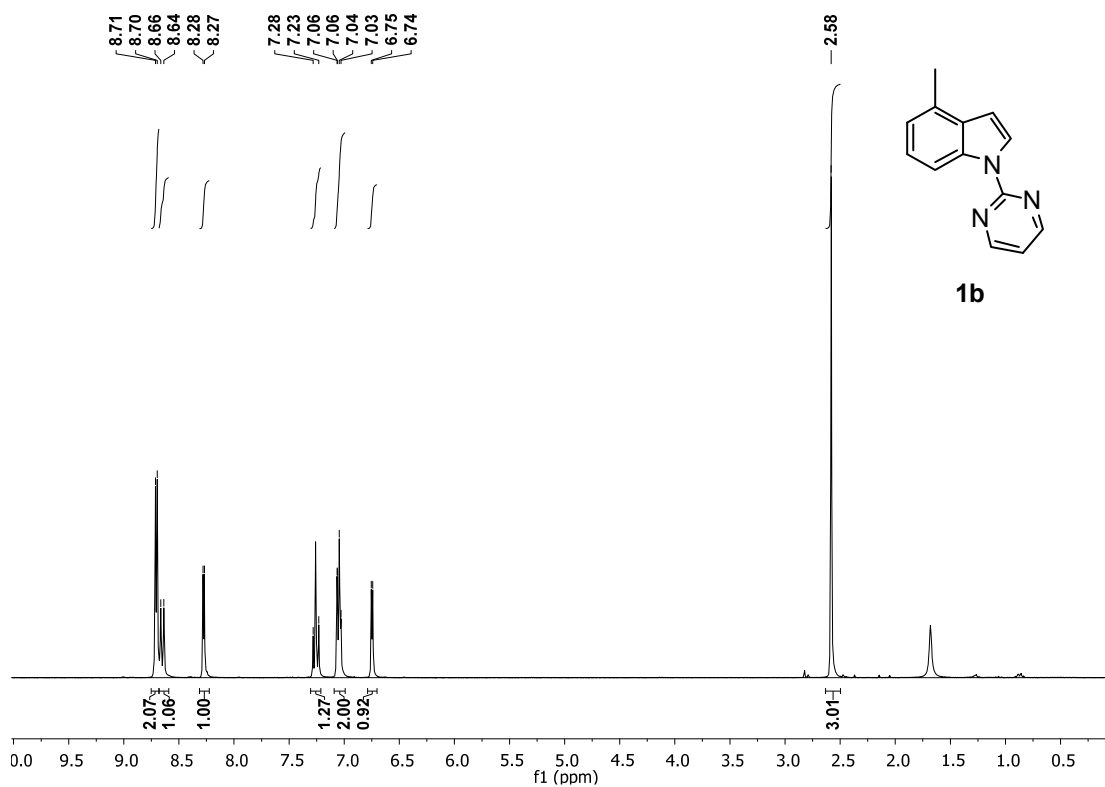
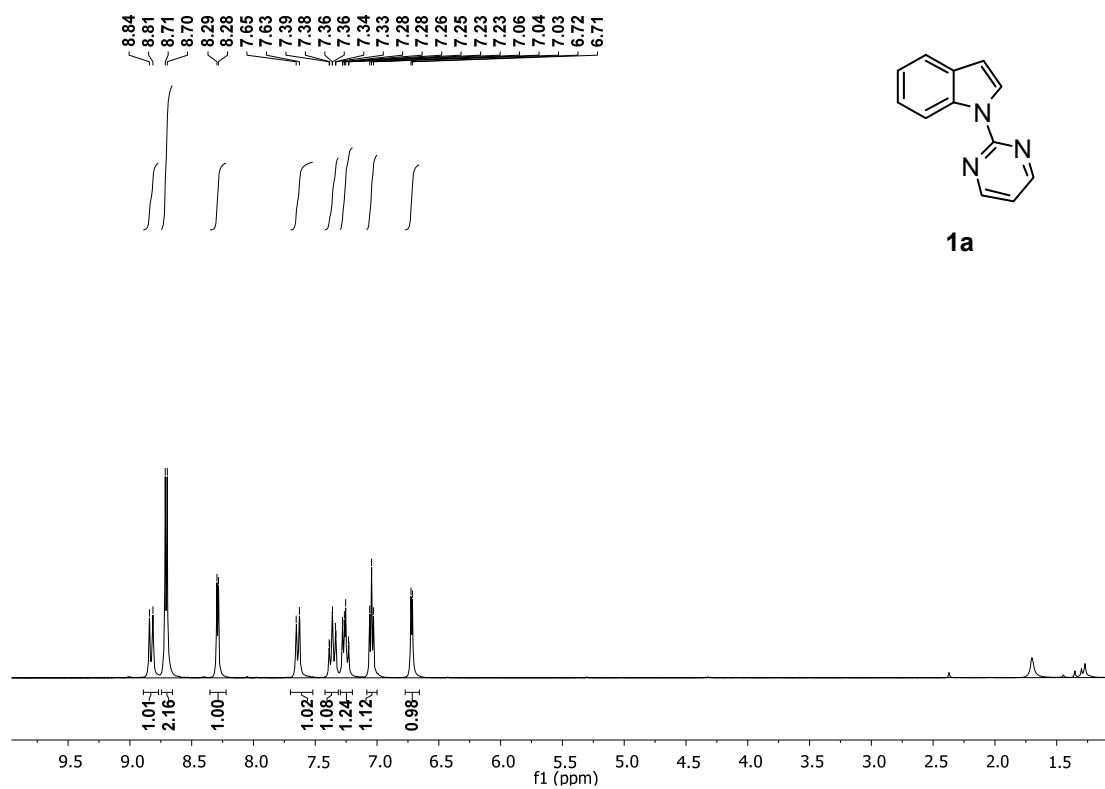


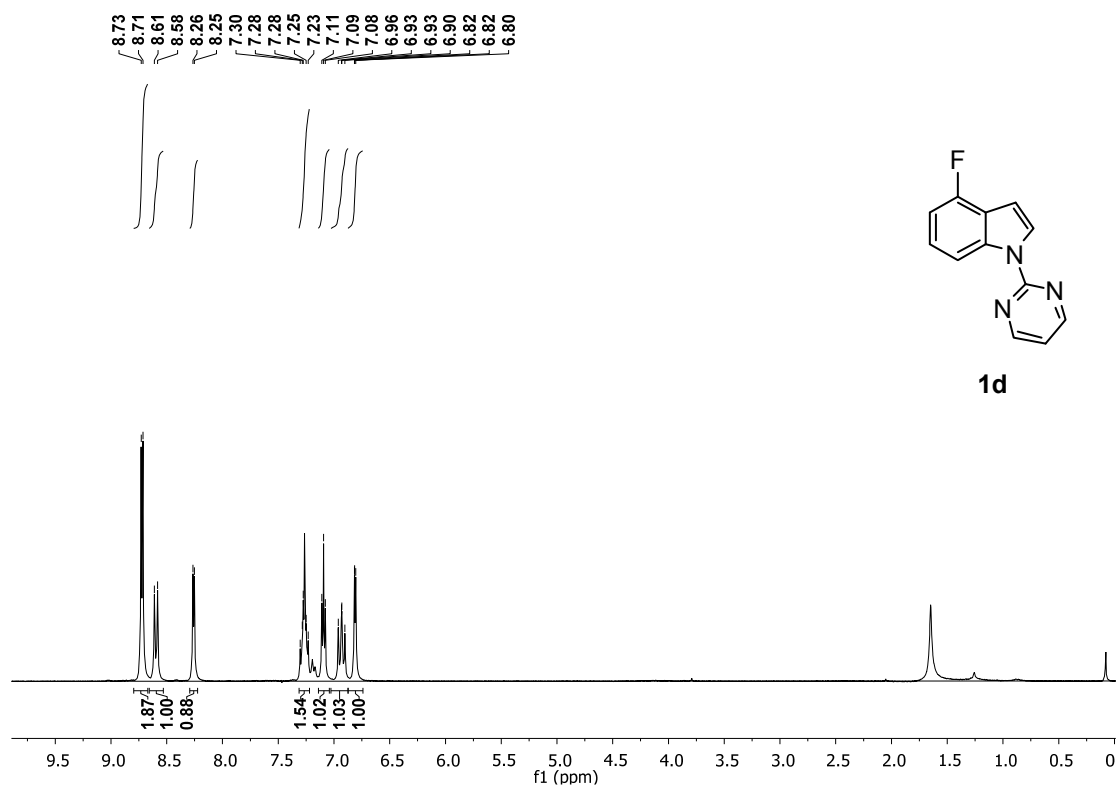
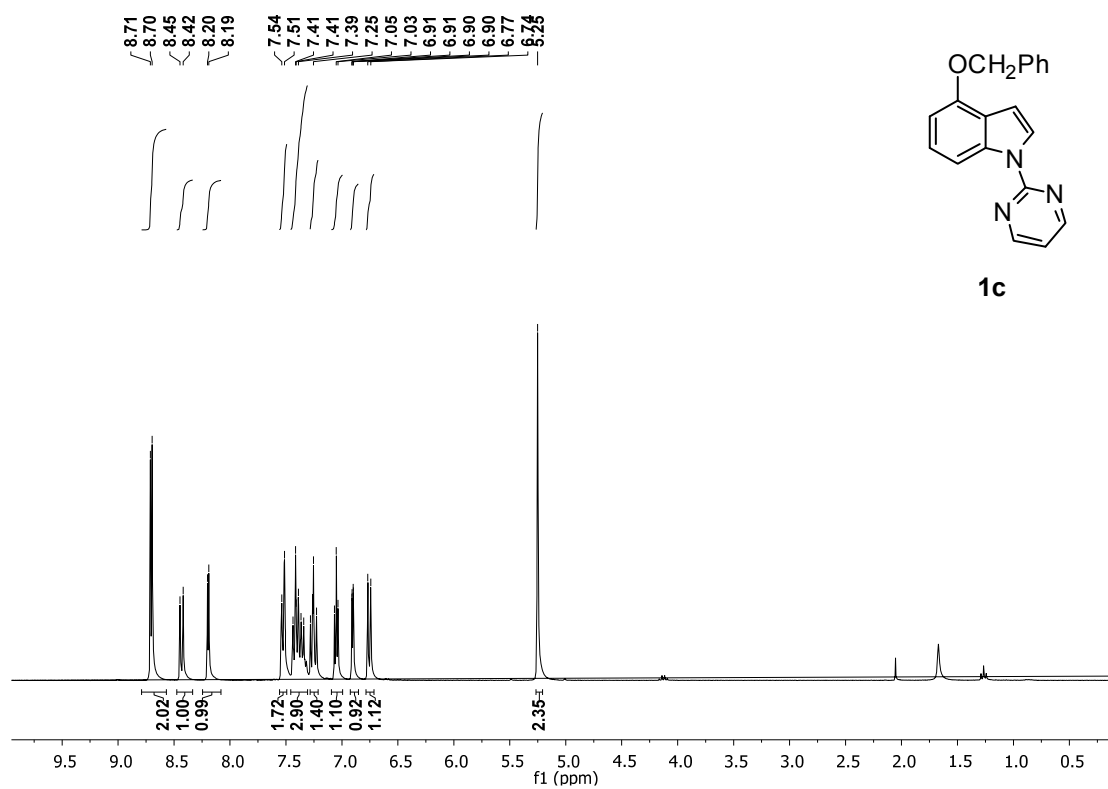
3-Chloro-1-phenyl-1H-indole: colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.73 (dd, *J* = 6.5, 2.3 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 3H), 7.51 (t, *J* = 4.2 Hz, 2H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.37 (s, 1H), 7.32 – 7.27 (m, 2H). The spectral data of the product was in accordance with that reported in the literature³.

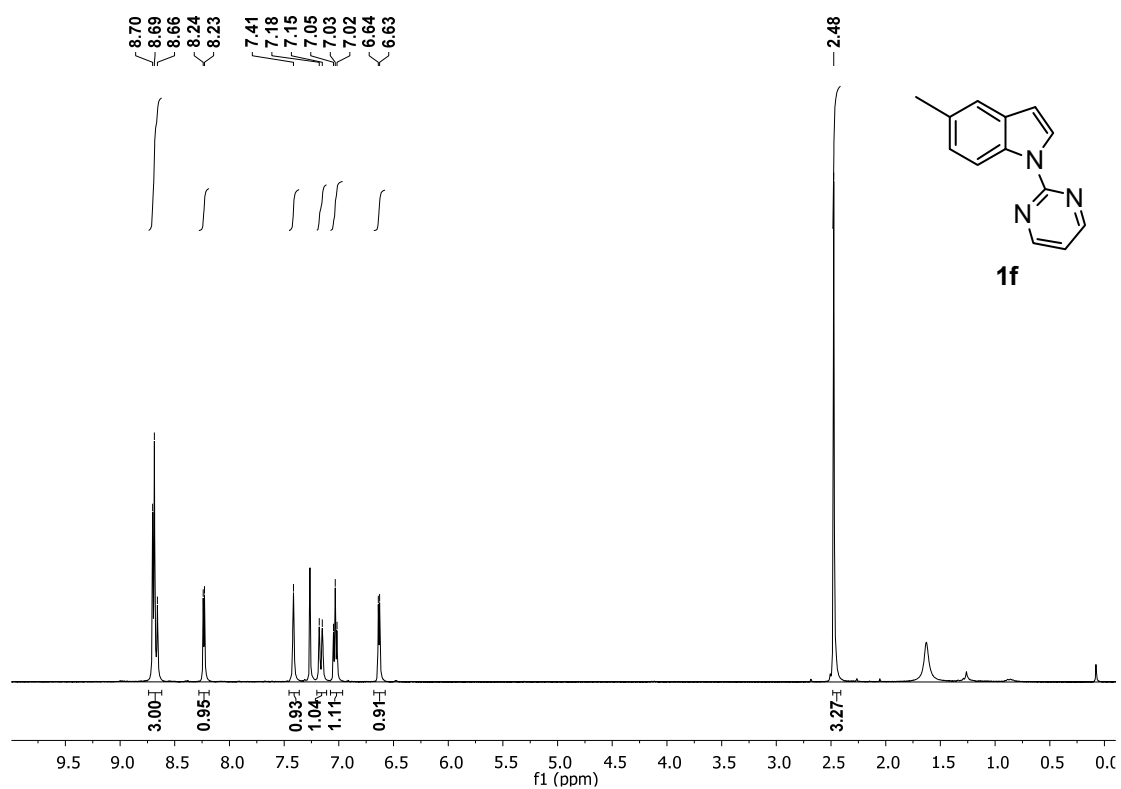
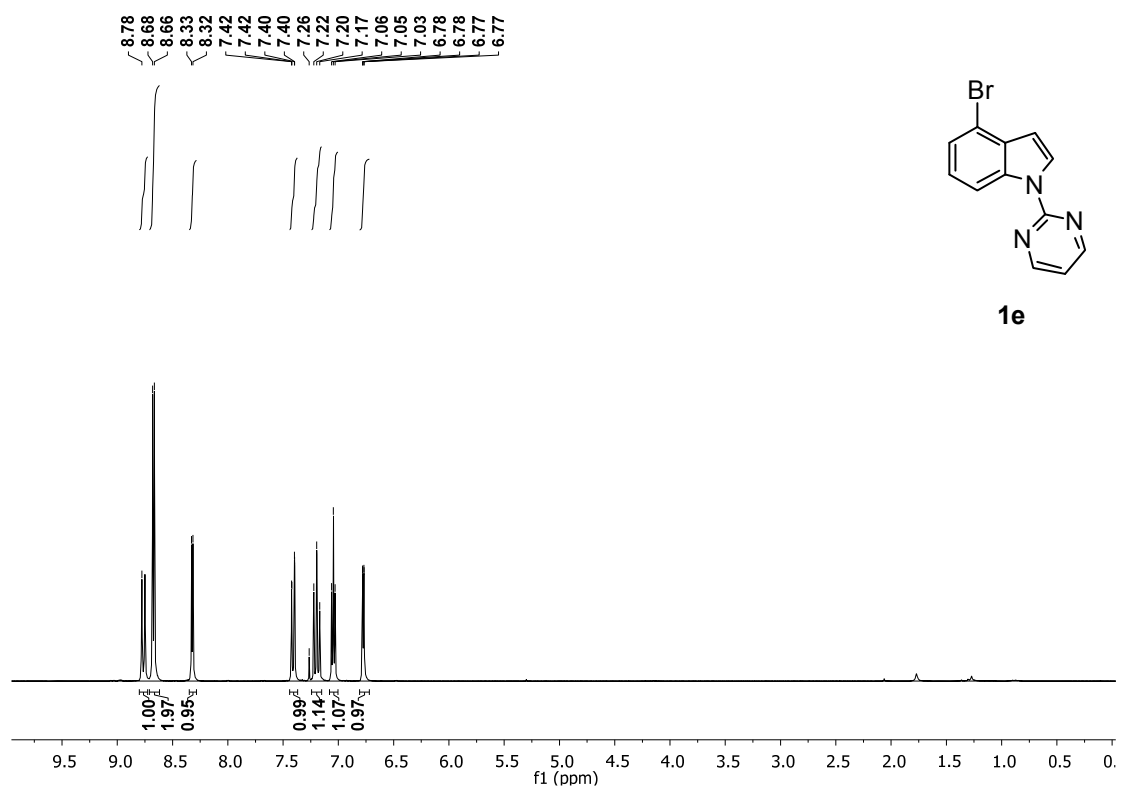
6. References

