Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Synthesis of 3,3'-Bisindoles via Demethylenation

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^{13}C NMR Spectrum of 17 58
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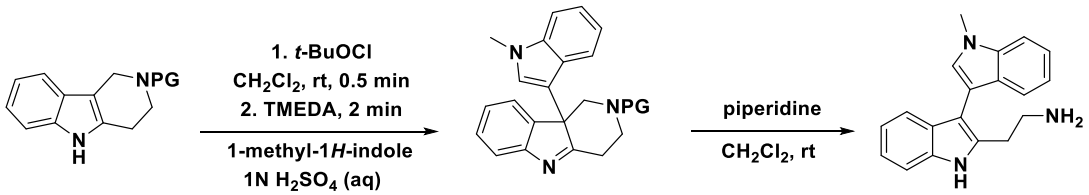
1. General Information

All reactions were performed under a designated atmosphere in flame-dried round bottom flasks, magnetically stirred, unless otherwise noted. All reactions were performed at room temperature (rt., 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) spectrum were recorded on a Bruker-400 (^{1}H, 400 MHz; ^{13}C, 101 MHz; ^{19}F 376 MHz) and JEOL-500 (^{1}H, 500 MHz; ^{13}C, 126 MHz; ^{19}F 471 MHz) spectrometer. 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 Fishec r Scientific Exactive Plus mass spectrometer. The 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 ^{o}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
t-BuOCl = *tert*-butyl hypochlorite
PE = petroleum ether
EtOAc = ethyl acetate
DMSO = dimethyl sulfoxide
TMEDA = *N, N, N′, N′*-tetramethylethylenediamine

2. Optimization of Reaction Conditions

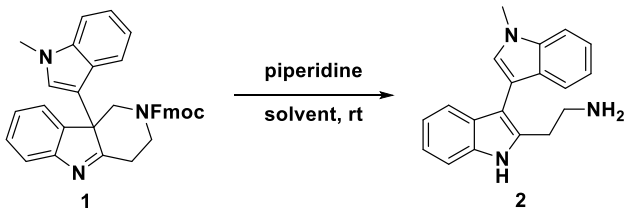
Table S1. Optimization of substrate expansion



Entry[a]	*N*-PG	Yield[b]
1	*N*-Ts	trace
2	*N*-Ac	trace
3	*N*-SO_2Ph	trace
4	*N*-CO_2Me	trace
5	***N*-Fmoc**	**81**

[a] Unless otherwise noted, all reactions were carried out with *N*-PG-TH*γ*Cs (0.1 mmol, 1.0 equiv) and *tert*-butyl hypochlorite (0.11 mmol, 1.1 equiv) in 1.0 mL CH_2Cl_2 at rt for 0.5 min, then TMEDA (0.1 mmol, 2.0 equiv) was added and the reaction mixture was stirred at rt for 2 min. *1-methyl-1H-indole* (0.15 mmol, 1.5 equiv) and 1 N H_2SO_4 solution (0.1 mL, 0.1 mmol) were added and the reaction mixture was stirred at rt for another 30 min. The resulting mixture was washed with H_2O (2 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in different solvent (0.8 mL) was added piperidine (0.2 mL). The mixture was stirred at rt for 20 min. [b] The yield was determined by silica gel column chromatography.

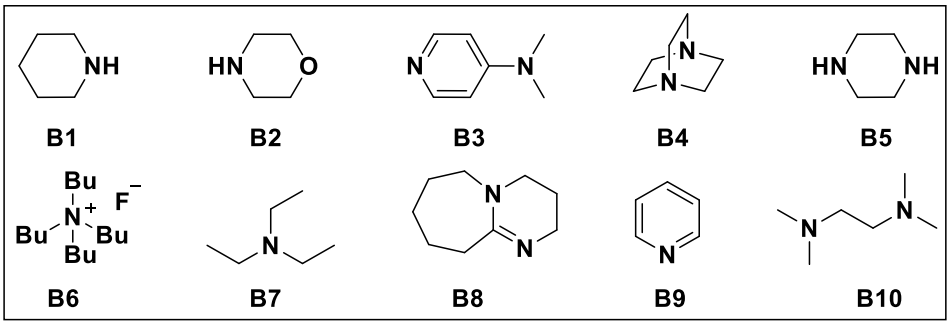
Table S2. Optimization of solvents

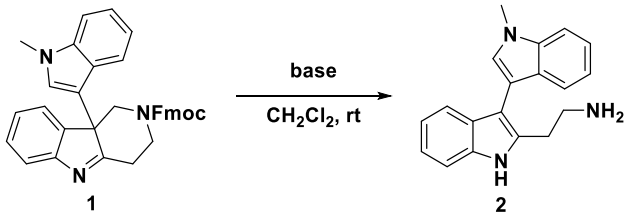


Entry[a]	solvent	Yield[b]	Entry[a]	solvent	Yield[b]
1	**CH_2Cl_2**	**81%**	8	DMSO	50%
2	$CHCl_3$	50%	9	Acetone	25%
3	CCl_4	30%	10	DMA	45%
4	THF	30%	11	1,4-Dioxane	50%
5	CH_3CN	30%	12	2-MeTHF	35%
6	DCE	30%	13	Ethyl acetate	35%
7	DMF	50%	14	MeOH	40%

[a] To a solution of **1** (0.1 mmol) in the solvent (0.8 mL) was added piperidine (0.2 mL). The mixture was stirred at rt for 20 min. [b] Isolated yield.

Table S3. Optimization of bases





Entry[a]	Base (equiv)	Stirring time (h)	Yield (%)[b]	Entry[a]	Base (equiv)	Stirring time (h)	Yield (%)[b]
1	**B1 (20 eq)**	**0.5 h**	**81%**	11	B6 (2 eq)	8 h	trace
2	B1 (13 eq)	3 h	70%	12	B7 (2 eq)	8 h	trace
3	B1 (2 eq)	8 h	40%	13	B8 (2 eq)	3 h	trace
4	B1 (1 eq)	8 h	20%	14	B9 (2 eq)	8 h	trace
5	B2 (20 eq)	0.5 h	trace	15	B10 (2 eq)	8 h	trace
6	B3 (2 eq)	8 h	trace	16	B5 (4 eq)	12 h	88%
7	B4 (2 eq)	8 h	trace	17	B5 (5 eq)	12 h	75%
8	B5 (2 eq)	8 h	60%	18	B5 (6 eq)	12 h	75%
9	B5 (10 eq)	2 h	75%	19	B5 (8 eq)	12 h	75%
10	B6 (1 eq)	8 h	trace	-	-	-	-

[a] To a solution of **1** in CH_2Cl_2 (0.8 mL) was added different base and the mixture was stirred at rt.
[b] Isolated yield.

3. Emission Spectra Data

Emission Spectrum Data for compound 3

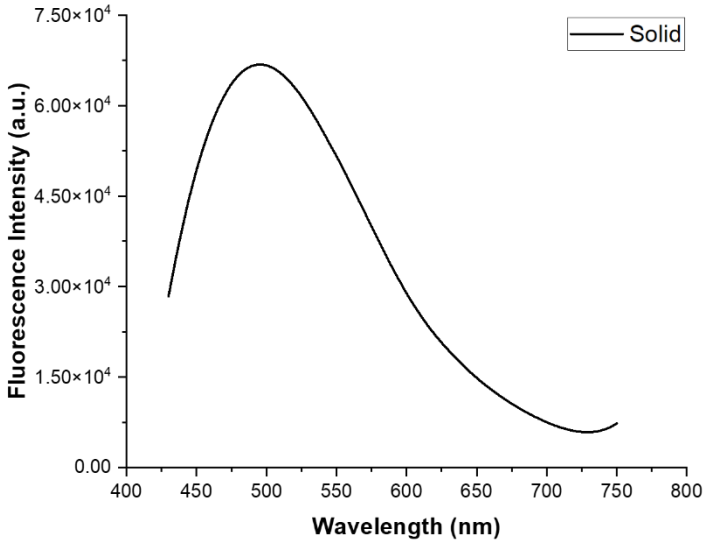


Figure S1. Emission spectrum of compound **3** in solid state was excited by 365 nm.

Emission Spectrum Data for compound 4

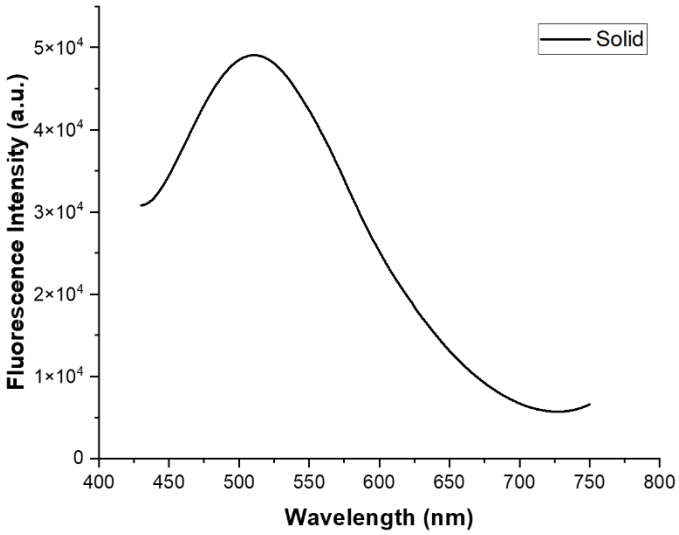


Figure S2. Emission spectrum of compound **4** in solid state was excited by 365 nm.

Emission Spectrum Data for compound 5

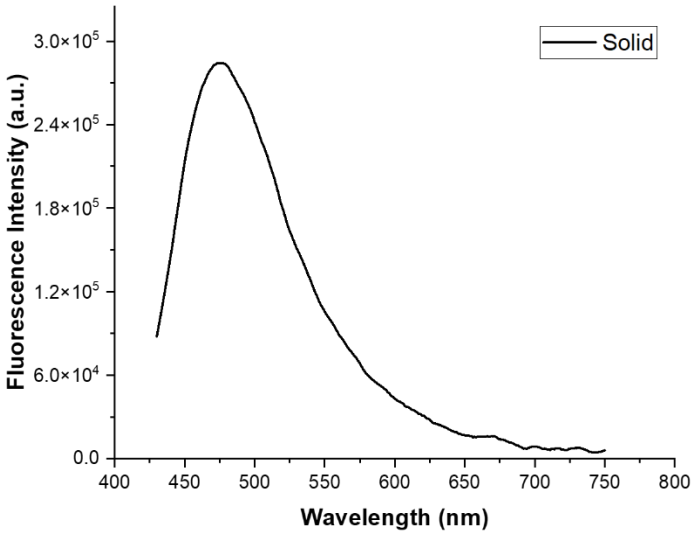


Figure S3. Emission spectrum of compound **5** in solid state was excited by 365 nm.

Emission Spectrum Data for compound 7

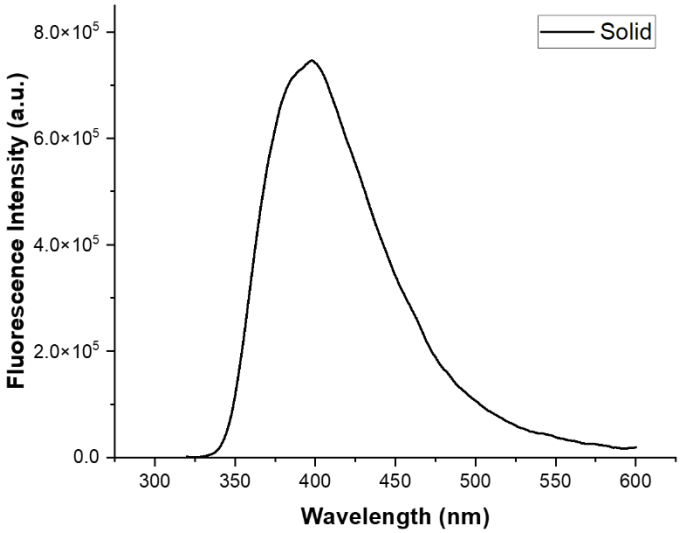


Figure S4. Emission spectrum of compound **7** in solid state was excited by 365 nm.

Emission Spectrum Data for compound 12

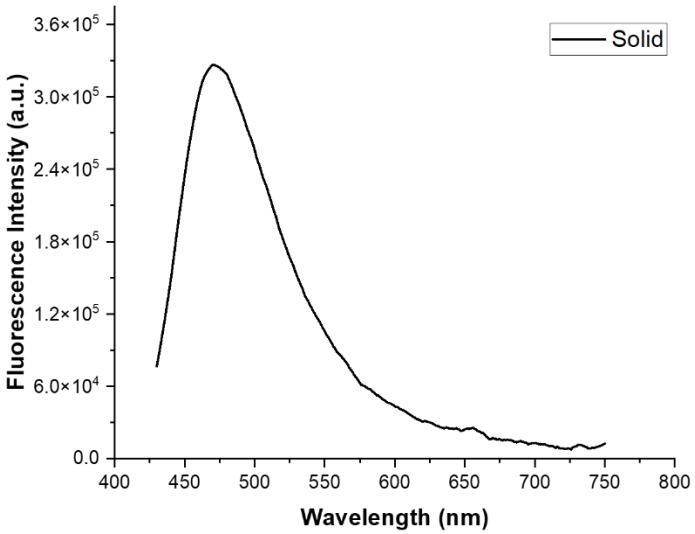


Figure S5. Emission spectrum of compound **12** in solid state was excited by 365 nm.

Emission Spectrum Data for compound 20 (Solid)

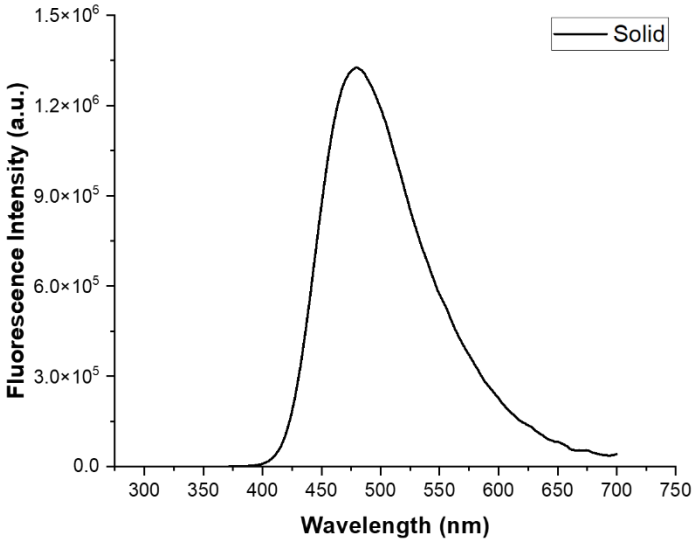


Figure S6. Emission spectrum of compound **20** in solid state was excited by 365 nm.

Emission Spectrum Data for compound 20 in THF

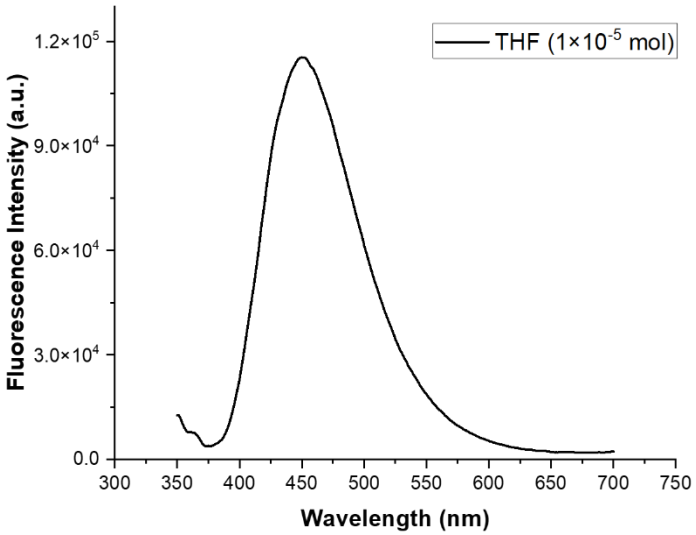


Figure S7. Emission spectrum of compound **20** in THF (1×10^{-5} mol/L) was excited by 365 nm.

Emission Spectrum Data for compound 21

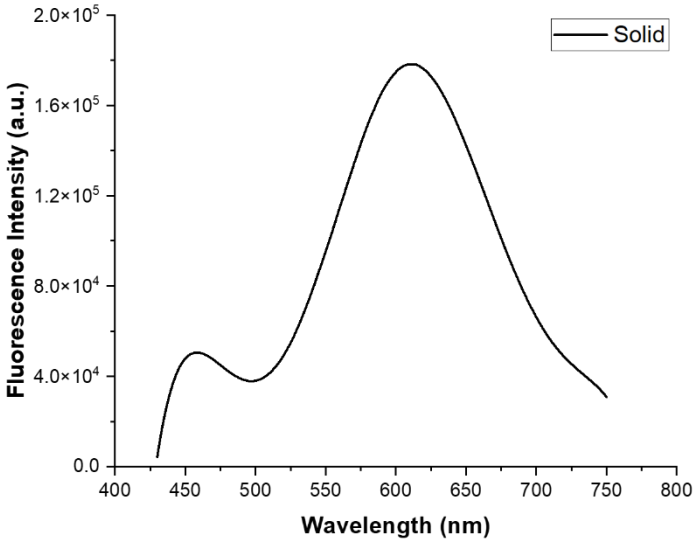


Figure S8. Emission spectrum of compound **21** in solid state was excited by 365 nm.

Emission Spectrum Data for compound 24 (Solid)

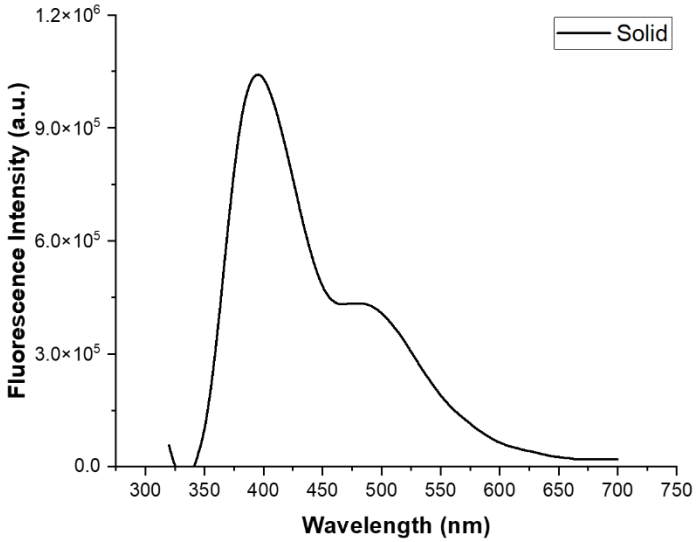


Figure S9. Emission spectrum of compound **24** in solid state was excited by 365 nm.

Emission Spectrum Data for compound 24 in THF

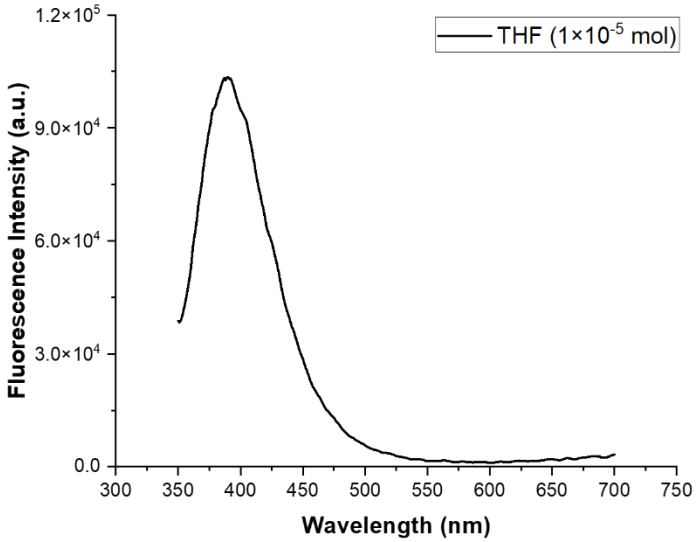


Figure S10. Emission spectrum of compound **24** in THF (1×10^{-5} mol/L) was excited by 365 nm.

Normalized Emission Spectra Data for compounds 20 and 24

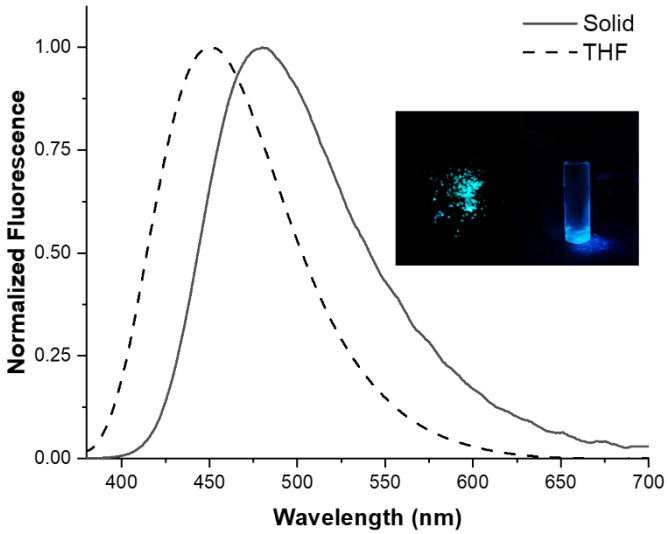


Figure S11. Normalized PL emission spectrum of compounds **20** in THF (1×10^{-5} mol/L) and in solid state was excited by 365 nm.

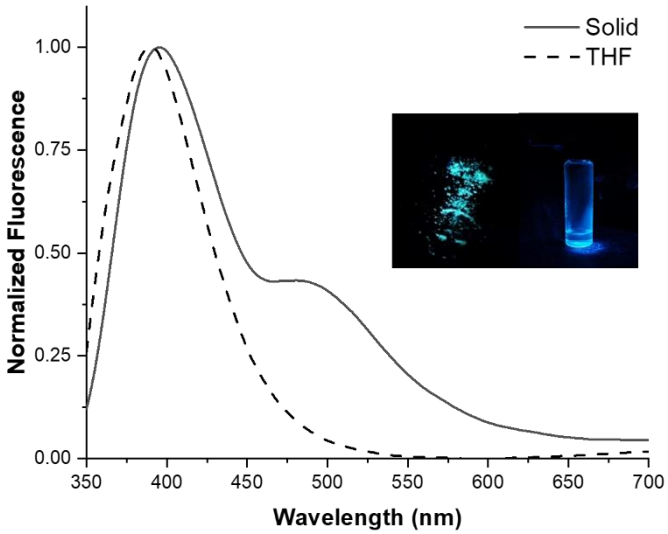


Figure S12. Normalized PL emission spectrum of compounds **24** in THF (1×10^{-5} mol) and in solid state was excited by 365 nm.

4. Mechanism Studies

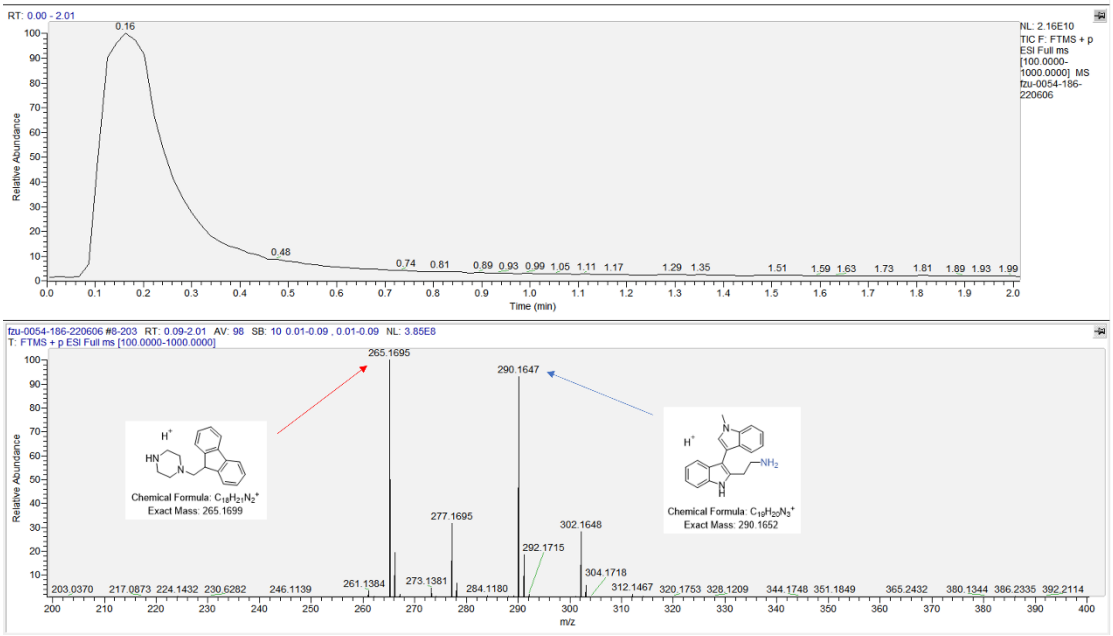


Figure S13. HRMS of DBF adduct.

HRMS (ESI): calcd for $C_{18}H_{21}N_2$ $[M + H]^+$*m/z* 265.1699, found 265.1695.

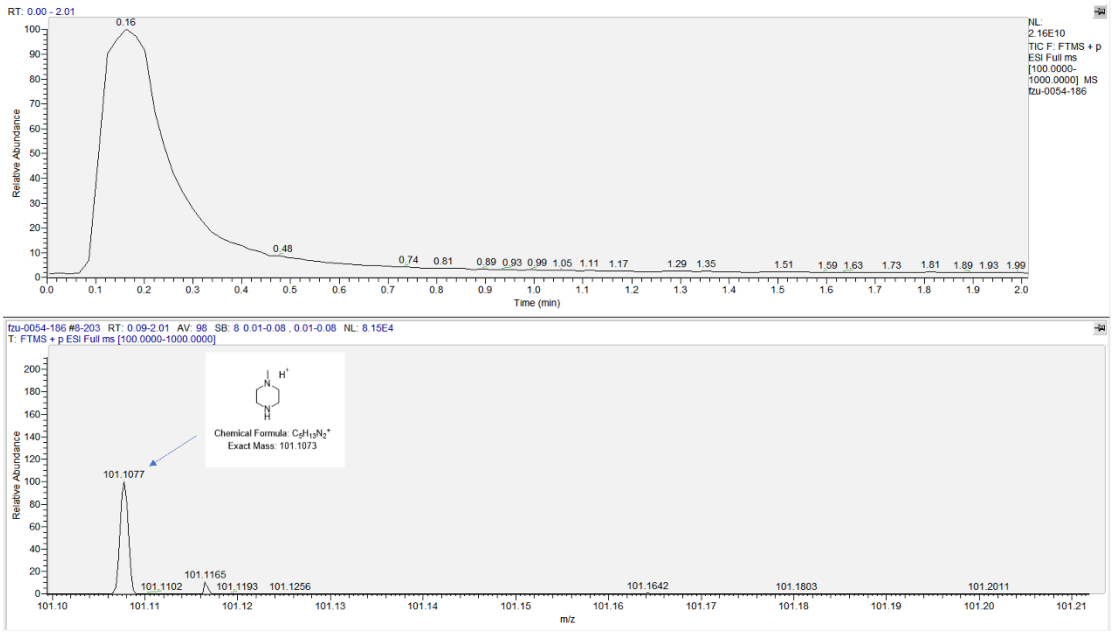


Figure S14. HRMS of 1-methylpiperazine.

HRMS (ESI): calcd for $C_5H_{13}N_2$ $[M + H]^+$*m/z* 101.1073, found 101.1077.

