Supporting Information

Cp*Co(III)-Catalyzed Synthesis of Isoquinolones *via* Controlled Annulation of Primary Arylamides with Internal Alkynes

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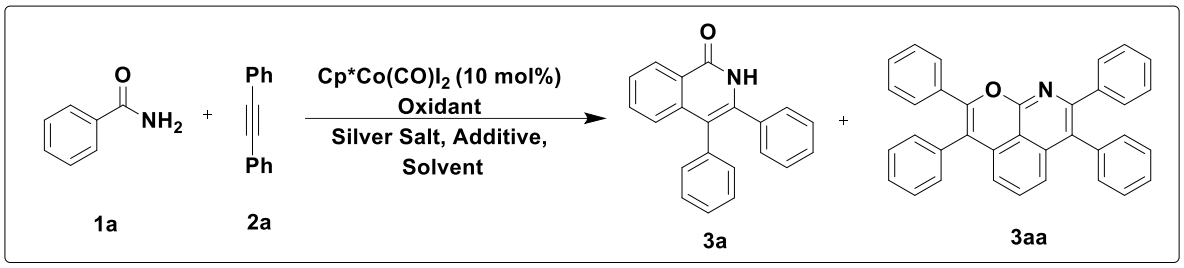
1. Table S1: Optimization table for the Cp*Co(III) catalyzed synthesis of isoquinolone.[a]



S.No.	Additive (20 mol%)	Solvent	Silver Salt (20 mol%)	Oxidant (2.0 equiv)	Temperature °C	Yield (%) 3a (3aa)
1	NaOAc	TFE	$AgBF_4$	CuO	120	53 (17)
2	**Ag_2CO_3**	TFE	$AgBF_4$	CuO	120	nr
3	**Na_2CO_3**	TFE	$AgBF_4$	CuO	120	nr
4	**AgOAc**	TFE	$AgBF_4$	CuO	120	71 (6)
5	**CsOAc**	TFE	$AgBF_4$	CuO	120	Trace
6	**KOAc**	TFE	$AgBF_4$	CuO	120	56 (13)
7	**LiOAc**	TFE	$AgBF_4$	CuO	120	43 (13)
8	**AgOAc**	TFE	$AgBF_4$	CuO	120	28 (3)[b]
9	-	TFE	$AgBF_4$	CuO	120	nr
10	AgOAc	**1,4 Dioxane**	$AgBF_4$	CuO	120	17
11	AgOAc	**THF**	$AgBF_4$	CuO	120	Trace
12	AgOAc	**DCE**	$AgBF_4$	CuO	120	Trace
13	AgOAc	**ACN**	$AgBF_4$	CuO	120	nr
14	AgOAc	**HFIP**	$AgBF_4$	CuO	120	44(8)
15	AgOAc	**TFE**	$AgBF_4$	CuO	120	56(18)[c]
16	AgOAc	TFE	**$AgSbF_6$**	CuO	120	25 (Trace)
17	AgOAc	TFE	**AgOTf**	CuO	120	45 (8)
18	AgOAc	TFE	**$AgNTf_2$**	CuO	120	31 (Trace)
19	AgOAc	TFE	**$AgBF_4$ (50 mol%)**	CuO	120	53 (5)
20	AgOAc	TFE	-	CuO	120	nr
21	AgOAc	TFE	$AgBF_4$	**$Cu(OAc)_2$**	120	nr
22	AgOAc	TFE	$AgBF_4$	**Ag_2O**	120	Trace
23	AgOAc	TFE	$AgBF_4$	-	120	Trace
24	AgOAc	TFE	$AgBF_4$	CuO	120	31 (Trace)[d]
25	AgOAc	TFE	$AgBF_4$	CuO	120	50 (15)[e]

26	AgOAc	TFE	$AgBF_4$	CuO	120	64 (7)[f]
27	AgOAc	TFE	$AgBF_4$	CuO	**140**	65 (12)
28	**AgOAc**	**TFE**	**$AgBF_4$**	**CuO**	**100**	**76 (5)**
29	AgOAc	TFE	$AgBF_4$	CuO	**80**	54 (7)
30	AgOAc	TFE	$AgBF_4$	CuO	100	74(10)[g]
31	AgOAc	TFE	$AgBF_4$	CuO	100	50(4)[h]

[a]Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (0.4 mmol, 2.0 equiv), Cp*Co(CO)I_2 (10 mol%), additive (20 mol%), oxidant (2.0 equiv), silver salt (20 mol%), solvent (2 ml) for 24 h. [b]1.0 equiv of additive was used. [c]1 ml of solvent was used. [d]5 mol% of catalyst was used. [e]3.0 equiv of **2a** was used. [f]1.5 equiv of **2a** was used. [g]Reaction time = 36 h. [h]Reaction time = 12 h

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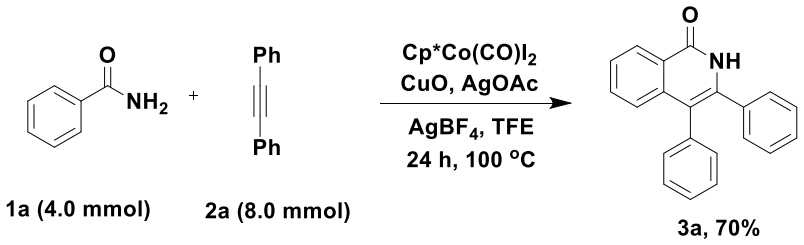
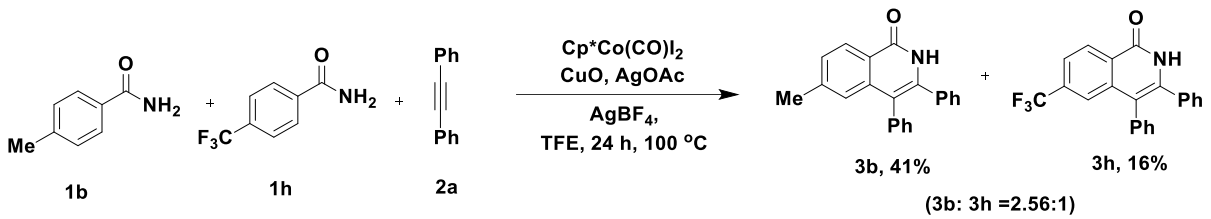
2. Procedure for scale-up synthesis.



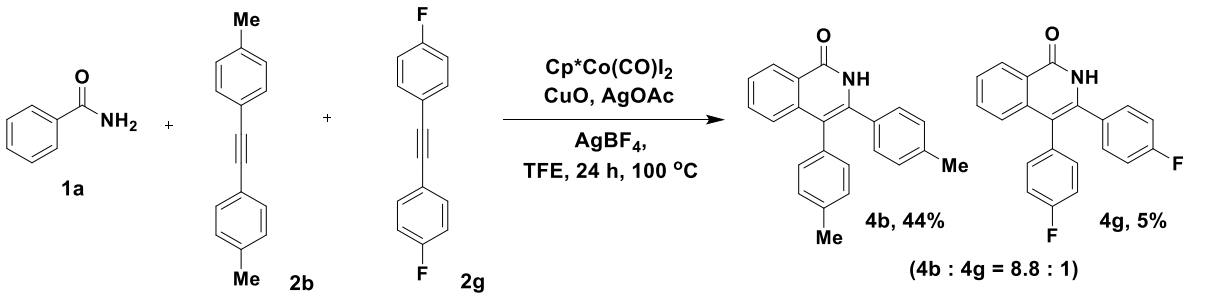
To a clean oven-dried sealed tube equipped with a magnetic stir bar was sequentially added benzamide **1a** (4.0 mmol, 1.0 equiv), diphenylacetylene **2b** (8.0 mmol, 2.0 equiv), Cp*Co(CO)I_2 (10 mol%), AgOAc (20 mol%), CuO (0.4 mmol, 2.0 equiv) in TFE (40 ml). Subsequently, $AgBF_4$ (20 mol%) was added under a nitrogen atmosphere, and the reaction tube was flushed with nitrogen. The tube was tightly closed, placed in a preheated oil bath at 100 ^oC, and stirred for 24 h. After completion, the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (100-200 mesh) using ethyl acetate/hexanes as eluent to give the desired product in 70 % yield (830 mg).

3. Procedure for Intermolecular Competition Experiment between 1b and 1h.



To a clean oven-dried 15ml sealed tube equipped with a magnetic stir bar was sequentially added 4-Me-benzamide **1b** (0.2 mmol, 1.0 equiv), 4-CF_3-benzamide **1h** (0.2 mmol, 1.0 equiv), diphenylacetylene **2a** (0.4 mmol, 2.0 equiv), Cp*Co(CO)I_2 (10 mol%), AgOAc (20 mol%), CuO (0.4 mmol, 2.0 equiv) in TFE (2 ml). Subsequently, $AgBF_4$ (20 mol%) was added under a nitrogen atmosphere, and the reaction tube was flushed with nitrogen. The tube was tightly closed, placed in a preheated oil bath at 100 °C, and stirred for 24 h. After completion, the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (100-200 mesh) using ethyl acetate/hexanes as eluent to give the desired product **3b** & **3h** in 41% and 16% yield respectively and the ratio was 2.56:1.

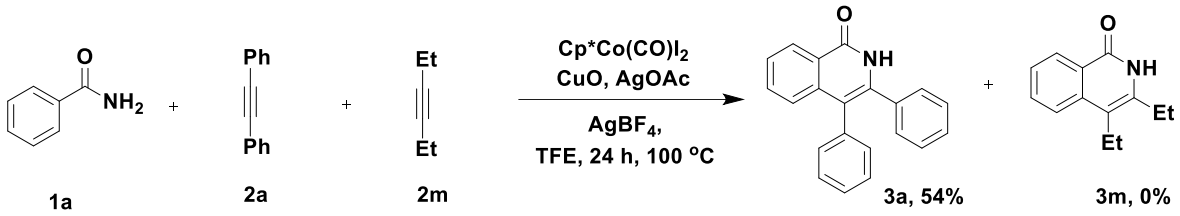
Procedure for Intermolecular Competition Experiment between 2b and 2g.



To a clean oven-dried 15ml sealed tube equipped with a magnetic stir bar was sequentially added benzamide **1a** (0.2 mmol, 1.0 equiv), acetylene **2b** (0.4 mmol, 2.0 equiv), acetylene **2g** (0.4 mmol, 2.0 equiv), Cp*Co(CO)I_2 (10 mol%), AgOAc (20 mol%), CuO (0.4 mmol, 2.0 equiv) in TFE (2 ml). Subsequently, $AgBF_4$ (20 mol%) was added under a nitrogen atmosphere, and the reaction tube was flushed with nitrogen. The tube was tightly closed,

placed in a preheated oil bath at 100 °C, and stirred for 24 h. After completion, the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (100-200 mesh) using ethyl acetate/hexanes as eluent to give the desired product **4b** & **4g** in 44% and 5% yield respectively and the ratio was 8.8:1.

Procedure for Intermolecular Competition Experiment between 2a and 2m.



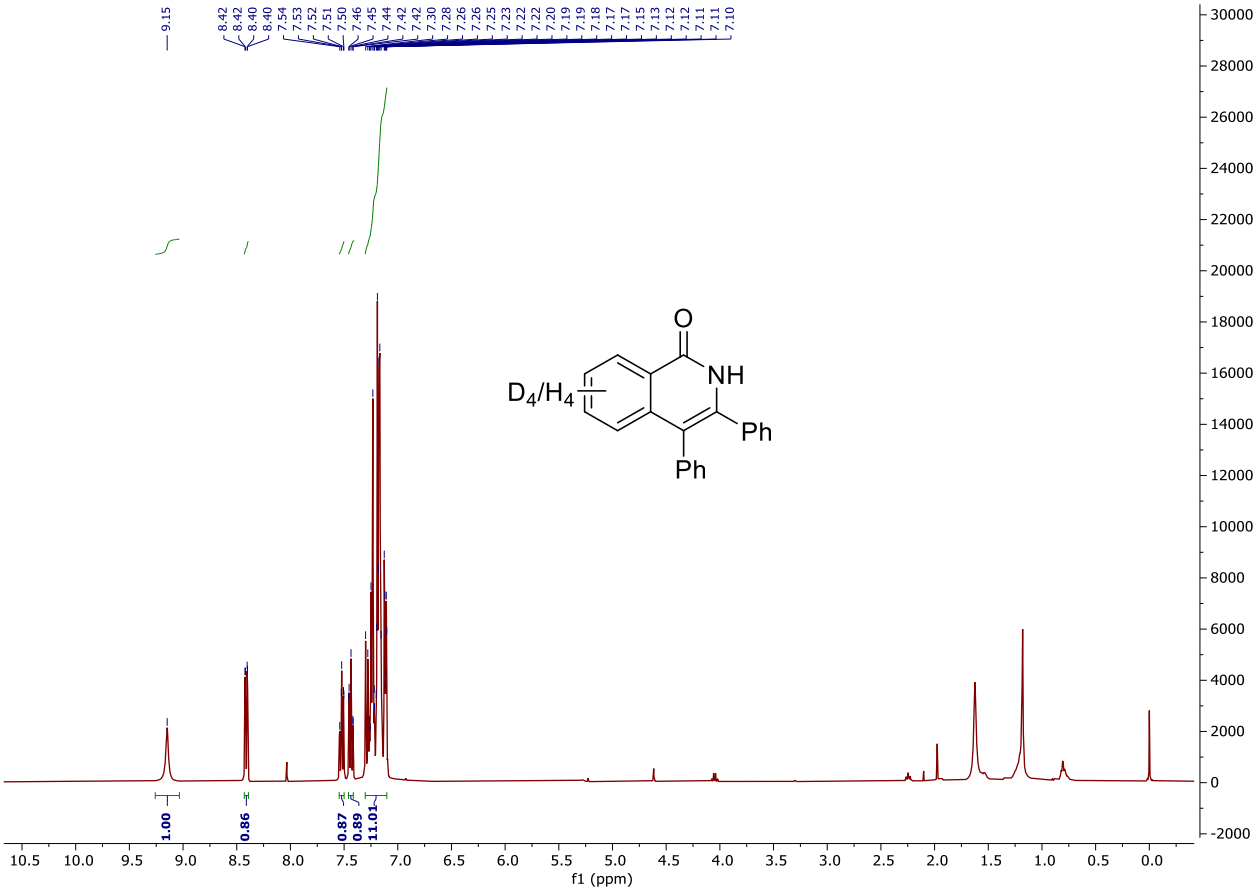
To a clean oven-dried 15ml sealed tube equipped with a magnetic stir bar was sequentially added benzamide **1a** (0.2 mmol, 1.0 equiv), acetylene **2a** (0.4 mmol, 2.0 equiv), acetylene **2m** (0.4 mmol, 2.0 equiv), Cp*Co(CO)I_2 (10 mol%), AgOAc (20 mol%), CuO (0.4 mmol, 2.0 equiv) in TFE (2 ml). Subsequently, $AgBF_4$ (20 mol%) was added under a nitrogen atmosphere, and the reaction tube was flushed with nitrogen. The tube was tightly closed, placed in a preheated oil bath at 100 °C, and stirred for 24 h. After completion, the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (100-200 mesh) using ethyl acetate/hexanes as eluent to give the product in **3a** 54%.

4. Procedure for KIE Experiment between 1a and 1a-d5.

i) Competition Reaction

To a clean oven-dried 15ml sealed tube equipped with a magnetic stir bar was sequentially added benzamide **1a** (0.2 mmol, 1.0 equiv), deuterated benzamide **1a-D_5** (0.2 mmol, 1.0 equiv), diphenylacetylene **2a** (0.4 mmol, 2.0 equiv), Cp*Co(CO)I_2 (10 mol%), AgOAc (20 mol%),

CuO (0.4 mmol, 2.0 equiv) in TFE (2 ml). Subsequently, $AgBF_4$ (20 mol%) was added under a nitrogen atmosphere, and the reaction tube was flushed with nitrogen. The tube was tightly closed, placed in a preheated oil bath at 100 ^oC, and stirred for 3 h. After that, the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (100-200 mesh) using ethyl acetate/hexanes as eluent to give 28% of the product in combined yield. The ratio of **3a** and **3a-D$_4$** was determined by ^{1}H NMR analysis and found to be $k_H/k_D \approx 6.1{:}1$ (3 h).



ii) Parallel Reaction

Reaction A. To a clean oven-dried 15ml sealed tube equipped with a magnetic stir bar was sequentially added benzamide **1a** (0.2 mmol, 1.0 equiv), diphenylacetylene **2a** (0.4 mmol, 2.0

equiv), Cp*Co(CO)I_2 (10 mol%), AgOAc (20 mol%), CuO (0.4 mmol, 2.0 equiv) in TFE (2 ml). Subsequently, $AgBF_4$ (20 mol%) was added under a nitrogen atmosphere, and the reaction tube was flushed with nitrogen. The tube was tightly closed, placed in a preheated oil bath at 100 ^oC, and stirred for 3 h.

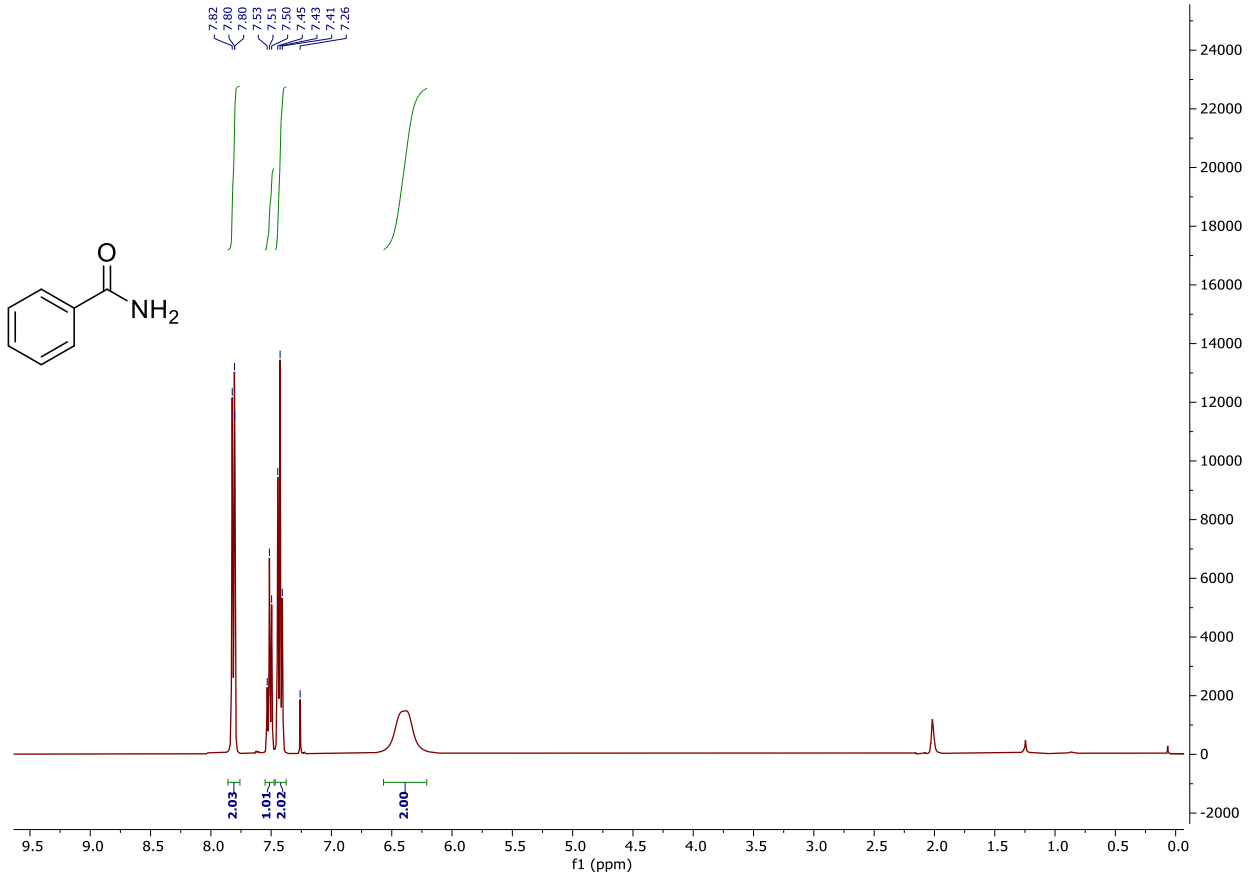
Reaction B. To a clean oven-dried 15ml sealed tube equipped with a magnetic stir bar was sequentially added deuterated benzamide **1a-D_5** (0.2 mmol, 1.0 equiv), diphenylacetylene **2a** (0.4 mmol, 2.0 equiv), Cp*Co(CO)I_2 (10 mol%), AgOAc (20 mol%), CuO (0.4 mmol, 2.0 equiv) in TFE (2 ml). Subsequently, $AgBF_4$ (20 mol%) was added under a nitrogen atmosphere, and the reaction tube was flushed with nitrogen. The tube was tightly closed, placed in a preheated oil bath at 100 ^oC, and stirred for 3 h.

After completion, reaction A and reaction B were cooled to room temperature, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography on silica gel (100-200 mesh) using ethyl acetate/hexanes as eluent to give **3a** and **3a-D_4** in 24% and 5% yield respectively. The kinetic isotopic effect (KIE) was found to be k_H/k_D ~ 4.8 through the independent parallel experiments.

5. Procedure for H/D exchange experiment without diphenylacetylene in CD_3OD.

To a clean oven-dried 15ml sealed tube equipped with a magnetic stir bar was sequentially added benzamide **1a** (0.2 mmol, 1.0 equiv), Cp*Co(CO)I_2 (10 mol%), AgOAc (20 mol%), CuO (0.4 mmol, 2.0 equiv) in TFE (2 ml). Subsequently, $AgBF_4$ (20 mol%) was added under a nitrogen atmosphere, and the reaction tube was flushed with nitrogen. The tube was tightly closed, placed in a preheated oil bath at 100 ^oC, and stirred for 24 h. After completion, the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (100-200 mesh) using ethyl acetate/hexanes as eluent. It was found *via* ^1H NMR analysis that no

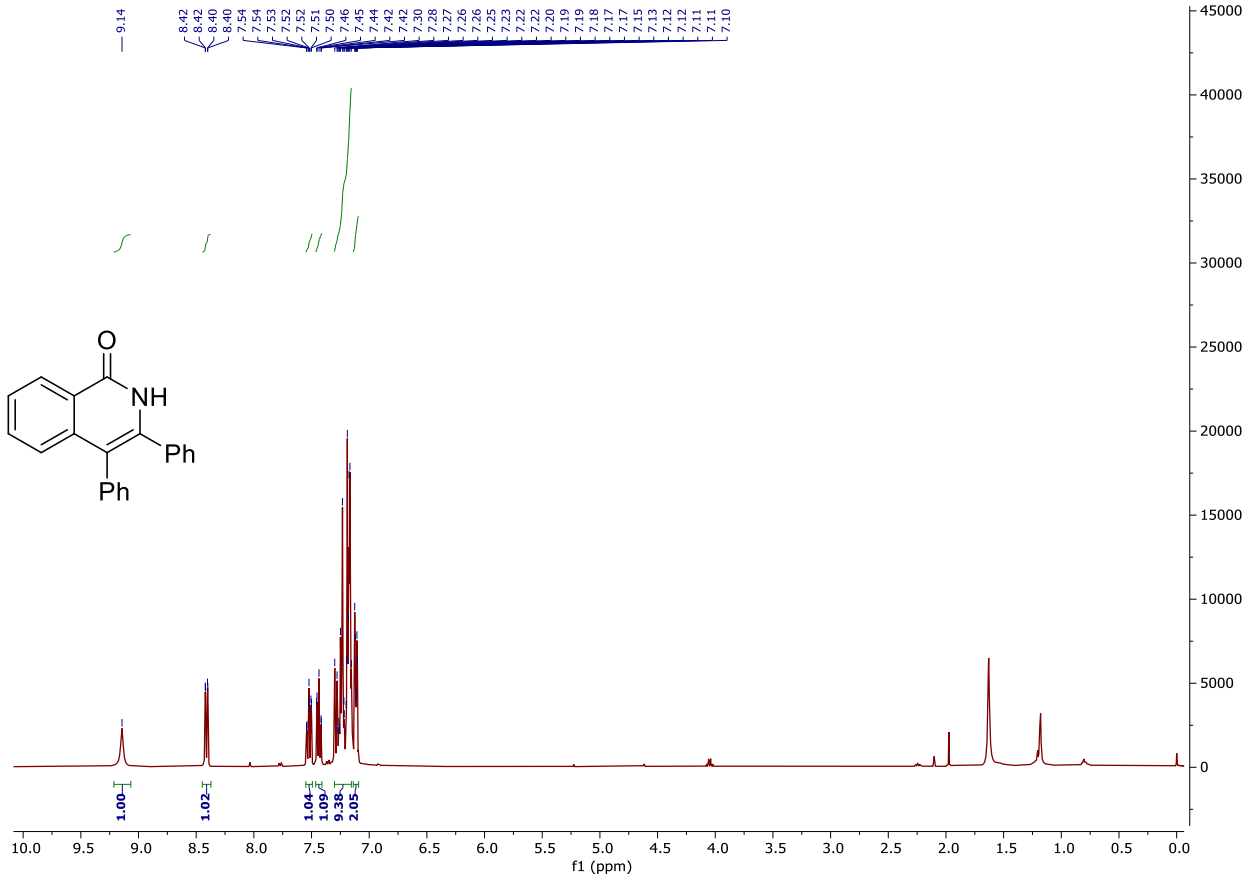
deuteration was incorporated into the product which suggests that the C-H activation step is non-reversible.



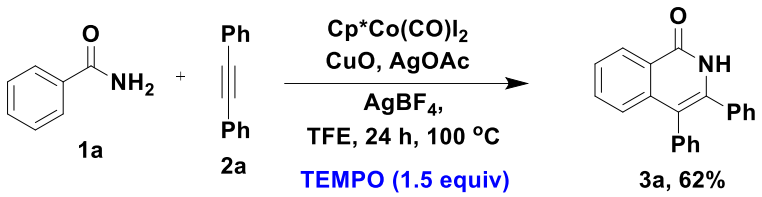
Procedure for H/D exchange experiment with diphenylacetylene in CD_3OD.

To a clean oven-dried 15ml sealed tube equipped with a magnetic stir bar was sequentially added benzamide **1a** (0.2 mmol, 1.0 equiv), diphenylacetylene **2a** (0.4 mmol, 2.0 equiv), Cp*Co(CO)I_2 (10 mol%), AgOAc (20 mol%), CuO (0.4 mmol, 2.0 equiv) in TFE (2 ml). Subsequently, $AgBF_4$ (20 mol%) was added under a nitrogen atmosphere, and the reaction tube was flushed with nitrogen. The tube was tightly closed, placed in a preheated oil bath at 100 ^oC, and stirred for 24 h. After completion, the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (100-200 mesh) using ethyl acetate/hexanes as eluent. Again, it

was found *via* ^{1}H NMR analysis that no deuteration was incorporated into the product which suggests that the C-H activation step is non-reversible.



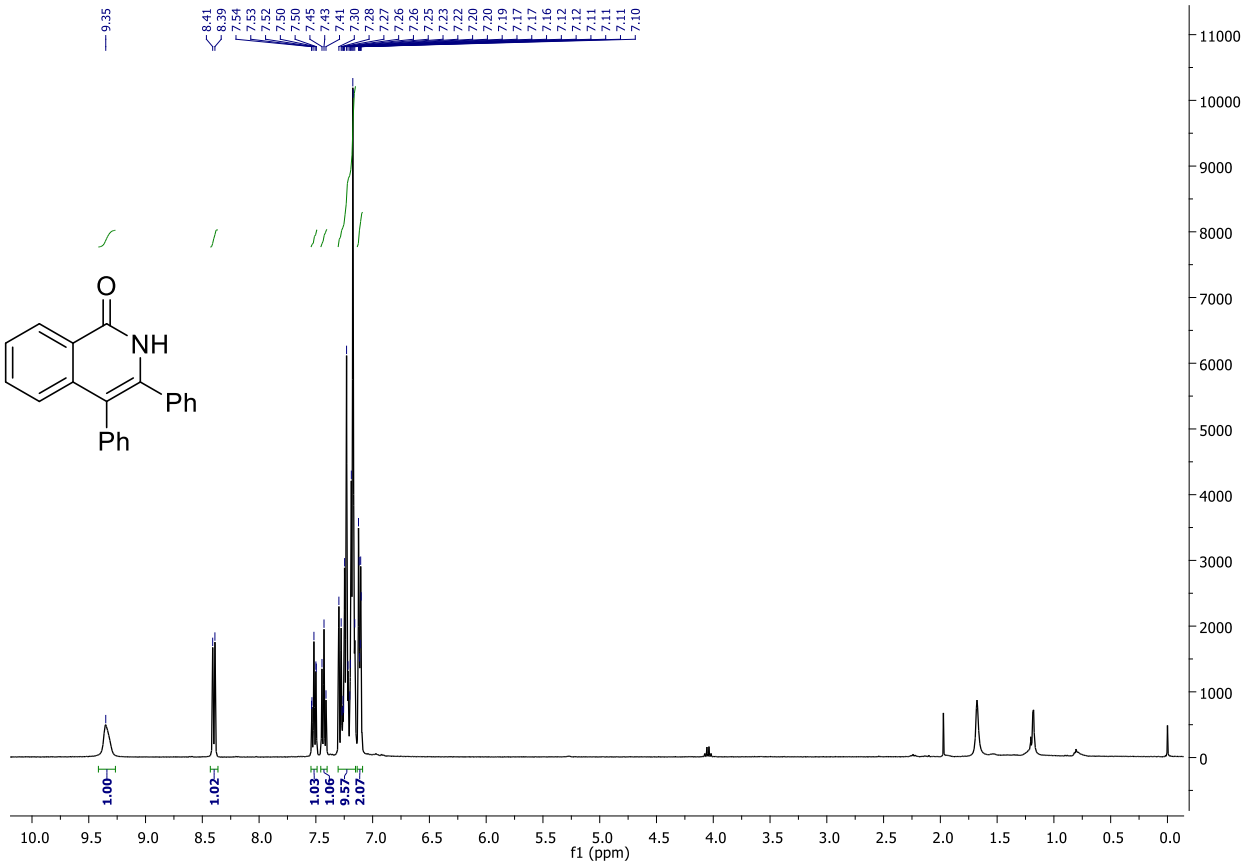
6. Procedure for radical inhibition experiment.

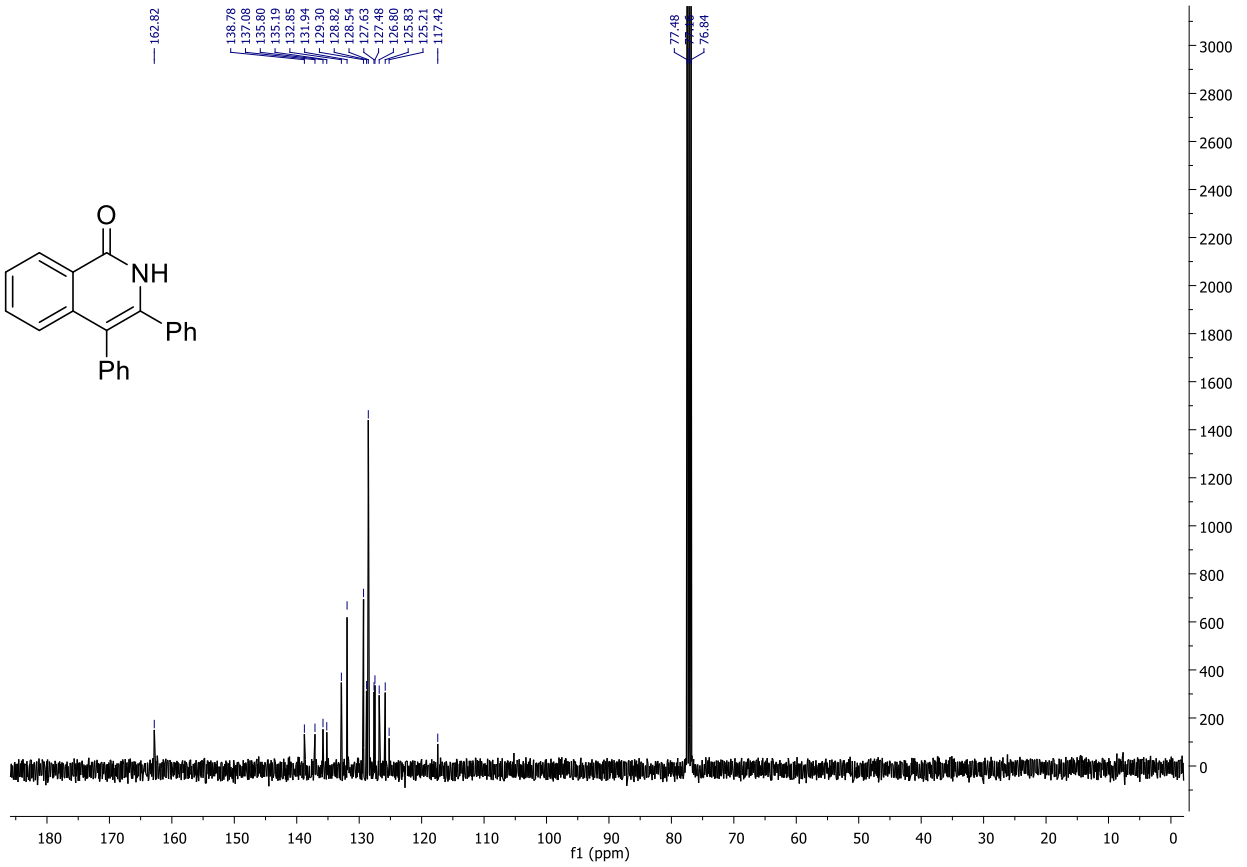


To a clean oven-dried 15ml sealed tube equipped with a magnetic stir bar was sequentially added benzamide **1a** (0.2 mmol, 1.0 equiv), diphenylacetylene **2a** (0.4 mmol, 2.0 equiv), Cp*Co(CO)I_2 (10 mol%), AgOAc (20 mol%), CuO (0.4 mmol, 2.0 equiv), and TEMPO (1.5 equiv) in TFE (2 ml). Subsequently, $AgBF_4$ (20 mol%) was added under a nitrogen atmosphere, and the reaction tube was flushed with nitrogen. The tube was tightly closed,

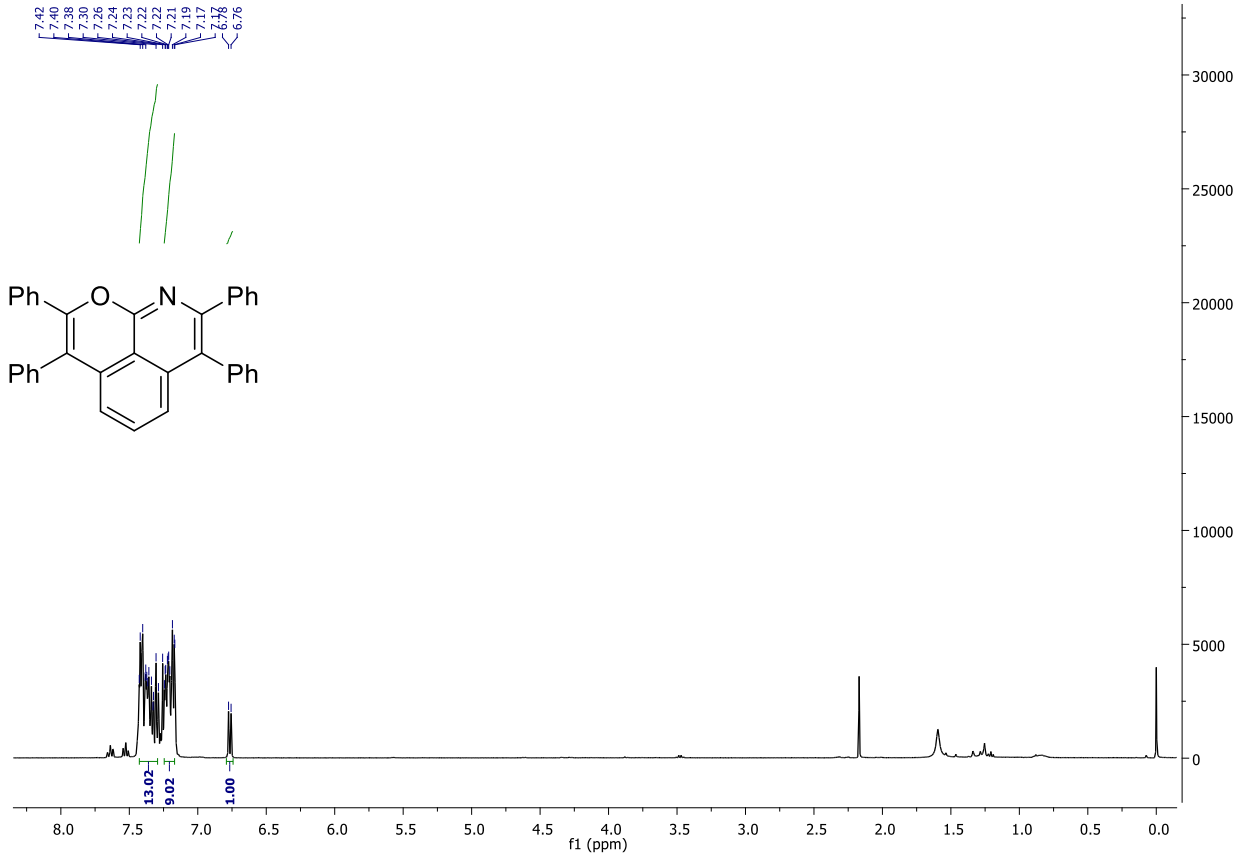
placed in a preheated oil bath at 100 ^{o}C, and stirred for 24 h. After completion, the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (100-200 mesh) using ethyl acetate/hexanes as eluent to give 62% of the desired product. The outcome rules out the involvement of the free radical mechanism in the catalytic cycle.