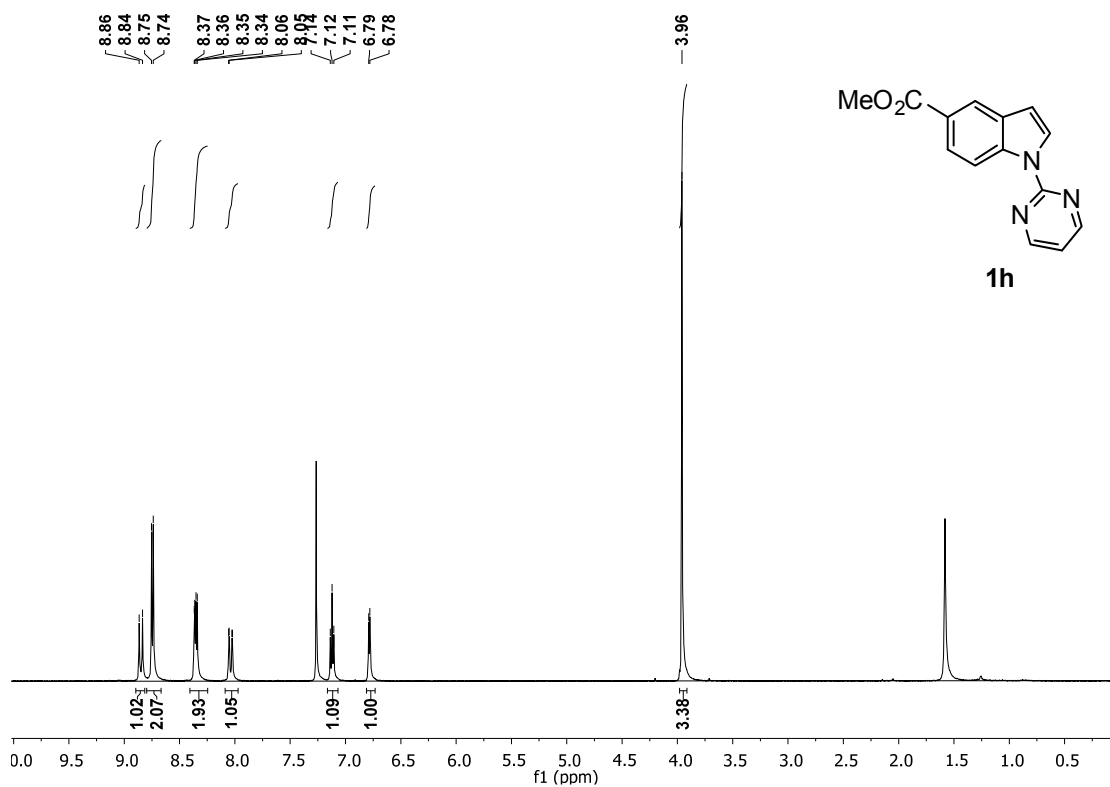
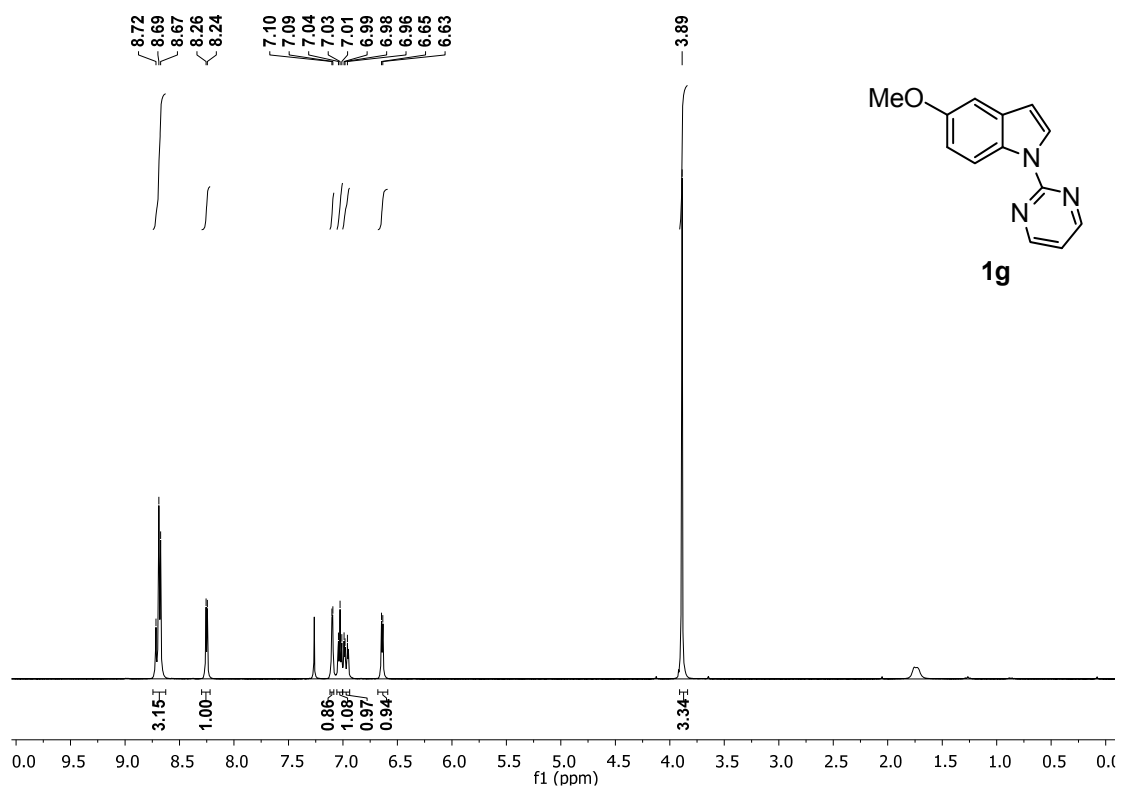
1. (a) L. Ackermann and A. V. Lygin, *Org. Lett.*, 2011, **13**, 3332-3335; (b) Z. Ding and N. Yoshikai, *Angew. Chem. Int. Ed. Engl.*, 2012, **51**, 4698-4701; (c) J. Shi, B. Zhou, Y. Yang and Y. Li, *Org. Biomol. Chem*, 2012, **10**, 8953-8955; (d) S. Xu, X. Huang, X. Hong and B. Xu, *Org. Lett.*, 2012, **14**, 4614-4617.
2. Q. Yang, Y. Wang, B. Zhang and M. Zhang, *Chin. J. Chem* . 2012, **30**, 2389-2393.
3. C. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1997, 2695-2700.

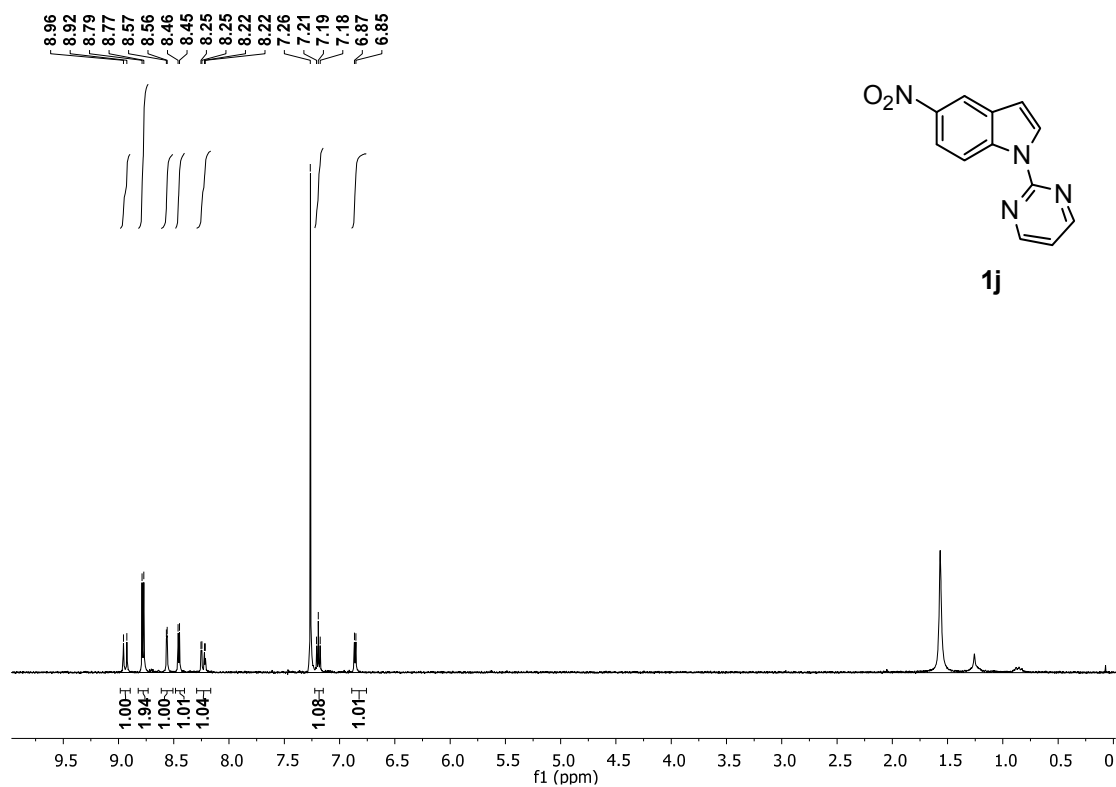
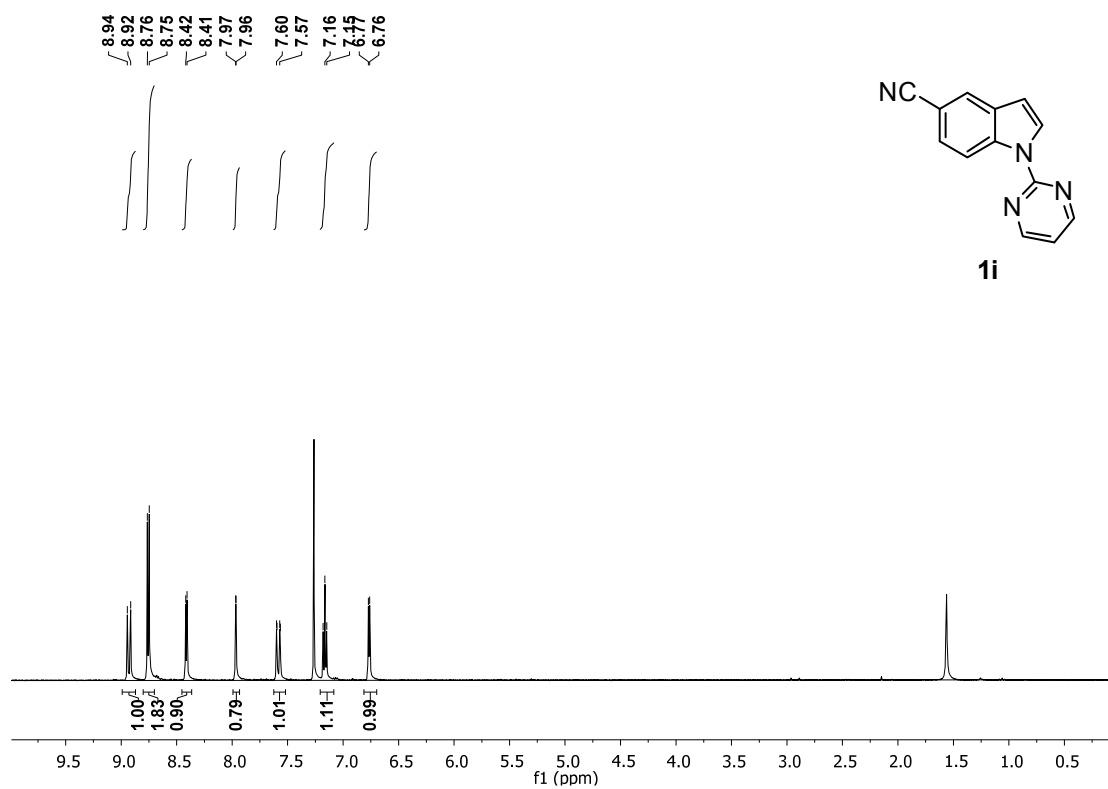
7. ^1H and ^{13}C NMR spectra of starting materials and products

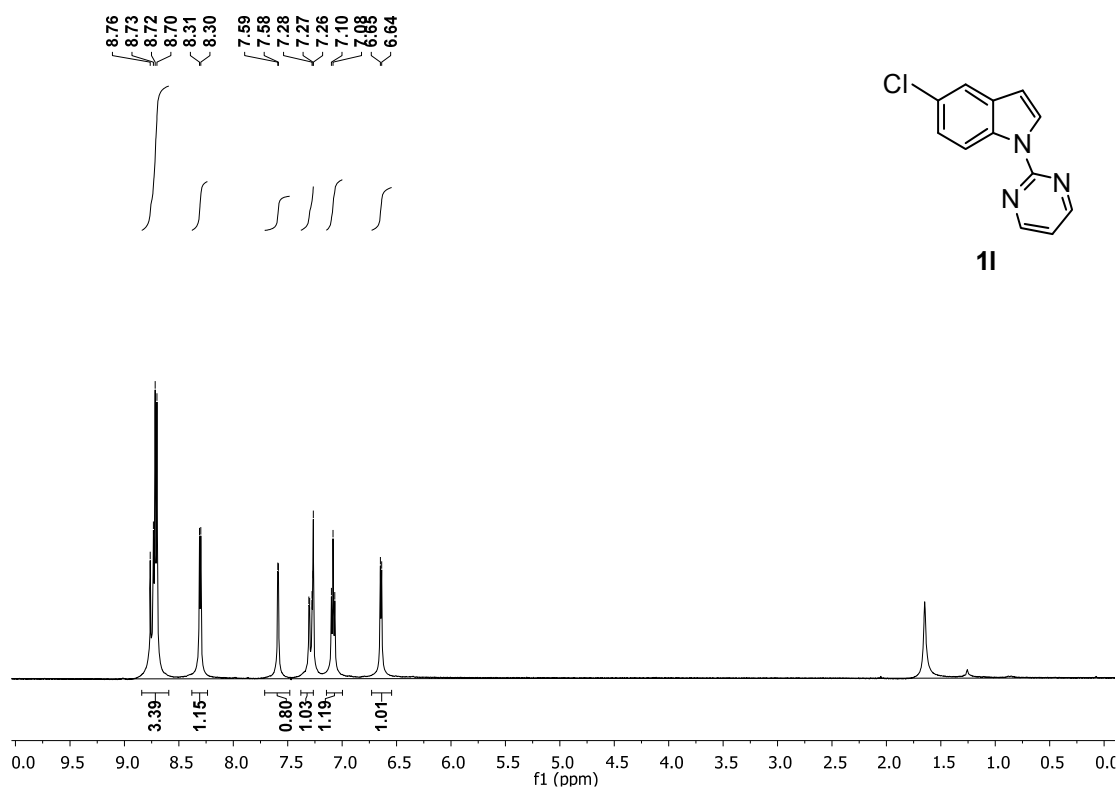
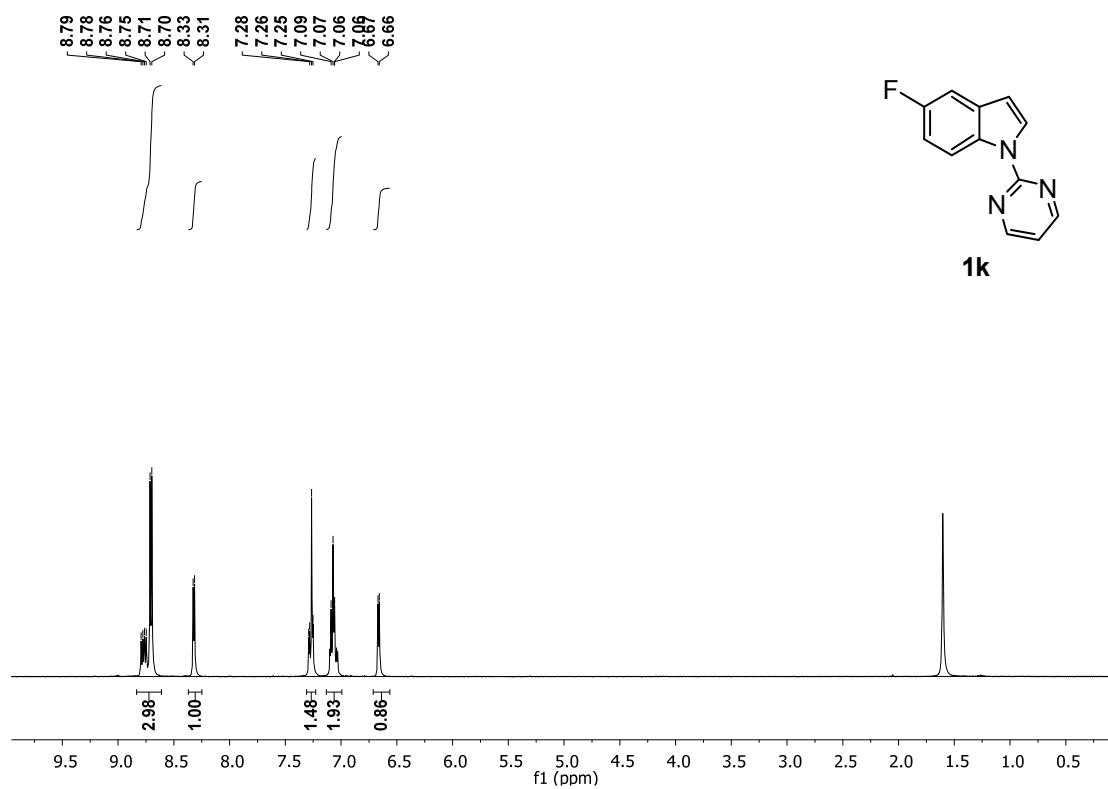


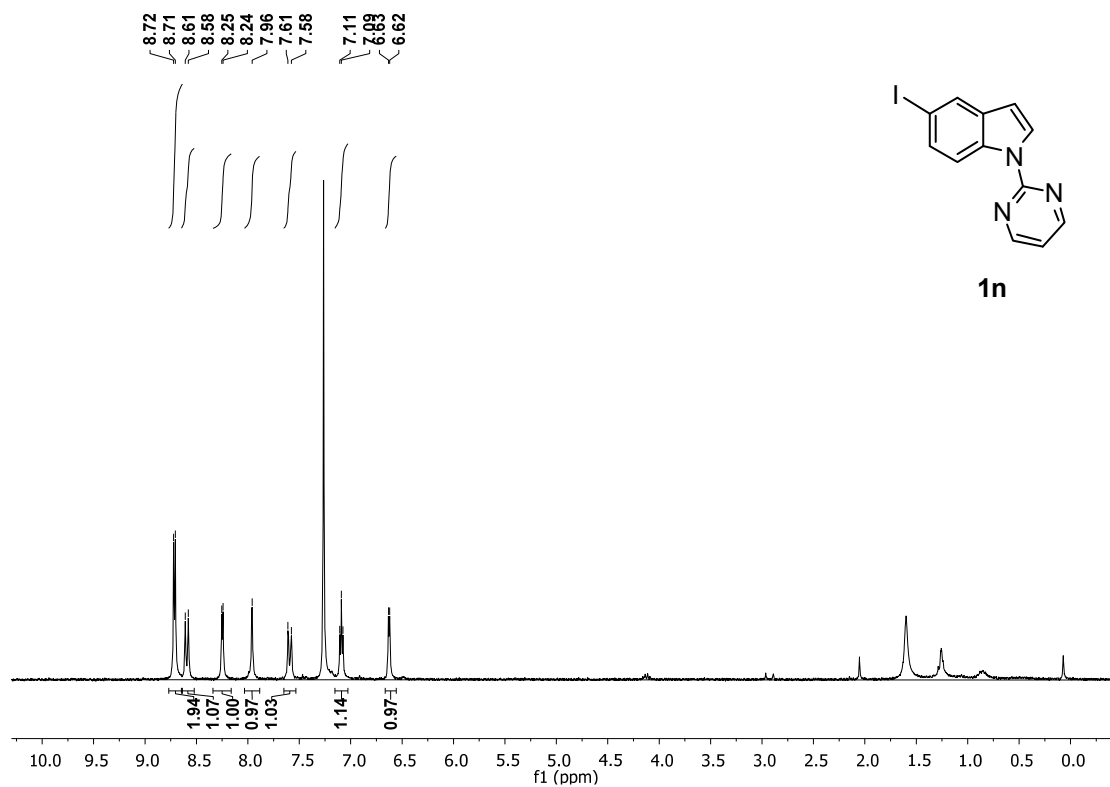
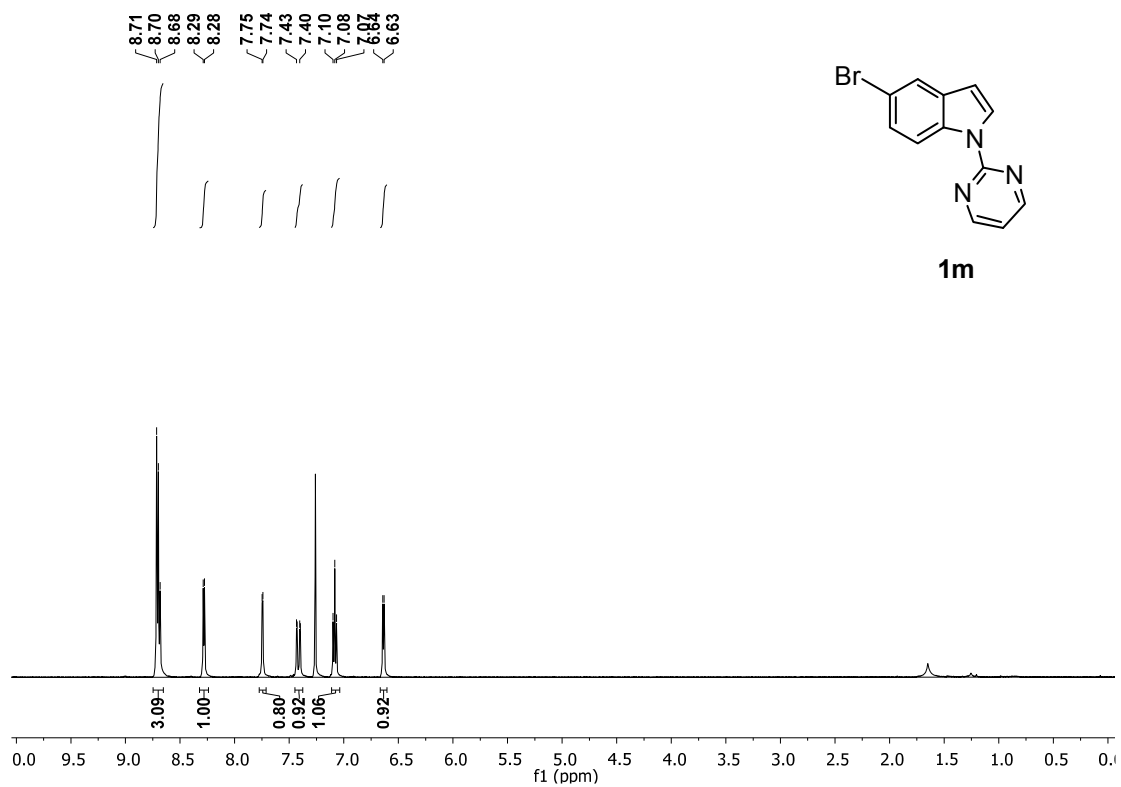


