Supporting information

Diversity-Oriented Chiral Phosphoric Acid Catalyzed Alkylation of Indolizines with Aminals

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1. General information

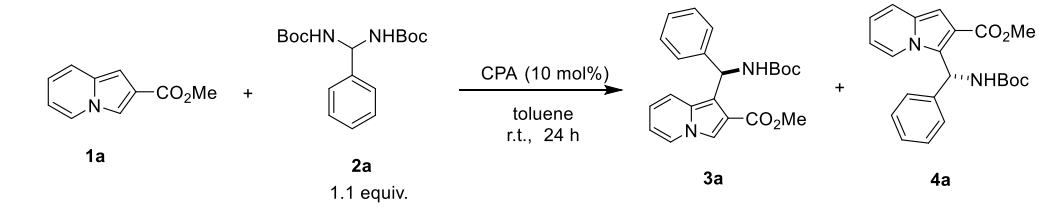
All reagents were purchased from Sigma-Aldrich, Ambeed and Fluorochem, and used without further purification. All solvents were of reagent grade quality and were dried over MS 3Å before use. Some of BINOL-based chiral phosphoric acid catalysts were purchased from Ambeed, and others were synthesized according to the literature procedure.[1-5] *H8*-BINOL-derived chiral phosphoric acid catalysts were all synthesized according to the literature procedure.[5-9] SPINOL-derived chiral phosphoric acid catalysts were also synthesized according to the literature procedure.[10-13] Solvents were dried with MS 3Å.

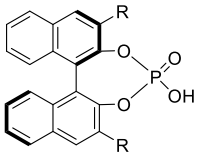
The ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on Varian Gemini 200, Bruker Avance III HD 400, Bruker model DRX Avance 500, Varian-Agilent 500 model and Varian-Agilent 600. Chemical shifts are reported in ppm. The splitting pattern of multiplets is described by abbreviations (s – singlet, bs – broad singlet, d – doublet, t – triplet, q –quartet, dd – doublet of doublets, ddd – doublet of doublet of doublets, m – complex multiplicity). Coupling constants values (*J*) are reported in Hz. Column chromatography was performed with Merck Kieselgel 60 (230-400 mesh). TLC was carried out on Merck Kieselgel F254 plates. Melting points were determined using a Boëtius M HMK hot-stage apparatus and were uncorrected. High resolution Mass spectrometry analysis was performed using Synapt G2-S mass spectrometer (Waters) equipped with the electrospray (ESI) ion source and quadrupole-Time-of-flight (qTOF) mass analyzer. Acetonitrile (Honeywell, LC-MS Chromasolv™, purity ≥ 99.9%) was used as a solvent and mobile phase with the flow rate 100 µl/min. Sample was dissolved and injected directly into the ESI source. Injection volume was 1 µl depending on concentration. The measurement was performed in the positive ion mode with the resolving power of TOF analyzer 30000 FWHM. The lock-spray spectrum of Leucine-enkephalin was generated by the lock-spray source and the correction was performed for the recorded spectrum. The exact mass measurement was performed within 3 mDa mass error. Nitrogen was used as desolvation and cone gas, and their flow values were set to 600 L/h and 100 L/h respectively. Desolvation gas temperature was set to 350°C. Nebulizer gas pressure was set to 5.0 bar. Capillary voltage was set to 3.0 kV, and sampling cone voltage and source offset were set to 30-50 V. The instrument was controlled and data were processed using the MassLynx V4.1 software package (Waters). Optical Rotations were measured in DCM on Jasco P-2000 digital polarimeter using a sodium lamp (λ 589 nm, D-line). [α]D values are reported at 25 °C in 10^{-1} degrees $cm^2 \cdot g^{-1}$ with concentration in $g \cdot 100cm^{-3}$. HPLC analyses for the determination of enantiomeric excesses were performed on a Hitachi Elite LaChrom HPLC

System With L-2400 UV detector, L-2200 Autosampler and L-2130 pump, equipped with Chiralpak AD-H column (5 μm, 4.6 x 250 mm), Chiralpak IC column (5 μm, 4.6 x 250 mm), Chiralcel OD-H column (5 μm, 4.6 x 250 mm). ECD values were measured on Jasco J-815 EDC Spectropolarimeter.

2. Optimization of reaction conditions

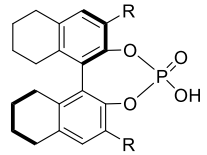
Table S1. Screening of catalysts for reaction between indolizine **1a** and *N*-Boc aminal **2a**[a]





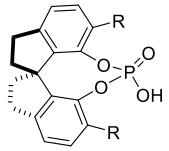
A

A1: R = 9-anthracyl
A2: R = 9-phenanthryl
A3: R = 2,4,6-$Cy_3C_6H_2$
A4: R = 3,5-^{t}BuC_6H_3
A5: R = 3,5-$(CF_3)_2C_6H_3$
A6: R = I
A7: R = 1-pyrenyl
A8: R = 4-PhC_6H_4
A9: R = 3,5-$Ph_2C_6H_3$
A10: R = 1-naphthyl
A11: R = $SiPh_3$
A12: R = 2,4,6-$Me_3C_6H_2$
A13: R = 2,4,6-^{i}Pr$_3C_6H_2$
A14: R = 3,5-$Me_2C_6H_3$
A15: R = 3,5-$Cl_2C_6H_3$



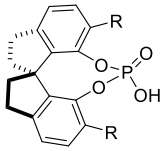
B

B1: R = 9-anthracyl
B2: R = 1-naphthyl
B3; R = 2,4,6-^{i}Pr$_3C_6H_2$
B4: R = 3,5-^{t}BuC_6H_3
B5: R = I
B6: R = Br
B6: R = 3,5-$(CF_3)_2C_6H_3$



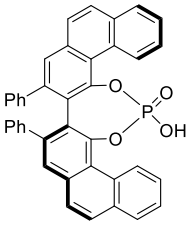
S

S1: R = 9-anthracyl
S2: R = 1-pyrenyl
S3: R = 1-naphthyl
S4: R = 2-naphthyl



D

D1: R = 9-phenanthryl
D2: R = 3,5-^{t}BuC_6H_3
D3: R = 3,5-$(CF_3)_2C_6H_3$



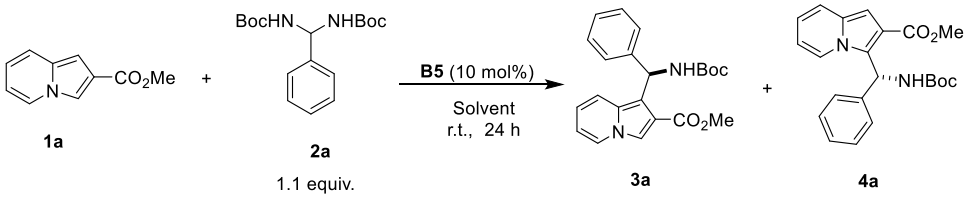
E

Entry	CPA	Conversion (%)[b]	**3a** e.e. (%)[c]	**4a** e.e. (%)[c]	Ratio **4a**:**3a**
1	**A1**, (*R*)-9-anthracenyl	66	19	8	1:1
2	**A2**, (*R*)-9-phenanthryl	66	36	5	1.1:1
3	**A3**, (*R*)-2,4,6-$Cy_3C_6H_2$	66	65	54	6.5:1
4	**A4**, (*R*)- 3,5-^{t}BuC_6H_3	64	12	-18	5.4:1
5	**A5**, (*R*)-3,5-$(CF_3)_2C_6H_3$	94	13	-37	7.5:1
6	**A6**, (*R*)-I	76	57	-1	1:1.4
7	**A7**, (*R*)-1-pyrenyl	73	5	13	1:1.1
8	**A8**, (*R*)-4-PhC_6H_4	78	9	-11	1:1.1
9	**A9**, (*R*)-3,5-$Ph_2C_6H_3$	85	1	-3	4:1
10	**A10**, (*R*)-1-naphthyl	83	3	1	1:1.2
11	**A11**, (*R*)-$SiPh_3$	84	7	-12	1.3:1

12	**A12**, (*R*)-2,4,6-$Me_3C_6H_2$	79	17	40	2.9:1
13	**A13**, (*R*)-2,4,6-$^{i}Pr_3C_6H_2$	68	-	11	>20:1
14	**A14**, (*R*)-3,5-$Me_2C_6H_3$	76	13	-31	1.8:1
15	**A15**, (*R*)-3,5-$Cl_2C_6H_3$	56	7	-10	1.4:1
16	**B1**, (*R*)-9-anthracenyl	90	37	12	2.4:1
17	**B2**, (*R*)-1-naphthyl	78	32	2	1:1.3
18	**B3**, (*R*)-2,4,6-$^{i}Pr_3C_6H_2$	52	60	48	9:1
19	**B4**, (*R*)- 3,5-$^{t}BuC_6H_3$	34	-10	-28	6.8:1
20	**B5**, (*R*)-I	80	78	12	1:1.1
21	**B6**, (*R*)-Br	80	66	18	1:1.2
22	**B7**, (*R*)-3,5-$(CF_3)_2C_6H_3$	70	-7	-33	4.2:1
23	**S1**, (*R*)-9-anthracenyl	77	63	41	13:1
24	**S2**, (*R*)-1-pyrenyl	74	72	76	6:1
25	**S3**, (*R*)-1-naphthyl	60	44	58	4.1:1
26	**S4**, (*R*)-2-naphthyl	73	44	66	6:1
27	**D1**, (*S*)-9-phenanthryl	72	-44	-57	12:1
28	**D2**, (*S*)- 3,5-$^{t}BuC_6H_3$	20	-	-	9:1
29	**D3**, (*S*)-3,5-$(CF_3)_2C_6H_3$	67	-52	-50	4.3:1
30	**E**, (*R*)-VAPOL	80	24	-14	2:1

[a]Reaction conditions: indolizine **1a** (0.030 mmol), *N*-Boc aminal **2a** (0.033 mmol), CPA (10 mol%), Toluene (0.3 mL). [b]Estimated by HPLC. [c]Determined by HPLC.

Table S2. Screening of solvents for reaction between indolizine **1a** and *N*-Boc aminal **2a** using **B5** catalyst[a]

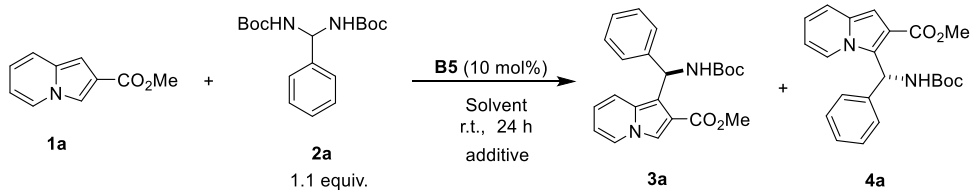


Entry	Solvent	Conversion (%)[b]	**3a** e.e. (%)[c]	**4a** e.e. (%)[c]	Ratio **4a**:**3a**
1	toluene	73	78	12	1:1.1
2	trifluorotoluene	87	67	-	1:1
3	chlorobenzene	80	76	-	1:1
4	*tert*-butylbenzene	78	73	-	1:1

5	*p*-xylene	84	81	-	1:1
6	benzene	75	82	-	1:1
7	hexafluorobenzene	70	55	-	3.3:1
8	DCM	78	45	2	1:1.4
9	DCE	72	32	-	1:1.7
10	tetrachloromethane	65	66	-	1.3:1
11	EtOAc	78	78	23	1:2
12	MeCN	0	-	-	-
13	isopropanol	62	10	-	1:1
14	hexane	80	64	-6	1.5:1

[a]Reaction conditions: indolizine **1a** (0.030 mmol), *N*-Boc aminal **2a** (0.033 mmol), CPA (10 mol%), Solvent (0.3 mL). [b]Estimated by HPLC. [c]Determined by HPLC.

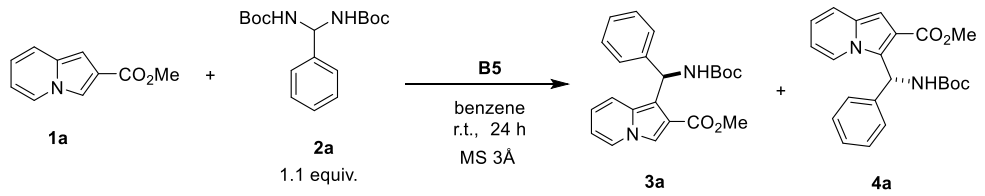
Table S3. Screening of additives for reaction between indolizine **1a** and *N*-Boc aminal **2a** using **B5** catalyst[a]



Entry	Additive	Conversion (%)[b]	**3a** e.e. (%)[c]	Ratio **4a**:**3a**
1	-	75	82	1:1
2	Na_2SO_4 (15 mg)	81	81	1.1:1
3	$MgSO_4$ (15 mg)	79	82	1.3:1
4	MS 3Å (15 mg)	84	91	1:1
5	MS 3Å (15 mg)	89	87	1:1
6	MS 3Å (7.5 mg)	82	91	1:1.1
7	MS 3Å (30 mg)	92	90	1:1

[a]Reaction conditions: indolizine **1a** (0.030 mmol), *N*-Boc aminal **2a** (0.033 mmol), **B5** (10 mol%), benzene (0.3 mL). [b]Estimated by HPLC. [c]Determined by HPLC.

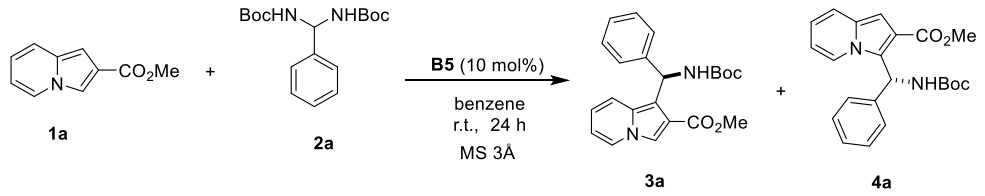
Table S4. Optimization of catalyst concentration for reaction between indolizine **1a** and *N*-Boc aminal **2a** using **B5** catalyst[a]



Entry	**B5** (%)	Conversion (%)[b]	**3a** e.e. (%)[c]	Ratio **4a**:**3a**
1	10	82	91	1:1.1
2	15	83	86	1:1.4
3	5	82	88	1:1

[a]Reaction conditions: indolizine **1a** (0.030 mmol), *N*-Boc aminal **2a** (0.033 mmol), MS 3Å (7.5 mg), benzene (0.3 mL). [b]Estimated by HPLC. [c]Determined by HPLC.

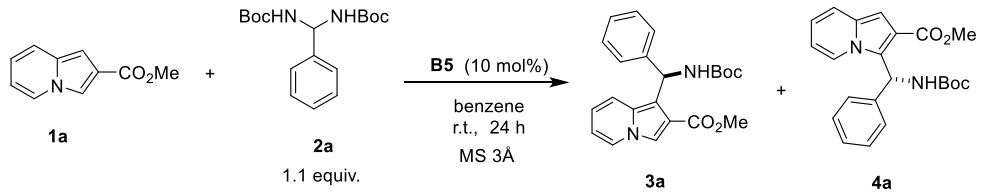
Table S5. Optimization of **2a** equivalents for reaction between indolizine **1a** and *N*-Boc aminal **2a** using **B5** catalyst[a]



Entry	**2a** (equiv.)	Conversion (%)[b]	**3a** e.e. (%)[c]	Ratio **4a**:**3a**
1	1.1	82	91	1:1.1
2	0.9	80	89	1:1.1
3	1.5	99	91	3.6:1
4	2.0	99	92	6.8:1
5	3.0	99	-	>20:1

[a]Reaction conditions: indolizine **1a** (0.030 mmol), MS 3Å (7.5 mg), **B5** (10 mol%), benzene (0.3 mL). [b]Estimated by HPLC. [c]Determined by HPLC.

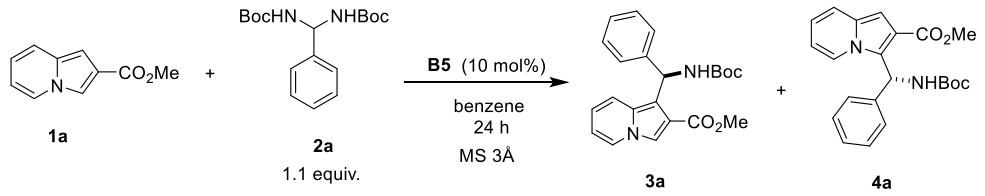
Table S6. Optimization of concentration of reaction between indolizine **1a** and *N*-Boc aminal **2a**[a] using **B5** catalyst



Entry	Concentration (mM)	Conversion (%)[b]	**3a** e.e. (%)[c]	Ratio **4a**:**3a**
1	0.10	82	91	1:1.1
2	0.15	80	88	1:1.2
3	0.05	88	93	1.1:1
4	0.03	83	93	1.4:1
5[d]	0.01	95	92	1.5:1

[a]Reaction conditions: indolizine **1a** (0.03 mmol), *N*-Boc aminal **2a** (0.033 mmol), **B5** (10 mol%), MS 3Å (7.5 mg). [b]Estimated by HPLC. [c]Determined by HPLC. [d]Time of the reaction = 72 hours.

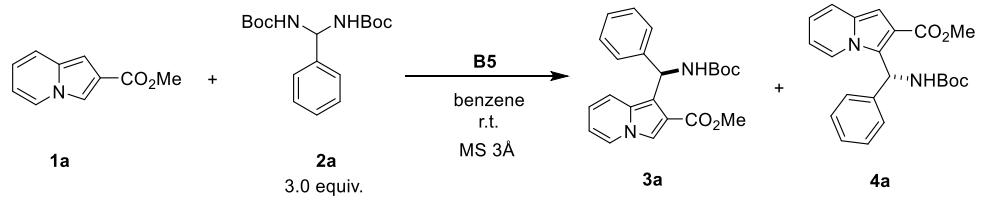
Table S7. Optimization of temperature of reaction between indolizine **1a** and *N*-Boc aminal **2a**[a] using **B5** catalyst



Entry	Solvent	T (°C)	Conversion (%)[b]	**3a** e.e. (%)[c]	Ratio **4a**:**3a**
1	benzene	r.t.	88	93	1.1:1
2	benzene	45	90	85	1.4:1
3	benzene	15	90	93	1:1
4[d]	benzene	10	95	94	1:1
5[e]	benzene:toluene (2:1)	-15	80	93	1:1
6[f]	benzene:toluene (1:2)	-30	84	94	1:1

[a]Reaction conditions: indolizine **1a** (0.030 mmol), *N*-Boc aminal **2a** (0.033 mmol), MS 3Å (7.5 mg), **B5** (10 mol%), benzene (0.6 mL). [b]Estimated by HPLC. [c]Determined by HPLC. [d]Time of the reaction = 48 hours. [e]Time of the reaction = 72 hours, solvent (1.0 mL). [f]Time of the reaction = 96 hours, solvent (2.0 mL).

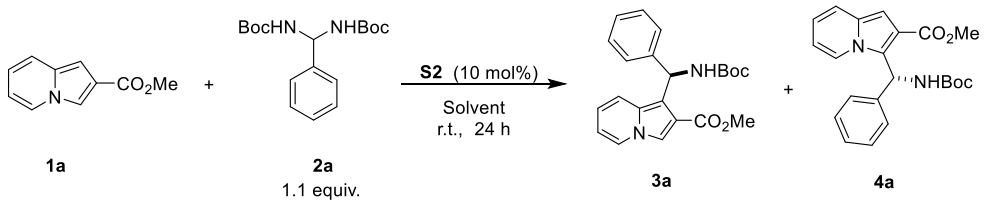
Table S8. Optimization of excess of **2a** equivalents for reaction between indolizine **1a** and *N*-Boc aminal **2a**[a] using **B5** catalyst



Entry	Solvent	**B5** (%)	Time (h)	Conversion (%)[b]	**3a** (e.e.) (%)[c]	Ratio **4a**:**3a**
1[d]	benzene	10	24	99	92	6.8:1
2	benzene	10	24	99	-	>20:1
3	benzene	15	0.67	99	-	17:1
4	toluene	15	0.67	99	92	1.6:1
5[e]	toluene	15	0.67	99	96	4.6:1
6[e]	toluene	18	0.67	99	98	3.3:1
7[e]	toluene	18	0.67	99	99	5:1

[a]Reaction conditions: indolizine **1a** (0.030 mmol), *N*-Boc aminal **2a** (0.09 mmol), MS 3Å (7.5 mg), solvent (0.3 mL). [b]Estimated by HPLC. [c]Determined by HPLC. [d]N-Boc aminal **2a** (0.06 mmol). [e]Toluene (1.0 mL).

Table S9. Screening of solvents for reaction between **1a** and **2a**[a] using **S2** catalyst



Entry	Solvent	Conversion (%)[b]	**4a** e.e. (%)[c]	**3a** e.e. (%)[c]	Ratio **4a**:**3a**
1	toluene	74	76	72	6:1

2	trifluorotoluene	55	81	-	>20:1
3	fluorobenzene	41	81	-	9:1
4	chlorobenzene	52	79	76	7:1
5	*tert*-butylbenzene	55	79	-	13:1
6	benzene	50	78	-	8:1
7	hexafluorobenzene	22	79	-	>20:1
8	*o*-xylene	55	80	-	12:1
9	*m*-xylene	50	81	-	13:1
10	*p*-xylene	76	81	-	>20:1
11	DCM	80	67	62	7:1
12	DCE	80	78	71	6.4:1
13	tetrachloromethane	67	74	-	7.5:1
14	$CHCl_3$	50	81	-	12:1
15	tetrachloroethylene	40	80	-	8:1
16[d]	1,1,1-trichloroethane	10	84	-	>20:1
17	EtOAc	12	62	42	1:1
18	Et_2O	48	79	-	15:1
19	vinyl acetate	No reaction	-	-	-

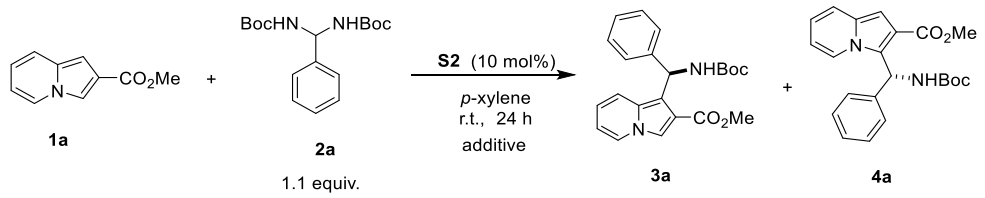
[a]Reaction conditions: indolizine **1a** (0.030 mmol), *N*-Boc aminal **2a** (0.033 mmol), **S2** (10 mol%), Solvent (0.3 mL). [b]Estimated by HPLC. [c]Determined by HPLC. [d]The reaction was left for additional one week of stirring but the conversion remained ≈ 10%.

Table S10. Optimization of **2a** equivalents for reaction between indolizine **1a** and *N*-Boc aminal **2a**[a] using **S2** catalyst

Entry	**2a** (equiv.)	Conversion (%)[b]	**4a** e.e. (%)[c]	Ratio **4a**:**3a**
1	1.1	76	81	>20:1
2[d]	1.1	73	80	9:1
3	0.8	55	75	16:1
4	2.0	85	77	17:1

[a]Reaction conditions: indolizine **1a** (0.03 mmol), **S2** (10 mol%), Solvent (0.3 mL). [b]Estimated by HPLC. [c]Determined by HPLC. [d]CPA (15 mol%).

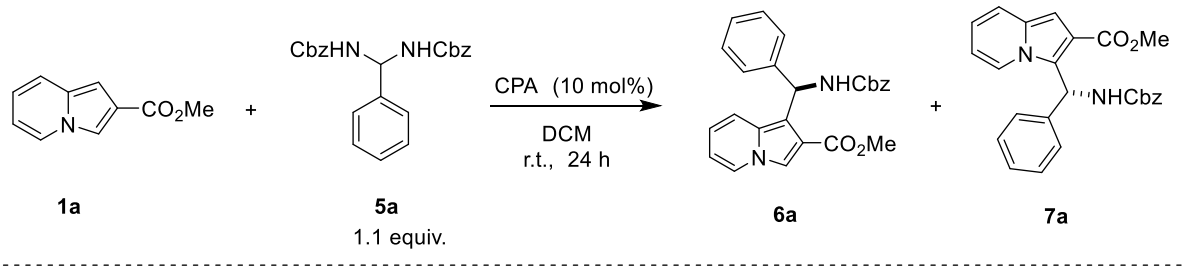
Table S11. Screening of additives for reaction between indolizine **1a** and *N*-Boc aminal **2a**[a] using **S2** catalyst



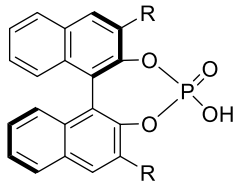
Entry	Additive	Conversion (%)[b]	**4a** e.e. (%)[c]	Ratio **4a:3a**
1	-	76	81	>20:1
2	MS 3Å	60	78	10:1
3	$MgSO_4$	80	78	7.5:1
4	Na_2SO_4	60	82	15:1

[a]Reaction conditions: indolizine **1a** (0.030 mmol), *N*-Boc aminal **2a** (0.033 mmol), **S2** (10 mol%), additive (15 mg), Solvent (0.3 mL). [b]Estimated by HPLC. [c]Determined by HPLC.

Table S12. Preliminary screening of catalysts for reaction between indolizine **1a** and *N*-Cbz aminal **5a**[a]

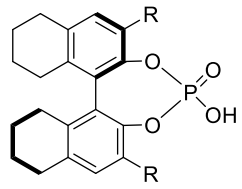


1a **5a** 1.1 equiv. **6a** **7a**



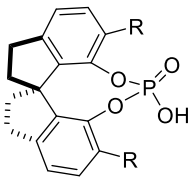
A

A1: R = 9-anthracyl
A2: R = 9-phenanthryl
A3: R = 2,4,6-$Cy_3C_6H_2$
A4: R = 3,5-^{t}BuC_6H_3
A5: R = 3,5-$(CF_3)_2C_6H_3$
A6: R = I
A8: R = 4-PhC_6H_4
A9: R = 3,5-$Ph_2C_6H_3$
A10: R = 1-naphthyl
A12: R = 2,4,6-$Me_3C_6H_2$
A13: R = 2,4,6-^{i}Pr$_3C_6H_2$
A14: R = 3,5-$Me_2C_6H_3$
A15: R = 3,5-$Cl_2C_6H_3$
A16: R = 3,5-$(NO_2)_2C_6H_3$
A17: R = 2-naphthyl
A18: R = C_6F_5
A19: R = 10-phenyl-9-anthracenyl



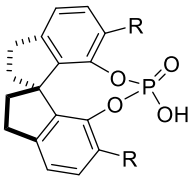
B

B1: R = 9-anthracyl
B2: R = 1-naphthyl
B3; R = 2,4,6-^{i}Pr$_3C_6H_2$
B4: R = 3,5-^{t}BuC_6H_3
B5: R = I
B6: R = Br
B7: R = 3,5-$(CF_3)_2C_6H_3$



S

S3: R = 1-naphthyl



D

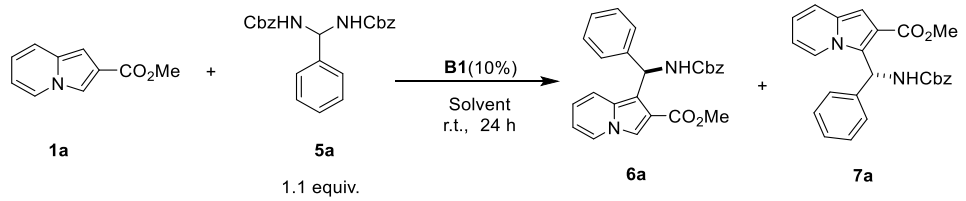
D1: R = 9-phenanthryl
D3: R = 3,5-$(CF_3)_2C_6H_3$

Entry	Catalyst	Conversion (%)[b]	**7a** e.e. (%)[c]	**6a** e.e. (%)[c]	Ratio **7a:6a**
1	**A1**, (*R*)-9-anthracenyl	82	22	78	1:1
2	**A2**, (*R*)-9-phenanthryl	70	4	12	1:1.5
3	**A3**, (*R*)-2,4,6-$Cy_3C_6H_2$	36	20	-	7.4:1
4	**A4**, (*R*)- 3,5-^{t}BuC_6H_3	68	-28	-	5:1
5	**A5**, (*R*)-3,5-$(CF_3)_2C_6H_3$	87	0	nd	1:1
6	**A6**, (*R*)-I	93	0	12	1:3.2
7	**A8**, (*R*)-4-PhC_6H_4	85	2	11	1:2

8	**A9**, (*R*)-3,5-$Ph_2C_6H_3$	85	-2	-6	1.3:1
9	**A10**, (*R*)-1-naphthyl	87	1	6	1:1.8
10	**A12**, (*R*)-2,4,6-$Me_3C_6H_2$	80	10	24	1.7:1
11	**A13**, (*R*)-2,4,6-$^{i}Pr_3C_6H_2$	63	24	-	4.9:1
12	**A14**, (*R*)-3,5-$Me_2C_6H_3$	76	-28	-24	1.9:1
13	**A15**, (*R*)-3,5-$Cl_2C_6H_3$	85	-1	-8	1:3.2
14	**A16**, (*R*)-3,5-$(NO_2)_2C_6H_3$	94	-4	4	1:2
15	**A17**, (*R*)-2-naphthyl	87	0	11	1:2.9
16	**A18**, (*R*)-C_6F_5	90	-4	-4	1:1.3
17	**A19**, 10-phenyl-9-anthracenyl	70	20	74	6.9:1
18	**B1**, (*R*)-9-anthracenyl	90	82	92	1.8:1
19	**B2**, (*R*)-1-naphthyl	78	6	36	1.8:1
20	**B3**, (*R*)-2,4,6-$^{i}Pr_3C_6H_2$	30	18	-	5.7:1
21	**B4**, (*R*)- 3,5-$^{t}BuC_6H_3$	35	-33	-	7.1:1
22	**B5**, (*R*)-I	93	2	12	1:3.8
23	**B6**, (*R*)-Br	96	4	4	1:3.1
24	**B7**, (*R*)-3,5-$(CF_3)_2C_6H_3$	72	-16	-2	3:1
25	**S3**, (*R*)-1-naphthyl	50	-30	-	4.6:1
26	**D1**, (*S*)-9-phenanthryl	65	2	54	4.6:1
27	**D3**, (*S*)-3,5-$(CF_3)_2C_6H_3$	61	-54	-	5.3:1

[a]Reaction conditions: indolizine **1a** (0.01 mmol), *N*-Cbz aminal **5a** (0.011 mmol), CPA (10 mol%), DCM (0.5 mL). [b]Estimated by HPLC. [c]Determined by HPLC. [d] Not determined.

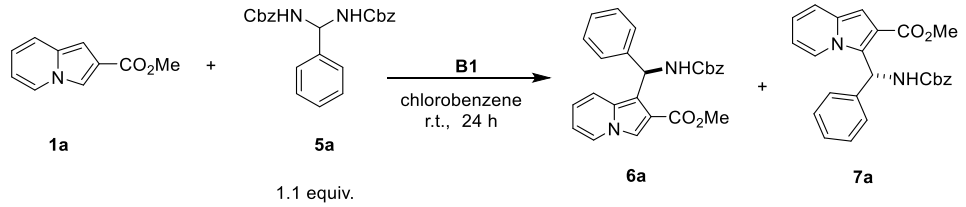
Table S13. Screening of solvents for reaction between indolizine **1a** and *N*-Cbz aminal **5a**[a]



Entry	Solvent	Conversion (%)[b]	**7a** e.e. (%)[c]	**6a** e.e. (%)[c]	Ratio **7a**:**6a**
1	toluene	93	84	86	5:1
2	trifluorotoluene	94	68	86	2.8:1
3	fluorobenzene	85	54	83	1.9:1
4	chlorobenzene	87	86	91	2.9:1
5	bromobenzene	82	80	89	3.3:1
6	*tert*-butylbenzene	90	60	70	3.1:1
7	*o*-xylene	100	71	80	1.9:1
8	*m*-xylene	95	71	81	2.8:1
9	*p*-xylene	88	67	78	2.4:1
10	benzene	86	63	87	1.7:1
11	hexafluorobenzene	71	3	24	1.8:1
12	DCM	90	82	92	1.8:1
13	DCE	72	76	90	2.2:1
14	$CHCl_3$	90	75	84	2.8:1
15	1,1,1-trichloroethane	<5	-	-	-
16	EtOAc	100	78	-	10:1
17	MeOH	95	4	10	1:1.2
18	Et_2O	<5	-	-	-
19	*tert*-butylmethyl ether	<5	-	-	-

[a]Reaction conditions: indolizine **1a** (0.010 mmol), *N*-Cbz aminal **5a** (0.011 mmol), **B1** (10 mol%), Solvent (0.5 mL). [b]Estimated by HPLC. [c]Determined by HPLC.

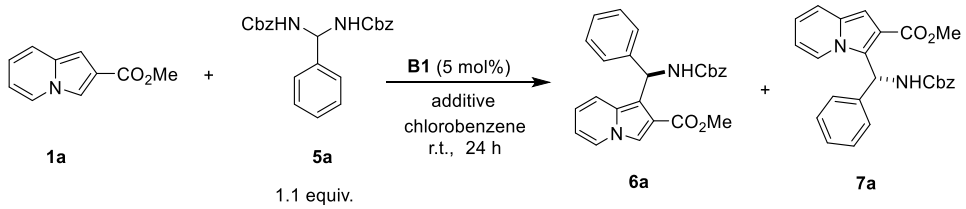
Table S14. Optimization of catalyst concentration for reaction between indolizine **1a** and *N*-Cbz aminal **5a**[a]



Entry	**B1** (%)	Conversion (%)[b]	**7a** e.e. (%)[c]	**6a** e.e. (%)[c]	Ratio **7a**:**6a**
1	10	87	86	91	2.9:1
2	20	95	82	89	2.7:1
3	5	90	89	-	5.1:1
4	2.5	68	89	-	4.7:1

[a]Reaction conditions: indolizine **1a** (0.010 mmol), *N*-Cbz aminal **5a** (0.011 mmol), chlorobenzene (0.5 mL). [b]Estimated by HPLC. [c]Determined by HPLC.

Table S15. Screening of additives for reaction between indolizine **1a** and *N*-Cbz aminal **5a**[a]

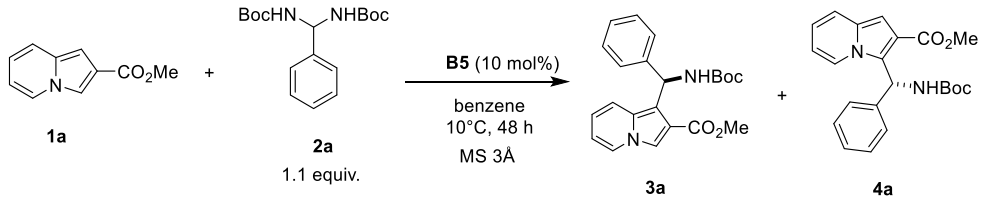


Entry	**5a** (equiv.)	Concen. (mM)	additive	Conv. (%)[b]	**7a** e.e. (%)[c]	Ratio **7a**:**6a**
1	1.1	0.02		90	89	5.1:1
2	1.1	0.02	MS 3Å	96	84	2.4:1
3	1.1	0.02	$MgSO_4$	90	86	4.4:1
4	1.1	0.02	Na_2SO_4	95	89	5.7:1
5	1.1	0.01	Na_2SO_4	83	92	9.2:1
6	1.1	0.005	Na_2SO_4	83	92	8.6:1
7	1.5	0.01	Na_2SO_4	98	92	9.2:1

8[d]	1.5	0.01	Na_2SO_4	23	93	19:1

[a]Reaction conditions: indolizine **1a** (0.01 mmol), **B1** (5 mol%), additive (12.5 mg). [b]Estimated by HPLC. [c]Determined by HPLC. [d]Temperature = 10 °C.

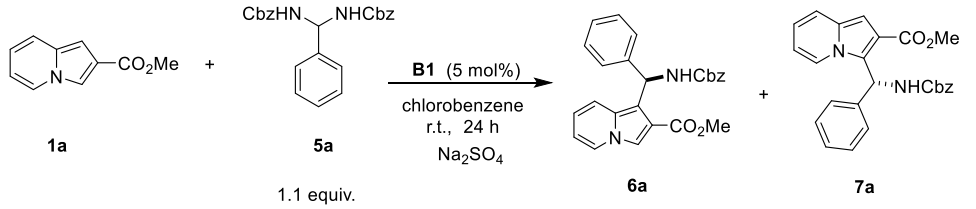
Table S16. Relation between overall e.e. of catalyst **B5** and e.e. of product **3a**[a]



Entry	Overall e.e. (%) of **B5**[b]	**3a** e.e. (%)[c]
1	100	94
2	90	86
3	70	70
4	50	53
5	40	43
6	20	22
7	0	3

[a]Reaction conditions: indolizine **1a** (0.030 mmol), *N*-Boc aminal **2a** (0.033 mmol), MS 3Å (7.5 mg), CPA (10 mol %), benzene (0.6 mL). [b] Enantiomeric excess of catalyst of catalyst **B5**. [c]Determined by HPLC.

Table S17. Relation between overall e.e. of catalyst **B1** and e.e. of product **7a**[a]



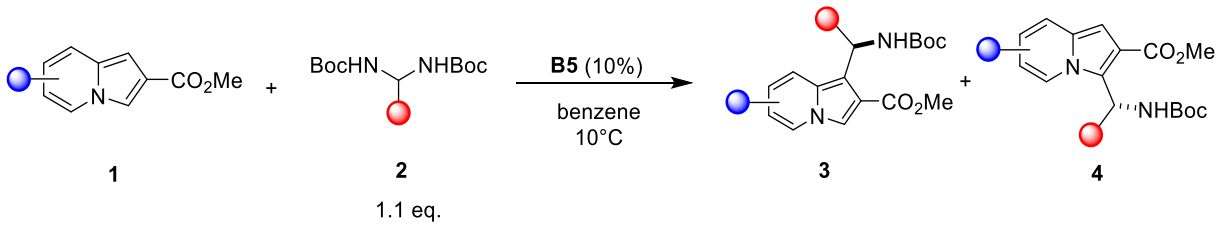
Entry	Overall e.e. (%) of **B1** [b]	**7a** e.e. (%)[c]
1	100	90
2	90	80
3	80	71
4	70	63

5	60	54
6	40	36
7	20	20
8	0	1

[a]Reaction conditions: indolizine **1a** (0.01 mmol), *N*-Cbz aminal **5a** (0.015 mmol), **B1** (5 mol%), Na_2SO_4 (12.5 mg) chlorobenzene (1.0 mL). [b]Enantiomeric excess of catalyst **B1**. [c]Determined by HPLC.

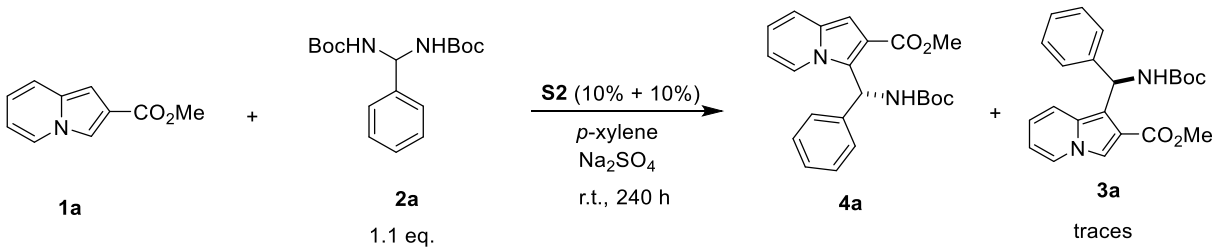
3. Asymmetric synthesis of chiral regioisomers

3.1. General procedure A



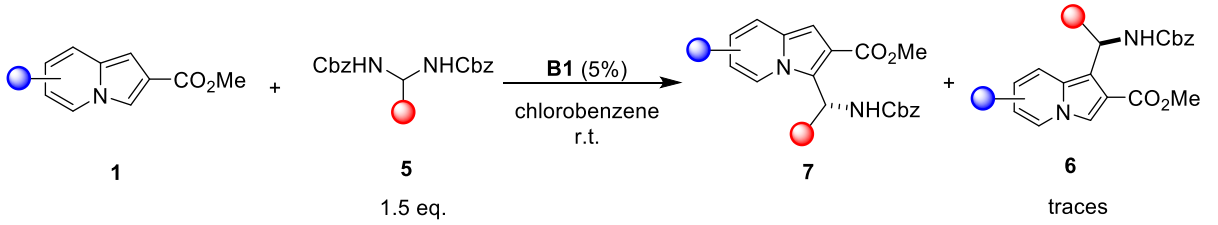
Indolizine **1** (0.457 mmol), catalyst **B5** (27.8 mg, 0.046 mmol) and Molecular sieves 3Å (114 mg) were dissolved in dry benzene (4.6 mL) at 10 °C under inert atmosphere. Then, a solution of *N*-Boc aminal **2** (0.503 mmol) in benzene (4.6 mL) was added to the reaction mixture and stirred at 10 °C until the starting material was finished (the reaction was followed by TLC).

3.3. Procedure B



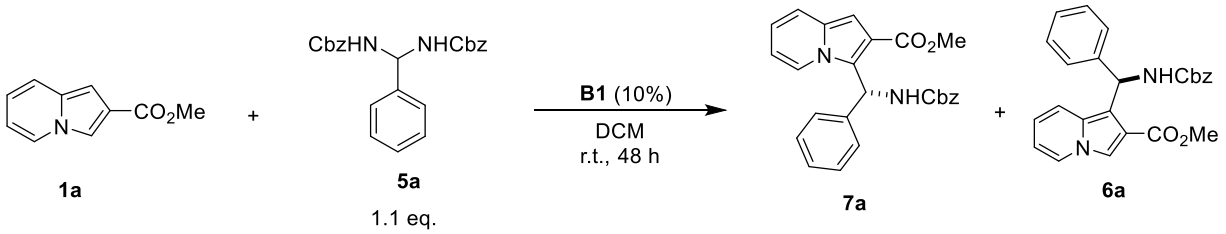
Indolizine **1a** (40.0 mg, 0.228 mmol), catalyst **S2** (16.3 mg, 0.023 mmol) and Na_2SO_4 (114.3 mg) were dissolved in dry *p*-xylene (1.15 mL) at room temperature under inert atmosphere. Then, a solution of *N*-Boc aminal **2a** (81.0 mg, 0.251 mmol) in dry *p*-xylene (1.15 mL) is added to the reaction mixture and stirred at room temperature for 10 days (additional 16.3 mg of **S2** catalyst was added after 5 days of the reaction). Purification of the reaction mixture by Flash chromatography (85:15 hexane/dichloromethane to 70:30 hexane/dichloromethane + 0.25% Et_3N).

3.4. General procedure C



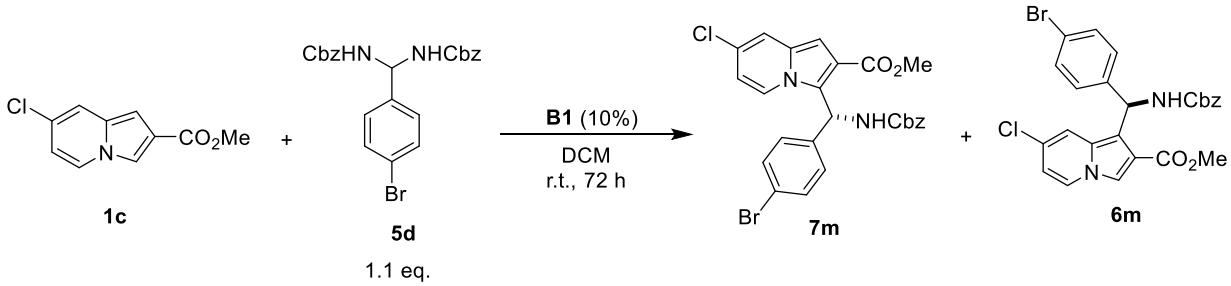
To a mixture of Indolizine **1** (0.342 mmol), *N*-Cbz aminal **5** (0.514 mmol), **B1** catalyst (12.1 mg, 0.071 mmol) and Na_2SO_4 (429 mg) was added dry chlorobenzene (34.3 mL) at room temperature under inert atmosphere. Then, the reaction mixture was stirred at room temperature until the starting material is finished (the reaction is followed by TLC).

3.5. Procedure D



Indolizine **1a** (210.0 mg, 1.20 mmol), *N*-Cbz aminal **5a** (515.0 mg, 1.32 mmol) and **B1** catalyst (85.1 mg, 0.12 mmol) were dissolved in dry DCM (60.0 mL) at room temperature under inert atmosphere. Then, the reaction mixture was stirred at room temperature for 48 h. Purification by Flash chromatography (80:20 hexane/dichloromethane to 70:30 hexane/dichloromethane + 0.25% Et_3N).

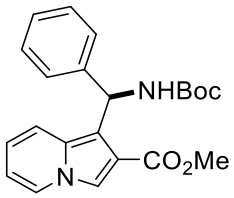
3.6. Procedure E



Indolizine **1c** (84.0 mg, 0.40 mmol), *N*-Cbz aminal **5d** (206.0 mg, 0.44 mmol) and **B1** catalyst (28.4 mg, 0.04 mmol) were dissolved in dry DCM (20.0 mL) at room temperature under inert atmosphere. Then, the reaction mixture was stirred at room temperature for 72 h. Purification by Flash chromatography (90:10 hexane/ethyl acetate to 80:20 hexane/ethyl acetate + 0.25% Et_3N).

3.7. Products with Boc-protecting group 3a-s, 4a-s and 10

Methyl (*R*)-1-(((tert-butoxycarbonyl)amino)(phenyl)methyl)indolizine-2-carboxylate 3a



3a and **4a** were prepared according to the **General Procedure A**. Purification by Flash chromatography (85:15 hexane/dichloromethane to 70:30 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 56 mg, 32% yield, 96% e.e..

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80-7.75 (m, 1H), 7.77 (s, 1H), 7.61 (d, *J* = 9.3 Hz, 1H), 7.26-7.21 (m, 4H), 7.19-7.13 (m, 1H), 7.08 (d, *J* = 9.9 Hz, 1H), 6.71 (dd, *J* = 9.3, 6.4 Hz, 1H), 6.58-6.50 (m, 2H), 3.73 (s, 3H), 1.48 (s, 9H).

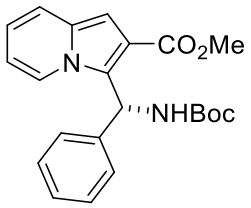
^{13}C NMR (151 MHz, $CDCl_3$) δ 165.9(C), 156.0(C), 143.1(C), 131.3(C), 128.1(2CH), 126.5(CH), 126.1(2CH), 125.2(CH), 118.7(CH), 118.5(CH), 117.7(CH), 116.4(C), 114.8(C), 112.8(CH), 79.2(C), 51.6(CH_3), 48.9(CH), 28.63(3CH_3).

HRMS $[M+Na]^+$ calculated for $C_{22}H_{24}N_2O_4Na$ 403.1634 found 403.1636.

$[\alpha]^{25}_D$ = 65.8 (*c* = 0.21, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 10% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 8.5 min (minor), 18.7 min (major).

Methyl (*R*)-3-(((tert-butoxycarbonyl)amino)(phenyl)methyl)indolizine-2-carboxylate 4a



Colorless oil, 73 mg, 42% yield, 37% e.e. (**Procedure A**).

Colorless oil, 75 mg, 86% yield, 82% e.e. (**Procedure B**).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.3 Hz, 1H), 7.40 (d, *J* = 9.1 Hz, 1H), 7.31-7.18 (m, 4H), 7.16 (d, *J* = 7.6 Hz, 2H), 6.92 (s, 1H), 6.76 (d, *J* = 9.8 Hz, 1H), 6.72 (dd, *J* = 9.1, 6.4 Hz, 1H), 6.61-6.57 (m, 1H), 3.80 (s, 3H), 1.46 (s, 9H).

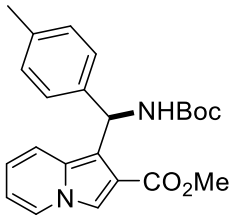
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.4(C), 156.1(C), 140.5(C), 131.7(C), 128.6(2CH), 128.2(C), 127.3(CH), 126.1(2CH), 122.4(CH), 120.7(CH), 118.2(CH), 116.8(C), 113.1(CH), 102.2(CH), 79.8(C), 51.9(CH_3), 48.7(CH), 28.6(3CH_3).

HRMS $[M+Na]^+$ calculated for $C_{22}H_{24}N_2O_4Na$ 403.1634 found 403.1639.

$[\alpha]^{25}_D$ = 11.9 (*c* = 0.25, CH_2Cl_2) (for 82% e.e.) (**Procedure B**).

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 1% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 14.1 min (minor), 18.5 min (major) (**Procedure B**).

Methyl (*R*)-1-(((tert-butoxycarbonyl)amino)(p-tolyl)methyl)indolizine-2-carboxylate 3b



The two regioisomers **3b** and **4b** were prepared according to the General **Procedure A** (reaction time = 4 h). Purification by Flash chromatography (90:10 hexane/dichloromethane to 80:20 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 55 mg, 31% yield, 94% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85-7.76 (m, 2H), 7.60 (d, *J* = 9.3 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 2H), 7.09-6.98 (m, 3H), 6.71 (ddd, *J* = 9.3, 6.5, 1.1 Hz, 1H), 6.58-6.46 (m, 2H), 3.76 (s, 3H), 2.28 (s, 3H), 1.46 (s, 9H).

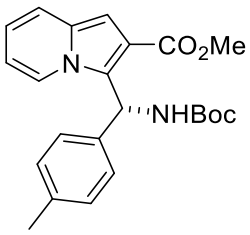
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 156.0, 140.2, 136.0, 131.3, 128.9(2C), 126.1(2C), 125.2, 118.64, 118.63, 117.7, 116.5, 115.1, 112.8, 79.1, 51.7, 48.8, 28.7(3C), 21.1.

HRMS $[M+Na]^+$ calculated for $C_{23}H_{26}N_2O_4Na$ 417.1790 found 417.1776.

$[\alpha]^{25}_D$ = 39.8 (*c* = 0.28, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 10% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 10.6 min (minor), 21.6 min (major).

Methyl (*R*)-3-(((*tert*-butoxycarbonyl)amino)(*p*-tolyl)methyl)indolizine-2-carboxylate 4b



Colorless oil, 86 mg, 48% yield, 43% e.e..

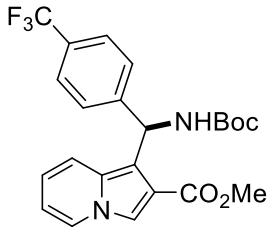
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08-7.97 (m, 1H), 7.39 (d, *J* = 9.1 Hz, 1H), 7.27 (bs, 1H), 7.10-7.01 (m, 4H), 6.91 (s, 1H), 6.76-6.67 (m, 2H), 6.61-6.54 (m, 1H), 3.81 (s, 3H), 2.28 (s, 3H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 156.1, 137.4, 136.9, 131.6, 129.3(2C), 128.3, 126.1(2C), 122.4, 120.6, 118.3, 116.8, 113.0, 102.2, 79.7, 51.8, 48.6, 28.6(3C), 21.1.

HRMS $[M+Na]^+$ calculated for $C_{23}H_{26}N_2O_4Na$ 417.1790 found 417.1783.

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 1% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 15.0 min (minor), 18.9 min (major).

Methyl (*R*)-1-(((*tert*-butoxycarbonyl)amino)(4-(trifluoromethyl)phenyl)methyl)indolizine-2-carboxylate 3c



The two regioisomers **3c** and **4c** were prepared according to the **General Procedure A** (reaction time = 38 h). Purification by Flash chromatography (80:20 hexane/dichloromethane to 65:35 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 98 mg, 48% yield, 87% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.4 Hz, 1H), 7.81 (s, 1H), 7.61 (d, *J* = 9.3 Hz, 1H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.04 (d, *J* = 9.8 Hz, 1H), 6.77 (dd, *J* = 9.3, 6.5 Hz, 1H), 6.61 – 6.53 (m, 2H), 3.76 (s, 3H), 1.47 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 156.0, 147.3, 131.5, 128.8, 126.5(2C), 125.4, 125.1(2C), 124.4 (d, *J* = 271.9 Hz), 119.2, 118.3, 117.9, 116.3, 114.0, 113.1, 79.6, 51.8, 48.7, 28.6(3C).

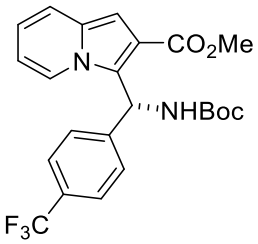
^{19}F NMR (470 MHz, $CDCl_3$) δ -62.35.

HRMS $[M+Na]^+$ calculated for $C_{23}H_{23}N_2O_4F_3Na$ 471.1508 found 471.1511.

$[\alpha]^{25}_D$ = 88.0 (*c* = 0.14, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 8.6 min (major), 12.5 min (minor).

Methyl (*R*)-3-(((*tert*-butoxycarbonyl)amino)(4-(trifluoromethyl)phenyl)methyl)indolizine-2-carboxylate 4c



Colorless oil, 86 mg, 42% yield, 63% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.3 Hz, 1H), 7.51 (d, *J* = 8.1 Hz, 2H), 7.42 (d, *J* = 9.1 Hz, 1H), 7.31 – 7.21 (m, 3H), 6.92 (s, 1H), 6.79 (d, *J* = 9.7 Hz, 1H), 6.75 (dd, *J* = 9.1, 6.5 Hz, 1H), 6.67 – 6.61 (m, 1H), 3.79 (s, 3H), 1.46 (s, 9H).

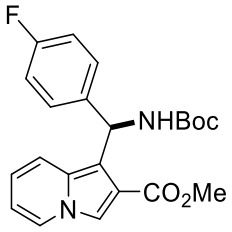
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 156.2, 144.7, 131.9, 129.6, 127.4, 126.4(2C), 125.5(2C), 124.3, 122.1, 120.8, 118.4, 116.9, 113.5, 102.4, 80.2, 52.0, 48.3, 28.6(3C).

^{19}F NMR (470 MHz, $CDCl_3$) δ -62.52.

HRMS $[M+Na]^+$ calculated for $C_{23}H_{23}N_2O_4F_3Na$ 471.1508 found 471.1512.

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 0.3% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 18.1 min (minor), 22.0 min (major).

Methyl (*R*)-1-(((tert-butoxycarbonyl)amino)(4-fluorophenyl)methyl)indolizine-2-carboxylate 3d



The two regioisomers **3d** and **4d** were prepared according to the **General Procedure A** (reaction time = 6 h). Purification by Flash chromatography (80:20 hexane/dichloromethane to 60:40 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 100 mg, 55% yield, 94% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 6.5 Hz, 1H), 7.80 (s, 1H), 7.60 (d, *J* = 9.3 Hz, 1H), 7.17 (dd, *J* = 8.4, 5.3 Hz, 2H), 6.99 (d, *J* = 9.8 Hz, 1H), 6.93 – 6.87(m, 2H), 6.74 (dd, *J* = 9.3, 6.4 Hz, 1H), 6.59 – 6.54 (m, 1H), 6.49 (d, *J* = 9.8 Hz, 1H), 3.76 (s, 3H), 1.46 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 161.7, 156.0, 138.9, 131.3, 127.8(2C), 125.3, 119.0, 118.5, 117.8, 116.4, 114.9(2C), 114.7, 113.0, 79.4, 51.8, 48.4, 28.7(3C).

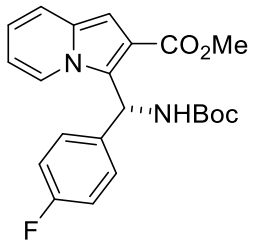
^{19}F NMR (470 MHz, $CDCl_3$) δ -117.30.

HRMS $[M+H]^+$ calculated for $C_{22}H_{23}FN_2O_4Na$ 421.1540 found 421.1537.

$[\alpha]^{25}_D$ = 74.2 (*c* = 0.13, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 13.1 min (major), 22.1 min (minor).

Methyl (*R*)-3-(((*tert*-butoxycarbonyl)amino)(4-fluorophenyl)methyl)indolizine-2-carboxylate 4d



Colorless oil, 74 mg, 41% yield, 54% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 6.1 Hz, 1H), 7.40 (d, *J* = 9.1 Hz, 1H), 7.28 (bs, 1H), 7.11 (dd, *J* = 8.5, 5.3 Hz, 2H), 6.94 (d, *J* = 8.5 Hz, 2H), 6.92 (s, 1H), 6.76 – 6.68 (m, 2H), 6.64 – 6.58 (m, 1H), 3.81 (s, 3H), 1.45 (s, 9H).

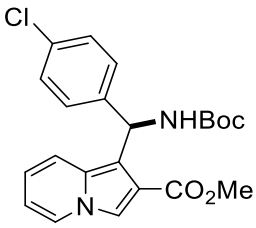
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 162.1, 156.1, 136.3, 131.7, 127.9, 127.8(2C), 122.2, 120.7, 118.3, 116.8, 115.4(2C), 113.3, 102.3, 79.9, 51.9, 48.1, 28.6(3C).

^{19}F NMR (470 MHz, $CDCl_3$) δ -115.78.

HRMS $[M+H]^+$ calculated for $C_{22}H_{23}FN_2O_4Na$ 421.1540 found 421.1544.

HPLC analysis of the product: Daicel CHIRALPAK IC column; 1% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 10.3 min (major), 12.6 min (minor).

Methyl (*R*)-1-(((*tert*-butoxycarbonyl)amino)(4-chlorophenyl)methyl)indolizine-2-carboxylate 3e



The two regioisomers **3e** and **4e** were prepared according to the **General Procedure A** (reaction time = 6 h). Purification by Flash chromatography (80:20 hexane/dichloromethane to 60:40 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 102 mg, 54% yield, 90% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.0 Hz, 1H), 7.80 (s, 1H), 7.60 (d, *J* = 9.3 Hz, 1H), 7.18 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 8.2 Hz, 2H), 6.98 (d, *J* = 9.8 Hz, 1H), 6.75 (dd, *J* = 9.3, 6.5 Hz, 1H), 6.60 – 6.54 (m, 1H), 6.48 (d, *J* = 9.8 Hz, 1H), 3.77 (s, 3H), 1.46 (s, 9H).

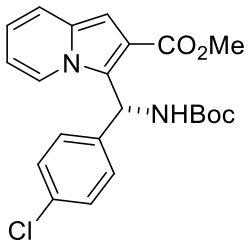
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 156.0, 141.8, 132.3, 131.4, 128.2(2C), 127.6(2C), 125.3, 119.1, 118.4, 117.8, 116.4, 114.4, 113.0, 79.5, 51.8, 48.4, 28.7(3C).

HRMS [M+Na]$^+$ calculated for $C_{22}H_{23}N_2O_4ClNa$ 437.1244 found 437.1248.

[α]$^{25}_D$ = 91.5 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 10% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 8.3 min (minor), 19.3 min (major).

Methyl (*R*)-3-(((*tert*-butoxycarbonyl)amino)(4-chlorophenyl)methyl)indolizine-2-carboxylate 4e



Colorless oil, 74 mg, 39% yield, 57% e.e..

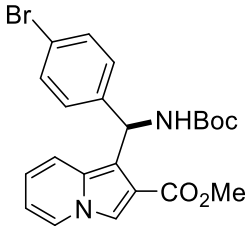
^{1}H NMR (200 MHz, CDCl3) δ 8.04 (d, *J* = 7.3 Hz, 1H), 7.40 (d, *J* = 8.9 Hz, 1H), 7.28 – 7.17 (m, 3H), 7.07 (d, *J* = 8.4 Hz, 2H), 6.91 (s, 1H), 6.78 – 6.66 (m, 2H), 6.66 – 6.57 (m, 1H), 3.80 (s, 3H), 1.45 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 156.1, 139.2, 133.1, 131.8, 128.7(2C), 127.7, 127.6(2C), 122.2, 120.8, 118.3, 116.8, 113.4, 102.3, 80.0, 52.0, 48.1, 28.6(3C).

HRMS [M+Na]$^+$ calculated for $C_{22}H_{23}N_2O_4ClNa$ 437.1244 found 437.1242.

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 0.3% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 22.5 min (minor), 26.0 min (major).

Methyl (*R*)-1-((4-bromophenyl)((tert-butoxycarbonyl)amino)methyl)indolizine-2-carboxylate 3f



The two regioisomers **3f** and **4f** were prepared according to the **General Procedure A** (reaction time = 6 h). Purification by Flash chromatography (90:10 hexane/dichloromethane to 80:20 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 113 mg, 54% yield, 93% e.e..

^{1}H NMR (500 MHz, CDCl3) δ 7.82 (d, *J* = 7.0 Hz, 1H), 7.80 (s, 1H), 7.59 (d, *J* = 9.3 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 6.98 (d, *J* = 9.8 Hz, 1H), 6.75 (dd, *J* = 9.3, 6.9 Hz, 1H), 6.60-6.54 (m, 1H), 6.46 (d, *J* = 9.8 Hz, 1H), 3.76 (s, 3H), 1.46 (s, 9H).

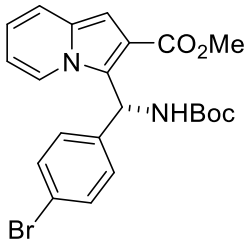
^{13}C NMR (126 MHz, CDCl3) δ 165.9, 156.0, 142.3, 131.4, 131.2(2C), 128.0(2C), 125.3, 120.4, 119.1, 118.4, 117.8, 116.4, 114.3, 113.0, 79.5, 51.8, 48.5, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{22}H_{23}N_2O_4BrNa$ 481.0739 found 481.0737.

$[\alpha]^{25}_D$ = 55.8 (*c* = 0.29, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 13.2 min (major), 20.4 min (minor).

Methyl (*R*)-3-((4-bromophenyl)((*tert*-butoxycarbonyl)amino)methyl)indolizine-2-carboxylate 4f



Colorless oil, 90 mg, 43% yield, 60% e.e..

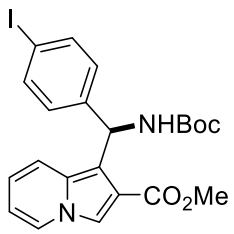
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 9.1 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.24 (bs, 1H), 7.02 (d, *J* = 8.2 Hz, 2H), 6.91 (s, 1H), 6.73 (dd, *J* = 9.1, 6.7 Hz, 1H), 6.69 (d, *J* = 9.8 Hz, 1H), 6.65 – 6.58 (m, 1H), 3.81 (s, 3H), 1.45 (s, 9H).

^{13}C NMR (126 MHz, $cdcl_3$) δ 166.4, 156.1, 139.7, 131.8, 131.6(2C), 127.9(2C), 127.6, 122.2, 121.3, 120.8, 118.3, 116.8, 113.4, 102.3, 80.0, 52.0, 48.2, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{22}H_{23}N_2O_4BrNa$ 481.0739 found 481.0735.

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 0.3% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 22.2 min (minor), 25.6 min (major).

Methyl (*R*)-1-(((*tert*-butoxycarbonyl)amino)(4-iodophenyl)methyl)indolizine-2-carboxylate 3g



The two regioisomers **3g** and **4g** were prepared according to the **General Procedure A** (reaction time = 48 h). Purification by Flash chromatography (80:20 hexane/dichloromethane to 60:40 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 97 mg, 42% yield, 90% e.e..

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.0 Hz, 1H), 7.79 (s, 1H), 7.59 (d, *J* = 9.2 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.01 – 6.98 (m, 1H), 6.97 (d, *J* = 8.4 Hz, 2H), 6.75 (ddd, *J* = 9.2, 6.4, 1.0 Hz, 1H), 6.59 – 6.54 (m, 1H), 6.45 (d, *J* = 9.9 Hz, 1H), 3.77 (s, 3H), 1.45 (s, 9H).

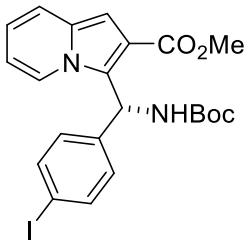
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 156.0, 143.1, 137.1(2C), 131.4, 128.3(2C), 125.3, 119.1, 118.4, 117.8, 116.4, 114.2, 113.0, 92.0, 79.5, 51.8, 48.6, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{22}H_{23}N_2O_4INa$ 529.0600 found 529.0595.

$[\alpha]^{25}_D$ = 48.0 (*c* = 0.26, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 14.0 min (major), 20.8 min (minor).

Methyl (*R*)-3-(((*tert*-butoxycarbonyl)amino)(4-iodophenyl)methyl)indolizine-2-carboxylate 4g



Colorless oil, 103 mg, 45% yield, 67% e.e..

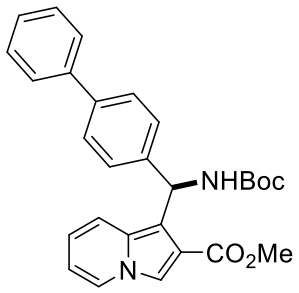
^{1}H NMR (200 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.3 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.9 Hz, 1H), 7.20 (bs, 1H), 6.95 – 6.84 (m, 3H), 6.80 – 6.57 (m, 3H), 3.81 (s, 3H), 1.45 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 156.1, 140.5, 137.6(2C), 131.8, 128.2(2C), 127.5, 122.2, 120.8, 118.3, 116.8, 113.4, 102.3, 92.9, 80.0, 52.0, 48.3, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{22}H_{23}N_2O_4INa$ 529.0600 found 529.0599.

HPLC analysis of the product: Daicel CHIRALPAK IC column; 1% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 11.8 min (major), 14.3 min (minor).

Methyl (*R*)-1-([1,1'-biphenyl]-4-yl((*tert*-butoxycarbonyl)amino)methyl)indolizine-2-carboxylate 3h



The two regioisomers **3h** and **4h** were prepared according to the **General Procedure A** (reaction time = 24 h). Purification by Flash chromatography (75:25 hexane/dichloromethane to 70:30 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 83 mg, 40% yield, 96% e.e..

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85 – 7.80 (m, 2H), 7.65 (d, *J* = 9.3 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.42 – 7.37 (m, 2H), 7.34 – 7.27 (m, 3H), 7.09 (d, *J* = 9.8 Hz, 1H), 6.75 (dd, *J* = 9.3, 6.5 Hz, 1H), 6.61 – 6.54 (m, 2H), 3.78 (s, 3H), 1.48 (s, 9H).

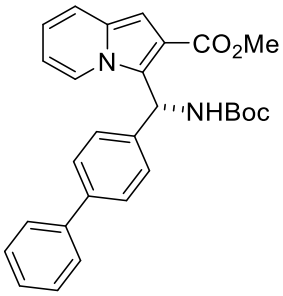
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.0, 156.1, 142.3, 141.2, 139.4, 131.4, 128.8(2C), 127.1, 127.1(2C), 126.9(2C), 126.6(2C), 125.3, 118.8, 118.6, 117.7, 116.5, 114.8, 113.0, 79.3, 51.8, 48.8, 28.7(3C).

HRMS $[M+Na]^+$ calculated for $C_{28}H_{28}N_2O_4Na$ 479.1947 found 479.1950.

$[\alpha]^{25}_D$ = 46.2 (*c* = 0.26, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 10% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 13.9 min (minor), 27.7min (major).

Methyl (*R*)-3-([1,1'-biphenyl]-4-yl((*tert*-butoxycarbonyl)amino)methyl)indolizine-2-carboxylate 4h



Colorless oil, 96 mg, 46% yield, 51% e.e..

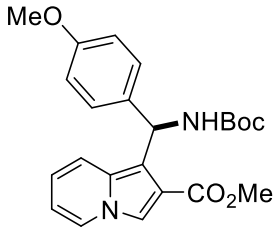
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.0 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 2H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.44 – 7.38 (m, 3H), 7.37 – 7.29 (m, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 6.95 (s, 1H), 6.81 (d, *J* = 9.4 Hz, 1H), 6.74 (ddd, *J* = 9.1, 6.4, 0.9 Hz, 1H), 6.65 – 6.59 (m, 1H), 3.83 (s, 3H), 1.48 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.5, 156.2, 140.9, 140.2, 139.6, 131.7, 128.8(2C), 128.1, 127.3, 127.3(2C), 127.1(2C), 126.6(2C), 122.4, 120.7, 118.2, 116.8, 113.2, 102.3, 79.8, 51.9, 48.5, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{28}H_{28}N_2O_4Na$ 479.1947 found 479.1950.

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 0.3% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 45.9 min (minor), 55.3 min (major).

Methyl (*R*)-1-(((tert-butoxycarbonyl)amino)(4-methoxyphenyl)methyl)indolizine-2-carboxylate 3i



The two regioisomers **3i** and **4i** were prepared according to the **General Procedure A** (reaction time = 4 h). Purification by Flash chromatography (50:50 hexane/dichloromethane to 30:70 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 48 mg, 26% yield, 68% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (m, 2H), 7.60 (d, *J* = 9.2 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 9.7 Hz, 1H), 6.76 (d, *J* = 8.4 Hz, 2H), 6.71 (ddd, *J* = 9.2, 6.5, 1.1 Hz, 1H), 6.58 – 6.52 (m, 1H), 6.48 (d, *J* = 9.7 Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 1.46 (s, 9H).

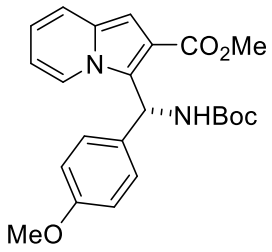
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 158.3, 156.0, 135.4, 131.2, 127.3(2C), 125.2, 118.7, 118.7, 117.7, 116.5, 115.1, 113.5(2C), 112.9, 79.2, 55.3, 51.7, 48.5, 28.7(3C).

HRMS $[M+Na]^+$ calculated for $C_{23}H_{26}N_2O_5Na$ 433.1739 found 433.1742.

$[\alpha]^{25}_D$ = 28.8 (*c* = 0.26, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 20% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 9.6 min (minor), 14.2 min (major).

Methyl (*R*)-3-(((tert-butoxycarbonyl)amino)(4-methoxyphenyl)methyl)indolizine-2-carboxylate 4i



Colorless oil, 131 mg, 70% yield, 21% e.e..

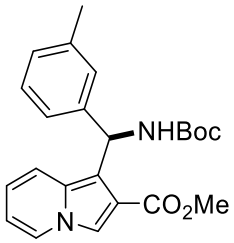
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 9.0 Hz, 1H), 7.30 (bs, 1H), 7.08 (d, *J* = 8.5 Hz, 2H), 6.91 (s, 1H), 6.78 (d, *J* = 8.5 Hz, 2H), 6.74 – 6.65 (m, 2H), 6.61 – 6.55 (m, 1H), 3.82 (s, 3H), 3.75 (s, 3H), 1.45 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 158.9, 156.1, 132.6, 131.6, 128.3, 127.4(2C), 122.4, 120.7, 118.1, 116.8, 114.0(2C), 113.1, 102.2, 79.7, 55.4, 51.9, 48.4, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{23}H_{26}N_2O_5Na$ 433.1739 found 433.1738.

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 1% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 27.5 min (minor), 31.2 min (major).

Methyl (*R*)-1-(((tert-butoxycarbonyl)amino)(m-tolyl)methyl)indolizine-2-carboxylate 3j



The two regioisomers **3j** and **4j** were prepared according to the **General Procedure A** (reaction time = 4 h). Purification by Flash chromatography (60:40 hexane/dichloromethane to 40:60 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 86 mg, 48% yield, 92% e.e..

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 – 7.78 (m, 2H), 7.61 (d, *J* = 9.3 Hz, 1H), 7.14 – 7.09 (m, 1H), 7.05 – 6.99 (m, 3H), 6.97 (d, *J* = 9.9 Hz, 1H), 6.72 (dd, *J* = 9.3, 6.4 Hz, 1H), 6.58 – 6.54 (m, 1H), 6.49 (d, *J* = 9.9 Hz, 1H), 3.76 (s, 3H), 2.27 (s, 3H), 1.46 (s, 9H).

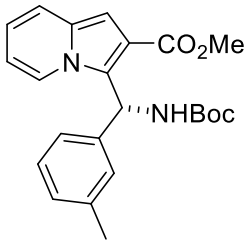
^{13}C NMR (151 MHz, $CDCl_3$) δ 166.0, 156.1, 143.1, 137.6, 131.4, 128.0, 127.4, 127.0, 125.2, 123.2, 118.7(2C), 117.7, 116.5, 115.0, 112.9, 79.2, 51.7, 48.9, 28.7, 21.7(3C).

HRMS $[M+Na]^+$ calculated for $C_{23}H_{26}N_2O_4Na$ 417.1790 found 417.1788.

$[\alpha]^{25}_D$ = 59.4 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 10% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 8.3 min (minor), 16.4 min (major).

Methyl (*R*)-3-(((*tert*-butoxycarbonyl)amino)(*m*-tolyl)methyl)indolizine-2-carboxylate 4j



Colorless oil, 70 mg, 39% yield, 39% e.e..

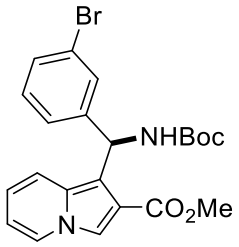
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 – 8.00 (m, 1H), 7.40 (d, *J* = 9.1 Hz, 1H), 8.25 (bs, 1H), 7.16 – 7.11 (m, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 6.98 (s, 1H), 6.94 – 6.90 (m, 2H), 6.74 – 6.68 (m, 2H), 6.62 – 6.57 (m, 1H), 3.81 (s, 3H), 2.27 (s, 3H), 1.45 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.5, 156.2, 140.4, 138.2, 131.6, 128.5, 128.3, 128.2, 126.9, 123.2, 122.4, 120.7, 118.1, 116.8, 113.1, 102.2, 79.7, 51.9, 48.7, 28.6, 21.7(3C).

HRMS $[M+Na]^+$ calculated for $C_{23}H_{26}N_2O_4Na$ 417.1790 found 417.1789.

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 1% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 12.0 min (minor), 14.7 min (major).

Methyl (*R*)-1-((3-bromophenyl)((*tert*-butoxycarbonyl)amino)methyl)indolizine-2-carboxylate 3k



The two regioisomers **3k** and **4k** were prepared according to the **General Procedure A** (reaction time = 22 h). Purification by Flash chromatography (50:50 hexane/dichloromethane to 40:60 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 111 mg, 53% yield, 85% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.0 Hz, 1H), 7.81 (s, 1H), 7.59 (d, *J* = 9.3 Hz, 1H), 7.32 (s, 1H), 7.28 (d, *J* = 7.9 Hz, 1H), 7.16 (d, *J* = 7.8 Hz, 1H), 7.12 – 7.06 (m, 1H), 6.95 (d, *J* = 9.8 Hz, 1H), 6.76 (dd, *J* = 9.3, 6.5 Hz, 1H), 6.61 – 6.54 (m, 1H), 6.49 (d, *J* = 9.8 Hz, 1H), 3.77 (s, 3H), 1.46 (s, 9H).

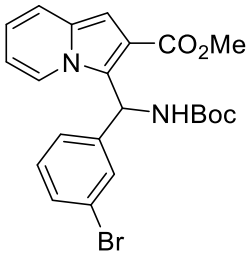
^{13}C NMR (126 MHz, $CDCl_3$) δ 165.9, 156.0, 145.6, 131.5, 129.7(2C), 129.4, 125.3, 124.9, 122.4, 119.1, 118.4, 117.8, 116.4, 114.0, 113.1, 79.5, 51.8, 48.5, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{22}H_{23}N_2O_4BrNa$ 481.0739 found 481.0740.

$[\alpha]^{25}_D$ = 59.9 (*c* = 0.24, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 10% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 8.4 min (minor), 17.1 min (major).

Methyl (*R*)-3-((3-bromophenyl)((*tert*-butoxycarbonyl)amino)methyl)indolizine-2-carboxylate 4k



Colorless oil, 83 mg, 40% yield, 41% e.e..

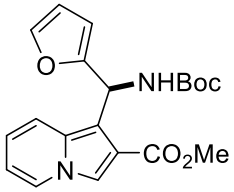
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.2 Hz, 1H), 7.41 (d, *J* = 9.1 Hz, 1H), 7.37 – 7.29 (m, 2H), 7.18 (bs, 1H), 7.14 – 7.08 (m, 1H), 7.04 (d, *J* = 7.9 Hz, 1H), 6.92 (s, 1H), 6.78 – 6.70 (m, 2H), 6.78 – 6.70 (m,1H), 3.81 (s, 3H), 1.46 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 156.1, 143.0, 131.8, 130.5, 130.1, 129.2, 127.3, 124.8, 122.8, 122.2, 120.8, 118.4, 116.9, 113.4, 102.4, 80.1, 51.9, 48.2, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{22}H_{23}N_2O_4BrNa$ 481.0739 found 481.0743.

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 0.3% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 18.2 min (minor), 25.2 min (major).

Methyl (*R*)-1-(((tert-butoxycarbonyl)amino)(furan-2-yl)methyl)indolizine-2-carboxylate 3l



The two regioisomers **3l** and **4l** were prepared according to the **General Procedure A** (reaction time = 3 h). Purification by Flash chromatography (70:30 hexane/dichloromethane to 40:60 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 88 mg, 52% yield, 87% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.77 (m, 2H), 7.57 (d, *J* = 9.3 Hz, 1H), 7.28 – 7.24 (m, 1H), 6.96 (d, *J* = 9.8 Hz, 1H), 6.73 (dd, *J* = 9.3, 6.4 Hz, 1H), 6.58 – 6.49 (m, 2H), 6.26 – 6.21 (m, 1H), 6.06 – 5.99 (m, 1H), 3.83 (s, 3H), 1.45 (s, 9H).

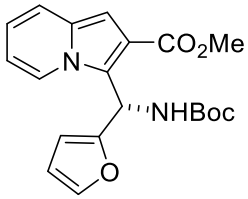
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 155.8, 155.5, 141.6, 131.3, 125.3, 118.9, 118.5, 117.5, 116.9, 112.9, 112.2, 110.3, 105.6, 79.4, 51.8, 44.5, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{20}H_{22}N_2O_5Na$ 393.1426 found 393.1424.

$[\alpha]^{25}_D$ = -14 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 10% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 10.6 min (minor), 19.8 min (major).

Methyl (*R*)-3-(((tert-butoxycarbonyl)amino)(furan-2-yl)methyl)indolizine-2-carboxylate 4l



Colorless oil, 75 mg, 44% yield, 6% e.e..

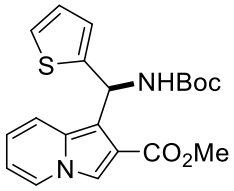
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.3 Hz, 1H), 7.38 (d, *J* = 9.1 Hz, 1H), 7.29 – 7.27 (m, 1H), 7.26 (bs, 1H), 6.89 (s, 1H), 6.81 – 6.74 (m, 1H), 6.72 (ddd, *J* = 9.1, 6.4, 1.0 Hz, 1H), 6.64 – 6.59 (m, 1H), 6.25 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.09 – 6.04 (m, 1H), 3.86 (s, 3H), 1.44 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.4, 155.8, 152.8, 142.2, 131.8, 125.5, 122.7, 120.6, 118.3, 117.1, 113.0, 110.5, 106.4, 102.2, 80.0, 51.9, 44.2, 28.5(3C).

HRMS $[M+Na]^+$ calculated for $C_{20}H_{22}N_2O_5Na$393.1426 found 393.1429.

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 10% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 15.6 min (minor), 19.9 min (major).

Methyl (*R*)-1-(((*tert*-butoxycarbonyl)amino)(thiophen-2-yl)methyl)indolizine-2-carboxylate 3m



The two regioisomers **3m** and **4m** were prepared according to the **General Procedure A** (reaction time = 6 h). Purification by Flash chromatography (80:20 hexane/dichloromethane to 70:30 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 81 mg, 46% yield, 89% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 – 7.80 (m, 2H), 7.59 (d, *J* = 9.3 Hz, 1H), 7.17 (d, *J* = 9.8 Hz, 1H), 7.09 (d, *J* = 5.0 Hz, 1H), 6.87 – 6.82 (m, 1H), 6.74 (dd, *J* = 9.3, 6.5 Hz, 1H), 6.71 – 6.65 (m, 2H), 6.59 – 6.55 (m, 1H), 3.80 (s, 3H), 1.46 (s, 9H).

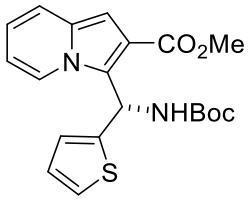
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 155.8, 148.7, 131.1, 126.7, 125.3, 124.0, 123.7, 119.0, 118.4, 117.7, 116.7, 114.3, 113.0, 79.5, 51.8, 46.0, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{20}H_{22}N_2O_4SNa$ 409.1198 found 409.1199.

$[\alpha]^{25}_D$ = 22.0 (*c* = 0.28, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 10% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 13.2 min (minor), 21.5 min (major).

Methyl (*R*)-3-(((*tert*-butoxycarbonyl)amino)(thiophen-2-yl)methyl)indolizine-2-carboxylate 4m



Colorless oil, 86 mg, 49% yield, 15% e.e..

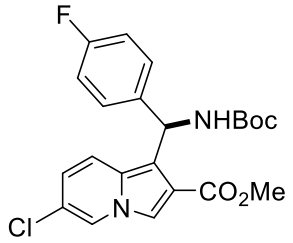
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 5.4 Hz, 1H), 7.47 (bs, 1H), 7.40 (d, *J* = 9.1 Hz, 1H), 7.15 (d, *J* = 5.0 Hz, 1H), 6.92 (s, 1H), 6.92 – 6.87 (m, 1H), 6.85 (dd, *J* = 5.0, 3.6 Hz, 1H), 6.73 (ddd, *J* = 9.1, 6.5, 1.0 Hz, 1H), 6.66 (d, *J*= 3.6 Hz, 1H), 6.64 – 6.57 (m, 1H), 3.85 (s, 3H), 1.45 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 155.8, 145.0, 131.7, 127.3, 126.9, 124.8, 124.4, 122.4, 120.7, 118.3, 116.9, 113.2, 102.3, 80.0, 52.0, 45.7, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{20}H_{22}N_2O_4SNa$ 409.1198 found 409.1200.

HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 18.0 min (major), 20.0 min (minor).

Methyl (*R*)-1-(((tert-butoxycarbonyl)amino)(4-fluorophenyl)methyl)-6-chloroindolizine-2-carboxylate 3n



The two regioisomers **3n** and **4n** were prepared according to the **General Procedure A** (reaction time = 18 h). Purification by Flash chromatography (65:35 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 52 mg, 26% yield, 91% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.77 (s, 1H), 7.56 (d, *J* = 9.7 Hz, 1H), 7.14 (dd, *J* = 8.4, 5.3 Hz, 2H), 6.95 – 6.87 (m, 3H), 6.71 (dd, *J* = 9.7, 1.7 Hz, 1H), 6.45 (d, *J* = 9.8 Hz, 1H), 3.76 (s, 3H), 1.45 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.5, 161.8, 156.0, 138.4, 129.7, 127.7(2C), 122.8, 121.55, 120.7, 119.1, 118.0, 117.1, 116.1, 115.0(2C), 79.6, 51.9, 48.4, 28.6(3C).

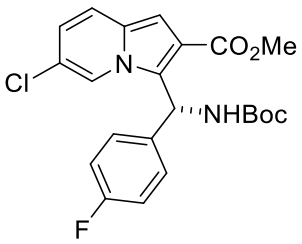
^{19}F NMR (470 MHz, $CDCl_3$) δ -116.92.

HRMS $[M+Na]^+$ calculated for $C_{22}H_{22}N_2O_4FClNa$ 455.1150 found 455.1157.

$[\alpha]^{25}_D$ = 42.3 (*c* = 0.16, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 1% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 17.4 min (minor), 20.6 min (major).

Methyl (*R*)-3-(((*tert*-butoxycarbonyl)amino)(4-fluorophenyl)methyl)-6-chloroindolizine-2-carboxylate 4n



Colorless oil, 143 mg, 72% yield, 81% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.35 (d, *J* = 9.5 Hz, 1H), 7.29 – 7.224 (m, 1H), 7.11 (dd, *J* = 8.4, 5.2 Hz, 2H), 6.98 – 6.92 (m, 3H), 6.70 (dd, *J* = 9.5, 1.6 Hz, 1H), 6.63 (d, *J* = 9.6 Hz, 1H), 3.81 (s, 3H), 1.46 (s, 9H).

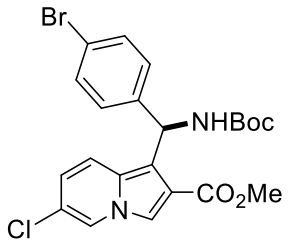
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 162.2, 156.0, 135.8, 129.9, 128.5, 127.9(2C), 122.1, 121.2, 120.1, 119.9, 117.5, 115.5(2C), 103.8, 80.1, 52.0, 48.3, 28.6(3C).

^{19}F NMR (470 MHz, $CDCl_3$) δ -115.30.

HRMS $[M+Na]^+$ calculated for $C_{22}H_{22}N_2O_4FClNa$ 455.1150 found 455.1154.

HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 1% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 13.2 min (minor), 17.4 min (major).

Methyl (*R*)-1-((4-bromophenyl)((*tert*-butoxycarbonyl)amino)methyl)-6-chloroindolizine-2-carboxylate 3o



The two regioisomers **3o** and **4o** were prepared according to the **General Procedure A** (reaction time = 24 h). Purification by Flash chromatography (65:35 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 68 mg, 30% yield, 92% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.76 (s, 1H), 7.56 (d, *J* = 9.7 Hz, 1H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.06 (d, *J* = 8.3 Hz, 2H), 6.91 (d, *J* = 9.8 Hz, 1H), 6.72 (dd, *J* = 9.7, 1.7 Hz, 1H), 6.42 (d, *J* = 9.8 Hz, 1H), 3.76 (s, 3H), 1.45 (s, 9H).

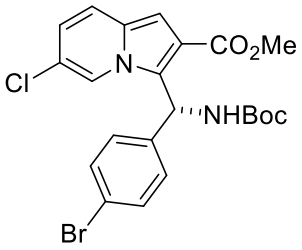
^{13}C NMR (151 MHz, $CDCl_3$) δ 165.5, 156.0, 141.8, 131.2(2C), 129.8, 128.0(2C), 122.8, 121.6, 120.8, 120.6, 119.0, 118.0, 117.0, 115.8, 79.6, 51.9, 48.5, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{22}H_{22}N_2O_4ClBrNa$ 515.0349 found 515.0340.

$[\alpha]^{25}_D$ = 175.1 (*c* = 0.10, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 2% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 13.4 min (minor), 15.8 min (major).

Methyl (*R*)-3-((4-bromophenyl)((*tert*-butoxycarbonyl)amino)methyl)-6-chloroindolizine-2-carboxylate 4o



Colorless oil, 144 mg, 64% yield, 82% e.e..

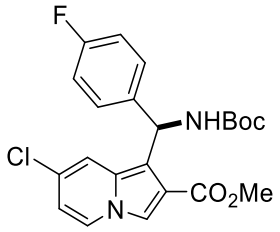
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 9.5 Hz, 1H), 7.24 (bs, 1H), 7.01 (d, *J* = 8.3 Hz, 2H), 6.96 (s, 1H), 6.70 (dd, *J* = 9.5, 1.6 Hz, 1H), 6.60 (d, *J* = 9.6 Hz, 1H), 3.81 (s, 3H), 1.46 (s, 9H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 166.0, 156.0, 139.1, 131.7(2C), 129.9, 128.2, 127.9(2C), 122.1, 121.5, 121.2, 120.1, 119.9, 117.5, 103.8, 80.2, 52.0, 48.3, 28.5(3C).

HRMS $[M+Na]^+$ calculated for $C_{22}H_{22}N_2O_4ClBrNa$ 515.0349 found 515.0346.

HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 6.6 min (minor), 8.8 min (major).

Methyl (*R*)--(((*tert*-butoxycarbonyl)amino)(4-fluorophenyl)methyl)-7-chloroindolizine-2-carboxylate 3p



The two regioisomers **3p** and **4p** were prepared according to the **General Procedure A** (reaction time = 24 h). Purification by Flash chromatography (85:15 hexane/dichloromethane to 70:30 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 138 mg, 70% yield, 92% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.73 (d, *J* = 7.4 Hz, 1H), 7.58 (s, 1H), 7.15 (dd, *J* = 8.4, 5.3 Hz, 2H), 7.00 – 6.86 (m, 3H), 6.52 (dd, *J* = 7.4, 2.1 Hz, 1H), 6.40 (d, *J* = 9.8 Hz, 1H), 3.76 (s, 3H), 1.46 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.5, 161.8, 156.0, 138.4, 130.9, 127.8(2C), 126.0, 125.4, 118.3, 117.5, 116.8, 115.0(2C), 114.71, 114.69, 79.6, 51.9, 48.4, 28.6(3C).

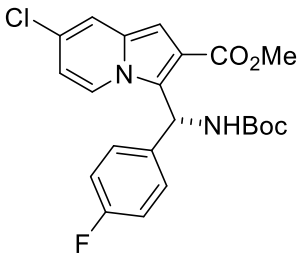
^{19}F NMR (470 MHz, $CDCl_3$) δ -121.62.

HRMS $[M+Na]^+$ calculated for $C_{22}H_{22}N_2O_4FClNa$ 455.1150 found 455.1154.

$[\alpha]^{25}_D$ = 43.8 (*c* = 0.21, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 11.1 min (major), 23.3 min (minor).

Methyl (*R*)-3-(((*tert*-butoxycarbonyl)amino)(4-fluorophenyl)methyl)-7-chloroindolizine-2-carboxylate 4p



Colorless oil, 55 mg, 28% yield, 68% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.7 Hz, 1H), 7.39 (s, 1H), 7.16 (bs, 1H), 7.09 (dd, *J* = 8.4, 5.3 Hz, 2H), 6.97 – 6.90 (m, 2H), 6.86 (s, 1H), 6.65 (d, *J* = 9.6 Hz, 1H), 6.57 (dd, *J* = 7.7, 2.2 Hz, 1H), 3.80 (s, 3H), 1.45 (s, 9H).

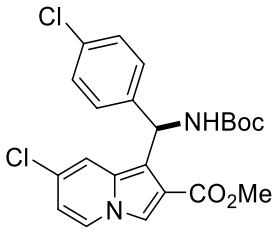
^{13}C NMR (126 MHz, $CDCl_3$) δ 165.9, 162.0, 155.9, 135.7, 131.2, 128.4, 127.6(2C), 124.5, 123.0, 118.8, 117.6, 115.3(2C), 114.7, 102.0, 80.0, 51.9, 48.1, 28.4(3C).

^{19}F NMR (470 MHz, $CDCl_3$) δ -115.43.

HRMS $[M+Na]^+$ calculated for $C_{22}H_{22}N_2O_4FClNa$ 455.1150 found 455.1155.

HPLC analysis of the product: Daicel CHIRALPAK IC column; 2.5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 6.7 min (major), 8.5 min (minor).

Methyl (*R*)-1-(((*tert*-butoxycarbonyl)amino)(4-chlorophenyl)methyl)-7-chloroindolizine-2-carboxylate 3q



The two regioisomers **3q** and **4q** were prepared according to the **General Procedure A** (reaction time = 24 h). Purification by Flash chromatography (85:15 hexane/dichloromethane to 70:30 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 148 mg, 72% yield, 94% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.74 (d, *J* = 7.4 Hz, 1H), 7.59 (s, 1H), 7.19 (d, *J* = 8.3 Hz, 2H), 7.12 (d, *J* = 8.3 Hz, 2H), 6.93 (d, *J* = 9.8 Hz, 1H), 6.53 (dd, *J* = 7.4, 2.1 Hz, 1H), 6.39 (d, *J* = 9.8 Hz, 1H), 3.76 (s, 3H), 1.46 (s, 9H).

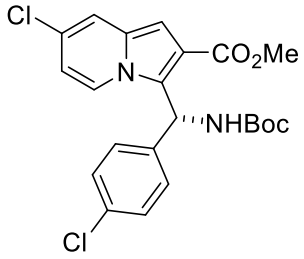
^{13}C NMR (126 MHz, $CDCl_3$) δ 165.5, 156.0, 141.3, 132.5, 131.0, 128.3(2C), 127.6(2C), 126.1, 125.5, 118.3, 117.5, 116.8, 114.7, 114.4, 79.6, 51.9, 48.4, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{22}H_{22}N_2O_4Cl_2Na$ 471.0854 found 455.1156.

$[\alpha]^{25}_D$ = 97.2 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 10.9 min (major), 19.6 min (minor).

Methyl (*R*)-3-(((*tert*-butoxycarbonyl)amino)(4-chlorophenyl)methyl)-7-chloroindolizine-2-carboxylate 4q



Colorless oil, 54 mg, 26% yield, 70% e.e..

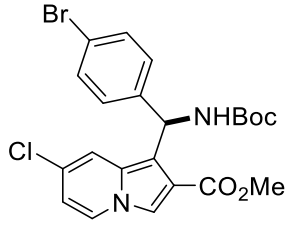
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.7 Hz, 1H), 7.39 (d, *J* = 1.8 Hz, 1H), 7.22 (d, *J* = 8.5 Hz, 2H), 7.13 (bs, 1H), 7.05 (d, *J* = 8.5 Hz, 2H), 6.85 (s, 1H), 6.65 (d, *J* = 9.7 Hz, 1H), 6.58 (dd, *J* = 7.7, 1.8 Hz, 1H), 3.80 (s, 3H), 1.45 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 156.1, 138.7, 133.3, 131.4, 128.8(2C), 128.3, 127.5(2C), 124.7, 123.1, 119.0, 117.8, 114.9, 102.2, 80.2, 52.1, 48.2, 28.5(3C).

HRMS $[M+Na]^+$ calculated for $C_{22}H_{22}N_2O_4Cl_2Na$ 471.0854 found 471.0858.

HPLC analysis of the product: Daicel CHIRALPAK IC column; 2.5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 6.8 min (major), 8.3 min (minor).

Methyl (*R*)-1-((4-bromophenyl)((tert-butoxycarbonyl)amino)methyl)-7-chloroindolizine-2-carboxylate 3r



The two regioisomers **3r** and **4r** were prepared according to the **General Procedure A** (reaction time = 24 h). Purification by Flash chromatography (85:15 hexane/dichloromethane to 70:30 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 155 mg, 69% yield, 97% e.e..

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.73 (d, *J* = 7.4 Hz, 1H), 7.58 (s, 1H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.06 (d, *J* = 8.2 Hz, 2H), 6.94 (d, *J* = 9.8 Hz, 1H), 6.52 (dd, *J* = 7.4, 2.1 Hz, 1H), 6.37 (d, *J* = 9.8 Hz, 1H), 3.76 (s, 3H), 1.46 (s, 9H).

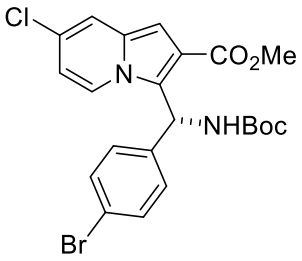
^{13}C NMR (151 MHz, $CDCl_3$) δ 165.5, 155.9, 141.8, 131.2(2C), 131.0, 128.0(2C), 126.1, 125.6, 120.6, 118.3, 117.4, 116.8, 114.7, 114.3, 79.6, 51.9, 48.4, 28.6(3C).

HRMS $[M+K]^+$ calculated for $C_{22}H_{22}N_2O_4ClBrK$ 531.0089 found 531.0095.

$[\alpha]^{25}_D$ = 94.1 (*c* = 0.26, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 10.5 min (major), 19.0 min (minor).

Methyl (*R*)-3-((4-bromophenyl)((tert-butoxycarbonyl)amino)methyl)-7-chloroindolizine-2-carboxylate 4r



Colorless oil, 53 mg, 23% yield, 73% e.e..

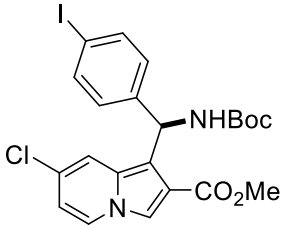
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 6.8 Hz, 1H), 7.44 – 7.34 (m, 3H), 7.12 (bs, 1H), 6.99 (d, *J* = 8.2 Hz, 2H), 6.85 (s, 1H), 6.63 (d, *J* = 9.4 Hz, 1H), 6.58 (d, *J* = 6.8 Hz, 1H), 3.80 (s, 3H), 1.45 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 156.1, 139.3, 131.7(2C), 131.4, 128.3, 127.8(2C), 124.7, 123.1, 121.5, 119.0, 117.8, 114.9, 102.2, 80.2, 52.1, 48.3, 28.5(3C).

HRMS $[M+K]^+$ calculated for $C_{22}H_{22}N_2O_4ClBrK$ 531.0089 found 531.0087.

HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 19.9 min (minor), 25.4 min (major).

Methyl (*R*)-1-(((*tert*-butoxycarbonyl)amino)(4-iodophenyl)methyl)-7-chloroindolizine-2-carboxylate 3s



The two regioisomers **3s** and **4s** were prepared according to the **General Procedure A** (reaction time = 48 h). Purification by Flash chromatography (90:10 hexane/dichloromethane to 70:30 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 173 mg, 70% yield, 90% e.e..

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.74 (d, *J* = 7.4 Hz, 1H), 7.59 (s, 1H), 7.54 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 8.4 Hz, 2H), 6.91 (s, 1H), 6.54 (dd, *J* = 7.4, 2.0 Hz, 1H), 6.36 (d, *J* = 9.8 Hz, 1H), 3.76 (s, 3H), 1.46 (s, 9H).

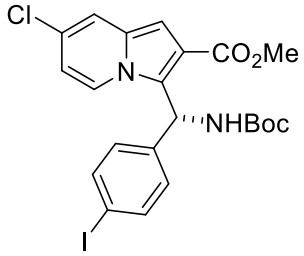
^{13}C NMR (126 MHz, $CDCl_3$) δ 165.5, 156.0, 142.6, 137.2(2C), 131.0, 128.3(2C), 126.1, 125.6, 118.3, 117.5, 116.8, 114.8, 114.3, 92.2, 79.6, 51.9, 48.5, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{22}H_{22}N_2O_4ClINa$ 563.0210 found 563.0215.

$[\alpha]^{25}_D$ = 78.3 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 11.8 min (major), 19.9 min (minor).

Methyl (*R*)-3-(((*tert*-butoxycarbonyl)amino)(4-iodophenyl)methyl)-7-chloroindolizine-2-carboxylate 4s



Colorless oil, 70 mg, 28% yield, 67% e.e..

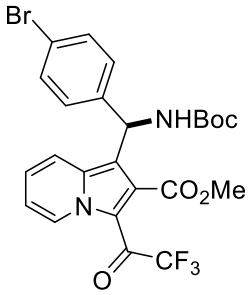
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.7 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 2.2 Hz, 1H), 7.09 (s, 1H), 6.92 – 6.83 (m, 3H), 6.63 (d, *J* = 9.6 Hz, 1H), 6.58 (dd, *J* = 7.7, 2.2 Hz, 1H), 3.80 (s, 3H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 156.1, 140.0, 137.7(2C), 131.4, 128.2, 128.1(2C), 124.8, 123.1, 119.0, 117.9, 114.9, 102.2, 93.0, 80.2, 52.1, 48.4, 28.6(3C).

HRMS $[M+Na]^+$ calculated for $C_{22}H_{22}N_2O_4ClINa$ 563.0210 found 563.0209.

HPLC analysis of the product: Daicel CHIRALPAK IC column; 2.5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 7.4 min (major), 9.0 min (minor).

Methyl (*R*)-1-((4-bromophenyl)((tert-butoxycarbonyl)amino)methyl)-3-(2,2,2-trifluoroacetyl)indolizine-2-carboxylate 10



Under argon atmosphere and room temperature, **3f** (45.9 mg, 0.10 mmol) was dissolved in dichloromethane (2.0 mL), which was added $^{i}Pr_2NEt$ (27.8 μL, 0.16 mmol). Then, TFAA (20.9 μL, 0.15 mmol) was added dropwise to the reaction mixture, which was further stirred at room temperature for 24 h. After the completion of the reaction indicated by TLC, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography (90:10 hexane/dichloromethane to 80:20 hexane/dichloromethane + 0.25% Et_3N) to give the product **10**.

Yellowish oil, 50 mg, 90% yield, 91% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (d, *J* = 7.2 Hz, 1H), 7.92 (d, *J* = 9.0 Hz, 1H), 7.48 – 7.42 (m, 1H), 7.40 (d, *J* = 8.2 Hz, 2H), 7.21 – 7.13 (m, 1H), 7.10 (d, *J* = 8.2 Hz, 2H), 6.48 (d, *J* = 9.6 Hz, 1H), 6.11 (d, *J* = 9.6 Hz, 1H), 3.58 (s, 3H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 165.7, 155.6, 139.3, 138.0, 131.5(2C), 128.9, 128.3(2C), 128.0, 127.7, 121.3, 120.2, 118.0, 117.7, 116.7, 115.8, 80.3, 52.7, 48.4, 28.5(3C).

^{19}F NMR (376 MHz, $CDCl_3$) δ -71.90.

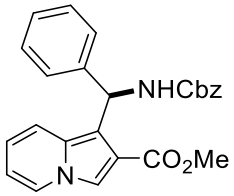
HRMS $[M+Na]^+$ calculated for $C_{24}H_{22}F_3BrN_2O_5Na$ 577.0562 found 577.0561.

$[\alpha]^{25}_D$ = -27.5 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 5.0% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 10.7 min (major), 23.1 min (minor).

3.8. Products with Cbz-protecting group 6a-m, 7a-m, 8 and 9

Methyl (*R*)-1-((((benzyloxy)carbonyl)amino)(phenyl)methyl)indolizine-2-carboxylate 6a



The product was prepared according to the **General Procedure D** (reaction time = 48 h). Purification by Flash chromatography (80:20 hexane/dichloromethane to 70:30 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 153 mg, 31% yield, 93% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.79 (d, *J* = 6.2 Hz, 1H), 7.64 (d, *J* = 9.3 Hz, 1H), 7.48 – 7.16 (m, 11H), 6.75 (dd, *J* = 9.3, 6.5 Hz, 1H), 6.64 (d, *J* = 9.9 Hz, 1H), 6.58 – 6.52 (td, *J* = 6.8, 1.2 Hz, 1H), 5.26 – 5.09 (m, 2H), 3.74 (s, 3H).

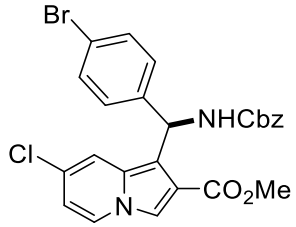
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 156.7, 142.6, 136.9, 131.4, 128.5(2C), 128.19(2C), 128.17(2C), 128.0, 126.7, 126.2(2C), 125.3, 118.9, 118.3, 117.8, 116.4, 114.4, 112.9, 66.8, 51.7, 49.6.

HRMS $[M+Na]^+$ calculated for $C_{25}H_{22}N_2O_4Na$ 437.1477 found 437.14779.

$[\alpha]^{25}_D$ = 21.1 (*c* = 0.28, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 20.0% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 15.3 min (major), 25.9 min (minor).

Methyl (*R*)-1-((((benzyloxy)carbonyl)amino)(4-bromophenyl)methyl)-7-chloroindolizine-2-carboxylate 6m



The product was prepared according to the **Procedure E** (reaction time = 72 h). Purification by Flash chromatography (90:10 hexane/ethyl acetate to 80:20 hexane/ethyl acetate + 0.25% Et_3N).

Colorless oil, 129 mg, 61% yield, 88% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.74 (d, *J* = 7.4 Hz, 1H), 7.60 (s, 1H), 7.44 – 7.21 (m, 8H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.54 (dd, *J* = 7.4, 2.1 Hz, 1H), 6.43 (d, *J* = 9.8 Hz, 1H), 5.24 – 5.04 (m, 2H), 3.74 (s, 3H).

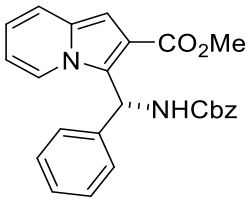
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 156.6, 141.2, 136.7, 131.3(2C), 131.1, 128.6(2C), 128.3, 128.2(2C), 128.0(2C), 126.1, 125.8, 120.8, 118.4, 117.4, 116.6, 114.8, 113.9, 67.0, 51.9, 49.1.

HRMS $[M+Na]^+$ calculated for $C_{25}H_{20}N_2O_4ClBrNa$ 549.0193 found 549.0190.

$[\alpha]^{25}_D$ = 54.3 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 20.0% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 9.2 min (major), 12.9 min (minor).

Methyl (*R*)-3-((((benzyloxy)carbonyl)amino)(phenyl)methyl)indolizine-2-carboxylate 7a



The product was prepared according to the **General Procedure C** (reaction time = 72 h). Purification by Flash chromatography (80:20 hexane/dichloromethane to 70:30 hexane/dichloromethane + 0.25% Et_3N).

The product was prepared according to the **Procedure D** (reaction time = 48 h). Purification by Flash chromatography (80:20 hexane/dichloromethane to 70:30 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 124 mg, 88% yield, 92% e.e. (**General Procedure C**).

Colorless oil, 335 mg, 67% yield, 84% e.e. (**Procedure D**).

^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.04 (d, *J* = 7.2 Hz, 1H), 7.61 (d, *J* = 9.1 Hz, 1H), 7.47 – 7.15 (m, 11H), 6.95 (s, 1H), 6.81 (d, *J* = 9.5 Hz, 1H), 6.75 (dd, *J* = 9.1, 6.4 Hz, 1H), 6.68 – 6.58 (m, 1H), 5.12 (q, *J* = 12.3 Hz, 2H), 3.80 (s, 3H).

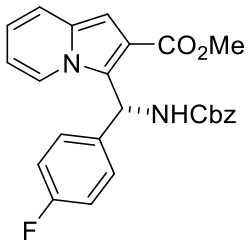
^{13}C NMR (101 MHz, CD_2Cl_2) δ 166.6, 156.6, 140.1, 136.9, 131.8, 128.6(2C), 128.5(2C), 128.1, 128.0(2C), 127.7, 127.5, 126.2(2C), 122.3, 120.6, 118.25, 116.9, 113.2, 102.3, 66.9, 51.8, 49.5.

HRMS $[M+H]^+$ calculated for $C_{25}H_{23}N_2O_4$ 415.1658 found 415.1656

$[\alpha]^{25}_D$ = -13.3 (*c* = 0.25, CH_2Cl_2) (**General Procedure C**).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 6.0% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 16.3 min (major), 24.4 min (minor) (**General Procedure C**).

Methyl (*R*)-3-((((benzyloxy)carbonyl)amino)(4-fluorophenyl)methyl)indolizine-2-carboxylate 7b



The product was prepared according to the **General Procedure C** (reaction time = 48 h). Purification by Flash chromatography (85:15 hexane/dichloromethane to 75:25 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 132 mg, 90% yield, 90% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.3 Hz, 1H), 7.69 (d, *J* = 9.7 Hz, 1H), 7.45 – 7.27 (m, 6H), 7.14 (dd, *J* = 8.4, 5.3 Hz, 2H), 6.99 – 6.90 (m, 3H), 6.80 – 6.70 (m, 2H), 6.67 – 6.58 (m, 1H), 5.22 – 5.07 (m, 2H), 3.81 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 162.2, 156.8, 136.6, 135.8, 131.8, 128.6(2C), 128.23(2C), 128.22, 128.0(2C), 127.4, 122.1, 120.8, 118.4, 116.9, 115.5(2C), 113.4, 102.5, 67.2, 52.0, 49.0.

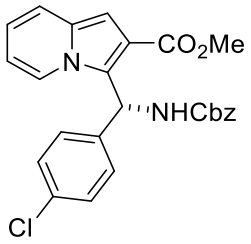
^{19}F NMR (376 MHz, $CDCl_3$) δ -115.34.

HRMS $[M+ Na]^+$ calculated for $C_{25}H_{21}FN_2O_4Na$ 455.1383 found 455.1380.

[α]$^{25}_{D}$ = -22.2 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 2.5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 17.4 min (major), 20.4 min (minor).

Methyl (*R*)-3-((((benzyloxy)carbonyl)amino)(4-chlorophenyl)methyl)indolizine-2-carboxylate 7c



The product was prepared according to the **General Procedure C** (reaction time = 72 h). Purification by Flash chromatography (90:10 hexane/dichloromethane to 80:20 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 130 mg, 85% yield, 88% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.3 Hz, 1H), 7.63 (d, *J* = 9.7 Hz, 1H), 7.45 – 7.28 (m, 6H), 7.22 (d, *J* = 8.6 Hz, 2H), 7.09 (d, *J* = 8.6 Hz, 2H), 6.93 (s, 1H), 6.80 – 6.70 (m, 2H), 6.67 – 6.59 (m, 1H), 5.23 – 5.05 (m, 2H), 3.80 (s, 3H).

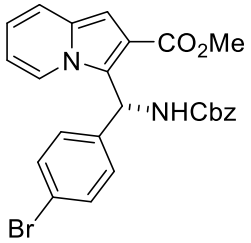
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 156.8, 138.6, 136.5, 133.4, 131.9, 128.7(2C), 128.6(2C), 128.24, 128.22(2C), 127.6(2C), 127.2, 122.1, 120.8, 118.4, 116.9, 113.4, 102.5, 67.2, 52.0, 48.9.

HRMS $[M+ Na]^+$ calculated for $C_{25}H_{21}ClN_2O_4Na$ 471.1088 found 471.1084.

[α]$^{25}_{D}$ = 5.1 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 2.5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 17.4 min (major), 19.9 min (minor).

Methyl (*R*)-3-((((benzyloxy)carbonyl)amino)(4-bromophenyl)methyl)indolizine-2-carboxylate 7d



The product was prepared according to the **General Procedure C** (reaction time = 72 h). Purification by Flash chromatography (85:15 hexane/dichloromethane to 75:25 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 153 mg, 91% yield, 88% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.3 Hz, 1H), 7.64 (d, *J* = 9.6 Hz, 1H), 7.46 – 7.27 (m, 8H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.93 (s, 1H), 6.79 – 6.70 (m, 2H), 6.68 – 6.58 (m, 1H), 5.22 – 5.06 (m, 2H), 3.80 (s, 3H).

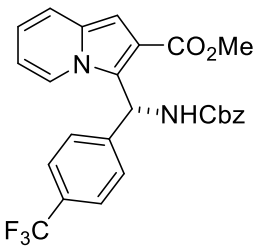
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 156.8, 139.2, 136.5, 131.9, 131.7(2C), 128.6(2C), 128.3, 128.2(2C), 128.0(2C), 127.1, 122.1, 121.5, 120.8, 118.4, 116.9, 113.5, 102.5, 67.2, 52.0, 49.0.

HRMS $[M+Na]^+$ calculated for $C_{25}H_{21}N_2O_4BrNa$ 515.0582 found 515.0576.

$[\alpha]^{25}_D$ = 13.7 (*c* = 0.26, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 2.5% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 21.5 min (major), 25.2 min (minor).

Methyl (*R*)-3-((((benzyloxy)carbonyl)amino)(4-(trifluoromethyl)phenyl)methyl)indolizine-2-carboxylate 7e



The product was prepared according to the **General Procedure C** (reaction time = 216 h). Additional 5% of catalyst were added over 8 days. Purification by Flash chromatography (90:10 hexane/dichloromethane to 80:20 hexane/dichloromethane + 0.25% Et_3N). (13 mg, 22% of indolizine **1a** recovered).

Colorless oil, 100 mg, 61% yield, 93% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.2 Hz, 1H), 7.64 (d, *J* = 9.1 Hz, 1H), 7.51 (d, *J* = 8.2 Hz, 2H), 7.45 – 7.27 (m, 8H), 6.94 (s, 1H), 6.84 (d, *J* = 9.6 Hz, 1H), 6.76 (dd, *J* = 9.1, 6.4 Hz, 1H), 6.70 – 6.61 (m, 1H), 5.24 – 5.07 (m, 2H), 3.79 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 156.9, 144.2, 136.5, 132.0, 129.8, 128.7(2C), 128.32, 128.28(2C), 126.9, 126.5(2C), 125.6(2C), 124.2, 122.0, 120.9, 118.5, 117.0, 113.6, 102.6, 67.3, 52.0, 49.1.

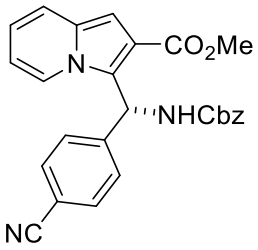
^{19}F NMR (376 MHz, $CDCl_3$) δ -62.54.

HRMS $[M+Na]^+$ calculated for $C_{26}H_{21}N_2O_4F_3Na$ 505.1351 found 505.1355.

[α]$^{25}_{D}$ = 11.5 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 5.0% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 17.9 min (minor), 20.2 min (major).

Methyl (*R*)-3-((((benzyloxy)carbonyl)amino)(4-cyanophenyl)methyl)indolizine-2-carboxylate 7f



The product was prepared according to the **General Procedure C** (reaction time = 144 h). Purification by Flash chromatography (85:15 hexane/dichloromethane to 70:30 hexane/dichloromethane + 0.25% Et_3N). (29 mg, 48% of indolizine **1a** recovered).

Colorless oil, 63 mg, 42% yield, 92% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.3 Hz, 1H), 7.60 – 7.49 (m, 3H), 7.43 (d, *J* = 9.1 Hz, 1H), 7.39 – 7.30 (m, 5H), 7.26 (d, *J* = 8.2 Hz, 2H), 6.93 (s, 1H), 6.83 (d, *J* = 9.6 Hz, 1H), 6.77 (dd, *J* = 9.1, 6.5 Hz, 1H), 6.72 – 6.62 (m, 1H), 5.23 – 5.06 (m, 2H), 3.77 (s, 3H).

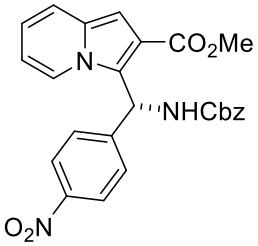
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 156.9, 145.6, 136.3, 132.4(2C), 132.1, 128.7(2C), 128.4, 128.3(2C), 126.9(2C), 126.5, 121.9, 120.9, 118.8, 118.7, 117.0, 113.7, 111.4, 102.6, 67.4, 52.0, 49.0.

HRMS $[M+H]^+$ calculated for $C_{26}H_{22}N_3O_4$ 440.1610 found 440.1613.

[α]$^{25}_{D}$ = 36.1 (*c* = 0.29, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK AD-H column; 30% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 29.7 min (minor), 34.7 min (major).

Methyl (*R*)-3-((((benzyloxy)carbonyl)amino)(4-nitrophenyl)methyl)indolizine-2-carboxylate 7g



The product was prepared according to the **General Procedure C** (reaction time = 192 h (96 h at r.t. and 96 h at 40 °C)). Additional 5% of catalyst were added over 8 days. Purification by Flash chromatography (90:10 hexane/dichloromethane to 80:20 hexane/dichloromethane + 0.25% Et_3N). (10 mg, 17% of indolizine **1a** recovered).

Colorless oil, 100 mg, 64% yield, 92% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 – 8.05 (m, 3H), 7.57 (d, *J* = 9.6 Hz, 1H), 7.44 (d, *J* = 9.1 Hz, 1H), 7.41 – 7.27 (m, 7H), 6.94 (s, 1H), 6.87 (d, *J* = 9.6 Hz, 1H), 6.78 (dd, *J* = 9.1, 6.4 Hz, 1H), 6.73 – 6.63 (m, 1H), 5.26 – 5.06 (m, 2H), 3.78 (s, 3H).

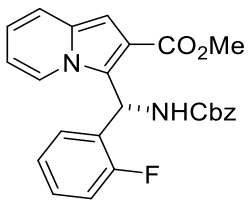
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 156.9, 147.6, 147.3, 136.3, 132.1, 128.7(2C), 128.4, 128.3(2C), 127.0(2C), 126.5, 123.8(2C), 121.9, 120.9, 118.7, 117.0, 113.8, 102.6, 67.5, 52.0, 48.9.

HRMS $[M+Na]^+$ calculated for $C_{25}H_{21}N_3O_6Na$ 482.1328 found 482.1333.

$[\alpha]^{25}_D$ = 49.6 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALCEL OD-H column; 20.0% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 20.4 min (major), 25.4 min (minor).

Methyl (*R*)-3-((((benzyloxy)carbonyl)amino)(2-fluorophenyl)methyl)indolizine-2-carboxylate 7h



The product was prepared according to the **General Procedure C** (reaction time = 192 h). Purification by Flash chromatography (95:05 hexane/dichloromethane to 90:10 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 142 mg, 97% yield, 93% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 7.2 Hz, 1H), 7.90 (d, *J* = 9.0 Hz, 1H), 7.59 – 7.52 (m, 1H), 7.42 – 7.27 (m, 6H), 7.23 – 7.16 (m, 1H), 7.12 – 7.04 (m, 1H), 7.00 – 6.92 (m, 2H), 6.87 (s, 1H), 6.73 (dd, *J* = 9.0, 6.4 Hz, 1H), 6.69 – 6.62 (m, 1H), 5.19 – 5.07 (m, 2H), 3.84 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 160.5, 156.3, 136.6, 131.7, 129.2, 128.6(2C), 128.5, 128.22, 128.17(2C), 127.0, 126.8, 124.1, 122.8, 120.5, 118.3, 116.6, 115.4, 113.0, 102.4, 67.1, 52.0, 44.3.

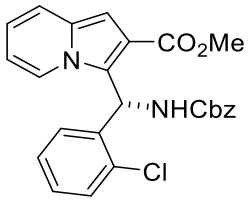
^{19}F NMR (376 MHz, $CDCl_3$) δ -116.53.

HRMS $[M+ Na]^+$ calculated for $C_{25}H_{21}FN_2O_4Na$ 455.1383 found 455.1378.

[α]$^{25}_{D}$ = 36.4 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 5.0% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 17.6 min (major), 21.8 min (minor).

Methyl (*R*)-3-((((benzyloxy)carbonyl)amino)(2-chlorophenyl)methyl)indolizine-2-carboxylate 7i



The product was prepared according to the **General Procedure C** (reaction time = 192 h). Purification by Flash chromatography (90:10 hexane/dichloromethane to 80:20 hexane/dichloromethane + 0.25% Et_3N).

Semisolid, 137 mg, 90% yield, 95% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.3 Hz, 1H), 7.53 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.45 – 7.27 (m, 8H), 7.23 – 7.14 (m, 2H), 6.92 (d, *J* = 9.8 Hz, 1H), 6.88 (s, 1H), 6.74 (dd, *J* = 9.0, 6.4 Hz, 1H), 6.69 – 6.61 (m, 1H), 5.22 – 5.06 (m, 2H), 3.80 (s, 3H).

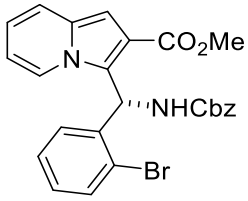
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 156.2, 136.7, 136.6, 133.7, 131.7, 129.9, 129.3, 128.9, 128.6(2C), 128.13, 128.09(2C), 126.6, 126.4, 122.9, 120.5, 118.3, 117.3, 113.0, 102.3, 67.1, 51.9, 47.8.

HRMS $[M+Na]^+$ calculated for $C_{25}H_{21}ClN_2O_4Na$ 471.1088 found 471.1093.

[α]$^{25}_{D}$ = -17.1 (*c* = 0.27, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 5.0% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 17.9 min (major), 21.9 min (minor).

Methyl (*R*)-3-((((benzyloxy)carbonyl)amino)(2-bromophenyl)methyl)indolizine-2-carboxylate 7j



The product was prepared according to the **General Procedure C** (reaction time = 144 h). Purification by Flash chromatography (90:10 hexane/dichloromethane to 80:20 hexane/dichloromethane + 0.25% Et_3N).

Semisolid, 156 mg, 93% yield, 94% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.2 Hz, 1H), 7.54 (dd, *J* = 9.0, 1.3 Hz, 1H), 7.49 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.43 – 7.18 (m, 8H), 7.10 (ddd, *J* = 7.9, 7.6 Hz, 1.7 Hz, 1H), 6.89 (s, 1H), 6.85 (d, *J* = 9.8 Hz, 1H), 6.74 (dd, *J* = 9.0, 6.4 Hz, 1H), 6.69 – 6.61 (m, 1H), 5.23 – 5.06 (m, 2H), 3.80 (s, 3H).

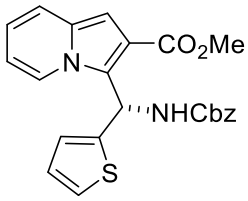
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 156.1, 138.1, 136.6, 133.3, 131.7, 129.7, 129.2, 128.5(2C), 128.1, 128.0(2C), 127.2, 126.3, 123.9, 123.0, 120.5, 118.4, 117.4, 113.0, 102.3, 67.0, 51.9, 50.2.

HRMS $[M+H]^+$ calculated for $C_{25}H_{22}N_2O_4Br$ 493.0763 found 493.0765.

$[\alpha]^{25}_D$ = -60.2 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 5.0% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 21.2 min (major), 25.9 min (minor).

Methyl (*R*)-3-((((benzyloxy)carbonyl)amino)(thiophen-2-yl)methyl)indolizine-2-carboxylate 7k



The product was prepared according to the **General Procedure C** (reaction time = 24 h). Purification by Flash chromatography (90:10 hexane/dichloromethane to 80:20 hexane/dichloromethane + 0.25% Et_3N).

Colorless oil, 136 mg, 95% yield, 88% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.3 Hz, 1H), 7.91 (d, *J* = 9.6 Hz, 1H), 7.45 – 7.27 (m, 6H), 7.17 (d, *J* = 5.1 Hz, 1H), 7.00 (d, *J* = 9.5 Hz, 1H), 6.95 (s, 1H), 6.87 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.78 – 6.68 (m, 2H), 6.66 – 6.56 (m, 1H), 5.25 – 5.08 (m, 2H), 3.85 (s, 3H).

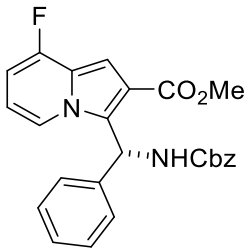
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 156.4, 144.2, 136.5, 131.8, 128.5(2C), 128.1(3C), 126.9, 126.8, 125.0, 124.6, 122.3, 120.6, 118.4, 116.9, 113.3, 102.4, 67.1, 52.0, 46.4.

HRMS $[M+Na]^+$ calculated for $C_{23}H_{20}N_2O_4SNa$ 443.1041 found 443.1040.

$[\alpha]^{25}_D$ = -55.2 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 10% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 11.4 min (major), 18.7 min (minor).

Methyl (*R*)-3-((((benzyloxy)carbonyl)amino)(phenyl)methyl)-8-fluoroindolizine-2-carboxylate 7l



The product was prepared according to the **General Procedure C** (reaction time = 192 h (96 h at r.t. and 96 h at 40 °C)). Additional 5% of **B1** catalyst were added over 8 days. Purification by Flash chromatography (90:10 hexane/dichloromethane + 0.25% Et_3N). (23 mg, 35% of indolizine **1d** recovered).

Colorless oil, 93 mg, 63% yield, 82% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.2 Hz, 1H), 7.65 (d, *J* = 9.6 Hz, 1H), 7.44 – 7.22 (m, 8H), 7.19 (d, *J* = 7.2 Hz, 2H), 7.13 (s, 1H), 6.83 (d, *J* = 9.6 Hz, 1H), 6.60 – 6.49 (m, 1H), 6.43 (dd, *J* = 10.2, 7.2 Hz, 1H), 5.26 – 5.08 (m, 2H), 3.81 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 156.8, 155.1, 139.5, 136.6, 129.7, 128.7(2C), 128.6(2C), 128.19, 128.18(2C), 127.7, 126.1(2C), 124.4, 118.7, 117.2, 112.3, 100.3, 100.2, 67.2, 52.0, 49.8.

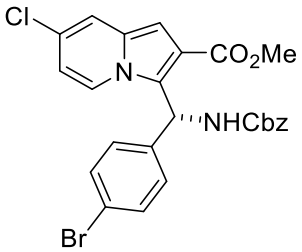
^{19}F NMR (376 MHz, $CDCl_3$) δ -124.21.

HRMS $[M+Na]^+$ calculated for $C_{25}H_{21}FN_2O_4Na$ 455.1383 found 455.1385.

$[\alpha]^{25}_D$ = -17.8 (*c* = 0.29, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 10.0% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 8.5 min (major), 12.2 min (minor).

Methyl (*R*)-3-((((benzyloxy)carbonyl)amino)(4-bromophenyl)methyl)-7-chloroindolizine-2-carboxylate 7m



The product was prepared according to the **Procedure E** (reaction time = 72 h). Purification by Flash chromatography (90:10 hexane/ethyl acetate to 80:20 hexane/ethyl acetate + 0.25% Et_3N).

Colorless oil, 80 mg, 38% yield, 26% e.e..

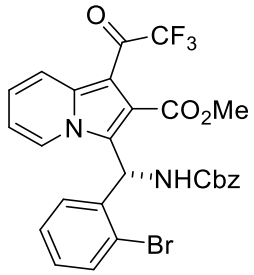
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.7 Hz, 1H), 7.55 (d, *J* = 9.8 Hz, 1H), 7.45 – 7.28 (m, 8H), 7.02 (d, *J* = 8.5 Hz, 2H), 6.87 (s, 1H), 6.70 (d, *J* = 9.8 Hz, 1H), 6.57 (d, *J* = 7.7 Hz, 1H), 5.23 – 5.05 (m, 2H), 3.79 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 156.8, 138.7, 136.4, 131.7(2C), 131.4, 128.6(2C), 128.3, 128.2(2C), 127.9(2C), 127.7, 124.8, 122.9, 121.6, 118.9, 117.8, 114.9, 102.3, 67.3, 52.1, 49.0.

HRMS $[M+Na]^+$ calculated for $C_{25}H_{20}N_2O_4ClBrNa$ 549.0193 found 549.0196.

HPLC analysis of the product: Daicel CHIRALPAK IC column; 10.0% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 8.2 min (major), 10.9 min (minor).

Methyl (*R*)-3-((((benzyloxy)carbonyl)amino)(2-bromophenyl)methyl)-1-(2,2,2-trifluoroacetyl)indolizine-2-carboxylate 8



Under argon atmosphere at room temperature, **7j** (49.3 mg, 0.1 mmol) was dissolved in dichloromethane (2.0 mL), which was added ^{i}Pr$_2$NEt (34.8 μL, 0.2 mmol). Then, TFAA (26.5 μL, 0.19 mmol) was added dropwise to the reaction mixture, which was further stirred at room temperature for 24 h. Another portions of ^{i}Pr$_2$NEt (34.8 μL, 0.2 mmol) and TFAA (26.5 μL, 0.19 mmol) were added again to the reaction mixture, which was stirred for another 24 h. After the completion of the reaction indicated by TLC, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography (80:20 hexane/dichloromethane + 0.25% Et_3N) to give the product **8**.

Colorless oil, 47 mg, 80% yield, 93% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 6.9 Hz, 1H), 8.29 (d, *J* = 9.3 Hz, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.45 – 7.28 (m, 7H), 7.23 – 7.15 (m, 1H), 7.11 – 7.02 (m, 1H), 6.69 (d, *J* = 9.3 Hz, 1H), 6.02 (d, *J* = 9.3 Hz, 1H), 5.23 – 5.08 (d, *J* = 2.4 Hz, 2H), 3.50 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.6, 166.4, 155.7, 137.2, 136.2, 136.0, 133.4, 130.0, 129.2, 128.7(2C), 128.5, 128.3(2C), 127.6, 127.5, 127.1, 124.8, 124.1, 122.3, 120.4, 116.8, 115.9, 105.3, 67.7, 52.6, 50.3.

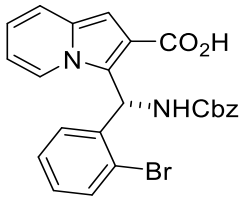
^{19}F NMR (376 MHz, $CDCl_3$) δ -73.58.

HRMS $[M+Na]^+$ calculated for $C_{27}H_{20}F_3BrN_2O_5Na$ 611.0405 found 611.0397.

$[\alpha]^{25}_D$ = 50.7 (*c* = 0.25, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 10.0% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 12.8 min (major), 16.5 min (minor).

(R)-3-((((benzyloxy)carbonyl)amino)(2-bromophenyl)methyl)indolizine-2-carboxylic acid 9



To a solution of **7j** (49.3 mg, 0.1 mmol) in THF (4 mL) and MeOH (4 mL) was added LiOH (33.5 mg, 1.4 mmol) in water (1 mL). After 5h of stirring at 70 °C, the solvent was completely evaporated under reduced pressure and the resulting residue was neutralized with 1M HCl to pH = 2-3). The solution was extracted with EtOAc (10 mL × 3), dried over Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography (50:50 hexane/dichloromethane to 100% dichloromethane + 0.25% Et_3N) to give the product **9**.

Colorless oil, 41 mg, 86% yield, 94% e.e..

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.3 Hz, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.47 – 7.37 (m, 2H),), 7.36 – 7.27 (m, 5H), 7.23 – 7.13 (m, 1H), 7.11 – 7.03 (m, 1H), 6.98 (d, *J* = 9.7 Hz, 1H), 6.94 (s, 1H), 6.83 (d, *J* = 9.7 Hz, 1H), 6.78 – 6.62 (m, 2H), 5.23 – 5.01 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.2, 156.1, 137.7, 136.5, 133.4, 131.9, 129.7, 129.3, 128.6(2C), 128.3, 128.2(2C), 127.2, 127.1, 123.9, 123.1, 120.7, 118.6, 116.4, 113.4, 103.2, 67.3, 50.1.

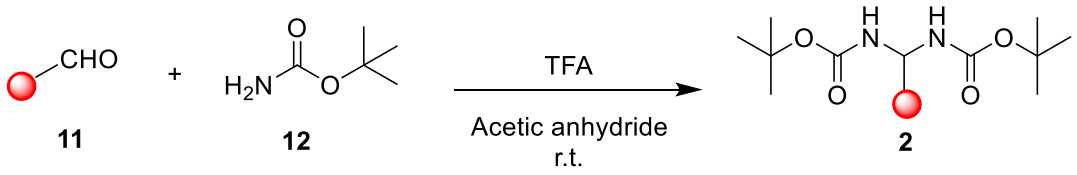
HRMS $[M+Na]^+$ calculated for $C_{24}H_{19}BrN_2O_4Na$ 501.0426 found 501.0425.

$[\alpha]^{25}_D$ = -74.8 (*c* = 0.26, CH_2Cl_2).

HPLC analysis of the product: Daicel CHIRALPAK IC column; 5.0% ^{i}PrOH in hexanes; 1.0 mL/min; λ = 254 nm; retention times: 20.4 min (major), 38.2 min (minor).

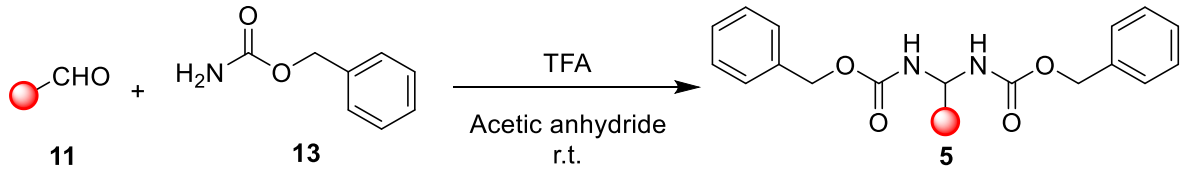
4. Synthesis of N-Boc aminals

4.1. General procedure F for synthesis of *N*-Boc aminals



The *N*-Boc-protected aminals **2** were synthesized according to the procedure in the literature.[4] Aldehyde (1 equiv.) and *tert*-butyl carbamate (1.67 equiv.) were added into acetic anhydride (0.2 mL/1 mmol of aldehyde). To this suspension was added trifluoroacetic acid (0.08 equiv.), and the mixture was stirred at room temperature until the product was solidified in acetic anhydride solvent as white solid. Then, it was filtered in vacuum, and washed several times with hexane. The *N*-Boc-protected aminals **2** were obtained as a white powder.

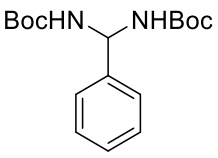
4.2. General procedure G for synthesis of *N*-Cbz aminals



The *N*-Cbz-protected aminals **5** were synthesized according to the procedure in the literature.[4] Aldehyde (1.0 equiv.) and benzyl carbamate (2.1 equiv.) were added into acetic anhydride (1 mL/3.33 mmol of aldehyde). To this suspension was added trifluoroacetic acid (0.1 equiv.), and the mixture was stirred at room temperature until the product was solidified in acetic anhydride solvent as white solid. Toluene was then added, and the product was collected by filtration. The white solid was washed two times with toluene and hexane, and recrystallized from toluene to give *N*-Cbz-protected aminals **5** was obtained as a white powder.

4.3. *N*-Boc aminals

di-*tert*-butyl (phenylmethylene)dicarbamate 2a



Following the **general procedure F** using benzaldehyde (5.77 mL, 56.54 mmol), *tert*-butyl carbamate (11.01 g, 93.98 mmol) and trifluoroacetic acid (357 μL, 4.66 mmol) under stirring for 24 h in acetic anhydride (12.9 mL) solution, the *N*-Boc aminal was obtained as a white powder (6.82 g, 21.144 mmol, 45%).

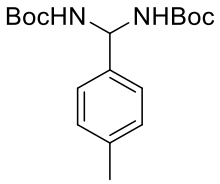
^{1}H NMR (400 MHz, CDCl3) δ 7.42–7.27 (m, 5H), 6.10 (t, *J* = 8.0 Hz, 1H), 5.44 (bs, 2H), 1.44 (s, 18H).

