Electronic Supporting Information

for

Switchable Regioselective Hydroalkylation of 2-Arylindoles with Maleimides

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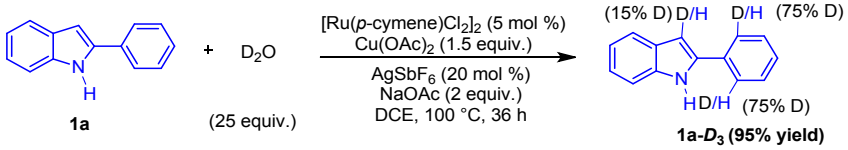
1. Mechanistic Studies:

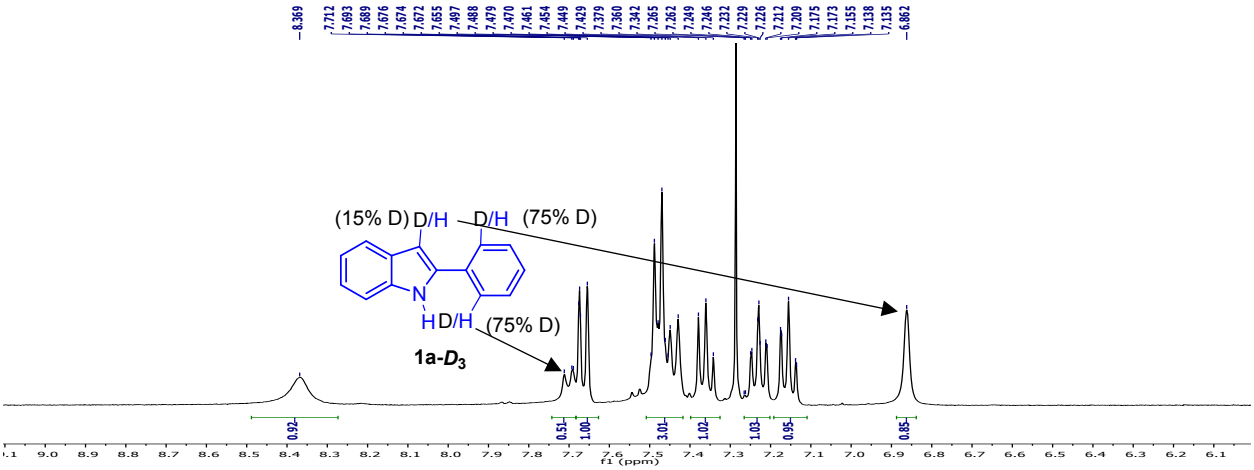
1.1 Deuterium exchange experiment:



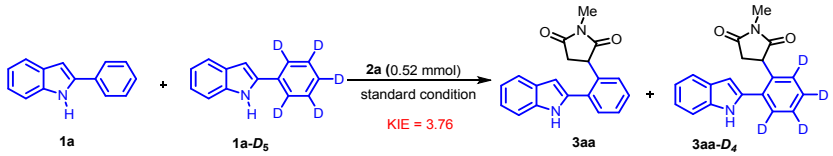
1a **1a-D_3 (95% yield)**

An oven dried 10 mL pressure tube charged with 2-phenylindole (**1a**, 0.26 mmol), $Cu(OAc)_2.H_2O$ (0.39 mmol), $AgSbF_6$ (20 mol %), NaOAc (0.52 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (2.5 mol %), D_2O (25 equiv.) and DCE (2 mL). The reaction mixture stirred at 100 °C in oil bath for 36 h. After completion of reaction, it was cooled to ambient temperature, quenched by water and extracted in ethyl acetate (10 mL × 3). The combined organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The resulting residue was purified by column chromatography (*n*-hexane/EtOAc) on (100-200 mm) size silica gel to afford the product **1a-D_3.** 75% of Deuterium

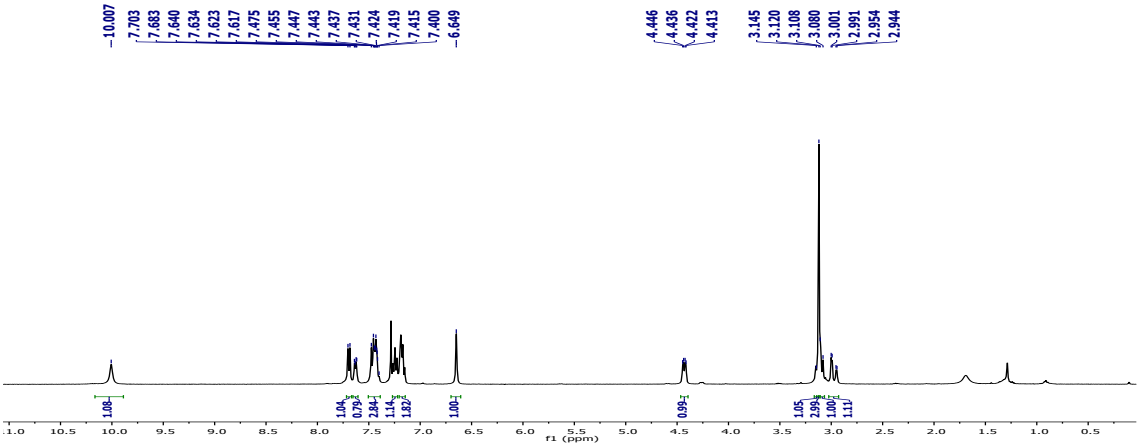
incorporation was observed at both *ortho* C−H bonds of 2-phenyl ring and 15% of deuterium incorporation was observed at C3-position to give **1a-*D*$_3$**.



1.2 Intermolecular KIE Experiment:

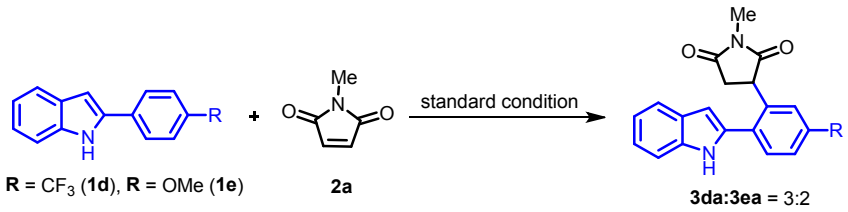


An oven dried 10 mL pressure tube charged with 2-phenylindole (**1a**, 50 mg, 0.26 mmol), 2-phenyl-D_5-indole (**1a-*D*$_5$**, 52 mg, 0.26 mmol), *N*-methyl maleimide (**2a**, 57 mg, 0.52 mmol), $Cu(OAc)_2.H_2O$ (77 mg, 0.39 mmol), $AgSbF_6$ (18 mg, 20 mol %), NaOAc (43 mg, 0.52 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (8 mg, 2.5 mol %), and DCE (2 mL). The reaction mixture stirred at 100 °C in oil bath for 36 h. After completion of reaction, it was cooled to ambient temperature, quenched by water and extracted in ethyl acetate (10 mL × 3). The combined organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The resulting residue was purified by column chromatography (*n*-hexane/EtOAc) on (100-200 mm) size silica gel to afford the mixture of products **3aa** and **3aa-*d*$_4$.** The isolated product was analyzed by ^{1}H NMR spectrum, the intermolecular KIE (k_H/k_D) was calculated as 3.76.

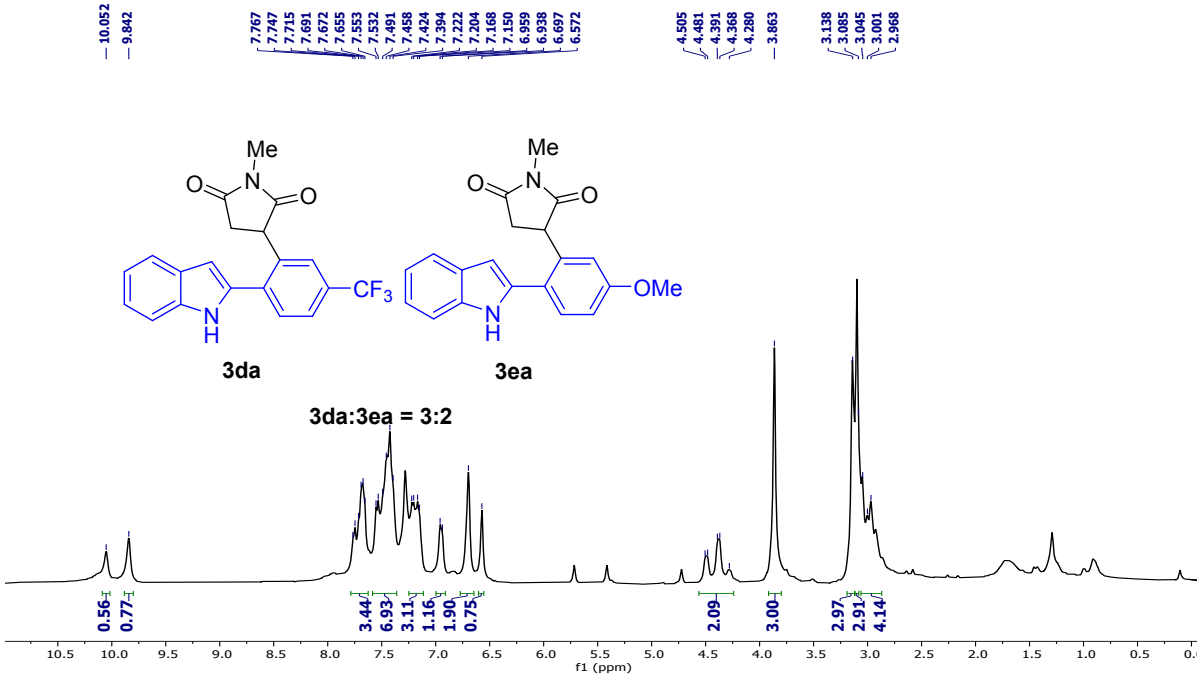


2. Competition Experiment

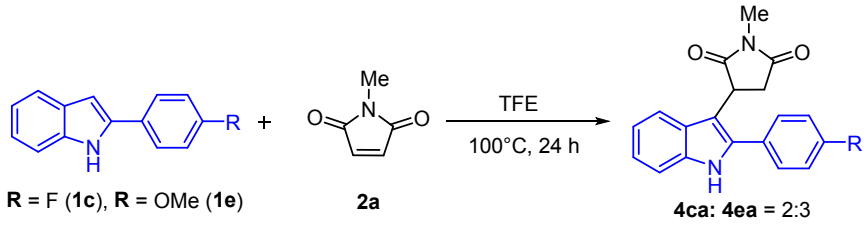
2.1. Competition Experiment for ortho-Hydroalkylation



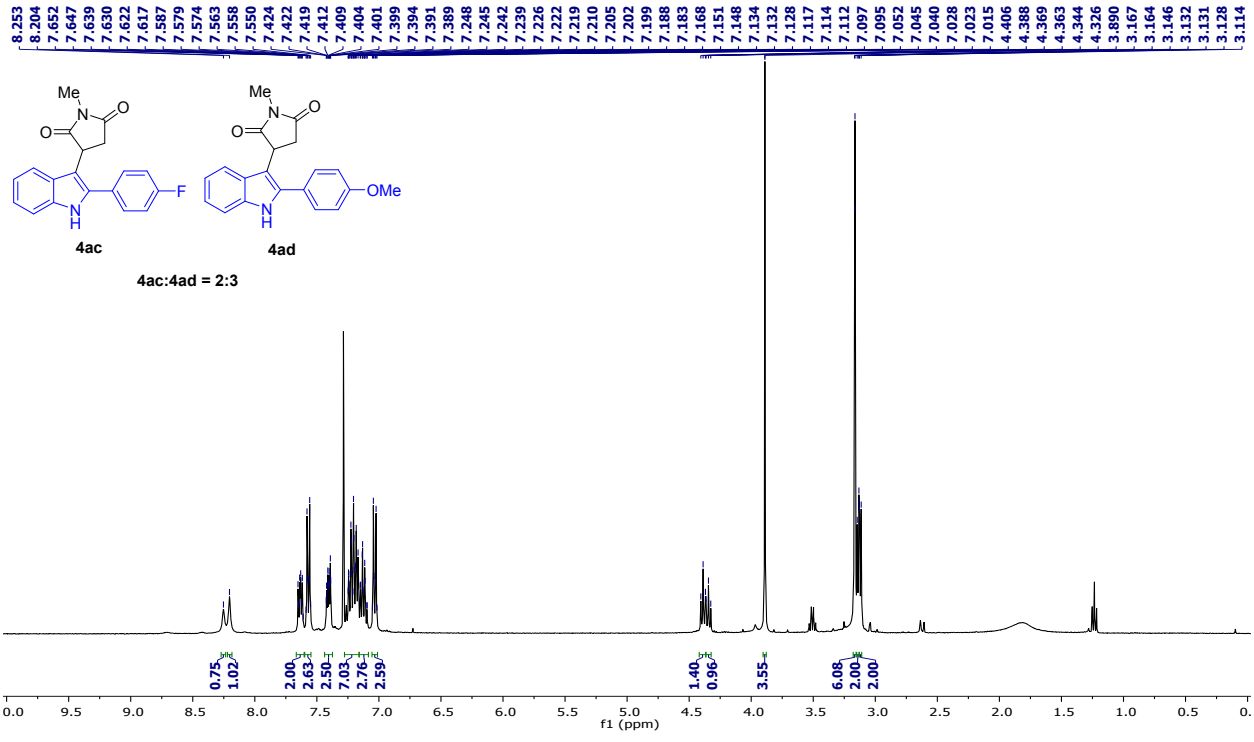
An oven dried 10 mL pressure tube charged with 2-(4-fluorophenyl)-1*H*-indole (**1d**, 0.26 mmol), 2-(4-methoxyphenyl)-1*H*-indole (**1d**, 0.26 mmol), *N*-methyl maleimide (**2a**, 0.52 mmol), $Cu(OAc)_2 \cdot H_2O$ (77 mg, 0.39 mmol), $AgSbF_6$ (18 mg, 20 mol %), NaOAc (43 mg, 0.52 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (8 mg, 2.5 mol %) in dichloro ethane (2 mL). The reaction tube was caped tightly and stirred at 100 °C in an oil bath for 36 h. After completion of reaction, it was cooled to ambient temperature, quenched by water and extracted in ethyl acetate (10 mL × 3). The combined organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The resulting residue was purified by column chromatography (*n*-hexane/EtOAc) on (100-200 mm) size silica gel to afford the mixture of products **3da** and **3ea**. The isolated product was analyzed by ^1H NMR spectrum, and ratio predicted as 3:2.



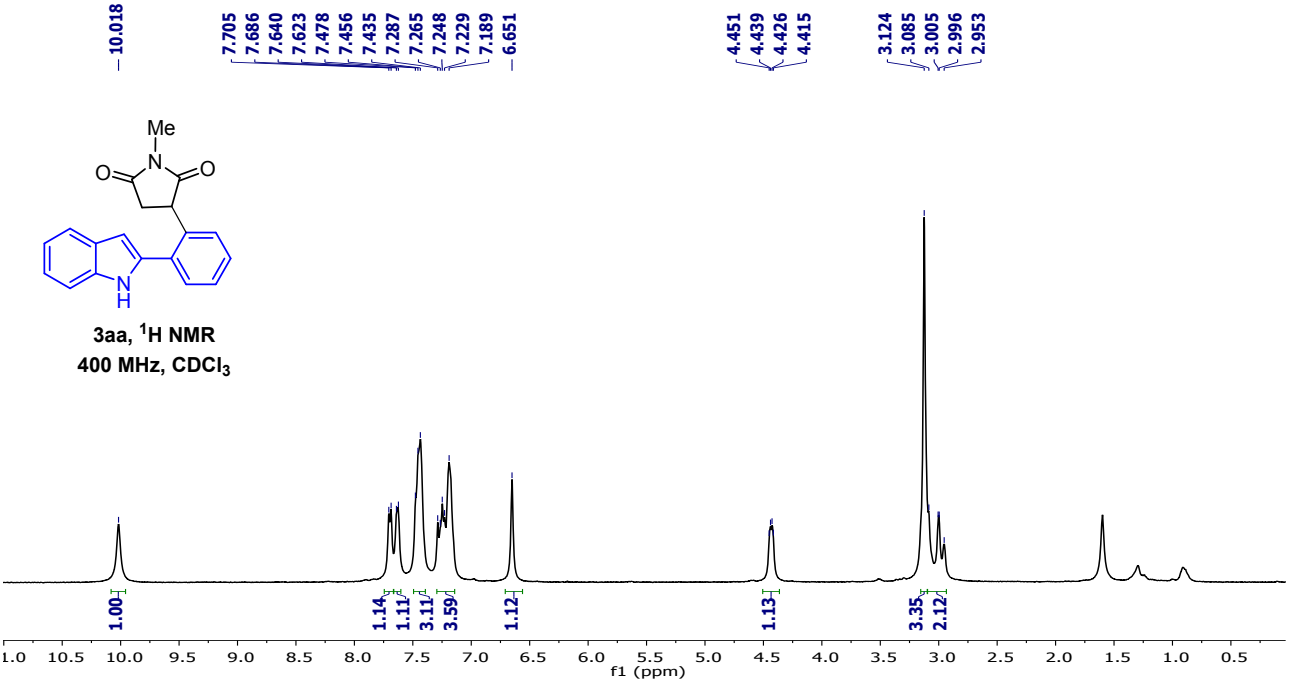
2.2 Competition Experiment for C3-Hydroalkylation:



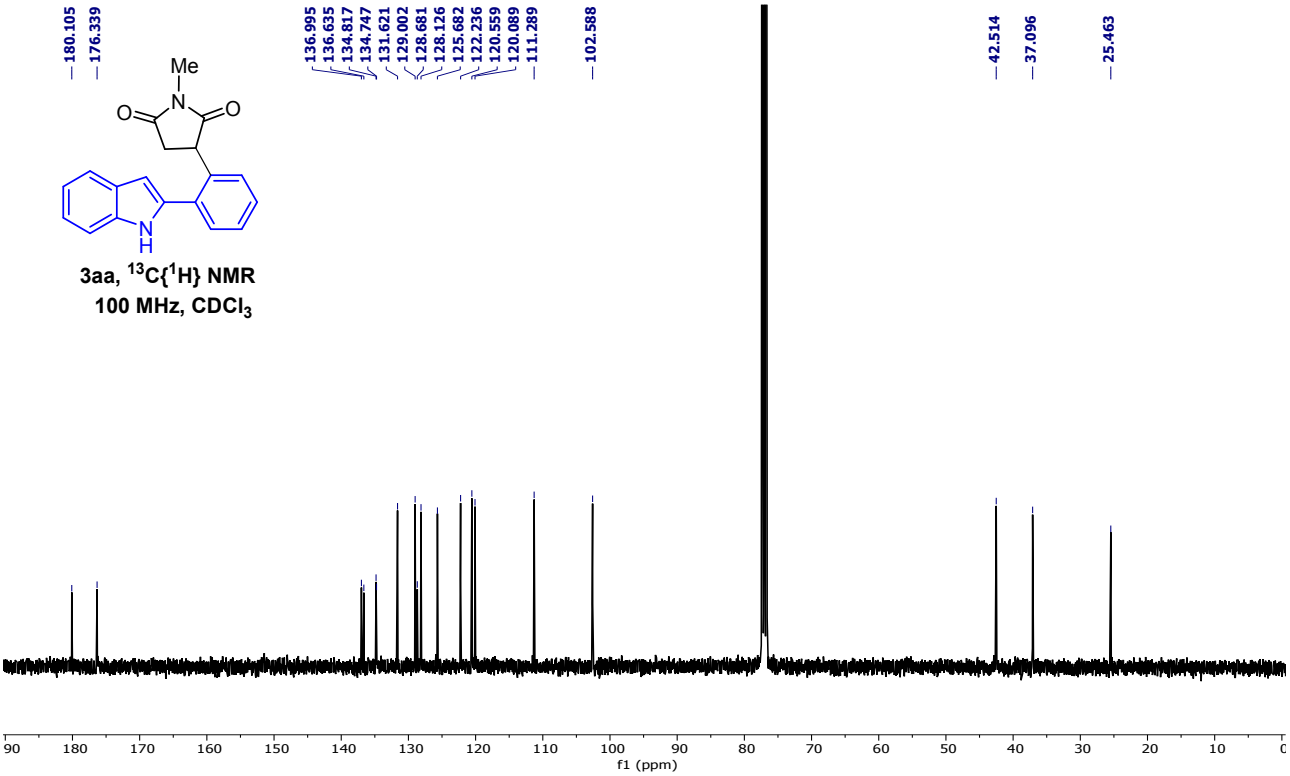
An oven dried 10 mL pressure tube charged with 2-(4-fluorophenyl)-1*H*-indole (**1c**, 0.26 mmol), 2-(4-methoxyphenyl)-1*H*-indole (**1d**, 0.26 mmol), *N*-methyl maleimide (**2a**, 0.52 mmol), and TFE (2 mL). The reaction mixture stirred at 100 °C in oil bath for 24 h. After completion of reaction, it was cooled to ambient temperature, quenched by water and extracted in ethyl acetate (10 mL × 3). The combined organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The resulting residue was purified by column chromatography (*n*-hexane/EtOAc) on (100-200 mm) size silica gel to afford the mixture of products **4ac** and **4ad**. The isolated product was analyzed by ^{1}H NMR spectrum, and ratio predicted as 2:3.



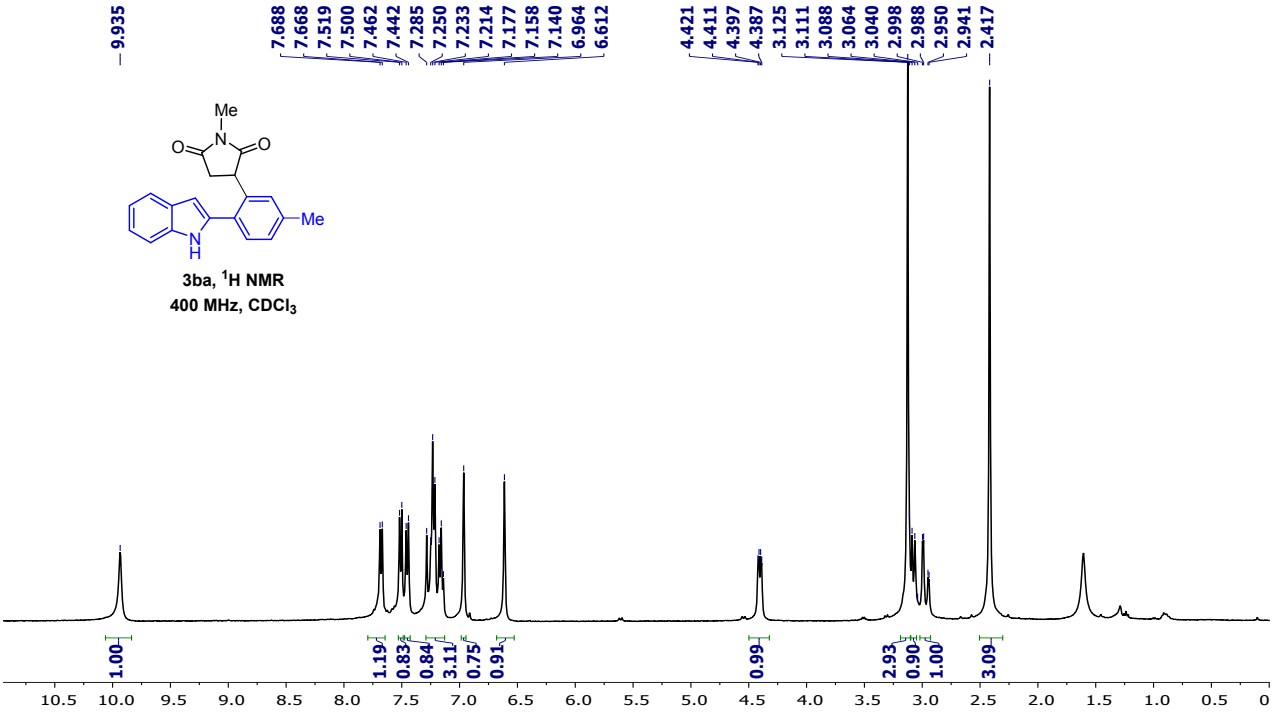
3. Copies of ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of 3 and 4



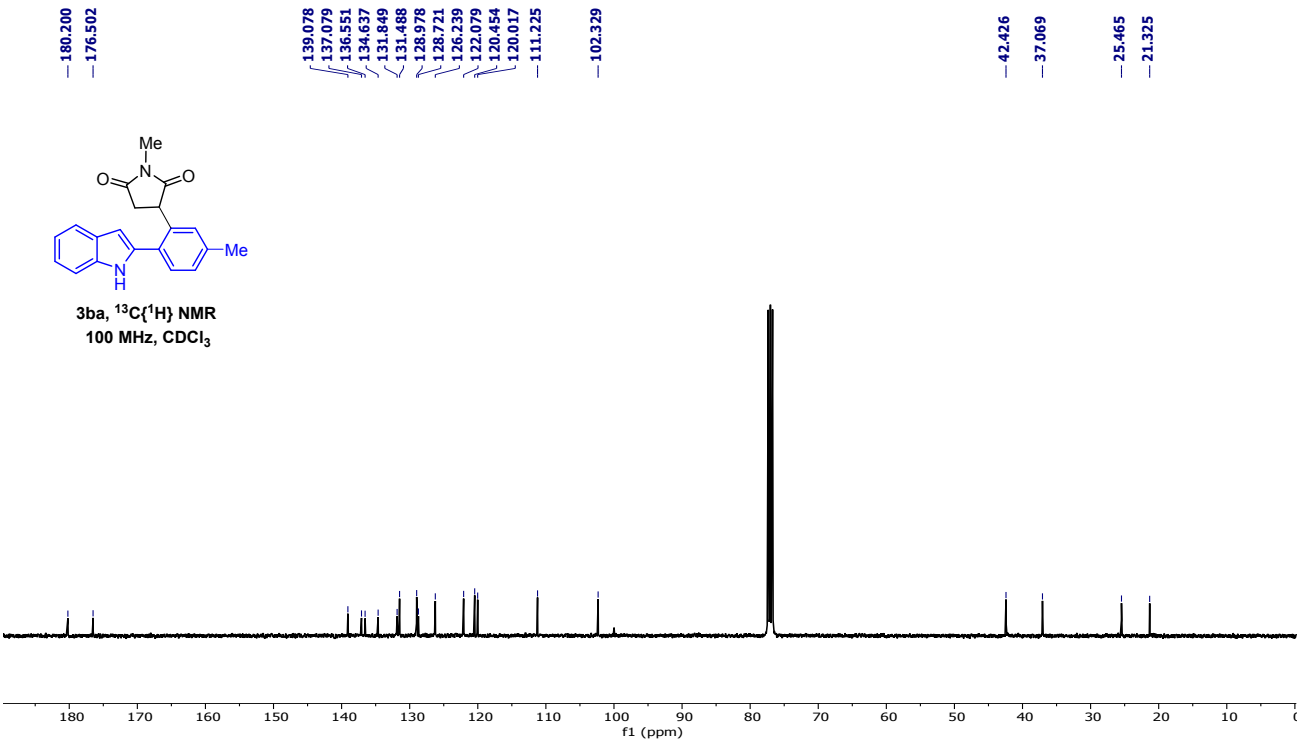
3aa, ^{1}H NMR
400 MHz, $CDCl_3$



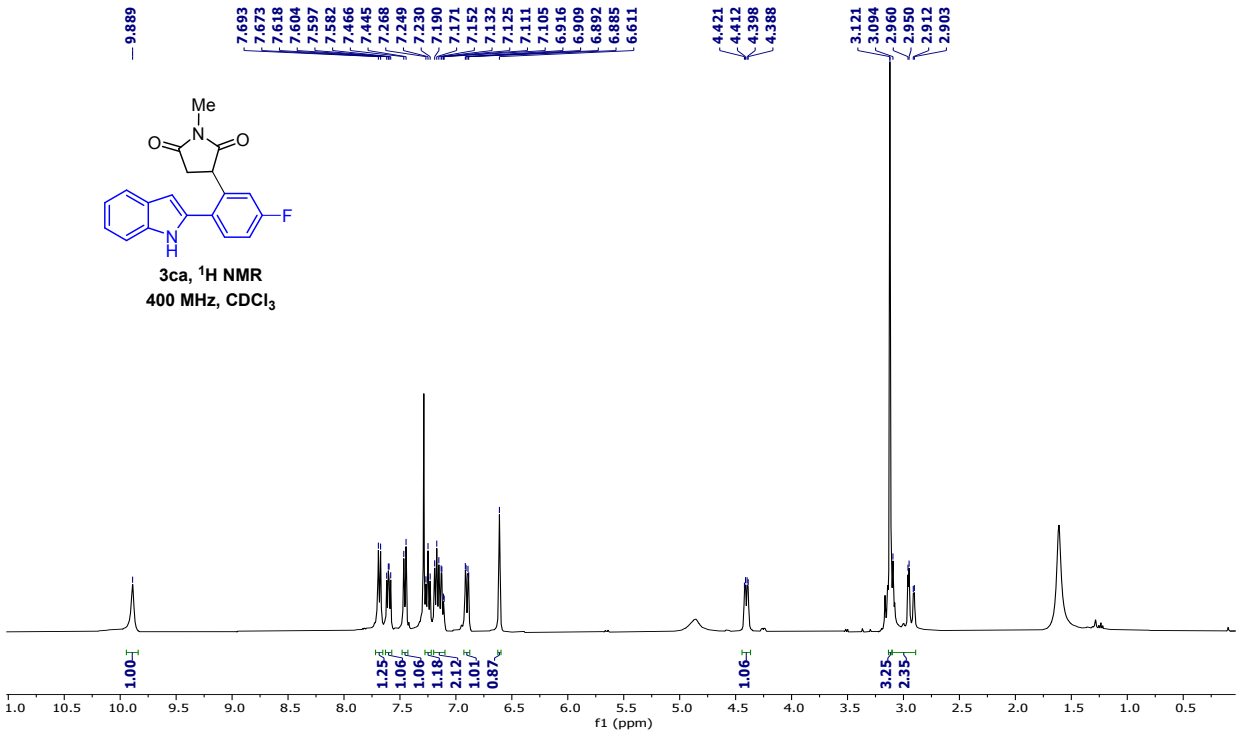
3aa, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



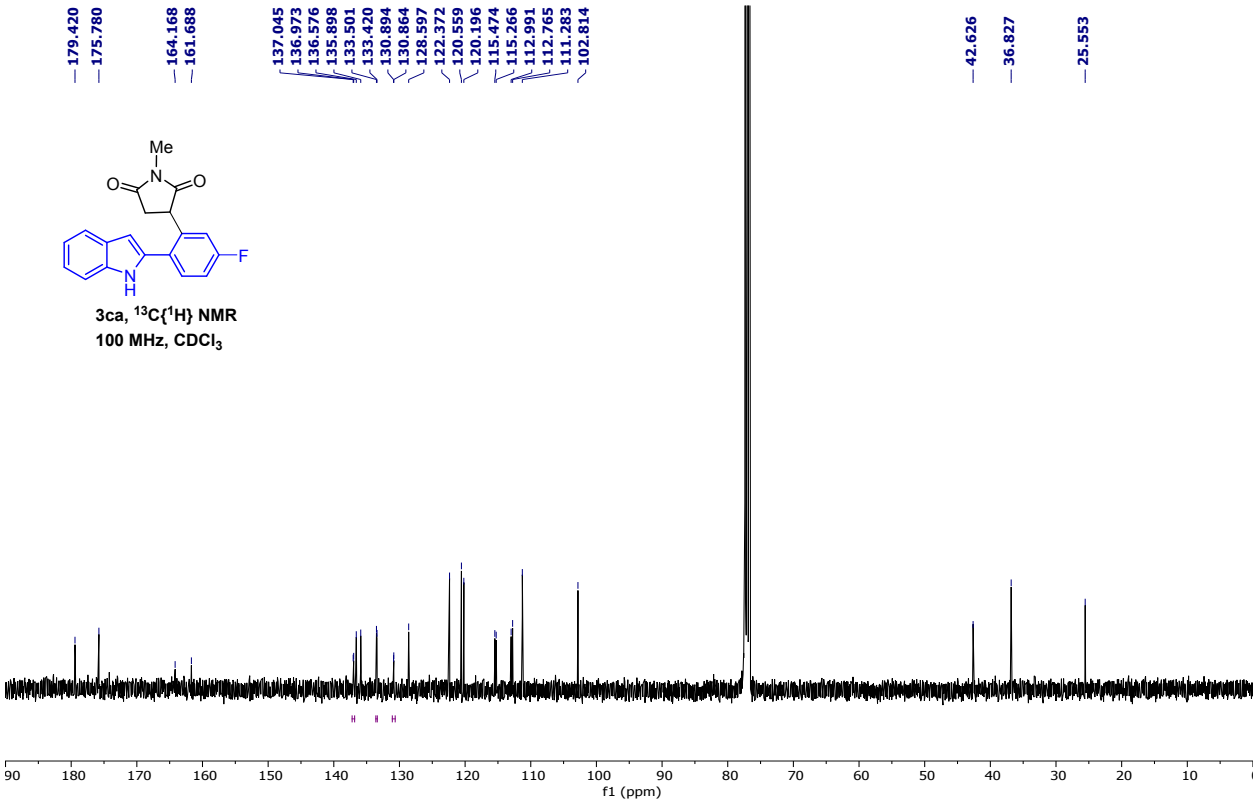
3ba, ^{1}H NMR
400 MHz, $CDCl_3$



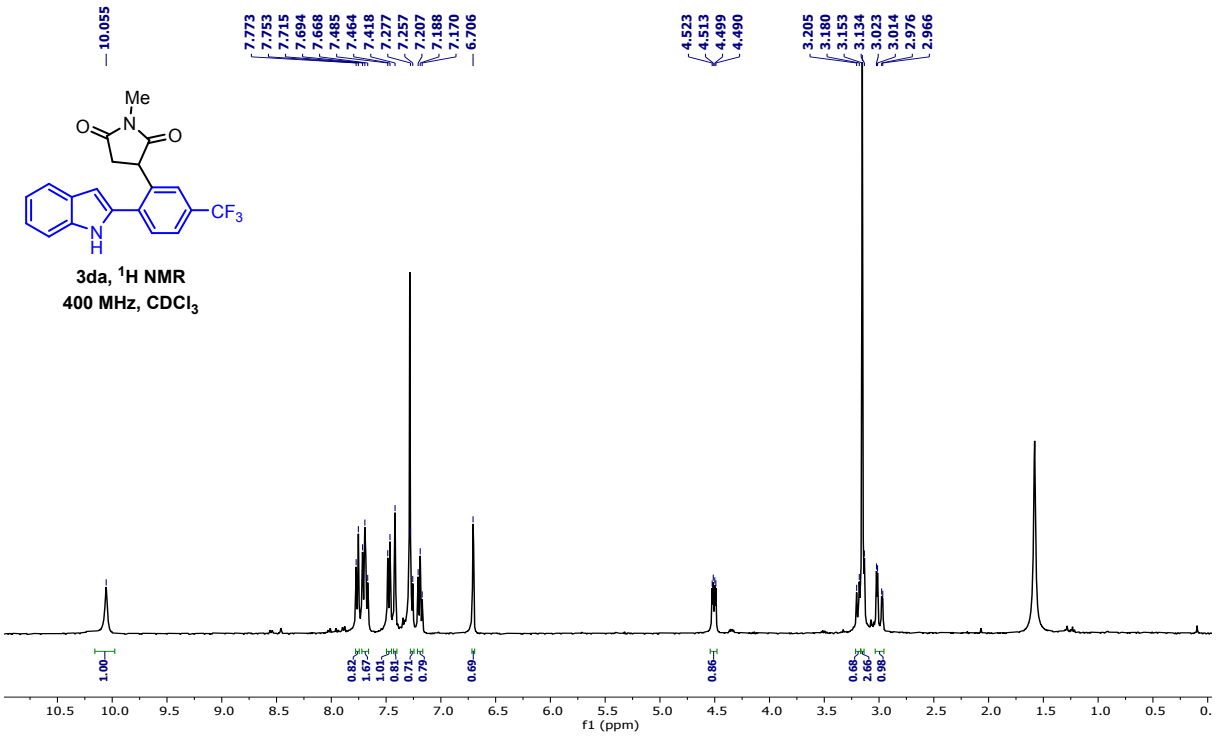
3ba, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