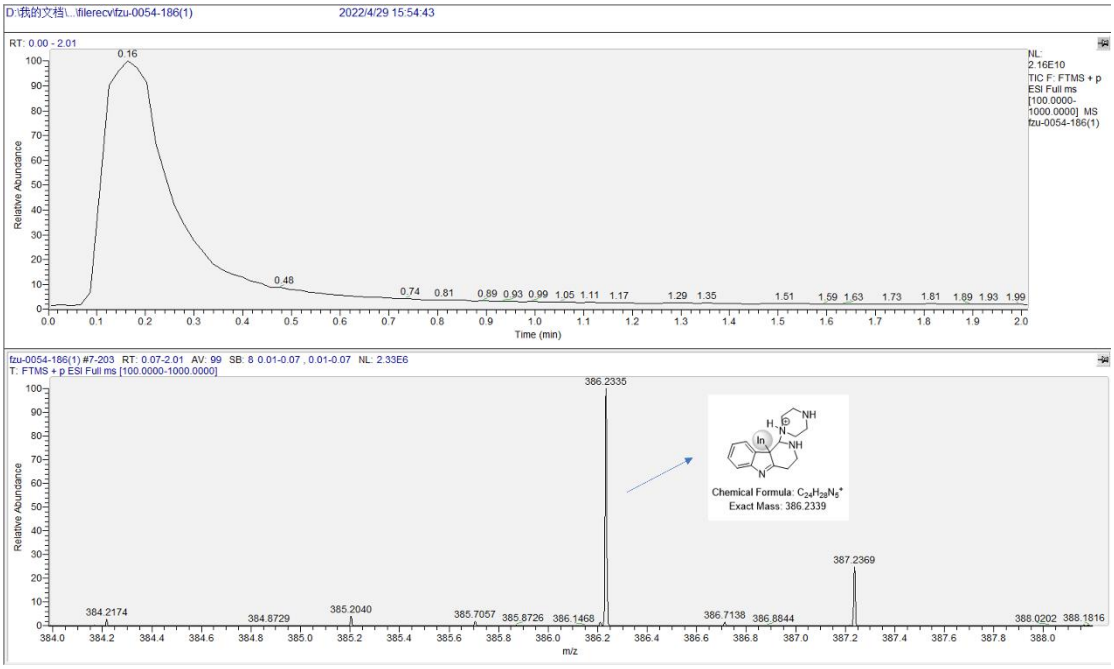


Figure S15. HRMS of B.

HRMS (ESI): calcd for $C_{24}H_{28}N_5$ $[M + H]^+$*m/z* 386.2339, found 386.2335.

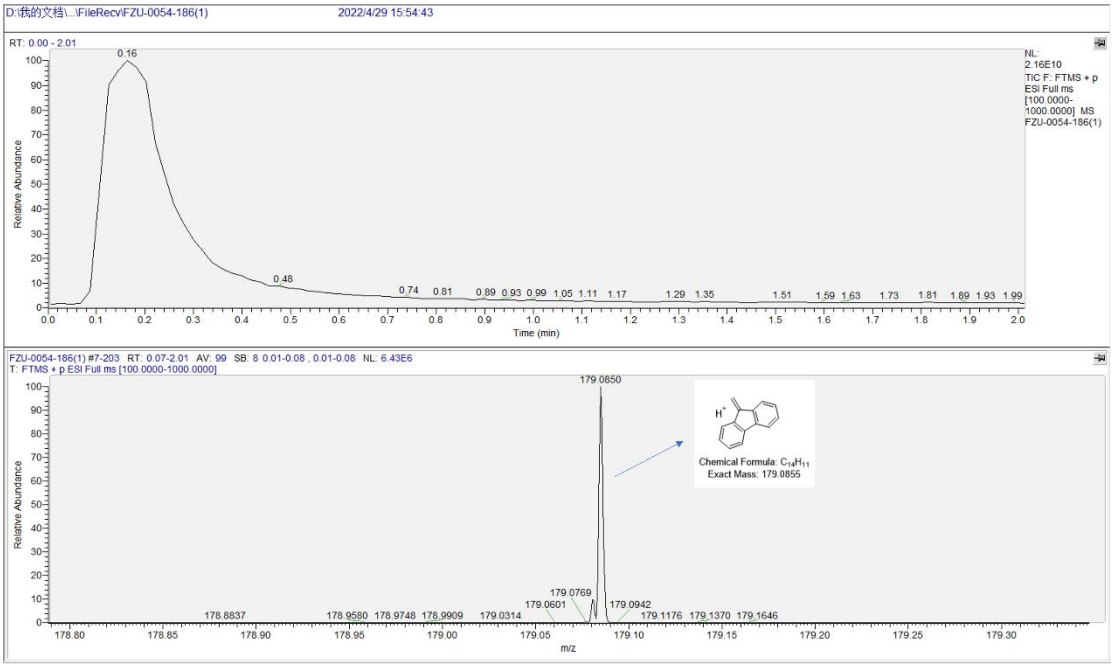
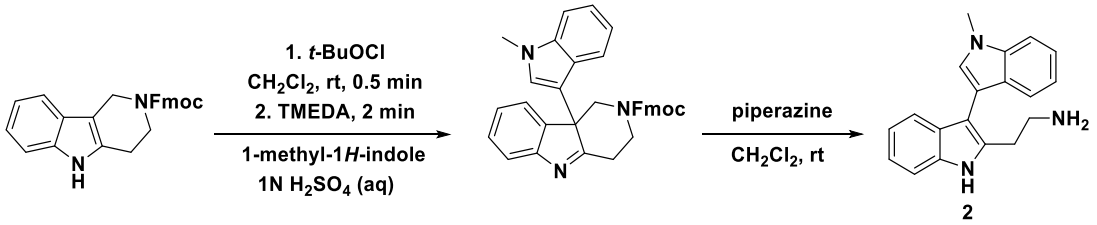


Figure S16. HRMS of C.

HRMS (ESI): calcd for $C_{14}H_{11}$ $[M + H]^+$*m/z* 179.0855, found 179.0850.

5. General Procedures

Compound 2



2-(1'-Methyl-1H,1'H-[3,3'-biindol]-2-yl)ethan-1-amine

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *1-methyl-1H-indole* (196 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 30 min. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (4 mL) was added piperazine (331 mg). The mixture was stirred at rt for 20 min. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with saturated aqueous $NaHCO_3$ solution (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) the desired product (234 mg, 85%) as a white solid.

Physical State: white solid

Melting Point: 160.2 – 163.5 °C.

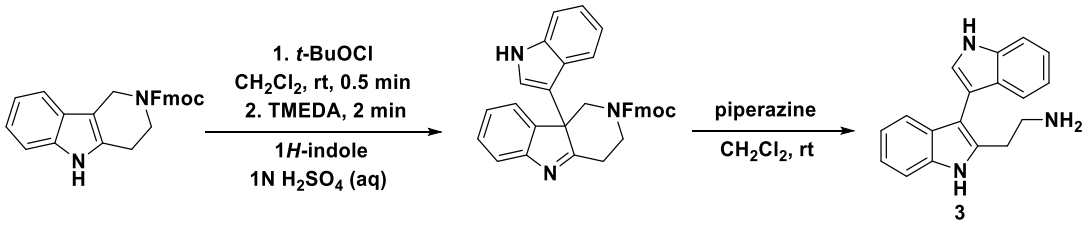
TLC: R_f = 0.33 (CH_2Cl_2/MeOH = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1H), 7.52 (d, *J* = 7.9 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 1H), 7.36 (d, *J* = 8.6 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.19 – 7.11 (m, 1H), 7.11 – 7.03 (m, 2H), 7.00 (s, 1H), 3.77 (s, 3H), 3.69 (s, 2H), 2.91 (s, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 137.03, 135.59, 133.55, 128.72, 128.10, 127.63, 121.69, 121.47, 120.54, 119.67, 119.37, 119.10, 110.89, 109.38, 108.34, 107.29, 40.96, 32.75, 27.82.

HRMS (ESI): calcd for $C_{19}H_{20}N_3$ $[M + H]^+$*m/z* 290.1652, found 290.1649.

Compound 3



2-(1H,1'H-[3,3'-Biindol]-2-yl)ethan-1-amine

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *1H-indole* (129 mg, 1.1 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 30 min. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (4 mL) was added piperazine (331 mg). The mixture was stirred at rt for 30 min. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with saturated aqueous $NaHCO_3$ solution (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give the desired product (146 mg, 53%) as a yellow solid.

Physical State: yellow solid.

Melting Point: 85.1 – 88.3 °C.

TLC: R_f = 0.35 (CH_2Cl_2/MeOH = 5:1).

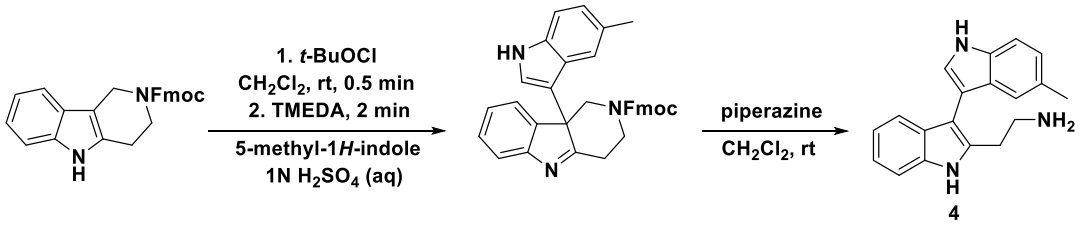
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (s, 1H), 8.36 (s, 1H), 7.45 (d, *J* = 43.2 Hz, 2H), 7.35 (d, *J* = 33.4 Hz, 2H), 7.27 – 7.20 (m, 2H), 7.20 – 7.14 (m, 2H), 7.14 – 6.96 (m, 3H), 3.35 (s, 2H), 2.90 (s, 4H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 136.85, 136.10, 135.26, 128.80, 127.80, 124.08, 121.39, 120.77, 120.12, 119.23, 118.95, 118.83, 112.10, 111.23, 109.23, 106.74, 42.29, 30.85.

^{13}C NMR (101 MHz, DMSO-d_6) δ 124.08, 121.39, 120.78, 120.13, 119.24, 118.95, 118.84, 112.10, 111.23, 42.29, 30.85.

HRMS (ESI): calcd for $C_{18}H_{18}N_3$ $[M + H]^+$*m/z* 276.1495, found 276.1486.

Compound 4



2-(5'-Methyl-1H,1'H-[3,3'-biindol]-2-yl)ethan-1-amine

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *5-methyl-1H-indole* (144 mg, 1.1 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 6 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 20 min. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with saturated aqueous $NaHCO_3$ solution (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give the desired product (150 mg, 52%) as a light yellow solid.

Physical State: light yellow solid.

Melting Point: 90.5 – 93.5 °C.

TLC: R_f = 0.39 (CH_2Cl_2/MeOH = 30:1).

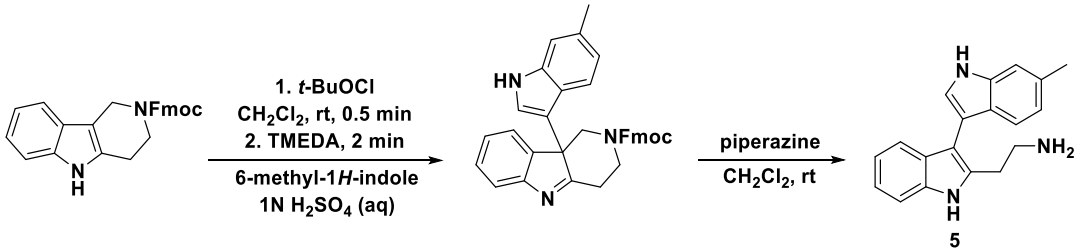
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61 (s, 1H), 8.20 (s, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.23 – 7.17 (m, 2H), 7.10 (d, *J* = 6.6 Hz, 2H), 3.08 – 3.01 (m, 2H), 2.99 – 2.91 (m, 2H), 2.43 (s, 3H), 2.04 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 135.48, 135.41, 134.62, 128.85, 128.78, 128.14, 123.67, 123.19, 121.25, 120.09, 119.63, 119.30, 110.89, 110.67, 109.75, 107.00, 41.74, 29.06, 21.55.

^{13}C NMR (101 MHz, $CDCl_3$) δ 123.67, 123.19, 121.25, 120.10, 119.63, 119.30, 110.89, 110.67, 41.74, 29.06, 21.54.

HRMS (ESI): calcd for $C_{19}H_{20}N_3$ $[M + H]^+$*m/z* 290.1652, found 290.1641.

Compound 5



2-(6'-Methyl-1H,1'H-[3,3'-biindol]-2-yl)ethan-1-amine

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *6-methyl-1H-indole* (144 mg, 1.1 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 30 min. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with saturated aqueous $NaHCO_3$ solution (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give the desired product (150 mg, 52%) as a yellow solid.

Physical State: yellow solid.

Melting Point: 93.3 – 95.2 °C.

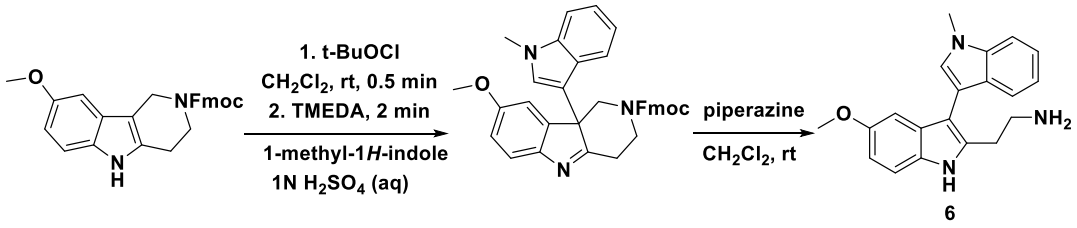
TLC: R_f = 0.36 (CH_2Cl_2/MeOH = 5:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 8.18 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 1H), 7.19 (d, *J* = 7.2 Hz, 2H), 7.10 – 7.03 (m, 2H), 6.96 (d, *J* = 8.0 Hz, 1H), 2.96 – 2.85 (m, 4H), 2.51 (s, 3H), 2.48 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 136.70, 135.48, 134.95, 131.87, 128.72, 125.67, 122.31, 121.31(2C), 120.20, 119.64, 119.30, 111.21, 110.72, 109.98, 107.09, 41.53, 28.75, 21.71.

HRMS (ESI): calcd for $C_{19}H_{20}N_3$ $[M + H]^+$*m/z* 290.1652, found 290.1641.

Compound 6



2-(5-methoxy-1'-methyl-1H,1'H-[3,3'-biindol]-2-yl)ethan-1-amine

To a solution of *(9H-fluoren-9-yl)methyl 8-methoxy-1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (424 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *1-methyl-1H-indole* (196 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 30 min. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (4 mL) was added piperazine (331 mg). The mixture was stirred at rt for 20 min. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with saturated aqueous $NaHCO_3$ solution (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 80:10:1) the desired product (220 mg, 69%) as a gray solid.

Physical State: gray solid

Melting Point: 142.3 – 145.1 °C.

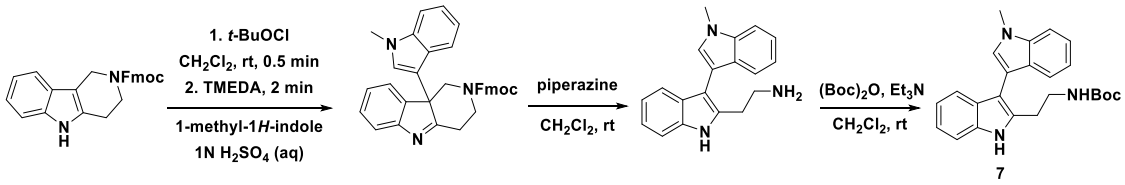
TLC: R_f = 0.38 (CH_2Cl_2/MeOH = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.55 (s, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 1H), 7.29 – 7.26 (m, 2H), 7.11 – 7.07 (m, 2H), 6.97 (d, *J* = 2.4 Hz, 1H), 6.82 (dd, *J* = 8.7, 2.5 Hz, 1H), 3.87 (s, 3H), 3.74 (s, 3H), 2.99 (t, *J* = 5.9 Hz, 2H), 2.91 (t, *J* = 6.0 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.11, 137.15, 136.25, 130.68, 129.29, 128.30, 127.60, 121.73, 120.78, 119.12, 111.47, 111.40, 109.42, 108.92, 106.83, 101.62, 56.06, 41.79, 32.95, 29.17.

HRMS (ESI): calcd for $C_{19}H_{20}N_3$ $[M + H]^+$ *m/z* 320.1757, found 320.1756.

Compound 7



tert-Butyl (2-(1'-methyl-1H,1'H-[3,3'-biindol]-2-yl)ethyl)carbamate

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *1-methyl-1H-indole* (196 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 30 min. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added $(Boc)_2O$ (436 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 50:1) to give the desired product (241 mg, 62%) as a yellow solid.

Physical State: yellow solid.

Melting Point: 145.2 – 146.2 °C.

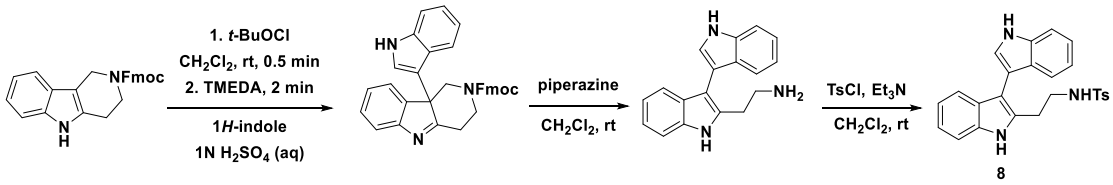
TLC: R_f = 0.42 (PE/EtOAc = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.53 (d, *J* = 7.9 Hz, 2H), 7.42 (t, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 7.2 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.14 (d, *J* = 6.1 Hz, 2H), 7.13 – 7.05 (m, 1H), 4.64 (s, 1H), 3.91 (s, 3H), 3.49 – 3.39 (m, 2H), 3.12 – 3.03 (m, 2H), 1.42 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.26, 137.12, 135.71, 133.19, 129.09, 128.28, 127.68, 121.72, 121.54, 120.67, 119.72, 119.49, 119.14, 110.69, 109.33, 108.48, 107.87, 79.60, 40.15, 32.88, 28.39(3C), 27.69.

HRMS (ESI): calcd for $C_{24}H_{28}N_3O_2$ $[M + H]^+$ *m/z* 390.2176, found 390.2175.

Compound 8



N-(2-(1H,1'H-[3,3'-biindol]-2-yl)ethyl)-4-methylbenzenesulfonamide

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *1H-indole* (175 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 10 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added TsCl (381 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 50:1) to give the desired product (223 mg, 52%) as a white solid.

Physical State: white solid.

Melting Point: 180 – 182 °C.

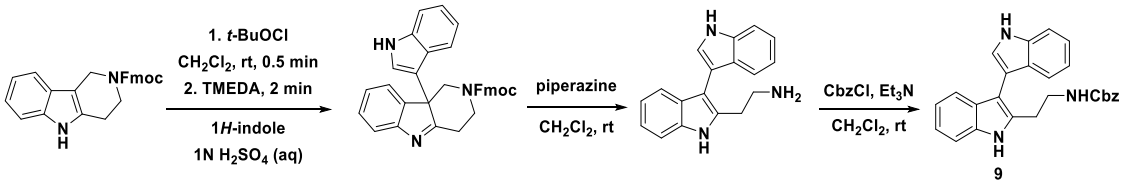
TLC: R_f = 0.47 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.27 (s, 1H), 11.13 (s, 1H), 7.79 – 7.71 (m, 1H), 7.66 (d, *J* = 7.5 Hz, 2H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.41 – 7.35 (m, 3H), 7.29 (d, *J* = 7.7 Hz, 2H), 7.18 (t, *J* = 7.0 Hz, 1H), 7.10 (t, *J* = 6.9 Hz, 1H), 7.05 – 6.95 (m, 2H), 3.20 – 3.09 (m, 2H), 3.05 – 2.93 (m, 2H), 2.34 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 142.99, 138.02, 136.87, 136.19, 133.31, 130.01(3C), 127.74, 126.96(2C), 124.02, 121.50, 121.11, 120.09, 119.43, 119.06, 118.99, 112.12, 111.32, 108.88, 107.24, 43.22, 27.67, 21.40.

HRMS (ESI): calcd for $C_{25}H_{24}N_3O_2S$ $[M + H]^+$ *m/z* 430.1584, found 430.1587.

Compound 9



Benzyl (2-(1H,1'H-[3,3'-biindol]-2-yl)ethyl)carbamate

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *1H-indole* (175 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 6 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (341 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 50:1) to give the desired product (310 mg, 76%) as a light yellow solid.

Physical State: light yellow solid.

Melting Point: 96.3 – 96.8 °C.

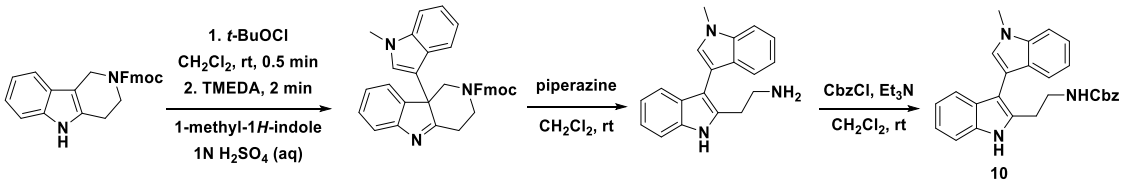
TLC: R_f = 0.52 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.24 (s, 1H), 7.52 (d, *J* = 7.4 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.41 – 7.34 (m, 4H), 7.33 (s, 1H), 7.28 (d, *J* = 7.4 Hz, 2H), 7.28 – 7.19 (m, 2H), 7.16 – 7.07 (m, 2H), 5.07 (s, 2H), 4.84 (s, 1H), 3.47 (s, 2H), 3.06 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.82, 136.52, 136.33, 135.77, 133.13, 129.04, 128.67(2C), 128.27, 128.11(3C), 127.84, 123.32, 122.20, 121.75, 120.53, 119.84, 119.72, 119.68, 111.49, 110.93, 107.94, 66.84, 40.88, 27.46.

HRMS (ESI): calcd for $C_{26}H_{24}N_3O_2$ $[M + H]^+$*m/z* 410.1863, found 410.1863.

Compound 10



Benzyl (2-(1'-methyl-1H,1'H-[3,3'-biindol]-2-yl)ethyl)carbamate

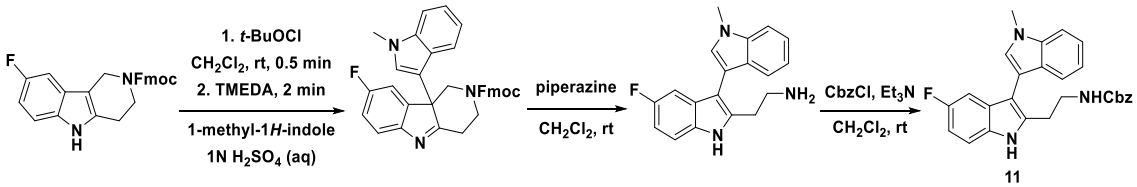
To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *1-methyl-1H-indole* (196 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 30 min. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (341 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 50:1) to give the desired product (288 mg, 68%) as a white solid.

Gram-scale:

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 5.0 mmol) in CH_2Cl_2 (30 mL) was added *tert*-butyl hypochlorite (648 mg, 6 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (580 mg, 5.0 mmol) was added. The solution was stirred at rt for 2 min. Then *1-methyl-1H-indole* (984 mg, 7.5 mmol) and 1 N H_2SO_4 solution (10.0 mL, 10.0 mmol) were added into the mixture. The solution was stirred at rt for 30 min. The resulting mixture was diluted with CH_2Cl_2 (100 mL) and then was washed with H_2O (150 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (15 mL) was added piperazine (1720 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (100 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (1705 mg, 10 mmol) and Et_3N (1010 mg, 10 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 50:1) to give the desired

product (1520 mg, 72%) as a white solid.
Physical State: white solid.
Melting Point: 83.3 – 86.1 °C.
TLC: R_f = 0.44 (PE/EtOAc = 2:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.62 (t, *J* = 8.3 Hz, 2H), 7.49 (d, *J* = 8.2 Hz, 1H), 7.41 (s, 4H), 7.38 (s, 2H), 7.30 (d, *J* = 6.8 Hz, 2H), 7.24 – 7.18 (m, 2H), 7.16 (s, 1H), 5.14 (s, 2H), 4.98 (s, 1H), 3.88 (s, 3H), 3.52 – 3.39 (m, 2H), 3.10 – 2.98 (m, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 156.80, 137.22, 136.55, 135.83, 133.07, 129.17, 128.74, 128.68, 128.34, 128.12, 127.92, 127.78, 121.89, 121.69, 120.71, 119.87, 119.71, 119.61, 119.26, 110.86, 109.51, 108.46, 108.01, 66.88, 40.92, 32.94, 27.57.
HRMS (ESI): calcd for $C_{27}H_{26}N_3O_2$ $[M + H]^+$ *m/z* 424.2020, found 424.2019.

Compound 11



Benzyl (2-(5-fluoro-1'-methyl-1H,1'H-[3,3'-biindol]-2-yl)ethyl)carbamate

To a solution of *(9H-fluoren-9-yl)methyl 8-fluoro-1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (412 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *1-methyl-1H-indole* (196 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 30 min. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (341 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 50:1) to give the desired product (255 mg, 58%) as a white solid.

Physical State: white solid.

Melting Point: 65 – 67.1 °C.

TLC: R_f = 0.57 (PE/EtOAc = 2:1).

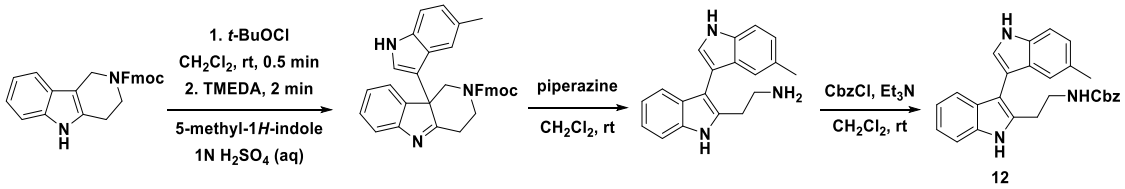
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (s, 1H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.41 (s, 1H), 7.34 (dt, *J* = 4.9, 2.5 Hz, 4H), 7.30 (d, *J* = 8.0 Hz, 3H), 7.22 – 7.10 (m, 3H), 7.07 (s, 1H), 6.95 – 6.91 (m, 1H), 5.06 (s, 2H), 4.91 (s, 1H), 3.84 (s, 3H), 3.45 (d, *J* = 6.2 Hz, 2H), 3.02 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.05, 157.19, 156.81, 137.18, 136.42, 134.99, 132.25, 129.66, 128.68, 128.32, 128.10, 127.76, 121.93, 120.44, 119.41, 111.37, 111.29, 109.94, 109.73, 109.52, 107.96, 104.74, 104.55, 66.92, 40.71, 32.93, 27.76.

^{19}F NMR (471 MHz, $CDCl_3$) δ -124.62.

HRMS (ESI): calcd for $C_{27}H_{26}N_3O_2$ $[M + H]^+$ *m/z* 442.1925, found 442.1926

Compound 12



Benzyl (2-(5'-methyl-1H,1'H-[3,3'-biindol]-2-yl)ethyl)carbamate

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *5-methyl-1H-indole* (196 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 10 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (341 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 50:1) to give the desired product (273 mg, 65%) as a gray solid.

Physical State: gray solid.

Melting Point: 90.1 – 95.3 °C.