^{13}C NMR (101 MHz, CDCl3) δ 154.9(2C), 140.0, 128.7(2C), 128.1, 125.9(2C), 80.3(2C), 61.8, 28.4(6C).

HRMS $[M+Na]^+$ calculated for $C_{17}H_{26}N_2O_4Na$ 345.1790 found 345.1793.

m.p. 153-155 °C.

di-*tert*-butyl (*p*-tolylmethylene)dicarbamate 2b



Following the **general procedure F** using 4-methylbenzaldehyde (2.0 g, 16.65 mmol), *tert*-butyl carbamate (3.25 g, 27.80 mmol) and trifluoroacetic acid (105 μL, 1.38 mmol) under stirring for 46 h in acetic anhydride (3.8 mL) solution, the *N*-Boc aminal was obtained as a white powder (2.43 g, 7.23 mmol, 52%).

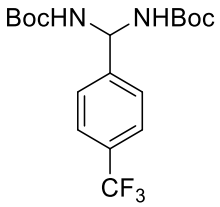
^{1}H NMR (400 MHz, CDCl3) δ 7.27 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.07 (t, *J* = 8.0 Hz, 1H), 5.38 (bs, 2H), 2.33 (s, 3H), 1.44 (s, 18H).

^{13}C NMR (101 MHz, CDCl3) δ 154.9(2C), 137.7, 137.0, 129.3(2C), 125.8(2C), 80.1(2C), 61.6, 28.4(6C), 21.1.

HRMS $[M+Na]^+$ calculated for $C_{18}H_{28}N_2O_4Na$ 359.1947 found 359.1951.

m.p. 135-136 °C.

di-*tert*-butyl ((4-(trifluoromethyl)phenyl)methylene)dicarbamate 2c



Following the **general procedure F** using 4-(Trifluoromethyl)benzaldehyde (5.00 g, 28.72 mmol), tert-butyl carbamate (5.62 g, 47.96 mmol) and trifluoroacetic acid (177 µL, 2.31 mmol) under stirring for 18 h in acetic anhydride (6.5 mL) solution, the *N*-Boc aminal was obtained as a white powder (6.86 g, 17.57 mmol, 73 %).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.2 Hz, 2H), 7.51 (d, *J* = 8.2 Hz, 2H), 6.14 – 6.03 (m, 1H), 5.82 (bs, 2H), 1.43 (s, 18H).

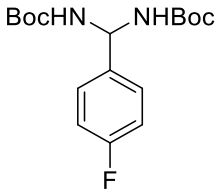
^{13}C NMR (126 MHz, $CDCl_3$) δ 155.0(2C), 143.9, 130.3, 126.4(2C), 125.6(2C), 124.2, 80.7(2C), 61.3, 28.4(6C).

^{19}F NMR (470 MHz, $CDCl_3$) δ -62.60.

HRMS $[M+Na]^+$ calculated for $C_{18}H_{25}N_2O_4F_3Na$ 413.1664 found 413.1665.

m.p. 154-155 °C.

di-tert-butyl ((4-fluorophenyl)methylene)dicarbamate 2d



Following the **general procedure F** using 4-fluorobenzaldehyde (2.50 g, 20.14 mmol), *tert*-butyl carbamate (3.94 g, 33.64 mmol) and trifluoroacetic acid (128 µL, 1.67 mmol) under stirring for 2 h in acetic anhydride (4.7 mL) solution, the *N*-Boc aminal was obtained as a white powder (3.25 g, 9.55 mmol, 57%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 8.4, 5.2 Hz, 2H), 7.06 – 6.98 (m, 2H), 6.04 (t, *J* = 8.0 Hz, 1H), 5.59 (bs, 2H), 1.43 (s, 18H).

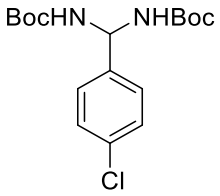
^{13}C NMR (126 MHz, $CDCl_3$) δ 162.5, 154.9(2C), 135.8, 127.7, 115.5, 80.5(2C), 61.3, 28.4(6C).

^{19}F NMR (470 MHz, $CDCl_3$) δ -114.89.

HRMS $[M+Na]^+$ calculated for $C_{17}H_{25}N_2O_4FNa$ 363.1696 found 363.1697.

m.p. 138-139 °C.

di-*tert*-butyl ((4-chlorophenyl)methylene)dicarbamate 2e



Following the **general procedure F** using 4-chlorobenzaldehyde (5.00 g, 35.57 mmol), *tert*-butyl carbamate (6.96 g, 59.40 mmol) and trifluoroacetic acid (227 µL, 2.97 mmol) under stirring for 5 h in acetic anhydride (8.2 mL) solution, the *N*-Boc aminal was obtained as a white powder (6.66 g, 18.66 mmol, 63%).

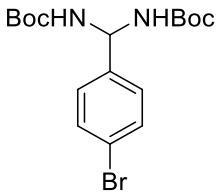
^{1}H NMR (200 MHz, $CDCl_3$) δ 7.46 – 7.15 (m, 4H), 6.02 (t, *J* = 8.0 Hz, 1H), 5.68 (bs, 2H), 1.43 (s, 18H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 154.9(2C), 138.5, 133.8, 128.7(2C), 127.4(2C), 80.5(2C), 61.2, 28.4(6C).

HRMS $[M+Na]^+$ calculated for $C_{17}H_{25}N_2O_4ClNa$ 379.1401 found 379.1402.

m.p. 158-159 °C.

di-*tert*-butyl ((4-bromophenyl)methylene)dicarbamate 2f



Following the **general procedure F** using 4-bromobenzaldehyde (2.5 g, 13.51 mmol), *tert*-butyl dicarbamate (2.65 g, 22.57 mmol) and trifluoroacetic acid (85 µL, 1.12 mmol) under stirring for 28 h in acetic anhydride (3.1 mL) solution, the *N*-Boc aminal was obtained as a white powder (3.14 g, 7.83 mmol, 69%).

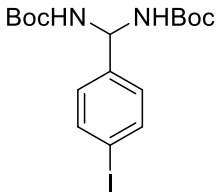
^{1}H NMR (400 MHz, CDCl3) δ 7.47 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 6.02 (t, *J* = 8.0 Hz, 1H), 5.63 (bs, 2H), 1.44 (s, 18H).

^{13}C NMR (101 MHz, CDCl3) δ 154.9, 139.1, 131.7, 127.8, 122.0, 80.5, 61.3, 28.4.

HRMS $[M+Na]^+$ calculated for $C_{17}H_{25}N_2O_4BrNa$ 423.0895 found 423.0899.

m.p. 156-157 °C.

di-*tert*-butyl ((4-iodophenyl)methylene)dicarbamate 2g



Following the **general procedure F** using 4-Iodobenzaldehyde (3.50 g, 15.09 mmol), *tert*-butyl carbamate (2.95 g, 25.19 mmol) and trifluoroacetic acid (95 μL, 1.25 mmol) under stirring for 3 h in acetic anhydride (3.5 mL) solution, the *N*-Boc aminal was obtained as a white powder (3.93 g, 8.76 mmol, 70%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.2 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 6.07 – 5.91 (m, 1H), 5.66 (bs, 2H), 1.43 (s, 18H).

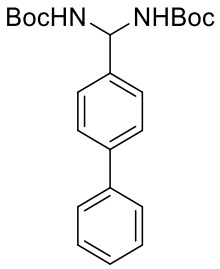
^{13}C NMR (126 MHz, $CDCl_3$) δ 155.0(2C), 139.7, 137.7(2C), 128.0(2C), 93.7, 80.6(2C), 61.3, 28.4(6C).

^{19}F NMR (470 MHz, $CDCl_3$) δ -62.60.

HRMS $[M+Na]^+$ calculated for $C_{17}H_{25}N_2O_4INa$ 471.0757 found 471.0763.

m.p. 154-155 °C.

di-*tert*-butyl ([1,1'-biphenyl]-4-ylmethylene)dicarbamate 2h



Following the **general procedure F** using biphenyl-4-carboxaldehyde (4.00 g, 21.95 mmol), *tert*-butyl carbamate (4.29 g, 36.66 mmol) and trifluoroacetic acid (136 μL, 1.78 mmol) under stirring for 2 h in acetic anhydride (5.0 mL) solution, the *N*-Boc aminal was obtained as a white powder (5.67 g, 14.24 mmol, 78%).

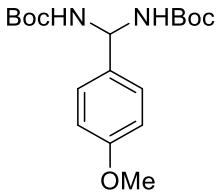
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 – 7.55 (m, 4H), 7.49 – 7.41 (m, 4H), 7.35 (t, *J* = 7.4 Hz, 1H), 6.15 (t, *J* = 8.1 Hz, 1H), 5.63 (bs, 2H), 1.46 (s, 18H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.0(2C), 141.0, 140.7, 138.9, 128.9(2C), 127.5, 127.4(2C), 127.2(2C), 126.4(2C), 80.3(2C), 61.6, 28.5(6C).

HRMS $[M+Na]^+$ calculated for $C_{23}H_{30}N_2O_4Na$ 421.2103 found 421.2108.

m.p. 170-171 °C.

di-*tert*-butyl ((4-methoxyphenyl)methylene)dicarbamate 2i



Following the **general procedure F** using 4-methoxybenzaldehyde (3.0 g, 22.03 mmol), *tert*-butyl carbamate (4.31 g, 36.79 mmol) and trifluoroacetic acid (139 µL, 1.82 mmol) under stirring for 24 h in acetic anhydride (5.0 mL) solution, the *N*-Boc aminal was obtained as a white powder (2.92 g, 8.29 mmol, 45%).

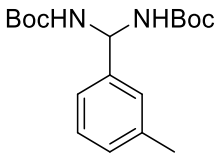
^{1}H NMR (400 MHz, CDCl3) δ 7.30 (d, *J* = 8.3 Hz, 2H), 6.87 (d, *J* = 8.3 Hz, 2H), 6.05 (t, *J* = 7.9 Hz, 1H), 5.38 (bs, 2H), 3.79 (s, 3H), 1.44 (s, 18H).

^{13}C NMR (50 MHz, CDCl3) δ 159.3, 154.9(2C), 132.1, 127.1(2C), 114.0(2C), 80.2(2C), 61.5, 55.4, 28.4(6C).

HRMS $[M+Na]^+$ calculated for $C_{18}H_{28}N_2O_5Na$ 375.1896 found 375.1899.

m.p. 134-135 °C.

di-*tert*-butyl (*m*-tolylmethylene)dicarbamate 2j



Following the **general procedure F** using 3-methylbenzaldehyde (4.0 g, 33.29 mmol), *tert*-butyl carbamate (6.51 g, 55.60 mmol) and trifluoroacetic acid (210 µL, 2.76 mmol) under stirring for 24 h in acetic anhydride (7.6 mL) solution, the *N*-Boc aminal was obtained as a white powder (7.75 g, 23.05 mmol, 83%).

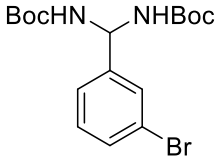
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.14 (m, 3H), 7.09 (d, *J* = 7.3 Hz, 1H), 6.07 (t, *J* = 8.0 Hz, 1H), 5.48 (bs, 2H), 2.34 (s, 3H), 1.44 (s, 18H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.9(2C), 139.9, 138.3, 128.8, 128.6, 126.7, 122.9, 80.2(2C), 61.8, 28.4(6C), 21.6.

HRMS $[M+Na]^+$ calculated for $C_{18}H_{28}N_2O_4Na$ 359.1947 found 359.1949.

m.p. 161-162 °C.

di-*tert*-butyl ((3-bromophenyl)methylene)dicarbamate 2k



Following the **general procedure F** using 3-bromobenzaldehyde (3.80 g, 20.53 mmol), *tert*-butyl carbamate (4.02 g, 34.29 mmol) and trifluoroacetic acid (131 µL, 1.71 mmol) under stirring for 2 h in acetic anhydride (4.7 mL) solution, the *N*-Boc aminal was obtained as a white powder (5.71 g, 14.23 mmol, 83%).

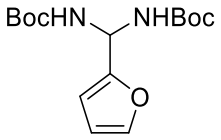
^{1}H NMR (200 MHz, $CDCl_3$) δ 7.62 – 7.11 (m, 4H), 6.03 (t, *J* = 8.0 Hz, 1H), 5.60 (bs, 1H), 1.44 (s, 18H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 154.9(2C), 142.3, 131.1, 130.2, 129.2, 124.7, 122.8, 80.6(2C), 61.1, 28.4(6C).

HRMS $[M+Na]^+$ calculated for $C_{17}H_{25}N_2O_4BrNa$ 423.0895 found 423.0895.

m.p. 148-149 °C.

di-*tert*-butyl (furan-2-ylmethylene)dicarbamate 2l



Following the **general procedure F** using 2-furaldehyde (2.0 g, 20.81 mmol), *tert*-butyl carbamate (4.07 g, 34.76 mmol) and trifluoroacetic acid (134 µL, 1.75 mmol) under stirring for 2 h in acetic anhydride (4.8 mL) solution, the *N*-Boc aminal was obtained as a white powder (4.06 g, 13.01 mmol, 75%).

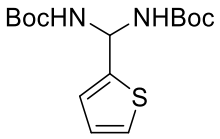
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (bs, 1H), 6.32 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.28 (d, *J* = 3.3 Hz, 1H), 6.11 (t, *J* = 8.5 Hz, 1H), 5.57 (bs, 2H), 1.44 (s, 18H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.6(2C), 151.9, 142.3, 110.6, 106.8, 80.5(2C), 56.9, 28.4(6C).

HRMS $[M+Na]^+$ calculated for $C_{15}H_{24}N_2O_5Na$ 335.1583 found 335.1586.

m.p. 146-147 °C.

di-*tert*-butyl (thiophen-2-ylmethylene)dicarbamate 2m



Following the **general procedure F** using 2-thiophenecarboxaldehyde (2.00 g, 17.83 mmol), *tert*-butyl carbamate (3.49 g, 29.78 mmol) and trifluoroacetic acid (114 μL, 1.49 mmol) under stirring for 8 h in acetic anhydride (4.1 mL) solution, the *N*-Boc aminal was obtained as a white powder (2.01 g, 6.12 mmol, 41%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 4.7 Hz, 1H), 7.01 – 6.90 (m, 2H), 6.31 – 6.21 (m, 1H), 5.72 (bs, 2H), 1.45 (s, 18H).

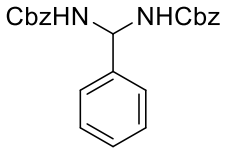
^{13}C NMR (126 MHz, $CDCl_3$) δ 154.7(2C), 144.6, 127.1, 125.2, 124.5, 80.5(2C), 58.9, 28.4(6C).

HRMS $[M+Na]^+$ calculated for $C_{15}H_{24}N_2O_4SNa$ 351.1354 found 351.1355.

m.p. 133-134 °C.

4.4. *N*-Cbz aminals

dibenzyl (phenylmethylene)dicarbamate 5a



Following the **general procedure G** using benzaldehyde (4.08 mL, 40.00 mmol), benzyl carbamate (12.70 g, 84.00 mmol) and trifluoroacetic acid (306 μL, 4.00 mmol) under stirring for 20 h in acetic anhydride (12.0 mL) solution, the *N*-Cbz aminal was obtained as a white powder (14.02 g, 35.91 mmol, 90% yield).

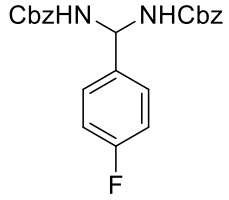
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.21 (m, 15H), 6.29 (t, *J* = 8.0 Hz, 1H), 5.80 (bs, 2H), 5.12 (d, *J* = 2.6 Hz, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5(2C), 138.9, 136.2(2C), 128.9(2C), 128.7(4C), 128.4, 128.3(4C), 128.3(2C), 125.9(2C), 67.2(2C), 62.2.

HRMS $[M+Na]^+$ calculated for $C_{23}H_{22}N_2O_4Na$ 413.1477 found 413.1470.

m.p. 174-175 °C.

dibenzyl ((4-fluorophenyl)methylene)dicarbamate 5b



Following the **general procedure G** using 4-fluorobenzaldehyde (1.24 mL, 10.00 mmol), benzyl carbamate (3.17 g, 21.00 mmol) and trifluoroacetic acid (77 μL, 1.00 mmol) under stirring for 1 h in acetic anhydride (3.0 mL) solution, the *N*-Cbz aminal was obtained as a white powder (1.63 g, 3.99 mmol, 40% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 12H), 7.05 – 6.95 (m, 2H), 6.24 (t, *J* = 8.0 Hz, 1H), 5.97 (bs, 2H), 5.17 – 5.03 (m, 4H).

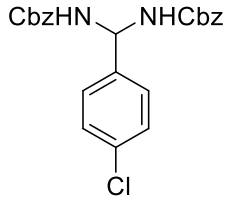
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 155.5(2C), 136.1(2C), 134.8, 128.7(4C), 128.4(2C), 128.3(4C), 127.8(2C), 115.7(2C), 67.3(2C), 61.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -114.02.

HRMS $[M+Na]^+$ calculated for $C_{23}H_{21}N_2O_4FNa$ 431.1383 found 431.1376.

m.p. 189-190 °C.

dibenzyl ((4-chlorophenyl)methylene)dicarbamate 5c



Following the **general procedure G** using 4-chlorobenzaldehyde (2.11 g, 15.00 mmol), benzyl carbamate (4.76 g, 31.50 mmol) and trifluoroacetic acid (115 μL, 1.50 mmol) under stirring for 1 h in acetic anhydride (4.5 mL) solution, the *N*-Cbz aminal was obtained as a white powder (1.63 g, 8.71 mmol, 58% yield).

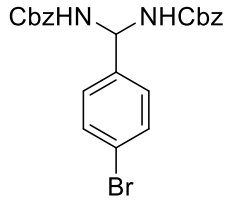
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.27 (m, 14H), 6.21 (t, *J* = 8.0 Hz, 1H), 5.92 (bs, 2H), 5.16 – 5.06 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5(2C), 137.5, 136.0(2C), 134.4, 129.0(2C), 128.7(4C), 128.5(2C), 128.3(4C), 127.4(2C), 67.4(2C), 61.7.

HRMS $[M+Na]^+$ calculated for $C_{23}H_{21}N_2O_4ClNa$ 447.1088 found 447.1089.

m.p. 190-191 °C.

dibenzyl ((4-bromophenyl)methylene)dicarbamate 5d



Following the **general procedure G** using 4-bromobenzaldehyde (2.78 g, 15.03 mmol), benzyl carbamate (4.76 g, 31.50 mmol) and trifluoroacetic acid (115 μL, 1.50 mmol) under stirring for 24 h in acetic anhydride (4.5 mL) solution, the *N*-Cbz aminal was obtained as a white powder (4.16 g, 8.86 mmol, 59% yield).

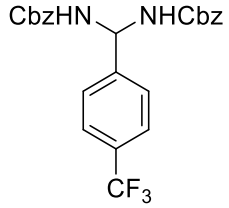
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.1 Hz, 2H), 7.42 – 7.19 (m, 12H), 6.18 (t, *J* = 8.0 Hz, 1H), 5.88 (bs, 2H), 5.18 – 5.05 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5(2C), 138.0, 136.0(2C), 132.0(2C), 128.7(4C), 128.5(2C), 128.3(4C), 127.8(2C), 122.5, 67.4(2C), 61.8.

HRMS $[M+Na]^+$ calculated for $C_{23}H_{21}N_2O_4BrNa$ 491.0582 found 491.0583.

m.p. 191-192 °C.

dibenzyl ((4-(trifluoromethyl)phenyl)methylene)dicarbamate 5e



Following the **general procedure G** using 4-(trifluoromethyl)benzaldehyde (1.74 g, 10.00 mmol), benzyl carbamate (3.17 g, 21.00 mmol) and trifluoroacetic acid (77 μL, 1.00 mmol) under stirring for 24 h in acetic anhydride (3.0 mL) solution, the *N*-Cbz aminal was obtained as a white powder (4.48 g, 9.77 mmol, 98% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.2 Hz, 2H), 7.50 (d, *J* = 8.2 Hz, 2H), 7.42 – 7.19 (m, 10H), 6.25 (t, *J* = 7.9 Hz, 1H), 6.04 (bs, 2H), 5.19 – 5.03 (m, 4H).

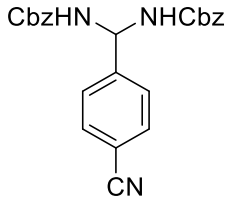
^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6(2C), 142.8, 136.0(2C), 130.7, 128.7(4C), 128.5(2C), 128.3(4C), 126.5(2C), 125.8(2C), 124.1, 67.5(2C), 61.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.65.

HRMS $[M+Na]^+$ calculated for $C_{24}H_{21}N_2O_4F_3Na$ 481.1351 found 481.1357.

m.p. 204-205 °C.

dibenzyl ((4-cyanophenyl)methylene)dicarbamate 5f



Following the **general procedure G** using 4-cyanobenzaldehyde (1.31 g, 10.00 mmol), benzyl carbamate (3.17 g, 21.00 mmol) and trifluoroacetic acid (77 μL, 1.00 mmol) under stirring for 24 h in acetic anhydride (3.0 mL) solution, the *N*-Cbz aminal was obtained as a white powder (3.80 g, 9.15 mmol, 92% yield).

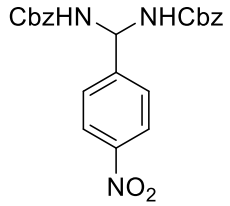
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.1 Hz, 2H), 7.50 (d, *J* = 8.1 Hz, 2H), 7.44 – 7.27 (m, 10H), 6.21 (t, *J* = 8.1 Hz, 1H), 6.03 (bs, 2H), 5.17 – 5.03 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6(2C), 144.1, 135.8(2C), 132.6(2C), 128.7(4C), 128.6(2C), 128.3(4C), 126.9(2C), 118.5, 112.3, 67.6(2C), 61.7.

HRMS $[M+Na]^+$ calculated for $C_{24}H_{21}N_3O_4Na$ 438.1430 found 438.1434.

m.p. 187-188 °C.

dibenzyl ((4-nitrophenyl)methylene)dicarbamate 5g



Following the **general procedure G** using 4-nitrobenzaldehyde (0.76 g, 5.00 mmol), benzyl carbamate (1.59 g, 10.50 mmol) and trifluoroacetic acid (38 μL, 0.50 mmol) under stirring for 24 h in acetic anhydride (1.5 mL) solution, the *N*-Cbz aminal was obtained as a white powder (1.90 g, 4.36 mmol, 87% yield).

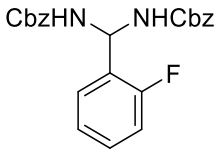
^{1}H NMR (400 MHz, DMSO-d_6) δ 8.30 (bs, 2H), 8.21 (d, *J* = 8.8 Hz, 2H), 7.66 (d, *J* = 8.8 Hz, 2H), 7.46 – 7.24 (m, 10H), 6.33 (t, *J* = 8.1 Hz, 1H), 5.07 (s, 4H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 155.3(2C), 147.22, 147.16, 136.8(2C), 128.4(4C), 128.0(2C), 127.94(4C), 127.88(2C), 123.5(2C), 65.8(2C), 61.4.

HRMS $[M+Na]^+$ calculated for $C_{23}H_{21}N_3O_6Na$ 458.1328 found 458.1331.

m.p. 197-198 °C.

dibenzyl ((2-fluorophenyl)methylene)dicarbamate 5h



Following the **general procedure G** using 2-fluorobenzaldehyde (3.10 g, 25.00 mmol), benzyl carbamate (7.94 g, 52.50 mmol) and trifluoroacetic acid (191 μL, 2.50 mmol) under stirring for 24 h in acetic anhydride (7.5 mL) solution, the *N*-Cbz aminal was obtained as a white powder (7.34 g, 17.98 mmol, 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.28 (m, 12H), 7.17 – 7.03 (m, 2H), 6.51 (t, *J* = 8.3 Hz, 1H), 5.87 (bs, 2H), 5.16 – 5.04 (m, 4H).

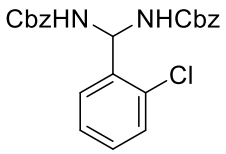
^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 155.1(2C), 136.1(2C), 130.4, 128.65(4C), 128.58, 128.4(2C), 128.3(4C), 126.3, 124.6, 116.1, 67.3(2C), 59.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -117.92.

HRMS $[M+Na]^+$ calculated for $C_{23}H_{21}N_2O_4FNa$ 431.1383 found 431.1382.

m.p. 174-175 °C.

dibenzyl ((2-chlorophenyl)methylene)dicarbamate 5i



Following the **general procedure G** using 2-chlorobenzaldehyde (1.41 g, 10.03 mmol), benzyl dicarbamate (3.17 g, 21.00 mmol) and trifluoroacetic acid (77 μL, 1.00 mmol) under stirring for 24 h in acetic anhydride (3.0 mL) solution, the *N*-Cbz aminal was obtained as a white powder (2.15 g, 5.06 mmol, 51% yield).

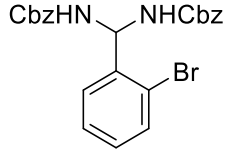
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.45 (m, 1H), 7.43 – 7.23 (m, 13H), 6.55 (t, *J* = 8.1 Hz, 1H), 5.99 (bs, 2H), 5.16 – 5.04 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.1(2C), 136.2, 136.1(2C), 132.5, 130.4, 129.9, 128.7(4C), 128.5, 128.4(2C), 128.3(4C), 127.2, 67.3(2C), 61.0.

HRMS $[M+Na]^+$ calculated for $C_{23}H_{21}N_2O_4ClNa$ 447.1088 found 447.1086.

m.p. 164-165 °C.

dibenzyl ((2-bromophenyl)methylene)dicarbamate 5j



Following the **general procedure G** using 2-bromobenzaldehyde (0.56 g, 3.03 mmol), benzyl carbamate (0.95 g, 6.30 mmol) and trifluoroacetic acid (23 μL, 0.30 mmol) under stirring for 24 h in acetic anhydride (0.9 mL) solution, the *N*-Cbz aminal was obtained as a white powder (0.93 g, 1.98 mmol, 65% yield).

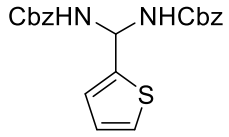
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 7.9, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.40 – 7.27 (m, 11H), 7.19 (ddd, *J* = 7.7, 7.6 Hz, 1.7 Hz, 1H), 6.50 (t, *J* = 7.9 Hz, 1H), 6.00 (bs, 2H), 5.17 – 5.04 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.1(2C), 137.8, 136.1(2C), 133.6, 130.2, 128.6(4C), 128.5, 128.35(2C), 128.27(4C), 127.8, 122.5, 67.3(2C), 62.6.

HRMS $[M+Na]^+$ calculated for $C_{23}H_{21}N_2O_4BrNa$ 491.0582 found 491.0583.

m.p. 168-169 °C.

dibenzyl (thiophen-2-ylmethylene)dicarbamate 5k



Following the **general procedure G** using 2-thiophenecarboxaldehyde (1.12 g, 10.00 mmol), benzyl carbamate (3.17 g, 21.00 mmol) and trifluoroacetic acid (77 μL, 1.00 mmol) under stirring for 24 h in acetic anhydride (3.0 mL) solution, the *N*-Cbz aminal was obtained as a white powder (3.24 g, 8.17 mmol, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.27 (s, 10H), 7.24 (dd, *J* = 5.1, 1.3 Hz, 1H), 7.01 (d, *J* = 3.6 Hz, 1H), 6.96 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.47 (t, *J* = 8.3 Hz, 1H), 5.92 (bs, 2H), 5.20 – 5.07 (m, 4H).

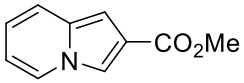
^{13}C NMR (101 MHz, $CDCl_3$) δ 155.2(2C), 143.3, 136.1(2C), 128.7(4C), 128.4(2C), 128.3(4C), 127.3, 125.7, 125.0, 67.4(2C), 59.5.

HRMS $[M+Na]^+$ calculated for $C_{21}H_{20}N_2O_4SNa$ 419.1041 found 419.1044.

m.p. 184-185 °C.

5. Synthesis of indolizines

methyl indolizine-2-carboxylate 1a



Under inert atmosphere, a round bottom flask was charged with 2-formyl pyridine (11.0 g, 102.70 mmol) and methyl acrylate (19.42 mL, 215.67 mmol). To this solution was added diazo[2.2.2]bicyclooctane (1.70 g, 15.15 mmol). The reaction mixture was stirred at room temperature for 21 h, after which the reaction mixture was filtered through silica using hexane and ethyl acetate as eluent. The solvent was removed and the residue was dissolved in 50 mL acetic anhydride. The solution was heated to 130 °C for 3 h. The acetic anhydride and acetic acid were removed on vacuo. The remaining solid was purified by flash chromatography (95:05 hexane/dichloromethane to 85:15 hexane/dichloromethane). Then recrystallization in hexane/dichloromethane to give the product as white powder (8.21 g, 46%).[14]

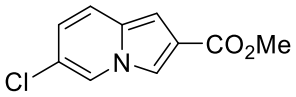
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.1 Hz, 1H), 7.78 (s, 1H), 7.34 (d, *J* = 9.1 Hz, 1H), 6.81 (s, 1H), 6.66 (ddd, *J* = 9.1, 6.5, 1.0 Hz, 1H), 6.54 – 6.48 (m, 1H), 3.88 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 132.9, 125.4, 120.4, 119.7, 118.2, 116.0, 112.4, 100.5, 51.5.

HRMS $[M+H]^+$ calculated for $C_{10}H_{10}NO_2$ 176.0712 found 176.0715.

m.p. 101-102 °C.

methyl 6-chloroindolizine-2-carboxylate 1b



Under inert atmosphere, a round bottom flask was charged with 5-chloro-2-formyl pyridine (3.50 g, 24.72 mmol) and methyl acrylate (5.36 mL, 59.52 mmol). To this solution was added diazo[2.2.2]bicyclooctane (0.33 g, 2.97 mmol). The reaction mixture was stirred at room temperature for 18 h, after which it was purified by flash chromatography (70:30 hexane/ethyl acetate). The solvent was removed and the residue was dissolved in 25 mL of acetic anhydride. The solution was heated to 135 °C for 3 h. The acetic anhydride and acetic acid were removed on vacuo. The remaining solid was purified by flash chromatography (95:05 hexane/dichloromethane to 80:20 hexane/dichloromethane) to give the product as white powder (3.63 g, 70%).

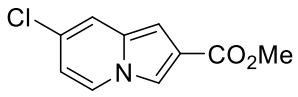
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.75 (s, 1H), 7.31 (d, *J* = 9.5 Hz, 1H), 6.86 (s, 1H), 6.65 (d, *J* = 9.5 Hz, 1H), 3.88 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.2, 131.2, 123.0, 120.9(2C), 120.6, 120.0, 116.4, 101.9, 51.7.

HRMS $[M+H]^+$ calculated for $C_{10}H_9NO_2Cl$ 210.0322 found 210.0325.

m.p. 109-110 °C.

methyl 7-chloroindolizine-2-carboxylate 1c



Under inert atmosphere, a round bottom flask was charged with 4-chloro-2-formyl pyridine (6.50 g, 45.92 mmol) and methyl acrylate (9.92 mL, 110.20 mmol). To this solution was added diazo[2.2.2]bicyclooctane (0.62 g, 5.51 mmol). The reaction mixture was stirred at room temperature for 16 h, after which it was purified by flash chromatography (75:25 hexane/ethyl acetate). The solvent was removed and the residue was dissolved in 46 mL acetic anhydride. The solution was heated to 140°C for 6 h. The acetic anhydride and acetic acid were removed on vacuo. The remaining solid was purified by flash chromatography (90:10 hexane/dichloromethane to 80:20 hexane/dichloromethane) to give the product as white powder (6.03 g, 63%).

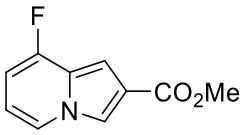
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 – 7.72 (m, 2H), 7.32 (s, 1H), 6.75 (s, 1H), 6.48 (dd, *J* = 7.4, 2.1 Hz, 1H), 3.87 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.2, 132.5, 126.1, 124.5, 120.9, 118.7, 116.4, 114.0, 100.7, 51.7.

HRMS $[M+H]^+$ calculated for $C_{10}H_9NO_2Cl$ 210.0322 found 210.0331.

m.p. 129-130 °C.

methyl 8-fluoroindolizine-2-carboxylate 1d



Under inert atmosphere, a round bottom flask was charged with 3-Fluoropicolinaldehyde (2.00 g, 16.00 mmol) and methyl acrylate (3.04 mL, 33.60 mmol). To this solution was added diazo[2.2.2]bicyclooctane (0.22 g, 1.90 mmol). The reaction mixture was stirred at room temperature for 16 h, after which it was purified by flash chromatography (70:30 hexane/dichloromethane). The

product was dissolved in 16 mL acetic anhydride. The solution was heated to 120 °C for 7 h. The acetic anhydride and acetic acid were removed on vacuo. The remaining solid was purified by flash chromatography (90:10 hexane/dichloromethan) to give the product as white powder (2.28 g, 74%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 2.9, 1.5 Hz, 1H), 7.67 (d, *J* = 6.9 Hz, 1H), 6.98 (s, 1H), 6.49 – 6.42 (m, 1H), 6.36 (dd, *J* = 10.5, 6.9 Hz, 1H), 3.88 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 155.1, 125.7, 121.8, 120.1, 117.7, 111.5, 100.3, 98.5 (d, *J* = 3.2 Hz), 51.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -124.50.

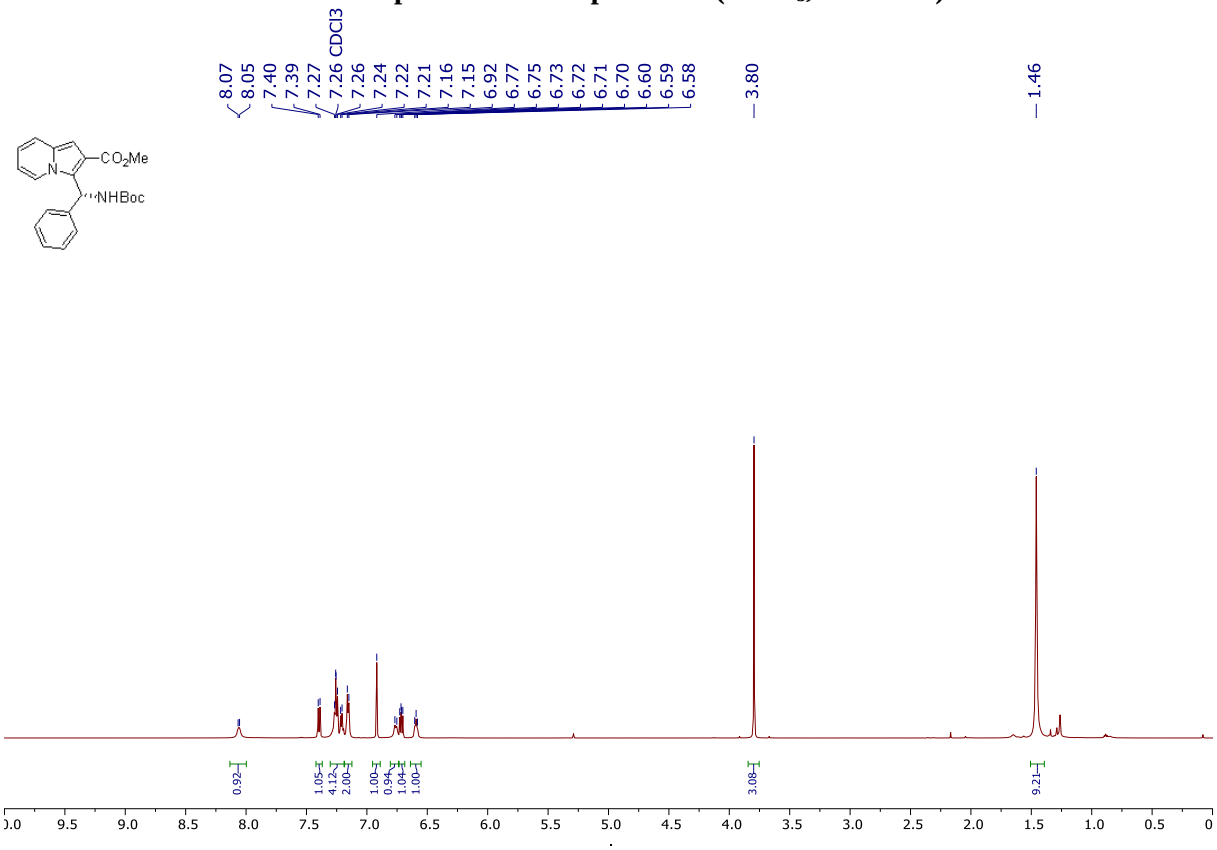
HRMS $[M+H]^+$ calculated for $C_{10}H_9NO_2F$ 194.0617 found 194.0626.

m.p. 79-80 °C.

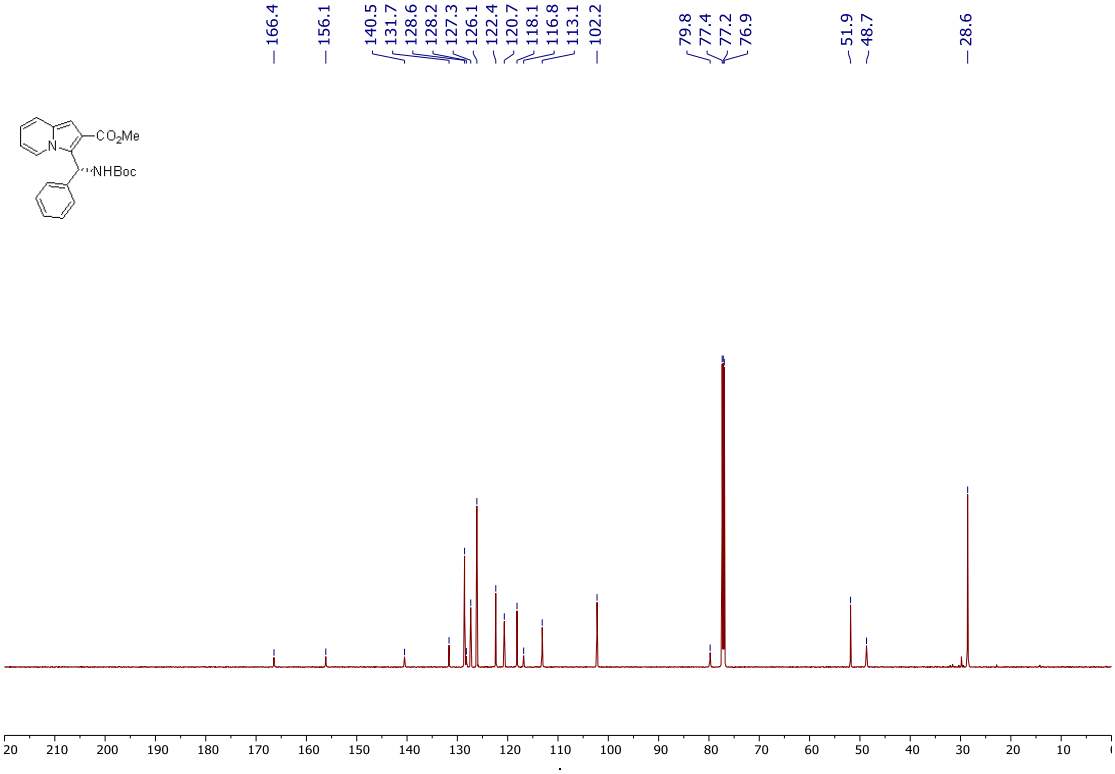
6. ^{1}H, ^{13}C and ^{19}F NMR Spectra

6.1. Products with Boc-protecting group 3a-s, 4a-s and 10

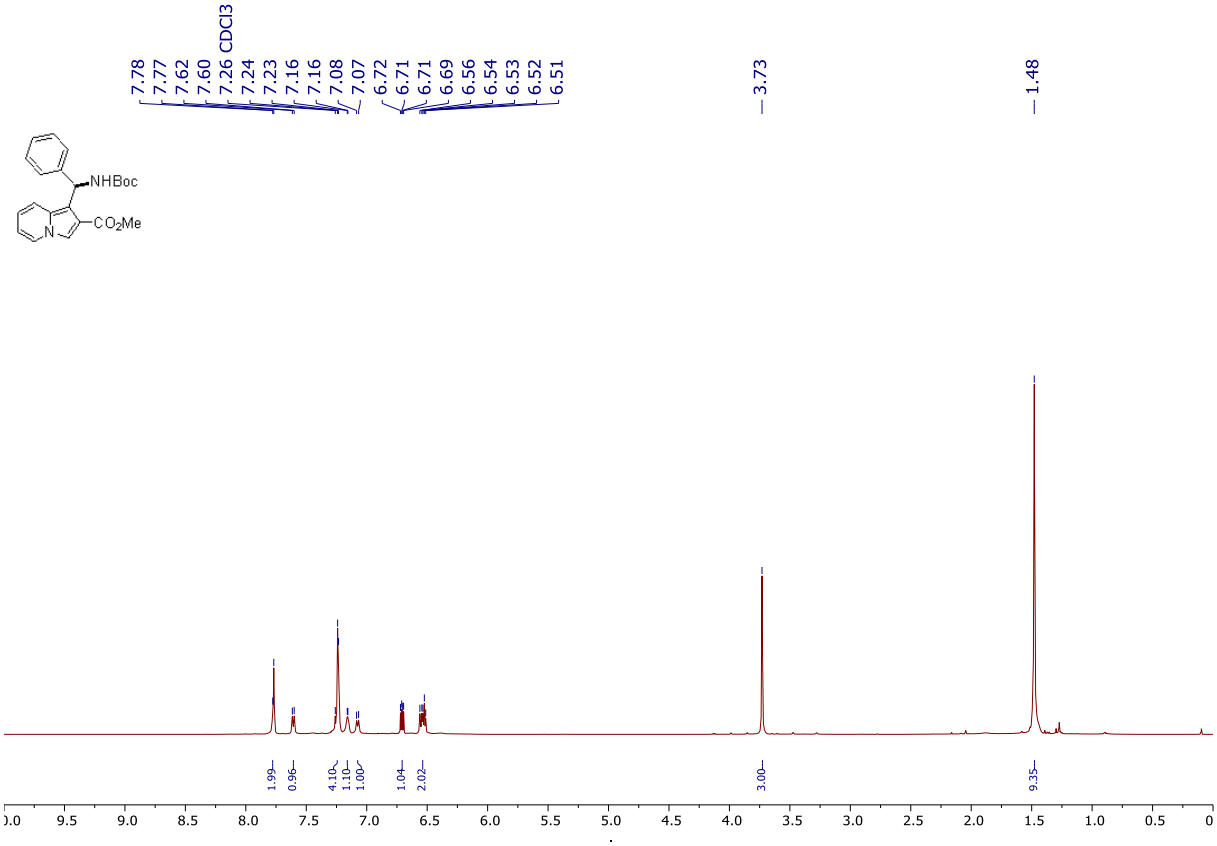
^{1}H NMR spectrum of compound 4a ($CDCl_3$, 600 MHz).



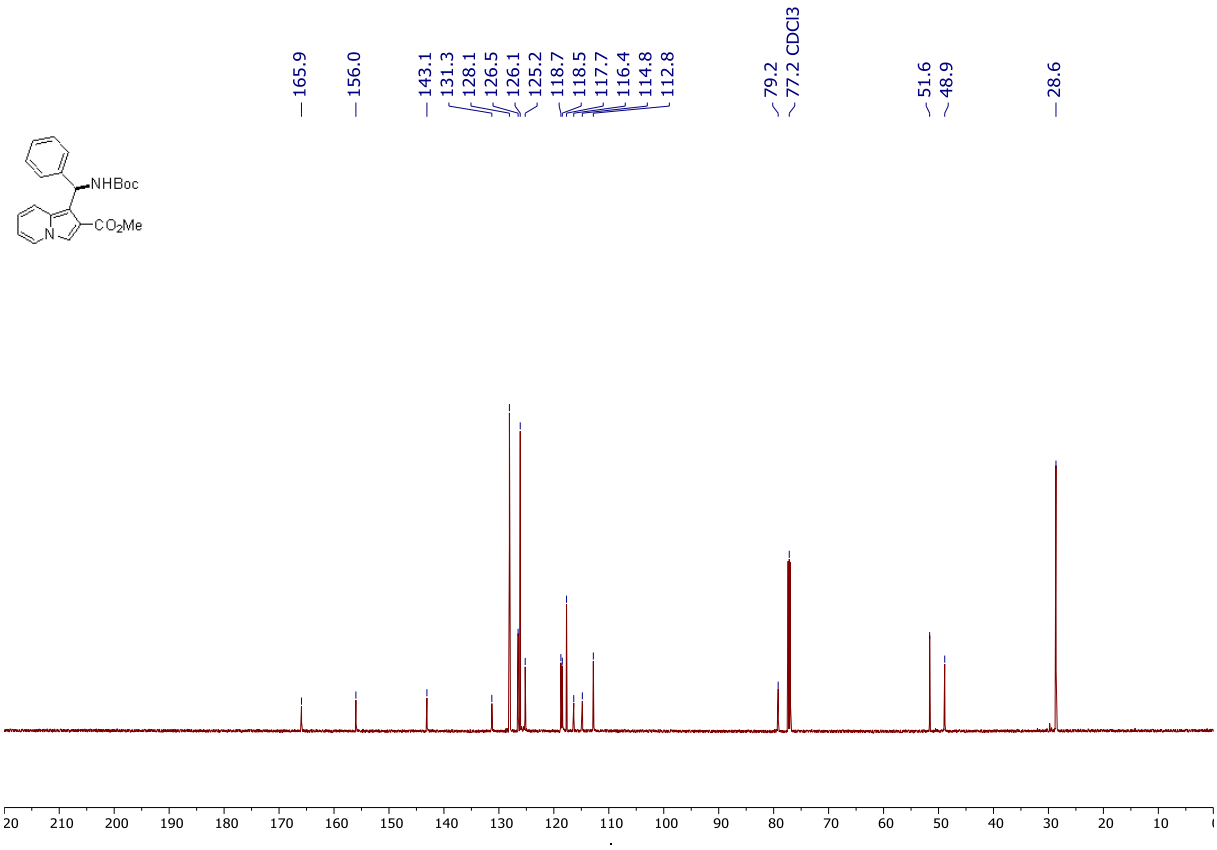
^{13}C NMR spectrum of compound 4a ($CDCl_3$, 151 MHz)



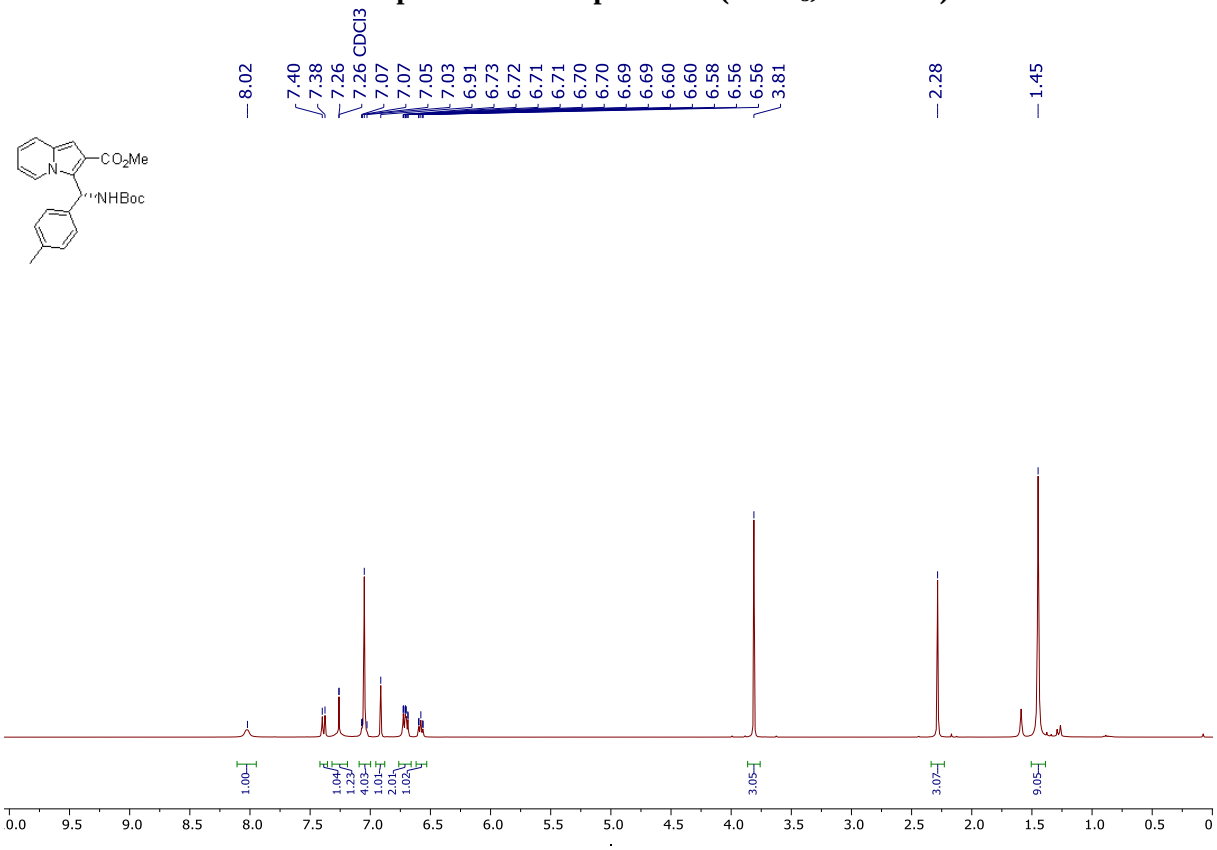
^{1}H NMR spectrum of compound 3a (CDCl3, 600 MHz)



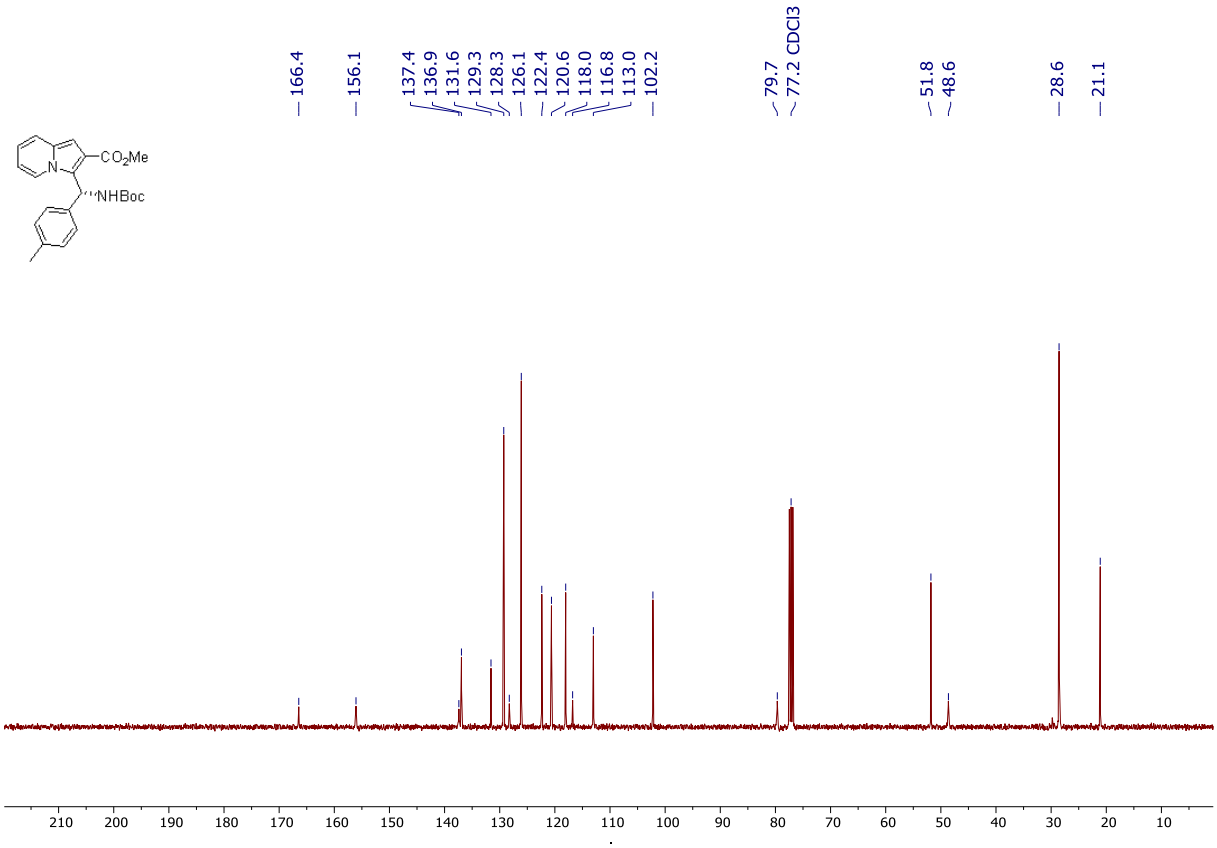
^{13}C NMR spectrum of compound 3a ($CDCl_3$, 151 MHz)



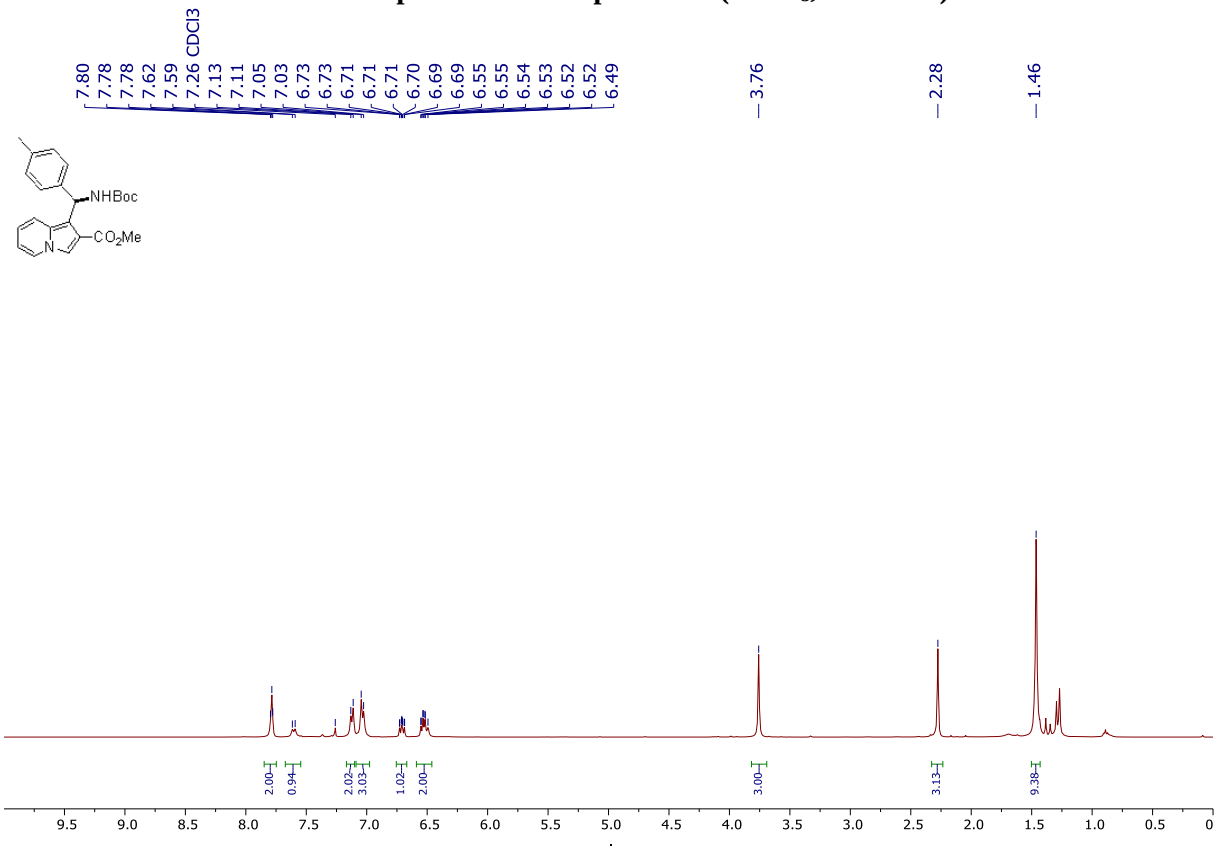
^{1}H NMR spectrum of compound 4b ($CDCl_3$, 400 MHz)



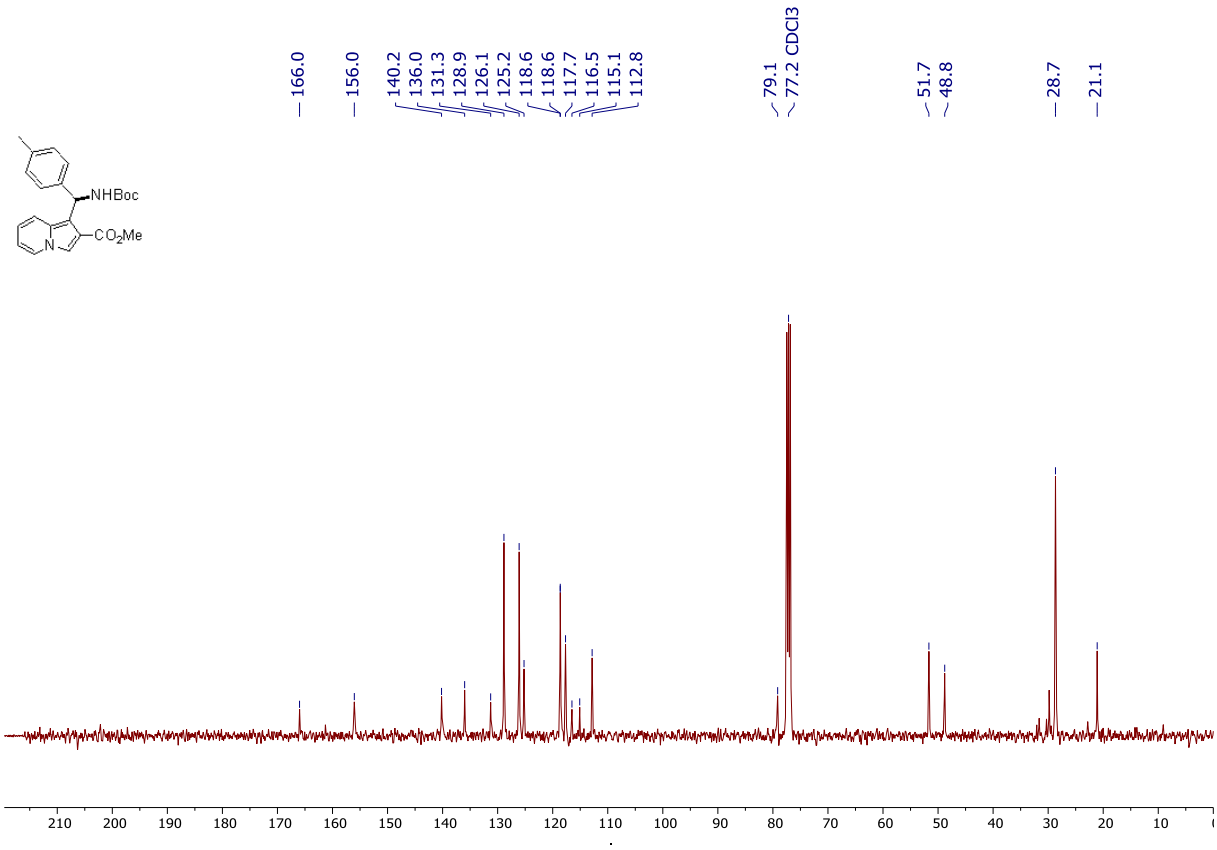
^{13}C NMR spectrum of compound 4b ($CDCl_3$, 101 MHz)



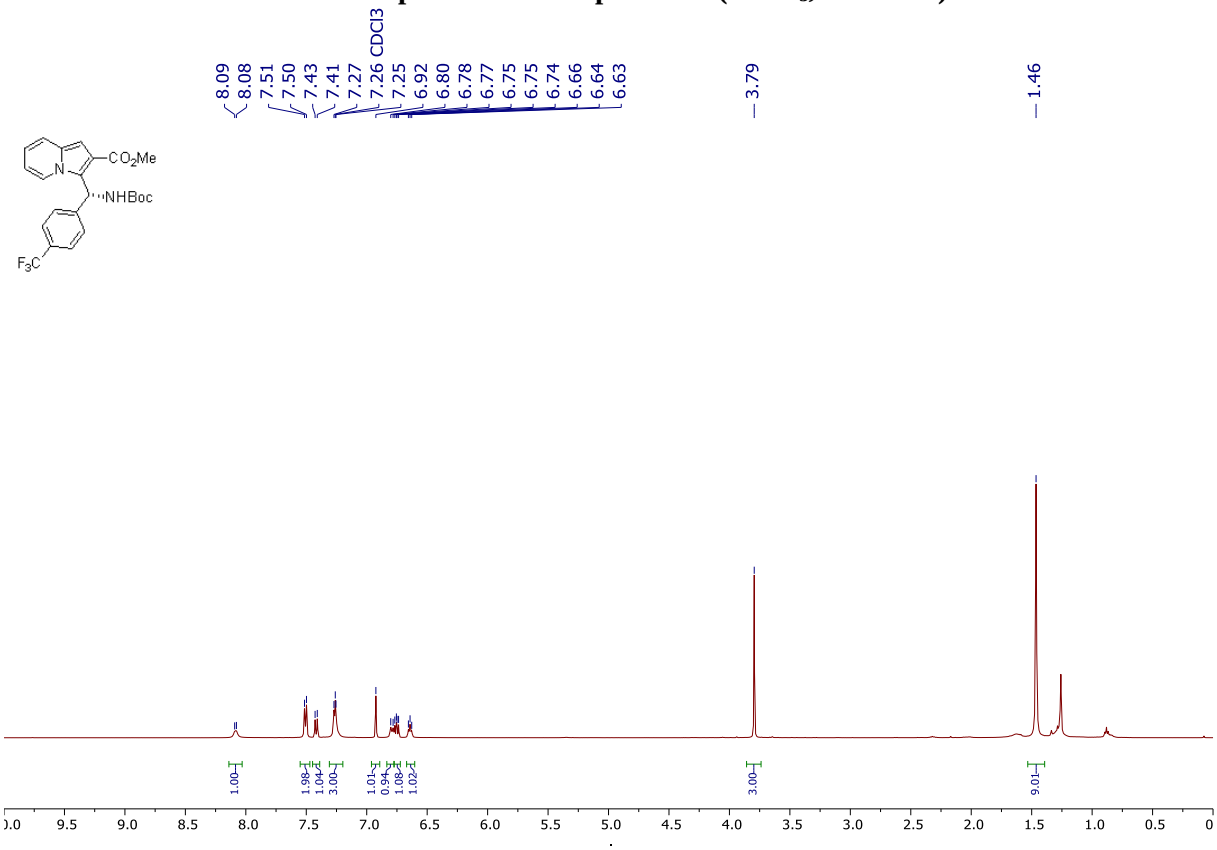
^{1}H NMR spectrum of compound 3b ($CDCl_3$, 400 MHz)



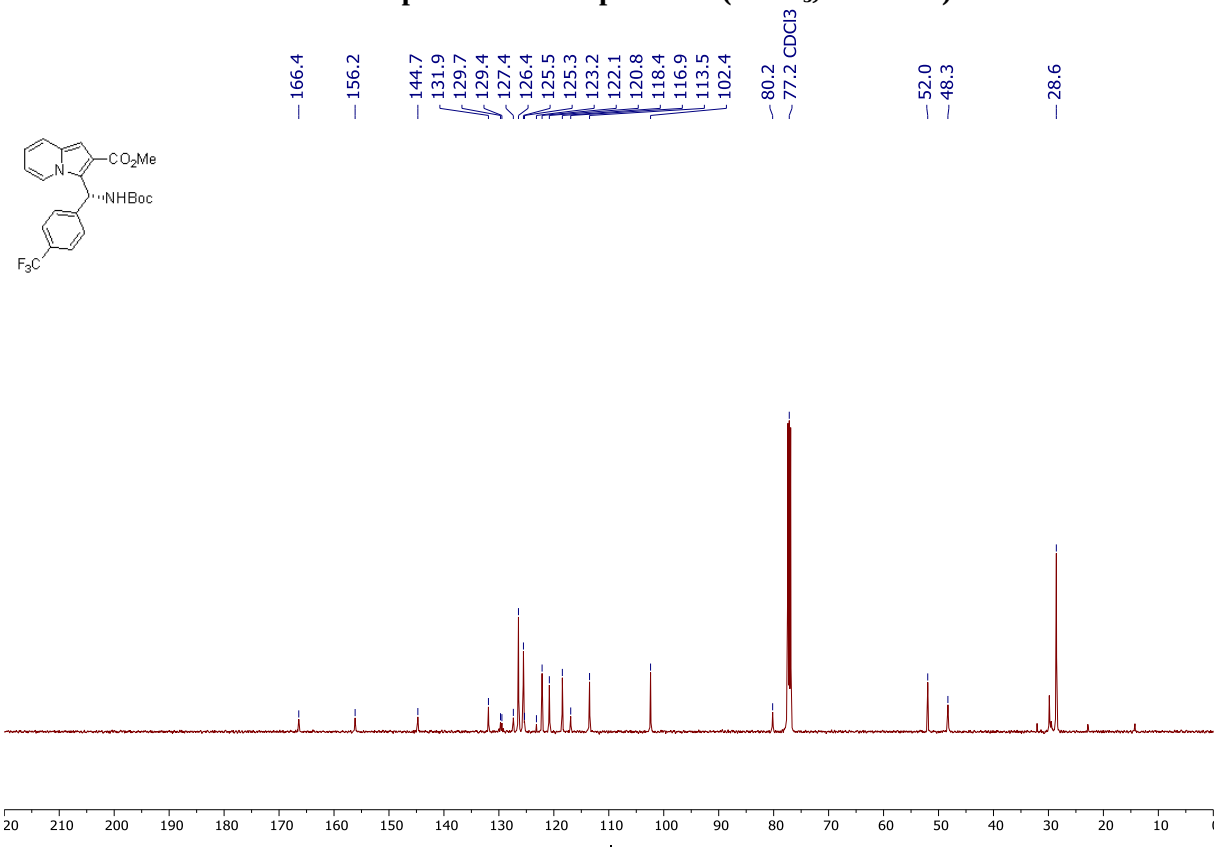
^{13}C NMR spectrum of compound 3b ($CDCl_3$, 101 MHz)



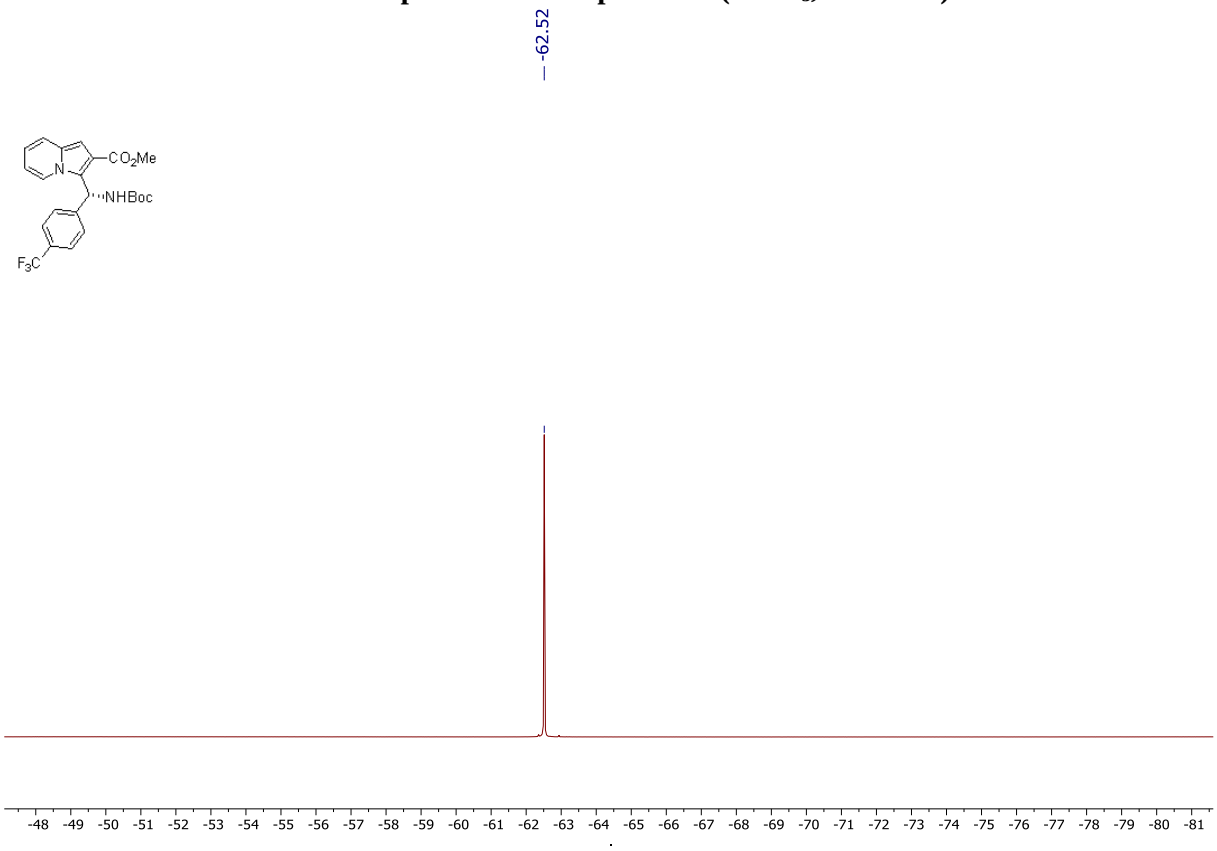
^{1}H NMR spectrum of compound 4c ($CDCl_3$, 500 MHz)



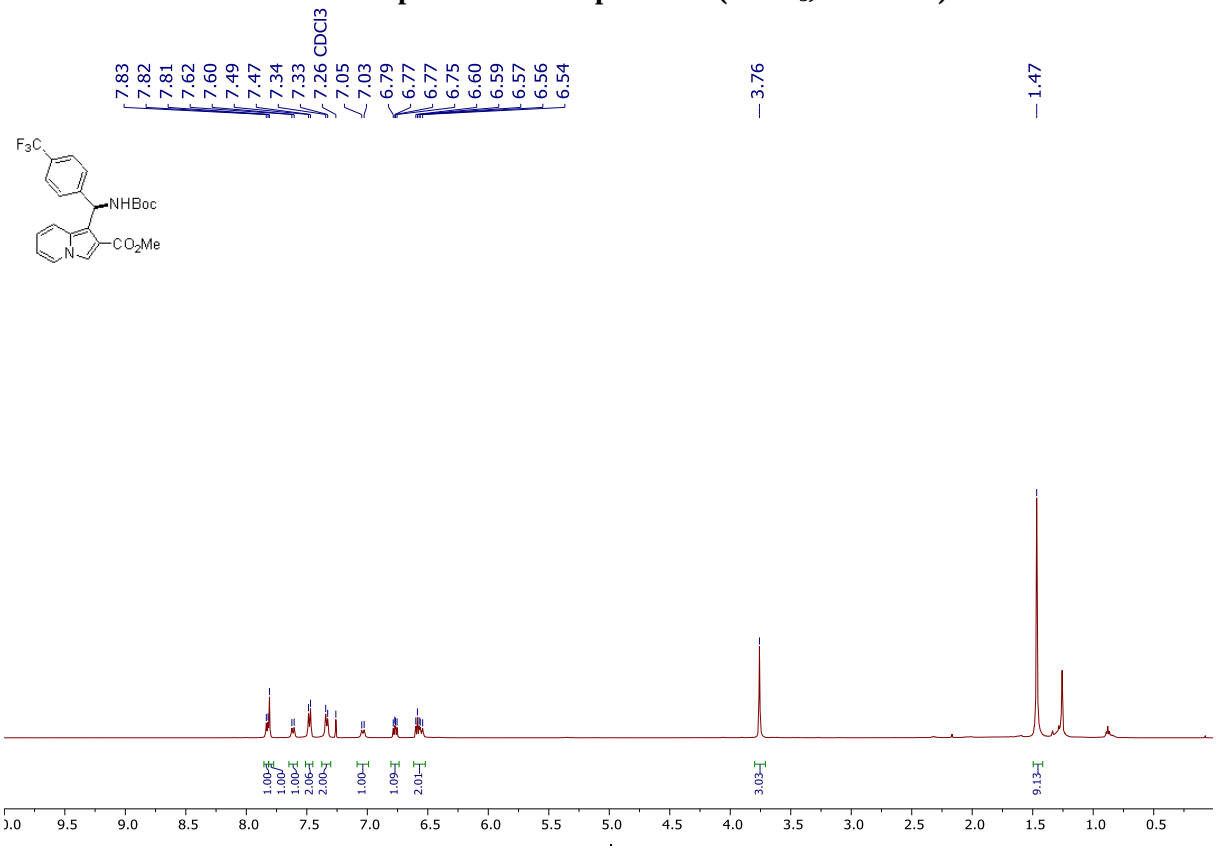
^{13}C NMR spectrum of compound 4c ($CDCl_3$, 126 MHz)



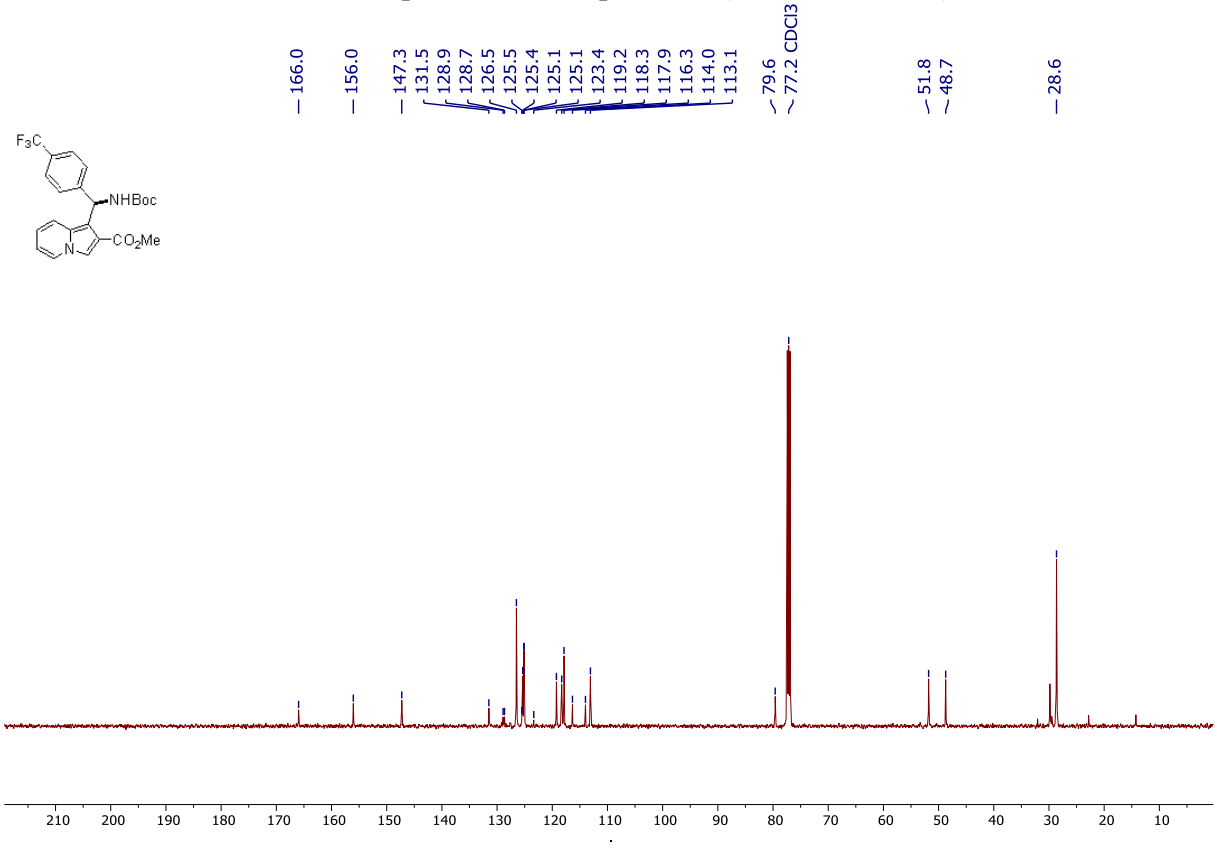
^{19}F NMR spectrum of compound 4c ($CDCl_3$, 470 MHz)



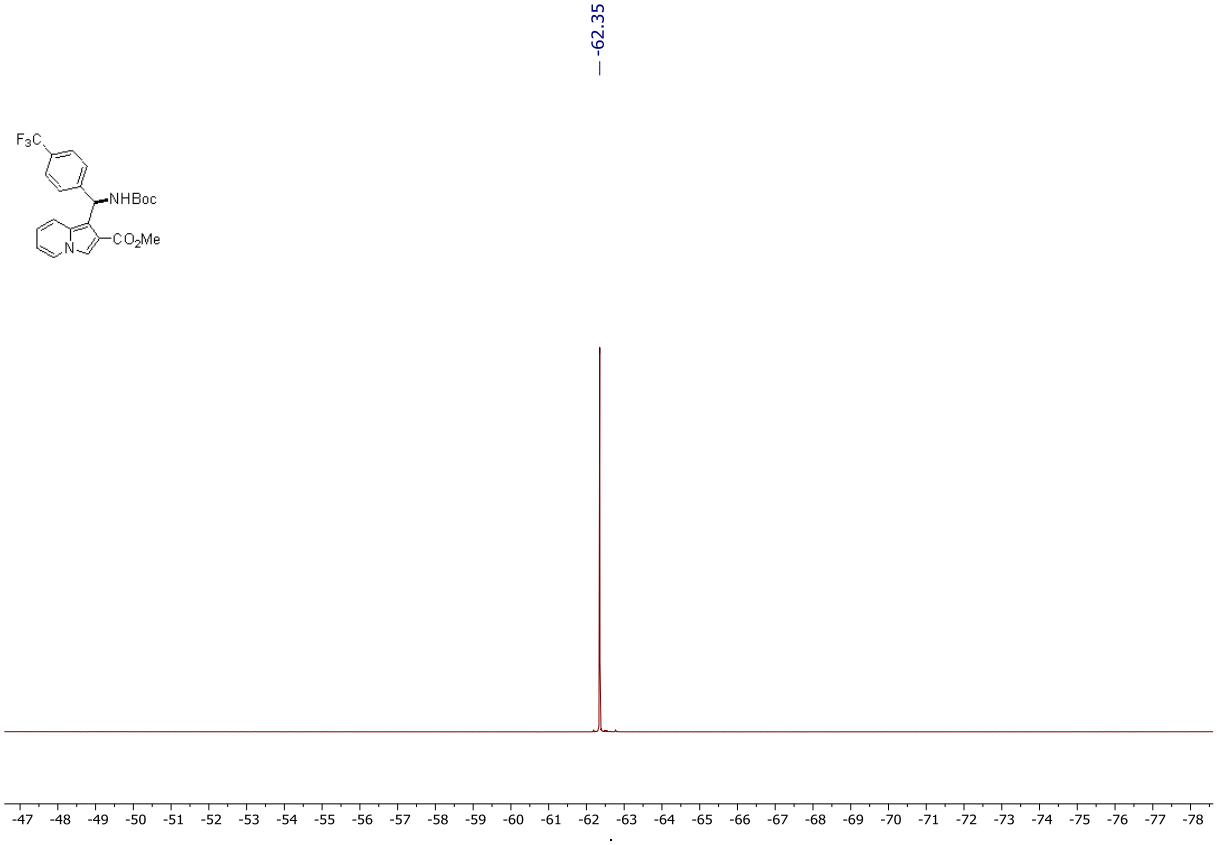
^{1}H NMR spectrum of compound 3c ($CDCl_3$, 500 MHz)



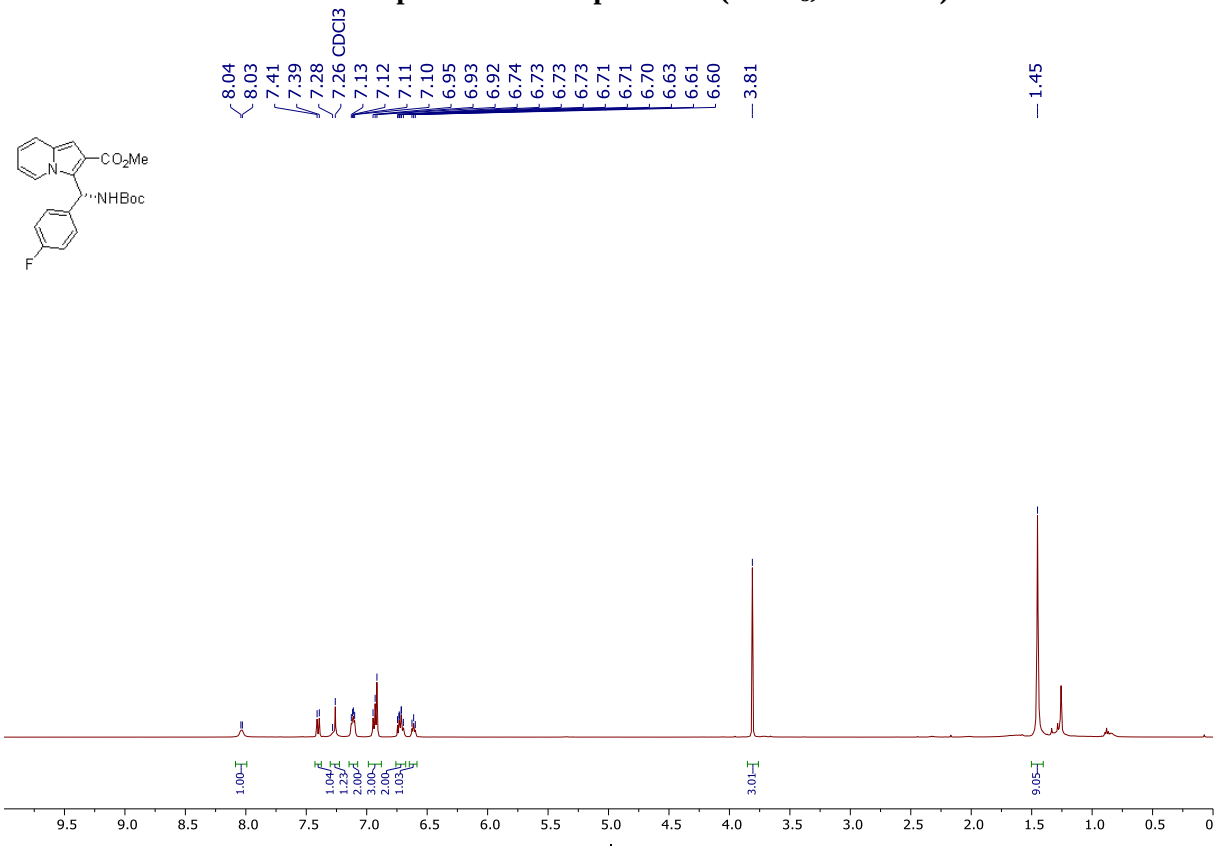
^{13}C NMR spectrum of compound 3c ($CDCl_3$, 126 MHz)



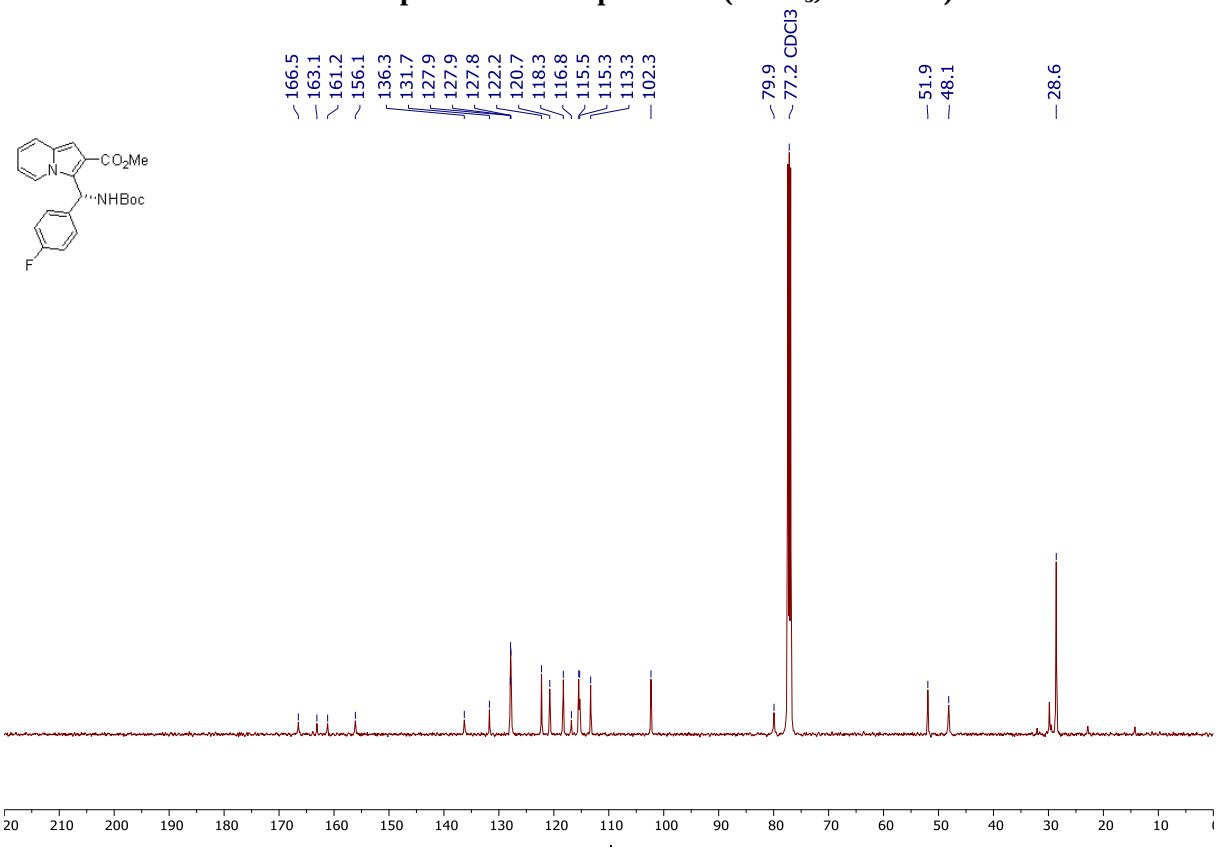
^{19}F NMR spectrum of compound 3c ($CDCl_3$, 470 MHz)



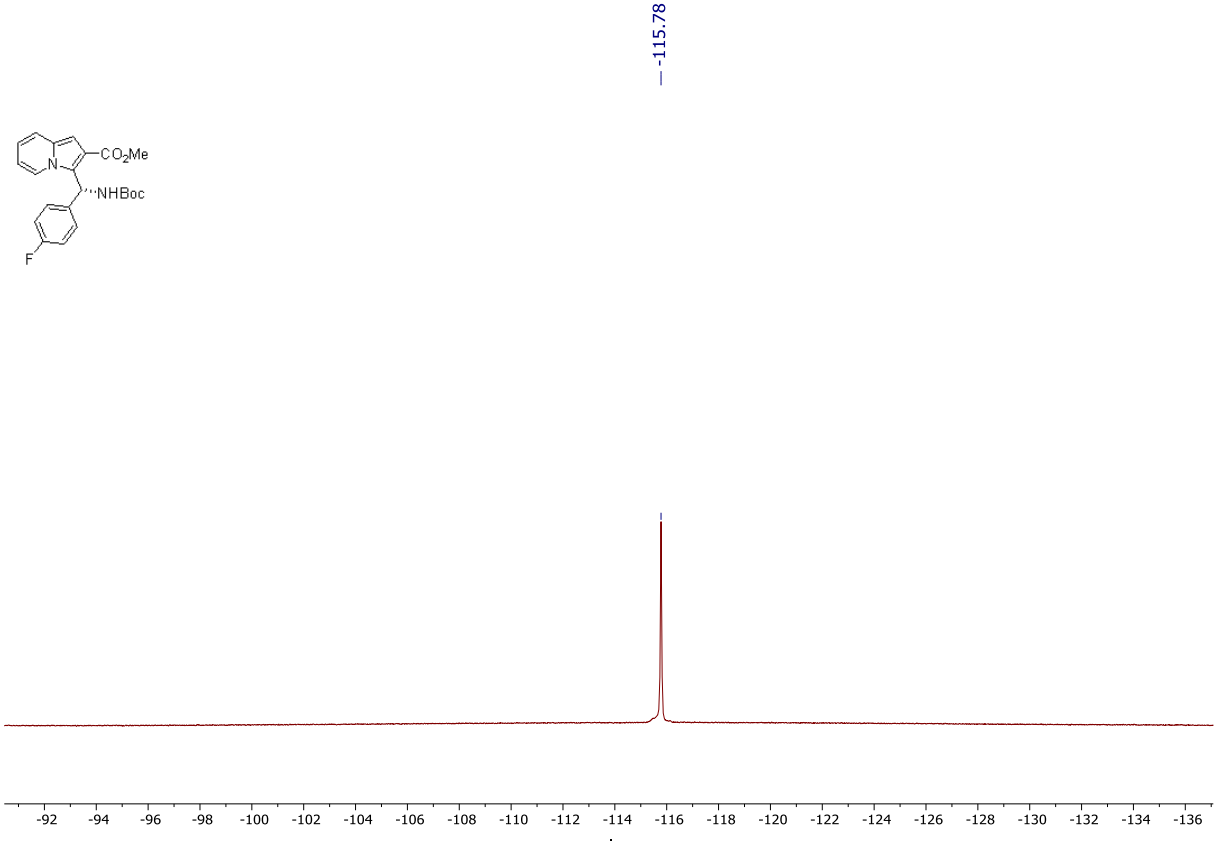
^{1}H NMR spectrum of compound 4d ($CDCl_3$, 500 MHz)



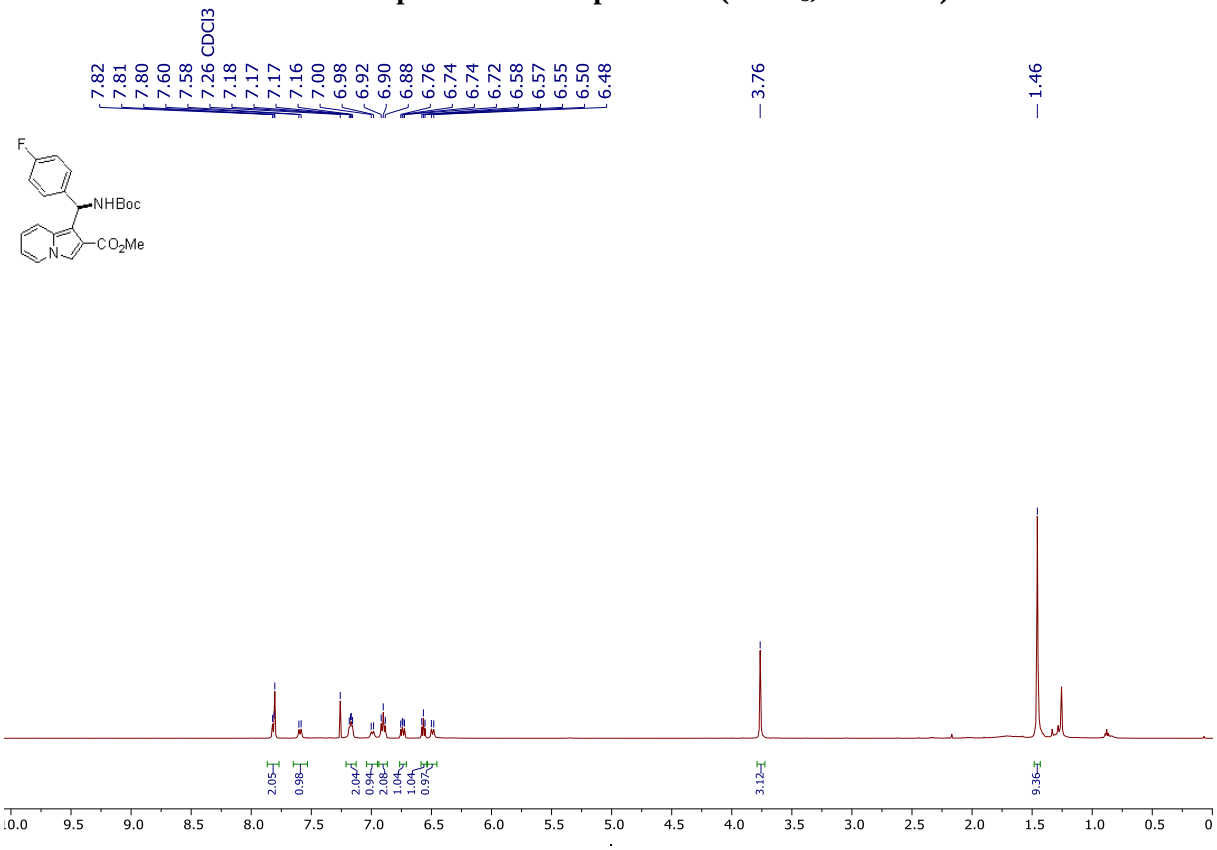
^{13}C NMR spectrum of compound 4d ($CDCl_3$, 126 MHz)



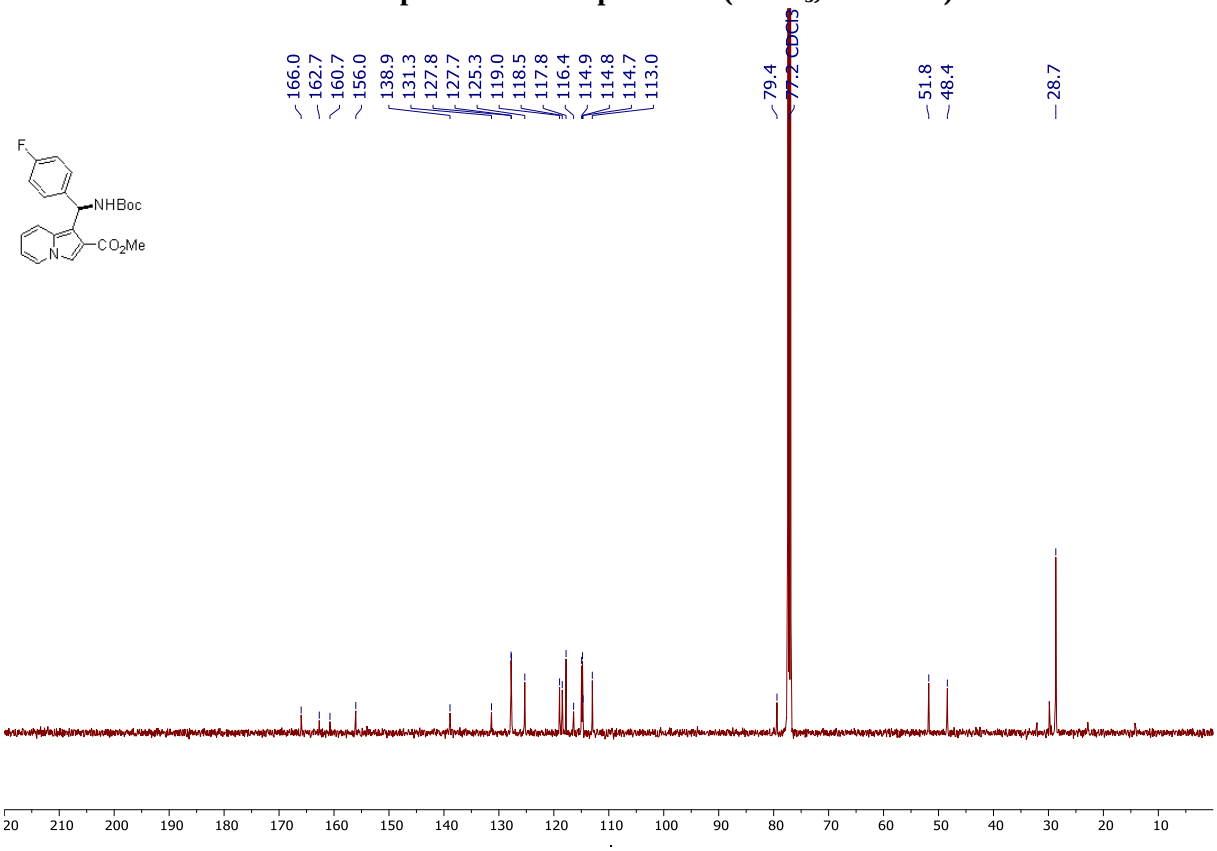
^{19}F NMR spectrum of compound 4d ($CDCl_3$, 470 MHz)



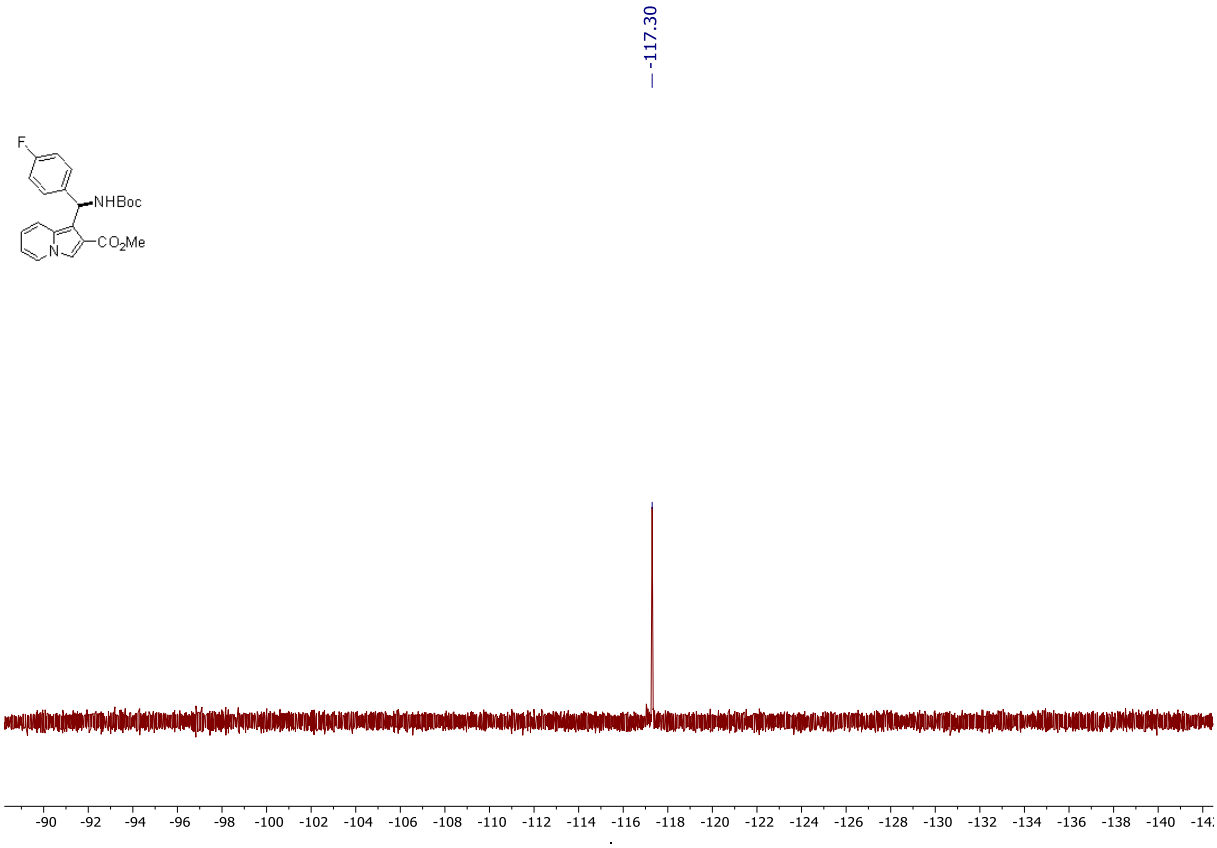
^{1}H NMR spectrum of compound 3d ($CDCl_3$, 500 MHz)



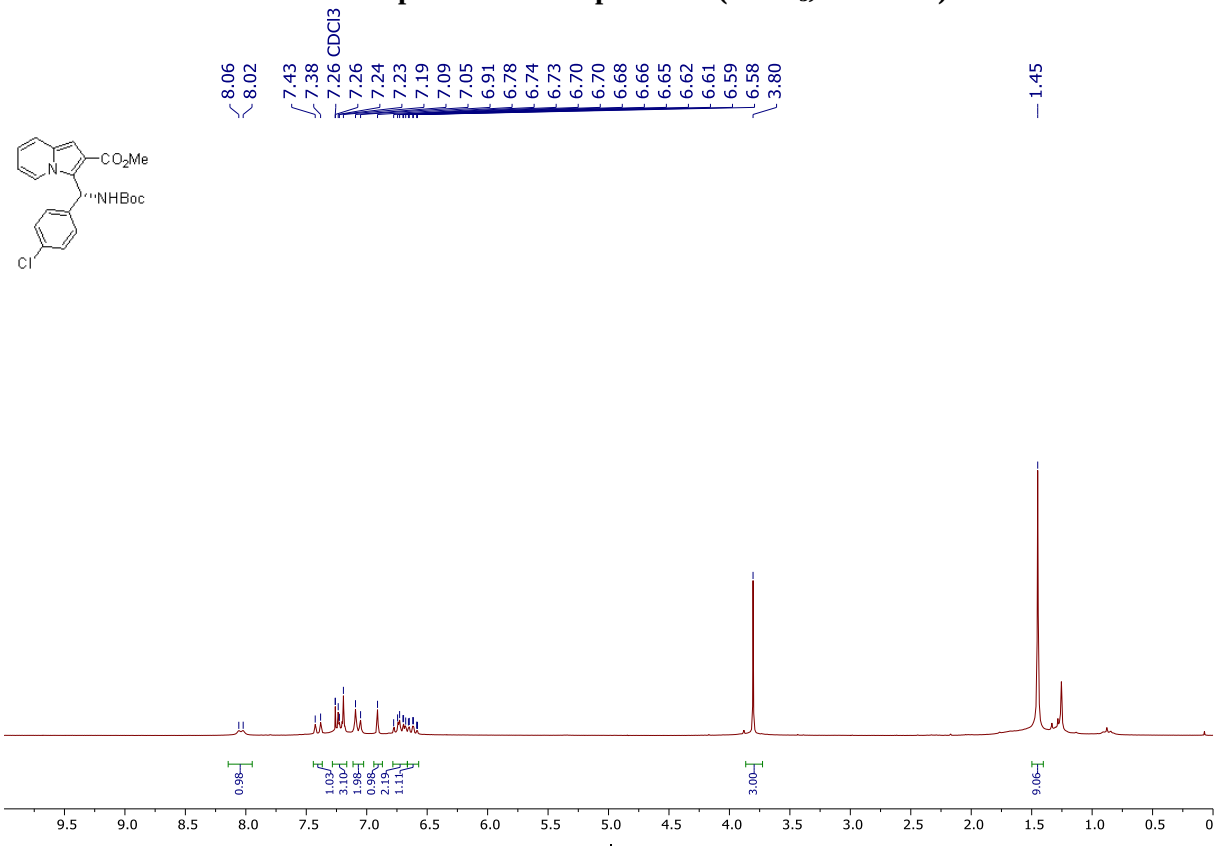
^{13}C NMR spectrum of compound 3d ($CDCl_3$, 126 MHz)



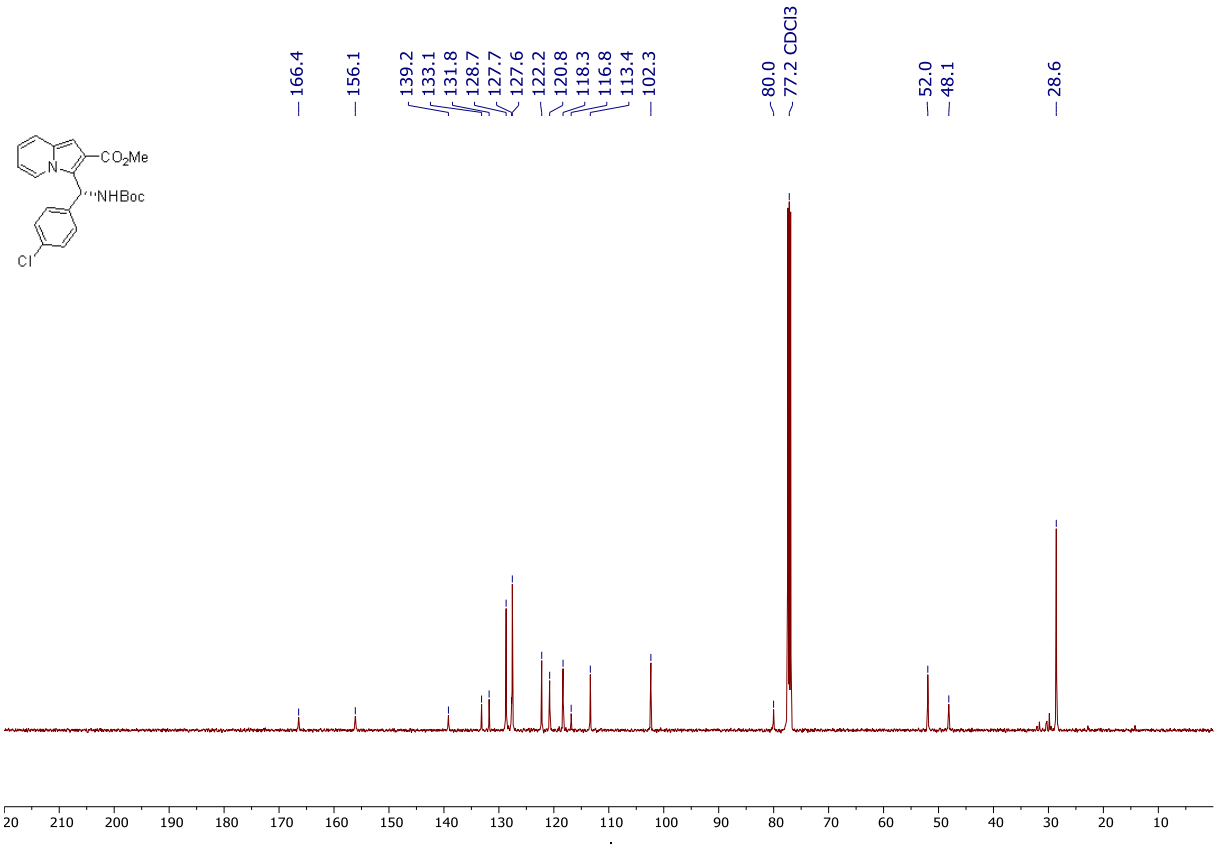
^{19}F NMR spectrum of compound **3d** ($CDCl_3$, 470 MHz)



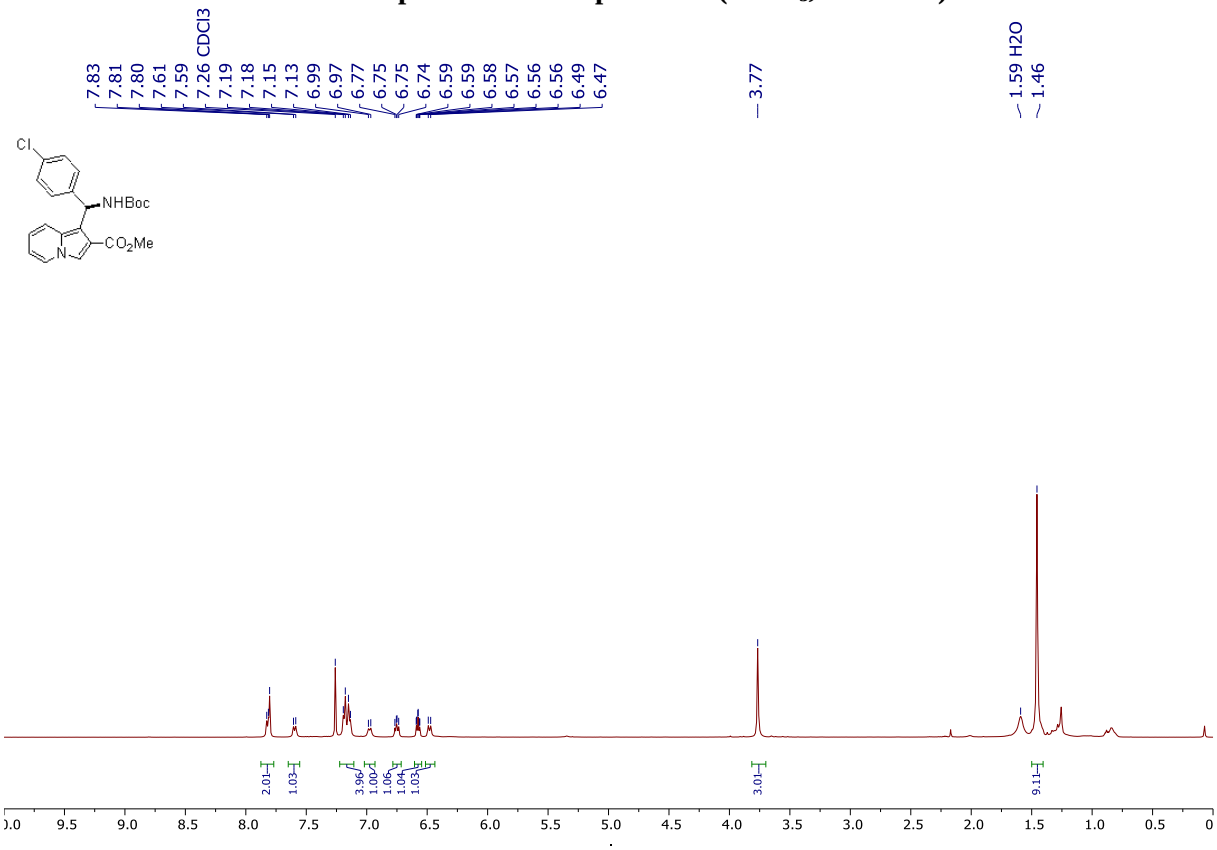
^{1}H NMR spectrum of compound 4e ($CDCl_3$, 200 MHz)



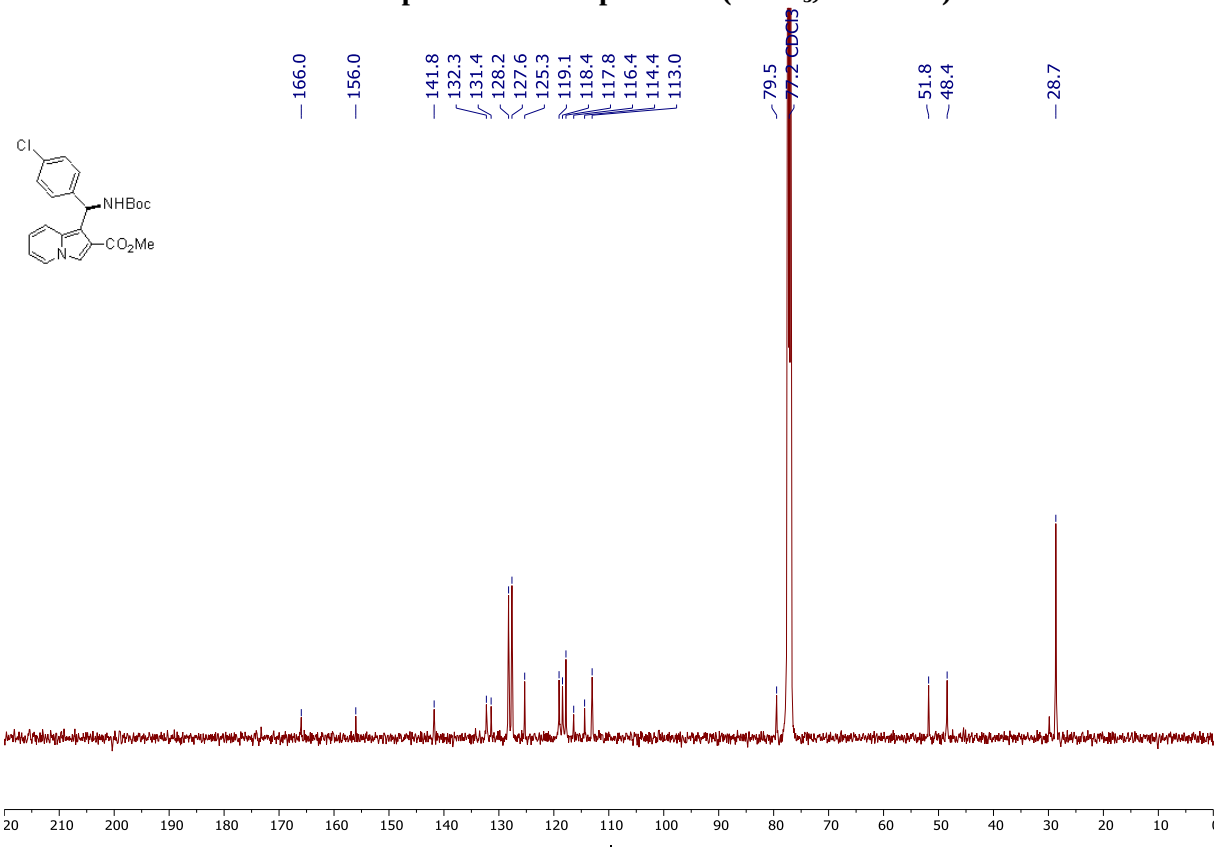
^{13}C NMR spectrum of compound 4e ($CDCl_3$, 126 MHz)



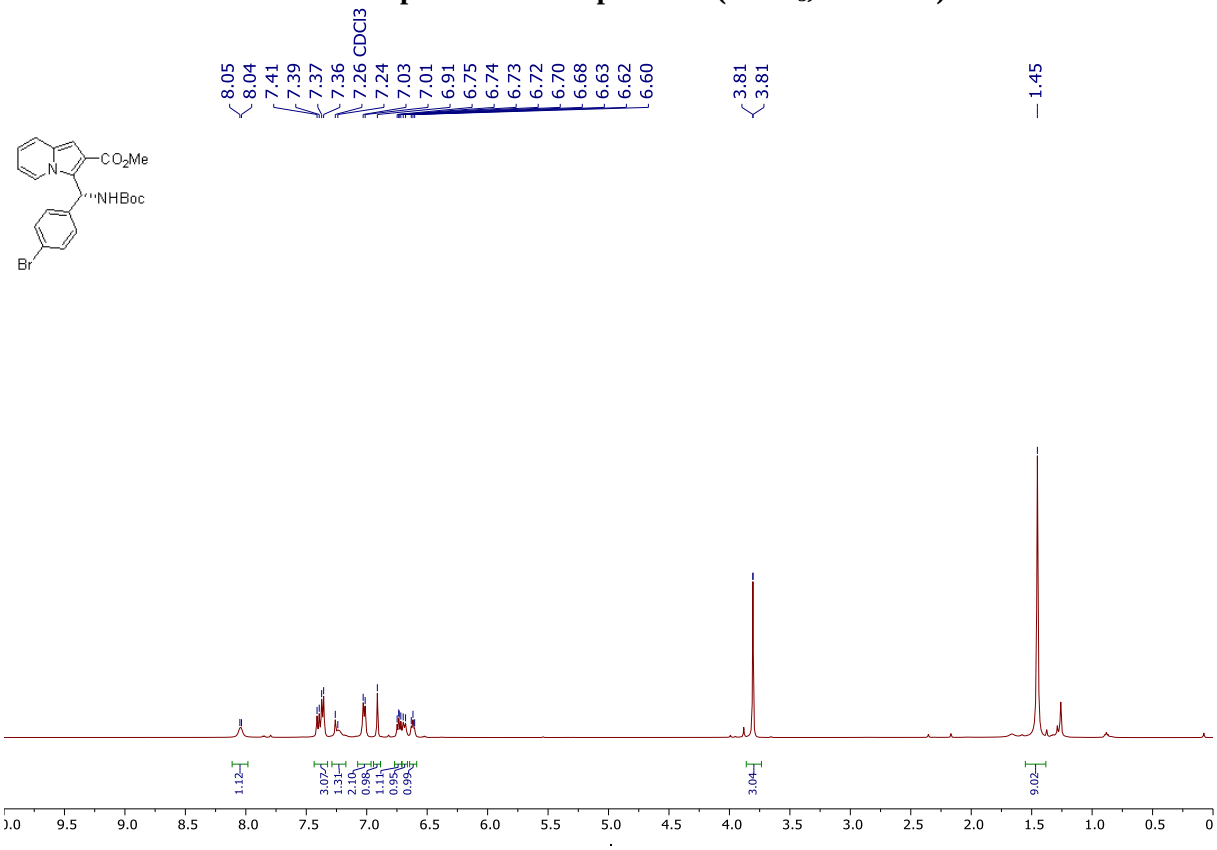
^{1}H NMR spectrum of compound 3e ($CDCl_3$, 500 MHz)



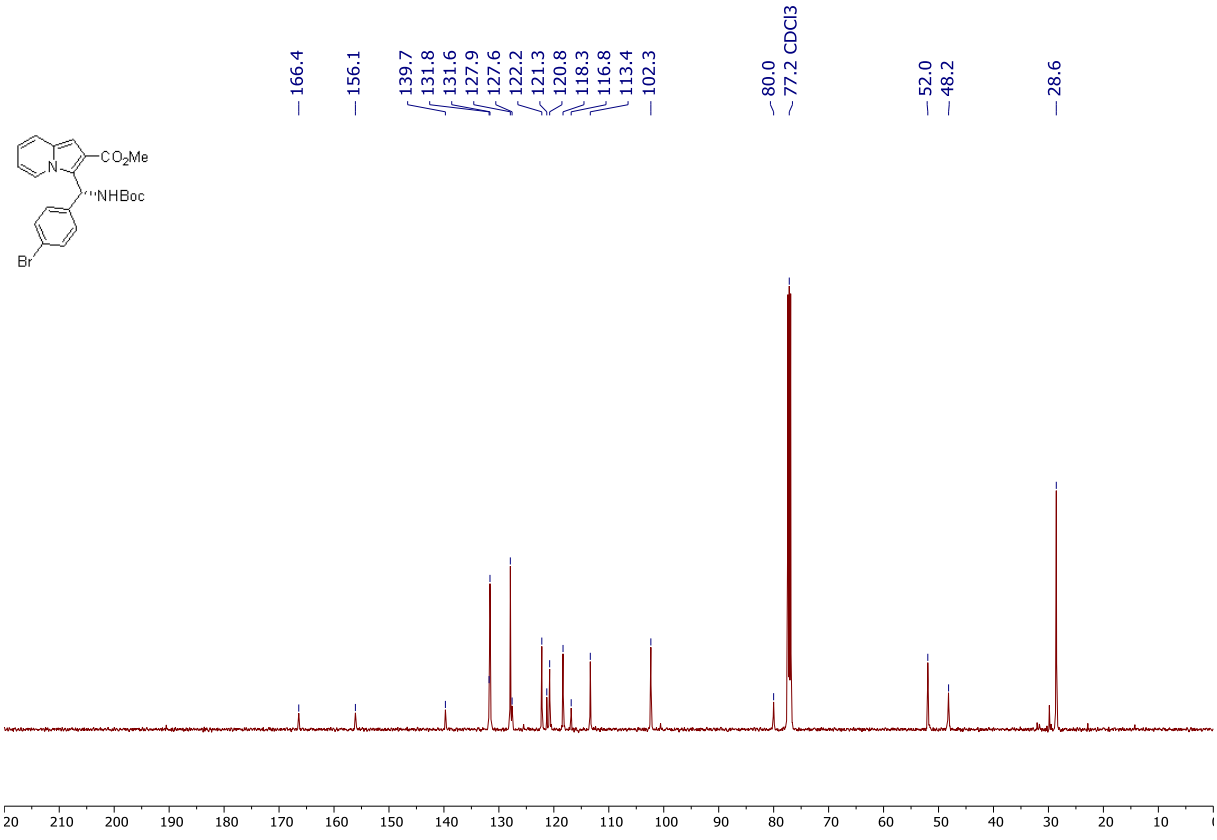
^{13}C NMR spectrum of compound 3e ($CDCl_3$, 126 MHz)



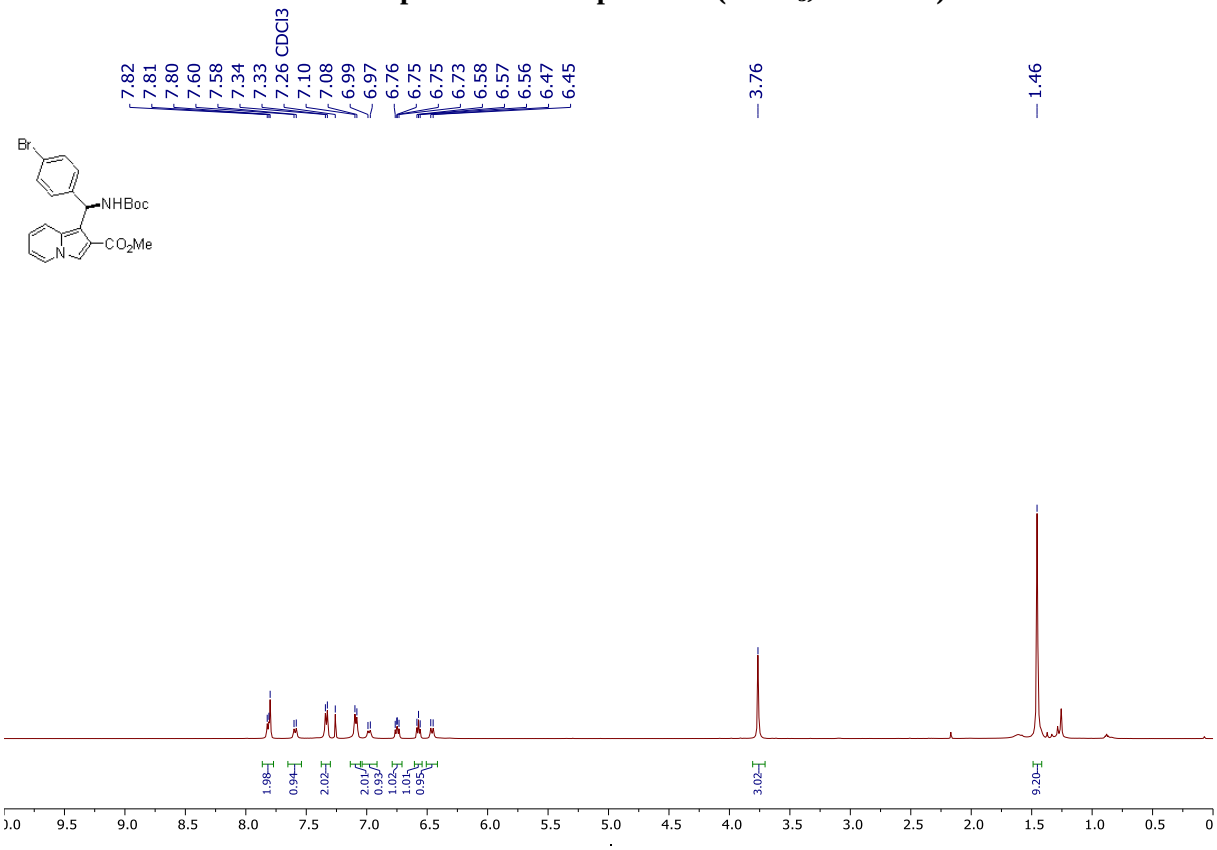
^{1}H NMR spectrum of compound 4f ($CDCl_3$, 500 MHz)



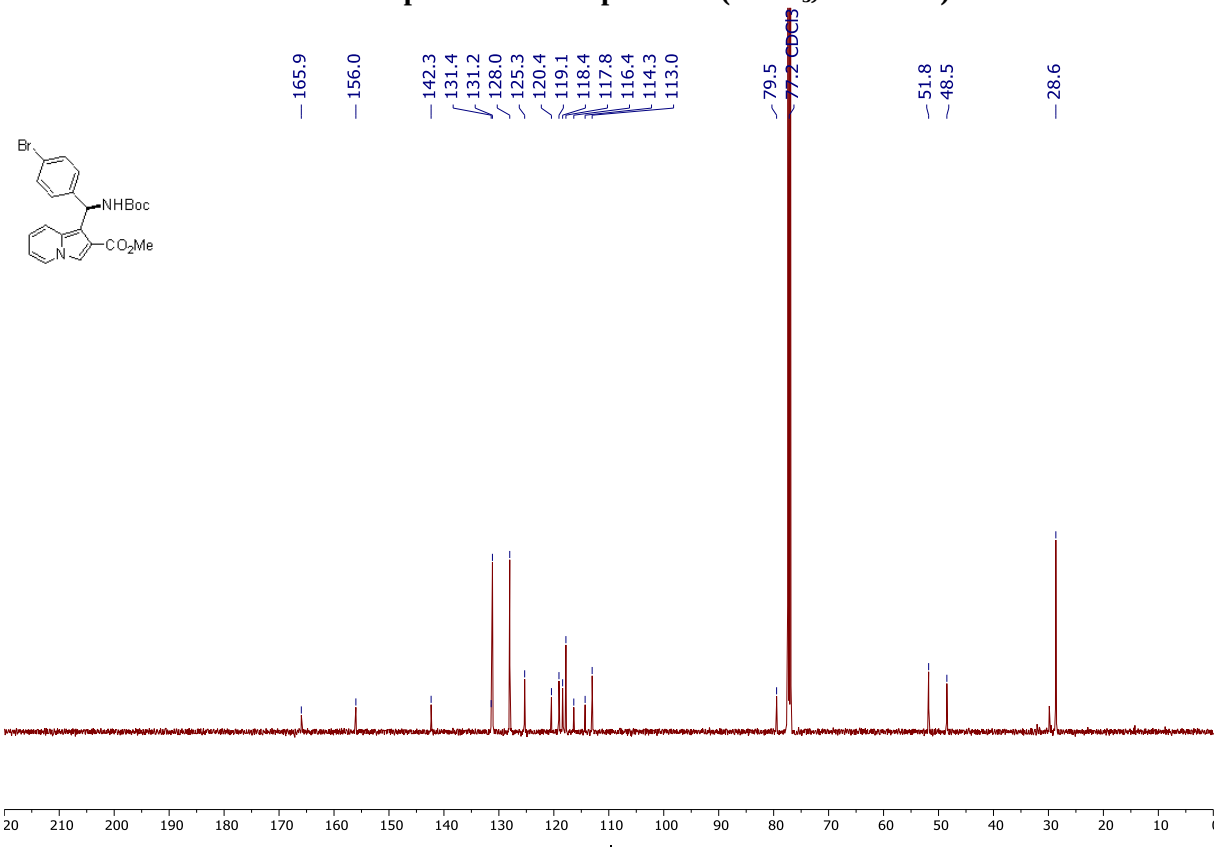
^{13}C NMR spectrum of compound **4f** ($CDCl_3$, 126 MHz)



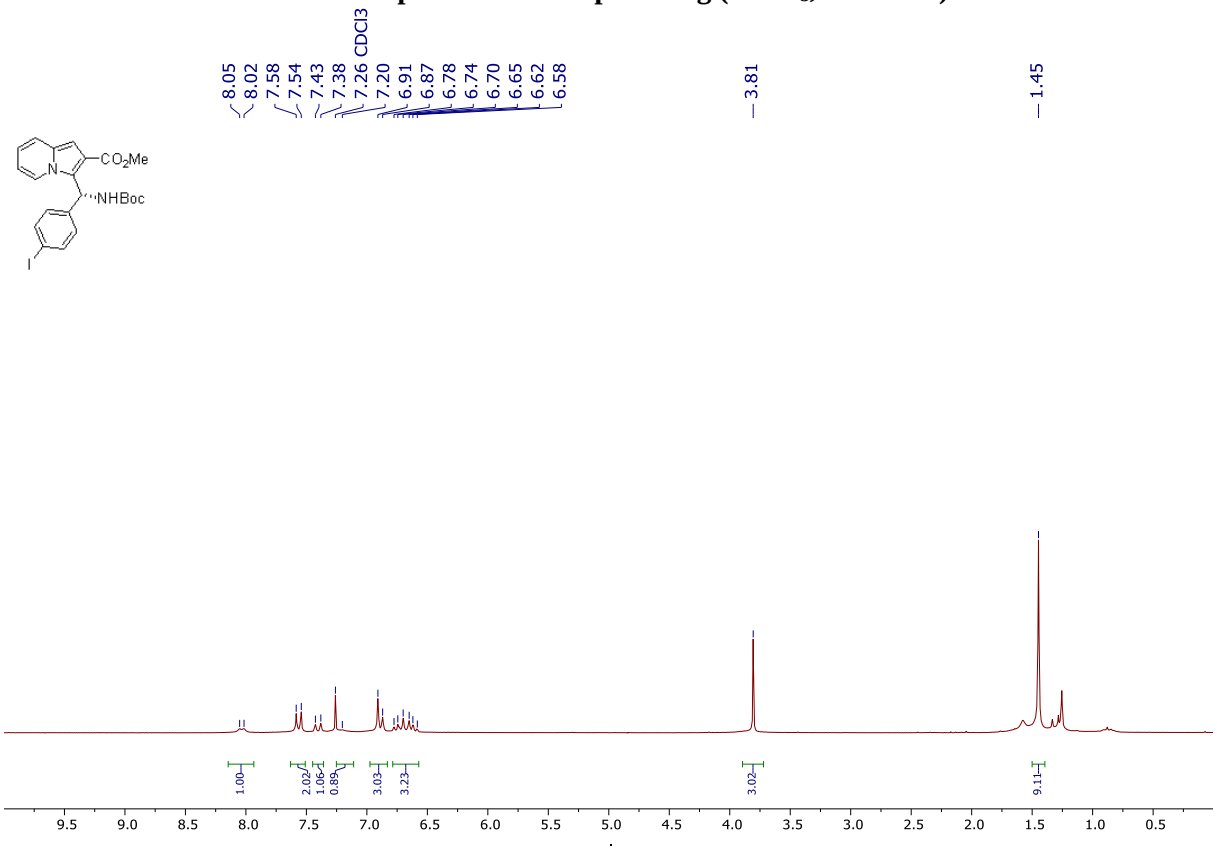
^{1}H NMR spectrum of compound 3f ($CDCl_3$, 500 MHz)



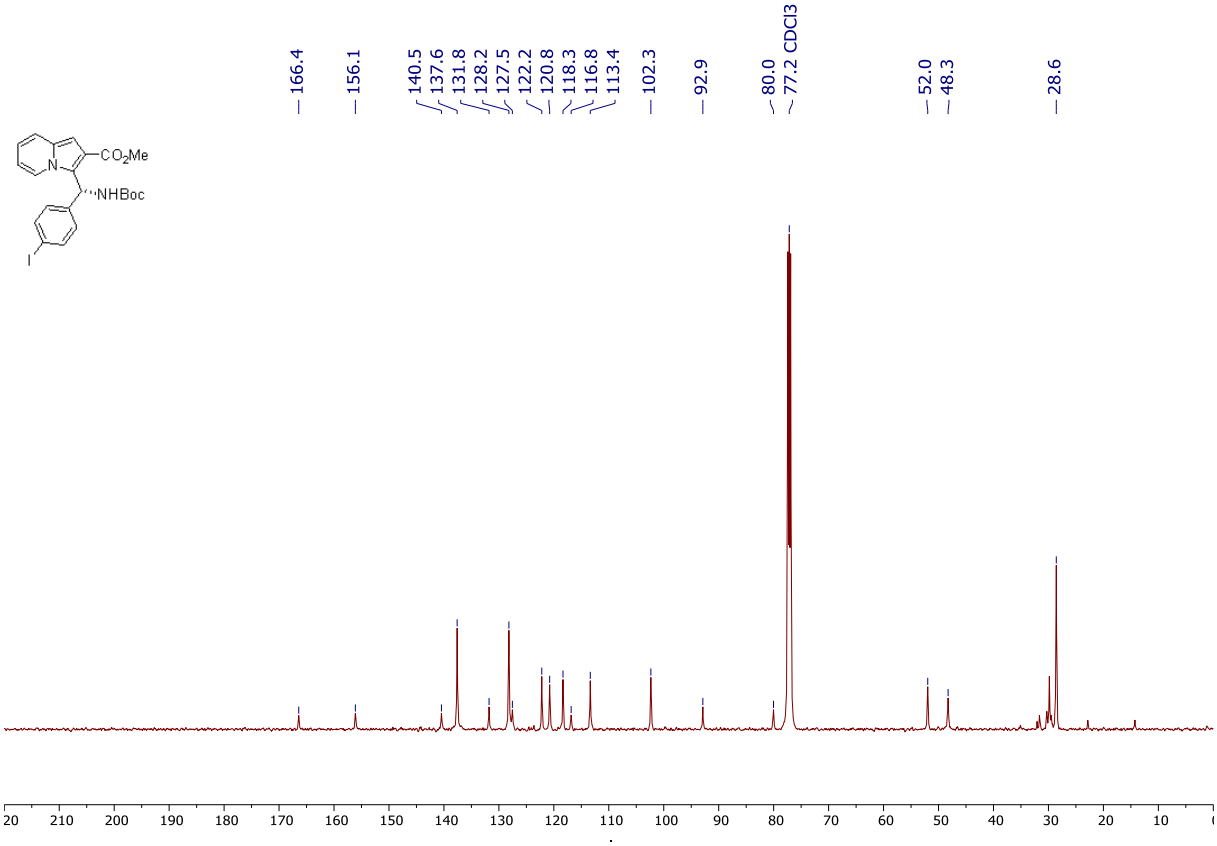
^{13}C NMR spectrum of compound 3f ($CDCl_3$, 126 MHz)