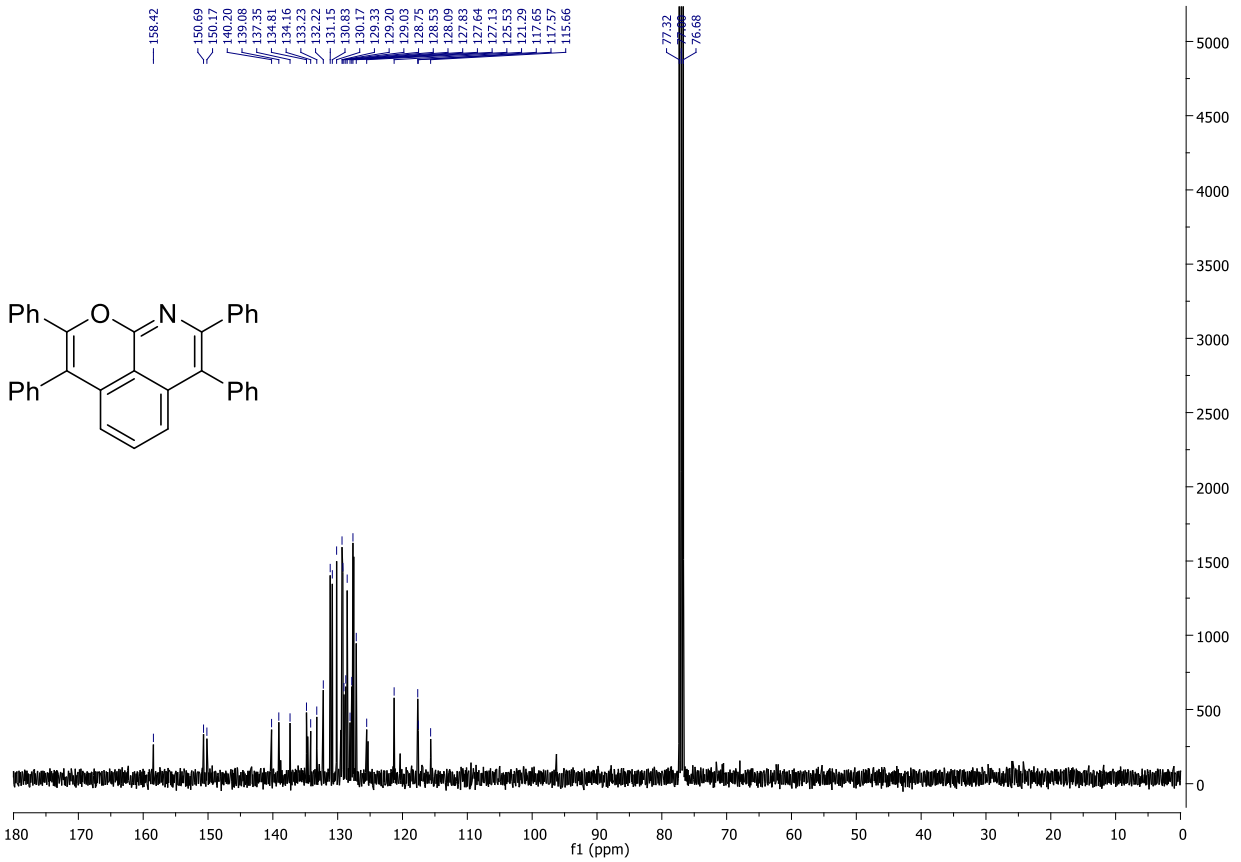
7. NMR Spectra. ^{1}H (400 MHz) and $^{13}C\{1H\}$ (100 MHz) spectra of 3a in $CDCl_3$



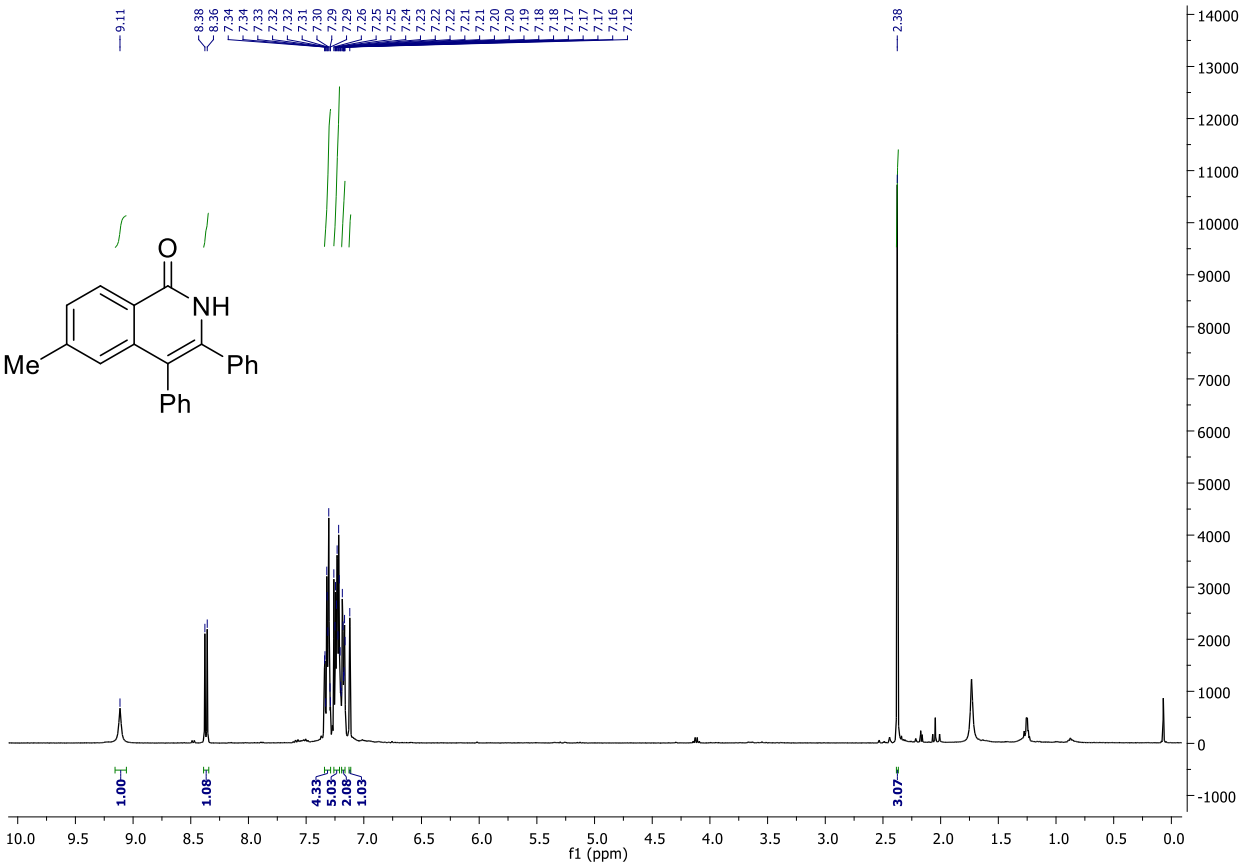


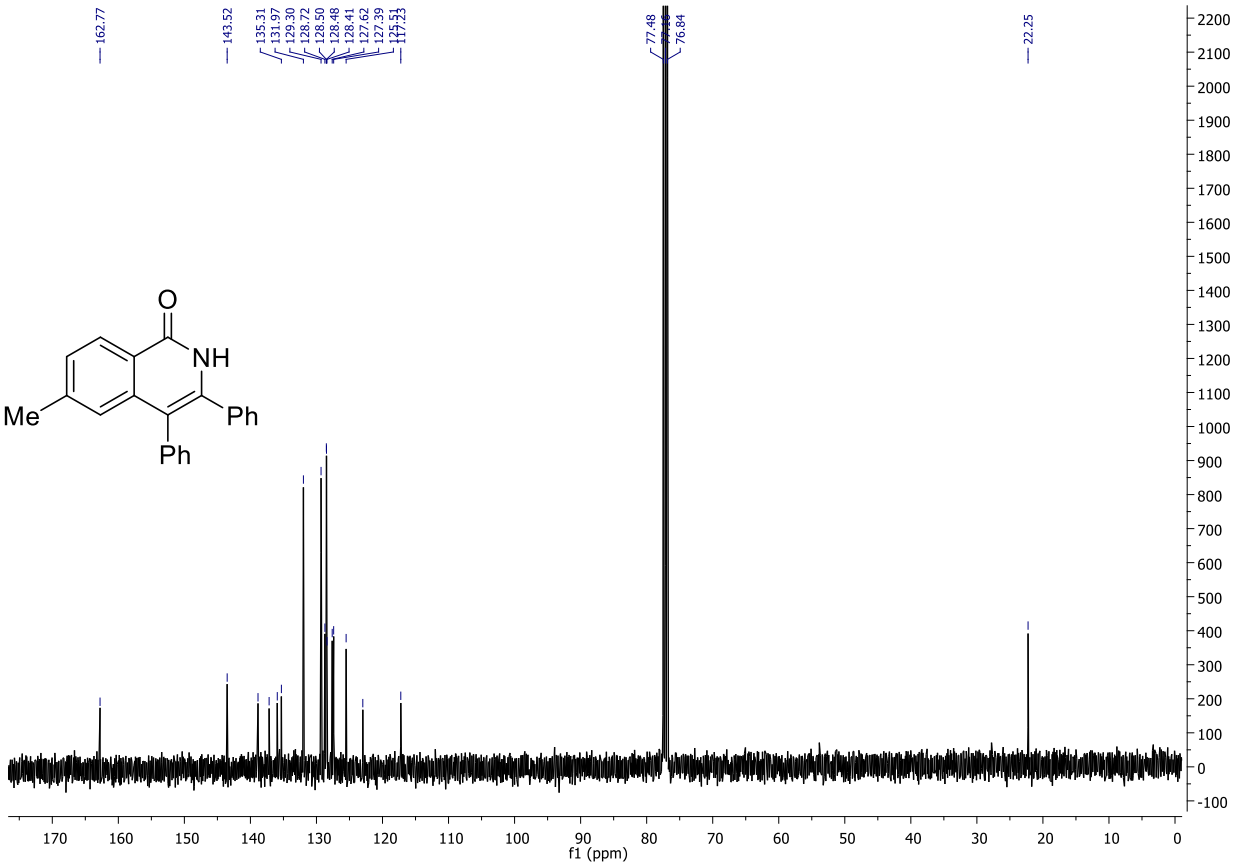
^{1}H (400 MHz) and $^{13}C\{1H\}$ (100 MHz) spectra of 3aa in $CDCl_3$



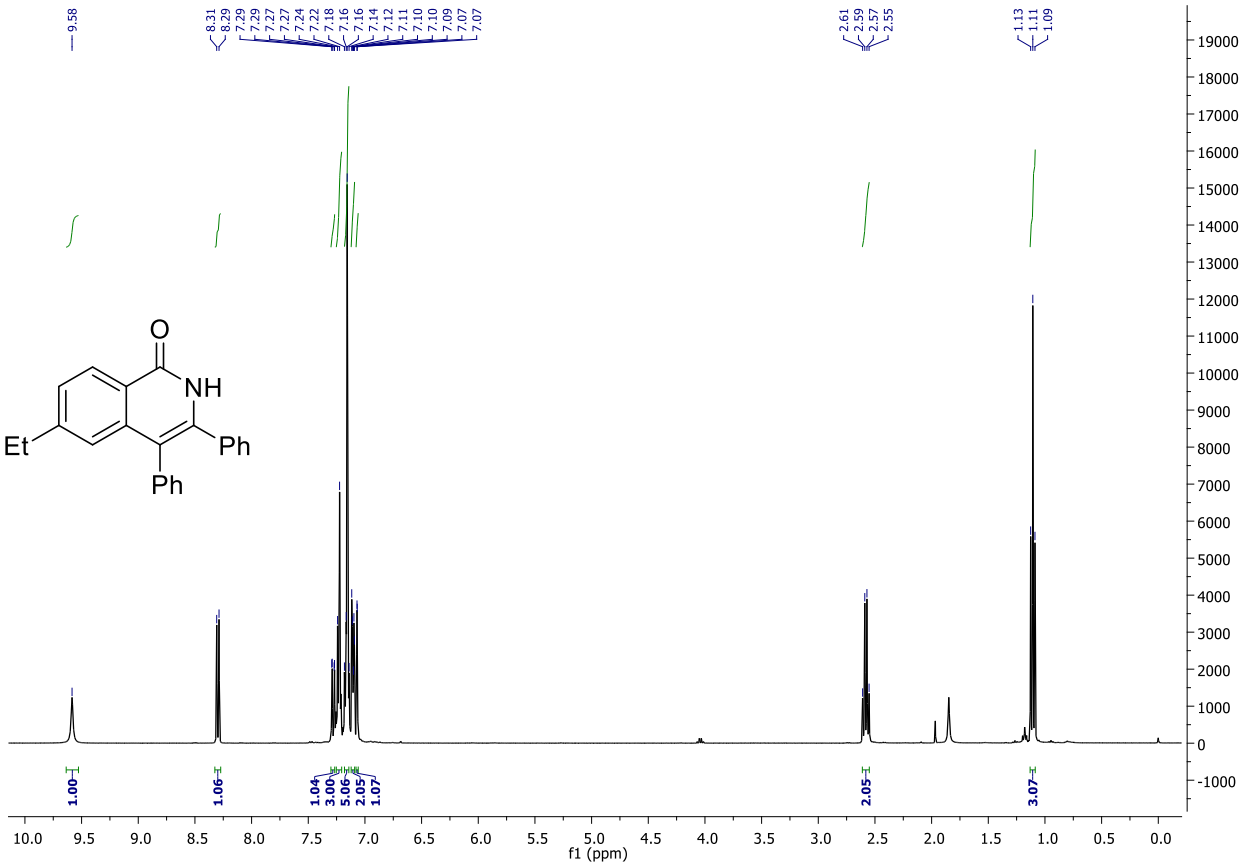


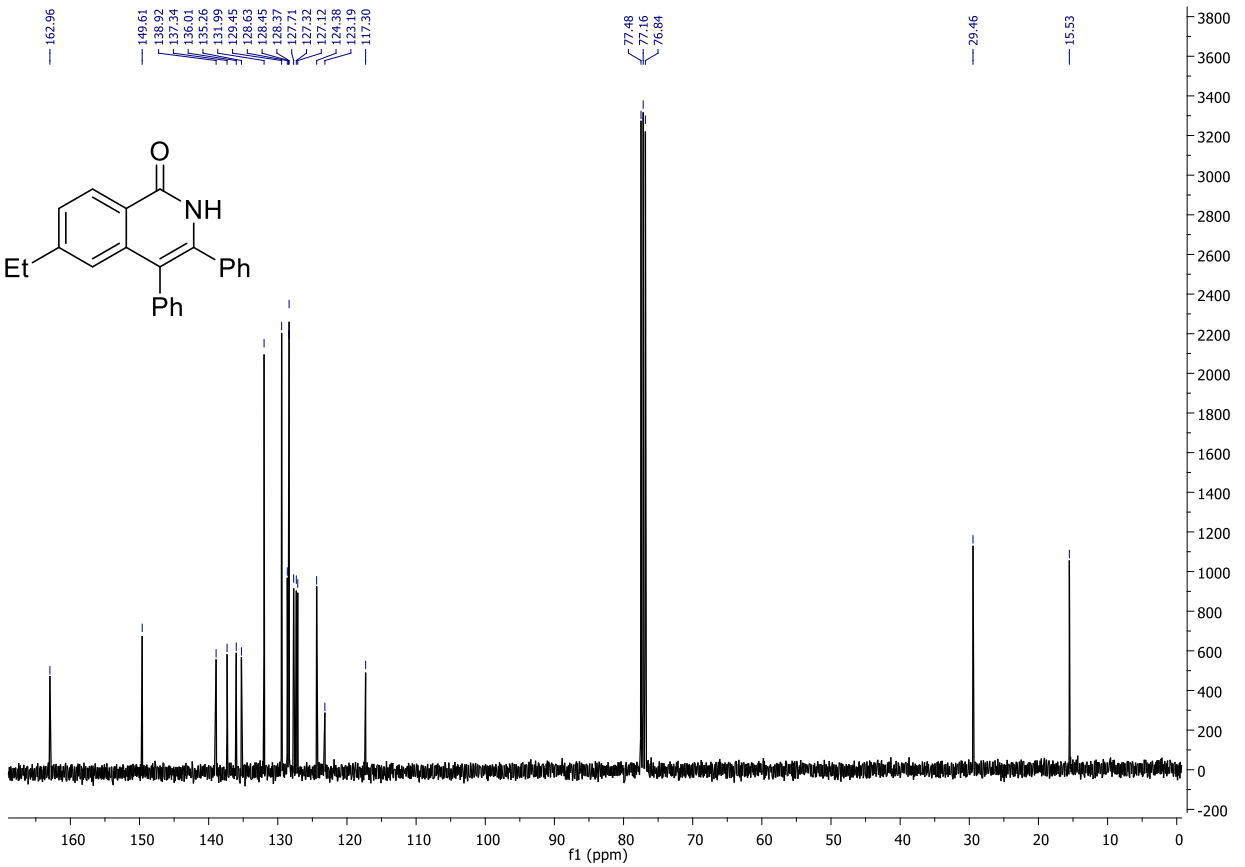
^{1}H (400 MHz) and ^{13}C{1H} (100 MHz) spectra of 3b in $CDCl_3$



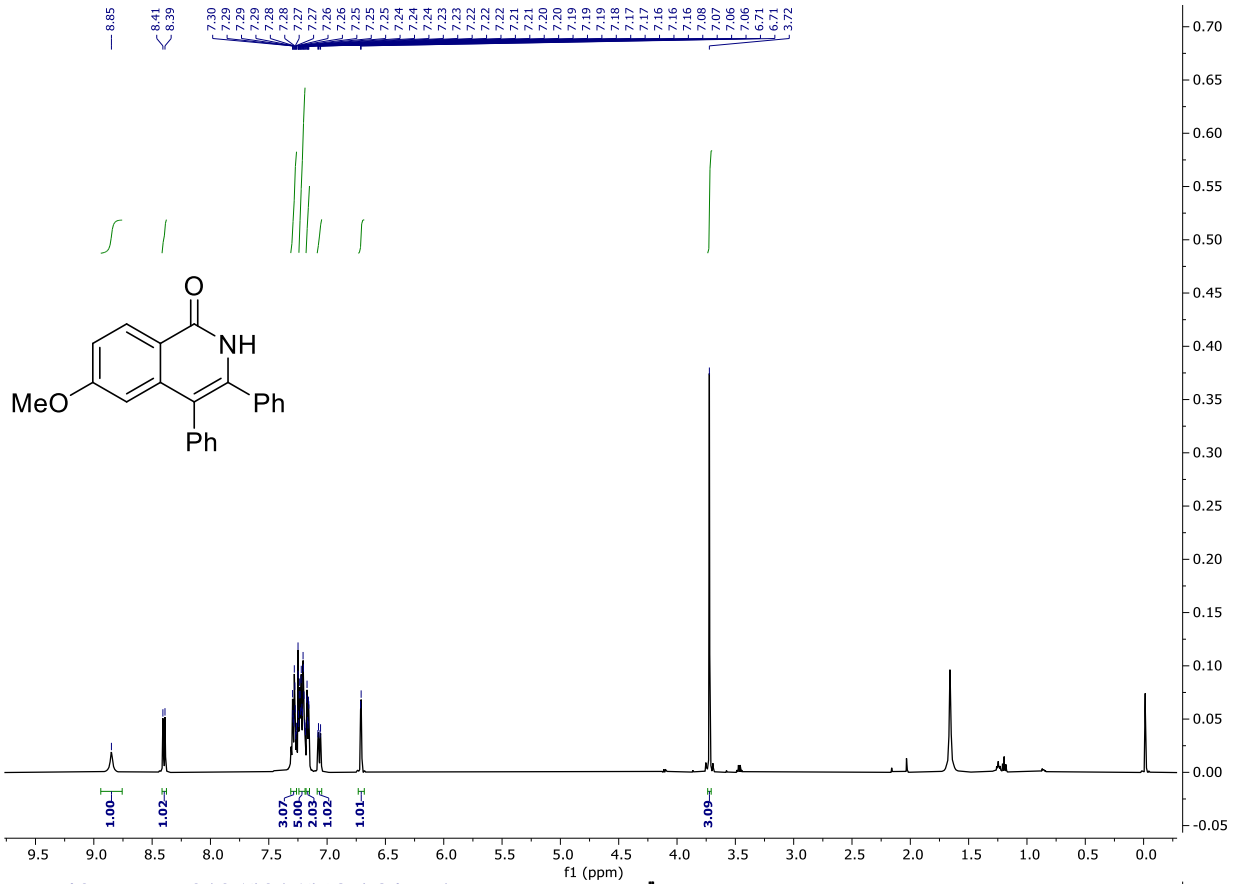


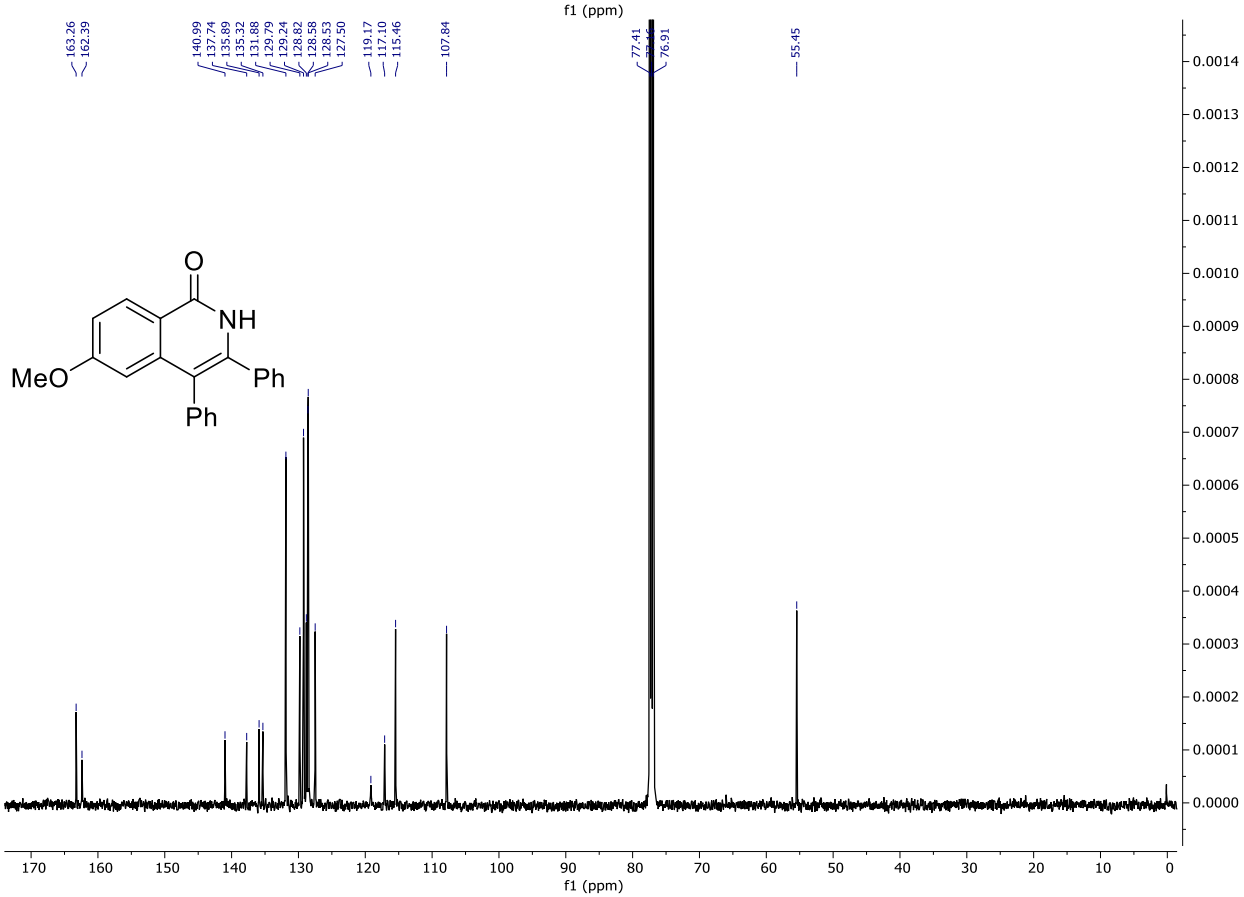
^{1}H (400 MHz) and ^{13}C{1H} (100 MHz) spectra of 3c in $CDCl_3$



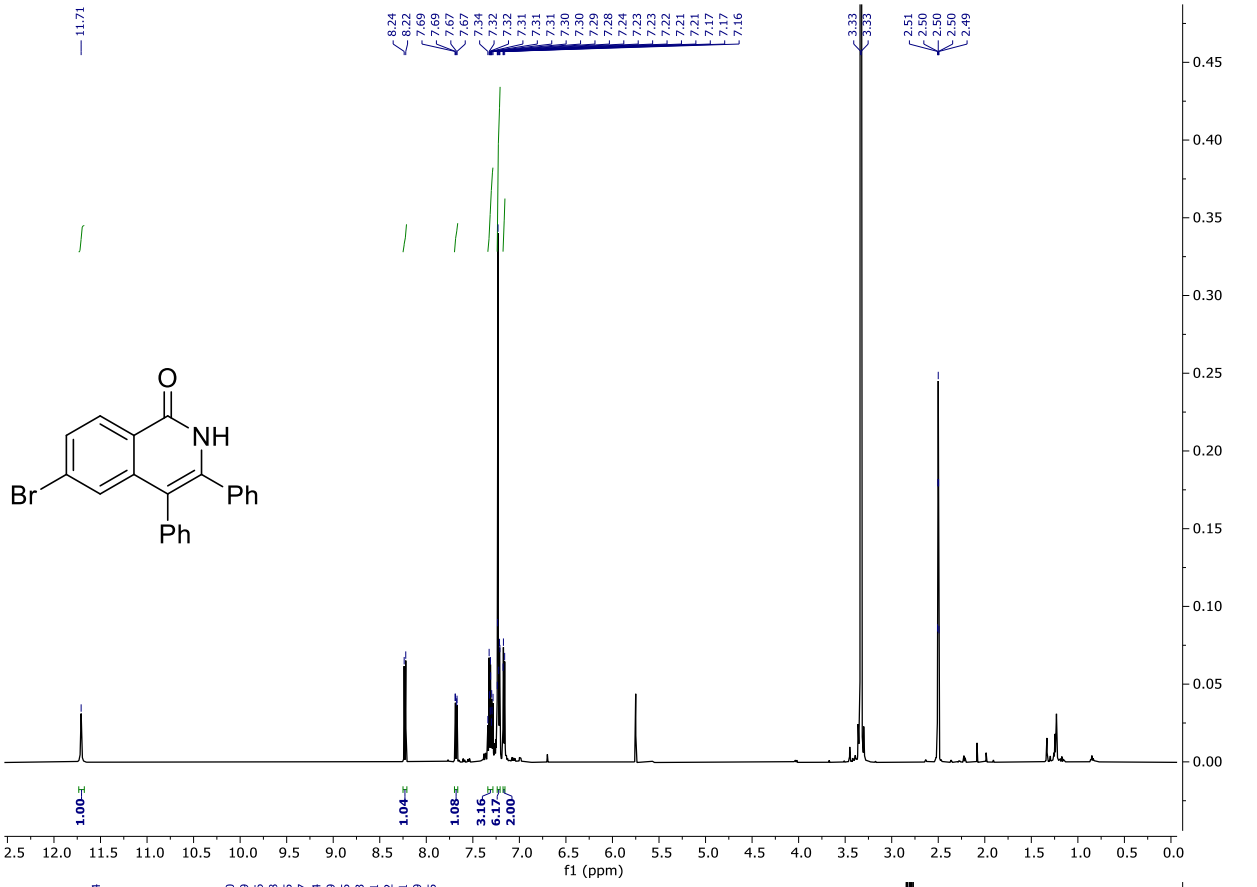


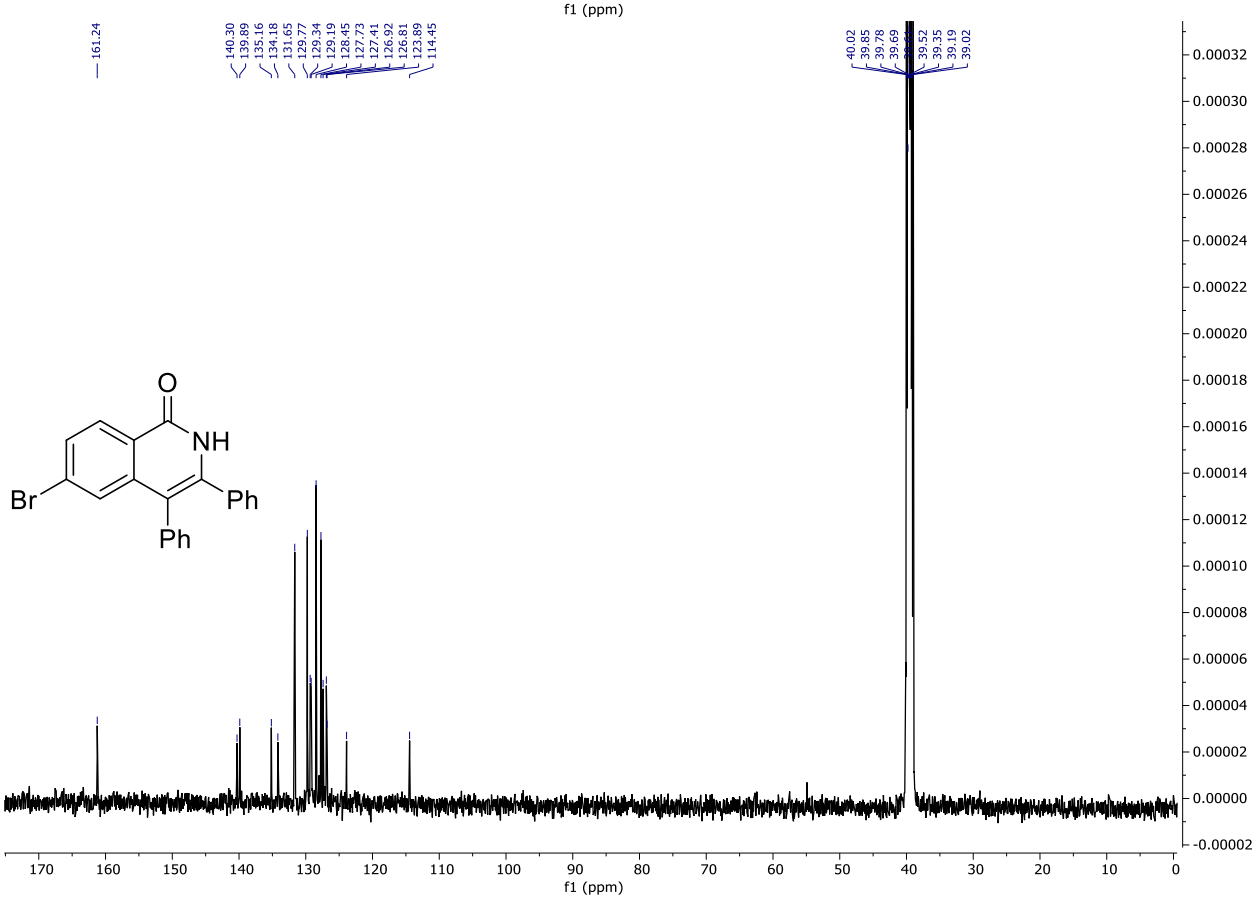
^{1}H (500 MHz) and ^{13}C{1H} (125 MHz) spectra of 3d in $CDCl_3$



