

Supporting Information

Photoredox C–F Quaternary Annulation Catalyzed by a Strongly Reducing Iridium Species

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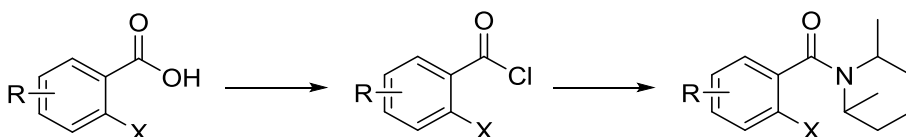
General Information

Commercially available reagents from HEOWNS, J&K Chemical, Energy Chemical were used as received. The solvents used in the reaction were distilled from the appropriate commercially available reagents. All visible-light induced reactions were carried out with standard procedures using Schlenk techniques under nitrogen atmosphere unless otherwise specified. Flash chromatography was performed with 300-400 mesh silica gel purchased from Qingdao Haiyang Chemical Co., Ltd.

^1H NMR spectra were recorded on Bruker Avance III 400 (400 MHz). Chemical shifts were reported in ppm downfield from tetramethylsilane with the solvent resonance as the internal standard (CDCl_3 , $\delta = 7.26$). ^{13}C NMR spectra were acquired on Bruker Avance III 400 (100 MHz). Chemical shifts are reported in ppm downfield from the tetramethylsilane with the solvent resonance as internal standard (CDCl_3 , $\delta = 77.16$). IR spectra were recorded on ThermoFisher Nicolet iS5. High resolution mass spectra were obtained on Agilent system equipped with an ESI source. Emission quenching experiments were performed on HITACHI F-7000FL-5J1-0004. Reverse phase high performance liquid chromatography (RP-HPLC) was performed with Shimadzu SPD-M20A diode array detector and FRC-10A fraction collector using YMC-Park ODS-A column as noted for specific compounds. The enantiomeric excesses of the products were determined by chiral HPLC analysis using Chiralcel OJ-H column or Chiralcel AD-H column as indicated for the specific cases.

1. General Procedure A:

Substituted benzoic acid (10mmol) was suspended in dichloromethane (30mL) and SOCl_2 (2mL) was added. DMF (3 drops) was used as accelerant and the mixture was refluxed for 3h. The reaction was concentrated to dryness under reduced pressure. The crude acid chloride was dissolved in anhydrous dichloromethane and cooled to 0°C with ice-bath. 2,6-Dimethylpiperidine (15mmol) was added and the resulting suspension was stirred at room temperature overnight. When the reaction completed, the mixture was washed with 2 M hydrochloric acid (3 times), saturated NaHCO_3 (3 times) and brine (3 times) in turn, dried over Na_2SO_4 and filtered. Solvent was removed under reduced pressure to yield the crude 2-halobenzamide which was recrystallized from ethyl acetate or purified by flash column chromatography (PE/EA, 9:1, v/v) if necessary.



Scheme S1. General Procedure A

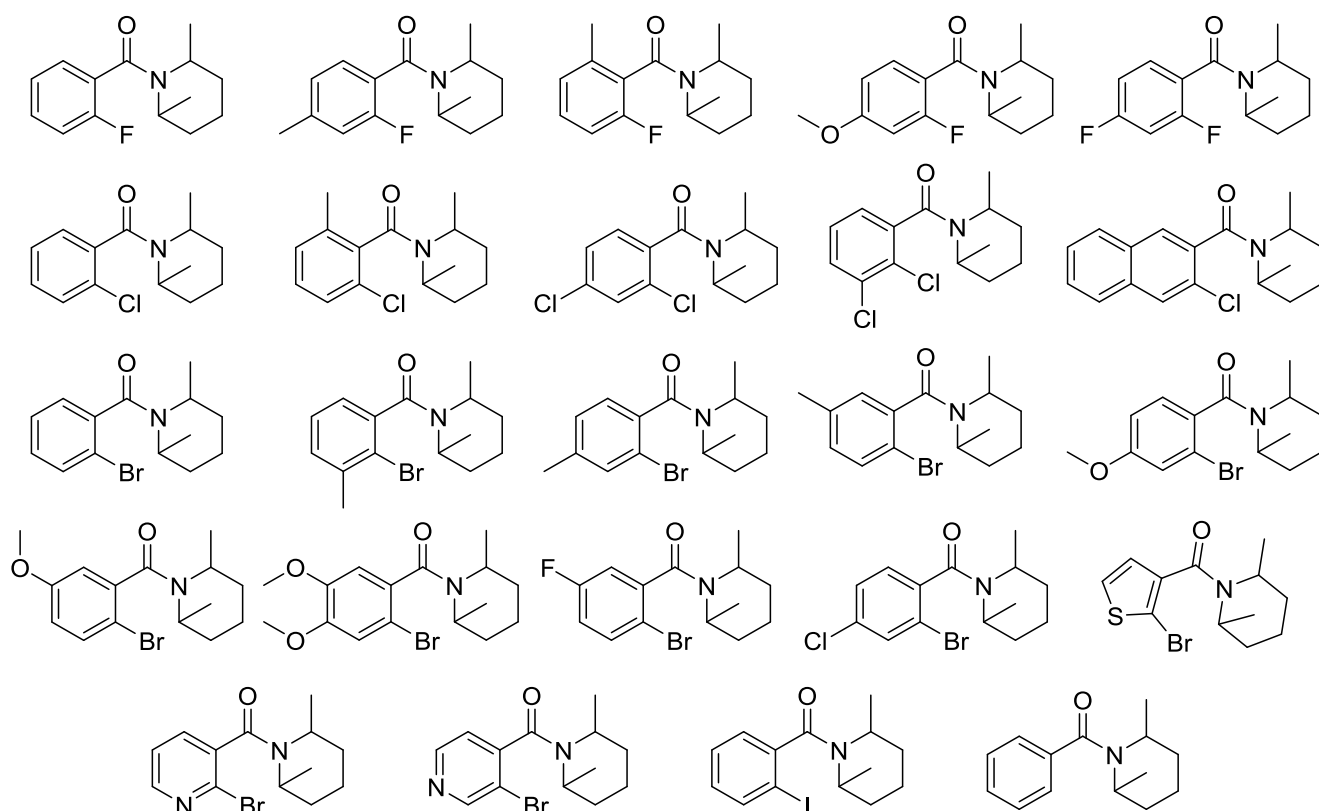
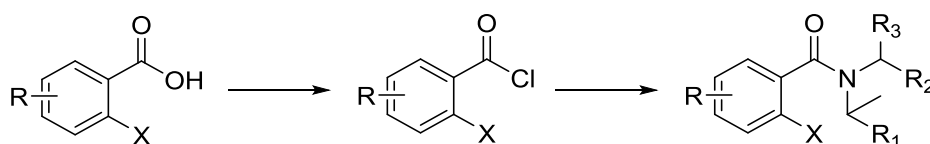


Figure S1. The Synthesized Amide Substrates with Procedure A.

2. General Procedure B:

Substituted benzoic acid (10mmol) was suspended in dichloromethane (30mL) and SOCl_2 (2mL) was added. DMF (3 drops) was used as accelerant and the mixture was refluxed for 3h. The reaction was concentrated to dryness under reduced pressure. The crude acid chloride was dissolved in anhydrous dichloromethane and cooled to 0 °C with ice-bath. The corresponding amine (15mmol) was added and the resulting suspension was stirred at room temperature overnight. When the reaction completed, the mixture was washed with 2 M hydrochloric acid (3 times), saturated NaHCO_3 (3 times) and brine (3 times) in turn, dried over Na_2SO_4 and filtered. Solvent was removed under reduced pressure to yield the crude amide which was recrystallized from ethyl acetate or purified by flash column chromatography (PE/EA, 9:1, v/v) if necessary.



Scheme S2. General Procedure B

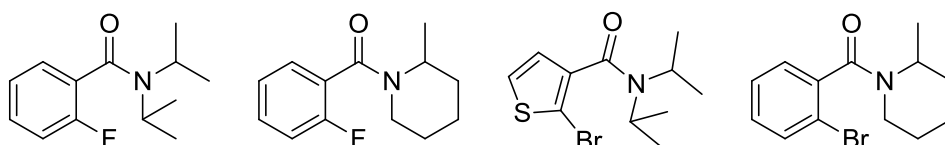
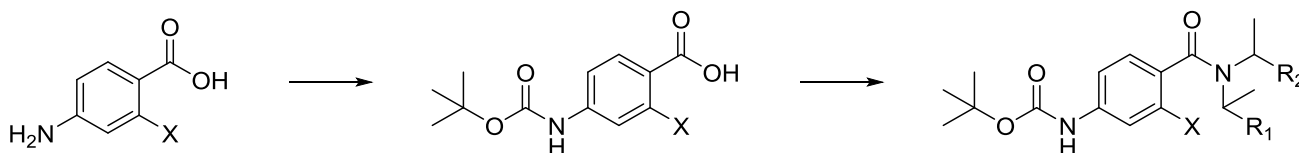


Figure S2. The Synthesized Amide Substrates with Procedure B.

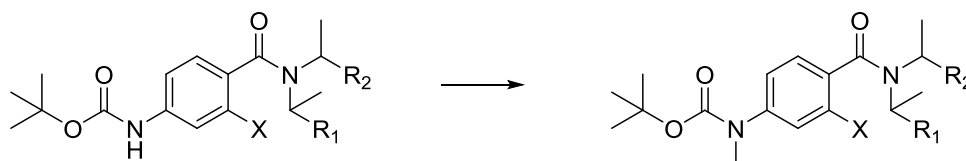
3. General Procedure C:

4-(*t*-Butoxycarbonylamino)-2-halobenzoic acid was acquired according to the literature.^[1] Following the general procedure B, 4-(*t*-Butoxycarbonylamino)-2-halobenzoic acid was reacted with the relevant amine to yield the amide.



Scheme S3. General Procedure C

The Boc-protected amide (10 mmol) and sodium hydride (15 mmol) was dissolved in anhydrous dimethylformamide (40 mL) under argon atmosphere and then the suspension was stirred for 0.5 h. Methyl iodide (15 mmol) was added via syringe and the reaction mixture was stirred overnight at room temperature. The reaction mixture was quenched with water and extracted with diethyl ether (2 × 20 mL). The ether phases were combined and dried over Na₂SO₄. Solvent was removed under reduced pressure to yield the crude amide which was recrystallized from ethyl acetate or purified by flash column chromatography (PE/EA, 9:1, v/v) if necessary.^[2]



Scheme S4. General Procedure C

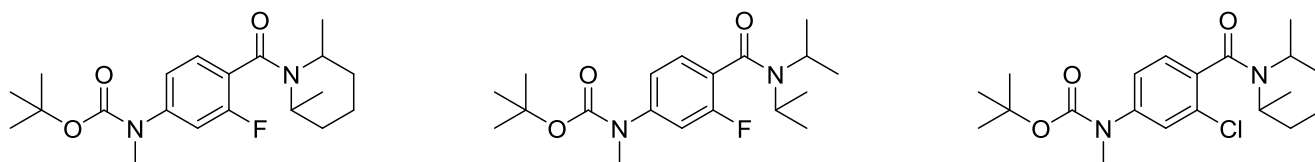
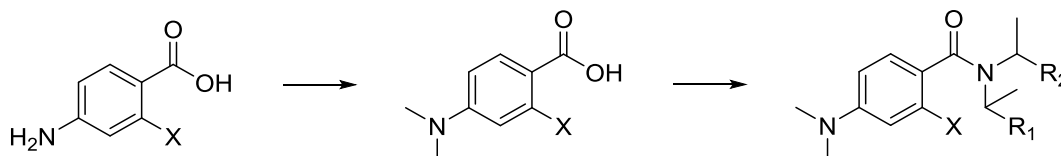


Figure S3. The Synthesized Boc-protected Amide Substrates with Procedure C.

4. General Procedure D:

According to the literature,^[3] 4-amino-2-halobenzoic acid (1.5 g) was dissolved in THF (18 mL) followed by 1.8 mL 20% formaldehyde solution and 0.6 mL glacial acetic acid. After stirring for 1.5h, 0.7 g sodium cyanoborohydride was added and the reaction mixture was stirred for 30 min. After that, 3.7 mL formaldehyde solution was added and the solution was stirred for another 30 min. Then 1.5 g sodium cyanoborohydride was added. The resulting solution was stirred at room temperature overnight. The suspension was filtered and the solvent of filtrate was removed under reduced pressure. The residue was used as 4-amino-2-halobenzoic acid in the preparation of amide according to the general procedure A without further purification.



Scheme S5. General Procedure D

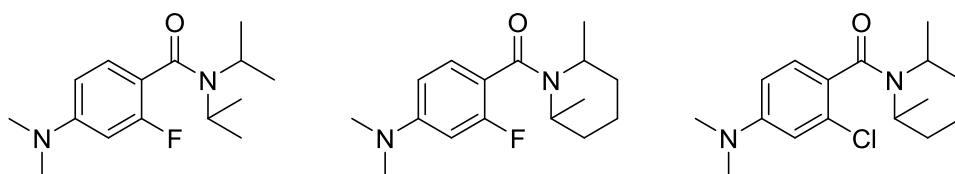
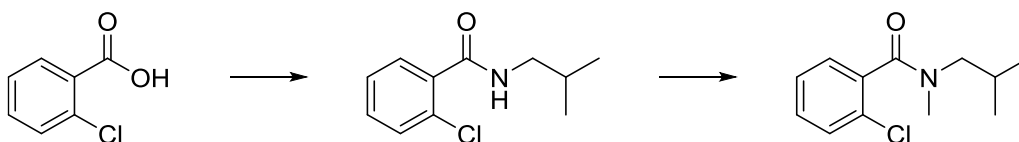


Figure S4. The Synthesized Amide Substrates with Procedure D.

5. Synthesis of 1k

2-chloro-N-isobutylbenzamide was synthesized according to general procedure B with 2-chlorobenzoic acid and 2-methylpropan-1-amine. 2-chloro-N-isobutylbenzamide (10 mmol) and sodium hydride (15 mmol) was dissolved in anhydrous dimethylformamide (40 mL) under argon atmosphere and then the suspension was stirred for 0.5h. Methyl iodide (15 mmol) was added via syringe and the reaction mixture was stirred overnight at room temperature. The reaction mixture was quenched with water and extracted with diethyl ether (2×20 mL). The ether phases were combined and dried over Na_2SO_4 . Solvent was removed under reduced pressure to yield oil product, which was purified by flash column chromatography (PE/EA, 9:1, v/v). 2-Chloro-N-isobutyl-N-methylbenzamide was obtained as light yellow oil.

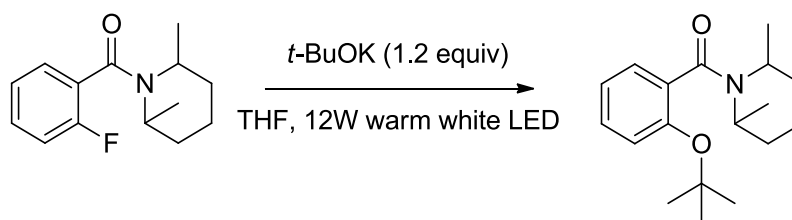


Scheme S6. Synthesis of 1k

6. Control Experiments

6.1 The Procedure for Visible-Light Induced Substitution Reaction without $\text{Ir}(\text{ppy})_3$

$t\text{-BuOK}$ (27 mg, 2.4 mmol, 1.2 eq.) was added into a Schlenk tube charged with **1a** (0.2 mmol, 1.0 eq.) in the glove box. Under N_2 atmosphere, anhydrous THF (2 mL) was added to the tube via syringe. The mixture was stirred with irradiation of 12 W warm white LED strip for 3h. Then the mixture was diluted with distilled water and extracted with EA (3 times). The combined organic layer was washed with brine, dried over Na_2SO_4 , and filtered. Solvent was removed under reduced pressure. The residue was purified by chromatography on silica gel (PE/EA, 5:1, v/v) to yield **3** (6.4 mg, 11%).



Scheme S7a. Reaction in the absence of *fac*- $\text{Ir}(\text{ppy})_3$

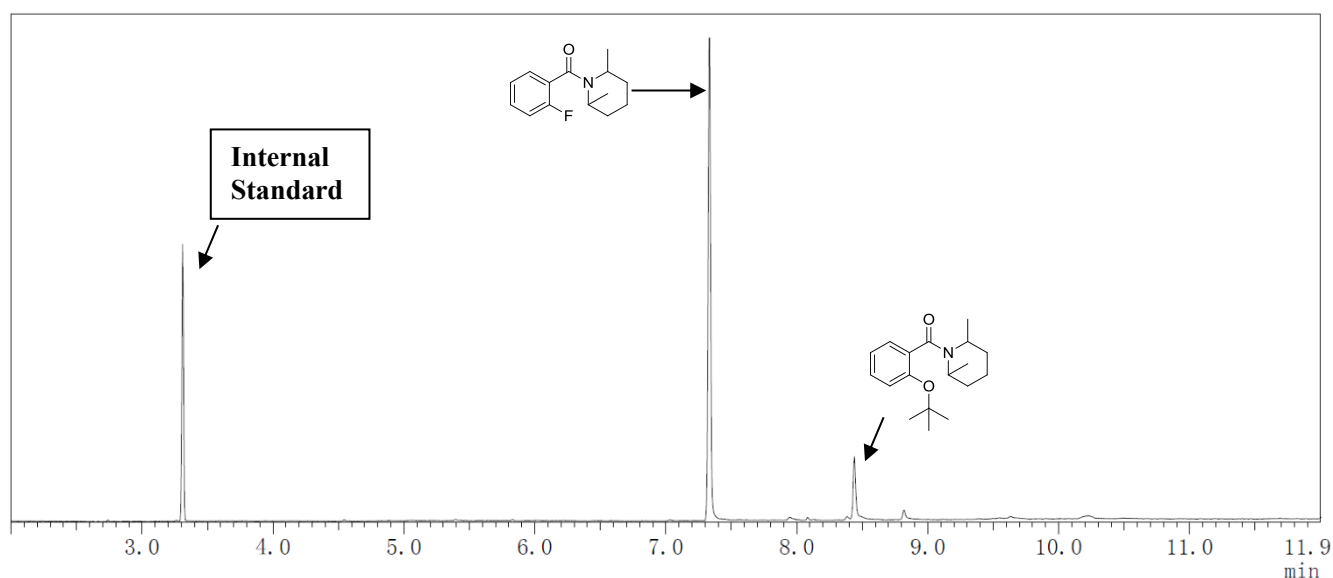
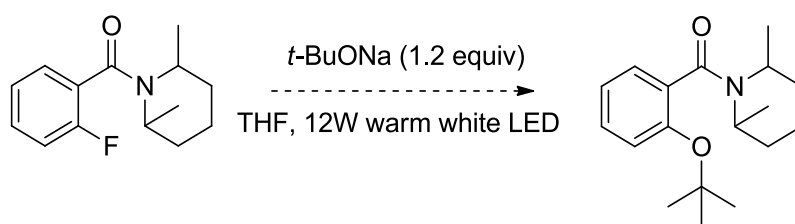


Figure S5a. GC-MS chromatography of **3**.

t-BuONa (23 mg, 2.4 mmol, 1.2 eq.) was added into a Schlenk tube charged with **1a** (0.2 mmol, 1.0 eq.) in the glove box. Under N₂ atmosphere, anhydrous THF (2 mL) was added to the tube via syringe. The mixture was stirred with irradiation of 12 W warm white LED strip for 3h. Then the mixture was diluted with distilled water and extracted with EA (3 times). The combined organic layer was washed with brine, dried over Na₂SO₄, and filtered. The filtrate was monitored by GC-MS.



Scheme S7b. Reaction in the absence of *fac*-Ir(ppy)₃

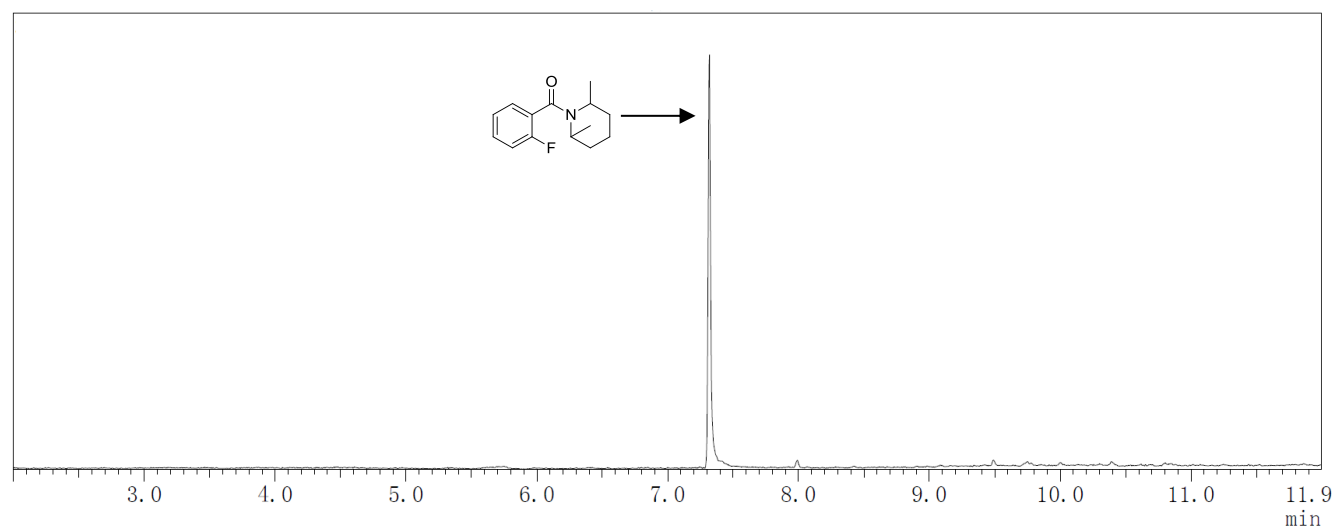
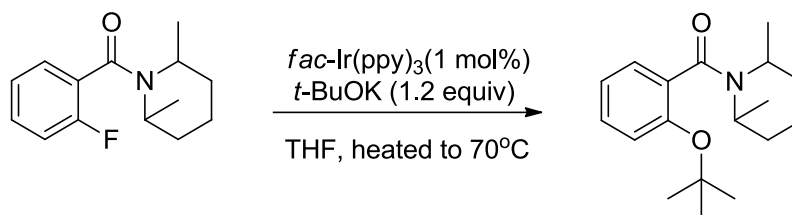


Figure S5b. GC-MS chromatography of reaction with *t*-BuONa.

6.2 The Procedure for Visible-Light Induced Substitution Reaction without Light

t-BuOK (27 mg, 2.4 mmol, 1.2 eq.) was added into a Schlenk tube charged with **1a** (0.2 mmol, 1.0 eq.) in the glove box. Under N₂ atmosphere, anhydrous THF (2 mL) was added to the tube via

syringe. The mixture was heated to 70 °C without light for 12h. Then the mixture was diluted with distilled water and extracted with EA (3 times). The combined organic layer was washed with brine, dried over Na₂SO₄, and filtered. Solvent was removed under reduced pressure. The residue was purified by chromatography on silica gel (PE/EA, 5:1, v/v) to yield **3** (9.9 mg, 17%).



Scheme S7c. Substitution Reaction

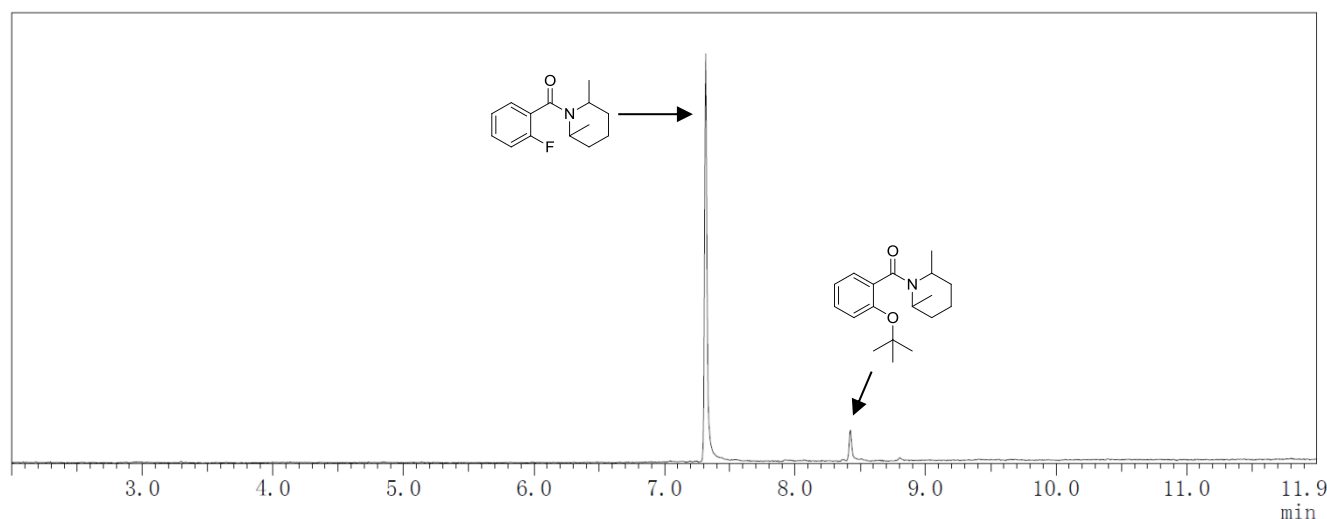
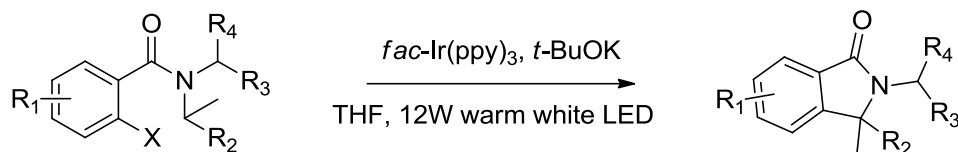


Figure S5c. GC-MS chromatography of **3**.

7. General Procedure E for Visible-Light Induced Intramolecular Quaternary Alkylation

t-BuOK (27 mg, 2.4 mmol, 1.2 eq.) was added into a Schlenk tube charged with *fac*-Ir(ppy)₃ (1.2 mg, 1 mol%) and the corresponding amide (0.2 mmol, 1.0 eq.) in the glove box. Under N₂ atmosphere, anhydrous THF (2 mL) was added to the tube via syringe. The sealed mixture was stirred with irradiation of 12 W warm white LED strip for the given time. During the reaction, the air temperature close to the reaction tube inside the covered reactor was about 70 °C with 1-2 degree variation because the heating generation from warm white LEDs was greater than normal white LEDs. The temperature was detected with a thermometer close to the external wall of sealing tube. Then the mixture was diluted with distilled water and extracted with EA (3 times). The combined organic layer was washed with brine, dried over Na₂SO₄, and filtered. Solvent was removed under reduced pressure. The residue was purified by chromatography on silica gel or semi-preparative RP HPLC if necessary to yield the corresponding product.

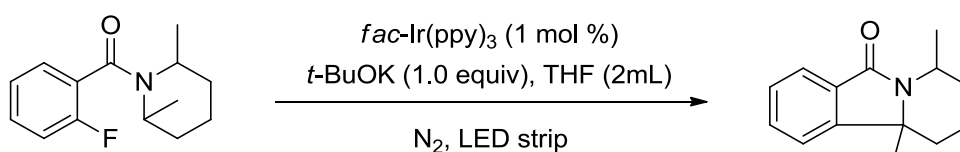


Scheme S8. Photoredox Annulation



8. Optimization of Reaction Conditions

8.1 Light Source Screening

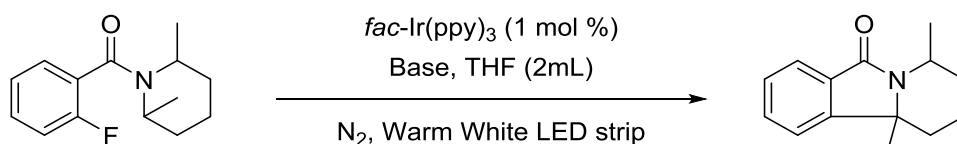


Entry ^a	Light	Time	Yield/% ^b
1	Cold White	12h	63%
2	Warm White	12h	80%
3	Blue	12h	37%
4	Green	12h	3%
5	—	12h	n.d.
6 ^c	—	36h	n.d.
7 ^d	—	12h	n.d.

^a Unless otherwise noted, the reaction of **1a** (0.2 mmol) was carried out in the presence of the catalyst (0.002 mmol, 1 mol%) in solvent (2.0 mL) using a LED strip. ^b Yields were the average of two runs and were determined by GC-MS.

^c Experiment was carried out without light and was heated to 50 °C. ^d Experiment was carried out without light and was heated to 70 °C.

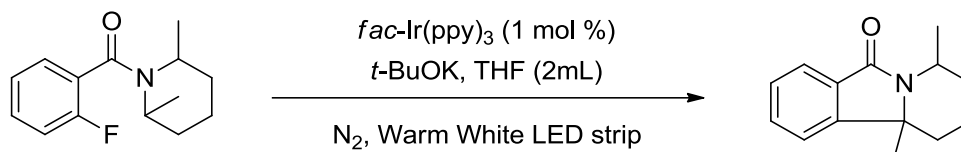
8.2 Base Screening



Entry	Base	Time	Yield/% ^b
1	—	12h	N.R.
2	Cs ₂ CO ₃	12h	N.R.
3	K ₂ CO ₃	12h	N.R.
4	<i>t</i> -BuONa	12h	N.R.

^a Unless otherwise noted, the reaction of **1a** (0.2 mmol) was carried out in the presence of the Catalyst (0.002 mmol, 1 mol%) in THF (2.0 mL) using a warm white LED strip. ^b Yields were determined by GC-MS.

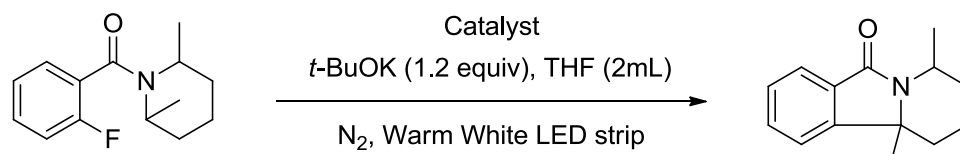
8.3 Base Loading Screening



Entry ^a	Base Loading	Time	Yield/% ^b
1	0.5 eq.	3h	32%
2	1.0 eq.	3h	74%
3	1.2 eq.	3h	100% (93% ^c)
4	1.5 eq.	3h	100%
5	2.0 eq.	3h	100%

^a Unless otherwise noted, the reaction of **1a** (0.2 mmol) was carried out in the presence of the catalyst (0.002 mmol, 1 mol%) in solvent (2.0 mL) using a warm white LED strip. ^b Yields were the average of two runs and were determined by GC-MS. ^c Isolated yield.

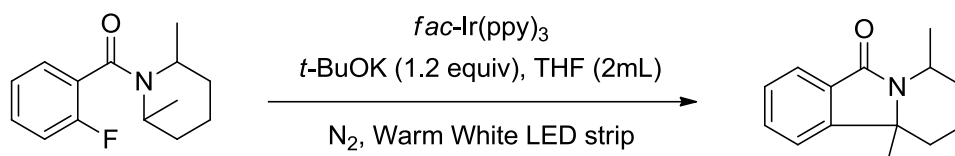
8.4 Catalyst Screening



Entry ^a	Catalyst	Time	Yield/% ^b
1	—	12h	n.d.
2	Safranine T	12h	trace
3	Eosin Y	12h	n.d.
4	Acridine	12h	n.d.
5	Rhodamine B	12h	n.d.
6	Acid Blue	12h	n.d.
7	Fe(OAc)_2	12h	n.d.
8	$\text{Ir(ppy)}_2(\text{dtbppy})\text{PF}_6$	12h	n.d.
9	$\text{Ir[dF(CF}_3\text{)ppy]}_2(\text{dtbppy})\text{PF}_6$	12h	n.d.
10	$fac\text{-Ir(ppy)}_3$	12h	81%

^a Unless otherwise noted, the reaction of **1a** (0.2 mmol) was carried out in the presence of the Catalyst (0.002 mmol, 1 mol%) in THF (2.0 mL) using a warm white LED strip. ^b Yields were the average of two runs and were determined by GC-MS.

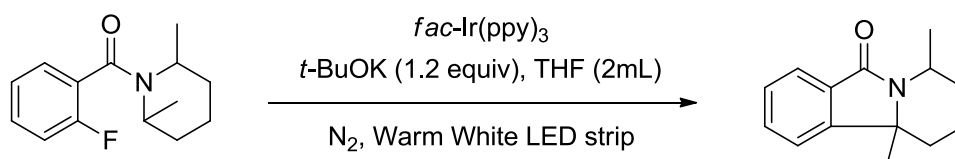
8.5 Catalyst Loading Screening



Entry ^a	Catalyst Loading	Time	Yield/% ^b
1	5 mol%	20h	95%
2	4 mol%	5h	83%
3	3 mol%	5h	90%
4	2 mol%	3h	100%
5	1 mol%	3h	100%
6	0.5 mol%	12h	98%
7	0.1 mol%	12h	98%
8	0.01 mol%	12h	99% (85.2% ^c)
9	0.005% mol%	12h	99% (88% ^c)
10	0.002 mol%	12h	9%
11	—	12h	n.d.

^a Unless otherwise noted, the reaction of **1a** (0.2 mmol) was carried out in the presence of the catalyst in solvent (2.0 mL) using a warm white LED strip. ^b Yields were the average of two runs and were determined by GC-MS. ^c Isolated yield.

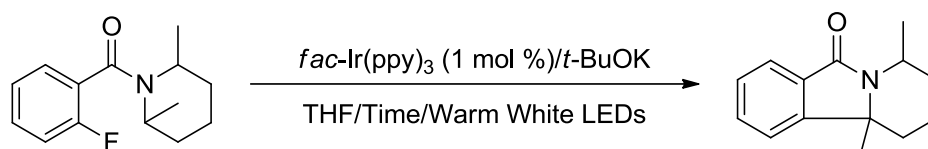
We checked the solubility of *fac*-Ir(ppy)₃ in THF and found 5 mol % *fac*-Ir(ppy)₃ could not dissolved completely at 70 °C. When the catalyst loading decreased to 3 mol%, complete dissolution was achieved. So we measured the conversion of **1a** to annulated product with varied catalyst loading from 3 mol% to at 70 °C in THF. The conversion was detected with GC-MS at 0.5 h, 1 h, 1.5 h, 2h, and 3h.



Entry ^a	Time	Yield/% ^b			
		5 mol%	1 mol%	0.1 mol%	0.005 mol%
1	0.5h	3%	3%	4%	trace
2	1h	40%	20%	21%	3%
3	1.5h	72%	44%	44%	5%
4	2h	85%	54%	56%	8%
5	3h	92%	69%	76%	18%

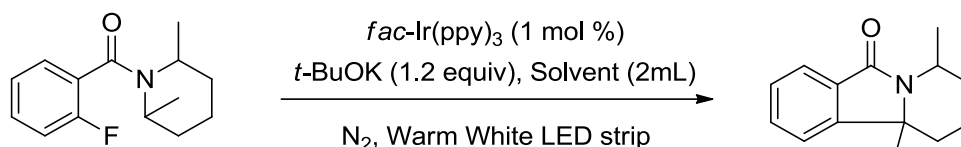
^a Unless otherwise noted, the reaction of **1a** (0.2 mmol) was carried out in the presence of the catalyst in solvent (2.0 mL) using a warm white LED strip. ^b Yields were the average of two runs and were determined by GC-MS.

In the above table, the conversion was slower in comparison with the result in table 1 of manuscript. In this catalyst loading experiments, the Teflon screwed Schlenk tube was used in the reaction with THF as solvent. Samplings at different time points required open of the Teflon screw cap. Because the reaction temperature was at 70 °C, higher than the boiling point of THF, it not safe to open the Teflon screw cap immediately after taking the sealing tube from light source. We used a general operation to let the reaction cool down for a while (ca. 5 minutes), open the Teflon screw cap, sampling, sealing again and move the Schlenck tube back to the original position in the light source. After several sampling operation, the difference got significant. To minimize this effect, five reactions with 1 mol % *fac*-Ir(ppy)₃ without sampling was carried out. Each reaction stopped and measured the conversion with GC-MS at different reaction time. The results listed below suggested that the conversion was similar to that found in the initial condition optimization. This experiment was repeated twice and the results were parallel. The data in the table were the average of two runs.



Time	0.5h	1h	1.5h	2h	3h
GC-MS Yields	7%	42%	65%	80%	98%

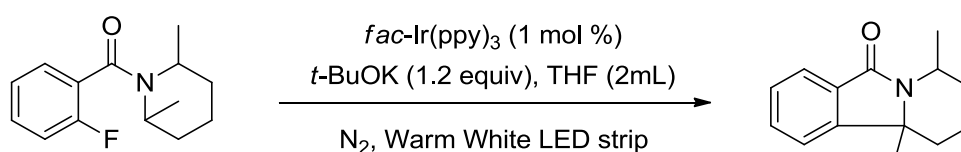
8.6 Solvent Screening



Entry ^a	Solvent	Time	Yield/% ^b
1	CH ₃ CN	3h	trace
2	Toluene	3h	99%
3	MBTE	3h	98% (86.5% ^c)
4	DCE	3h	N.R.
5	DMSO	3h	N.R.
6	DMF	3h	7%
7	MeOH	3h	N.R.
8	Dioxane	3h	89%
9	DCM	3h	N.R.
10	Pentane	3h	N.R.

^a Unless otherwise noted, the reaction of **1a** (0.2 mmol) was carried out in the presence of the catalyst (0.002 mmol, 1 mol%) in solvent (2.0 mL) using a warm white LED strip. ^b Yields were the average of two runs and were determined by GC-MS. ^c Isolated yield.

8.7 Temperature Screening

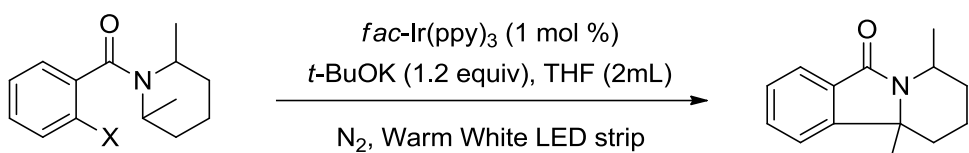


Entry ^a	Time	Yield/% ^b
1 ^c	20h	55%
2 ^d	20h	N.R.

^a Unless otherwise noted, the reaction of **1a** (0.2 mmol) was carried out in the presence of the catalyst (0.002 mmol, 1 mol%) in solvent (2.0 mL) using a warm white LED strip. ^b Yields were the average of two runs and were determined by GC-MS. ^c Reaction temperature was cooled to 47.5 °C. ^d Reaction temperature was cooled to 22 °C.

9. Relative Reactivity of Aryl Fluorides, Chlorides and Bromides

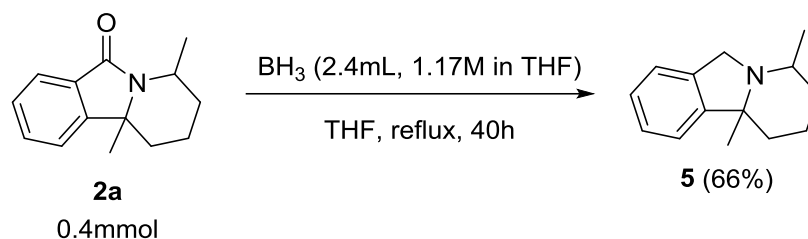
As mentioned in Section 8.7, **1a** would not convert to **2a** when the reaction temperature was cooled to room temperature. So the relative reactivity was compared between aryl chlorides (**1j** was taken as an example) and bromides (**1o** was taken as an example) according to the different GC-MS yields tested at the same time.

		
Time ^a	Yield/% ^b	
	Cl	Br
10 min	2%	13%
20 min	10%	38%
40 min	31%	73%
60 min	56%	90%
80 min	72%	95%

^a The reaction of **1j** or **1o** (0.2 mmol) was carried out in the presence of the Catalyst (0.002 mmol, 1 mol%) in THF (2.0 mL) using a LED strip. Reaction temperature was cooled to 22 °C. ^b Yields were determined by GC-MS.

10. Synthesis of 5

To a THF solution (4 mL) of **2a** (86 mg, 0.4 mmol) was added 1.17 M borane/THF solution (2.40 mL) while stirring at 0 °C. The mixture was refluxed for 40 h. The reaction was monitored by TLC until completion. 4 mL of 1 M hydrochloric acid was added to the reaction system with cooling and then refluxed for 1 h. The reaction was made basic with aqueous 5 M NaOH solution and then extracted three times with chloroform. The combined organic layer was washed with brine, dried over Na₂SO₄ and the solvent was evaporated away under reduced pressure. The crude product was purified by chromatography on silica gel (PE/EA = 95:5, v/v) to yield **5** (53 mg, 66%) as pale yellow oil.^[4]



Scheme S9. Synthesis of **5**

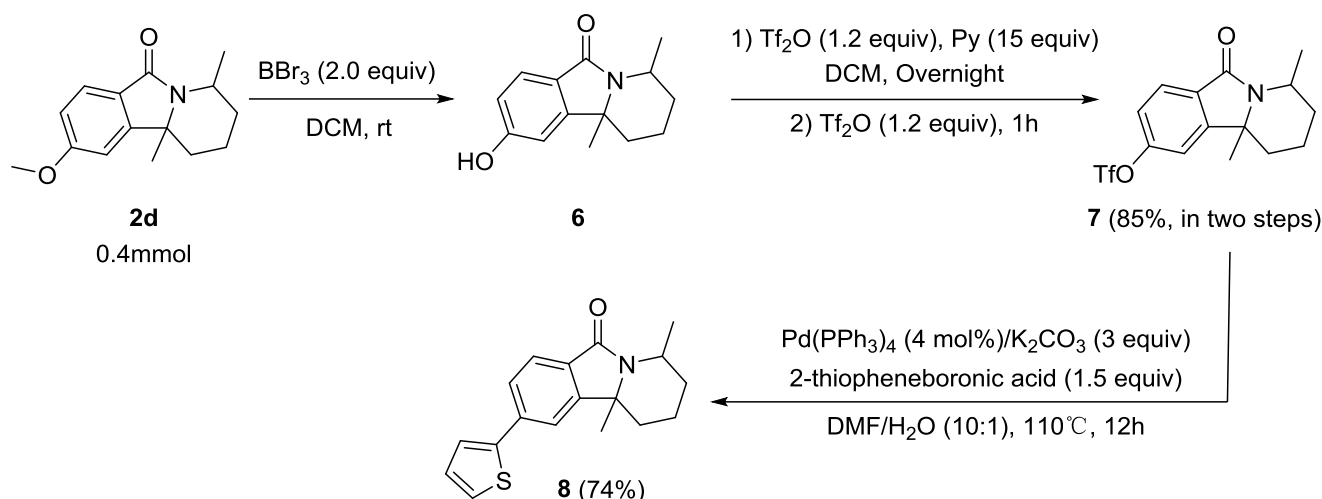
11. Synthesis of 8

An oven-dried 10 mL flask was charged with **2d** (100 mg, 0.4 mmol) and dry DCM (3 mL) under N₂ atmosphere. BBr₃ (204 mg, 1 M in DCM) was added dropwise into the mixture at room temperature. Stirring was kept while the reaction was monitored by TLC. Upon completion, ice-water was added and the aqueous phase was extracted three times with ethyl acetate. The combined organic layer was washed with brine, dried over Na₂SO₄ and filtered. Solvent was removed under reduced pressure to give the crude product which was used in the next step without further purification.

The crude product acquired in the last step was dissolved in anhydrous DCM (2 mL). Pyridine (0.5 mL) and trifluoromethanesulfonic anhydride (136 mg) was added dropwise at 0 °C. The resulting mixture was further stirred at room temperature overnight. Afterwards, additional trifluoromethanesulfonic anhydride (136 mg) was added. The solution was stirred at room temperature for another 1 h. Then the resulting mixture was washed with brine, dried over Na₂SO₄, and evaporated under reduced pressure to yield the OTf-protected product as light yellow oil which was further purified by chromatography on silica gel (PE/EA = 9:1, v/v) to give white solid (123 mg, 85%, two

steps).^[5]

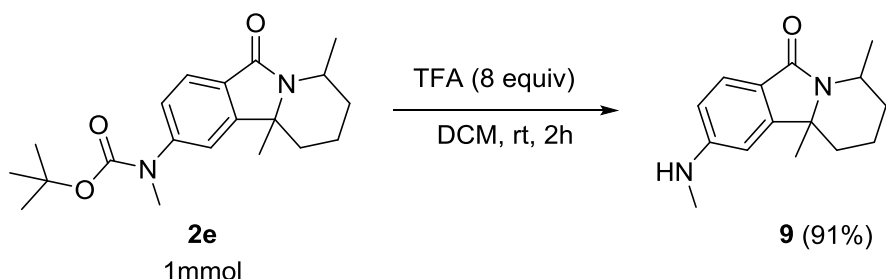
The white solid (36.3 mg, 0.1 mmol) obtained in the last step, 2-thiopheneboronic acid (19.2 mg, 0.15 mmol), Pd(PPh₃)₄ (5 mg, 4 mol%), K₂CO₃ (41.5 mg), distilled water (0.15 mL) was suspended in DMF (1.5 mL). The resulting mixture was stirred at 110 °C for 12h. The heating was removed and the reaction mixture was filtered through a short pad of silica gel. The filtrate was extracted with EtOAc/Et₂O (1:1) for three times. The combined organic layers were washed with saturated NaCl solution for three times and dried over Na₂SO₄. Solvent was removed and the crude residue was purified by silica gel chromatography (PE/EA = 9:1, v/v) to yield the coupling product (22 mg, 74%).^[6]



Scheme S10. Synthesis of **8**

12. Synthesis of **9**

The Boc-protected amide **2e** (1 mmol) was dissolved in a stirred mixture of dichloromethane (10 mL) and trifluoroacetic acid (0.6 mL). The mixture was stirred at room temperature for 2h. The resulting solution was washed with saturated aqueous sodium bicarbonate solution (3 times), dried over Na₂SO₄ and filtered. Solvent was removed under reduced pressure and the resulting residue was purified by chromatography on silica gel (PE/EA = 9:1, v/v) to give product **9** (222.2 mg, 91%).



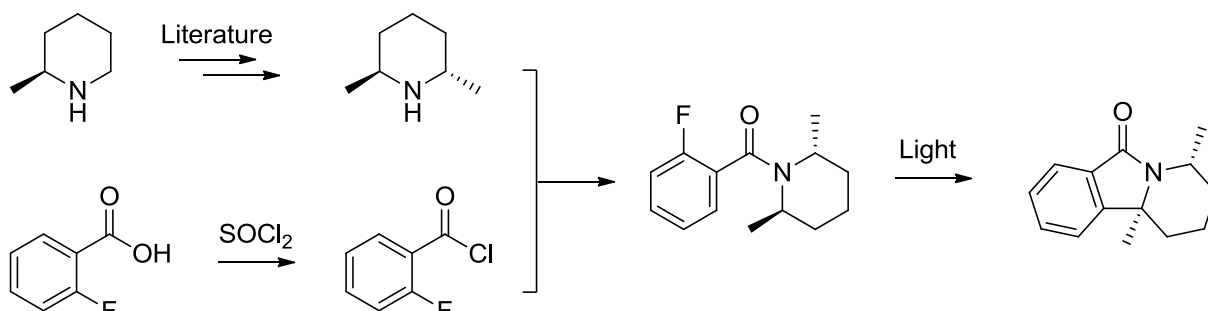
Scheme S11. Synthesis of **9**

13. Substrate-induced Enantioselectivity Transformation

trans-(+)-2,6-Lupetidine was successfully prepared according to the literature.^[7] Following general procedure A, *trans*-(+)-**1a** ($[\alpha]_D^{26.4} = +70.6^\circ$ (CHCl_3 , $c=0.05$, 86% ee)) of 86% ee was synthesized with 2-fluorobenzoic acid and *trans*-(+)-2,6-lupetidine. GC-MS retention time of *trans*-**1a**

was different from *cis*-**1a**. The enantiomeric excesses of *trans*-(+)-**1a** was determined by chiral HPLC analysis on a Chiralcel OJ-H column (**Figure S7c**). *Rac-trans*-(±)-2,6-lupetidine was also prepared according to the same literature except with *rac*-(±)-2-methylpiperidine. Following general procedure A, *rac-trans*-(±)-**1a** was easily acquired with 2-fluorobenzoic acid and *rac-trans*-(±)-2,6-lupetidine. GC-MS analysis showed only one peak, which is totally different from *cis*-**1a**. Chiral HPLC equipped with Chiralcel OJ-H column showed two peaks, one for each enantiomer, with the peak area ratio of 1:1 (**Figure S7b**).

Following general procedure E, *trans*-(+)-**1a** of 86% ee afforded *cis*-(+)-**2a** ($[\alpha]_D^{27.2} = +19.0^\circ$ (CHCl₃, *c* 0.38, 86% ee)) as the only diastereomer in 90% yield with no loss of ee as judged by chiral HPLC equipped with Chiralcel AD-H column (**Figure S9b**). When *rac-trans*-(±)-**1a** was employed, *rac-cis*-(±)-**2a** was obtained as the only diastereomer in 91% yield as judged by chiral HPLC equipped with Chiralcel AD-H column (**Figure S9a**).



Scheme S12. Synthesis of *trans*-(+)-**1a** and *cis*-(+)-**2a**

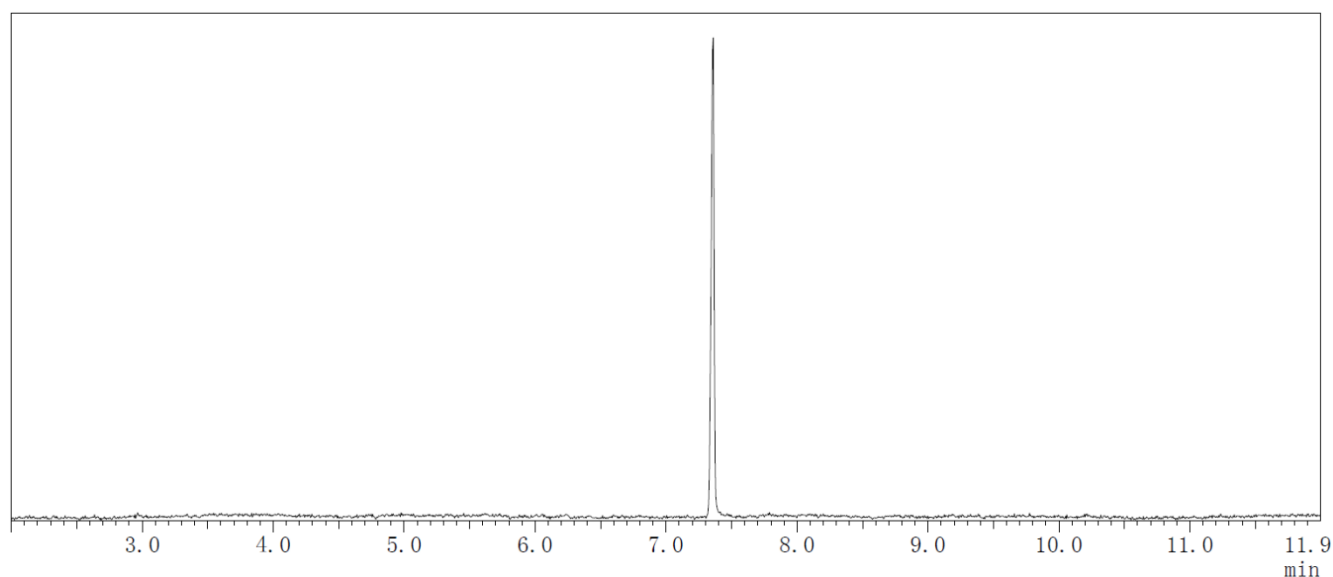


Figure S6a. GC-MS Monitoring of *cis*-**1a**.

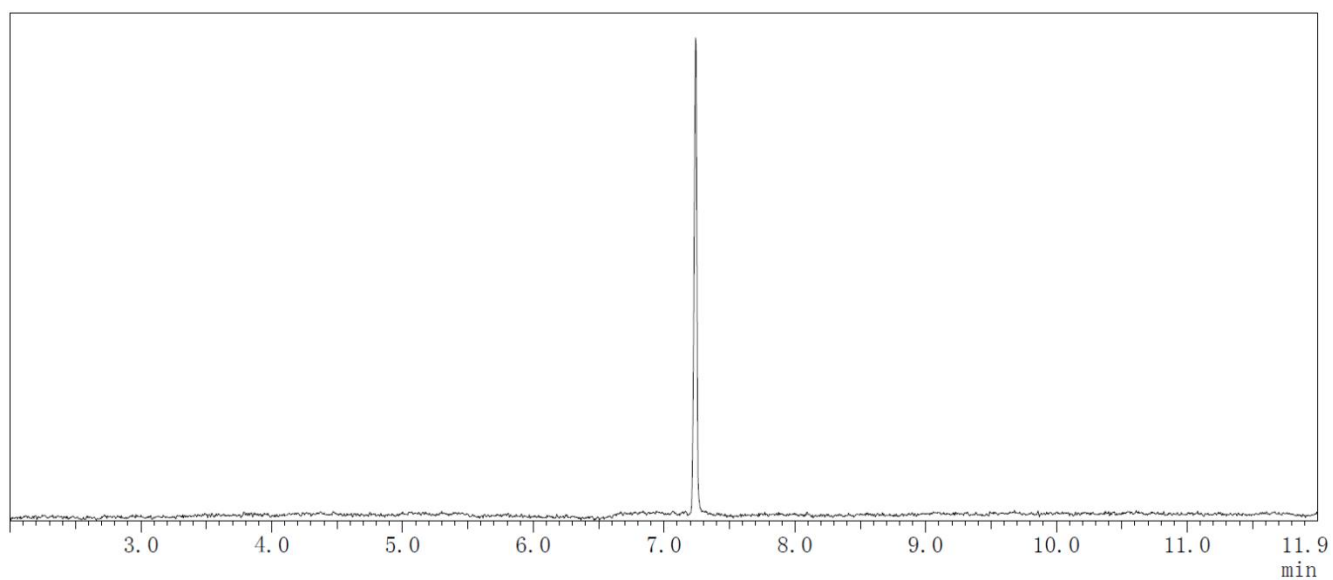


Figure S6b. GC-MS Monitoring of *rac-trans*-(\pm)-**1a**.

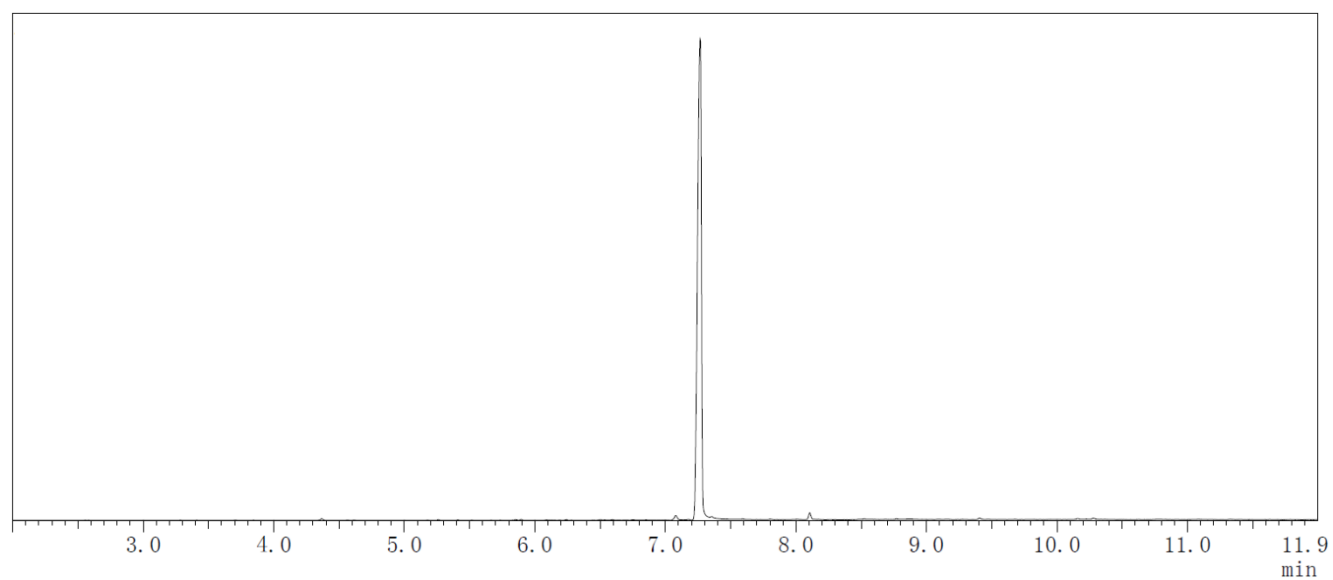


Figure S6c. GC-MS Monitoring of *trans*-(+)-**1a**.

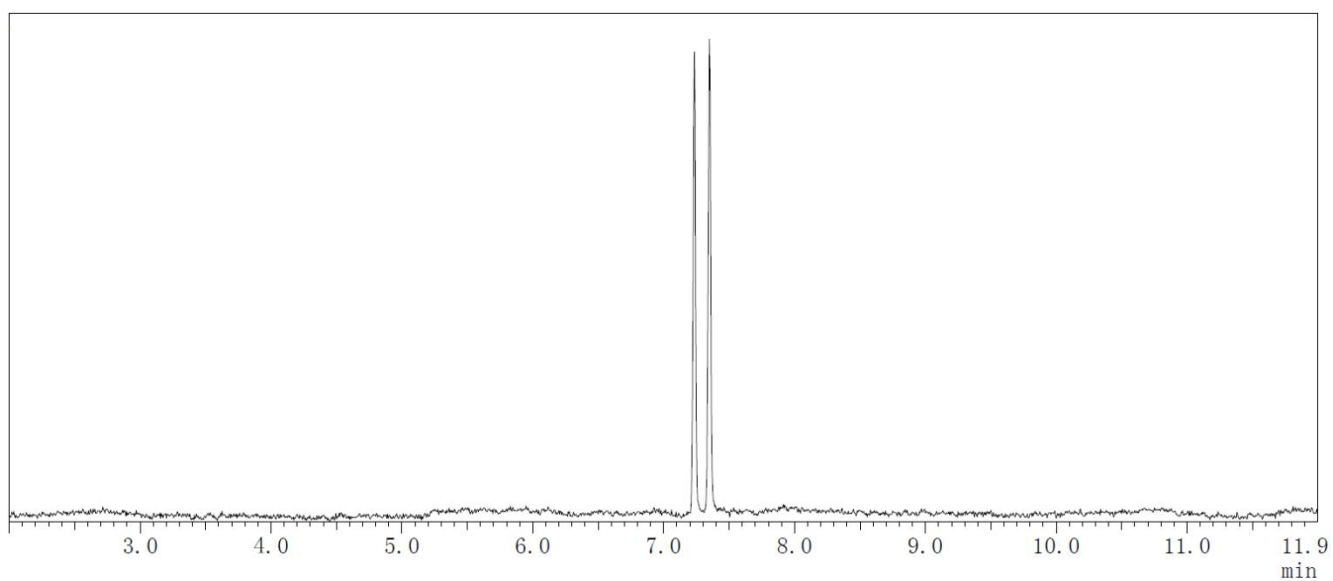


Figure S6d. GC-MS Monitoring of the mixture of *cis*-**1a** and *rac-trans*-(\pm)-**1a**.

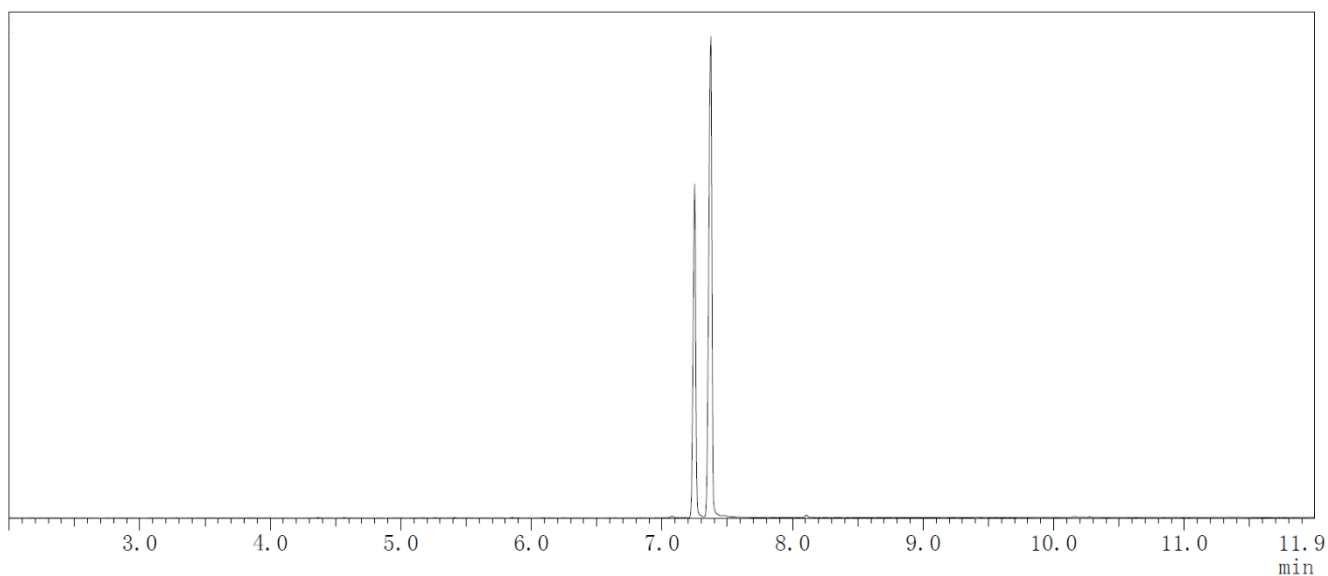


Figure S6e. GC-MS Monitoring of the mixture of *cis*-**1a** and *trans*-(+)-**1a**.

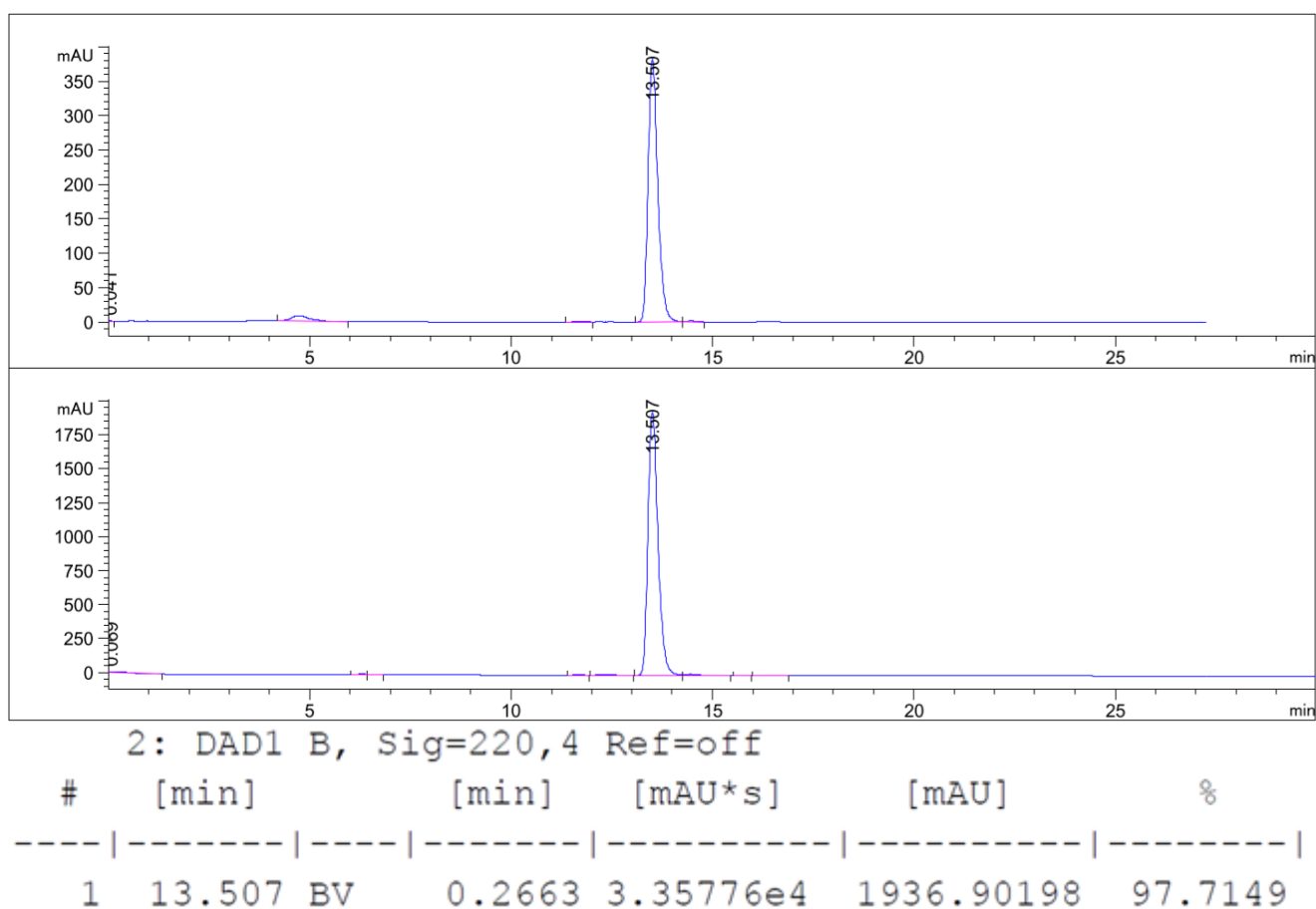
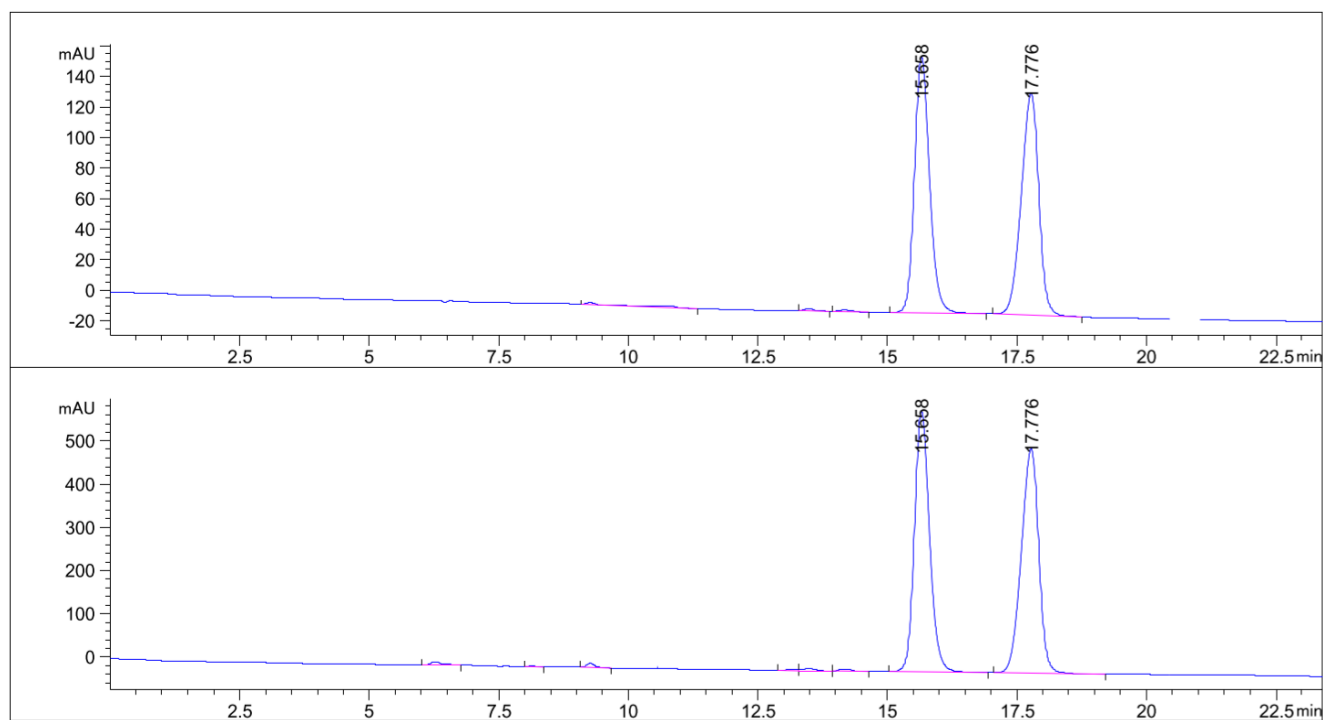


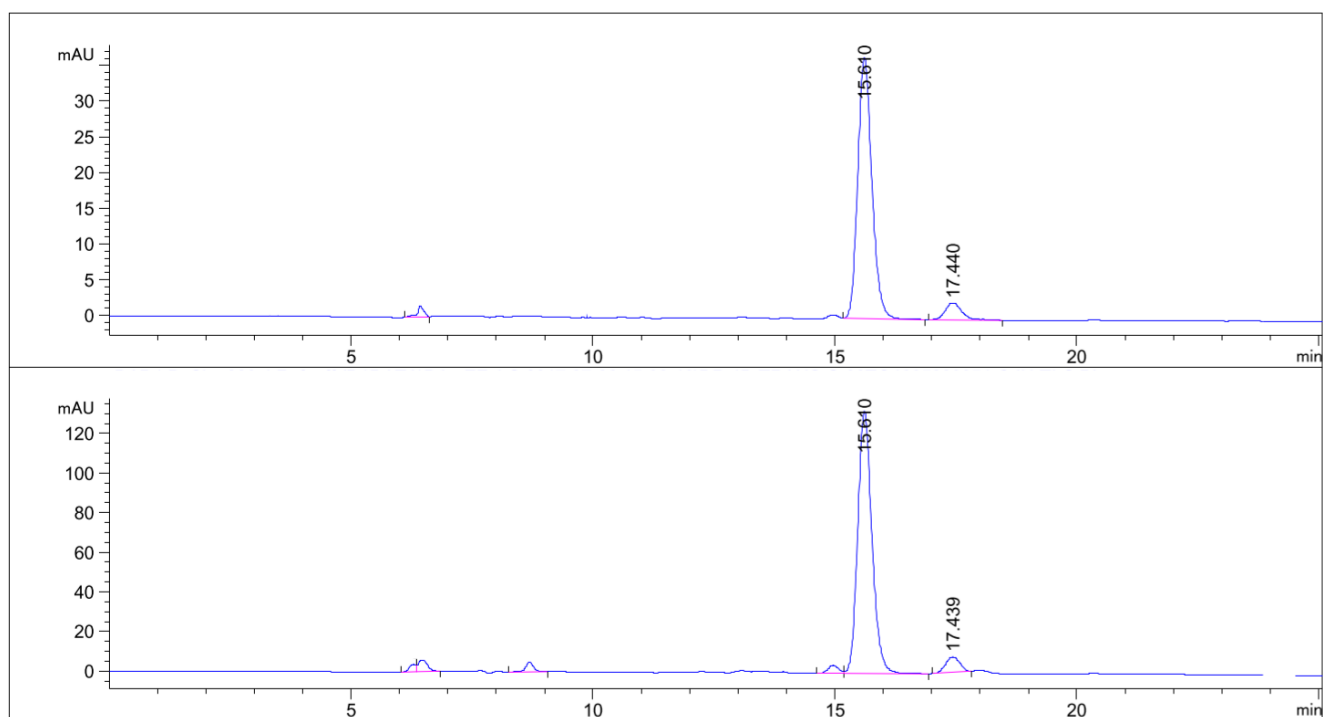
Figure S7a. Chiral HPLC Enantiomeric Excess Spectra of *cis*-**1a** (HPLC conditions: Chiralcel OJ-H column, 220 nm & 254nm, flow rate: 0.5 ml/min, *i*-PrOH/hexanes = 1/9, t = 13.507 min).



2: DAD1 B, Sig=220,4 Ref=off

#	[min]		[min]	[mAU*s]	[mAU]	%
1	15.658	BB	0.3113	1.21362e4	601.71521	49.2009
2	17.776	BBA	0.3617	1.20758e4	518.46271	48.9559

Figure S7b. Chiral HPLC Enantiomeric Excess Spectra of *rac-trans*-(±)-**1a** (HPLC conditions: Chiralcel OJ-H column, 220 nm & 254nm, flow rate: 0.5 ml/min, *i*-PrOH/hexanes = 1/9, t_1 = 15.058 min, t_2 = 17.776 min).



1: DAD1 A, Sig=254,4 Ref=off						
#	[min]		[min]	[mAU*s]	[mAU]	%
1	15.610	BB	0.3124	739.59113	36.49695	91.2989
2	17.440	BB	0.3537	56.27003	2.36373	6.9463

Figure S7c. Chiral HPLC Enantiomeric Excess Spectra of *trans*-(+)-**1a** (HPLC conditions: Chiralcel OJ-H column, 220 nm & 254nm, flow rate: 0.5 ml/min, *i*-PrOH/hexanes = 1/9, t_{major} = 15.610 min, t_{minor} = 17.440 min; 86% ee.).

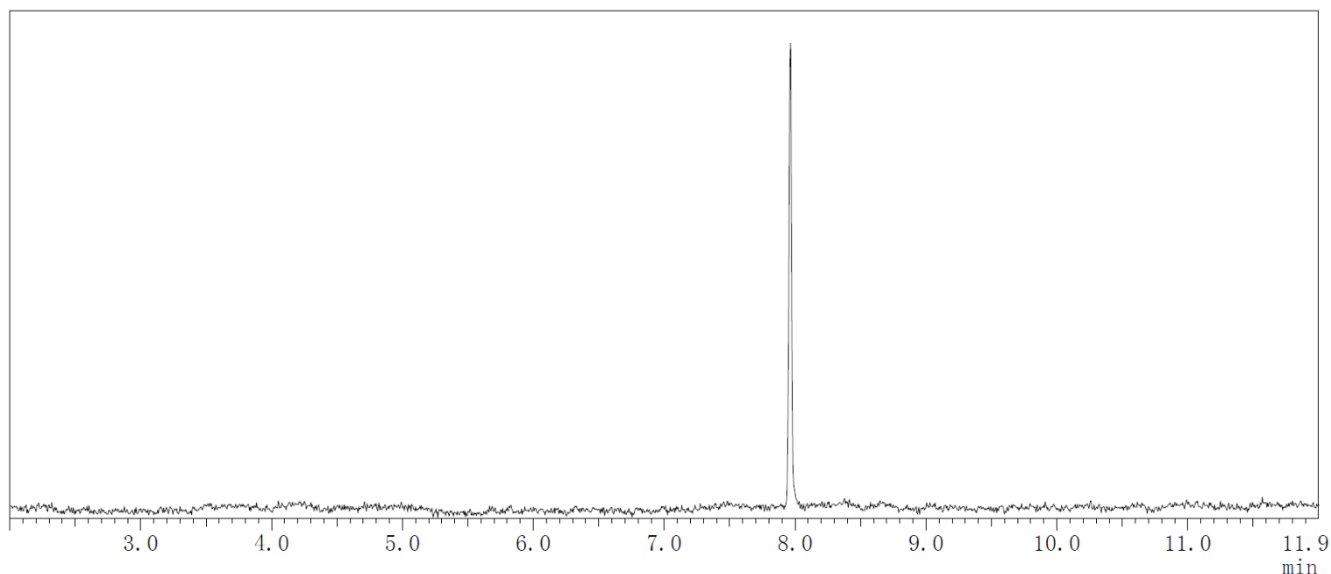


Figure S8a. GC-MS Monitoring of racemic *cis*-**2a**.

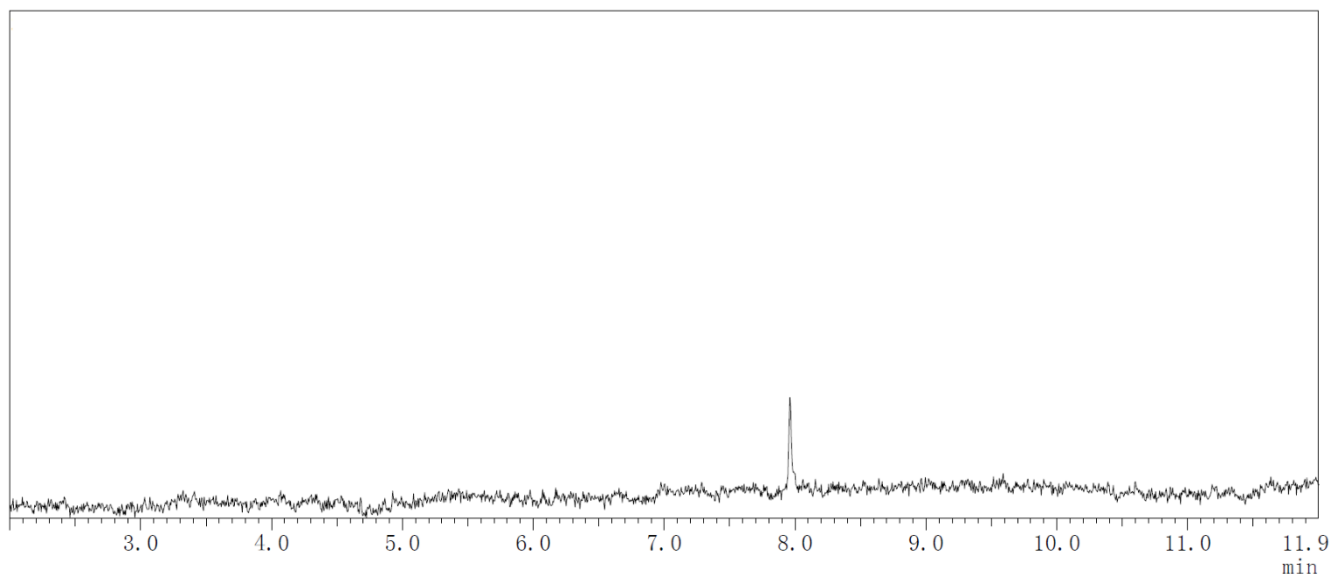


Figure S8b. GC-MS Monitoring of product in Scheme S12.

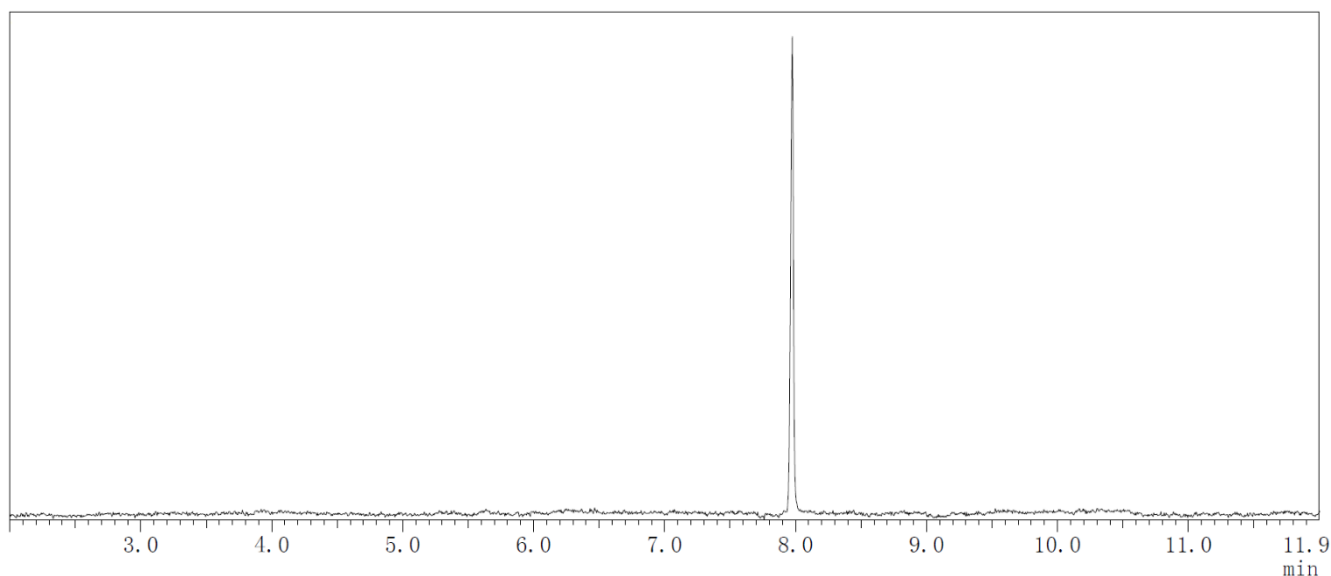
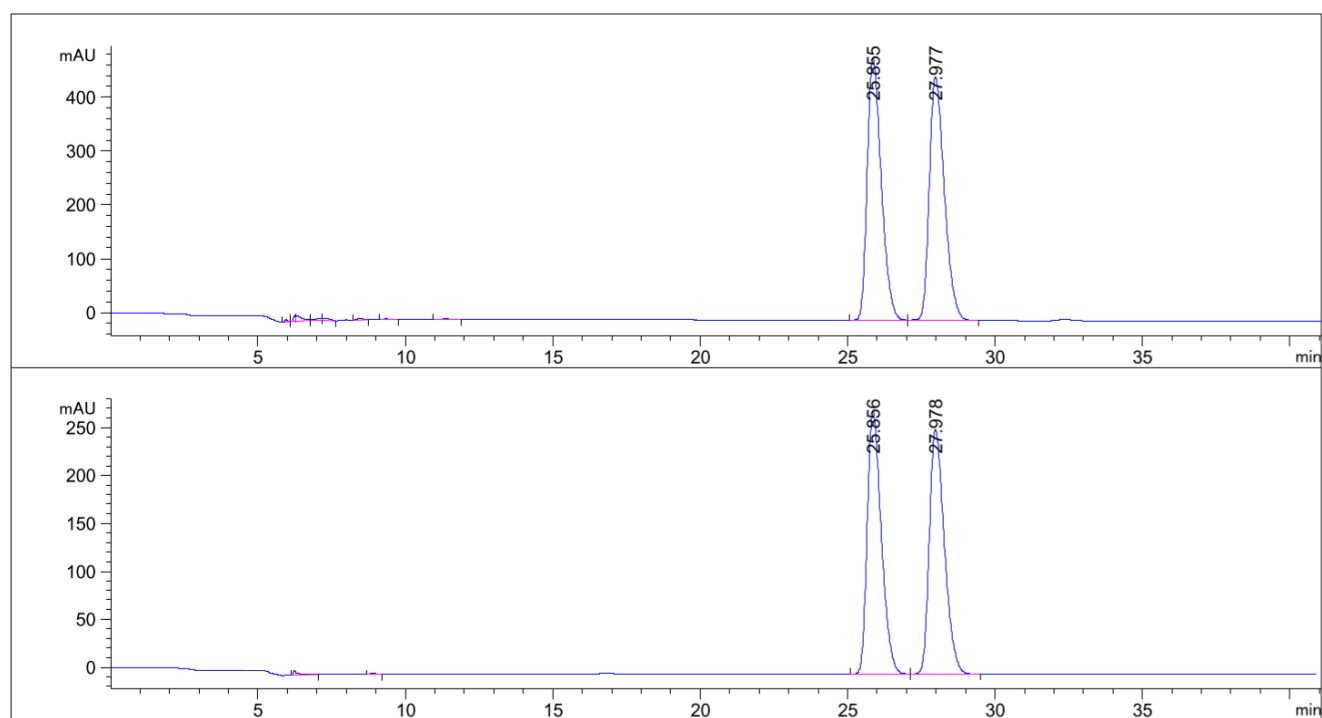


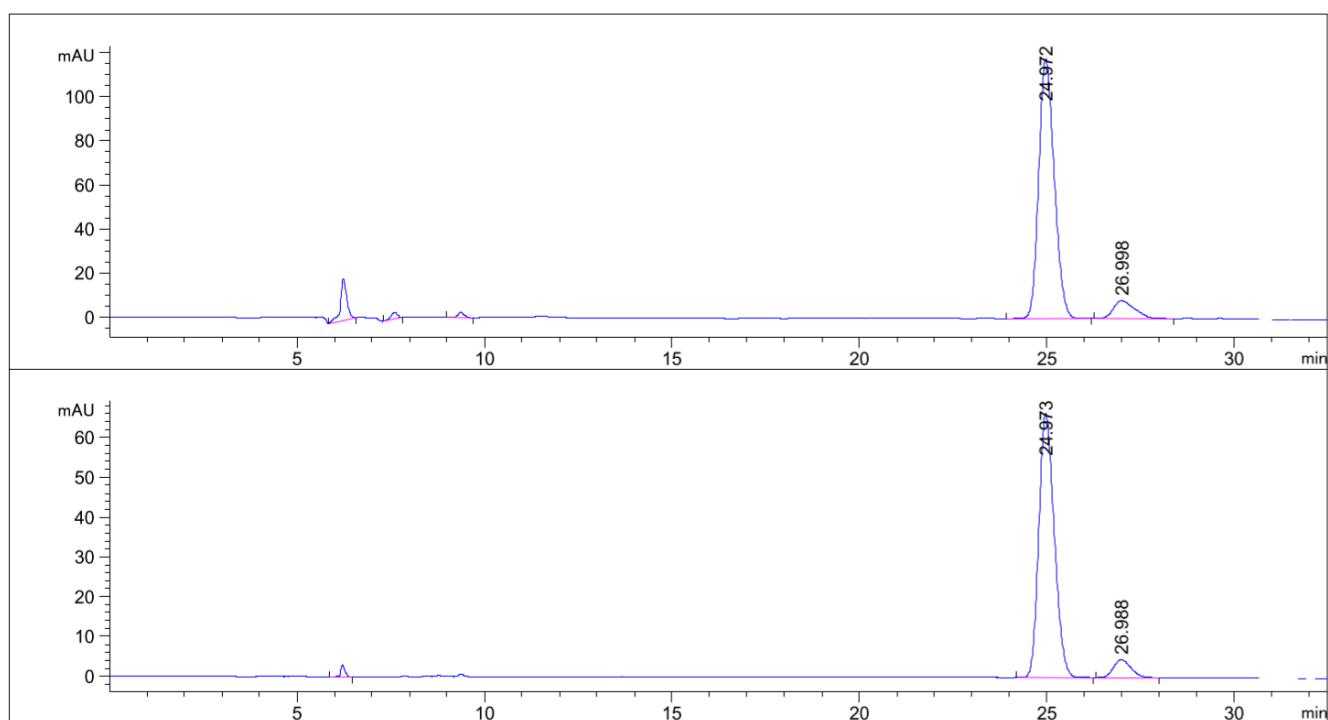
Figure S8c. GC-MS Monitoring of the mixture of *cis*-**2a** and product from **Scheme S12**.



