Supplementary Material

Copper-catalyzed radical oxyallylation of olefins for the construction of alkene-containing isoxazolines

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Table of Contents

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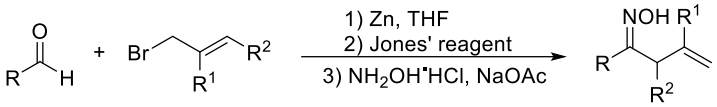
1. Substrates preparation

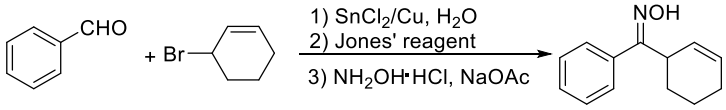
Synthetic procedure for oximes



1) To a solution of the allylbromide (2.0 equiv) in anhydrous THF was slowly added zinc dust (2.0 equiv) at 0 °C. Aldehyde (1.0 equiv) was dissolved in anhydrous THF and added to the solution. The resulting suspension was stirred overnight at this temperature. The reaction was quenched with saturated aqueous NH_4Cl carefully at 0 °C, filtered and extracted with ethyl acetate for 3 times. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo. The crude homoallylic alcohol product was directly used in the next step without further purification.

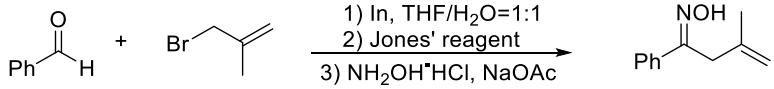
2) A solution of the homoallylic alcohol in diethyl ether was stirred at 0 °C while Jones reagent (2.0 - 4.0 equiv) was added dropwise. The resulting mixture was allowed to warm to room temperature and stirred for 1 hour. The diethyl ether layer was separated and the aqueous layer was extracted with ethyl acetate for 3 times. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo. The crude *β,γ*-unsaturated ketone product was directly used in the next step without further purification.

3) To a solution of *β,γ*-unsaturated ketone (1.0 equiv) in pyridine was added hydroxylamine hydrochloride (2.0 equiv). The mixture was stirred at room temperature (110 °C for **1k**) for 4 h and concentrated in vacuo. Then, the mixture was diluted with water and extracted with ethyl acetate, the combined organic layers were dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel to afford the *β,γ*-unsaturated ketoxime.



1) To a mixture of benzaldehyde (1.0 equiv) and 3-bromo-1-cyclohexene (1.8 equiv) in water, $SnCl_2{\cdot}H_2O$ (2.0 equiv) and copper powder (1.0 equiv) were added. This mixture was vigorously stirred at room temperature for 24 h. Then the mixture was extracted with ethyl acetate (3×30 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and evaporated. The crude material was purified by flash chromatography on silica gel to afford the product.

Steps 2) and 3) are same as above-mentioned.



1) A round bottomed flask charged with a solution of the 3-bromo-2-methylprop-1-eneor its analogues (1.1 equiv) and indium (1.1 equiv) in THF/H_2O (1:1) was kept at room temperature with stirring. The benzaldehyde was added to the solution and the resulting suspension was stirred overnight. Saturated ammonium chloride solution was slowly added at 0 ℃. The resulting mixture was extracted with ethyl acetate for 3 times. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo.

Steps 2) and 3) are same as above-mentioned

The starting substrates 1a-1d, 1g-h, 1k-l, 1o[1], 1e, 1j[2], 1f[3], 1p[4], 1m[5], 1n[6] are known compounds, and their NMR data were identical with those found in the literature.

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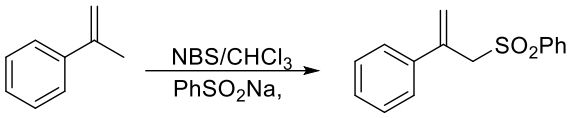
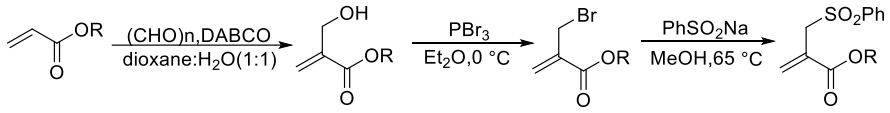
Synthetic procedure for allyl sulfones.



a) A solution of a-methyl styrene (8.3 mL, 64 mmol) and N-bromosuccinimide (NBS, 15.0 g， 84 mmol) in $CHCl_3$ (15 mL) was heated to reflux for 3 h. The mixture was cooled down after reflux and the filtrated was evaporated and purified by chromatography to afford l-bromo-2-phenyl-2-propene.

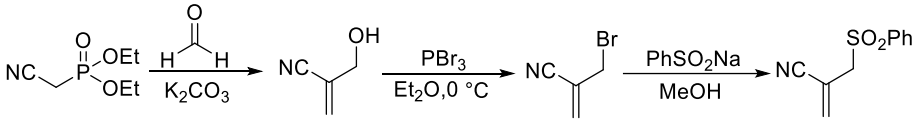
b) To a solution of the l-bromo-2-phenyl-2-propene (2.61 g, 13.2 mmol) in dry DMF (40 mL) was added sodium benzenesulfinate. This mixture was heated to 80 °C for 4 h, cooled, and diluted with EtOAc (100 mL). The mixture was washed with water (3 ×50 mL), brine, dried with Na_2SO_4, filtered and the filtrate was evaporated and purified by flash chromatography (Petroleum ether / EtOAc = 10:1, TLC R_f = 0.22) afforded (2-phenylallyl)sulfonyl)benzene as a white solid.



1) To a solution of paraformaldehyde (1.3 equiv) and acrylate (1.0 equiv) in dioxanewater (1:1, v/v) was added DABCO (1.3 equiv) and the reaction progress was monitored by TLC. Upon completion, the reaction mixture was partitioned with EtOAc and water. The organic layer was separated and washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel to afford corresponding alcohols.

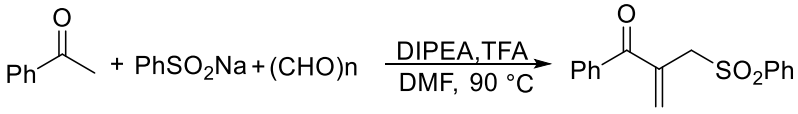
2) To a solution of alcohol was added phosphorus (III) bromide (0.33 equiv) in dry Et_2O (20 mL) at -10 °C. The temperature was allowed to rise to 20 °C and stirring was continued for 3 h. Water (50 mL) was then added and the mixture was extracted with petroleum ether (3 ×50 mL). The organic phase was washed with saturated aq. NaCl(50 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel to give corresponding alkyl bromide.

Steps 3) are same as above-mentioned.



1) To a mixture of diethyl(cyanomethyl)phosphonate (20 mmol) and a 37% aqueous solution of formaldehyde (80 mmol), a saturated aqueous solution of K_2CO_3 (37.5 mmol) was added at room temperature dropwise over 30 min. After stirring for an additional 2 h, the reaction was quenched with saturated aq. NH_4Cl (20 mL). Afterwards, the reaction mixture was extracted with Et_2O (3 × 20 mL). The organic layers were combined and dried over Na_2SO_4. The solvent was evaporated using a rotary evaporator, and the remaining colorless oil was purified by flash chromatography giving the 2-(hydroxymethyl)acrylonitrile as a colorless oil.

Steps 2) and 3) are same as above-mentioned.



A mixture of acetophenone (1.0 equiv), DIPEA (1.0 equiv), TFA (2.0 equiv), sodium benzenesulfinate (1.0 equiv) and paraformaldehyde (4.0 equiv) in DMF was heated to 90 °C in a sealed vessel for 20 h. The reaction mixture was cooled to room temperature, diluted with EtOAc, washed with 3 × 20 mL LiCl (5 wt%) and dried over Na_2SO_4. The solid was filtered off and the organic solvent evaporated. The viscous crude oil was purified by flash column chromatography to afford the product as a white solid.

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The starting substrates 2a-2e[7] are known compounds, and their NMR data were identical with those found in the literature.

2. Optimization details

Table S1 Optimization of reaction conditions[a,b]

Entry	base	**2a** (eq.)	Temp.(°C)	Yield[b]/(%)
1	Na_2CO_3	1.5	80	58
2	$NaHCO_3$	1.5	80	43
3	K_2CO_3	1.5	80	35
4	Na_2CO_3	2	80	64
5	Na_2CO_3	2.5	80	70
6	Na_2CO_3	3	80	84
7	Na_2CO_3	3.5	80	88
8	Na_2CO_3	3	60	86
9	Na_2CO_3	3	50	84
10	Na_2CO_3	3	rt	<10

[a]Reaction conditions: 1a (0.1 mmol), $Cu(OTf)_2$ (0.005 mmol), bpy (0.01 mmol), base (0.15 mmol), MeCN (1 mL), 12 h, under argon. [b]HPLC yields using Naphthalene as an internal standard.

3. References

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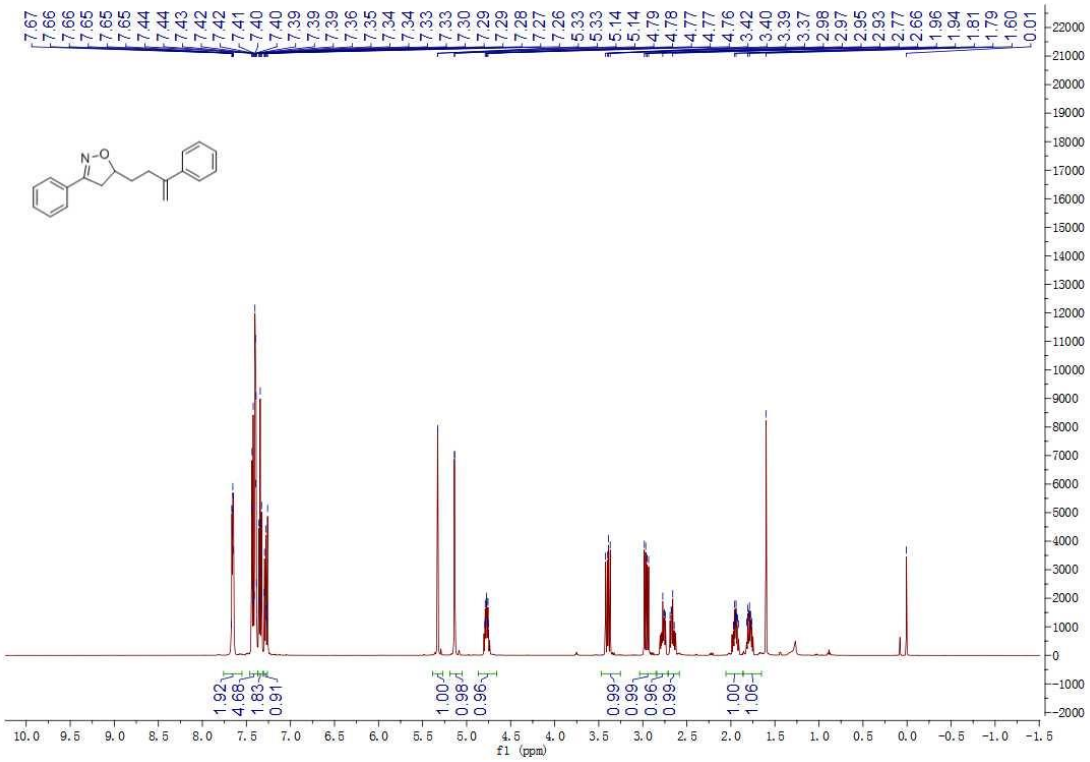
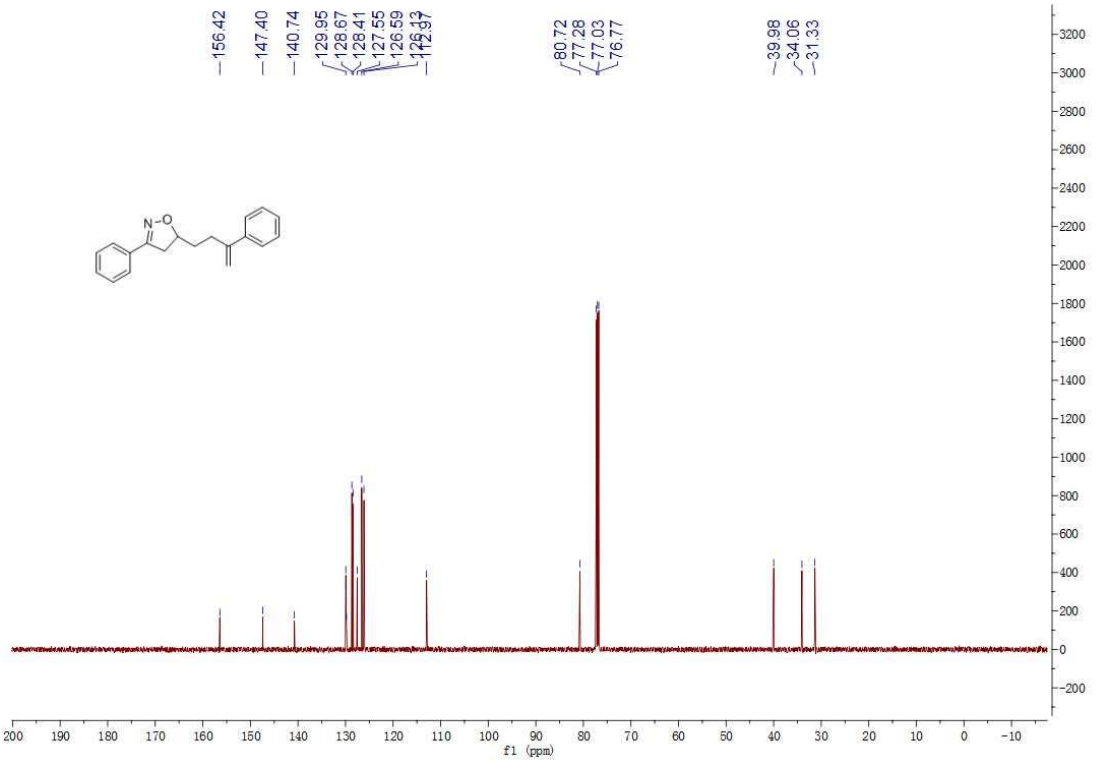
4. ^{1}H NMR , ^{13}C NMR and ^{19}F NMR Spectra of the Products

