Supplementary Information (SI) for Organic & Biomolecular Chemistry.

Synthesis of Bis(indolyl)methanes Using N-Heterocyclic Carbene Salts as C1 Precursor

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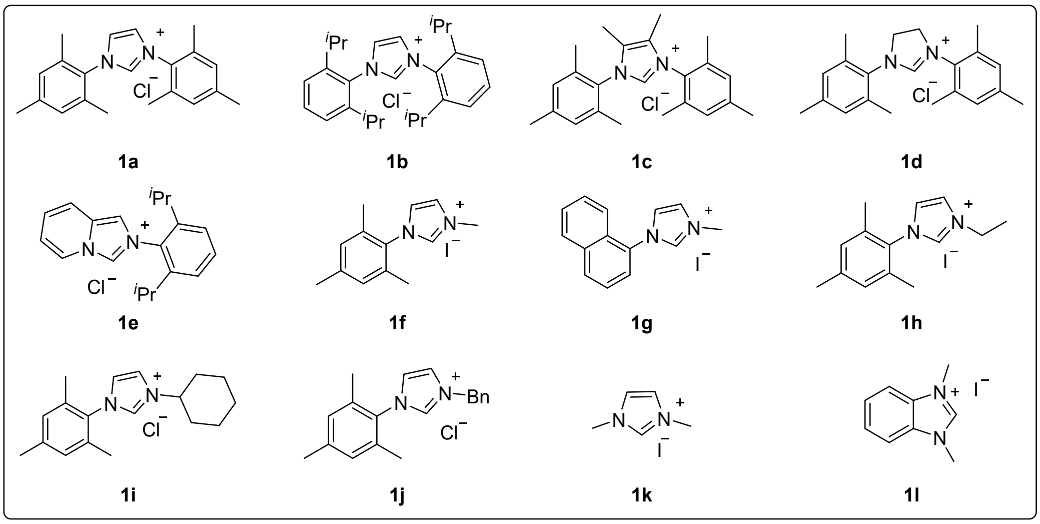
1. General Information

Unless otherwise noted, all reactions were carried out in flame-dried reaction vessels with Teflon screw caps under nitrogen. Solvents were purified and dried according to standard methods prior to use. All commercially available reagents were obtained from chemical suppliers and used after proper purification if necessary. Flash column chromatography was performed on silica gel (200-300 mesh) with the indicated solvent mixtures. TLC analysis was performed on pre-coated, glass-backed silica gel plates and visualized with UV light.

The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 or 500 AV spectrometers. Chemical shifts (δ) were reported as parts per million (ppm) downfield from tetramethylsilane and the following abbreviations were used to identify the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, br = broad and all combinations thereof can be explained by their integral parts. Coupling constant (*J*) was reported in hertz unit (Hz). High-resolution mass spectra (HRMS) were recorded with an Agilent 6210 LC/TOF spectrometer.

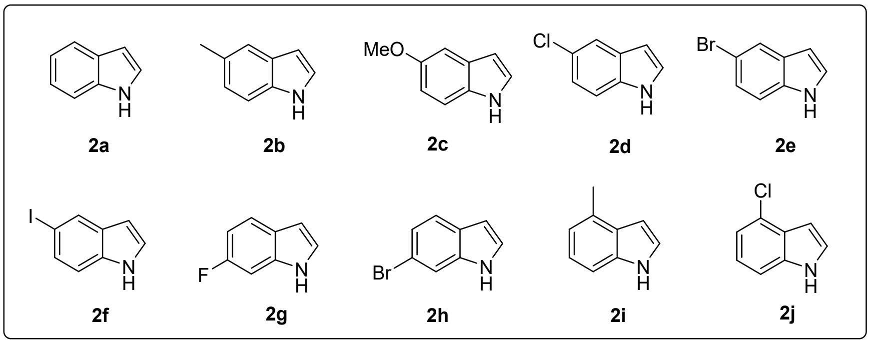
2. Preparation of Substrates

2.1 Preparation of NHC salts



The substrates **1a**, **1b** and **1d** are commercially available and used as received. The other substrates are prepared from the known literature.[1-6]

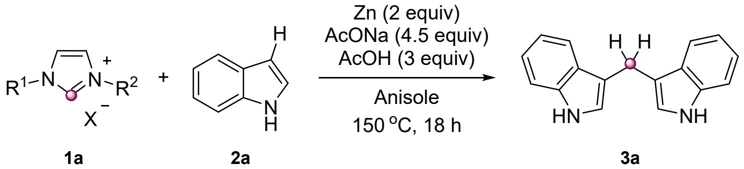
2.2 List of indoles

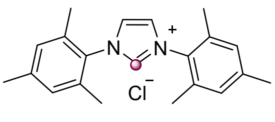


All of the indoles are commercial available and used as received.

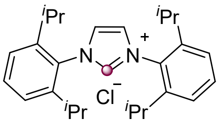
3. Synthesis Bis(indolyl)methanes from Indoles with NHC Salts

3.1 Evaluation of the structurally varied NHC salts.

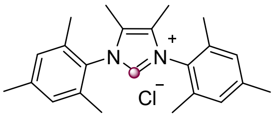




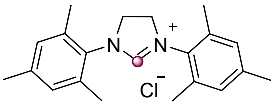
1a [**3a**: 50%]



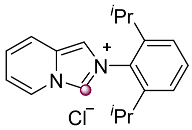
1b [**3a**: 3%]



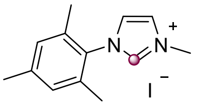
1c [**3a**: 8%]



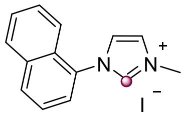
1d [**3a**: 25%]



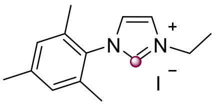
1e [**3a**: 0%]



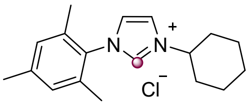
1f [**3a**: 45%]



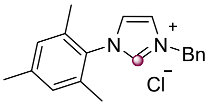
1g [**3a**: 25%]



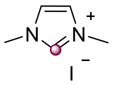
1h [**3a**: 22%]



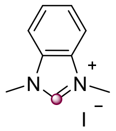
1i [**3a**: 20%]



1j [**3a**: 52%]

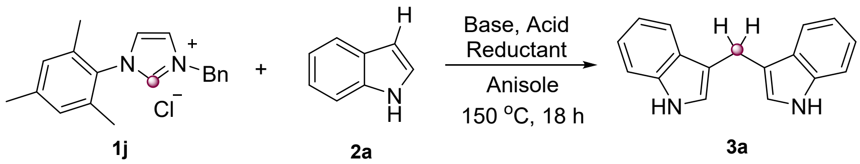


1k [**3a**: 0%]



1l [**3a**: 30%]

3.2 Optimization of reaction conditions

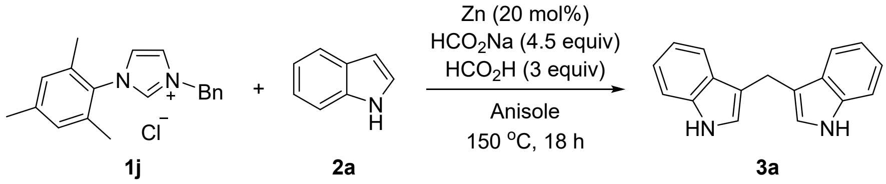


Entry	Base/equiv	Acid/equiv	Reductant/equiv	Yield/%
1	NaOAc/4.5	HOAc/3	Zn/7	53
2	NaOAc/4.5	HOAc/3	Zn/5	52
3	NaOAc /4.5	HOAc /3	Zn/3	45
4	NaOAc /4.5	HOAc /3	Zn/1	10
5	NaOAc /4.5	HOAc /3	Zn/0.5	5
6	NaOAc /4.5	HOAc /3	-	NR
7	NaOAc /4.5	HOAc/3	Sn/5	20
8	NaOAc /4.5	HOAc/3	Mg/5	NR
9	NaOAc /4.5	HOAc/3	$Zn(OAc)_2$/5	NR
10	NaOAc /4.5	HOAc/3	$ZnBr_2$/5	NR
11	NaOAc /3	HOAc/3	Zn/5	43
12	NaOAc /1	HOAc/3	Zn/5	30
13	-	HOAc/3	Zn/5	Trace
14	NaOAc /4.5	HOAc /1	Zn/5	12
15	NaOAc /4.5	-	Zn/5	NR
16	-	-	Zn/5	NR

17	^{t}BuONa/4.5	^{t}BuOH/3	Zn/5	NR
18	EtONa/4.5	EtOH/3	Zn/5	NR
19	AdCO$_2$Na/4.5	AdCO$_2$H/3	Zn/5	82
20	PivONa/4.5	PivOH$_2$/3	Zn/5	45
21	HCO$_2$Na/4.5	HCOOH/3	Zn/5	72
22	HCO$_2$Na/4.5	HCOOH/3	Zn/0.2	68
23	AdCO$_2$Na/4.5	AdCO$_2$H/3	Zn/0.2	NR
24	HCO$_2$Na/4.5	HCOOH/3	Zn/0.1	42
25	HCO$_2$Na/4.5	HCOOH/3	Zn(OAc)$_2$/0.2	53
26	HCO$_2$Na/4.5	HCOOH/3	ZnBr$_2$/0.2	55
27	HCO$_2$Na/4.5	HCOOH/3	Zn(OTf)$_2$/0.2	20
28	-	HCOOH/3	Zn/0.2	Trace
29	HCO$_2$Na/4.5	-	Zn/0.2	NR
30	HCO$_2$Na/4.5	HCOOH/3	-	NR

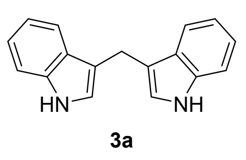
^{a}Conditions: **1j** (0.2 mmol), **2a** (0.4 mmol), Base, Acid, Reductant, Anisole (1 mL), at 150 °C for 18 h.

3.3 Experimental details and characterization of products



To a 25 mL flame-dried Schlenk tube containing a stirring bar was added 1-(2,4,6-Trimethylphenyl)-3-(benzyl)imidazolium chloride **1j** (0.2 mmol), indole **2a** (0.4 mmol), Zn (0.04 mmol, 2.6 mg), HCO$_2$Na (0.9 mmol), HCO$_2$H (0.6 mmol) and anisole (1 mL) sequentially under nitrogen. The tube was sealed and stirred at 150 °C for 18 h. After completion, the reaction mixture was concentrated and purified by silica gel column chromatography to give the pure product.

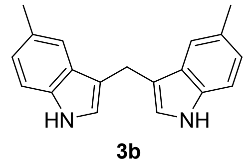
3,3'-Diindolylmethane (3a) [7]


3a

Purified by silica gel column chromatography as white solid, 68% (33 mg).

^{1}H NMR (400 MHz, DMSO-*d$_6$*) δ 10.74 (s, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 2.4 Hz, 2H), 7.05 – 7.01 (m, 2H), 6.94 – 6.90 (m, 2H), 4.13 (s, 2H).

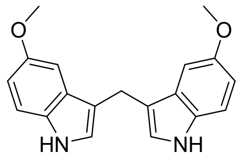
3,3'-Methylenebis[5-methyl-1H-indole] (3b) [7]


3b

Purified by silica gel column chromatography as white solid, 58% (32 mg).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.46 (s, 2H), 5.95 (d, J = 8.4 Hz, 2H), 5.71 (t, J = 7.6 Hz, 2H), 5.46 (d, J = 6.8 Hz, 4H), 3.25 (s, 2H), 1.34 (s, 6H).

3,3'-Methylenebis[5-methoxy-1H-indole] (3c) [7]

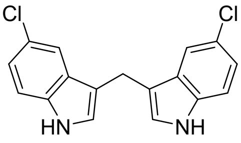


3c

Purified by silica gel column chromatography as white solid, 55% (34 mg).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.71 (s, 2H), 6.35 (d, J = 8.8 Hz, 2H), 6.23 (d, J = 2.0 Hz, 2H), 6.16 (d, J = 2.0 Hz, 2H), 5.83 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 2H), 3.20 (s, 2H), 2.85 (s, 6H).

5,5'-chlorine-3,3'-diindolylmethane (3d) [7]



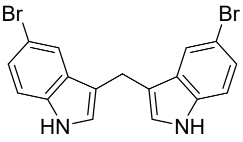
3d

Purified by silica gel column chromatography as white solid, 45% (28 mg).

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.14 (s, 2H), 6.67 (d, J = 2.0 Hz, 2H), 6.50 (d, J = 8.5 Hz, 2H), 6.45 (d, J = 2.0 Hz, 2H), 6.18 (dd, J_1 = 8.5 Hz, J_2 = 2.0 Hz, 2H), 3.26 (s, 2H).

^{13}C NMR (125 MHz, DMSO) δ 135.39, 128.71, 125.27, 123.29, 121.24, 118.37, 114.31, 113.41, 21.08.

5,5'-dibromo-3,3'-diindolylmethane (3e) [7]



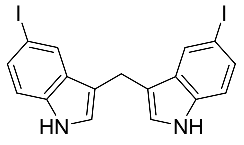
3e

Purified by silica gel column chromatography as white solid, 70% (58 mg).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 2H), 7.70 (d, J = 1.5 Hz, 2H), 7.28 – 7.23 (m, 4H), 6.96 (d, J = 2.5 Hz, 2H), 4.14 (s, 2H).

^{13}C NMR (125 MHz, DMSO) δ 135.62, 129.45, 125.10, 123.78, 121.43, 114.22, 113.91, 111.31, 21.09.

5,5'-iodine-3,3'-diindolylmethane (3f) [7]

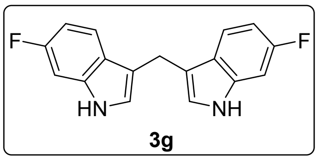


3f

Purified by silica gel column chromatography as white solid, 48% (48 mg).

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.12 (s, 2H), 6.99 (d, J = 1.5 Hz, 2H), 6.44 (dd, J_1 = 8.5 Hz, J_2 = 2.0 Hz, 2H), 6.35 (d, J = 8.5 Hz, 2H), 6.33 (d, J = 2.0 Hz, 2H), 3.22 (s, 2H).

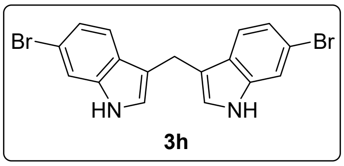
6,6'-fluorine-3,3'-diindolylmethane (3g) [7]



Purified by silica gel column chromatography as white solid, 62% (35 mg).

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.86 (s, 2H), 7.50 (dd, J_1 = 8.5 Hz, J_2 = 5.5 Hz, 2H), 7.18 (d, J = 1.5 Hz, 2H), 7.12 (dd, J_1 = 10.0 Hz, J_2 = 2.5 Hz, 2H), 6.82 – 6.78 (m, 2H), 4.12 (s, 2H).

6,6'-dibromo-3,3'-diindolylmethane (3h) [7]

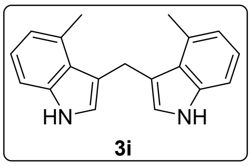


Purified by silica gel column chromatography as white solid, 52% (42 mg).

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.08 (s, 2H), 6.66 (d, J = 1.5 Hz, 2H), 6.59 (d, J = 7.5 Hz, 2H), 6.33 (d, J = 2.0 Hz, 2H), 6.19 (dd, J_1 = 8.5 Hz, J_2 = 2.0 Hz, 2H), 3.25 (s, 2H).

^{13}C NMR (125 MHz, DMSO) δ 137.75, 126.62, 124.41, 121.45, 120.87, 114.77, 114.38, 114.14, 21.09.

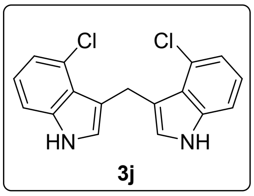
3,3'-Methylenebis[4-methyl-1H-indole] (3i) [7]



Purified by silica gel column chromatography as yellow oil liquid, 65% (36 mg).

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.73 (s, 2H), 6.45 (s, 2H), 6.36 (d, J = 8.4 Hz, 2H), 6.18 (d, J = 2.0 Hz, 2H), 6.01 (d, J = 8.0 Hz, 2H), 3.21 (s, 2H), 1.48 (s, 6H).

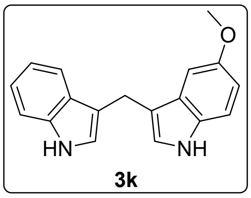
4,4'-chlorine-3,3'-diindolylmethane (3j) [7]



Purified by silica gel column chromatography as yellow oil liquid, 46% (29 mg).

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.27 (s, 2H), 6.49 (d, J = 8.0 Hz, 2H), 6.18 (t, J = 7.6 Hz, 2H), 6.12 (d, J = 7.6 Hz, 2H), 6.04 (s, 2H), 3.78 (s, 2H).

3-(1H-Indol-3-ylmethyl)-5-methoxy-1H-indole (3k) [8]

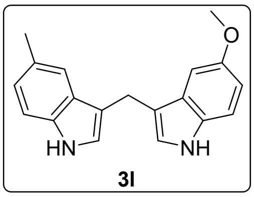


Purified by silica gel column chromatography as white solid, 40% (22 mg).

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.73 (s, 1H), 10.57 (s, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.21 (d, J =

8.8 Hz, 1H), 7.15 (s, 1H), 7.07 – 7.00 (m, 3H), 6.93 (t, J = 7.4 Hz, 1H), 6.69 (d, J = 8.8 Hz, 1H), 4.09 (s, 2H), 3.70 (s, 3H).

5-Methoxy-3-[(5-methyl-1H-indol-3-yl) methyl]-1H-indole (3l) [8]

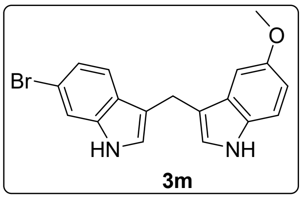


3l

Purified by silica gel column chromatography as white solid, 39% (23 mg).