2: DAD1 B, Sig=254,4 Ref=off

#	[min]		[min]	[mAU*s]	[mAU]	%
1	25.856	BB	0.5043	9014.13867	273.64005	49.8115
2	27.978	BB	0.5419	9010.92773	255.24171	49.7937

Figure S9a. Chiral HPLC chromatography of *cis*-**2a** (HPLC conditions: Chiralcel AD-H column, 220 nm & 254nm, flow rate: 0.5 ml/min, *i*-PrOH/hexanes = 1/19, t_1 = 25.9 min, t_2 = 8.0 min).



2: DAD1 B, Sig=254,4 Ref=off

#	[min]		[min]	[mAU*s]	[mAU]	%
1	24.973	BB	0.4438	1898.74976	66.36482	91.6292
2	26.988	BB	0.4812	147.62039	4.56634	7.1238

Figure S9b. Chiral HPLC chromatography of product from **Scheme S12** (HPLC conditions: Chiralcel AD-H column, 220 nm, flow rate:0.5 ml/min, *i*-PrOH/hexanes = 1/19, t_{major} = 25.0 min, t_{minor} = 27.0 min; 86% ee.).

14. Mechanism Study

14.1 Emission Quenching Experiments

In order to determine the wavelength of emission quenching, the UV-Vis absorption of *fac*-Ir(ppy)₃ in THF was measured. As shown in **Figure S10**, 377 nm, the maximum absorption wavelength of *fac*-Ir(ppy)₃, was chosen as the irradiation wavelength. The fluorescence was recorded from the direction 90° to the inlet of light at 377 nm (**Figure S11a**).

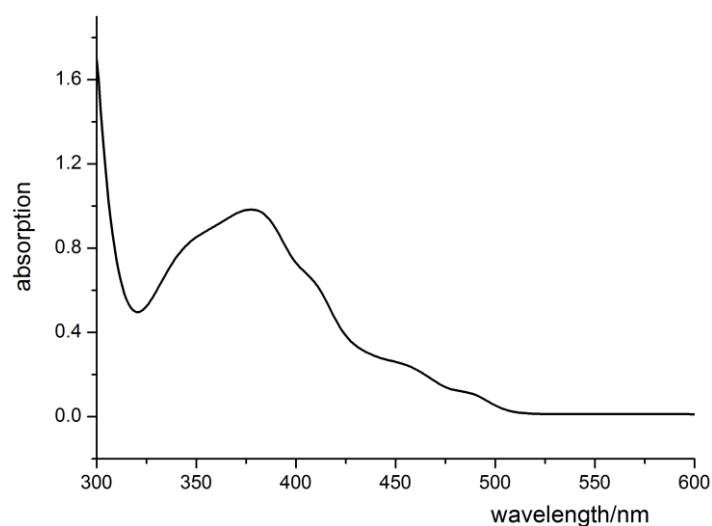


Figure S10. The UV-Vis absorption of *fac*-Ir(ppy)₃.

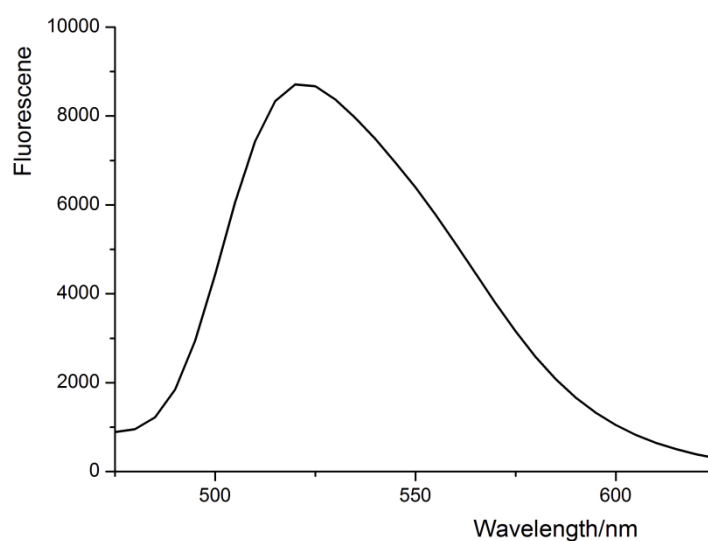


Figure S11a. The emission of *fac*-Ir(ppy)₃ with irradiation at 377 nm used in the emission quenching of *fac*-Ir(ppy)₃ by *t*-BuOK.

All *fac*-Ir(ppy)₃ solutions were irradiated at 377 nm and the emission intensity from 400 to 700 nm was recorded by F-7000 FL Spectrophotometer with EX Slit:10, EM Slit:10, PMT Voltage: 650V, Scan speed: 1200 nm/min. In a typical experiment, *t*-BuOK (0.4 mmol, 0.4 mmol, 0.4 mmol, 0.4 mmol, 0.4 mmol, 0.4 mmol, 0.4 mmol, 1.2 mmol) was added continuously to a 2 mL (0.001 mmol/mL) solution of *fac*-Ir(ppy)₃ in THF in the cuvette at 70 °C. Then the emission spectrum of the solution was collected at each addition. (**Figure S11b**)

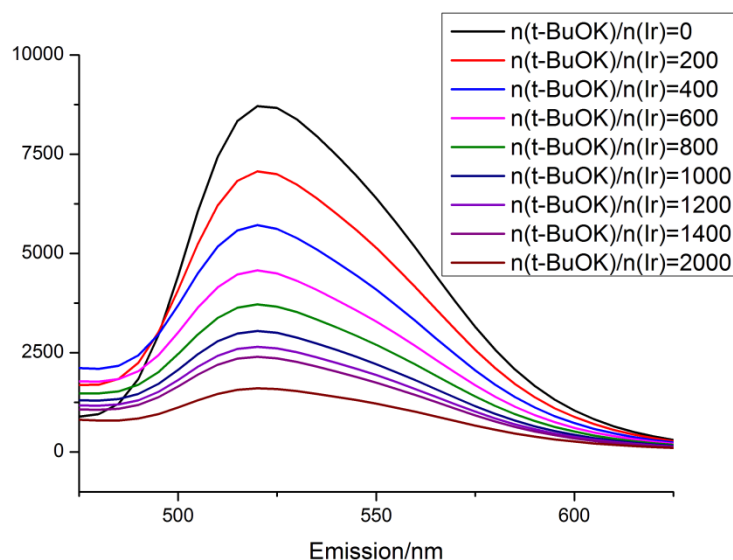


Figure S11b. The emission quenching of *fac*-Ir(ppy)₃ by *t*-BuOK at 377 nm.

All *fac*-Ir(ppy)₃ solutions were irradiated at 377 nm and the emission intensity from 400 to 700 nm was recorded by F-7000 FL Spectrophotometer with EX Slit:10, EM Slit:20, PMT Voltage: 740V, Scan speed: 1200 nm/min. In a typical experiment, **1a** (0.1 mmol, 0.1 mmol, 0.2 mmol, 0.2 mmol, 0.4 mmol, 0.2 mmol, 0.4 mmol) was added continuously to a 2 mL (0.001 mmol/mL) solution of *fac*-Ir(ppy)₃ in THF in the sealing cuvette at 70 °C. Then the emission spectrum of the solution was collected at each addition. (**Figure S12**)

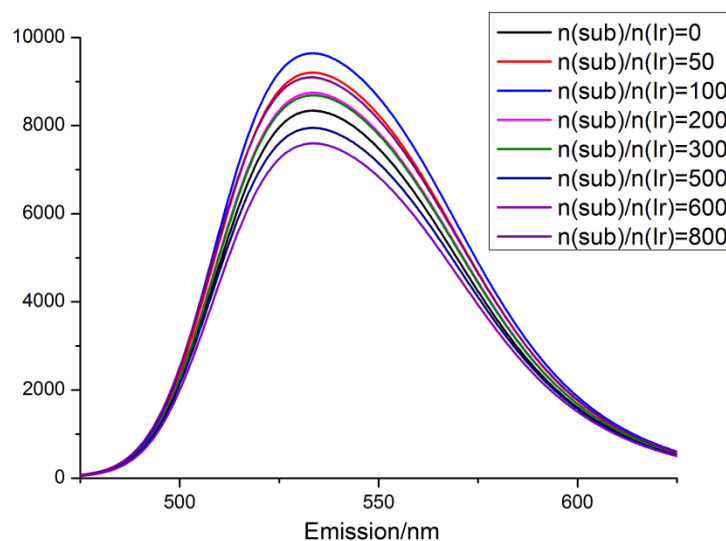


Figure S12. The emission quenching of *fac*-Ir(ppy)₃ by **1a** at 377 nm.

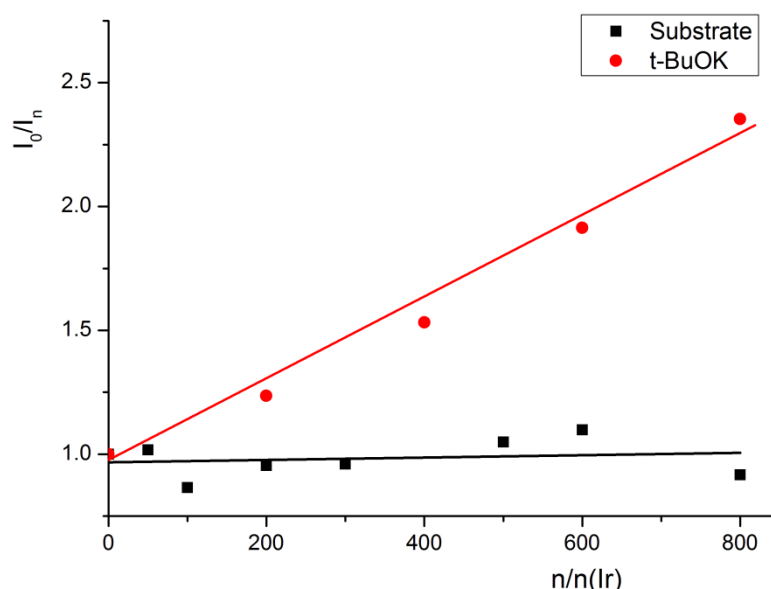
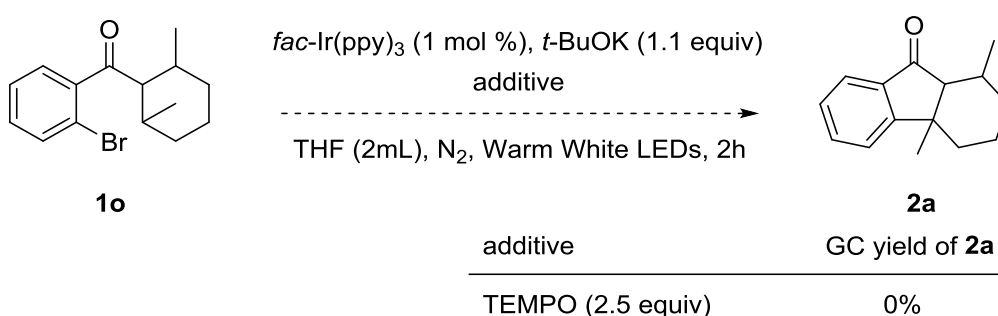


Figure S13. The comparison of emission quenching of *fac*-Ir(ppy)₃ by **1a** and *t*-BuOK at 377 nm at 70 °C in THF.

14.2 Radical Trapping Experiments

In order to confirm the radical pathway of this conversion, radical-trapping experiment was carried out. When TEMPO (2.5 equiv) was used as the radical-trapping reagent, formation of desired product **2** was totally suppressed (**Scheme S13**), which means this reaction probably proceeds by a radical pathway.

t-BuOK (27 mg, 2.4 mmol, 1.2 eq.) was added into a Schlenk tube charged with *fac*-Ir(ppy)₃ (1.2 mg, 1 mol%) and **1o** (0.2 mmol, 1.0 eq.) in the glove box. Under N₂ atmosphere, anhydrous THF (2 mL) was added to the tube via syringe. The mixture was stirred with irradiation of 12 W warm white LED strip for 2h. When the reaction was completed, the solvent was removed under reduced pressure. The residue was monitored by GC-MS.



Scheme S13. Effect of radical scavenger

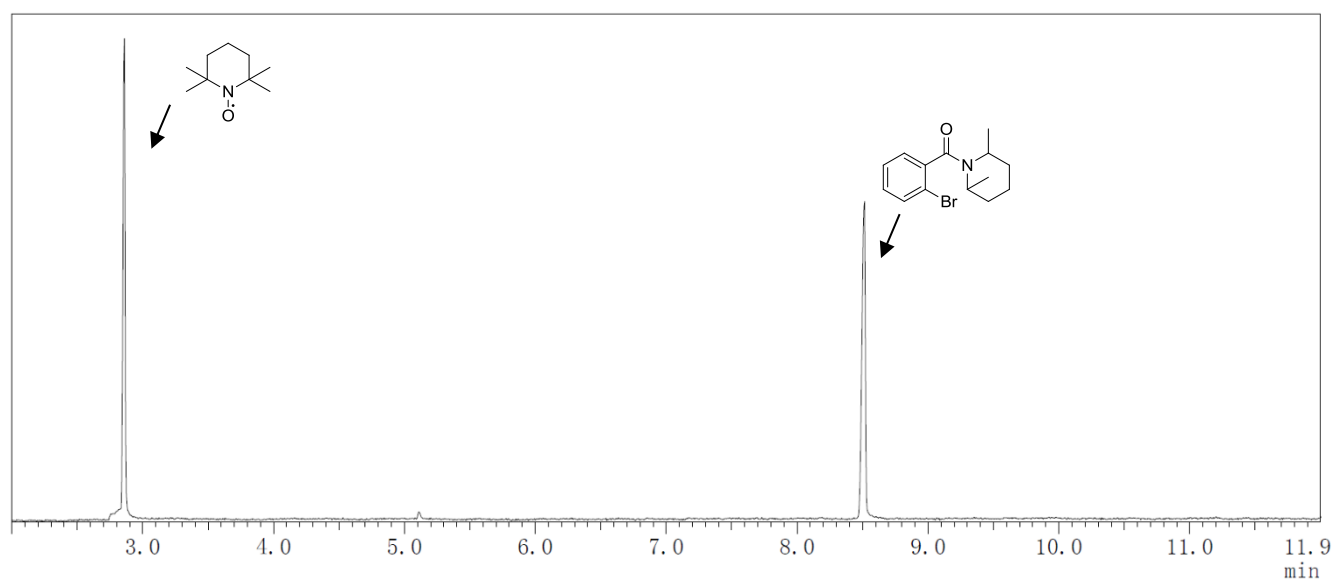
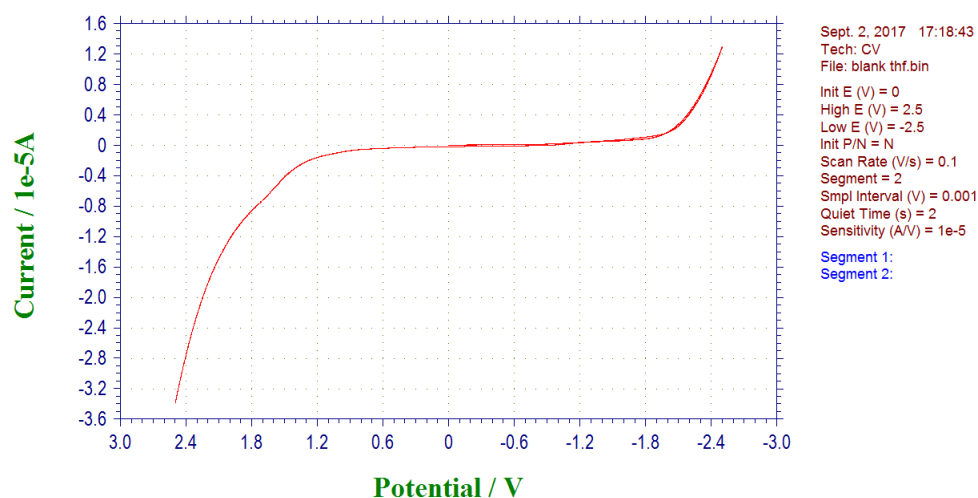
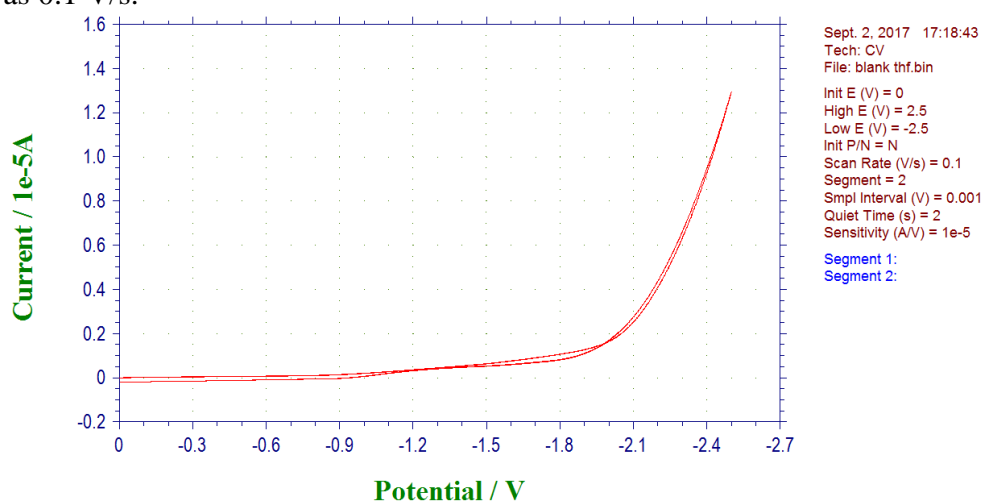


Figure S14. GC-MS of reaction quenched with TEMPO.

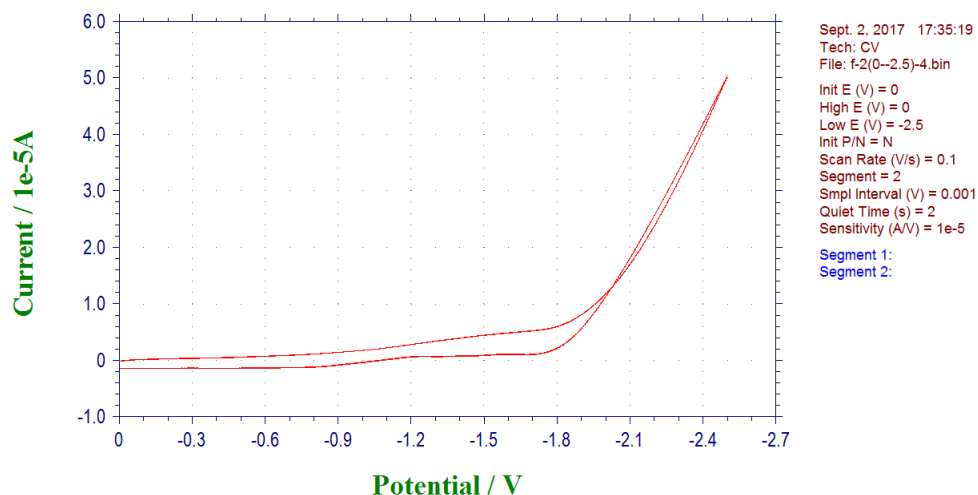
15. The Cyclic Voltammetry Experiments



Cyclic voltammogram of blank in 0.1 M TBAP/THF at a Pt working electrode with a Pt counter electrode and saturated calomel electrode (SCE). Ferrocene was used as an internal standard; potential sweep rate was 0.1 V/s.

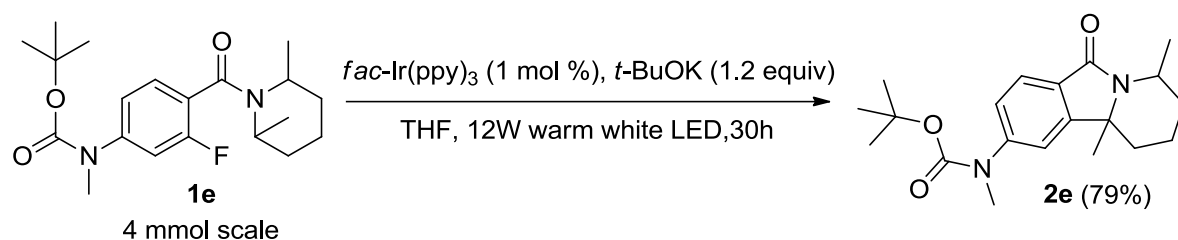


Cyclic voltammogram of blank in 0.1 M TBAP/THF at a Pt working electrode with a Pt counter electrode and saturated calomel electrode (SCE). Ferrocene was used as an internal standard; potential sweep rate was 0.1 V/s.



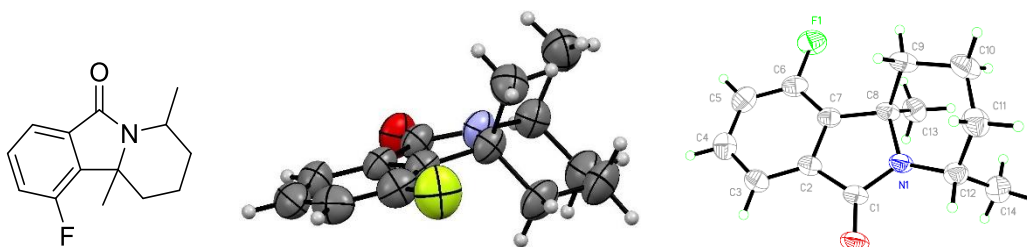
Cyclic voltammogram of **1a** in 0.1 M TBAP/THF at a Pt working electrode with a Pt counter electrode and saturated calomel electrode (SCE). Ferrocene was used as an internal standard; potential sweep rate was 0.1 V/s.

16. Scale Up Experiment



t-BuOK (538.6 mg, 4.8 mmol, 1.2 eq.) was added into a 20mL Schlenk tube charged with *fac*-Ir(ppy)₃ (24 mg, 1 mol%) and **1e** (1.45 g, 4 mmol) in the glove box. Under N₂ atmosphere, anhydrous THF (15 mL) was added to the tube via syringe. The mixture was stirred with irradiation of 12 W warm white LED strip for 30h. Then the mixture was diluted with distilled water and extracted with EA (3 times). The combined organic layer was washed with brine, dried over Na₂SO₄, and filtered. Solvent was removed under reduced pressure. The residue was purified by chromatography on silica gel (PE/EA = 9:1, v/v) to yield **2e** (1.08g, 79%).

17. X-Ray Crystallographic Data for 2t



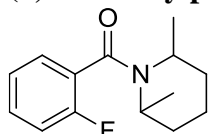
Identification code	170419a
Empirical formula	C ₁₄ H ₁₆ FNO
Formula weight	233.28
Temperature/K	293(2)
Wavelength	1.54178
Crystal system	Monoclinic
Space group	P2(1)/n
a/Å	10.7587(8)
b/Å	10.0218(7)
c/Å	11.9403(8)
α/°	90.00
β/°	107.695(3)
γ/°	90.00
Volume/Å ³	1226.51(15)
Z	4
Calculated density	1.263 g/cm ³
F(000)	496
Crystal size/mm ³	0.25*0.21*0.20 mm ³
Radiation	CuKα
Index ranges	-9<=h<=12, -11<=k<=11, -14<=l<=10
Theta range for data collection	4.85 to 66.05°
Data/restraints/parameters	2137/0/156
Goodness-of-fit on F ²	1.075
Final R indexes [I>=2σ (I)]	0.0559
Final R indexes [all data]	0.0698
Largest diff. peak/hole / e Å ⁻³	0.315/-0.203 e Å ⁻³

18. References

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- [2] Jaika, D.; Till, P.; Alexandra, S.; Marc, S.; Sven D. *Angew. Chem.* **2014**, 53, 7918–7922.
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- [5] Anitha, N.; Reddy, K. V.; Rao, Y. J. *Heterocycl. Commun.* **2014**, 20, 129–132.
- [6] Mohammad, L. H.; Ye F.; Liu Z. X.; Xia, Y.; Shi, Y.; Zhou, L.; Zhang, Y.; Wang J. B. *J. Org. Chem.* **2014**, 79, 8689–8699.
- [7] Mauro F. A. A.; Varinder K. A.; Matthew A. S. *Synth. Commun.* **1999**, 29, 1747–1756.

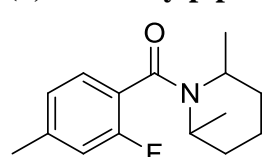
19. Synthesis and Characterization of New Compounds

(2,6-dimethylpiperidin-1-yl)(2-fluorophenyl)methanone (1a)



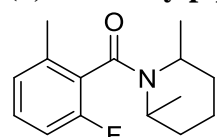
Following general procedure A, 2-fluorobenzoic acid and 2,6-dimethylpiperidine provided **1a** after recrystallization from ethyl acetate as white solid (963.5 mg, 41%). M.P. 152 – 153 °C. IR (neat) 2967, 2933, 2913, 1629, 1469, 1424, 1381, 1242, 1117, 767 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.32 – 7.00 (m, 4H), 4.89 (brs, 1H), 3.81 (brs, 1H), 1.83 – 1.16 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.1, 130.3, 128.4, 127.5, 125.8, 125.6, 124.4, 115.6, 49.6, 44.3, 30.1, 21.0, 14.0. ^{19}F NMR (376 MHz, CDCl_3) δ -115.81, -116.28. HRMS (ESI): calcd. for $\text{C}_{14}\text{H}_{18}\text{FNO}$ ($[\text{M}+\text{H}]^+$): 236.1445. found: 236.1453. HPLC conditions: Chiralcel OJ-H column, 220 nm & 254nm, flow rate: 0.5 ml/min, i-PrOH/hexanes = 1/9, t = 13.507 min.

(2,6-dimethylpiperidin-1-yl)(2-fluoro-4-methylphenyl)methanone (1b)



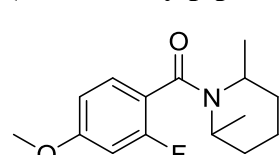
Following general procedure A, 2-fluoro-4-methylbenzoic acid and 2,6-dimethylpiperidine provided **1b** after recrystallization from ethyl acetate as white solid (1.34g, 54%). M.P. 116 – 118 °C. IR (neat) 2970, 2939, 1625, 1424, 1367, 1274, 1120, 1052, 943, 831, 749 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.19 – 6.78 (m, 3H), 4.83 (brs, 1H), 3.83 (brs, 1H), 2.27 (s, 3H), 1.82 – 1.11 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.3, 141.0, 128.0, 125.0, 122.7, 122.5, 116.0, 49.3, 44.4, 30.0, 21.0, 21.0, 14.0. ^{19}F NMR (376 MHz, CDCl_3) δ -116.84, -117.17. HRMS (ESI): calcd. for $\text{C}_{15}\text{H}_{20}\text{FNO}$ ($[\text{M}+\text{H}]^+$): 250.1602. found: 250.1604.

(2,6-dimethylpiperidin-1-yl)(2-fluoro-6-methylphenyl)methanone (1c)



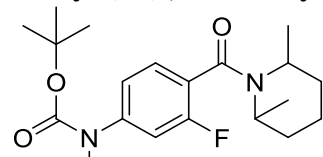
Following general procedure A, 2-fluoro-6-methylbenzoic acid and 2,6-dimethylpiperidine provided **1c** after recrystallization from ethyl acetate as white solid (1.17g, 47%). M.P. 127 – 130 °C. IR (neat) 2970, 2948, 2933, 1621, 1462, 1420, 1367, 793, 758, 747 cm^{-1} . ^1H NMR (600 MHz, CDCl_3) δ 7.23 – 7.16 (m, 1H), 7.02 – 6.86 (m, 2H), 5.08 – 4.99 (m, 1H), 3.85 – 3.66 (m, 1H), 2.35 – 2.26 (m, 3H), 1.66 – 1.11 (m, 12H). ^{13}C NMR (151 MHz, CDCl_3) δ 165.8, 165.7, 159.4, 158.6, 157.8, 157.0, 137.5, 137.5, 136.2, 136.2, 129.6, 129.5, 129.4, 129.3, 126.4, 126.4, 125.6, 125.6, 113.4, 113.2, 112.6, 112.5, 49.8, 49.8, 44.1, 43.9, 31.4, 30.9, 30.1, 29.9, 21.8, 21.3, 21.3, 21.1, 20.7, 19.2, 19.1, 18.7, 18.7, 14.3, 14.2. ^{19}F NMR (376 MHz, CDCl_3) δ -116.52, -117.13. HRMS (ESI): calcd. for $\text{C}_{15}\text{H}_{20}\text{FNO}$ ($[\text{M}+\text{H}]^+$): 250.1602. found: 250.1604.

(2,6-dimethylpiperidin-1-yl)(2-fluoro-4-methoxyphenyl)methanone (1d)



Following general procedure A, 2-fluoro-4-methoxybenzoic acid and 2,6-dimethylpiperidine provided **1d** after recrystallization from ethyl acetate as white solid (1.40g, 53%). M.P. 84 – 87 °C. IR (neat) 2970, 2937, 2870, 1616, 1507, 1287, 1156, 1119, 950, 834, 544 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.06 (brs, 1H), 6.61 – 6.43 (m, 2H), 4.56 (brs, 2H), 3.64 (s, 3H), 1.73 – 1.05 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.0, 161.0, 160.9, 128.6, 117.7, 117.5, 110.0, 110.0, 101.4, 101.2, 55.2, 48.4, 44.9, 29.8, 20.7, 13.8. ^{19}F NMR (376 MHz, CDCl_3) δ -113.90. HRMS (ESI): calcd. for $\text{C}_{15}\text{H}_{20}\text{FNO}_2$ ($[\text{M}+\text{H}]^+$): 266.1551. found: 266.1553.

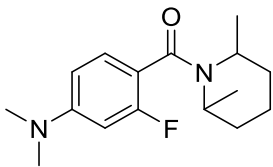
t-butyl (4-(2,6-dimethylpiperidine-1-carbonyl)-3-fluorophenyl)(methyl)carbamate (1e)



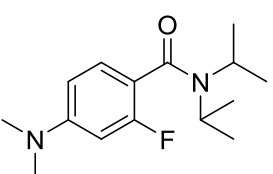
Following general procedure C, 4-amino-2-fluorobenzoic acid and 2,6-dimethylpiperidine provided **1e** after flash column chromatography (PE/EA, 9:1, v/v) and recrystallization from ethyl acetate as white solid (2.88g, 79%). M.P. 119 – 124 °C. IR (neat) 2973, 2936, 1706, 1624, 1416, 1367, 1276, 1152, 1118, 764, 749 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.27 – 7.04 (m, 3H), 5.49 – 3.46 (m, 2H), 3.25 (s, 3H), 1.47 (s, 9H), 2.00 – 1.11 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.1, 154.3, 145.7, 128.1, 122.3, 122.1, 120.7, 120.7, 112.7, 81.2, 37.1, 30.2, 28.4,

21.1, 14.2. ^{19}F NMR (376 MHz, CDCl_3) δ -114.97. HRMS (ESI): calcd. for $\text{C}_{20}\text{H}_{29}\text{FN}_2\text{O}_3$ ($[\text{M}+\text{H}]^+$): 365.2235. found: 365.2236.

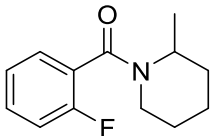
(4-(dimethylamino)-2-fluorophenyl)(2,6-dimethylpiperidin-1-yl)methanone (1f)

 Following general procedure **D**, 4-amino-2-fluorobenzoic acid and 2,6-dimethylpiperidine provided **1f** after flash column chromatography (PE/EA, 9:1, v/v) and recrystallization from ethyl acetate as white solid (1.69g, 61%). M.P. 109 – 112 °C. IR (neat) 2935, 1626, 1410, 1365, 1276, 1232, 1119, 1101, 763, 749 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.14 (t, J = 8.3 Hz, 1H), 6.45 (dd, J = 8.6, 2.5 Hz, 1H), 6.32 (dd, J = 13.3, 2.4 Hz, 1H), 4.41 (brs, 2H), 2.95 (s, 6H), 1.86 – 1.23 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 167.3, 152.4, 152.3, 129.2, 112.9, 112.7, 108.0, 98.8, 98.5, 40.3, 30.3, 21.2, 14.3. ^{19}F NMR (376 MHz, CDCl_3) δ -114.64. HRMS (ESI): calcd. for $\text{C}_{16}\text{H}_{23}\text{FN}_2\text{O}$ ($[\text{M}+\text{H}]^+$): 279.1867. found: 279.1866.

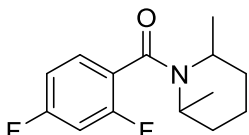
4-(dimethylamino)-2-fluoro-N,N-diisopropylbenzamide (1g)

 Following general procedure **D**, 4-amino-2-fluorobenzoic acid and diisopropylamine provided **1g** after flash column chromatography (PE/EA, 9:1, v/v) and recrystallization from ethyl acetate as white solid (2.07g, 78%). M.P. 149 – 151 °C. IR (neat) 2972, 2935, 1624, 1435, 1369, 1338, 1275, 1238, 810, 764, 749 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.12 (t, J = 8.4 Hz, 1H), 6.44 (dd, J = 8.6, 2.4 Hz, 1H), 6.32 (dd, J = 13.2, 2.4 Hz, 1H), 3.84 (s, 1H), 3.50 (brs, 1H), 2.96 (brs, 6H), 1.33 (d, J = 150.8 Hz, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.9, 160.6, 158.2, 152.3, 152.2, 128.9, 128.8, 114.4, 114.2, 108.0, 108.0, 98.8, 98.5, 40.3, 20.8. ^{19}F NMR (376 MHz, CDCl_3) δ -114.92. HRMS (ESI): calcd. for $\text{C}_{15}\text{H}_{23}\text{FN}_2\text{O}$ ($[\text{M}+\text{H}]^+$): 267.1867. found: 267.1865.

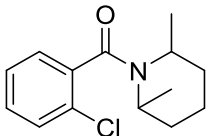
(2-fluorophenyl)(2-methylpiperidin-1-yl)methanone (1h)

 Following general procedure **B**, 2-fluorobenzoic acid and 2-methylpiperidine provided **1h** after after flash column chromatography (PE/EA, 9:1, v/v) as light yellow solid (1.66g, 75%). M.P. 59 – 61 °C. IR (neat) 2938, 2865, 1634, 1488, 1454, 1428, 1315, 1222, 1030, 755 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.13 – 7.00 (m, 2H), 6.95 – 6.75 (m, 2H), 4.92 – 4.23 (m, 1H), 3.69 – 2.58 (m, 2H), 1.64 – 0.92 (m, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ 164.4, 158.6, 156.2, 130.2, 130.1, 128.0, 127.5, 124.7, 124.5, 123.9, 123.9, 115.2, 115.0, 114.8, 49.7, 43.5, 36.0, 30.1, 29.1, 25.5, 25.0, 18.1, 15.9, 15.0. ^{19}F NMR (376 MHz, CDCl_3) δ -115.85, -116.44, -116.58. HRMS (ESI): calcd. for $\text{C}_{13}\text{H}_{16}\text{FNO}$ ($[\text{M}+\text{H}]^+$): 222.1289. found: 222.1290.

(2,4-difluorophenyl)(2,6-dimethylpiperidin-1-yl)methanone (1i)

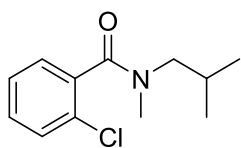
 Following general procedure **A**, 2,4-difluorobenzoic acid and 2,6-dimethylpiperidine provided **1i** after recrystallization from ethyl acetate as white solid (1.06g, 42%). M.P. 150 – 151 °C. IR (neat) 3062, 2969, 2933, 1627, 1429, 1369, 1267, 1145, 1116, 764, 749 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.32 – 7.11 (m, 1H), 6.87 – 6.72 (m, 2H), 4.79 (brs, 1H), 3.78 (brs, 1H), 1.96 – 0.83 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 165.2, 164.1, 161.7, 159.2, 156.8, 129.4, 122.0, 122.0, 121.8, 121.8, 111.8, 111.6, 104.1, 49.3, 44.5, 30.0, 20.9, 13.9. ^{19}F NMR (376 MHz, CDCl_3) δ -108.46, -108.78, -111.65, -111.89. HRMS (ESI): calcd. for $\text{C}_{14}\text{H}_{17}\text{F}_2\text{NO}$ ($[\text{M}+\text{H}]^+$): 254.1351. found: 254.1351.

(2-chlorophenyl)(2,6-dimethylpiperidin-1-yl)methanone (1j)

 Following general procedure **A**, 2-chlorobenzoic acid and 2,6-dimethylpiperidine provided **1j** after recrystallization from ethyl acetate as white solid (1.18g, 47%). M.P. 134 – 136 °C. IR (neat) 2983, 2964, 2933, 1625, 1435, 1422, 1369, 1116, 771, 751 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.62 – 7.51 (m, 1H), 7.36 – 7.29 (m, 1H), 7.26 – 7.15 (m, 2H), 5.08 – 4.86 (m, 1H), 3.88 – 3.59 (m, 1H), 1.89 – 1.14 (m, 12H).

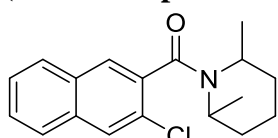
^{13}C NMR (101 MHz, CDCl_3) δ 168.0, 167.6, 137.4, 137.0, 130.7, 130.3, 130.0, 129.6, 129.6, 129.4, 127.5, 127.1, 127.0, 126.8, 50.0, 49.4, 44.1, 44.0, 30.7, 29.9, 21.7, 21.4, 20.6, 14.3, 14.2. HRMS (ESI): calcd. for $\text{C}_{14}\text{H}_{18}\text{ClNO}$ ($[\text{M}+\text{H}]^+$): 252.1150. found: 252.1159.

2-chloro-N-isobutyl-N-methylbenzamide (1k)



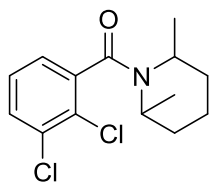
According to the synthesis of 21e', 2-chlorobenzoic acid and 2-methylpropan-1-amine provided **1k** after flash column chromatography (PE/EA, 9:1, v/v) as light yellow oil (1.51g, 67%). IR (neat) 3058, 2959, 2929, 2871, 1644, 1489, 1465, 1433, 1403, 1292, 1115, 1079, 1044, 771, 747 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.43 – 7.22 (m, 4H), 3.52 – 2.80 (m, 5H), 2.14 – 1.89 (m, 1H), 1.00 (d, J = 6.7 Hz, 3H), 0.77 (dd, J = 16.5, 6.7 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 168.9, 168.7, 137.1, 136.5, 130.6, 130.2, 130.0, 130.0, 129.7, 129.7, 128.6, 127.8, 127.3, 127.0, 58.0, 54.5, 36.8, 32.7, 26.9, 26.7, 20.3, 20.1, 19.6. HRMS (ESI): calcd. for $\text{C}_{12}\text{H}_{16}\text{ClNO}$ ($[\text{M}+\text{H}]^+$): 226.0993. found: 226.0991.

(3-chloronaphthalen-2-yl)(2,6-dimethylpiperidin-1-yl)methanone (1l)



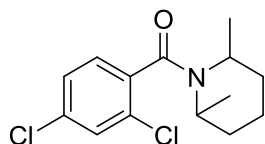
Following general procedure A, 3-chloro-2-naphthoic acid and 2,6-dimethylpiperidine provided **1l** after recrystallization from ethyl acetate as white solid (1.72g, 57%). M.P. 171 – 174 $^{\circ}\text{C}$. IR (neat) 2969, 2936, 2868, 1628, 1458, 1417, 1368, 1275, 1057, 750 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.96 – 7.70 (m, 4H), 7.55 – 7.48 (m, 2H), 5.18 – 4.90 (m, 1H), 4.02 – 3.61 (m, 1H), 1.82 – 1.15 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 168.0, 167.6, 135.4, 134.7, 133.6, 131.7, 131.4, 128.6, 128.2, 128.0, 127.9, 127.8, 127.7, 127.5, 127.1, 127.0, 126.9, 126.9, 126.8, 126.1, 50.1, 44.3, 30.8, 30.0, 21.3, 20.6, 14.3, 14.2. HRMS (ESI): calcd. for $\text{C}_{18}\text{H}_{20}\text{ClNO}$ ($[\text{M}+\text{H}]^+$): 302.1306. found: 302.1302.

(2,3-dichlorophenyl)(2,6-dimethylpiperidin-1-yl)methanone (1m)



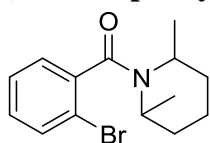
Following general procedure A, 2,3-dichlorobenzoic acid and 2,6-dimethylpiperidine provided **1m** after recrystallization from ethyl acetate as white solid (1.31g, 46%). M.P. 143 – 146 $^{\circ}\text{C}$. IR (neat) 2986, 2939, 2871, 1624, 1424, 1410, 1367, 1275, 764, 749 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.48 – 7.41 (m, 1H), 7.26 – 7.08 (m, 2H), 5.02 – 4.90 (m, 1H), 3.85 – 3.58 (m, 1H), 1.75 – 1.10 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 167.1, 166.8, 139.4, 139.0, 134.2, 133.4, 130.3, 129.2, 128.6, 128.0, 127.8, 125.6, 125.0, 50.2, 49.6, 44.4, 44.1, 30.8, 30.7, 29.9, 29.8, 21.7, 21.5, 20.7, 20.6, 14.2, 14.2. HRMS (ESI): calcd. for $\text{C}_{14}\text{H}_{17}\text{Cl}_2\text{NO}$ ($[\text{M}+\text{H}]^+$): 286.0760. found: 286.0763.

(2,4-dichlorophenyl)(2,6-dimethylpiperidin-1-yl)methanone (1n)



Following general procedure A, 2,4-dichlorobenzoic acid and 2,6-dimethylpiperidine provided **1n** after recrystallization from ethyl acetate as white solid (1.17g, 41%). M.P. 124 – 126 $^{\circ}\text{C}$. IR (neat) 2970, 2937, 2869, 1631, 1587, 1420, 1378, 1365, 765, 750 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.45 – 7.31 (m, 1H), 7.28 – 7.23 (m, 1H), 7.22 – 7.07 (m, 1H), 5.18 – 4.64 (m, 1H), 3.92 – 3.40 (m, 1H), 1.85 – 1.11 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 167.0, 166.6, 135.8, 135.4, 134.8, 134.8, 131.6, 130.9, 130.1, 129.3, 128.4, 127.8, 127.5, 127.2, 50.1, 44.3, 30.6, 29.8, 21.4, 20.5, 14.1, 14.1. HRMS (ESI): calcd. for $\text{C}_{14}\text{H}_{17}\text{Cl}_2\text{NO}$ ($[\text{M}+\text{H}]^+$): 286.0760. found: 286.0760.

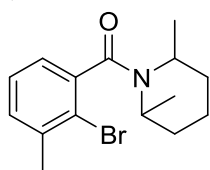
(2-bromophenyl)(2,6-dimethylpiperidin-1-yl)methanone (1o)



Following general procedure A, 2-bromobenzoic acid and 2,6-dimethylpiperidine provided **1o** after recrystallization from ethyl acetate as white solid (1.74g, 59%). M.P. 135 – 137 $^{\circ}\text{C}$. IR (neat) 2966, 2932, 1622, 1421, 1367, 1275, 1157, 1057, 772, 750 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.61 – 7.49 (m, 1H), 7.36 – 7.27 (m, 1H), 7.26 – 7.13 (m, 2H), 5.07 – 4.86 (m, 1H), 3.90 – 3.50 (m, 1H), 1.90 – 1.10 (m, 12H).

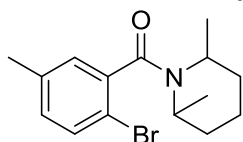
^{13}C NMR (101 MHz, CDCl_3) δ 168.7, 168.4, 139.5, 139.0, 133.5, 132.6, 129.8, 129.7, 127.6, 127.5, 127.4, 127.0, 119.5, 119.1, 50.0, 49.5, 44.1, 43.9, 30.7, 29.9, 29.8, 21.6, 21.4, 20.7, 20.6, 14.3, 14.2. HRMS (ESI): calcd. for $\text{C}_{14}\text{H}_{18}\text{BrNO}$ ($[\text{M}+\text{H}]^+$): 296.0645. found: 296.0646.

(2-bromo-3-methylphenyl)(2,6-dimethylpiperidin-1-yl)methanone (1p)



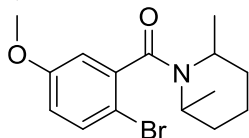
Following general procedure A, 2-bromo-3-methylbenzoic acid and 2,6-dimethylpiperidine provided **1p** after recrystallization from ethyl acetate as white solid (1.61g, 52%). M.P. 149 – 151 °C. IR (neat) 2966, 2935, 2865, 1627, 1424, 1376, 1365, 1275, 1117, 1057, 802, 749 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.25 – 7.18 (m, 2H), 7.08 – 6.96 (m, 1H), 5.06 – 4.95 (m, 1H), 3.90 – 3.61 (m, 1H), 2.44 – 2.40 (m, 3H), 1.82 – 1.11 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 169.2, 168.8, 140.1, 139.7, 139.6, 138.8, 130.5, 130.4, 127.5, 127.3, 124.8, 124.4, 121.9, 121.4, 50.0, 49.5, 44.1, 43.8, 30.8, 30.0, 29.8, 23.5, 23.4, 21.6, 21.4, 20.8, 20.6, 14.3, 14.2. HRMS (ESI): calcd. for $\text{C}_{15}\text{H}_{20}\text{BrNO}$ ($[\text{M}+\text{H}]^+$): 310.0801. found: 310.0800.

(2-bromo-5-methylphenyl)(2,6-dimethylpiperidin-1-yl)methanone (1q)



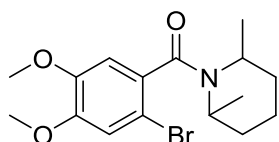
Following general procedure A, 2-bromo-5-methylbenzoic acid and 2,6-dimethylpiperidine provided **1q** after recrystallization from ethyl acetate as white solid (1.39g, 45%). M.P. 127 – 132 °C. IR (neat) 2969, 2935, 1629, 1422, 1377, 1363, 1275, 1143, 1057, 764, 749 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.47 – 7.36 (m, 1H), 7.07 – 6.96 (m, 2H), 5.08 – 4.83 (m, 1H), 3.94 – 3.59 (m, 1H), 2.31 – 2.28 (m, 3H), 1.84 – 1.12 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 168.9, 168.5, 139.3, 138.8, 137.7, 137.5, 133.2, 132.3, 130.6, 130.6, 128.1, 127.5, 116.1, 115.6, 50.0, 49.4, 44.1, 43.9, 30.8, 30.7, 29.9, 29.8, 21.7, 21.4, 21.0, 20.7, 20.6, 14.3, 14.2. HRMS (ESI): calcd. for $\text{C}_{15}\text{H}_{20}\text{BrNO}$ ($[\text{M}+\text{H}]^+$): 310.0801. found: 310.0801.

(2-bromo-5-methoxyphenyl)(2,6-dimethylpiperidin-1-yl)methanone (1r)



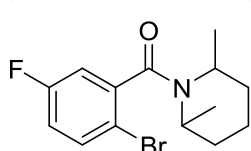
Following general procedure A, 2-bromo-5-methoxybenzoic acid and 2,6-dimethylpiperidine provided **1r** after recrystallization from ethyl acetate as white solid (1.88g, 58%). M.P. 119 – 122 °C. IR (neat) 2969, 2936, 1629, 1446, 1423, 1364, 1275, 1261, 1059, 764, 750 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.49 – 7.38 (m, 1H), 6.84 – 6.69 (m, 2H), 5.07 – 4.91 (m, 1H), 3.91 – 3.66 (m, 1H), 3.82 – 3.75 (m, 3H), 1.81 – 1.24 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 168.5, 168.2, 159.2, 158.9, 140.3, 139.8, 134.3, 133.4, 116.0, 115.9, 113.0, 112.5, 109.9, 109.4, 55.7, 50.1, 49.5, 44.2, 30.9, 30.0, 21.9, 21.4, 20.6, 14.3, 14.2. HRMS (ESI): calcd. for $\text{C}_{15}\text{H}_{20}\text{BrNO}_2$ ($[\text{M}+\text{H}]^+$): 326.0750. found: 326.0749.

(2-bromo-4,5-dimethoxyphenyl)(2,6-dimethylpiperidin-1-yl)methanone (1s)



Following general procedure A, 2-bromo-4,5-dimethoxybenzoic acid and 2,6-dimethylpiperidine provided **1s** after recrystallization from ethyl acetate as white solid (1.42g, 40%). M.P. 141 – 145 °C. IR (neat) 2968, 2935, 1626, 1505, 1420, 1384, 1274, 1255, 1211, 1183, 764, 749 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.00 – 6.61 (m, 2H), 5.20 – 4.62 (m, 1H), 3.99 – 3.61 (m, 7H), 1.80 – 1.07 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 168.6, 168.3, 149.5, 149.5, 148.7, 148.5, 131.3, 130.9, 116.0, 115.2, 110.3, 109.8, 109.6, 109.3, 56.2, 56.2, 56.2, 55.6, 49.9, 49.4, 44.1, 30.7, 29.8, 21.3, 20.5, 14.1, 14.1. HRMS (ESI): calcd. for $\text{C}_{16}\text{H}_{22}\text{BrNO}_3$ ($[\text{M}+\text{H}]^+$): 356.0856. found: 356.0860.

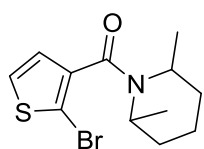
(2-bromo-5-fluorophenyl)(2,6-dimethylpiperidin-1-yl)methanone (1t)



Following general procedure A, 2-bromo-5-fluorobenzoic acid and 2,6-dimethylpiperidine provided **1t** after recrystallization from ethyl acetate as white solid (1.34g, 43%). M.P. 124 – 126 °C. IR (neat) 2991, 2971, 2935, 1620, 1461, 1431, 1379, 1364, 1256, 779, 764, 750 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.60 – 7.44 (m, 1H), 7.05 – 6.87 (m, 2H), 5.07 – 4.81 (m, 1H), 3.89 – 3.57 (m,

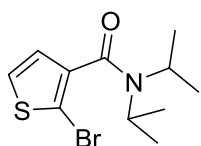
1H), 1.86 – 1.16 (m, 12H). ¹³C NMR (101 MHz, CDCl₃) δ 167.4, 167.1, 163.2, 163.0, 160.7, 160.5, 141.2, 141.1, 140.6, 140.5, 135.1, 135.1, 134.2, 134.2, 117.3, 117.2, 117.1, 117.0, 115.0, 114.8, 114.4, 114.2, 113.4, 113.4, 50.2, 49.6, 44.3, 44.2, 30.8, 29.9, 21.8, 21.4, 20.7, 20.6, 14.2, 14.2. ¹⁹F NMR (376 MHz, CDCl₃) δ -113.61, -114.00. HRMS (ESI): calcd. for C₁₄H₁₇BrFNO ([M+H]⁺): 314.0550. found: 314.0552.

(2-bromothiophen-3-yl)(2,6-dimethylpiperidin-1-yl)methanone (1u)



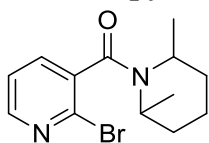
Following general procedure A, 2-bromothiophene-3-carboxylic acid and 2,6-dimethylpiperidine provided **1u** after recrystallization from ethyl acetate as white solid (1.50g, 50%). M.P. 106 – 107 °C. IR (neat) 2970, 2939, 2868, 1618, 1424, 1373, 1333, 1275, 1260, 1120, 1056, 749 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.28 (d, *J* = 5.5 Hz, 1H), 6.89 (d, *J* = 5.6 Hz, 1H), 5.24 – 3.33 (m, 2H), 1.96 – 1.25 (m, 12H). ¹³C NMR (101 MHz, CDCl₃) δ 165.4, 138.6, 127.3, 126.5, 109.6, 50.8, 45.3, 30.3, 21.3, 14.1. HRMS (ESI): calcd. for C₁₂H₁₆BrNOS ([M+H]⁺): 302.0209. found: 302.0207.

2-bromo-N,N-diisopropylthiophene-3-carboxamide (1v)



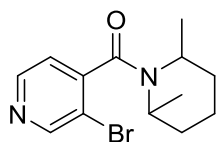
Following general procedure B, 2-bromothiophene-3-carboxylic acid and diisopropylamine provided **1v** after recrystallization from ethyl acetate as white solid (1.18g, 41%). M.P. 79 – 81 °C. IR (neat) 2970, 2932, 1633, 1444, 1370, 1318, 1275, 1260, 1122, 749 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.25 (dd, *J* = 20.4, 3.3 Hz, 2H), 3.62 (dt, *J* = 60.6, 6.7 Hz, 2H), 1.56 (d, *J* = 6.8 Hz, 6H), 1.17 (d, *J* = 6.6 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 164.8, 139.7, 123.9, 122.3, 108.5, 51.2, 46.1, 20.9, 20.5. HRMS (ESI): calcd. for C₁₁H₁₆BrNOS ([M+H]⁺): 290.0209. found: 290.0212.

(2-bromopyridin-3-yl)(2,6-dimethylpiperidin-1-yl)methanone (1w)



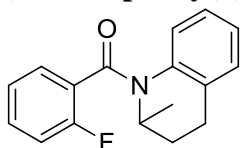
Following general procedure A, 2-bromonicotinic acid and 2,6-dimethylpiperidine provided **1w** after recrystallization from ethyl acetate as white solid (1.36g, 46%). M.P. 148 – 149 °C. IR (neat) 2970, 2938, 2870, 1632, 1578, 1420, 1396, 1367, 1073, 801, 759, 688, 644 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 8.49 – 8.30 (m, 1H), 7.65 – 7.46 (m, 1H), 7.34 – 7.26 (m, 1H), 4.94 (brs, 1H), 3.82 – 3.57 (m, 1H), 1.86 – 1.14 (m, 12H). ¹³C NMR (101 MHz, CDCl₃) δ 166.6, 166.2, 166.0, 149.9, 149.8, 149.6, 149.6, 147.6, 147.1, 138.7, 136.7, 136.5, 135.9, 135.8, 135.3, 133.7, 133.3, 122.9, 122.7, 122.6, 122.4, 50.4, 49.7, 44.4, 30.8, 30.5, 29.9, 21.8, 21.6, 21.4, 20.7, 20.4, 20.4, 14.2, 14.2, 14.1. HRMS (ESI): calcd. for C₁₃H₁₇BrN₂O ([M+H]⁺): 297.0597. found: 297.0599.

(3-bromopyridin-4-yl)(2,6-dimethylpiperidin-1-yl)methanone (1x)



Following general procedure A, 3-bromoisonicotinic acid and 2,6-dimethylpiperidine provided **1x** after recrystallization from ethyl acetate as white solid (1.42 g, 48%). M.P. 142 – 146 °C. IR (neat) 2970, 2937, 1632, 1424, 1396, 1369, 1274, 763, 749, 654 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 8.80 – 8.66 (m, 1H), 8.58 – 8.48 (m, 1H), 7.21 – 7.07 (m, 1H), 5.02 – 4.82 (m, 1H), 3.77 – 3.48 (m, 1H), 1.79 – 1.12 (m, 12H). ¹³C NMR (101 MHz, CDCl₃) δ 166.2, 165.9, 153.0, 152.0, 148.6, 148.2, 146.7, 146.2, 121.8, 121.3, 117.8, 117.3, 50.3, 49.7, 44.4, 44.2, 30.7, 29.8, 29.7, 21.8, 21.6, 20.6, 20.6, 14.2, 14.1. HRMS (ESI): calcd. for C₁₃H₁₇BrN₂O ([M+H]⁺): 297.0597. found: 297.0597.

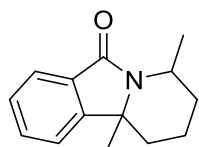
(2-fluorophenyl)(2-methyl-3,4-dihydroquinolin-1(2H)-yl)methanone (S2)



Following general procedure A, 2-fluorobenzoic acid and 2-methyl-1,2,3,4-tetrahydroquinoline provided **S2** after recrystallization from ethyl acetate as white solid (1.08g, 40%). M.P. 119 – 121 °C. IR (neat) 2934, 2868, 1642, 1614, 1490, 1452, 1356, 1346, 1304, 1147, 753 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.57 – 6.63 (m, 8H), 4.90 (s, 1H), 2.58 (d, *J* = 112.2 Hz, 3H), 1.52 –

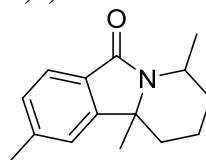
1.23 (m, 4H). ^{13}C NMR (101 MHz, CDCl_3) δ 165.5, 131.3, 131.2, 129.9, 127.2, 125.6, 125.6, 125.4, 125.4, 125.3, 124.2, 124.2, 115.6, 115.4, 49.4, 32.2, 25.7, 19.9. ^{19}F NMR (376 MHz, CDCl_3) δ -114.05. HRMS (ESI): calcd. for $\text{C}_{17}\text{H}_{16}\text{FNO}$ ($[\text{M}+\text{H}]^+$): 270.1289. found: 270.1282.

4,10b-dimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2a)



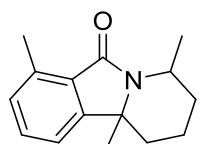
Following general procedure E, **1a**, **1j**, **1o** provided the product **2a** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow solid (40.0 mg, 93% from **1a**; 39.5 mg, 92% from **1j**; 38.7 mg, 90% from **1o**). M.P. 64 – 67 °C. IR (neat) 2970, 2936, 2867, 1682, 1467, 1391, 1360, 1332, 1311, 760, 698 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.82 (dt, J = 7.6, 1.0 Hz, 1H), 7.50 (td, J = 7.5, 1.2 Hz, 1H), 7.40 (td, J = 7.5, 1.0 Hz, 1H), 7.32 (dt, J = 7.5, 0.9 Hz, 1H), 4.90 – 4.80 (m, 1H), 2.21 – 1.41 (m, 6H), 1.56 (s, 3H), 1.37 (d, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.9, 152.9, 131.4, 130.5, 127.8, 123.8, 120.3, 77.4, 77.1, 76.8, 61.4, 43.4, 36.1, 30.0, 25.5, 19.7, 16.5. HRMS (ESI): calcd. for $\text{C}_{14}\text{H}_{17}\text{NO}$ ($[\text{M}+\text{H}]^+$): 216.1383. found: 216.1380.

4,9,10b-trimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2b)



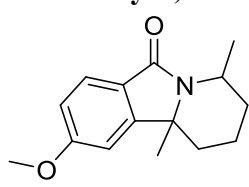
Following general procedure E, **1b** provided the product **2b** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow oil (42.1 mg, 92%). IR (neat) 2970, 2935, 2866, 1683, 1618, 1391, 1360, 1332, 1308, 1196, 784, 697 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.69 (d, J = 7.7 Hz, 1H), 7.20 (d, J = 7.7 Hz, 1H), 7.11 (s, 1H), 4.83 (p, J = 7.1 Hz, 1H), 2.43 (s, 3H), 2.13 – 1.48 (m, 6H), 1.54 (s, 3H), 1.36 (d, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.9, 153.3, 142.0, 128.9, 128.0, 123.6, 120.8, 77.4, 77.1, 76.8, 61.2, 43.4, 36.2, 30.0, 25.5, 22.0, 19.7, 16.5. HRMS (ESI): calcd. for $\text{C}_{15}\text{H}_{19}\text{NO}$ ($[\text{M}+\text{H}]^+$): 230.1539. found: 230.1540.

4,7,10b-trimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2c)



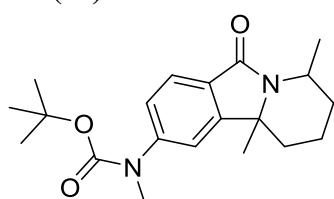
Following general procedure E, **1c** provided the product **2c** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow oil (41.2 mg, 90%). IR (neat) 2970, 2935, 2867, 1678, 1603, 1480, 1390, 1331, 1309, 1099, 804, 783, 700 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.35 (t, J = 7.5 Hz, 1H), 7.12 (d, J = 7.6 Hz, 2H), 4.82 (t, J = 7.5 Hz, 1H), 2.72 (s, 3H), 2.12 – 1.50 (m, 6H), 1.52 (s, 3H), 1.35 (d, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 167.7, 153.6, 137.6, 130.9, 129.8, 117.7, 60.4, 43.0, 36.3, 30.0, 25.7, 19.7, 17.4, 16.6. HRMS (ESI): calcd. for $\text{C}_{15}\text{H}_{19}\text{NO}$ ($[\text{M}+\text{H}]^+$): 230.1539. found: 230.1536.

9-methoxy-4,10b-dimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2d)



Following general procedure E, **1d** provided the product **2d** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow oil (44.1 mg, 90%). IR (neat) 2935, 1675, 1611, 1488, 1390, 1332, 1286, 1218, 1061, 696 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.74 (d, J = 8.3 Hz, 1H), 6.93 (dd, J = 8.4, 2.2 Hz, 1H), 6.79 (d, J = 2.2 Hz, 1H), 4.85 – 4.78 (m, 1H), 3.86 (s, 3H), 2.11 – 1.53 (m, 6H), 1.55 (s, 3H), 1.36 (d, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.7, 162.8, 155.2, 125.2, 123.3, 114.0, 105.6, 61.1, 55.7, 43.4, 36.2, 30.0, 25.7, 19.9, 16.6. HRMS (ESI): calcd. for $\text{C}_{15}\text{H}_{19}\text{NO}_2$ ($[\text{M}+\text{H}]^+$): 246.1489. found: 246.1488.

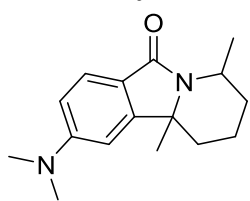
t-butyl(4,10b-dimethyl-6-oxo-1,2,3,4,6,10b-hexahydropyrido[2,1-a]isoindol-9-yl)(methyl)carbamate (2e)



Following general procedure E, **1e** provided the product **2e** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow solid (67.4 mg, 98%). M.P. 140 – 143 °C. IR (neat) 2973, 2935, 1687, 1617, 1488, 1454, 1392, 1362, 1309, 1275, 1150, 764, 749, 701 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.77 – 7.72 (m, 1H), 7.24 (d, J = 7.6 Hz, 2H), 4.82 (p, J = 7.2, 6.7 Hz, 1H), 3.29 (s, 3H), 2.13 – 1.54 (m, 6H), 1.55 (s, 3H), 1.44 (s, 9H), 1.36 (d, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.3, 154.4, 153.3, 146.9, 127.2, 124.4,

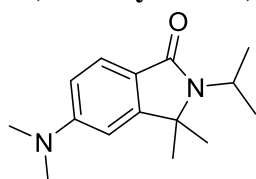
123.9, 117.5, 80.8, 61.2, 43.5, 37.4, 36.1, 29.9, 28.3, 25.5, 19.7, 16.5. HRMS (ESI): calcd. for $C_{20}H_{28}N_2O_3$ ($[M+H]^+$): 345.2173. found: 345.2173.

9-(dimethylamino)-4,10b-dimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2f)



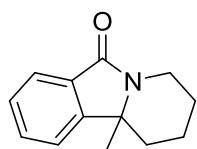
Following general procedure E, **1f** provided the product **2f** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow oil (48.5 mg, 94%). IR (neat) 2932, 1667, 1613, 1510, 1389, 1361, 1330, 1308, 1251, 1230, 1169, 1108, 780, 698 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.5 Hz, 1H), 6.70 (dd, J = 8.6, 2.3 Hz, 1H), 6.48 (d, J = 2.2 Hz, 1H), 4.88 – 4.71 (m, 1H), 3.03 (s, 6H), 2.13 – 1.46 (m, 6H), 1.54 (s, 3H), 1.35 (d, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 155.2, 153.1, 124.7, 118.4, 111.8, 102.3, 61.0, 43.1, 40.6, 36.4, 30.1, 25.8, 20.0, 16.6. HRMS (ESI): calcd. for $C_{16}H_{22}N_2O$ ($[M+H]^+$): 259.1805. found: 259.1806.

5-(dimethylamino)-2-isopropyl-3,3-dimethylisoindolin-1-one (2g)



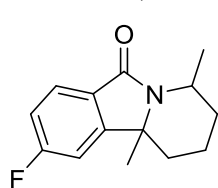
Following general procedure E, **1g** provided the product **2g** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow oil (46.7 mg, 95%). IR (neat) 2967, 2928, 2810, 1671, 1614, 1511, 1410, 1346, 1200, 854, 782, 749, 700 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.5 Hz, 1H), 6.69 (dd, J = 8.5, 2.3 Hz, 1H), 6.49 (d, J = 2.2 Hz, 1H), 3.59 (p, J = 6.8 Hz, 1H), 3.03 (s, 6H), 1.53 (d, J = 6.8 Hz, 6H), 1.43 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 153.5, 153.0, 124.2, 120.0, 111.8, 102.7, 62.9, 44.4, 40.6, 25.8, 20.8. HRMS (ESI): calcd. for $C_{15}H_{22}N_2O$ ($[M+H]^+$): 247.1805. found: 247.1808.

10b-methyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2h)



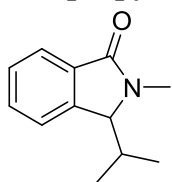
Following general procedure E, **1h** provided the product **2h** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow oil (36.2 mg, 90%). IR (neat) 2933, 2852, 1679, 1469, 1443, 1403, 1291, 1275, 1260, 1102, 698 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ 7.85 (dt, J = 7.6, 1.0 Hz, 1H), 7.52 (td, J = 7.5, 1.2 Hz, 1H), 7.43 (td, J = 7.5, 1.1 Hz, 1H), 7.38 (dt, J = 7.6, 1.0 Hz, 1H), 4.41 (dd, J = 13.2, 5.2 Hz, 1H), 2.96 (td, J = 13.2, 3.2 Hz, 1H), 2.29 – 1.51 (m, 6H), 1.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 152.6, 131.4, 131.0, 128.0, 123.9, 120.5, 60.9, 36.6, 36.3, 25.6, 21.1, 20.5. HRMS (ESI): calcd. for $C_{13}H_{15}NO$ ($[M+H]^+$): 202.1226. found: 202.1226.

9-fluoro-4,10b-dimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2i)

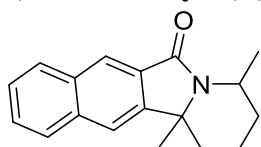


Following general procedure E and anhydrous MBTE was used as solvent, **1i** provided the product **2i** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow solid (16 mg, 34%). M.P. 114 – 116 $^{\circ}C$. IR (neat) 2988, 2938, 1683, 1621, 1394, 1361, 1332, 1275, 1260, 1208, 693 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.75 (m, 1H), 7.10 (t, J = 8.8 Hz, 1H), 7.01 (d, J = 8.2 Hz, 1H), 4.83 (t, J = 7.1 Hz, 1H), 2.17 – 1.52 (m, 6H), 1.56 (s, 3H), 1.37 (d, J = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 165.9, 164.0, 155.3, 155.2, 126.6, 126.6, 125.9, 125.8, 115.7, 115.5, 108.0, 107.7, 61.2, 61.2, 43.6, 36.0, 29.9, 25.5, 19.7, 16.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -107.75. HRMS (ESI): calcd. for $C_{14}H_{16}FNO$ ($[M+H]^+$): 234.1289. found: 234.1290.

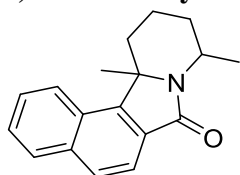
3-isopropyl-2-methylisoindolin-1-one (2k)



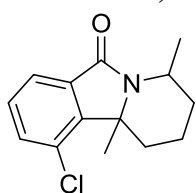
Following general procedure E, **1k** provided the product **2k** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow oil (6.8 mg, 18%). IR (neat) 2935, 1697, 1681, 1646, 1275, 1260, 1054, 1032, 764, 749 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.79 (m, 1H), 7.53 – 7.41 (m, 3H), 4.35 (d, J = 3.2 Hz, 1H), 3.12 (s, 3H), 2.43 (td, J = 7.0, 3.3 Hz, 1H), 1.17 (d, J = 7.1 Hz, 3H), 0.58 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 143.5, 133.4, 130.9, 128.1, 123.6, 123.0, 67.1, 29.5, 28.1, 18.7, 15.6. HRMS (ESI): calcd. for $C_{12}H_{15}NO$ ($[M+H]^+$): 190.1226. found: 190.1226.

4,12b-dimethyl-1,3,4,12b-tetrahydrobenzo[f]pyrido[2,1-a]isoindol-6(2H)-one (2l)

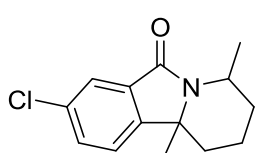
Following general procedure E, **1l** provided the mixture of **2l** and **2l'** after flash column chromatography (PE/EA = 9:1, v/v) which was further separated by semi-preparative high performance liquid chromatography (MeOH/H₂O = 65:35, 1.5mL/min on YMC-Park ODS-A) to yield **2l** as light yellow solid (13.2 mg, 25%). M.P. 72 – 75 °C. IR (neat) 2936, 2853, 1681, 1398, 1380, 1361, 1333, 1274, 1259, 1106, 765 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 8.08 – 7.96 (m, 2H), 7.90 (s, 2H), 7.65 – 7.54 (m, 2H), 4.95 (p, *J* = 6.3 Hz, 1H), 2.75 – 1.57 (m, 6H), 1.82 (s, 3H), 1.47 (d, *J* = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 149.7, 135.9, 130.0, 129.3, 128.5, 126.9, 126.8, 126.7, 124.1, 120.3, 63.0, 43.8, 36.2, 30.4, 25.4, 20.2, 16.6. HRMS (ESI): calcd. for C₁₈H₁₉NO ([M+H]⁺): 266.1539. found: 266.1539.

9,12a-dimethyl-10,11,12,12a-tetrahydrobenzo[g]pyrido[2,1-a]isoindol-7(9H)-one (2l')

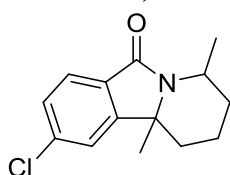
Following general procedure E, **1l** provided the mixture of **2l** and **2l'** after flash column chromatography (PE/EA = 9:1, v/v) which was further separated by semi-preparative high performance liquid chromatography (MeOH/H₂O = 65:35, 1.5mL/min on YMC-Park ODS-A) to yield **2l'** as light yellow solid (30.2 mg, 57%). M.P. 149 – 151 °C. IR (neat) 2922, 2851, 1680, 1393, 1358, 1309, 1275, 1141, 1111, 764, 749 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 8.36 (s, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.74 (s, 1H), 7.54 (dt, *J* = 18.7, 7.1 Hz, 2H), 4.92 (p, *J* = 7.2 Hz, 1H), 2.32 – 1.55 (m, 6H), 1.68 (s, 3H), 1.43 (d, *J* = 5.9 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 166.6, 148.5, 135.3, 133.1, 129.6, 129.0, 128.1, 127.5, 126.1, 124.0, 119.1, 61.5, 43.6, 36.7, 30.0, 26.5, 19.9, 16.6. HRMS (ESI): calcd. for C₁₈H₁₉NO ([M+H]⁺): 266.1539. found: 266.1542.

10-chloro-4,10b-dimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2m)

Following general procedure E and anhydrous MBTE was used as solvent, **1m** provided the mixture of **2m** and **2m'** after flash column chromatography (PE/EA = 9:1, v/v) which was further separated by semi-preparative high performance liquid chromatography (MeOH/H₂O = 80:20, 1.5mL/min on YMC-Park ODS-A) to yield **2m** as light yellow solid (26 mg, 52%). M.P. 80 – 83 °C. IR (neat) 2938, 2856, 1693, 1461, 1394, 1375, 1361, 1334, 1311, 1275, 1259, 750 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.75 (dd, *J* = 7.4, 1.1 Hz, 1H), 7.45 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.36 (t, *J* = 7.7 Hz, 1H), 4.85 (p, *J* = 6.6 Hz, 1H), 2.70 – 1.69 (m, 6H), 1.71 (s, 3H), 1.40 (d, *J* = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 165.4, 148.1, 133.5, 132.7, 129.4, 128.2, 122.4, 62.9, 43.9, 33.4, 29.9, 22.5, 19.8, 16.2. HRMS (ESI): calcd. for C₁₄H₁₆ClNO ([M+H]⁺): 250.0993. found: 250.0995.

8-chloro-4,10b-dimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2m')

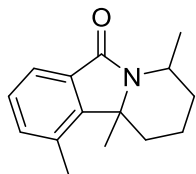
Following general procedure E and anhydrous MBTE was used as solvent, **1m** provided the mixture of **2m** and **2m'** after flash column chromatography (PE/EA = 9:1, v/v) which was further separated by semi-preparative high performance liquid chromatography (MeOH/H₂O = 80:20, 1.5mL/min on YMC-Park ODS-A) to yield **2m'** as light yellow oil (19 mg, 38%). IR (neat) 2921, 2850, 1686, 1429, 1358, 1332, 1275, 1260, 750, 708 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.80 (d, *J* = 1.9 Hz, 1H), 7.48 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.28 (s, 1H), 4.84 (t, *J* = 7.1 Hz, 1H), 2.24 – 1.64 (m, 6H), 1.56 (s, 3H), 1.38 (d, *J* = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 165.5, 151.1, 134.1, 132.4, 131.6, 124.0, 121.7, 61.4, 43.7, 36.1, 29.9, 25.5, 19.6, 16.5. HRMS (ESI): calcd. for C₁₄H₁₆ClNO ([M+H]⁺): 250.0993. found: 250.0996.

9-chloro-4,10b-dimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2n)

Following general procedure E and anhydrous MBTE was used as solvent, **1n** provided the product **2n** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow solid (14.5 mg, 29%). M.P. 109 – 112 °C. IR (neat) 2988, 2936, 1687, 1460, 1392, 1360, 1333, 1275, 1260, 1153, 749, 707, 691 cm⁻¹. ¹H NMR (400

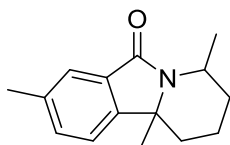
MHz, CDCl₃) δ 7.75 (d, J = 8.1 Hz, 1H), 7.39 (dd, J = 8.1, 1.7 Hz, 1H), 7.32 (d, J = 1.7 Hz, 1H), 4.83 (p, J = 7.0 Hz, 1H), 2.15 – 1.45 (m, 6H), 1.56 (s, 3H), 1.37 (d, J = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 165.9, 154.4, 137.8, 129.1, 128.5, 125.2, 121.0, 61.3, 43.7, 36.0, 29.9, 25.5, 19.7, 16.5. HRMS (ESI): calcd. for C₁₄H₁₆ClNO ([M+H]⁺): 250.0993. found: 250.0999.

4,10,10b-trimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2p/2q)



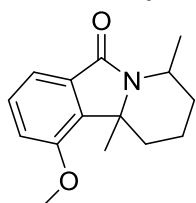
Following general procedure E, **1p** and **1q** provided the mixture of **2p/2q** and **2p'/2q'** after flash column chromatography (PE/EA = 9:1, v/v) which was further separated by semi-preparative high performance liquid chromatography (MeOH/H₂O = 70:30, 1.5mL/min on YMC-Park ODS-A) to yield **2p/2q** as light yellow oil (29.7 mg, 65% from **1p**; 30.0 mg, 66% from **1q**). IR (neat) 2927, 2853, 1685, 1388, 1332, 1309, 1160, 818, 791, 571 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, J = 7.2 Hz, 1H), 7.31 (dd, J = 14.8, 7.5 Hz, 2H), 4.87 (p, J = 7.2 Hz, 1H), 2.46 (s, 3H), 2.09 – 1.59 (m, 6H), 1.62 (s, 3H), 1.40 (d, J = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 166.9, 149.9, 134.0, 131.4, 131.2, 127.9, 121.5, 77.4, 77.3, 77.1, 76.8, 62.7, 43.5, 34.1, 29.8, 23.4, 19.9, 18.7, 16.4. HRMS (ESI): calcd. for C₁₅H₁₉NO ([M+H]⁺): 230.1539. found: 230.1540.

4,8,10b-trimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2p'/2q')



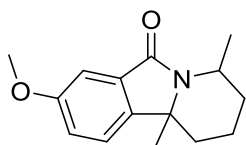
Following general procedure E, **1p** and **1q** provided the mixture of **2p/2q** and **2p'/2q'** after flash column chromatography (PE/EA = 9:1, v/v) which was further separated by semi-preparative high performance liquid chromatography (MeOH/H₂O = 70:30, 1.5mL/min on YMC-Park ODS-A) to yield **2p'/2q'** as light yellow solid (13.3 mg, 29% from **2p**; 13.4 mg, 29% from **2q**). M.P. 115 – 118 °C. IR (neat) 2935, 2853, 1685, 1484, 1394, 1374, 1361, 1334, 1312, 1156, 975, 762 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.64 (s, 1H), 7.33 (d, J = 7.7 Hz, 1H), 7.22 (d, J = 7.7 Hz, 1H), 4.85 (t, J = 7.0 Hz, 1H), 2.43 (s, 3H), 2.17 – 1.58 (m, 6H), 1.55 (s, 3H), 1.38 (d, J = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 150.4, 137.9, 132.4, 130.7, 124.1, 120.1, 61.3, 43.5, 36.4, 30.1, 25.6, 21.4, 19.7, 16.6. HRMS (ESI): calcd. for C₁₅H₁₉NO ([M+H]⁺): 230.1539. found: 230.1539.

10-methoxy-4,10b-dimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2r)

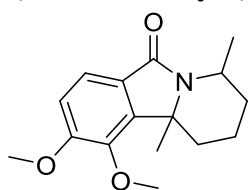


Following general procedure E, **1r** provided the mixture of **2r** and **2r'** after flash column chromatography (PE/EA = 9:1, v/v) which was further separated by semi-preparative high performance liquid chromatography (MeOH/H₂O = 65:35, 1.5mL/min on YMC-Park ODS-A) to yield **2r** as light yellow oil (29.4 mg, 60%). IR (neat) 2937, 2855, 1686, 1602, 1490, 1393, 1360, 1266, 1066, 754 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.43 (d, J = 7.5 Hz, 1H), 7.36 (t, J = 7.7 Hz, 1H), 6.98 (d, J = 7.9 Hz, 1H), 4.83 (p, J = 7.1 Hz, 1H), 3.88 (s, 3H), 2.50 – 1.53 (m, 6H), 1.62 (s, 3H), 1.38 (d, J = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 166.6, 154.2, 139.7, 132.6, 129.3, 115.8, 113.2, 61.9, 55.4, 43.6, 34.3, 30.2, 22.9, 19.9, 16.2. HRMS (ESI): calcd. for C₁₅H₁₉NO₂ ([M+H]⁺): 246.1489. found: 246.1488.

