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Zirconium-Hydride-Catalyzed Transfer Hydrogenation of Quinoline and Indole with Ammonia Borane

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General Information

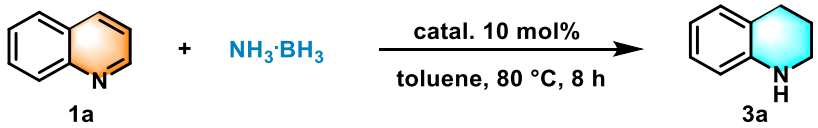
Manipulations were carried out under an atmosphere of dry and deoxygenated N_2 using Schlenk line or in a glovebox (H_2O and O_2 < 0.01 ppm). Glassware was pre-dried in an oven at 150 °C for several hours and cooled prior to use. Solvents were purchased as super dry solvent or purified via standard purification operations. All reagents were purchased from Sigma-Aldrich, TCI, Acros, Energy, Adamas, Bidepharm, Macklin company and used without further purification. $D_3N{\cdot}BH_3$, $H_3N{\cdot}BD_3$, were synthesized according to literature procedures.[1] NMR spectra were recorded Bruker Advance Neo 400 MHz NMR at room temperature. Chemical shifts (δ) are given in parts per million (ppm). Coupling constants (*J*) are given in Hertz (Hz). Thin-layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in petroleum (bp. 60-90 °C).

General Procedure for the Transfer Hydrogenation of Quinolines

In a nitrogen-filled glovebox, to a 15 mL pressure tube equipped with a magnetic stirrer were added Cp_2ZrH_2 (4.5 mg, 0.02 mmol), $H_3N{\cdot}BH_3$ (12.3 mg, 0.4 mmol), toluene (1 mL), and quinolines or indoles (0.2 mmol) in a sequence manner. The pressure tube was taken out the glove box and was heated at 80 ºC for 8 h. Upon completion, all the solvent was evaporated, and the crude product was isolated on silica gel using flash chromatography with petroleum ether/ethyl acetate as the eluent to give the corresponding products.

Condition Optimization Tables

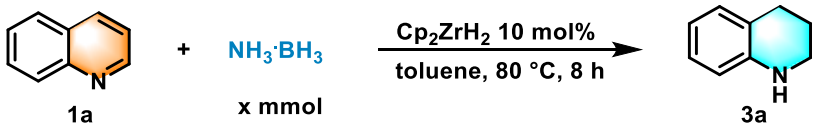
Table S1. Zirconium-catalyzed transfer hydrogenation of quinoline with **AB**: catalyst effect[a]



Entry	Catal.	yield **3a** [%][b]
1	**Cp_2ZrH_2**	**85**
2	Cp_2ZrCl_2	15
3	Cp_2ZrHCl	19
4[c]	Cp_2ZrCl_2	45
5[c]	Cp_2ZrHCl	36
6	-	10

[a]Reaction conditions: **1a** (0.2 mmol), $NH_3{\cdot}BH_3$ (0.6 mmol, 3.0 equiv.), Catal (10 mol%), 1 mL of toluene in 15 mL pressure tube at 80 °C for 8 h; [b]yields of **3a** was determined by GC with dodecane as internal standard; [c]reaction was performed with 1 equiv. MeOLi.

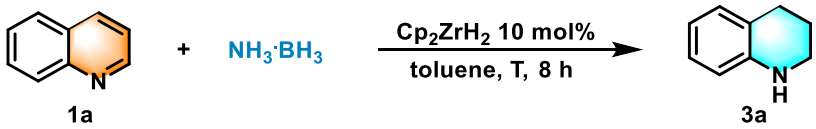
Table S2. Zirconium-catalyzed transfer hydrogenation of quinoline with **AB**: **AB** amount effect[a]



Entry	x [mmol]	yield **3a** [%][b]
1	0.6	85
2	**0.4**	**90**
3	0.2	61
4	0.1	15

[a]Reaction conditions: **1a** (0.2 mmol), $NH_3{\cdot}BH_3$ (x mmol.), Cp_2ZrH_2 (10 mol%), 1 mL of toluene in 15 mL pressure tube at 80 °C for 8 h; [b]yields of **3a** was determined by GC with dodecane as internal standard.

Table S3. Zirconium-catalyzed transfer hydrogenation of quinoline with **AB**: temperature effect[a]

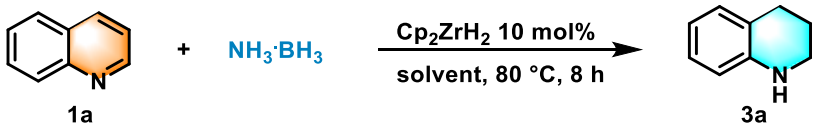


1a **3a**

Entry	T (°C)	yield **3a** [%][b]
1	**80**	**90**
2	60	47
3	40	31
4	25	18

[a]Reaction conditions: **1a** (0.2 mmol), $NH_3{\cdot}BH_3$ (0.4 mmol.), Cp_2ZrH_2 (10 mol%), 1 mL of toluene in 15 mL pressure tube at various temperatures for 8 h; [b]yields of **3a** was determined by GC with dodecane as internal standard.

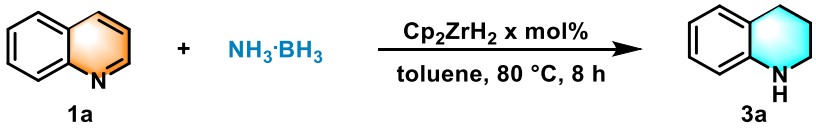
Table S4. Zirconium-catalyzed transfer hydrogenation of quinoline with **AB**: solvent effect[a]



Entry	Solvent	yield **3a** [%][b]
1	DCE	21
2	DME	7
3	Hexane	41
4	1,4-Dioxane	34
5	THF	84
6	MTBE	85
7	**Toluene**	**90**
8	MeOH	30

[a]Reaction conditions: **1a** (0.2 mmol), $NH_3{\cdot}BH_3$ (0.4 mmol.), Cp_2ZrH_2 (10 mol%), 1 mL of different solvent in 15 mL pressure tube at 80 °C for 8 h; [b]yields of **3a** was determined by GC with dodecane as internal standard.

Table S5. Zirconium-catalyzed transfer hydrogenation of quinoline with **AB**: catalyst loading effect[a]



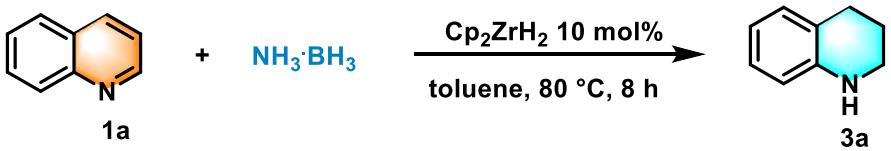
Entry	x [mol%]	yield **3a** [%][b]
1	2	32
2	5	46
3	**10**	**90**
4	15	88
5	20	87

[a]Reaction conditions: **1a** (0.2 mmol), $NH_3{\cdot}BH_3$ (0.4 mmol.), Cp_2ZrH_2 (x mol%), 1 mL of toluene in 15 mL pressure tube at 80 °C for 8 h; [b]yields of **3a** was determined by GC with dodecane as internal standard.

Mechanistic studies

Reaction with substituted ammonia boranes

Table S6. Transfer hydrogenation of quinoline using different substituted ammonia boranes.[a]



	$NH_3{\cdot}BH_3$	$MeNH_2{\cdot}BH_3$	$Me_2NH{\cdot}BH_3$	$Me_3N{\cdot}BH_3$	$BEt_3{\cdot}NH_3$
yield of 3a	**91%**	**88%**	**36%**	**27%**	**nr**

[a]yields were determined by GC with dodecane as internal standard.

In a nitrogen-filled glovebox, to a 15 mL pressure tube equipped with a magnetic stirrer were added Cp_2ZrH_2 (4.5 mg, 0.02 mmol), different substituted ammonia boranes (0.4 mmol), toluene (1 mL) and quinoline (25.8 mg, 23.6 uL, 0.2 mmol) in a sequence manner. The pressure tube was taken out the glove box and was heated at 80 ºC for 8 h and the yields of **3a** was analyzed by GC.

Deuterium Labelling Experiments

In a nitrogen-filled glovebox, to a 15 mL pressure tube equipped with a magnetic stirrer were added Cp_2ZrH_2 (4.5 mg, 0.02 mmol), $ND_3{\cdot}BH_3$ (12.3 mg, 0.4 mmol), toluene (1 mL) and indole (20.3 uL, 0.2 mmol) in a sequence manner. The pressure tube was taken out the glove box and was heated at 80 ºC for 8 h. Upon completion, all the solvent was evaporated, and the crude product was isolated on silica gel using flash chromatography with petroleum ether/ethyl acetate as the eluent to give the corresponding products, the ratio of H-atom incorporation was determined by ^{1}H NMR signal peaks around 2.98 ppm.

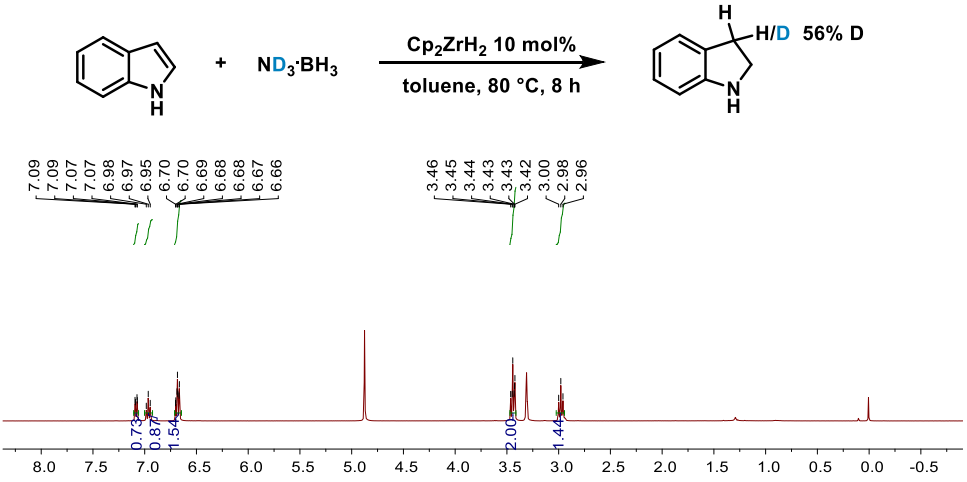


Figure S1. ^{1}H NMR spectrum of labelling product **4a** (400 MHz, CD_3OD).

In a nitrogen-filled glovebox, to a 15 mL pressure tube equipped with a magnetic stirrer were added Cp_2ZrH_2 (4.5 mg, 0.02 mmol), $NH_3{\cdot}BD_3$ (12.3 mg, 0.4 mmol), toluene (1 mL) and indole (20.3 uL, 0.2 mmol) in a sequence manner. The pressure tube was taken out the glove box and was heated at 80 ºC for 8 h. Upon completion, all the solvent was evaporated, and the crude product was isolated on silica gel using flash chromatography with petroleum ether/ethyl acetate as the eluent to give the corresponding products, the ratio of H-atom incorporation was determined by ^{1}H NMR signal peak around 3.42 ppm.

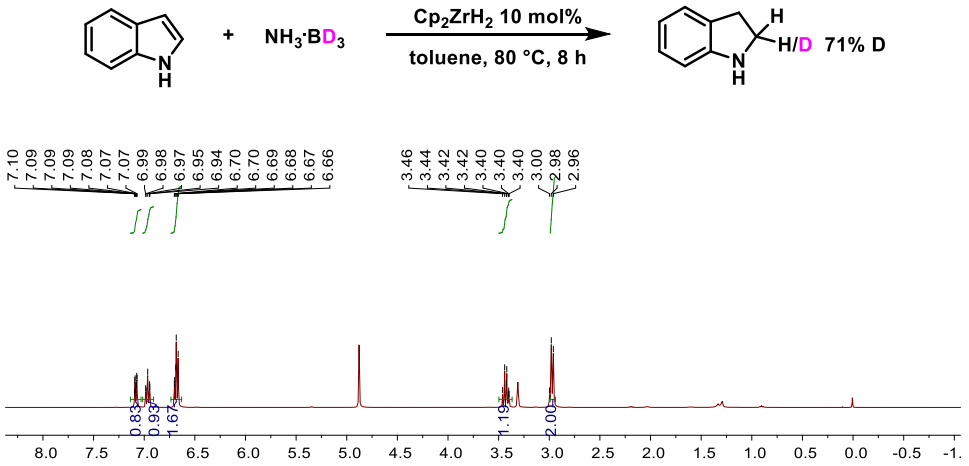
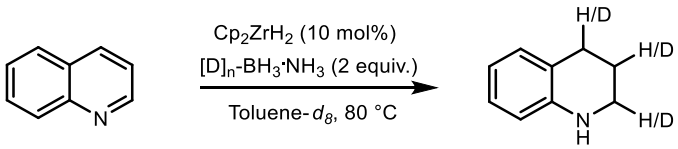


Figure S2. ^{1}H NMR spectrum of labelling product **4a** (400 MHz, CD_3OD)

Scheme S1. Reaction of quinoline with stoichiometric amount of Cp_2ZrH_2, GC yield is given.

In a nitrogen-filled glovebox, to a 15 mL pressure tube equipped with a magnetic stirrer were added Cp_2ZrH_2 (45 mg, 0.2 mmol), toluene (1 mL) and quinoline (25.8 mg, 23.6 uL, 0.2 mmol) in a sequence manner. The pressure tube was taken out the glove box and was heated at 80 ºC for 8 h and the yield of **3a** was determined by GC with dodecane as internal standard.

Kinetic Isotope Effects



0.2 mmol **3a/3a-D**

A J-Young NMR tube was charged with Cp_2ZrH_2 (4.5 mg, 0.02 mmol), $[D]_n$-ammonia-borane (0.4 mmol), toluene-d_8 (1 mL) and quinoline (25.8 mg, 23.6 uL, 0.2 mmol). The NMR tube was heated at 80 °C for 1 h. KIE were calculated by comparing the yield of independent reactions [KIE = Yield($NH_3{\cdot}BH_3$)/Yield($[D]_n$-$NH_3{\cdot}BH_3$)].

Table S7. Yields of **3a** with different labeled ammonia-boranes after 1 h.

Entry	$[D]_n$-$NH_3{\cdot}BH_3$	**3a yield (%)**[a]	**KIE**
1	$NH_3{\cdot}BH_3$	21.5	-
2	$ND_3{\cdot}BH_3$	10.9	1.97
3	$NH_3{\cdot}BD_3$	6.3	3.41

[a]NMR yield using 1,3,5-trimethoxybenzene as internal standard.

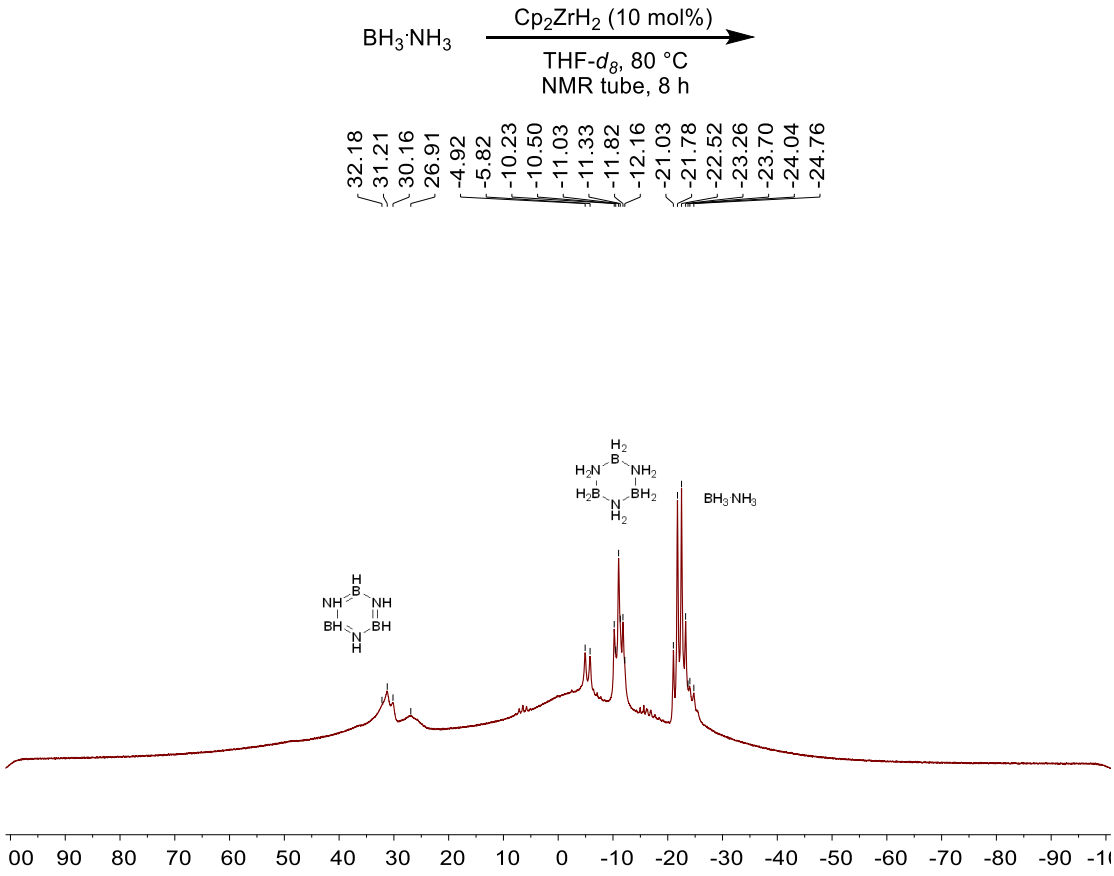


Figure S3. ^{11}B NMR spectrum of Cp_2ZrH_2 catalyzed dehydrogenation of ammonia borane.

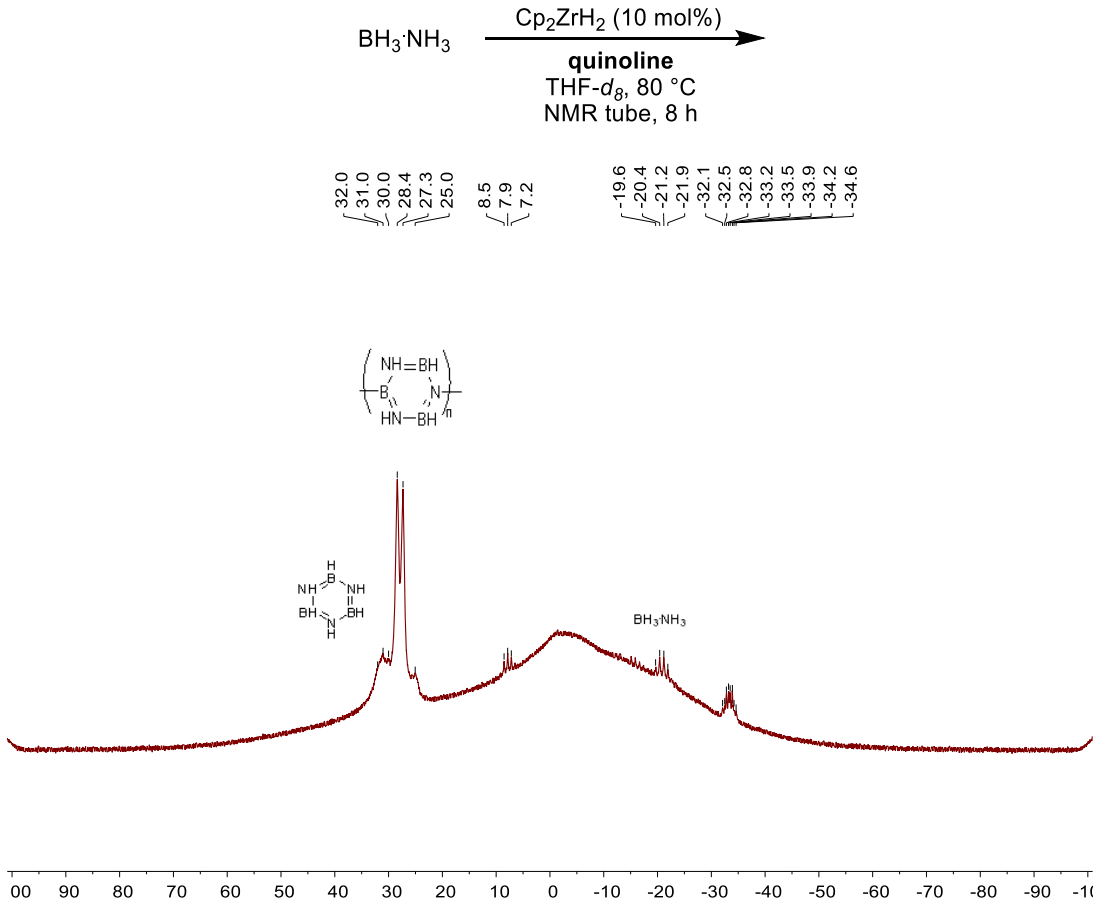
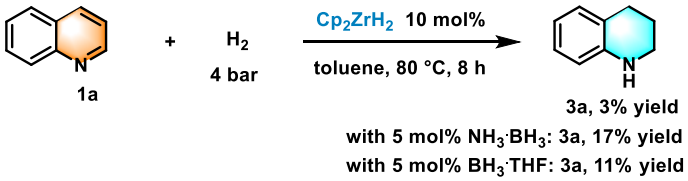


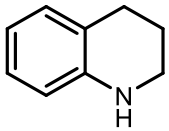
Figure S4. ^{11}B NMR spectrum of Cp_2ZrH_2 catalyzed dehydrogenation of ammonia borane in the presence of quinoline.

Catalytic Hydrogenation with H_2 Gas



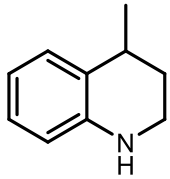
In a nitrogen-filled glovebox, to a 5 mL reaction vials equipped with a magnetic stirrer were added Cp_2ZrH_2 (4.5 mg, 0.02 mmol), toluene (1 mL) and indole (20.3 uL, 0.2 mmol) and *B*-additives if necessary in a sequence manner. The vials was placed in an autoclave and filled with 4 bar H_2 gas, after which the autoclave was heated at 80 ºC for 8 h. Upon completion, the yields of **3a** were determined by GC with dodecane as internal standard.