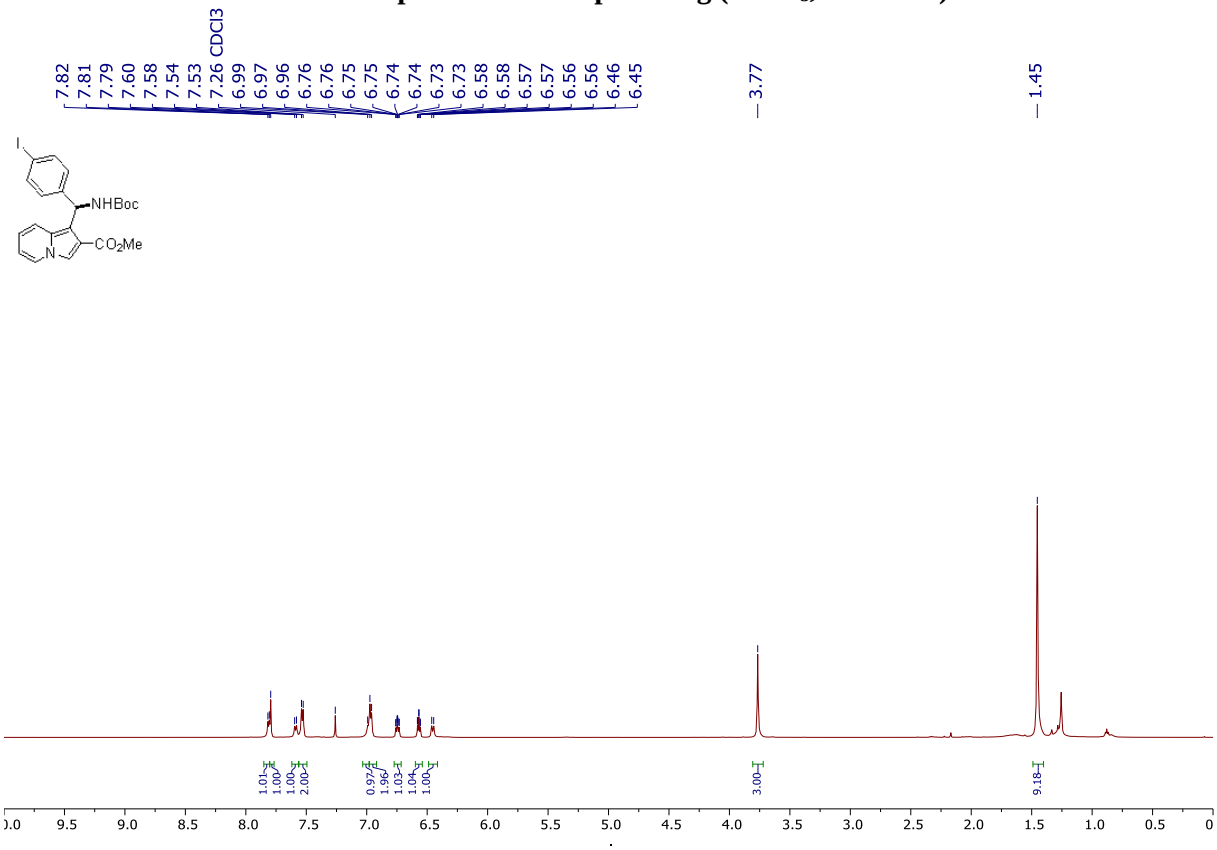
^{1}H NMR spectrum of compound 4g ($CDCl_3$, 200 MHz)



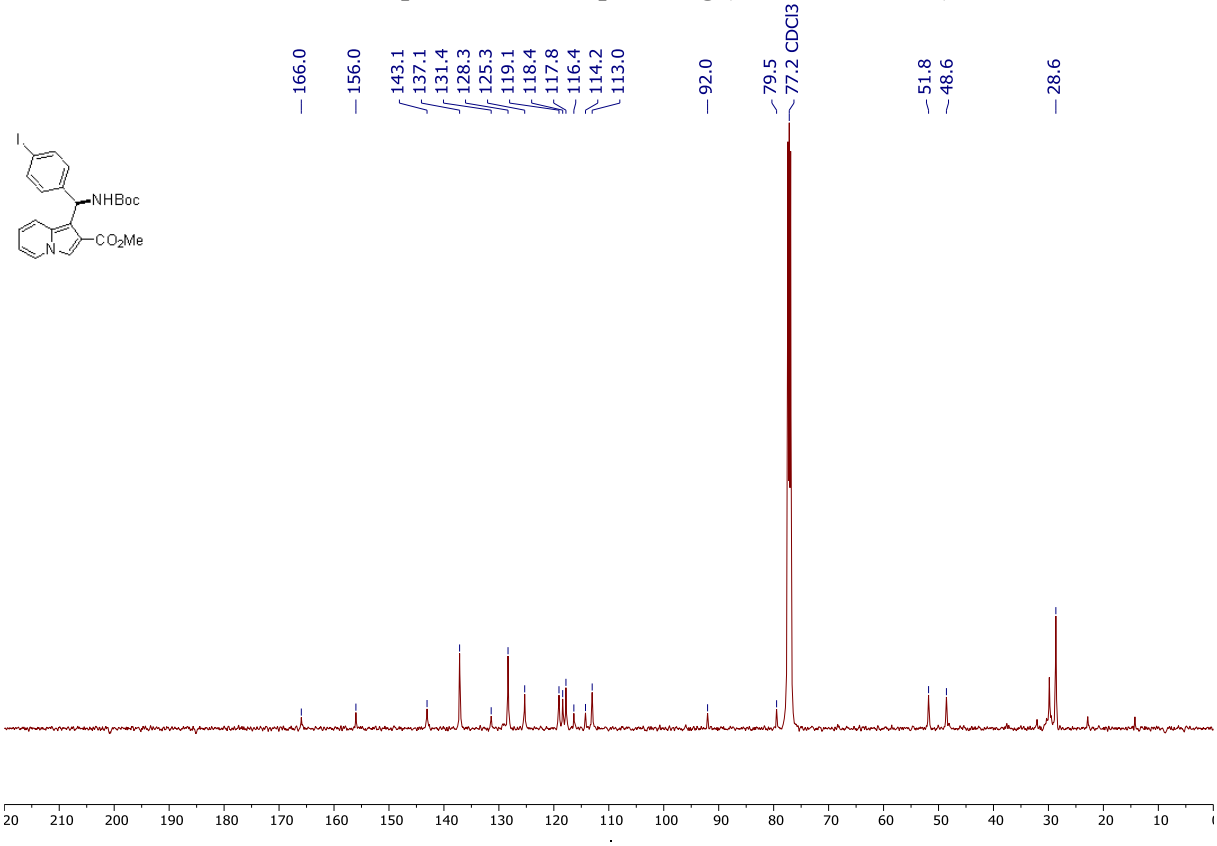
^{13}C NMR spectrum of compound 4g ($CDCl_3$, 126 MHz)



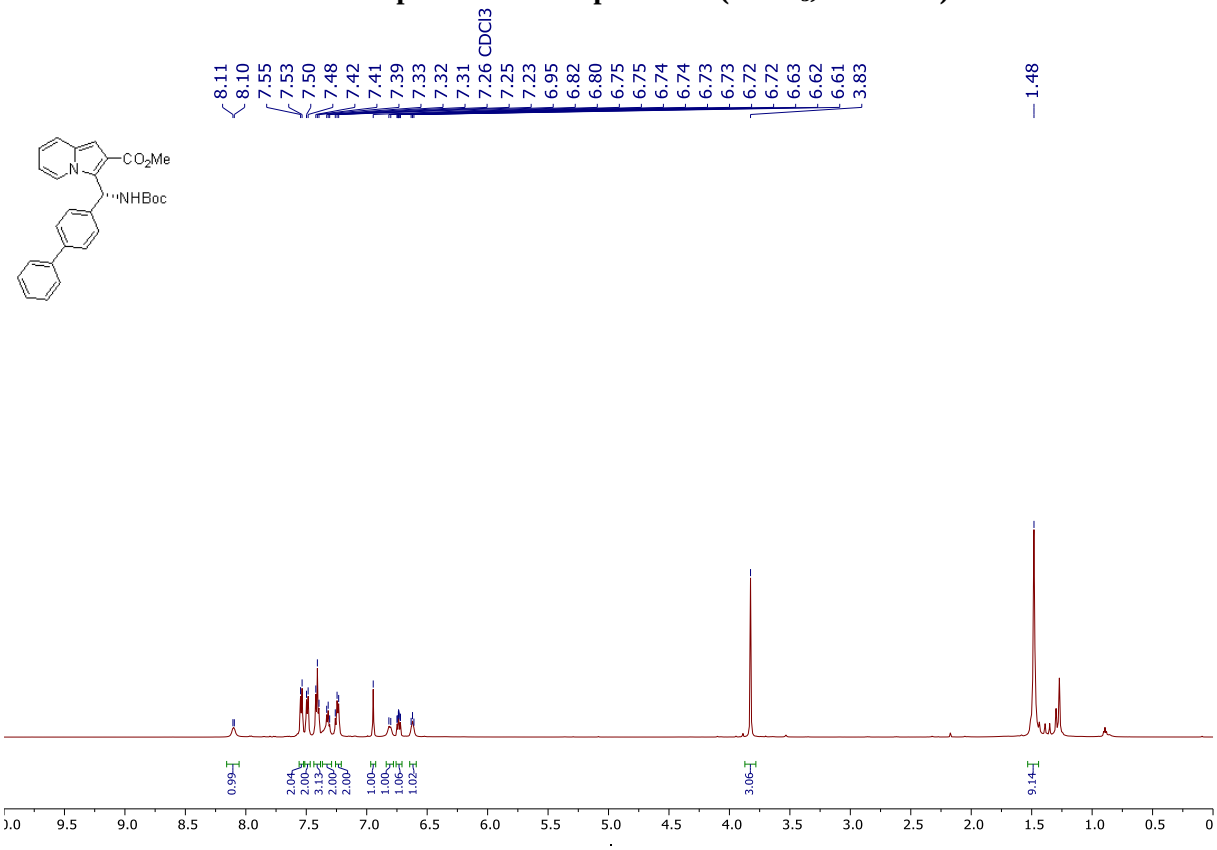
^{1}H NMR spectrum of compound 3g ($CDCl_3$, 600 MHz)



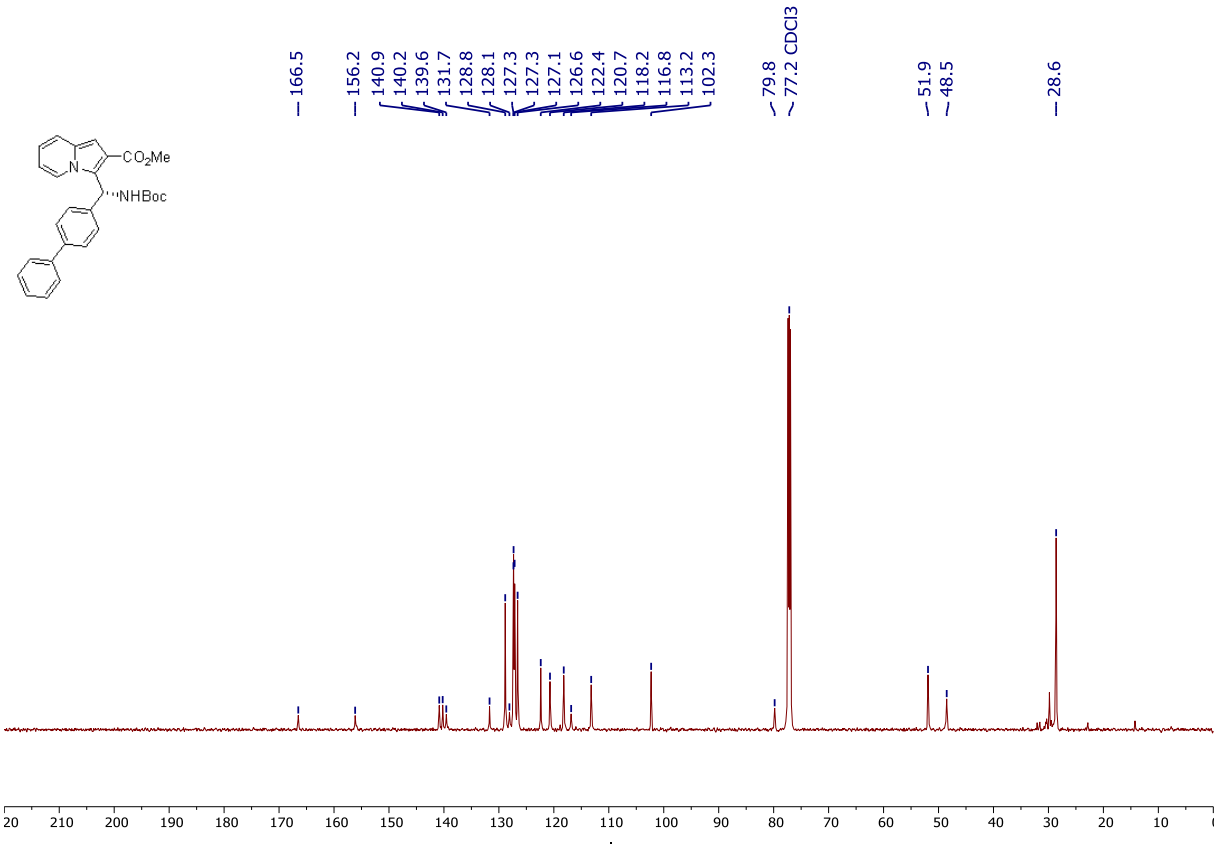
^{13}C NMR spectrum of compound 3g ($CDCl_3$, 126 MHz)



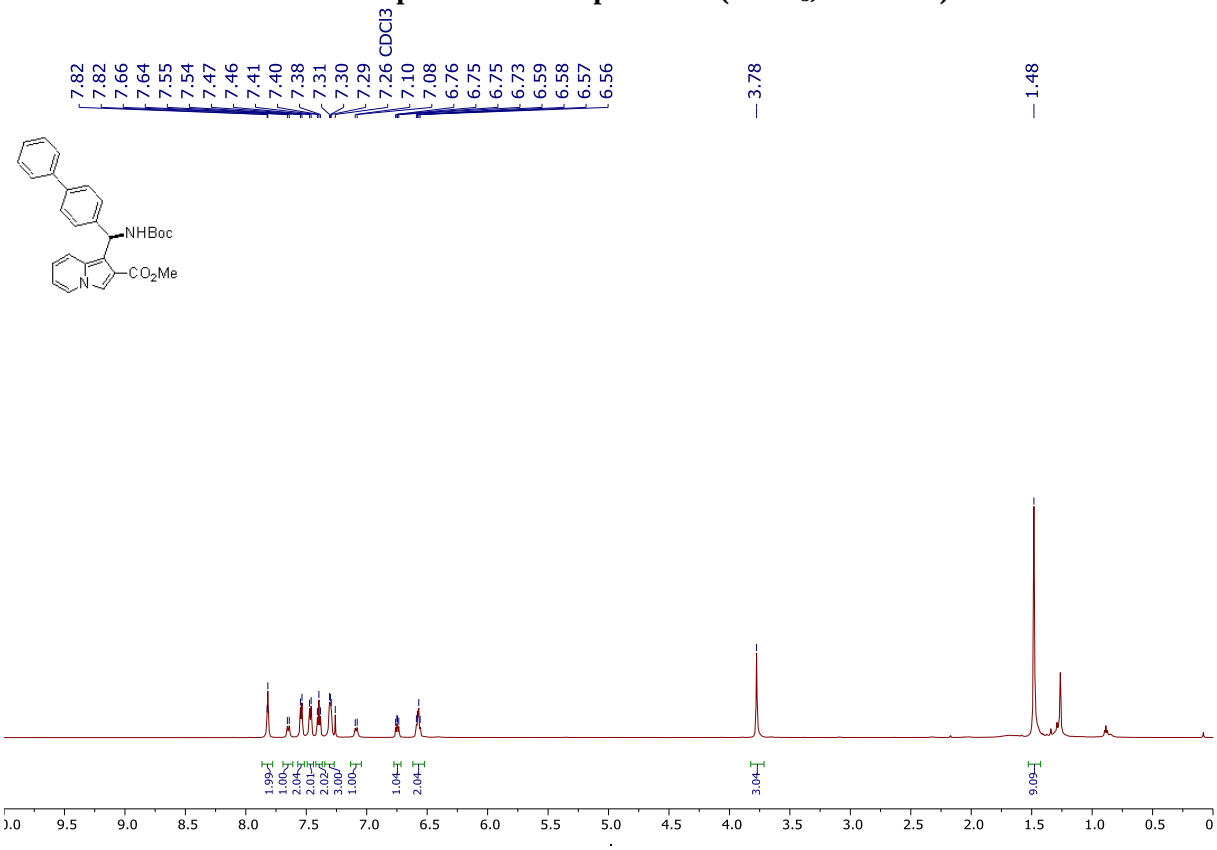
^{1}H NMR spectrum of compound 4h ($CDCl_3$, 600 MHz)



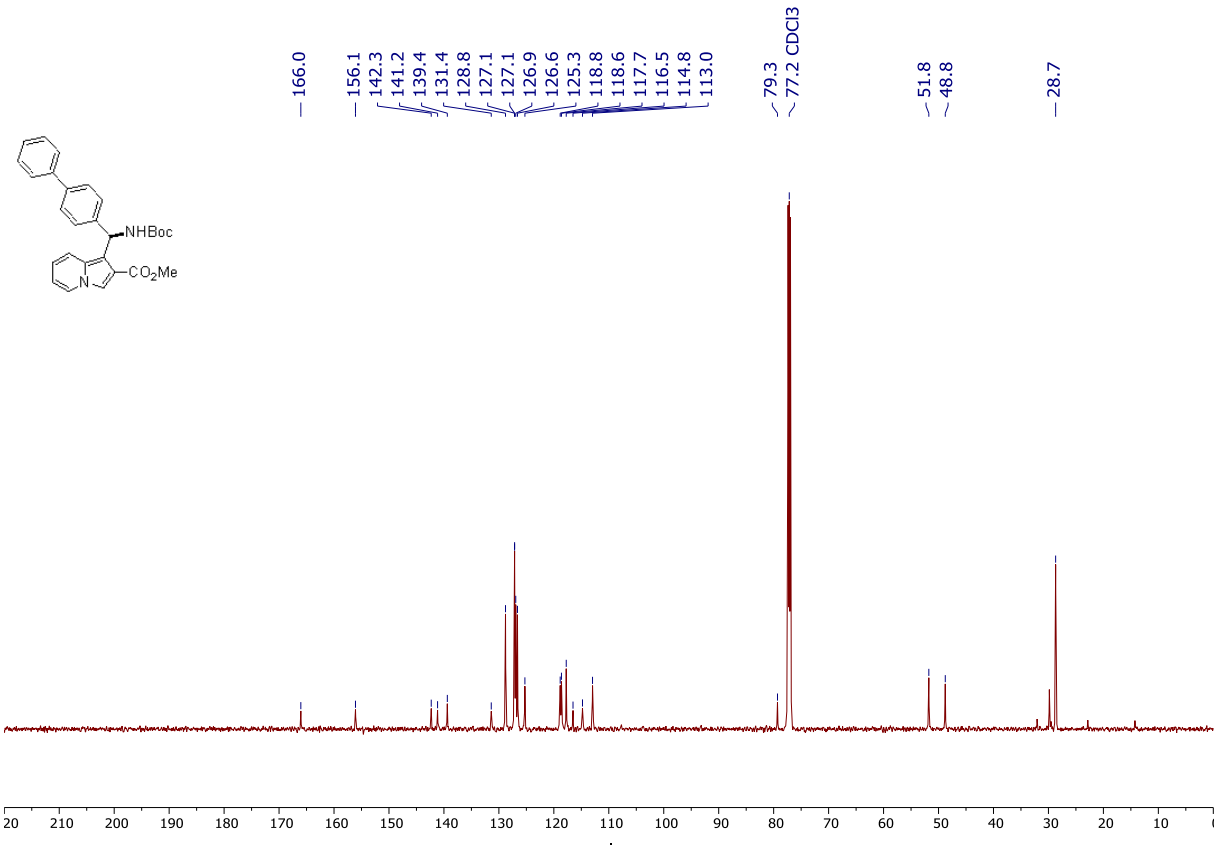
^{13}C NMR spectrum of compound 4h ($CDCl_3$, 151 MHz)



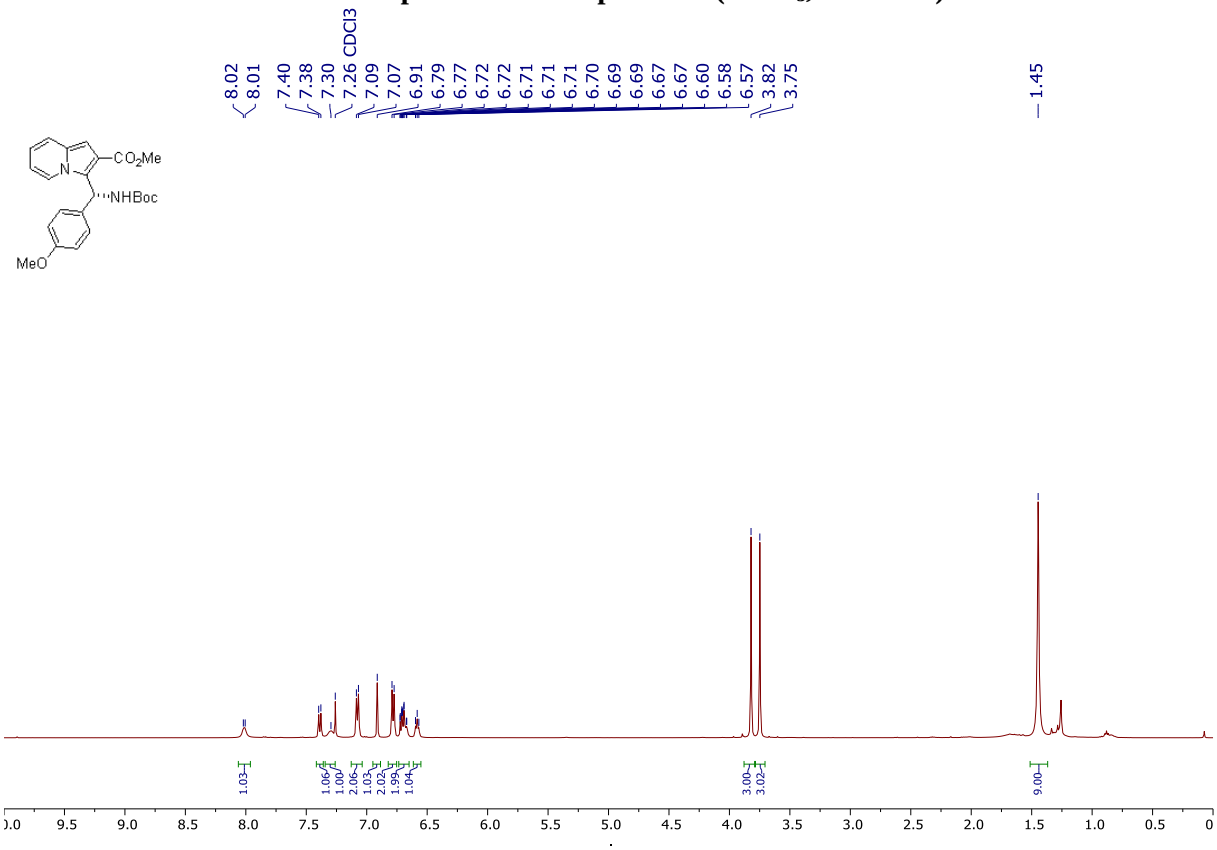
^{1}H NMR spectrum of compound 3h ($CDCl_3$, 600 MHz)



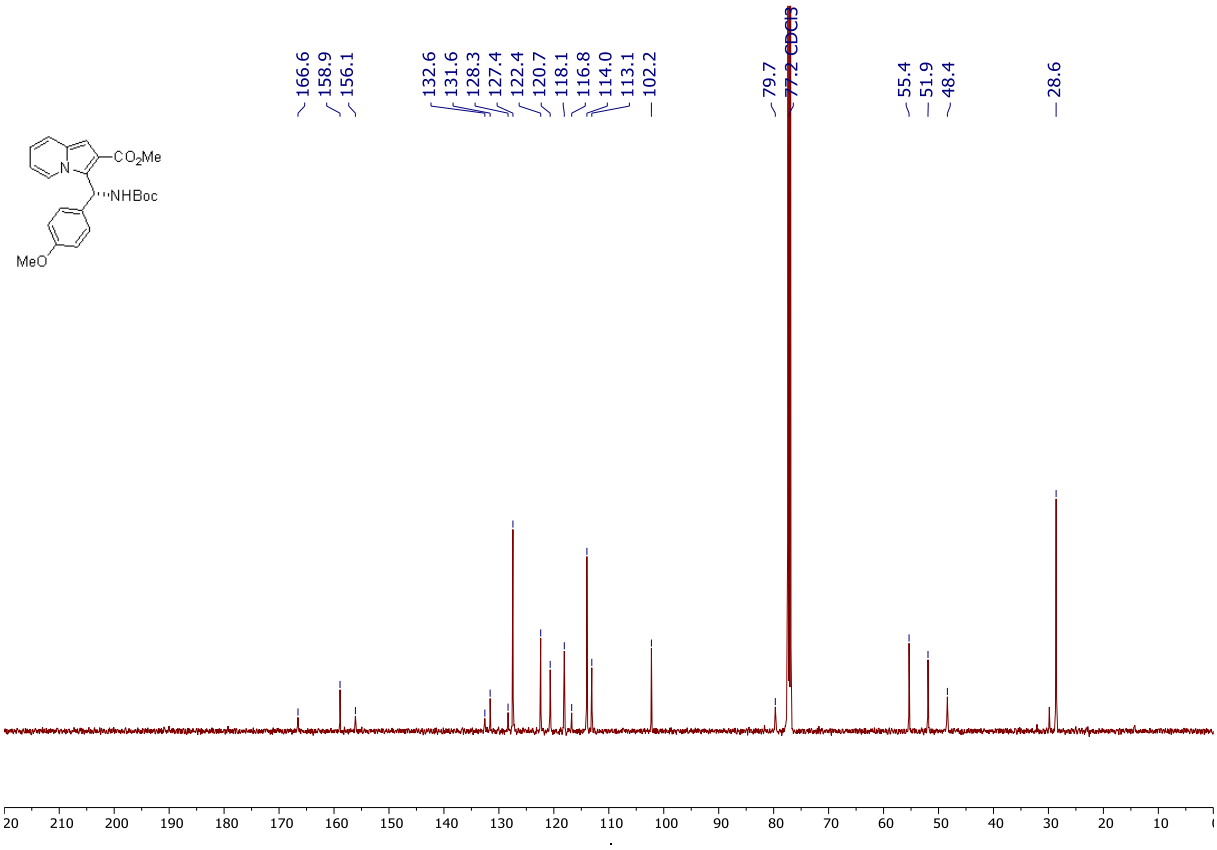
^{13}C NMR spectrum of compound 3h ($CDCl_3$, 151 MHz)



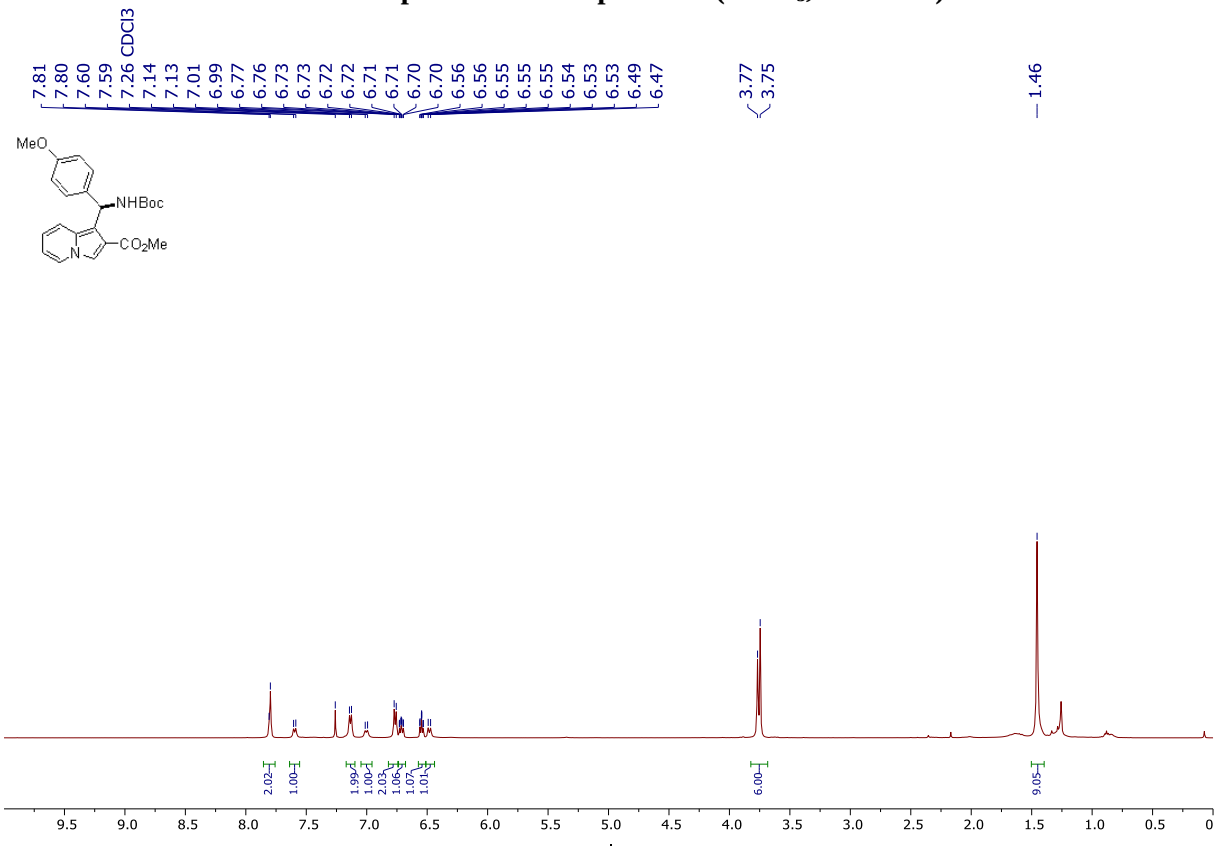
^{1}H NMR spectrum of compound 4i ($CDCl_3$, 400 MHz)



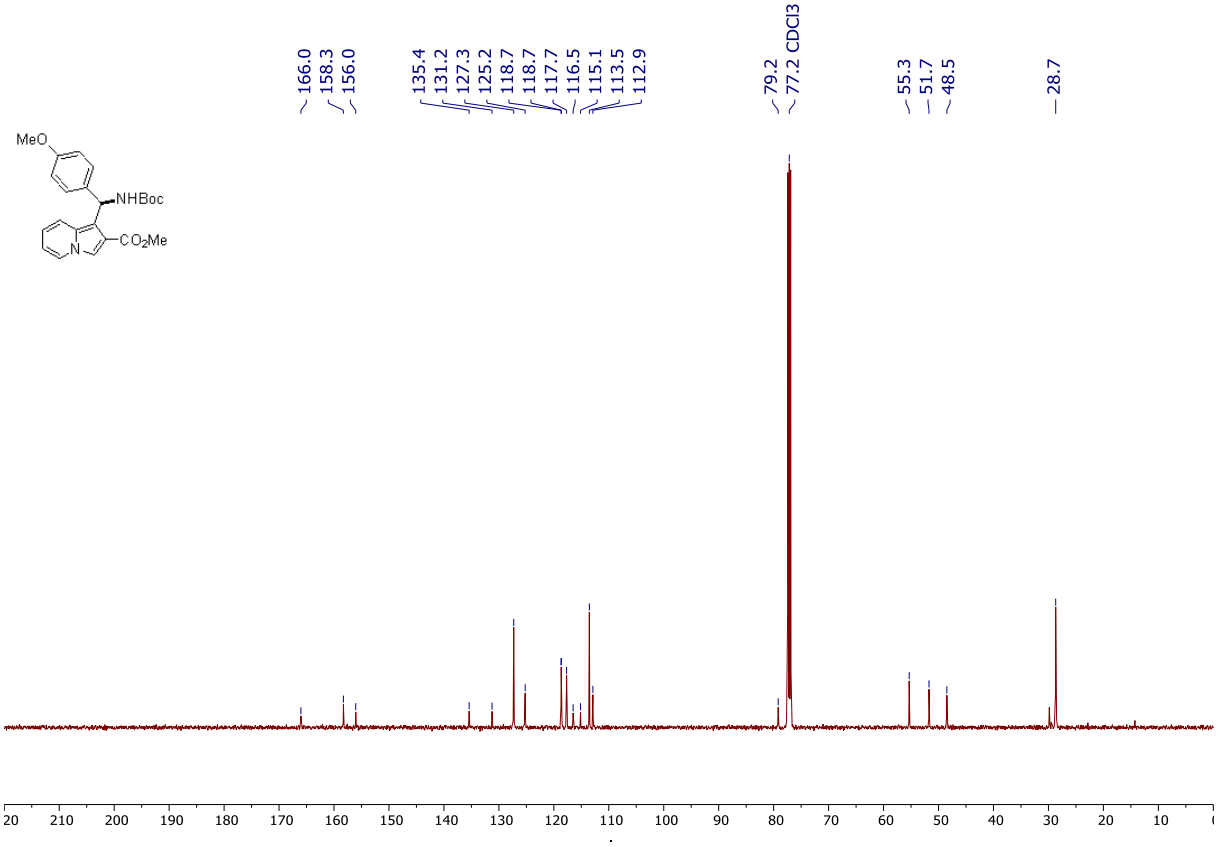
^{13}C NMR spectrum of compound 4i ($CDCl_3$, 101 MHz)



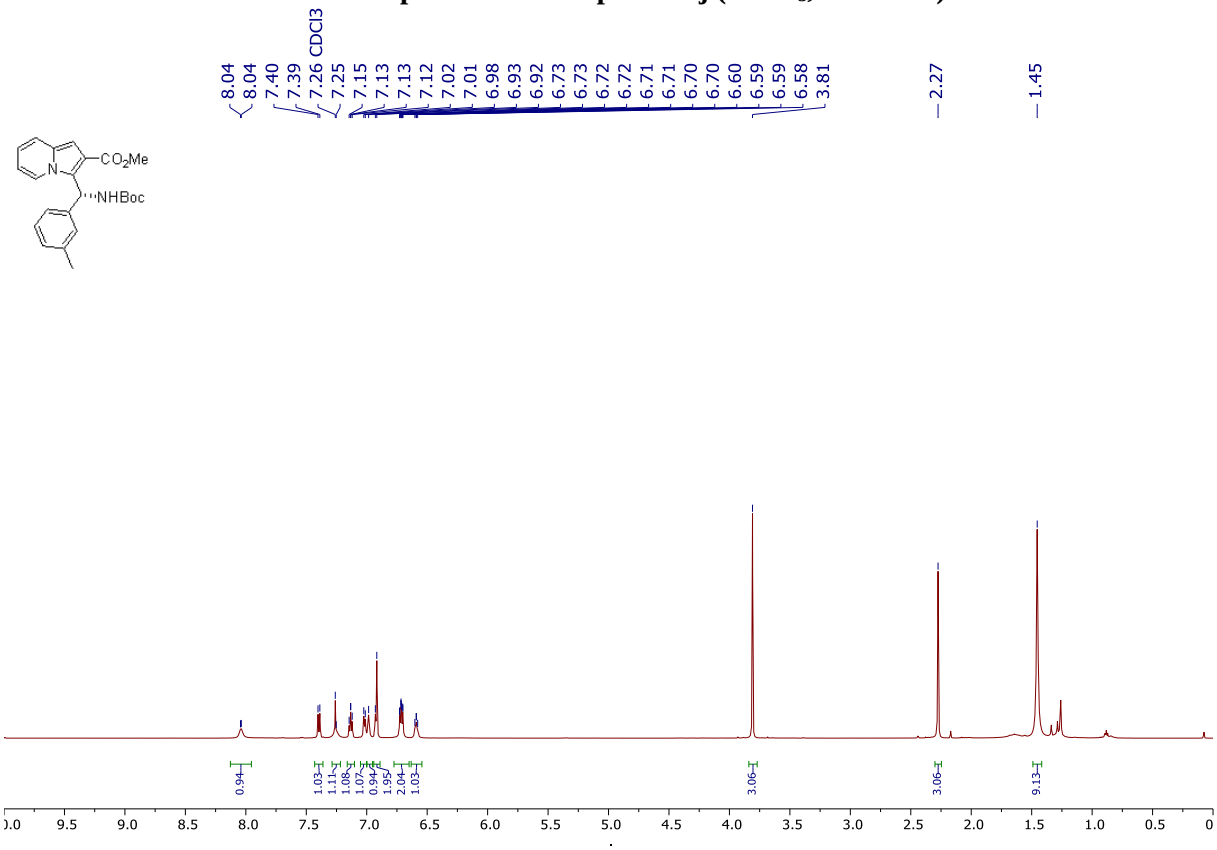
^{1}H NMR spectrum of compound 3i ($CDCl_3$, 400 MHz)



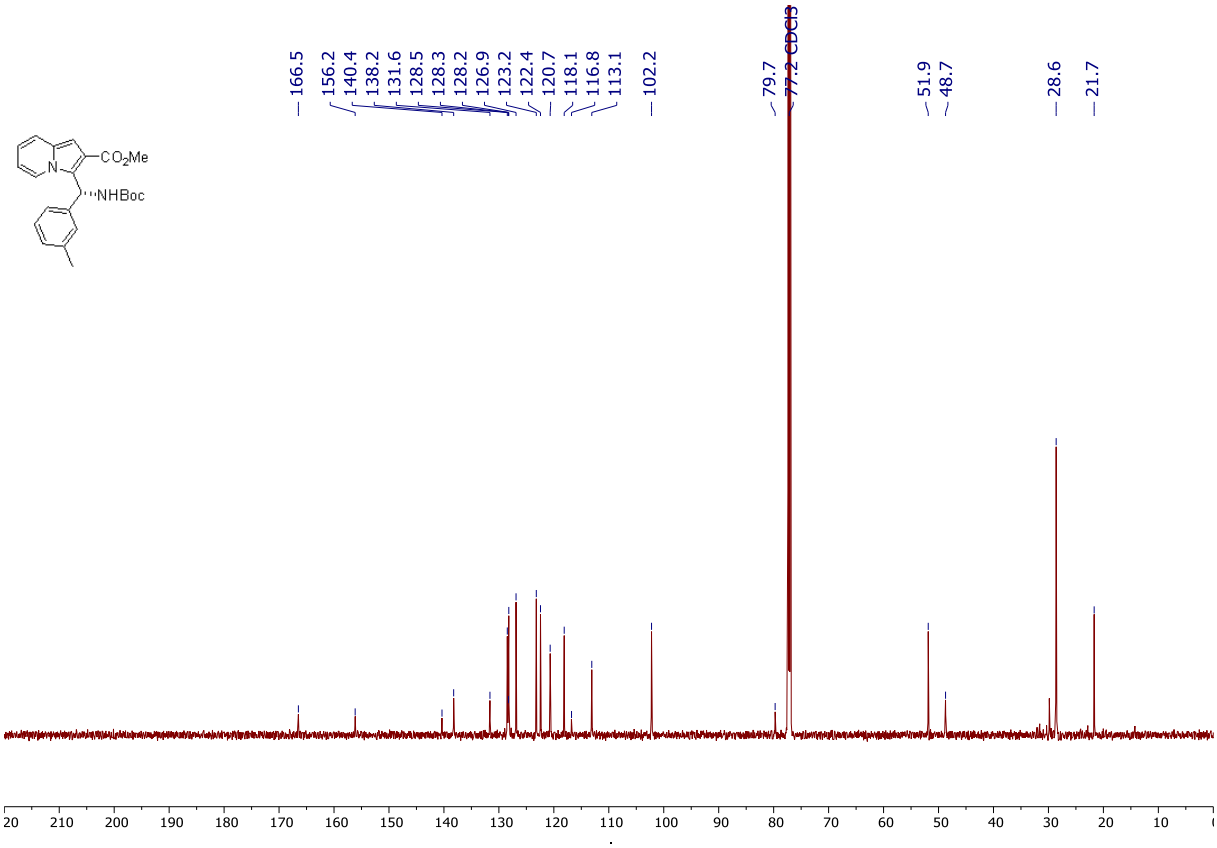
^{13}C NMR spectrum of compound 3i ($CDCl_3$, 101 MHz)



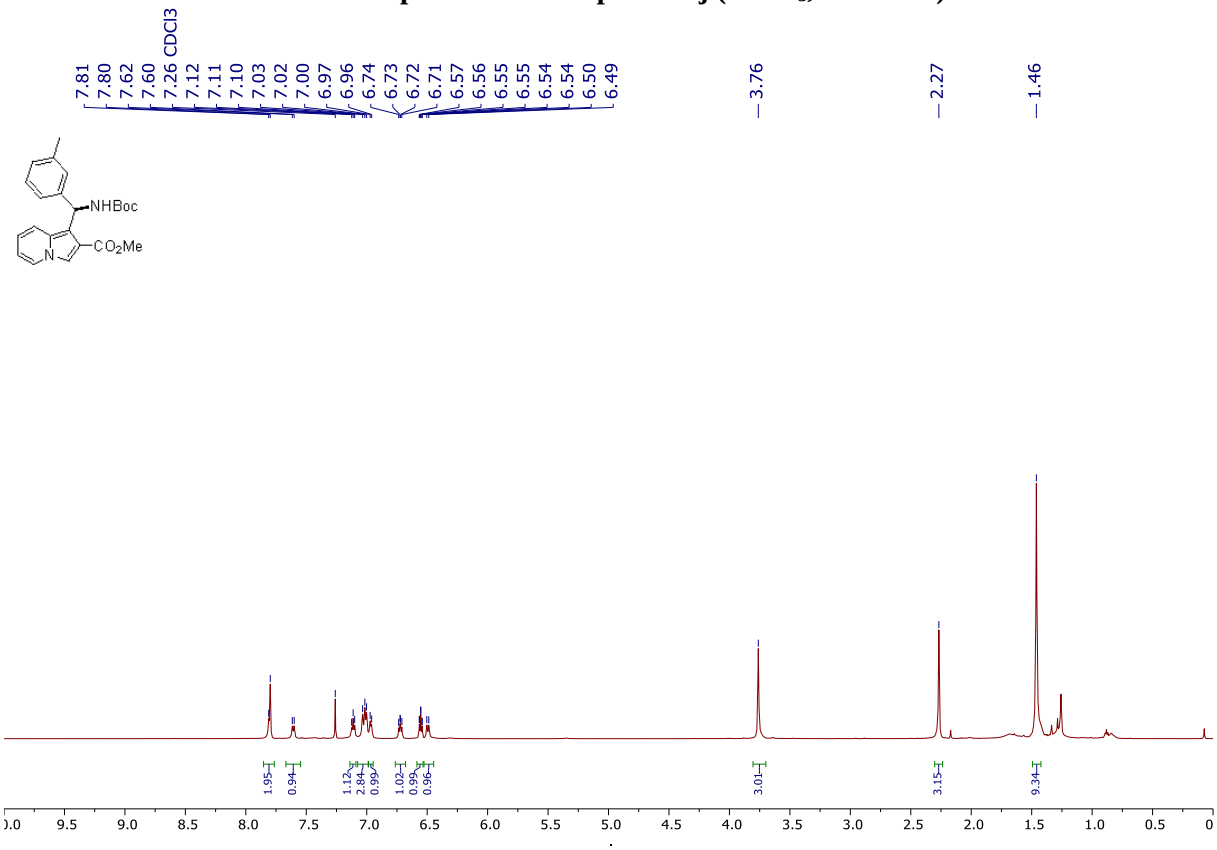
^{1}H NMR spectrum of compound 4j ($CDCl_3$, 600 MHz)



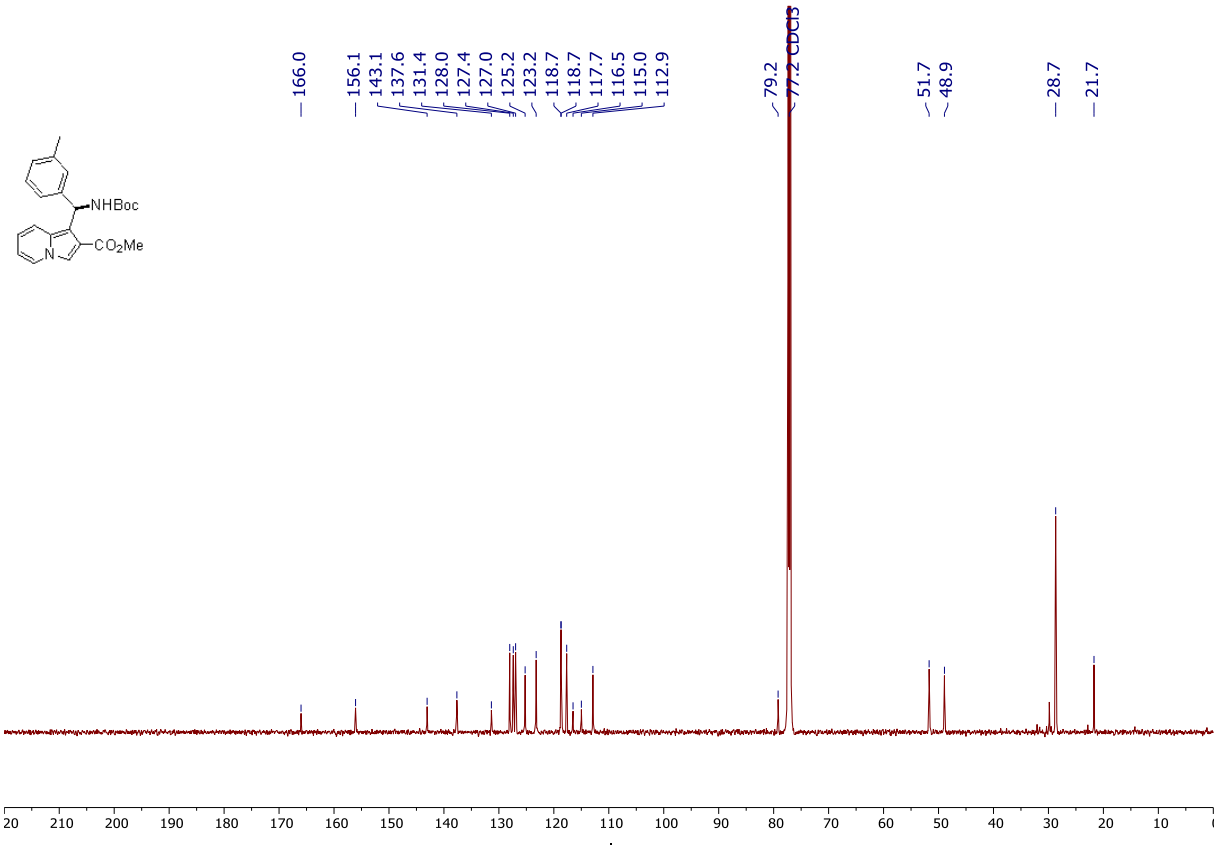
^{13}C NMR spectrum of compound 4j ($CDCl_3$, 151 MHz)



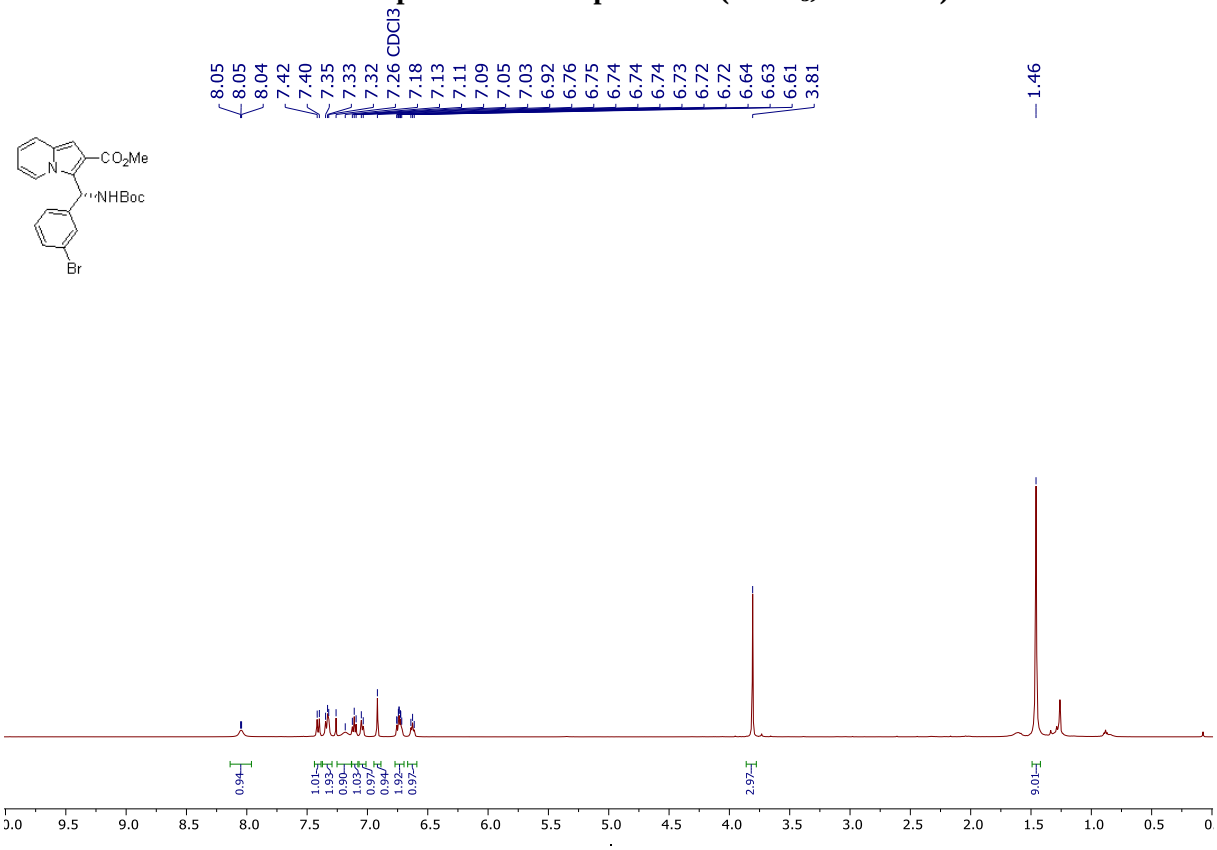
^{1}H NMR spectrum of compound 3j ($CDCl_3$, 600 MHz)



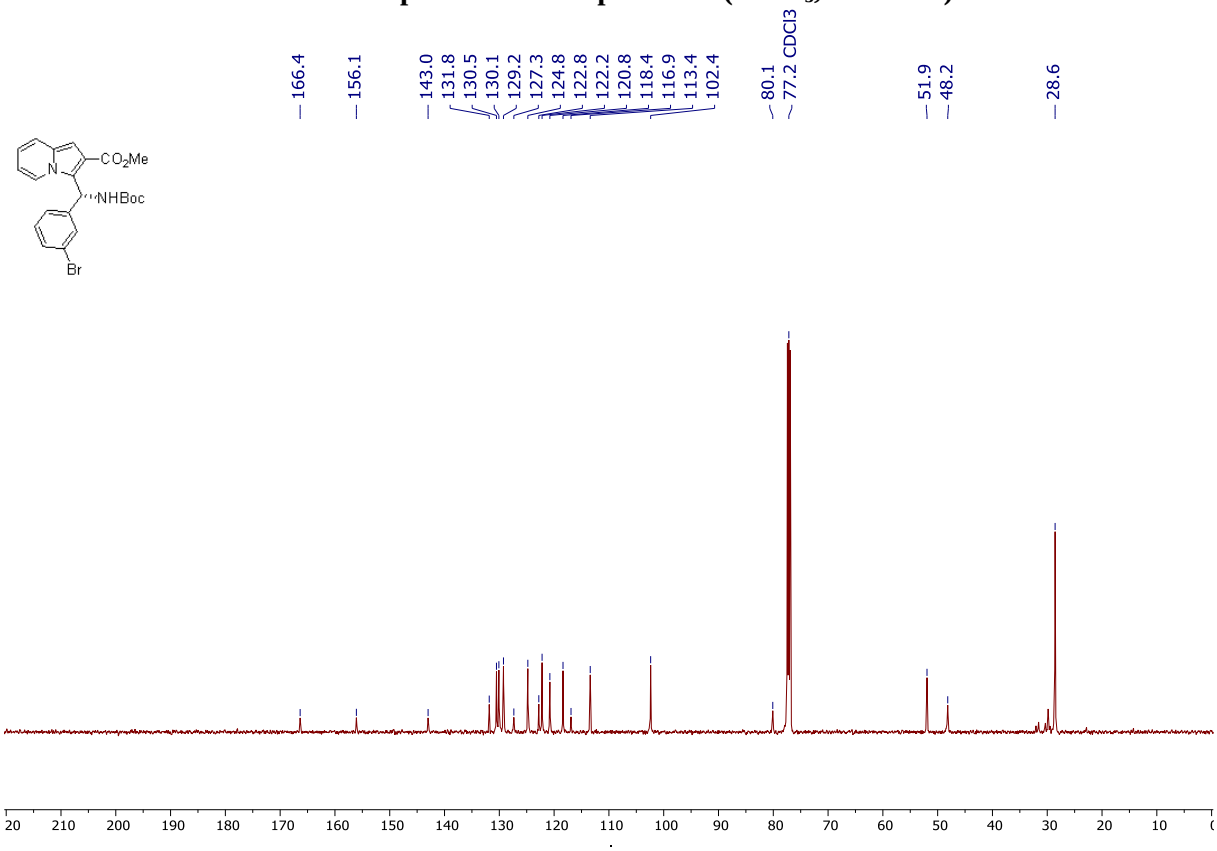
^{13}C NMR spectrum of compound 3j ($CDCl_3$, 151 MHz)



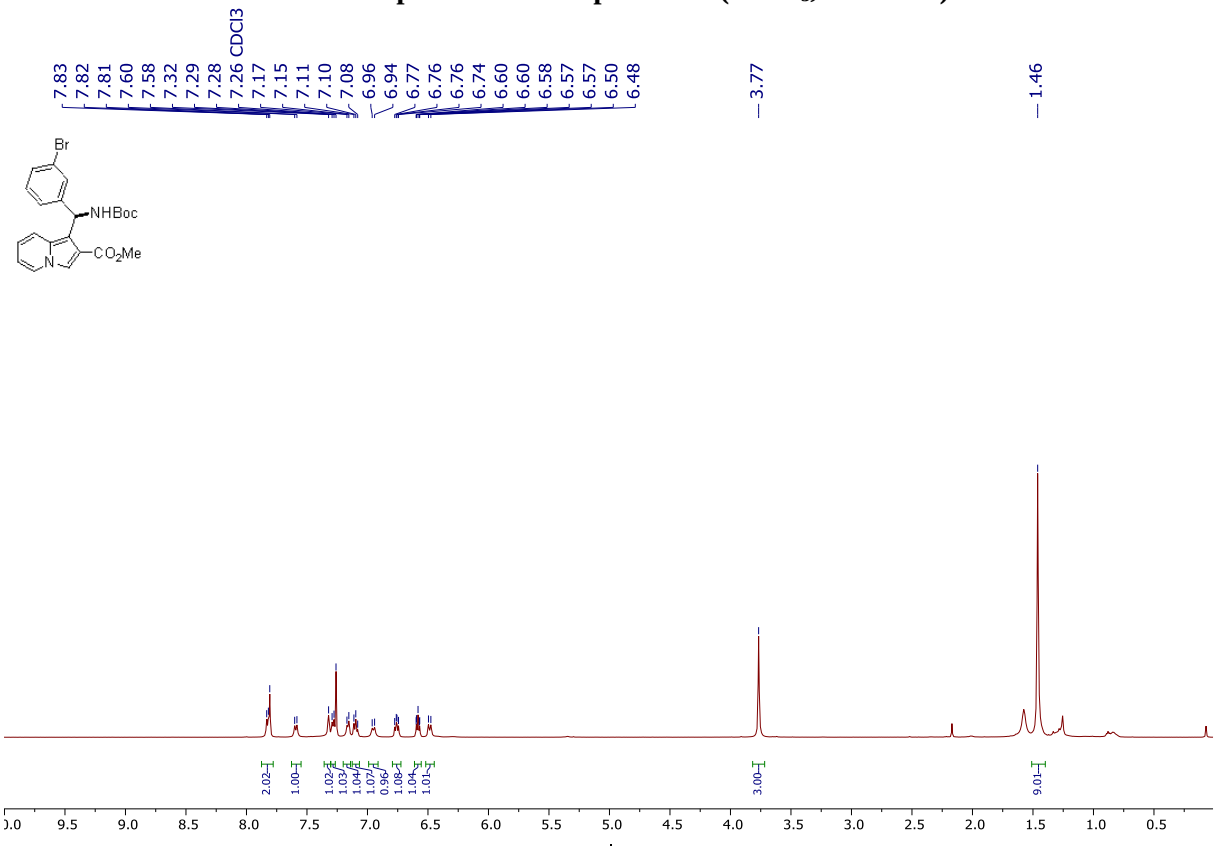
^{1}H NMR spectrum of compound 4k ($CDCl_3$, 500 MHz)



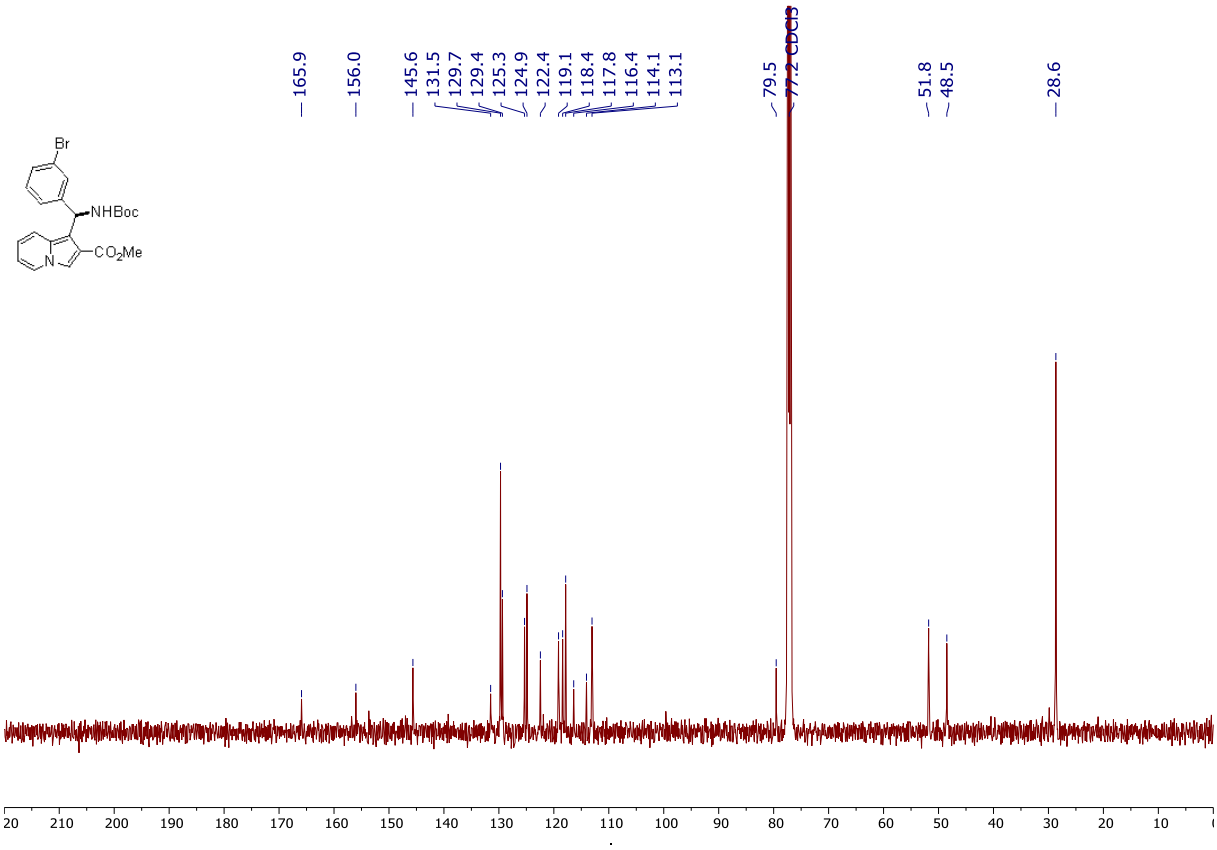
^{13}C NMR spectrum of compound 4k ($CDCl_3$, 126 MHz)



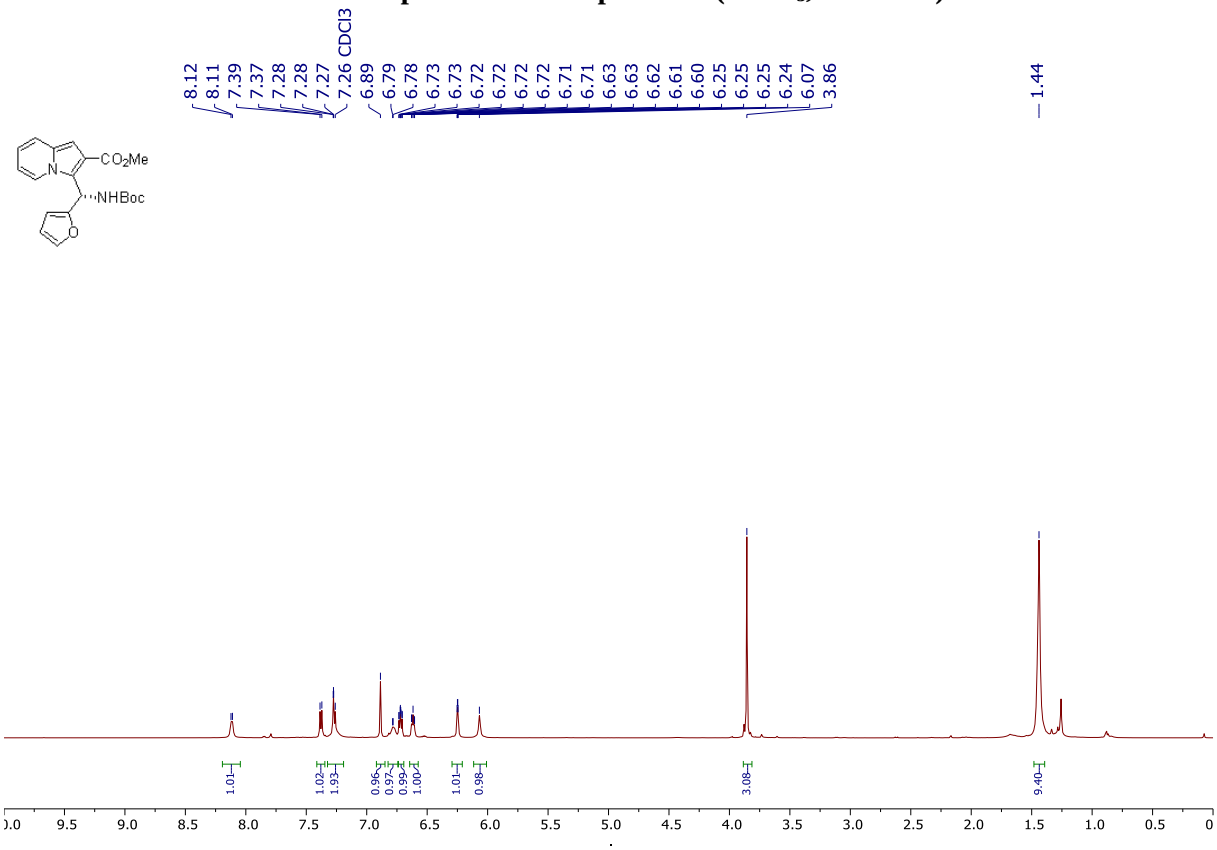
^{1}H NMR spectrum of compound 3k ($CDCl_3$, 500 MHz)



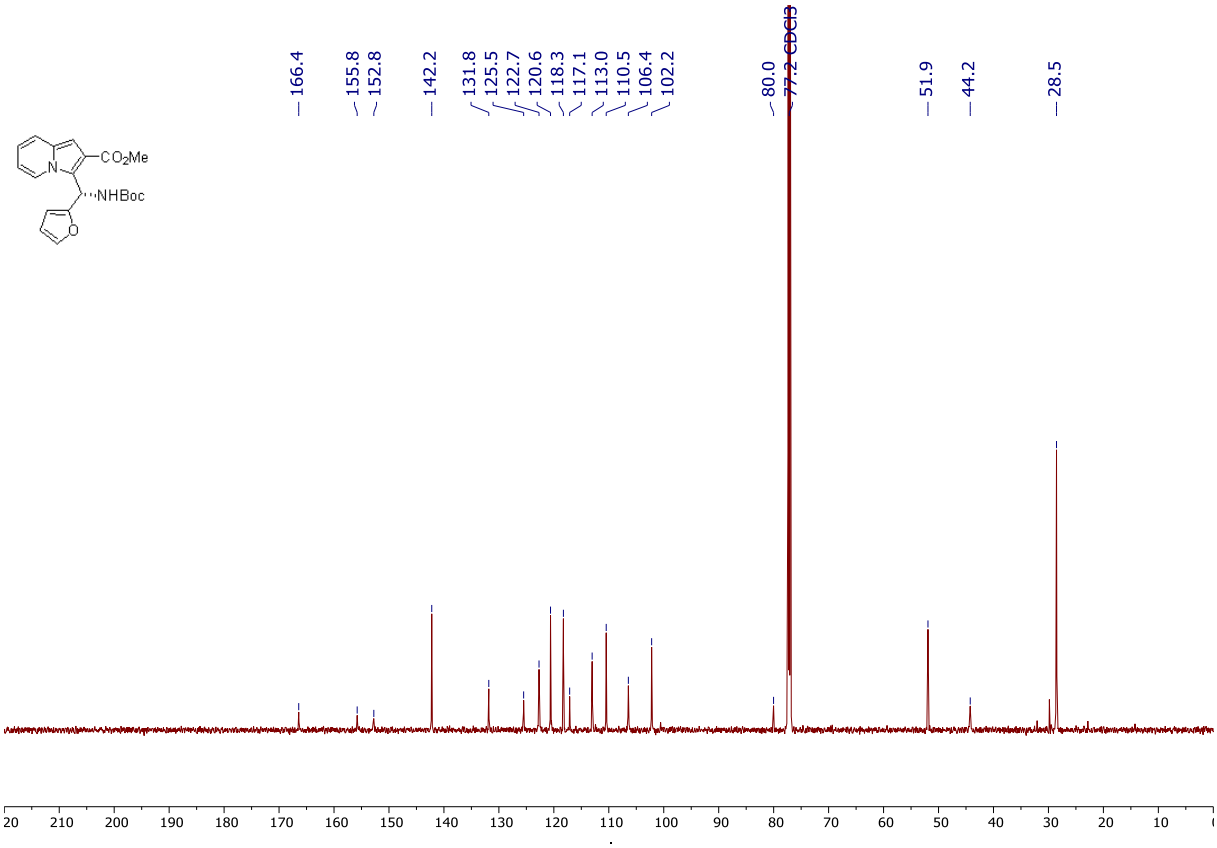
^{13}C NMR spectrum of compound 3k ($CDCl_3$, 126 MHz)



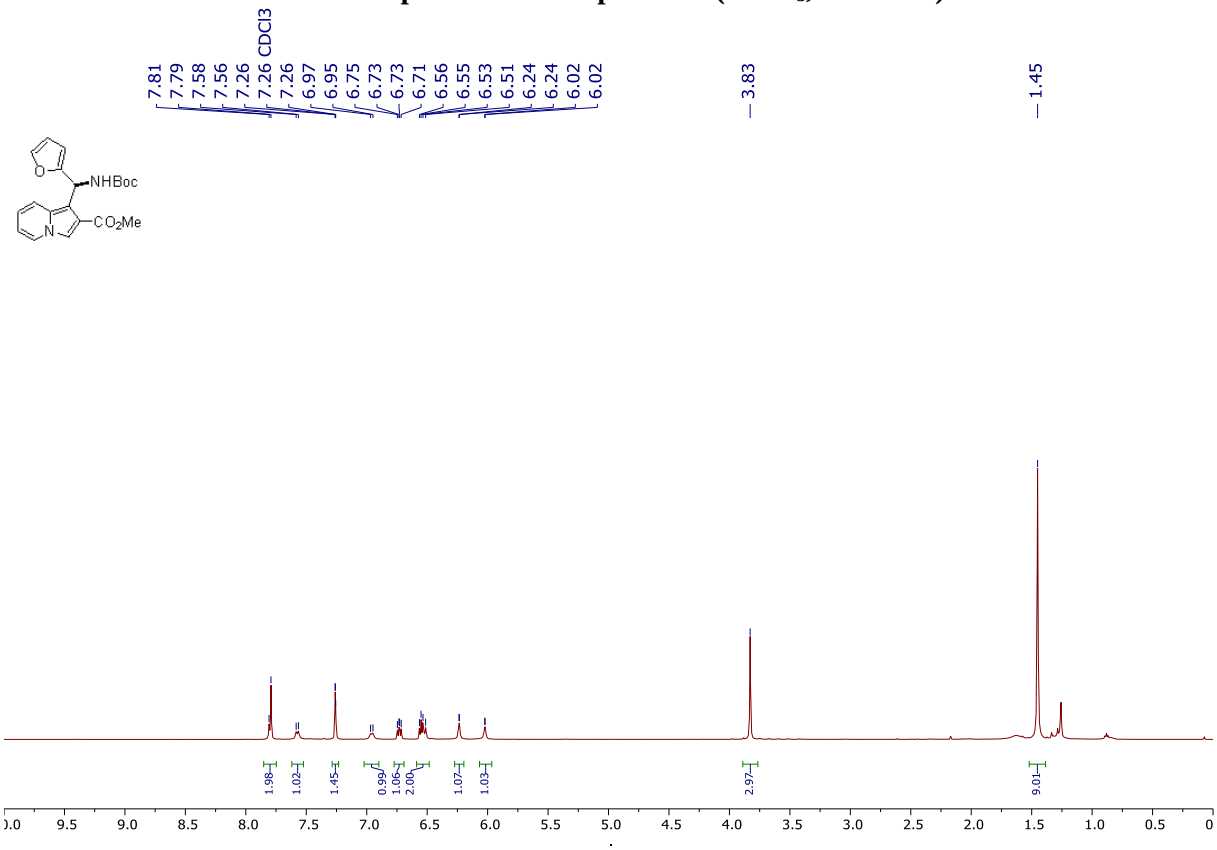
^{1}H NMR spectrum of compound 4l ($CDCl_3$, 600 MHz)



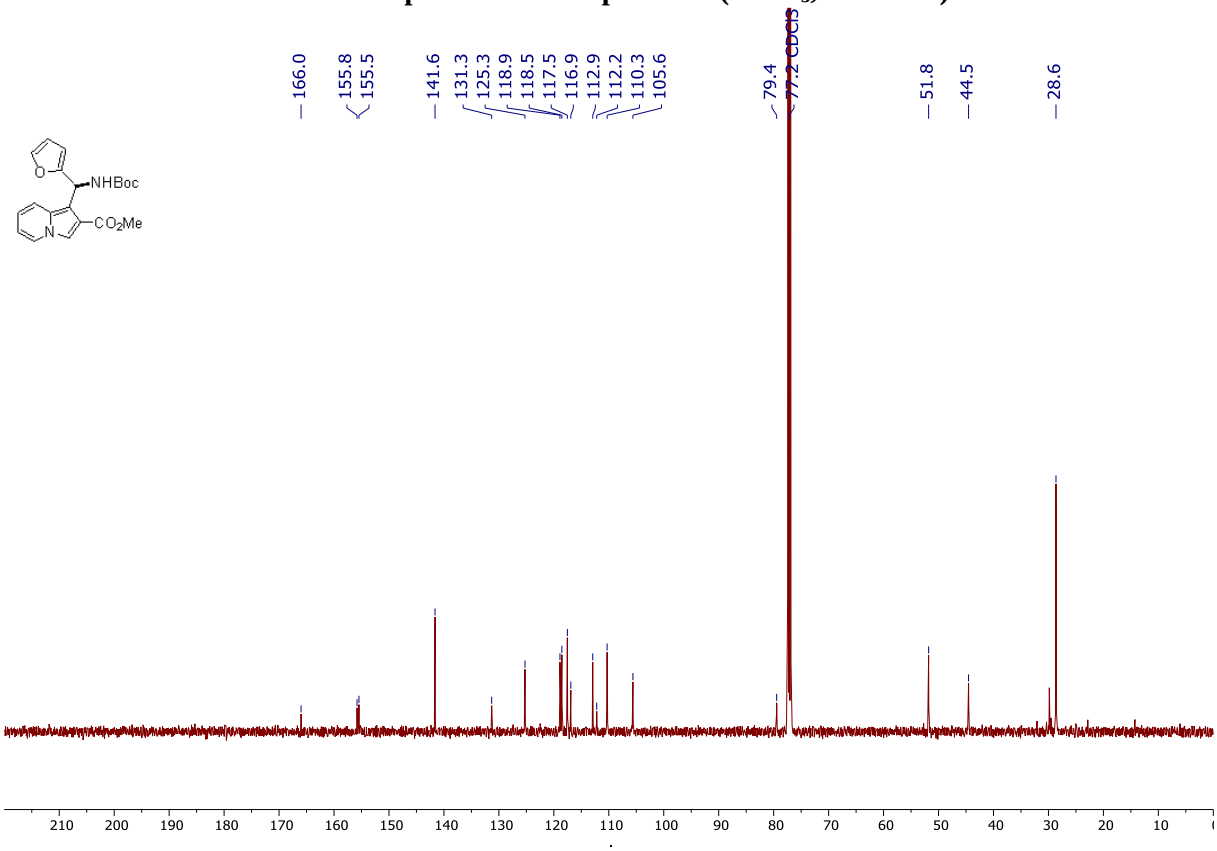
^{13}C NMR spectrum of compound 4l ($CDCl_3$, 151 MHz)



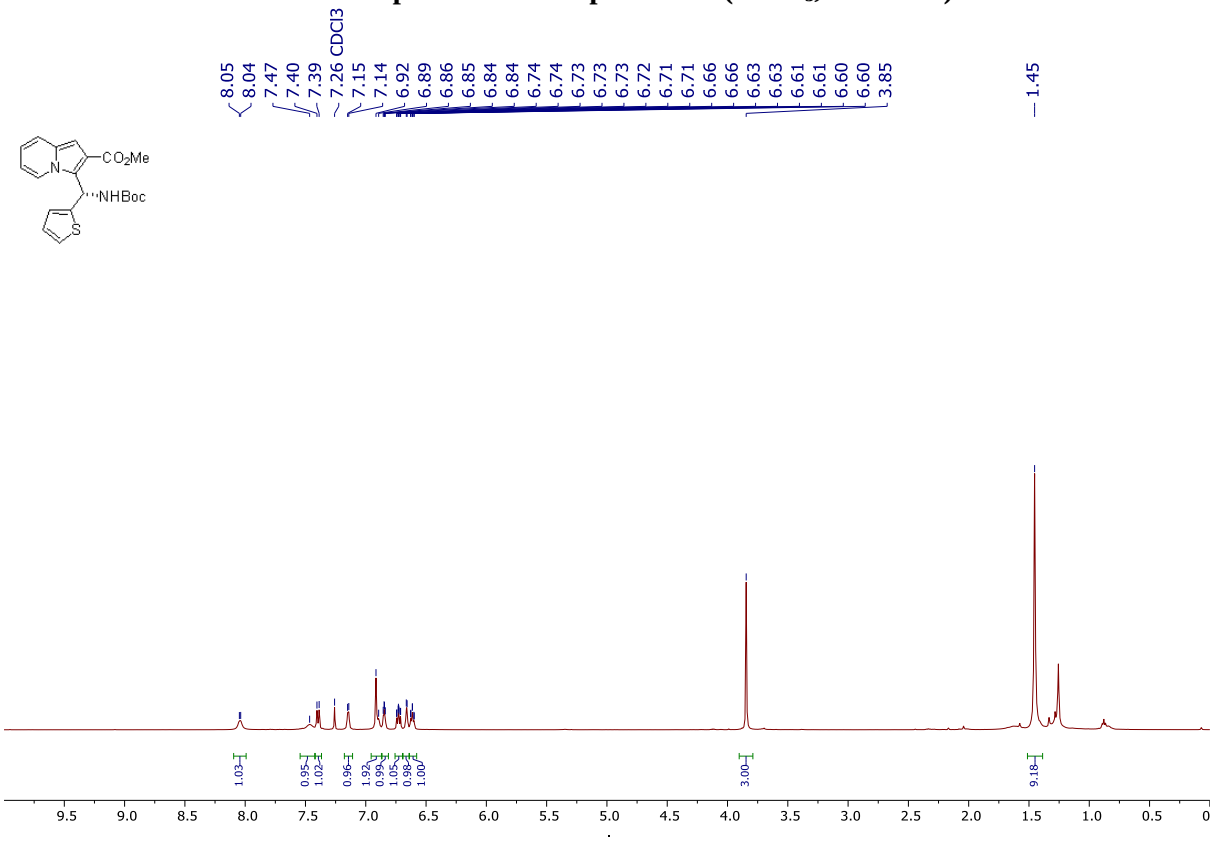
^{1}H NMR spectrum of compound 3l ($CDCl_3$, 500 MHz)



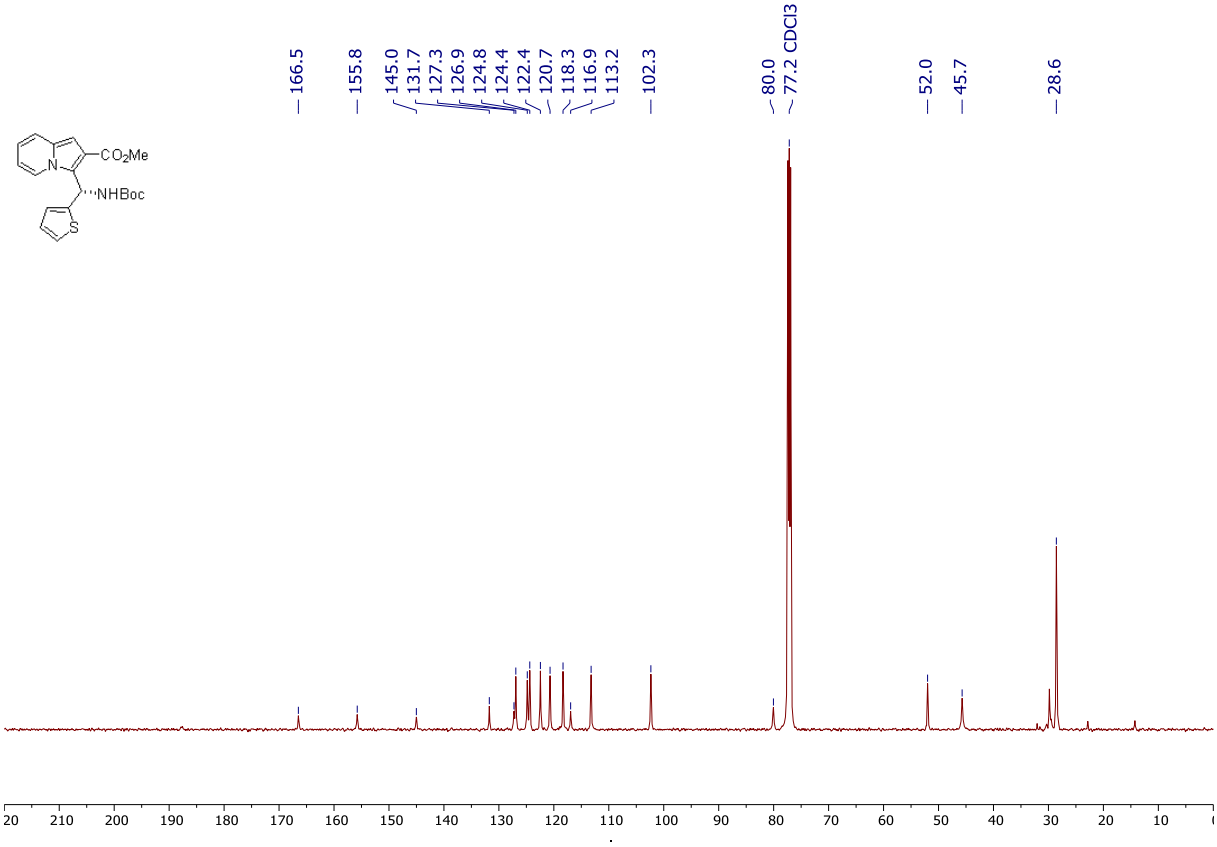
^{13}C NMR spectrum of compound 3l ($CDCl_3$, 126 MHz)



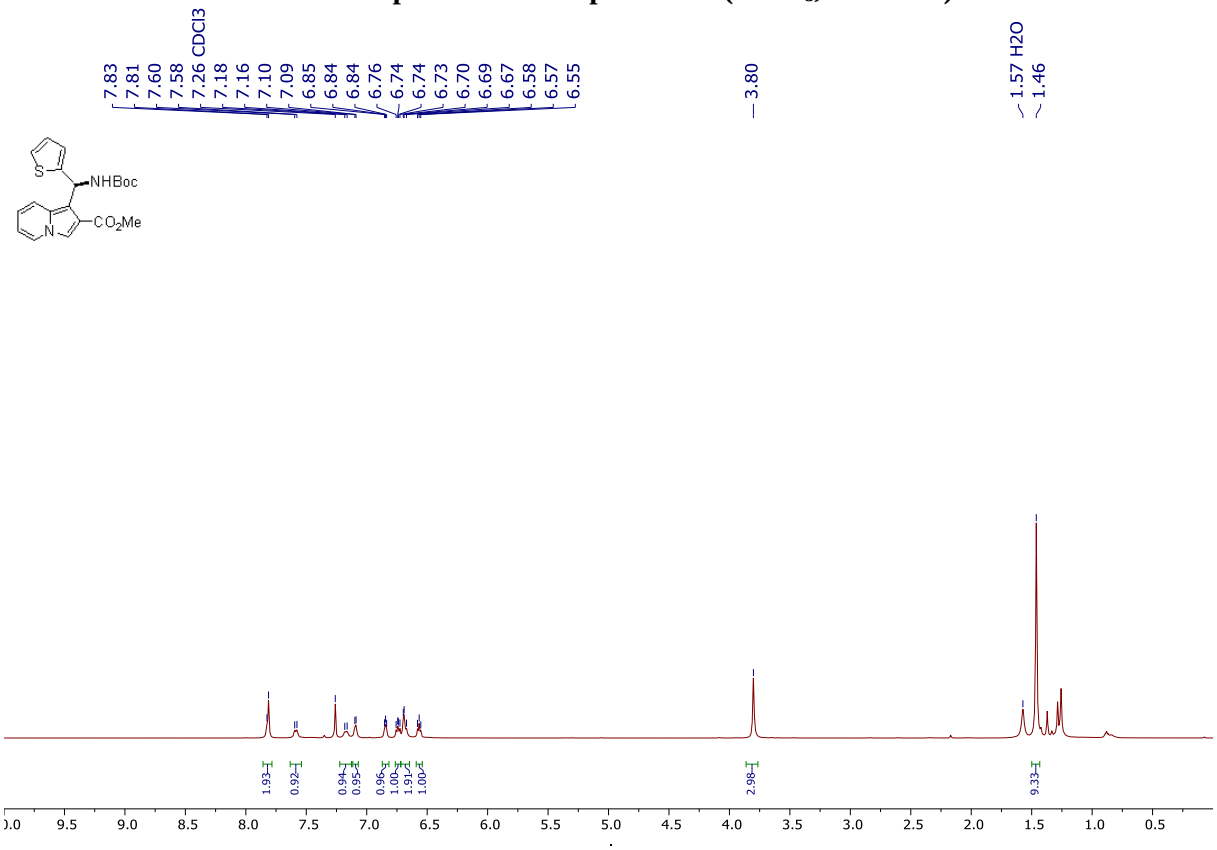
^{1}H NMR spectrum of compound 4m ($CDCl_3$, 500 MHz)



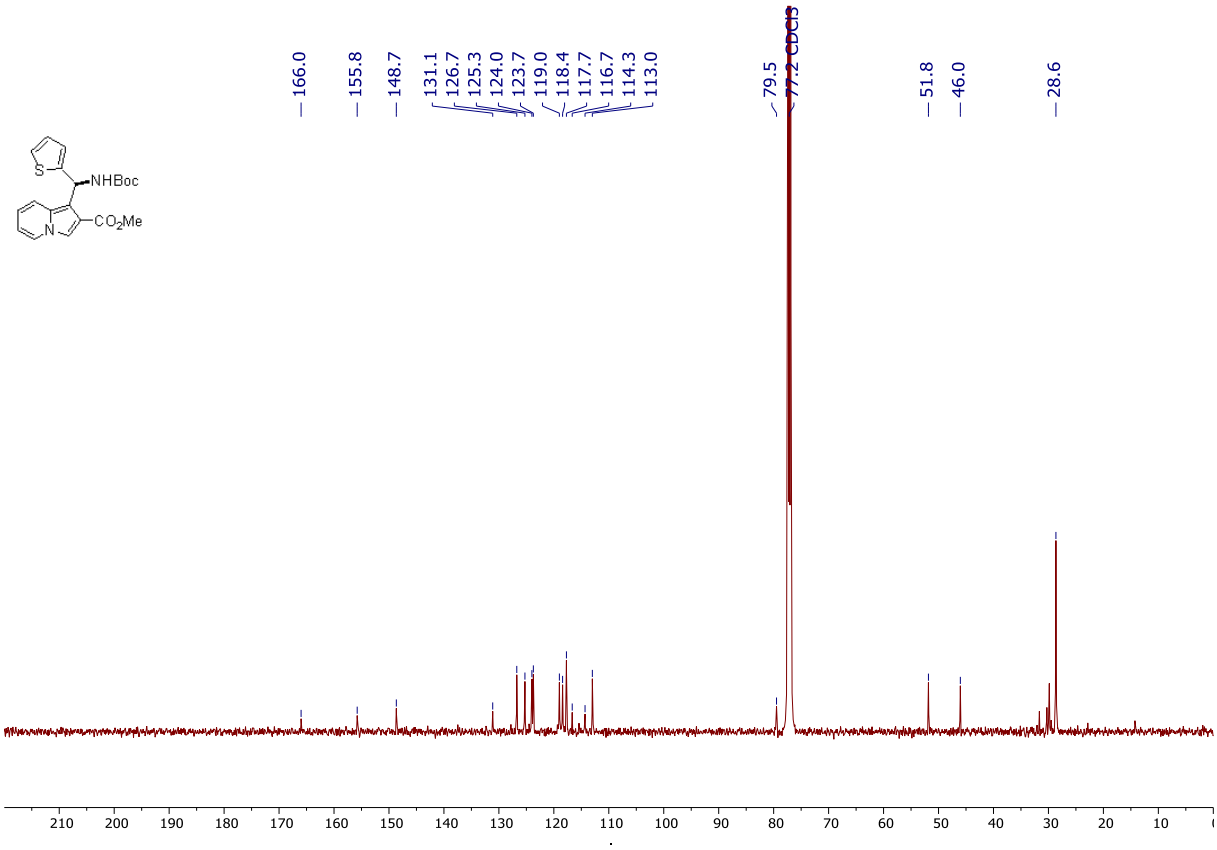
^{13}C NMR spectrum of compound 4m ($CDCl_3$, 126 MHz)



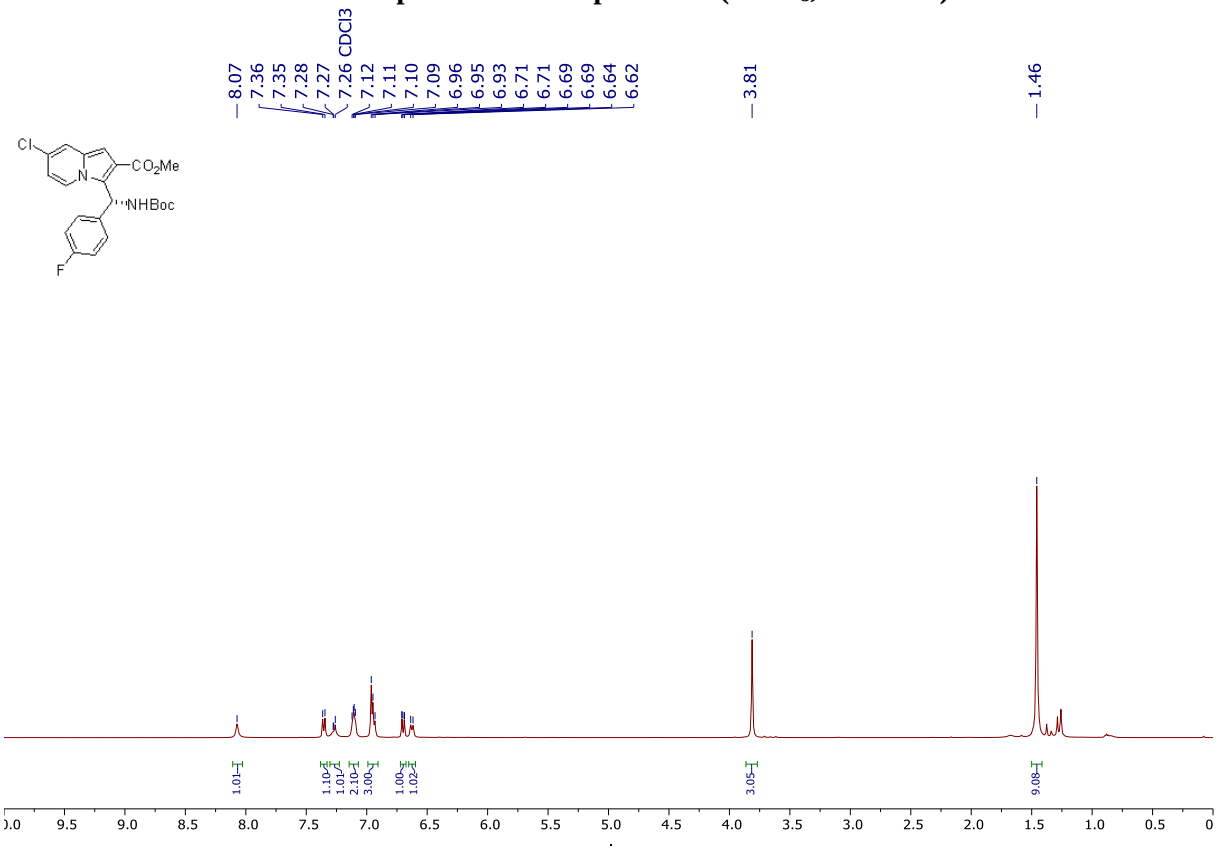
^{1}H NMR spectrum of compound 3m ($CDCl_3$, 500 MHz)



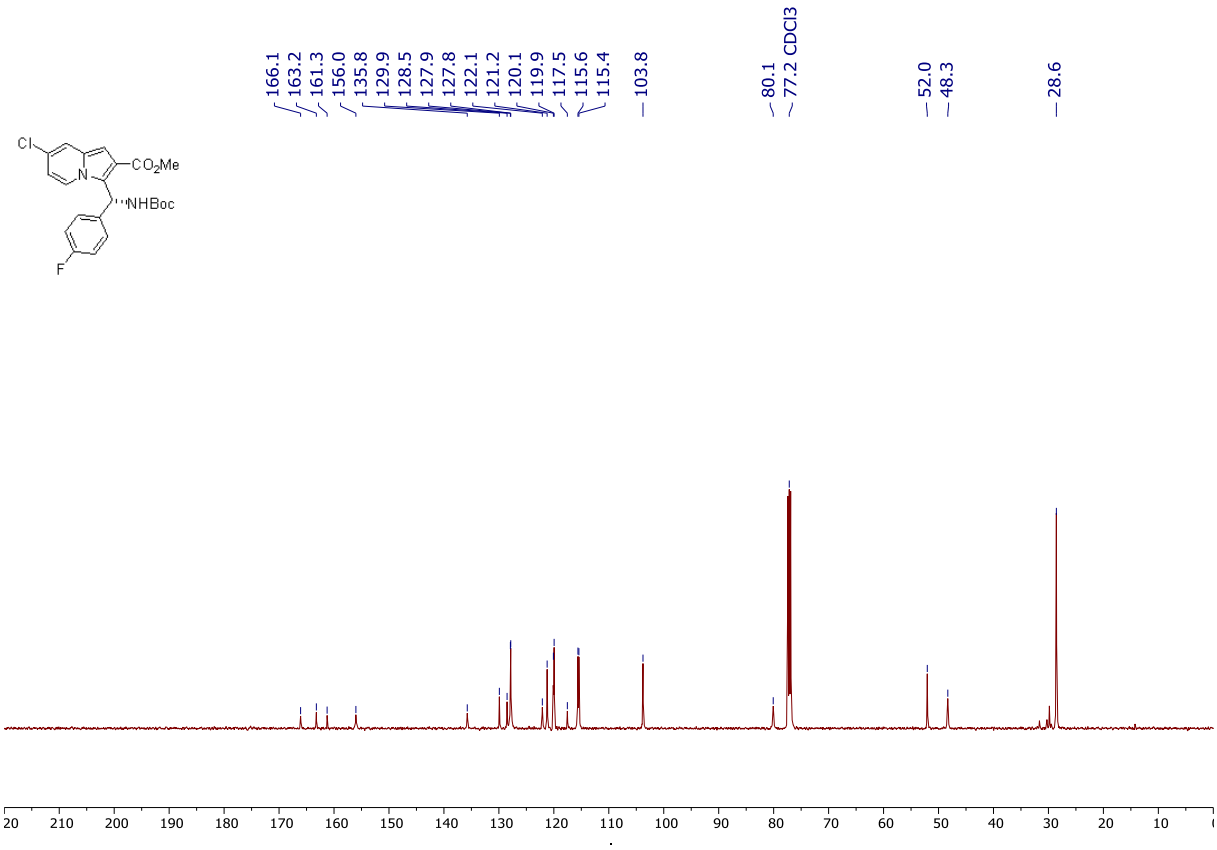
^{13}C NMR spectrum of compound 3m ($CDCl_3$, 126 MHz)



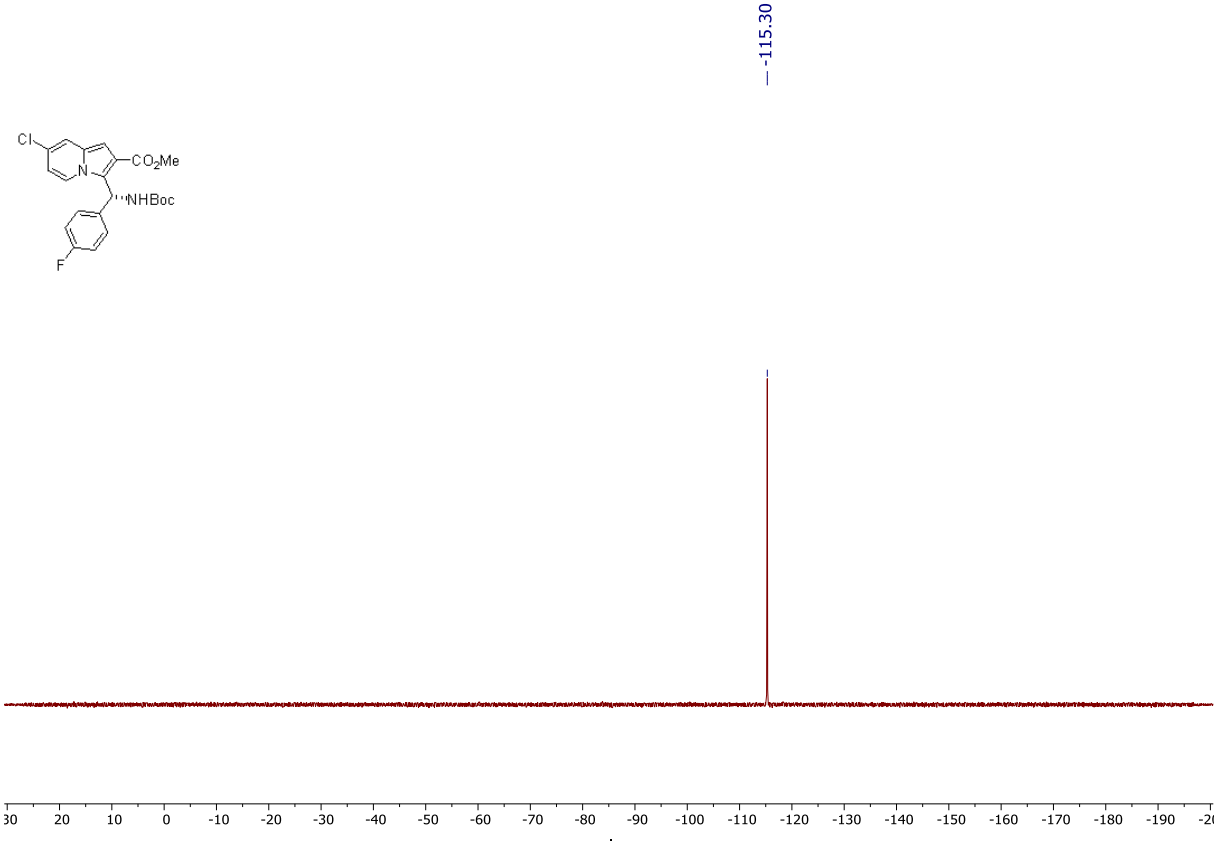
^{1}H NMR spectrum of compound 4n ($CDCl_3$, 500 MHz)



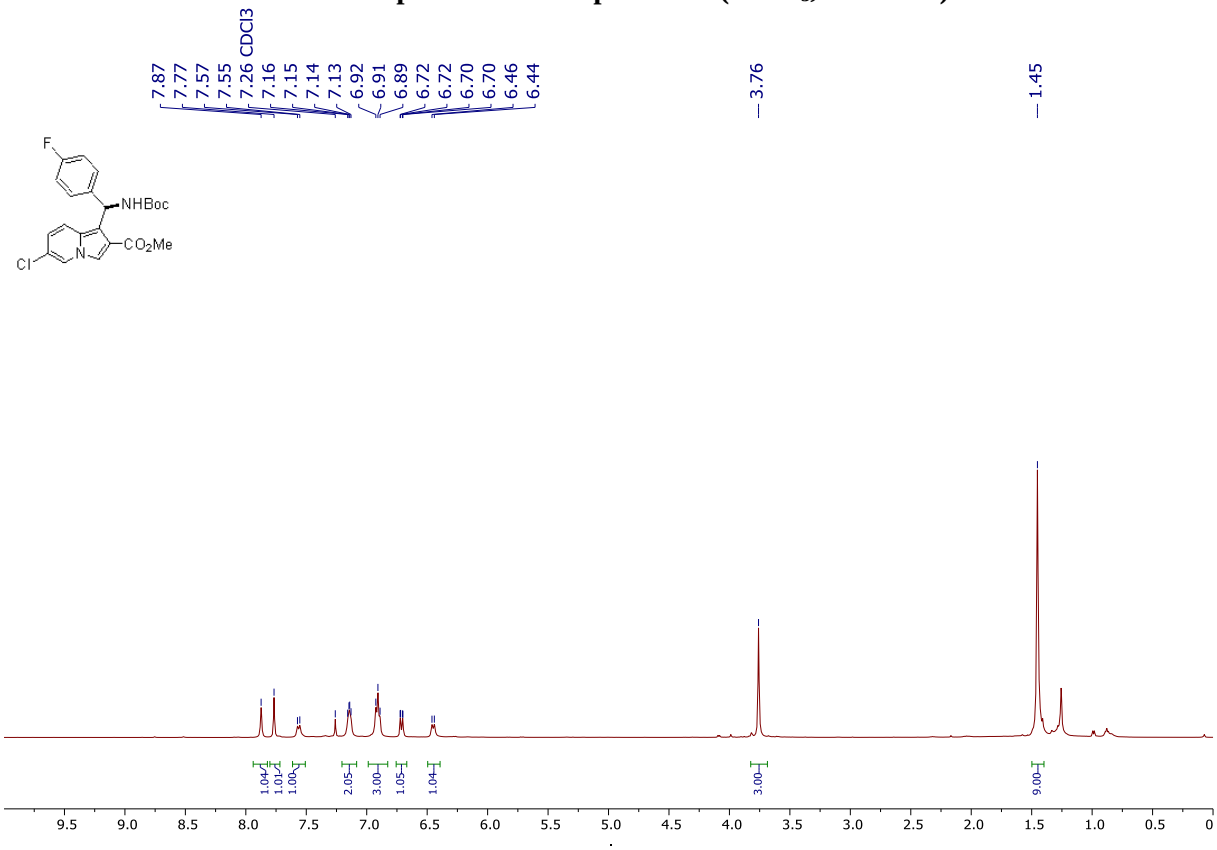
^{13}C NMR spectrum of compound 4n ($CDCl_3$, 126 MHz)



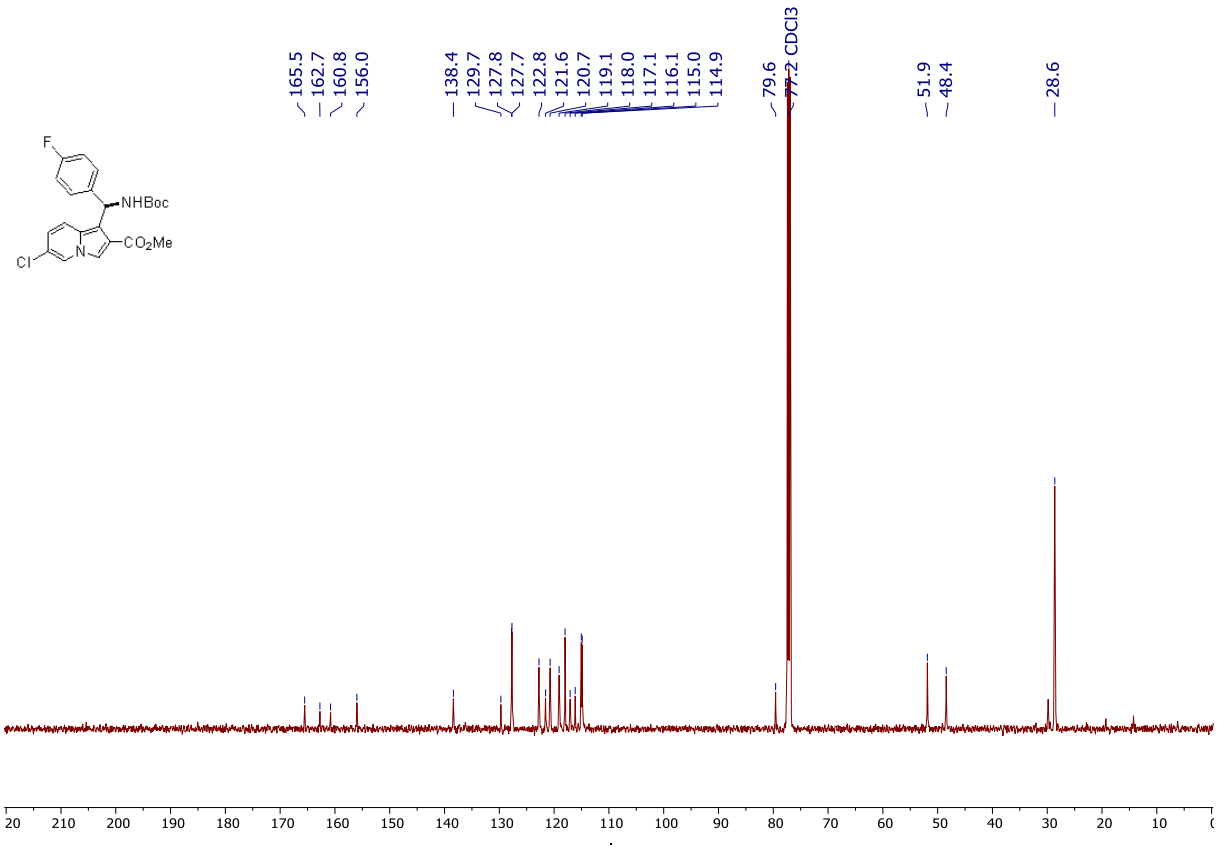
^{19}F NMR spectrum of compound 4n ($CDCl_3$, 470 MHz)



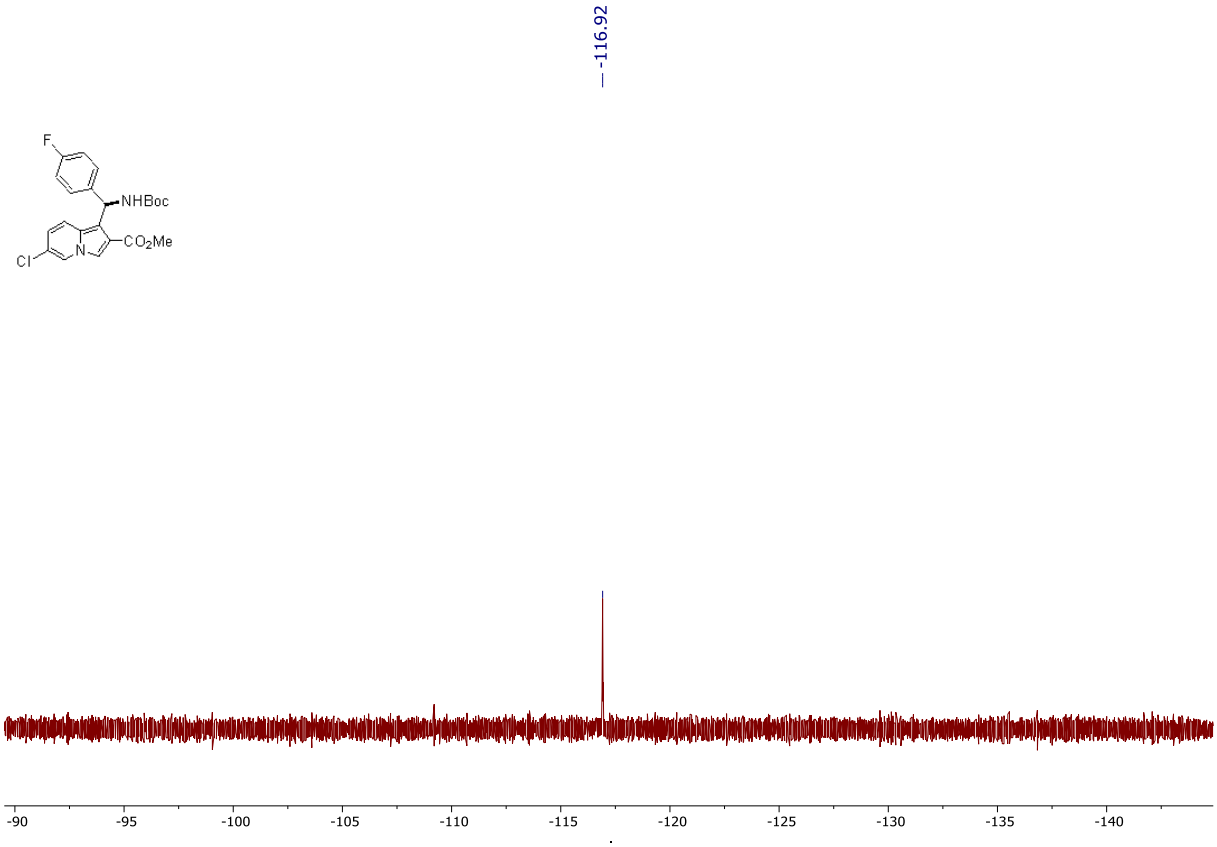
^{1}H NMR spectrum of compound 3n ($CDCl_3$, 500 MHz)



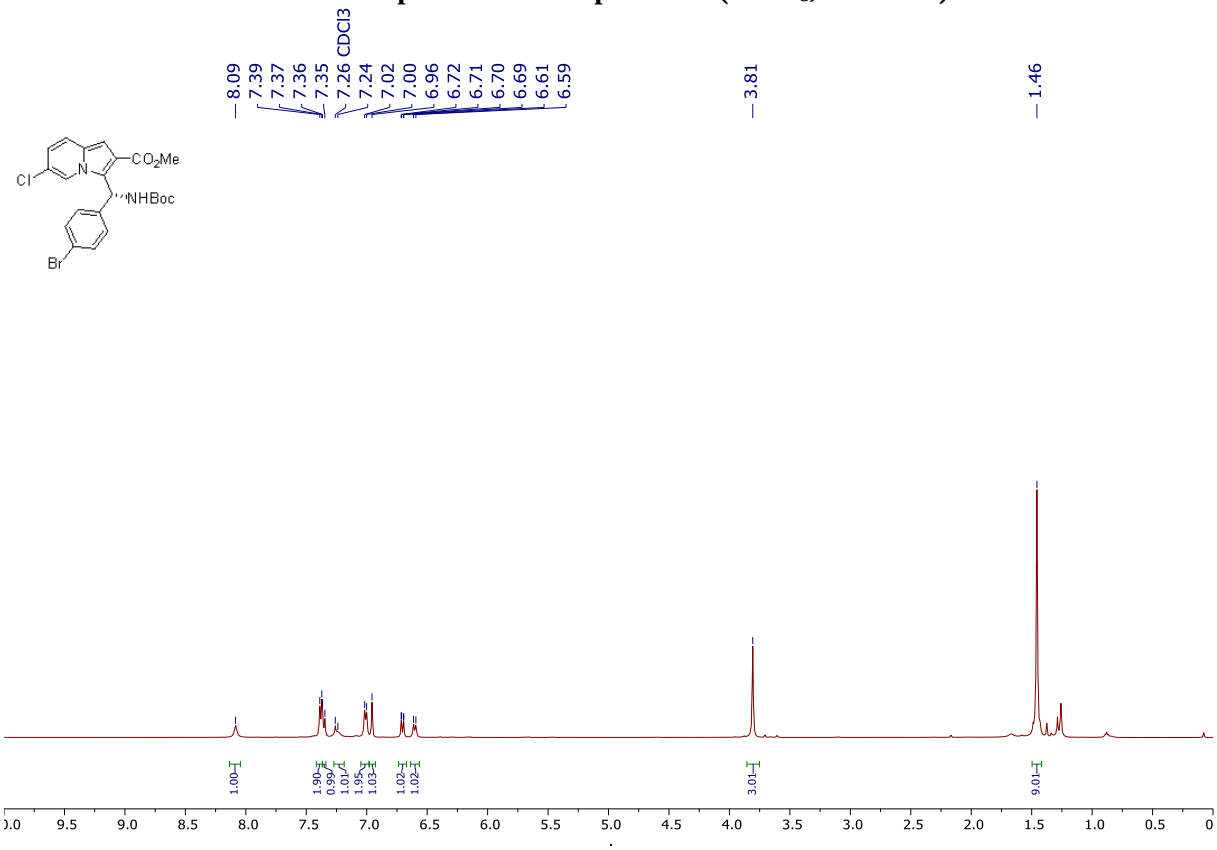
^{13}C NMR spectrum of compound 3n ($CDCl_3$, 126 MHz)



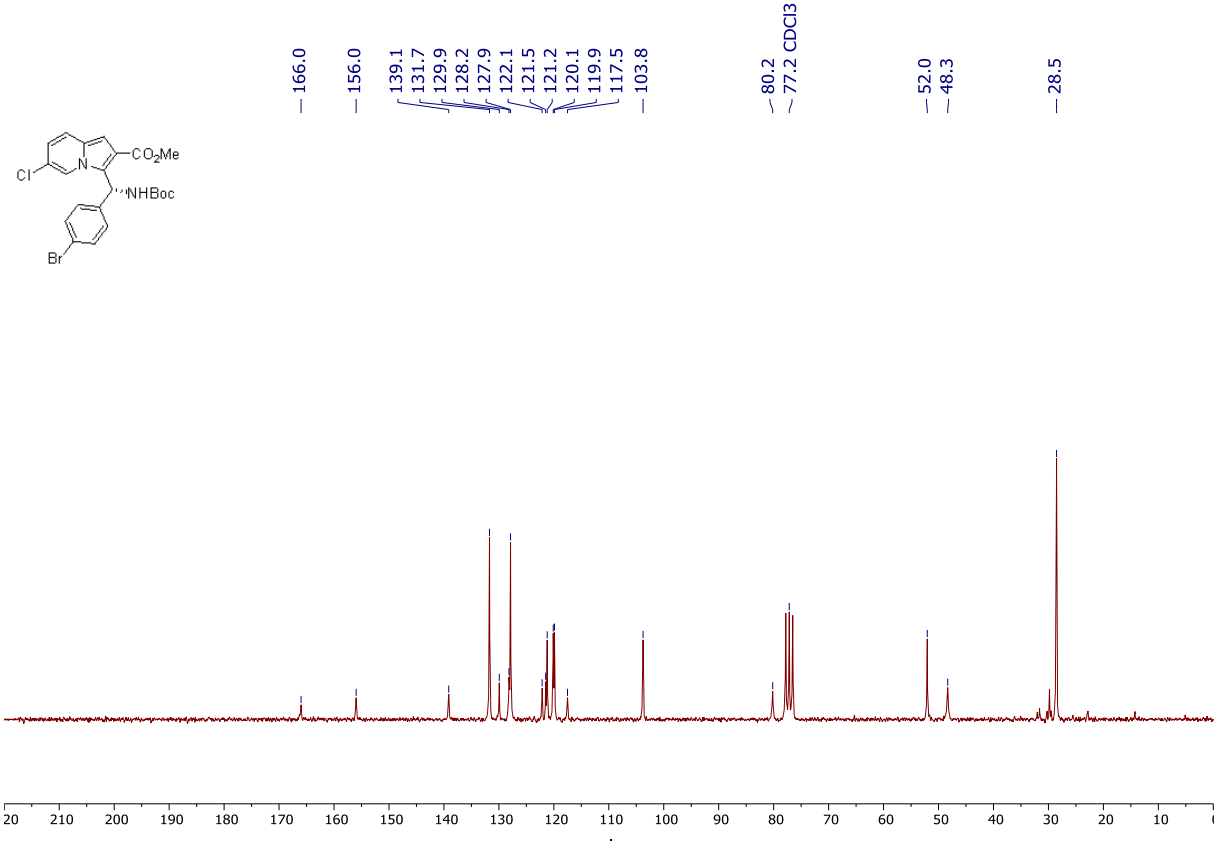
^{19}F NMR spectrum of compound 3n ($CDCl_3$, 470 MHz)



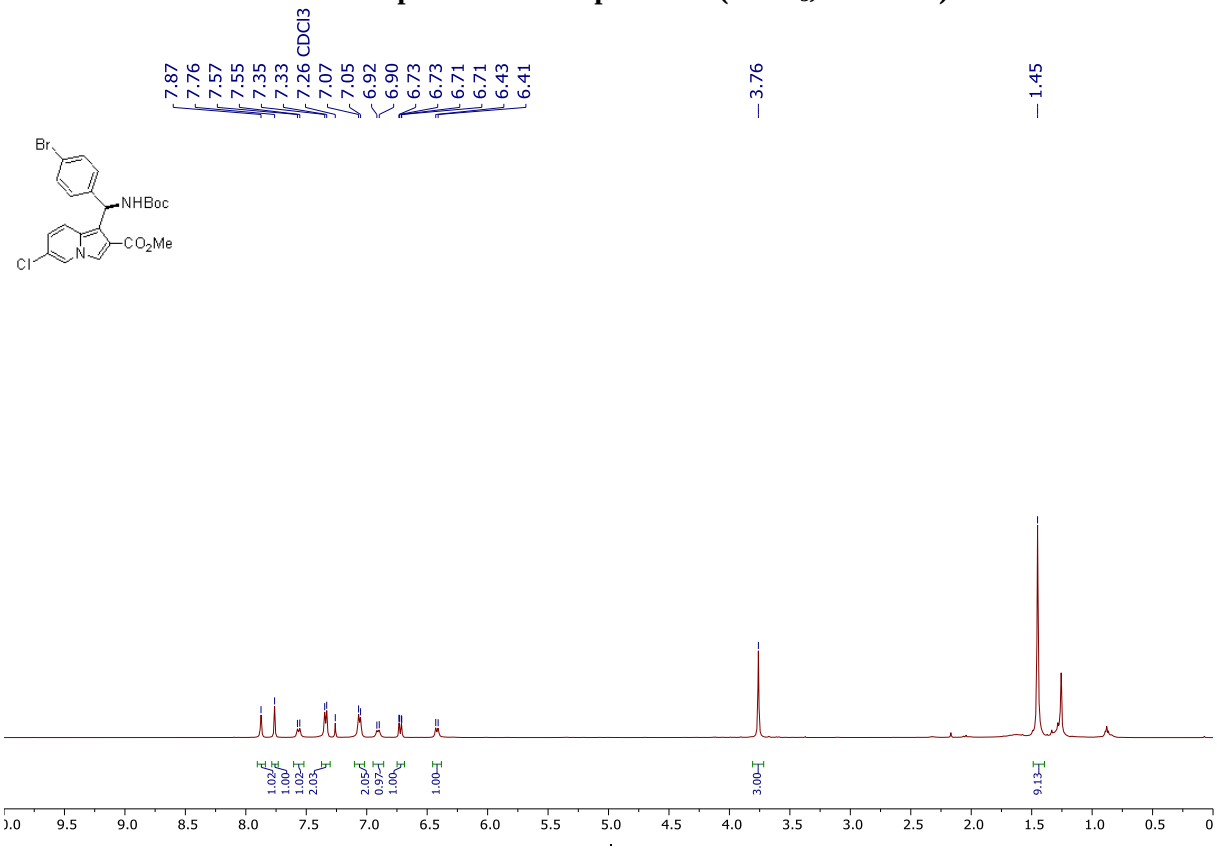
^{1}H NMR spectrum of compound 4o ($CDCl_3$, 500 MHz)



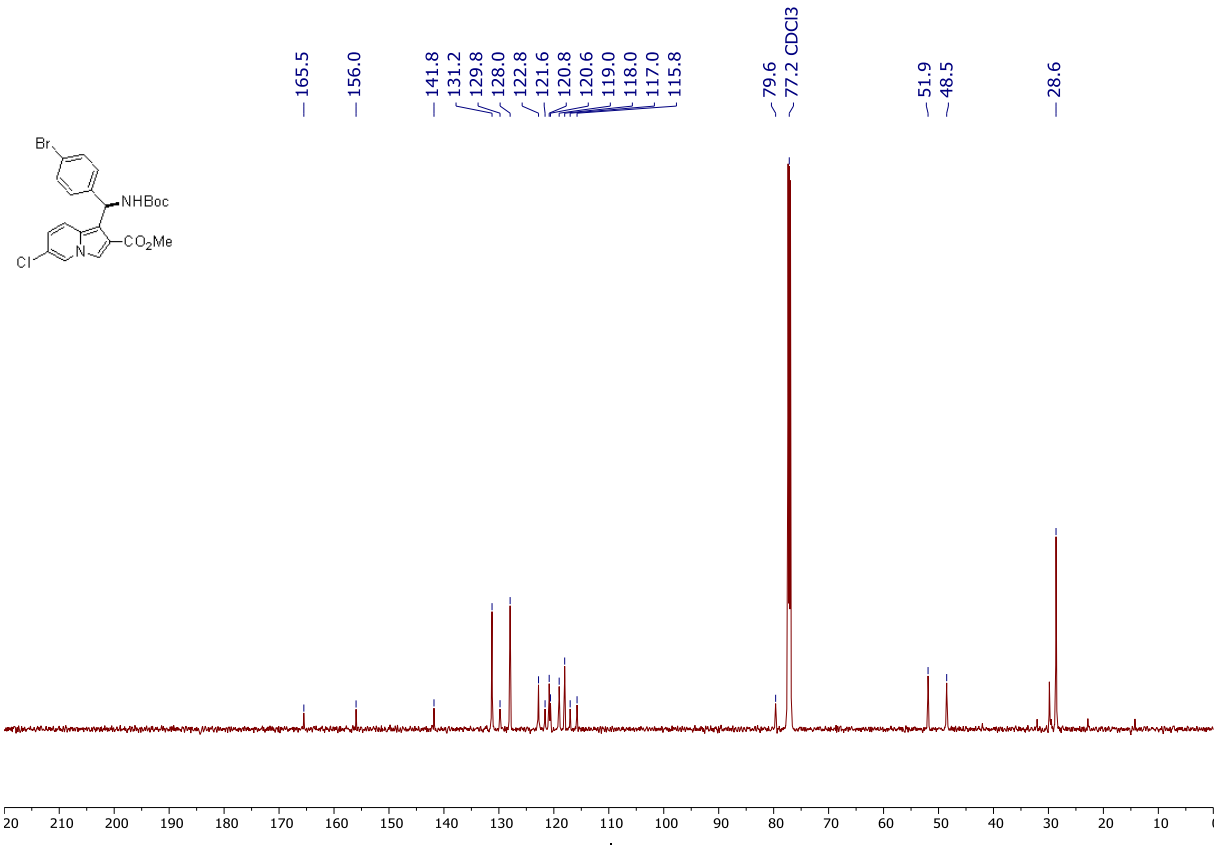
^{13}C NMR spectrum of compound 4o ($CDCl_3$, 50 MHz)



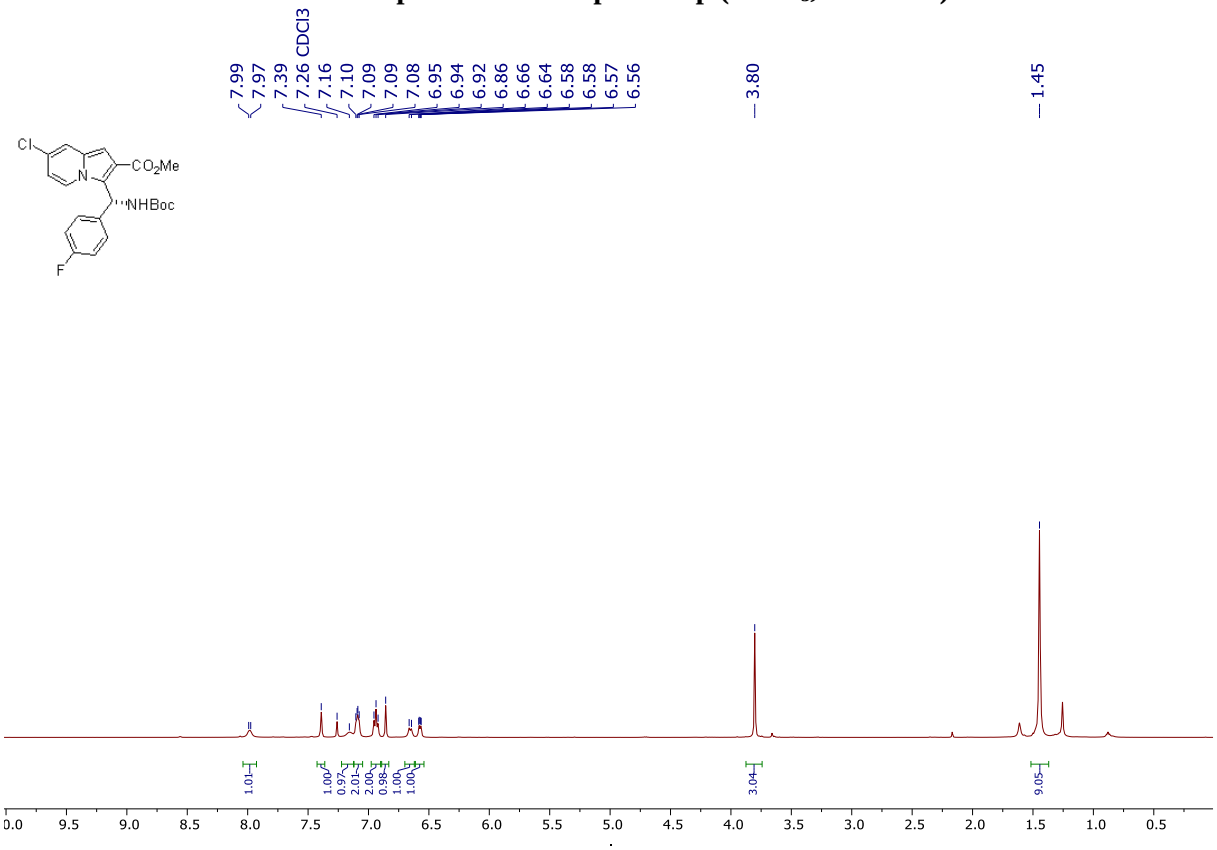
^{1}H NMR spectrum of compound 3o ($CDCl_3$, 500 MHz)



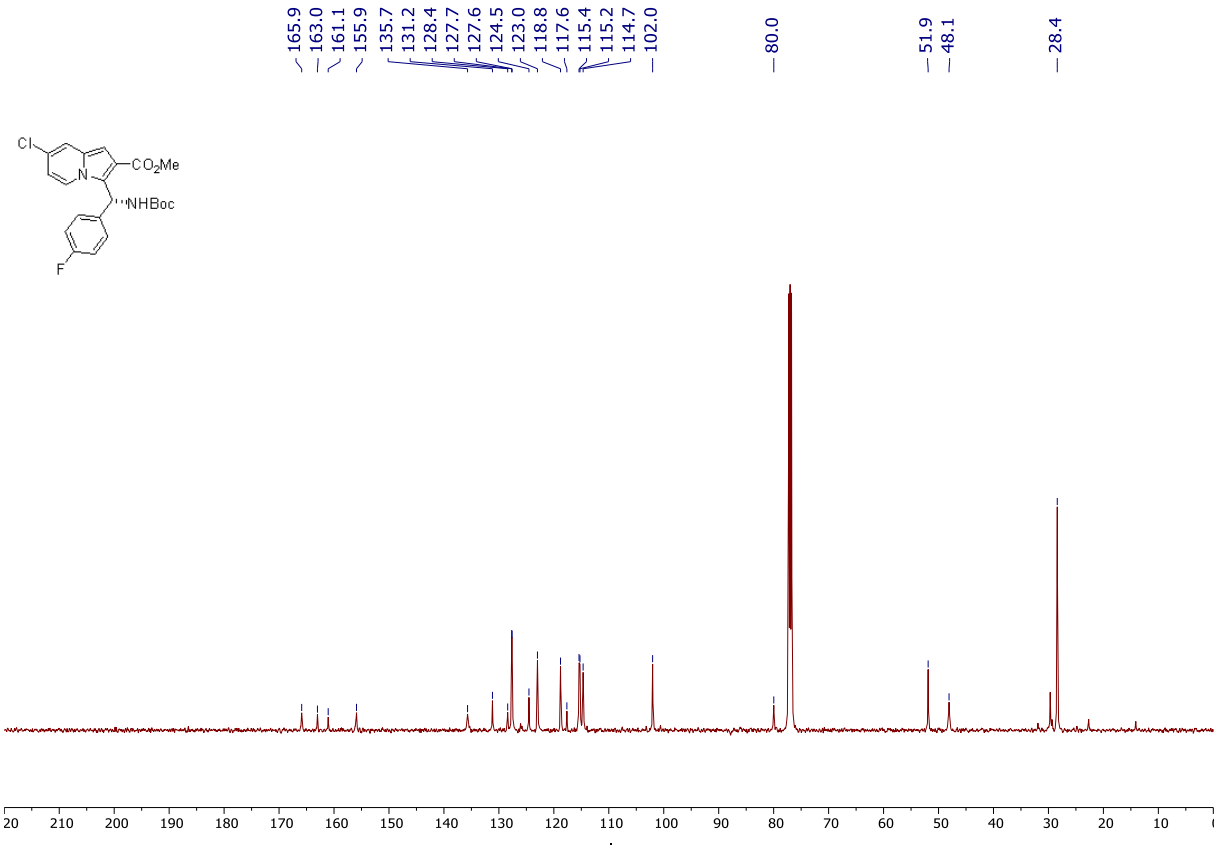
^{13}C NMR spectrum of compound 3o ($CDCl_3$, 151 MHz)



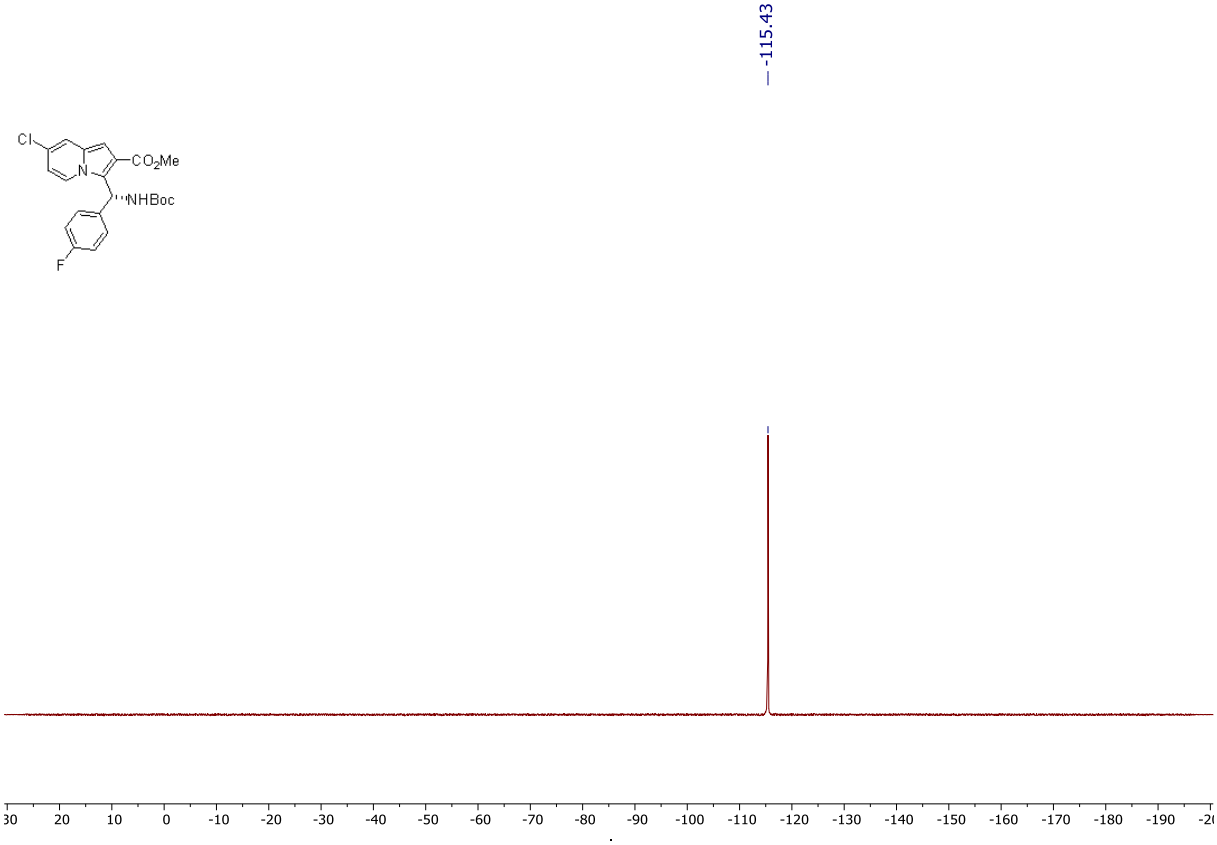
^{1}H NMR spectrum of compound 4p ($CDCl_3$, 500 MHz)



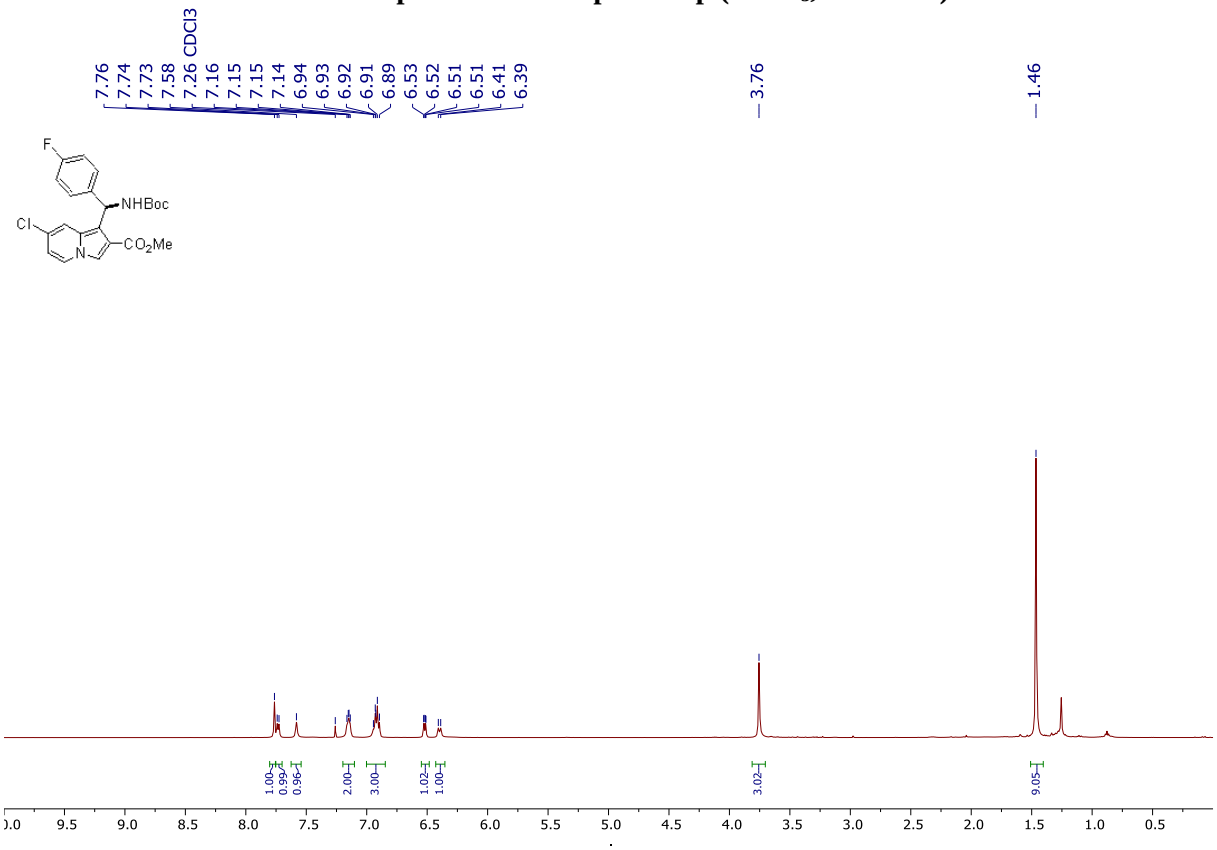
^{13}C NMR spectrum of compound 4p ($CDCl_3$, 126 MHz)