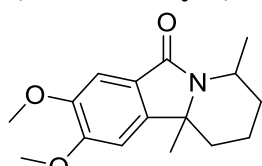
8-methoxy-4,10b-dimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2r')



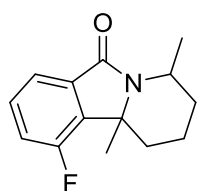
Following general procedure E, **1r** provided the mixture of **2r** and **2r'** after flash column chromatography (PE/EA = 9:1, v/v) which was further separated by semi-preparative high performance liquid chromatography (MeOH/H₂O = 65:35, 1.5mL/min on YMC-Park ODS-A) to yield **2r'** as light yellow oil (9.8 mg, 20%). IR (neat) 2923, 2852, 1683, 1491, 1359, 1336, 1276, 1260, 1067, 764, 749 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.32 (s, 1H), 7.23 (d, J = 8.3 Hz, 1H), 7.08 (d, J = 7.9 Hz, 1H), 4.85 (t, J = 7.0 Hz, 1H), 3.86 (s, 3H), 2.14 – 1.63 (m, 6H), 1.54 (s, 3H), 1.38 (d, J = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 166.8, 159.8, 145.5, 131.9, 121.3, 119.8, 106.4, 61.1, 55.8, 43.6, 36.5, 30.0, 25.6, 19.7, 16.6. HRMS (ESI): calcd. for C₁₅H₁₉NO₂ ([M+H]⁺): 246.1489. found: 246.1486.

9,10-dimethoxy-4,10b-dimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2s)

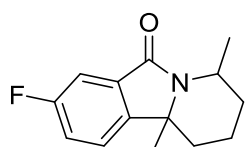
Following general procedure E, **1s** provided the mixture of **2s** and **2s'** after flash column chromatography (PE/EA = 9:1, v/v) which was further separated by semi-preparative high performance liquid chromatography (MeOH/H₂O = 65:35, 1.5mL/min on YMC-Park ODS-A) to yield **2s** light yellow solid (31.9 mg, 58%). M.P. 184 – 188 °C. IR (neat) 2925, 2853, 1680, 1495, 1395, 1374, 1361, 1274, 1251, 1106, 1045, 738 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, *J* = 8.2 Hz, 1H), 6.97 (d, *J* = 8.2 Hz, 1H), 3.91 (d, *J* = 4.9 Hz, 6H), 2.07 – 1.52 (m, 6H), 1.62 (s, 3H), 1.36 (d, *J* = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 166.3, 155.5, 144.7, 143.3, 124.6, 119.6, 112.4, 61.6, 60.8, 56.2, 43.5, 35.0, 30.0, 23.9, 19.9, 16.3. HRMS (ESI): calcd. for C₁₆H₂₁NO₃ ([M+H]⁺): 276.1594. found: 276.1594.

8,9-dimethoxy-4,10b-dimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2s')

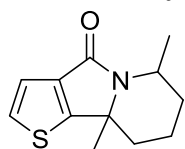
Following general procedure E, **1s** provided the mixture of **2s** and **2s'** after flash column chromatography (PE/EA = 9:1, v/v) which was further separated by semi-preparative high performance liquid chromatography (MeOH/H₂O = 65:35, 1.5mL/min on YMC-Park ODS-A) to yield **2s'** as light yellow solid (18.7 mg, 34%). M.P. 103 – 107 °C. IR (neat) 2932, 2853, 1673, 1497, 1470, 1422, 1389, 1360, 1330, 1301, 1213, 1060, 759 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.27 (s, 1H), 6.75 (s, 1H), 4.79 (p, *J* = 7.8, 7.4 Hz, 1H), 3.91 (d, *J* = 8.7 Hz, 6H), 2.22 – 1.41 (m, 6H), 1.52 (s, 3H), 1.34 (d, *J* = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 152.6, 149.4, 146.6, 122.6, 105.4, 102.6, 61.0, 56.3, 56.2, 43.5, 36.4, 30.0, 25.5, 19.7, 16.5. HRMS (ESI): calcd. for C₁₆H₂₁NO₃ ([M+H]⁺): 276.1594. found: 276.1596.

10-fluoro-4,10b-dimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2t)

Following general procedure E, **1t** provided the mixture of **2t** and **2t'** after flash column chromatography (PE/EA = 9:1, v/v) which was further separated by semi-preparative high performance liquid chromatography (MeOH/H₂O = 65:35, 1.5mL/min on YMC-Park ODS-A) to yield **2t** as light yellow solid (24.2 mg, 52%). M.P. 105 – 107 °C. IR (neat) 2937, 2853, 1693, 1597, 1484, 1393, 1361, 1281, 1243, 1009, 779, 758 cm⁻¹. ¹H NMR (600 MHz, CDCl₃) δ 7.63 (d, *J* = 7.4 Hz, 1H), 7.42 – 7.36 (m, 1H), 7.16 (t, *J* = 8.4 Hz, 1H), 4.83 (t, *J* = 6.9 Hz, 1H), 2.14 – 1.52 (m, 6H), 1.66 (s, 3H), 1.39 (d, *J* = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 165.7, 158.4, 156.0, 138.1, 138.0, 133.9, 133.9, 129.9, 129.9, 119.7, 119.7, 118.6, 118.4, 61.1, 61.1, 43.8, 34.9, 30.0, 24.0, 19.8, 16.2. ¹⁹F NMR (376 MHz, CDCl₃) δ -122.27. HRMS (ESI): calcd. for C₁₄H₁₆FNO ([M+H]⁺): 234.1289. found: 234.1299. Recrystallization of the product from ethyl acetate at room temperature afforded crystals suitable for XRD analysis.

8-fluoro-4,10b-dimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (2t')

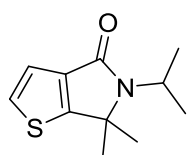
Following general procedure E, **1t** provided the mixture of **2t** and **2t'** after flash column chromatography (PE/EA = 9:1, v/v) which was further separated by semi-preparative high performance liquid chromatography (MeOH/H₂O = 65:35, 1.5mL/min on YMC-Park ODS-A) to yield **2t'** as light yellow solid (8.4 mg, 18%). M.P. 96 – 98 °C. IR (neat) 2937, 1684, 1485, 1359, 1335, 1274, 1261, 1158, 787, 764, 747 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.48 (d, *J* = 7.0 Hz, 1H), 7.29 (dd, *J* = 8.4, 4.5 Hz, 1H), 7.21 (t, *J* = 8.7 Hz, 1H), 4.88 – 4.81 (m, 1H), 2.14 – 1.54 (m, 6H), 1.56 (s, 3H), 1.38 (d, *J* = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 165.8, 163.9, 161.5, 148.4, 148.4, 132.7, 132.6, 121.9, 121.8, 119.0, 118.8, 110.6, 110.3, 61.3, 43.7, 36.3, 29.9, 25.6, 19.6, 16.5. ¹⁹F NMR (376 MHz, CDCl₃) δ -113.91. HRMS (ESI): calcd. for C₁₄H₁₆FNO ([M+H]⁺): 234.1289. found: 234.1297.

6,9a-dimethyl-7,8,9,9a-tetrahydrothieno[2,3-a]indolizin-4(6H)-one (2u)

Following general procedure E, **1u** provided the product **2u** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow solid (4.4 mg, 10%). M.P. 114 –

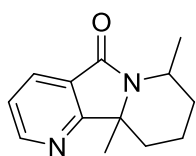
118 °C. IR (neat) 2969, 2935, 2853, 1681, 1403, 1381, 1327, 1301, 1003, 800, 721 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.27 (d, J = 4.9 Hz, 1H), 7.19 (d, J = 4.8 Hz, 1H), 4.78 (t, J = 7.1 Hz, 1H), 2.13 – 1.57 (m, 6H), 1.60 (s, 3H), 1.34 (d, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 163.7, 162.2, 137.7, 128.6, 120.3, 61.4, 44.0, 37.5, 30.1, 26.8, 19.9, 16.4. HRMS (ESI): calcd. for $\text{C}_{12}\text{H}_{15}\text{NOS}$ ($[\text{M}+\text{H}]^+$): 222.0947. found: 222.0950.

5-isopropyl-6,6-dimethyl-5,6-dihydro-4H-thieno[2,3-c]pyrrol-4-one (2v)



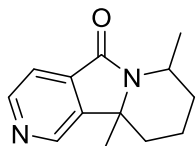
Following general procedure E, **1v** provided the product **2v** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow solid (12.5 mg, 30%). M.P. 97 – 100 °C. IR (neat) 2967, 2927, 1673, 1464, 1418, 1380, 1329, 1277, 1207, 1074, 825, 715 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.27 (d, J = 3.4 Hz, 1H), 7.15 (d, J = 4.9 Hz, 0H), 3.57 (p, J = 6.9 Hz, 1H), 1.52 (d, J = 6.9 Hz, 6H), 1.52 (s, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 164.1, 160.3, 139.2, 128.5, 120.3, 62.9, 45.2, 26.6, 20.7. HRMS (ESI): calcd. for $\text{C}_{11}\text{H}_{15}\text{NOS}$ ($[\text{M}+\text{H}]^+$): 210.0947. found: 210.0951.

7,10a-dimethyl-8,9,10,10a-tetrahydropyrido[2,3-a]indolizin-5(7H)-one (2w)



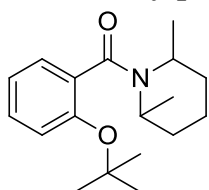
Following general procedure E, **1w** provided the product **2w** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow solid (38.9 mg, 90%). M.P. 100 – 103 °C. IR (neat) 2932, 2953, 1689, 1606, 1417, 1390, 1359, 1334, 1275, 1260, 764, 749 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 8.69 (dd, J = 5.0, 1.6 Hz, 1H), 8.11 (dd, J = 7.6, 1.6 Hz, 1H), 7.35 (dd, J = 7.6, 4.9 Hz, 1H), 4.90 (p, J = 6.3 Hz, 1H), 2.32 – 1.67 (m, 6H), 1.64 (s, 3H), 1.40 (d, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 170.9, 165.1, 152.2, 132.1, 124.1, 123.1, 62.2, 43.4, 34.4, 30.1, 24.0, 19.6, 16.2. HRMS (ESI): calcd. for $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}$ ($[\text{M}+\text{H}]^+$): 217.1335. found: 217.1333.

7,10a-dimethyl-8,9,10,10a-tetrahydropyrido[3,4-a]indolizin-5(7H)-one (2x)



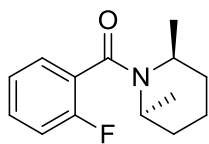
Following general procedure E, **1x** provided the product **2x** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow solid (15.1 mg, 35%). M.P. 138 – 140 °C. IR (neat) 2935, 1693, 1419, 1392, 1360, 1334, 1275, 1260, 764, 749, 701 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 8.74 (s, 2H), 7.72 (s, 1H), 4.86 (t, J = 7.2 Hz, 1H), 2.29 – 1.65 (m, 6H), 1.64 (s, 3H), 1.39 (d, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 165.0, 149.3, 147.0, 143.3, 138.1, 117.8, 61.4, 43.9, 35.9, 29.8, 25.4, 19.4, 16.3. HRMS (ESI): calcd. for $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}$ ($[\text{M}+\text{H}]^+$): 217.1335. found: 217.1331.

(2-(t-butoxy)phenyl)(2,6-dimethylpiperidin-1-yl)methanone (3)



Following general procedure E without $\text{Ir}(\text{ppy})_3$, **1a** provided the product **3** as light yellow oil (6.4 mg, 11%). IR (neat) 3068, 2973, 2934, 2870, 1632, 1597, 1447, 1416, 1366, 1160, 898, 853, 763, 647, 515 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.26 – 6.98 (m, 4H), 5.18 – 4.73 (m, 1H), 3.92 – 3.68 (m, 1H), 1.81 – 1.17 (m, 21H). ^{13}C NMR (101 MHz, CDCl_3) δ 169.54, 169.43, 152.73, 151.29, 133.34, 132.78, 129.17, 128.68, 128.27, 126.82, 123.29, 122.49, 122.47, 121.75, 80.02, 79.81, 49.91, 48.95, 44.15, 43.59, 30.81, 30.53, 30.05, 29.38, 21.70, 21.17, 20.72, 20.61, 14.37, 14.32. HRMS (ESI): calcd. for $\text{C}_{18}\text{H}_{27}\text{NO}_2$ ($[\text{M}+\text{H}]^+$): 290.2115. found: 290.2112.

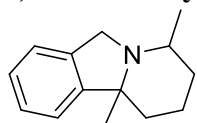
((2R,6R)-2,6-dimethylpiperidin-1-yl)(2-fluorophenyl)methanone (4)



Following the procedure for synthesis of **4**, 2-fluorobenzoic acid (0.2 mmol) and *trans*-(+)-2,6-lupetidine (0.6 mmol) provided the product **4** after flash column chromatography (PE/EA = 5:1, v/v) as light yellow oil (36.4 mg; 58%). $[\alpha]_D^{26.4} = +70.6^\circ$ (CHCl_3 , $c=0.05$, 86% ee). IR (neat) 2930, 1632, 1488, 1452, 1406, 1374, 1275, 1260, 1221, 1029, 764, 750 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.52 – 6.90 (m, 4H), 4.10 (d, J = 7.2 Hz, 2H), 2.26 – 1.26 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.26, 166.82, 130.61, 130.54, 128.67, 128.63, 126.46, 126.27, 124.51, 124.48, 116.03, 115.82, 60.50, 29.80, 27.02, 21.13, 14.30. HRMS (ESI): calcd. for $\text{C}_{14}\text{H}_{18}\text{FNO}$ ($[\text{M}+\text{H}]^+$): 236.1445. found: 236.1451. HPLC conditions:

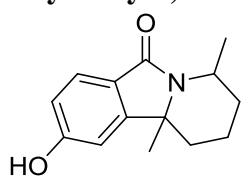
Chiralcel OJ-H column, 220 nm & 254nm, flow rate: 0.5 ml/min, i-PrOH/hexanes = 1/9, t_{major} = 15.610 min, t_{minor} = 17.440 min; 86% ee.

4,10b-dimethyl-1,2,3,4,6,10b-hexahydropyrido[2,1-a]isoindole (5)



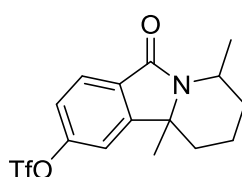
Following the procedure for synthesis of **5**, the **2a** (0.4 mmol) provided the product **5** after flash column chromatography (PE/EA = 95:5, v/v) as light yellow oil (53 mg; 66%). IR (neat) 3471, 2936, 2858, 2795, 2480, 1446, 1417, 1367, 1239, 1206, 1113, 826, 749, 667, 566 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.26 – 7.12 (m, 3H), 7.08 (d, J = 7.1 Hz, 1H), 4.28 (d, J = 14.6 Hz, 1H), 3.89 (d, J = 14.6 Hz, 1H), 2.47 – 2.37 (m, 1H), 1.60 – 1.10 (m, 12H). ^{13}C NMR (101 MHz, CDCl_3) δ 130.06, 128.98, 126.99, 126.62, 123.34, 121.03, 56.52, 53.80, 33.22, 30.93, 29.55, 27.36, 22.85, 18.94. HRMS (ESI): calcd. for $\text{C}_{14}\text{H}_{19}\text{N}$ ($[\text{M}+\text{H}]^+$): 202.1590. found: 202.1592.

9-hydroxy-4,10b-dimethyl-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (6)



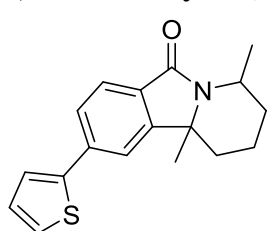
Following the procedure for synthesis of **6**, **2d** provided the product **6** as off-white soli. M.P. 202 – 205 $^{\circ}\text{C}$. IR (neat) 3170, 2938, 2854, 1648, 1610, 1463, 1405, 1375, 1306, 1214, 1181, 1105, 784, 701 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 9.55 (brs, 1H), 7.62 (d, J = 8.2 Hz, 1H), 6.94 (dd, J = 8.3, 1.9 Hz, 1H), 6.85 (d, J = 2.0 Hz, 1H), 4.81 (p, J = 7.1 Hz, 1H), 2.09 – 1.47 (m, 6H), 1.52 (s, 3H), 1.35 (d, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 167.8, 161.3, 155.6, 125.3, 121.2, 116.1, 107.5, 61.7, 43.8, 36.1, 30.1, 25.5, 19.8, 16.4. HRMS (ESI): calcd. for $\text{C}_{14}\text{H}_{17}\text{NO}_2$ ($[\text{M}+\text{H}]^+$): 232.1332. found: 232.1329.

4,10b-dimethyl-6-oxo-1,2,3,4,6,10b-hexahydropyrido[2,1-a]isoindol-9-yl trifluoromethanesulfonate (7)



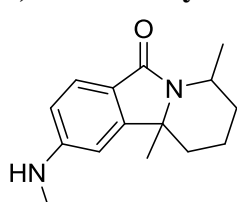
Following the procedure for synthesis of **7**, **6** provided the product **7** as off-white solid (123 mg, 85% in two steps). M.P. 128 – 131 $^{\circ}\text{C}$. IR (neat) 3054, 2980, 2943, 2870, 1676, 1419, 1380, 1311, 1206, 1141, 934, 887, 822, 692 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.90 (d, J = 8.3 Hz, 1H), 7.32 (dd, J = 8.3, 2.1 Hz, 1H), 7.25 (d, J = 2.1 Hz, 1H), 4.83 (q, J = 7.0 Hz, 1H), 2.20 – 1.57 (m, 6H), 1.59 (s, 3H), 1.38 (d, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 165.0, 155.0, 151.7, 130.6, 126.0, 121.3, 120.4, 117.2, 114.1, 43.9, 35.9, 29.8, 25.5, 19.6, 16.4. ^{19}F NMR (376 MHz, CDCl_3) δ -72.72. HRMS (ESI): calcd. for $\text{C}_{15}\text{H}_{16}\text{F}_3\text{NO}_4\text{S}$ ($[\text{M}+\text{H}]^+$): 364.0825. found: 364.0823.

4,10b-dimethyl-9-(thiophen-2-yl)-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (8)



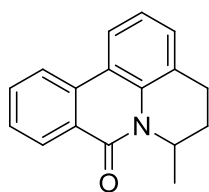
Following the procedure for synthesis of **8**, **7** provided the product **8** as colorless oil (22 mg, 74%). IR (neat) 3071, 2969, 2935, 2867, 1682, 1614, 1480, 1391, 1332, 1107, 828, 803, 786, 695 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.82 (d, J = 7.9 Hz, 1H), 7.66 (dd, J = 7.9, 1.6 Hz, 1H), 7.52 (d, J = 1.5 Hz, 1H), 7.39 (dd, J = 3.6, 1.2 Hz, 1H), 7.33 (dd, J = 5.1, 1.2 Hz, 1H), 7.10 (dd, J = 5.1, 3.6 Hz, 1H), 4.85 (t, J = 7.5 Hz, 1H), 2.21 – 1.62 (m, 6H), 1.61 (s, 3H), 1.39 (d, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.5, 153.8, 143.7, 137.7, 129.6, 128.3, 125.9, 125.9, 124.4, 124.3, 117.6, 61.5, 43.5, 36.2, 30.0, 25.6, 19.7, 16.5. HRMS (ESI): calcd. for $\text{C}_{18}\text{H}_{19}\text{NOS}$ ($[\text{M}+\text{H}]^+$): 298.1260. found: 298.1261.

4,10b-dimethyl-9-(methylamino)-1,3,4,10b-tetrahydropyrido[2,1-a]isoindol-6(2H)-one (9)



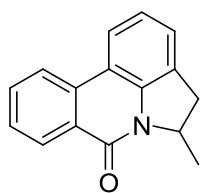
Following the procedure for synthesis of **9**, **2e** provided the product **9** as red solid (222.2 mg, 91%). M.P. 155 – 157 $^{\circ}\text{C}$. IR (neat) 3334, 2971, 2936, 1659, 1613, 1525, 1392, 1333, 1307, 1237, 1104, 783, 701 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.60 (d, J = 8.3 Hz, 1H), 6.58 (dd, J = 8.3, 2.1 Hz, 1H), 6.41 (d, J = 2.1 Hz, 1H), 4.79 (dq, J = 7.4, 5.9 Hz, 1H), 4.22 (brs, 1H), 2.88 (s, 3H), 2.11 – 1.52 (m, 6H), 1.53 (s, 3H), 1.34 (d, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 167.4, 155.5, 152.5, 124.9, 119.5, 112.6, 102.2, 60.9, 43.1, 36.3, 30.6, 30.1, 25.7, 20.0, 16.6. HRMS (ESI): calcd. for $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}$ ($[\text{M}+\text{H}]^+$): 245.1648. found: 245.1650.

6-methyl-5,6-dihydropyrido[3,2,1-de]phenanthridin-8(4H)-one (S3)



Following general procedure E, S2 provided the product S3 after flash column chromatography (PE/EA = 9:1, v/v) as light yellow solid (5.5 mg, 11%). M.P. 106 – 109 °C. IR (neat) 2921, 2850, 1643, 1609, 1587, 1480, 1423, 1334, 1318, 1239, 1161, 754 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 8.56 (d, *J* = 9.4 Hz, 1H), 8.29 (d, *J* = 8.2 Hz, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.75 (t, *J* = 7.7 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 7.3 Hz, 1H), 7.23 (t, *J* = 7.7 Hz, 1H), 5.50 (dt, *J* = 7.1, 3.5 Hz, 1H), 3.24 (ddd, *J* = 18.7, 13.2, 6.3 Hz, 1H), 2.96 – 2.87 (m, 1H), 2.12 – 2.01 (m, 2H), 1.36 (d, *J* = 6.7 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.7, 133.8, 133.8, 132.3, 129.9, 128.7, 127.9, 125.6, 124.9, 121.9, 121.8, 121.4, 119.5, 46.1, 25.9, 23.2, 17.9. HRMS (ESI): calcd. for C₁₇H₁₅NO ([M+H]⁺): 250.1226. found: 250.1224.

5-methyl-4H-pyrrolo[3,2,1-de]phenanthridin-7(5H)-one (S5)



Following general procedure E, S4 provided the product S5 after flash column chromatography (PE/EA = 9:1, v/v) as light yellow solid (4.2 mg, 9%). M.P. 93 – 95 °C. IR (neat) 3360, 3004, 2961, 2923, 2851, 1651, 1601, 1482, 1388, 1275, 1260, 1096, 750 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 8.59 (d, *J* = 9.4 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.79 (t, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 7.3 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 5.17 (ddt, *J* = 9.8, 6.5, 3.1 Hz, 1H), 3.68 (dd, *J* = 16.5, 9.5 Hz, 1H), 3.03 (dd, *J* = 16.5, 3.6 Hz, 1H), 1.67 (d, *J* = 6.4 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 139.3, 134.0, 132.1, 129.6, 128.5, 127.9, 127.9, 124.8, 123.5, 122.1, 120.0, 116.9, 56.1, 36.5, 20.8. HRMS (ESI): calcd. for C₁₆H₁₃NO ([M+H]⁺): 236.1070. found: 236.1070.

20 Additional Substrates

Several substrates S1, S2, S4, S6, S7, S8, S9, S10 was synthesized and subjected to general procedure E for annulation reaction. S1 did not offer the corresponding product. S2 and S4 gave C-C bonds between aromatic rings. S6-S8 gave adducts of *t*-BuO⁻. S9 gave complex mixture. S10 gave trace annulation product as detected on GC-MS.

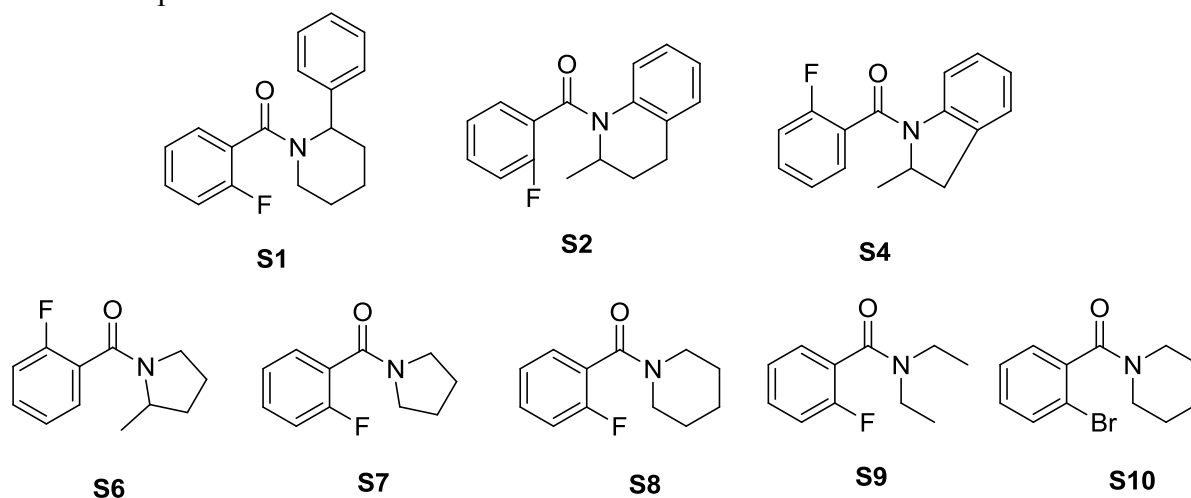
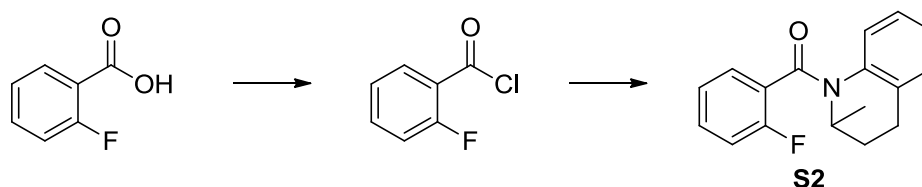


Figure S15. Additional Amide Substrates.

20.1 Synthesis of S2

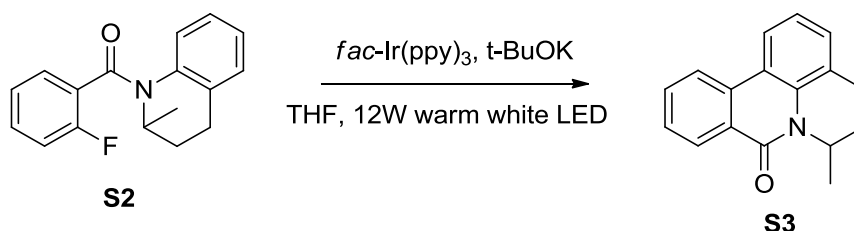
2-fluorobenzoic acid (10mmol) was suspended in dichloromethane (30mL) and SOCl₂ (2mL) was

added. DMF (3 drops) was used as accelerant and the mixture was refluxed for 3h. The reaction was concentrated to dryness under reduced pressure. The crude acid chloride was dissolved in anhydrous dichloromethane and cooled to 0 °C with ice-bath. 2-methyl-1,2,3,4-tetrahydroquinoline (15mmol) was added and the resulting suspension was stirred at room temperature overnight. When the reaction completed, the mixture was washed with 2 M hydrochloric acid (3 times), saturated NaHCO₃ (3 times) and brine (3 times) in turn, dried over Na₂SO₄ and filtered. Solvent was removed under reduced pressure to yield the crude **S2** which was recrystallized from ethyl acetate.



Scheme S14. Synthesis of **S2**

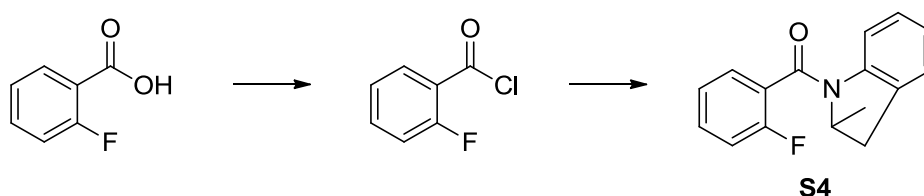
Following general procedure **E**, **S2** provided the product **S4** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow solid (5.5 mg, 11%).



Scheme S15. Photoredox Annulation of **S2**

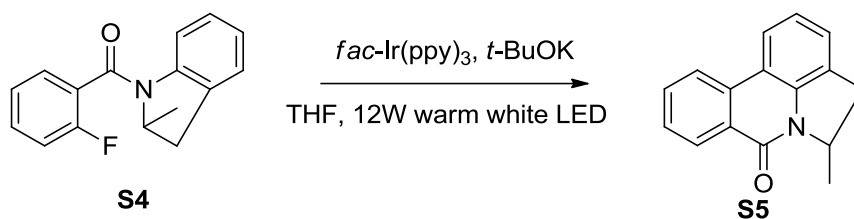
20.2 Synthesis of **S4**

2-fluorobenzoic acid (10mmol) was suspended in dichloromethane (30mL) and SOCl₂ (2mL) was added. DMF (3 drops) was used as accelerant and the mixture was refluxed for 3h. The reaction was concentrated to dryness under reduced pressure. The crude acid chloride was dissolved in anhydrous dichloromethane and cooled to 0 °C with ice-bath. 2-methylindoline (15mmol) was added and the resulting suspension was stirred at room temperature overnight. When the reaction completed, the mixture was washed with 2 M hydrochloric acid (3 times), saturated NaHCO₃ (3 times) and brine (3 times) in turn, dried over Na₂SO₄ and filtered. Solvent was removed under reduced pressure to yield the crude **S4** which was recrystallized from ethyl acetate.



Scheme S16. Synthesis of **S4**

Following general procedure **E**, **S4** provided the product **S5** after flash column chromatography (PE/EA = 9:1, v/v) as light yellow solid (4.2 mg, 9%).



Scheme S17. Photoredox Annulation of **S4**

20.3 Photoredox Annulation of **S11**

When **S11** was subject to the photoredox procedure E, trace amount of annulation product was detected on GC-MS. It was too depleted to isolate.

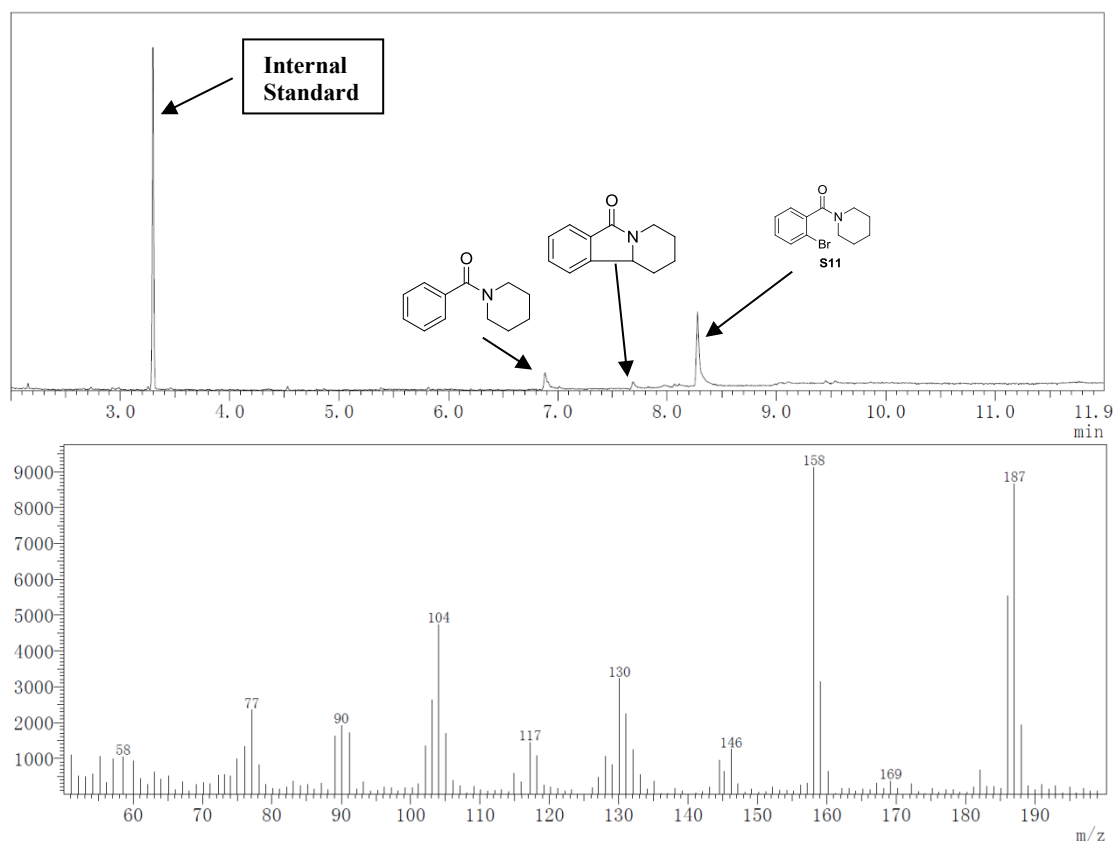


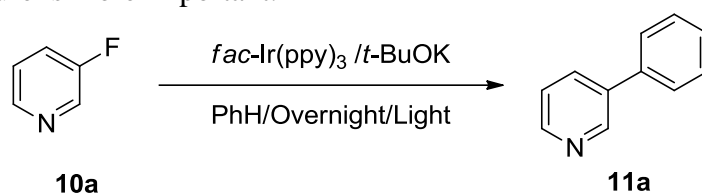
Figure S16. GC-MS Monitoring of the reaction of **S11**.

20.4 Photoredox intermolecular C-X arylation reaction

General procedure F: To a Schlenk tube equipped with a stir bar was added halogen-substituted arene **10** (0.2 mmol), *t*-BuOK (26.9 mg, 0.24 mmol) and *fac*-Ir(ppy)₃ (1 or 5 mol %) under argon. Anhydrous benzene (2.0 mL) was added via syringe. Then the Schlenk tube was sealed with Teflon screw cap. The mixture was irradiated with 100 W white LED for 6 hours. The residue was cooled to rt and diluted with water. Organic layer was extracted with EA three times. The combined organic layer was washed with brine, dried (Na₂SO₄), and concentrated. The residue was purified with silica gel chromatography with PE/EA as eluent, giving desired product **11**.

Several control experiments were carried out to investigate the major factor that enables this transformation with 1 mol % *fac*-Ir(ppy)₃ and *t*-BuOK (1.2 equiv). We found both *fac*-Ir(ppy)₃ and

t-BuOK are necessary to achieved the conversion. Increased luminescence could benefit the reactivity and increased temperature is more important.



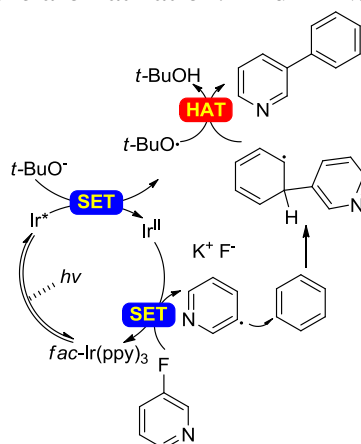
Entry ^a	Catalytic condtions	Light power	Temperature	Conversion by GC-MS
1 ^c	Ir/ <i>t</i> -BuOK	100 W	100-104 °C	96%
2	Ir/ <i>t</i> -BuOK	100 W	70 °C	15%
3	Ir/ <i>t</i> -BuOK	12 W	70 °C	trace
4	Ir/ <i>t</i> -BuOK	No light	103 °C	N. R.
5	<i>t</i> -BuOK	100 W	100-104 °C	N. R.
6	Ir	100 W	100-104 °C	N. R.

The device of 100 W LED and 100 °C reaction using it was depicted here in **Figure S17**.



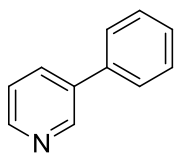
Figure S17. 100 W white LED and reaction.

A plausible mechanism was proposed in **Scheme S18**. In this pathway, *t*-BuO[•] radical work as a hydrogen atom abstractor to furnish the aromatization. And KF would be a side product.



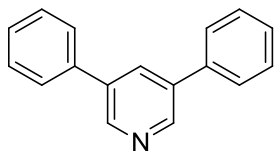
Scheme S18 A plausible pathway of the intermolecular C-F arylation

3-phenylpyridine (11a)



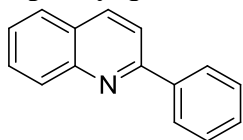
This compound was prepared using general procedure **F** with 3-fluoropyridine **10a** (18.8 mg, 0.2 mmol), *t*-BuOK (26.9 mg, 0.24 mmol) and *fac*-Ir(ppy)₃ (1 mol %) in benzene (2 mL). 70.5 mg, 91%. ¹H NMR (400 MHz, CDCl₃) δ 8.86 (s, 1H), 8.60 (d, *J* = 5.7 Hz, 1H), 7.88 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.58 (d, *J* = 7.5 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.45 – 7.33 (m, 2H). The data is consistent with reported value.^[1]

3,5-diphenylpyridine (11b)



This compound was prepared using general procedure **F** with 3,5-difluoropyridine **10b** (23 mg, 0.2 mmol), *t*-BuOK (56 mg, 0.50 mmol) and *fac*-Ir(ppy)₃ (5 mol %) in benzene (2 mL). 21.7 mg, 47%. ¹H NMR (400 MHz, CDCl₃) δ 8.27 – 8.13 (m, 4H), 7.87 (d, *J* = 8.6 Hz, 1H), 7.83 (d, *J* = 8.1 Hz, 1H), 7.74 (t, *J* = 7.7 Hz, 1H), 7.61 – 7.43 (m, 1H). The data is consistent with reported value.^[2] Because the 11b was accompanied with some *t*-BuO adduct with very close R_f on silica gel, carefully chromatography resulted in some loss of yield of **11b**.

2-phenylquinoline (11c)

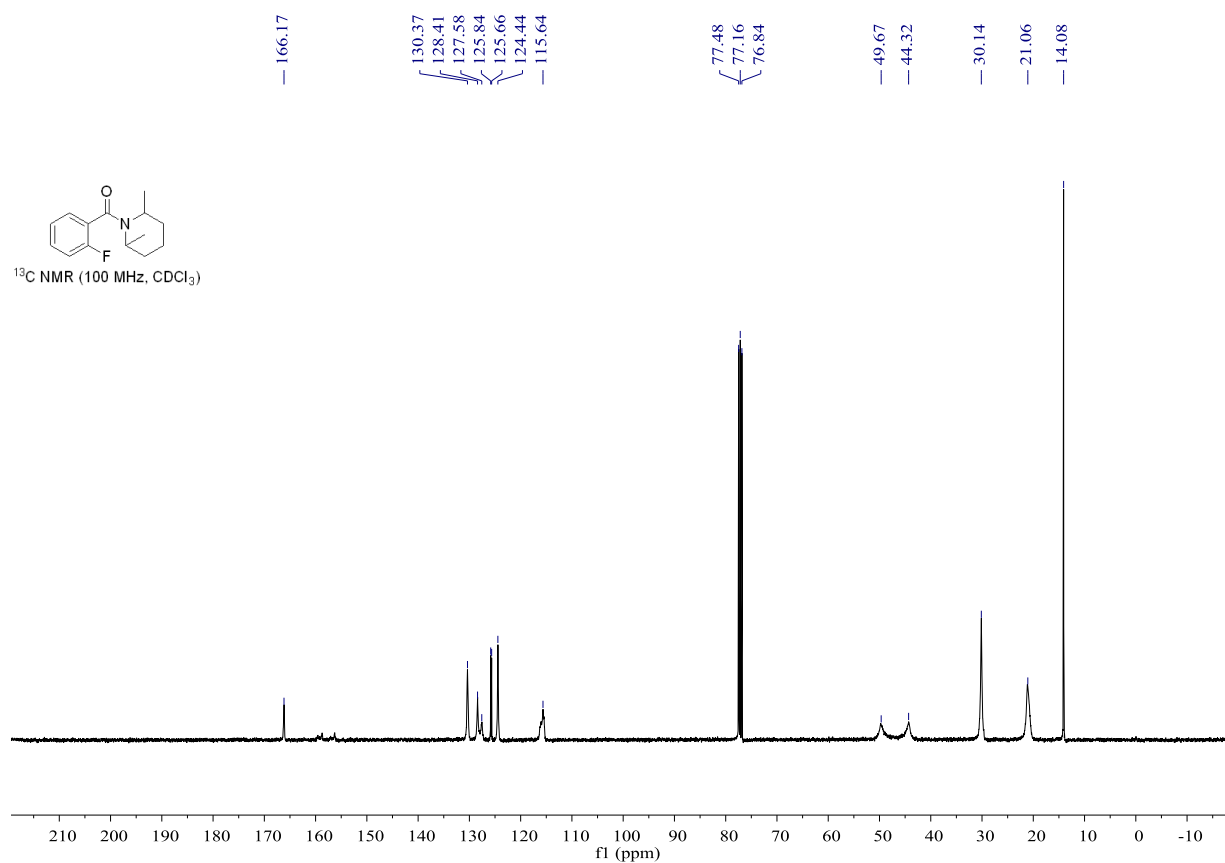
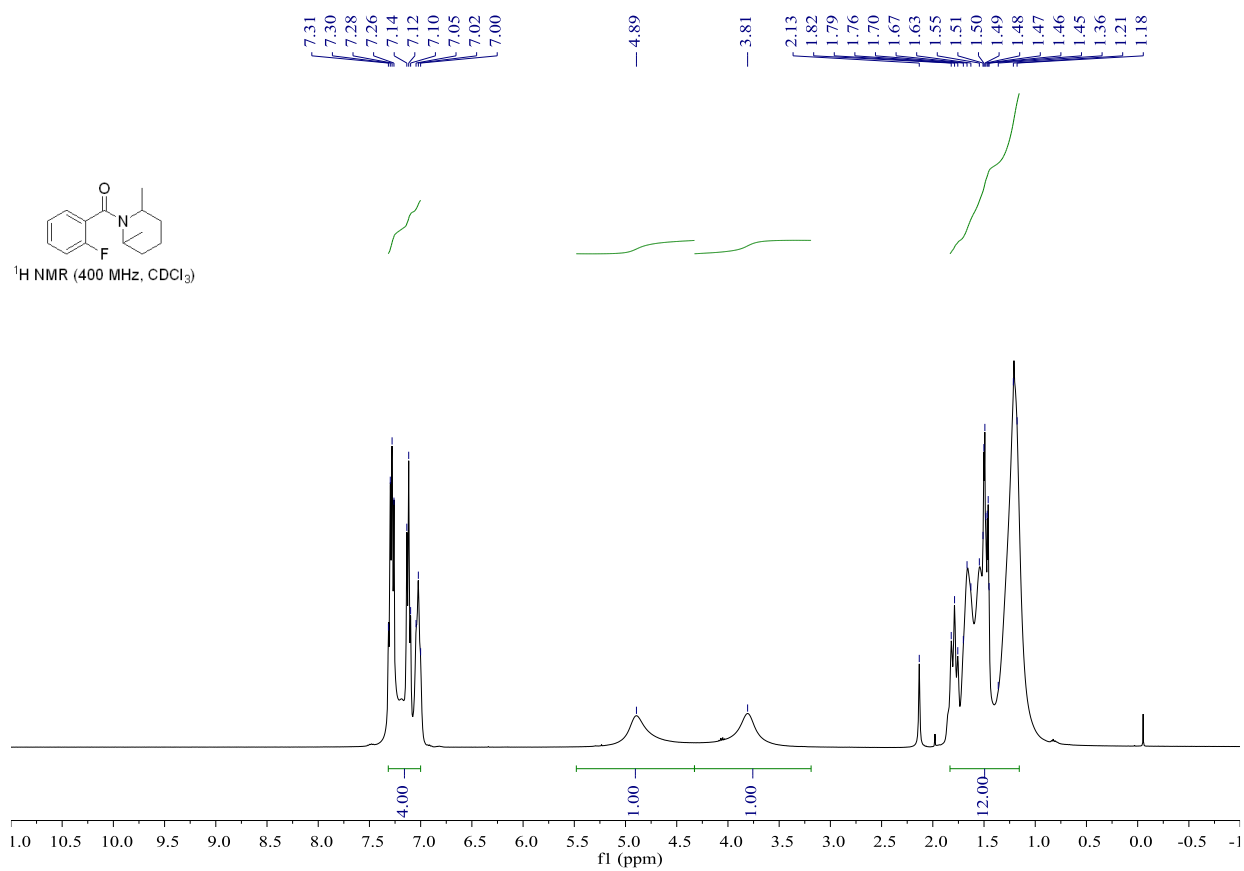


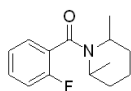
This compound was prepared using general procedure **F** (except using 12 W warm white LEDs at 70 °C) with 2-chloroquinoline (32.6 mg, 0.20 mmol), *t*-BuOK (26.9 mg, 0.24 mmol) and *fac*-Ir(ppy)₃ (1 mol %) in benzene (2 mL). 35.7 mg, 87%. ¹H NMR (400 MHz, CDCl₃) δ 8.83 (s, 2H), 8.06 (s, 1H), 7.65 (d, *J* = 7.3 Hz, 4H), 7.51 (t, *J* = 7.5 Hz, 4H), 7.44 (t, *J* = 7.3 Hz, 2H). Because the 2-fluoroquinoline was highly reactive in the S_NAr reaction with *t*-BuOK as nucleophile, 2-chloroquinoline was used instead. The data is consistent with reported value.^[1]

[1] Ogawa, H.; Yang, Z.-K.; Minami, H.; Kojima, K.; Saito, T.; Wang, C.; Uchiyama, M. *ACS Catal.* **2017**, 7, 3988.

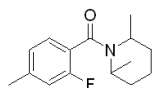
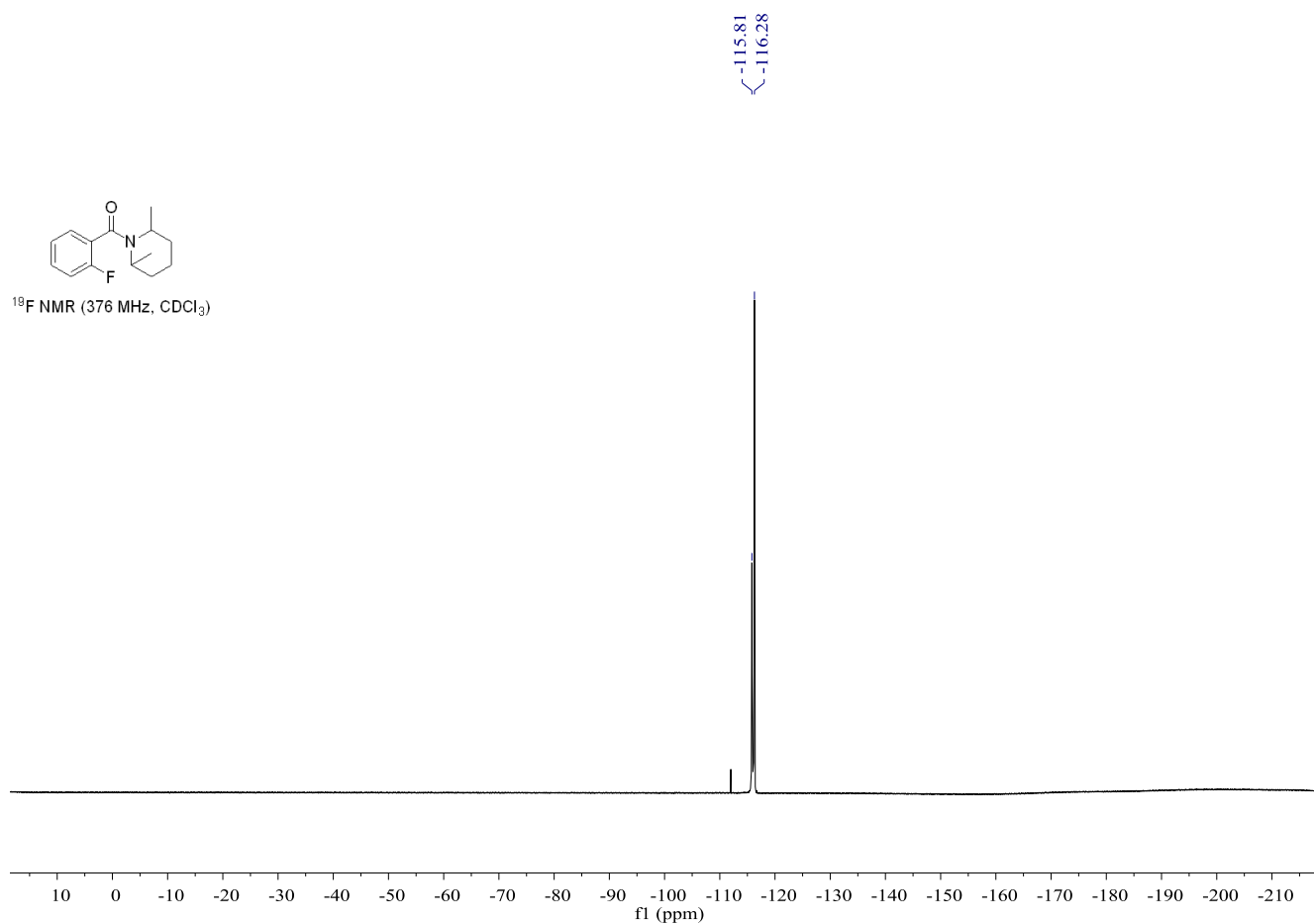
[2] Ye, Z.; Wang, W.; Luo, F.; Zhang, S.; Cheng, J. *Org. Lett.* **2009**, 11, 3974.

21. ^1H -NMR, ^{13}C -NMR and ^{19}F -NMR Spectra

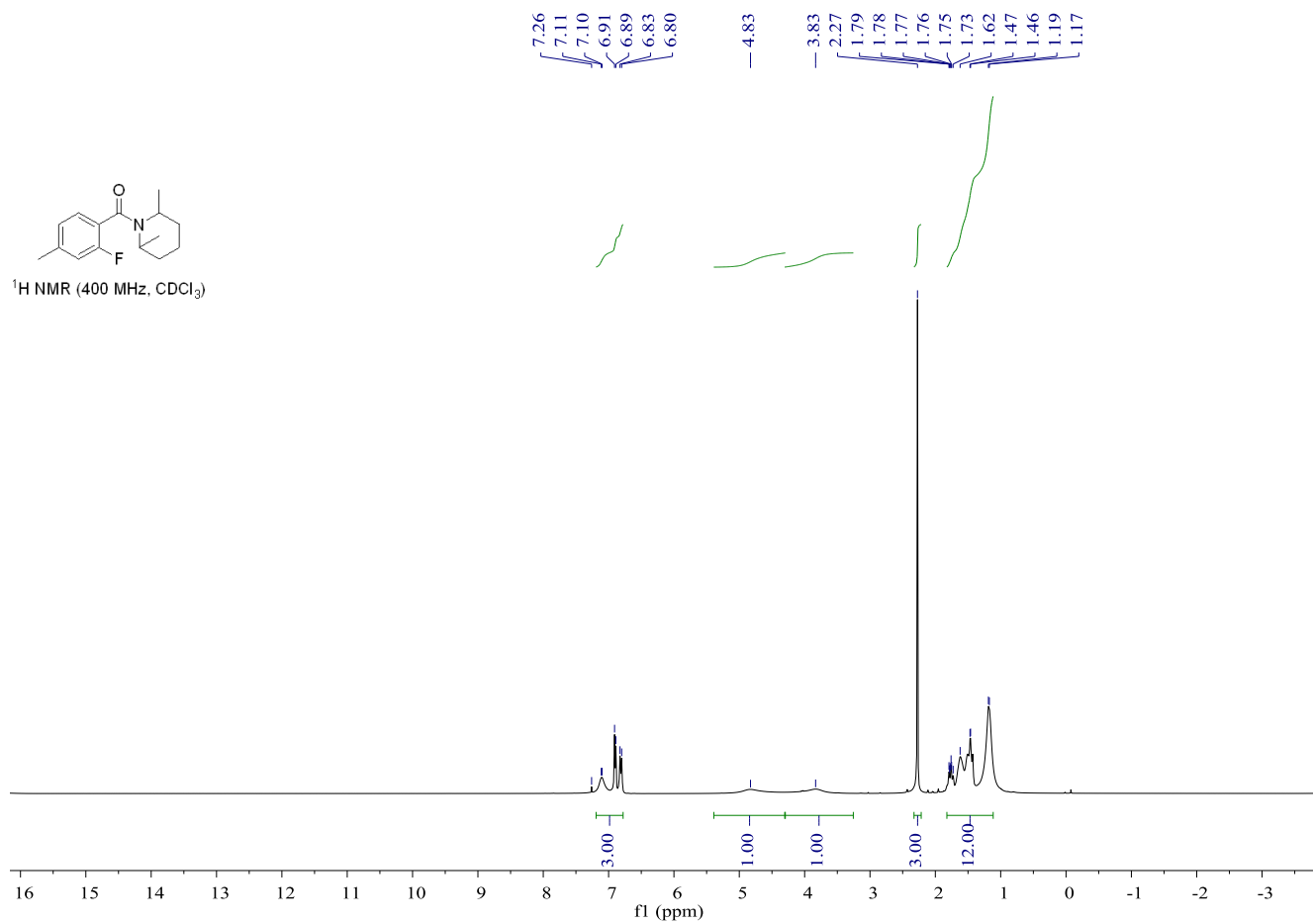


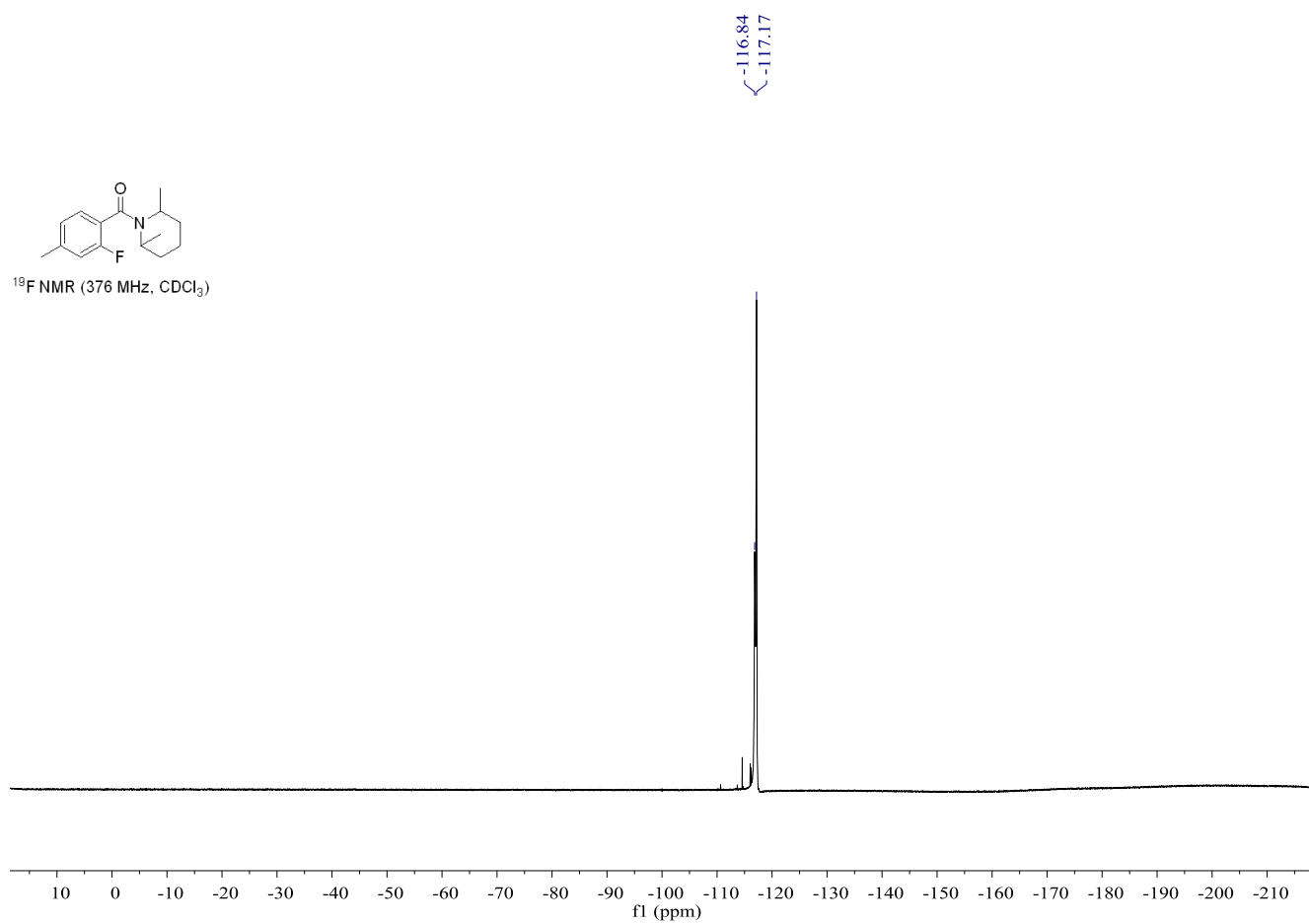
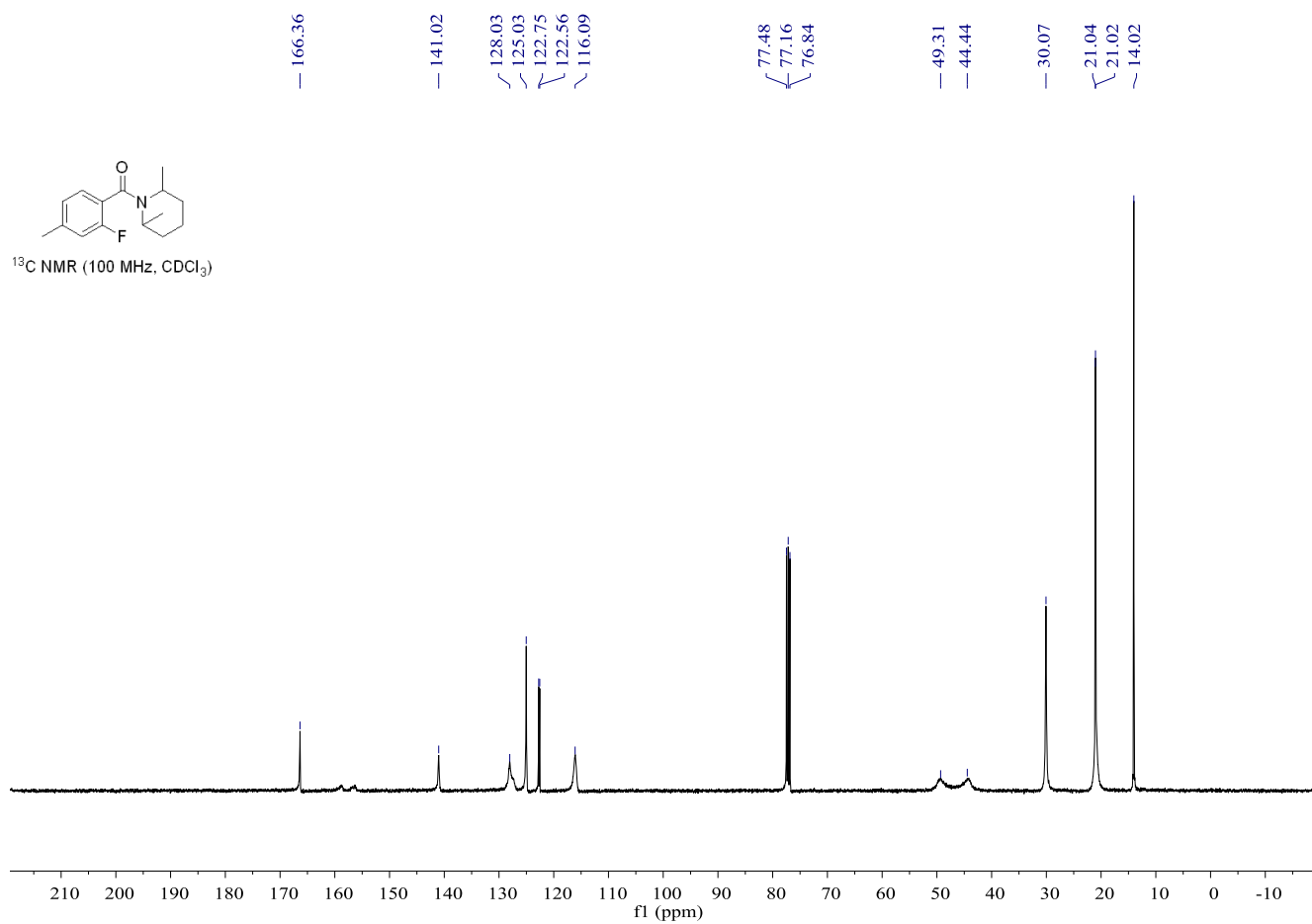


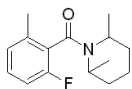
^{19}F NMR (376 MHz, CDCl_3)



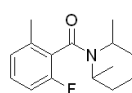
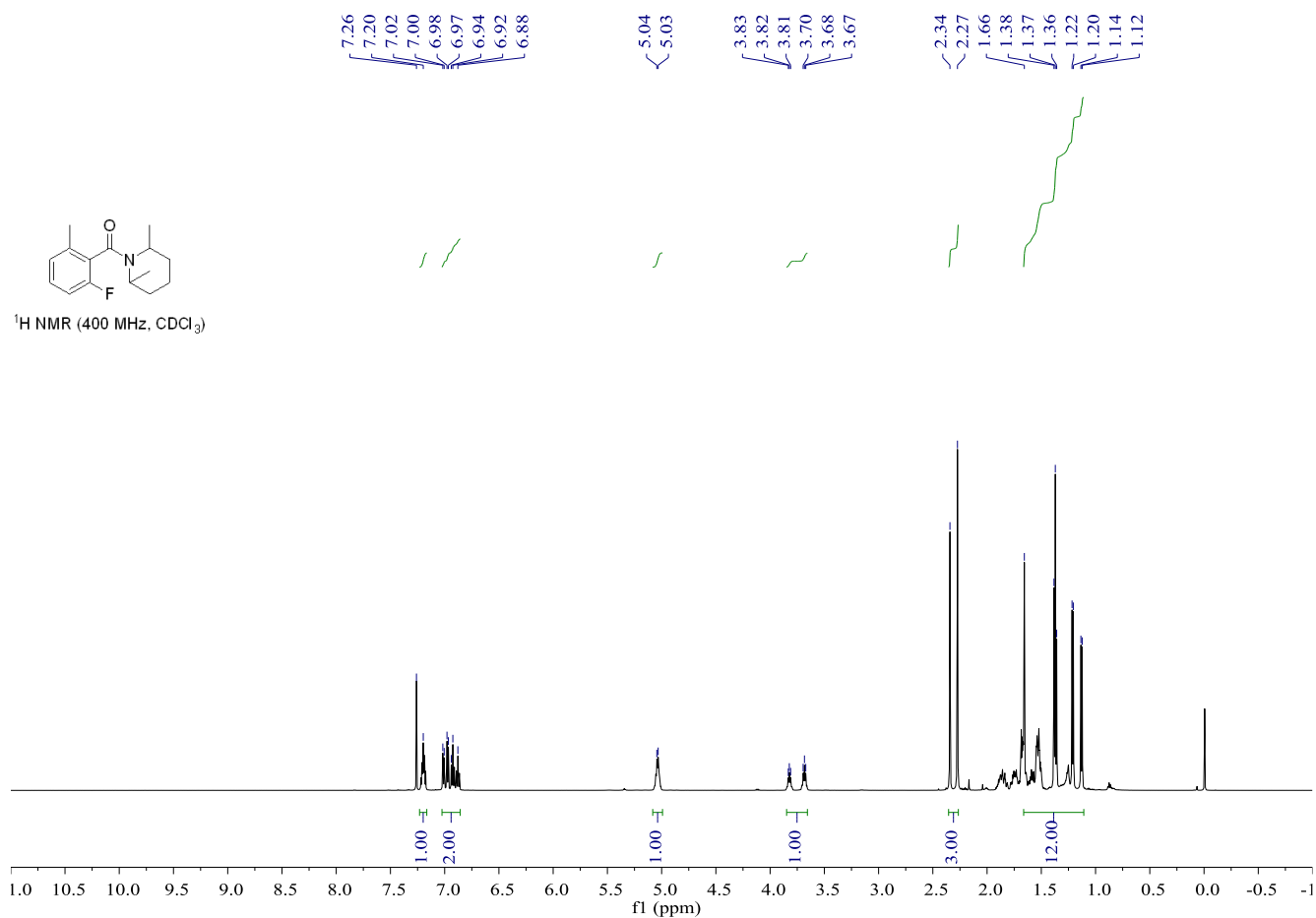
^1H NMR (400 MHz, CDCl_3)



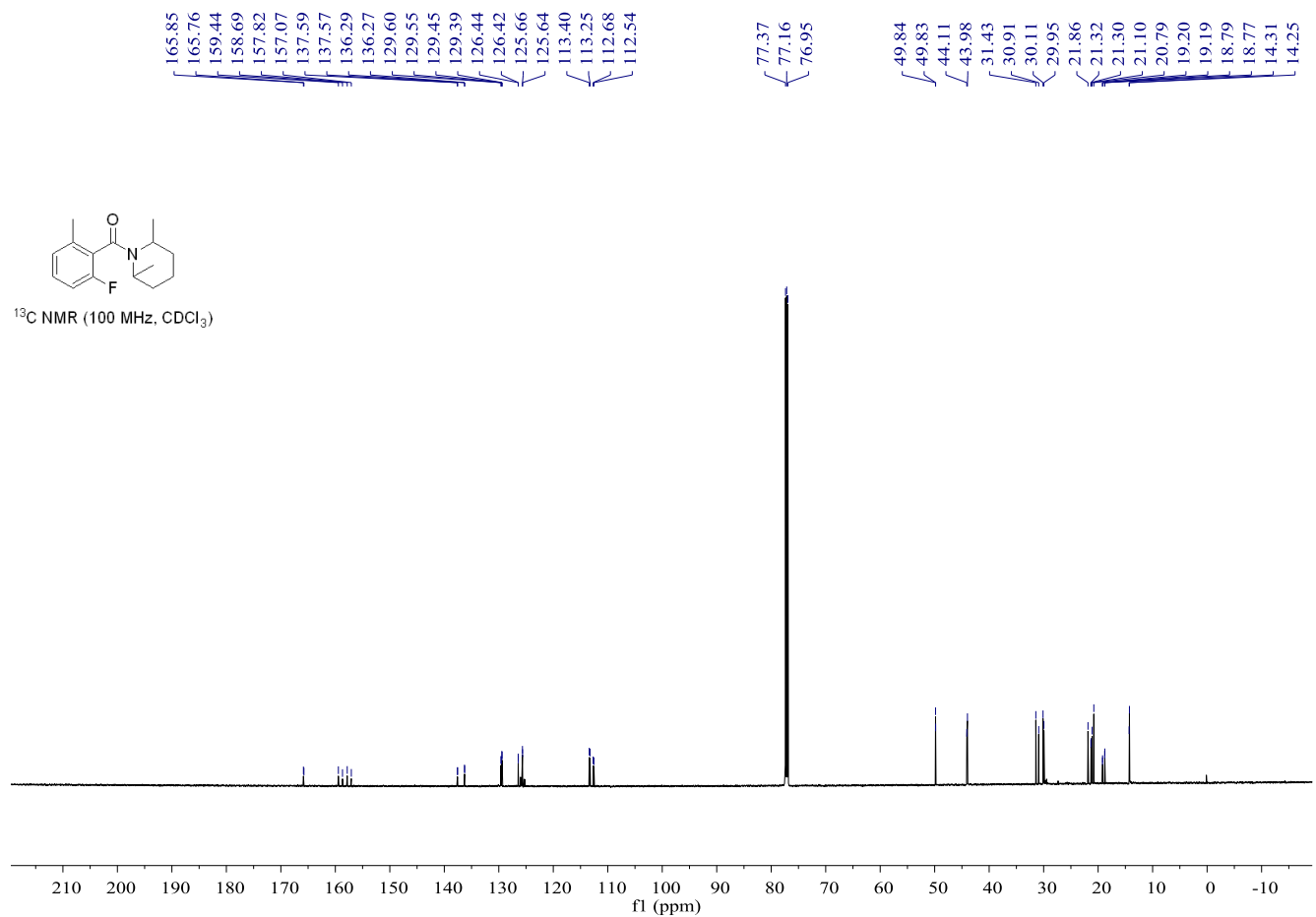


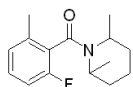


¹H NMR (400 MHz, CDCl₃)

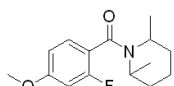
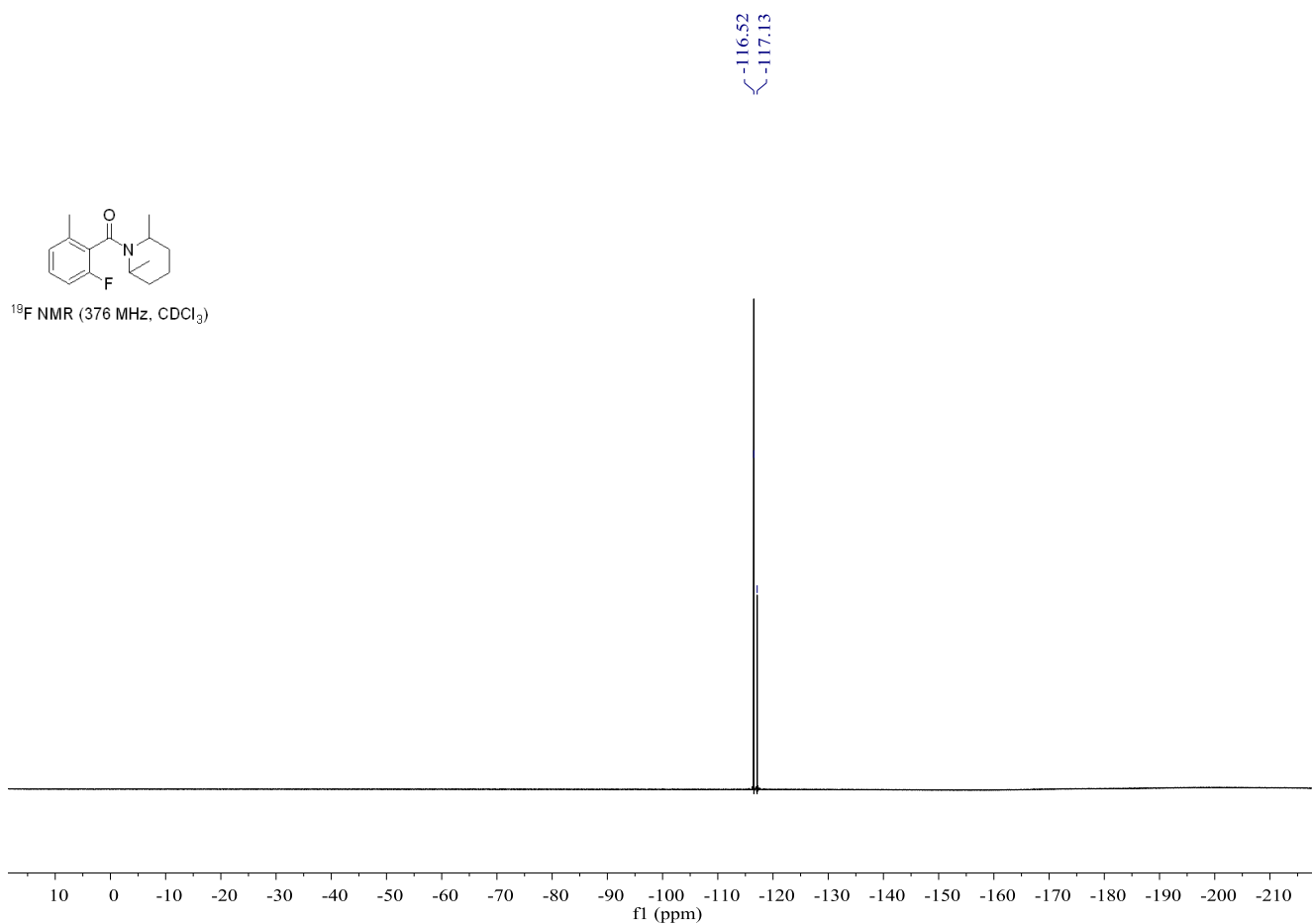


¹³C NMR (100 MHz, CDCl₃)

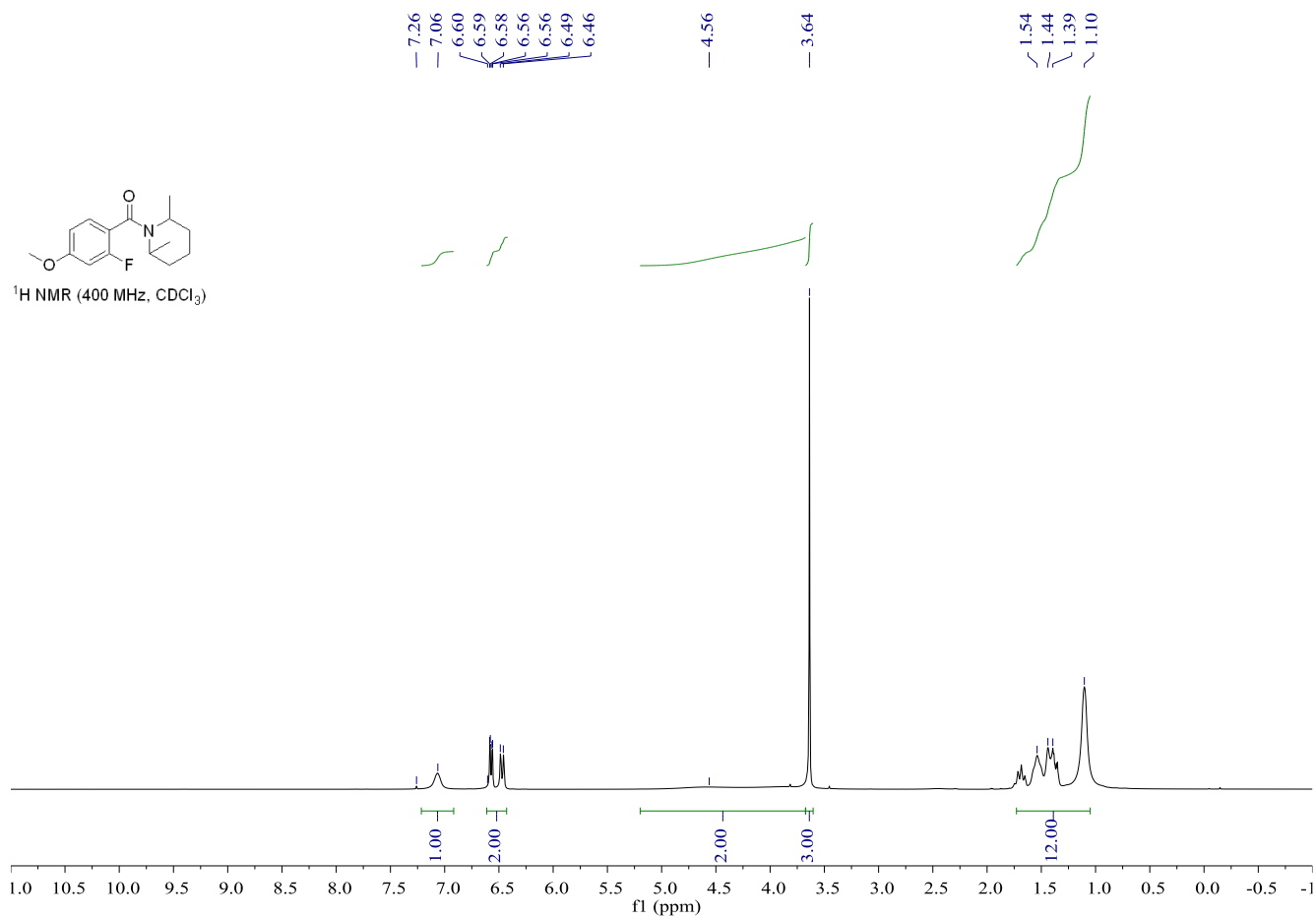


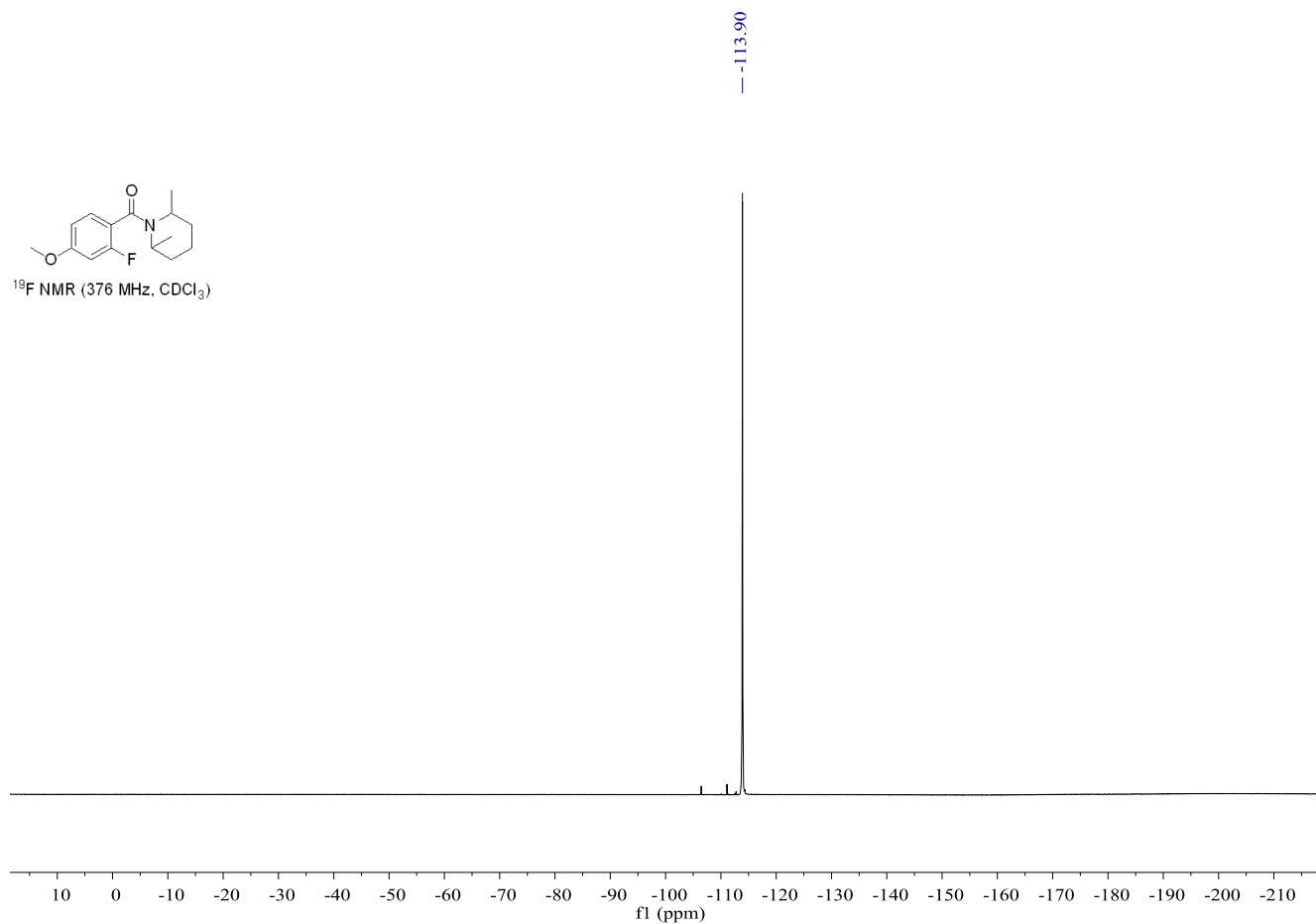
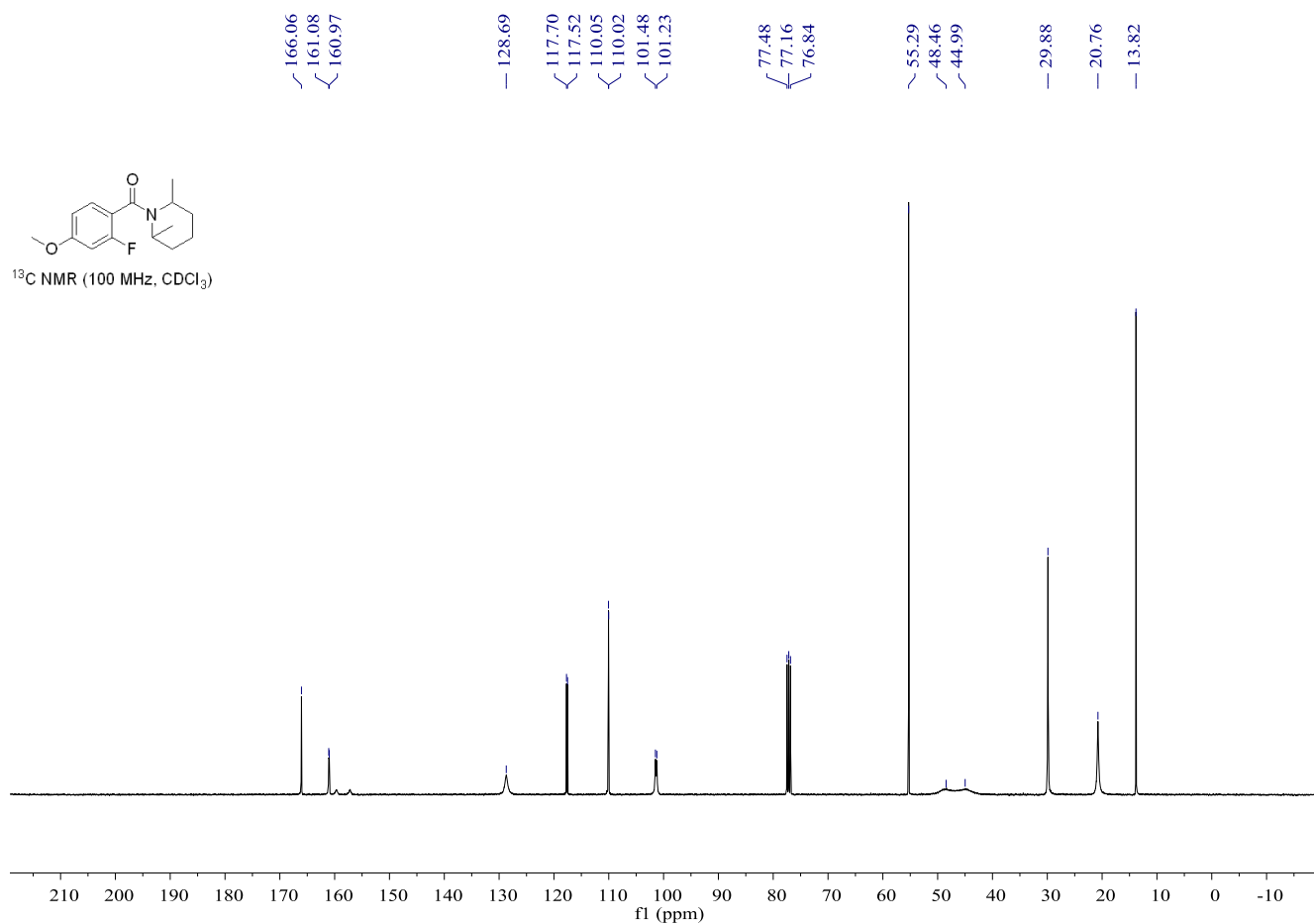