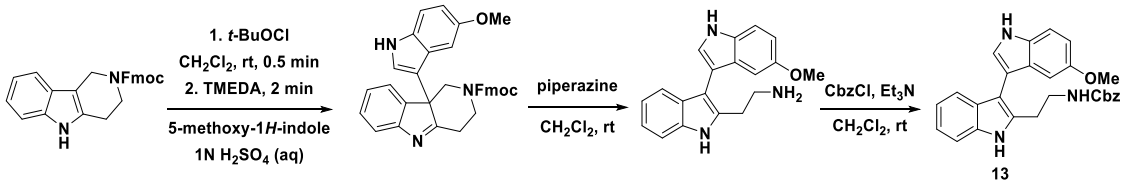
TLC: R_f = 0.59 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.15 (s, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 12.4 Hz, 3H), 7.36 (s, 2H), 7.33 (s, 1H), 7.30 (s, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.17 (s, 1H), 7.11 (t, *J* = 7.7 Hz, 2H), 5.07 (s, 2H), 4.85 (s, 1H), 3.45 (s, 2H), 3.04 (s, 2H), 2.41 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.89, 136.56, 135.80, 134.72, 133.20, 129.13, 129.00, 128.70(2C), 128.29, 128.19, 128.12(2C), 123.90, 123.59, 121.74, 120.09, 119.91, 119.69, 111.23, 110.98, 109.22, 108.10, 66.87, 40.96, 27.45, 21.68.

HRMS (ESI): calcd for $C_{27}H_{26}N_3O_2$ $[M + H]^+$ *m/z* 424.2020, found 424.2019.

Compound 13



Benzyl (2-(5'-methoxy-1H,1'H-[3,3'-biindol]-2-yl)ethyl)carbamate

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *5-methoxy-1H-indole* (221 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 10 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (341 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 30:1) to give the desired product (299 mg, 68%) as a yellow solid.

Physical State: yellow solid.

Melting Point: 68.8 – 71.8 °C.

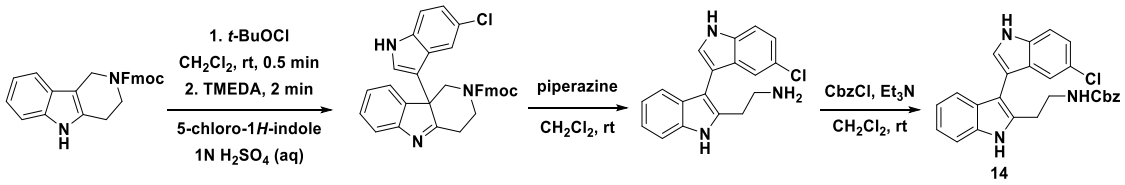
TLC: R_f = 0.48 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.16 (s, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.39 (s, 2H), 7.38 – 7.34 (m, 3H), 7.33 (s, 1H), 7.32 (s, 1H), 7.24 – 7.19 (m, 1H), 7.17 (s, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 6.93 (d, *J* = 7.6 Hz, 2H), 5.07 (s, 2H), 4.87 (s, 1H), 3.73 (s, 3H), 3.50 – 3.34 (m, 2H), 3.11 – 3.00 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.01, 154.20, 136.59, 135.92, 133.25, 131.64, 129.01, 128.82, 128.74, 128.36, 128.32, 128.18, 128.10, 124.32, 121.81, 119.95, 119.73, 112.70, 112.44, 111.14, 109.56, 108.03, 102.09, 66.89, 55.92, 41.08, 27.47.

HRMS (ESI): calcd for $C_{27}H_{26}N_3O_2$ $[M + H]^+$*m/z* 440.1969, found 440.1972.

Compound 14



Benzyl (2-(5'-chloro-1H,1'H-[3,3'-biindol]-2-yl)ethyl)carbamate

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *5-chloro-1H-indole* (226 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 10 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (341 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 50:1) to give the desired product (284 mg, 64%) as a light yellow solid.

Physical State: light yellow solid.

Melting Point: 96.2 – 100.3 °C.

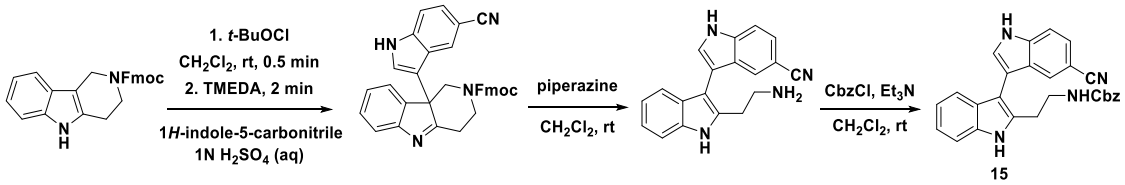
TLC: R_f = 0.48 (PE/EtOAc = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.26 (s, 1H), 7.46 (d, *J* = 8.1 Hz, 2H), 7.38 (d, *J* = 11.5 Hz, 2H), 7.37 – 7.33 (m, 2H), 7.34 – 7.30 (m, 2H), 7.29 (s, 1H), 7.25 (s, 1H), 7.24 – 7.19 (m, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 5.07 (s, 2H), 4.85 (s, 1H), 3.51 – 3.39 (m, 2H), 3.09 – 2.95 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.03, 136.51, 135.87, 134.82, 133.49, 129.06, 128.97, 128.79(2C), 128.41, 128.11(2C), 125.45, 124.91, 122.55, 121.99, 119.98, 119.79, 119.68, 112.77, 111.17, 109.54, 107.37, 66.98, 41.01, 27.41.

HRMS (ESI): calcd for $C_{26}H_{23}ClN_3O_2$ $[M + H]^+$*m/z* 444.1473, found 444.1477.

Compound 15



Benzyl (2-(5'-cyano-1H,1'H-[3,3'-biindol]-2-yl)ethyl)carbamate

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *1H-indole-5-carbonitrile* (213 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 10 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (341 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 30:1) to give the desired product (135 mg, 31%) as a light yellow solid.

Physical State: light yellow solid.

Melting Point: 83.3 – 85.2 °C.

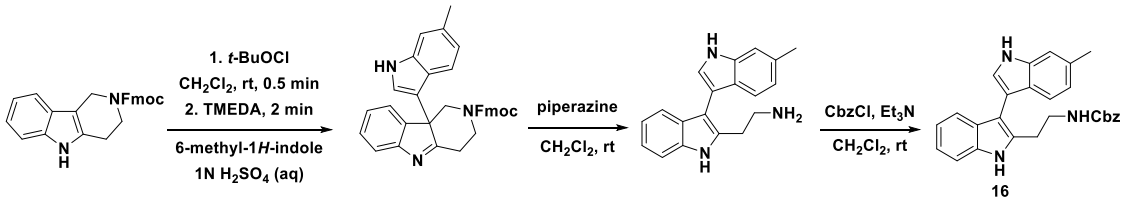
TLC: R_f = 0.30 (PE/EtOAc = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.50 (s, 1H), 7.86 (s, 1H), 7.49 (s, 2H), 7.41 (d, *J* = 7.1 Hz, 2H), 7.39 – 7.35 (m, 2H), 7.34 – 7.30 (m, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 7.24 (d, *J* = 7.7 Hz, 1H), 7.13 (t, *J* = 7.2 Hz, 1H), 5.07 (s, 2H), 4.87 (s, 1H), 3.56 – 3.42 (m, 2H), 3.13 – 2.95 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.73, 137.99, 136.32, 135.71, 133.45, 128.65, 128.62(2C), 128.25, 128.05(2C), 127.66, 126.03, 125.21, 124.94, 121.99, 121.03, 119.98, 119.23, 112.37, 110.99, 110.81, 106.52, 102.34, 66.84, 40.80, 27.45.

HRMS (ESI): calcd for $C_{27}H_{23}N_4O_2$ $[M + H]^+$*m/z* 435.1816, found 435.1816.

Compound 16



Benzyl (2-(6'-methyl-1H,1'H-[3,3'-biindol]-2-yl)ethyl)carbamate

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *6-methyl-1H-indole* (196 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 10 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (341 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 50:1) to give the desired product (237 mg, 56%) as a yellow solid.

Physical State: yellow solid.

Melting Point: 90 – 91 °C.

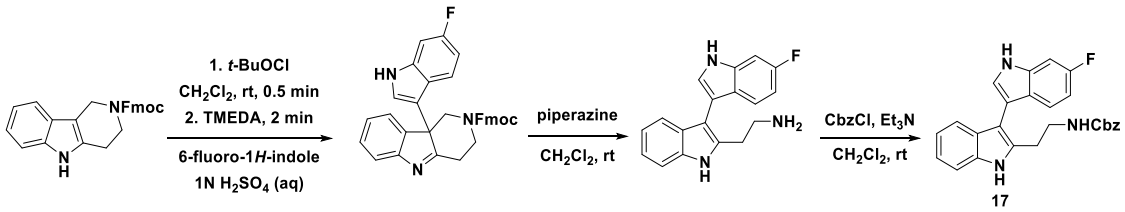
TLC: R_f = 0.42 (PE/EtOAc = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.12 (s, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 2H), 7.37 (s, 1H), 7.36 (s, 2H), 7.32 (d, *J* = 7.3 Hz, 2H), 7.29 (s, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.16 – 7.11 (m, 1H), 7.10 – 7.05 (m, 1H), 6.96 (d, *J* = 8.1 Hz, 1H), 5.07 (s, 2H), 4.84 (s, 1H), 3.54 – 3.36 (m, 2H), 3.10 – 2.98 (m, 2H), 2.52 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.98, 136.93, 136.66, 135.91, 133.20, 132.05, 129.13, 128.78(2C), 128.36, 128.17(2C), 125.84, 122.83, 121.82, 121.64, 120.34, 120.01, 119.76, 111.64, 111.10, 109.62, 108.19, 66.92, 41.04, 27.48, 21.97.

HRMS (ESI): calcd for $C_{27}H_{26}N_3O_2$ $[M + H]^+$ *m/z* 424.2020, found 424.2019.

Compound 17



Benzyl (2-(6'-fluoro-1H,1'H-[3,3'-biindol]-2-yl)ethyl)carbamate

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *6-fluoro-1H-indole* (202 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 10 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (341 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 50:1) to give the desired product (332 mg, 78%) as a light yellow solid.

Physical State: light yellow solid.

Melting Point: 150.6 – 151.8 °C.

TLC: R_f = 0.42 (PE/EtOAc = 3:1).

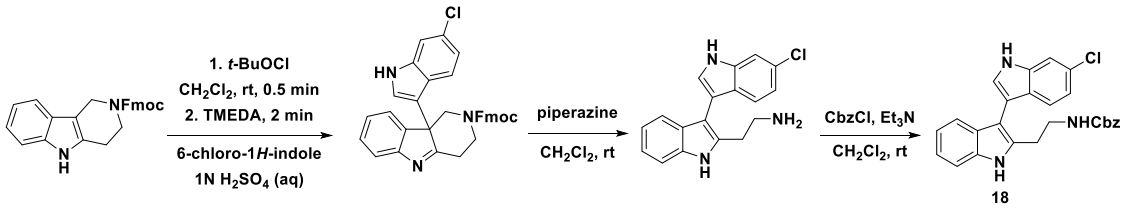
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.20 (s, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 5.3 Hz, 2H), 7.37 (d, *J* = 5.7 Hz, 3H), 7.34 – 7.30 (m, 2H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.17 (s, 1H), 7.13 (s, 1H), 7.10 (d, *J* = 7.7 Hz, 1H), 6.87 (t, *J* = 9.1 Hz, 1H), 5.07 (s, 2H), 4.85 (s, 1H), 3.55 – 3.41 (m, 2H), 3.11 – 2.97 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.14 (d, *J* = 237.3 Hz), 157.00, 136.47, 136.29 (d, *J* = 12.5 Hz), 135.87, 133.34, 128.98, 128.76(2C), 128.39, 128.10(2C), 124.49, 123.57, 123.56, 121.93, 121.26 (d, *J* = 10.2 Hz), 119.84 (d, *J* = 2.9 Hz), 111.13, 109.83, 108.46 (d, *J* = 24.3 Hz), 107.69, 97.77 (d, *J* = 26.0 Hz), 66.96, 41.00, 27.40.

^{19}F NMR (376 MHz, $CDCl_3$) δ -120.81.

HRMS (ESI): calcd for $C_{26}H_{23}N_3O_2$ $[M + H]^+$*m/z* 428.1769, found 428.1769.

Compound 18



Benzyl (2-(6'-chloro-1H,1'H-[3,3'-biindol]-2-yl)ethyl)carbamate

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *6-chloro-1H-indole* (226 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 10 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (341 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 50:1) to give the desired product (332 mg, 75%) as a brown solid.

Physical State: brown solid.

Melting Point: 53.6 – 54.5 °C.

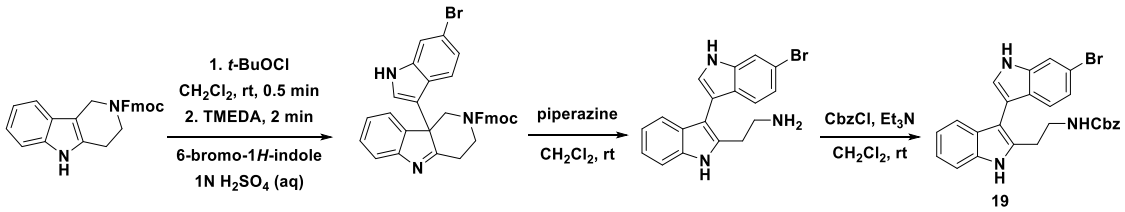
TLC: R_f = 0.46 (PE/EtOAc = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 8.22 (s, 1H), 7.45 (d, *J* = 11.0 Hz, 2H), 7.39 (d, *J* = 8.7 Hz, 3H), 7.36 (s, 2H), 7.34 – 7.30 (m, 2H), 7.22 (t, *J* = 7.7 Hz, 1H), 7.19 (s, 1H), 7.14 – 7.03 (m, 2H), 5.06 (s, 2H), 4.84 (t, *J* = 6.3 Hz, 1H), 3.56 – 3.33 (m, 2H), 3.09 – 3.00 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.09, 136.83, 136.51, 135.95, 133.49, 129.02, 128.85(2C), 128.48, 128.15(2C), 128.04, 126.55, 124.11, 122.03, 121.50, 120.47, 119.97, 119.85, 111.57, 111.26, 109.93, 107.57, 67.04, 41.07, 27.44.

HRMS (ESI): calcd for $C_{26}H_{23}ClN_3O_2$ $[M + H]^+$*m/z* 444.1473, found 444.1477.

Compound 19



Benzyl (2-(6'-bromo-1H,1'H-[3,3'-biindol]-2-yl)ethyl)carbamate

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *6-bromo-1H-indole* (294 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 10 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (341 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 50:1) to give the desired product (254 mg, 59%) as a light yellow solid.

Physical State: light yellow solid.

Melting Point: 70.2 – 72.9 °C.

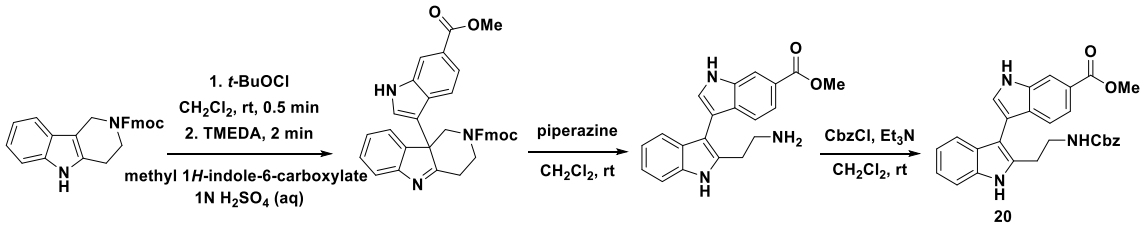
TLC: R_f = 0.45 (PE/EtOAc = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.23 (s, 1H), 7.60 (s, 1H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.37 (s, 4H), 7.31 (d, *J* = 13.7 Hz, 3H), 7.26 – 7.18 (m, 2H), 7.17 (s, 1H), 7.15 – 7.07 (m, 1H), 5.06 (s, 2H), 4.84 (s, 1H), 3.63 – 3.24 (m, 2H), 3.24 – 2.92 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.96, 137.20, 136.44, 135.85, 133.39, 128.93, 128.77(2C), 128.40, 128.12(2C), 126.77, 123.93, 122.95, 121.95, 121.80, 119.88, 119.74, 115.70, 114.45, 111.14, 109.94, 107.44, 66.96, 40.97, 27.41.

HRMS (ESI): calcd for $C_{26}H_{23}BrN_3O_2$ $[M + H]^+$ *m/z* 488.0968, found 488.0971.

Compound 20



Methyl 2'-(2-(((benzyloxy)carbonyl)amino)ethyl)-1H,1'H-[3,3'-biindole]-6-carboxylate

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *methyl 1H-indole-6-carboxylate* (263 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 10 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (341 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 10:1) to give the desired product (243 mg, 52%) as a light yellow solid.

Physical State: light yellow solid.

Melting Point: 83.3 – 85.8 °C.

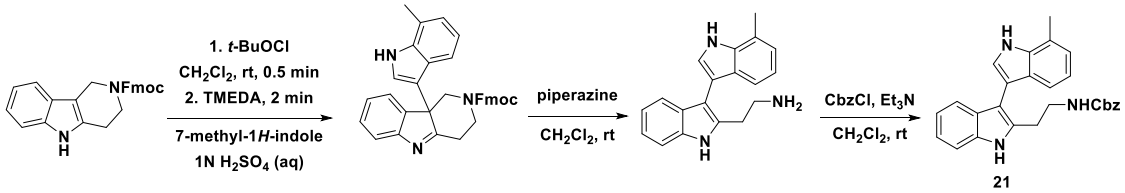
TLC: R_f = 0.37 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.53 (s, 1H), 8.23 (s, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 7.35 (s, 4H), 7.32 (s, 2H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 7.3 Hz, 1H), 5.06 (s, 2H), 4.87 (s, 1H), 3.98 (s, 3H), 3.55 – 3.40 (m, 2H), 3.13 – 2.96 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.99, 157.01, 136.46, 135.93, 135.84, 133.53, 131.53, 128.93, 128.68(2C), 128.28, 128.02(2C), 127.14, 123.46, 121.88, 120.61, 120.16, 119.81, 119.69, 114.22, 111.13, 110.25, 107.33, 66.88, 52.25, 41.01, 27.45.

HRMS (ESI): calcd for $C_{28}H_{26}N_3O_4$ $[M + H]^+$*m/z* 468.1918, found 468.1920.

Compound 21



Benzyl (2-(7'-methyl-1H,1'H-[3,3'-biindol]-2-yl)ethyl)carbamate

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *7-methyl-1H-indole* (196 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 6 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (20 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (341 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 50:1) to give the desired product (169 mg, 40%) as a light yellow solid.

Physical State: light yellow solid.

Melting Point: 84.4 – 87.5 °C.

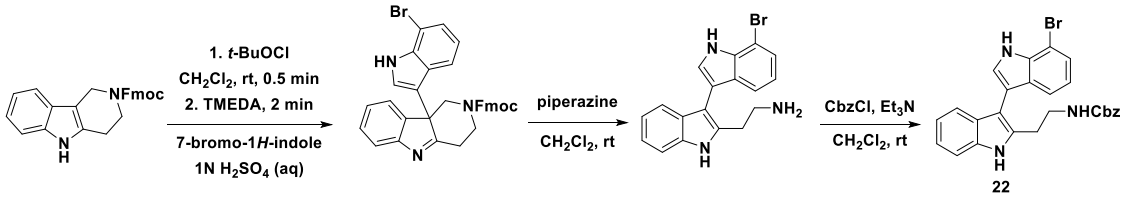
TLC: R_f = 0.40 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.15 (s, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.41 – 7.38 (m, 2H), 7.37 – 7.35 (m, 2H), 7.34 – 7.30 (m, 2H), 7.29 (s, 1H), 7.22 (t, *J* = 7.1 Hz, 2H), 7.11 (d, *J* = 7.8 Hz, 1H), 7.06 (d, *J* = 8.1 Hz, 2H), 5.08 (s, 2H), 4.84 (s, 1H), 3.52 – 3.39 (m, 2H), 3.13 – 2.95 (m, 2H), 2.58 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.69, 136.50, 135.84, 135.70, 132.98, 129.02, 128.62(2C), 128.22, 128.15(2C), 127.38, 122.96, 122.70, 121.69, 120.53, 119.91, 119.81, 119.60, 118.25, 110.80, 110.26, 108.15, 66.78, 40.82, 27.49, 16.68.

HRMS (ESI): calcd for $C_{27}H_{26}N_3O_2$ $[M + H]^+$*m/z* 424.2020, found 424.2019.

Compound 22



Benzyl (2-(7'-bromo-1H,1'H-[3,3'-biindol]-2-yl)ethyl)carbamate

To a solution of *(9H-fluoren-9-yl)methyl 1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate* (394 mg, 1.0 mmol) in CH_2Cl_2 (8 mL) was added *tert*-butyl hypochlorite (130 mg, 1.2 mmol). The solution was stirred at rt for 0.5 min and then TMEDA (116 mg, 1.0 mmol) was added. The solution was stirred at rt for 2 min. Then *7-bromo-1H-indole* (294 mg, 1.5 mmol) and 1 N H_2SO_4 solution (1.0 mL, 1.0 mmol) were added into the mixture. The solution was stirred at rt for 10 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum to give the crude product. To a solution of this crude product in CH_2Cl_2 (5 mL) was added piperazine (331 mg). The mixture was stirred at rt for 12 h. The resulting solution was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) to give primary amine. To a solution of this primary amine in CH_2Cl_2 (5 mL) was added CbzCl (341 mg, 2 mmol) and Et_3N (202 mg, 2 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 50:1) to give the desired product (342 mg, 70%) as a light yellow solid.

Physical State: light yellow solid.

Melting Point: 70.1 – 70.9 °C.

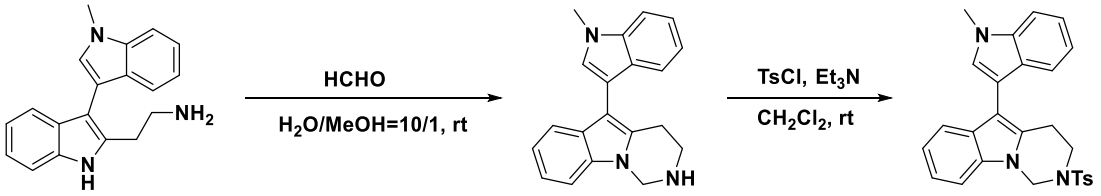
TLC: R_f = 0.40 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.40 (s, 1H), 7.49 – 7.43 (m, 2H), 7.41 (d, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 5.5 Hz, 3H), 7.35 – 7.31 (m, 2H), 7.25 (d, *J* = 4.8 Hz, 1H), 7.22 (d, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 7.3 Hz, 1H), 6.99 (t, *J* = 7.7 Hz, 1H), 5.08 (s, 2H), 4.84 (s, 1H), 3.58 – 3.36 (m, 2H), 3.14 – 2.92 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.92, 136.52, 135.84, 135.06, 133.46, 129.24, 128.94, 128.77(2C), 128.41, 128.24(2C), 128.17, 124.63, 124.02, 121.95, 120.99, 119.88, 119.77, 111.15, 111.08, 107.61, 105.02, 66.96, 40.96, 27.47.

HRMS (ESI): calcd for $C_{26}H_{23}BrN_3O_2$ $[M + H]^+$ *m/z* 488.0968, found 488.0917.

Compound 23



23

5-(1-Methyl-1H-indol-3-yl)-2-tosyl-1,2,3,4-tetrahydropyrimido[1,6-a]indole

To a solution of *2-(1'-methyl-1H,1'H-[3,3'-biindol]-2-yl)ethan-1-amine* (145 mg, 0.5 mmol) in H_2O/MeOH=10/1 (5.5 mL) was added 36% formaldehyde solution (50 mg, 0.6 mmol) and AcOH (0.5 mL). The solution was stirred at rt for 24 h. The resulting solution was filtered to give the crude product as pale yellow solid. To a solution of the crude product in CH_2Cl_2 (20 mL) was added TsCl (190 mg, 1 mmol) and Et_3N (101 mg, 1 mmol). The mixture was stirred at rt for 20 min. The resulting solution was purified by silica gel column chromatography (PE/EtOAc = 4:1) to give the desired product (85 mg, 37%) as a white solid.

Physical State: white solid.

Melting Point: 170.2 – 176.3 °C.

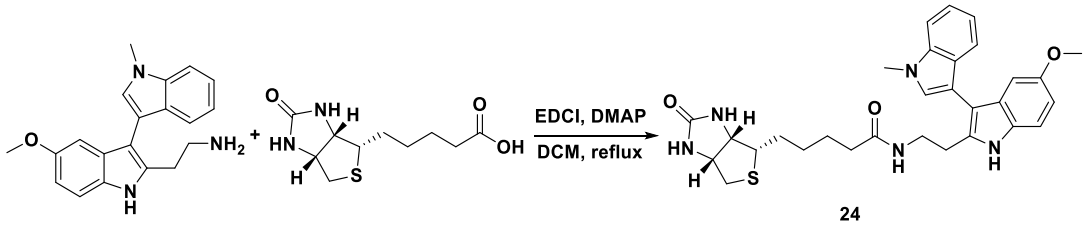
TLC: R_f = 0.51 (PE/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 7.9 Hz, 1H), 7.40 (t, *J* = 7.3 Hz, 2H), 7.30 (d, *J* = 7.3 Hz, 1H), 7.29 – 7.24 (m, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.99 (s, 1H), 5.64 (s, 2H), 3.88 (s, 3H), 3.72 (t, *J* = 6.3 Hz, 2H), 2.88 (t, *J* = 6.3 Hz, 2H), 2.38 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.11, 137.00, 135.80, 134.77, 129.86(2C), 129.66, 128.48, 127.71, 127.30(2C), 127.27, 121.75, 121.50, 120.49, 120.27, 119.89, 119.08, 109.42, 108.48, 107.72, 106.99, 57.92, 42.93, 32.90, 22.15, 21.56.

HRMS (ESI): calcd for $C_{27}H_{26}N_3O_2S$ $[M + H]^+$ *m/z* 456.1740, found 456.1741.

Compound 24



24

N-(2-(5-methoxy-1'-methyl-1H,1'H-[3,3'-biindol/]-2-yl)ethyl)-5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamide

To a solution of *2-(5-methoxy-1'-methyl-1H,1'H-[3,3'-biindol]-2-yl)ethan-1-amine* (160 mg, 0.5 mmol) in CH_2Cl_2 (4 mL) was added biotin (146 mg, 0.6mmol). The solution was stirred at 50℃ for 6 h. The resulting mixture was diluted with CH_2Cl_2 (40 mL) and then was washed with H_2O (60 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated to dryness under vacuum. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_3•H_2O = 100:10:1) the desired product (147 mg, 54%) as a white solid.

Physical State: white solid

Melting Point: 135.9 – 141.3 °C.

TLC: R_f = 0.43 (CH_2Cl_2/MeOH = 10:1).

