Visible-Light Mediated Oxidative C−H/N-H Cross-Coupling between Tetrahydrofuran and Azoles using Air

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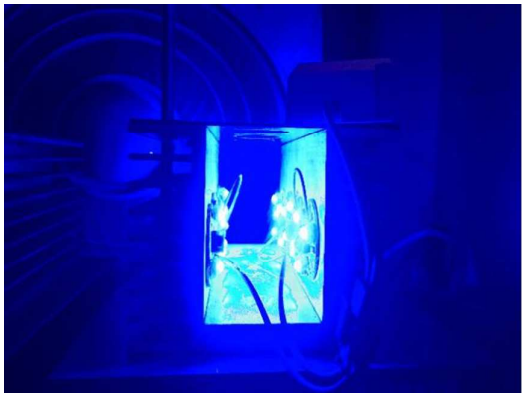
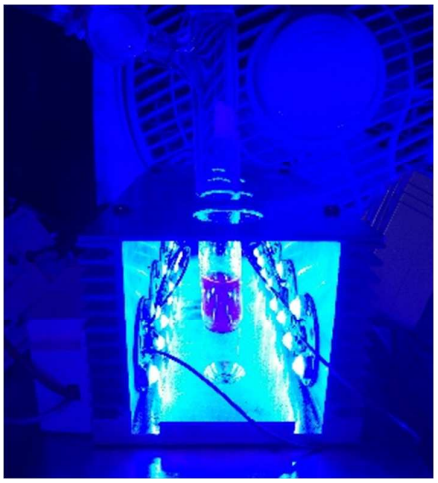
1. General Information

All manipulations were carried out by standard schlenk techniques. Unless otherwise noted, analytical grade solvents and commercially available reagents were used to conduct the reactions. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in petroleum (boiling point is between 60-90 ^{o}C). Gradient flash chromatography was conducted eluting with a continuous gradient using petroleum ether and ethyl acetate. The known compounds were characterized by ^{1}H NMR and ^{13}C NMR. GC-MS spectra were recorded on a Varian GC-MS 3900-2100T. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Advance III 400 MHz NMR spectrometer with tetramethylsilane as an internal standard. The chemical shifts (δ) were given in part per million relative to internal tetramethyl silane (TMS, 0 ppm for ^{1}H), $CDCl_3$ (for ^{13}C). The photocatalyst Acr^+ - Mes ClO_4^- is commercial available from the company of TokyoChemicalIndustry (TCI). The CAS number is 674783-97-2. The source of the blue LEDs is common LED lights. The power of each light is 3W. There is 3.0 cm distance between the reactor and LEDs. This reaction could be well-performed using a round bottle (25 mL). Below we will add two pictures of our instrument.





2. General Procedures for Oxidative Amination

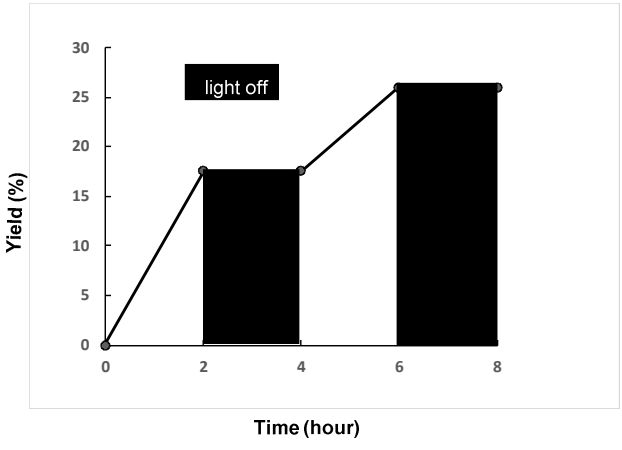
2.1 Visible Light Mediated Aerobic Oxidative C−H Amination of Tetrahydrofuran under mild conditions

In a dried schlenk tube, azoles **1** (0.5 mmol), Acr^+ - Mes ClO_4^- (3 mol%, 0.015 mmol) were stirred in 3.0 mL THF for 24 hours at room temperature under an air atmosphere irradiated by blue LEDs. After completion of the reaction, as indicated by TLC and GC-MS, the mixture was diluted by ethyl acetate. The pure product was obtained by flash column chromatography on silica gel using petroleum ether and ethyl acetate.

3. Mechanism Studies

3.1 Time Profile of Photocatalytic Reaction with and without Visible Light.

A solution of the 3-phenyl-1H-pyrazole **1g** (0.5 mmol), and Acr^+ - Mes ClO_4^- (3 mol%, 0.015 mmol) were stirred in 3 mL THF for 24 hours at room temperature under an air atmosphere. The process of photocatalytic reaction with and without light was monitored by GC using biphenyl as internal standard.



3.2 Radical-inhibiting experiment

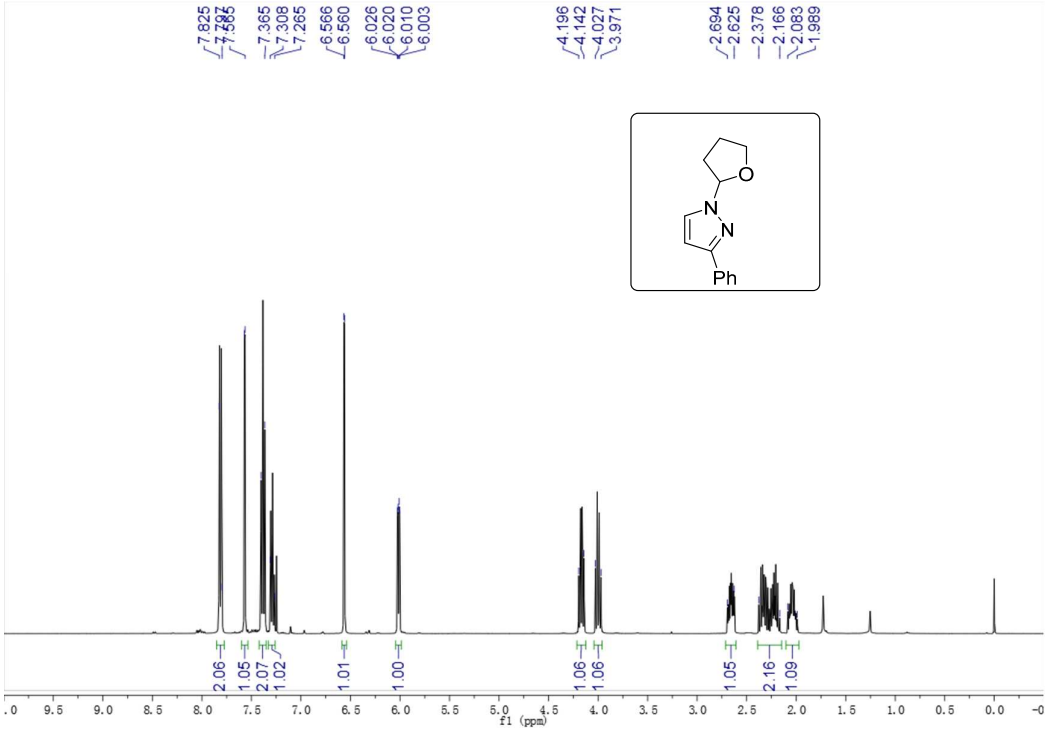
In a dried schlenk tube, 3-phenyl-1H-pyrazole **1a** (0.3 mmol), Acr^+ - Mes ClO_4^- (3

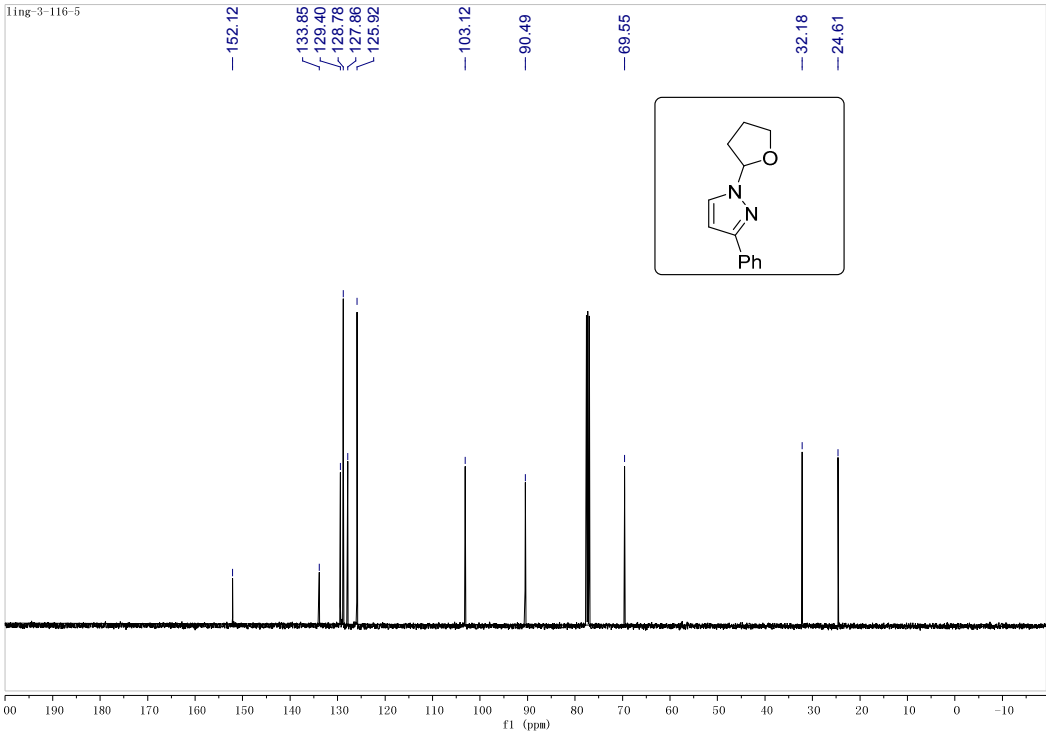
mol%, 0.015 mmol) and 2,2,6,6-tetramethlpiperidinooxy (TEMPO, 0.6 mmol) were stirred in 3.0 mL THF for 24 hours at room temperature under an air atmosphere irradiated by blue LEDs. After completion of the reaction, the mixture was detected by GC.