Products Characterization



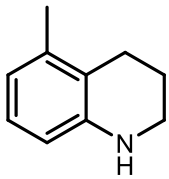
1,2,3,4-tetrahydroquinoline 3a

Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.10 – 7.04 (m, 1H), 7.00 – 6.94 (m, 1H), 6.78 – 6.61 (m, 1H), 6.52 (dd, *J* = 8.0, 2.9 Hz, 1H), 3.85 (br, 1H), 3.42 – 3.22 (m, 2H), 2.83 (t, *J* = 6.3 Hz, 2H), 2.11 – 1.90 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 144.7, 129.5, 126.7, 121.4, 116.9, 114.1, 41.9, 26.9, 22.1. Spectroscopic data are in agreement with those previously reported.[2]



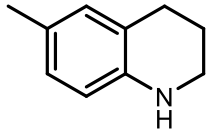
4-methyl-1,2,3,4-tetrahydroquinoline 3b

Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.07 (dt, *J* = 7.6, 1.4 Hz, 1H), 6.98 (td, *J* = 7.6, 1.6 Hz, 1H), 6.65 (tt, *J* = 7.3, 1.4 Hz, 1H), 6.49 (dd, *J* = 8.0, 1.4 Hz, 1H), 3.79 (s, 1H), 3.31 (dtd, *J* = 15.4, 11.1, 6.0 Hz, 2H), 2.92 (p, *J* = 6.6 Hz, 1H), 2.07 – 1.93 (m, 1H), 1.70 (dtd, *J* = 12.8, 6.3, 3.5 Hz, 1H), 1.31 (dd, *J* = 7.0, 1.8 Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 144.2, 128.4, 126.7, 126.6, 116.9, 114.1, 39.0, 30.2, 29.9, 22.6. Spectroscopic data are in agreement with those previously reported.[3]



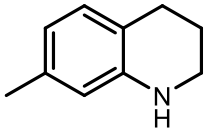
5-methyl-1,2,3,4-tetrahydroquinoline 3c

Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.90 (t, *J* = 7.7 Hz, 1H), 6.53 (d, *J* = 7.4 Hz, 1H), 6.38 (d, *J* = 8.0 Hz, 1H), 3.75 – 3.41 (m, 1H), 3.32 – 3.19 (m, 2H), 2.65 (t, *J* = 6.6 Hz, 2H), 2.19 (s, 3H), 2.12 – 1.87 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ143.9, 136.2, 125.2, 119.2, 117.9, 111.4, 40.6, 23.0, 21.5, 18.3. Spectroscopic data are in agreement with those previously reported.[3]



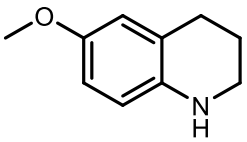
6-methyl-1,2,3,4-tetrahydroquinoline 3d

Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.81 (d, *J* = 5.9 Hz, 2H), 6.43 (dd, *J* = 8.8, 2.2 Hz, 1H), 3.65 (br, 1H), 3.32 – 3.26 (m, 2H), 2.79 – 2.73 (m, 2H), 2.24 (s, 3H), 2.00 - 1.90 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 142.4, 130.0, 127.2, 126.2, 121.6, 114.4, 42.2, 26.9, 22.4, 20.4. Spectroscopic data are in agreement with those previously reported.[3]



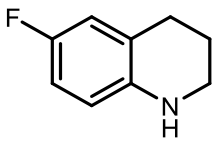
7-methyl-1,2,3,4-tetrahydroquinoline 3e

Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.84 (d, *J* = 7.5 Hz, 1H), 6.44 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.31 (d, *J* = 1.7 Hz, 1H), 3.72 (br, 1H), 3.35 – 3.20 (m, 2H), 2.73 (t, *J* = 6.4 Hz, 2H), 2.22 (s, 3H), 2.04 – 1.87 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 144.6, 136.3, 129.4, 118.5, 117.9, 114.8, 42.0, 26.6, 22.4, 21.1. Spectroscopic data are in agreement with those previously reported.[3]



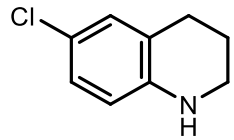
6-methoxy-1,2,3,4-tetrahydroquinoline 3f

Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.68 – 6.53 (m, 2H), 6.45 (d, *J* = 8.5 Hz, 1H), 3.73 (s, 3H), 3.31 – 3.14 (m, 2H), 2.76 (t, *J* = 6.5 Hz, 2H), 1.97 – 1.97 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 151.9, 138.9, 122.9, 115.6, 114.9, 112.9, 55.8, 42.3, 27.2, 22.5. Spectroscopic data are in agreement with those previously reported.[3]



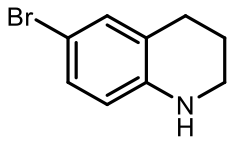
6-fluoro-1,2,3,4-tetrahydroquinoline 3g

Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.88 – 6.53 (m, 2H), 6.40 (dd, *J* = 9.5, 4.8 Hz, 1H), 3.69 (br, 1H), 3.41 – 3.14 (m, 2H), 2.74 (t, *J* = 6.5 Hz, 2H), 2.03 – 1.85 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 155.46 (d, *J* = 234.6 Hz), 140.92 (d, *J* = 1.6 Hz), 122.76 (d, *J* = 6.6 Hz), 115.58 (d, *J* = 21.6 Hz), 114.87 (d, *J* = 7.5 Hz), 113.17 (d, *J* = 22.3 Hz) 42.1, 27.0, 22.0. Spectroscopic data are in agreement with those previously reported.[4]



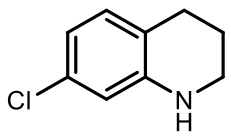
6-chloro-1,2,3,4-tetrahydroquinoline **3h**

Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.06 – 6.79 (m, 2H), 6.47 – 6.23 (m, 1H), 3.80 (br, 1H), 3.40 – 3.08 (m, 2H), 2.73 (t, *J* = 6.4 Hz, 2H), 2.06 – 1.79 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 143.3, 129.0, 126.5, 122.8, 121.2, 115.1, 41.8, 26.9, 21.7. Spectroscopic data are in agreement with those previously reported.[4]



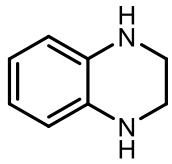
6-bromo-1,2,3,4-tetrahydroquinolineb 3i

Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.23 – 6.78 (m, 2H), 6.33 (d, *J* = 8.3 Hz, 1H), 3.83 (s, 1H), 3.33 – 3.24 (m, 2H), 2.73 (t, *J* = 6.4 Hz, 2H), 1.95 – 1.86 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 143.7, 131.9, 129.4, 123.4, 115.5, 108.2, 41.8, 26.8, 21.7. Spectroscopic data are in agreement with those previously reported.[5]



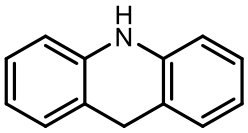
7-chloro-1,2,3,4-tetrahydroquinoline 3j

Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.83 (dd, *J* = 8.0, 1.1 Hz, 1H), 6.54 (dd, *J* = 8.0, 2.1 Hz, 1H), 6.43 (d, *J* = 2.1 Hz, 1H), 3.90 (br, 1H), 3.41 – 3.24 (m, 2H), 2.70 (t, *J* = 6.4 Hz, 2H), 1.98 – 1.82 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 145.7, 131.9, 130.4, 119.6, 116.5, 113.4, 41.7, 26.5, 21.8. Spectroscopic data are in agreement with those previously reported.[6]



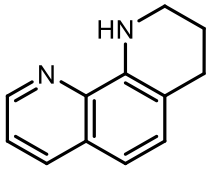
1,2,3,4-tetrahydroquinoxaline **3k**

Eluent: petroleum ether/ethyl acetate (10:1). White solid. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.67 – 6.35 (m, 4H), 3.60 (br, 2H), 3.42 (d, *J* = 1.9 Hz, 4H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 133.6, 118.7, 114.6, 41.3. Spectroscopic data are in agreement with those previously reported.[2]



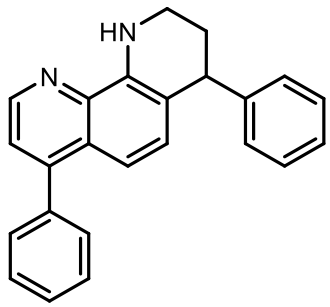
9,10-dihydroacridine **3l**

Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.19 – 7.00 (m, 4H), 6.92 – 6.82 (m, 2H), 6.67 (dd, *J* = 7.9, 1.2 Hz, 2H), 5.95 (s, 1H), 4.06 (s, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 140.1, 128.6, 127.0, 120.6, 120.0, 113.4, 31.4. Spectroscopic data are in agreement with those previously reported.[3]



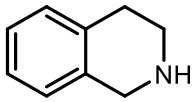
1,2,3,4,4a,10b-hexahydro-1,10-phenanthroline **3m**

Eluent: petroleum ether/ethyl acetate (10:1). Yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.67 (s, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.29 (dd, *J* = 8.6, 4.5 Hz, 1H), 7.15 (d, *J* = 8.2 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 5.92 (s, 1H), 3.53 (t, *J* = 5.5 Hz, 2H), 2.92 (t, *J* = 6.4 Hz, 2H), 2.22 – 1.98 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 146.9, 135.8, 129.1, 120.5, 113.1, 41.3, 27.0, 21.8. Spectroscopic data are in agreement with those previously reported.[3]



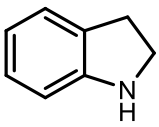
4,7-diphenyl-1,2,3,4-tetrahydro-1,10-phenanthroline **3n**

Eluent: petroleum ether/ethyl acetate (10:1). Yellow soild. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.67 (d, *J* = 4.3 Hz, 1H), 7.45 – 7.32 (m, 5H), 7.23 – 7.16 (m, 3H), 7.13 (d, *J* = 7.2 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 2H), 6.96 – 6.78 (m, 2H), 6.19 (br, 1H), 4.23 (t, *J* = 5.6 Hz, 1H), 3.54 – 3.25 (m, 2H), 2.29 – 1.93 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 148.3, 146.6, 146.5, 141.4, 138.7, 138.0, 129.5, 128.7, 128.3, 128.3, 128.1, 126.2, 126.0, 121.3, 117.8, 111.2, 42.7, 38.2, 30.7.



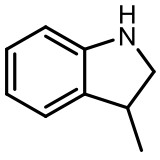
1,2,3,4-tetrahydroisoquinoline **3o**

Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.17 – 7.05 (m, 3H), 7.05 – 6.91 (m, 1H), 4.01 (s, 2H), 3.14 (t, *J* = 6.0 Hz, 2H), 2.80 (t, *J* = 6.0 Hz, 2H), 1.73 (s, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 136.0, 134.7, 129.2, 126.1, 125.9, 125.6, 48.3, 43.9, 29.1. Spectroscopic data are in agreement with those previously reported.[2]



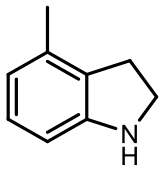
indoline **4a**

Eluent: petroleum ether/ethyl acetate (15:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.16 (d, *J* = 7.2 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.75 (dd, *J* = 8.6, 6.3 Hz, 1H), 6.68 (d, *J* = 7.7 Hz, 1H), 3.76 (br, 1H), 3.63 – 3.50 (m, 2H), 3.06 (t, *J* = 8.3 Hz, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 151.5, 129.3, 127.2, 124.6, 118.6, 109.4, 47.3, 29.8. Spectroscopic data are in agreement with those previously reported.[7]



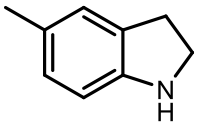
3-methylindoline **4b**

Eluent: petroleum ether/ethyl acetate (15:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.10 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.07 – 7.00 (m, 1H), 6.79 – 6.71 (m, 1H), 6.65 (d, *J* = 7.7 Hz, 1H), 3.71 (t, *J* = 8.6 Hz, 2H), 3.12 (t, *J* = 8.6 Hz, 1H), 1.34 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 151.2, 134.3, 127.3, 123.3, 118.7, 109.5, 55.4, 36.6, 18.6. Spectroscopic data are in agreement with those previously reported.[8]



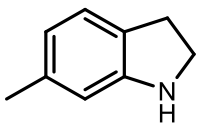
4-methylindoline **4c**

Eluent: petroleum ether/ethyl acetate (15:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.95 (t, *J* = 7.6 Hz, 1H), 6.53 (dd, *J* = 19.2, 7.6 Hz, 2H), 3.75 (br, 1H), 3.57 (t, *J* = 8.4 Hz, 2H), 2.98 (t, *J* = 8.4 Hz, 2H), 2.24 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 151.3, 134.2, 128.0, 127.2, 119.8, 106.9, 46.9, 28.6, 18.8. Spectroscopic data are in agreement with those previously reported.[9]



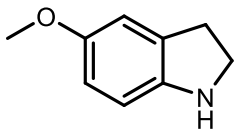
5-methylindoline **4d**

Eluent: petroleum ether/ethyl acetate (15:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.97 (s, 1H), 6.85 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.59 (d, *J* = 7.8 Hz, 1H), 3.54 (t, *J* = 8.3 Hz, 3H), 3.01 (t, *J* = 8.3 Hz, 2H), 2.28 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 148.2, 128.7, 127.0, 126.5, 124.4, 108.4, 46.5, 28.9, 19.7. Spectroscopic data are in agreement with those previously reported.[7]



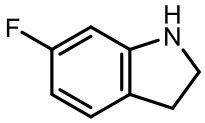
6-methylindoline **4e**

Eluent: petroleum ether/ethyl acetate (15:1). Colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.02 (d, *J* = 7.4 Hz, 1H), 6.67 – 6.43 (m, 2H), 3.55 (t, *J* = 8.3 Hz, 3H), 3.00 (t, *J* = 8.3 Hz, 2H), 2.28 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 151.8, 137.0, 126.3, 124.2, 119.3, 110.3, 47.5, 29.5, 21.4. Spectroscopic data are in agreement with those previously reported.[8]



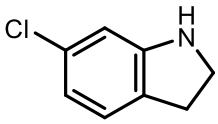
5-methoxyindoline **4f**

Eluent: petroleum ether/ethyl acetate (15:1). brown oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.77 (d, *J* = 1.0 Hz, 1H), 6.60 (d, *J* = 2.1 Hz, 2H), 3.75 (s, 3H), 3.53 (t, *J* = 8.3 Hz, 2H), 3.40 (s, 1H), 3.01 (t, *J* = 8.3 Hz, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.5, 145.4, 131.1, 112.2, 111.6, 110.0, 56.0, 47.7, 30.4. Spectroscopic data are in agreement with those previously reported.[7]



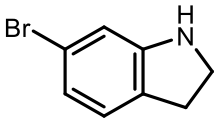
6-fluoroindoline **4g**

Eluent: petroleum ether/ethyl acetate (15:1). brown oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.98 (ddt, *J* = 8.0, 5.7, 1.3 Hz, 1H), 6.47 – 6.21 (m, 2H), 3.77 (br, 1H), 3.59 (t, *J* = 8.4 Hz, 2H), 2.97 (tt, *J* = 8.4, 1.5 Hz, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 163.1 (d, *J* = 240.6 Hz), 153.1 (d, *J* = 11.7 Hz), 124.8 (d, *J* = 10.4 Hz), 124.5 (d, *J* = 2.2 Hz), 104.4 (d, *J* = 22.6 Hz), 97.0 (d, *J* = 26.3 Hz), 48.0, 28.9. Spectroscopic data are in agreement with those previously reported.[8]



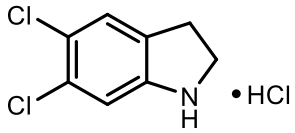
6-chloroindoline **4h**

Eluent: petroleum ether/ethyl acetate (15:1). brown oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.05 (s, 1H), 6.95 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.52 (d, *J* = 8.2 Hz, 1H), 3.72 (br, 1H), 3.55 (t, *J* = 8.4 Hz, 2H), 3.00 (t, *J* = 8.4 Hz, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 150.2, 131.2, 126.9, 124.8, 123.0, 109.9, 47.6, 29.8. Spectroscopic data are in agreement with those previously reported.[10]



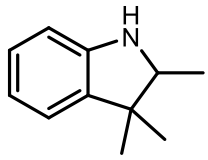
6-bromoindoline **4i**

Eluent: petroleum ether/ethyl acetate (15:1). brown liquid. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.94 (d, *J* = 7.7 Hz, 1H), 6.79 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.74 (d, *J* = 1.8 Hz, 1H), 3.80 (br, 1H), 3.57 (t, *J* = 8.4 Hz, 2H), 2.97 (t, *J* = 8.4 Hz, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.2, 128.3, 125.7, 121.1, 120.6, 112.1, 47.6, 29.2. Spectroscopic data are in agreement with those previously reported.[10]



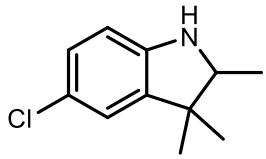
5,6-dichloroindoline hydrochloride **4j**·HCl

Precipitate after acidified with 2 mL 1N HCl in Et_2O. **^{1}H NMR** (400 MHz, D_2O) δ 7.69 (d, *J* = 7.8 Hz, 2H), 3.96 (t, *J* = 7.8 Hz, 2H), 3.34 (t, *J* = 7.8 Hz, 2H). **^{13}C NMR** (101 MHz, D_2O) δ 136.4, 135.0, 133.6, 131.4, 127.7,121.1, 46.9, 28.5. Spectroscopic data are in agreement with those previously reported.[11]



2,3,3-trimethylindoline **4k**

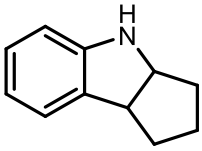
Eluent: petroleum ether/ethyl acetate (15:1). White solid. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.11 – 6.97 (m, 2H), 6.81 – 6.71 (m, *J* = 7.4, 0.9 Hz, 1H), 6.64 (d, *J* = 7.6 Hz, 1H), 3.77 (br, 1H), 3.53 (q, *J* = 6.5 Hz, 1H), 1.30 (s, 3H), 1.20 (d, *J* = 6.5 Hz, 3H), 1.06 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 149.3, 139.1, 127.1, 122.2, 118.8, 109.4, 65.1, 43.4, 26.2, 22.3, 15.1. Spectroscopic data are in agreement with those previously reported.[12]



5-chloro-2,3,3-trimethylindoline **4l**

Eluent: petroleum ether/ethyl acetate (15:1). yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.05 – 6.85 (m, 2H), 6.51 (d, *J* = 8.8 Hz, 1H), 3.75 (br, 1H), 3.53 (q, *J* = 6.5 Hz, 1H), 1.26 (s, 3H), 1.17 (d, *J* = 6.5 Hz, 3H), 1.04 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 147.8, 141.0,

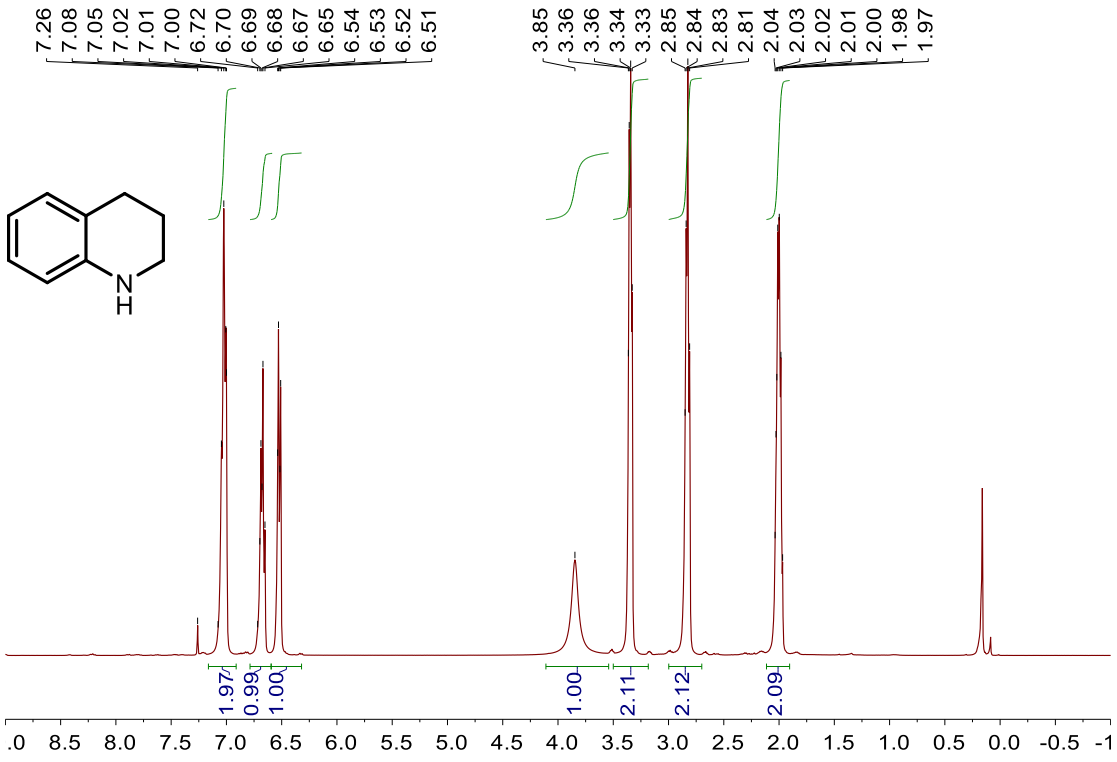
126.8, 123.3, 122.6, 110.1, 65.5, 43.7, 26.1, 22.2, 15.1. Spectroscopic data are in agreement with those previously reported.[13]



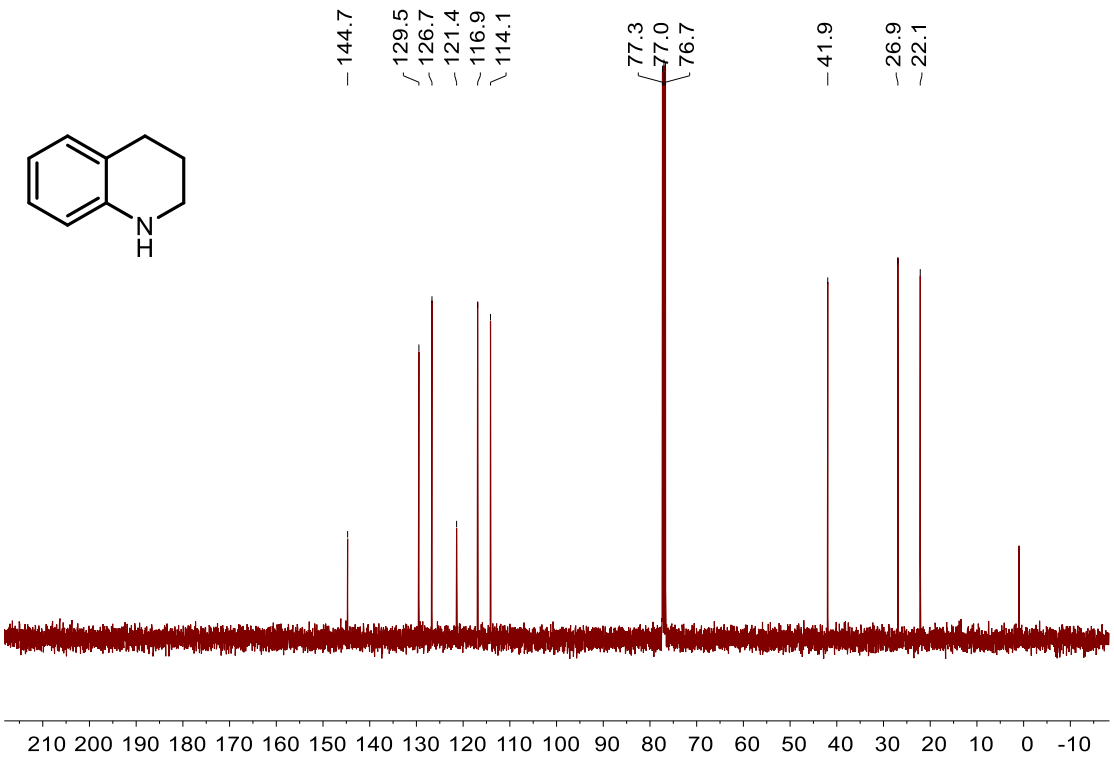
1,2,3,3a,4,8b-hexahydrocyclopenta[*b*]indole **4m**

Eluent: petroleum ether/ethyl acetate (15:1). White solid. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.05 (d, *J* = 7.3 Hz, 1H), 7.03 – 6.96 (m, 1H), 6.72 – 6.64 (m, 1H), 6.53 (d, *J* = 7.8 Hz, 1H), 4.45 – 4.30 (m, 1H), 3.84 – 3.75 (m, *J* = 8.8, 2.7 Hz, 1H), 3.65 (br, 1H), 2.03 – 1.89 (m, 1H), 1.87 – 1.50 (m, 5H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 151.4, 133.3, 127.3, 124.5, 118.2, 108.4, 63.3, 47.2, 36.9, 34.9, 24.4. Spectroscopic data are in agreement with those previously reported.[7]

