Supplementary Material

Selective aliphatic thiol conjugation to *α*-benzylidene succinimides: A versatile route to advanced succinimide functionalization

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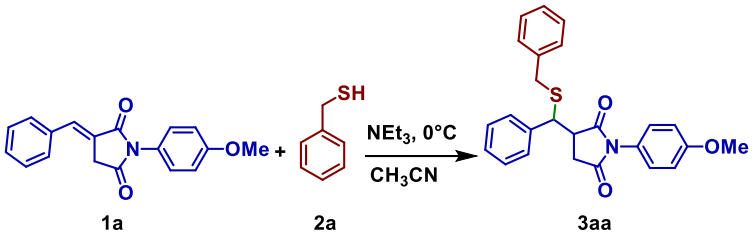
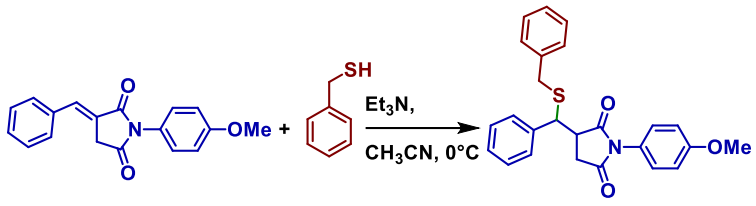
1. The study of base (NEt_3) equivalents



Entry	Et_3N (equiv.)	Time (h)	[a]Yield (%)
1	-	24	-
2	0.5	24	55
3	1	8	76
4	1.5	7	72
5	2	6	60

Reaction Condition: **1a** (50 mg, 0.17 mmol, 1 equiv.), **2a** (32 mg, 0.30 µL, 1.5 equiv.), **Et_3N** (17 mg, 0.17 mmol, 1 equiv., 24 µL), **CH_3CN** (3 mL) at 0 °C temperature. [a]Isolated yield.

2. Scale up condition for the synthesis of 3-((benzylthio)(phenyl)methyl)-1-(4-methoxyphenyl)pyrrolidine-2,5-dione (3aa):



In a 25 mL oven-dried round-bottom flask, (E)-3-benzylidene-1-(4-methoxyphenyl) pyrrolidine-2,5-dione **1a** (3.4 mmol, 1 equiv.) and benzyl mercaptan **2a** (3.74 mmol, 1.1 equiv.) were dissolved in CH_3CN, and the resulting mixture was stirred at 0 °C. After 10 minutes, NEt_3 (3.4 mmol, 1 equiv.) was added slowly to the reaction mixture. The progress of the reaction was then monitored by TLC. Upon completion of the reaction (after 11 h), the mixture was concentrated under reduced pressure and purified by column chromatography on silica gel (100–200 mesh) using a gradient of 8–20% ethyl acetate in hexane, affording compound 3aa in 87% yield.

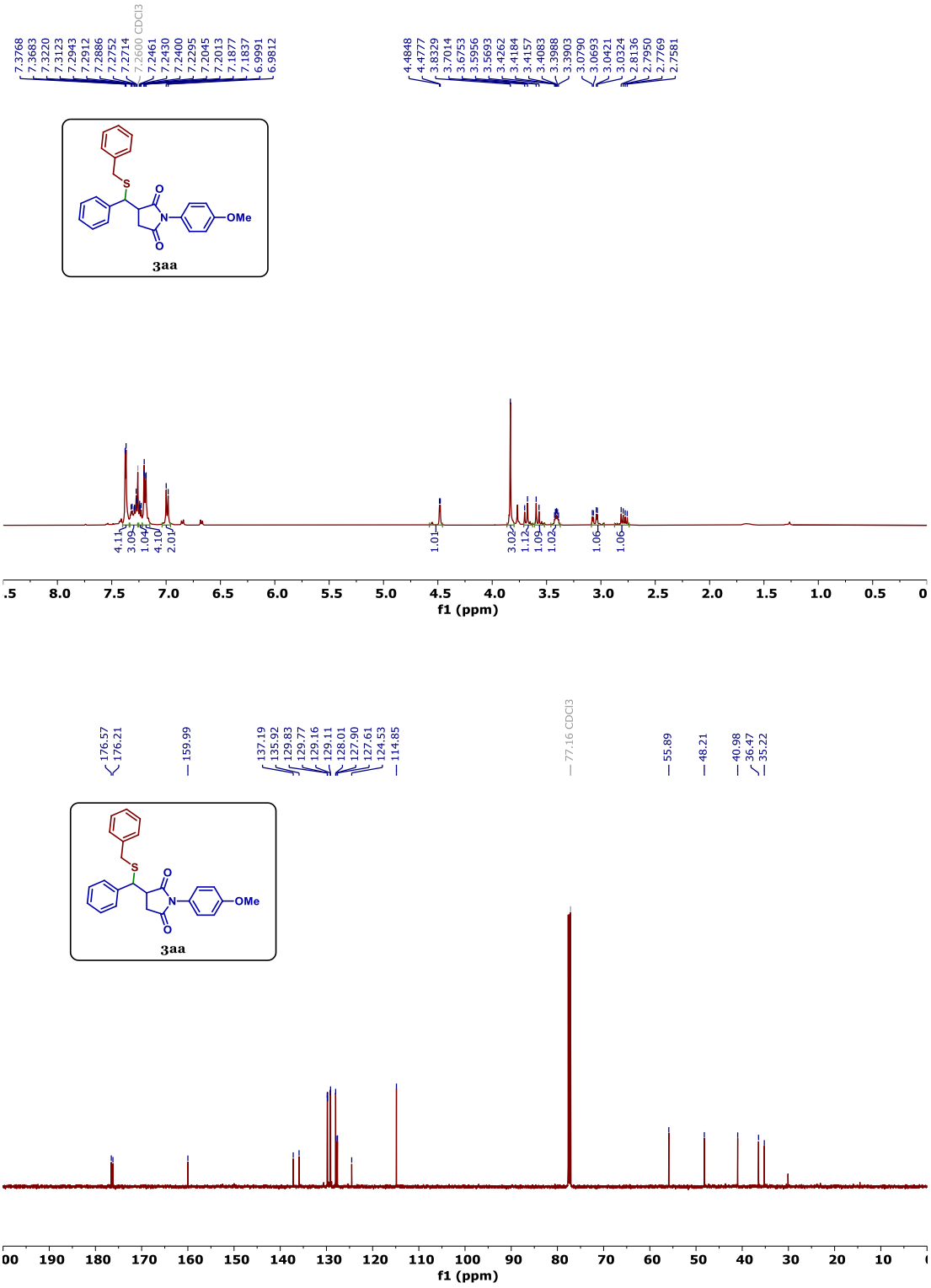
3. Recycling of diethylaminomethyl-polystyrene for the synthesis of 3aa:

(*E*)-3-Benzylidene-1-(4-methoxyphenyl)pyrrolidine-2,5-dione **1a** (500 mg, 1.7 mmol, 1 equiv.) and benzyl mercaptan **2a** (232 mg, 1.87 mmol, 1.1 equiv.) were dissolved in acetonitrile (CH_3CN) and the mixture was stirred at 50°C. After 10 minutes, diethylaminomethyl-polystyrene (N-content 3.2 mmol/g, 30 mol %, 0.2 mmol, 75 mg) was slowly added to the reaction. The reaction progress was monitored by TLC. After 14 hours, when the reaction was complete, the solid residue (the supported-amine diethylaminomethyl-polystyrene catalyst) was filtered out, and the remaining material was washed with 20 mL of ethyl acetate (EtOAc) and 20 mL of dichloromethane (CH_2Cl_2). The combined filtrate was concentrated under reduced pressure to yield the crude product, which was then purified by column chromatography on silica gel (100–200 mesh) using a gradient of 8–20% ethyl acetate in hexane, resulting in compound **3aa** with an 89% yield.

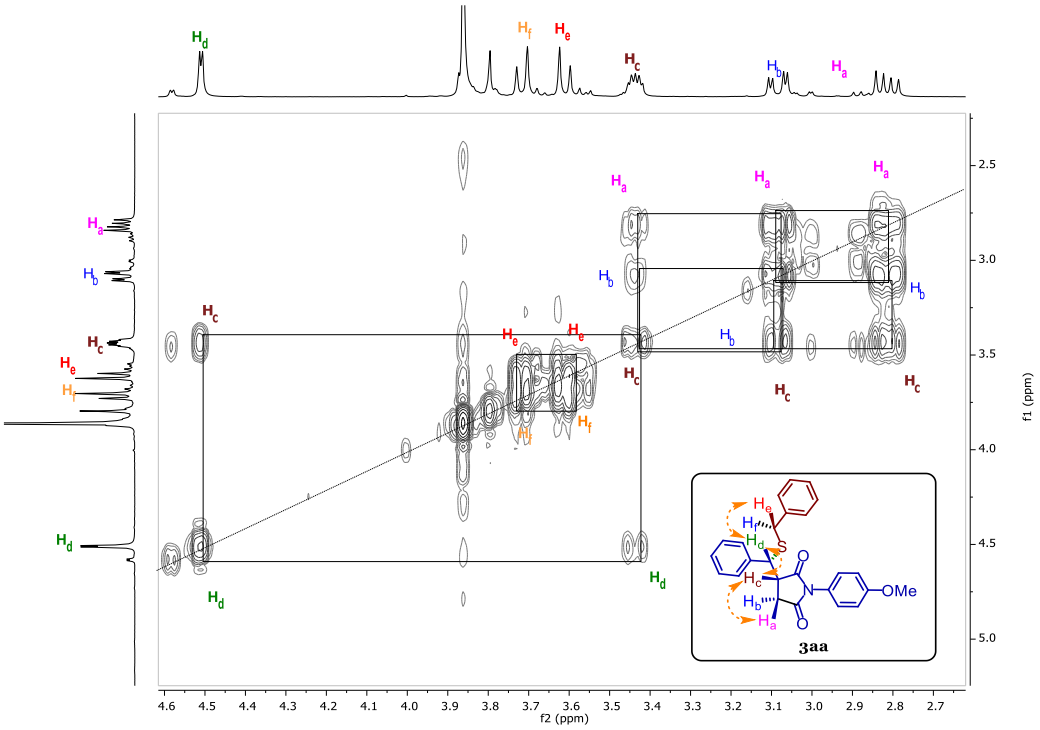
The recovered diethylaminomethyl-polystyrene catalyst collected by filtration was washed sequentially with methanol (2 × 2 mL), dichloromethane (2 × 2 mL), and acetone (2 × 2 mL), followed by drying before re-use.