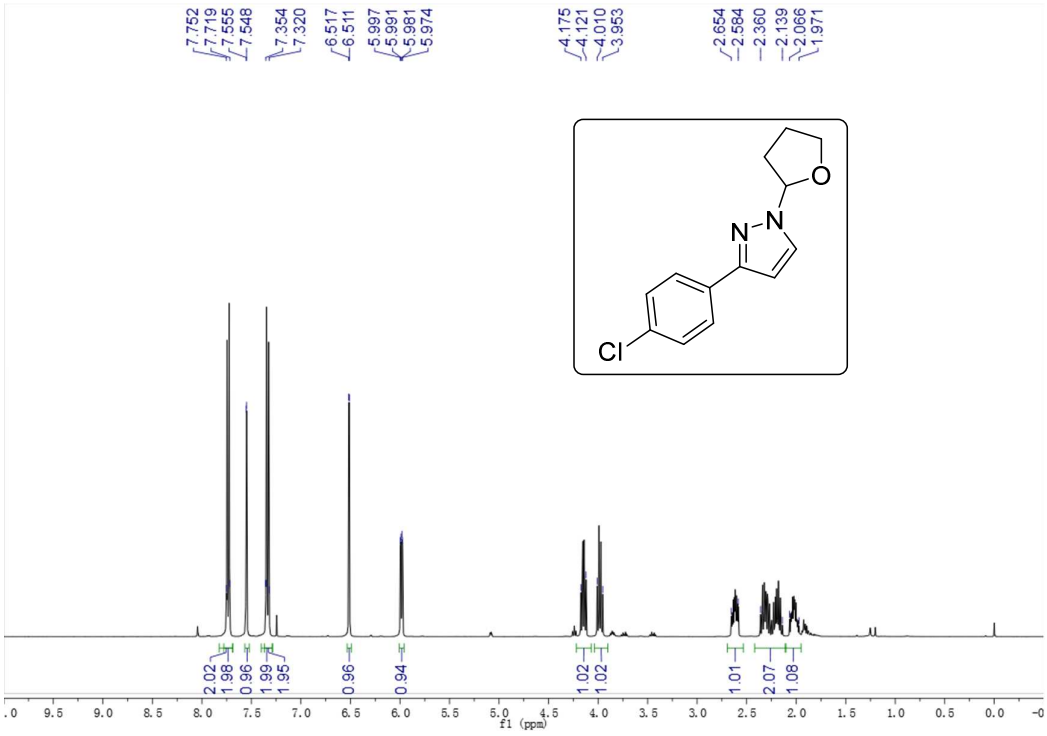
3.3 Kinetics of Isotopic Effect Experiment

A schlenk tube equipped with a stir-bar was charged with 3-phenyl-1H-pyrazole **1a** (0.3 mmol), Acr^+ - Mes ClO_4^- (3 mol%, 0.015 mmol). After that, the reaction tube was purged under an air atmosphere. Then 1.5 mL of THF and 1.5 mL of THF-d8 were added into the reaction tube via a syringe. Finally, the schlenk tube was under irradiation of blue LED and stirred for 24 h. Then the mixture was diluted by ethyl acetate, the pure product was obtained by flash column chromatography on silica gel to afford a mixture of the products deuterium-**3a** (**3a-D**) and **3a**. The ratio of the products was calculated from ^{1}H NMR spectra.