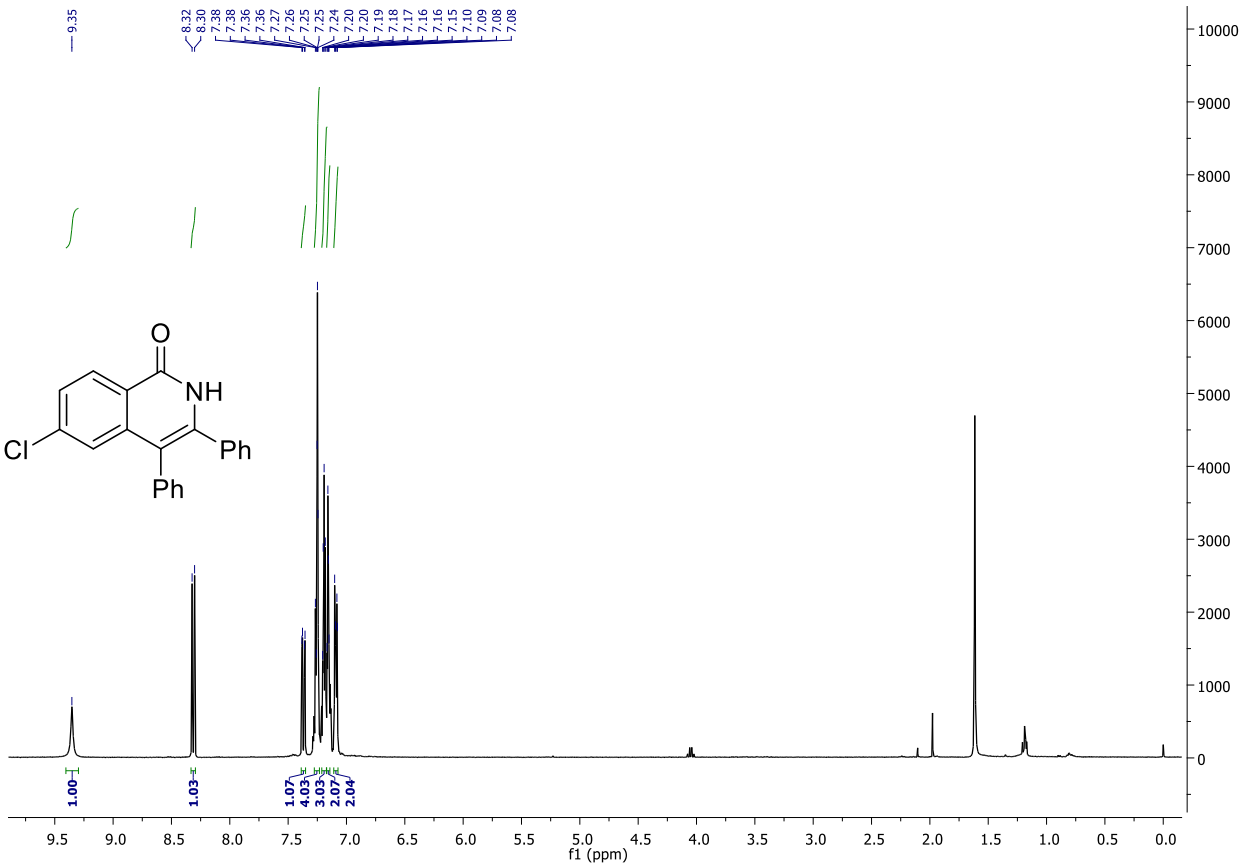


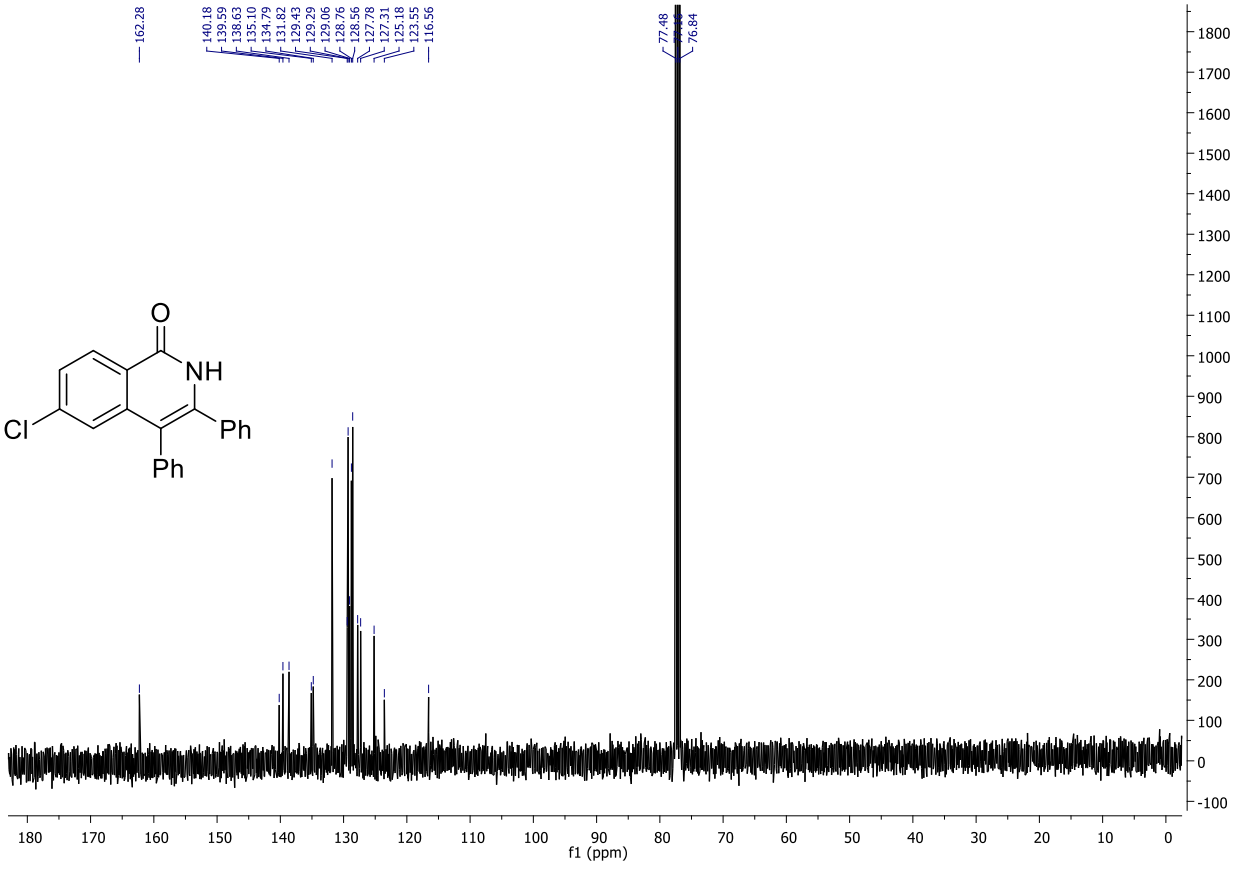
^{1}H (500 MHz) and ^{13}C{1H} (125 MHz) spectra of 3e in DMSO



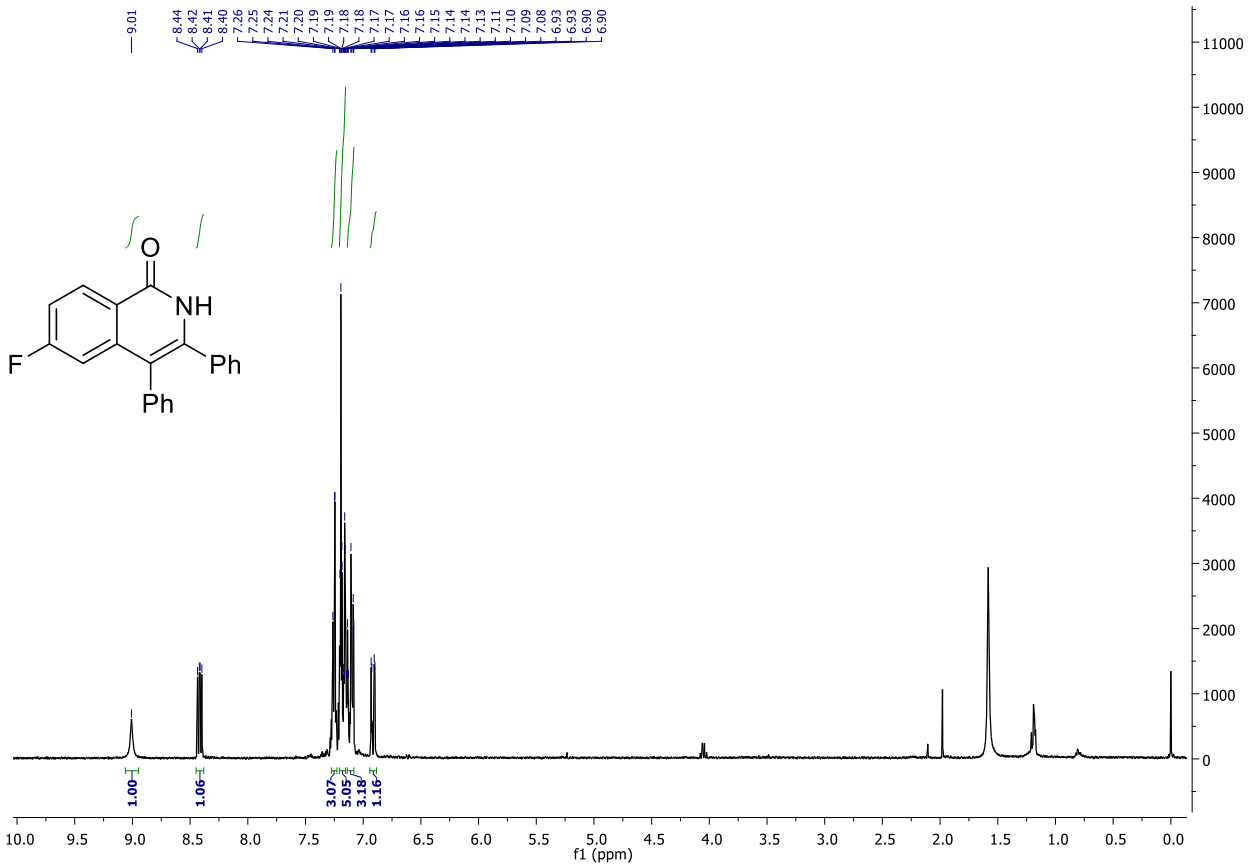


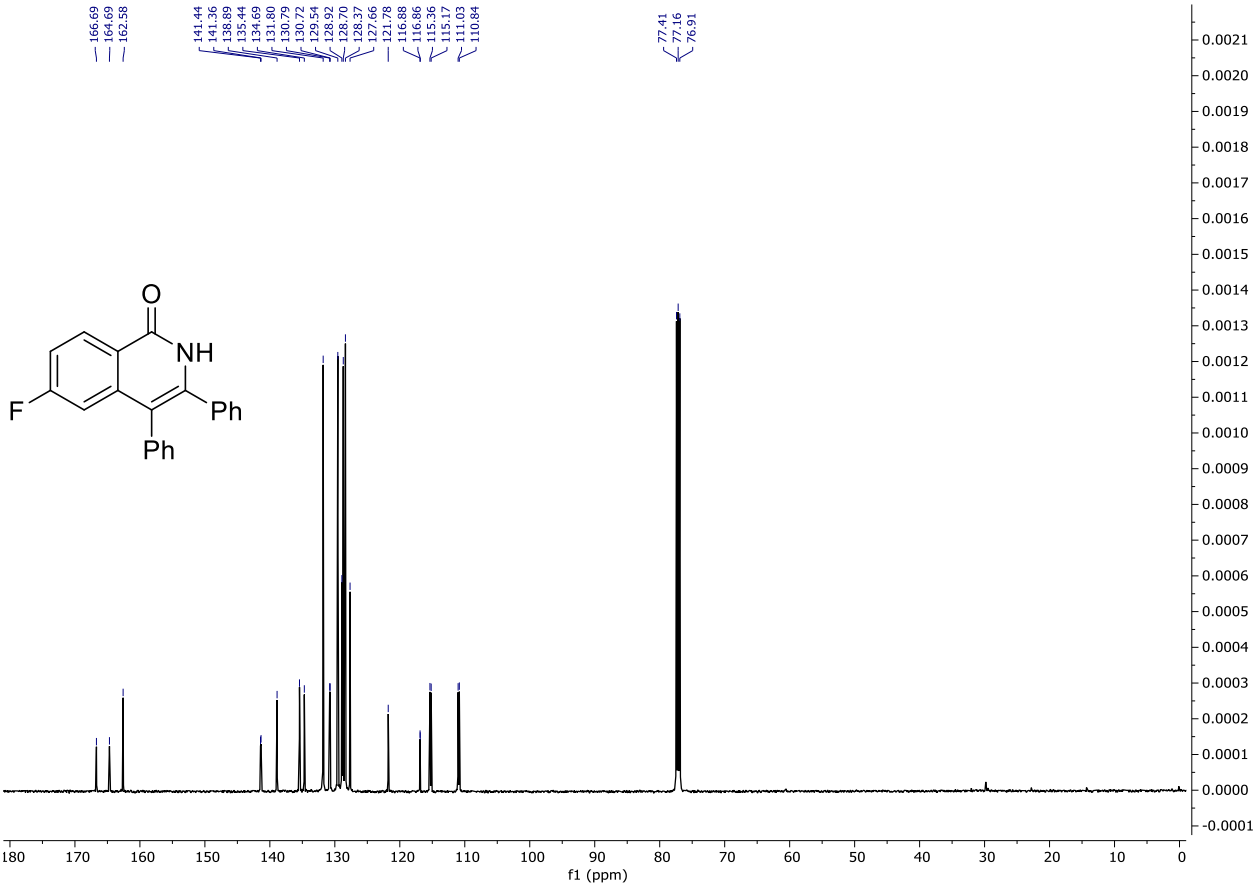
^{1}H (400 MHz) and ^{13}C{1H} (100 MHz) spectra of 3f in $CDCl_3$



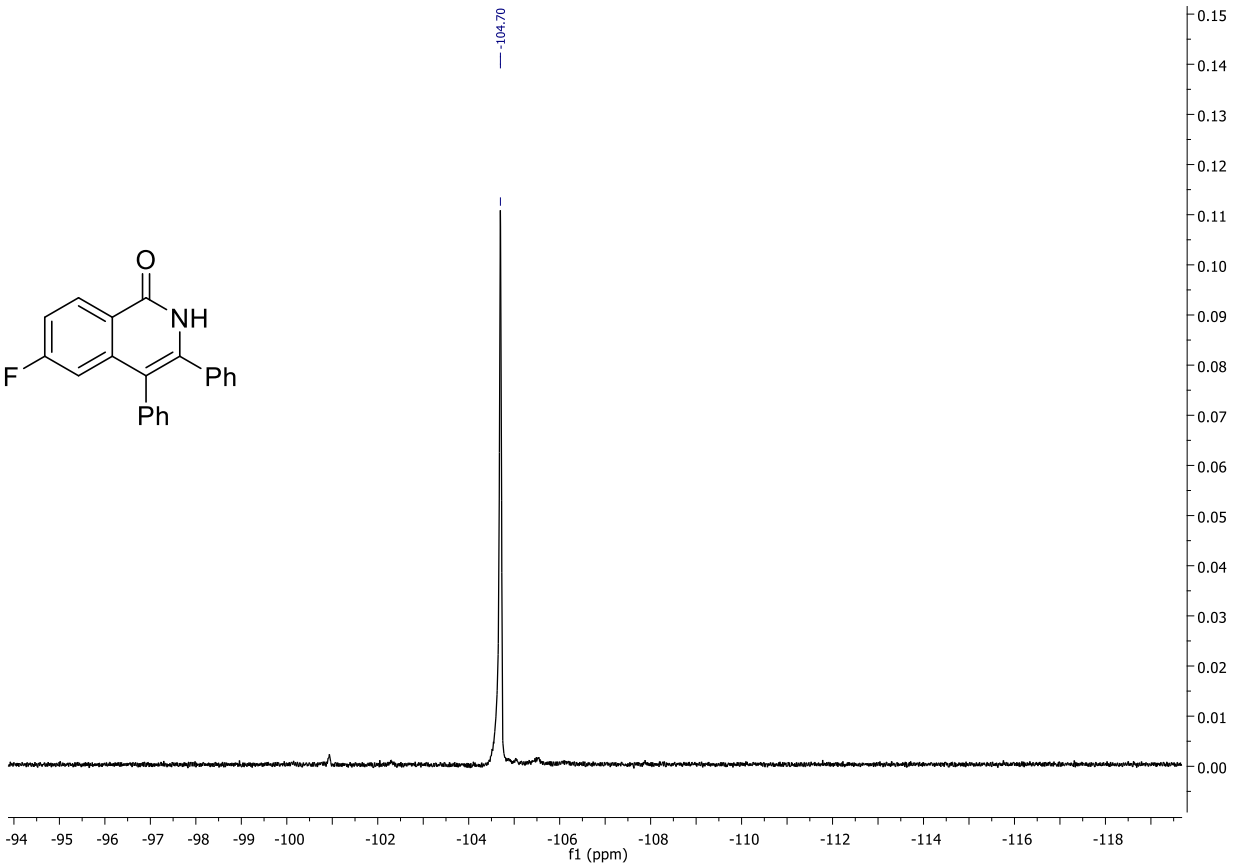


^{1}H (400 MHz) and ^{13}C{1H} (125 MHz) spectra of 3g in $CDCl_3$





$^{19}F\{^{1}H\}$ (471 MHz) NMR spectra of 3g in $CDCl_3$


-104.70
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F
Ph
Ph
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0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
0.05
0.04
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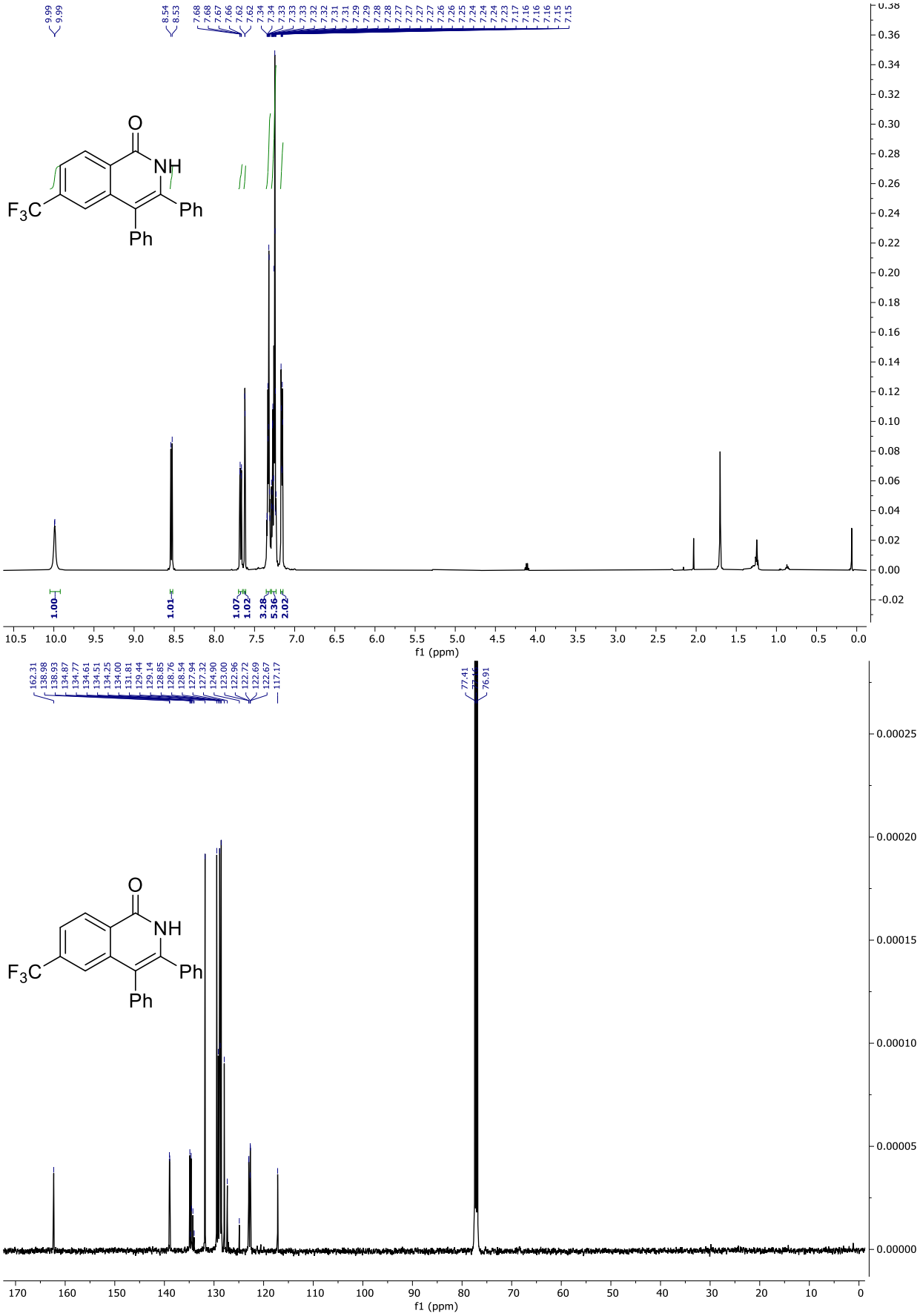
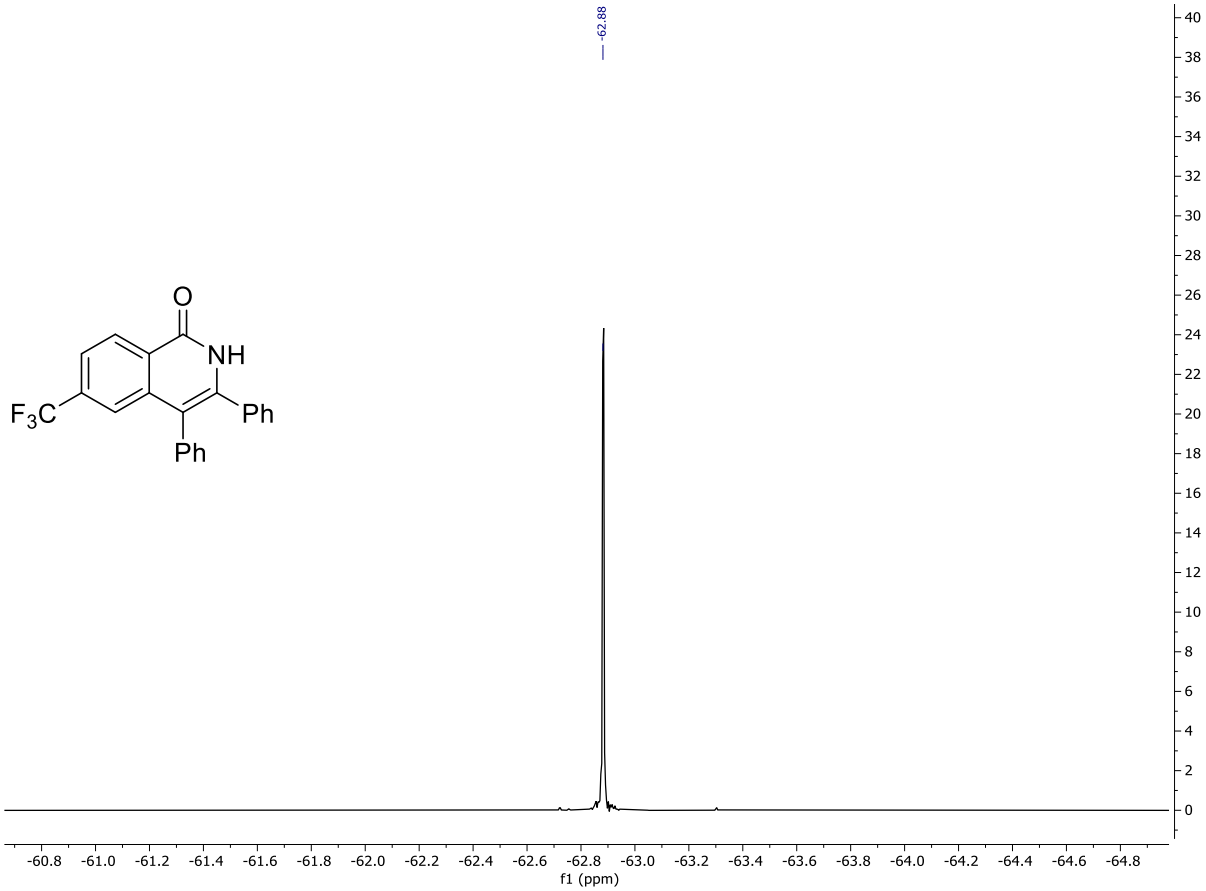
0.02
0.01
0.00
-94
-95
-96
-97
-98
-99
-100
-102
-104
-106
-108
-110
-112
-114
-116
-118
f1 (ppm)

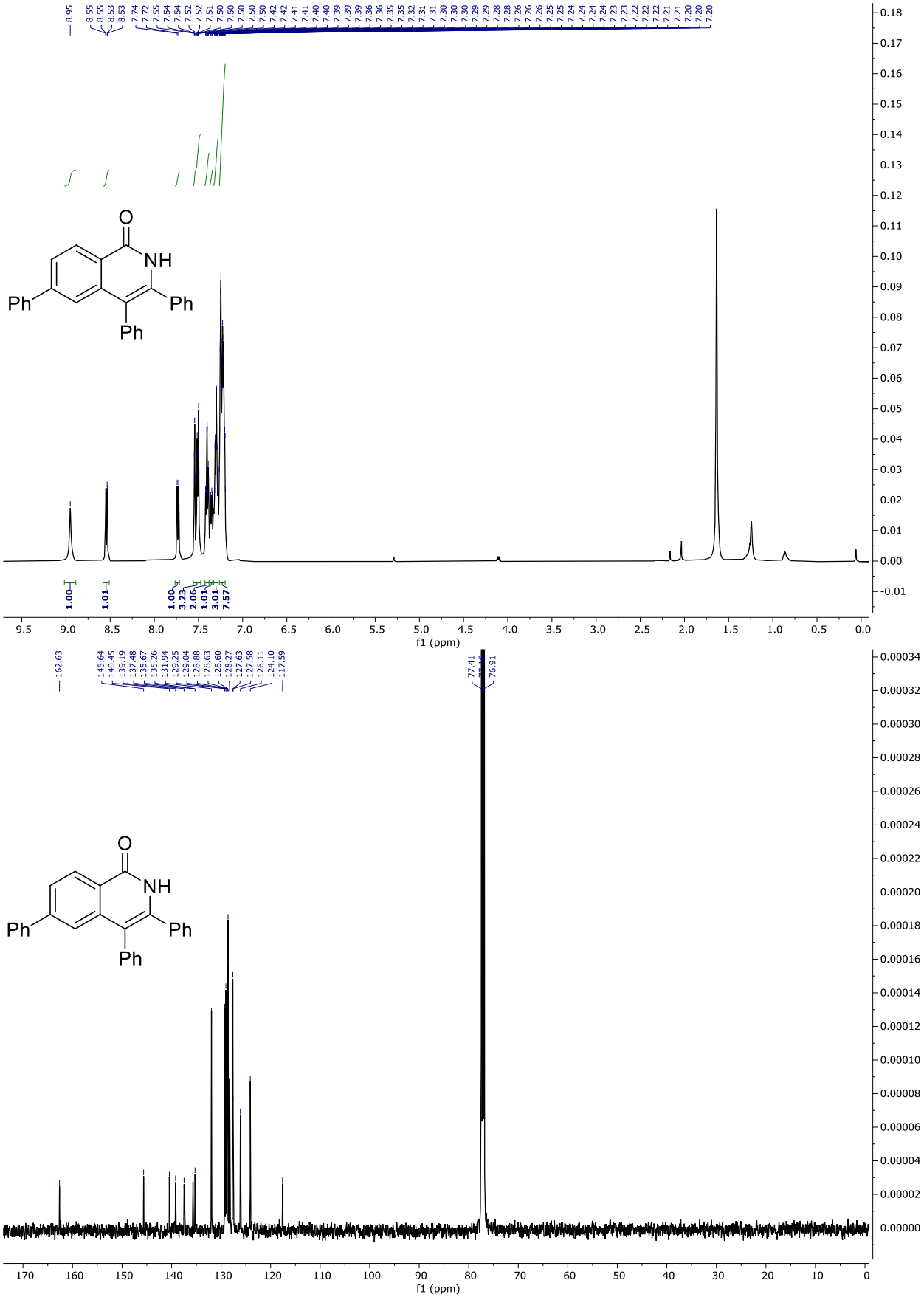
^{1}H (500 MHz) and ^{13}C{1H} (125 MHz) spectra of 3h in $CDCl_3$



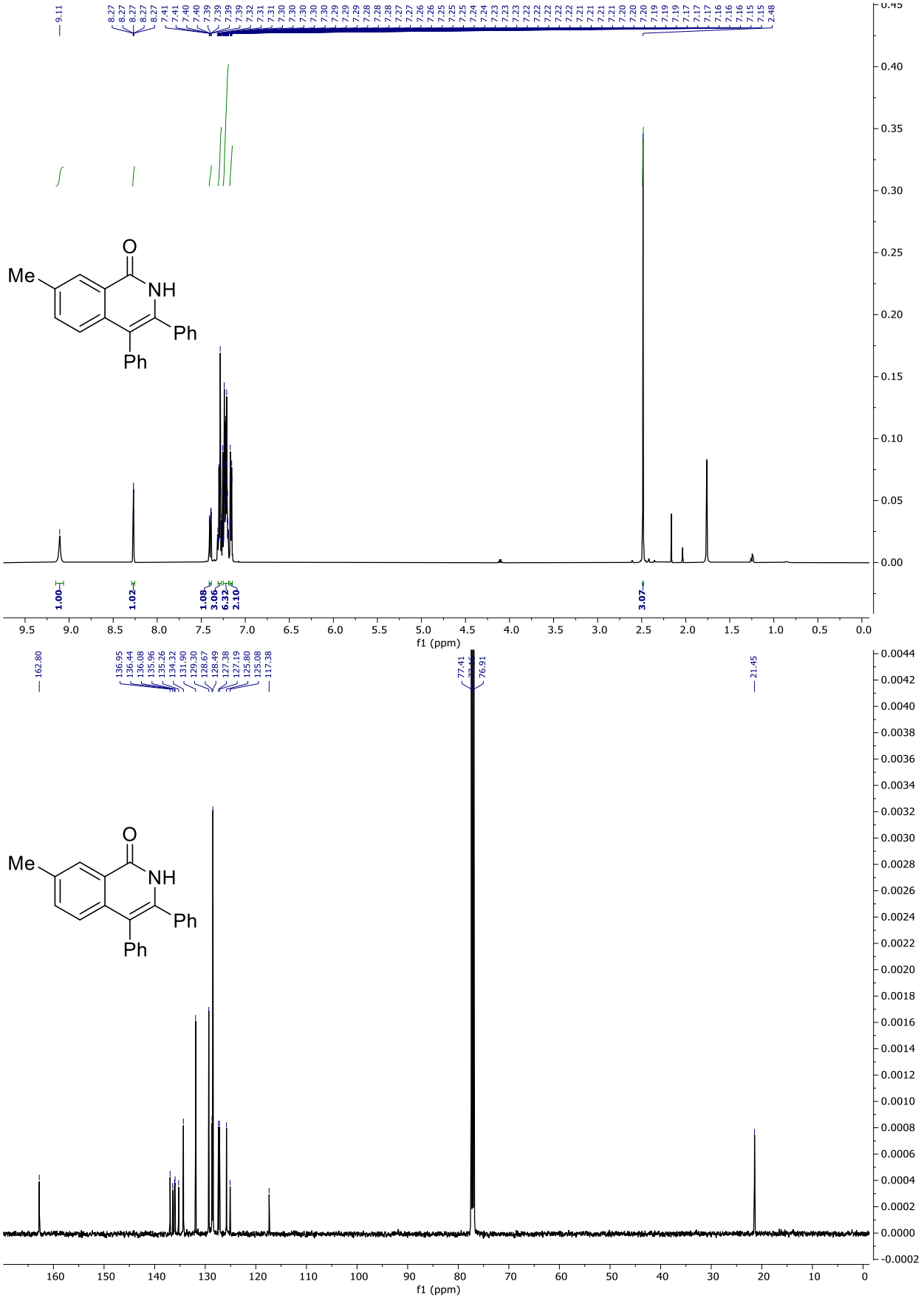
$^{19}F\{^{1}H\}$ (471 MHz) NMR spectra of 3h in $CDCl_3$