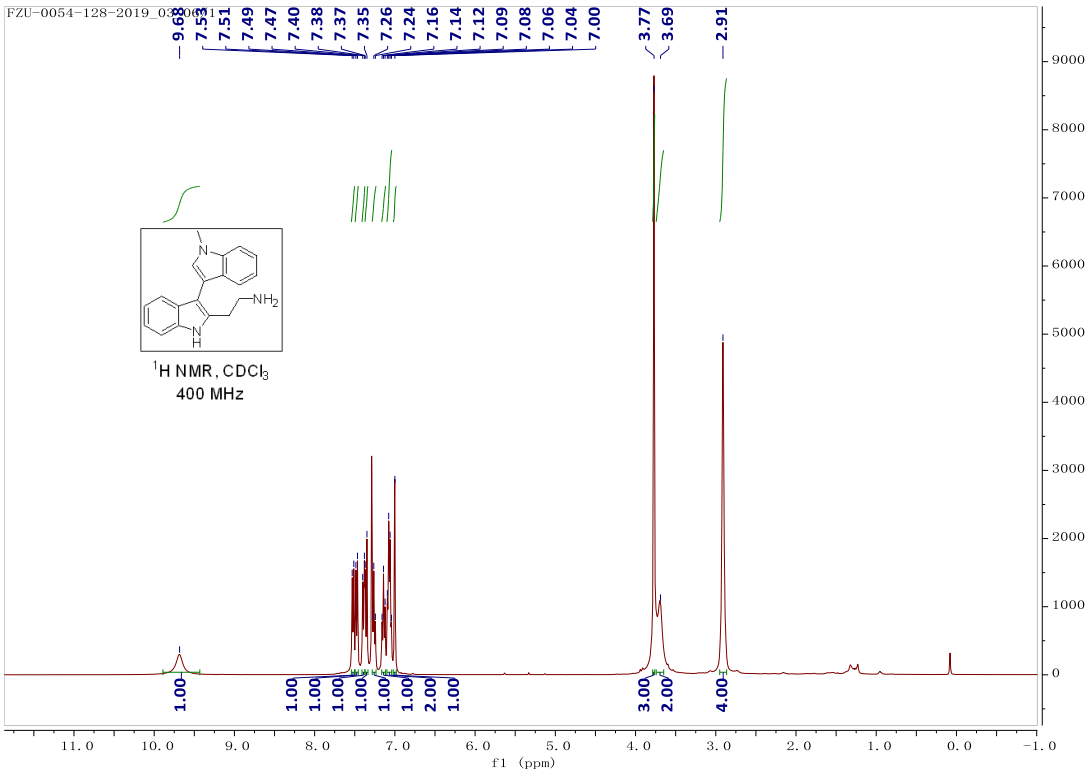
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.52 (s, 1H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 8.3 Hz, 1H), 7.25 (s, 1H), 7.09 – 7.05 (m, 2H), 6.91 (d, *J* = 2.2 Hz, 1H), 6.78 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.65 (s, 1H), 6.34 (t, *J* = 5.6 Hz, 1H), 4.27 – 4.23 (m, 1H), 4.06 – 4.02 (m, 1H), 3.83 (s, 3H), 3.69 (s, 3H), 3.56 – 3.33 (m, 3H), 2.98 (t, *J* = 6.5 Hz, 2H), 2.90 – 2.86 (m, 1H), 2.73 (dd, *J* = 12.8, 4.8 Hz, 1H), 2.52 (d, *J* = 12.8 Hz, 1H), 1.92 (d, *J* = 7.7 Hz, 1H), 1.53 (d, *J* = 8.1 Hz, 1H), 1.48 – 1.42 (m, 3H), 1.22 – 1.17 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 174.11, 153.98, 137.16, 134.56, 130.96, 129.28, 128.22, 127.62, 121.79, 120.63, 119.17, 111.78, 111.43, 109.51, 108.65, 107.19, 101.54, 61.66, 60.24, 55.99, 55.64, 40.48, 39.31, 35.72, 32.93, 27.93, 27.05, 25.59.

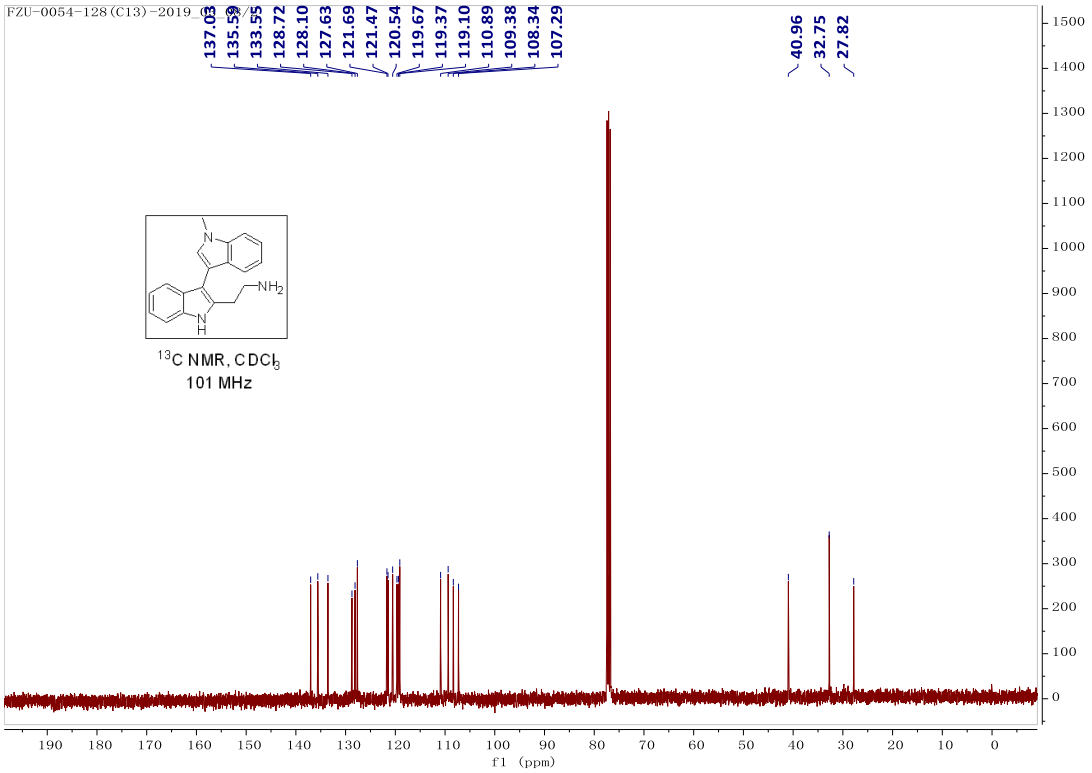
HRMS (ESI): calcd for $C_{19}H_{20}N_3$ $[M + H]^+$*m/z* 546.2533, found 546.2513.