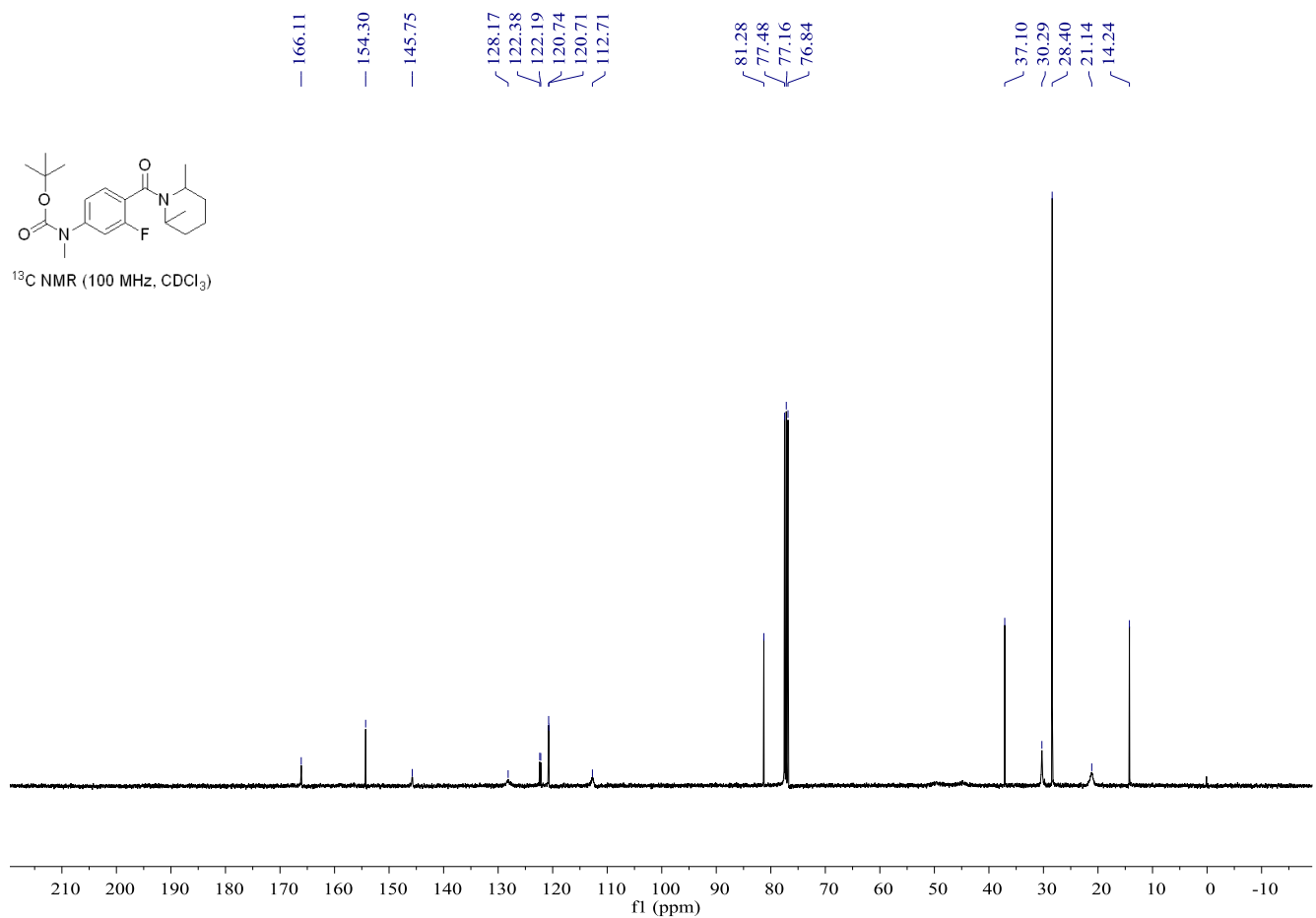
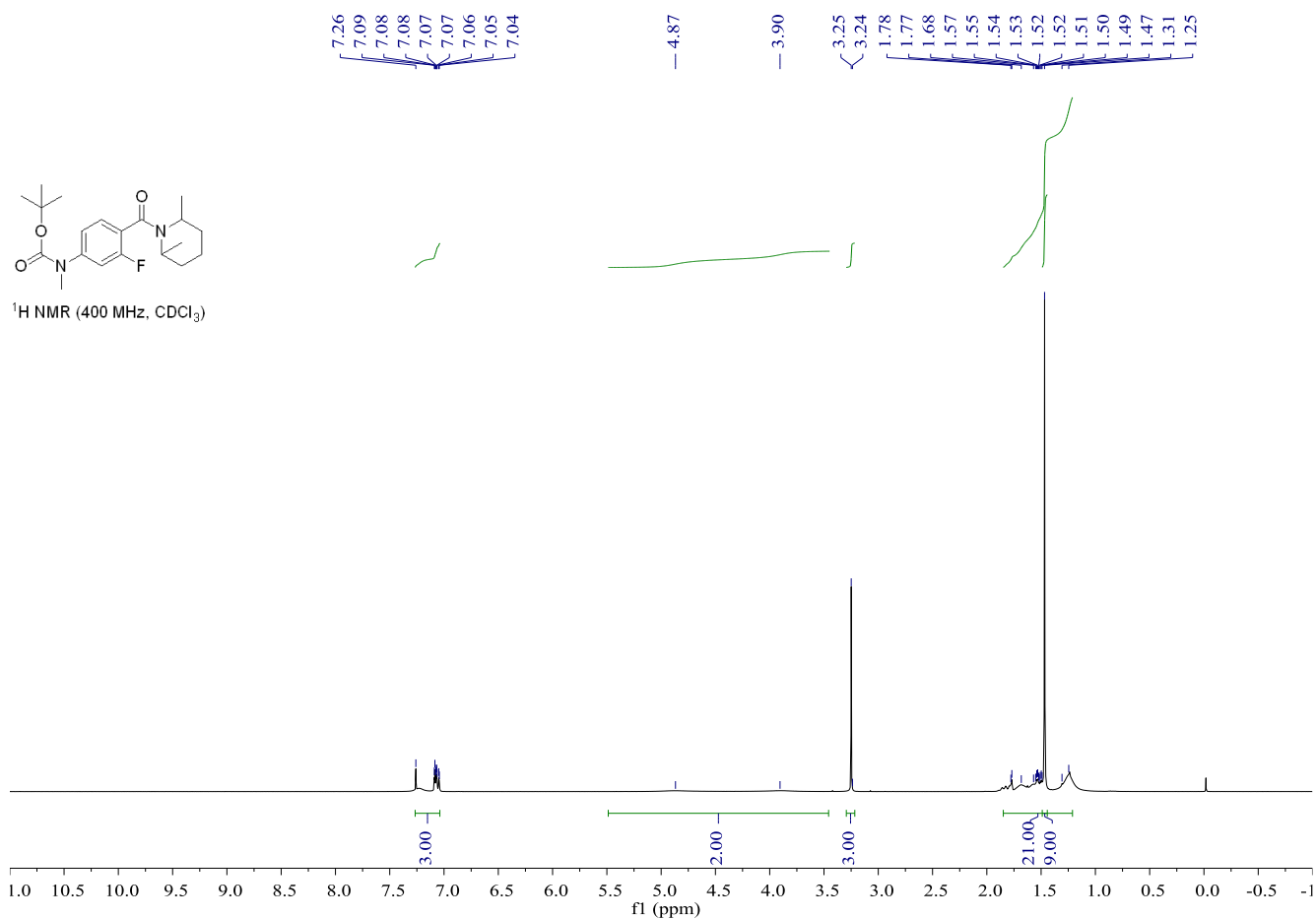
^{19}F NMR (376 MHz, CDCl_3)

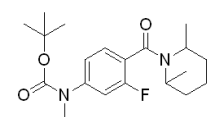


^1H NMR (400 MHz, CDCl_3)

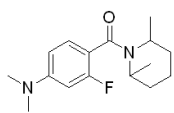
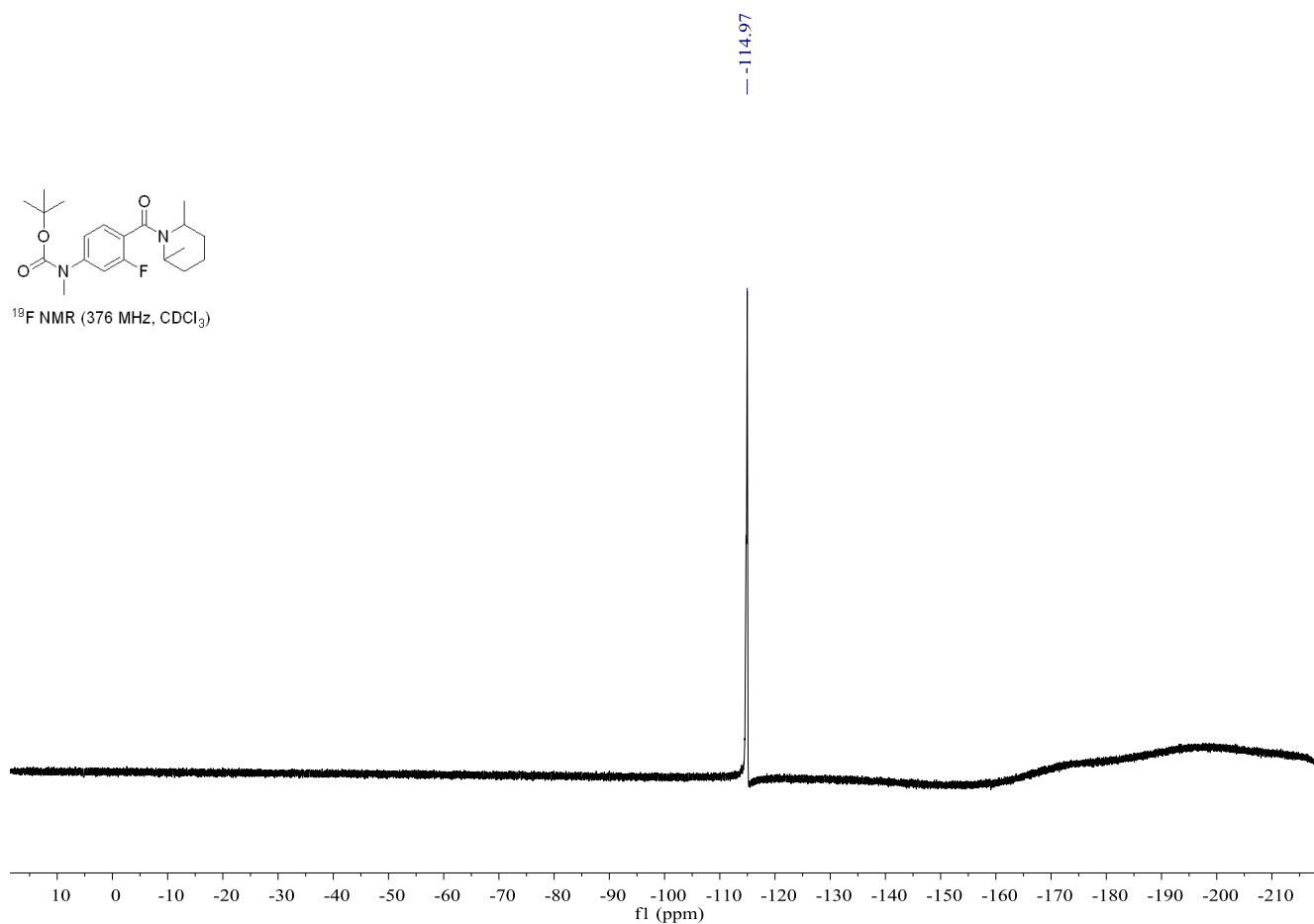




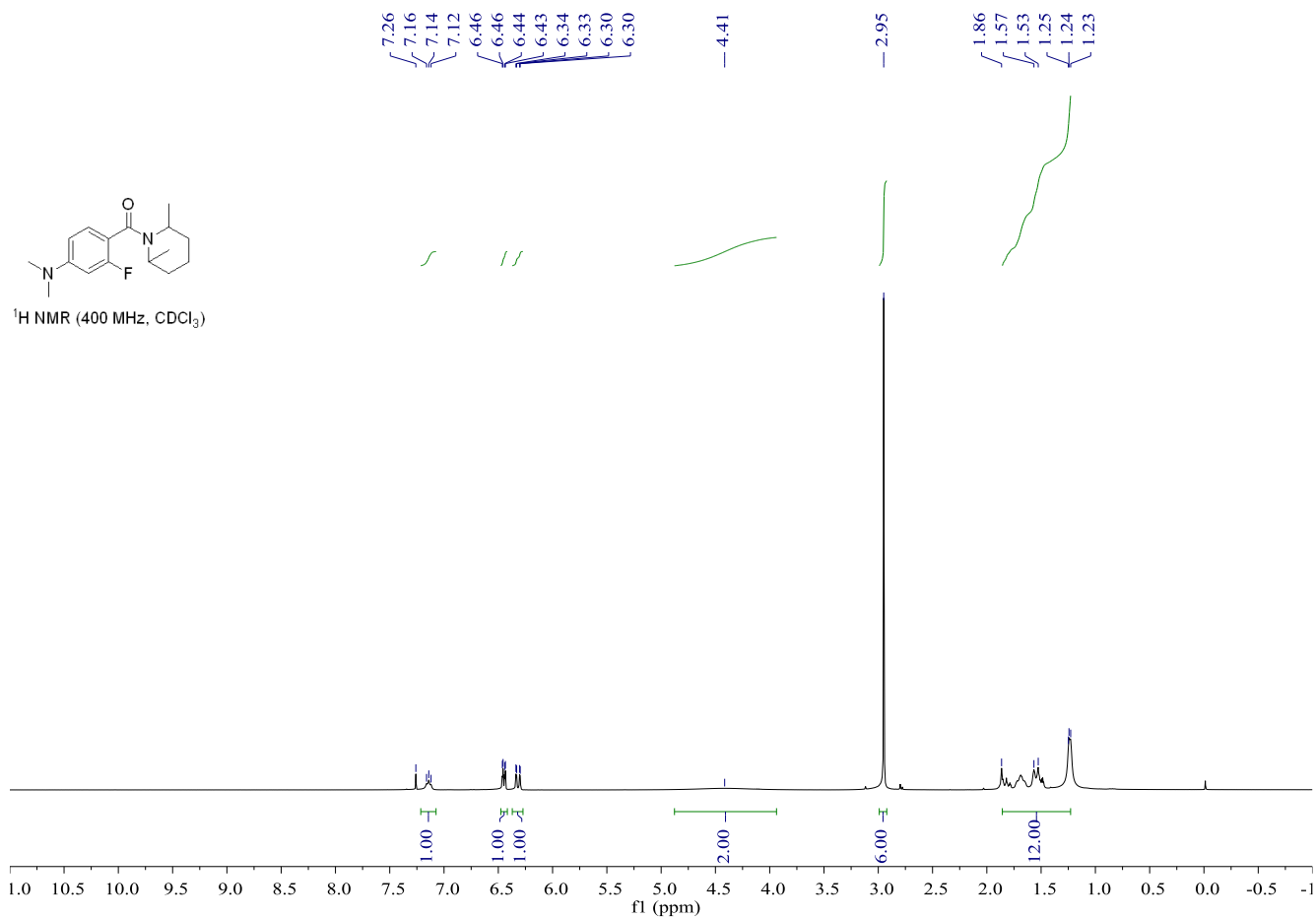


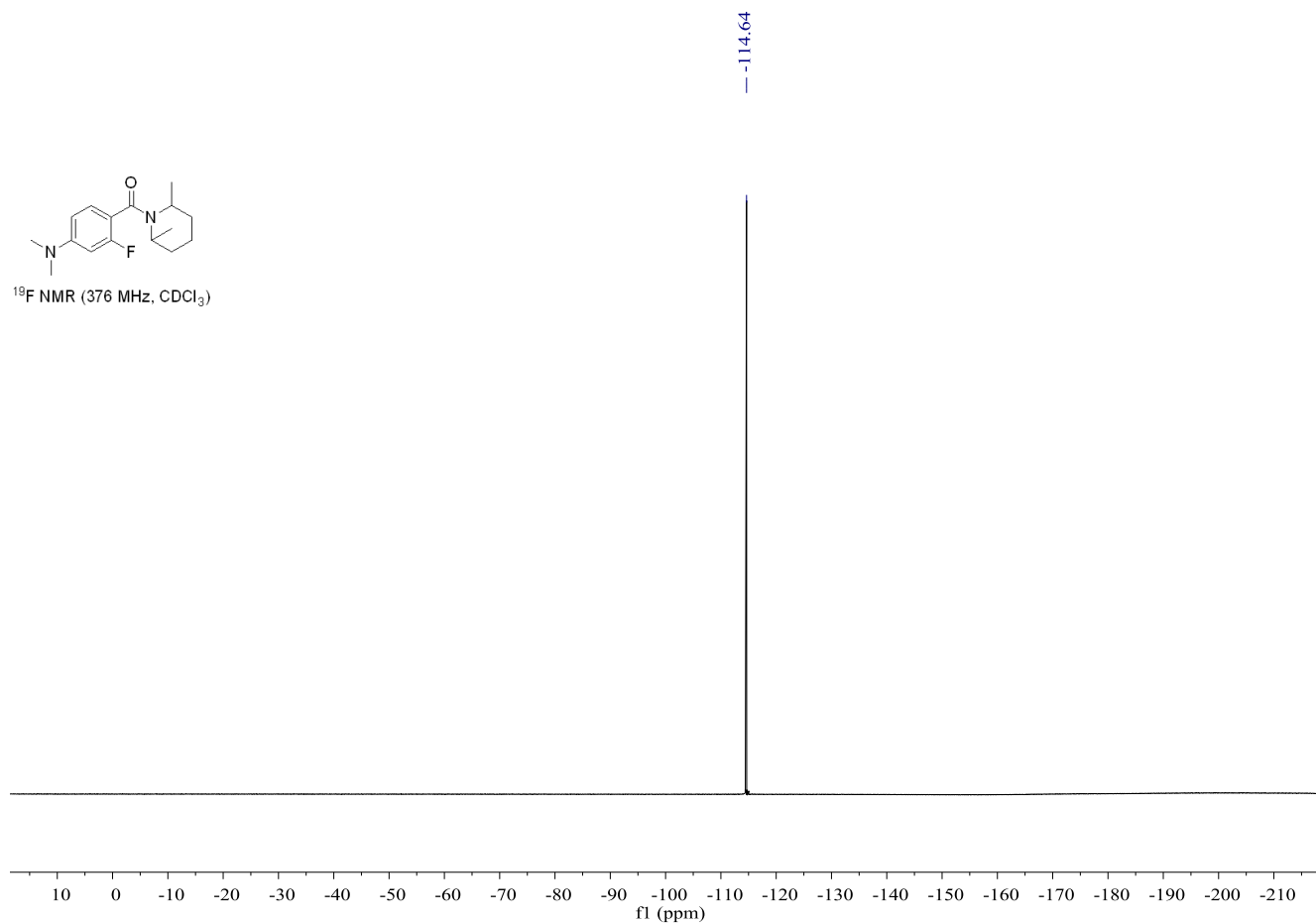
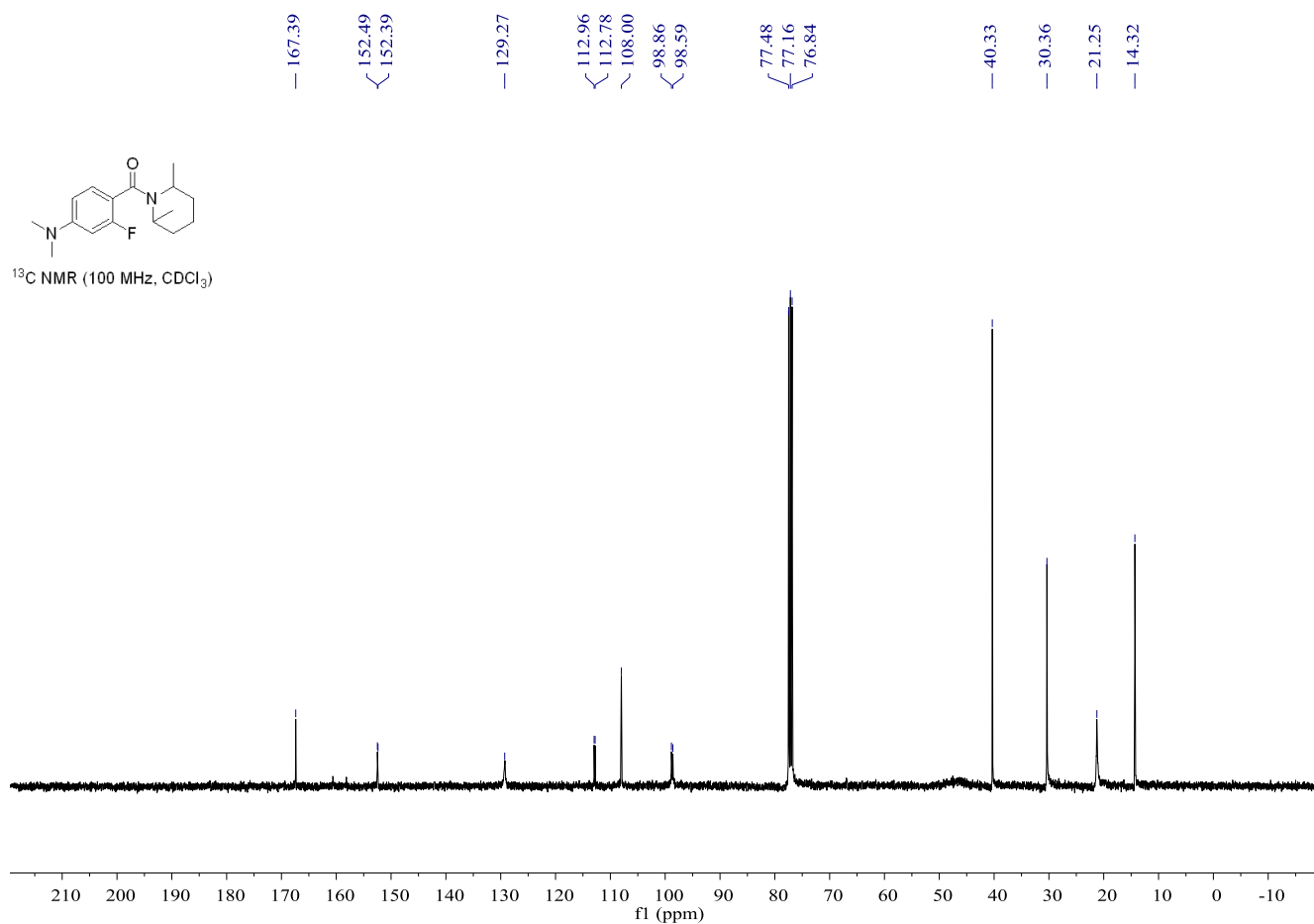


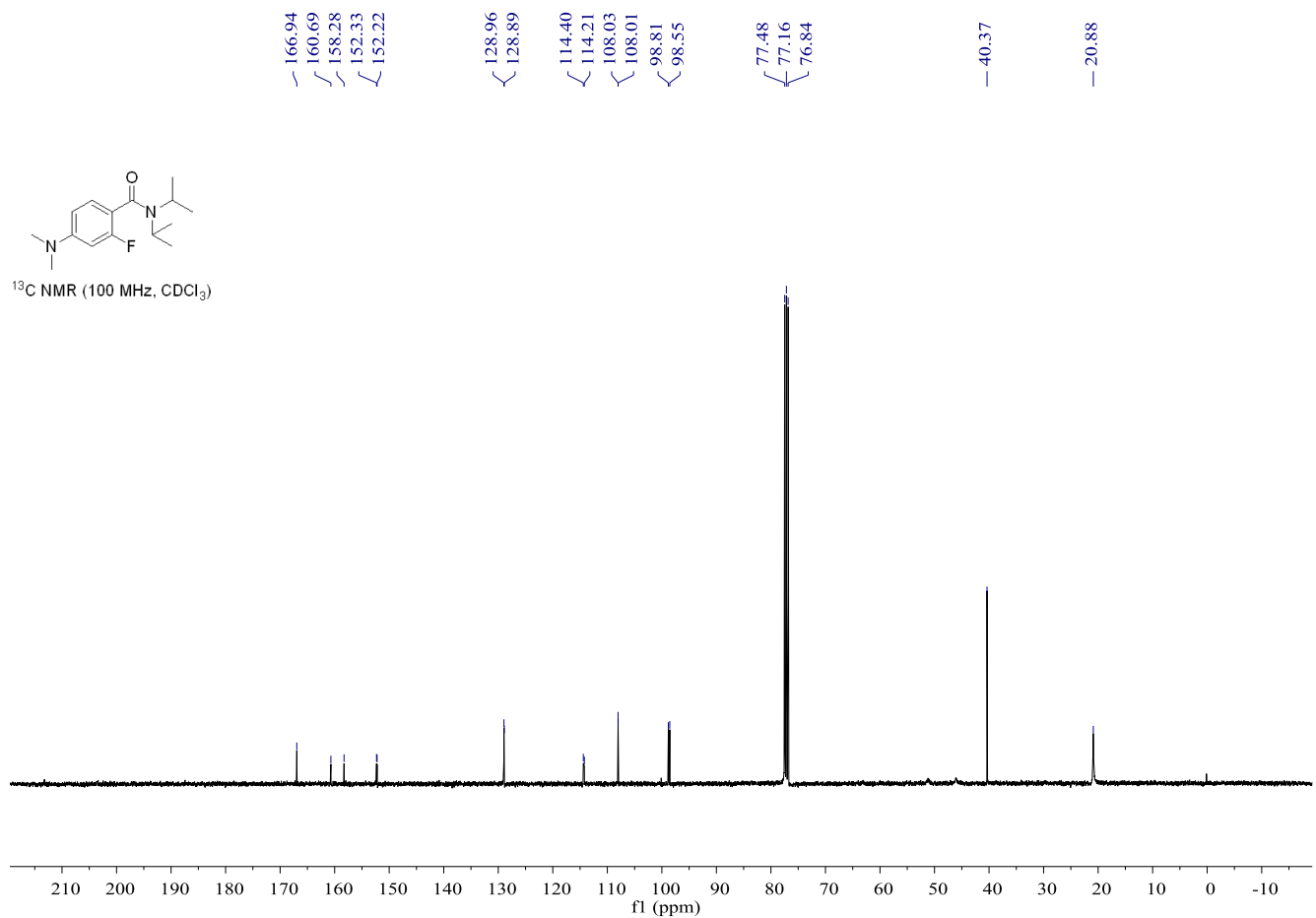
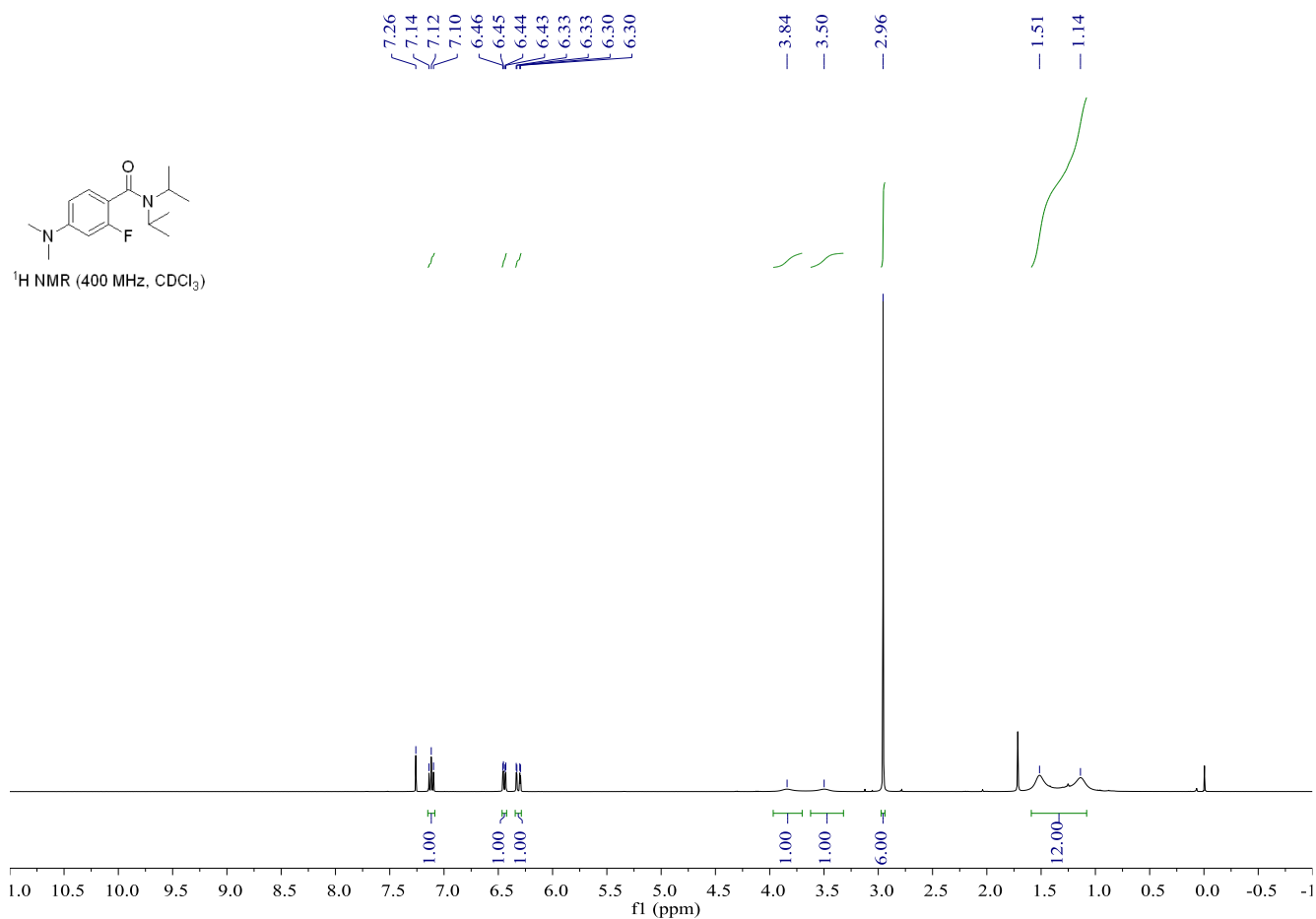
^{19}F NMR (376 MHz, CDCl_3)

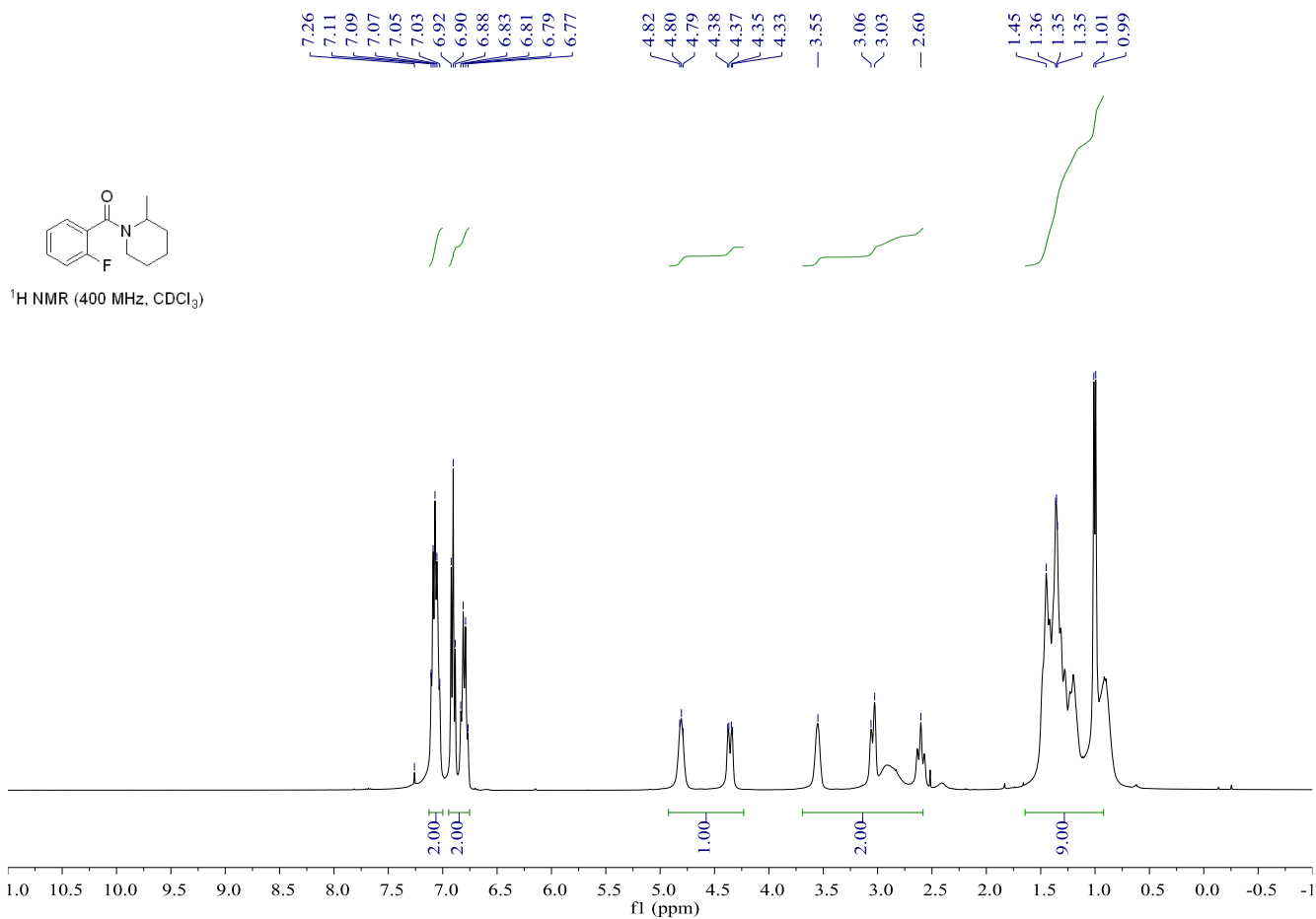
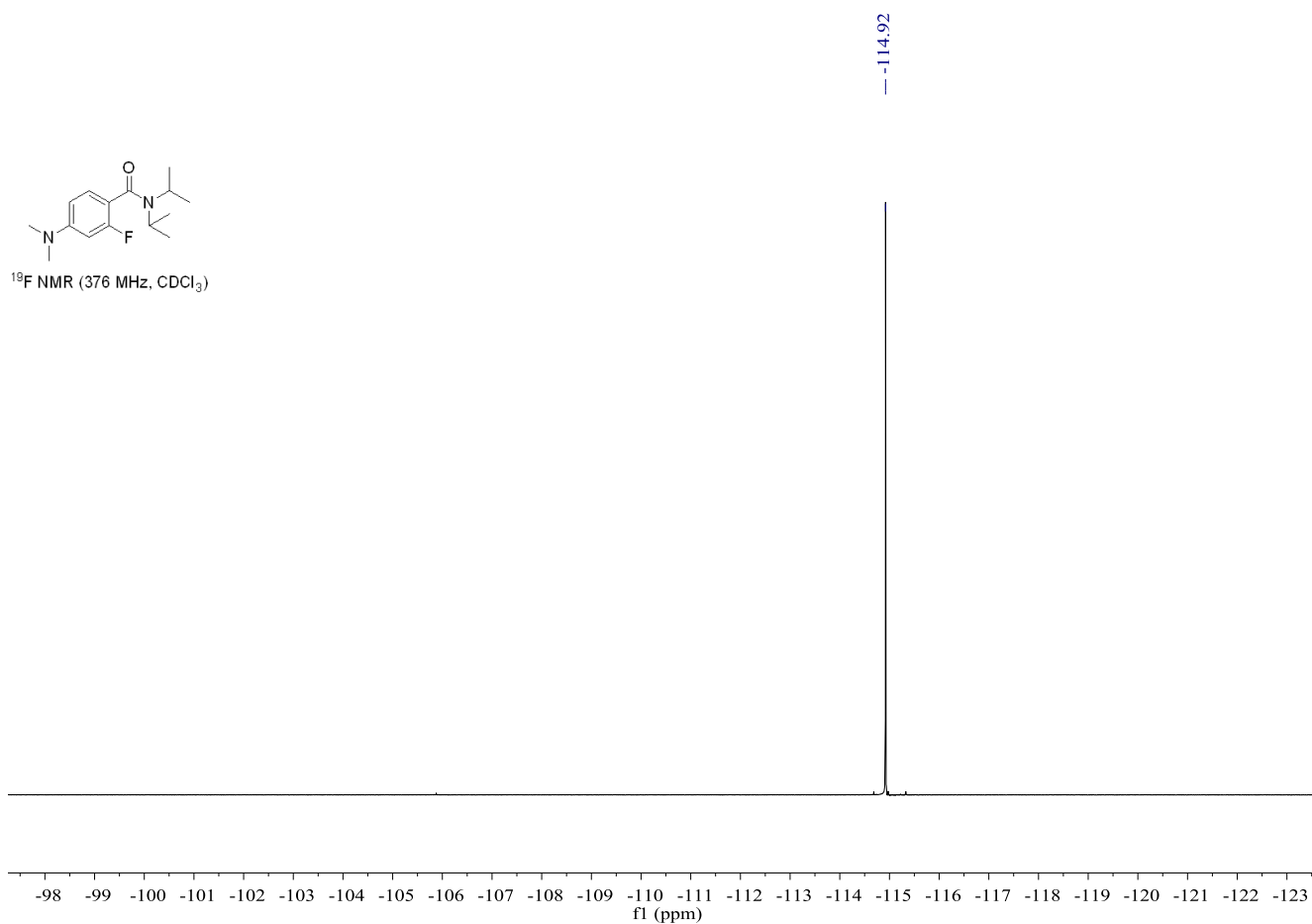
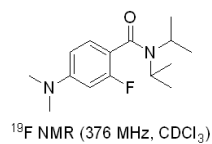


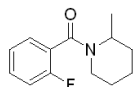
^1H NMR (400 MHz, CDCl_3)



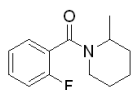
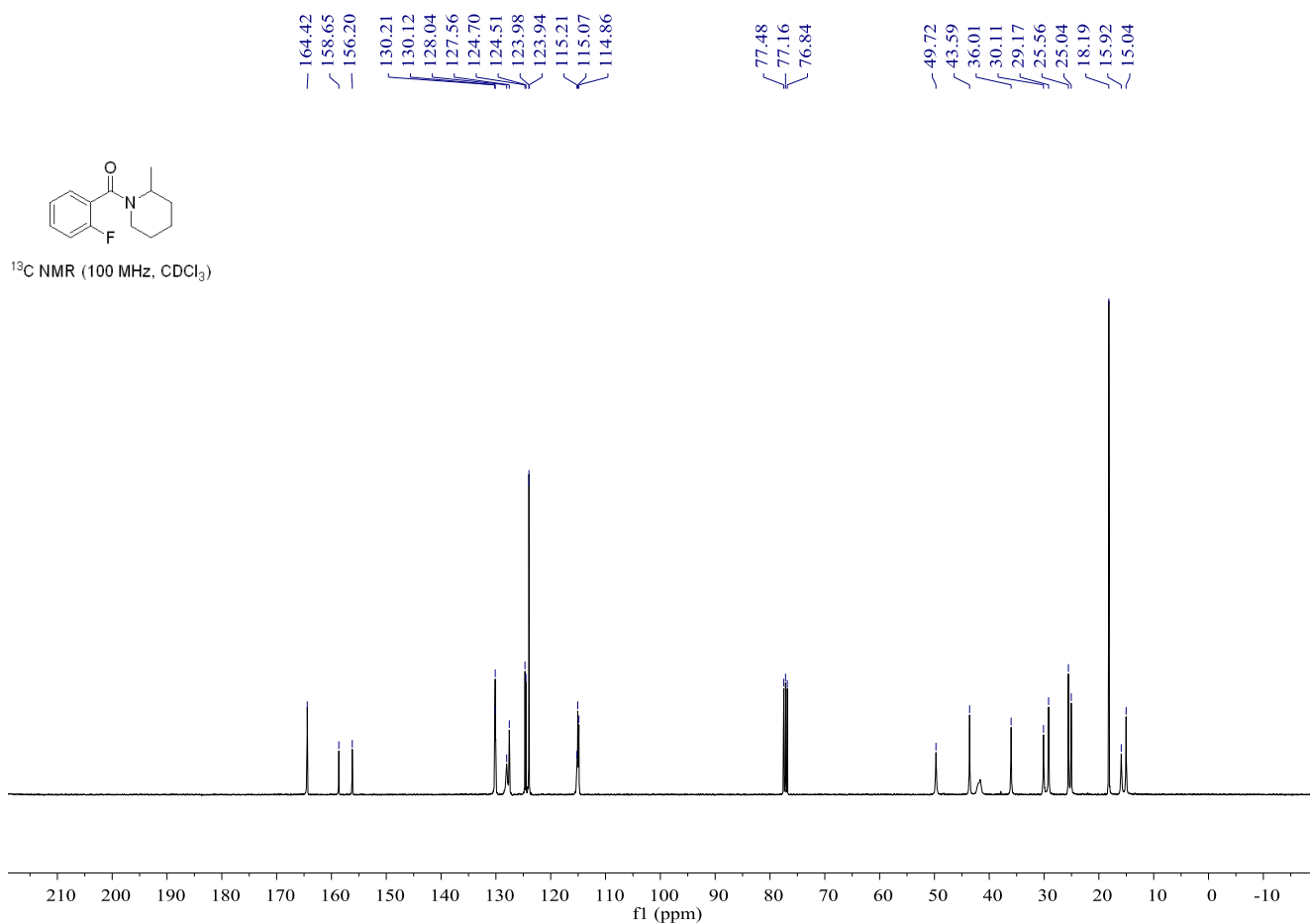




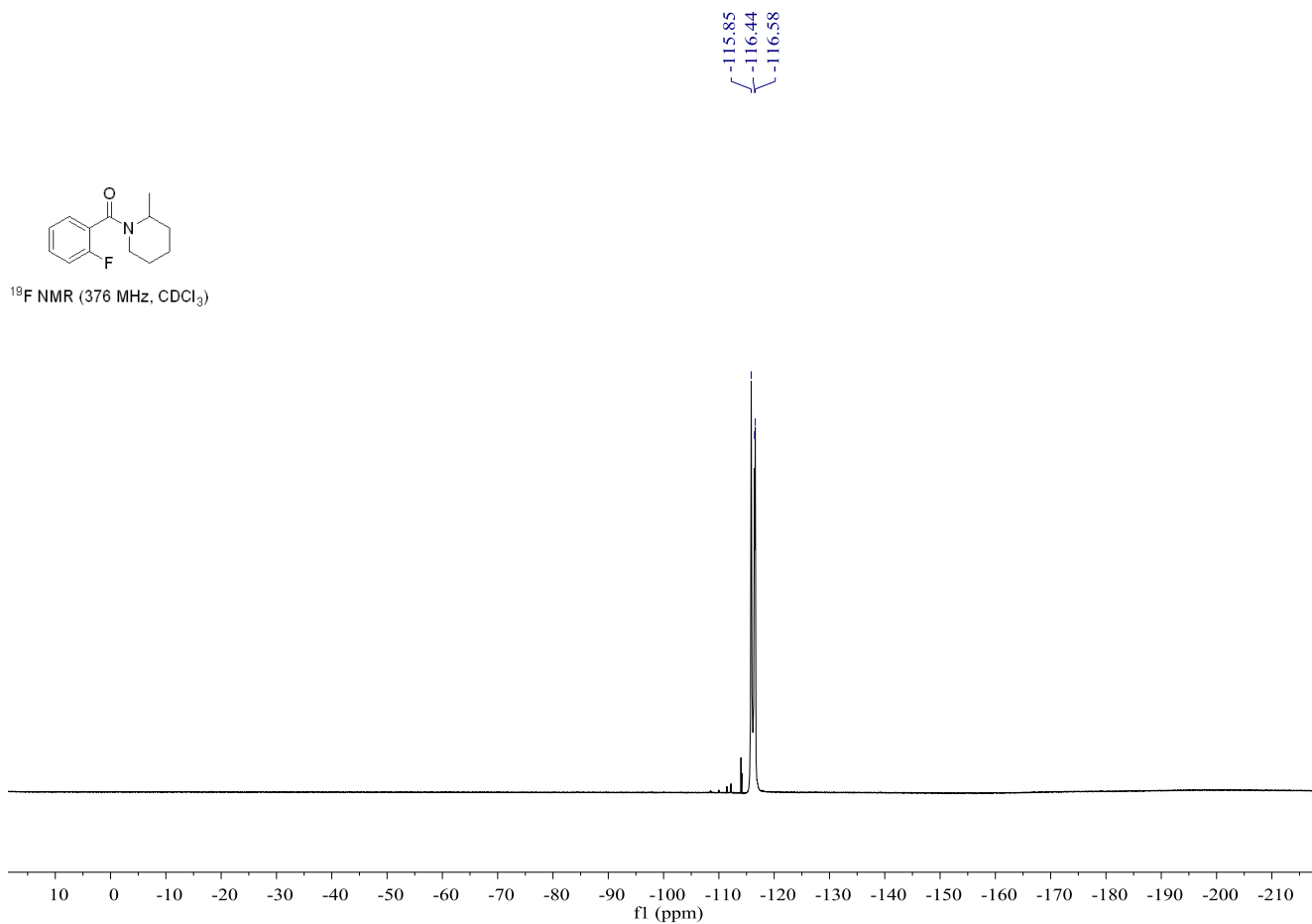


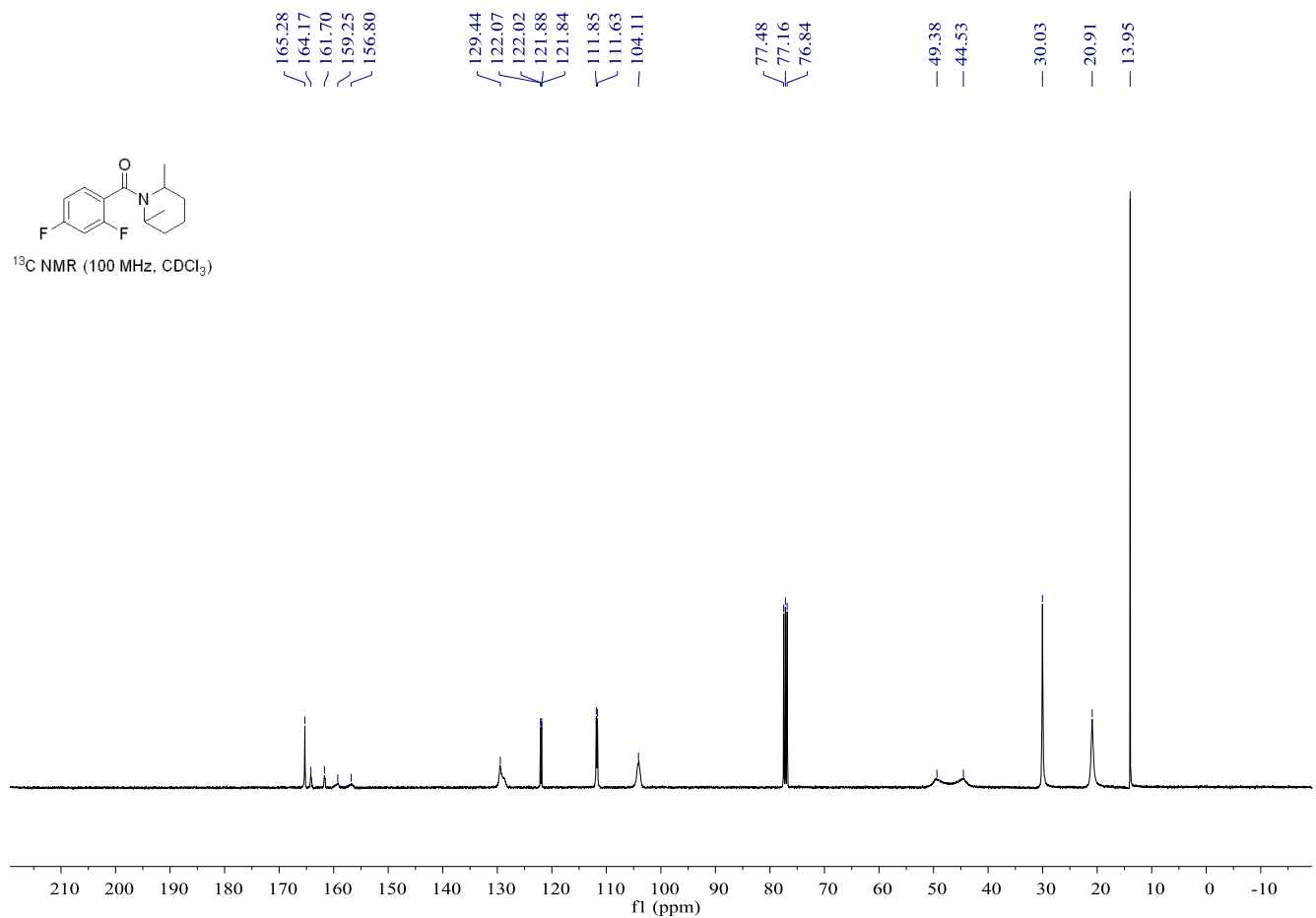
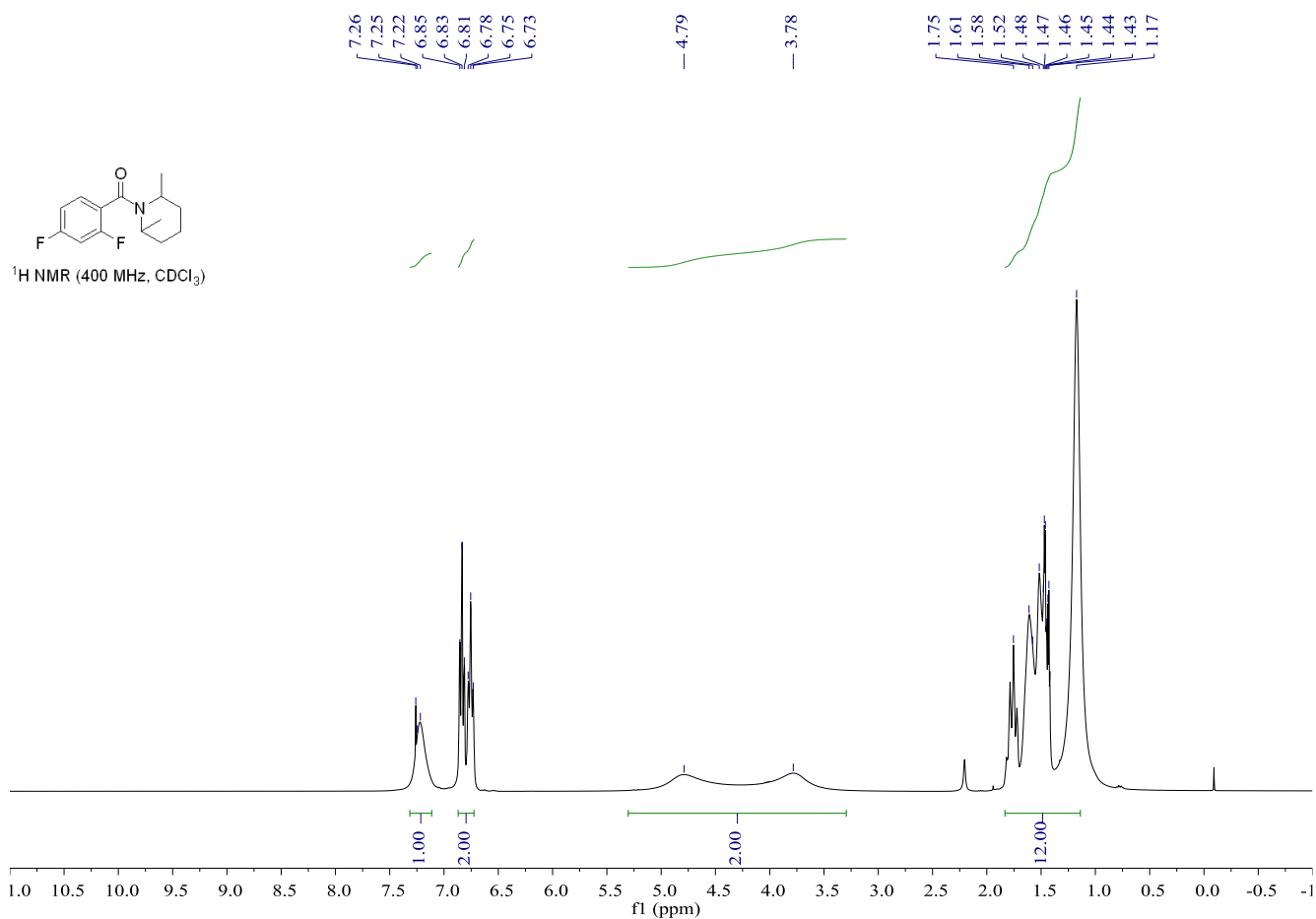


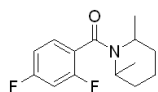
^{13}C NMR (100 MHz, CDCl_3)



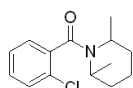
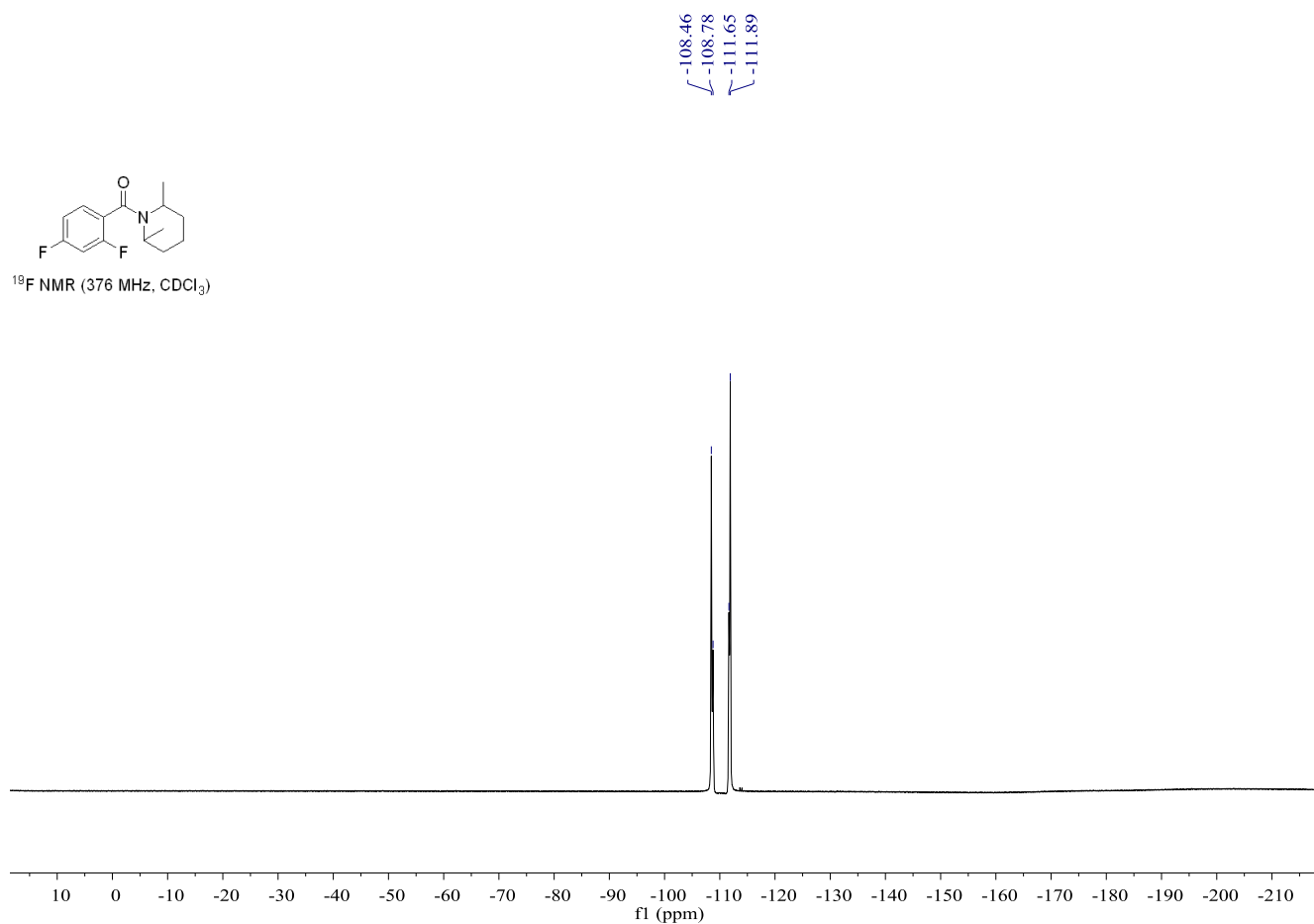
^{19}F NMR (376 MHz, CDCl_3)



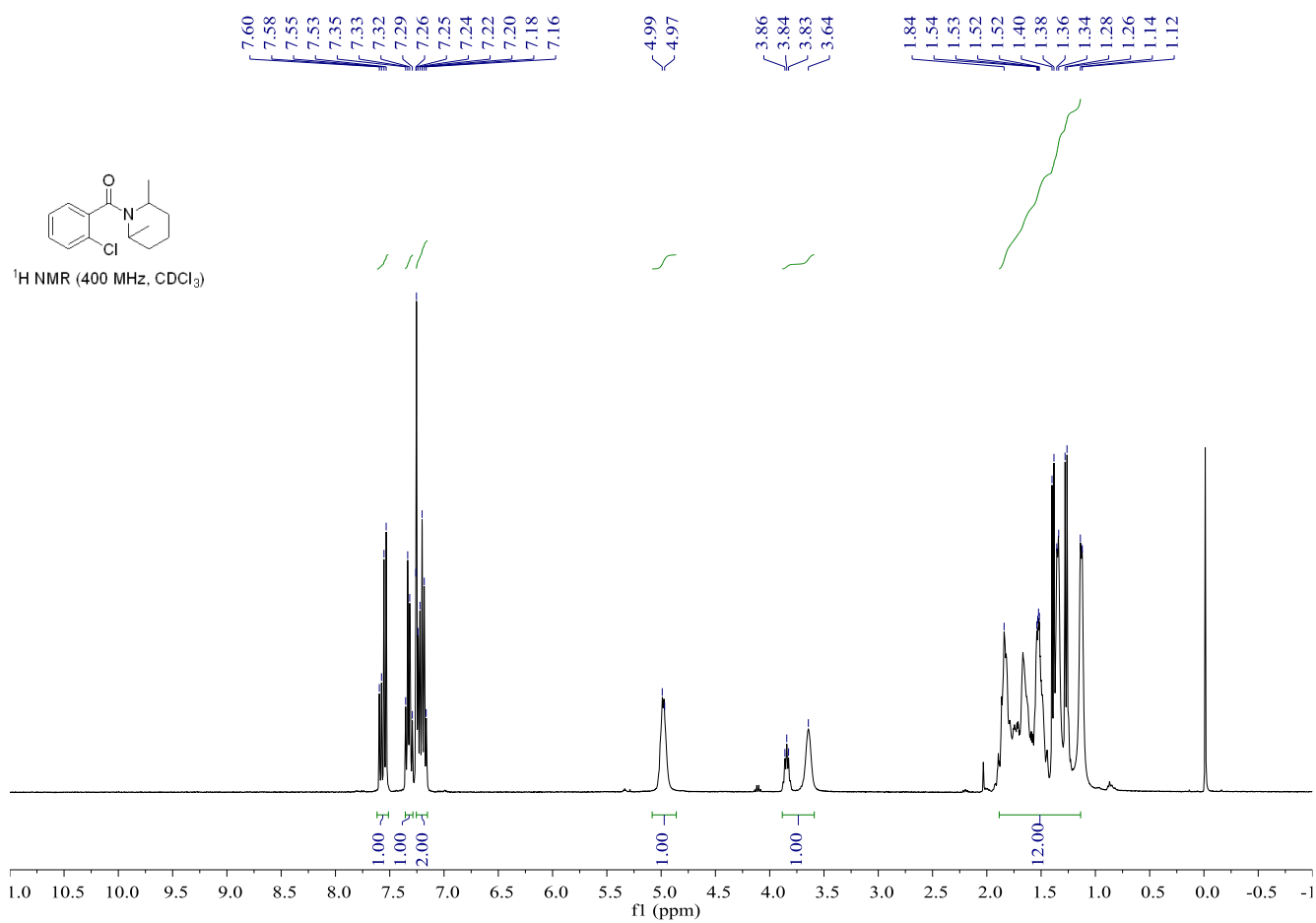


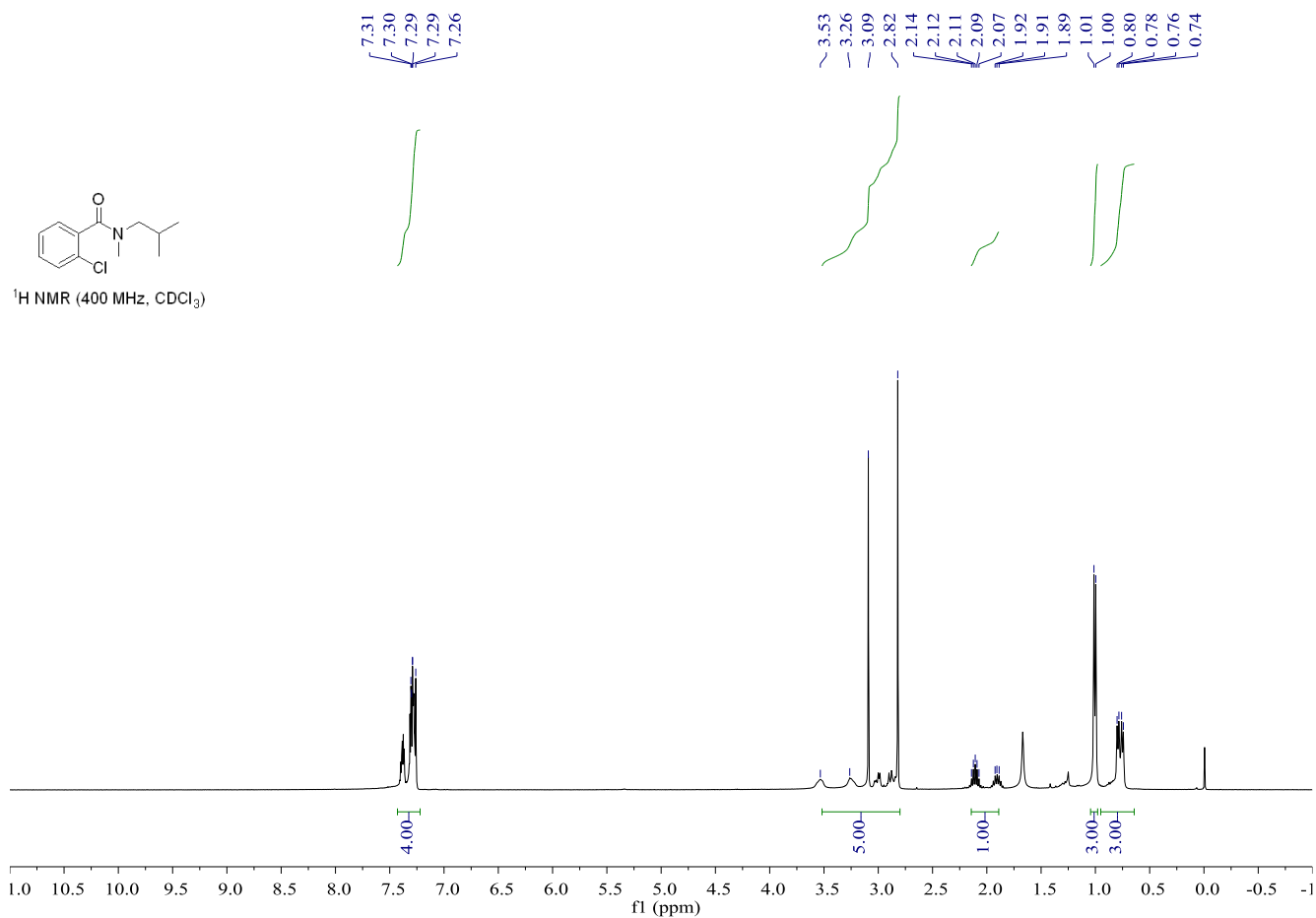
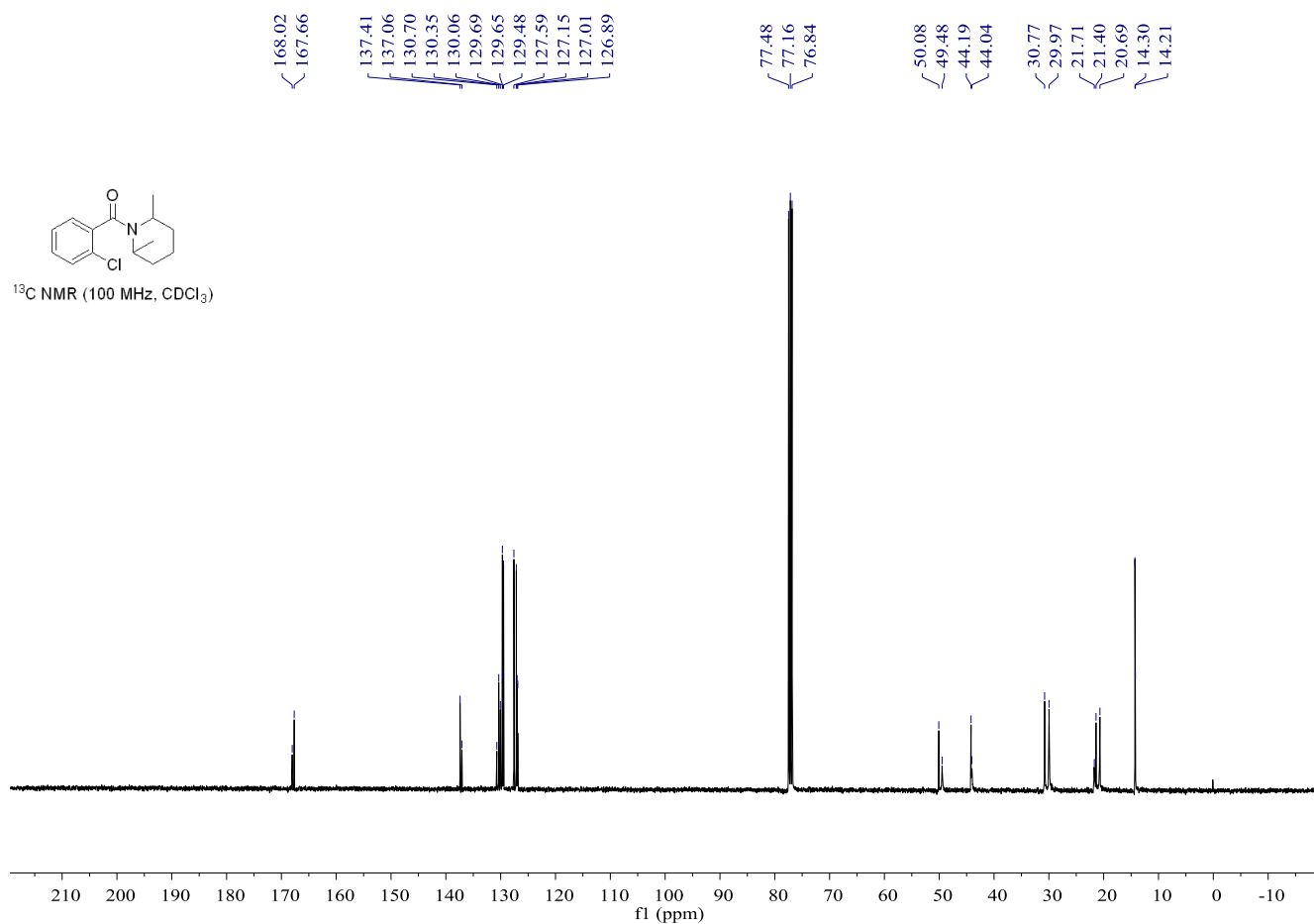


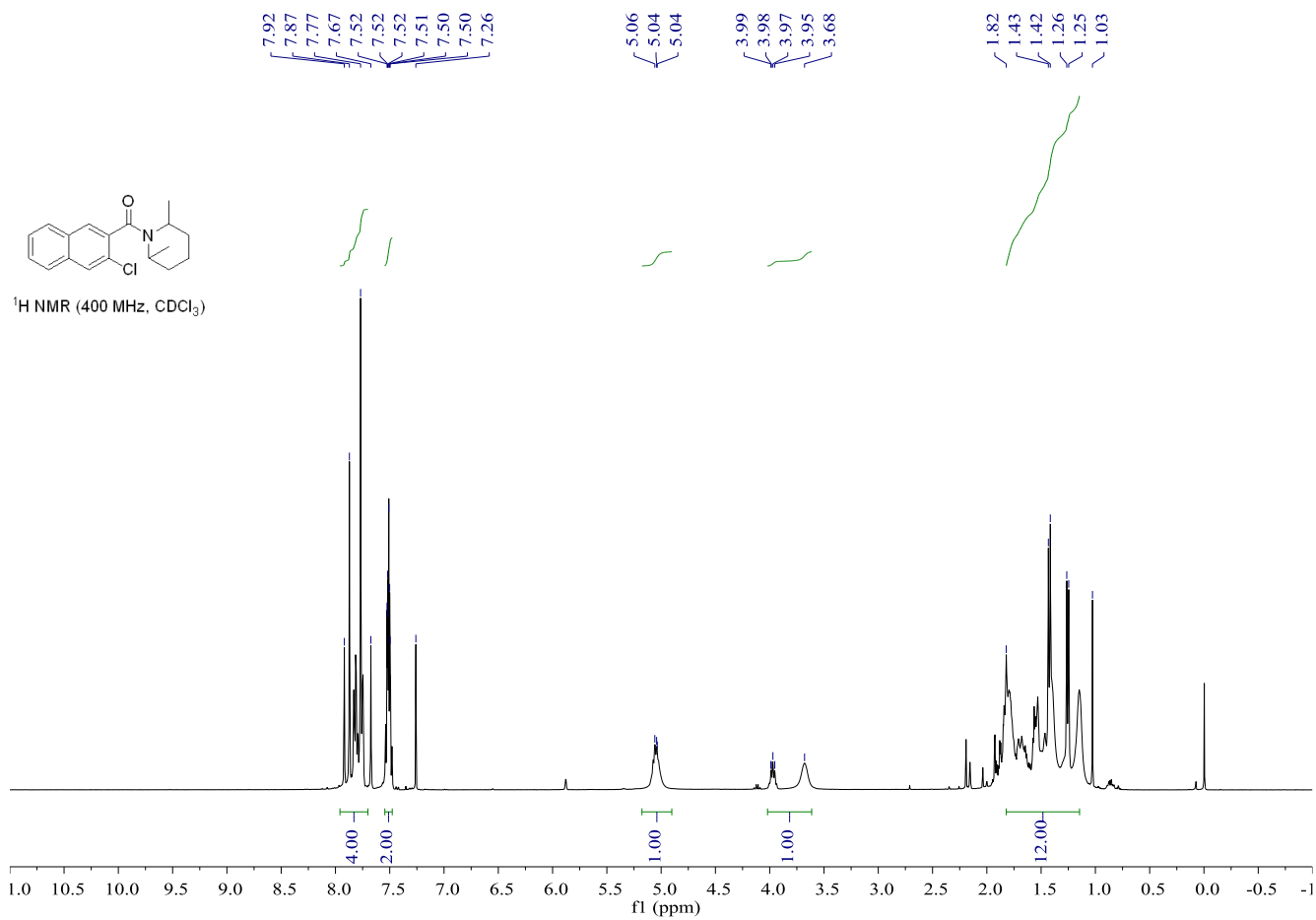
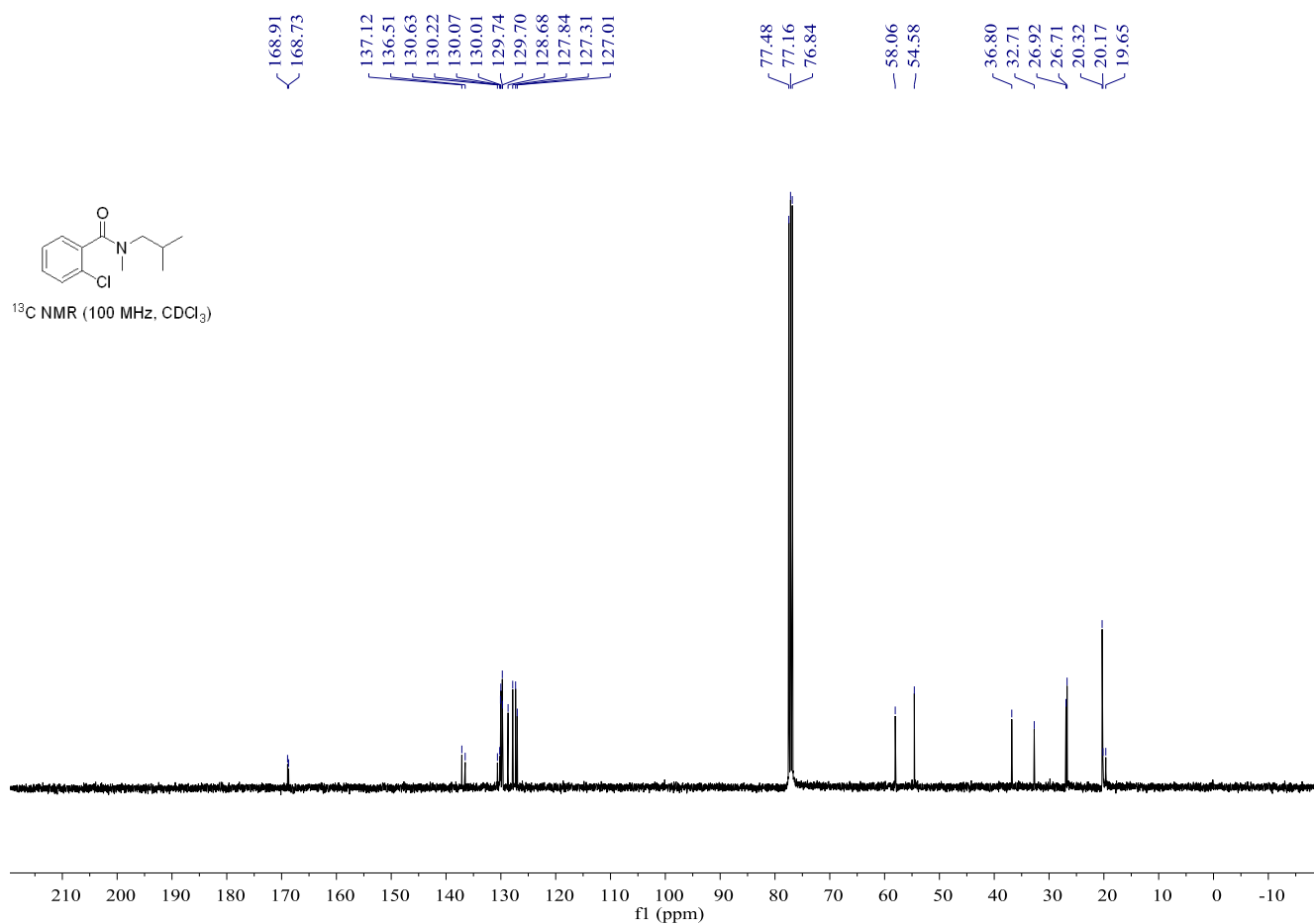
^{19}F NMR (376 MHz, CDCl_3)

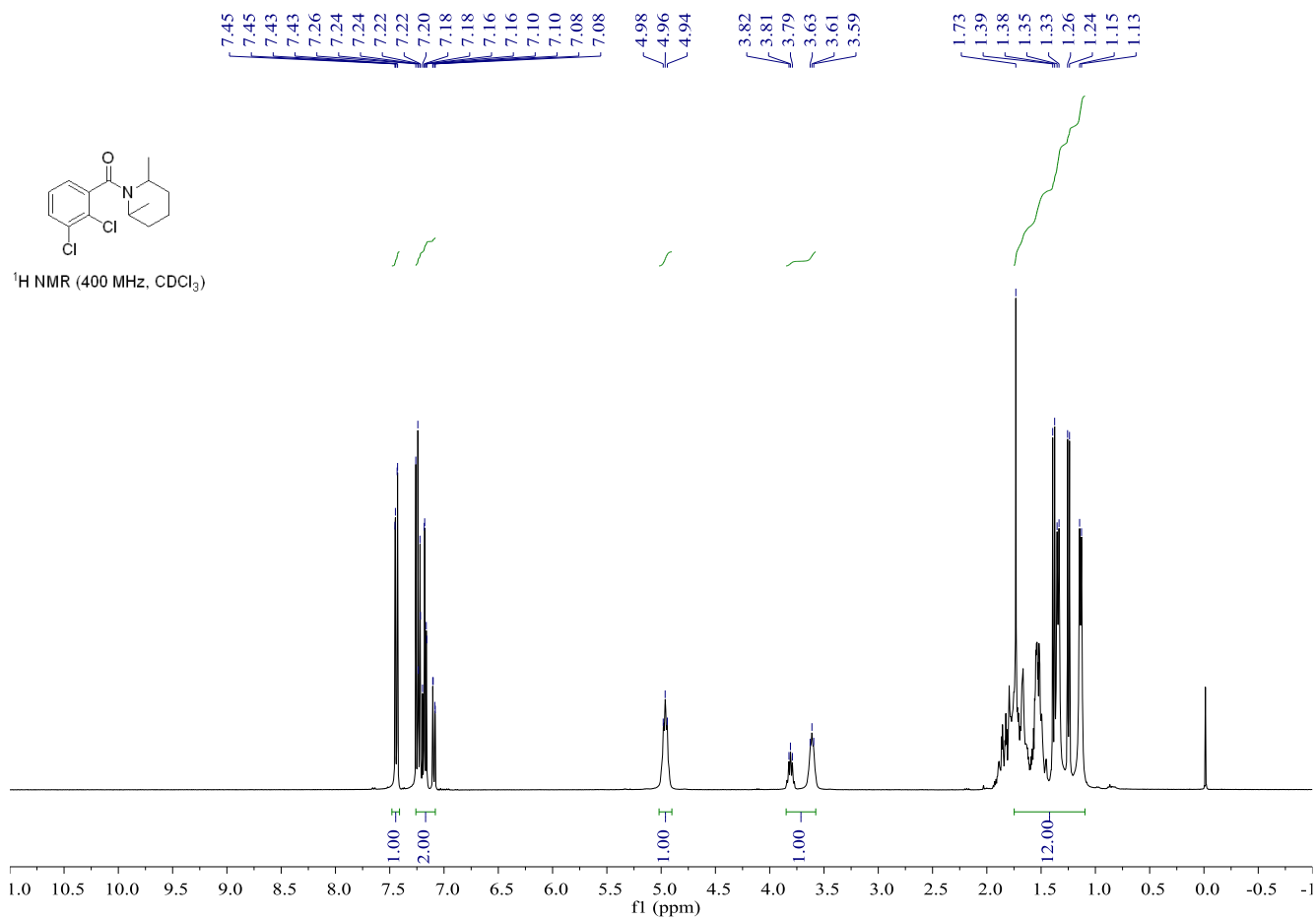
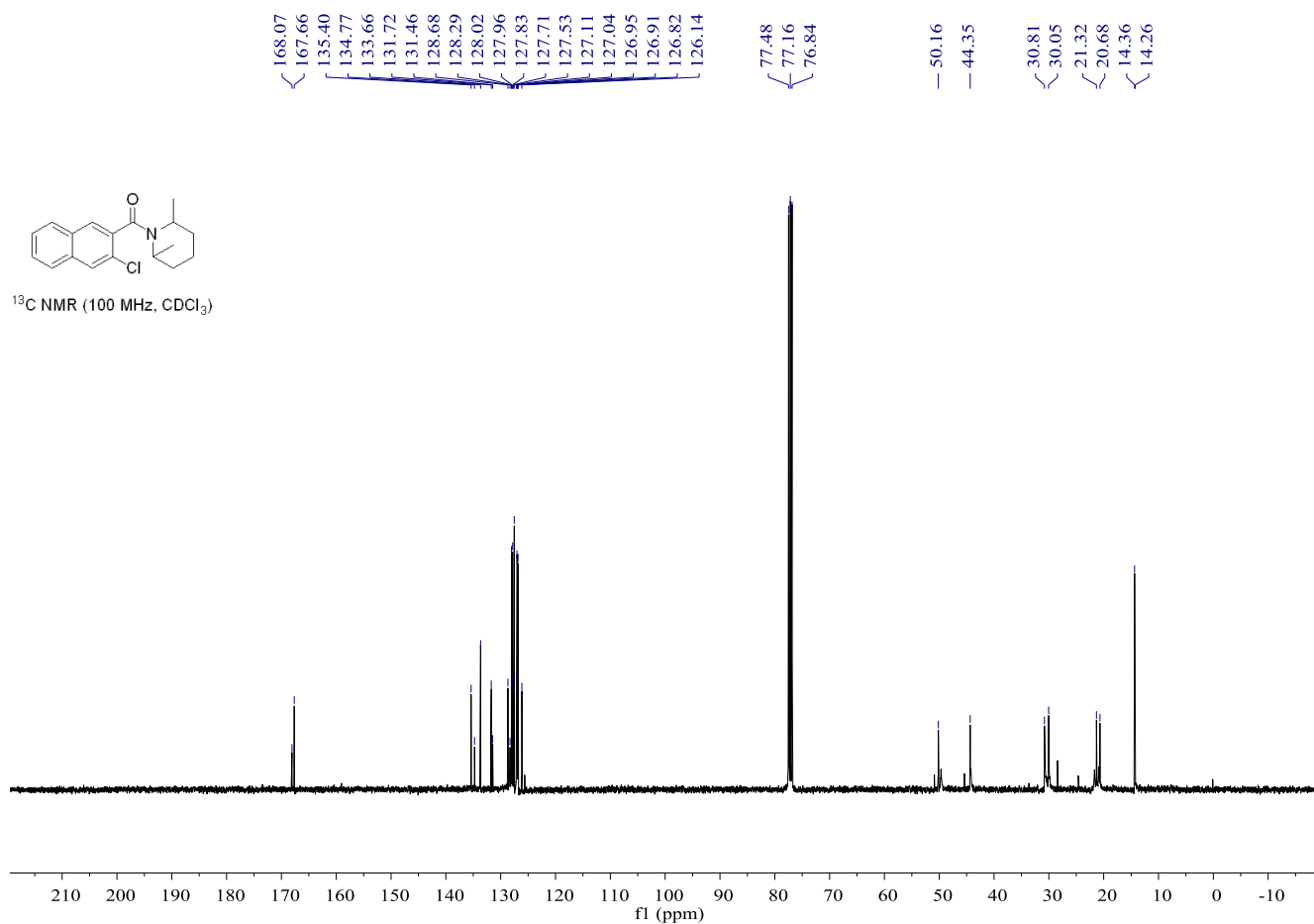