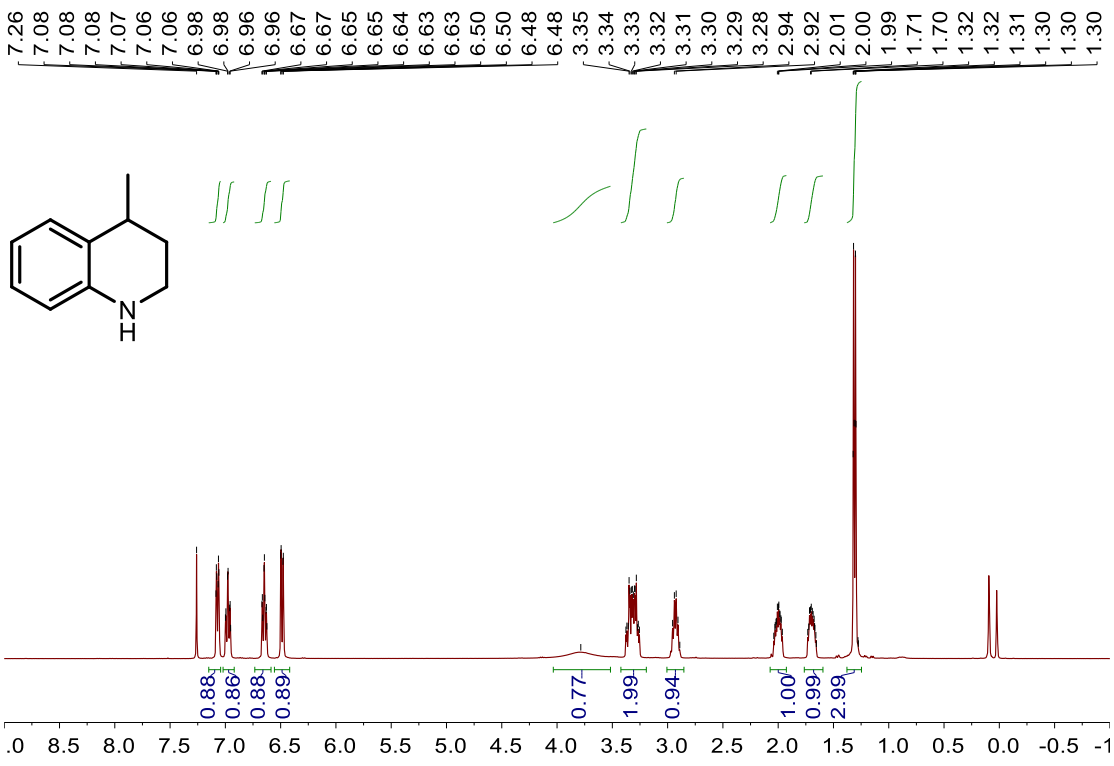
NMR Spectra



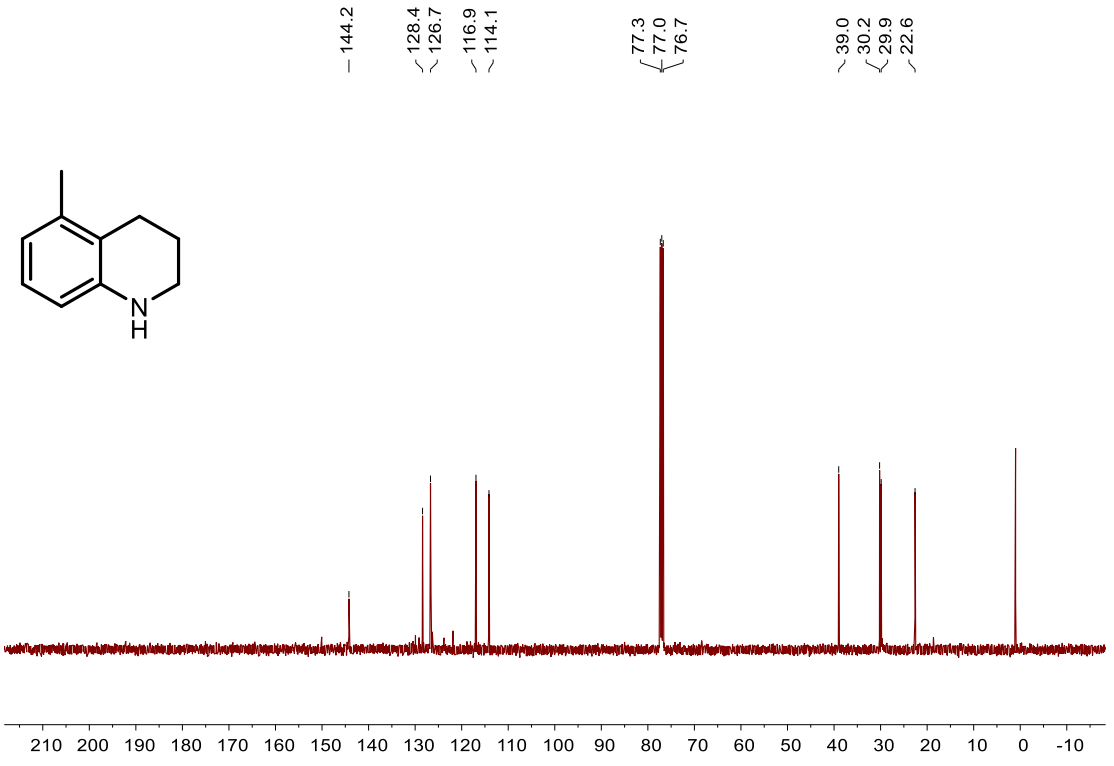
^{1}H NMR spectrum of **3a** (400 MHz, Chloroform-*d*)



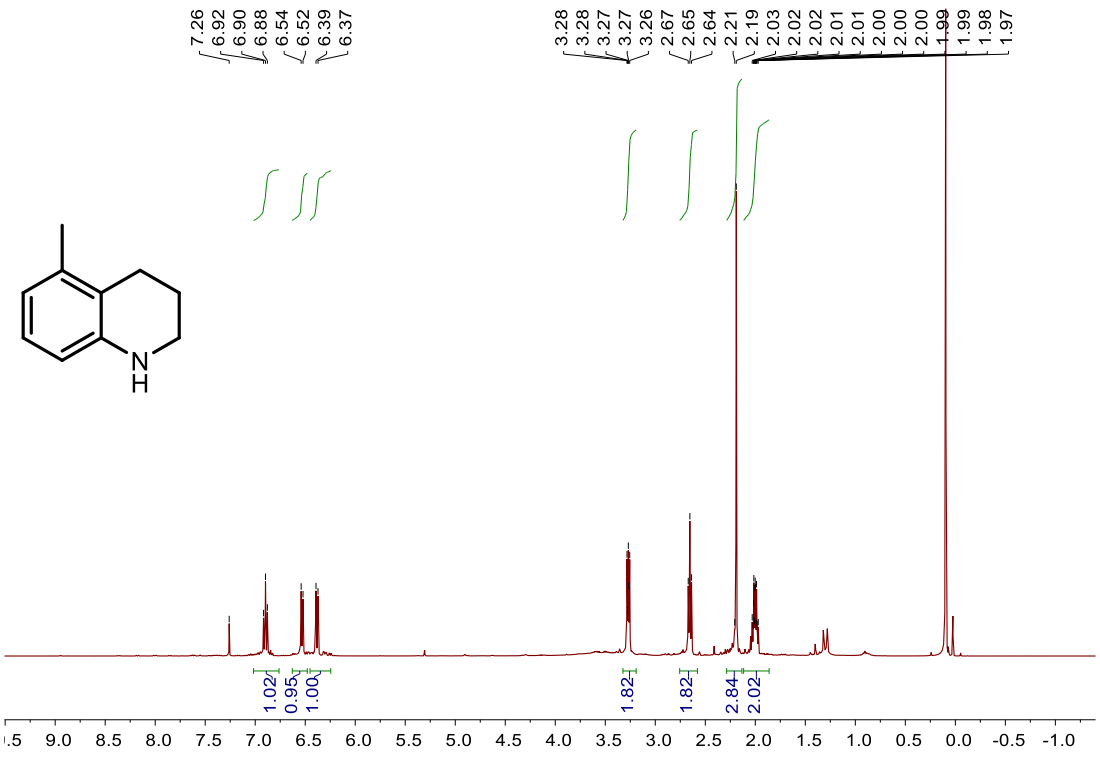
^{13}C NMR spectrum of **3a** (101 MHz, Chloroform-*d*)



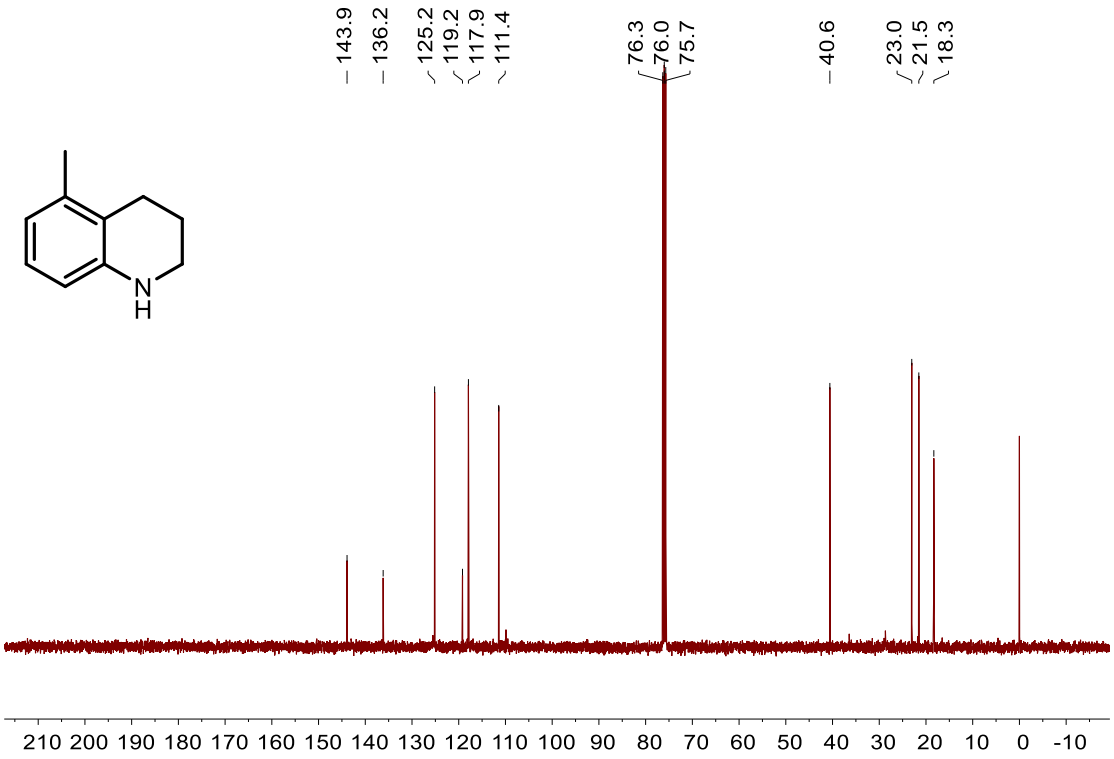
^{1}H NMR spectrum of **3b** (400 MHz, Chloroform-*d*)



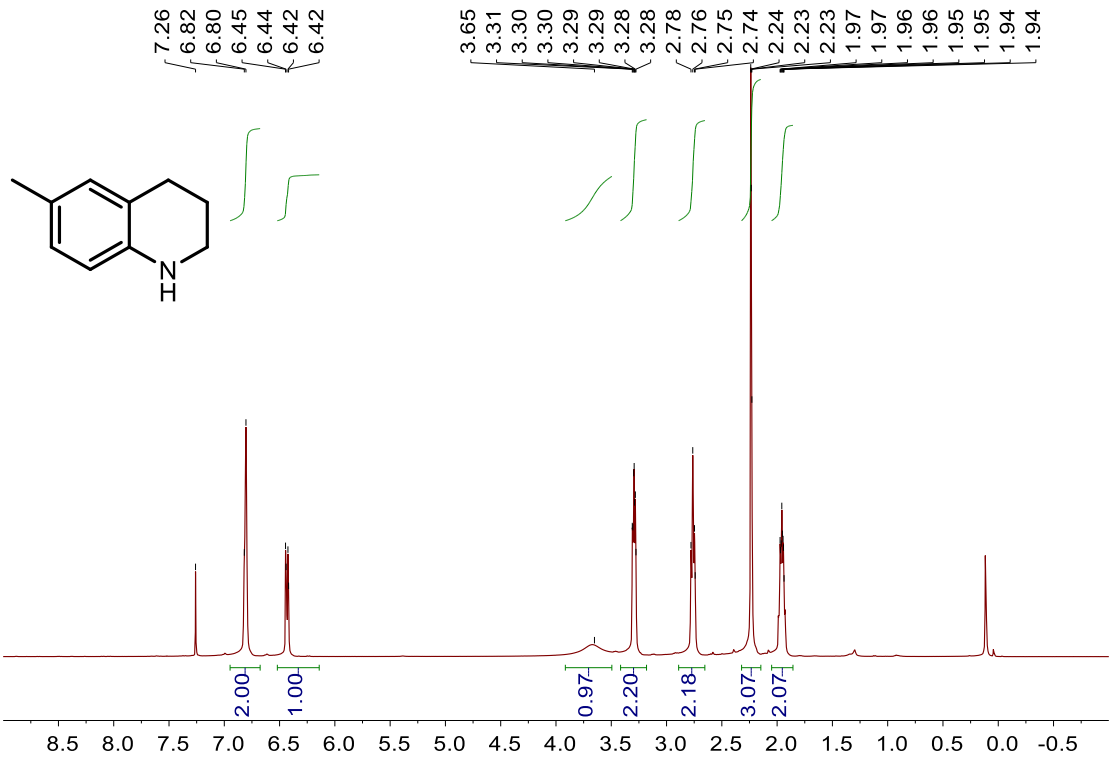
^{13}C NMR spectrum of **3b** (101 MHz, Chloroform-*d*)



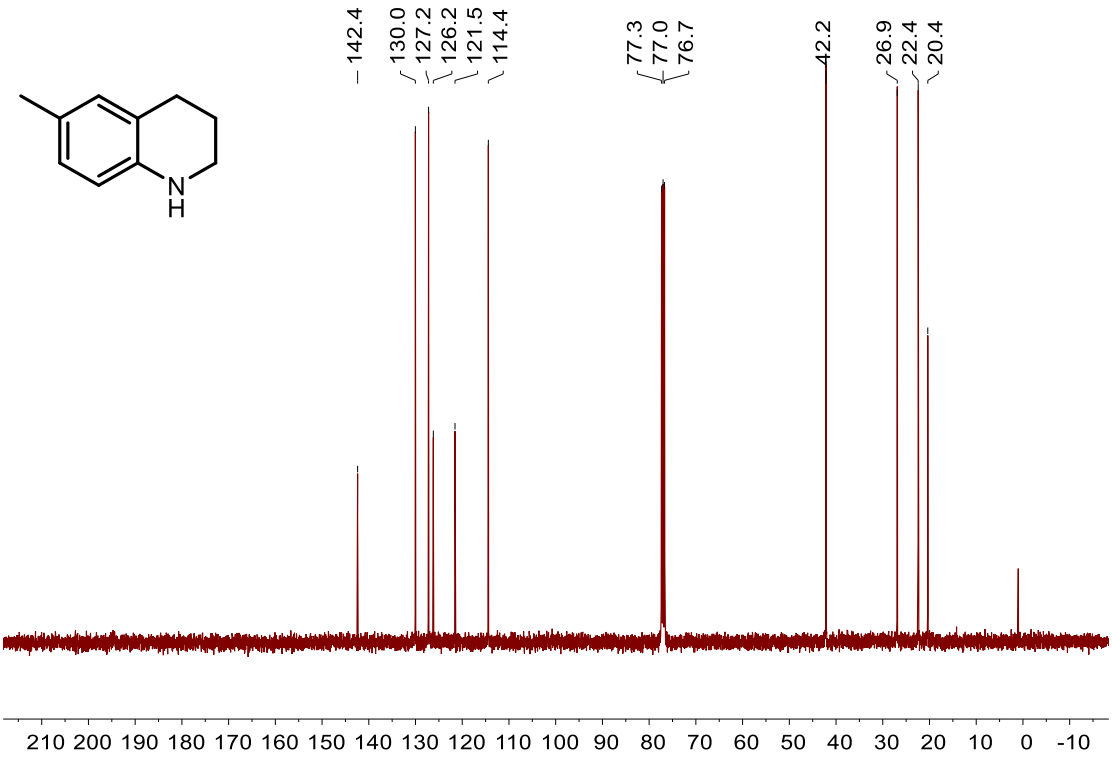
^{1}H NMR spectrum of **3c** (400 MHz, Chloroform-*d*)



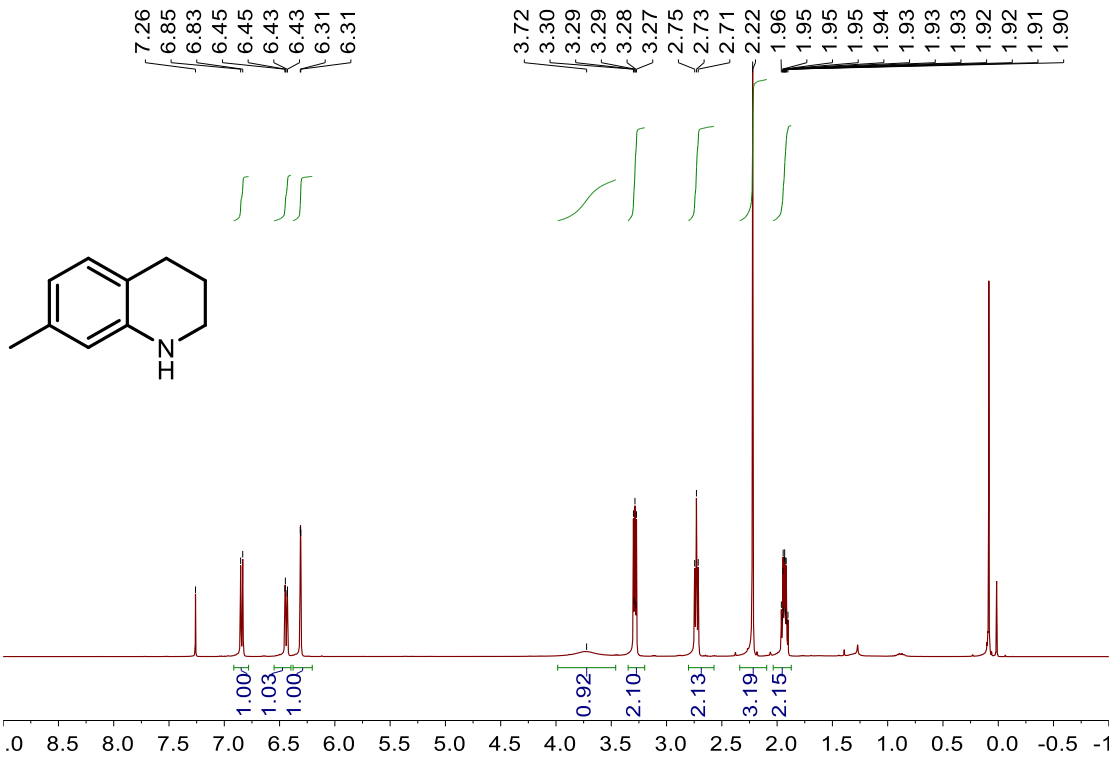
^{13}C NMR spectrum of **3c** (101 MHz, Chloroform-*d*)



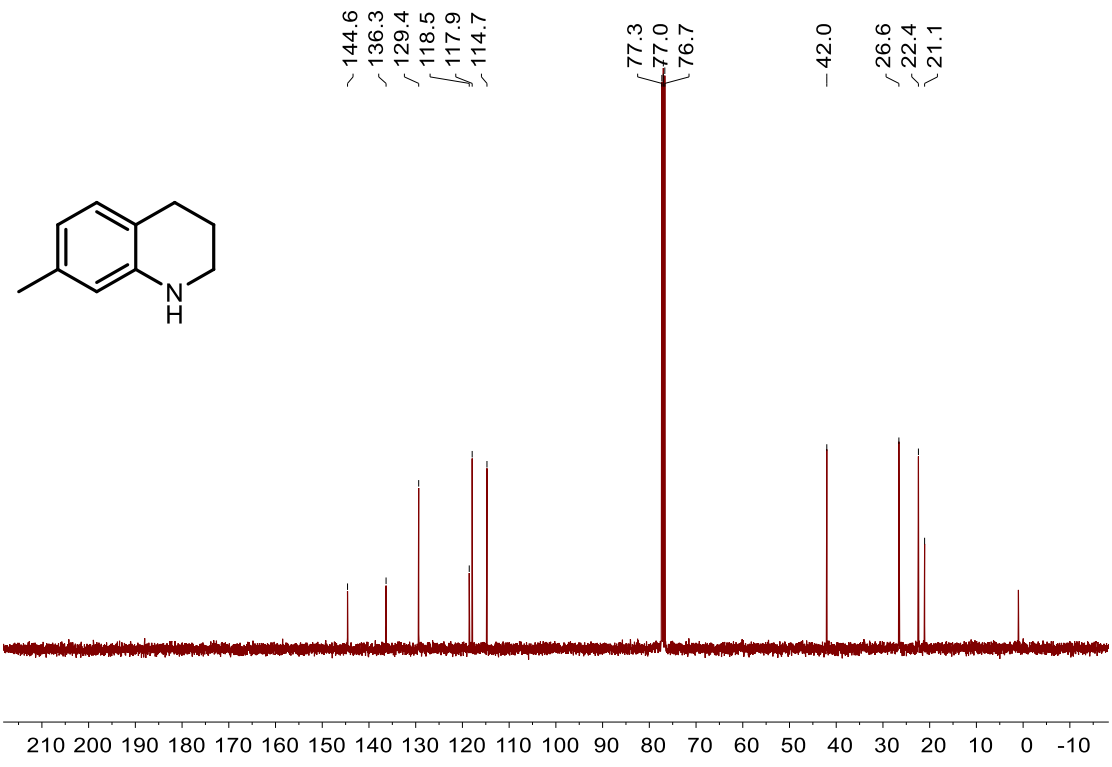
^{1}H NMR spectrum of **3d** (400 MHz, Chloroform-*d*)



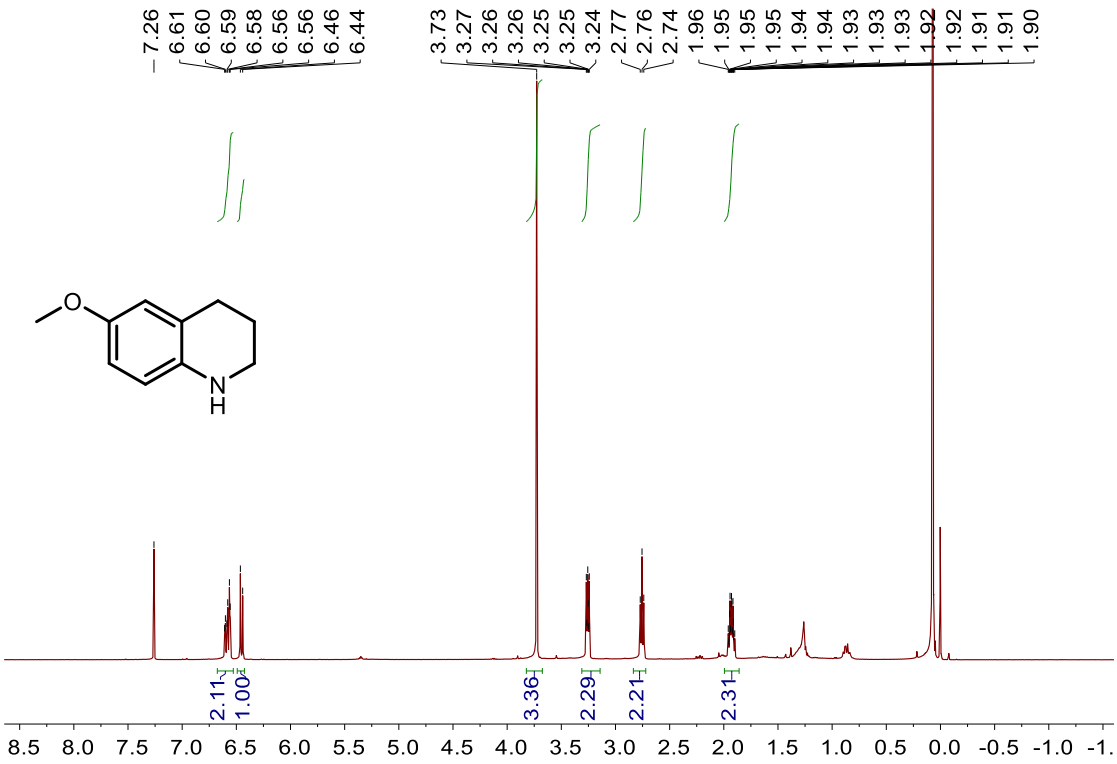
^{13}C NMR spectrum of **3d** (101 MHz, Chloroform-*d*)



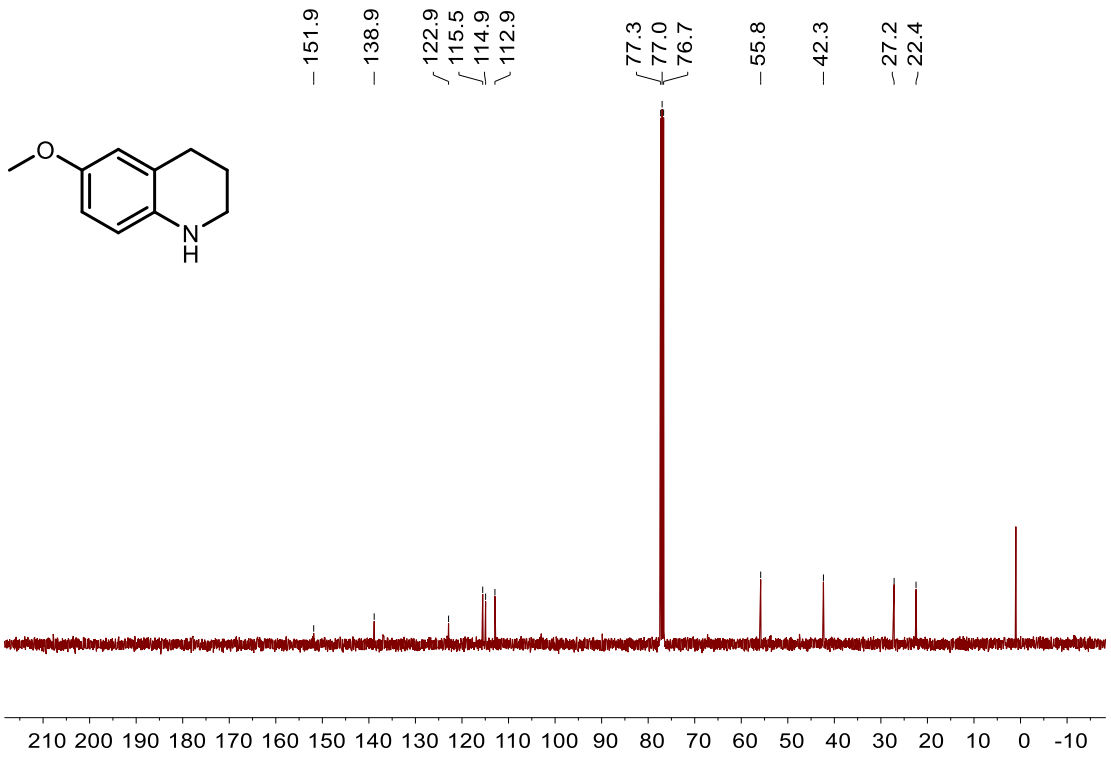
^{1}H NMR spectrum of **3e** (400 MHz, Chloroform-*d*)