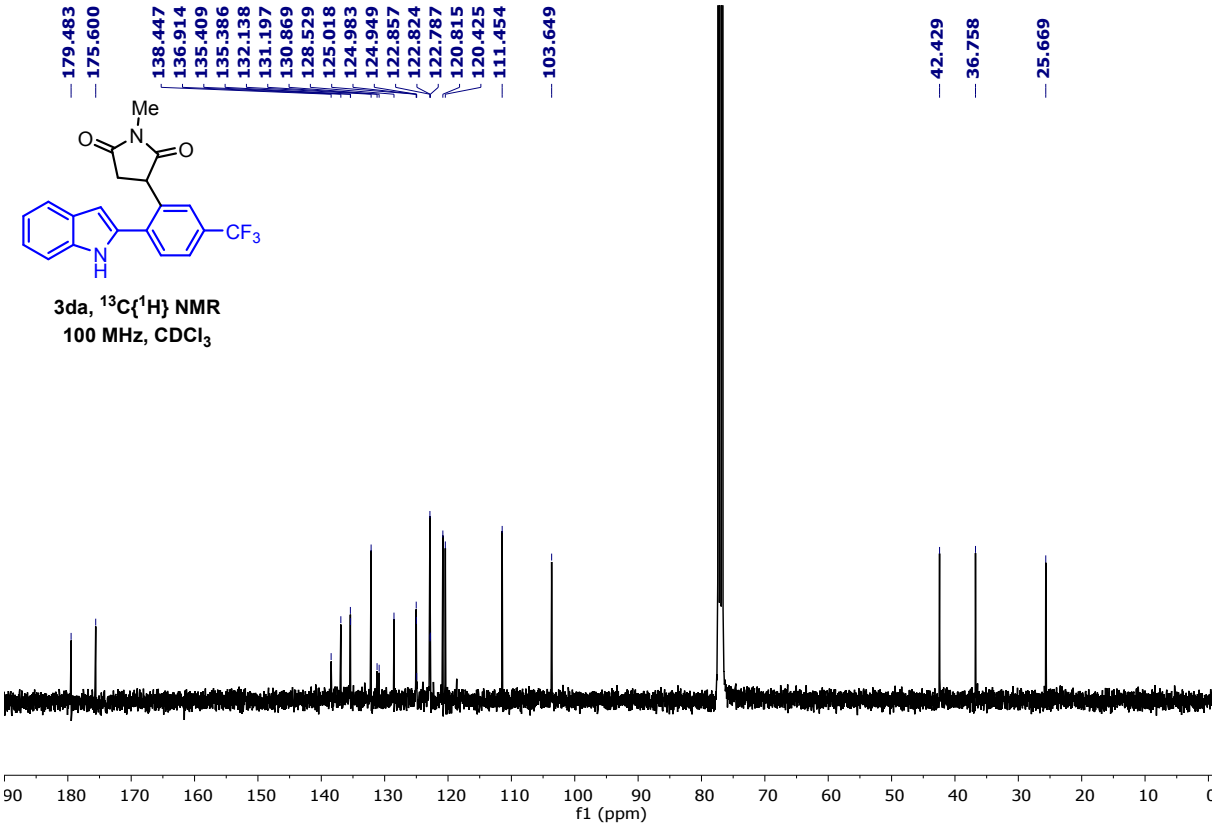
3ca, ^{1}H NMR
400 MHz, $CDCl_3$



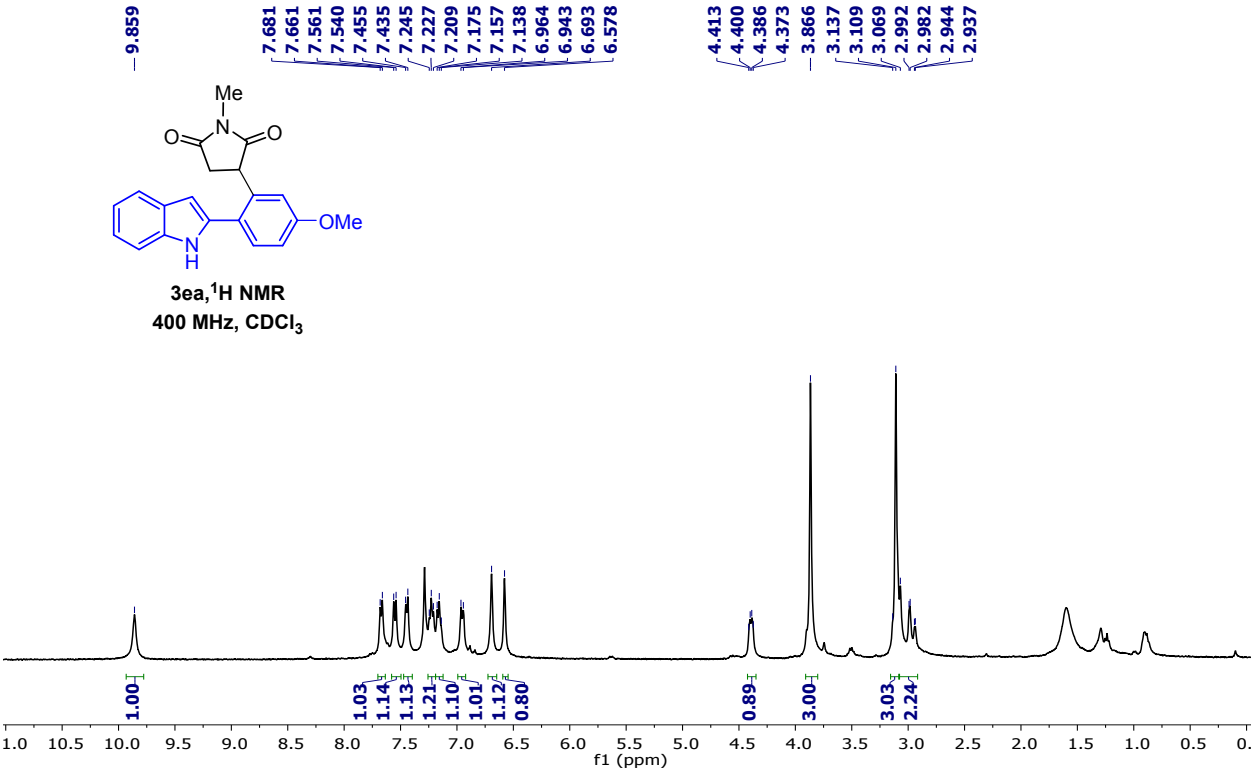
3ca, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



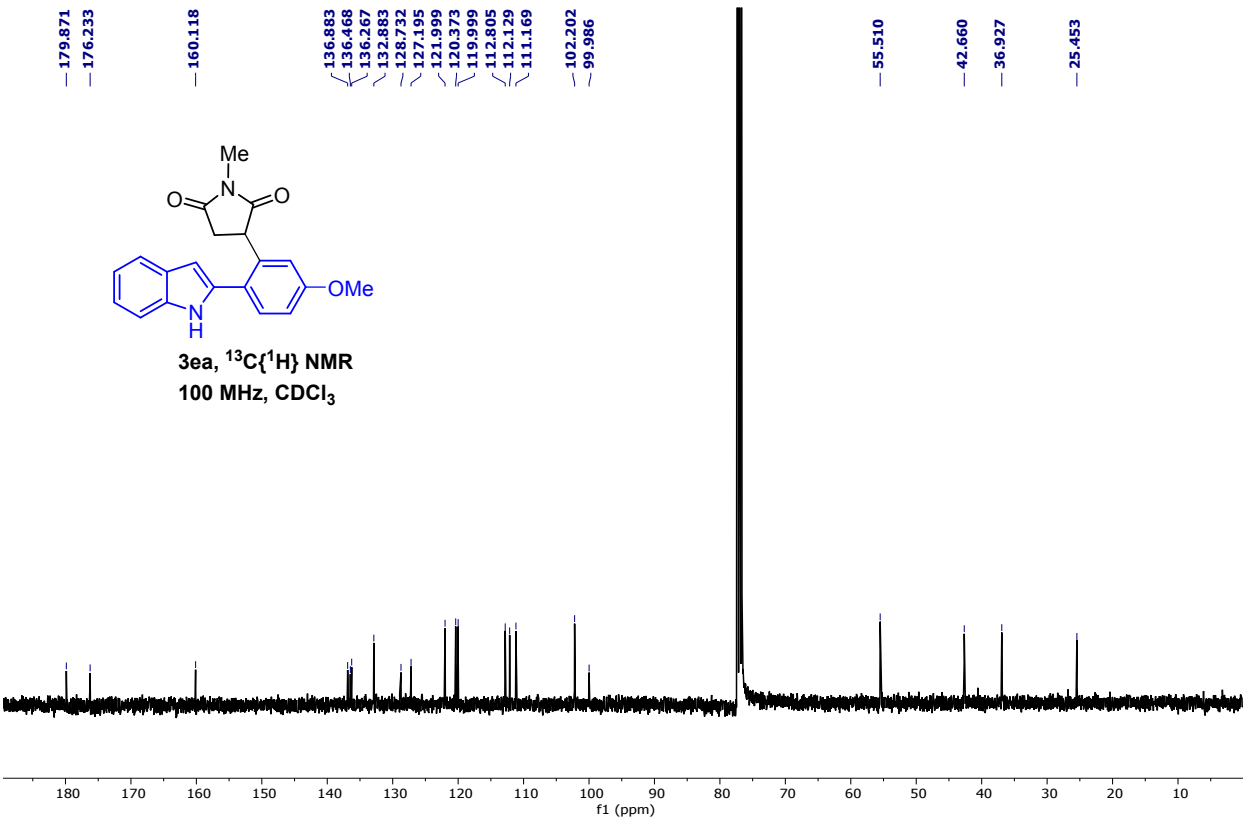
3da, ^{1}H NMR
400 MHz, $CDCl_3$



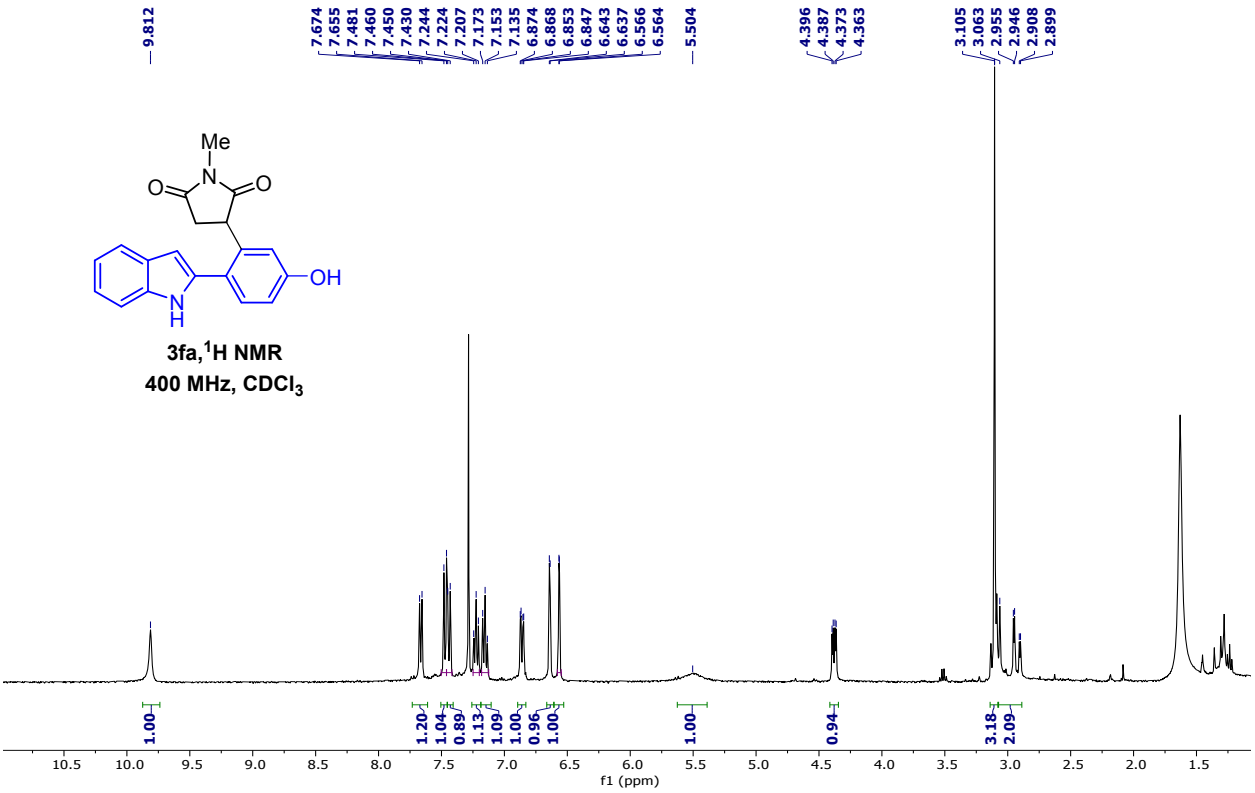
3da, ^{13}C{^{1}H} NMR
100 MHz, $CDCl_3$



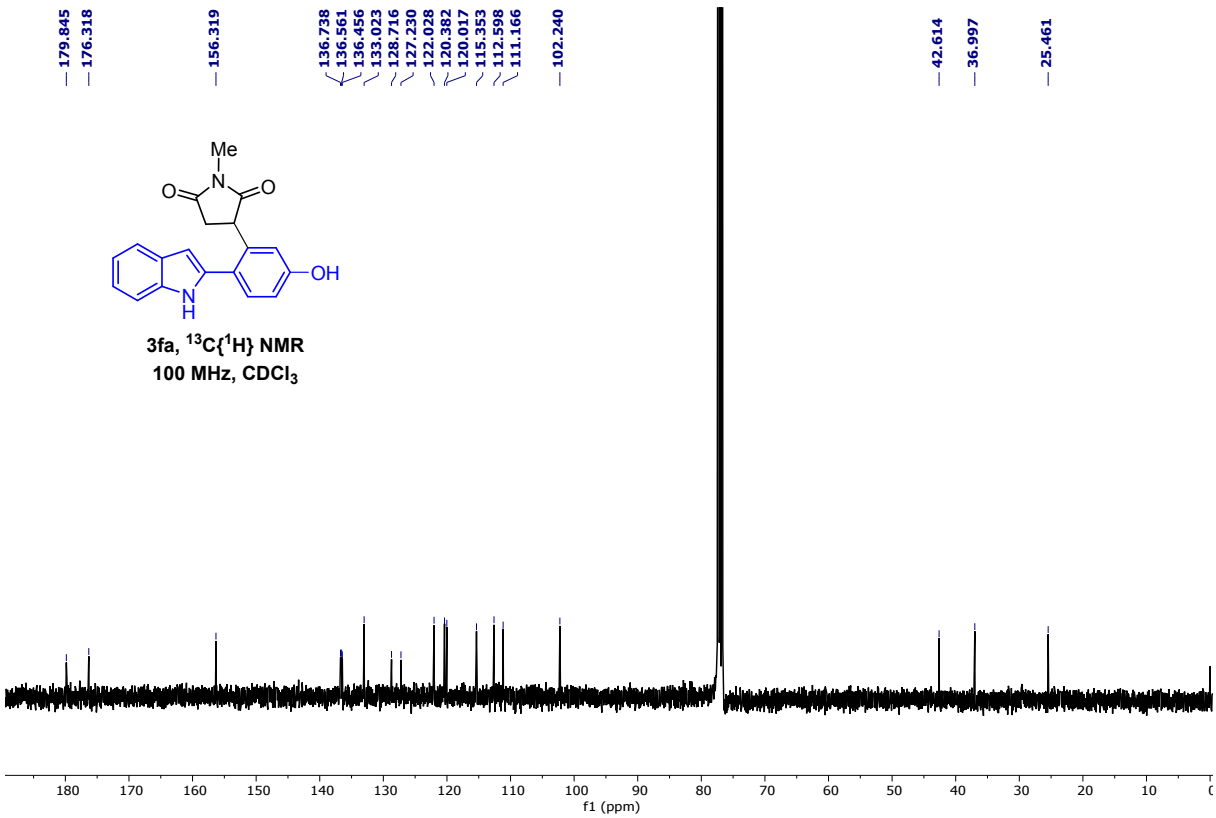
3ea, ^{1}H NMR
400 MHz, $CDCl_3$



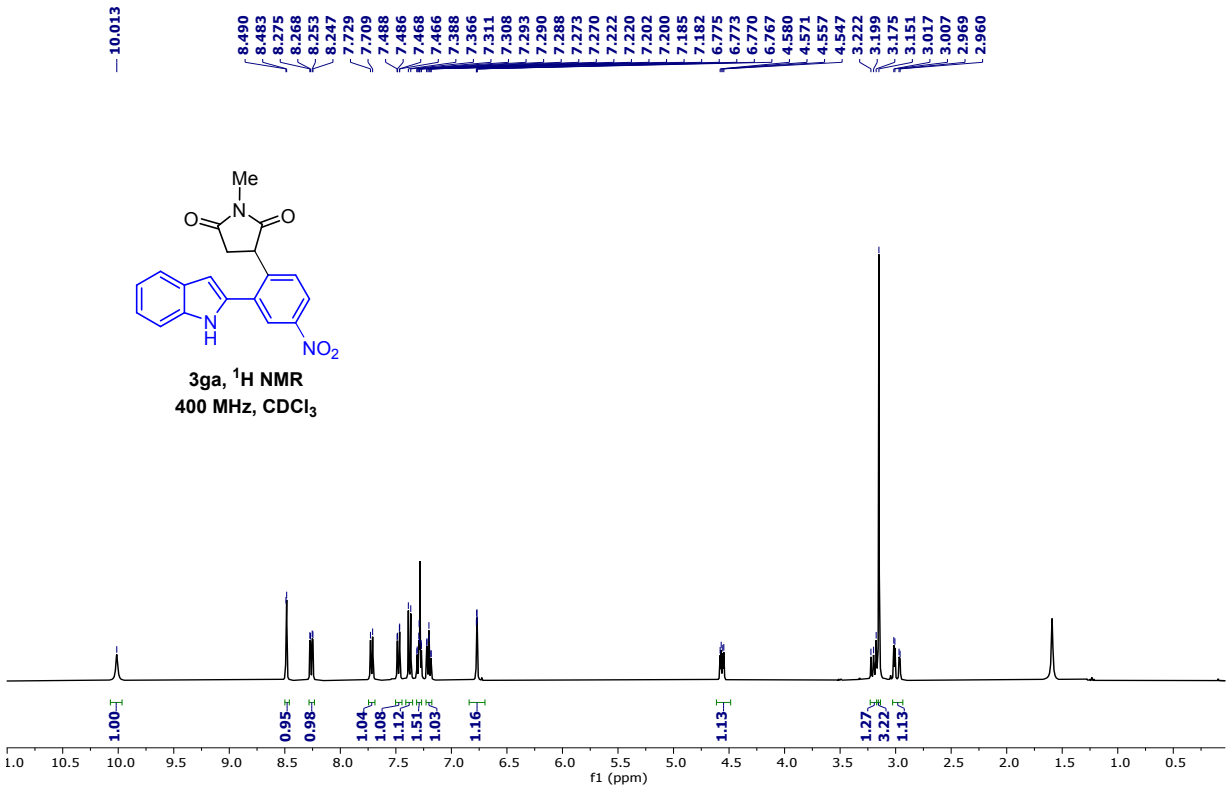
3ea, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



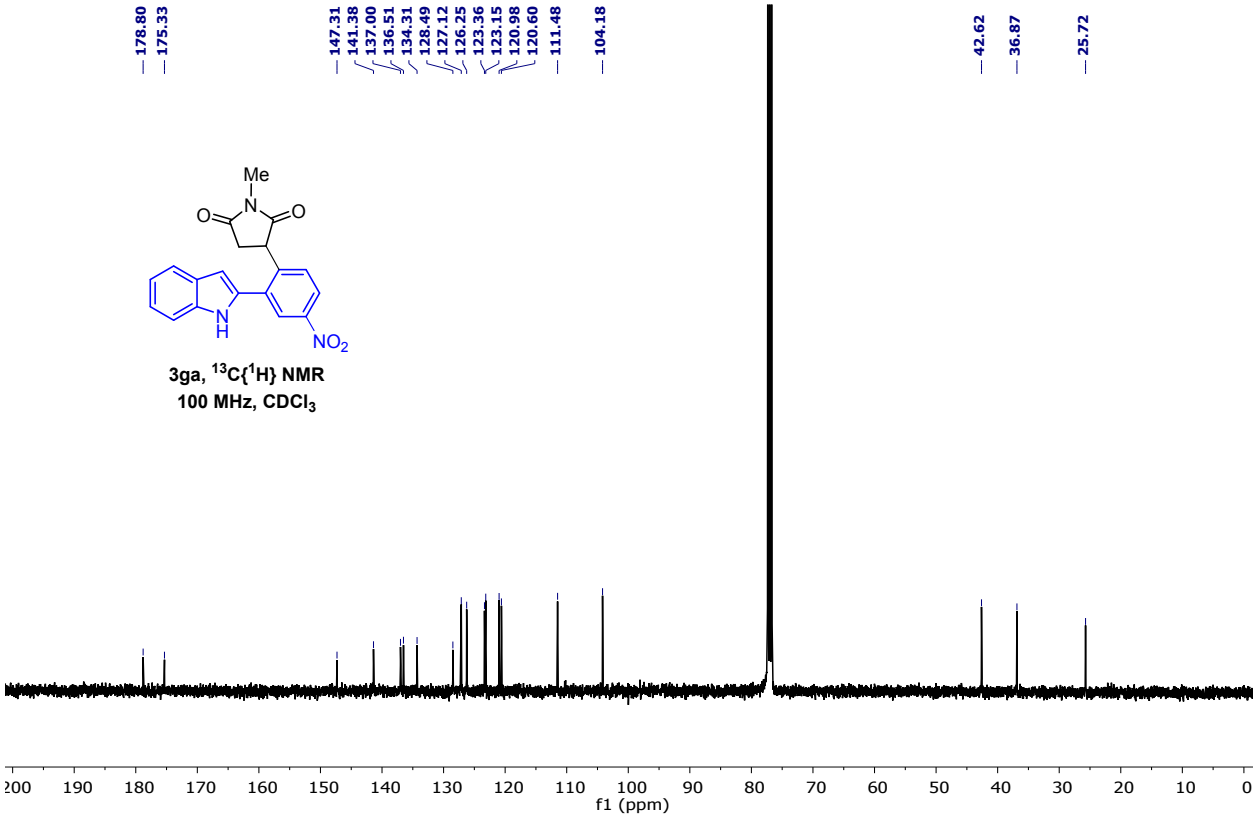
3fa,^{1}H NMR
400 MHz, $CDCl_3$



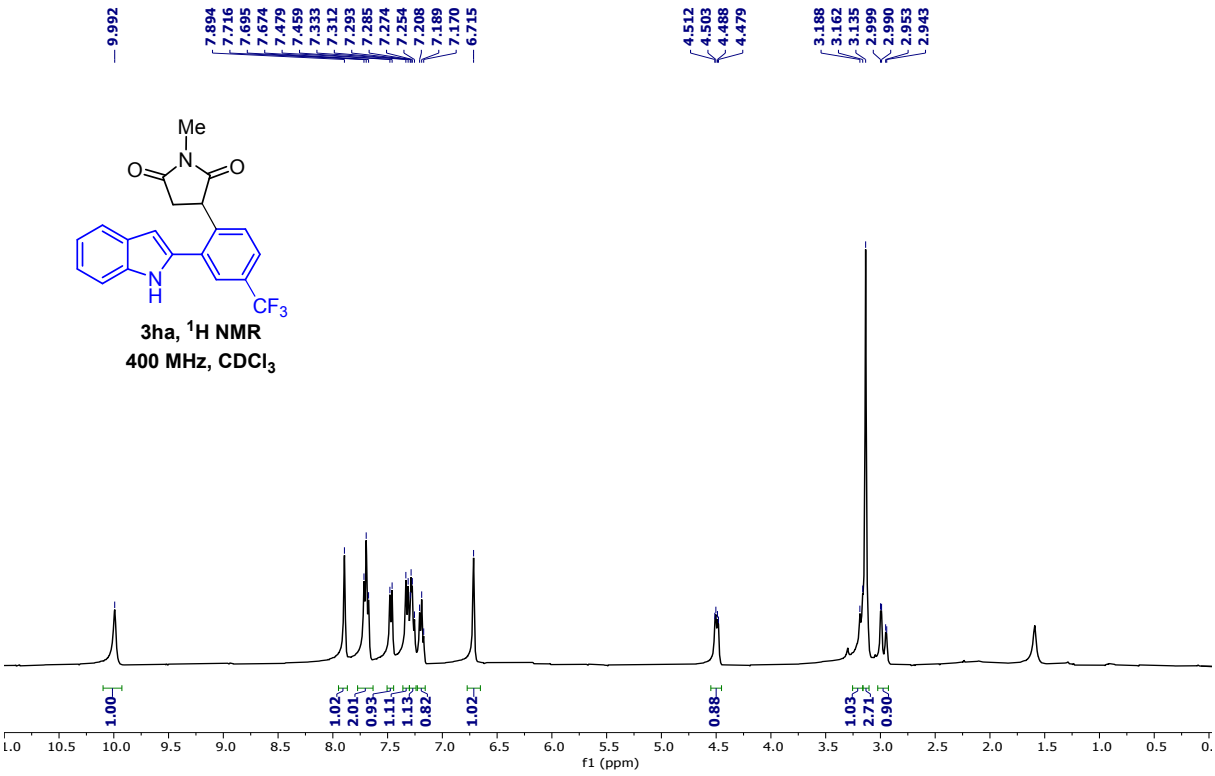
3fa, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



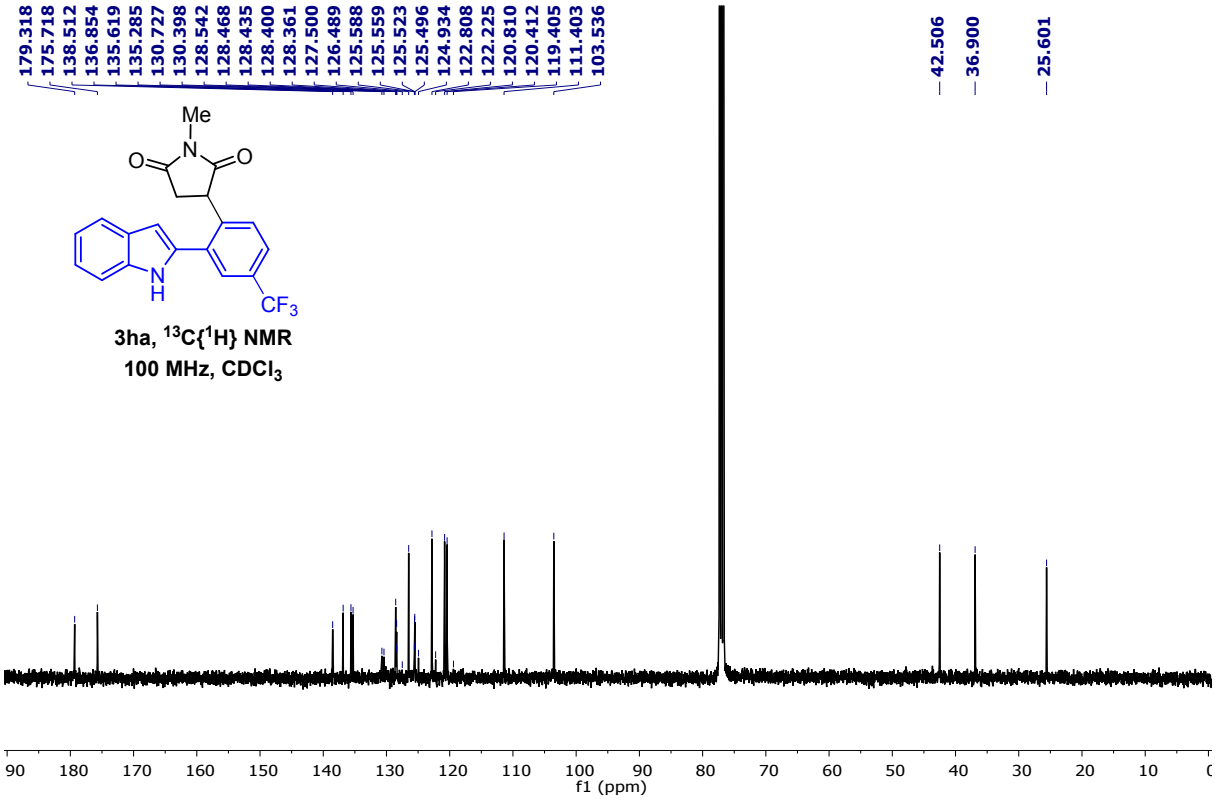
3ga, ^{1}H NMR
400 MHz, $CDCl_3$



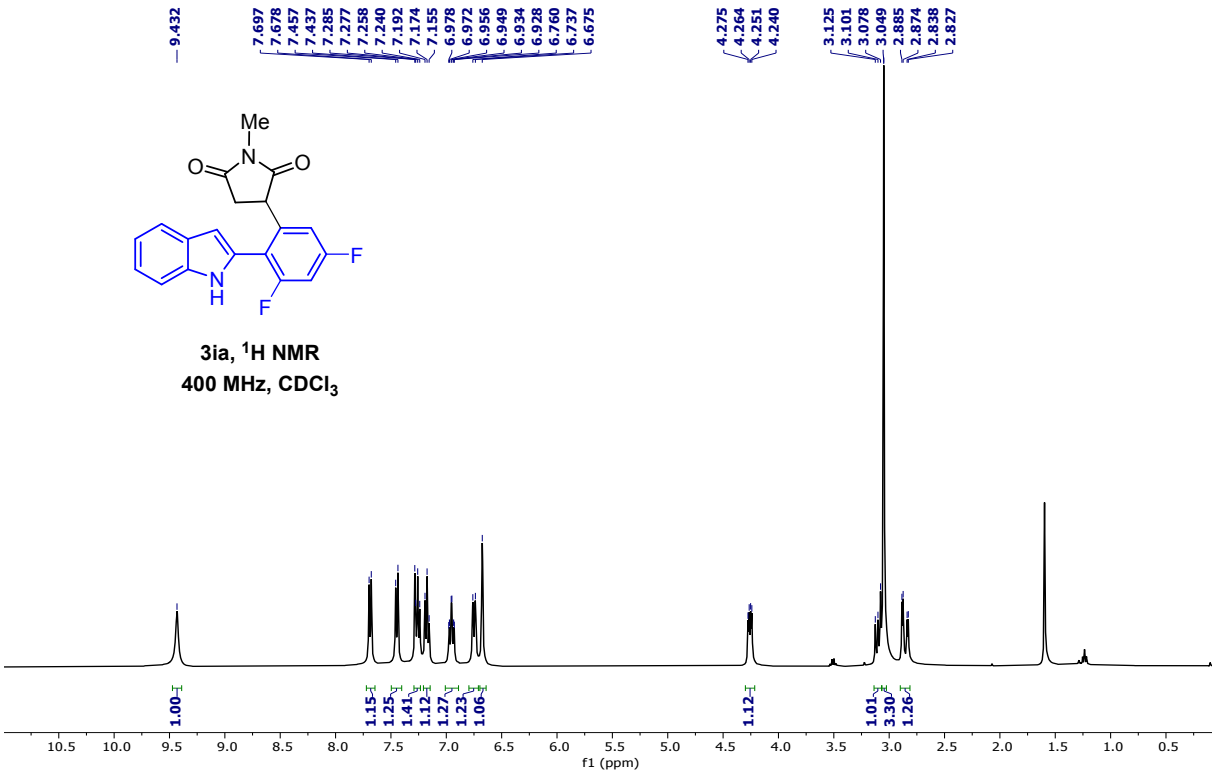
3ga, ^{13}C{^{1}H} NMR
100 MHz, $CDCl_3$



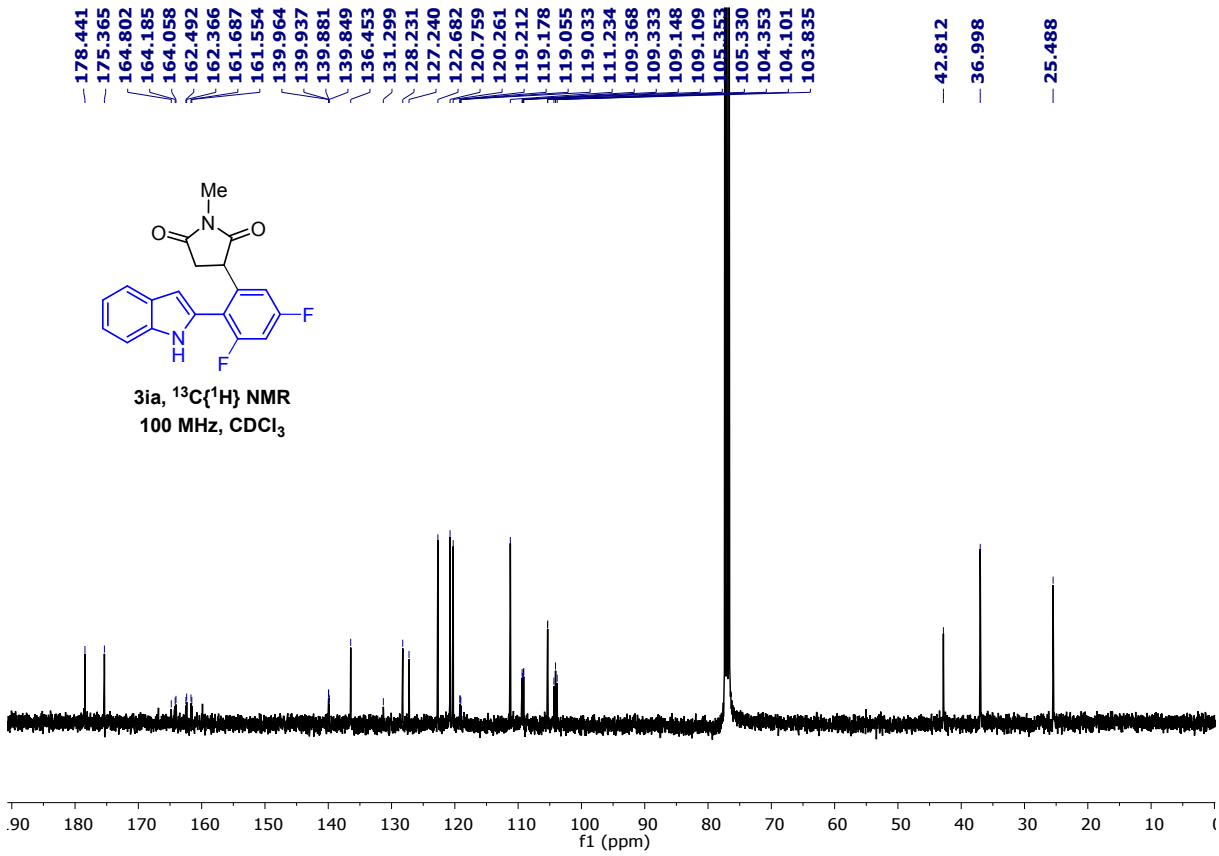
3ha, ^{1}H NMR
400 MHz, $CDCl_3$



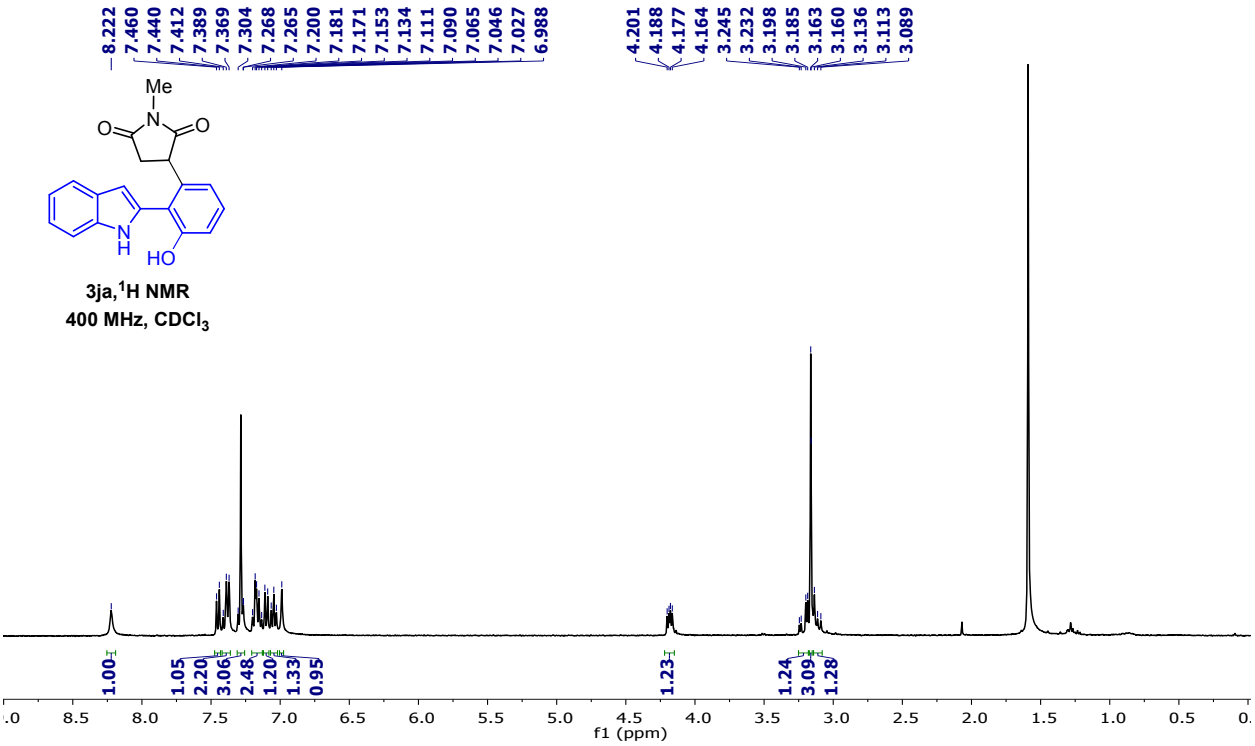
3ha, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



3ia, ^{1}H NMR
400 MHz, $CDCl_3$



3ia, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



3ja,^{1}H NMR
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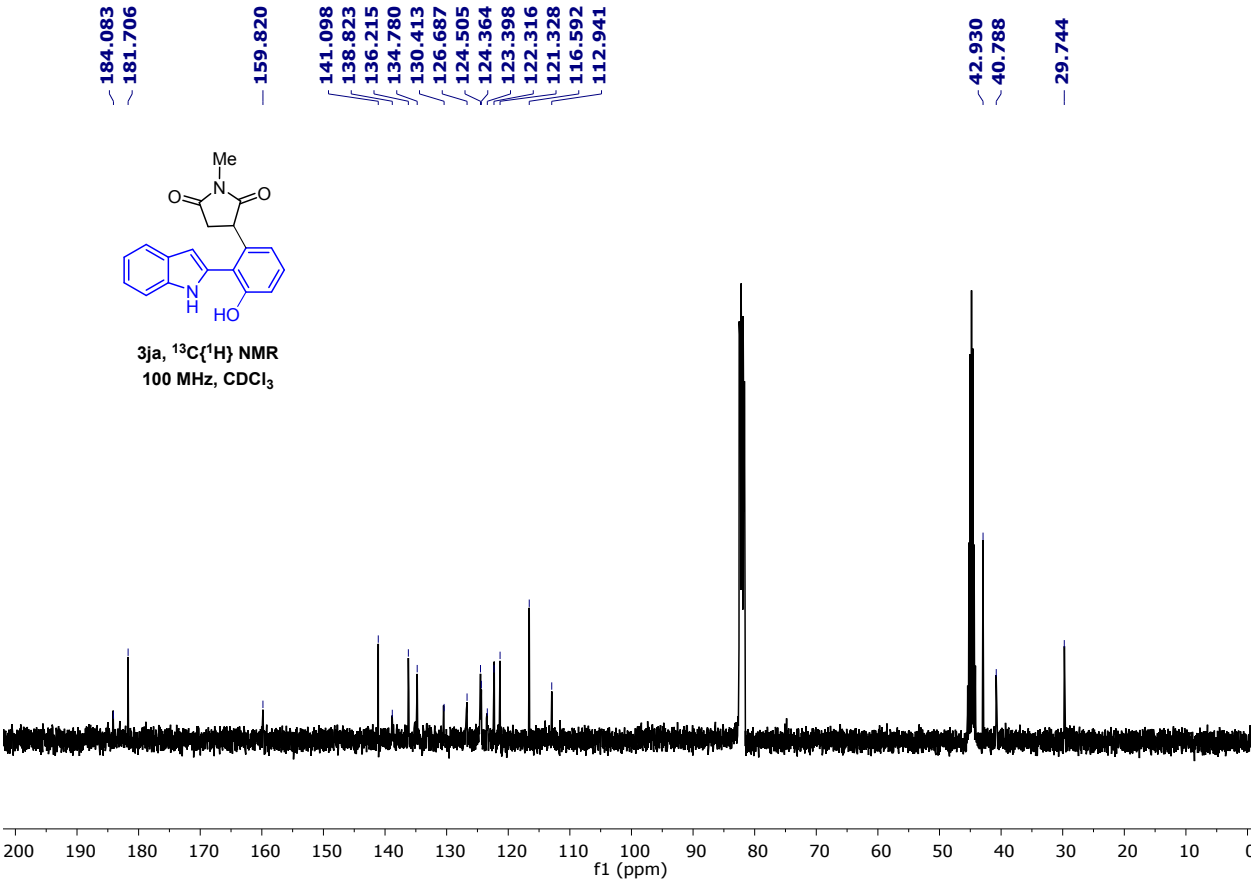

