Supporting Information

Oxidation of Tetrahydro-β-carbolines by Persulfate

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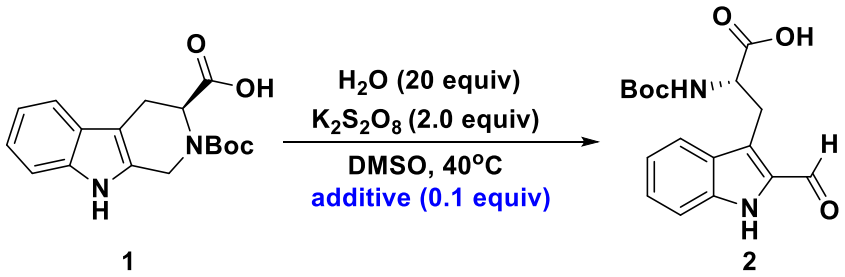
1. General Information

All reactions were performed under a designated atmosphere with anhydrous solvent in flame-dried round bottom flasks, magnetically stirred, unless otherwise noted. All reactions were performed at room temperature (r.t., approximately 25 °C), unless otherwise noted. Preparative column chromatography was performed using silica gel 60, particle size 0.063–0.200 mm (70–230 mesh, flash). Analytical TLC was carried out employing silica gel 60 F254 plates (Merck, Darmstadt). Visualization of the developed chromatograms was performed with detection by UV (254 nm and 365 nm). Preparative thin layer chromatography (PTLC) separations were carried out on 0.20 mm Yantai Jiangyou silica gel plates (HSGF254). ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on a Bruker-400 (^{1}H, 400 MHz; ^{13}C, 101 MHz) spectrometer in a suitable deuterated solvent. Chemical shifts for protons are reported in parts per million and are references to the NMR solvent peak ($CDCl_3$: δ 7.26; DMSO-d_6: 2.50). Chemical shifts for carbons are reported in parts per million and are referenced to the carbon resonances of the NMR solvent ($CDCl_3$: δ 77.16; DMSO-d_6: 39.52). Signals are listed in ppm, and multiplicity identified as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Chemical shifts were expressed in ppm, and *J* values were given in Hz. High resolution mass Spectrum (HRMS) were obtained from Thermo Fisher Scientific Exactive Plus mass spectrometer. Melting point was determined using the X-4A melting point apparatus (Shanghai Yidian Co., Ltd.) and uncorrected. Concentration under reduced pressure was performed by rotary evaporation at 25-35 °C at appropriate pressure. Purified compounds were further dried under high vacuum (0.01-0.10 Torr). Yields refer to purified and spectroscopically pure compounds, unless otherwise noted. All commercially available starting materials and solvents were reagent grade, and used without further purification.

Abbreviations used: TLC = thin layer chromatography; DMA = *N,N*-dimethylacetamide; DMF = dimethylformamide; DMSO = dimethyl sulfoxide; EtOAc = ethyl acetate; THF = tetrahydrofuran; NMA = *N*-methylacetamide; $TEAPF_6$ = tetraethylammonium hexafluorophosphate; TOAS = methyltrioctyl ammonium hydrogen sulfate; TMAC = tetrabutyl ammonium chloride; TBAC = tetrabutyl ammonium chloride; TEACl = tetraethylammonium Chloride; TMACl = tetramethylammonium chloride; TBAI = tetrabutylammonium iodide; TEAB = tetraethyl ammonium bromide; $TBAF_4$ = tetrabutylammonium tetrafluoroborate; 2-MeTHF = 2-methyltetra-hydrofuran; TBAC = *tert*-butyl acetate; AcOH = acetic acid; PE = petroleum ether; Vc = ascorbic acid; TEMPO = 2,2,6,6-tetramethylpiperidine-1-oxyl.

2. Optimization Studies

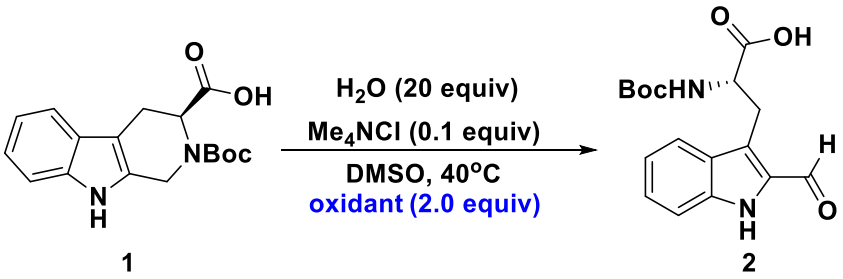
Table S1: Investigation of Additives



Entry[a]	Additive	Yield[b]	Entry	Additive	Yield[b]
1	**TMACl**	**93**	6	$TBAF_4$	<72
2	TEACl	<75	7	TMAC	<78
3	TBAI	<70	8	TBAC	<80
4	TEAB	<65	9	$TEAPF_6$	<62
5	TOAS	<67	10	-	66

[a] Reaction conditions: Unless otherwise noted, all reactions were carried out with THβC **1** (0.1 mmol) in 1.0 mL of DMSO, different additive (0.1 eqiuv) and $K_2S_2O_8$ (2.0 equiv) was added. Then H_2O (20 equiv) was added into the mixture. The reaction mixture was stirred for another 6 h. [b] All yields were determined by ^1H NMR analysis of the crude products using 1,3,5-trimethoxybenzene as an internal standard.

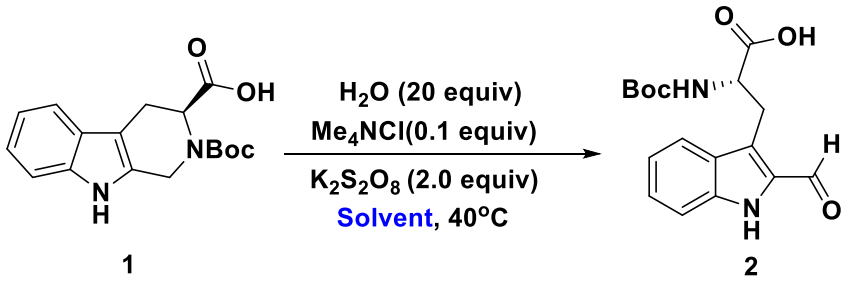
Table S2: Investigation of oxidants



Entry[a]	Oxidant	equiv	Yield[b]
1	$K_2S_2O_8$	0	0
2	$K_2S_2O_8$	1	82
3	**$K_2S_2O_8$**	**2**	**93**
4	$K_2S_2O_8$	5	<90
5	$Na_2S_2O_8$	1	<70
7	$Na_2S_2O_8$	2	82
8	$(NH_4)_2S_2O_8$	1	<30
9	$(NH_4)_2S_2O_8$	2	38

[a] Reaction conditions: Unless otherwise noted, all reactions were carried out with THβC **1** (0.1 mmol) in 1.0 mL of DMSO, different oxidant (0-5 equiv), Me_4NCl (0.1 equiv) was added. Then H_2O (20 equiv) was added into the mixture. The reaction mixture was stirred for another 6 h. [b] All yields were determined by ^1H NMR analysis of the crude products using 1,3,5-trimethoxybenzene as an internal standard.

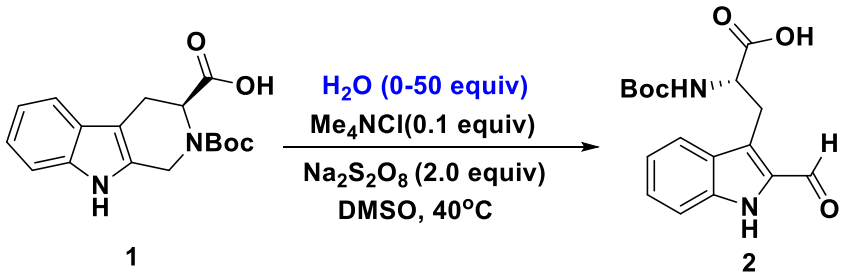
Table S3: Investigation of solvents



Entry[a]	Solvent	Yield[b]	Entry	Solvent	Yield[b]
1	DMF	trace	9	NMR	<35
2	2-MeTHF	<30	10	EtOAc	trace
3	MeOAc	<50	11	DMA	46
4	THF	trace	12	CH_2ClCH_2Cl	trace
5	CH_3CN	trace	**13**	**DMSO**	**93**
6	DMF	trace	14	H_2O	trace
7	$CHCl_3$	<60	15	MeOH	<40
8	EtOH	trace	16	$CHCl_2$	<30

[a] Reaction conditions: Unless otherwise noted, all reactions were carried out with THβC **1** (0.1 mmol) in different solvent (1 mL), Me_4NCl (0.1 equiv) and $Na_2S_2O_8$ (2.0 equiv) was added. Then H_2O (20 equiv) was added into the mixture. The reaction mixture was stirred for another 6 h. [b] All yields were determined by ^1H NMR analysis of the crude products using 1,3,5-trimethoxybenzene as an internal standard.

Table S4: Investigation of H_2O



Entry[a]	H_2O (equiv)	Yield[b]	Entry	H_2O (equiv)	Yield[b]
1	0	0	4	10	82
2	1	<56	**5**	**20**	**93**
3	5	75	6	50	<88

[a] Reaction conditions: Unless otherwise noted, all reactions were carried out with THβC **1** (0.1 mmol) in DMSO (1 mL), Me_4NCl (0.1 equiv) and $Na_2S_2O_8$ (2.0 equiv) was added. Then H_2O (0-50 equiv) was added into the mixture. The reaction mixture was stirred for another 6 h. [b] All yields were determined by ^1H NMR analysis of the crude products using 1,3,5-trimethoxybenzene as an internal standard.

3. Graphical Procedure for Gram-scale Preparation of 25

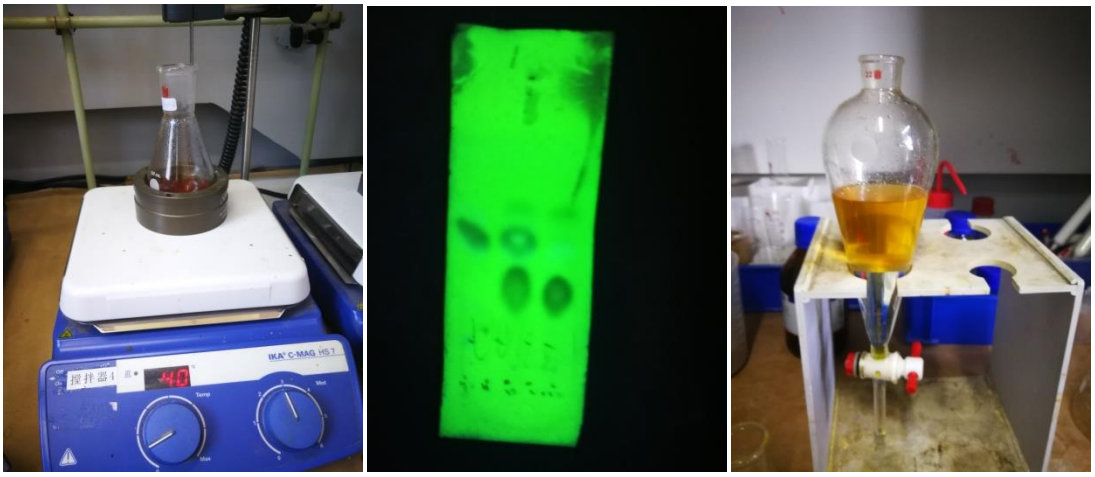
(Left) Evodiamine (1.21 g, 4 mmol); **(Center)** $Na_2S_2O_8$ (2.16 g, 8 mmol); **(Right)** Me_4NCl (43 mg, 0.4 mmol).

(Left) Addition of H_2O (1.4 mL, 80 mmol); **(Center)** Dissolved in DMSO (25 mL); **(Right)** TLC under UV (PE/EtOAc = 2:1).

(Left) The reaction mixture was diluted with water (100 mL); **(Center)** Purified by filtered; **(Right)** Product after filtered.

4. Graphical Procedure for Gram-scale Preparation of 2

(Left) 1 (1.26 g, 4 mmol); **(Center)** $Na_2S_2O_8$ (2.16 g, 8 mmol); **(Right)** Me_4NCl (43 mg, 0.4 mmol).

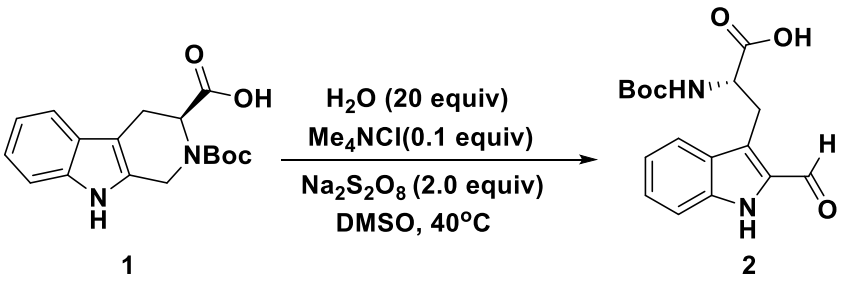


(Left) Stirred at 40 °C for 10 h; **(Center)** TLC under UV (PE/EtOAc = 2:1); **(Right)** Extracted with EtOAc and H_2O.

(Left) dried with Na_2SO_4; **(Center)** Purified by chromatography on silica gel (PE/EtOAc = 2:1); **(Right)** Product after column chromatography.

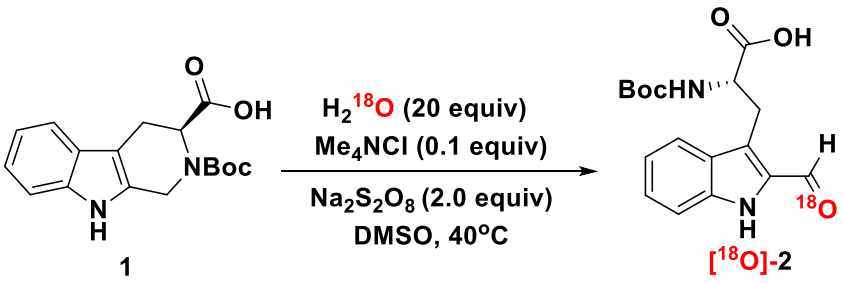
5. Mechanism Studies

Table S5: Investigation of the free radical inhibitor

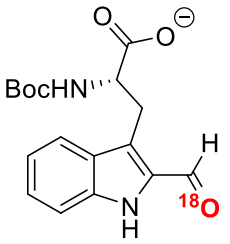


Entry[a]	Inhibitor	equiv	Yield[b]
1	Vc	2	0
2	TEMPO	2	0

[a] Reaction conditions: Unless otherwise noted, all reactions were carried out with THβC **1** (0.1 mmol) in DMSO (1 mL), Me_4NCl (0.1 equiv) and Inhibitor was added. Then H_2O (0-50 equiv) was added into the mixture. The reaction mixture was stirred for another 6 h. [b] All yields were determined by ^1H NMR analysis of the crude products.



To a solution of THβC **1** (32 mg, 0.1 mmol) in DMSO (1 mL) was added $K_2S_2O_8$ (54 mg, 0.2 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (1 mg, 0.01 mmol) and $H_2{}^{18}O$ (36 μL, 2 mmol) was added into the mixture. After stirring for 7 h, the reaction mixture was diluted with EtOAc (50 mL) and extracted with saturated $NaHCO_3$ (5 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 1:2) to give the desired product (28 mg, 84%) as a white solid.



Exact Mass: 333.1342

Found: 333.1348

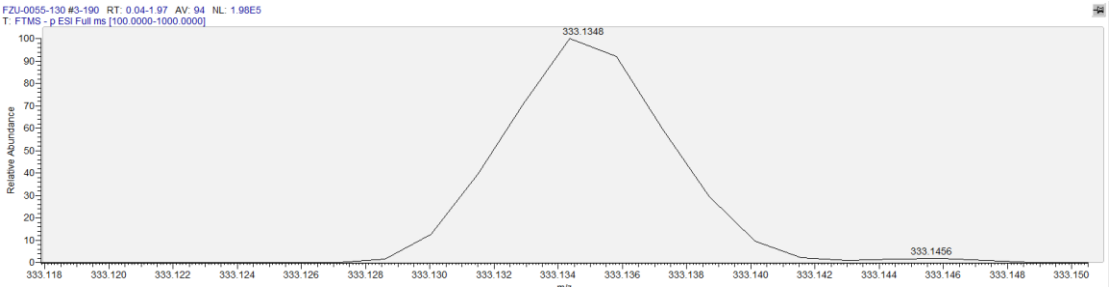
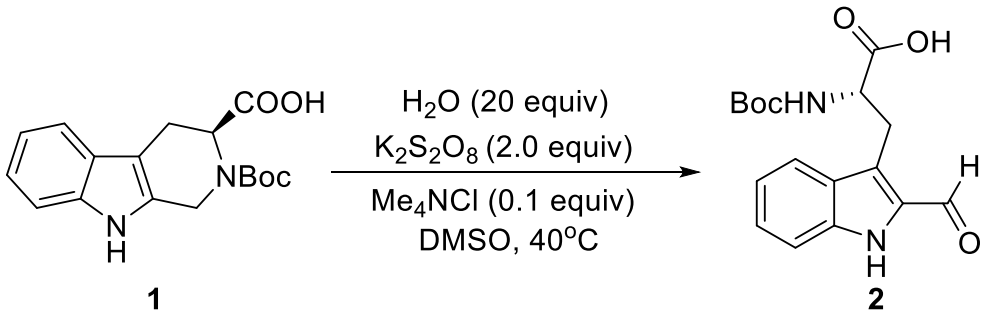


Figure S1. HRMS of **[^{18}O]-2**.

6. General Procedures

Compound 2



2-((tert-butoxycarbonyl)amino)-3-(2-formyl-1H-indol-3-yl)propanoic acid

To a solution of *(S)-2-(tert-butoxycarbonyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole-3-carboxylic acid* (316 mg, 1 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (540 mg, 2 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (11 mg, 0.1 mmol) and H_2O (360 µL, 20 mmol) was added into the mixture. After stirring for 7 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 1:2) to give the desired product (298 mg, 90%) as a white solid.

Gram-scale preparation of 2

To a solution of *(S)-2-(tert-butoxycarbonyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole-3-carboxylic acid* (1.26 g, 4 mmol) in DMSO (20 mL) was added $K_2S_2O_8$ (2.16 g, 8 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (44 mg, 0.4 mmol) and H_2O (1.4 mL, 80 mmol) was added into the mixture. After stirring for 10 h, the reaction mixture was diluted with EtOAc (200 mL) and extracted with saturated $NaHCO_3$ (200 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 1:2) to give the desired product (1.15 g, 87%) as a white solid.

Physical State: white solid.

Melting Point: 151.3 – 152.5 °C.

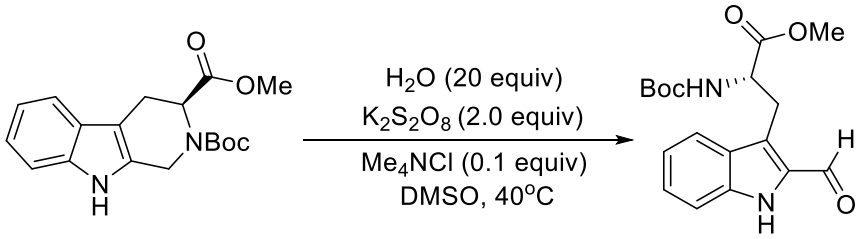
TLC: R_f = 0.21 (PE/EtOAc = 1:2).

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.73 (s, 1H), 11.69 (s, 1H), 9.98 (s, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.42 (d, *J* = 8.2 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.22 – 7.01 (m, 2H), 4.27 – 4.14 (m, 1H), 3.58 – 3.48 (m, 1H), 3.43 – 3.37 (m, 1H), 1.29 (s, 9H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 182.62, 173.53, 155.70, 138.06, 133.76, 127.44, 126.89, 123.51, 121.52, 120.41, 113.26, 78.63, 55.17, 28.52 (3C), 25.96.

HRMS (ESI): calcd for $C_{17}H_{20}N_2O_5$ $[M + H]^+$ *m/z* 333.1445, found 333.1420.

Compound 3



3

Methyl (S)-2-((tert-butoxycarbonyl)amino)-3-(2-formyl-1H-indol-3-yl)propanoate

To a solution of *2-(tert-butyl) 3-methyl (R)-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indole-2,3-dicarboxylate* (330 mg, 1 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (540 mg, 2 mmol). The reaction mixture was stirred at 40 °C for 1 min, then NMe_4Cl (11 mg, 0.1 mmol) and H_2O (360 µL, 20 mmol) was added into the mixture. After stirring for 8 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 2:1) to give the desired product (253 mg, 73%) as a white solid.

Physical State: white solid.

Melting Point: 147.2 - 147.8 °C.

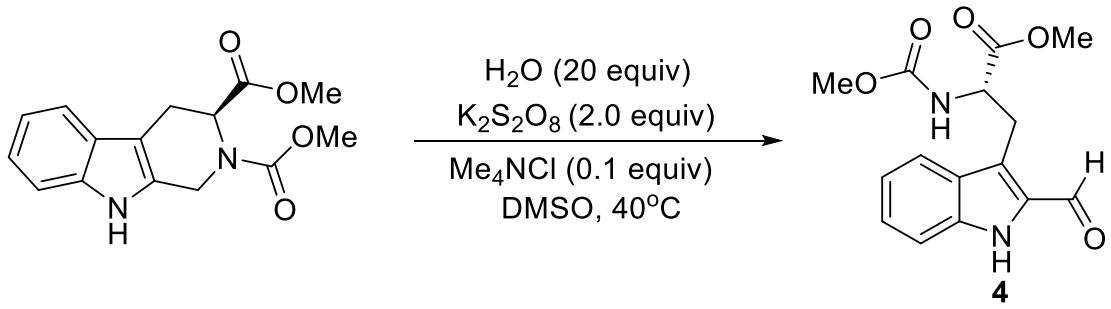
TLC: R_f = 0.55 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$)δ 9.89 (s, 1H), 9.12 (s, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.41 (s, 2H), 7.21 – 7.17 (m, 1H), 5.25 (d, *J* = 6.6 Hz, 1H), 4.80 – 4.74 (m, 1H), 3.67 (s, 3H), 3.67 – 3.63 (m, 2H), 1.47 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 181.07, 171.68, 154.97, 137.46, 133.36, 127.71, 127.51, 121.99, 121.35, 120.85, 112.56, 80.27, 54.36, 52.53, 28.27 (3C), 26.83.

HRMS (ESI): calcd for $C_{18}H_{22}N_2O_5$ $[M + H]^+$ *m/z* 347.1601, found 347.1588.

Compound 4



4

Methyl 3-(2-formyl-1H-indol-3-yl)-2-((methoxycarbonyl)amino)propanoate

To a solution of *dimethyl 1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indole-2,3-dicarboxylate* (144 mg, 0.5 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (270 mg, 1 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then Me_4NCl (6 mg, 0.05 mmol) and H_2O (180 µL, 10 mmol) was added into the mixture. After stirring for 8 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 2:1) to give the desired product (118 mg, 78%) as a white solid.

Physical State: white solid.

Melting Point: 128.3 - 129.8 °C.

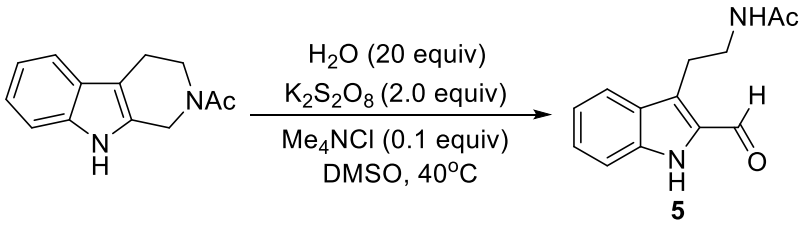
TLC: R_f = 0.30 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 9.63 (s, 1H), 7.69 (d, *J* = 8.2 Hz, 1H), 7.35 (s, 2H), 7.19 – 7.14 (m, 1H), 5.69 (d, *J* = 7.5 Hz, 1H), 4.90 – 4.80 (m, 1H), 3.70 (s, 3H), 3.67 (s, 3H), 3.65 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 181.09, 171.72, 156.44, 137.52, 133.23, 127.56 (2C), 121.76, 121.14, 120.94, 112.65, 54.84, 52.63 (2C), 26.90.

HRMS (ESI): calcd for $C_{15}H_{16}N_2O_5$ $[M + H]^+$ *m/z* 305.1132, found 305.1124.

Compound 5



5

N-(2-(2-formyl-1H-indol-3-yl)ethyl)acetamide

To a solution of *1-(1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indol-2-yl)ethan-1-one* (214 mg, 1 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (540 mg, 2 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (11 mg, 0.1 mmol) and H_2O (360 µL, 20 mmol) was added into the mixture. After stirring for 5 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (CH_2Cl_2/MeOH = 10:1) to give the desired product (180 mg, 80%) as a white solid.

Physical State: white solid.

Melting Point: 111.2 – 112.5 °C.

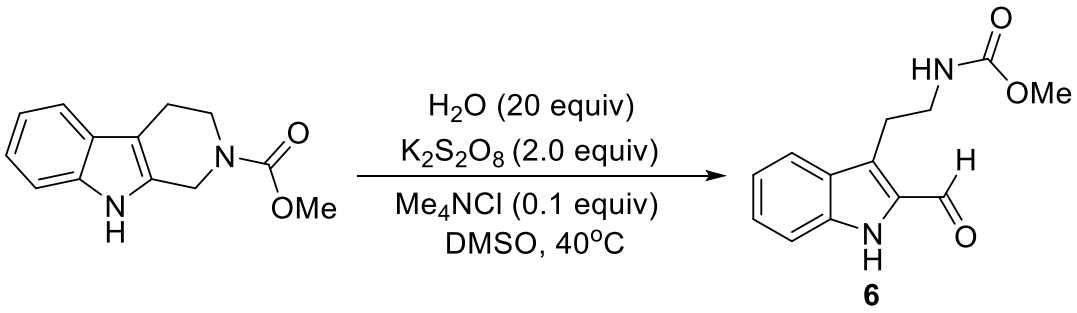
TLC: R_f = 0.26 (PE/EtOAc = 1:2).