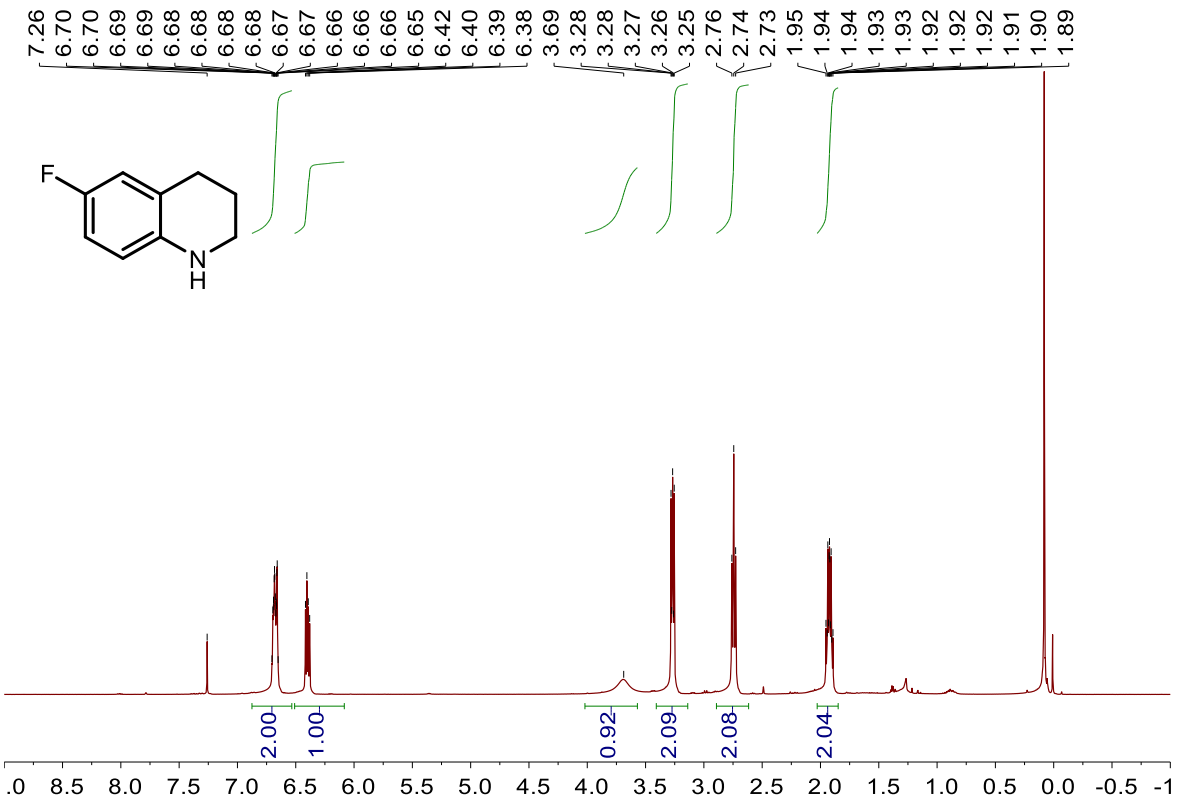
^{13}C NMR spectrum of **3e** (101 MHz, Chloroform-*d*)



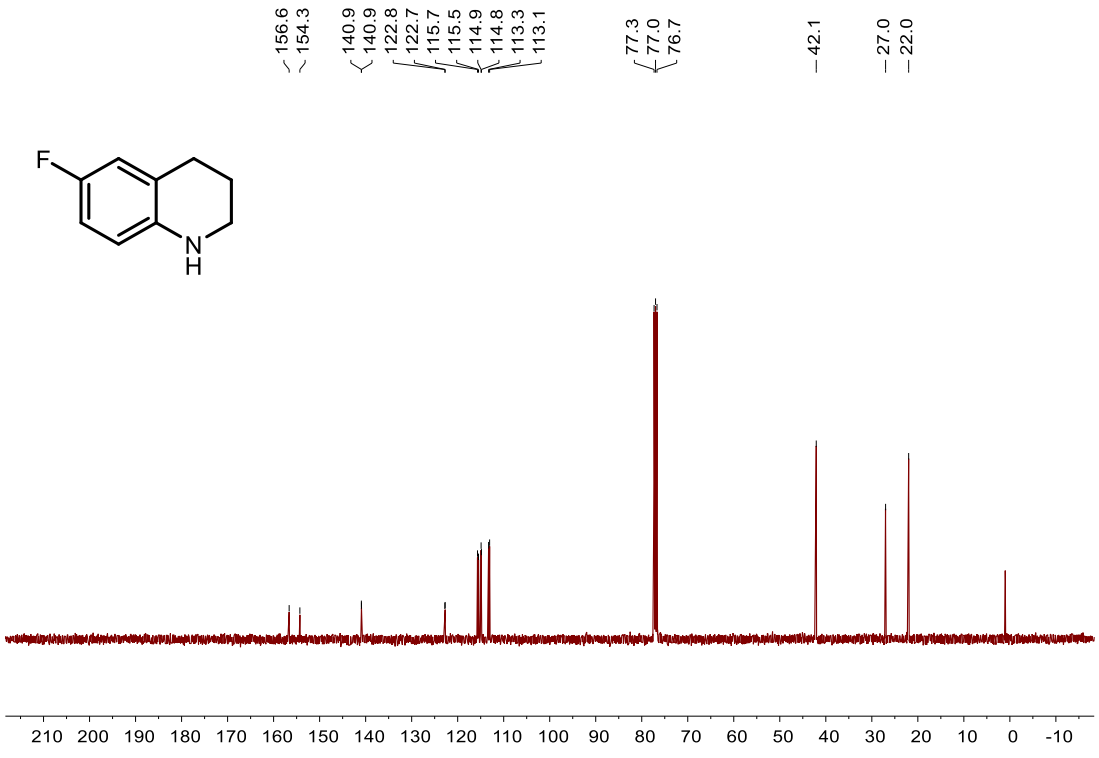
^{1}H NMR spectrum of **3f** (400 MHz, Chloroform-*d*)



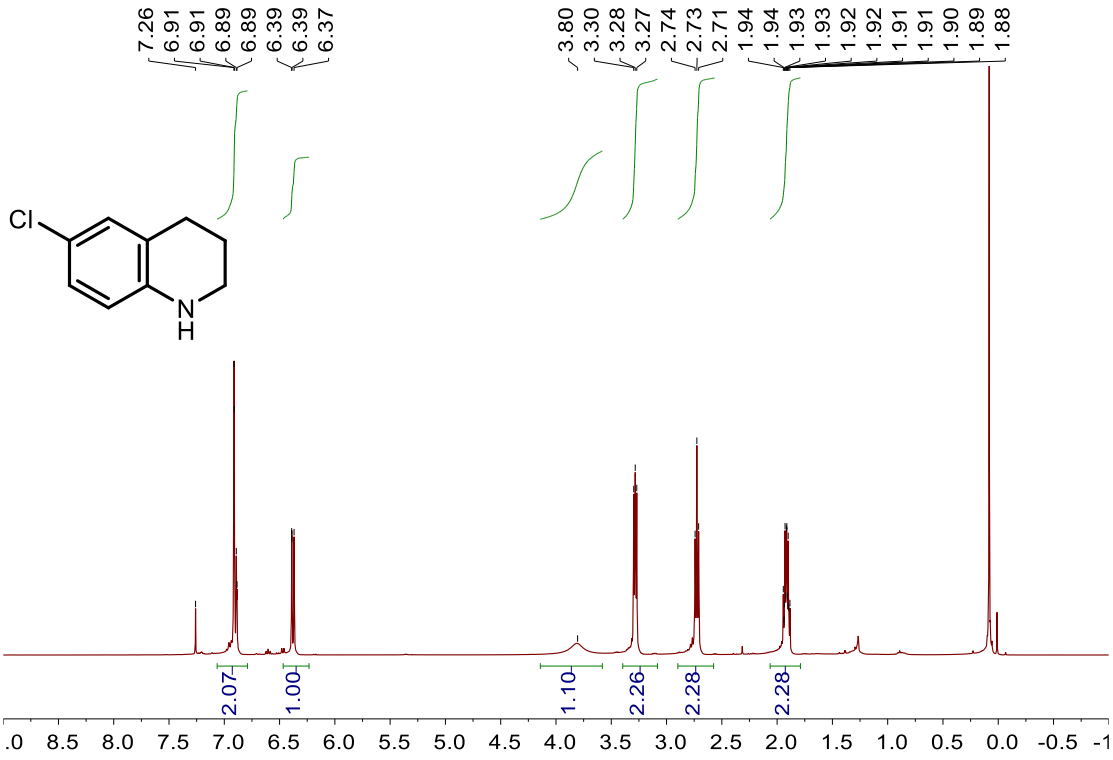
^{13}C NMR spectrum of **3f** (101 MHz, Chloroform-*d*)



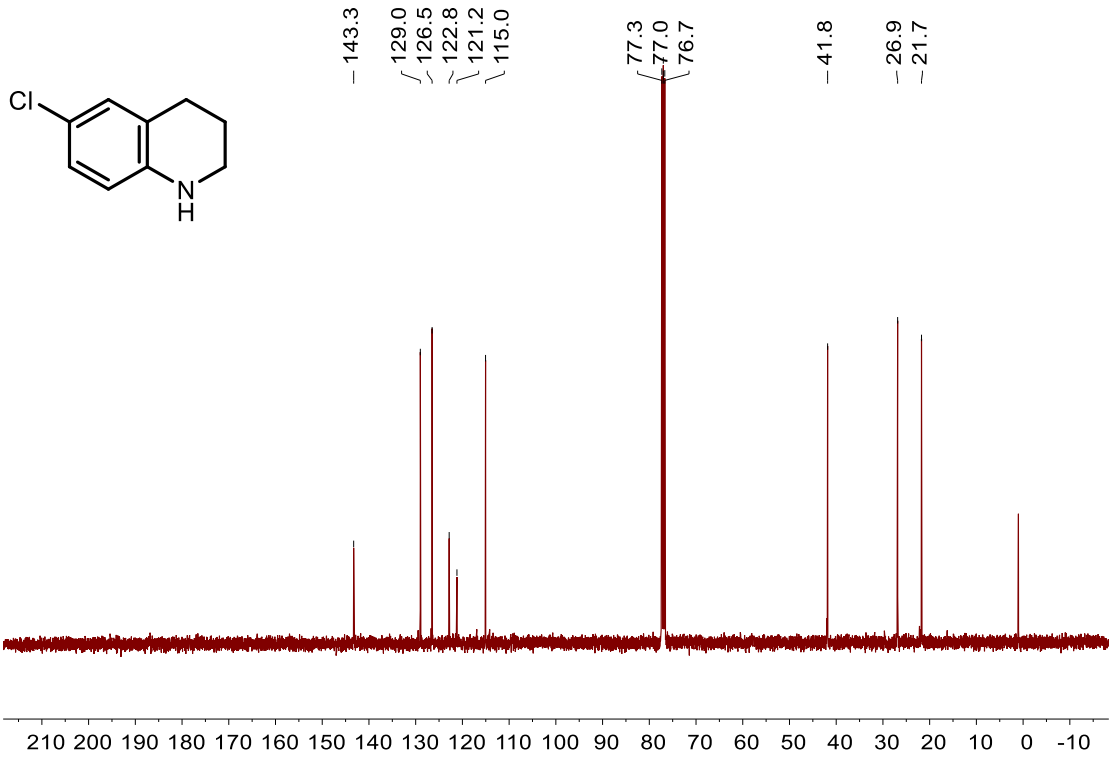
^{1}H NMR spectrum of **3g** (400 MHz, Chloroform-*d*)



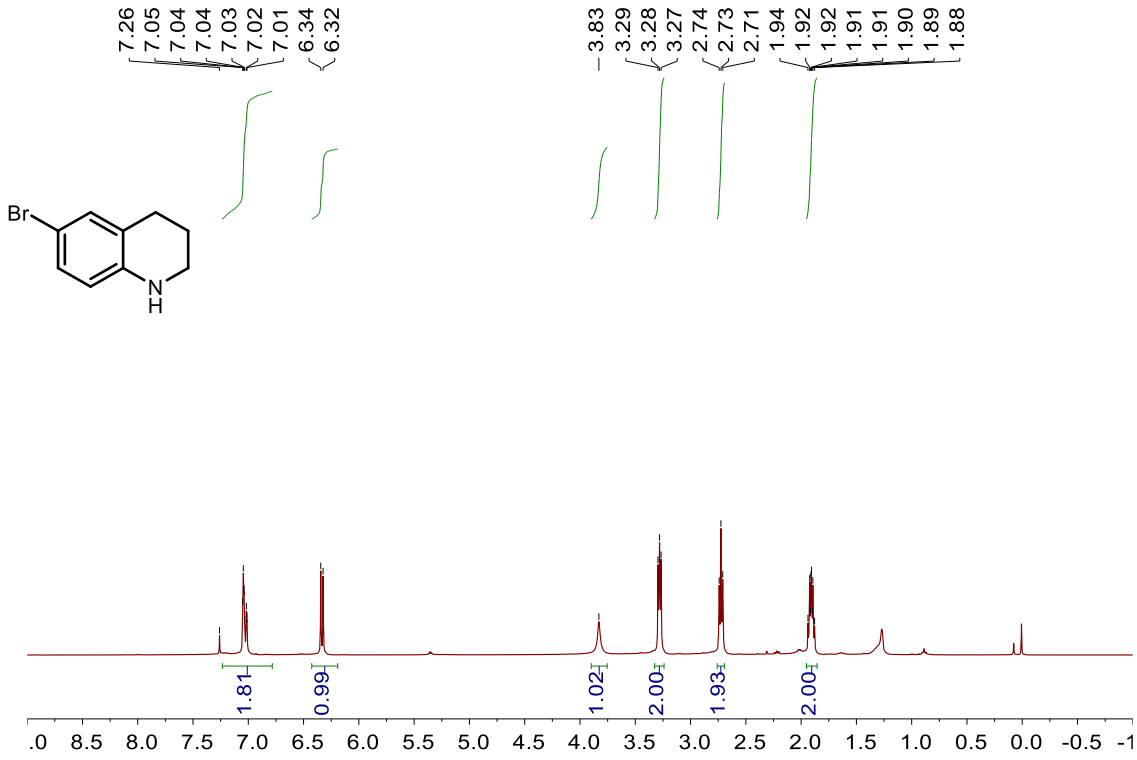
^{13}C NMR spectrum of **3g** (101 MHz, Chloroform-*d*)



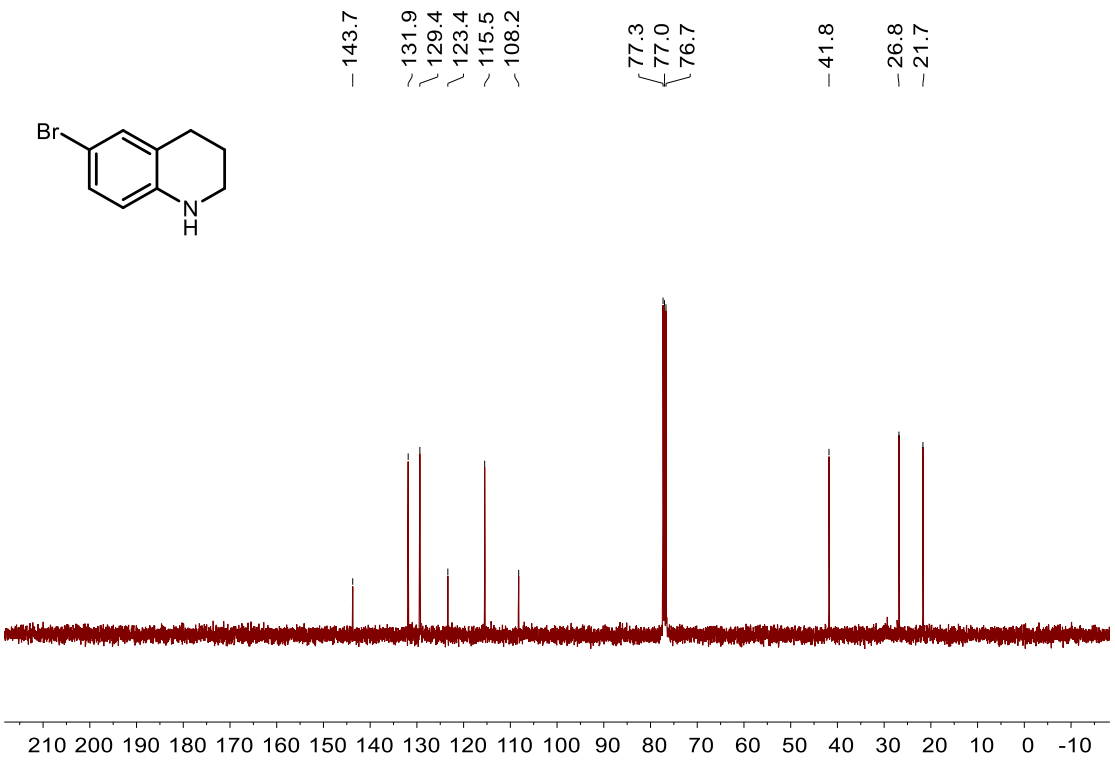
^{1}H NMR spectrum of **3h** (400 MHz, Chloroform-*d*)



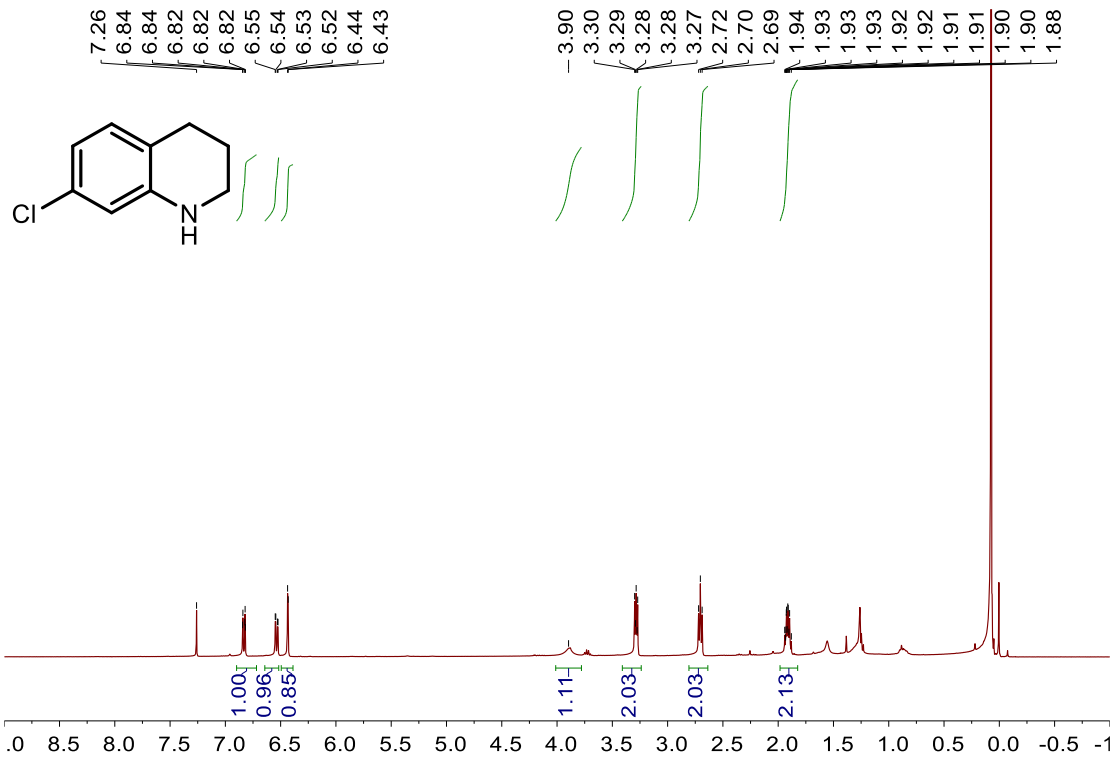
^{13}C NMR spectrum of **3h** (101 MHz, Chloroform-*d*)



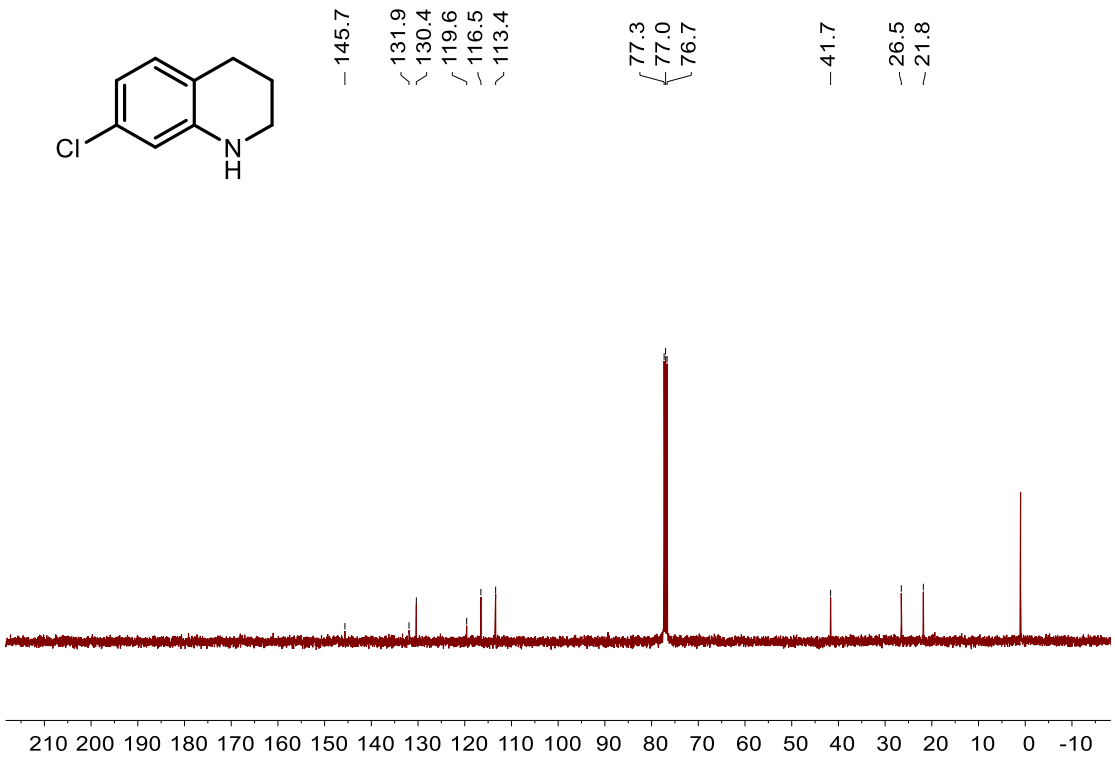
^{1}H NMR spectrum of **3i** (400 MHz, Chloroform-*d*)



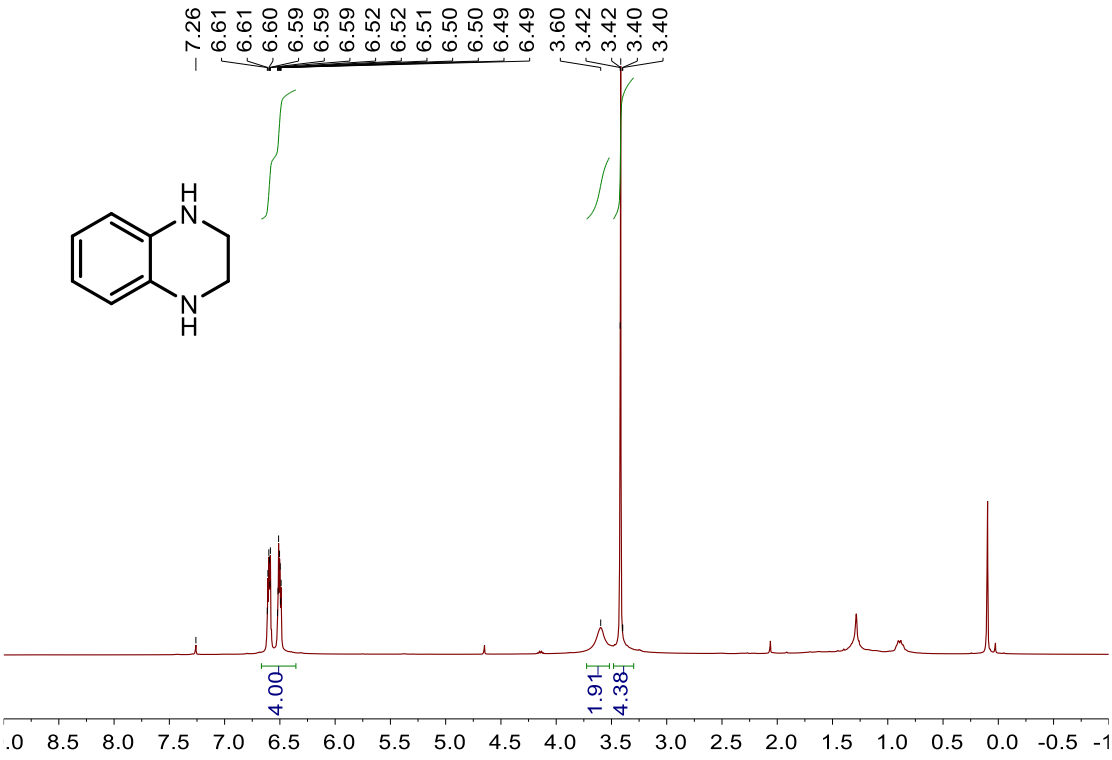
^{13}C NMR spectrum of **3i** (101 MHz, Chloroform-*d*)