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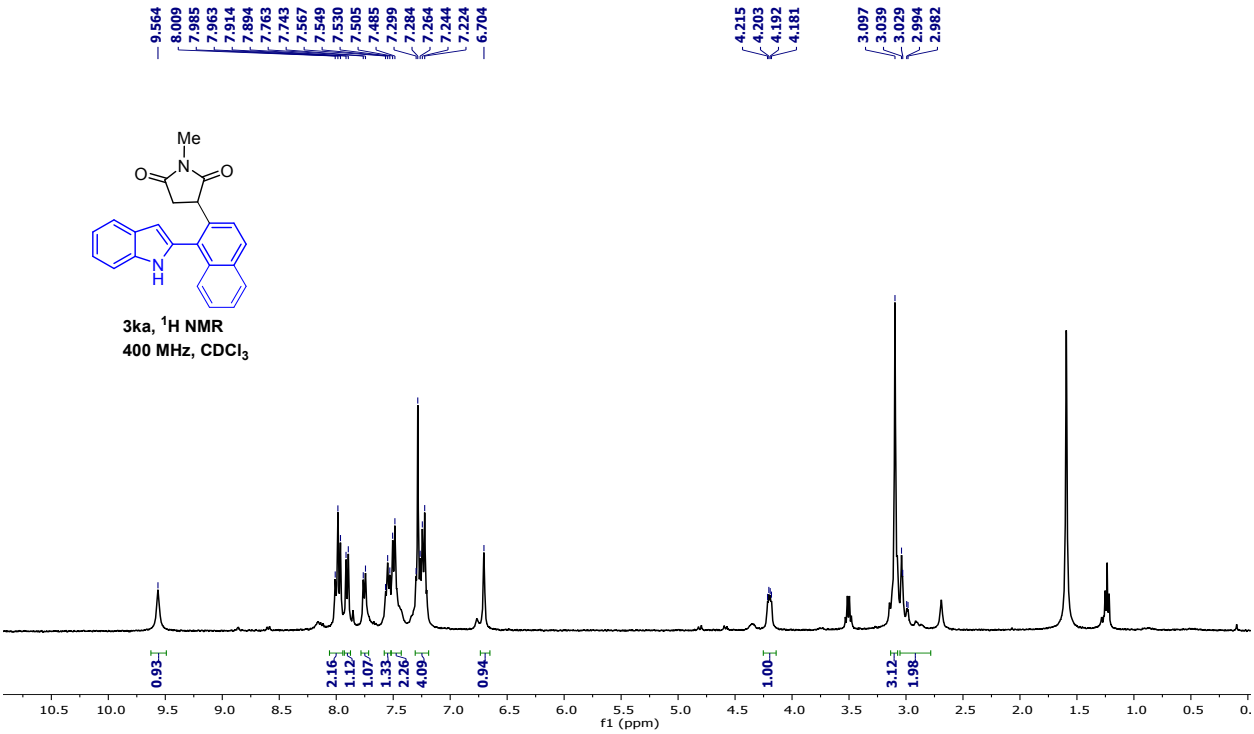

3ka, ^{1}H NMR
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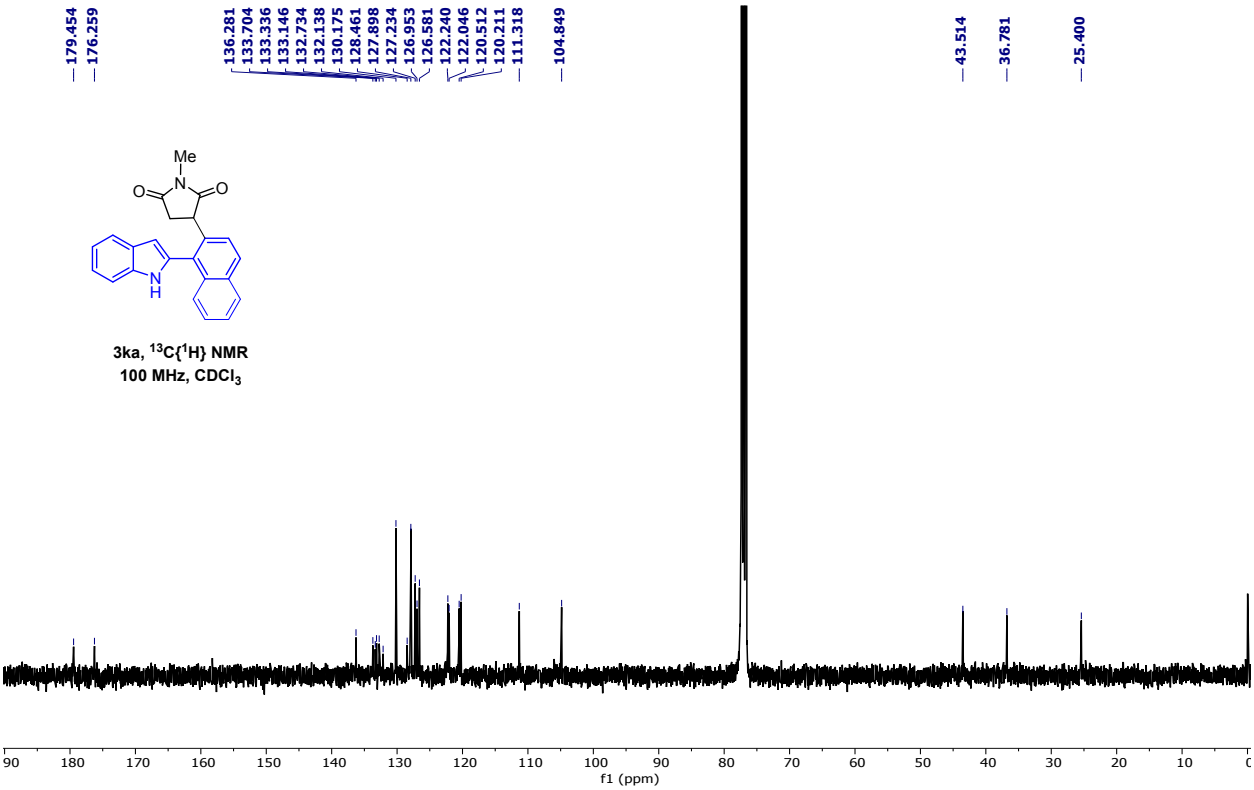

3ka, $^{13}C\{^{1}H\}$ NMR
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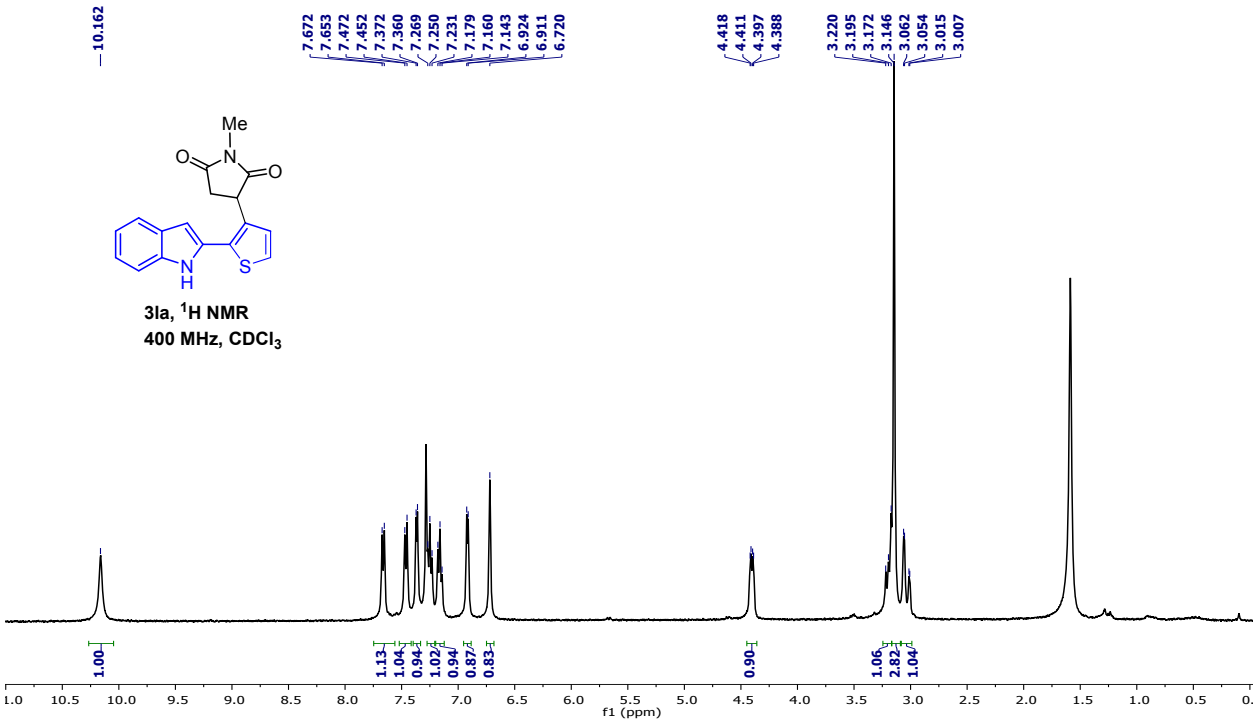
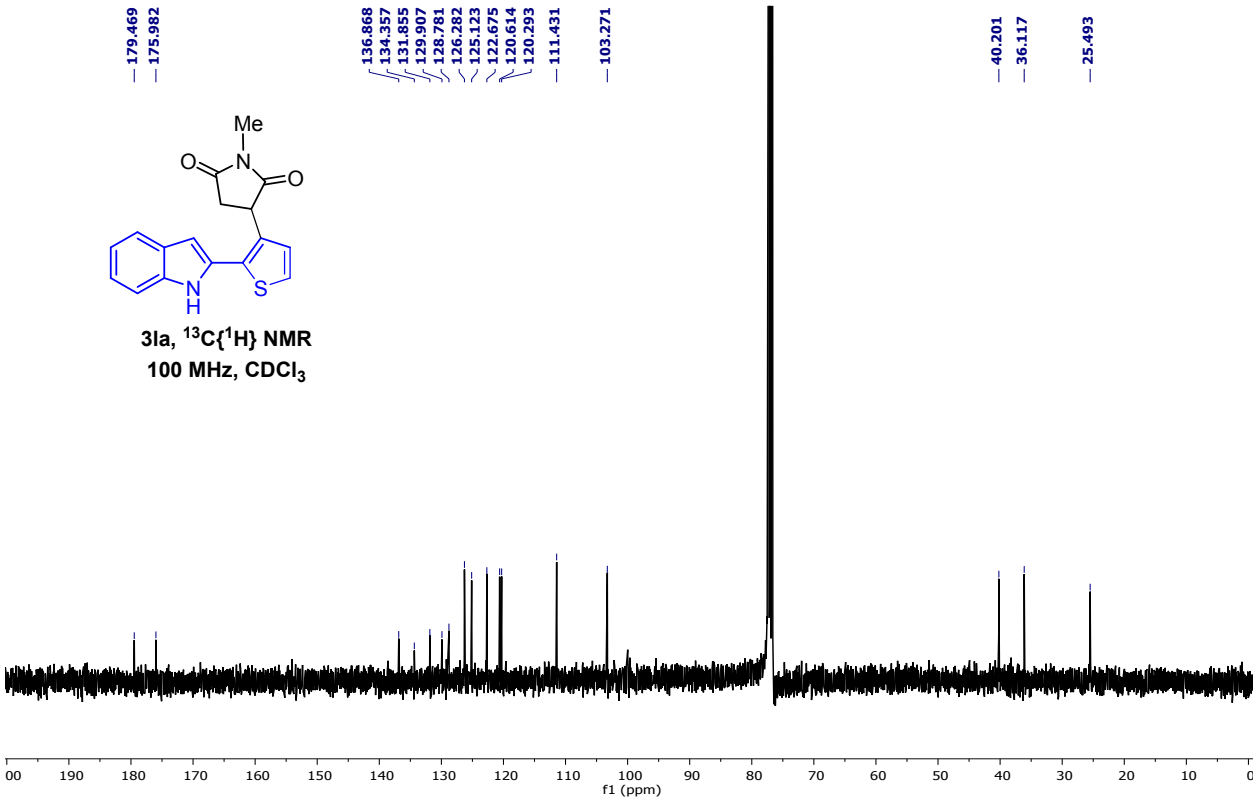


3Ia, ^{1}H NMR
400 MHz, $CDCl_3$



3Ia, ^{13}C{^{1}H} NMR
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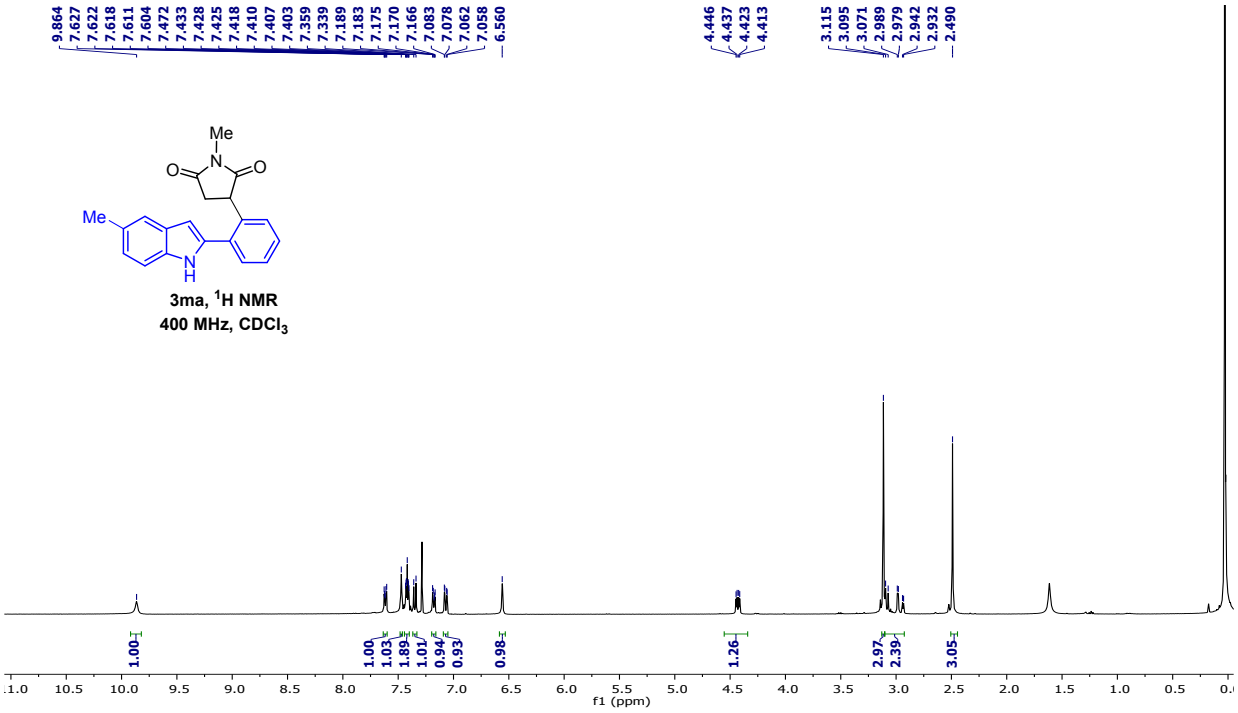
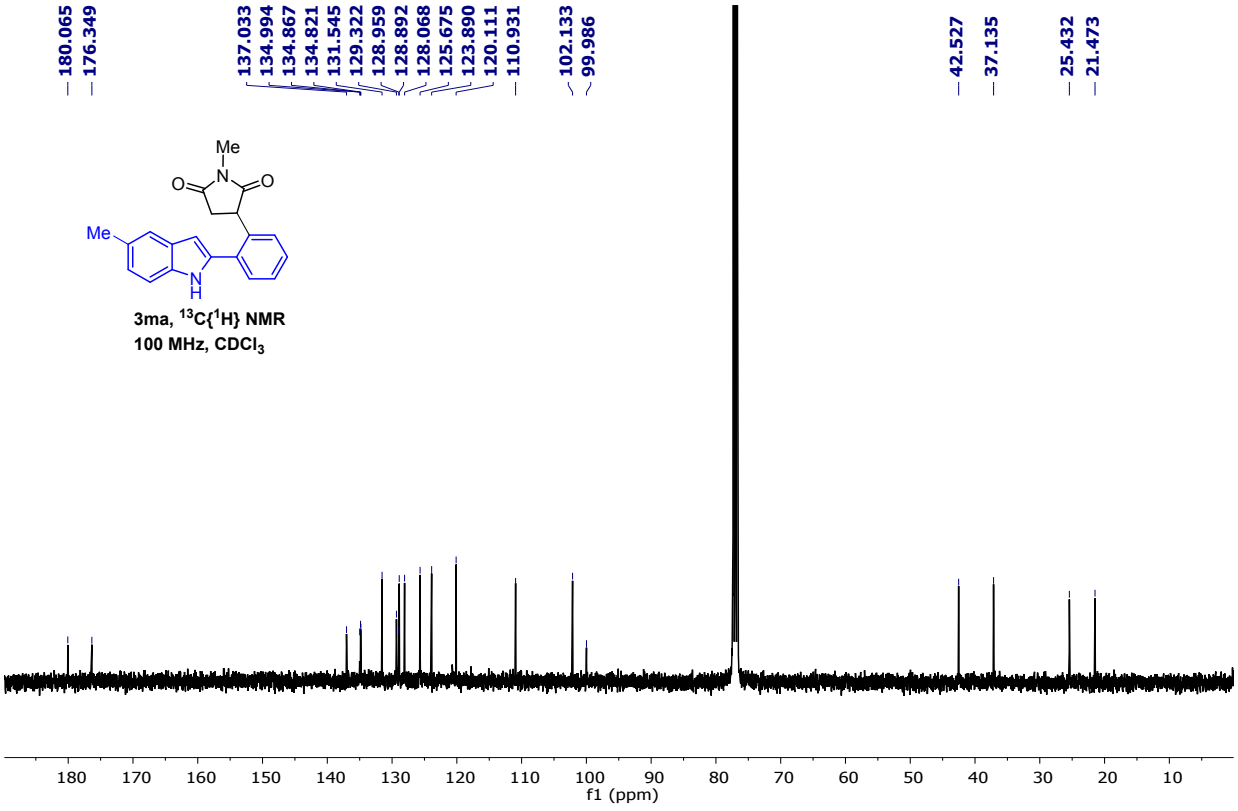
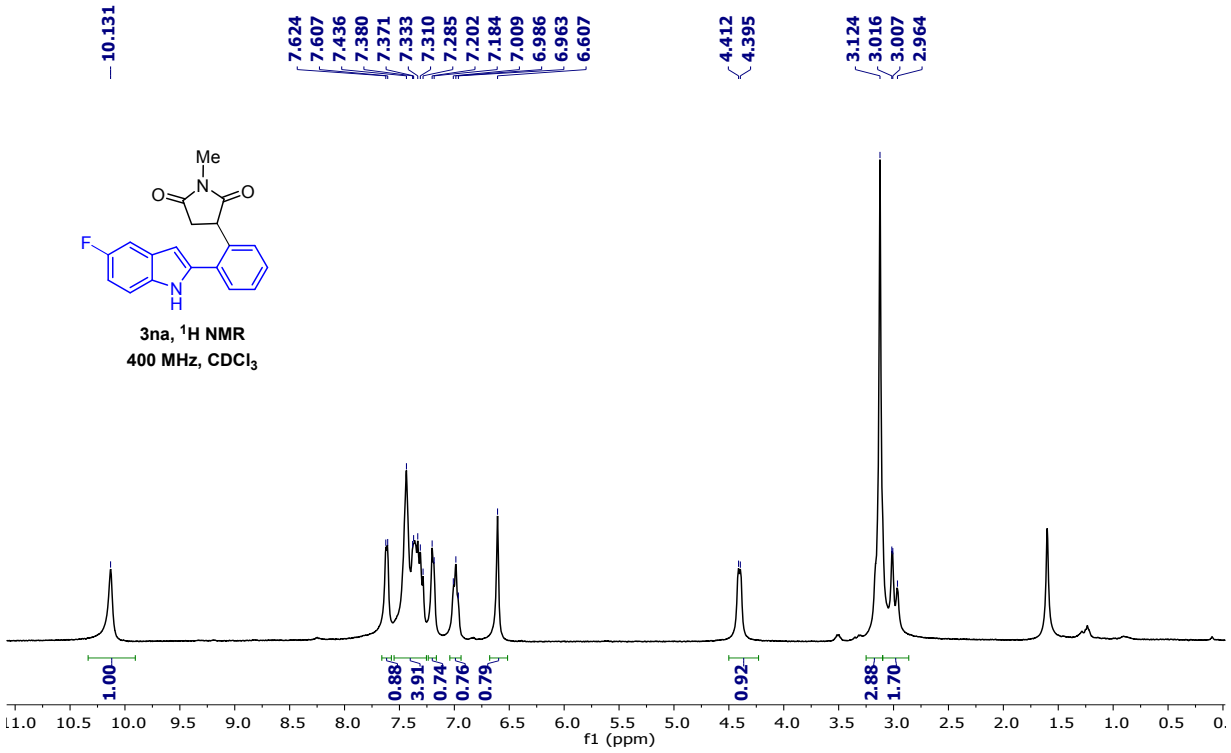


3ma, ^{1}H NMR
400 MHz, $CDCl_3$



3ma, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



3na, ^{1}H NMR
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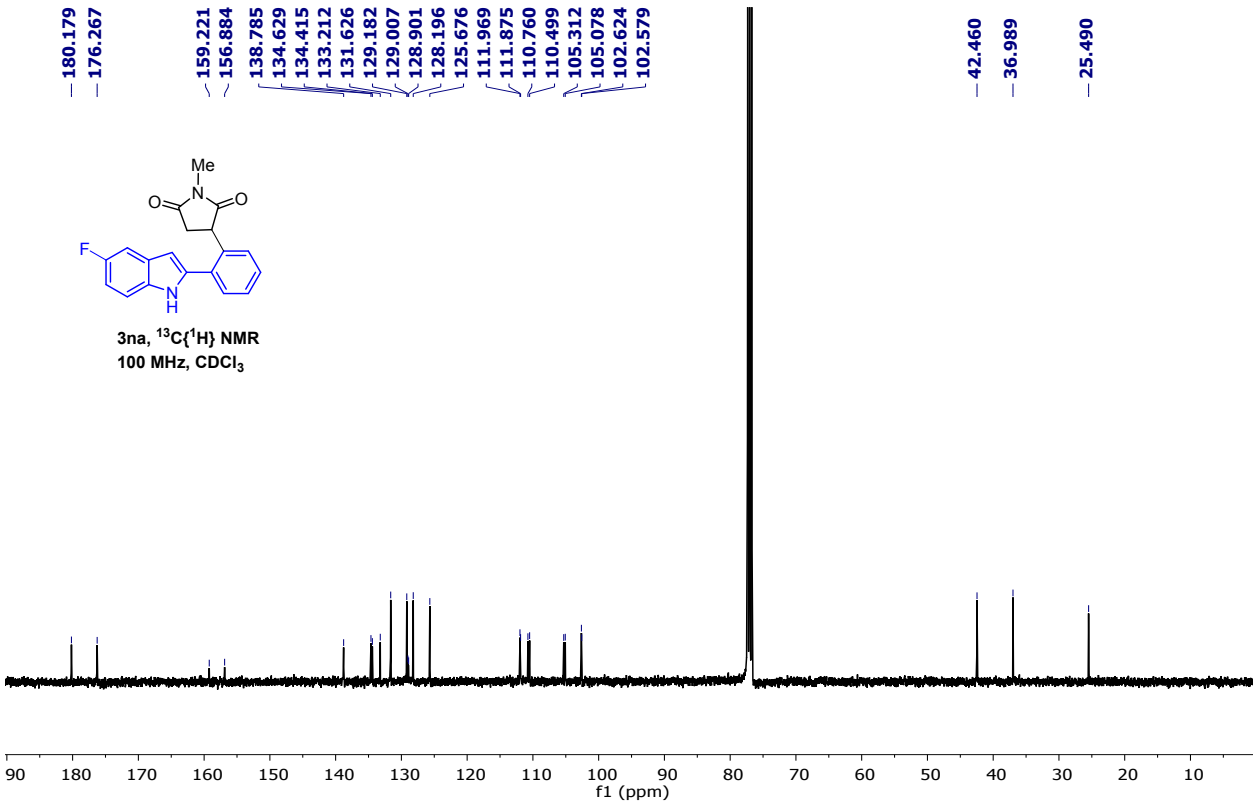
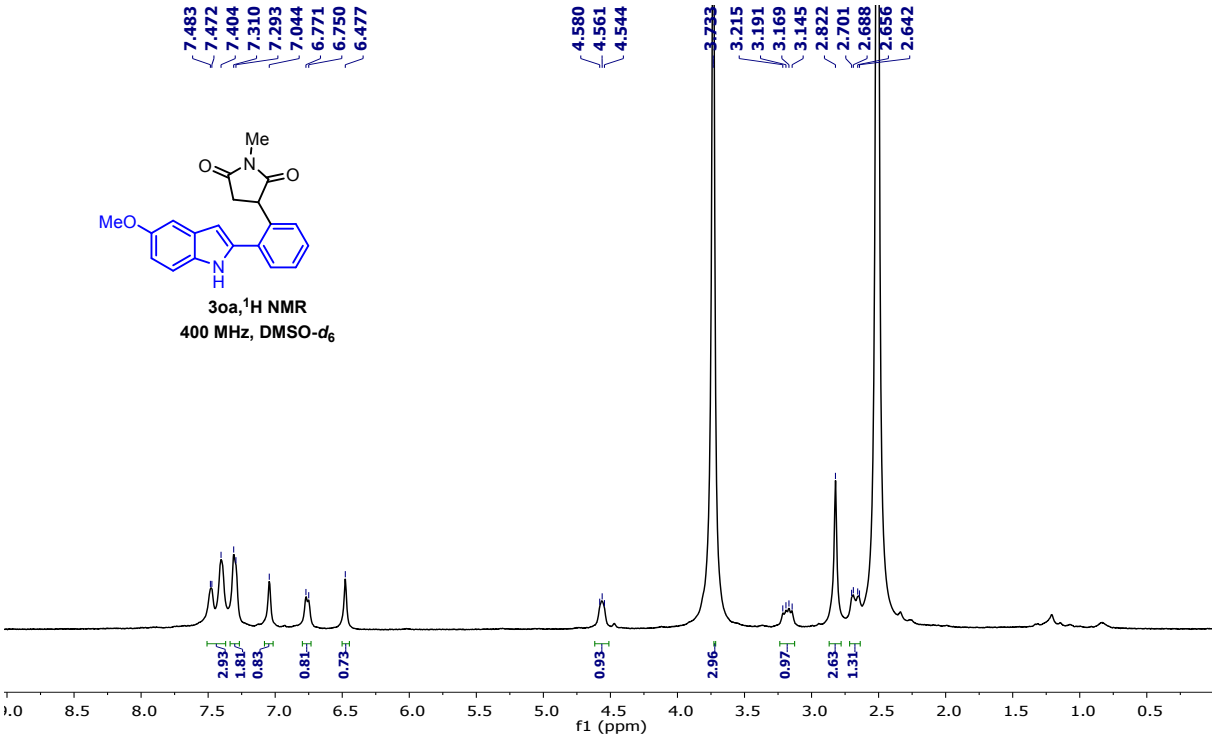
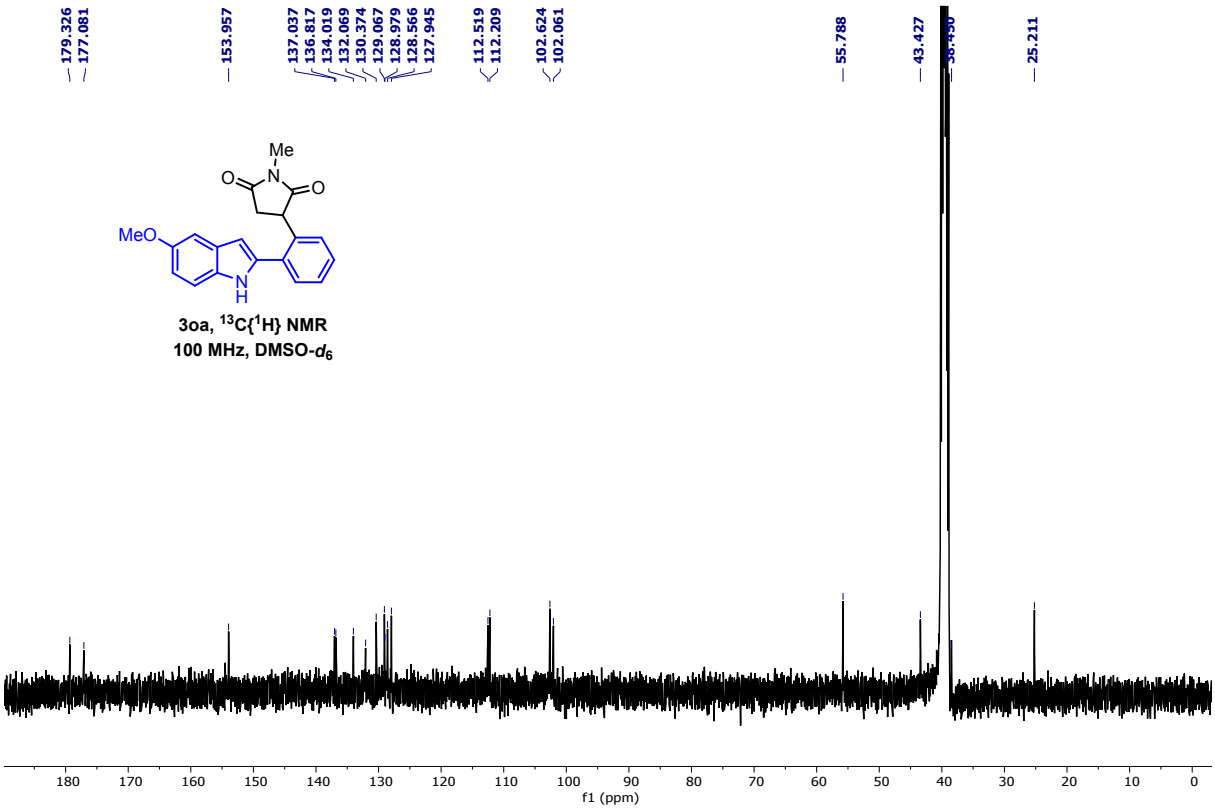


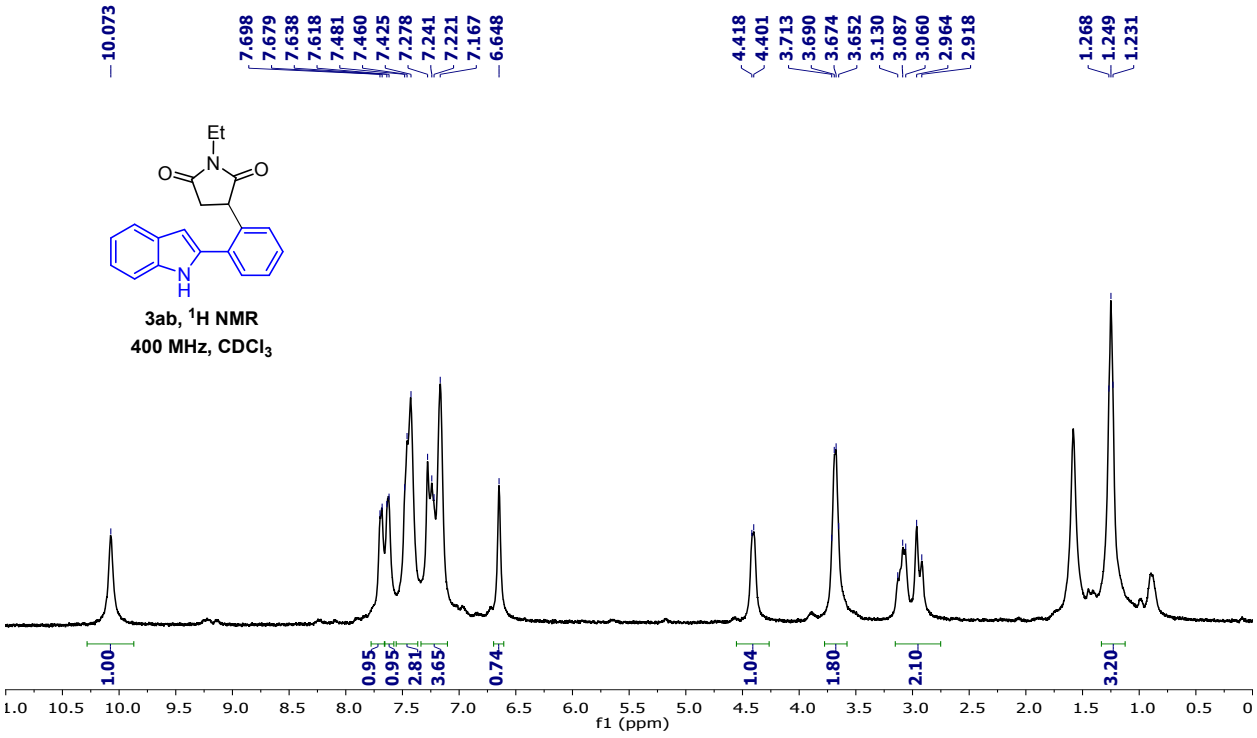
3na, ^{13}C{^{1}H} NMR
100 MHz, $CDCl_3$



3oa,^{1}H NMR
400 MHz, DMSO-d_6



3oa, ^{13}C{^{1}H} NMR
100 MHz, DMSO-d_6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7.679
7.638
7.618
7.481
7.460
7.425
7.278
7.241
7.221
7.167
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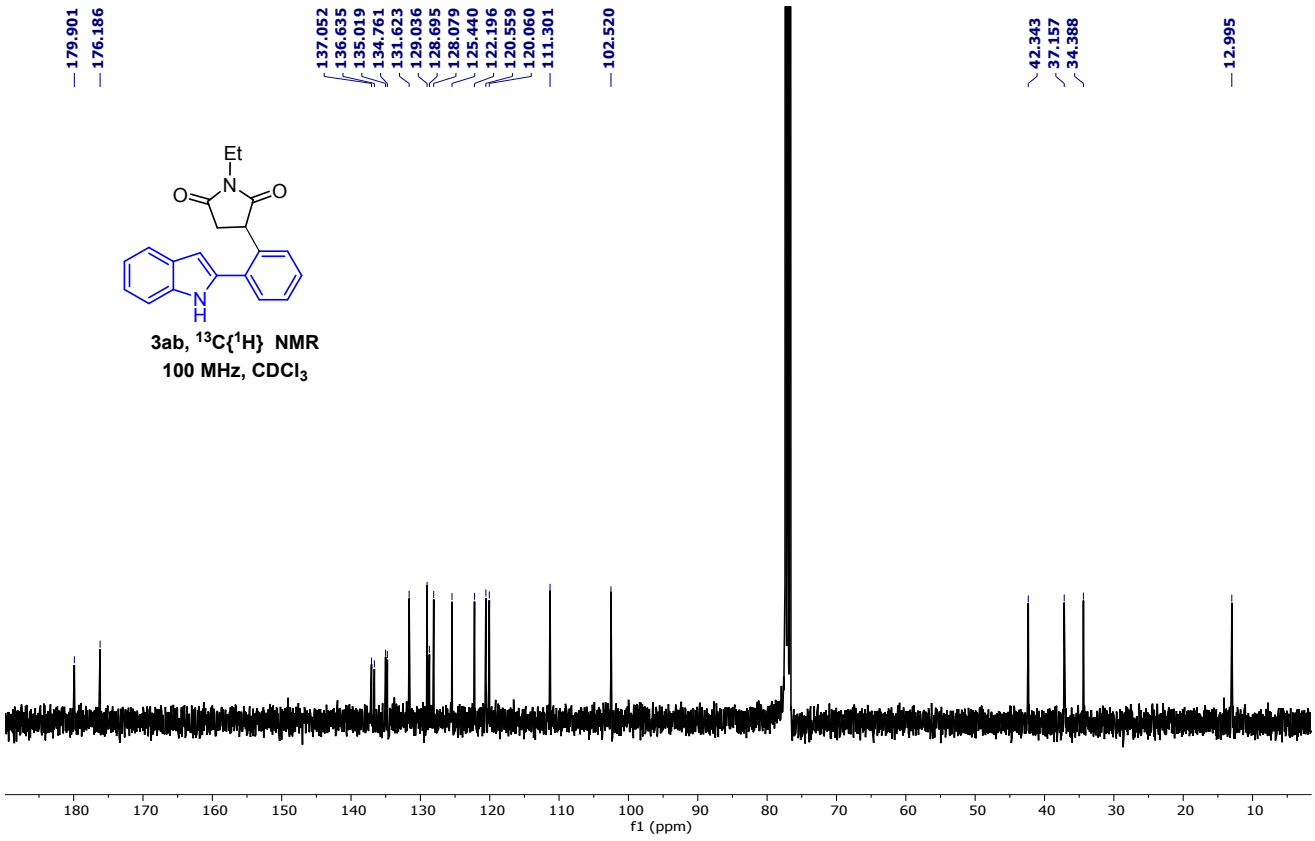
4.418
4.401
3.713
3.690
3.674
3.652
3.130
3.087
3.060
2.964
2.918
1.268
1.249
1.231
Et
N
O
O
N
H
3ab, 1H NMR
400 MHz, CDCl3
1.00
0.95
0.95
2.81
3.65
0.74
1.04
1.80
2.10
3.20
f1 (ppm)