2-phenyl-5-(3-phenylbut-3-en-1-yl)-4,5-dihydroisoxazole (3a)





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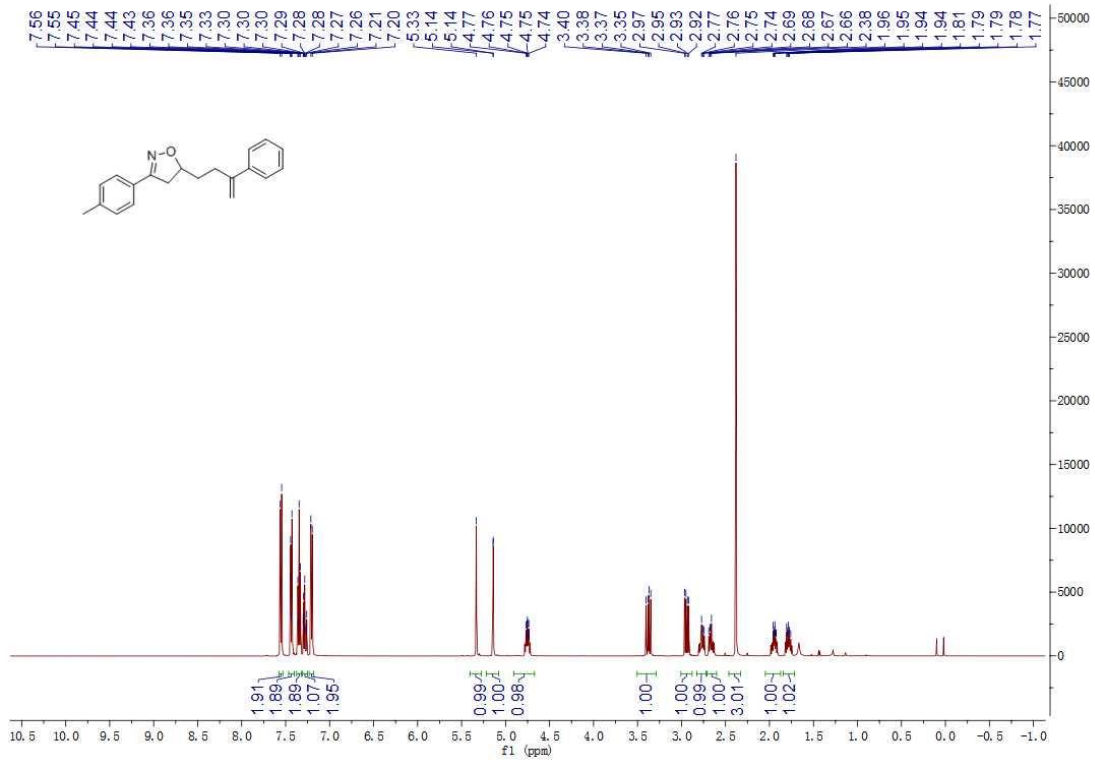

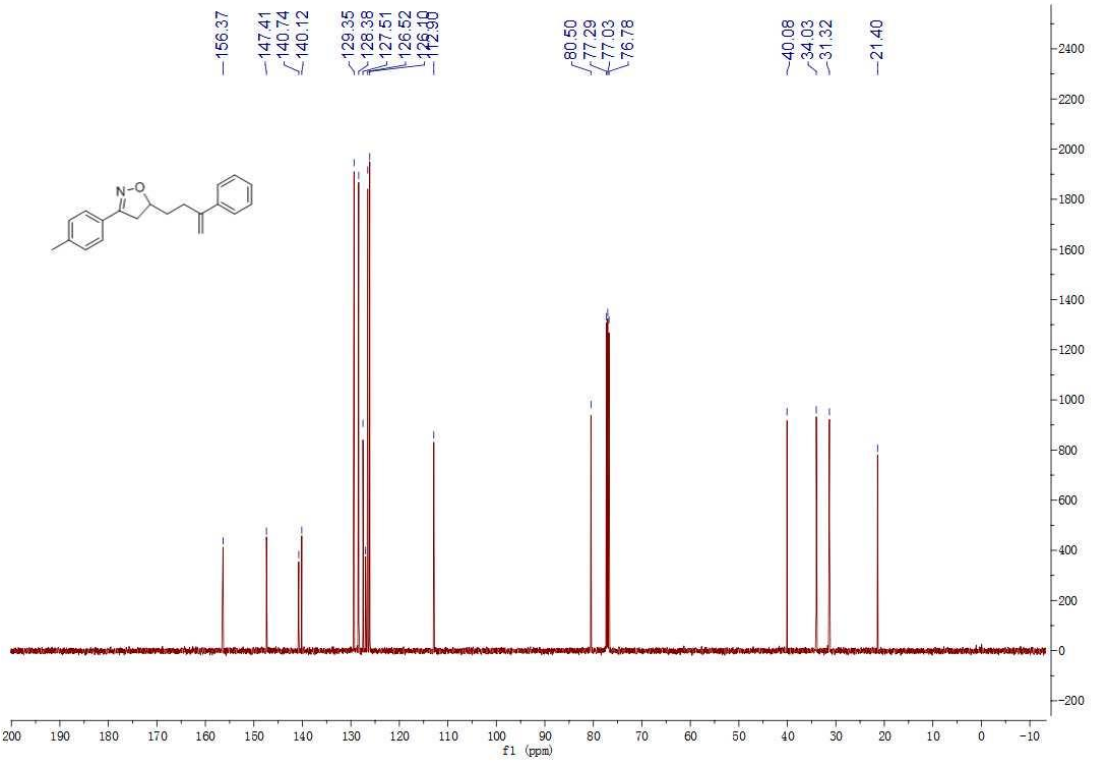

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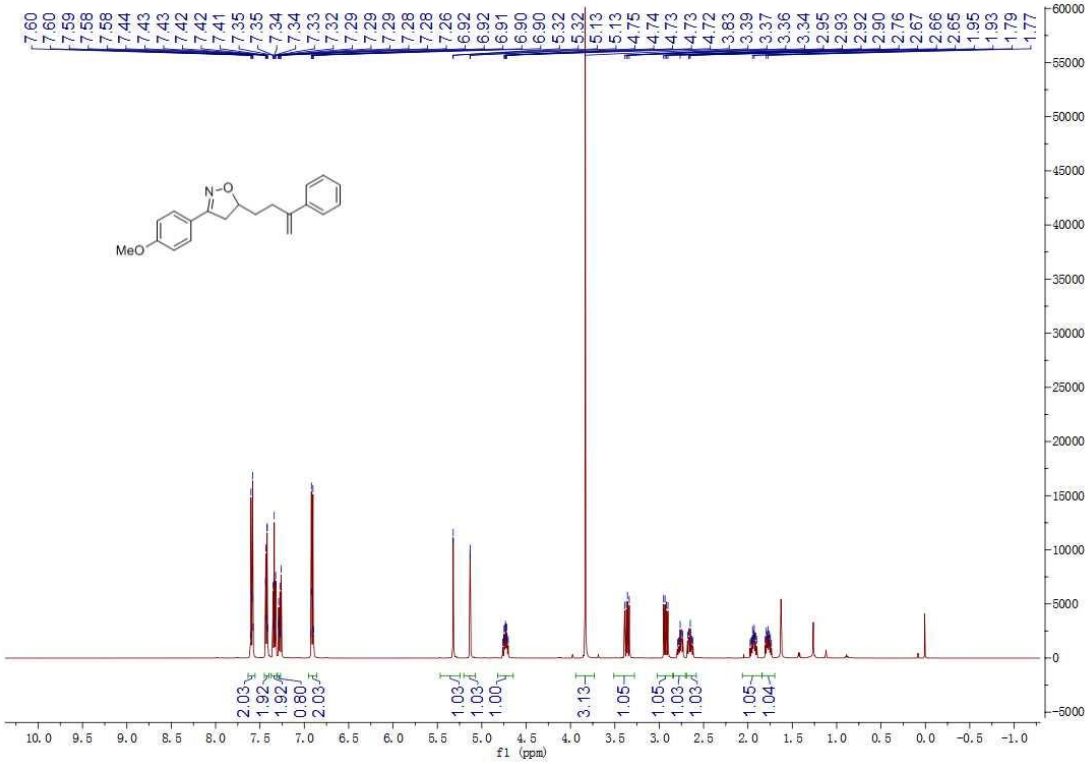