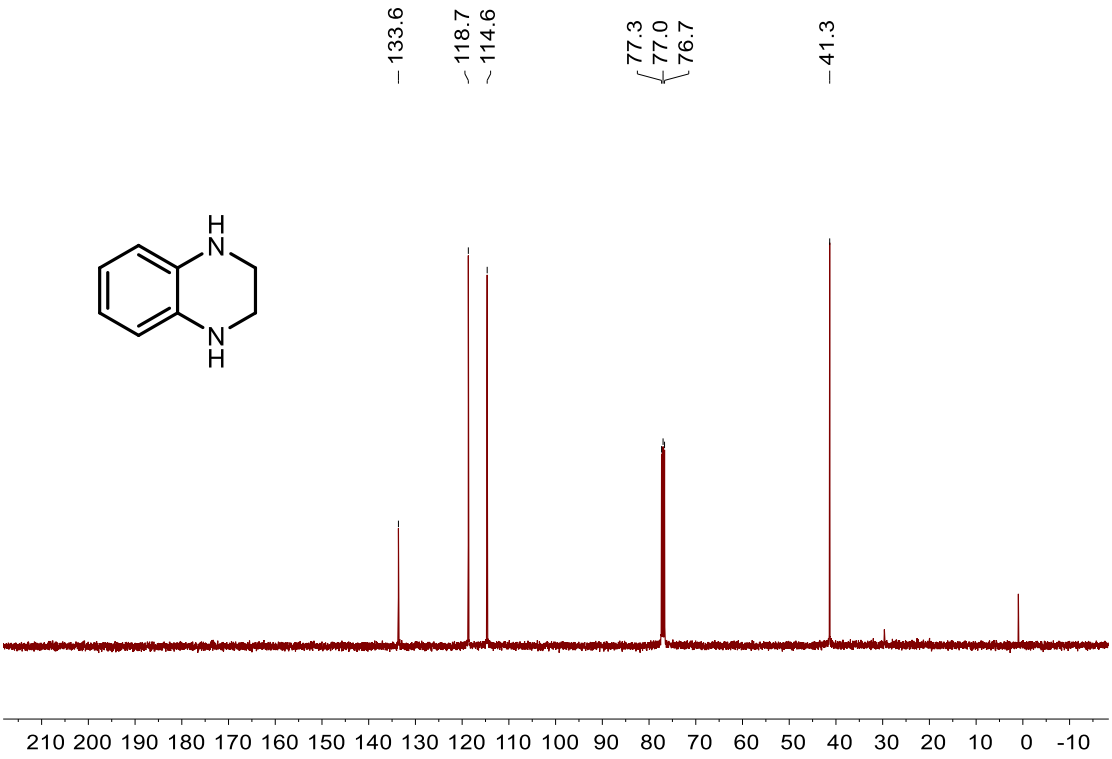
^{1}H NMR spectrum of **3j** (400 MHz, Chloroform-*d*)



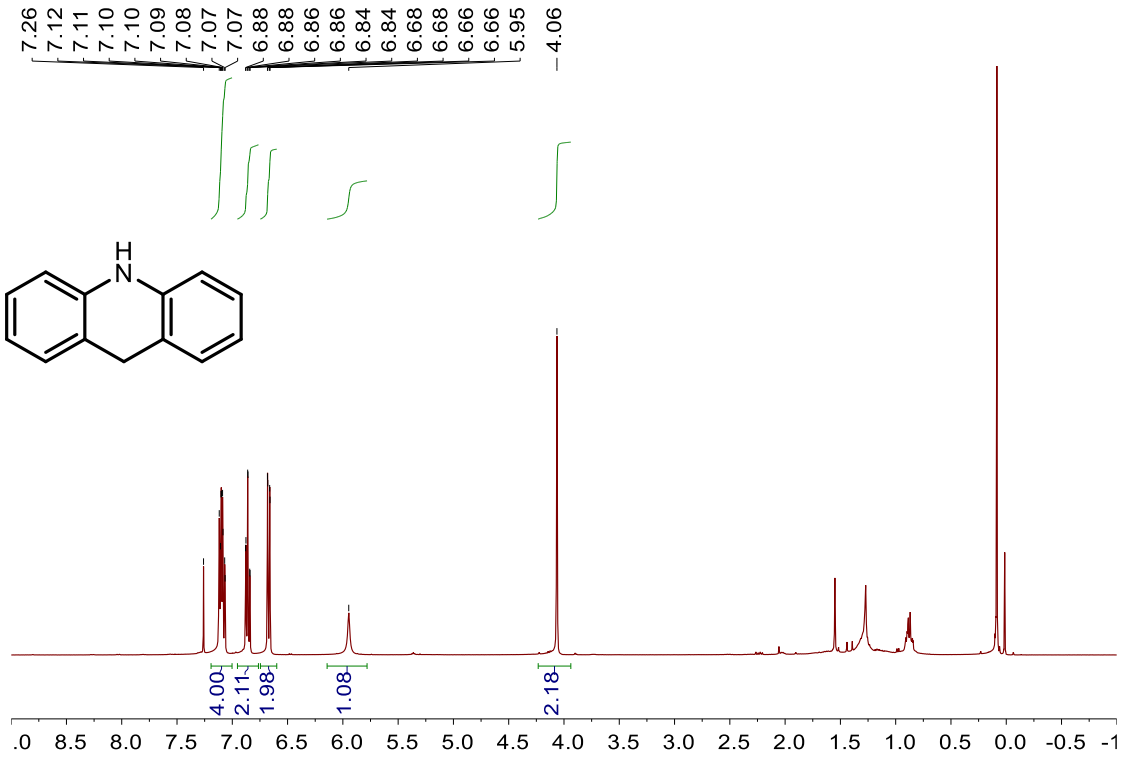
^{13}C NMR spectrum of **3j** (101 MHz, Chloroform-*d*)



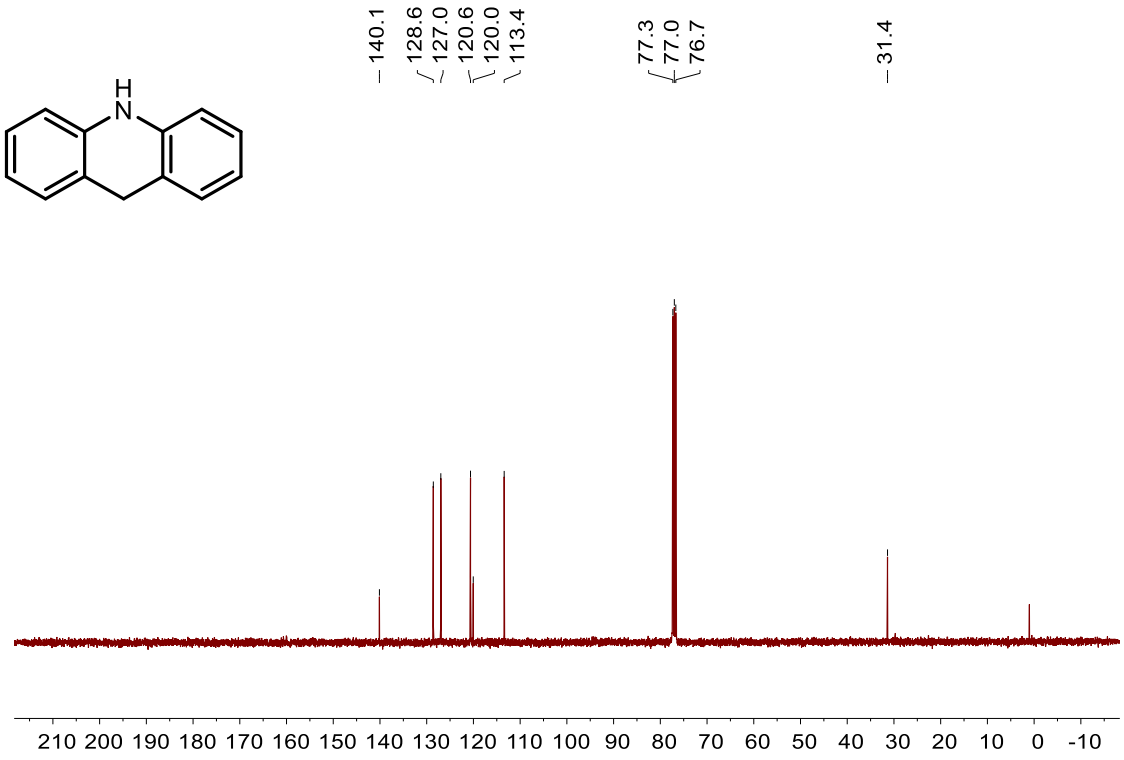
^{1}H NMR spectrum of **3k** (400 MHz, Chloroform-*d*)



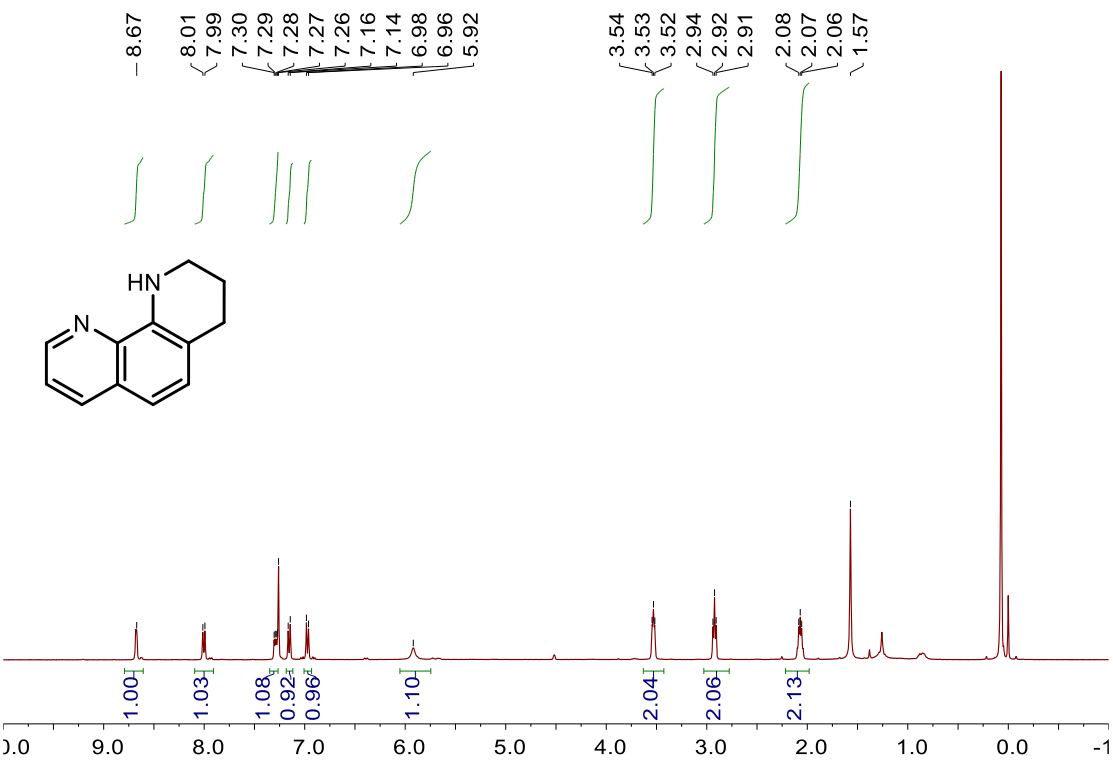
^{13}C NMR spectrum of **3k** (101 MHz, Chloroform-*d*)



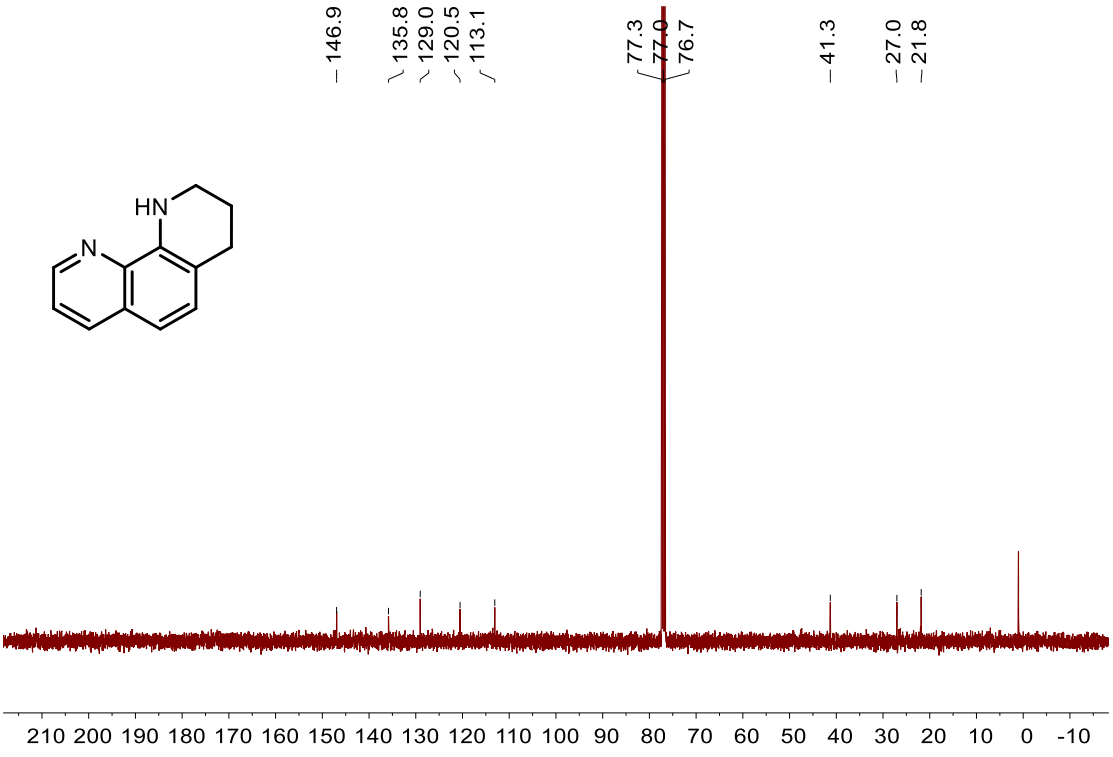
^{1}H NMR spectrum of **3l** (400 MHz, Chloroform-*d*)



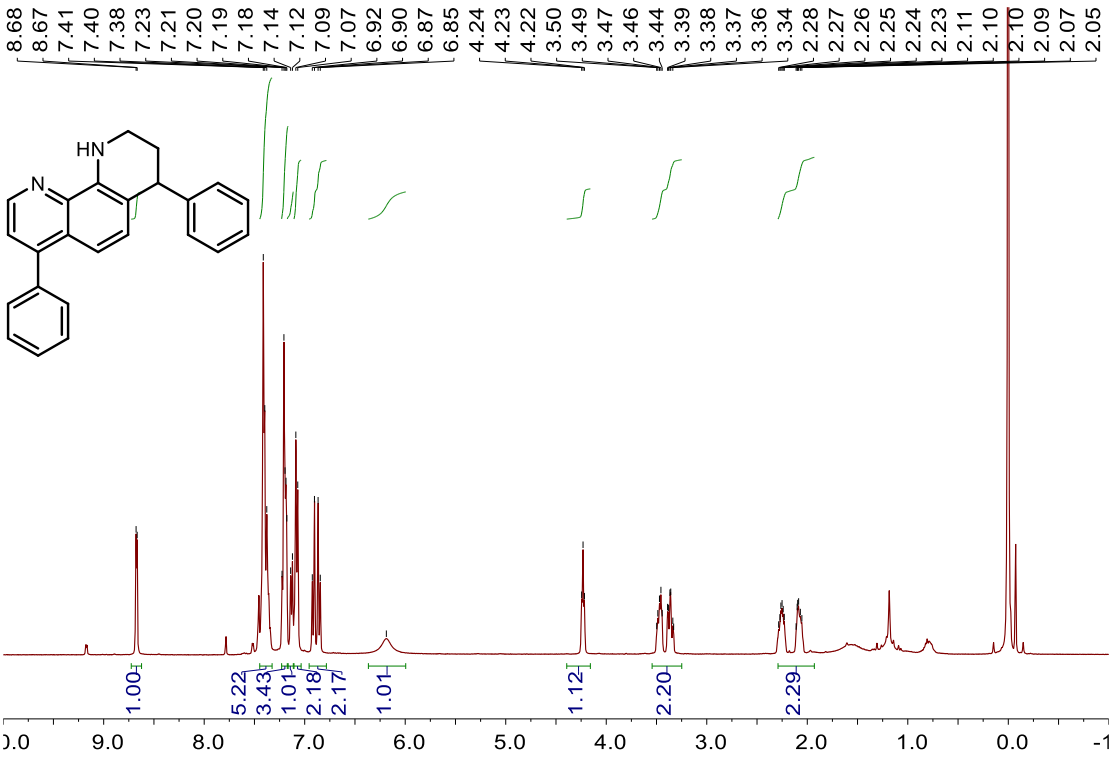
^{13}C NMR spectrum of **3l** (101 MHz, Chloroform-*d*)



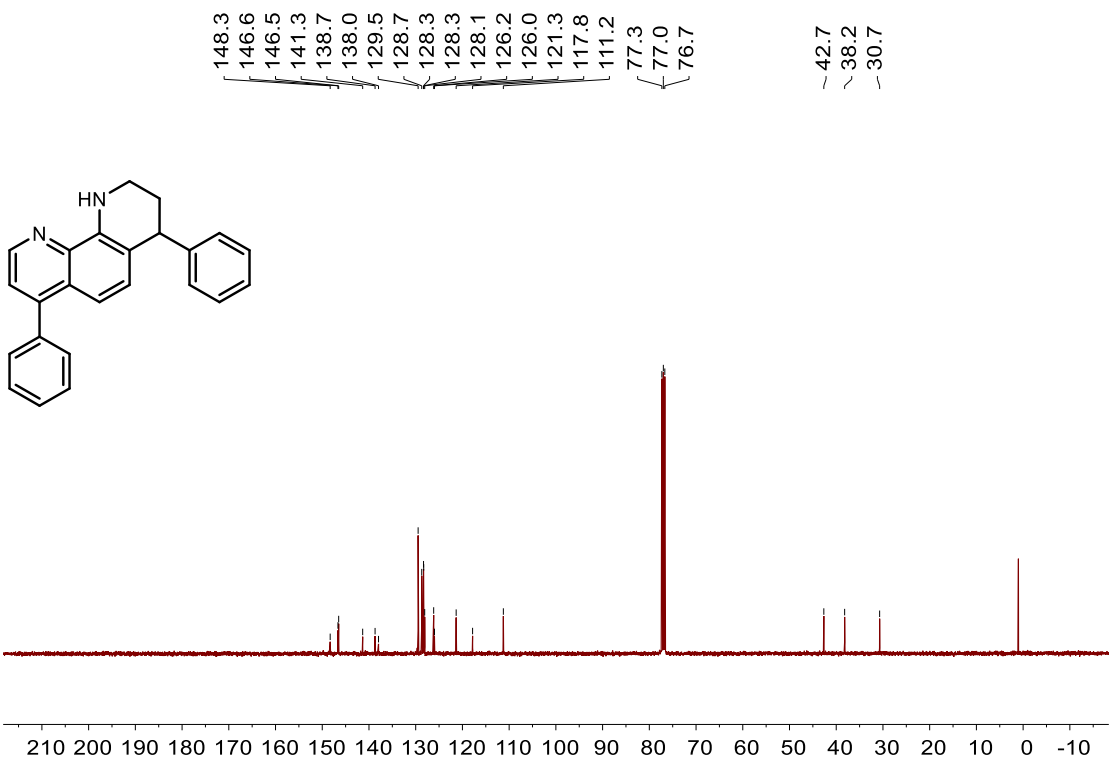
^{1}H NMR spectrum of **3m** (400 MHz, Chloroform-*d*)



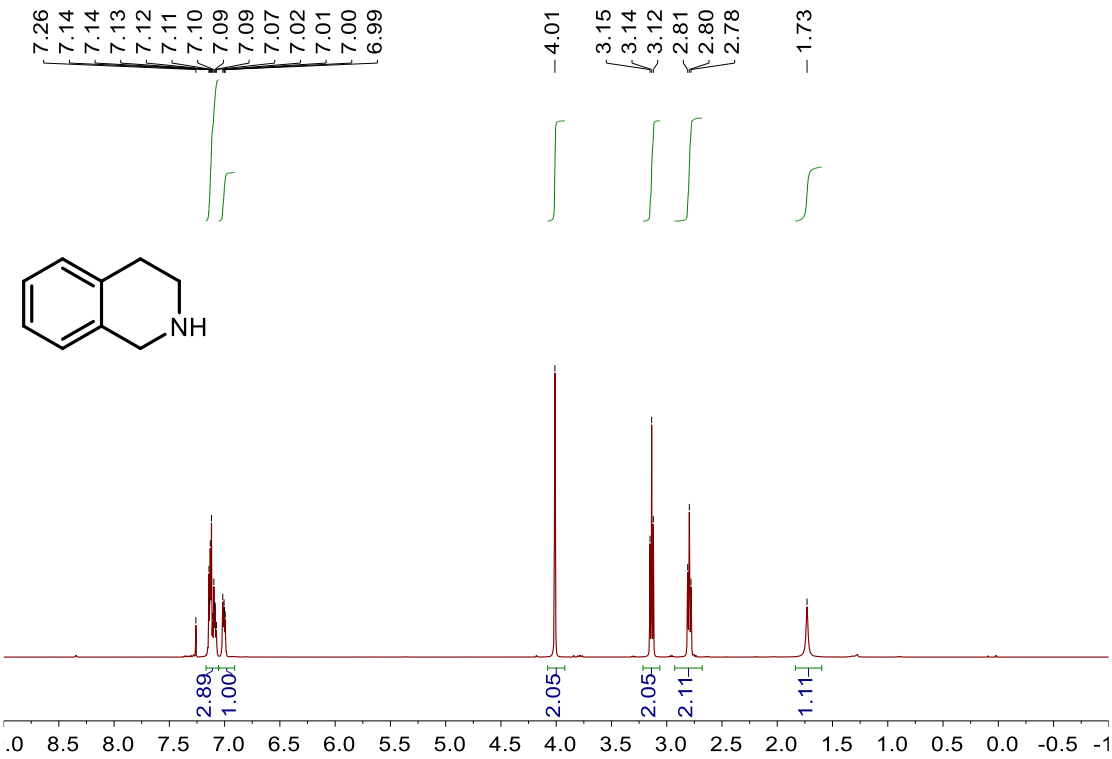
^{13}C NMR spectrum of **3m** (101 MHz, Chloroform-*d*)