4. NMR Spectra of Products



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N
Cl
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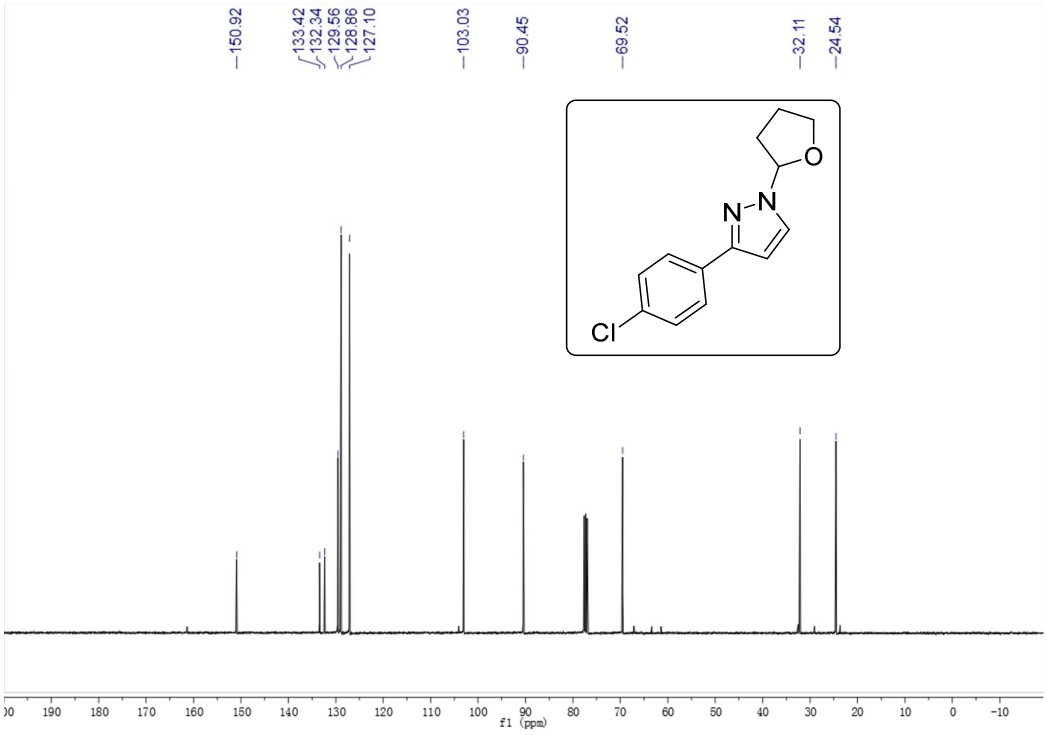
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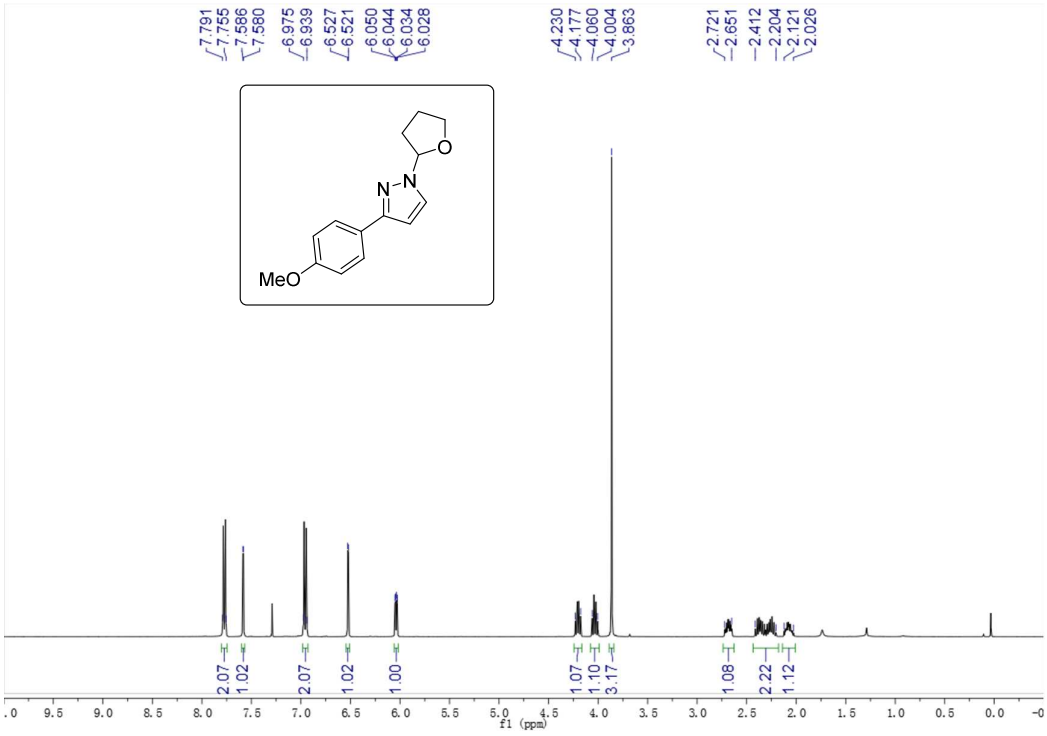
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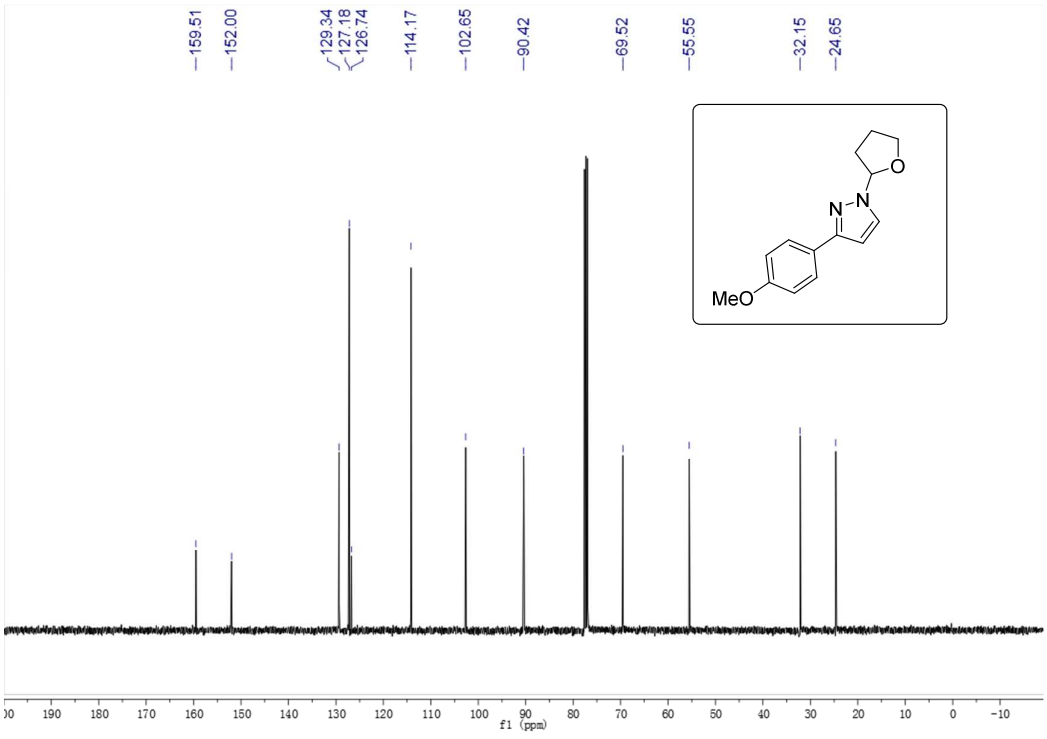
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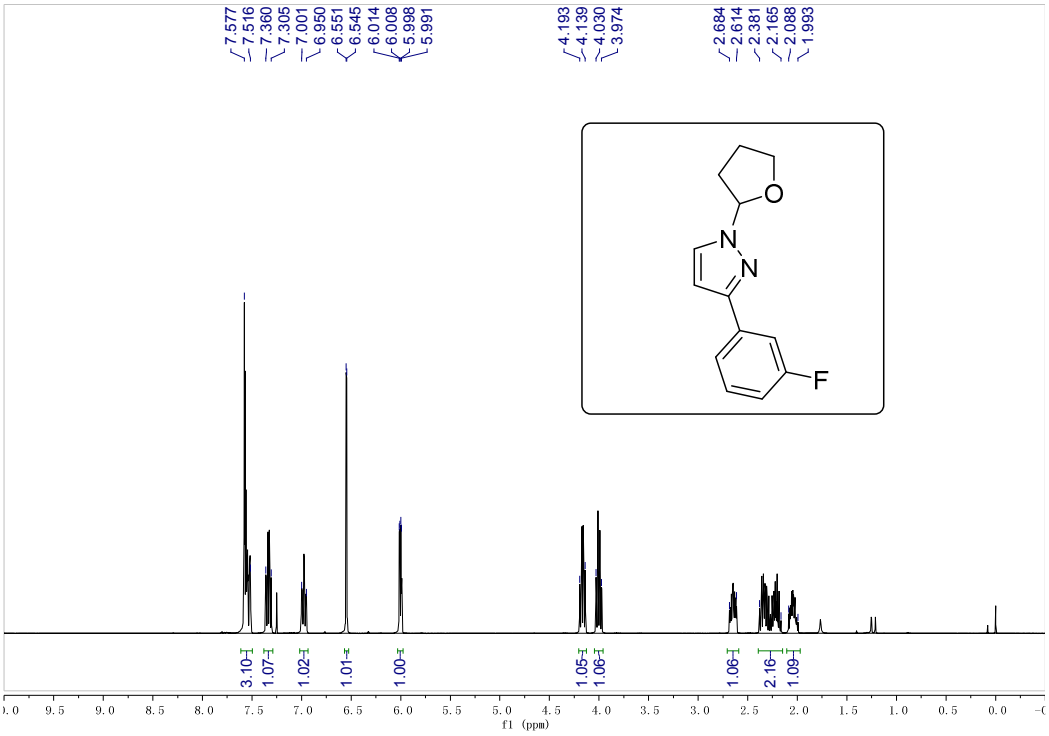
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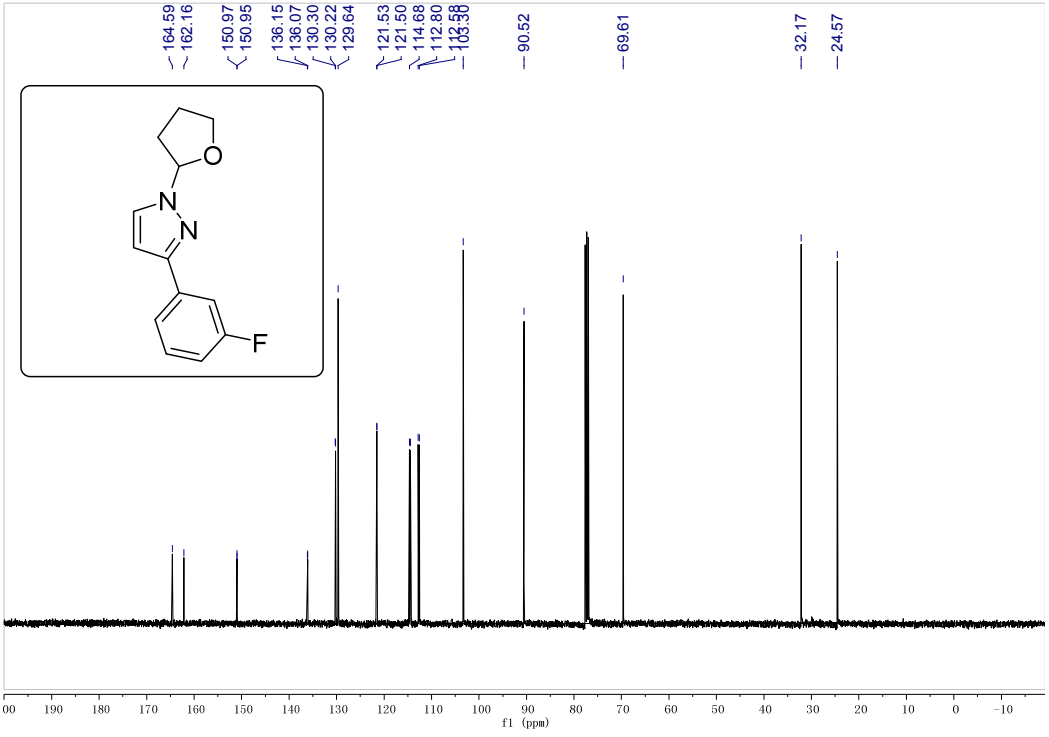