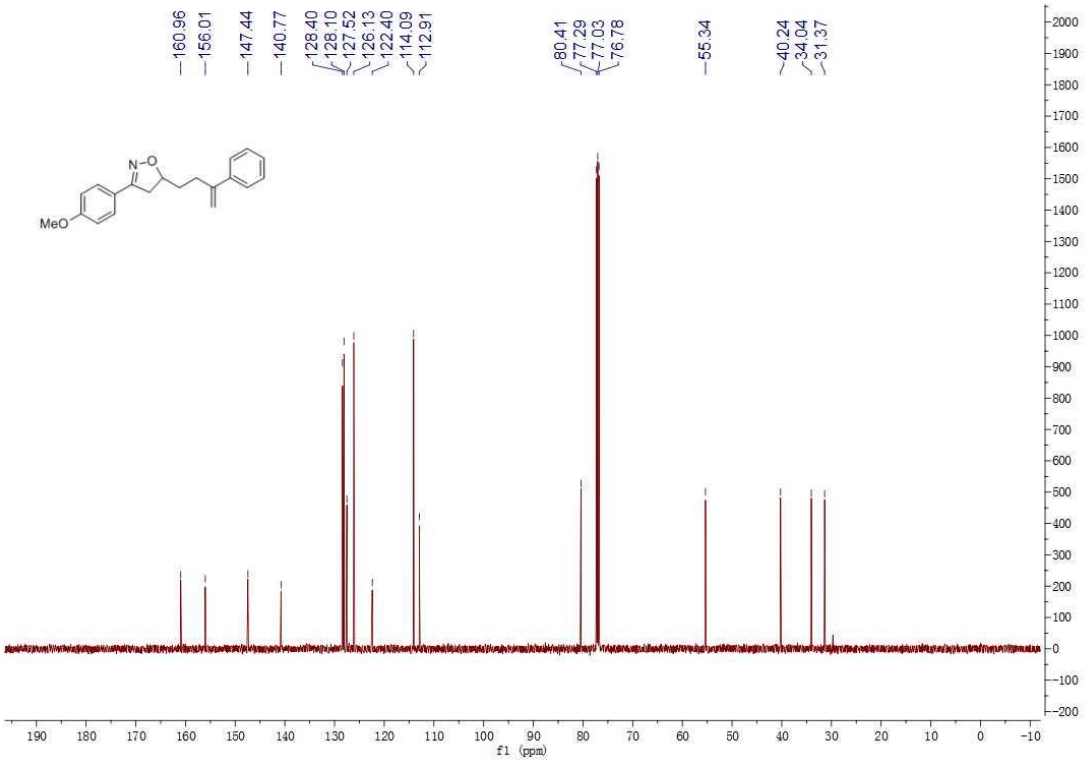

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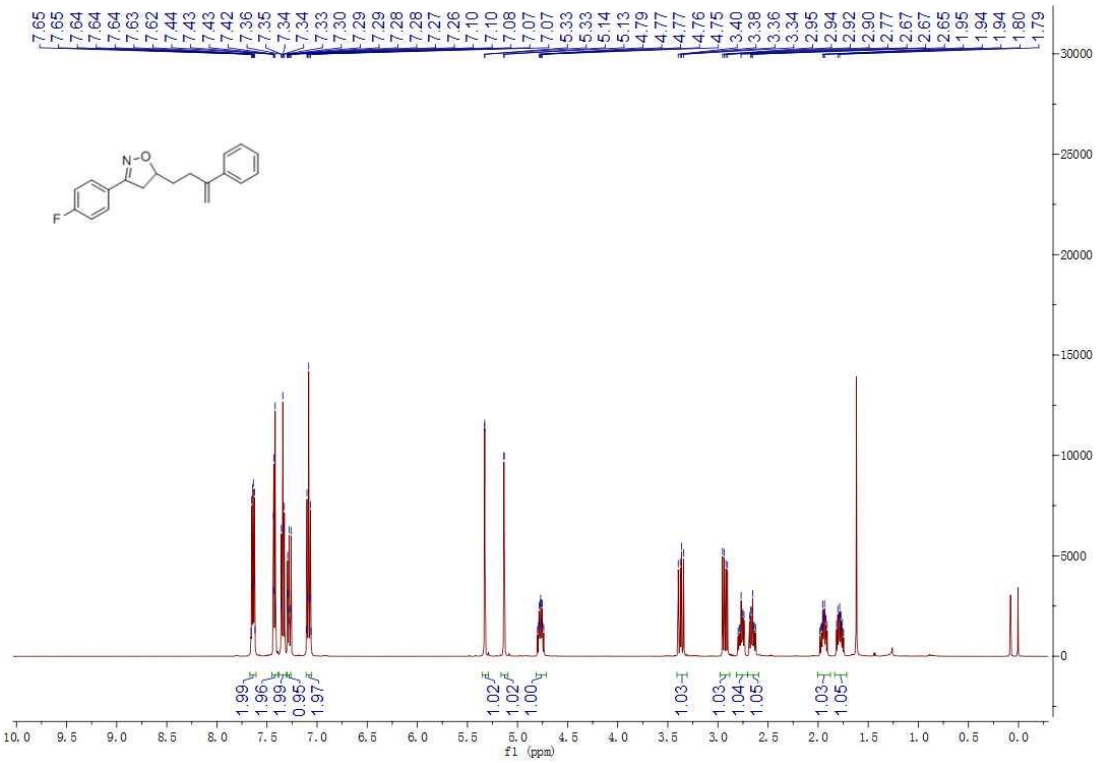

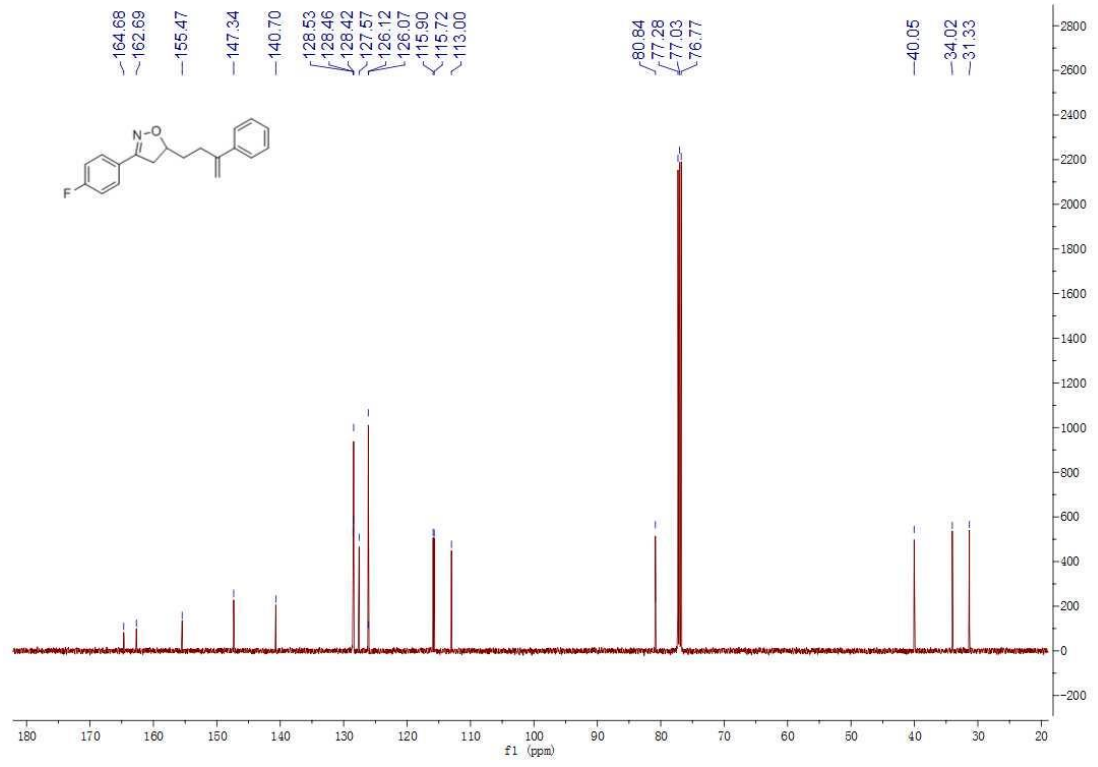

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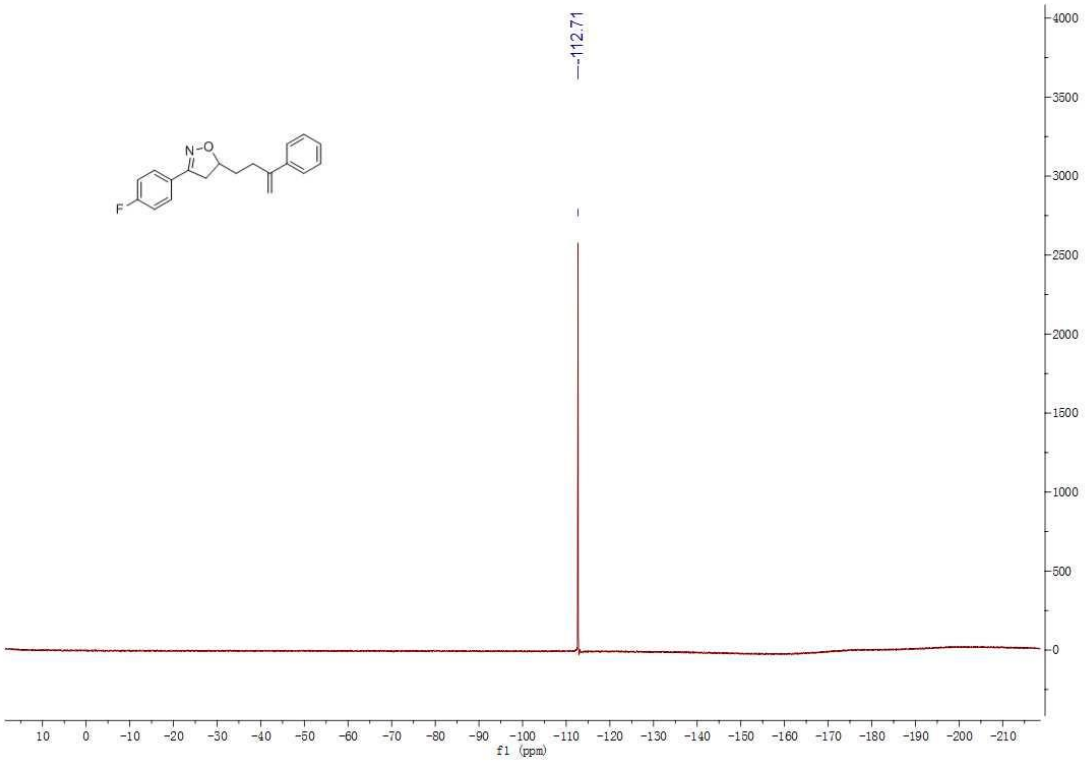
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f1 (ppm)

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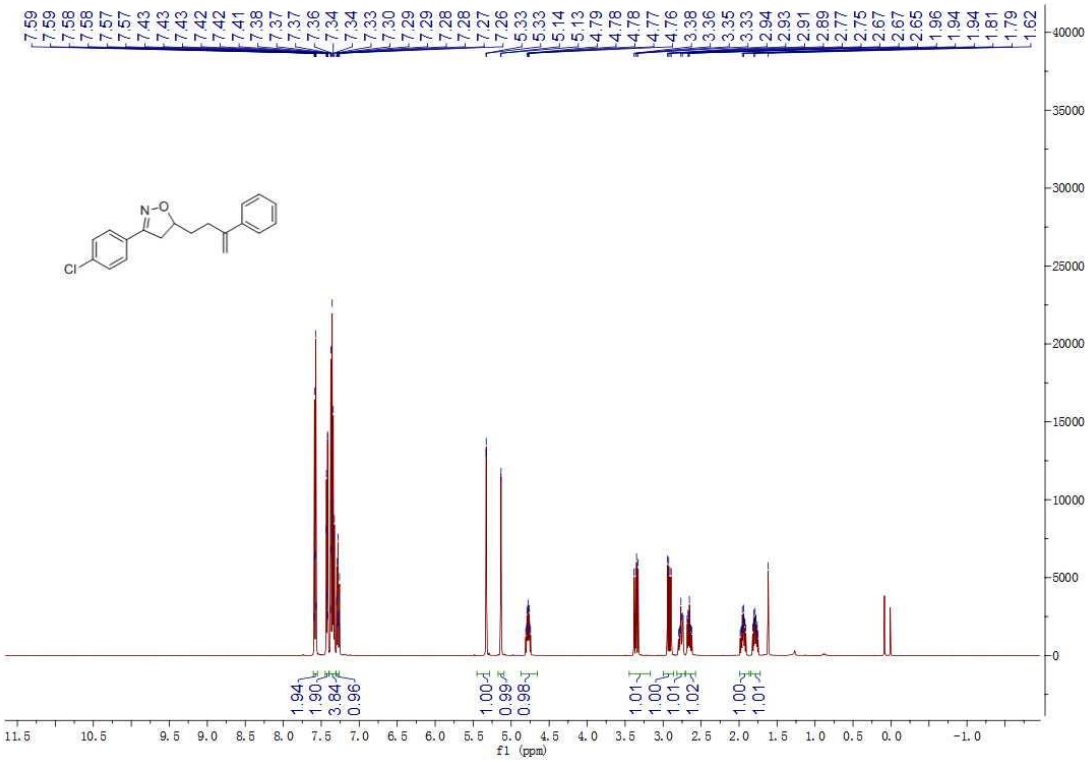