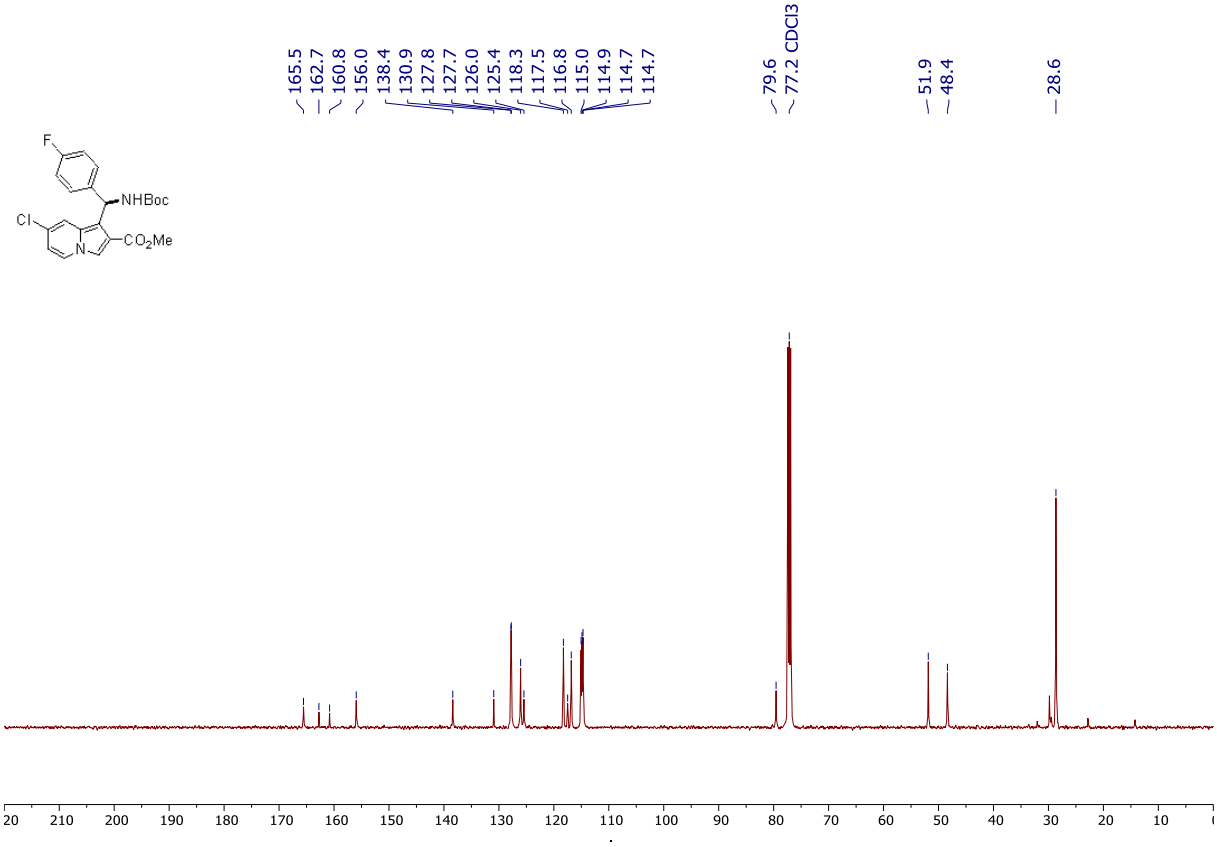
^{19}F NMR spectrum of compound 4p ($CDCl_3$, 470 MHz)



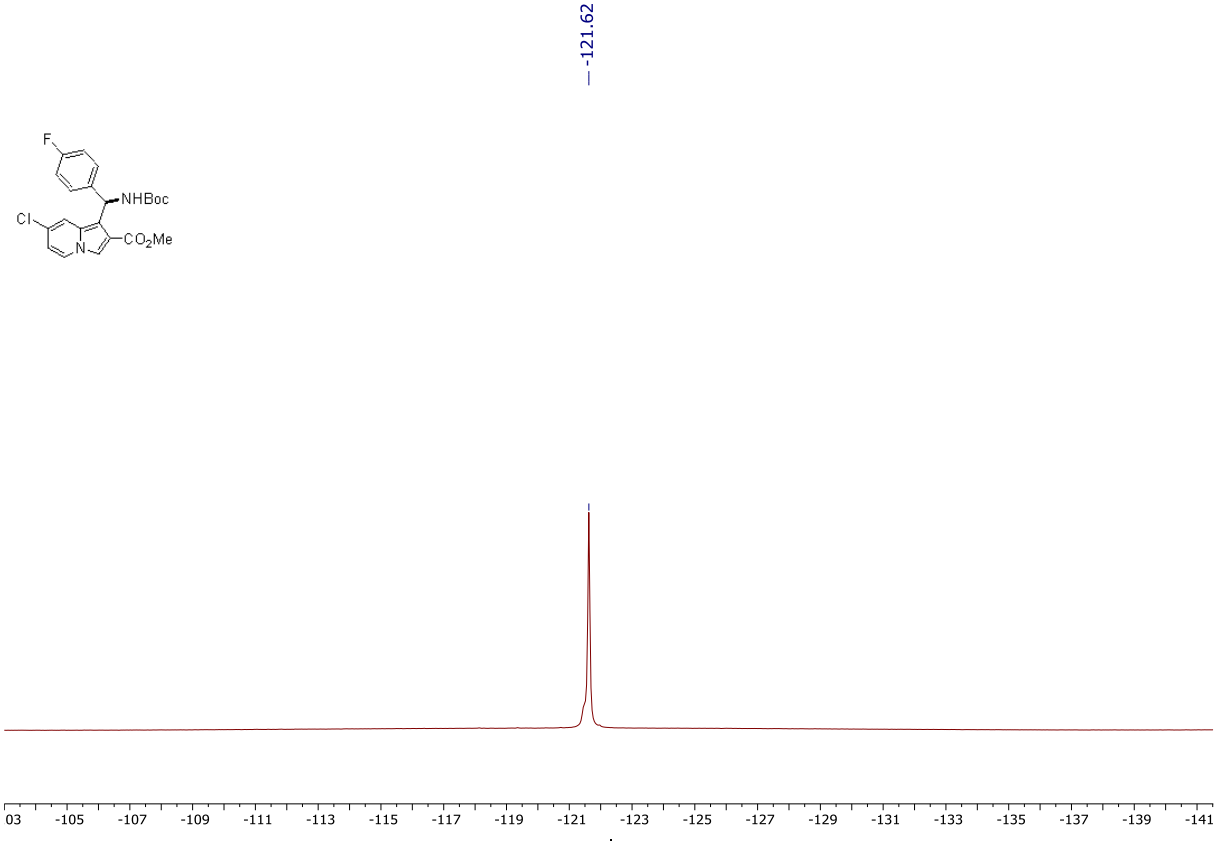
^{1}H NMR spectrum of compound 3p ($CDCl_3$, 500 MHz)



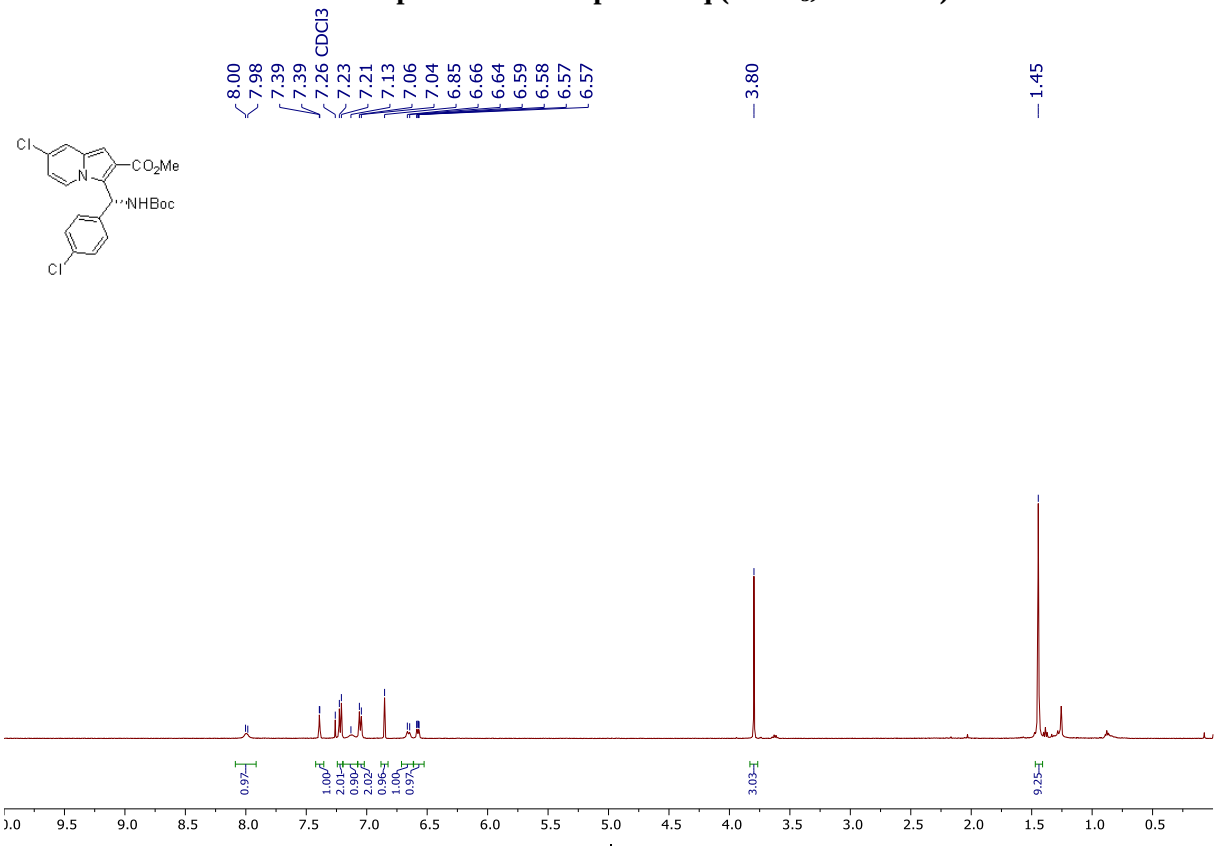
^{13}C NMR spectrum of compound 3p ($CDCl_3$, 126 MHz)



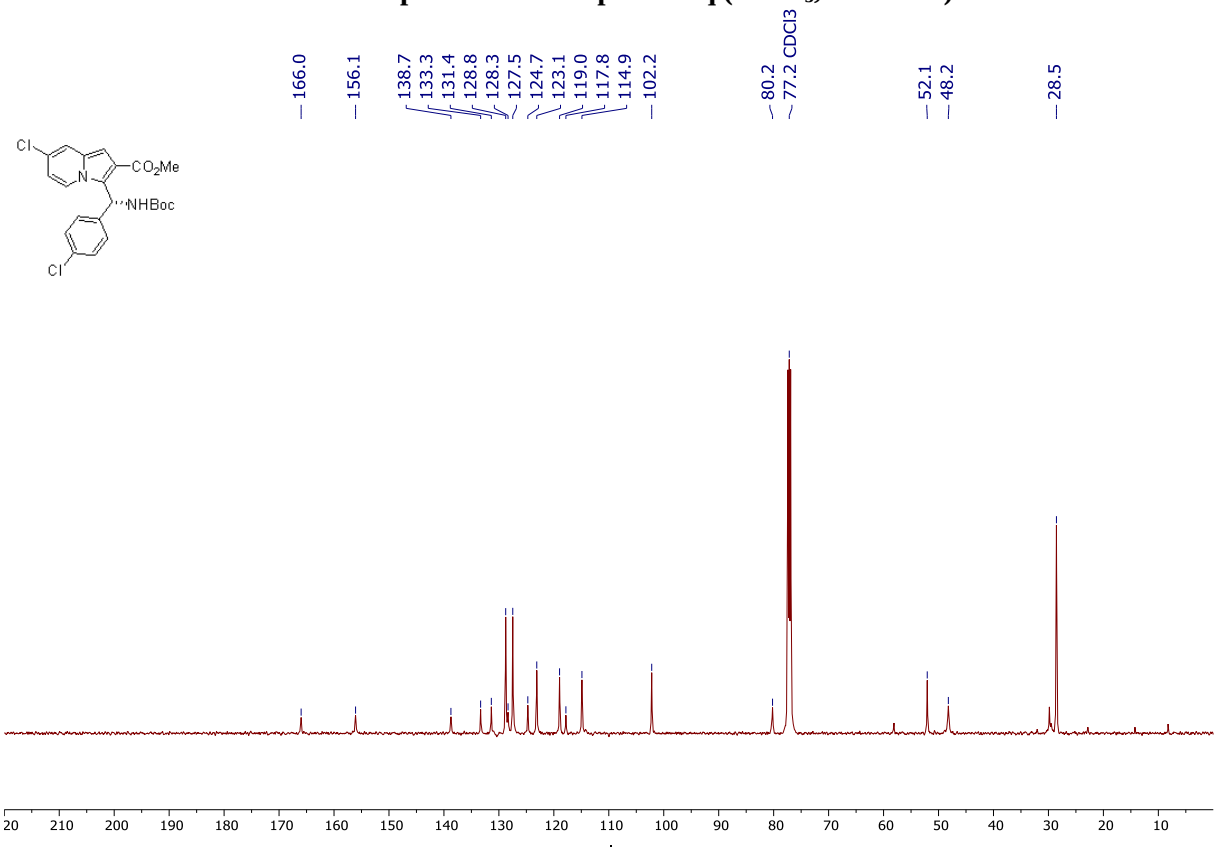
^{19}F NMR spectrum of compound 3p ($CDCl_3$, 470 MHz)



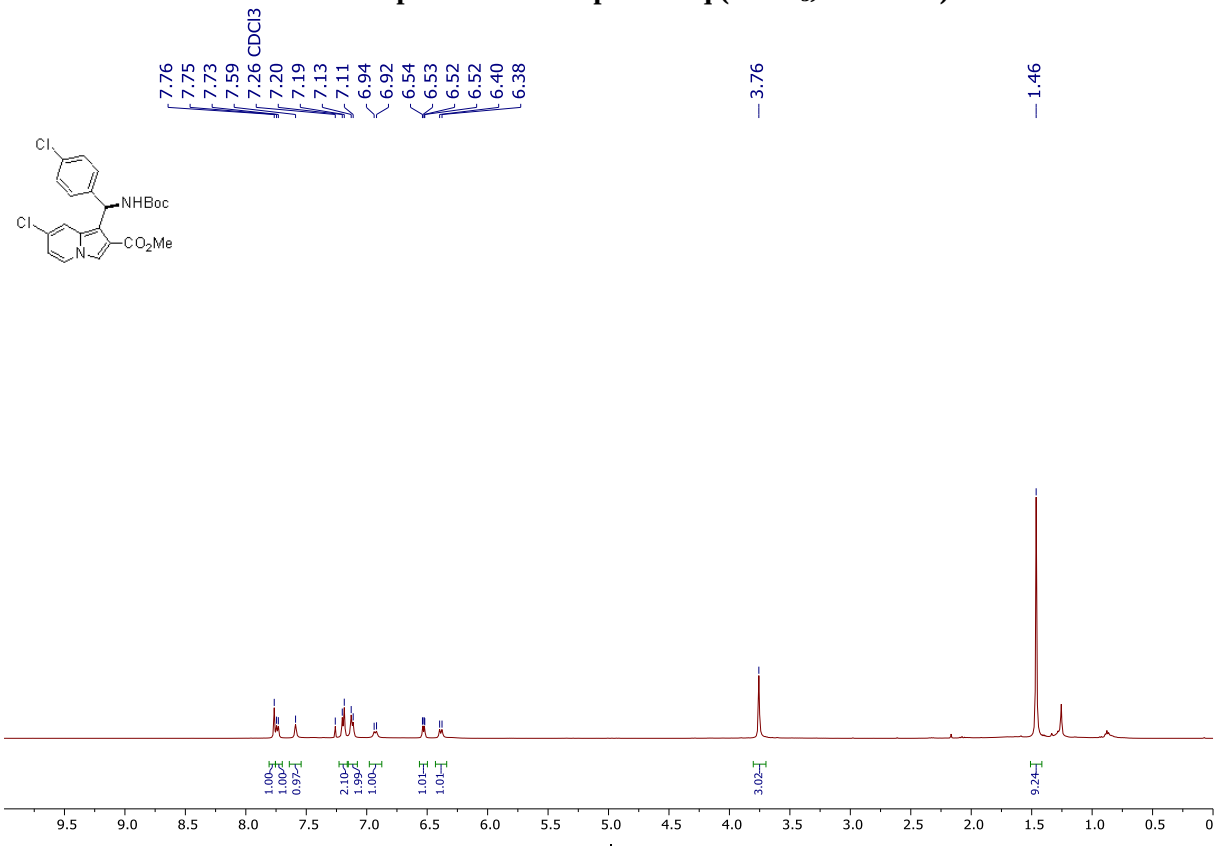
^{1}H NMR spectrum of compound 4q ($CDCl_3$, 500 MHz)



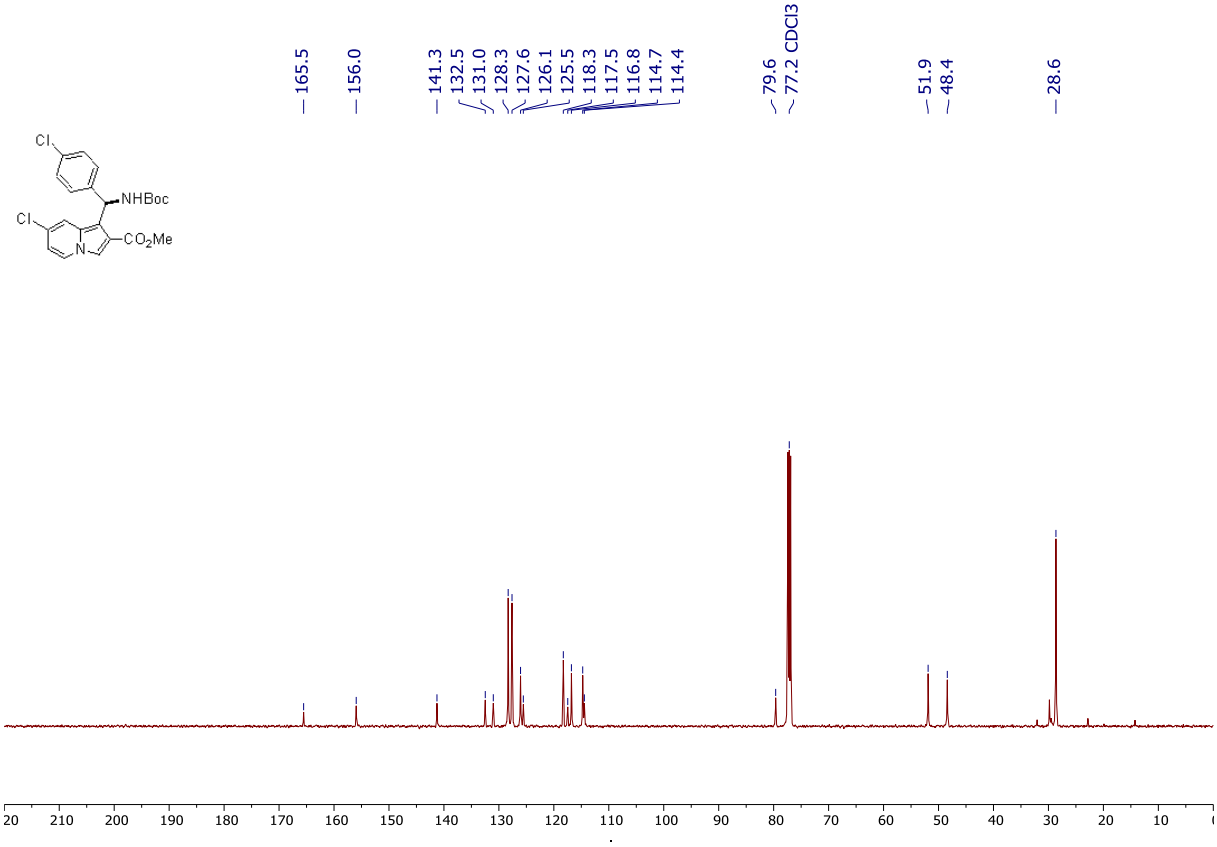
^{13}C NMR spectrum of compound 4q ($CDCl_3$, 126 MHz)



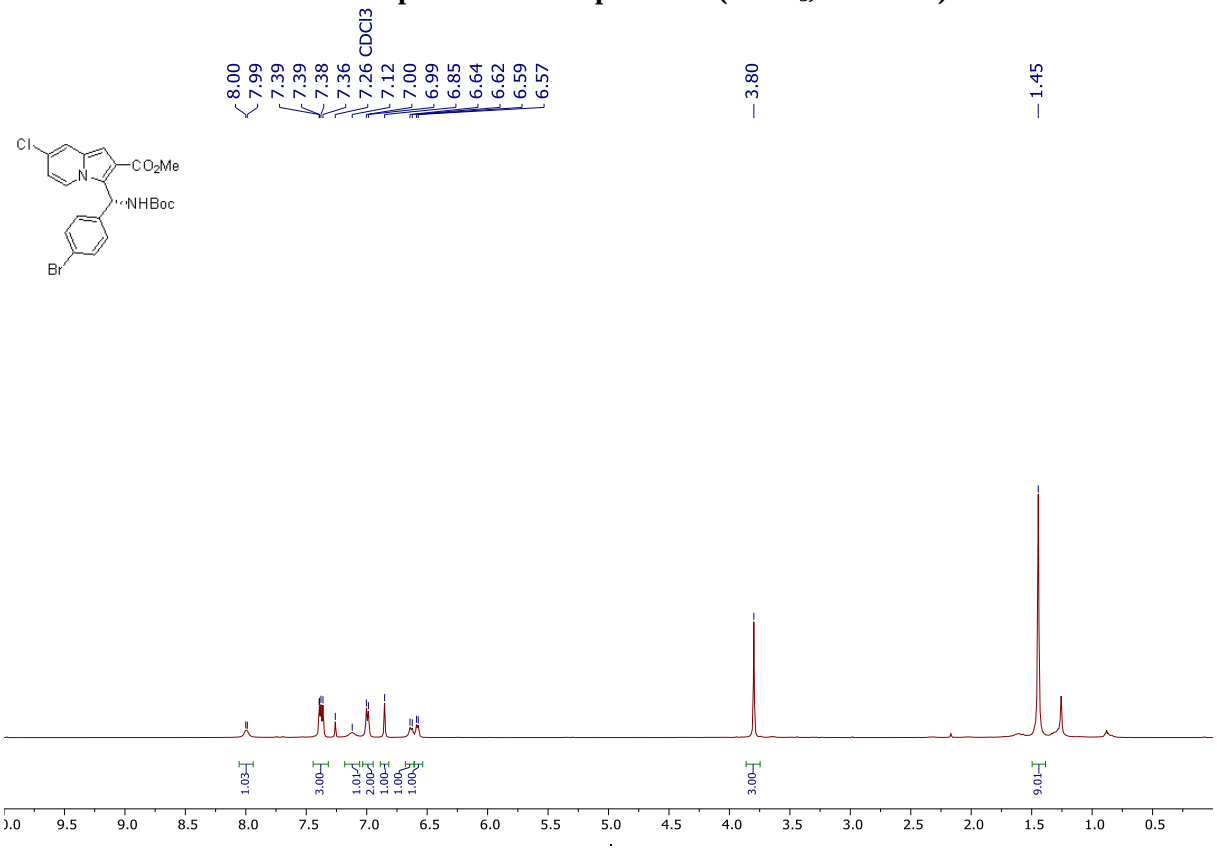
^{1}H NMR spectrum of compound 3q ($CDCl_3$, 500 MHz)



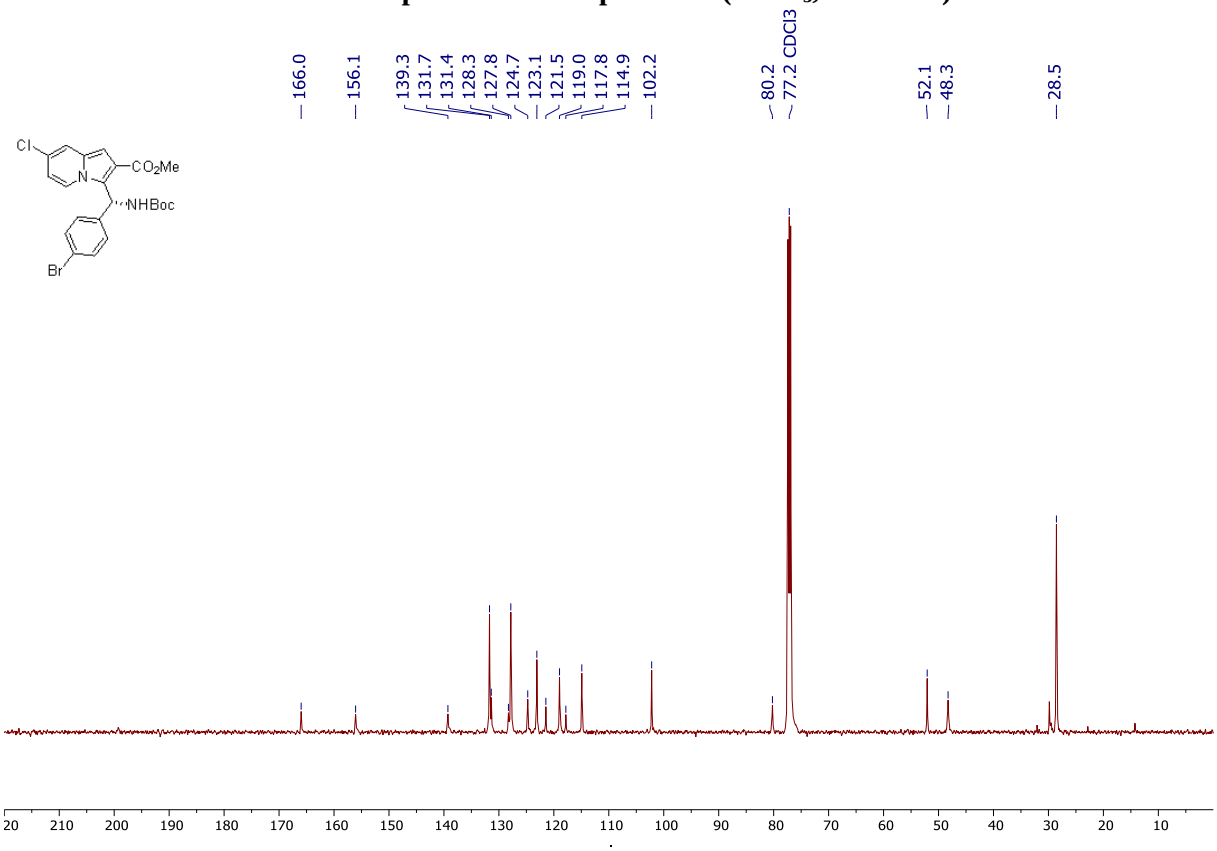
^{13}C NMR spectrum of compound 3q ($CDCl_3$, 126 MHz)



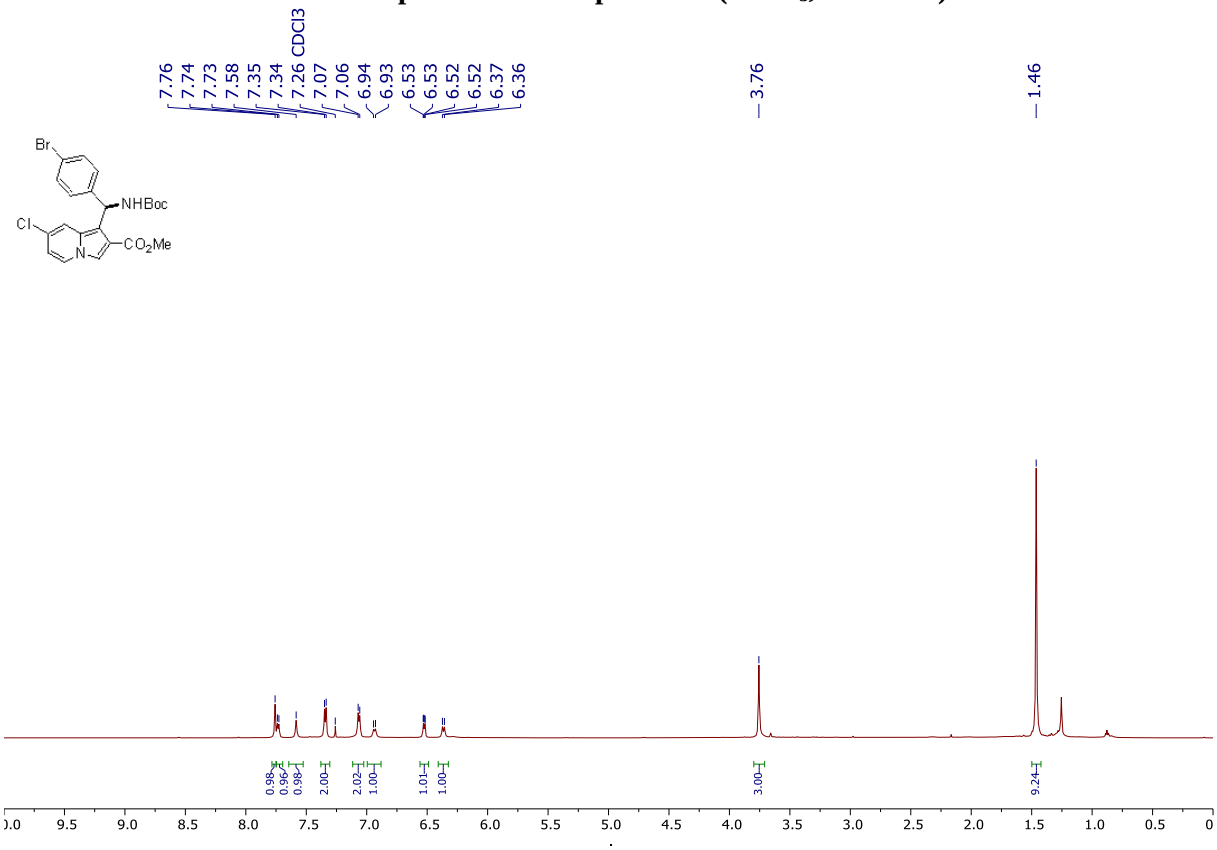
^{1}H NMR spectrum of compound 4r ($CDCl_3$, 500 MHz)



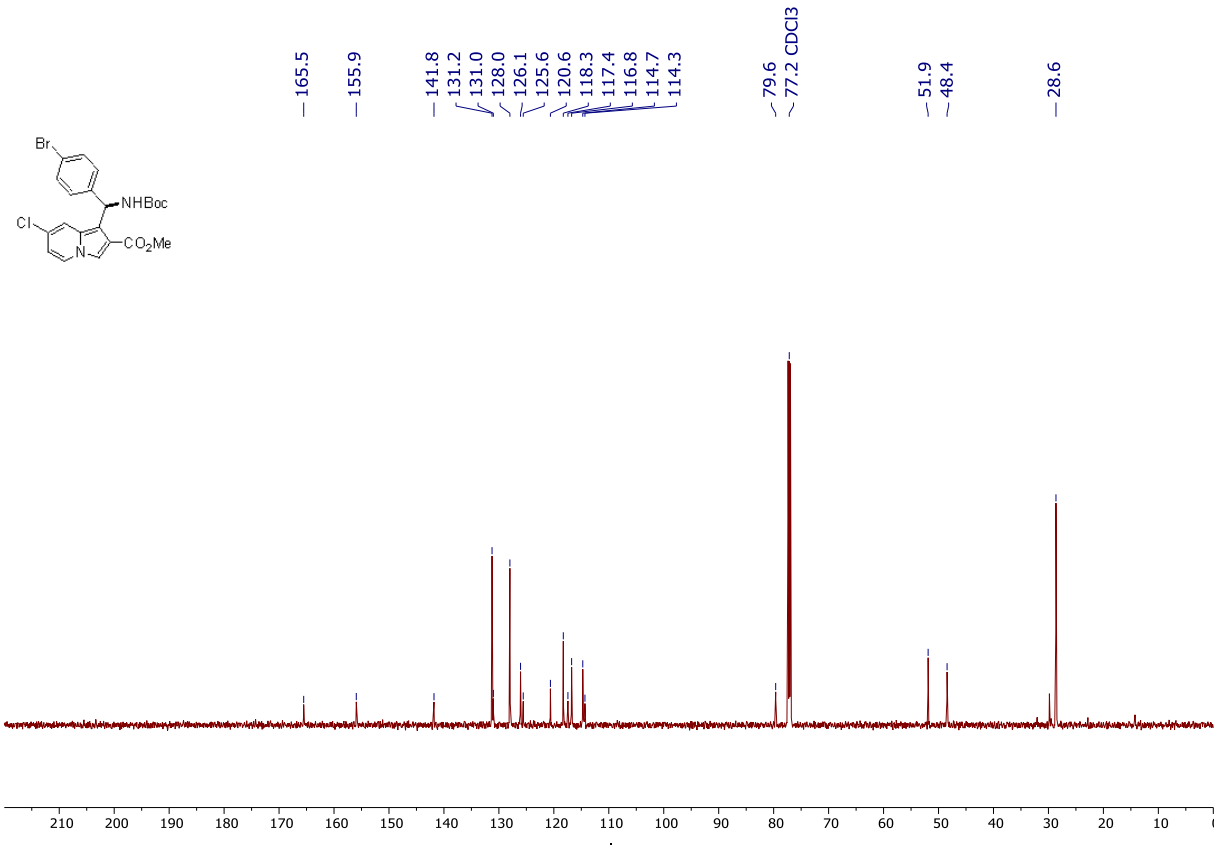
^{13}C NMR spectrum of compound 4r ($CDCl_3$, 126 MHz)



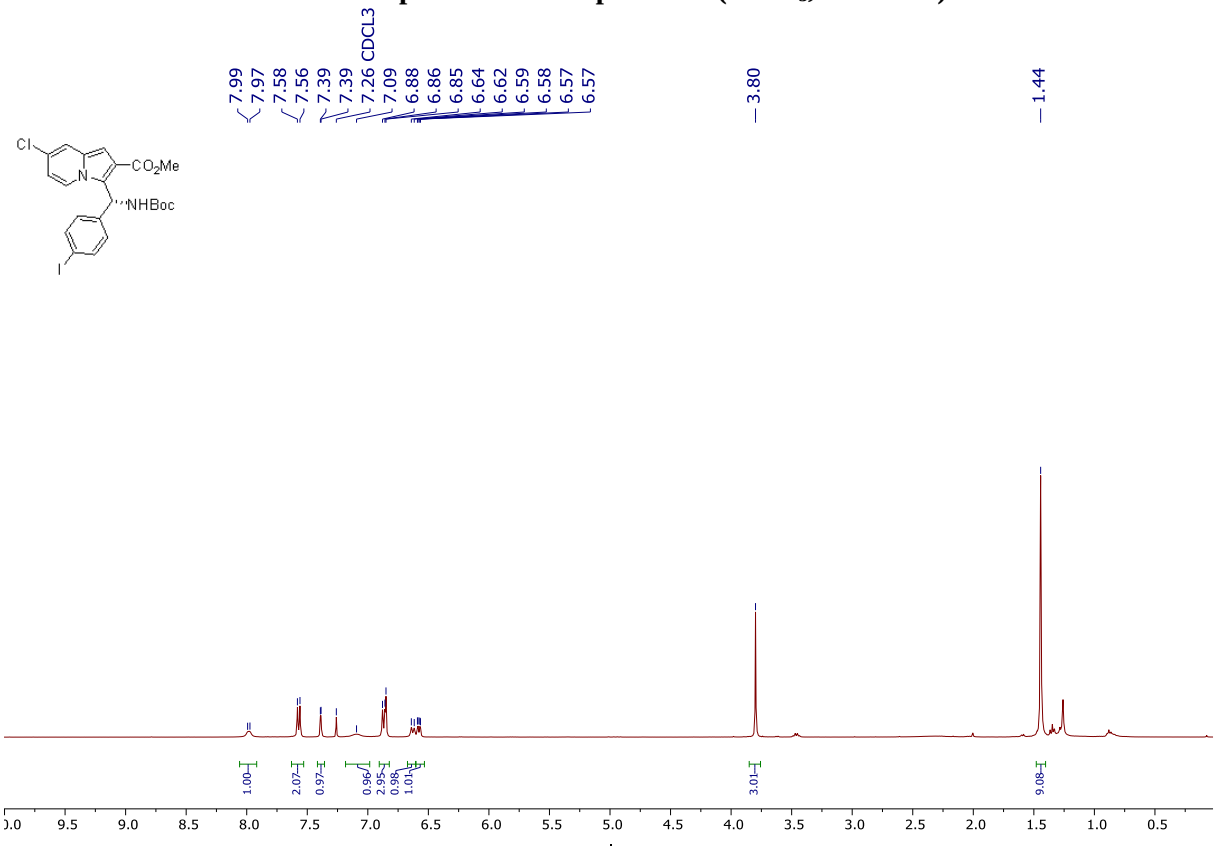
^{1}H NMR spectrum of compound 3r ($CDCl_3$, 600 MHz)



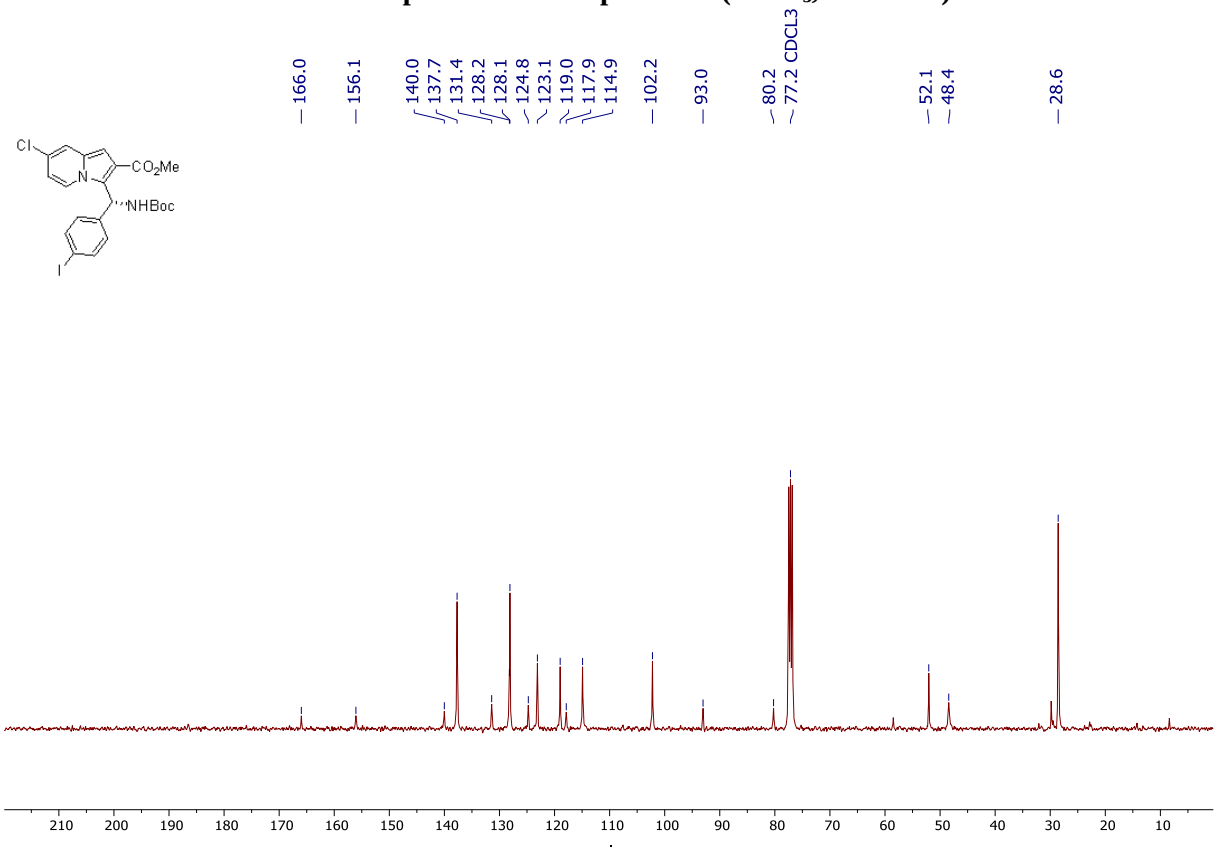
^{13}C NMR spectrum of compound 3r ($CDCl_3$, 151 MHz)



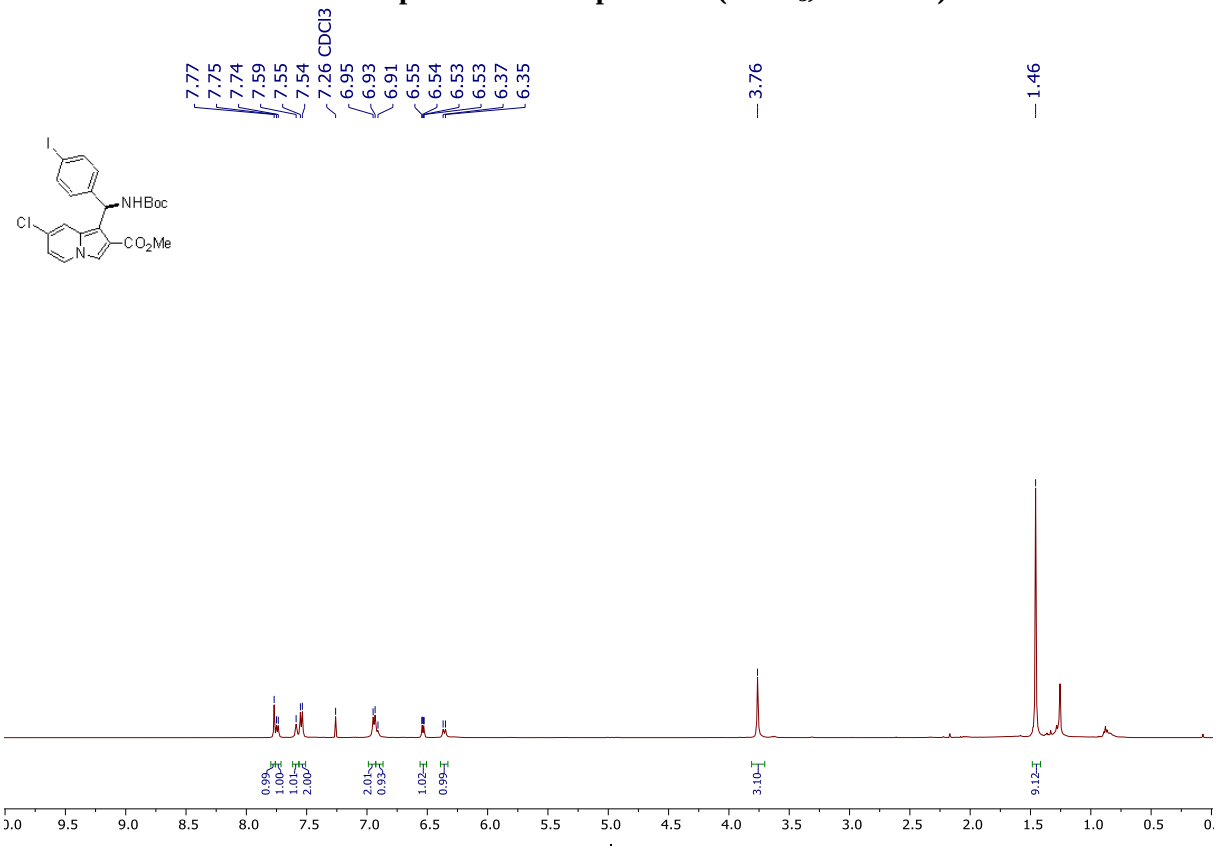
^{1}H NMR spectrum of compound 4s ($CDCl_3$, 400 MHz)



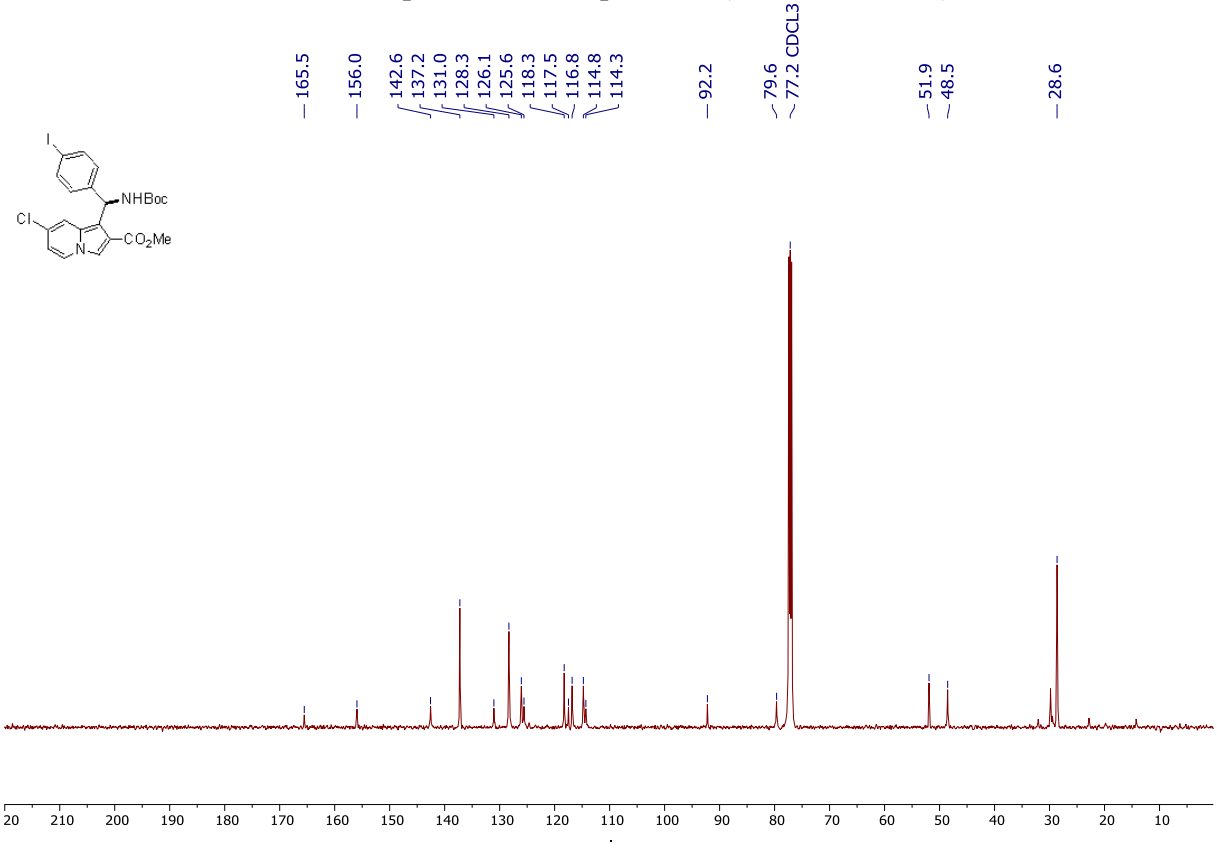
^{13}C NMR spectrum of compound 4s ($CDCl_3$, 101 MHz)



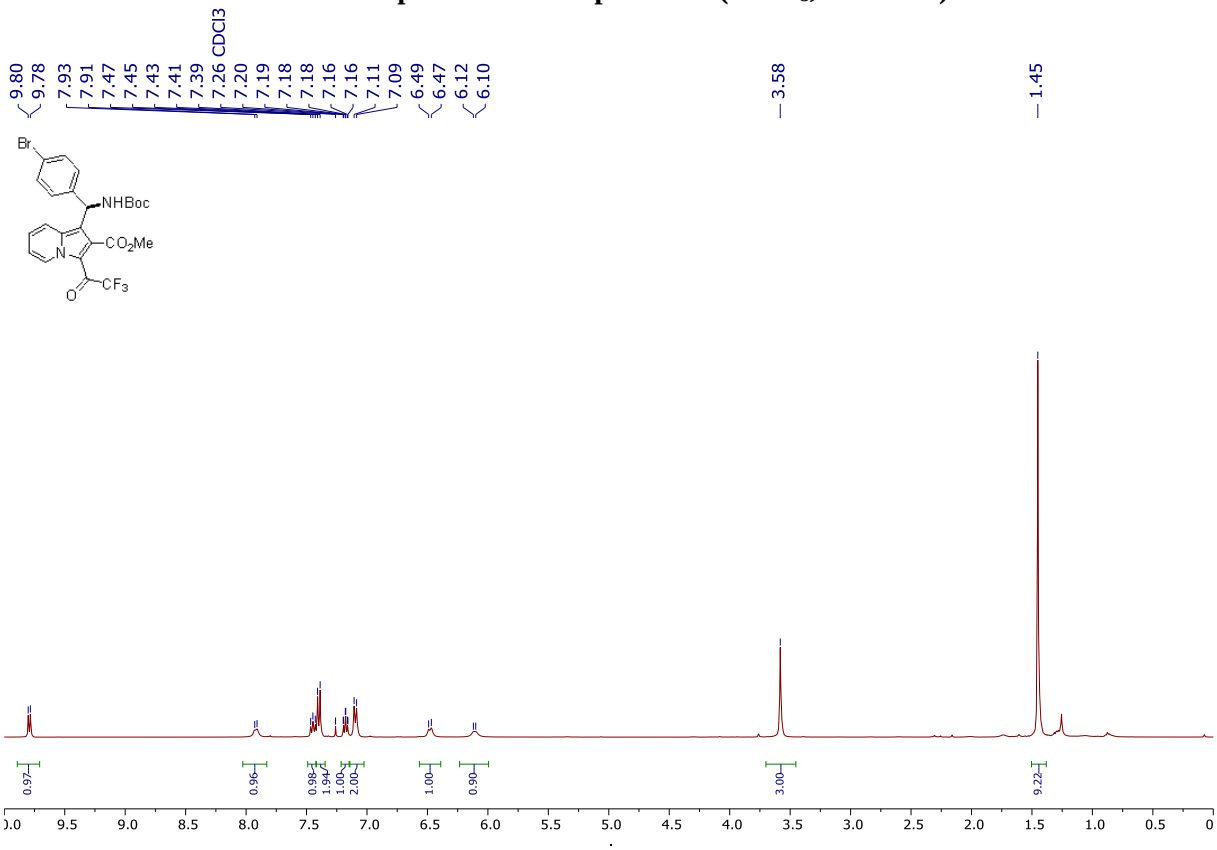
^{1}H NMR spectrum of compound 3s ($CDCl_3$, 500 MHz)



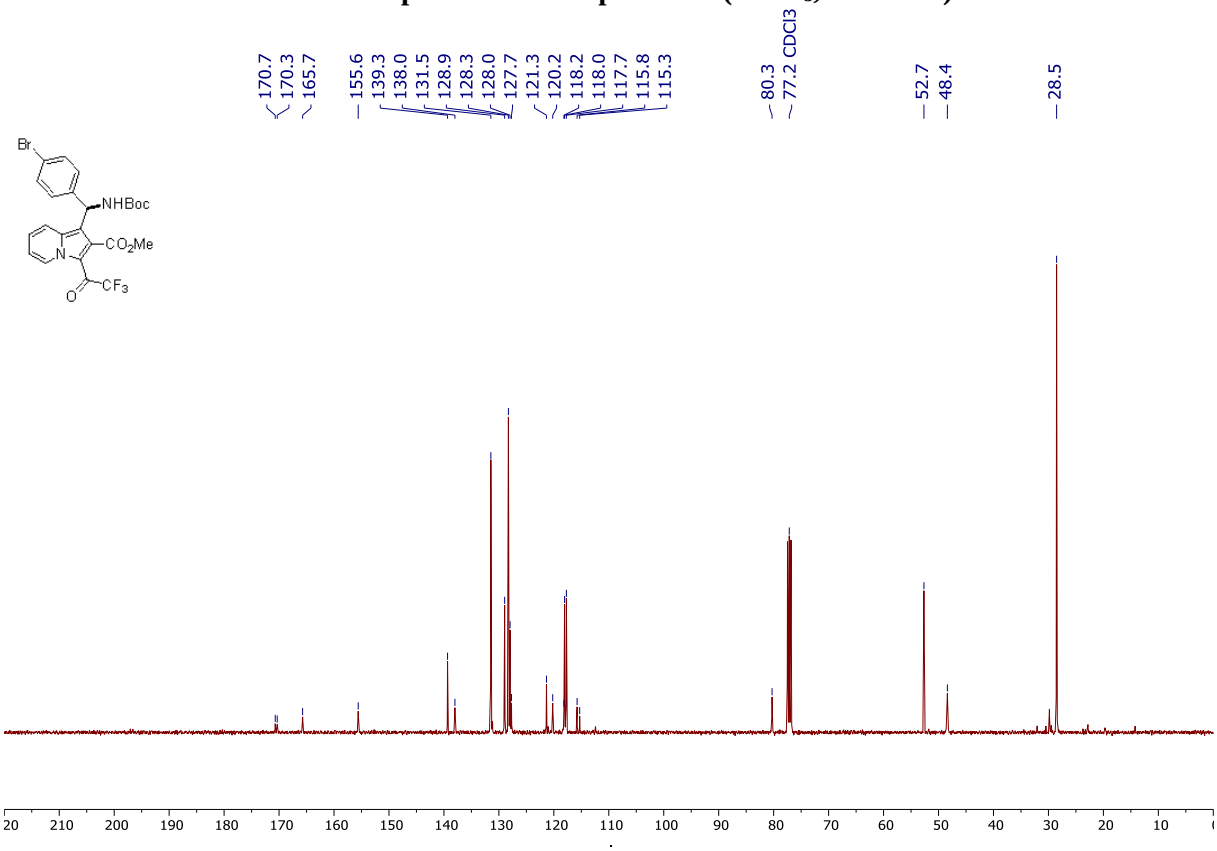
^{13}C NMR spectrum of compound 3s ($CDCl_3$, 126 MHz)



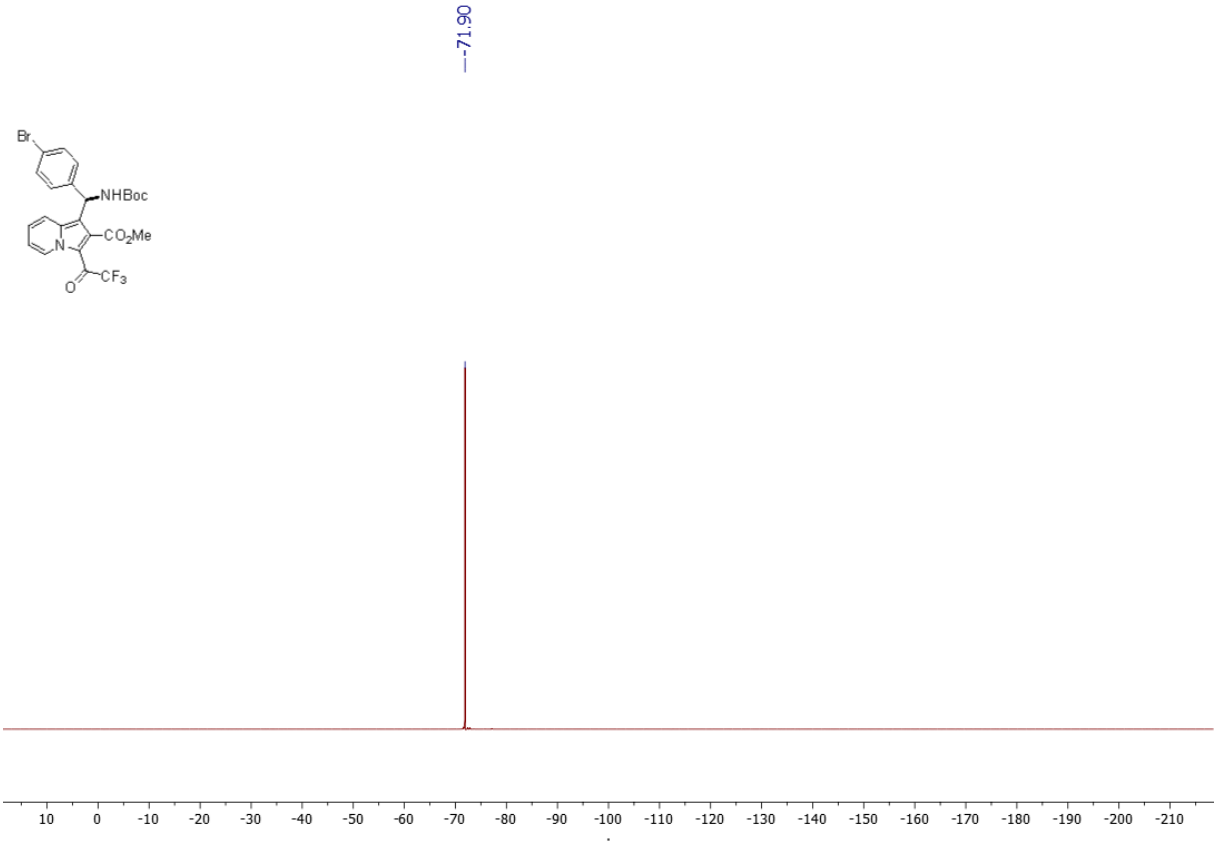
^{1}H NMR spectrum of compound 10 ($CDCl_3$, 500 MHz)



^{13}C NMR spectrum of compound 10 ($CDCl_3$, 101 MHz)

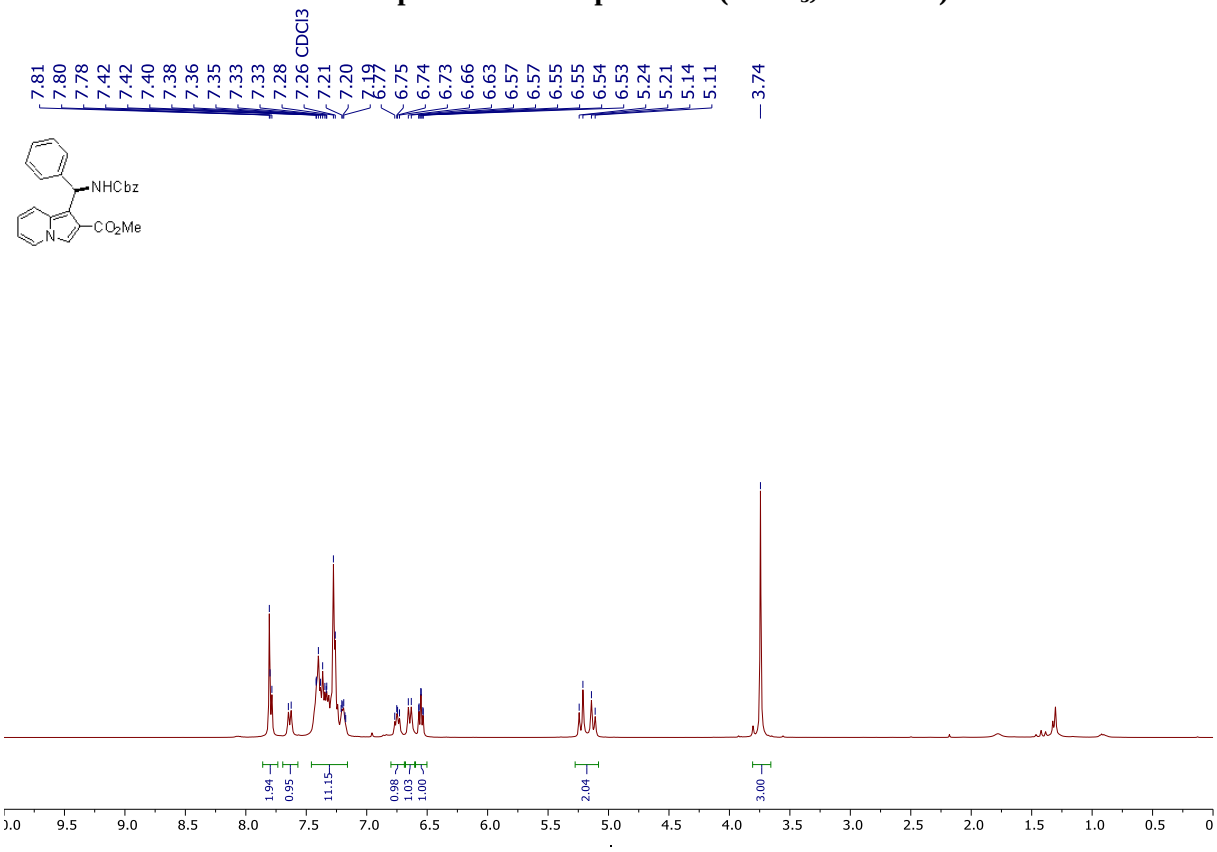


^{19}F NMR spectrum of compound 10 ($CDCl_3$, 376 MHz)

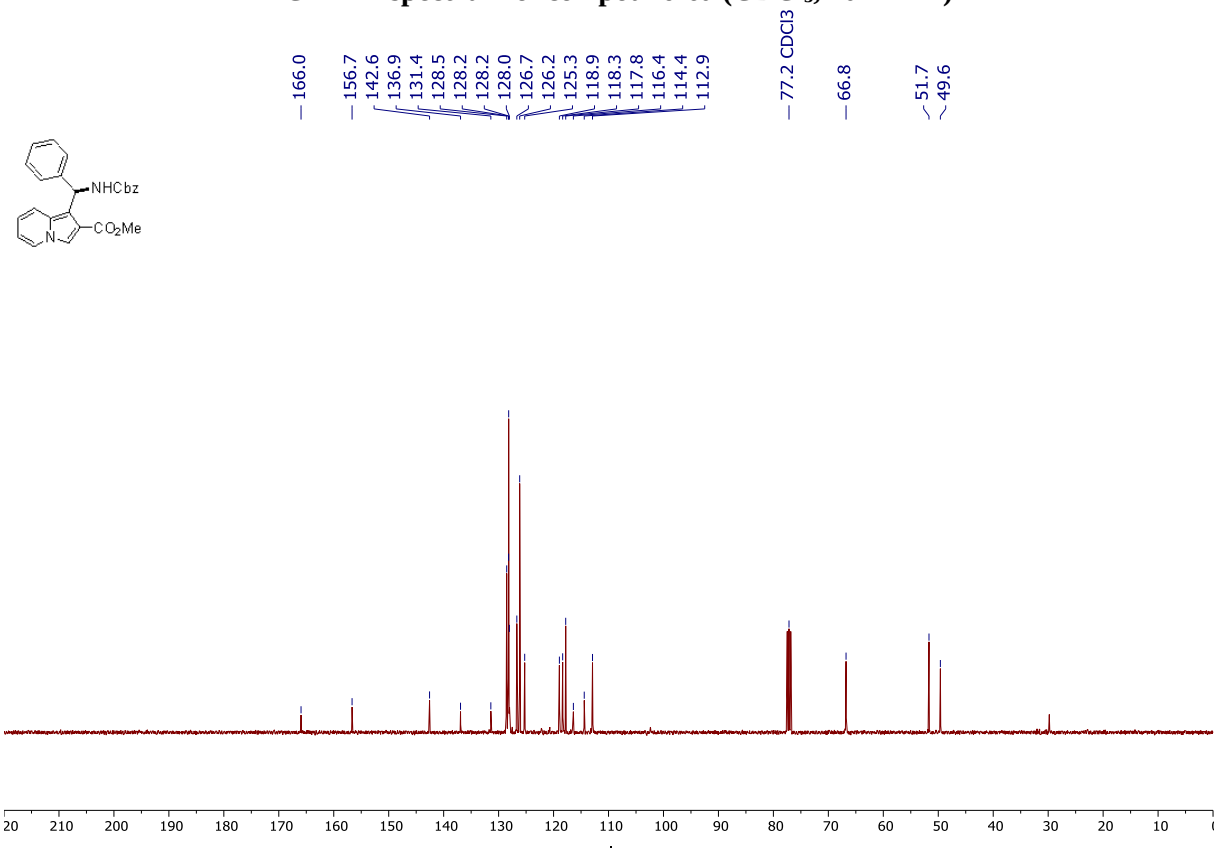


6.2. Products with Cbz-protecting group 6a-m, 7a-m, 8 and 9

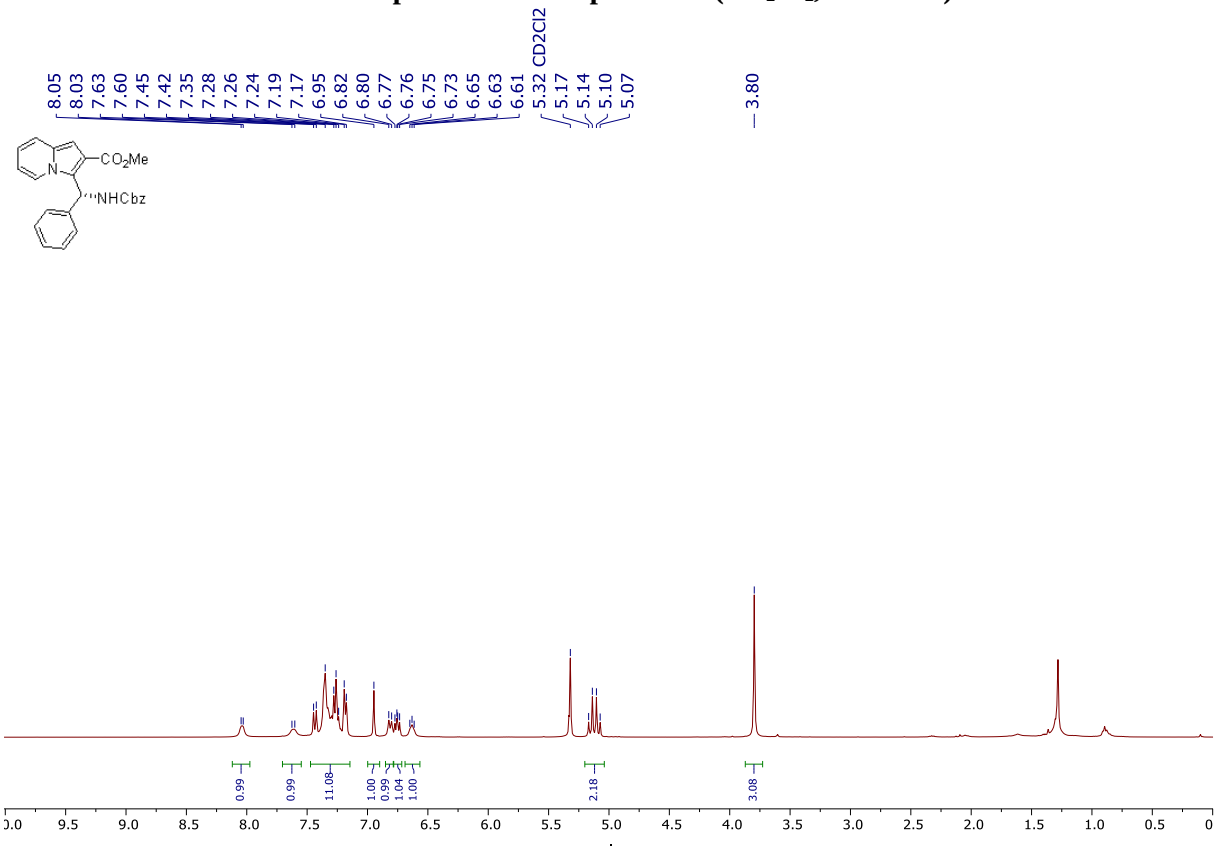
^{1}H NMR spectrum of compound 6a ($CDCl_3$, 400 MHz)



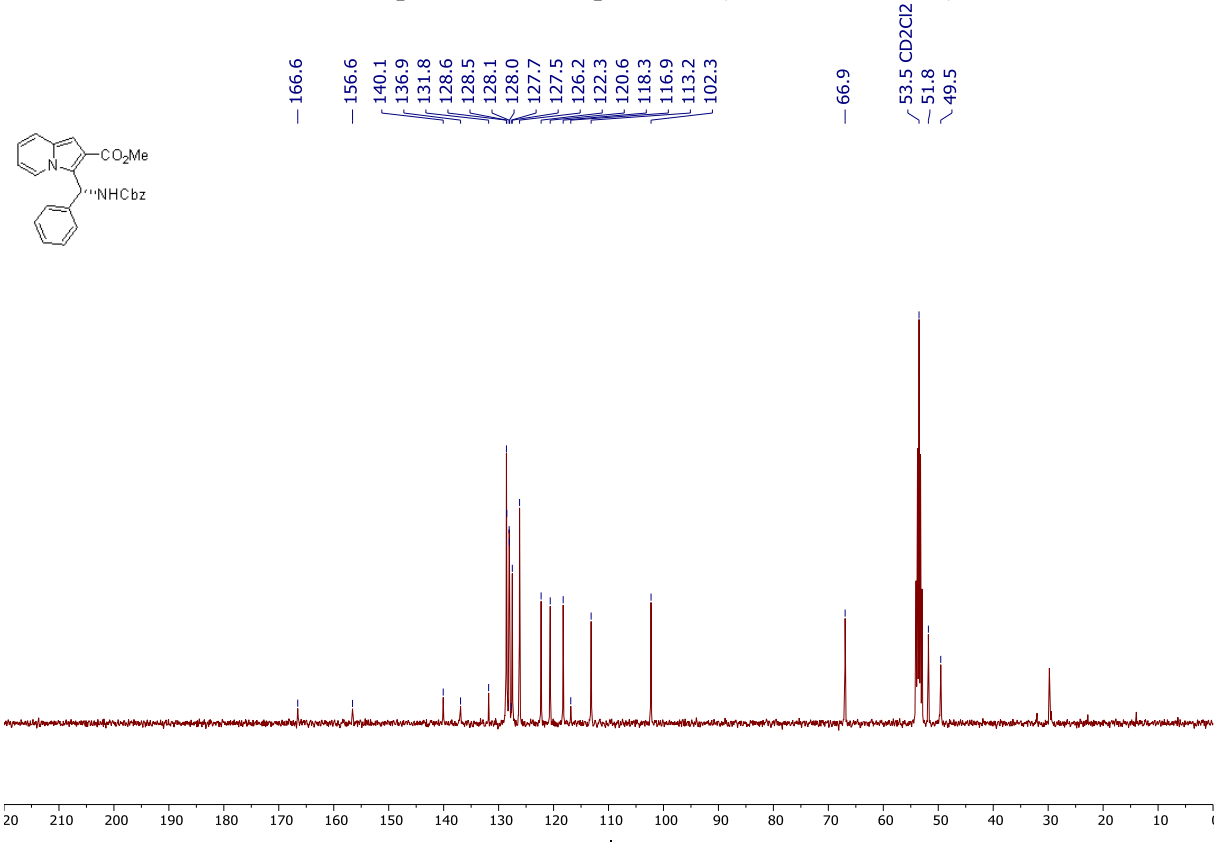
^{13}C NMR spectrum of compound 6a ($CDCl_3$, 101 MHz)



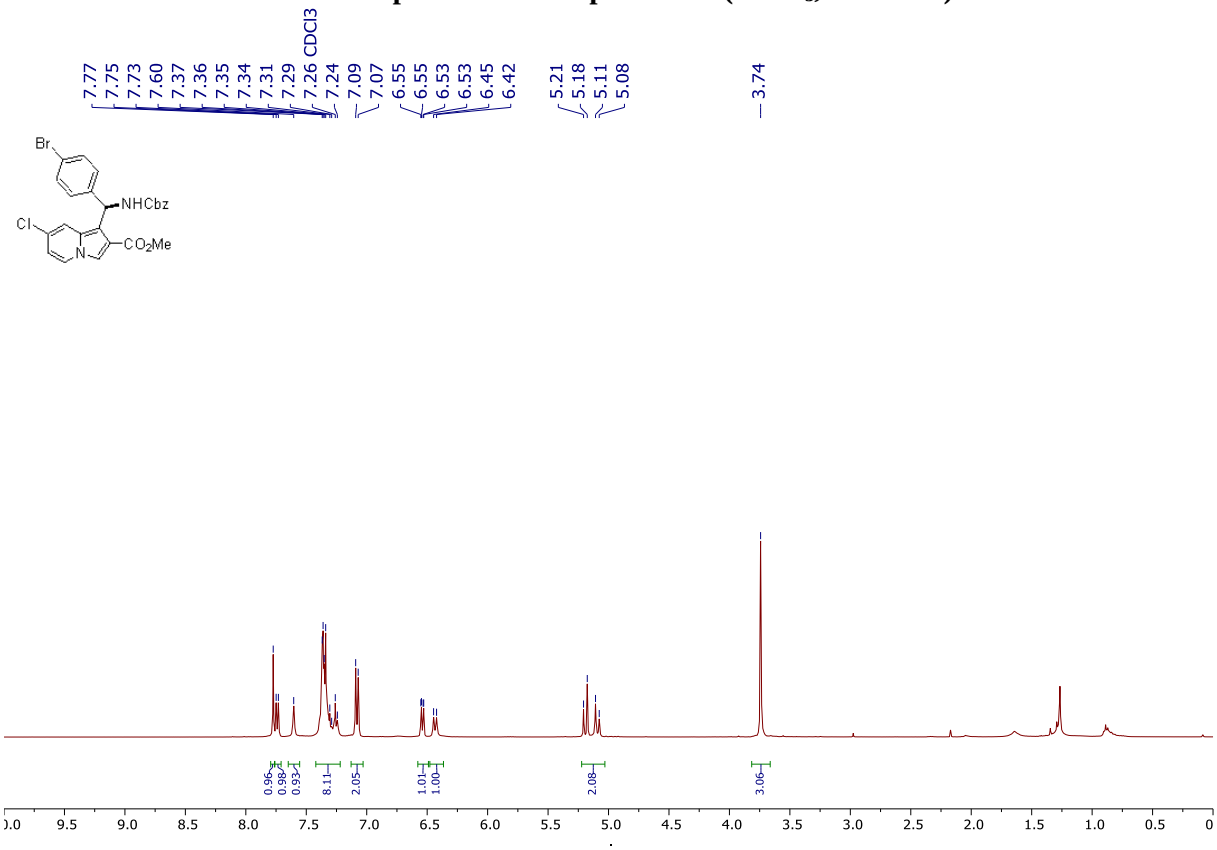
^{1}H NMR spectrum of compound 7a (CD_2Cl_2, 400 MHz)



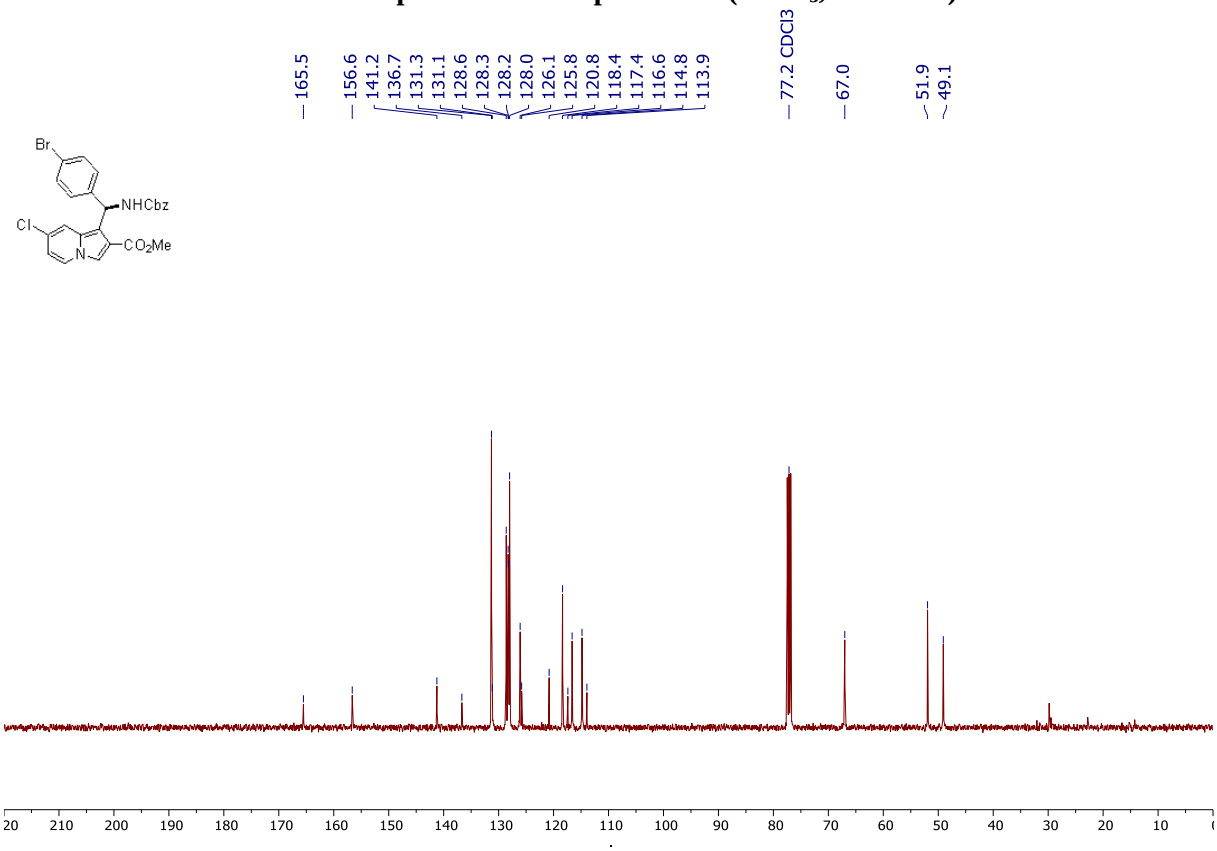
^{13}C NMR spectrum of compound 7a (CD_2Cl_2, 101 MHz)



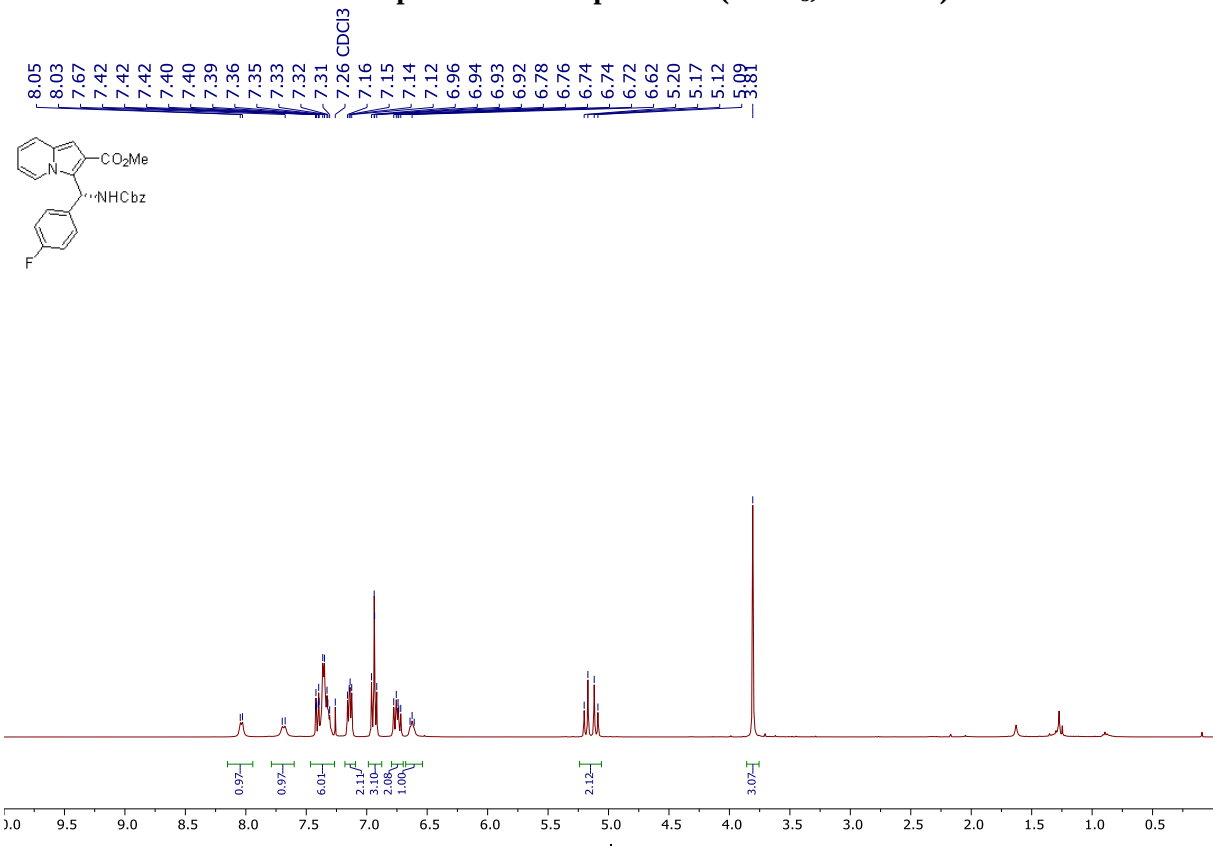
^{1}H NMR spectrum of compound 6m ($CDCl_3$, 400 MHz)



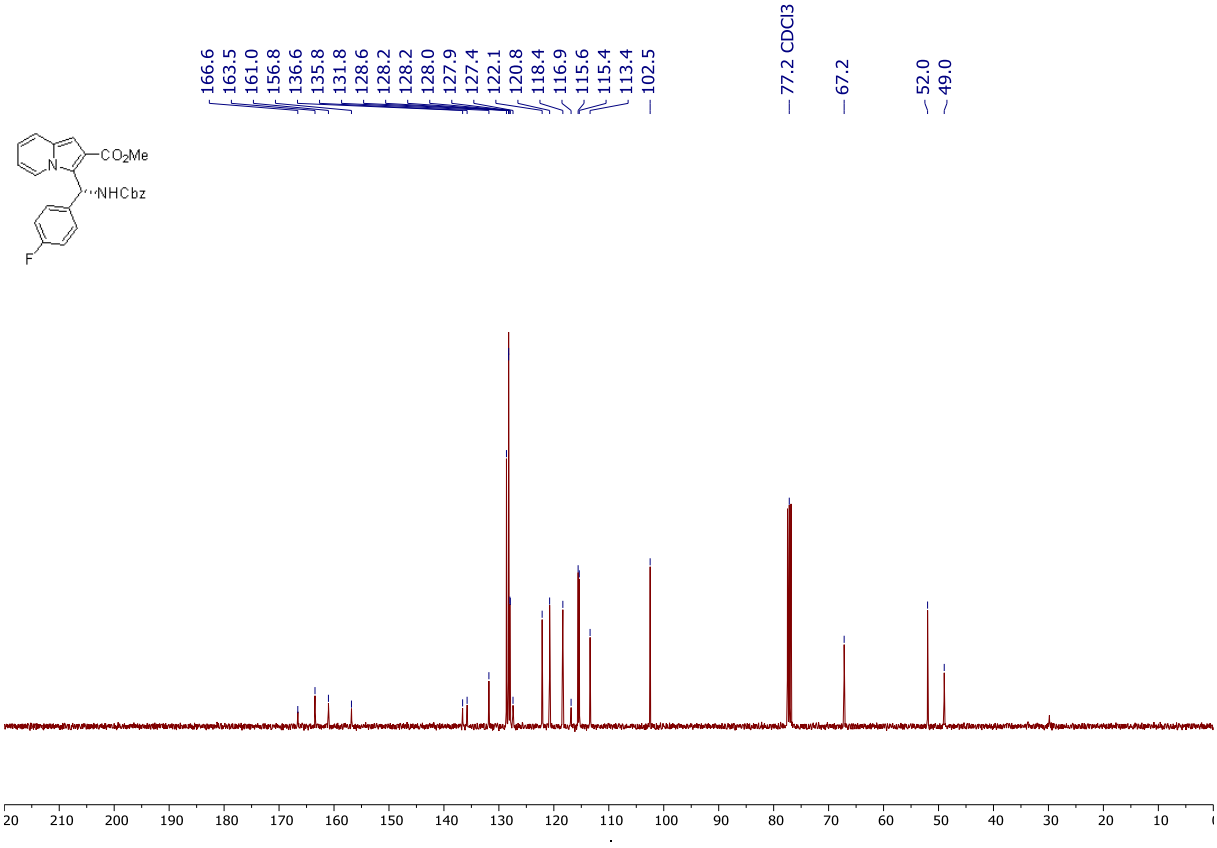
^{13}C NMR spectrum of compound 6m ($CDCl_3$, 101 MHz)



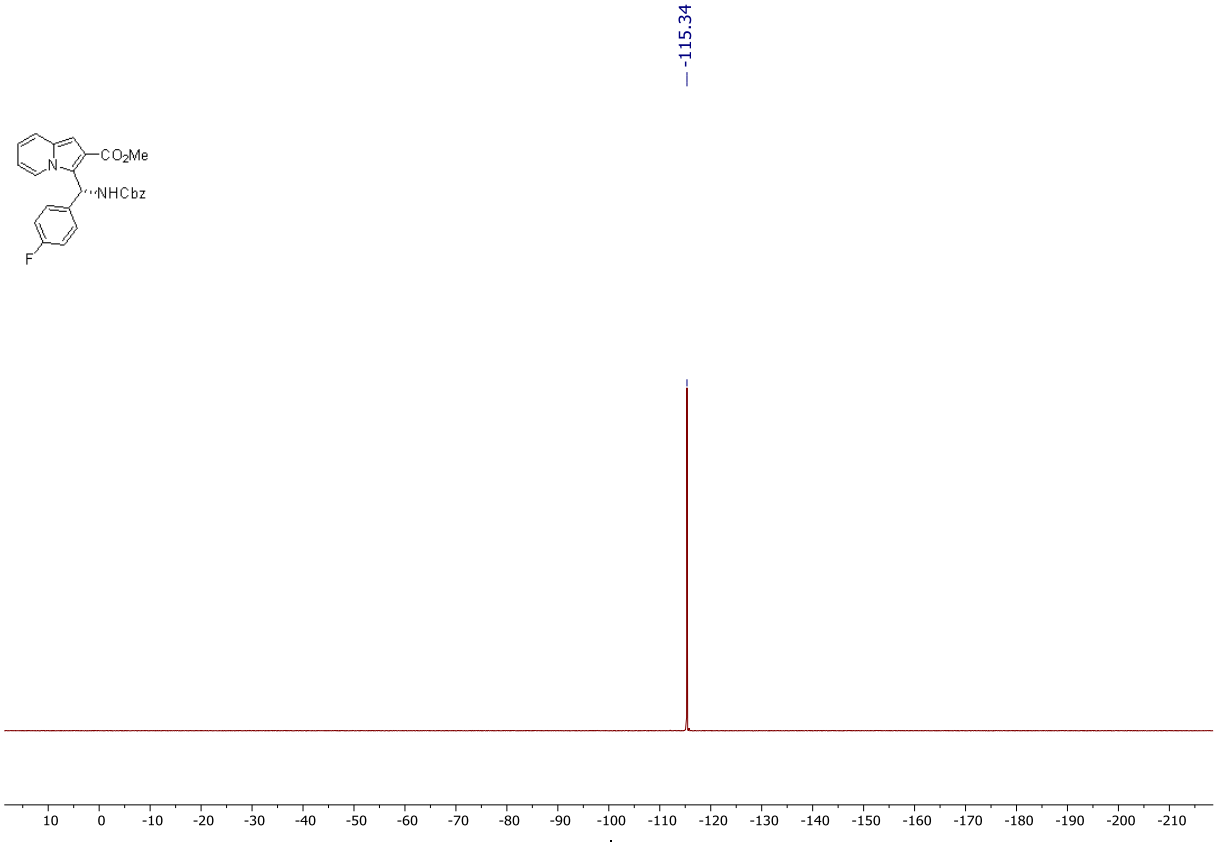
^{1}H NMR spectrum of compound 7b ($CDCl_3$, 400 MHz)



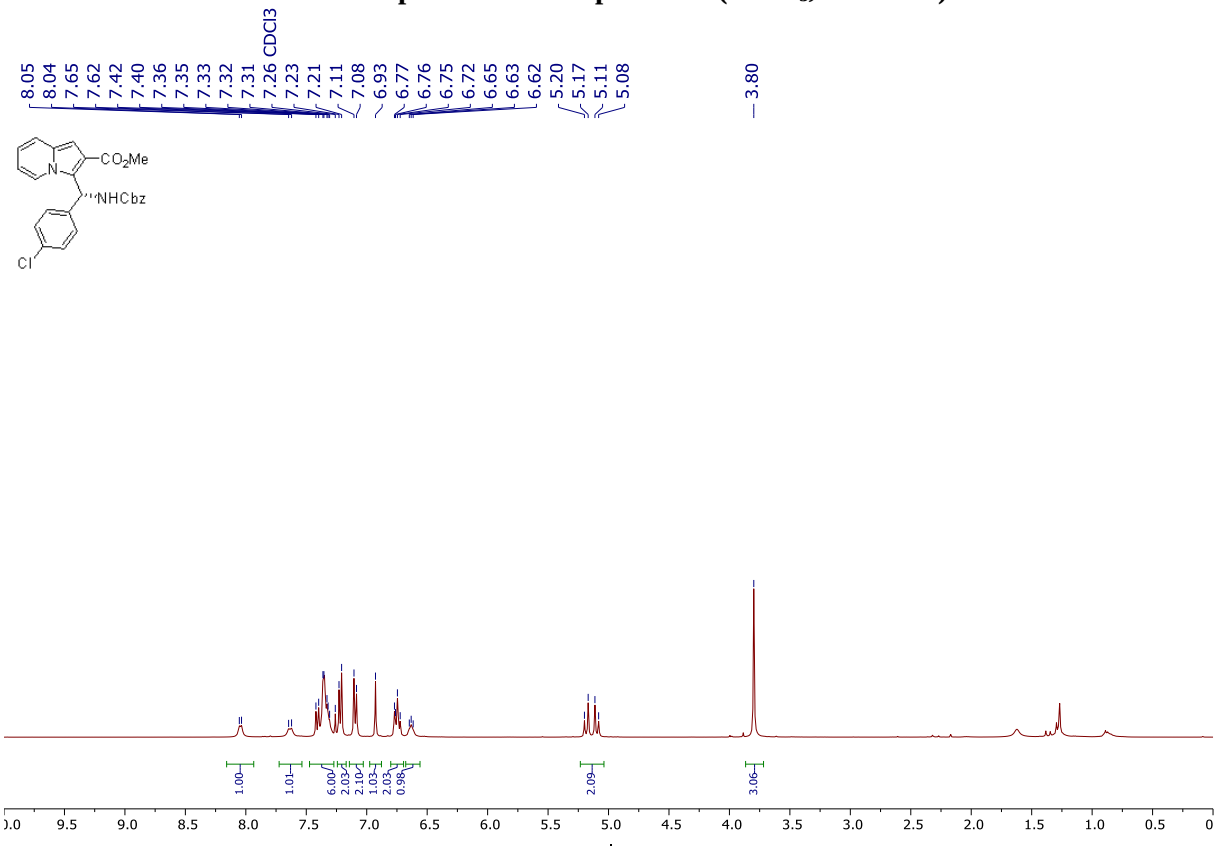
^{13}C NMR spectrum of compound 7b ($CDCl_3$, 101 MHz)



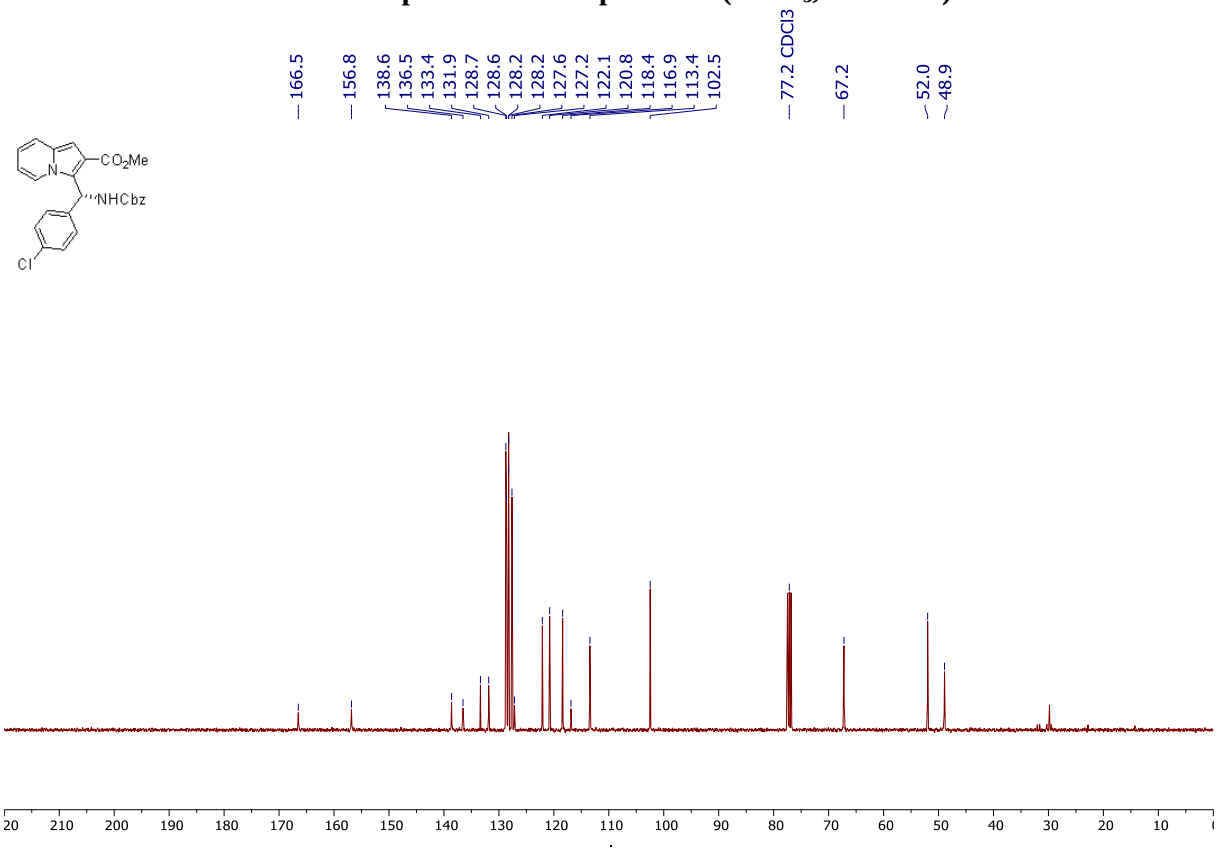
^{19}F NMR spectrum of compound 7b ($CDCl_3$, 376 MHz)



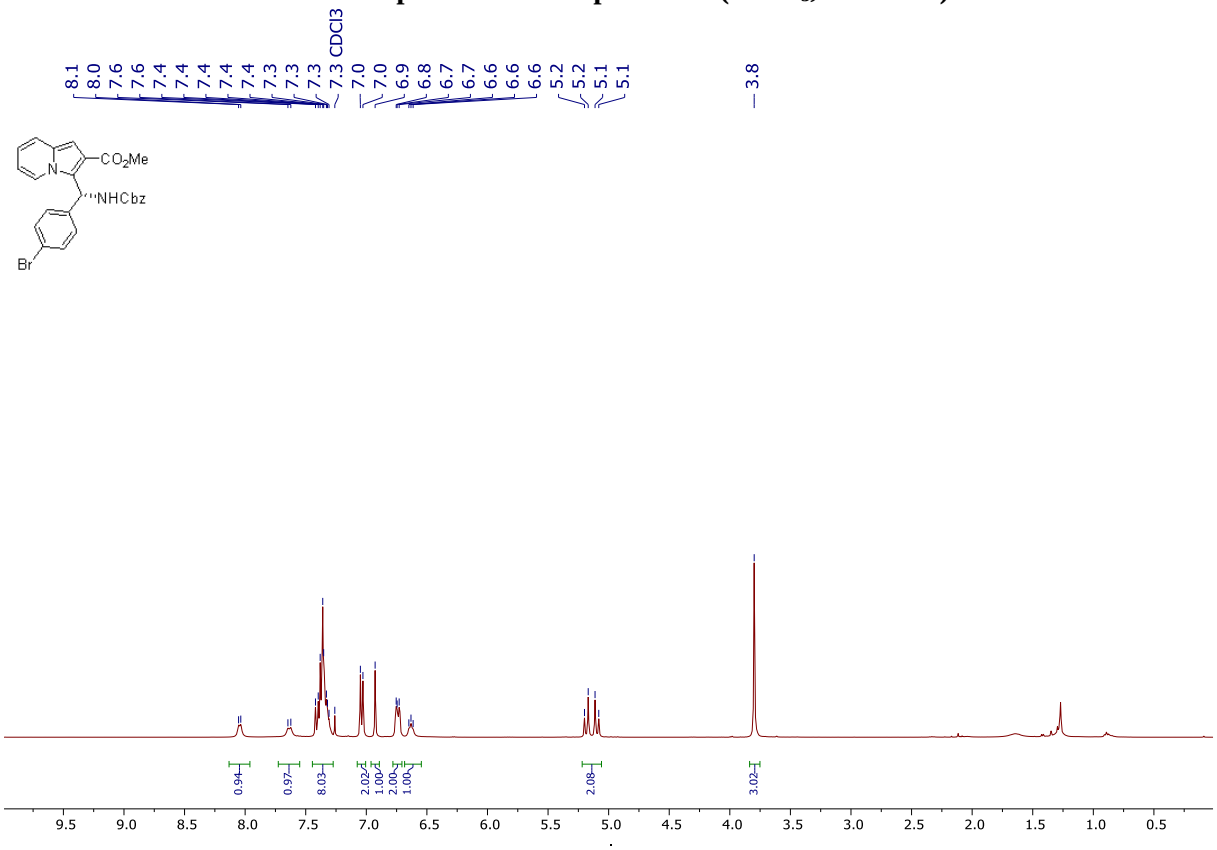
^{1}H NMR spectrum of compound 7c ($CDCl_3$, 400 MHz)



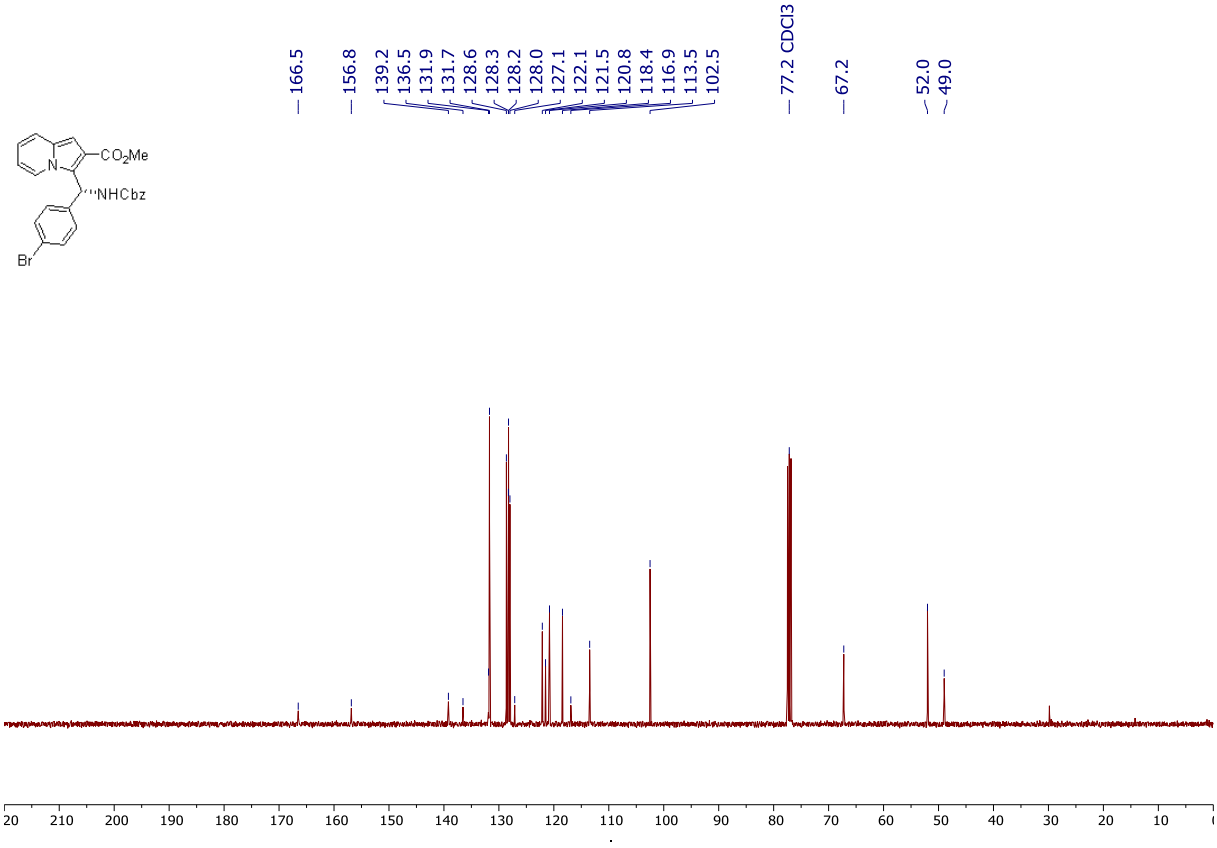
^{13}C NMR spectrum of compound 7c ($CDCl_3$, 101 MHz)



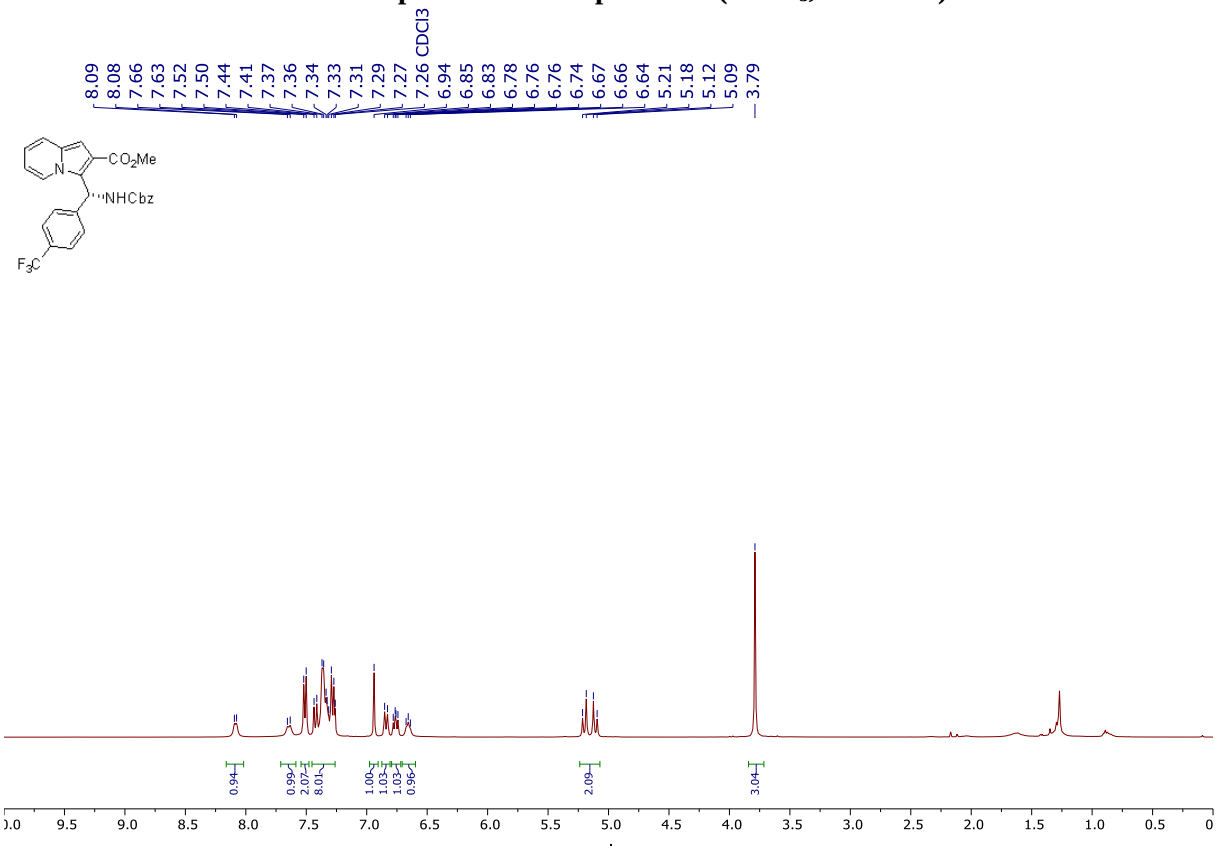
^{1}H NMR spectrum of compound 7d ($CDCl_3$, 400 MHz)



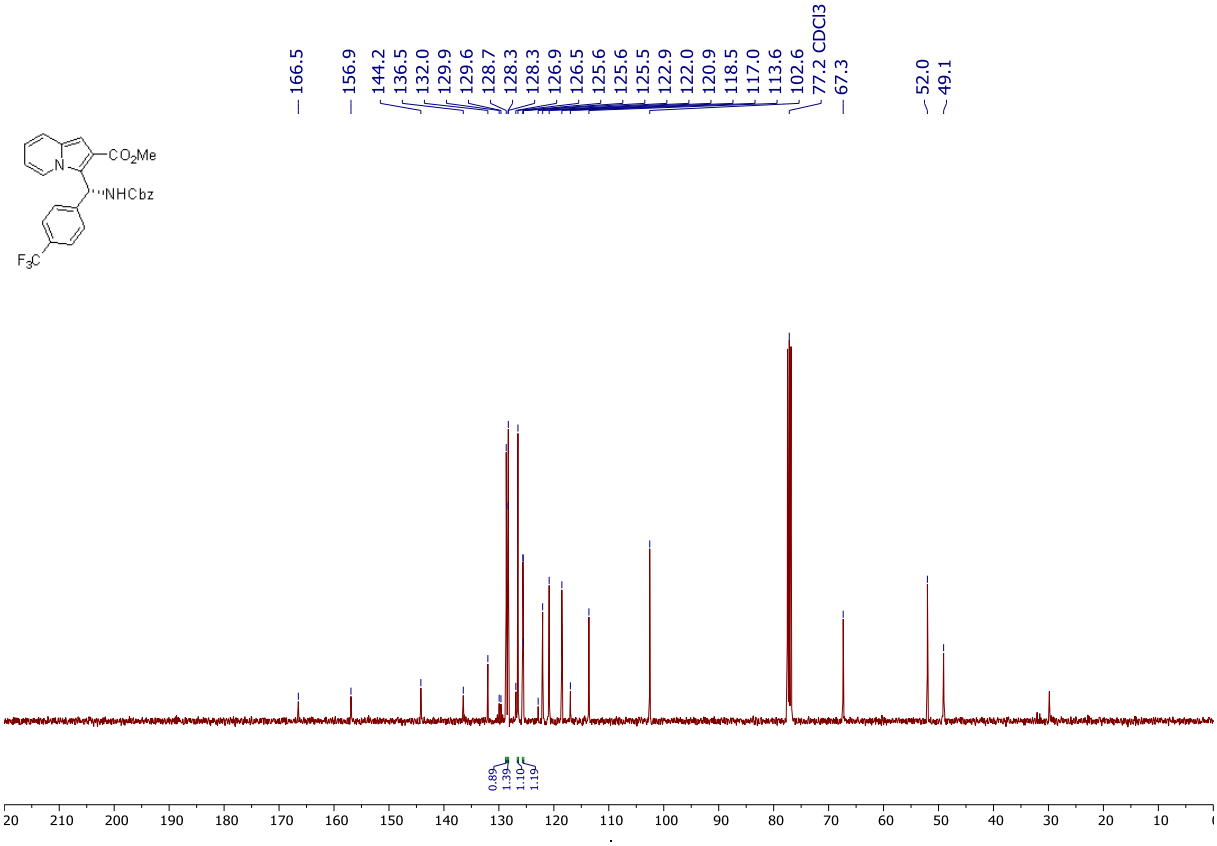
^{13}C NMR spectrum of compound 7d ($CDCl_3$, 101 MHz)



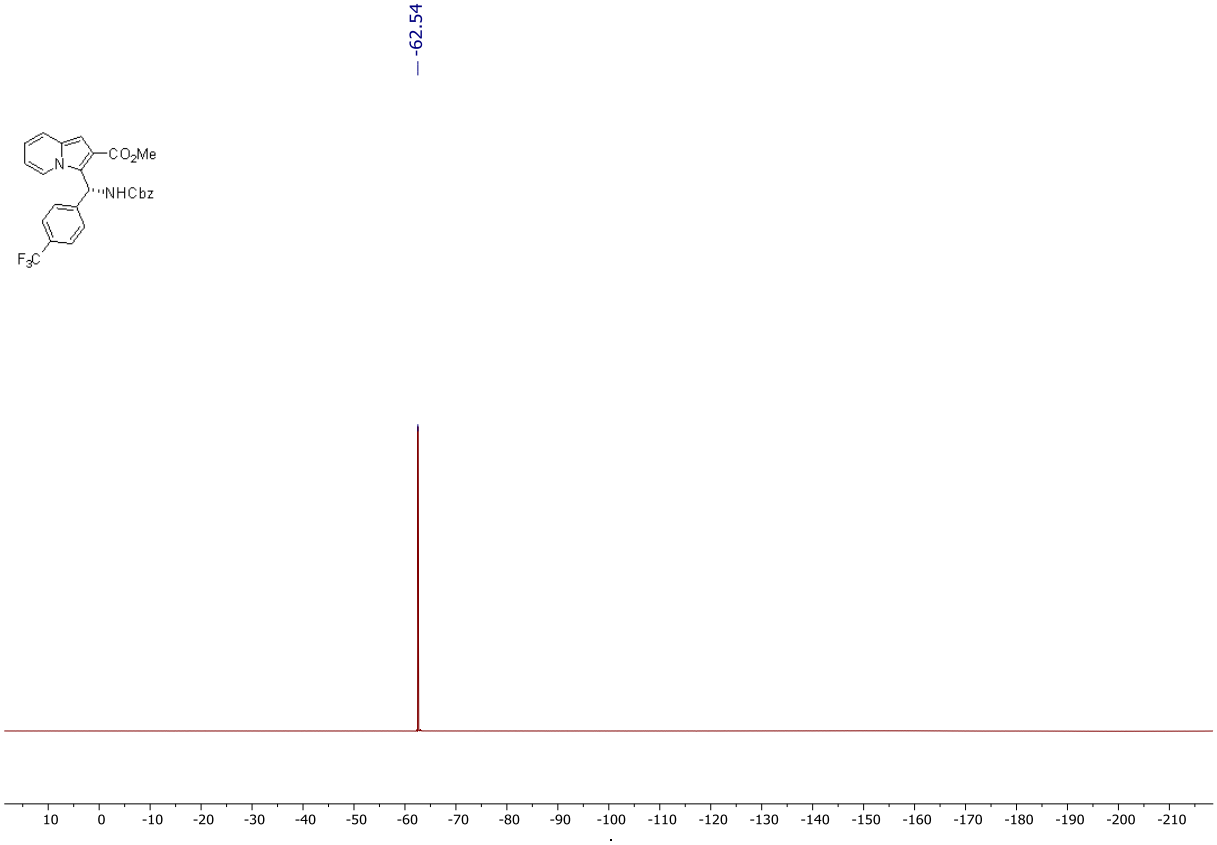
^{1}H NMR spectrum of compound 7e ($CDCl_3$, 400 MHz)



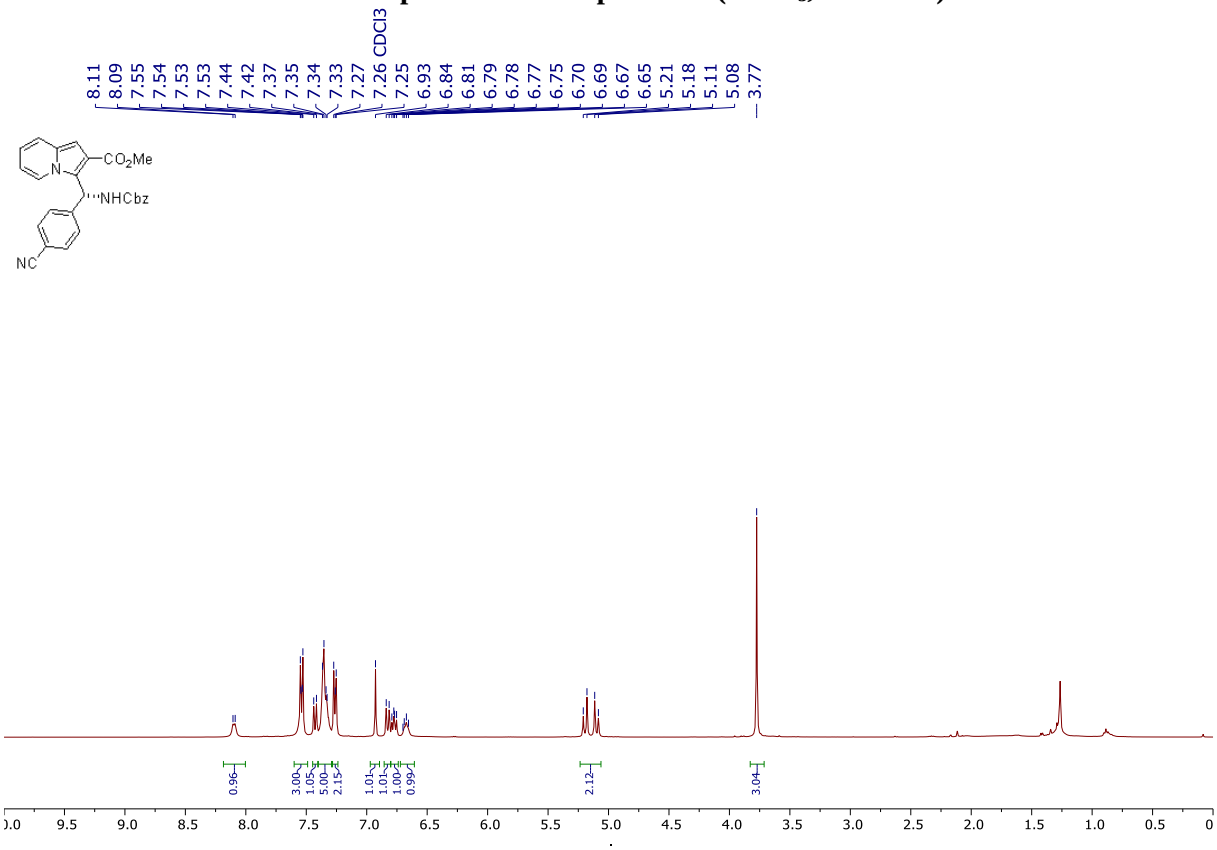
^{13}C NMR spectrum of compound 7e ($CDCl_3$, 101 MHz)



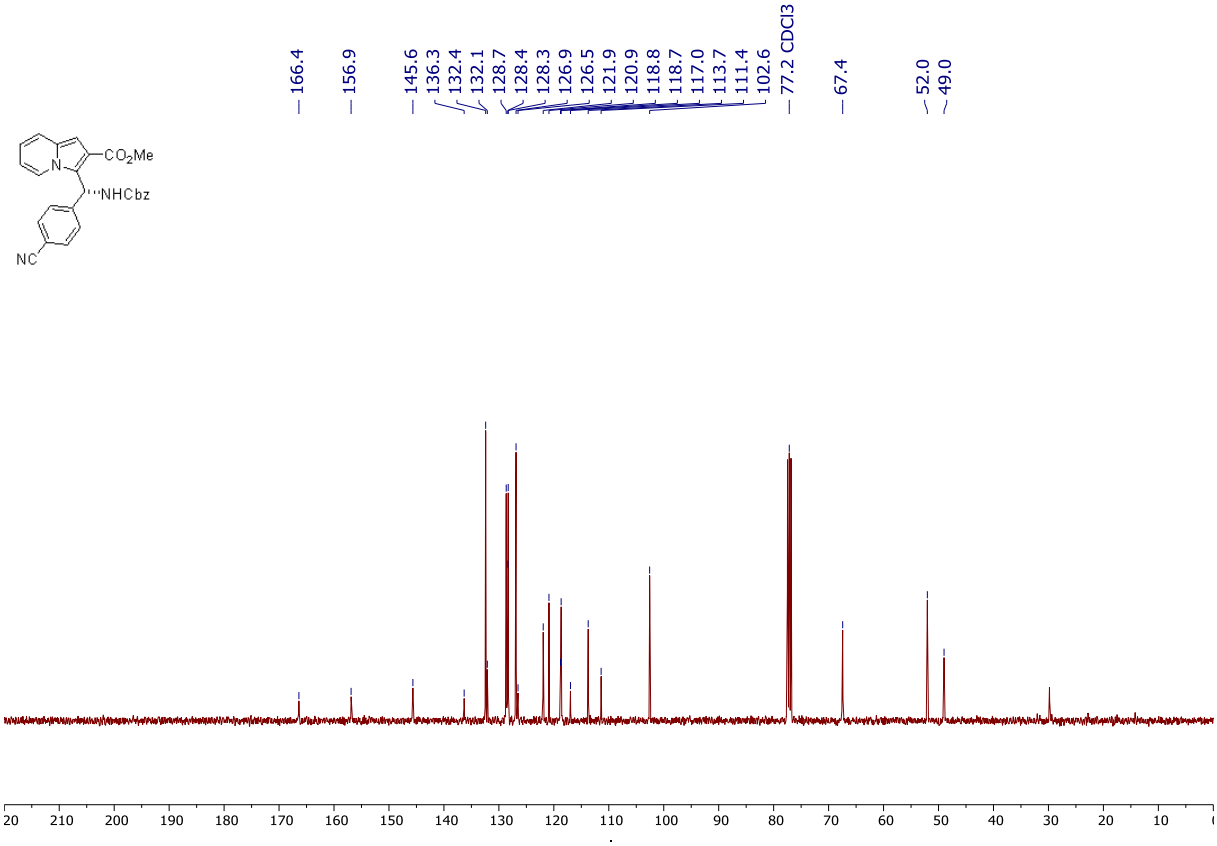
^{19}F NMR spectrum of compound 7e ($CDCl_3$, 376 MHz)



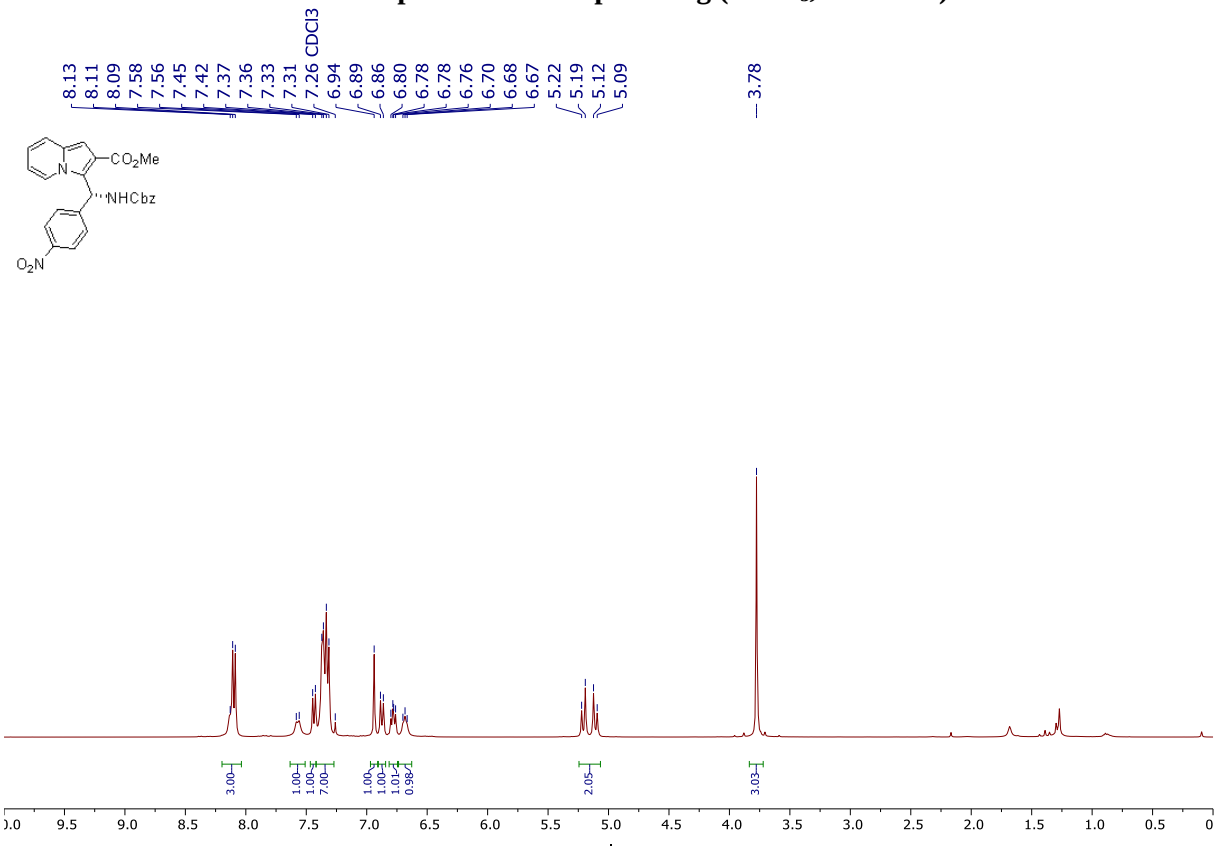
^{1}H NMR spectrum of compound 7f ($CDCl_3$, 400 MHz)



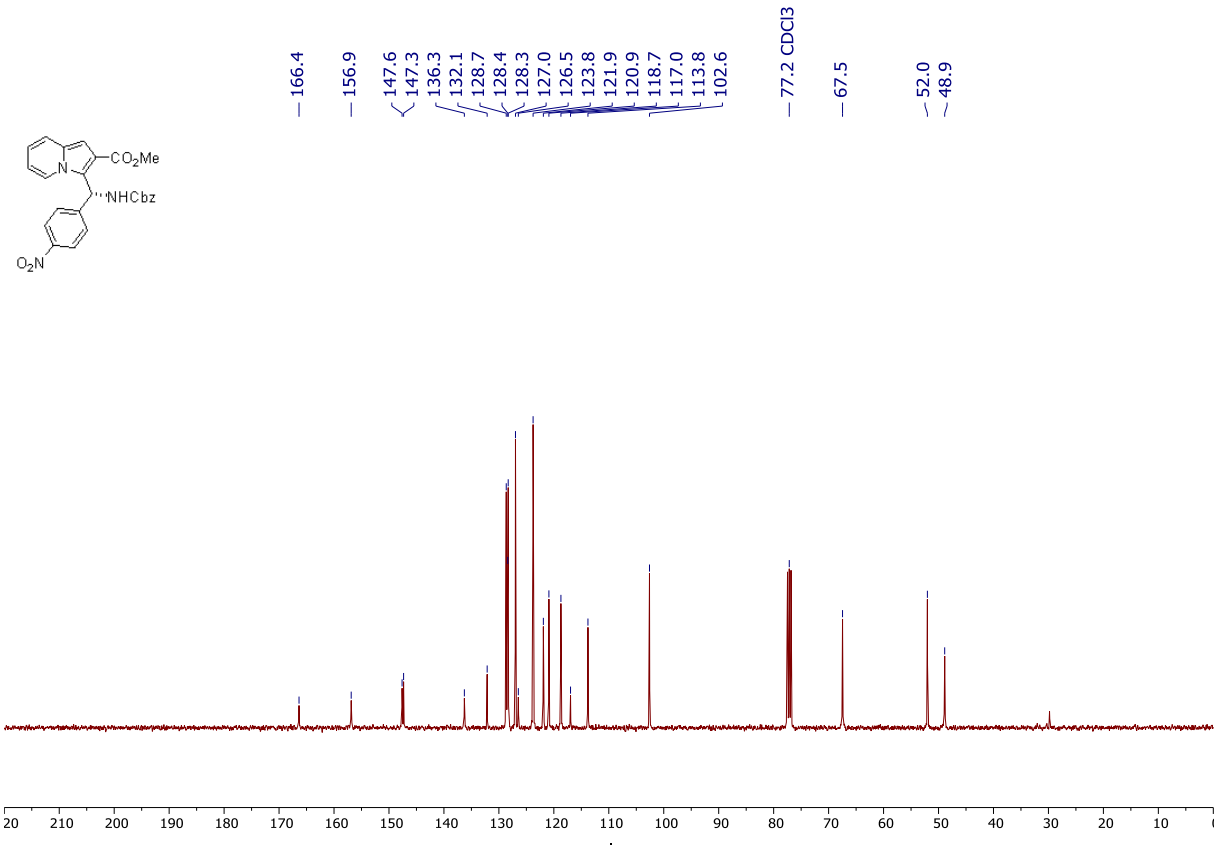
^{13}C NMR spectrum of compound 7f ($CDCl_3$, 101 MHz)



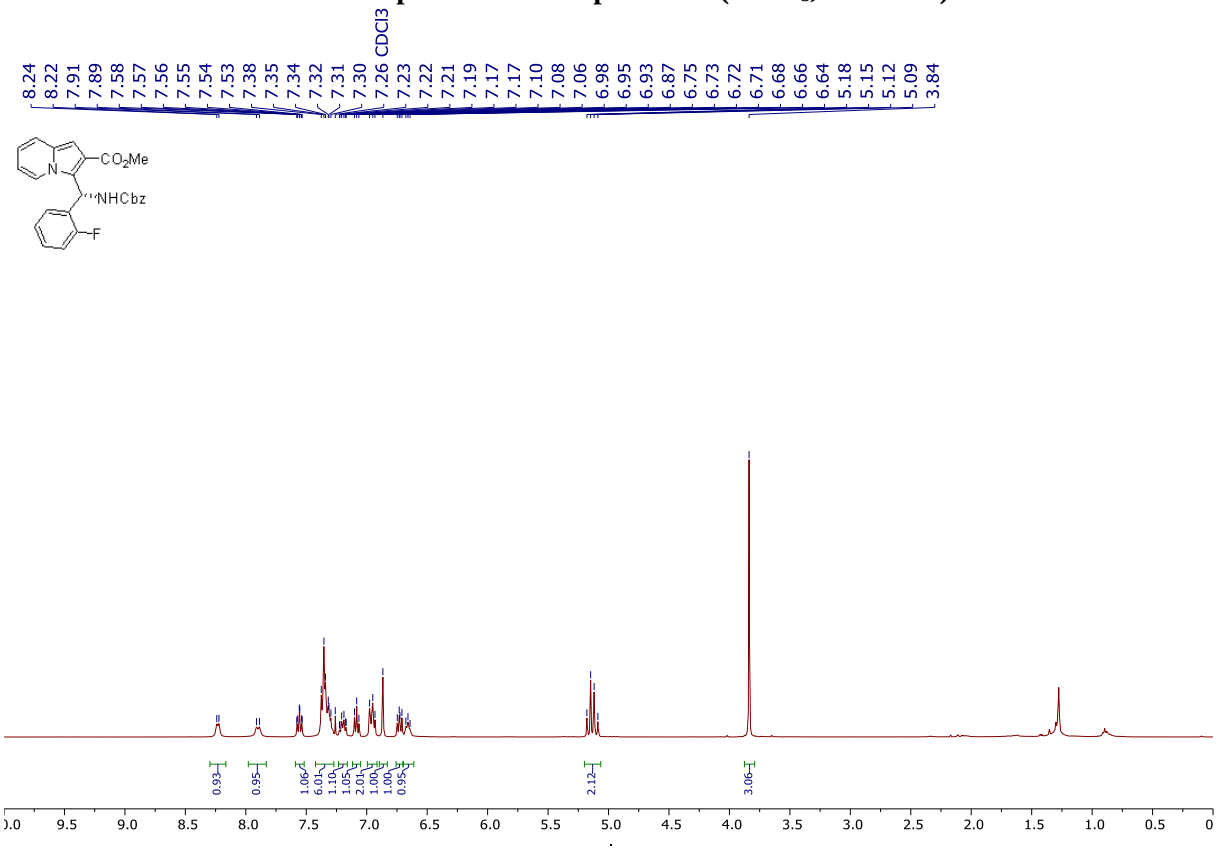
^{1}H NMR spectrum of compound 7g ($CDCl_3$, 400 MHz)



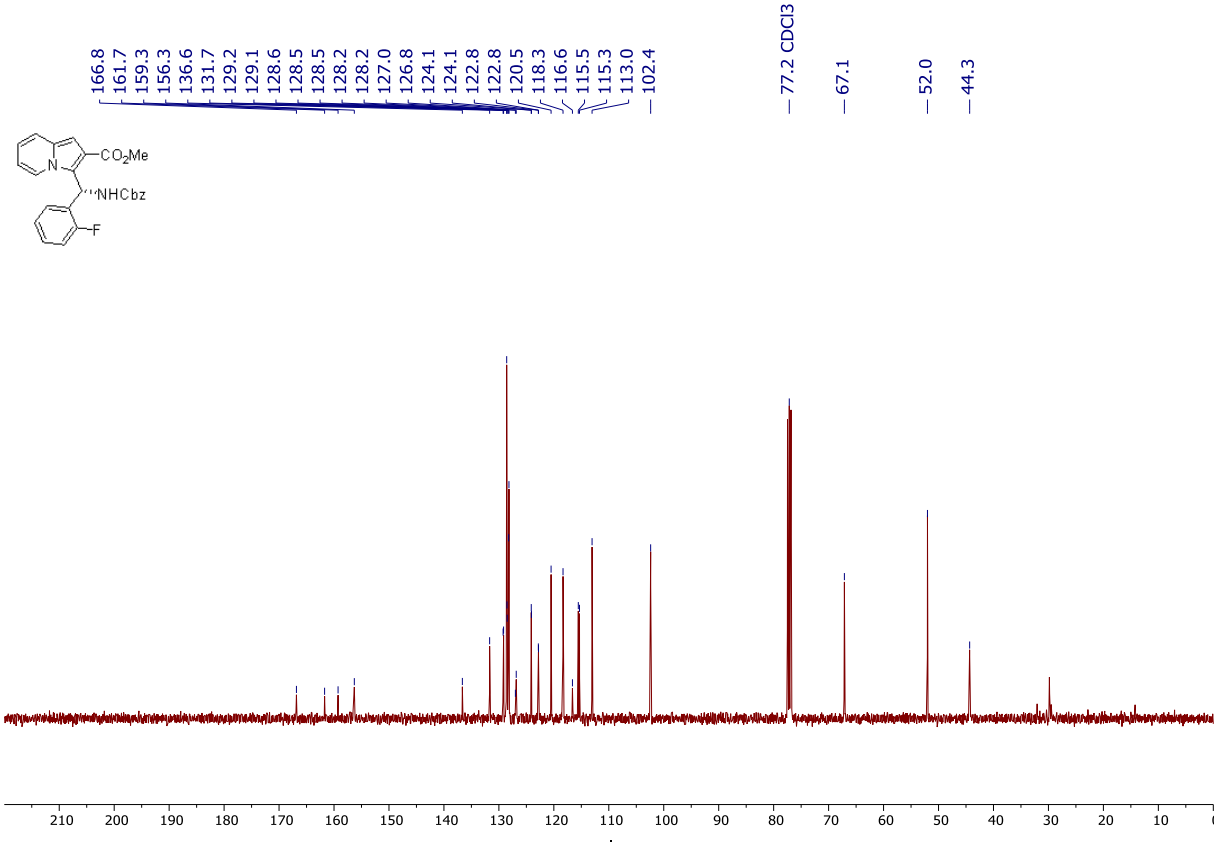
^{13}C NMR spectrum of compound 7g ($CDCl_3$, 101 MHz)