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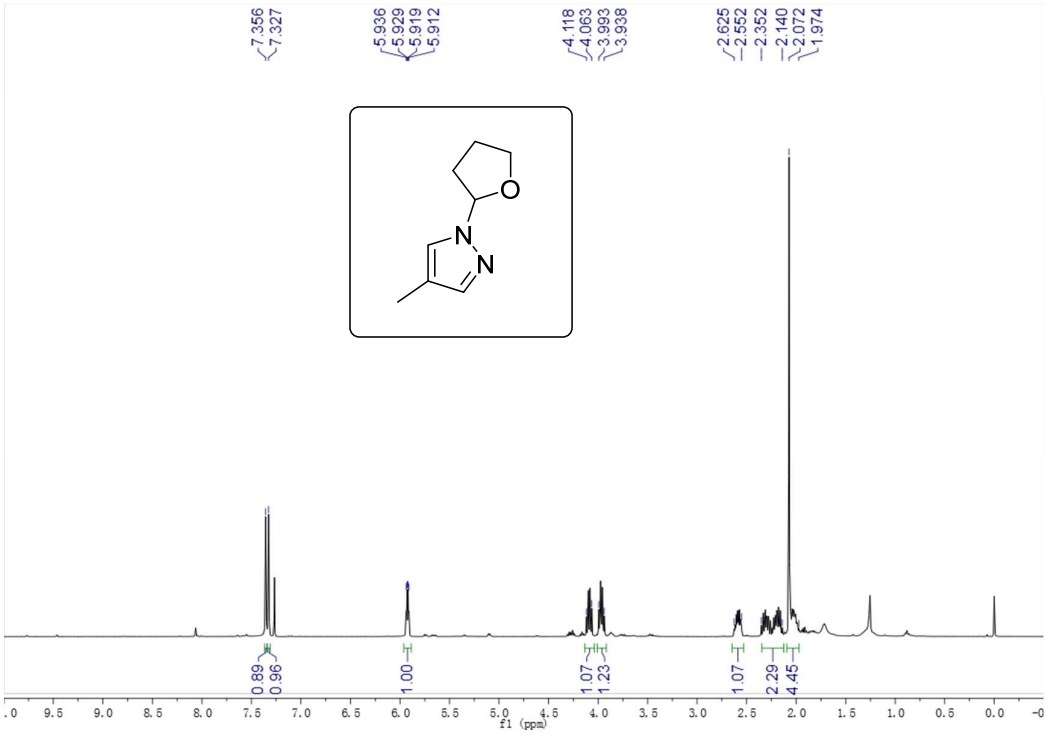
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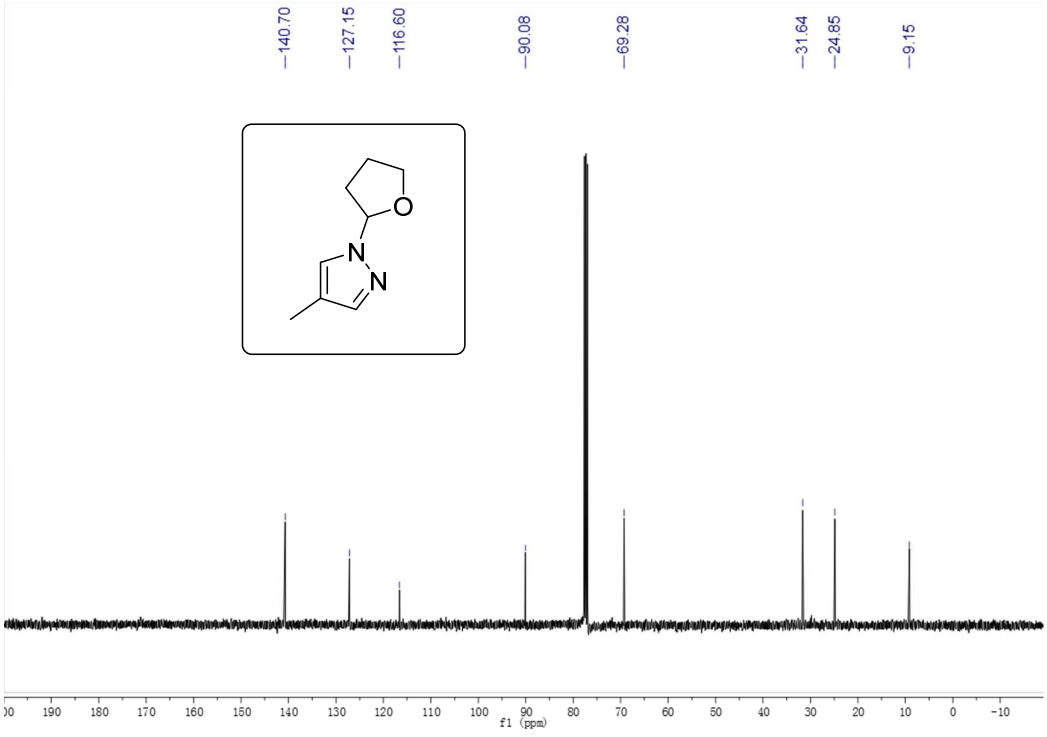
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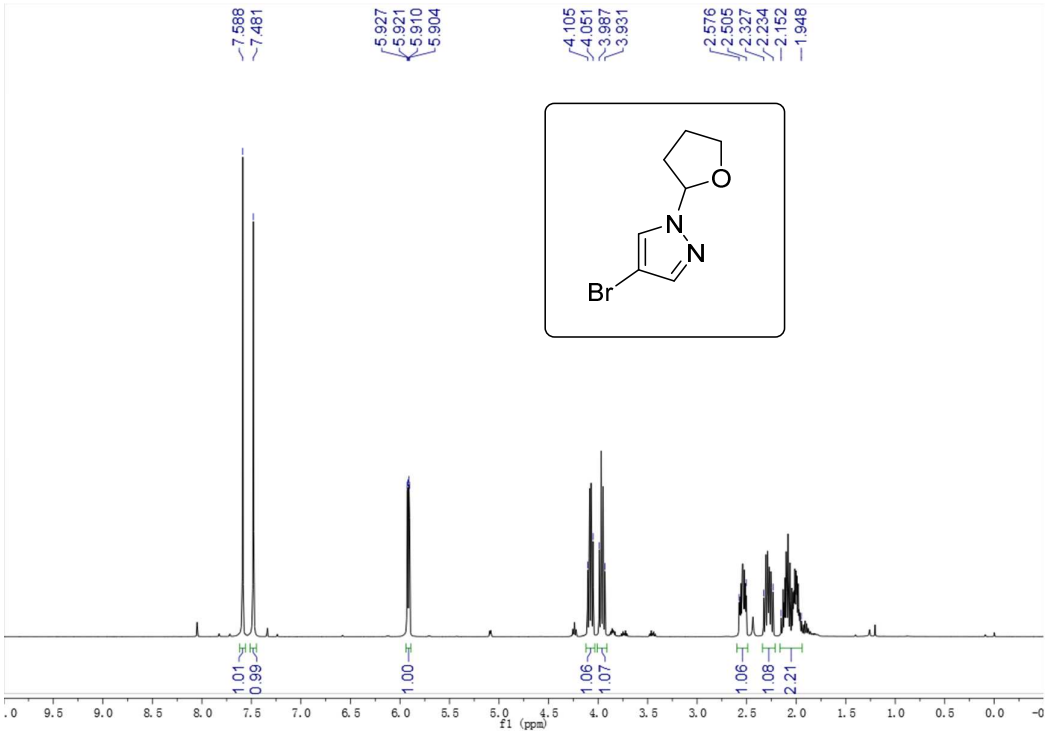
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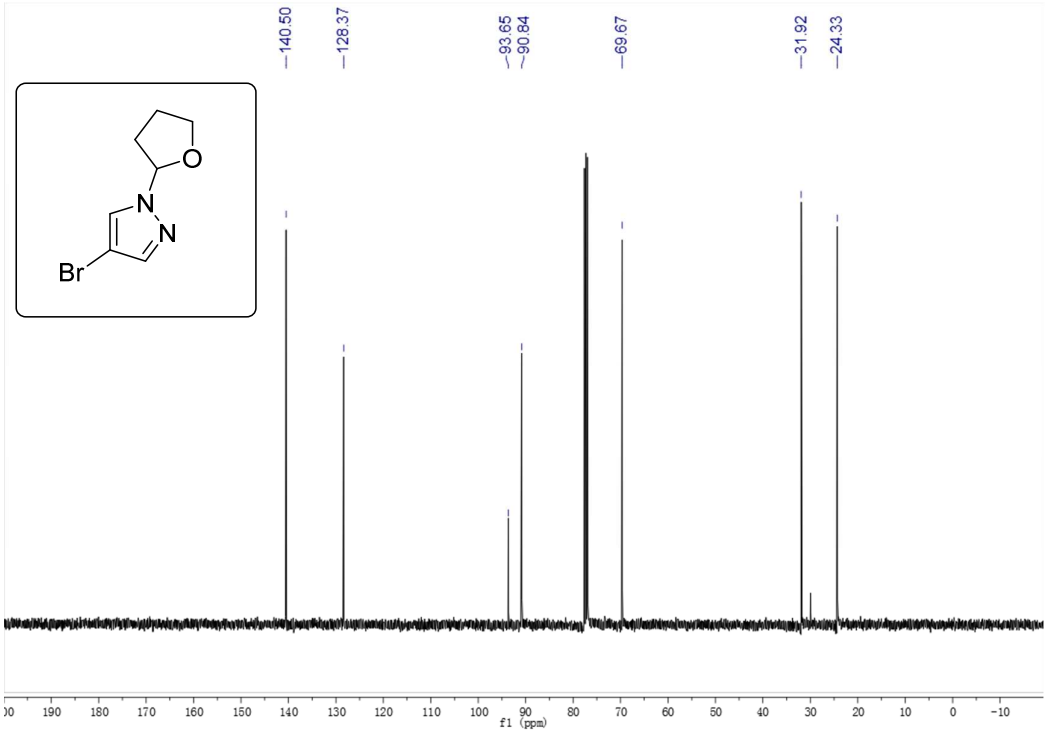
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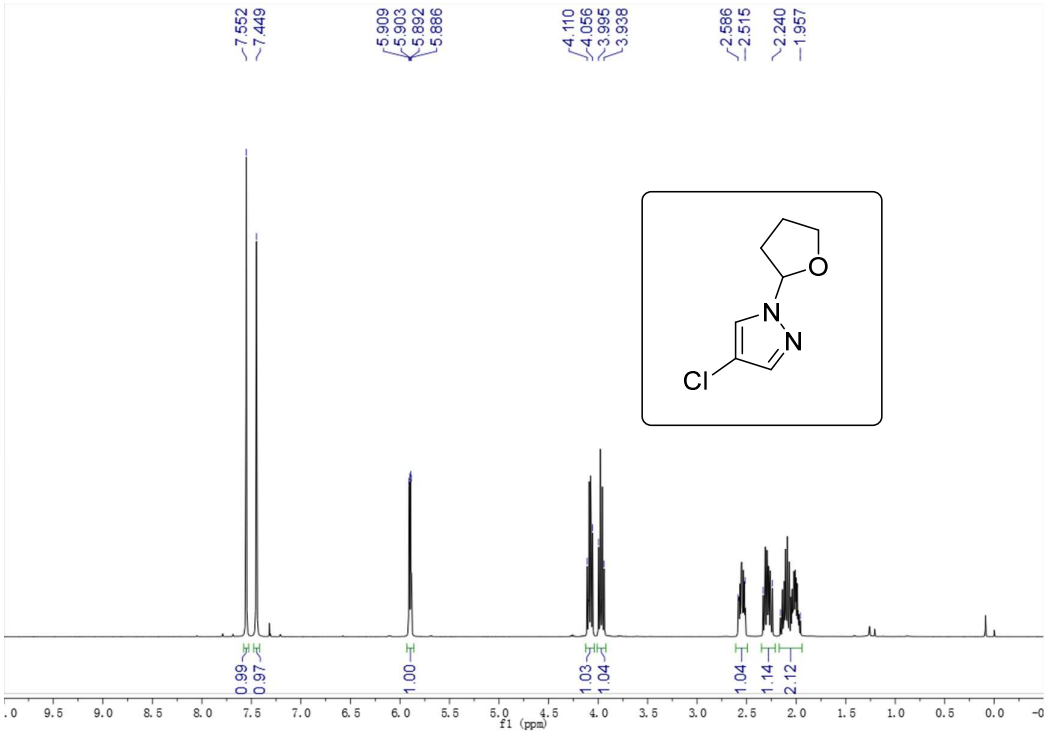
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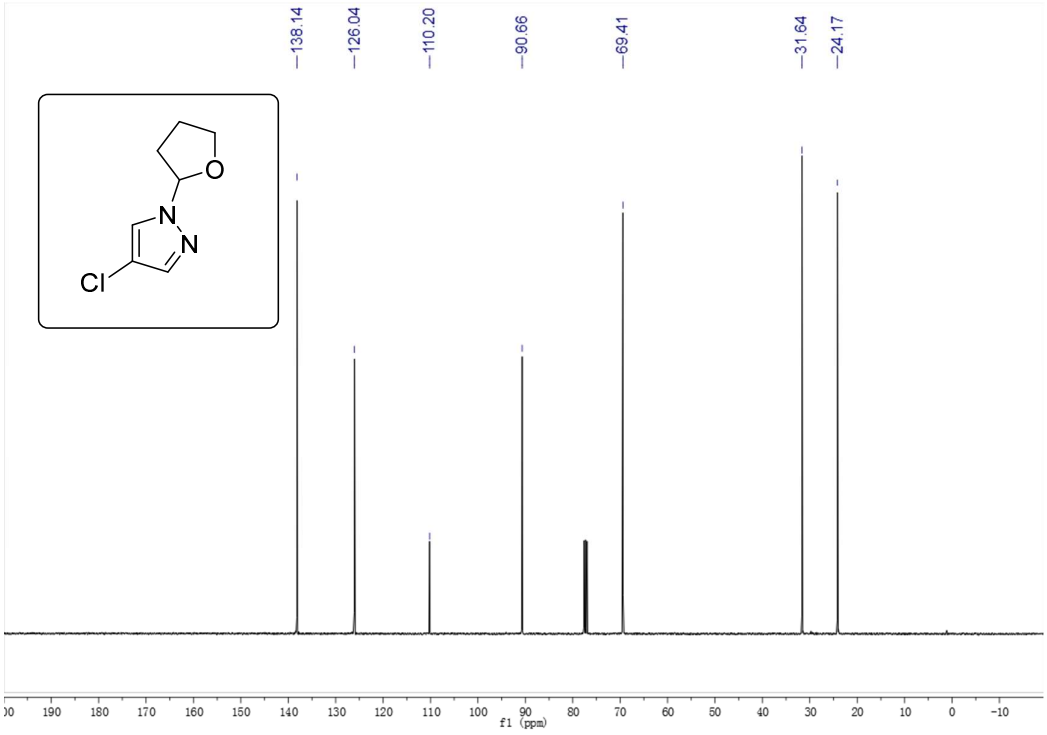