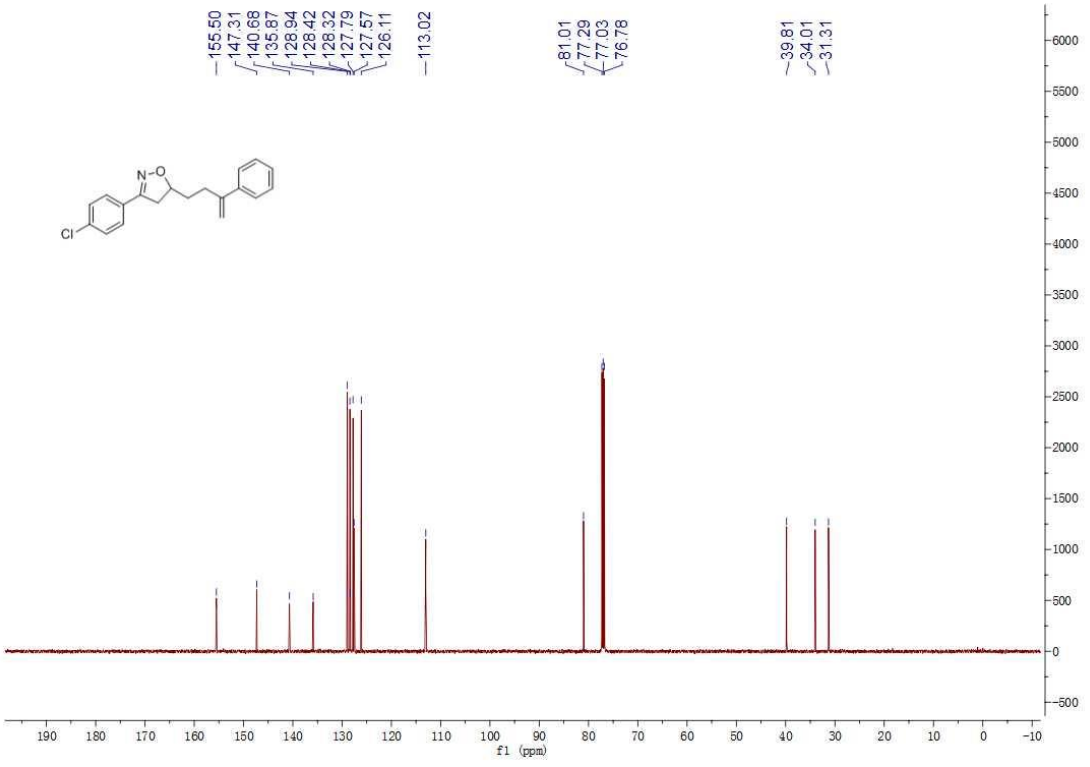

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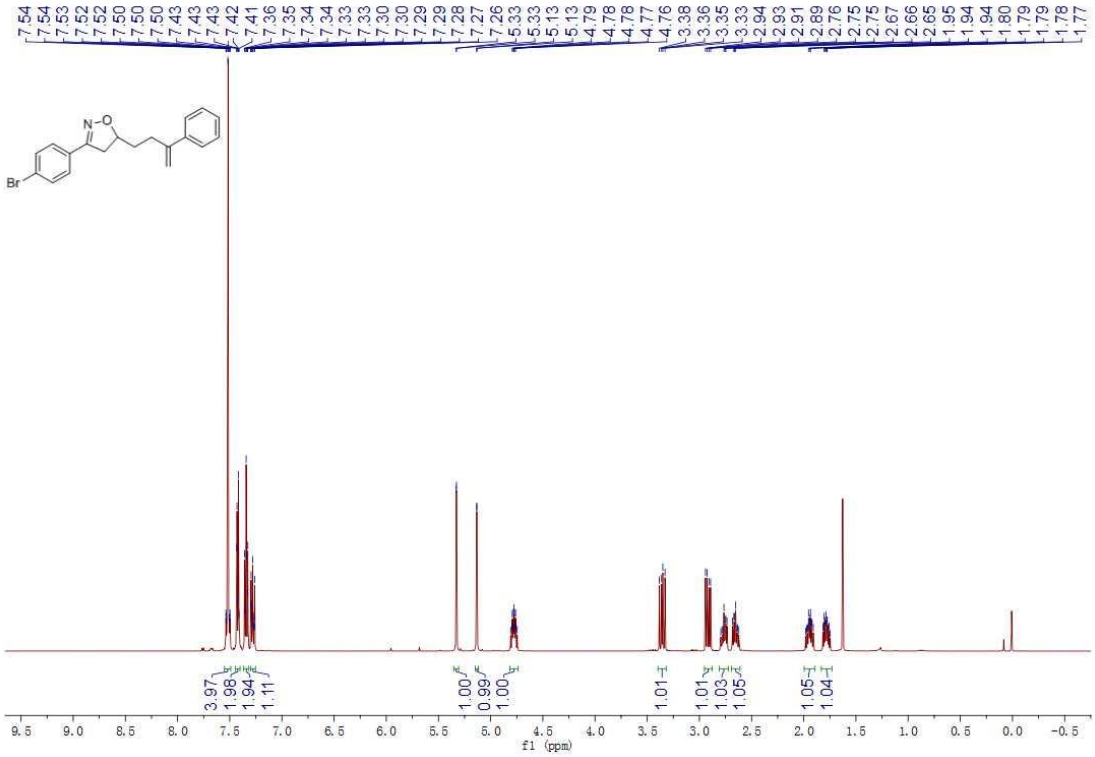

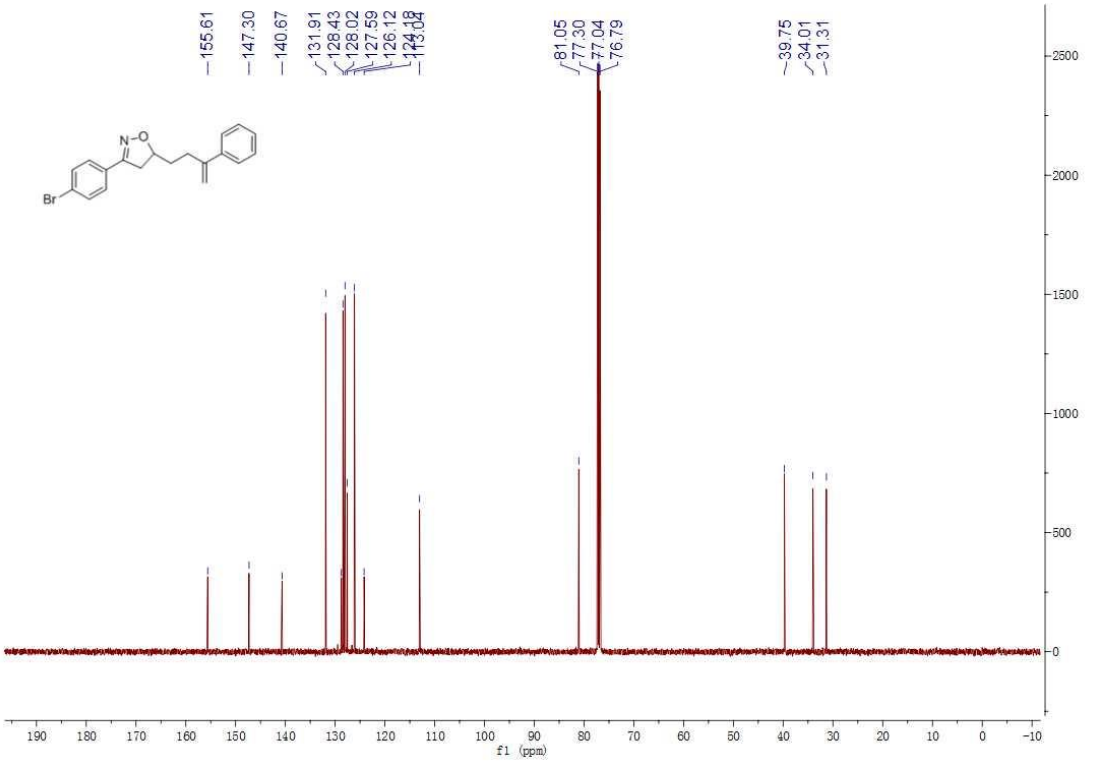

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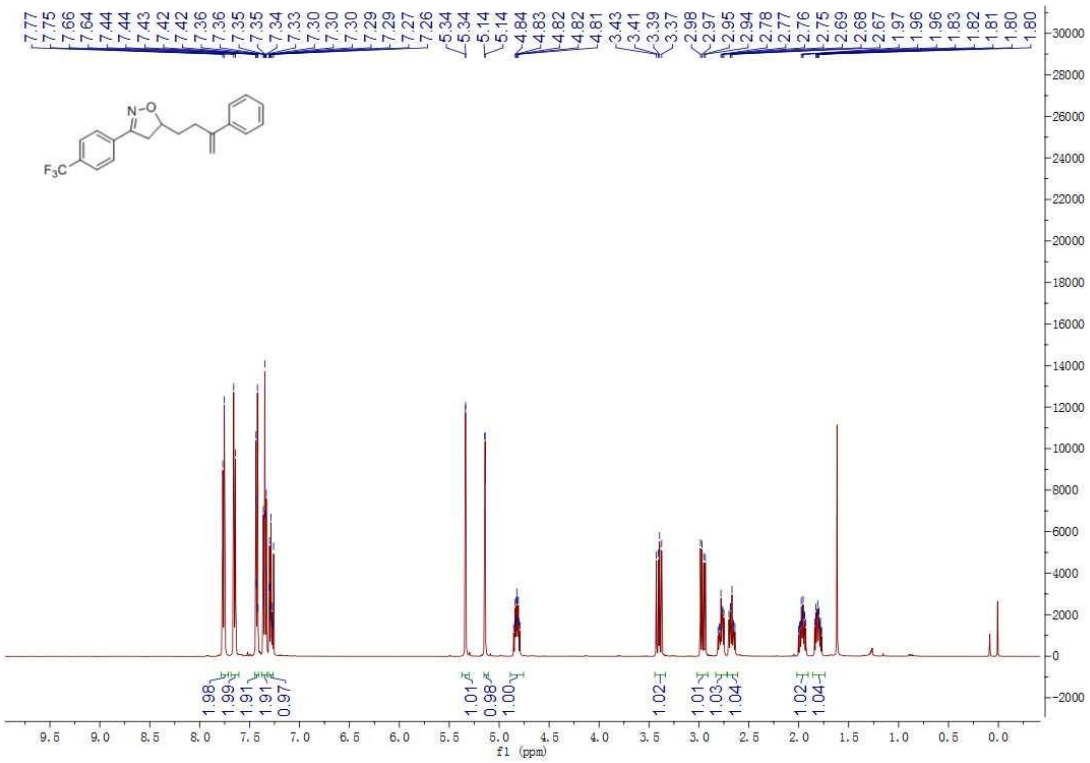