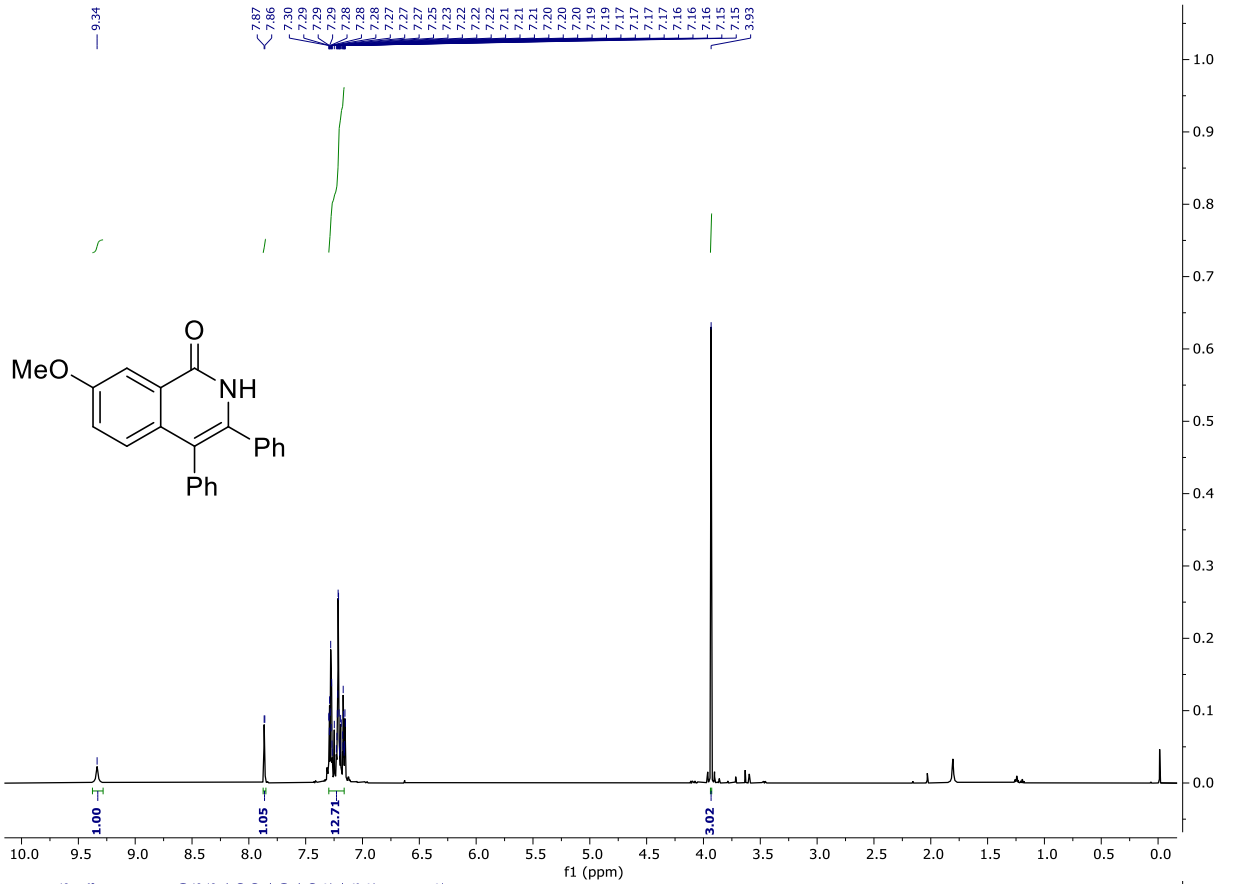
^{1}H (500 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 3i in $CDCl_3$

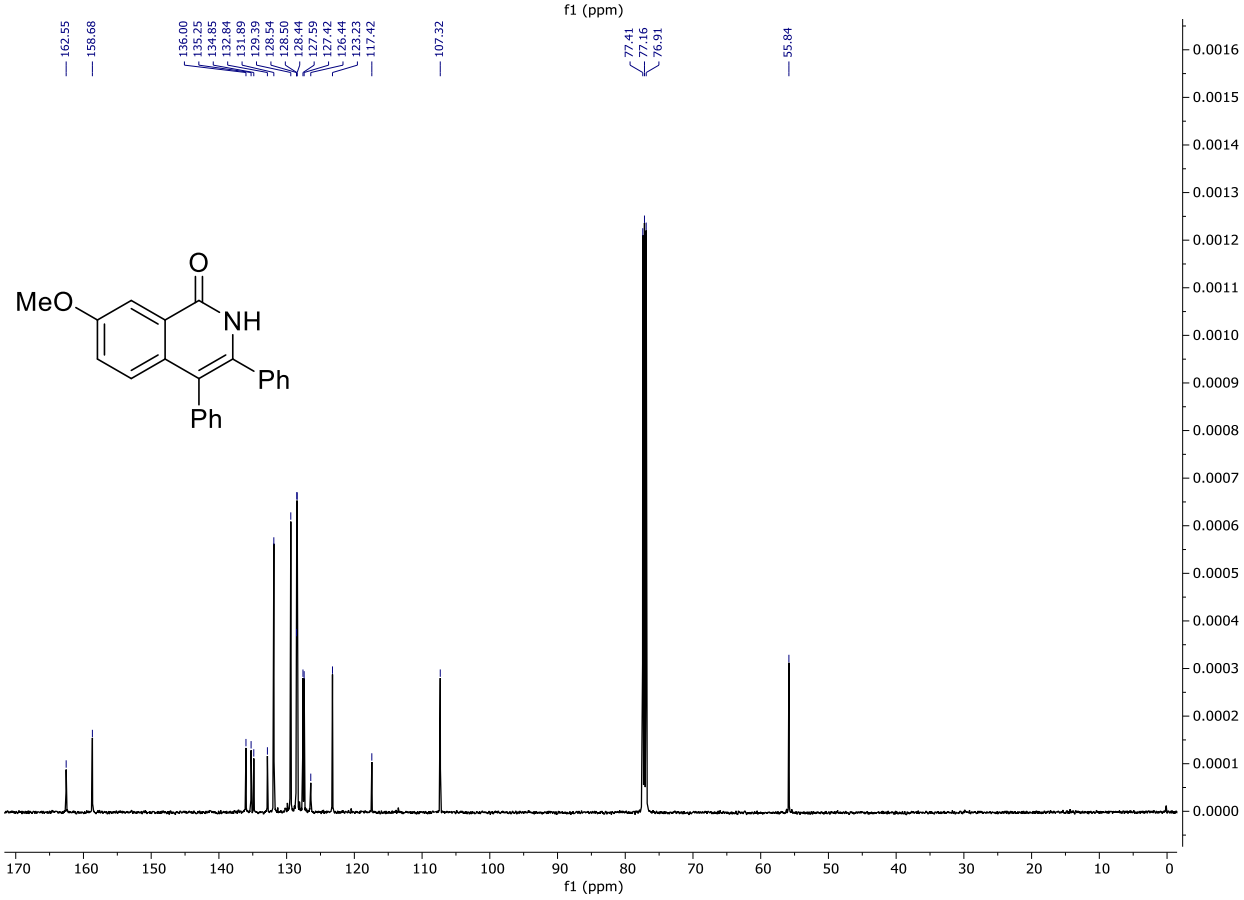


^{1}H (500 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 3j in $CDCl_3$

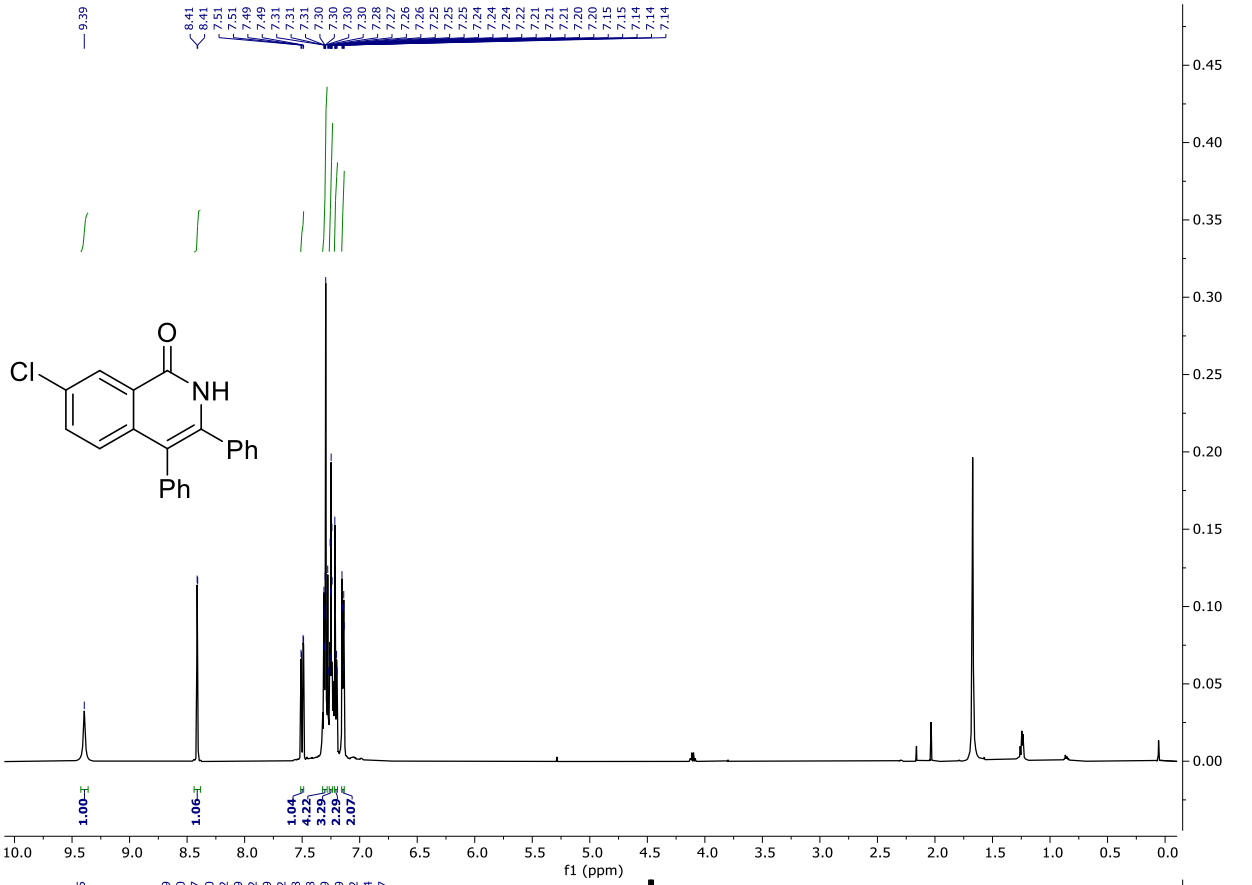


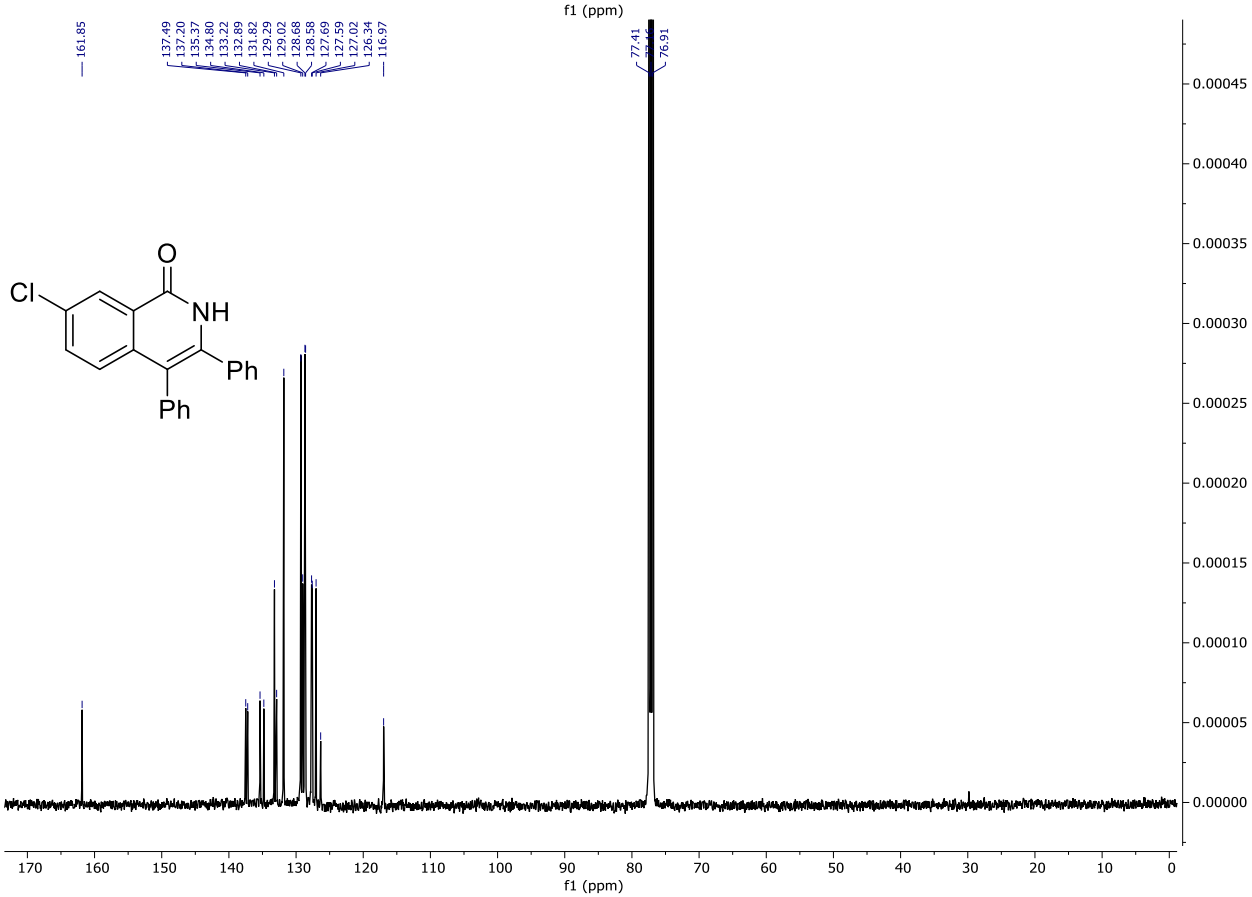
^{1}H (500 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 3k in $CDCl_3$



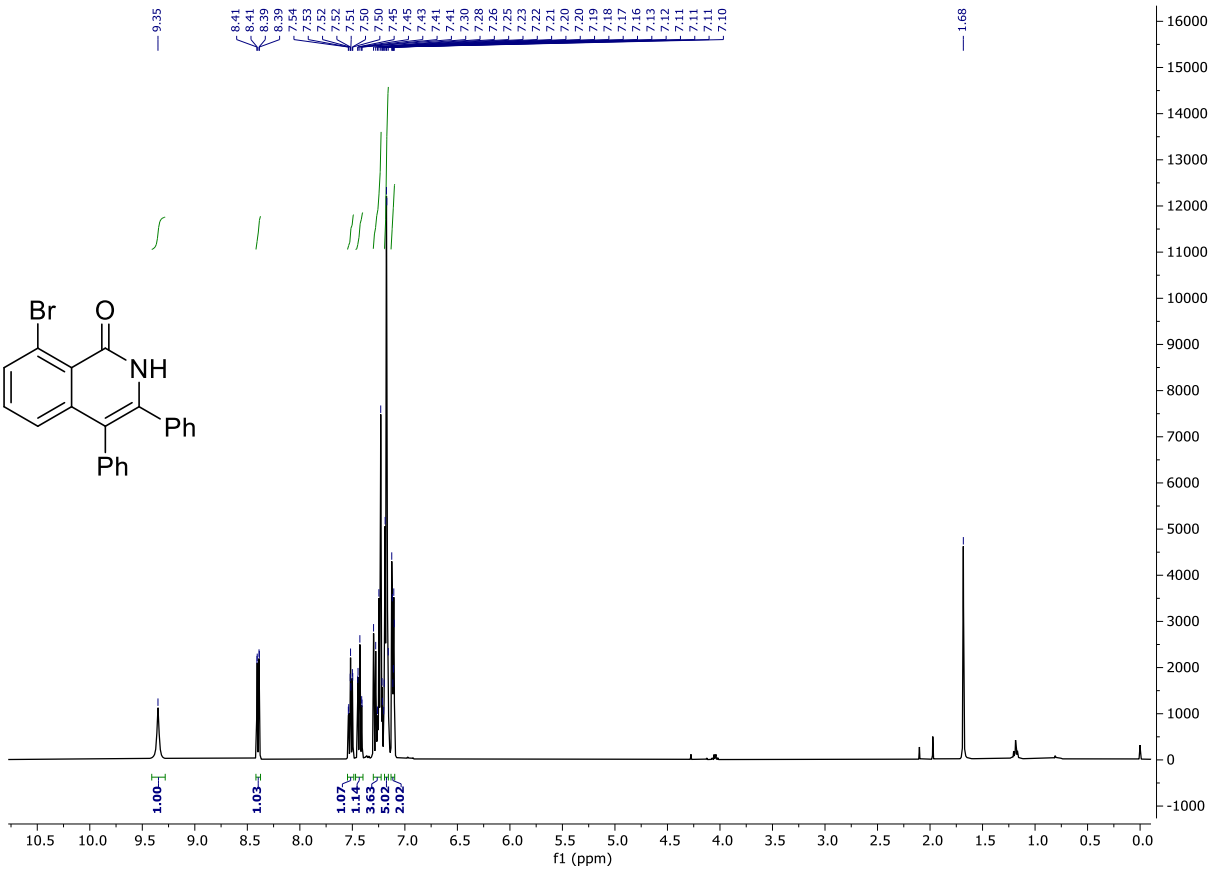


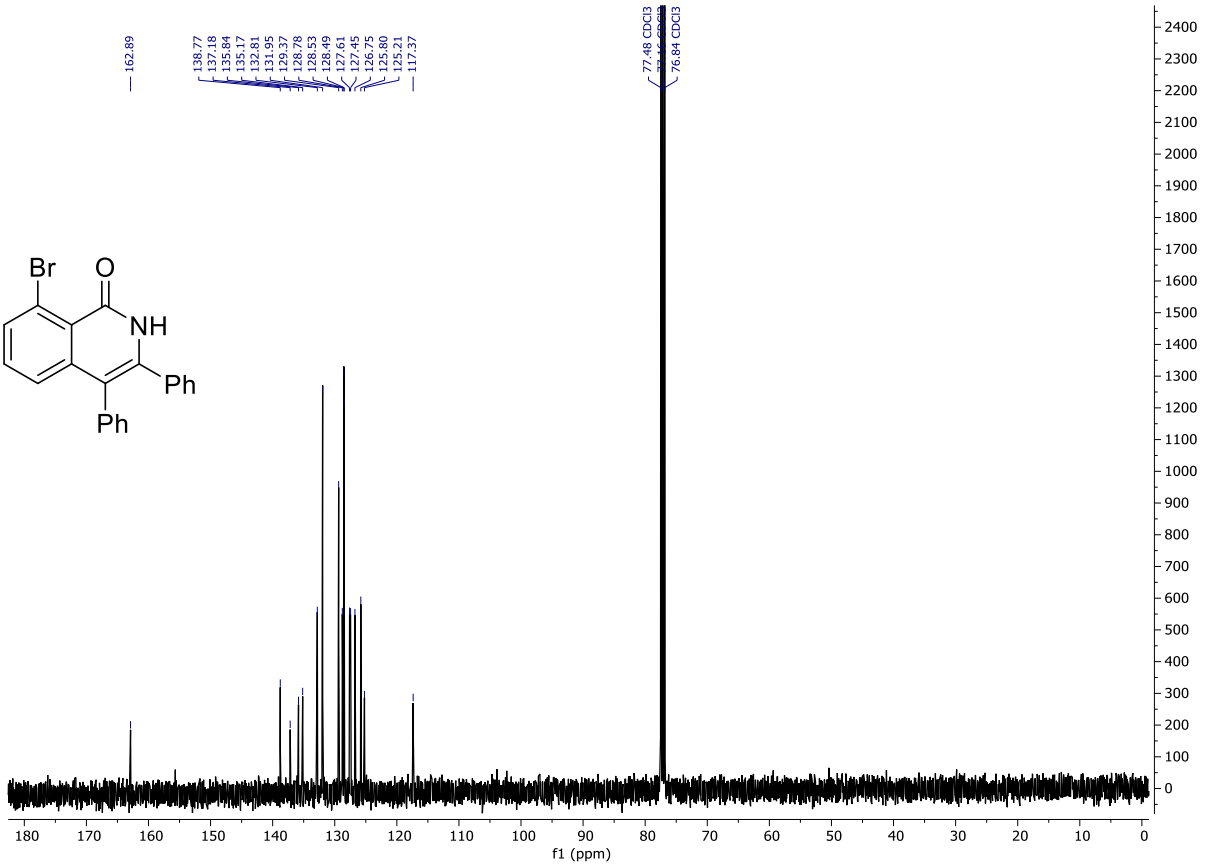
^{1}H (500 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 3l in $CDCl_3$



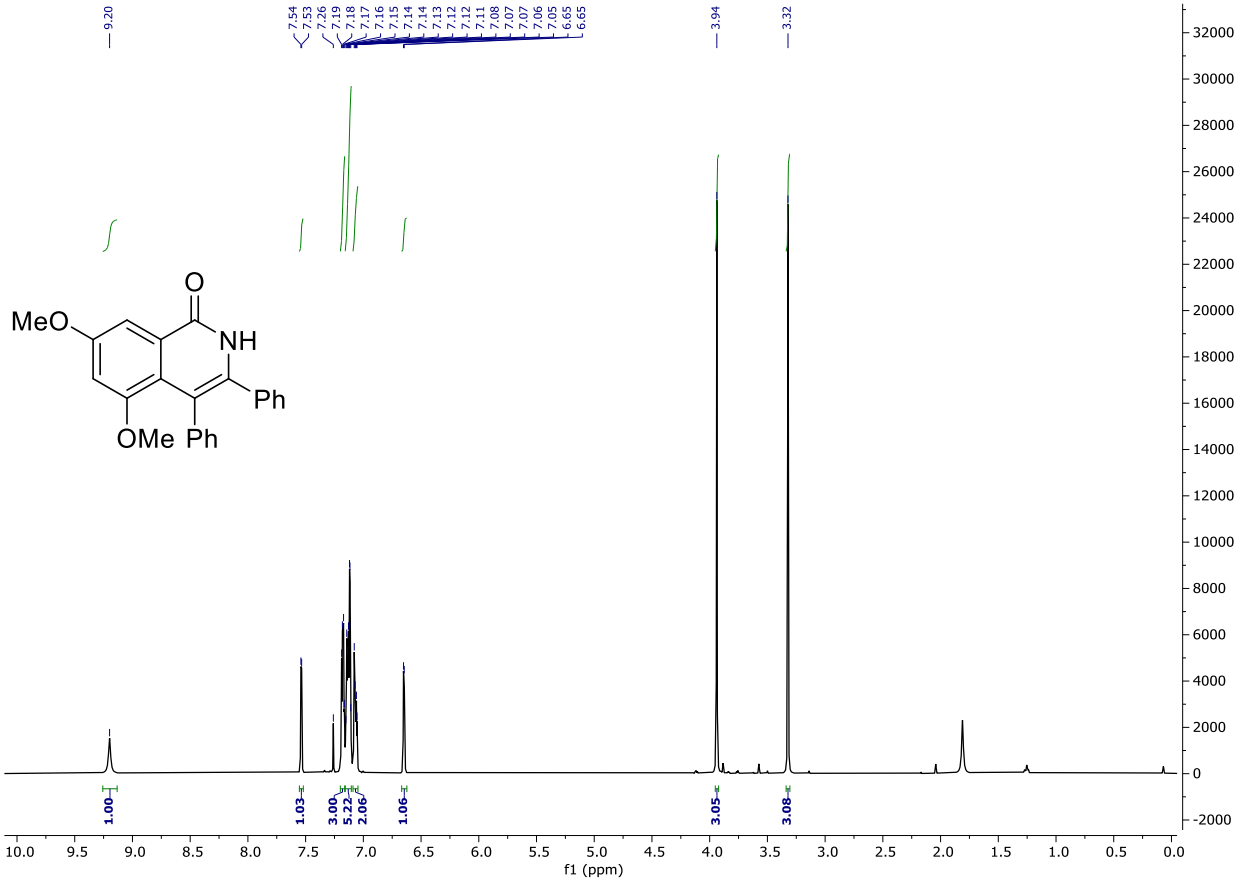


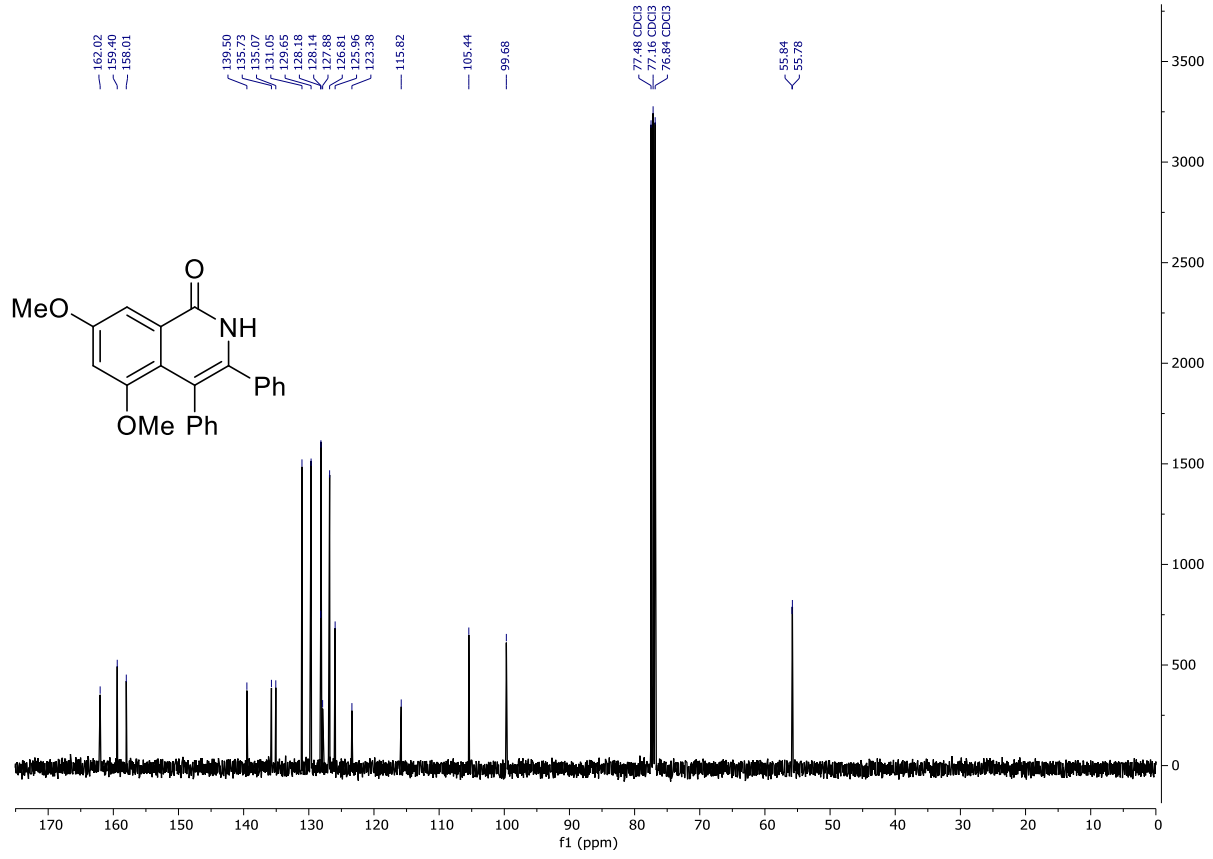
^{1}H (400 MHz) and ^{13}C{1H} (100 MHz) spectra of 3m in $CDCl_3$



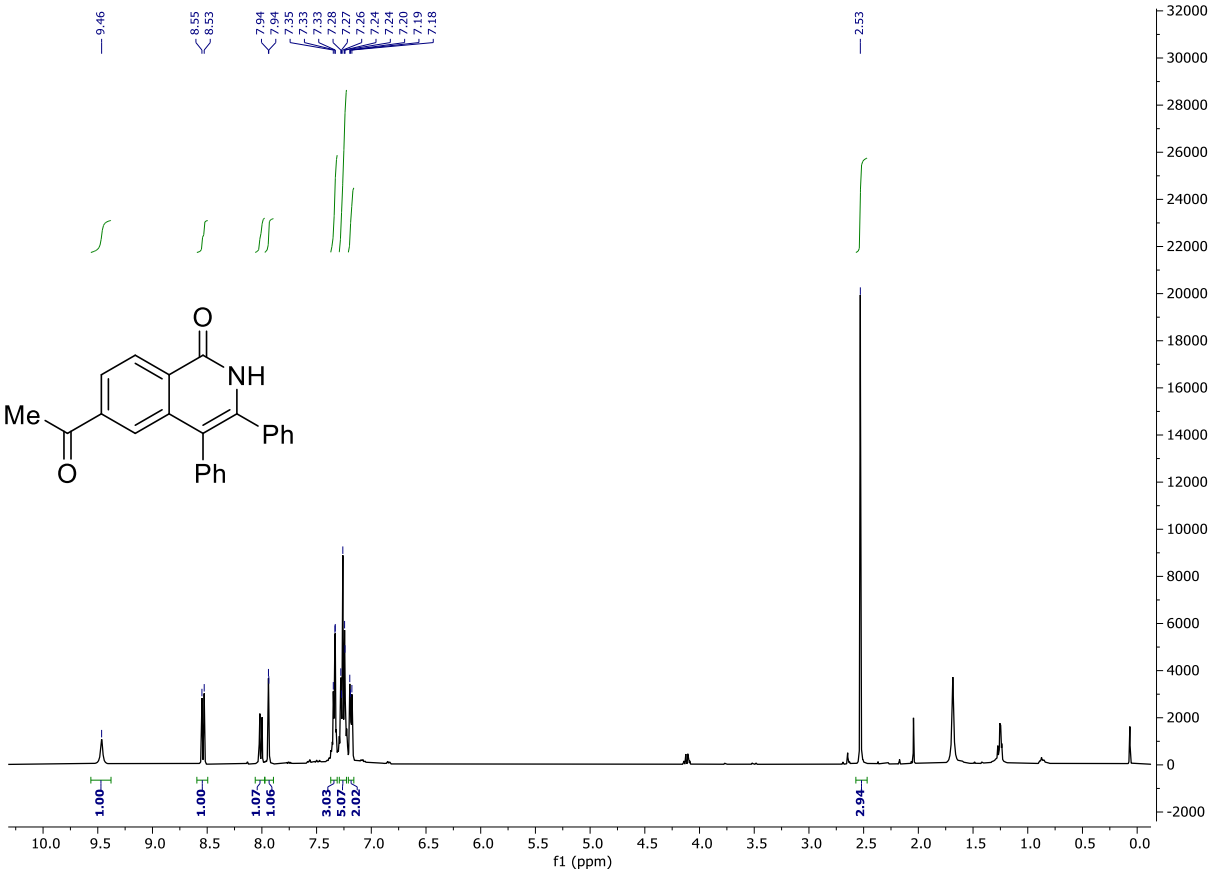


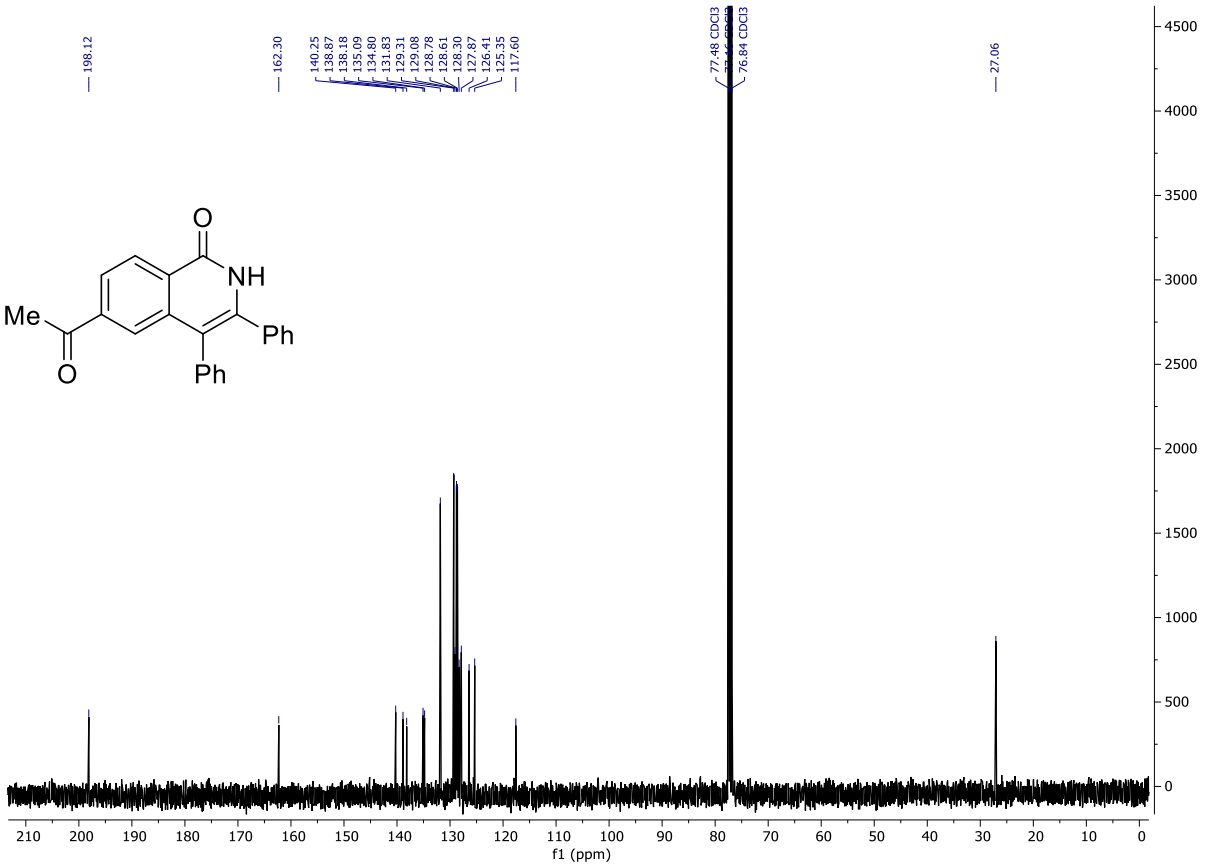
^{1}H (400 MHz) and $^{13}C\{1H\}$ (100 MHz) spectra of 3n in $CDCl_3$