179.901
176.186
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120.559
120.060
111.301
102.520
42.343
37.157
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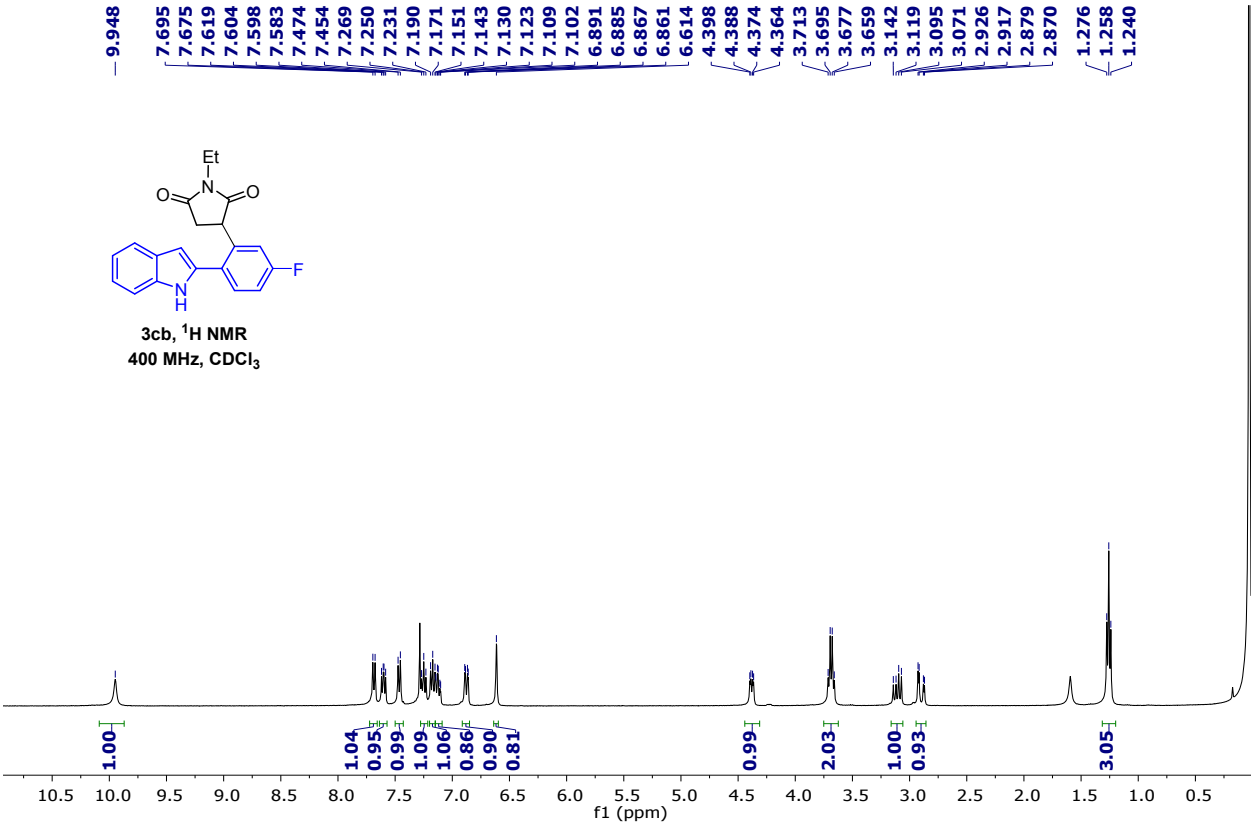
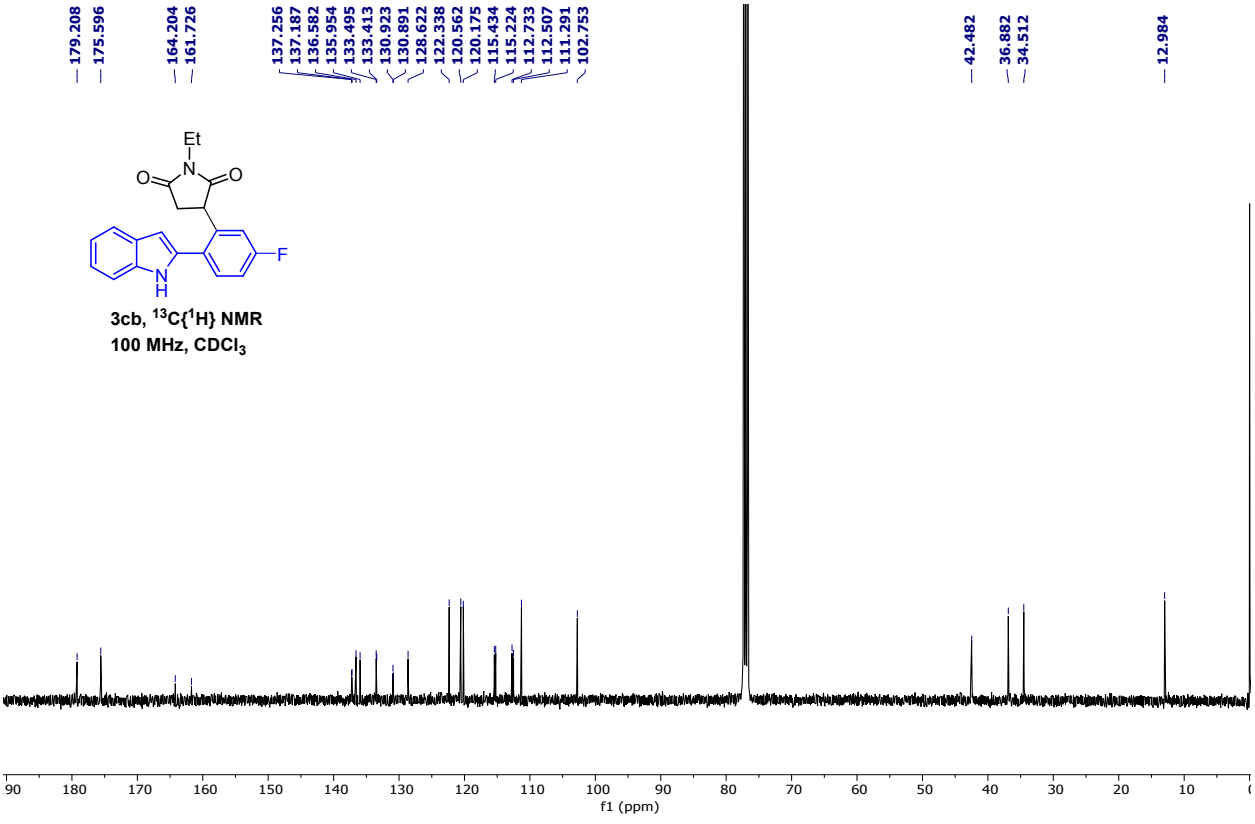
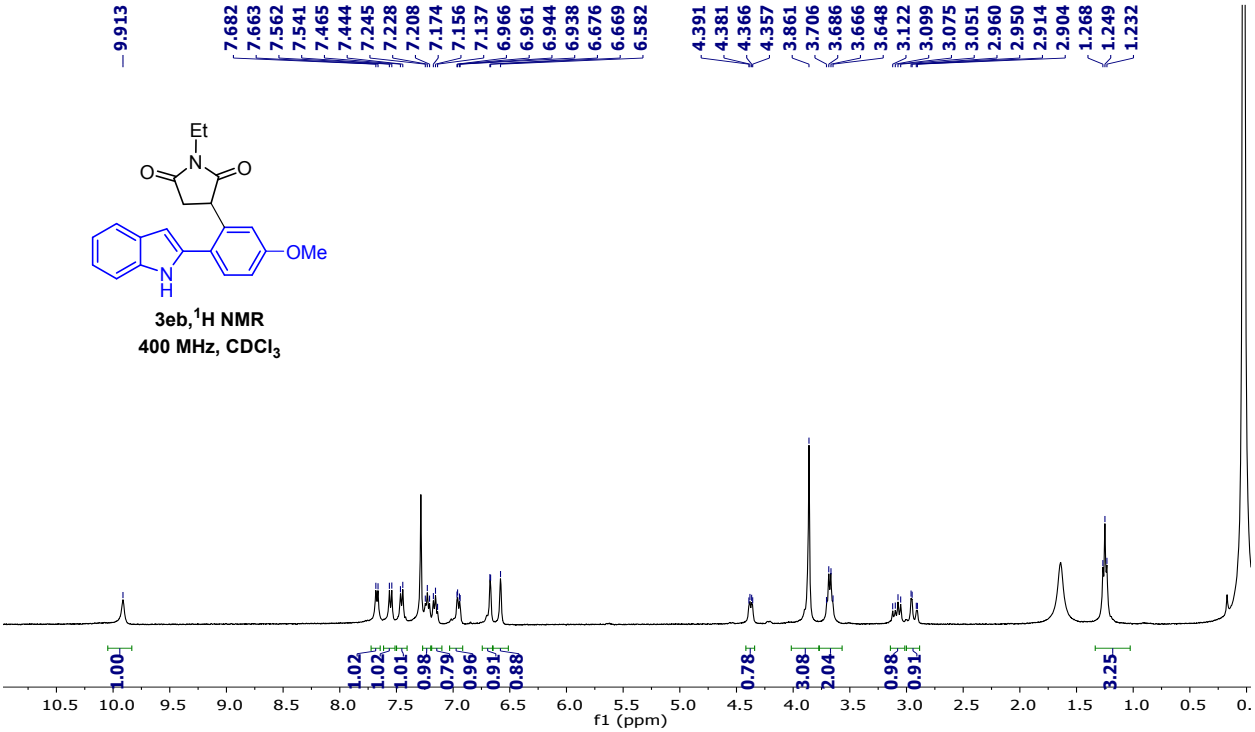
12.995
Et
N
O
O
N
H
3ab, 13C{1H} NMR
100 MHz, CDCl3
f1 (ppm)



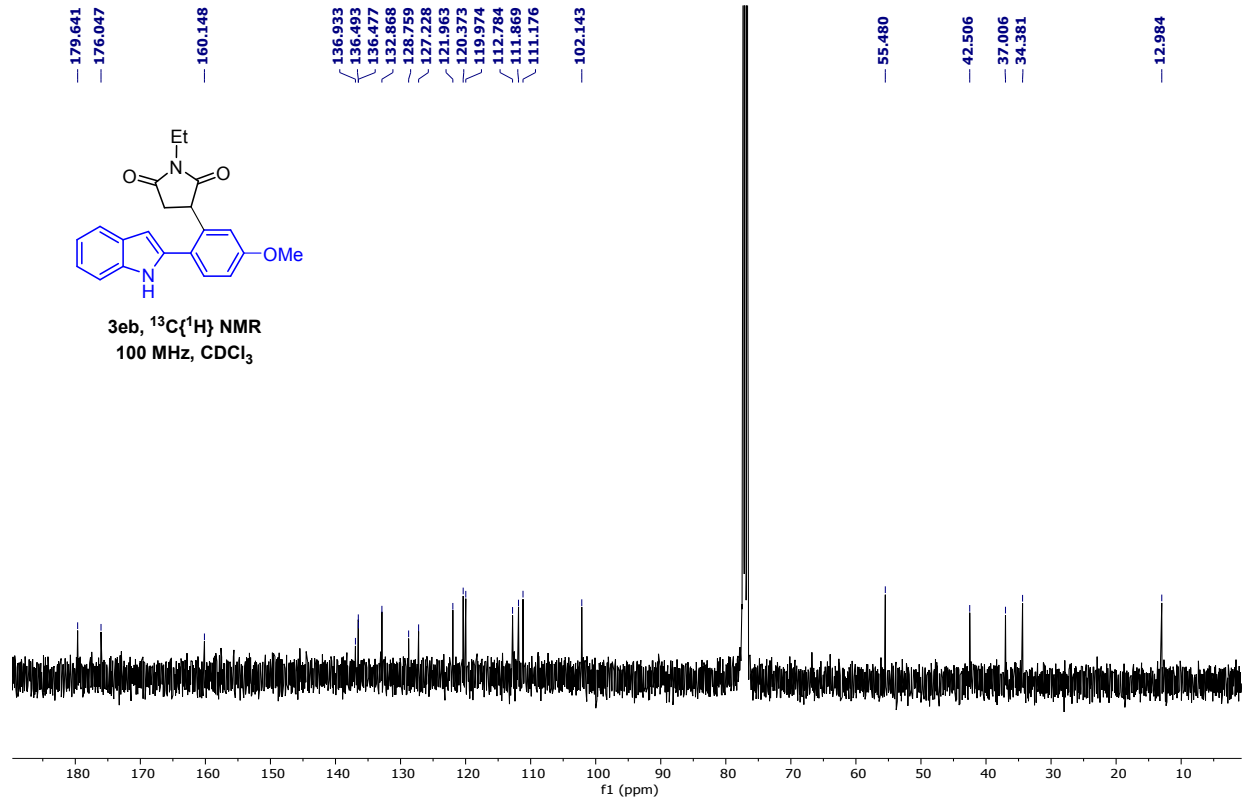
3cb, ^{1}H NMR
400 MHz, $CDCl_3$



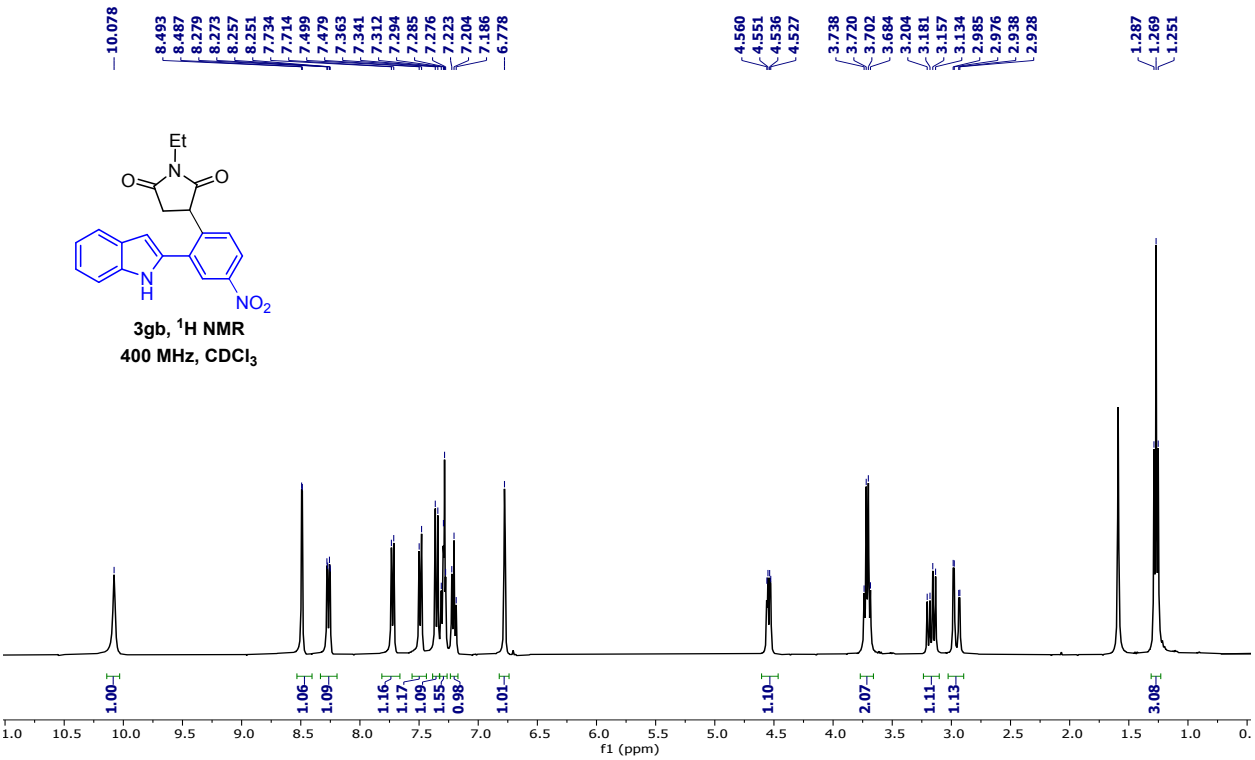
3cb, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



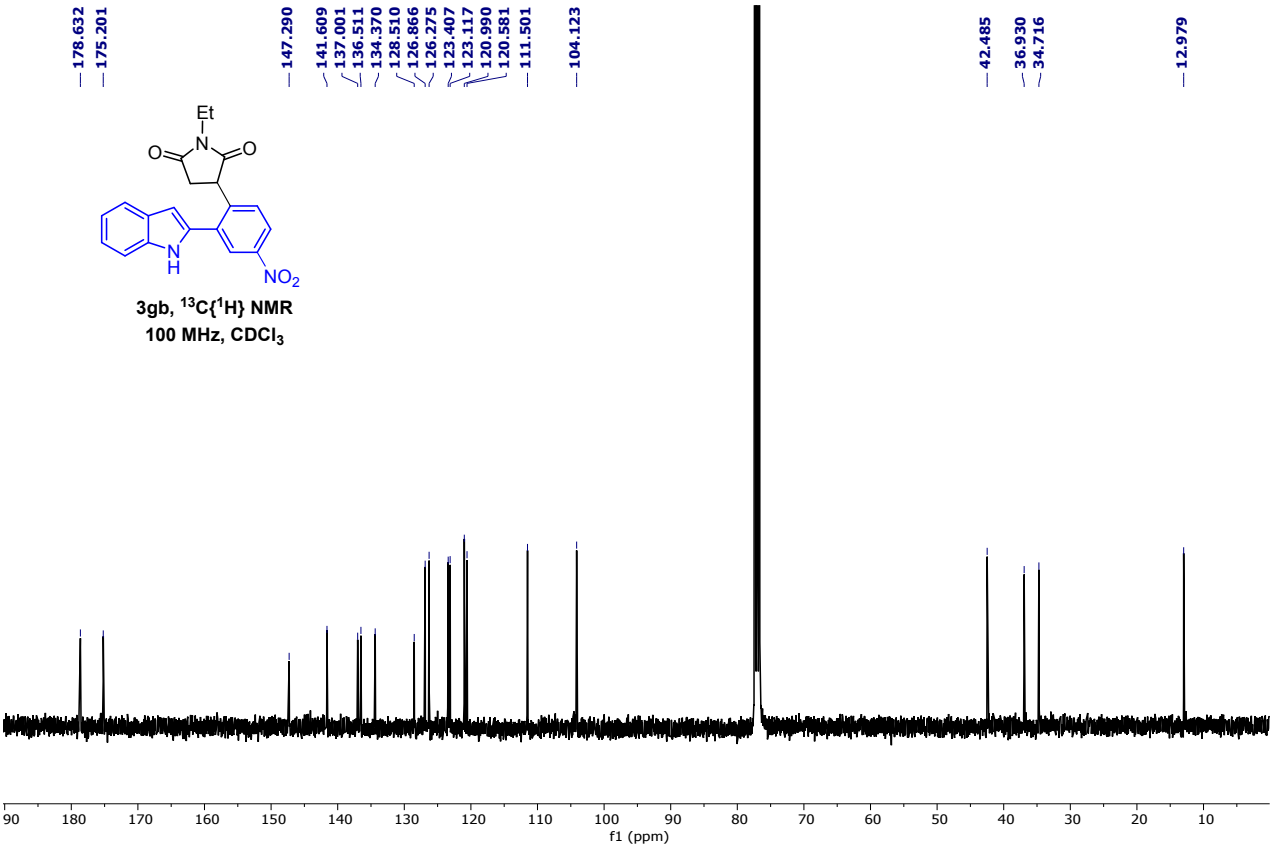
3eb, ^{1}H NMR
400 MHz, $CDCl_3$



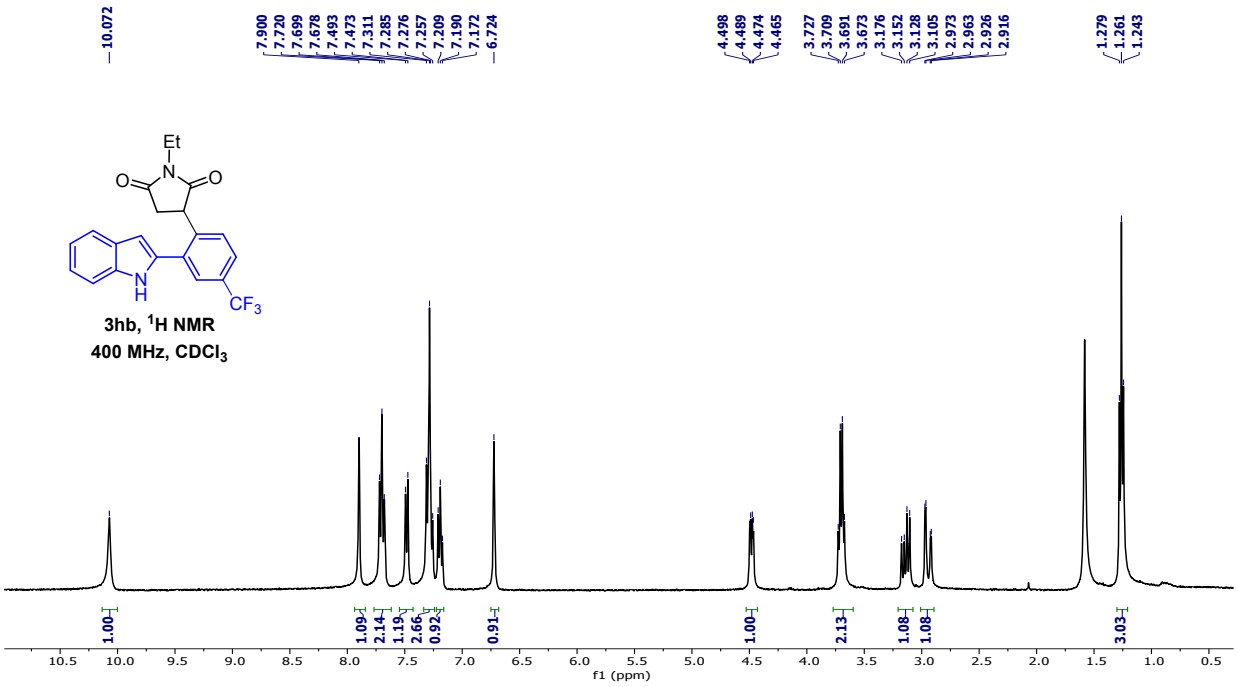
3eb, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



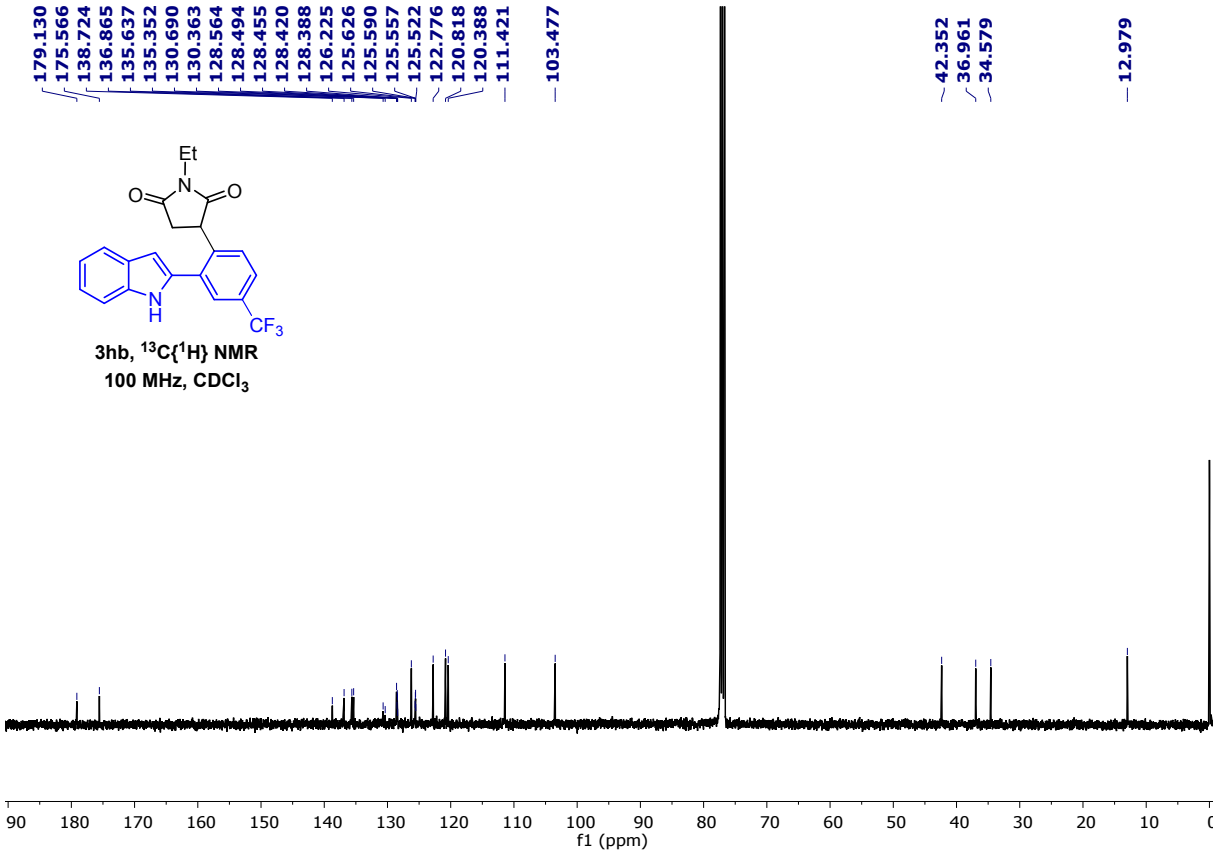
3gb, ^{1}H NMR
400 MHz, $CDCl_3$



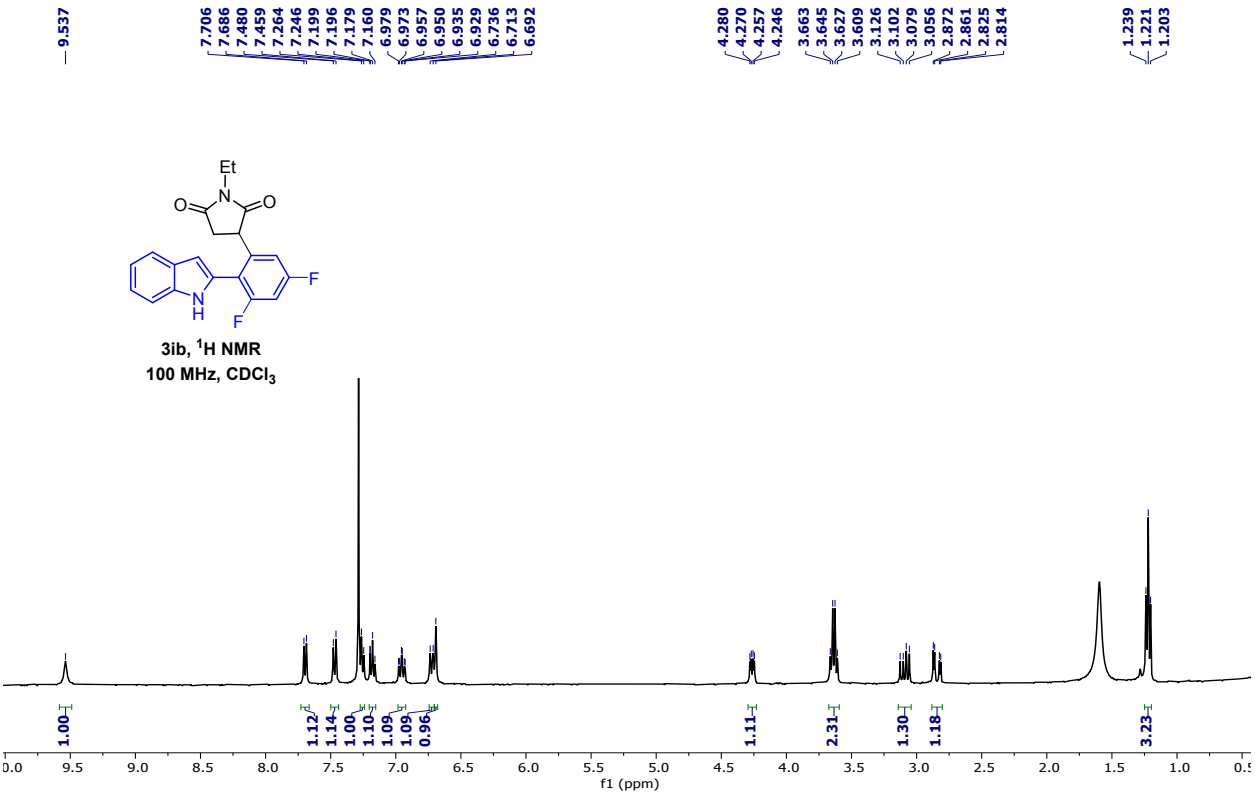
3gb, ^{13}C{^{1}H} NMR
100 MHz, $CDCl_3$



3hb, ^{1}H NMR
400 MHz, $CDCl_3$



3hb, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$


9.537
7.706
7.686
7.480
7.459
7.264
7.246
7.199
7.196
7.179
7.160
6.979
6.973
6.957
6.950
6.935
6.929
6.736
6.713
6.692
4.280
4.270
4.257
4.246
3.663
3.645
3.627
3.609
3.126
3.102
3.079
3.056
2.872
2.861
2.825
2.814
1.239
1.221
1.203
Et
N
O
O
F
N
H
F
3ib, 1H NMR
100 MHz, CDCl3
1.00
1.12
1.14
1.00
1.10
1.09
1.09
0.96
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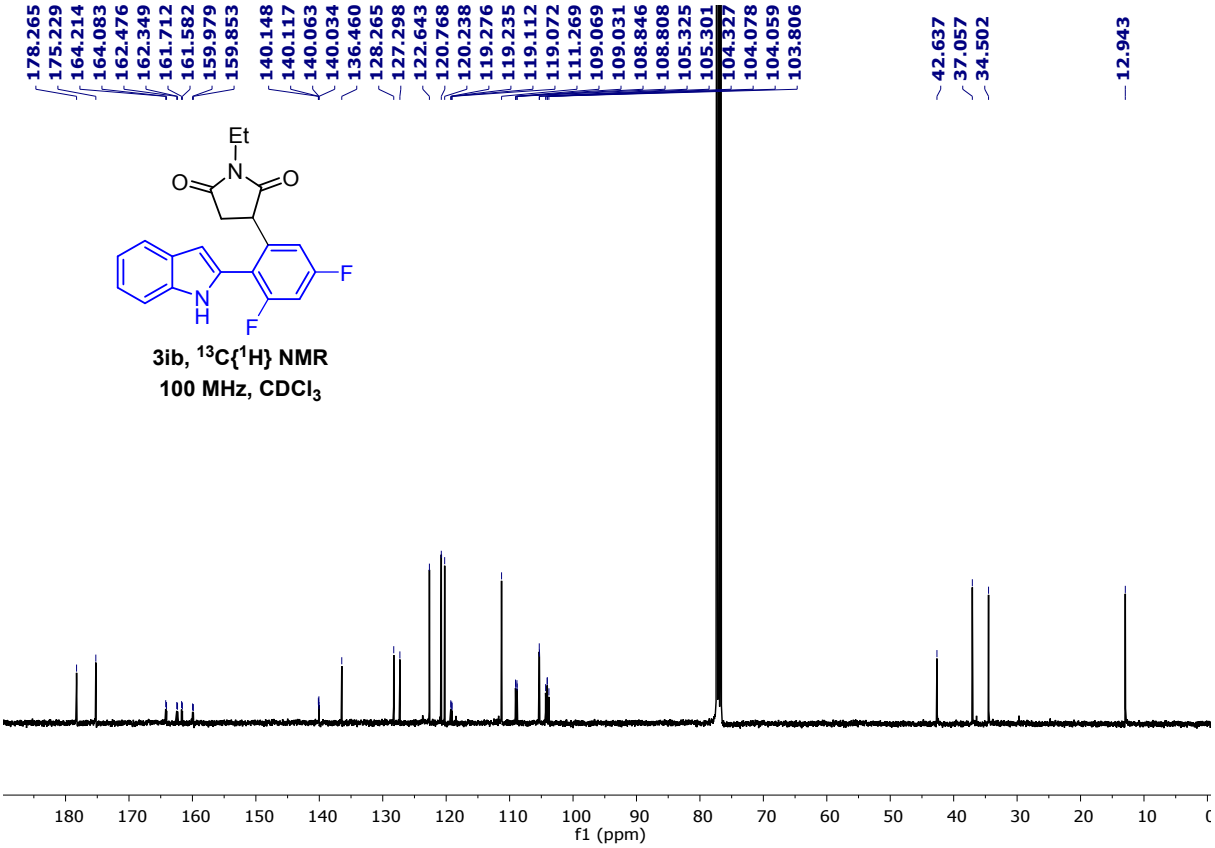
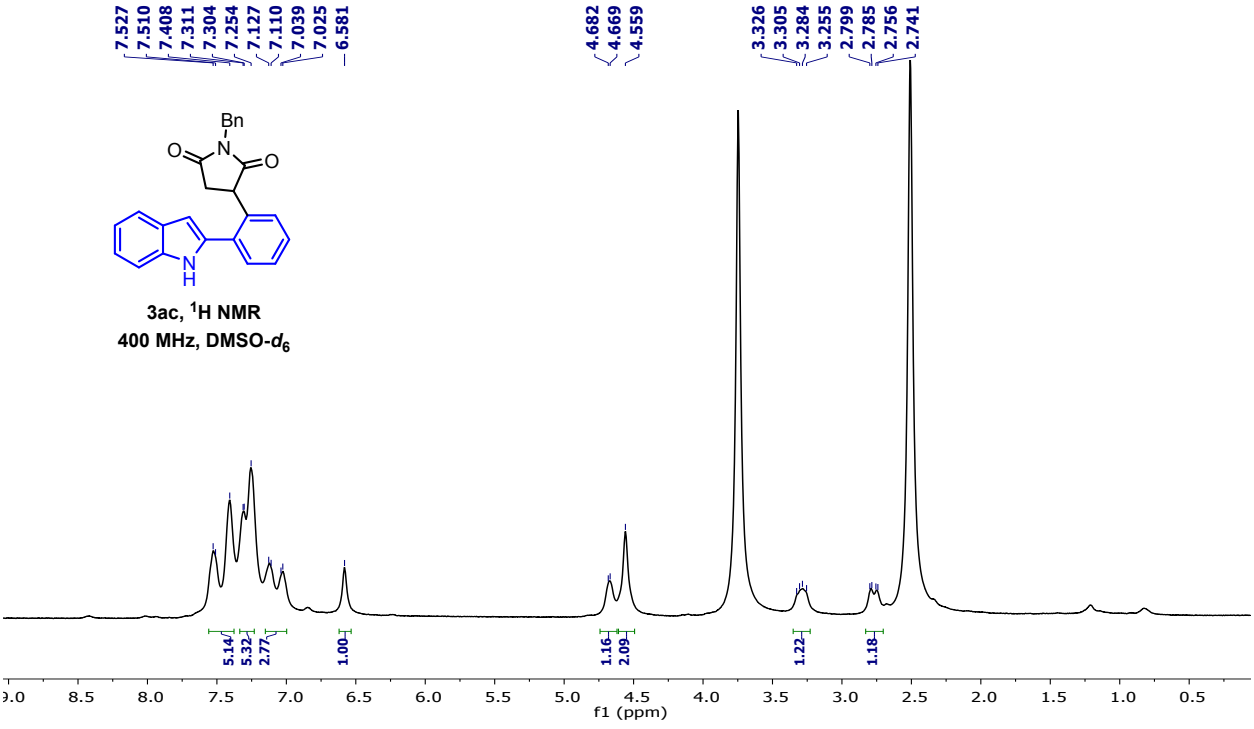
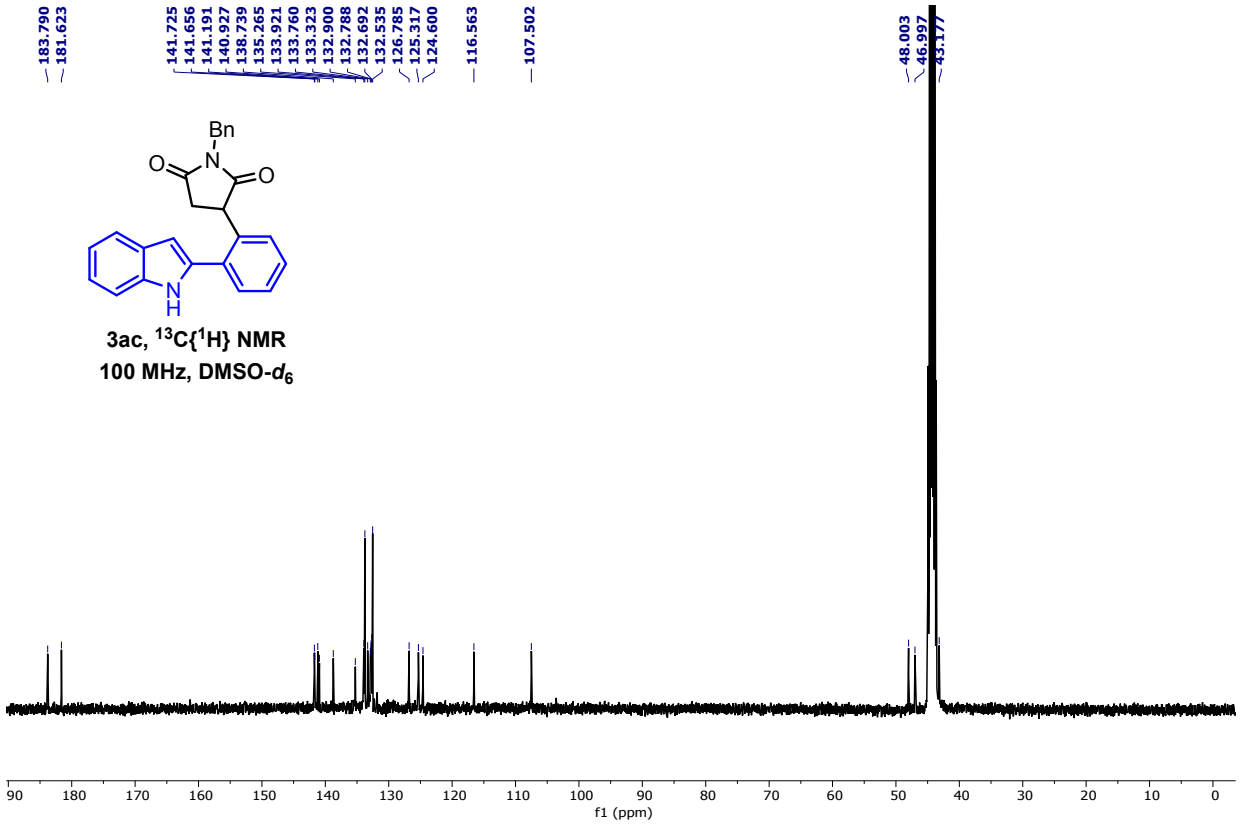
2.31
1.30
1.18
3.23
f1 (ppm)