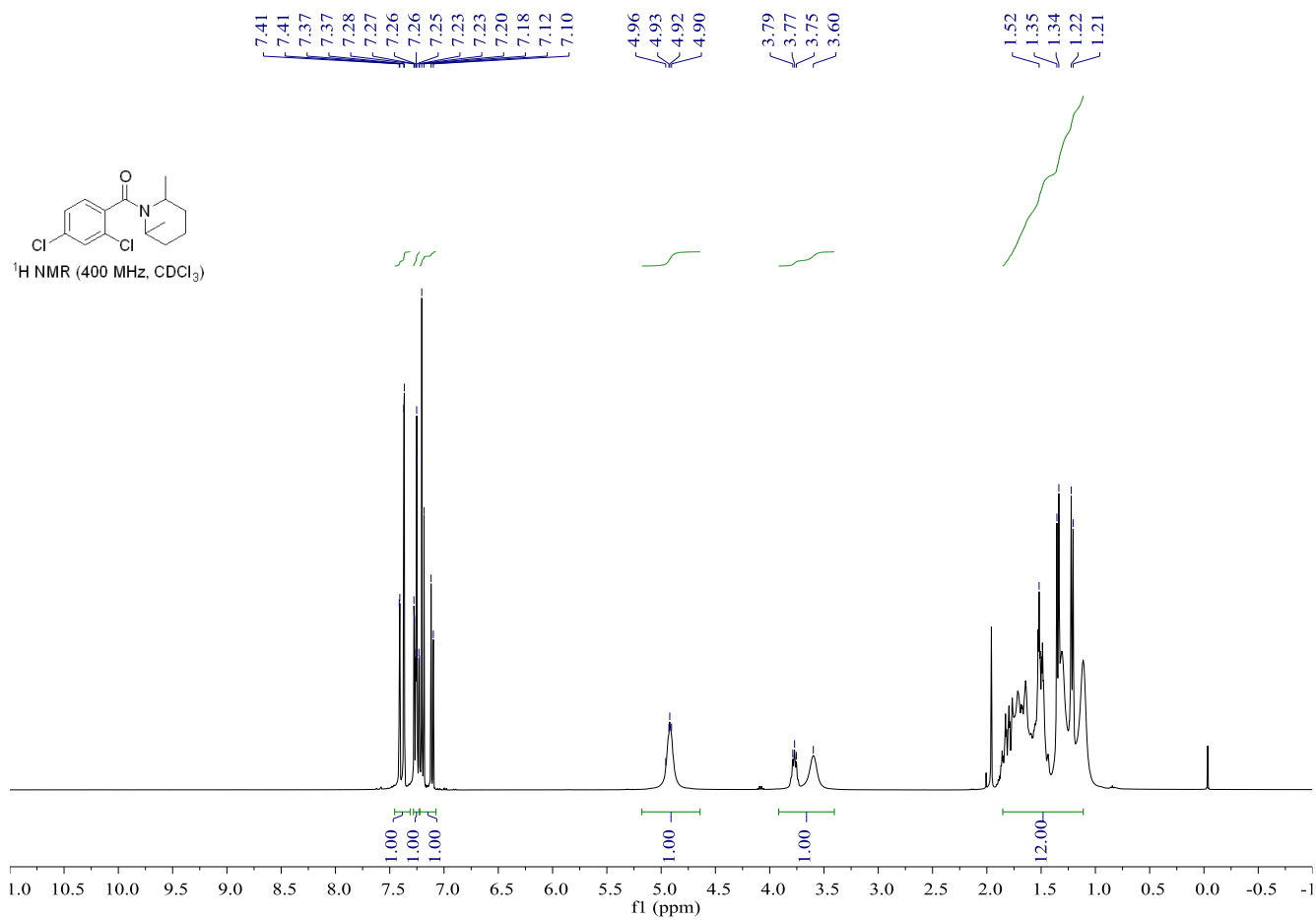
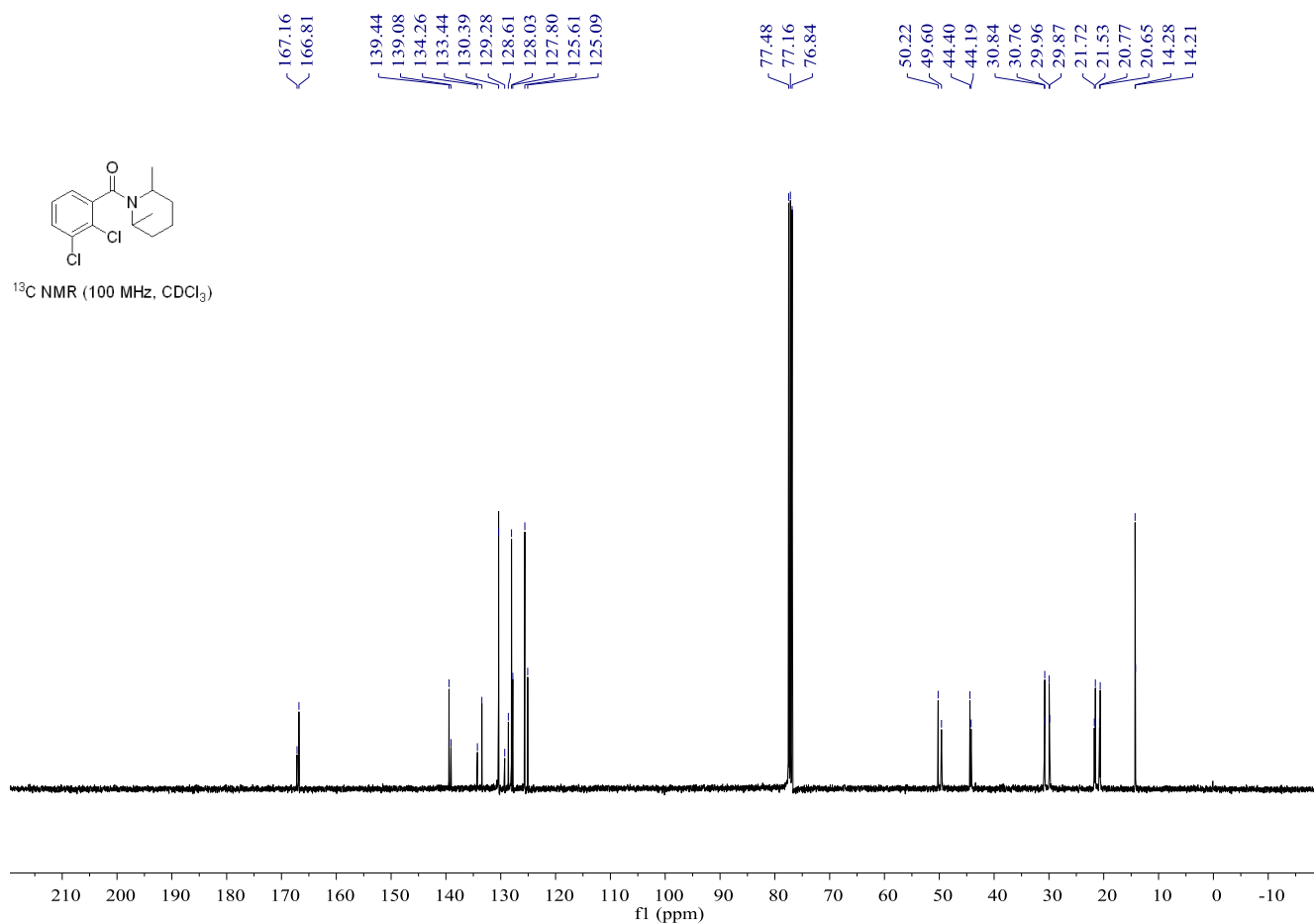
^1H NMR (400 MHz, CDCl_3)

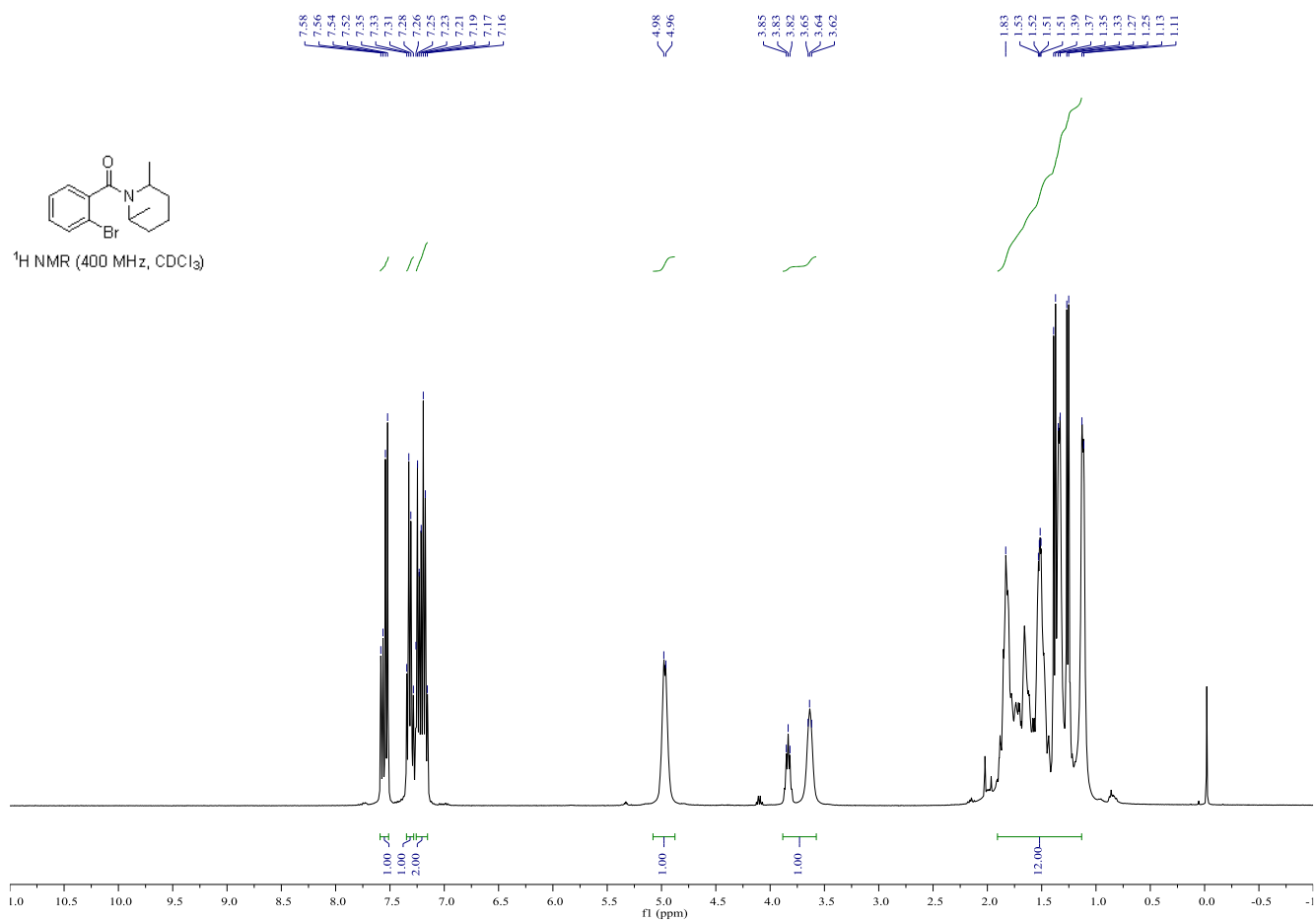
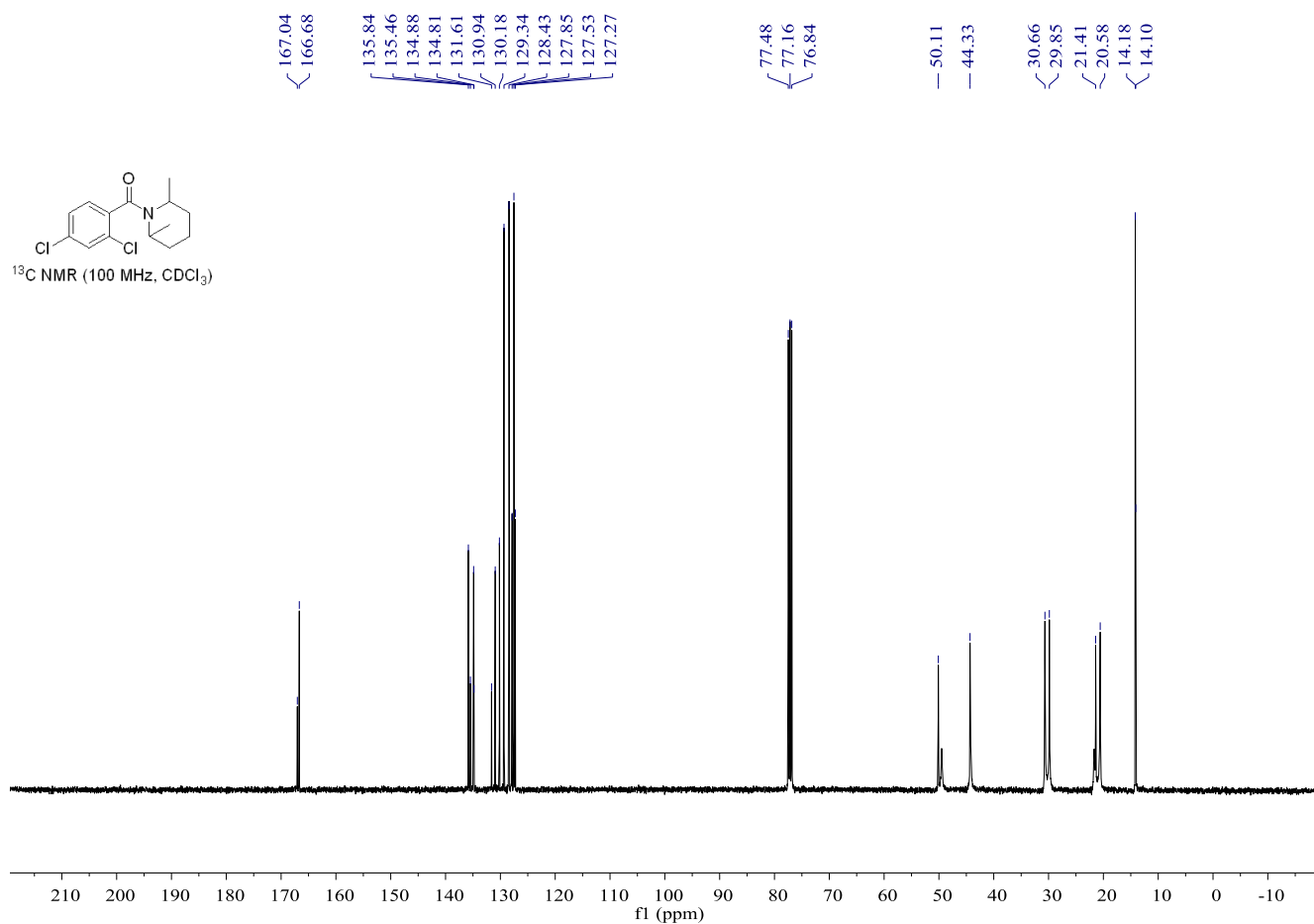


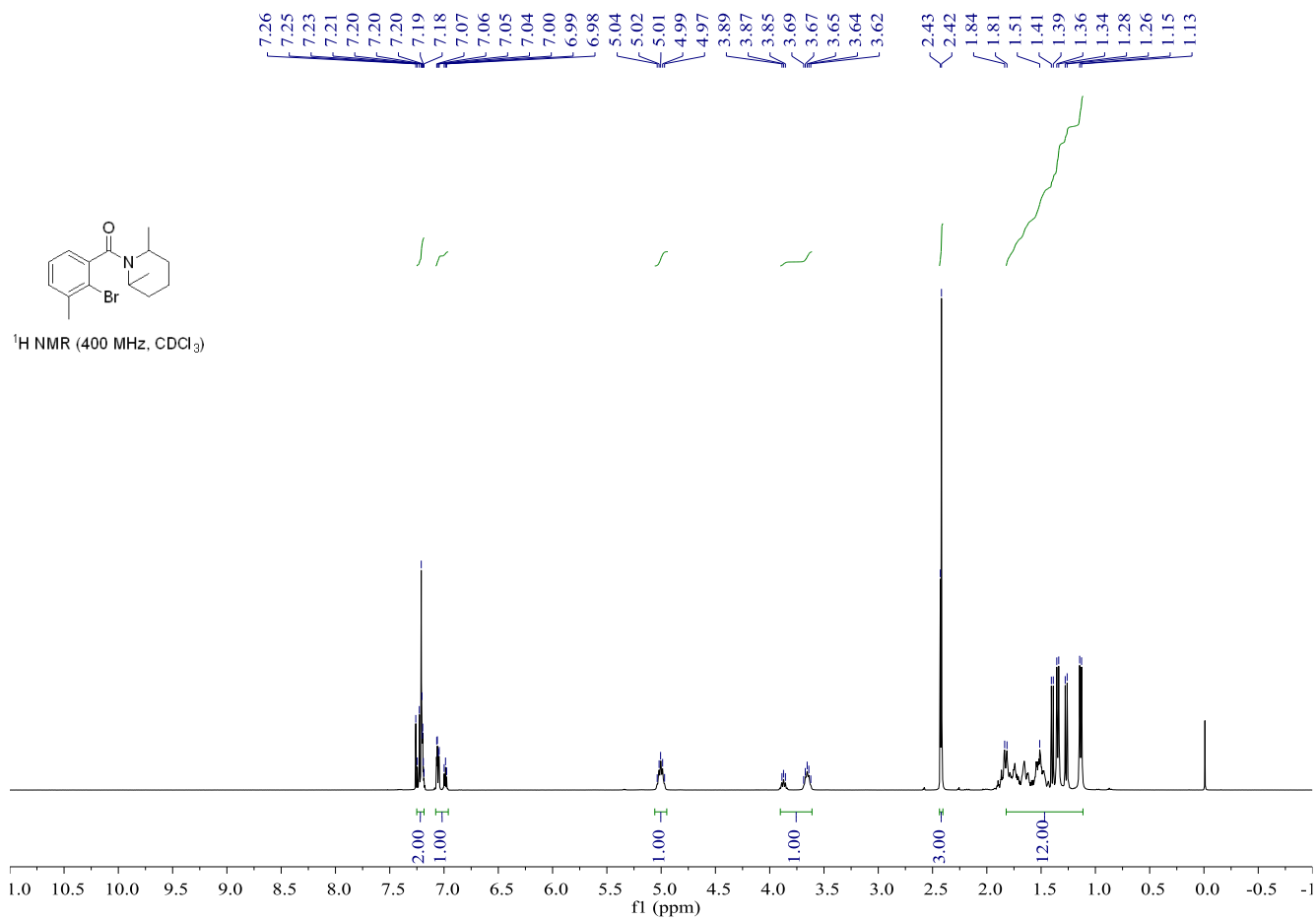
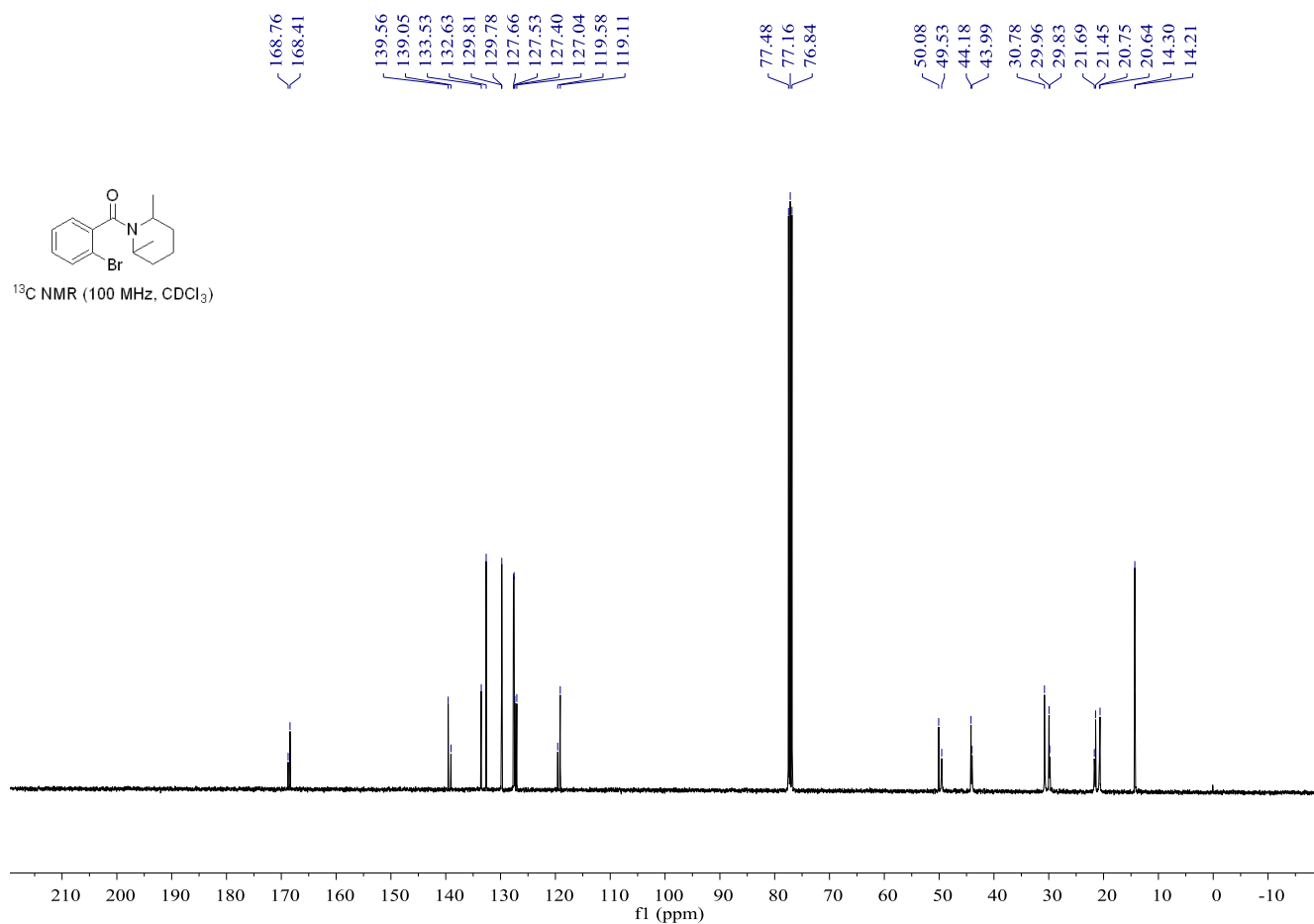


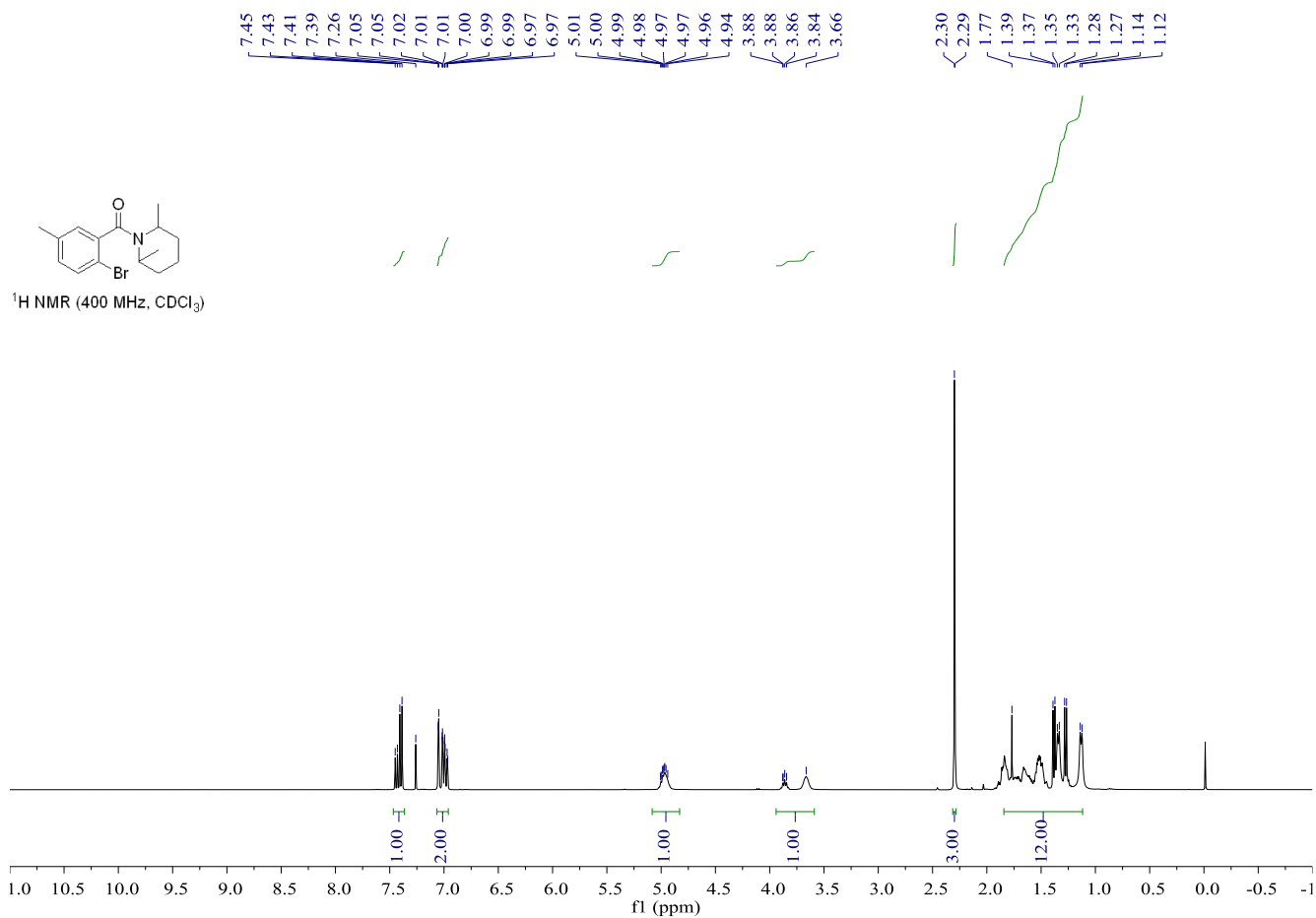
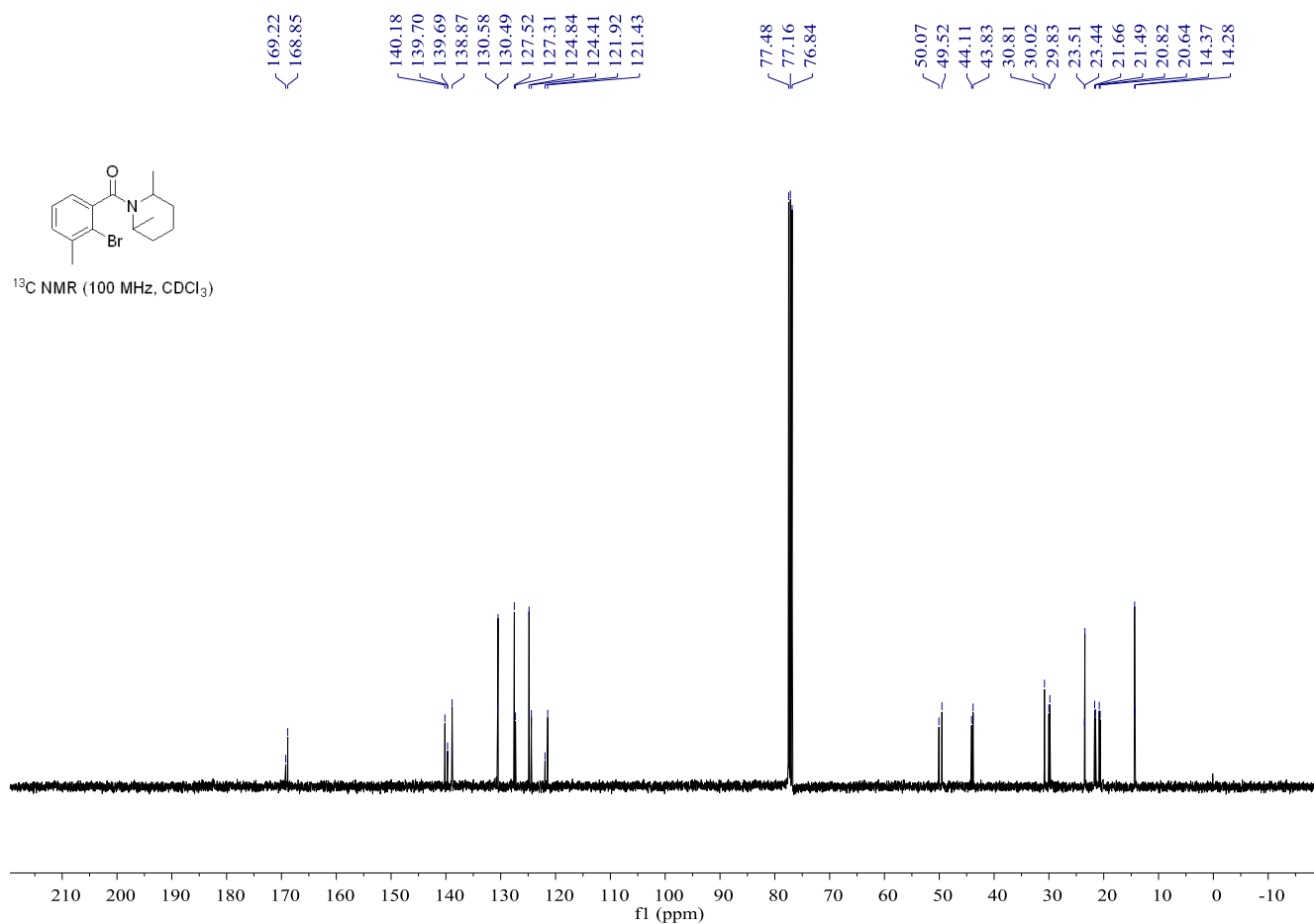


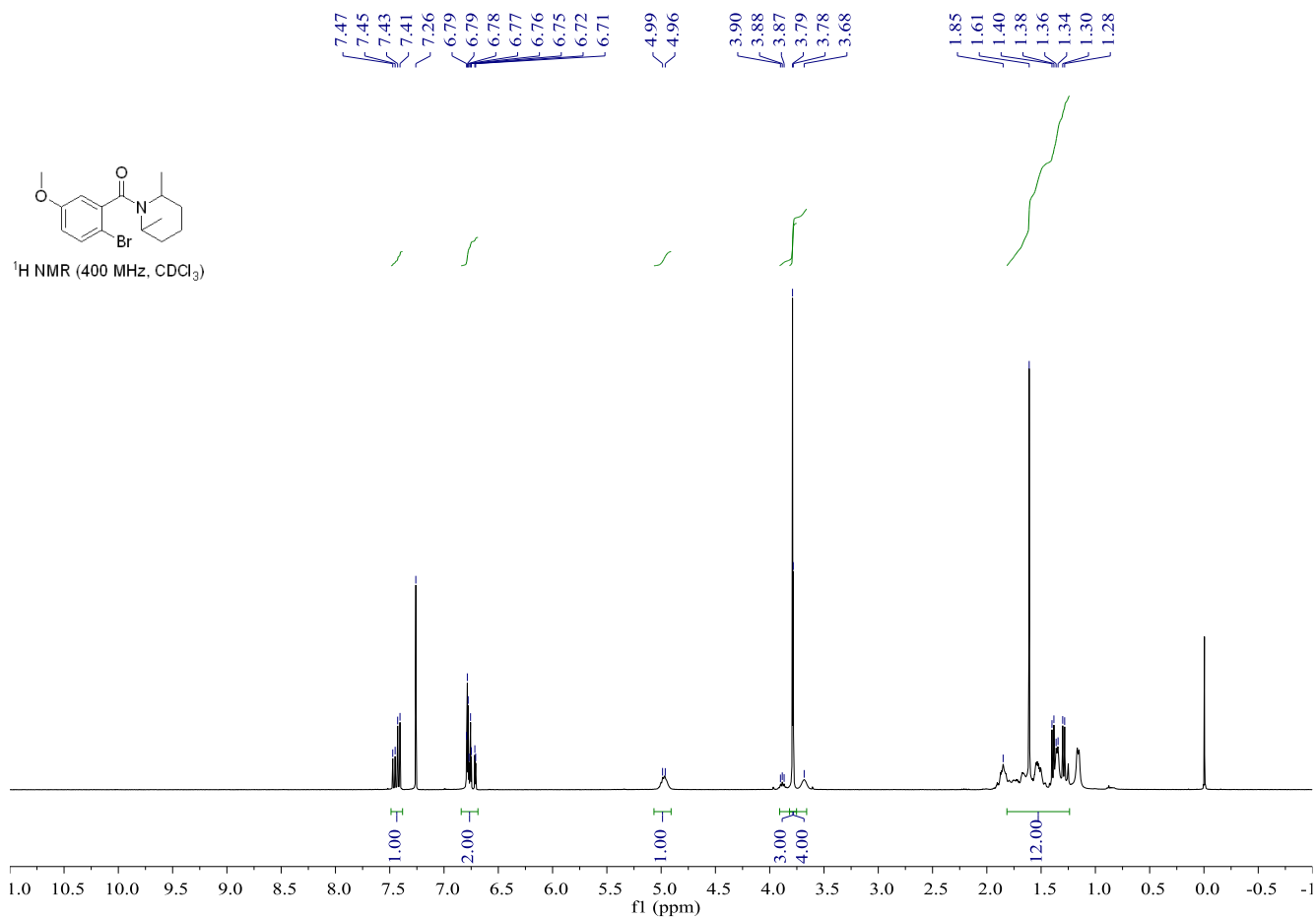
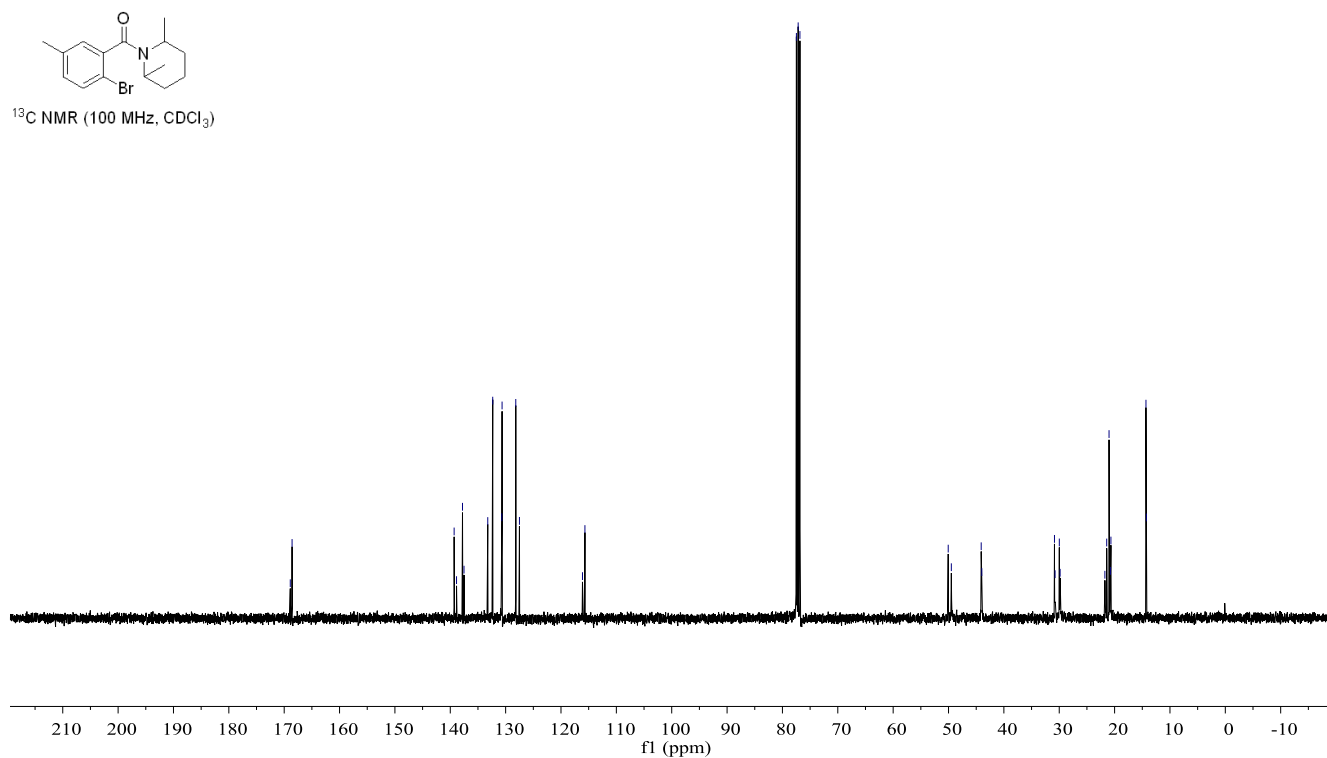


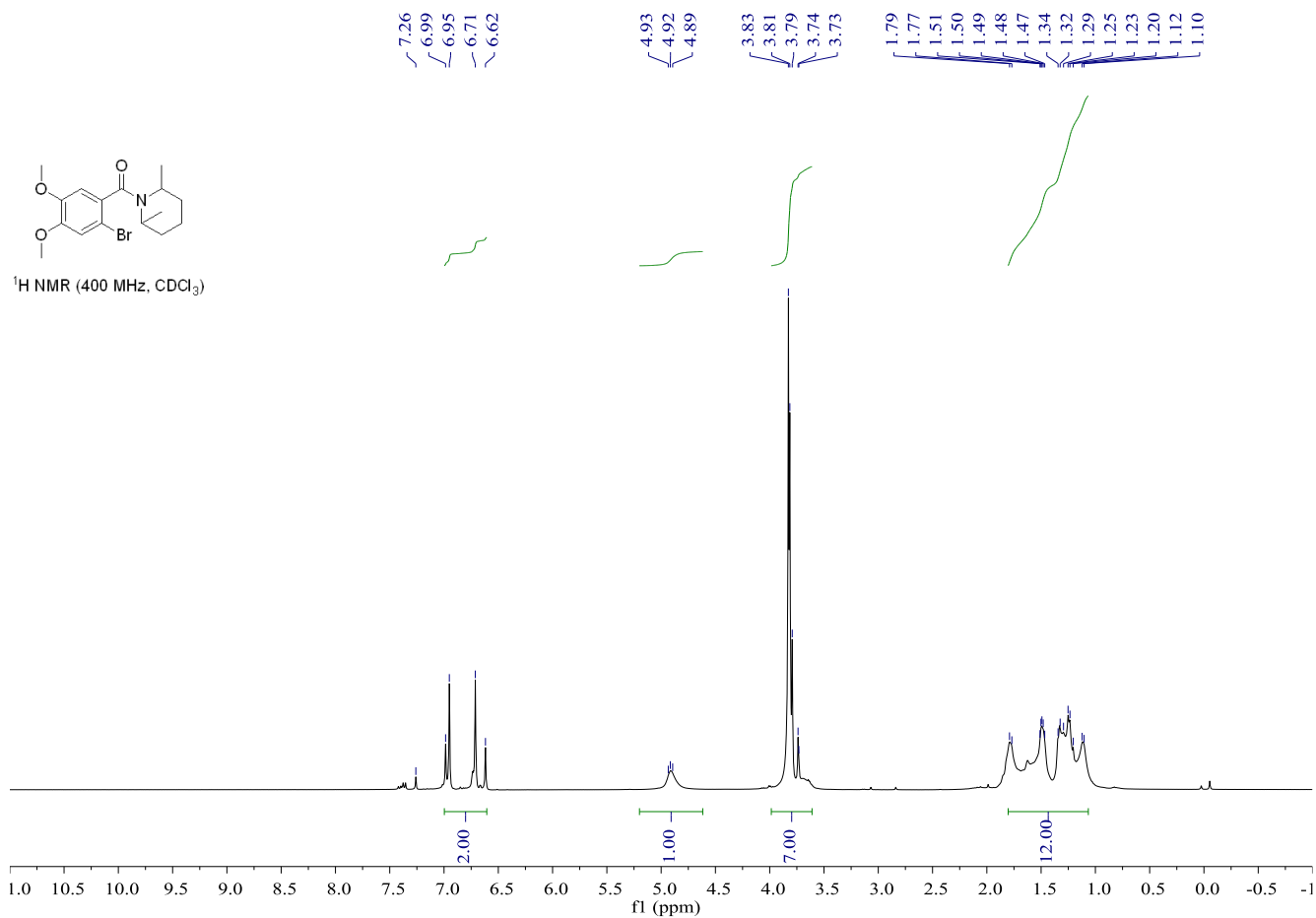
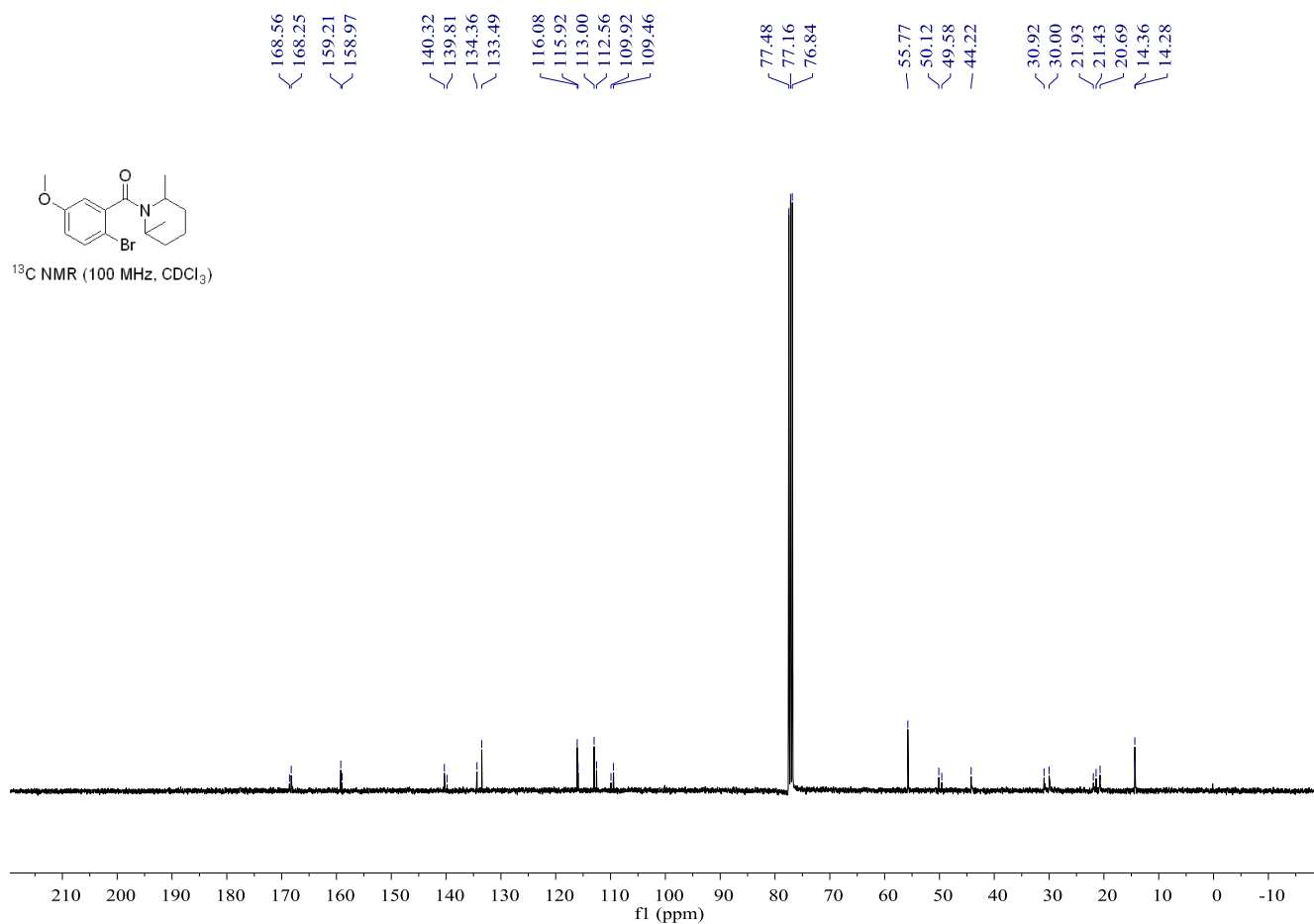


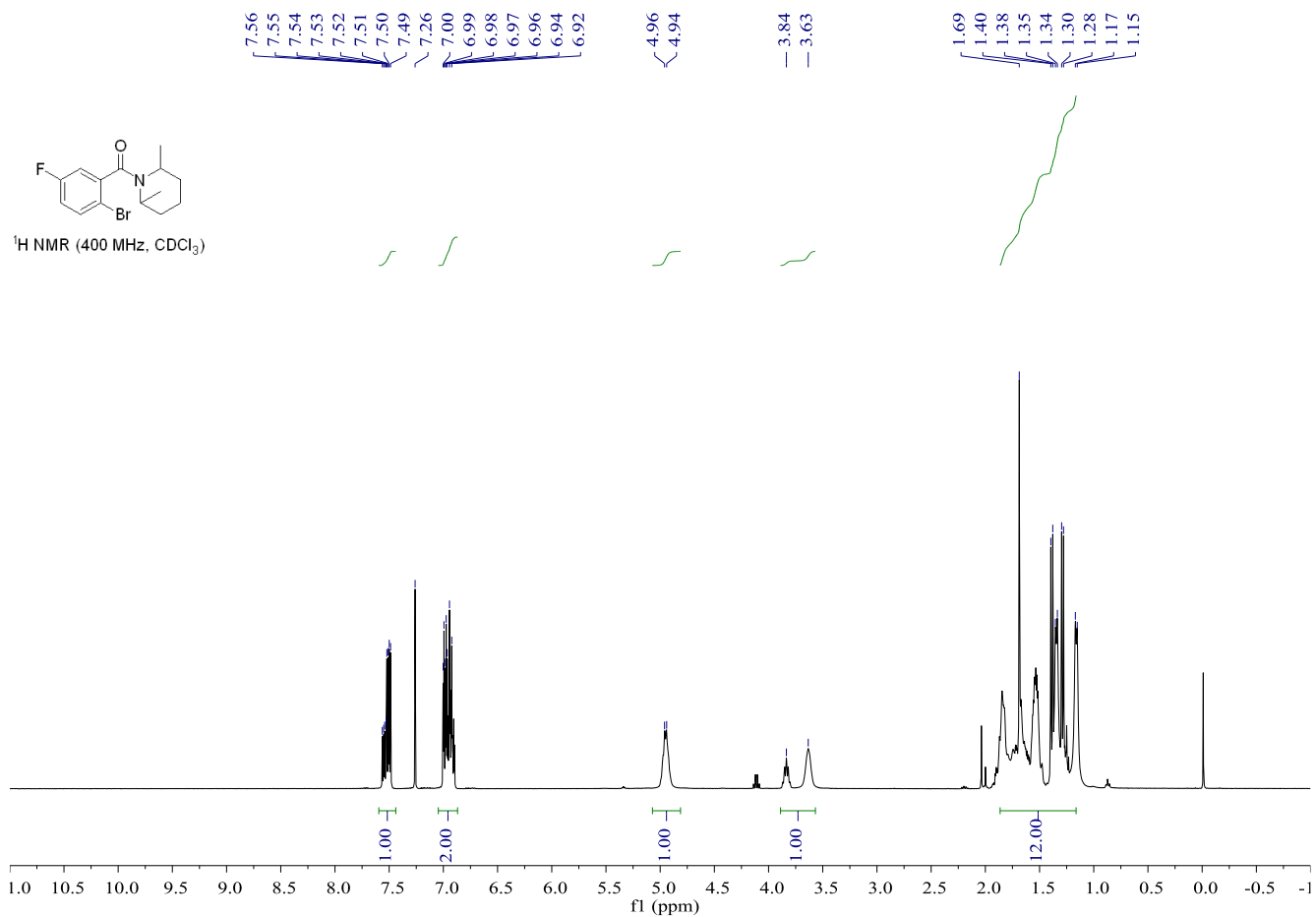
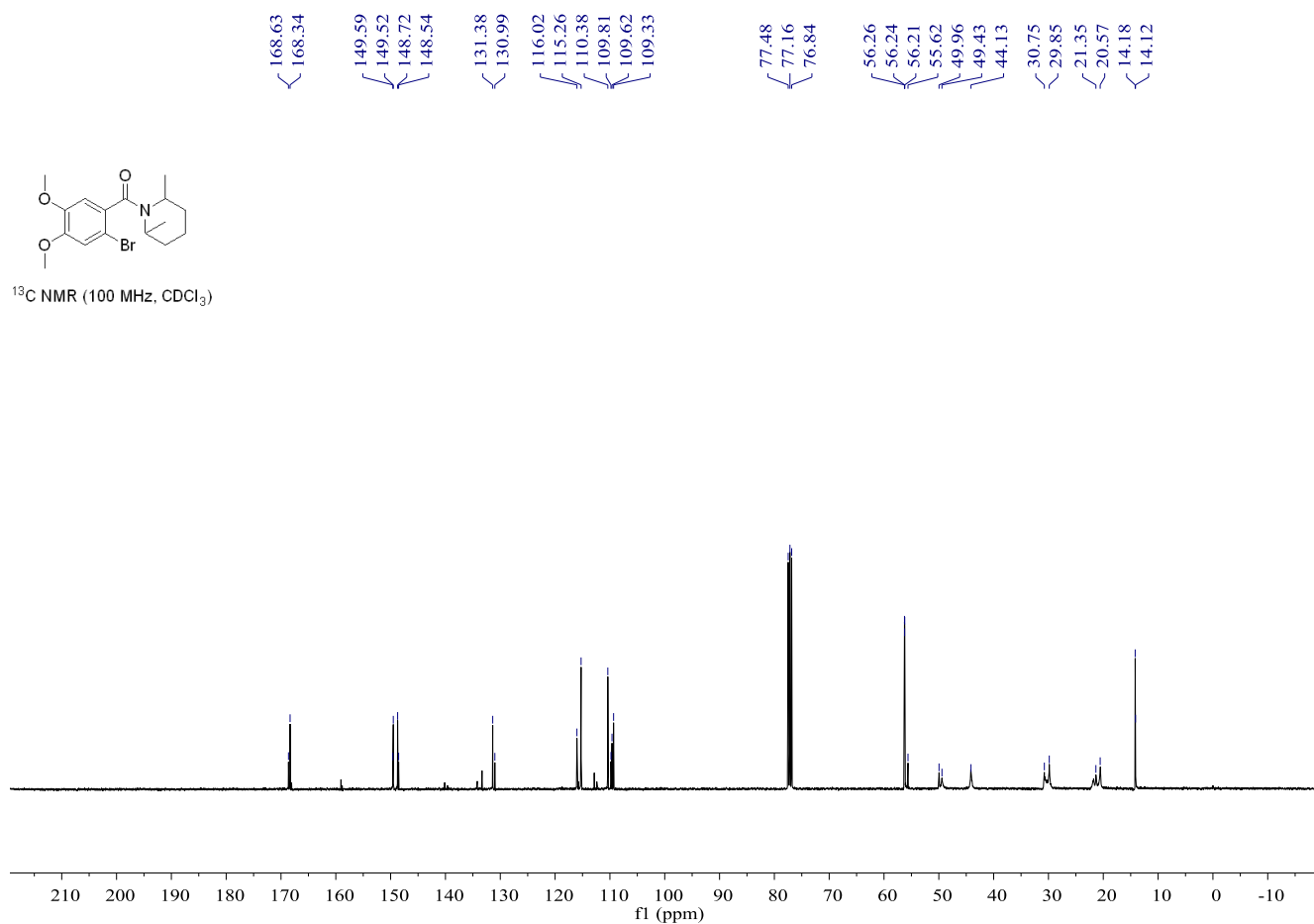


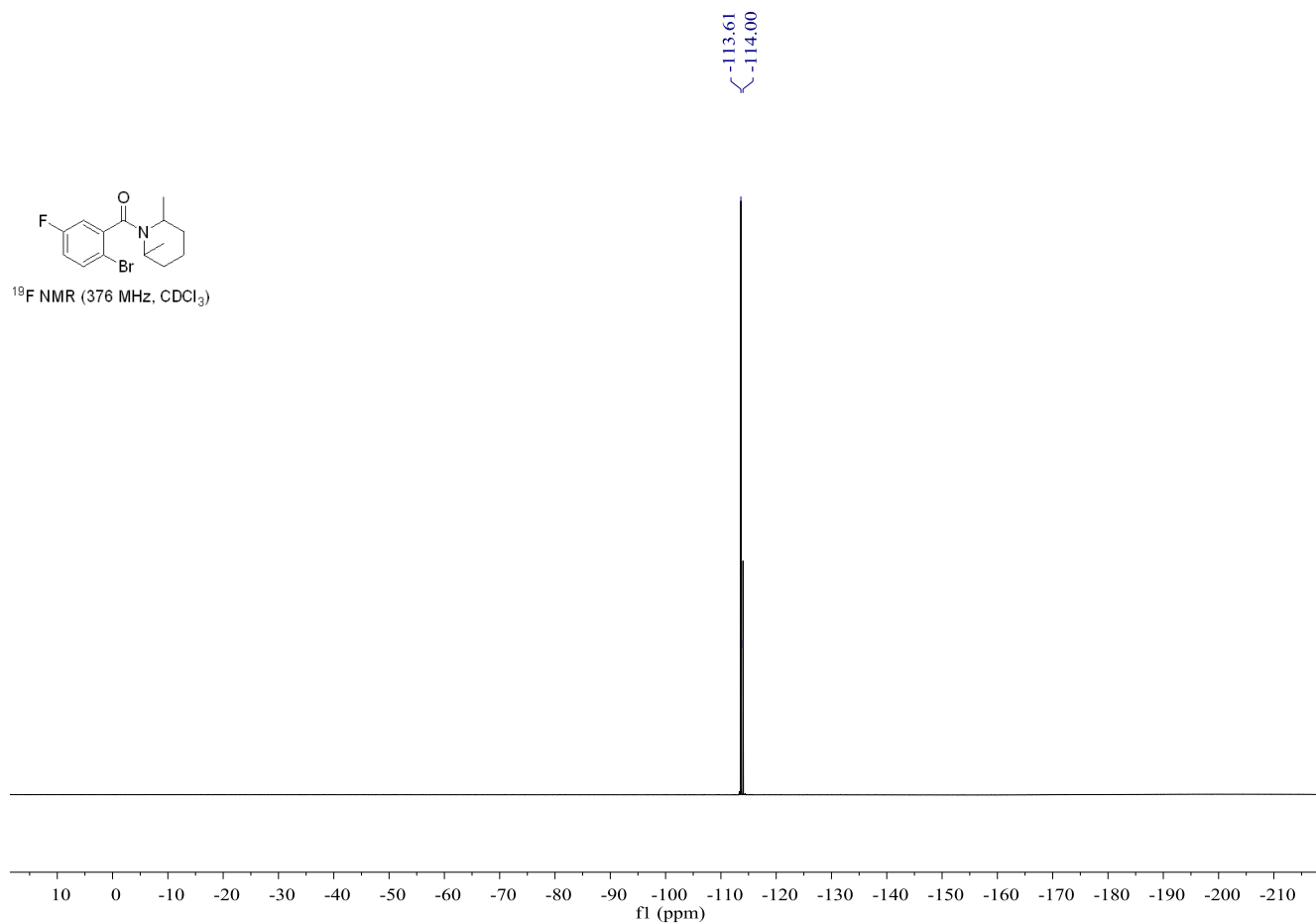
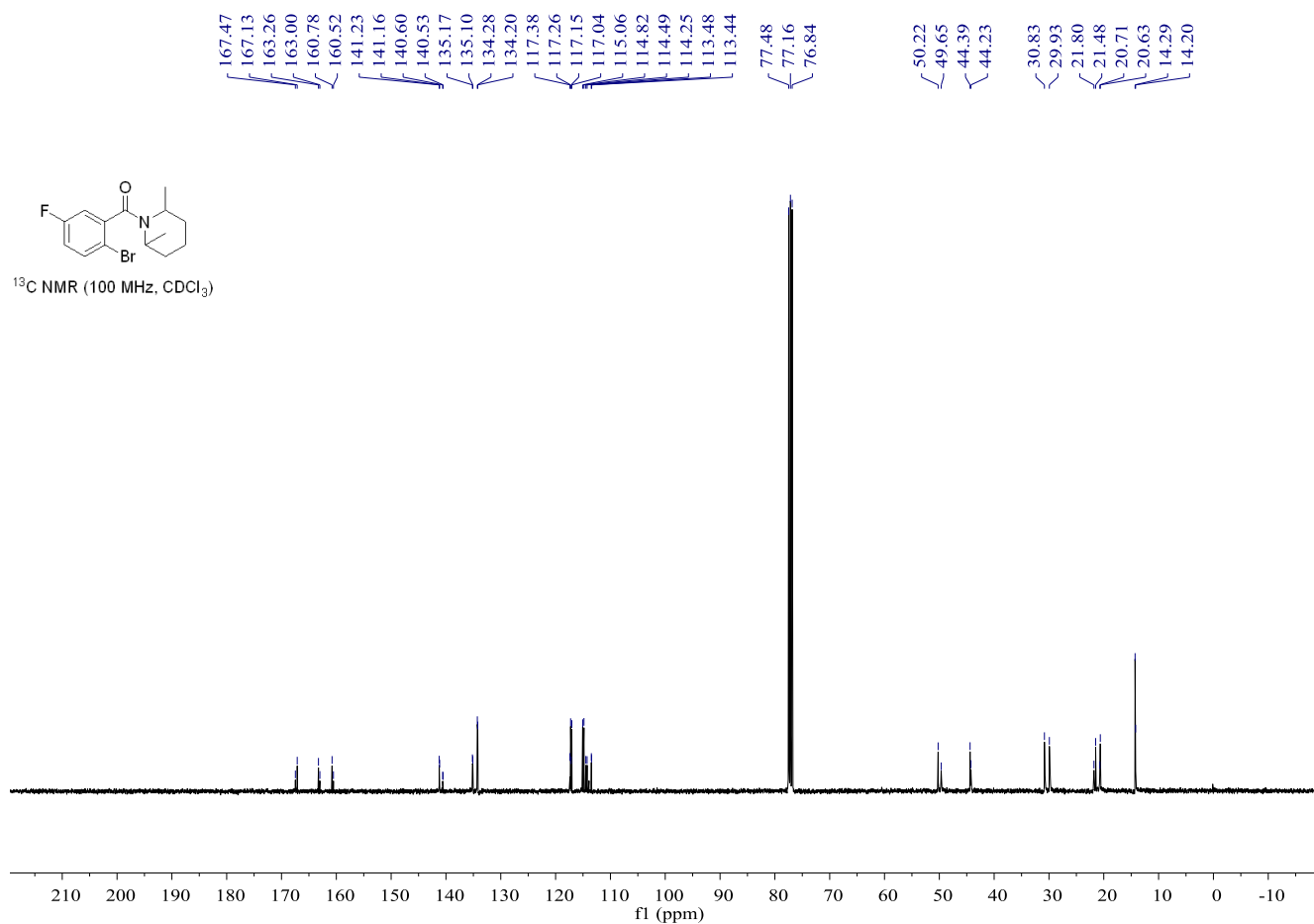


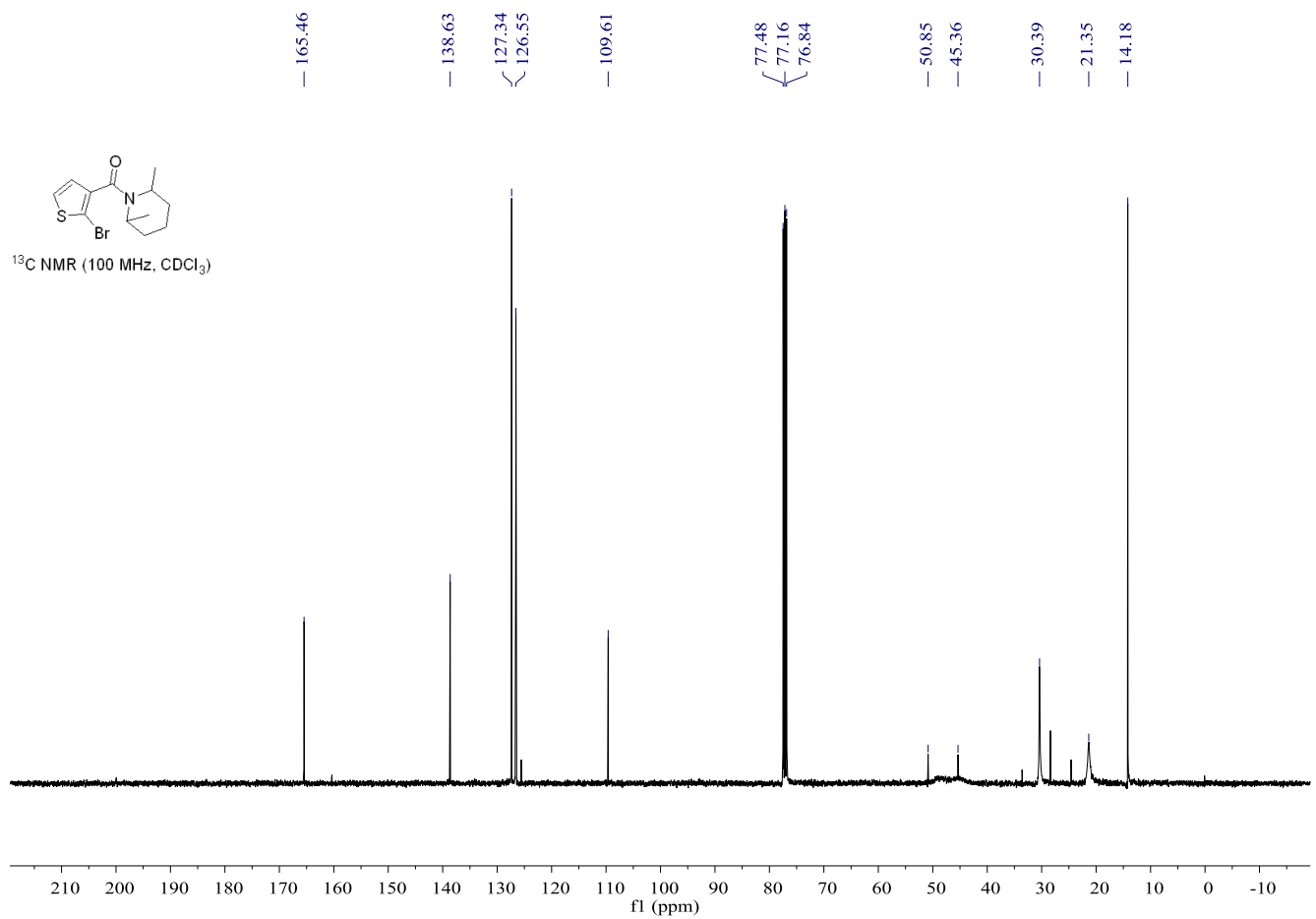
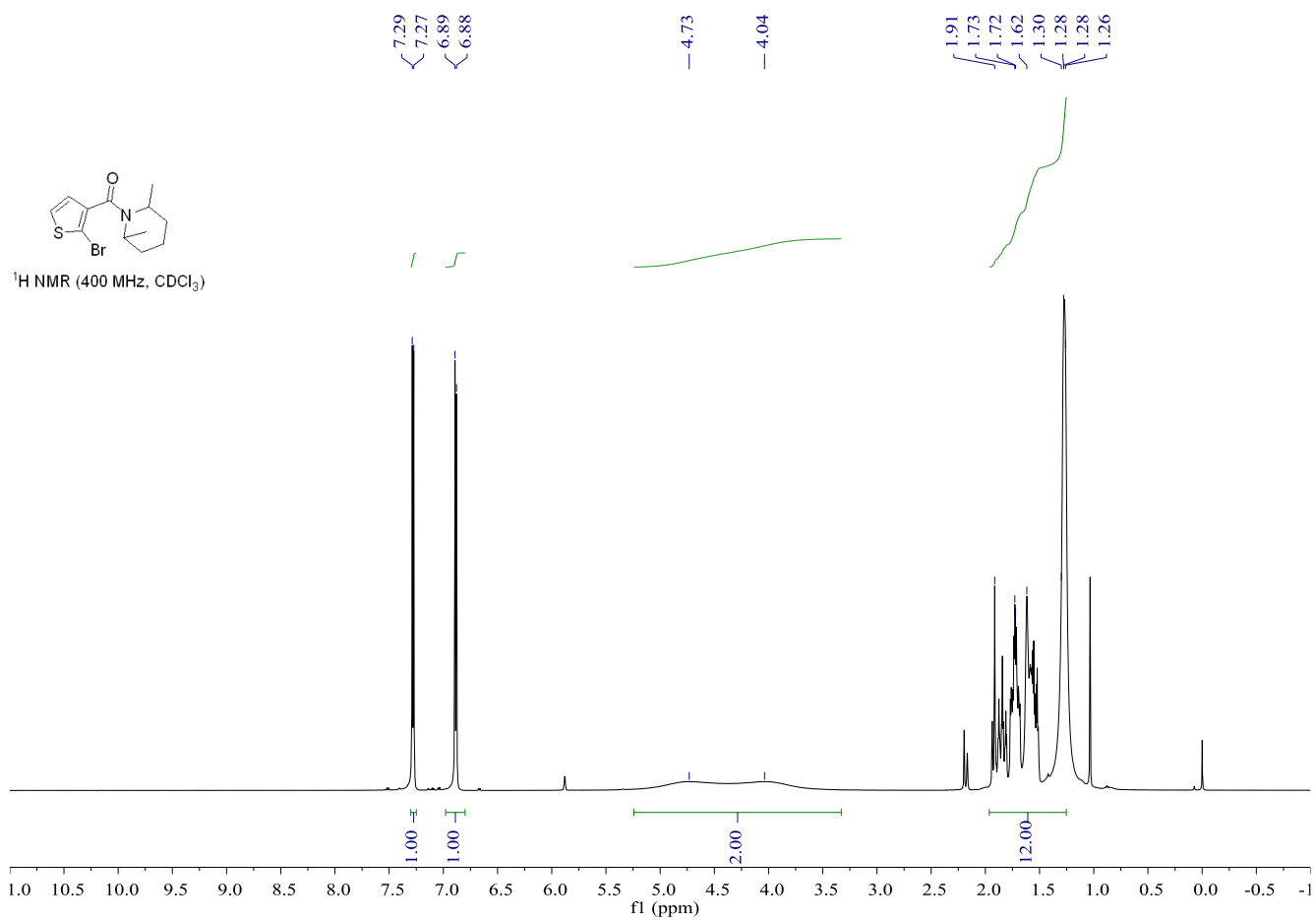


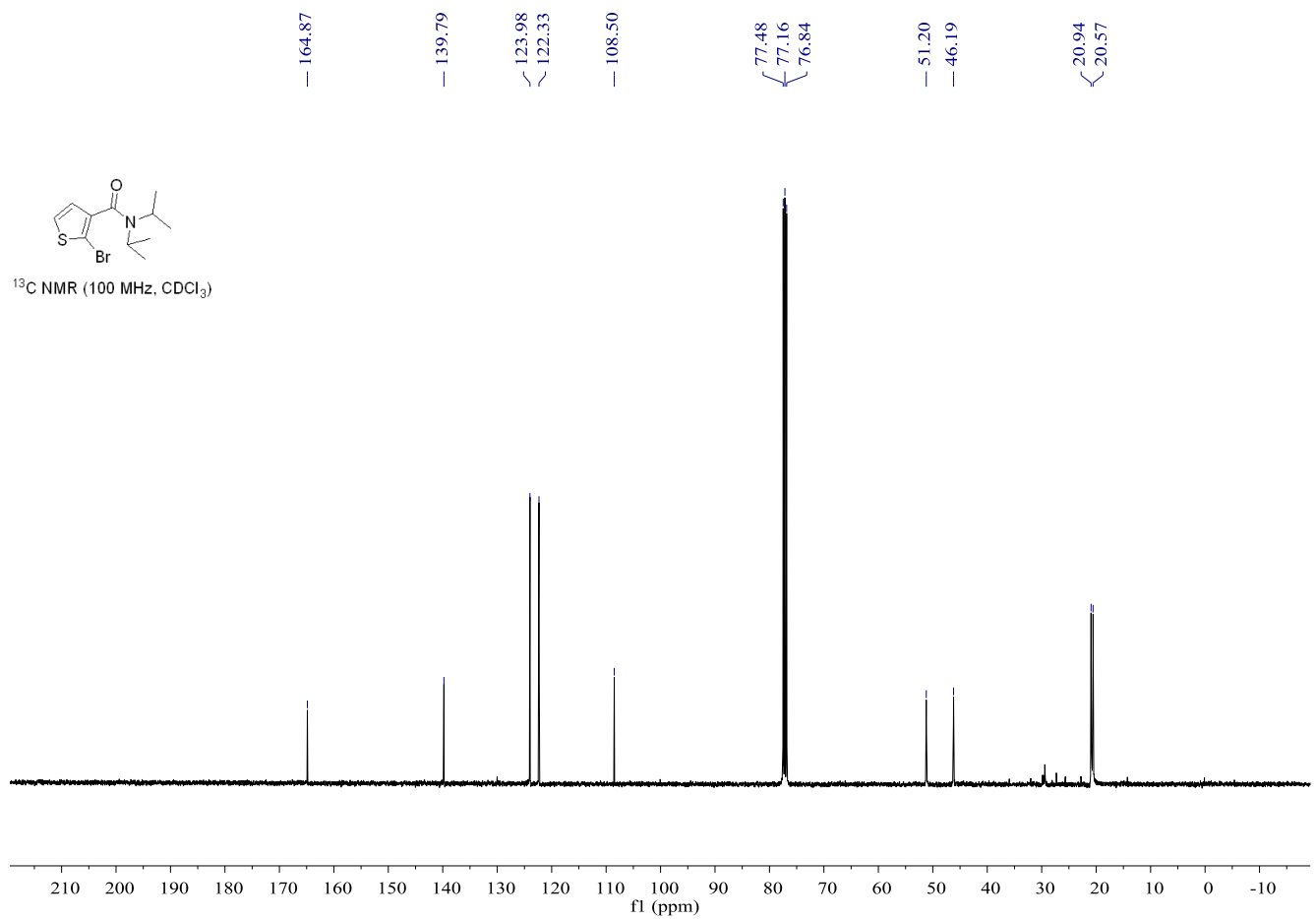
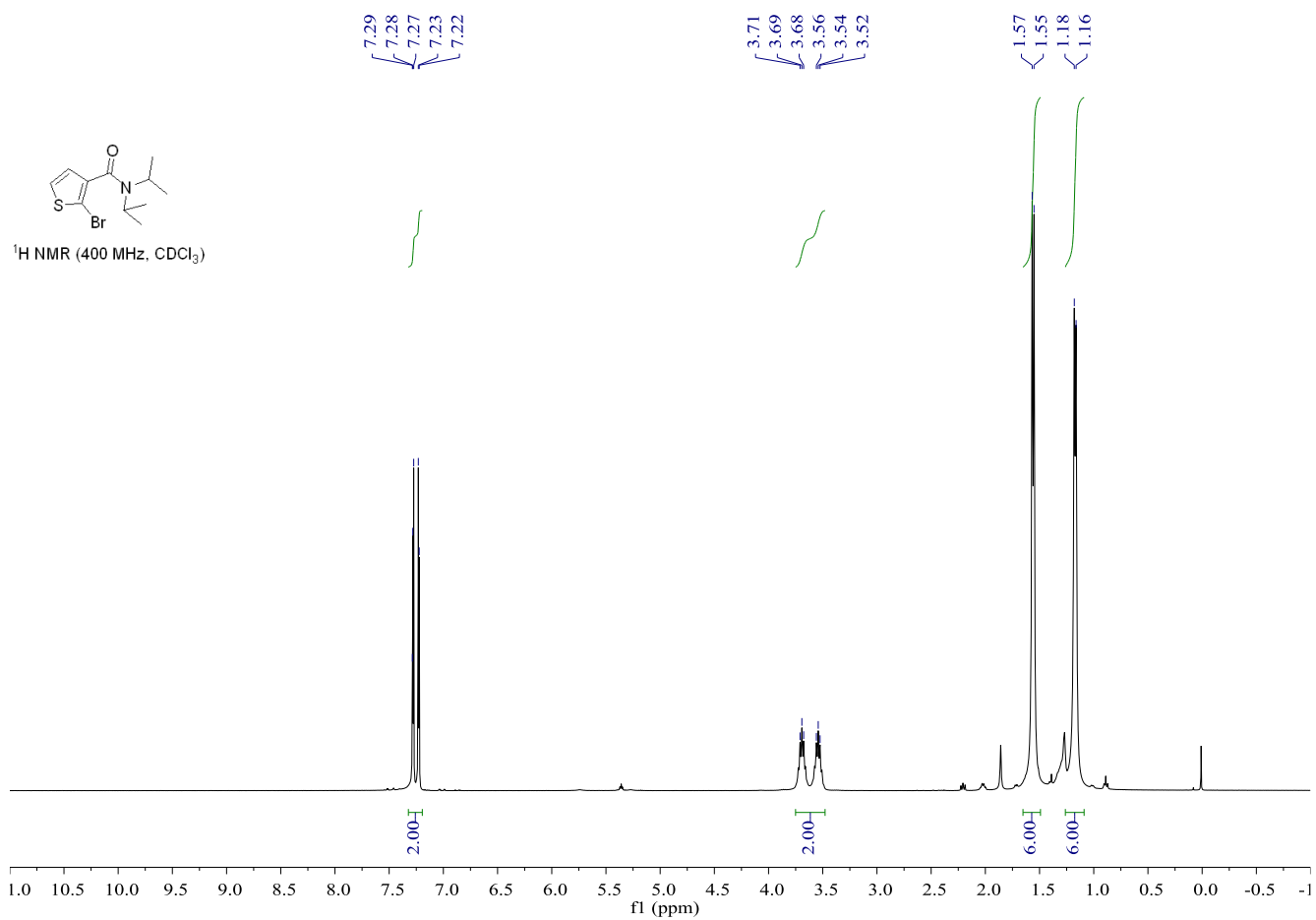


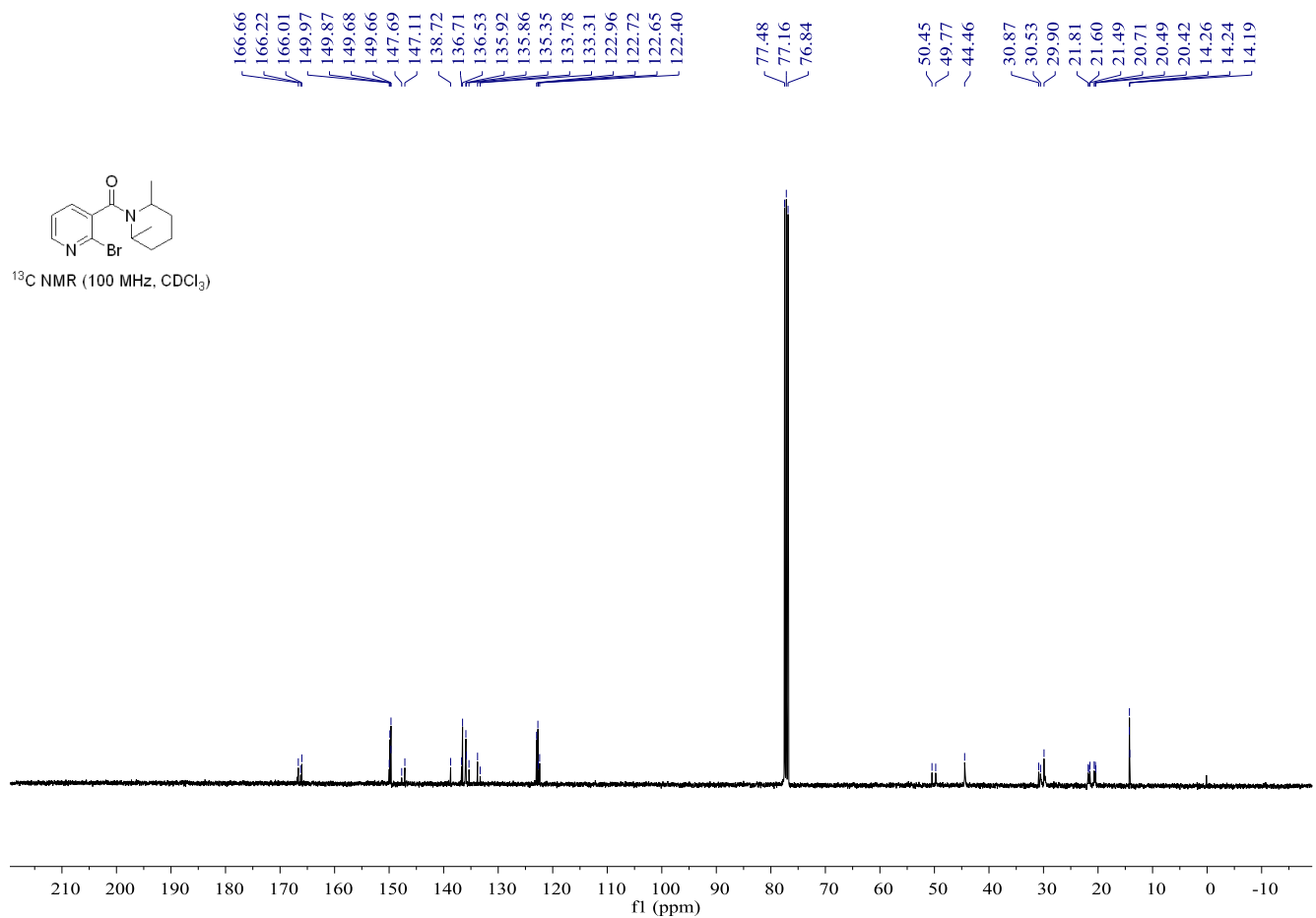
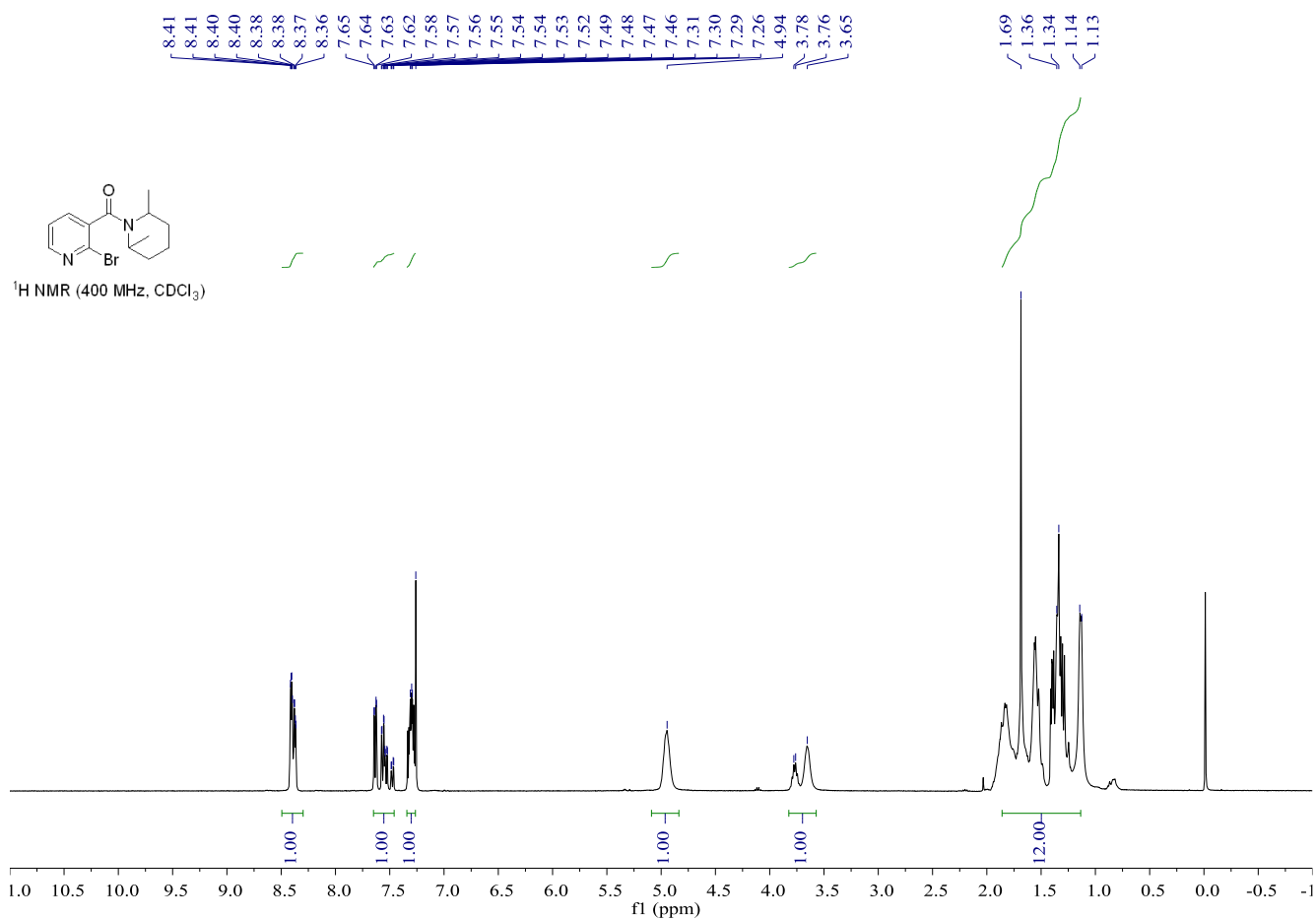