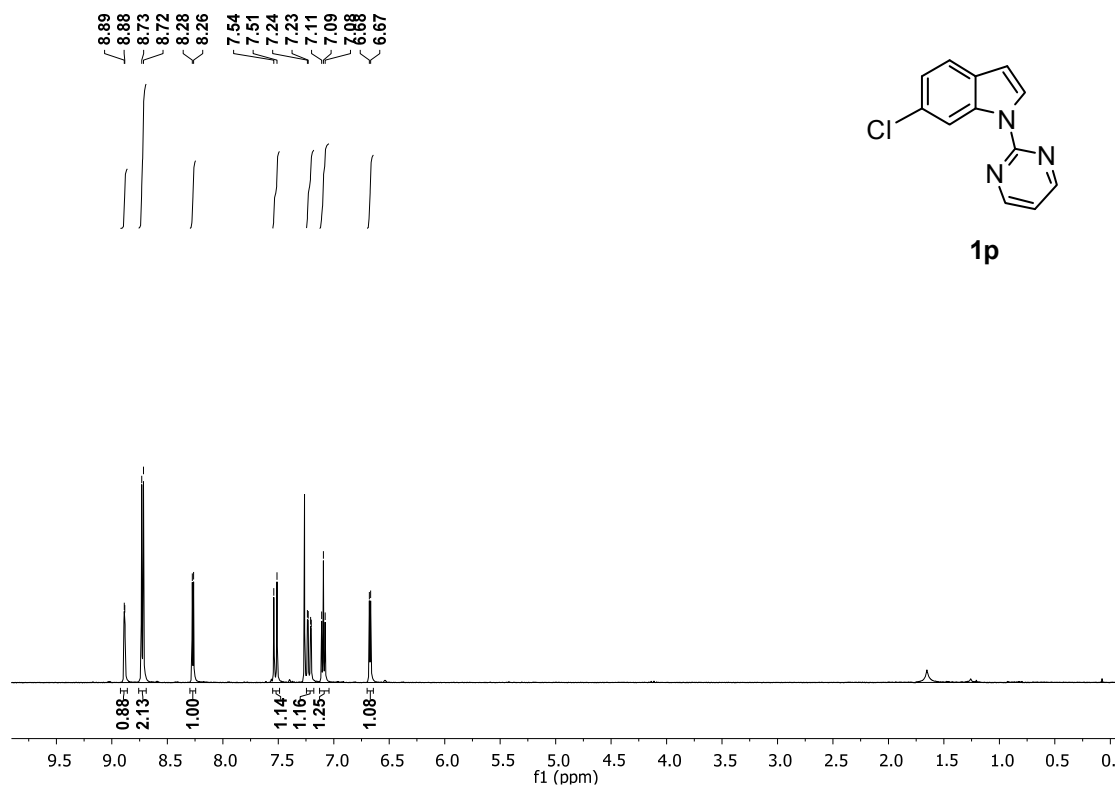
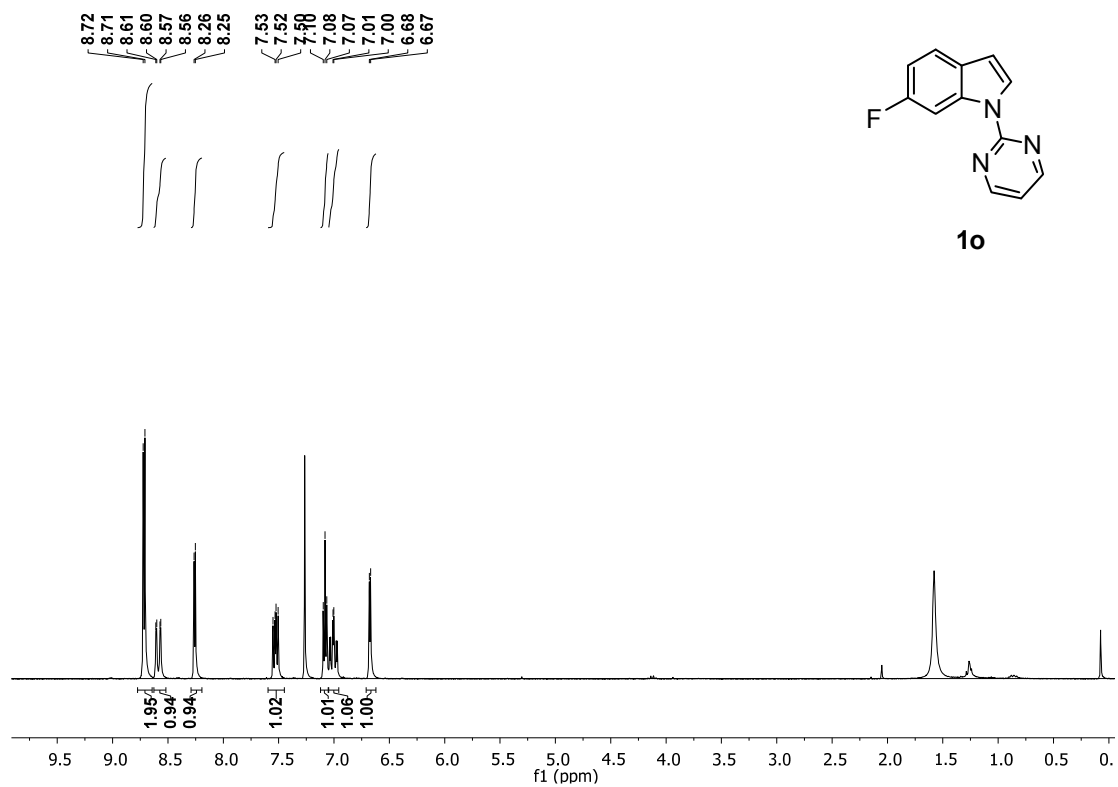


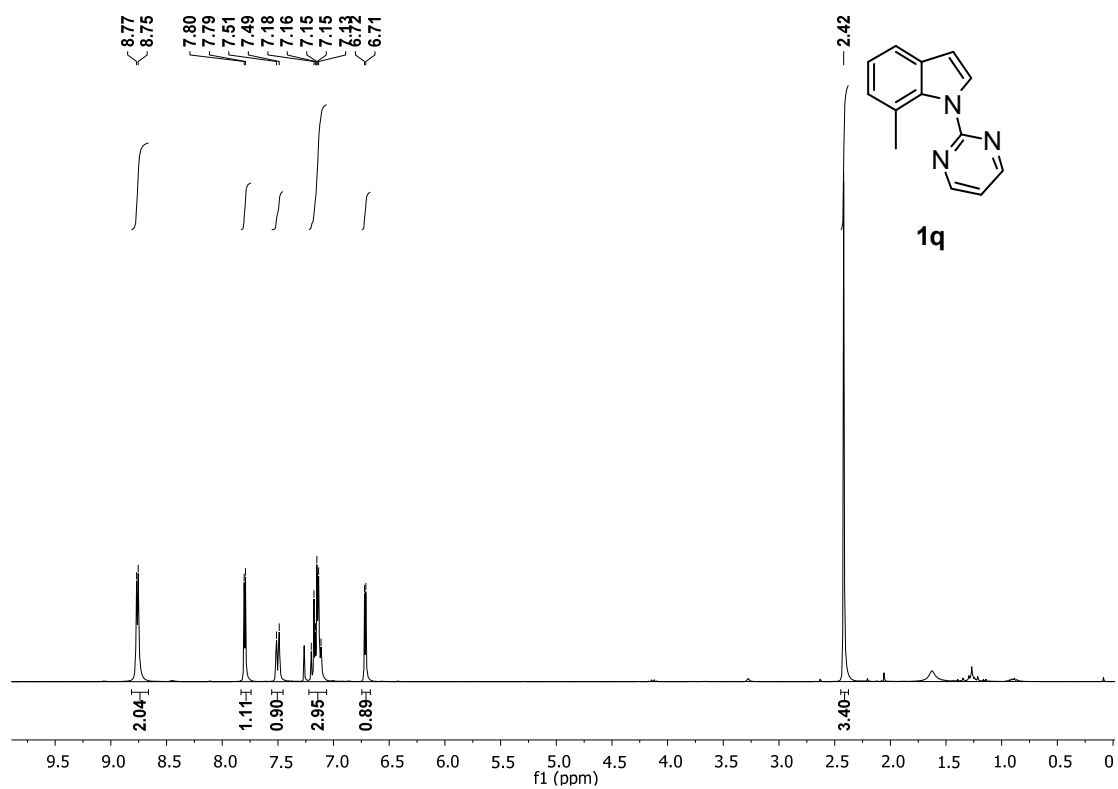


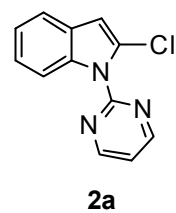
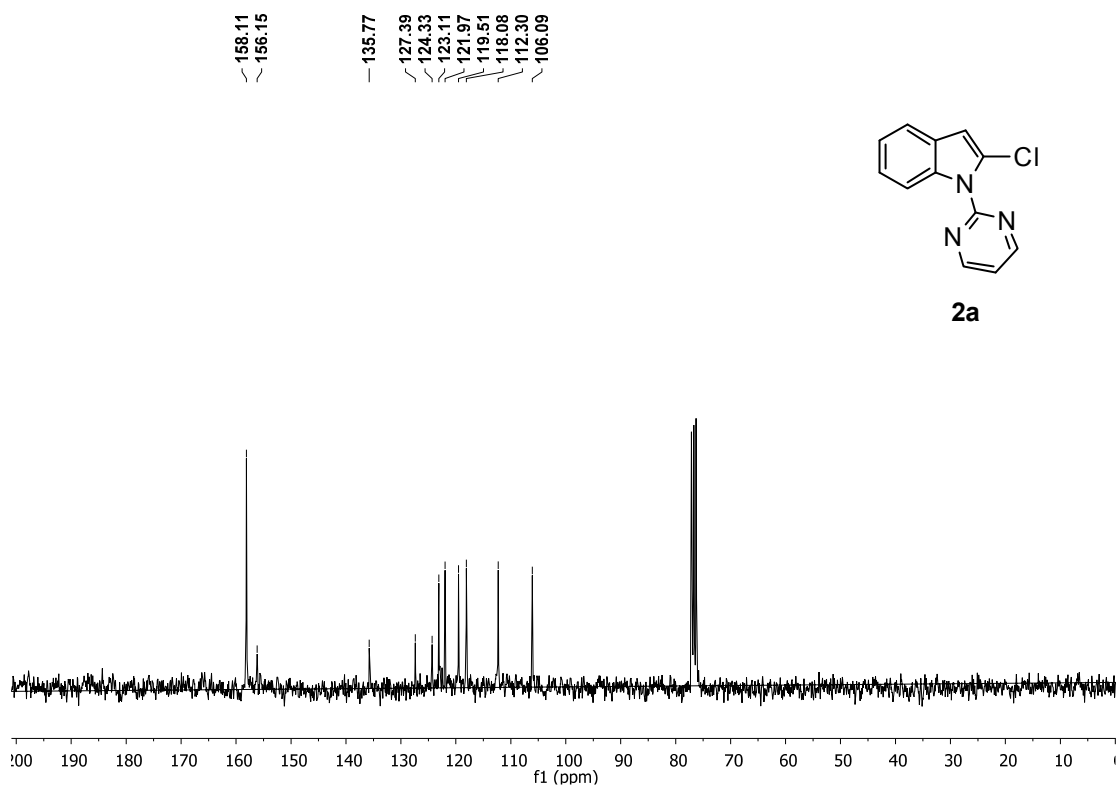
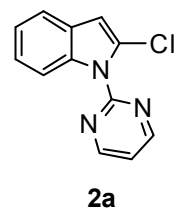
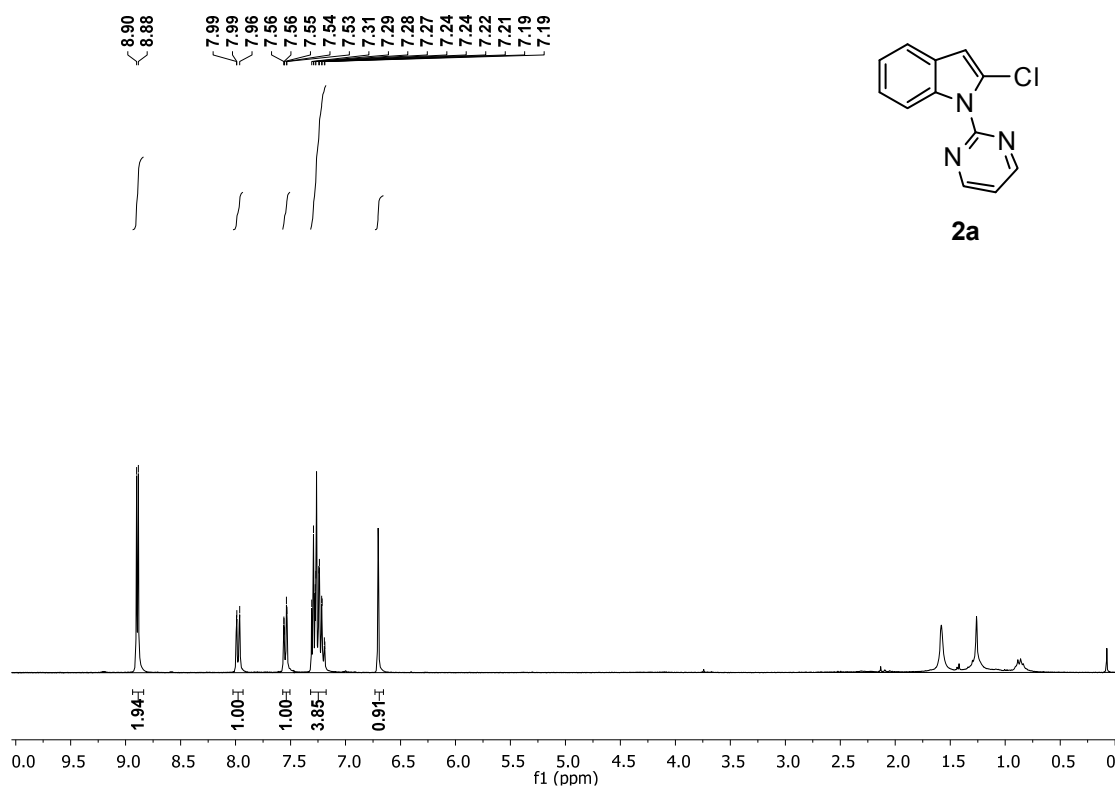


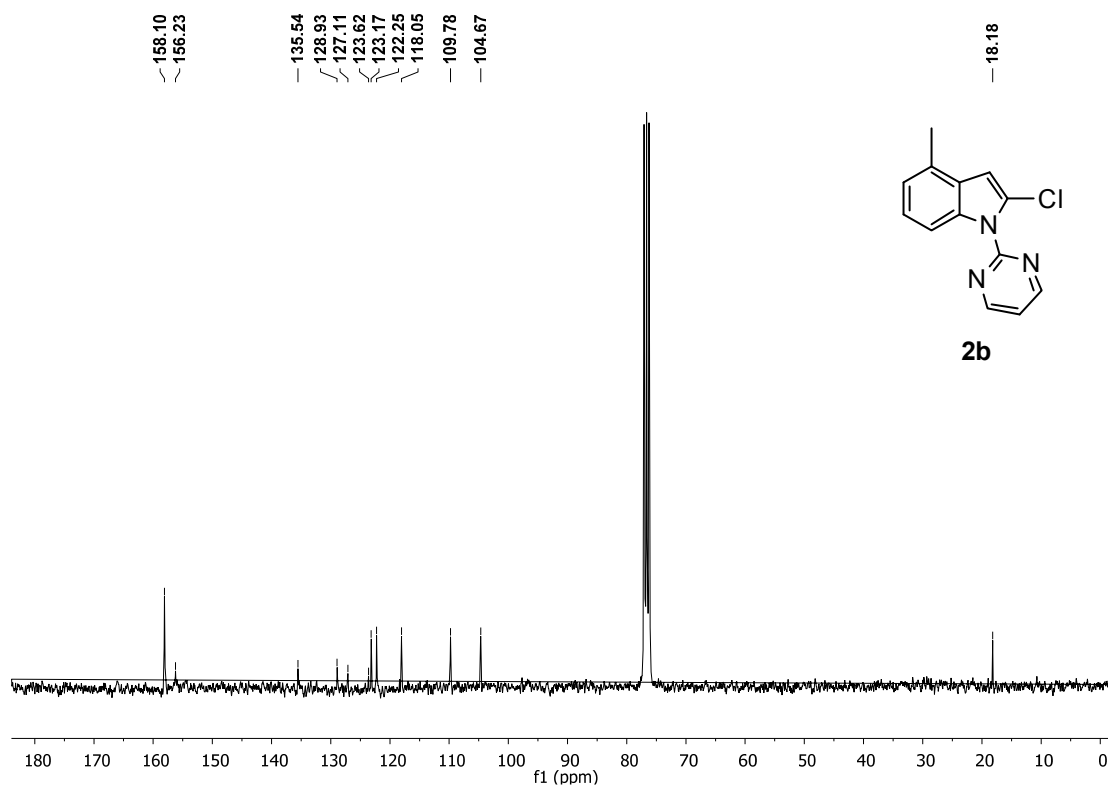
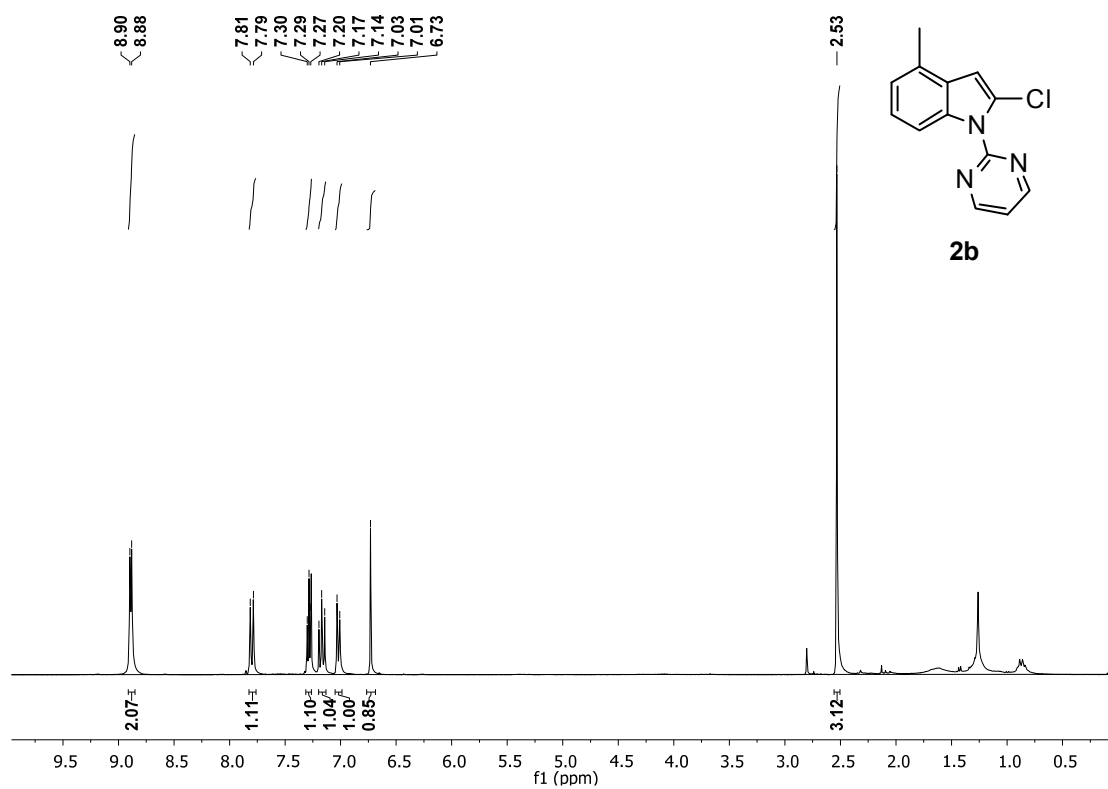