Cycle	Weight of Product **3aa** (g)	% Yield of 3aa	Polymer Weight (mg)	Polymer Loss (mg)	% Recovery of Polymer
1	0.4459	89	529.8	1.2	99.8
2	0.4437	89	528.9	0.9	99.8
3	0.4329	87	527.3	1.6	99.7
4	0.4089	82	524.7	2.6	99.5
5	0.4025	81	522.8	1.9	99.6

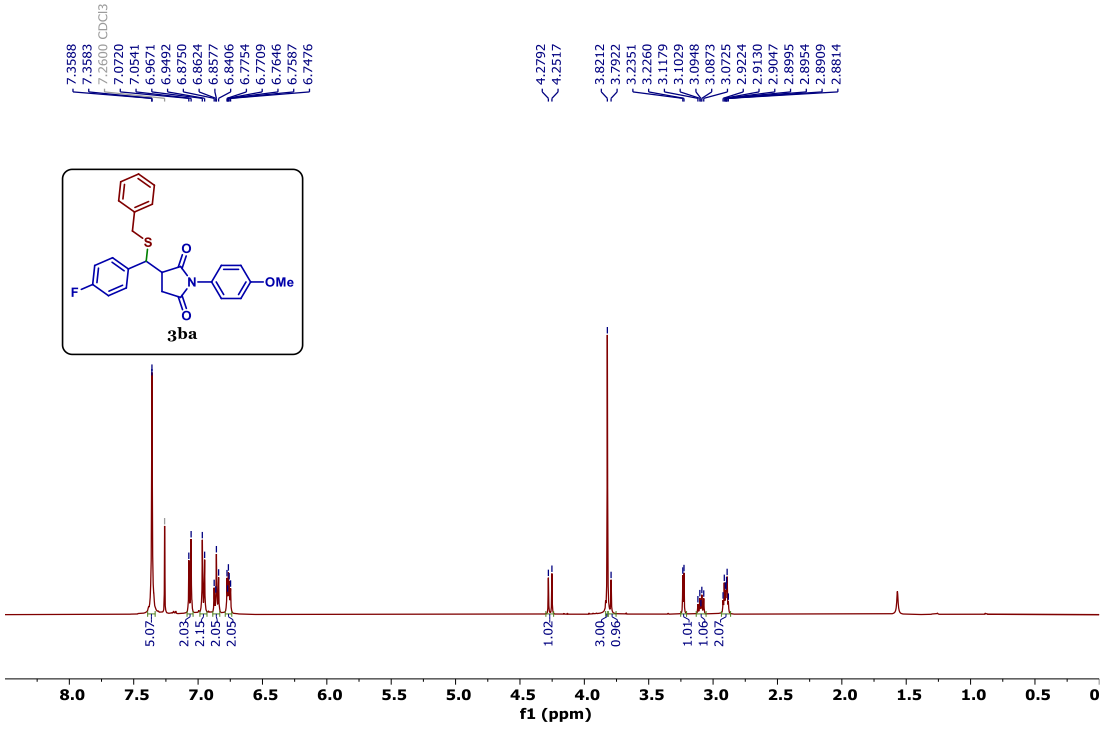
4. ^{1}H and ^{13}C NMR Spectra:



$CDCl_3$, 500 MHz ^{1}H NMR and 125 MHz ^{13}C{^{1}H} NMR Spectra of **3aa**



500 MHz ^{1}H-^{1}H COSY Spectra of **3aa**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2.9047
2.8995
2.8954
2.8909
2.8814
S
O
N
F
OMe
3ba
5.07
2.03
2.15
2.05
2.05
1.02
3.00
0.96
1.01
1.06
2.07
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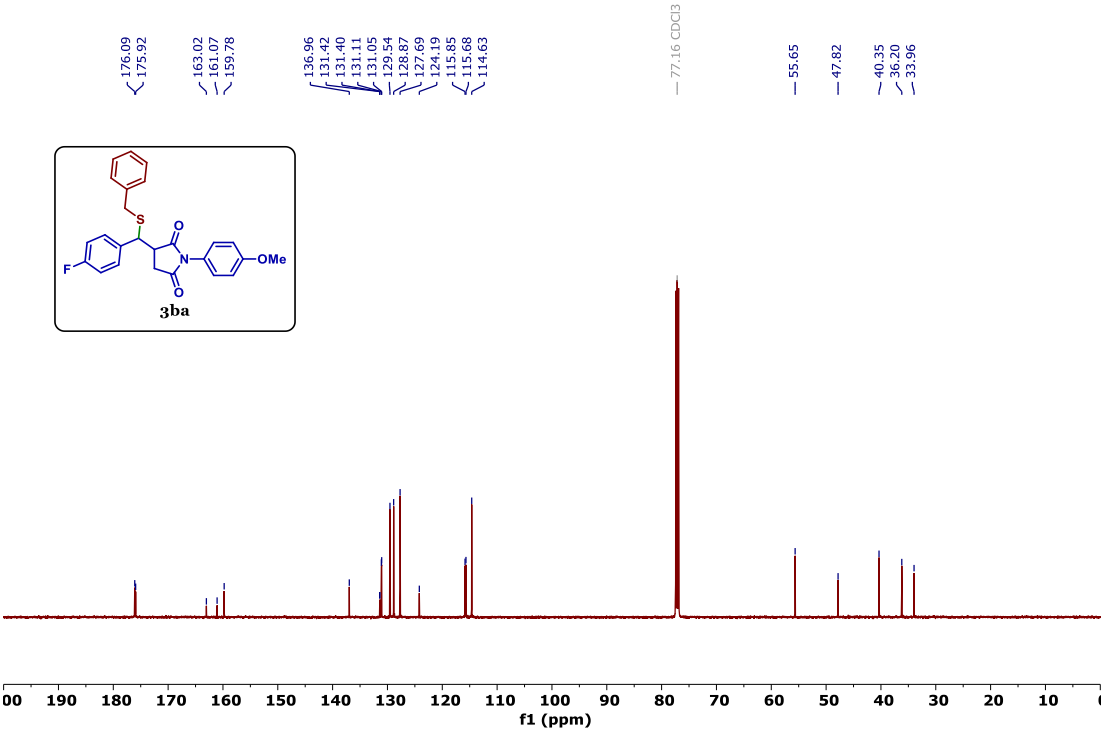
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124.19
115.85
115.68
114.63
77.16 CDCl3
55.65
47.82
40.35
36.20
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S
O
N
F
OMe
3ba
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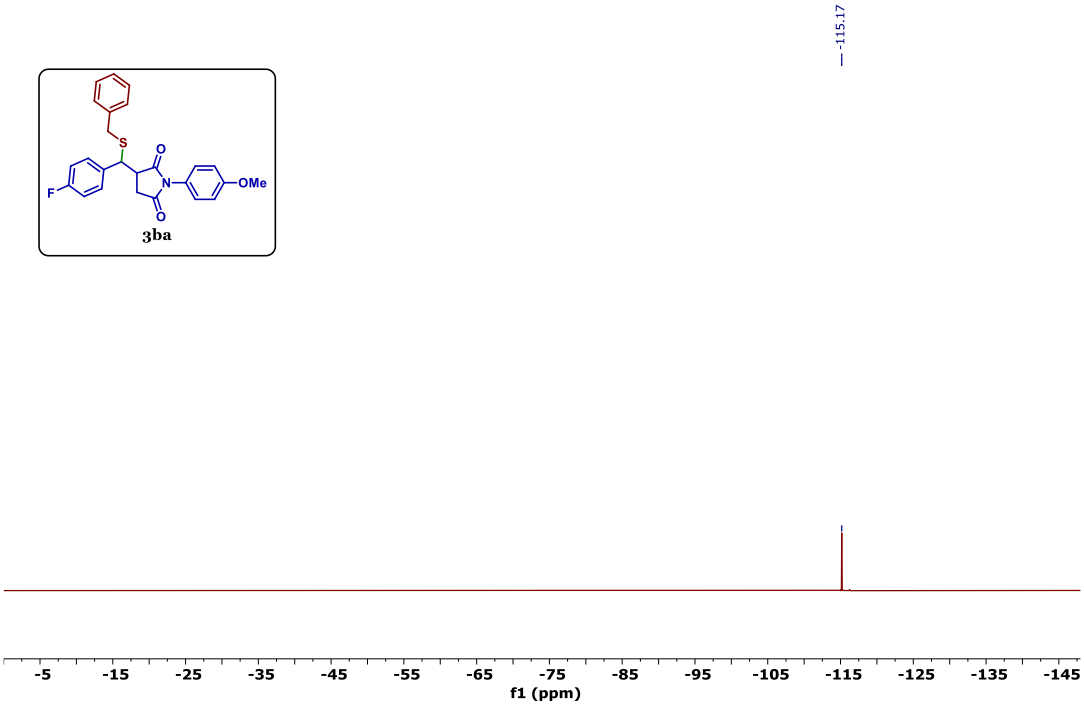
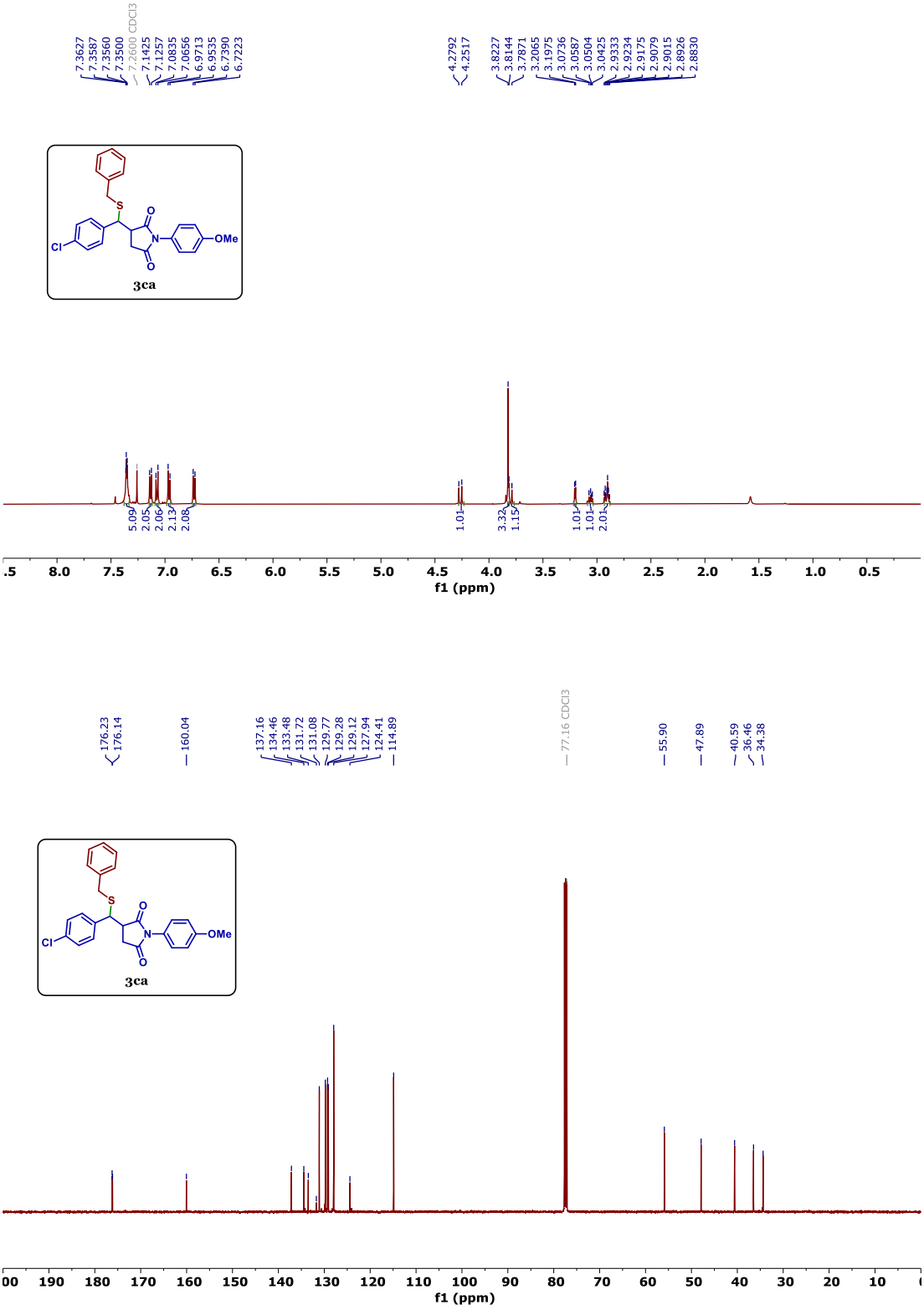
f1 (ppm)



$CDCl_3$, 500 MHz ^1H NMR, 125 MHz $^{13}C\{^1H\}$ NMR and ^{19}F NMR Spectra of **3ba**