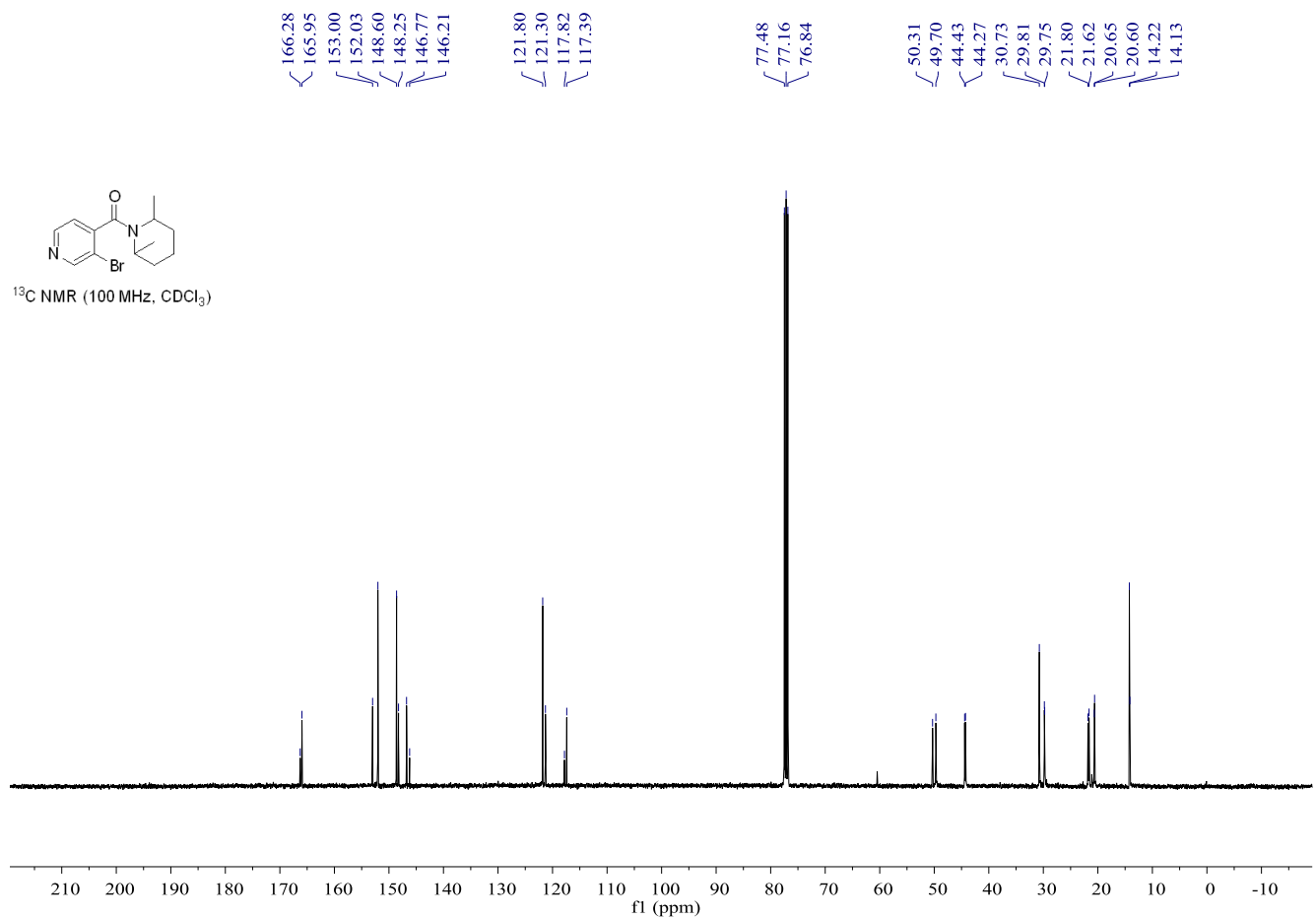
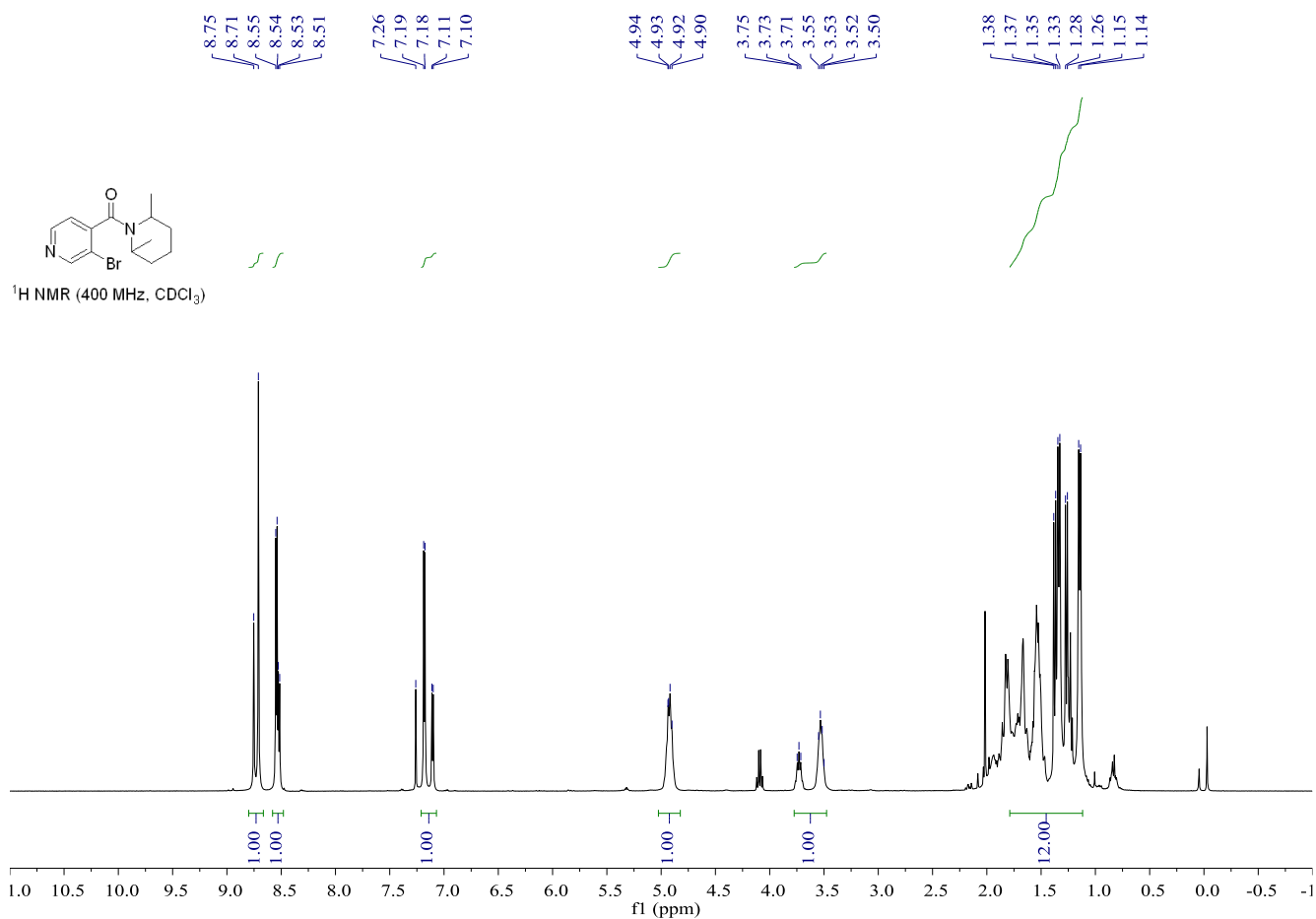


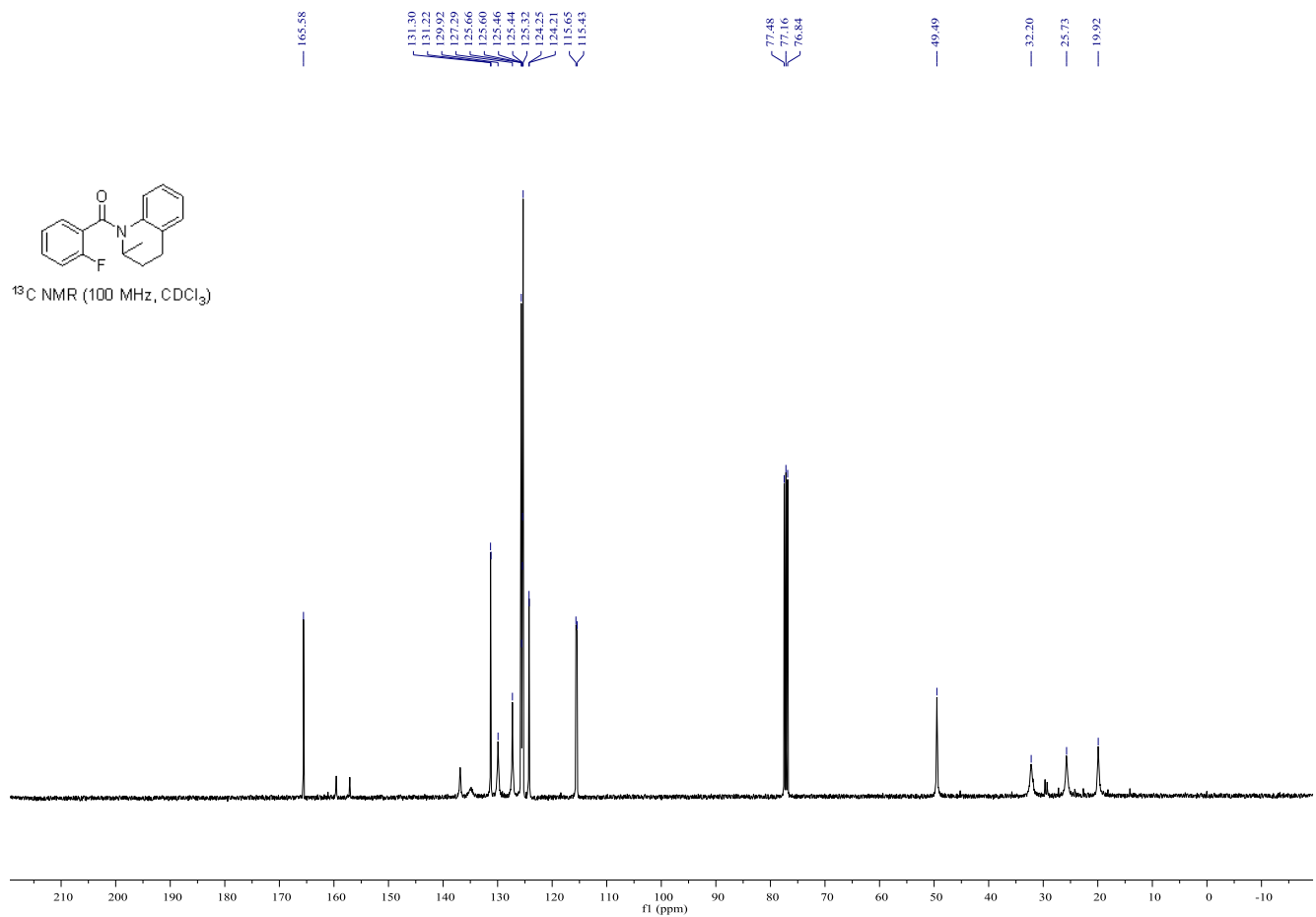
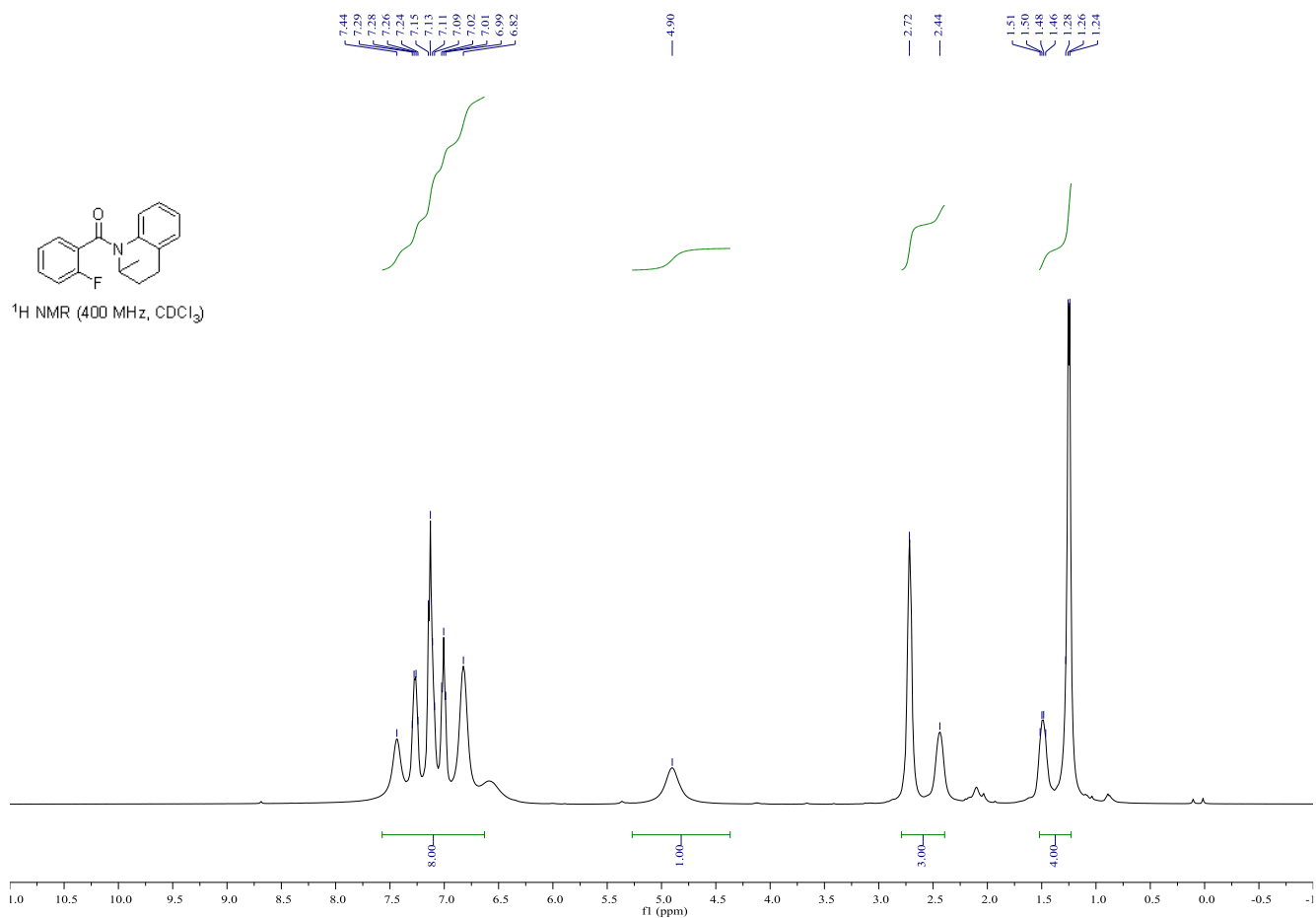


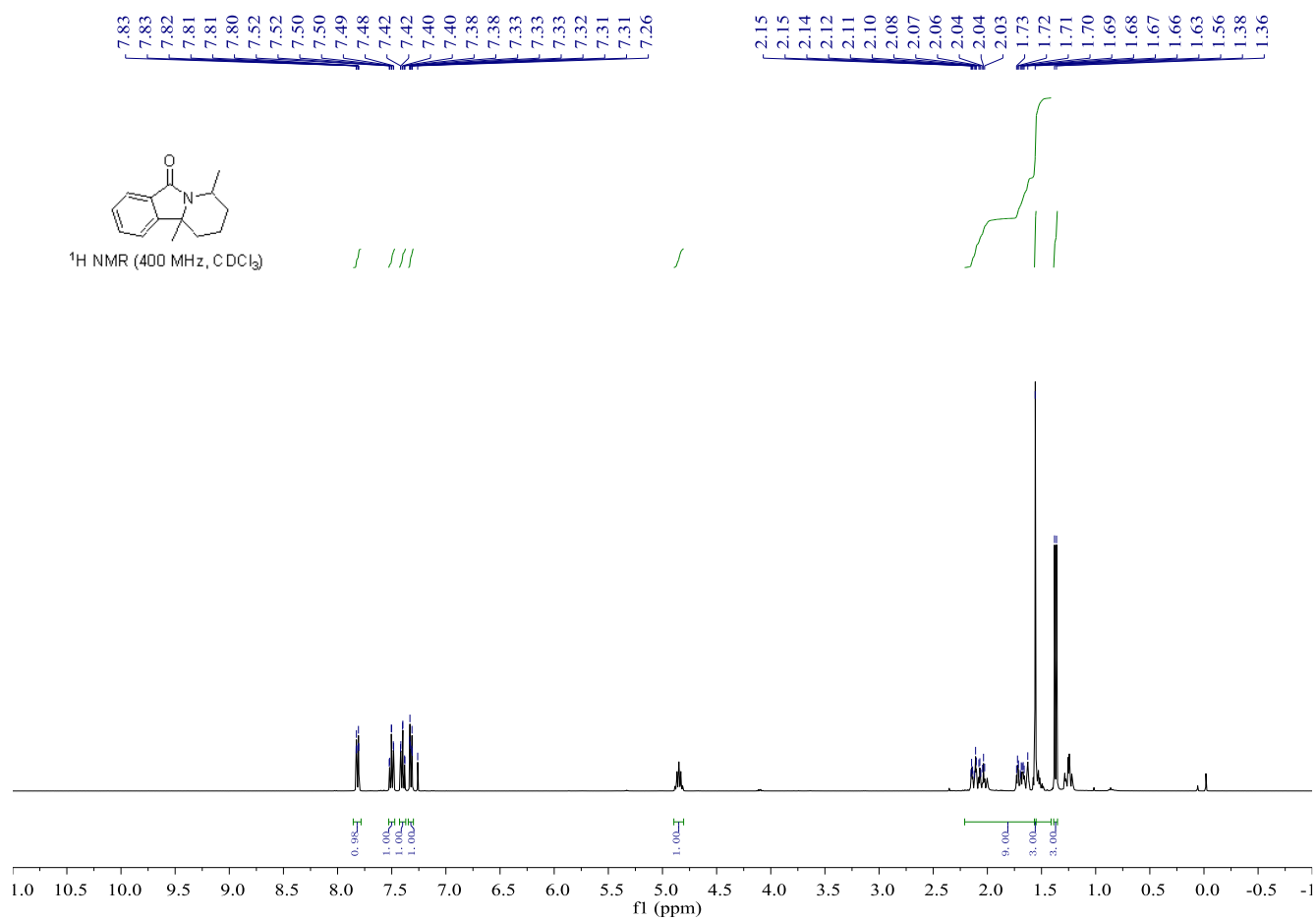
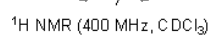
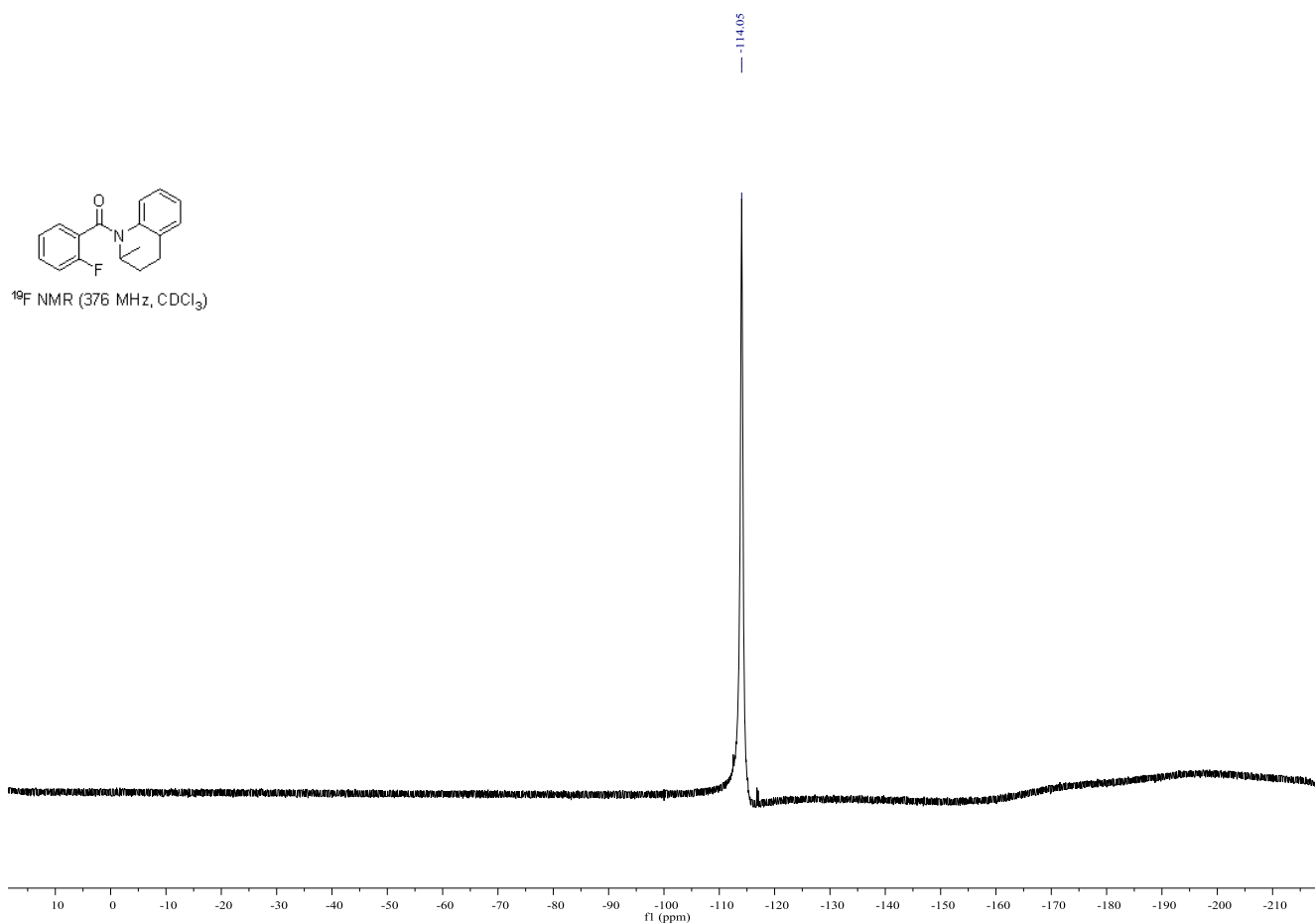


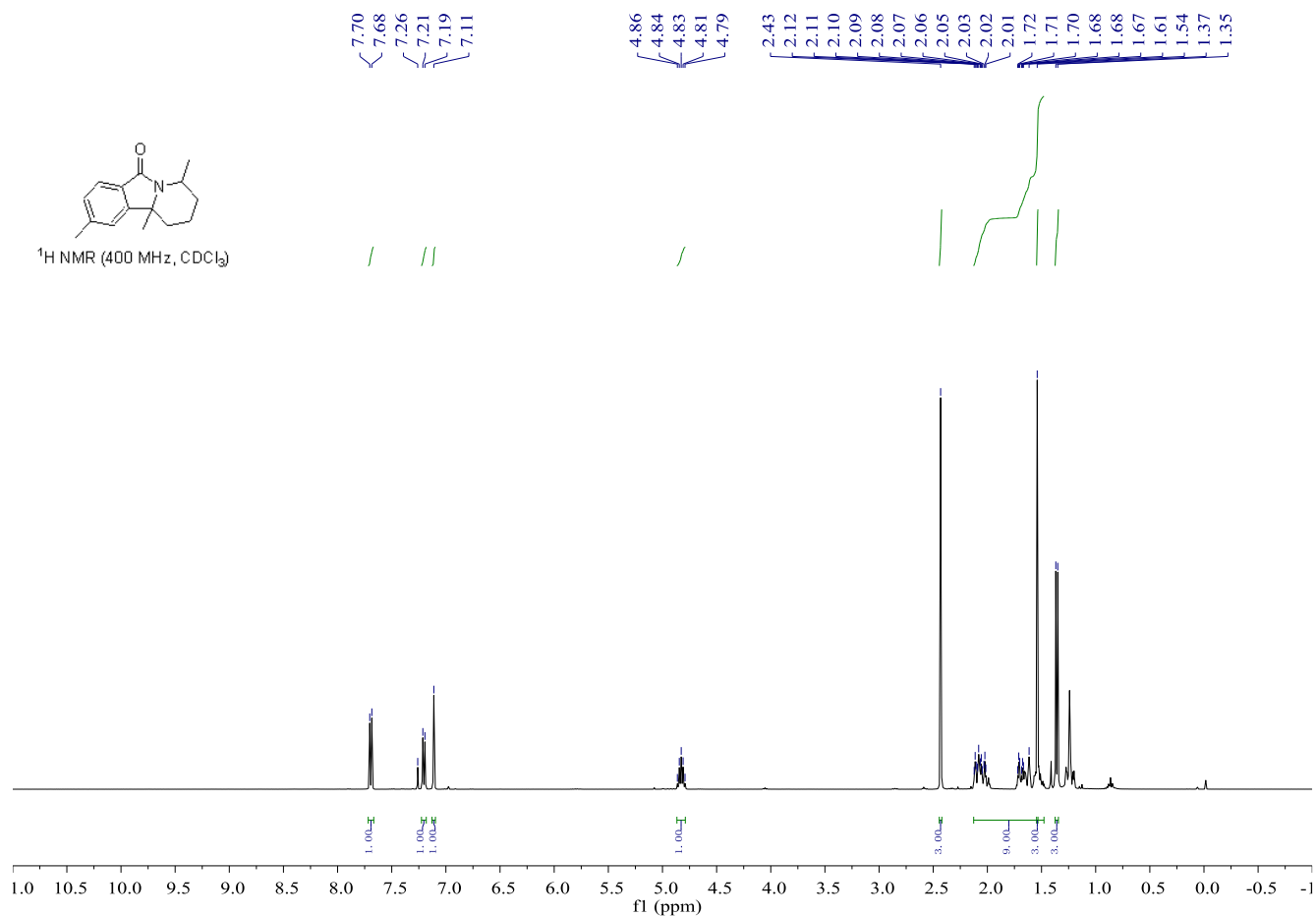
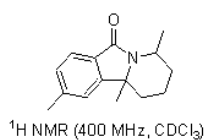
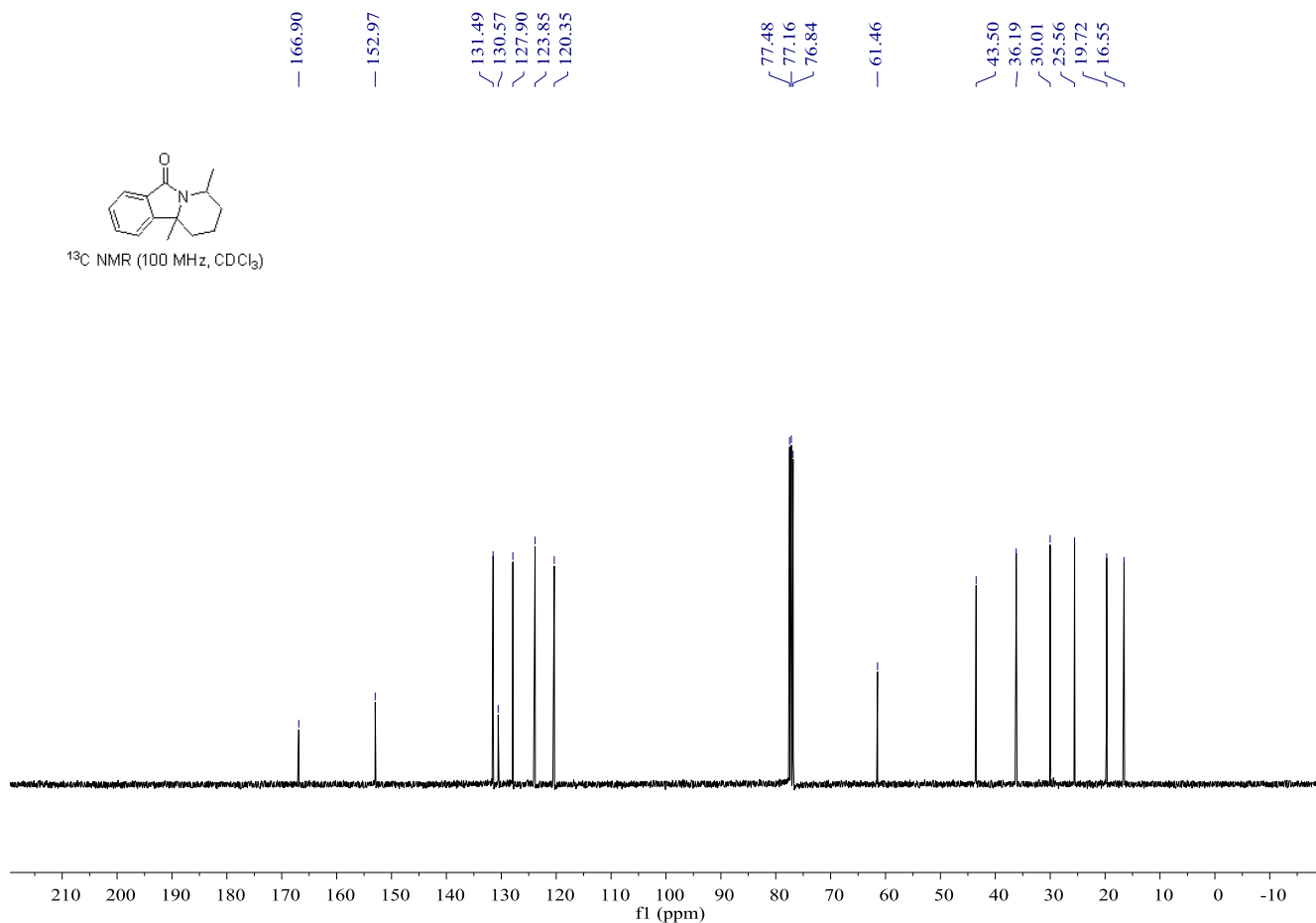
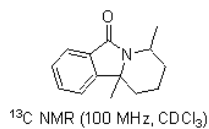


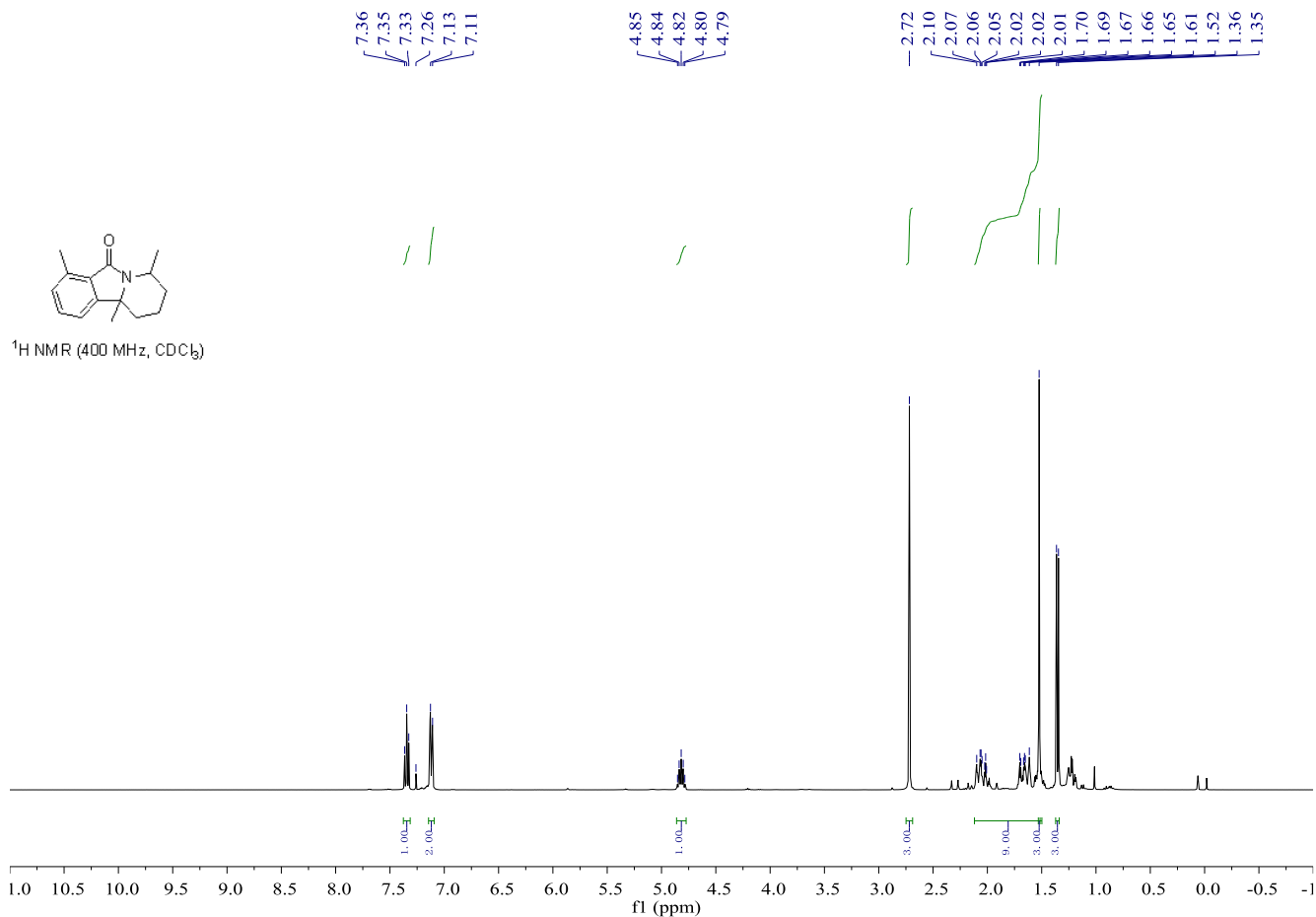
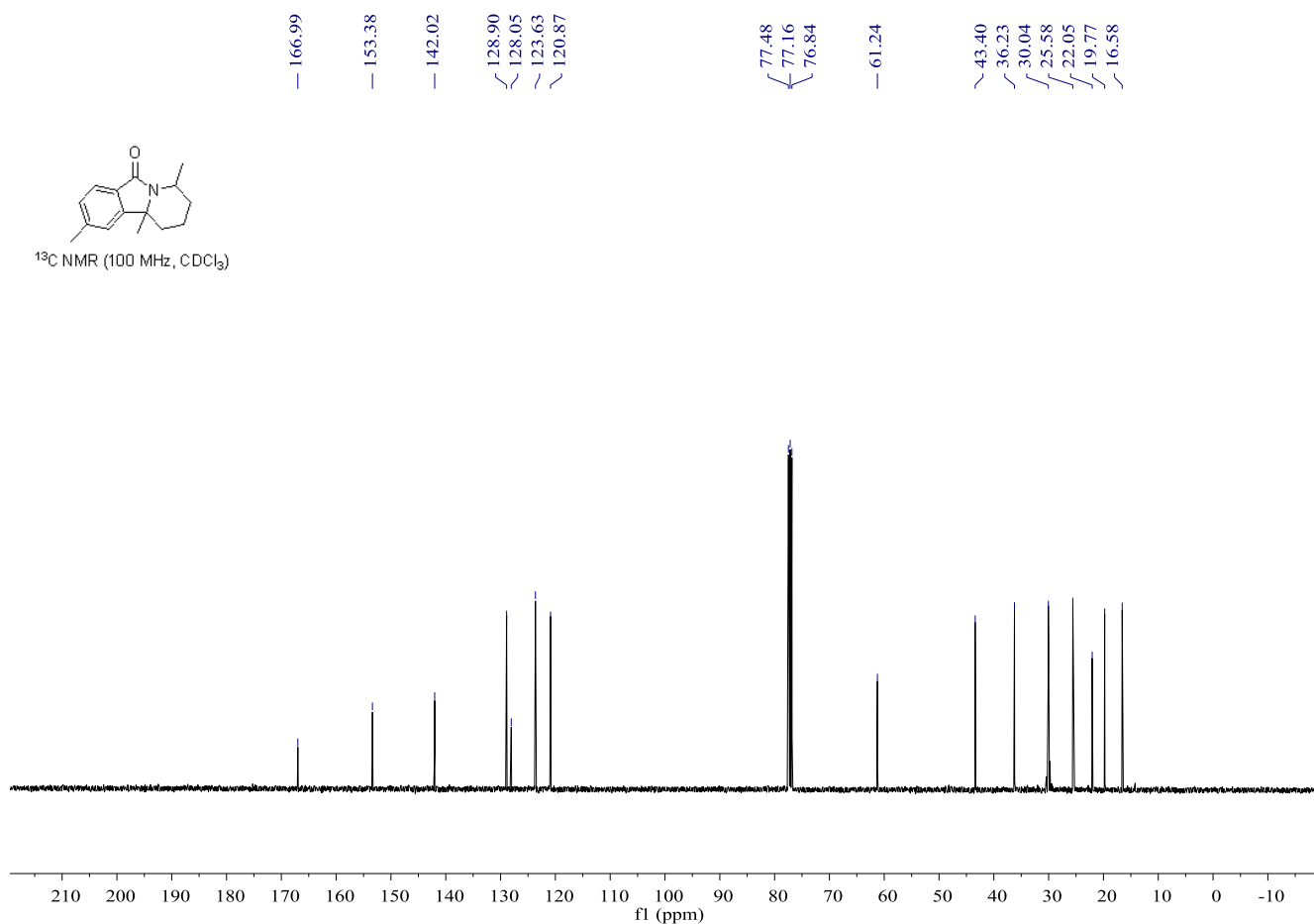
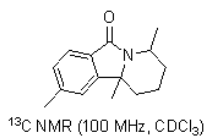


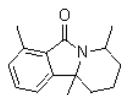










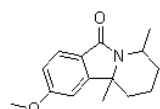
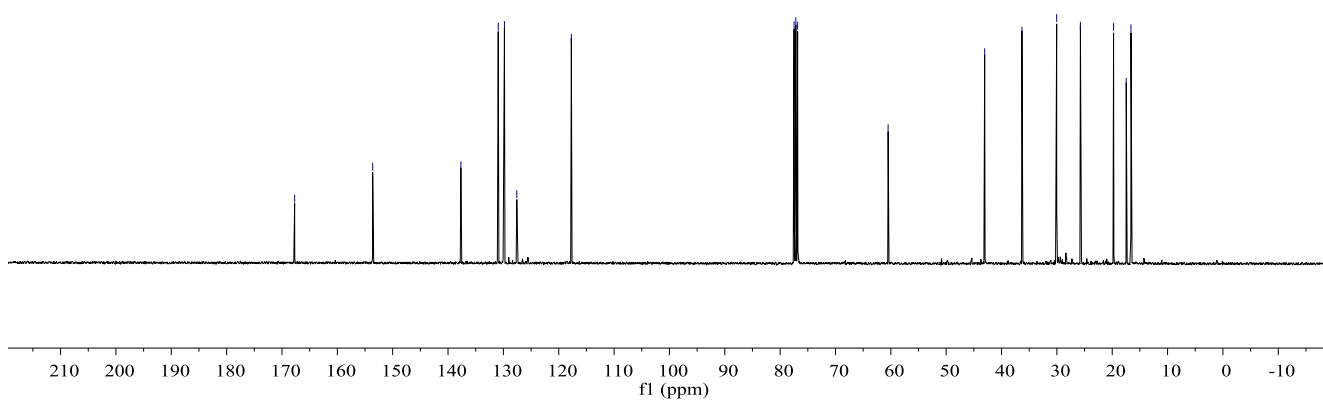


¹³C NMR (100 MHz, CDCl₃)

— 167.72
— 153.61
~ 137.68
/ 130.93
/ 129.81
~ 127.58
— 117.72

{ 77.48
{ 77.16
{ 76.84
— 60.49

~ 43.04
/ 36.32
/ 30.04
/ 25.75
/ 19.76
/ 17.47
/ 16.61

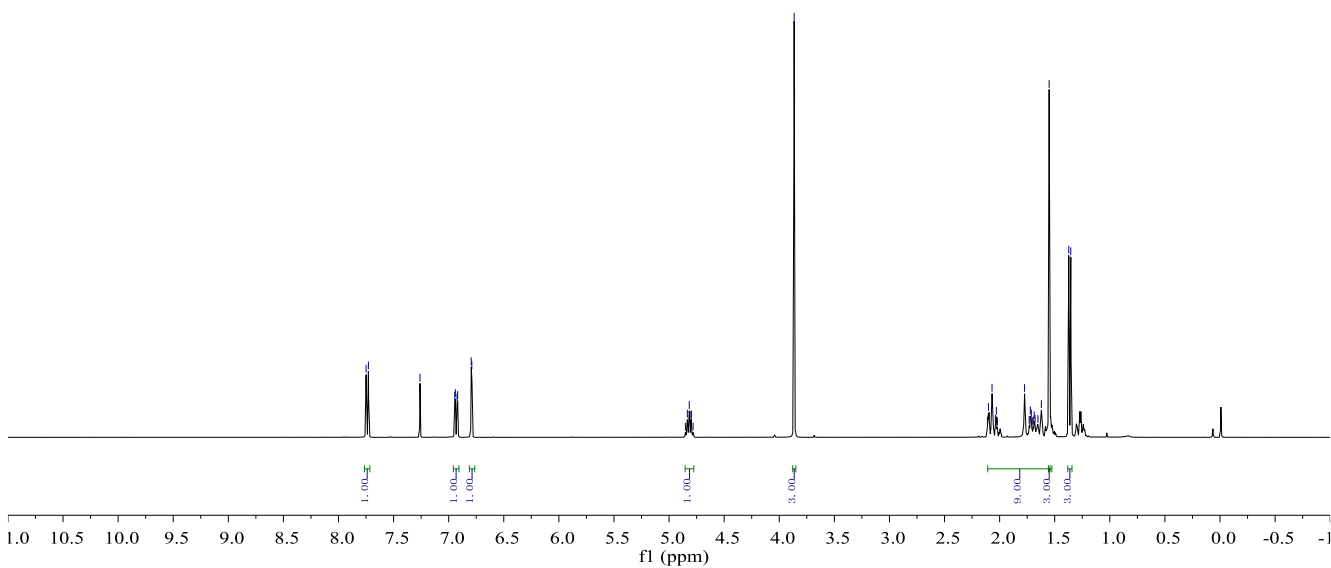


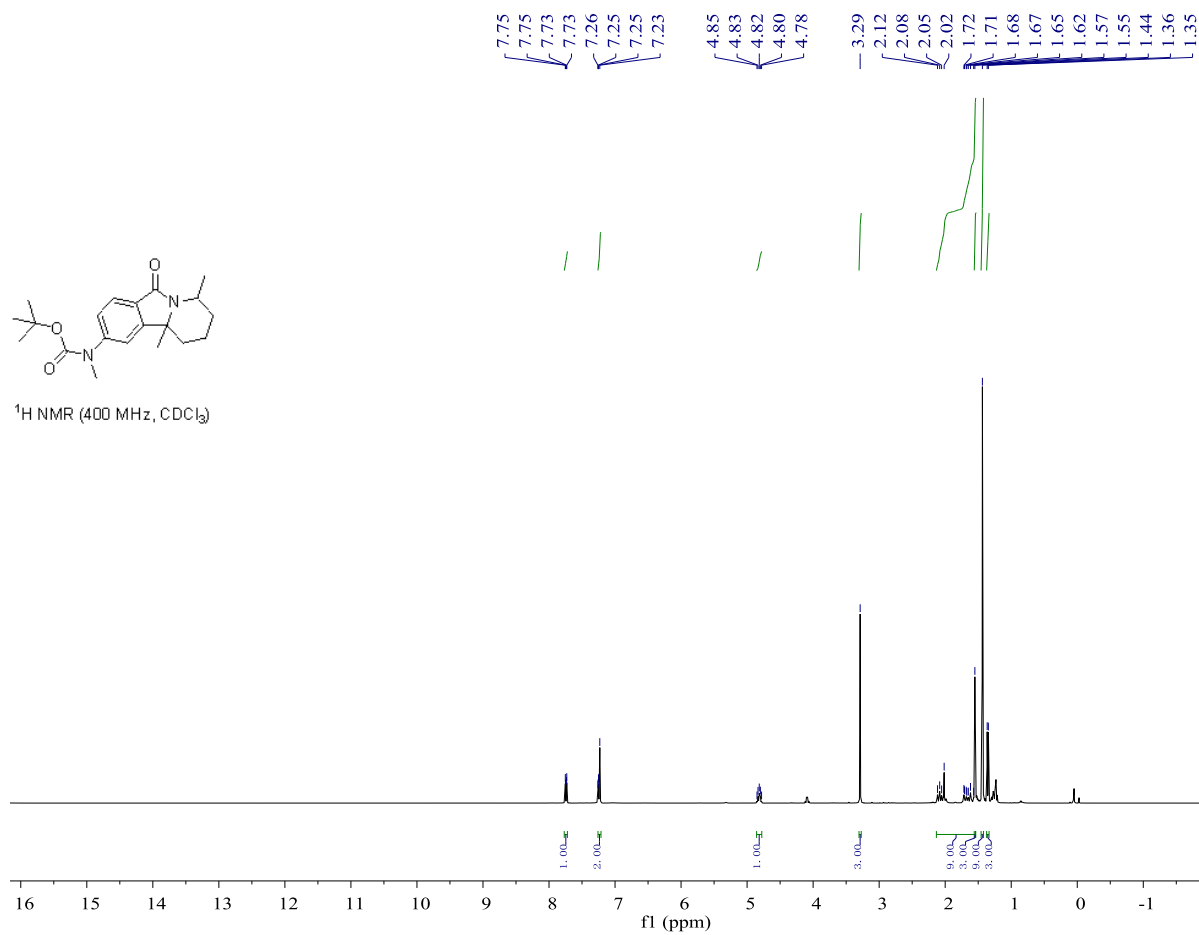
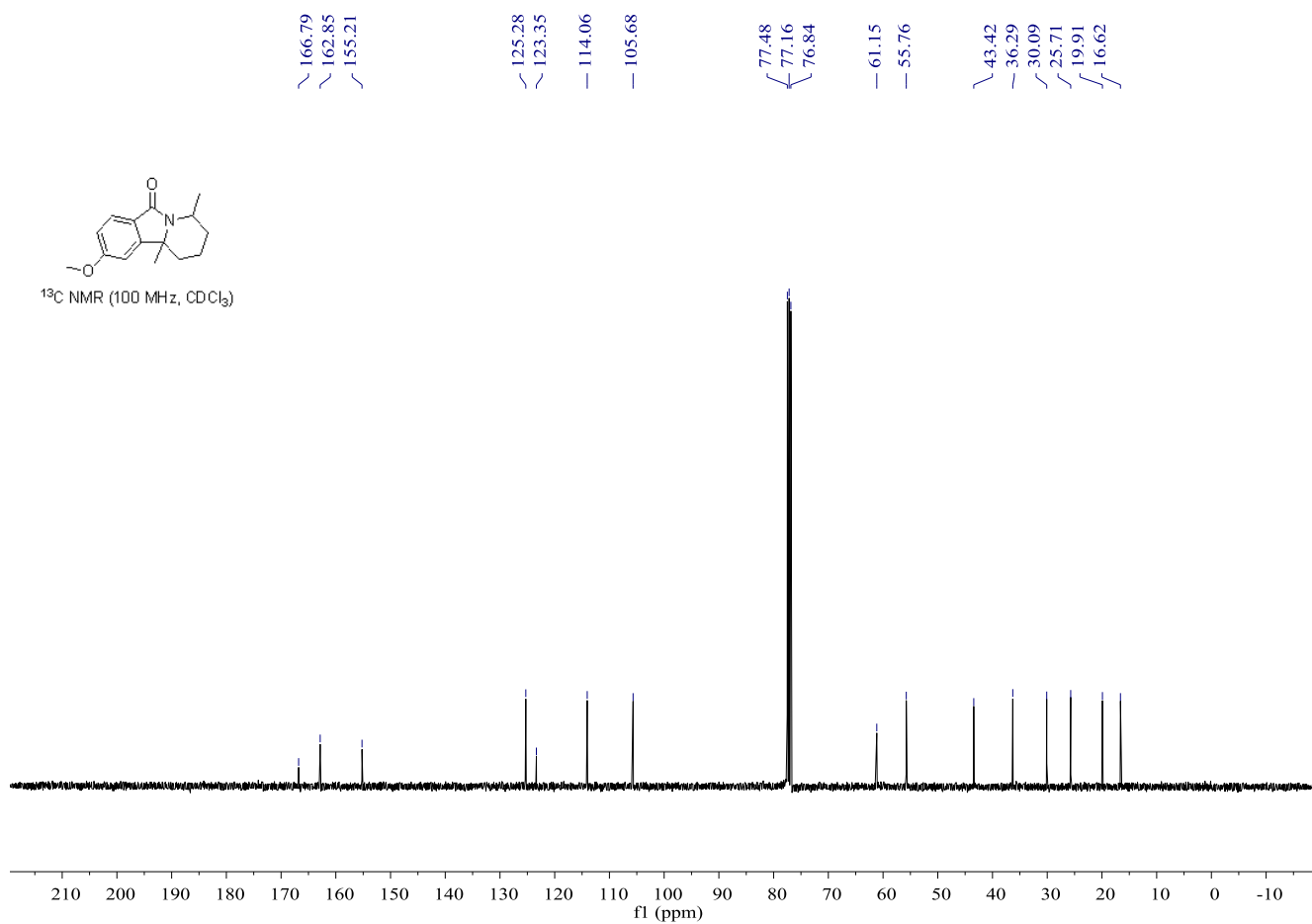
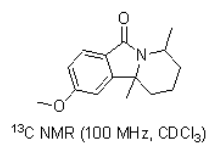
¹H NMR (400 MHz, CDCl₃)

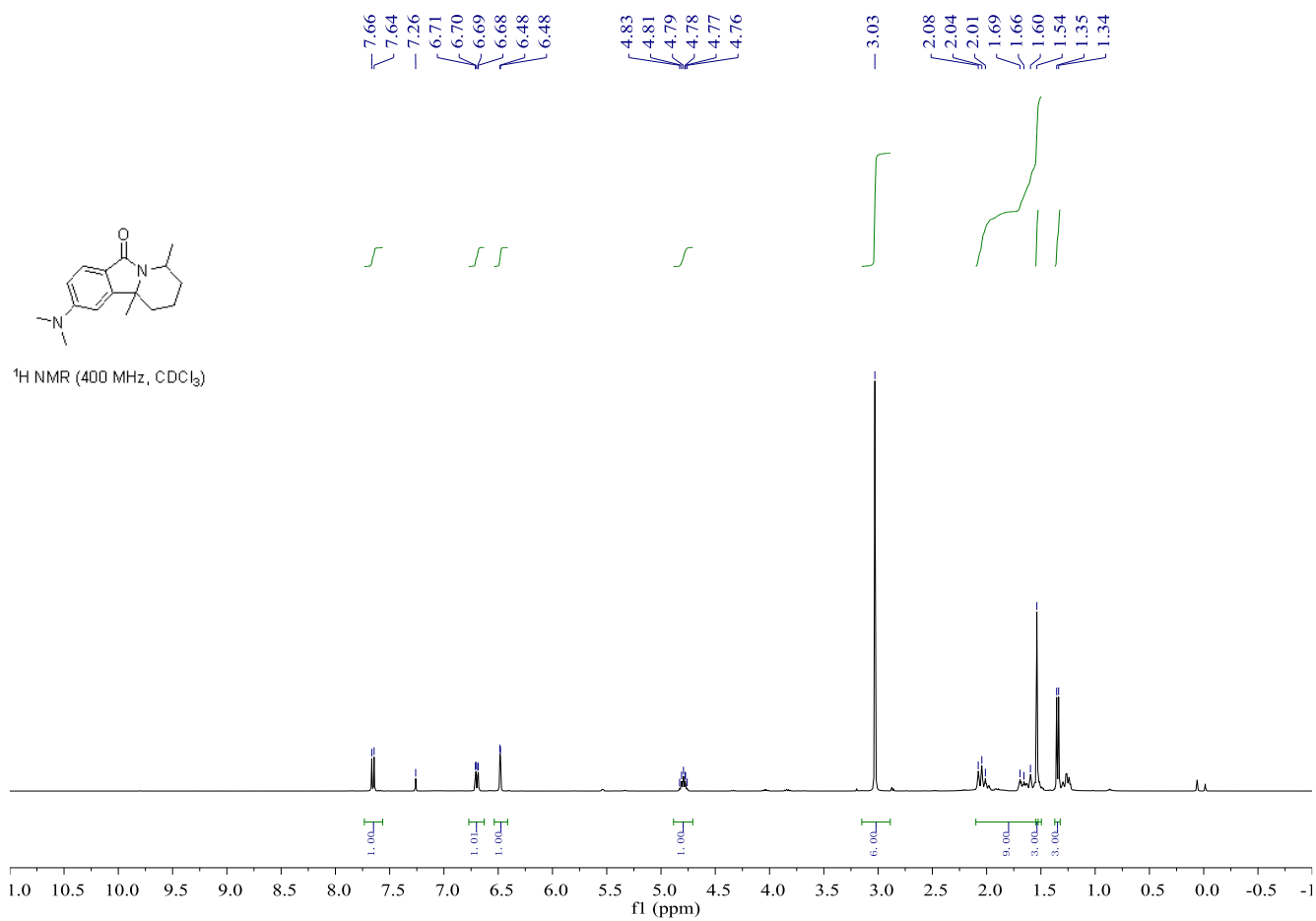
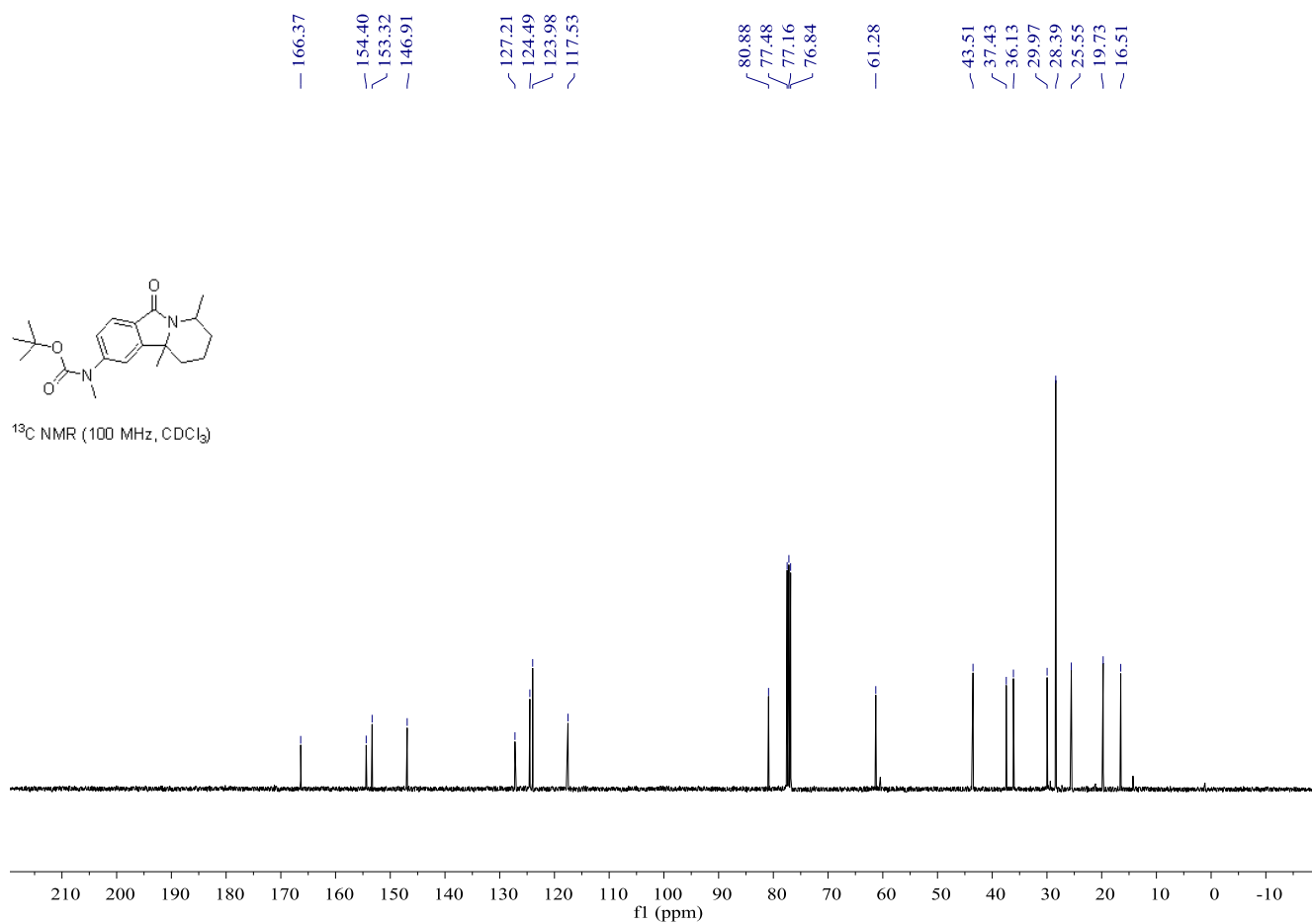
{ 7.75
{ 7.73
/ 7.26
/ 6.95
/ 6.94
/ 6.92
/ 6.92
/ 6.80
/ 6.79

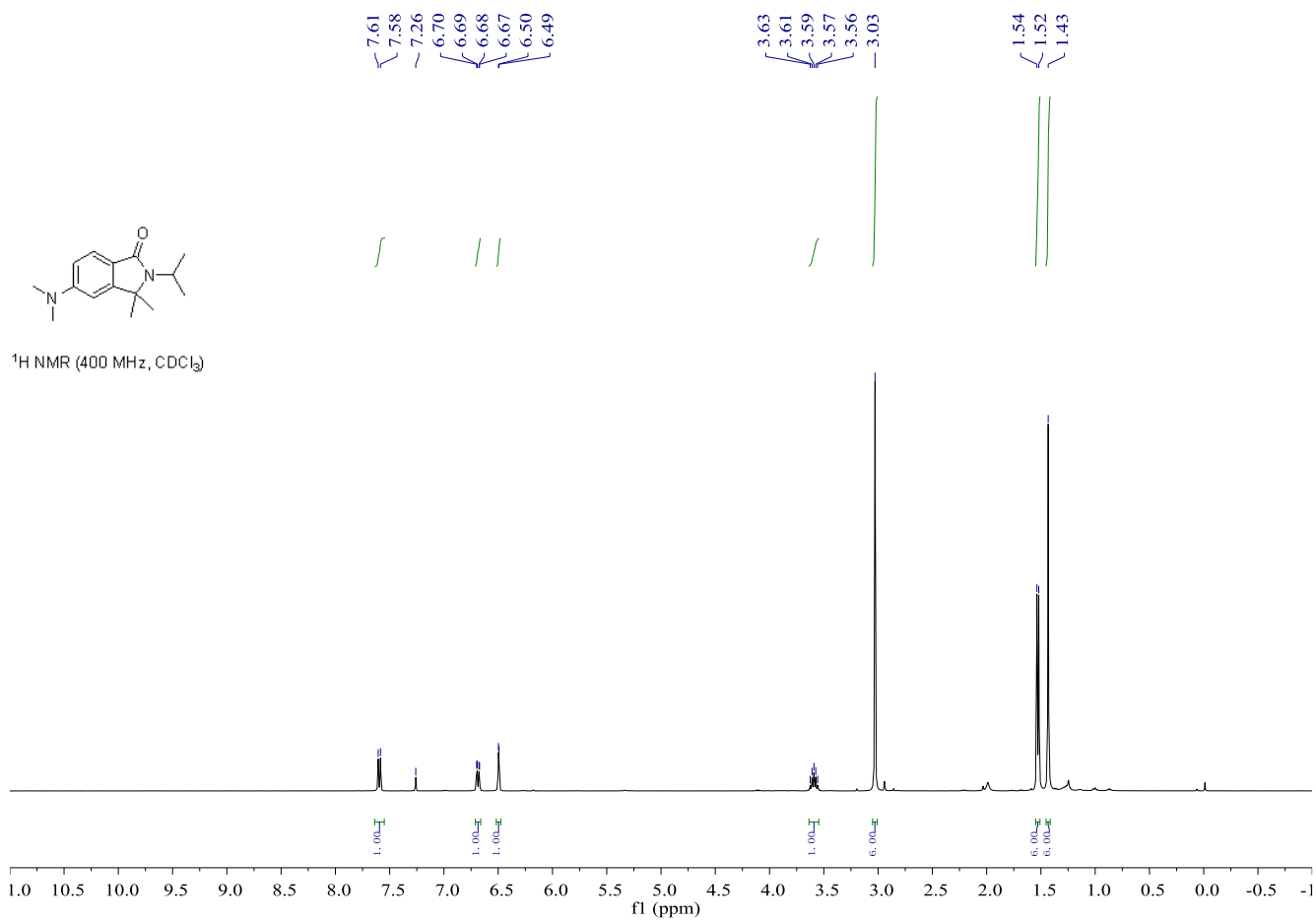
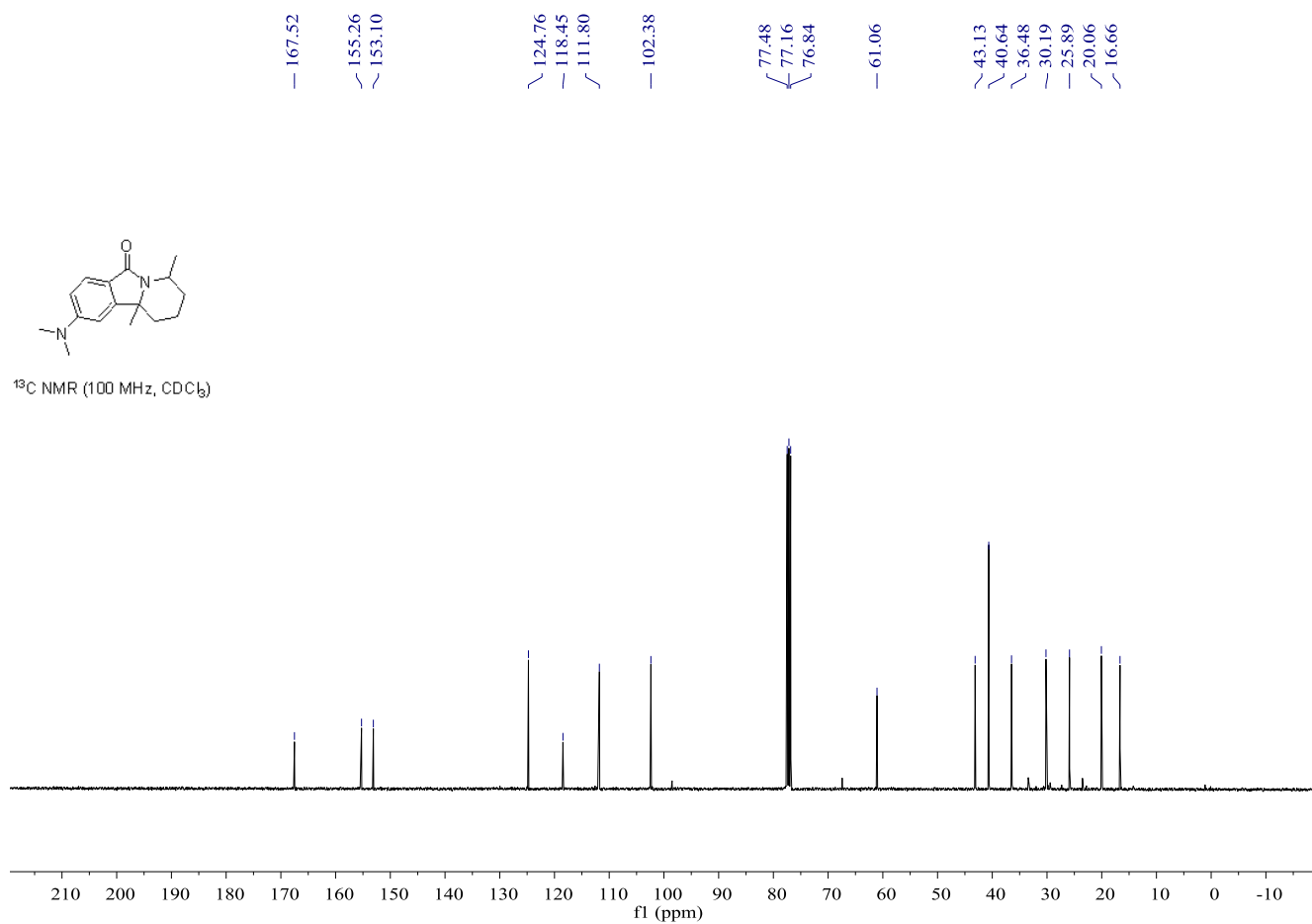
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/ 4.83
/ 4.82
/ 4.80
/ 4.80
/ 4.78

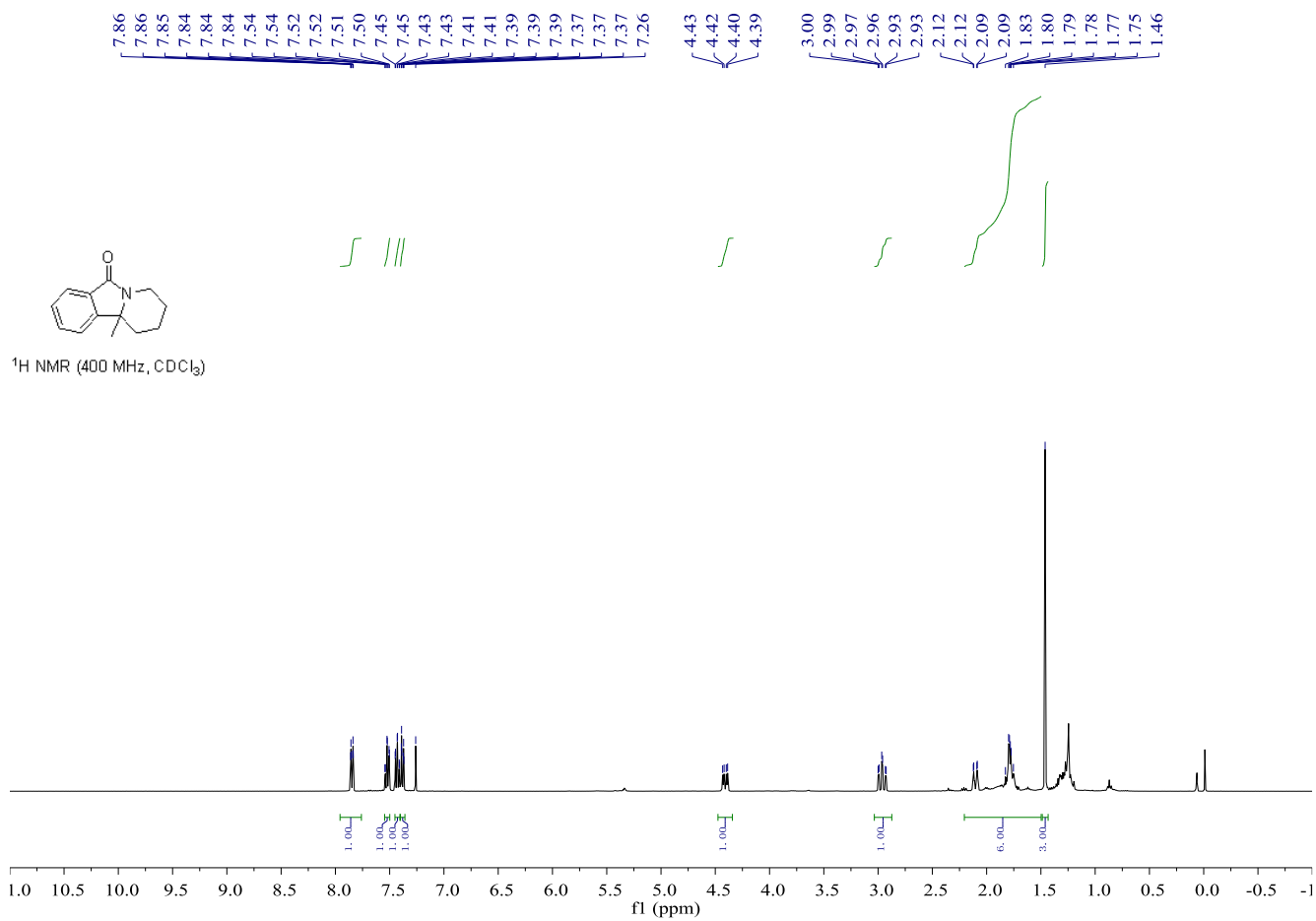
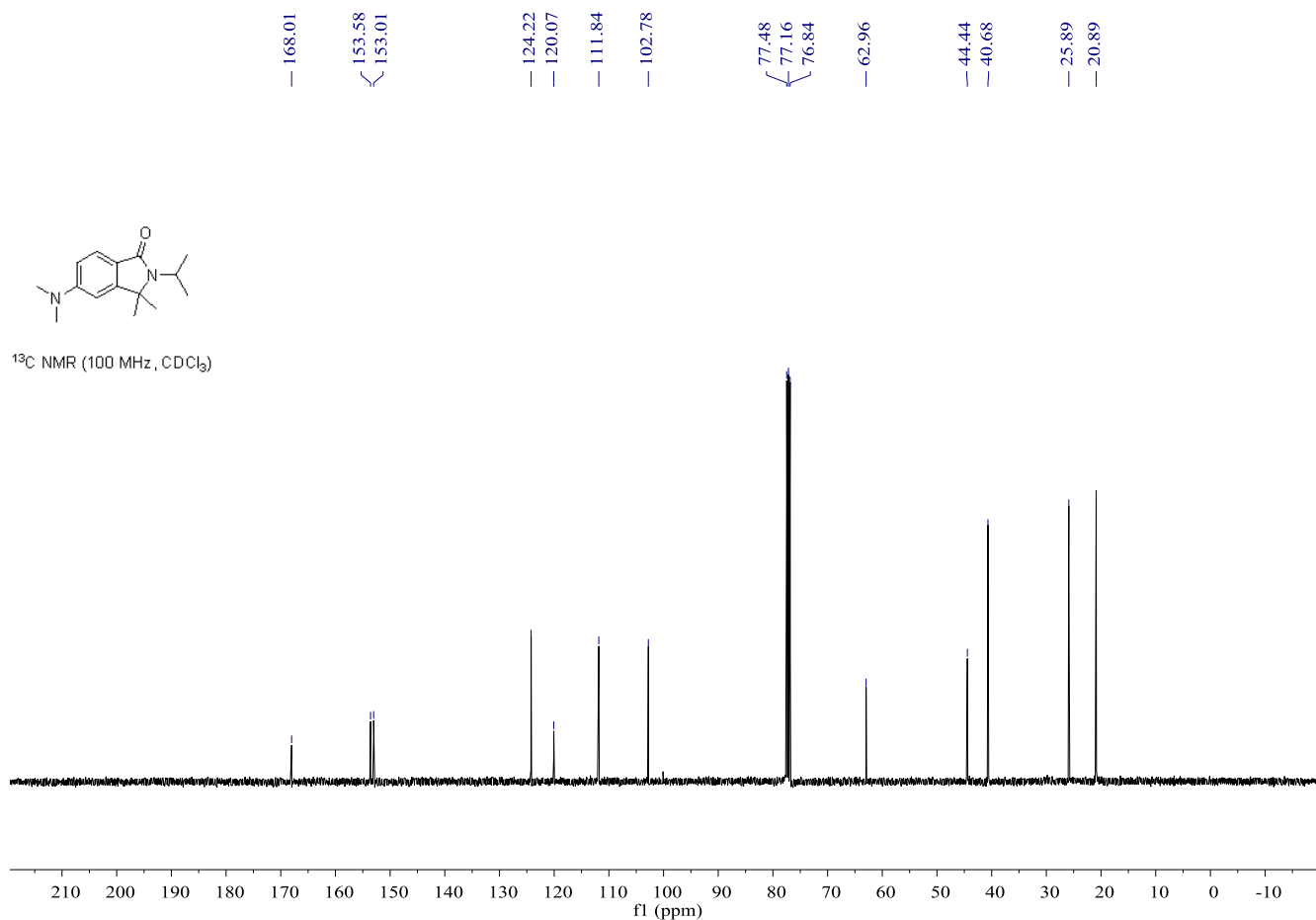
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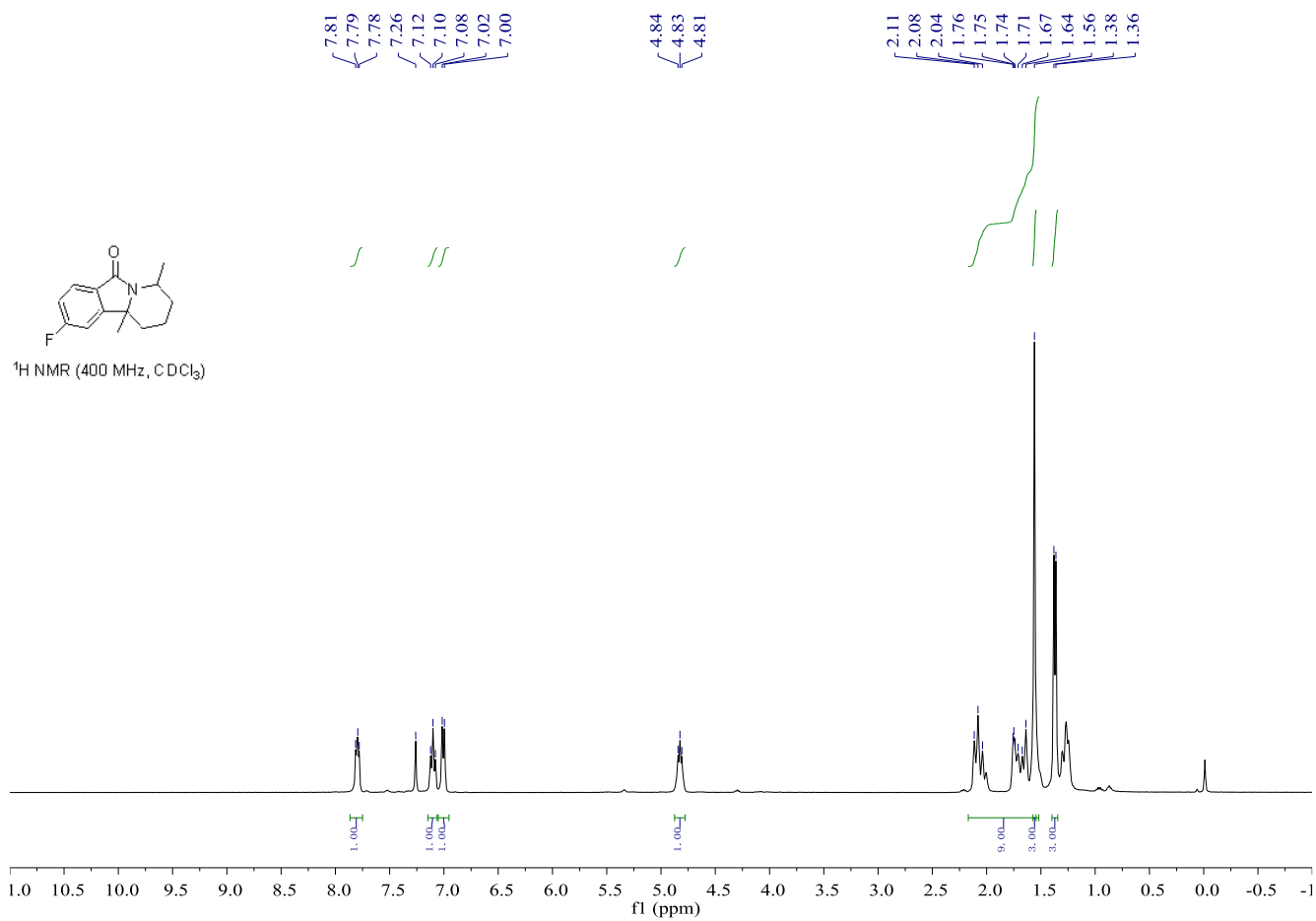
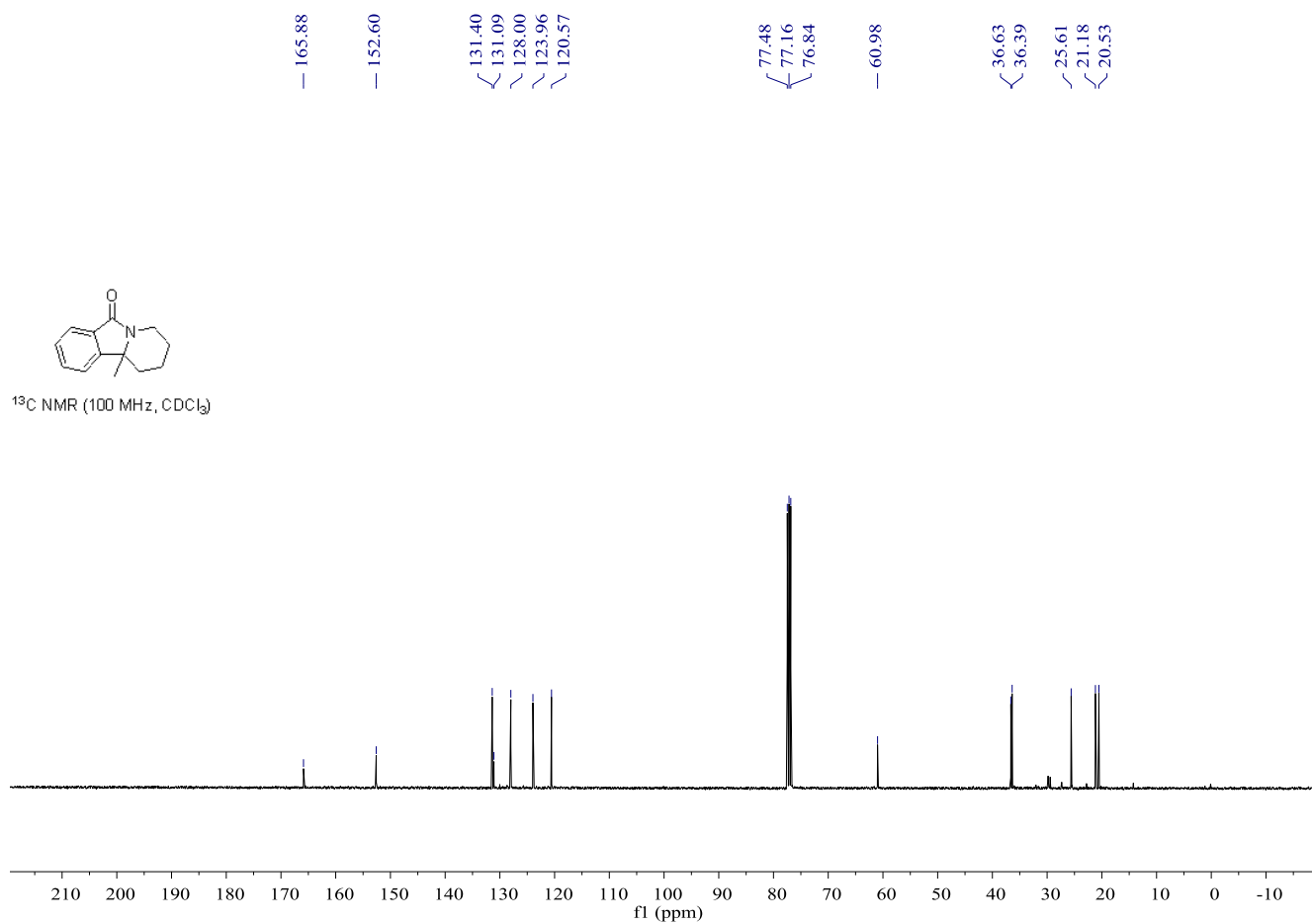