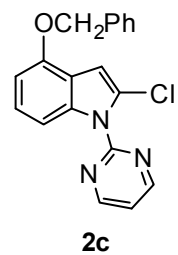
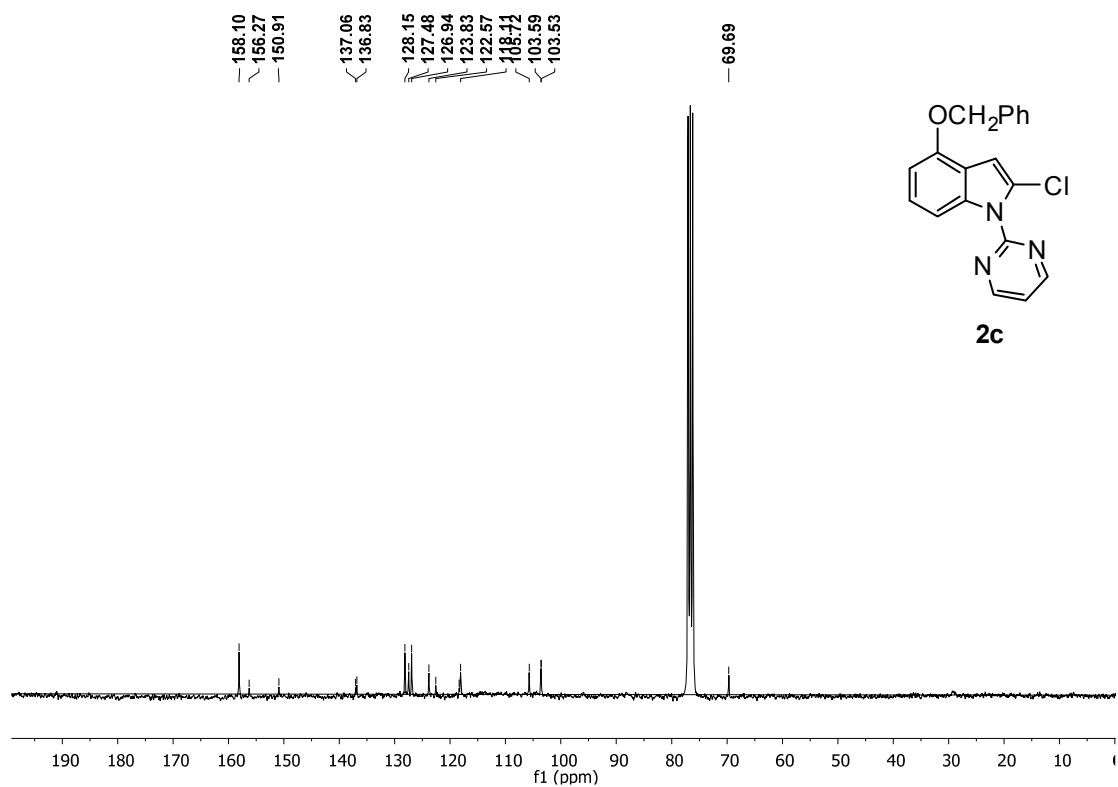
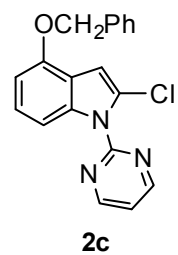
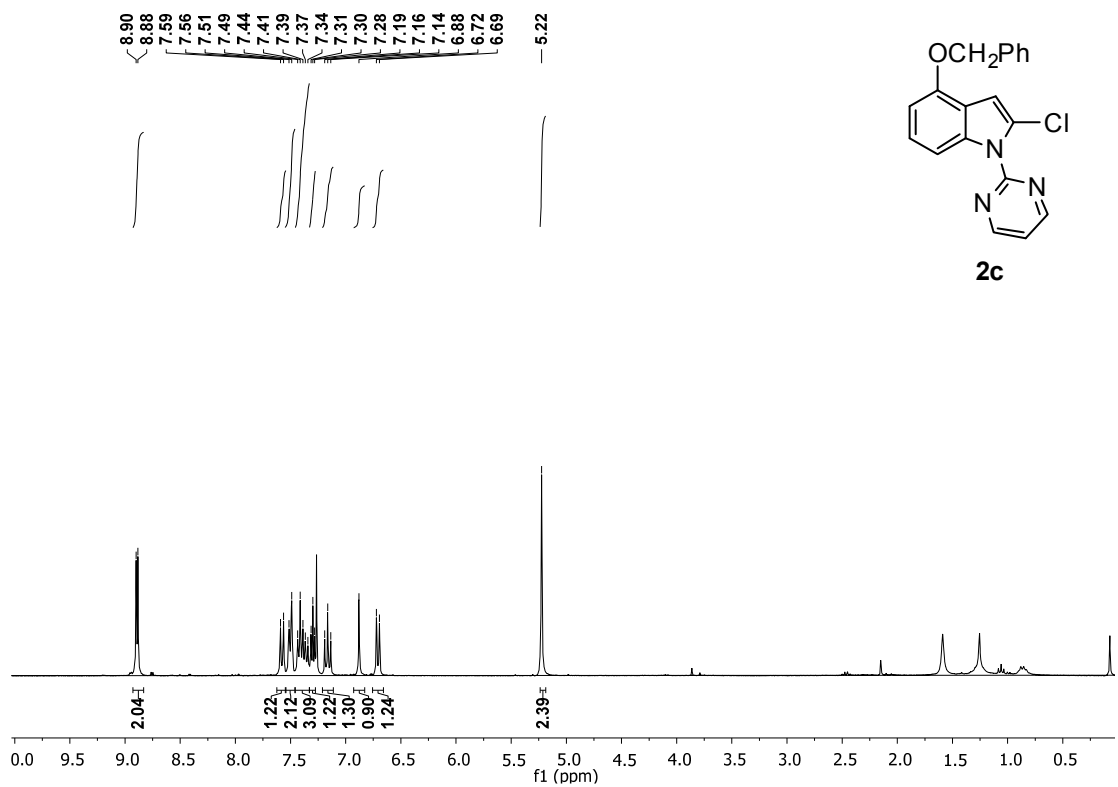


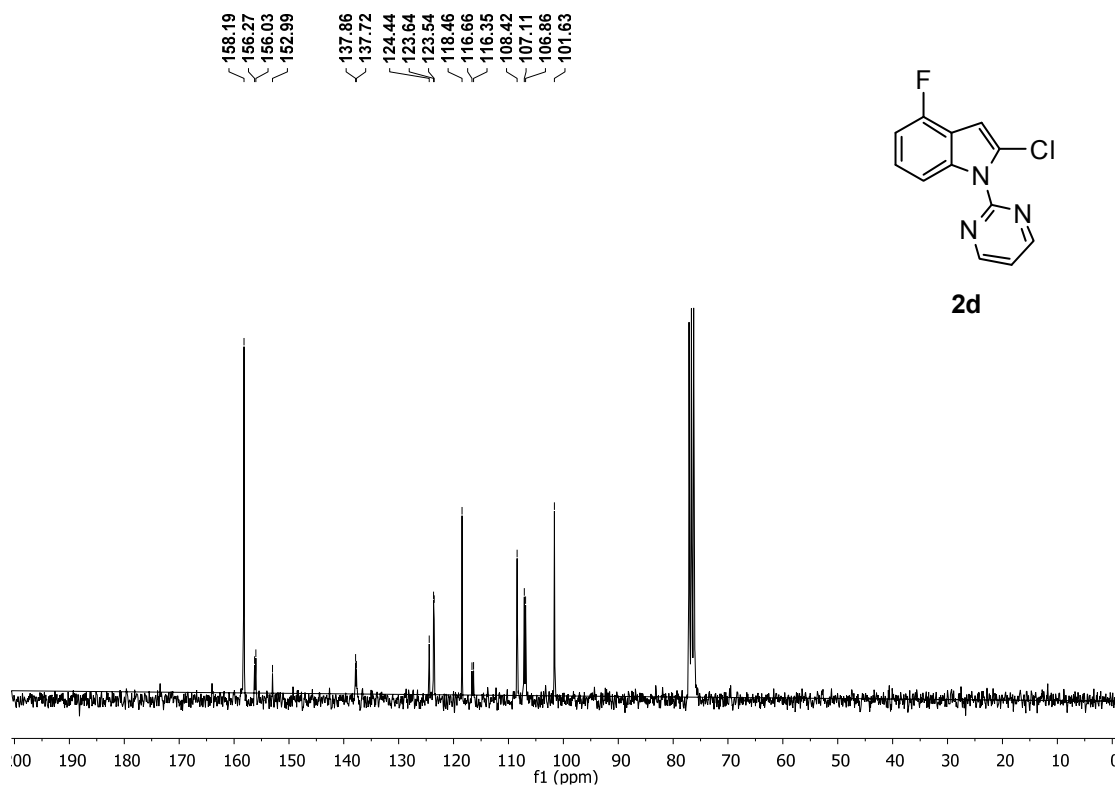
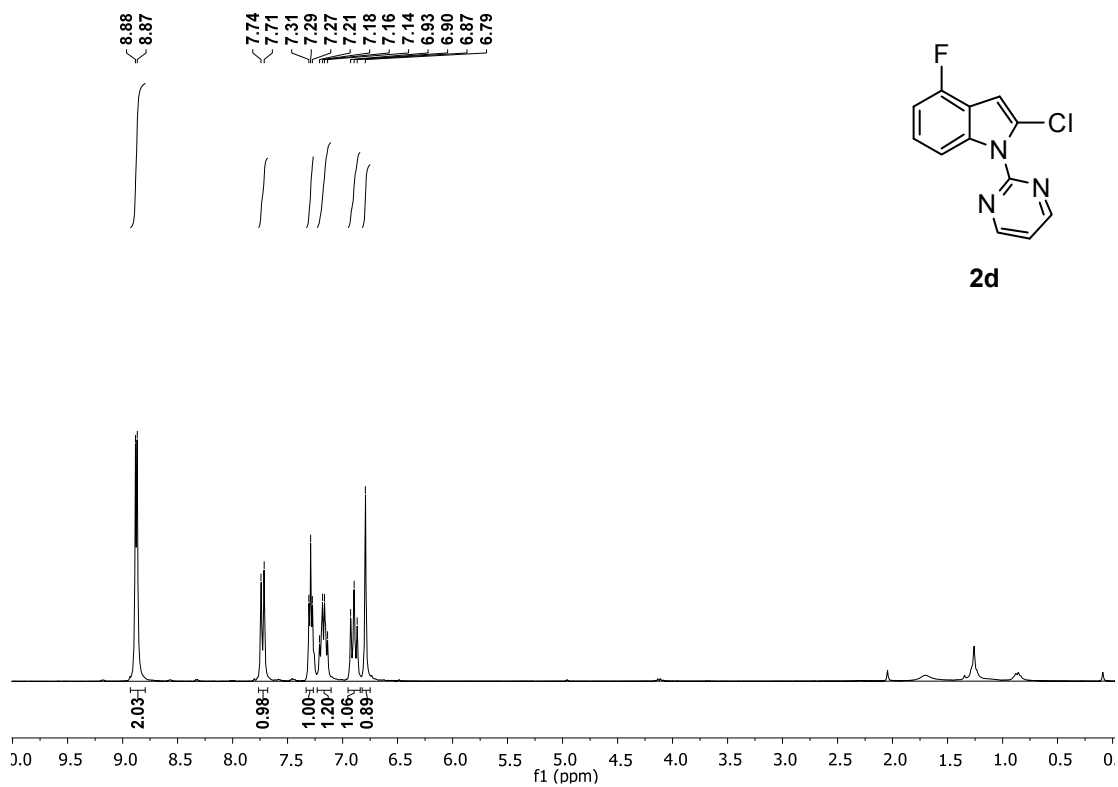


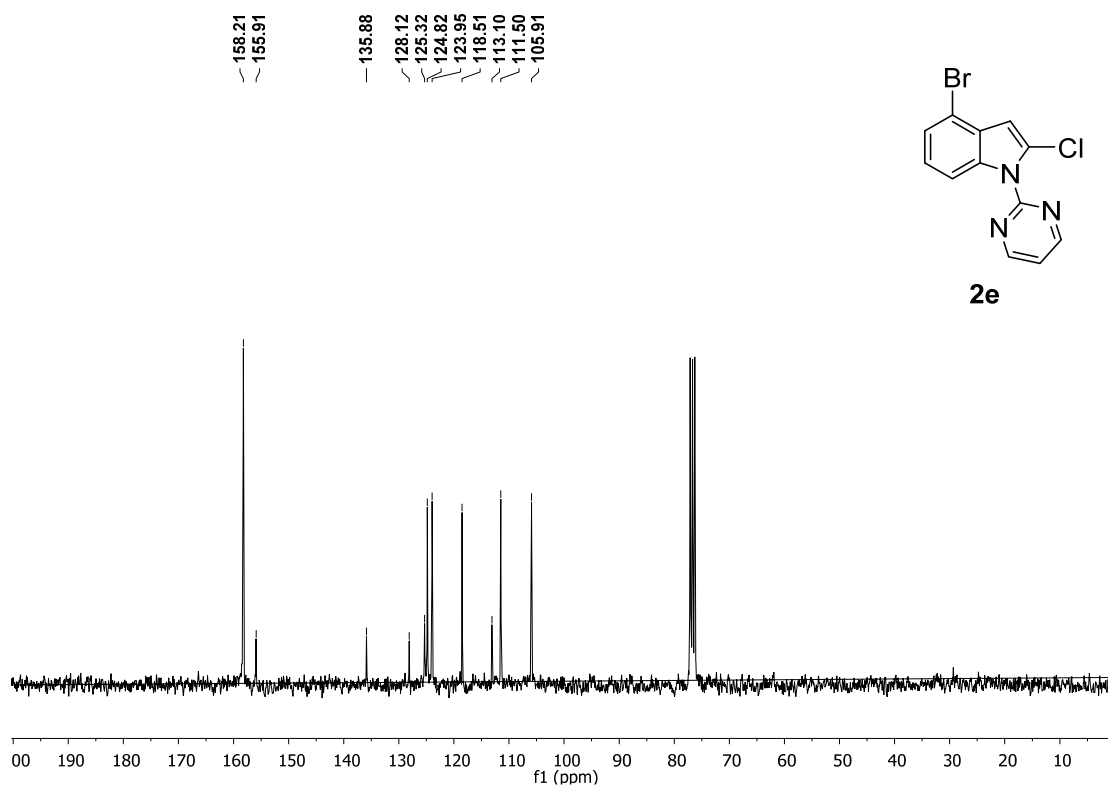
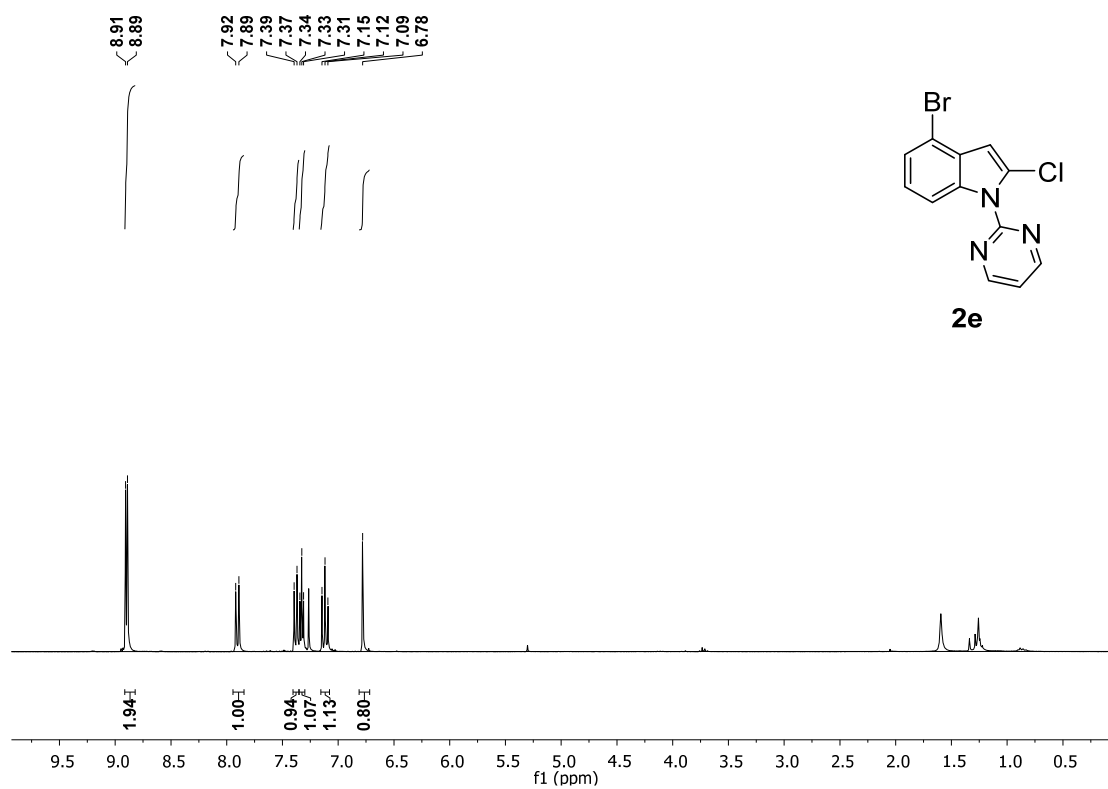


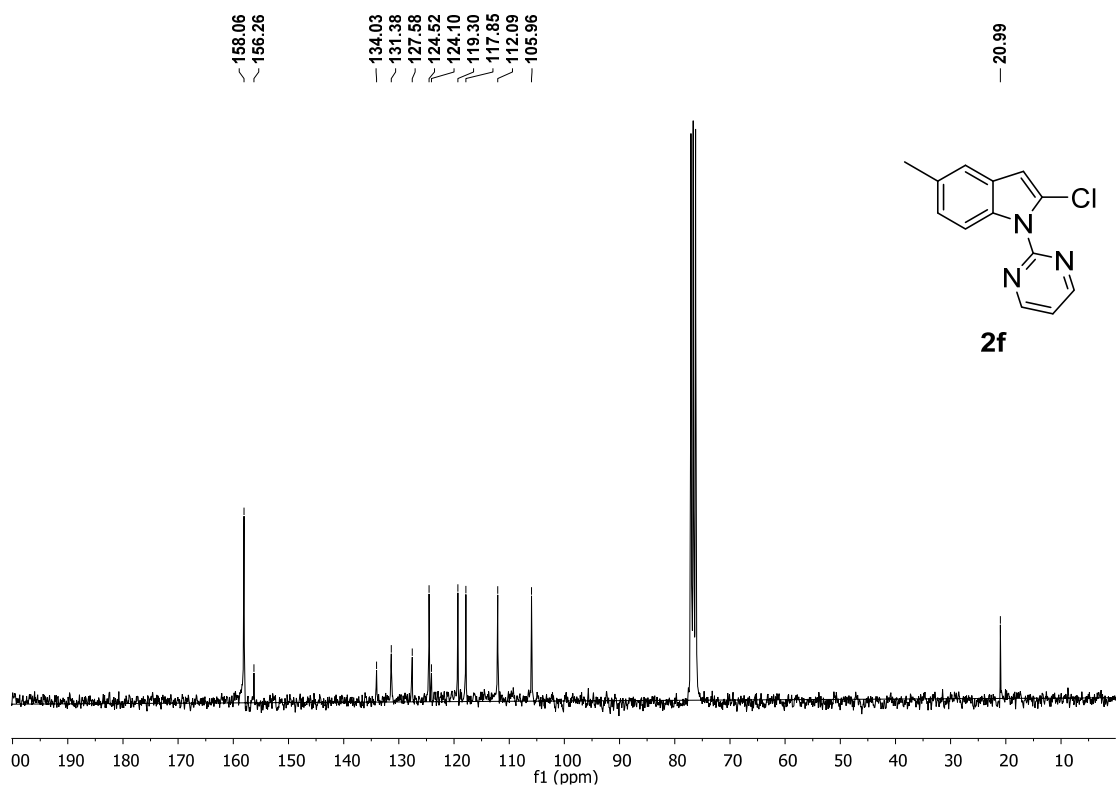
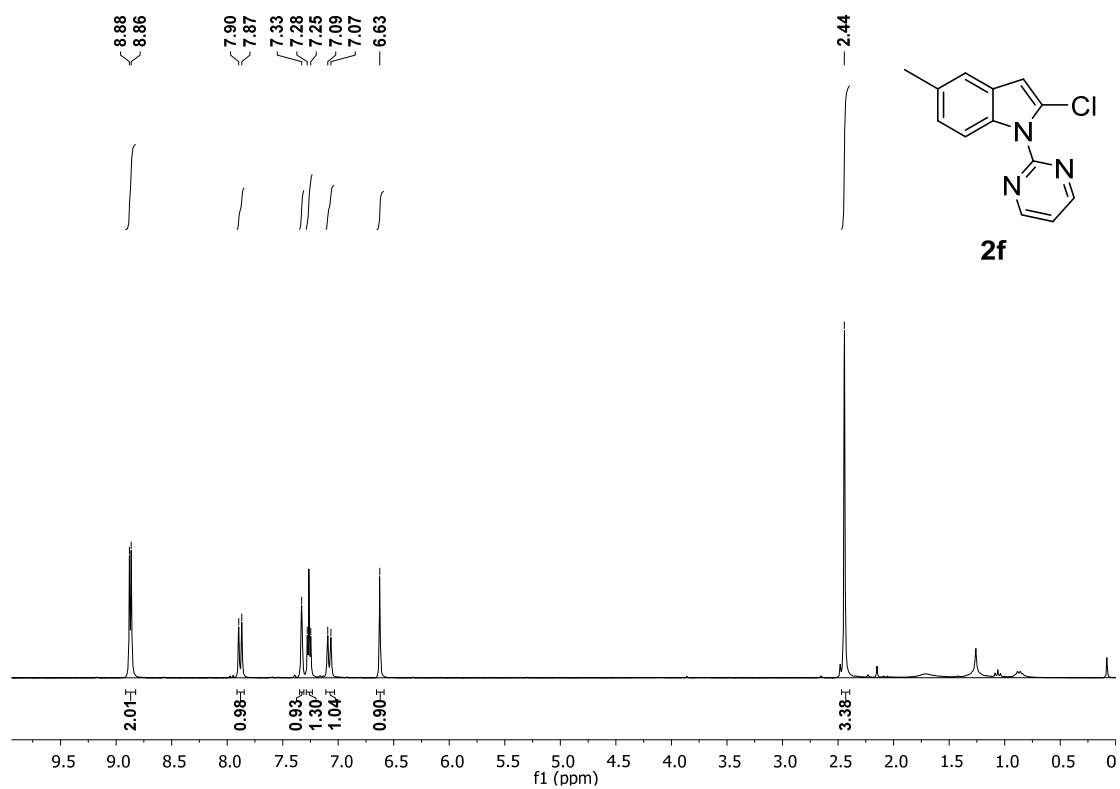