6. NMR Spectra

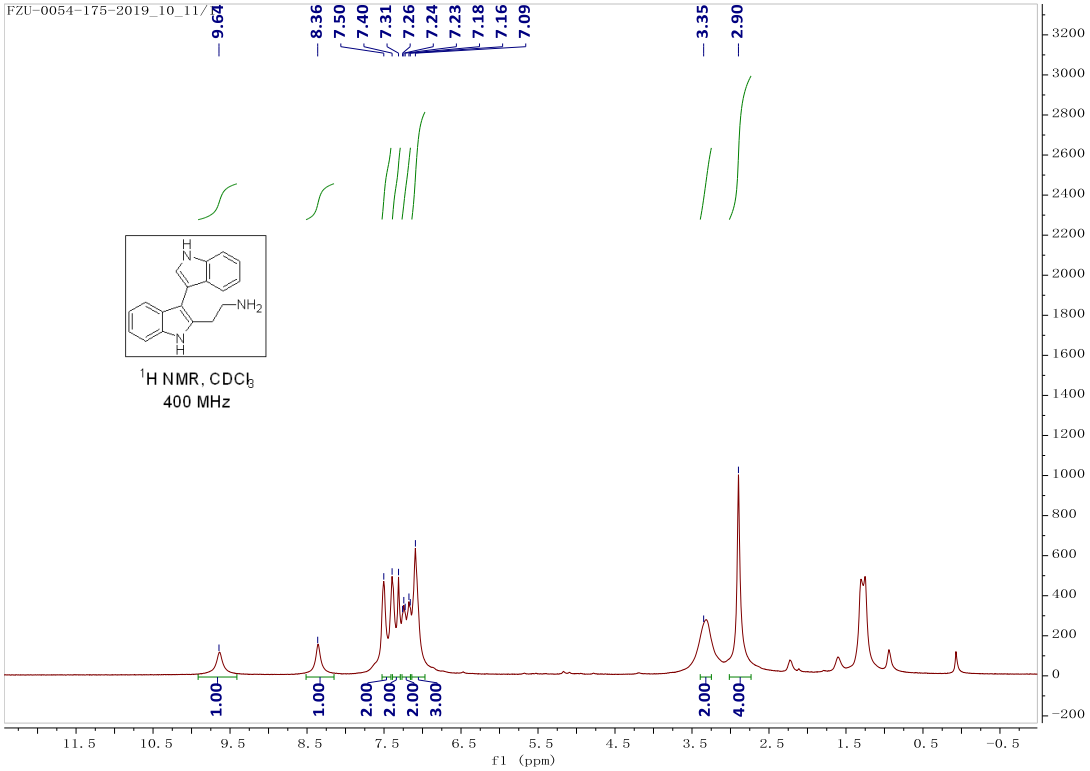
^{1}H NMR Spectrum of 2



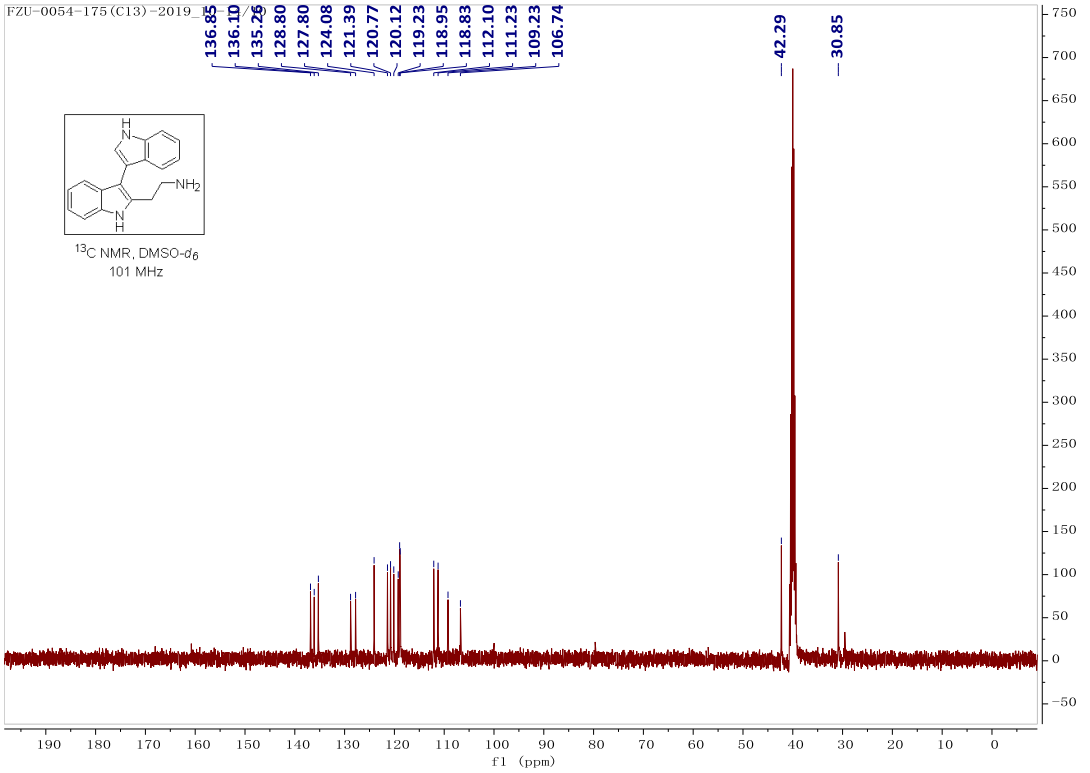
^{13}C NMR Spectrum of 2



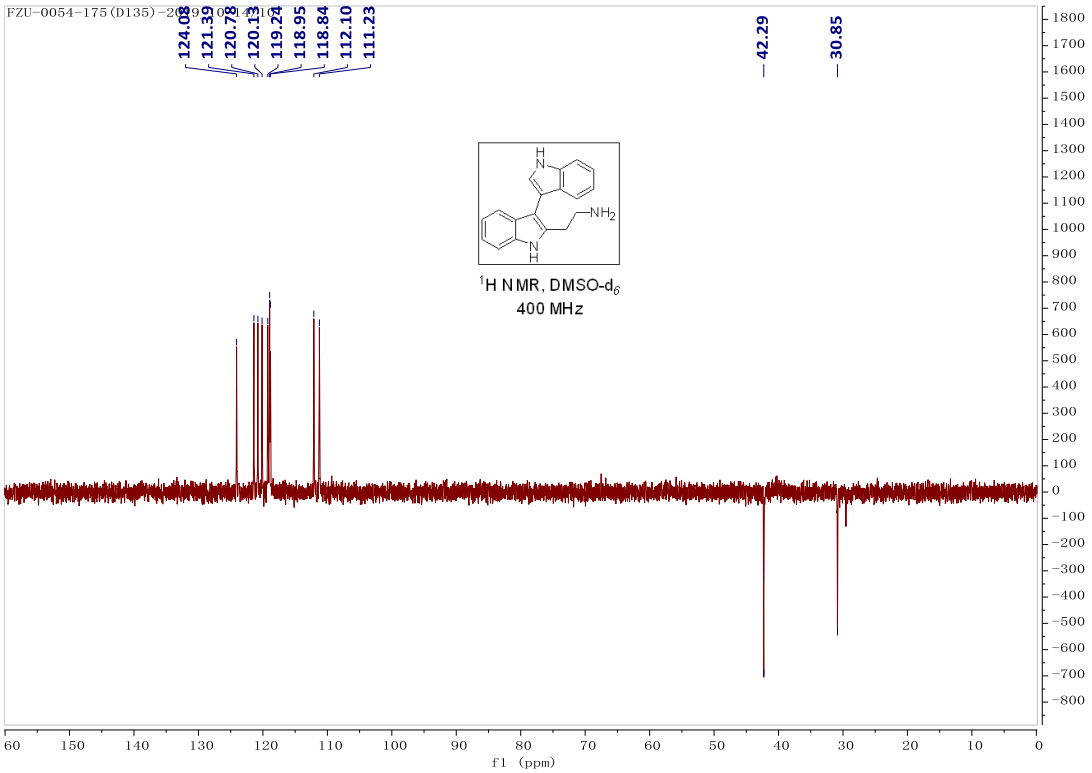
^{1}H NMR Spectrum of 3



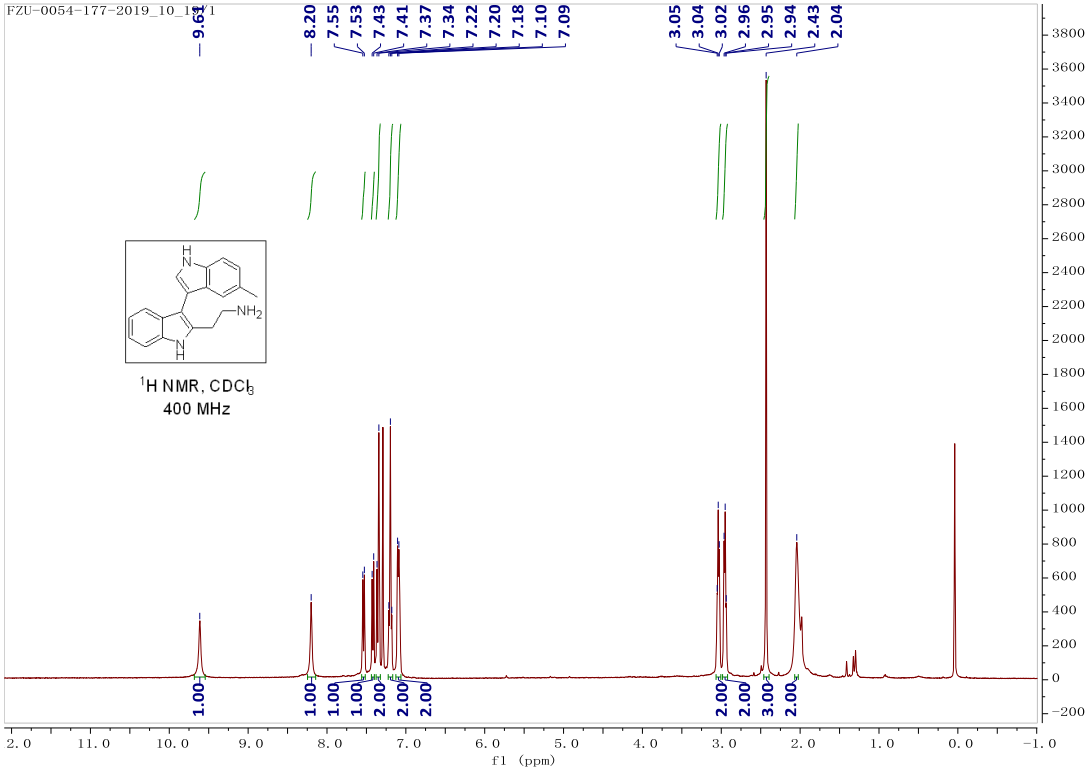
^{13}C NMR Spectrum of 3



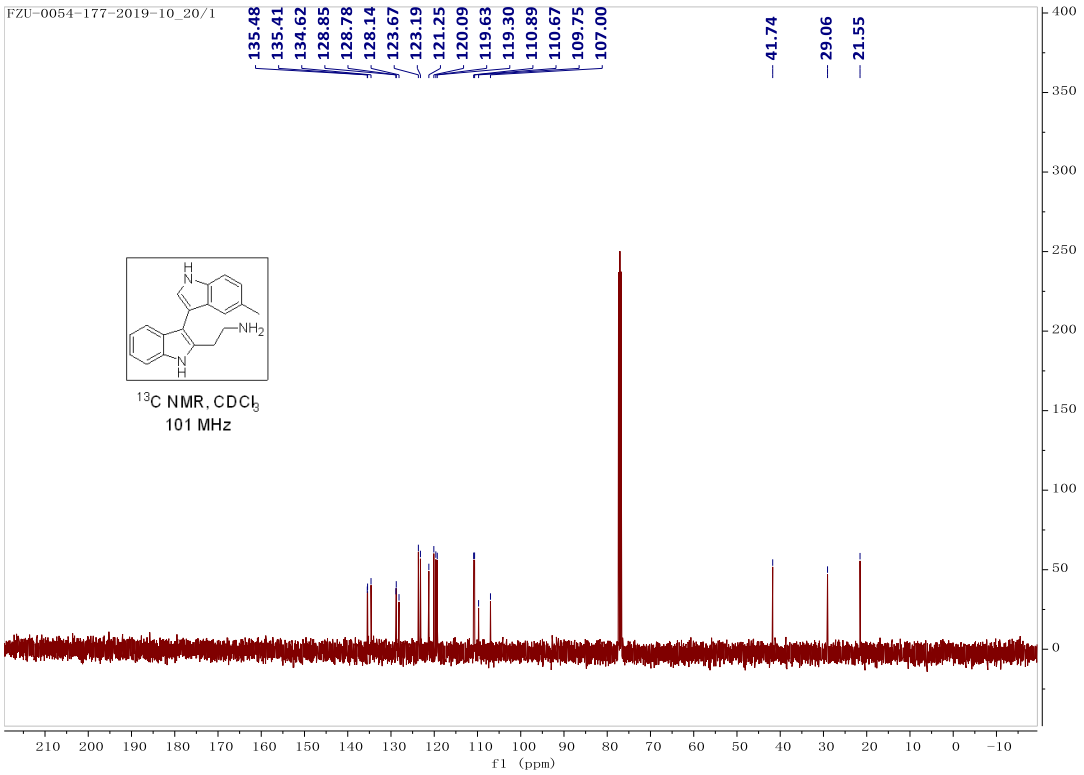
^{13}C NMR Spectrum (dept 135) of 3



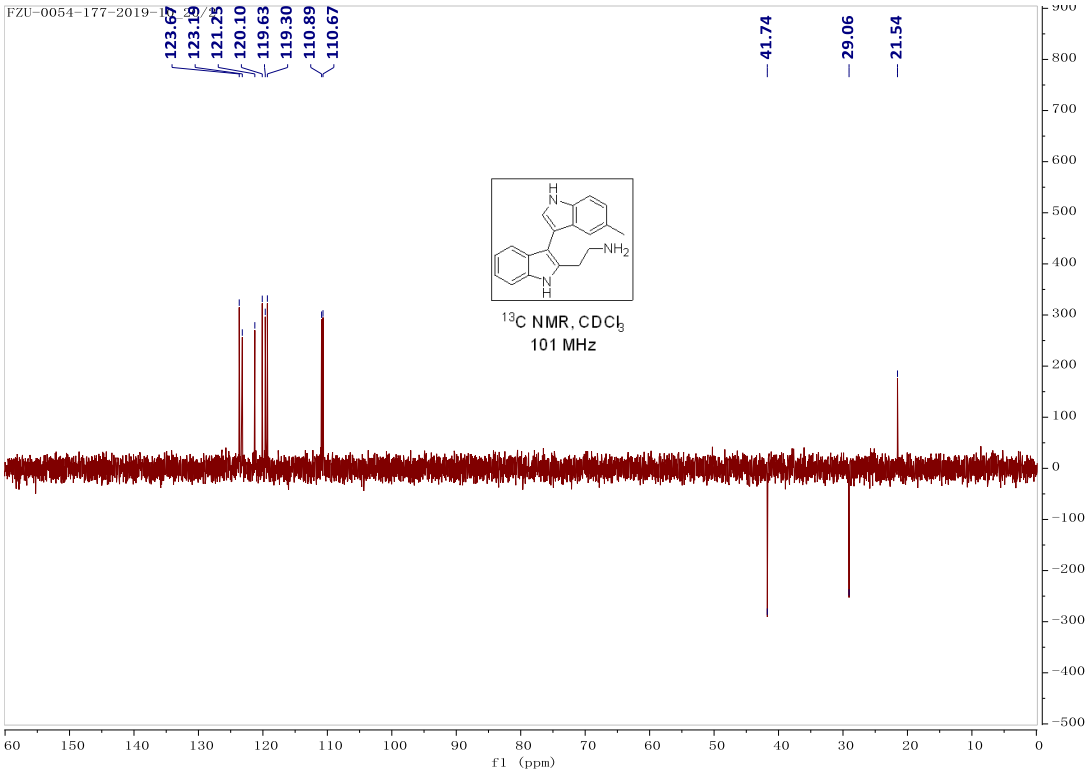
^{1}H NMR Spectrum of 4



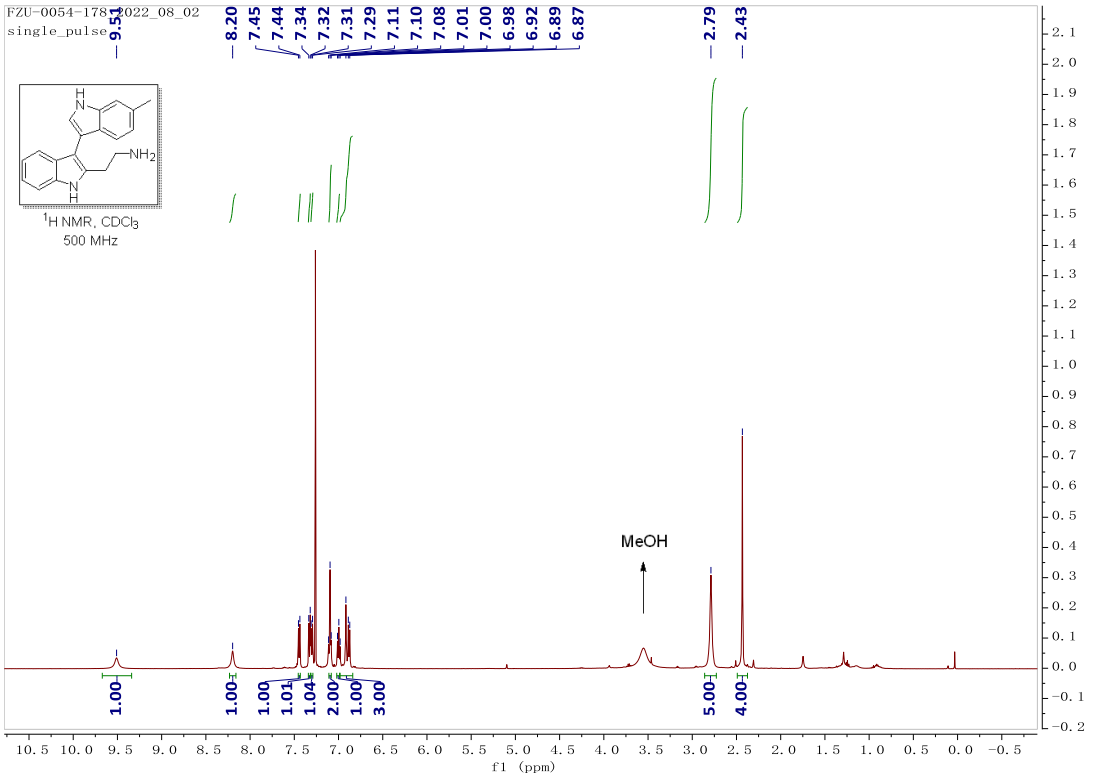
^{13}C NMR Spectrum of 4



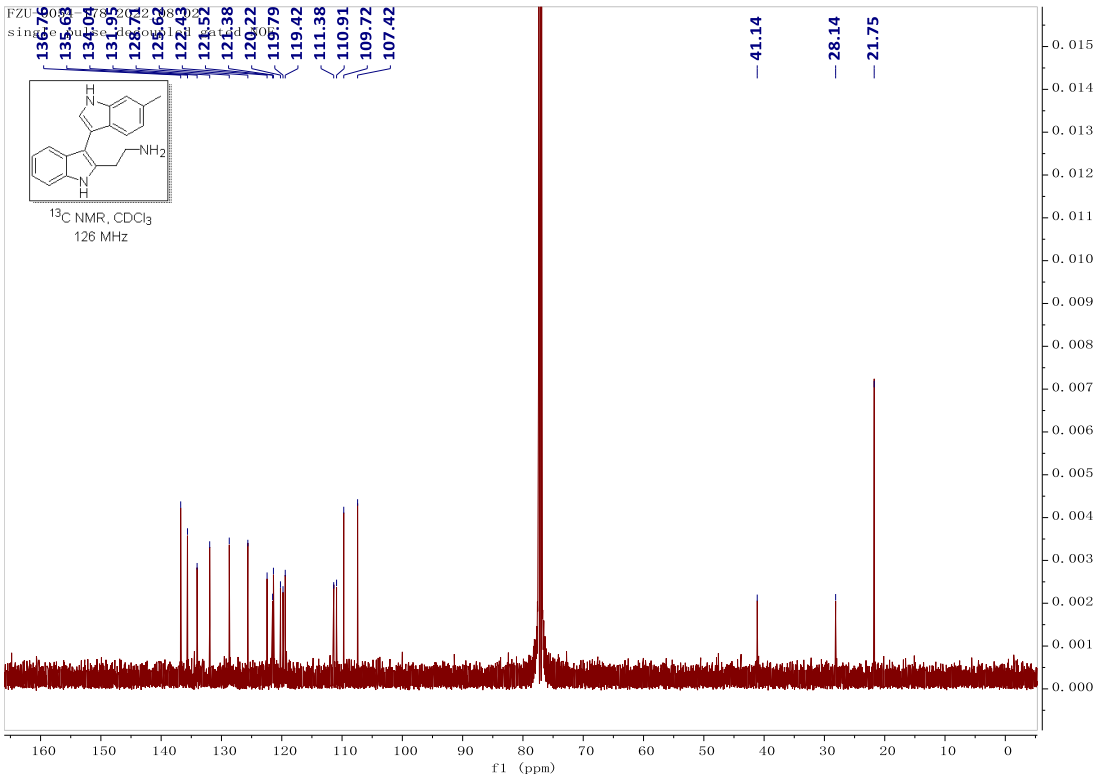
^{13}C NMR Spectrum (dept 135) of 4



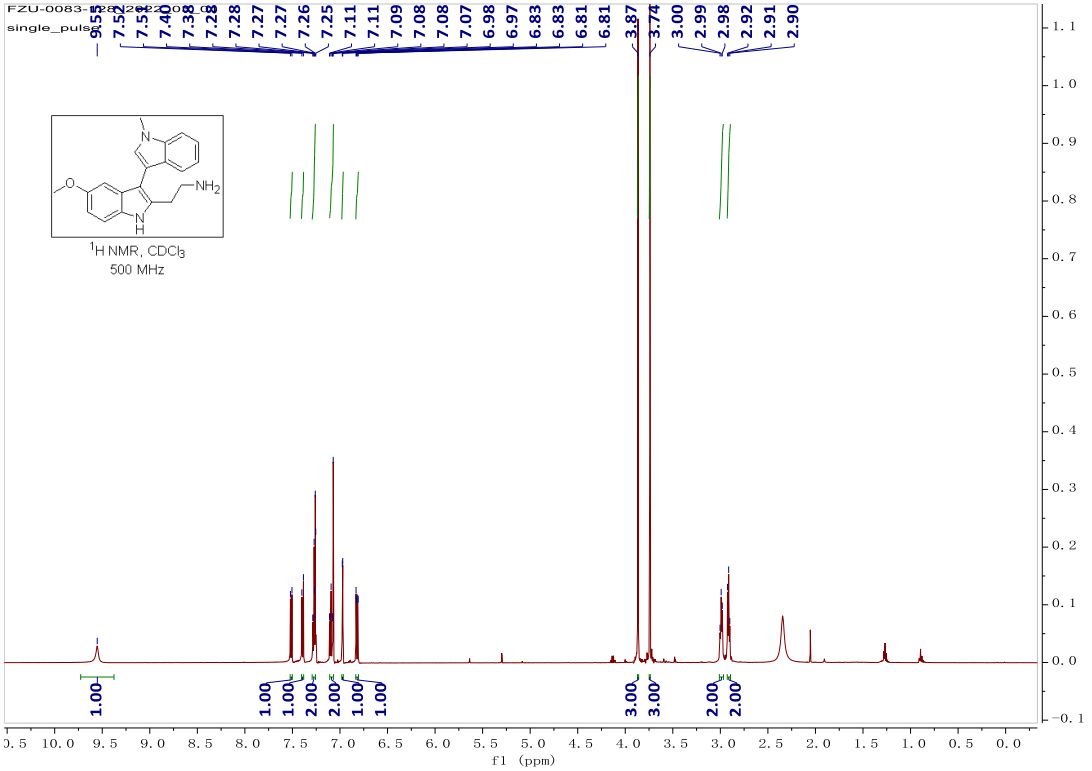
^{1}H NMR Spectrum of 5



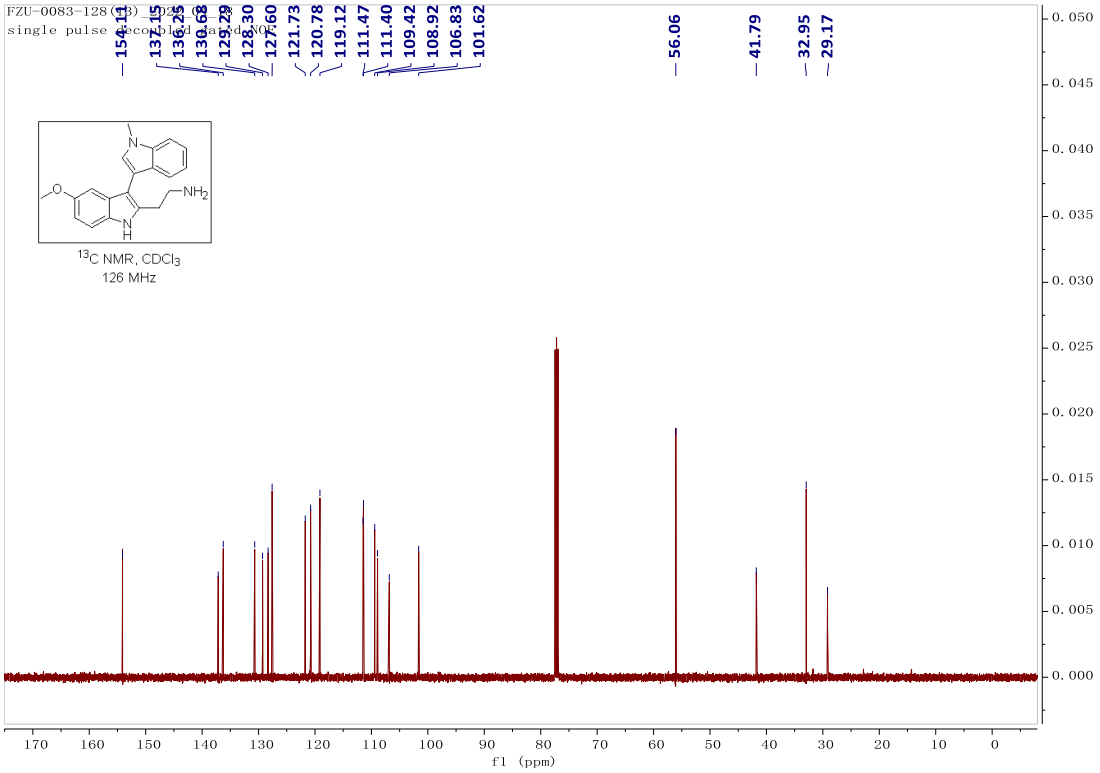
^{13}C NMR Spectrum of 5



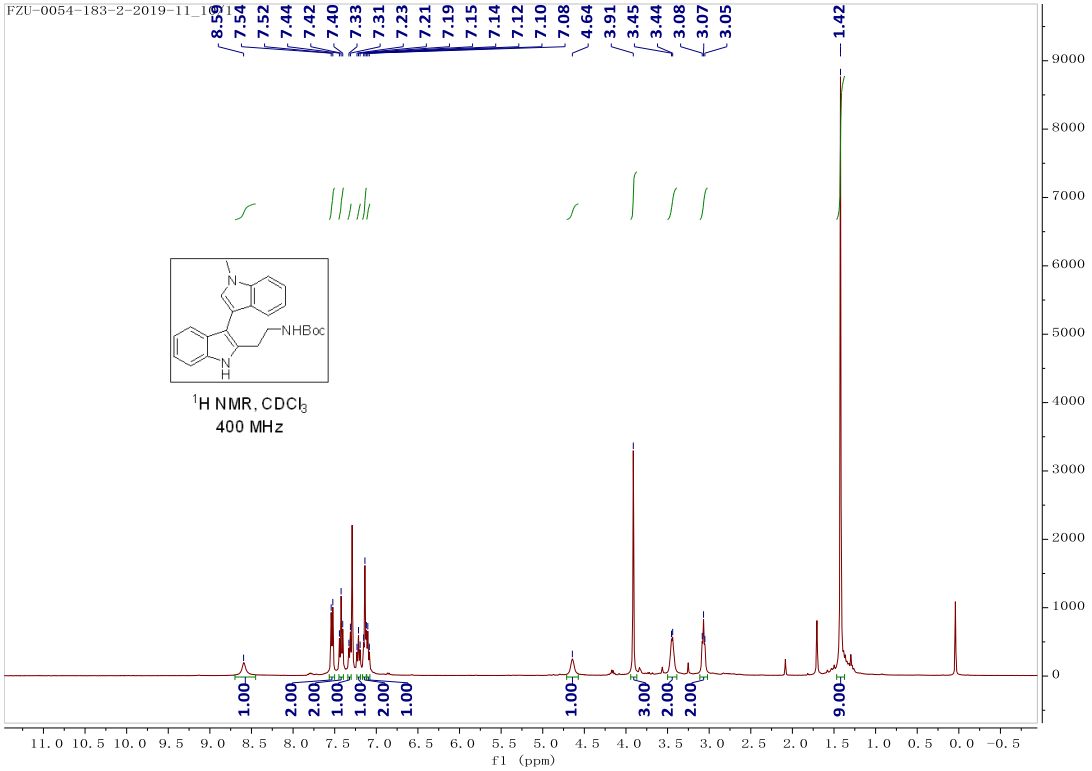
^{1}H NMR Spectrum of 6



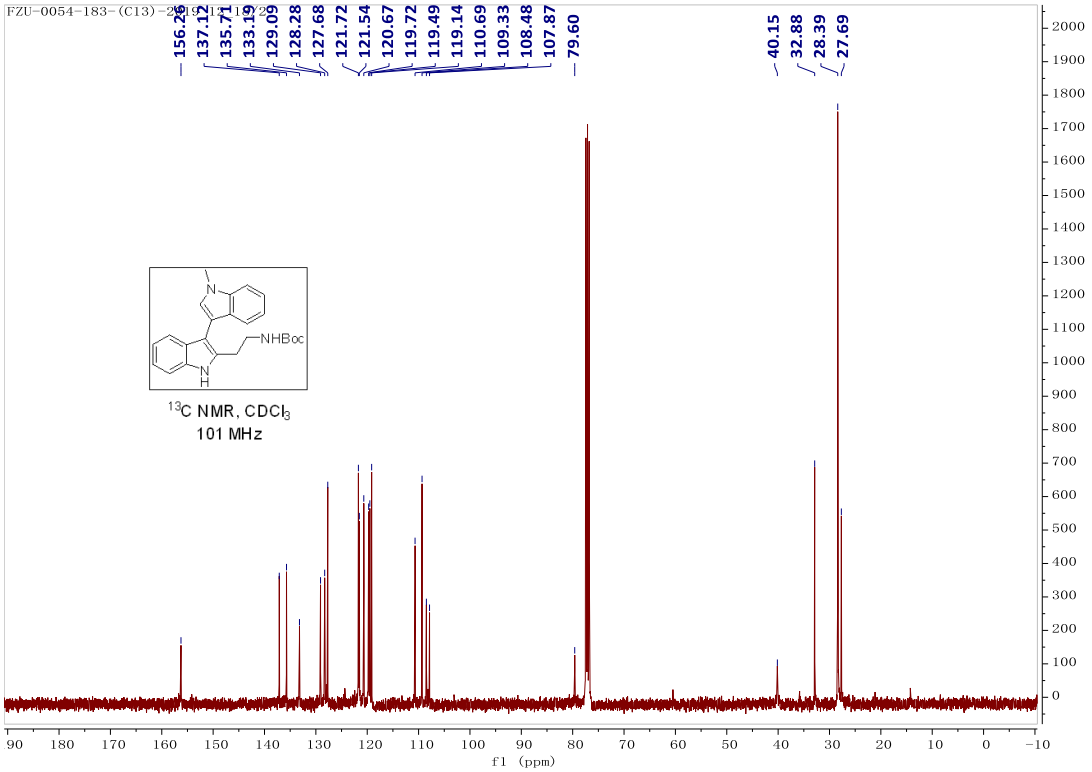
^{13}C NMR Spectrum of 6



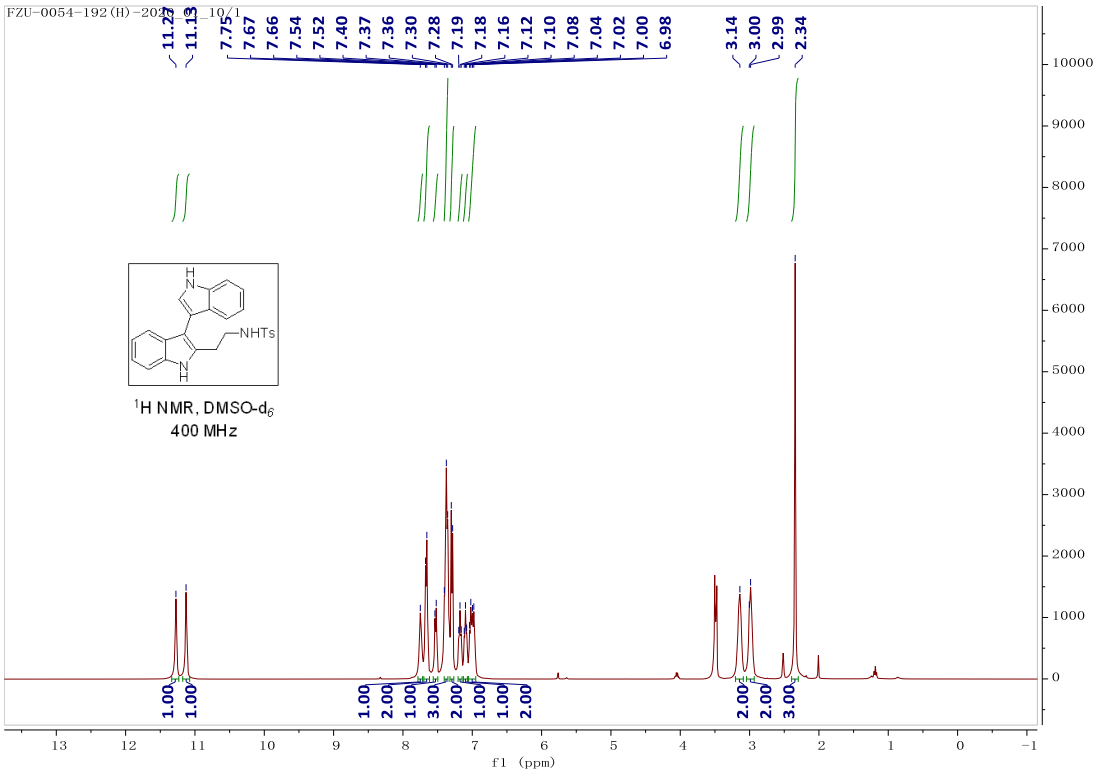
^{1}H NMR Spectrum of 7



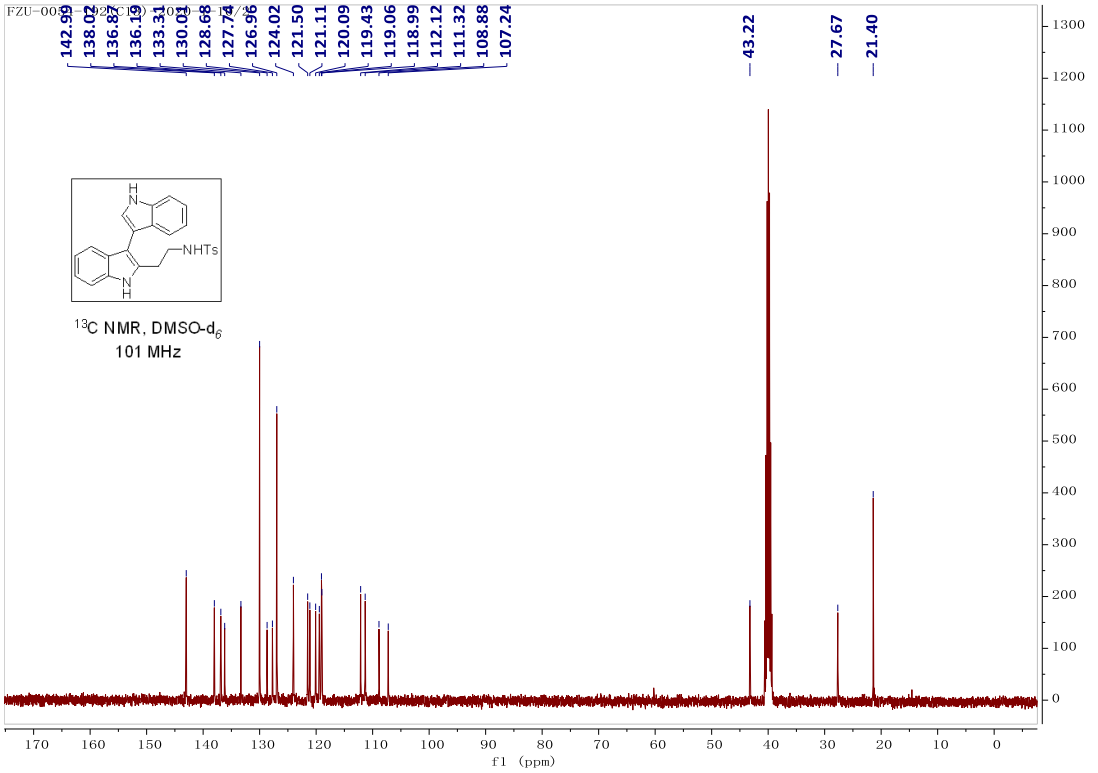
^{13}C NMR Spectrum of 7



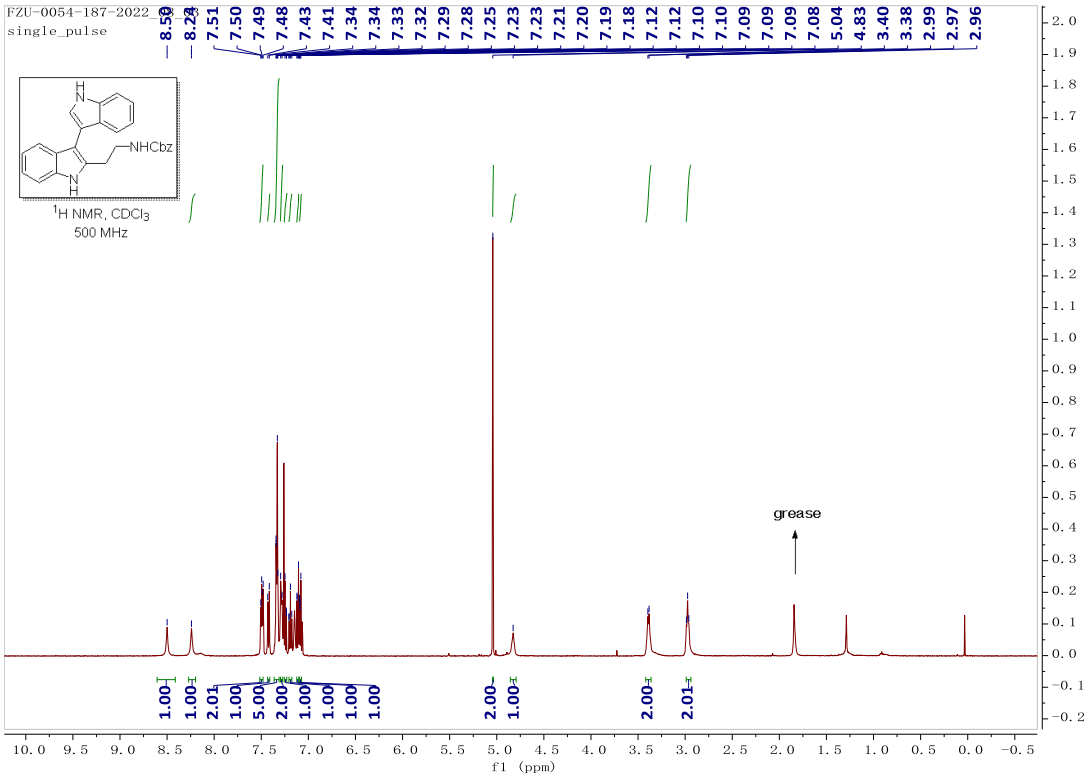
^{1}H NMR Spectrum of 8



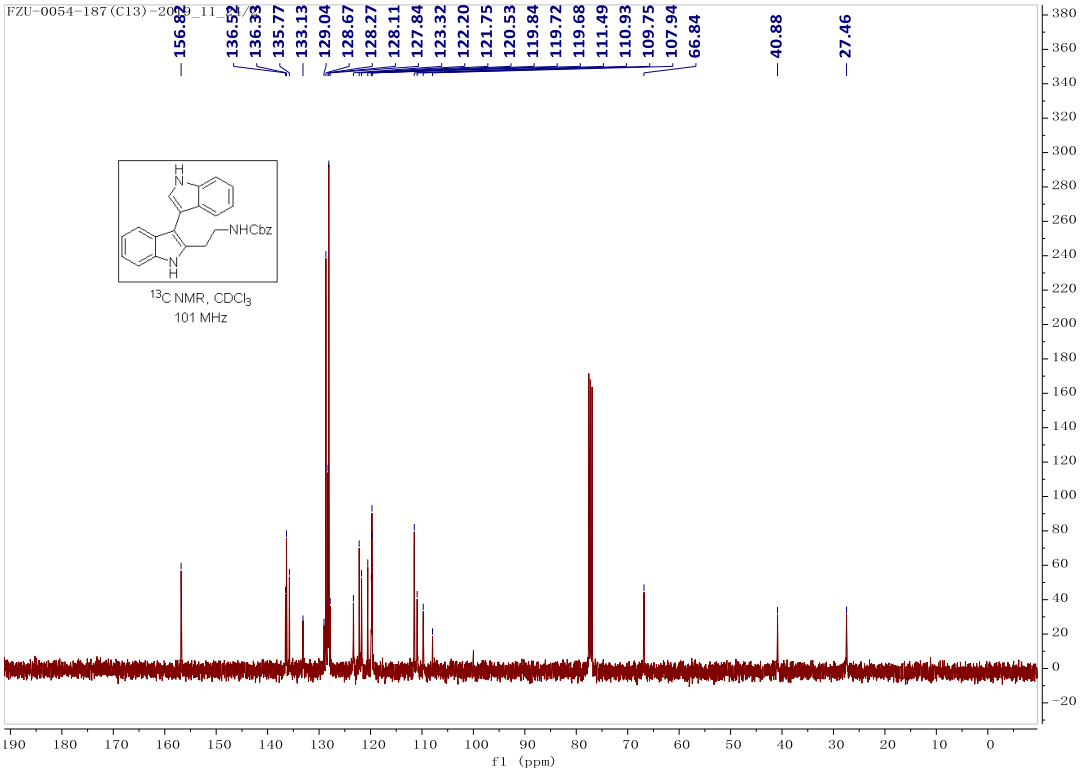
^{13}C NMR Spectrum of 8



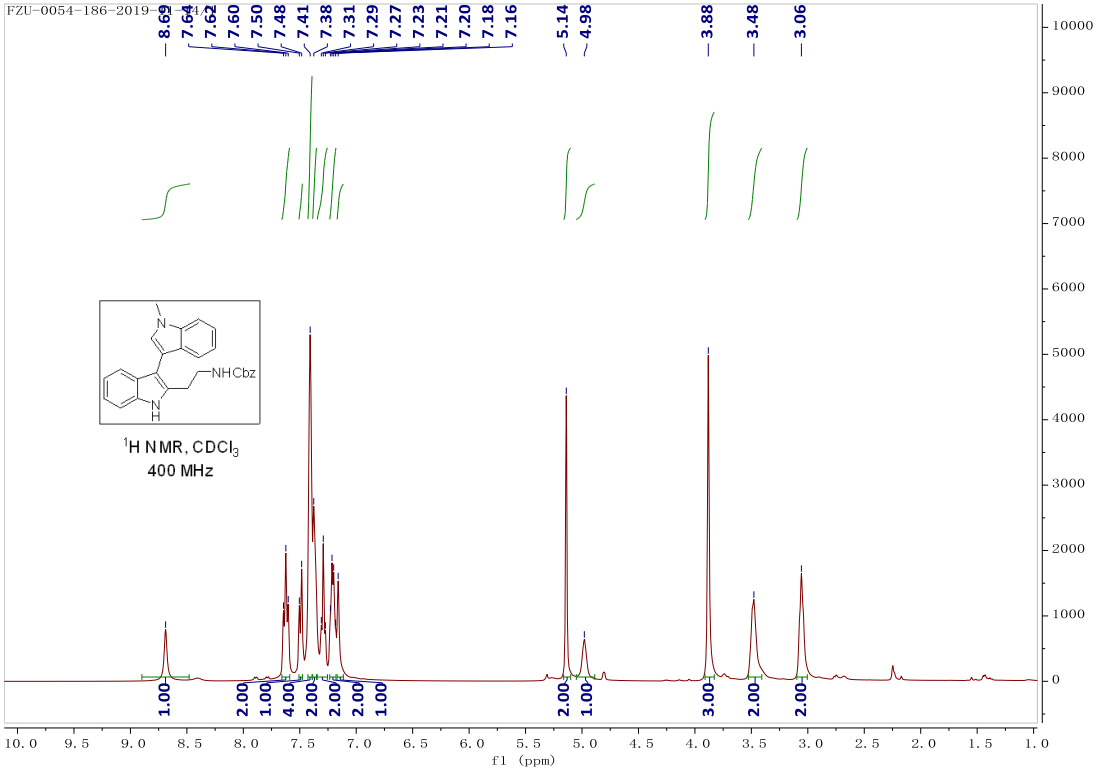
^{1}H NMR Spectrum of 9



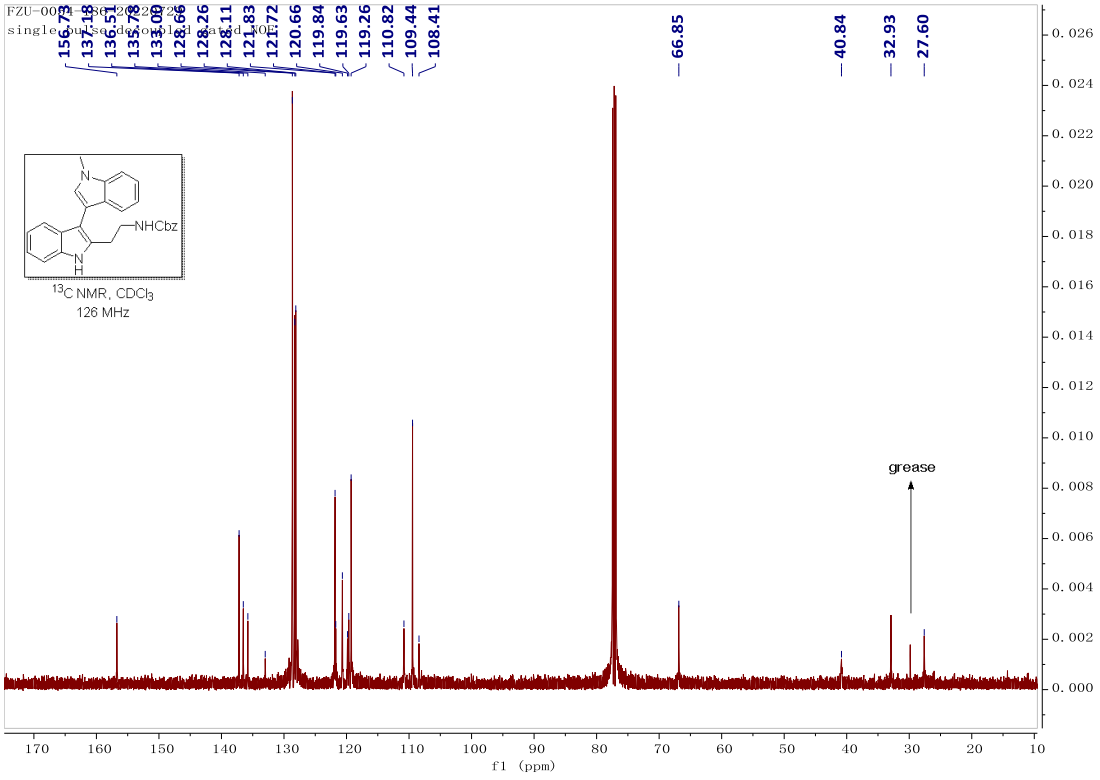