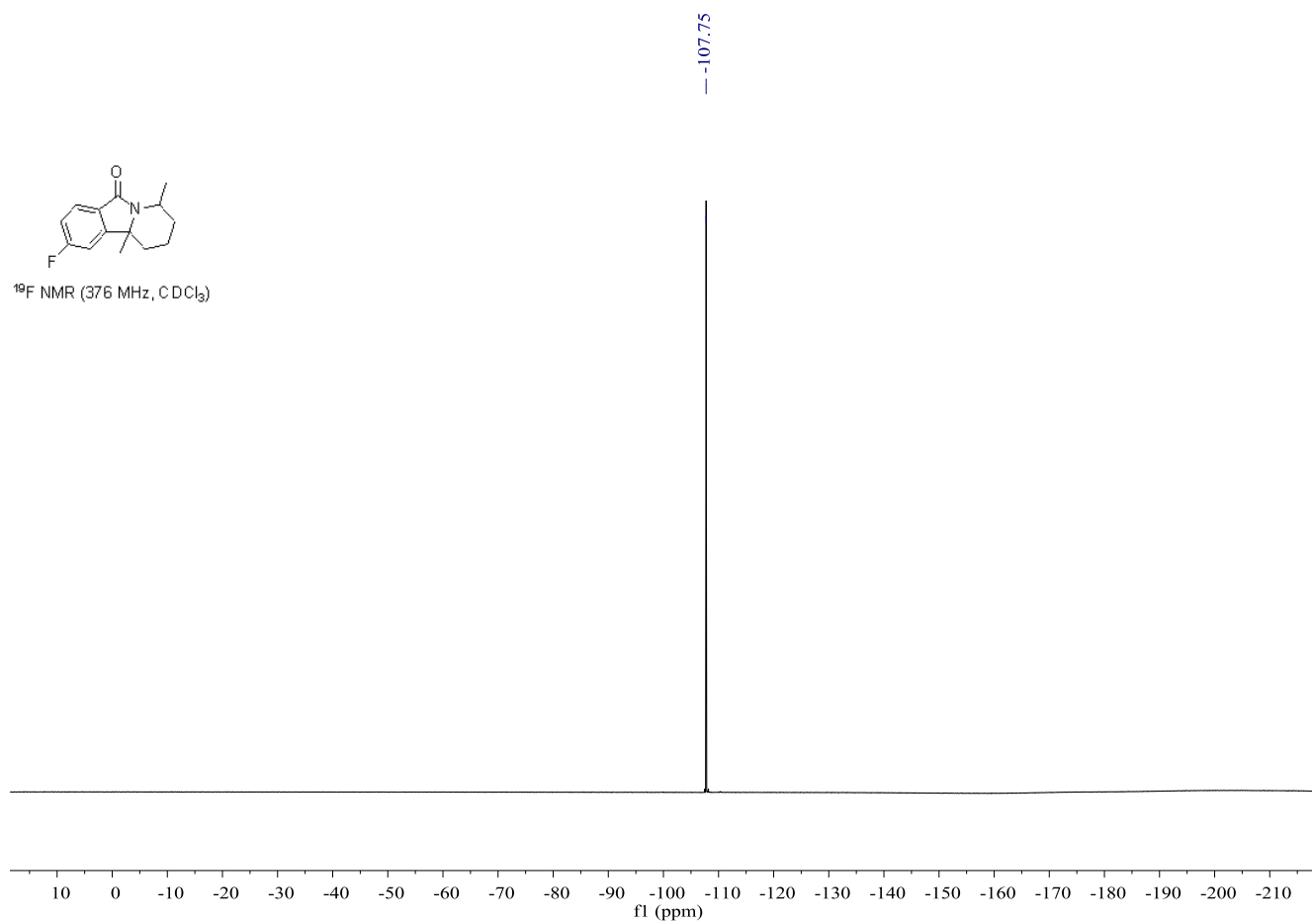
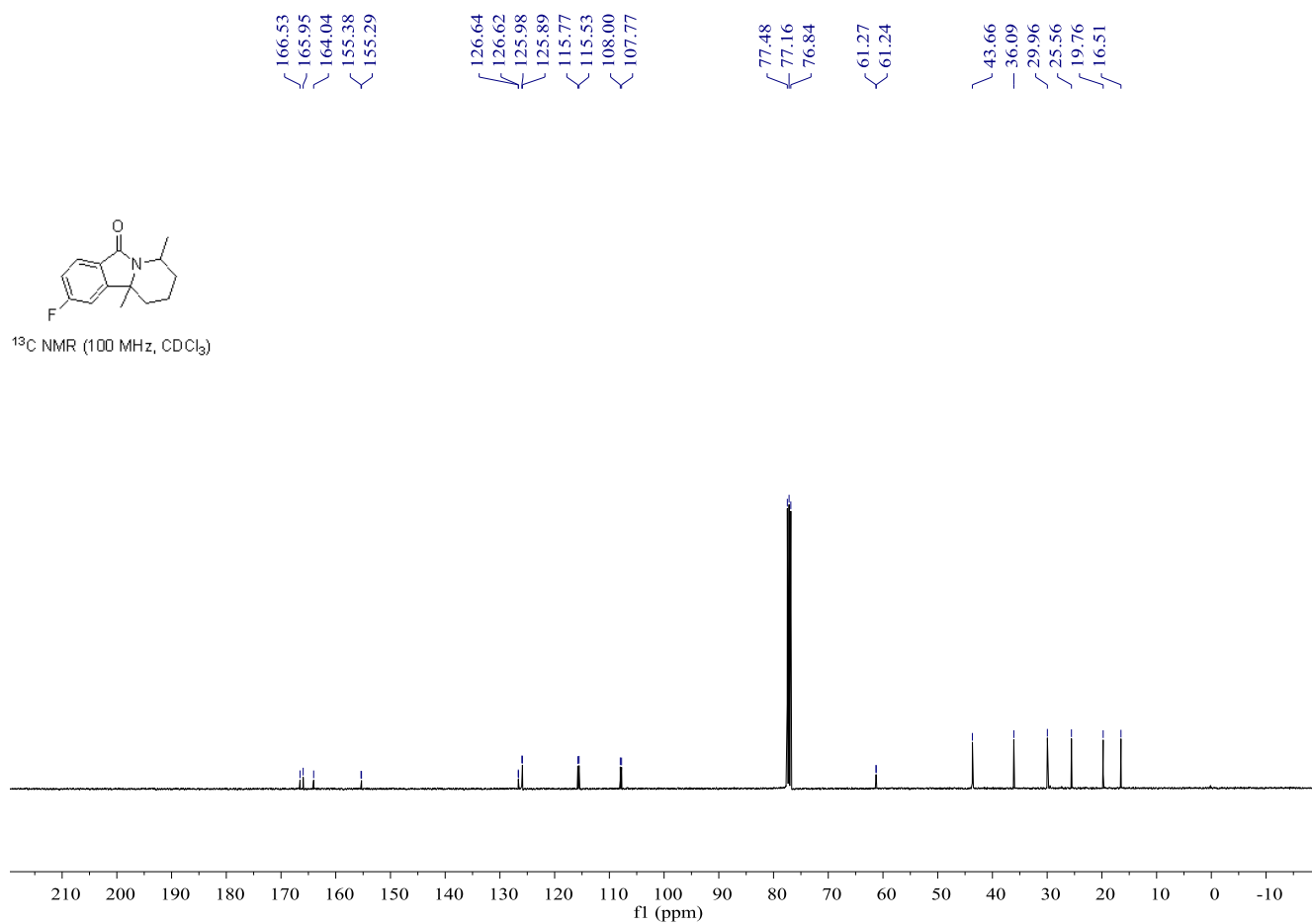


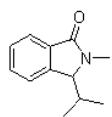




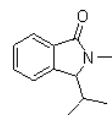
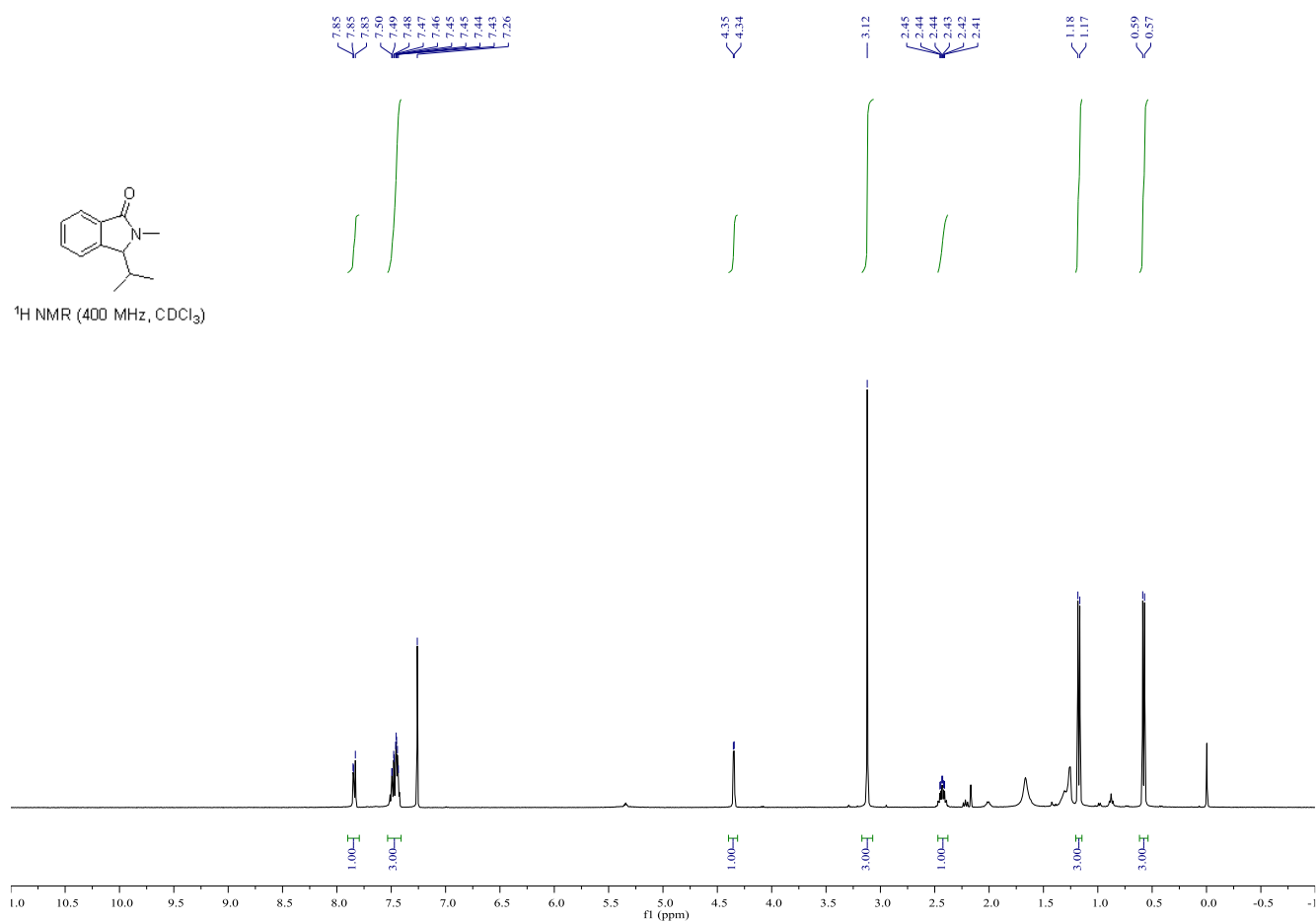




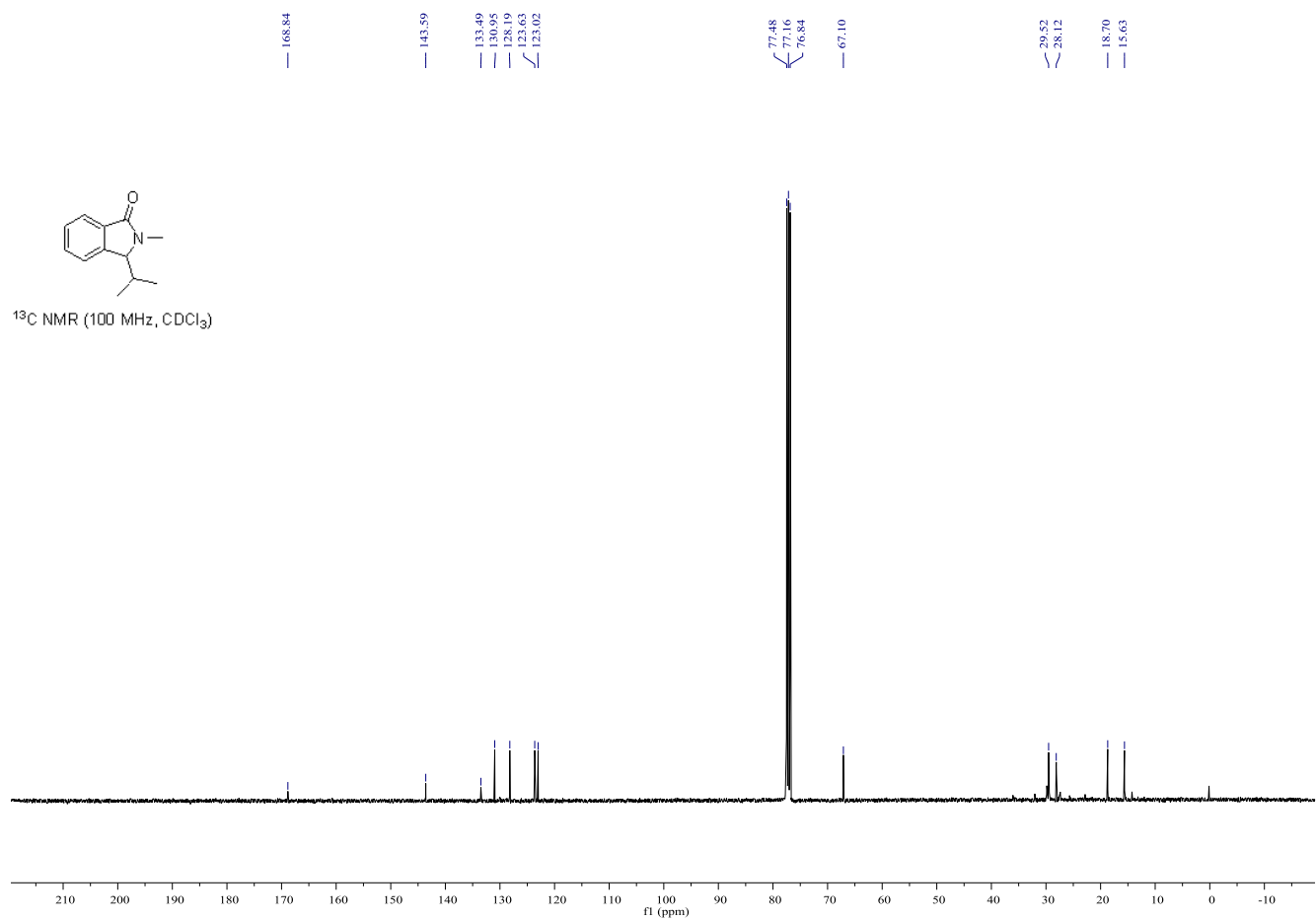


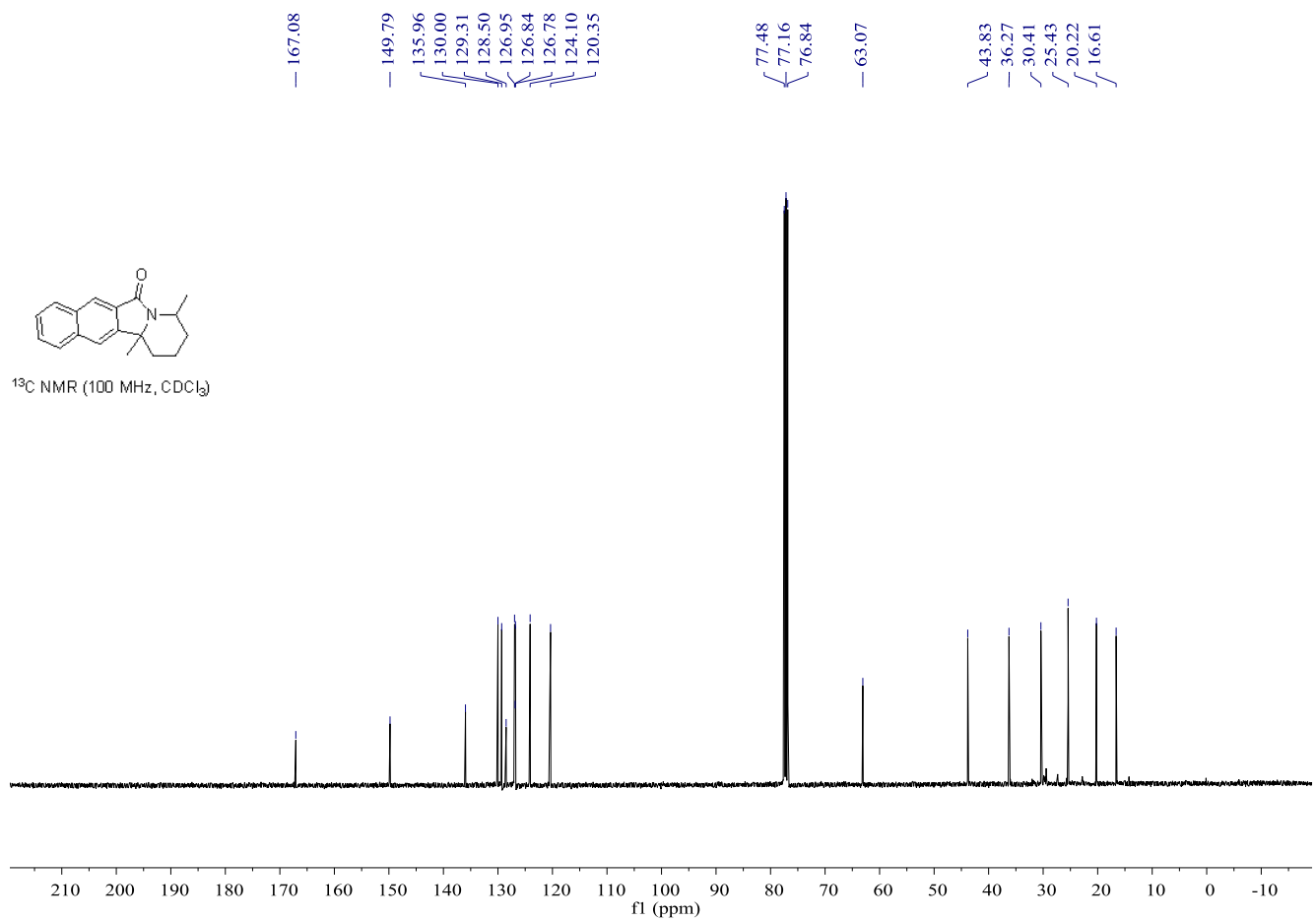
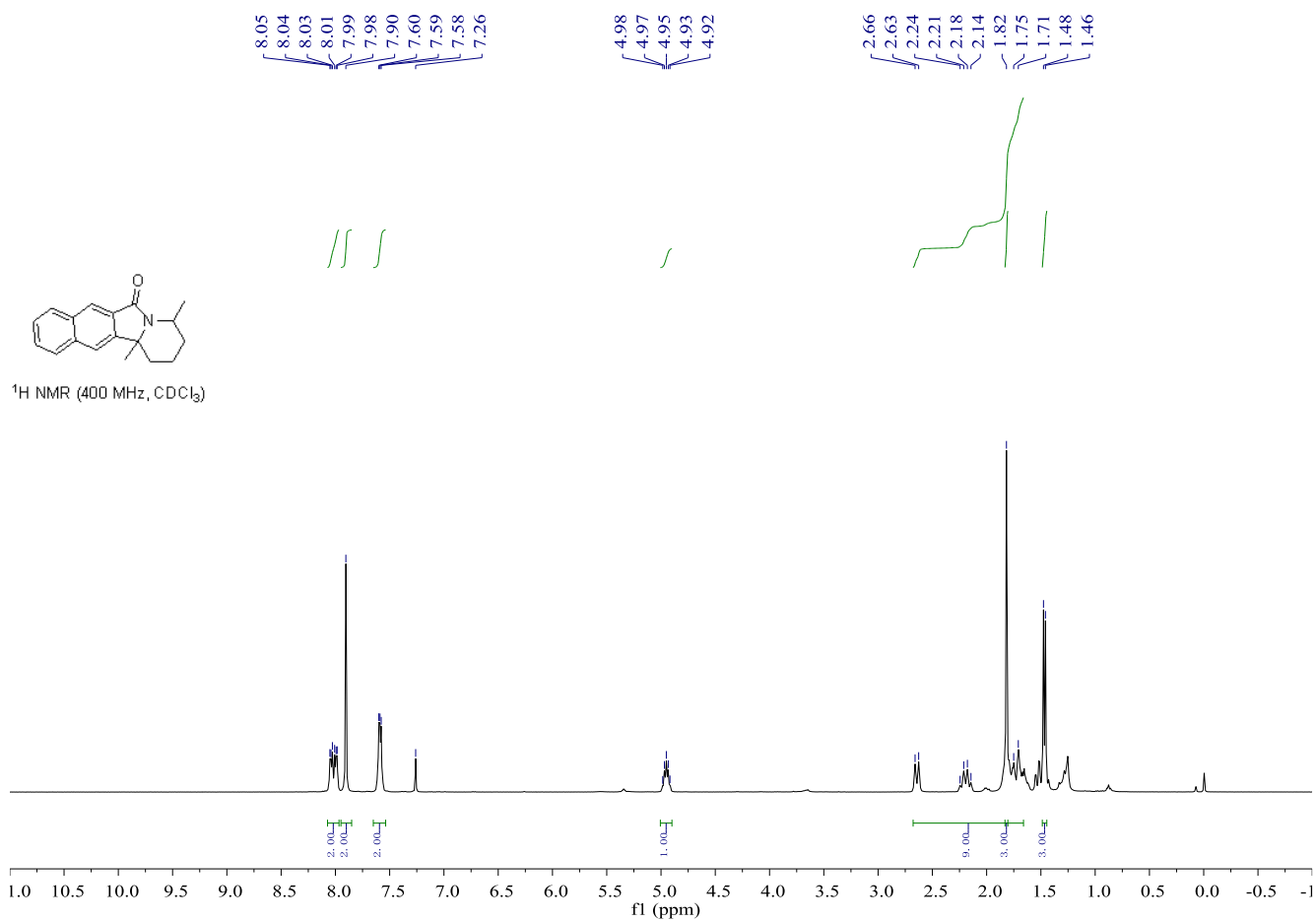


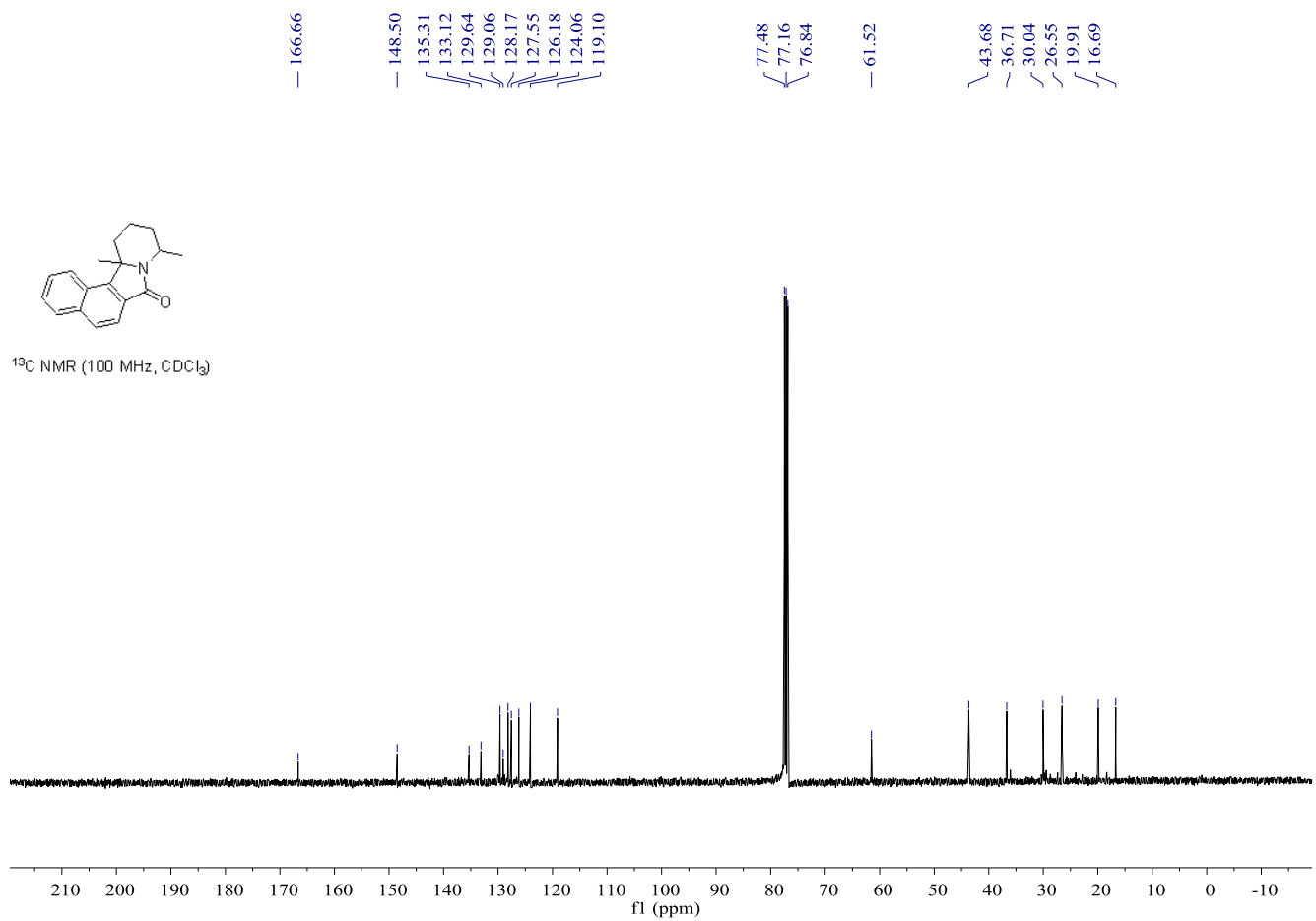
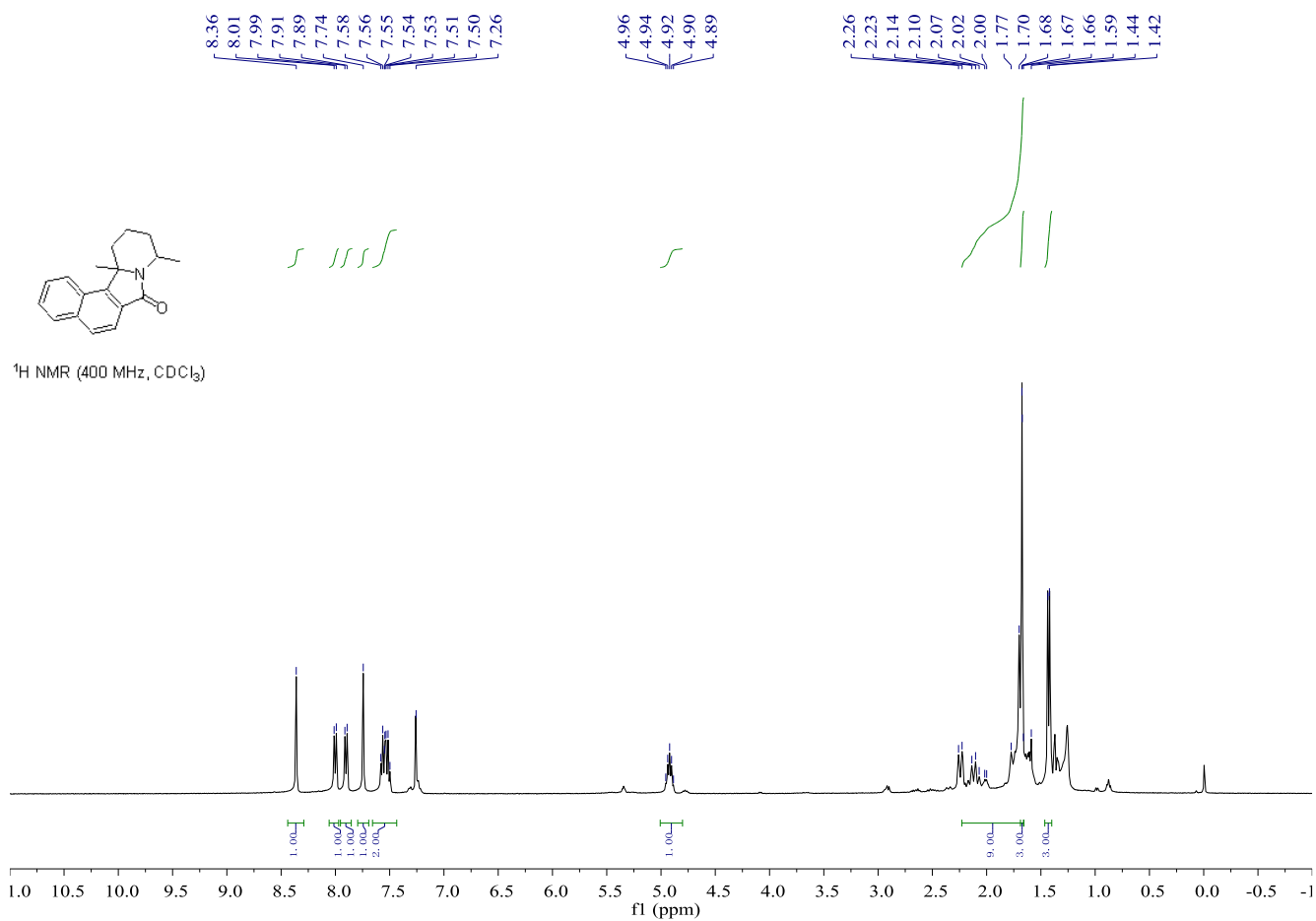
^1H NMR (400 MHz, CDCl_3)

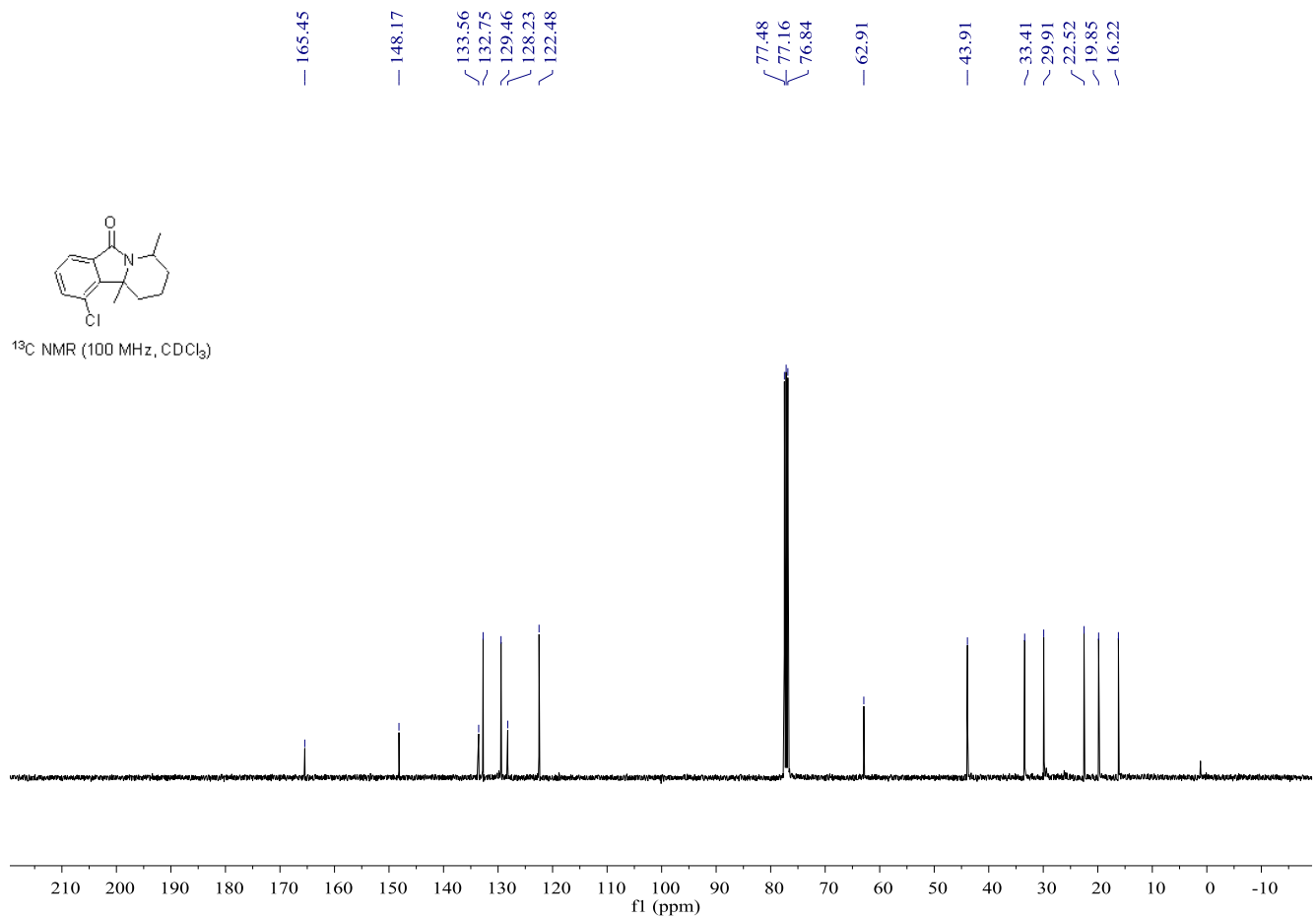
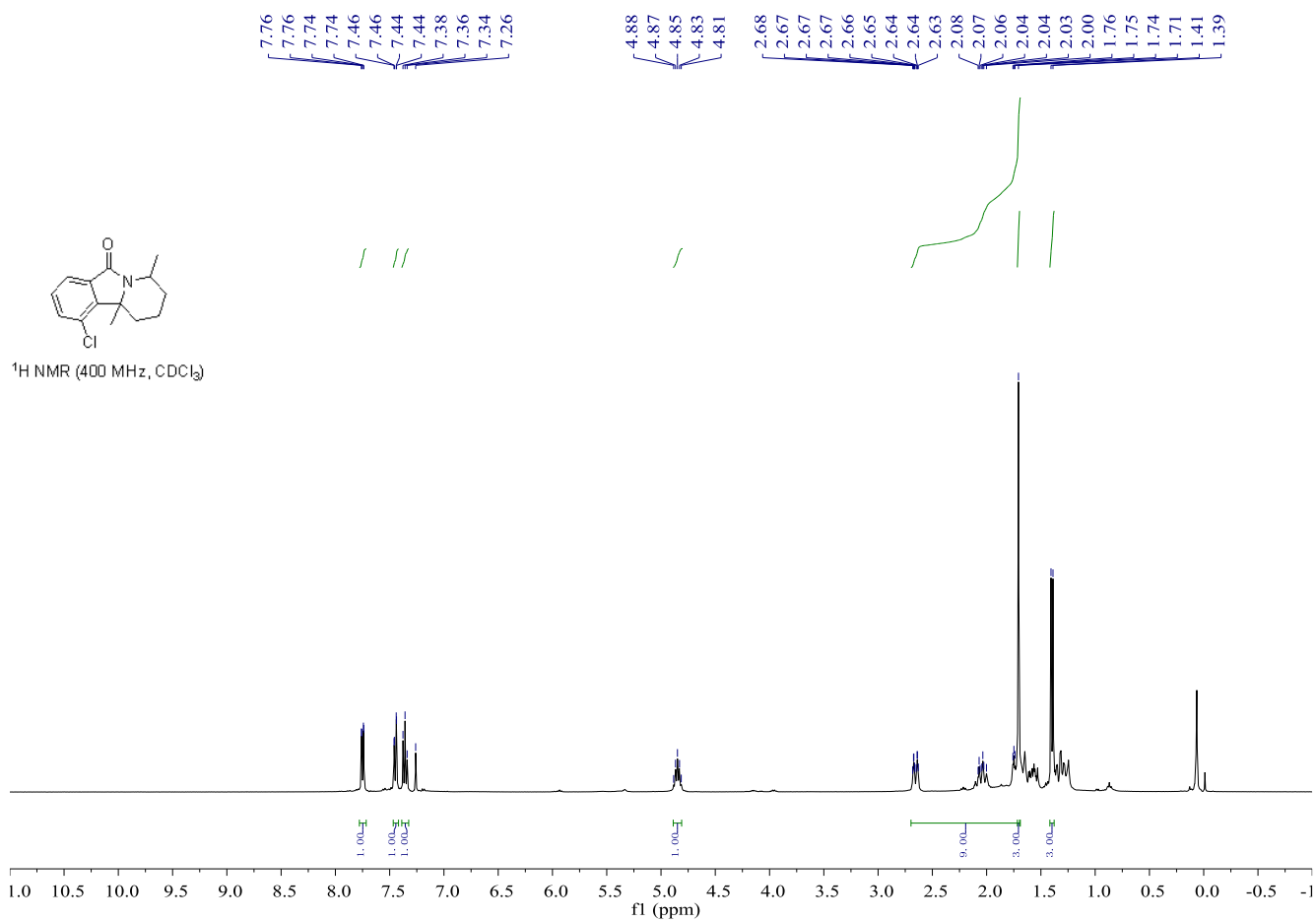


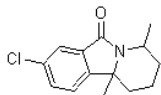
^{13}C NMR (100 MHz, CDCl_3)



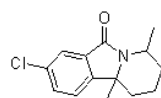
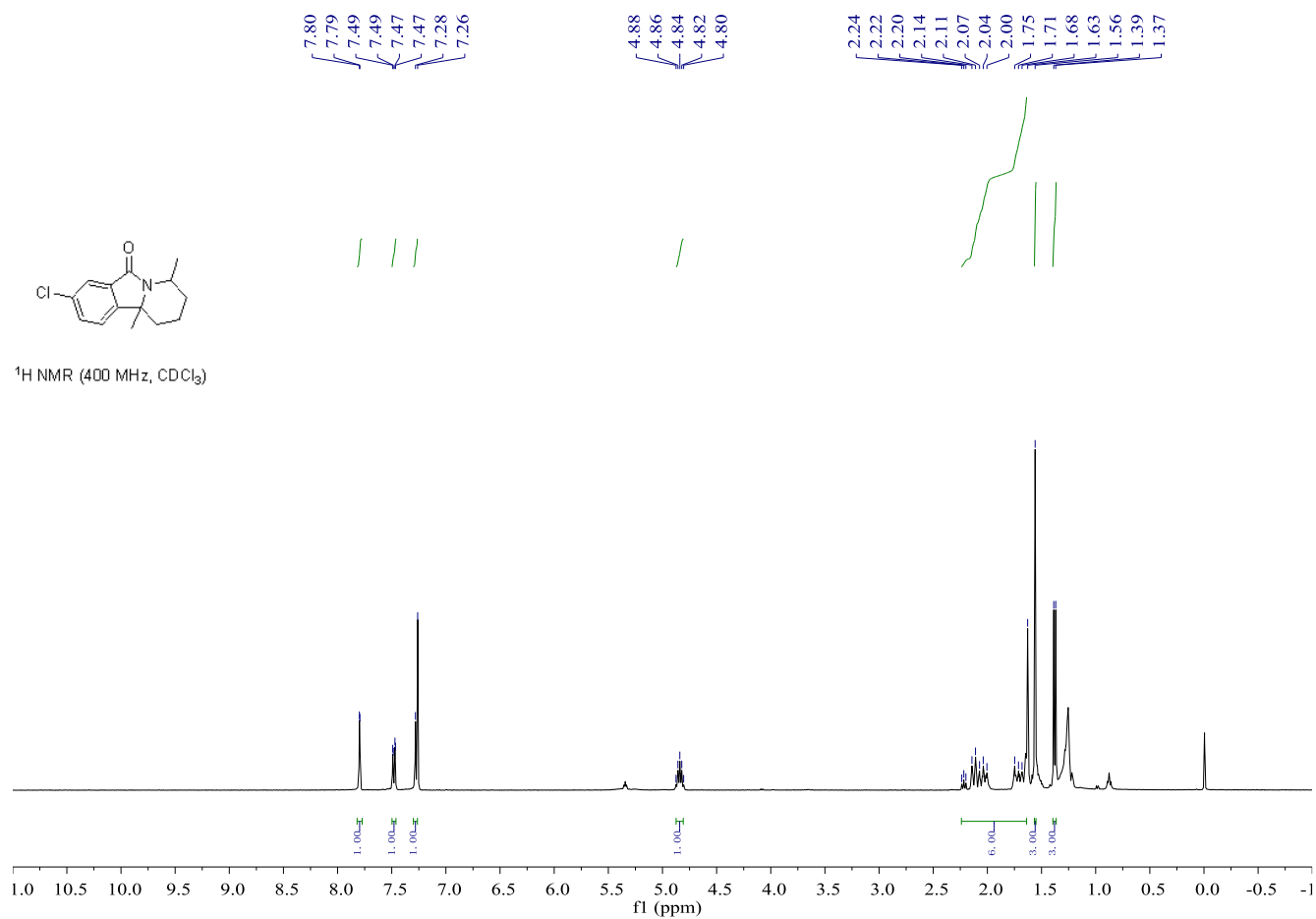




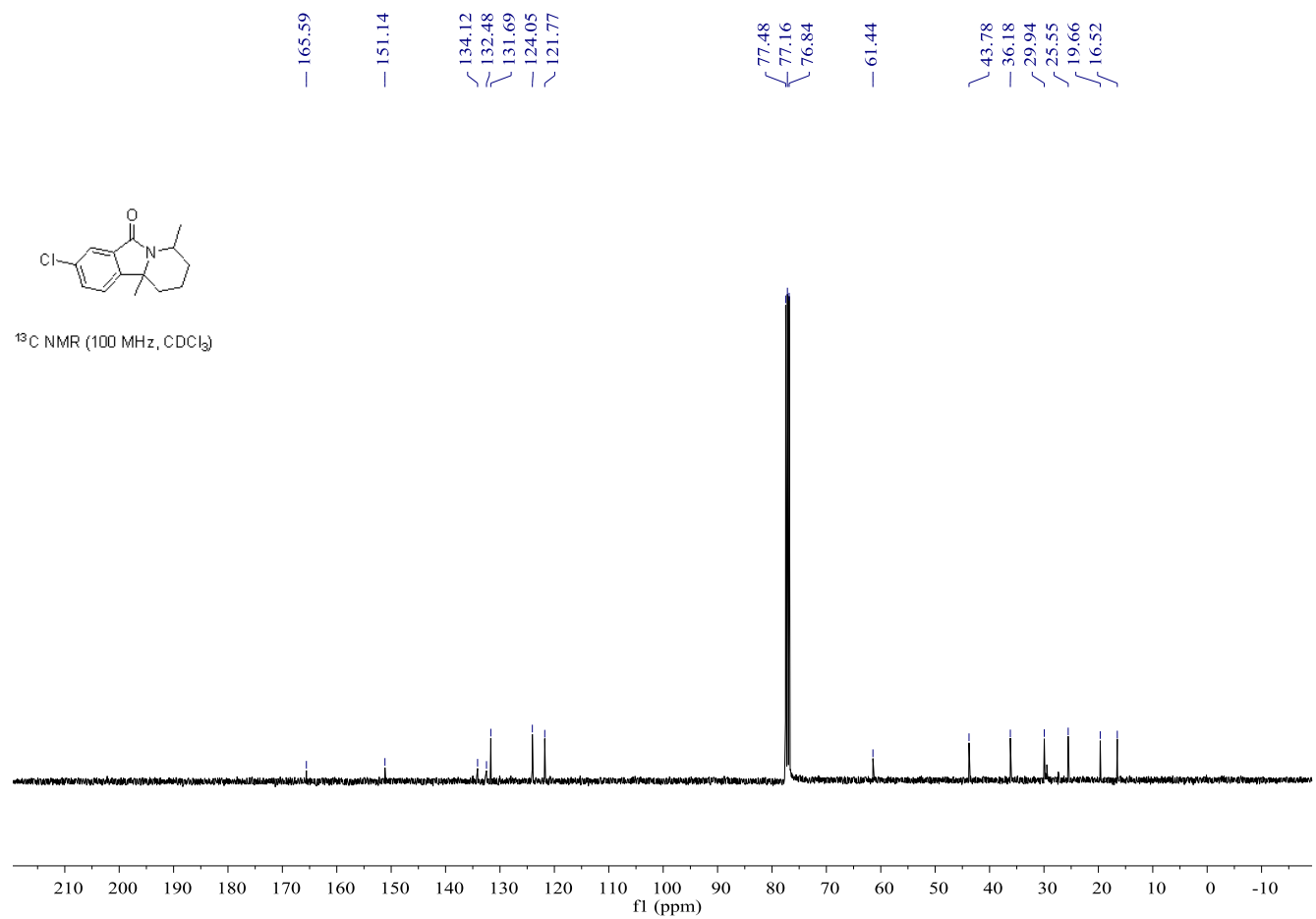


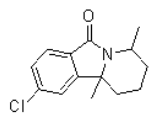


^1H NMR (400 MHz, CDCl_3)

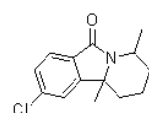
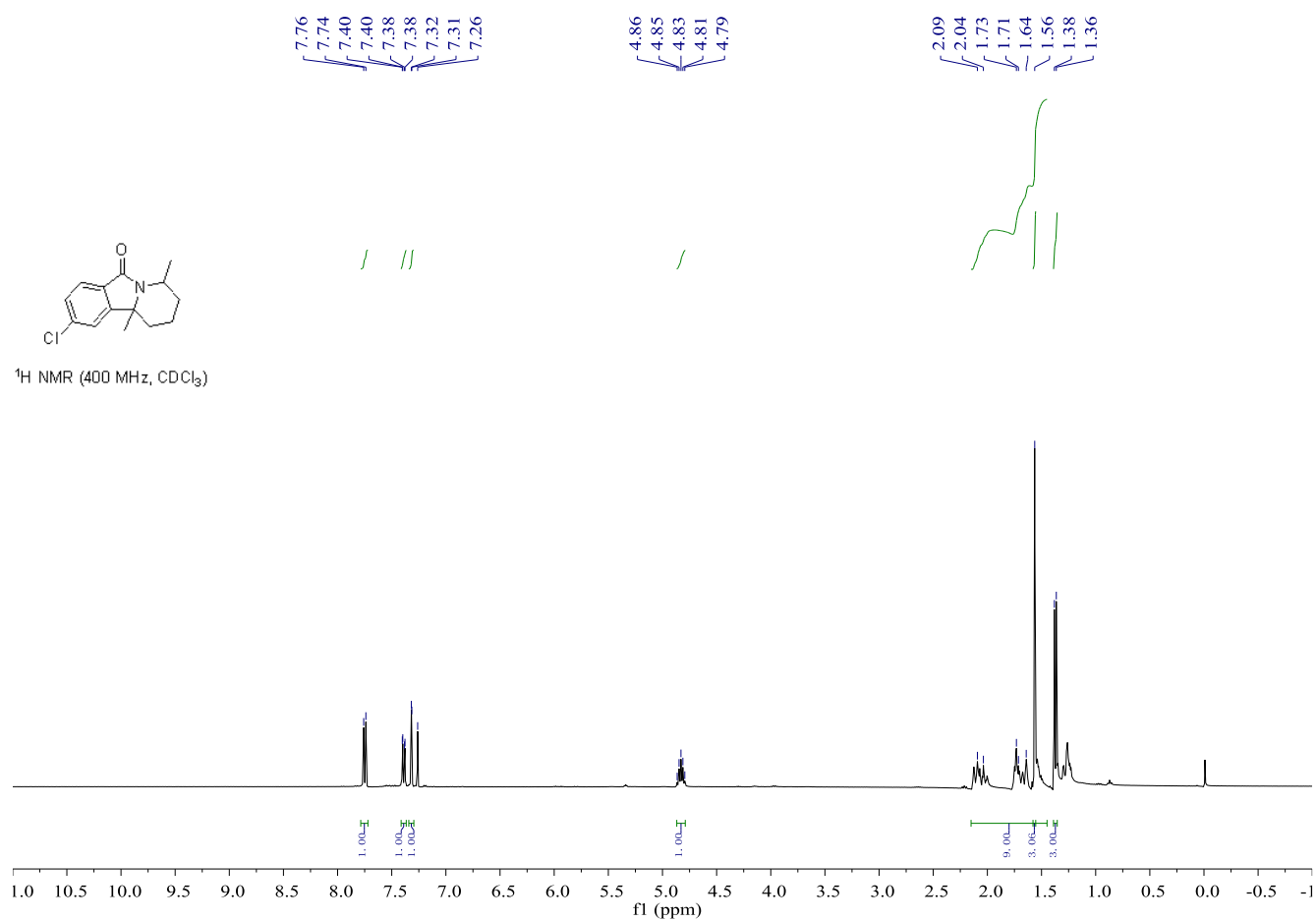


^{13}C NMR (100 MHz, CDCl_3)

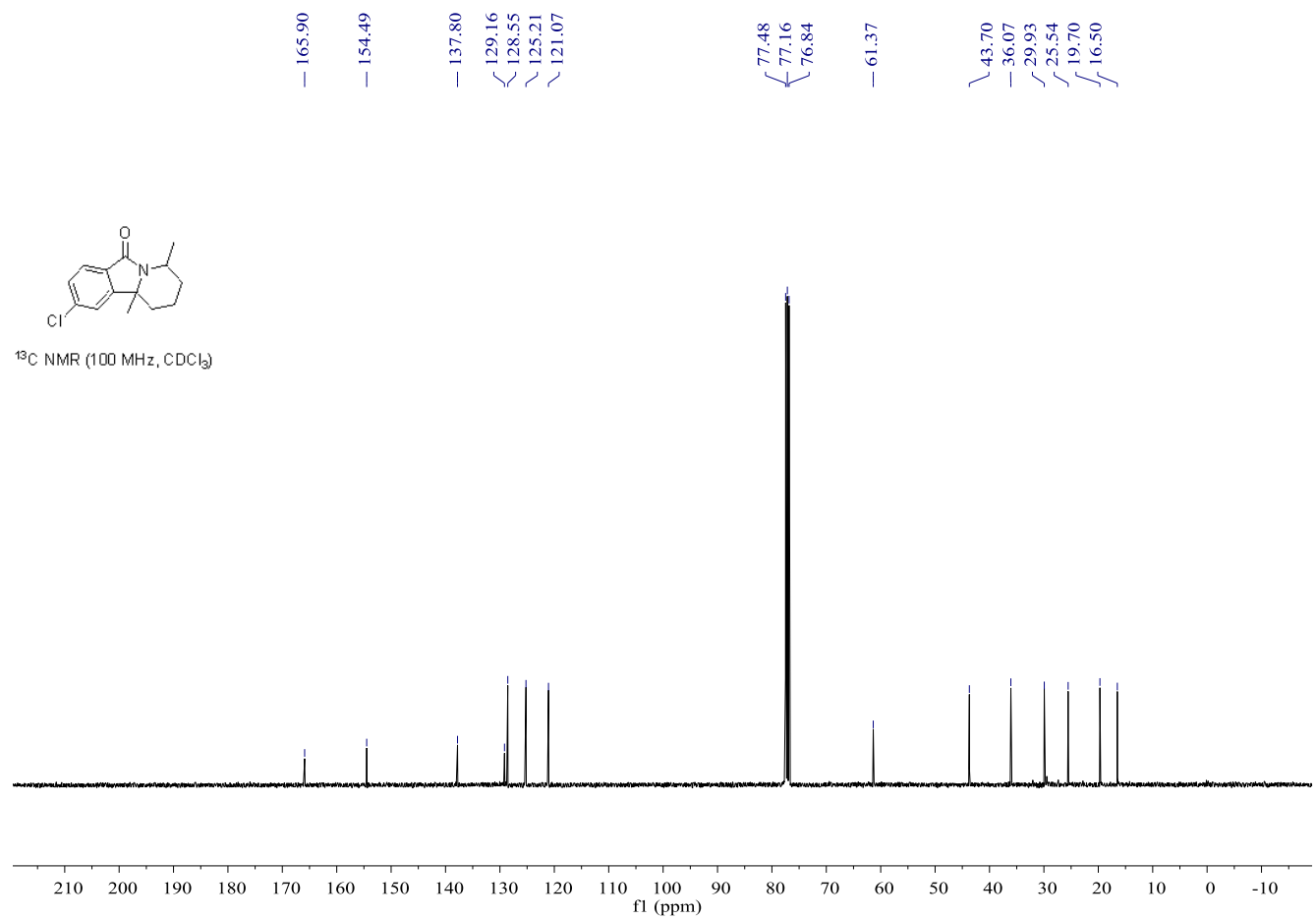


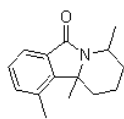


^1H NMR (400 MHz, CDCl_3)

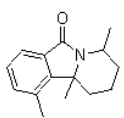
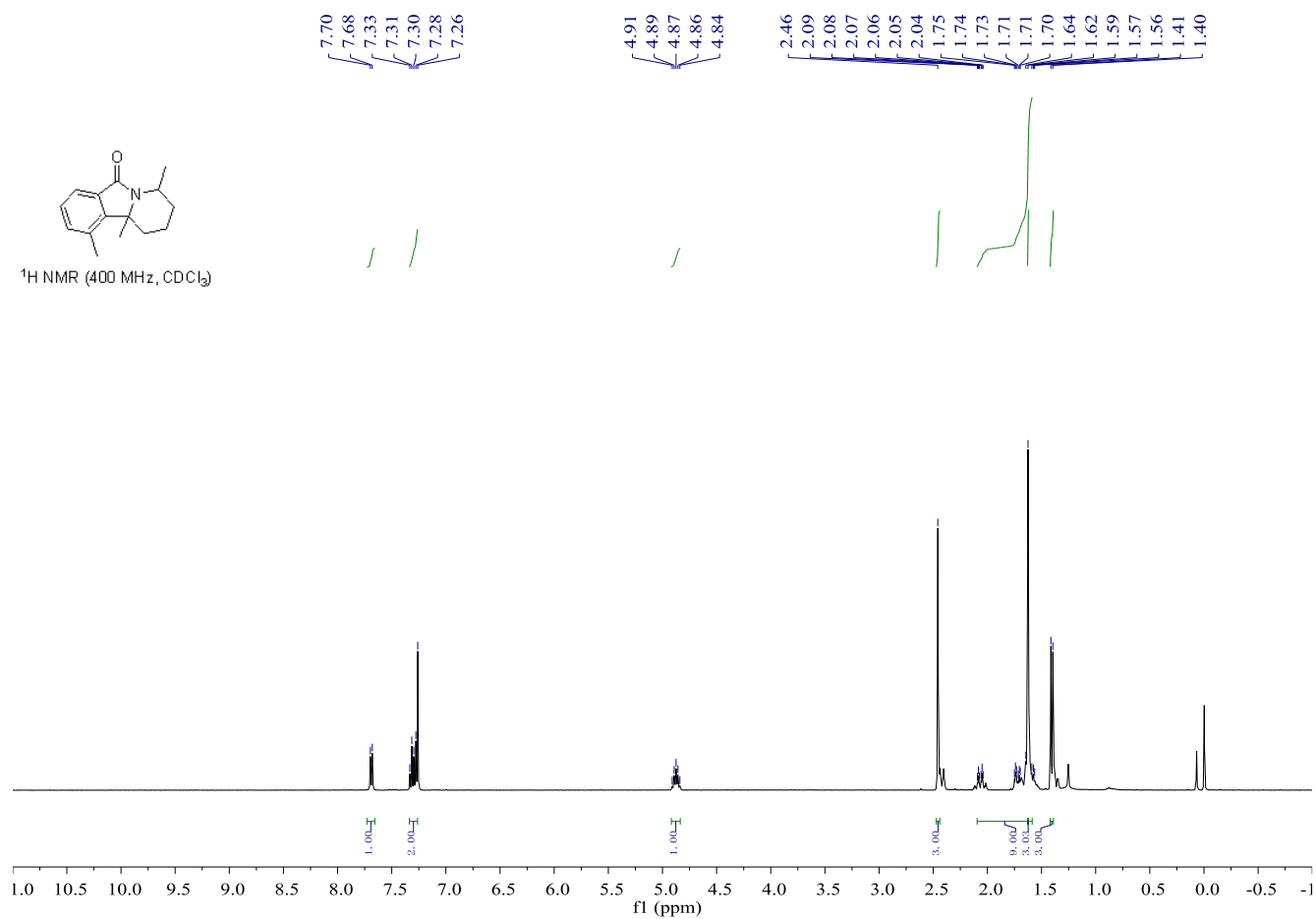


^{13}C NMR (100 MHz, CDCl_3)

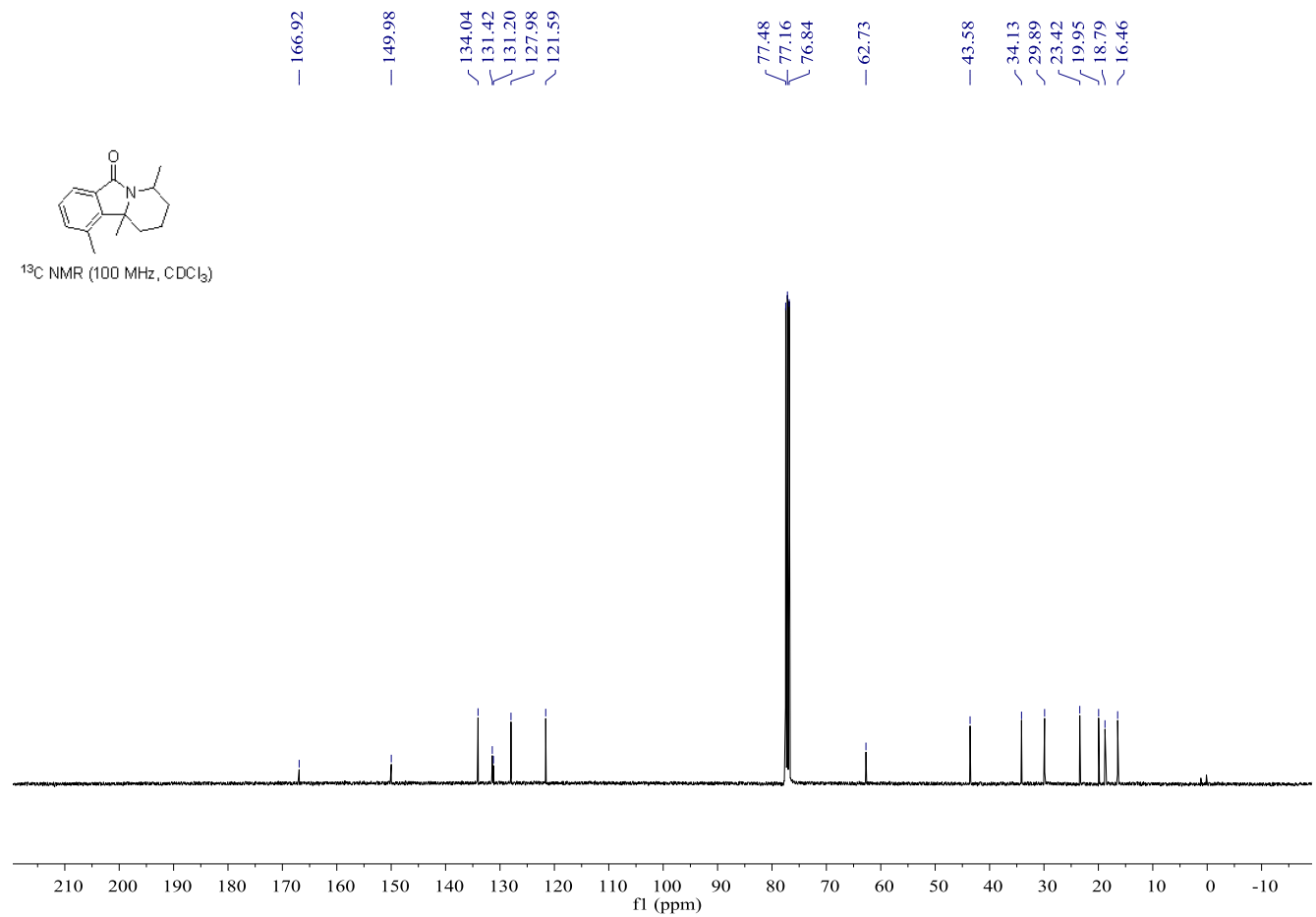


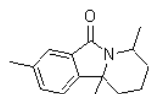


¹H NMR (400 MHz, CDCl₃)



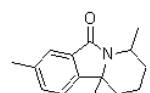
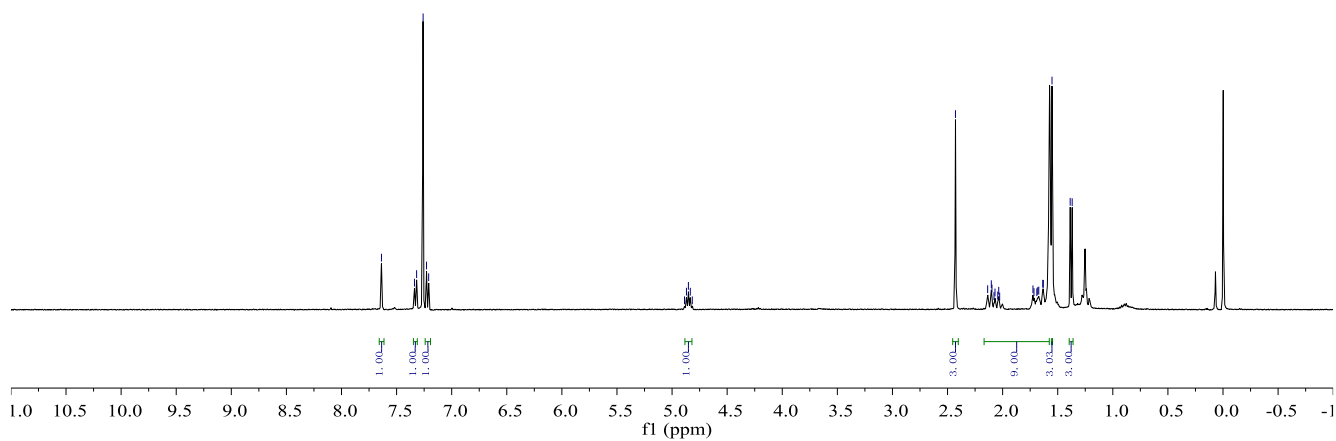
¹³C NMR (100 MHz, CDCl₃)





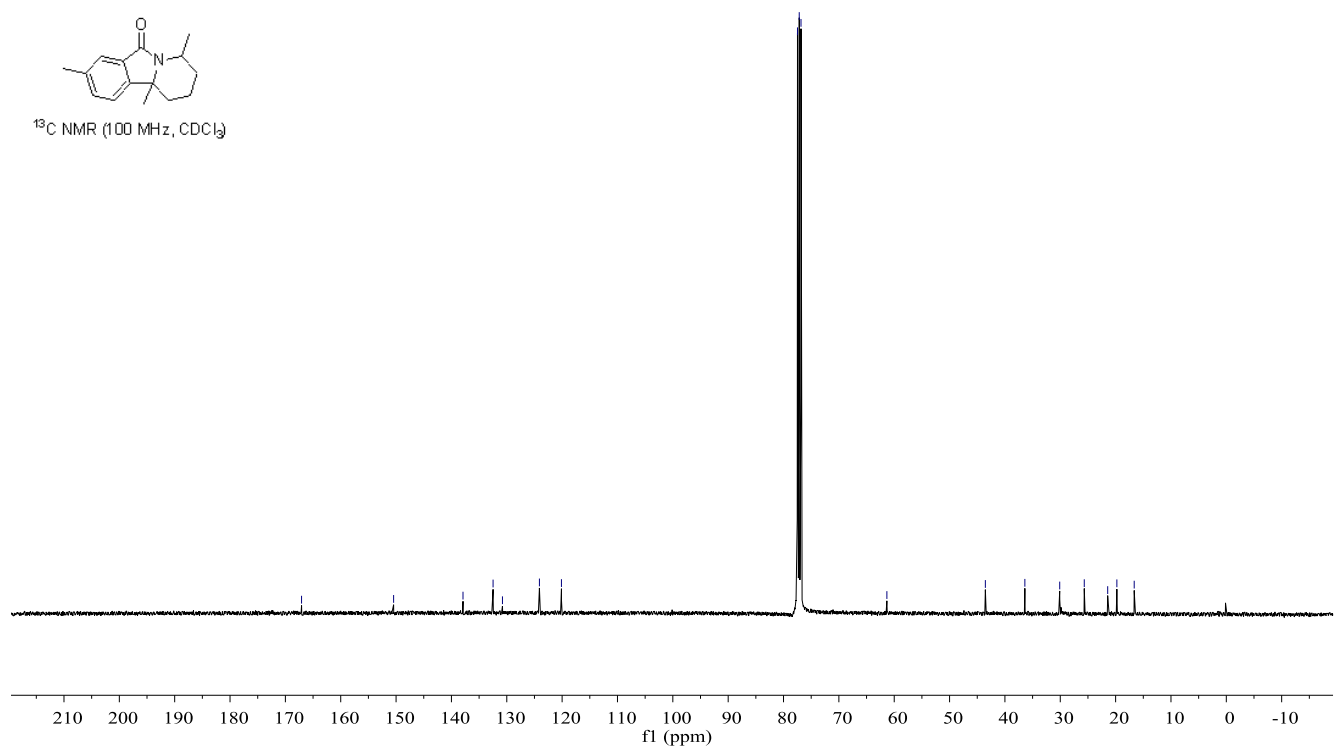
¹H NMR (400 MHz, CDCl₃)

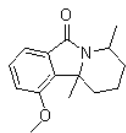
7.64, 7.34, 7.32, 7.26, 7.23, 7.21, 4.89, 4.87, 4.85, 4.83, 4.82, 2.43, 2.14, 2.10, 2.10, 2.08, 2.07, 2.04, 2.04, 2.03, 1.72, 1.72, 1.69, 1.68, 1.67, 1.64, 1.63, 1.55, 1.39, 1.37



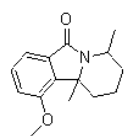
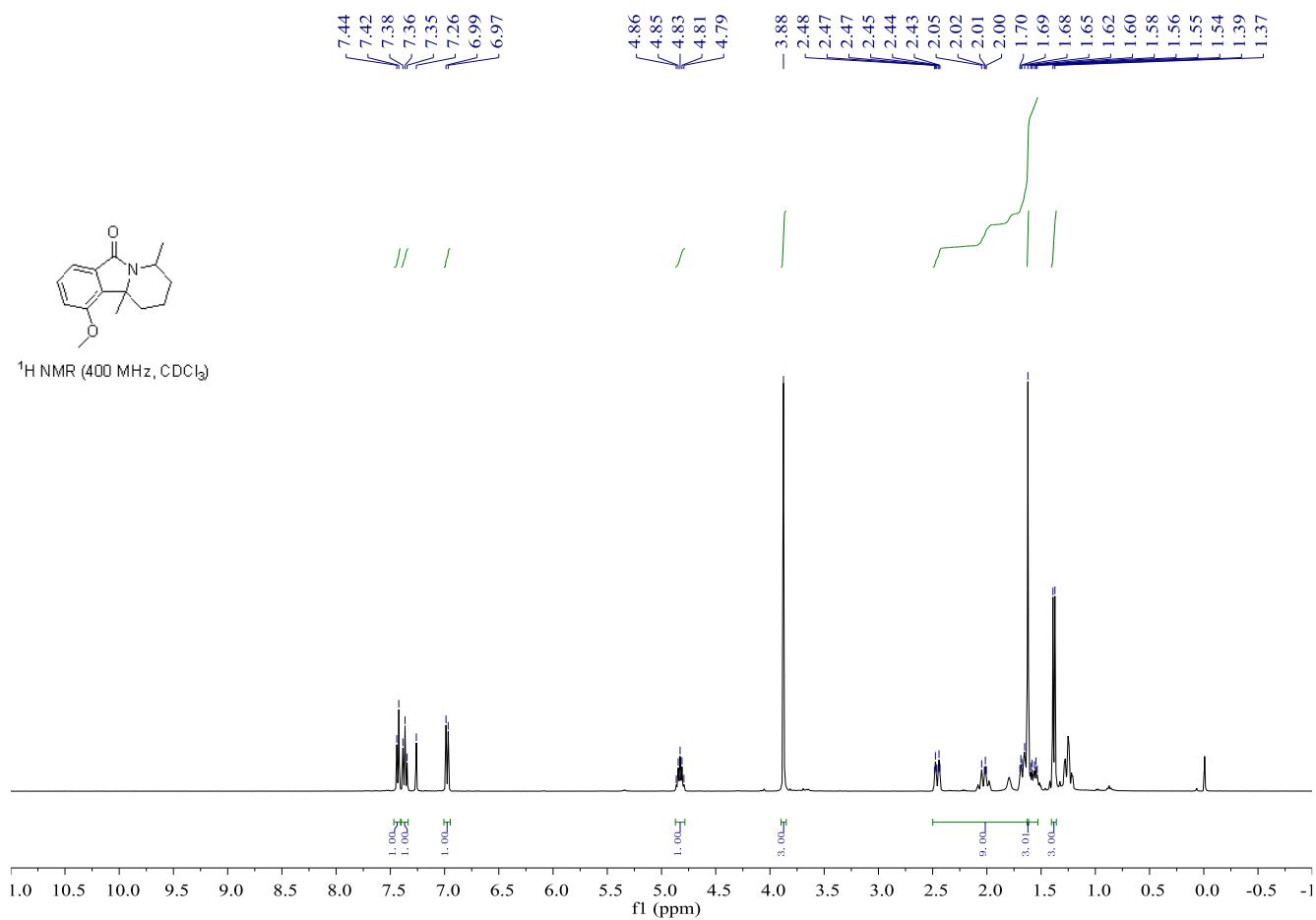
¹³C NMR (100 MHz, CDCl₃)

167.08, 150.44, 137.91, 132.48, 130.78, 124.10, 120.12, 77.48, 77.16, 76.84, 61.33, 43.54, 36.40, 30.10, 25.67, 21.43, 19.78, 16.64

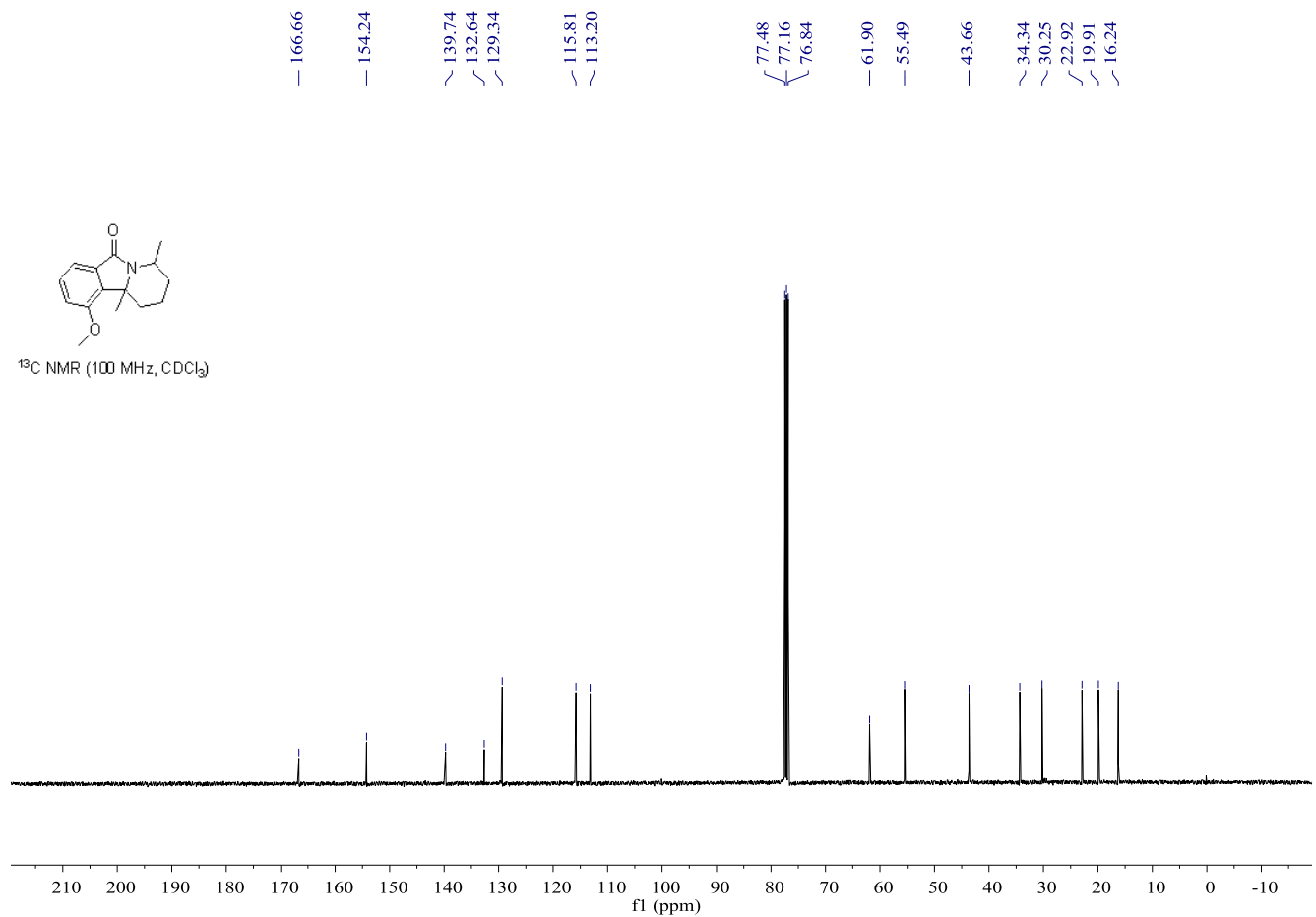


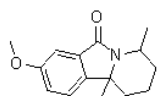


¹H NMR (400 MHz, CDCl₃)

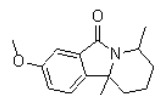
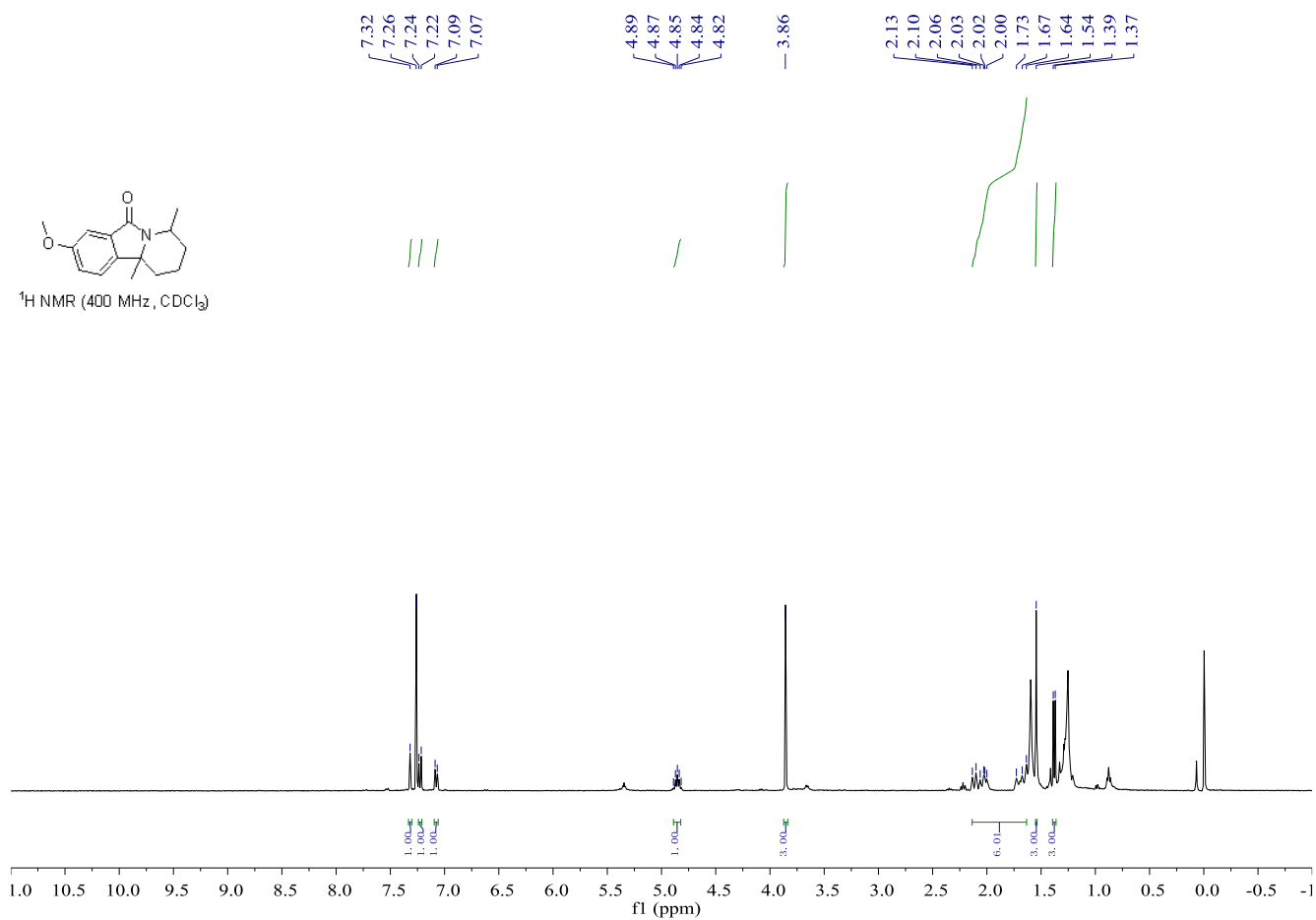


¹³C NMR (100 MHz, CDCl₃)

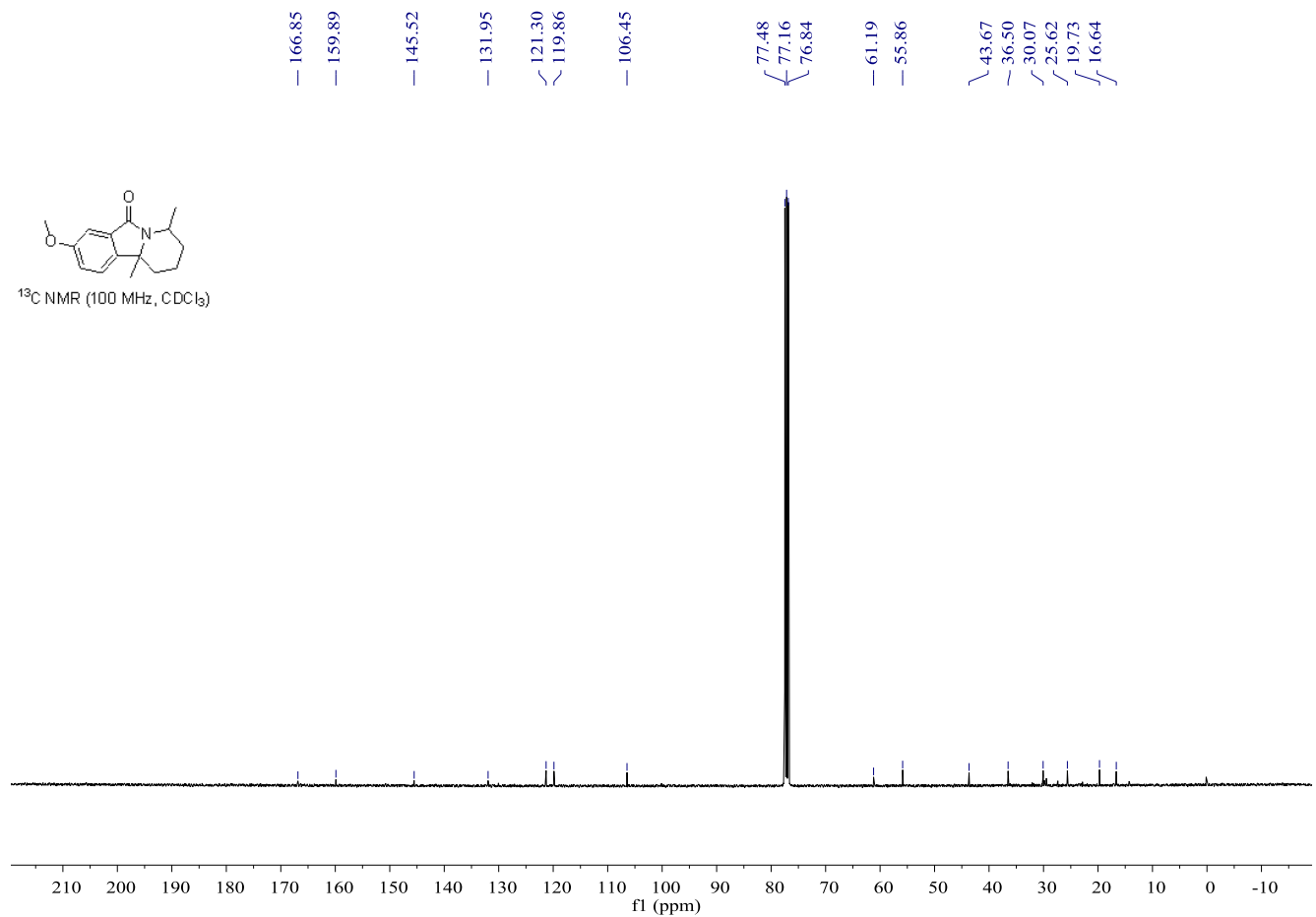


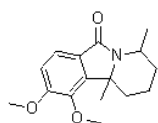


¹H NMR (400 MHz, CDCl₃)

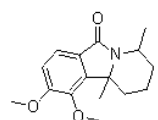
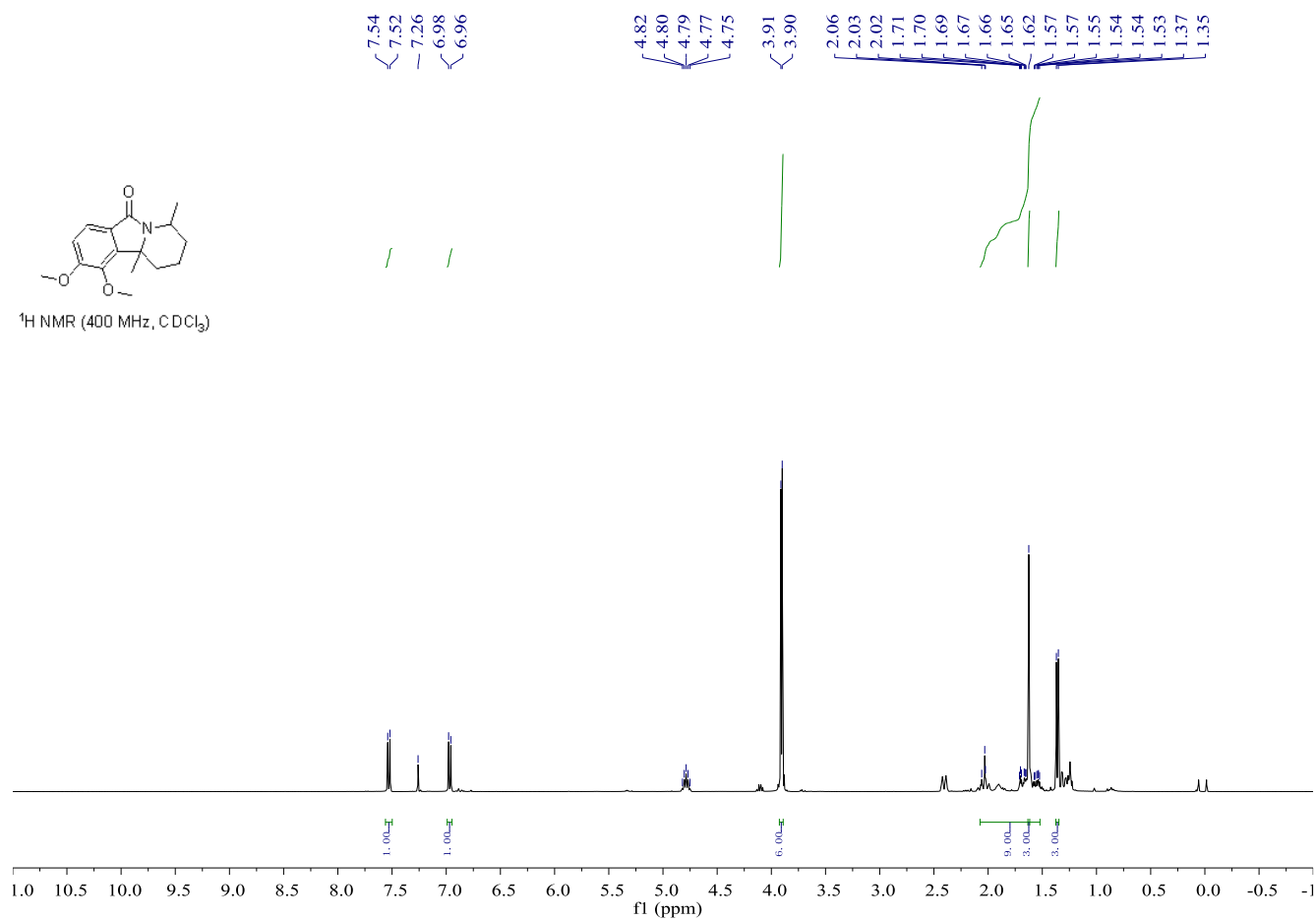


¹³C NMR (100 MHz, CDCl₃)