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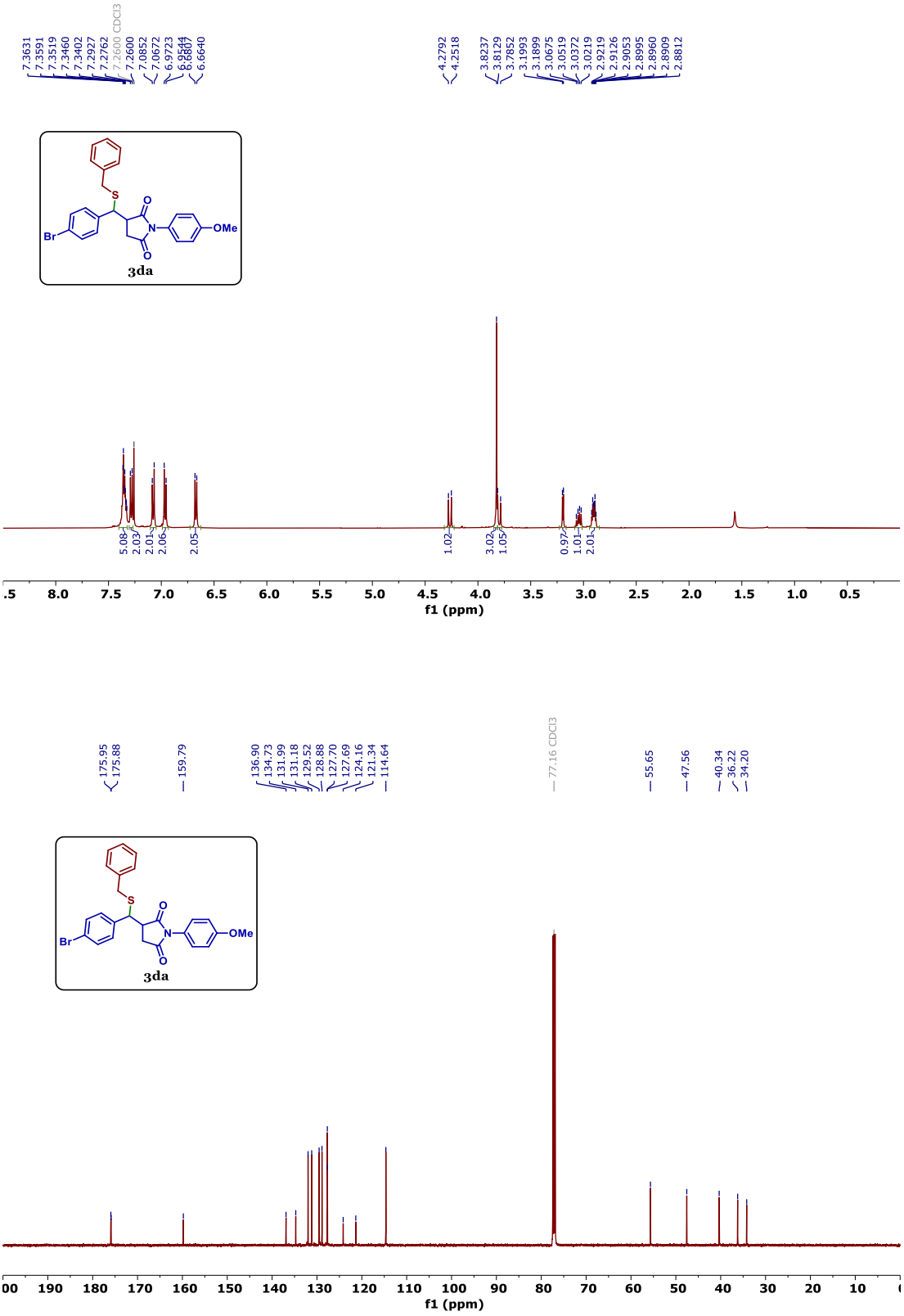

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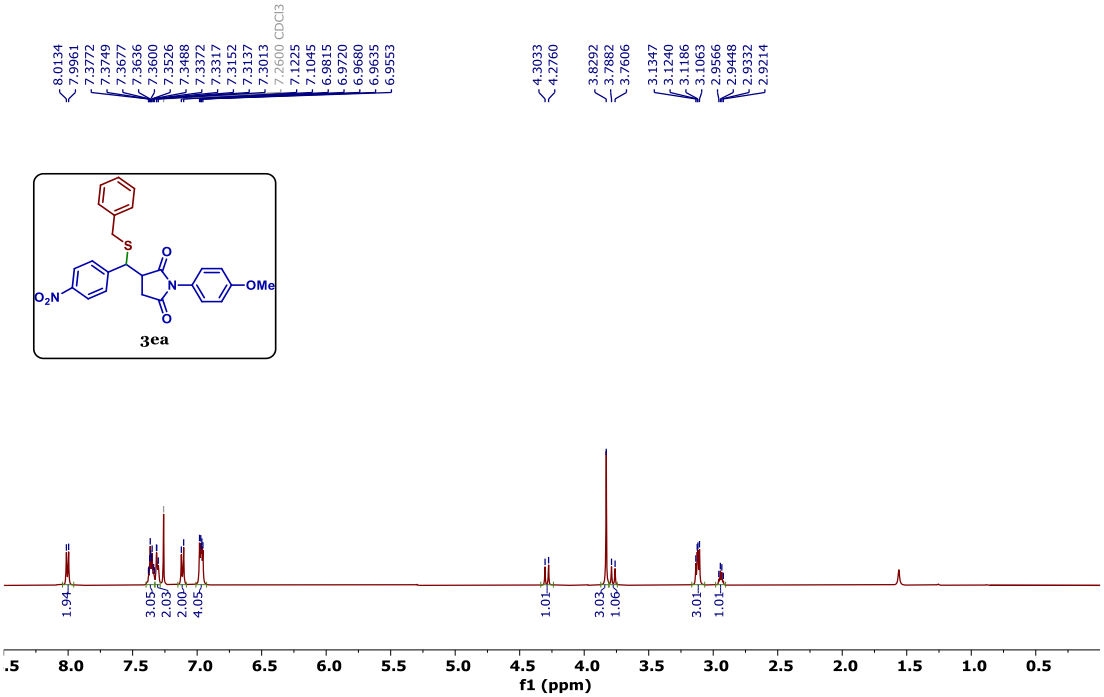
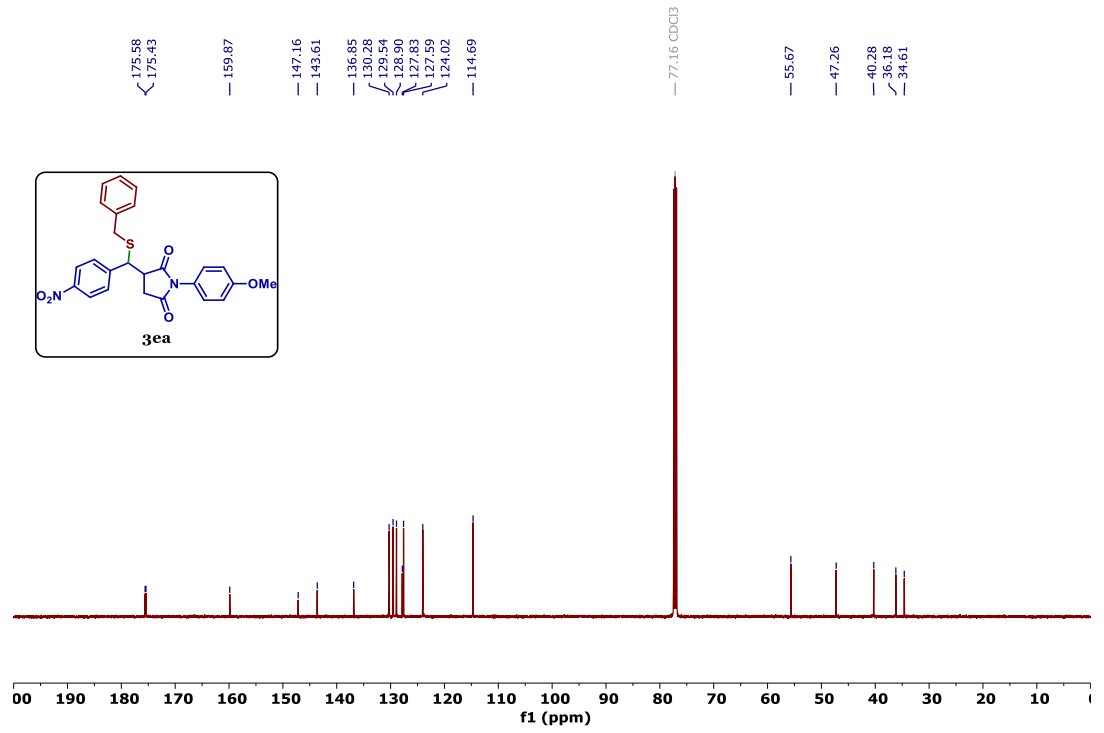
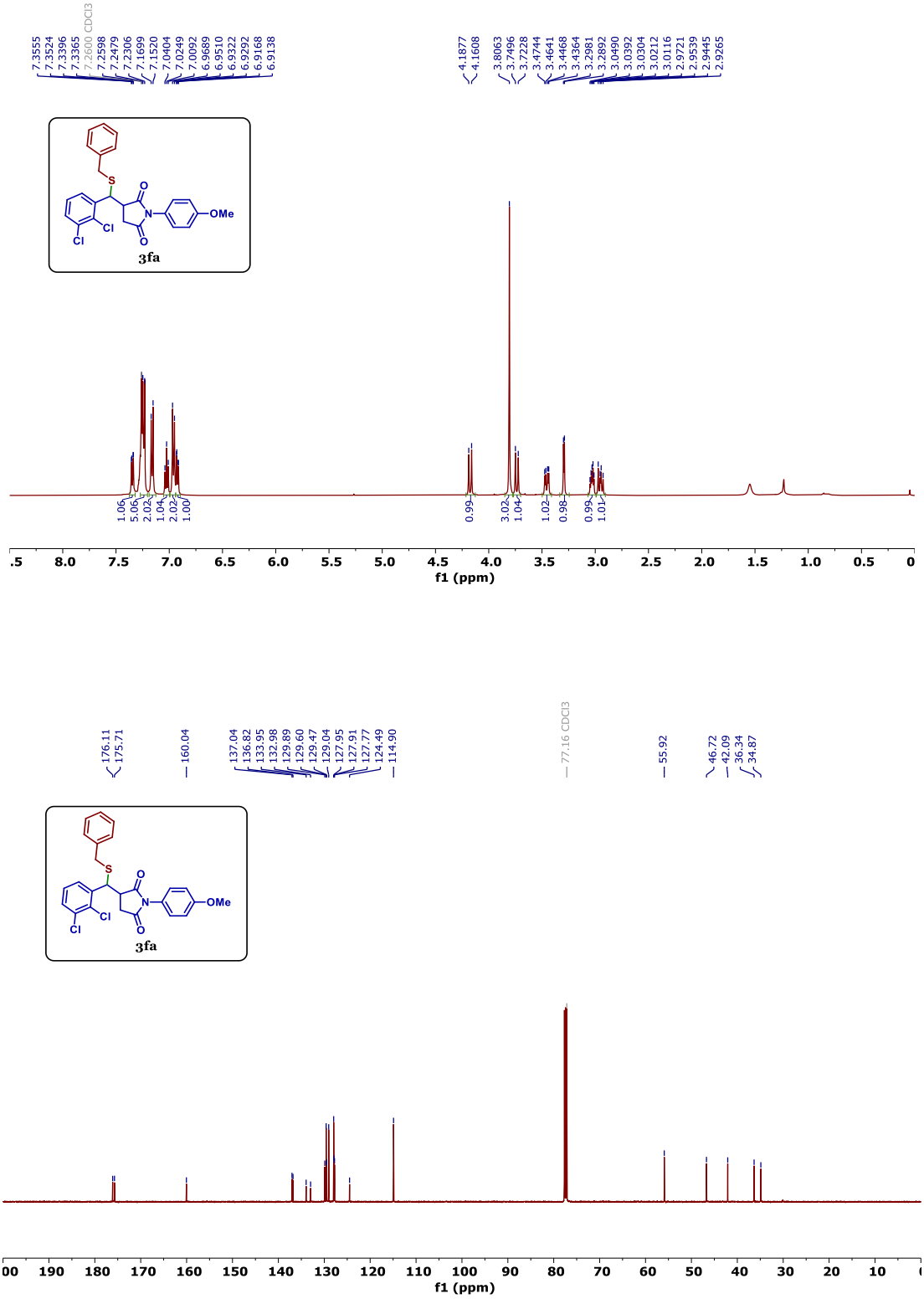
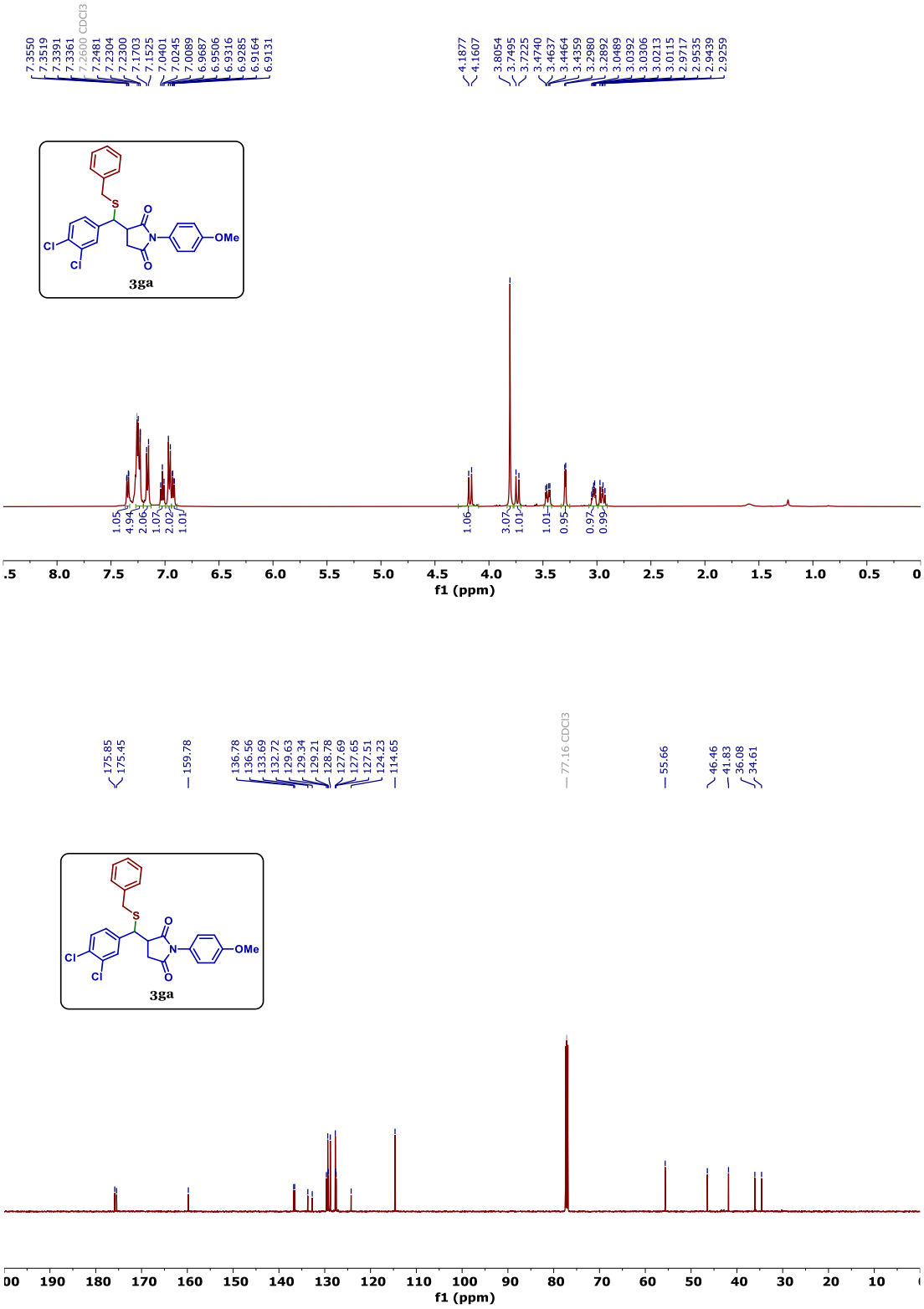