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.59 (s, 1H), 10.55 (s, 1H), 7.33 (s, 1H), 7.23 (d, J = 2.8 Hz, 1H), 7.21 (d, J = 2.8 Hz, 1H), 7.09 (s, 1H), 7.05 (s, 1H), 7.02 (d, J = 2.4 Hz, 1H), 6.88 (d, J = 8.4 Hz, 1H), 6.70 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H), 4.07 (s, 2H), 3.71 (d, J = 1.6 Hz, 3H), 2.34 (s, 3H).

3-[(6-Bromine-1H-indol-3-yl)methyl]-5-methoxy-1H-indole (3m)



3m

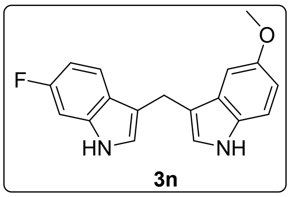
Purified by silica gel column chromatography as white solid, 46% (33 mg).

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.89 (s, 1H), 10.58 (s, 1H), 7.51 (s, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.21 (d, J = 9.2 Hz, 2H), 7.07 – 7.03 (m, 2H), 6.97 (s, 1H), 6.70 – 6.67 (m, 1H), 4.07 (s, 2H), 3.69 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 153.26, 137.73, 132.04, 127.88, 126.72, 124.34, 123.97, 121.36, 120.91, 115.06, 114.32, 114.06, 112.38, 111.20, 101.16, 60.22, 55.80, 21.21.

HRMS (ESI): m/z $[M-H]^-$ calcd for $C_{18}H_{14}BrN_2O$: 353.0295; found: 353.0289.

3-[(6-Fluoro-1H-indol-3-yl)methyl]-5-methoxy-1H-indole (3n) [8]

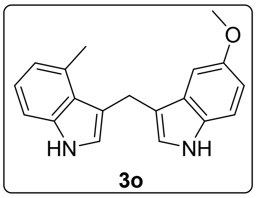


3n

Purified by silica gel column chromatography as white solid, 42% (25 mg).

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.80 (s, 1H), 10.57 (s, 1H), 7.48 (dd, J_1 = 8.8 Hz, J_2 = 5.6 Hz, 2H), 7.21 (d, J = 8.8 Hz, 1H), 7.15 (d, J = 2.0 Hz, 1H), 7.09 (dd, J_1 = 10.4 Hz, J_2 = 2.4 Hz, 2H), 6.99 (d, J = 2.0 Hz, 1H), 6.80 – 6.75 (m, 1H), 6.69 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 2H), 4.07 (s, 2H), 3.69 (s, 3H).

5-Methoxy-3-[(4-methyl-1H-indol-3-yl)methyl]-1H-indole (3o)



3o

Purified by silica gel column chromatography as white solid, 52% (30 mg).

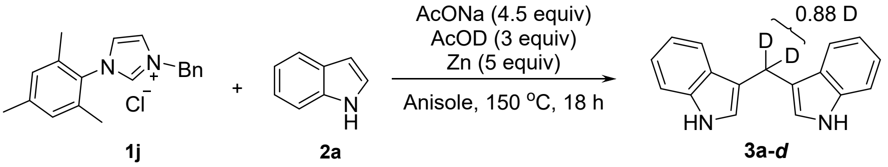
^{1}H NMR (400 MHz, DMSO-*d_6*) δ 10.74 (s, 1H), 10.59 (s, 1H), 7.26 (d, *J* = 8.8 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 2.0 Hz, 1H), 6.98 (s, 1H), 6.93 (t, *J* = 7.6 Hz, 1H), 6.80 (s, 1H), 6.74 (dd, J_1 = 8.8 Hz, J_2 = 2.0 Hz, 1H), 6.67 (d, *J* = 7.2 Hz, 1H), 4.27 (s, 2H), 3.72 (s, 3H), 2.54 (s, 3H).

^{13}C NMR (126 MHz, DMSO-*d_6*) δ 153.33, 137.44, 132.13, 130.35, 127.75, 126.33, 124.13, 123.87, 121.33, 120.13, 115.77, 115.03, 112.44, 111.31, 109.81, 101.06, 55.79, 23.46, 20.28.

HRMS (ESI): m/z [M-H]$^-$ calcd for $C_{19}H_{17}N_2O$: 289.1346; found: 289.1341.

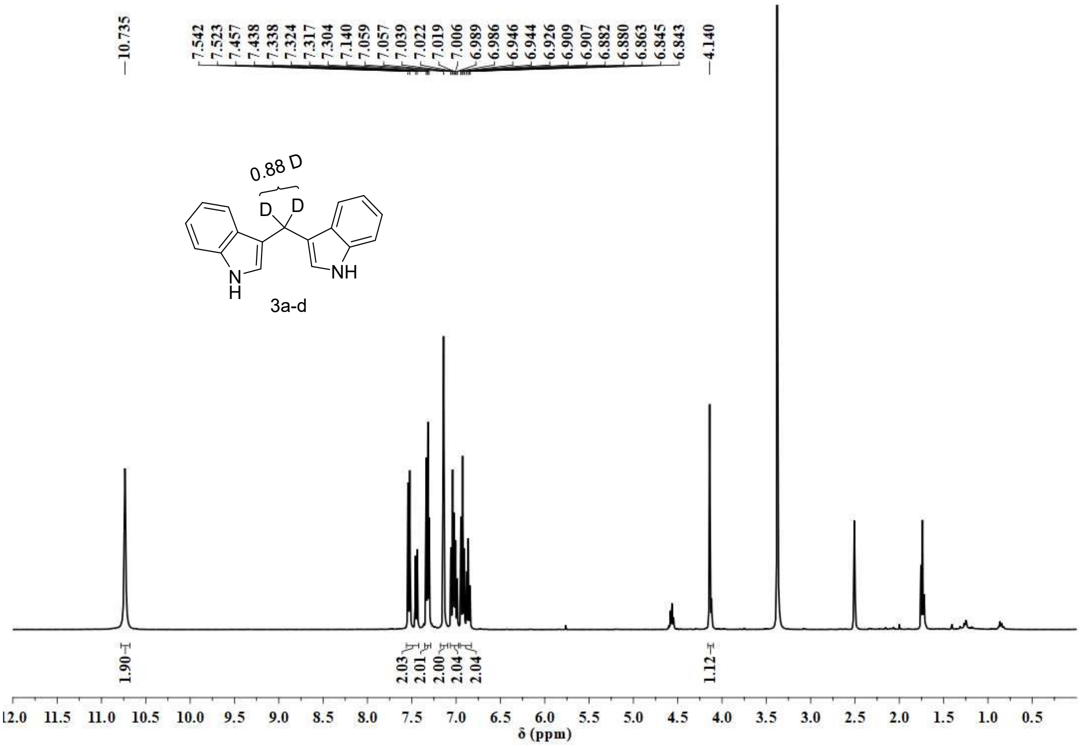
4. Mechanistic Studies

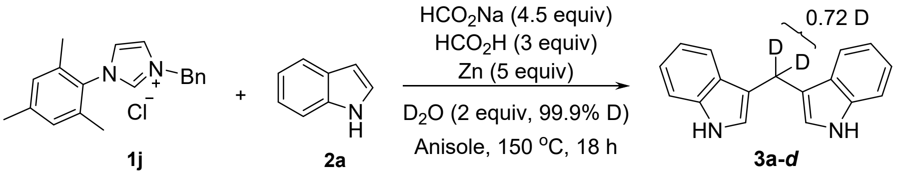
4.1 Deuterium-labelling experiment



Experimental procedure:

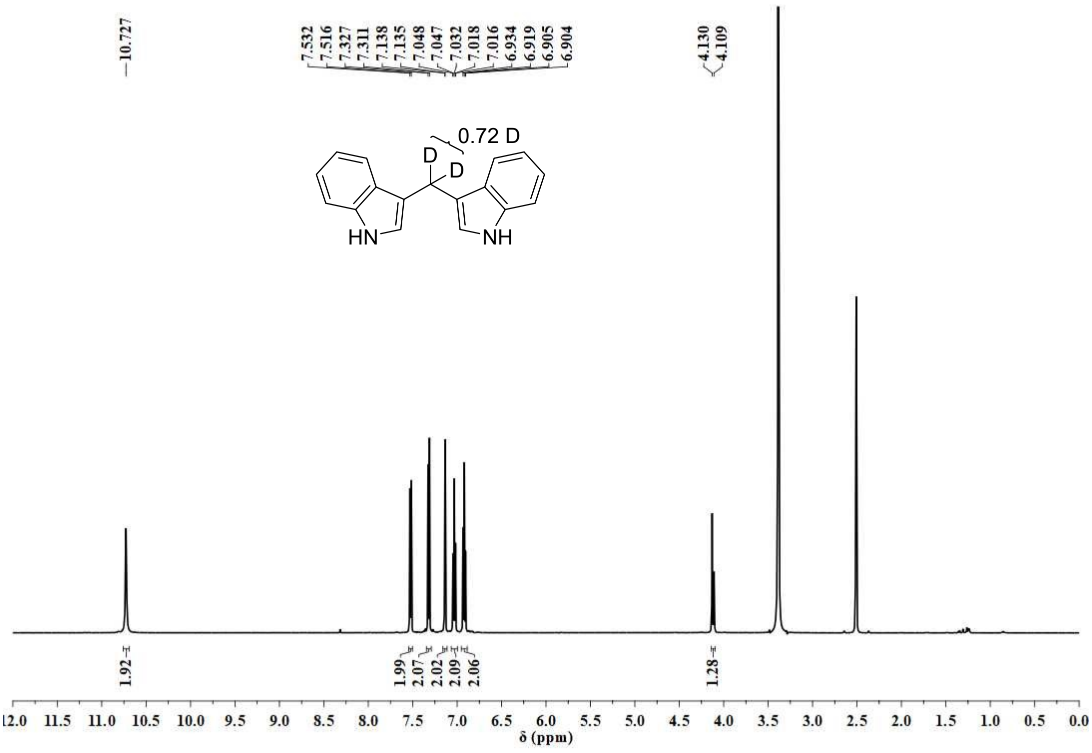
To a 25 mL flame-dried Schlenk tube containing a stirring bar was added 1-(2,4,6-Trimethylphenyl)-3-(benzyl)imidazolium chloride **1j** (0.2 mmol, 63 mg), indole **2a** (0.4 mmol, 47 mg, 1 equiv), Zn (1 mmol, 65 mg, 5 equiv), AcONa (0.9 mmol, 74 mg, 4.5 equiv), AcOD (0.6 mmol, 37 mg, 3 equiv) and anisole (1 mL), sequentially under nitrogen. The tube was sealed and stirred at 150 °C for 18 h. After completion, the reaction mixture was concentrated and purified by silica gel column chromatography to provide the product **3a-*d*** (44% D). **^{1}H NMR (400 MHz, DMSO-*d_6*)** δ 10.74 (s, 2H), 7.49 (dd, J_1 = 34.0 Hz, J_2= 7.6 Hz, 2H), 7.32 (dd, J_1 = 8.4 Hz, J_2=5.6 Hz, 2H), 7.14 (s, 2H), 7.06-6.99 (m, 2H), 6.95-6.84 (m, 2H), 4.14 (s, 1.12H).

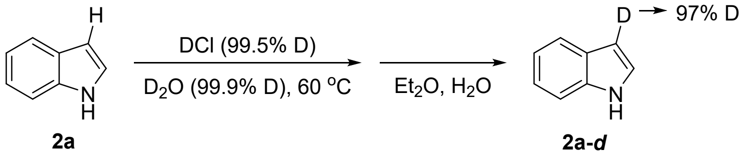




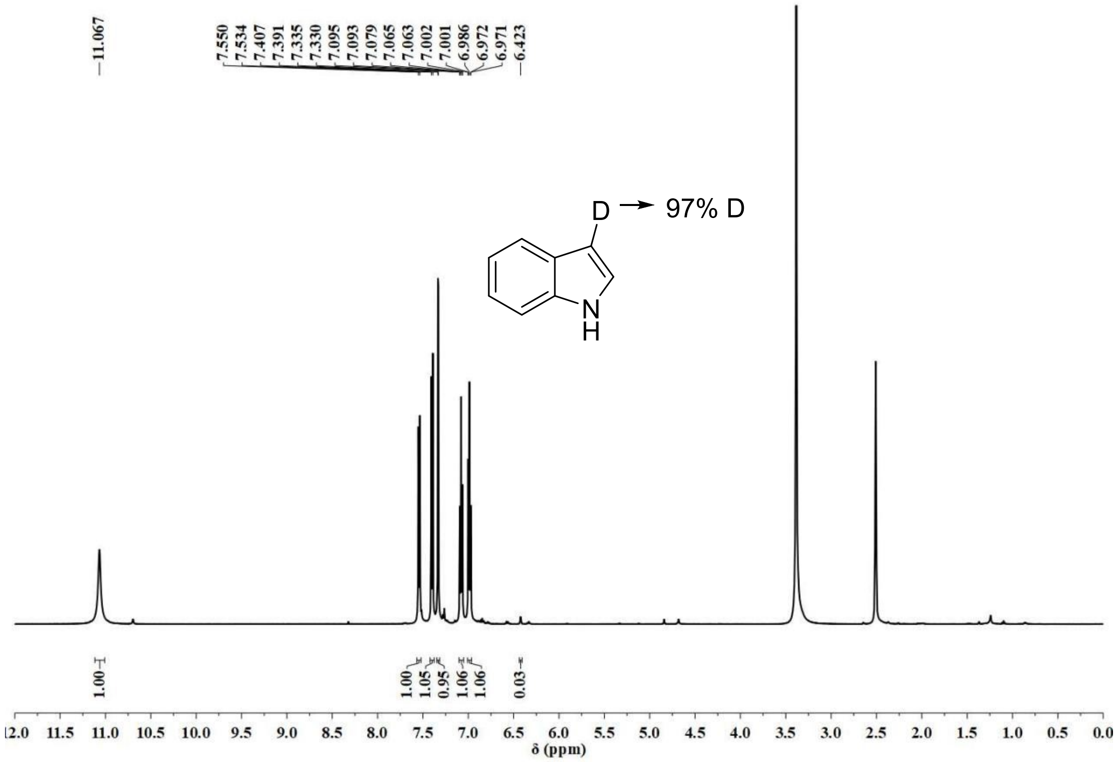
Experimental procedure:

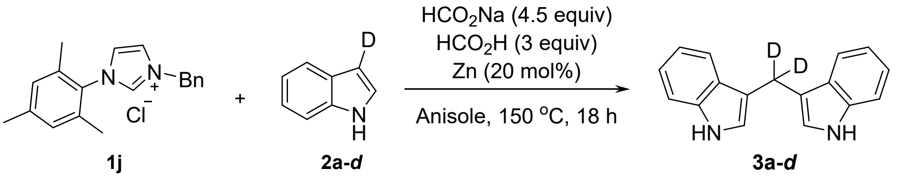
To a 25 mL flame-dried Schlenk tube containing a stirring bar was added 1-(2,4,6-Trimethylphenyl)-3-(benzyl)imidazolium chloride **1j** (0.2 mmol, 63 mg, 1 equiv), indole **2a** (0.4 mmol, 47 mg, 1 equiv), Zn (1 mmol, 65 mg, 5 equiv), HCOONa (0.9 mmol, 61 mg, 4.5 equiv), anisole (1 mL), HCOOH (0.6 mmol, 24 μL, 3 equiv) and D_2O (0.4 mmol, 8 μL, 2 equiv) sequentially under nitrogen. The tube was sealed and stirred at 150 °C for 18 h. After completion, the reaction mixture was concentrated and purified by silica gel column chromatography to provide the product **3a-*d*** (36% D). **^{1}H NMR (500 MHz, DMSO-d_6)** δ 10.73 (s, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 1.5 Hz, 2H), 7.05 – 7.02 (m, 2H), 6.92 (dd, J_1 =14.5 Hz, J_2 =7.5 Hz, 2H), 4.12 (m, 1.28H).



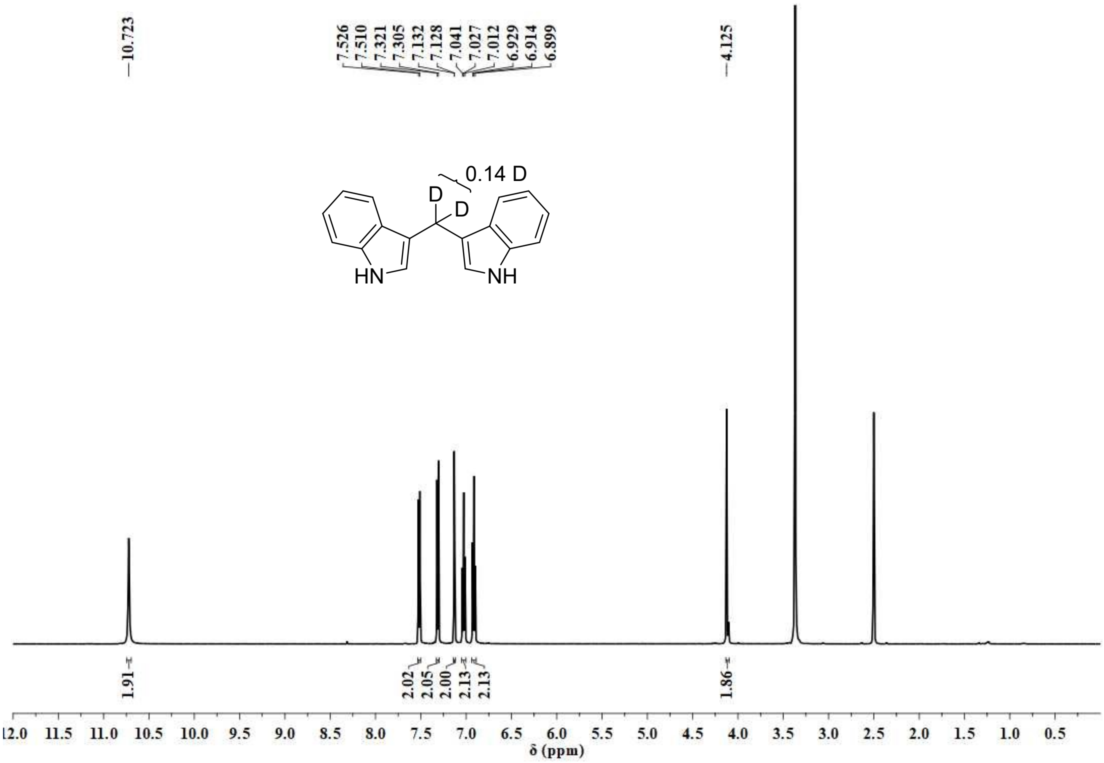


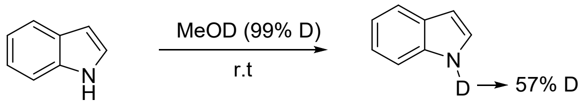
Indole **2a** (2.0 g, 17 mmol) and D_2O (20 mL) of 0.01 M DCl were added to a 25 mL flame-dried Schlenk tube containing a stirring bar under N_2 atmosphere, and the mixture was stirred at 60 °C for 4 hours. After the reaction was cooled, it was extracted with anhydrous Et_2O (20 mL) for three times. The organic layers were combined, dried with magnesium sulfate, filtered and reduced in vacuum. The obtained oil was ground in n-hexane to obtain a colorless solid. Ether (20 ml) and H_2O (10mL) were mixed, and the obtained colorless solid was dissolved in the solution and stirred at room temperature for 2 hours. The layers were separated, and the aqueous layer was extracted three times with Et_2O (20 mL). The organic layers were combined, dried with magnesium sulfate, filtered and reduced under vacuum to obtain white solids **2a-*d***.[9] **^{1}H NMR (500 MHz, DMSO-*d₆*)** δ 11.07 (s, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 2.5 Hz, 1H), 7.10 – 7.06 (m, 1H), 7.00 – 6.97 (m, 1H), 6.42 (s, 0.03H).