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.68 (s, 1H), 9.95 (s, 1H), 8.01 (s, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.43 (d, *J* = 8.3 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.11 (t, J = 7.5 Hz, 1H), 3.36 – 3.32 (m, 2H), 3.21 (t, J = 6.6 Hz, 2H), 1.77 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 181.98, 169.80, 138.21, 133.24, 127.45, 127.05, 125.65, 121.57, 120.34, 113.26, 40.80, 23.84, 23.01.

HRMS (ESI): calcd for $C_{13}H_{14}N_2O_2$ $[M + H]^+$ *m/z* 231.1128, found 231.1121.

Compound 6



6

Methyl (2-(2-formyl-1H-indol-3-yl)ethyl)carbamate

To a solution of *methyl 1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indole-2-carboxylate* (230 mg, 1 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (540 mg, 2 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (11 mg, 0.1 mmol) and H_2O (360 µL, 20 mmol) was added into the mixture. After stirring for 5 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 2:1) to give the desired product (209 mg, 85%) as a white solid.

Physical State: white solid.

Melting Point: 125.3 – 126.5 °C.

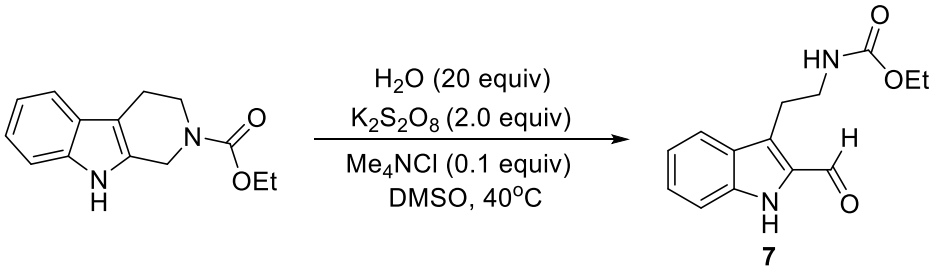
TLC: R_f = 0.33 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.92 (s, 1H), 9.70 (s, 1H), 7.74 – 7.69 (m, 1H), 7.42 (d, *J* = 8.2 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 5.08 (s, 1H), 3.66 (s, 3H), 3.55 – 3.49 (m, 2H), 3.31 (t, J = 6.0 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 180.81, 157.18, 137.86, 132.84, 127.64, 127.34, 125.72, 121.23, 120.76, 112.70, 52.21, 42.26, 24.33.

HRMS (ESI): calcd for $C_{13}H_{14}N_2O_3$ $[M + H]^+$ *m/z* 247.1077, found 247.1071.

Compound 7



7

N-(2-(2-formyl-1H-indol-3-yl)ethyl)propionamide

To a solution of *1-(1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indol-2-yl)propan-1-one* (244 mg, 1 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (540 mg, 2 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (11 mg, 0.1 mmol) and H_2O (360 µL, 20 mmol) was added into the mixture. After stirring for 5 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 2:1) to give the desired product (182 mg, 70%) as a white solid.

Physical State: white solid.

Melting Point: 117.5 – 118.6 °C.

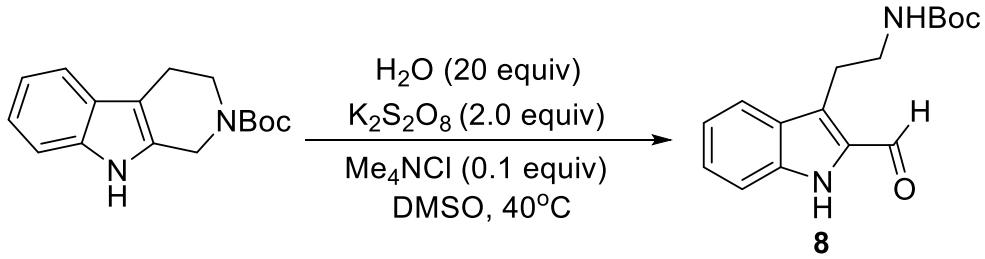
TLC: R_f = 0.40 (PE/EtOAc = 2:1).

1H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H), 9.89 (s, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 8.3 Hz, 1H), 7.33 (d, J = 7.2 Hz, 1H), 7.09 (t, J = 7.4 Hz, 1H), 5.23 (s, 1H), 4.15 – 4.08 (m, 2H), 3.51 – 3.46 (m, 2H), 3.26 (t, J = 6.1 Hz, 2H), 1.22 – 1.17 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 181.02, 156.90, 138.06, 132.85, 127.54, 127.32, 126.02, 121.21, 120.62, 112.81, 60.92, 42.19, 24.29, 14.64.

HRMS (ESI): calcd for $C_{14}H_{16}N_2O_3$ $[M + H]^+$ *m/z* 261.1234, found 261.1226.

Compound 8



8

Tert-butyl (2-(2-formyl-1H-indol-3-yl)ethyl)carbamate

To a solution of *tert-butyl 1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indole-2-carboxylate* (136 mg, 0.5 mmol) in DMSO (4 mL) was added $K_2S_2O_8$ (270 mg, 1 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (6 mg, 0.05 mmol) and H_2O (180 µL, 10 mmol) was added into the mixture. After stirring for 4 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 2:1) to give the desired product (98 mg, 68%) as a white solid.

Physical State: white solid.

Melting Point: 144.9 – 145.6 °C.

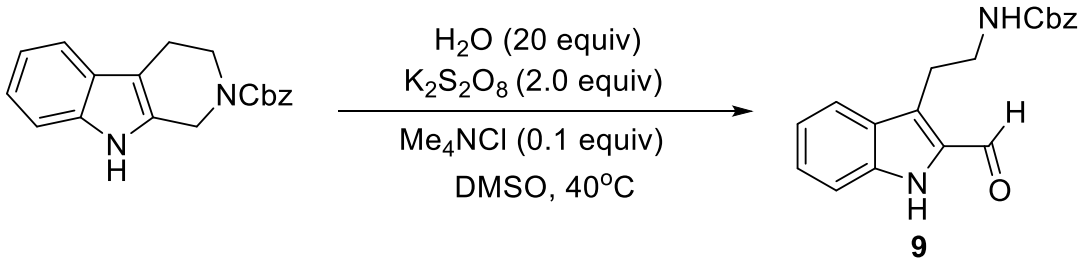
TLC: R_f = 0.34 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 9.56 (s, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.43 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.14 (t, *J* = 7.2 Hz, 2H), 4.74 (s, 1H), 3.50 – 3.42 (m, 4H), 3.29 (t, *J* = 7.1 Hz, 3H), 1.44 (s, 13H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 180.84, 155.95, 137.82, 132.96, 127.59, 127.40, 125.96, 121.33, 120.69, 112.62, 79.54, 41.78, 28.37 (3C), 24.25.

HRMS (ESI): calcd for $C_{16}H_{20}N_2O_3$ $[M + H]^+$ *m/z* 289.1547, found 289.1526.

Compound 9



9

Benzyl (2-(2-formyl-1H-indol-3-yl)ethyl)carbamate

To a solution of *benzyl 1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indole-2-carboxylate* (153 mg, 0.5 mmol) in DMSO (4 mL) was added $K_2S_2O_8$ (270 mg, 1 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (6 mg, 0.05 mmol) and H_2O (180 µL, 10 mmol) was added into the mixture. After stirring for 4 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 2:1) to give the desired product (105 mg, 65%) as a white solid.

Physical State: white solid.

Melting Point: 142.5 - 143.8 °C.

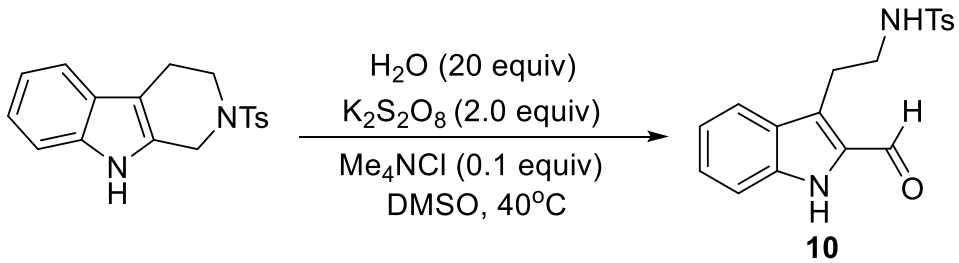
TLC: R_f = 0.47 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.68 (s, 1H), 9.98 (s, 1H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.36 – 7.28 (m, 6H), 7.08 (t, *J* = 7.2 Hz, 1H), 4.99 (s, 2H), 3.34 – 3.30 (m, 2H), 3.25 (t, *J* = 5.6 Hz, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 182.00, 156.62, 138.21, 137.68, 133.28, 128.79 (2C), 128.17, 128.04 (2C), 127.53, 126.99, 125.34, 121.57, 120.32, 113.26, 65.62, 42.47, 24.17.

HRMS (ESI): calcd for $C_{19}H_{18}N_2O_3$ $[M + H]^+$ *m/z* 323.1390, found 323.1379.

Compound 10



10

N-(2-(2-formyl-1H-indol-3-yl)ethyl)-4-methylbenzenesulfonamide

To a solution of *2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole* (326 mg, 1 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (540 mg, 2 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (11 mg, 0.1 mmol) and H_2O (360 µL, 20 mmol) was added into the mixture. After stirring for 5 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 2:1) to give the desired product (273 mg, 80%) as a white solid.

Physical State: white solid.

Melting Point: 126.3 – 127.1 °C.

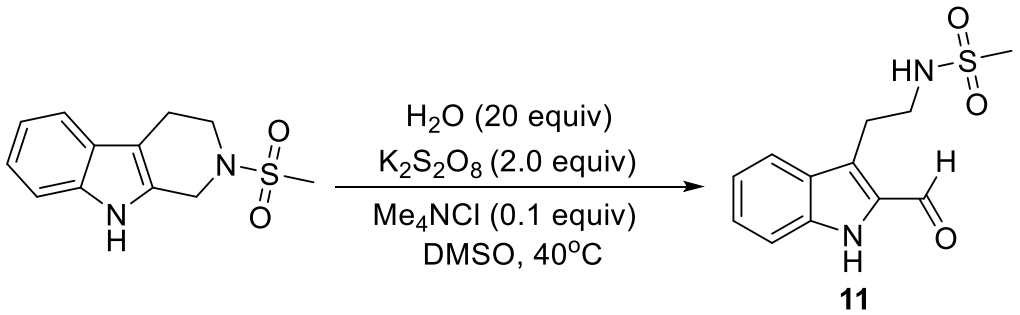
TLC: R_f = 0.34 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 9.61 (s, 1H), 7.70 (d, *J* = 7.4 Hz, 2H), 7.60 (d, *J* = 8.1 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.25 (d, *J* = 7.9 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 5.55 (s, 1H), 3.41 – 3.35 (m, 2H), 3.33 (t, *J* = 5.1 Hz, 2H), 2.40 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 182.24, 143.01, 138.13, 137.98, 133.26, 130.01, 127.22, 126.93, 126.90, 124.35, 121.38, 120.37, 113.29, 44.32, 24.37, 21.42.

HRMS (ESI): calcd for $C_{18}H_{18}N_2O_3S$ $[M + H]^+$ *m/z* 343.1111, found 343.1099.

Compound 11



N-(2-(2-formyl-1H-indol-3-yl)ethyl)methanesulfonamide

To a solution of *2-(methylsulfonyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole* (250 mg, 1 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (540 mg, 2 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (11 mg, 0.1 mmol) and H_2O (360 µL, 20 mmol) was added into the mixture. After stirring for 8 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 2:1) to give the desired product (244 mg, 92%) as a white solid.

Physical State: white solid.

Melting Point: 151.9 – 152.8 °C.

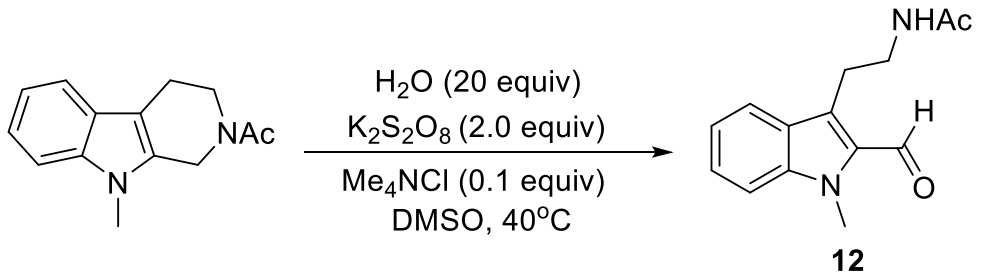
TLC: R_f = 0.60 (PE/EtOAc = 1:2).

^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 11.72 (s, 1H), 10.02 (s, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 1H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.18 – 7.09 (m, 2H), 3.37 (s, 1H), 3.27 (s, 2H), 3.02 (d, *J* = 15.4 Hz, 1H), 2.82 (s, 3H).

^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 182.36, 138.16, 133.31, 127.33, 127.01, 124.63, 121.57, 120.42, 113.30, 44.39, 42.59, 24.87.

HRMS (ESI): calcd for $C_{12}H_{14}N_2O_3S$ $[M + H]^+$ *m/z* 267.0798, found 267.0797.

Compound 12



12

N-(2-(2-formyl-1-methyl-1H-indol-3-yl)ethyl)acetamide

To a solution of *1-(9-methyl-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indol-2-yl)ethan-1-one* (66 mg, 0.3 mmol) in DMSO (2 mL) was added $K_2S_2O_8$ (160 mg, 0.6 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (3 mg, 0.03 mmol) and H_2O (108 µL, 6 mmol) was added into the mixture. After stirring for 6 h, the reaction mixture was diluted with EtOAc (10 mL) and extracted with saturated $NaHCO_3$ (10 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 1:1) to give the desired product (36 mg, 52%) as a white solid.

Physical State: white solid.

Melting Point: 146.4 – 147.5 °C.

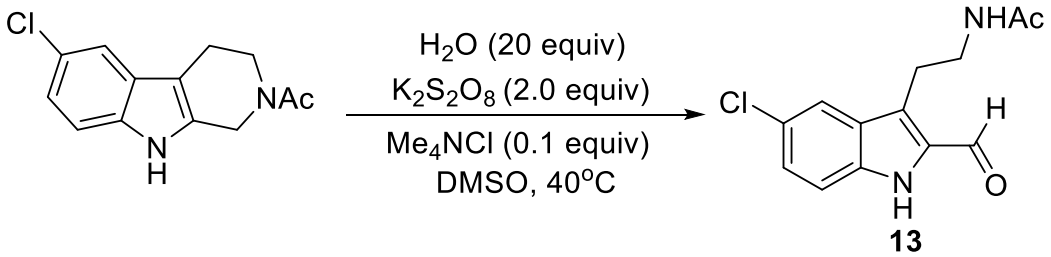
TLC: R_f = 0.28 (PE/EtOAc = 1:2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.08 (s, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 5.78 (s, 1H), 4.04 (s, 3H), 3.56 – 3.52 (m, 2H), 3.30 (t, *J* = 6.2 Hz, 2H), 1.91 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 181.62, 170.25, 139.73, 131.72, 127.46, 127.00, 126.31, 121.20, 120.70, 110.40, 41.25, 31.52, 23.75, 23.25.

HRMS (ESI): calcd for $C_{14}H_{16}N_2O_2$ $[M + H]^+$ *m/z* 245.1285, found 245.1277.

Compound 13



13

N-(2-(5-chloro-2-formyl-1H-indol-3-yl)ethyl)acetamide

To a solution of *1-(6-chloro-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indol-2-yl)ethan-1-one* (214 mg, 1 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (540 mg, 2 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (11 mg, 0.1 mmol) and H_2O (360 µL, 20 mmol) was added into the mixture. After stirring for 5 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (CH_2Cl_2/MeOH = 10:1) to give the desired product (210 mg, 79%) as a white solid.

Physical State: white solid.

Melting Point: 116.8 – 117.8 °C.

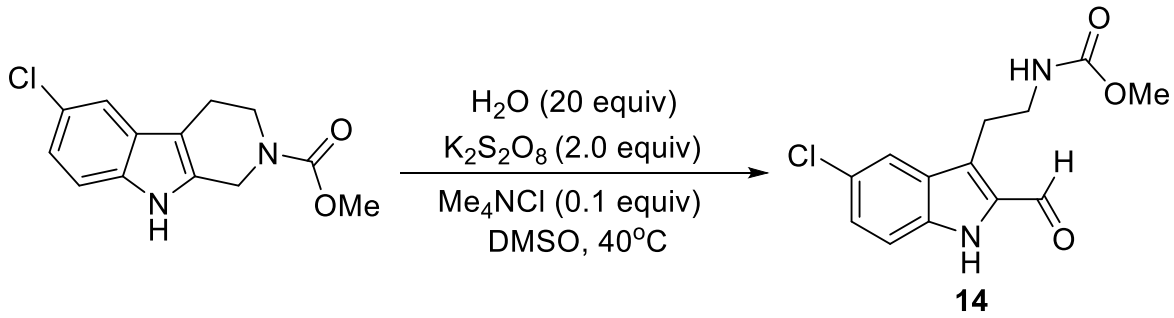
TLC: R_f = 0.29 (PE/EtOAc = 1:2).

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.86 (s, 1H), 9.94 (s, 1H), 7.97 (s, 1H), 7.84 (s, 1H), 7.42 (d, *J* = 8.7 Hz, 1H), 7.32 (d, *J* = 8.7 Hz, 1H), 3.31 – 3.28 (m, 2H), 3.19 (t, *J* = 6.7 Hz 2H), 1.73 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 182.32, 169.83, 136.47, 134.32, 128.47, 127.01, 124.91(2C), 120.72, 114.96, 40.65, 23.65, 22.96.

HRMS (ESI): calcd for $C_{13}H_{13}ClN_2O_2$ $[M + H]^+$ *m/z* 265.0738, found 265.0730.

Compound 14



14

Methyl (2-(5-chloro-2-formyl-1H-indol-3-yl)ethyl)carbamate

To a solution of *methyl 6-chloro-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indole-2-carboxylate* (264 mg, 1 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (540 mg, 2 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (11 mg, 0.1 mmol) and H_2O (360 µL, 20 mmol) was added into the mixture. After stirring for 5 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 2:1) to give the desired product (229 mg, 82%) as a white solid.

Physical State: white solid.

Melting Point: 178.9 – 179.5 °C.

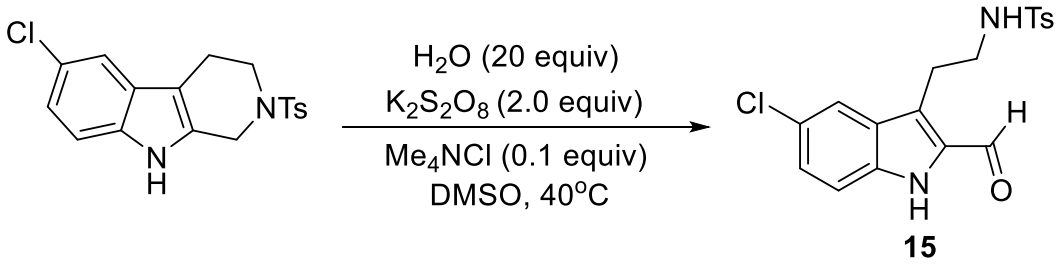
TLC: R_f = 0.32 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.87 (s, 1H), 9.96 (s, 1H), 7.84 (s, 1H), 7.43 (d, *J* = 8.8 Hz, 1H), 7.33 (d, *J* = 8.8 Hz, 1H), 7.24 (s, 1H), 3.34 (s, 3H), 3.29 – 3.24 (m, 2H), 3.21 (t, *J* = 5.7 Hz, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 182.36, 157.22, 136.46, 134.36, 128.54, 126.98, 124.89, 124.64, 120.68, 114.96, 51.68, 42.30, 23.92.

HRMS (ESI): calcd for $C_{13}H_{14}ClN_2O_3$ $[M + H]^+$ *m/z* 281.0698, found 281.0688.

Compound 15



15

N-(2-(5-chloro-2-formyl-1H-indol-3-yl)ethyl)-4-methylbenzenesulfonamide

To a solution of *6-chloro-2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole* (361 mg, 1 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (540 mg, 2 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (11 mg, 0.1 mmol) and H_2O (360 µL, 20 mmol) was added into the mixture. After stirring for 5 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 2:1) to give the desired product (250 mg, 67%) as a white solid.

Physical State: white solid.

Melting Point: 118.7 – 119.5 °C.

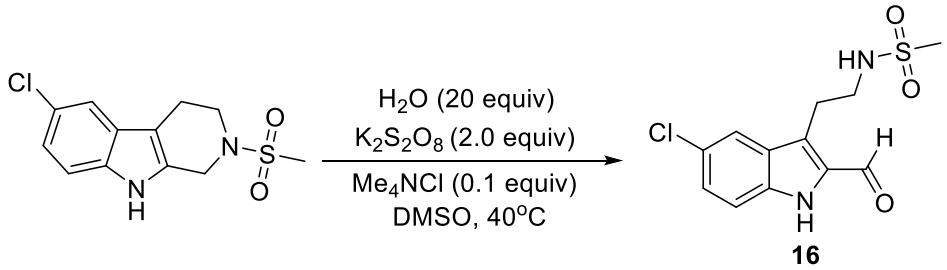
TLC: R_f = 0.38 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.85 (s, 1H), 9.94 (s, 1H), 7.71 (s, 1H), 7.64 (t, *J* = 5.5 Hz, 1H), 7.59 (s, 1H), 7.57 (s, 1H), 7.40 (d, *J* = 8.9 Hz, 1H), 7.32 – 7.29 (m, 3H), 3.16 (m, 2H), 3.01 (t, *J* = 6.1 Hz, 2H), 2.36 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 182.66, 143.00, 137.88, 136.39, 134.41, 129.97 (2C), 128.25, 126.91, 126.84 (2C), 124.91, 123.66, 120.57, 114.98, 44.18, 24.08, 21.43.

HRMS (ESI): calcd for $C_{18}H_{17}ClN_2O_3S$ $[M + H]^+$ *m/z* 377.0721, found 377.0711.

Compound 16



16

N-(2-(2-formyl-1H-indol-3-yl)ethyl)methanesulfonamide

To a solution of *6-chloro-2-(methylsulfonyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole* (143 mg, 0.5 mmol) in DMSO (3 mL) was added $K_2S_2O_8$ (270 mg, 1 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (6 mg, 0.05 mmol) and H_2O (180 µL, 10 mmol) was added into the mixture. After stirring for 5 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 2:1) to give the desired product (129 mg, 86%) as a white solid.

Physical State: white solid.

Melting Point: 162.9 – 163.5 °C.

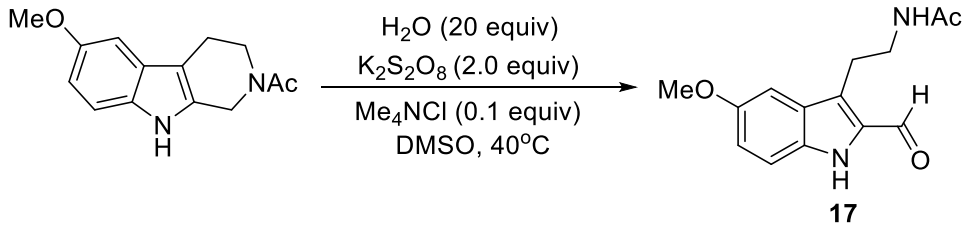
TLC: R_f = 0.48 (PE/EtOAc = 1:2).

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.92 (s, 1H), 10.02 (s, 1H), 7.86 (s, 1H), 7.45 (d, *J* = 8.7 Hz, 1H), 7.33 (d, *J* = 8.7 Hz, 1H), 7.14 (s, 1H), 3.25 (s, 4H), 2.83 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 182.75, 136.41, 134.42, 128.35, 127.04, 125.00, 123.99, 120.73, 115.02, 44.25, 39.77, 24.58.

HRMS (ESI): calcd for $C_{12}H_{13}ClN_2O_3S$ $[M + H]^+$ *m/z* 301.0408, found 301.0435.

Compound 17



17

N-(2-(2-formyl-5-methoxy-1H-indol-3-yl)ethyl)acetamide

To a solution of *1-(6-methoxy-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indol-2-yl)ethan-1-one* (122 mg, 0.5 mmol) in DMSO (4 mL) was added $K_2S_2O_8$ (270 mg, 1 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (6 mg, 0.05 mmol) and H_2O (180 µL, 10 mmol) was added into the mixture. After stirring for 8 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 1:4) to give the desired product (92 mg, 71%) as a white solid.

Physical State: white solid.

Melting Point: 181.9 – 182.8 °C.

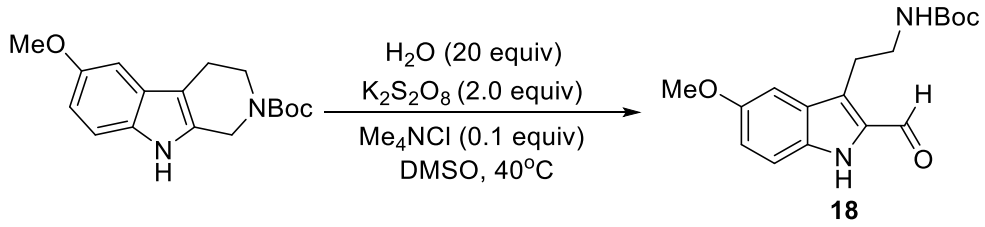
TLC: R_f = 0.34 (PE/EtOAc = 1:2).

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.55 (s, 1H), 9.89 (s, 1H), 7.99 (s, 1H), 7.32 (d, *J* = 8.8 Hz, 1H), 7.21 (s, 1H), 7.00 (d, *J* = 9.1 Hz, 1H), 3.80 (s, 3H), 3.33 – 3.30 (m, 2H), 3.17 (t, *J* = 6.7 Hz, 2H), 1.76 (s, 3H).

^{13}C NMR (101 MHz, DMSO) δ 181.71, 169.73, 154.22, 133.69, 133.65, 127.71, 124.98, 118.87, 114.26, 101.24, 55.79, 40.69, 23.86, 23.04.

HRMS (ESI): calcd for $C_{14}H_{16}N_2O_3$ $[M + H]^+$ *m/z* 261.1234, found 261.1226.