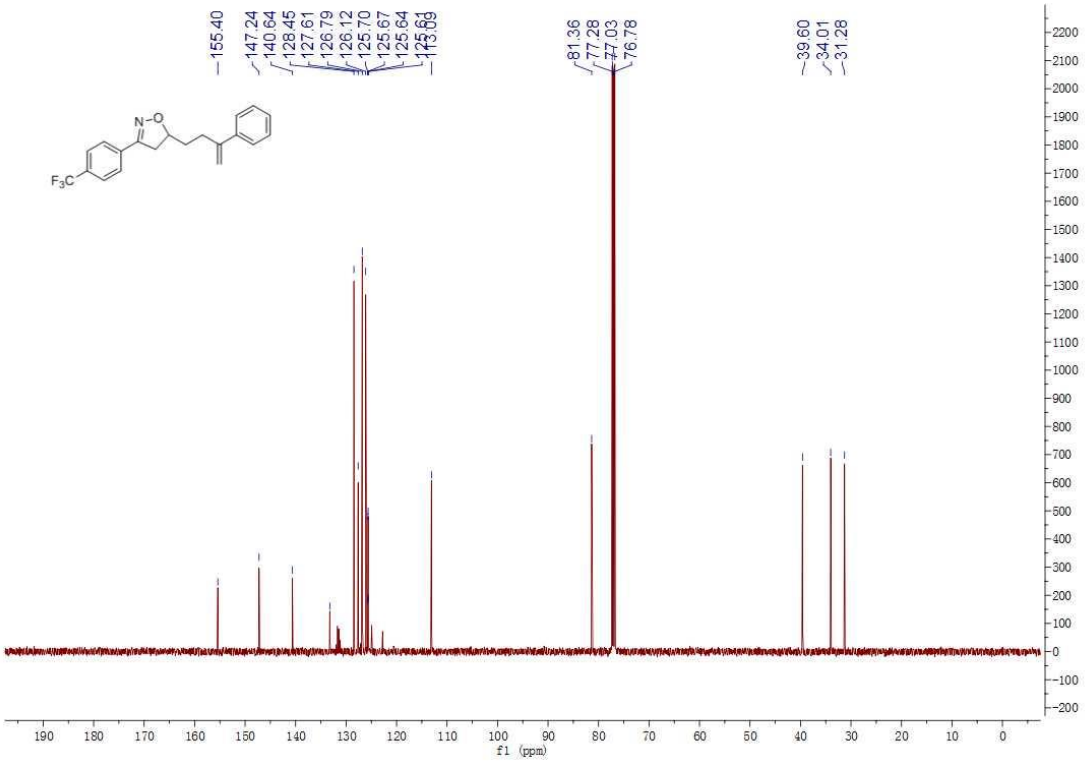

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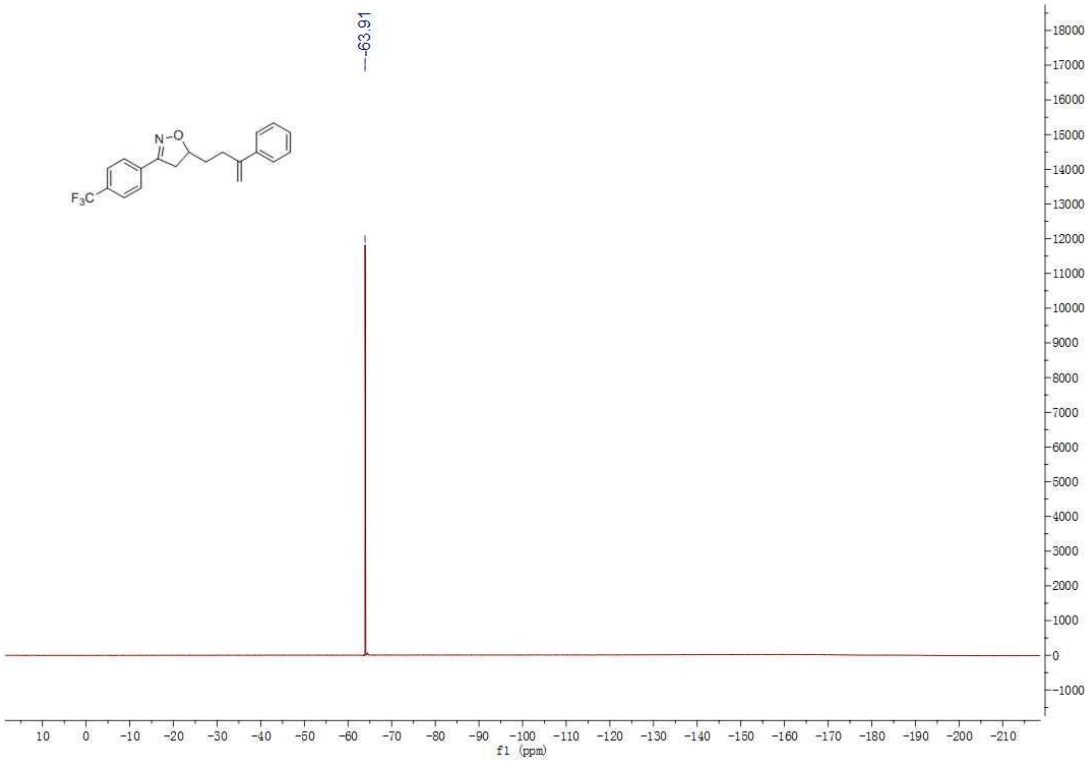
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f1 (ppm)

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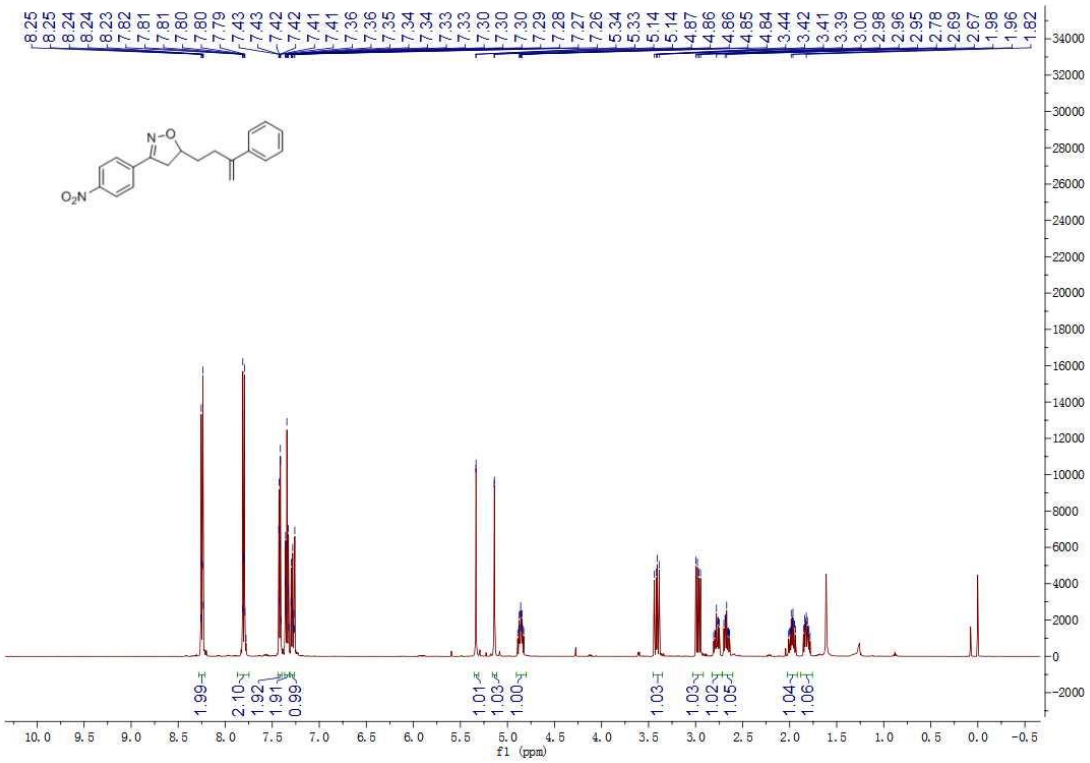