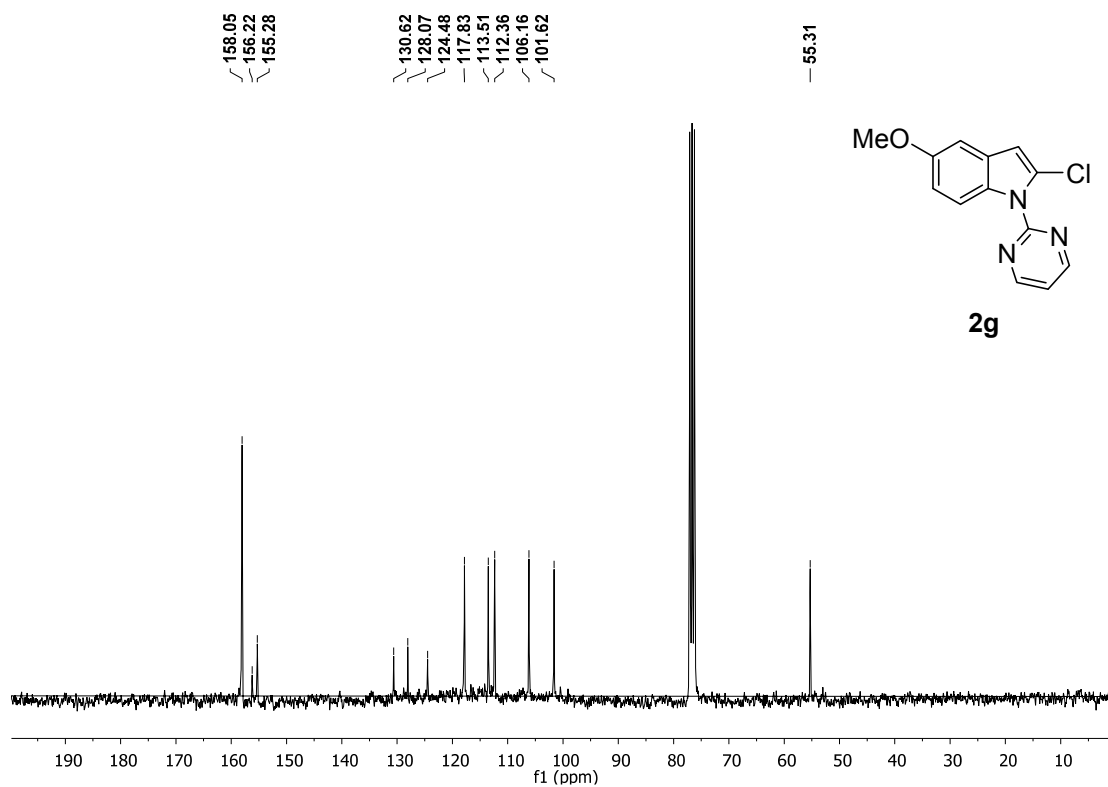
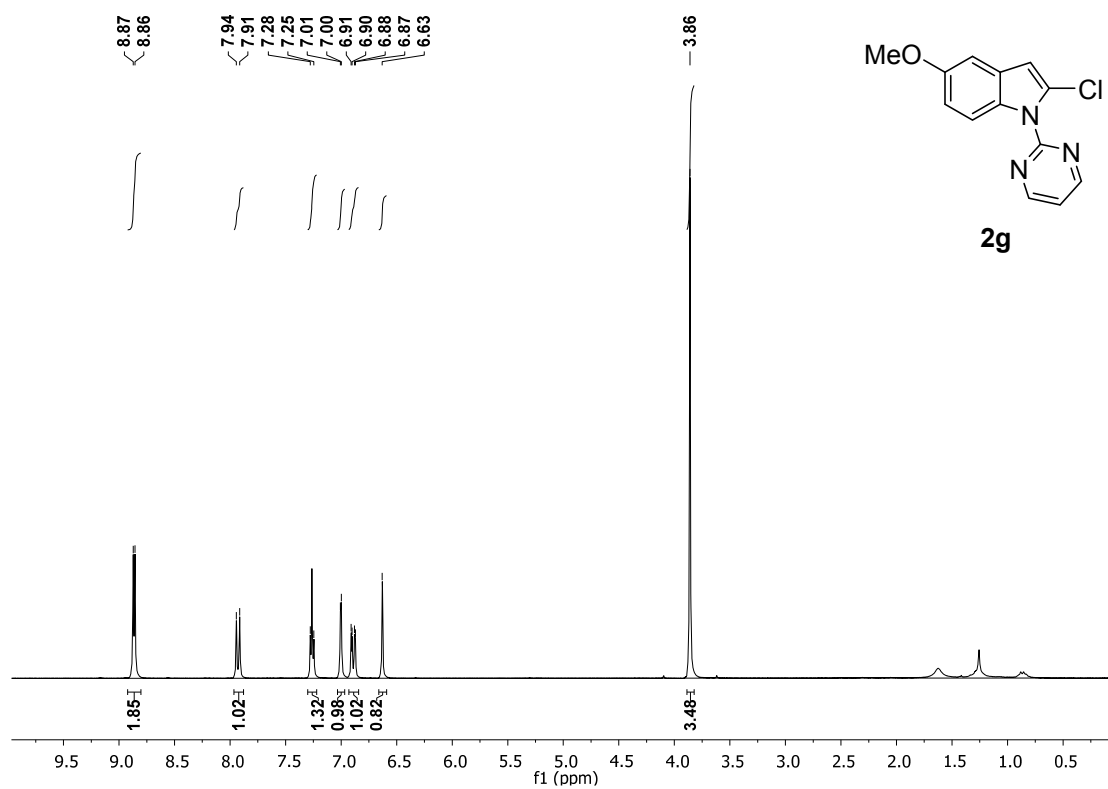


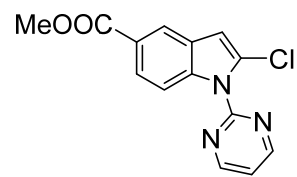
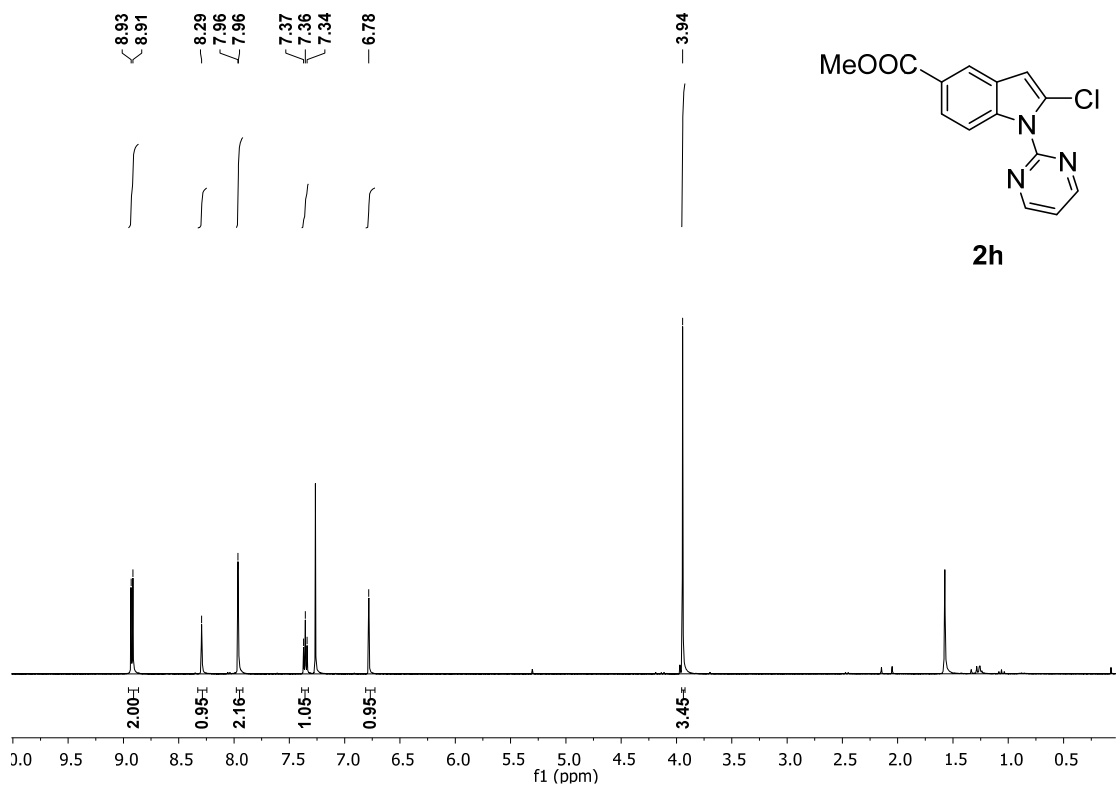




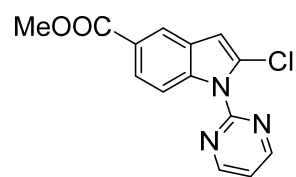
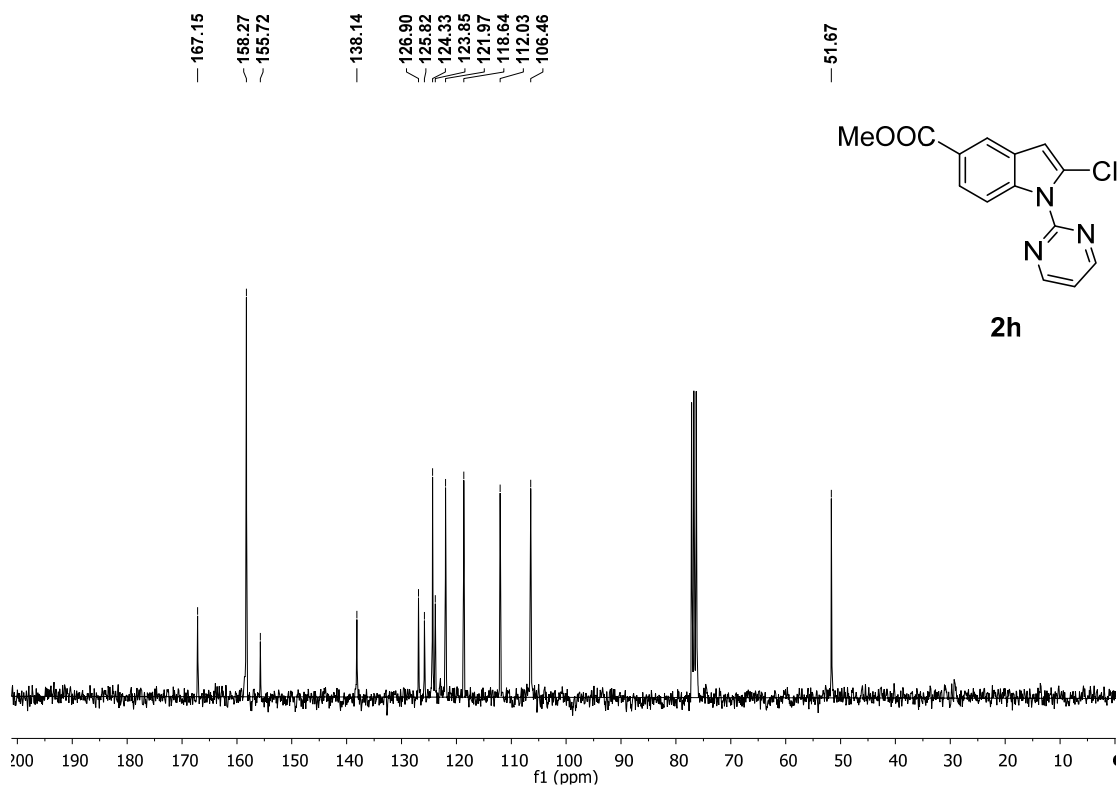




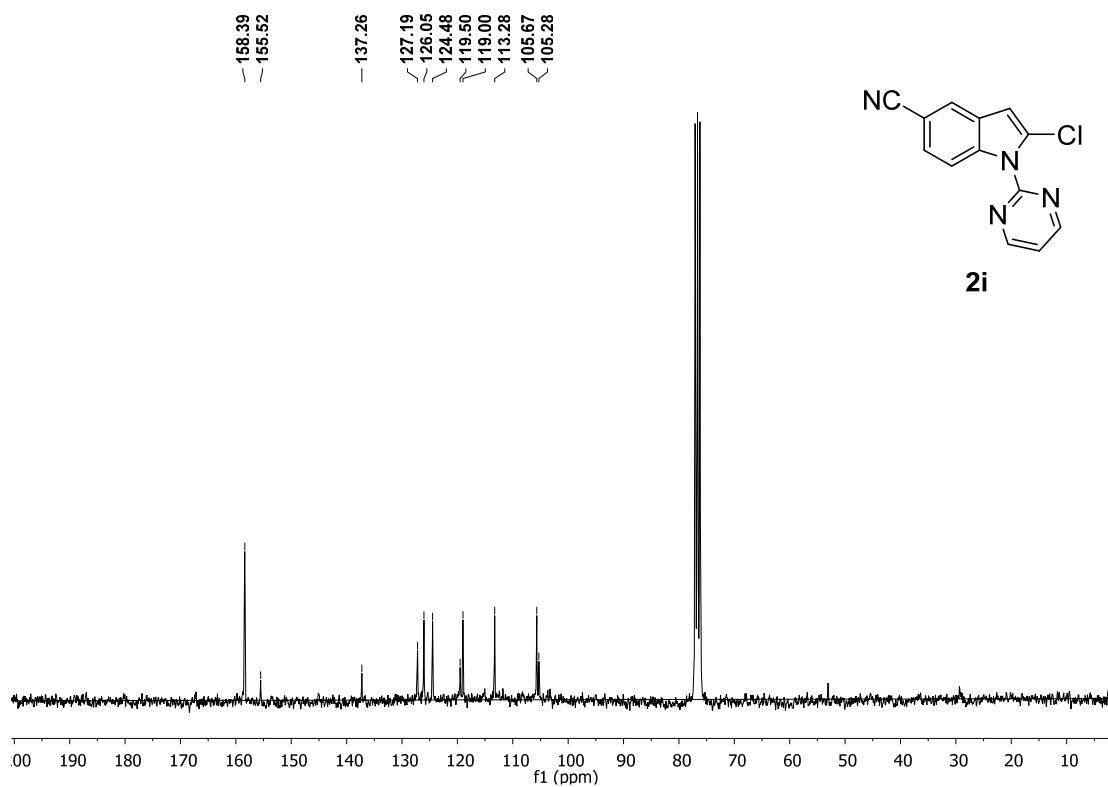
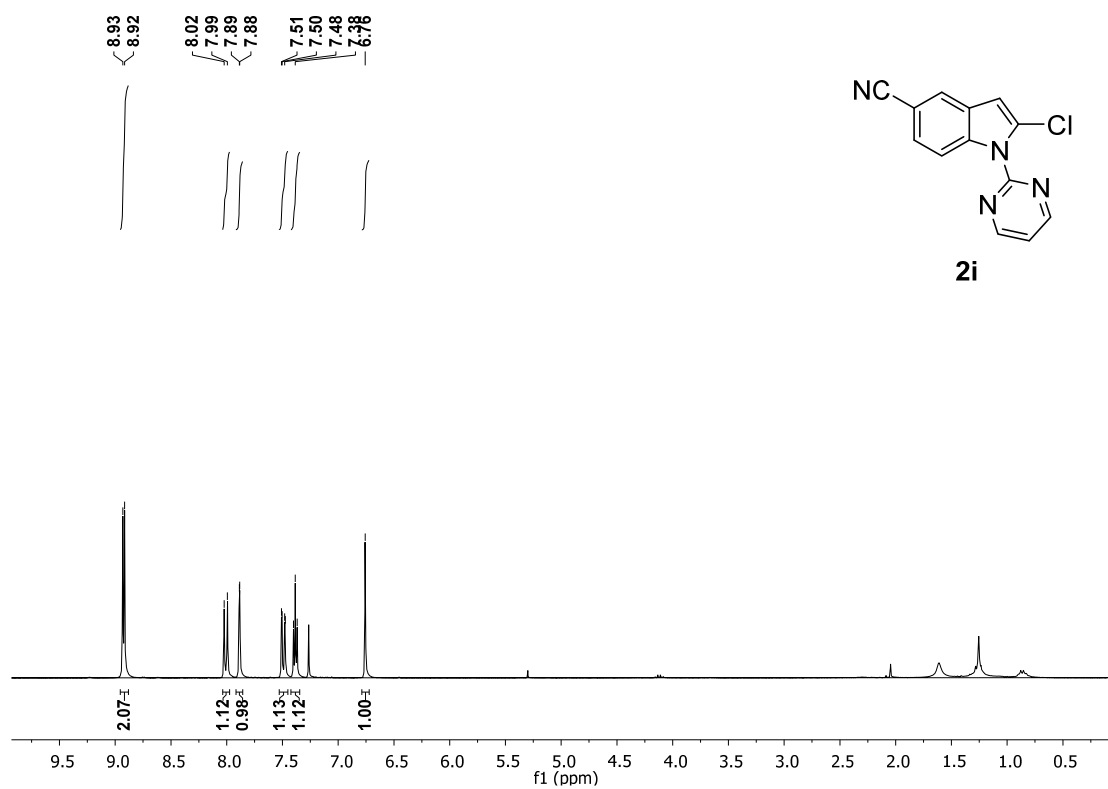


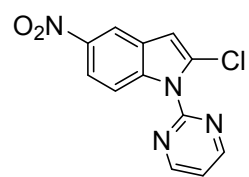
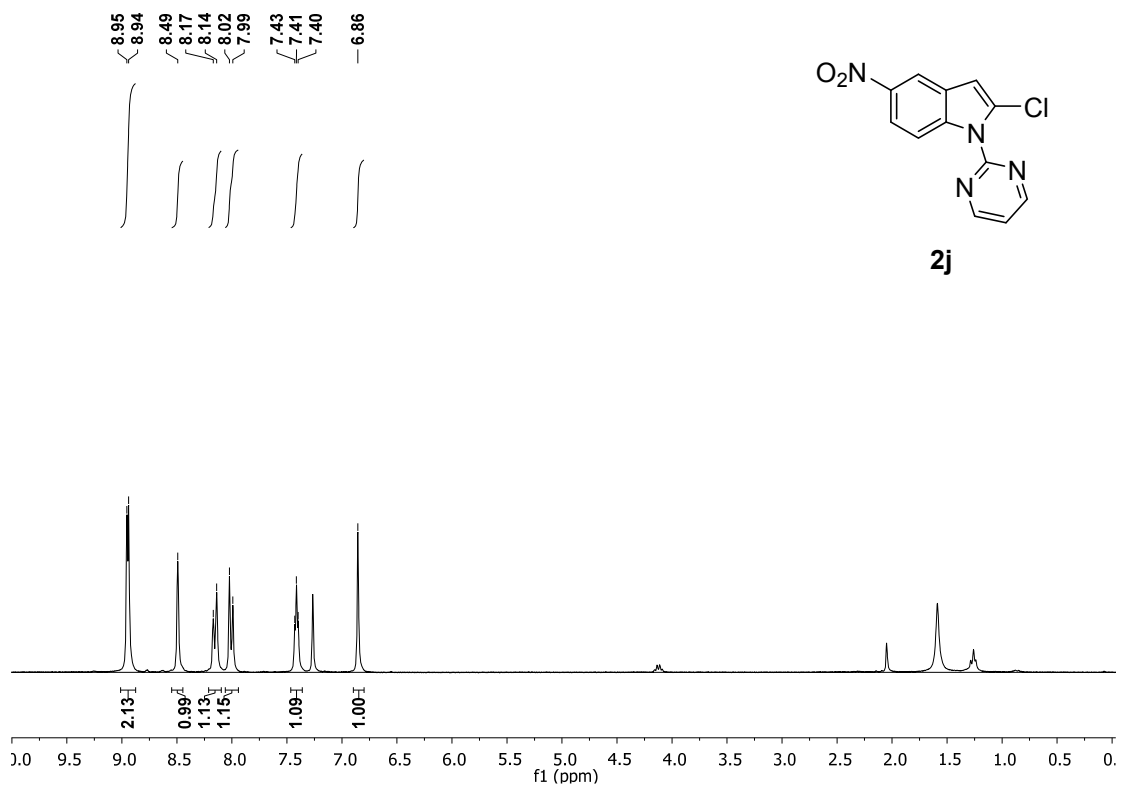