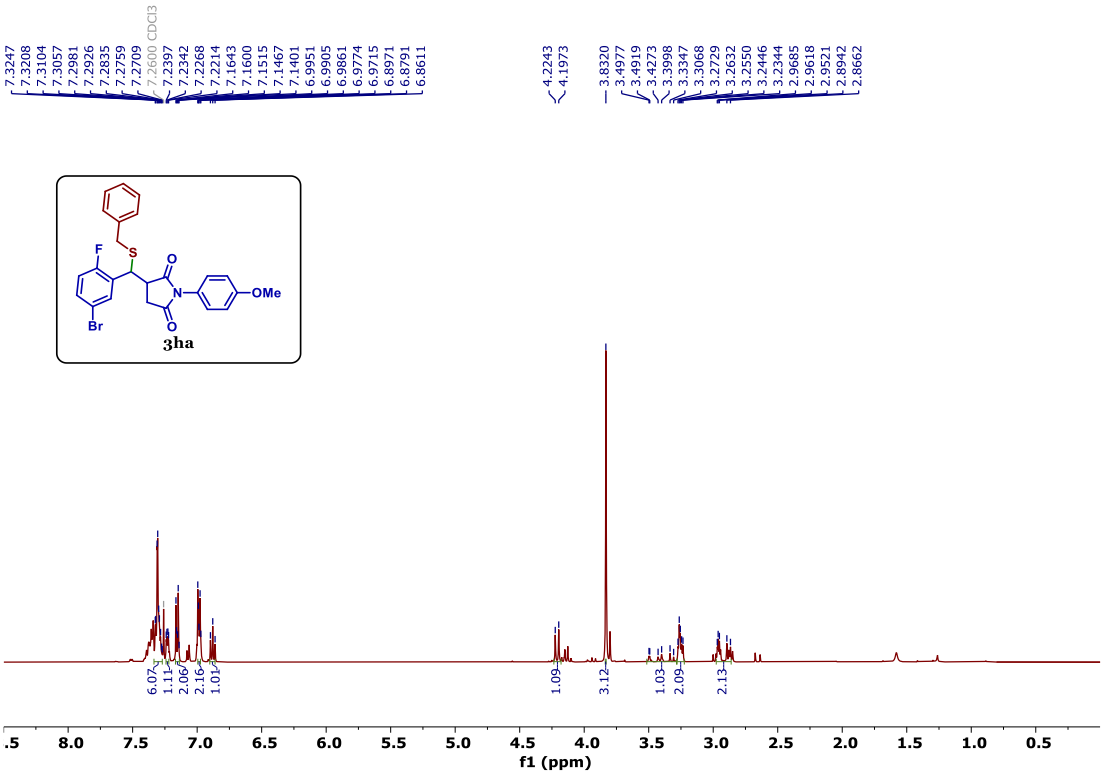
$CDCl_3$, 500 MHz ^1H NMR and 125 MHz $^{13}C\{^1H\}$ NMR Spectra of **3ea**