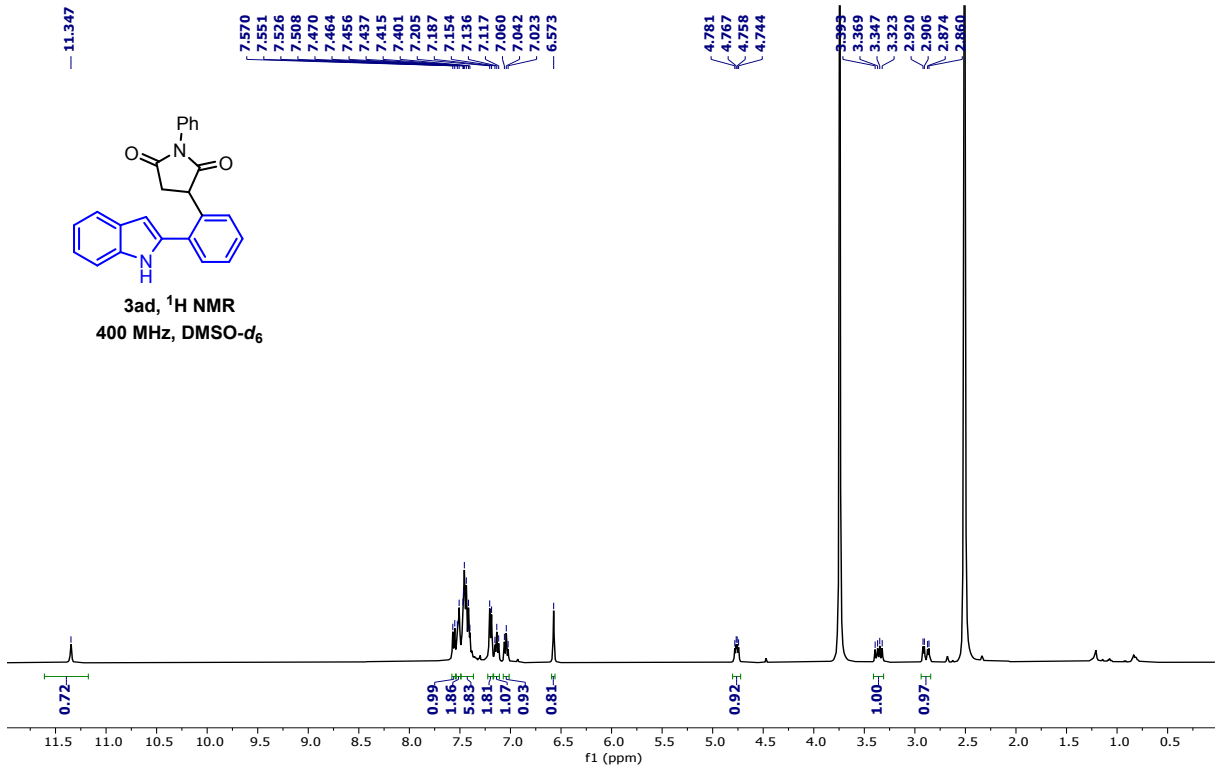
3ib, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



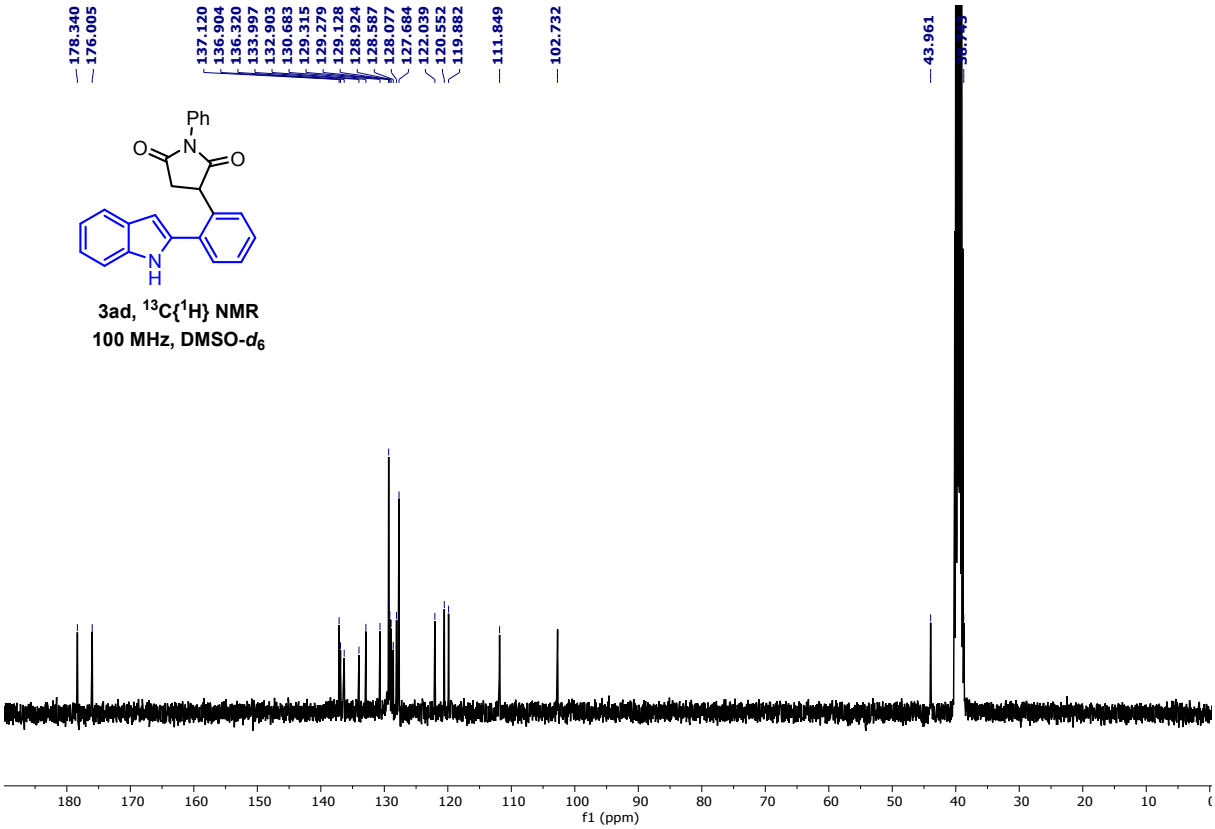
3ac, ^{1}H NMR
400 MHz, DMSO-d_6



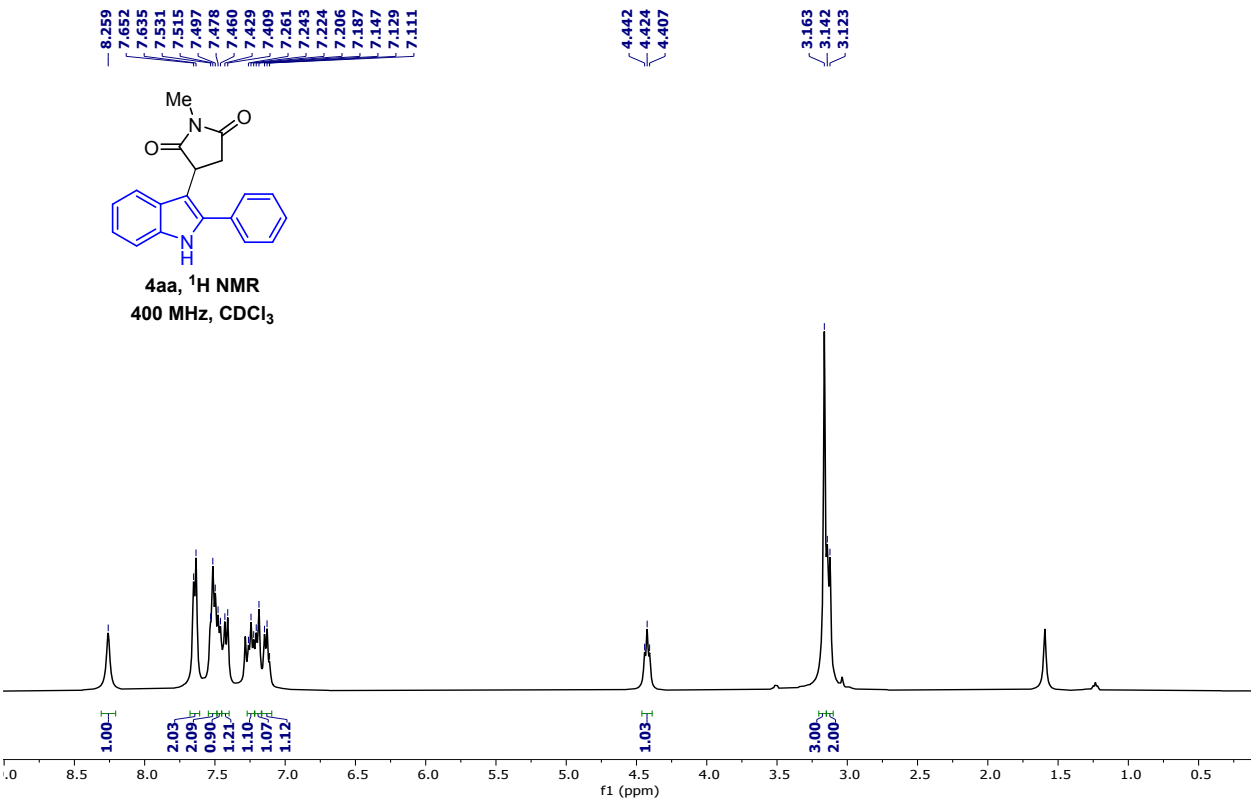
3ac, $^{13}C\{^{1}H\}$ NMR
100 MHz, DMSO-d_6



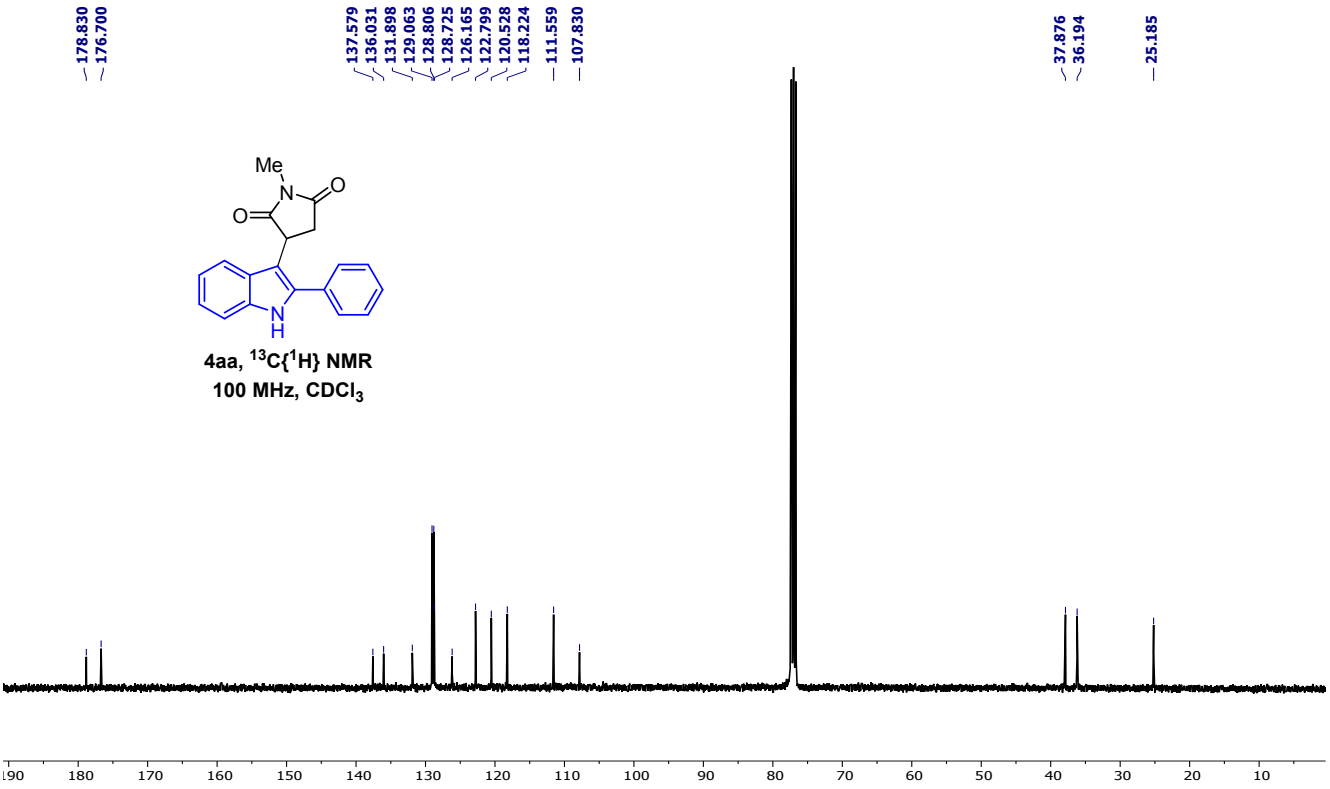
3ad, ^{1}H NMR
400 MHz, DMSO-d_6



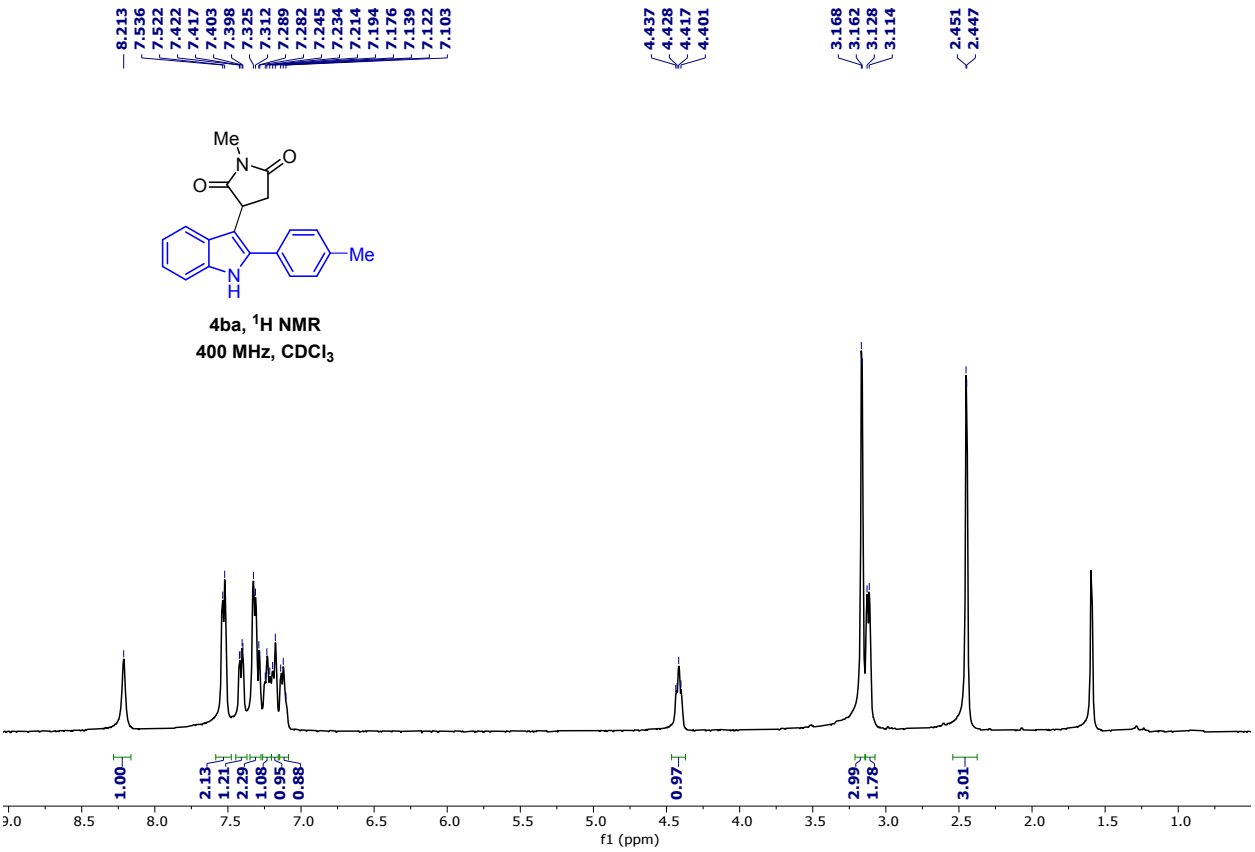
3ad, $^{13}C\{^{1}H\}$ NMR
100 MHz, DMSO-d_6



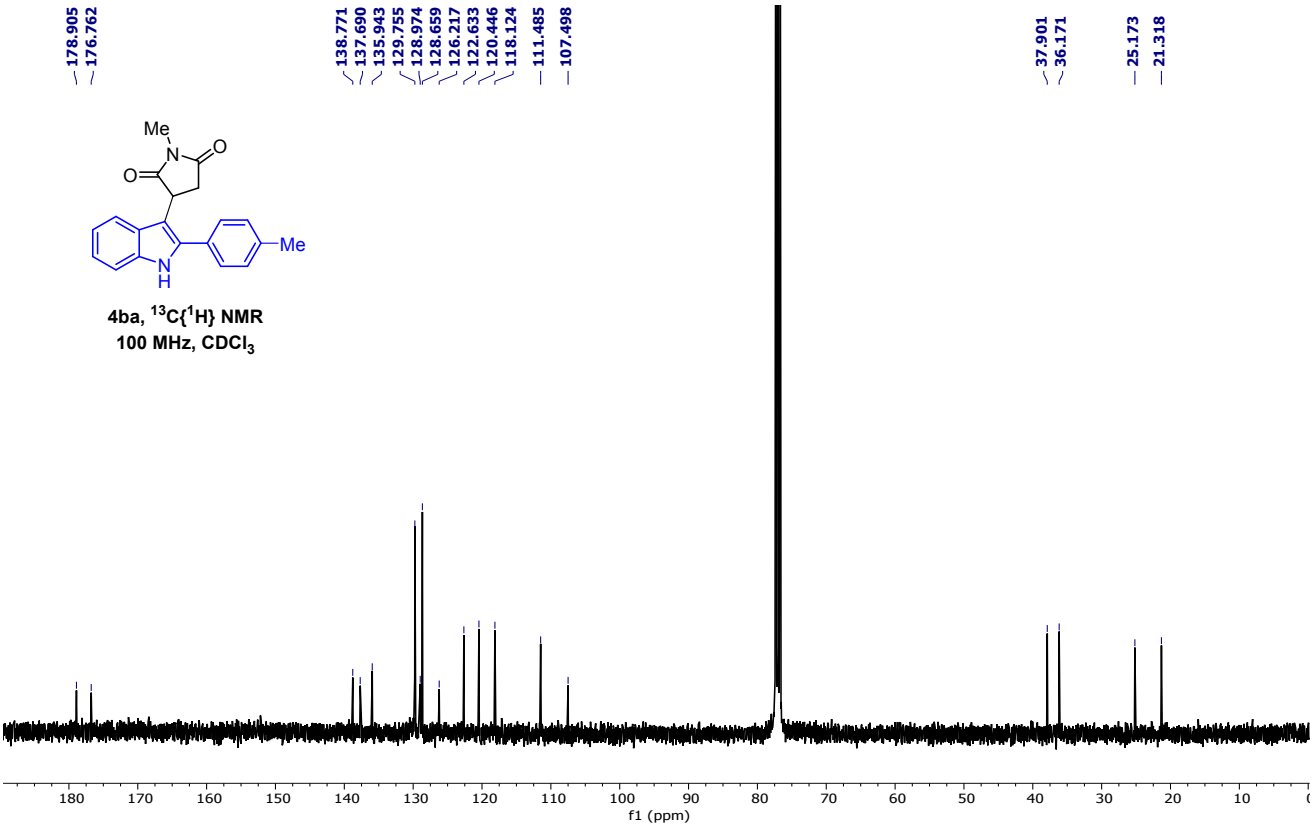
4aa, ^{1}H NMR
400 MHz, $CDCl_3$



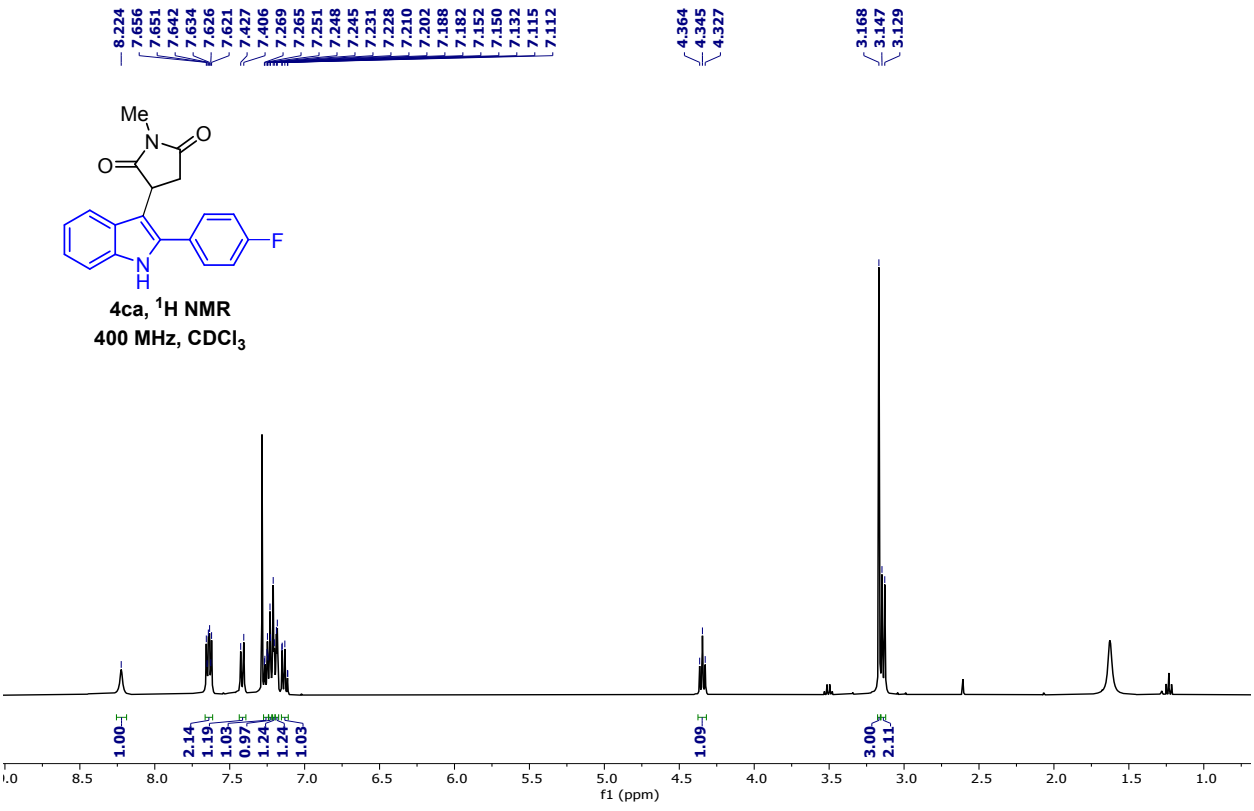
4aa, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



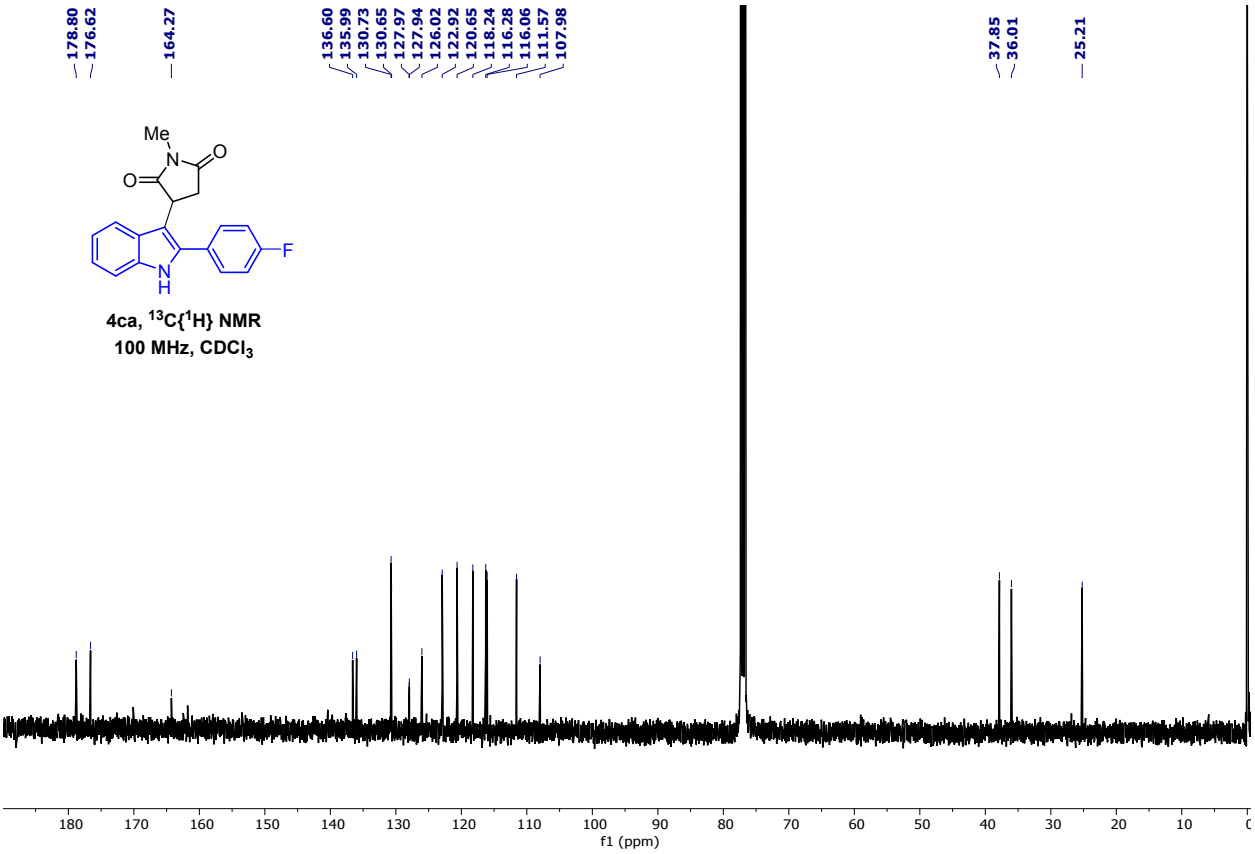
4ba, ^{1}H NMR
400 MHz, $CDCl_3$



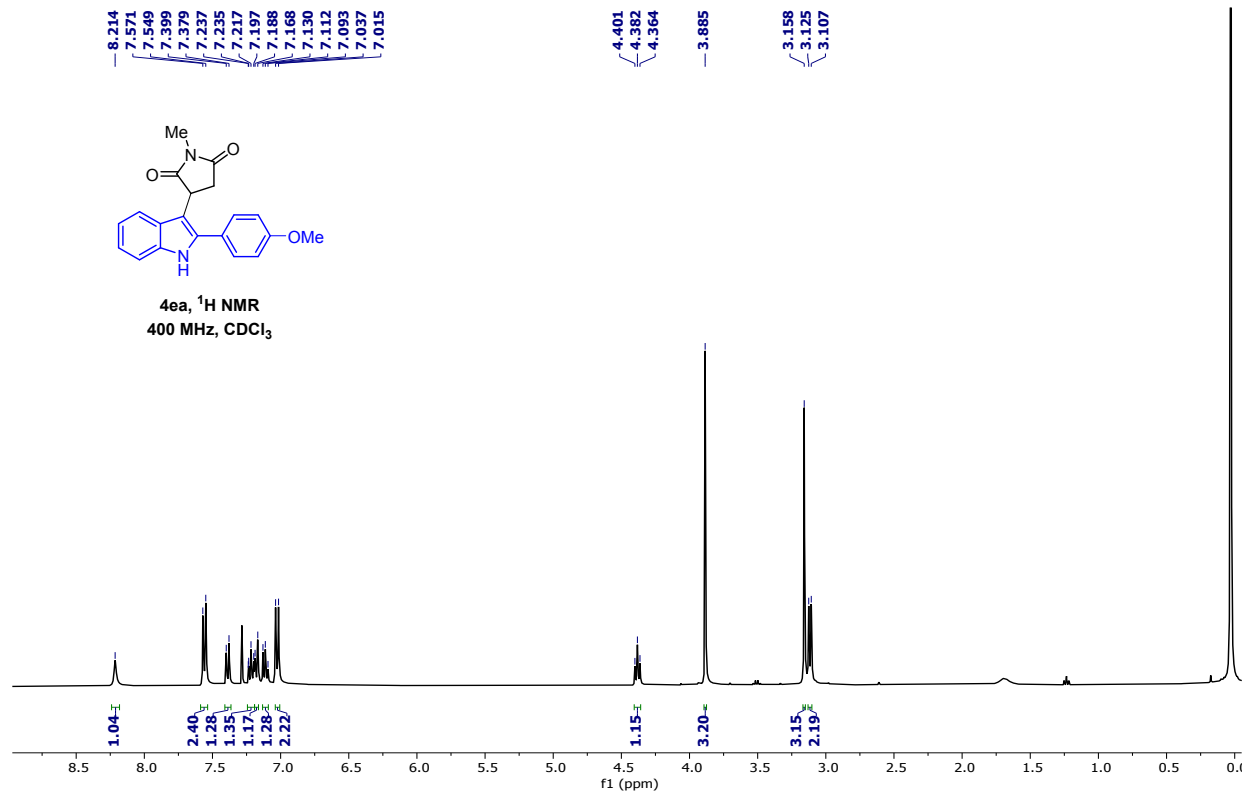
4ba, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



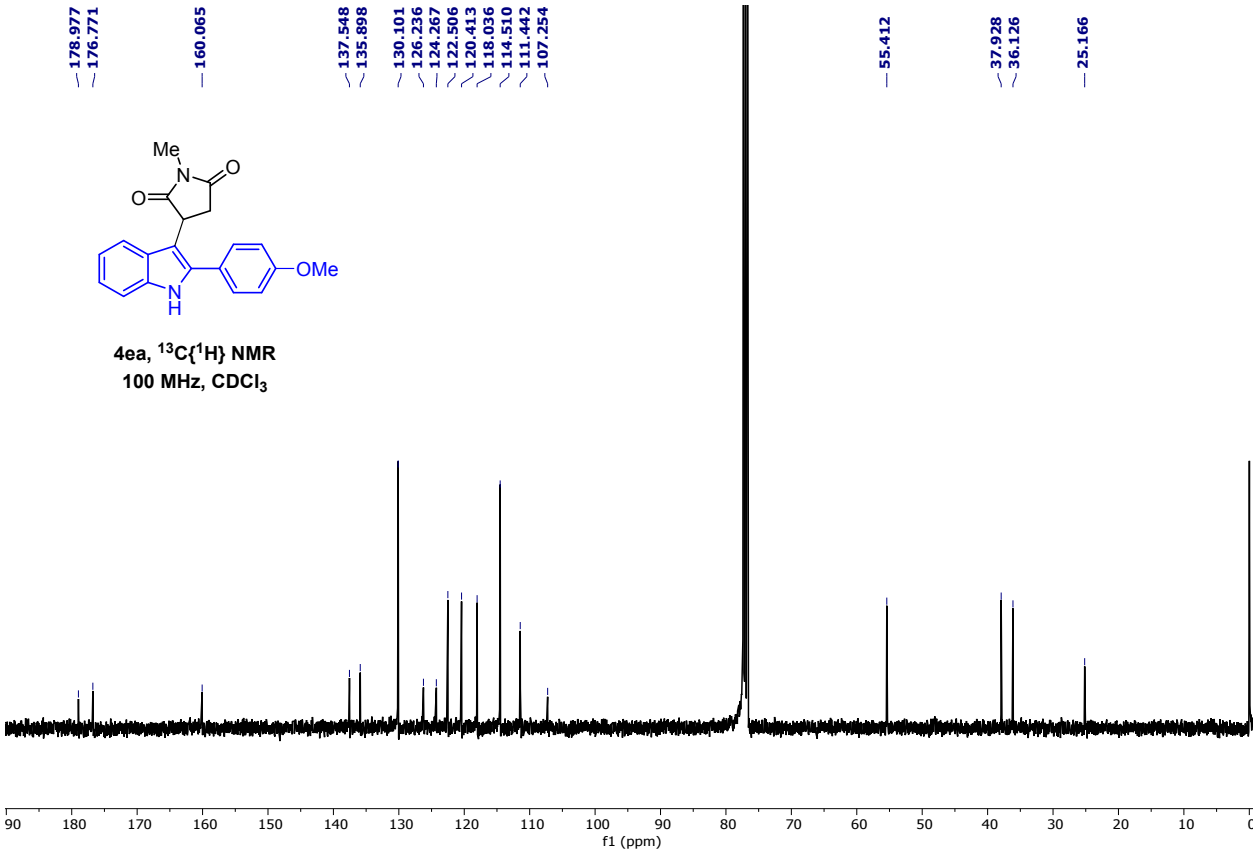
4ca, ^{1}H NMR
400 MHz, $CDCl_3$



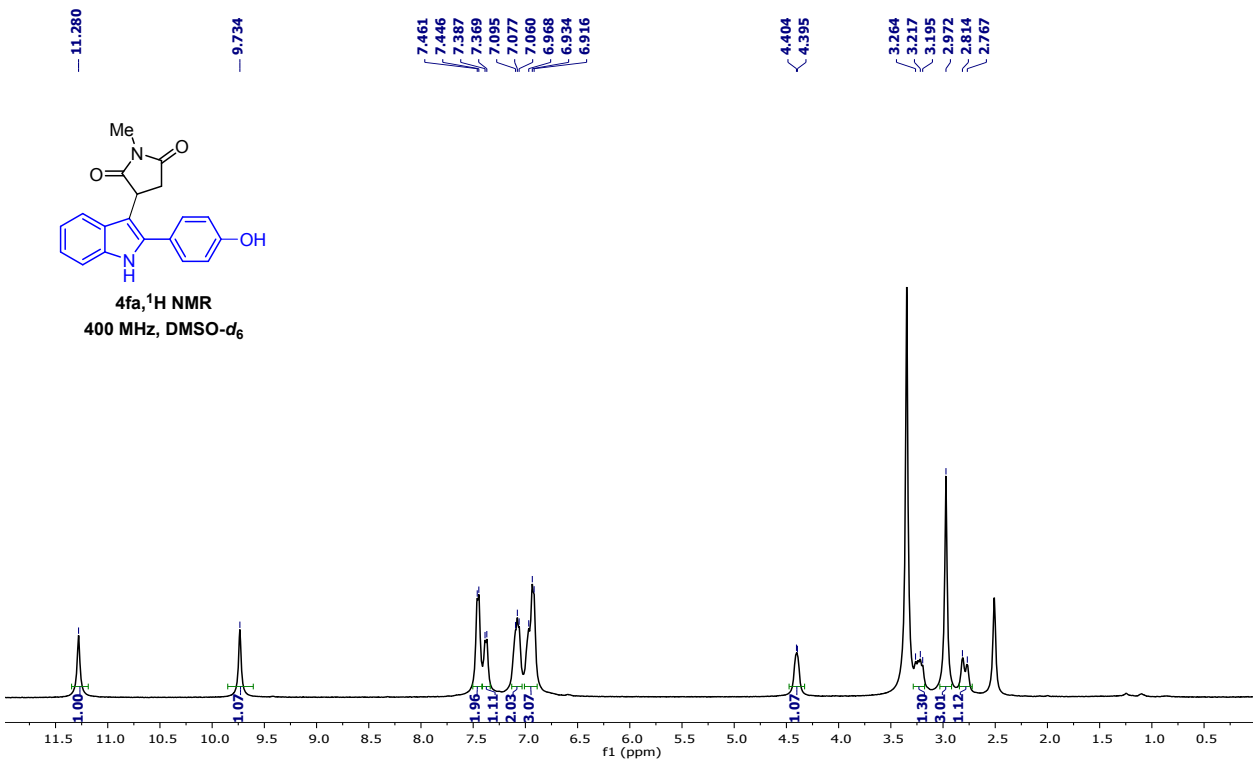
4ca, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



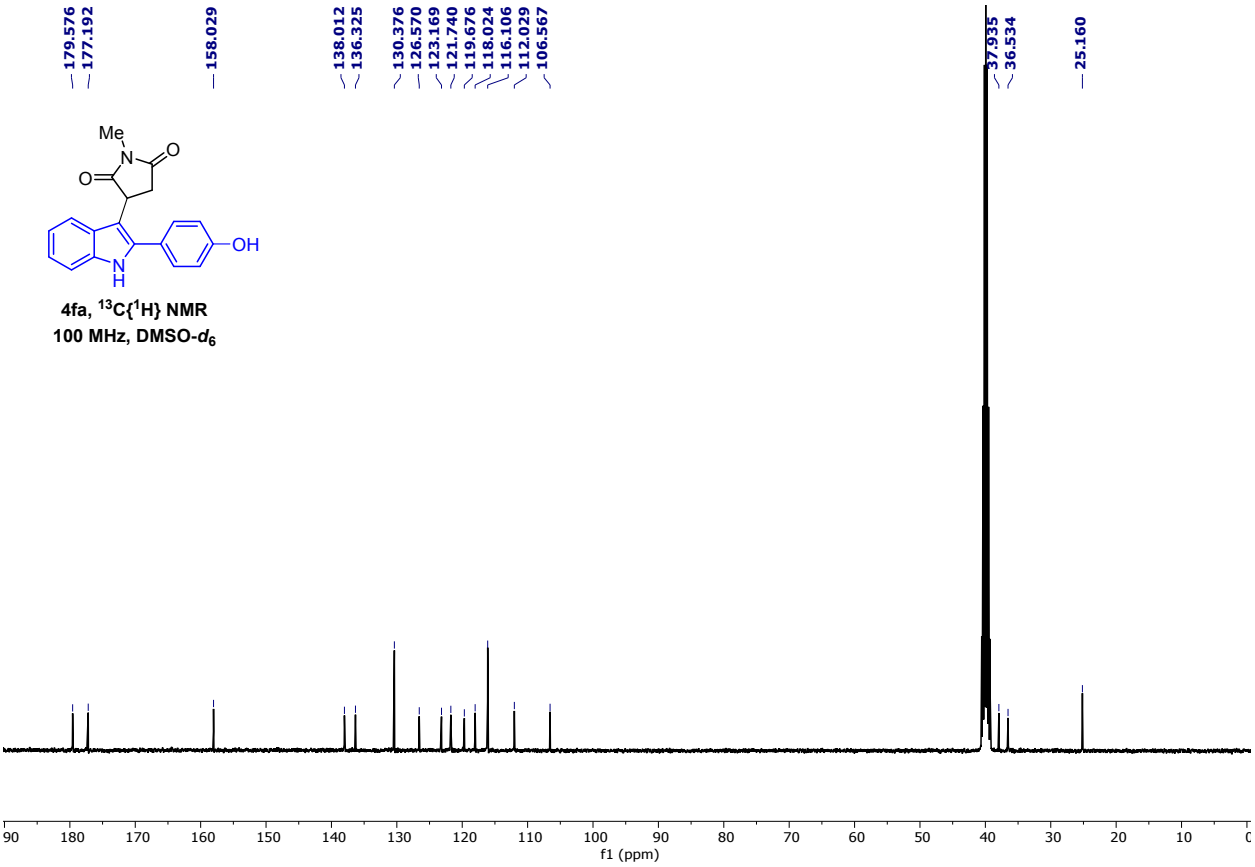
4ea, ^{1}H NMR
400 MHz, $CDCl_3$



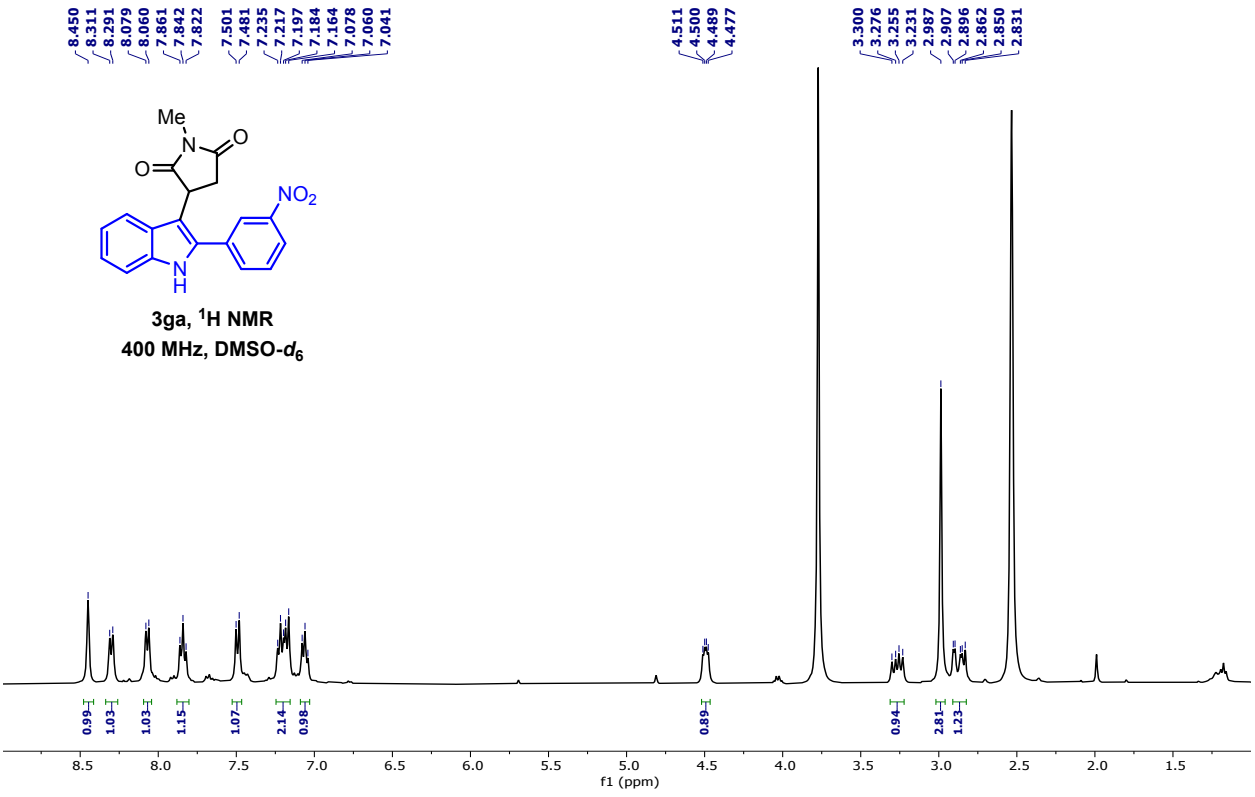
4ea, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