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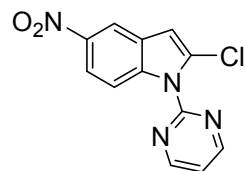
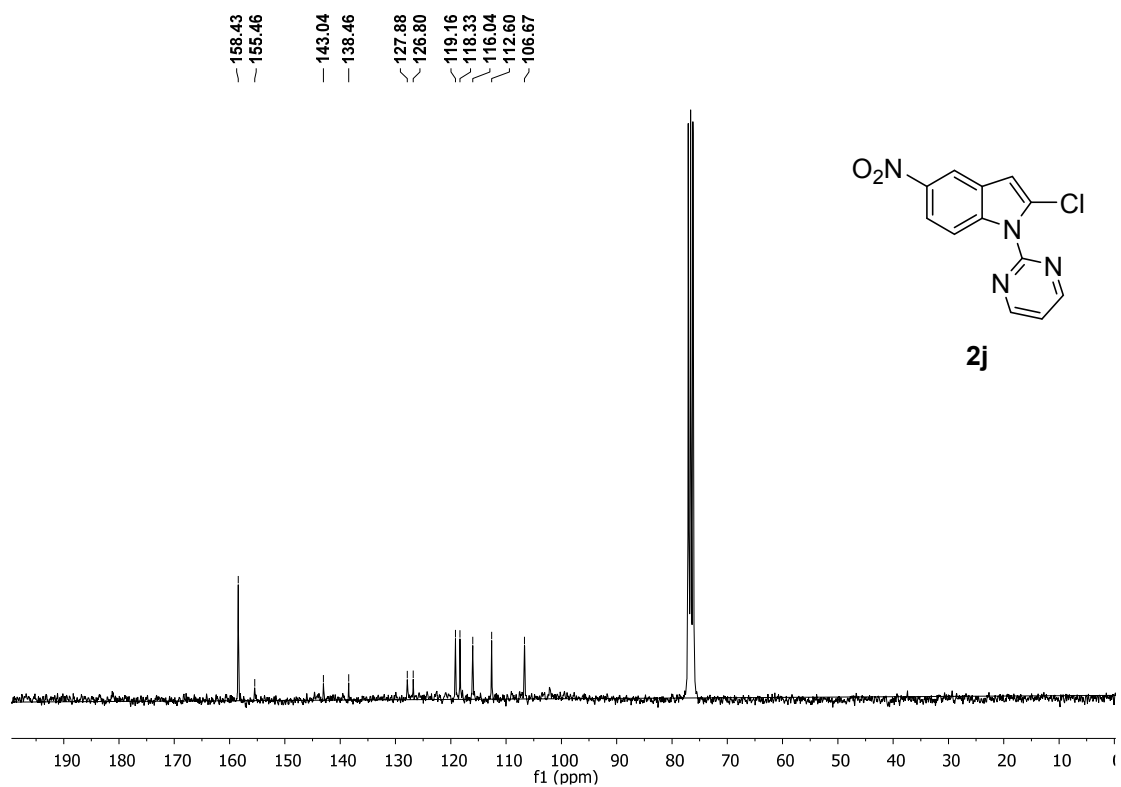


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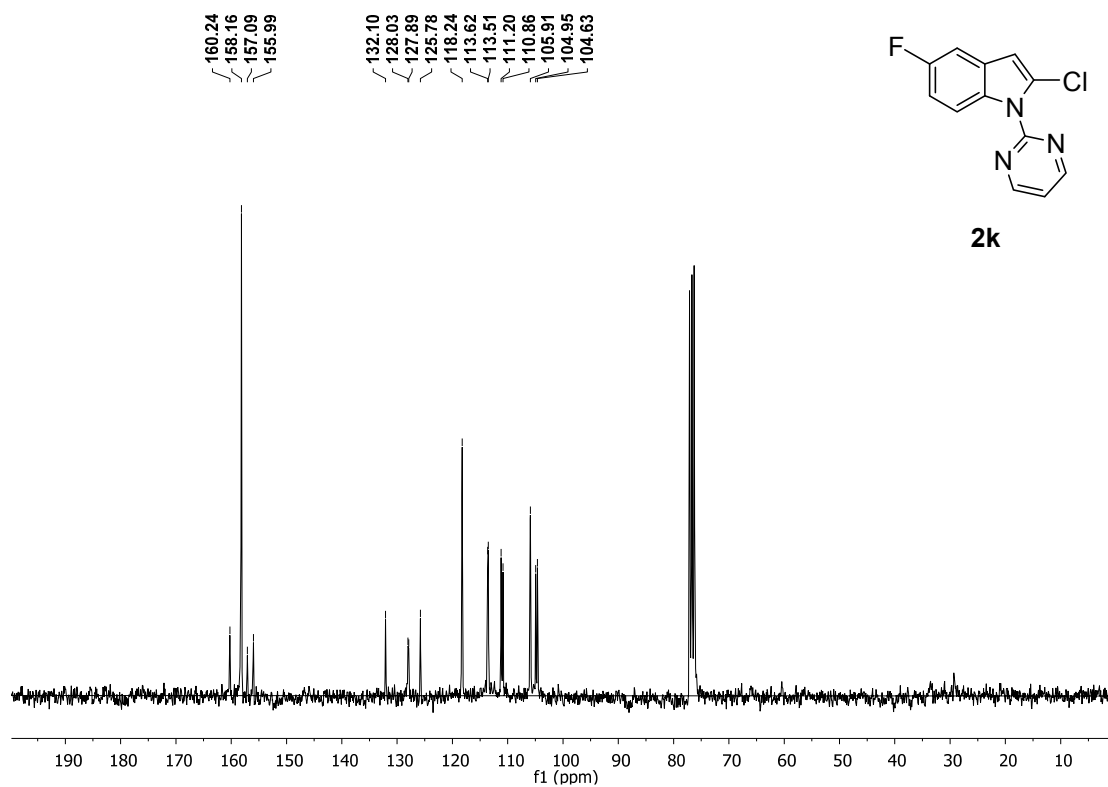
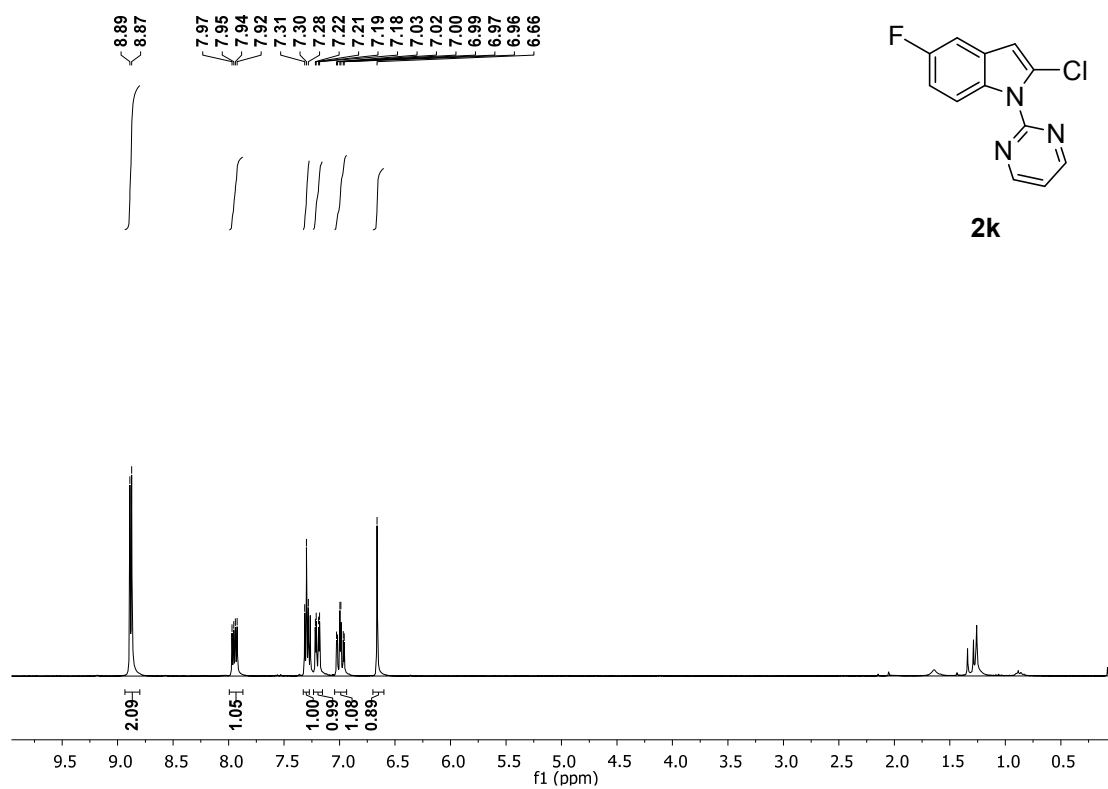


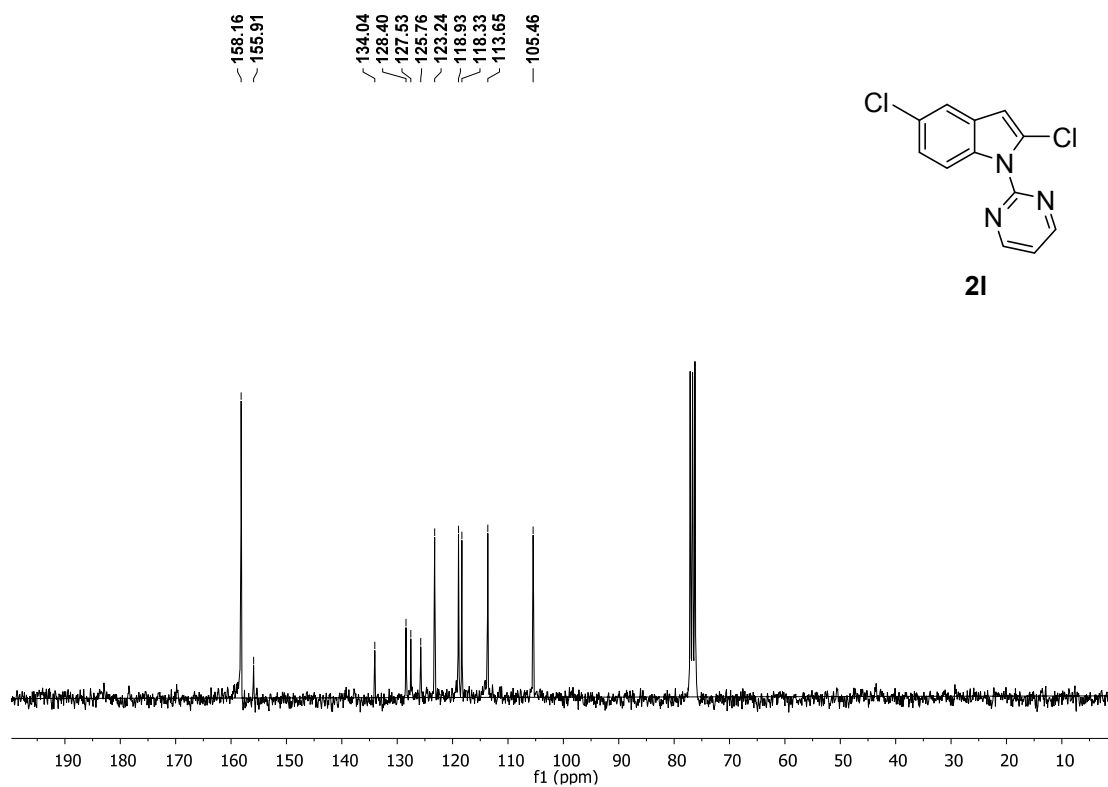
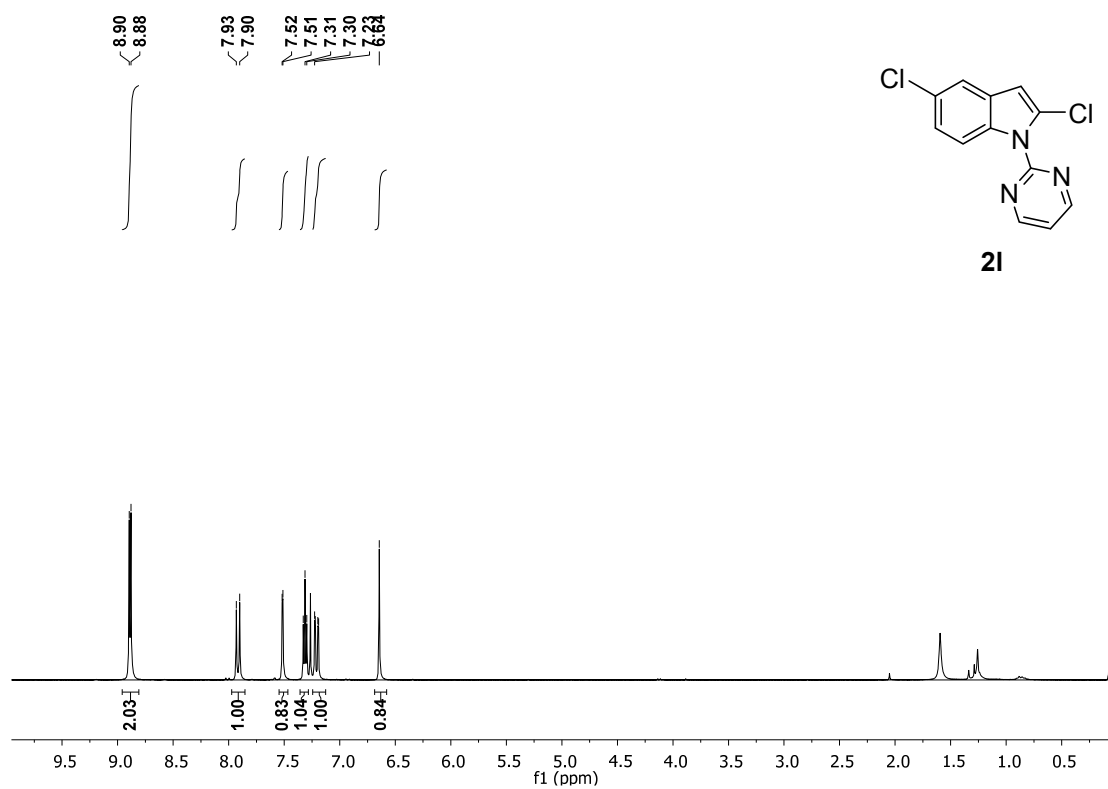