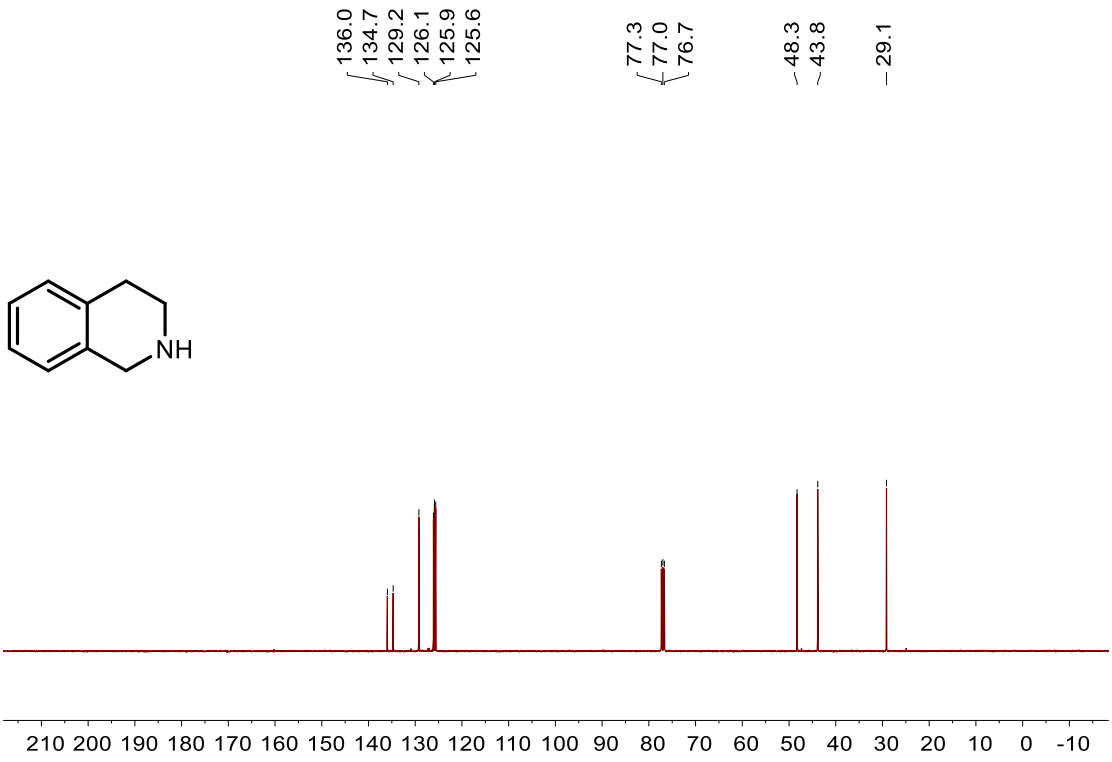
^{1}H NMR spectrum of **3n** (400 MHz, Chloroform-*d*)



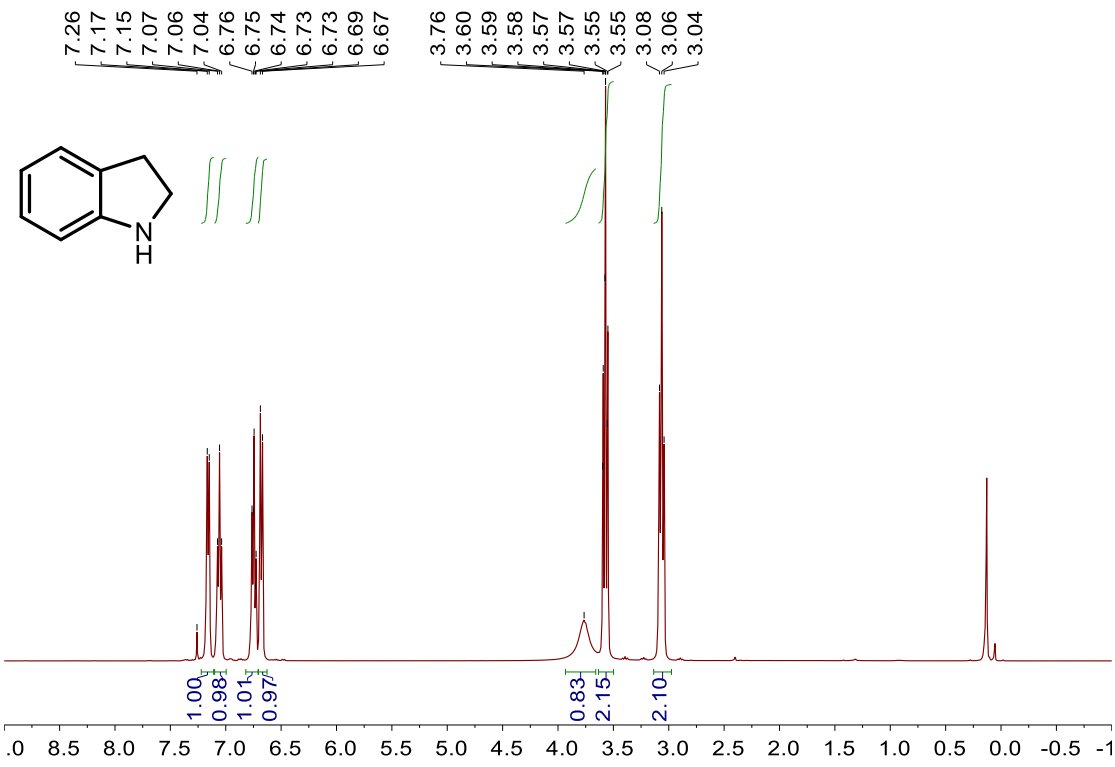
^{13}C NMR spectrum of **3n** (101 MHz, Chloroform-*d*)



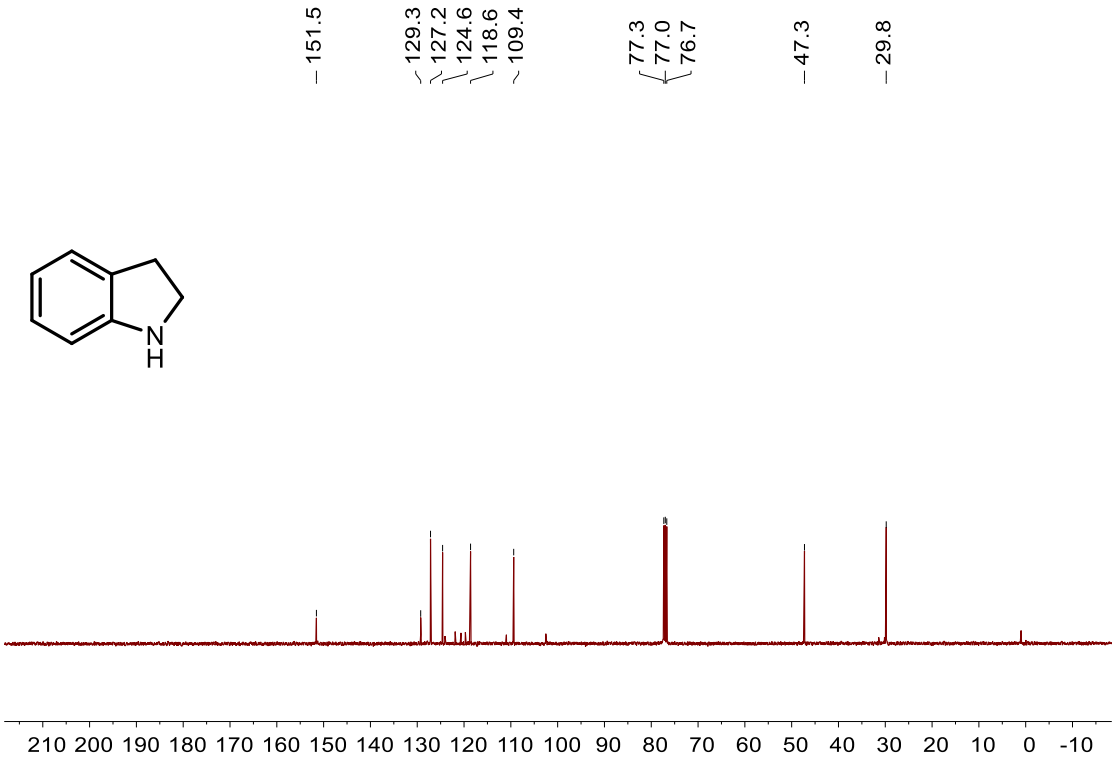
^{1}H NMR spectrum of **3o** (400 MHz, Chloroform-*d*)



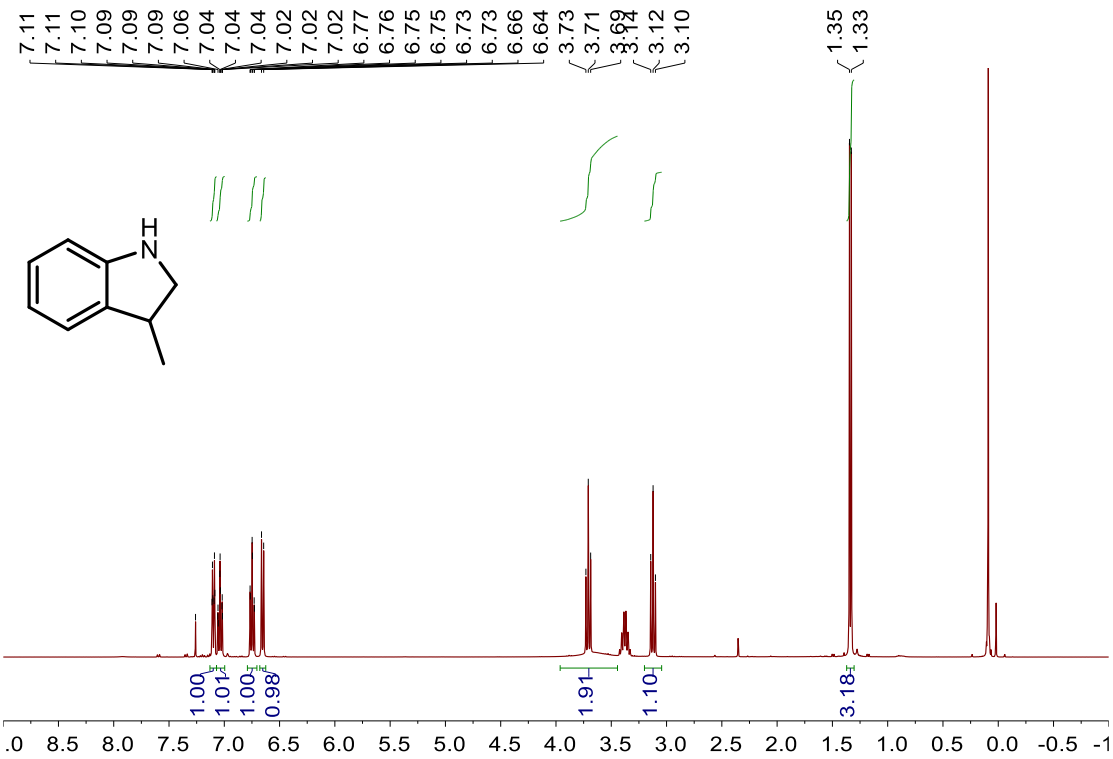
^{13}C NMR spectrum of **3o** (101 MHz, Chloroform-*d*)



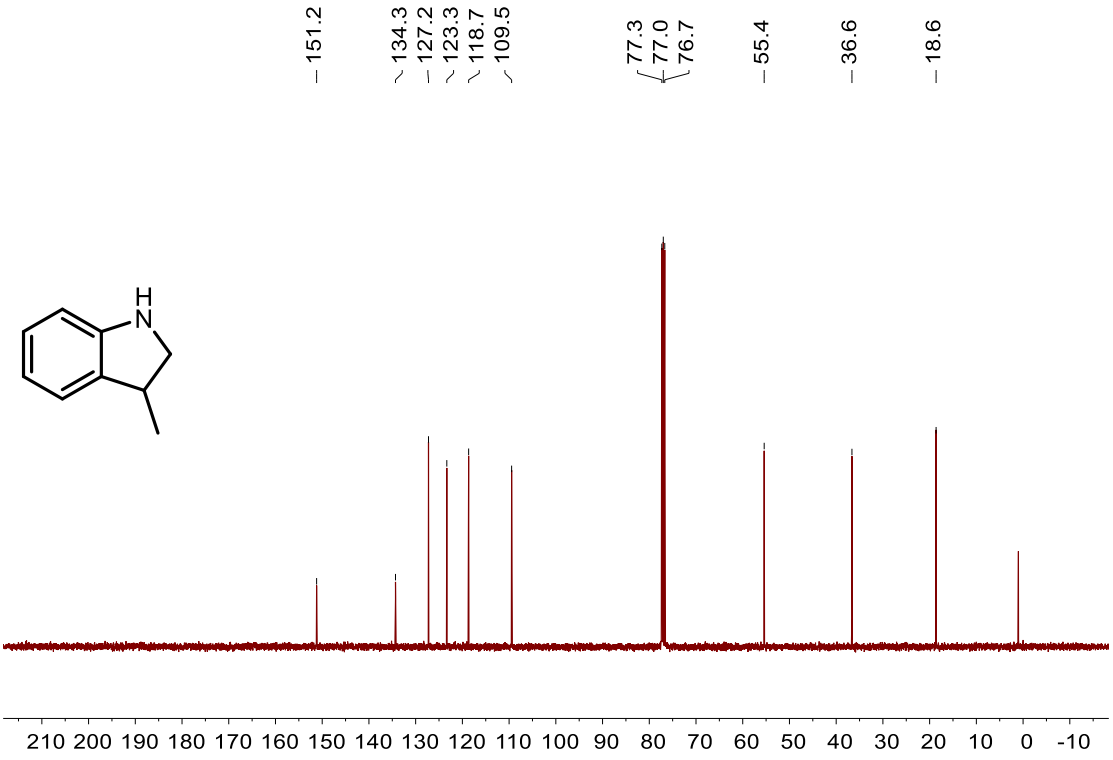
^{1}H NMR spectrum of **4a** (400 MHz, Chloroform-*d*)



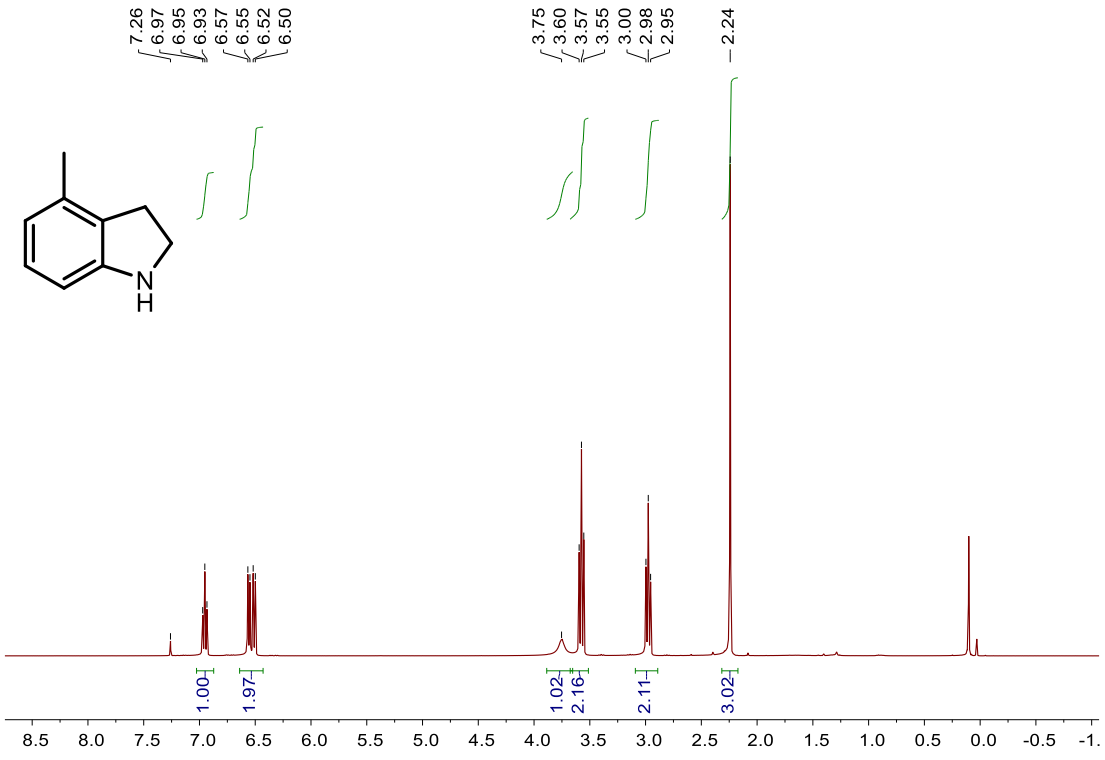
^{13}C NMR spectrum of **4a** (101 MHz, Chloroform-*d*)



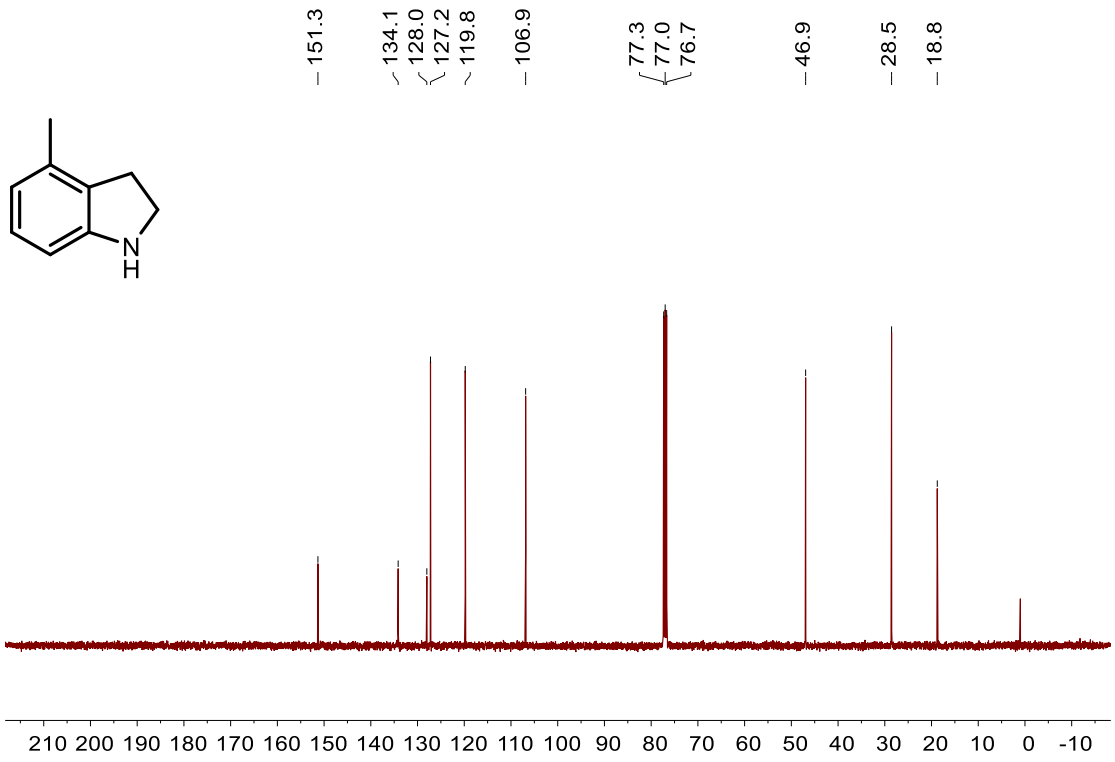
^{1}H NMR spectrum of **4b** (400 MHz, Chloroform-*d*)



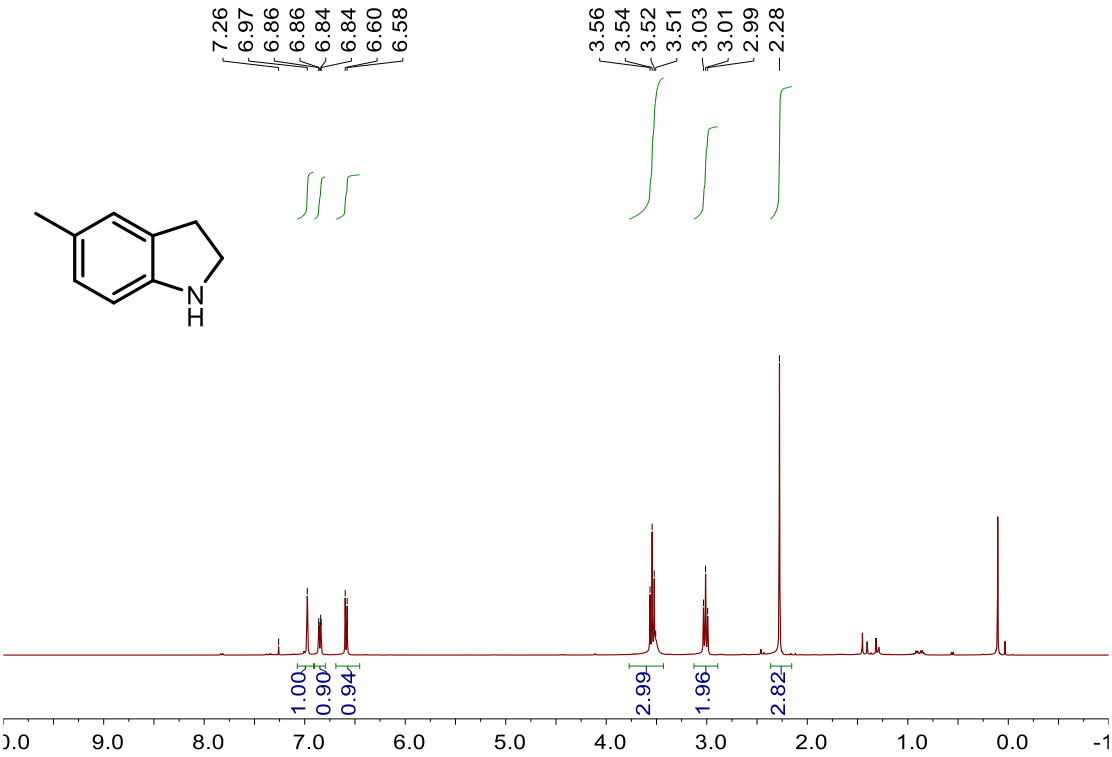
^{13}C NMR spectrum of **4b** (101 MHz, Chloroform-*d*)



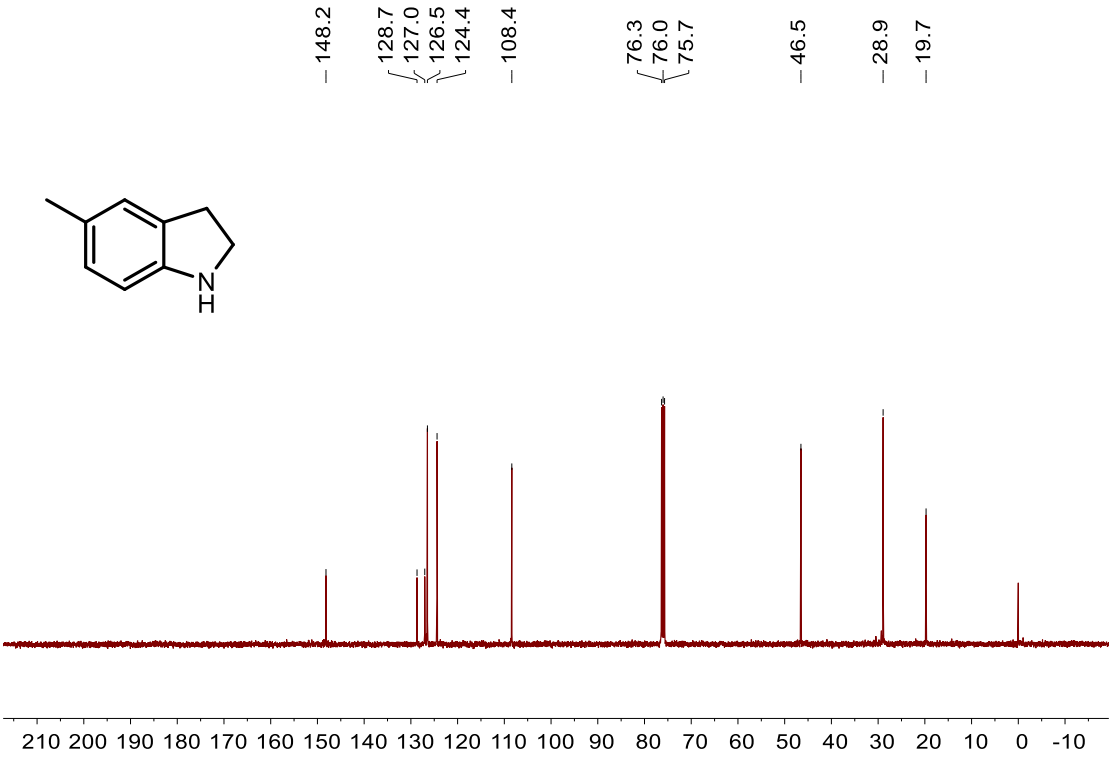
^{1}H NMR spectrum of **4c** (400 MHz, Chloroform-*d*)