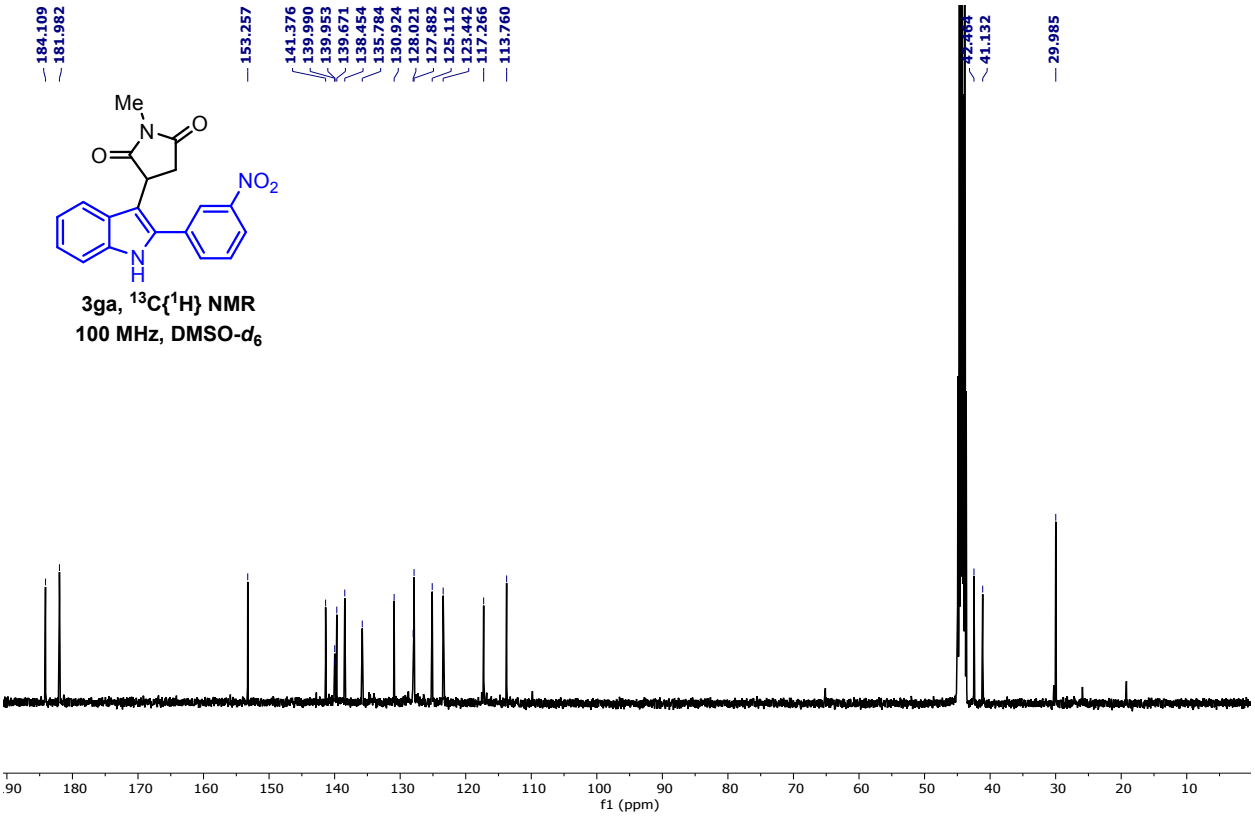
4fa,^{1}H NMR
400 MHz, DMSO-d_6



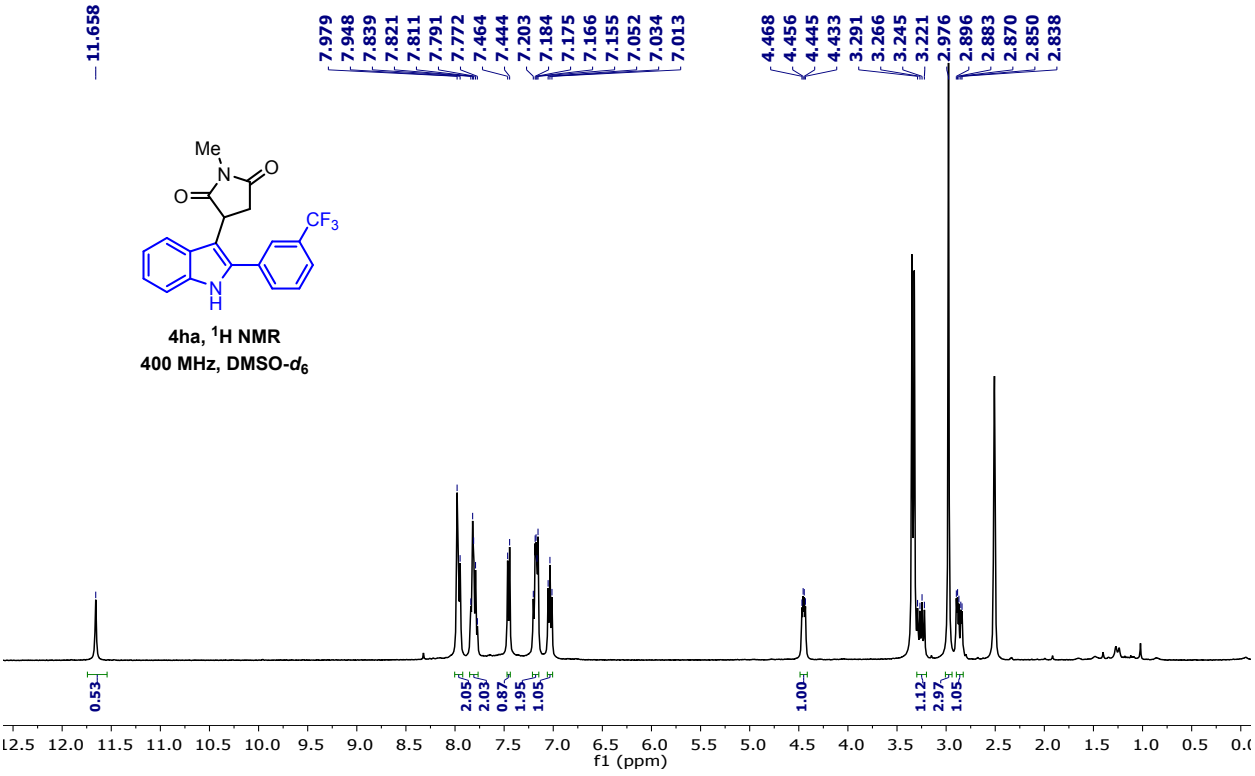
4fa, $^{13}C\{^{1}H\}$ NMR
100 MHz, DMSO-d_6



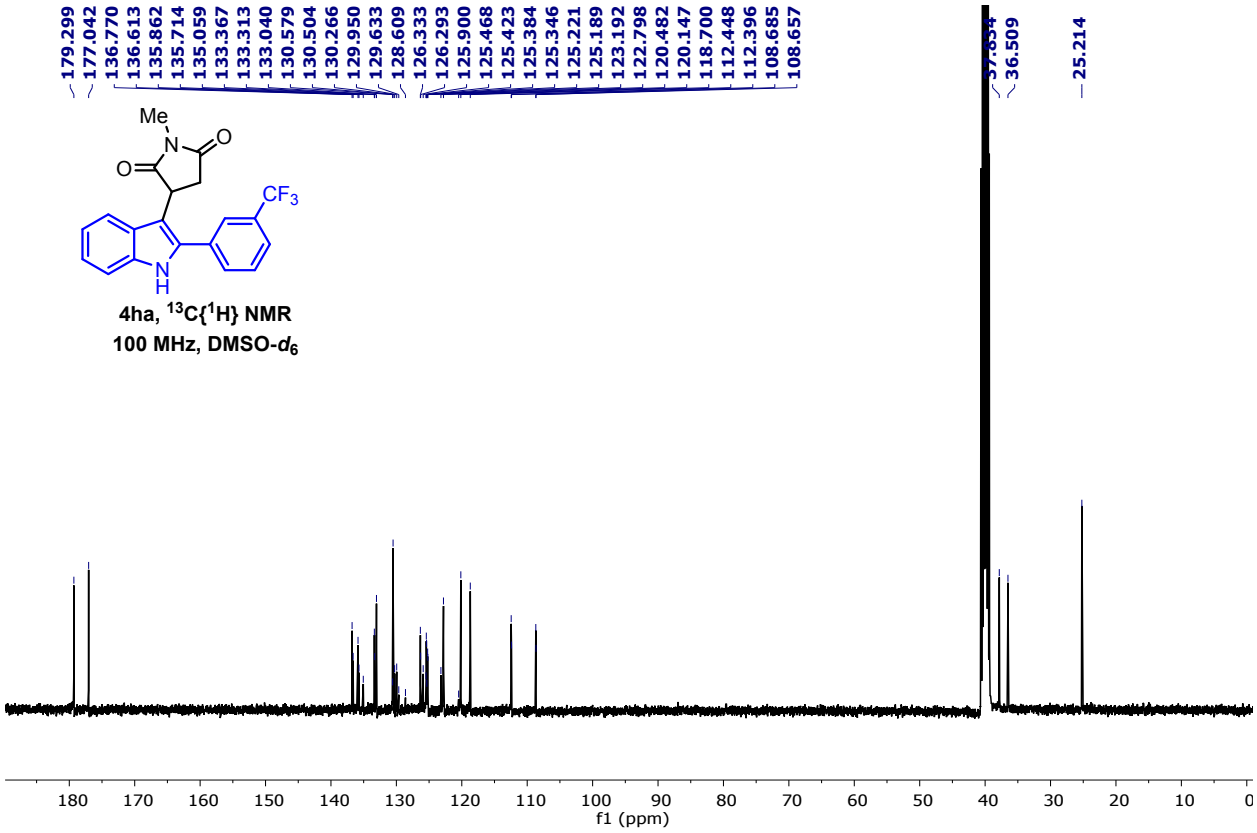
3ga, ^{1}H NMR
400 MHz, DMSO-d_6



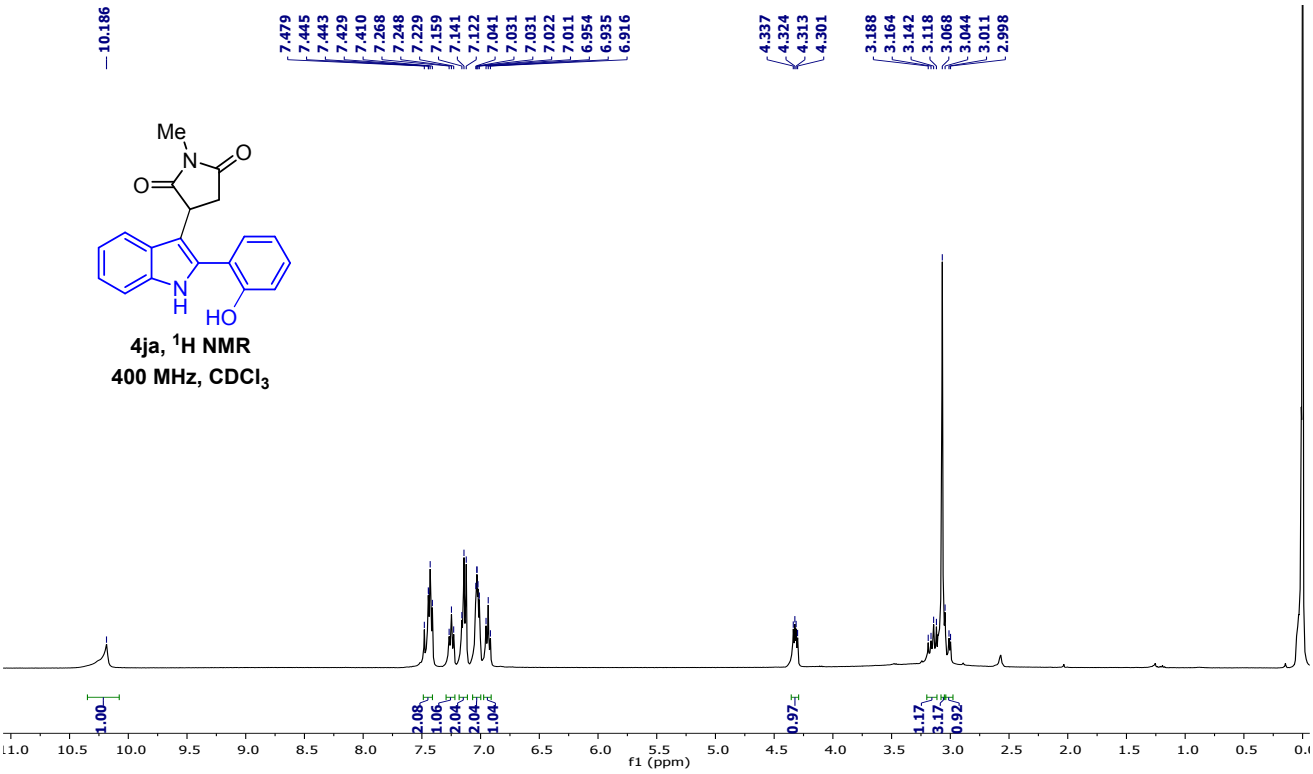
3ga, $^{13}C\{^{1}H\}$ NMR
100 MHz, DMSO-d_6



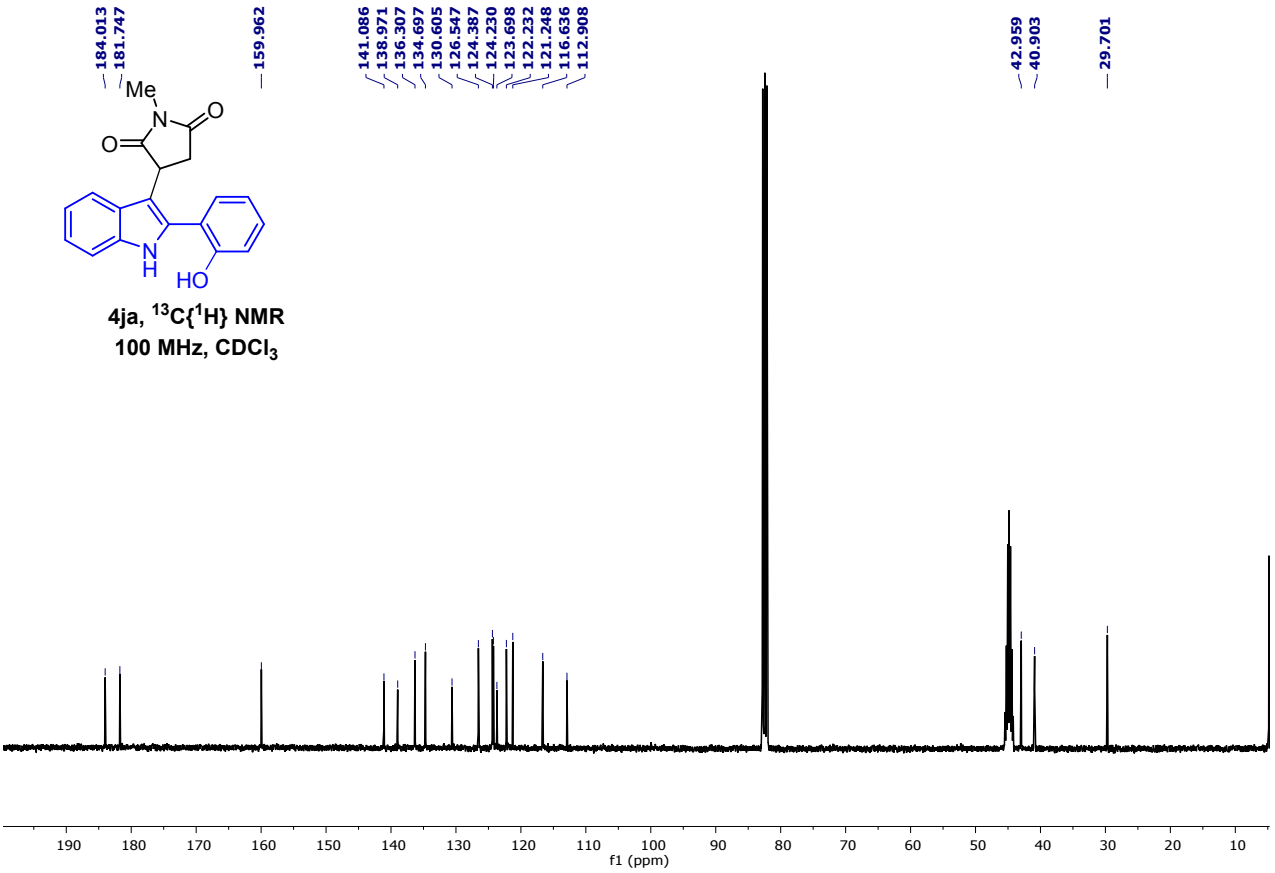
4ha, ^{1}H NMR
400 MHz, DMSO-d_6



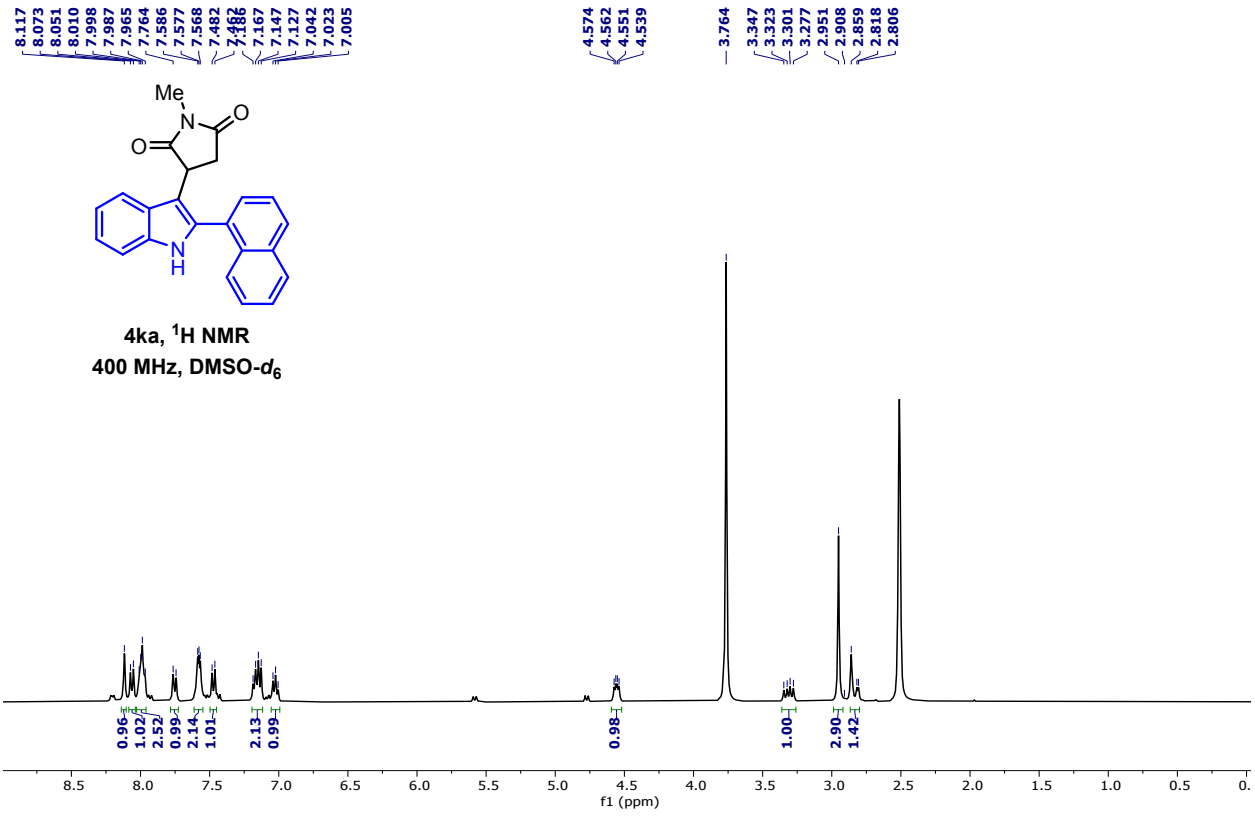
4ha, $^{13}C\{^{1}H\}$ NMR
100 MHz, DMSO-d_6



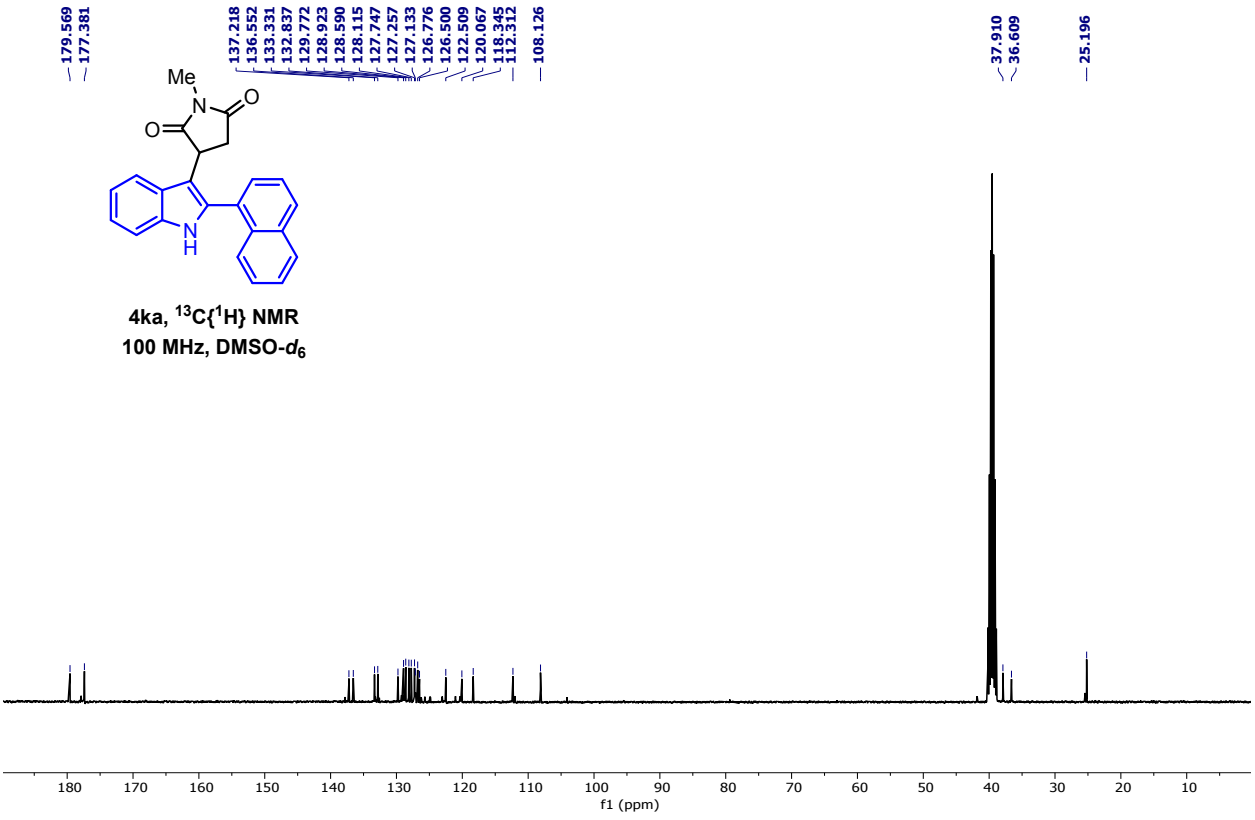
4ja, ^{1}H NMR
400 MHz, $CDCl_3$



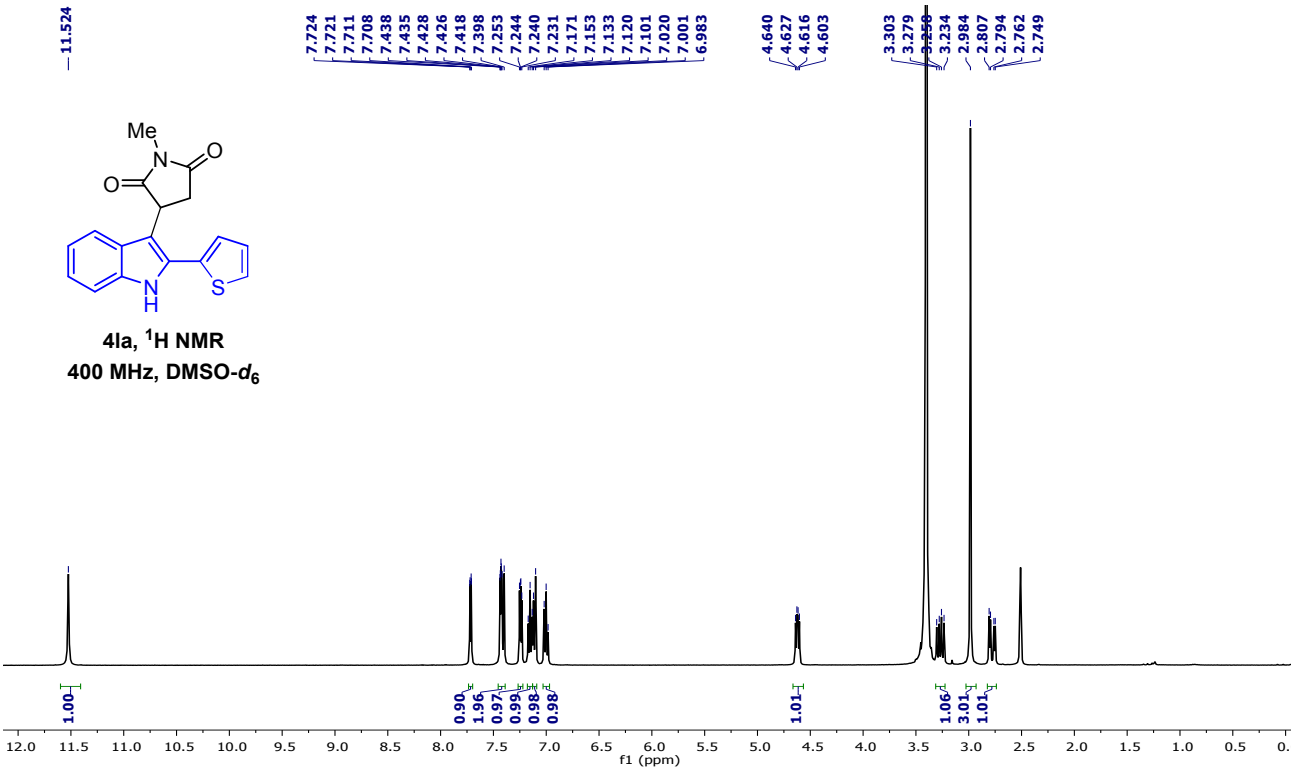
4ja, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



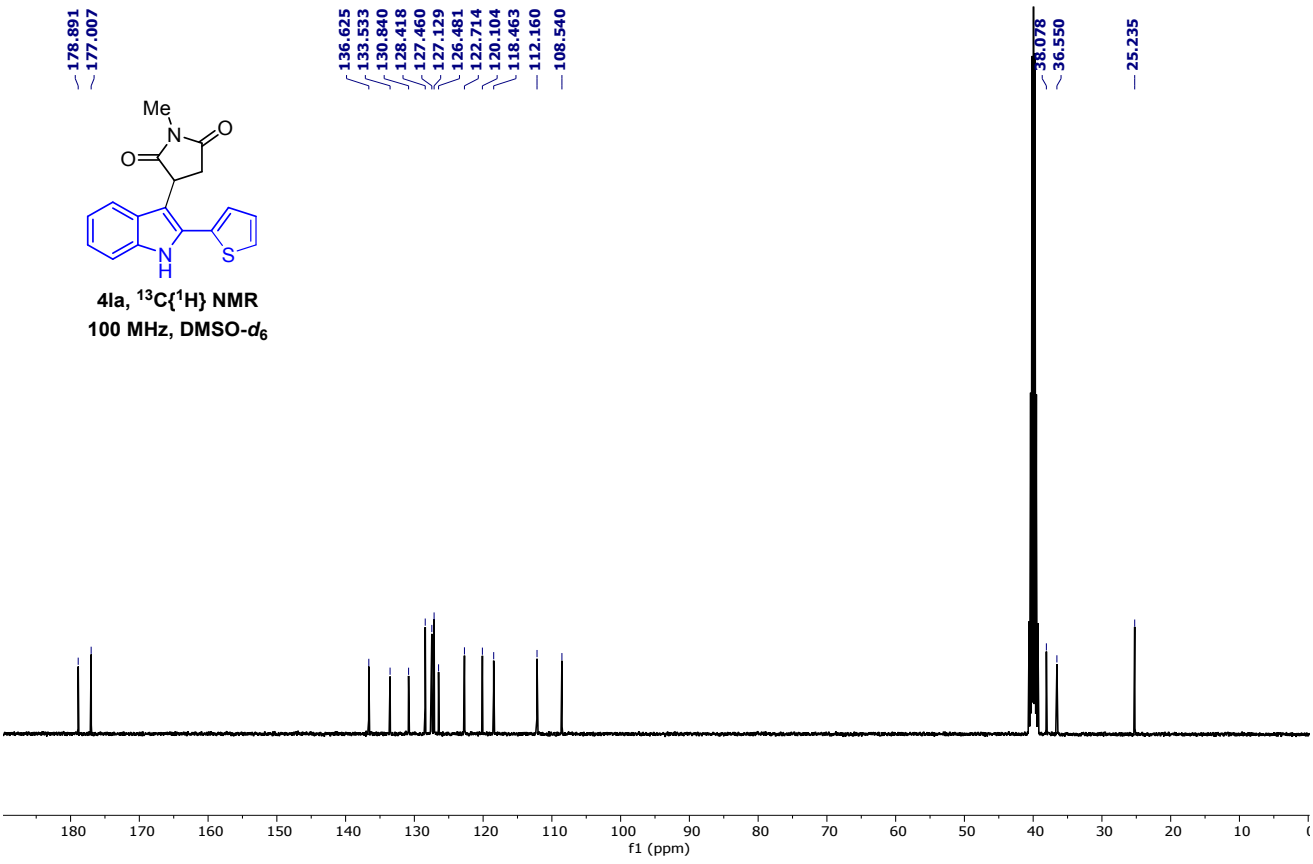
4ka, ^{1}H NMR
400 MHz, DMSO-d_6



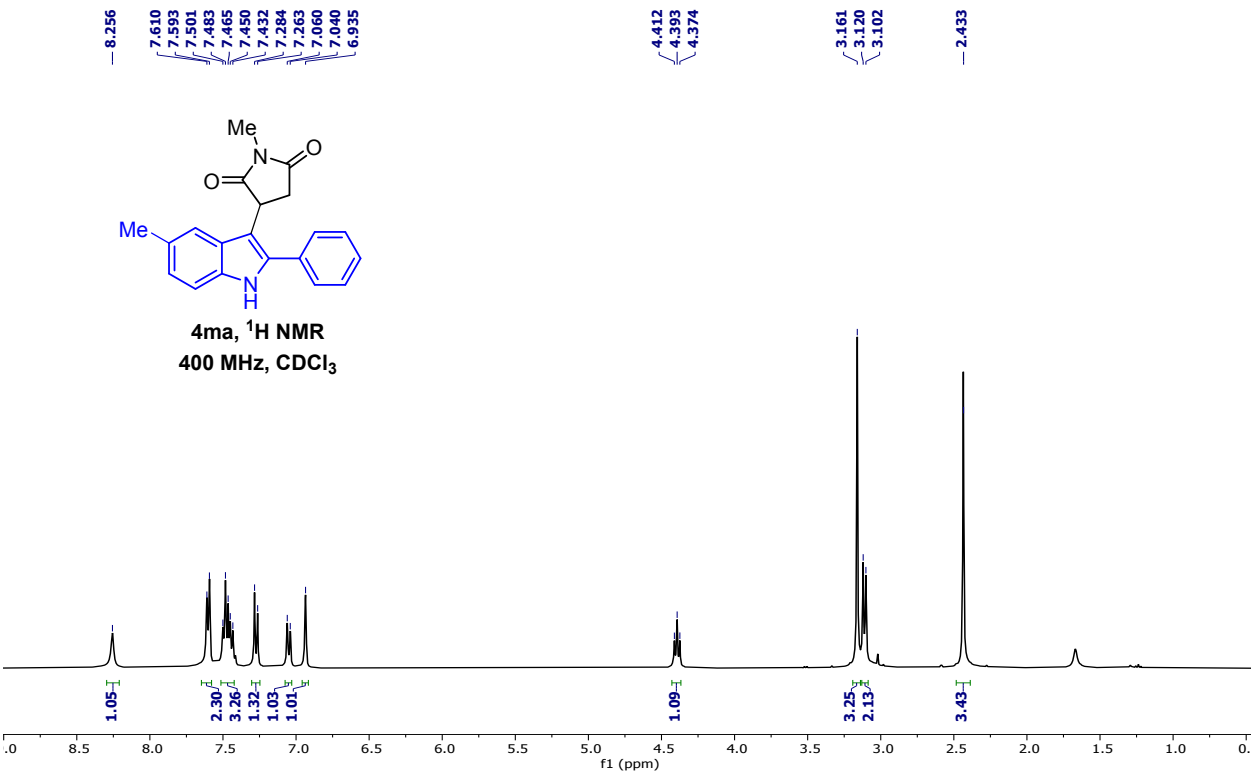
4ka, ^{13}C{^{1}H} NMR
100 MHz, DMSO-d_6