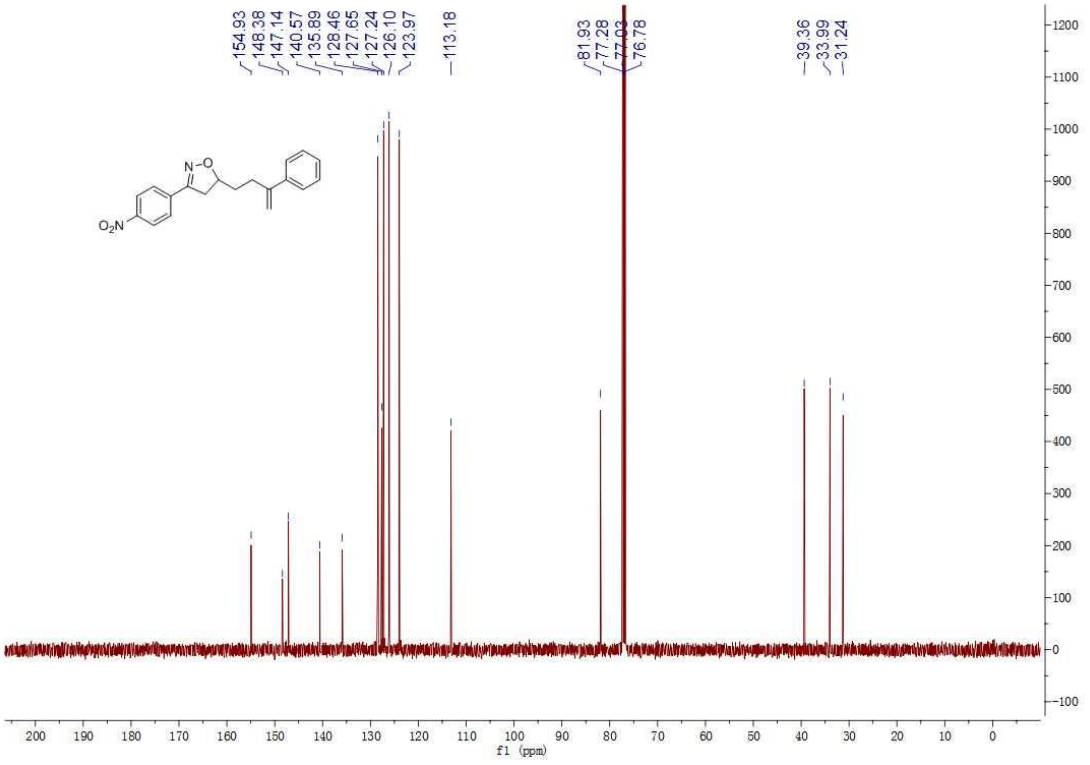

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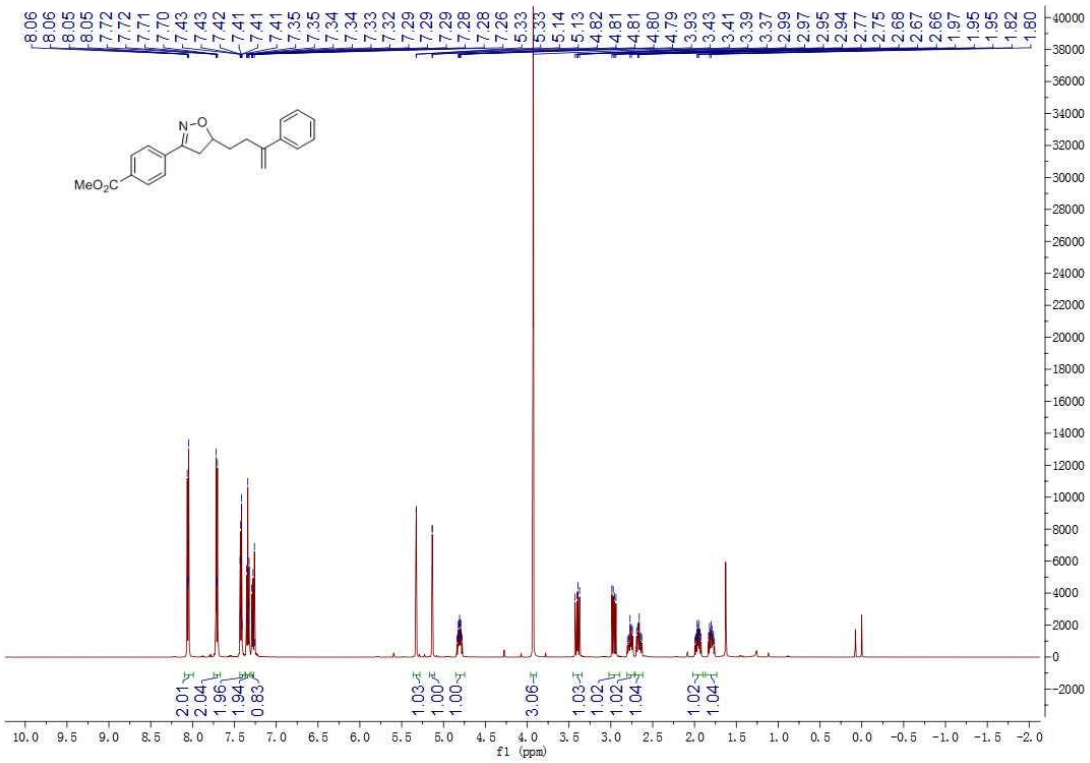

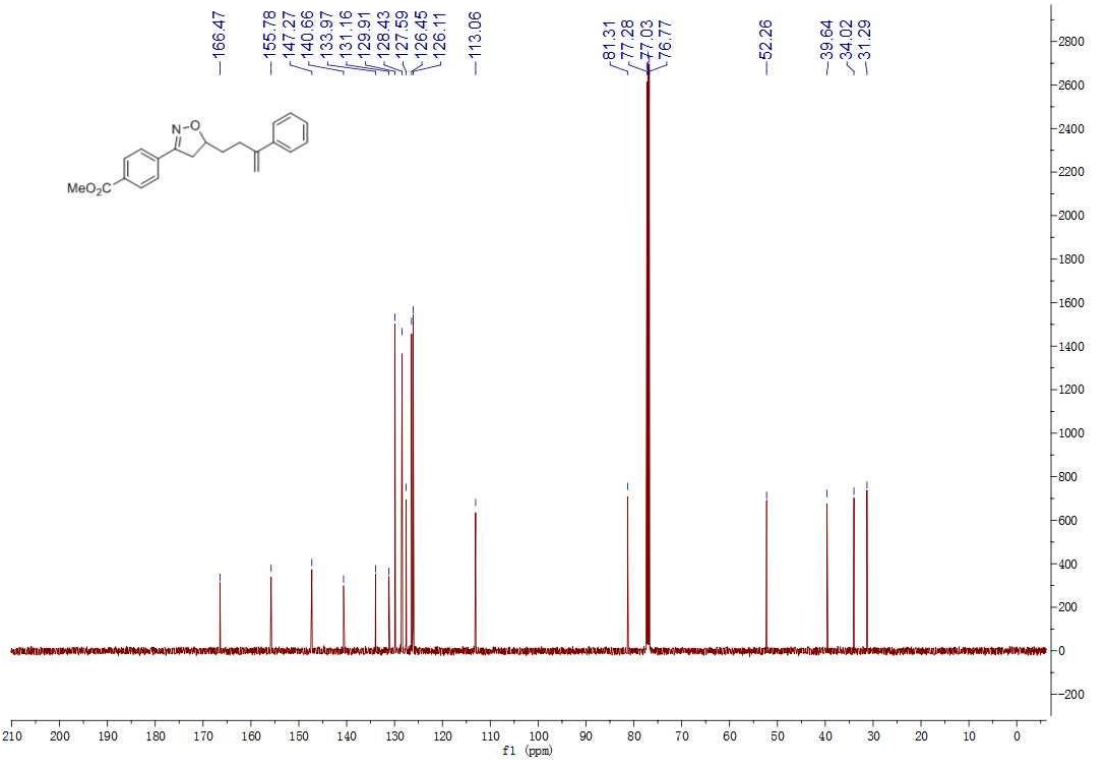

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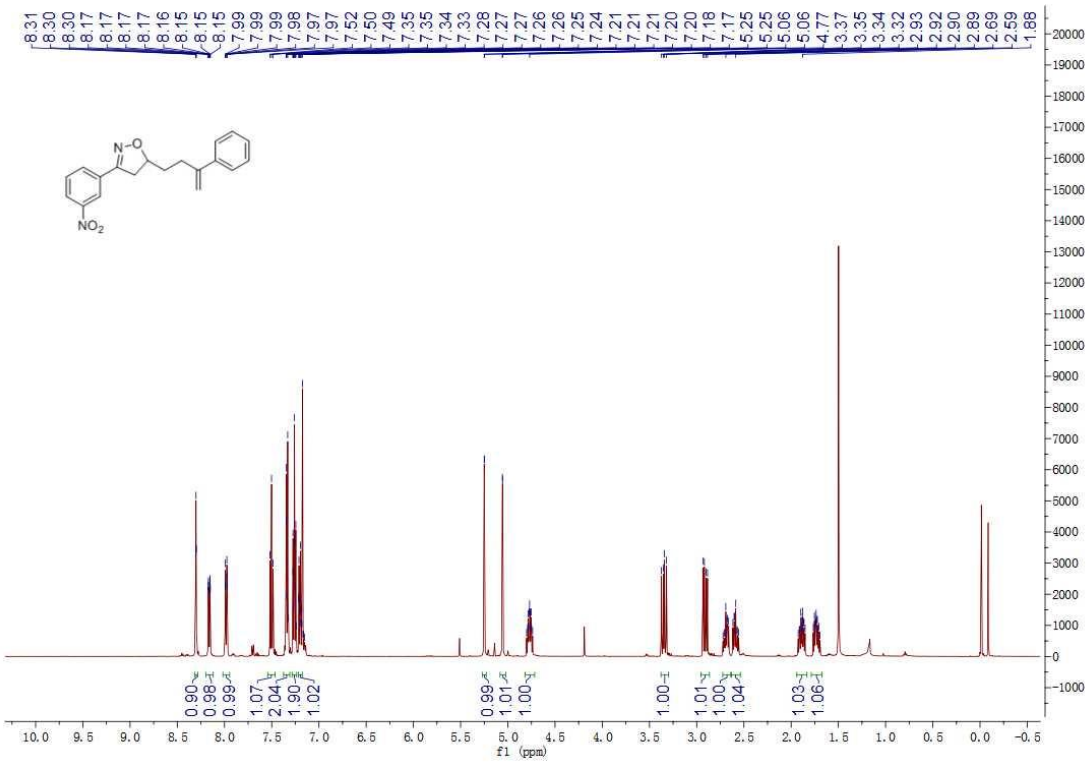

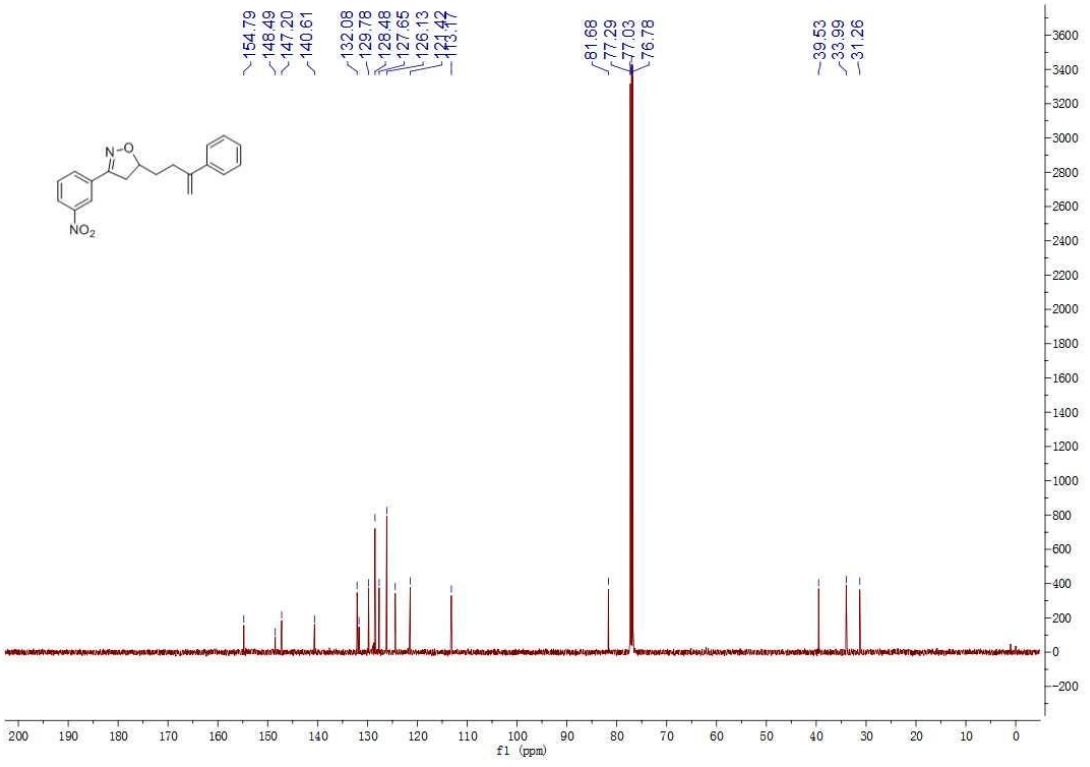

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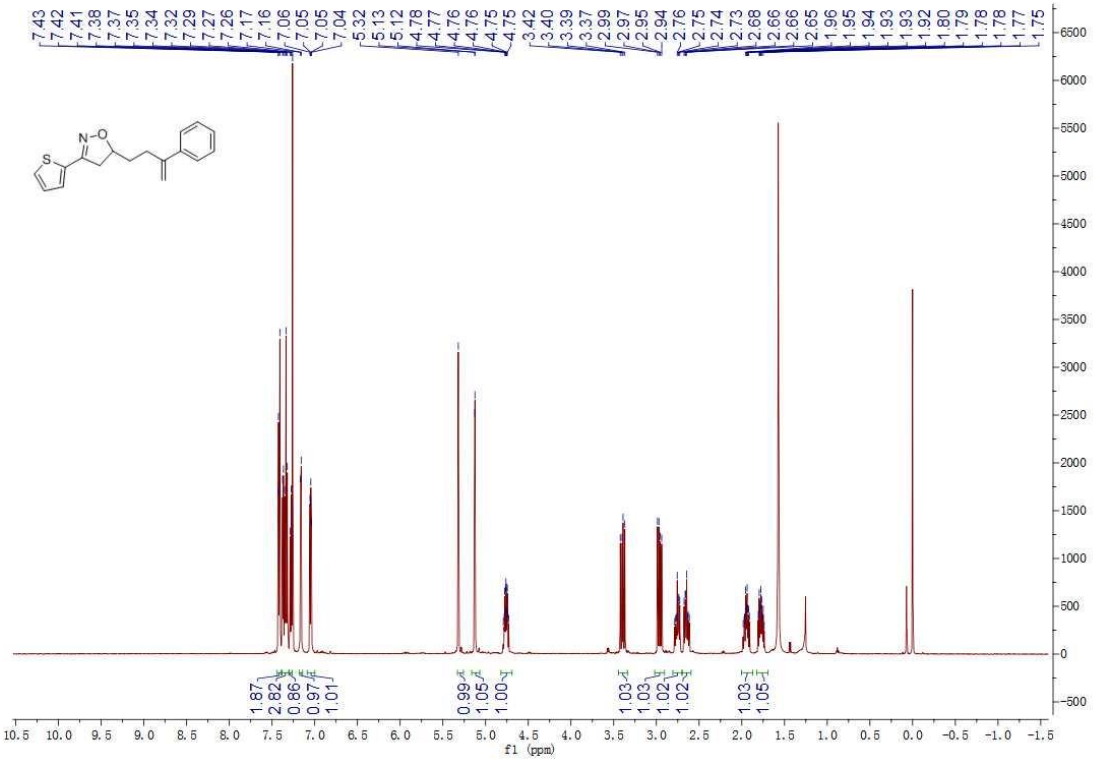