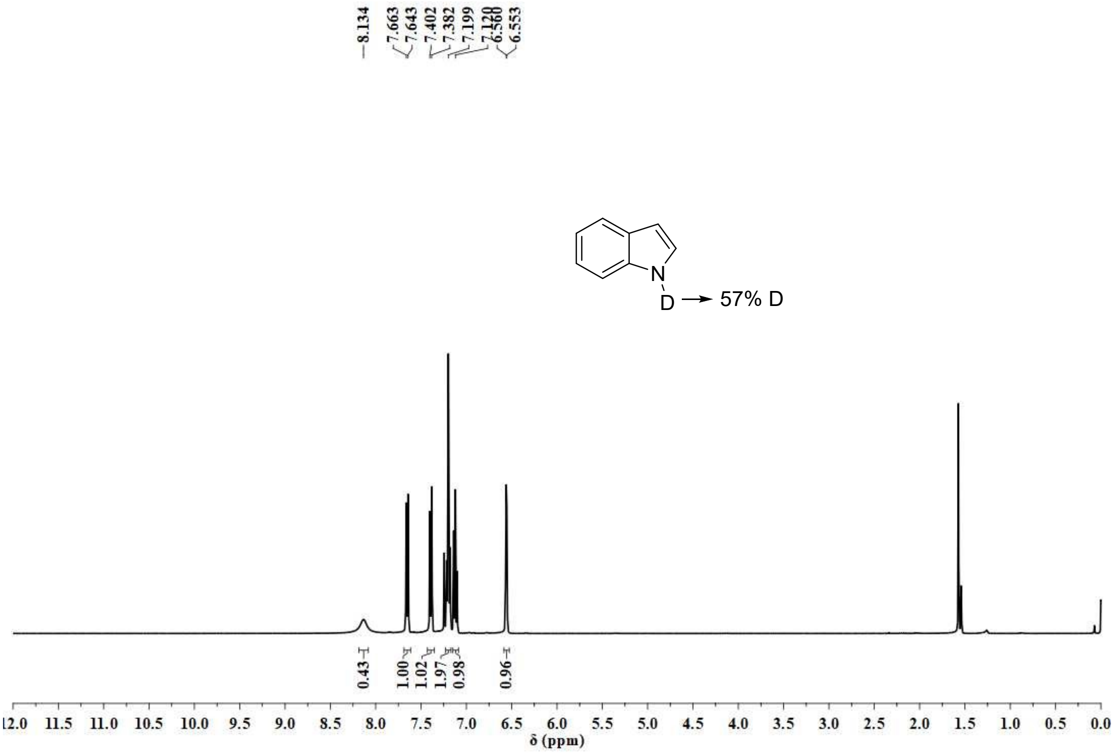
To a 25 mL flame-dried Schlenk tube containing a stirring bar was added 1-(2,4,6-Trimethylphenyl)-3-(benzyl)imidazolium chloride **1j** (0.2 mmol, 63 mg, 1 equiv), **2a-*d*** (0.4 mmol, 47 mg, 1 equiv), Zn (0.04 mmol, 2.6 mg, 0.2 equiv), HCOONa (0.9 mmol, 61 mg, 4.5 equiv), anisole (1 mL) and HCOOH (0.6 mmol, 24 μL, 3 equiv) sequentially under nitrogen. The tube was sealed and stirred at 150 ℃ for 18 h. After completion, the reaction mixture was concentrated and purified by silica gel column chromatography to provide the product **3a-*d*** (7% D). **^{1}H NMR (400 MHz, DMSO-d_6)** δ 10.72 (s, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 2.0 Hz, 2H), 7.03 (t, *J* = 7.5 Hz, 2H), 6.91 (t, *J* = 7.5 Hz, 2H), 4.13 (s, 1.86H).

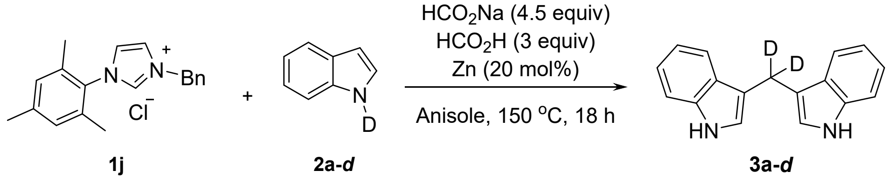




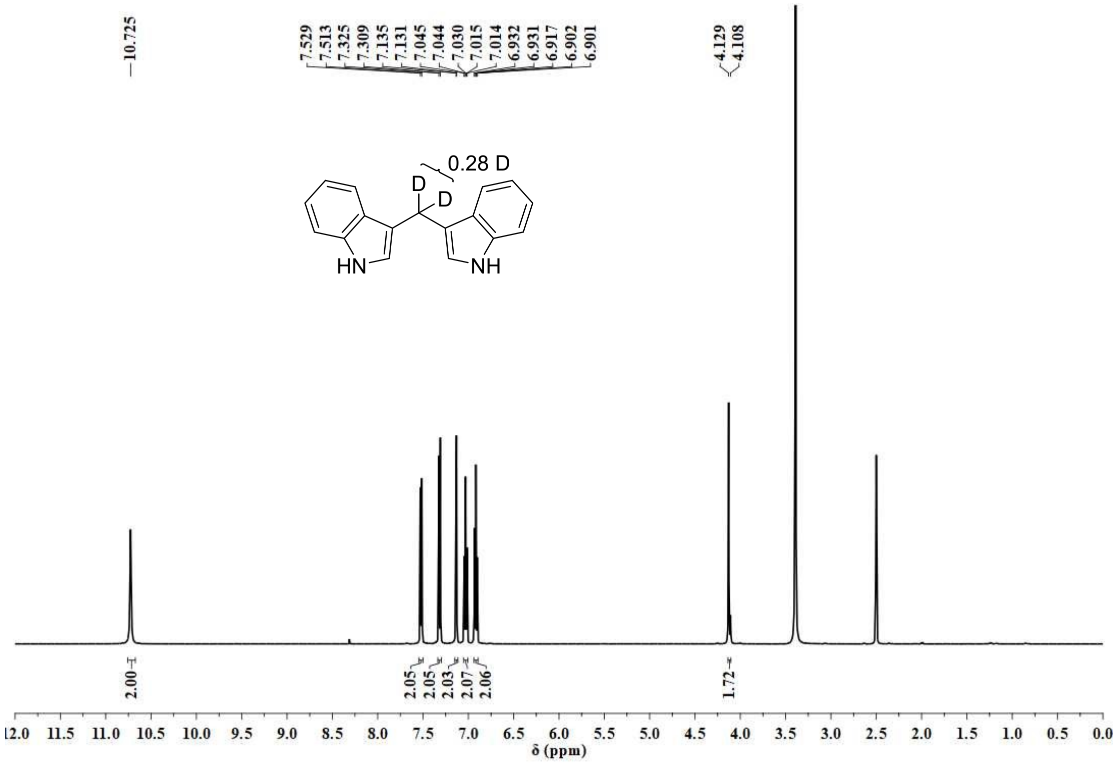
2a **2a-*d***

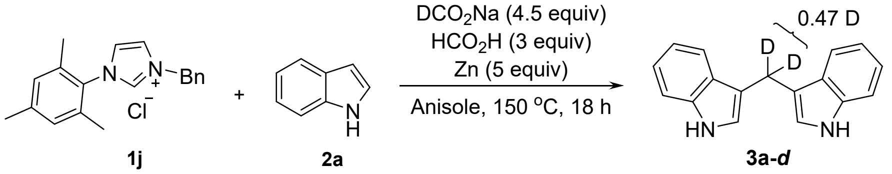
Indole (1.0 g, 8.55 mmol) and MeOD (6 mL, 230 mmol) were added to a dried 25 mL Schlenk tube under nitrogen atmosphere and stirred at room temperature for 4 hours. After the reaction, the solvent was removed by vacuum concentration. MeOD (6 mL) was added to the Schlenk tube again and stirred at room temperature for another 4 hours. The MeOD was removed by vacuum concentration and the product **2a-*d*** was obtained with deuteration rate of 57% D.[10] **^{1}H NMR (400 MHz, CDCl$_3$)** δ 8.13 (s, 0.43H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.22 – 7.18 (m, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 6.56 (d, *J* = 2.8 Hz, 1H).





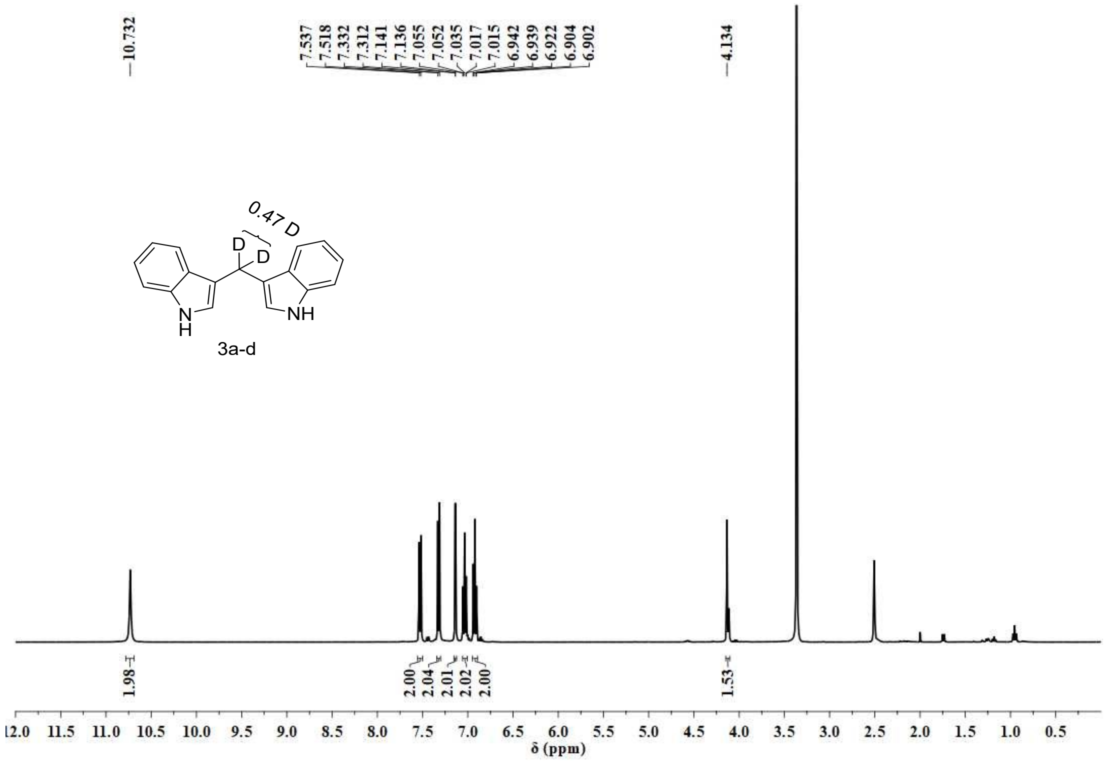
To a 25 mL flame-dried Schlenk tube containing a stirring bar was added 1-(2,4,6-Trimethylphenyl)-3-(benzyl)imidazolium chloride **1j** (0.2 mmol, 63 mg, 1 equiv), **2a-*d*** (0.4 mmol, 47 mg, 1 equiv), Zn (0.04 mmol, 2.6 mg, 0.2 equiv), HCOONa (0.9 mmol, 61 mg, 4.5 equiv), anisole (1 mL), HCOOH (0.5 mmol, 24 μL, 3 equiv), and D_2O (18 μL, 5 equiv) sequentially under nitrogen. The tube was sealed and stirred at 150 °C for 18 h. After completion, the reaction mixture was concentrated and purified by silica gel column chromatography to provide the product **3a-*d*** (14% D). **^{1}H NMR (500 MHz, DMSO-*d$_6$*)** δ 10.73 (s, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 2.0 Hz, 2H), 7.05 – 7.01 (m, 2H), 6.93 – 6.90 (m, 2H), 4.12 (m, 1.72H).

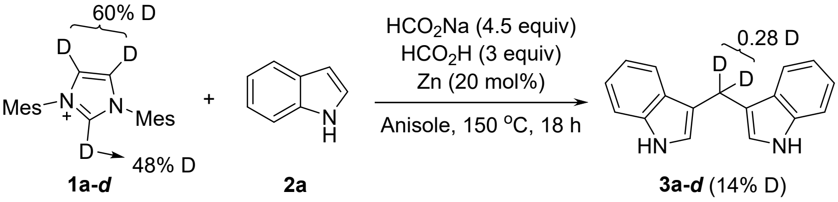




Experimental procedure:

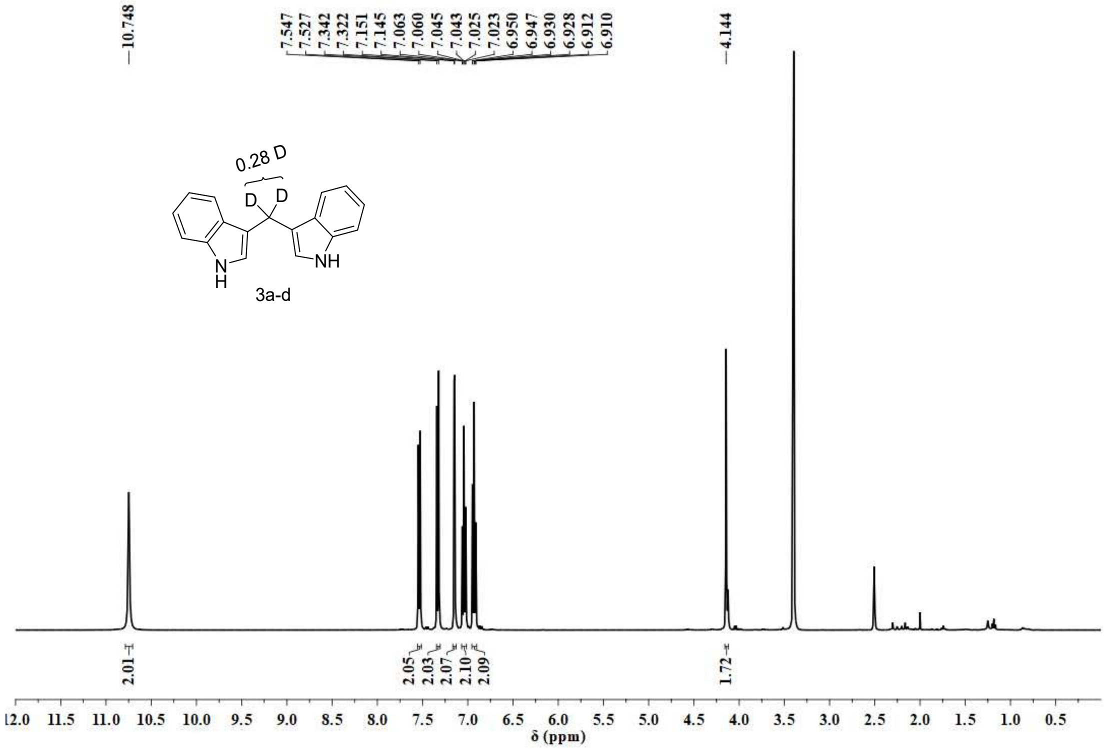
To a 25 mL flame-dried Schlenk tube containing a stirring bar was added 1-(2,4,6-Trimethylphenyl)-3-(benzyl)imidazolium chloride **1j** (0.2 mmol, 63 mg, 1 equiv), indole **2a** (0.4 mmol, 47 mg, 1 equiv), Zn (1 mmol, 65 mg, 5 equiv), DCOONa (0.9 mmol, 61 mg, 4.5 equiv), HCOOH (0.6 mmol, 24 µL, 3 equiv) and anisole (1 mL), sequentially under nitrogen. The tube was sealed and stirred at 150 °C for 18 h. After completion, the reaction mixture was concentrated and purified by silica gel column chromatography to provide the product **3a-*d*** (24% D).**^{1}H NMR (400 MHz, DMSO-d_6)** δ 10.73 (s, 2H), 7.53 (d, *J* = 7.6 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 2.0 Hz, 2H), 7.06-7.02 (m, 2H), 6.94-6.90 (m, 2H), 4.13 (s, 1.53H).