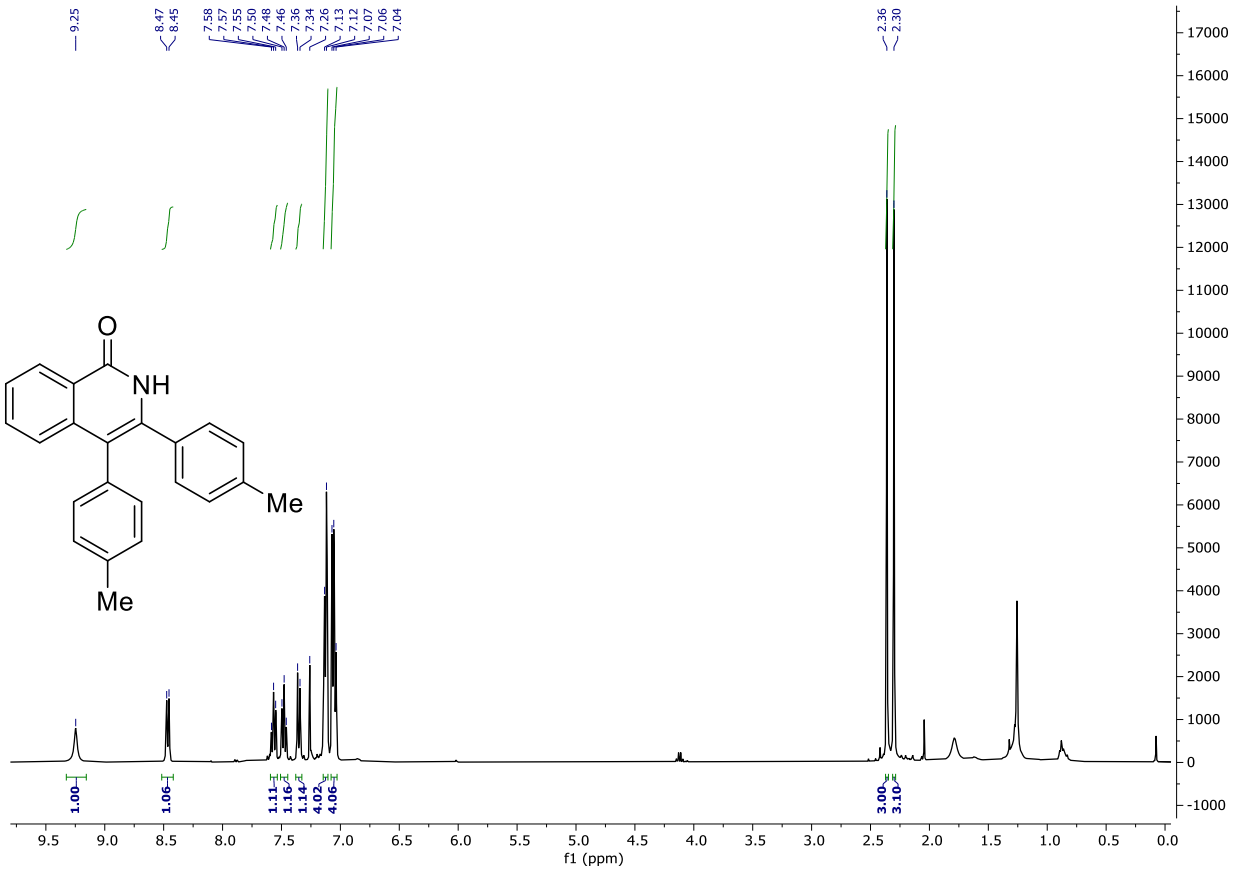


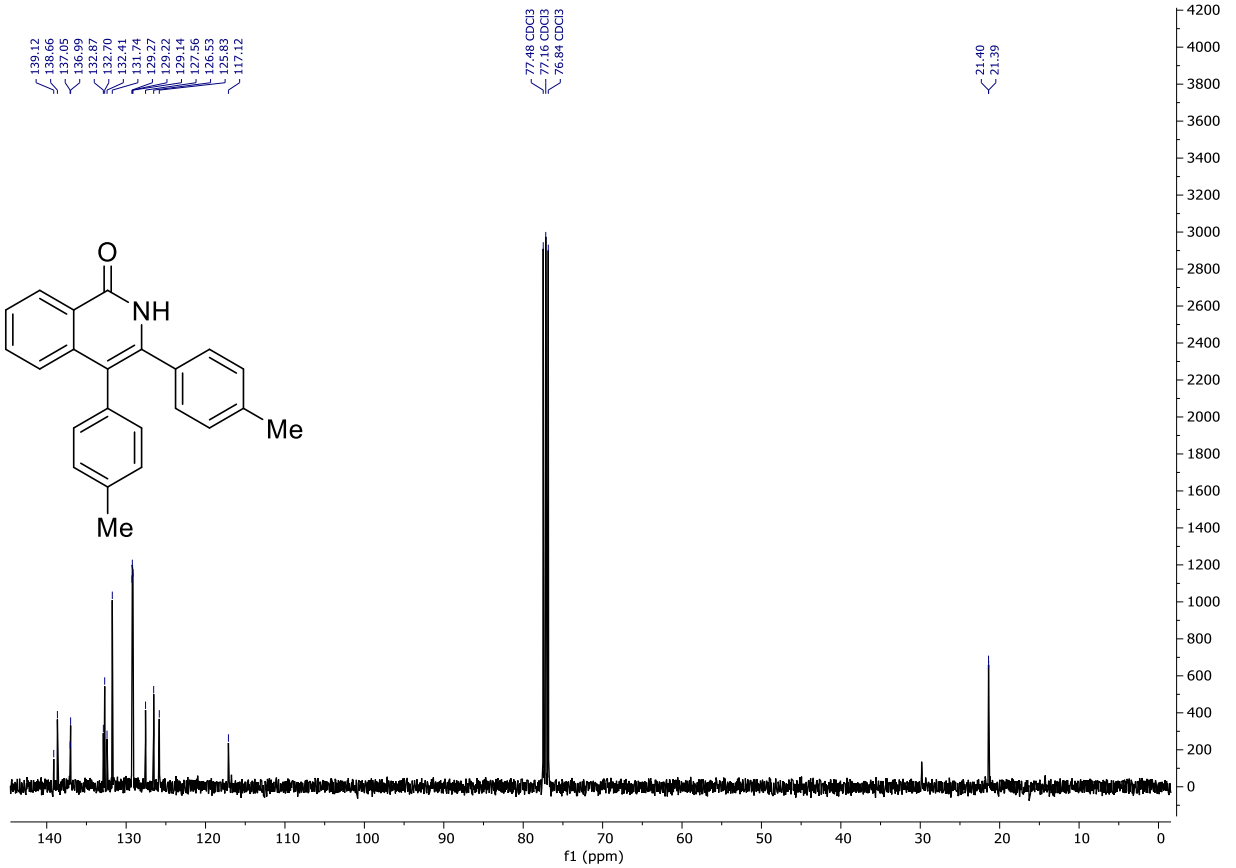
^{1}H (400 MHz) and ^{13}C{1H} (100 MHz) spectra of 3o in $CDCl_3$



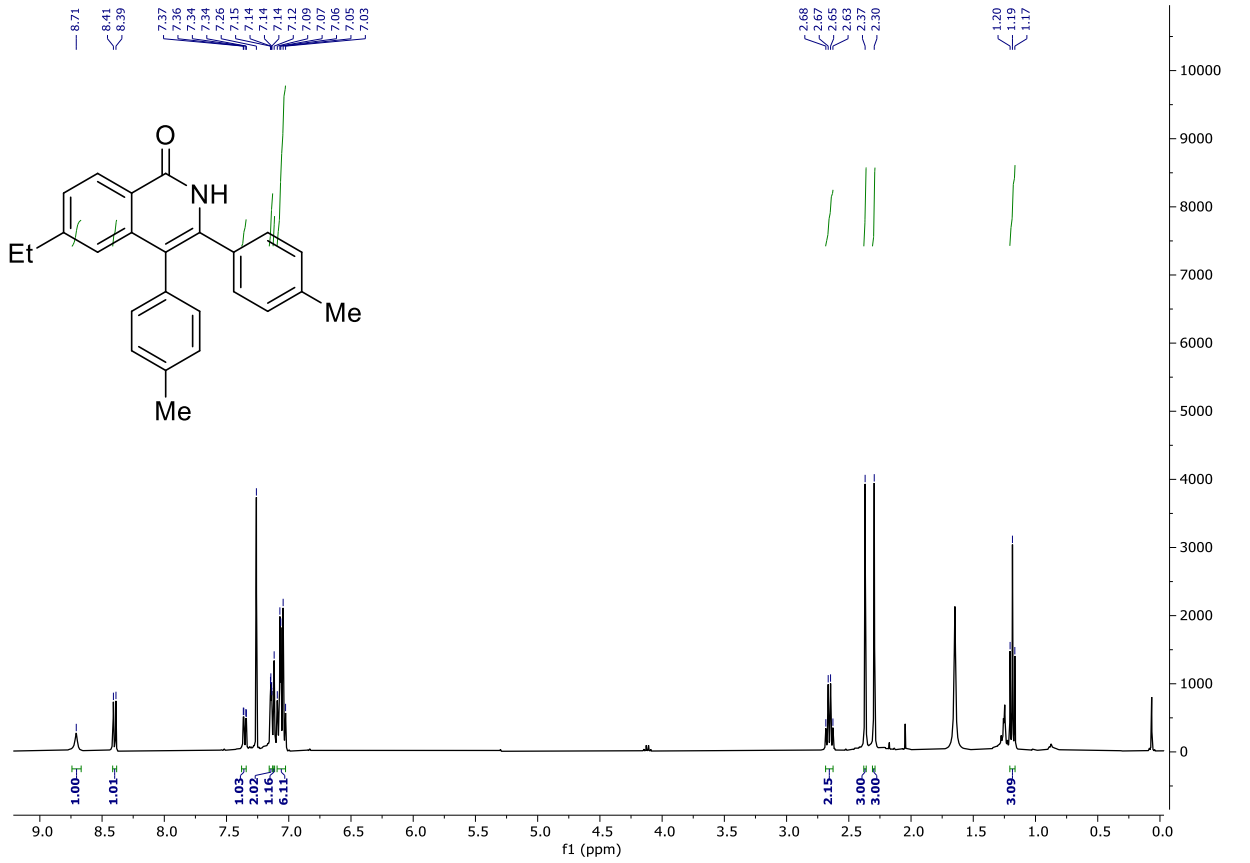


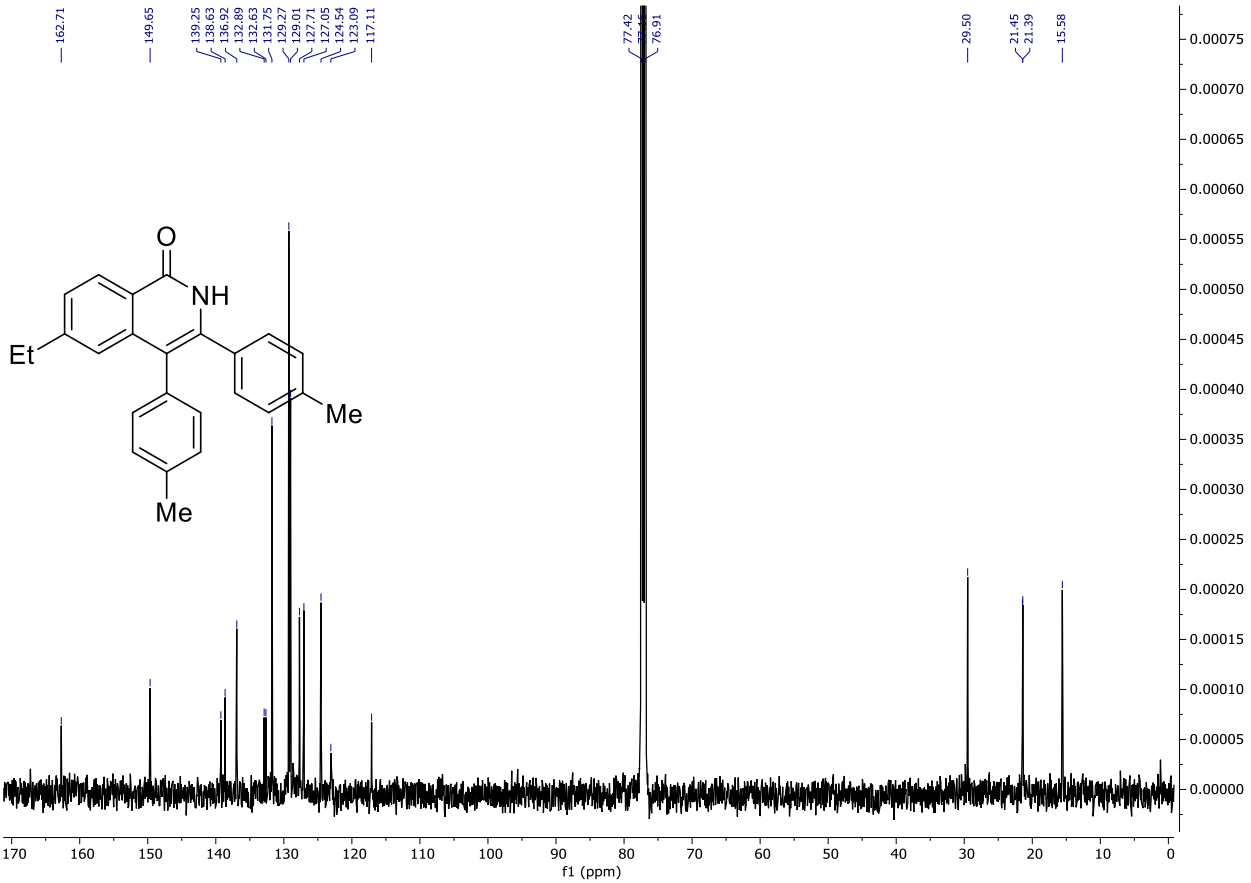
^{1}H (400 MHz) and ^{13}C{1H} (100 MHz) spectra of 4b in $CDCl_3$



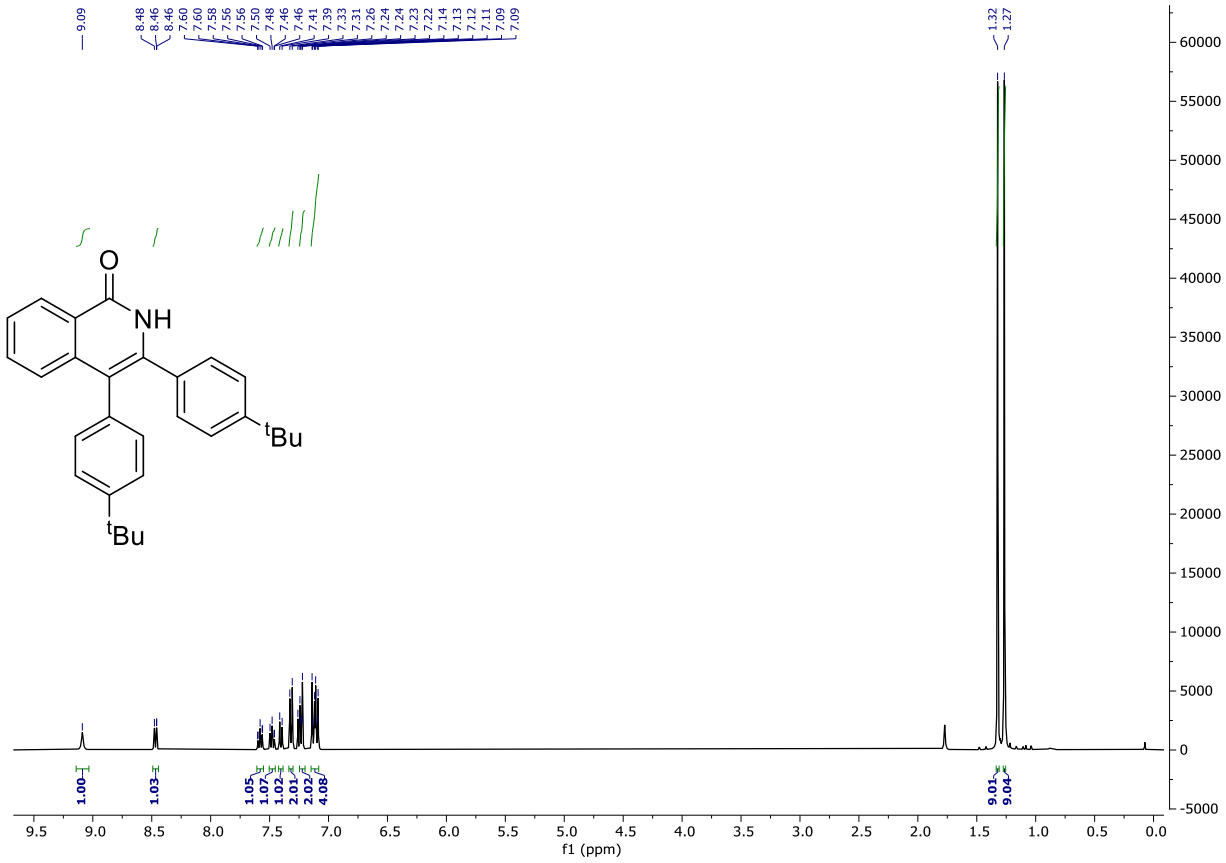


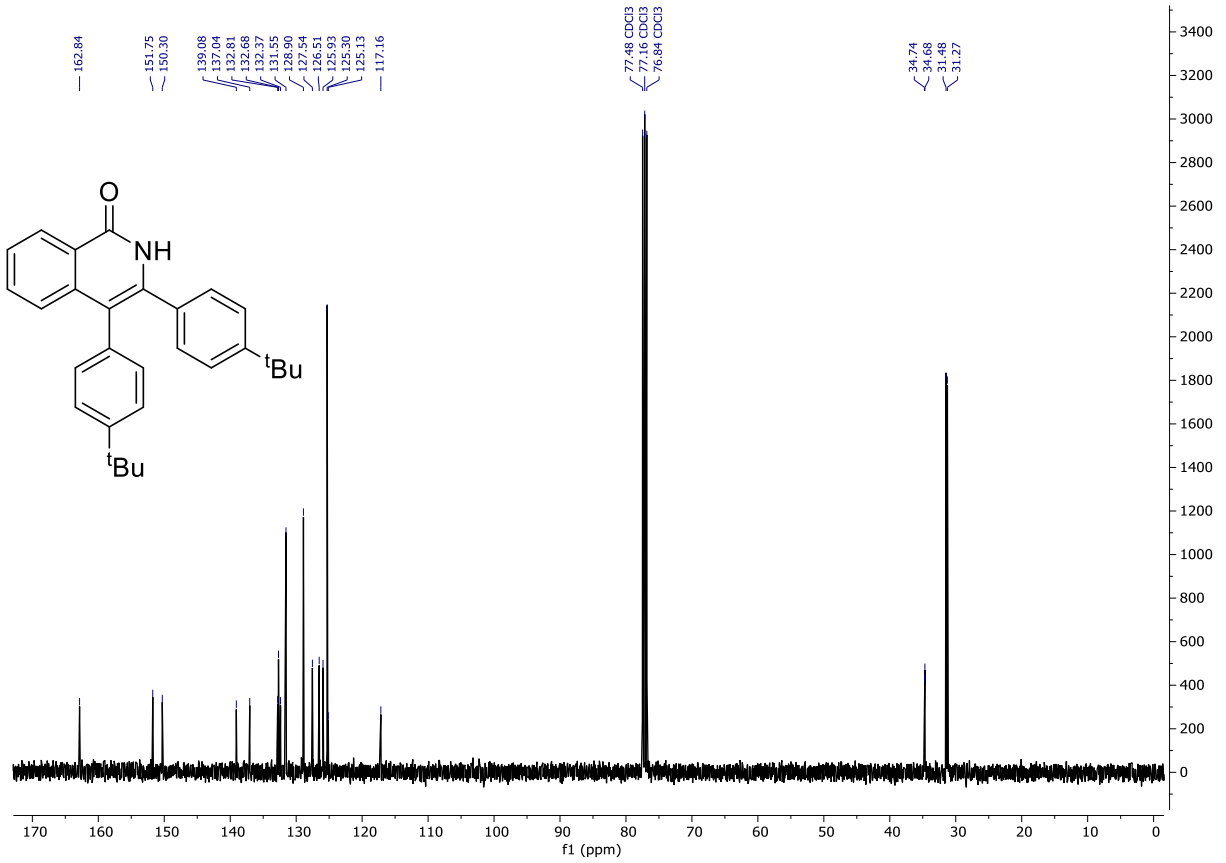
^{1}H (400 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 4c in $CDCl_3$



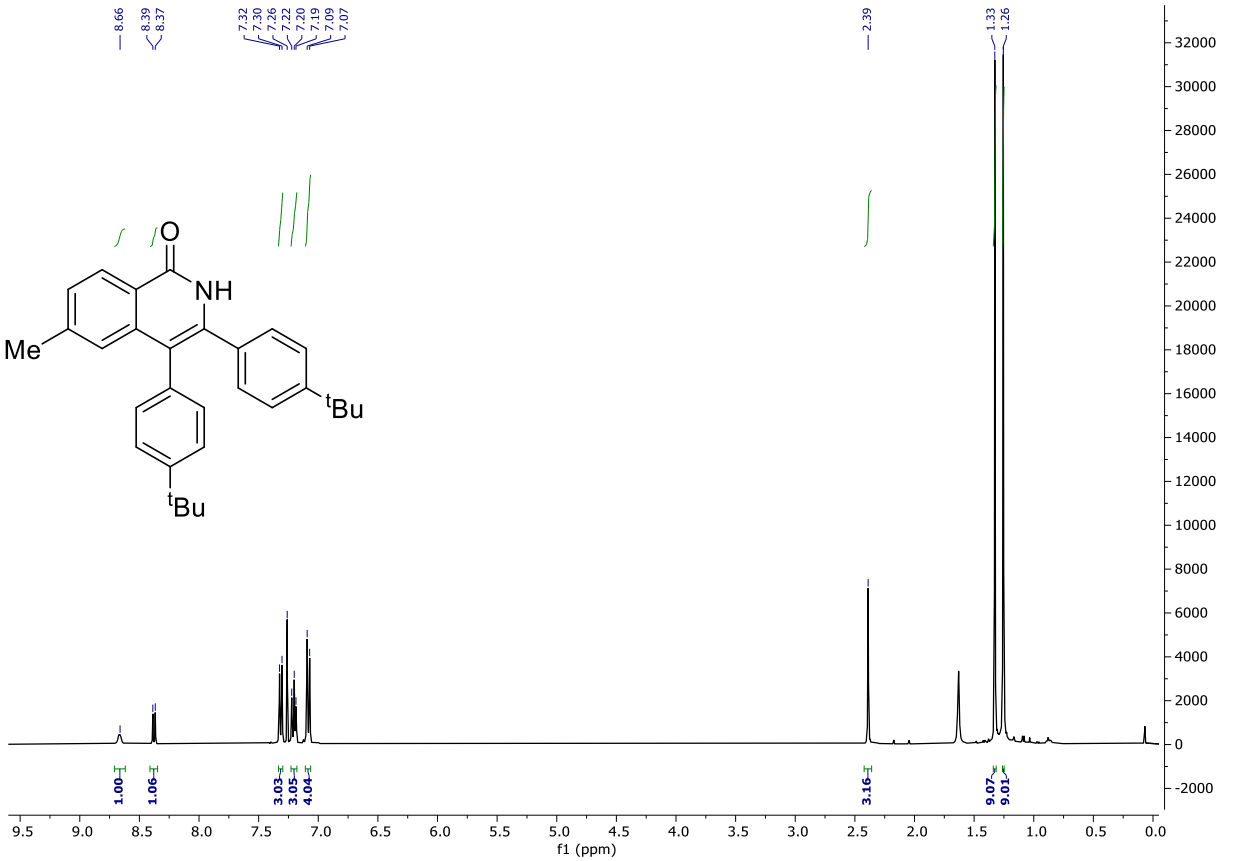


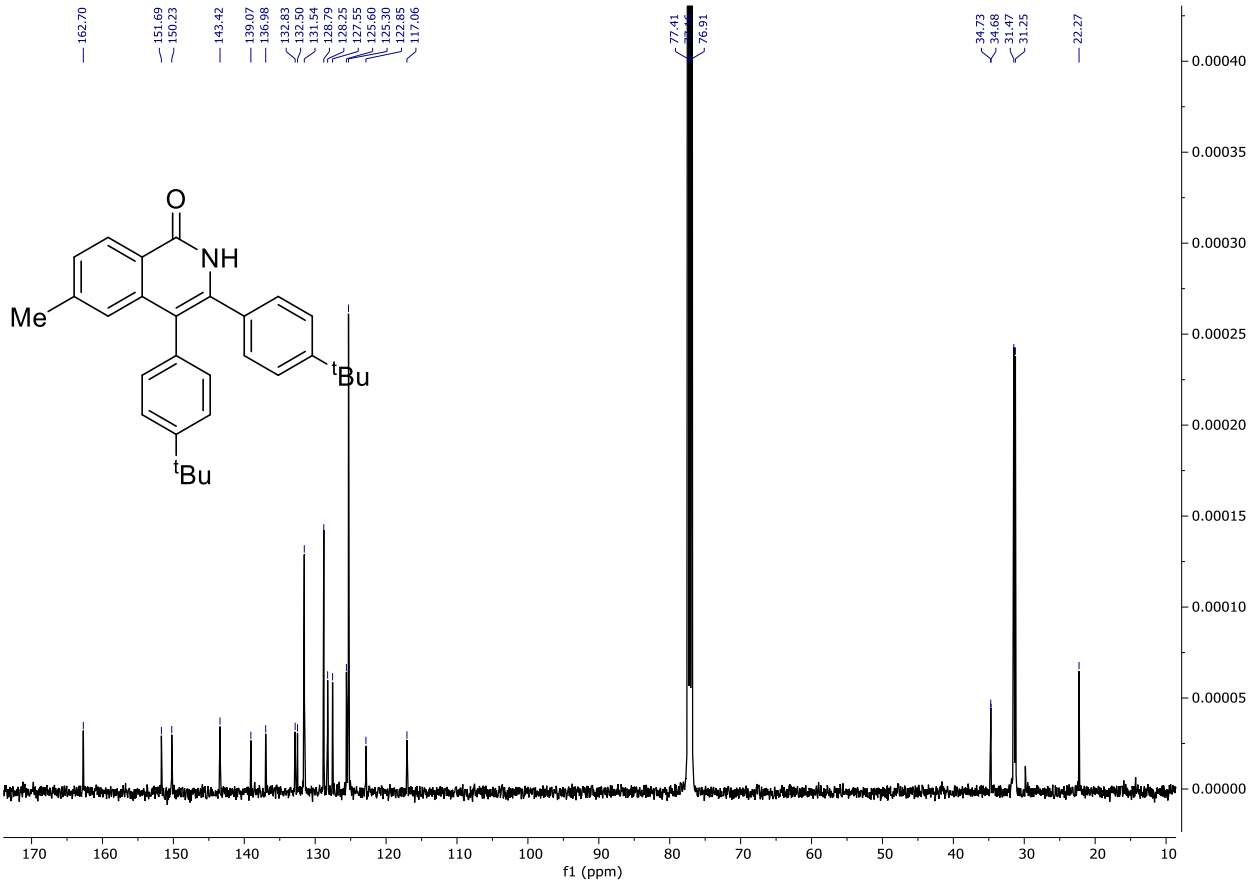
^{1}H (400 MHz) and $^{13}C\{1H\}$ (100 MHz) spectra of 4d in $CDCl_3$



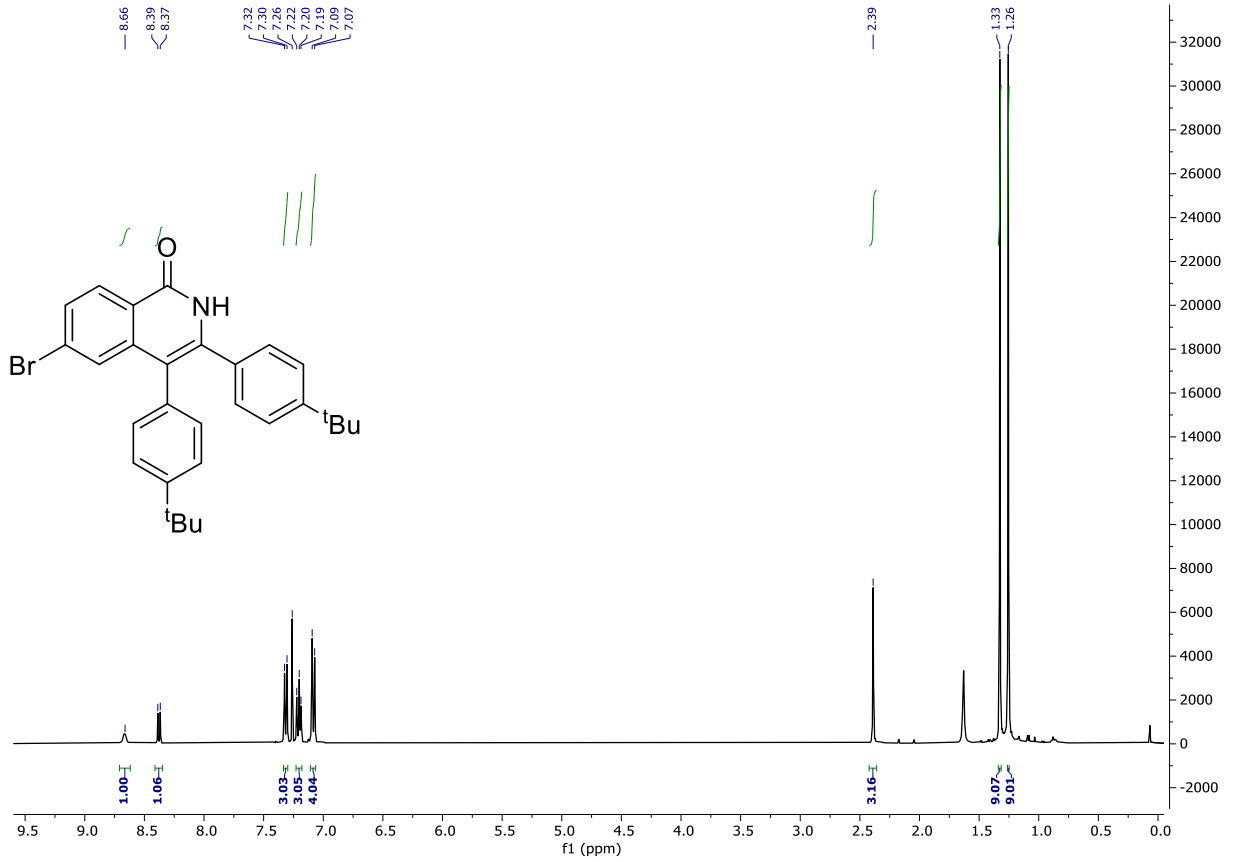


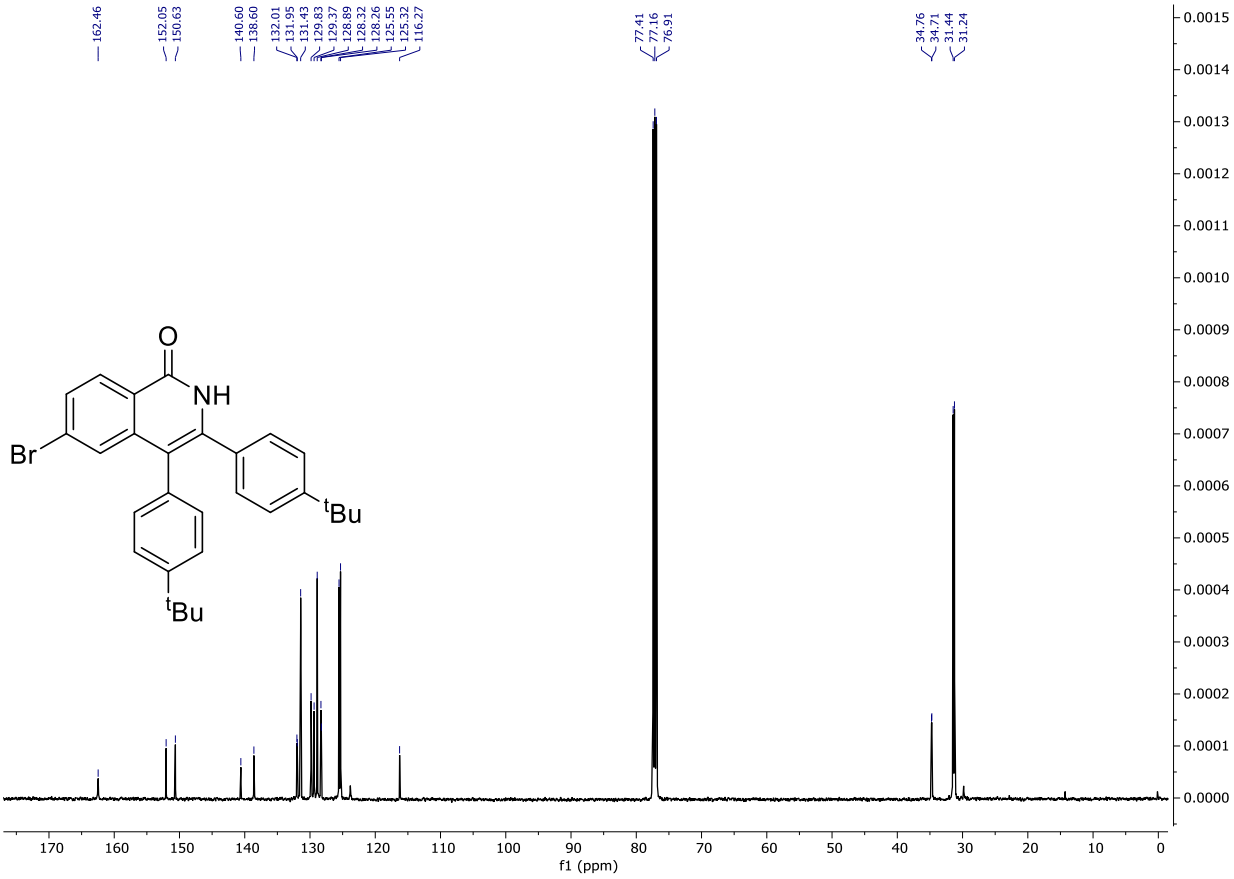
^{1}H (400 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 4e in $CDCl_3$