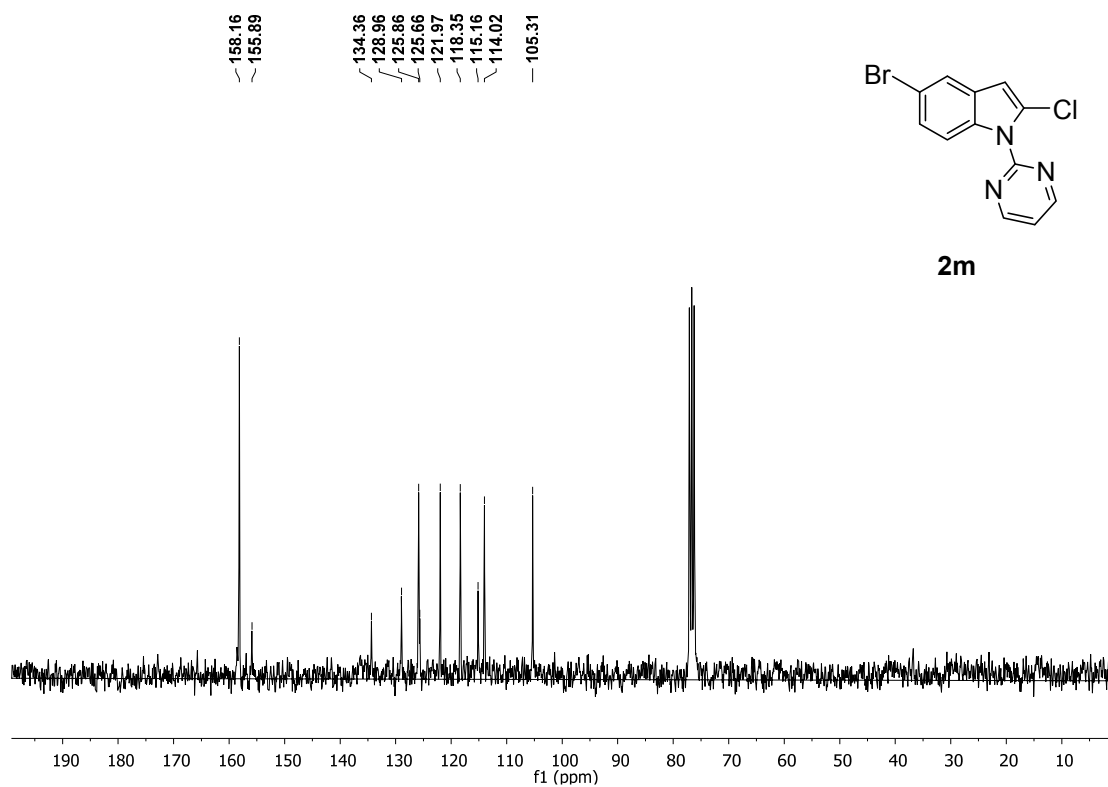
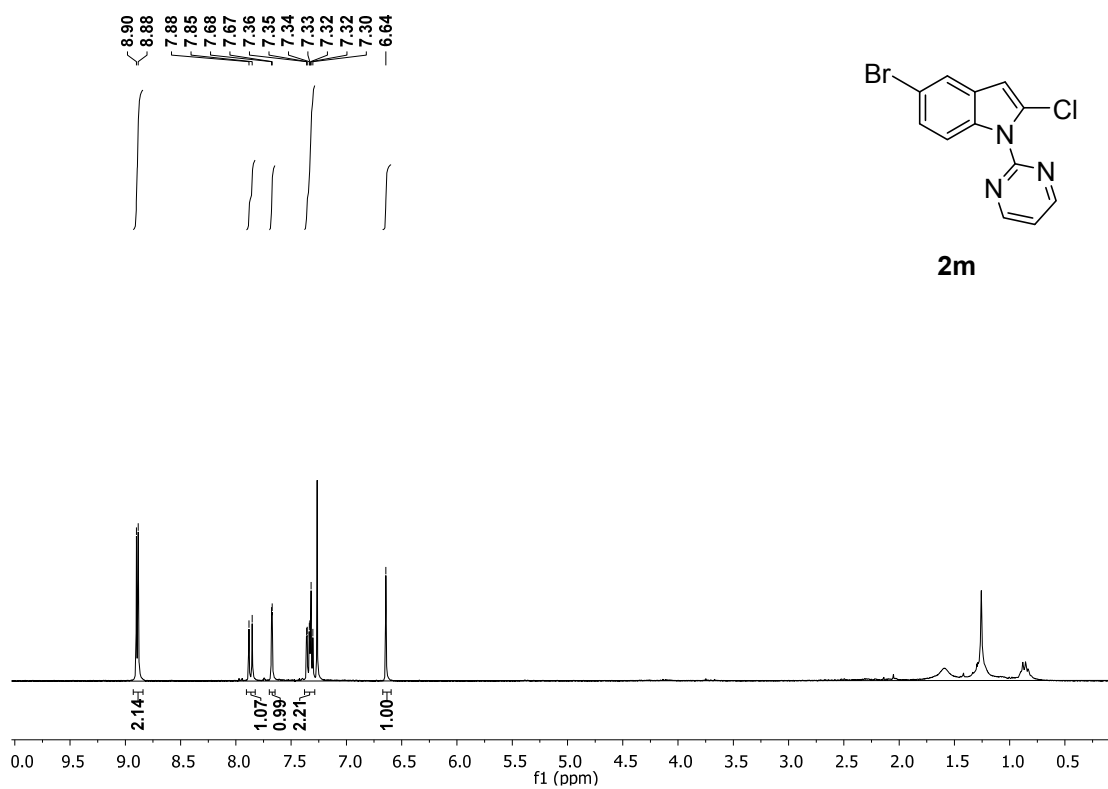
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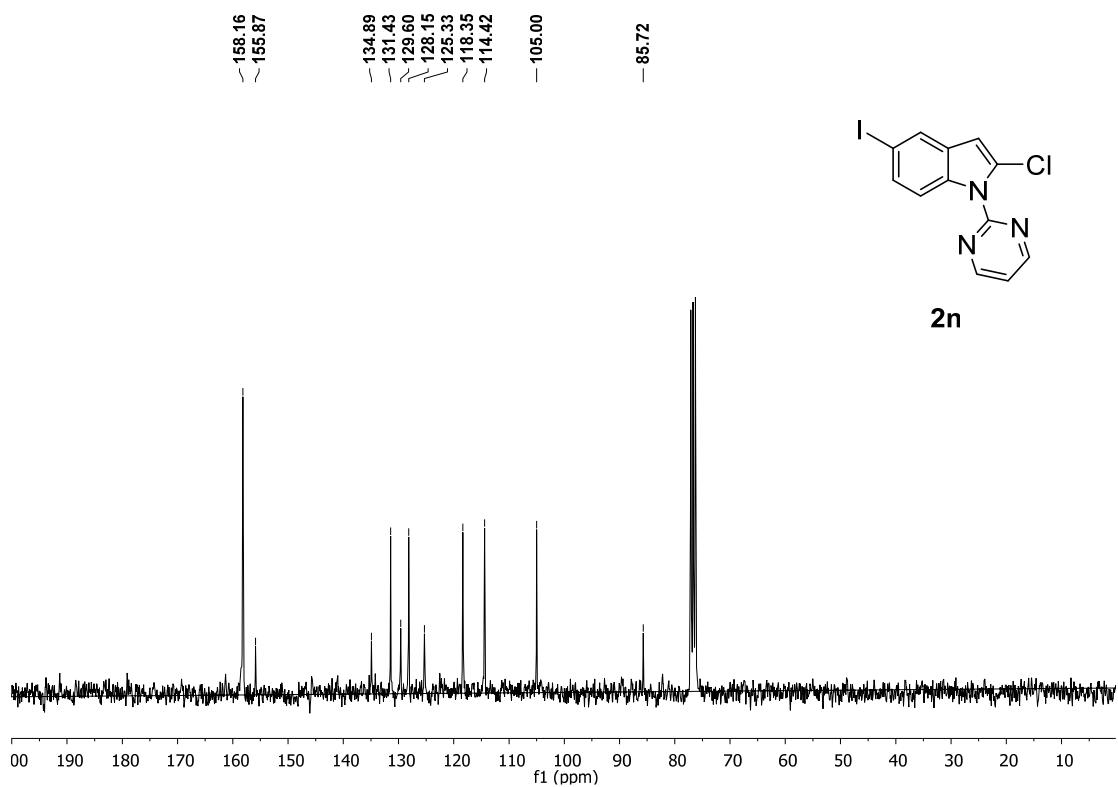
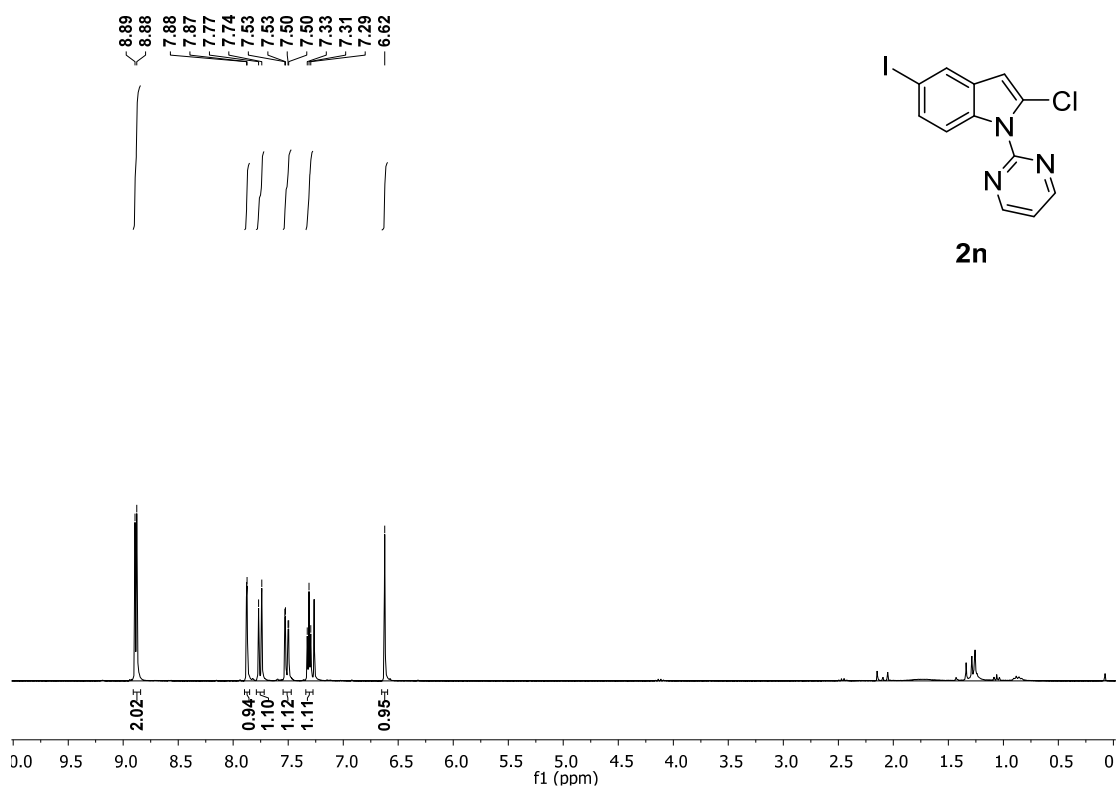


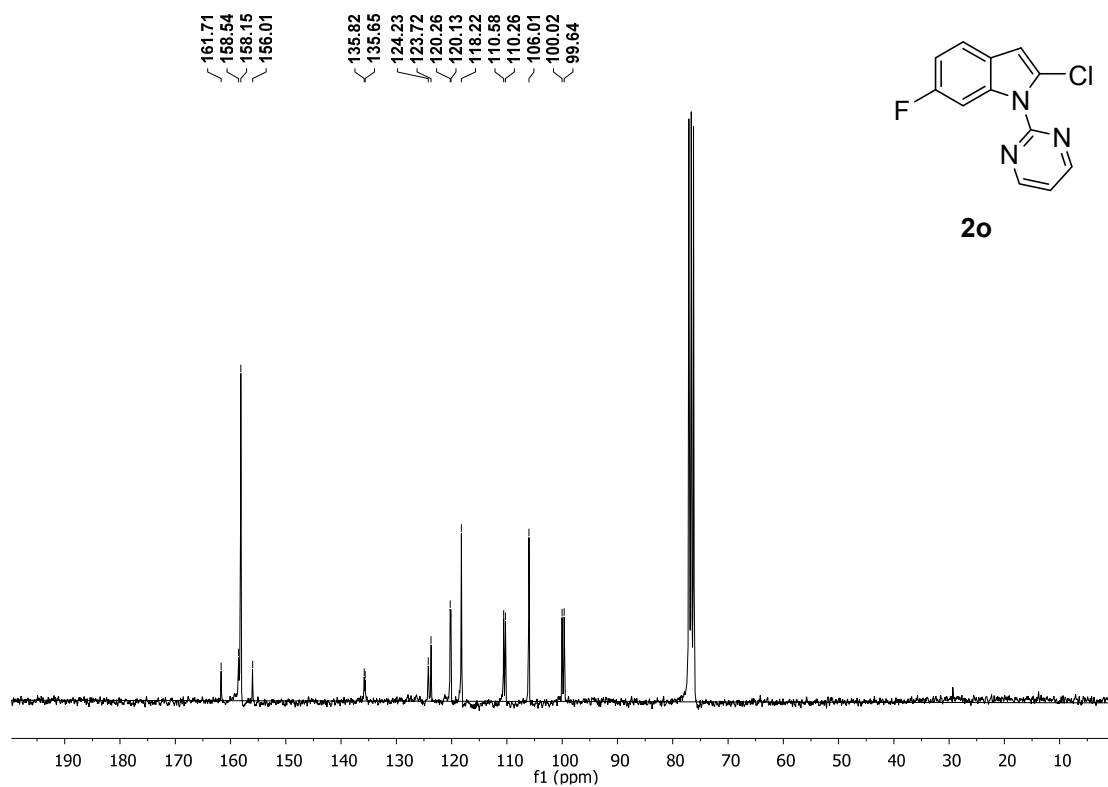
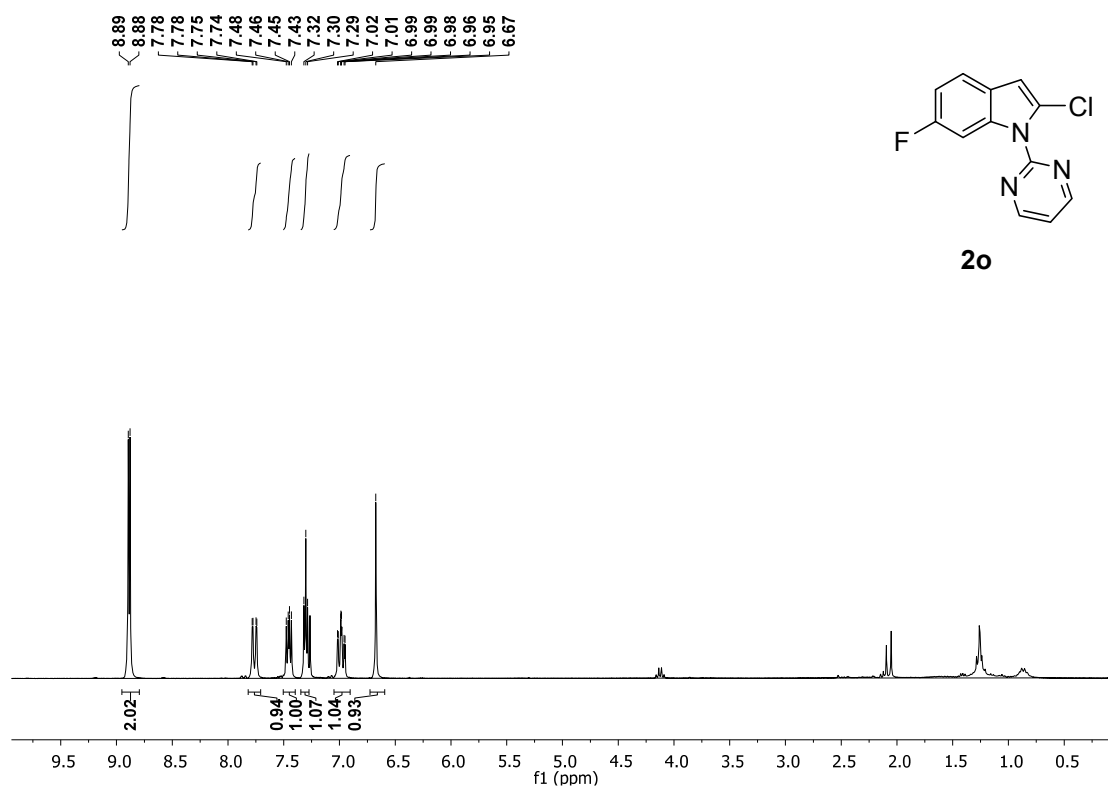
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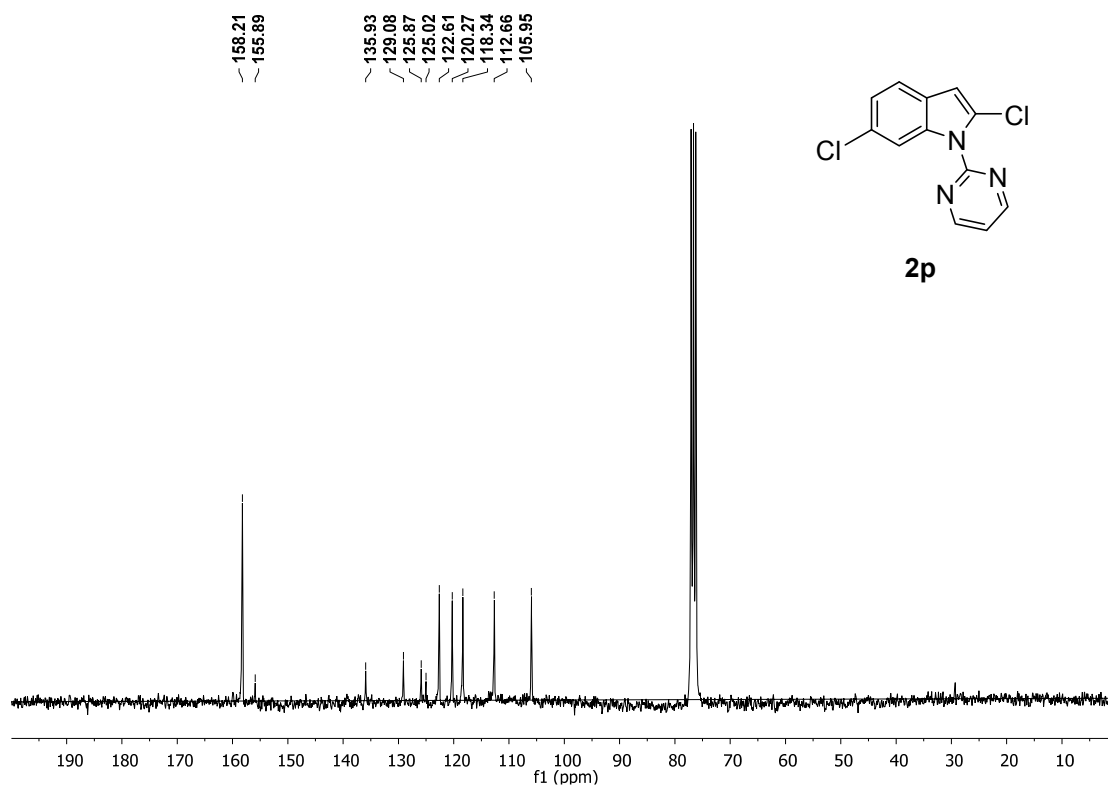
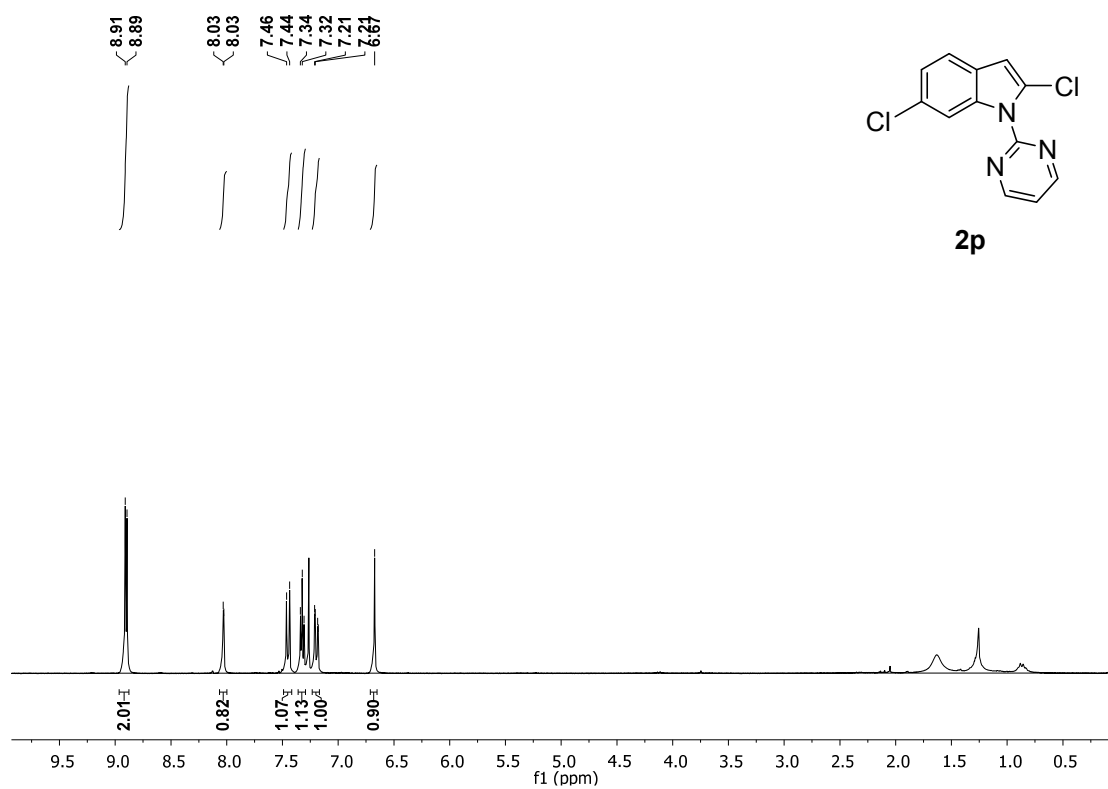