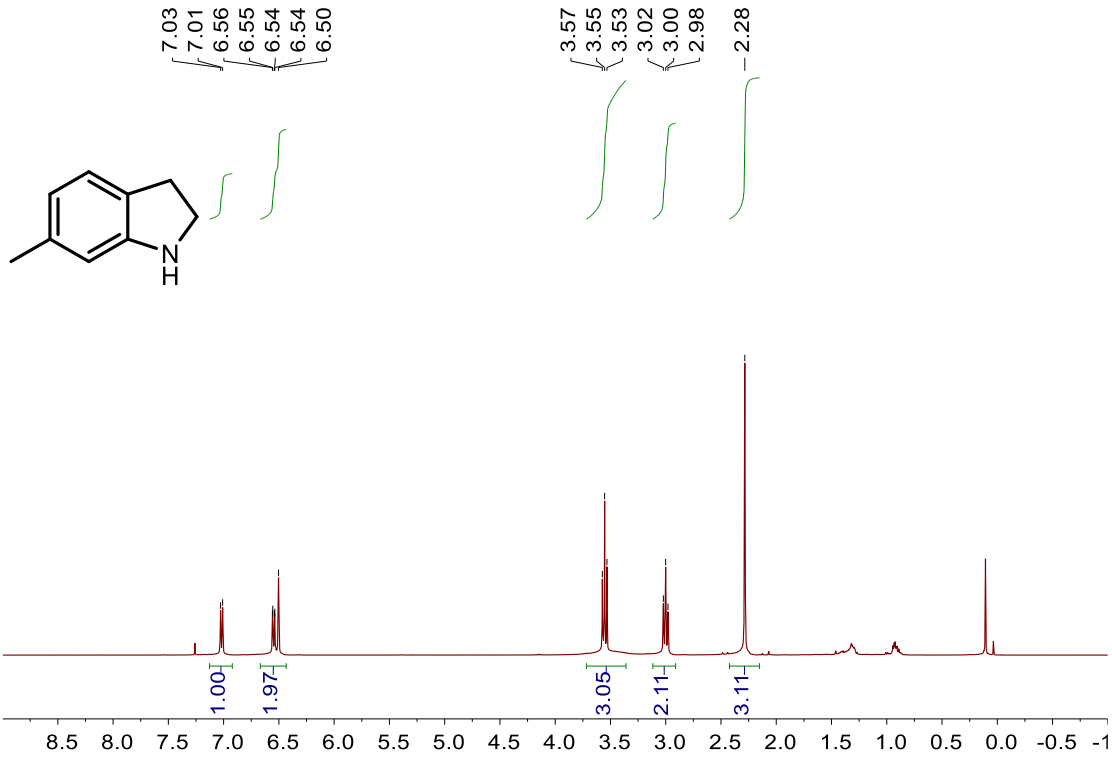
^{13}C NMR spectrum of **4c** (101 MHz, Chloroform-*d*)



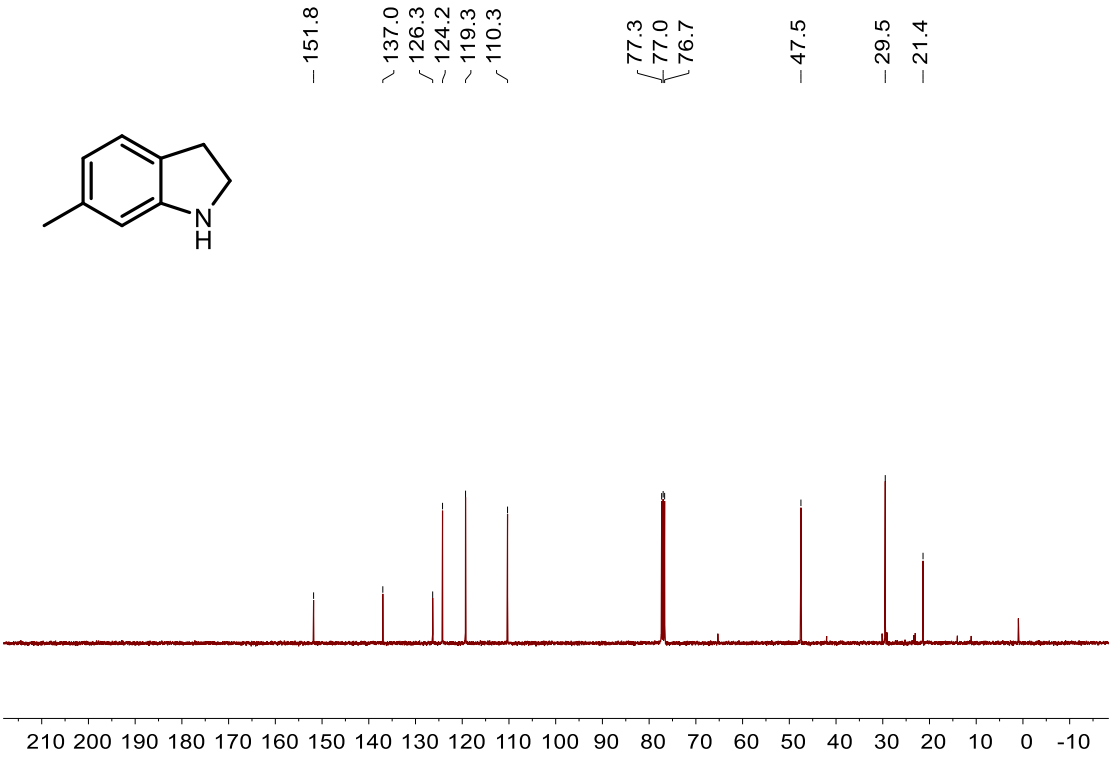
^{1}H NMR spectrum of **4d** (400 MHz, Chloroform-*d*)



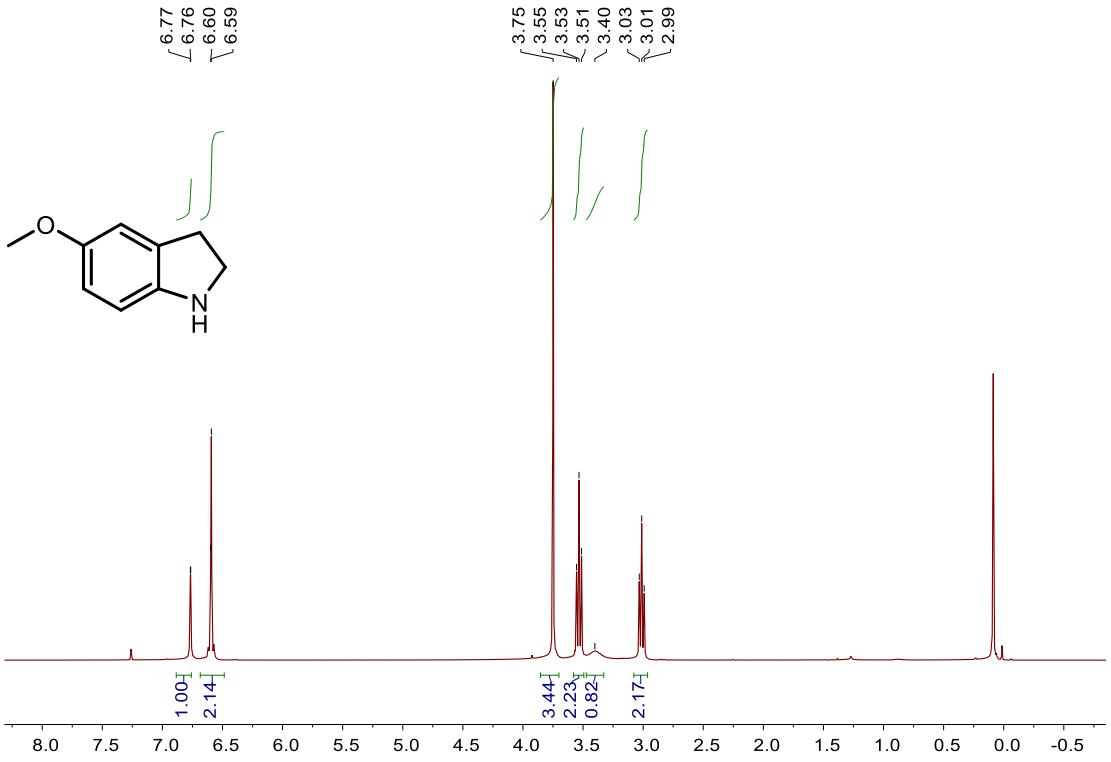
^{13}C NMR spectrum of **4d** (101 MHz, Chloroform-*d*)



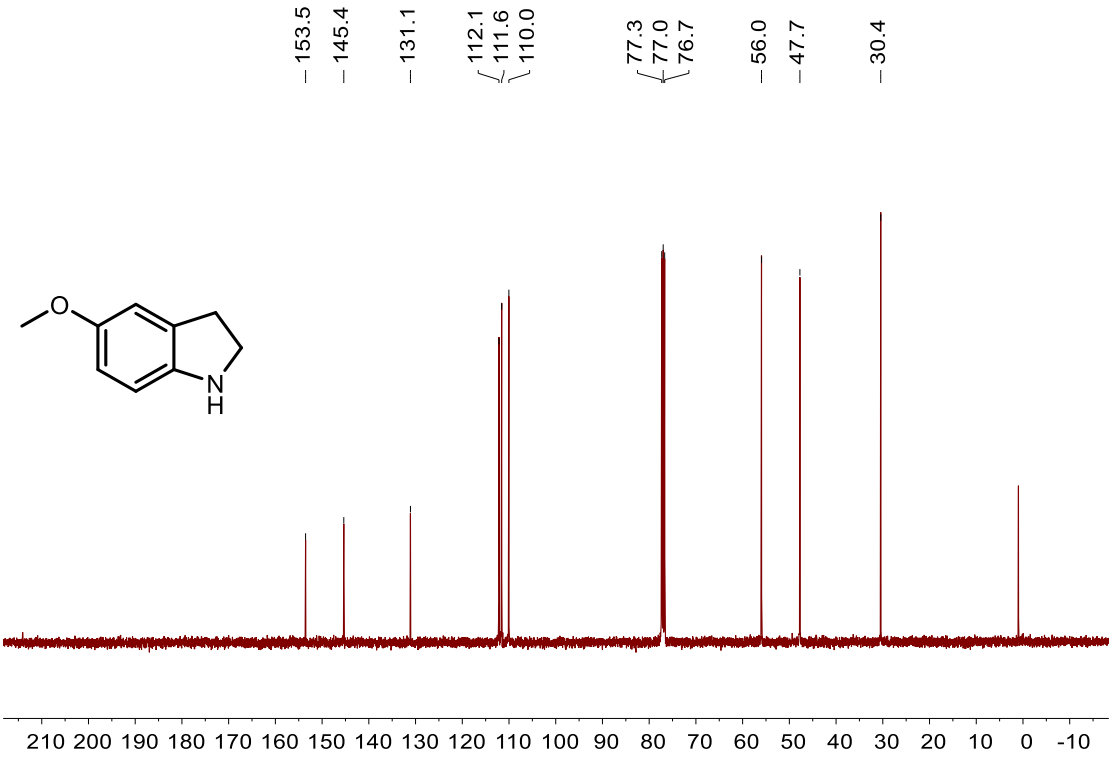
^{1}H NMR spectrum of **4e** (400 MHz, Chloroform-*d*)



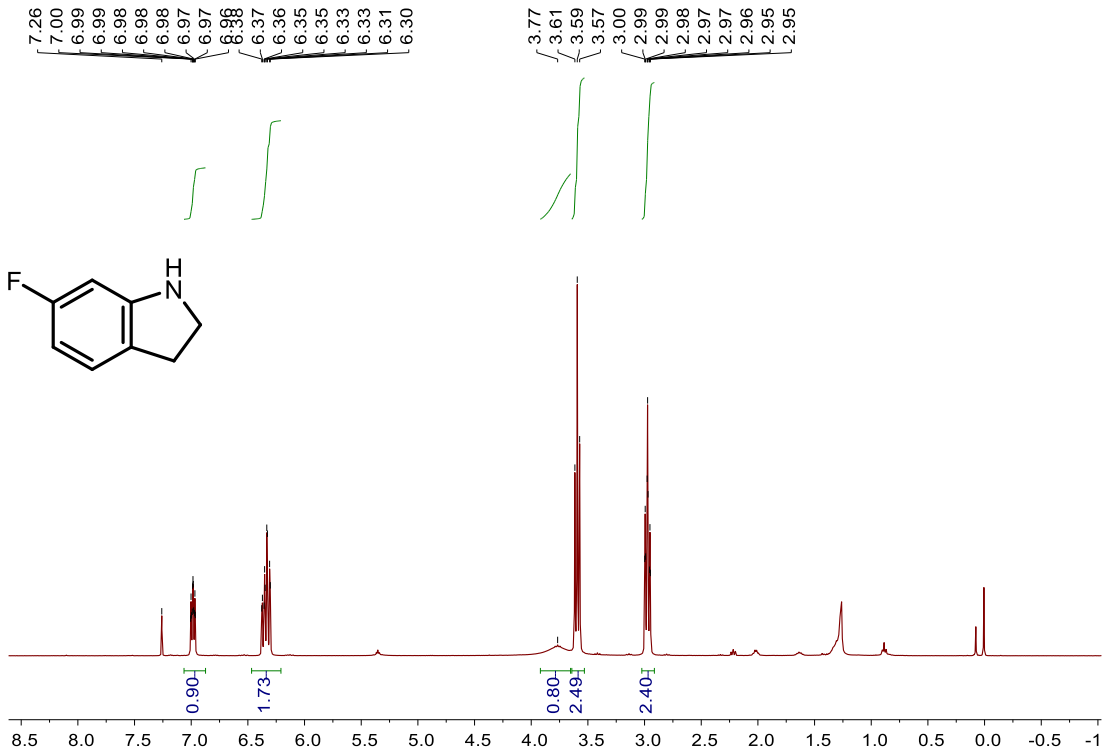
^{13}C NMR spectrum of **4e** (101 MHz, Chloroform-*d*)



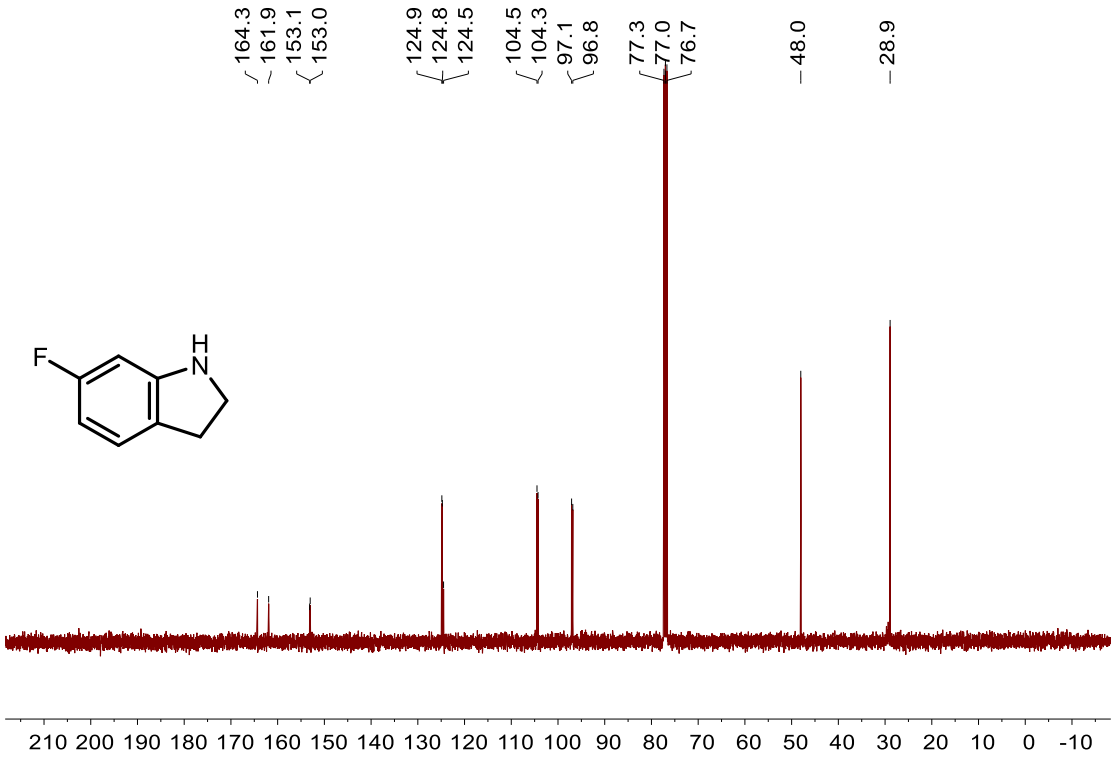
^{1}H NMR spectrum of **4f** (400 MHz, Chloroform-*d*)



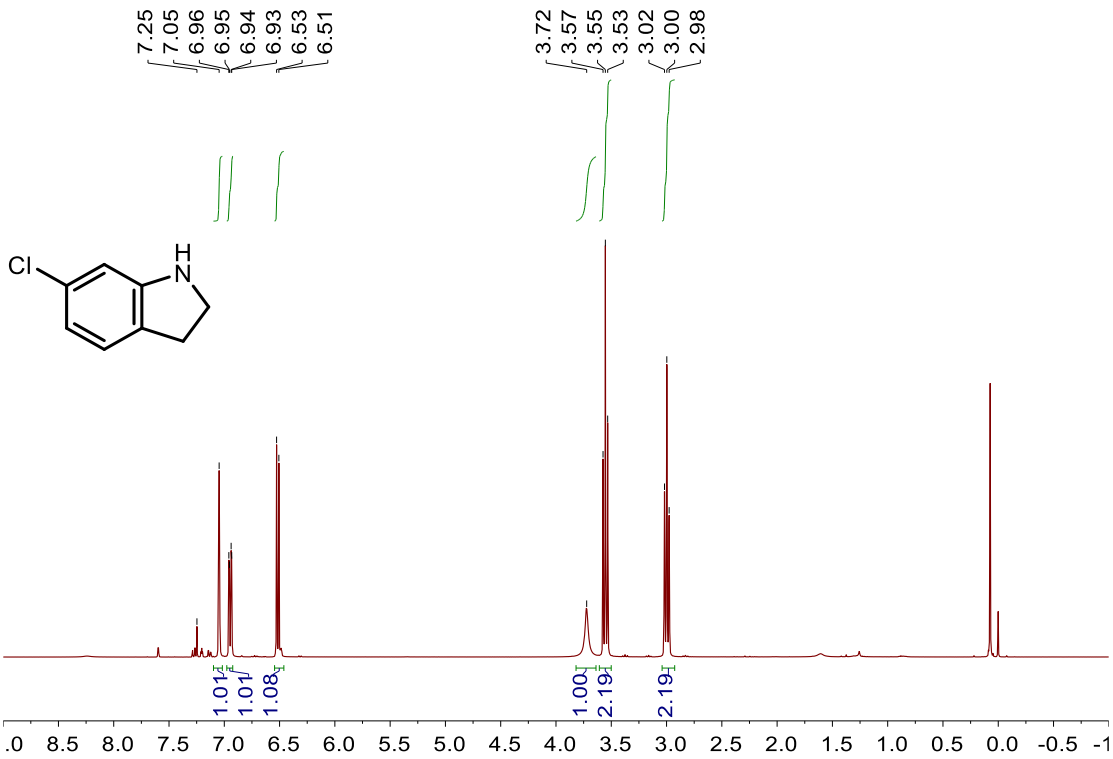
^{13}C NMR spectrum of **4f** (101 MHz, Chloroform-*d*)



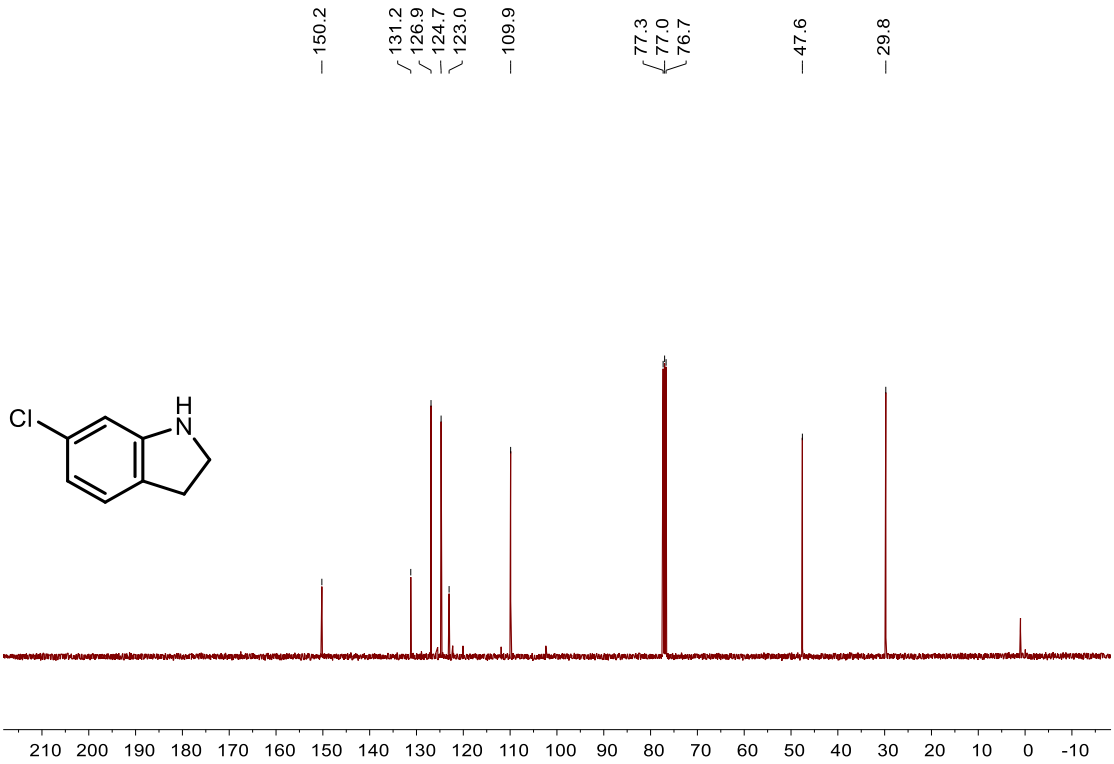
^{1}H NMR spectrum of **4g** (400 MHz, Chloroform-*d*)



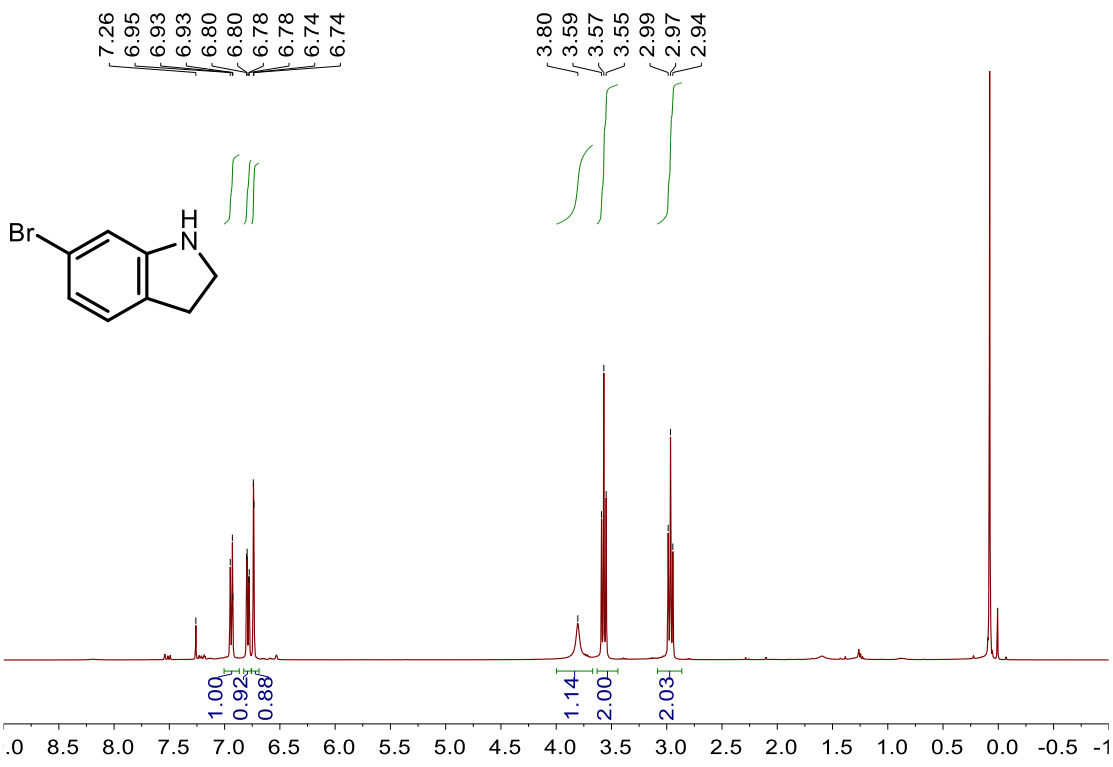
^{13}C NMR spectrum of **4g** (101 MHz, Chloroform-*d*)