Compound 18



18

N-(2-(2-formyl-5-methoxy-1H-indol-3-yl)ethyl)acetamide

To a solution of *tert-butyl 6-methoxy-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indole-2-carboxylate* (151 mg, 0.5 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (270 mg, 1 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (6 mg, 0.05 mmol) and H_2O (180 µL, 10 mmol) was added into the mixture. After stirring for 6 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 2:1) to give the desired product (87 mg, 55%) as a brown oil.

Physical State: brown oil.

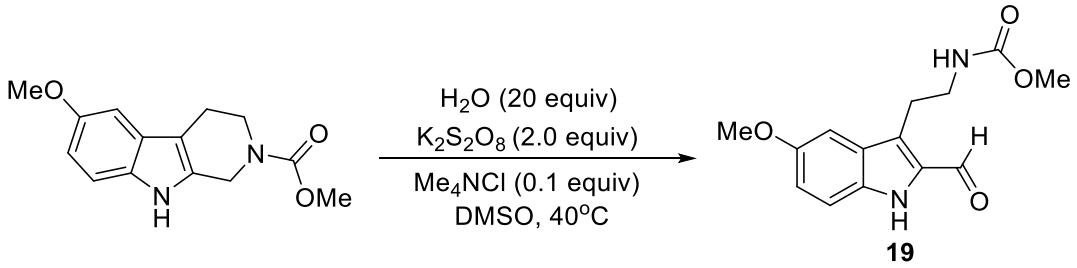
TLC: R_f = 0.23 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.46 (s, 1H), 6.97 (s, 1H), 6.88 – 6.72 (m, 2H), 3.89 (d, *J* = 6.9 Hz, 1H), 3.82 (s, 3H), 3.76 – 3.72 (m, 1H), 3.47 (s, 1H), 2.20 (d, *J* = 11.3 Hz, 2H), 1.56 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.57, 162.94, 155.77, 152.26, 135.01, 130.13, 112.71, 111.39, 110.21, 84.23, 55.81, 44.45, 37.74, 28.79, 28.02 (3C).

HRMS (ESI): calcd for $C_{17}H_{22}N_2O_4$ $[M + H]^+$ *m/z* 318.1580, found 318.1622.

Compound 19



19

Methyl (2-(2-formyl-5-methoxy-1H-indol-3-yl)ethyl)carbamate

To a solution of *methyl 6-methoxy-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indole-2-carboxylate* (130 mg, 0.5 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (270 mg, 1 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (6 mg, 0.05 mmol) and H_2O (180 µL, 10 mmol) was added into the mixture. After stirring for 10 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 2:1) to give the desired product (88 mg, 65%) as a white solid.

Physical State: white solid.

Melting Point: 168.2 – 169.1 °C.

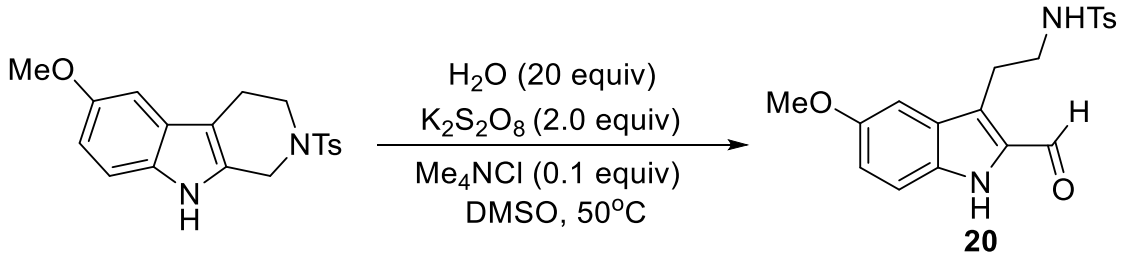
TLC: R_f = 0.22 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.93 (s, 1H), 9.22 (s, 1H), 7.35 (d, *J* = 9.1 Hz, 1H), 7.10 (d, *J* = 6.7 Hz, 2H), 4.94 (s, 1H), 3.89 (s, 3H), 3.70 (s, 3H), 3.55 - 3.58 (m, 2H), 3.30 (t, *J* = 6.0 Hz, 2H).

^{13}C NMR (101 MHz, DMSO) δ 181.72, 157.23, 154.22, 133.68, 133.66, 127.72, 124.74, 118.84, 114.25, 101.23, 55.76, 51.69, 42.32, 24.14.

HRMS (ESI): calcd for $C_{14}H_{16}N_2O_4$ $[M + H]^+$ *m/z* 277.1183, found 277.1176.

Compound 20



20

N-(2-(2-formyl-5-methoxy-1H-indol-3-yl)ethyl)-4-methylbenzenesulfonamide

To a solution of *6-methoxy-2-tosyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole* (180 mg, 0.5 mmol) in DMSO (5 mL) was added $K_2S_2O_8$ (270 mg, 1 mmol). The reaction mixture was stirred at 50 °C. for 1 min, then NMe_4Cl (6 mg, 0.05 mmol) and H_2O (180 µL, 10 mmol) was added into the mixture. After stirring for 100 h, the reaction mixture was diluted with EtOAc (10 mL) and extracted with saturated $NaHCO_3$ (10 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 2:1) to give the desired product (131 mg, 70%) as a white solid.

Physical State: white solid.

Melting Point: 130.4 – 131.5 °C.

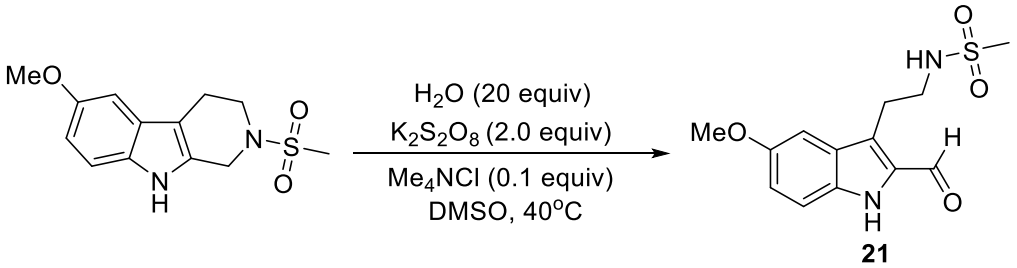
TLC: R_f = 0.65 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, DMSO-d_6) ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.56 (s, 1H), 9.90 (s, 1H), 7.71 – 7.68 (m, 1H), 7.63 (d, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 7.6 Hz, 2H), 7.08 (s, 1H), 6.98 (d, *J* = 8.8 Hz, 1H), 3.78 (s, 3H), 3.17 (t, *J* = 6.3 Hz, 2H), 3.00 – 3.05 (m, *J* = 6.0 Hz, 2H), 2.37 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 181.97, 154.24, 143.00, 137.98, 133.65, 133.62, 129.99, 127.49, 126.89, 123.69, 118.77, 114.29, 101.14, 55.78, 44.18, 24.39, 21.41.

HRMS (ESI): calcd for $C_{19}H_{20}N_2O_4S$ $[M + H]^+$ *m/z* 373.1217, found 373.1203.

Compound 21



21

N-(2-(2-formyl-5-methoxy-1H-indol-3-yl)ethyl)methanesulfonamide

To a solution of *6-methoxy-2-(methylsulfonyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole* (140 mg, 0.5 mmol) in DMSO (4 mL) was added $K_2S_2O_8$ (270 mg, 1 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (6 mg, 0.05 mmol) and H_2O (180 µL, 10 mmol) was added into the mixture. After stirring for 10 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 1:1) to give the desired product (110 mg, 75%) as a white solid.

Physical State: white solid.

Melting Point: 162.5 – 163.4 °C.

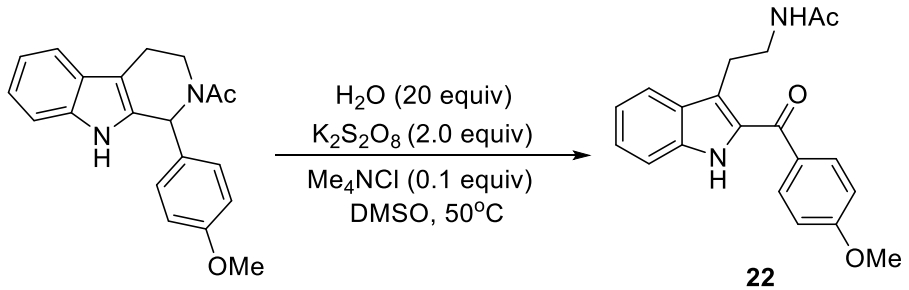
TLC: R_f = 0.26 (PE/EtOAc = 1:1).

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.60 (s, 1H), 9.97 (s, 1H), 7.33 (d, *J* = 8.8 Hz, 1H), 7.21 (s, 1H), 7.15 (s, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 3.81 (s, 3H), 3.25 (s, 4H), 2.83 (s, 3H).

^{13}C NMR (101 MHz, DMSO) δ 182.11, 154.26, 133.71, 133.64, 127.62, 124.04, 118.83, 114.30, 101.34, 55.80, 44.26, 39.79, 24.87.

HRMS (ESI): calcd for $C_{13}H_{16}N_2O_4S$ $[M + H]^+$ *m/z* 297.0904, found 297.0946.

Compound 22



22

N-(2-(2-(4-methoxybenzoyl)-1H-indol-3-yl)ethyl)acetamide

To a solution of *1-(1-(4-methoxyphenyl)-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indol-2-yl)ethan-1-one* (162 mg, 0.5 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (270 mg, 1 mmol). The reaction mixture was stirred at 50 °C. for 1 min, then NMe_4Cl (6 mg, 0.05 mmol) and H_2O (180 µL, 10 mmol) was added into the mixture. After stirring for 10 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 1:1) to give the desired product (118 mg, 70%) as a white solid.

Physical State: white solid.

Melting Point: 170.4 – 171.5 °C.

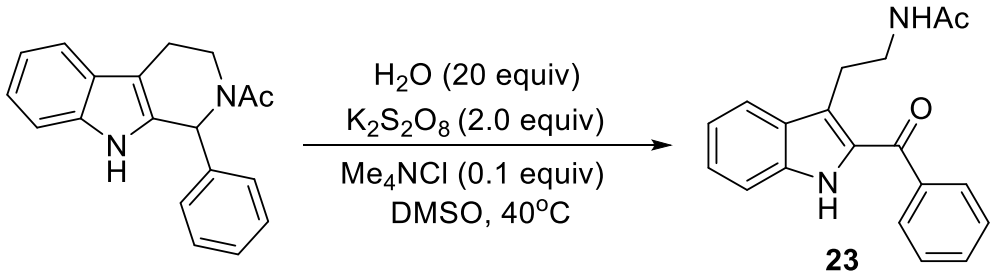
TLC: R_f = 0.32 (PE/EtOAc = 1:2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 7.86 (d, *J* = 7.4 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 8.3 Hz, 1H), 7.38 (d, *J* = 7.1 Hz, 1H), 7.21 (d, *J* = 7.3 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 3H), 3.90 (d, *J* = 1.7 Hz, 3H), 3.54 - 3.56 (m, 2H), 3.21 (t, *J* = 5.9 Hz, 2H), 1.86 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.06, 170.51, 163.51, 136.49, 132.14, 131.94 (2C), 130.87, 127.76, 126.12, 121.91, 120.77, 120.74, 114.03 (2C), 112.24, 55.57, 41.08, 23.98, 23.11.

HRMS (ESI): calcd for $C_{20}H_{20}N_2O_3$ $[M + H]^+$ *m/z* 336.1474, found 336.1496.

Compound 23



23

N-(2-(2-benzoyl-1H-indol-3-yl)ethyl)acetamide

To a solution of *1-(1-phenyl-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indol-2-yl)ethan-1-one* (116 mg, 0.4 mmol) in DMSO (6 mL) was added $K_2S_2O_8$ (216 mg, 0.8 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then NMe_4Cl (5 mg, 0.04 mmol) and H_2O (144 µL, 8 mmol) was added into the mixture. After stirring for 48 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 1:1) to give the desired product (91 mg, 75%) as a white solid.

Physical State: white solid.

Melting Point: 102.6 – 103.5 °C.

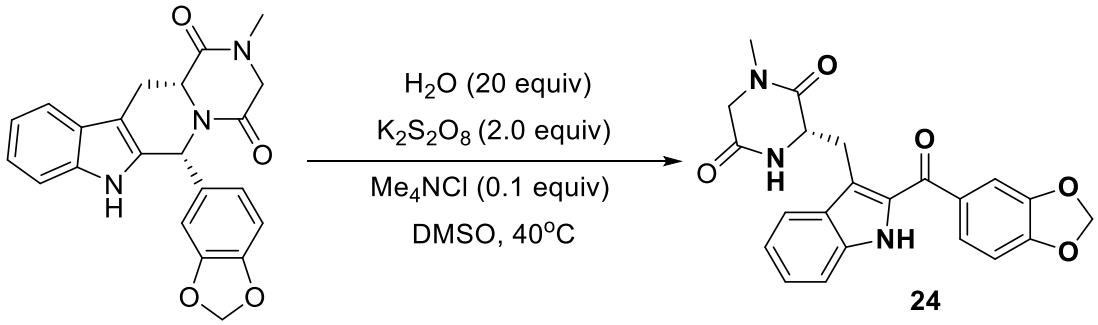
TLC: R_f = 0.33 (PE/EtOAc = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.86 (s, 2H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.66 (t, *J* = 7.1 Hz, 1H), 7.57 (t, *J* = 7.1 Hz, 2H), 7.42 (s, 2H), 7.25 – 7.20 (m, 1H), 6.55 (s, 1H), 3.57 - 3.59 (m, 2H), 3.23 (t, *J* = 5.2 Hz, 2H), 1.90 (d, *J* = 2.4 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 189.01, 169.46, 139.38, 137.21, 132.72, 131.90, 129.39 (2C), 129.06 (2C), 128.04, 125.73, 121.47, 121.16, 120.25, 113.25, 30.32, 25.47, 23.05.

HRMS (ESI): calcd for $C_{19}H_{18}N_2O_2$ $[M + H]^+$ *m/z* 307.1441, found 307.1456.

Compound 24



3-((2-(Benzo[d][1,3]dioxole-5-carbonyl)-1H-indol-3-yl)methyl)-1-methylpiperazine-2,5-dione

To a solution of *6-(benzo[d][1,3]dioxol-5-yl)-2-methyl-2,3,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione* (117 mg, 0.3 mmol) in DMSO (4 mL) was added $K_2S_2O_8$ (160 mg, 0.6 mmol). The reaction mixture was stirred at 40 °C. for 1 min, then Me_4NCl (4 mg, 0.03 mmol) and H_2O (108 µL, 6 mmol) was added into the mixture. After stirring for 18 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (CH_2Cl_2/MeOH = 20:1) to give the desired product (96 mg, 79%) as a white solid.

Physical State: white solid.

Melting Point: 187.6 – 188.5 °C.

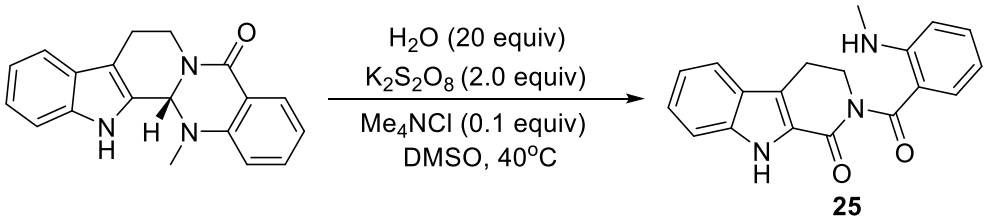
TLC: R_f = 0.20 (PE/EtOAc = 1:2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 7.71 (d, *J* = 8.1 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 1H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.28 (s, 1H), 7.22 – 7.16 (m, 2H), 6.82 (d, *J* = 7.8 Hz, 1H), 6.72 (s, 1H), 6.05 (s, 2H), 4.35 (s, 1H), 3.78 – 3.71 (m, 1H), 3.62 (d, *J* = 16.5 Hz, 1H), 3.50 (d, *J* = 17.4 Hz, 1H), 2.92 (d, *J* = 17.5 Hz, 1H), 2.73 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 186.84, 166.24, 165.37, 151.57, 148.16, 136.30, 132.68, 132.58, 127.42, 126.46, 125.63, 121.29, 121.12, 118.22, 112.35, 109.39, 108.13, 101.96, 56.17, 51.02, 33.81, 28.89.

HRMS (ESI): calcd for $C_{22}H_{19}N_3O_5$ $[M + H]^+$ *m/z* 406.1397, found 406.1386.

Compound 25



25

2-(2-(Methylamino)benzoyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-one

To a solution of evodiamine (303 mg, 1 mmol) in DMSO (3 mL) was added $K_2S_2O_8$ (540 mg, 2 mmol). The reaction mixture was stirred at 40 °C for 1 min, then NMe_4Cl (11 mg, 0.1 mmol) and H_2O (360 µL, 20 mmol) was added into the mixture. After stirring for 10 h, After cooling, the mixtures poured into H_2O and the precipitate was collected by filtration to give the desired product as a white solid (277 mg, 87%).

Procedure for gram-scale of 25

To a solution of evodiamine (1.21 g, 4 mmol) in DMSO (25 mL) was added $K_2S_2O_8$ (2.16 g, 8 mmol). The reaction mixture was stirred at 40 °C for 1 min, then NMe_4Cl (44 mg, 0.4 mmol) and H_2O (1.4 mL, 80 mmol) was added into the mixture. After stirring for 15 h, After cooling, the mixtures poured into H_2O and the precipitate was collected by filtration to give the desired product as a white solid (1.06 g, 83%).

Physical State: white solid.

Melting Point: 119.7 – 120.6 °C.

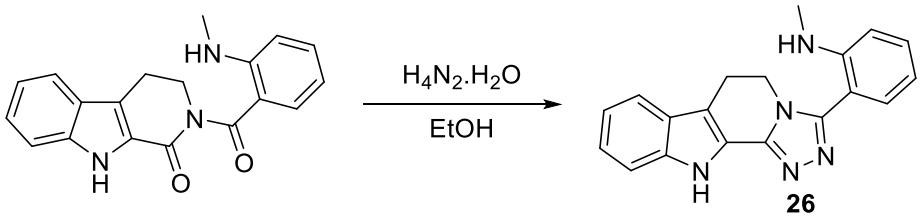
TLC: R_f = 0.23 (PE/EtOAc = 1:1).

^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 11.75 (s, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.31 (t, *J* = 7.4 Hz, 3H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.90 (d, *J* = 4.9 Hz, 1H), 6.70 (d, *J* = 8.3 Hz, 1H), 6.49 (t, *J* = 7.4 Hz, 1H), 4.11 (t, *J* = 6.0 Hz, 2H), 3.18 (t, *J* = 6.0 Hz, 2H), 2.82 (d, *J* = 4.6 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 175.25, 161.56, 150.24, 138.89, 134.03, 131.94, 126.47, 126.16, 124.92, 123.03, 121.35, 120.54, 117.36, 114.70, 113.28, 111.37, 47.38, 29.99, 21.00.

HRMS (ESI): calcd for $C_{19}H_{17}N_3O_2$ $[M + H]^+$ *m/z* 320.1394, found 320.1384.

Compound 26



26

2-(6,11-dihydro-5H-[1,2,4]triazolo[4',3':1,2]pyrido[3,4-b]indol-3-yl)-N-methylaniline

To a solution of *2-(2-(methylamino)benzoyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-one* (319 mg, 1 mmol) in EtOH (3 mL) was added $H_4H_2.H_2O$ (0.6 mL, 2 mmol). The reaction mixture was stirred at 70 °C for 2 h, the reaction mixture was diluted with EtOAc (20 mL) and extracted with saturated $NaHCO_3$ (20 mL), The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford the crude product, which was purified by silica gel chromatography (PE/EtOAc = 1:1) to give the desired product (277 mg, 88%) as a yellow solid.

Physical State: yellow solid.

Melting Point: 110.5 – 111.6 °C.

TLC: R_f = 0.25 (PE/EtOAc = 1:1).

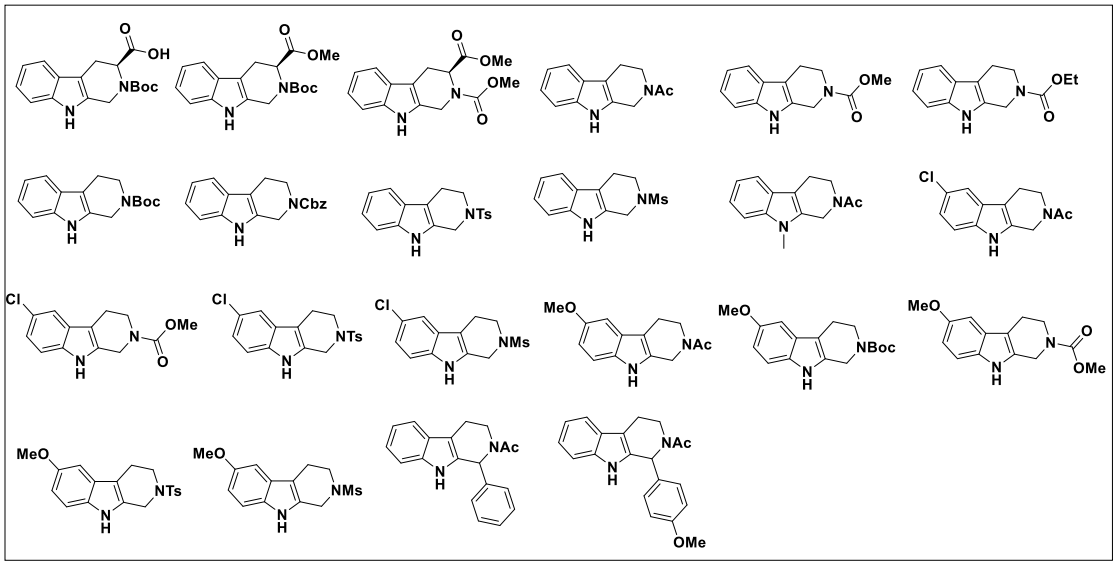
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.95 (s, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.3 Hz, 1H), 7.42 (d, *J* = 7.7 Hz, 1H), 7.33 (m, *J* = 13.3, 7.2 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.02 (s, 1H), 6.68 (d, *J* = 8.4 Hz, 1H), 6.58 (t, *J* = 7.5 Hz, 1H), 3.68 (t, *J* = 6.9 Hz, 2H), 3.05 (t, *J* = 6.9 Hz, 2H), 2.87 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.93, 163.94, 150.48, 137.71, 133.18, 127.37, 126.35, 125.20, 125.07, 120.25, 120.11, 119.96, 114.65, 113.27, 112.73, 111.07, 42.06, 29.69, 20.81.

HRMS (ESI): calcd for $C_{19}H_{17}N_5$ $[M + H]^+$ *m/z* 316.1557, found 316.1555.