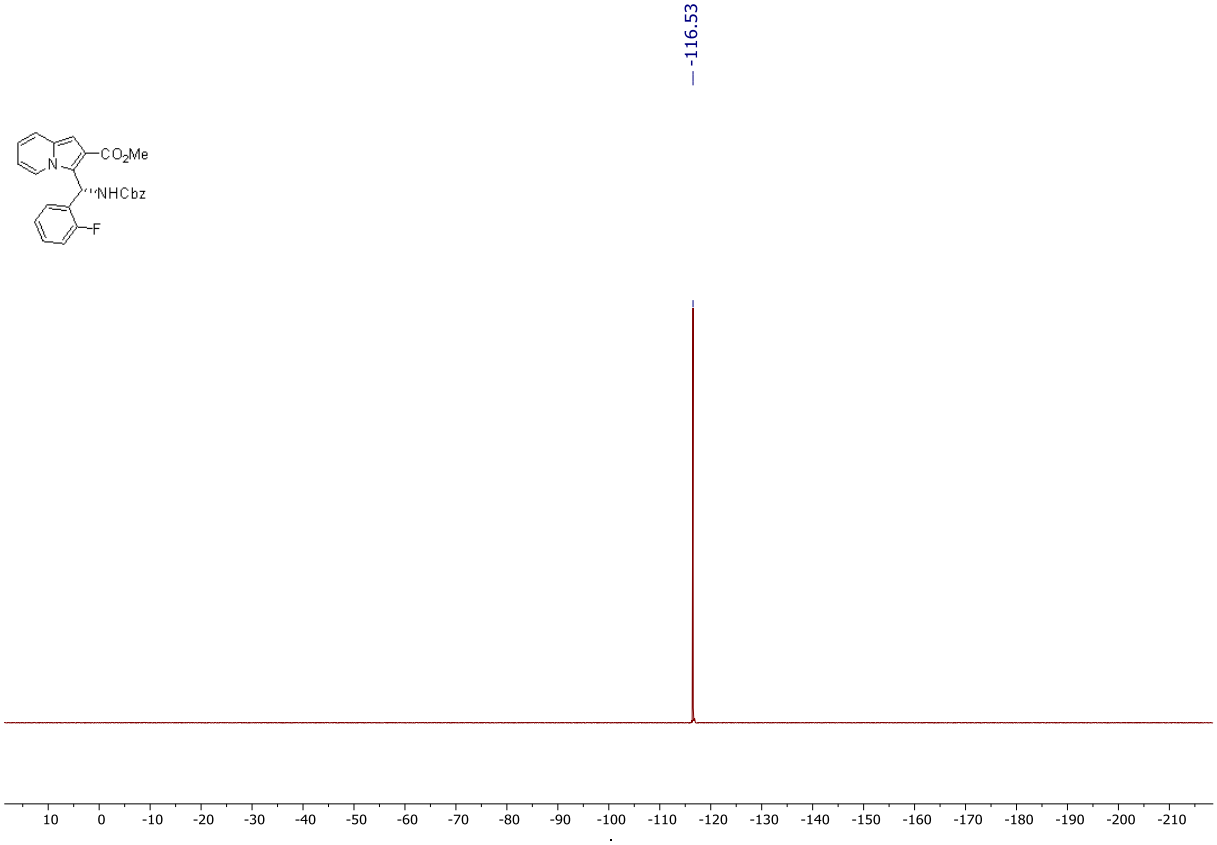
^{1}H NMR spectrum of compound 7h ($CDCl_3$, 400 MHz)



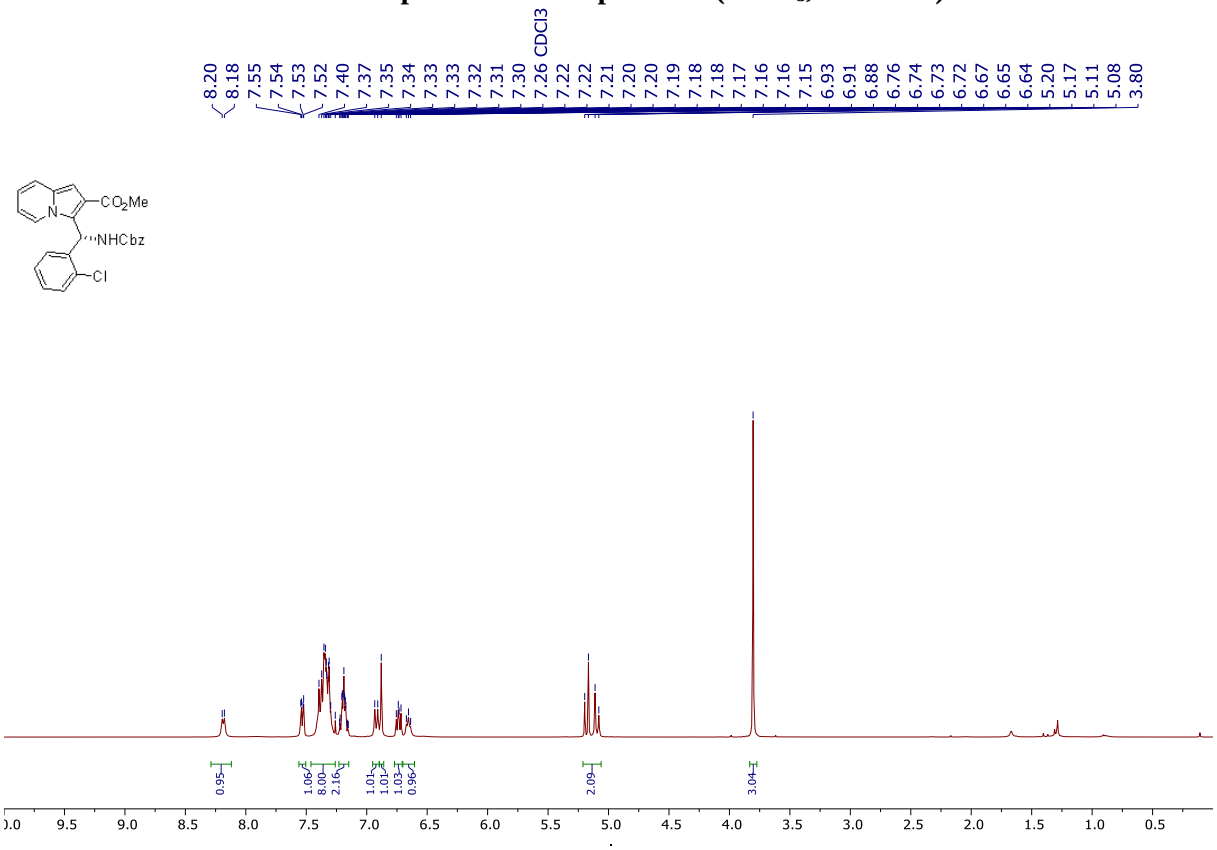
^{13}C NMR spectrum of compound 7h ($CDCl_3$, 101 MHz)



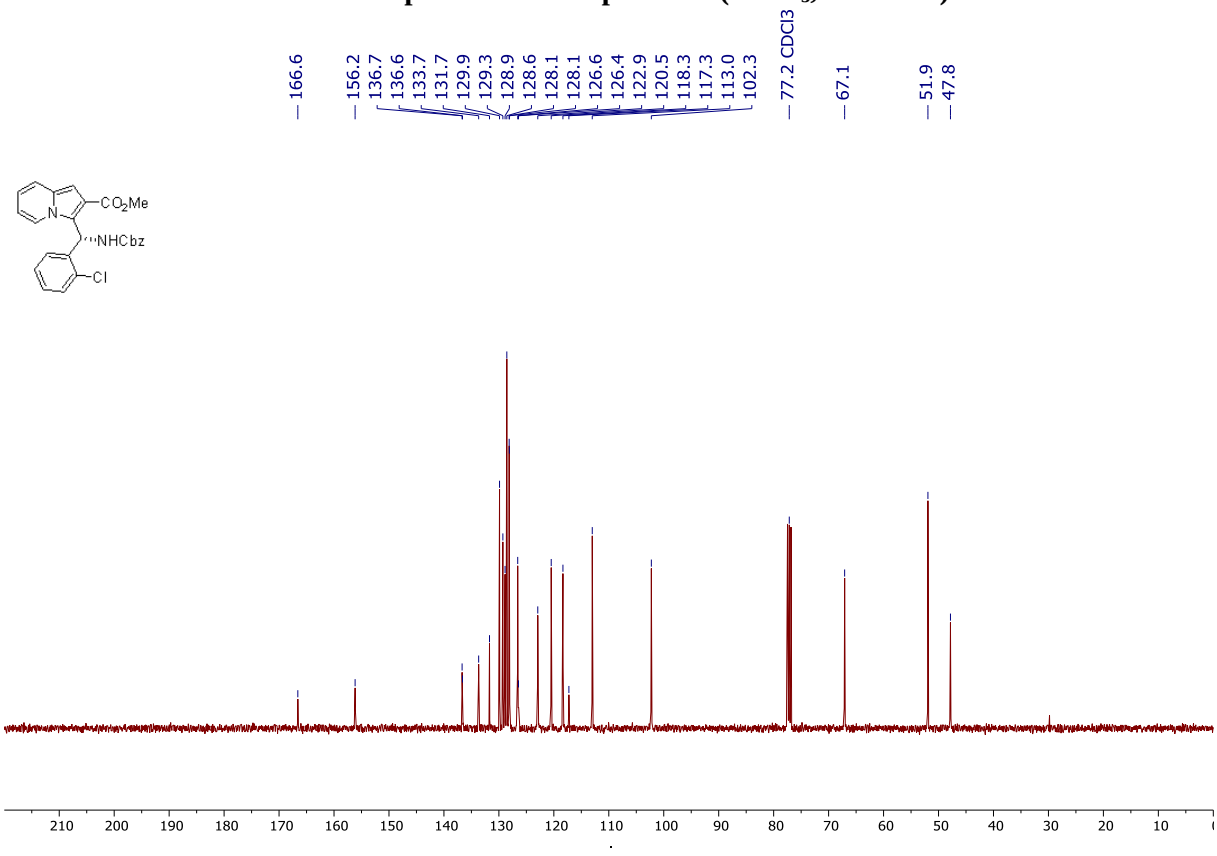
^{19}F NMR spectrum of compound 7h ($CDCl_3$, 376 MHz)



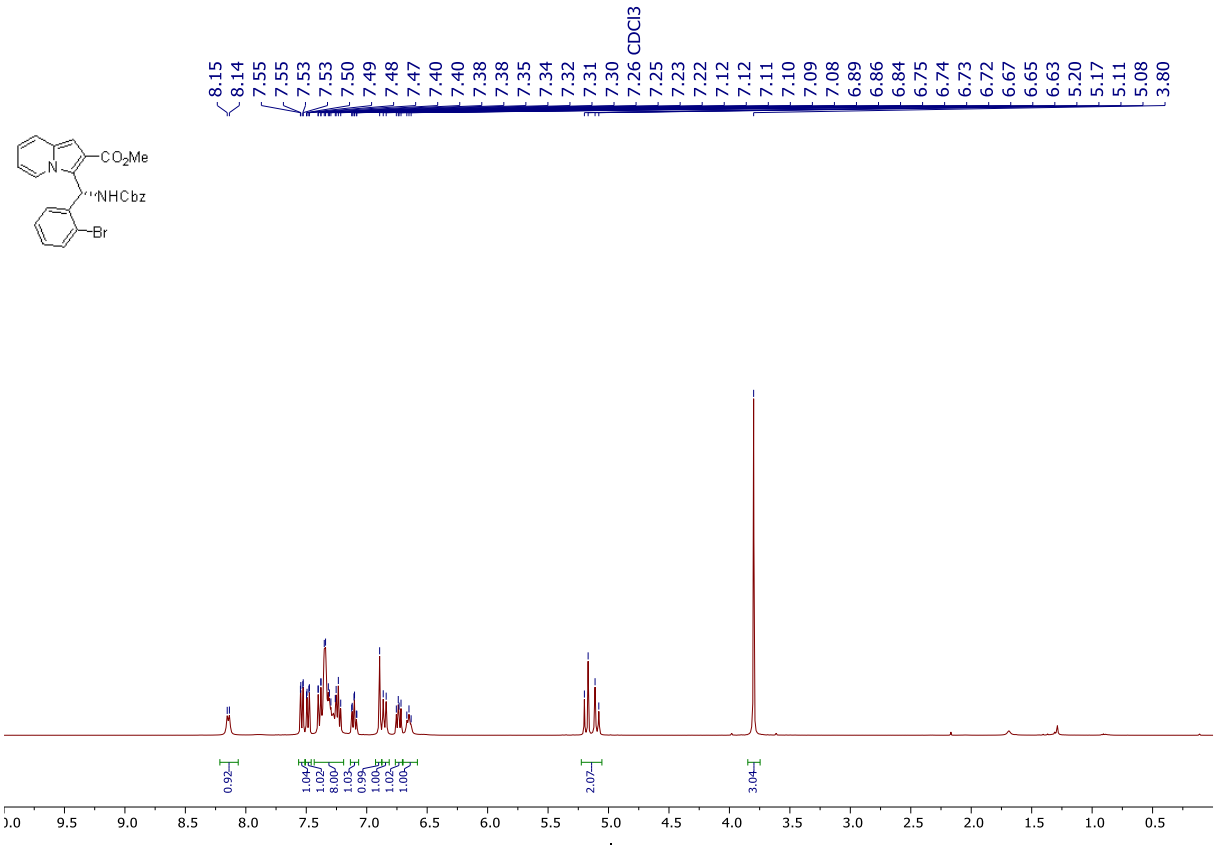
^{1}H NMR spectrum of compound 7i ($CDCl_3$, 400 MHz)



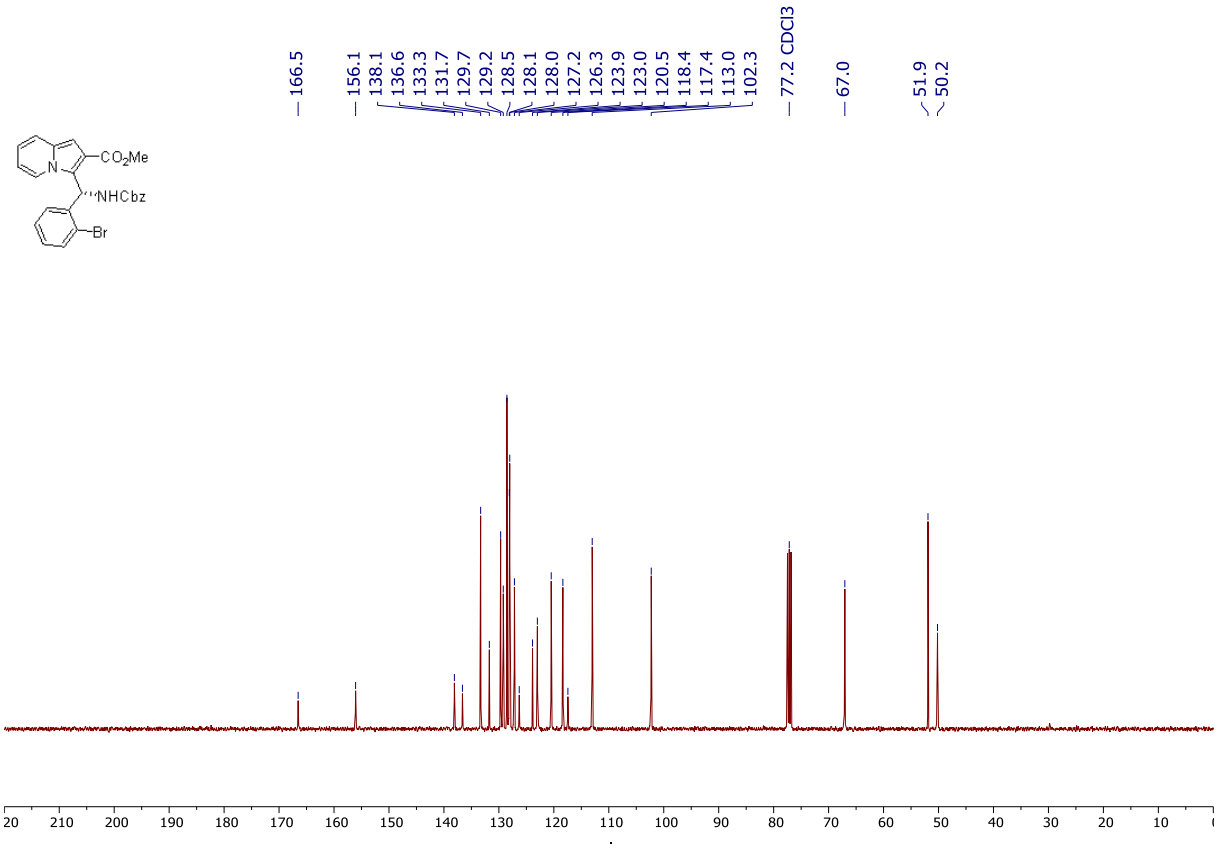
^{13}C NMR spectrum of compound 7i ($CDCl_3$, 101 MHz)



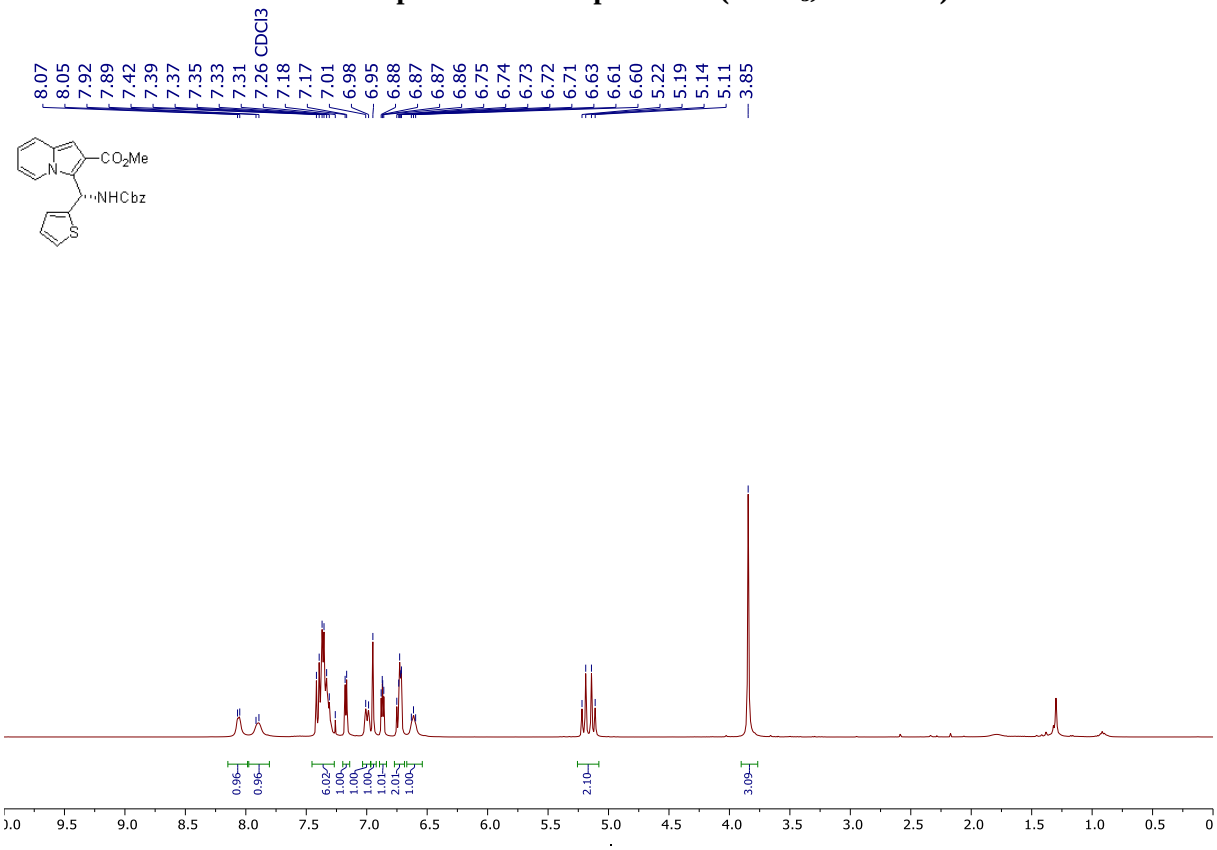
^{1}H NMR spectrum of compound 7j ($CDCl_3$, 400 MHz)



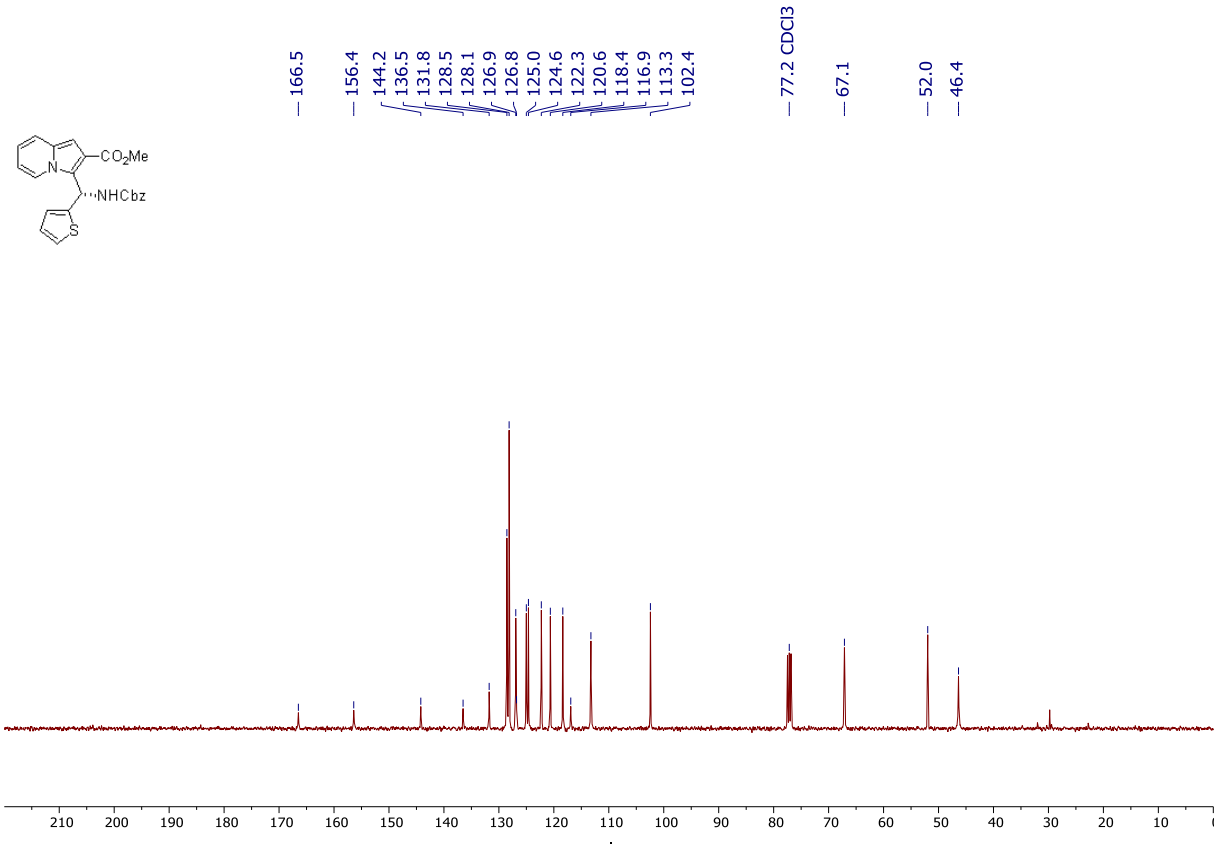
^{13}C NMR spectrum of compound 7j ($CDCl_3$, 101 MHz)



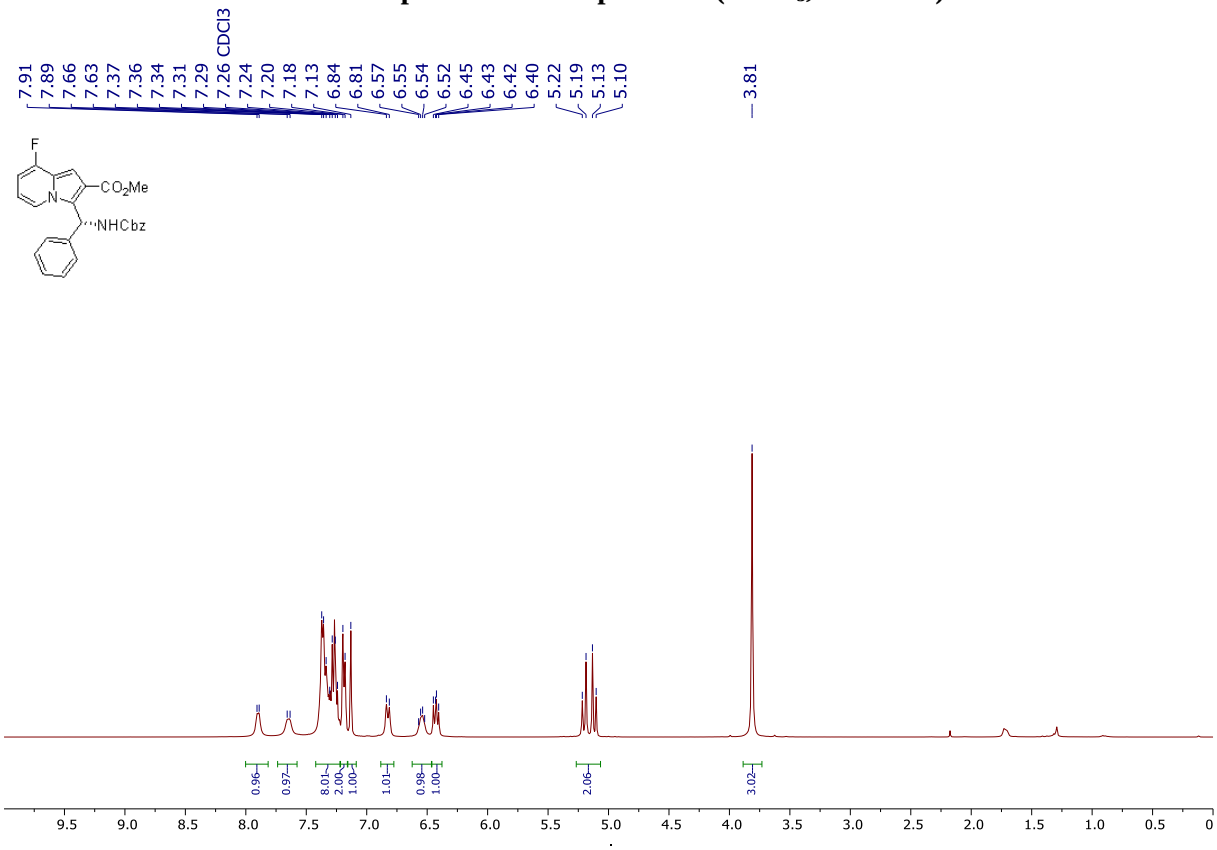
^{1}H NMR spectrum of compound 7k ($CDCl_3$, 400 MHz)



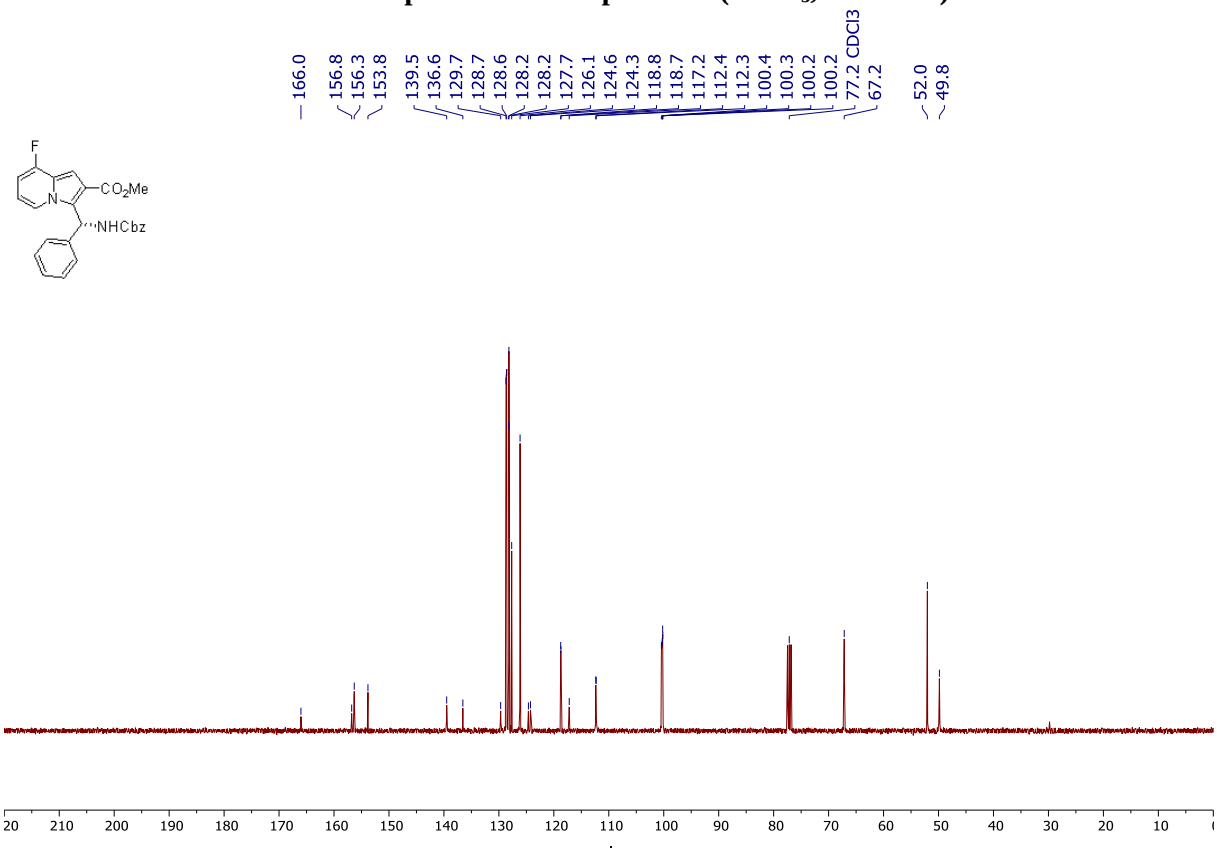
^{13}C NMR spectrum of compound 7k ($CDCl_3$, 101 MHz)



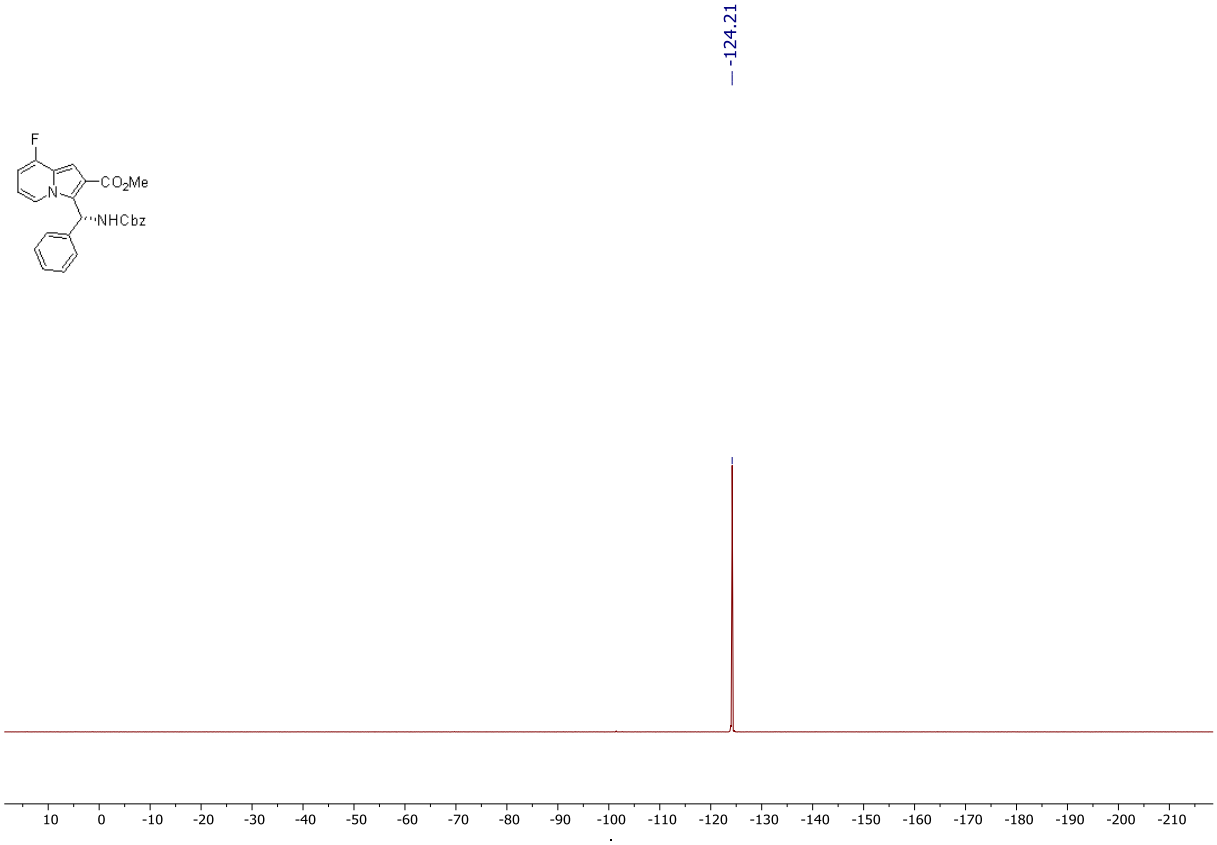
^{1}H NMR spectrum of compound 7l ($CDCl_3$, 400 MHz)



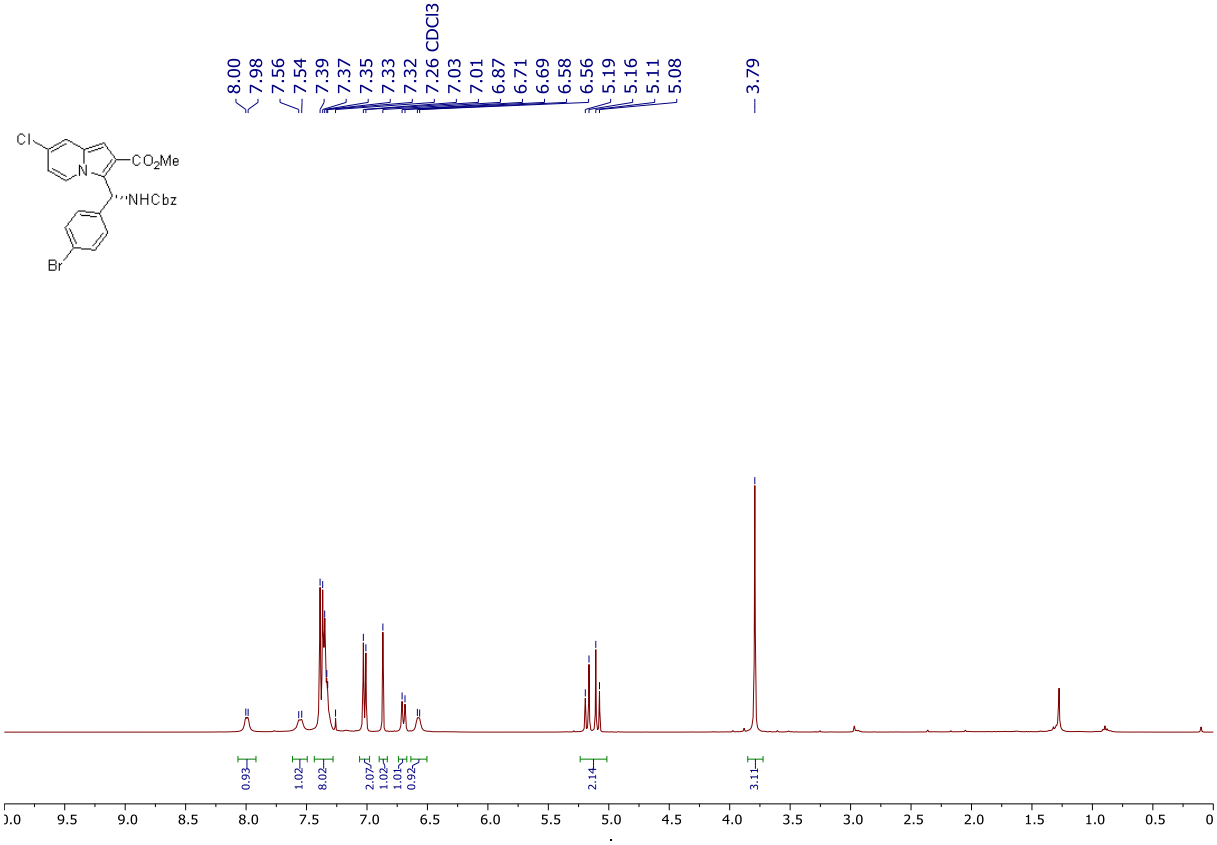
^{13}C NMR spectrum of compound 7l ($CDCl_3$, 101 MHz)



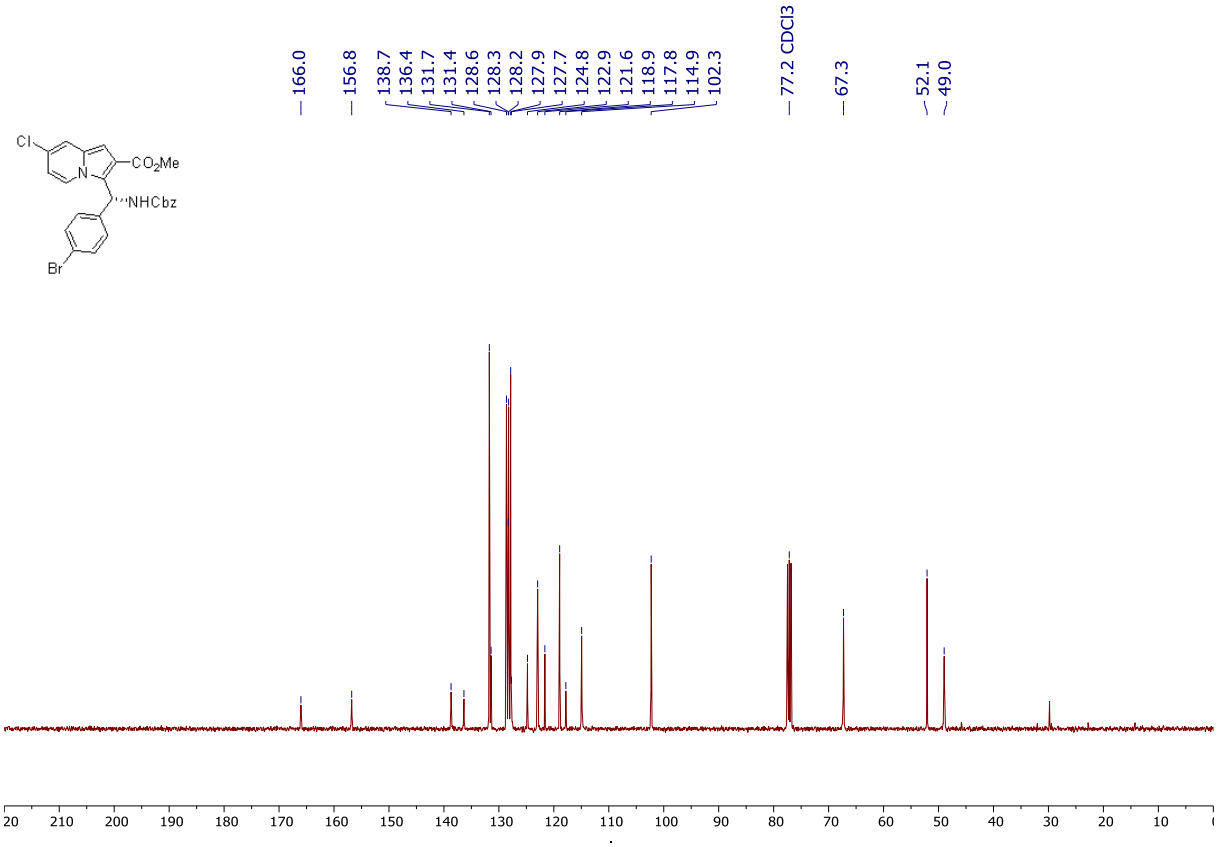
^{19}F NMR spectrum of compound 7l ($CDCl_3$, 376 MHz)



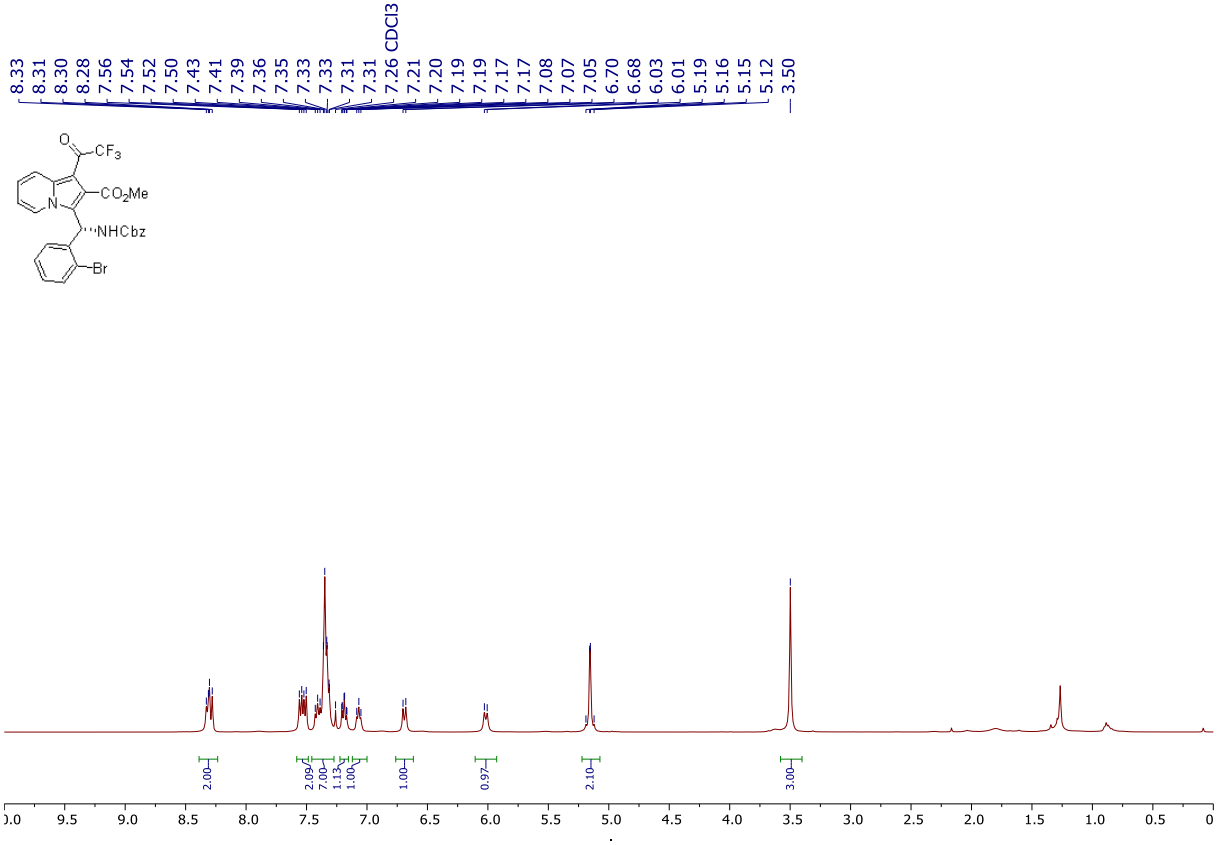
^{1}H NMR spectrum of compound 7m ($CDCl_3$, 400 MHz)



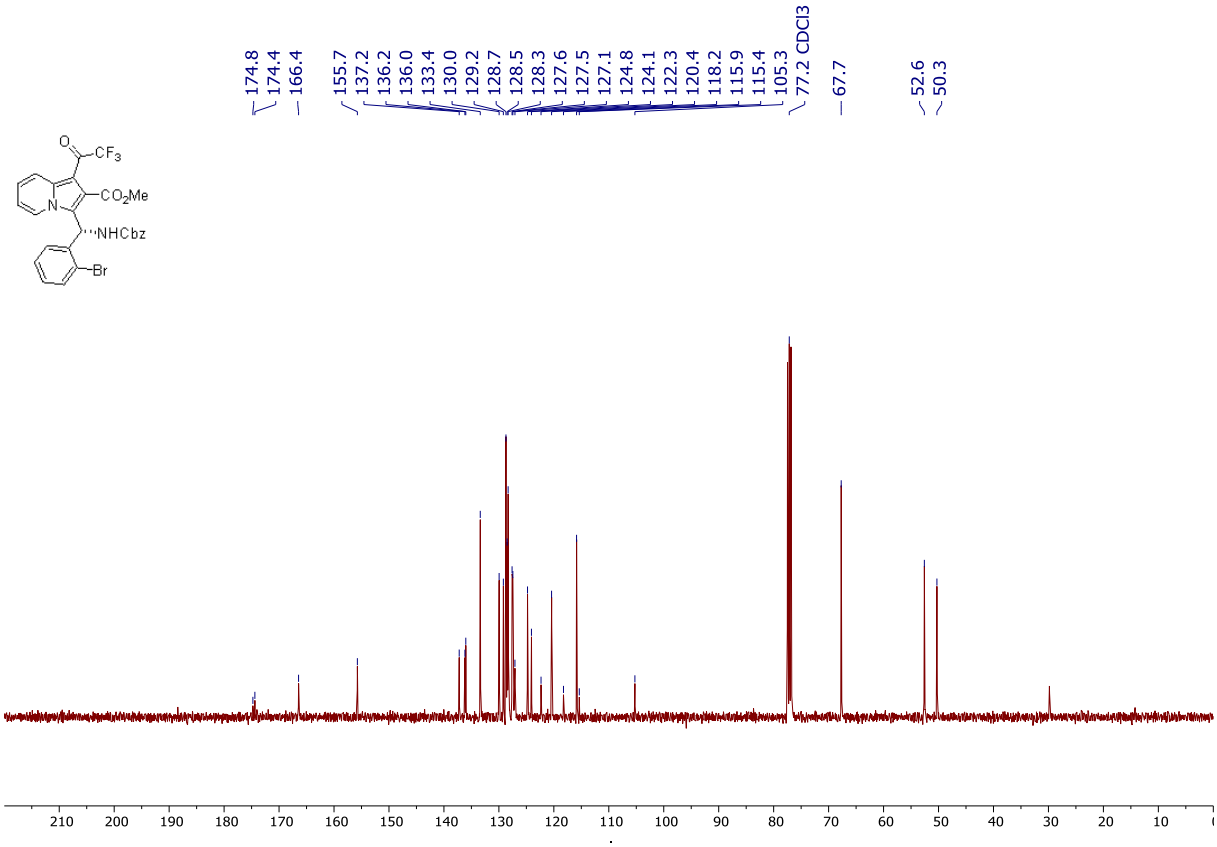
^{13}C NMR spectrum of compound 7m ($CDCl_3$, 101 MHz)



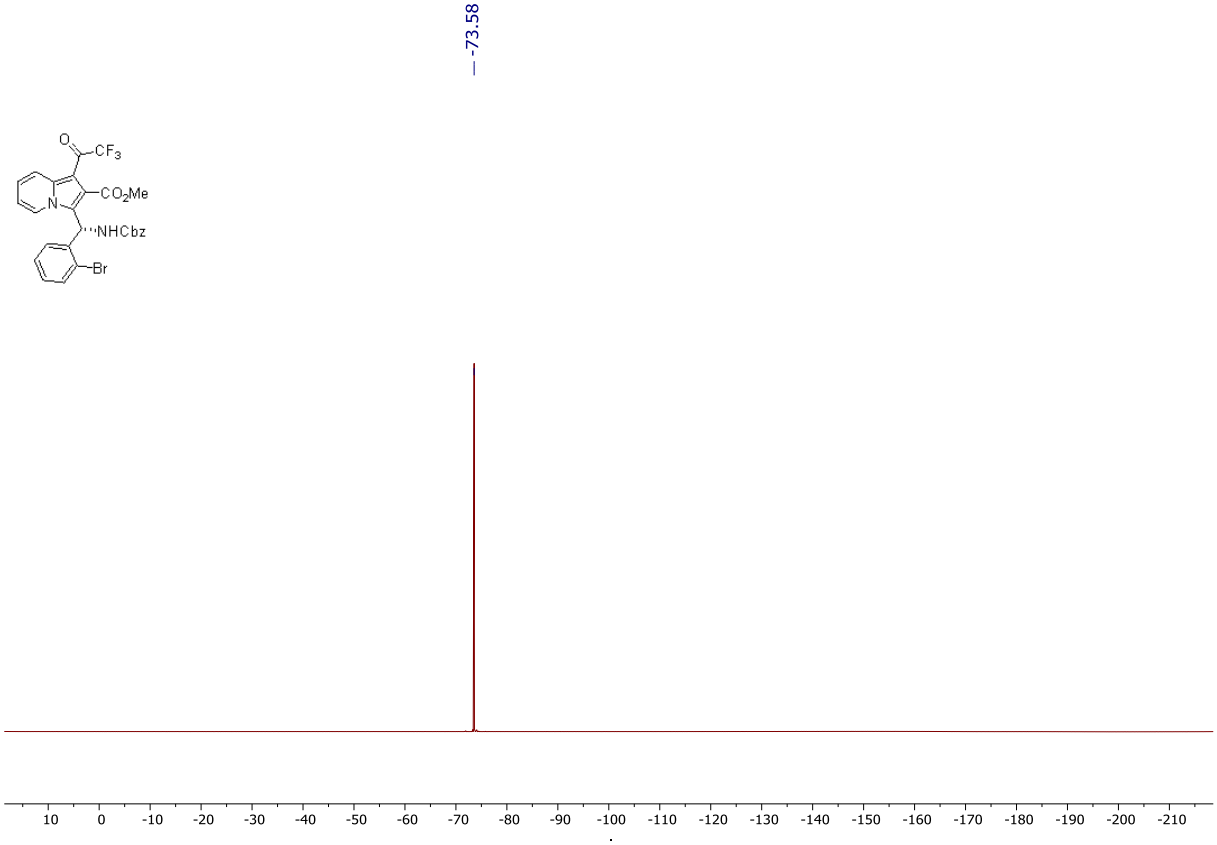
^{1}H NMR spectrum of compound 8 ($CDCl_3$, 500 MHz)



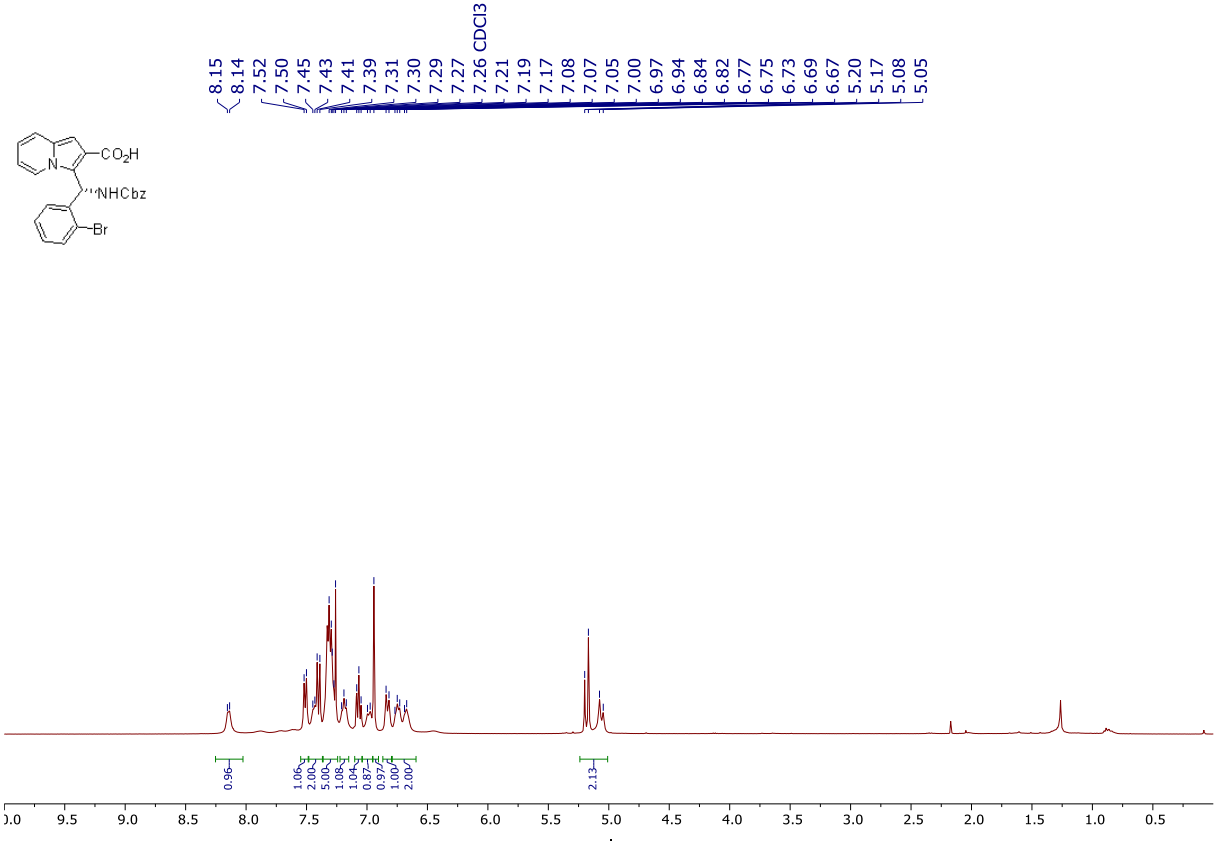
^{13}C NMR spectrum of compound 8 ($CDCl_3$, 101 MHz)



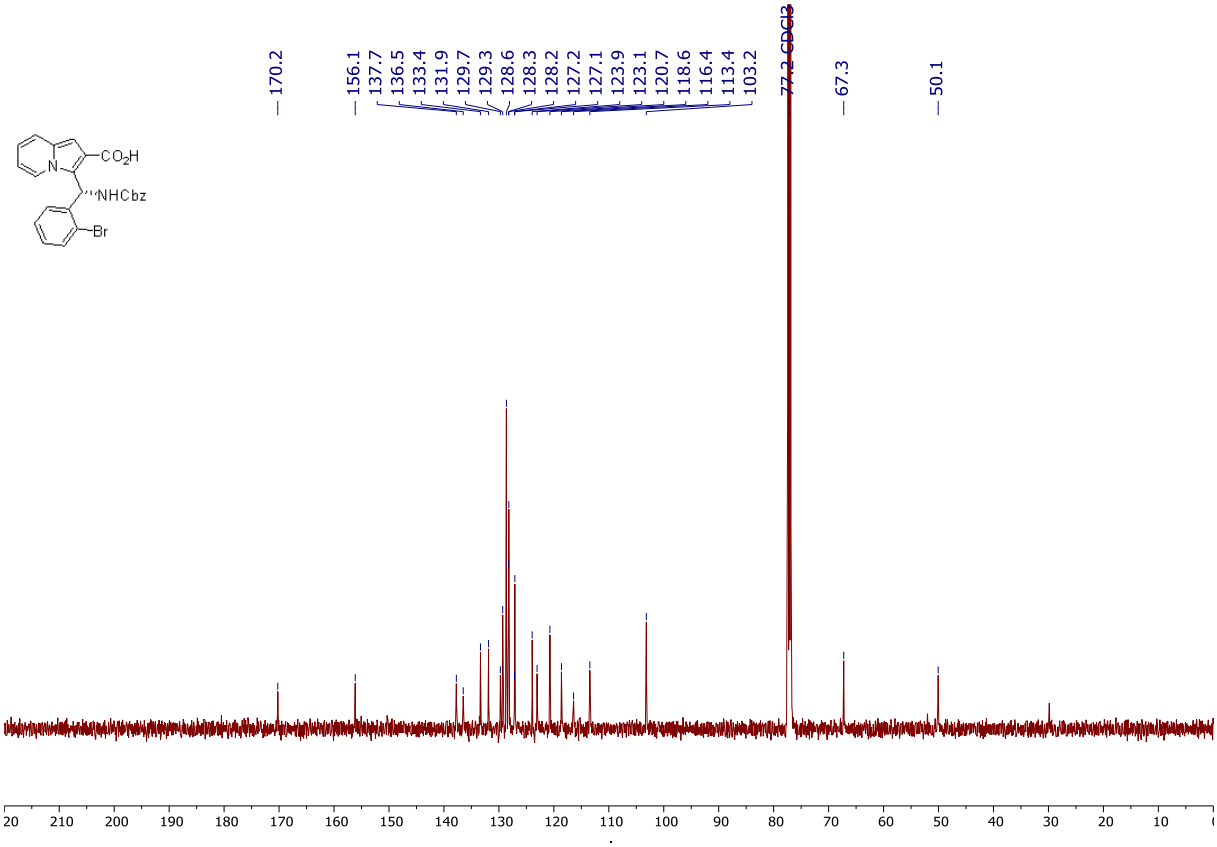
^{19}F NMR spectrum of compound 8 ($CDCl_3$, 376 MHz)



^{1}H NMR spectrum of compound 9 ($CDCl_3$, 400 MHz)

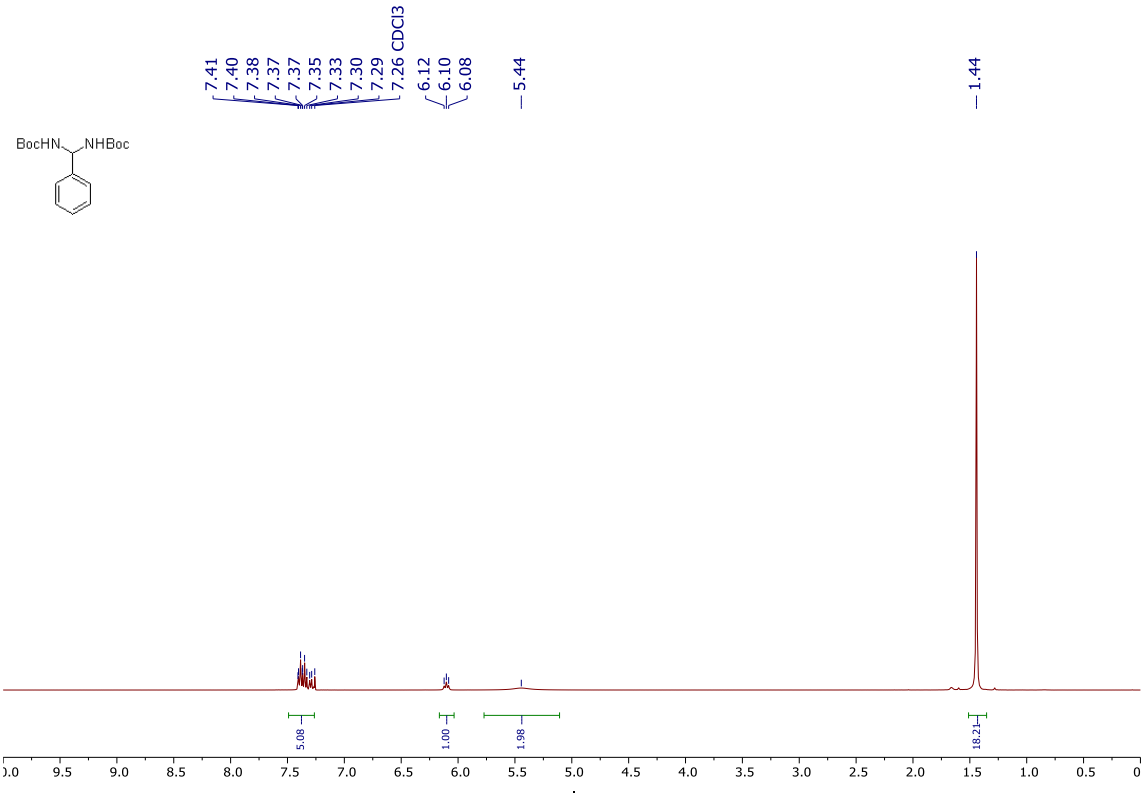


^{13}C NMR spectrum of compound X ($CDCl_3$, 126 MHz)

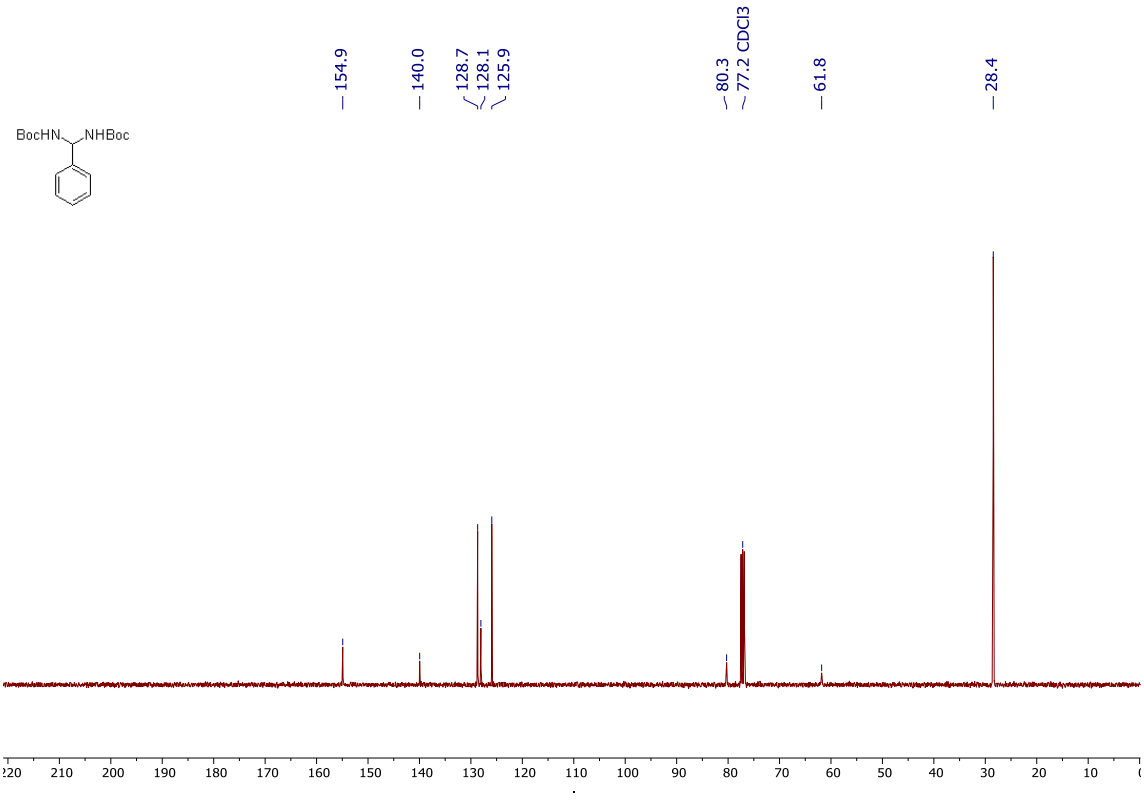


6.3. *N*-Boc aminals 2a-m

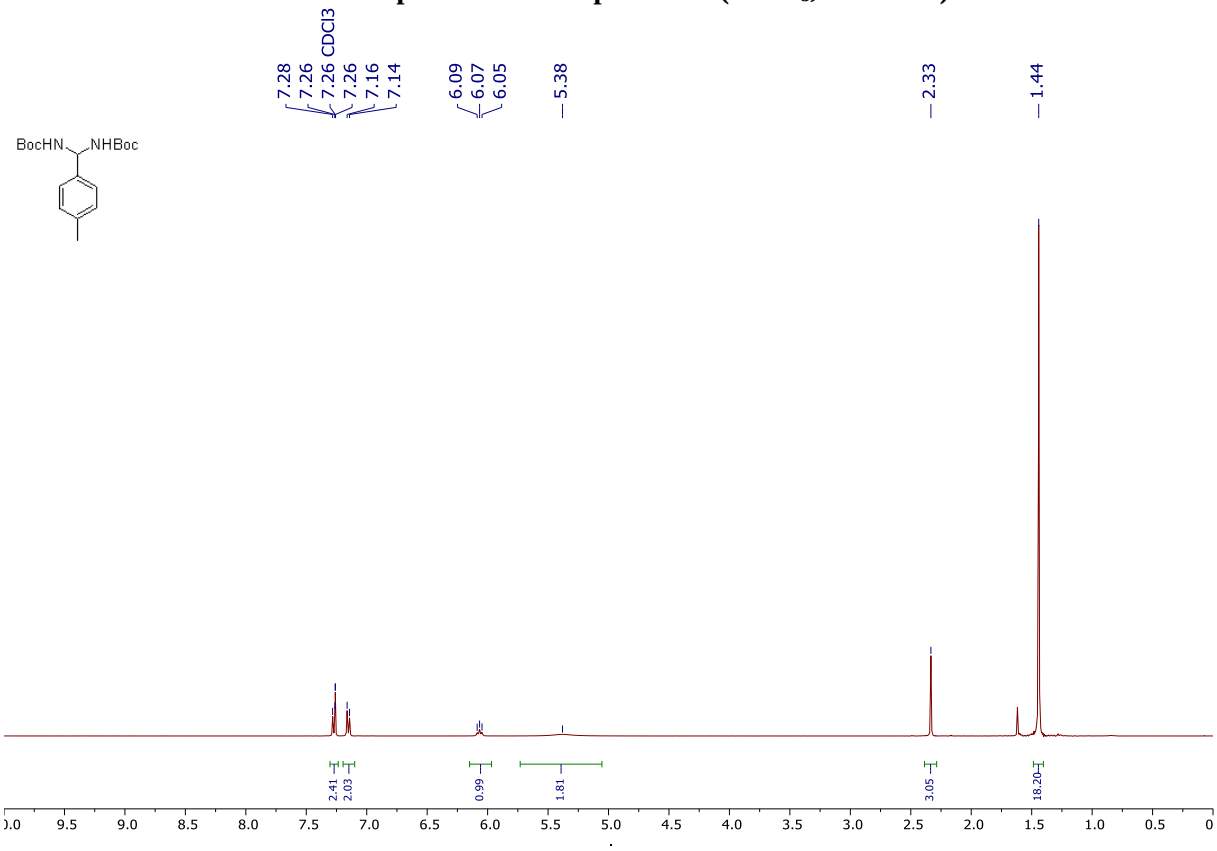
^{1}H NMR spectrum of compound 2a ($CDCl_3$, 400 MHz)



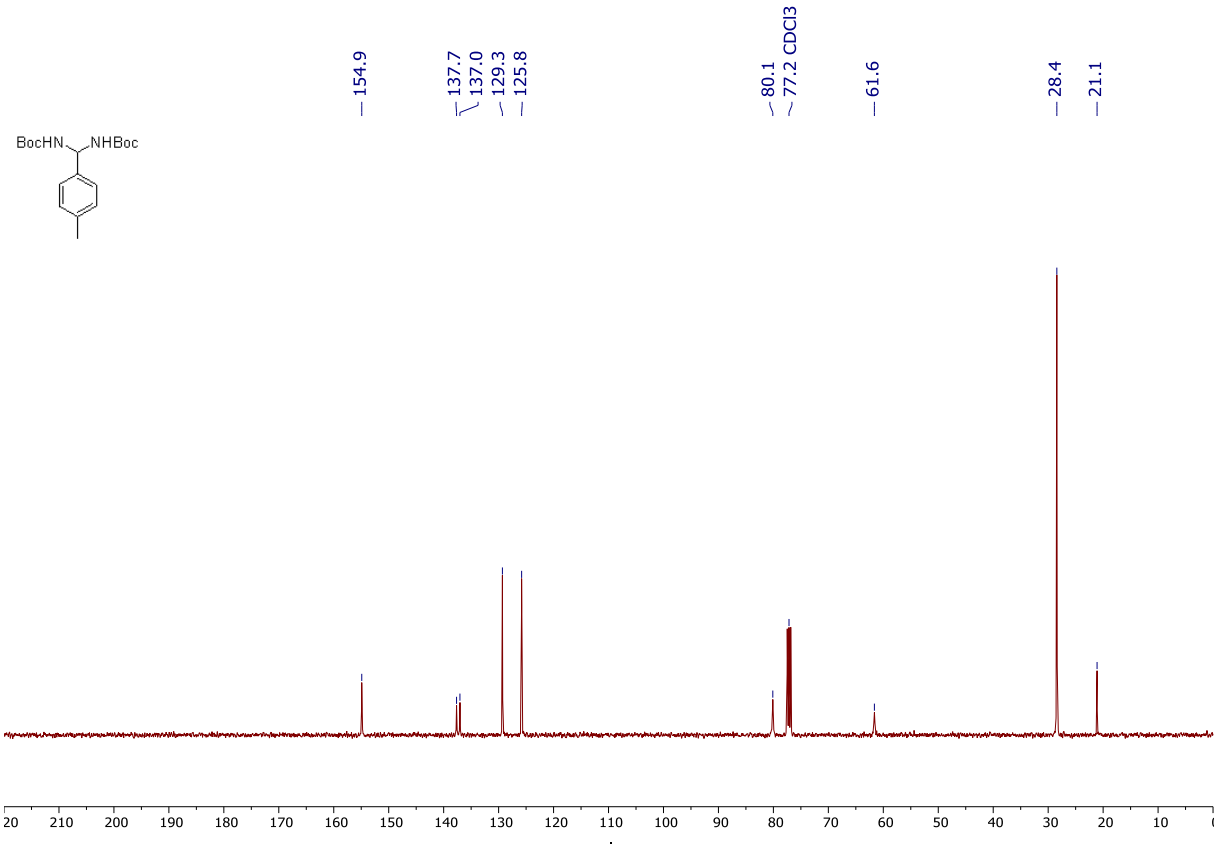
^{13}C NMR spectrum of compound 2a (CDCl3, 100 MHz)



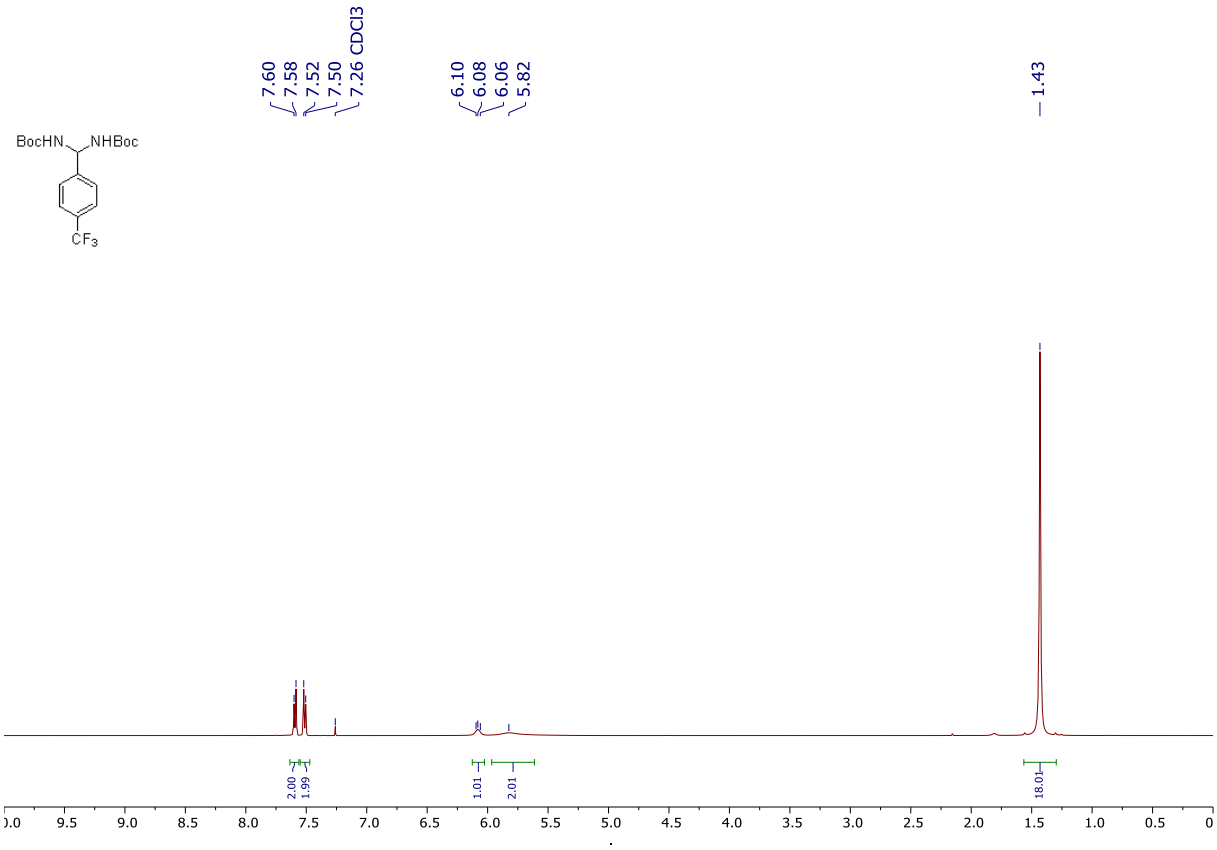
^{1}H NMR spectrum of compound 2b ($CDCl_3$, 400 MHz)



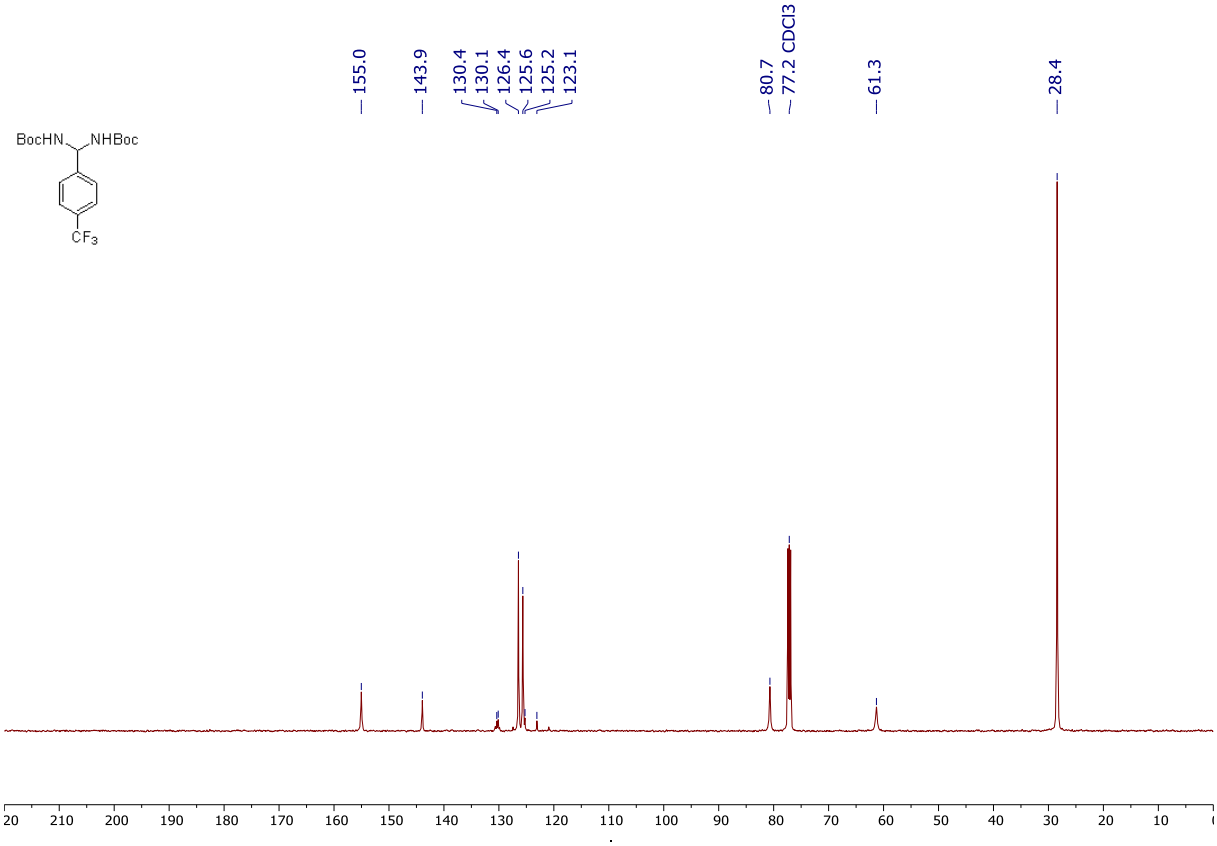
^{13}C NMR spectrum of compound 2b ($CDCl_3$, 100 MHz)



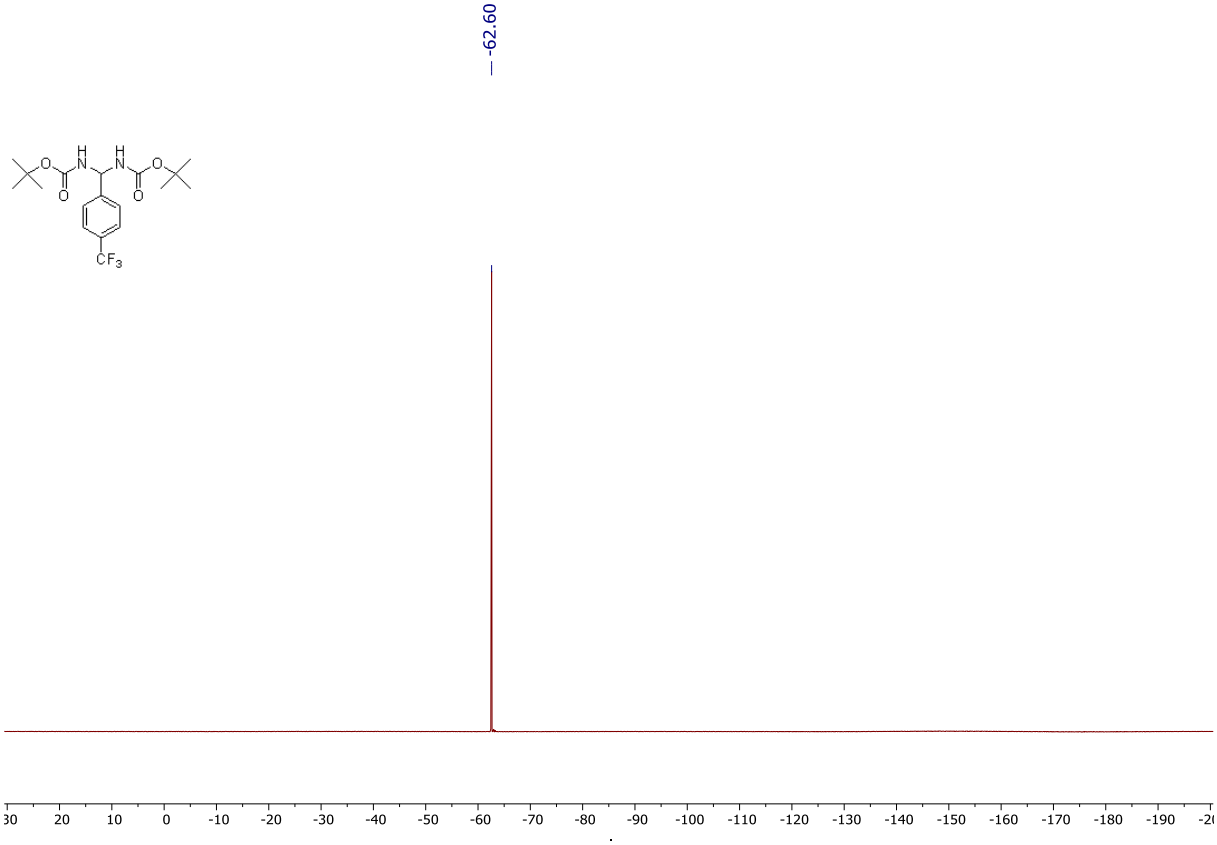
^{1}H NMR spectrum of compound 2c ($CDCl_3$, 400 MHz)



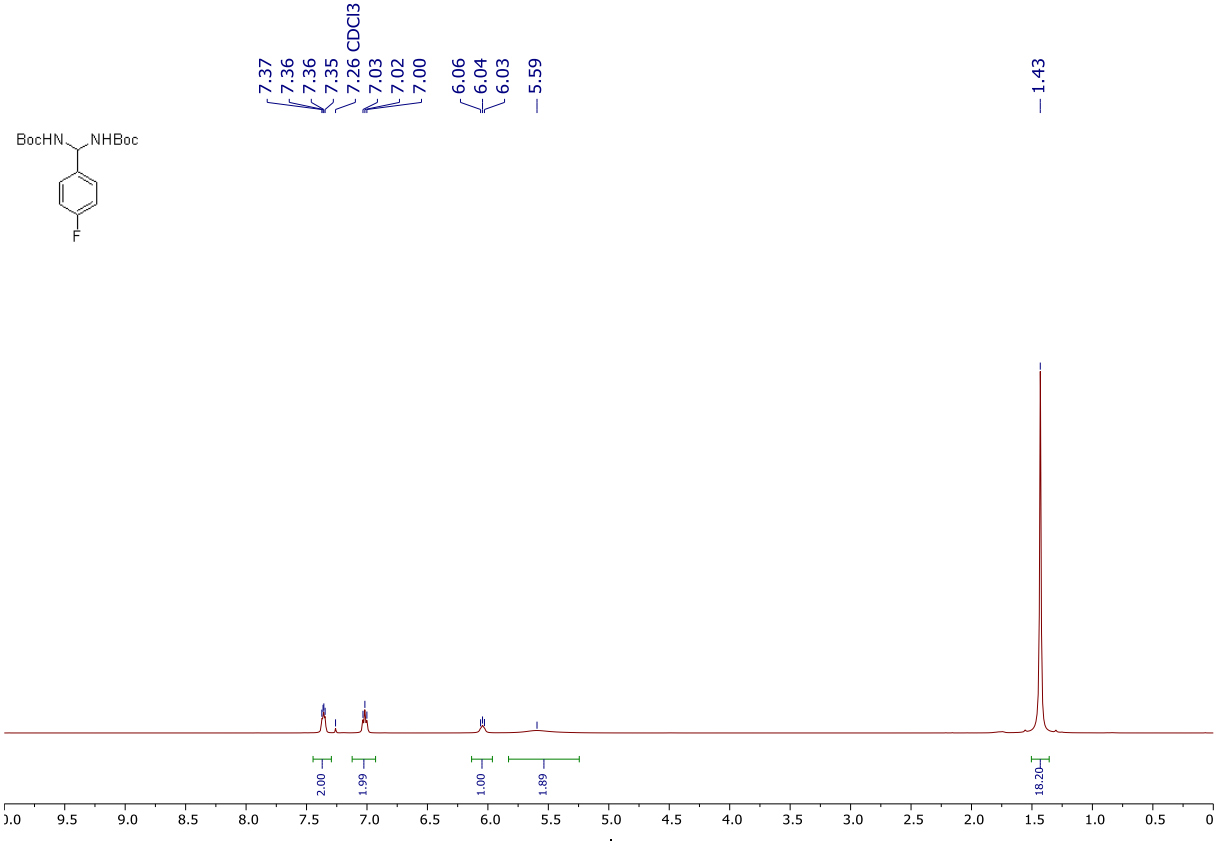
^{13}C NMR spectrum of compound 2c ($CDCl_3$, 100 MHz)



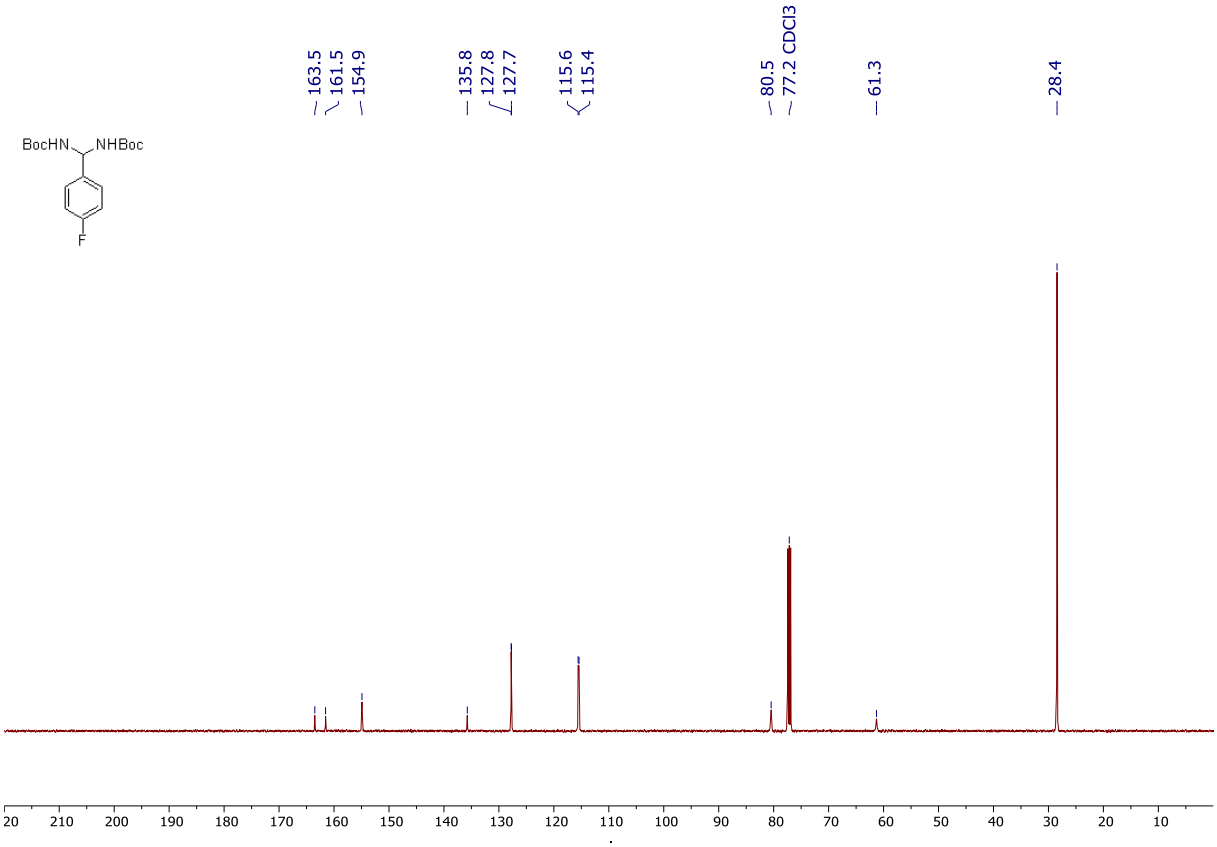
^{19}F NMR spectrum of compound 2c ($CDCl_3$, 376 MHz)



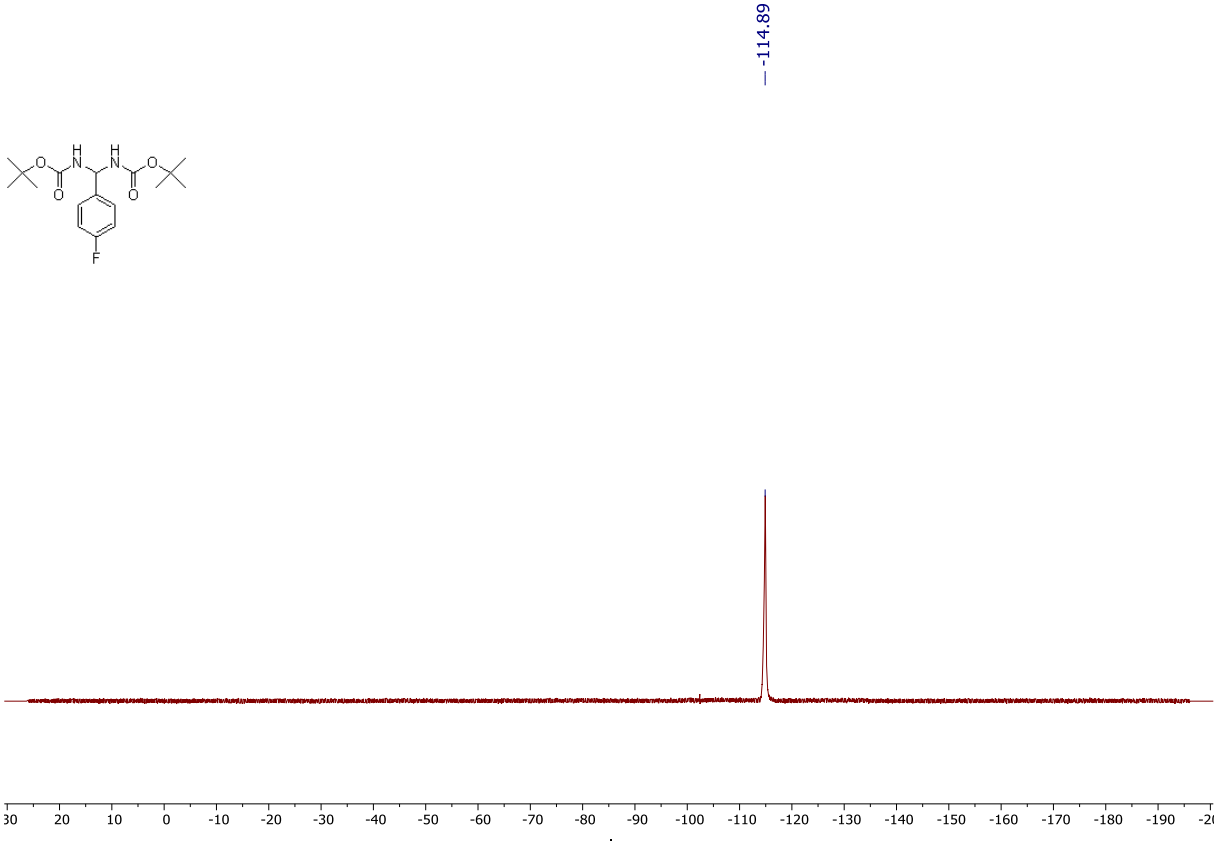
^{1}H NMR spectrum of compound 2d ($CDCl_3$, 400 MHz)



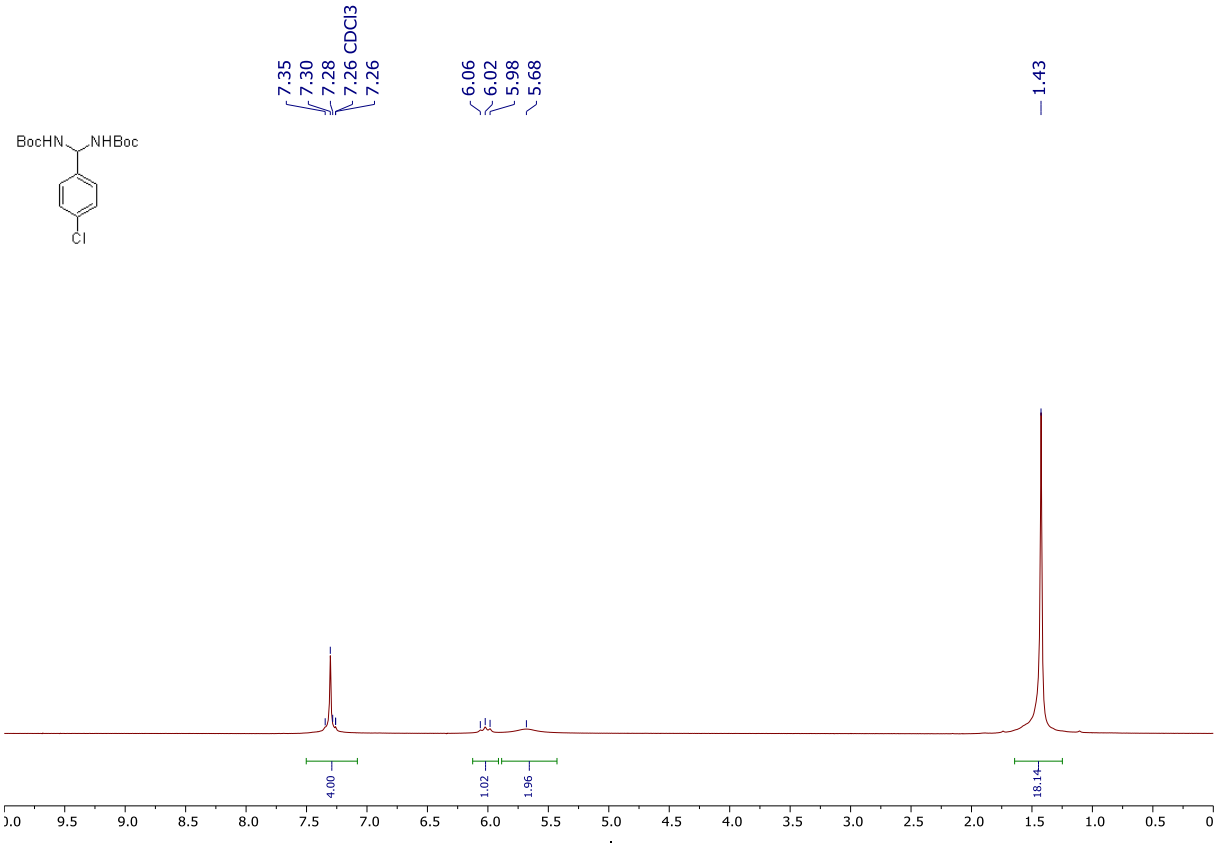
^{13}C NMR spectrum of compound 2d ($CDCl_3$, 100 MHz)



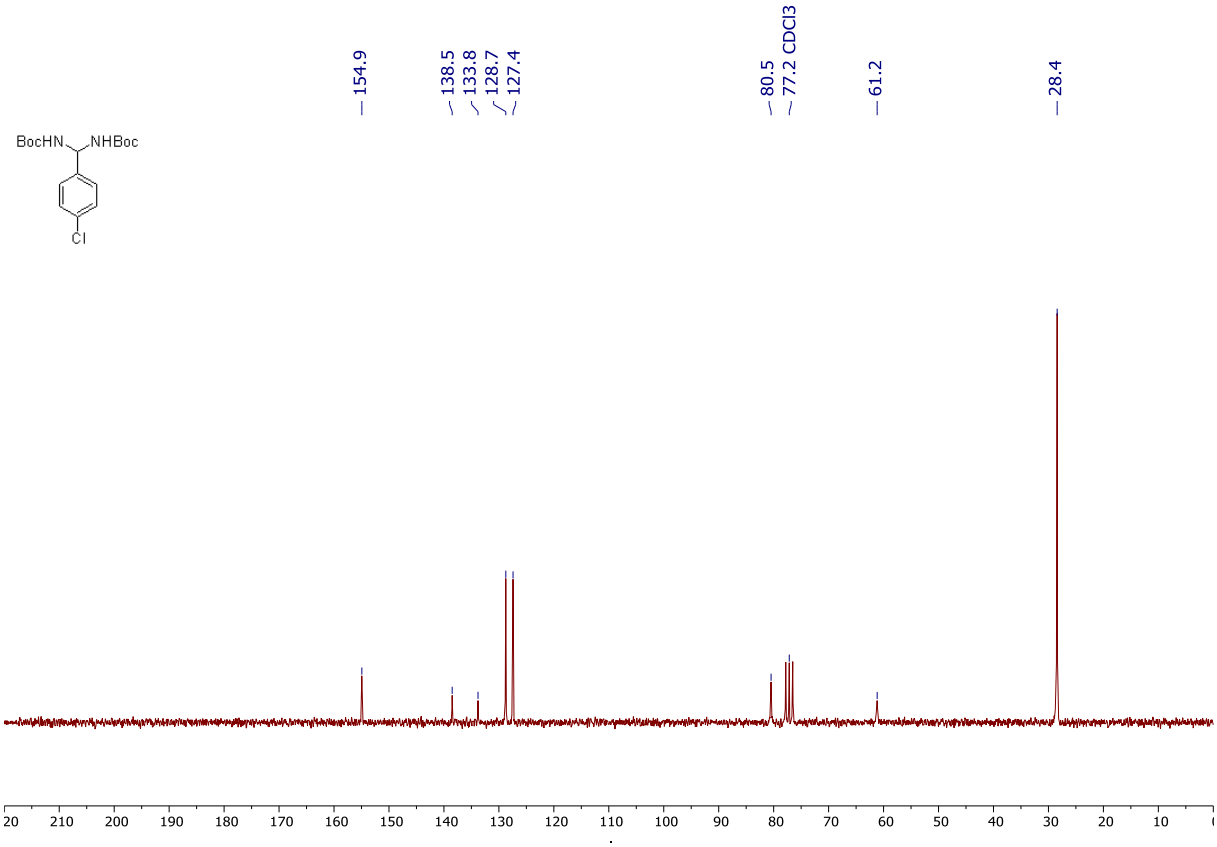
^{19}F NMR spectrum of compound 2d ($CDCl_3$, 376 MHz)



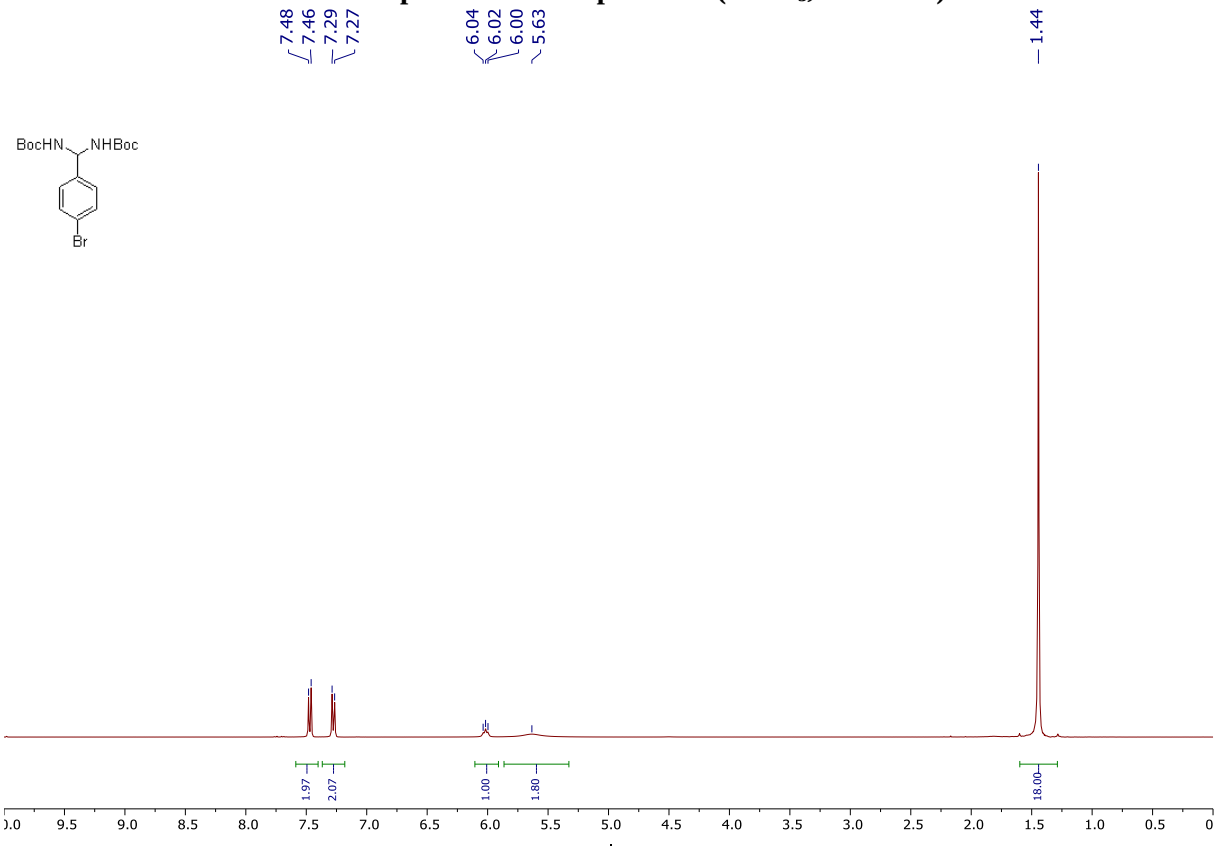
^{1}H NMR spectrum of compound 2e ($CDCl_3$, 200 MHz)



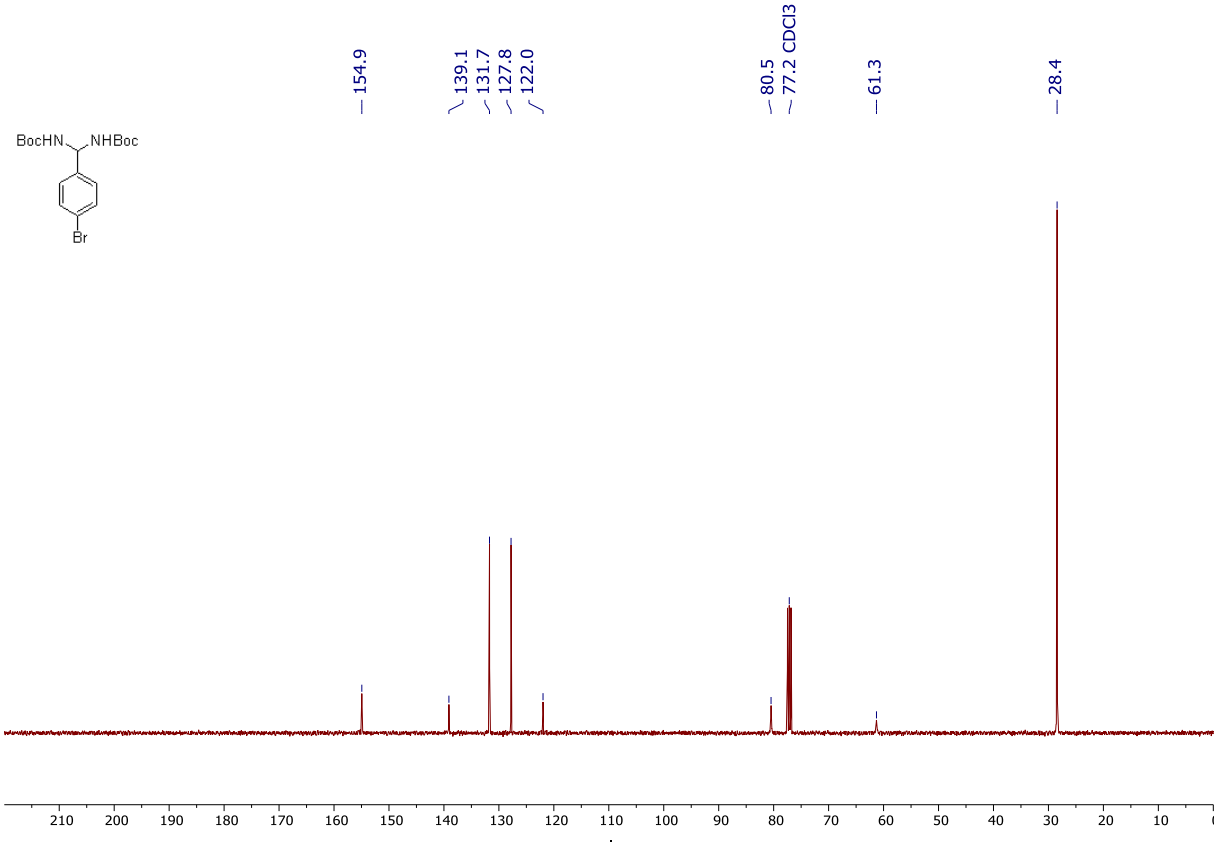
^{13}C NMR spectrum of compound 2e ($CDCl_3$, 50 MHz)



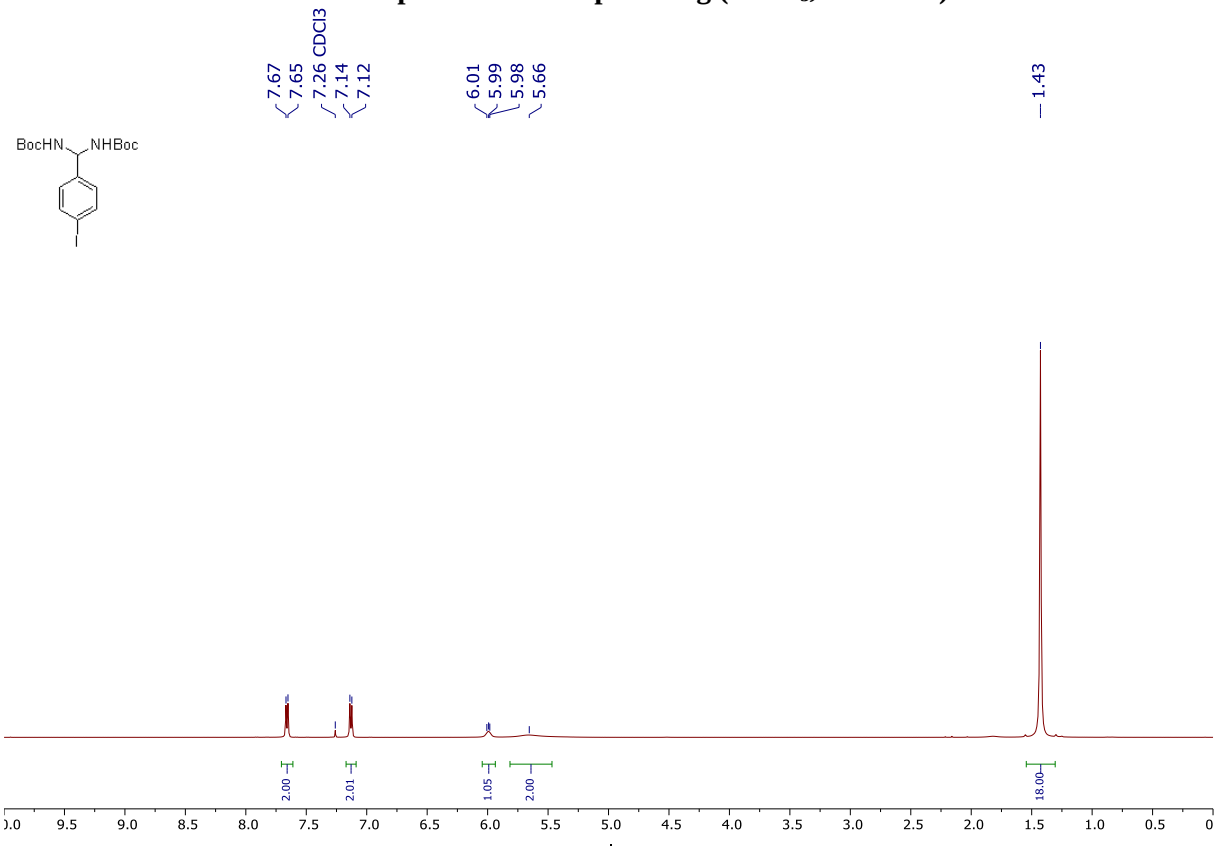
^{1}H NMR spectrum of compound 2f ($CDCl_3$, 400 MHz)



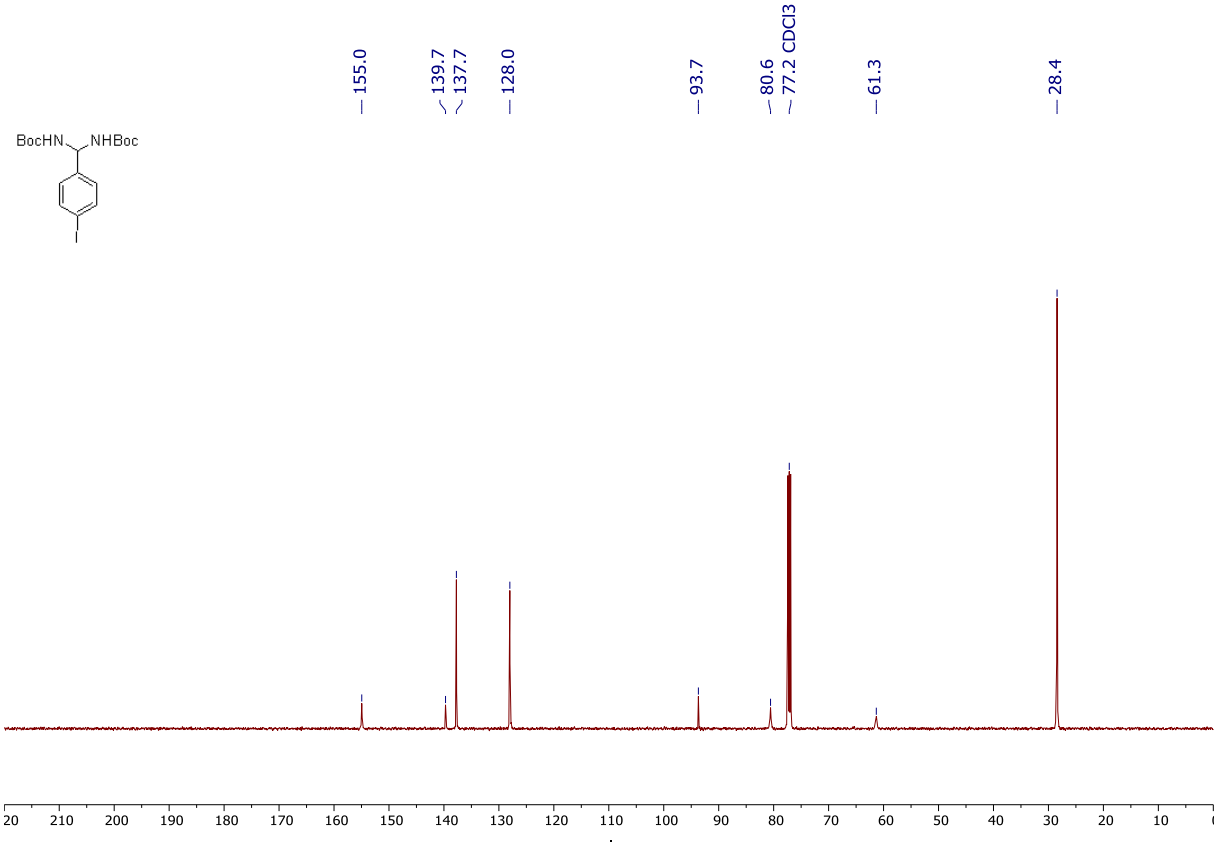
^{13}C NMR spectrum of compound 2f ($CDCl_3$, 100 MHz)



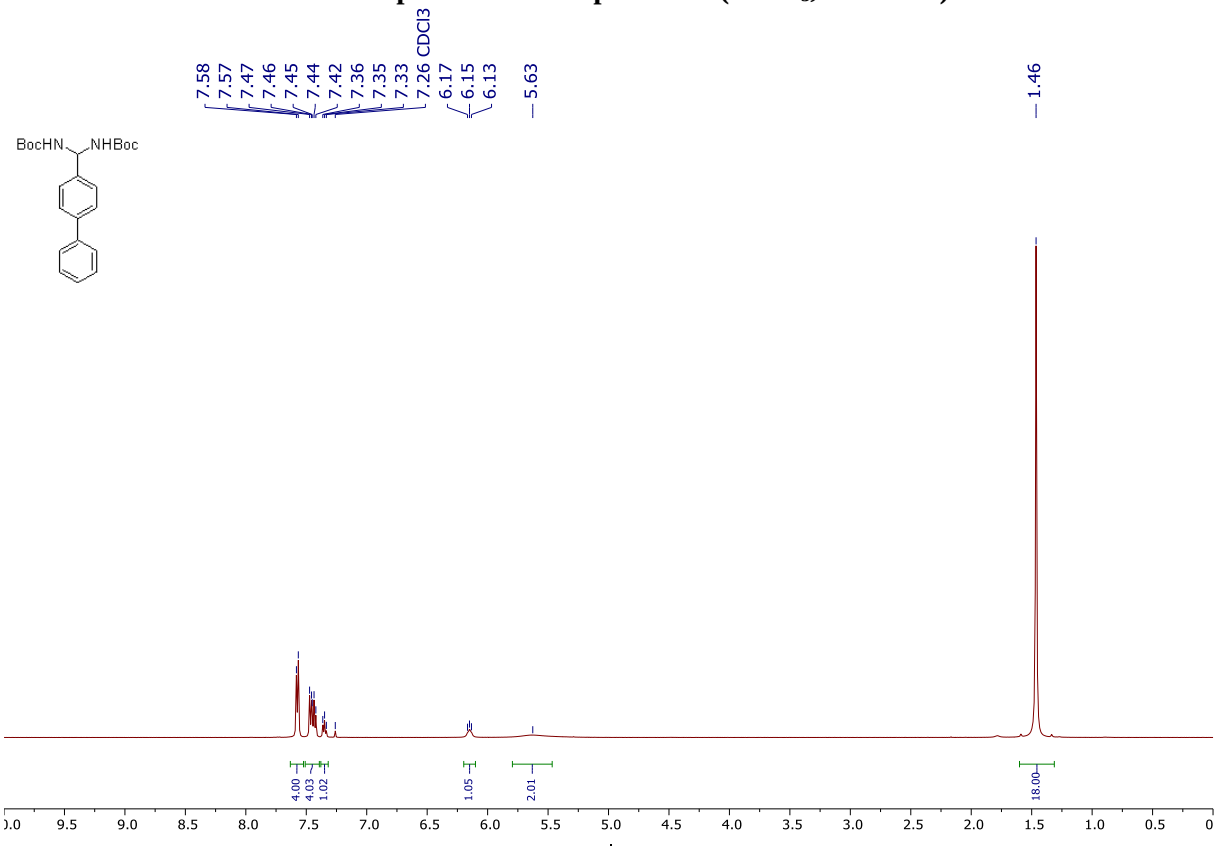
^{1}H NMR spectrum of compound 2g ($CDCl_3$, 400 MHz)



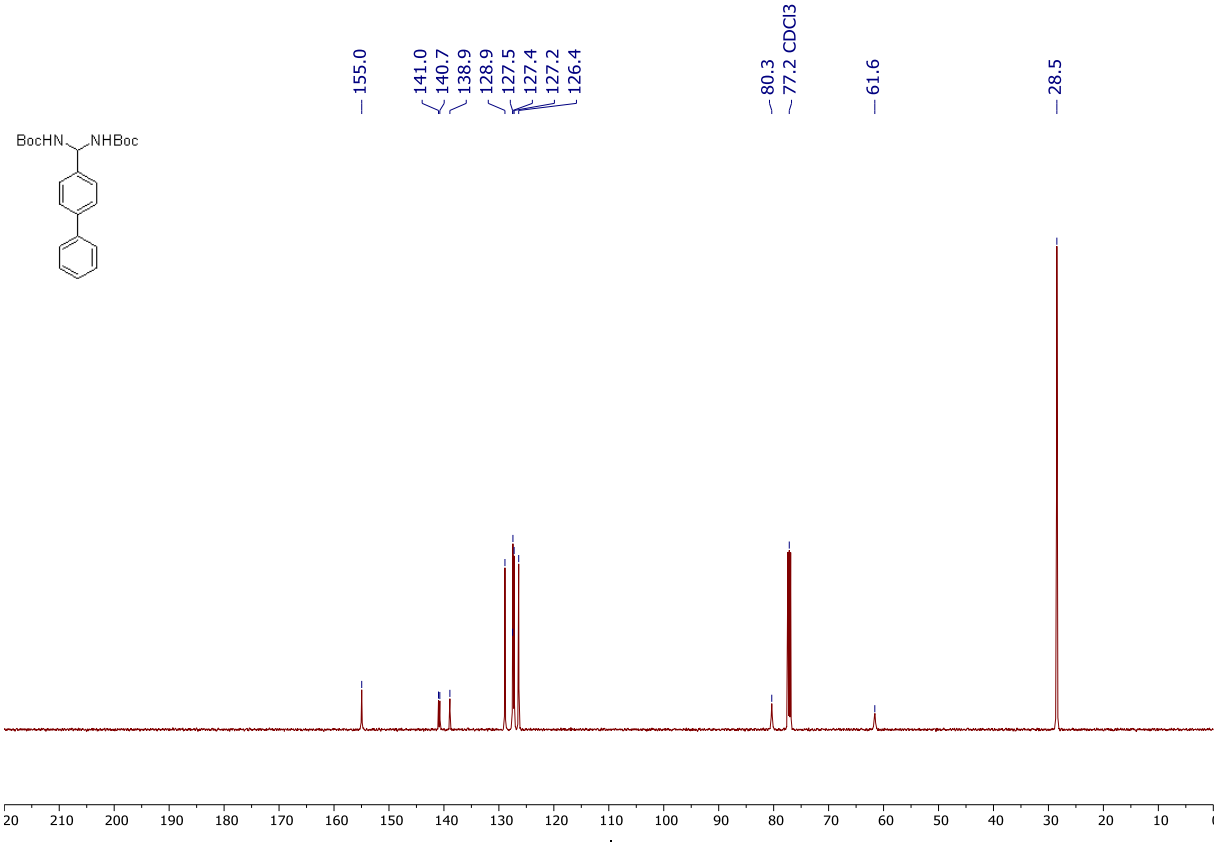
^{13}C NMR spectrum of compound 2g ($CDCl_3$, 100 MHz)



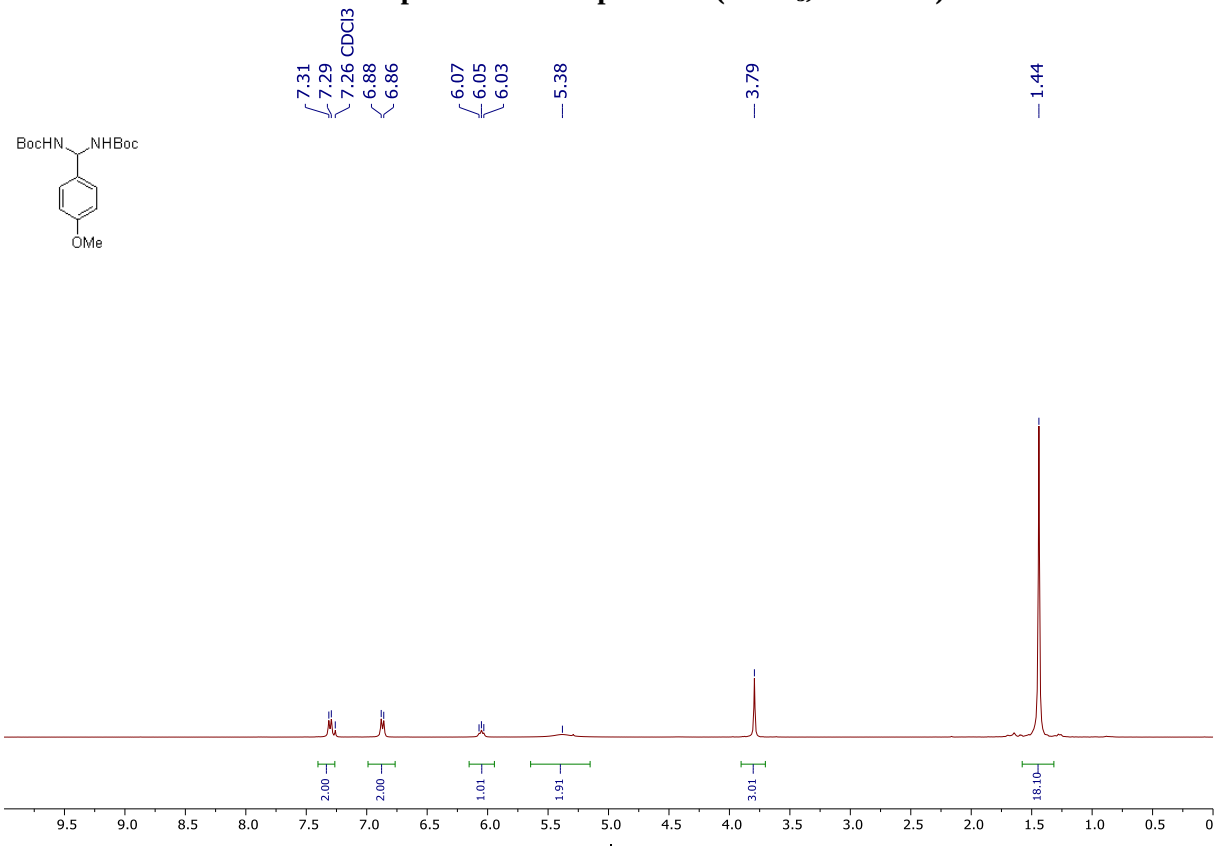
^{1}H NMR spectrum of compound 2h ($CDCl_3$, 400 MHz)



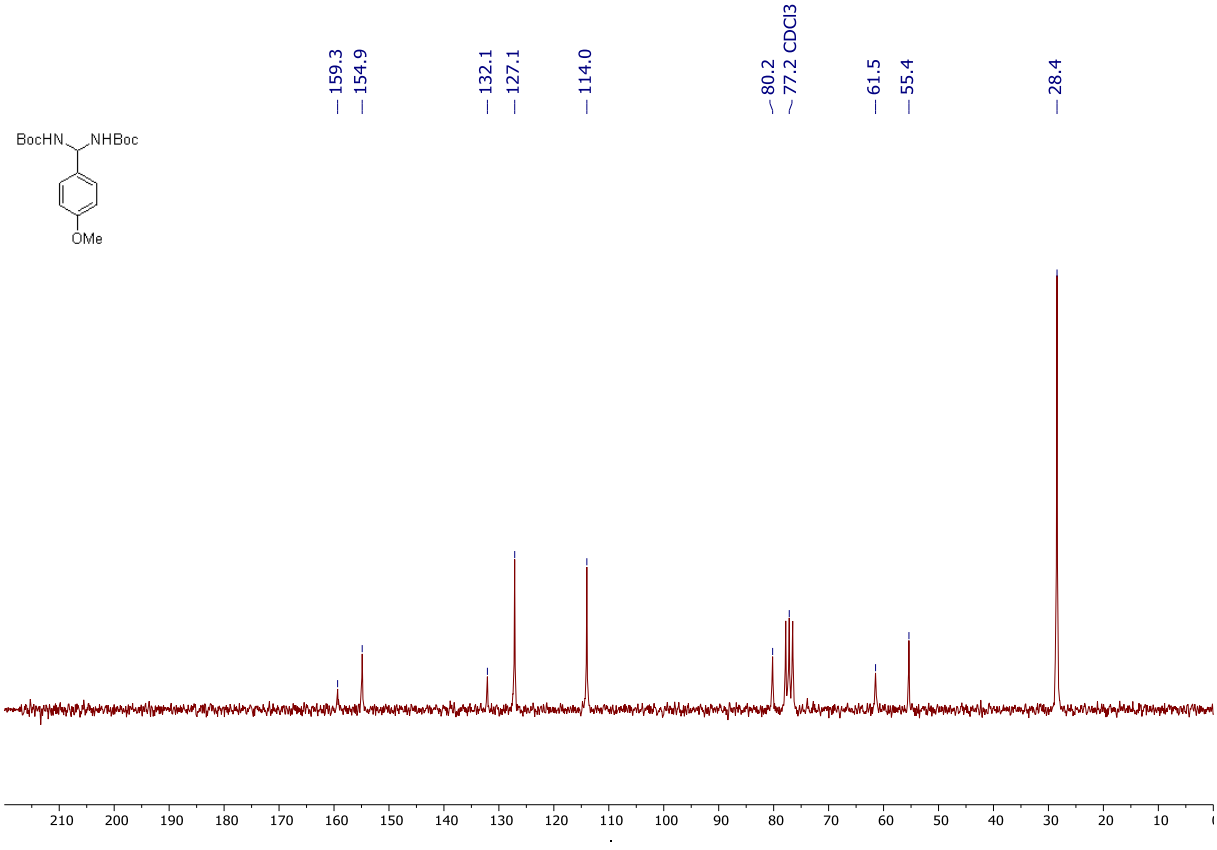
^{13}C NMR spectrum of compound 2h ($CDCl_3$, 100 MHz)



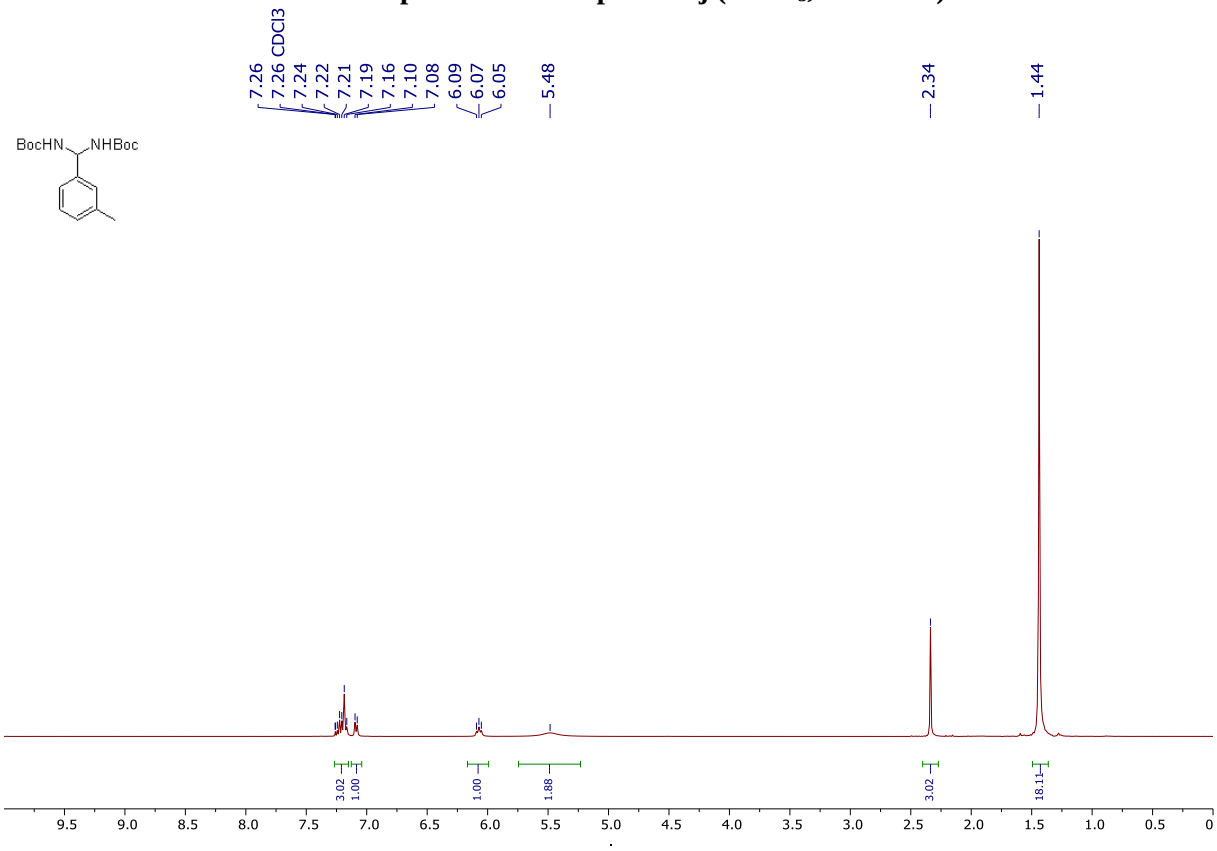
^{1}H NMR spectrum of compound 2i ($CDCl_3$, 400 MHz)



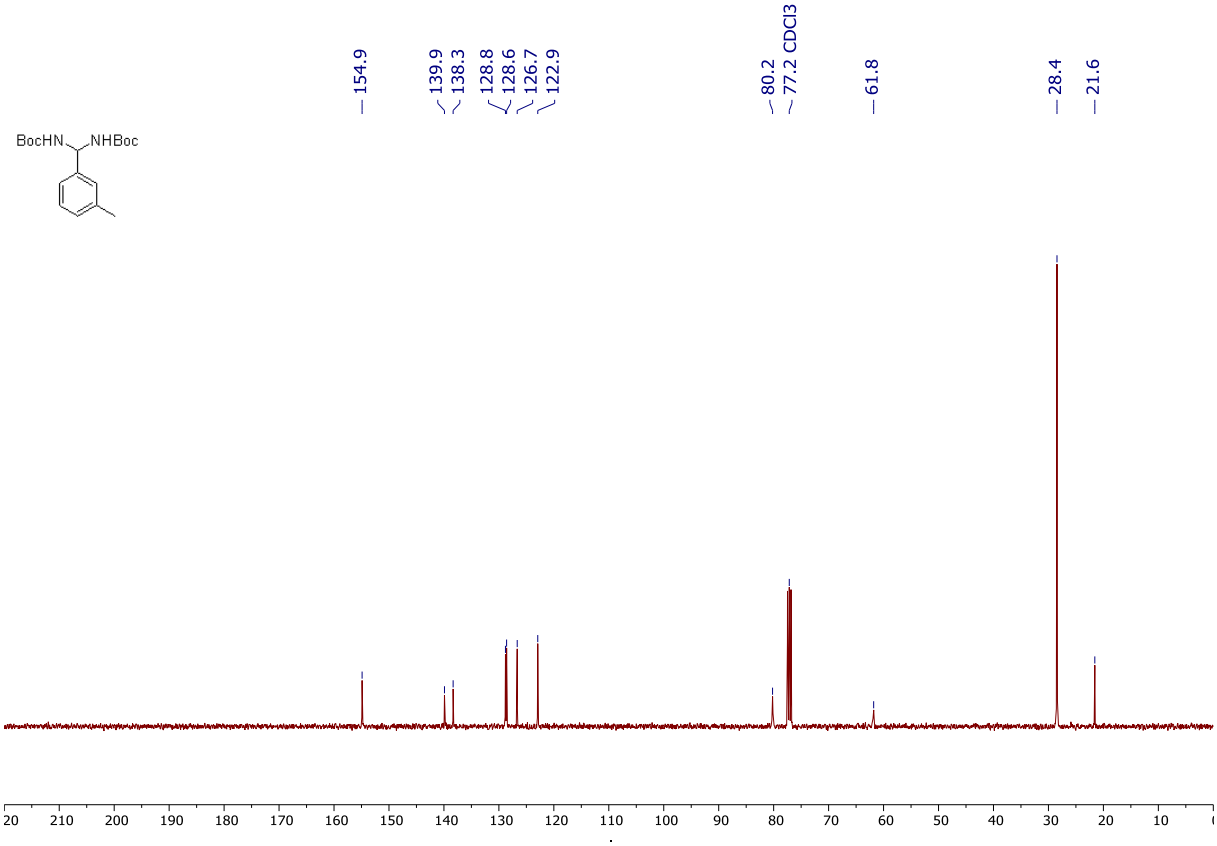
^{13}C NMR spectrum of compound 2i ($CDCl_3$, 100 MHz)



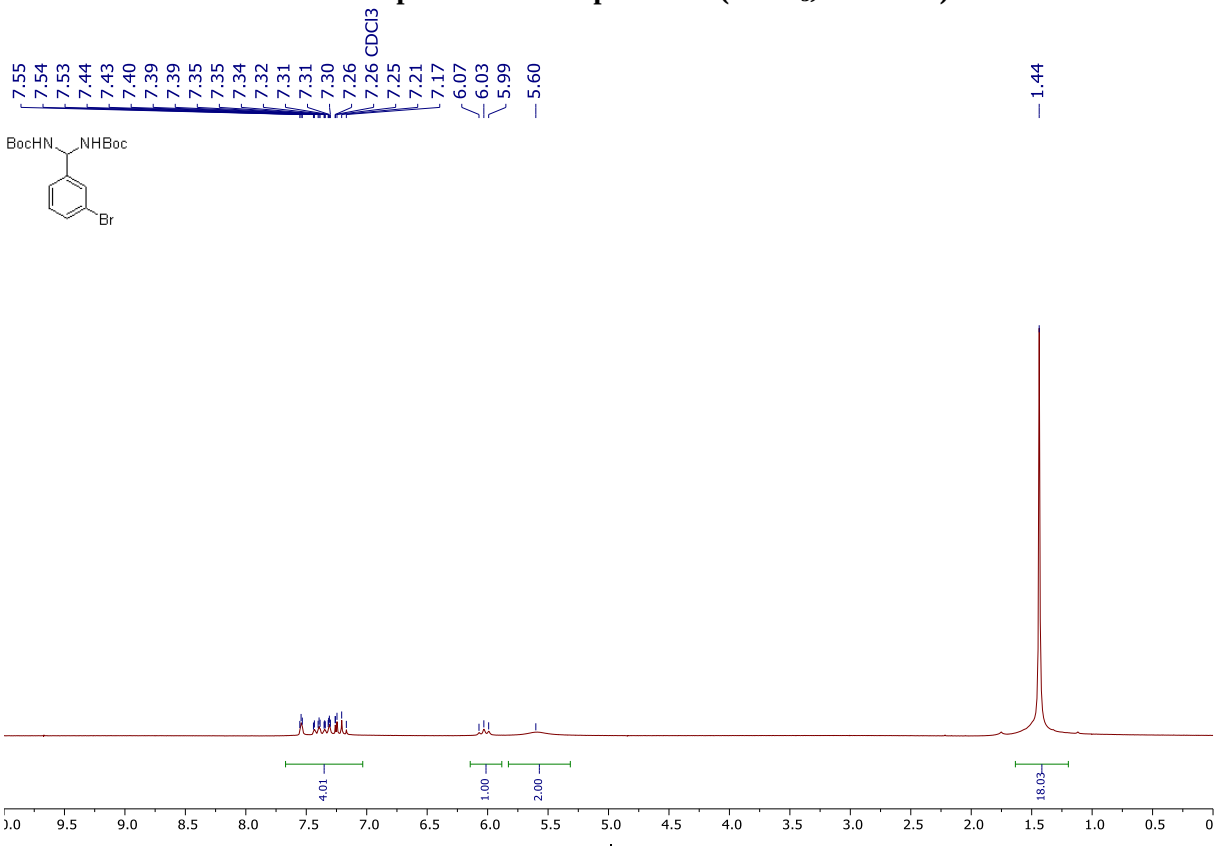
^{1}H NMR spectrum of compound 2j ($CDCl_3$, 400 MHz)