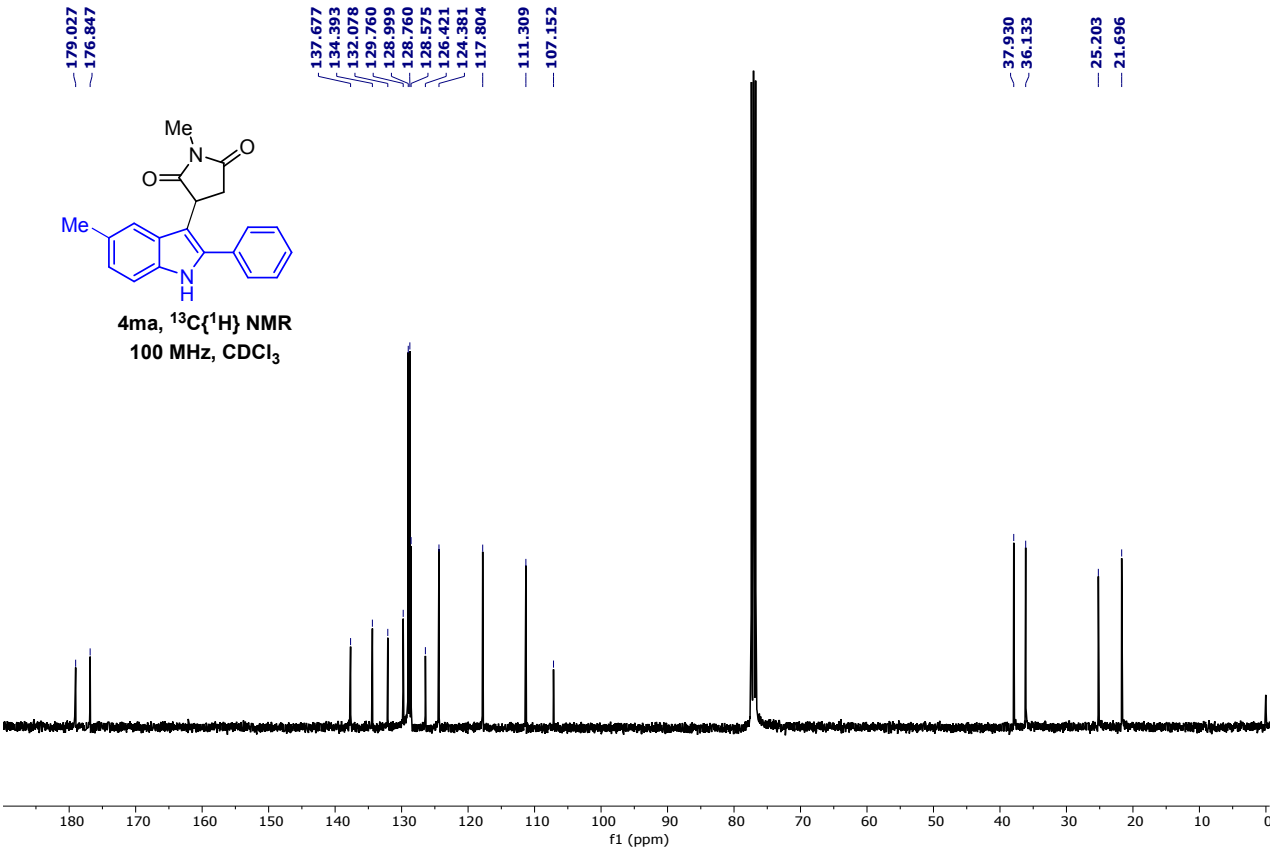
4la, ^{1}H NMR
400 MHz, DMSO-d_6



4la, ^{13}C{^{1}H} NMR
100 MHz, DMSO-d_6



4ma, ^{1}H NMR
400 MHz, $CDCl_3$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132.078
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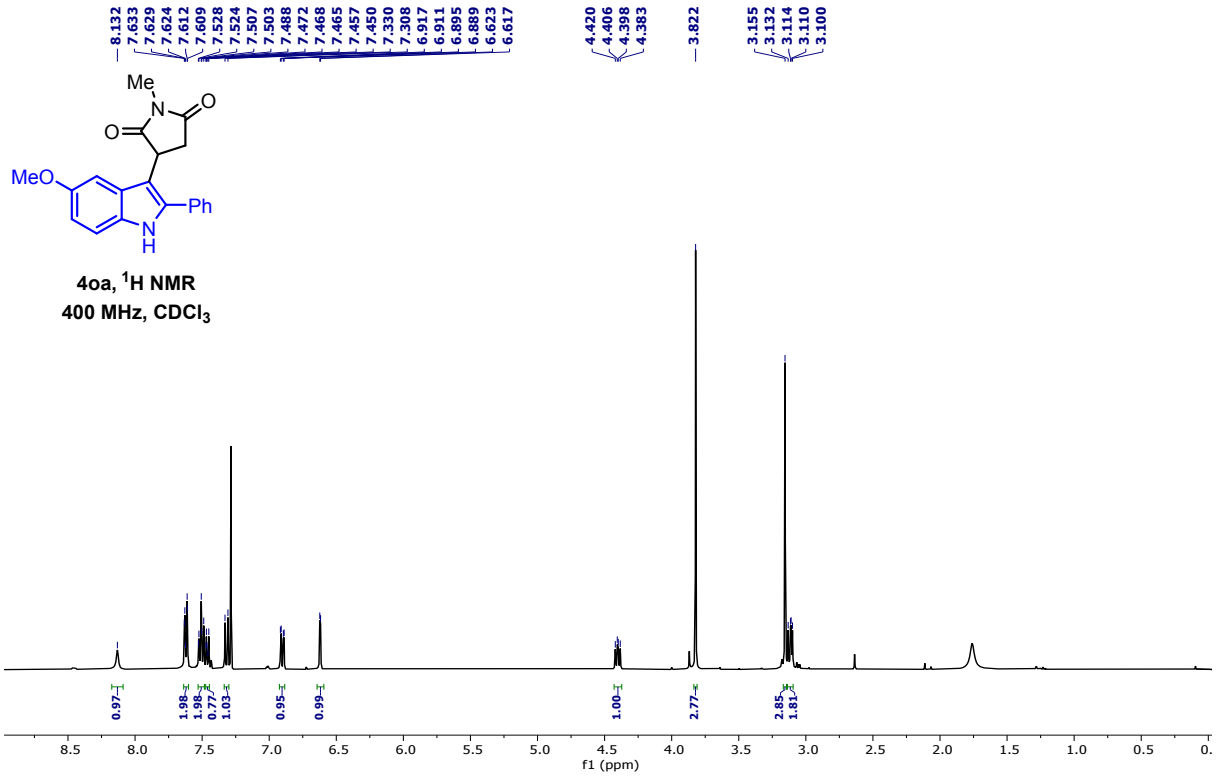
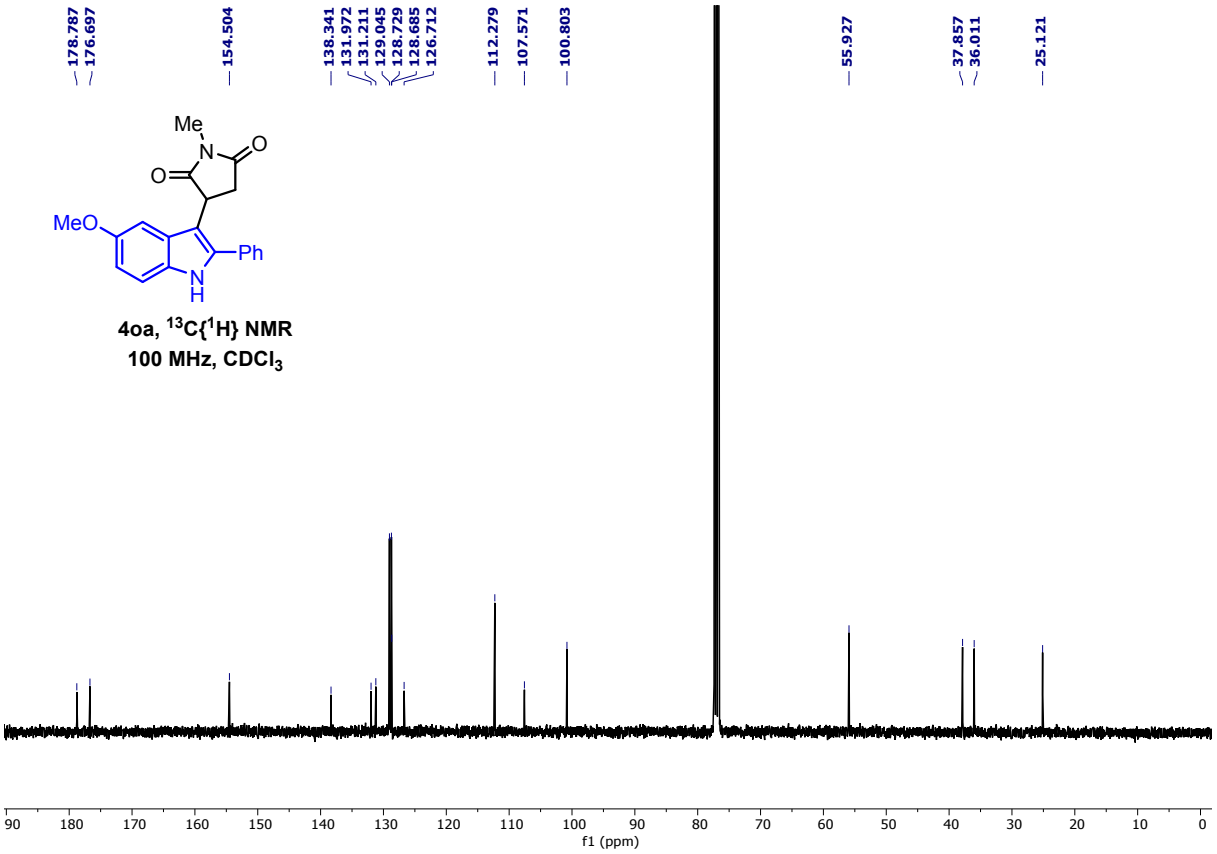
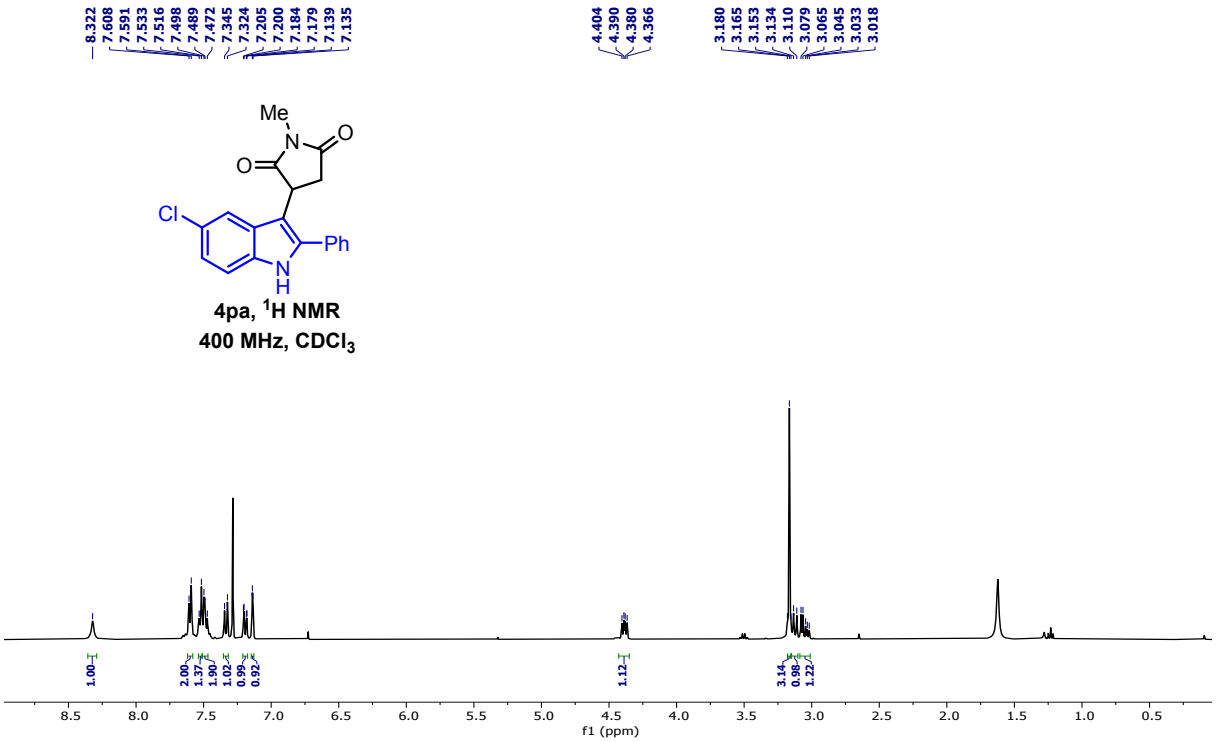
128.760
128.575
126.421
124.381
117.804
111.309
107.152
37.930
36.133
25.203
21.696
Me
N
O
O
Me
N
H
4ma, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



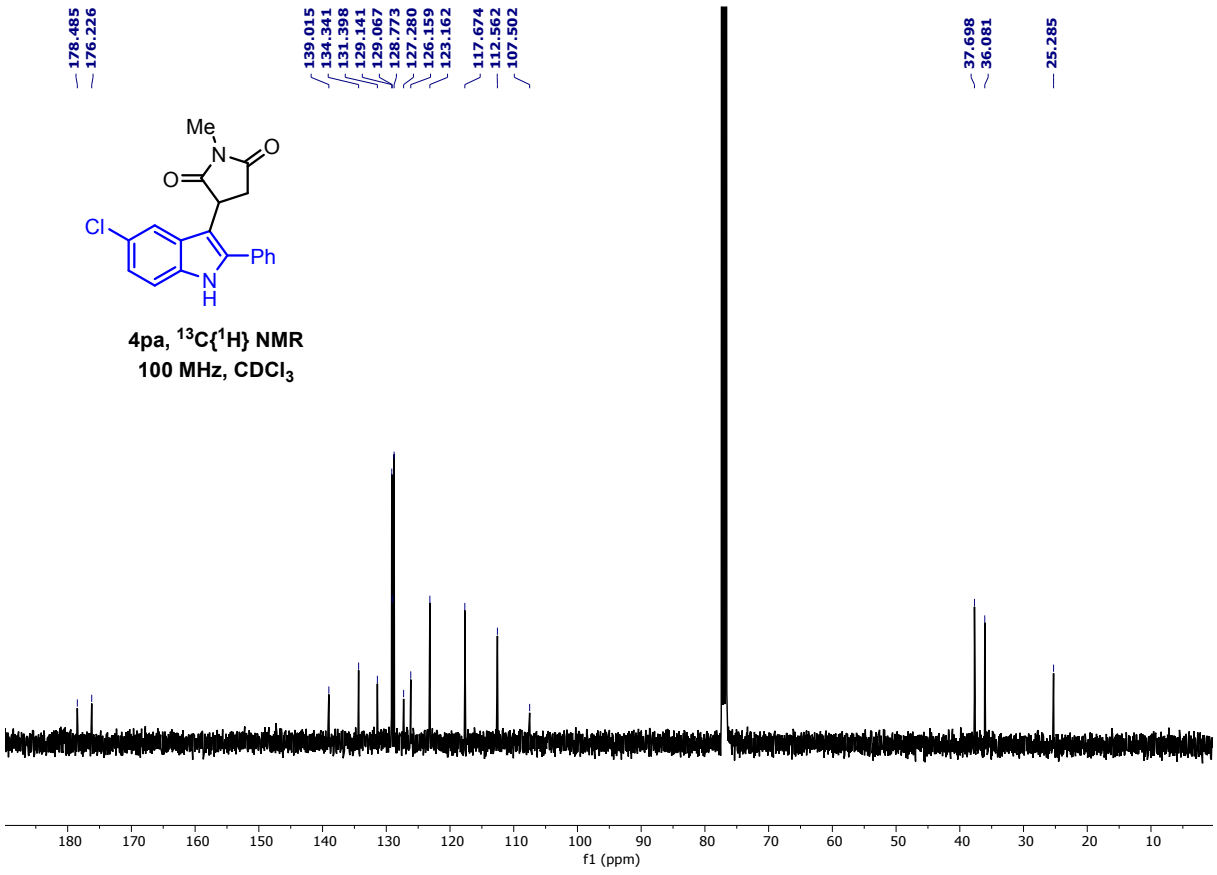
4oa, ^{1}H NMR
400 MHz, $CDCl_3$



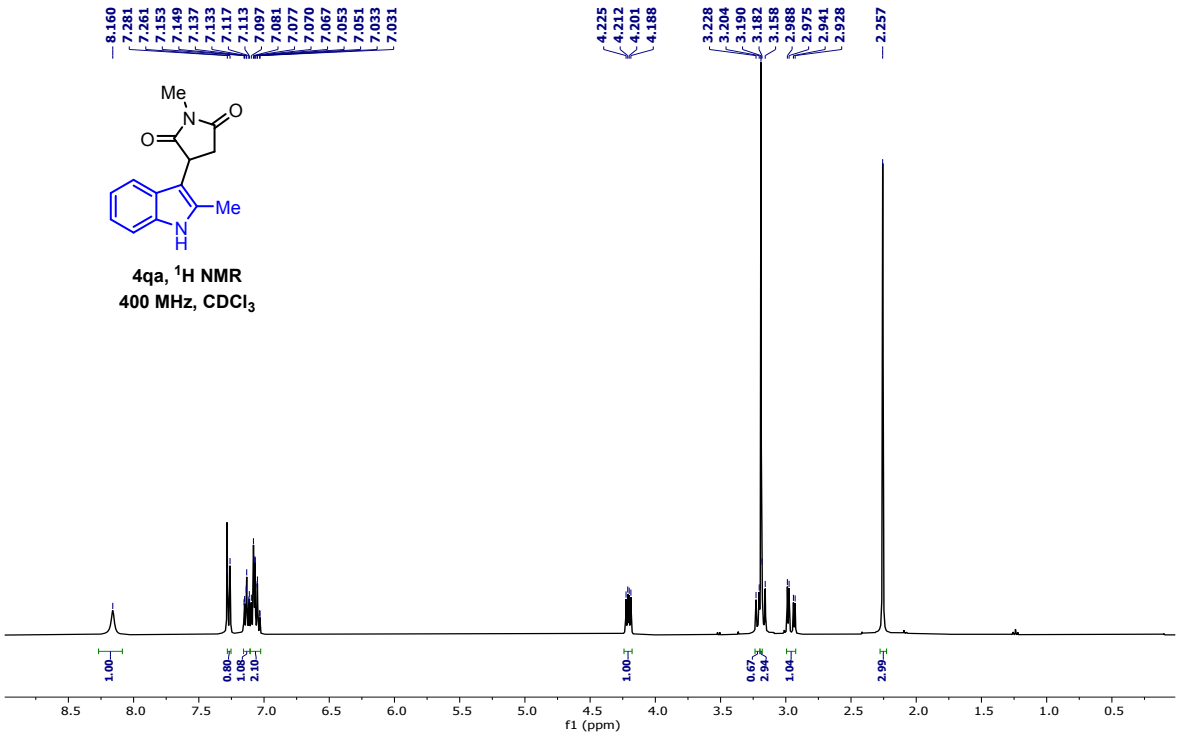
4oa, ^{13}C{^{1}H} NMR
100 MHz, $CDCl_3$



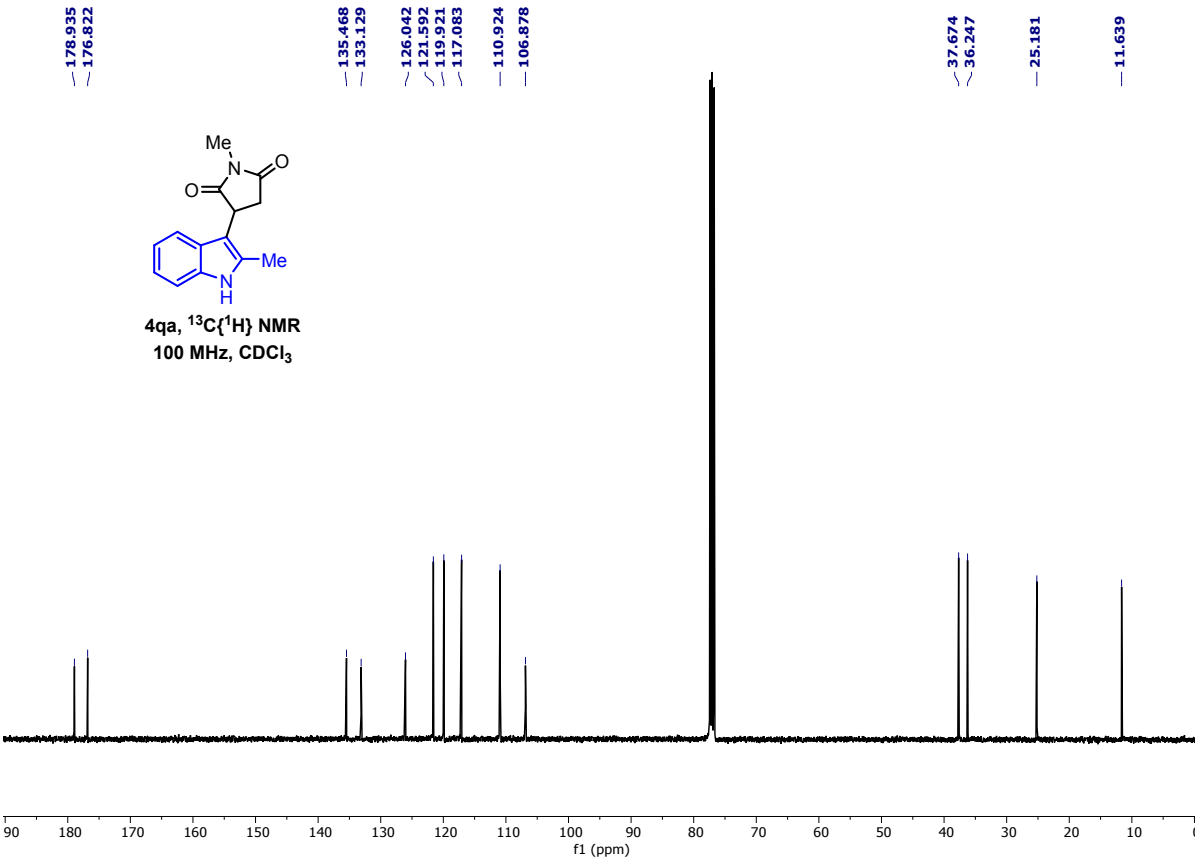
4pa, ^{1}H NMR
400 MHz, $CDCl_3$



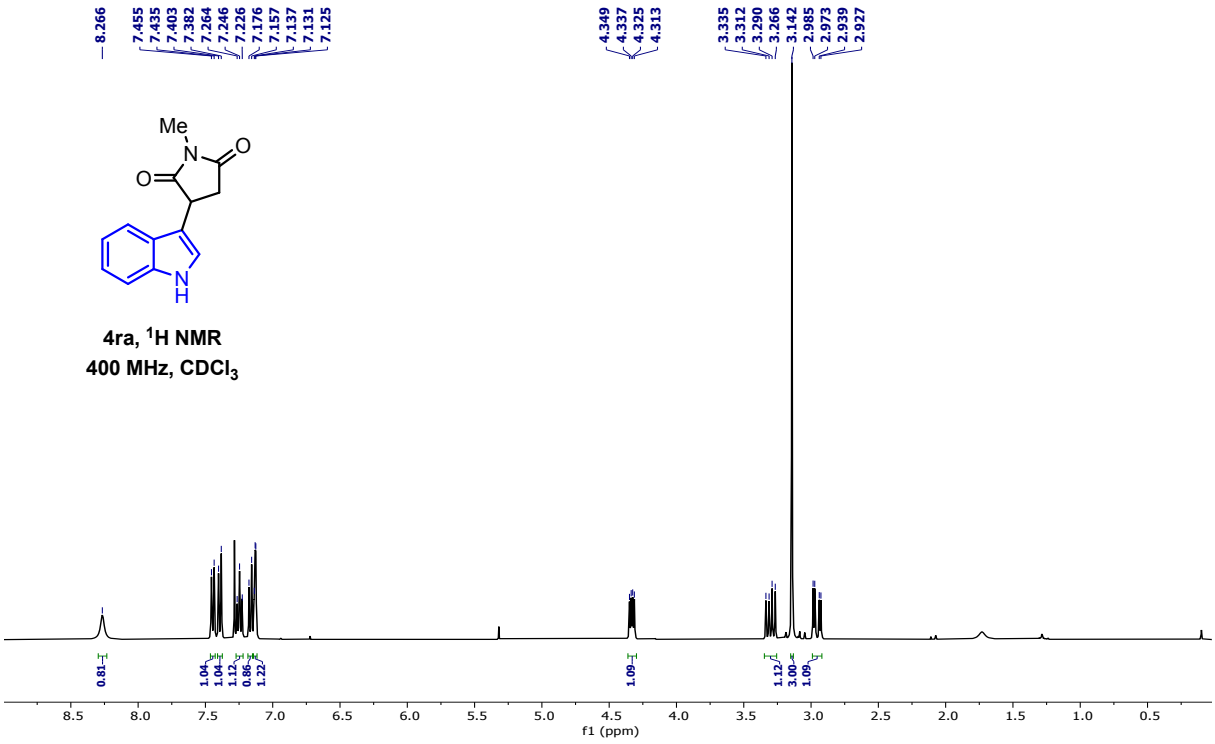
4pa, ^{13}C{^{1}H} NMR
100 MHz, $CDCl_3$



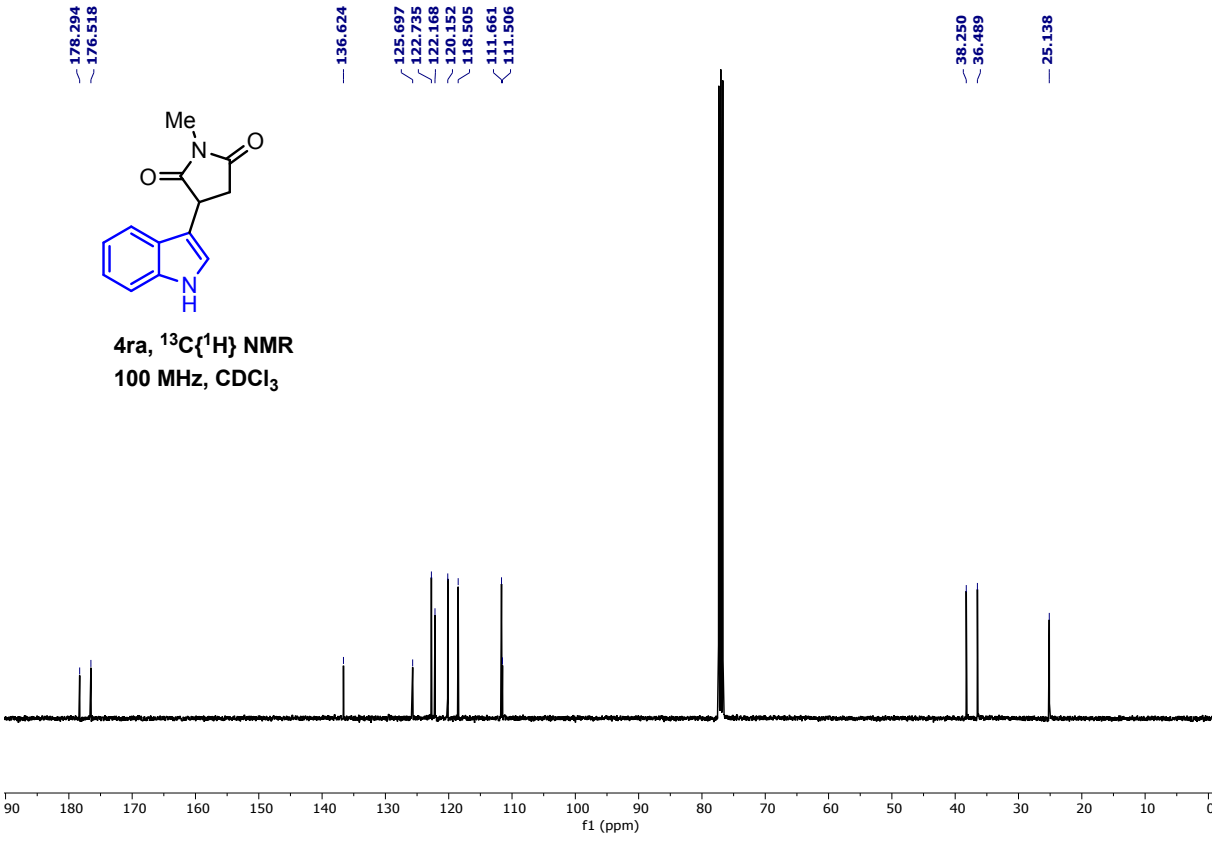
4qa, ^{1}H NMR
400 MHz, $CDCl_3$



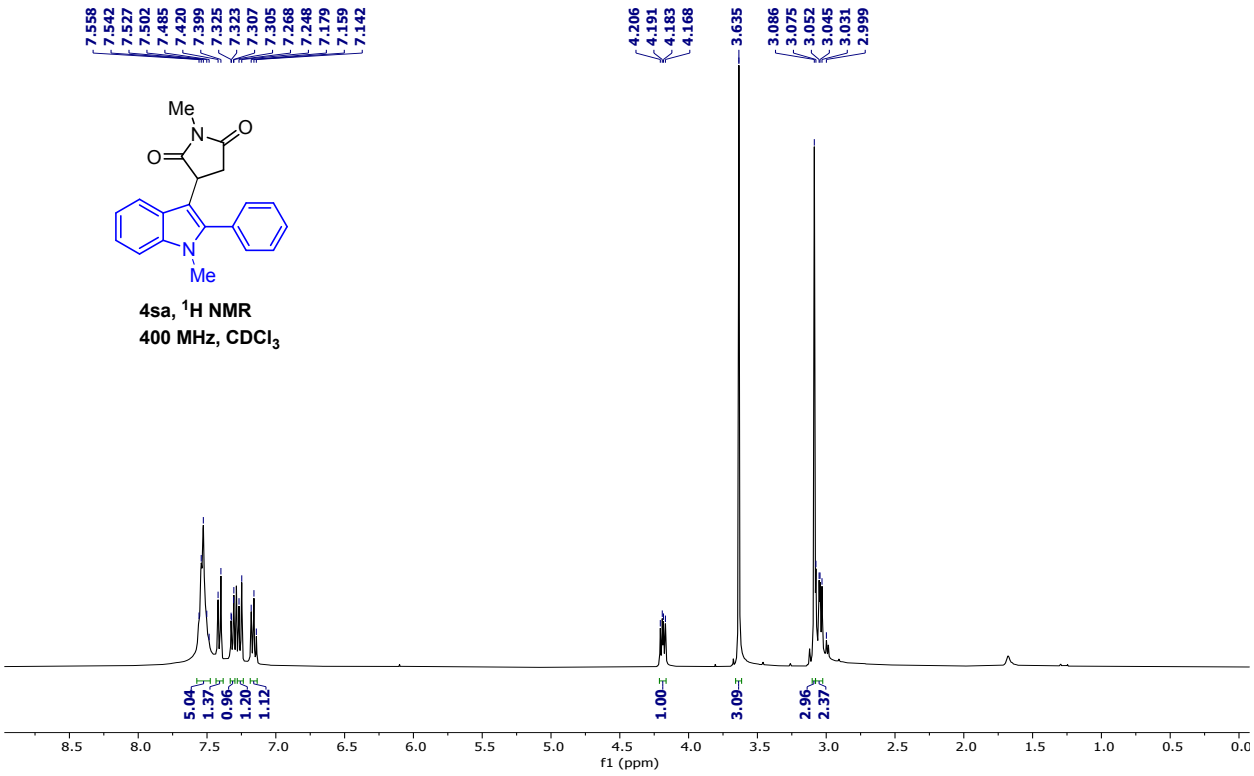
4qa, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



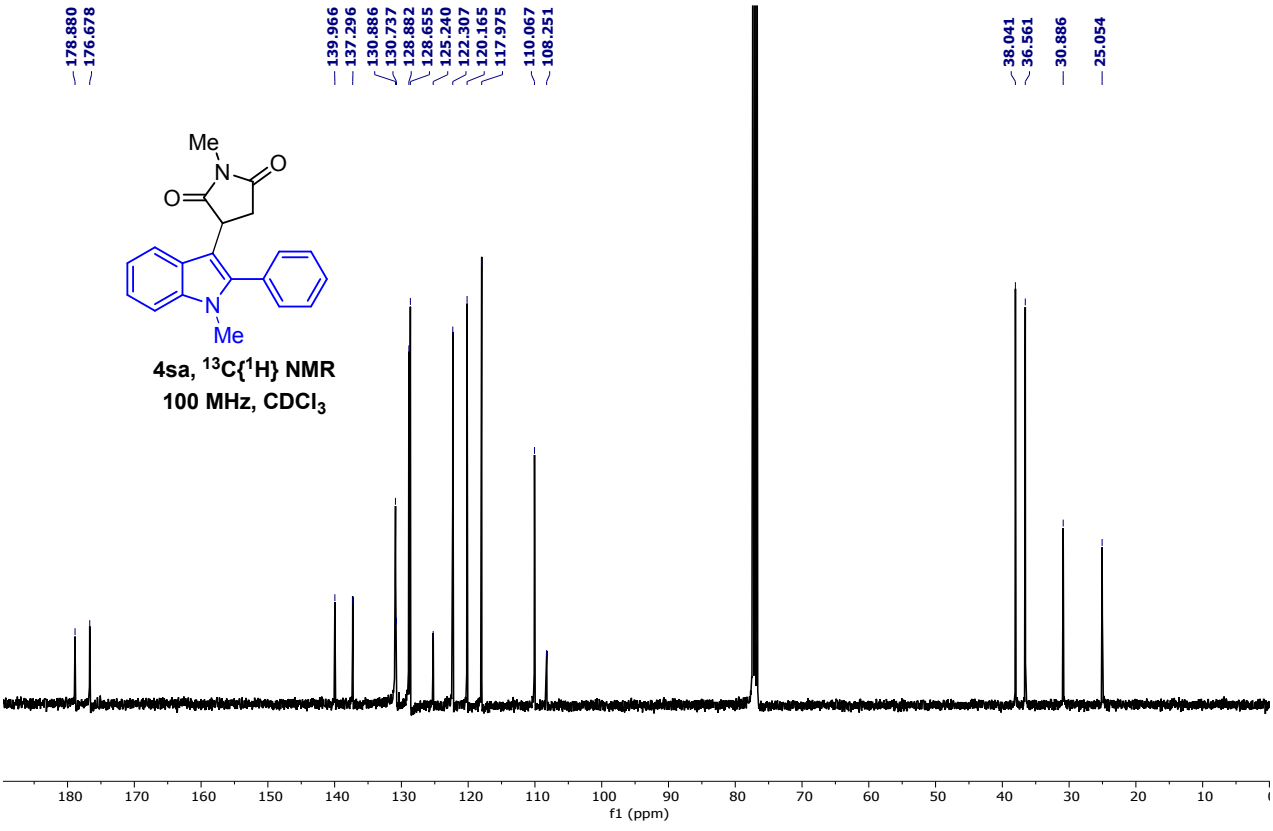
4ra, ^{1}H NMR
400 MHz, $CDCl_3$



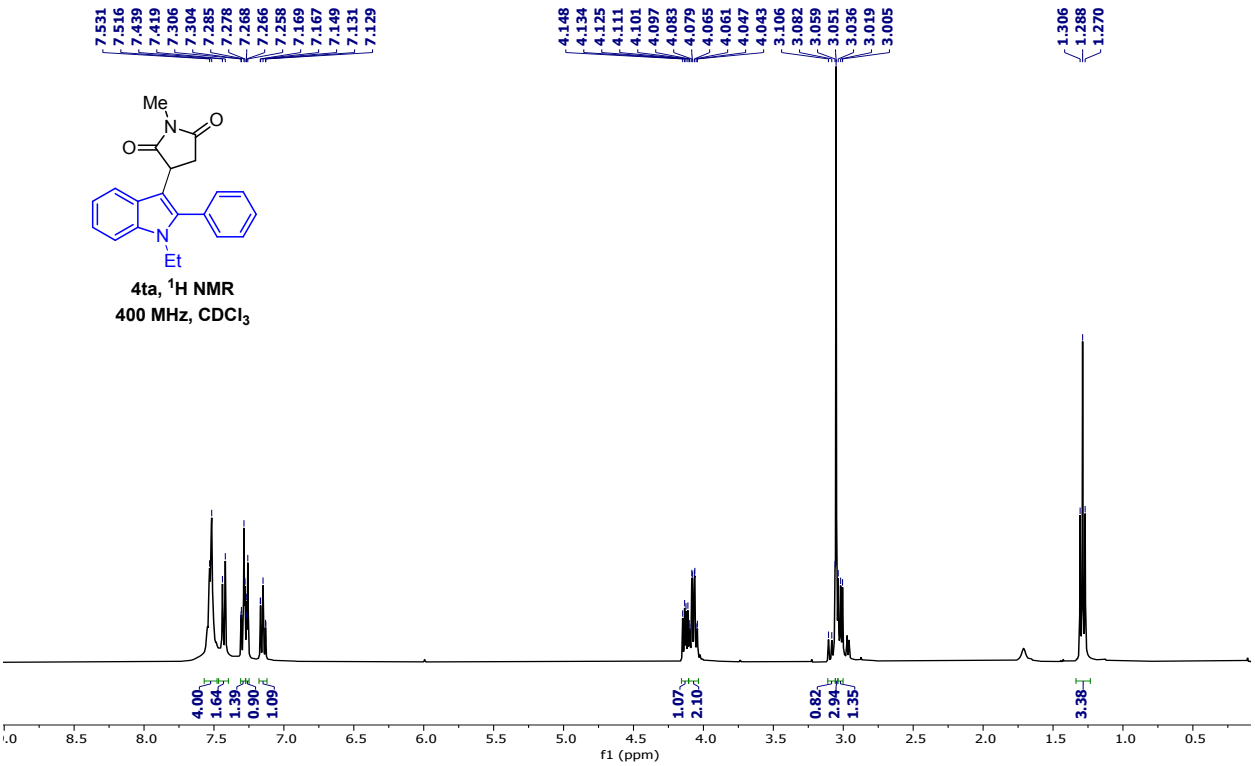
4ra, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



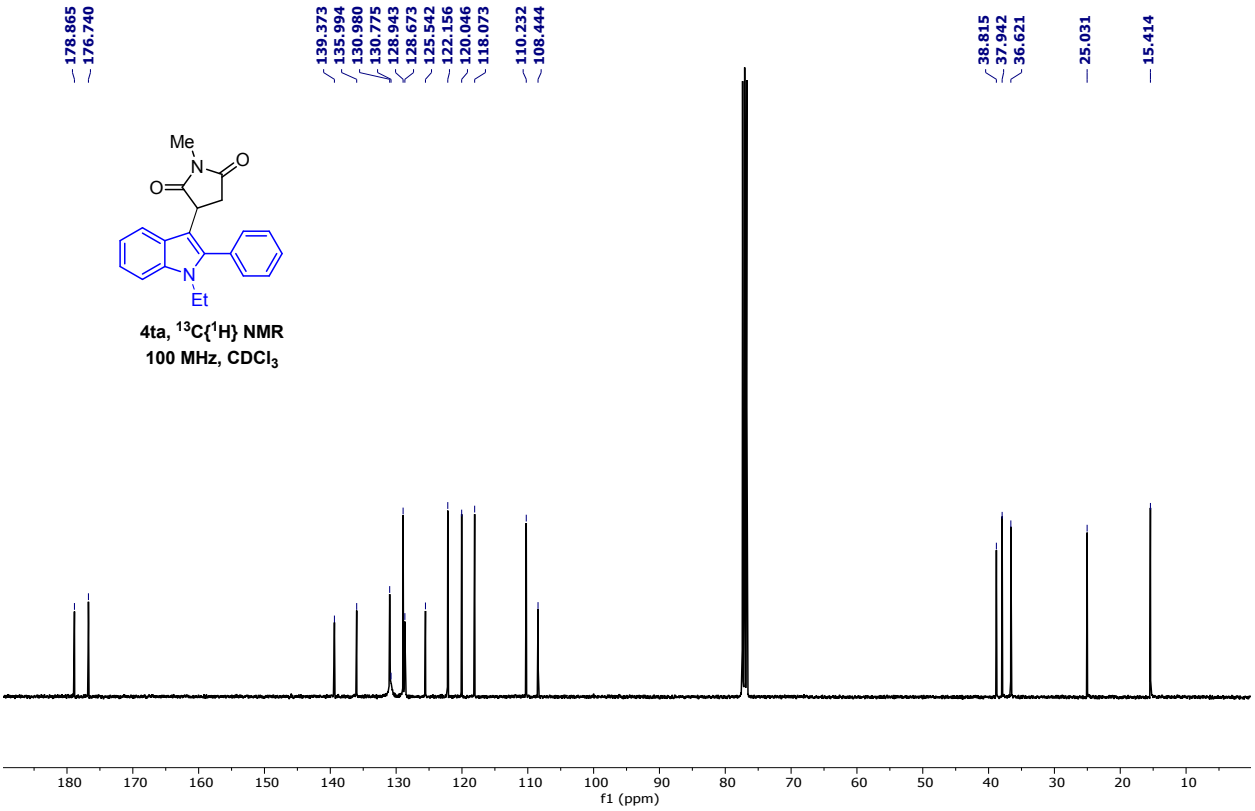
4sa, ^{1}H NMR
400 MHz, $CDCl_3$



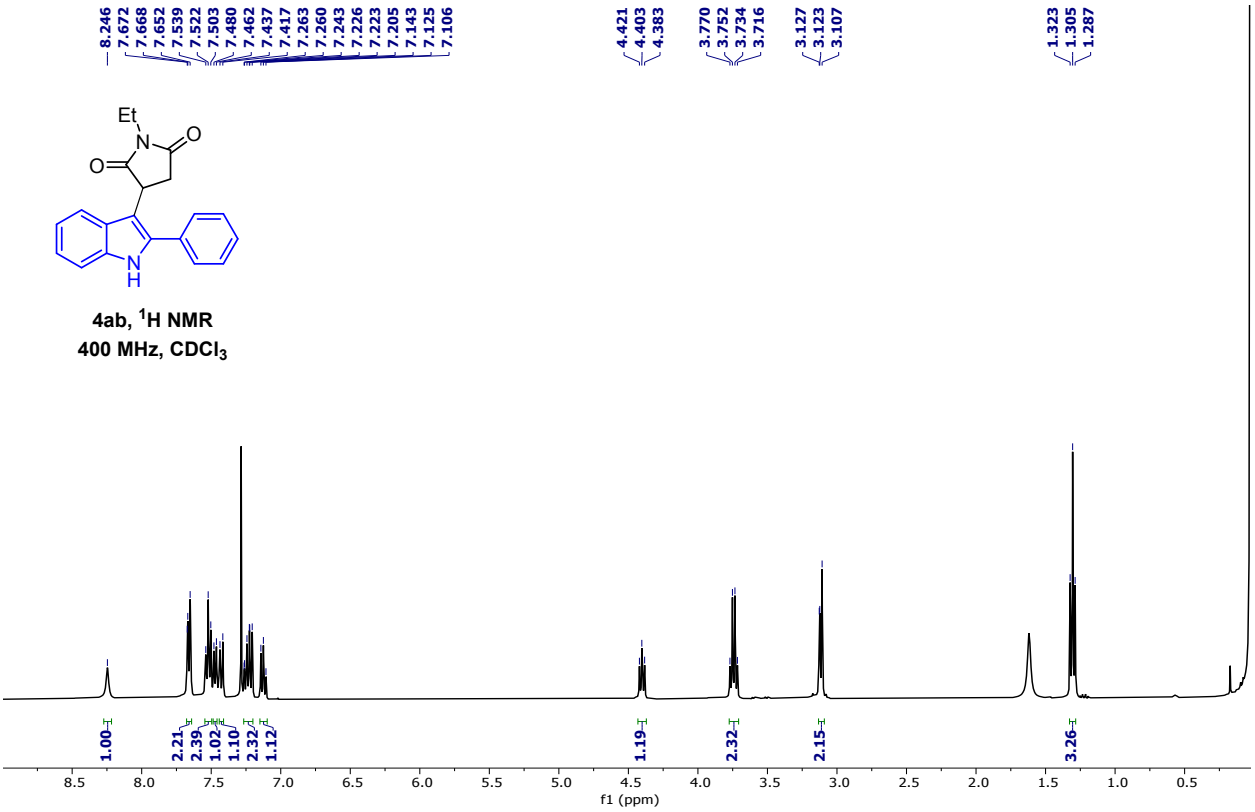
4sa, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