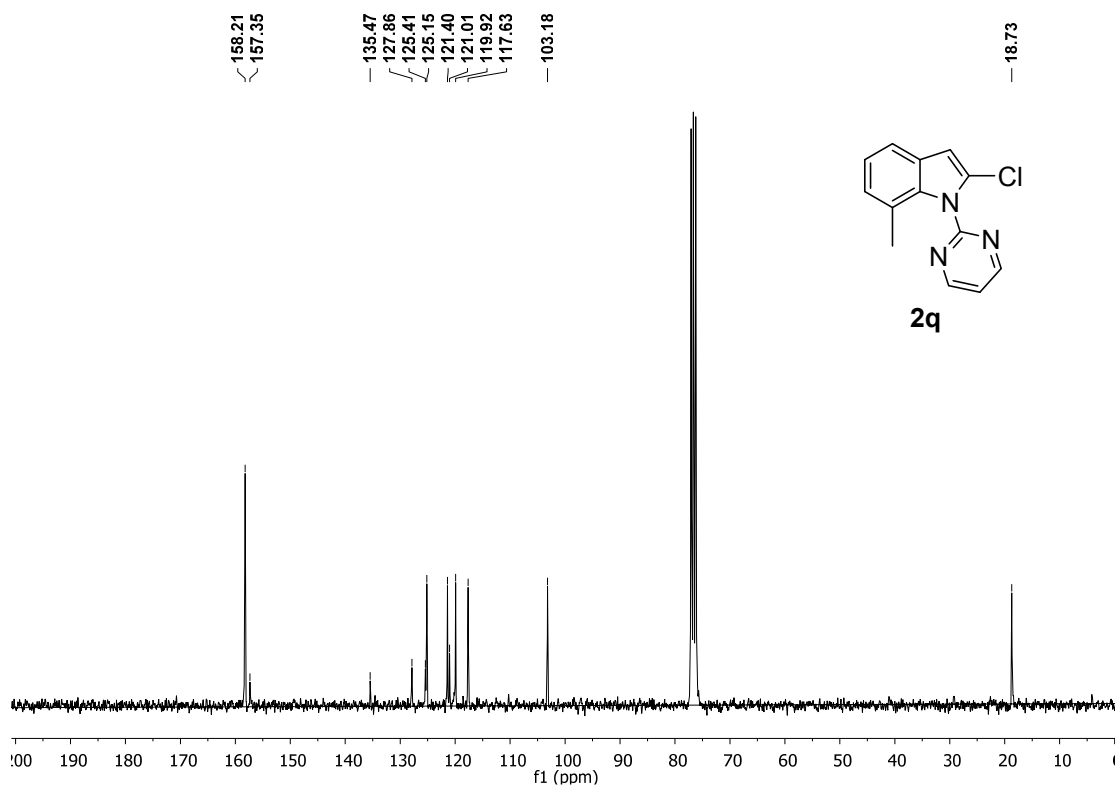
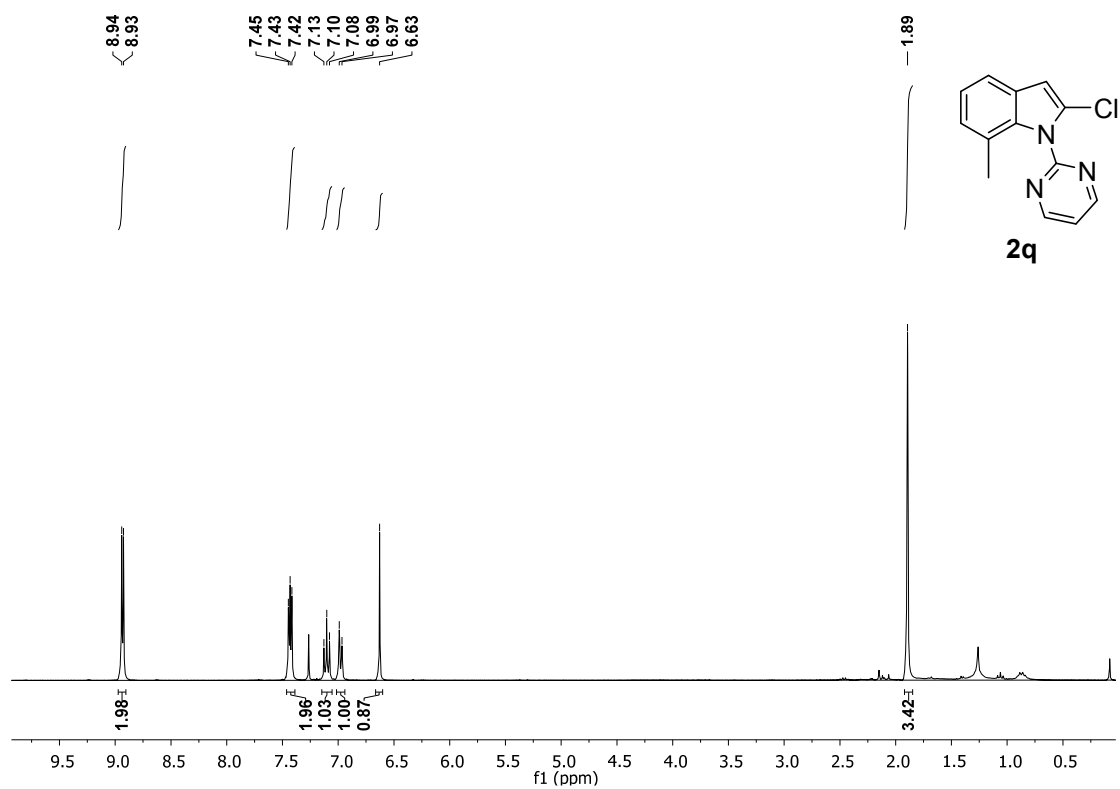


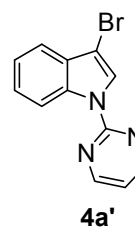
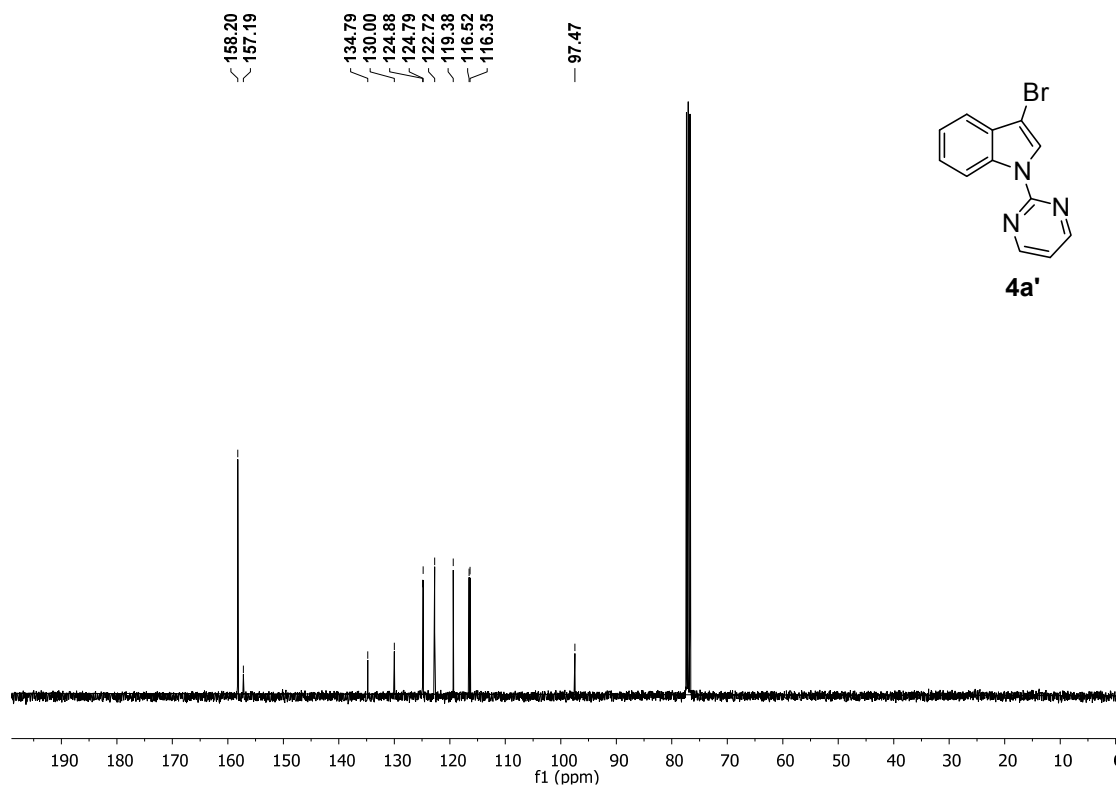
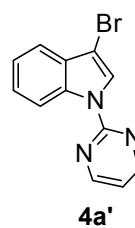
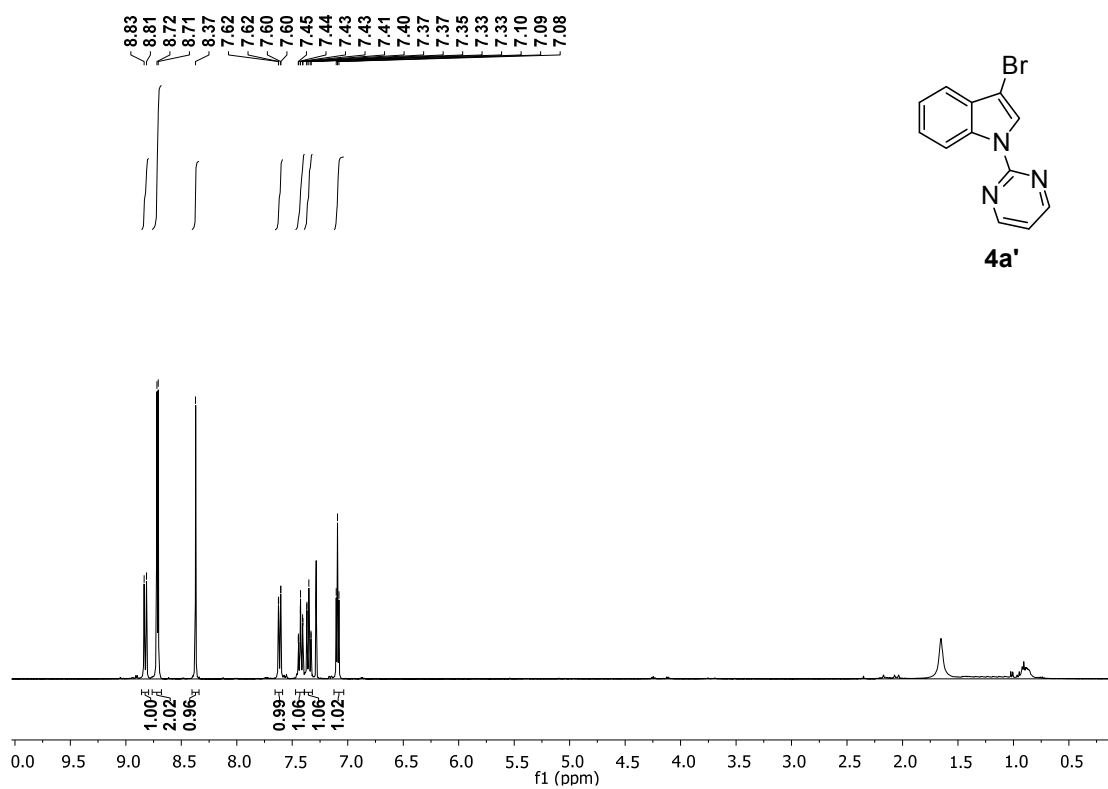


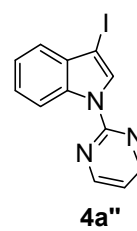
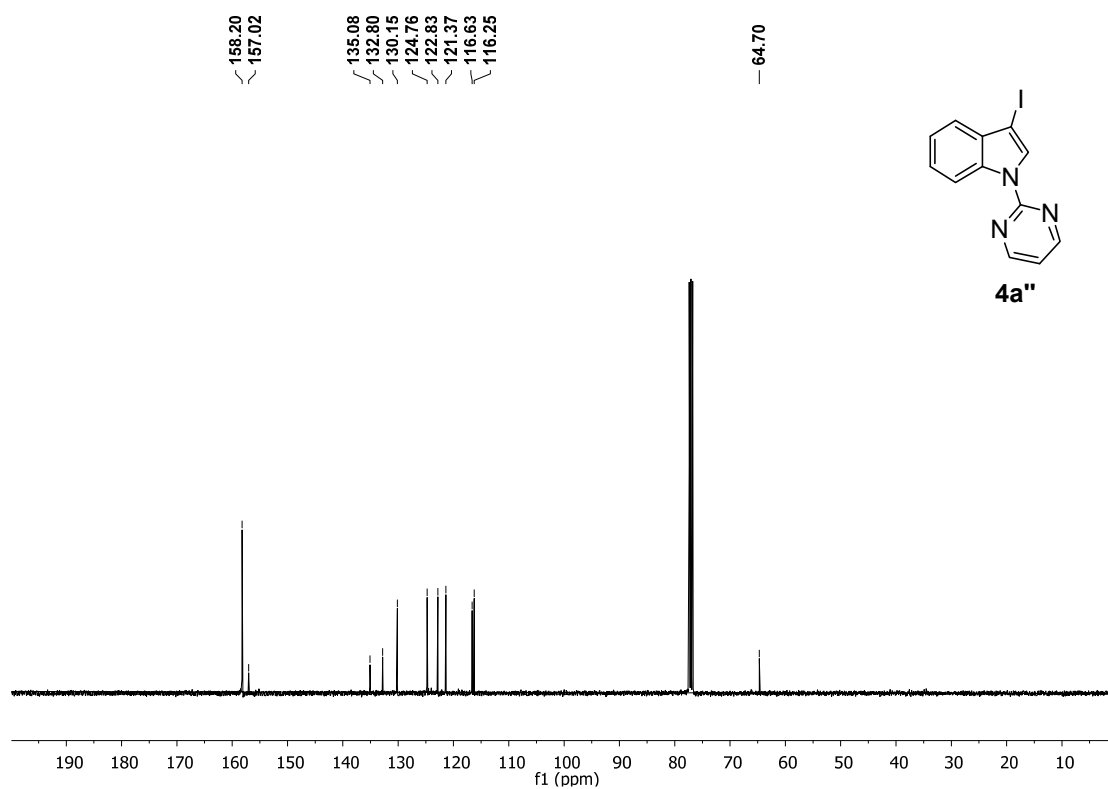
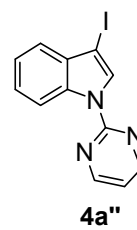
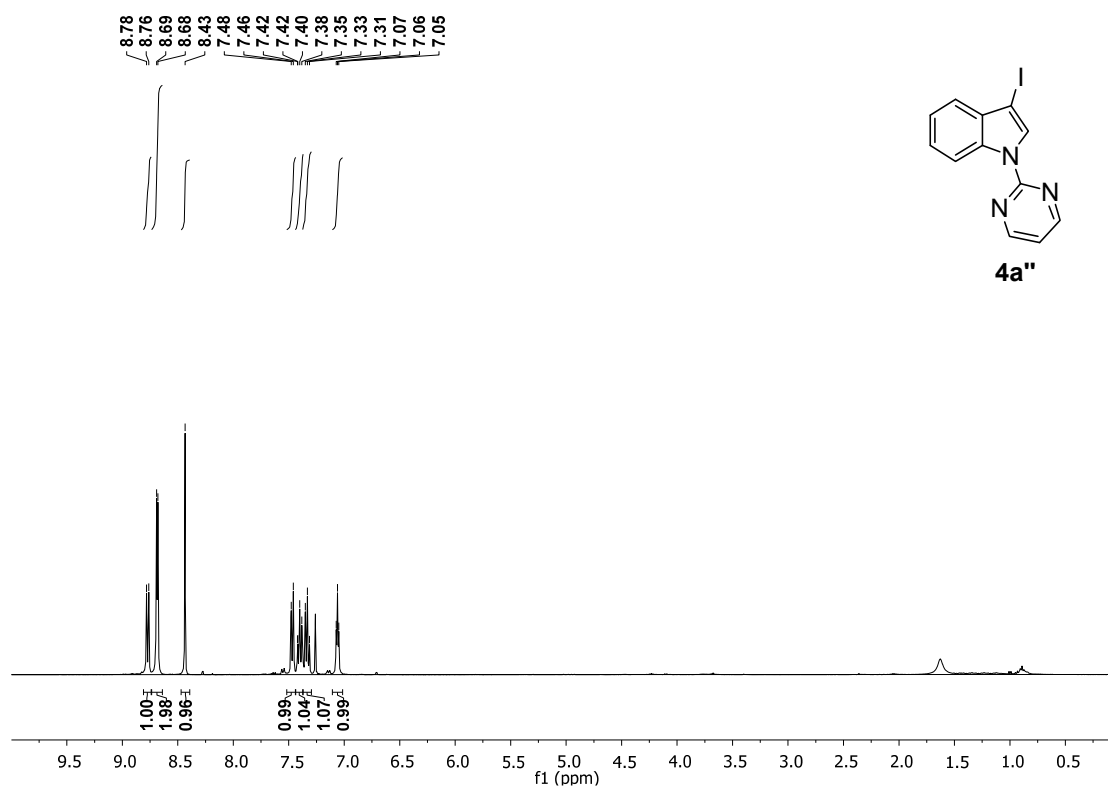


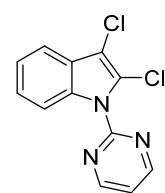
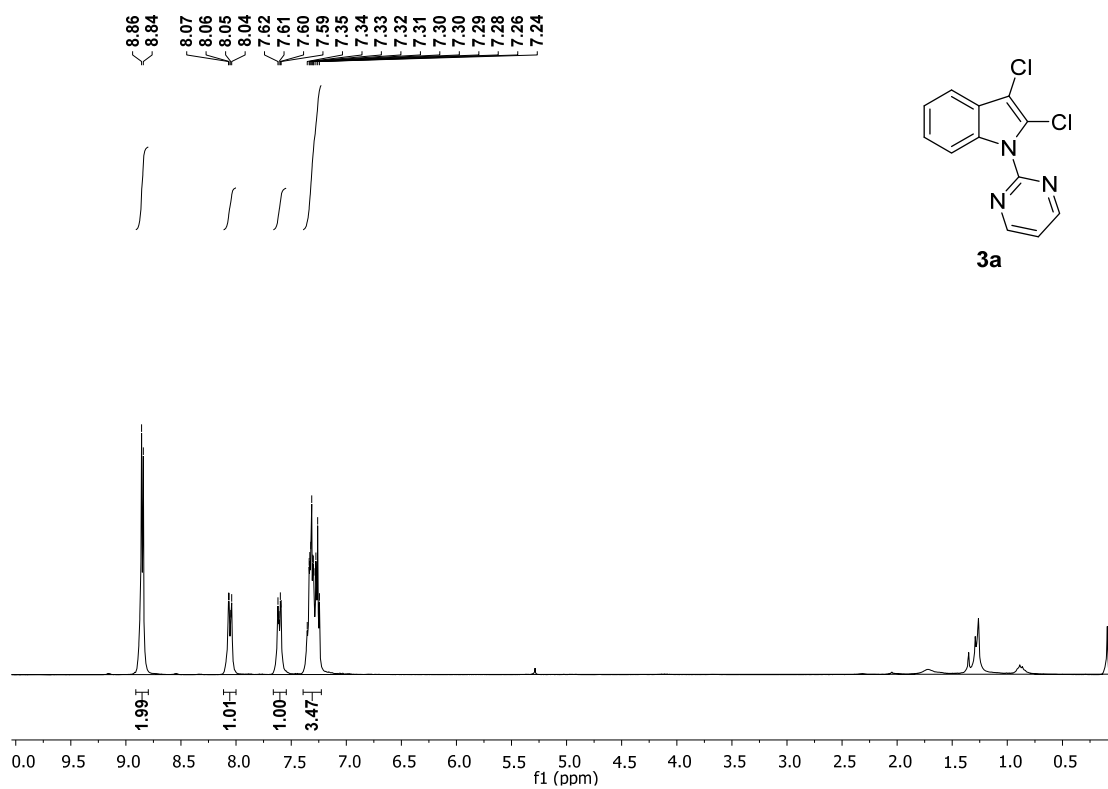




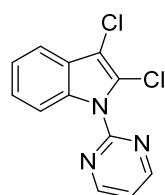
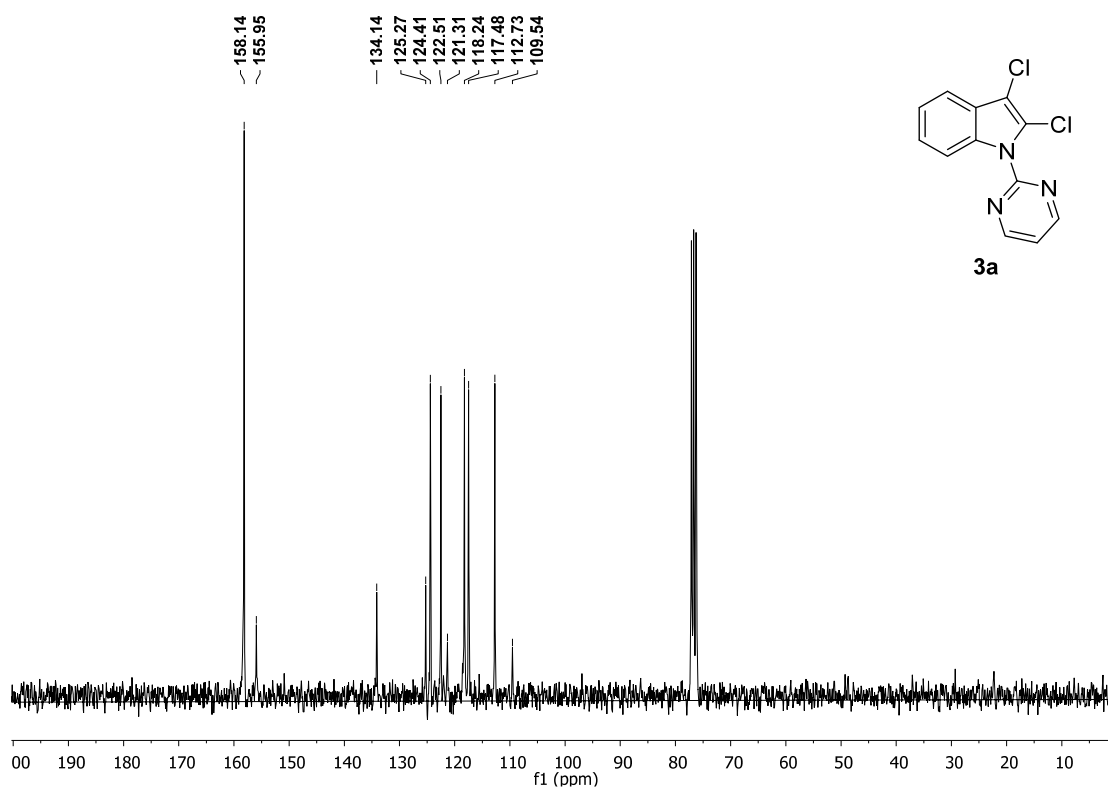








3a



3a