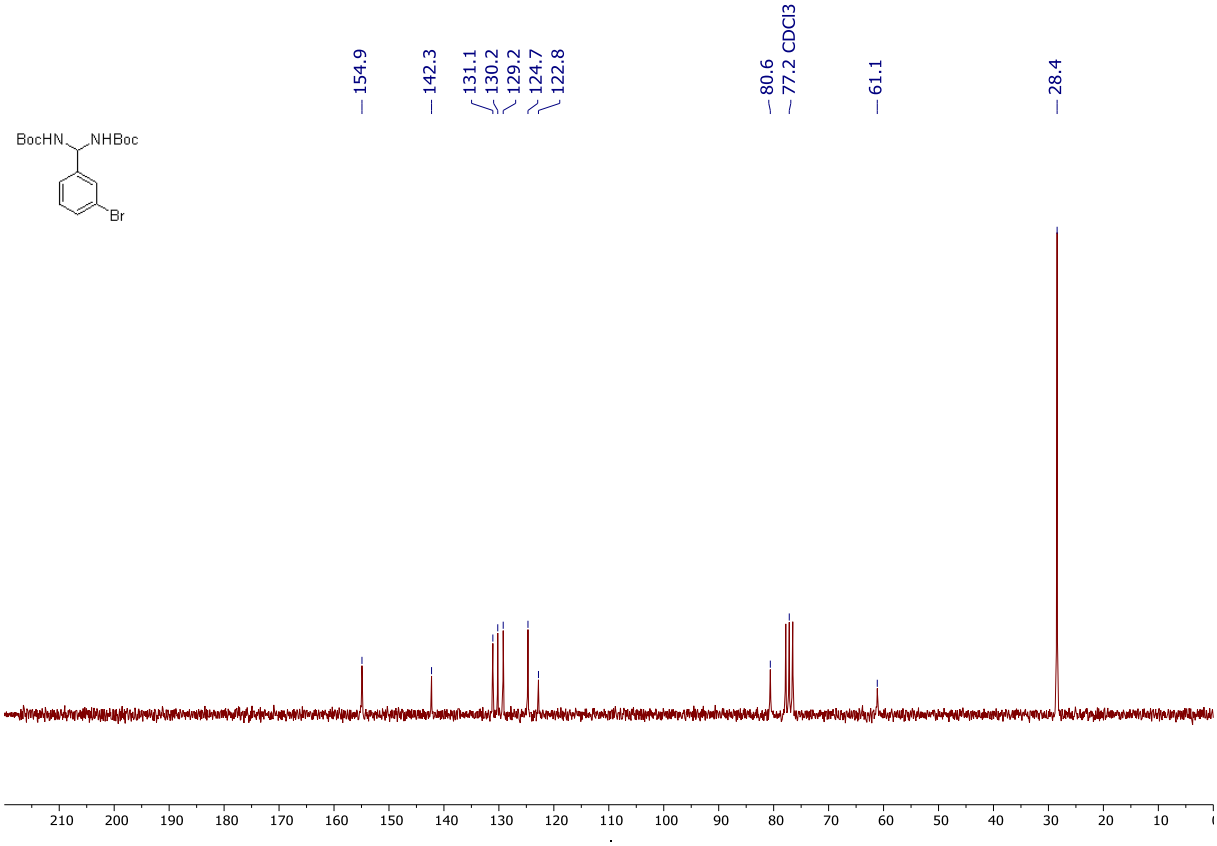
^{13}C NMR spectrum of compound 2j ($CDCl_3$, 100 MHz)



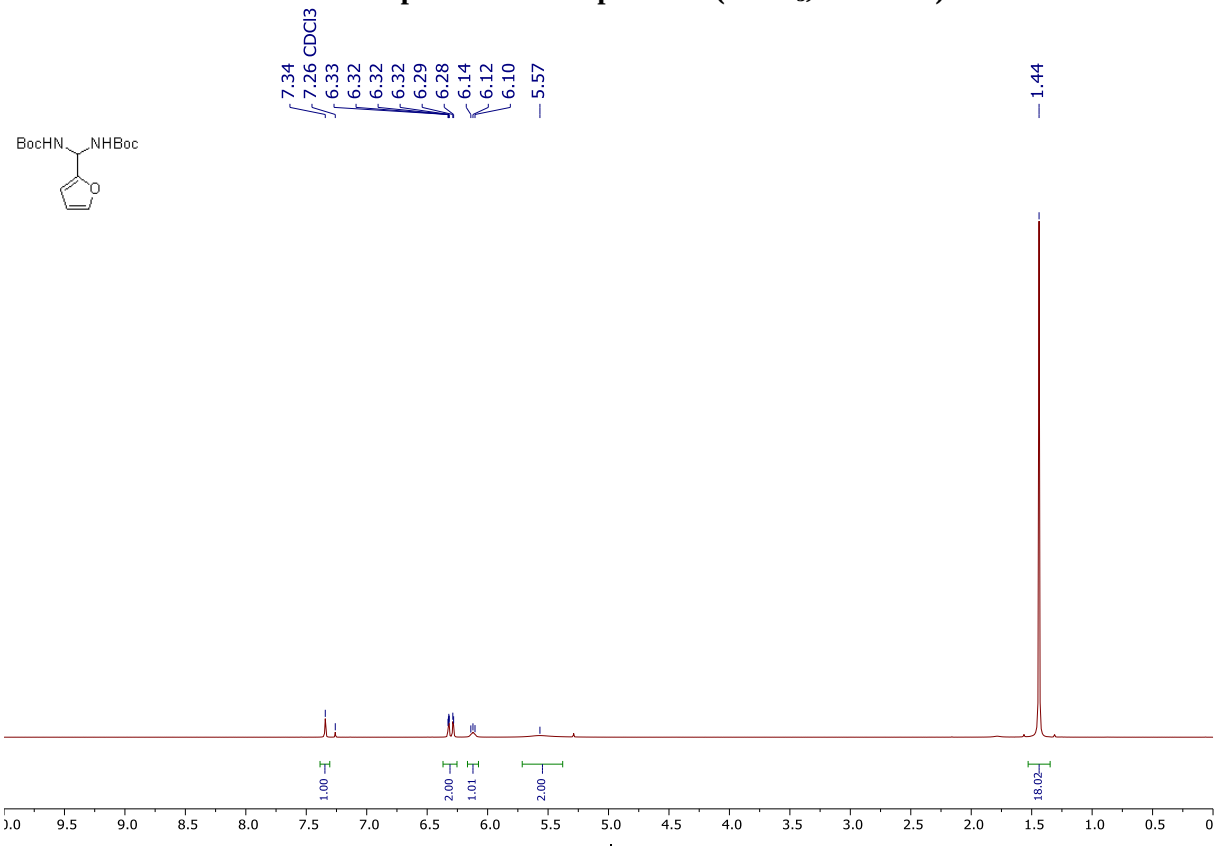
^{1}H NMR spectrum of compound 2k ($CDCl_3$, 200 MHz)



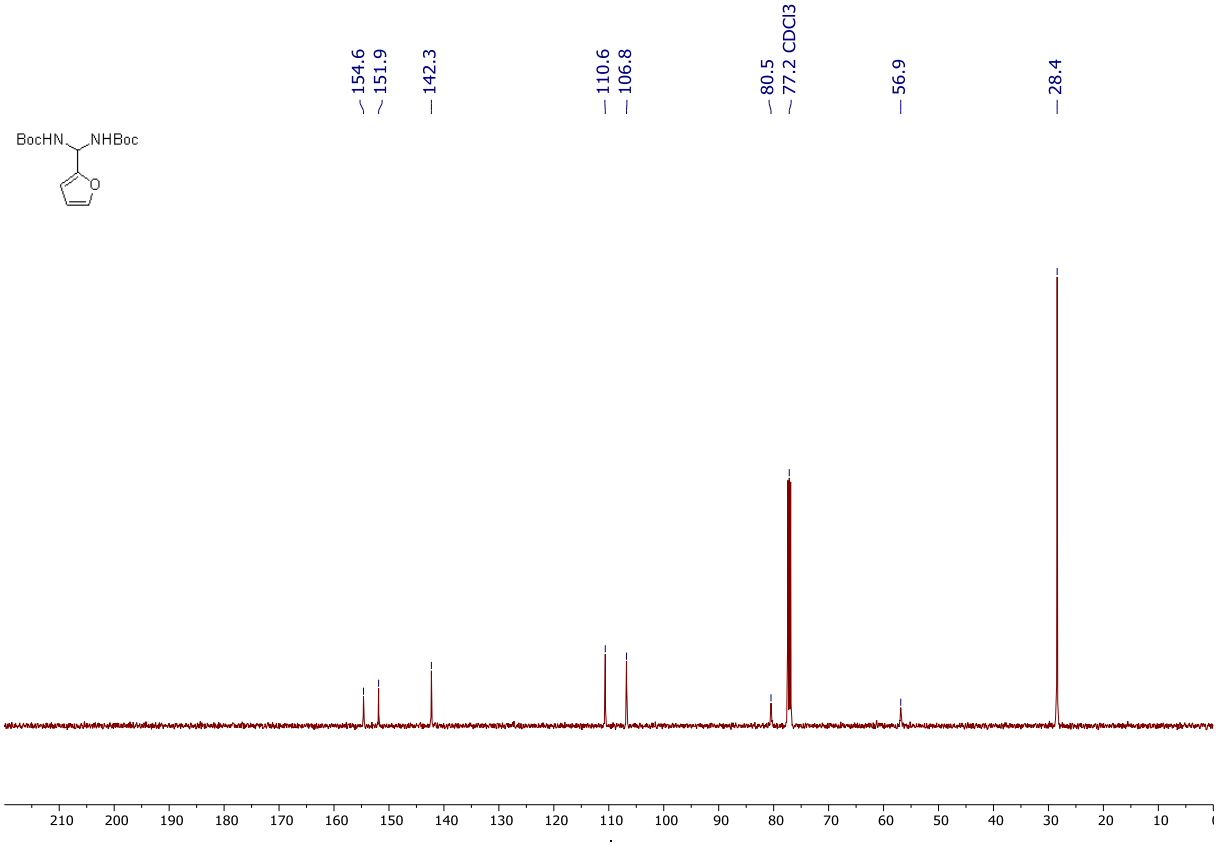
^{13}C NMR spectrum of compound 2k ($CDCl_3$, 100 MHz)



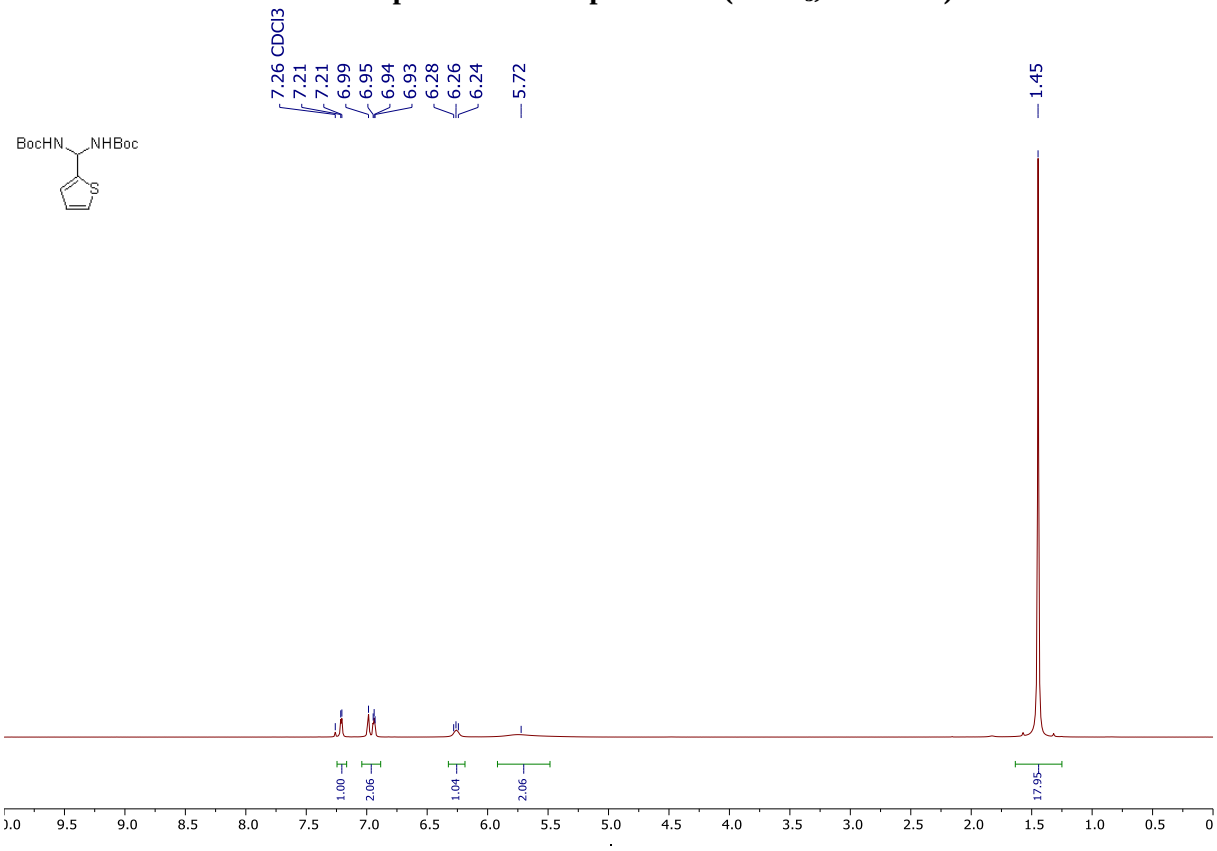
^{1}H NMR spectrum of compound 2l ($CDCl_3$, 400 MHz)



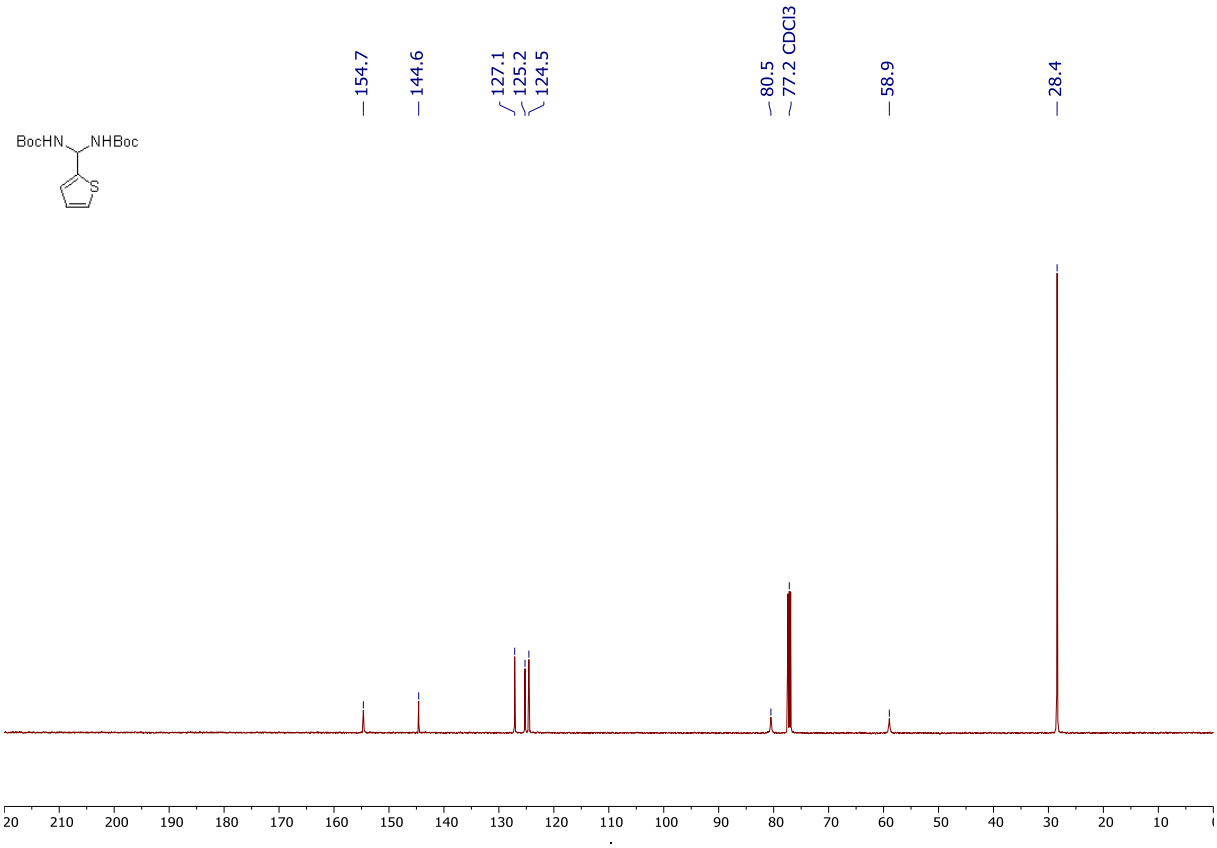
^{13}C NMR spectrum of compound 2l ($CDCl_3$, 100 MHz)



^{1}H NMR spectrum of compound 2m ($CDCl_3$, 400 MHz)

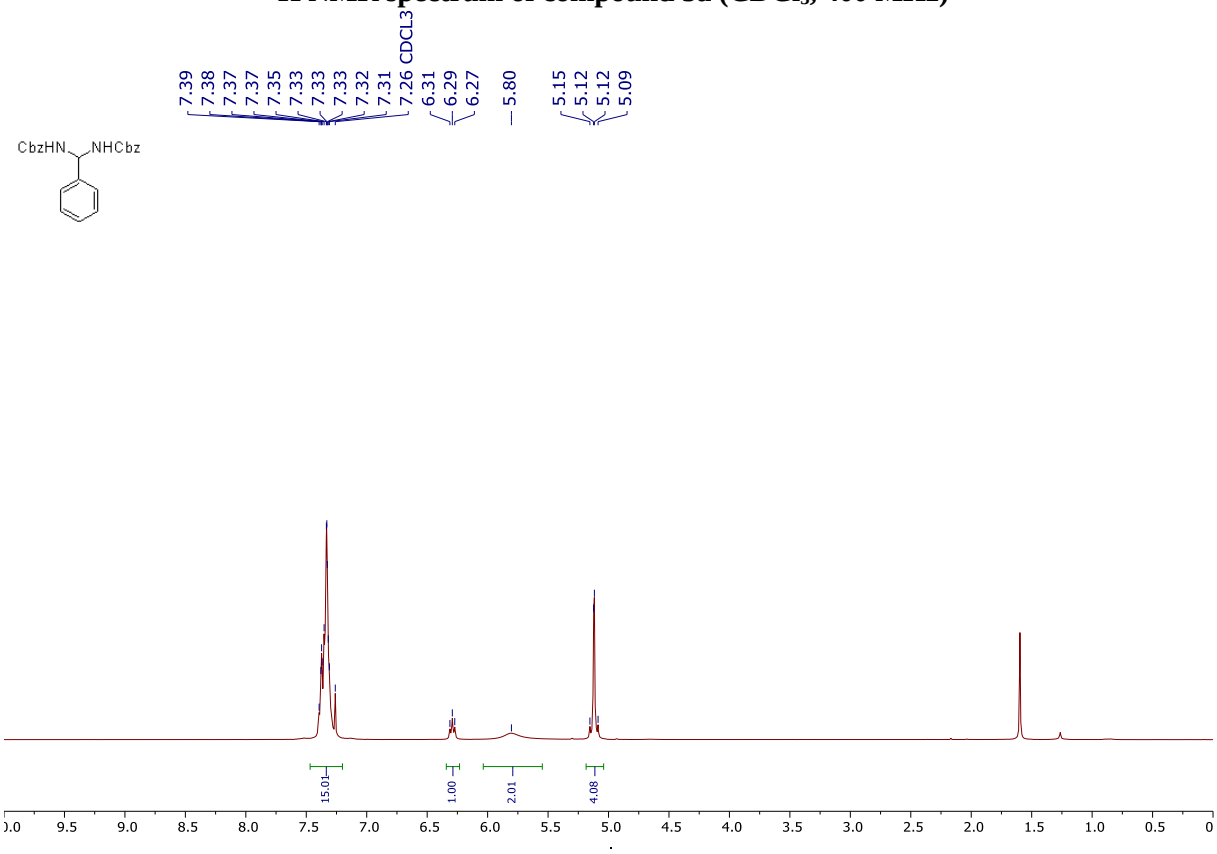


^{13}C NMR spectrum of compound 2m ($CDCl_3$, 100 MHz)

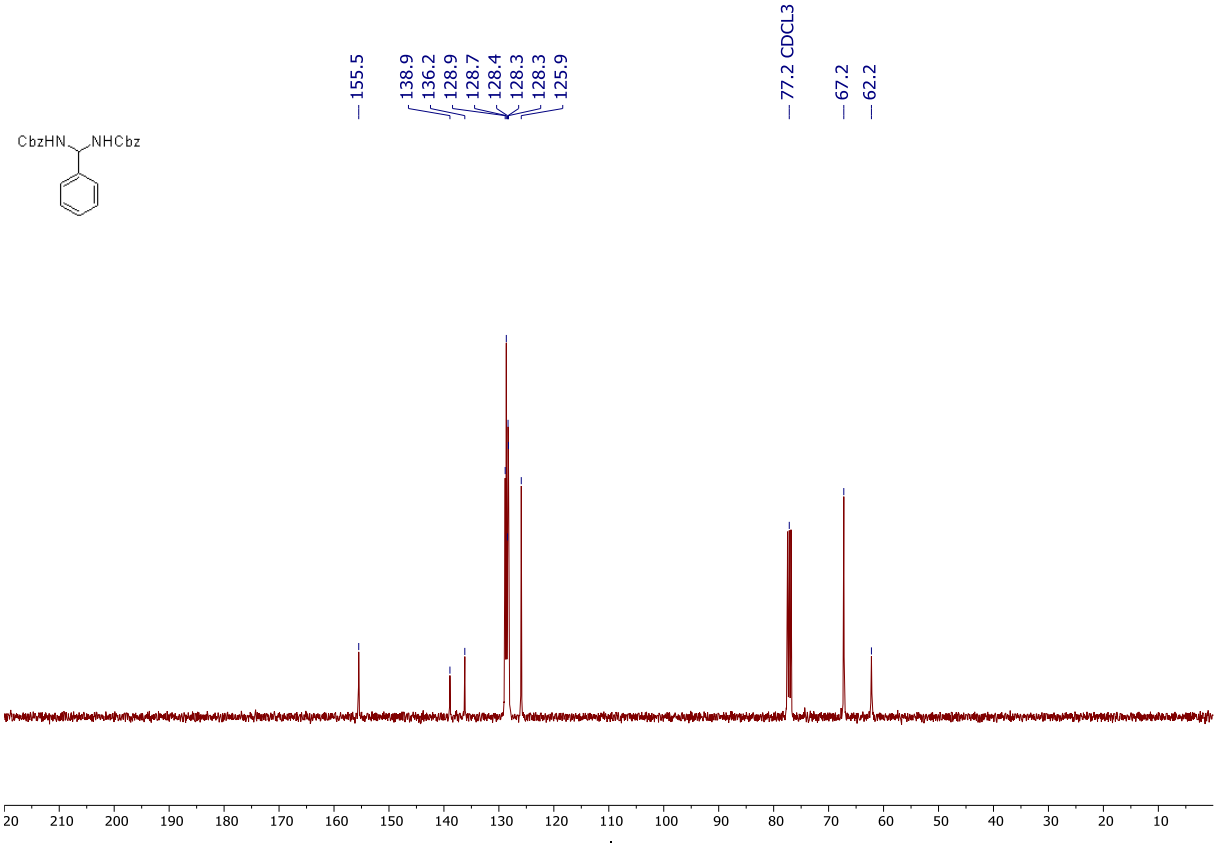


6.4. *N*-Cbz aminals 5a-k

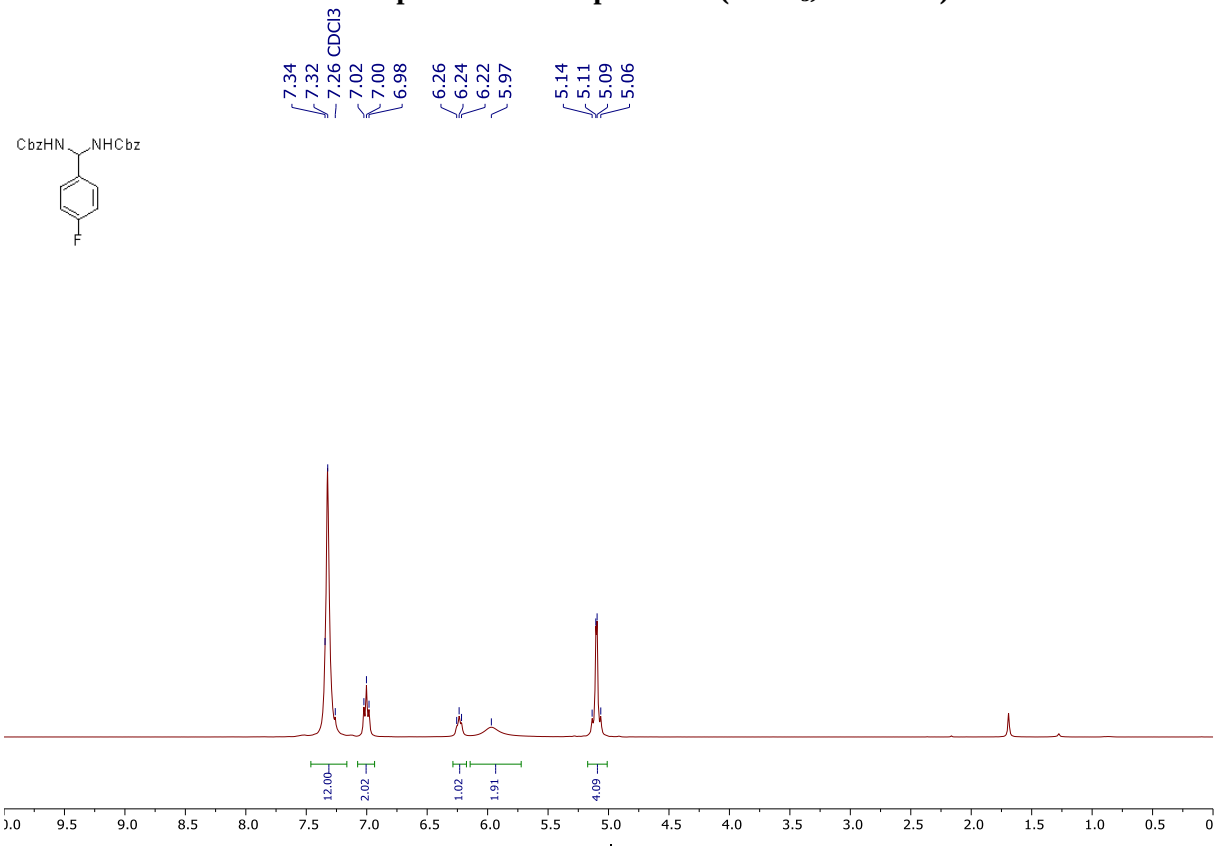
^{1}H NMR spectrum of compound 5a ($CDCl_3$, 400 MHz)



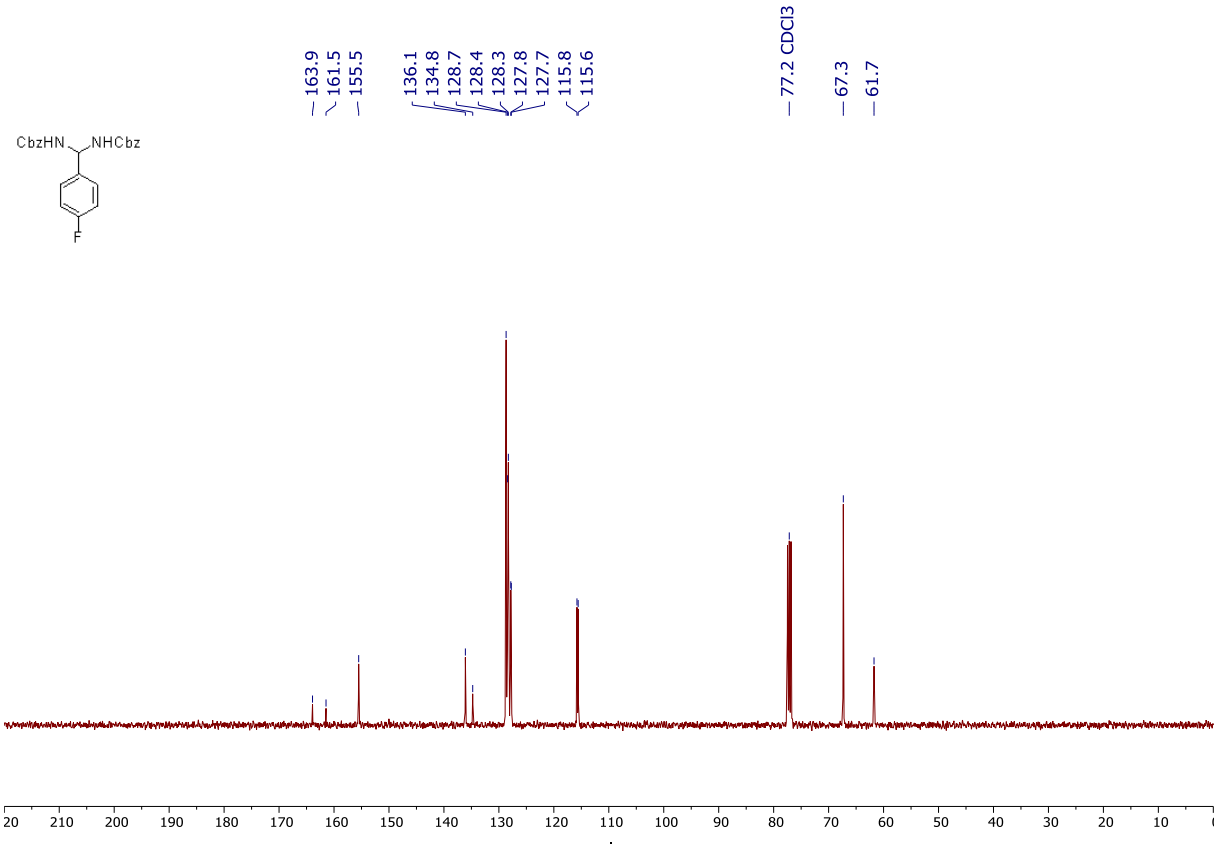
^{13}C NMR spectrum of compound 5a ($CDCl_3$, 100 MHz)



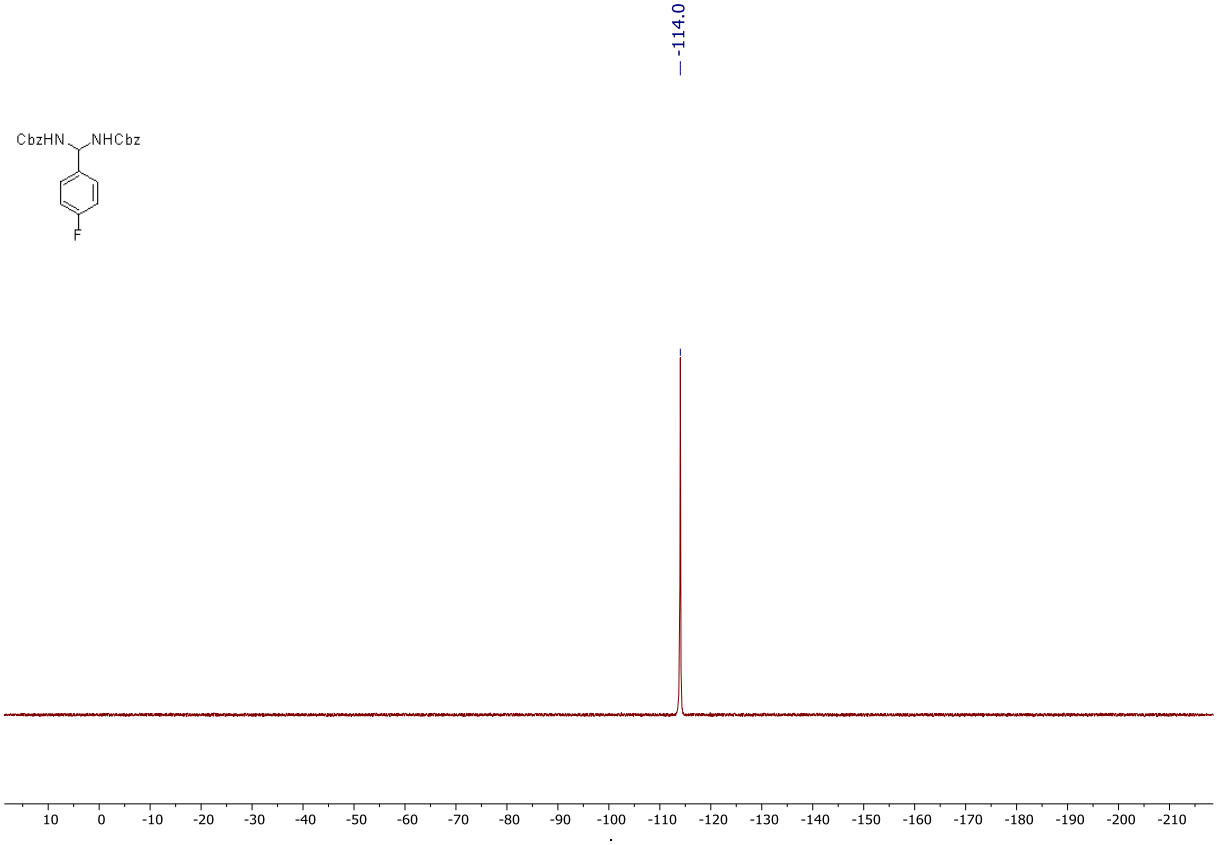
^{1}H NMR spectrum of compound 5b ($CDCl_3$, 400 MHz)



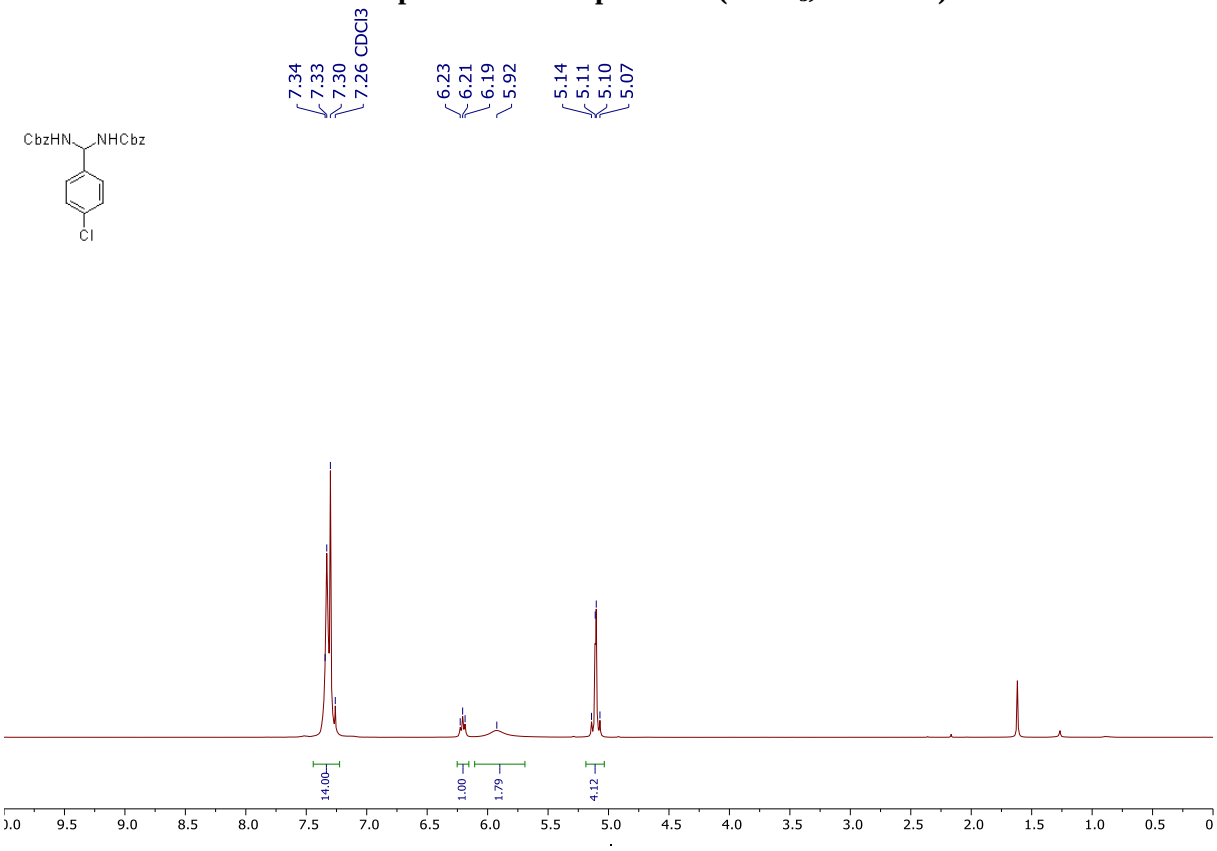
^{13}C NMR spectrum of compound 5b ($CDCl_3$, 100 MHz)



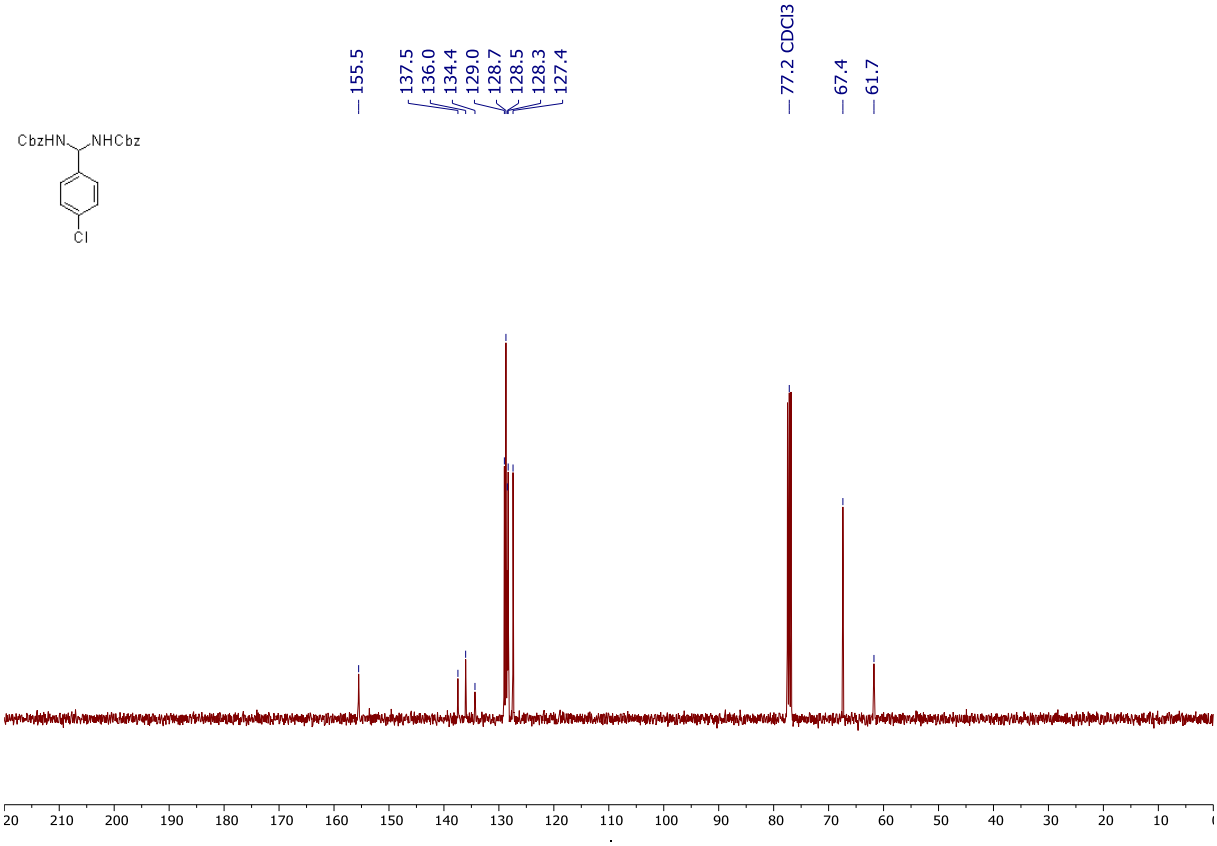
^{19}F NMR spectrum of compound 5b ($CDCl_3$, 376 MHz)



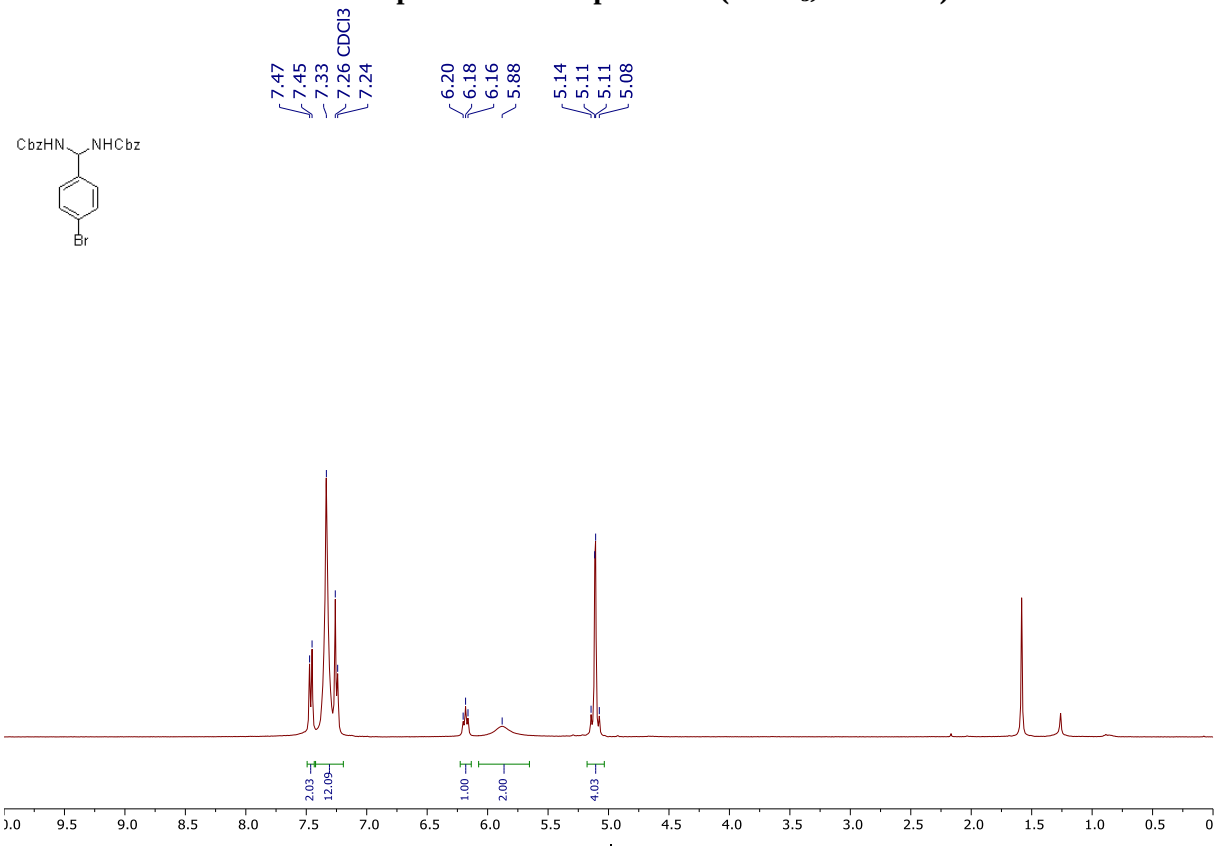
^{1}H NMR spectrum of compound 5c ($CDCl_3$, 400 MHz)



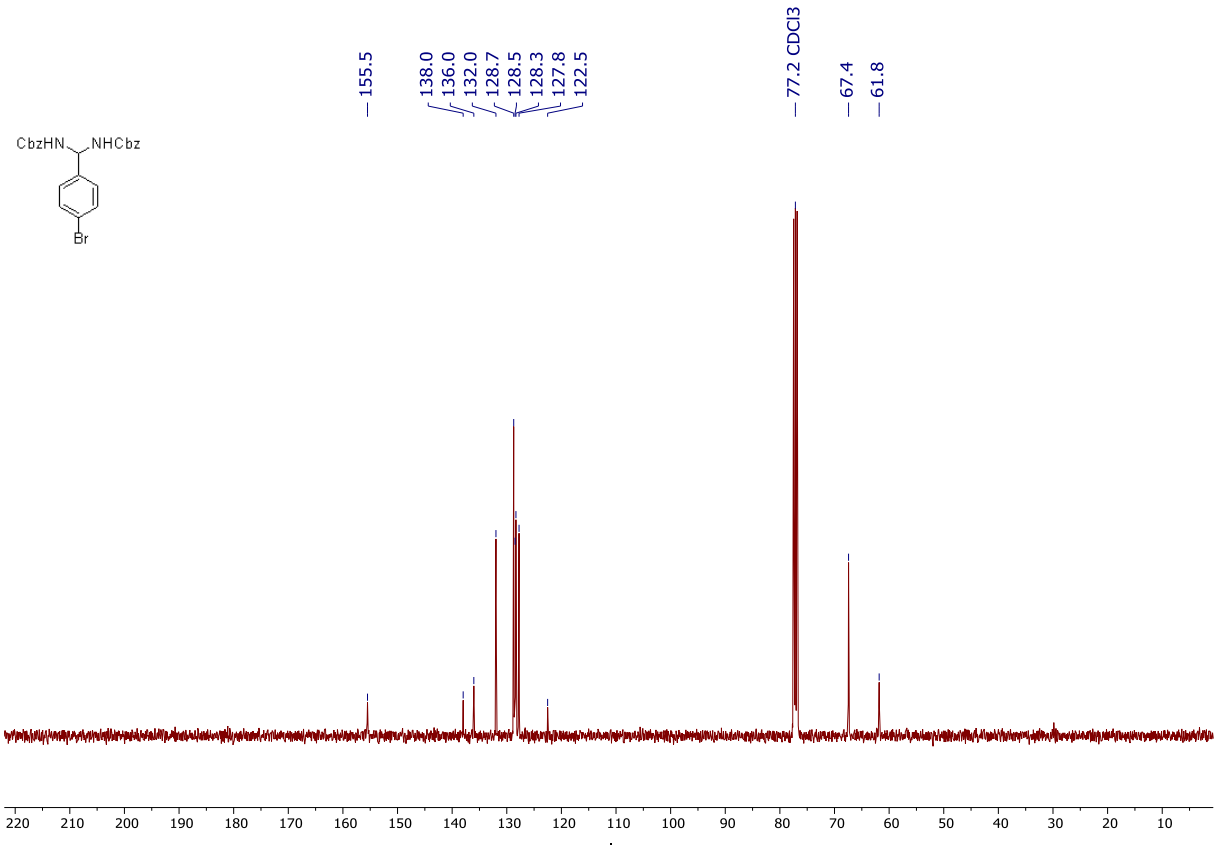
^{13}C NMR spectrum of compound 5c ($CDCl_3$, 100 MHz)



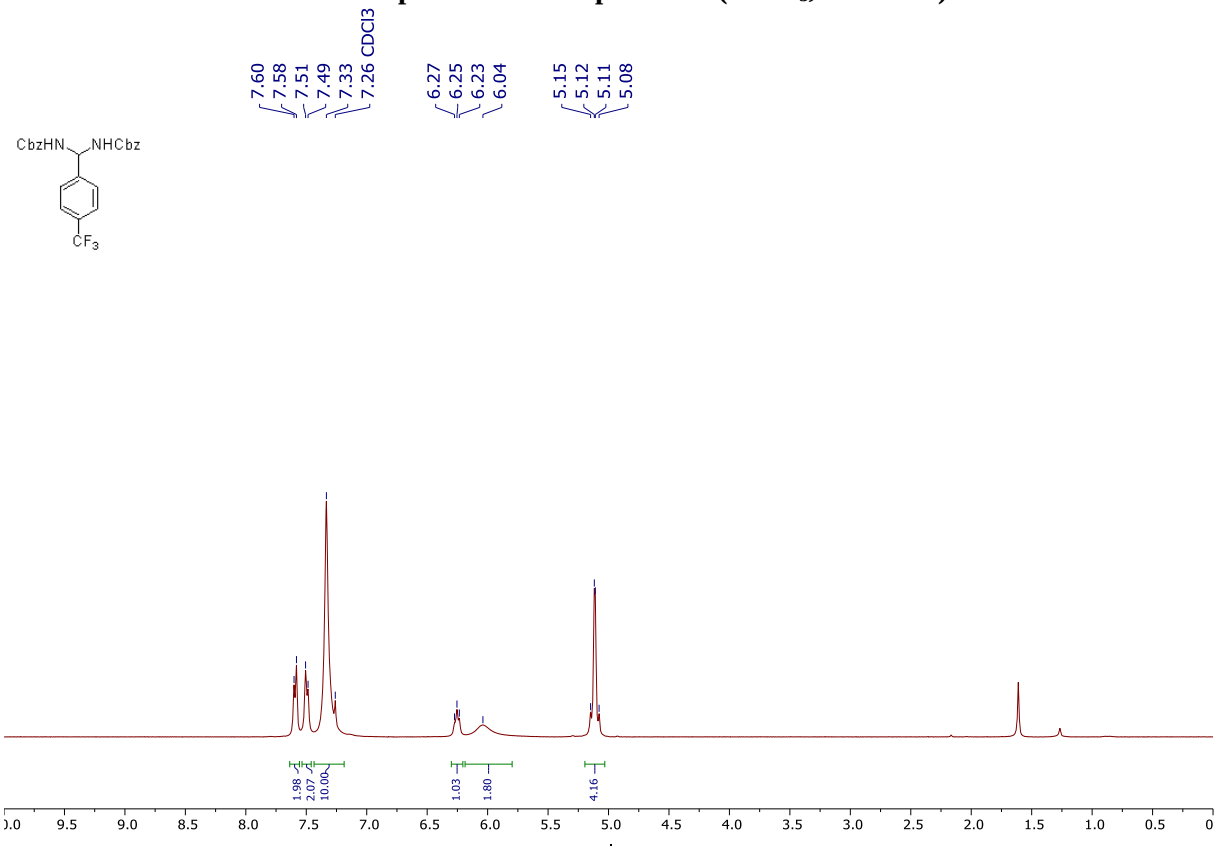
^{1}H NMR spectrum of compound 5d ($CDCl_3$, 400 MHz)



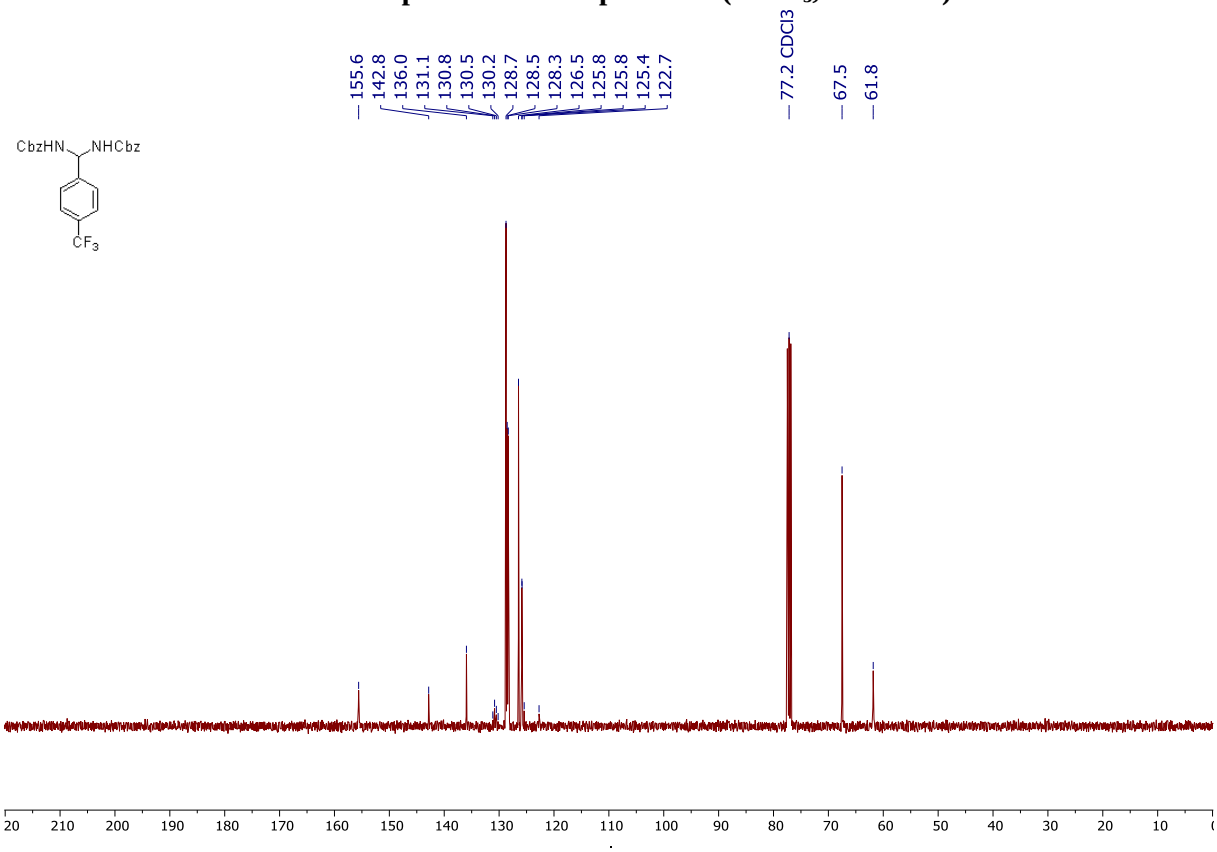
^{13}C NMR spectrum of compound 5d ($CDCl_3$, 100 MHz)



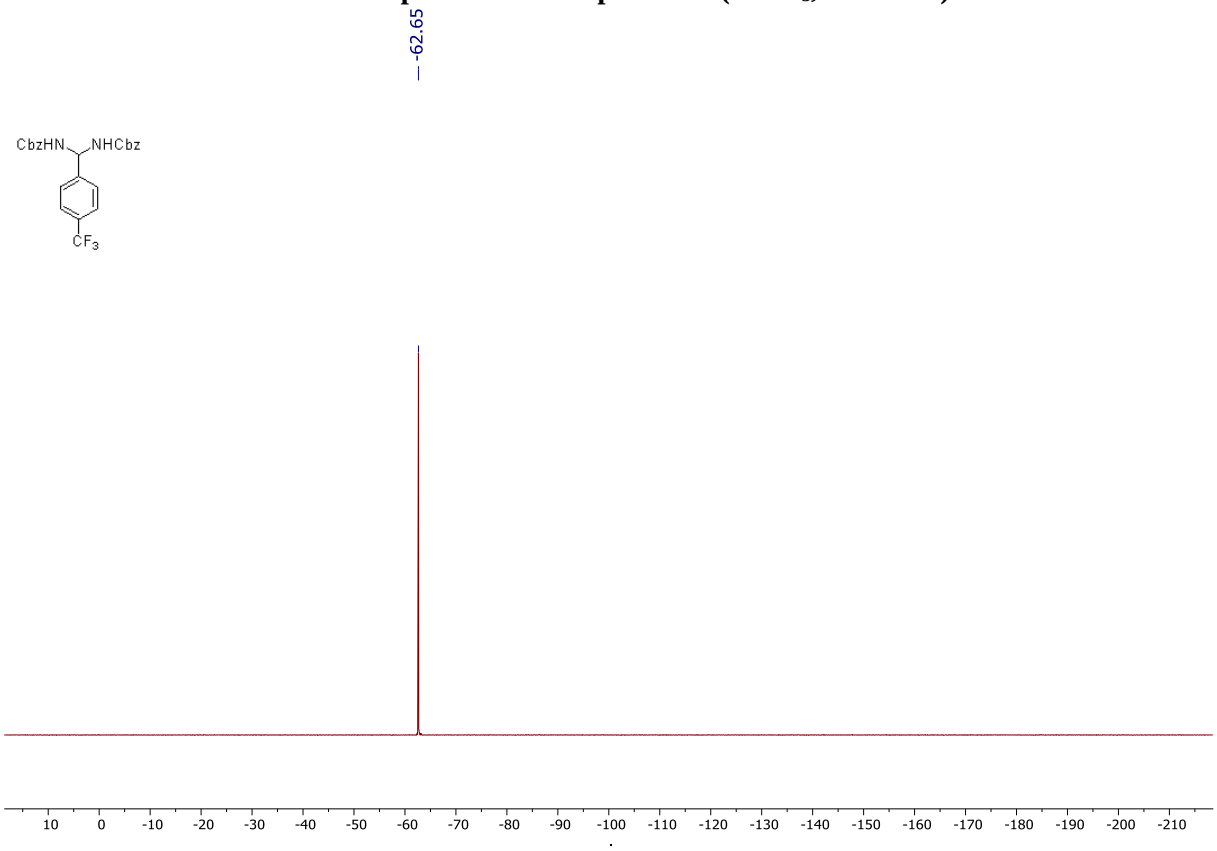
^{1}H NMR spectrum of compound 5e ($CDCl_3$, 400 MHz)



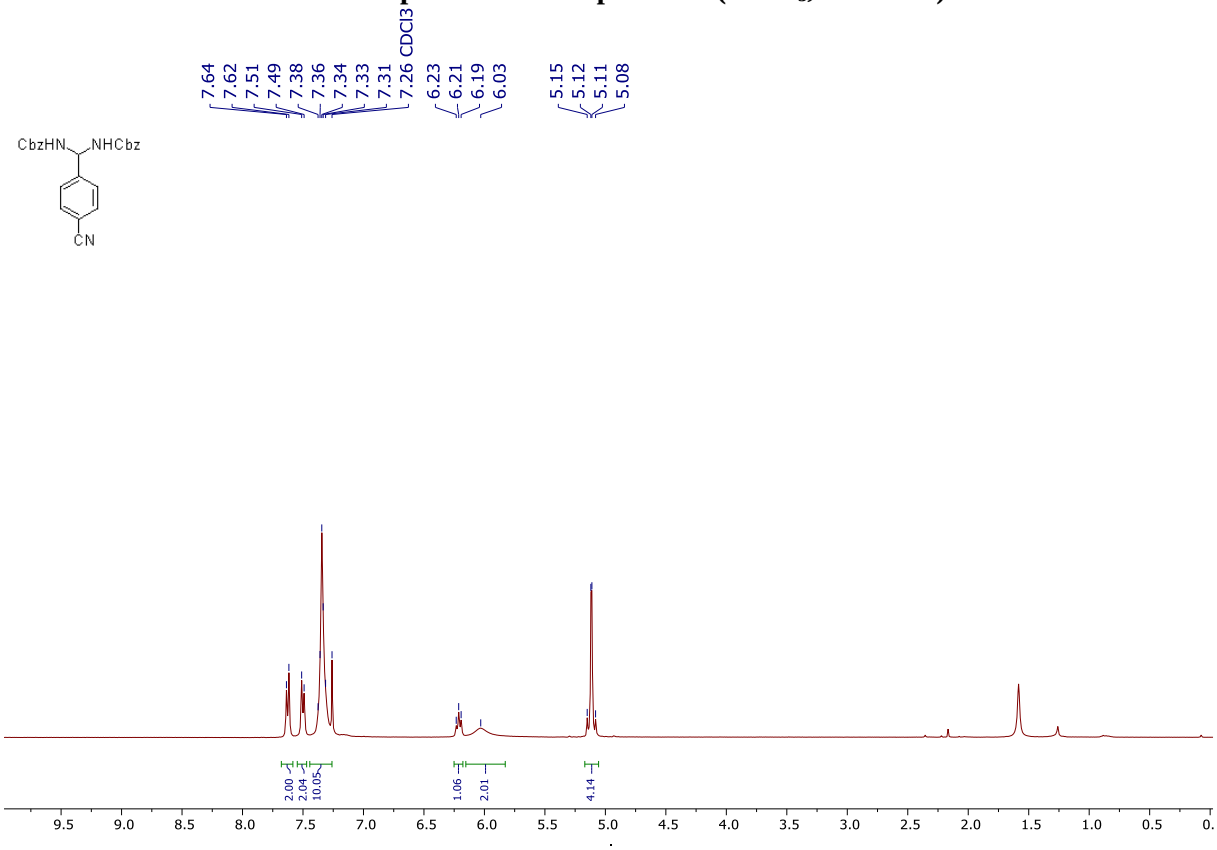
^{13}C NMR spectrum of compound 5e ($CDCl_3$, 100 MHz)



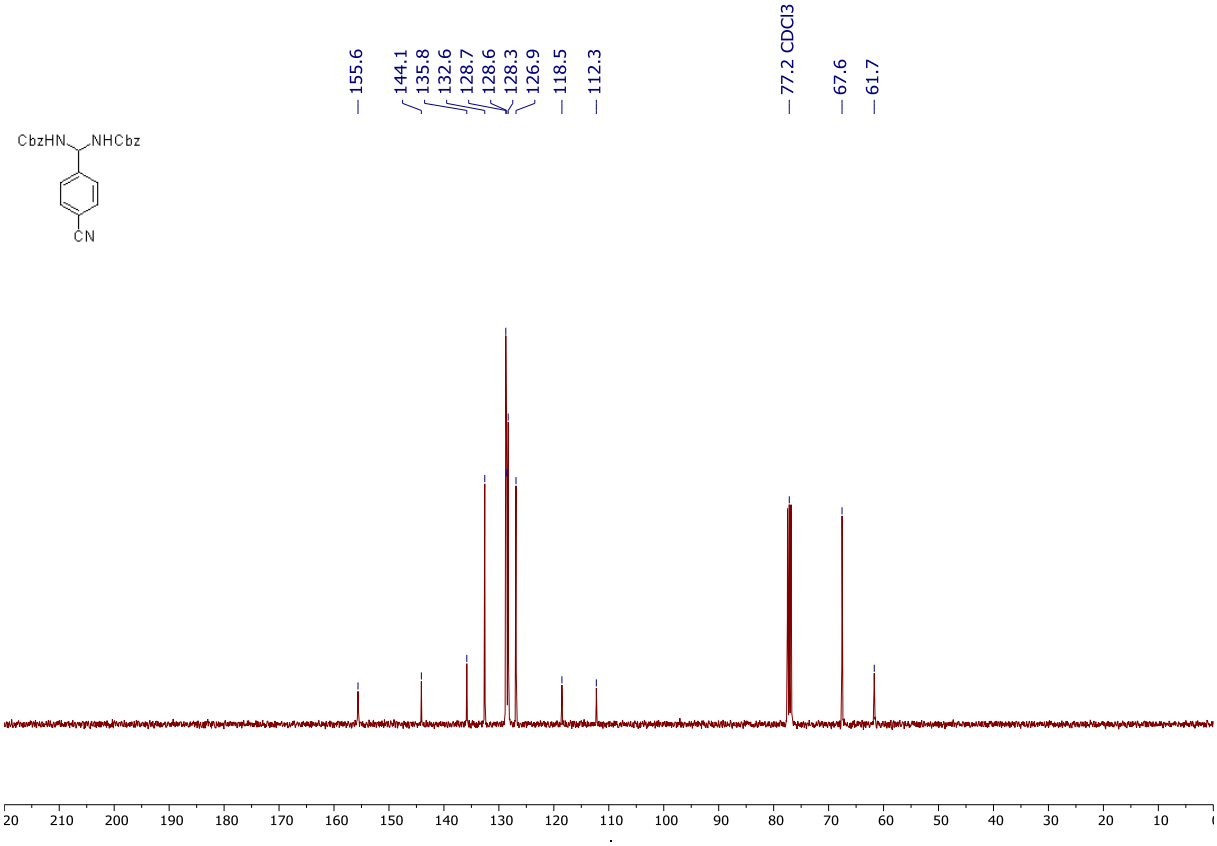
^{19}F NMR spectrum of compound 5e ($CDCl_3$, 376 MHz)



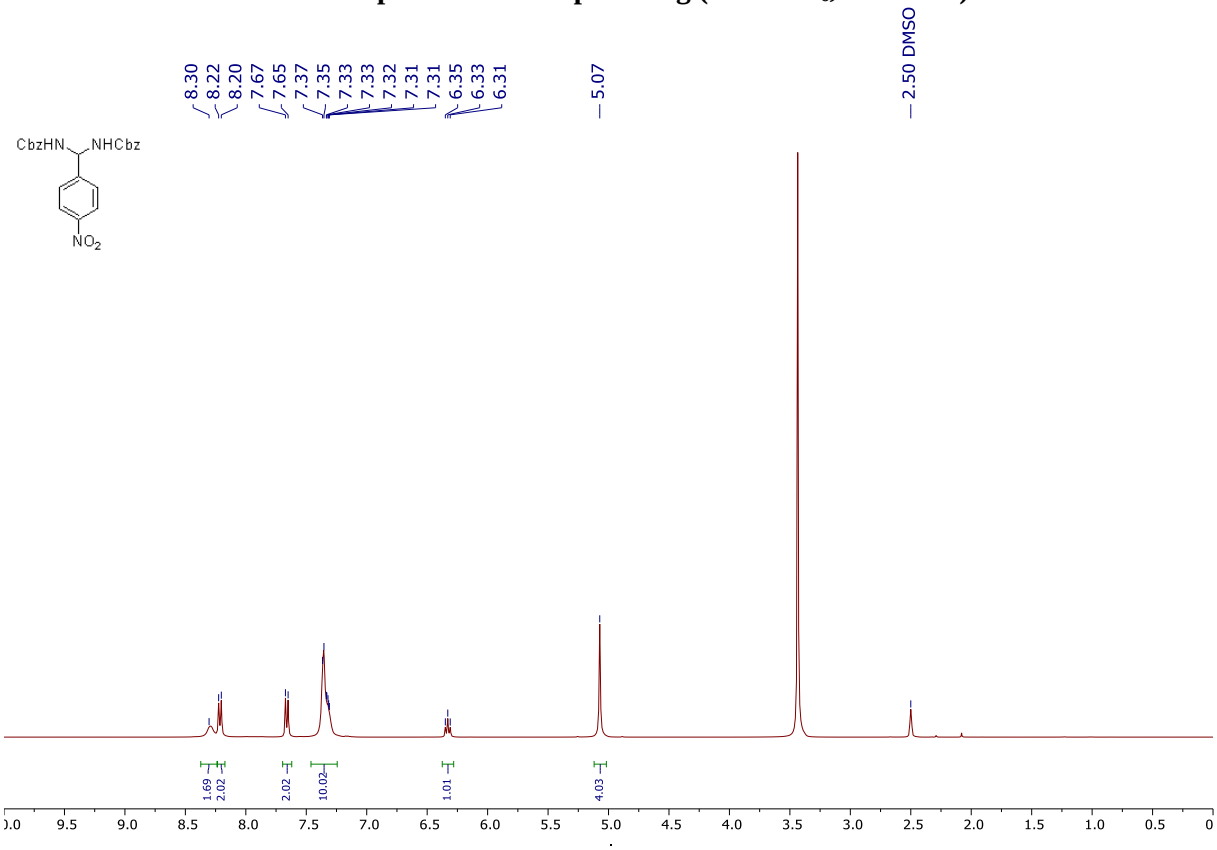
^{1}H NMR spectrum of compound 5f ($CDCl_3$, 400 MHz)



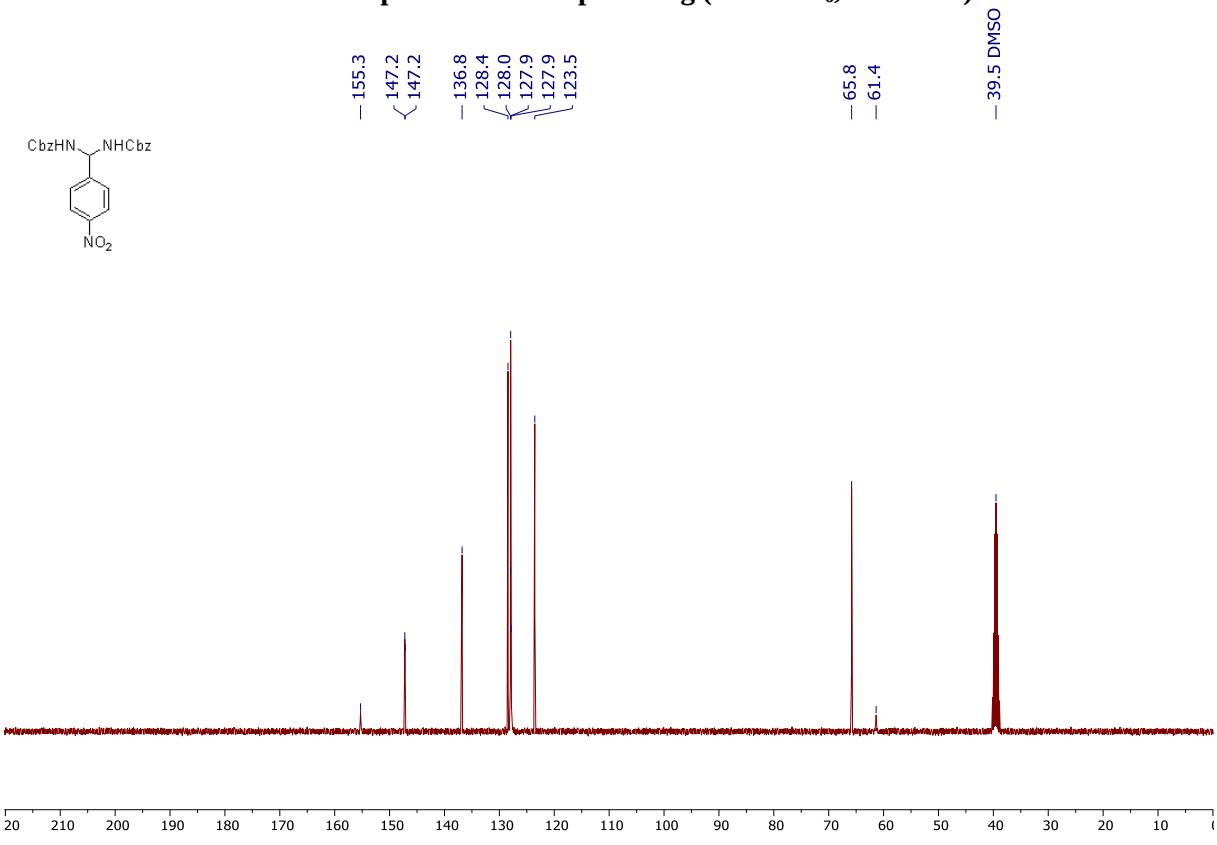
^{13}C NMR spectrum of compound 5f ($CDCl_3$, 100 MHz)



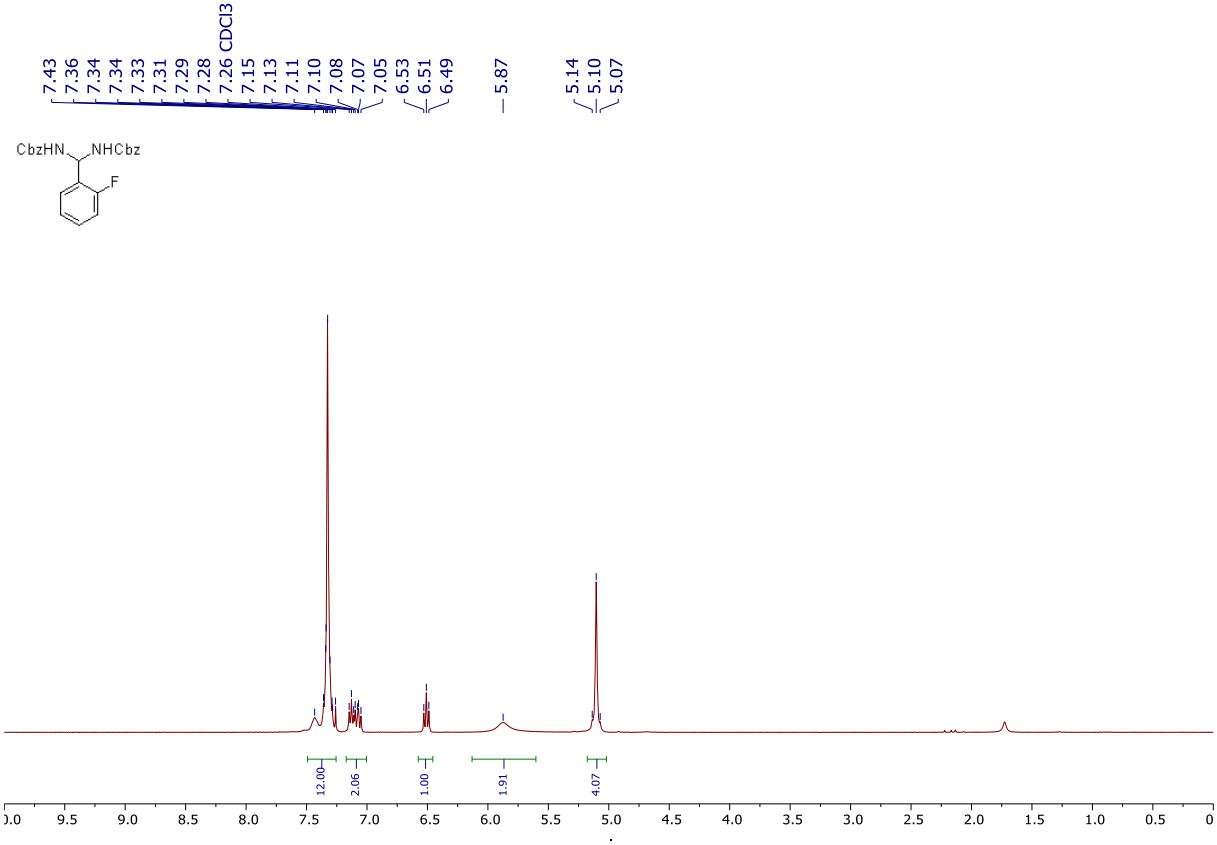
^{1}H NMR spectrum of compound 5g (DMSO-d_6, 400 MHz)



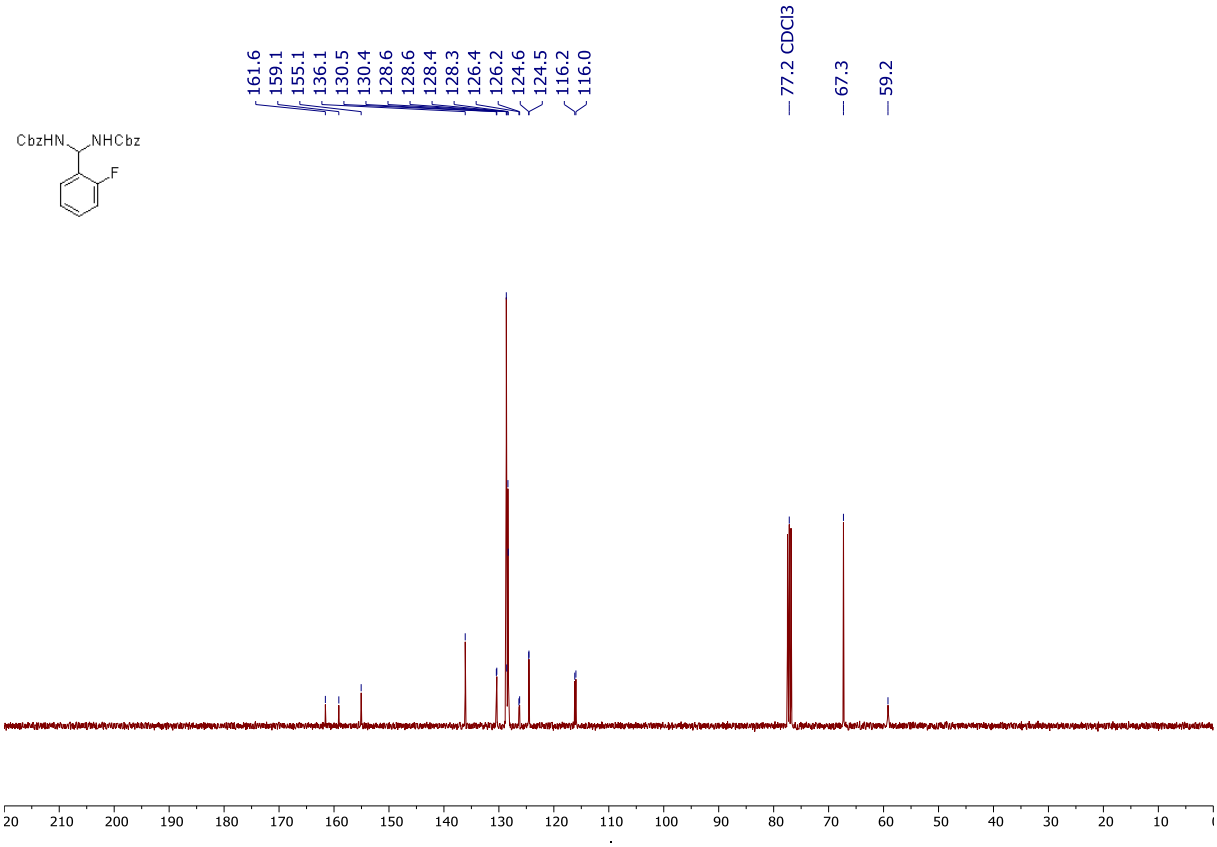
^{13}C NMR spectrum of compound 5g (DMSO-d_6, 100 MHz)



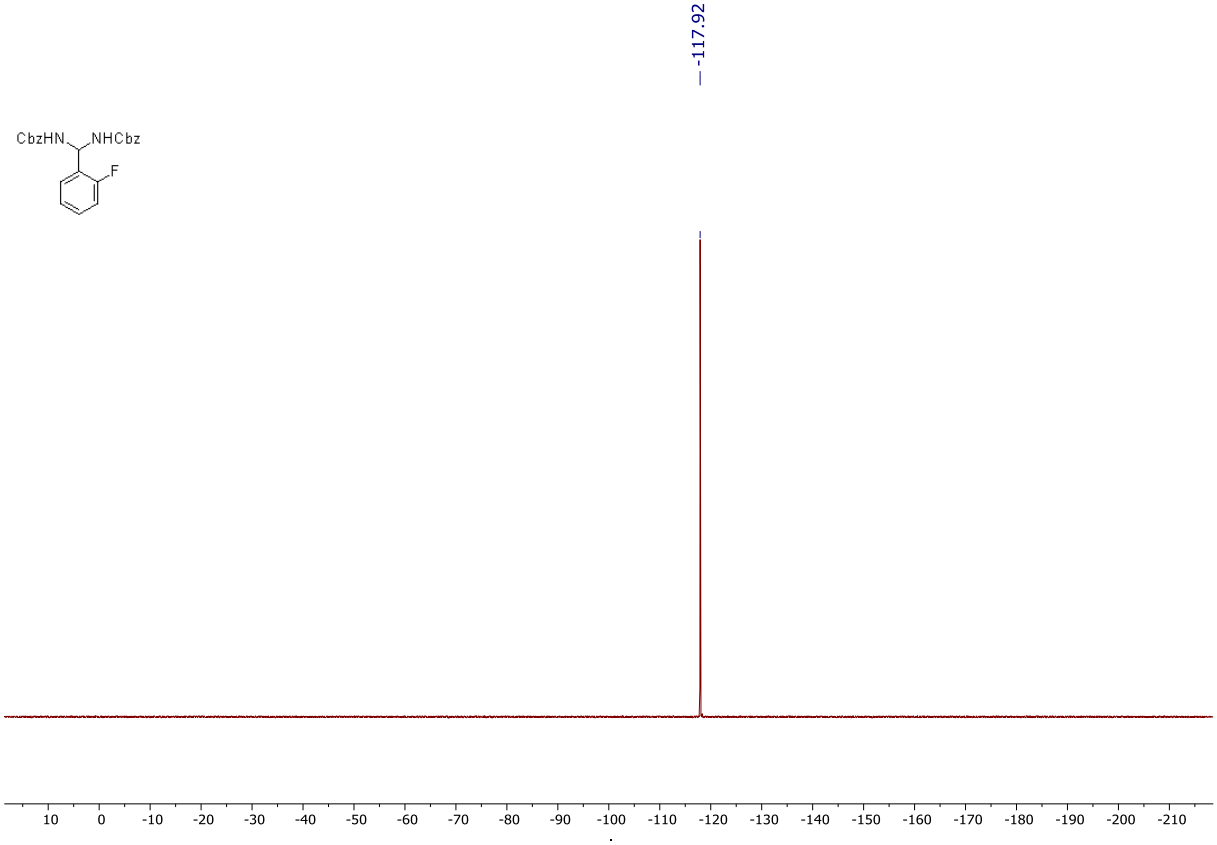
^{1}H NMR spectrum of compound 5h ($CDCl_3$, 400 MHz)



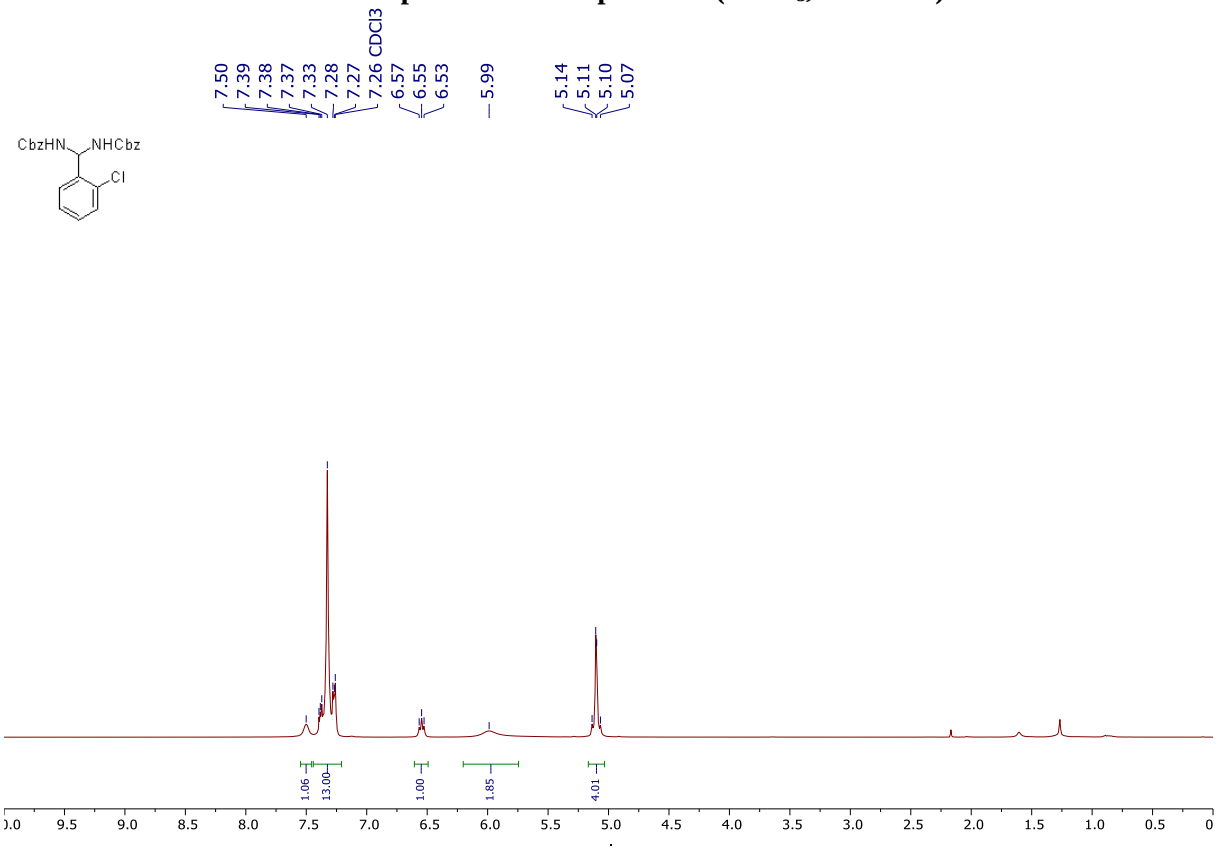
^{13}C NMR spectrum of compound 5h ($CDCl_3$, 100 MHz)



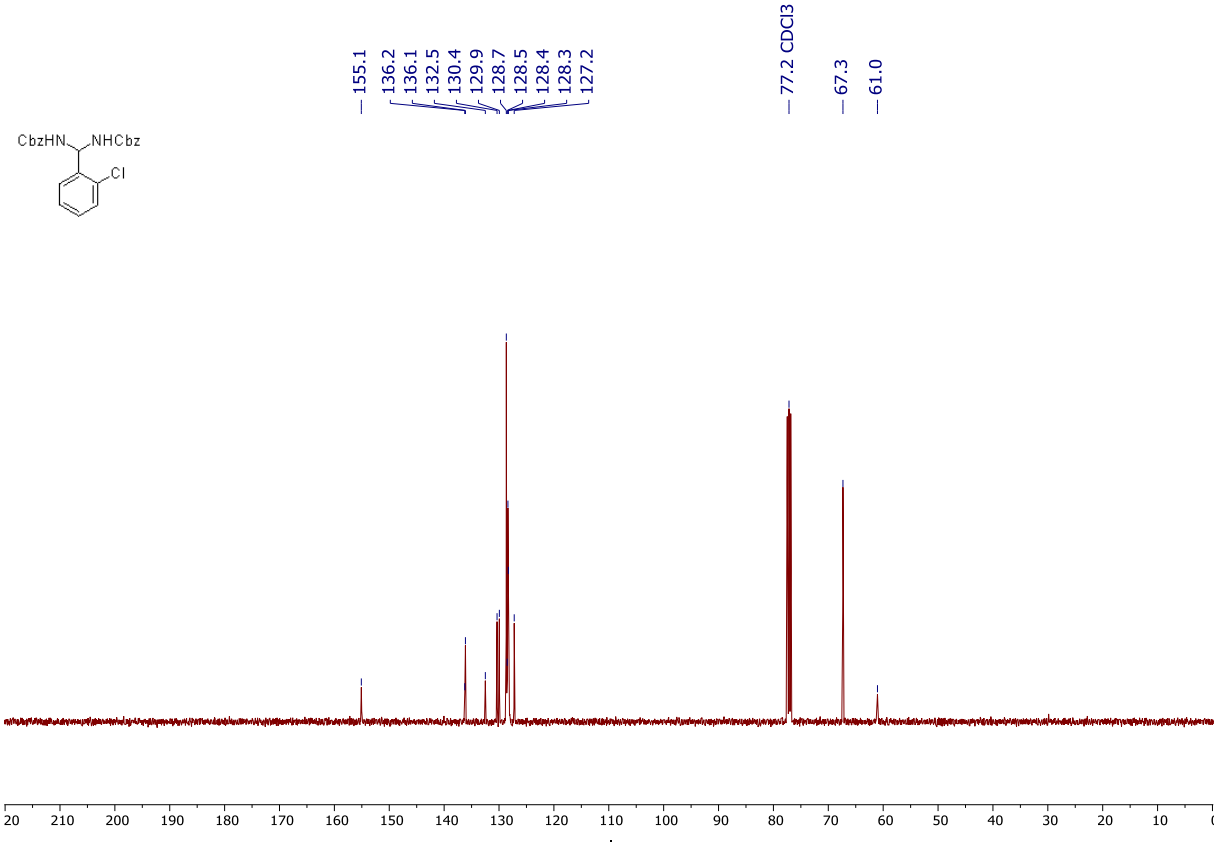
^{19}F NMR spectrum of compound 5h ($CDCl_3$, 376 MHz)



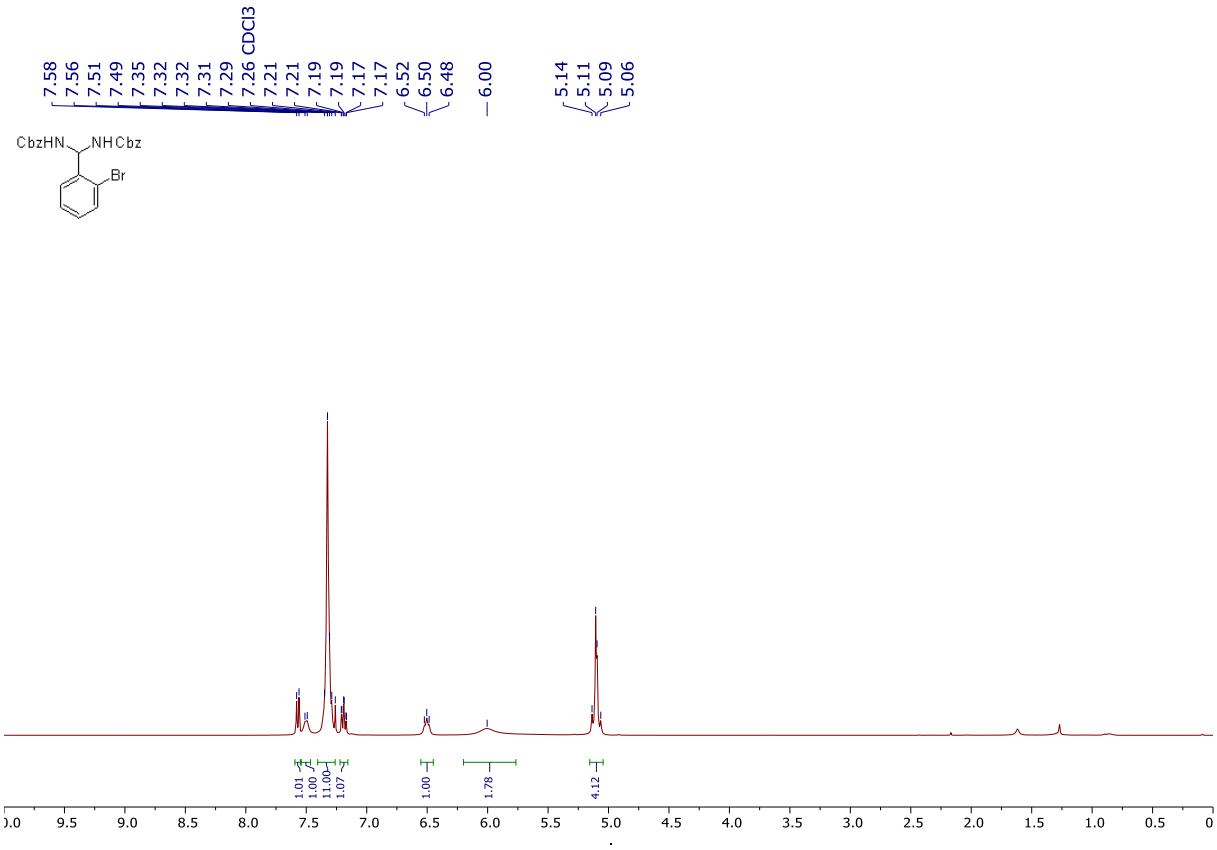
^{1}H NMR spectrum of compound 5i ($CDCl_3$, 400 MHz)



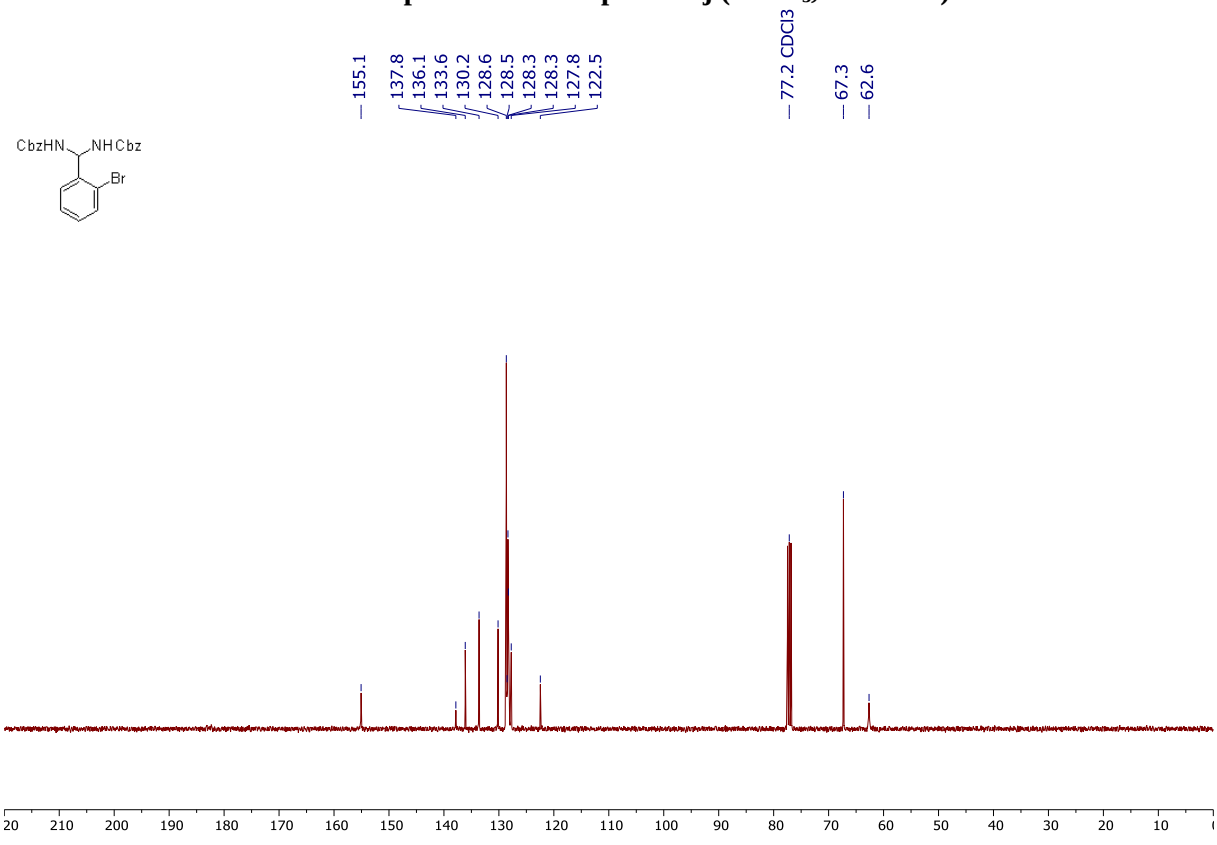
^{13}C NMR spectrum of compound 5i ($CDCl_3$, 100 MHz)



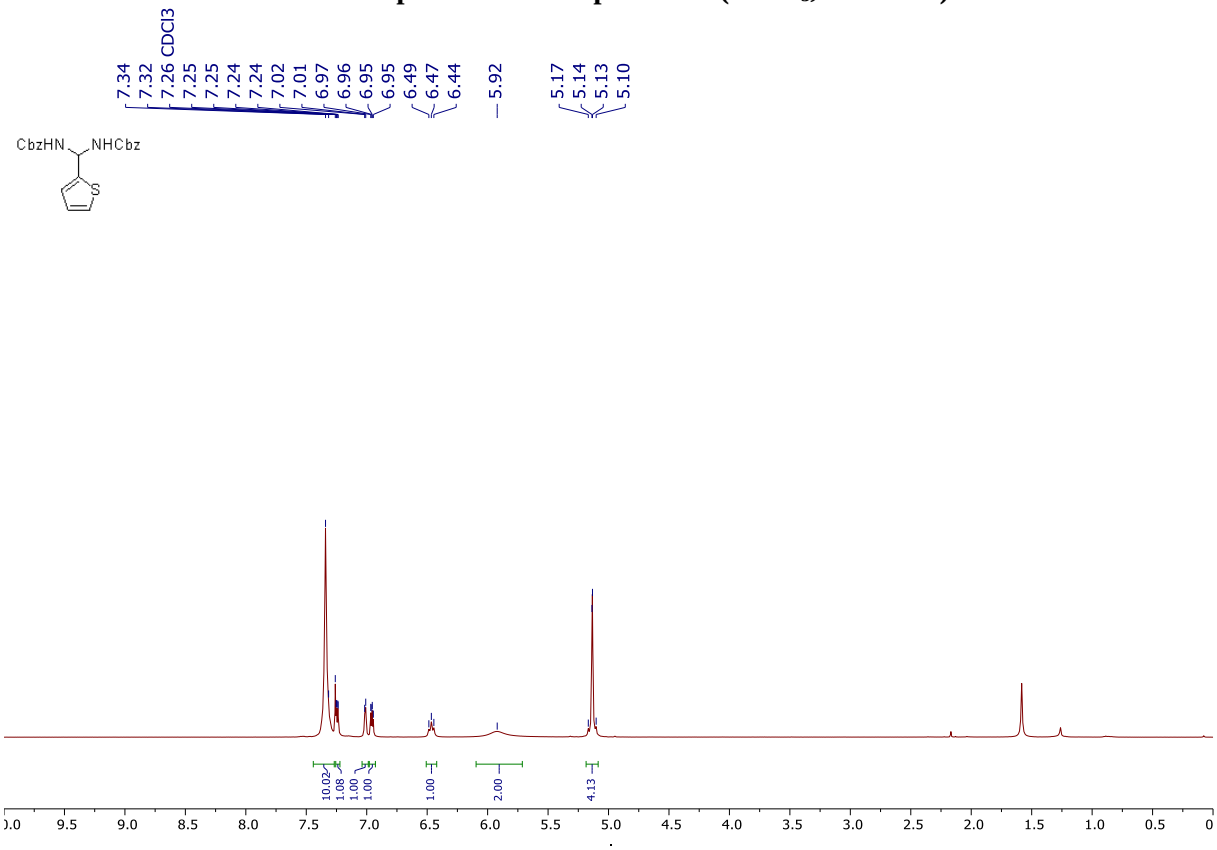
^{1}H NMR spectrum of compound 5j ($CDCl_3$, 400 MHz)



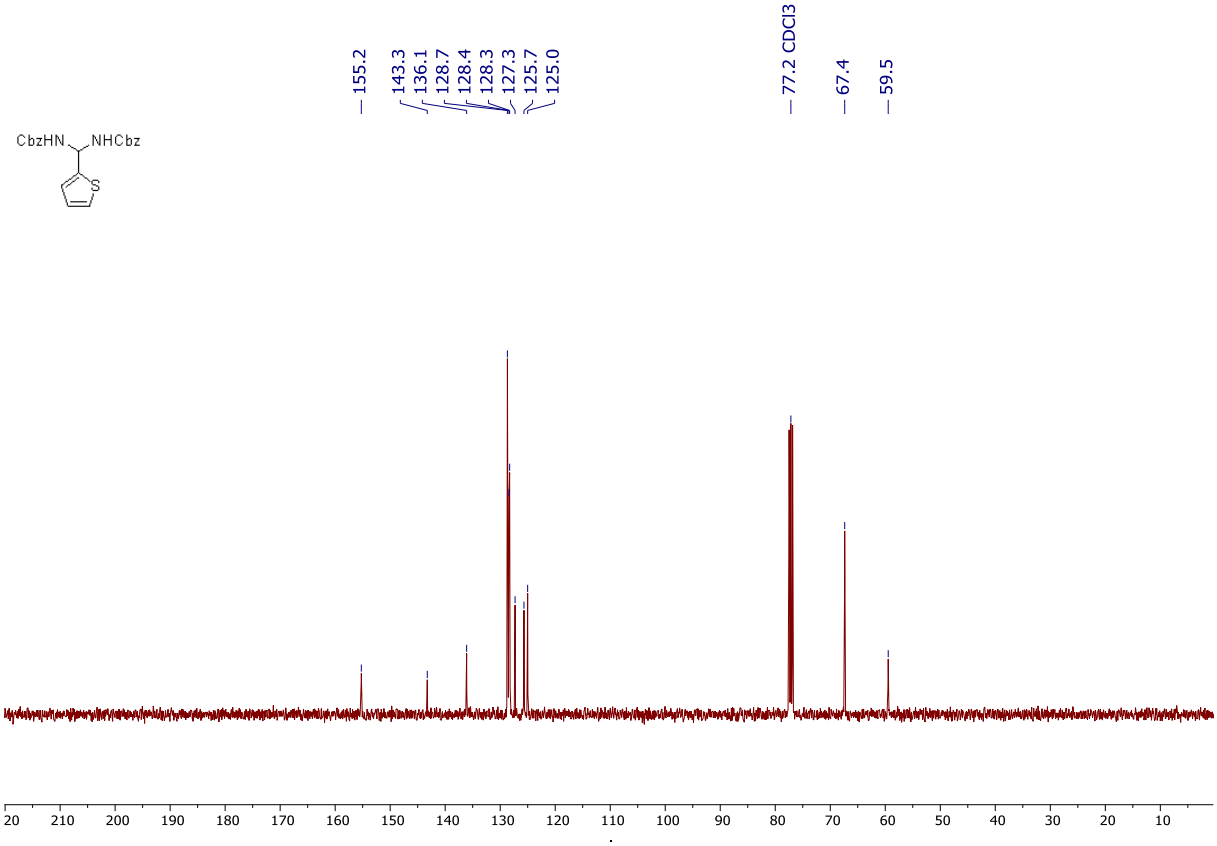
^{13}C NMR spectrum of compound 5j ($CDCl_3$, 100 MHz)



^{1}H NMR spectrum of compound 5k ($CDCl_3$, 400 MHz)

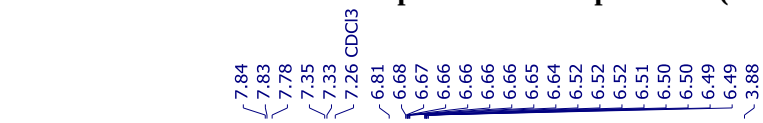


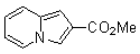
^{13}C NMR spectrum of compound 5k ($CDCl_3$, 100 MHz)

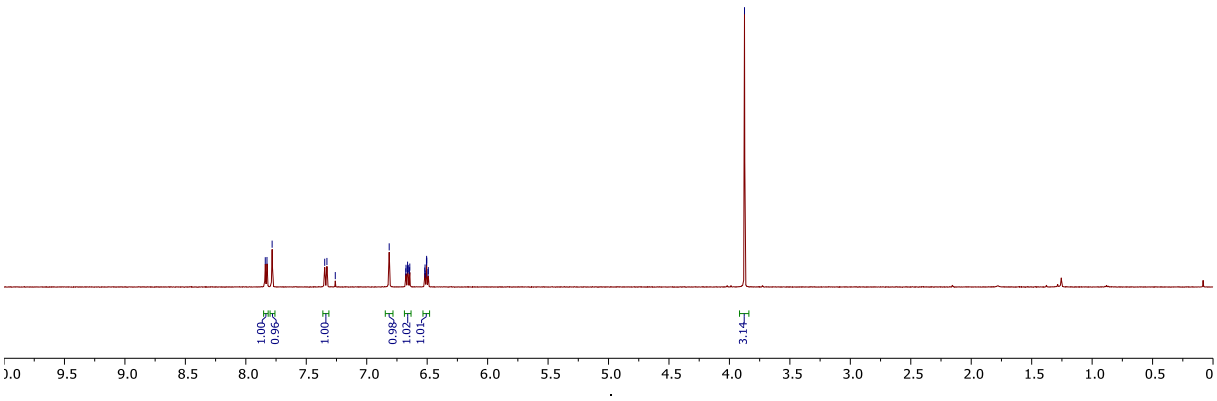


6.5. Indolizines 1a-d

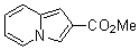
^{1}H NMR spectrum of compound 1a ($CDCl_3$, 500 MHz)

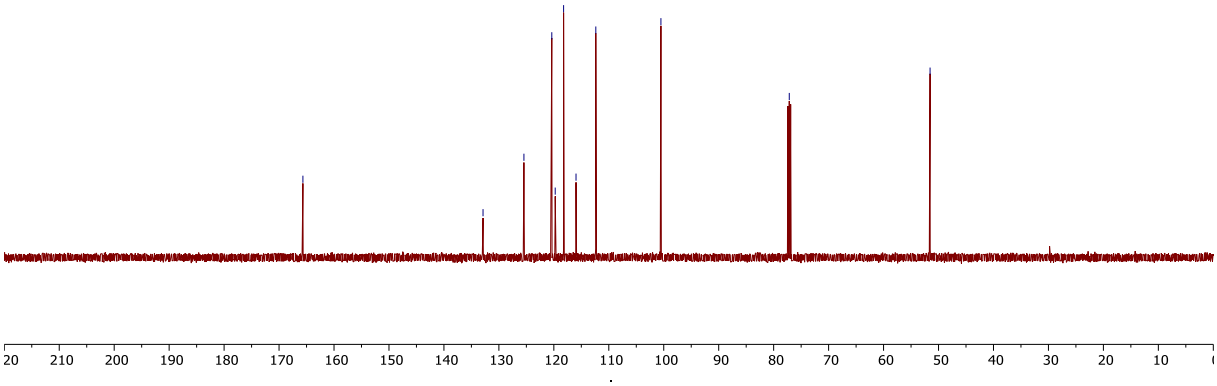




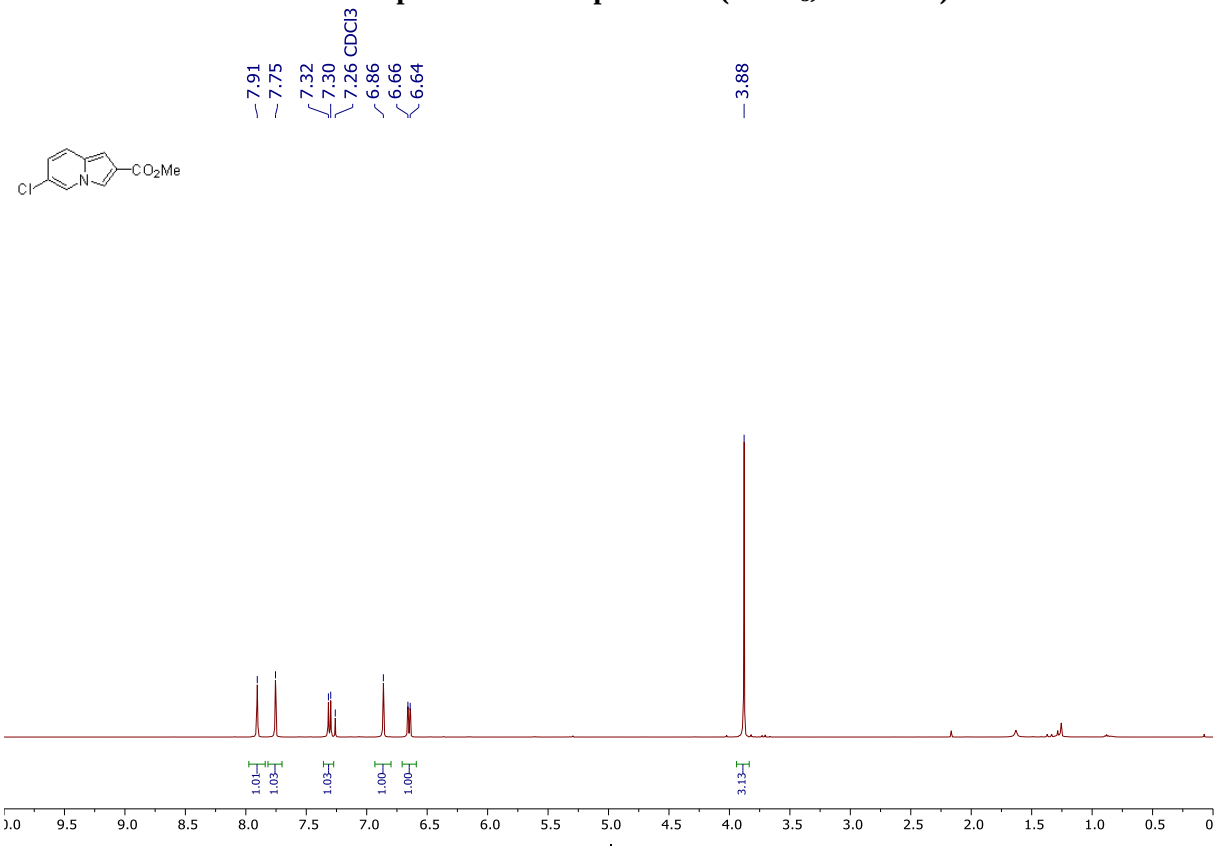


^{13}C NMR spectrum of compound 1a ($CDCl_3$, 126 MHz)

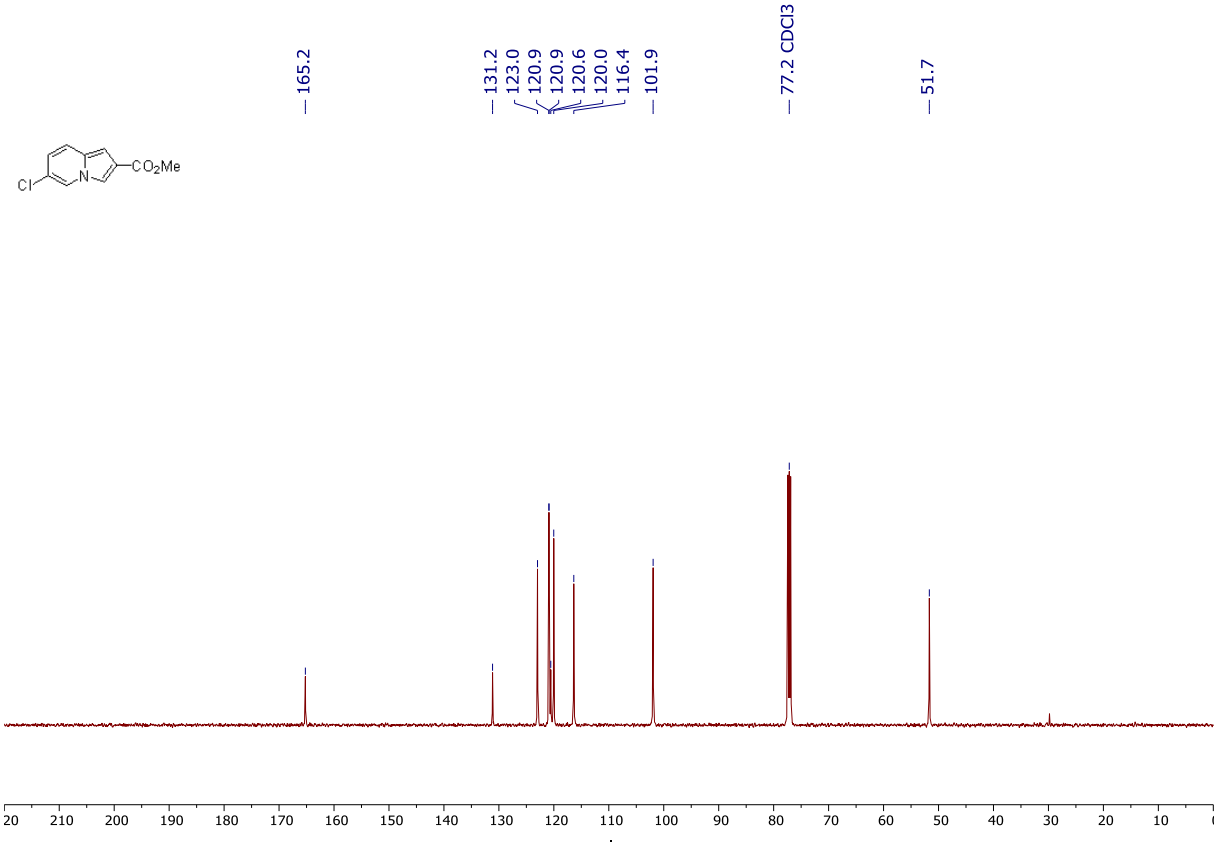




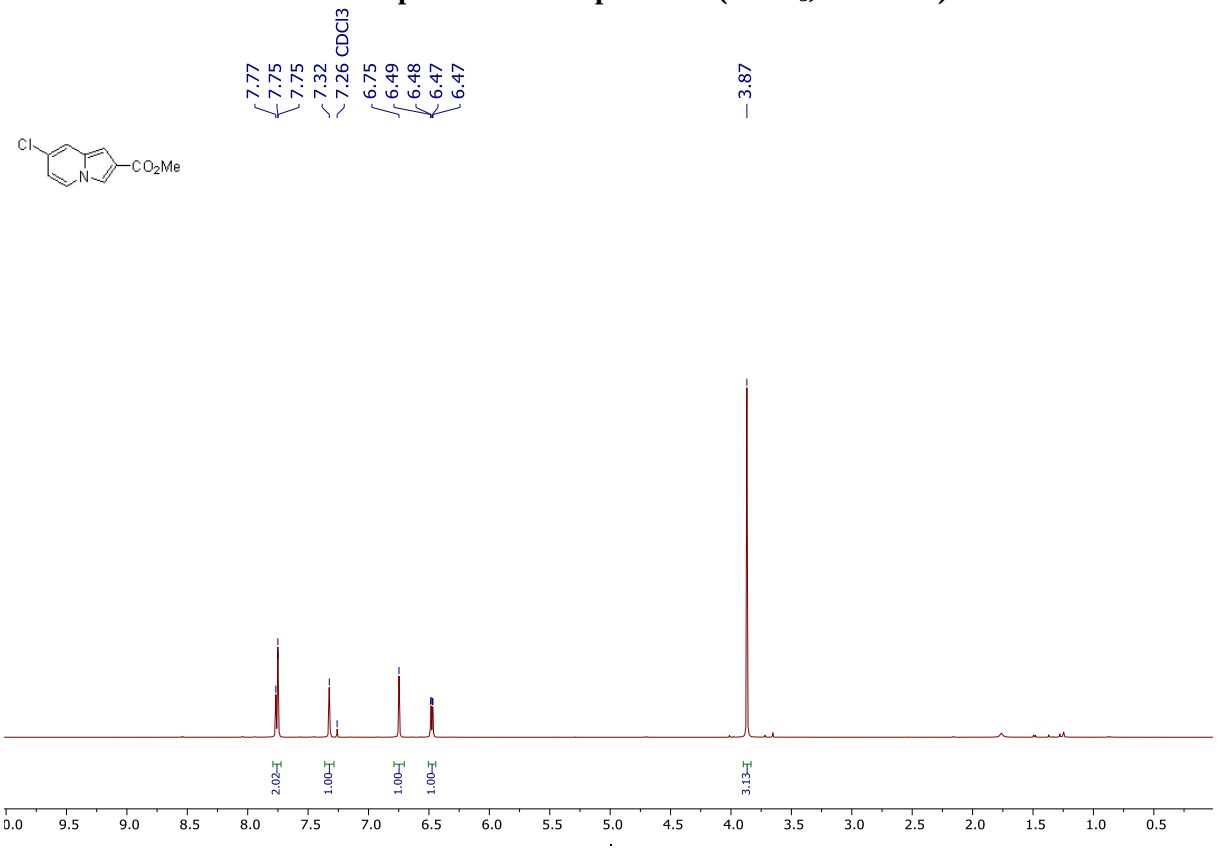
^{1}H NMR spectrum of compound 1b ($CDCl_3$, 500 MHz)



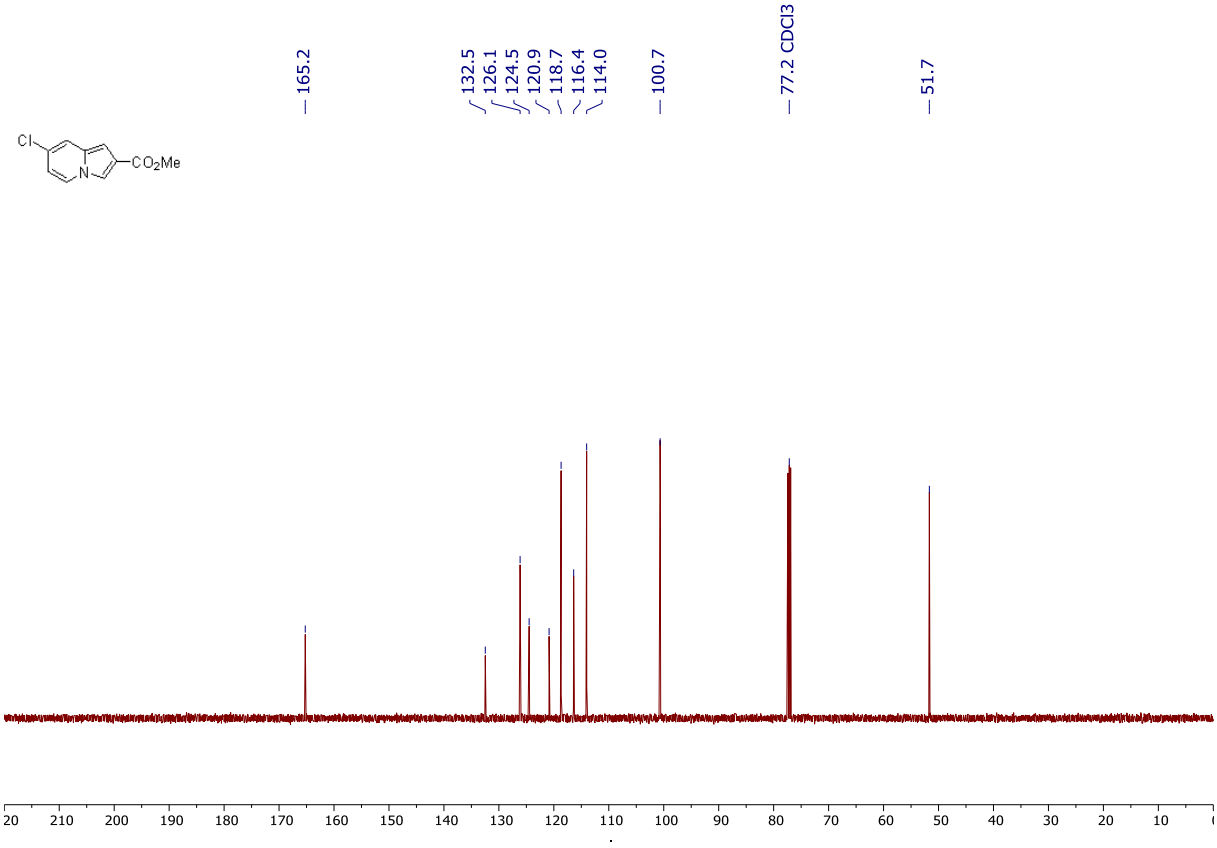
^{13}C NMR spectrum of compound 1b ($CDCl_3$, 126 MHz)



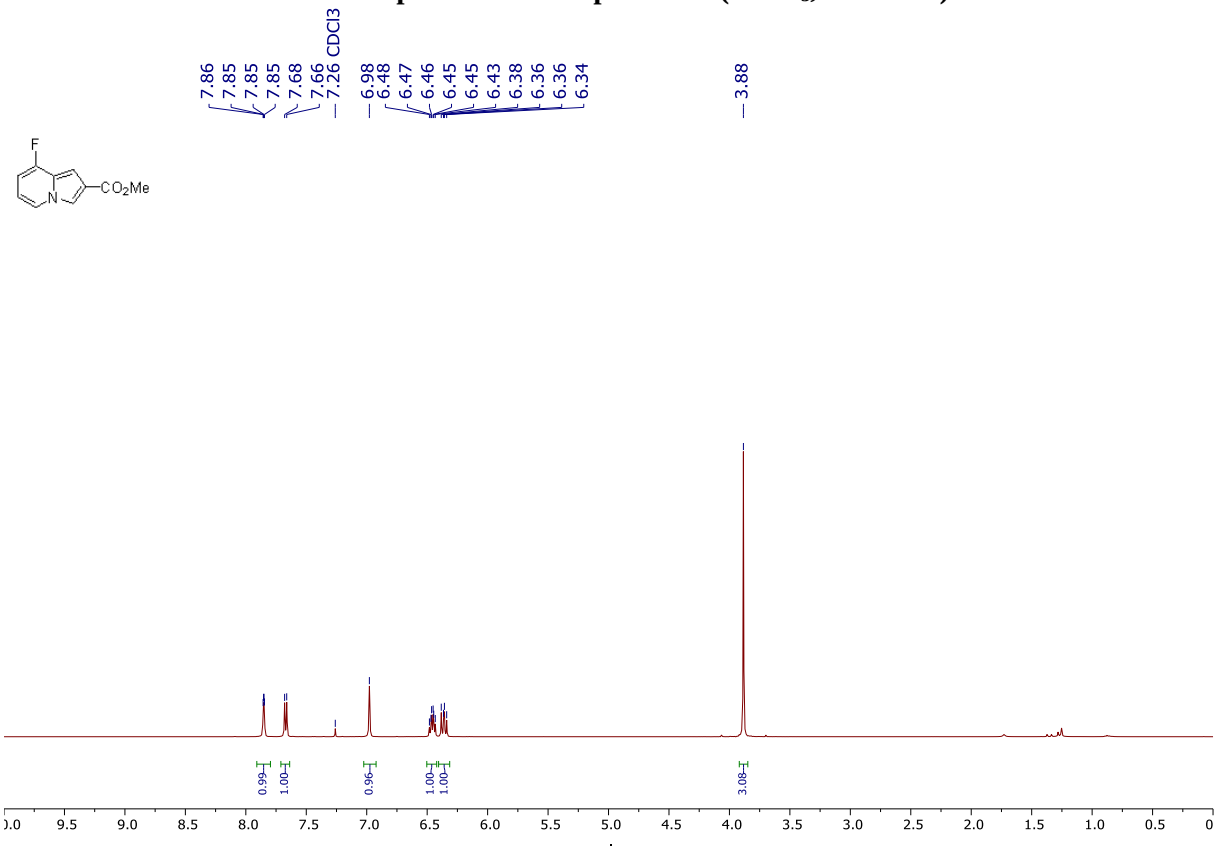
^{1}H NMR spectrum of compound 1c ($CDCl_3$, 500 MHz)



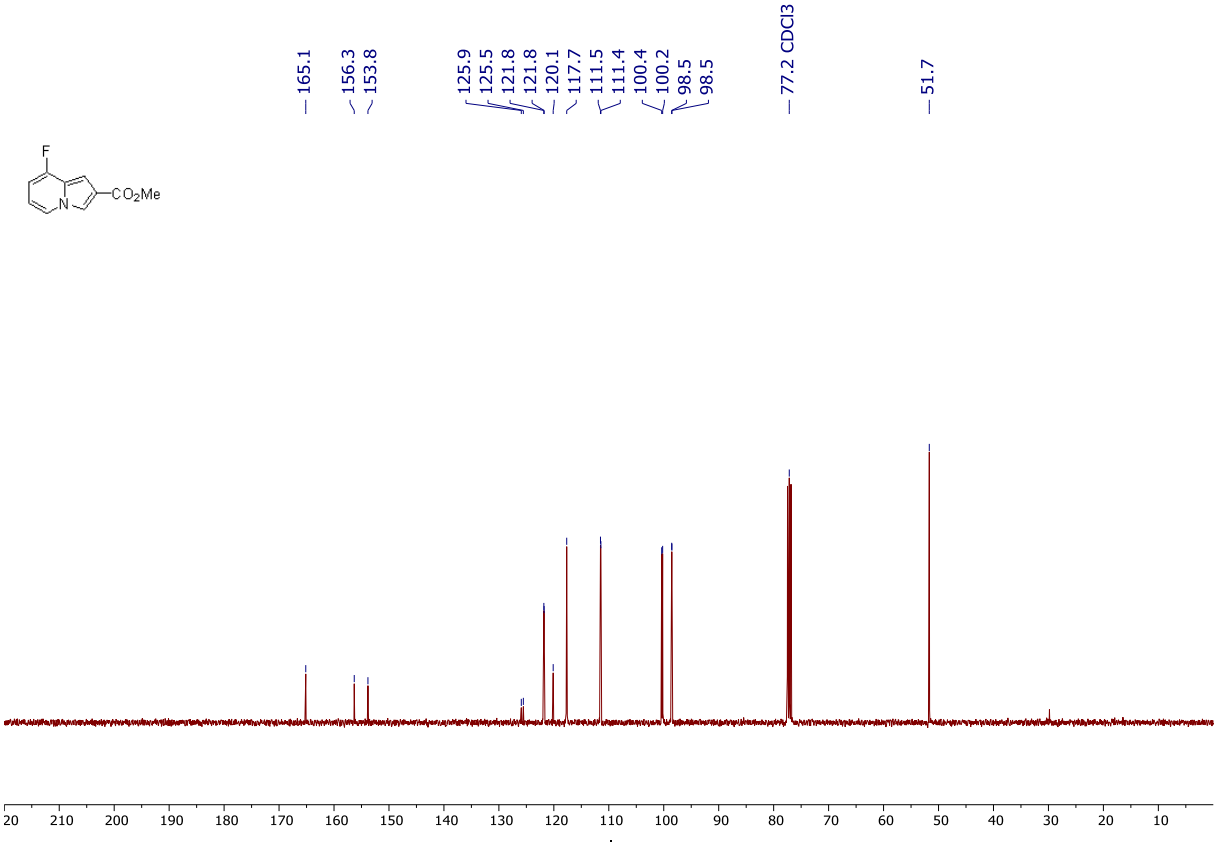
^{13}C NMR spectrum of compound 1c ($CDCl_3$, 126 MHz)



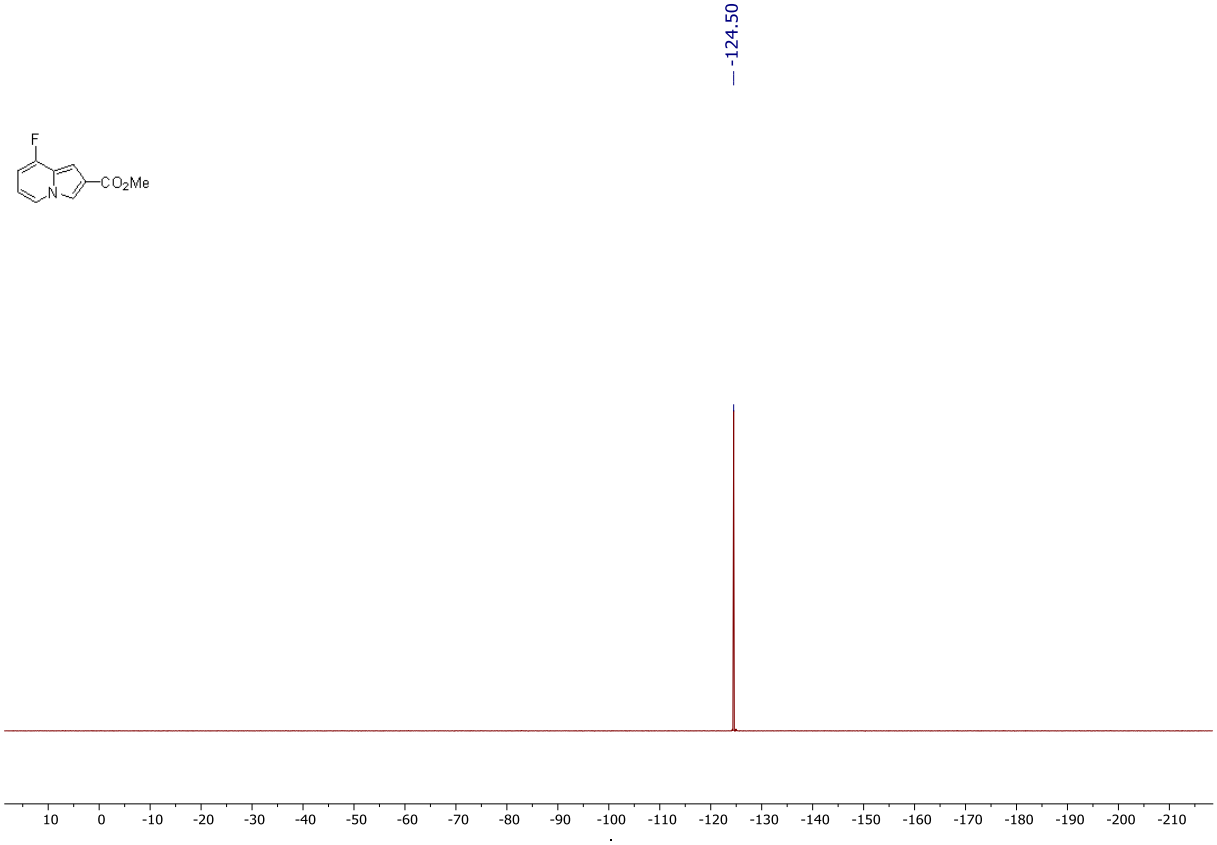
^{1}H NMR spectrum of compound 1d ($CDCl_3$, 400 MHz)



^{13}C NMR spectrum of compound 1d ($CDCl_3$, 101 MHz)



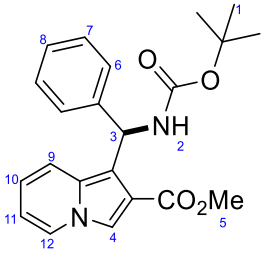
^{19}F NMR spectrum of compound 1d ($CDCl_3$, 376 MHz)



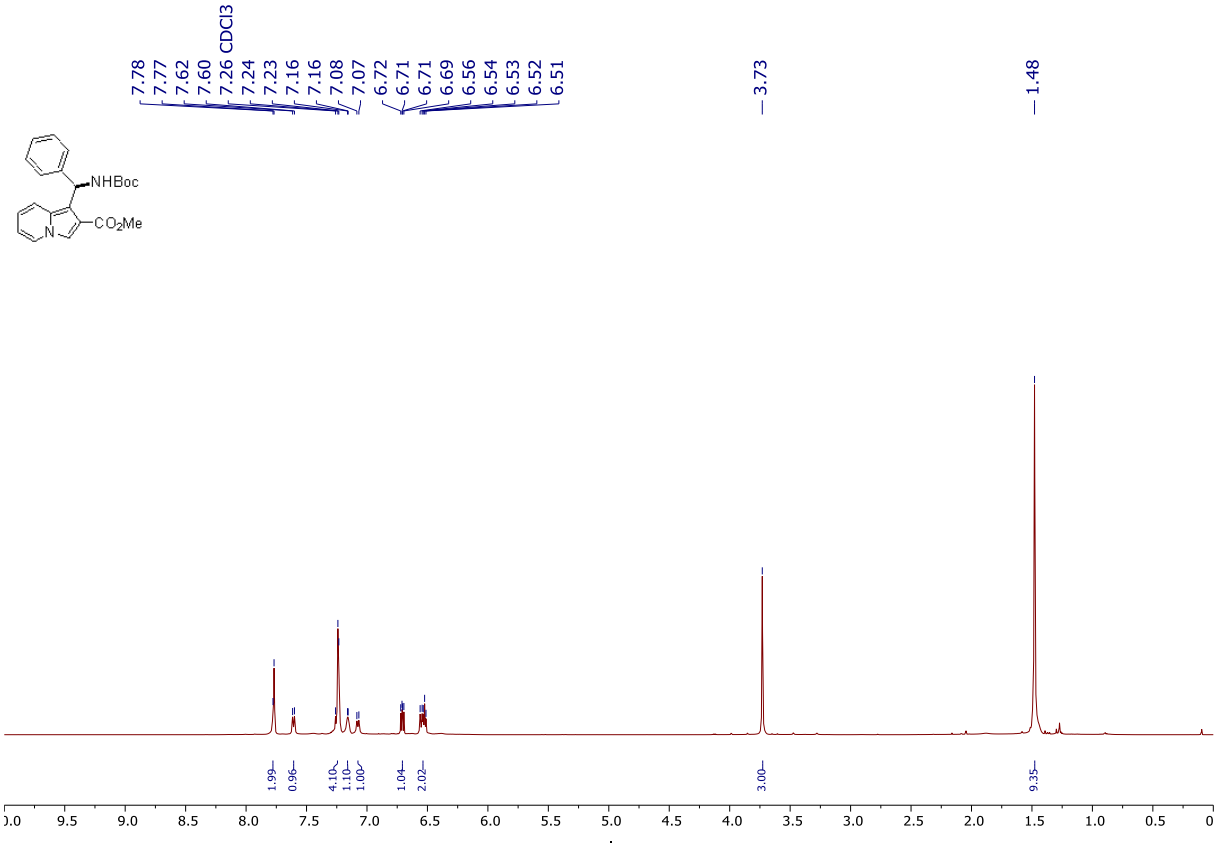
6.6. All NMR spectra of compounds 3a and 4a

6.6.1. Compound 3a

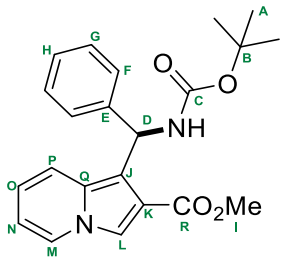
^{1}H NMR spectrum of compound 3a ($CDCl_3$, 600 MHz)



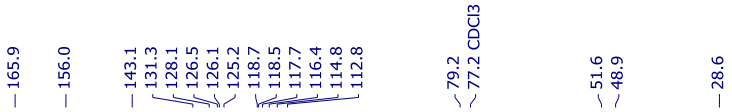
H	δH
1	1.48
2	7.08
3	6.58-6.50
4	7.77
5	3.73
6	7.26-7.21
7	7.26-7.21
8	7.19-7.13
9	7.61
10	6.71
11	6.58-6.50
12	7.80-7.75

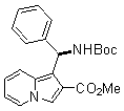


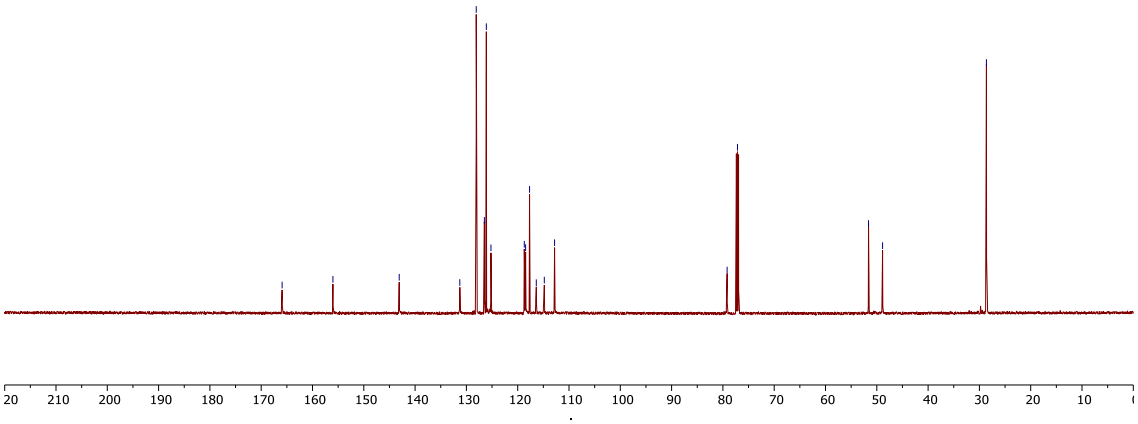
^{13}C NMR spectrum of compound 3a ($CDCl_3$, 151 MHz)