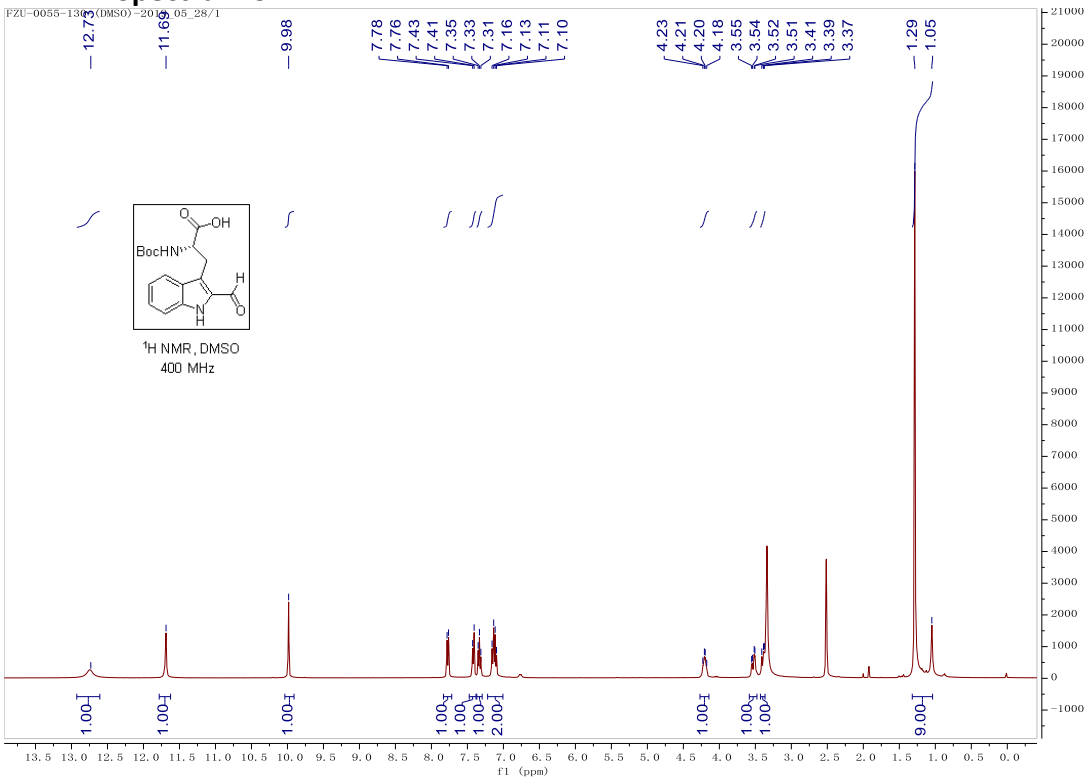
7. Preparation of Substrates

Substrates were prepared according to the published procedures.[1-6]