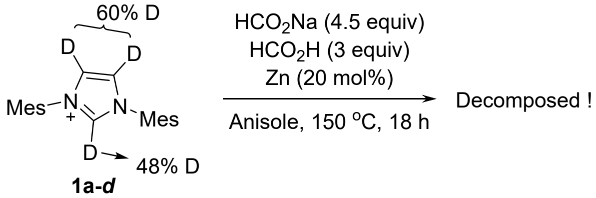




Experimental procedure:

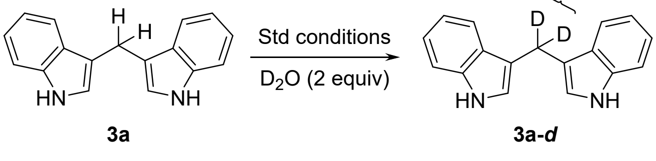
To a 25 mL flame-dried Schlenk tube containing a stirring bar was added 1-(2,4,6-Trimethylphenyl)-3-(benzyl)imidazolium chloride **1a-d** (0.2 mmol, 63 mg, 1 equiv), indole **2a** (0.4 mmol, 47 mg, 1 equiv), Zn (0.04 mmol, 2.6 mg, 0.2 equiv), HCOONa (0.9 mmol, 61 mg, 4.5 equiv), HCOOH (0.6 mmol, 24 μL, 3 equiv) and anisole (1 mL) sequentially under nitrogen. The tube was sealed and stirred at 150 °C for 18 h. After completion, the reaction mixture was concentrated and purified by silica gel column chromatography to provide the product **3a-*d*** (14% D).**^{1}H NMR (400 MHz, DMSO-*d$_6$*)** δ 10.75 (s, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 2.4 Hz, 2H), 7.06 – 7.02 (m, 2H), 6.95 – 6.91 (m, 2H), 4.14 (s, 1.72H).





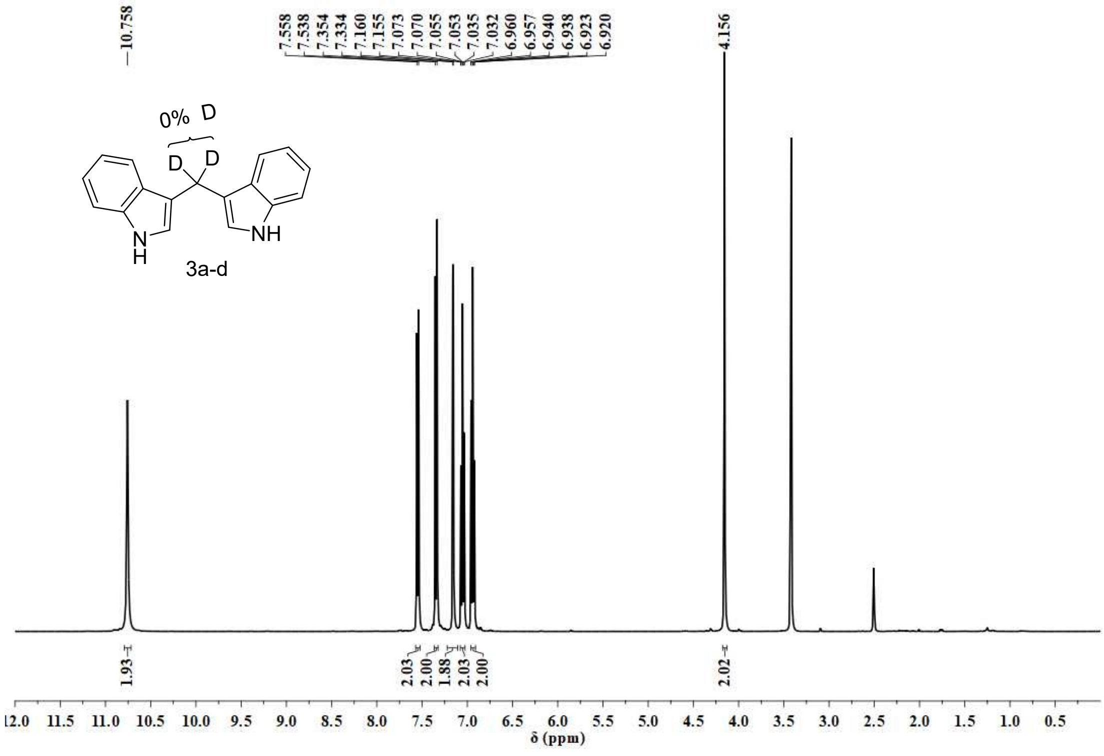
Experimental procedure:

To a 25 mL flame-dried Schlenk tube containing a stirring bar was added 1-(2,4,6-Trimethylphenyl)-3-(benzyl)imidazolium chloride **1a-d** (0.2 mmol, 63 mg, 1 equiv), Zn (0.04 mmol, 2.6 mg, 0.2 equiv), HCOONa (0.9 mmol, 61 mg, 4.5 equiv), HCOOH (0.6 mmol, 24 μL, 3 equiv) and anisole (1 mL) sequentially under nitrogen. The tube was sealed and stirred at 150 °C for 18 h. After completion, product was decomposed.

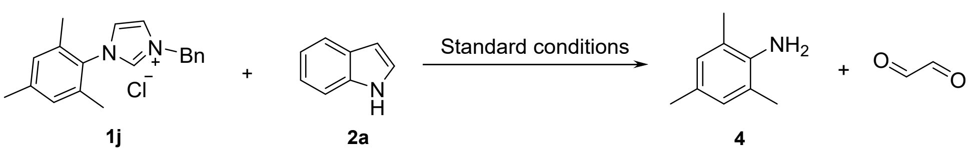


Experimental procedure:

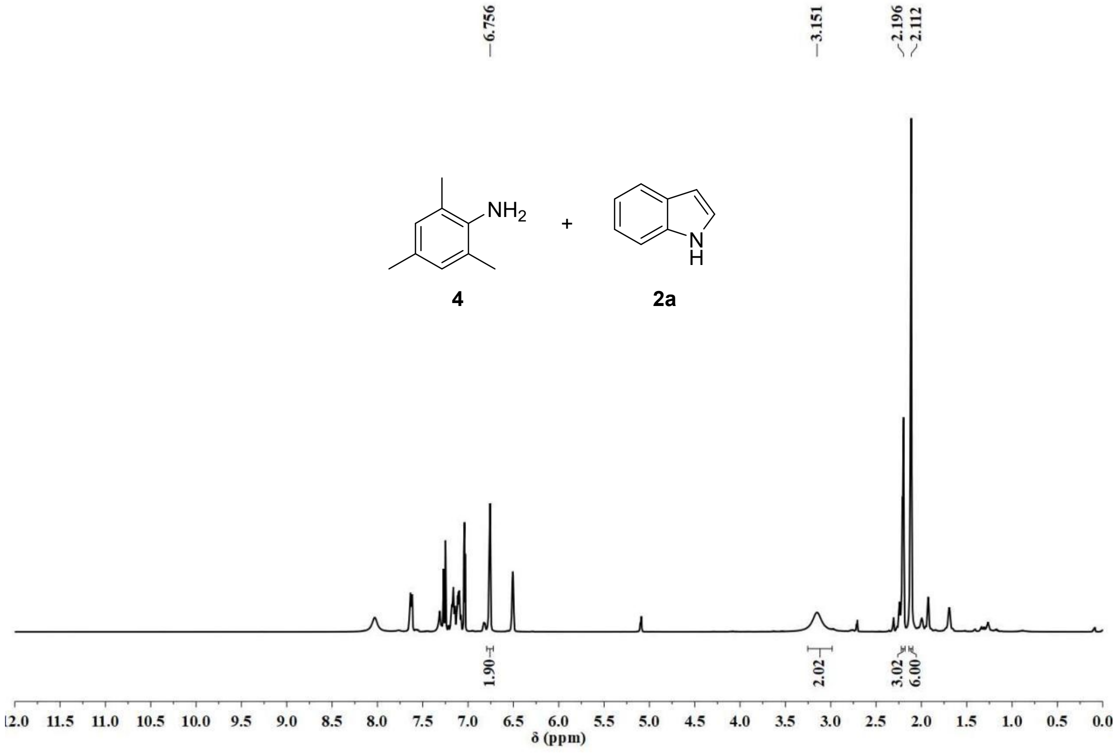
To a 25 mL flame-dried Schlenk tube containing a stirring bar was added di(1H-indol-3-yl)methane 3a (0.2 mmol, 49 mg, 1 equiv), Zn (0.04 mmol, 2.6 mg, 0.2 equiv), HCOONa (0.9 mmol, 61 mg, 4.5 equiv),HCOOH (0.6 mmol, 24 μL, 3 equiv) and D_2O (0.4 mmol, 8 μL, 2 equiv) and anisole (1 mL)sequentially under nitrogen. The tube was sealed and stirred at 150 °C for 18 h. After completion, the reaction mixture was concentrated and purified by silica gel column chromatography to provide the product 3a-d (0% D).^{1}**H NMR (400 MHz, DMSO-*d*$_6$)** δ 10.76 (s, 2H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 2.0 Hz, 2H), 7.07 – 7.03 (m, 2H), 6.96 – 6.92 (m, 2H), 4.16 (s, 2H).



4.1 The detection of the side product



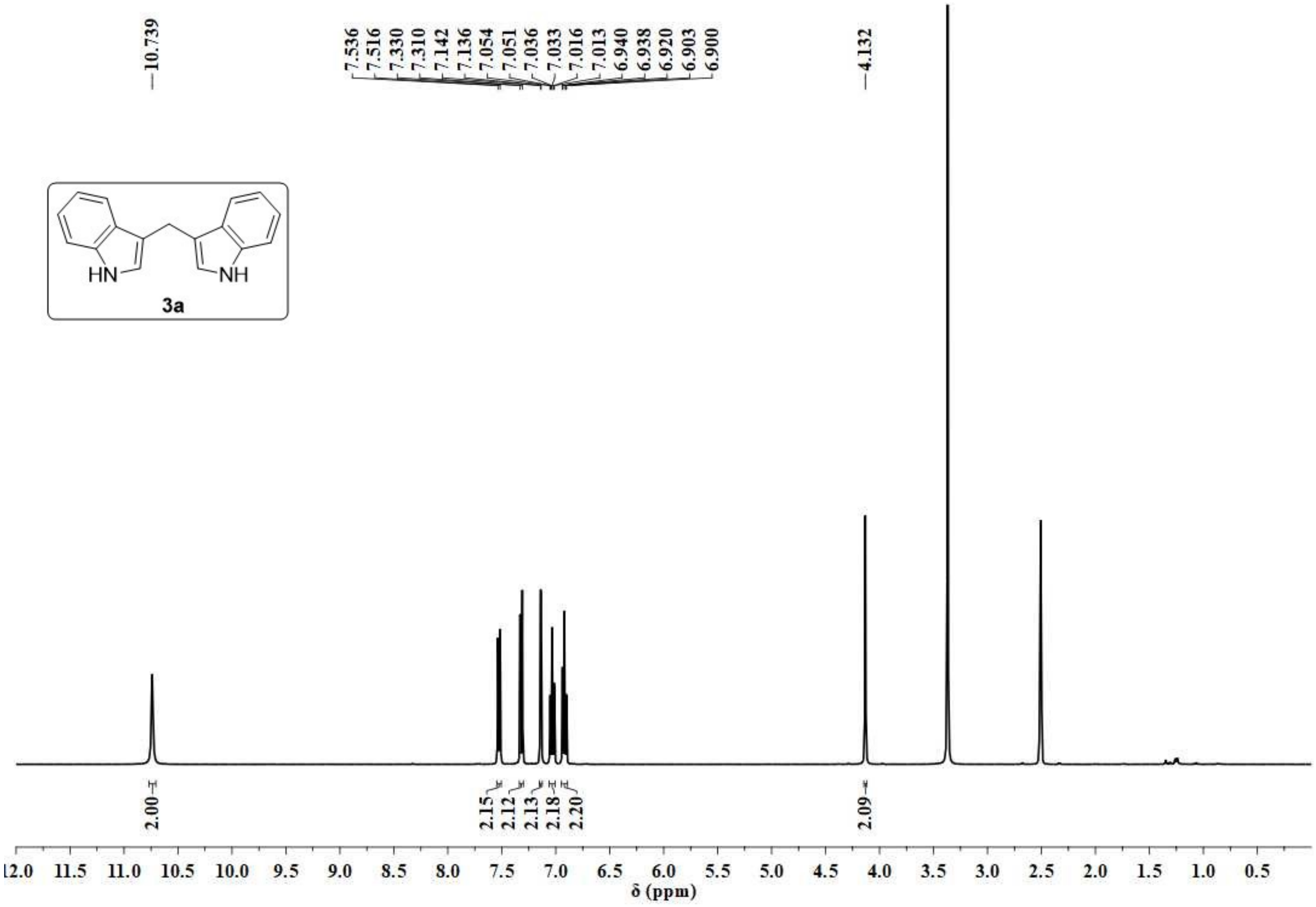
To a 25 mL flame-dried Schlenk tube containing a stirring bar was added 1-(2,4,6-trimethylphenyl)-3-(benzyl)imidazolium chloride **1j** (0.2 mmol, 63 mg, 1 equiv), indole **2a** (0.4 mmol, 47 mg, 1 equiv), Zn (0.04 mmol, 2.6 mg, 0.2 equiv), HCOONa (0.9 mmol, 61 mg, 4.5 equiv), HCOOH (0.6 mmol, 24 μL, 3 equiv) and anisole (1 mL) sequentially under nitrogen. The tube was sealed and stirred at 150 °C for 18 h. After completion, the unseparable mixture was isolated and the structure of side product **4** was determined by ^{1}H NMR analysis. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 6.73 (s, 1H), 2.42 (s, 3H), 2.33 (s, 6H).

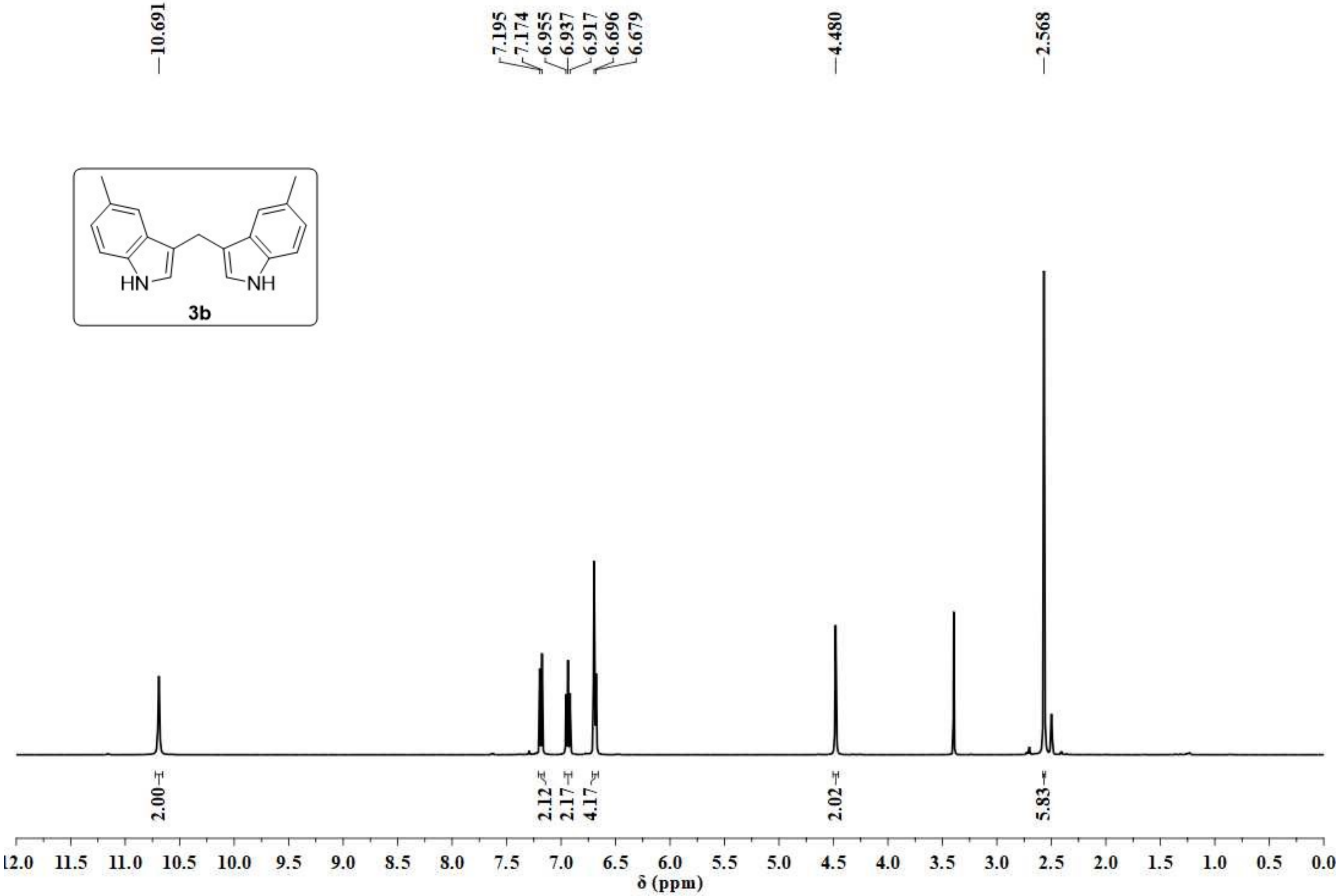


5. Reference

1. A. Beillard, X. Bantreil, T.-X. Metro and J. Martinez, *Green Chem.*, 2018, **20**, 964.
2. M. Hans and L. Delaude, *Org. Synth.*, 2010, **87**, 77.
3. P.-Q. Huang and H. Chen, *Chem. Comm.,* 2017, **53**, 12584.
4. A. Levens, F. An, M. Breugst, H. Mayr and D. Lupton, *Org. Lett.*, 2016, **18**, 3566.
5. E. Kolychev, I. Portnyagin, V. Shuntikov, V. Khrustalev and M. Nechaev, *J. Org. Chem.*, 2009, **694**, 2454.
6. T. Maishal, J. Alauzun, J.-M. Basset, C. Coperet, R. Corriu, E. Jeanneau, A. Mehdi, C. Reye, L. Veyre and C. Thieuleux, *Angew. Chem. Int. Ed.*, 2008, **47**, 8654.
7. W. Qiang, X. Liu and T.-P. Loh, *ACS Sustainable Chem. Eng.*, 2019, **7**, 8429.
8. T. Pillaiyar, E. Gorska, G. Schnakenburg and C. Mueller, *J. Org. Chem.,* 2018, **83**, 9902.
9. G. Li, C. Wang, Y. Li, K. Shao, G. Yu and S. Wang, *Chem. Commun.*, 2020, **56**, 7333.
10. H. Zhang, H.-Y. Wang, Y. Luo and C. Chen, *ACS Catal.*, 2018, **8**, 2173.