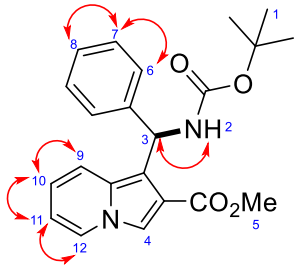
C	δC
A	28.6
B	79.2
C	156.0
D	48.9
E	143.1
F	126.1
G	128.1
H	126.5
I	51.6
J	114.8
K	116.4
L	117.7
M	125.2
N	112.8
O	118.7
P	118.5
Q	131.3
R	165.9



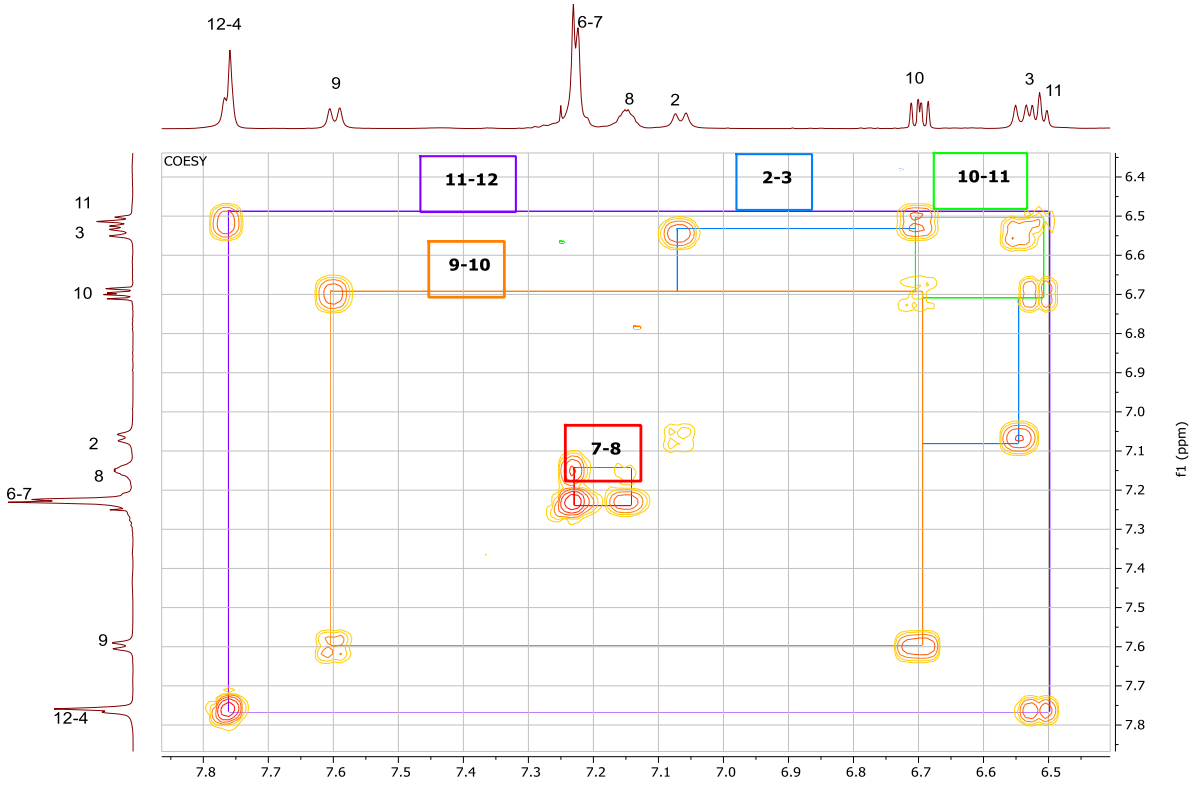




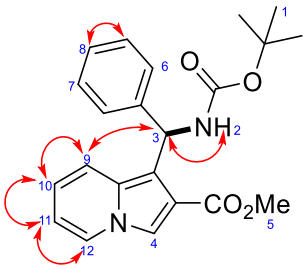
COSY spectrum of compound 3a ($CDCl_3$)



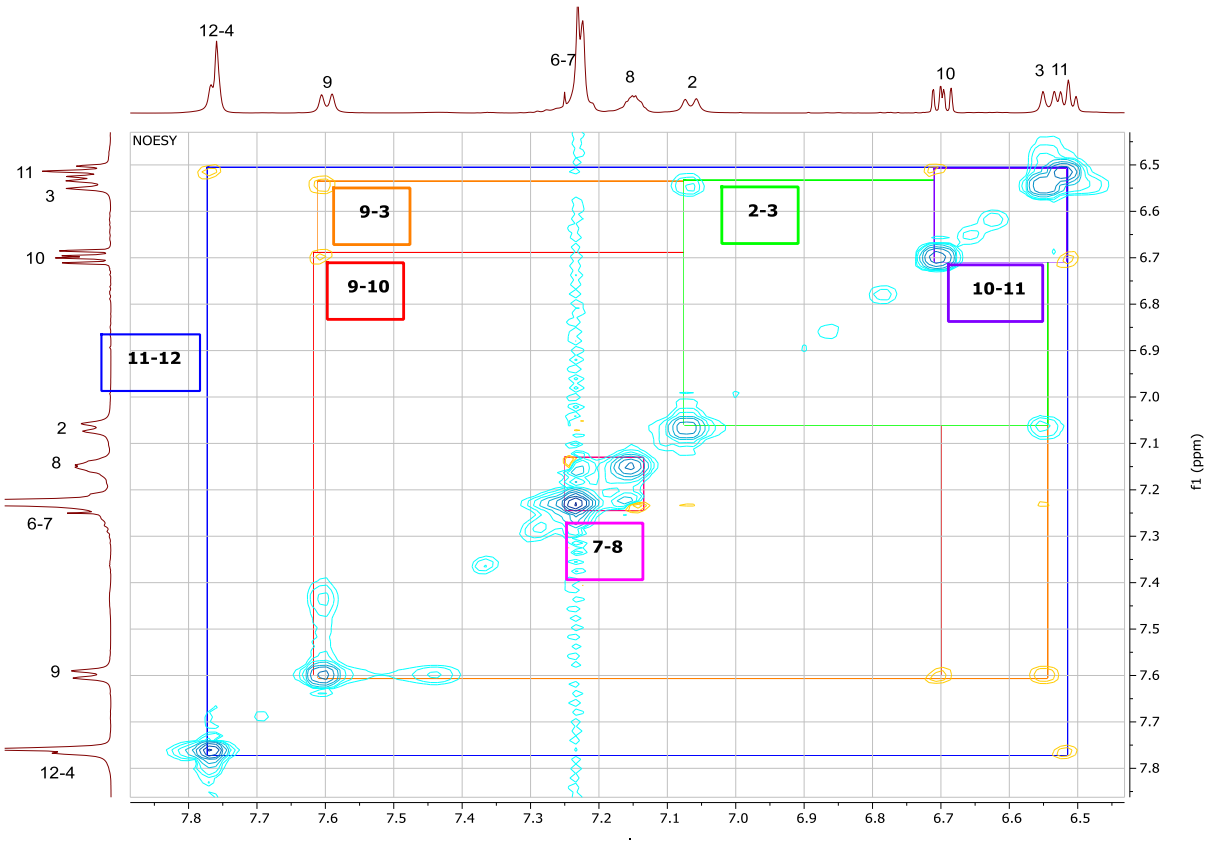
H	δH	^{3}JH-H
2	7.08	H2-H3
3	6.58-6.50	H2-H3
6	7.26-7.21	H6-H7
7	7.26-7.21	H6-H7, H8-H7
8	7.19-7.13	H8-H7
9	7.61	H9-H10
10	6.71	H9-H10, H10-H11
11	6.58-6.50	H10-H11, H11-H12
12	7.80-7.75	H11-H12



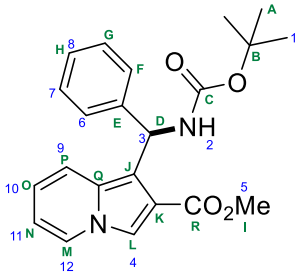
NOESY spectrum of compound 3a ($CDCl_3$)



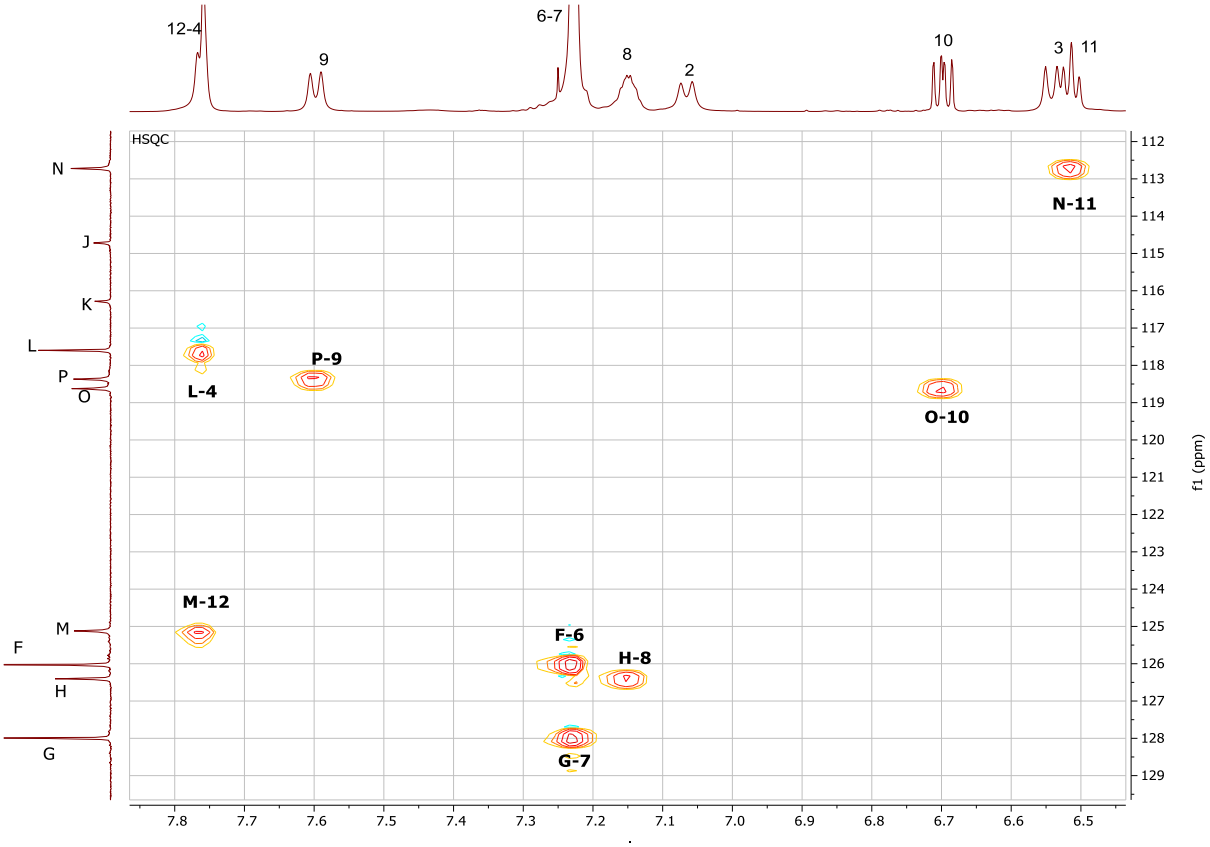
H	δH	H-H
2	7.08	H2-H3
3	6.58-6.50	H2-H3; H3-H9
7	7.26-7.21	H8-H7
8	7.19-7.13	H8-H7
9	7.61	H9-H10; H3-H9
10	6.71	H9-H10; H10-H11
11	6.58-6.50	H11-H12; H10-H11
12	7.80-7.75	H11-H12



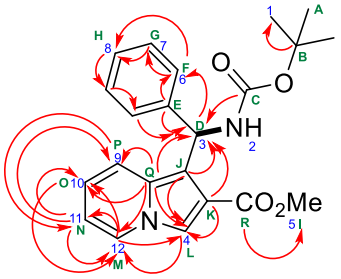
HSQC spectrum of compound 3a ($CDCl_3$)



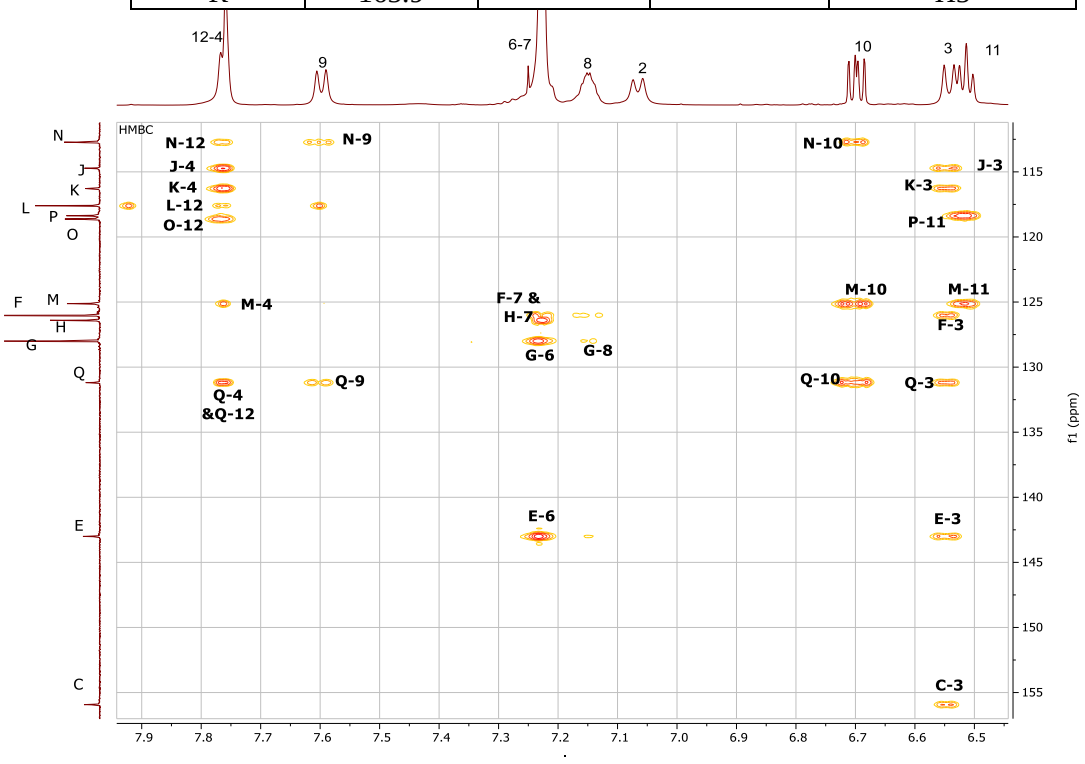
C	H	δC	δH
A	1	28.6	1.48
D	3	48.9	6.58-6.50
F	6	126.1	7.26-7.21
G	7	128.1	7.26-7.21
H	8	126.5	7.19-7.13
I	5	51.6	3.73
P	9	118.5	7.61
O	10	118.7	6.71
N	11	112.8	6.58-6.50
M	12	125.2	7.80-7.75



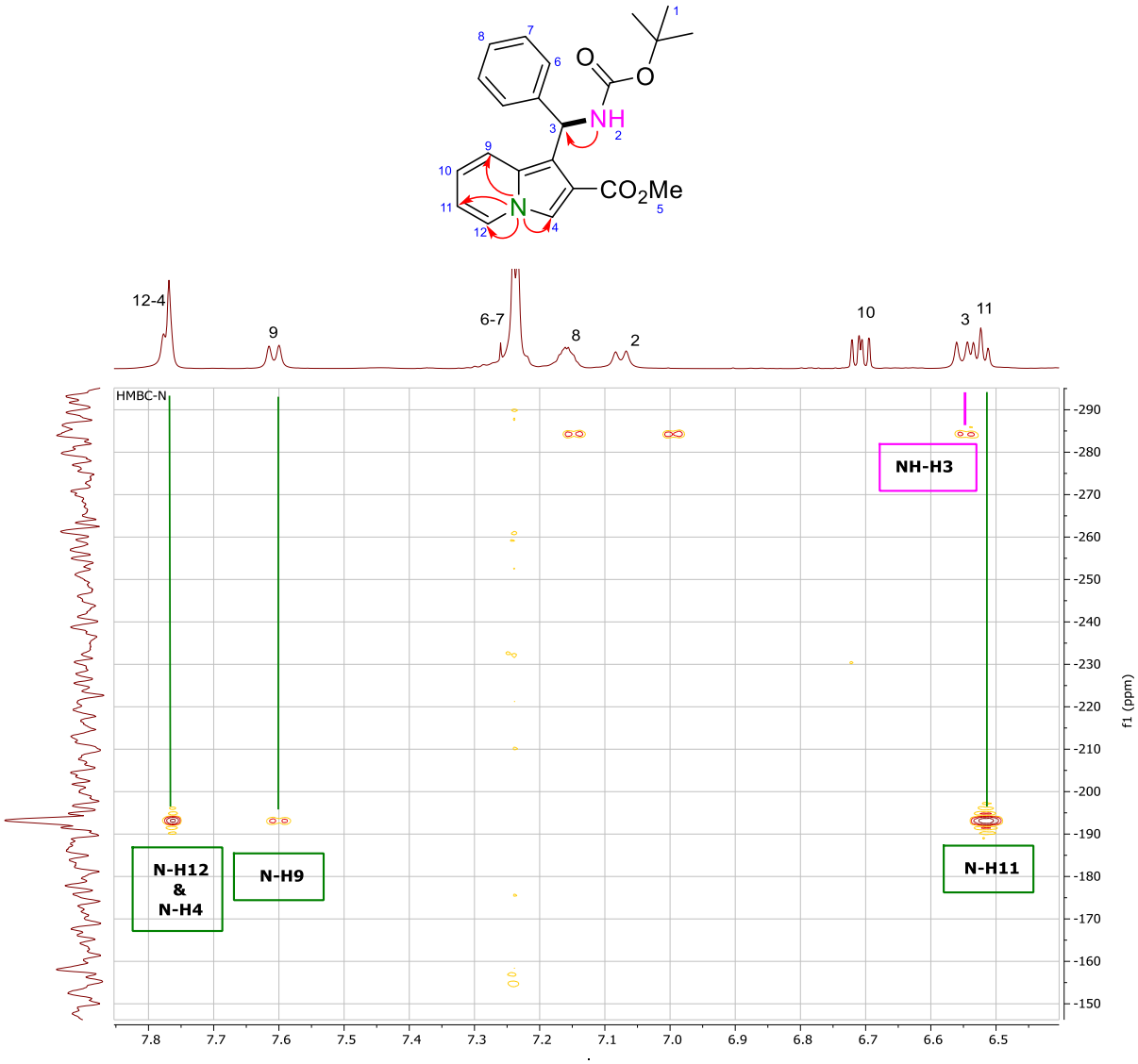
HMBC spectrum of compound 3a ($CDCl_3$)



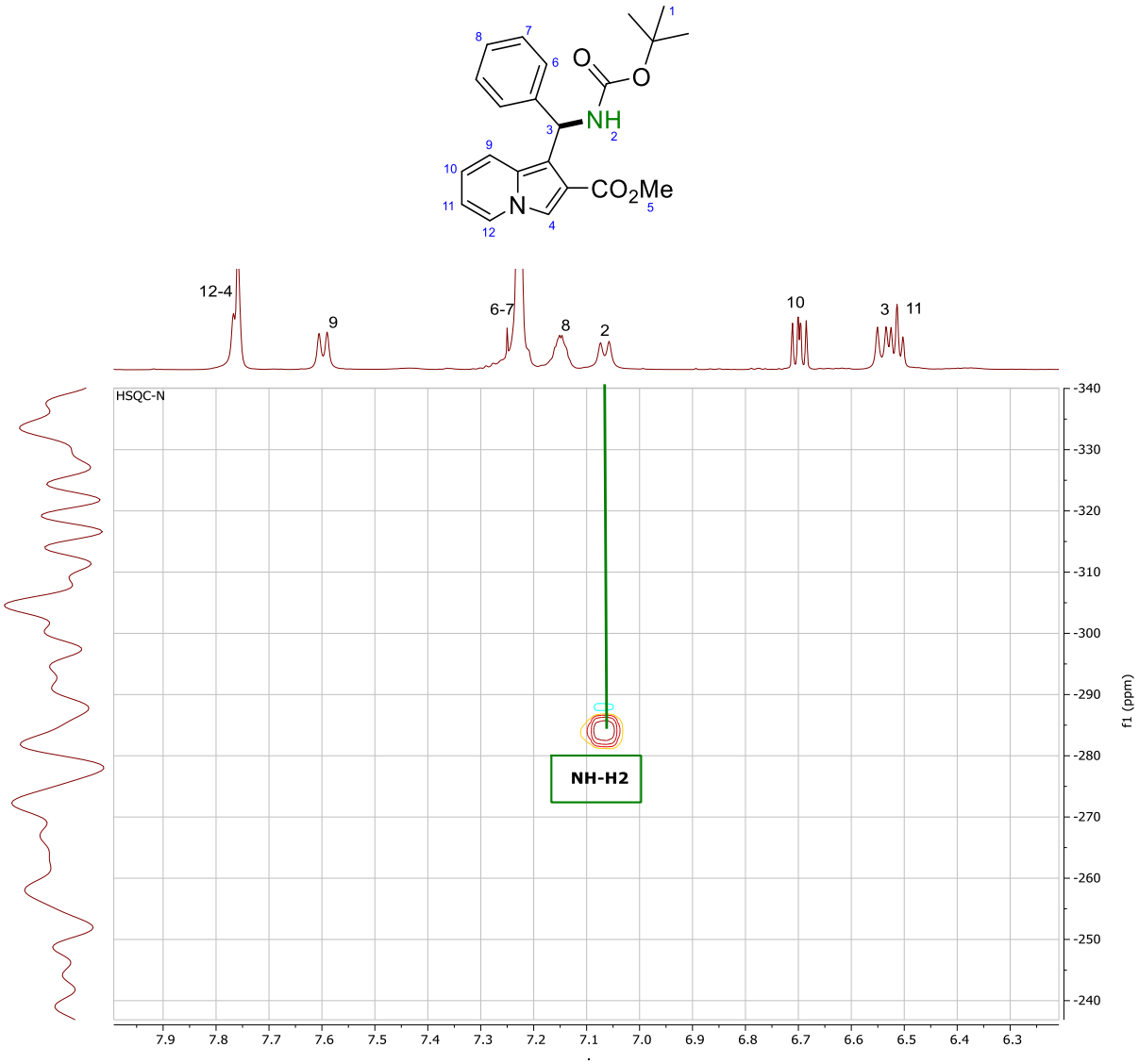
CH	δC	δH	^2JCH	^3JCH
D	48.9	6.58-6.50		H6
N	112.8	6.58-6.50	H10;H12	H9
L	117.7	7.77		H12
O	118.7	6.71		H12
P	118.5	7.61		H11
M	125.2	7.80-7.75	H10	H4;H11
F	126.1	7.26-7.21	H7	H3;F8
H	126.5	7.19-7.13	H7	
G	128.1	7.26-7.21	H6;H8	
C	**δC**	**δH**	**^2JCH**	**^3JCH**
B	79.2		H1	
J	114.8		H3	H4
K	116.4		H4	H3
Q	131.3		H9	H3;H4;H10;H12
E	143.1		H3;H6	
C	156.0			H3
R	165.9			H5



HMBC-N spectrum of compound 3a ($CDCl_3$)

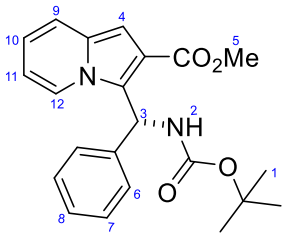


HSQC-N spectrum of compound 3a ($CDCl_3$)

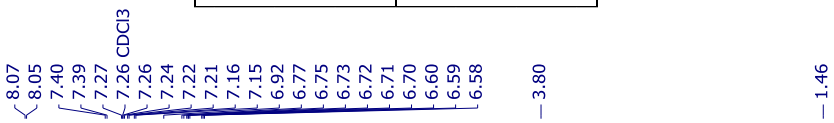


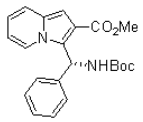
6.6.2. Compound 4a

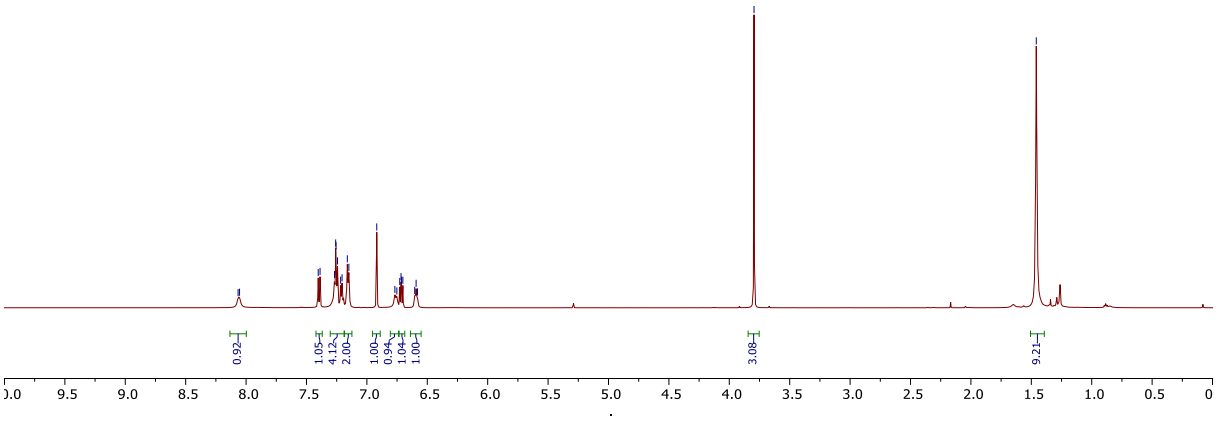
^{1}H NMR spectrum of compound 4a ($CDCl_3$, 600 MHz)



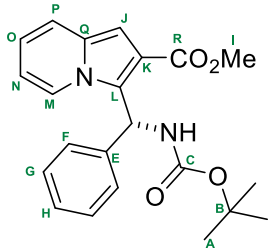
H	δH
1	1.46
2	7.31-7.18
3	6.76
4	6.92
5	3.80
6	7.16
7	7.31-7.18
8	7.31-7.18
9	7.40
10	6.72
11	6.61-6.57
12	8.06



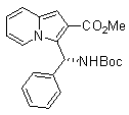


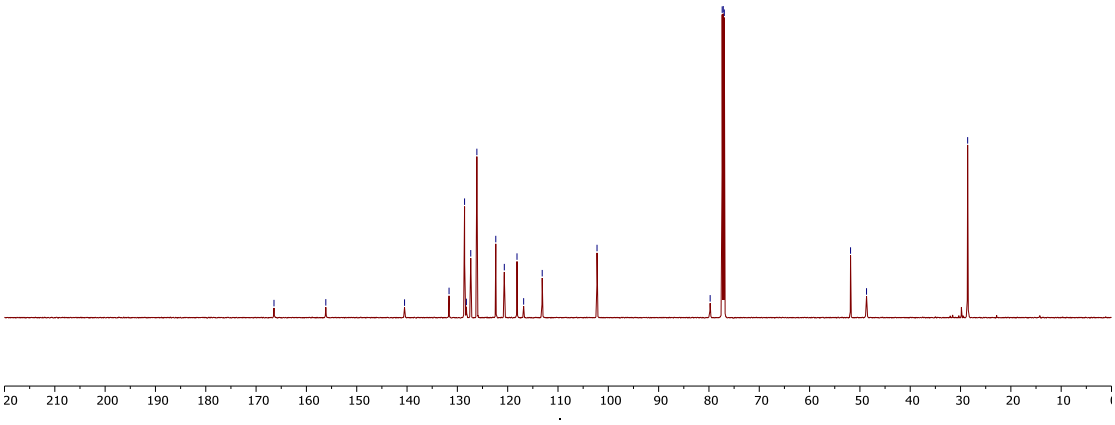


^{13}C NMR spectrum of compound 4a ($CDCl_3$, 151 MHz)

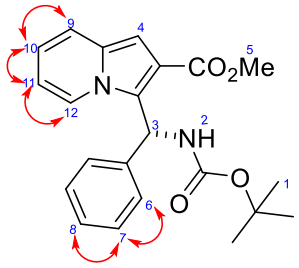


C	δC
A	28.6
B	79.8
C	156.1
D	48.7
E	140.5
F	126.1
G	128.6
H	127.3
I	51.9
J	102.2
K	128.2
L	116.8
M	122.4
N	113.1
O	118.2
P	120.7
Q	131.7
R	166.4

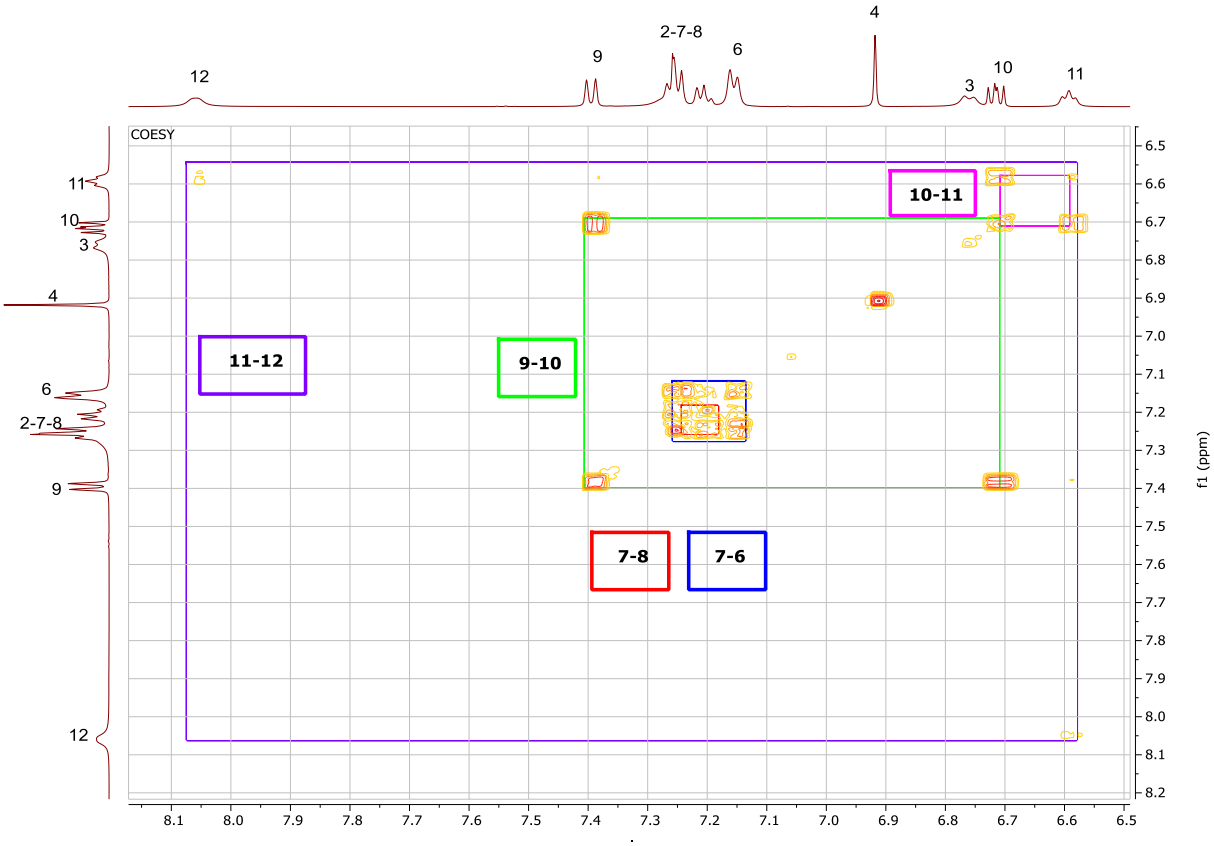




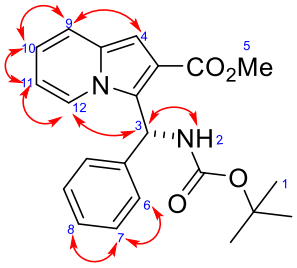
COSY spectrum of compound 4a ($CDCl_3$)



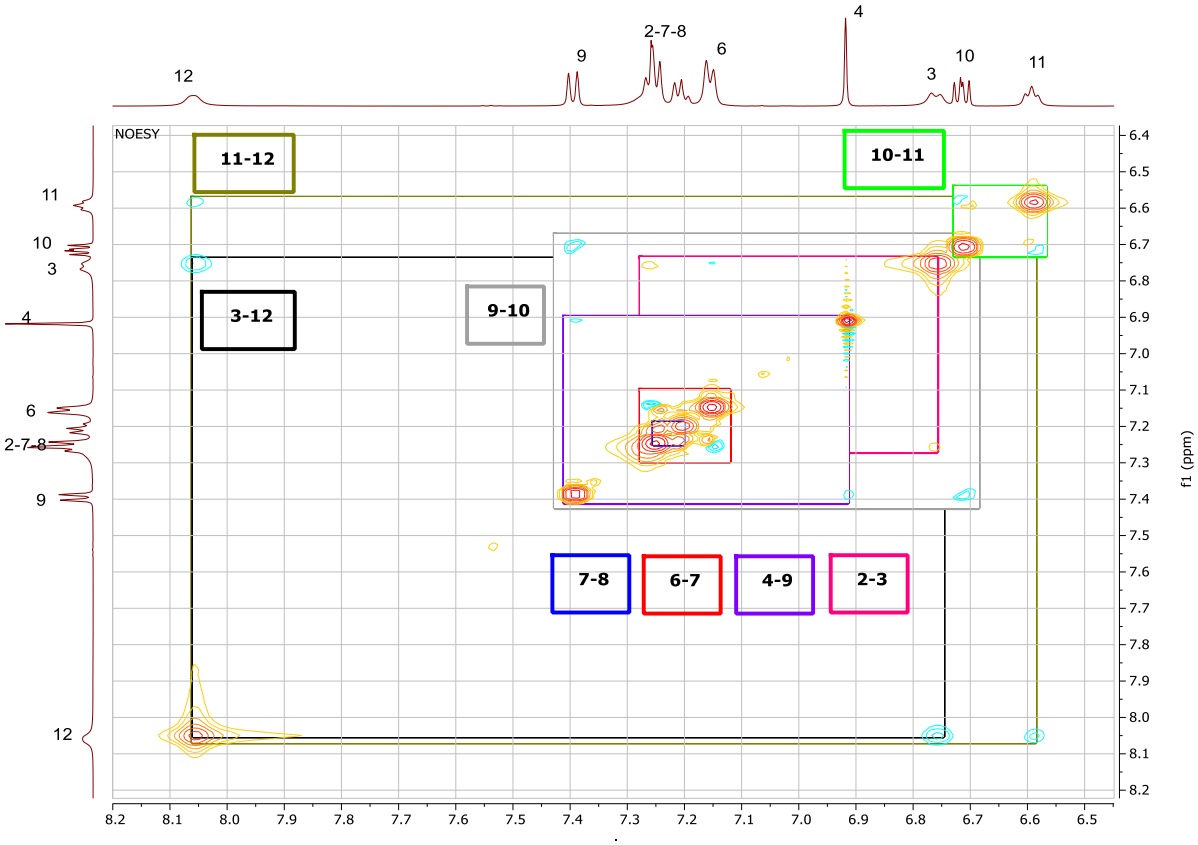
H	δH	^{3}JH-H
6	7.16	H6-H7
7	7.31-7.18	H6-H7;H7-H8
8	7.31-7.18	H7-H8
9	7.40	H9-H10
10	6.72	H9-H10;H10-H11
11	6.61-6.57	H10-H11;H11-H12
12	8.06	H11-H12



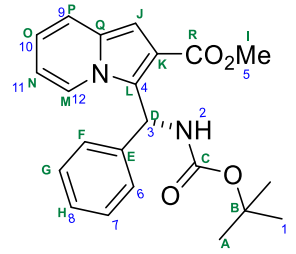
NOESY spectrum of compound 4a ($CDCl_3$)



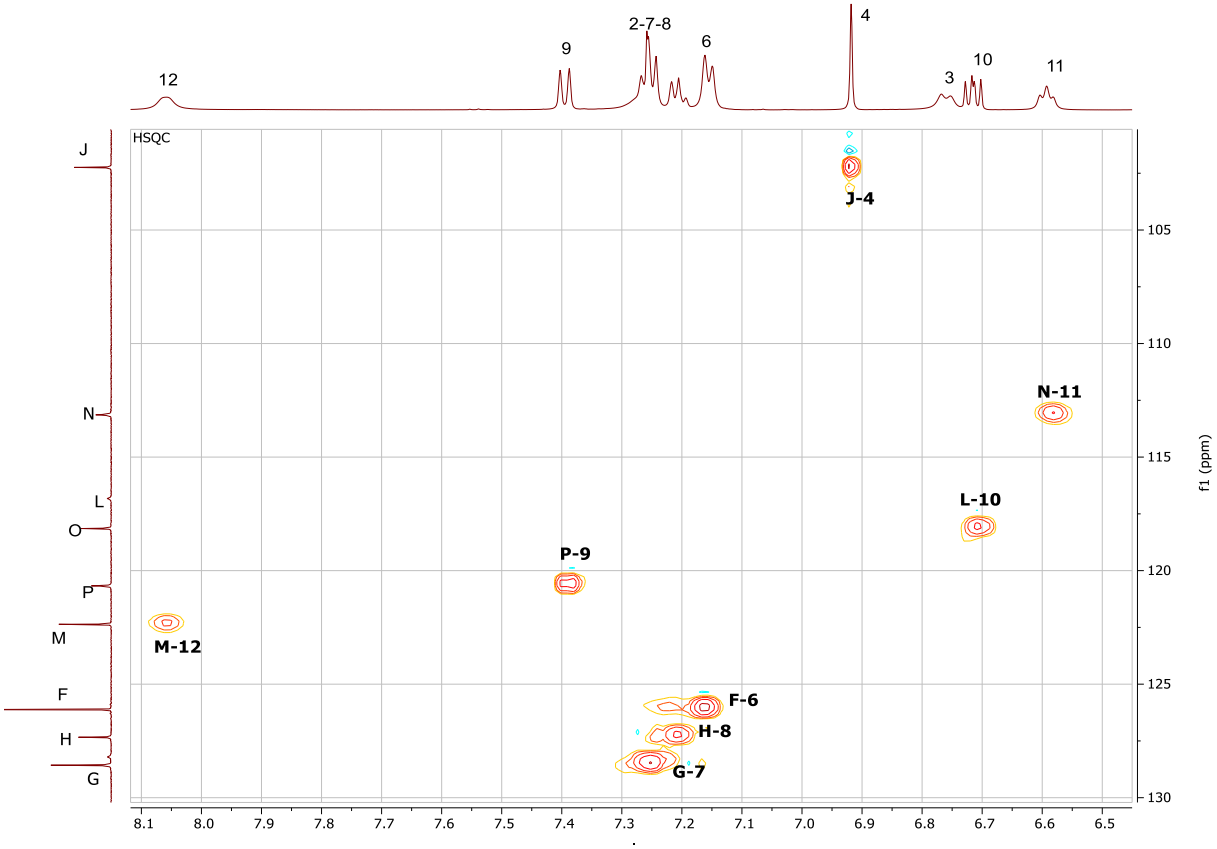
H	δH	H-H
2	7.31-7.18	H2-H3
3	6.76	H2-H3; H3-H12
4	6.92	H4-H9
6	7.16	H6-H7
7	7.31-7.18	H6-H7;H7-H8
8	7.31-7.18	H7-H8
9	7.40	H4-H9;H9-H10
10	6.72	H9-H10;H10-H11
11	6.61-6.57	H10-H11;H11-H12
12	8.06	H3-H12;H11-H12



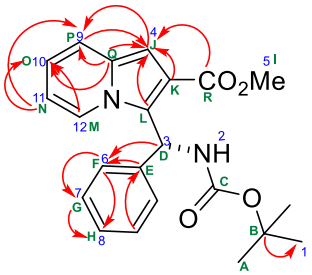
HSQC spectrum of compound 4a ($CDCl_3$)



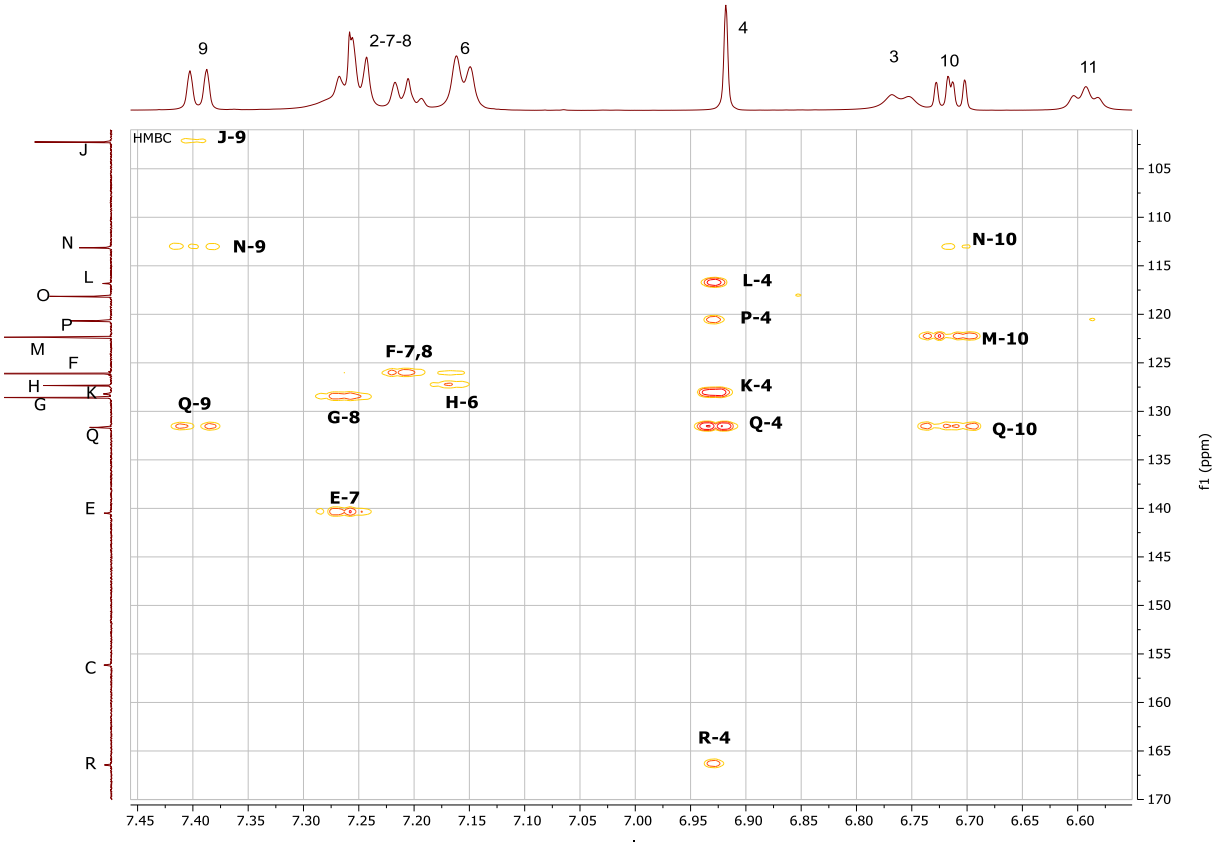
C	H	δC	δH
A	1	28.6	1.46
D	3	48.7	6.76
I	5	51.9	3.80
J	4	102.2	6.92
N	11	113.1	6.61-6.57
O	10	118.1	6.72
P	9	120.7	7.40
M	12	122.4	8.06
F	6	126.1	7.16
H	8	127.3	7.31-7.18
G	7	128.6	7.31-7.18



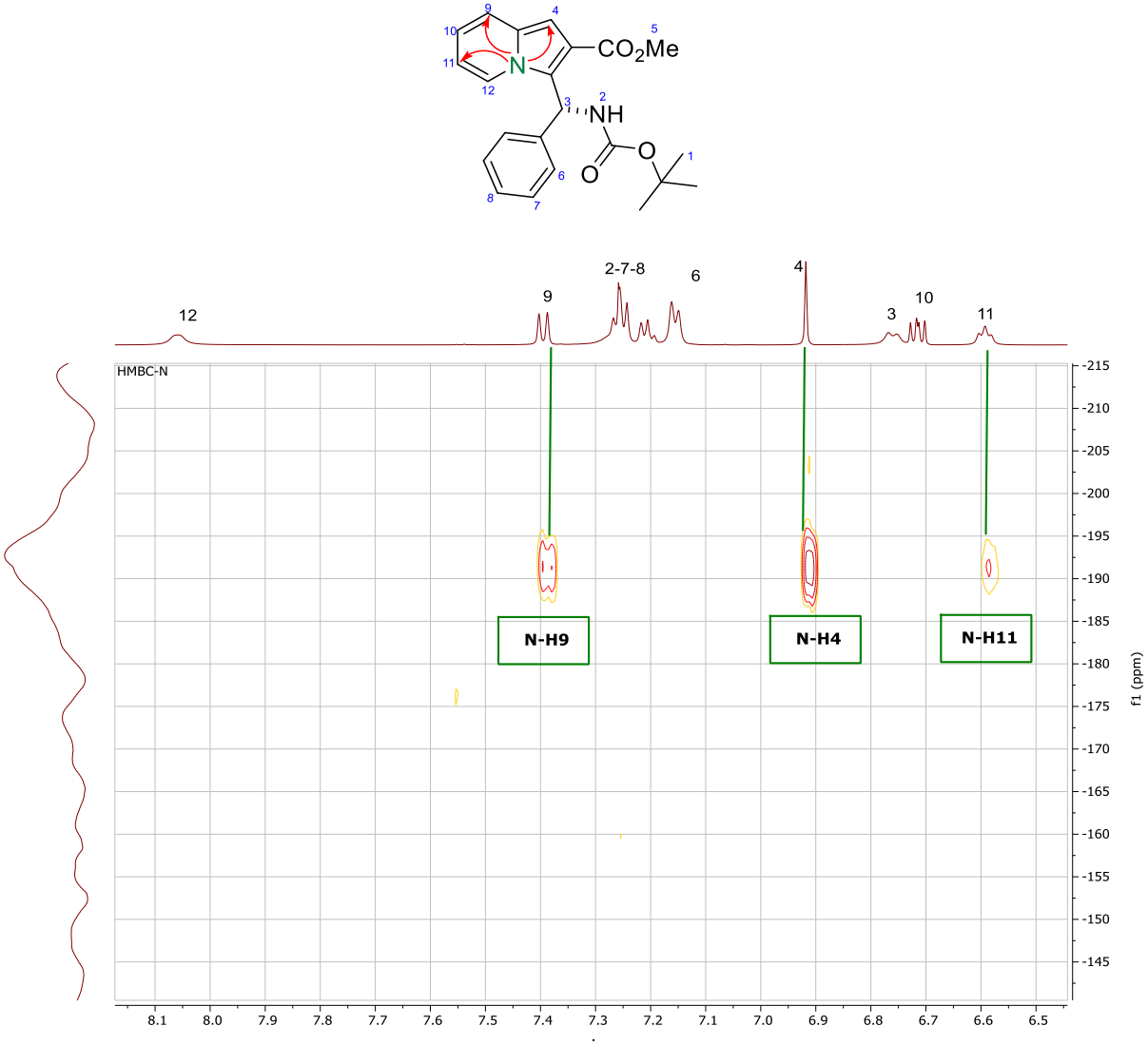
HMBC spectrum of compound 4a ($CDCl_3$)



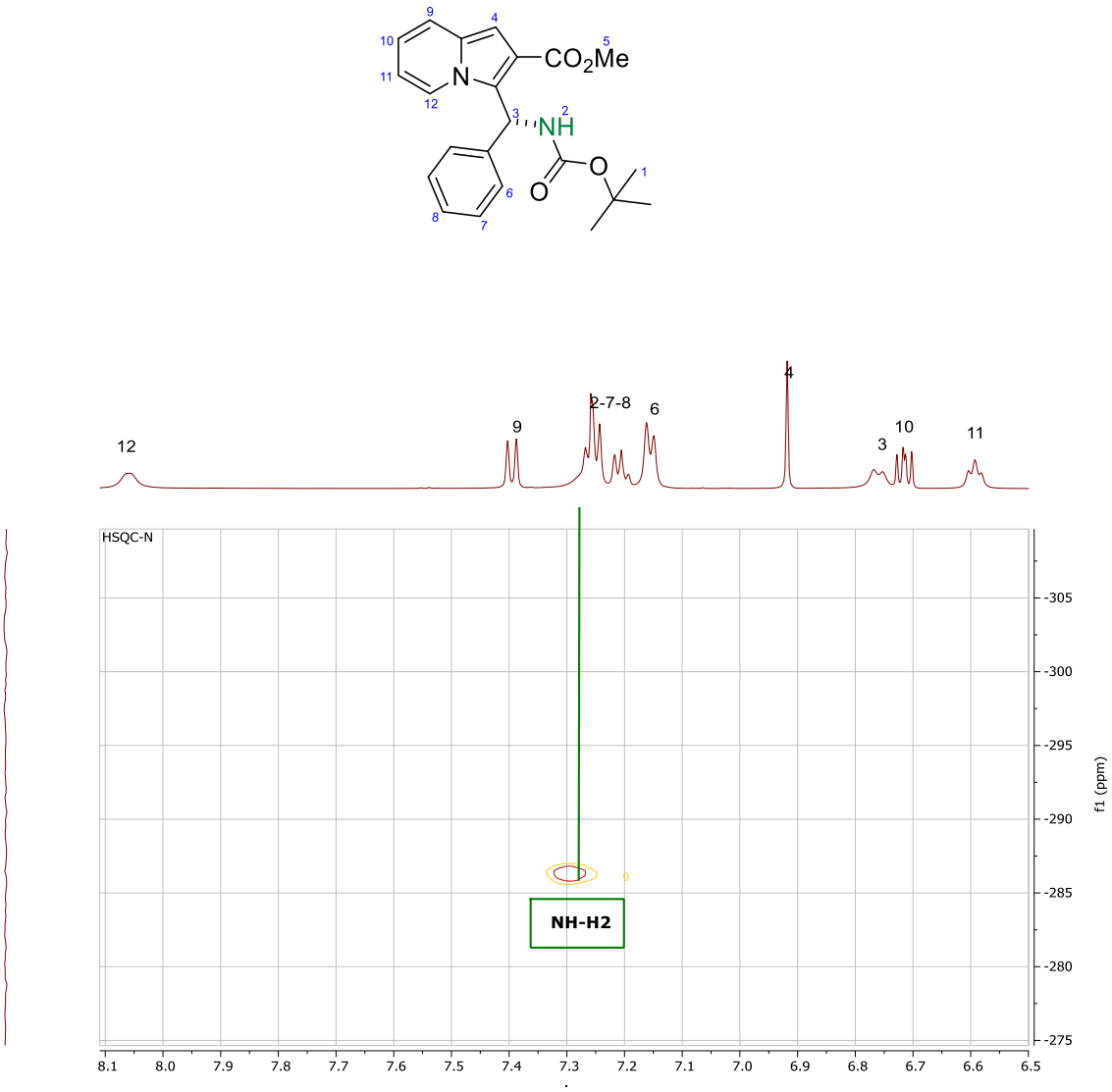
CH	δC	δH	^2JCH	^3JCH
J	102.2	6.92		H9
N	113.1	6.61-6.57	H10	H9
P	120.7	7.40		H4
M	122.4	8.06		H10
F	126.1	7.16	H7	H8
H	127.3	7.31-7.18		H6
G	128.6	7.31-7.18	H8	
C	**δC**	**δH**	**^2JCH**	**^3JCH**
B	79.8		H1	
L	116.8			H4
K	128.2		H4	
Q	131.7		H4;H9	H10
E	140.5		H6	
R	166.4			H4;H5



HMBC-N spectrum of compound 4a ($CDCl_3$)



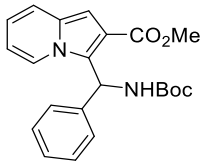
HSQC-N spectrum of compound 4a ($CDCl_3$)

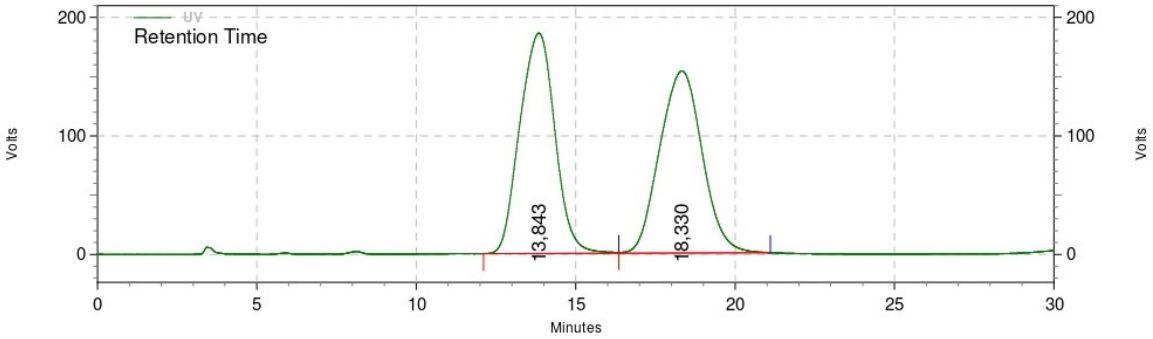


8. HPLC Chiral spectra

8.1. Products with Boc-protecting group 3a-s, 4a-s and 10

Chiral HPLC chromatogram of racemic 4a



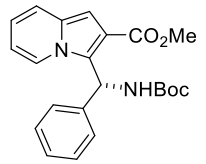


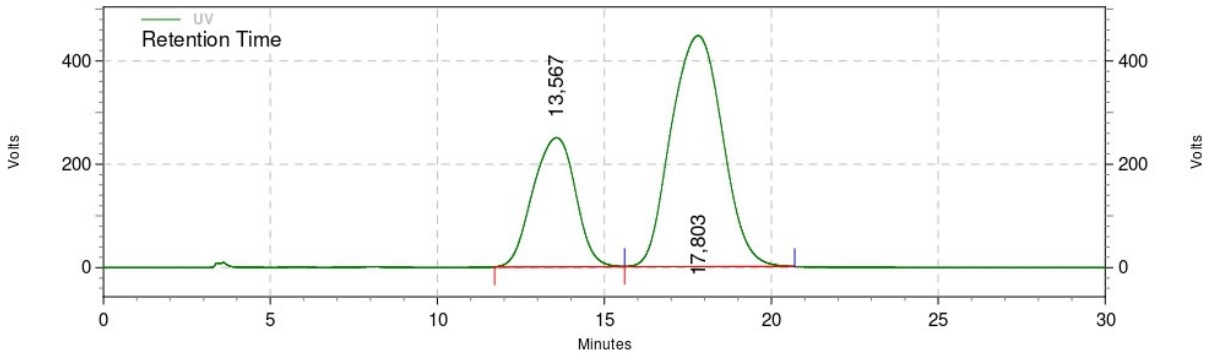
UV Results

Retention Time	Area	Area %	Height	Height %
13,843	57015316	50,00	744080	54,75
18,330	57017925	50,00	614933	45,25

Totals	114033241	100,00	1359013	100,00

Chiral HPLC chromatogram of chiral 4a



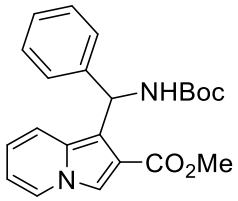


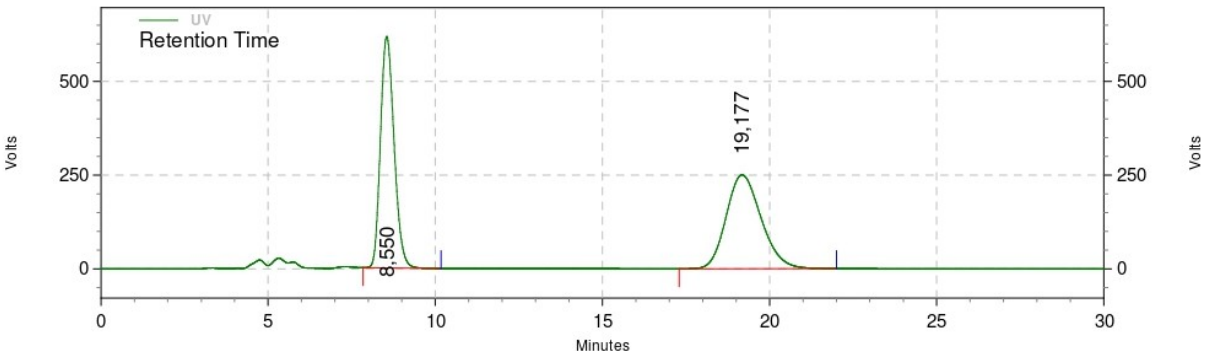
UV Results

Retention Time	Area	Area %	Height	Height %
13,567	88631047	31,66	999718	35,87
17,803	191344584	68,34	1787454	64,13

Totals	279975631	100,00	2787172	100,00

Chiral HPLC chromatogram of racemic 3a



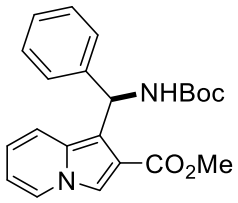


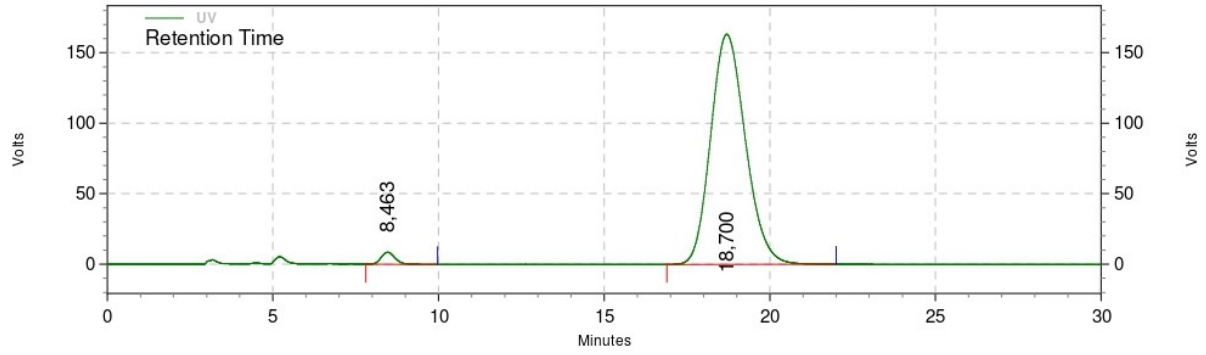
UV Results

Retention Time	Area	Area %	Height	Height %
8,550	69984599	48,97	2470174	71,15
19,177	72928830	51,03	1001623	28,85

Totals	142913429	100,00	3471797	100,00

Chiral HPLC chromatogram of chiral 3a



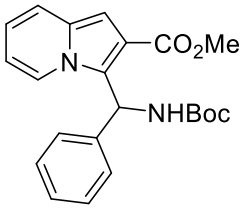


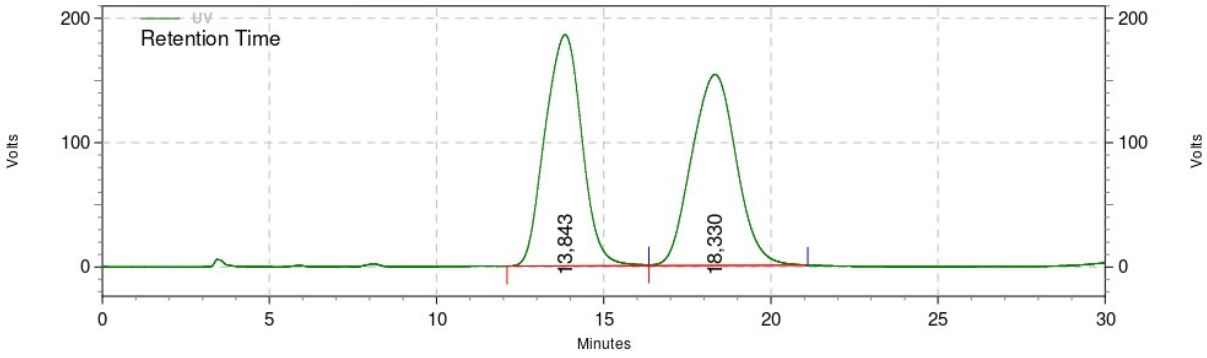
UV Results

Retention Time	Area	Area %	Height	Height %
8,463	1001400	2,06	34069	4,96
18,700	47674180	97,94	653034	95,04

Totals	48675580	100,00	687103	100,00

Chiral HPLC chromatogram of racemic 4a

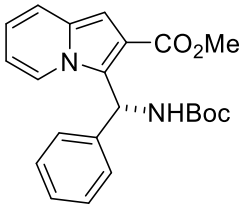


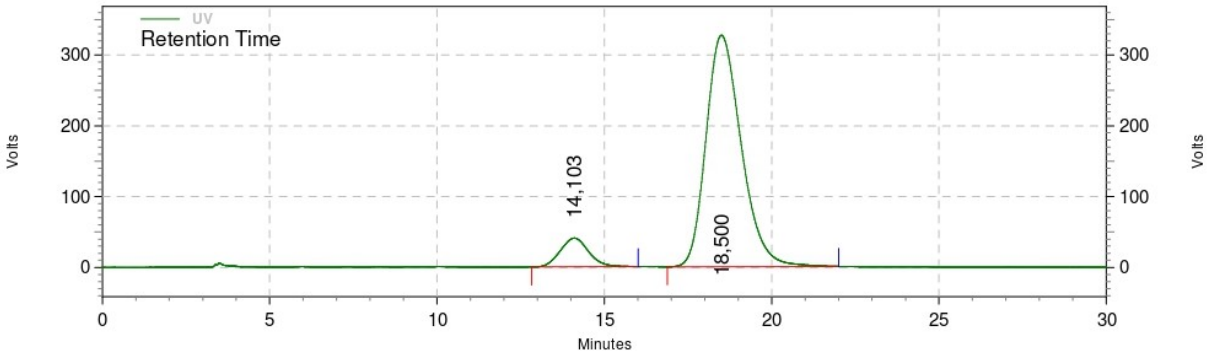


UV Results

Retention Time	Area	Area %	Height	Height %
13,843	57015316	50,00	744080	54,75
18,330	57017925	50,00	614933	45,25
Totals	114033241	100,00	1359013	100,00

Chiral HPLC chromatogram of chiral 4a (procedure B)

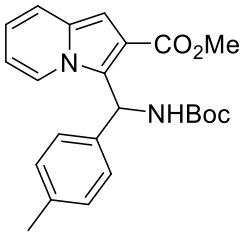


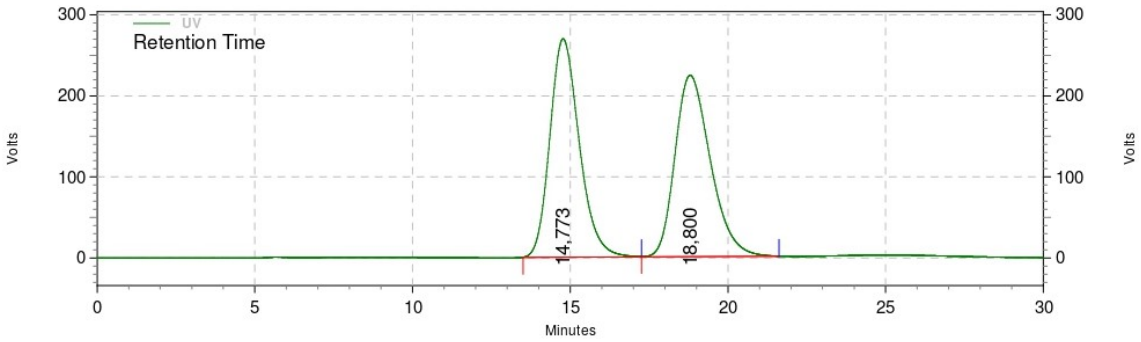


UV Results

Retention Time	Area	Area %	Height	Height %
14,103	9587778	9,10	162251	11,04
18,500	95796648	90,90	1307472	88,96
Totals	105384426	100,00	1469723	100,00

Chiral HPLC chromatogram of racemic 4b

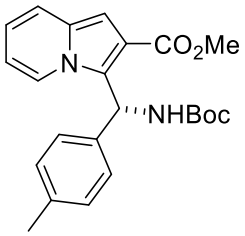


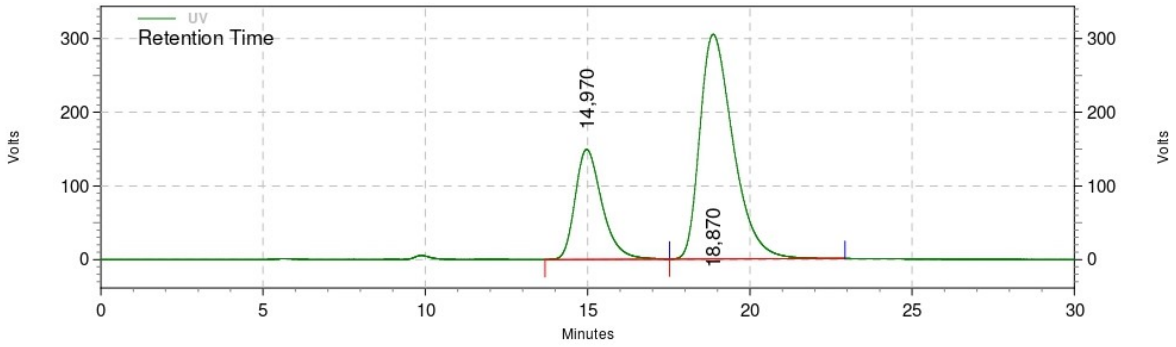


UV Results

Retention Time	Area	Area %	Height	Height %
14,773	69818719	50,00	1077547	54,62
18,800	69817369	50,00	895194	45,38
Totals	139636088	100,00	1972741	100,00

Chiral HPLC chromatogram of chiral 4b

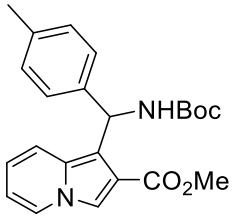


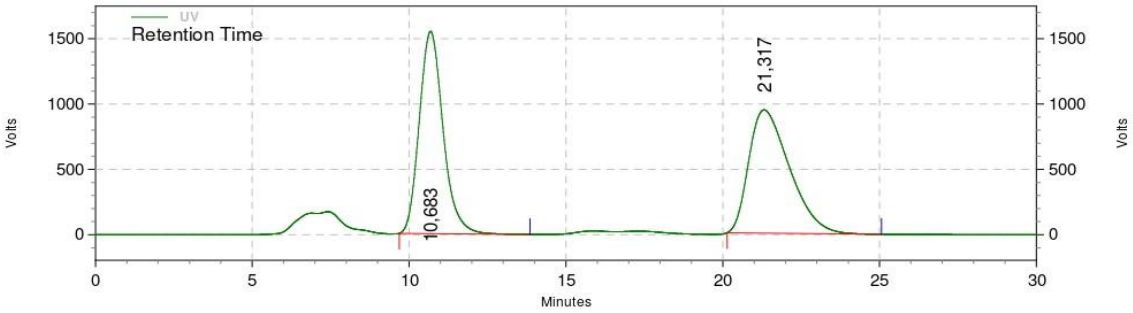


UV Results

Retention Time	Area	Area %	Height	Height %
14,970	34421300	28,31	598360	32,91
18,870	87168179	71,69	1219979	67,09
Totals	121589479	100,00	1818339	100,00

Chiral HPLC chromatogram of racemic 3b

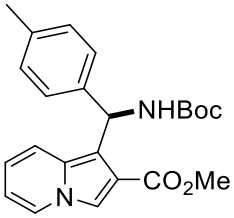


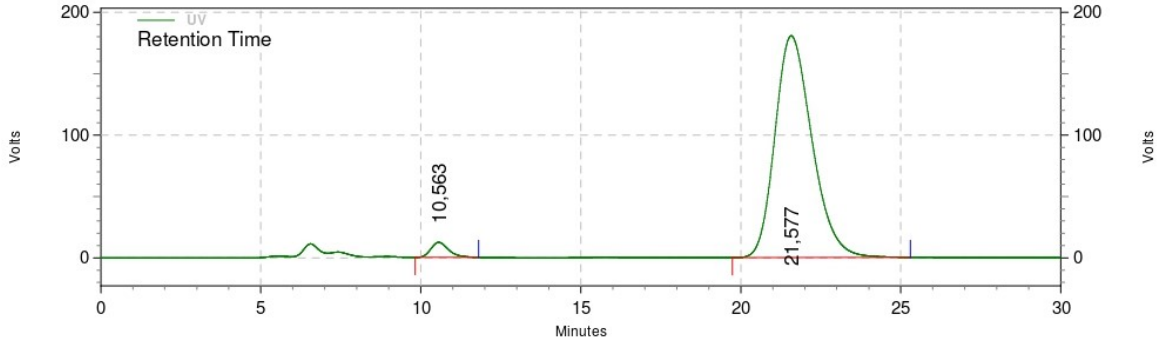


UV Results

Retention Time	Area	Area %	Height	Height %
10,683	326551193	49,01	6190814	62,14
21,317	339798926	50,99	3771438	37,86
Totals	666350119	100,00	9962252	100,00

Chiral HPLC chromatogram of chiral 3b

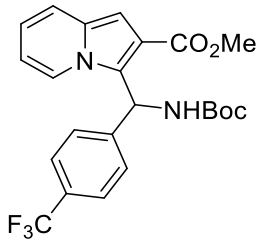


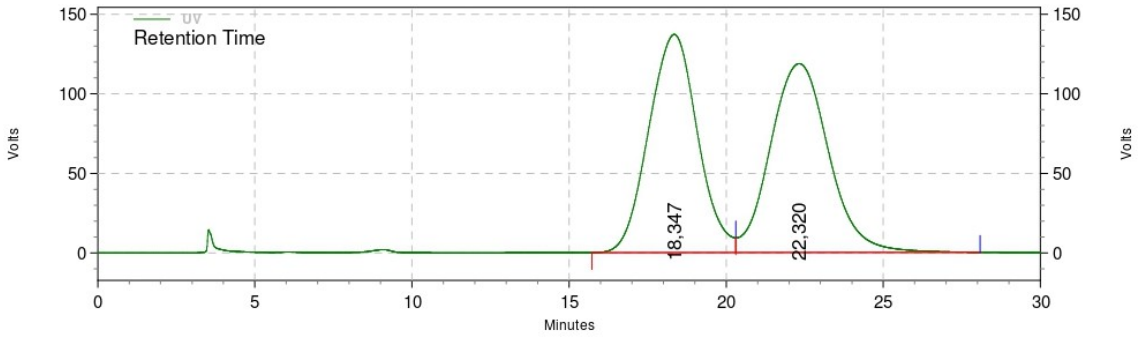


UV Results

Retention Time	Area	Area %	Height	Height %
10,563	1917542	3,19	49113	6,37
21,577	58159709	96,81	722343	93,63
Totals	60077251	100,00	771456	100,00

Chiral HPLC chromatogram of racemic 4c



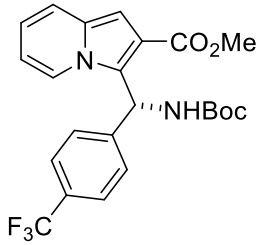


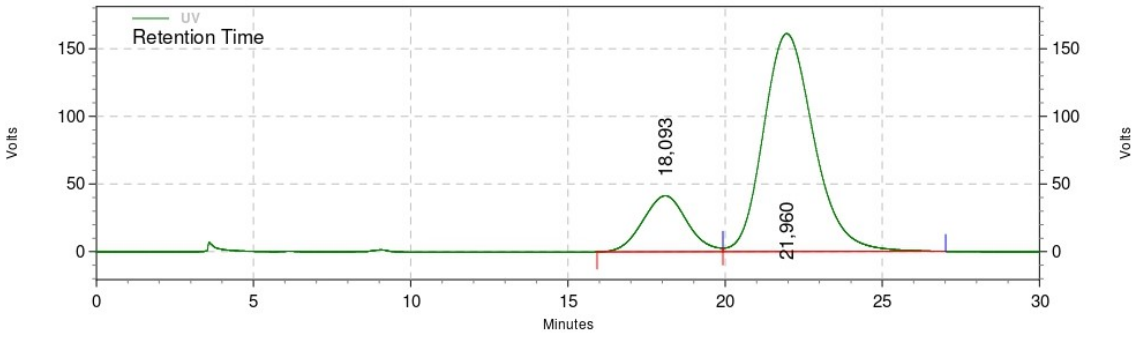
UV Results

Retention Time	Area	Area %	Height	Height %
18,347	59155829	49,19	547905	53,59
22,320	61096077	50,81	474464	46,41

Totals	120251906	100,00	1022369	100,00

Chiral HPLC chromatogram of chiral 4c



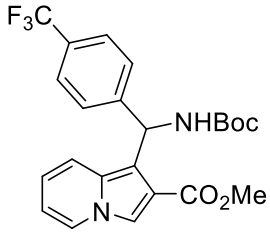


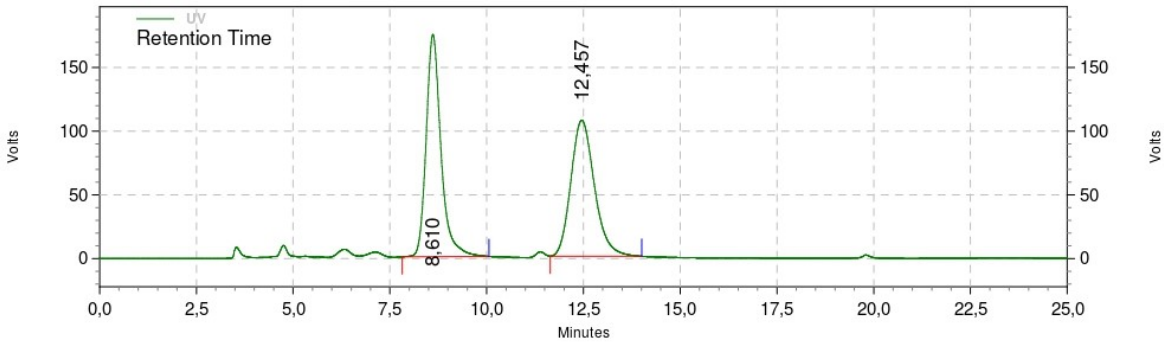
UV Results

Retention Time	Area	Area %	Height	Height %
18,093	16183126	18,42	165826	20,47
21,960	71680645	81,58	644239	79,53

Totals	87863771	100,00	810065	100,00

Chiral HPLC chromatogram of racemic 3c

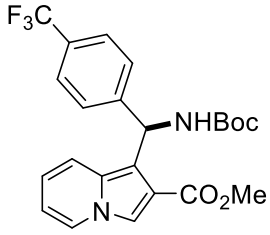


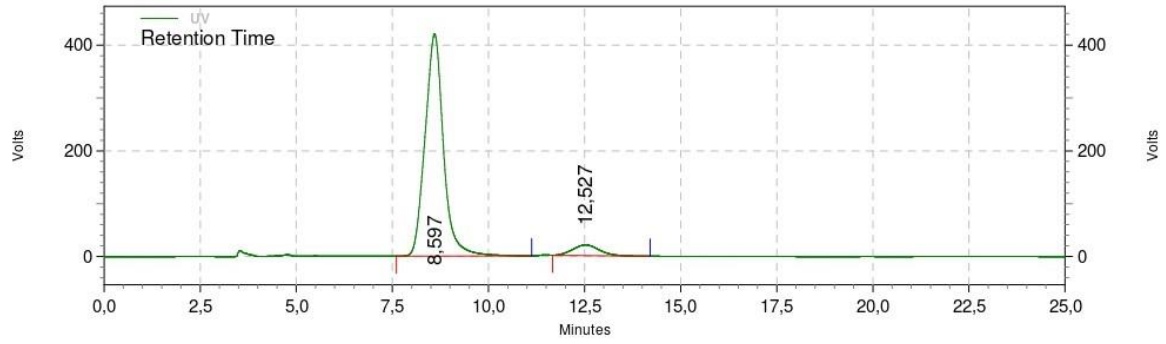


UV Results

Retention Time	Area	Area %	Height	Height %
8,610	18564812	50,65	697950	62,01
12,457	18087139	49,35	427681	37,99
Totals	36651951	100,00	1125631	100,00

Chiral HPLC chromatogram of chiral 3c

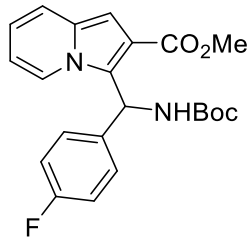


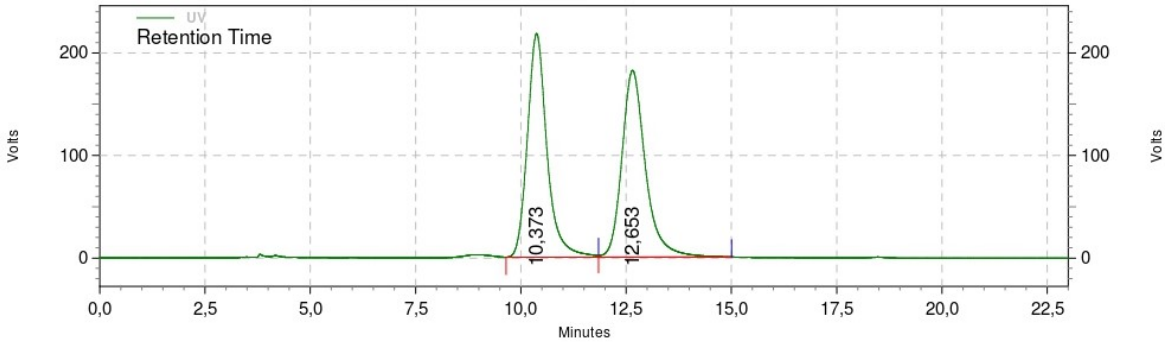


UV Results

Retention Time	Area	Area %	Height	Height %
8,597	56085747	93,45	1682161	95,41
12,527	3933280	6,55	80920	4,59
Totals	60019027	100,00	1763081	100,00

Chiral HPLC chromatogram of racemic 4d

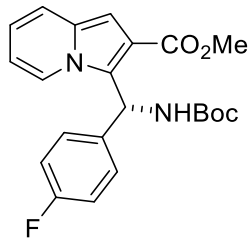


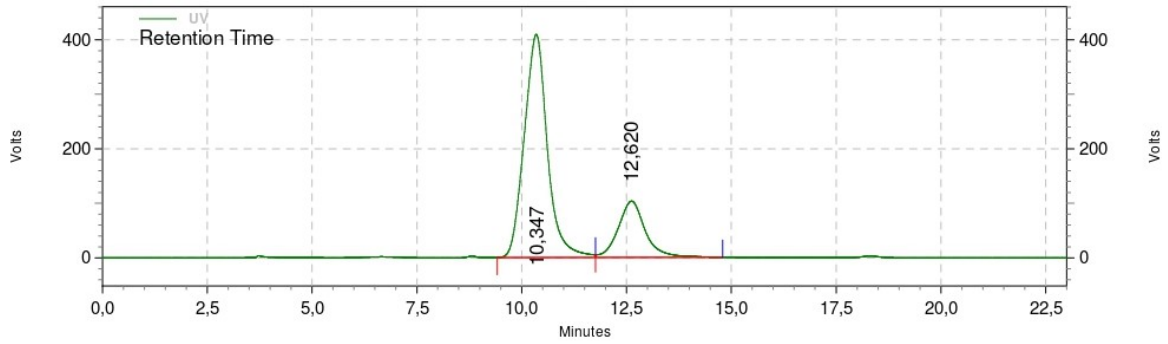


UV Results

Retention Time	Area	Area %	Height	Height %
10,373	28194791	49,87	871453	54,50
12,653	28347419	50,13	727495	45,50
Totals	56542210	100,00	1598948	100,00

Chiral HPLC chromatogram of chiral 4d

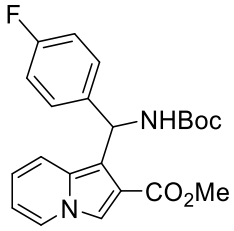


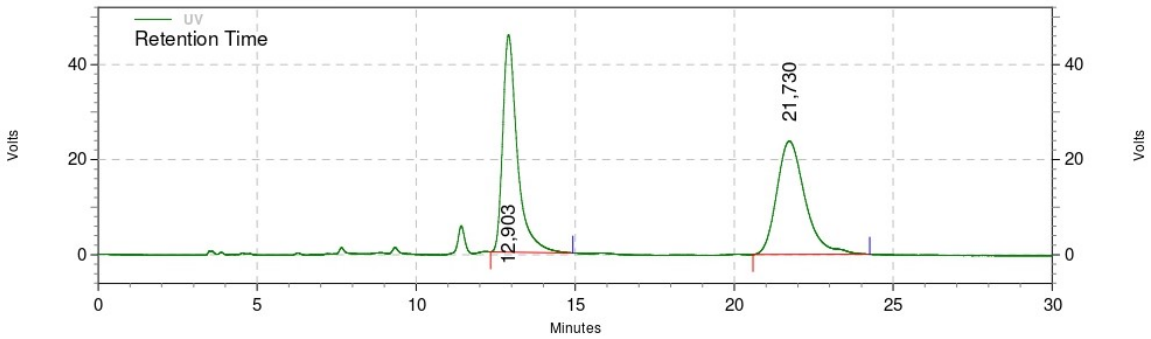


UV Results

Retention Time	Area	Area %	Height	Height %
10,347	62807919	77,19	1636167	79,84
12,620	18555046	22,81	413153	20,16
Totals	81362965	100,00	2049320	100,00

Chiral HPLC chromatogram of racemic 3d

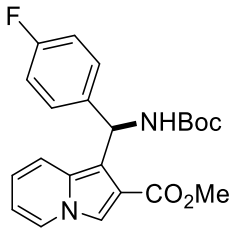


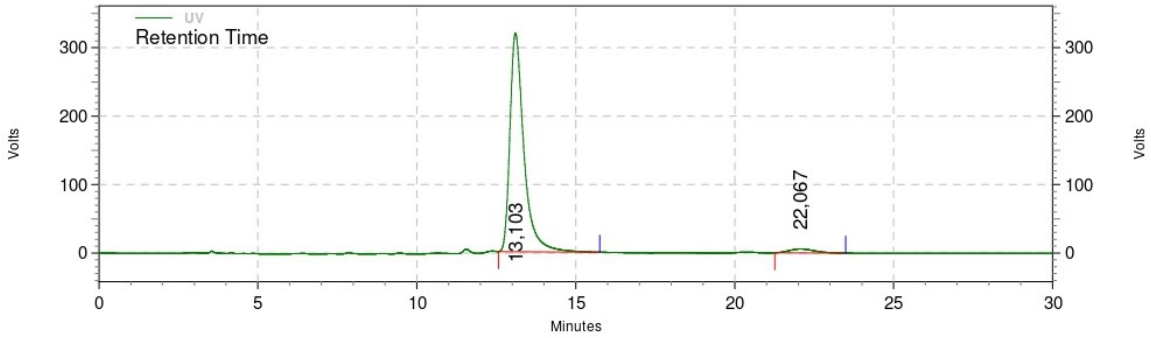


UV Results

Retention Time	Area	Area %	Height	Height %
12,903	5836341	49,72	182886	65,69
21,730	5901016	50,28	95517	34,31
Totals	11737357	100,00	278403	100,00

Chiral HPLC chromatogram of chiral 3d

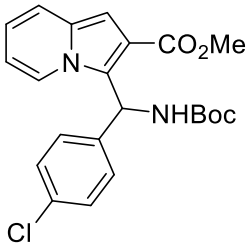


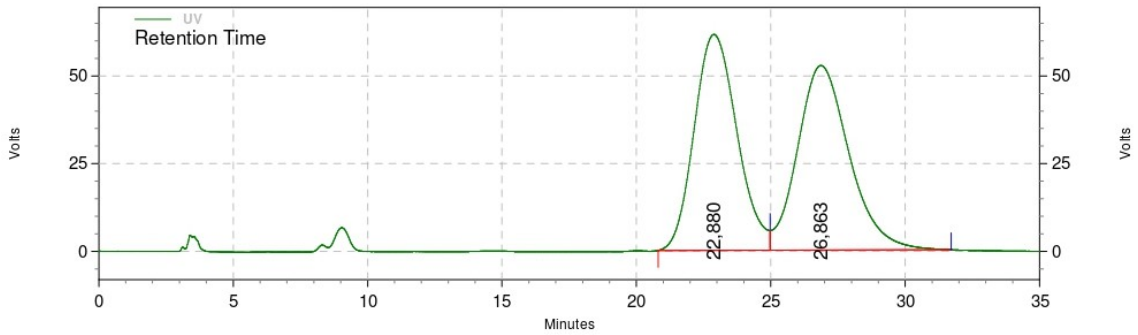


UV Results

Retention Time	Area	Area %	Height	Height %
13,103	39048408	96,84	1276314	98,25
22,067	1272773	3,16	22692	1,75
Totals	40321181	100,00	1299006	100,00

Chiral HPLC chromatogram of racemic 4e

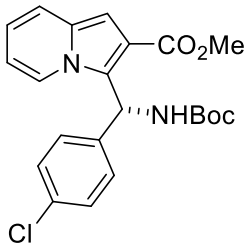


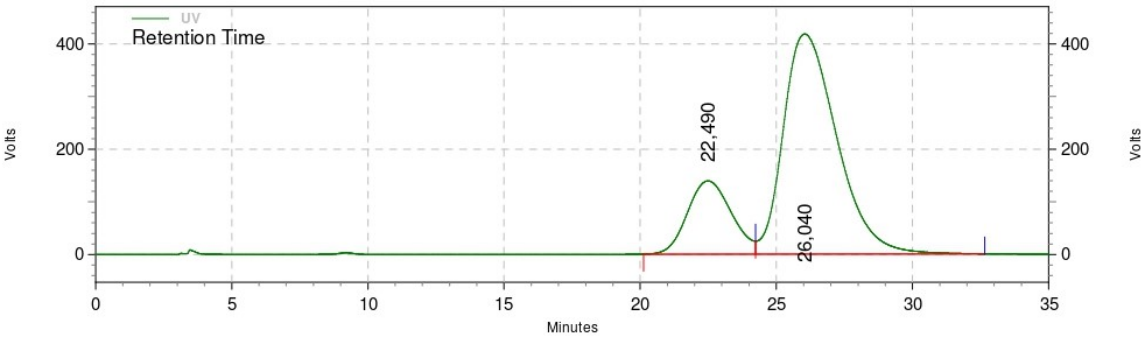


UV Results

Retention Time	Area	Area %	Height	Height %
22,880	27251563	49,25	246034	53,92
26,863	28082220	50,75	210273	46,08
Totals	55333783	100,00	456307	100,00

Chiral HPLC chromatogram of chiral 4e

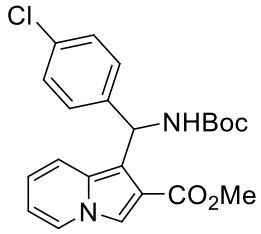


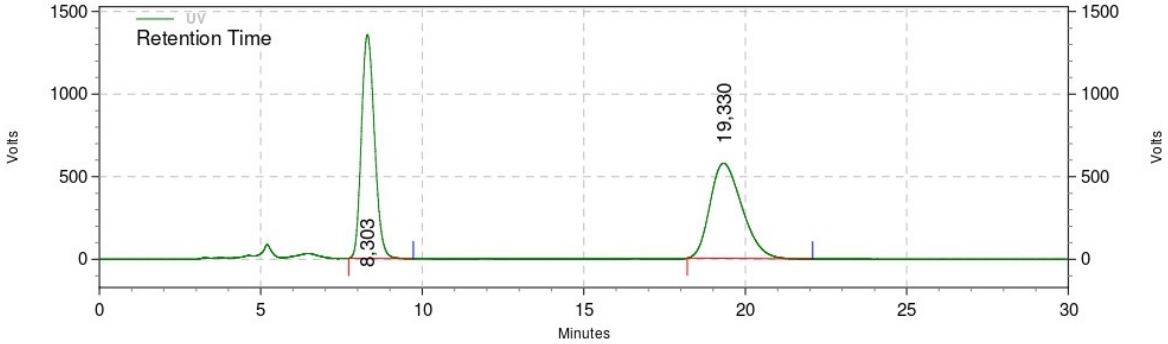


UV Results

Retention Time	Area	Area %	Height	Height %
22,490	62179727	21,40	556255	24,97
26,040	228418982	78,60	1671880	75,03
Totals	290598709	100,00	2228135	100,00

Chiral HPLC chromatogram of racemic 3e

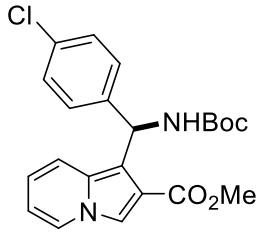


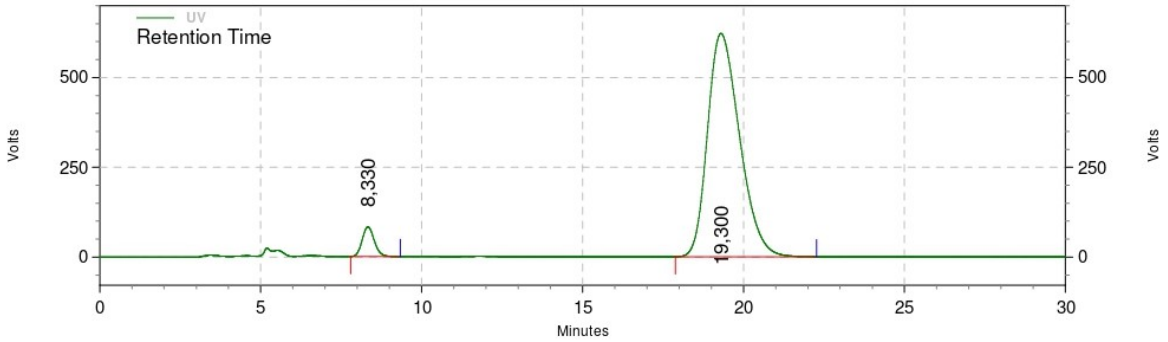


UV Results

Retention Time	Area	Area %	Height	Height %
8,303	152989548	49,09	5418360	70,14
19,330	158644455	50,91	2306879	29,86
Totals	311634003	100,00	7725239	100,00

Chiral HPLC chromatogram of chiral 3e

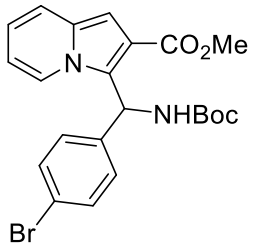


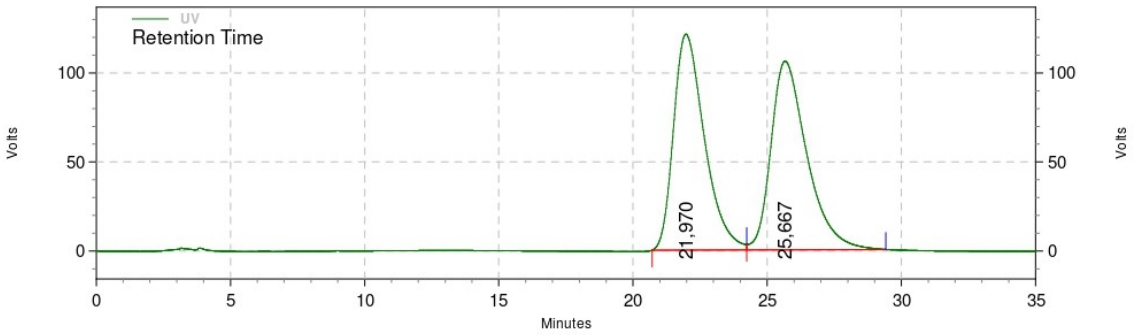


UV Results

Retention Time	Area	Area %	Height	Height %
8,330	8662946	4,78	330986	11,74
19,300	172415471	95,22	2487606	88,26
Totals	181078417	100,00	2818592	100,00

Chiral HPLC chromatogram of racemic 4f

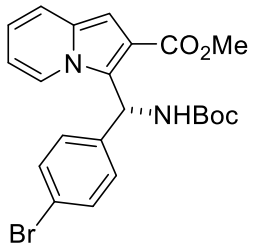


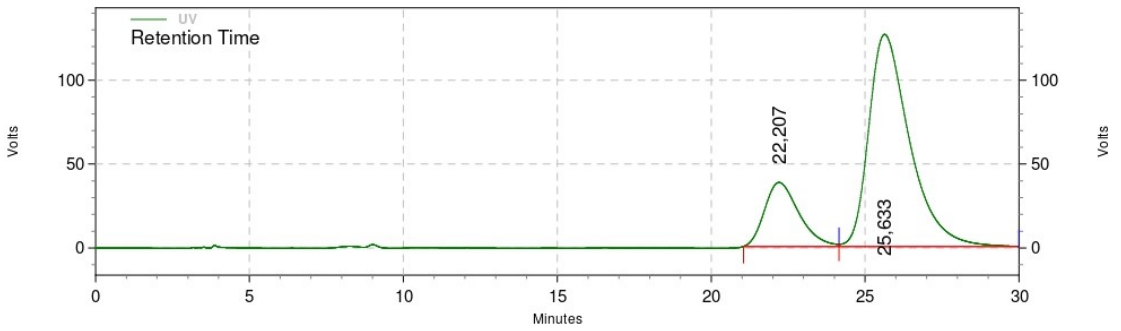


UV Results

Retention Time	Area	Area %	Height	Height %
21,970	38775658	49,59	485056	53,37
25,667	39412010	50,41	423766	46,63
Totals	78187668	100,00	908822	100,00

Chiral HPLC chromatogram of chiral 4f

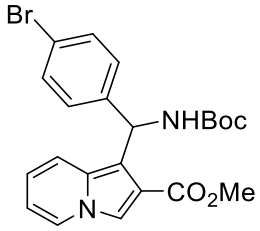


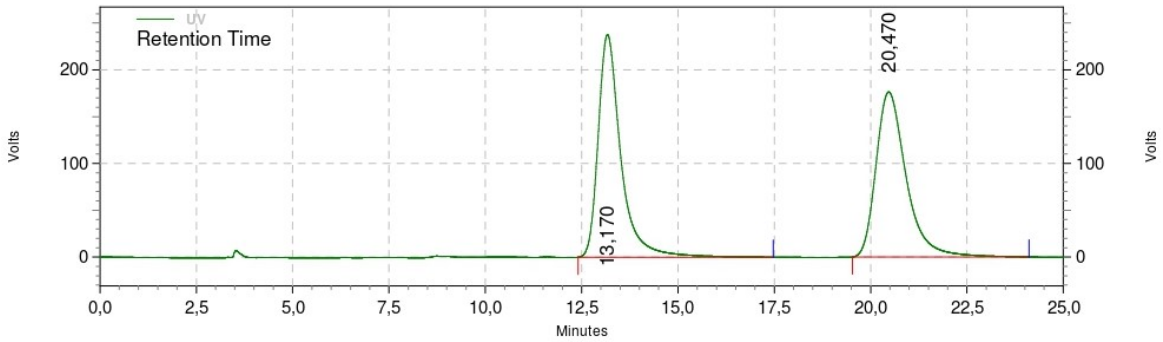


UV Results

Retention Time	Area	Area %	Height	Height %
22,207	11829174	20,24	152605	23,17
25,633	46614556	79,76	505893	76,83
Totals	58443730	100,00	658498	100,00

Chiral HPLC chromatogram of racemic 3f



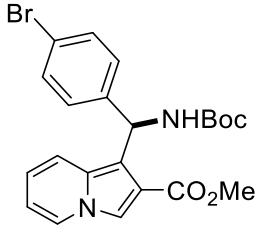


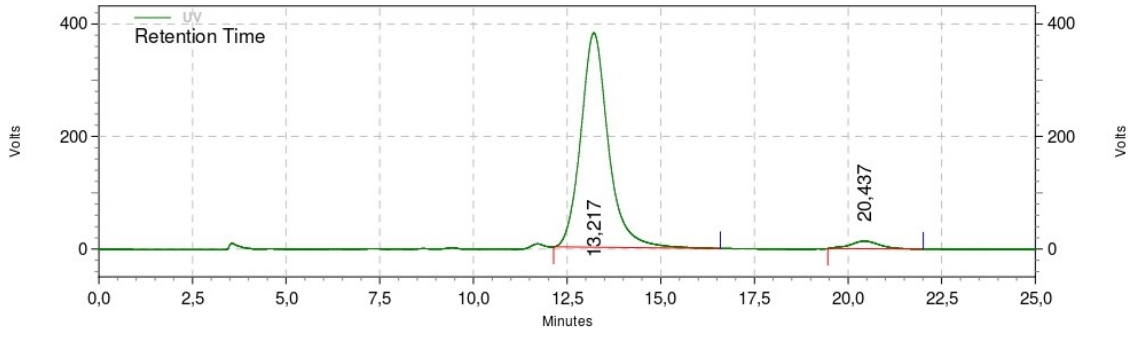
UV Results

Retention Time	Area	Area %	Height	Height %
13,170	38948744	50,37	951174	57,42
20,470	38382878	49,63	705464	42,58

Totals	77331622	100,00	1656638	100,00

Chiral HPLC chromatogram of chiral 3f



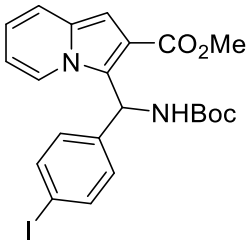


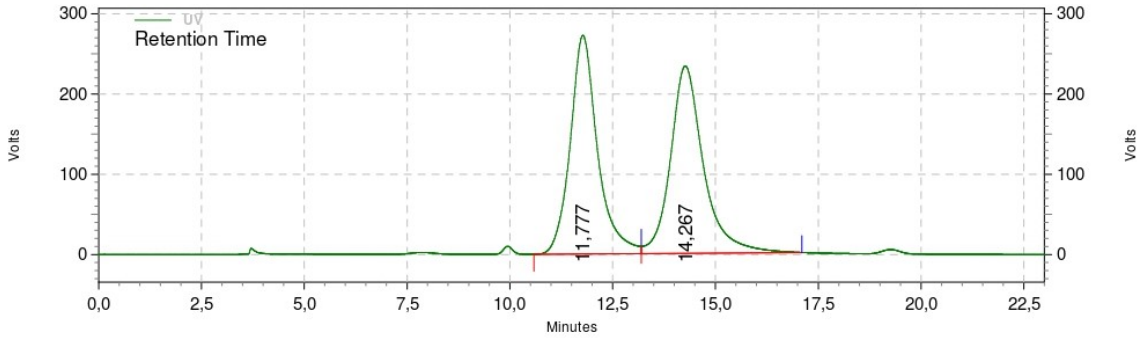
UV Results

Retention Time	Area	Area %	Height	Height %
13,217	77671067	96,31	1523542	96,55
20,437	2979225	3,69	54370	3,45

Totals	80650292	100,00	1577912	100,00

Chiral HPLC chromatogram of racemic 4g

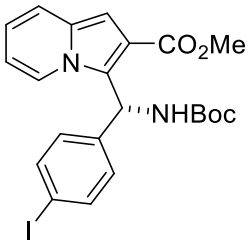


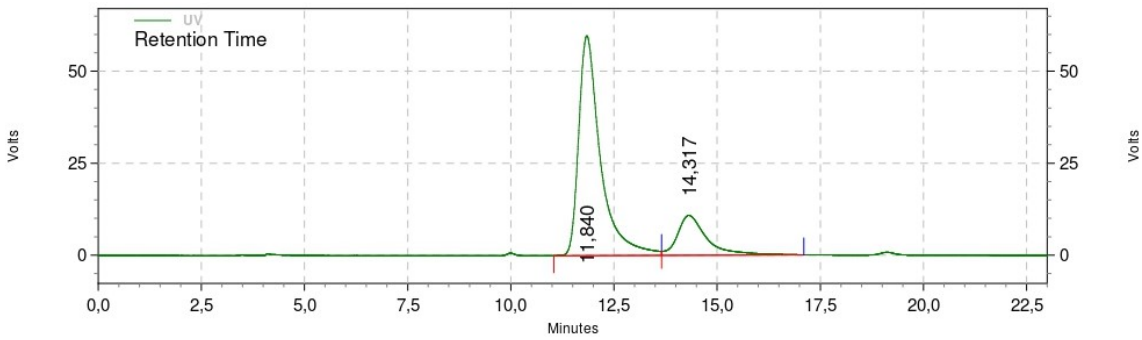


UV Results

Retention Time	Area	Area %	Height	Height %
11,777	50337746	49,18	1089135	53,83
14,267	52025693	50,82	934177	46,17
Totals	102363439	100,00	2023312	100,00

Chiral HPLC chromatogram of chiral 4g

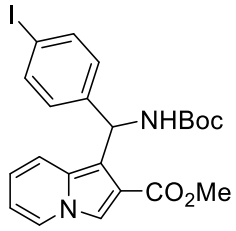


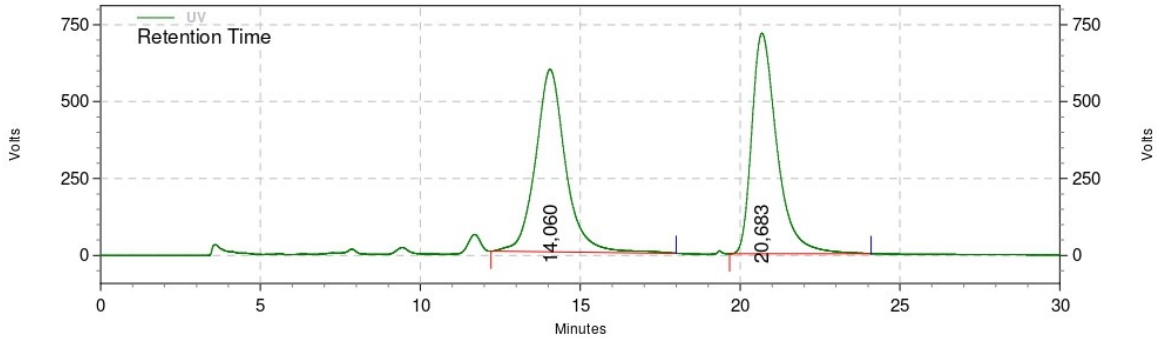


UV Results

Retention Time	Area	Area %	Height	Height %
11,840	8750995	80,53	238750	84,65
14,317	2115123	19,47	43291	15,35
Totals	10866118	100,00	282041	100,00

Chiral HPLC chromatogram of racemic 3g



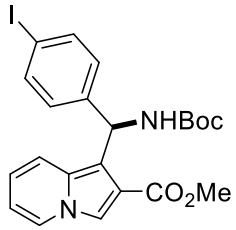


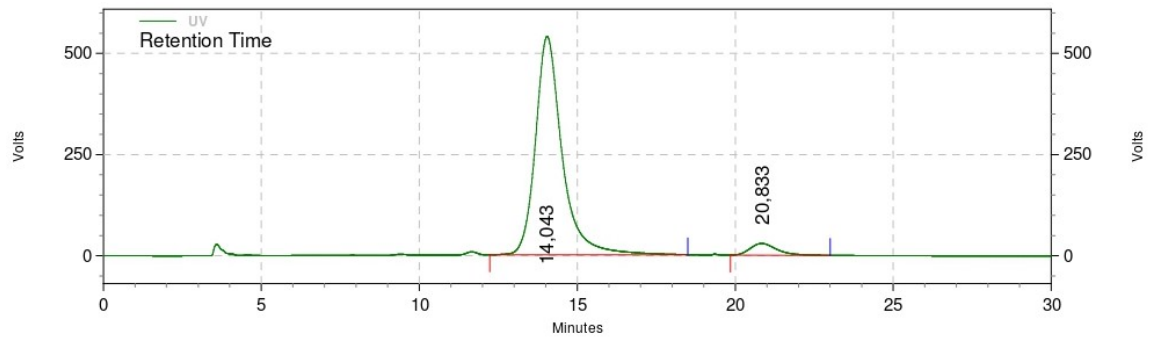
UV Results

Retention Time	Area	Area %	Height	Height %
14,060	155133263	49,66	2372929	45,28
20,683	157285204	50,34	2867954	54,72

Totals	312418467	100,00	5240883	100,00

Chiral HPLC chromatogram of chiral 3g



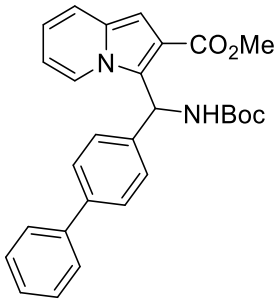


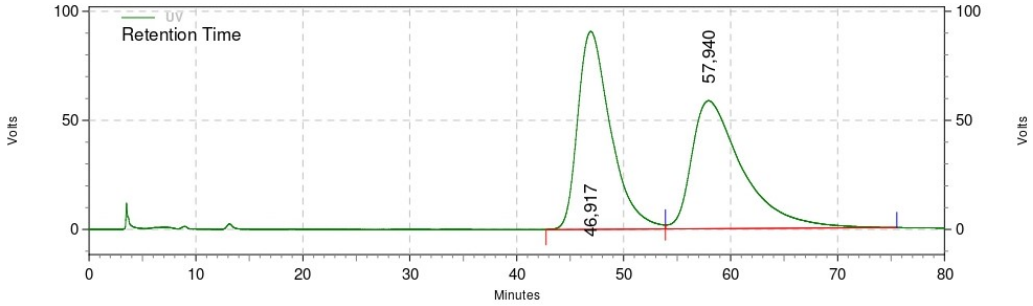
UV Results

Retention Time	Area	Area %	Height	Height %
14,043	127151776	94,92	2158714	94,91
20,833	6805488	5,08	115758	5,09

Totals	133957264	100,00	2274472	100,00

Chiral HPLC chromatogram of racemic 4h

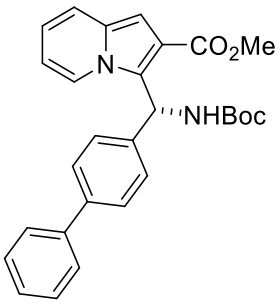


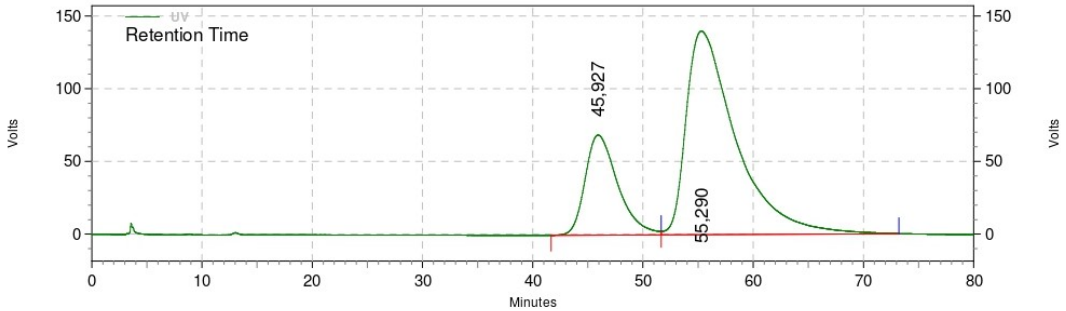


UV Results

Retention Time	Area	Area %	Height	Height %
46,917	77672077	50,15	362630	60,72
57,940	77218864	49,85	234540	39,28
Totals	154890941	100,00	597170	100,00

Chiral HPLC chromatogram of chiral 4h

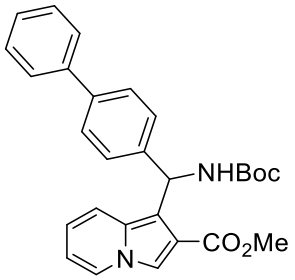


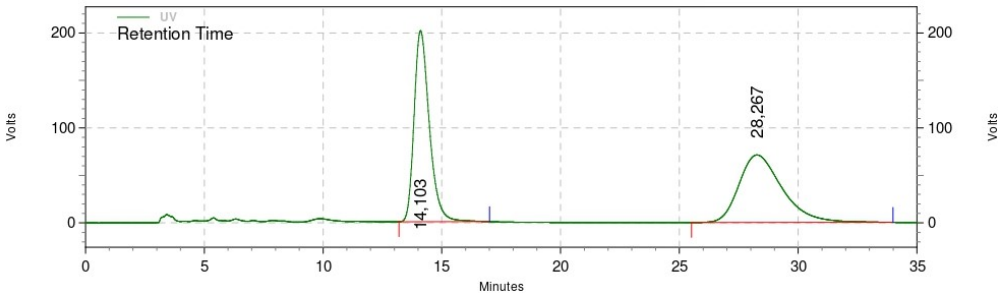


UV Results

Retention Time	Area	Area %	Height	Height %
45,927	56670974	24,42	275296	32,97
55,290	175401003	75,58	559723	67,03
Totals	232071977	100,00	835019	100,00

Chiral HPLC chromatogram of racemic 3h

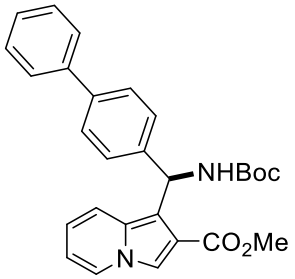


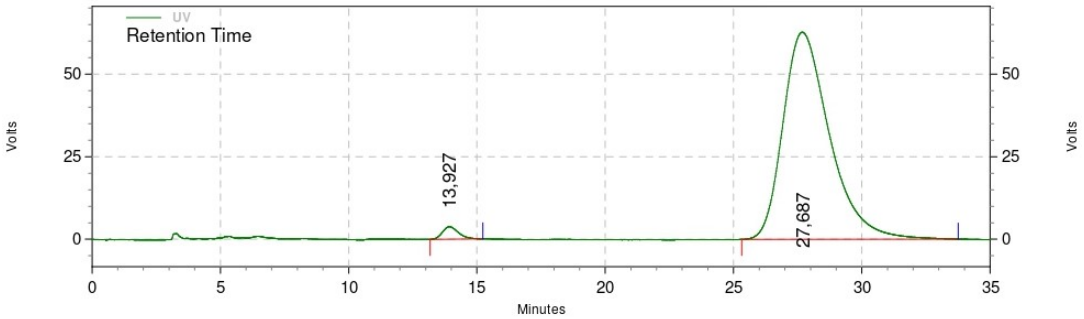


UV Results

Retention Time	Area	Area %	Height	Height %
14,103	35979376	50,00	804698	73,89
28,267	35973592	50,00	284390	26,11
Totals	71952968	100,00	1089088	100,00

Chiral HPLC chromatogram of chiral 3h

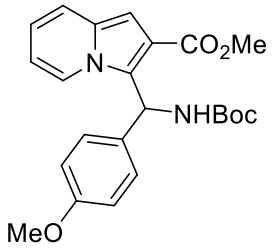


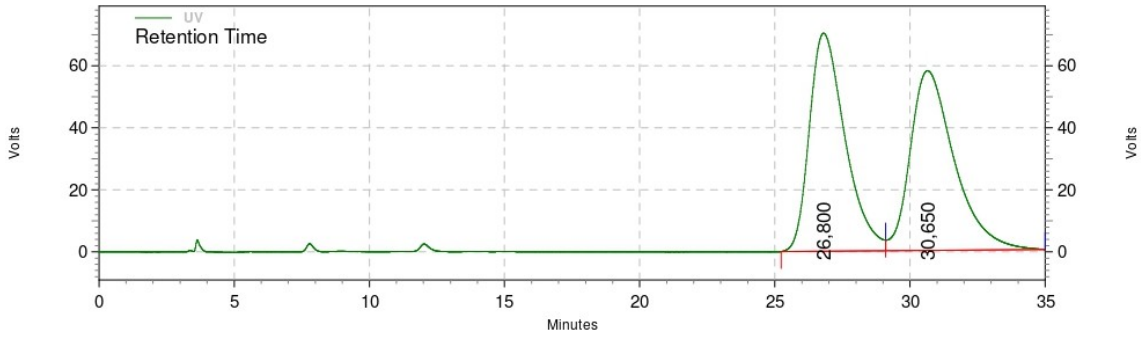


UV Results

Retention Time	Area	Area %	Height	Height %
13,927	650696	2,02	15073	5,67
27,687	31638076	97,98	250826	94,33
Totals	32288772	100,00	265899	100,00

Chiral HPLC chromatogram of racemic 4i

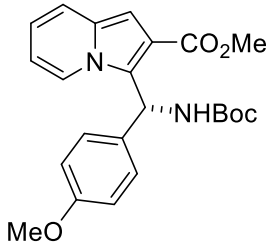


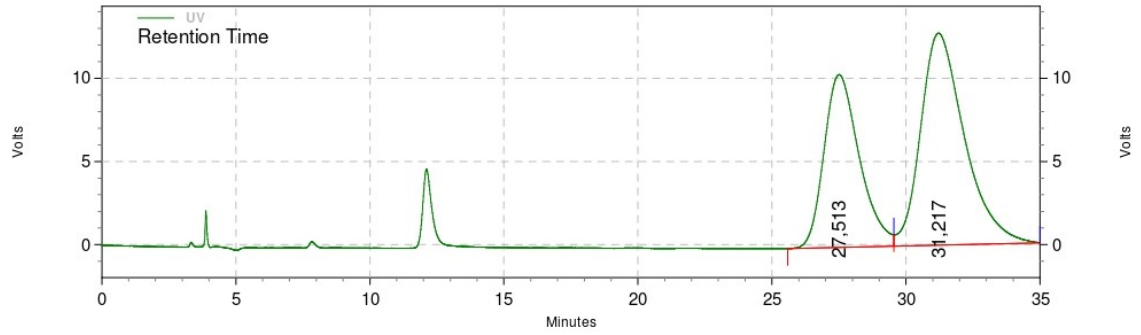


UV Results

Retention Time	Area	Area %	Height	Height %
26,800	25787071	49,55	281163	54,82
30,650	26256268	50,45	231760	45,18
Totals	52043339	100,00	512923	100,00

Chiral HPLC chromatogram of chiral 4i

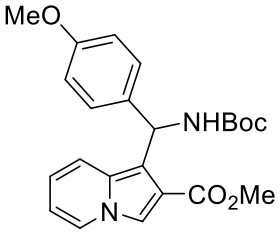


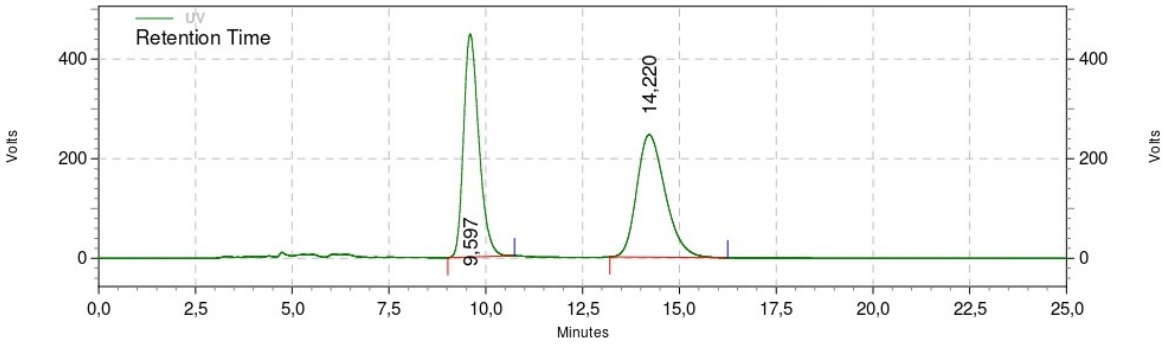


UV Results

Retention Time	Area	Area %	Height	Height %
27,513	3805754	39,63	41566	44,91
31,217	5797016	60,37	50991	55,09
Totals	9602770	100,00	92557	100,00

Chiral HPLC chromatogram of racemic 3i

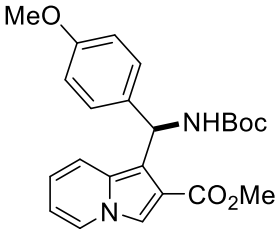


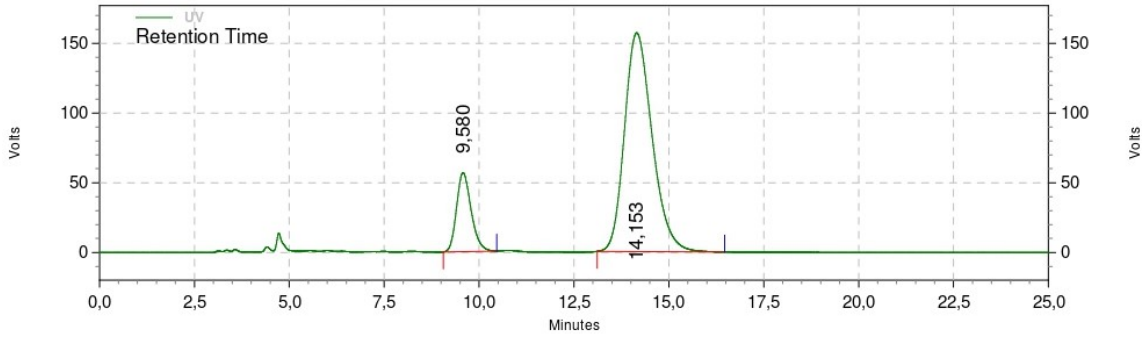


UV Results

Retention Time	Area	Area %	Height	Height %
9,597	49344175	49,50	1791299	64,53
14,220	50345015	50,50	984751	35,47
Totals	99689190	100,00	2776050	100,00

Chiral HPLC chromatogram of chiral 3i

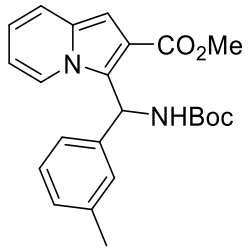


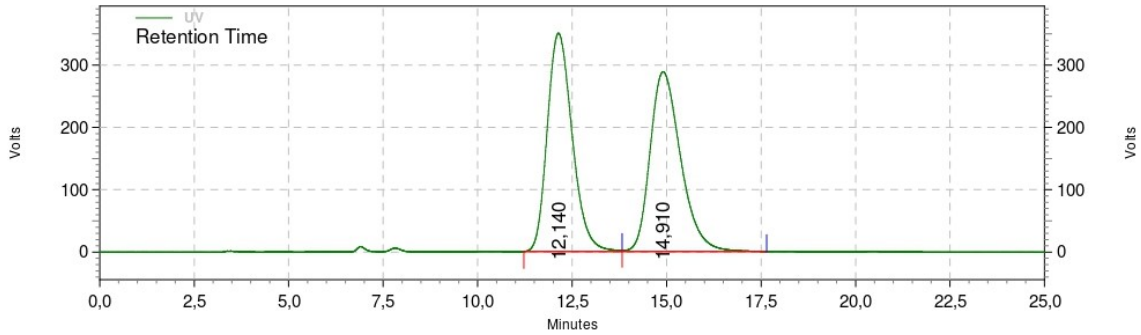


UV Results

Retention Time	Area	Area %	Height	Height %
9,580	6057180	15,99	226492	26,53
14,153	31814308	84,01	627316	73,47
Totals	37871488	100,00	853808	100,00

Chiral HPLC chromatogram of racemic 4j



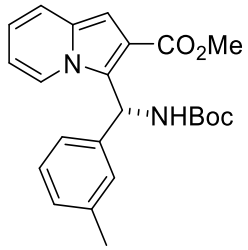


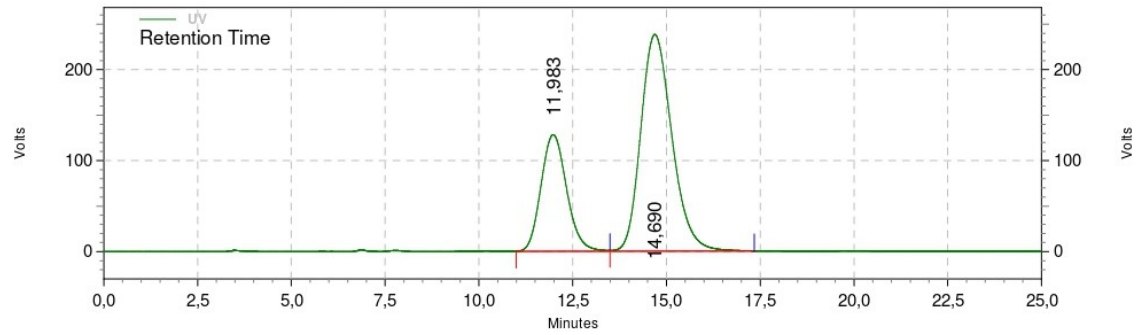
UV Results

Retention Time	Area	Area %	Height	Height %
12,140	64379837	49,81	1400738	54,85
14,910	64881108	50,19	1153095	45,15

Totals	129260945	100,00	2553833	100,00

Chiral HPLC chromatogram of chiral 4j



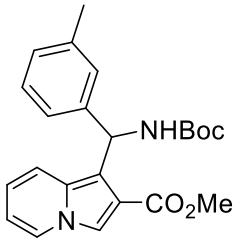


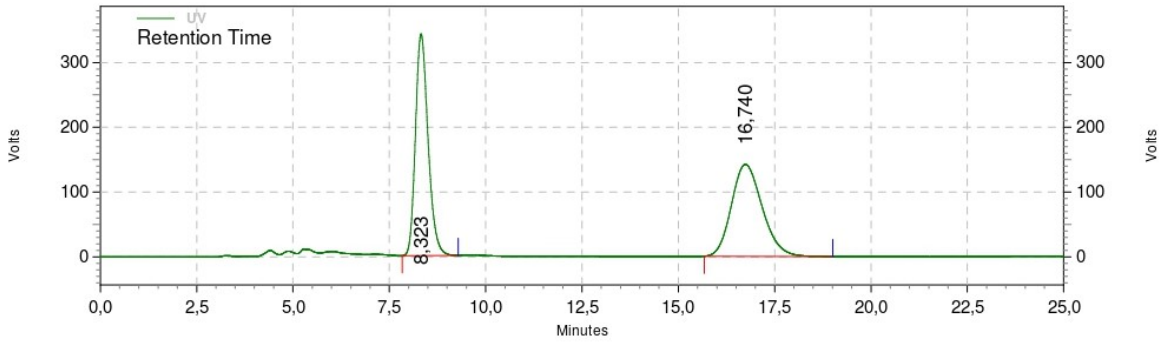
UV Results

Retention Time	Area	Area %	Height	Height %
11,983	24378989	30,74	512721	35,00
14,690	54918891	69,26	952325	65,00

Totals	79297880	100,00	1465046	100,00

Chiral HPLC chromatogram of racemic 3j

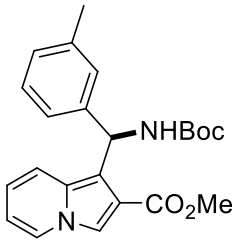


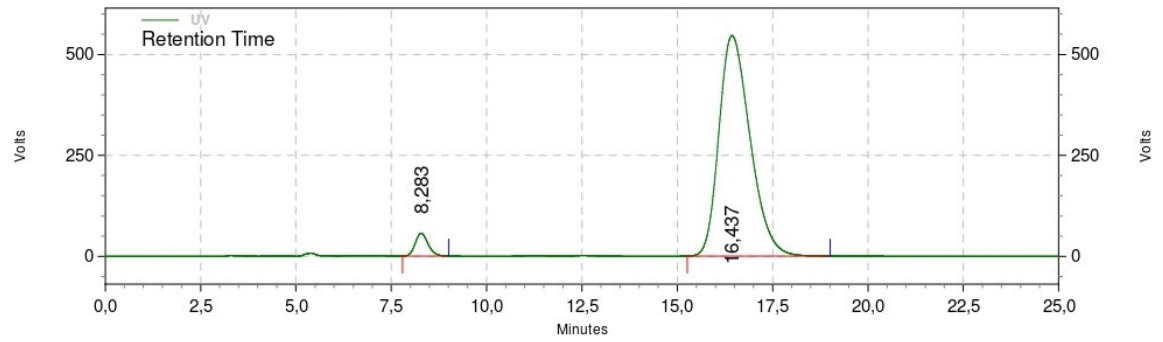


UV Results

Retention Time	Area	Area %	Height	Height %
8,323	31167327	49,70	1368776	70,67
16,740	31549426	50,30	568026	29,33
Totals	62716753	100,00	1936802	100,00

Chiral HPLC chromatogram of chiral 3j

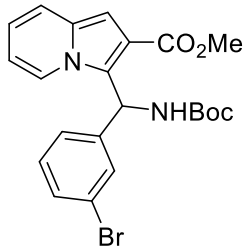


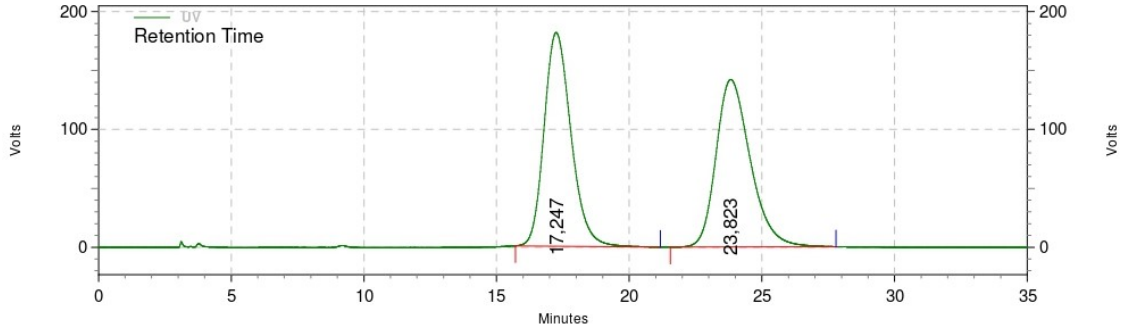


UV Results

Retention Time	Area	Area %	Height	Height %
8,283	5356214	4,13	227205	9,42
16,437	124246528	95,87	2184483	90,58
Totals	129602742	100,00	2411688	100,00

Chiral HPLC chromatogram of racemic 4k

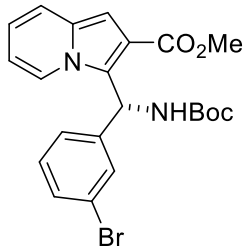


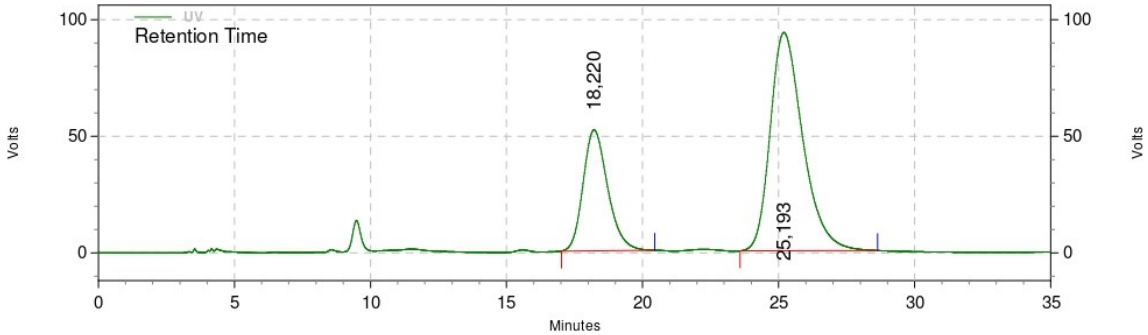


UV Results

Retention Time	Area	Area %	Height	Height %
17,247	51205008	50,05	725274	56,04
23,823	51099737	49,95	568924	43,96
Totals	102304745	100,00	1294198	100,00

Chiral HPLC chromatogram of chiral 4k

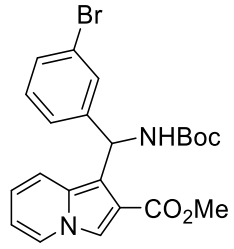


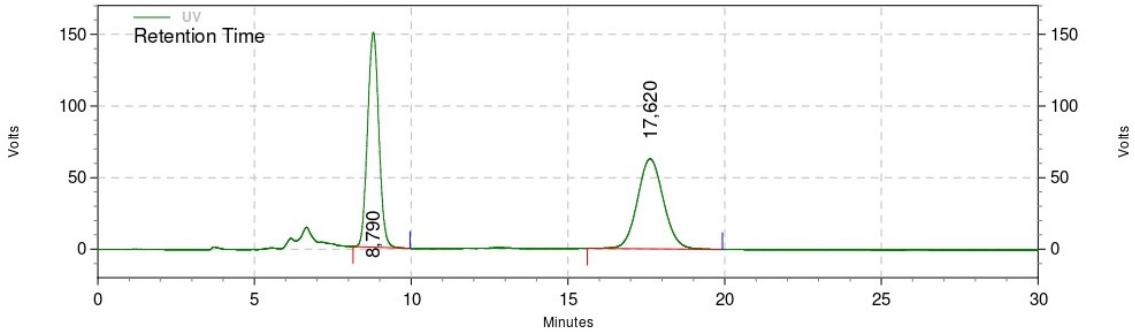


UV Results

Retention Time	Area	Area %	Height	Height %
18,220	13034520	29,46	207559	35,65
25,193	31213349	70,54	374622	64,35
Totals	44247869	100,00	582181	100,00

Chiral HPLC chromatogram of racemic 3k



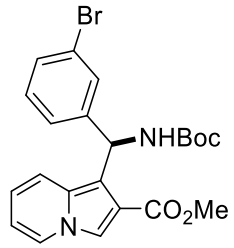


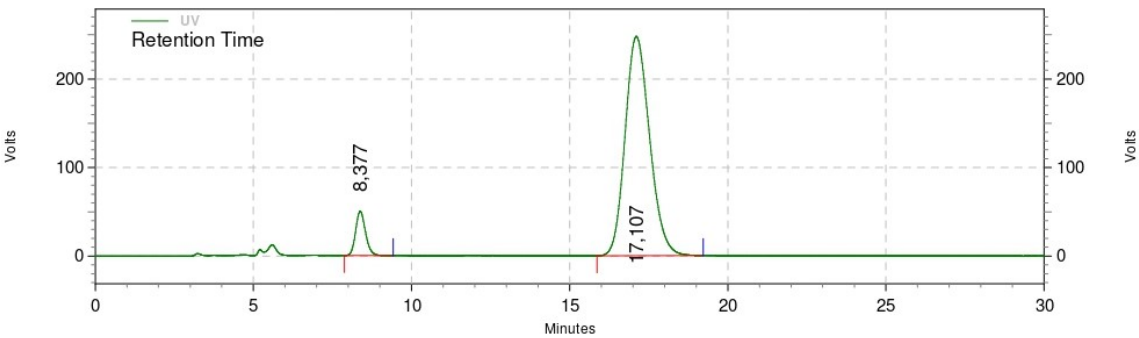
UV Results

Retention Time	Area	Area %	Height	Height %
8,790	15038327	50,92	599545	70,44
17,620	14494176	49,08	251572	29,56

Totals	29532503	100,00	851117	100,00

Chiral HPLC chromatogram of chiral 3k



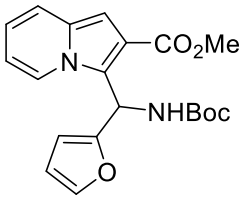


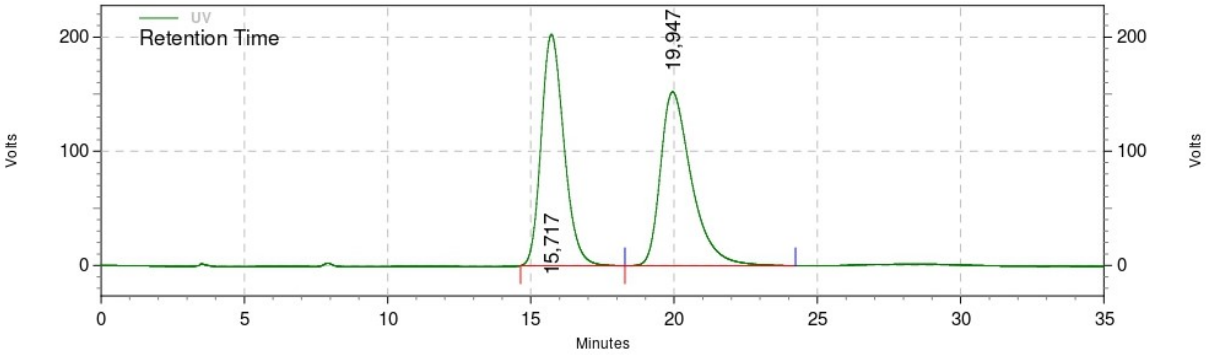
UV Results

Retention Time	Area	Area %	Height	Height %
8,377	4381626	7,57	200835	16,85
17,107	53493565	92,43	990925	83,15