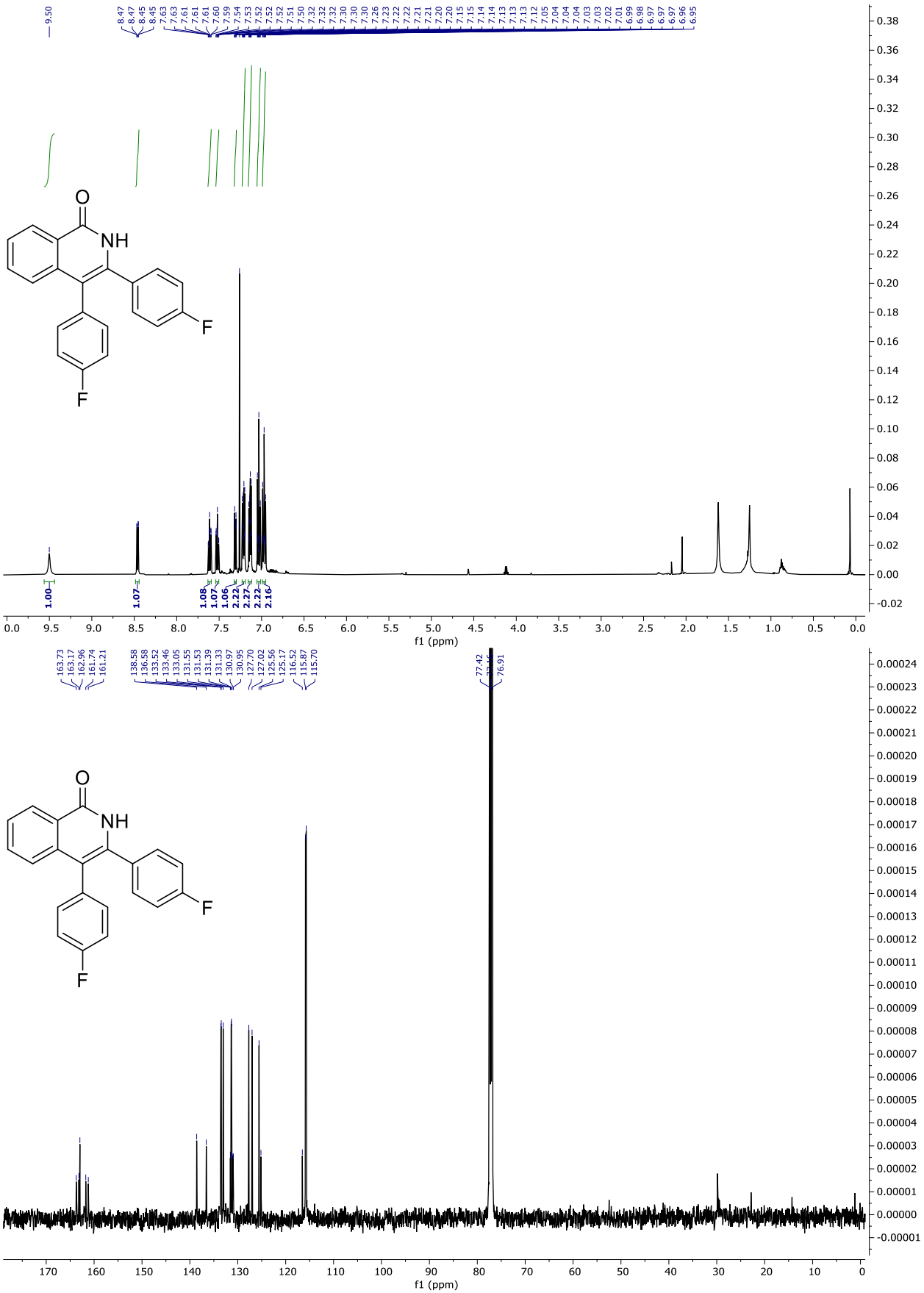


^{1}H (400 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 4f in $CDCl_3$

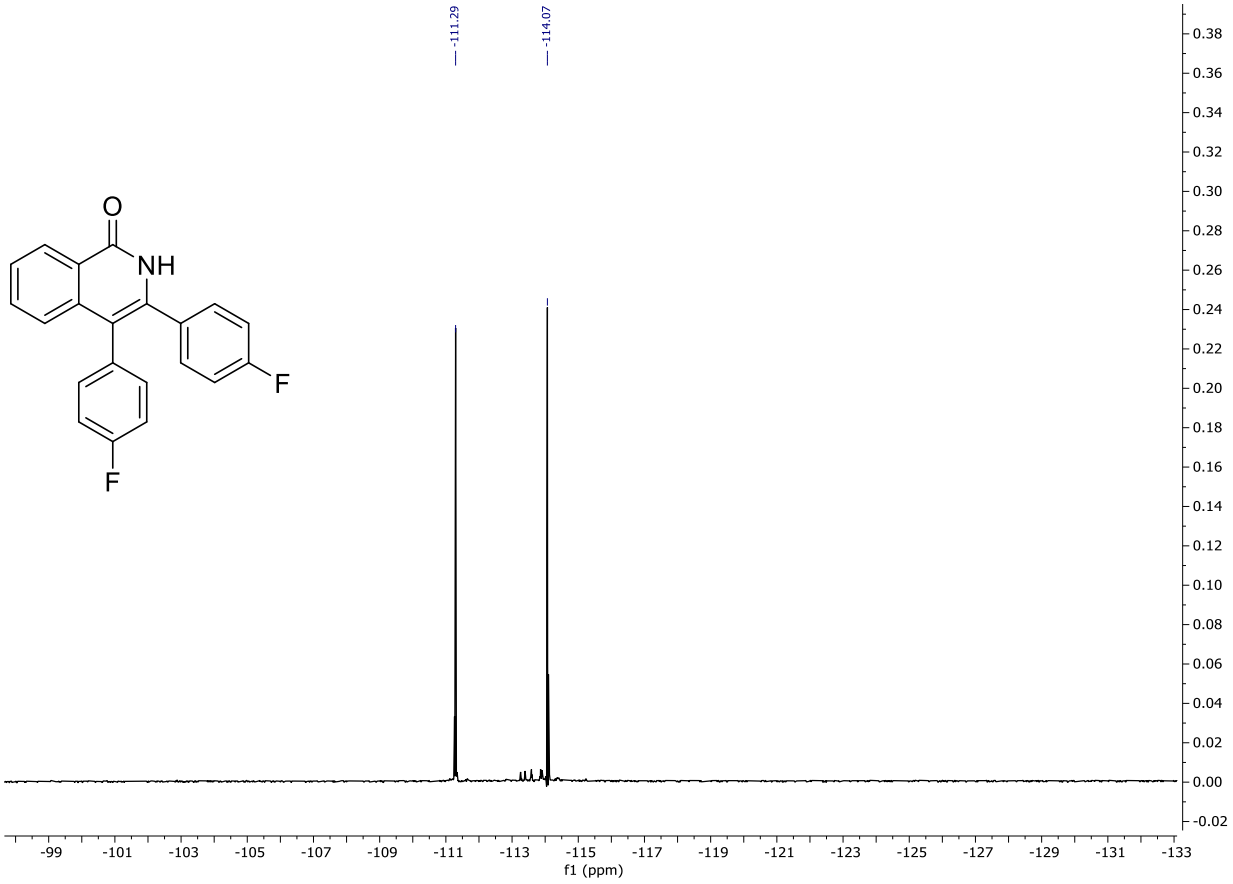




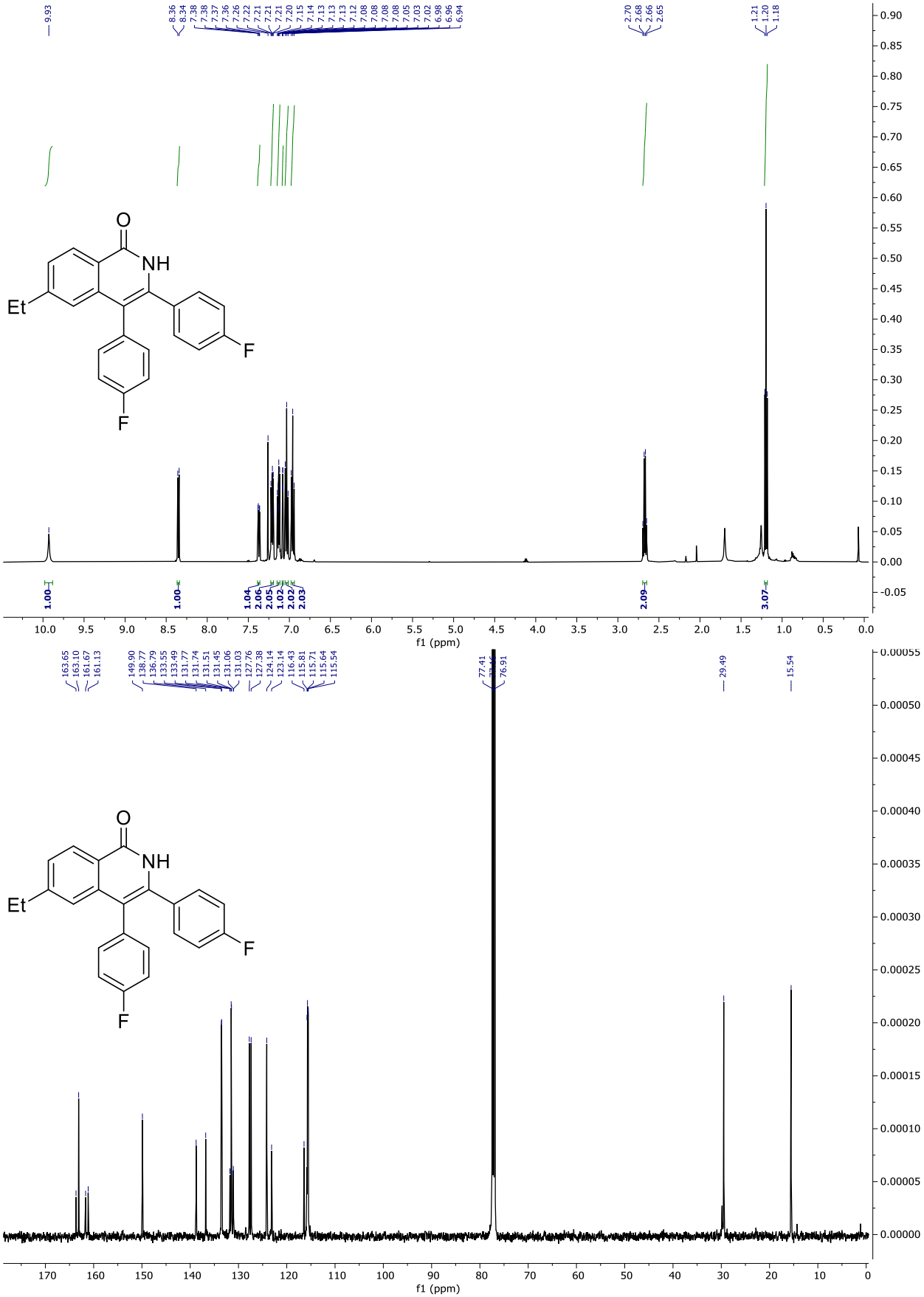
^{1}H (500 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 4g in $CDCl_3$



$^{19}F\{^{1}H\}$ (471 MHz) NMR spectra of 4g in $CDCl_3$

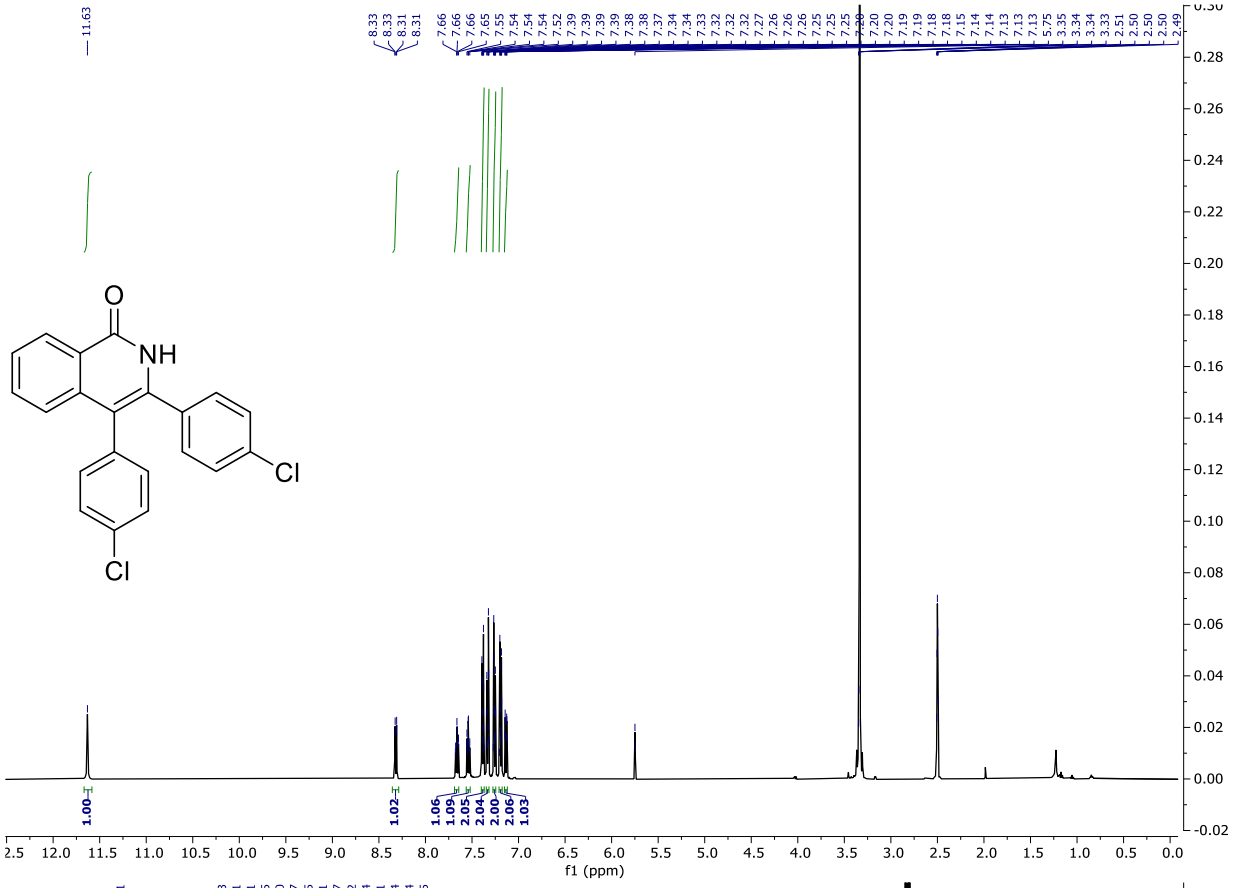


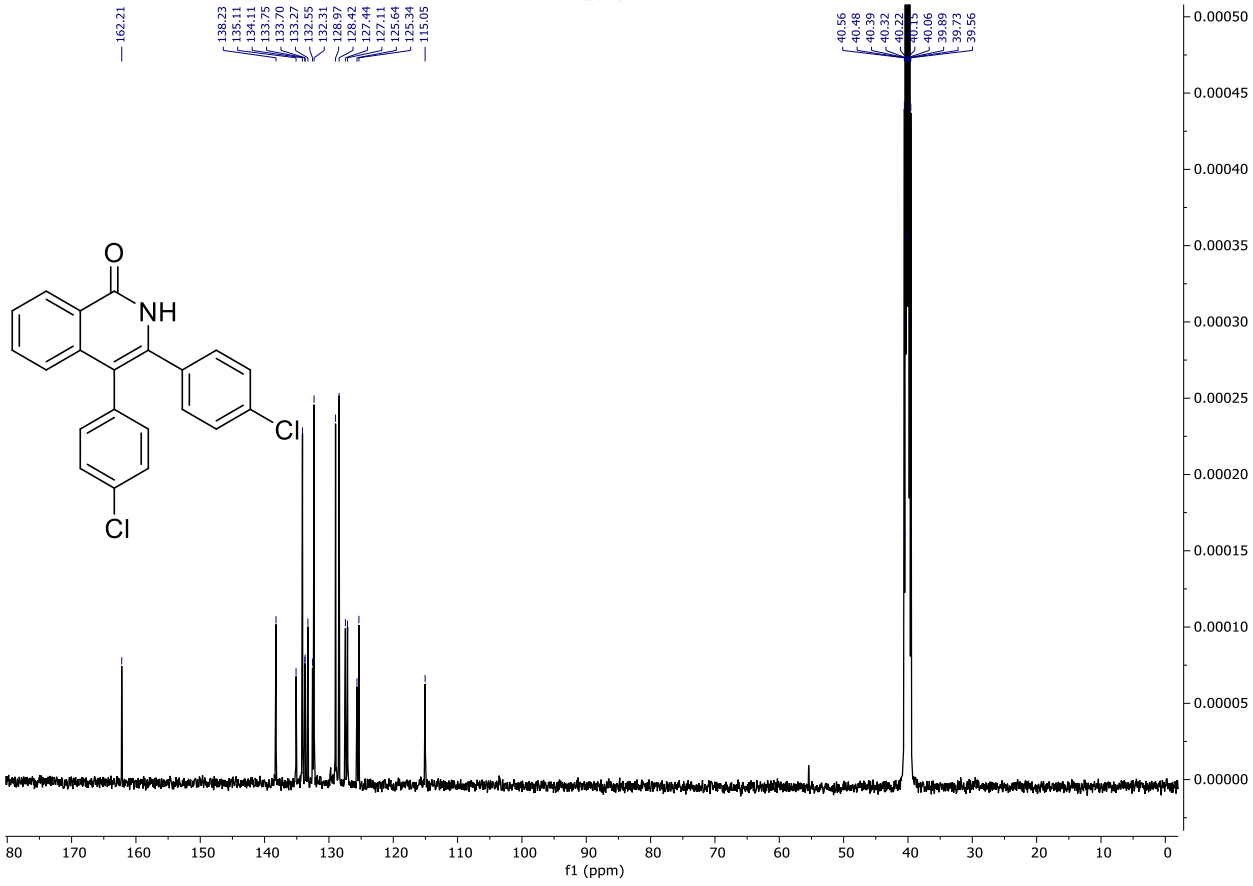
^{1}H (500 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 4h in $CDCl_3$



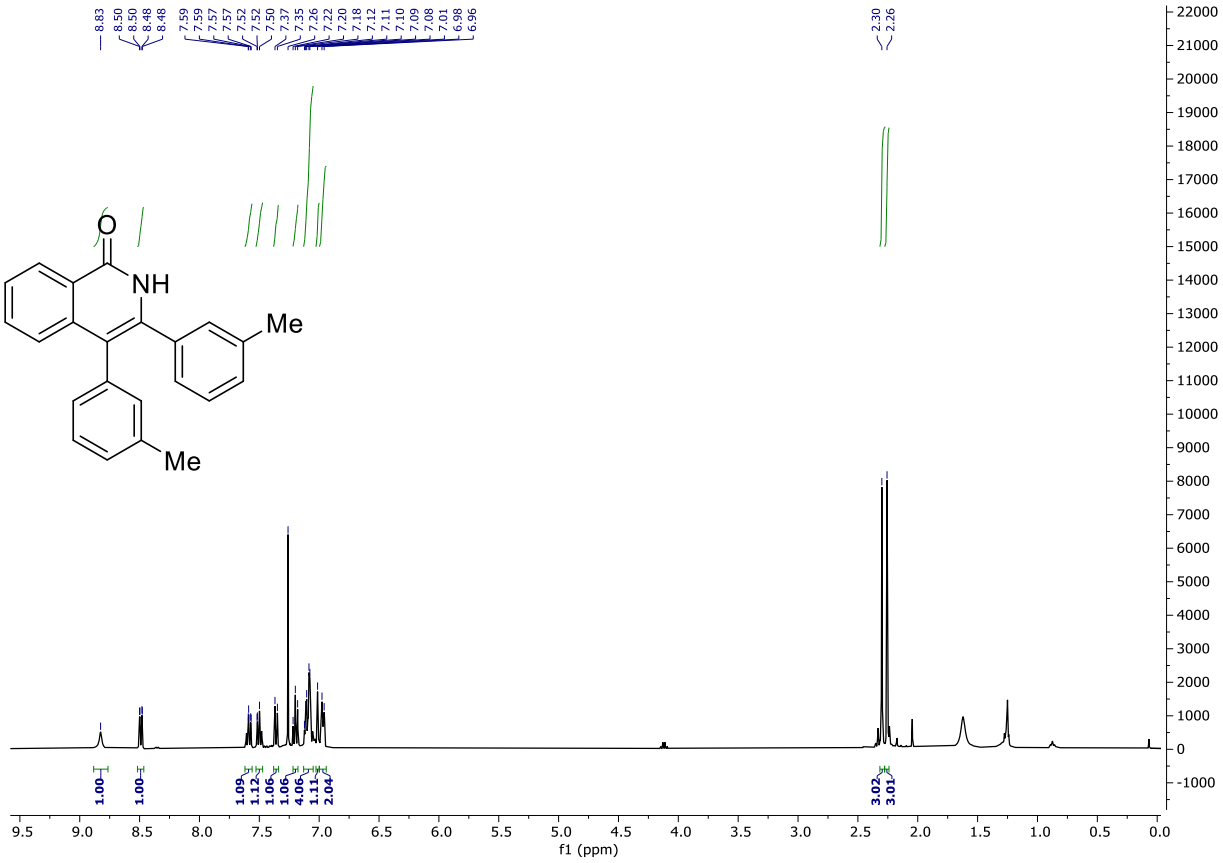
$^{19}F\{^{1}H\}$ (471 MHz) NMR spectra of 4h in $CDCl_3$

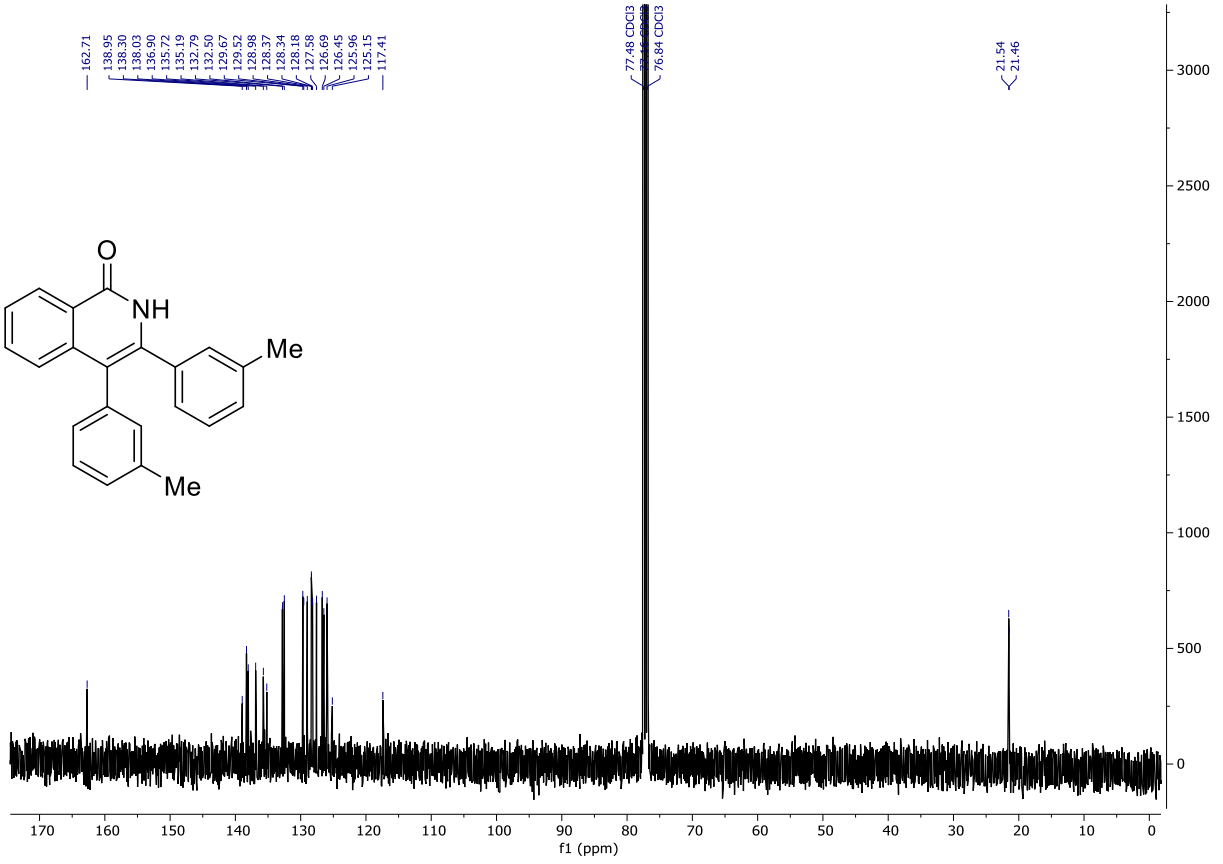
^{1}H (500 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 4i in DMSO



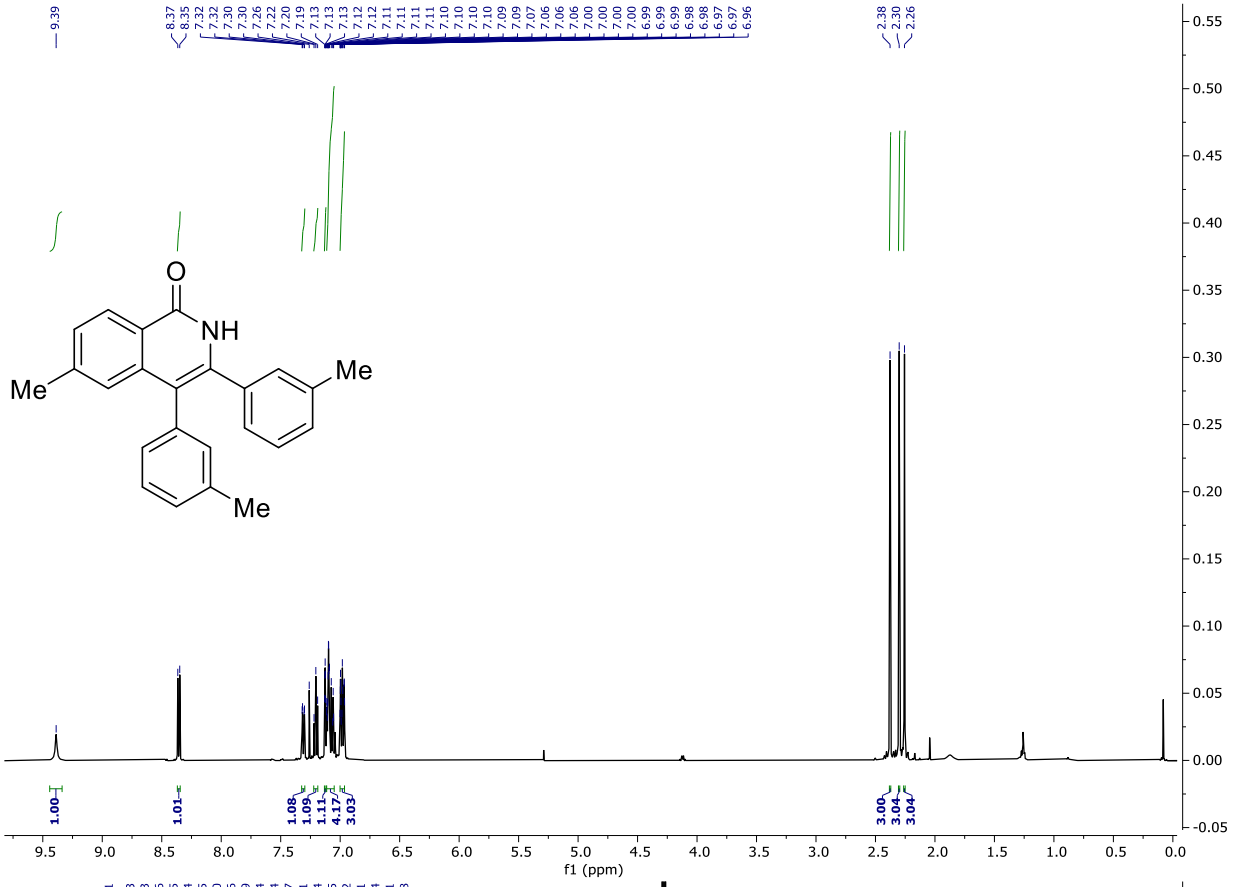


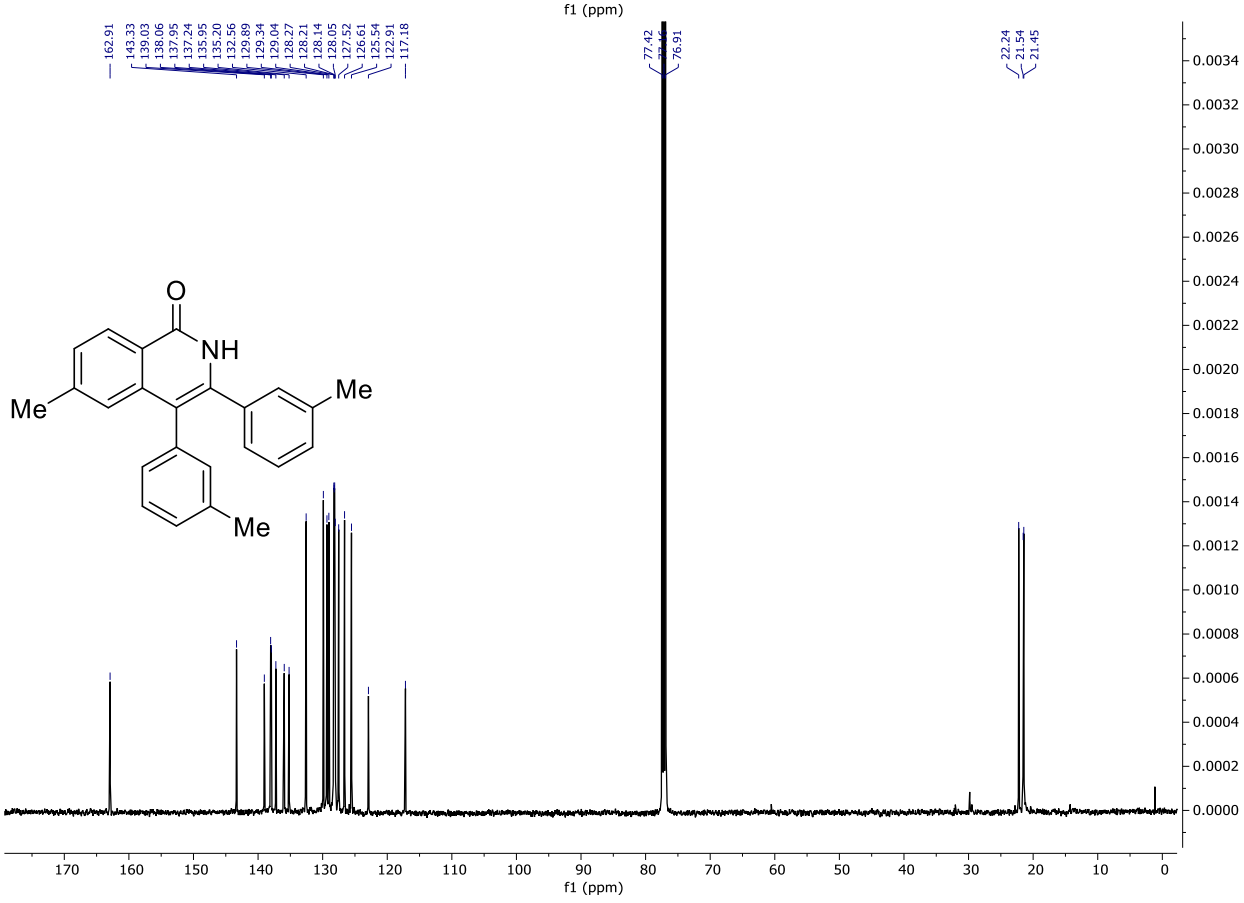
^{1}H (400 MHz) and $^{13}C\{1H\}$ (100 MHz) spectra of 4j in $CDCl_3$