$CDCl_3$, 500 MHz ^1H NMR and 125 MHz $^{13}C\{^1H\}$ NMR Spectra of **3fa**



$CDCl_3$, 500 MHz ^1H NMR and 125 MHz $^{13}C\{^1H\}$ NMR Spectra of **3ga**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3.2344
2.9685
2.9618
2.9521
2.8942
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F
S
O
N
OMe
Br
O
3ha
6.07
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1.09
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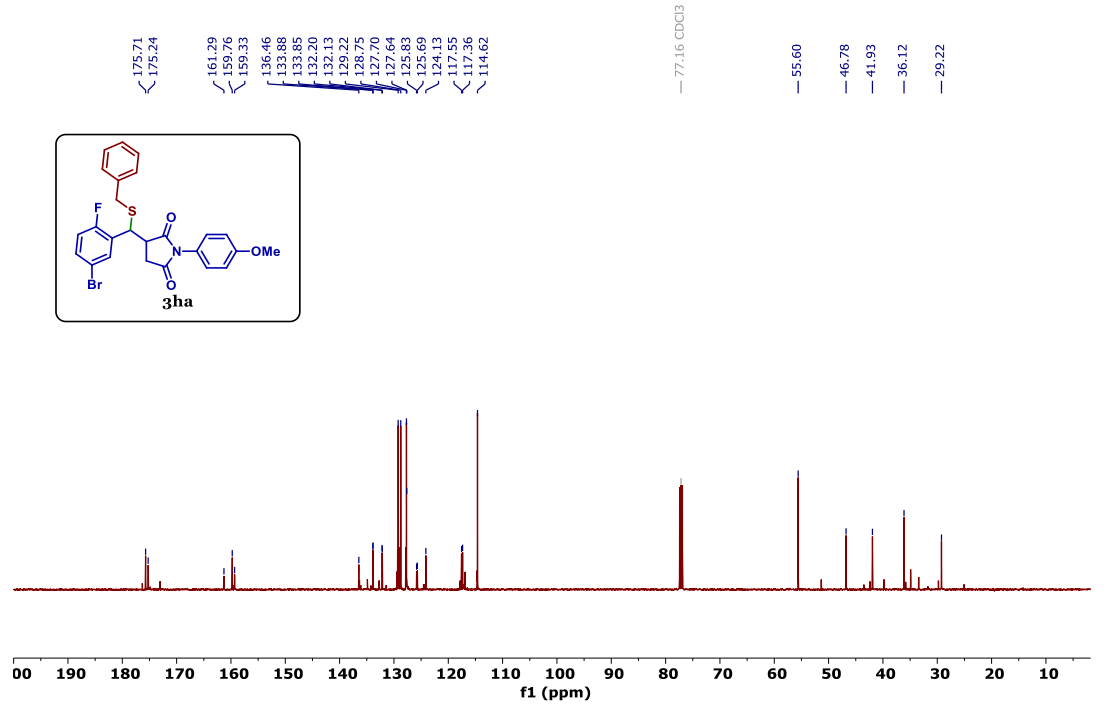
2.13
f1 (ppm)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117.55
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77.16 CDCl3
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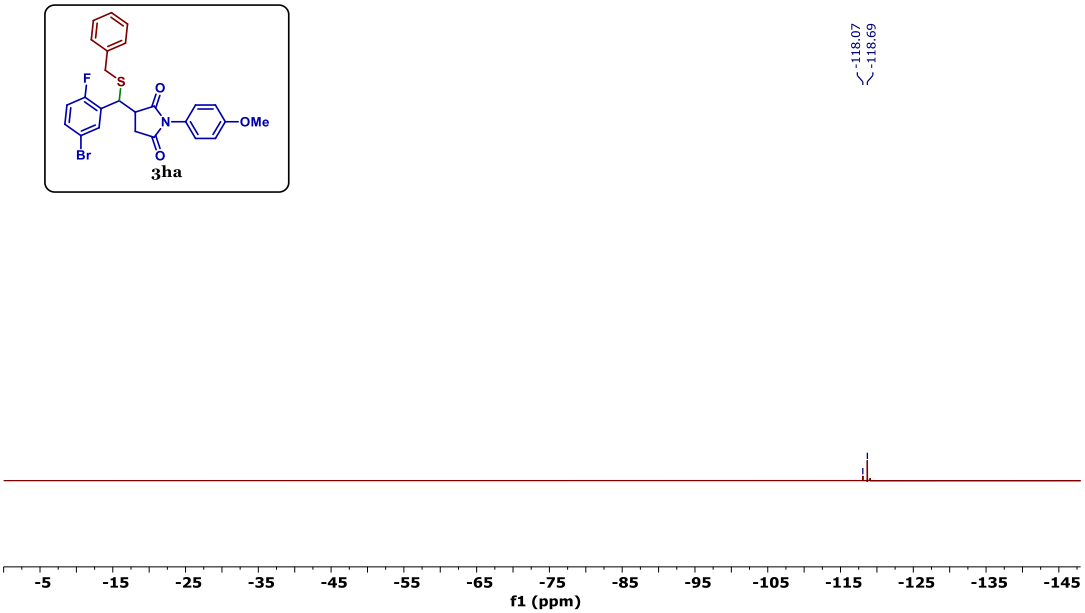
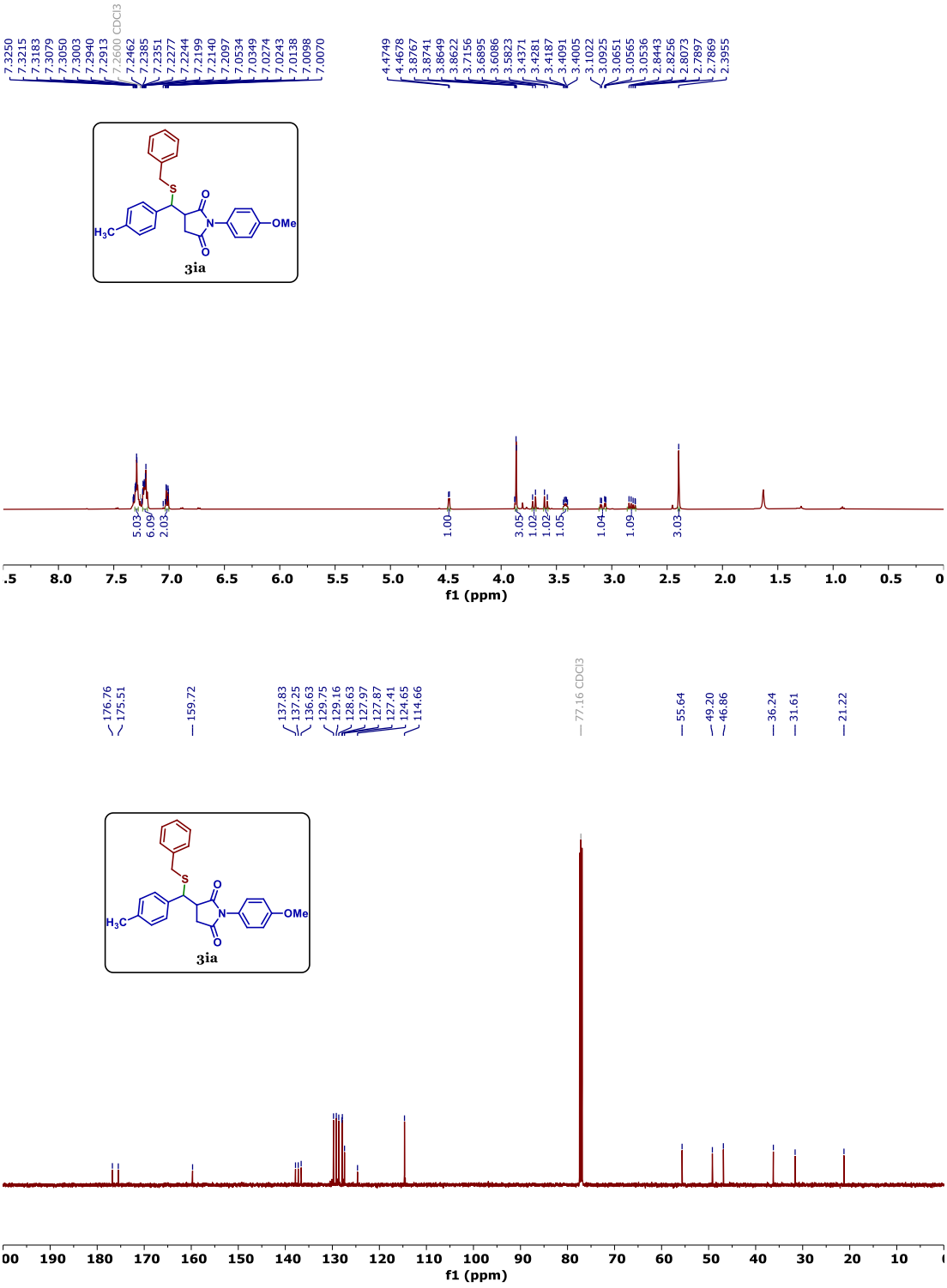
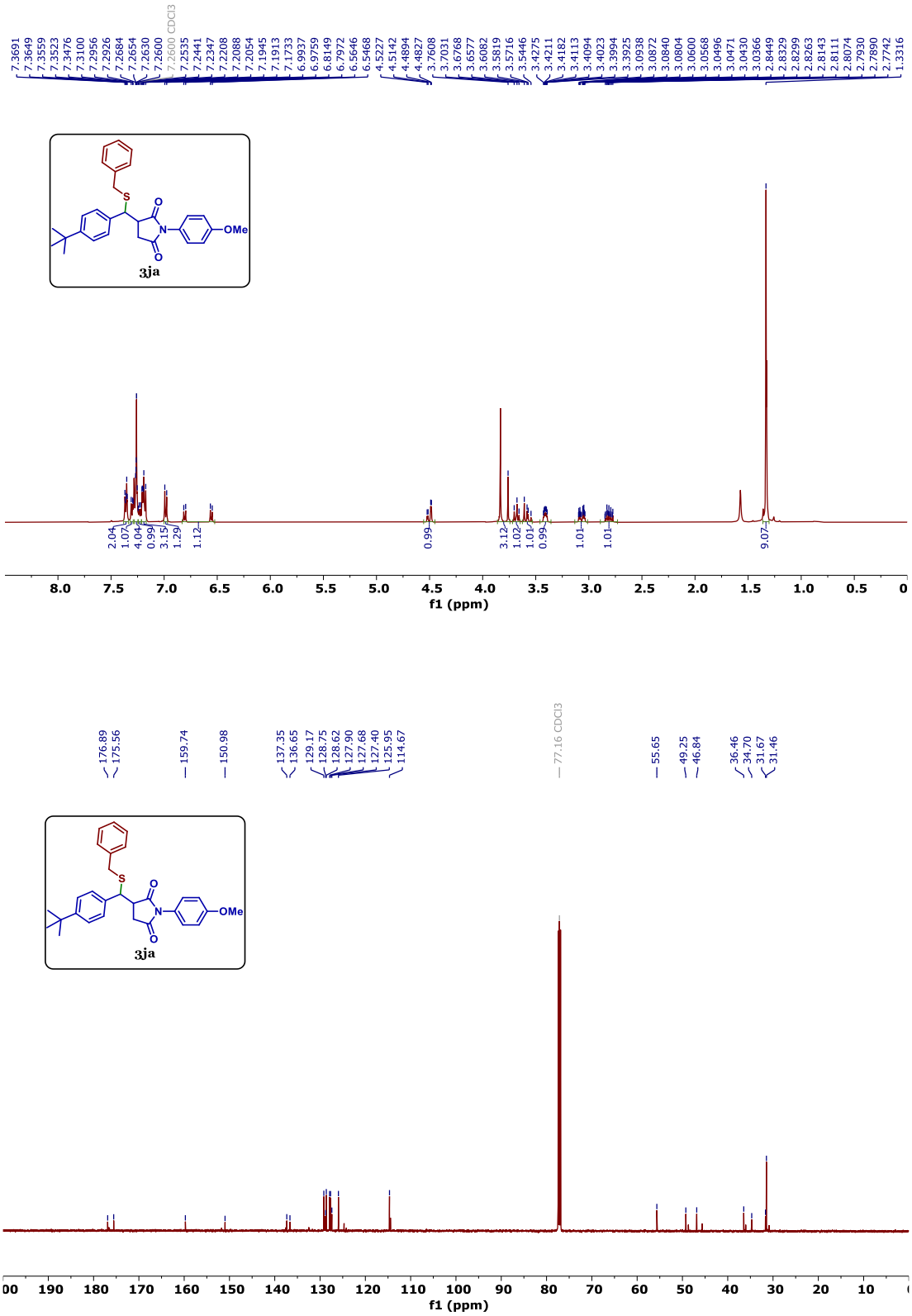
O
3ha
f1 (ppm)



$CDCl_3$, 500 MHz ^1H NMR, 125 MHz $^{13}C\{^1H\}$ NMR and ^{19}F NMR Spectra of **3ha**



$CDCl_3$, 500 MHz ^1H NMR and 125 MHz $^{13}C\{^1H\}$ NMR Spectra of **3ia**



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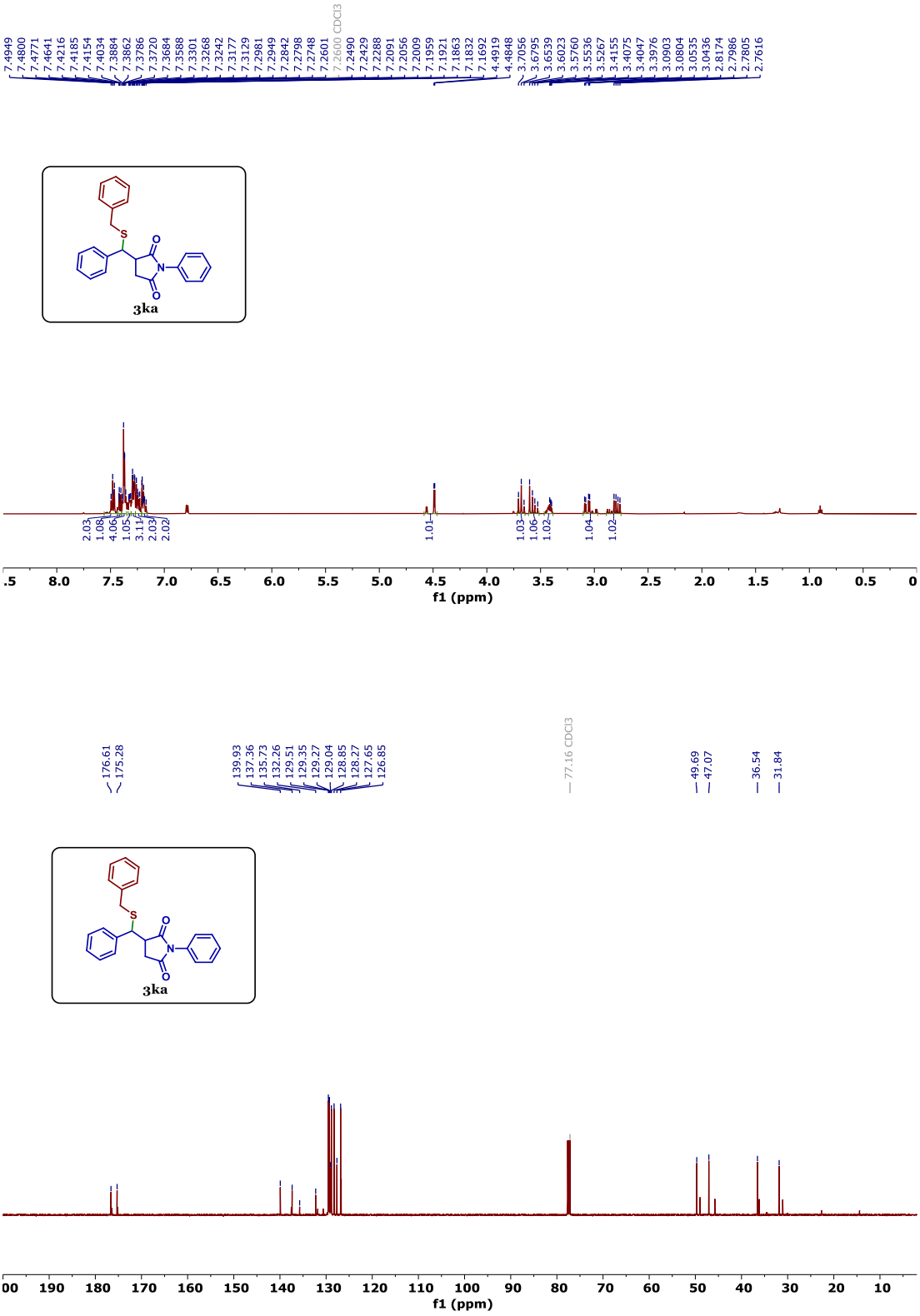
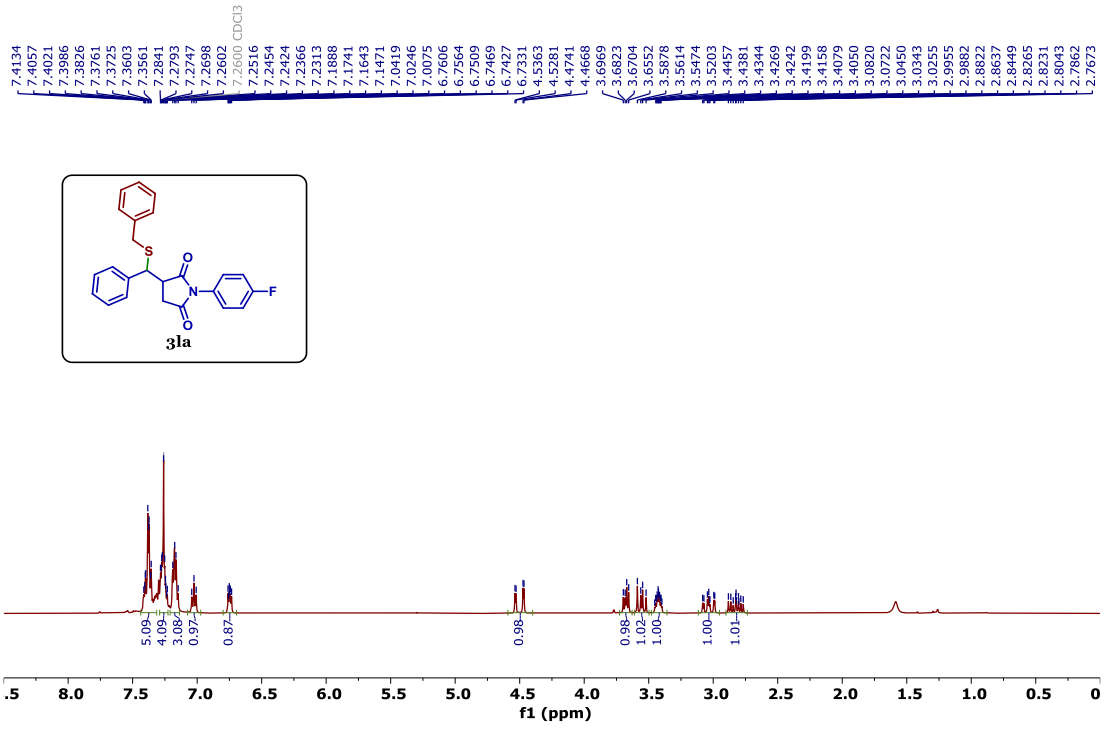