Totals	57875191	100,00	1191760	100,00

Chiral HPLC chromatogram of racemic 4l

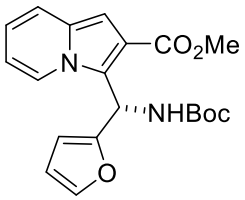


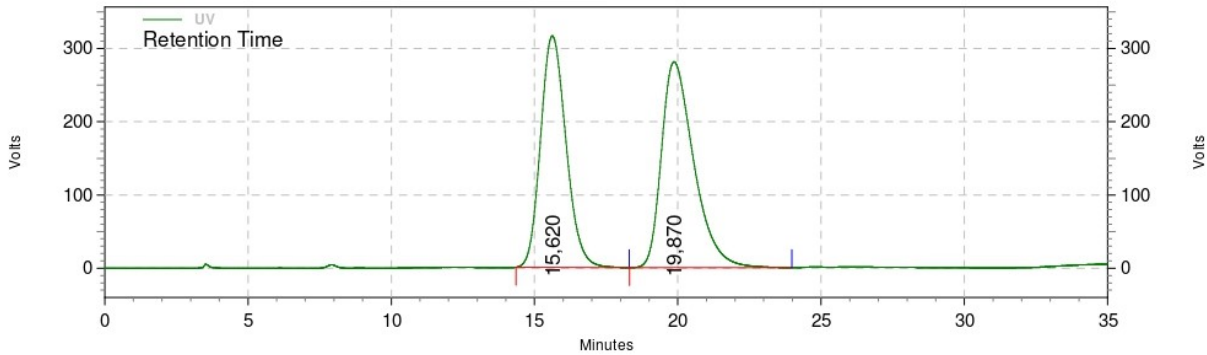


UV Results

Retention Time	Area	Area %	Height	Height %
15,717	44674800	49,31	810544	57,08
19,947	45932149	50,69	609449	42,92
Totals	90606949	100,00	1419993	100,00

Chiral HPLC chromatogram of chiral 4l

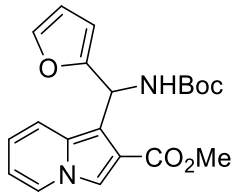


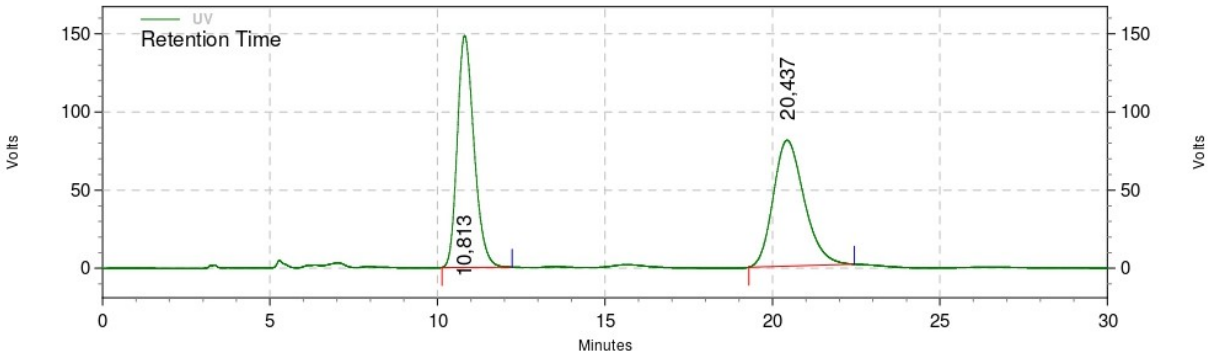


UV Results

Retention Time	Area	Area %	Height	Height %
15,620	78217572	47,00	1264228	52,94
19,870	88185589	53,00	1123858	47,06
Totals	166403161	100,00	2388086	100,00

Chiral HPLC chromatogram of racemic 3l

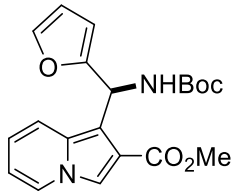


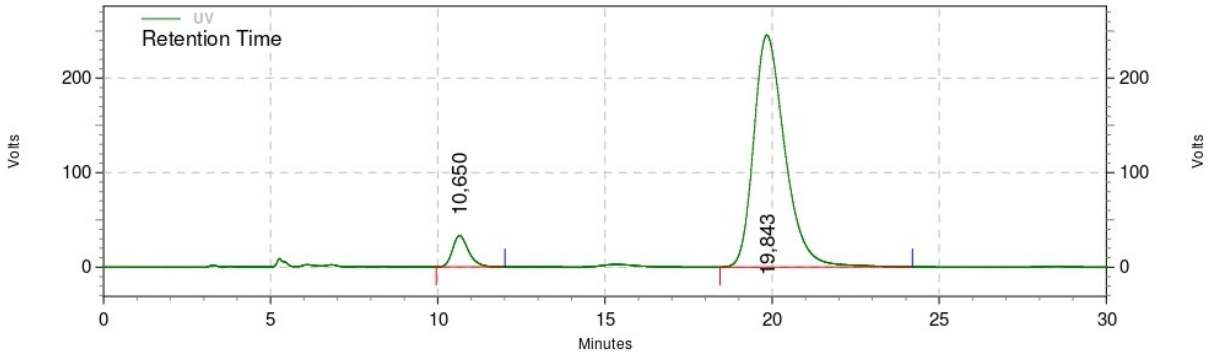


UV Results

Retention Time	Area	Area %	Height	Height %
10,813	20635314	49,98	592887	64,80
20,437	20648416	50,02	322027	35,20
Totals	41283730	100,00	914914	100,00

Chiral HPLC chromatogram of chiral 3l

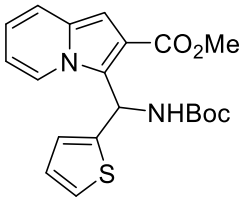


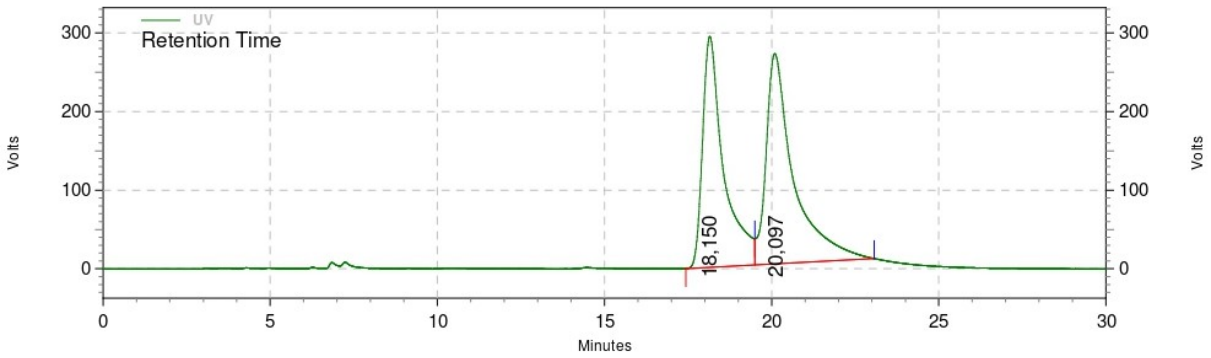


UV Results

Retention Time	Area	Area %	Height	Height %
10,650	4433978	6,51	132711	11,90
19,843	63643391	93,49	982265	88,10
Totals	68077369	100,00	1114976	100,00

Chiral HPLC chromatogram of racemic 4m

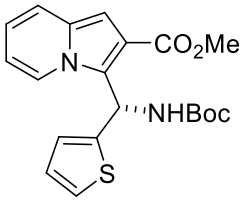


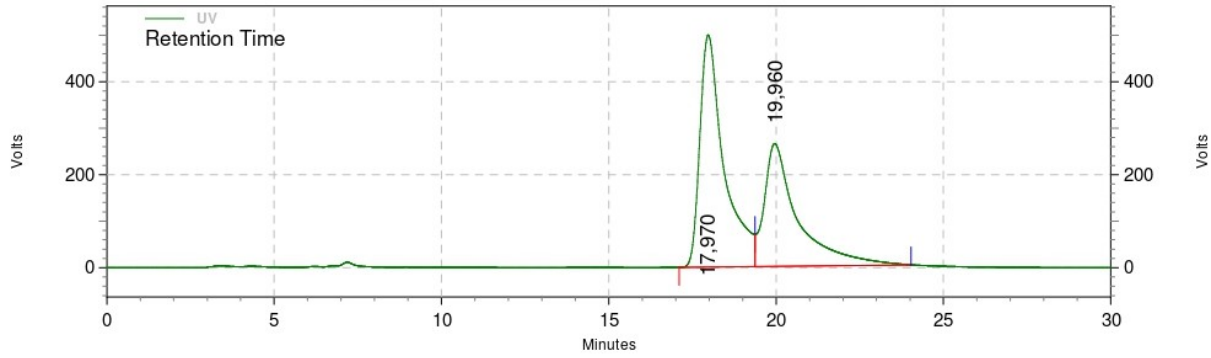


UV Results

Retention Time	Area	Area %	Height	Height %
18,150	51417152	45,60	1174076	52,35
20,097	61331138	54,40	1068865	47,65
Totals	112748290	100,00	2242941	100,00

Chiral HPLC chromatogram of chiral 4m

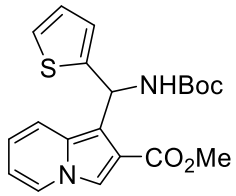


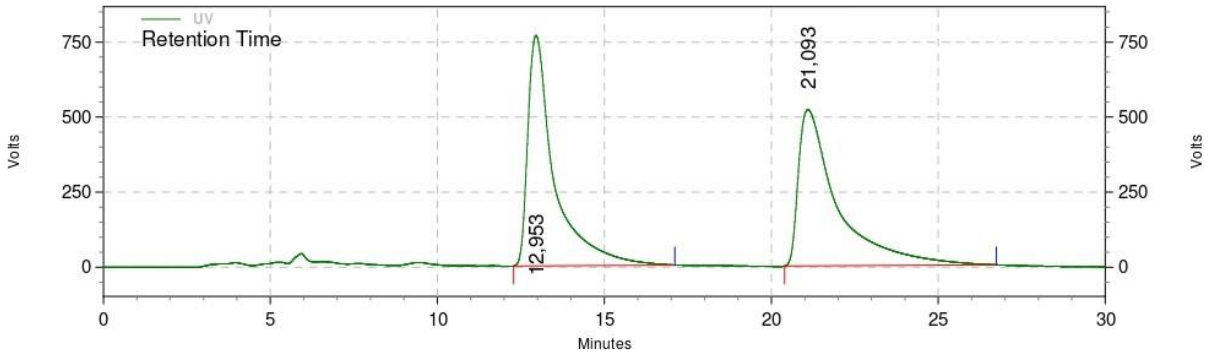


UV Results

Retention Time	Area	Area %	Height	Height %
17,970	99854384	57,71	1997846	65,40
19,960	73180870	42,29	1056916	34,60
Totals	173035254	100,00	3054762	100,00

Chiral HPLC chromatogram of racemic 3m

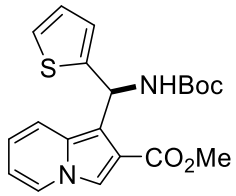


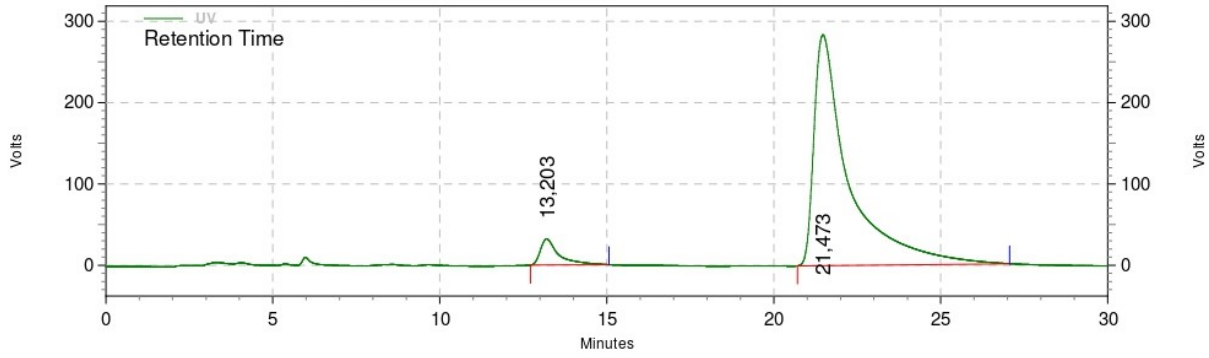


UV Results

Retention Time	Area	Area %	Height	Height %
12,953	169043090	50,00	3071260	59,57
21,093	169032737	50,00	2084610	40,43
Totals	338075827	100,00	5155870	100,00

Chiral HPLC chromatogram of chiral 3m

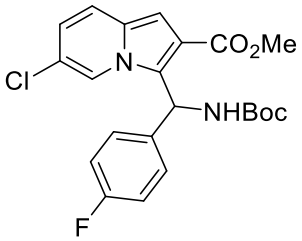


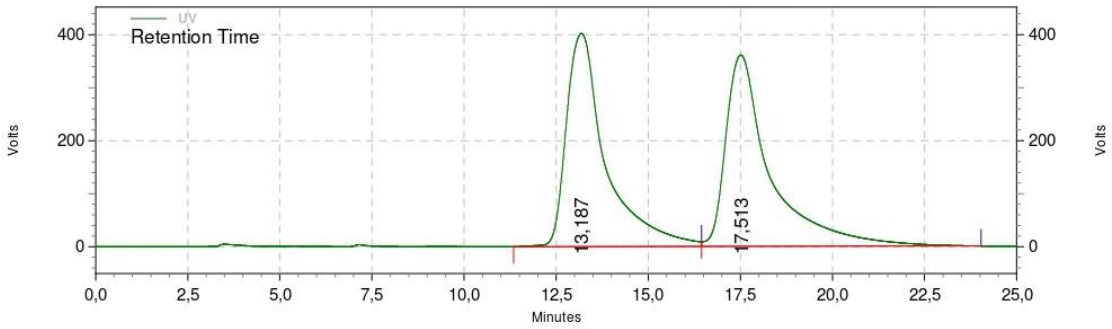


UV Results

Retention Time	Area	Area %	Height	Height %
13,203	4923712	5,67	128563	10,17
21,473	81950492	94,33	1135042	89,83
Totals	86874204	100,00	1263605	100,00

Chiral HPLC chromatogram of racemic 4n



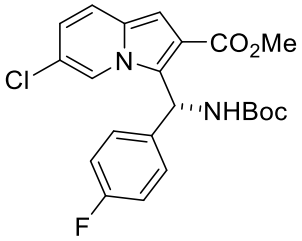


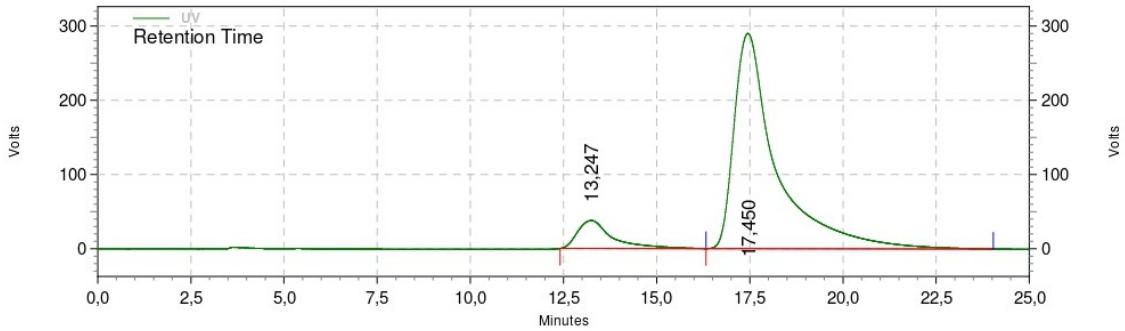
UV Results

Retention Time	Area	Area %	Height	Height %
13,187	118528905	49,49	1607833	52,68
17,513	120983617	50,51	1444327	47,32

Totals	239512522	100,00	3052160	100,00

Chiral HPLC chromatogram of chiral 4n



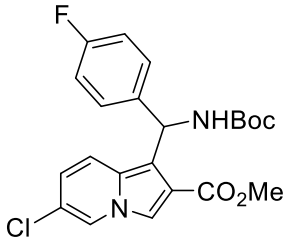


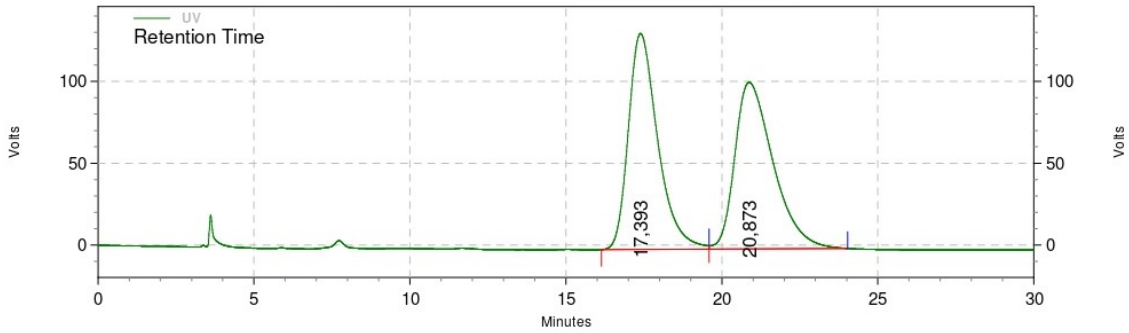
UV Results

Retention Time	Area	Area %	Height	Height %
13,247	9850667	9,70	151069	11,52
17,450	91659546	90,30	1160618	88,48

Totals	101510213	100,00	1311687	100,00

Chiral HPLC chromatogram of racemic 3n

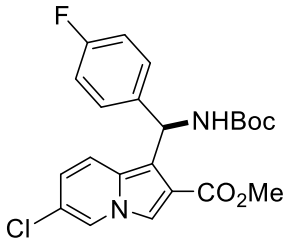


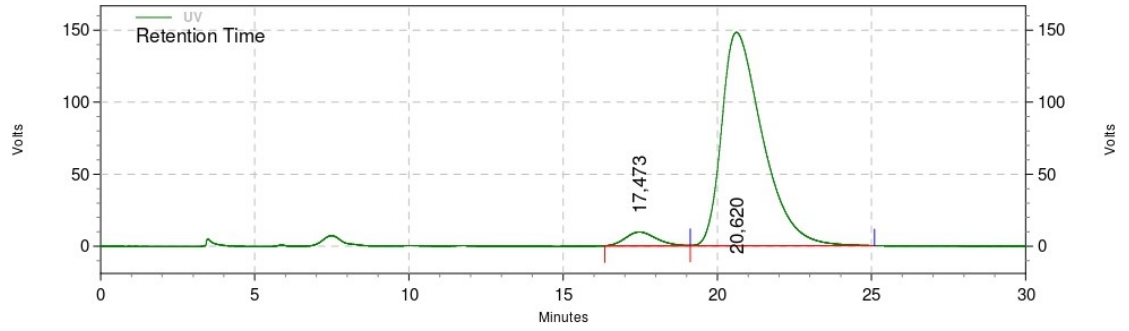


UV Results

Retention Time	Area	Area %	Height	Height %
17,393	34623027	49,86	528243	56,45
20,873	34815377	50,14	407582	43,55
Totals	69438404	100,00	935825	100,00

Chiral HPLC chromatogram of chiral 3n

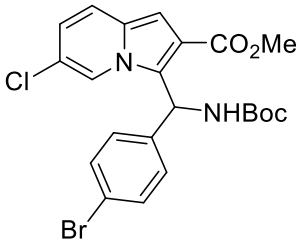


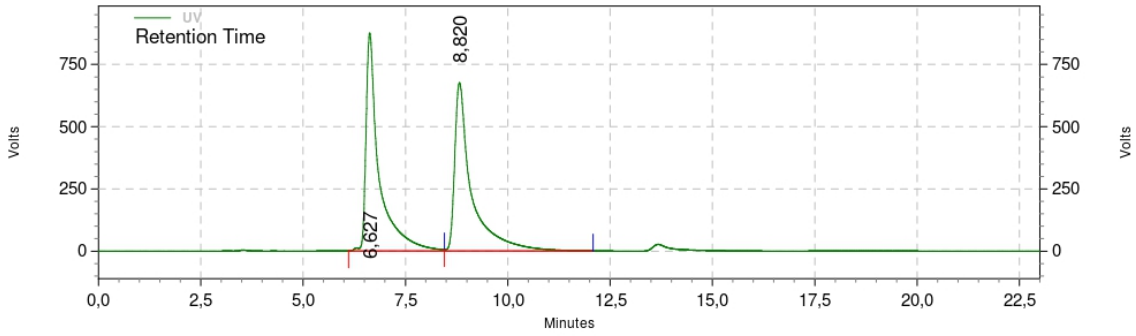


UV Results

Retention Time	Area	Area %	Height	Height %
17,473	2645841	4,62	38205	6,06
20,620	54562601	95,38	591872	93,94
Totals	57208442	100,00	630077	100,00

Chiral HPLC chromatogram of racemic 4o

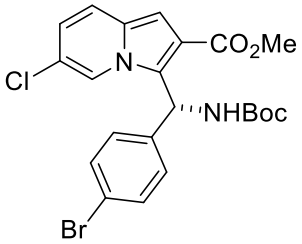


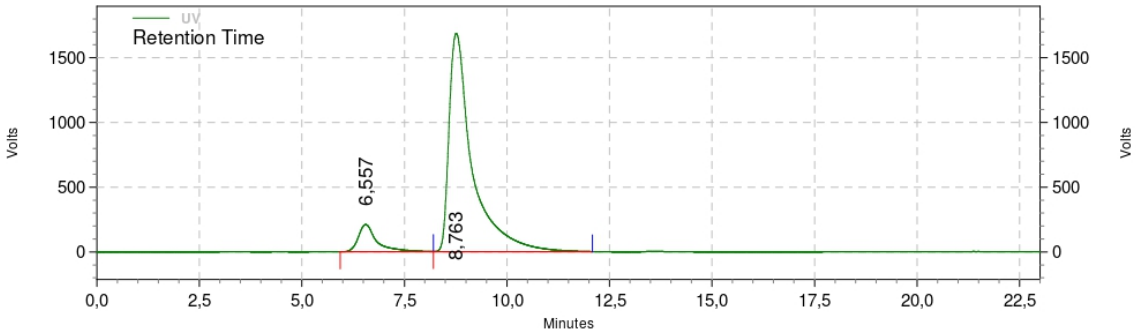


UV Results

Retention Time	Area	Area %	Height	Height %
6,627	77790690	50,33	3501343	56,42
8,820	76758625	49,67	2704899	43,58
Totals	154549315	100,00	6206242	100,00

Chiral HPLC chromatogram of chiral 4o

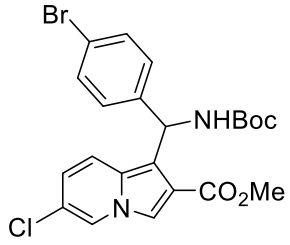


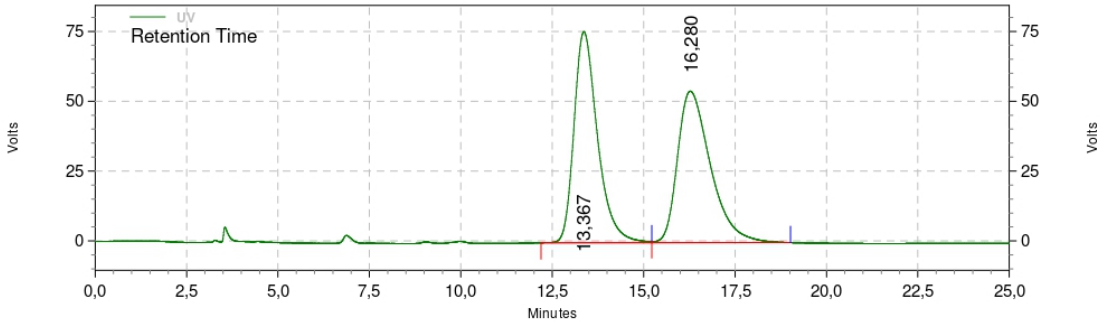


UV Results

Retention Time	Area	Area %	Height	Height %
6,557	26577923	9,12	840443	11,08
8,763	264758608	90,88	6744832	88,92
Totals	291336531	100,00	7585275	100,00

Chiral HPLC chromatogram of racemic 3o

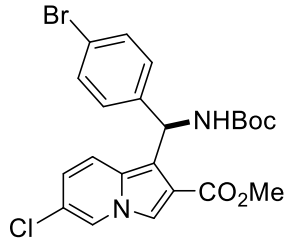


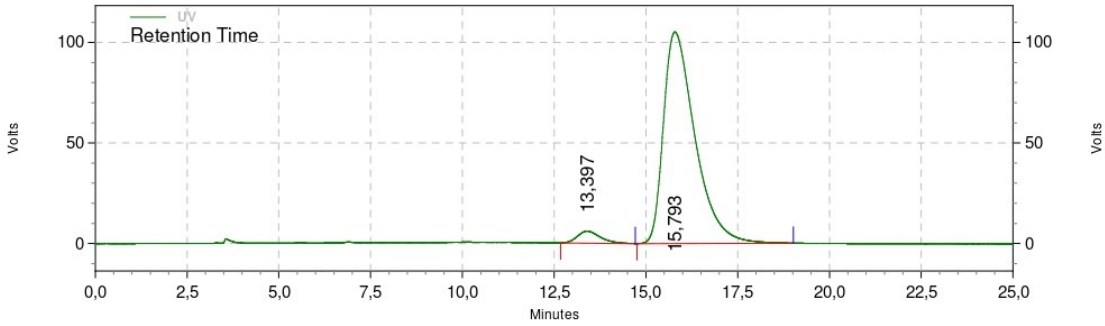


UV Results

Retention Time	Area	Area %	Height	Height %
13,367	13521189	49,88	302187	58,20
16,280	13587891	50,12	217014	41,80
Totals	27109080	100,00	519201	100,00

Chiral HPLC chromatogram of chiral 3o

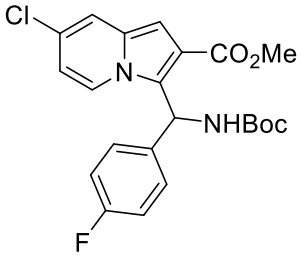


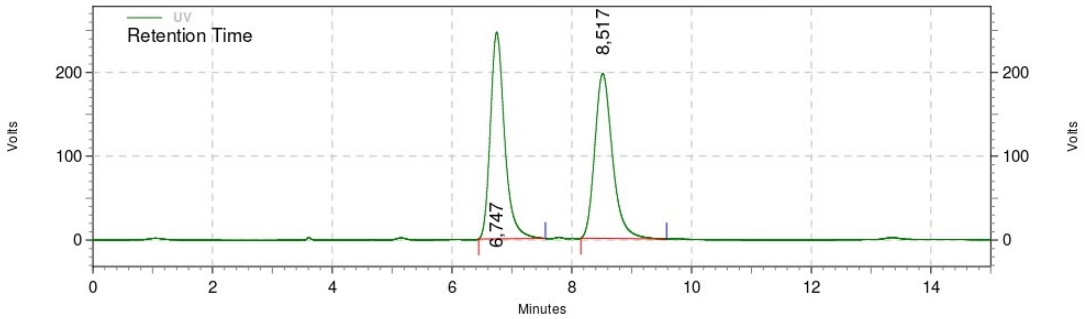


UV Results

Retention Time	Area	Area %	Height	Height %
13,397	1024337	3,93	23782	5,35
15,793	25065047	96,07	420686	94,65
Totals	26089384	100,00	444468	100,00

Chiral HPLC chromatogram of racemic 4p

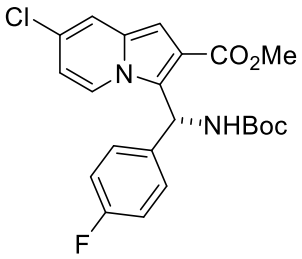


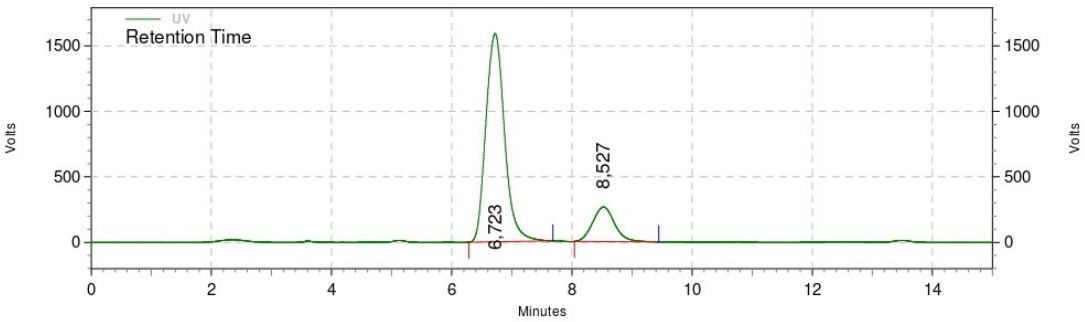


UV Results

Retention Time	Area	Area %	Height	Height %
6,747	16285939	50,23	985252	55,61
8,517	16133609	49,77	786339	44,39
Totals	32419548	100,00	1771591	100,00

Chiral HPLC chromatogram of chiral 4p

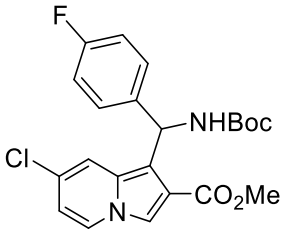


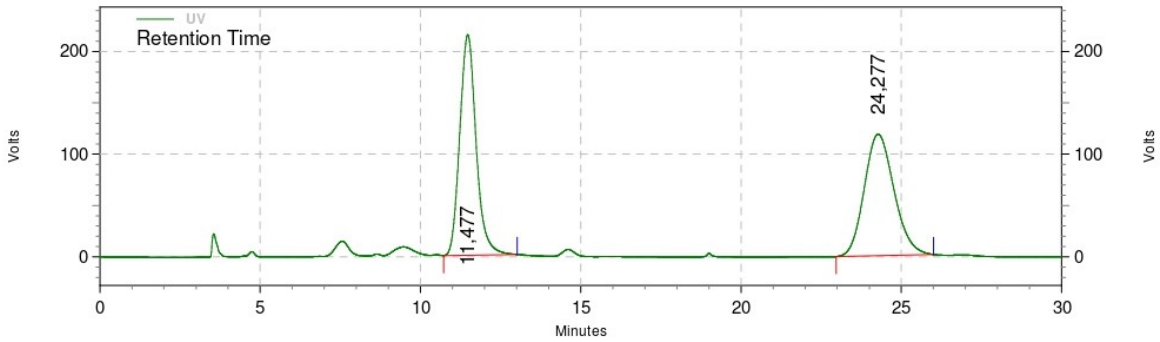


UV Results

Retention Time	Area	Area %	Height	Height %
6,723	137449272	83,77	6355920	85,74
8,527	26623279	16,23	1057190	14,26
Totals	164072551	100,00	7413110	100,00

Chiral HPLC chromatogram of racemic 3p



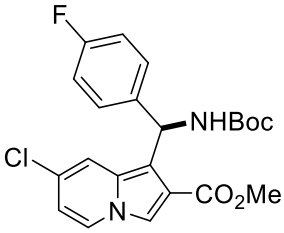


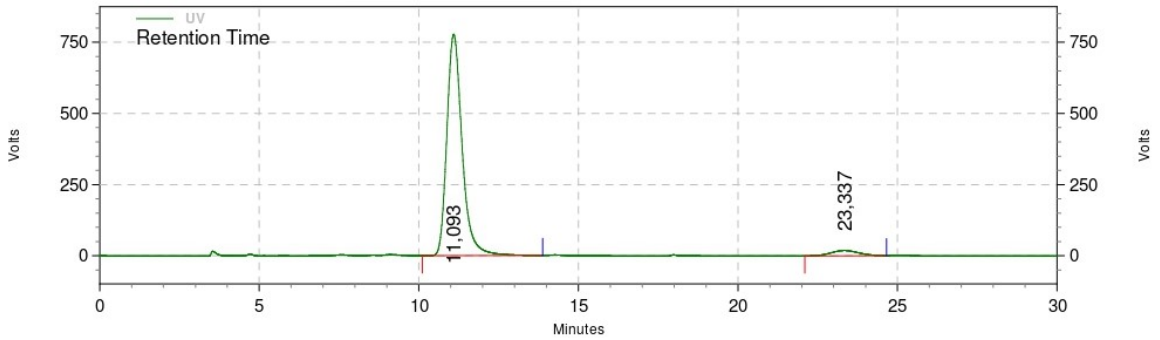
UV Results

Retention Time	Area	Area %	Height	Height %
11,477	30459204	49,95	859213	64,46
24,277	30521565	50,05	473826	35,54

Totals	60980769	100,00	1333039	100,00

Chiral HPLC chromatogram of chiral 3p



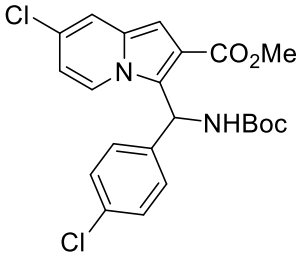


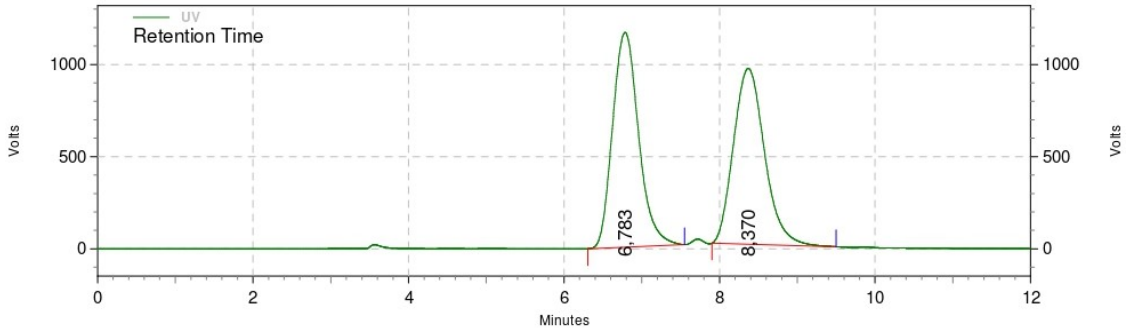
UV Results

Retention Time	Area	Area %	Height	Height %
11,093	103740857	95,94	3113573	97,70
23,337	4389948	4,06	73326	2,30

Totals	108130805	100,00	3186899	100,00

Chiral HPLC chromatogram of racemic 4q

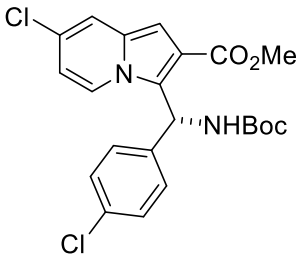


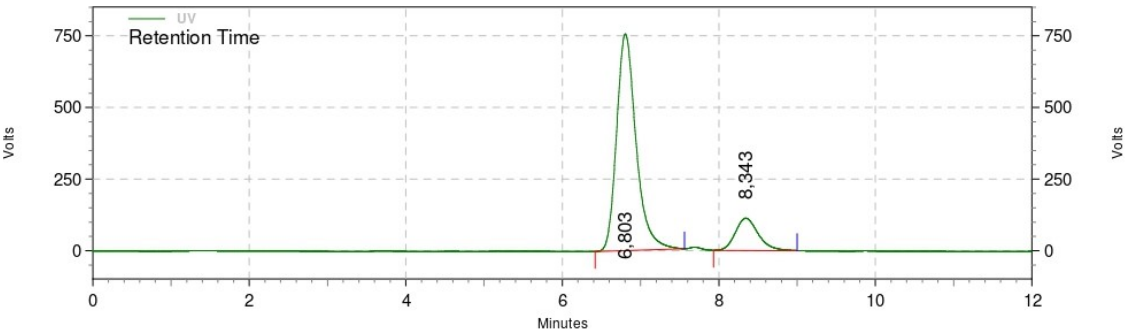


UV Results

Retention Time	Area	Area %	Height	Height %
6,783	108477417	50,59	4657823	54,96
8,370	105938569	49,41	3817204	45,04
Totals	214415986	100,00	8475027	100,00

Chiral HPLC chromatogram of chiral 4q

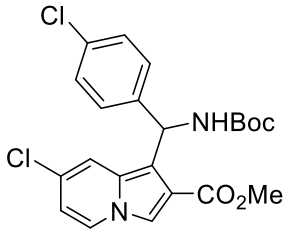


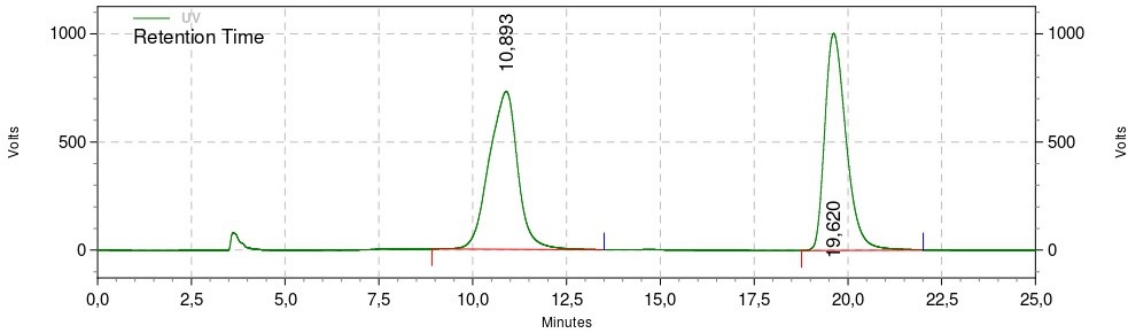


UV Results

Retention Time	Area	Area %	Height	Height %
6,803	52285006	85,15	3023314	87,06
8,343	9118776	14,85	449425	12,94
Totals	61403782	100,00	3472739	100,00

Chiral HPLC chromatogram of racemic 3q

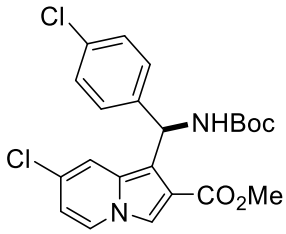


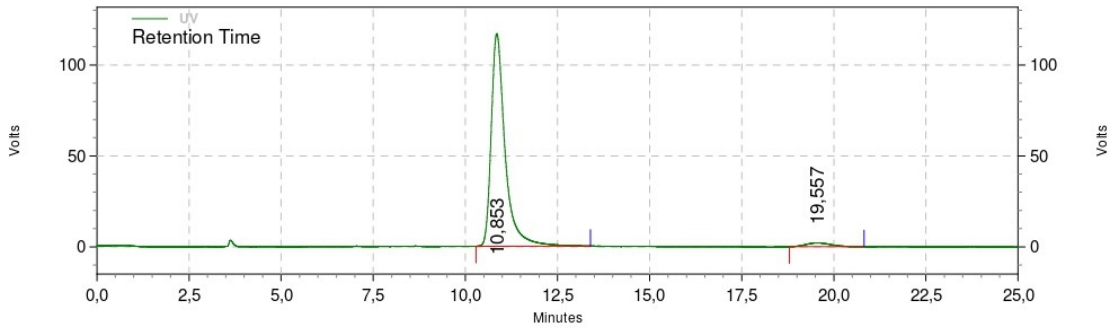


UV Results

Retention Time	Area	Area %	Height	Height %
10,893	154799078	49,50	2918242	42,12
19,620	157953520	50,50	4009883	57,88
Totals	312752598	100,00	6928125	100,00

Chiral HPLC chromatogram of chiral 3q

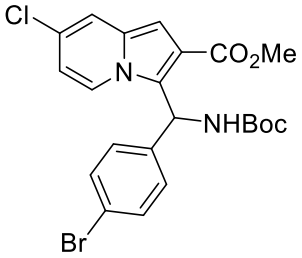


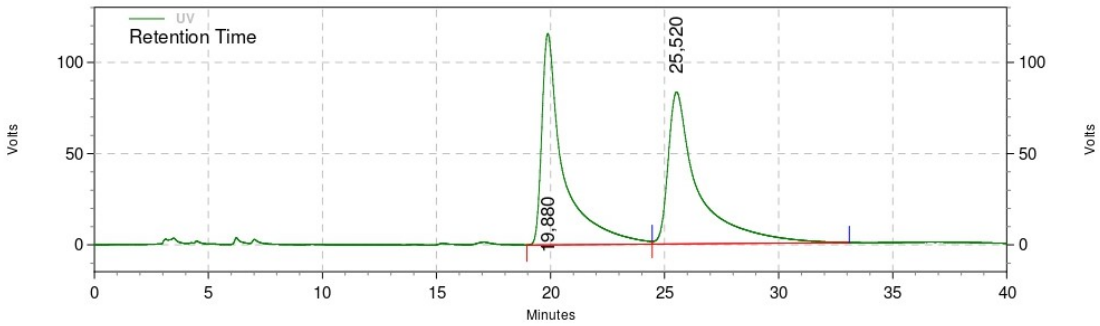


UV Results

Retention Time	Area	Area %	Height	Height %
10,853	12249702	96,79	467443	98,21
19,557	406769	3,21	8505	1,79
Totals	12656471	100,00	475948	100,00

Chiral HPLC chromatogram of racemic 4r

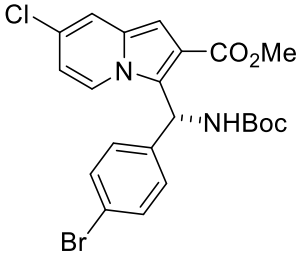


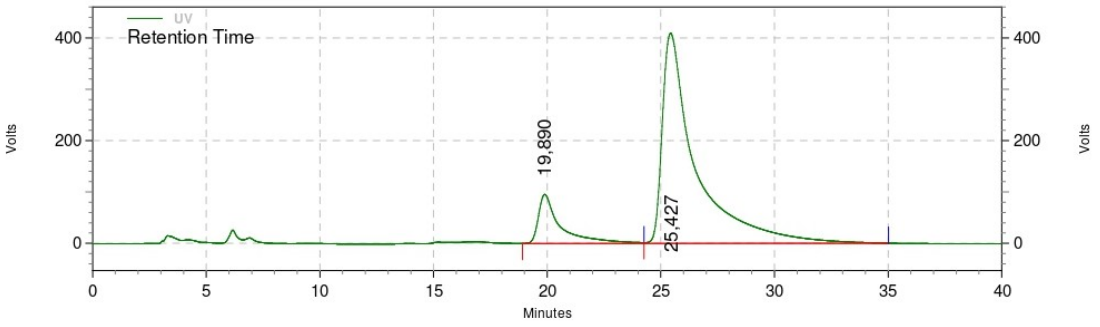


UV Results

Retention Time	Area	Area %	Height	Height %
19,880	30234417	49,83	462768	58,18
25,520	30442331	50,17	332634	41,82
Totals	60676748	100,00	795402	100,00

Chiral HPLC chromatogram of chiral 4r

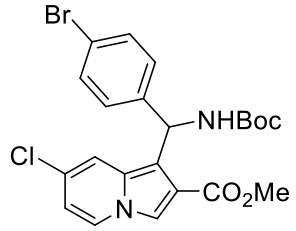


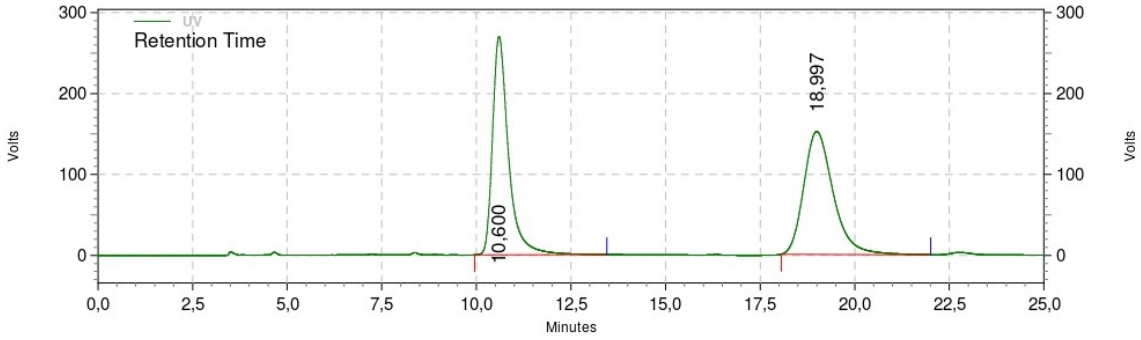


UV Results

Retention Time	Area	Area %	Height	Height %
19,890	25544819	13,27	381653	18,90
25,427	166965521	86,73	1637737	81,10
Totals	192510340	100,00	2019390	100,00

Chiral HPLC chromatogram of racemic 3r

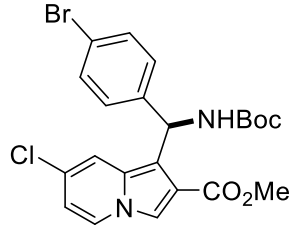


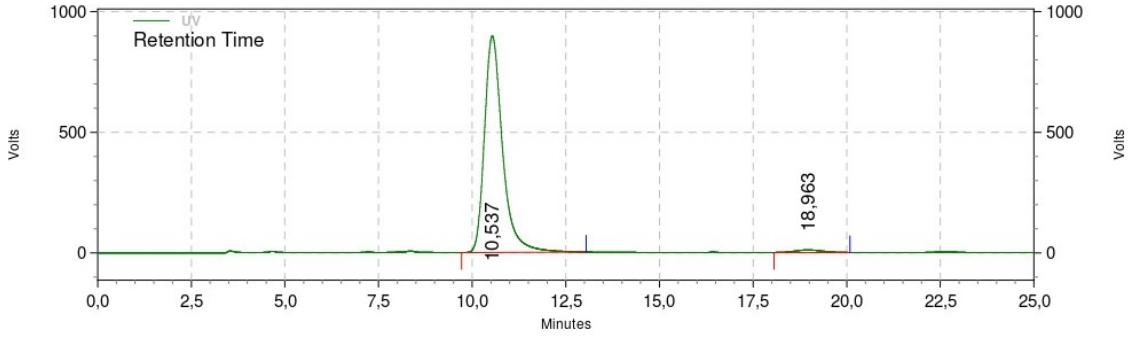


UV Results

Retention Time	Area	Area %	Height	Height %
10,600	31735217	49,16	1078983	63,98
18,997	32823291	50,84	607484	36,02
Totals	64558508	100,00	1686467	100,00

Chiral HPLC chromatogram of chiral 3r

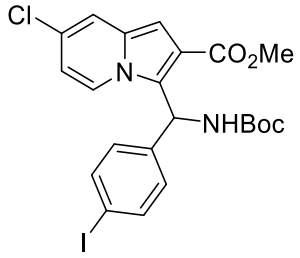


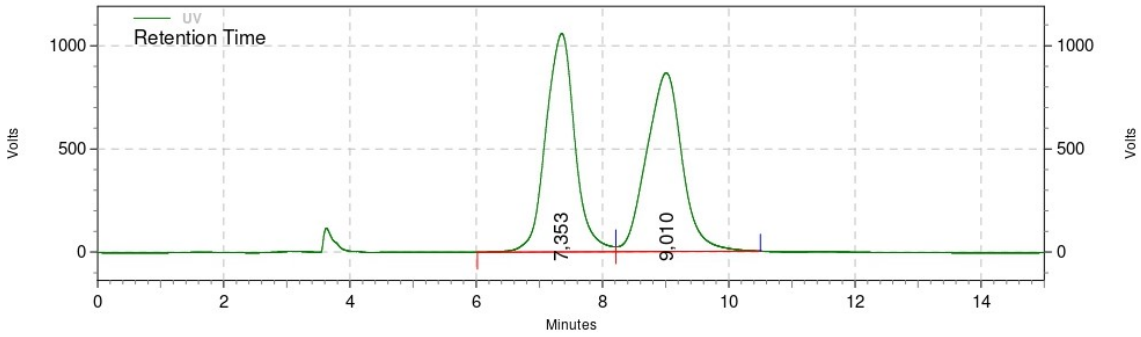


UV Results

Retention Time	Area	Area %	Height	Height %
10,537	120885567	98,26	3591485	98,85
18,963	2146028	1,74	41828	1,15
Totals	123031595	100,00	3633313	100,00

Chiral HPLC chromatogram of racemic 4s

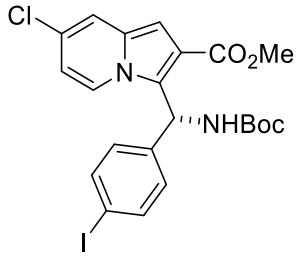


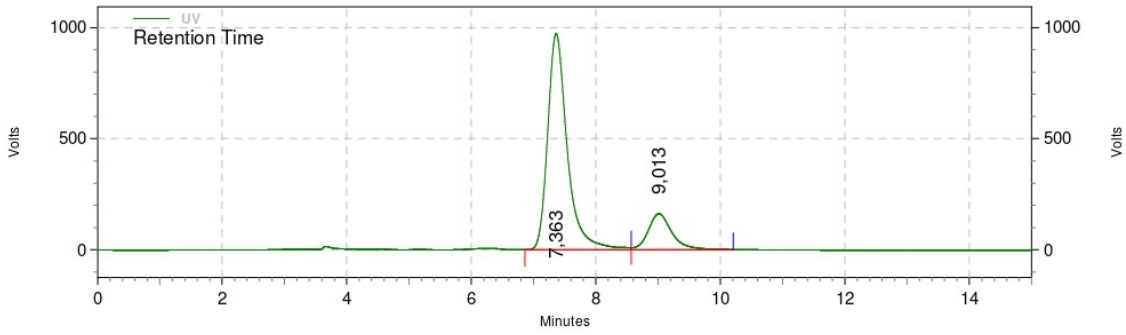


UV Results

Retention Time	Area	Area %	Height	Height %
7,353	135463638	50,00	4231862	54,99
9,010	135443752	50,00	3463222	45,01
Totals	270907390	100,00	7695084	100,00

Chiral HPLC chromatogram of chiral 4s

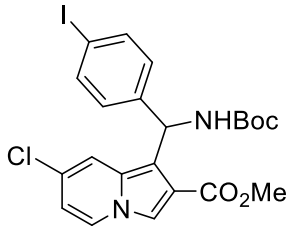


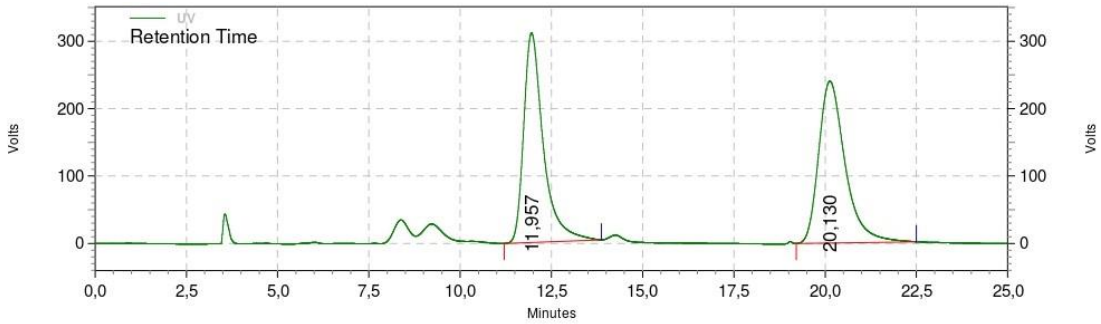


UV Results

Retention Time	Area	Area %	Height	Height %
7,363	85013464	83,33	3888435	85,76
9,013	17004335	16,67	645863	14,24
Totals	102017799	100,00	4534298	100,00

Chiral HPLC chromatogram of racemic 3s

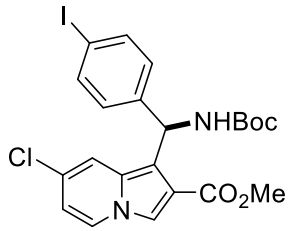


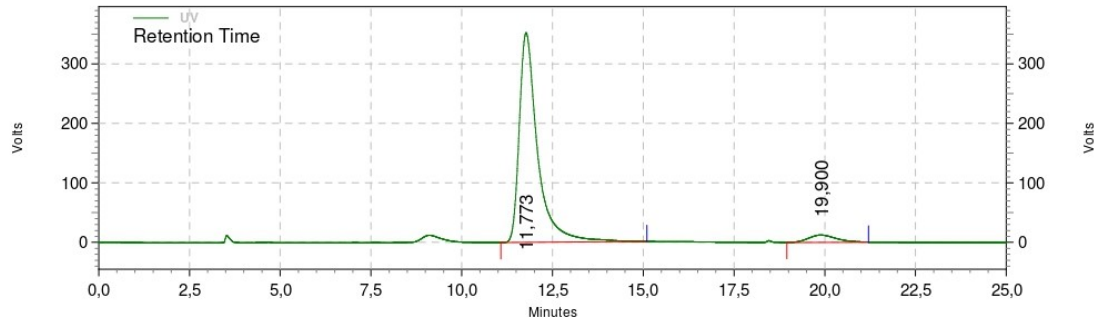


UV Results

Retention Time	Area	Area %	Height	Height %
11,957	46519908	49,06	1243455	56,42
20,130	48299321	50,94	960497	43,58
Totals	94819229	100,00	2203952	100,00

Chiral HPLC chromatogram of chiral 3s

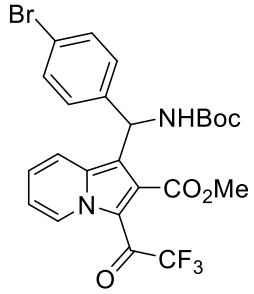


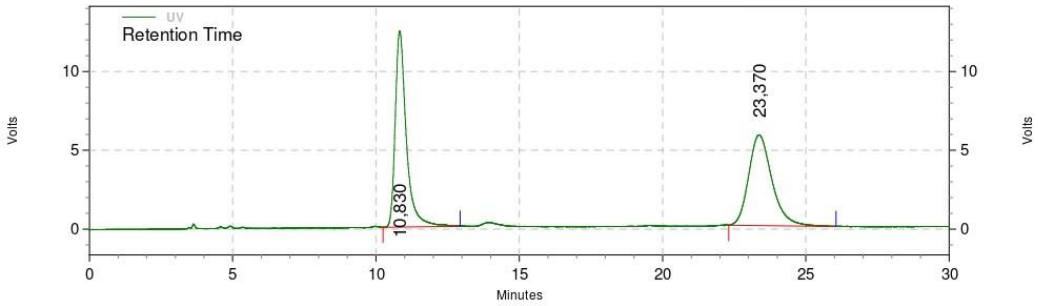


UV Results

Retention Time	Area	Area %	Height	Height %
11,773	49567689	95,09	1410597	96,67
19,900	2556816	4,91	48527	3,33
Totals	52124505	100,00	1459124	100,00

Chiral HPLC chromatogram of racemic 10

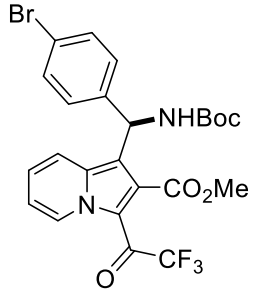


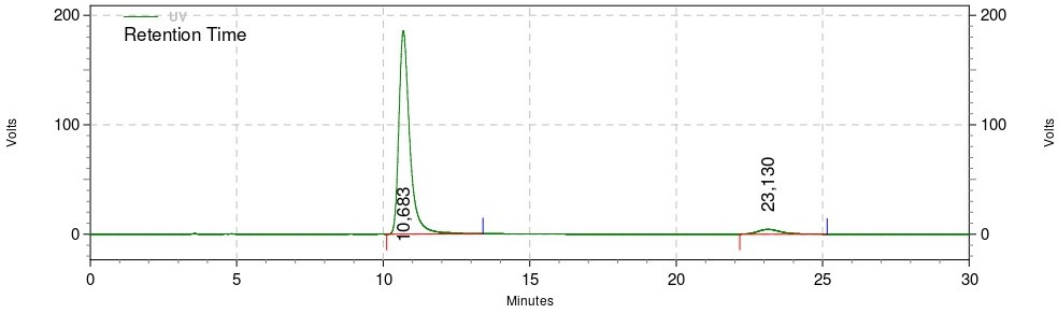


UV Results

Retention Time	Area	Area %	Height	Height %
10,830	1340137	50,76	49733	68,37
23,370	1299840	49,24	23005	31,63
Totals	2639977	100,00	72738	100,00

Chiral HPLC chromatogram of chiral 10



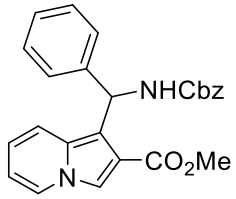


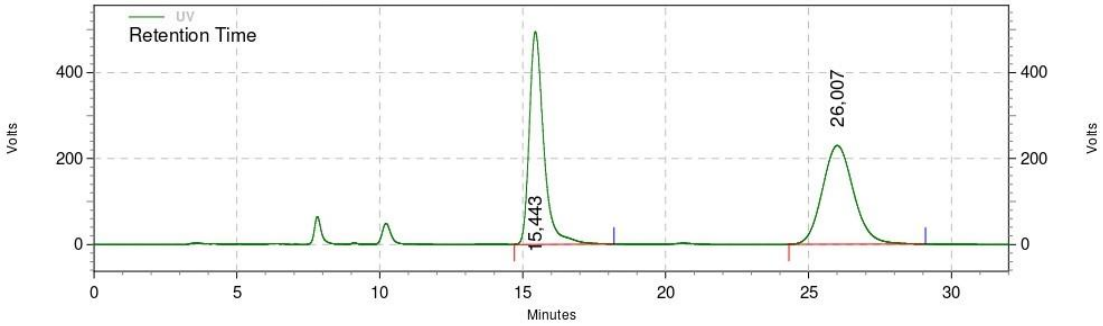
UV Results

Retention Time	Area	Area %	Height	Height %
10,683	19107318	95,31	742401	97,71
23,130	940529	4,69	17415	2,29
Totals	20047847	100,00	759816	100,00

8.2. Cbz-protected products 6a-m, 7a-m, 8 and 9

Chiral HPLC chromatogram of racemic 6a

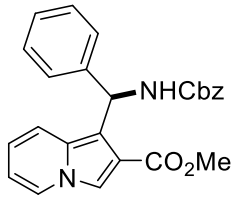


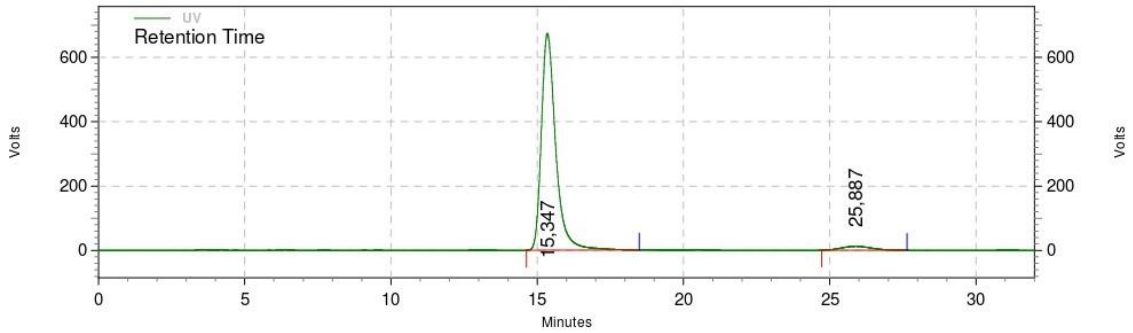


UV Results

Retention Time	Area	Area %	Height	Height %
15,443	69365685	49,83	1978993	68,28
26,007	69840348	50,17	919150	31,72
Totals	139206033	100,00	2898143	100,00

Chiral HPLC chromatogram of chiral 6a

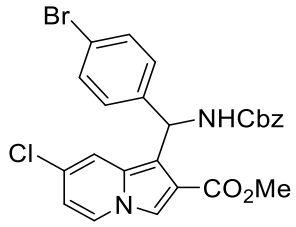


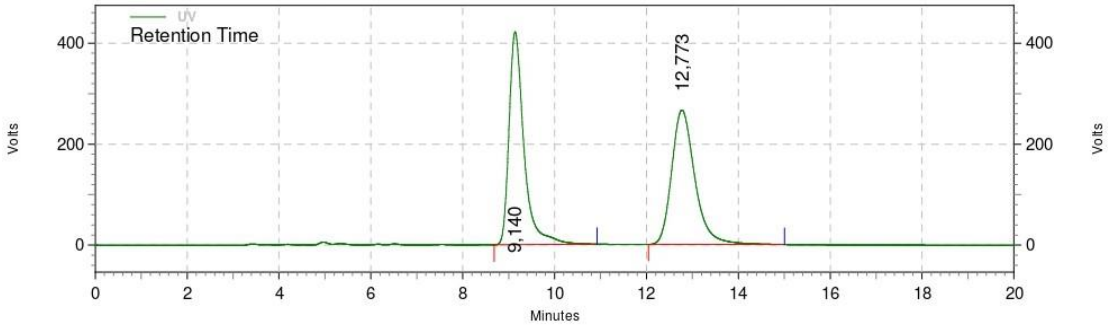


UV Results

Retention Time	Area	Area %	Height	Height %
15,347	91942914	96,29	2694190	98,21
25,887	3545400	3,71	49093	1,79
Totals	95488314	100,00	2743283	100,00

Chiral HPLC chromatogram of racemic 6m



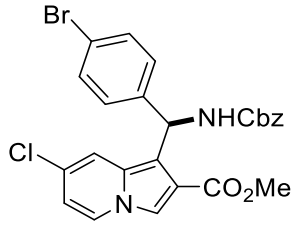


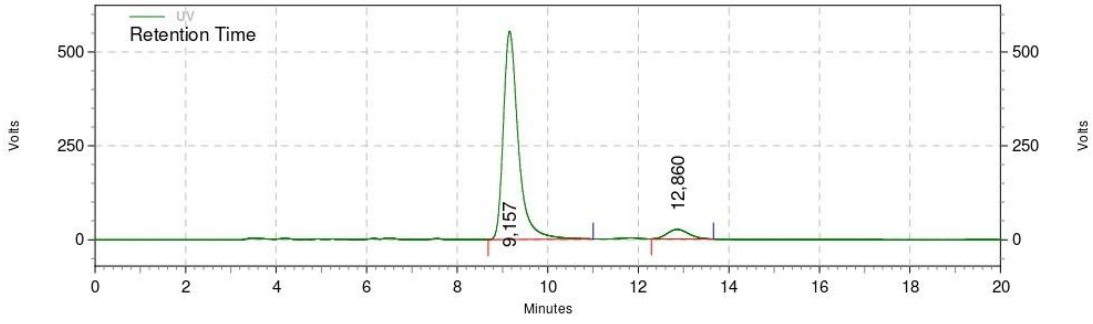
UV Results

Retention Time	Area	Area %	Height	Height %
9,140	38140437	50,48	1685982	61,27
12,773	37411700	49,52	1065617	38,73

Totals	75552137	100,00	2751599	100,00

Chiral HPLC chromatogram of chiral 6m



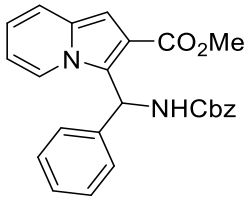


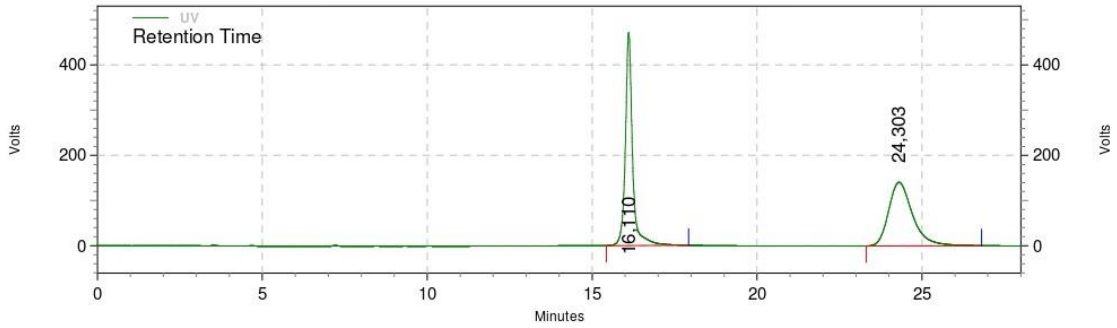
UV Results

Retention Time	Area	Area %	Height	Height %
9,157	50895054	93,76	2217860	95,61
12,860	3385925	6,24	101862	4,39

Totals	54280979	100,00	2319722	100,00

Chiral HPLC chromatogram of racemic 7a

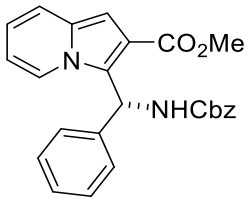


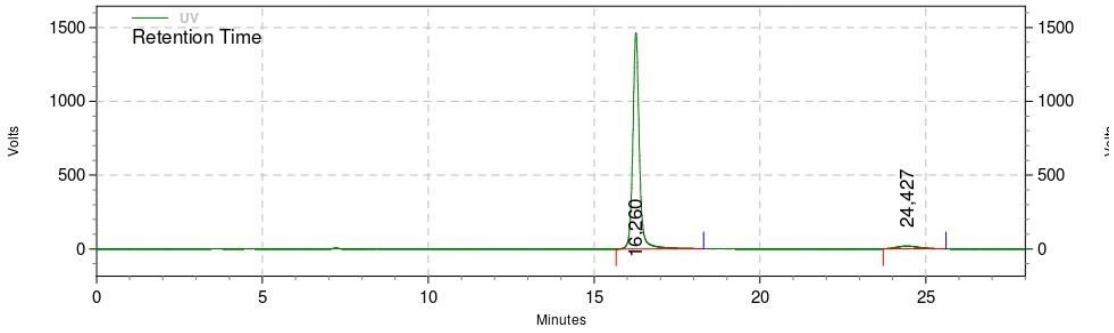


UV Results

Retention Time	Area	Area %	Height	Height %
16,110	28594506	50,22	1883409	76,98
24,303	28347647	49,78	563283	23,02
Totals	56942153	100,00	2446692	100,00

Chiral HPLC chromatogram of chiral 7a

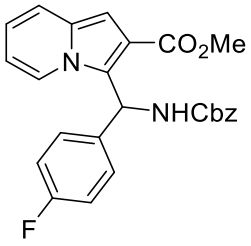


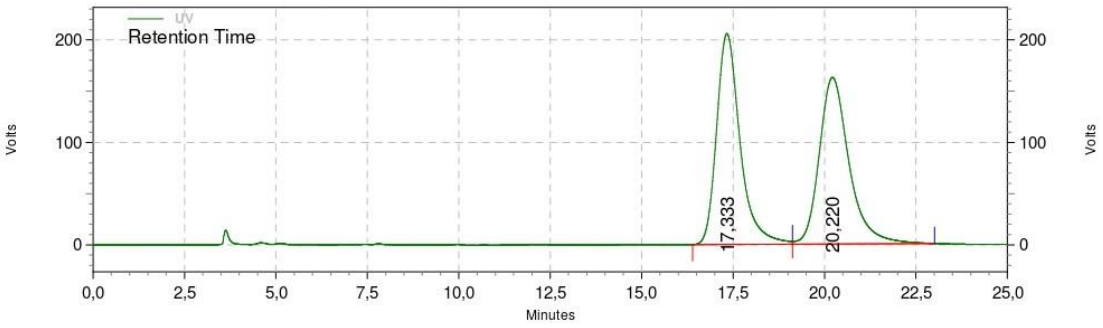


UV Results

Retention Time	Area	Area %	Height	Height %
16,260	80241847	95,78	5851310	98,74
24,427	3537931	4,22	74863	1,26
Totals	83779778	100,00	5926173	100,00

Chiral HPLC chromatogram of racemic 7b

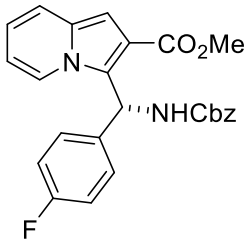


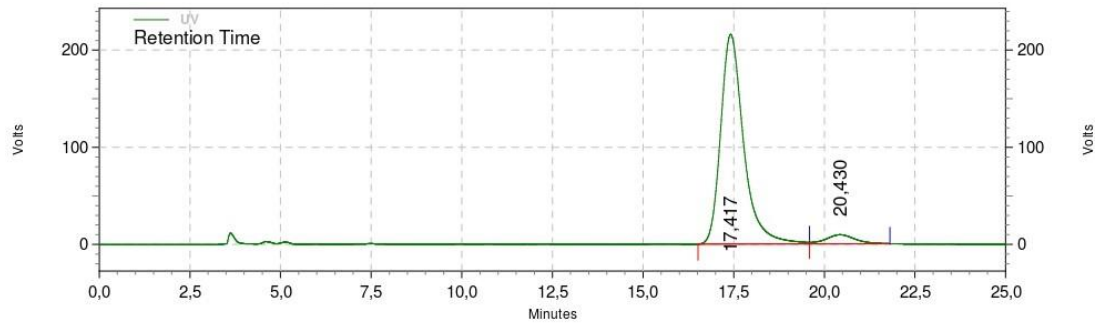


UV Results

Retention Time	Area	Area %	Height	Height %
17,333	36789410	49,98	823145	55,86
20,220	36816227	50,02	650431	44,14
Totals	73605637	100,00	1473576	100,00

Chiral HPLC chromatogram of chiral 7b

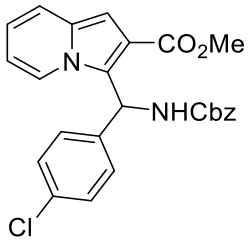


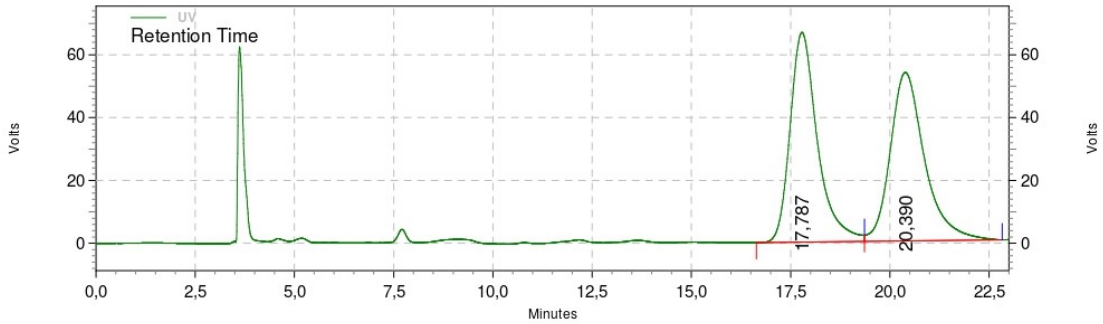


UV Results

Retention Time	Area	Area %	Height	Height %
17,417	38047717	94,85	863073	95,86
20,430	2065399	5,15	37258	4,14
Totals	40113116	100,00	900331	100,00

Chiral HPLC chromatogram of racemic 7c

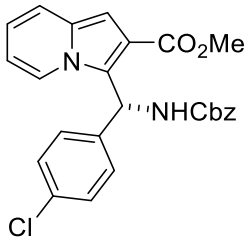


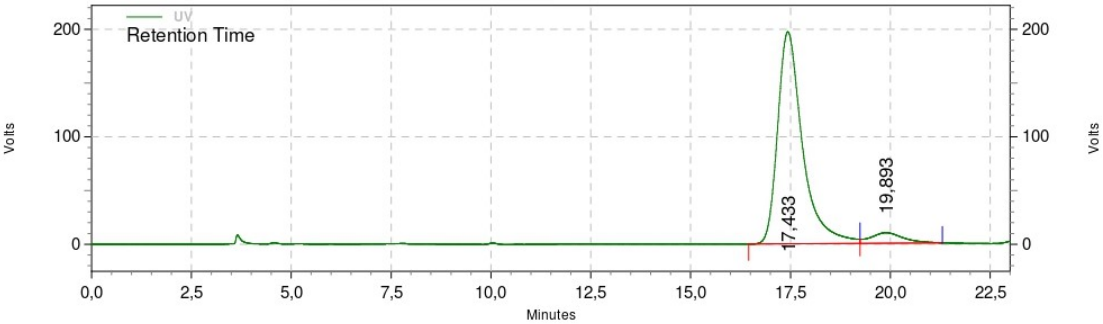


UV Results

Retention Time	Area	Area %	Height	Height %
17,787	12813197	49,81	267084	55,43
20,390	12912551	50,19	214722	44,57
Totals	25725748	100,00	481806	100,00

Chiral HPLC chromatogram of chiral 7c

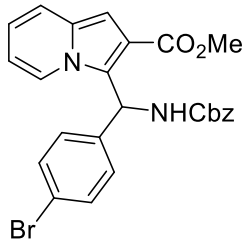


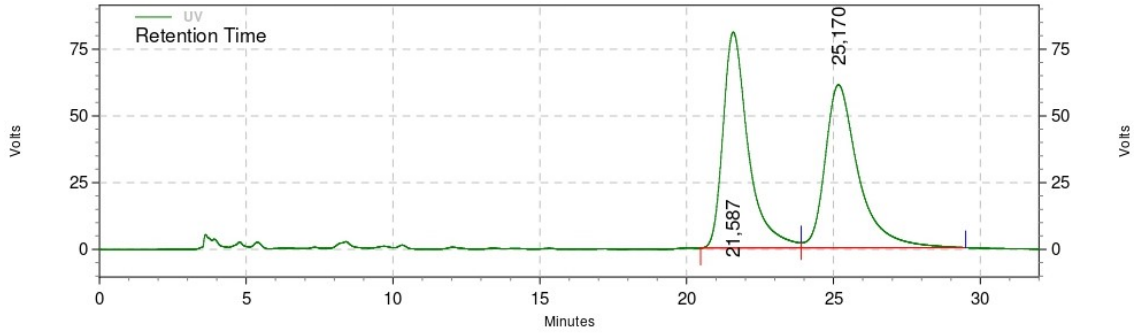


UV Results

Retention Time	Area	Area %	Height	Height %
17,433	34130624	93,99	788667	95,29
19,893	2182029	6,01	39023	4,71
Totals	36312653	100,00	827690	100,00

Chiral HPLC chromatogram of racemic 7d

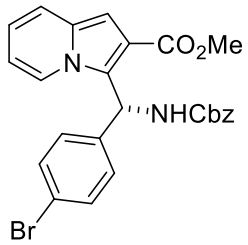


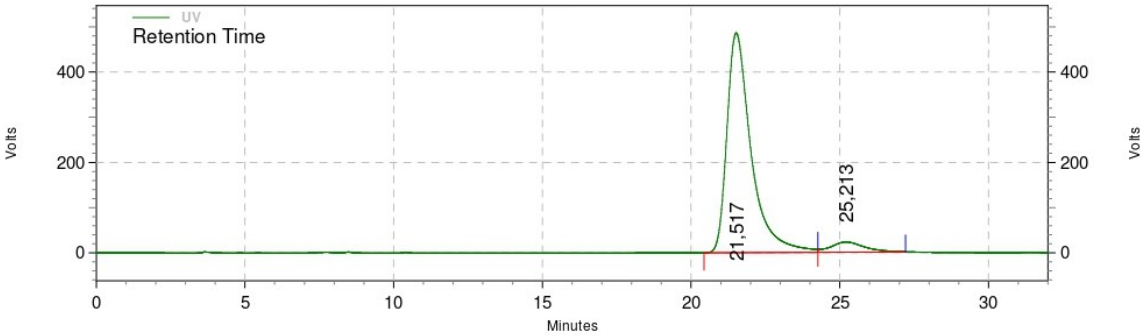


UV Results

Retention Time	Area	Area %	Height	Height %
21,587	19347005	50,14	323315	56,95
25,170	19241111	49,86	244381	43,05
Totals	38588116	100,00	567696	100,00

Chiral HPLC chromatogram of chiral 7d

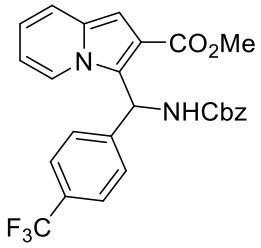


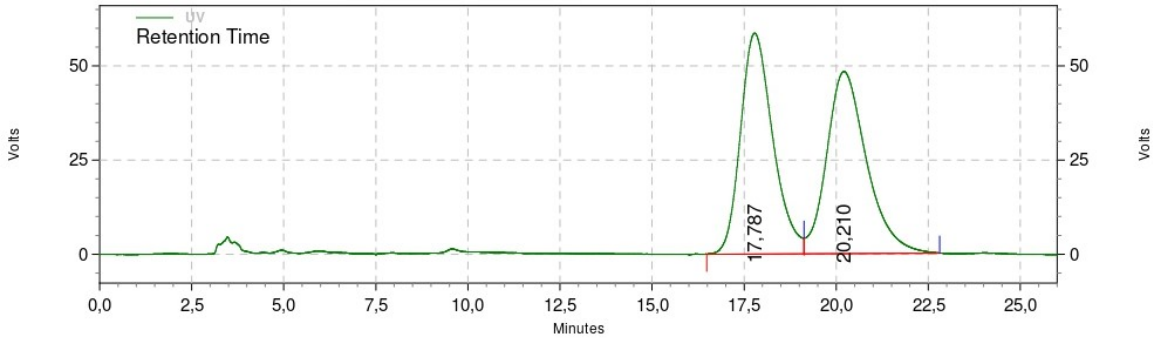


UV Results

Retention Time	Area	Area %	Height	Height %
21,517	110020102	94,03	1944345	95,57
25,213	6981304	5,97	90097	4,43
Totals	117001406	100,00	2034442	100,00

Chiral HPLC chromatogram of racemic 7e

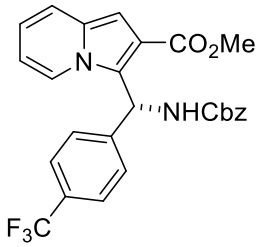


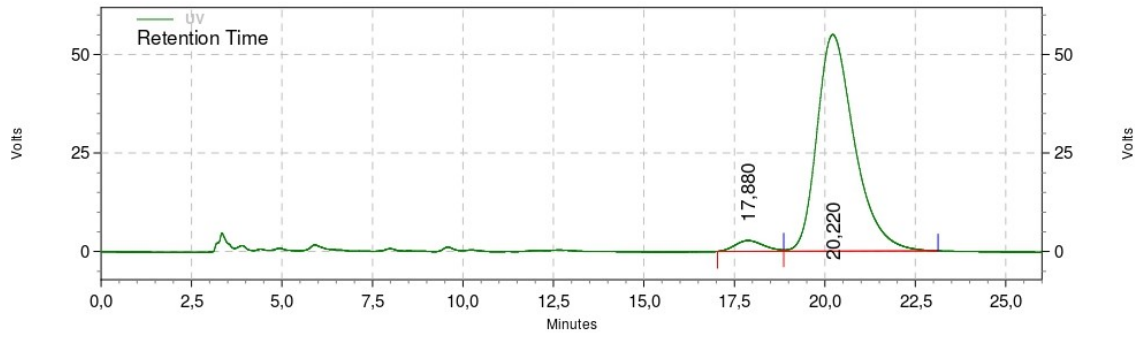


UV Results

Retention Time	Area	Area %	Height	Height %
17,787	14328865	49,61	234570	54,81
20,210	14556071	50,39	193383	45,19
Totals	28884936	100,00	427953	100,00

Chiral HPLC chromatogram of chiral 7e

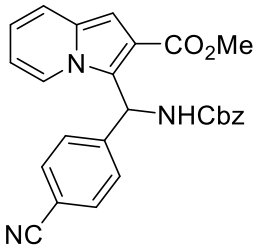


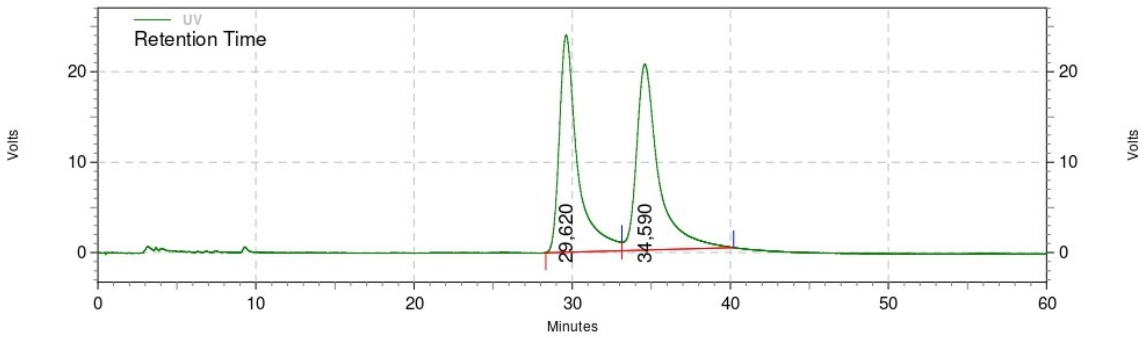


UV Results

Retention Time	Area	Area %	Height	Height %
17,880	598905	3,65	10904	4,73
20,220	15802317	96,35	219819	95,27
Totals	16401222	100,00	230723	100,00

Chiral HPLC chromatogram of racemic 7f

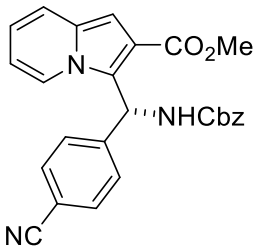


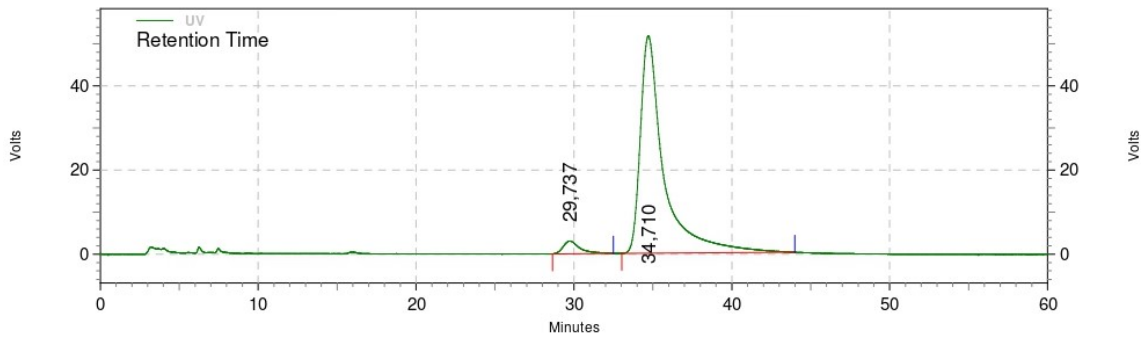


UV Results

Retention Time	Area	Area %	Height	Height %
29,620	7664783	49,06	96033	53,90
34,590	7957432	50,94	82150	46,10
Totals	15622215	100,00	178183	100,00

Chiral HPLC chromatogram of chiral 7f

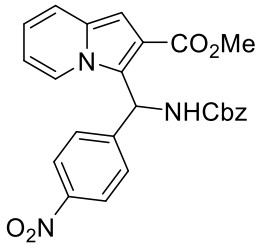


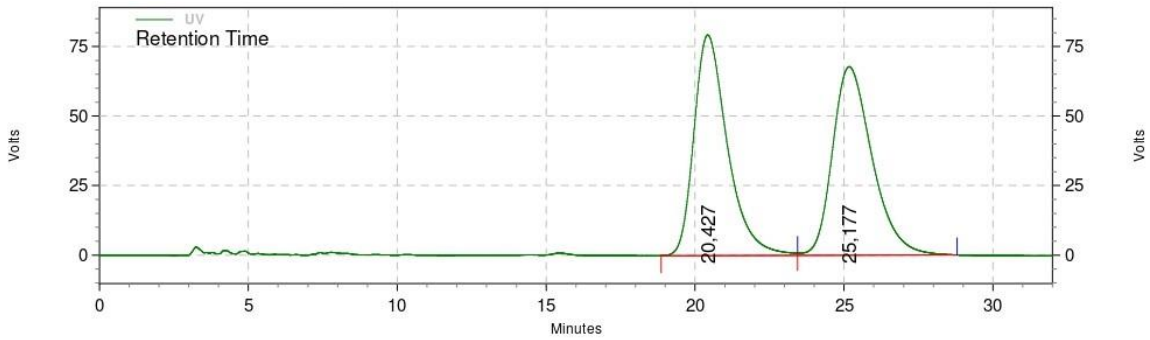


UV Results

Retention Time	Area	Area %	Height	Height %
29,737	872864	3,95	12060	5,51
34,710	21231728	96,05	206721	94,49
Totals	22104592	100,00	218781	100,00

Chiral HPLC chromatogram of racemic 7g



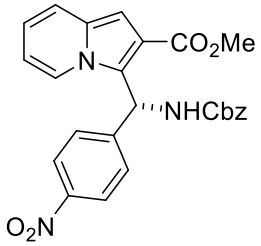


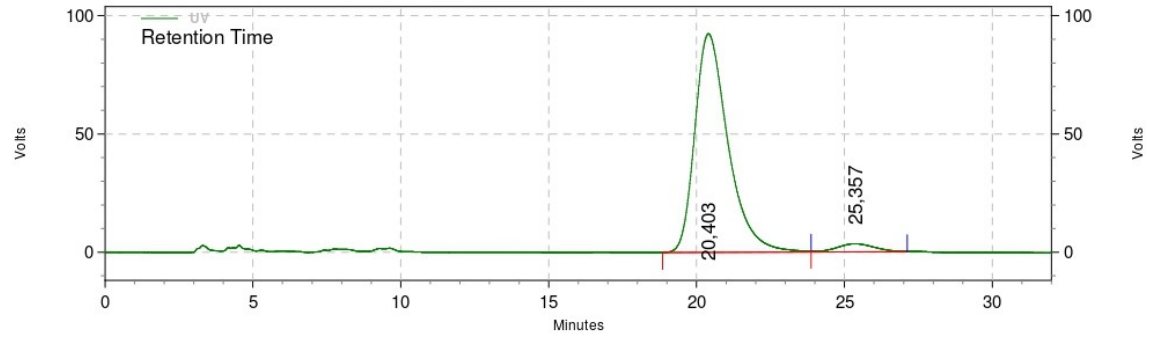
UV Results

Retention Time	Area	Area %	Height	Height %
20,427	24814643	49,75	317107	53,91
25,177	25065541	50,25	271064	46,09

Totals	49880184	100,00	588171	100,00

Chiral HPLC chromatogram of chiral 7g



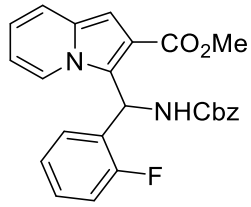


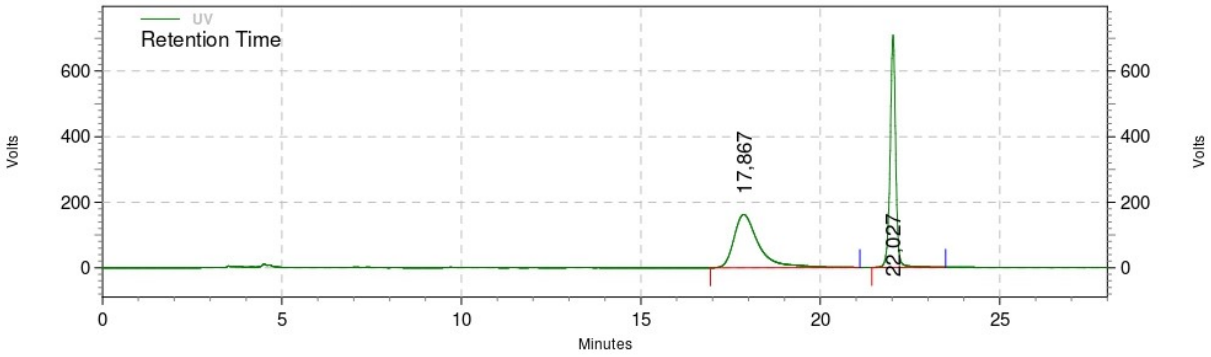
UV Results

Retention Time	Area	Area %	Height	Height %
20,403	28897309	96,12	369681	96,48
25,357	1167012	3,88	13495	3,52

Totals	30064321	100,00	383176	100,00

Chiral HPLC chromatogram of racemic 7h

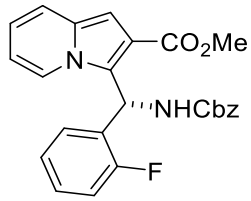


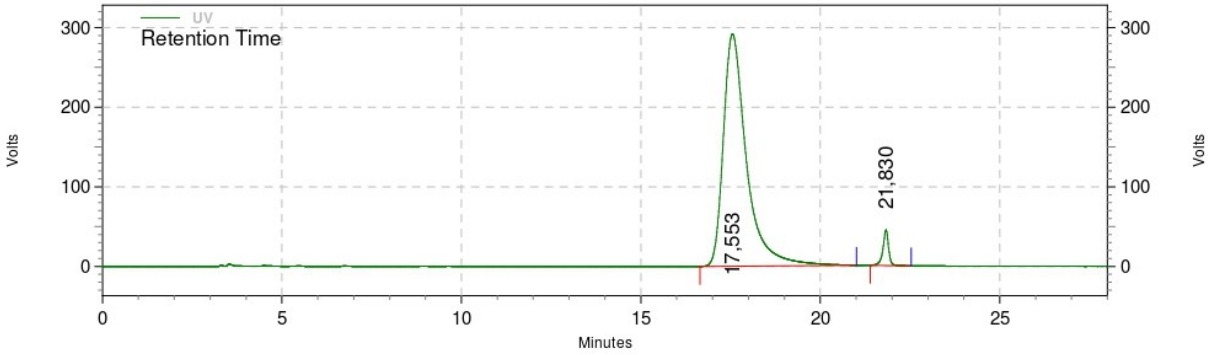


UV Results

Retention Time	Area	Area %	Height	Height %
17,867	30850719	50,25	649380	18,65
22,027	30541502	49,75	2832603	81,35
Totals	61392221	100,00	3481983	100,00

Chiral HPLC chromatogram of chiral 7h

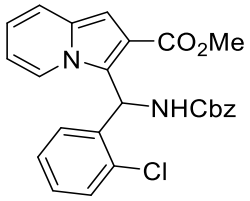


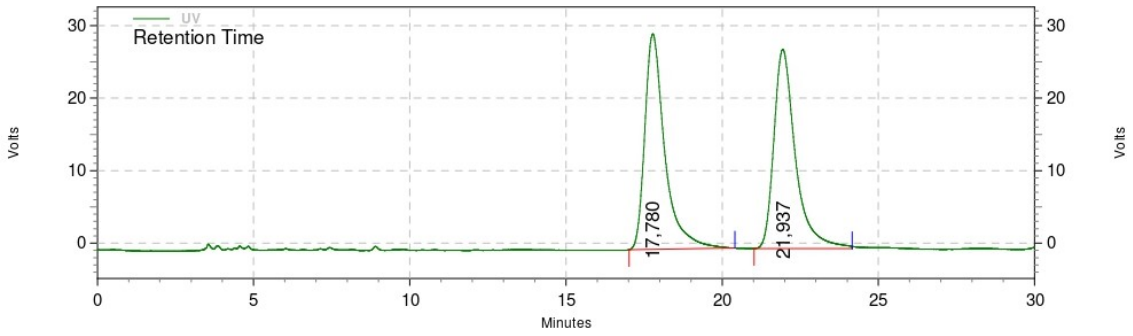


UV Results

Retention Time	Area	Area %	Height	Height %
17,553	52242219	96,42	1166984	86,68
21,830	1941787	3,58	179386	13,32
Totals	54184006	100,00	1346370	100,00

Chiral HPLC chromatogram of racemic 7i

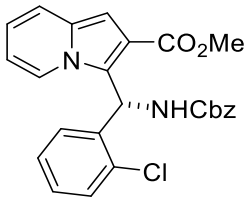


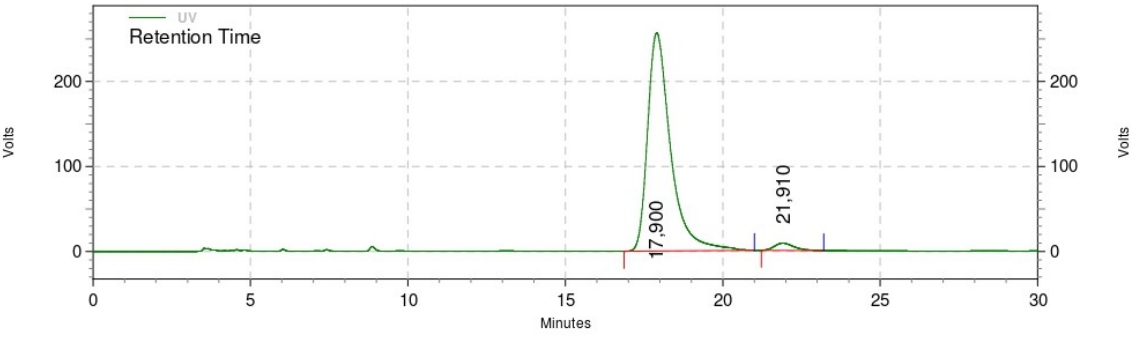


UV Results

Retention Time	Area	Area %	Height	Height %
17,780	5288274	50,01	118878	51,95
21,937	5287074	49,99	109953	48,05
Totals	10575348	100,00	228831	100,00

Chiral HPLC chromatogram of chiral 7i

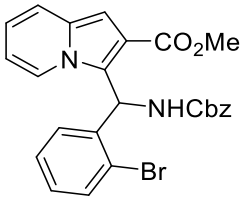


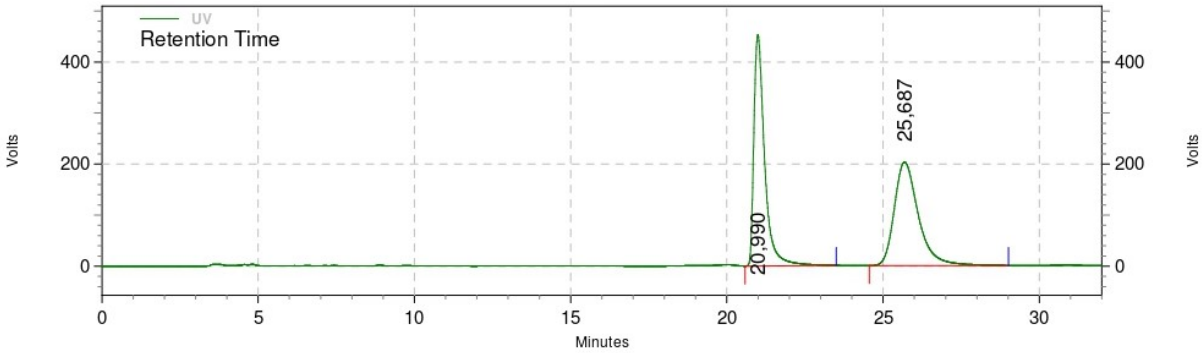


UV Results

Retention Time	Area	Area %	Height	Height %
17,900	52070667	97,29	1026479	96,78
21,910	1451321	2,71	34177	3,22
Totals	53521988	100,00	1060656	100,00

Chiral HPLC chromatogram of racemic 7j

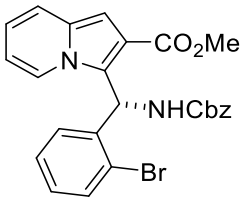


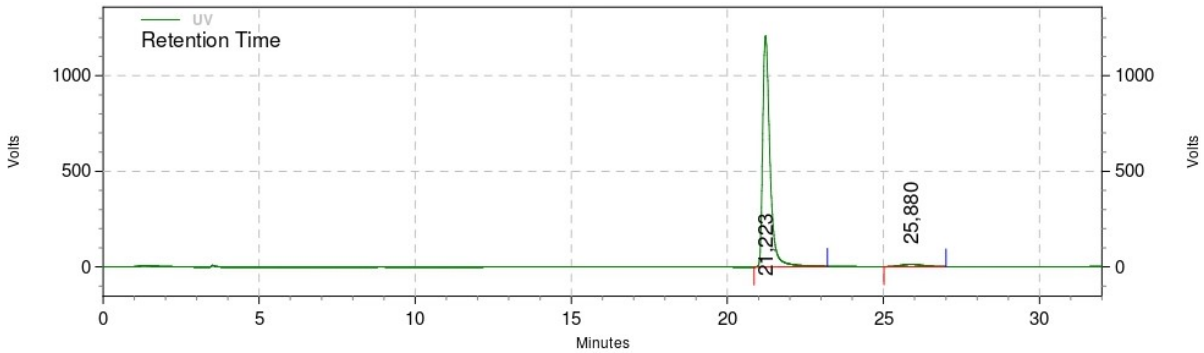


UV Results

Retention Time	Area	Area %	Height	Height %
20,990	43321883	49,93	1810862	69,06
25,687	43448102	50,07	811370	30,94
Totals	86769985	100,00	2622232	100,00

Chiral HPLC chromatogram of chiral 7j

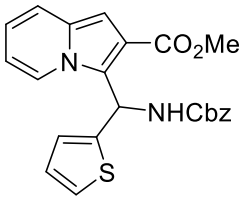


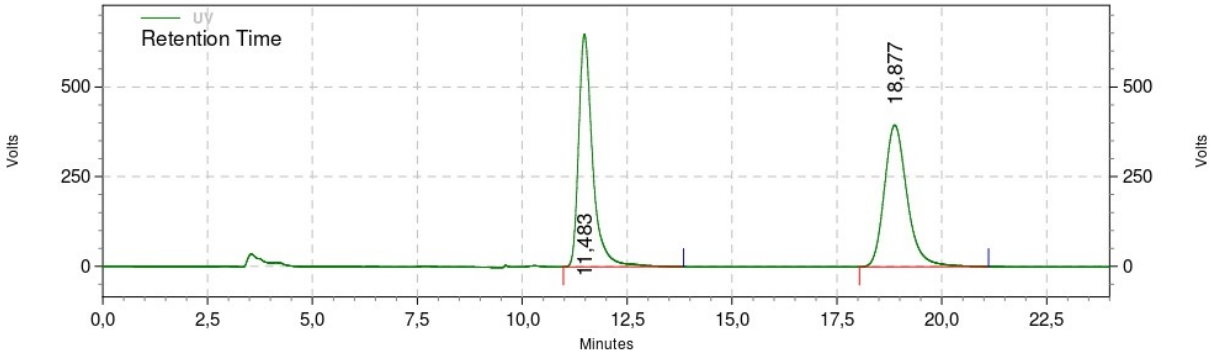


UV Results

Retention Time	Area	Area %	Height	Height %
21,223	78409346	96,93	4831179	99,00
25,880	2485160	3,07	48843	1,00
Totals	80894506	100,00	4880022	100,00

Chiral HPLC chromatogram of racemic 7k

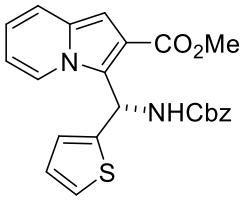


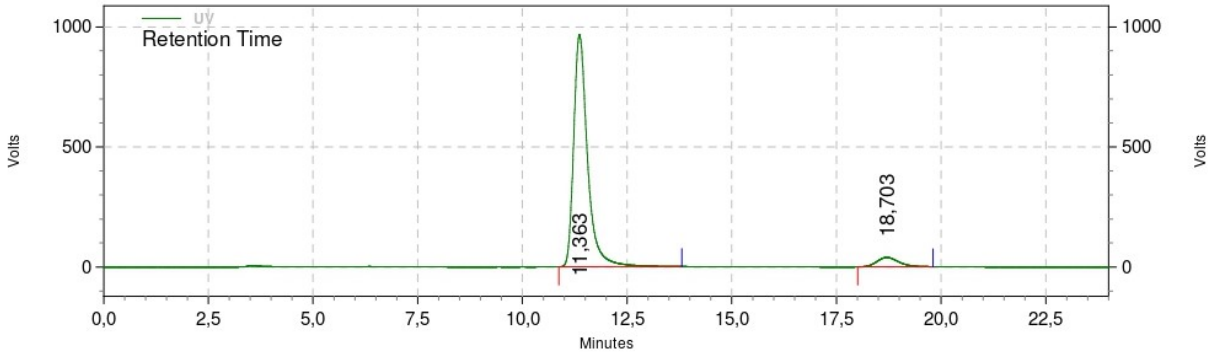


UV Results

Retention Time	Area	Area %	Height	Height %
11,483	60177896	50,23	2593052	62,13
18,877	59628645	49,77	1580638	37,87
Totals	119806541	100,00	4173690	100,00

Chiral HPLC chromatogram of chiral 7k

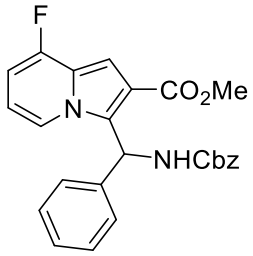


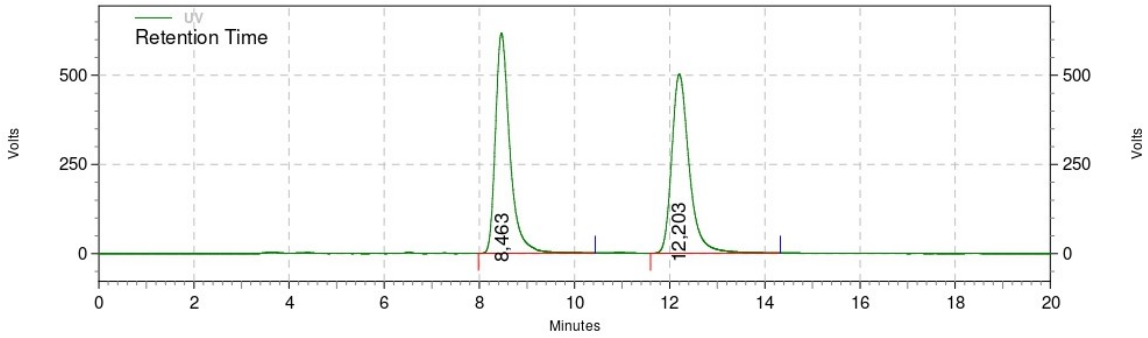


UV Results

Retention Time	Area	Area %	Height	Height %
11,363	88960921	93,95	3867149	96,09
18,703	5725310	6,05	157233	3,91
Totals	94686231	100,00	4024382	100,00

Chiral HPLC chromatogram of racemic 7l

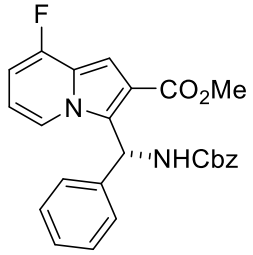


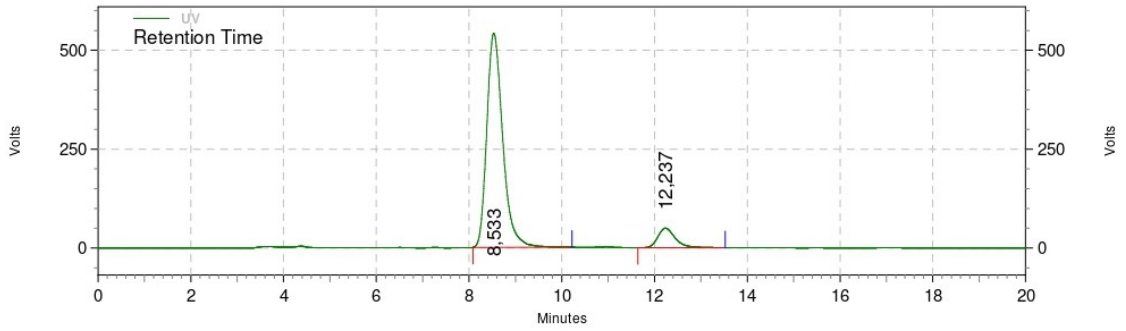


UV Results

Retention Time	Area	Area %	Height	Height %
8,463	52188780	50,39	2469300	55,12
12,203	51383098	49,61	2010967	44,88
Totals	103571878	100,00	4480267	100,00

Chiral HPLC chromatogram of chiral 7l

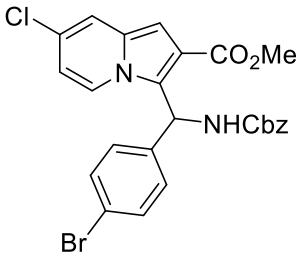


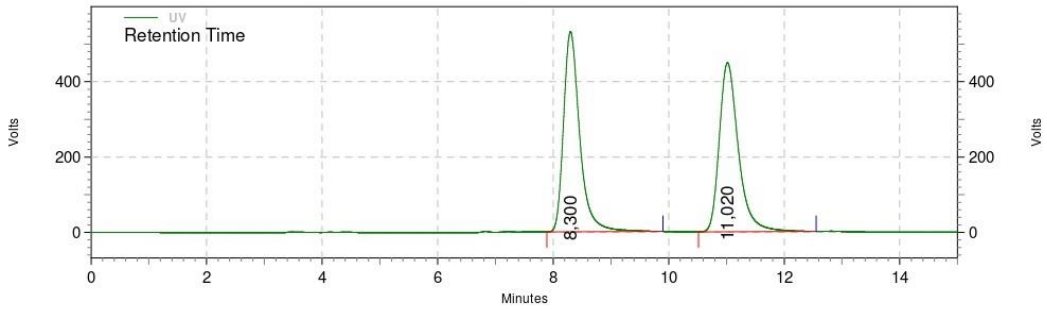


UV Results

Retention Time	Area	Area %	Height	Height %
8,533	51734767	90,85	2164605	91,61
12,237	5207490	9,15	198210	8,39
Totals	56942257	100,00	2362815	100,00

Chiral HPLC chromatogram of racemic 7m

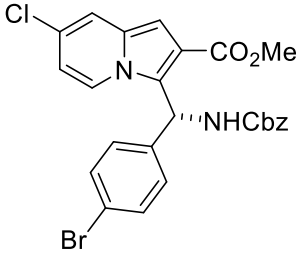


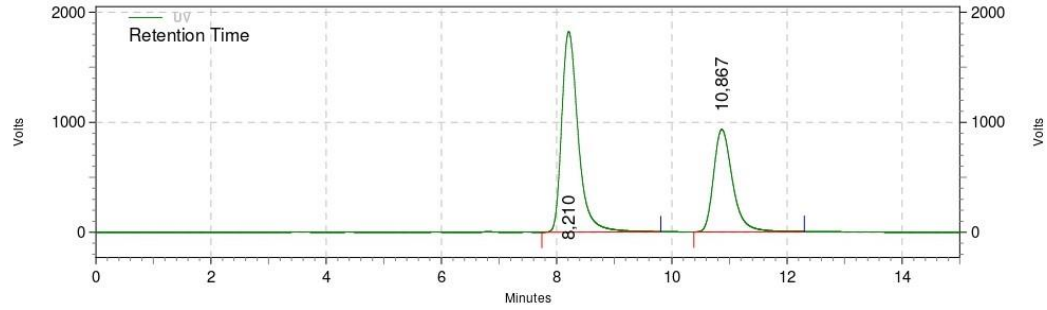


UV Results

Retention Time	Area	Area %	Height	Height %
8,300	41488099	50,15	2125774	54,22
11,020	41236167	49,85	1794511	45,78
Totals	82724266	100,00	3920285	100,00

Chiral HPLC chromatogram of chiral 7m

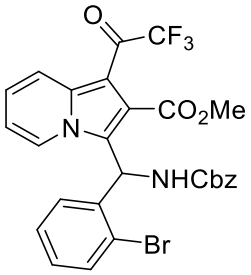


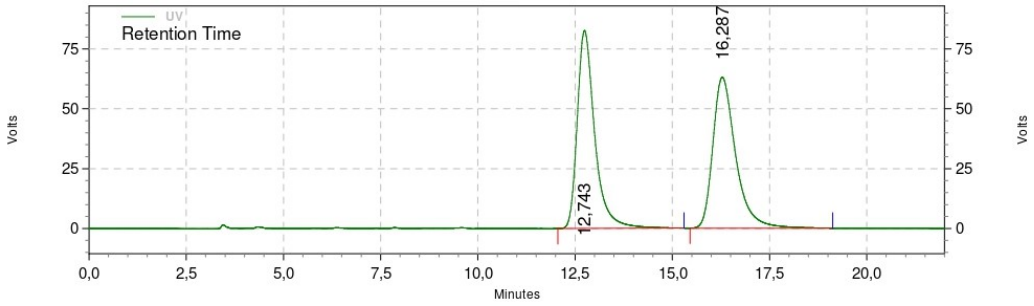


UV Results

Retention Time	Area	Area %	Height	Height %
8,210	144359751	62,95	7291592	66,17
10,867	84962970	37,05	3728600	33,83
Totals	229322721	100,00	11020192	100,00

Chiral HPLC chromatogram of racemic 8

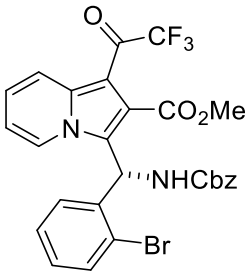


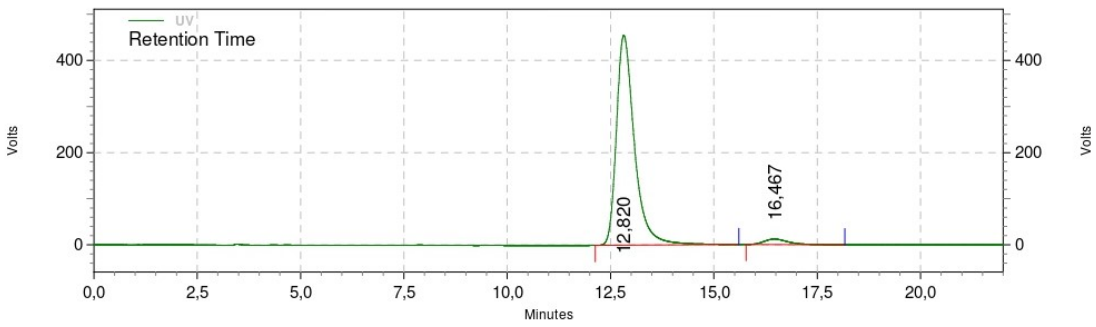


UV Results

Retention Time	Area	Area %	Height	Height %
12,743	10371314	50,23	330848	56,73
16,287	10276489	49,77	252325	43,27
Totals	20647803	100,00	583173	100,00

Chiral HPLC chromatogram of chiral 8

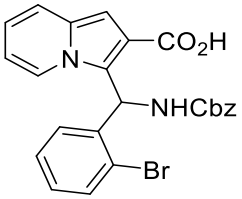


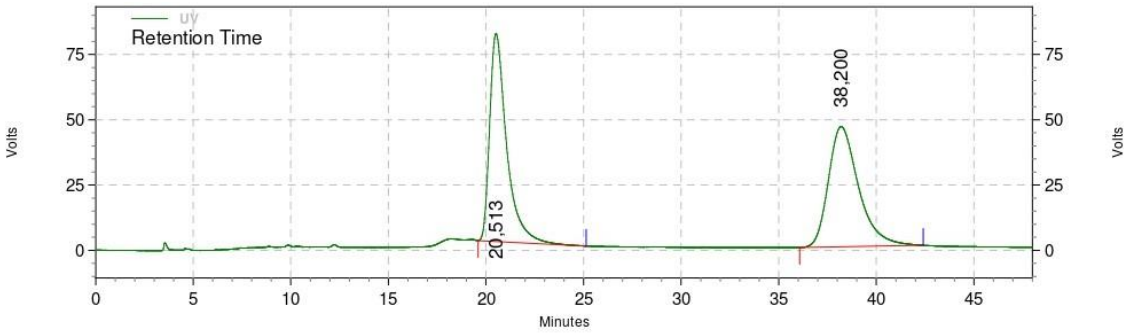


UV Results

Retention Time	Area	Area %	Height	Height %
12,820	55418881	96,61	1821714	97,43
16,467	1942638	3,39	47972	2,57
Totals	57361519	100,00	1869686	100,00

Chiral HPLC chromatogram of racemic 9

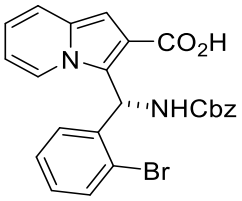


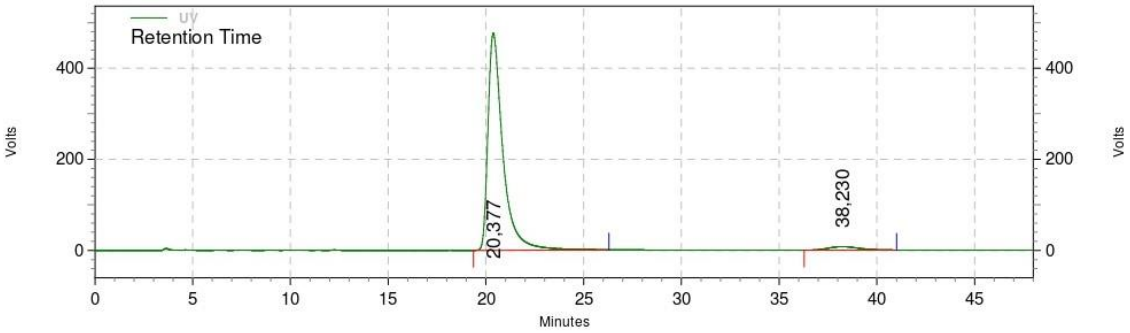


UV Results

Retention Time	Area	Area %	Height	Height %
20,513	19278788	49,35	318383	63,35
38,200	19788952	50,65	184203	36,65
Totals	39067740	100,00	502586	100,00

Chiral HPLC chromatogram of chiral 9





UV Results

Retention Time	Area	Area %	Height	Height %
20,377	101138266	96,76	1907348	98,40
38,230	3385743	3,24	30985	1,60
Totals	104524009	100,00	1938333	100,00

9. Absolute configuration assignment for compounds 3a, 4a, 6a, 7a using circular dichroism

The conformational search was performed using CREST conformational searching tool within energy threshold of 6 kcal/mol.[15] The obtained conformers were then initially preselected using isostat conformer selection tool from molclus package[16] with energy threshold of 0.25 kcal/mol and cutoff of 0.5A. The geometry of selected conformers was optimized using Gaussian 16[17] using density functional theory (DFT) using B3LYP functional with D3 (Becke–Johnson) dispersion correction "empiricaldispersion=gd3bj" along with def2SVP basis set with inclusion of CPCM solvation model via the keyword "scrf=(cpcm, solvent = acetonitrile)". The local minima were confirmed by frequency calculations. The TD-DFT calculations were performed for the first twenty lowest excitation energies on previously obtained geometries using ωB97XD functional with def2TZVP basis set and included solvent effects in acetonitrile via CPCM solvation model. The computed CD spectra were obtained employing Boltzmann averaging using SpecDis software[18] and compared with experimental results. In all cases the *R* configuration was assigned.

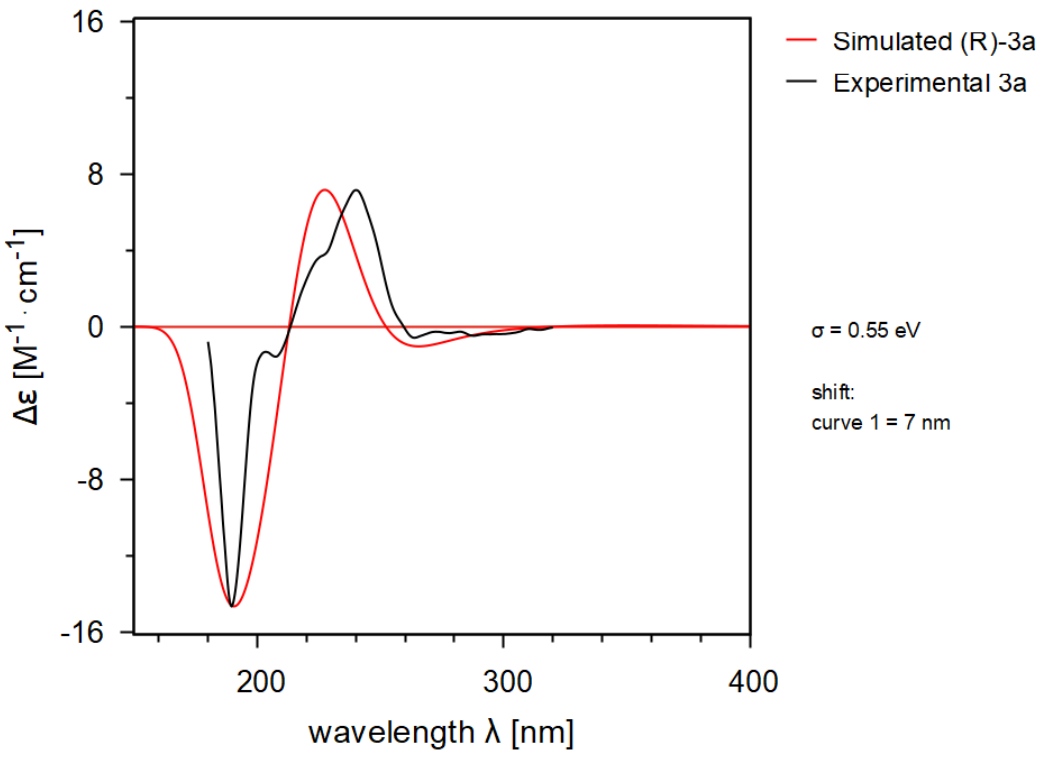


Figure S1. Comparison of experimental and simulated electronic dichroism spectra for compound **3a**.

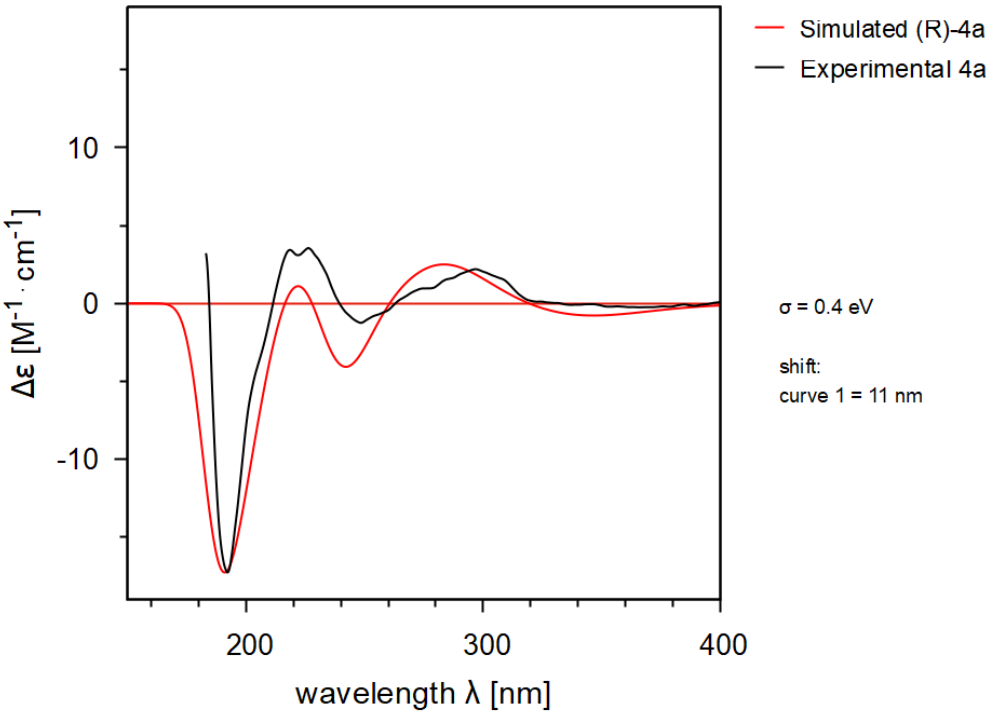


Figure S2. Comparison of experimental electronic dichroism spectra and simulated for compound **4a**.

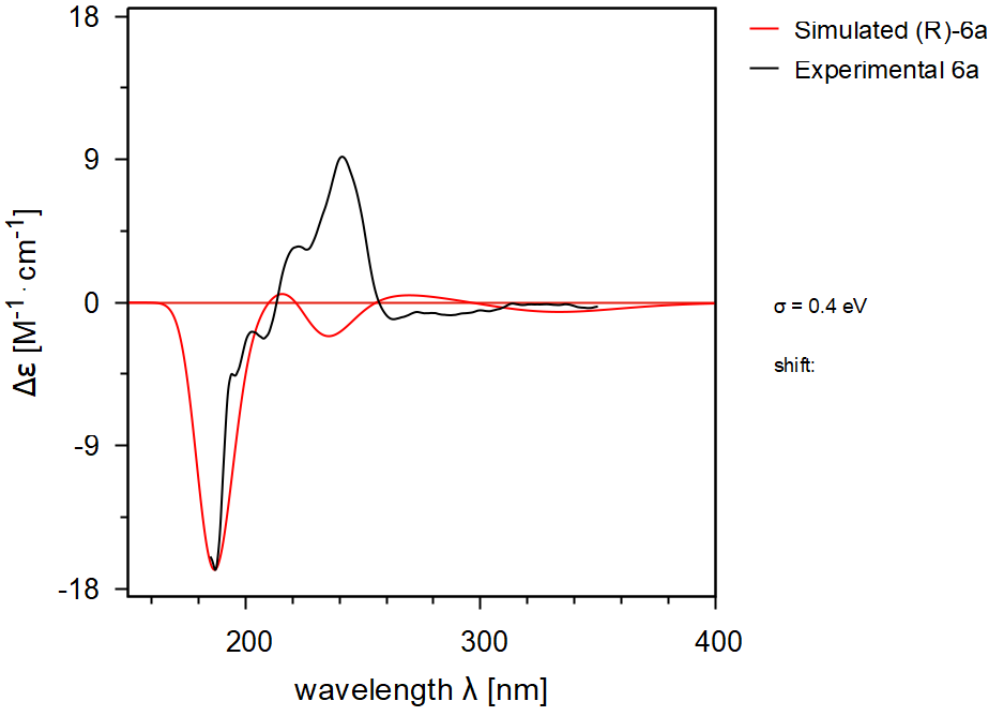


Figure S3. Comparison of experimental electronic dichroism spectra and simulated for compound **6a**.

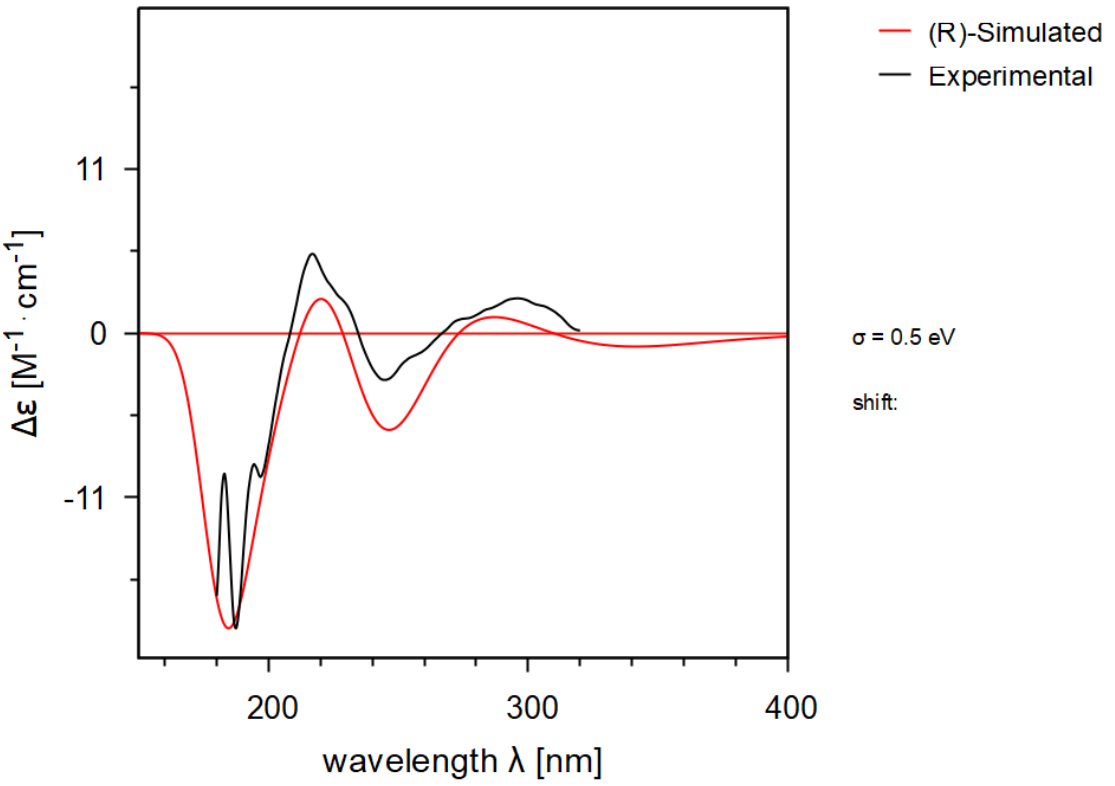


Figure S4. Comparison of experimental electronic dichroism spectra and simulated for compound **7a**.

Table S18. Energies and Gibbs free energies (in Hartrees) calculated for conformers of (*R*)-**3a** calculated at B3LYP-D3(BJ)/def2svp/CPCM (acetonitrile) and their Boltzmann distribution factors.

Structure (*R*)-**3a** Conformer	E $_{(solv\text{-}B3LYP\text{-}D3(BJ))}$	G$_{(solv\text{-}B3LYP\text{-}D3(BJ))}$	Boltzmann distribution (%)
1	-1262.454627	-1262.089741	78.01
2	-1262.453795	-1262.087623	8.26
3	-1262.45478	-1262.087325	6.03
4	-1262.451997	-1262.087128	4.89
5	-1262.451535	-1262.085613	0.98

Table S19. Energies and Gibbs free energies (in Hartrees) calculated for conformers of (*R*)-**4a** calculated at B3LYP-D3(BJ)/def2svp/CPCM (acetonitrile) and their Boltzmann distribution factors.

Structure (*R*)-**4a** Conformer	E $_{(solv\text{-}B3LYP\text{-}D3(BJ))}$	G$_{(solv\text{-}B3LYP\text{-}D3(BJ))}$	Boltzmann distribution (%)
1	-1262,453670	-1262,087924	51.17
2	-1262,452843	-1262,086832	16.09
3	-1262,452905	-1262,086761	14.93
4	-1262,450919	-1262,085839	5.62
5	-1262,452702	-1262,085812	5.46
6	-1262,450758	-1262,085419	3.60
7	-1262,450385	-1262,084329	1.13

Table S20. Energies and Gibbs free energies (in Hartrees) calculated for conformers of (*R*)-**6a** calculated at B3LYP-D3(BJ)/def2svp/CPCM (acetonitrile) and their Boltzmann distribution factors.

Structure (*R*)-**6a** Conformer	E $_{(solv\text{-}B3LYP\text{-}D3(BJ))}$	$G_{(solv\text{-}B3LYP\text{-}D3(BJ))}$	Boltzmann distribution (%)
1	-1375.492701	-1375.128097	16.94
2	-1375.493002	-1375.127939	14.33
3	-1375.493139	-1375.127769	11.97
4	-1375.493877	-1375.127594	9.94
5	-1375.49195	-1375.126603	3.48
6	-1375.491949	-1375.126594	3.44
7	-1375.489697	-1375.126508	3.14
8	-1375.491433	-1375.126499	3.11
9	-1375.490292	-1375.12646	2.99
10	-1375.491435	-1375.126401	2.81
11	-1375.491723	-1375.126298	2.52
12	-1375.492248	-1375.126192	2.25
13	-1375.489406	-1375.126186	2.23
14	-1375.492247	-1375.126185	2.23
15	-1375.489947	-1375.126	1.83
16	-1375.487644	-1375.125928	1.70
17	-1375.491418	-1375.125575	1.17
18	-1375.489975	-1375.125514	1.09
19	-1375.49201	-1375.125484	1.06
20	-1375.489954	-1375.125433	1.00

Table S21. Energies and Gibbs free energies (in Hartrees) calculated for conformers of (*R*)-**7a** calculated at B3LYP-D3(BJ)/def2svp/CPCM (acetonitrile) and their Boltzmann distribution factors.

Structure (*R*)-**7a** Conformer	E $_{(solv\text{-}B3LYP\text{-}D3(BJ))}$	$G_{(solv\text{-}B3LYP\text{-}D3(BJ))}$	Boltzmann distribution (%)
1	-1375.491575	-1375.127142	12.88
2	-1375.492108	-1375.126995	11.02
3	-1375.492587	-1375.126994	11.01
4	-1375.491204	-1375.126935	10.34
5	-1375.490972	-1375.126885	9.81
6	-1375.487185	-1375.125822	3.18
7	-1375.488481	-1375.125761	2.98
8	-1375.490649	-137512576	2.98
9	-1375.490601	-1375.125751	2.95
10	-1375.490855	-1375.125599	2.51
11	-1375.490706	-1375.125554	2.39
12	-1375.490111	-1375.125524	2.32
13	-1375.488619	-1375.125519	2.30
14	-1375.490766	-1375.12539	2.01
15	-1375.488803	-1375.125373	1.97
16	-137.,48739	-1375.125328	1.88
17	-1375.487163	-1375.125059	1.41
18	-1375.489332	-1375.124995	1.32
19	-1375.488003	-1375.124855	1.14
20	-1375.490948	-1375.124817	1.10
21	-1375.486469	-1375.124733	1.00

10. Computational investigation of indolizine alkylation selectivity

Conformational search was performed using CREST to find the structure of the lowest energy conformer of each catalyst.[15] All descriptors mentioned below were computed with MORFEUS Python package. [19] The data collected during catalyst screening from Table S1 and Table S12 were combined, giving data for 30 catalyst for *N*-Boc aminals and similarly data for 27 catalyst for *N*-Cbz aminals. The CPA catalyst **A11** with pyramidal (sp3-hybridized) triphenylsilyl substituent at the 3,3' positions was removed from the dataset as well as CPA catalyst **E** with completely different VAPOL backbone.

We found the optimal parameters for % buried volume descriptor (% V_{bur}) by varying the center of sphere and its radius. All buried volumes were computed without hydrogens. As a criteria for parameters optimization we used Pearson correlation coefficient (PCC) between difference of free energies of two regioisomers and catalyst %buried volume. The results are given in the Table S22.

Table S22. Pearson correlation coefficient for different location of % buried volume descriptor.

Center	Best radius, A	PCC
P	4.5	-0.77
O1	5.5	-0.76
O2	4.5	-0.79

To elucidate to effect of aminal substituents on the regioselectivity, the dataset was splited into two groups: reaction with *N*-Boc aminals (28 reactions) and with *N*-Cbz aminal (27 reactions). Figure S5 and Table S23 is showing similar relationship between observed C3/C1 selectivity for both *N*-Boc aminals and *N*-Cbz aminals and %V_{bur} although the reactions for these two groups were performed in two different solvents, toluene and dichloromethane, respectively. Combining the substituents effect of catalyst and aminals we can conclude, that bigger free volume in catalyst pocket facilitate formation of C1-product. However, when active center is crowded the preferable is C3-product.

The effect of other catalyst properties on the regioselectivity were also tested. Computed SASA (solvent accessibility surface area) descriptor placed at the oxygen of CPA and similarly dispersion descriptor placed at oxygen of catalyst also showed also good correlation with regioselectivity (PCC was 0.78). While, the Sterimol and Octants descriptors gave a low correlation with observed selectivity.

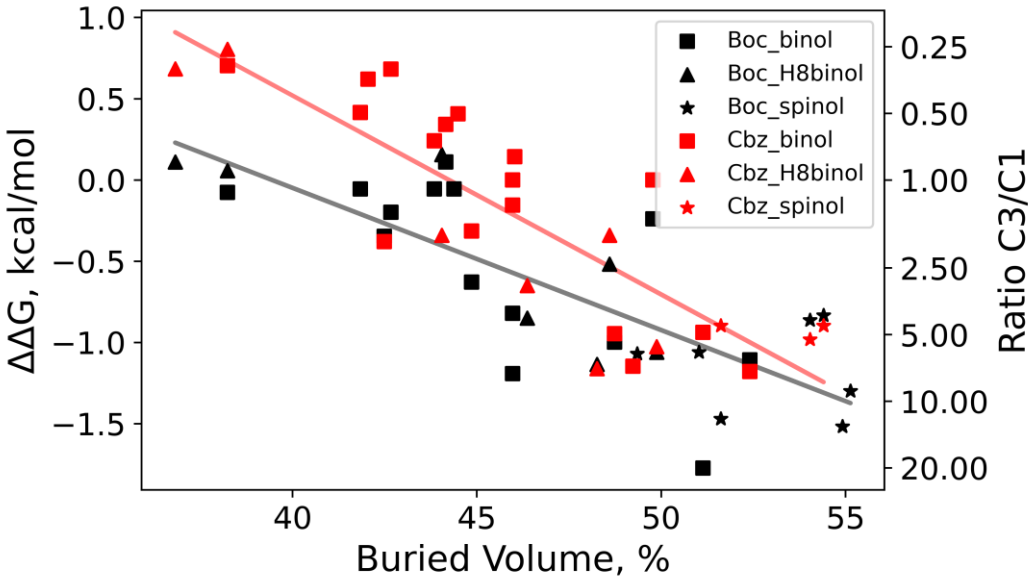


Figure S5. Plot showing correlations of C3/C1 selectivity (ΔΔG) for *N*-Boc aminals (black) and *N*-cbz aminals (red) and $\%V_{bur}$ of the catalyst for model reactions with distinction of different CPA catalyst subgroups.

Table S23. Comparison of Pearson correlation coefficients for *N*-Boc and *N*-Cbz aminals.

Aminal Protecting Group	PCC(Pearson coefficient)	slope	intercept
Boc	-0.79	-0.0875	3.451
Cbz	-0.85	-0.1224	5.4155

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