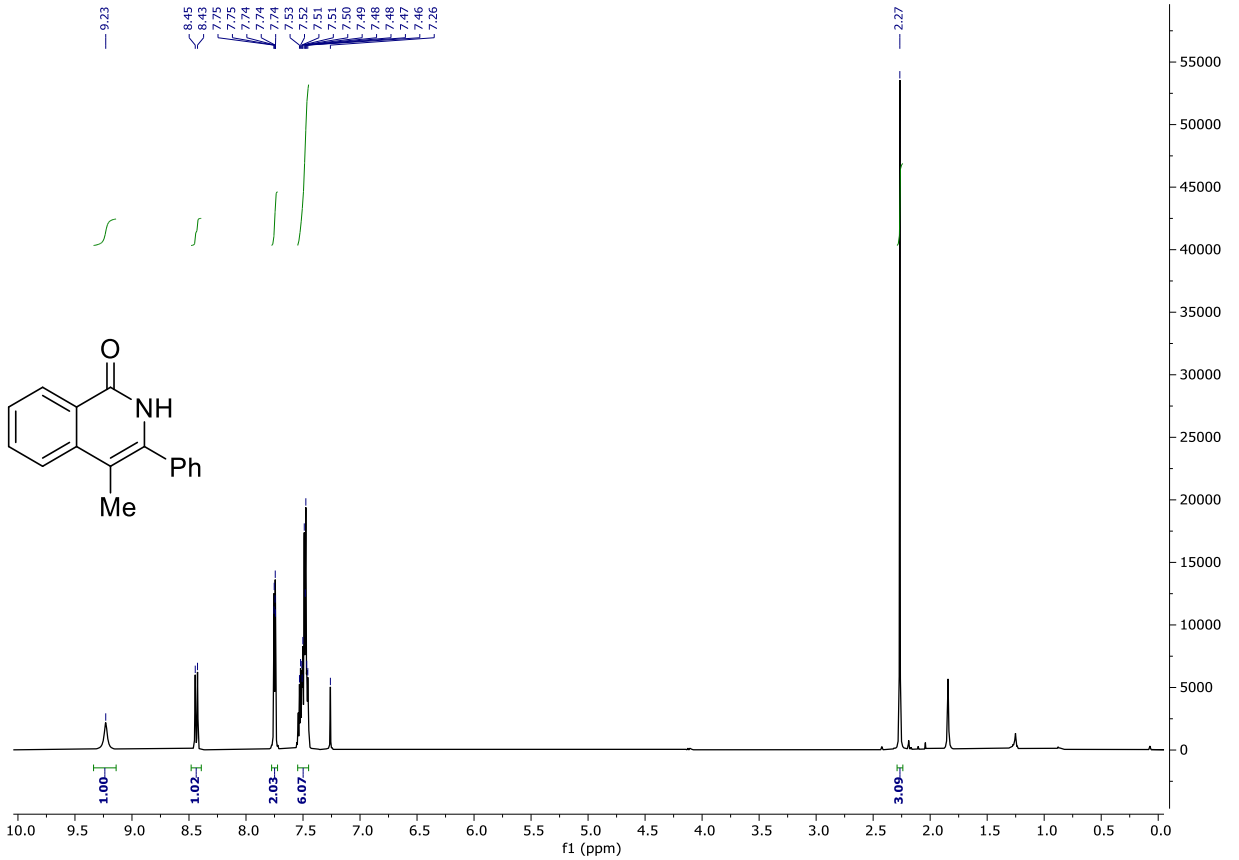


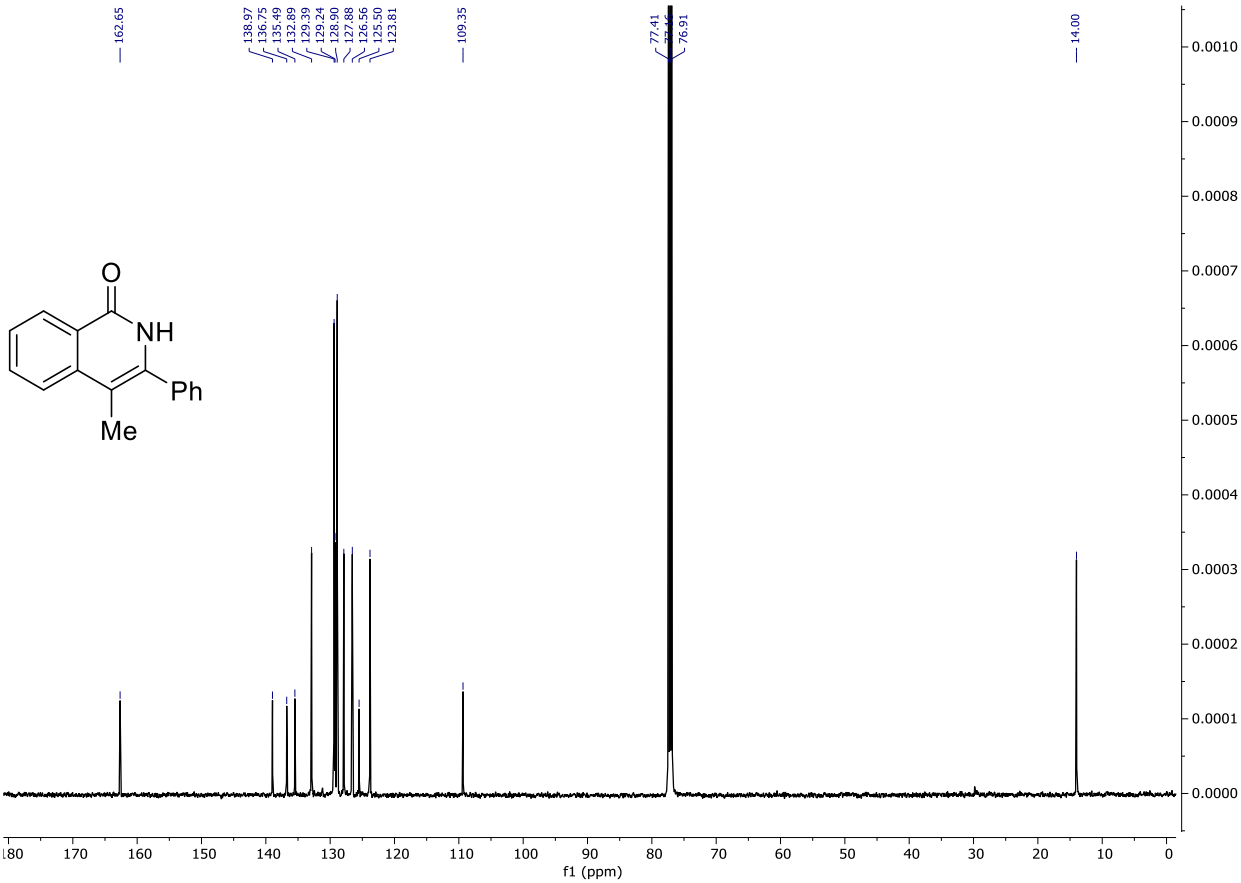
^{1}H (500 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 4k in $CDCl_3$



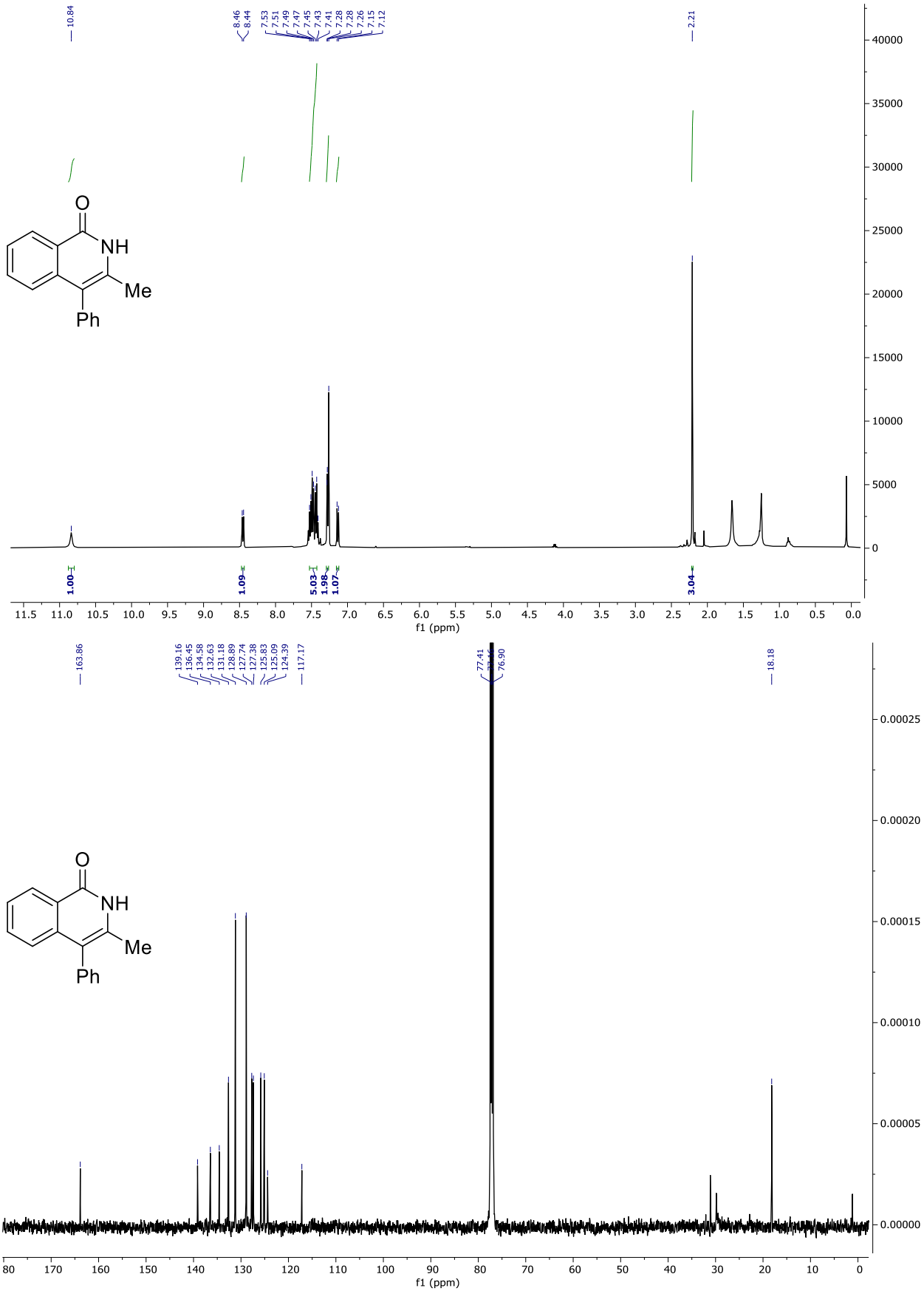


^{1}H (400 MHz) and ^{13}C{1H} (125 MHz) spectra of 4l in $CDCl_3$

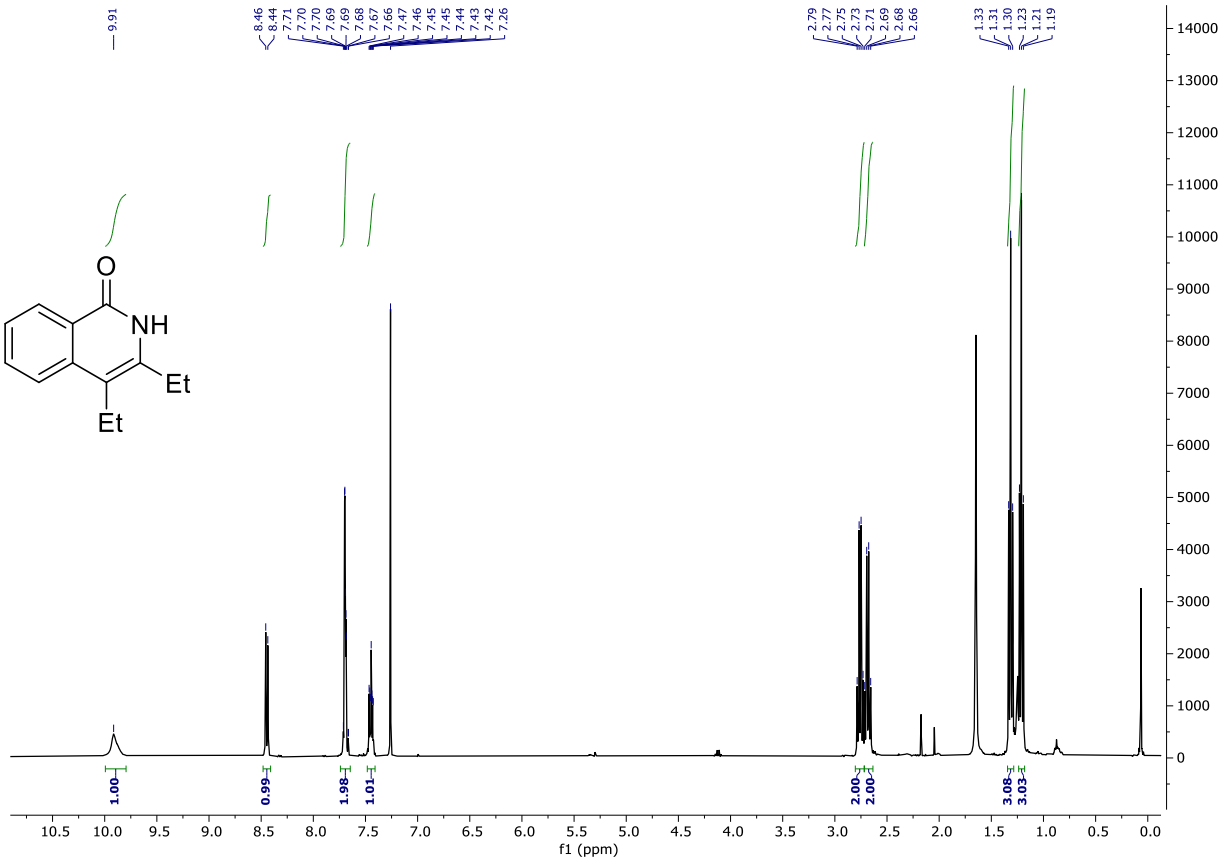


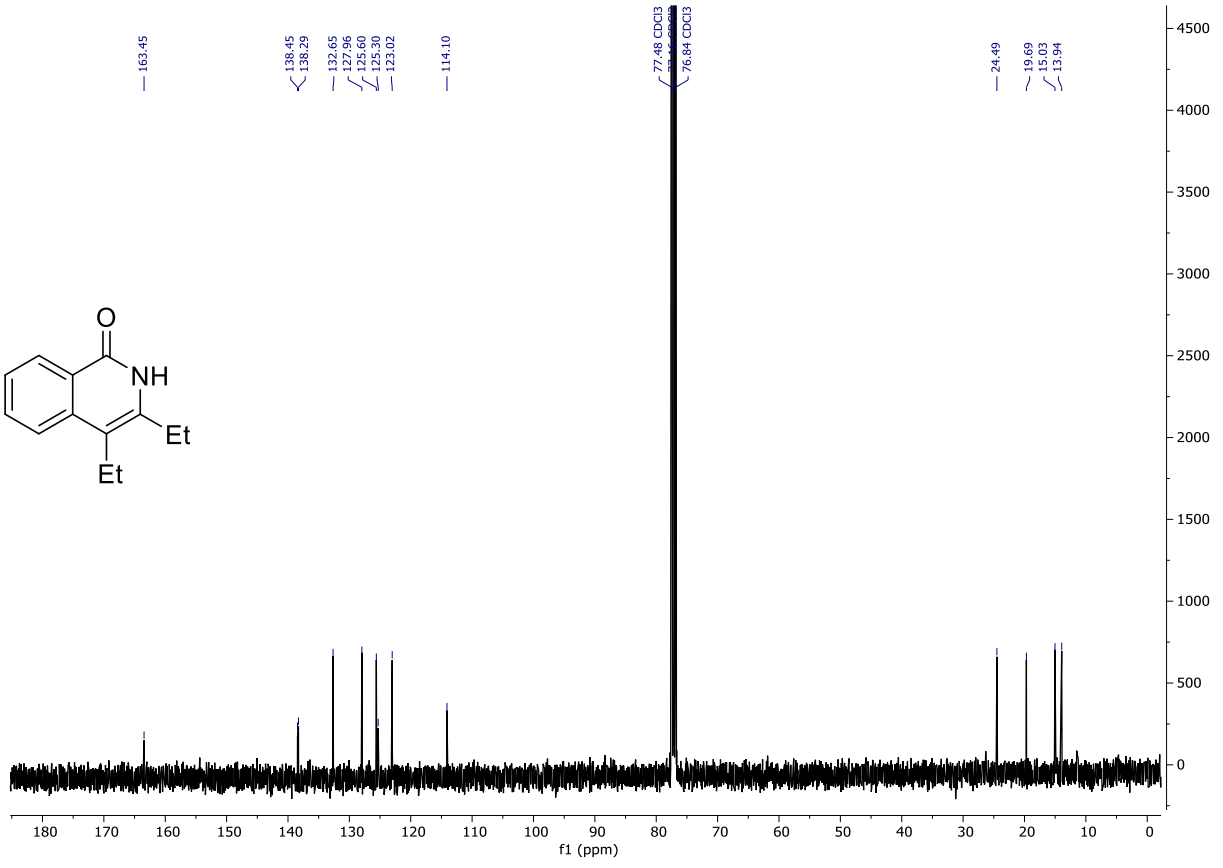


^{1}H (400 MHz) and ^{13}C{1H} (125 MHz) spectra of 4l' in $CDCl_3$

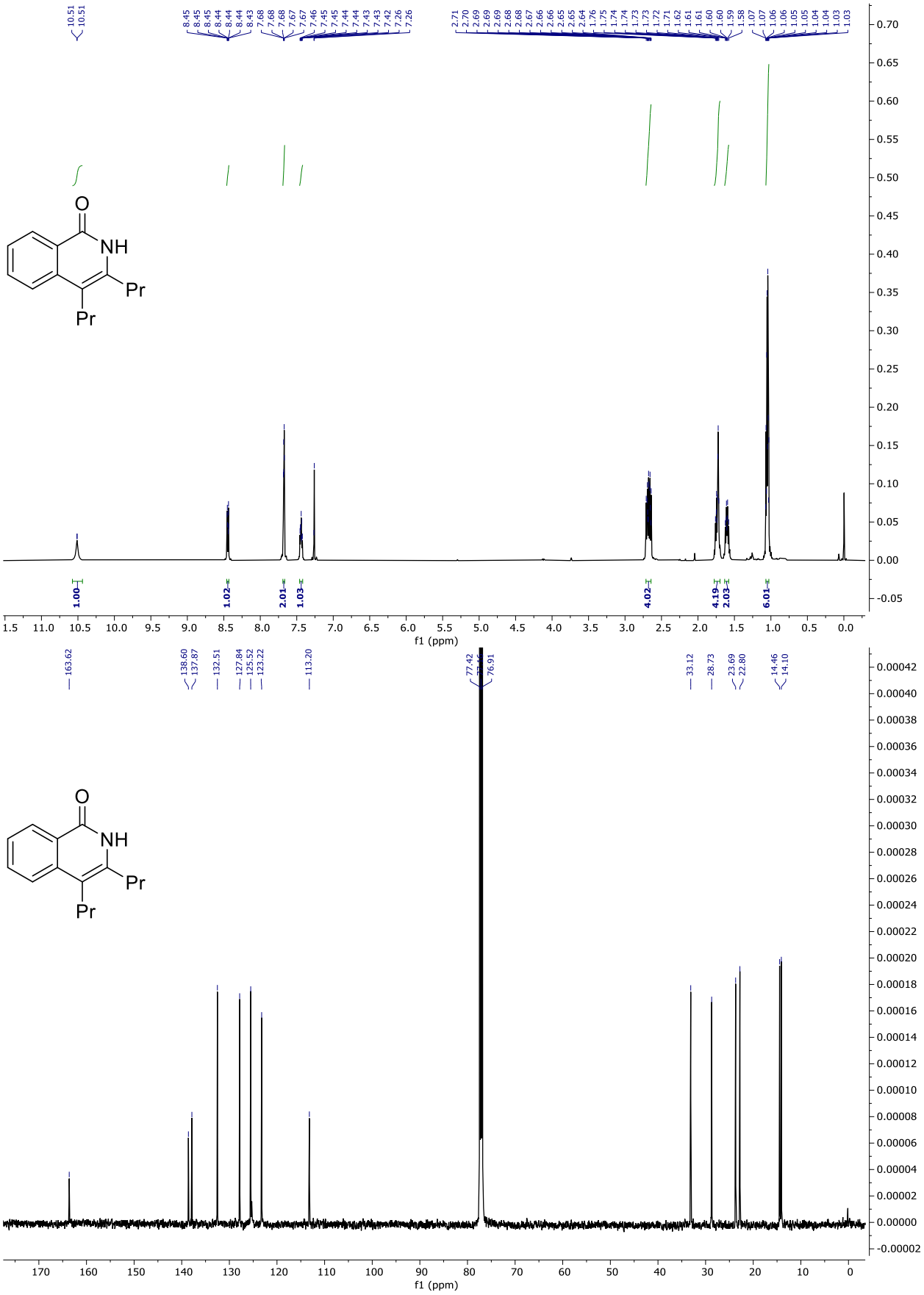


^{1}H (400 MHz) and ^{13}C{1H} (100 MHz) spectra of 4m in $CDCl_3$

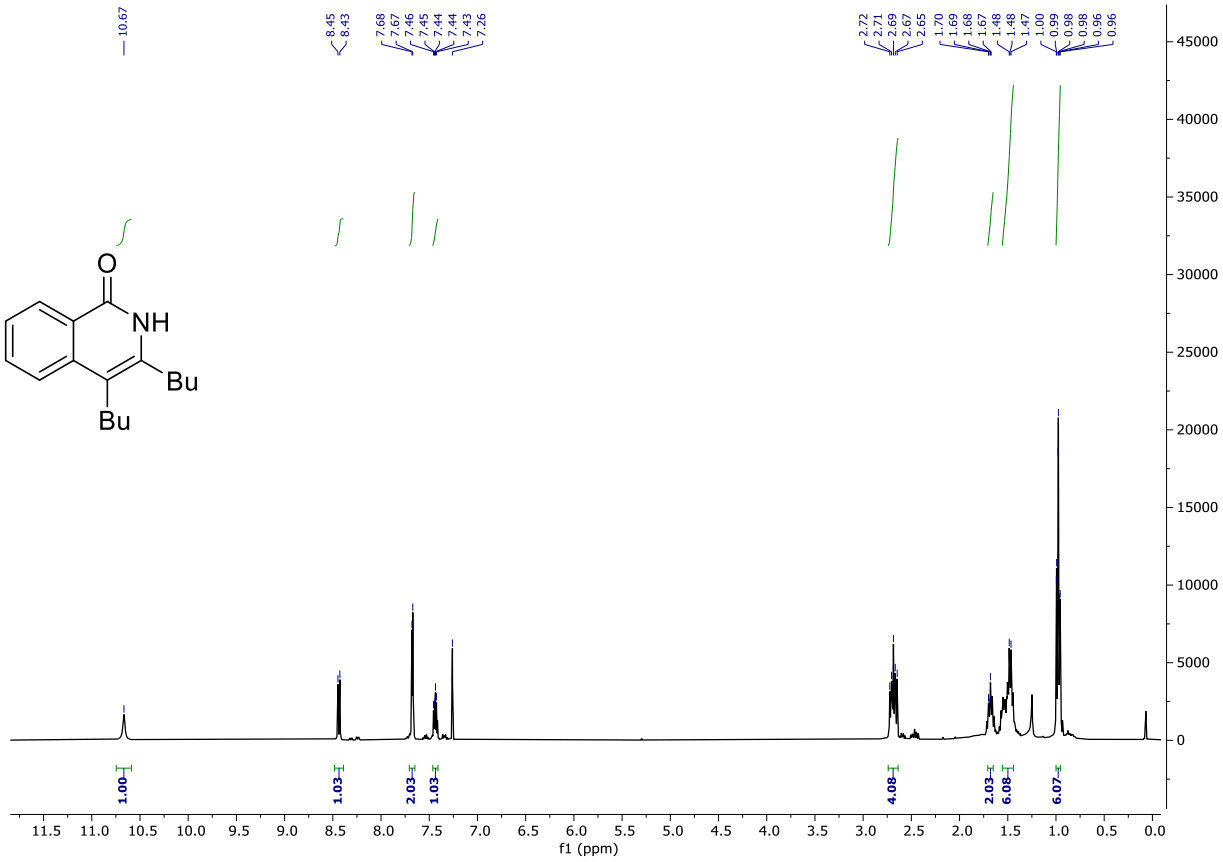


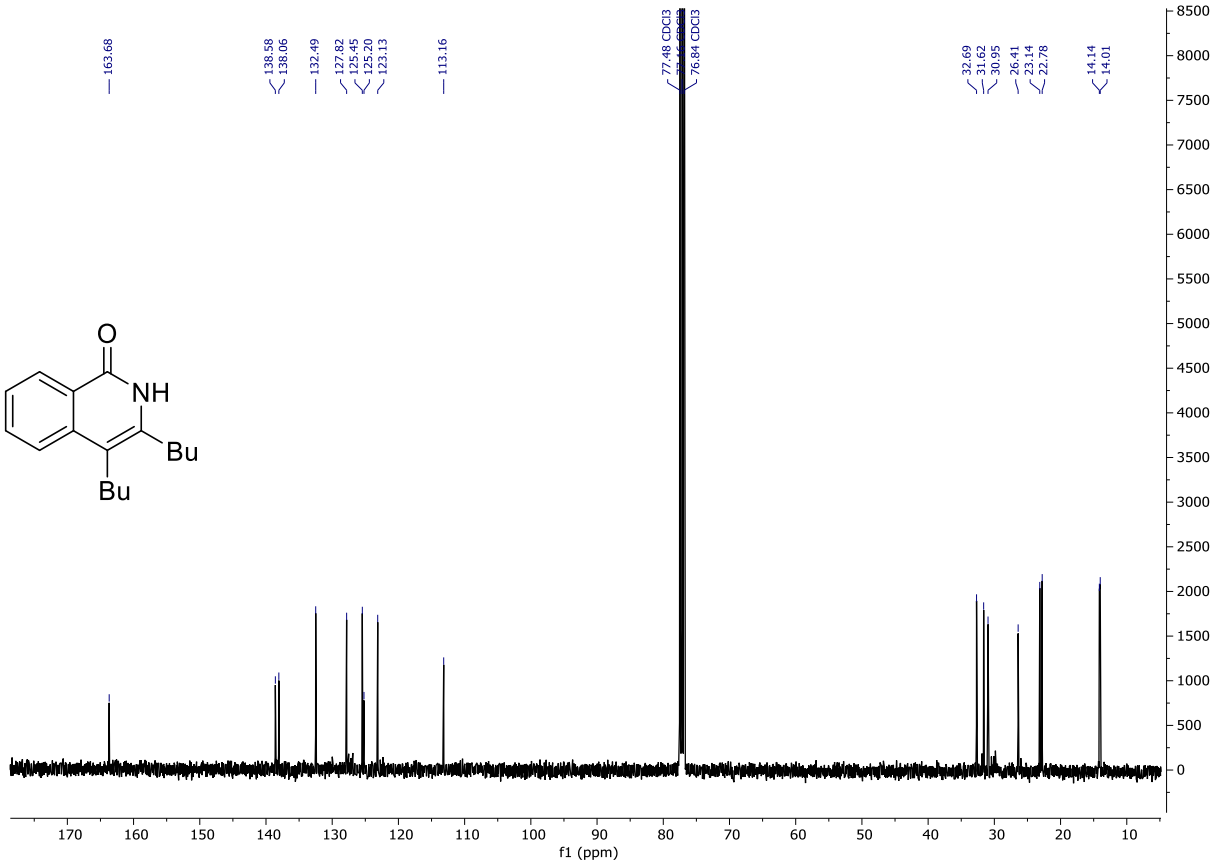


^{1}H (400 MHz) and $^{13}C\{1H\}$ (100 MHz) spectra of 4n in $CDCl_3$

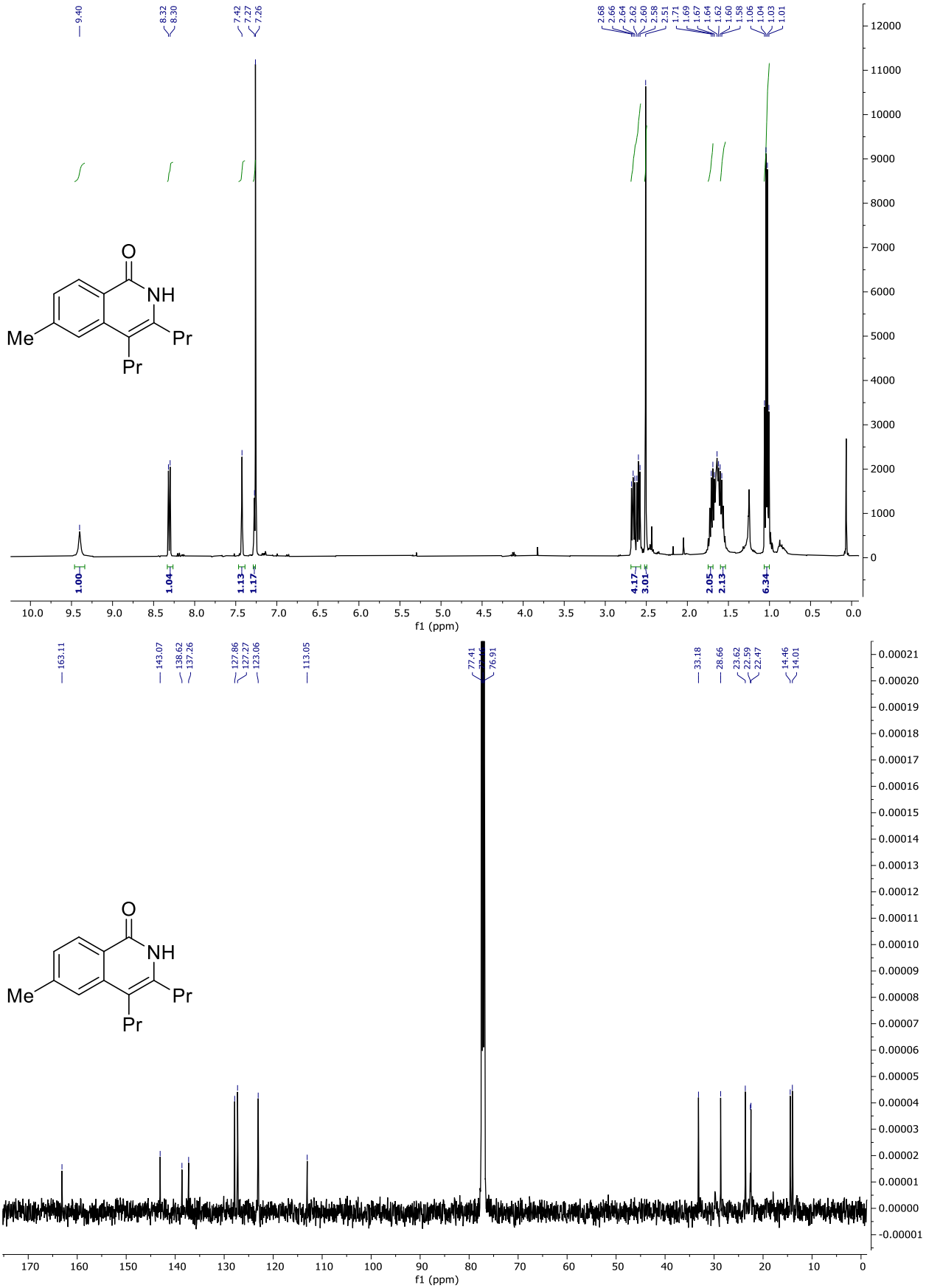


^{1}H (400 MHz) and ^{13}C{1H} (100 MHz) spectra of 4o in $CDCl_3$

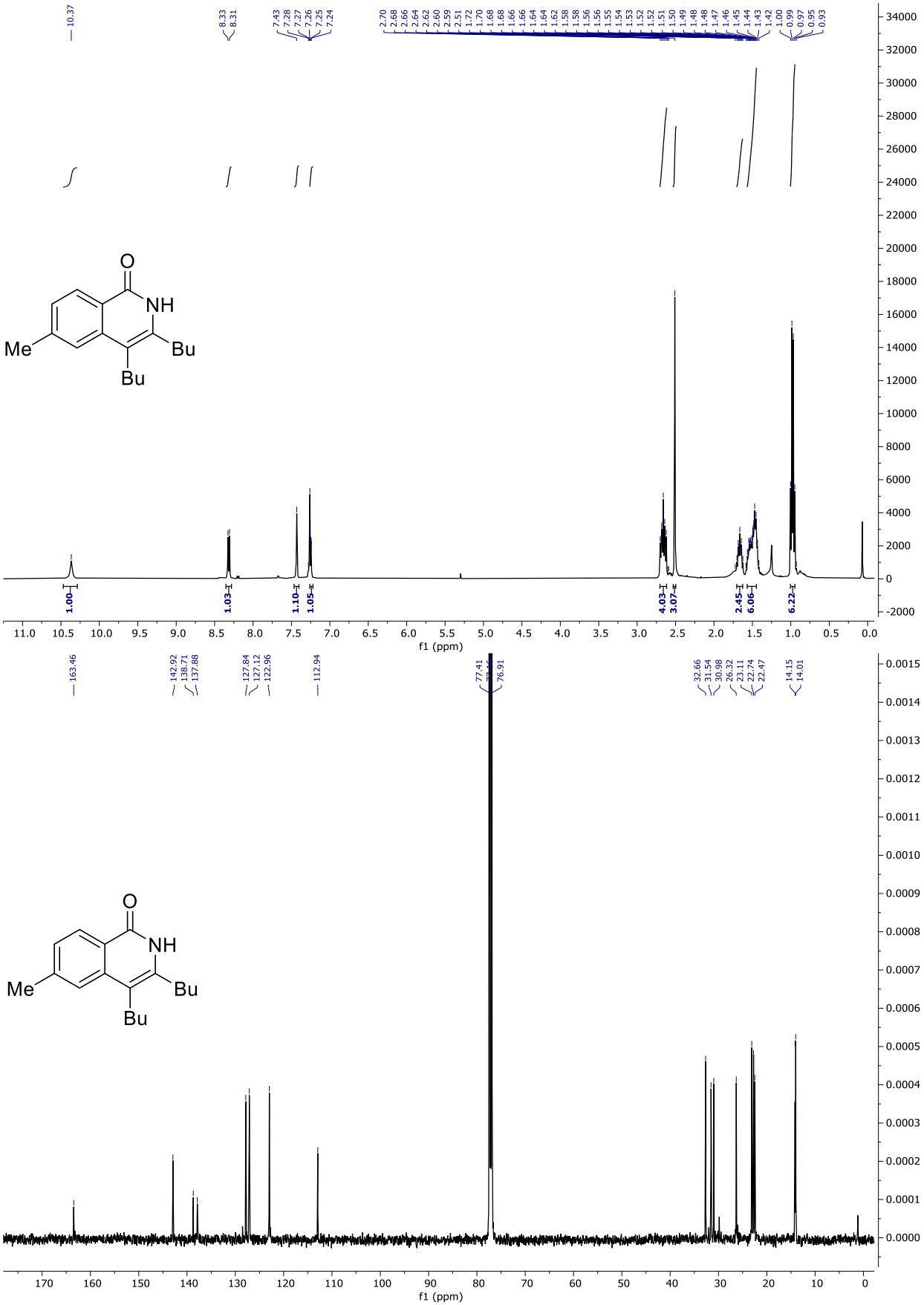




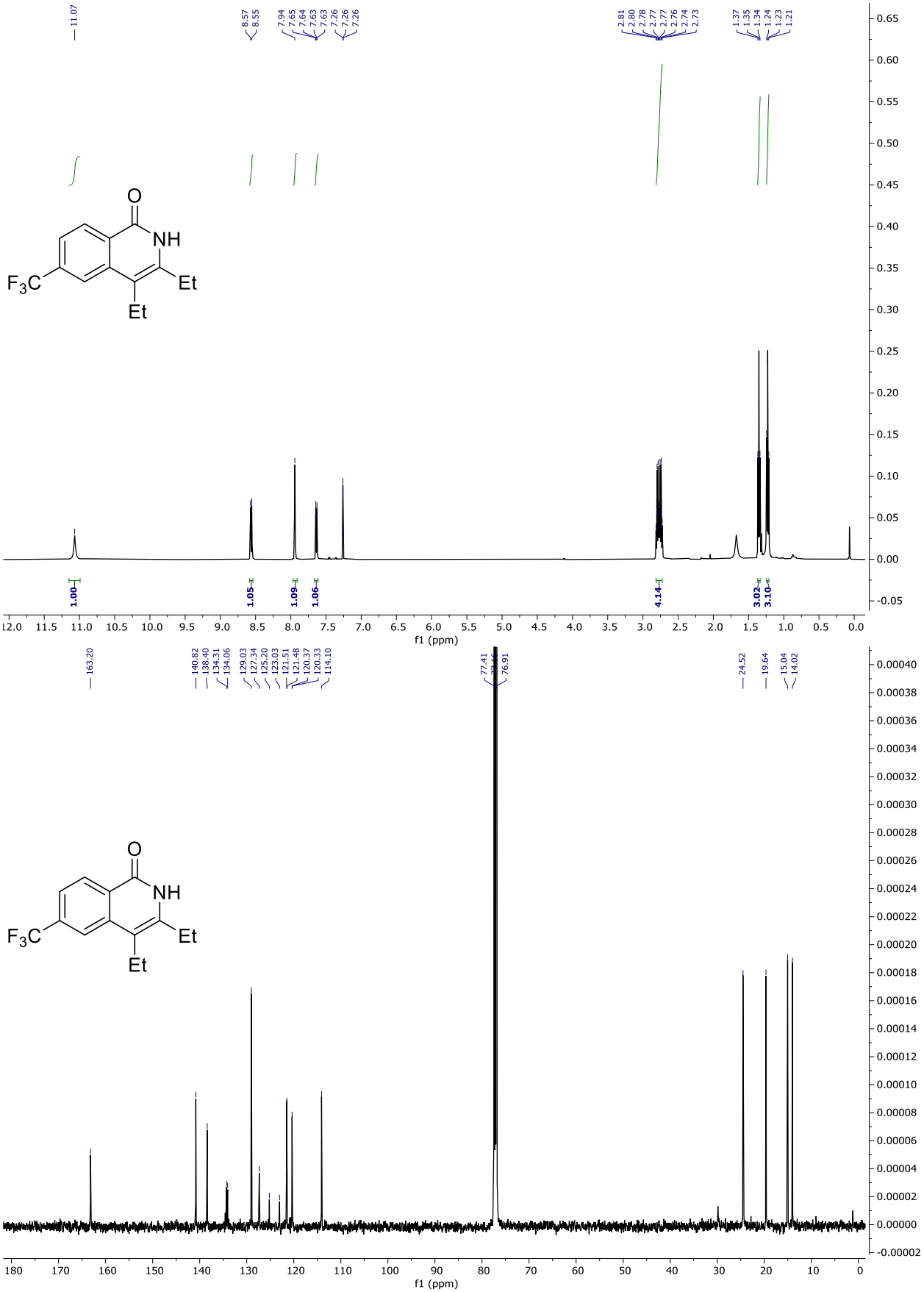
^{1}H (400 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 4p in $CDCl_3$