$CDCl_3$, 500 MHz ^1H NMR and 125 MHz $^{13}C\{^1H\}$ NMR Spectra of **3ka**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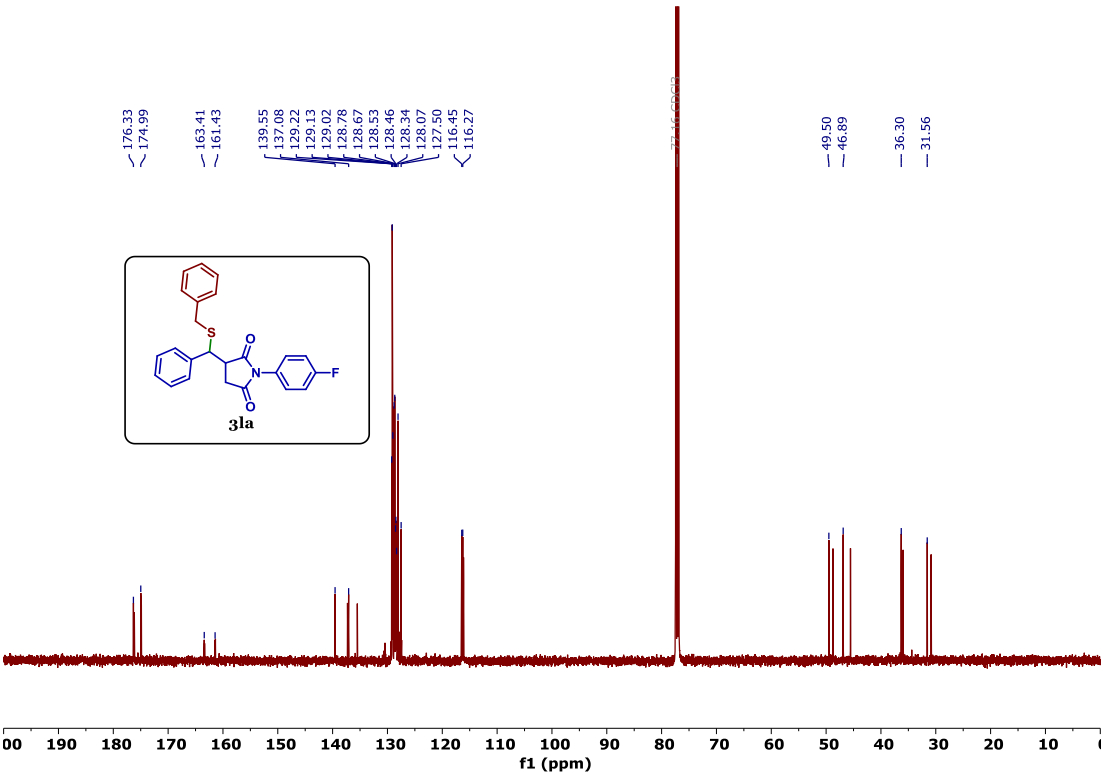
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128.34
128.07
127.50
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O
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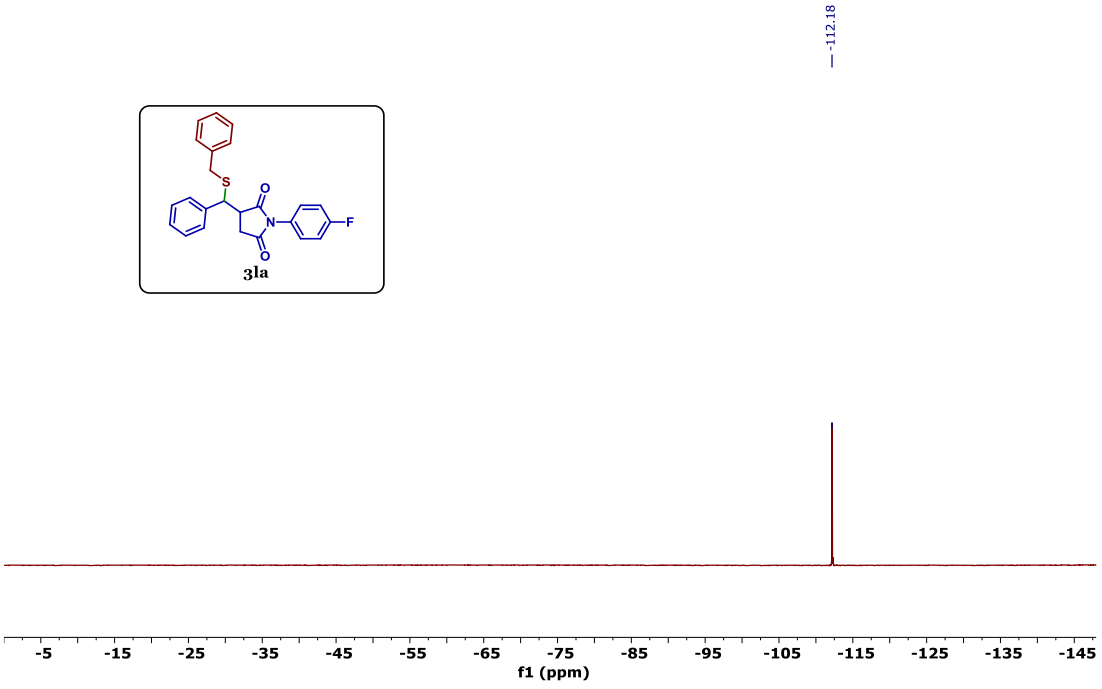
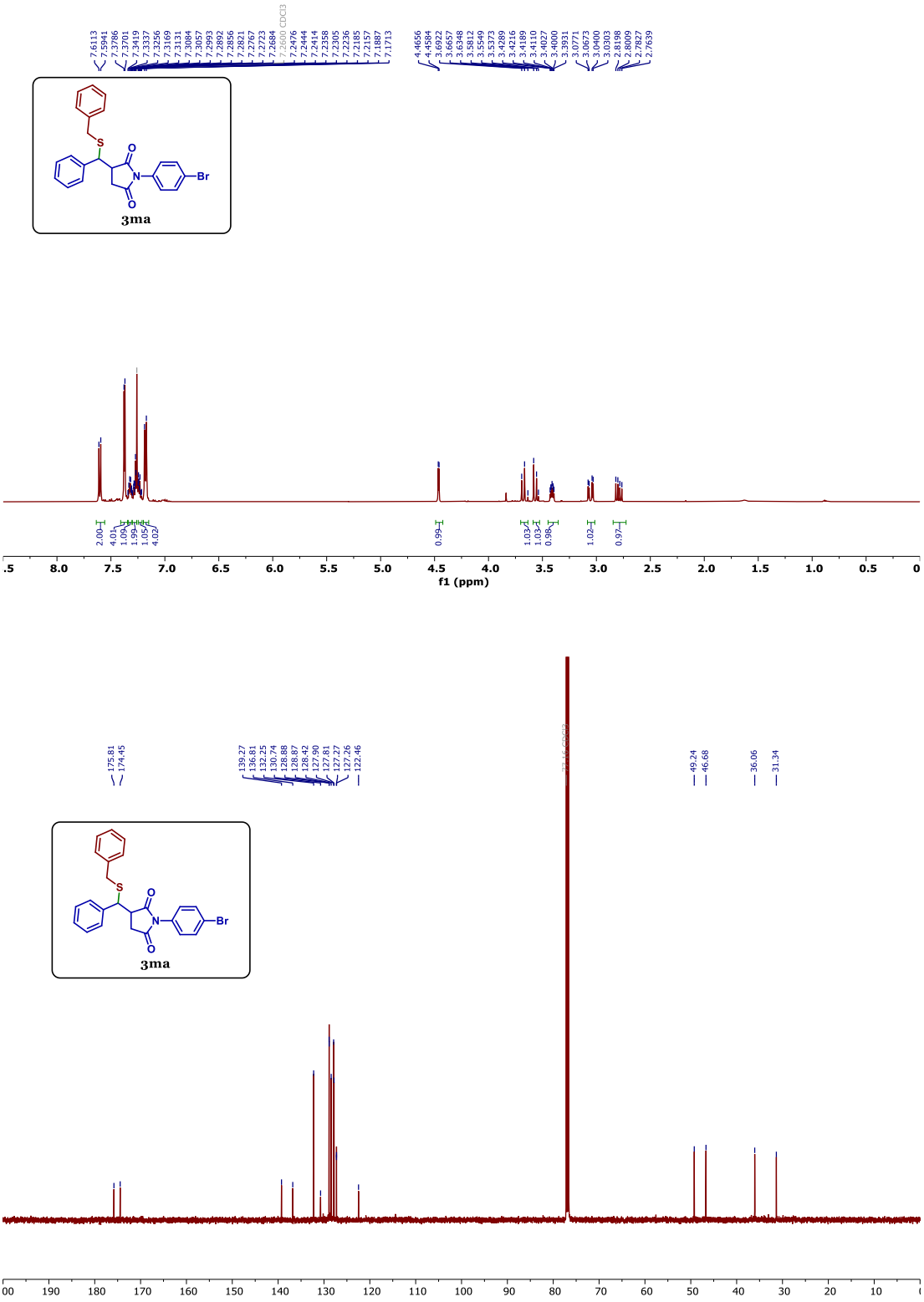


$CDCl_3$, 500 MHz ^1H NMR, 125 MHz $^{13}C\{^1H\}$ NMR and ^{19}F NMR Spectra of **3la**