^{13}C NMR Spectrum of 9



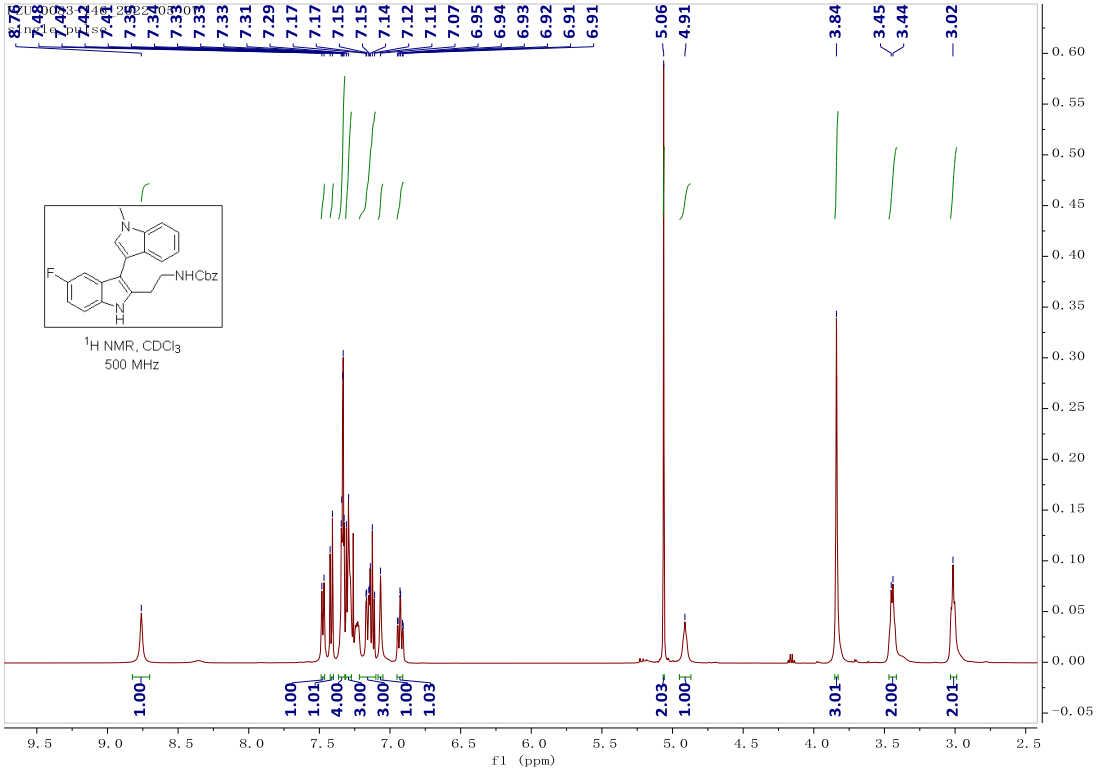
^{1}H NMR Spectrum of 10



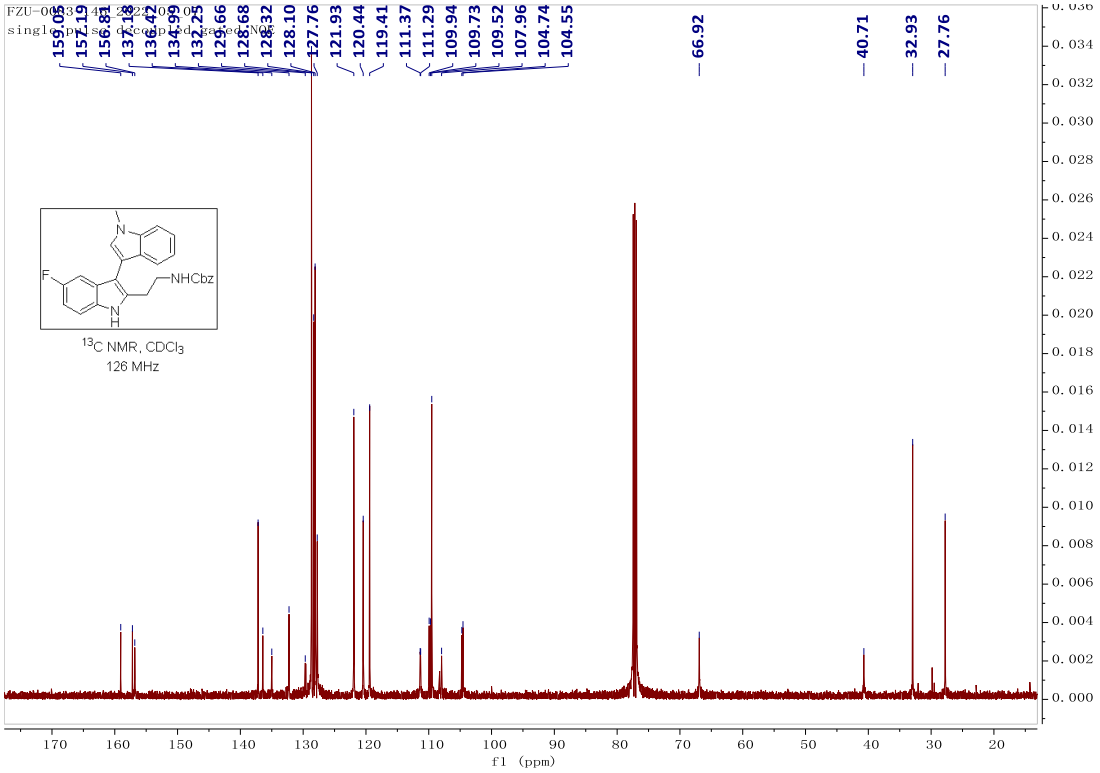
^{13}C NMR Spectrum of 10



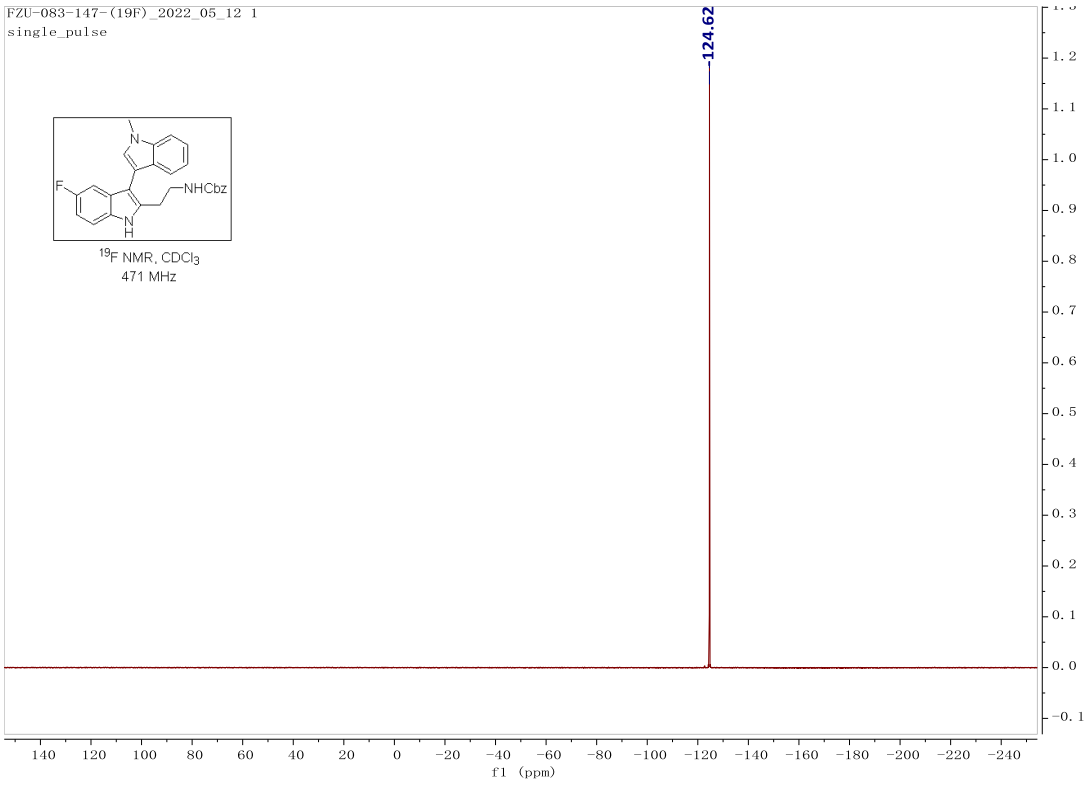
^{1}H NMR Spectrum of 11



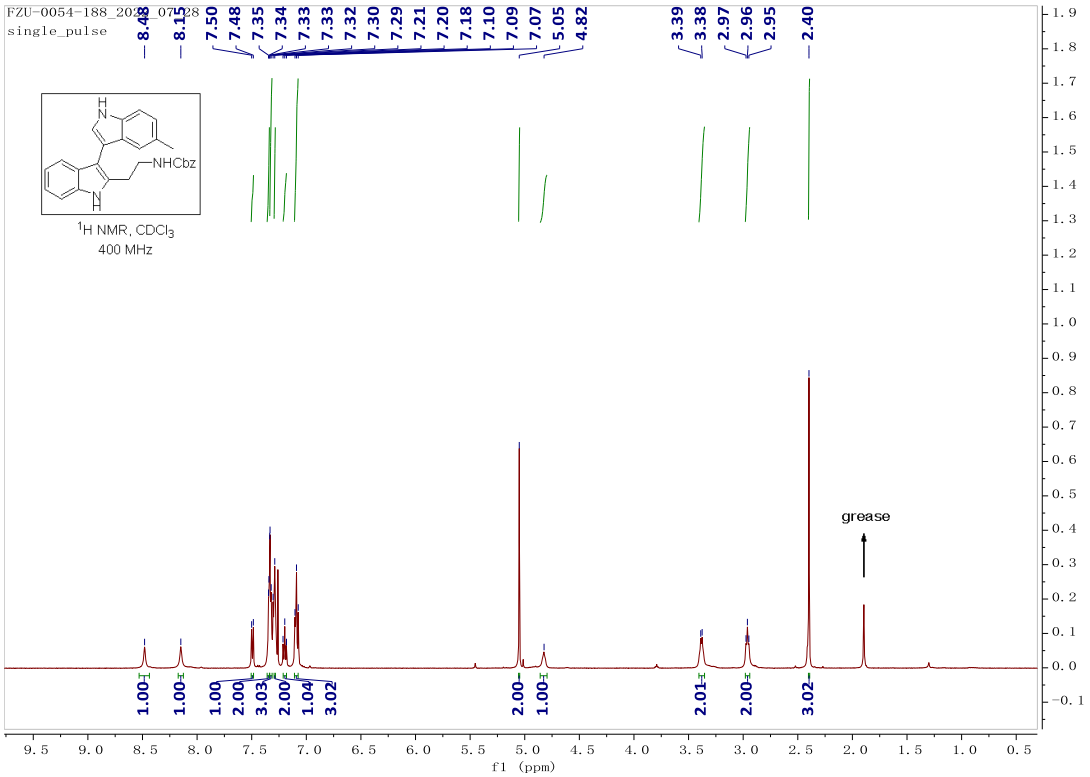
^{13}C NMR Spectrum of 11



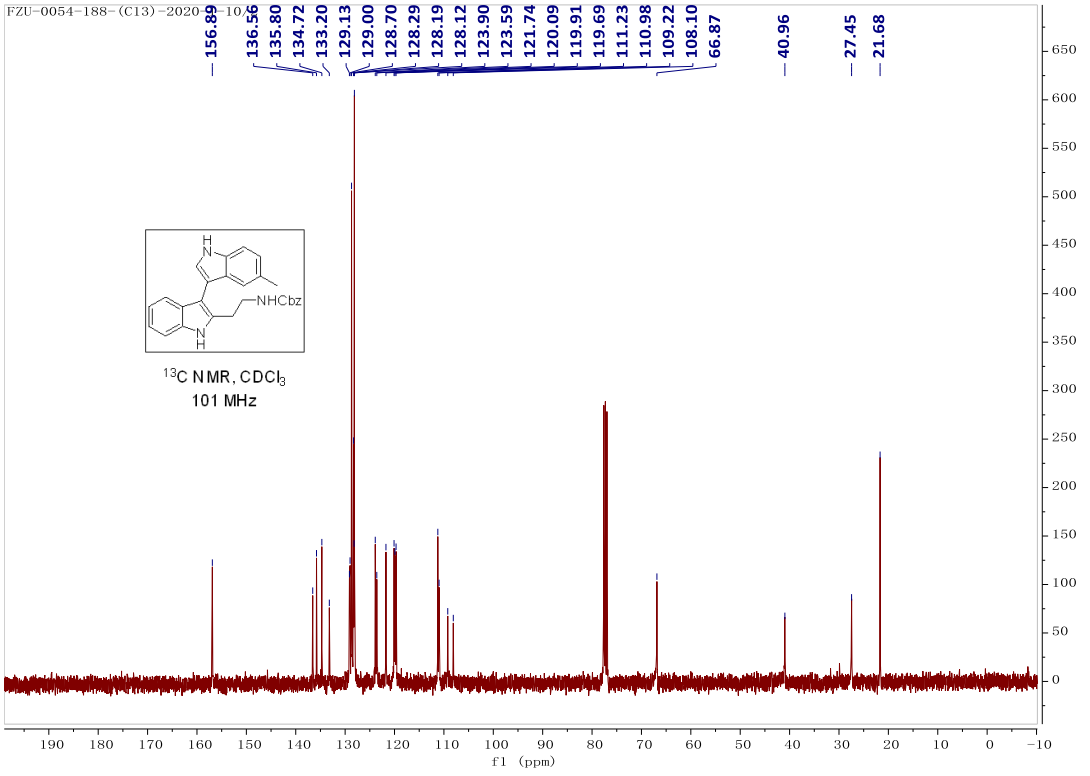
^{19}F NMR Spectrum of 11



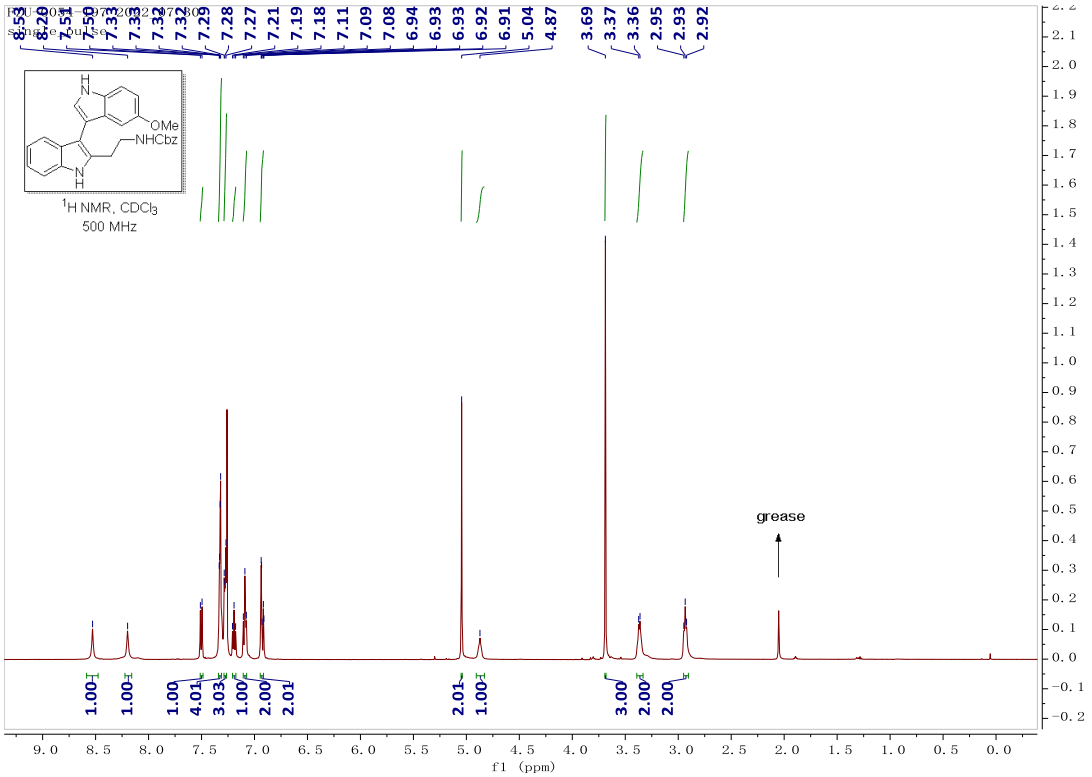
^{1}H NMR Spectrum of 12



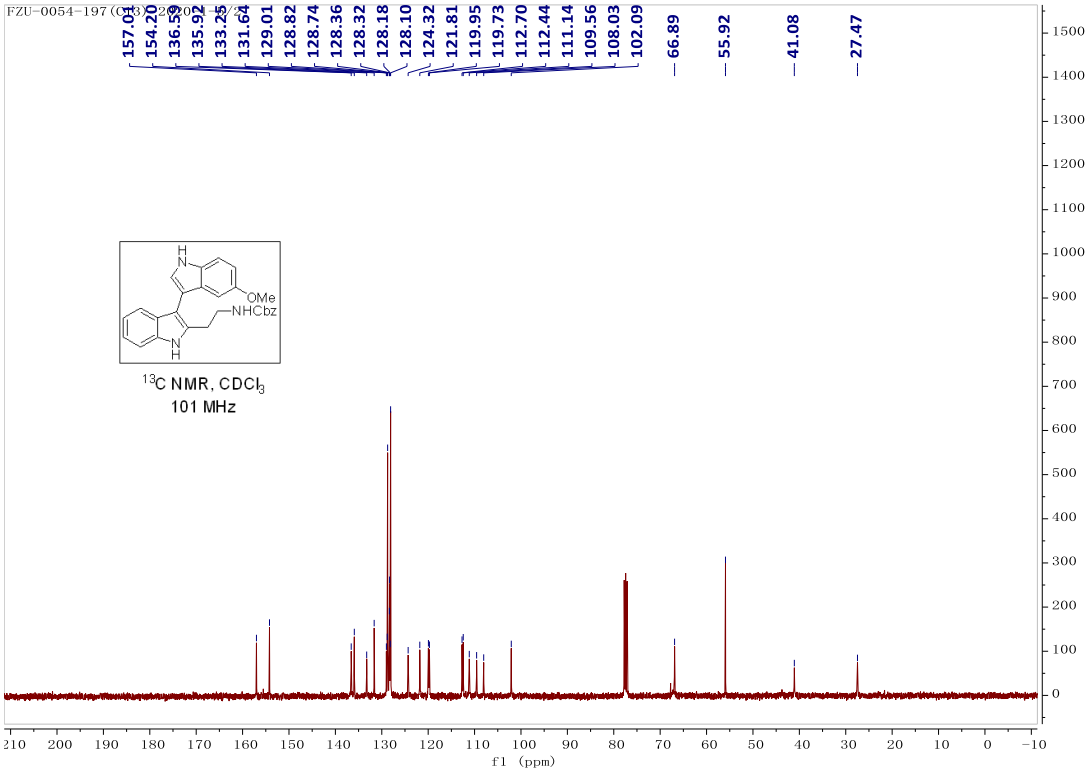
^{13}C NMR Spectrum of 12



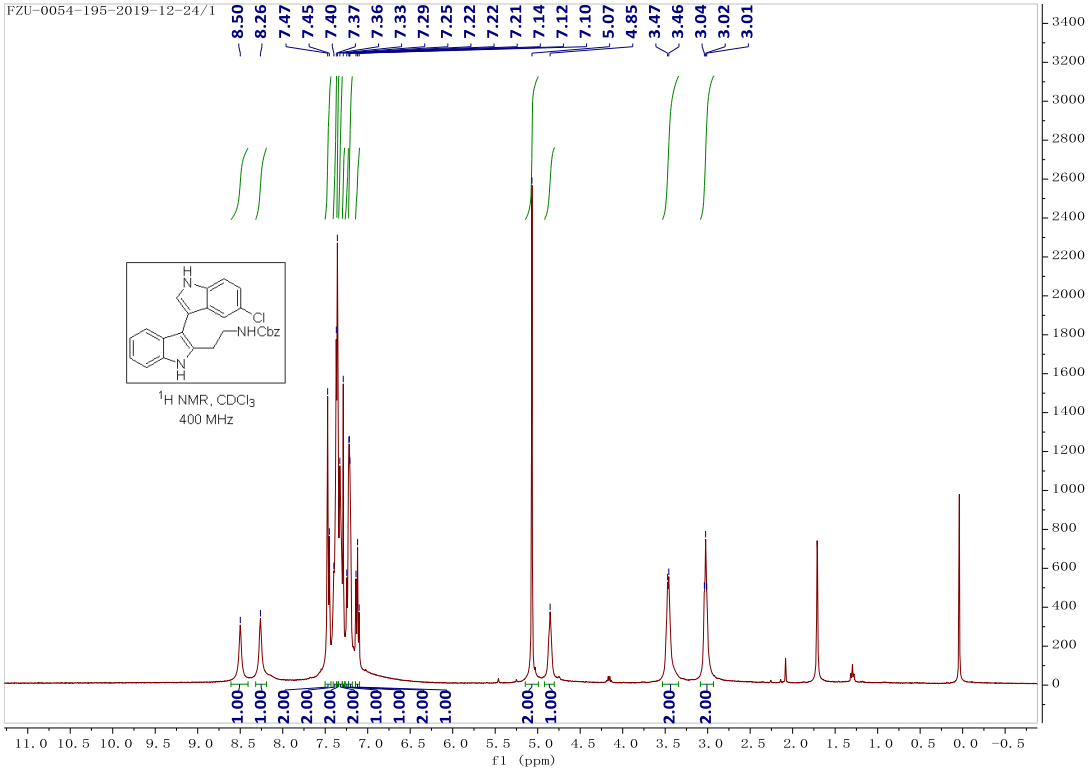
^{1}H NMR Spectrum of 13



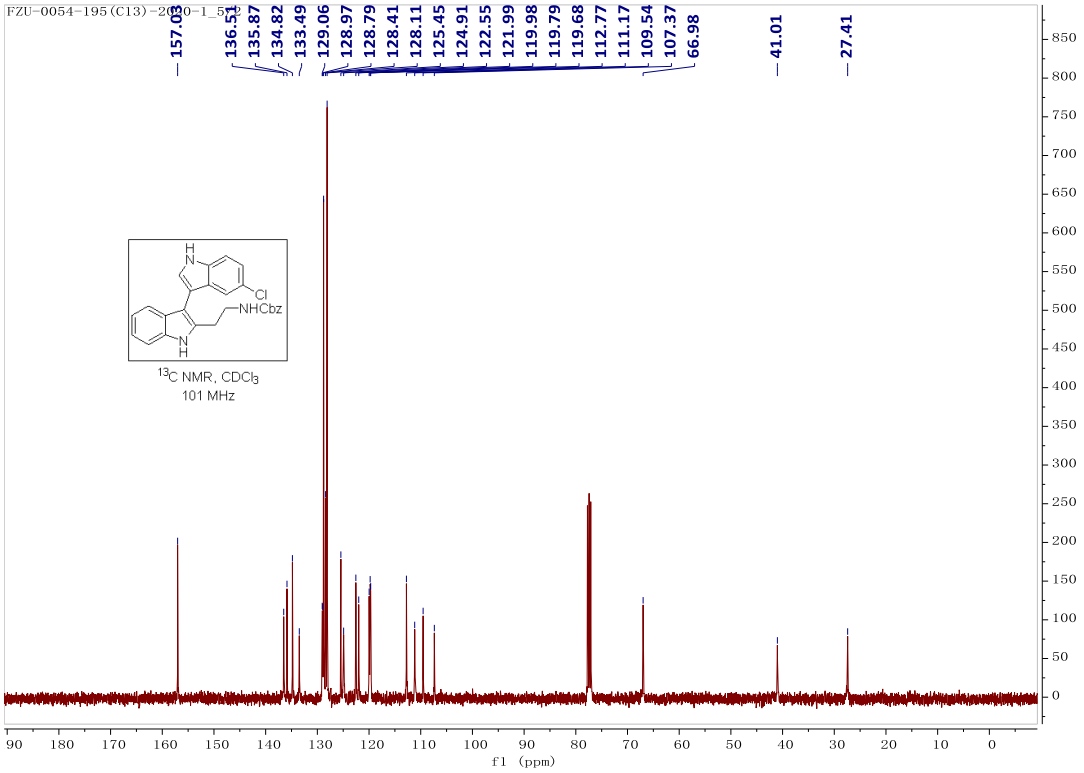
^{13}C NMR Spectrum of 13



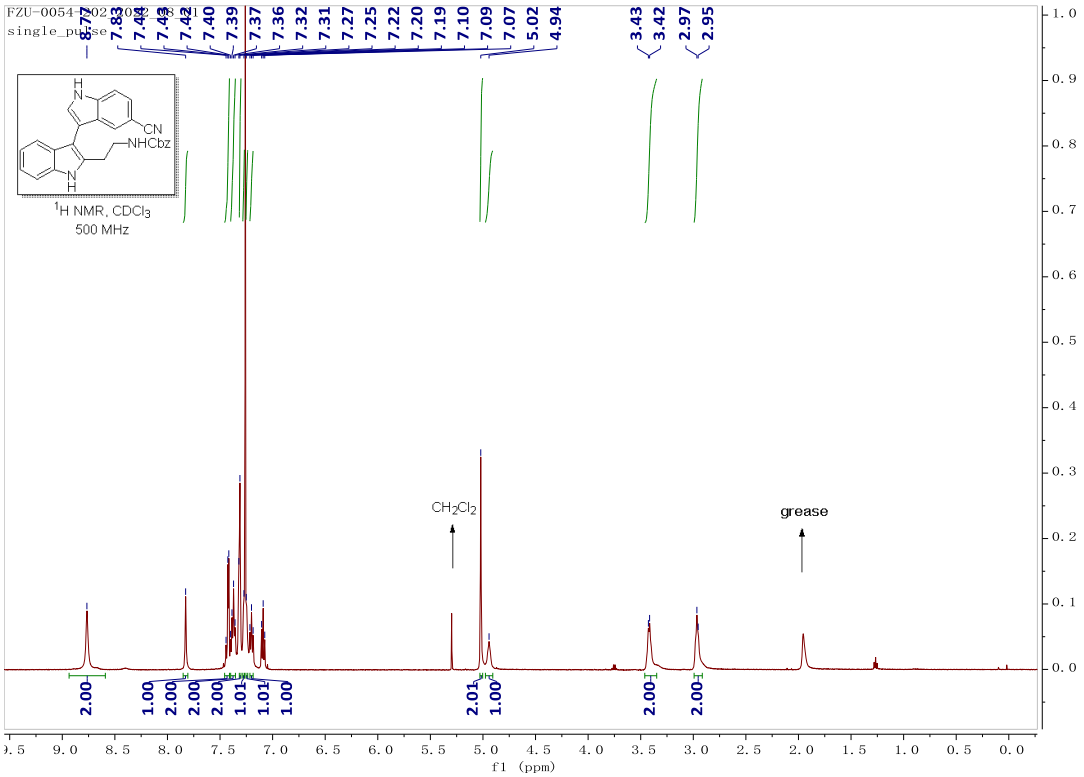
^{1}H NMR Spectrum of 14



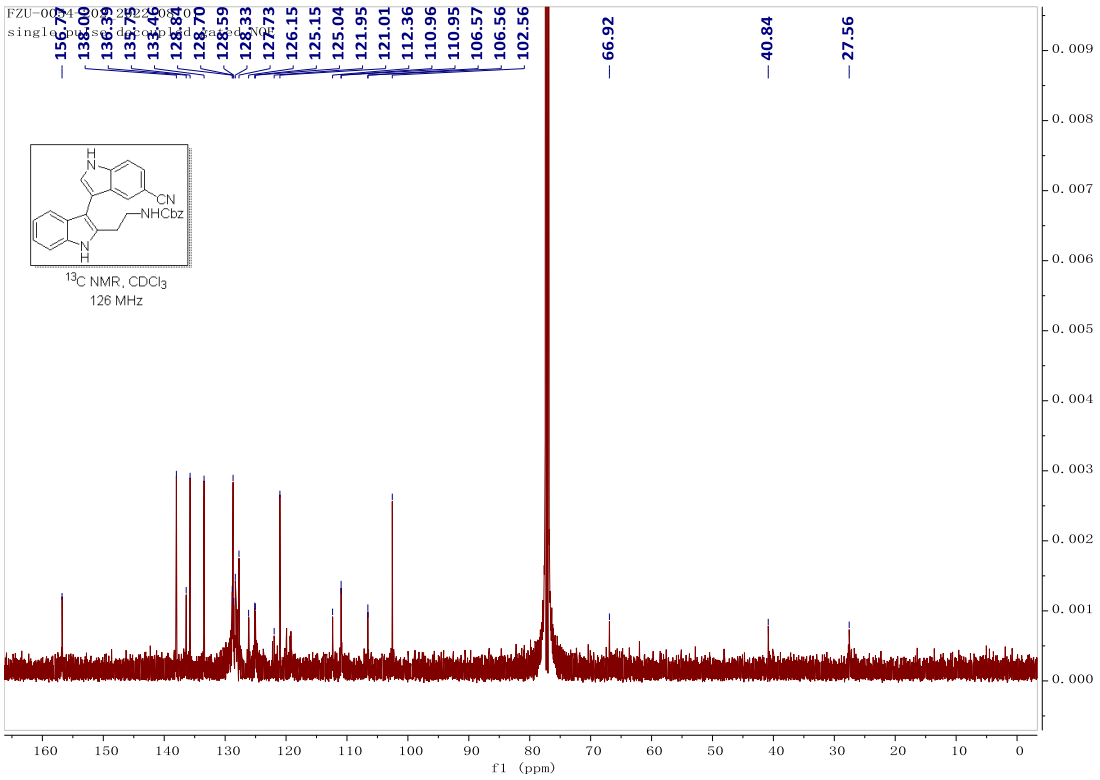
^{13}C NMR Spectrum of 14



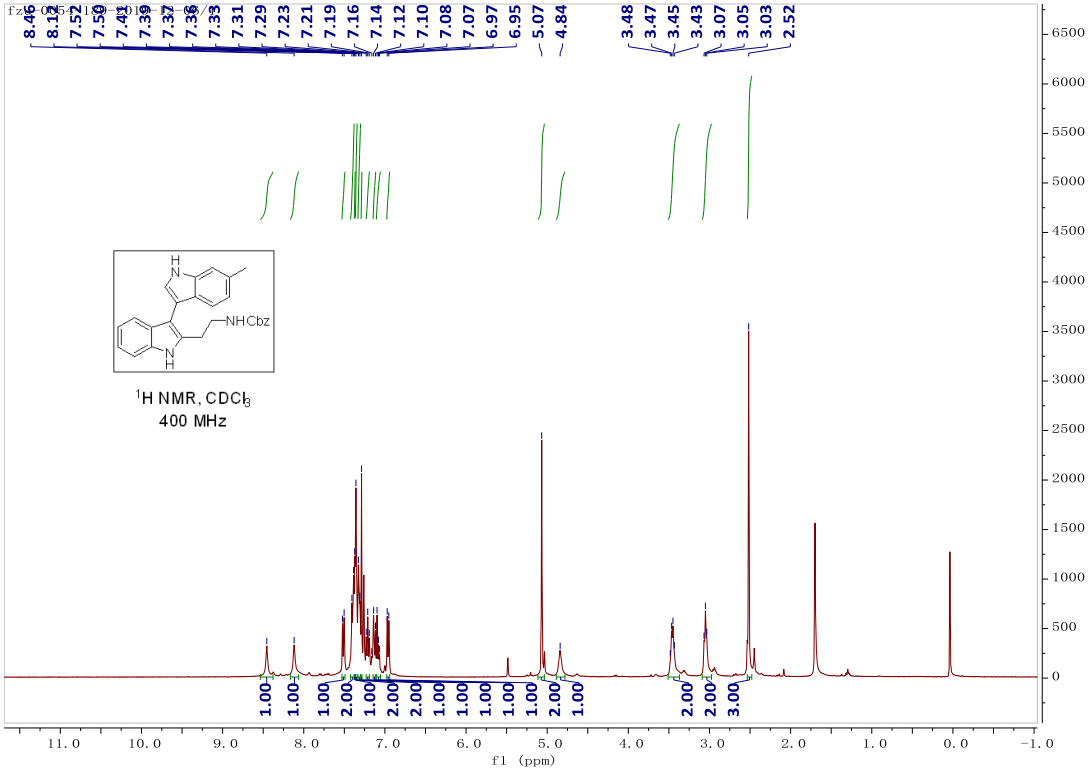
^{1}H NMR Spectrum of 15



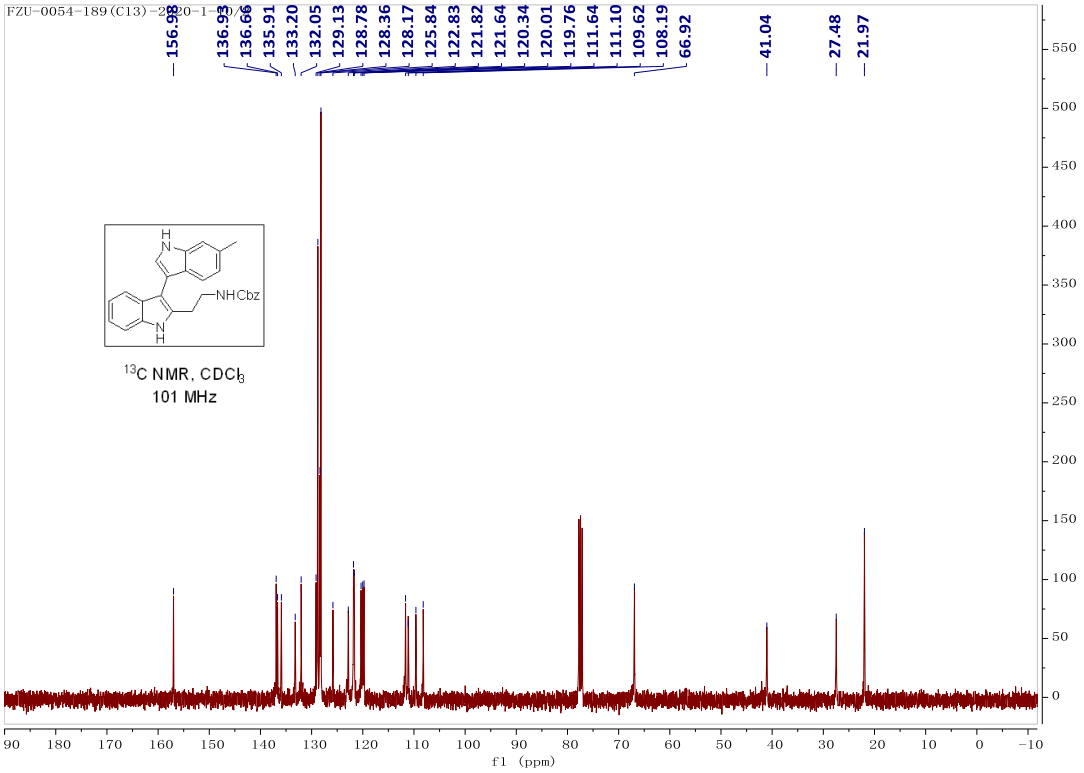
^{13}C NMR Spectrum of 15



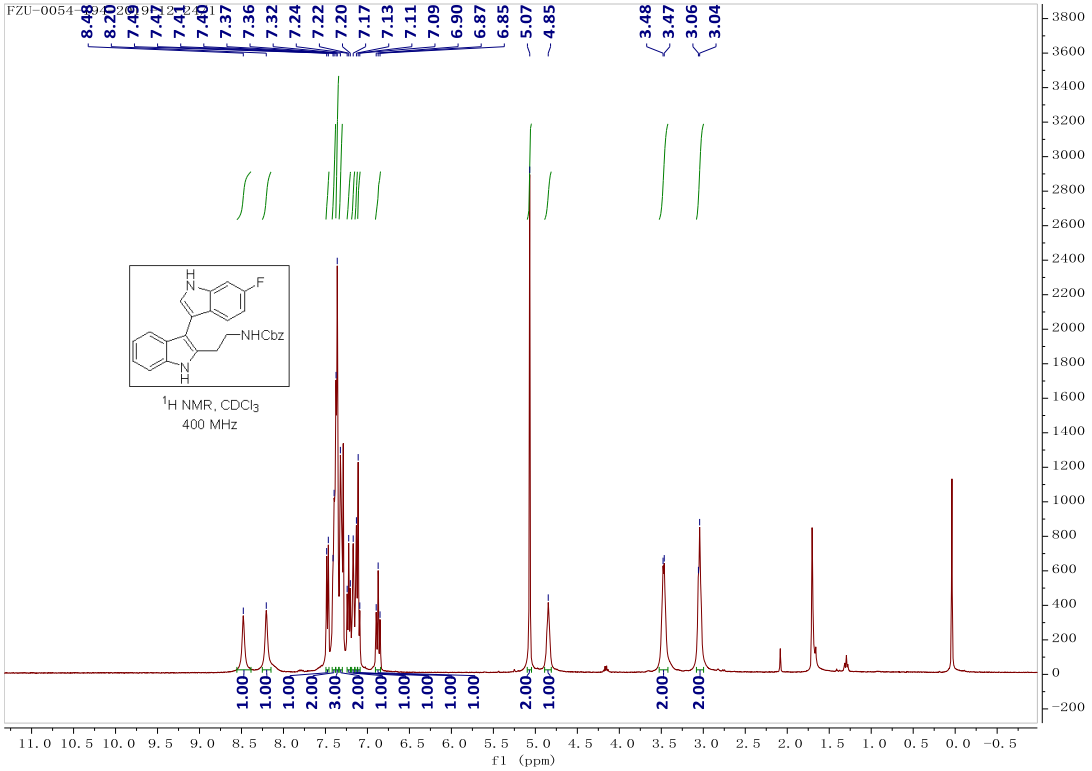
^{1}H NMR Spectrum of 16



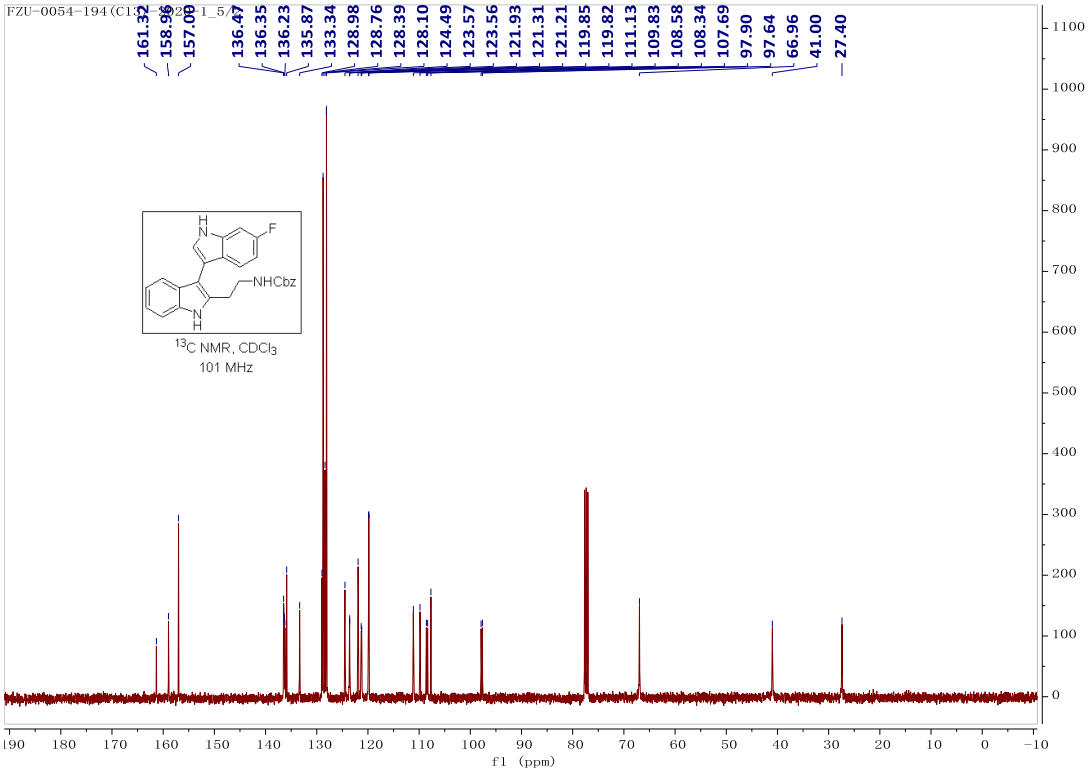
^{13}C NMR Spectrum of 16



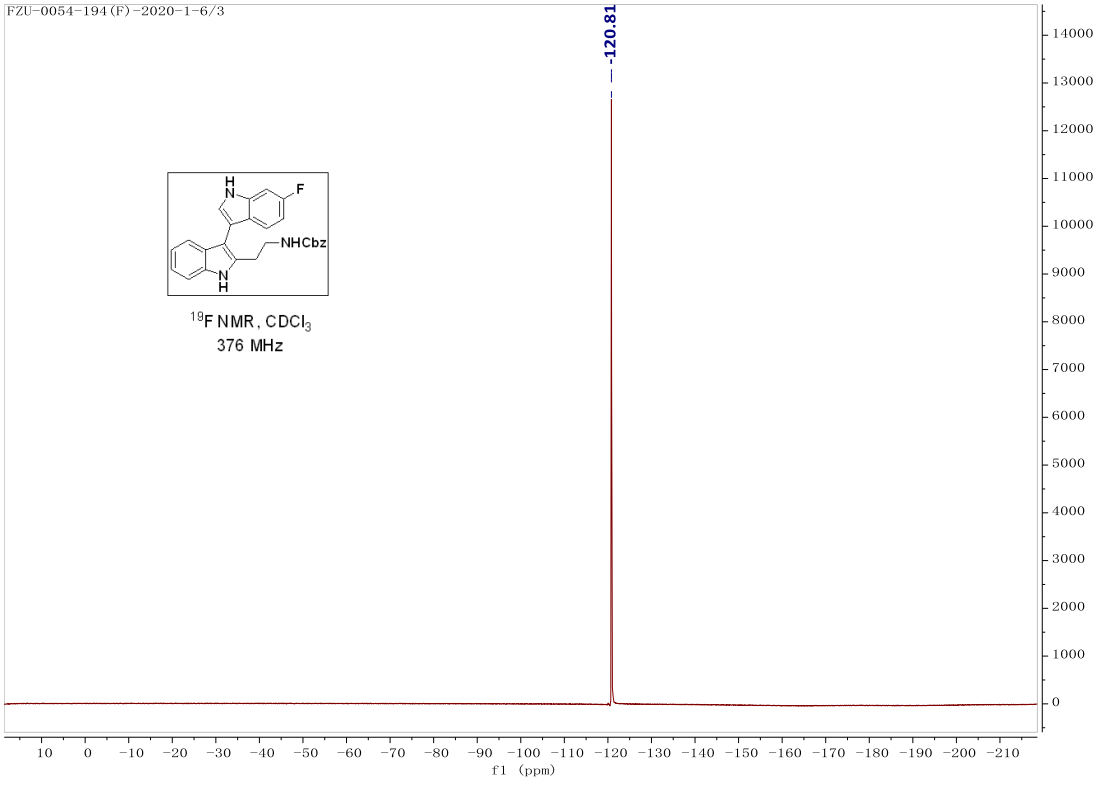
^{1}H NMR Spectrum of 17



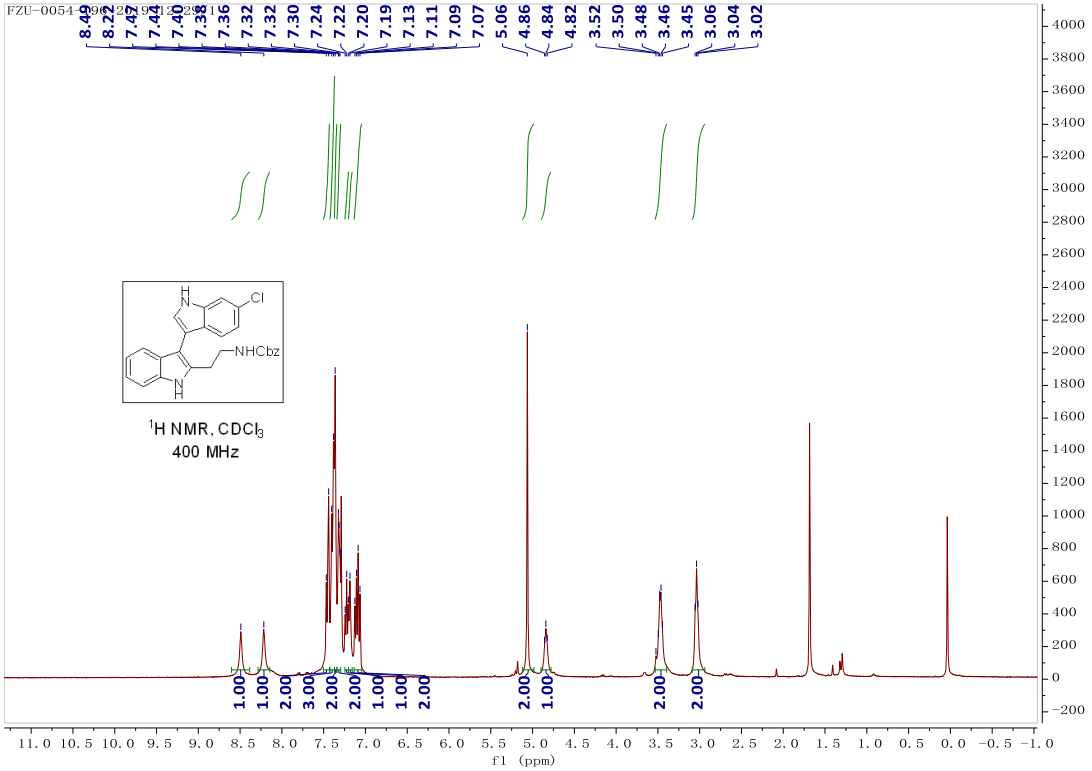
^{13}C NMR Spectrum of 17



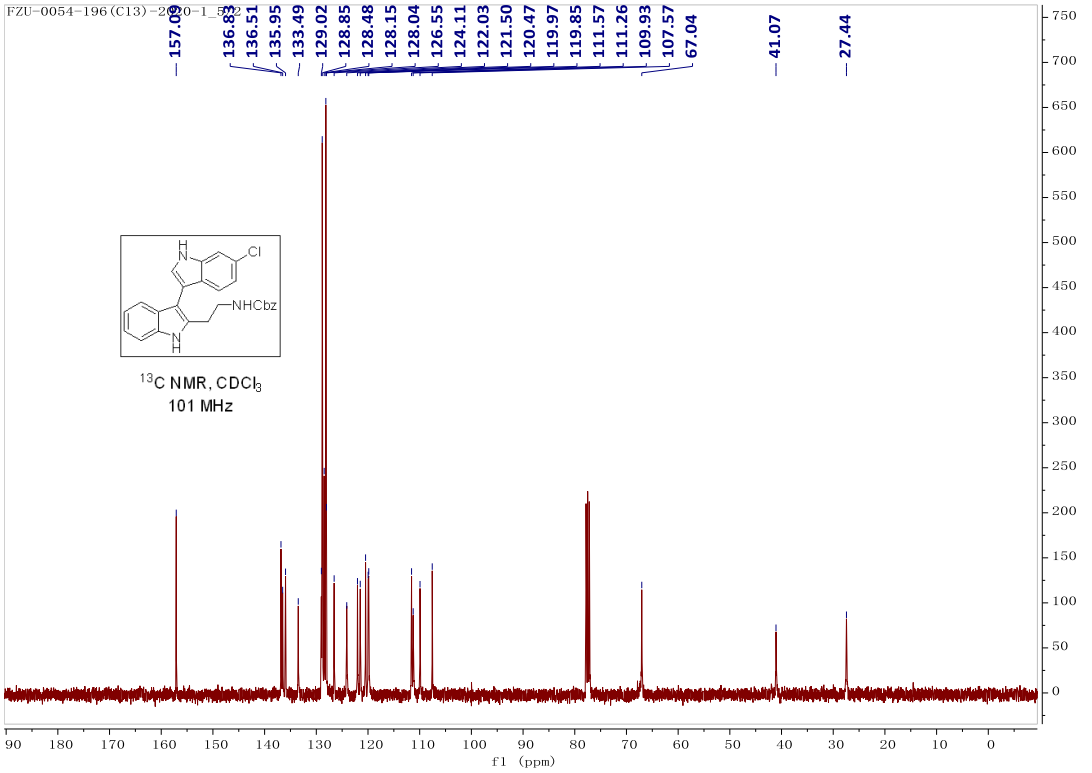