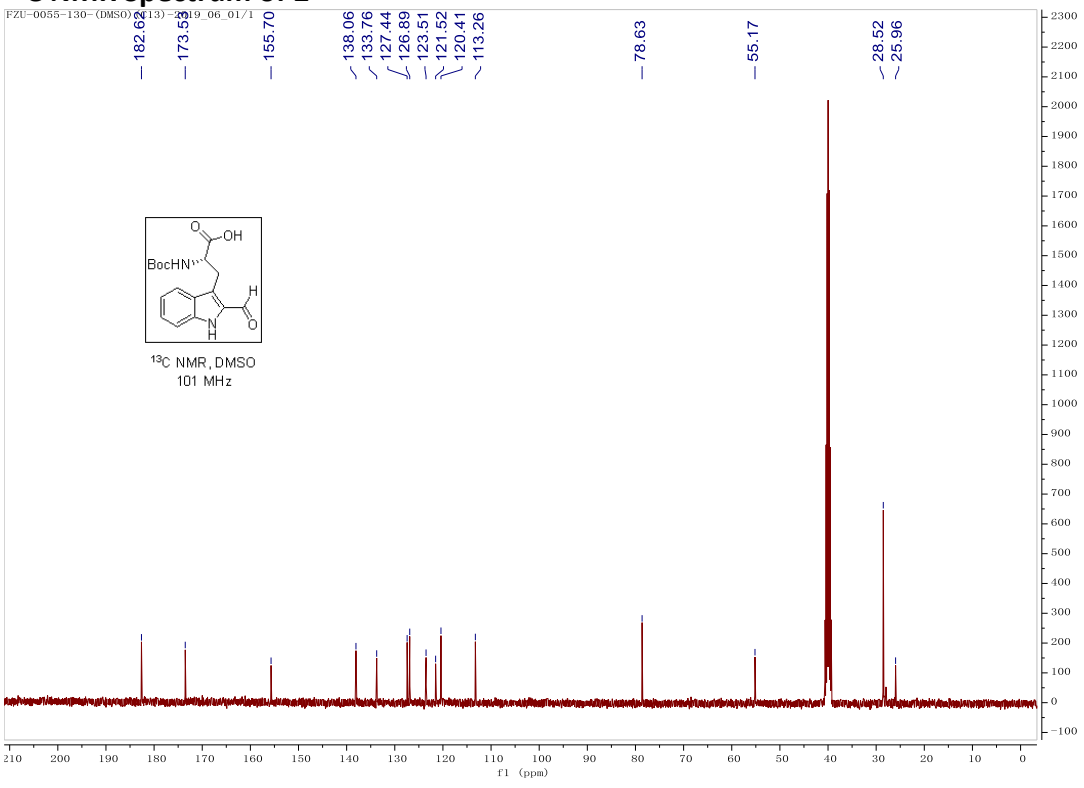


8. NMR Spectrum

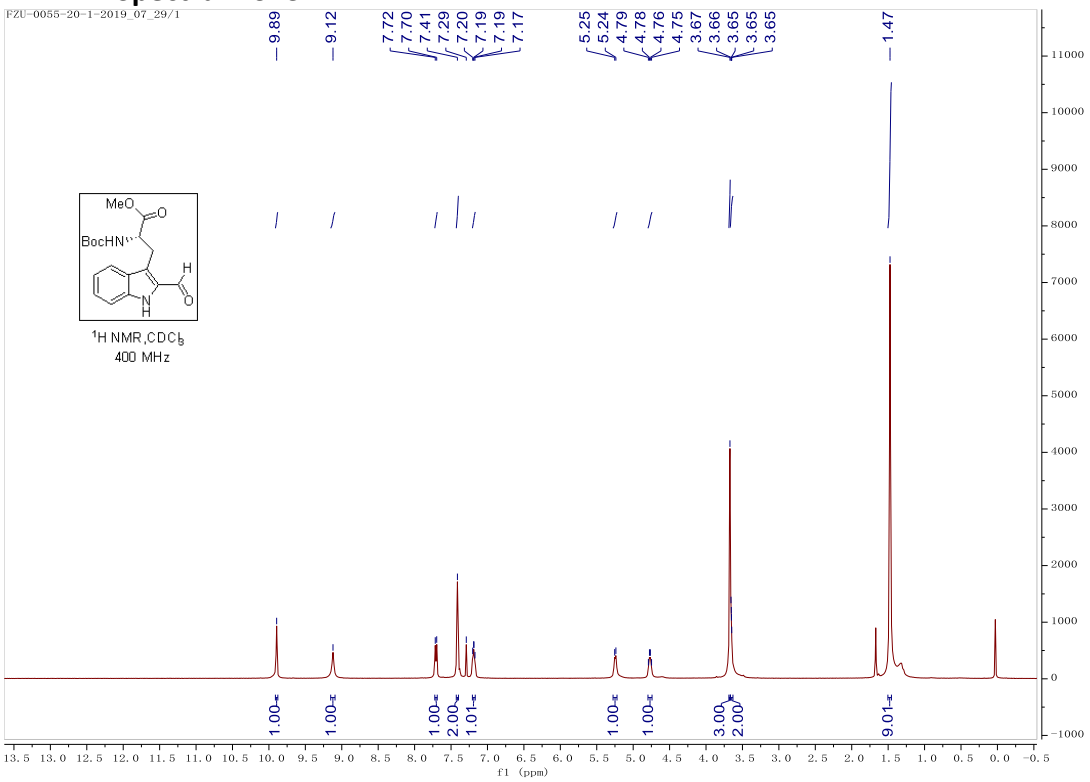
^{1}H NMR Spectrum of 2



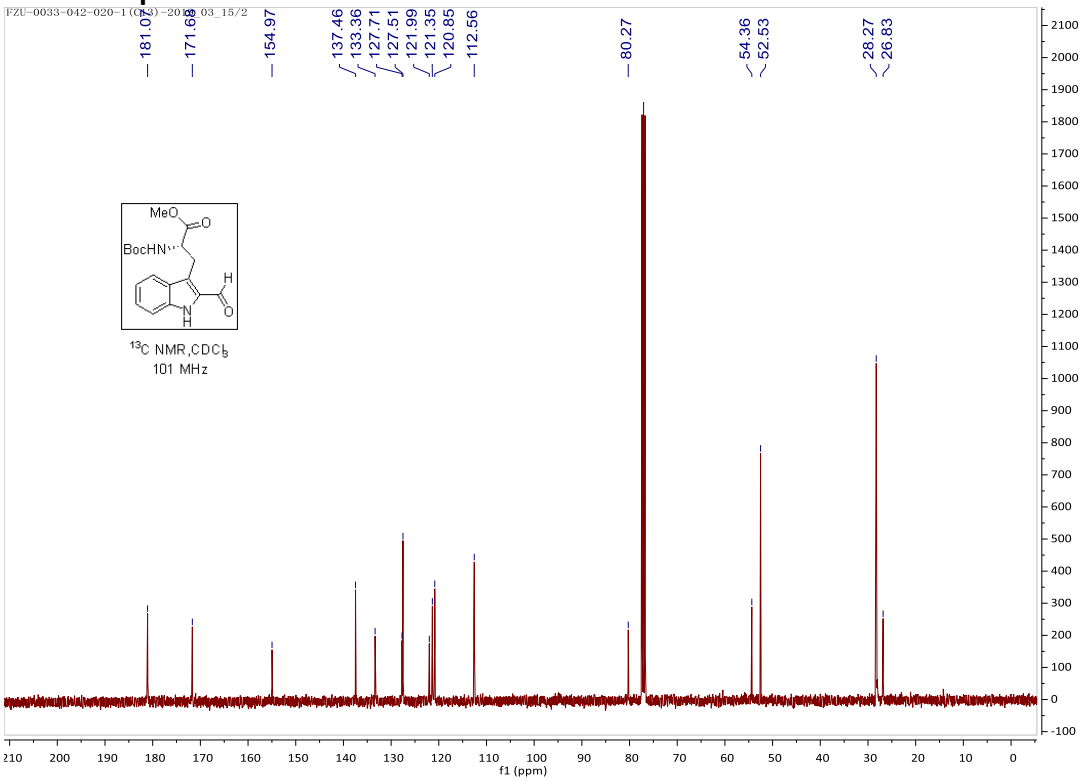
^{13}C NMR Spectrum of 2



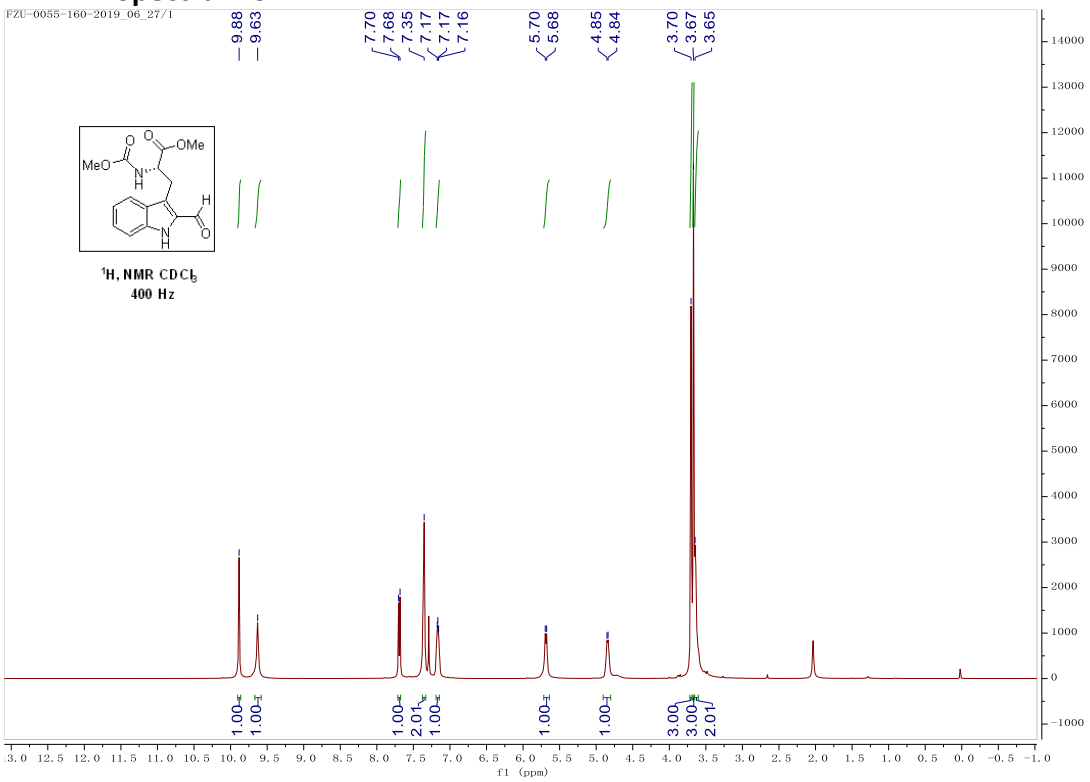
^{1}H NMR Spectrum of 3



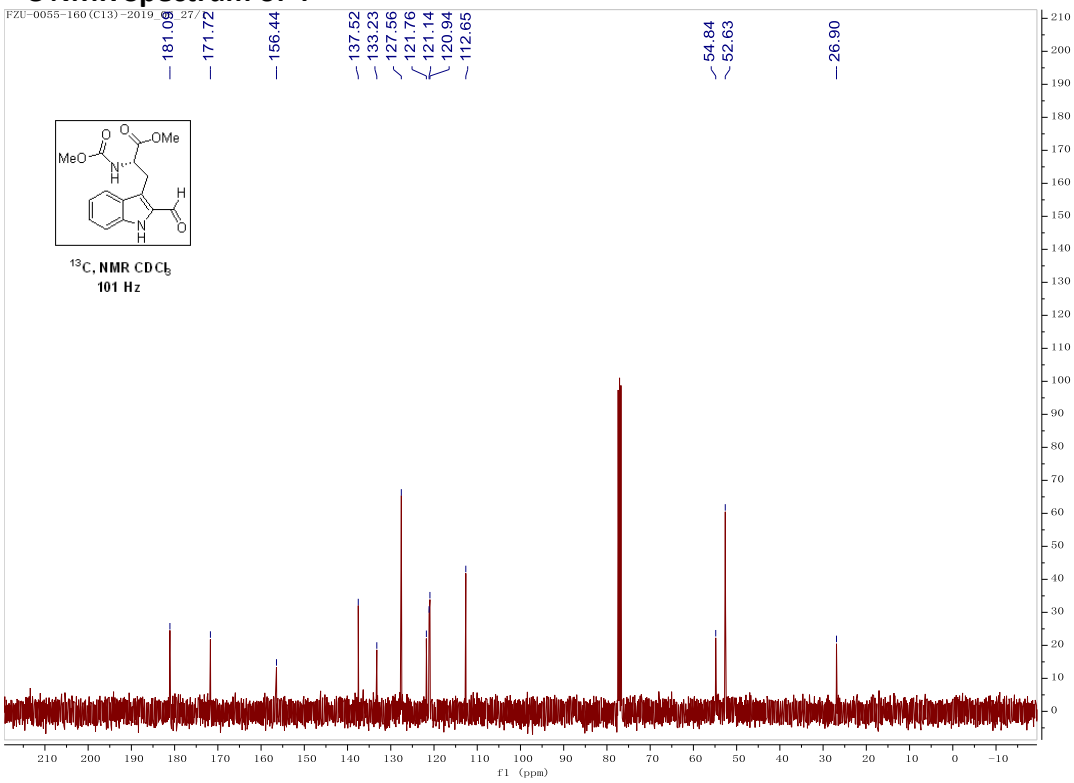
^{13}C NMR Spectrum of 3



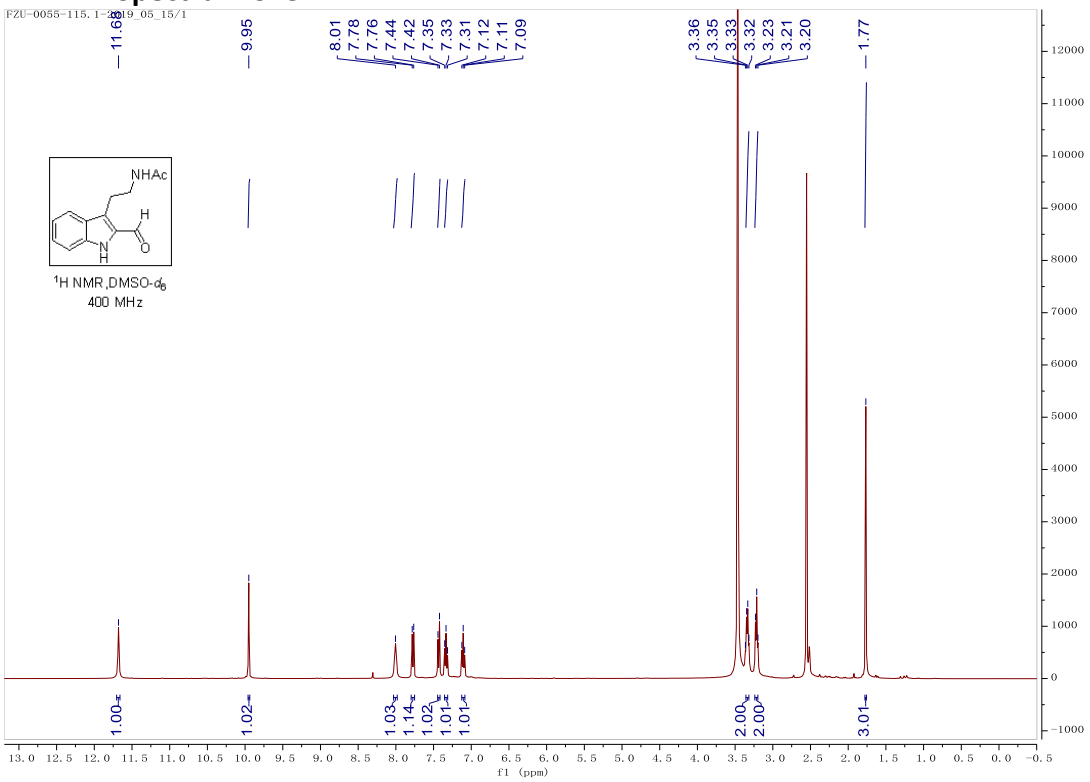
^{1}H NMR Spectrum of 4



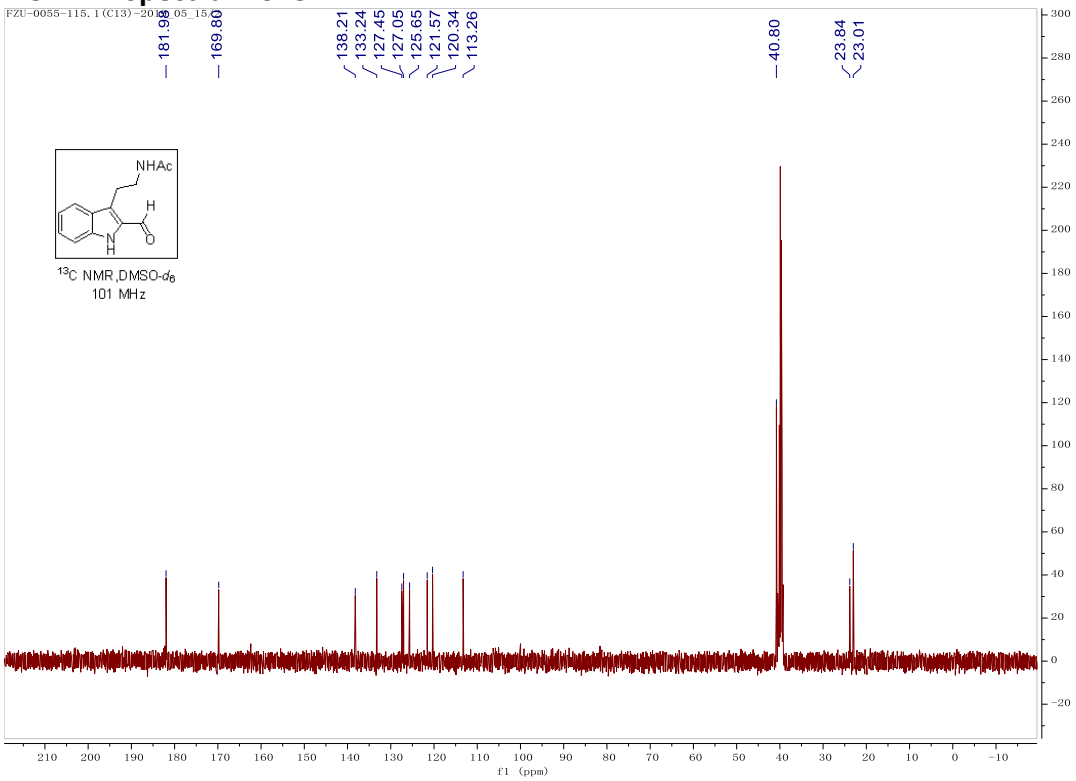
^{13}C NMR Spectrum of 4



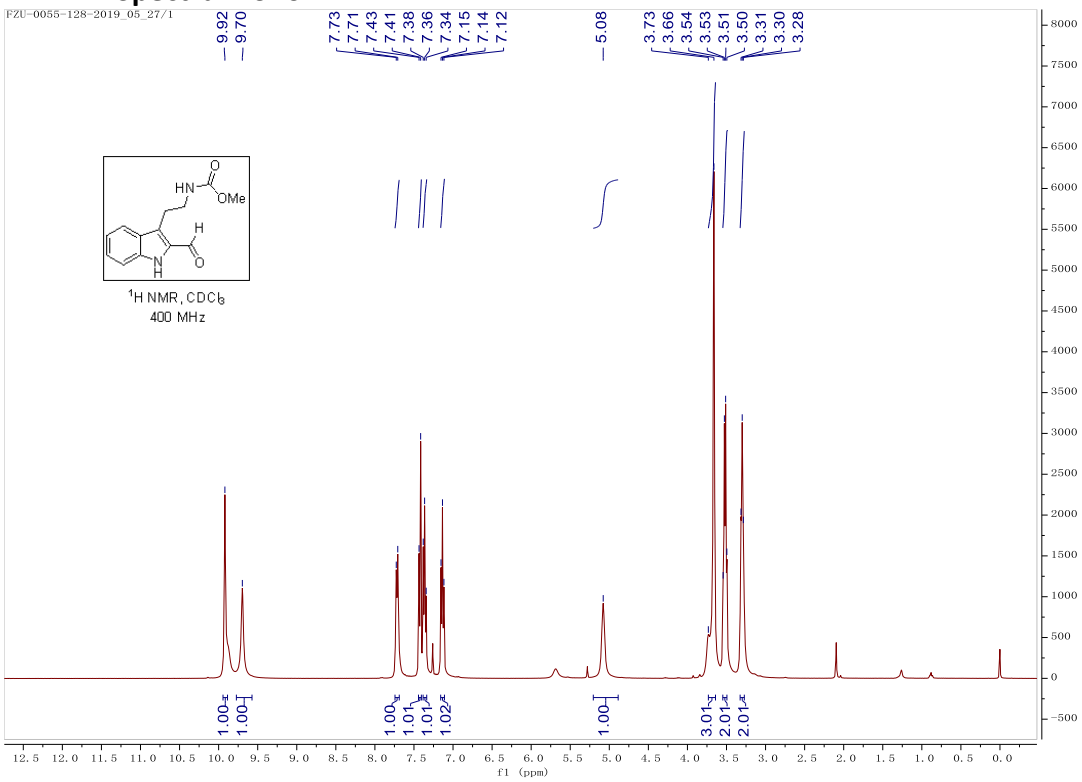
^{1}H NMR Spectrum of 5



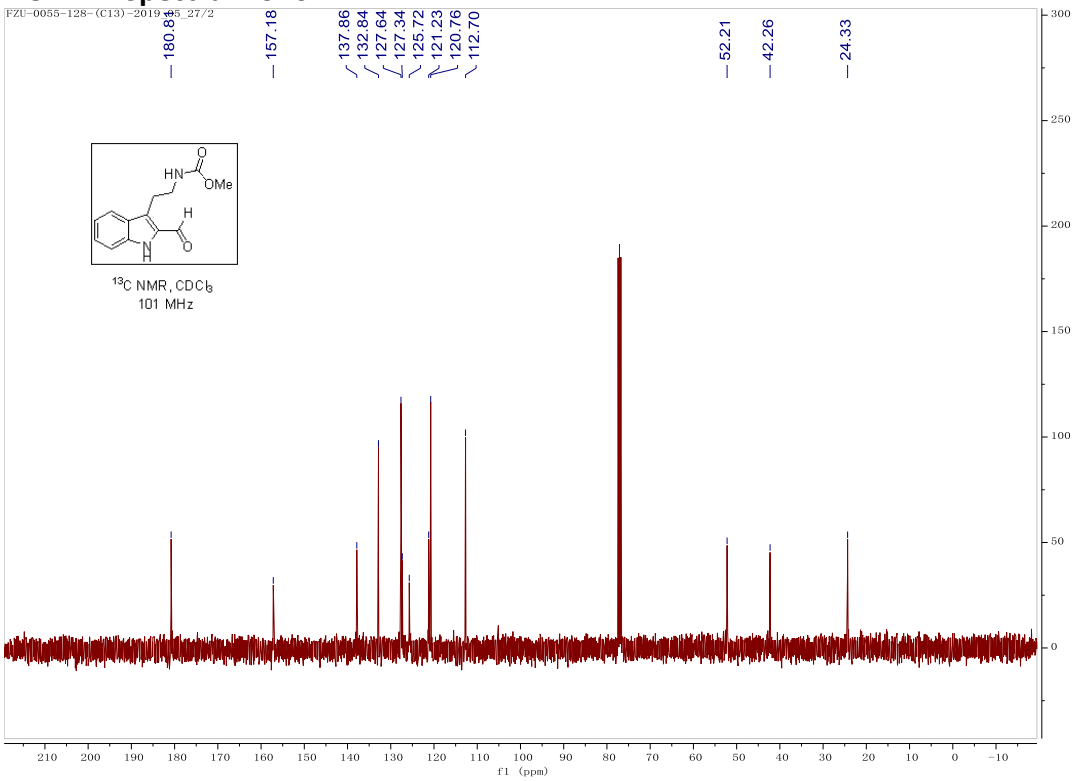
^{13}C NMR Spectrum of 5



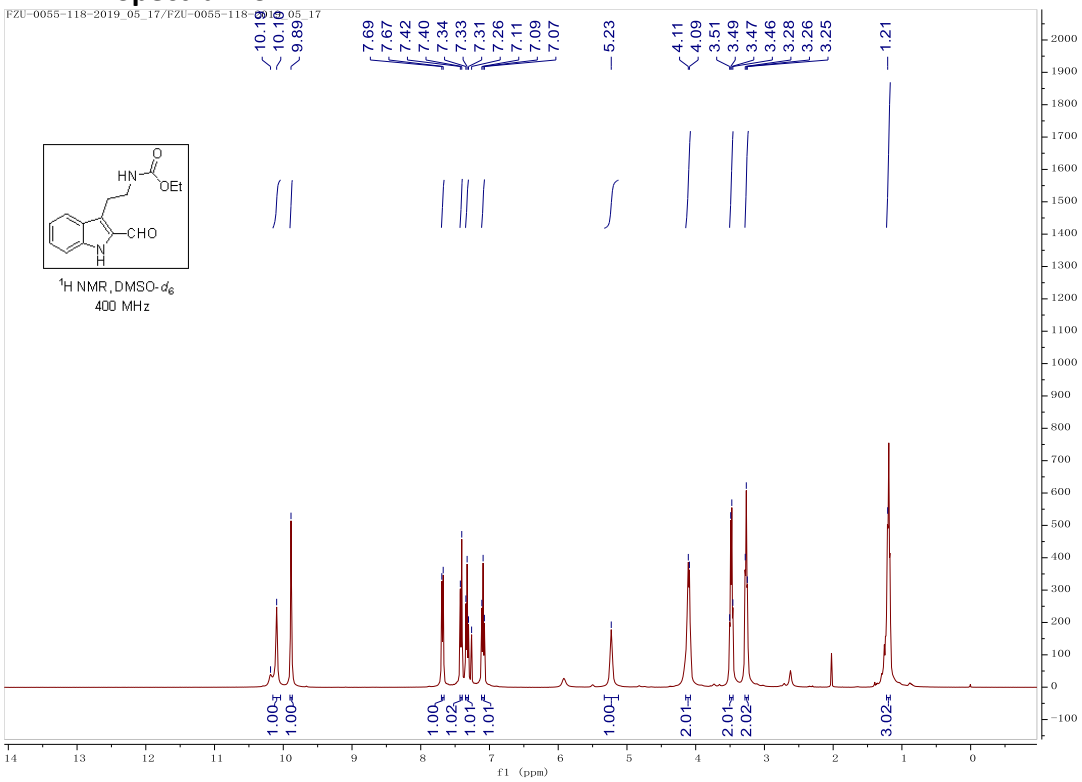
^{1}H NMR Spectrum of 6



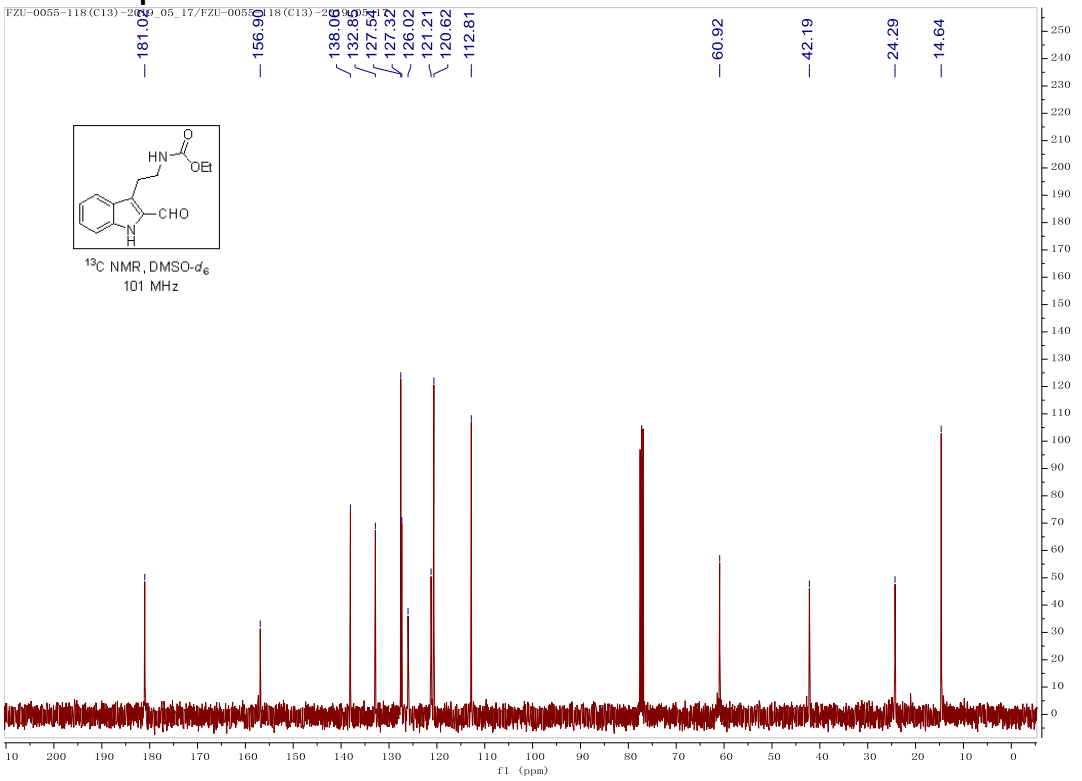
^{13}C NMR Spectrum of 6



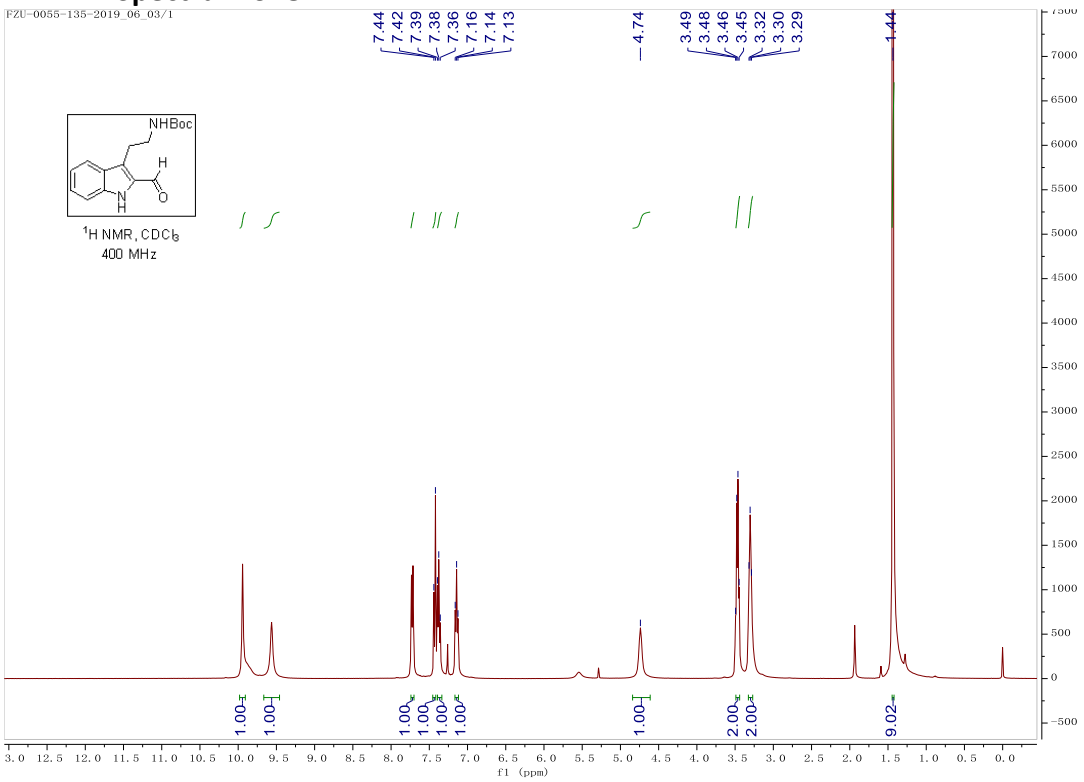
^{1}H NMR Spectrum of 7



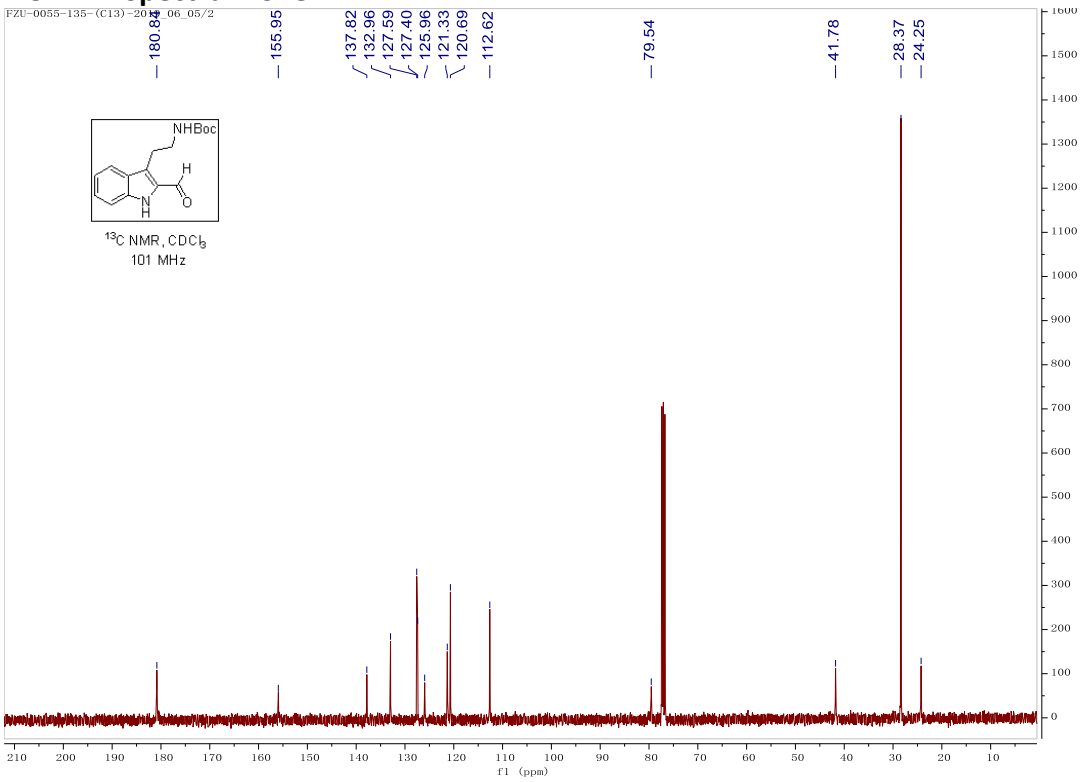
^{13}C NMR Spectrum of 7