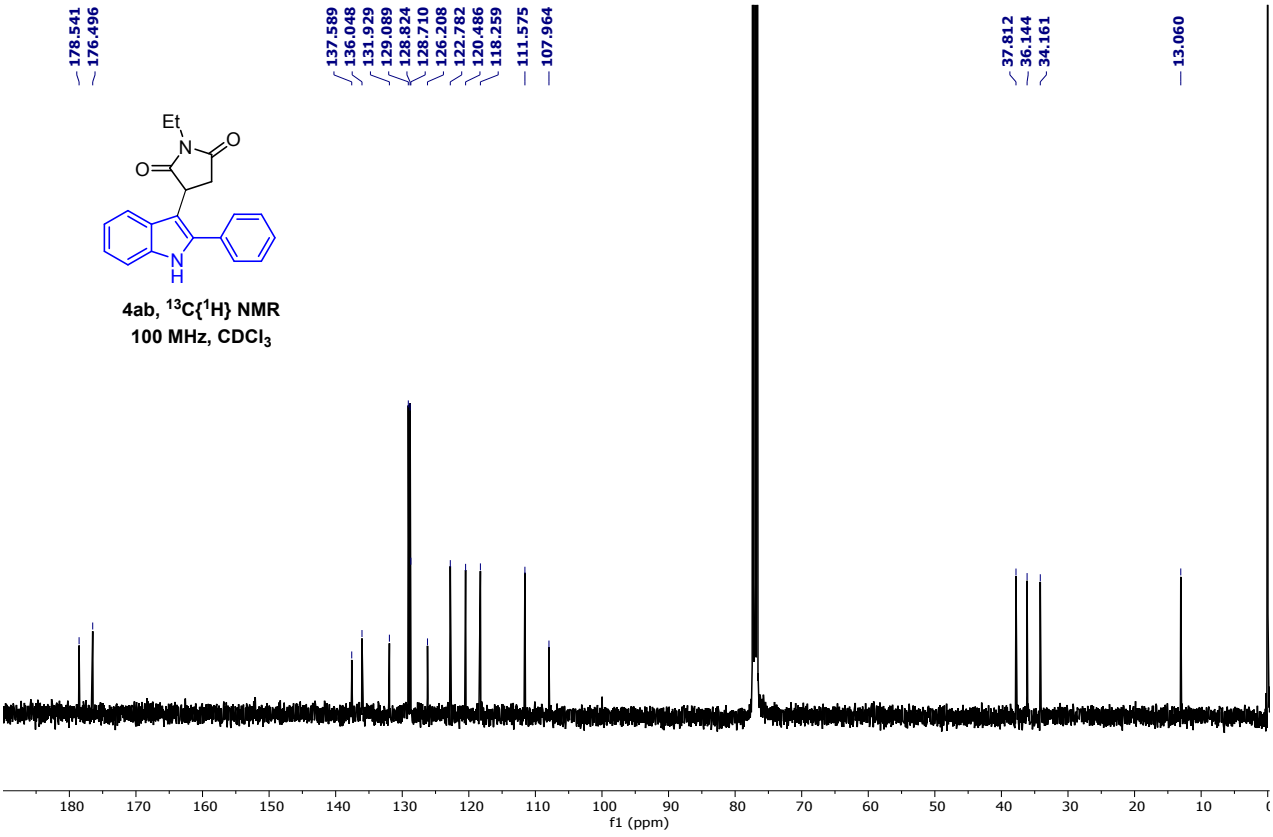
4ta, ^{1}H NMR
400 MHz, $CDCl_3$



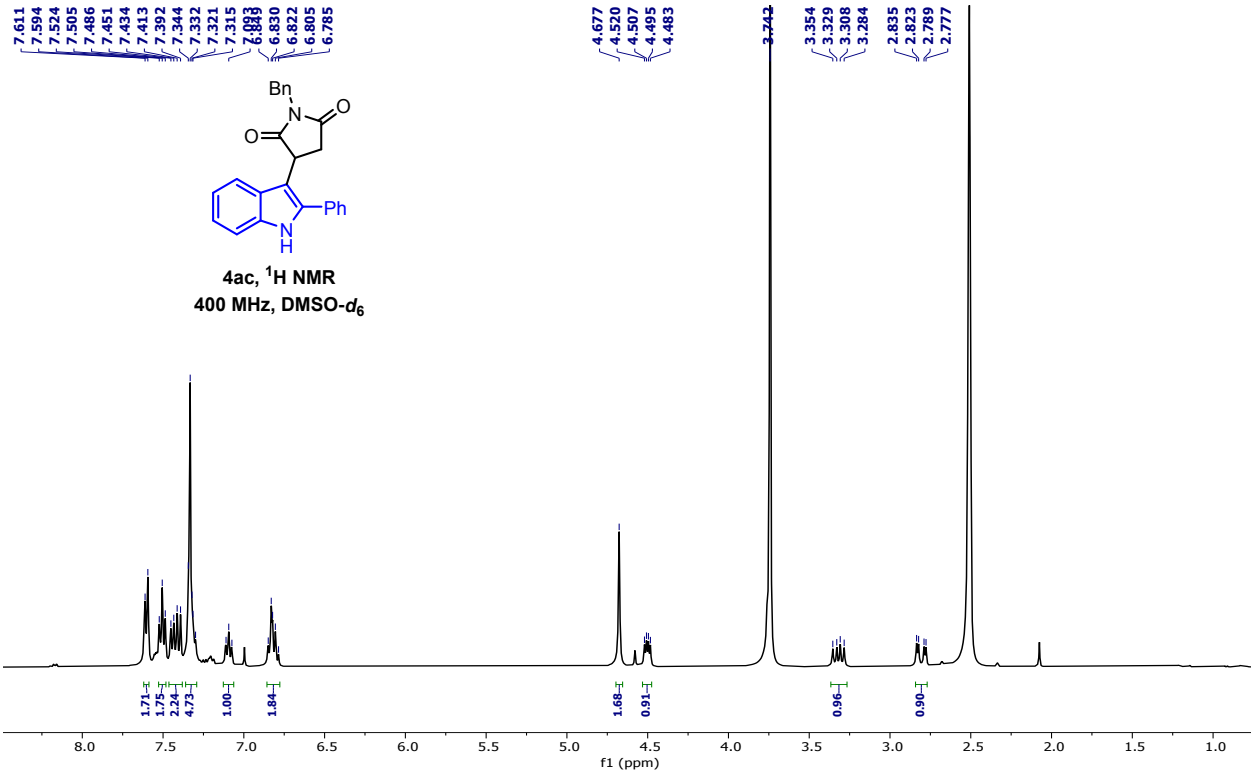
4ta, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



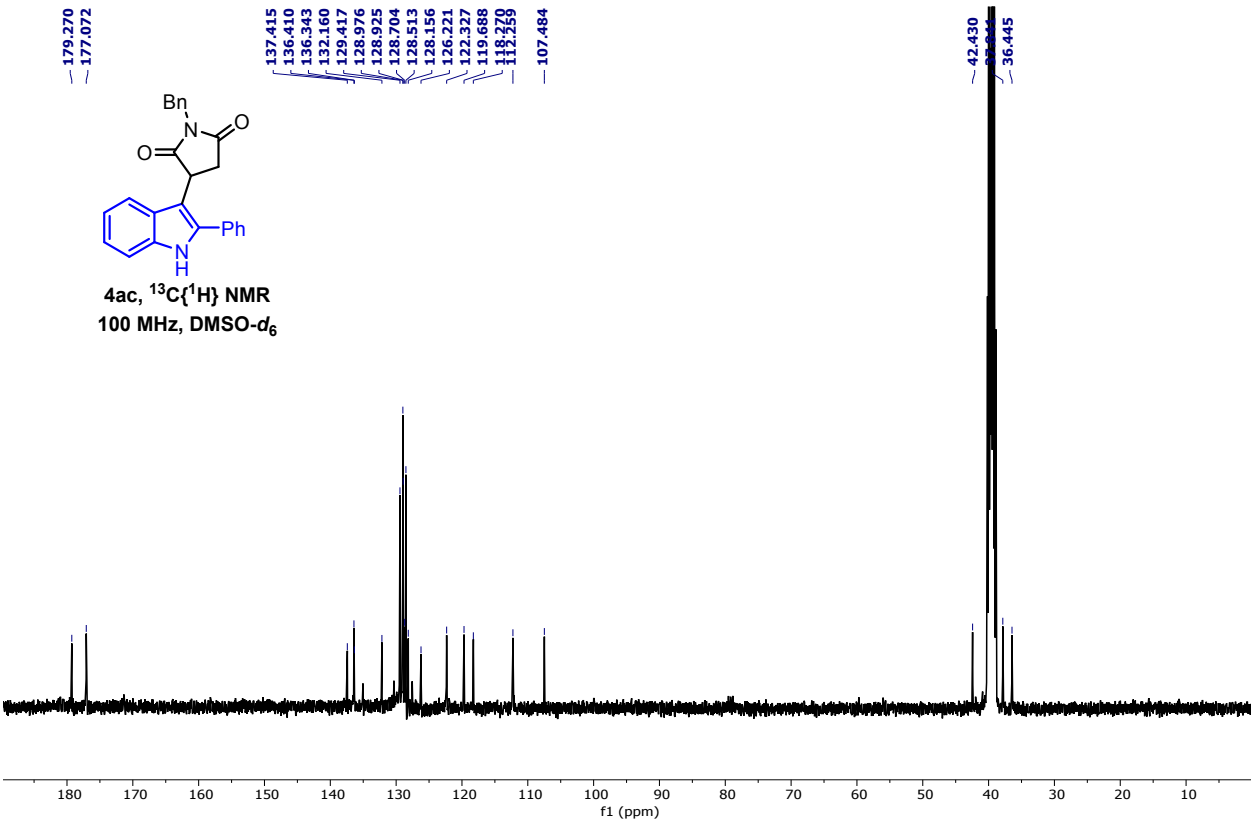
4ab, ^{1}H NMR
400 MHz, $CDCl_3$



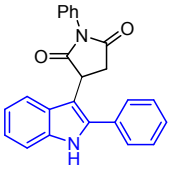
4ab, ^{13}C{^{1}H} NMR
100 MHz, $CDCl_3$



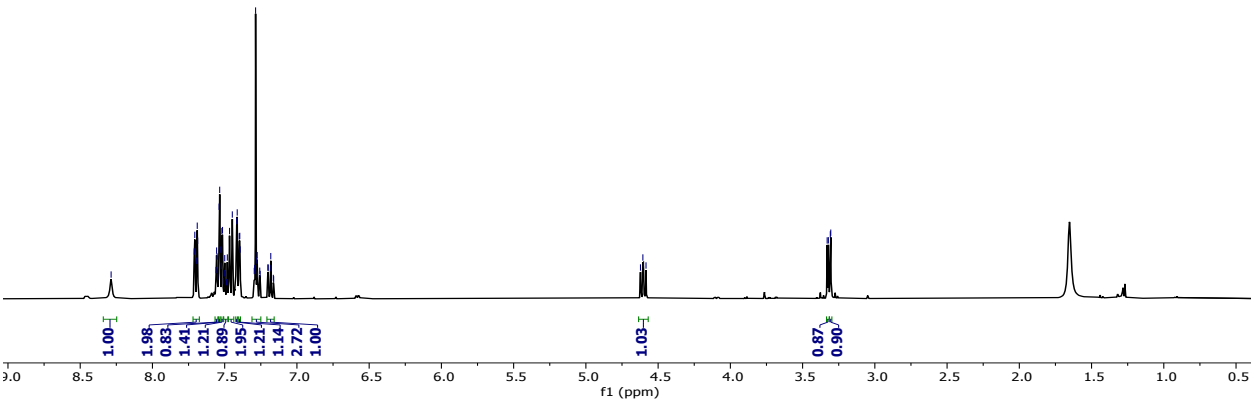
4ac, ^{1}H NMR
400 MHz, DMSO-d_6

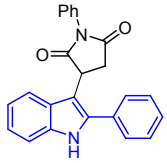


4ac, ^{13}C{^{1}H} NMR
100 MHz, DMSO-d_6

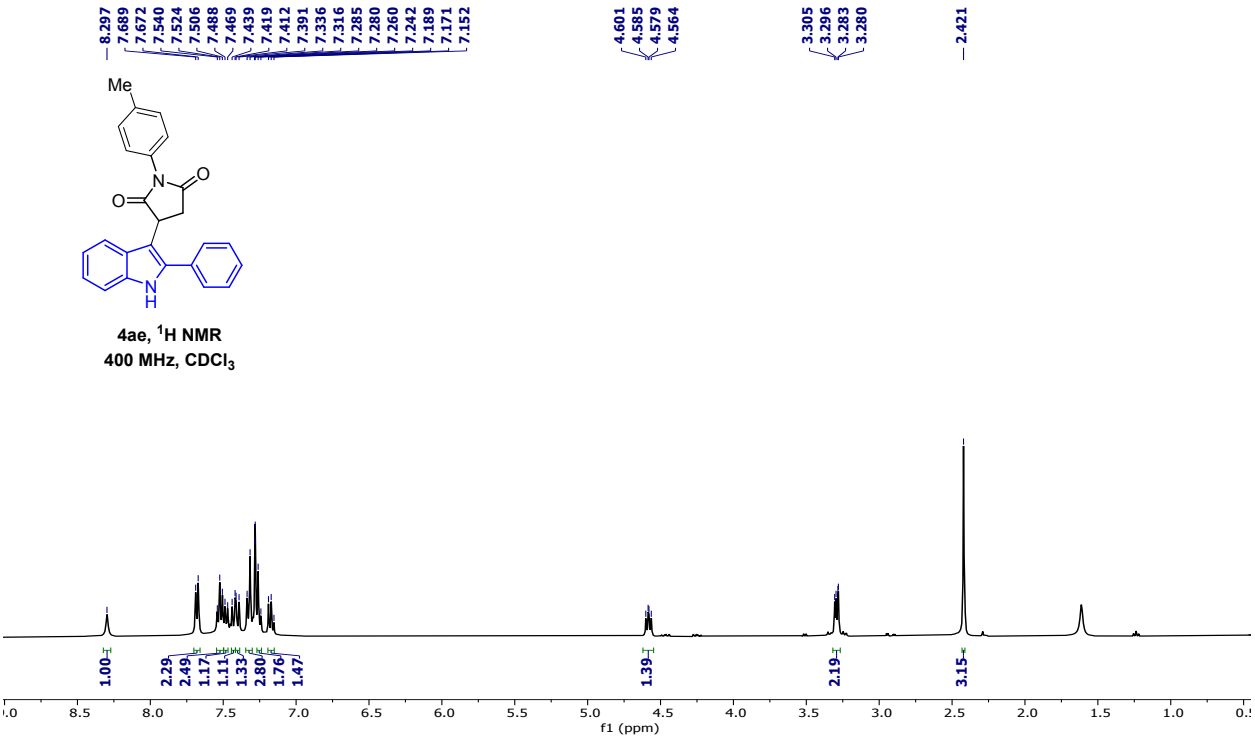


4ad, ^{1}H NMR
400 MHz, $CDCl_3$

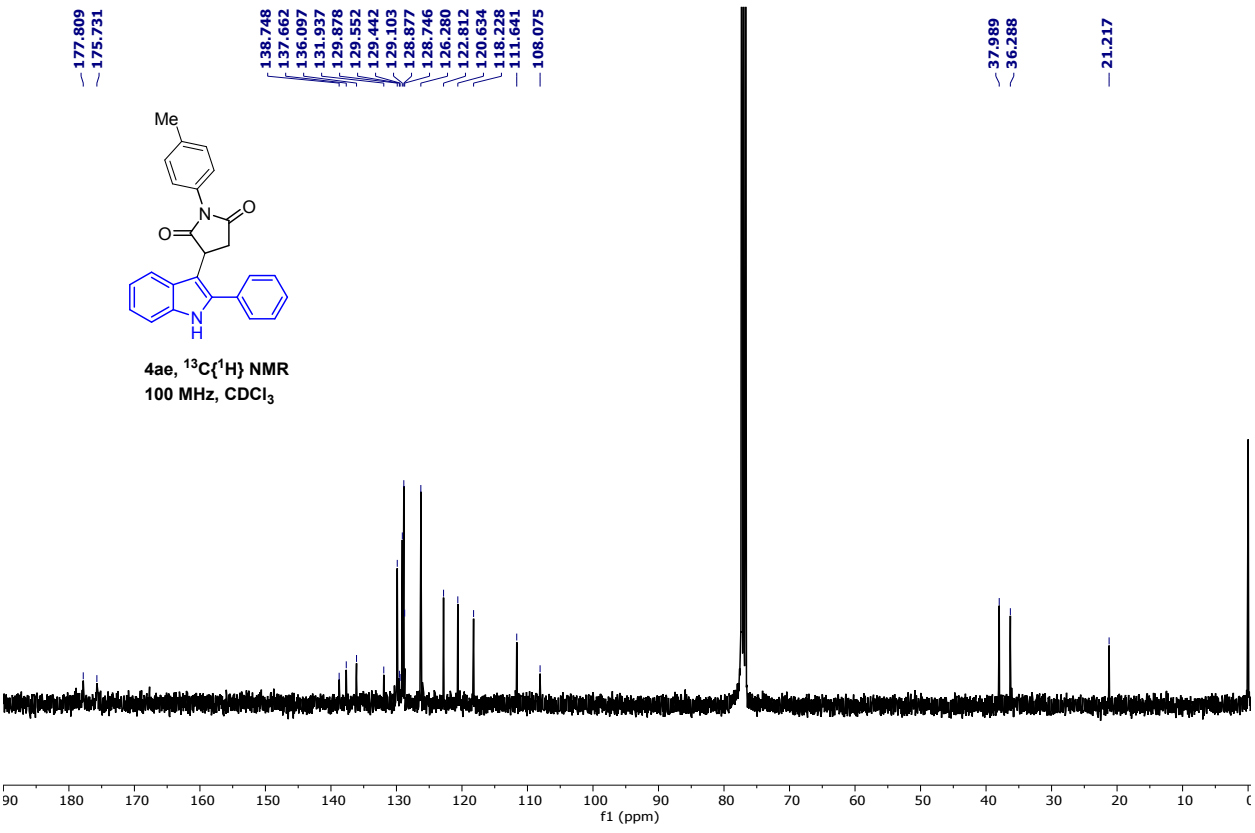




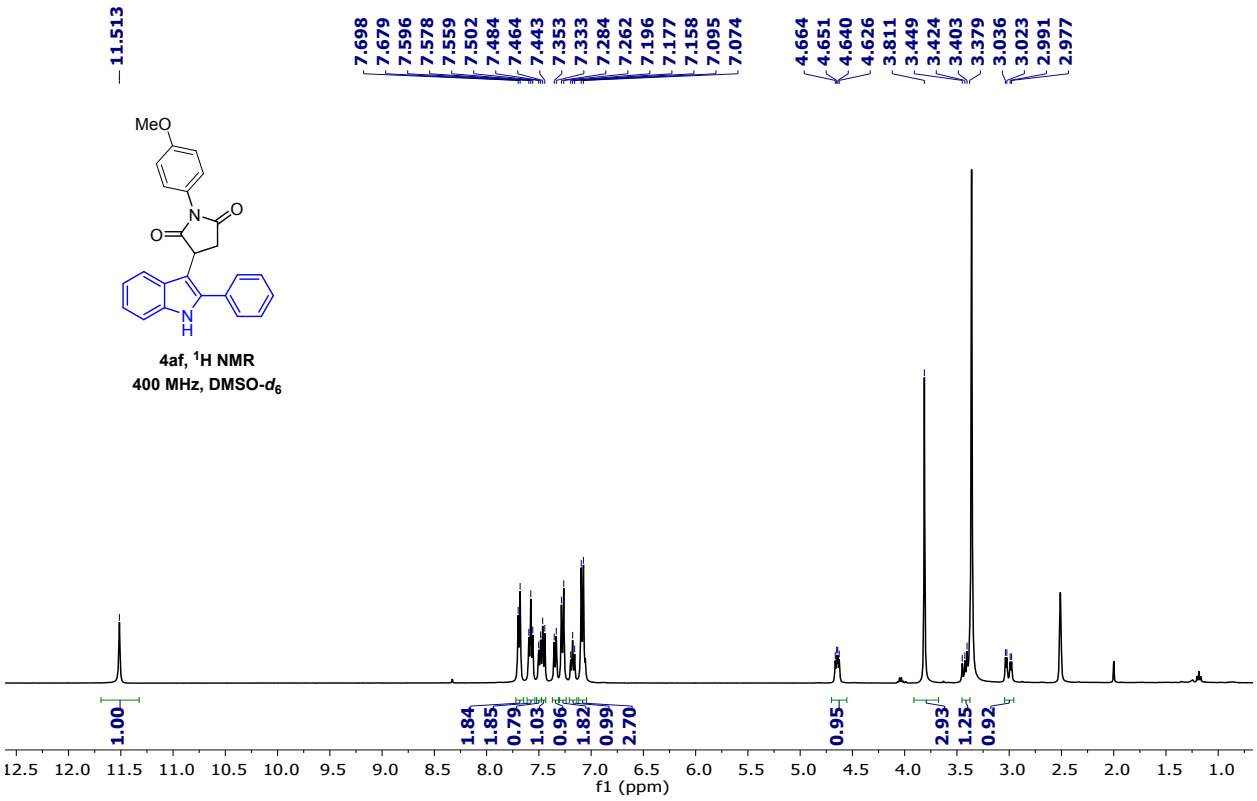
4ad, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



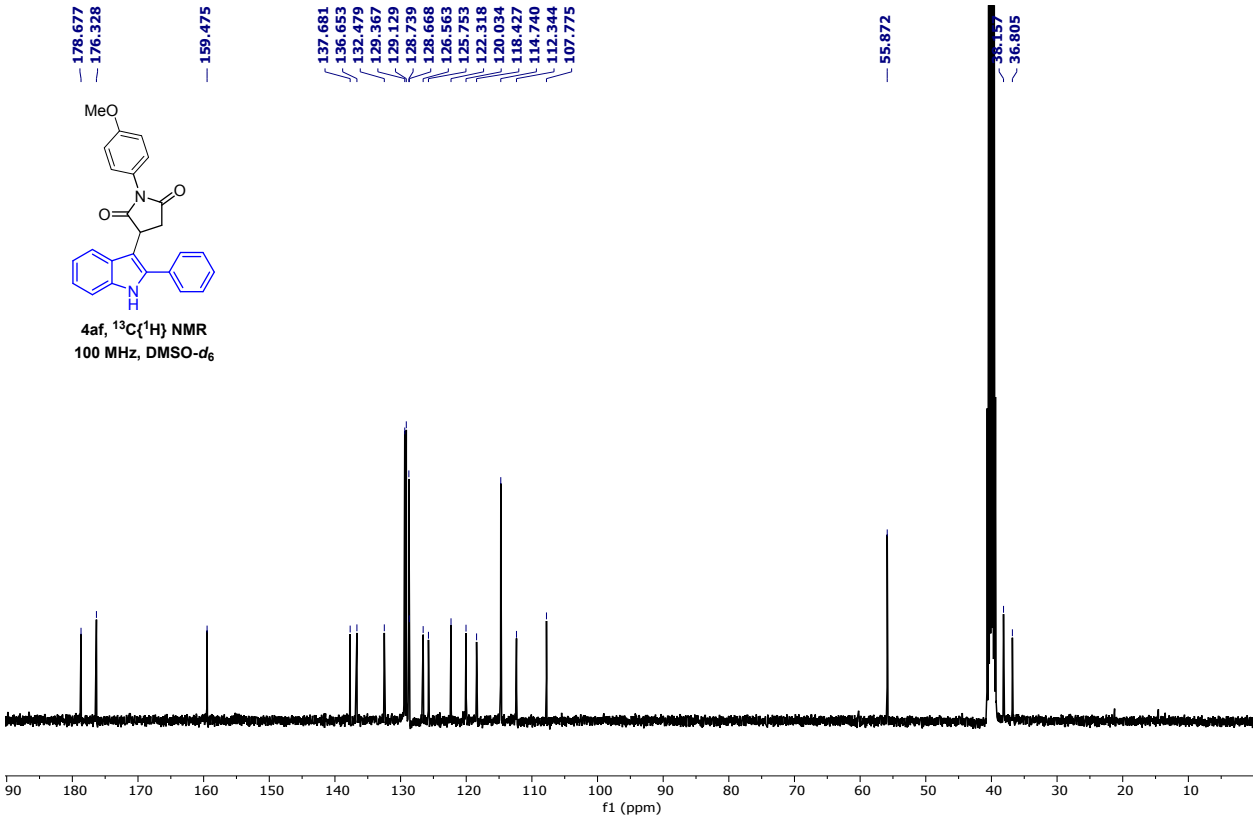
4ae, ^{1}H NMR
400 MHz, $CDCl_3$



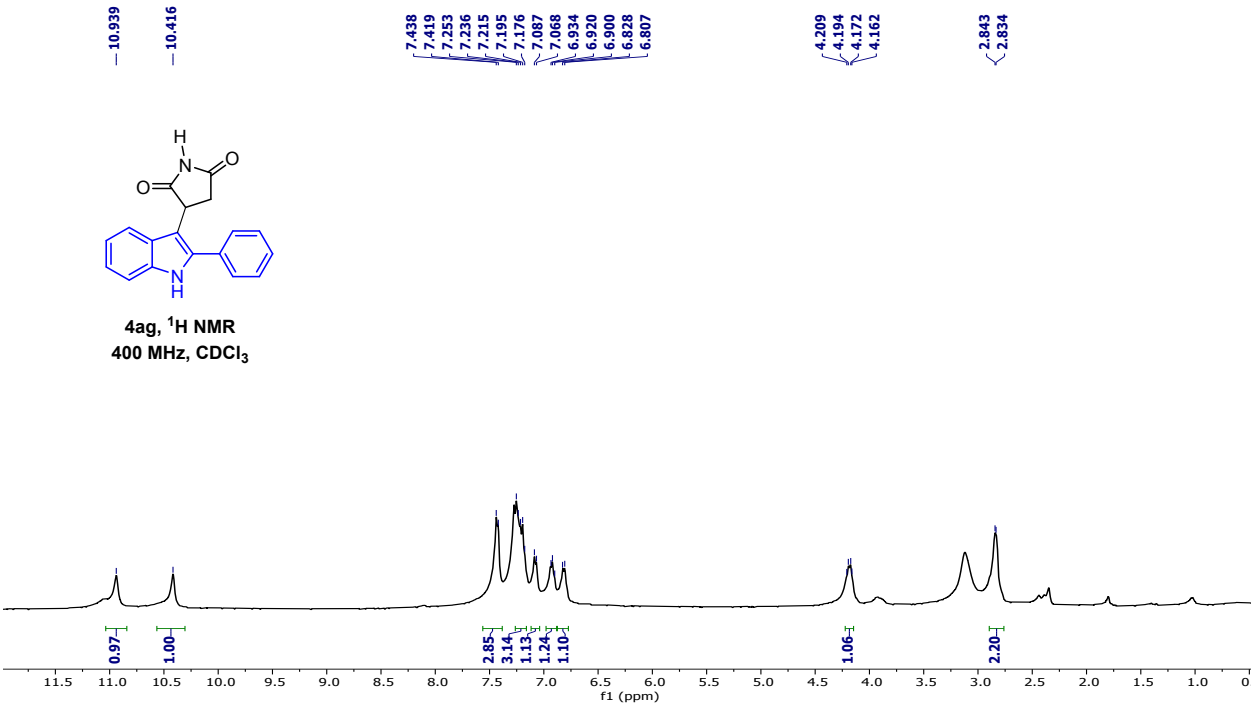
4ae, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$



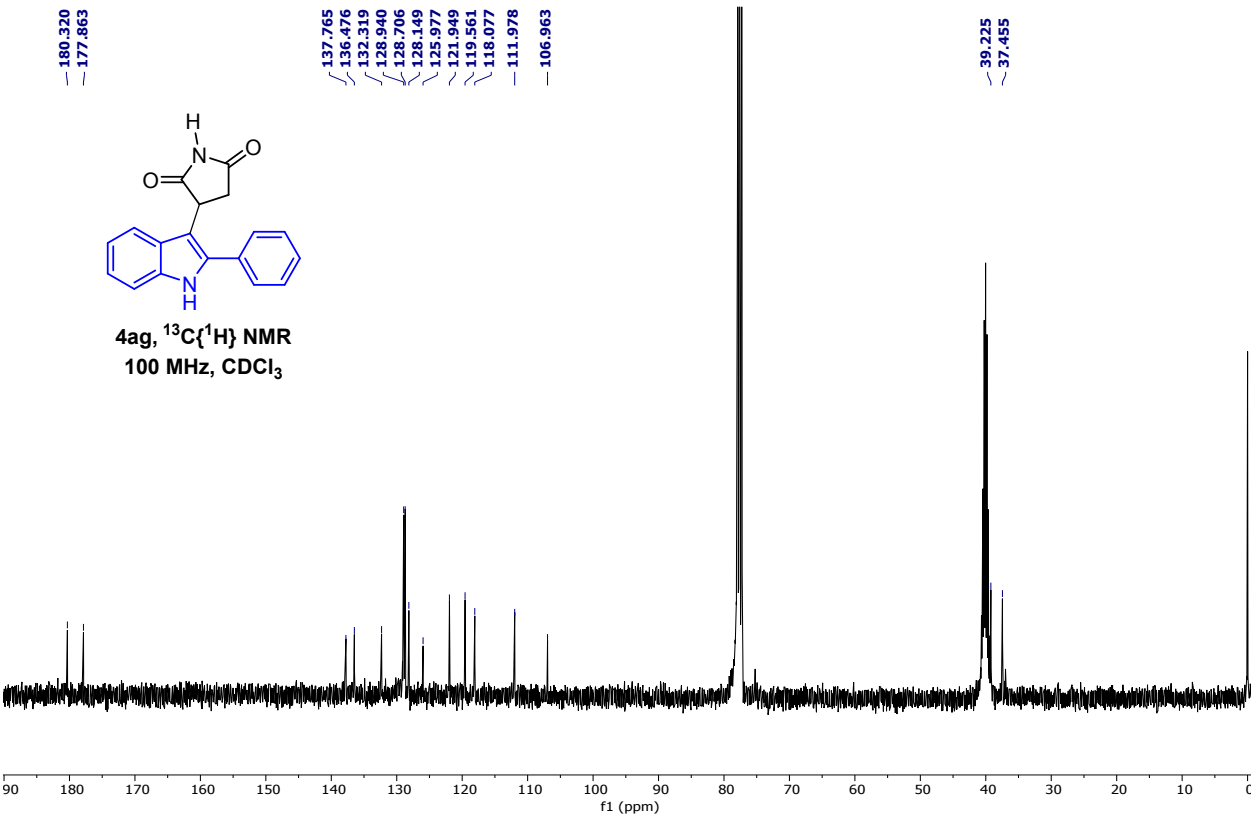
4af, ^{1}H NMR
400 MHz, DMSO-d_6



4af, ^{13}C{^{1}H} NMR
100 MHz, DMSO-d_6



4ag, ^{1}H NMR
400 MHz, $CDCl_3$



4ag, $^{13}C\{^{1}H\}$ NMR
100 MHz, $CDCl_3$

4. X-ray Crystallographic Analysis of 3aa

The single crystals of the compound **3aa** were obtained as yellow blocks from chloroform-hexane solvent mixture. The crystal data collection and data reduction were performed using CrysAlis PRO on a single crystal Rigaku Oxford XtaLab Pro diffractometer. The crystals were kept at 93(2) K during data collection using CuKα (λ = 1.54184) radiation. Using Olex2,[1] the structure was solved with the ShelXT[2] structure solution program using Intrinsic Phasing and refined with the ShelXL[3] refinement package using Least Squares minimization.

Table S1 Crystal data and structure refinement for 3aa.

Identification code	exp_687-AK-DNS-59
Empirical formula	$C_{19}H_{16}N_2O_2$
Formula weight	304.34
Temperature/K	93(2)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	12.4146(6)
b/Å	9.1711(5)
c/Å	13.5882(8)
α/°	90
β/°	105.086(5)
γ/°	90
Volume/Å^3	1493.77(14)
Z	4
ρ_{calc}g/cm^3	1.353
μ/mm^{-1}	0.716
F(000)	640.0
Crystal size/mm^3	0.15 × 0.1 × 0.04
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	6.738 to 159.198
Index ranges	-15 ≤ h ≤ 14, -11 ≤ k ≤ 6, -16 ≤ l ≤ 17
Reflections collected	8879
Independent reflections	4340 [R_{int} = 0.0685, R_{sigma} = 0.0914]
Data/restraints/parameters	4340/1/417
Goodness-of-fit on F^2	1.094
Final R indexes [I>=2σ (I)]	R_1 = 0.0862, wR_2 = 0.2693
Final R indexes [all data]	R_1 = 0.0903, wR_2 = 0.2721
Largest diff. peak/hole / e Å^{-3}	0.66/-0.49
Flack parameter	-0.1(4)

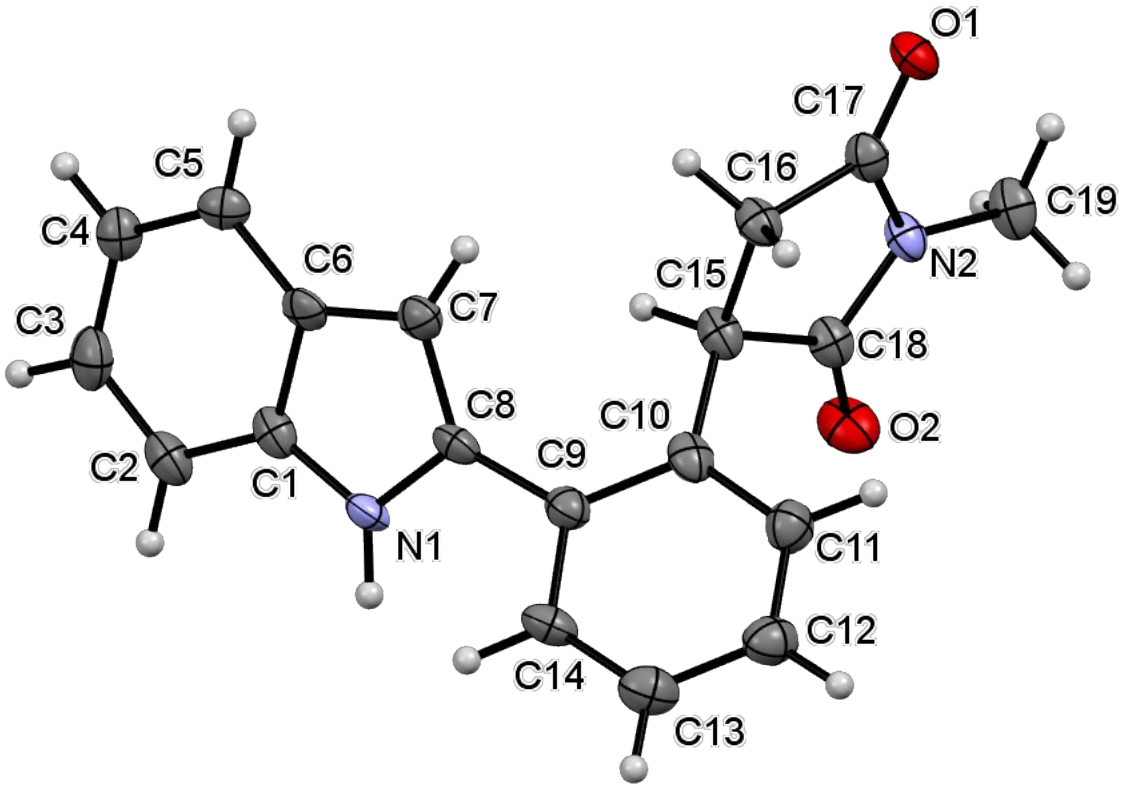


Figure S1. The crystal structure ORTEP diagram of the compound **3aa**. Only one of the two molecules appear in an asymmetric unit is shown for clarity. The thermal ellipsoids are drawn at 50 % probability level. CCDC number 2068507.

5. References

1. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Cryst.*, 2009, **42**, 339-341.
2. G. Sheldrick, *Acta Cryst. A*, 2015, **71**, 3-8.
3. G. Sheldrick, *Acta Cryst. C*, 2015, **71**, 3-8.