^{19}F NMR Spectrum of 17



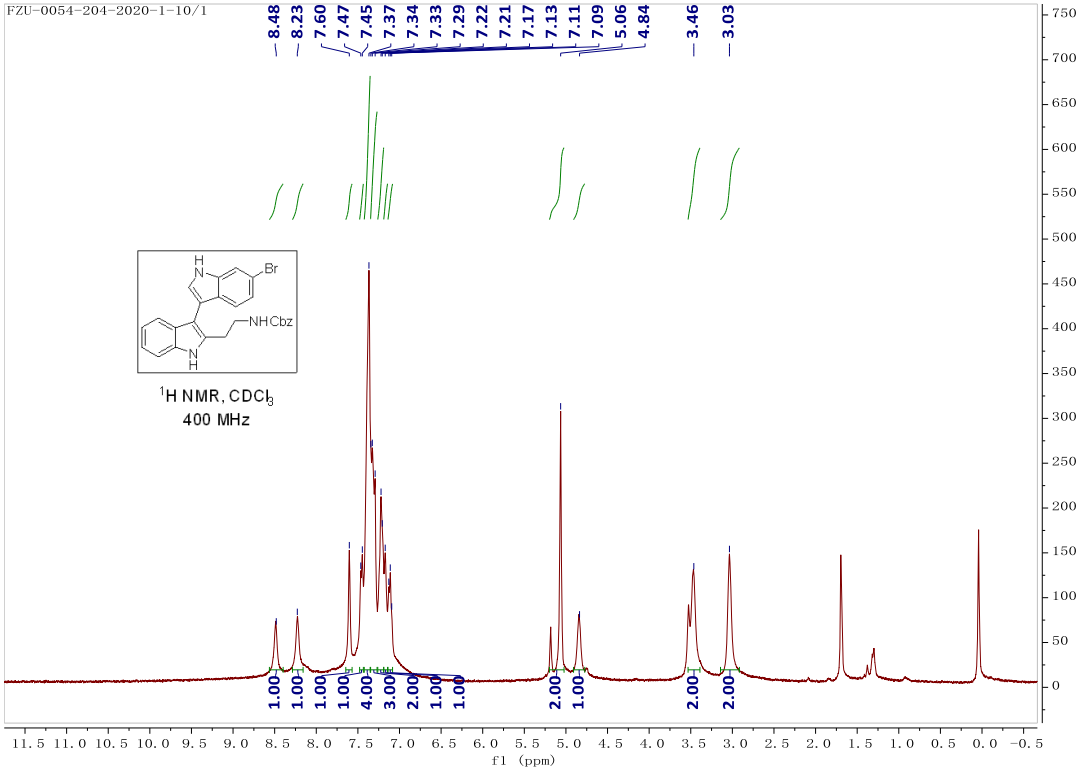
^{1}H NMR Spectrum of 18



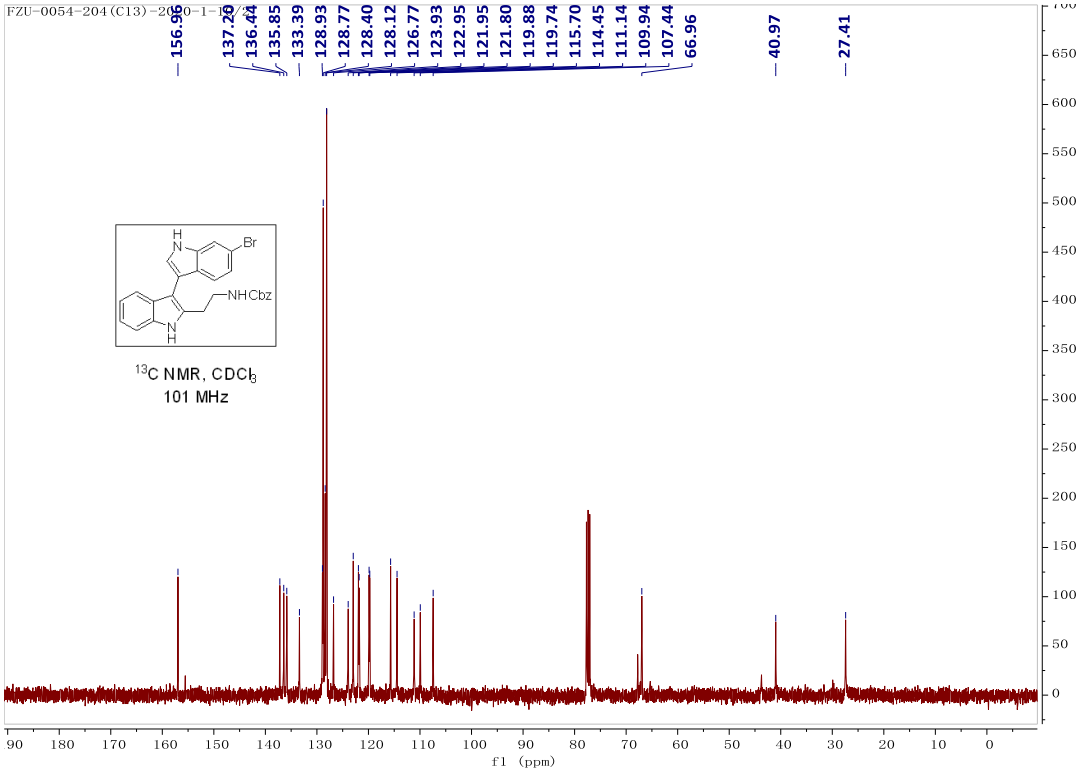
^{13}C NMR Spectrum of 18



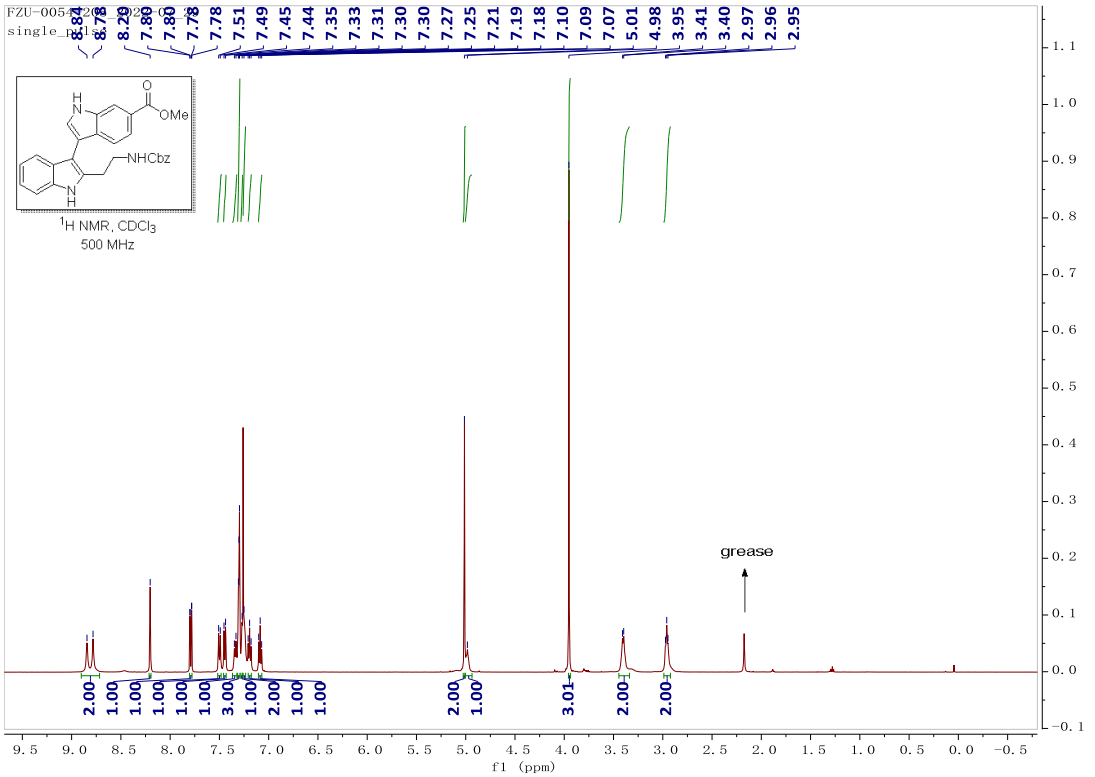
^{1}H NMR Spectrum 19



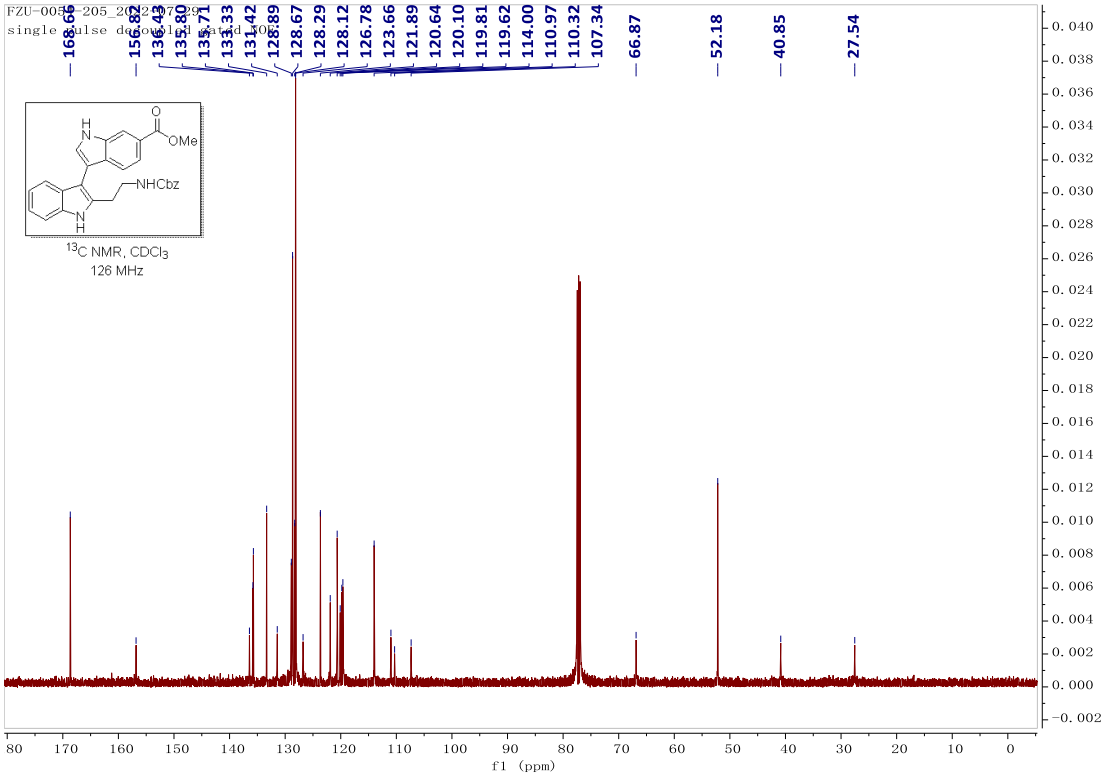
^{13}C NMR Spectrum of 19



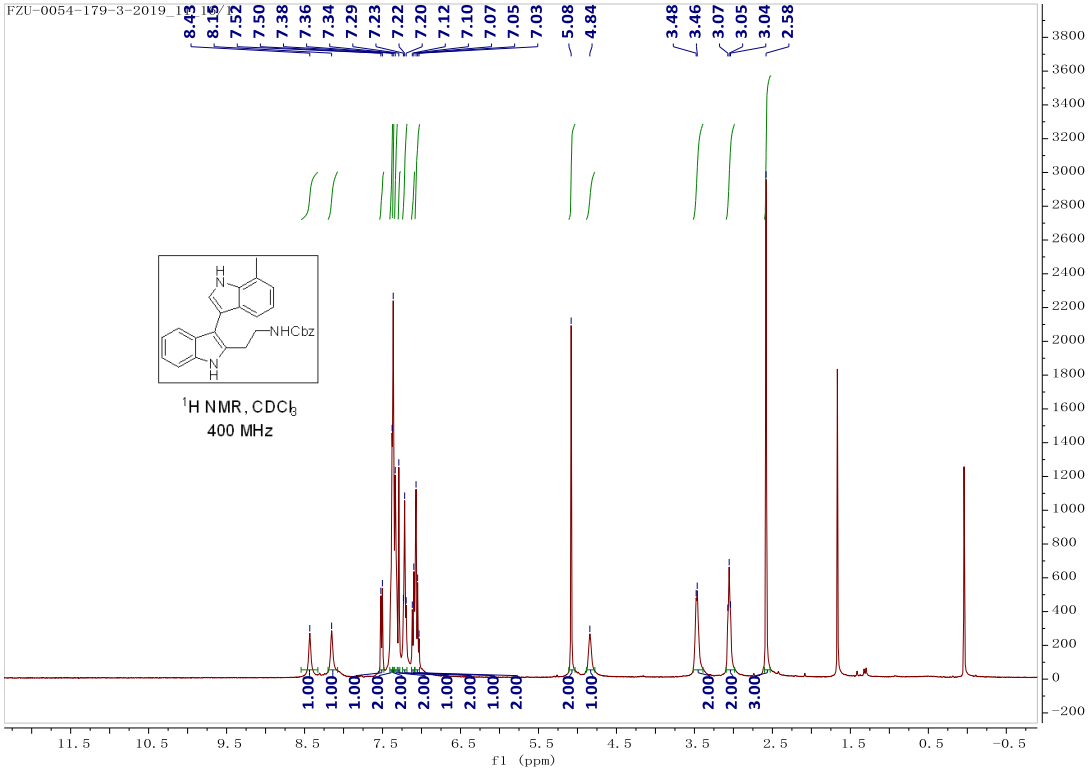
^{1}H NMR Spectrum of 20



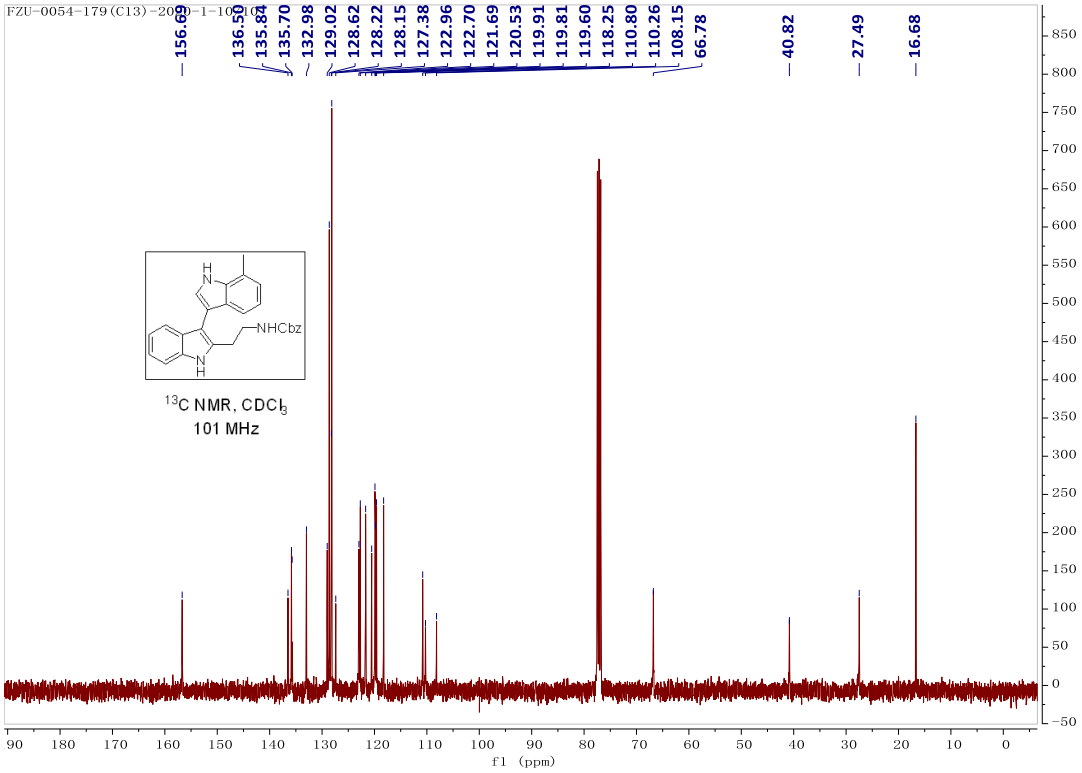
^{13}C NMR Spectrum of 20



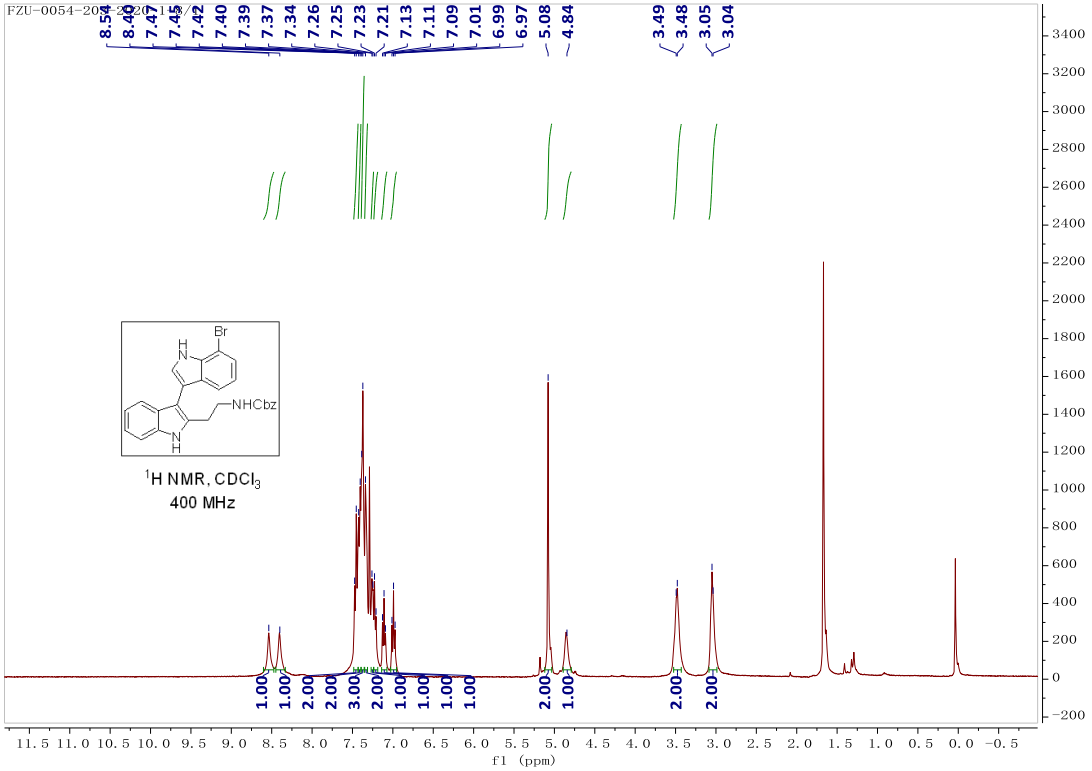
^{1}H NMR Spectrum of 21



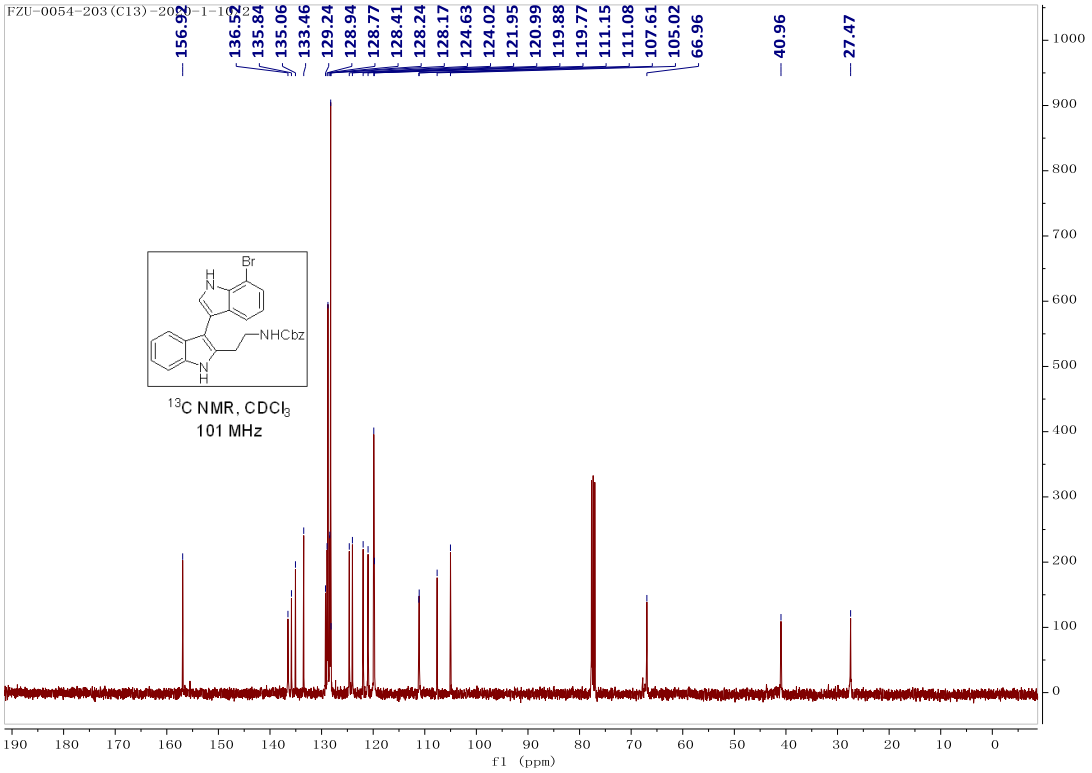
^{13}C NMR Spectrum of 21



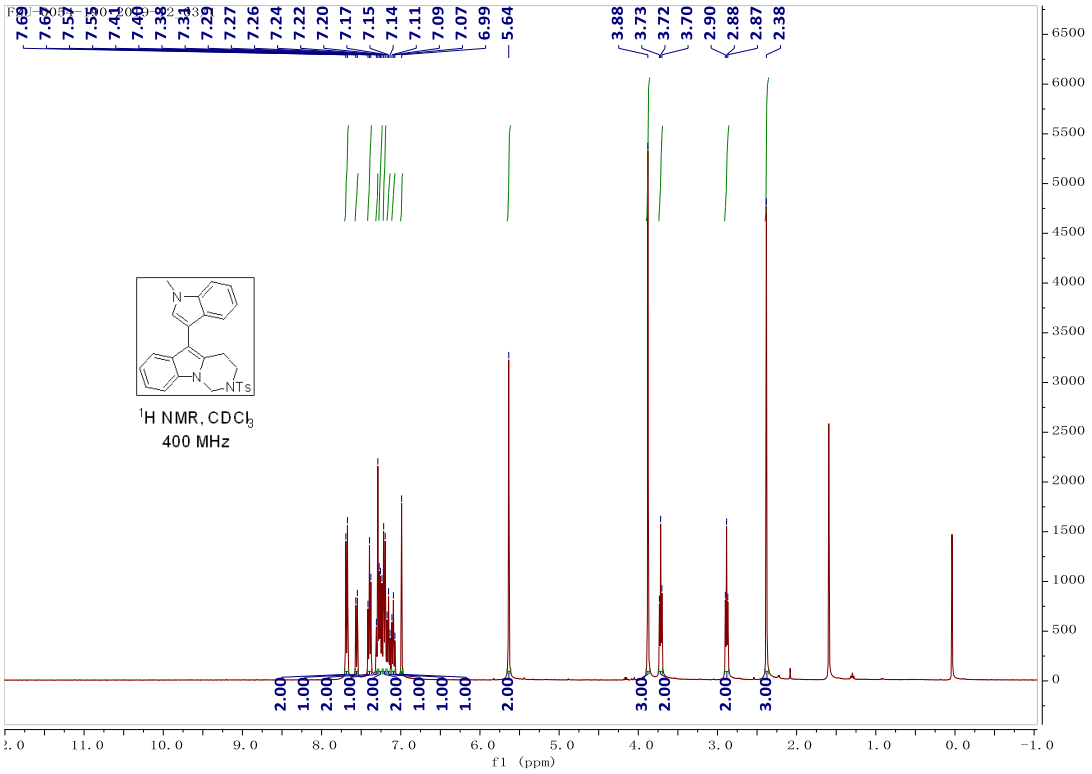
^{1}H NMR Spectrum of 22



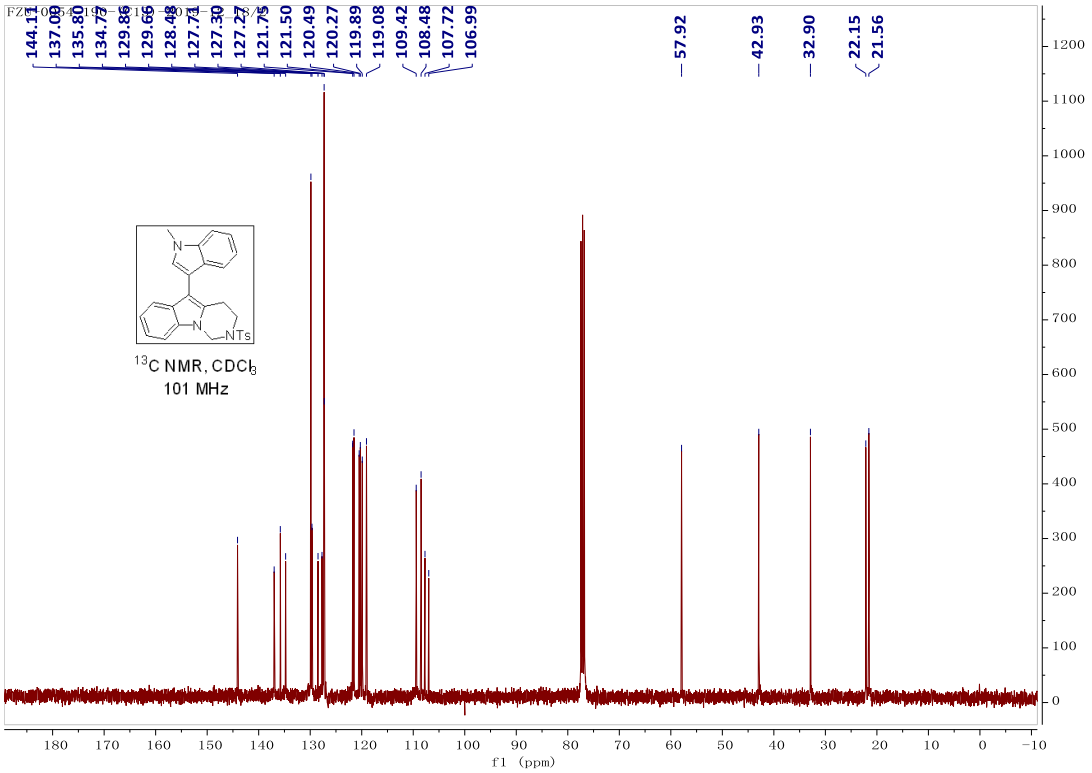
^{13}C NMR Spectrum of 22



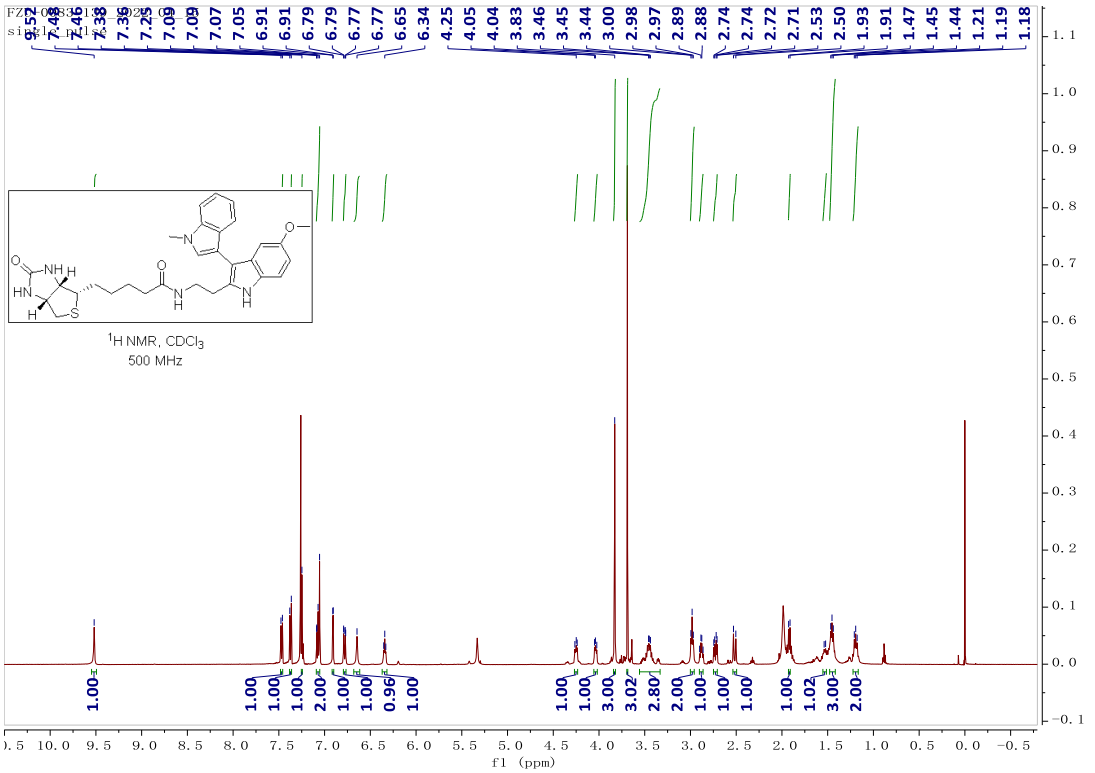
^{1}H NMR Spectrum of 23



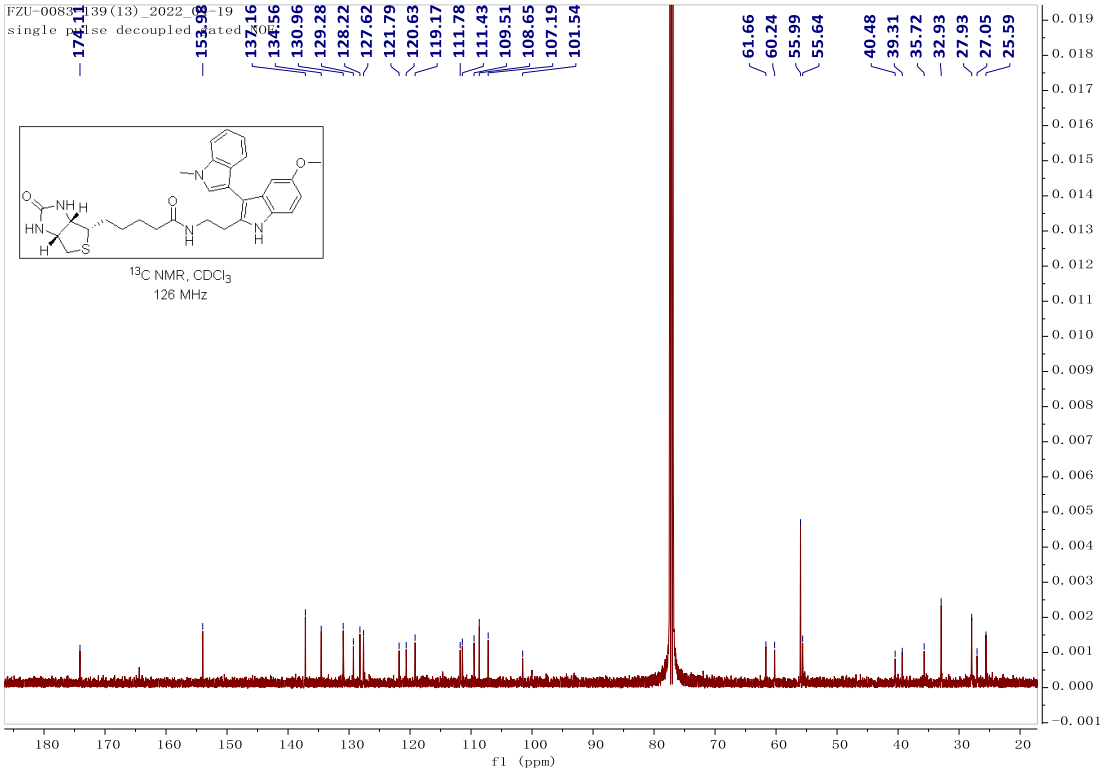
^{13}C NMR Spectrum of 23



^{1}H NMR Spectrum of 24

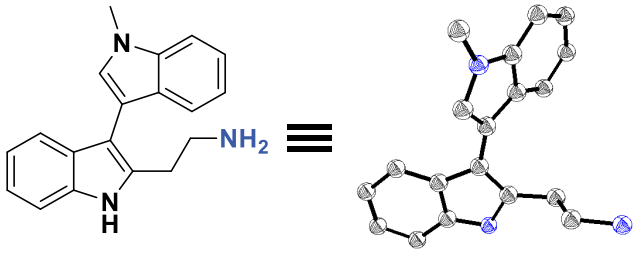


^{13}C NMR Spectrum of 24



7. X-ray Crystal Structure Data

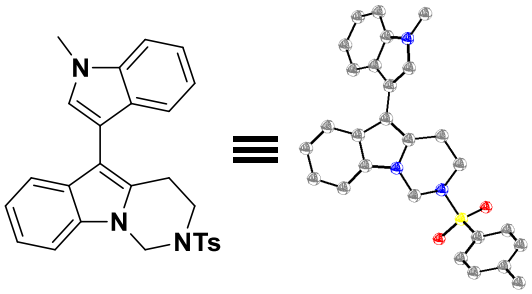
X-ray Crystal Structure Data for compound 2



CCDC 1906299

Identification code	2	
Bond precision	C-C = 0.0031 Å Wavelength=1.34139	
Cell	a=7.1136(3) b=8.1451(3) c=13.7212(5) alpha=80.702(3) beta=83.059(3) gamma=78.561(3)	