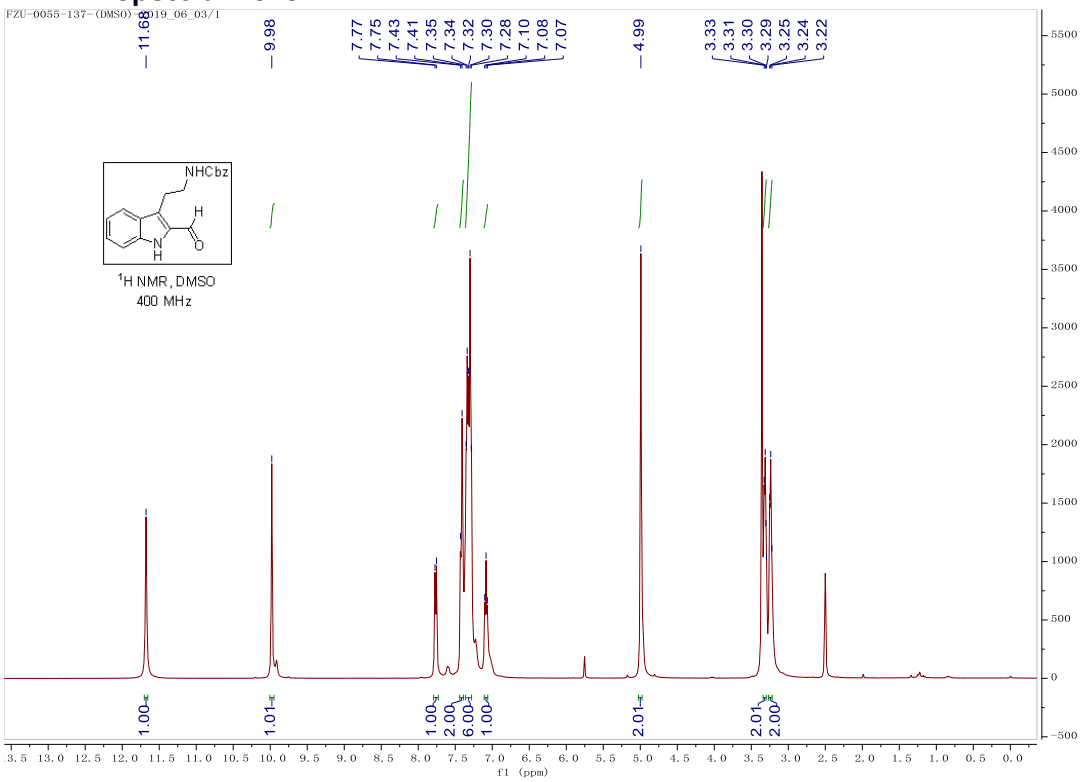
^{1}H NMR Spectrum of 8



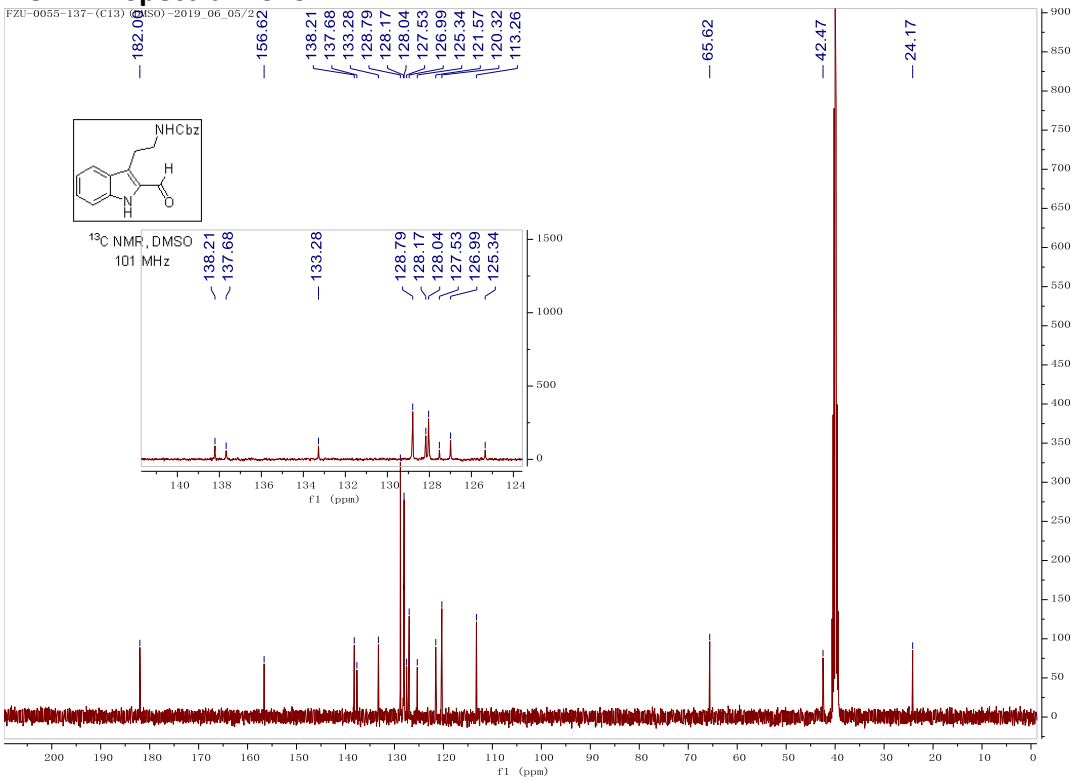
^{13}C NMR Spectrum of 8



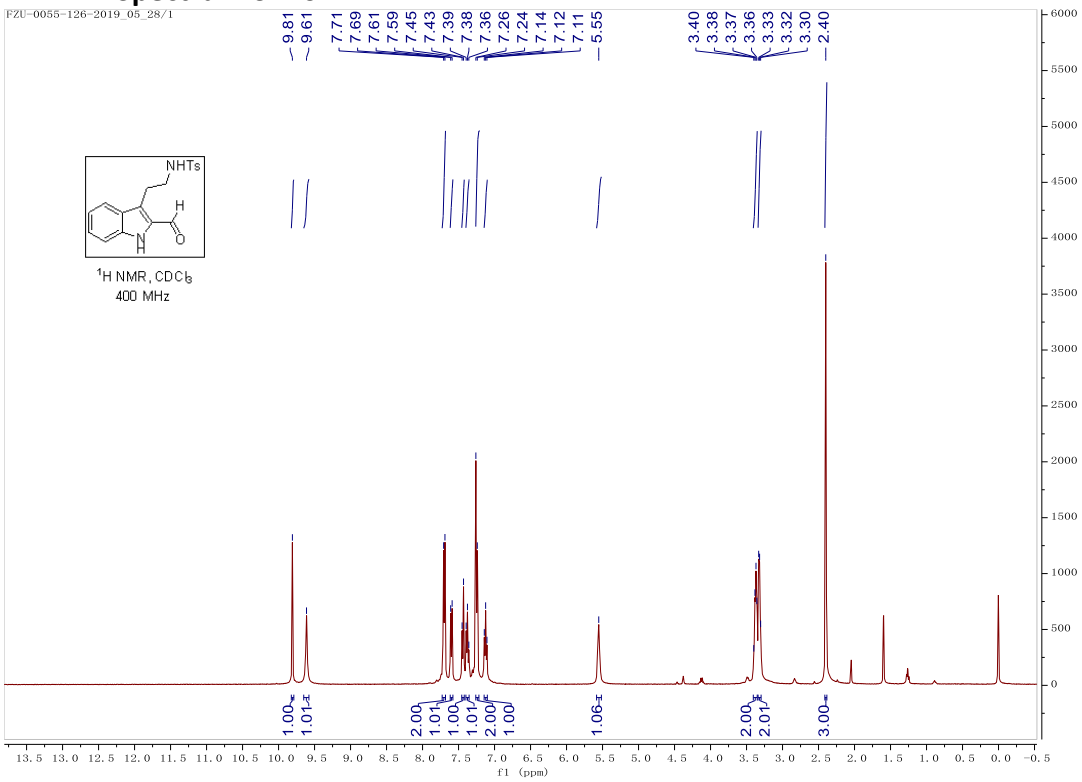
^{1}H NMR Spectrum of 9



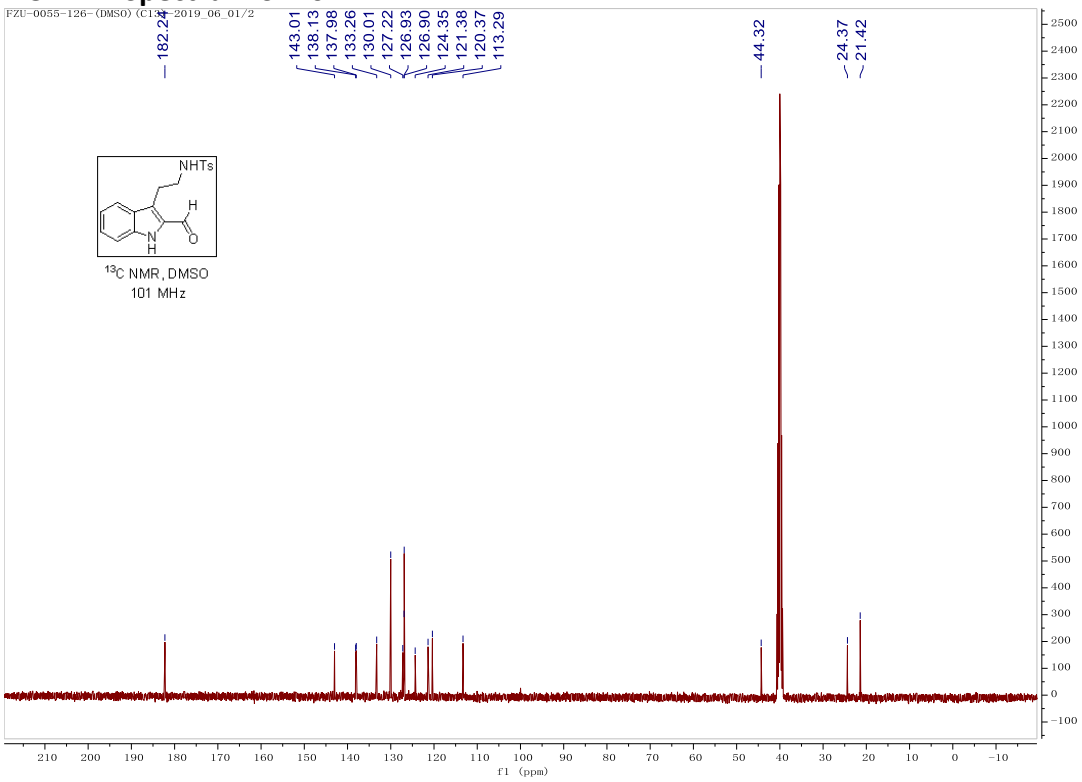
^{13}C NMR Spectrum of 9



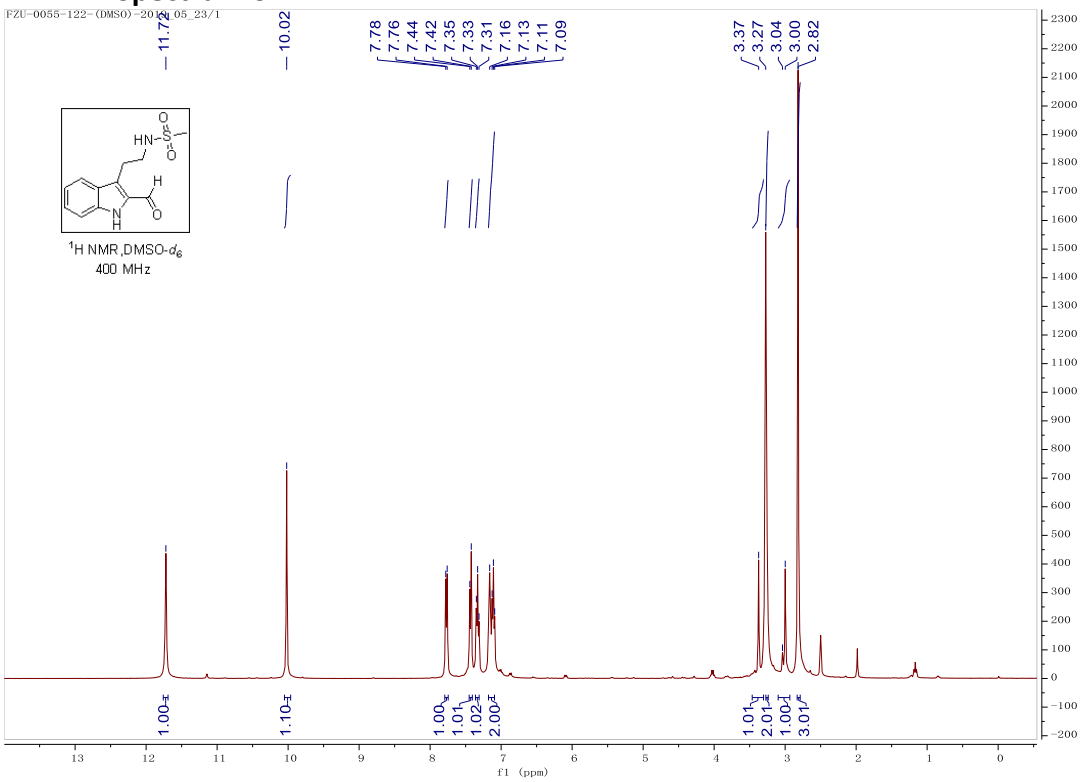
^{1}H NMR Spectrum of 10



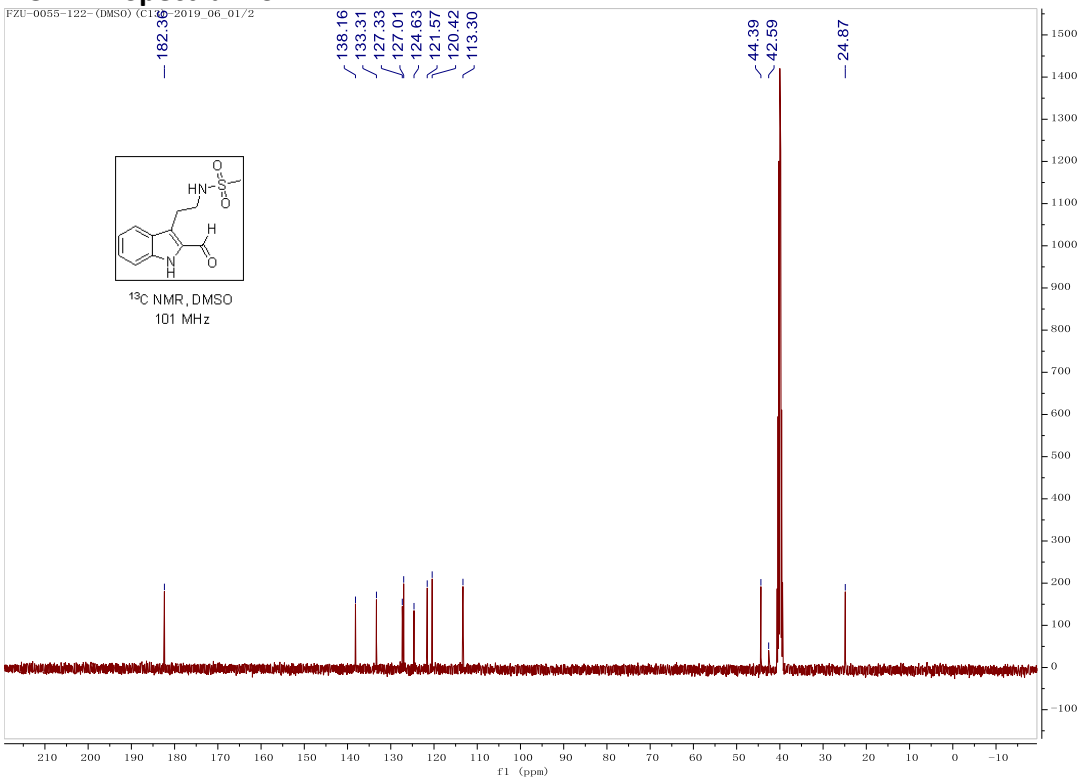
^{13}C NMR Spectrum of 10



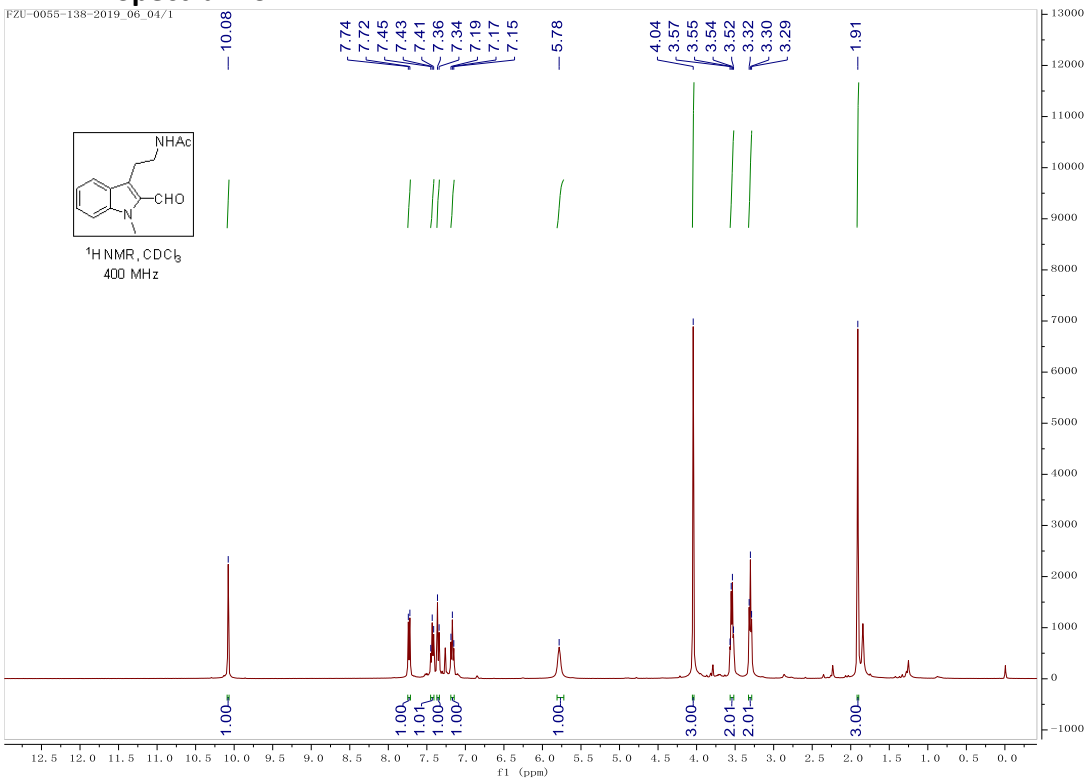
^{1}H NMR Spectrum of 11



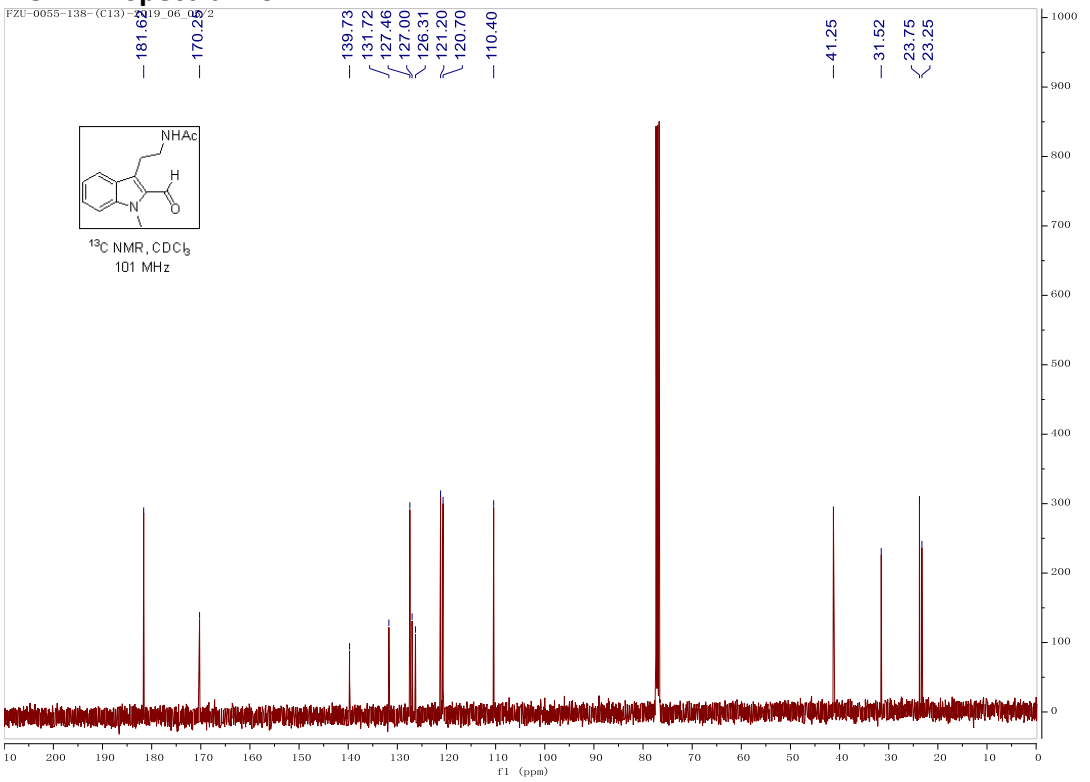
^{13}C NMR Spectrum of 11



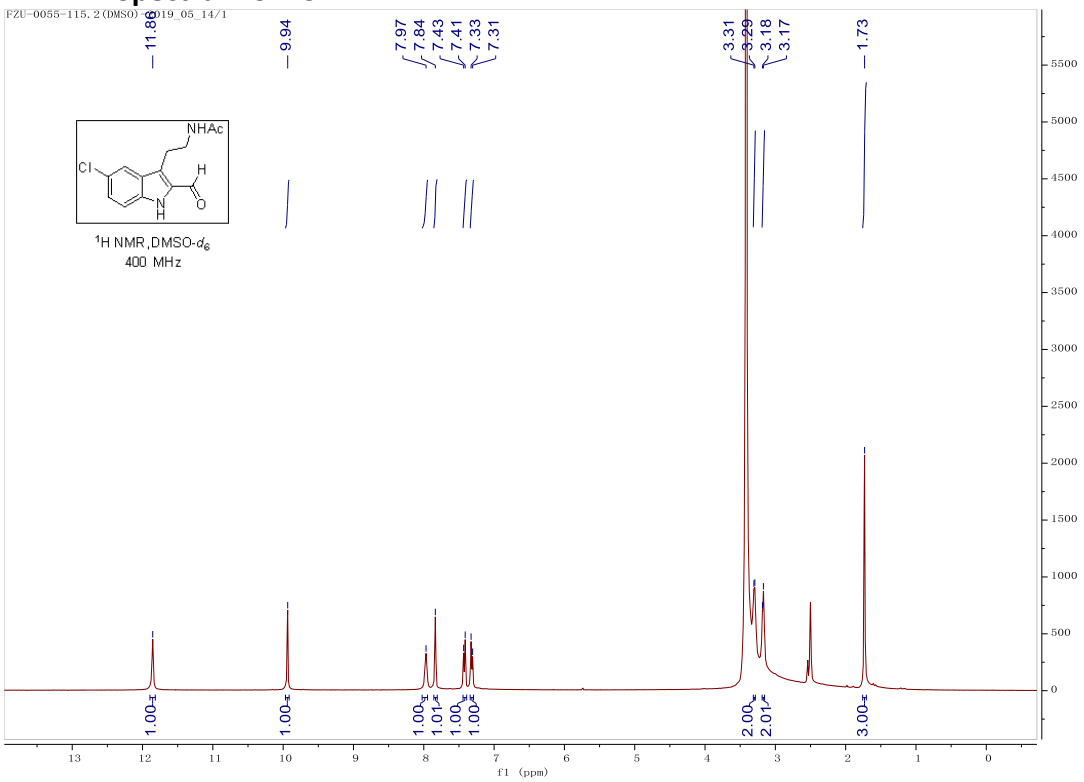
^{1}H NMR Spectrum of 12



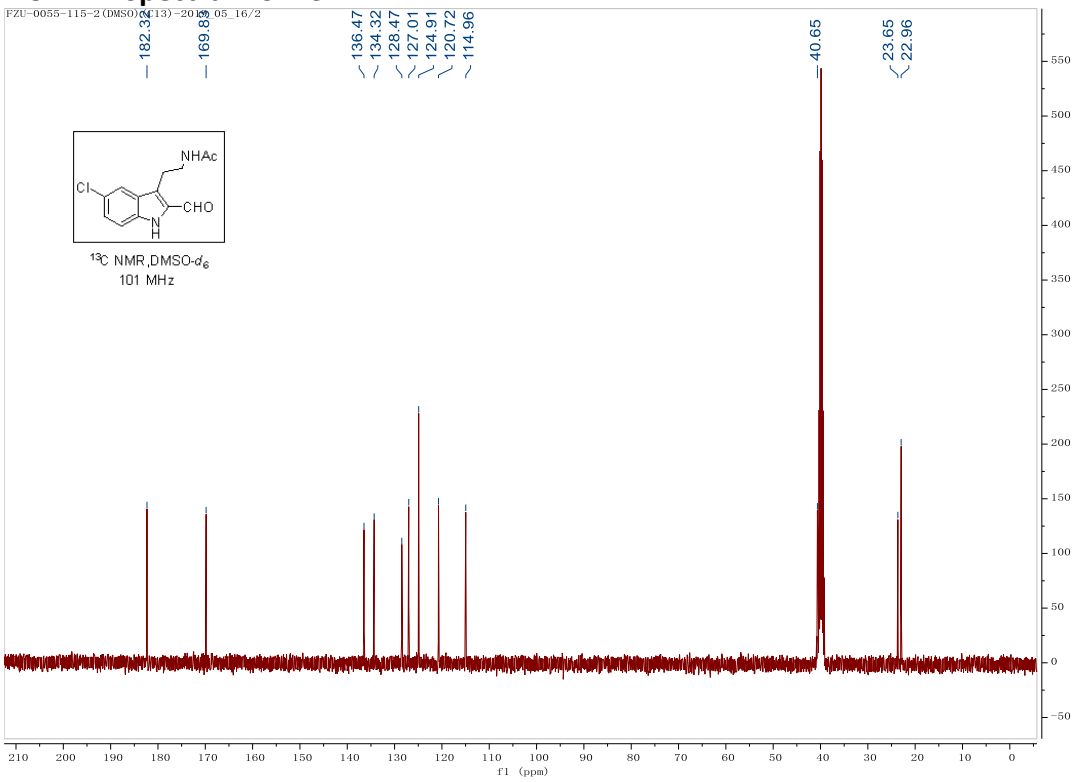
^{13}C NMR Spectrum of 12



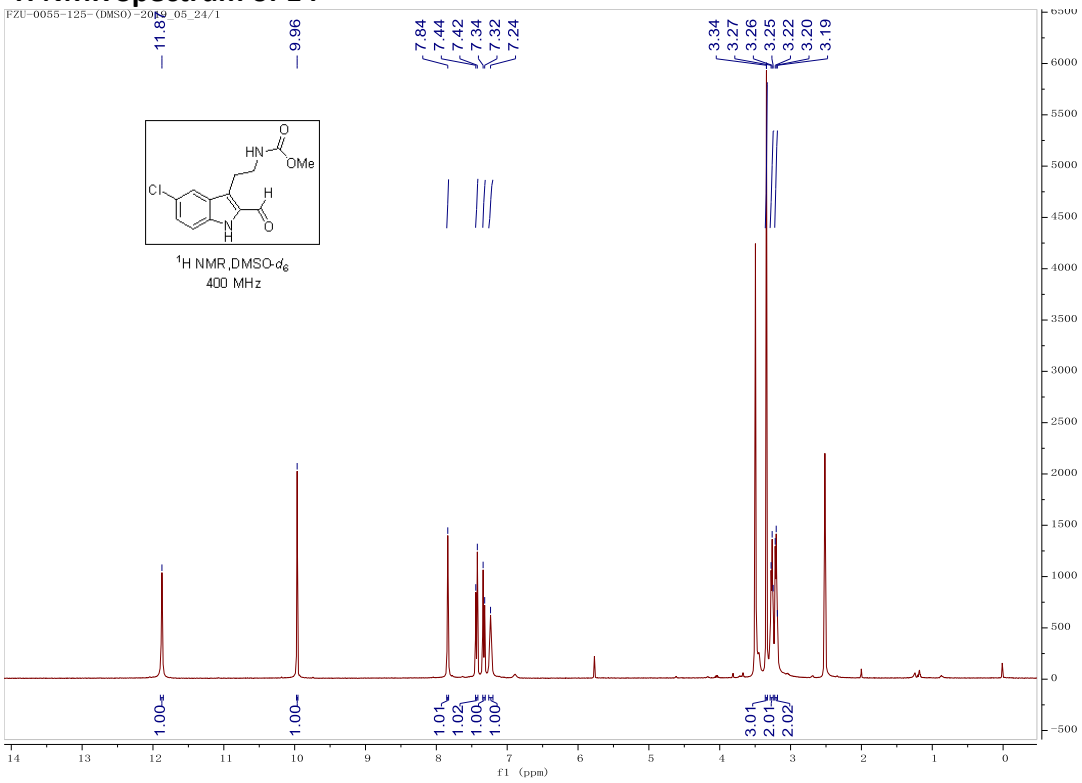
^{1}H NMR Spectrum of 13



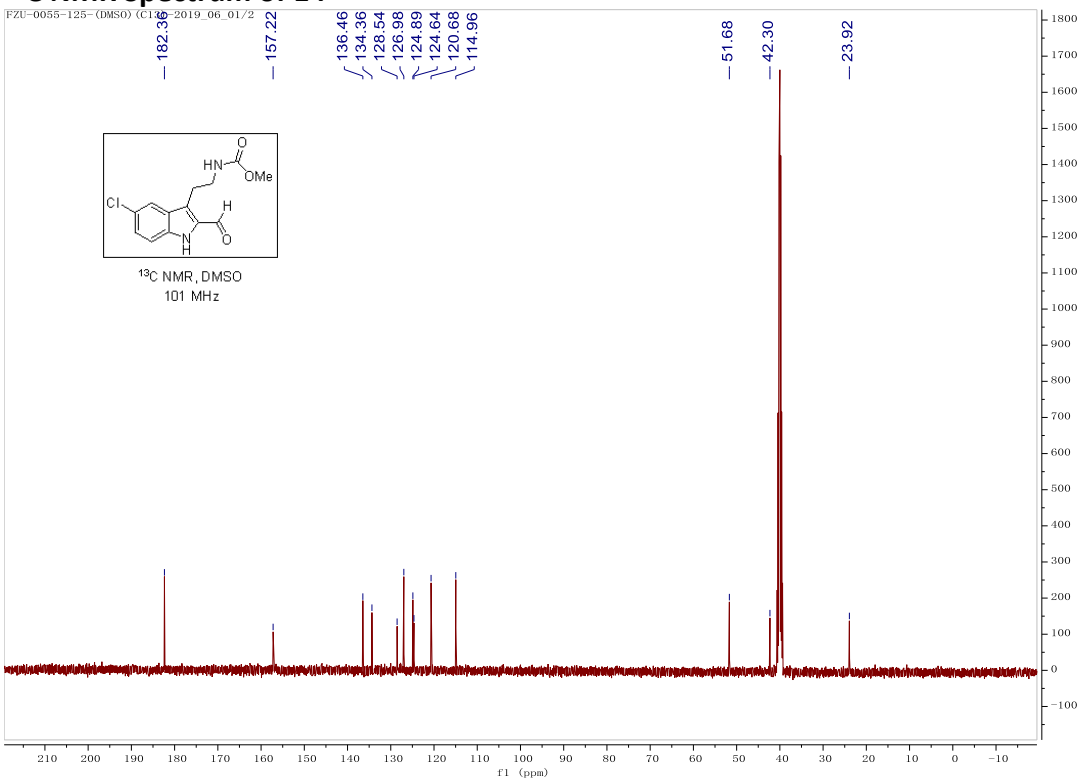
^{13}C NMR Spectrum of 13



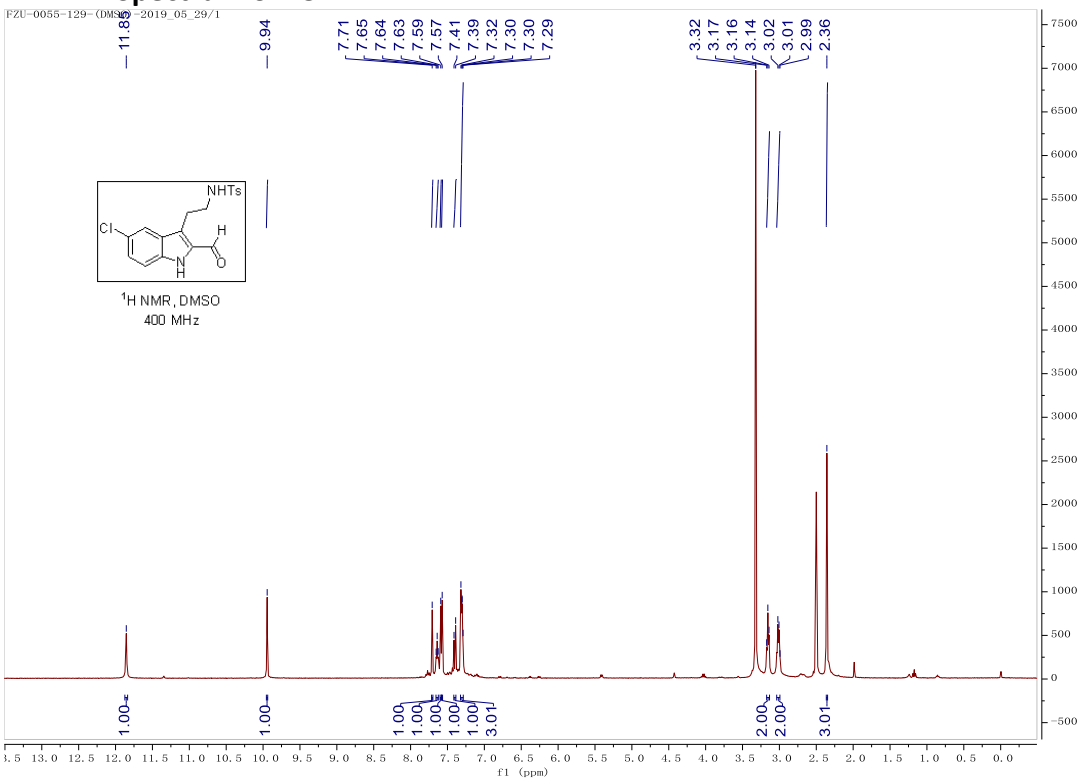