6. ^{1}H and ^{13}C NMR spectra

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6.679
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NH
3b
2.00
2.12
2.17
4.17
2.02
5.83
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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1.5
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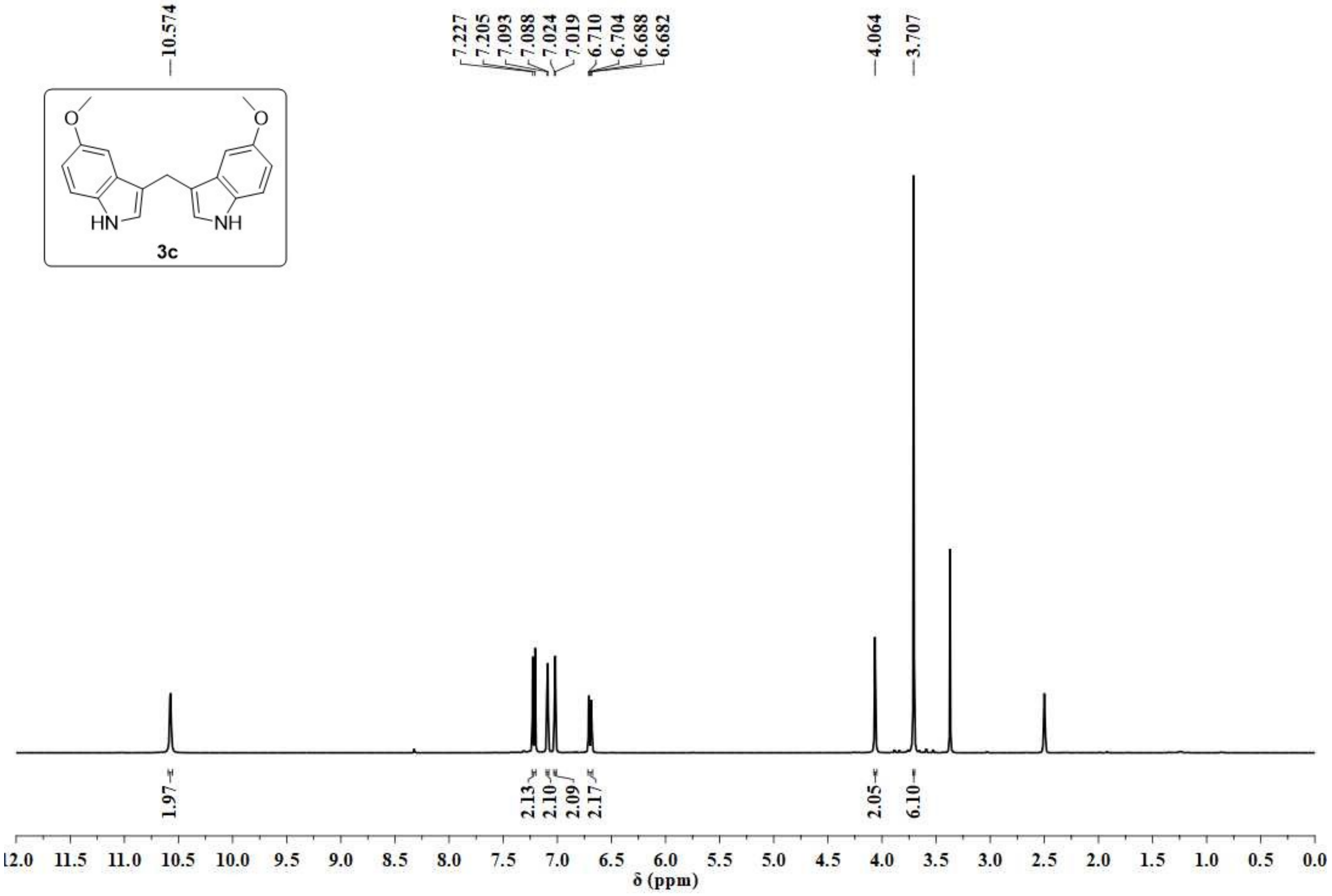
δ (ppm)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O
O
HN
NH
3c
1.97
2.13
2.10
2.09
2.17
2.05
6.10
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
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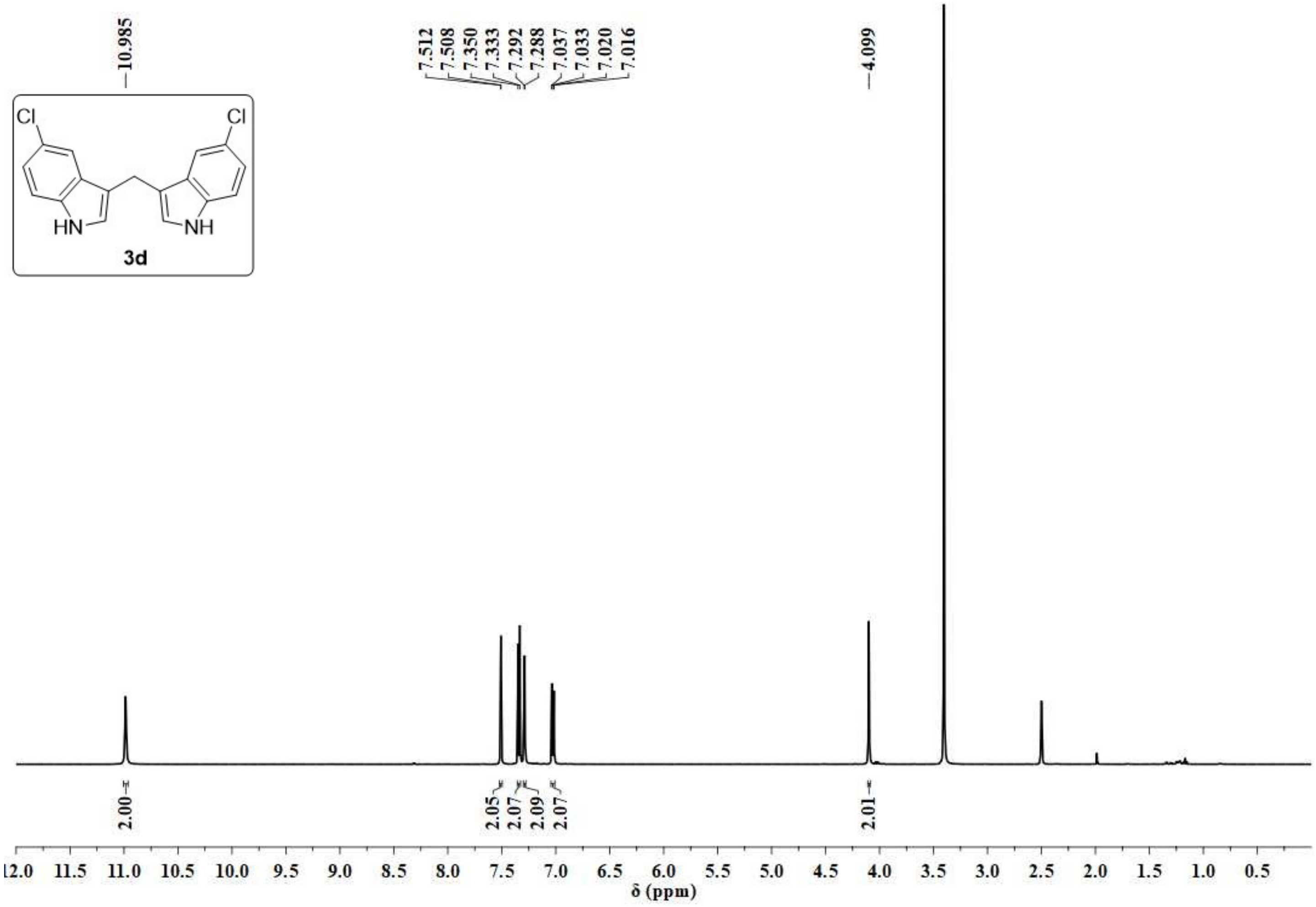
δ (ppm)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Cl
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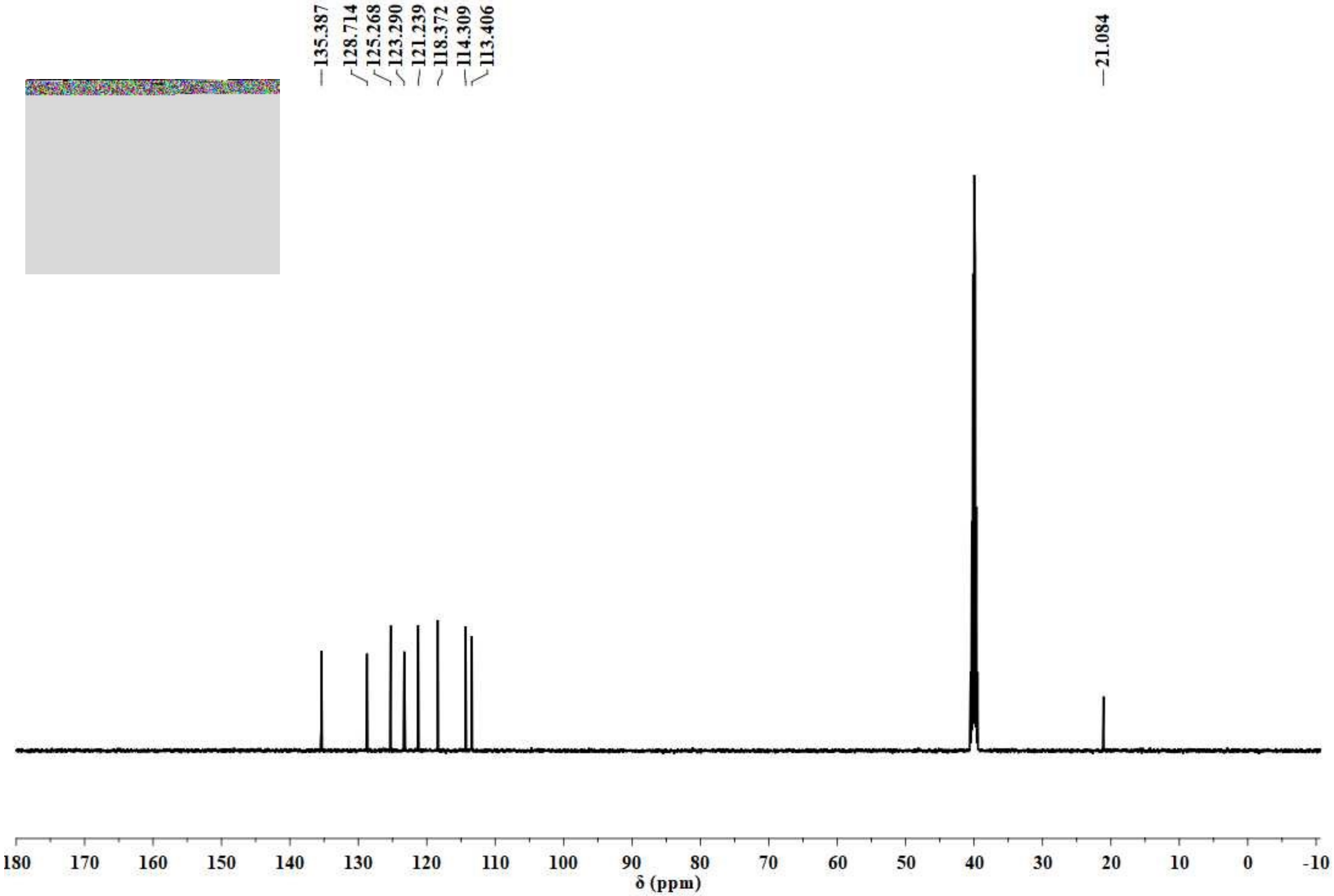
NH
2.00
2.05
2.07
2.09
2.07
2.01
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
δ (ppm)