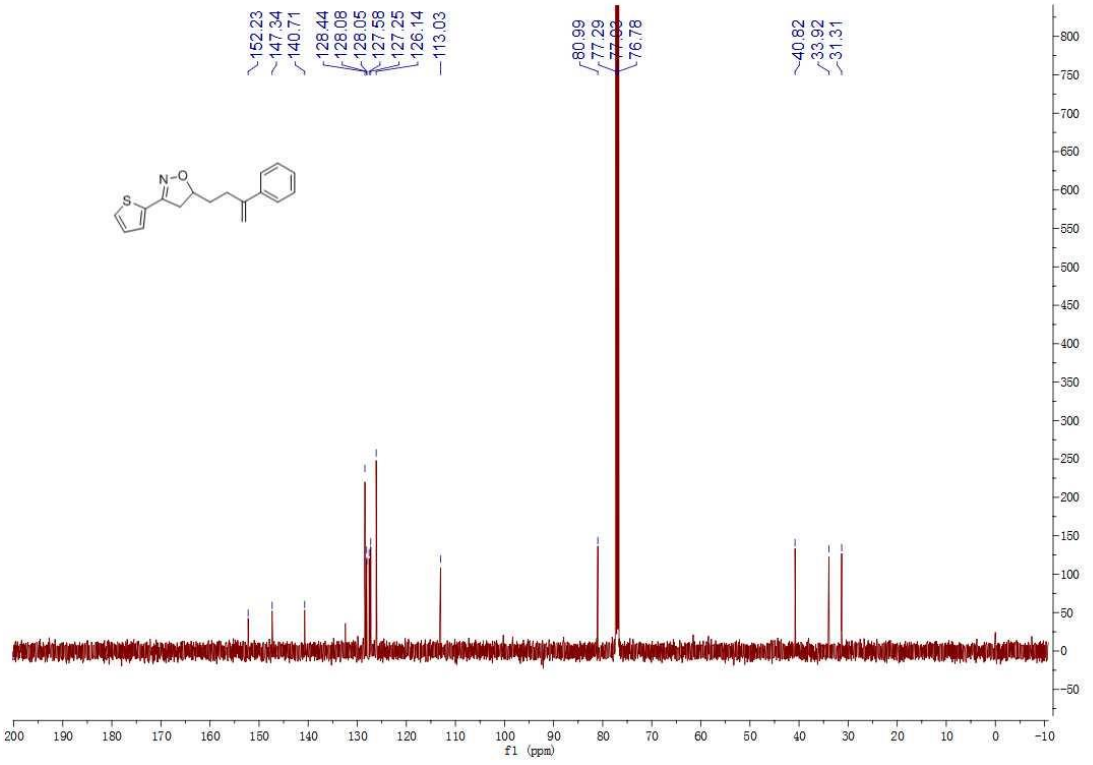

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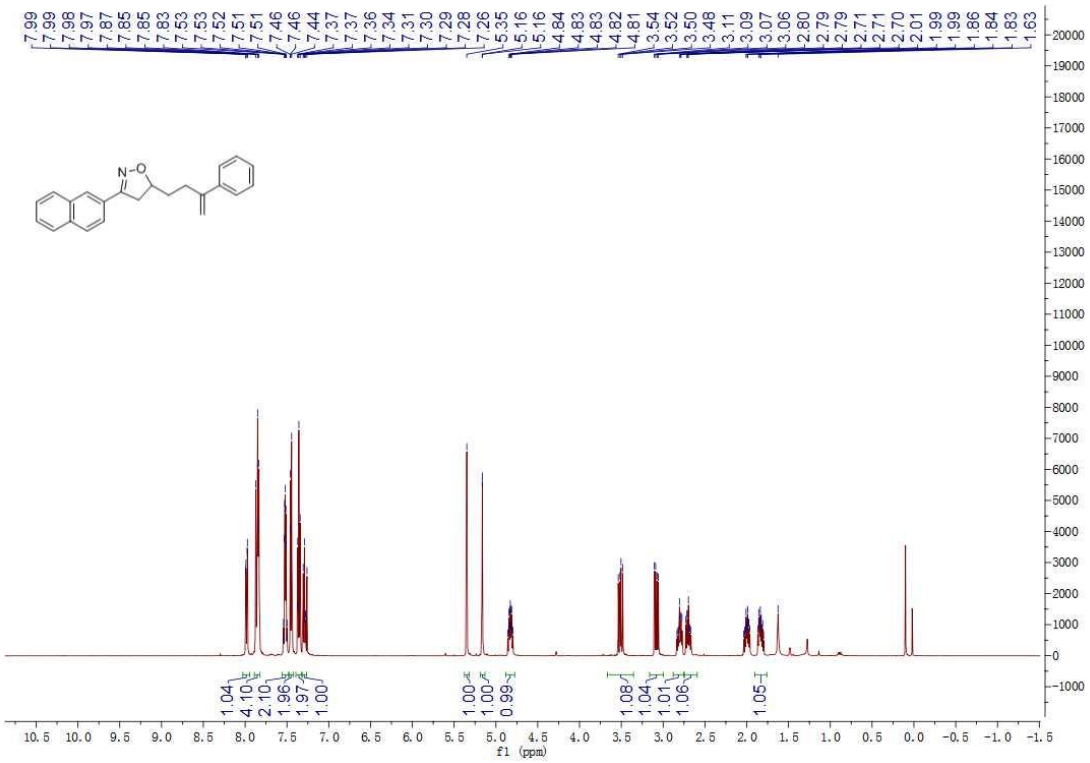

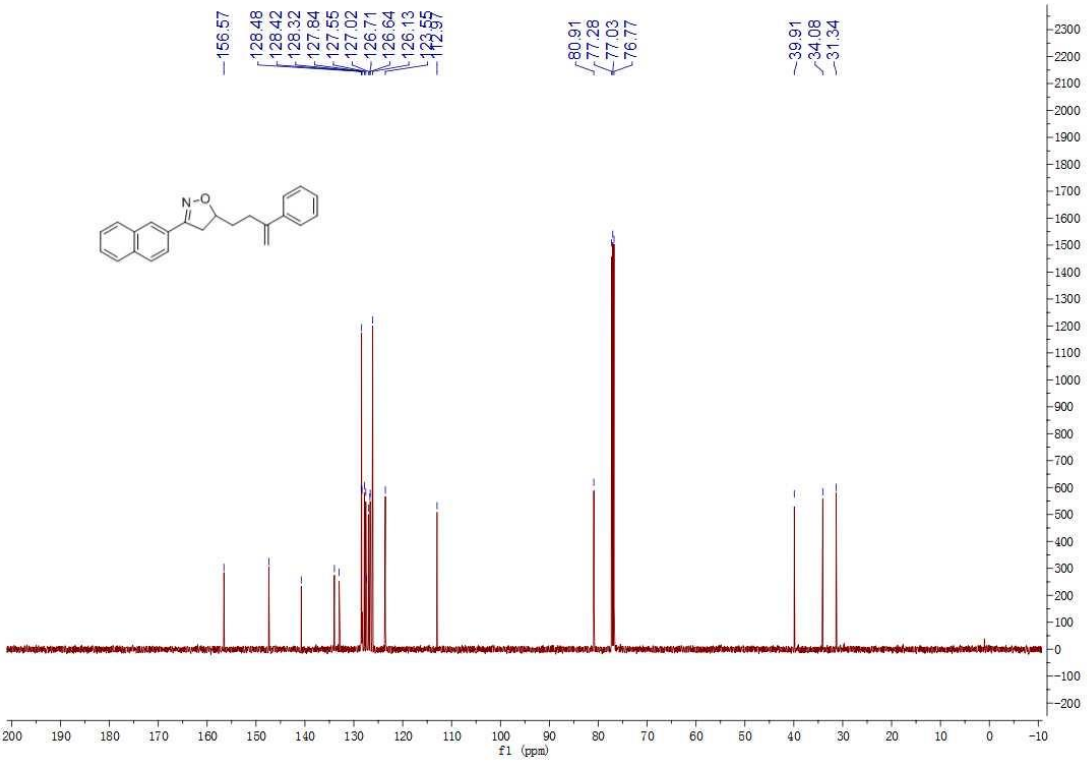

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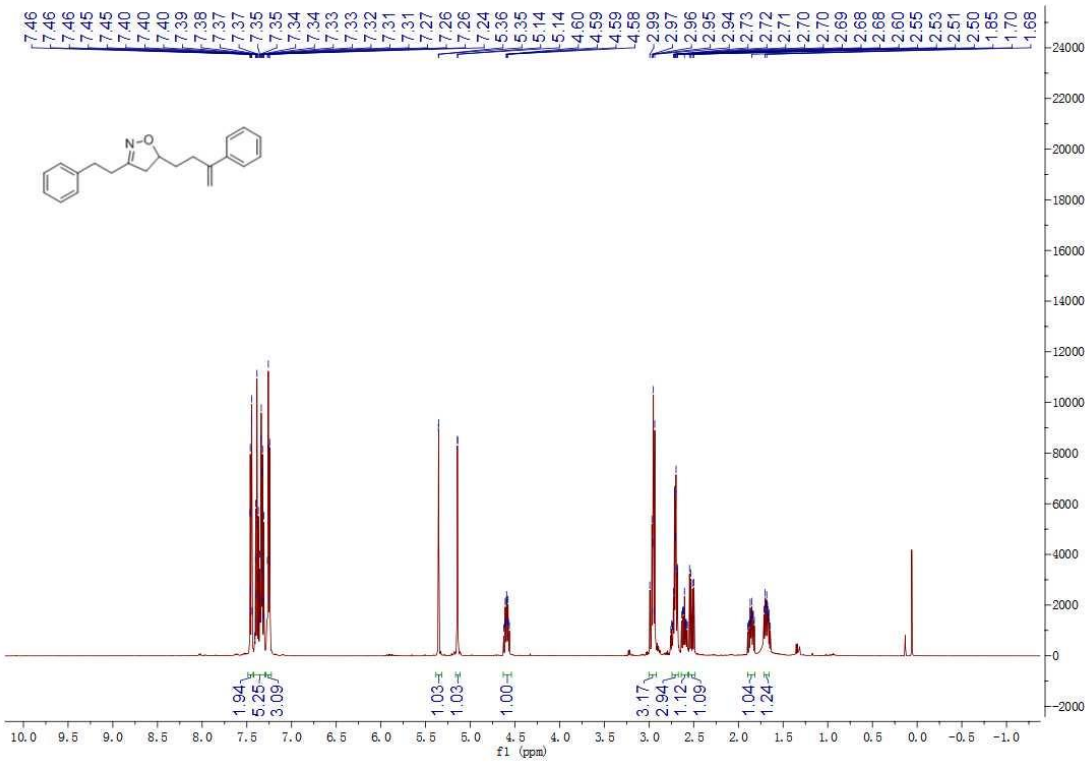