^{1}H NMR Spectrum of 14



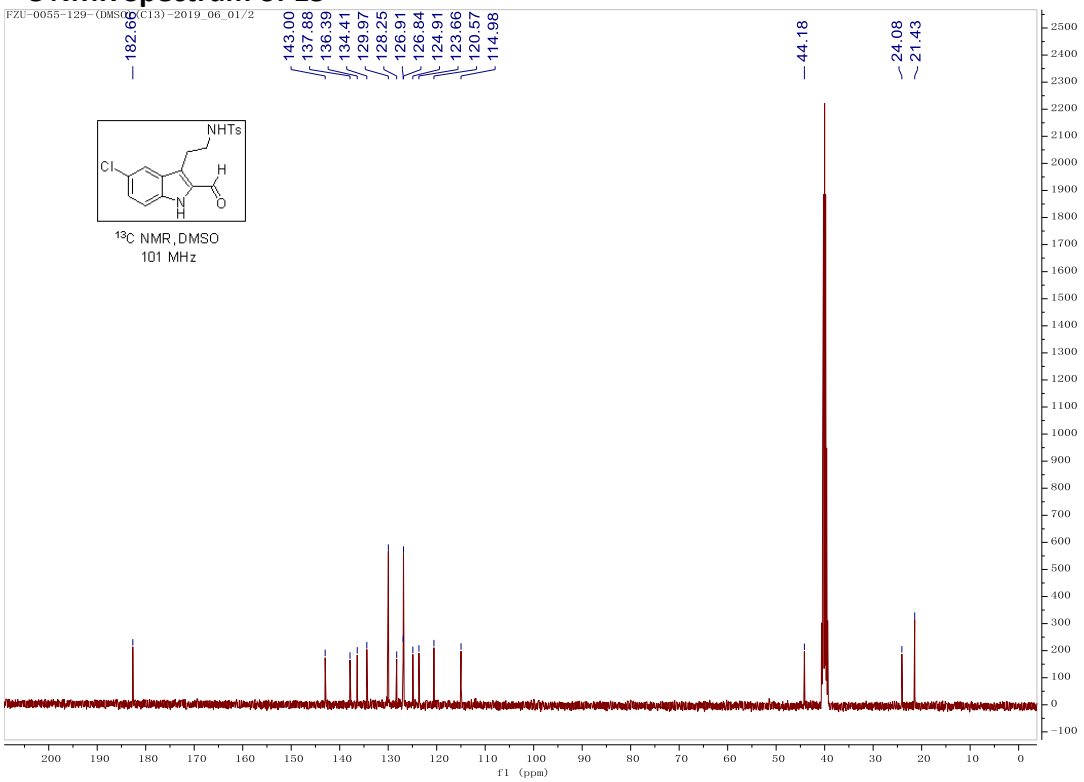
^{13}C NMR Spectrum of 14



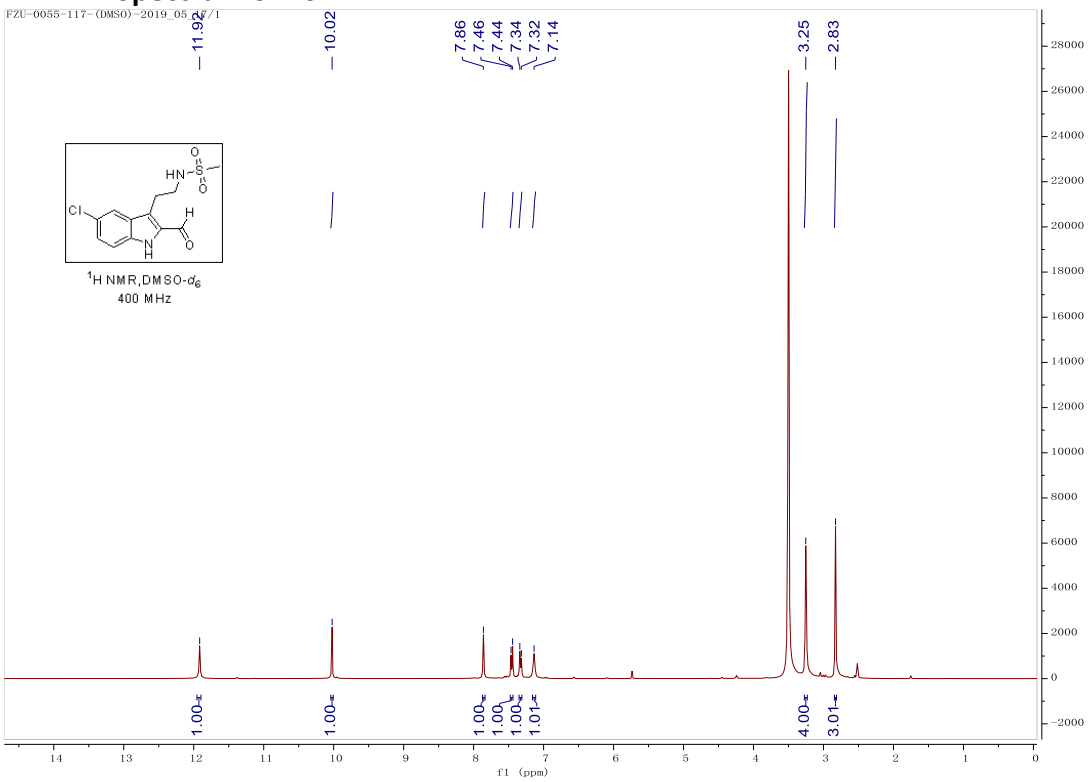
^{1}H NMR Spectrum of 15



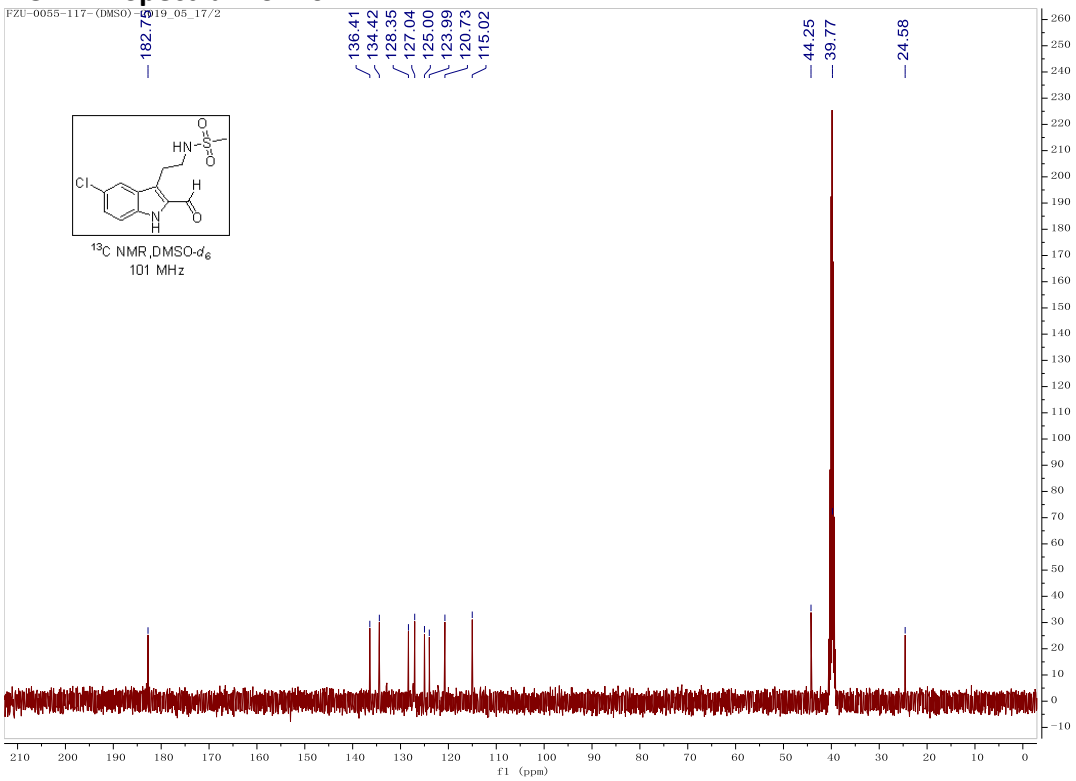
^{13}C NMR Spectrum of 15



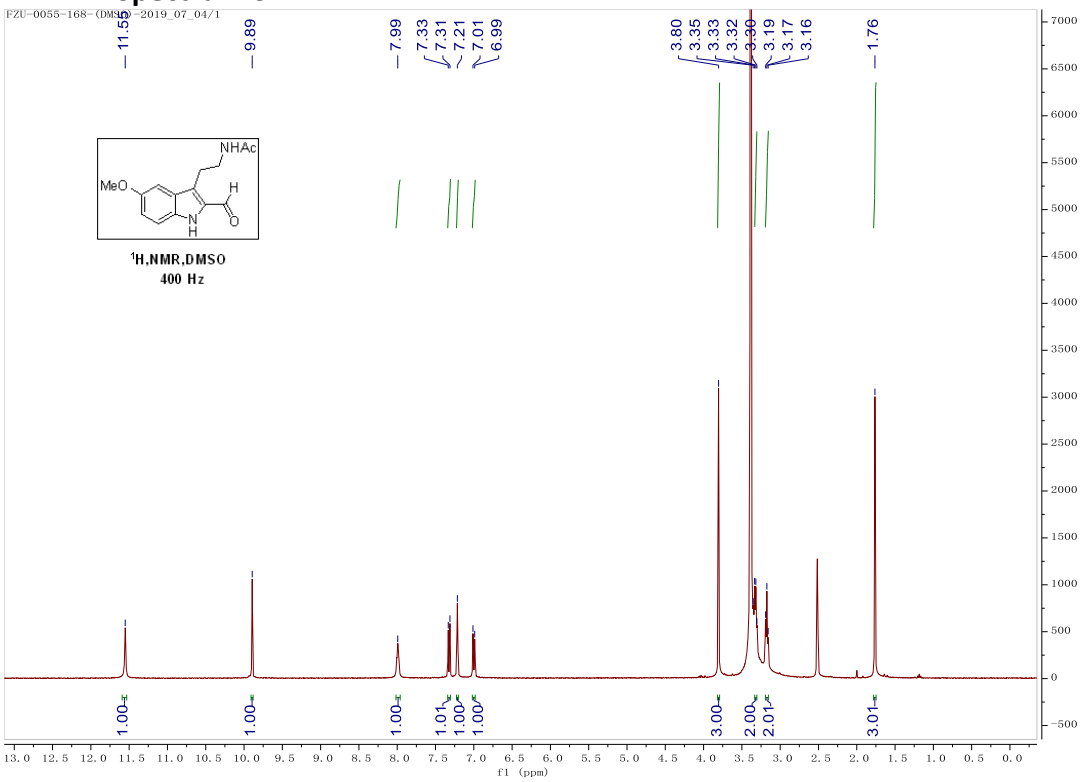
^{1}H NMR Spectrum of 16



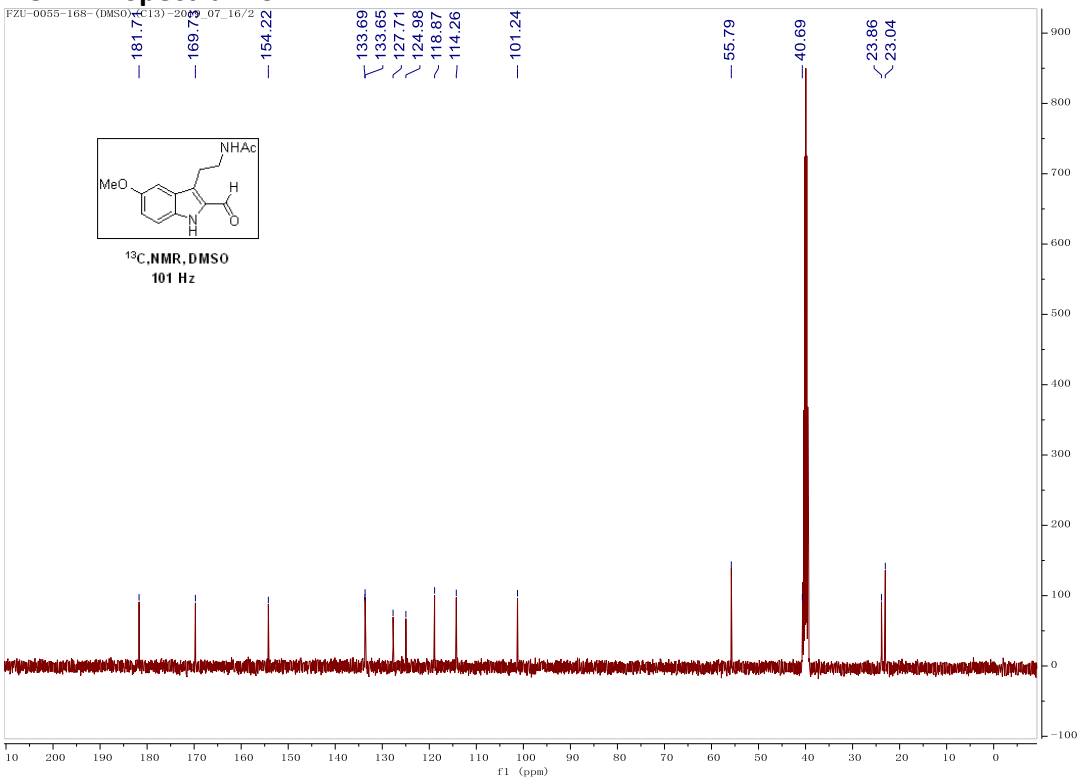
^{13}C NMR Spectrum of 16



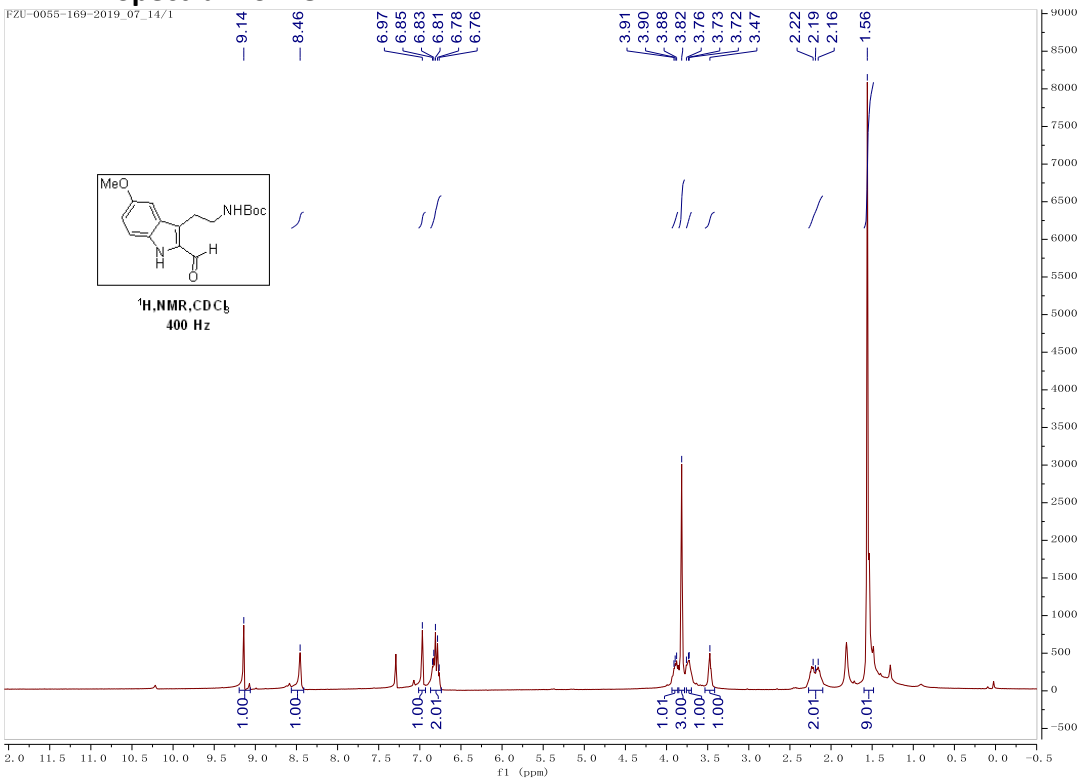
^{1}H NMR Spectrum of 17



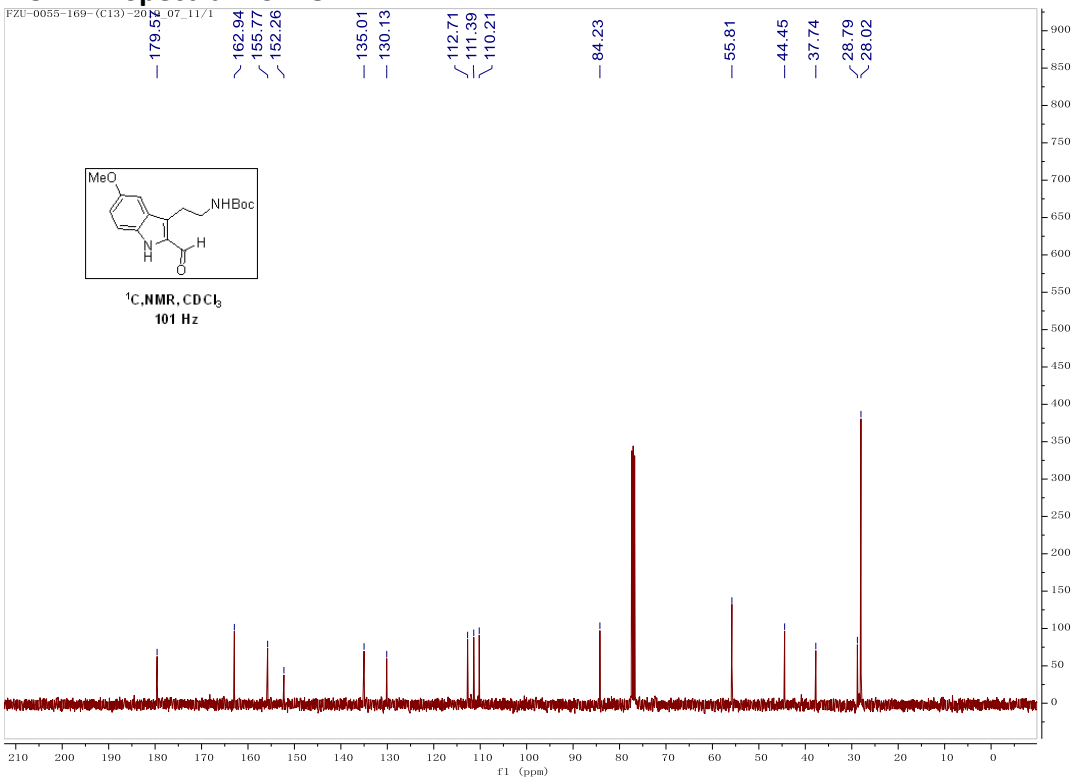
^{13}C NMR Spectrum of 17



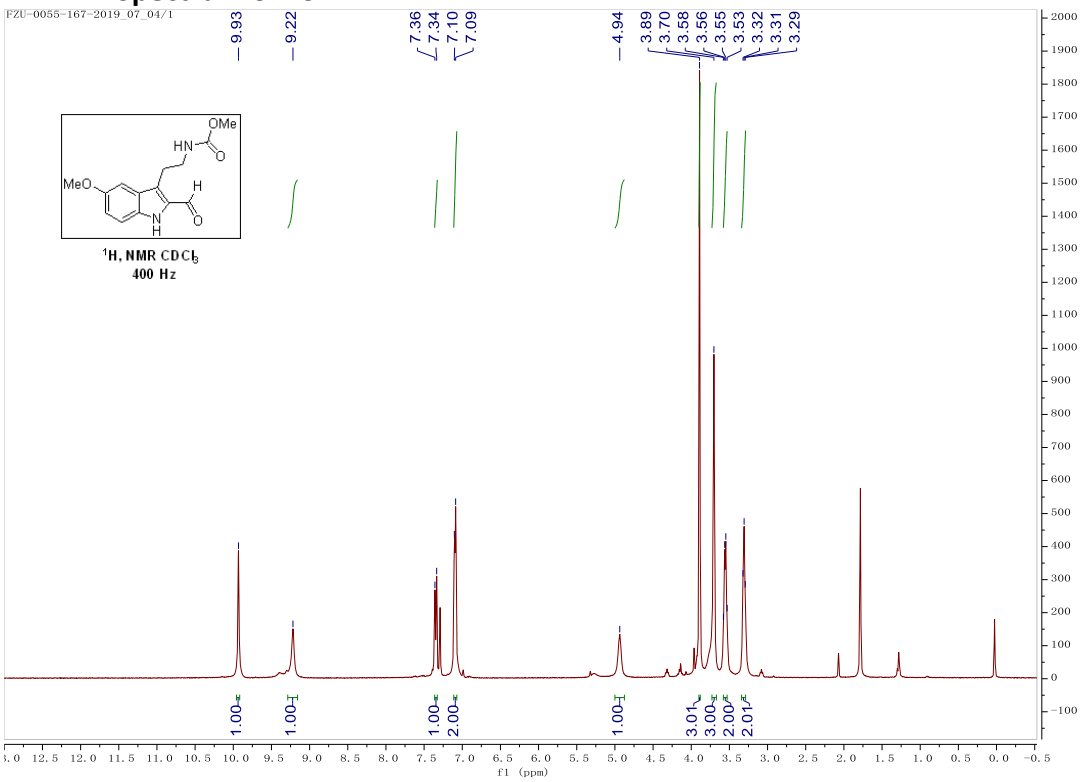
^{1}H NMR Spectrum of 18



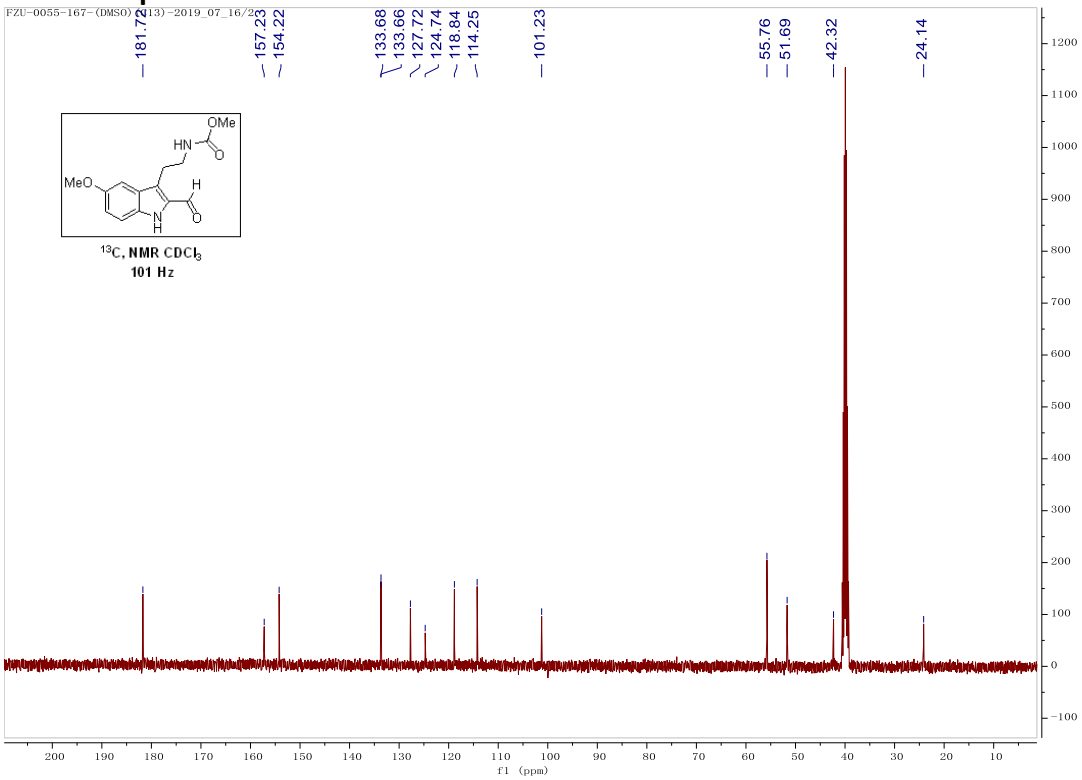
^{13}C NMR Spectrum of 18



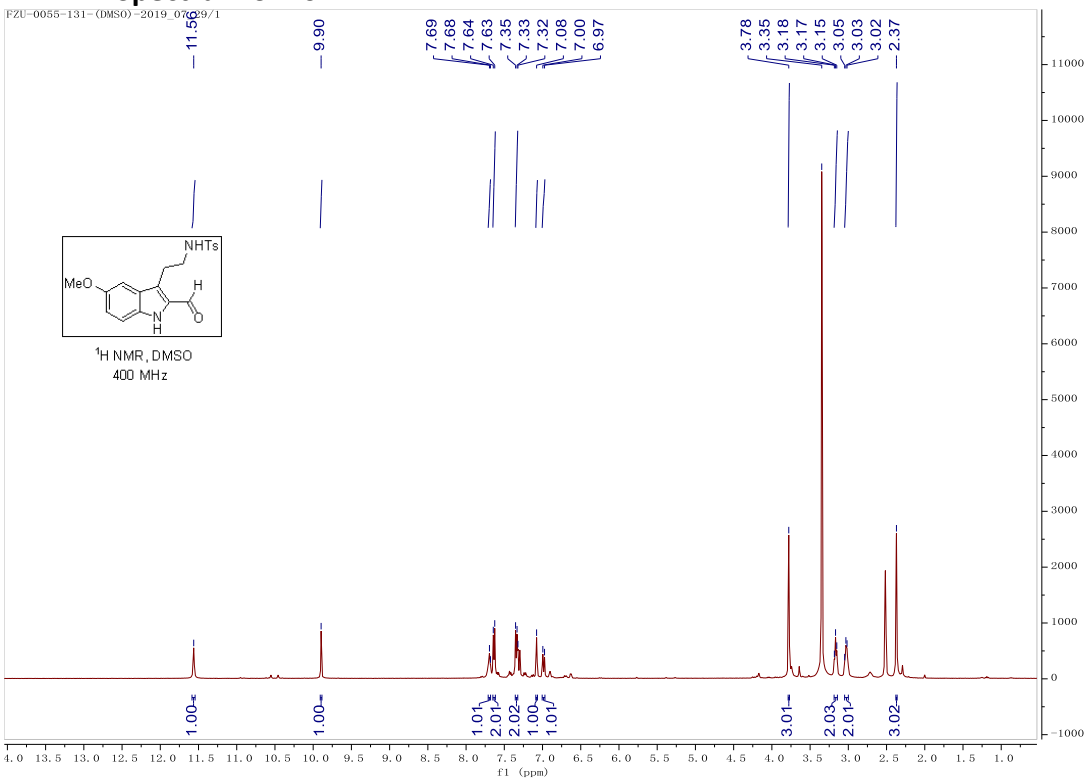
^{1}H NMR Spectrum of 19



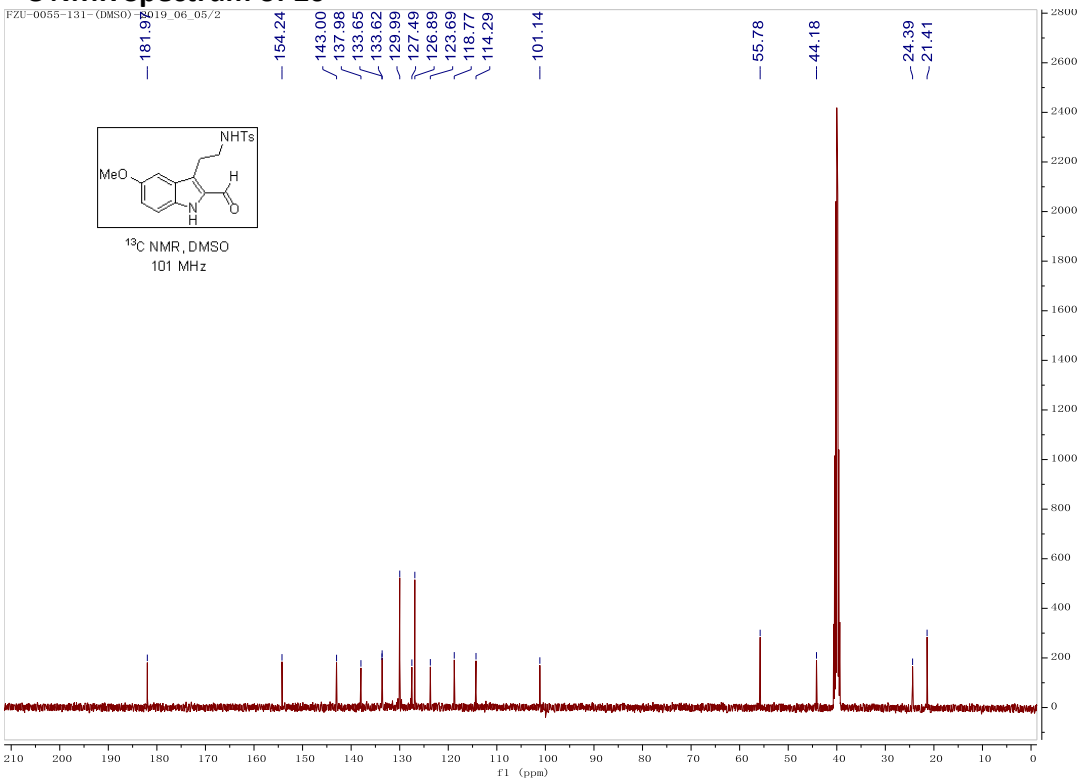
^{13}C NMR Spectrum of 19



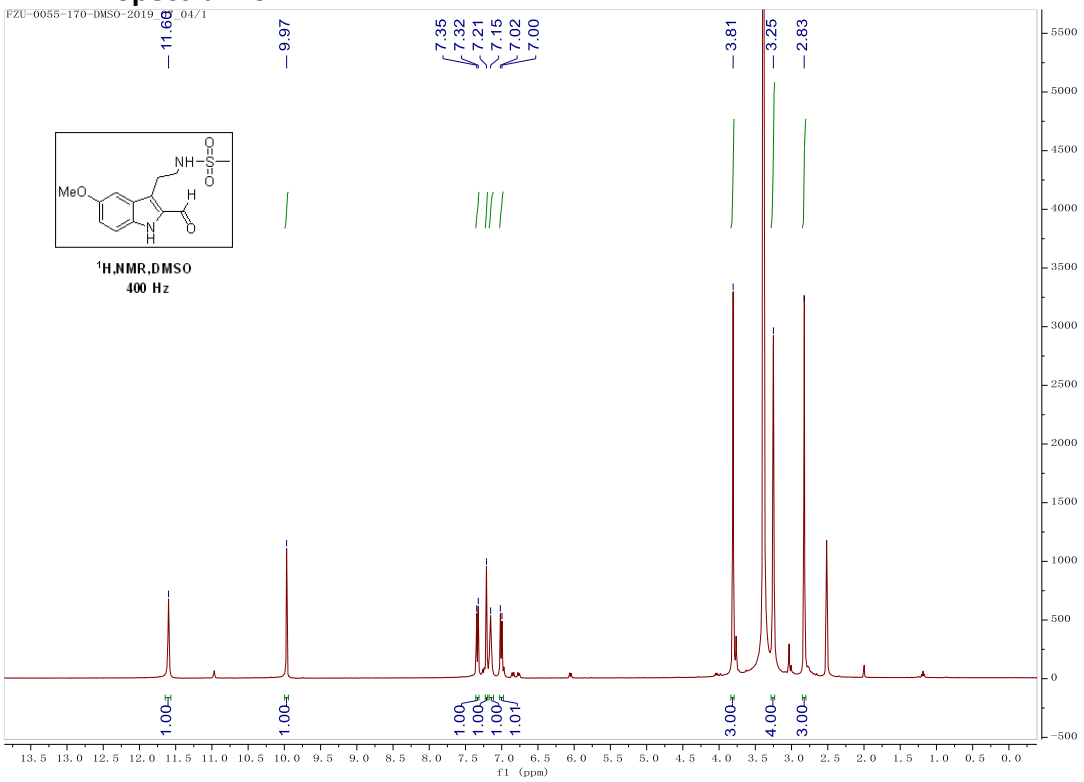
^{1}H NMR Spectrum of 20



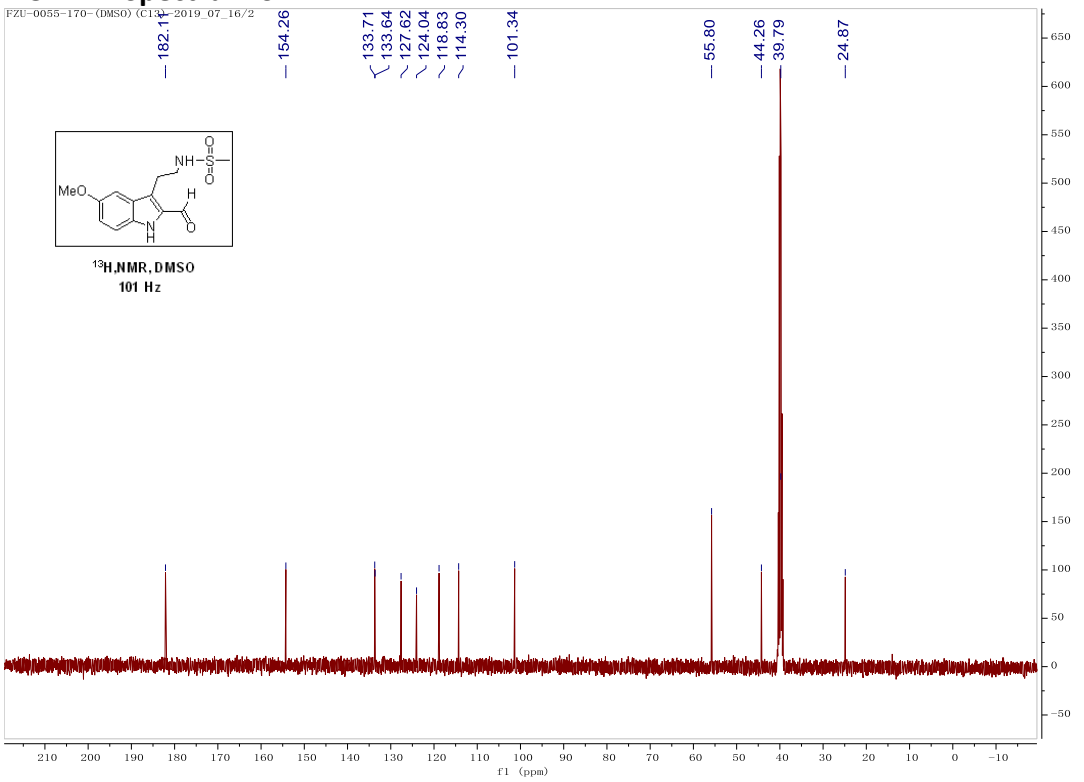