Temperature	170 K	
	Calculated	Reported
Volume	765.74(5)	765.74(5)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C19 H19 N3	C19 H19 N3
Sum formula	C19 H19 N3	C19 H19 N3
Mr	289.37	289.37
Dx,g cm-3	1.255	1.255
Z	2	2
Mu (mm-1)	0.372	0.376
F000	308.0	308.0
F000’	308.60	/
h,k,lmax	8,9,16	8,9,16
Nref	2910	2900
Tmin,Tmax	0.987,0.993	0.578,0.751
Tmin’	0.963	/
Data completeness	0.997	
Theta(max)	55.001	
R(reflections)	0.0605(2010)	
wR2(reflections)	0.1793(2900)	
S	1.044	
Npar	208	

X-ray Crystal Structure Data for compound 23



CCDC 1976118

Identification code	23	
Bond precision	C-C = 0.0032 Å Wavelength=0.71073	
Cell	a=9.3339(6) b=10.3228(7) c=12.9971(9) alpha=88.652(2) beta=69.740(2) gamma=77.801(2)	
Temperature	293 K	
	Calculated	Reported
Volume	1146.61(13)	1146.61(13)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C27 H25 N3 O2 S	?
Sum formula	C27 H25 N3 O2 S	C27 H25 N3 O2 S
Mr	455.56	455.56
Dx,g cm-3	1.319	1.319
Z	2	2
Mu (mm-1)	0.171	0.171
F000	480.0	480.0
F000’	480.43	/
h,k,lmax	11,12,16	11,12,16
Nref	4514	4501
Tmin,Tmax	0.966,0.986	0.644,0.746
Tmin’	0.966	/
Data completeness	0.997	
Theta(max)	25.996	
R(reflections)	0.0457(3420)	
wR2(reflections)	0.1203(4501)	
S	1.042	
Npar	301	