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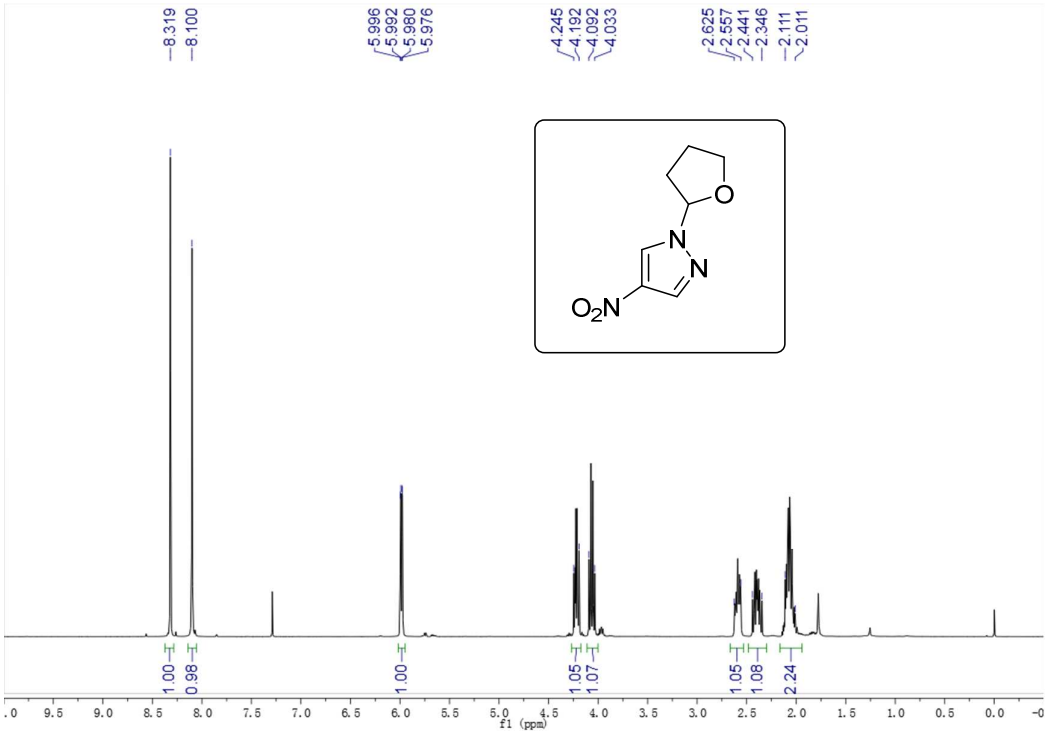
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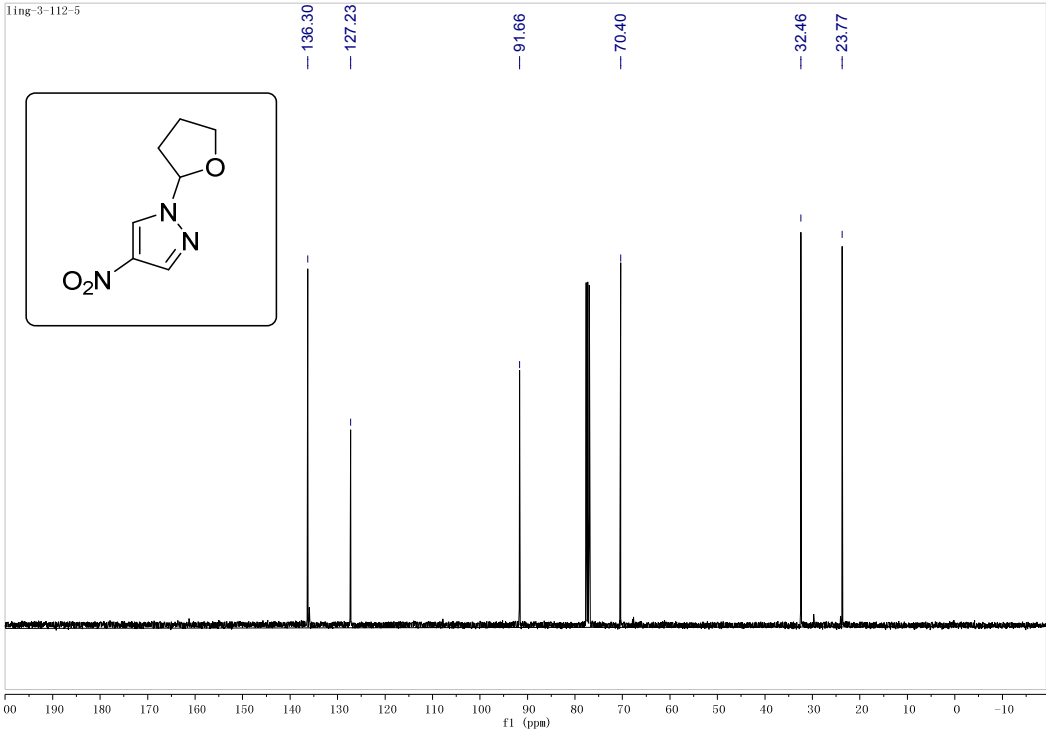
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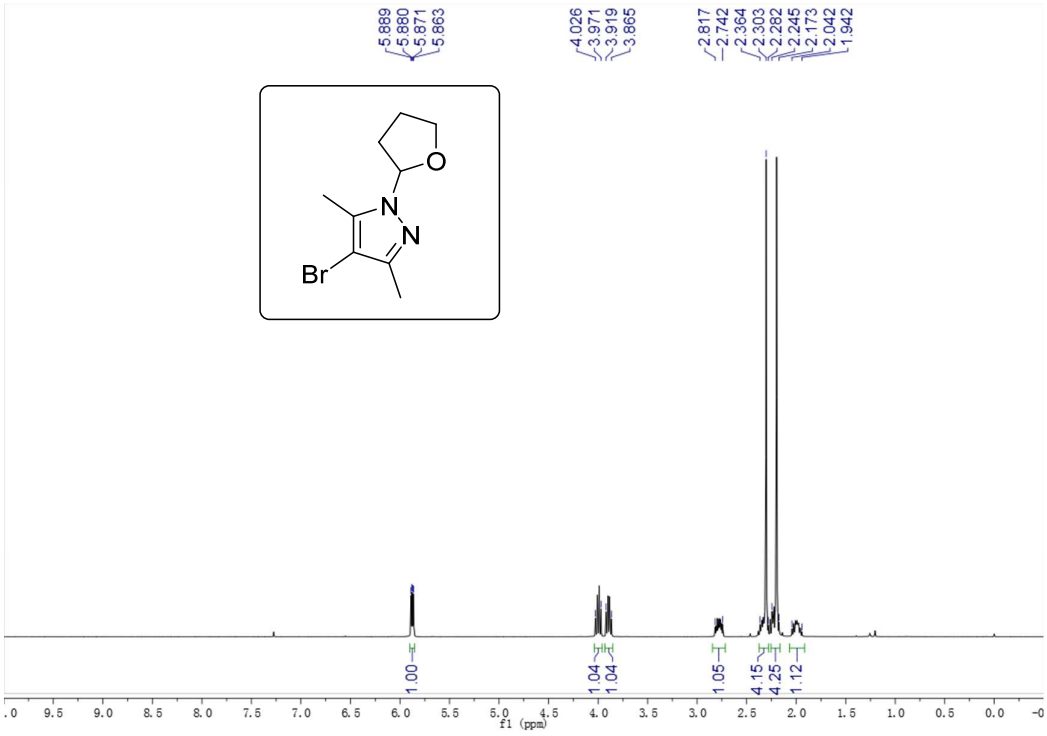
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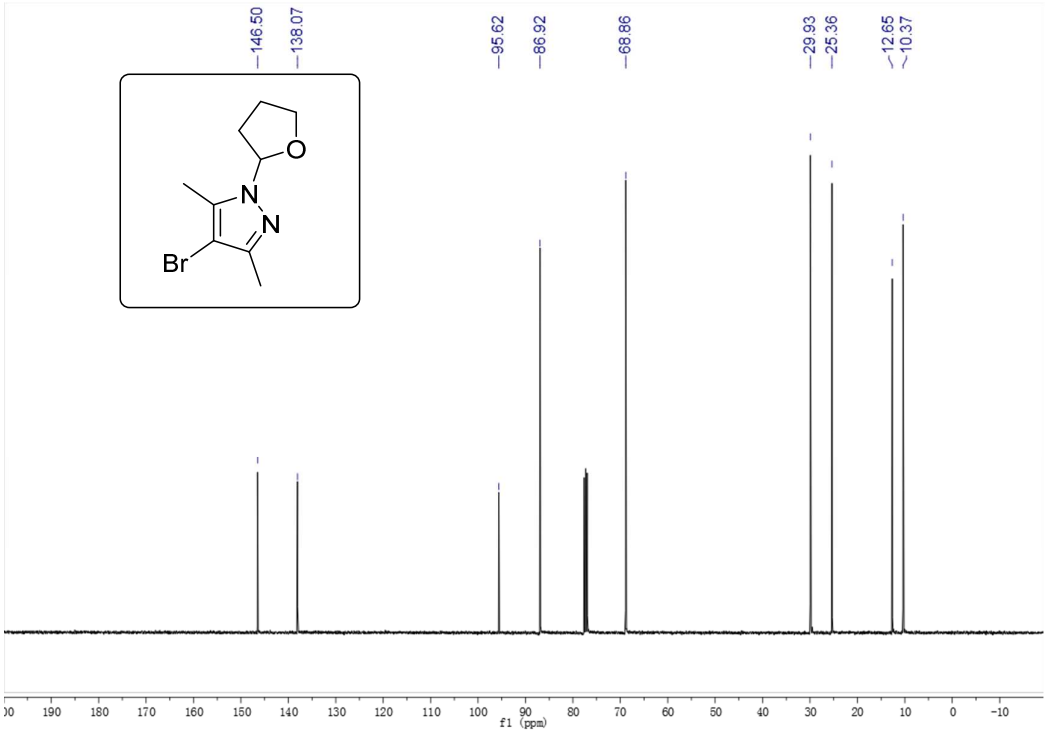
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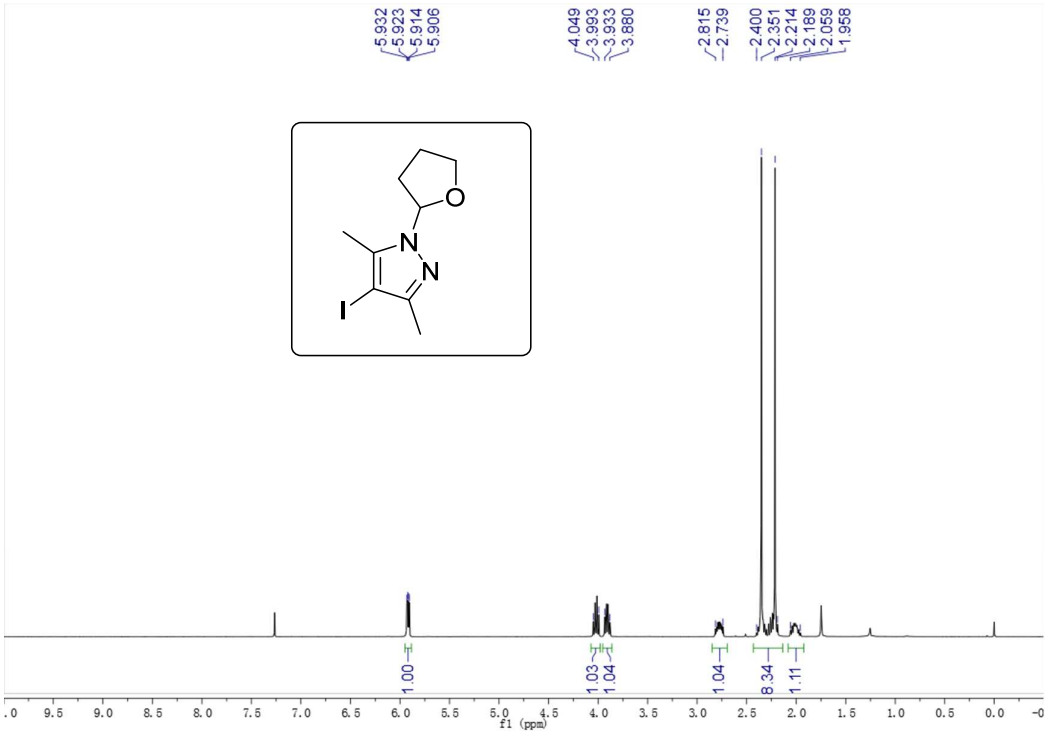