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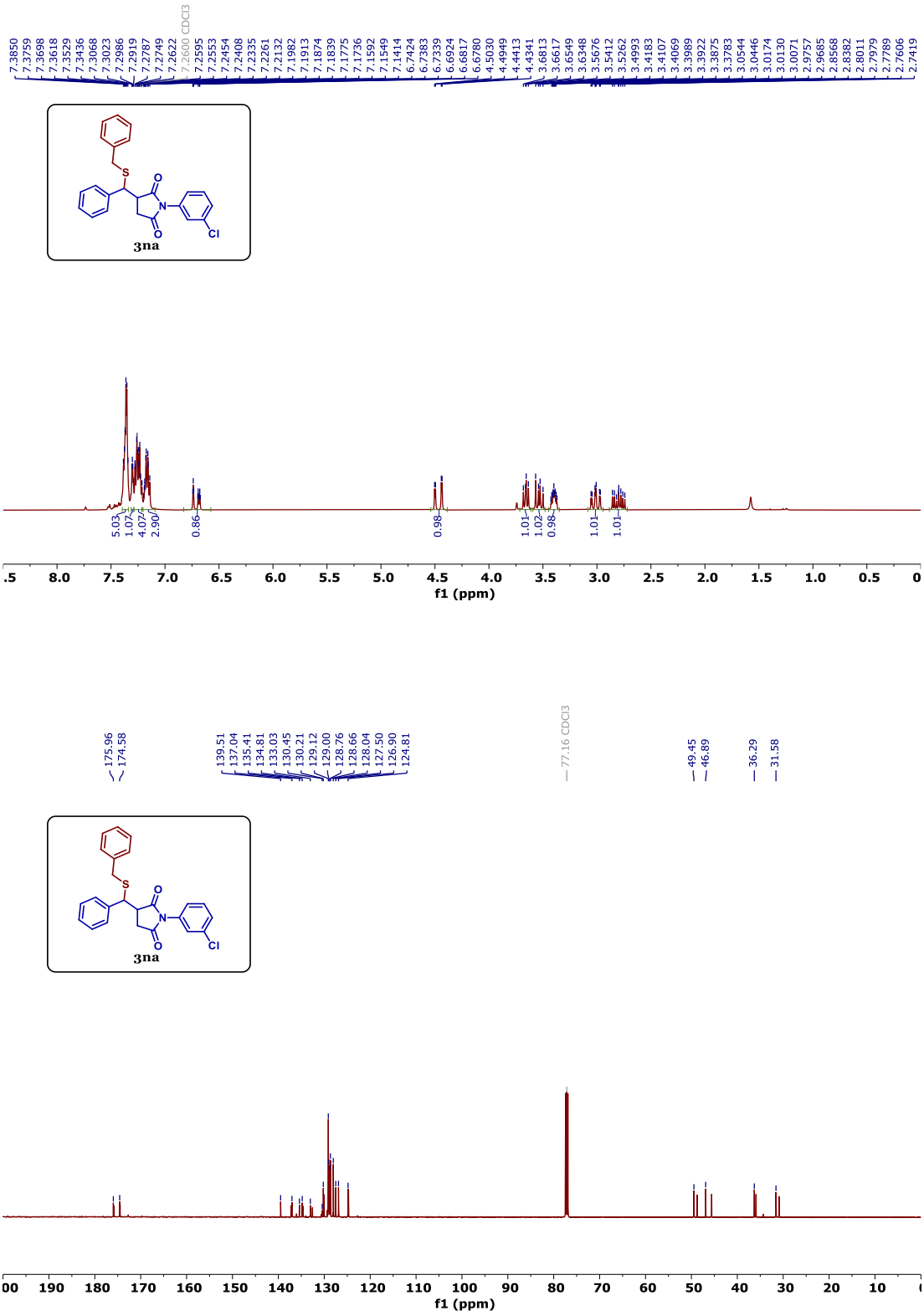

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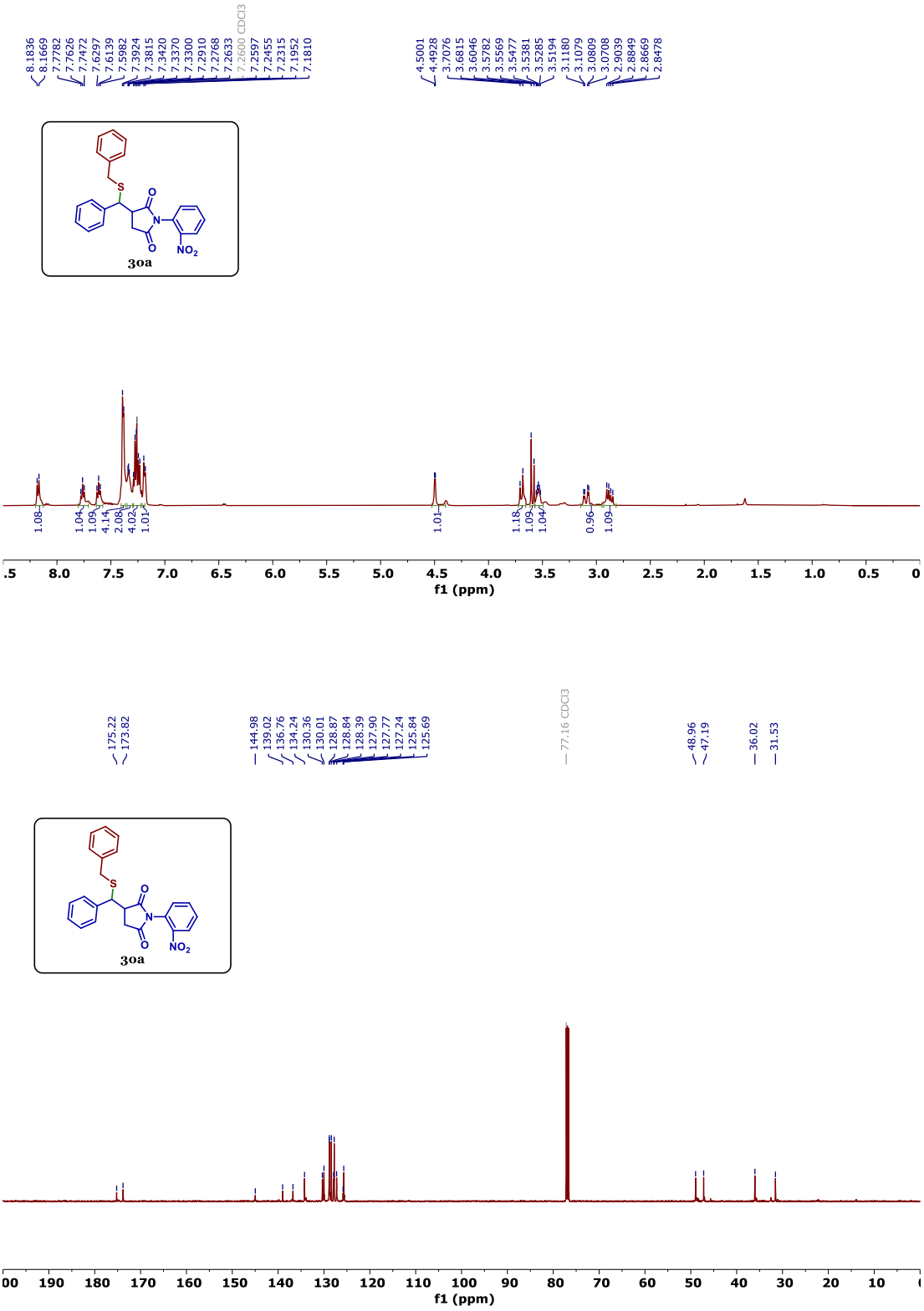

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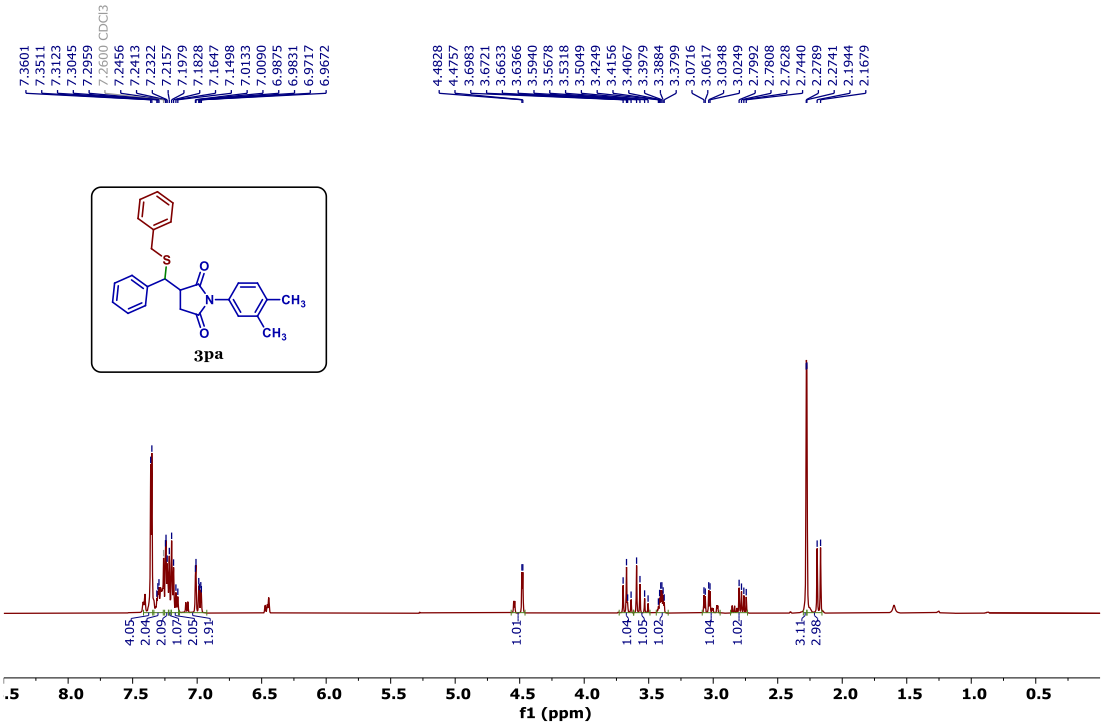