^{13}C NMR Spectrum of 20



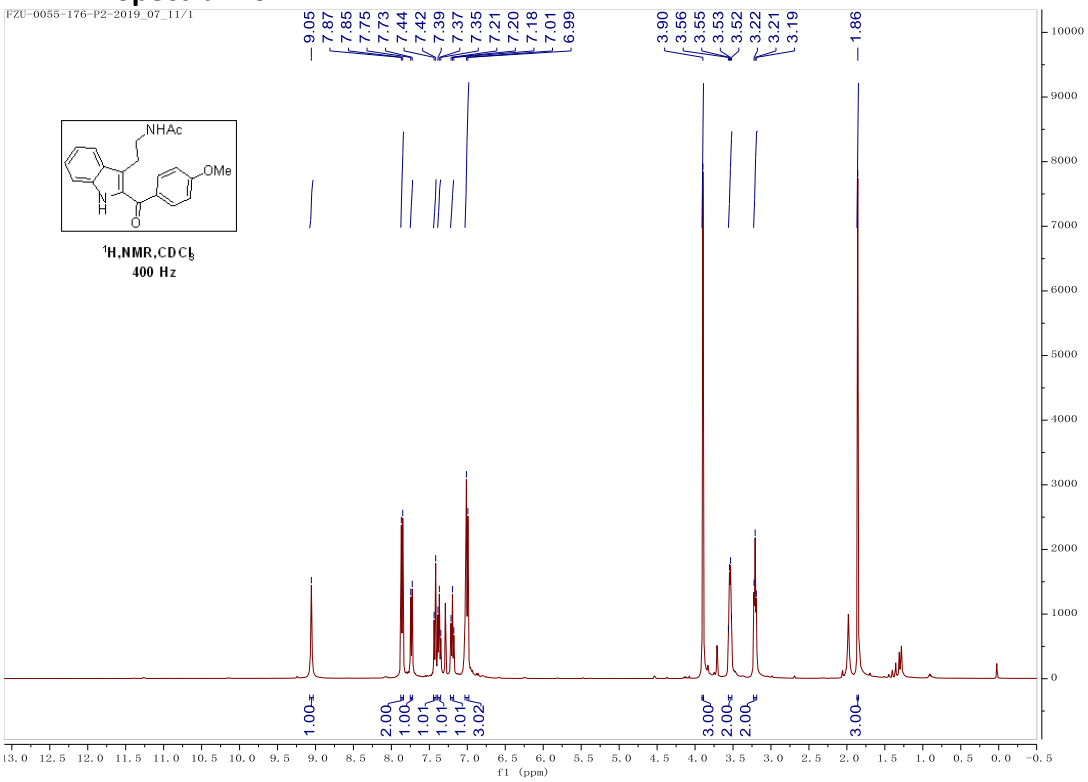
^{1}H NMR Spectrum of 21



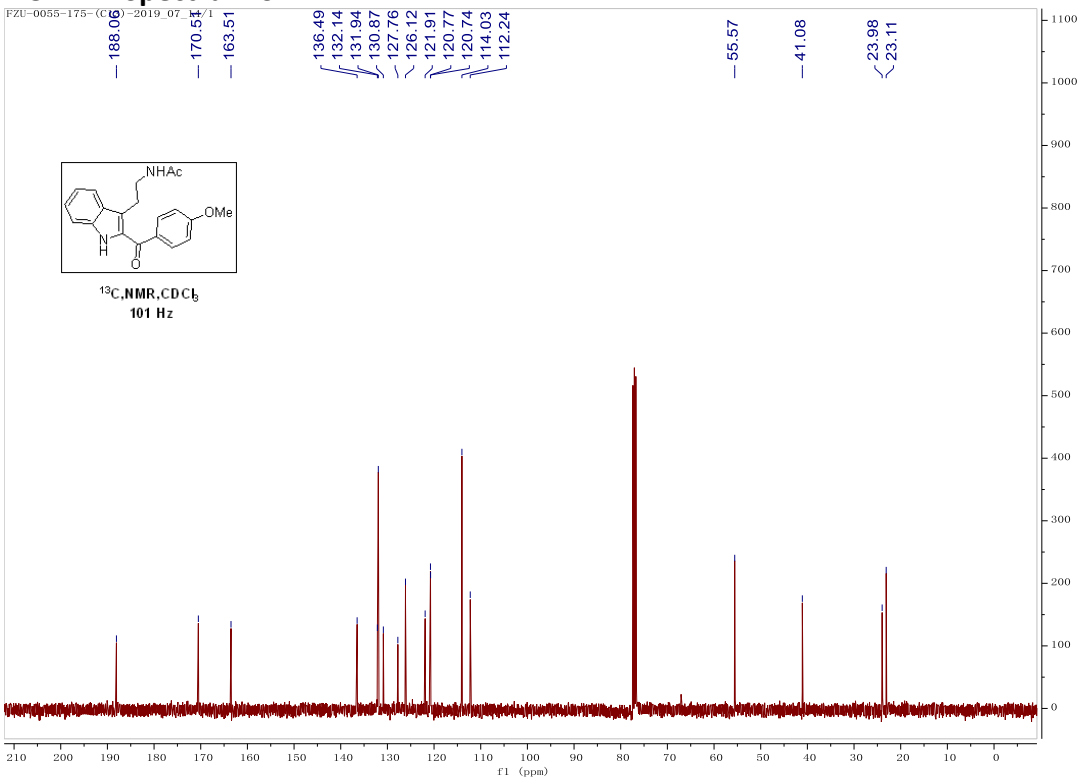
^{13}C NMR Spectrum of 21



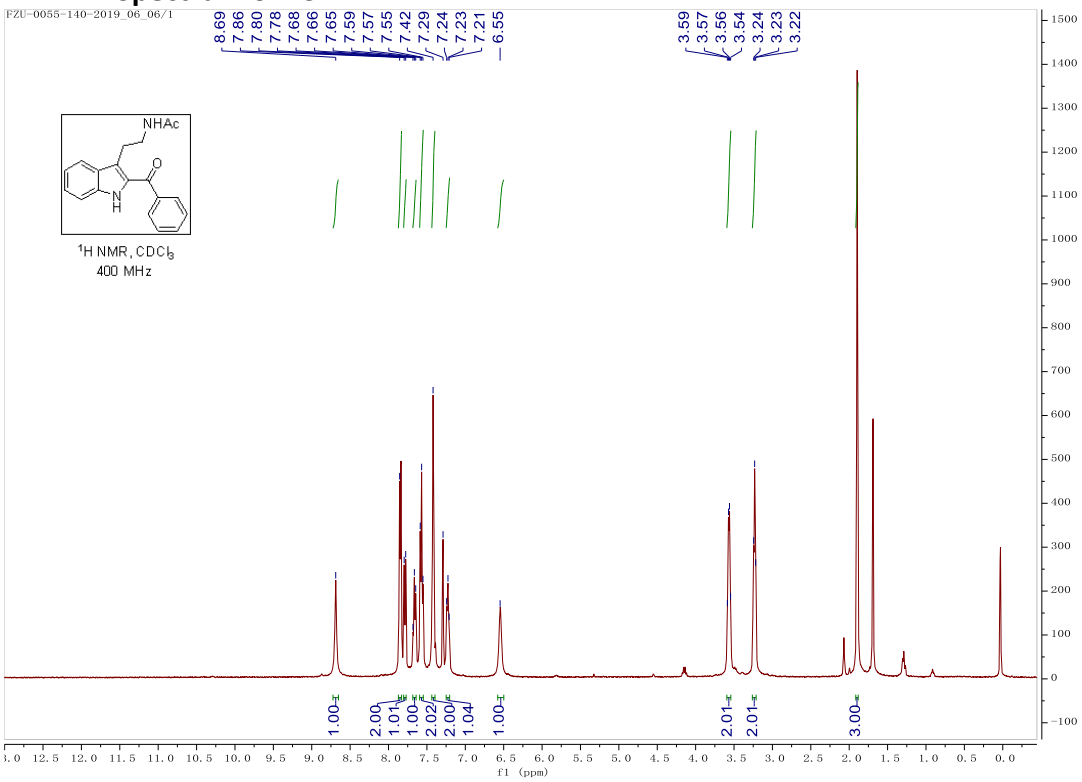
^{1}H NMR Spectrum of 22



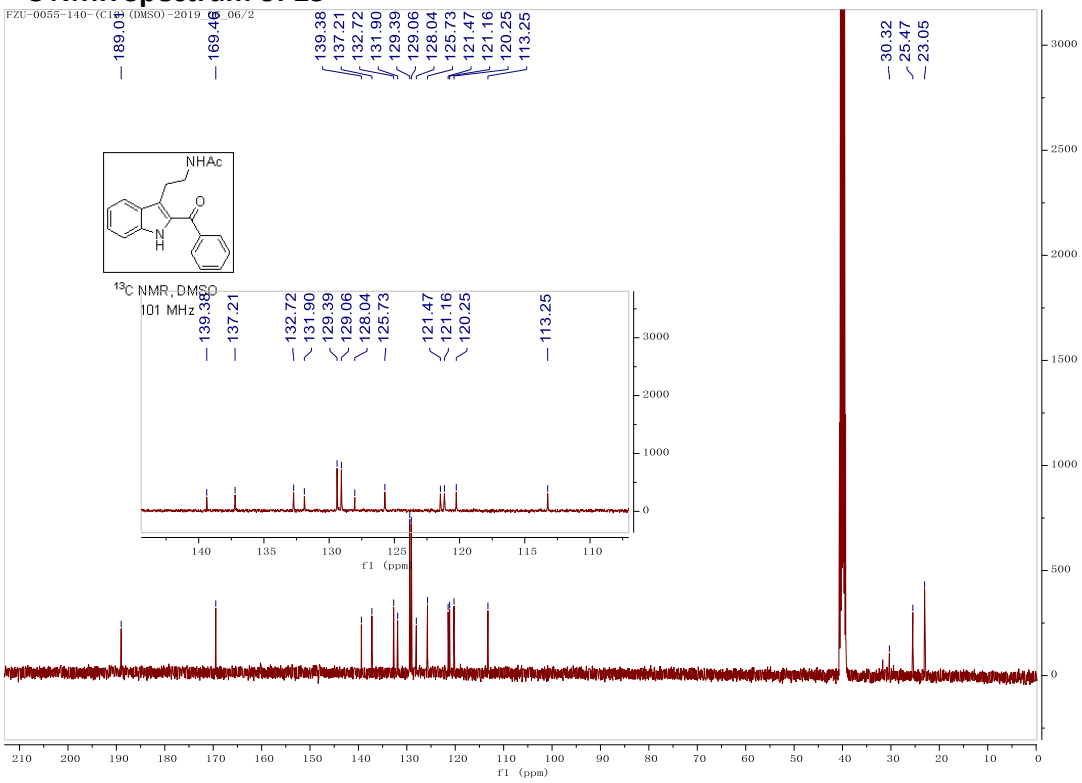
^{13}C NMR Spectrum of 22



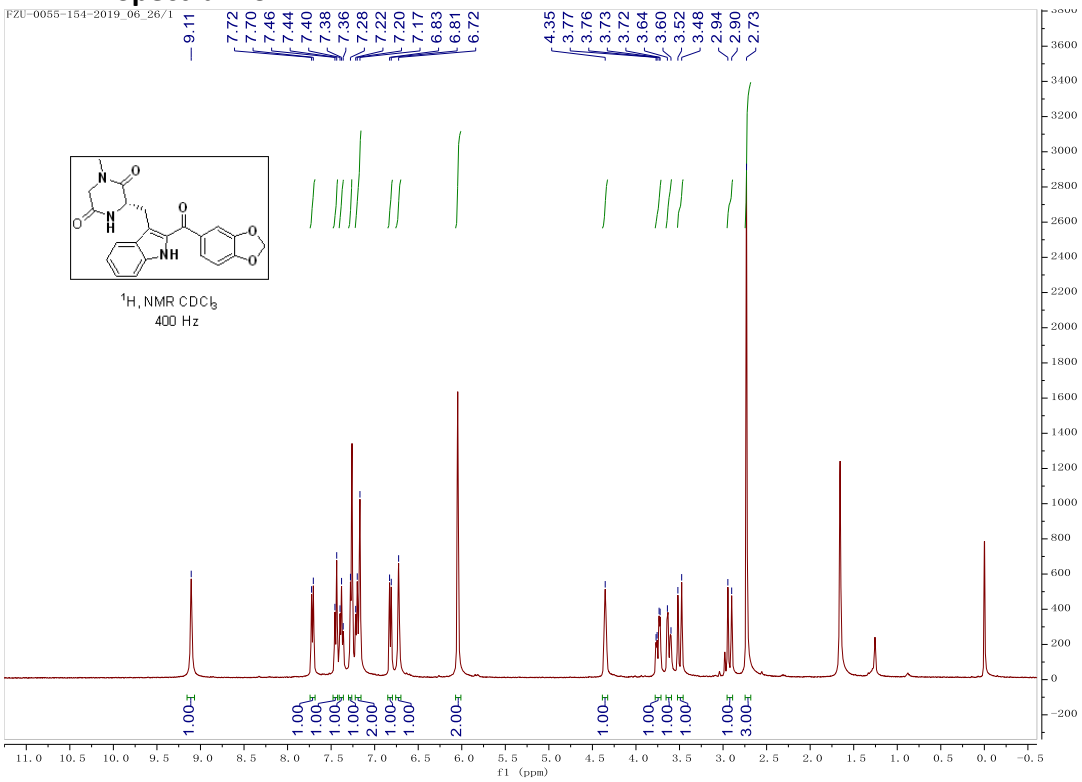
^{1}H NMR Spectrum of 23



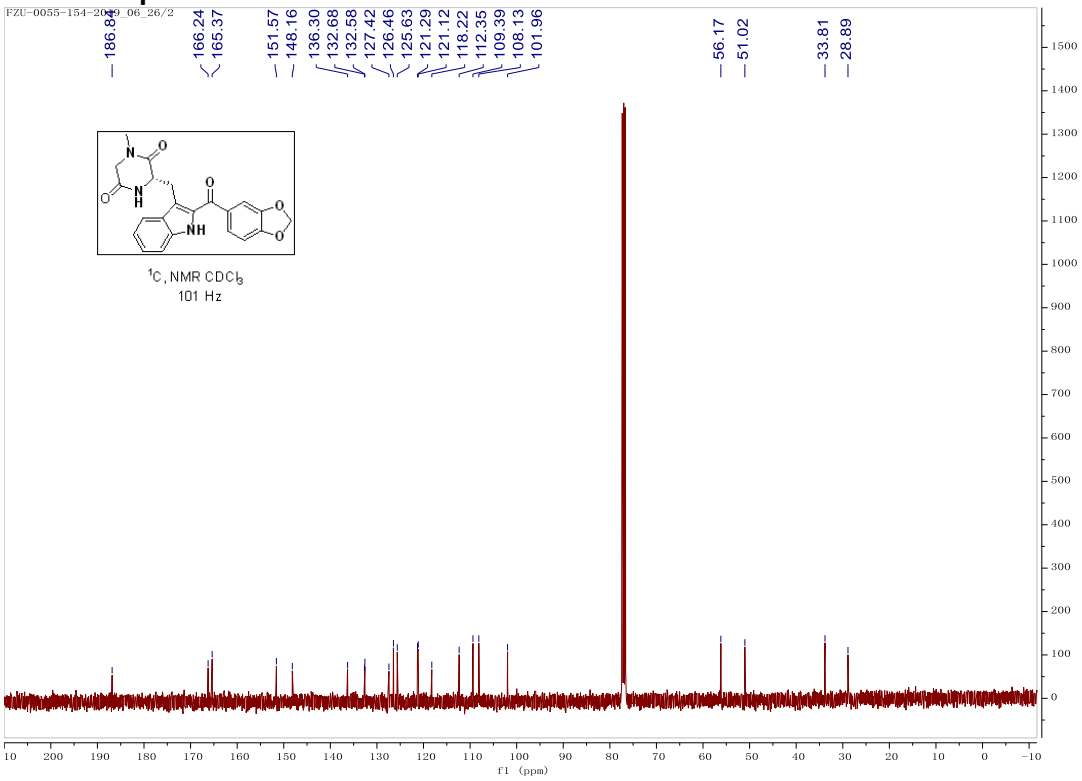
^{13}C NMR Spectrum of 23



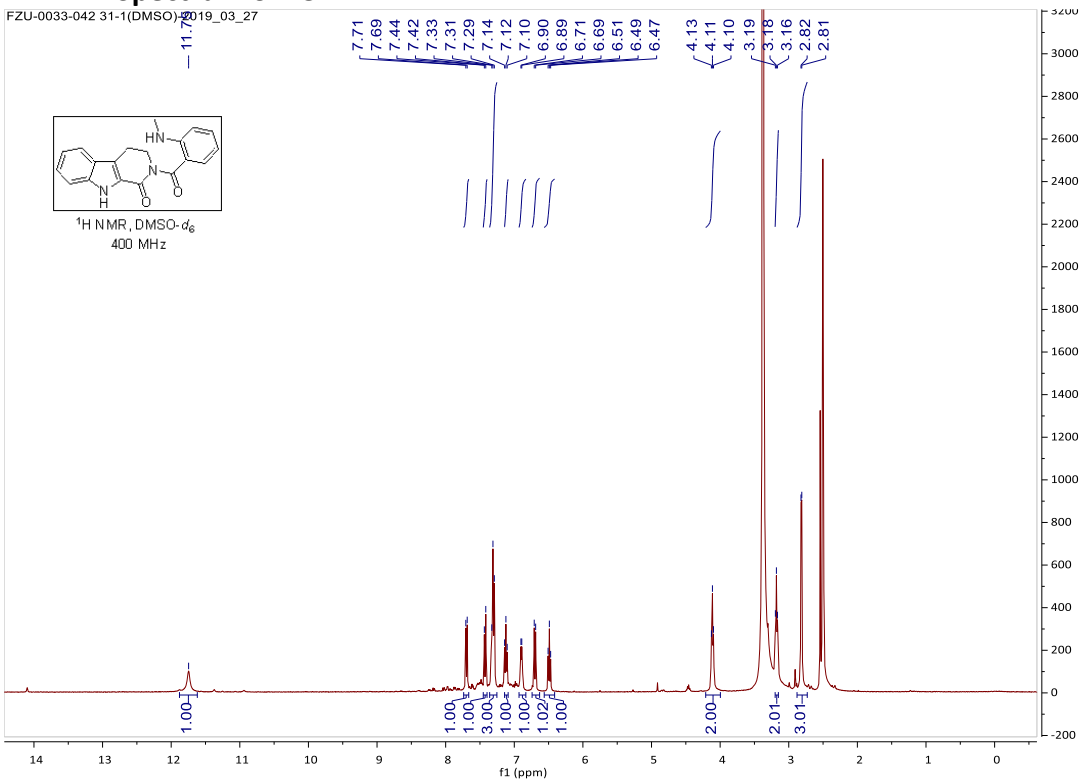
^{1}H NMR Spectrum of 24



^{13}C NMR Spectrum of 24

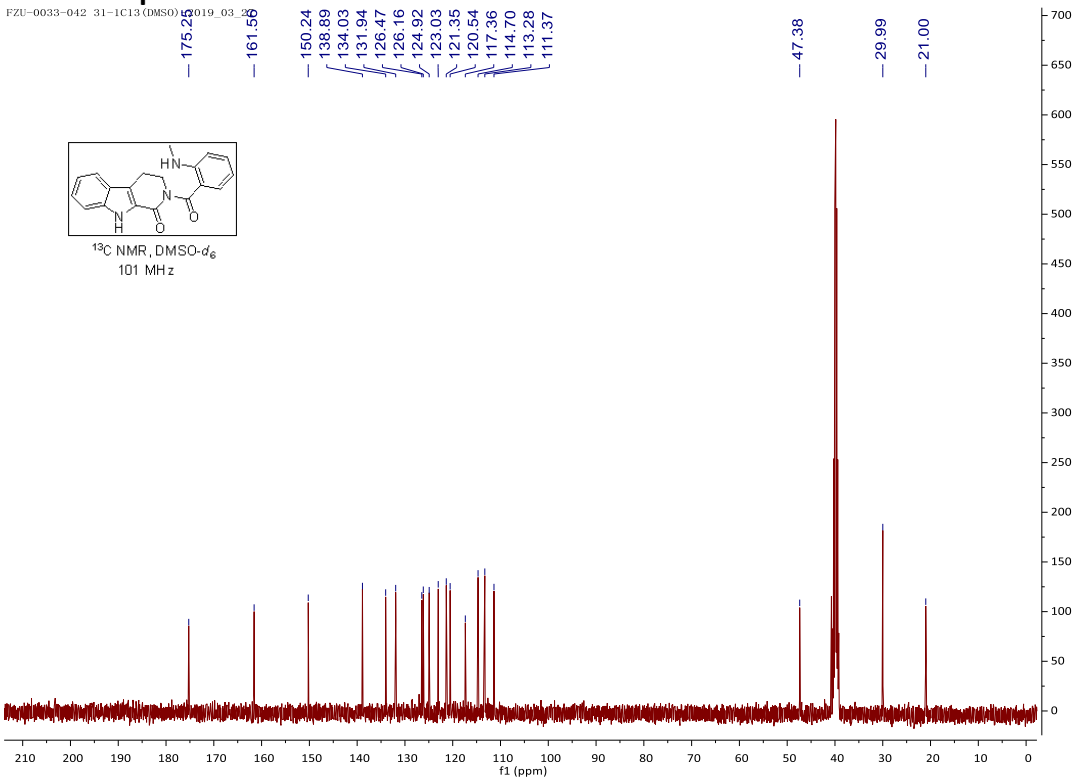


^{1}H NMR Spectrum of 25

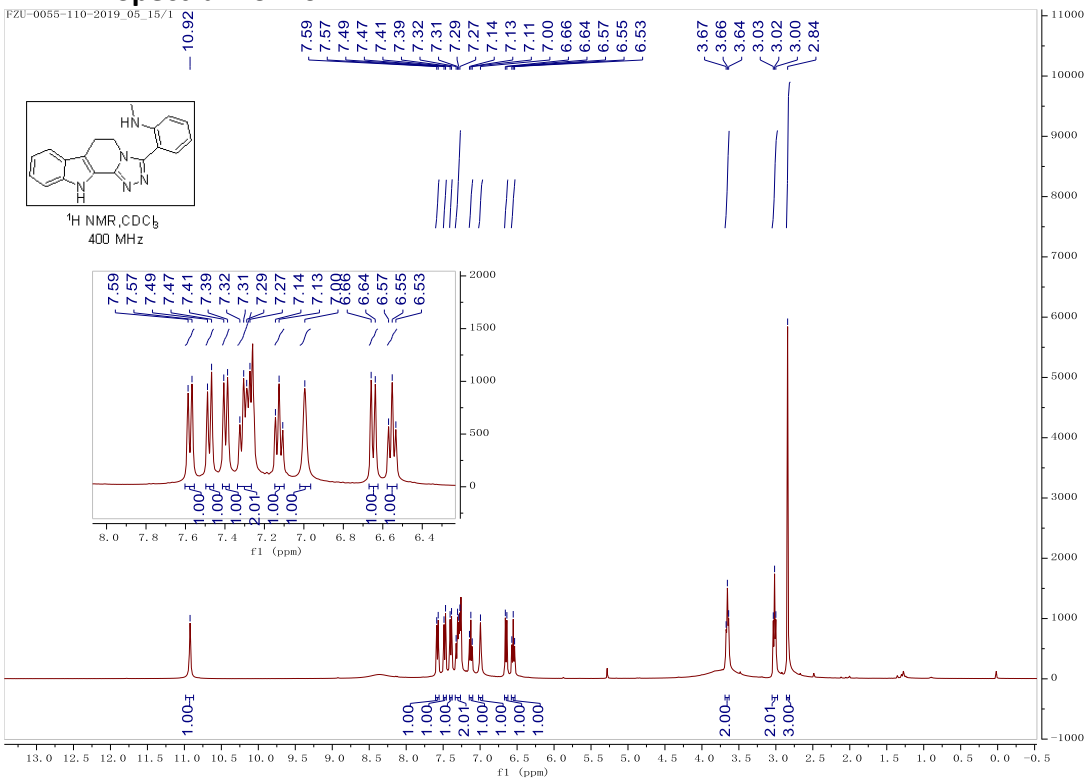


Note: *Compound 25 is unstable.*

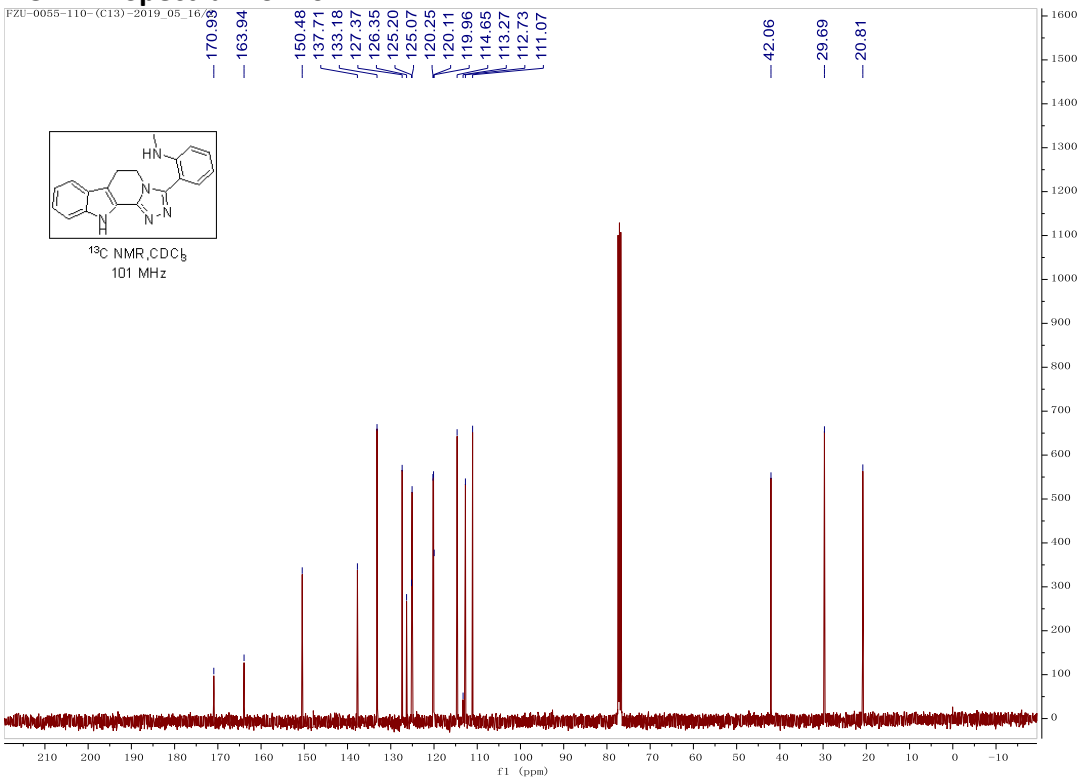
^{13}C NMR Spectrum of 25



^{1}H NMR Spectrum of 26



^{13}C NMR Spectrum of 26



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