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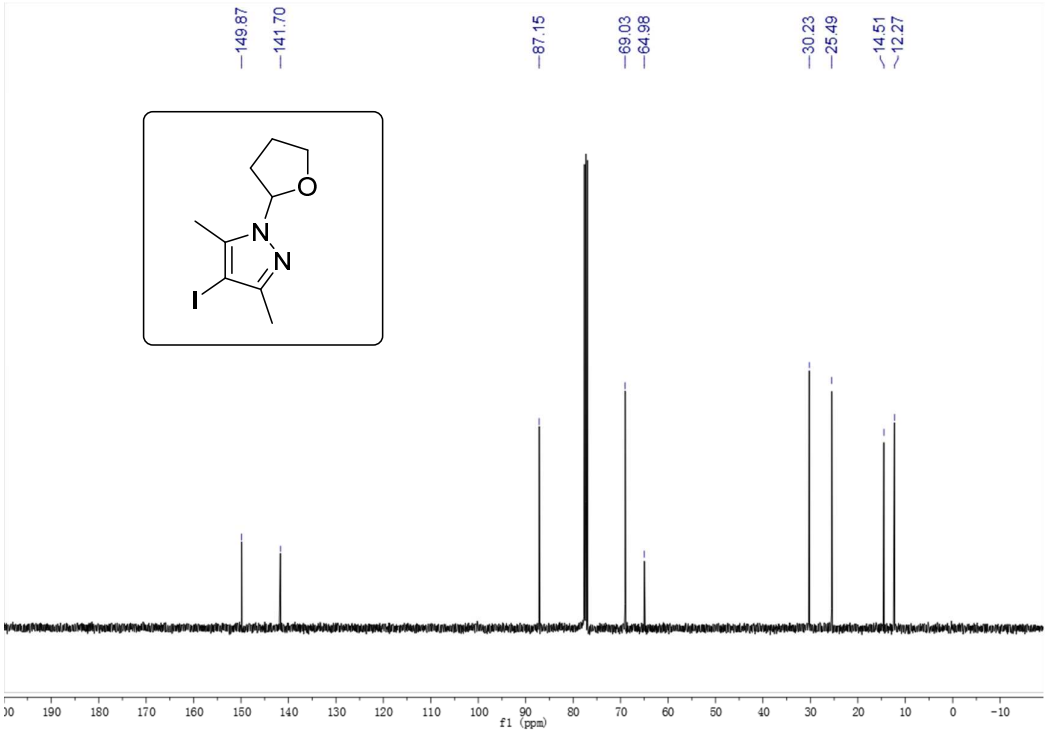
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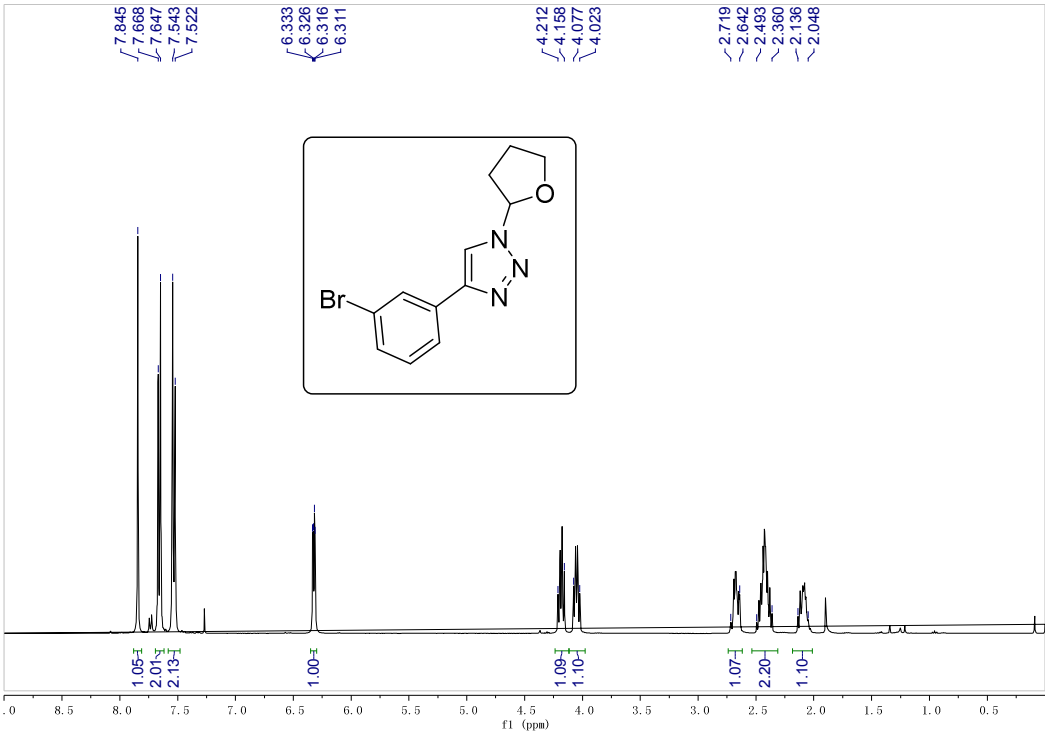
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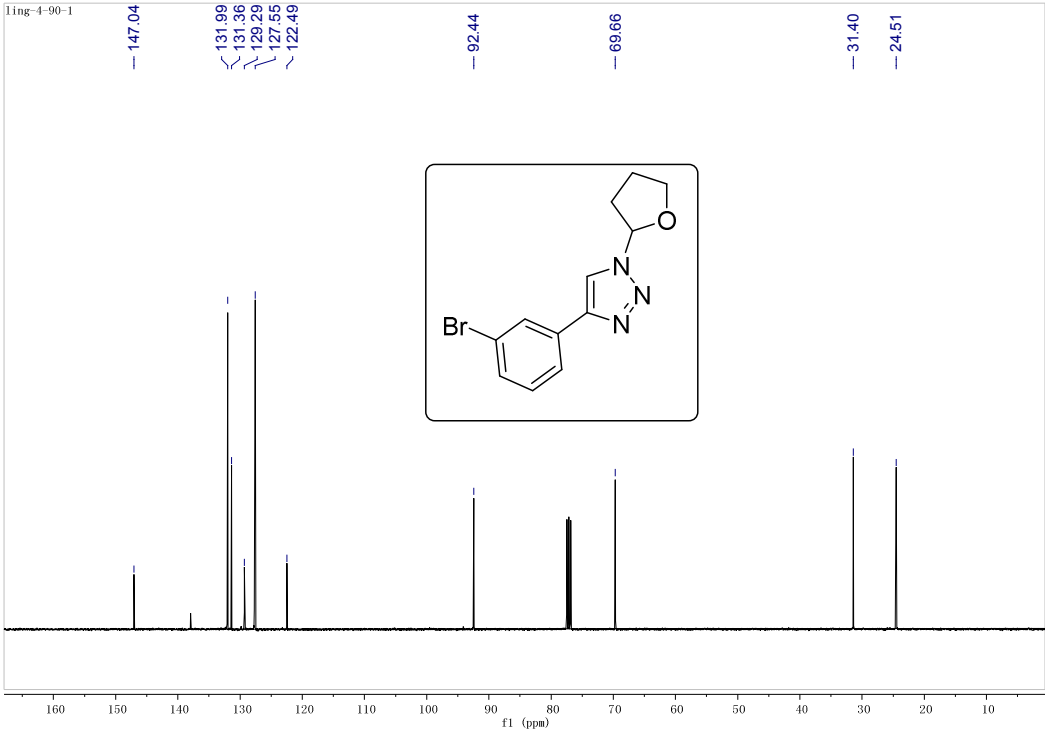
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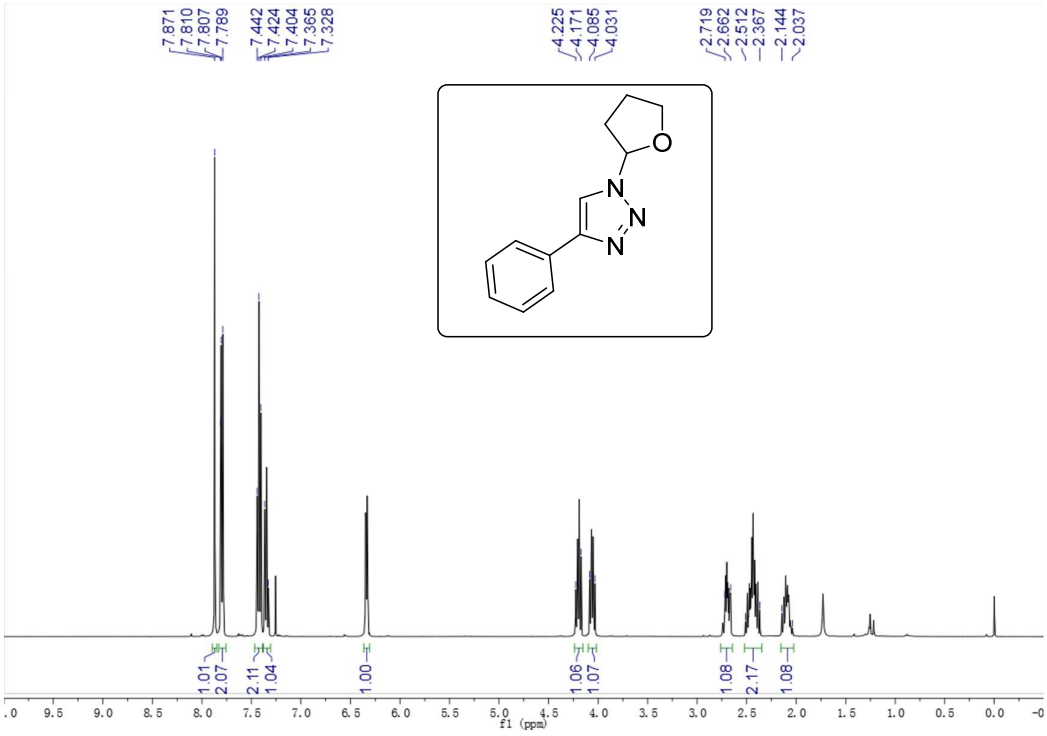
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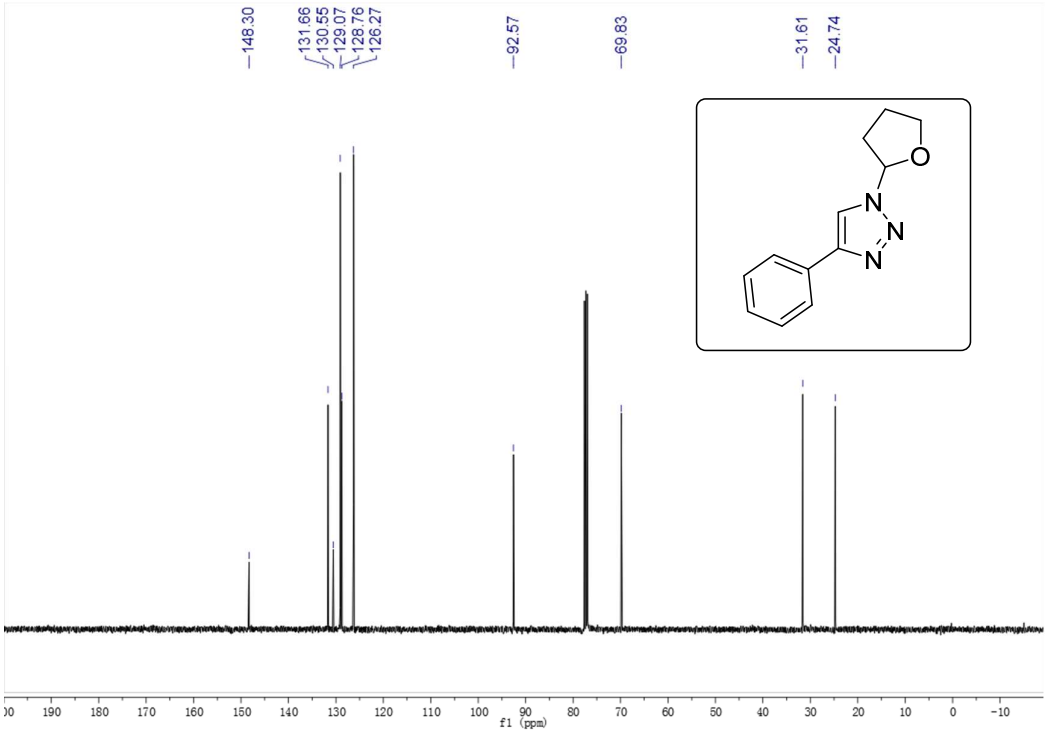
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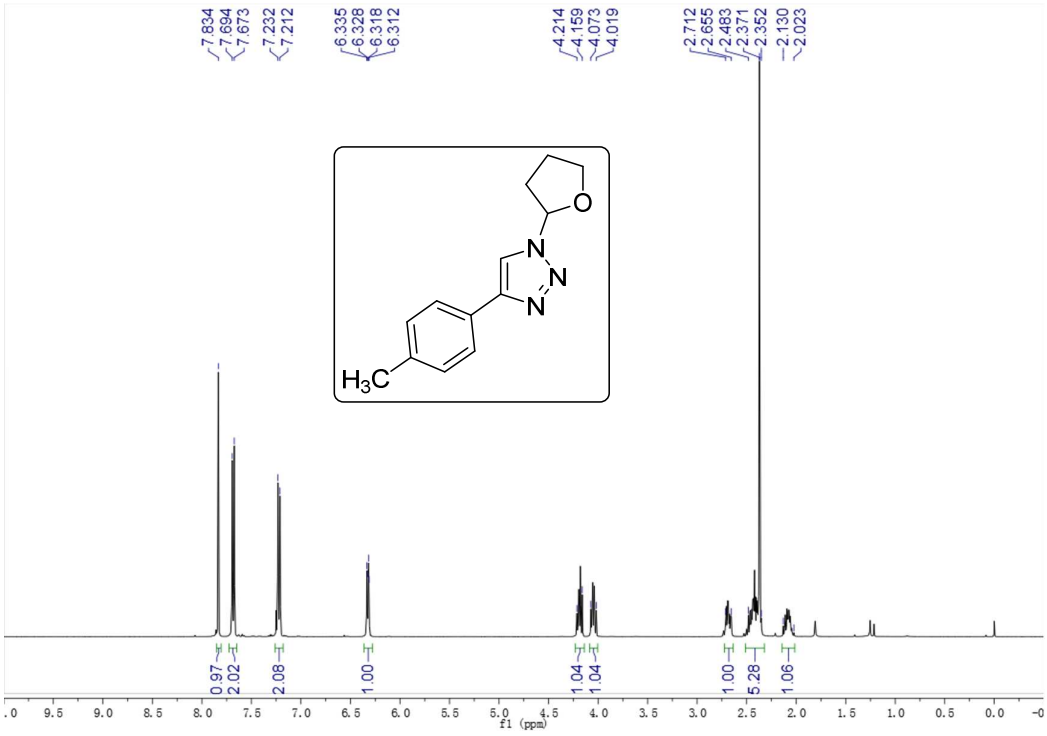