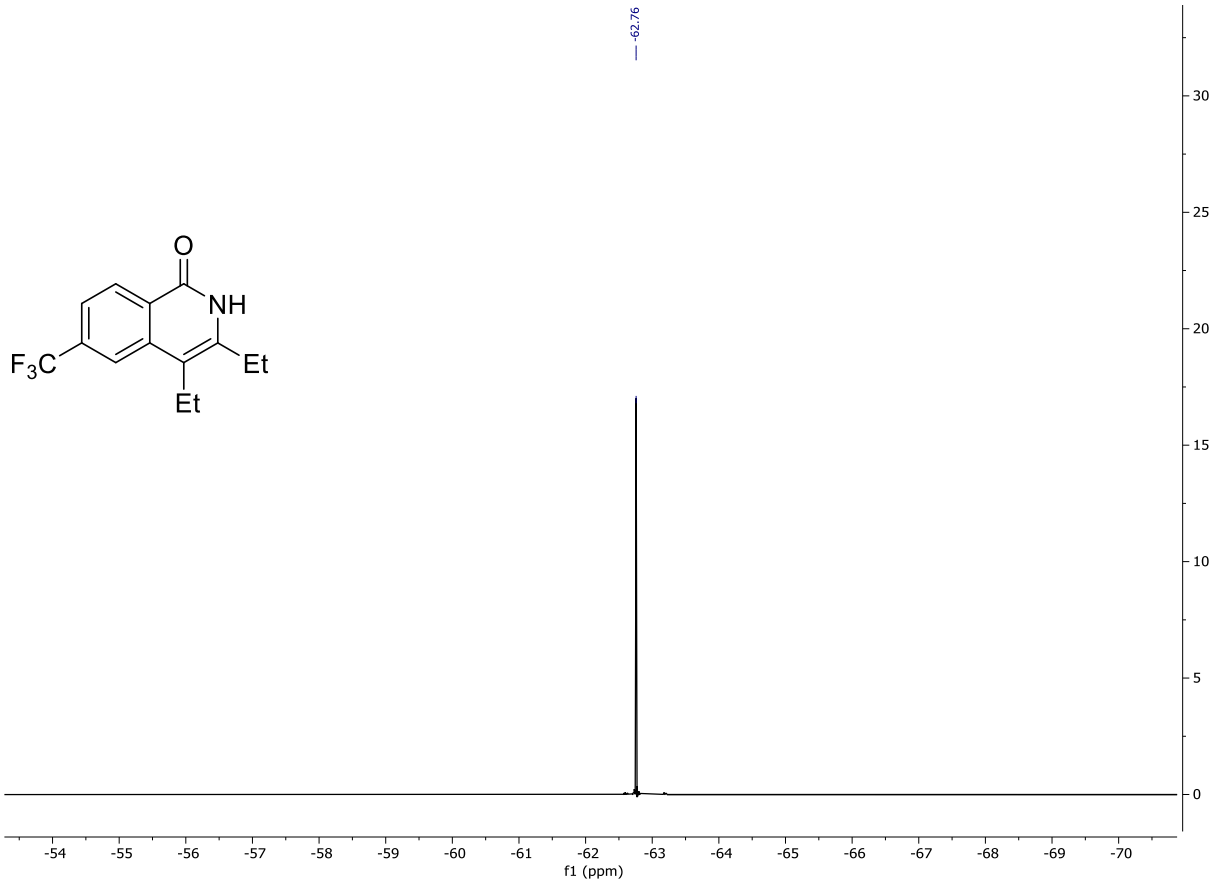
^{1}H (400 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 4q in $CDCl_3$



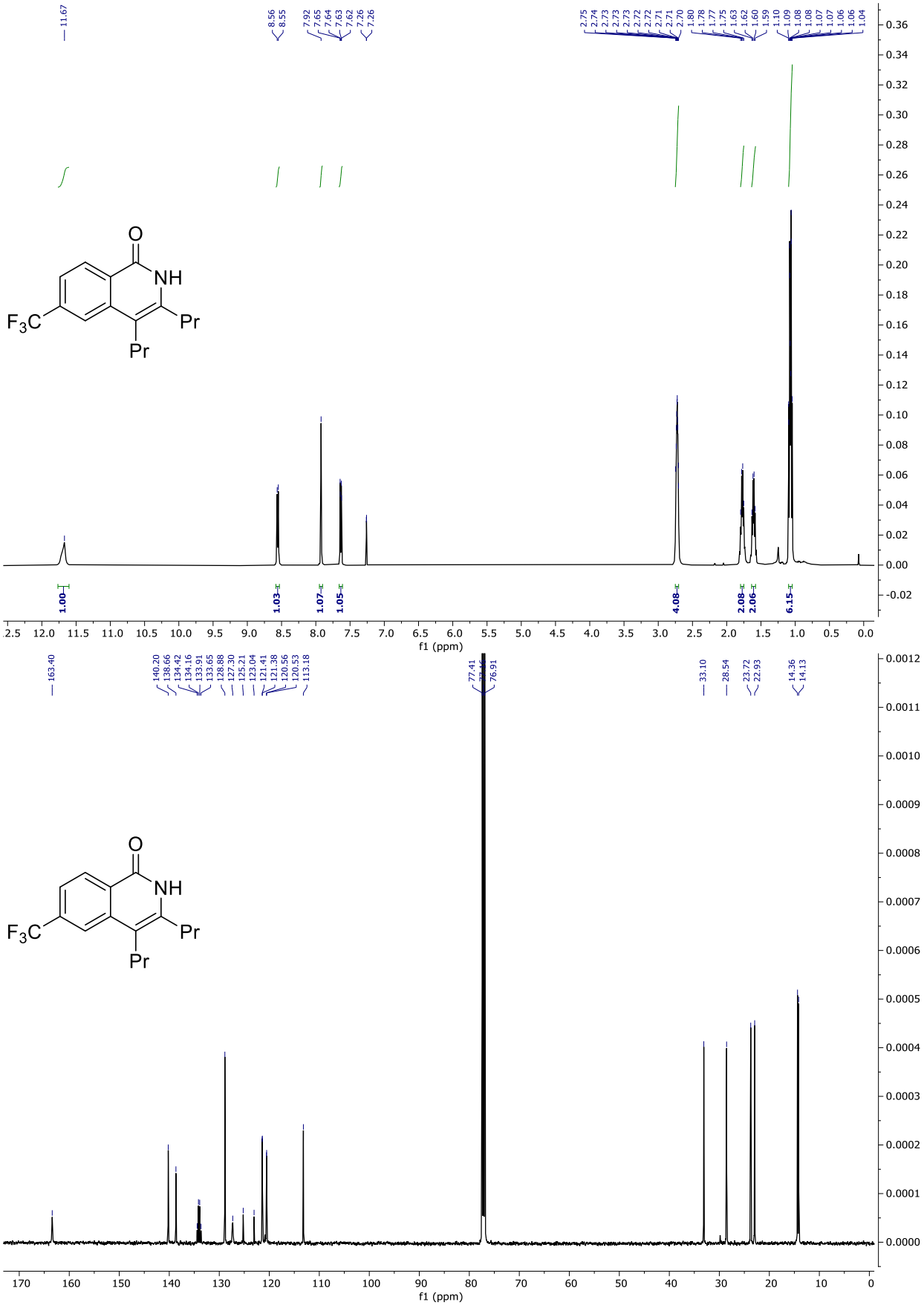
^{1}H (500 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 4r in $CDCl_3$



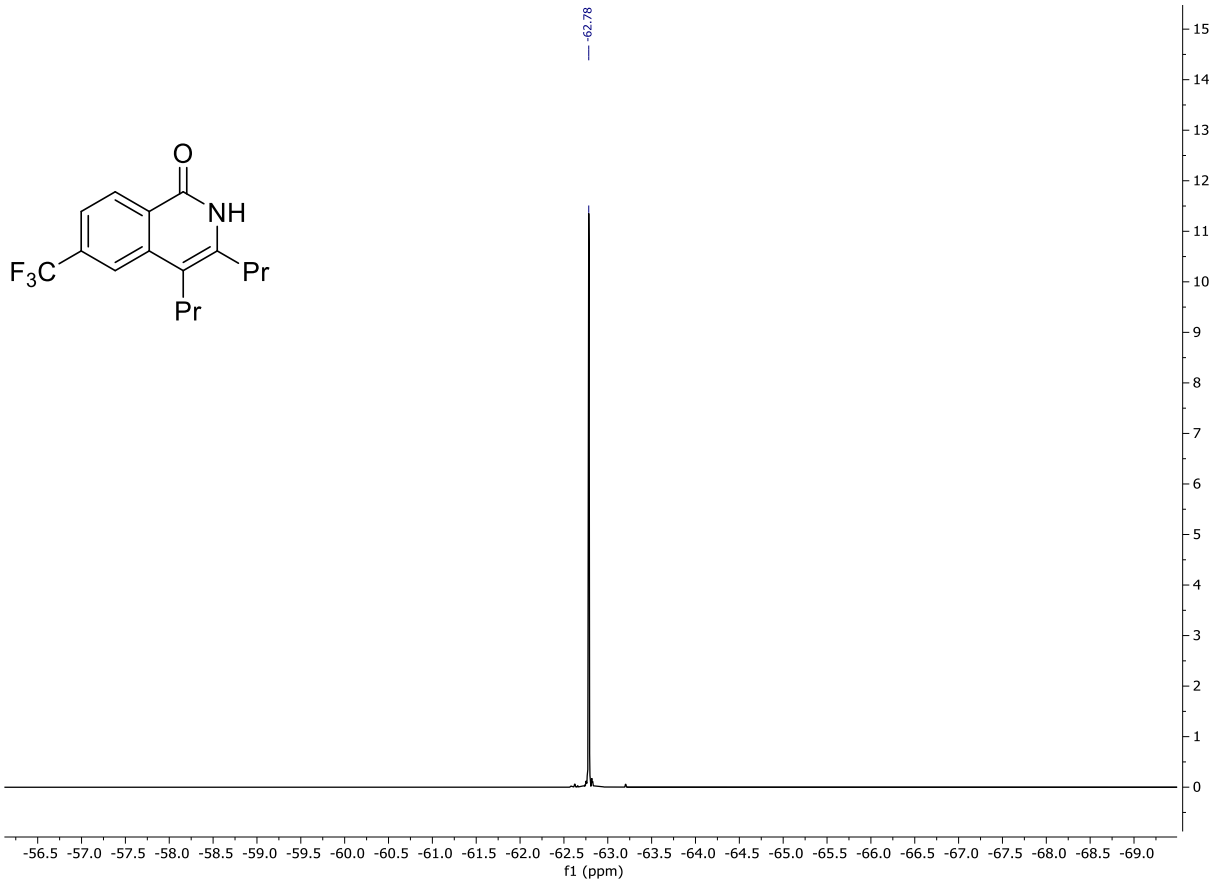
$^{19}F\{^{1}H\}$ (471 MHz) NMR spectra of 4r in $CDCl_3$



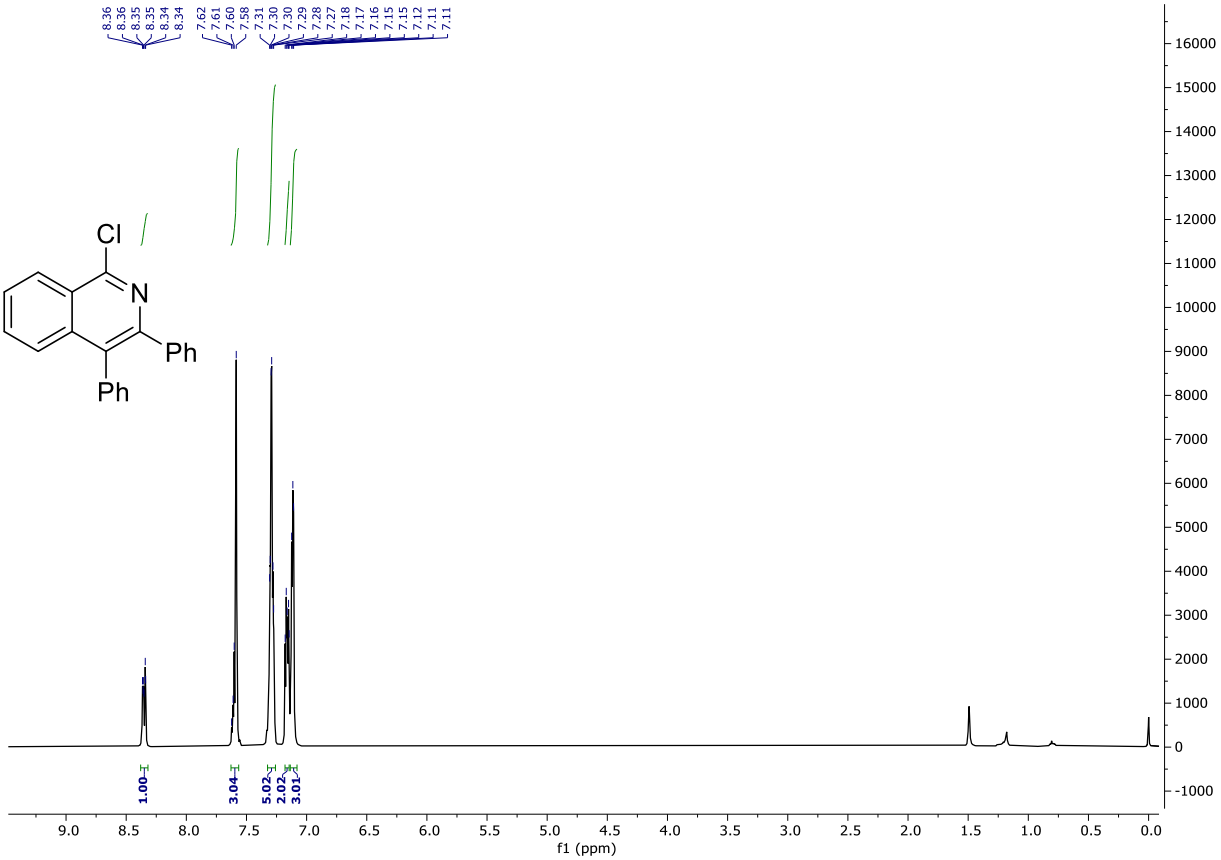
^{1}H (500 MHz) and ^{13}C{1H} (125 MHz) spectra of 4s in $CDCl_3$

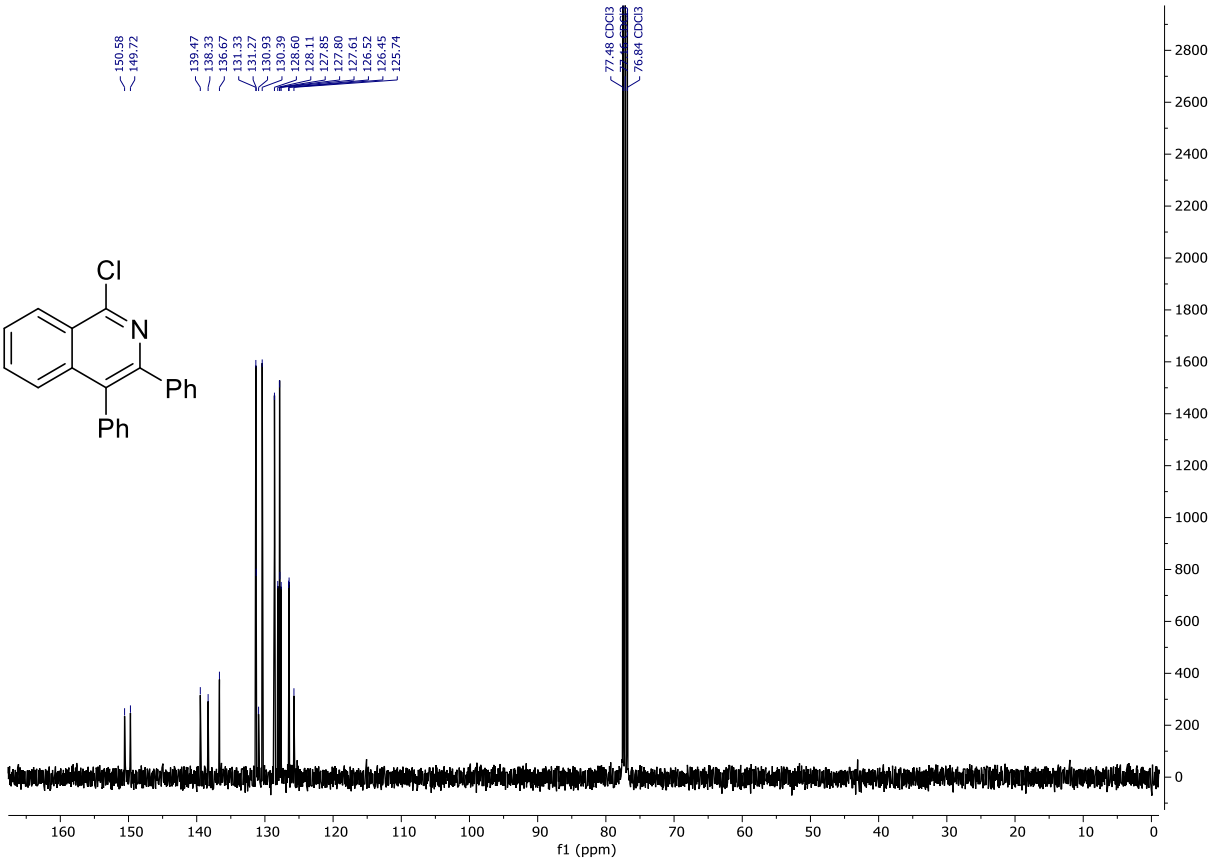


$^{19}F\{^{1}H\}$ (471 MHz) NMR spectra of 4s in $CDCl_3$

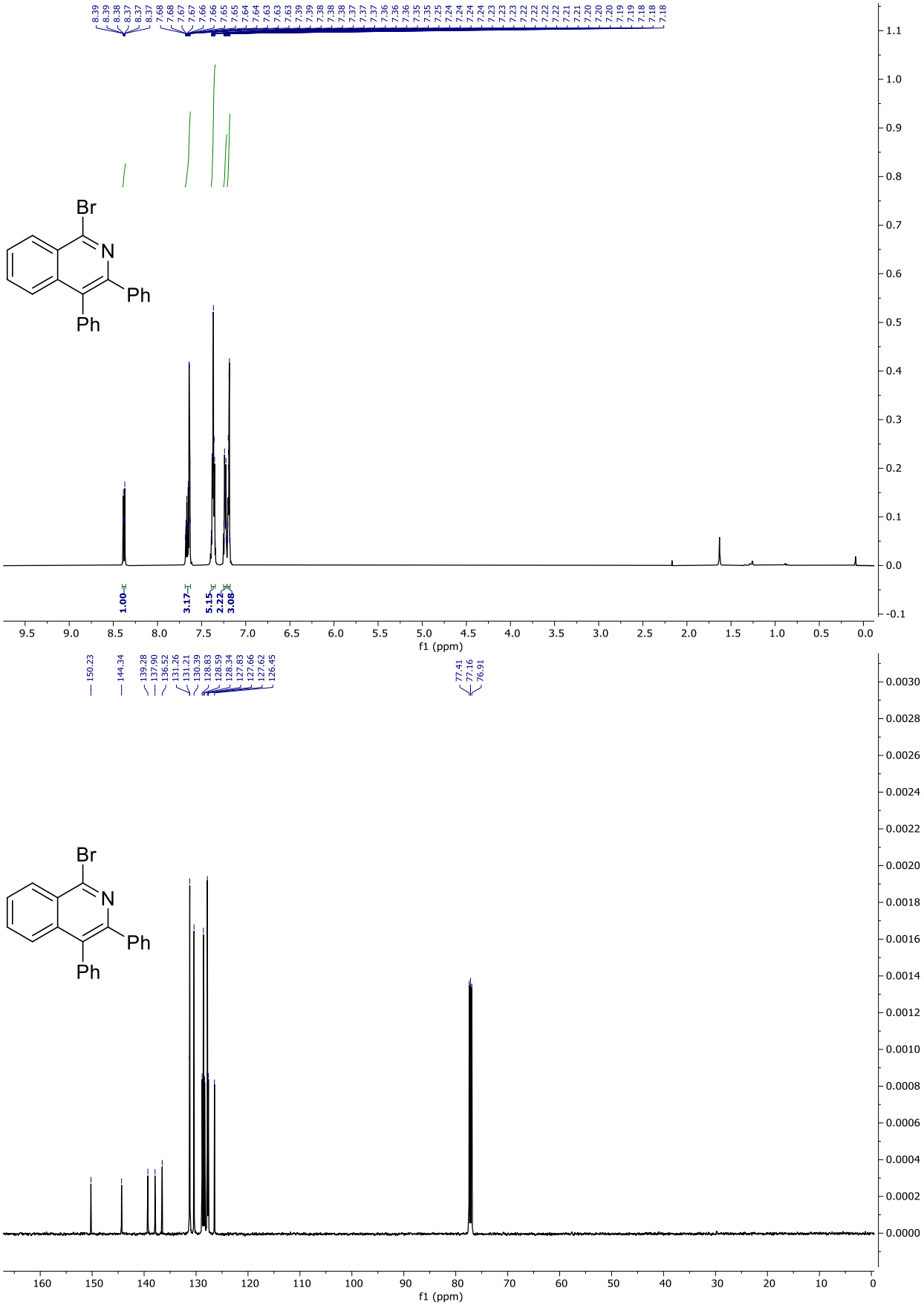


^{1}H (400 MHz) and ^{13}C{1H} (100 MHz) spectra of 5a in $CDCl_3$

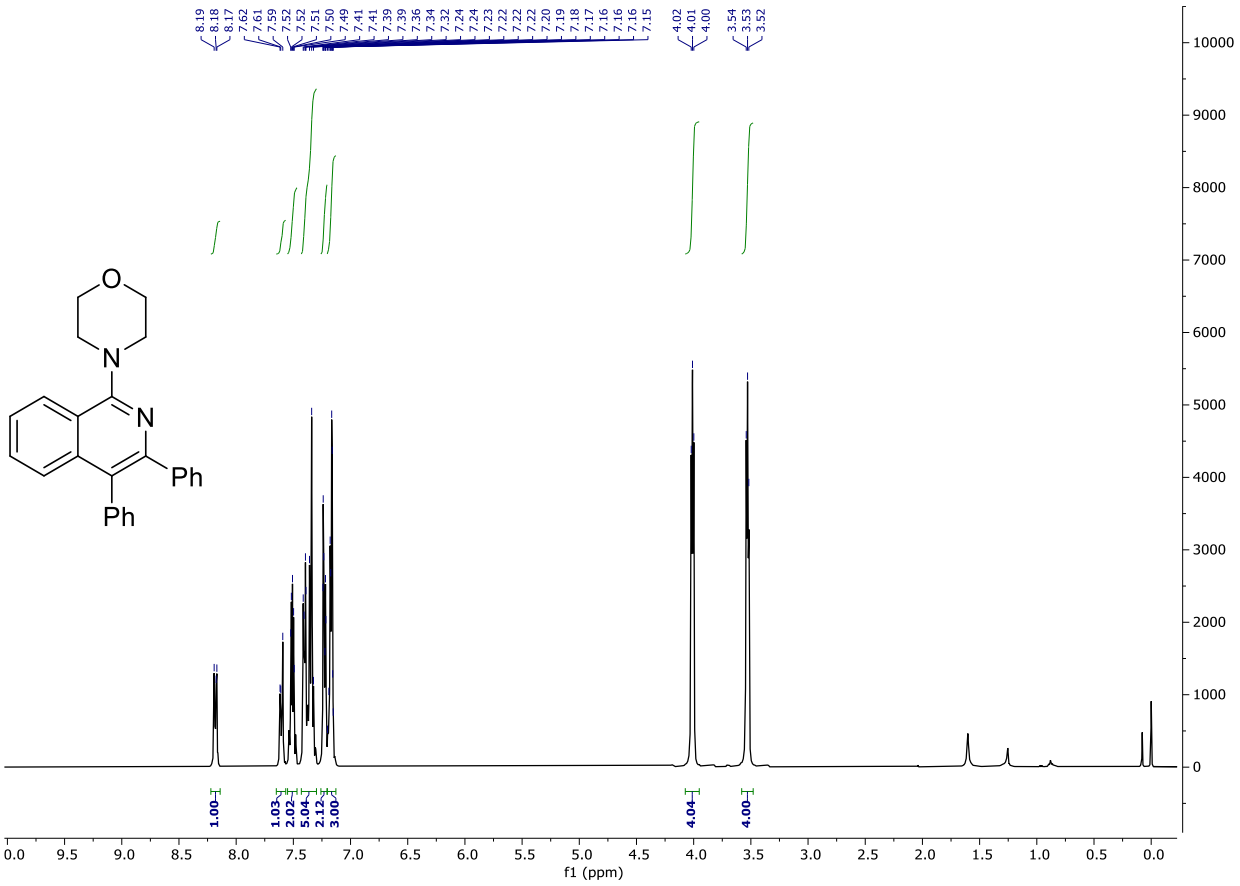


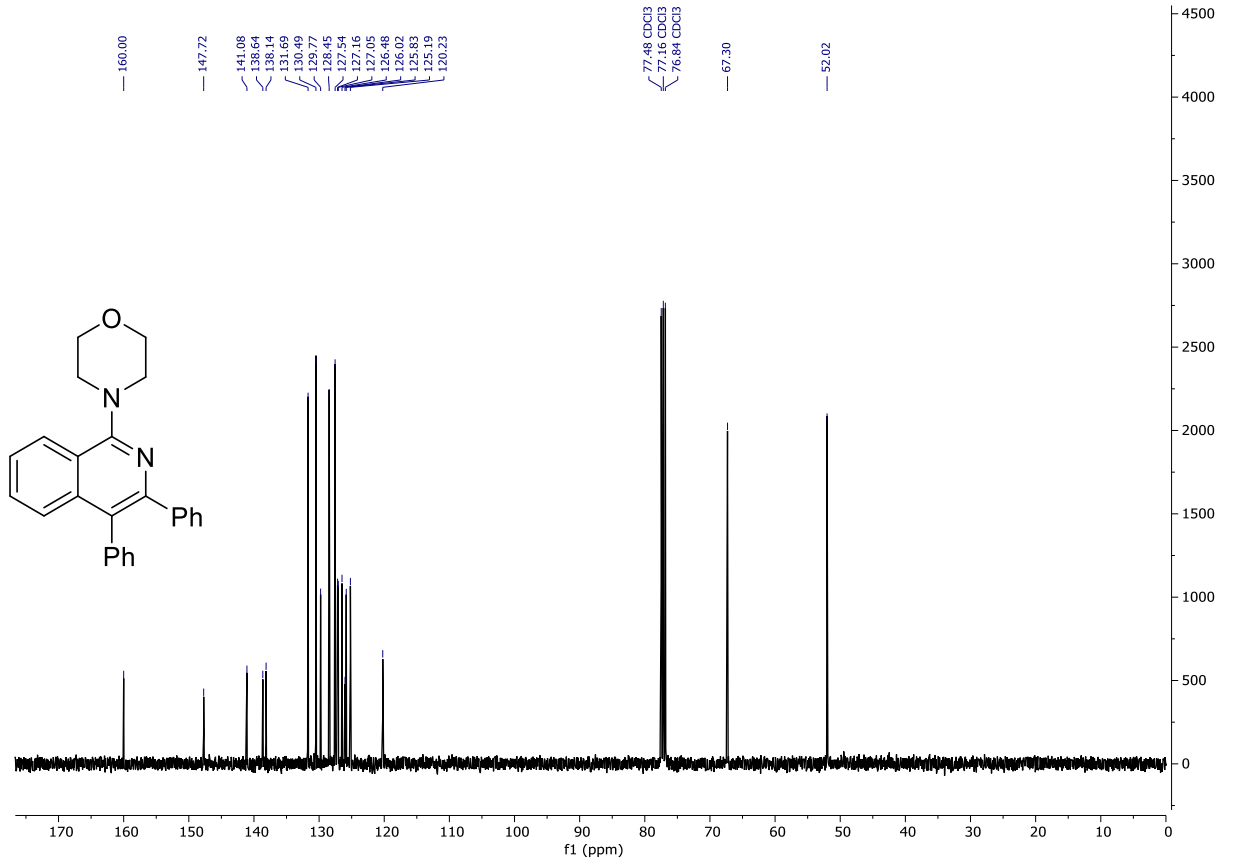


^{1}H (500 MHz) and ^{13}C{1H} (125 MHz) spectra of 5b in $CDCl_3$

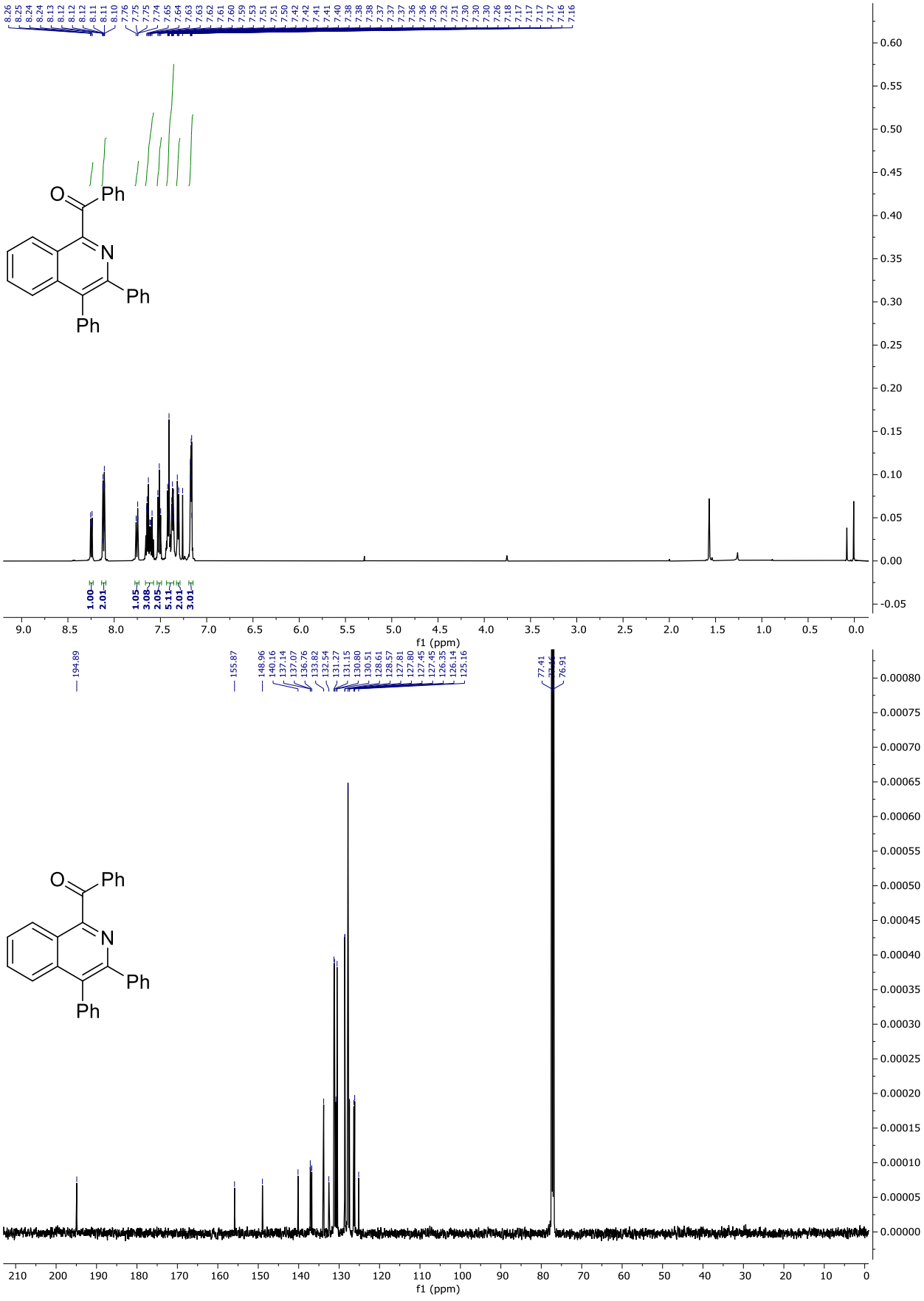


^{1}H (400 MHz) and $^{13}C\{1H\}$ (100 MHz) spectra of 5c in $CDCl_3$





^{1}H (500 MHz) and $^{13}C\{1H\}$ (125 MHz) spectra of 5d in $CDCl_3$



^{1}H (400 MHz) and ^{13}C{1H} (100 MHz) spectra of 6a in $CDCl_3$