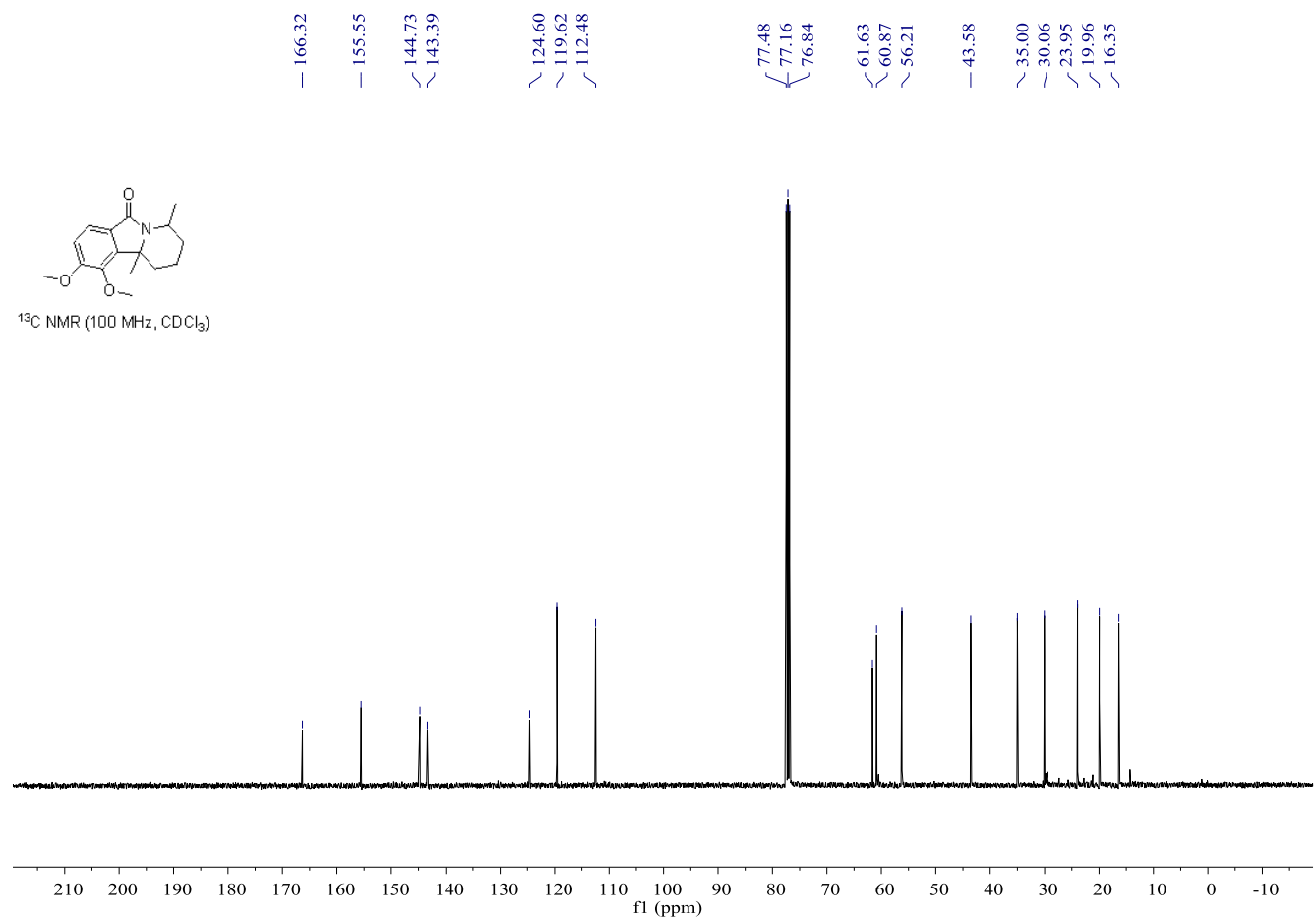


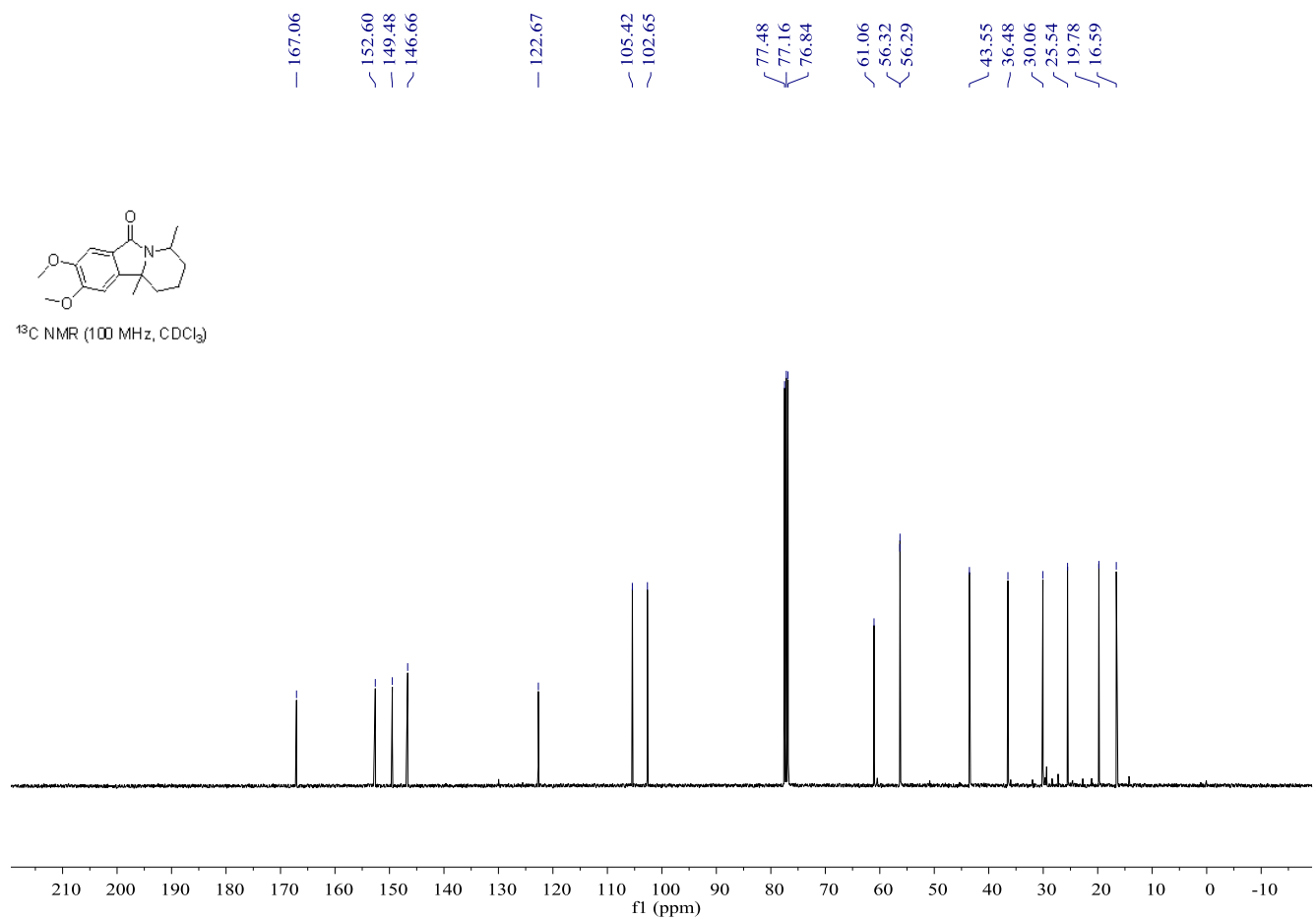
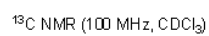
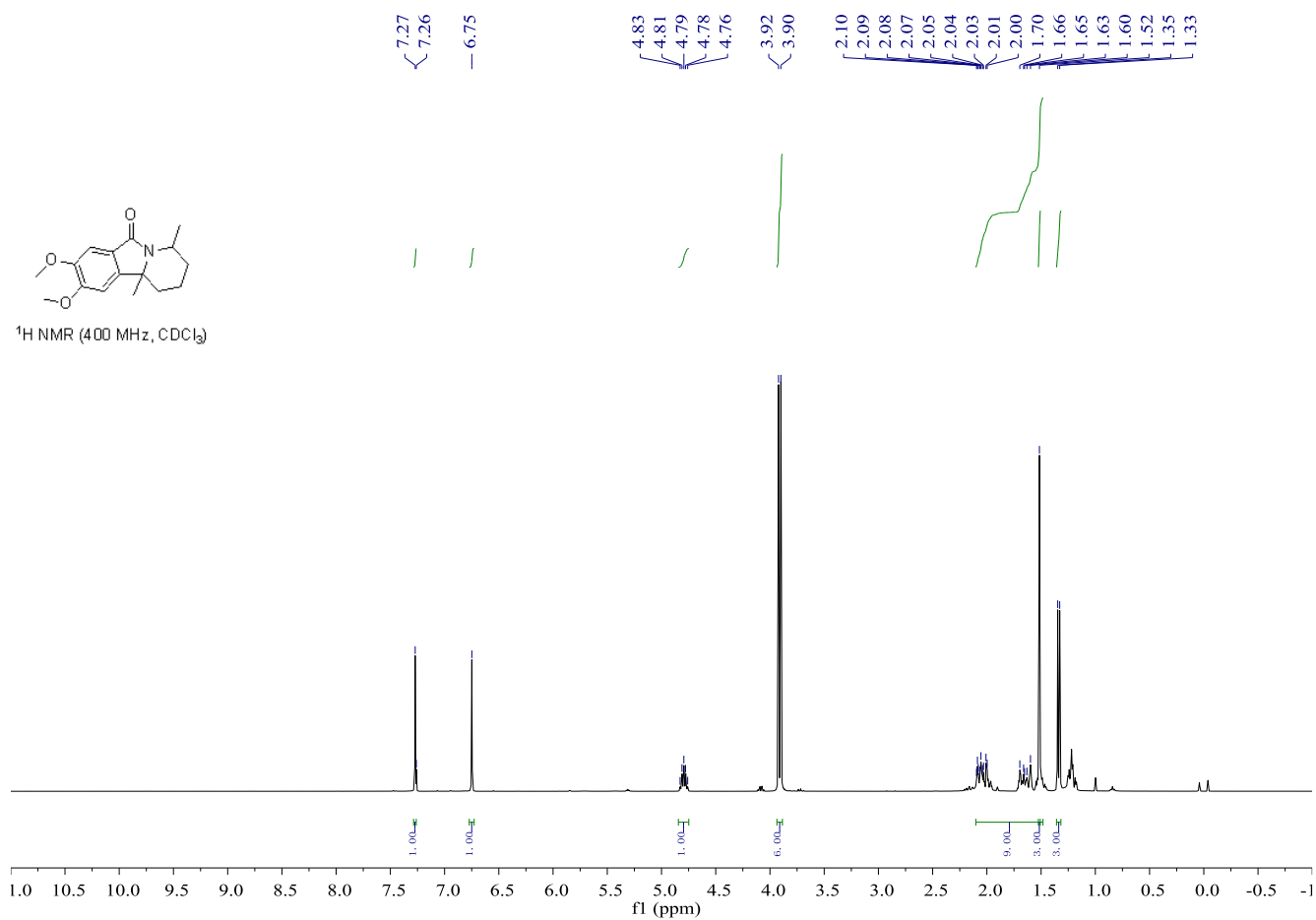
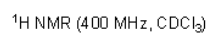


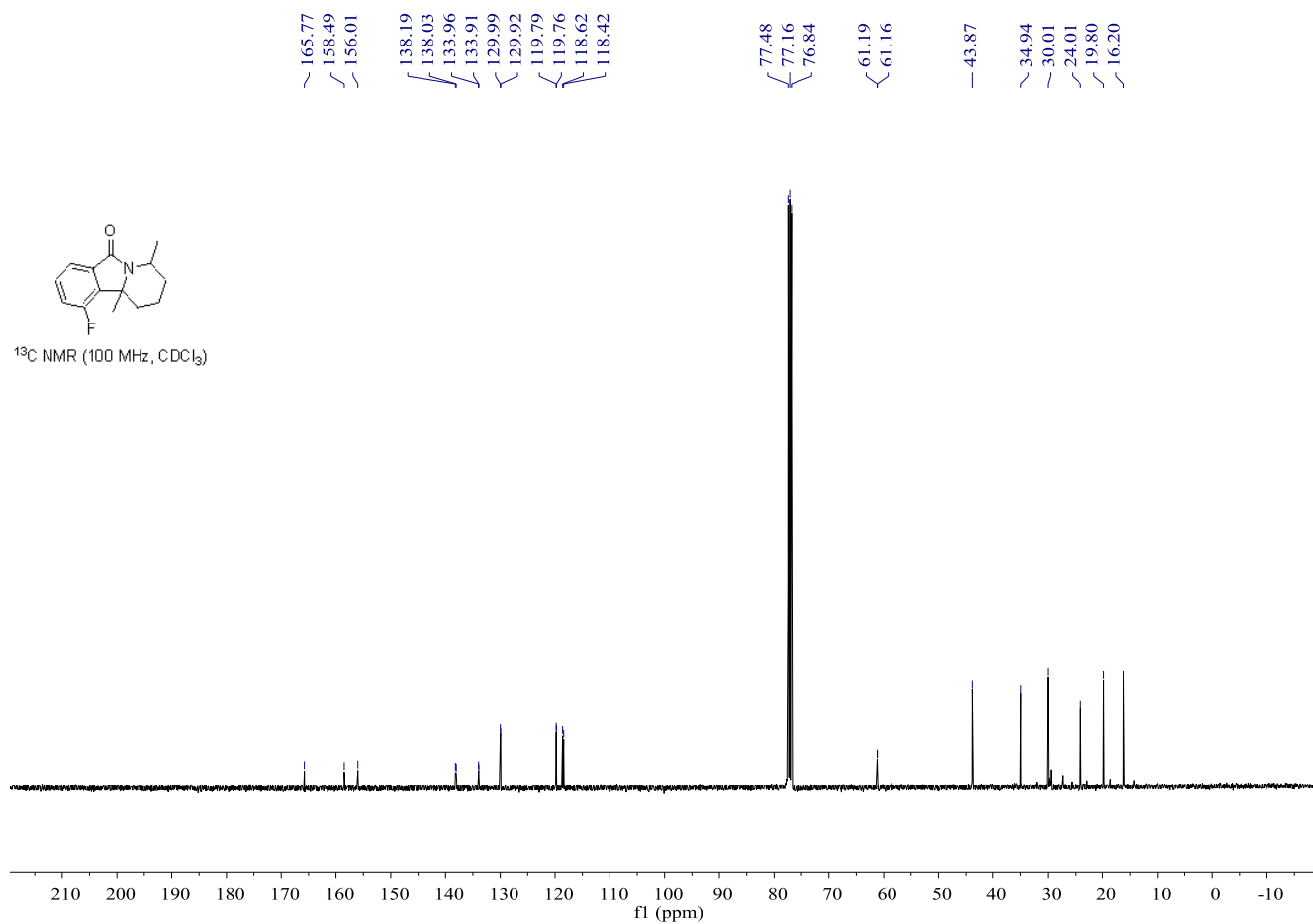
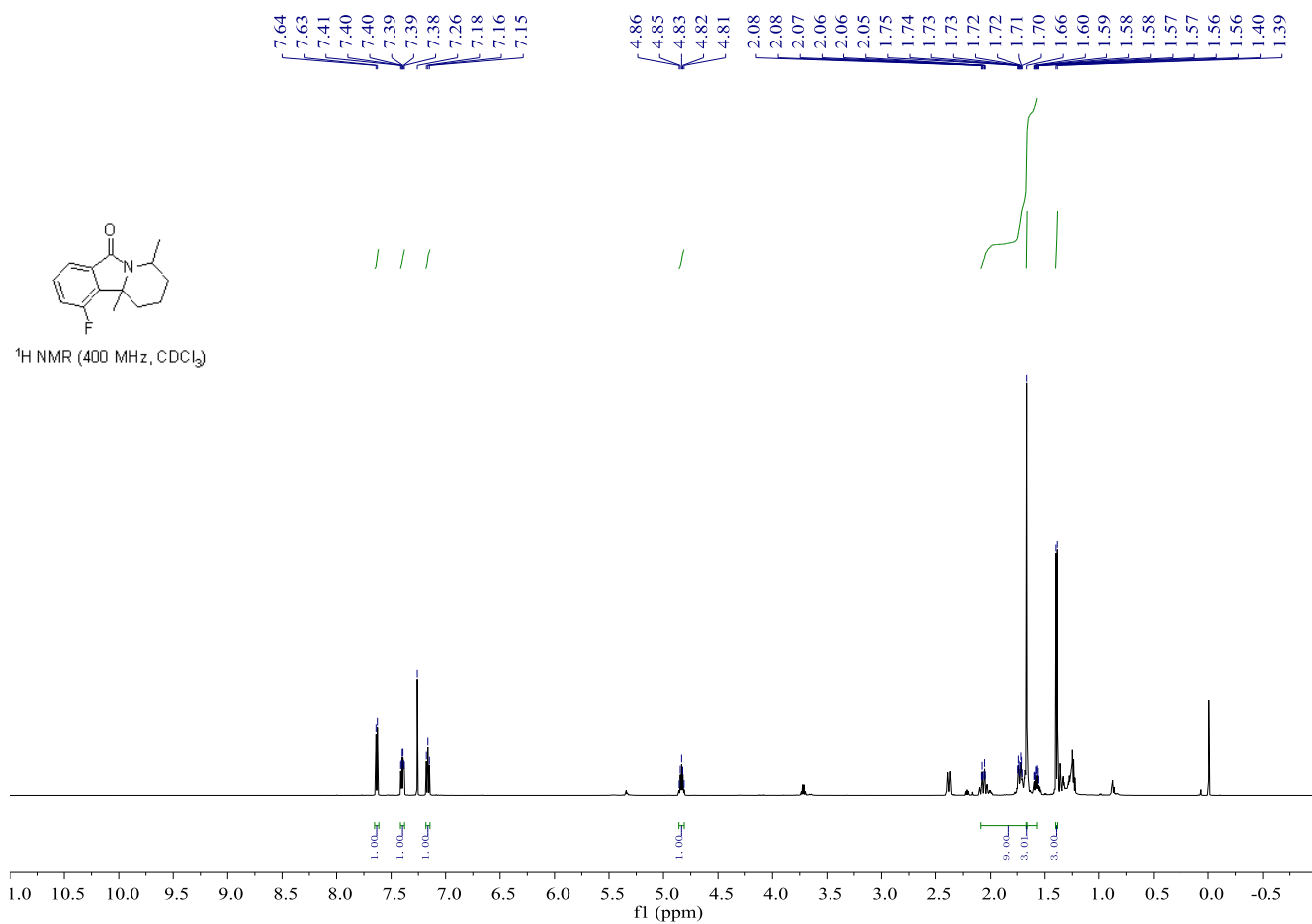
^1H NMR (400 MHz, CDCl_3)

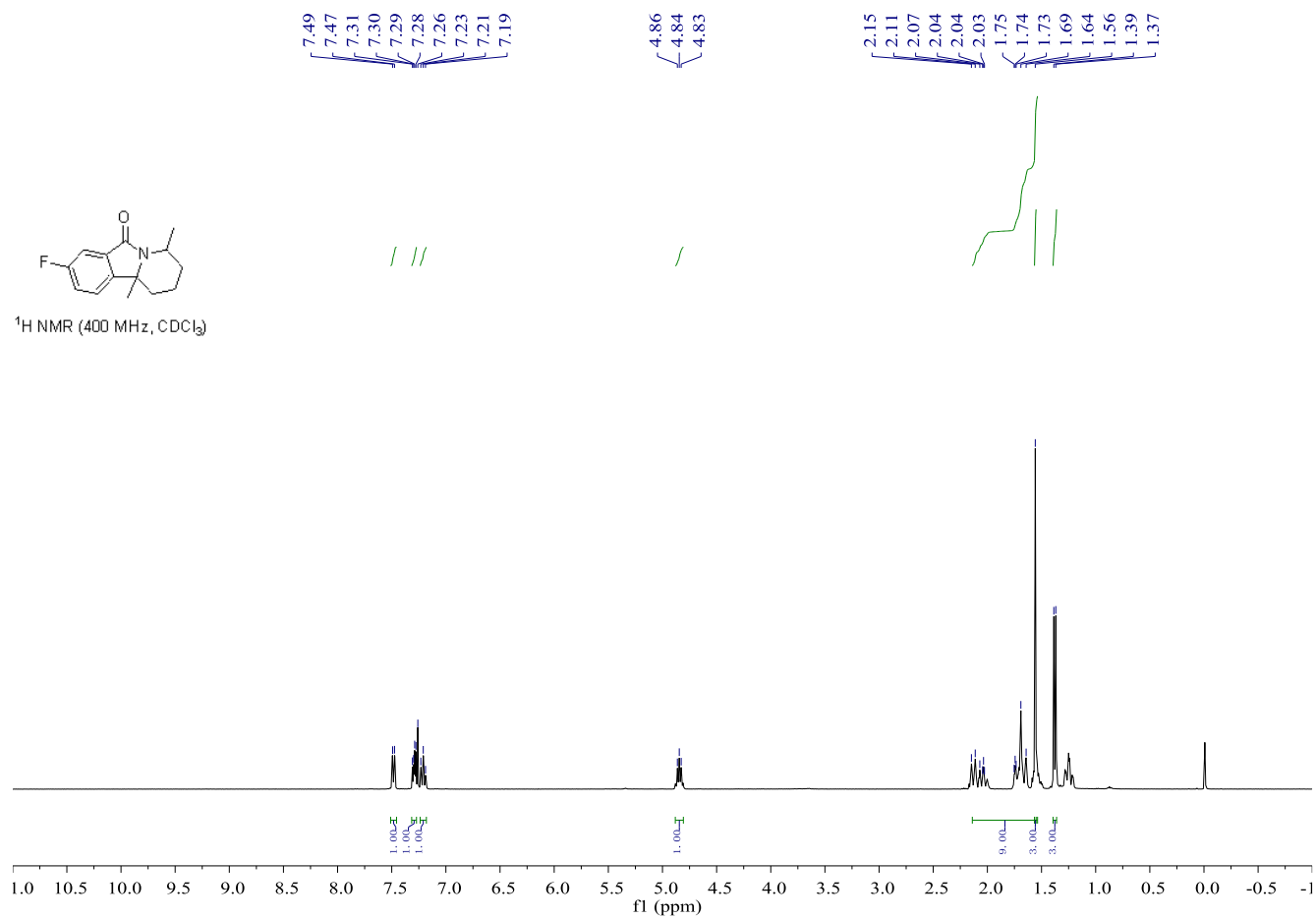
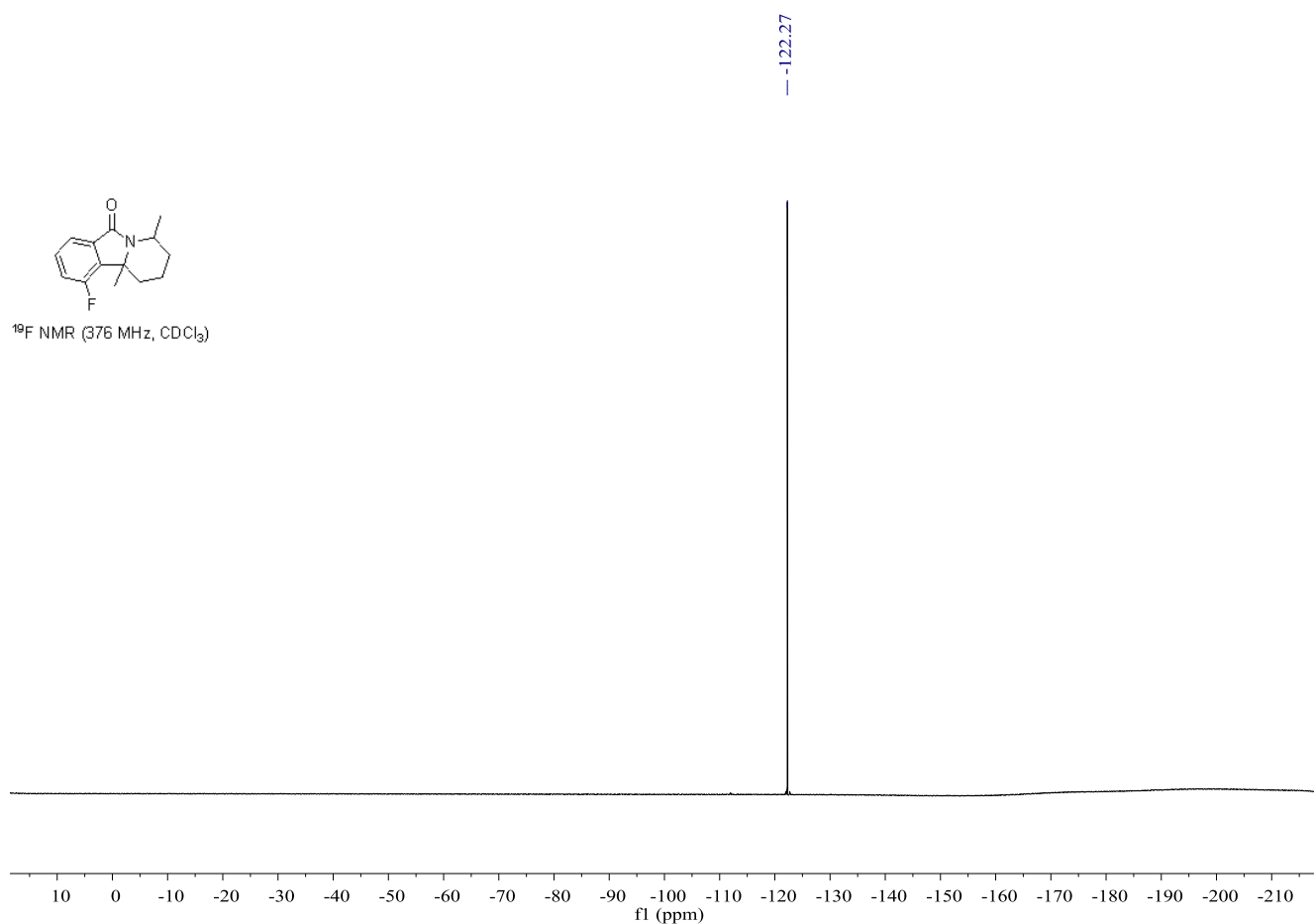
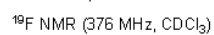


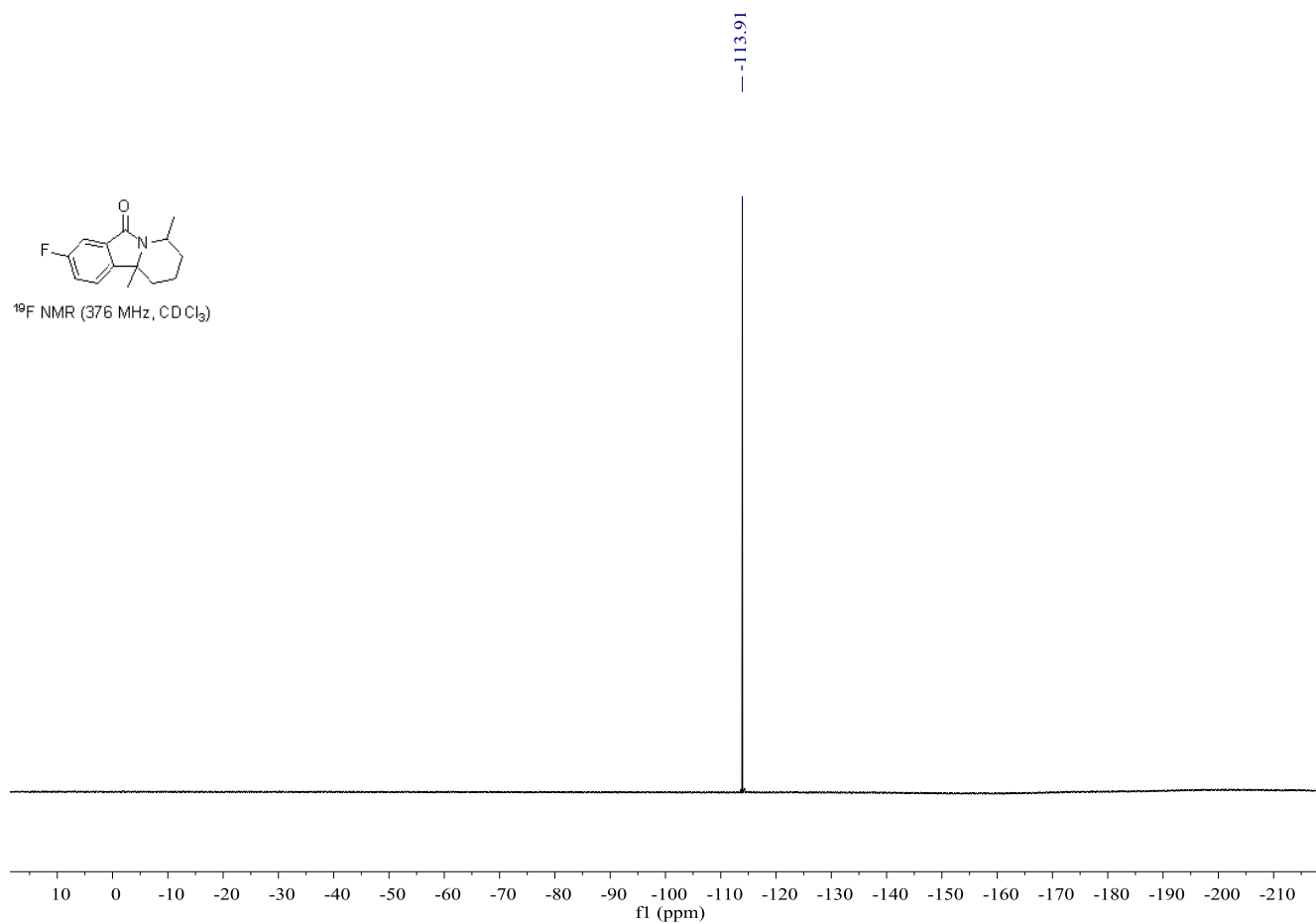
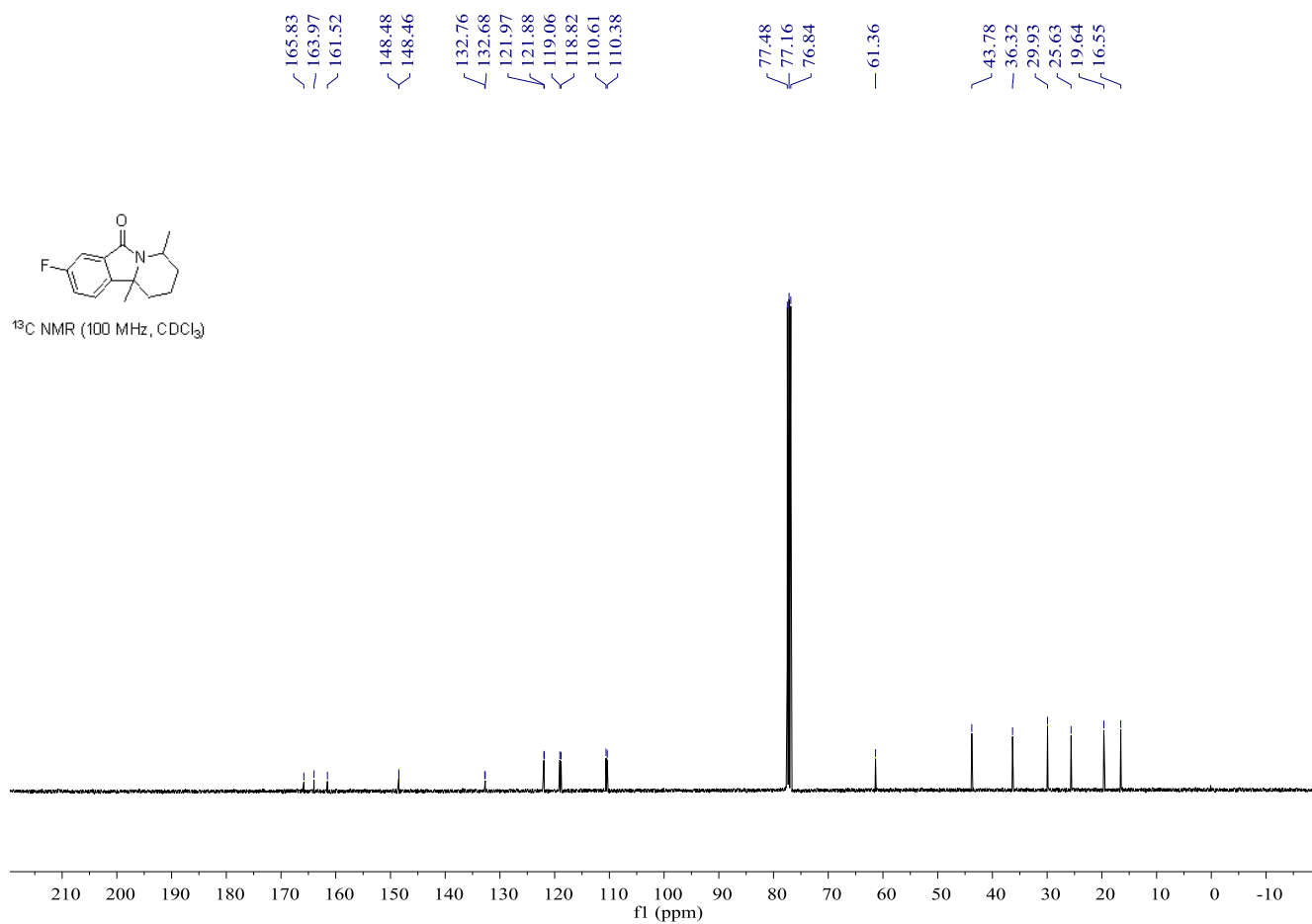
^{13}C NMR (100 MHz, CDCl_3)

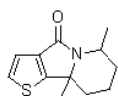




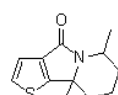
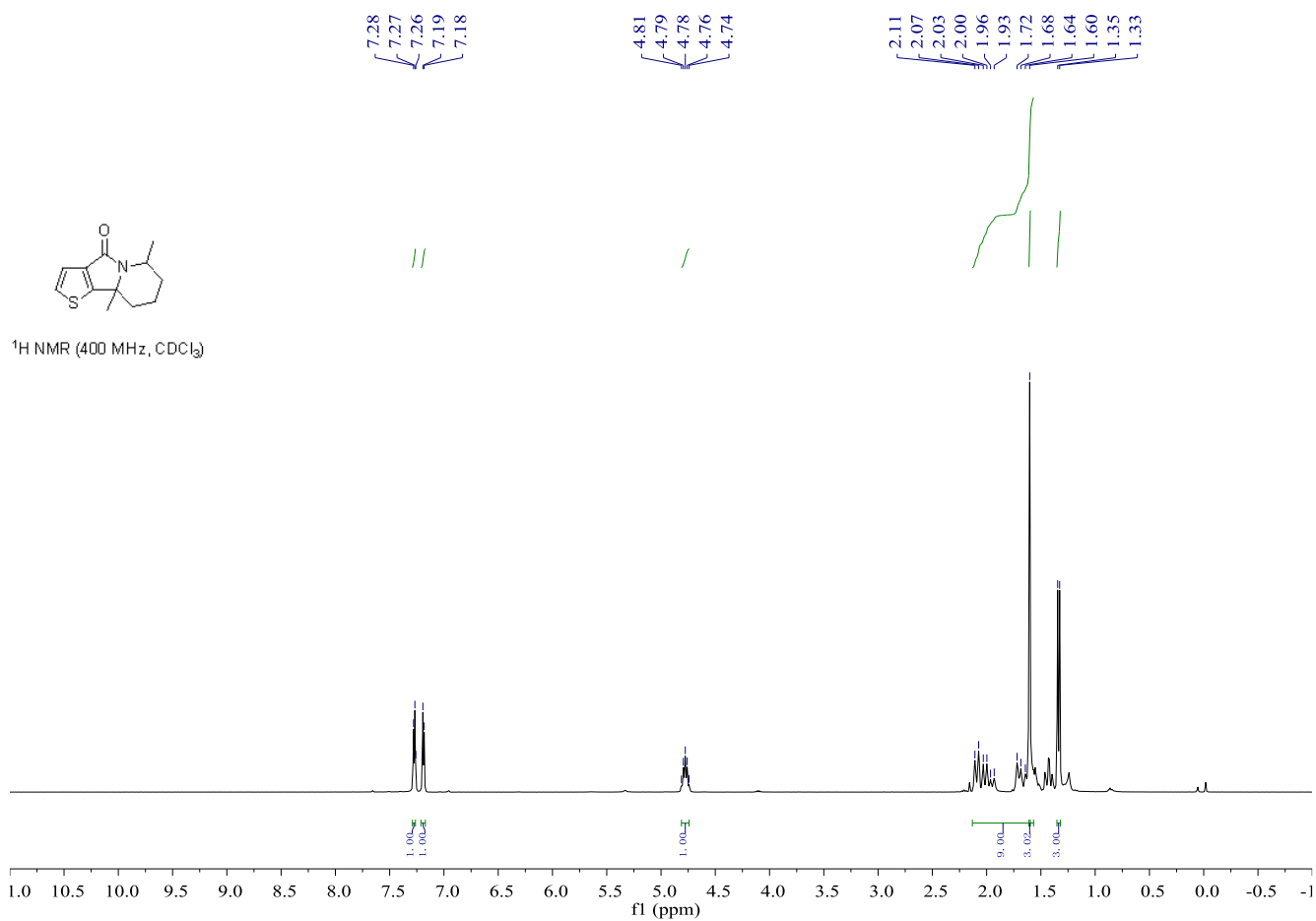




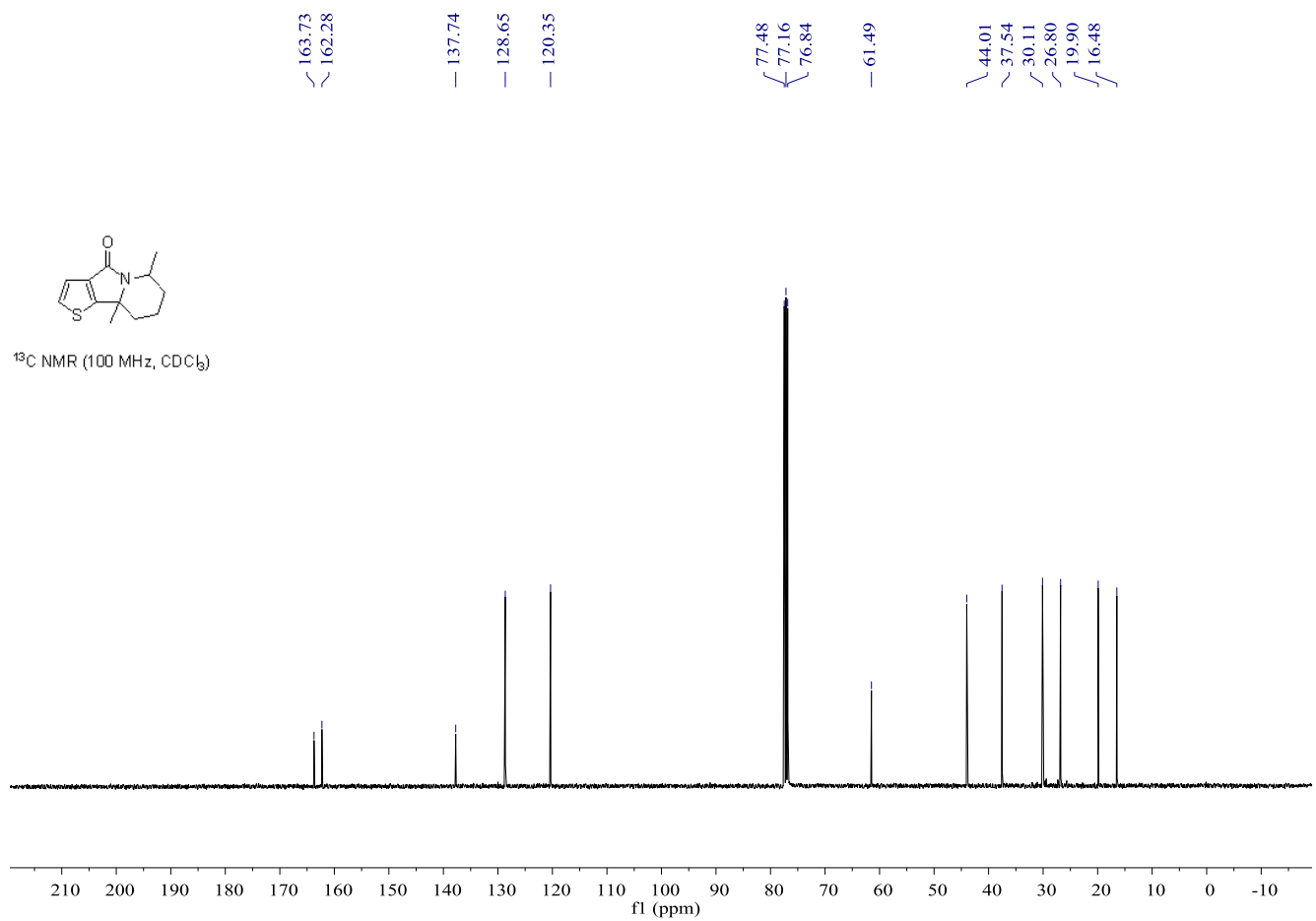


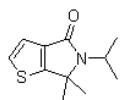


¹H NMR (400 MHz, CDCl₃)

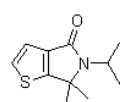
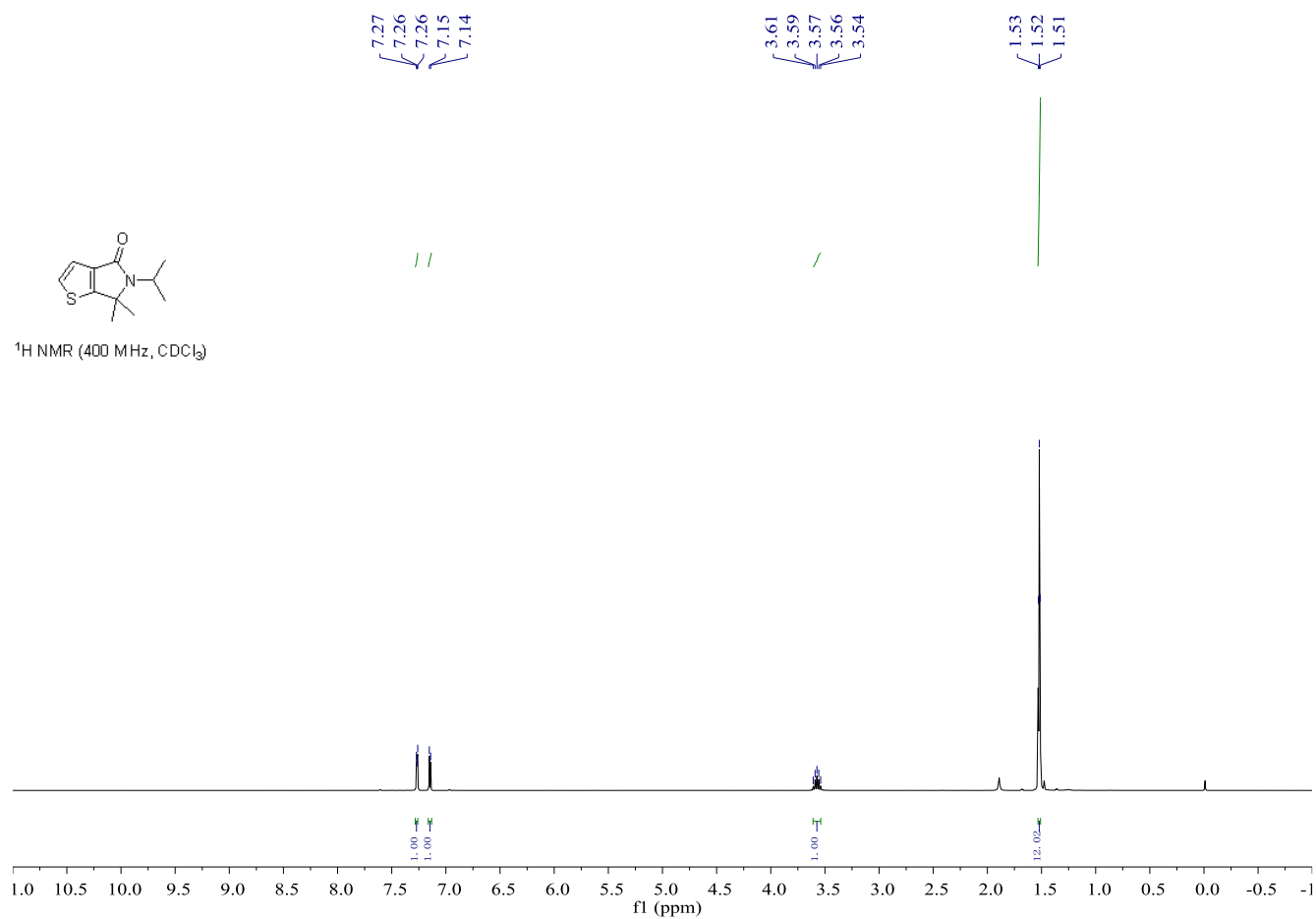


¹³C NMR (100 MHz, CDCl₃)

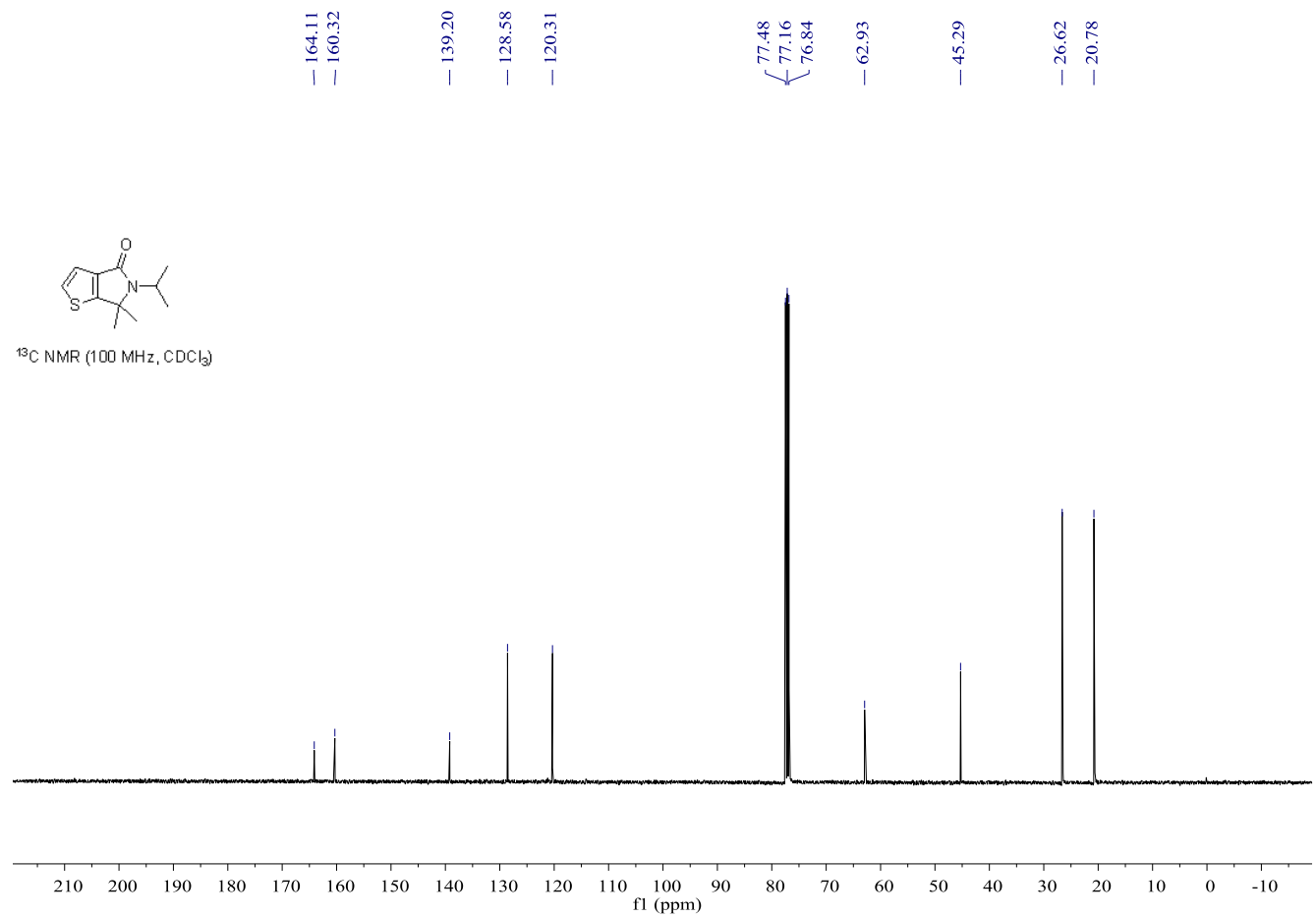


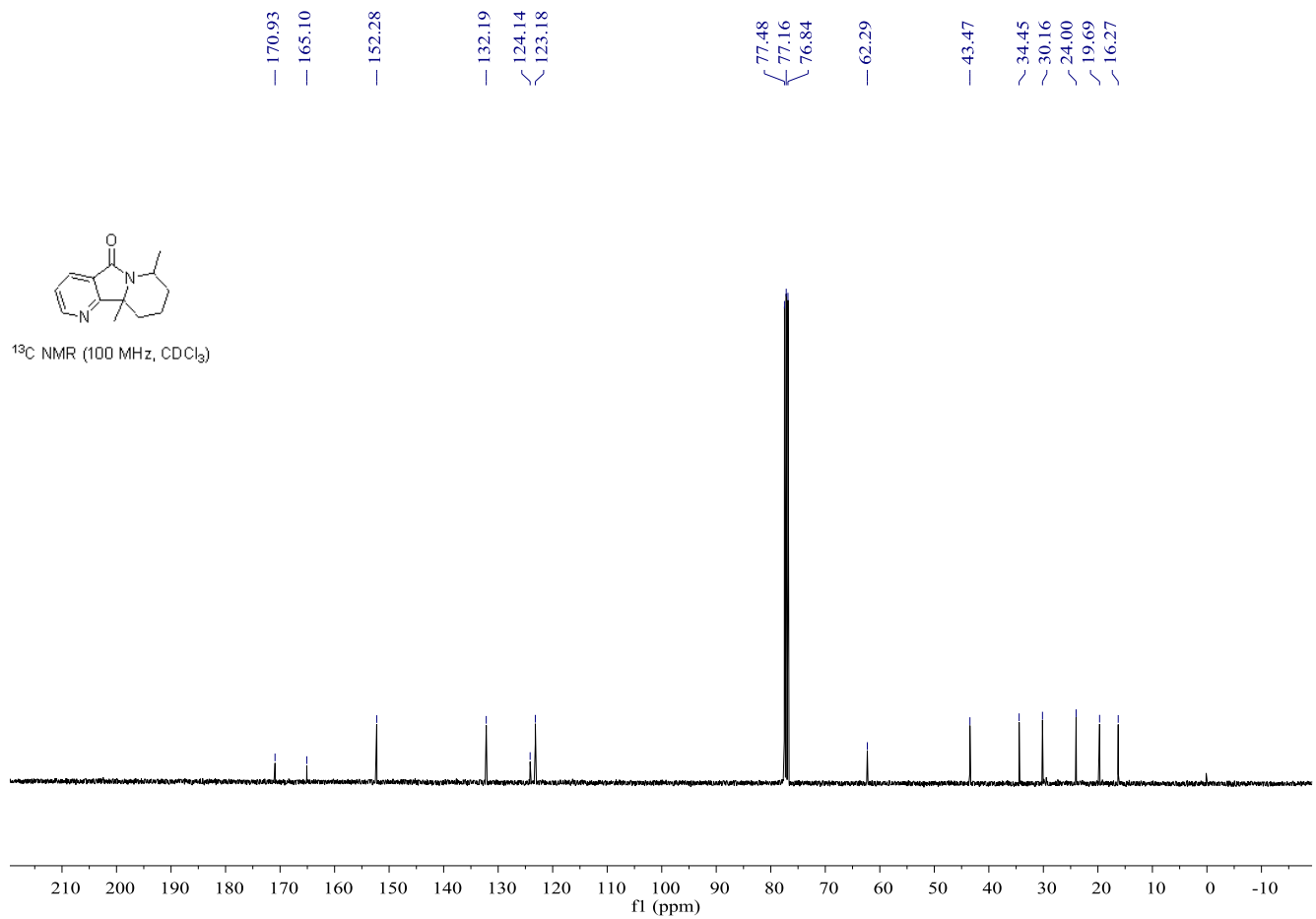
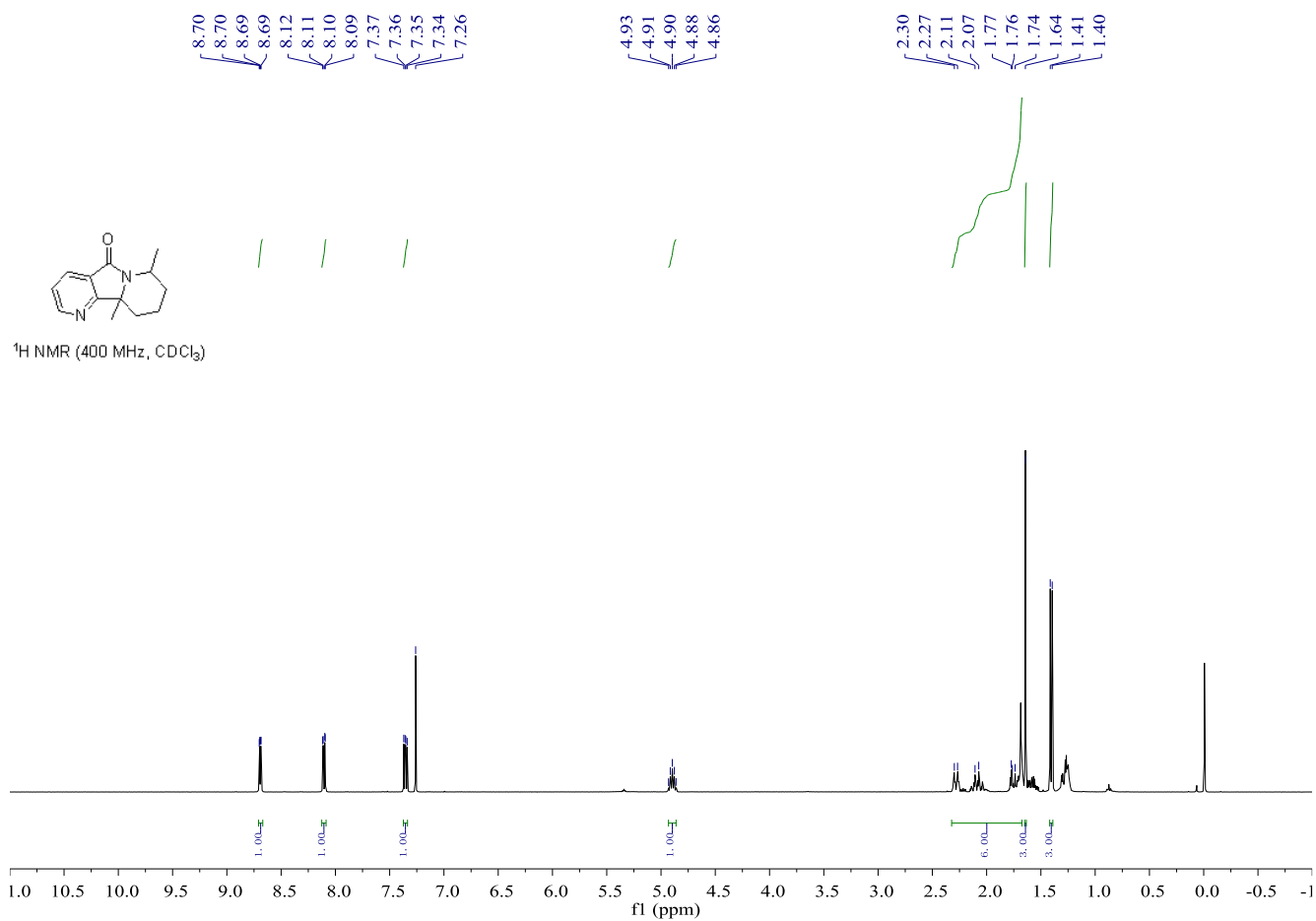


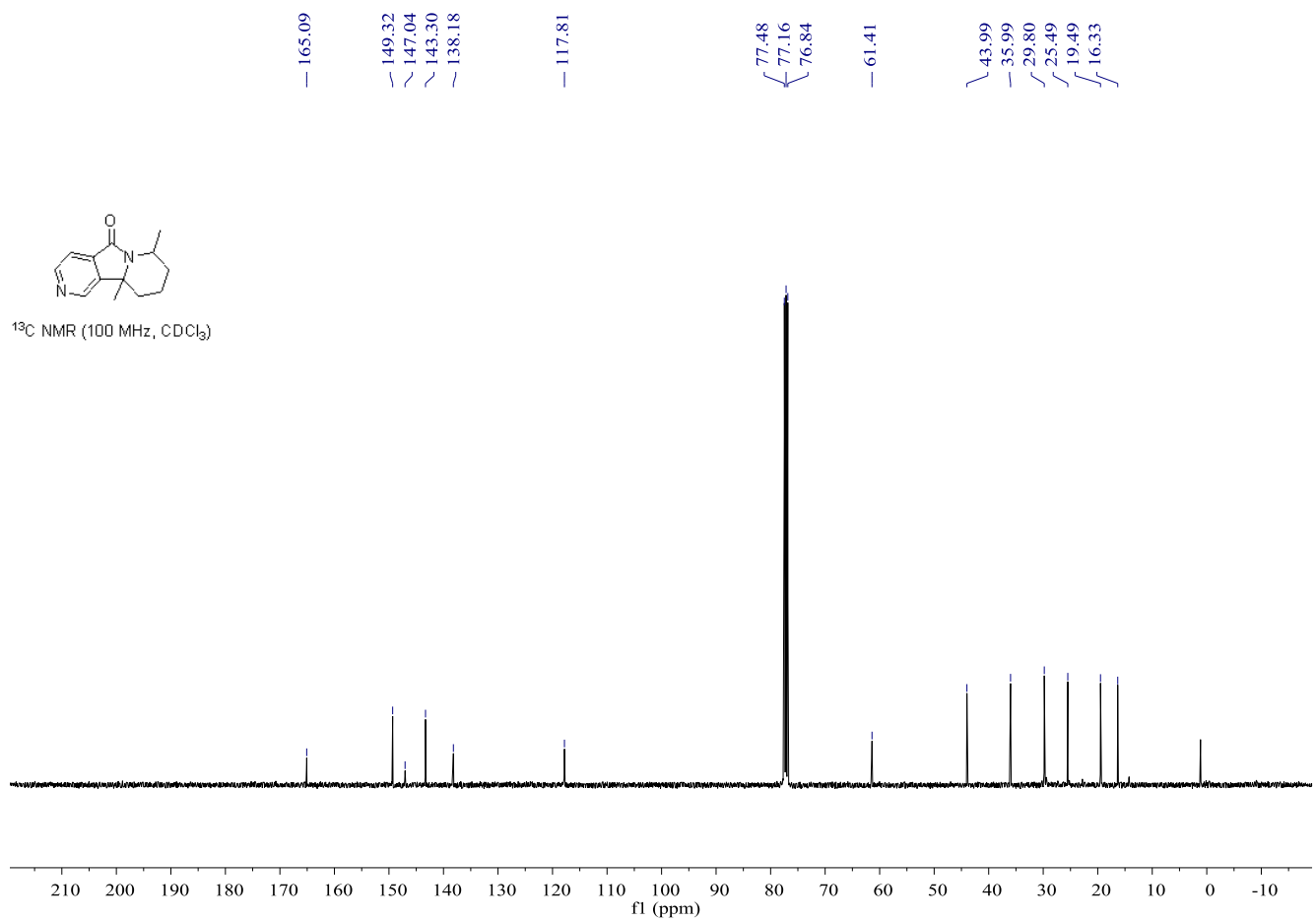
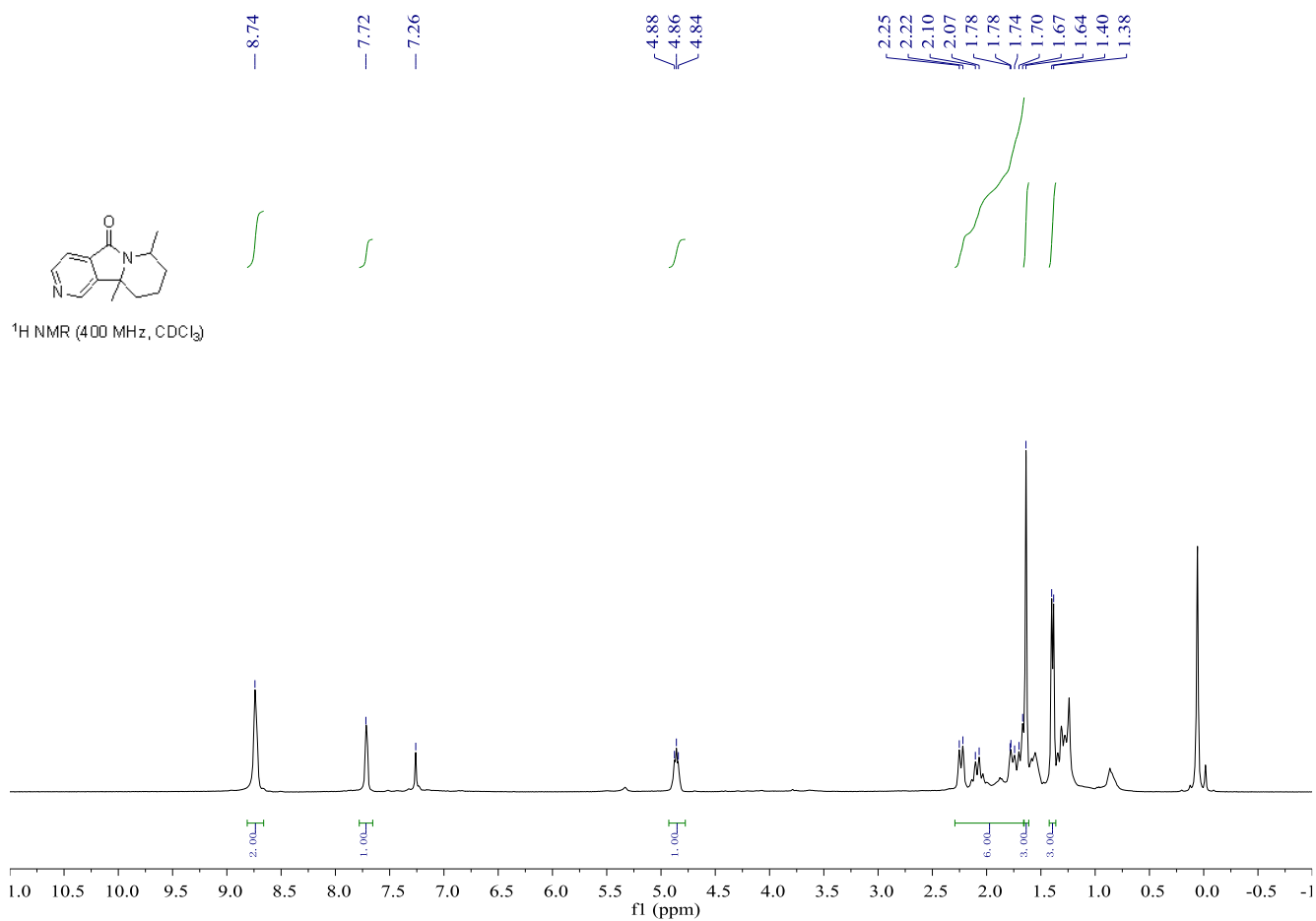
¹H NMR (400 MHz, CDCl₃)

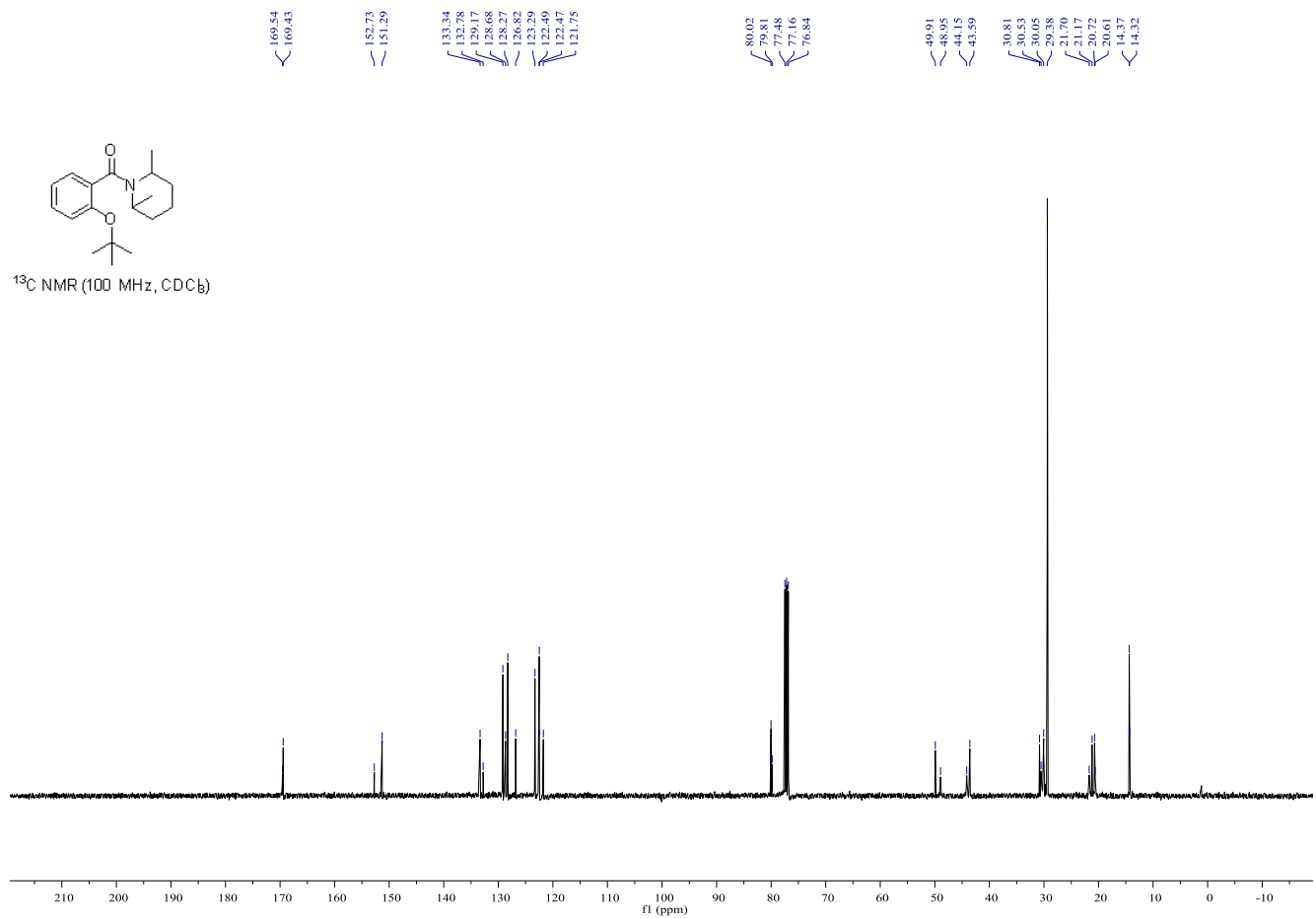
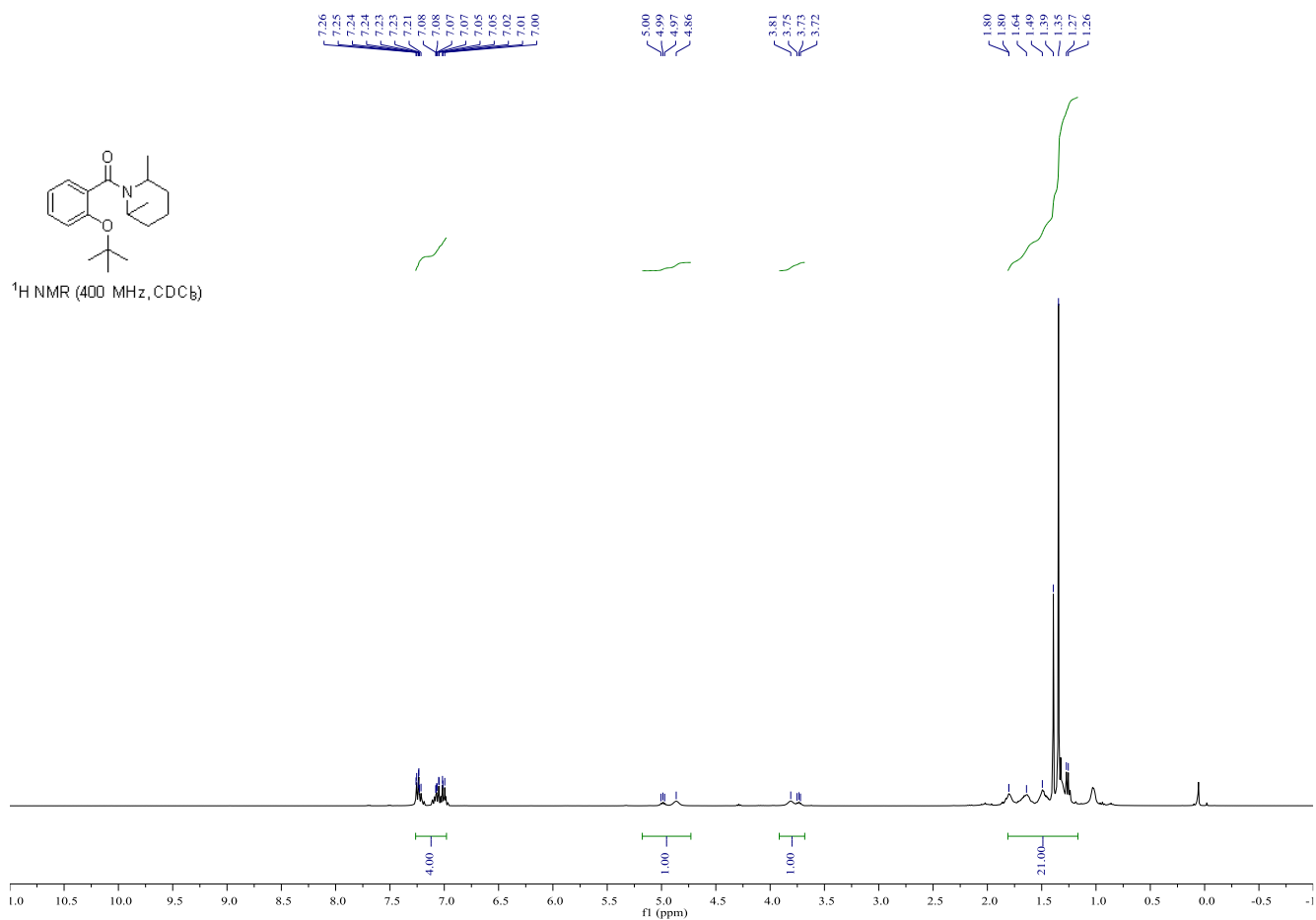


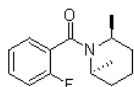
¹³C NMR (100 MHz, CDCl₃)



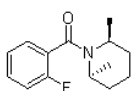
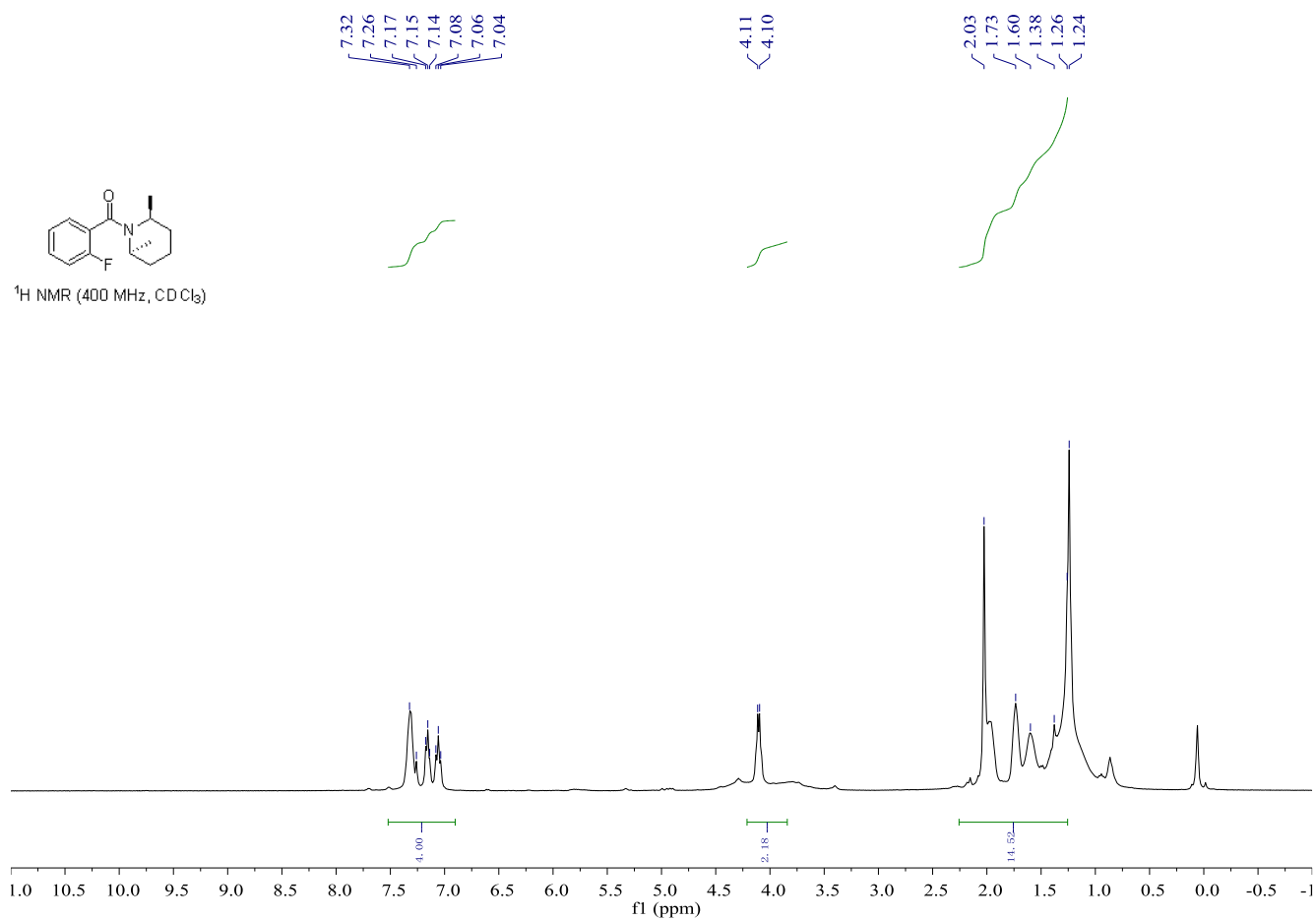




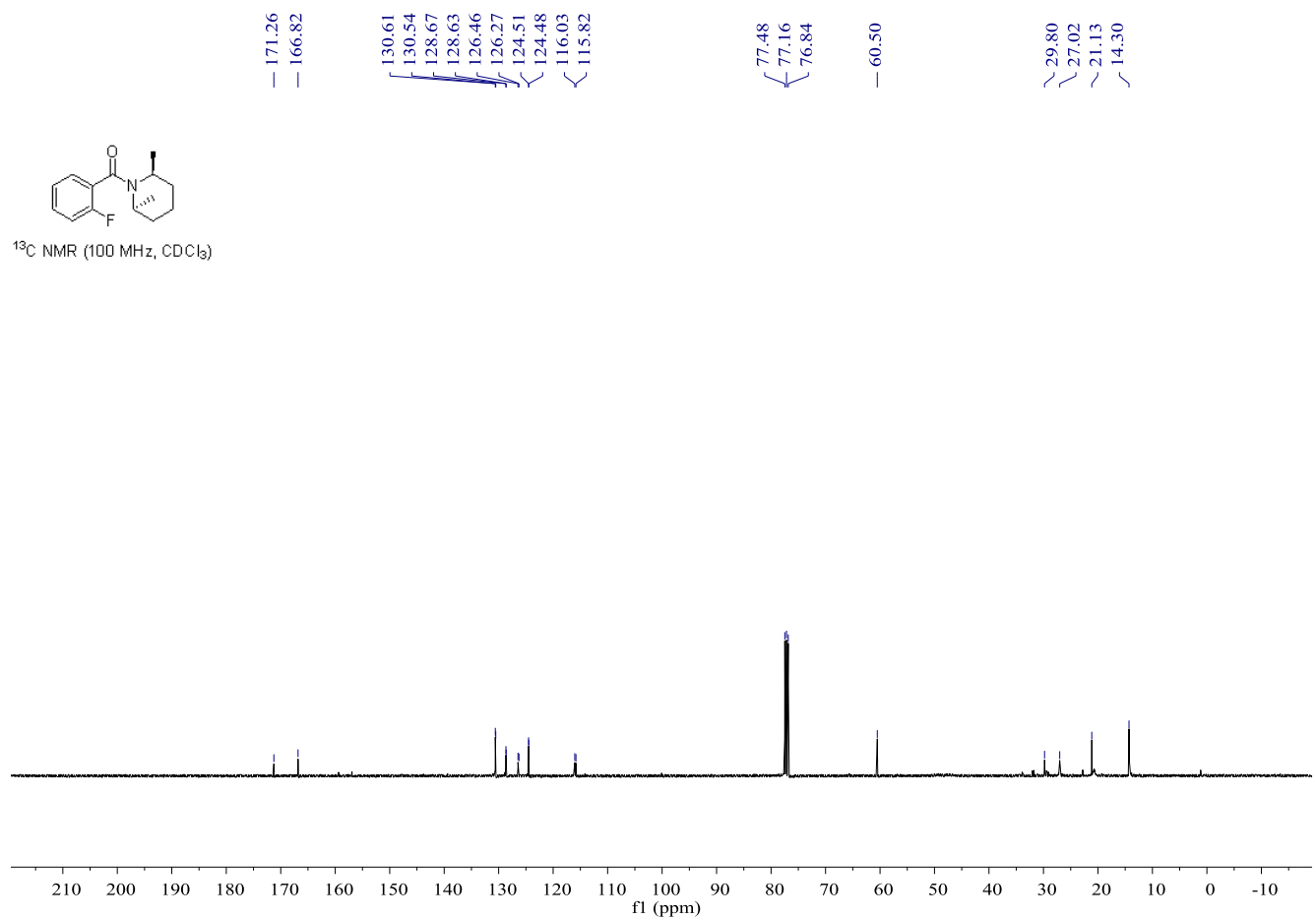


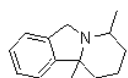


¹H NMR (400 MHz, CDCl₃)

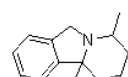
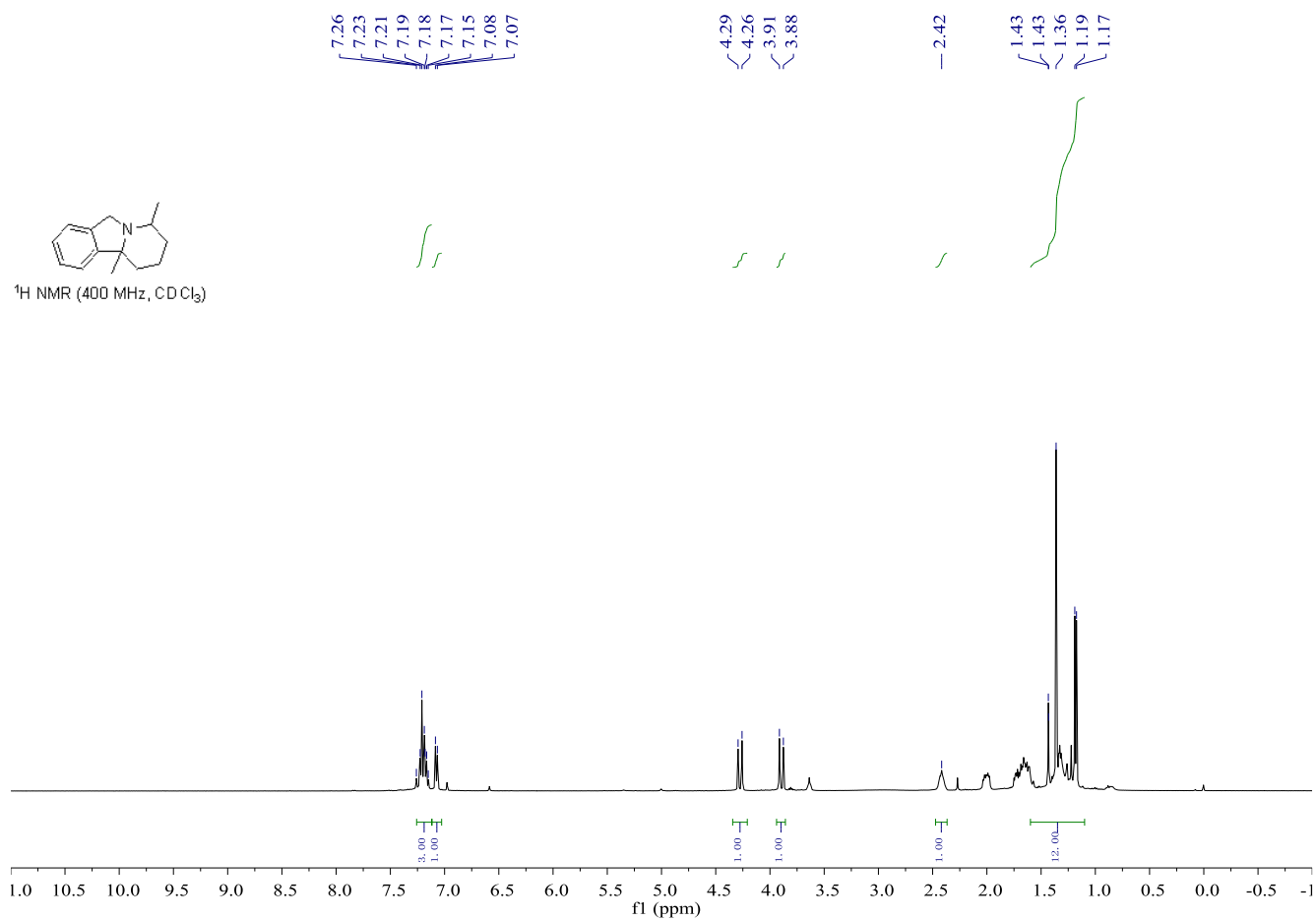


¹³C NMR (100 MHz, CDCl₃)





^1H NMR (400 MHz, CDCl_3)



^{13}C NMR (100 MHz, CDCl_3)