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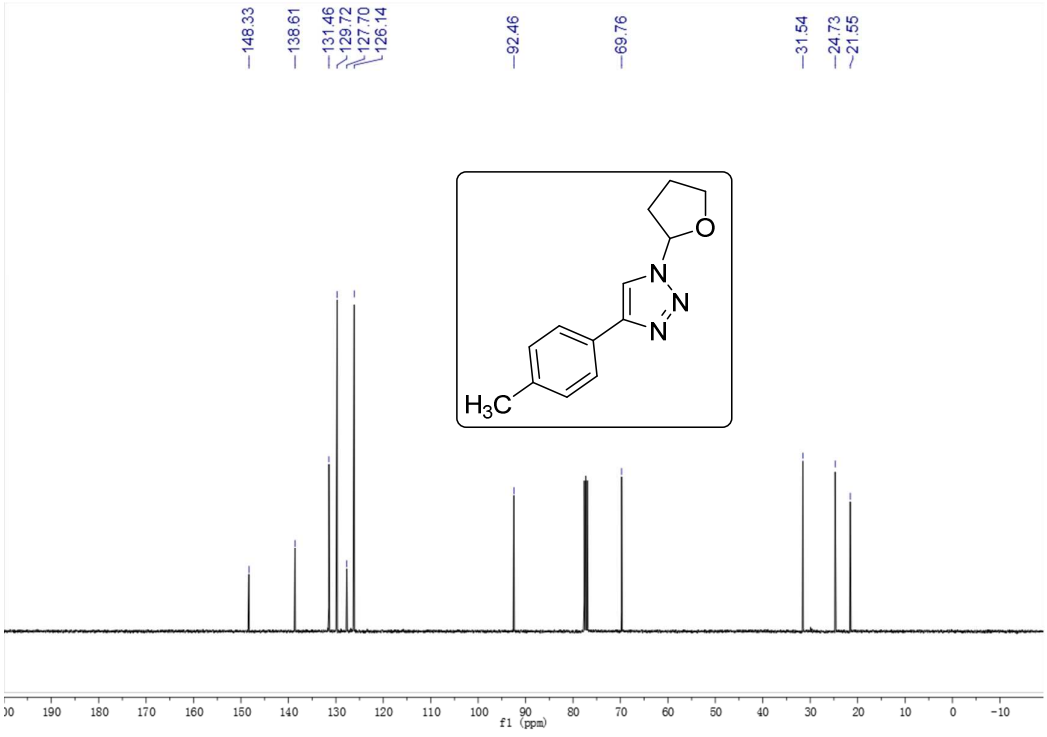
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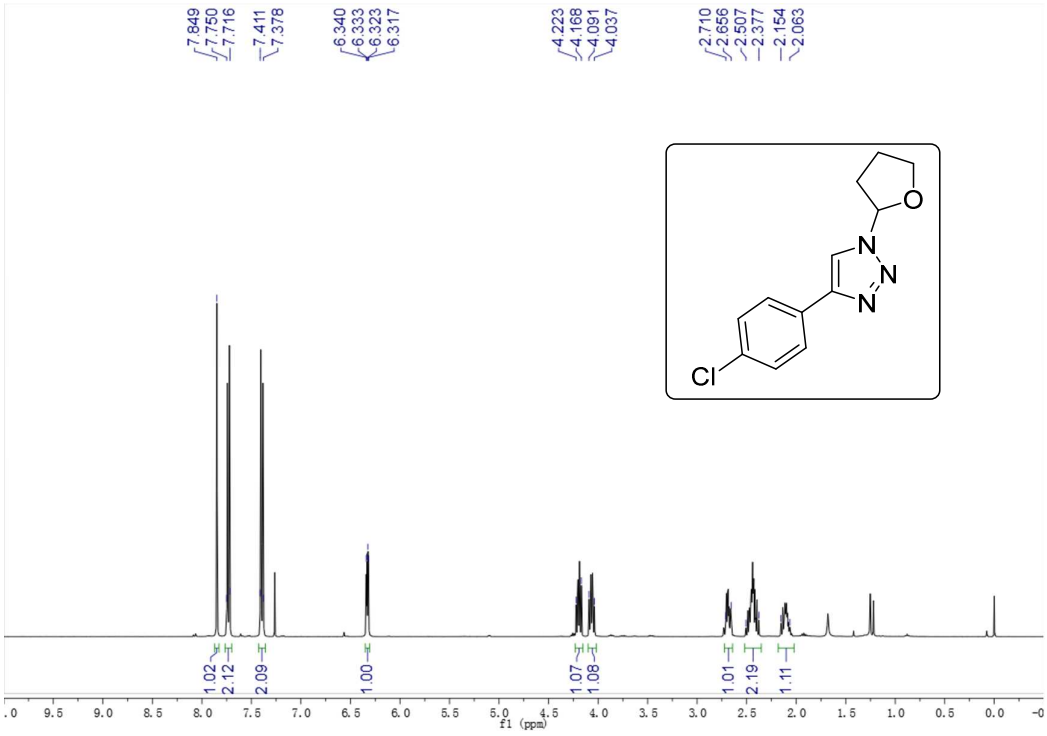
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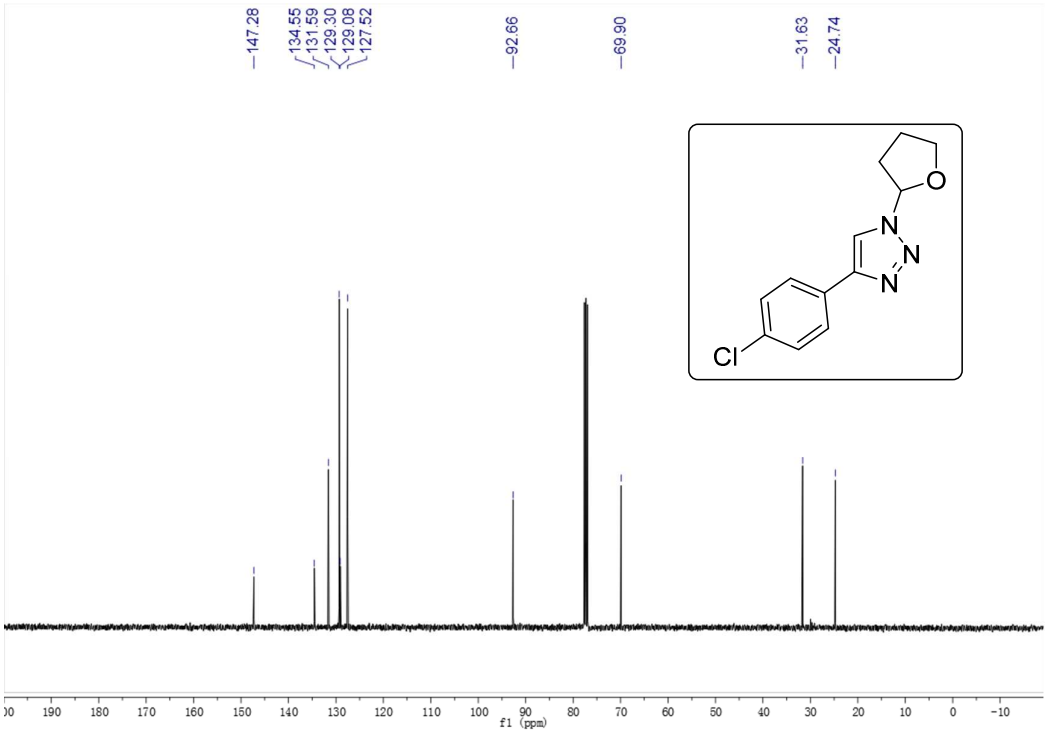
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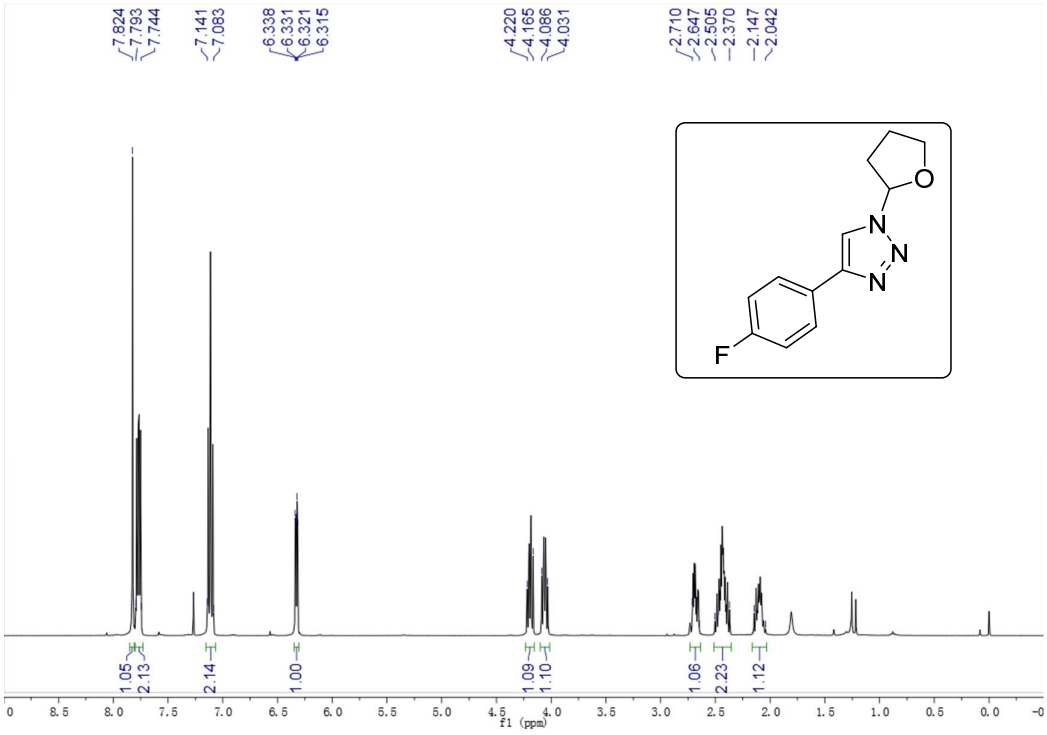
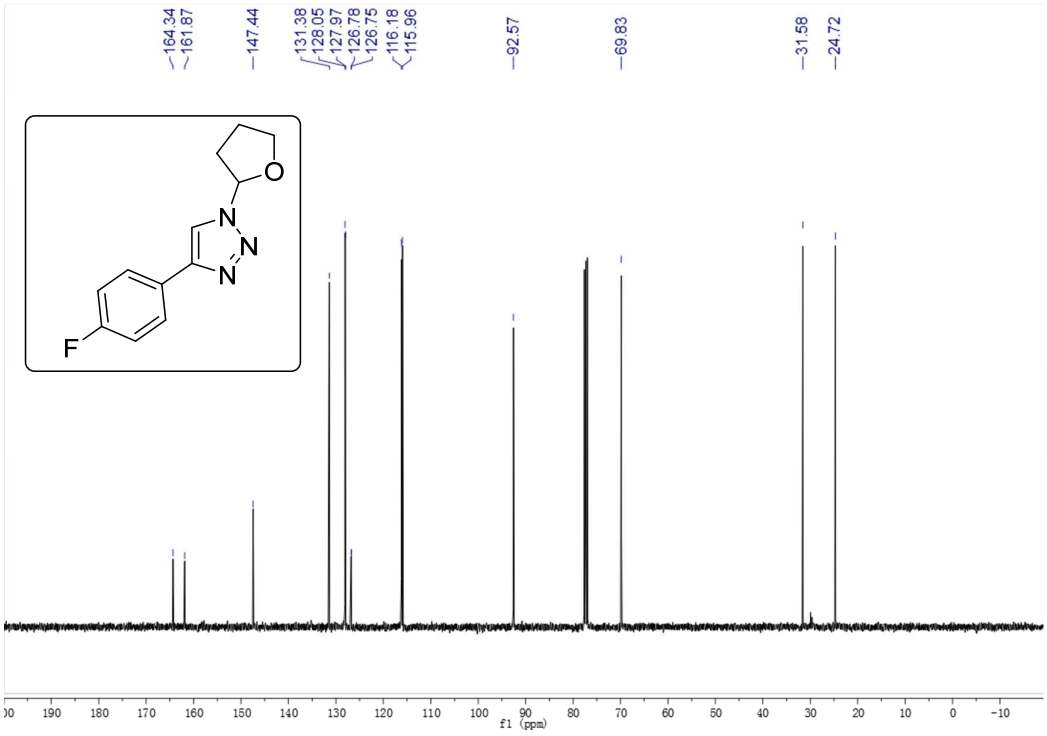
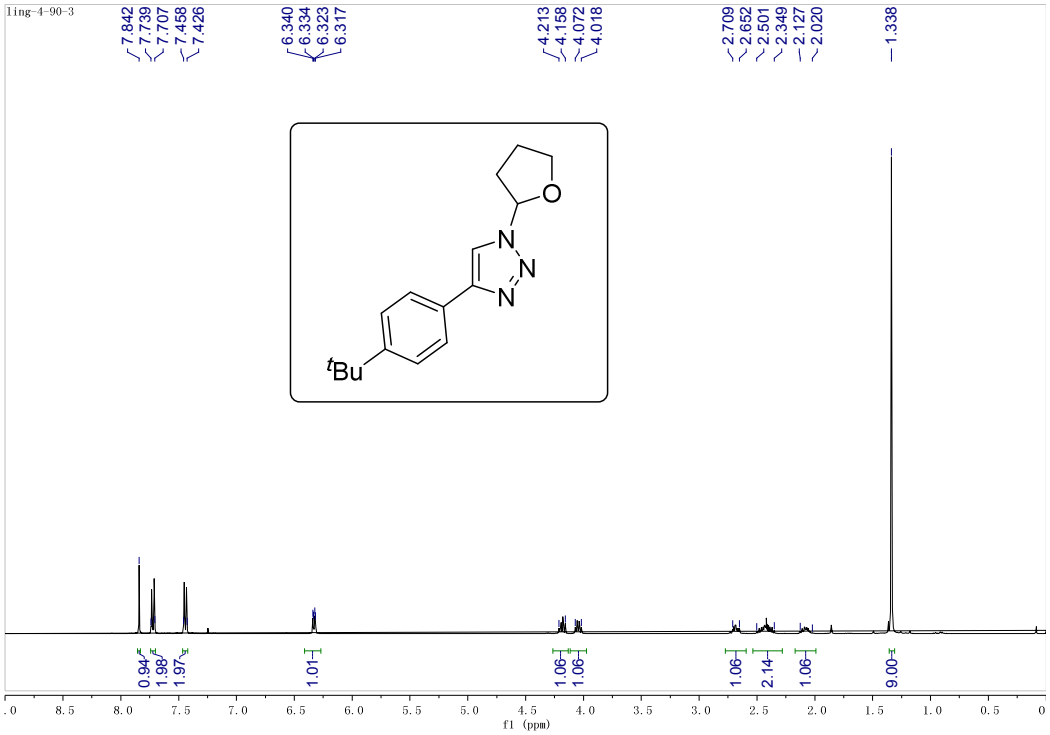
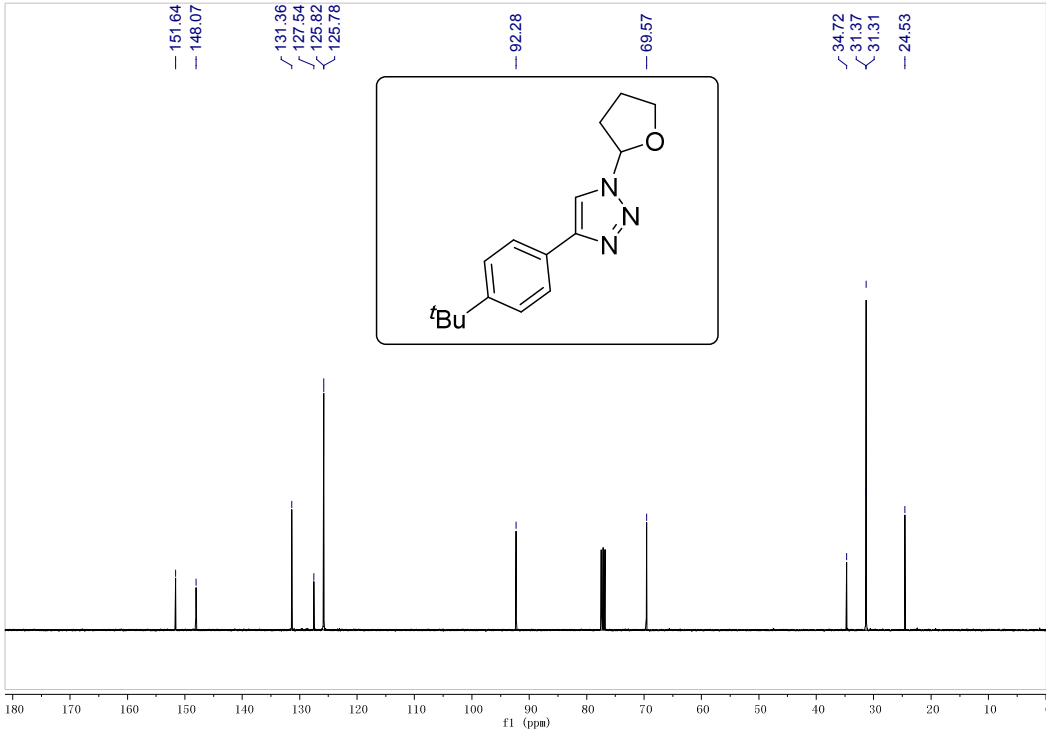
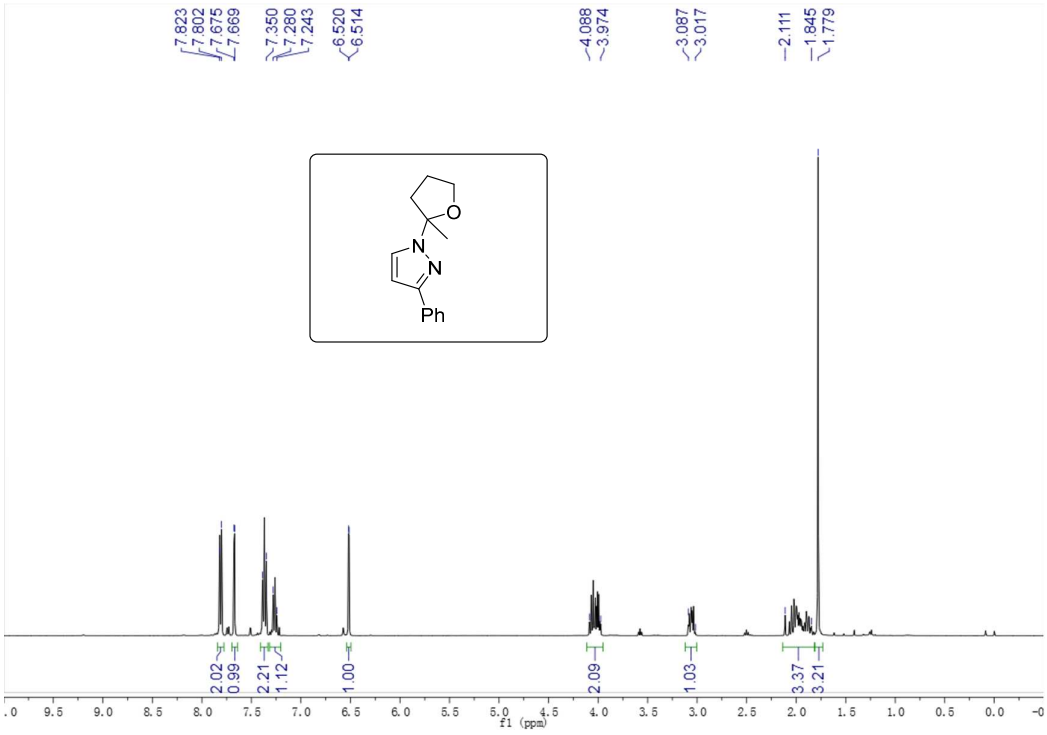
Cl
f1 (ppm)