3d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120
110
100
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40
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20
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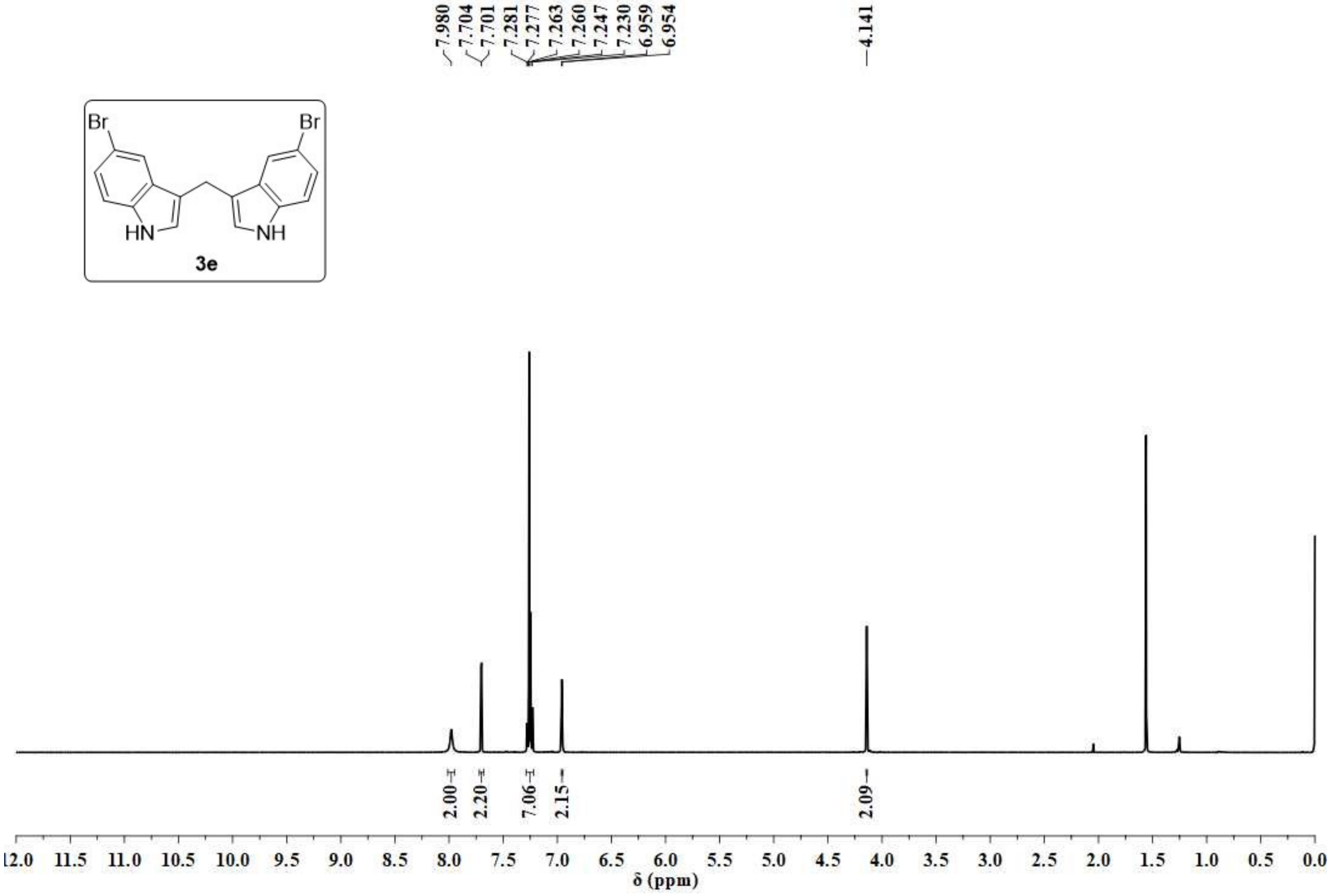
δ (ppm)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2.09
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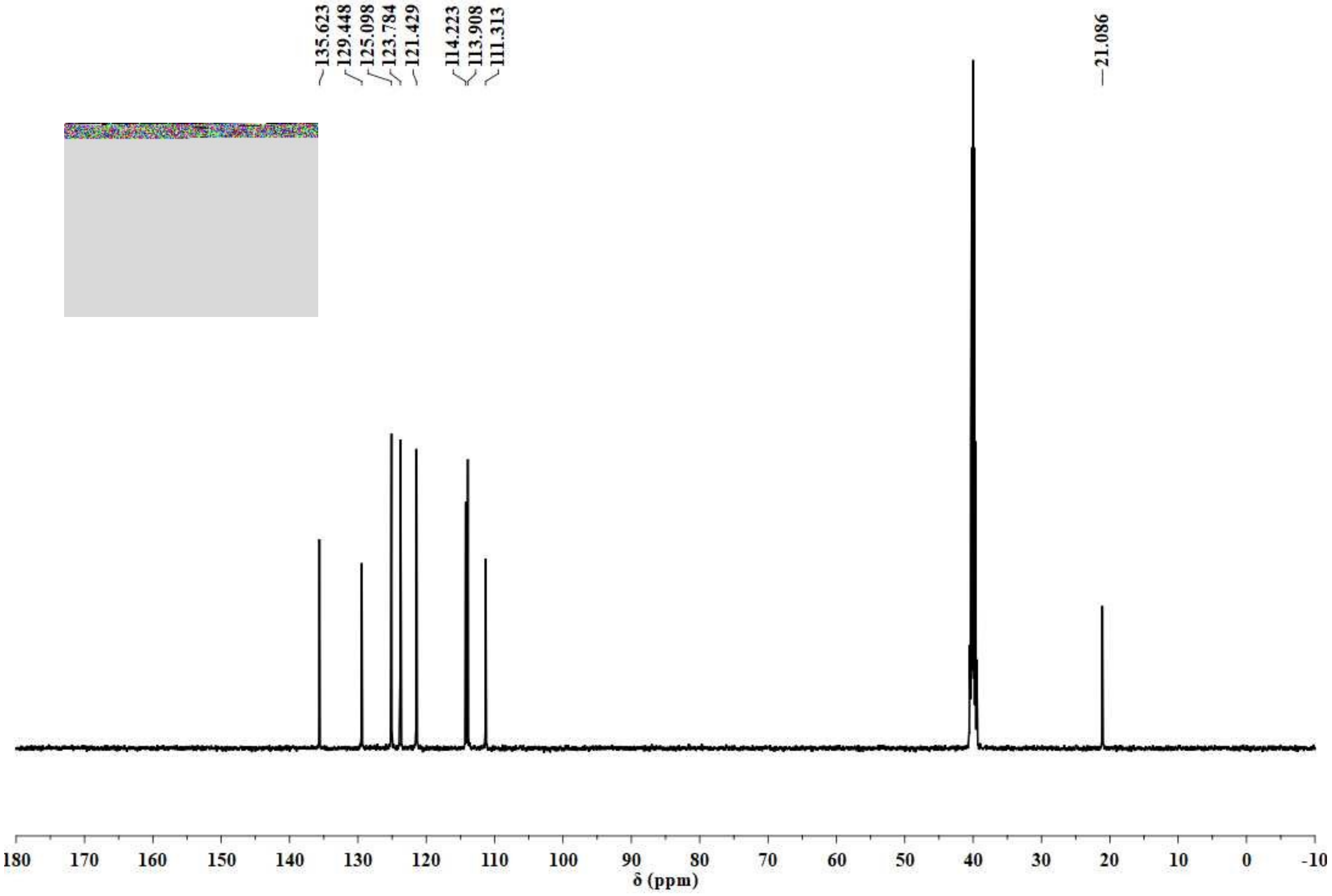
δ (ppm)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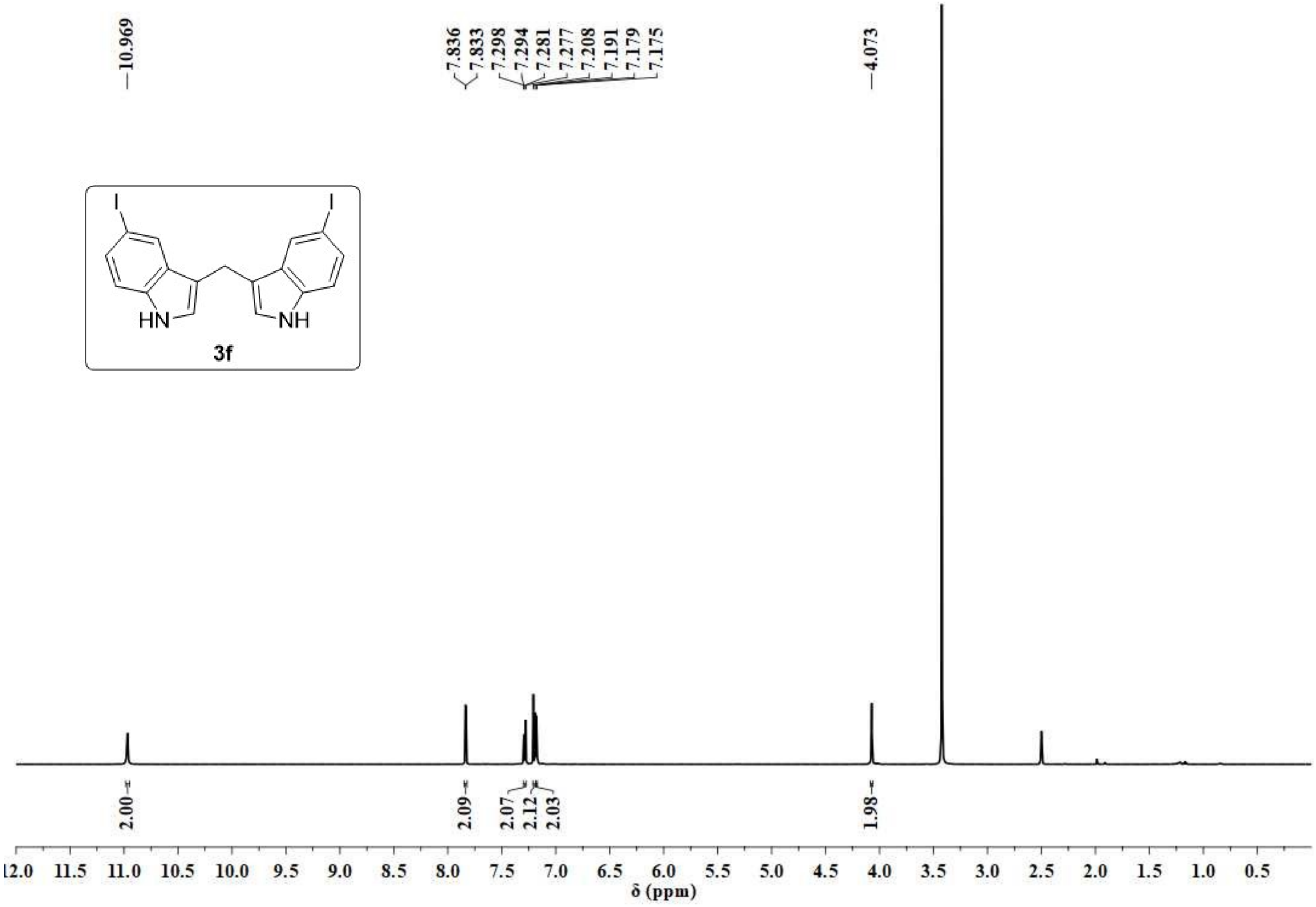
δ (ppm)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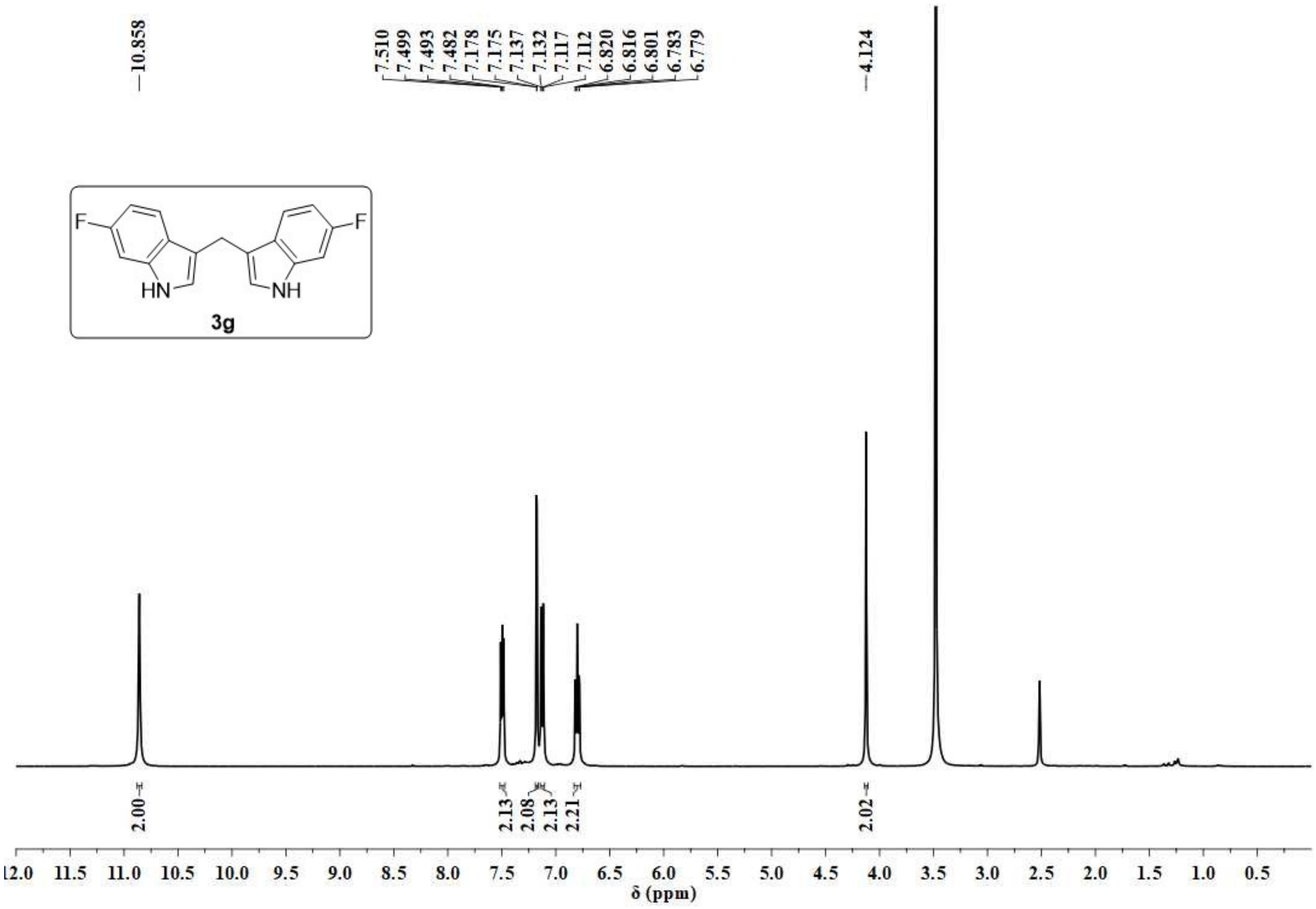
2.09
2.07
2.12
2.03
1.98
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
δ (ppm)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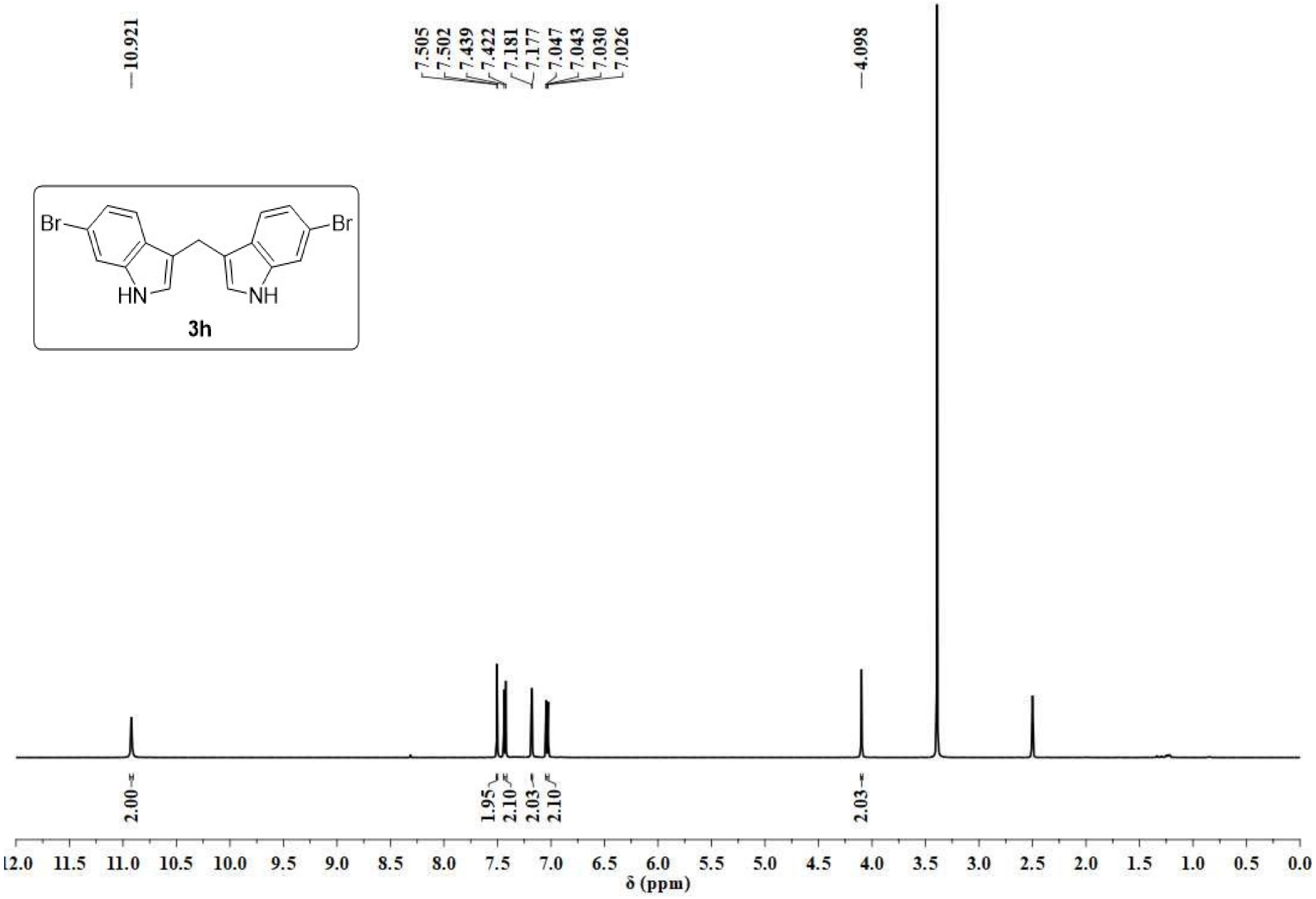
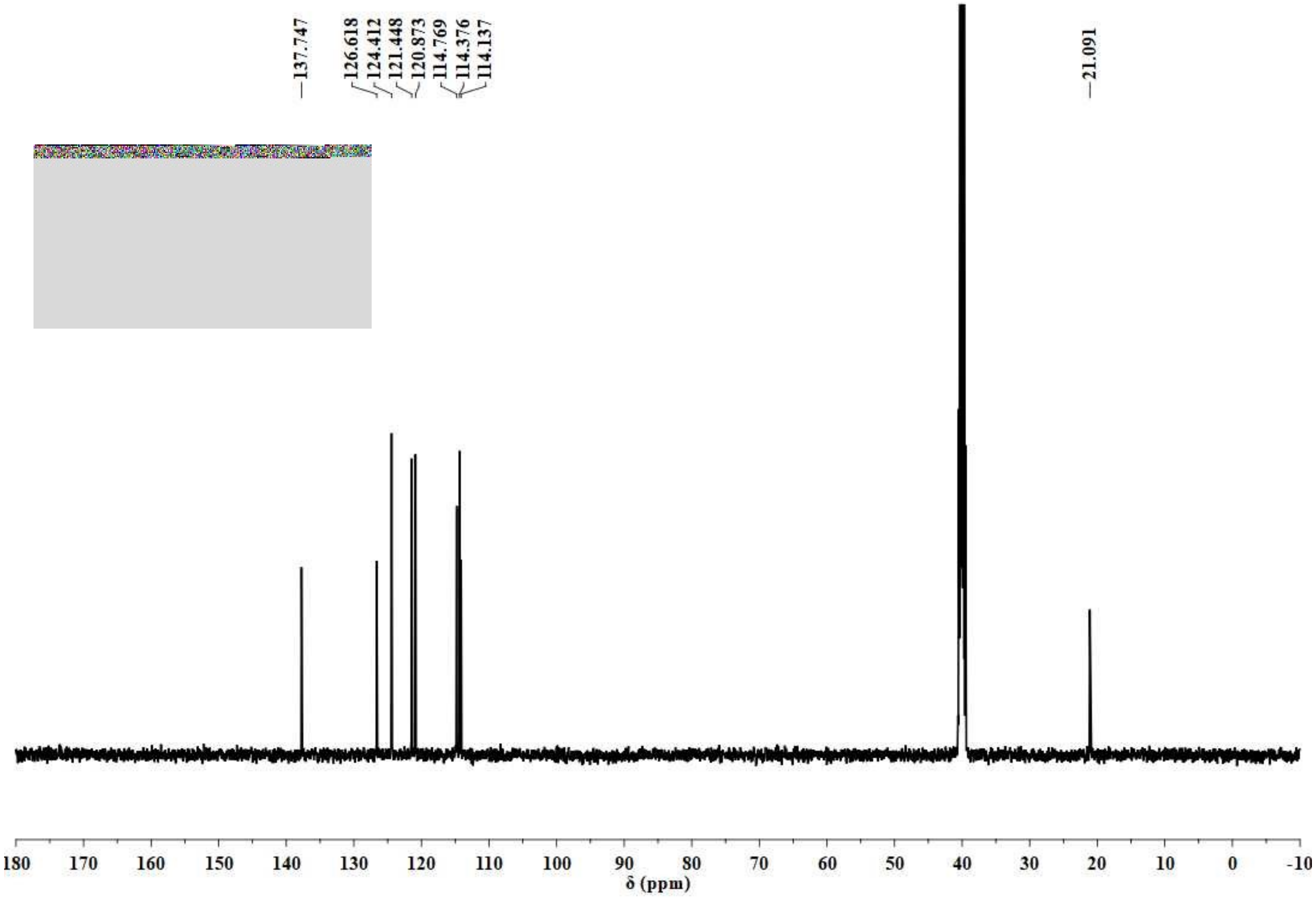
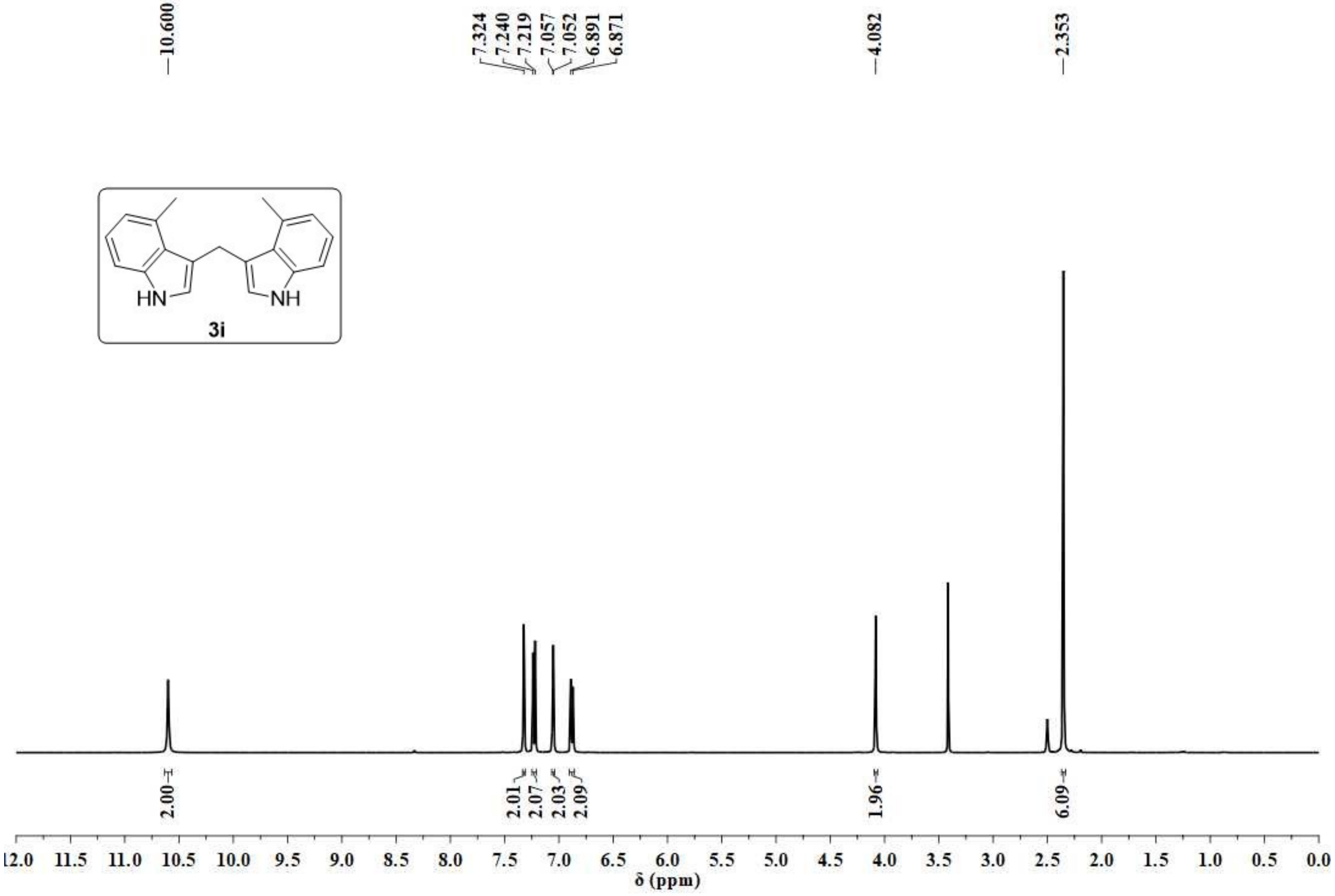
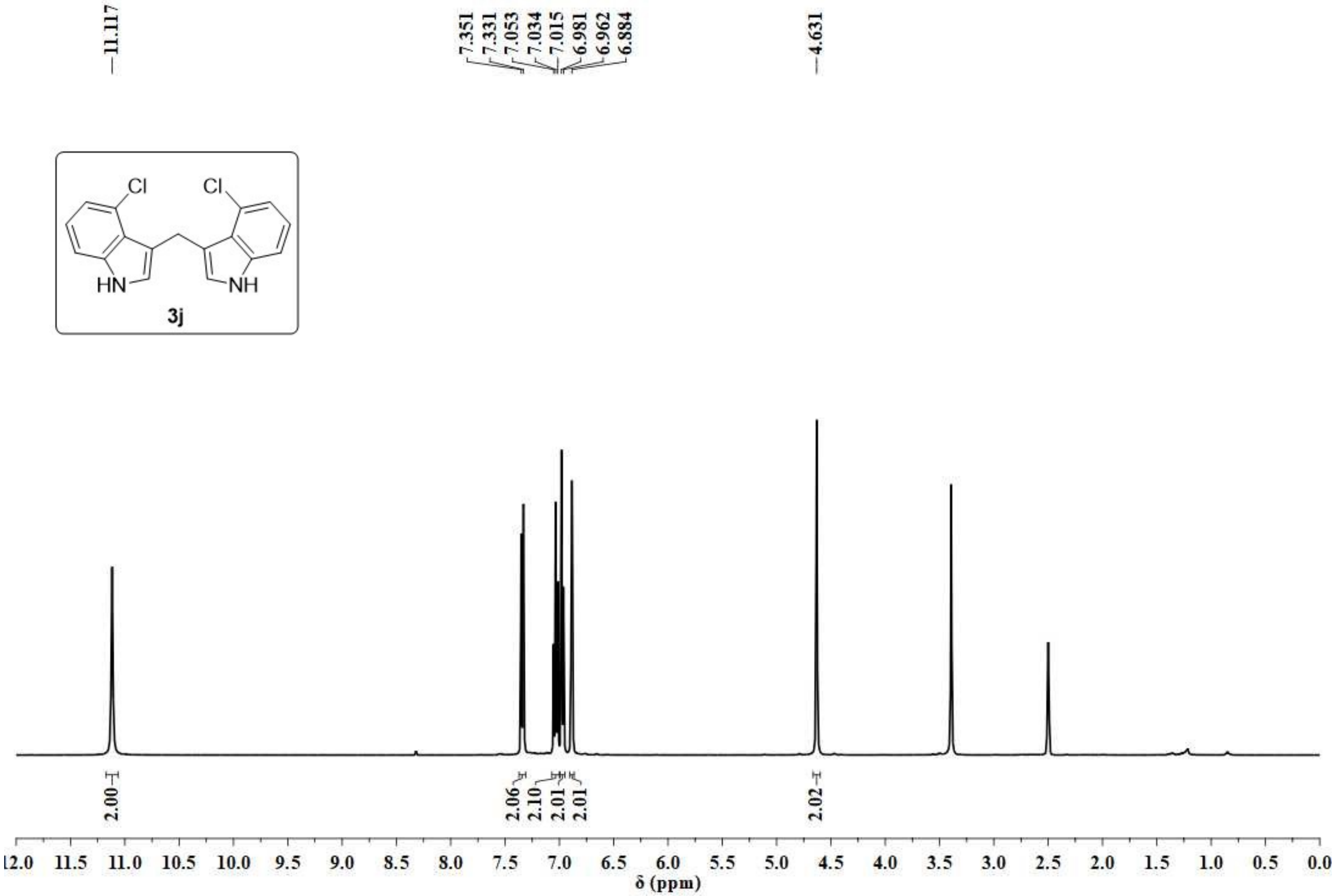
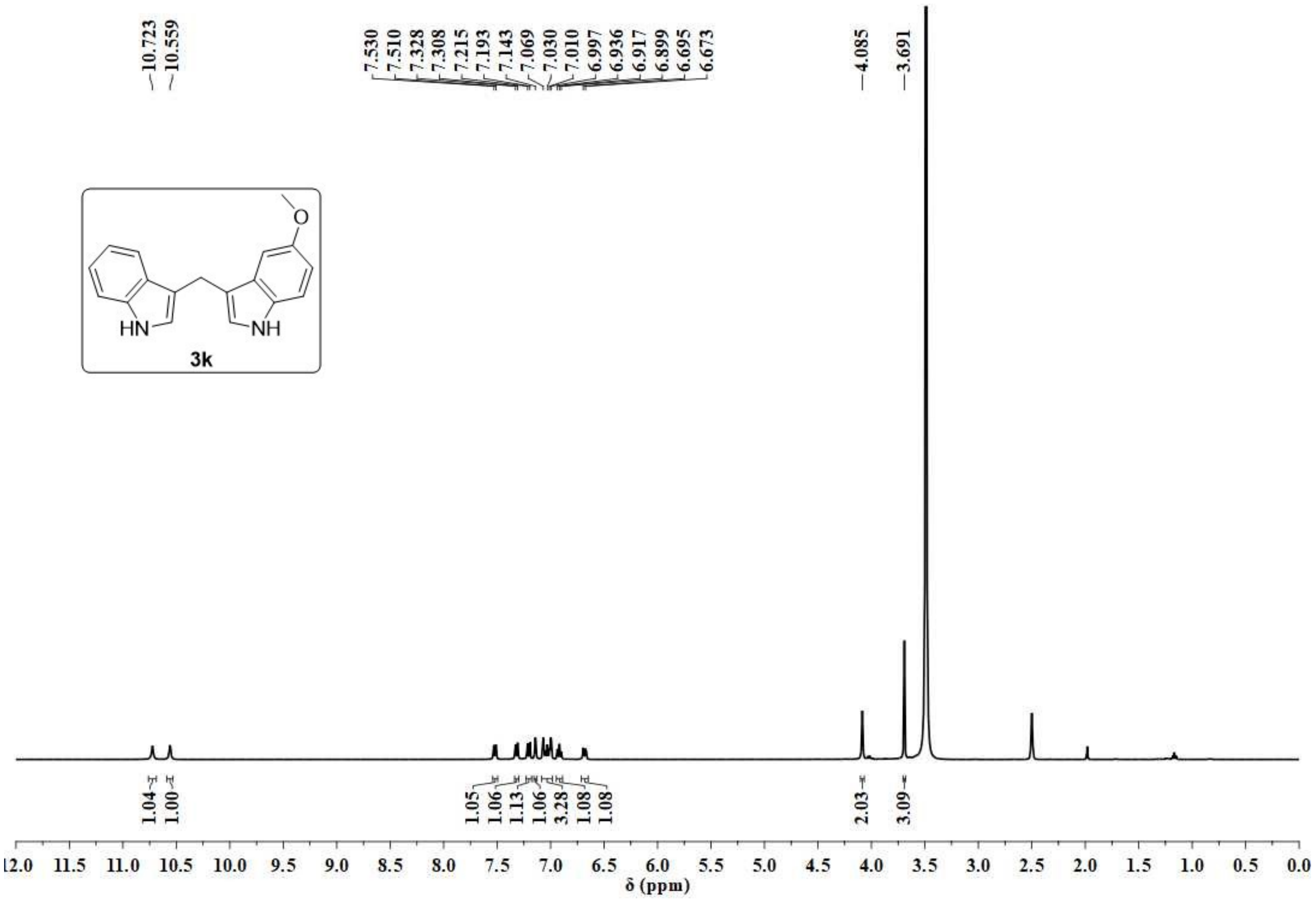
7.510
7.499
7.493
7.482
7.178
7.175
7.137
7.132
7.117
7.112
6.820
6.816
6.801
6.783
6.779
4.124
F
F
HN
NH
3g
2.00
2.13
2.08
2.13
2.21
2.02
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
δ (ppm)