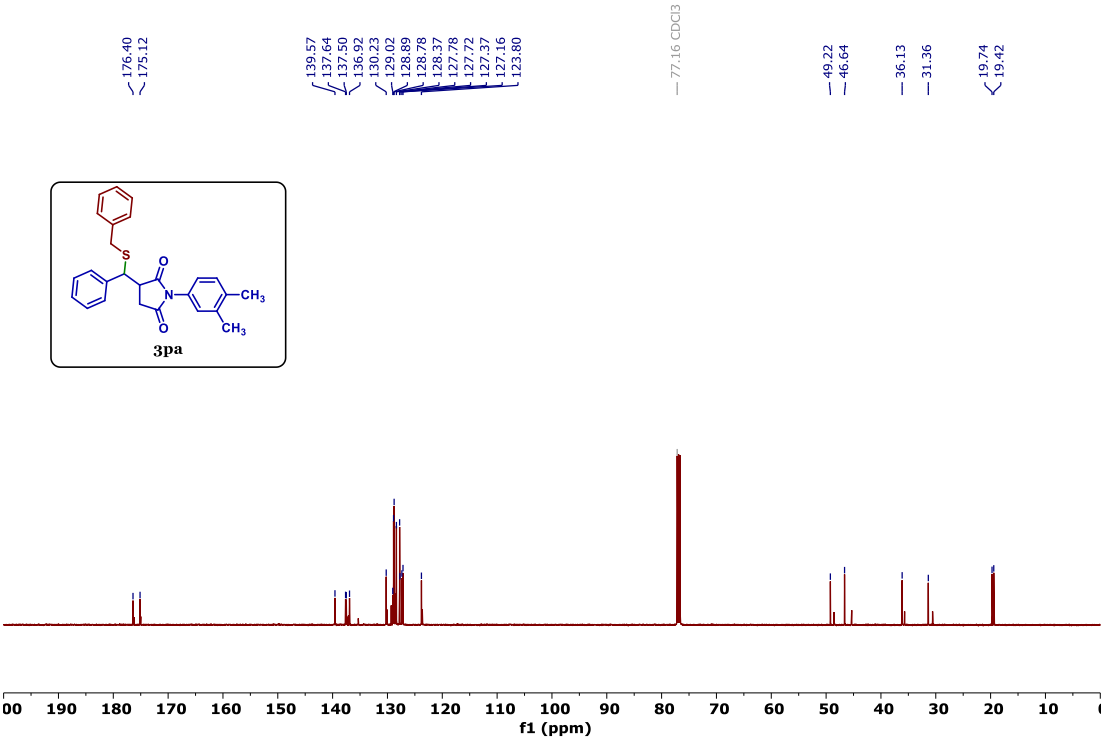

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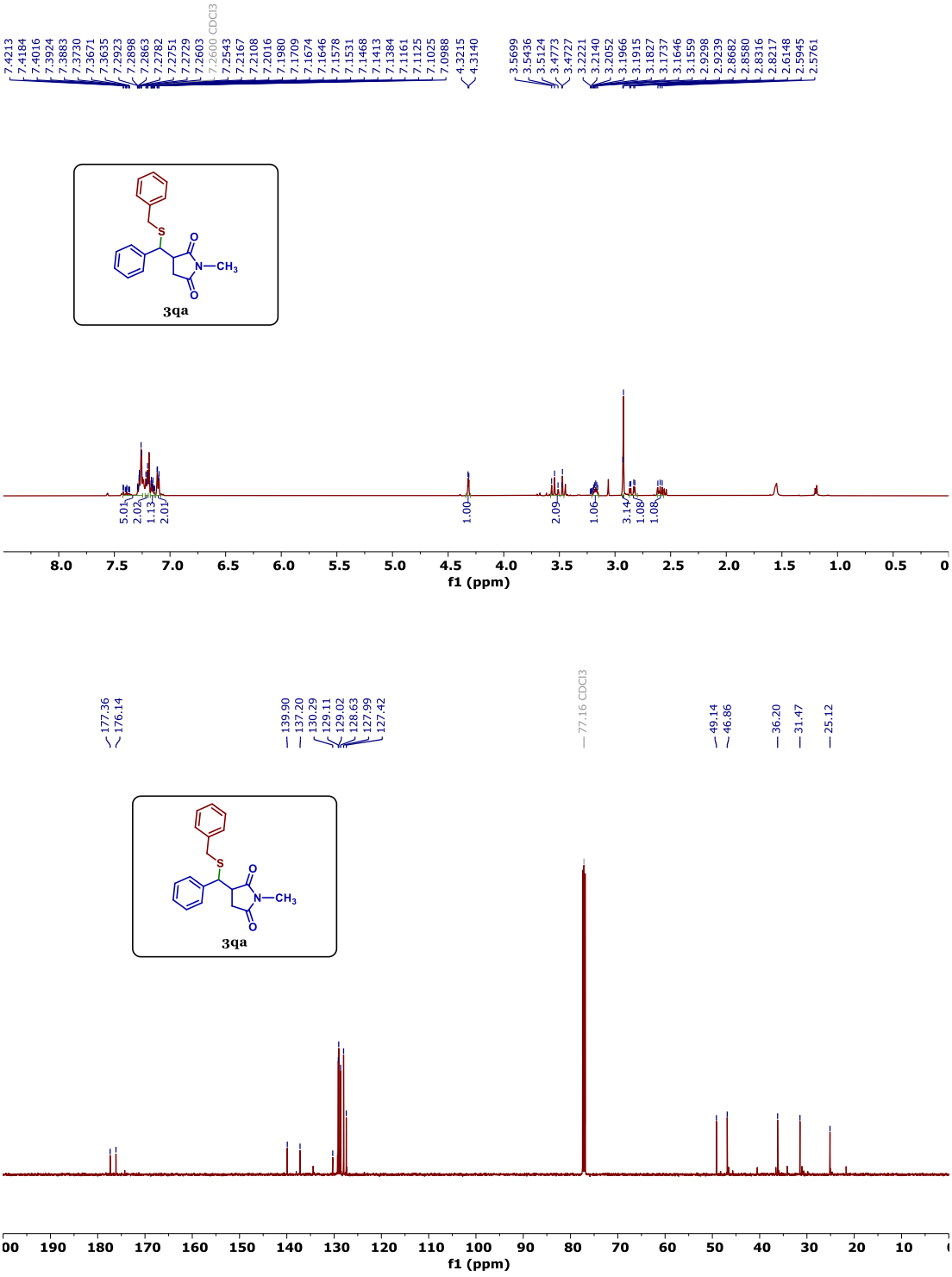

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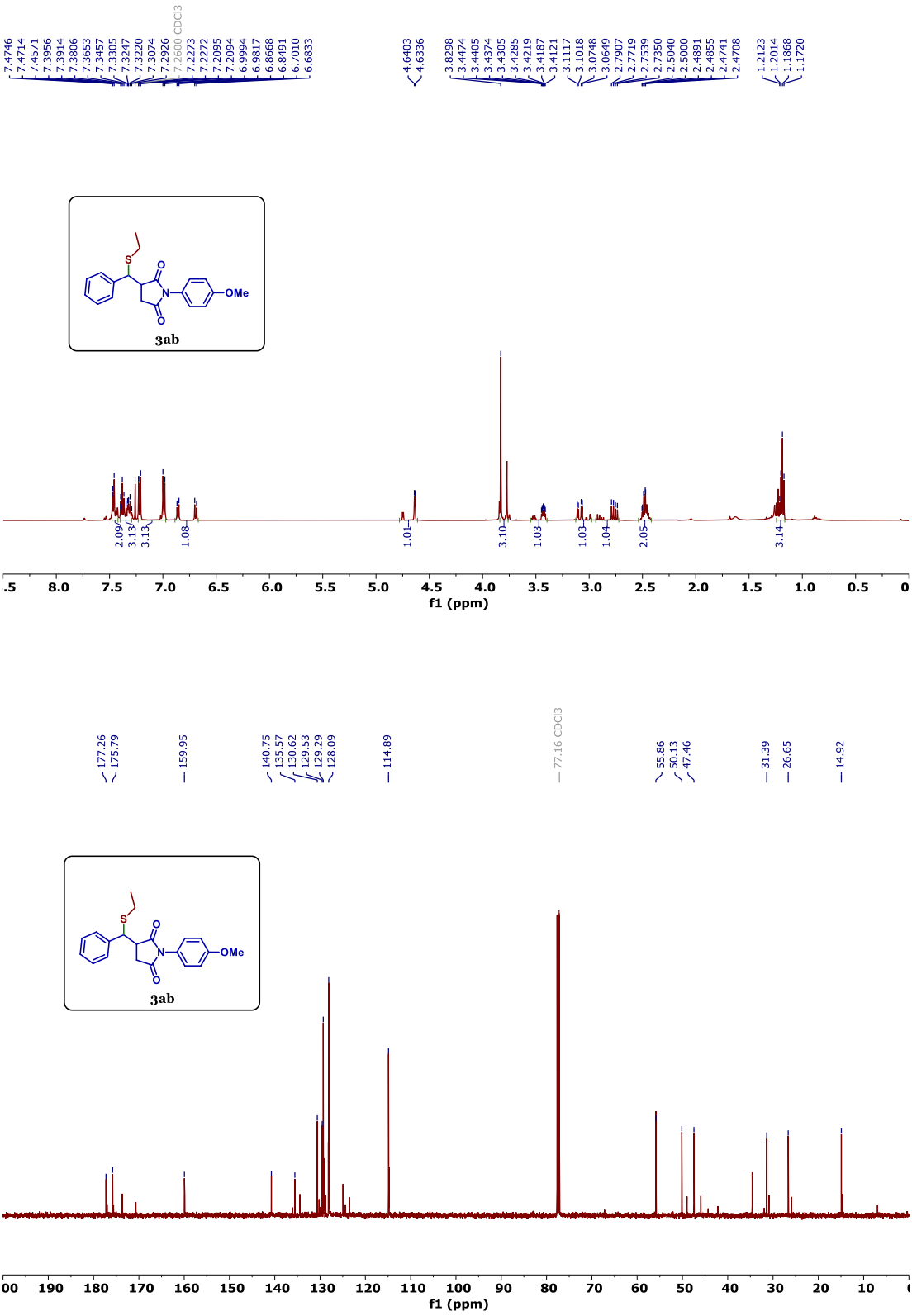

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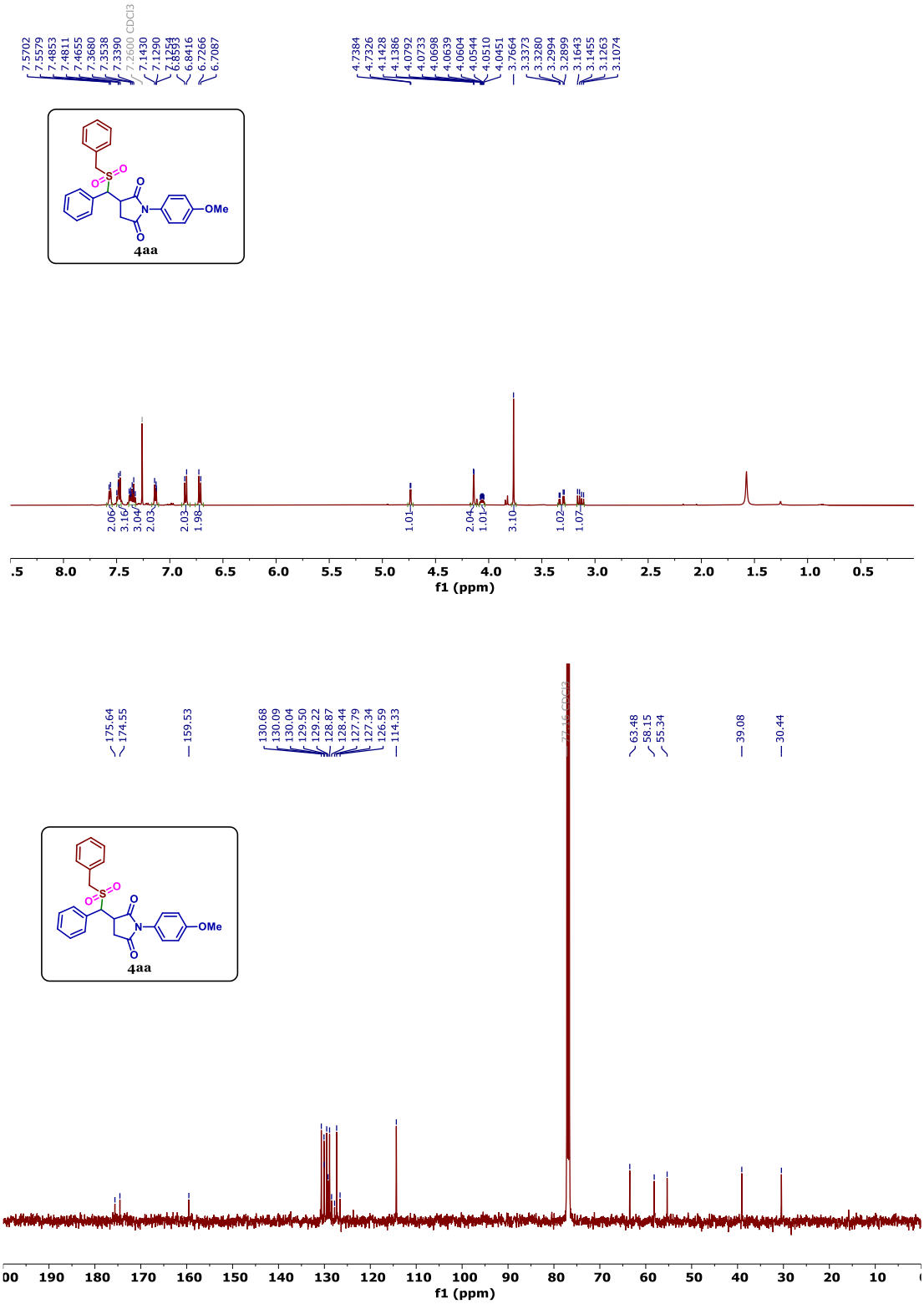

$CDCl_3$, 500 MHz ^1H NMR and 125 MHz $^{13}C\{^1H\}$ NMR Spectra of **4aa**