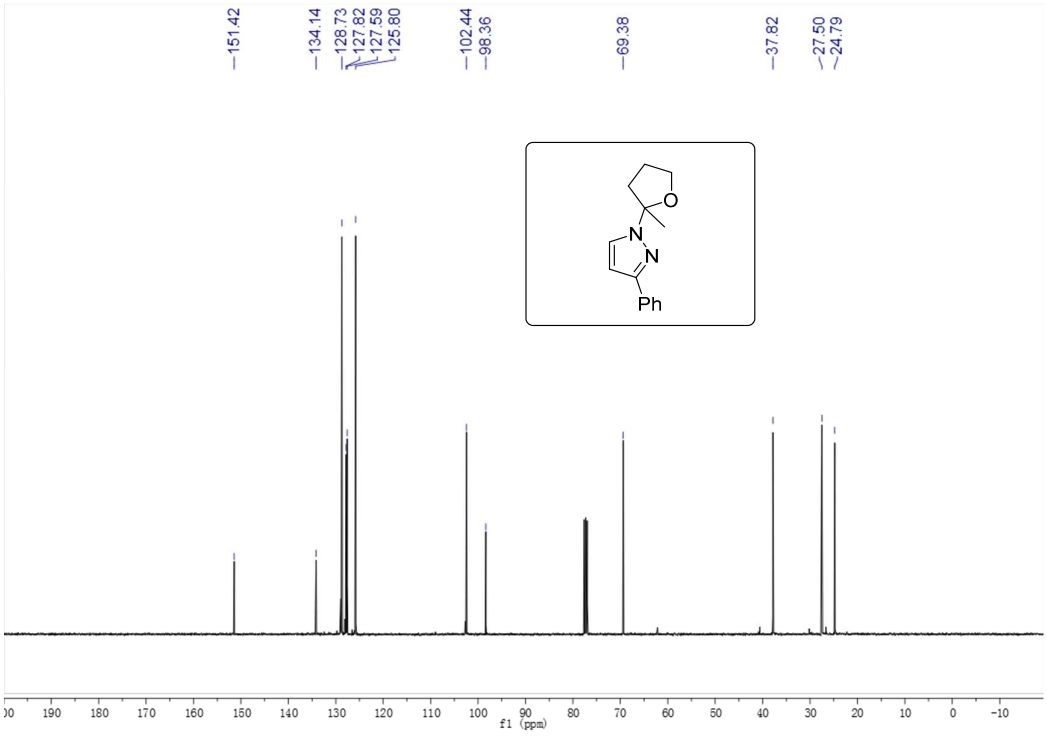

7.824
7.793
7.744
7.141
7.083
6.338
6.331
6.321
6.315
4.220
4.165
4.086
4.031
2.710
2.647
2.505
2.370
2.147
2.042
O
N
N
N
F
1.05
2.13
2.14
1.00
1.09
1.10
1.06
2.23
1.12
f1 (ppm)


164.34
161.87
147.44
131.38
128.05
127.97
126.78
126.75
116.18
115.96
92.57
69.83
31.58
24.72
O
N
N
N
F
f1 (ppm)


ling-4-90-3
7.842
7.739
7.707
7.458
7.426
6.340
6.334
6.323
6.317
4.213
4.158
4.072
4.018
2.709
2.652
2.501
2.349
2.127
2.020
1.338
O
N
N
N
tBu
0.94
1.98
1.97
1.01
1.06
1.06
1.06
2.14
1.06
9.00
f1 (ppm)


151.64
148.07
131.36
127.54
125.82
125.78
92.28
69.57
34.72
31.37
31.31
24.53
O
N
N
N
tBu
f1 (ppm)


7.823
7.802
7.675
7.669
7.350
7.280
7.243
6.520
6.514
4.088
3.974
3.087
3.017
2.111
1.845
1.779
O
N
N
Ph
2.02
0.99
2.21
1.12
1.00
2.09
1.03
3.37
3.21
f1 (ppm)


151.42
134.14
128.73
127.82
127.59
125.80
102.44
98.36
69.38
37.82
27.50
24.79
O
N
N
Ph
f1 (ppm)