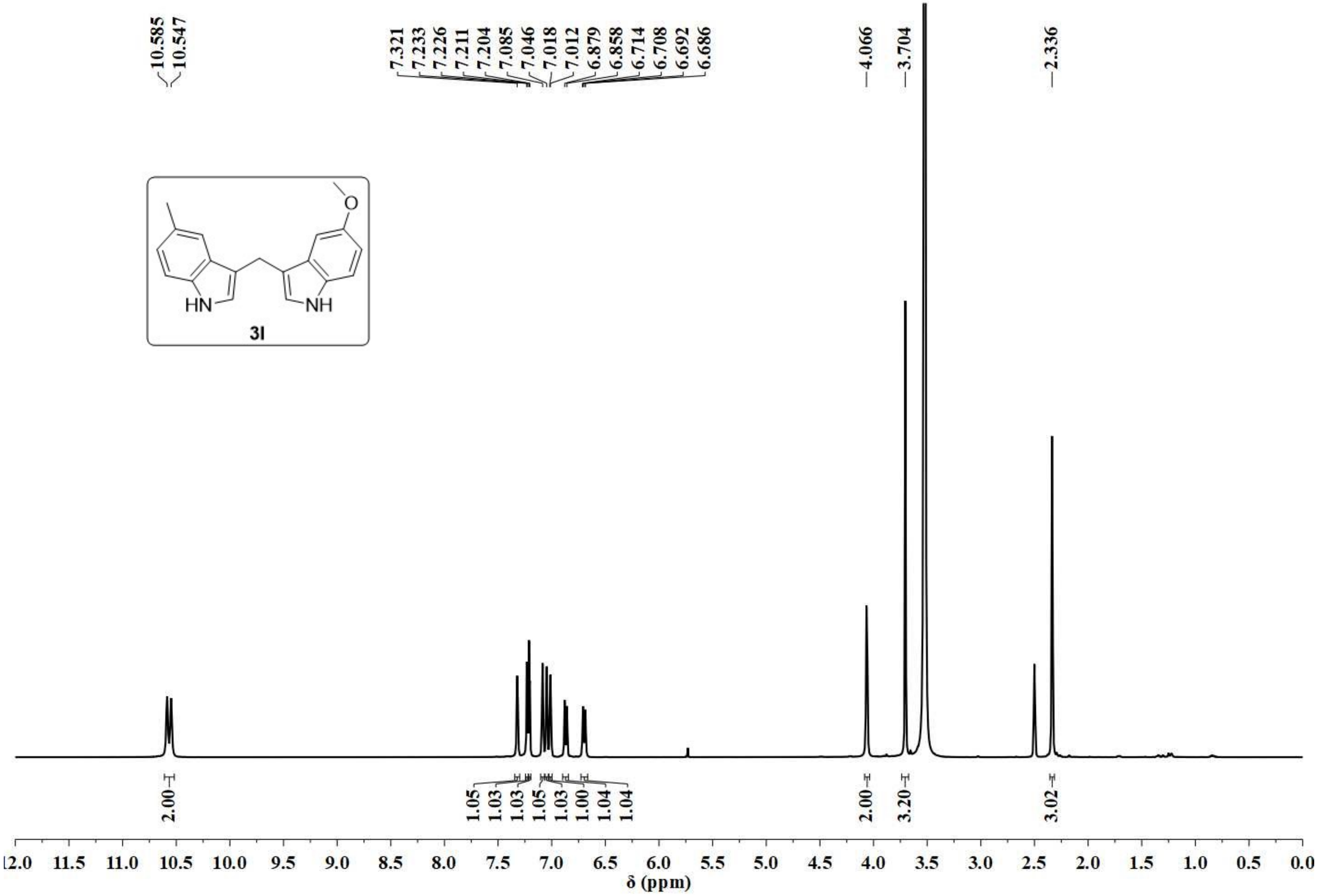

10.921
7.505
7.502
7.439
7.422
7.181
7.177
7.047
7.043
7.030
7.026
4.098
Br
Br
HN
NH
3h
2.00
1.95
2.10
2.03
2.10
2.03
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)

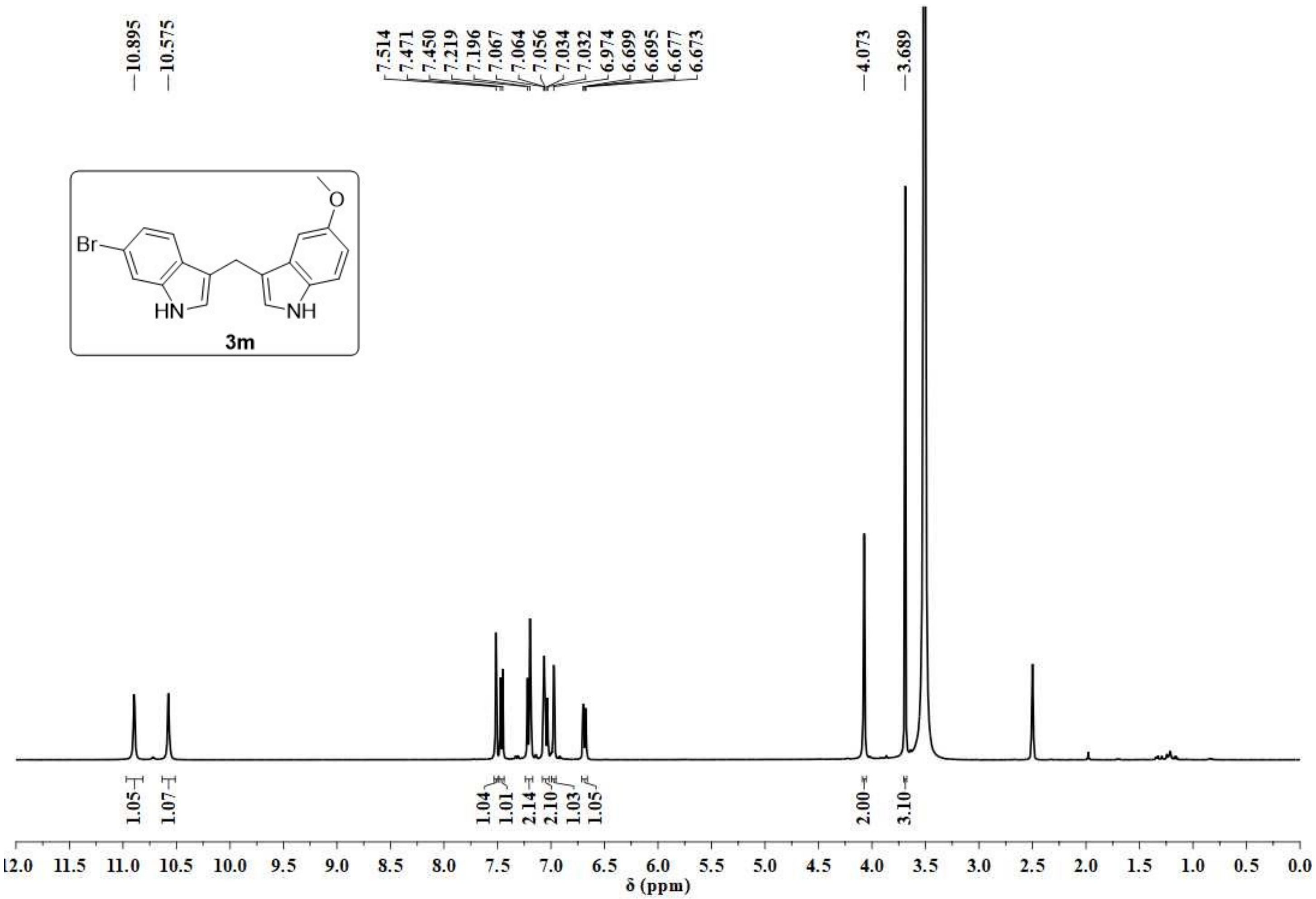

137.747
126.618
124.412
121.448
120.873
114.769
114.376
114.137
21.091
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
δ (ppm)