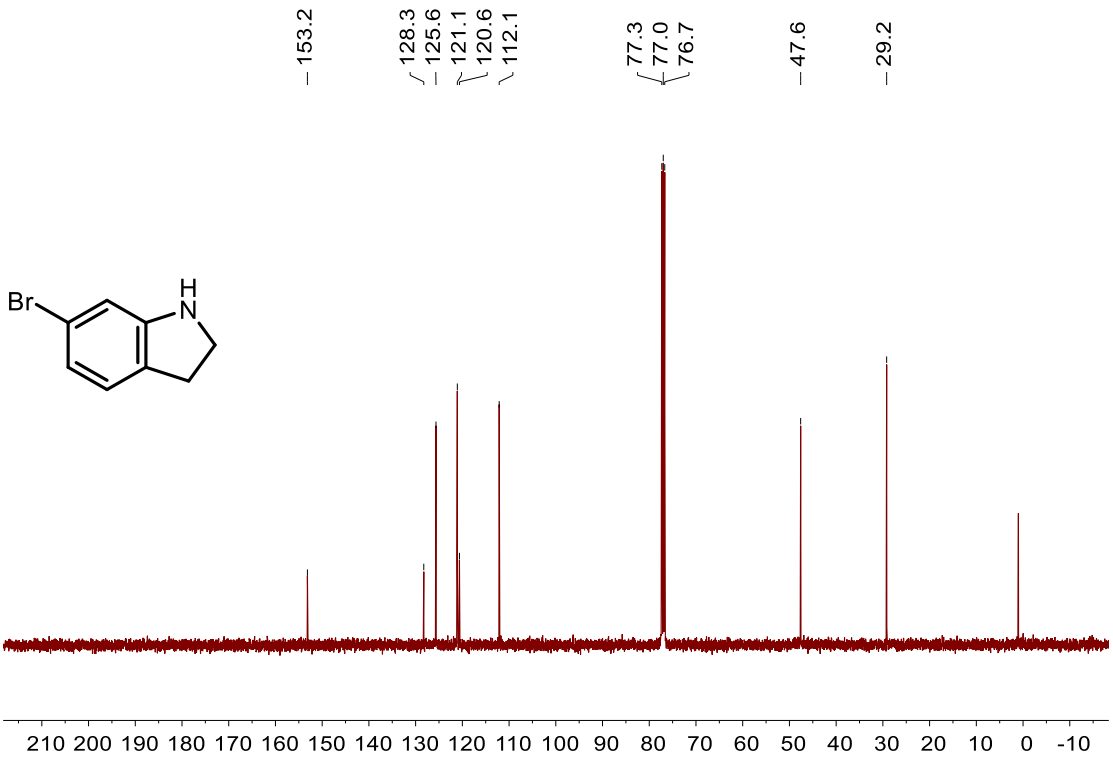
^{1}H NMR spectrum of **4h** (400 MHz, Chloroform-*d*)



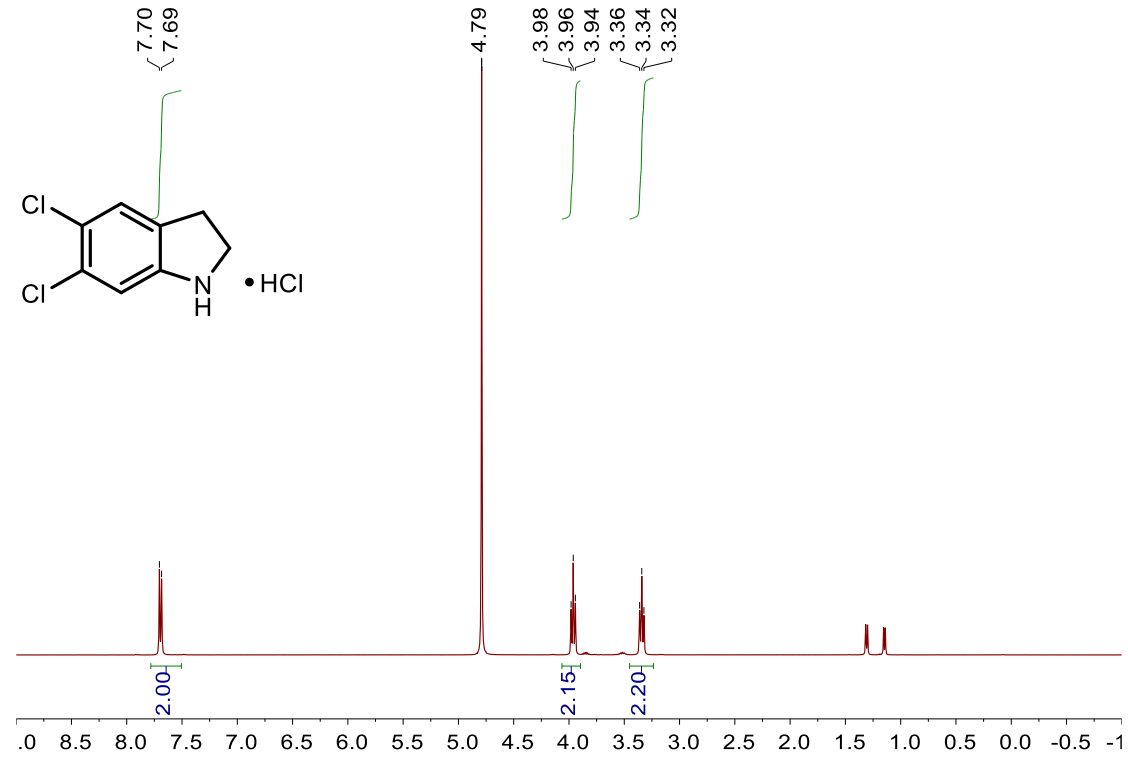
^{13}C NMR spectrum of **4h** (101 MHz, Chloroform-*d*)



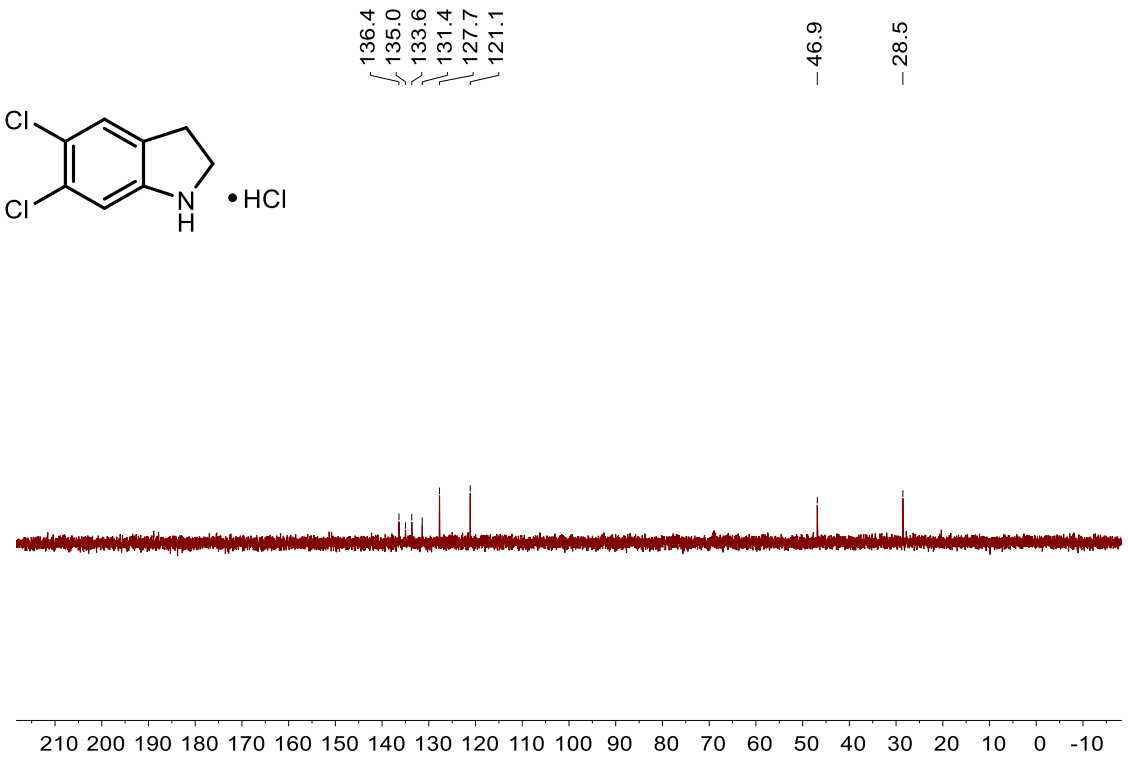
^{1}H NMR spectrum of **4i** (400 MHz, Chloroform-*d*)



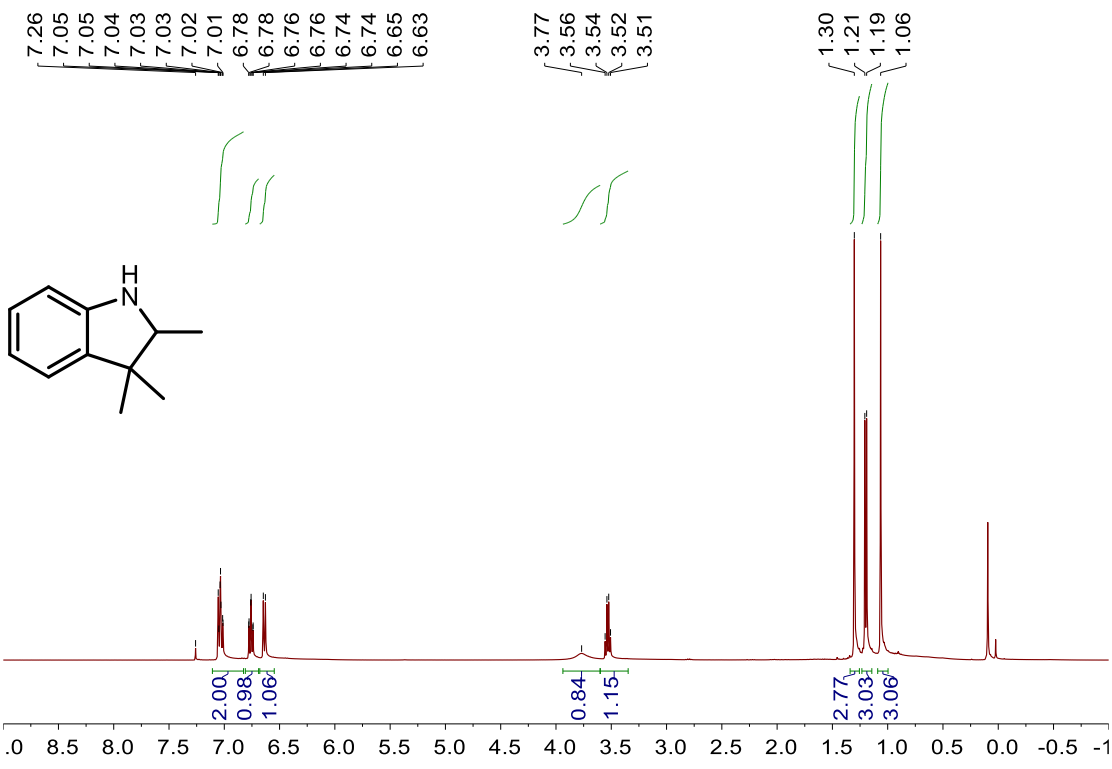
^{13}C NMR spectrum of **4i** (101 MHz, Chloroform-*d*)



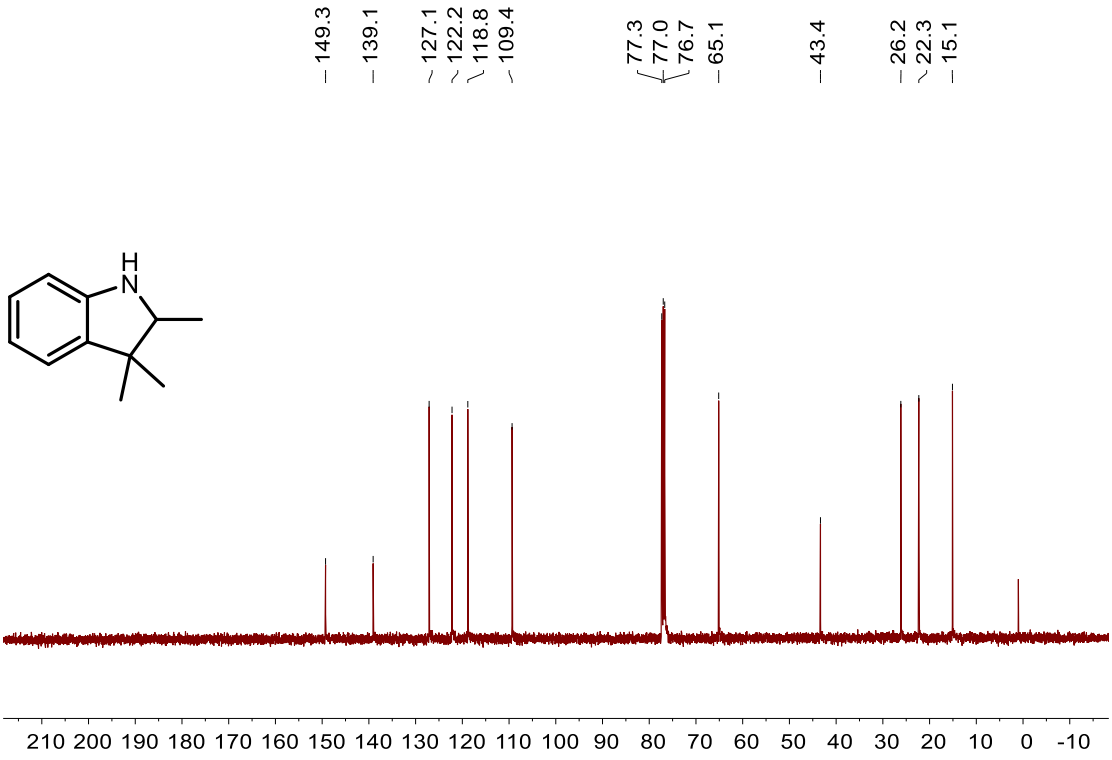
^{1}H NMR spectrum of **4j·HCl** (400 MHz, D_2O)



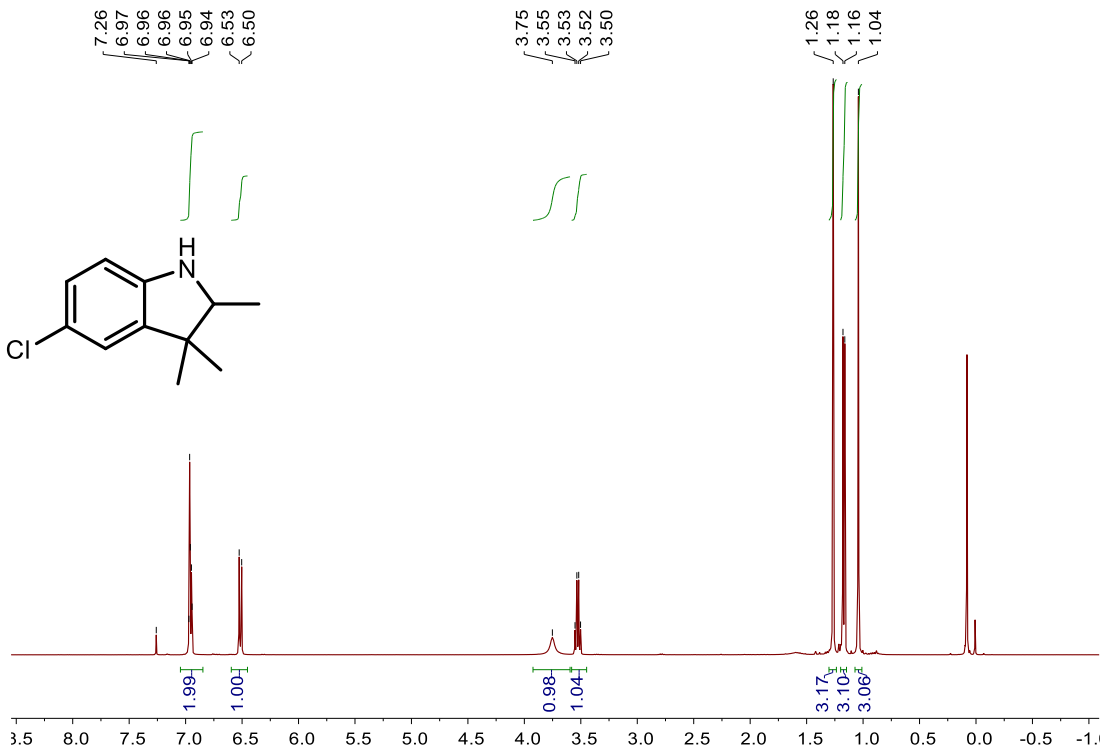
^{13}C NMR spectrum of **4j·HCl** (400 MHz, D_2O)



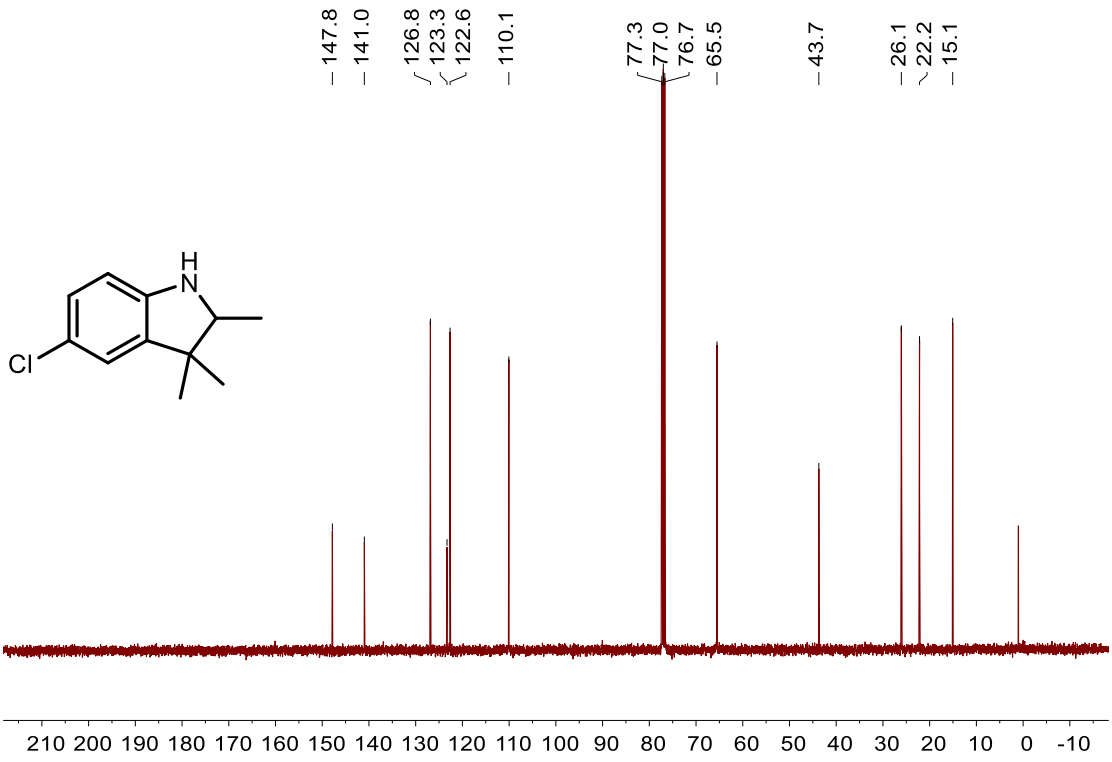
^{1}H NMR spectrum of **4k** (400 MHz, Chloroform-*d*)



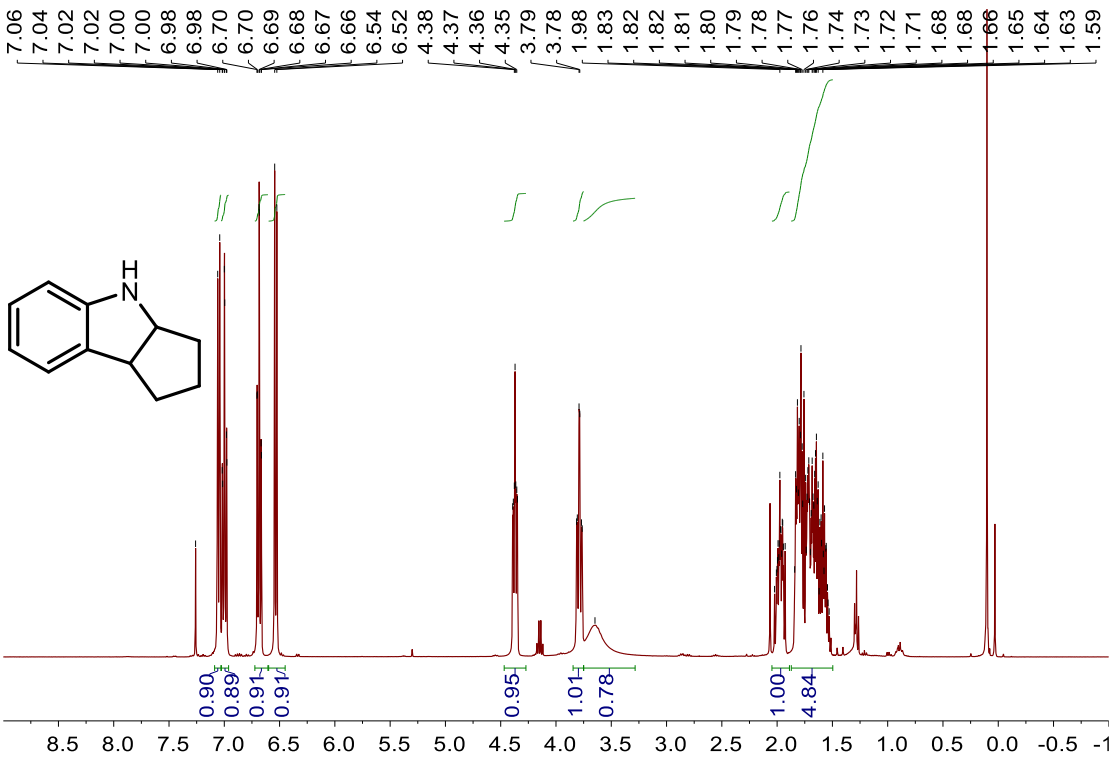
^{13}C NMR spectrum of **4k** (400 MHz, Chloroform-*d*)



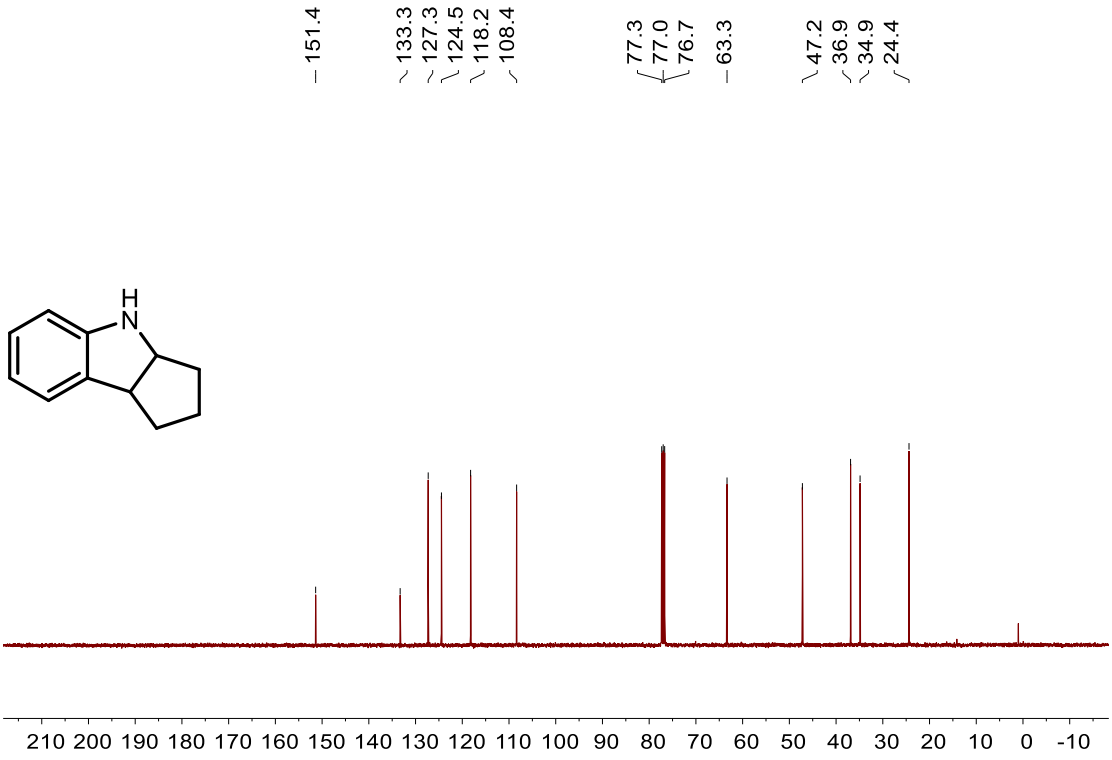
^{1}H NMR spectrum of **4l** (400 MHz, Chloroform-*d*)



^{13}C NMR spectrum of **4l** (400 MHz, Chloroform-*d*)



^{1}H NMR spectrum of **4m** (400 MHz, Chloroform-*d*)



^{13}C NMR spectrum of **4m** (400 MHz, Chloroform-*d*)

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