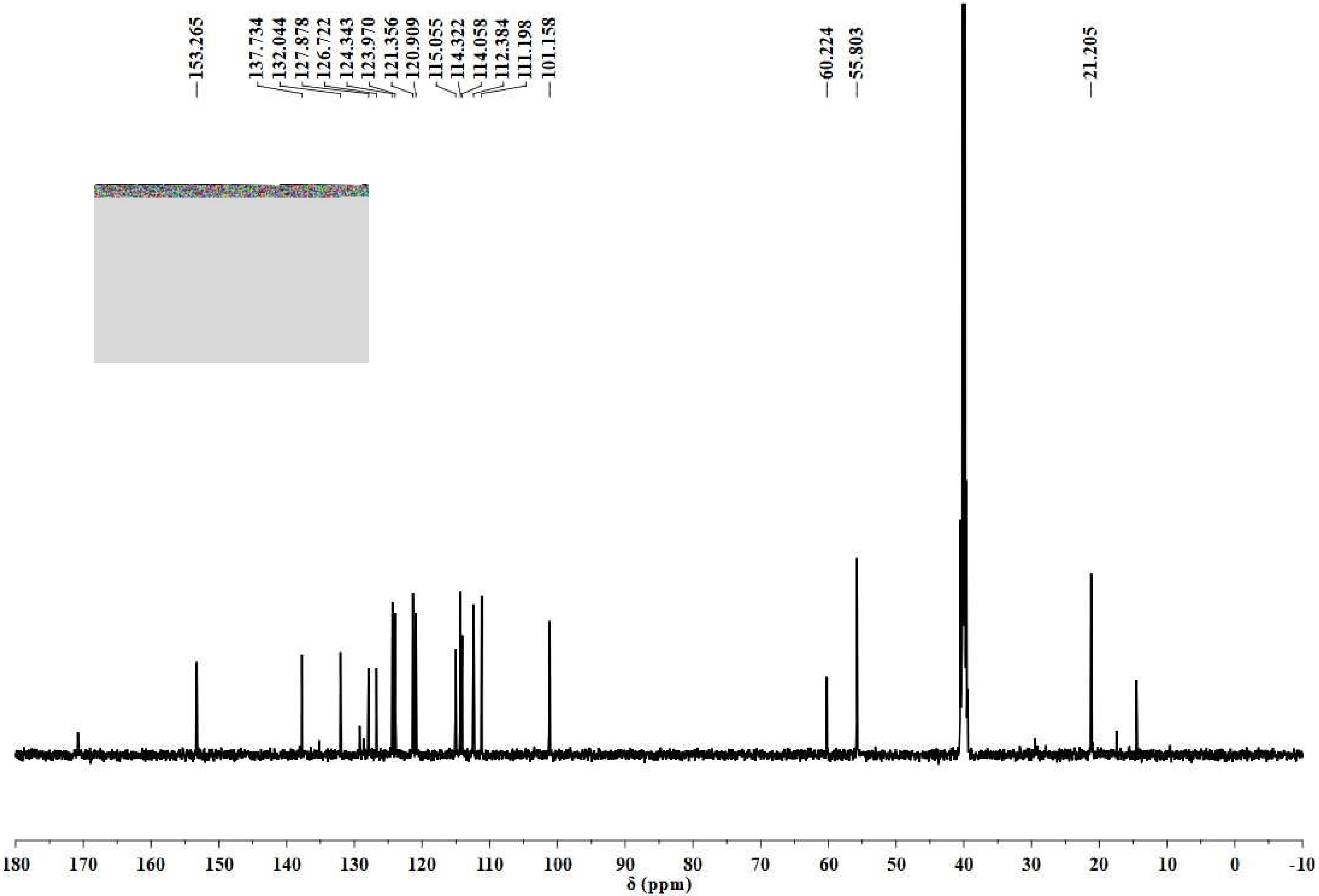

10.600
7.324
7.240
7.219
7.057
7.052
6.891
6.871
4.082
2.353
HN
NH
3i
2.00
2.01
2.07
2.03
2.09
1.96
6.09
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)

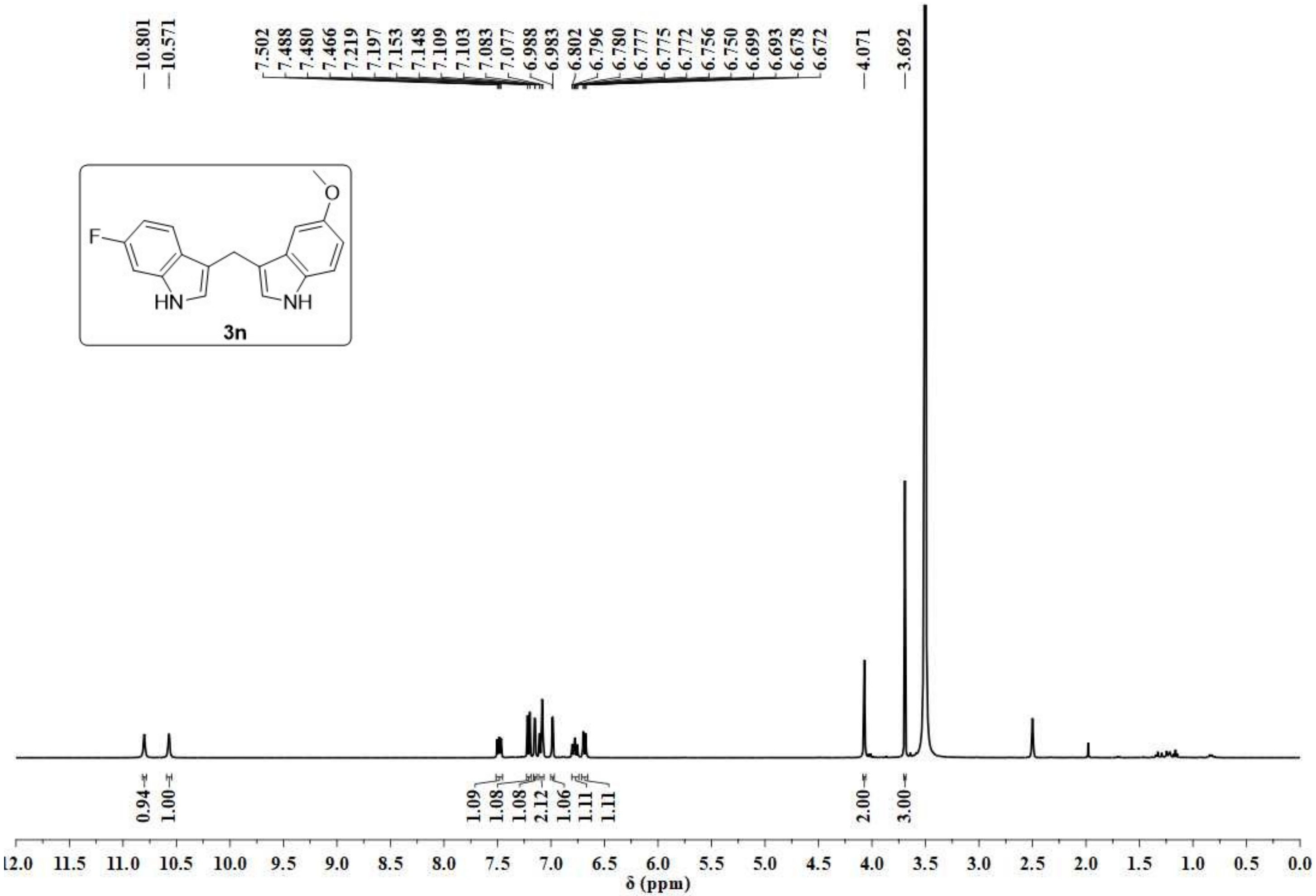

11.117
7.351
7.331
7.053
7.034
7.015
6.981
6.962
6.884
4.631
Cl
Cl
HN
NH
3j
2.00
2.06
2.10
2.01
2.01
2.02
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)

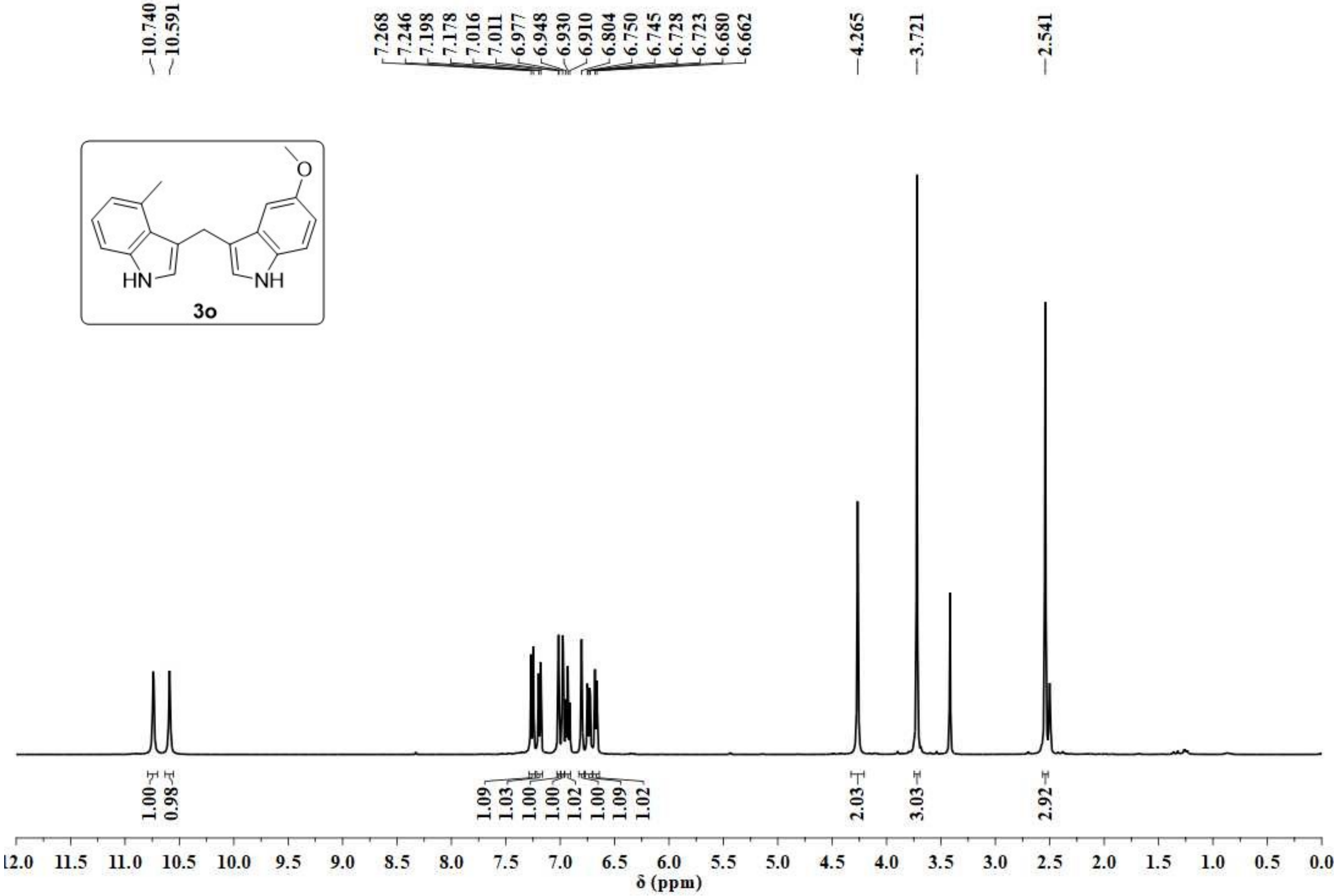

10.723
10.559
7.530
7.510
7.328
7.308
7.215
7.193
7.143
7.069
7.030
7.010
6.997
6.936
6.917
6.899
6.695
6.673
4.085
3.691
O
HN
NH
3k
1.04
1.00
1.05
1.06
1.13
1.06
3.28
1.08
1.08
2.03
3.09
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)

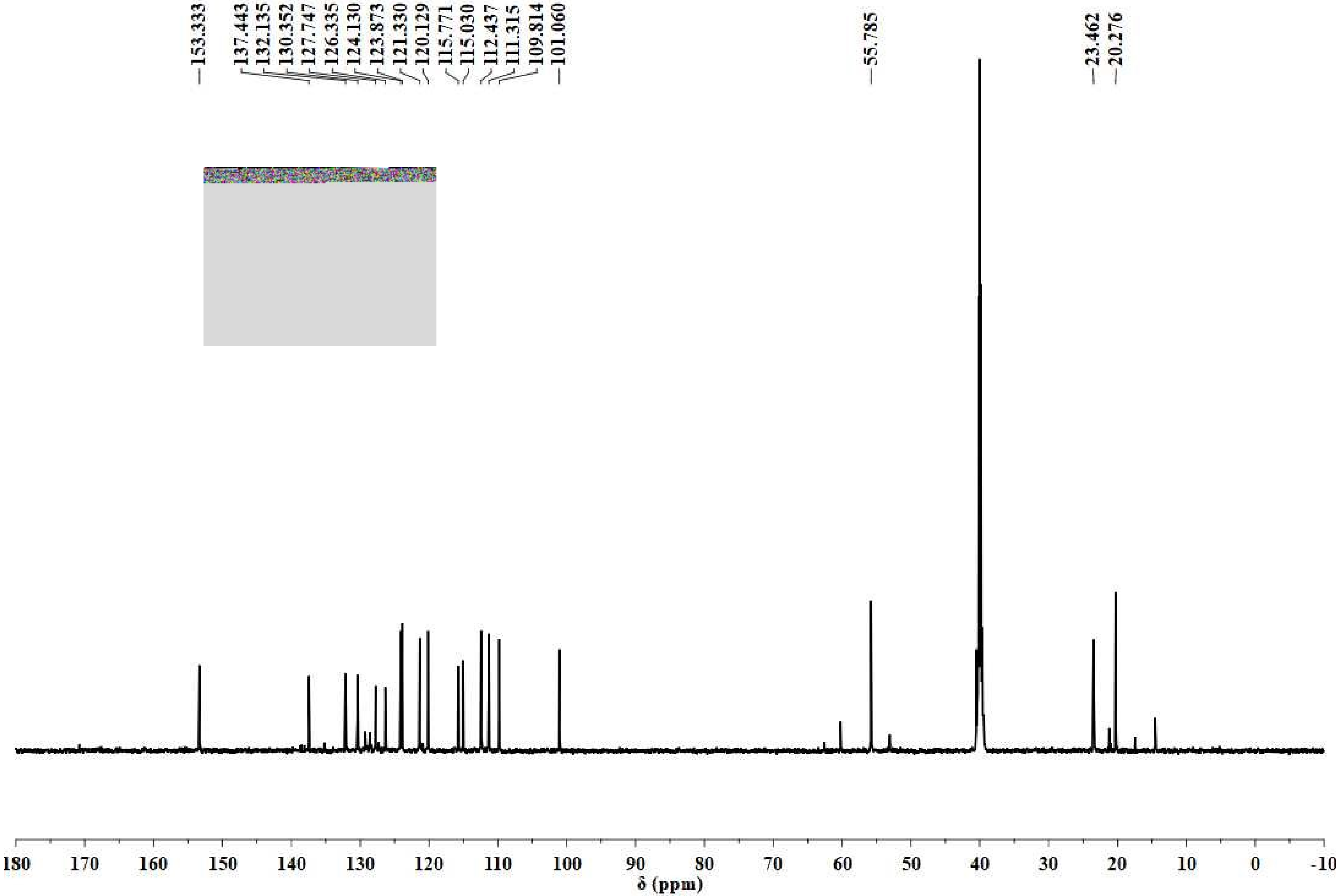

10.585
10.547
7.321
7.233
7.226
7.211
7.204
7.085
7.046
7.018
7.012
6.879
6.858
6.714
6.708
6.692
6.686
4.066
3.704
2.336
O
HN
NH
3l
2.00
1.05
1.03
1.03
1.05
1.03
1.00
1.04
1.04
2.00
3.20
3.02
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)


10.895
10.575
7.514
7.471
7.450
7.219
7.196
7.067
7.064
7.056
7.034
7.032
6.974
6.699
6.695
6.677
6.673
4.073
3.689
Br
HN
NH
O
3m
1.05
1.07
1.04
1.01
2.14
2.10
1.03
1.05
2.00
3.10
12.0
11.5
11.0
10.5
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
δ (ppm)


153.265
137.734
132.044
127.878
126.722
124.343
123.970
121.356
120.909
115.055
114.322
114.058
112.384
111.198
101.158
60.224
55.803
21.205
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
δ (ppm)


10.801
10.571
7.502
7.488
7.480
7.466
7.219
7.197
7.153
7.148
7.109
7.103
7.083
7.077
6.988
6.983
6.802
6.796
6.780
6.777
6.775
6.772
6.756
6.750
6.699
6.693
6.678
6.672
4.071
3.692
F
O
HN
NH
3n
0.94
1.00
1.09
1.08
1.08
2.12
1.06
1.11
1.11
2.00
3.00
12.0
11.5
11.0
10.5
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
δ (ppm)


10.740
10.591
7.268
7.246
7.198
7.178
7.016
7.011
6.977
6.948
6.930
6.910
6.804
6.750
6.745
6.728
6.723
6.680
6.662
4.265
3.721
2.541
HN
NH
O
3o
1.00
0.98
1.09
1.03
1.00
1.00
1.02
1.00
1.09
1.02
2.03
3.03
2.92
12.0
11.5
11.0
10.5
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
δ (ppm)


153.333
137.443
132.135
130.352
127.747
126.335
124.130
123.873
121.330
120.129
115.771
115.030
112.437
111.315
109.814
101.060
55.785
23.462
20.276
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
δ (ppm)