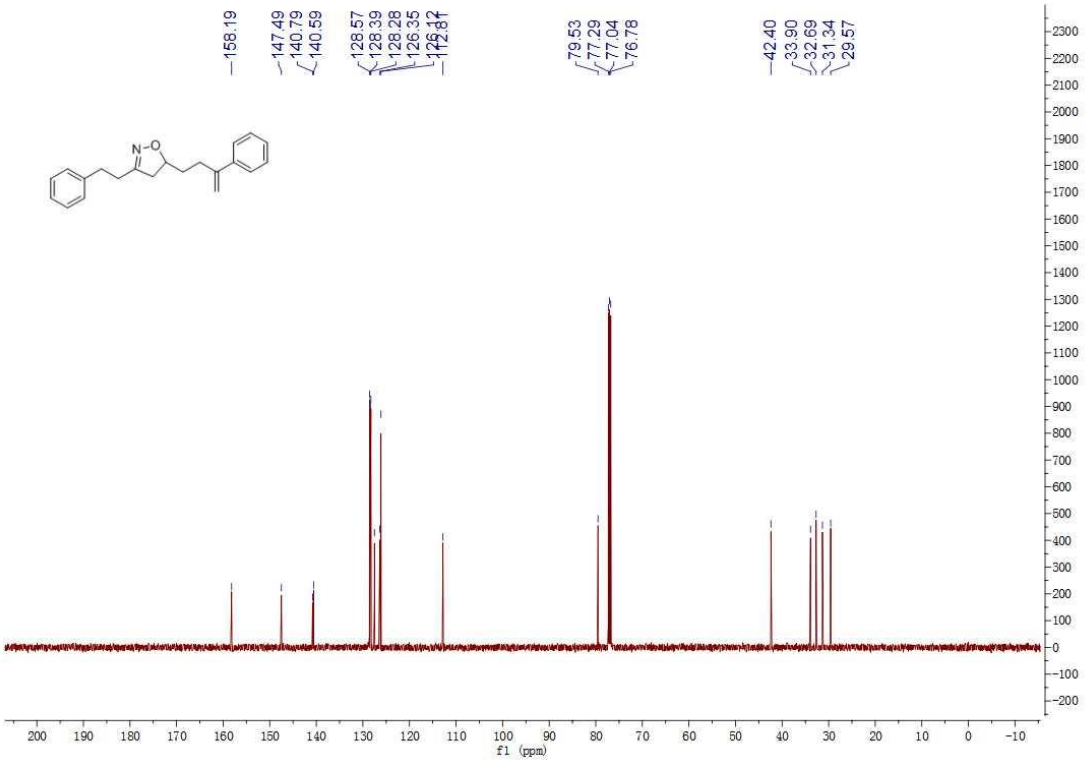

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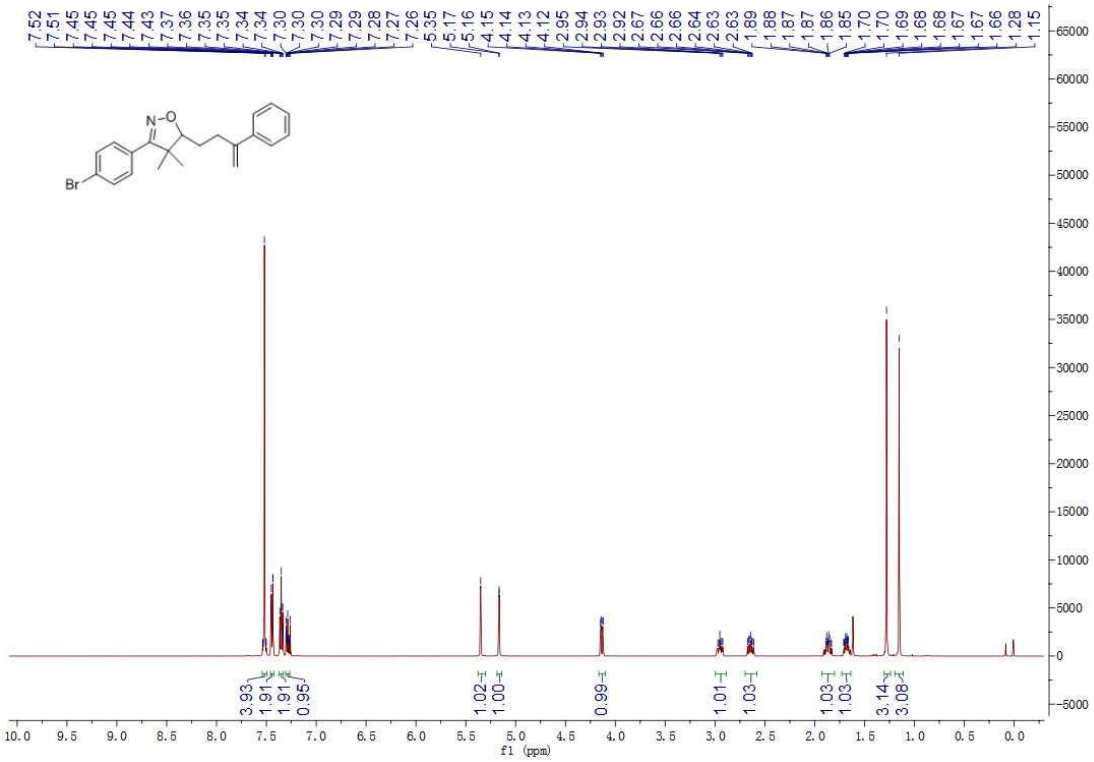
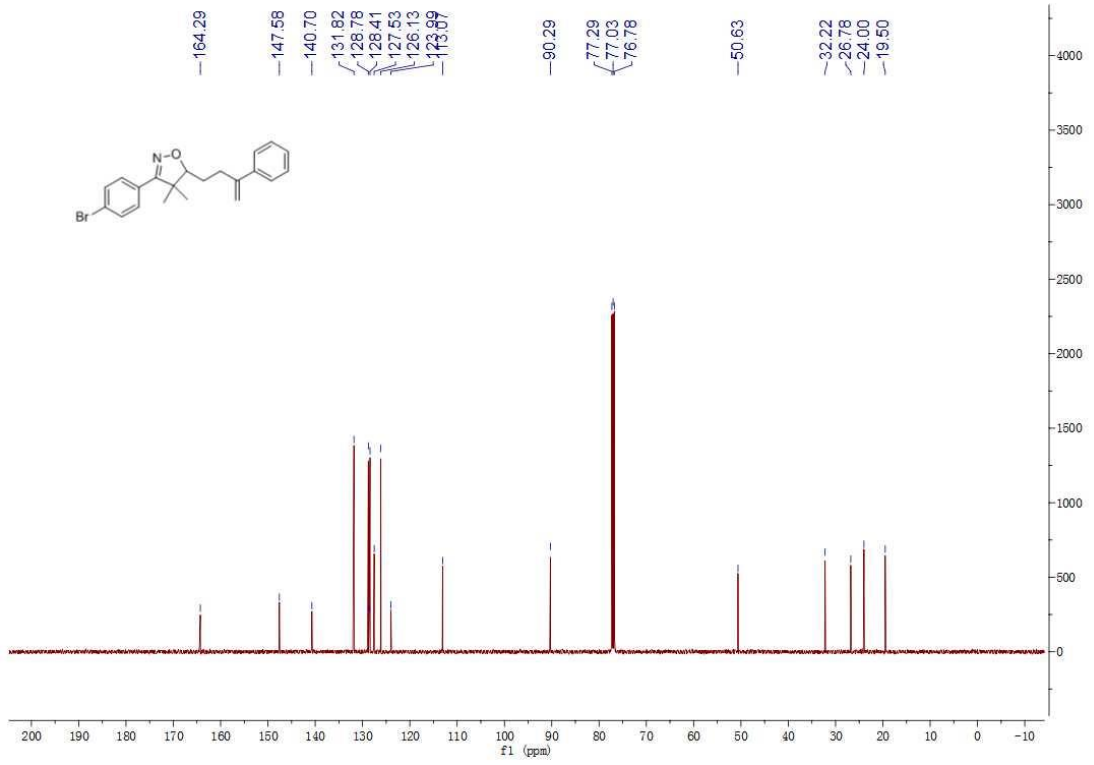
3-(4-bromophenyl)-4,4-dimethyl-5-(3-phenylbut-3-en-1-yl)-4,5-dihydroisoxazole (3n)





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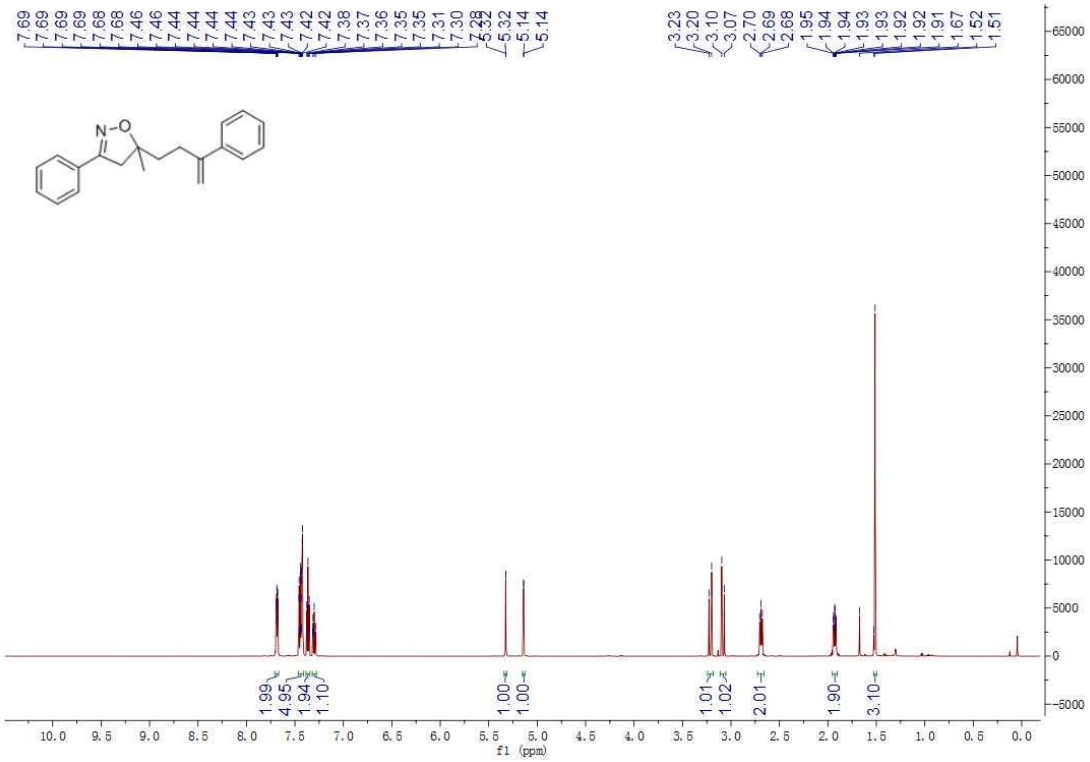
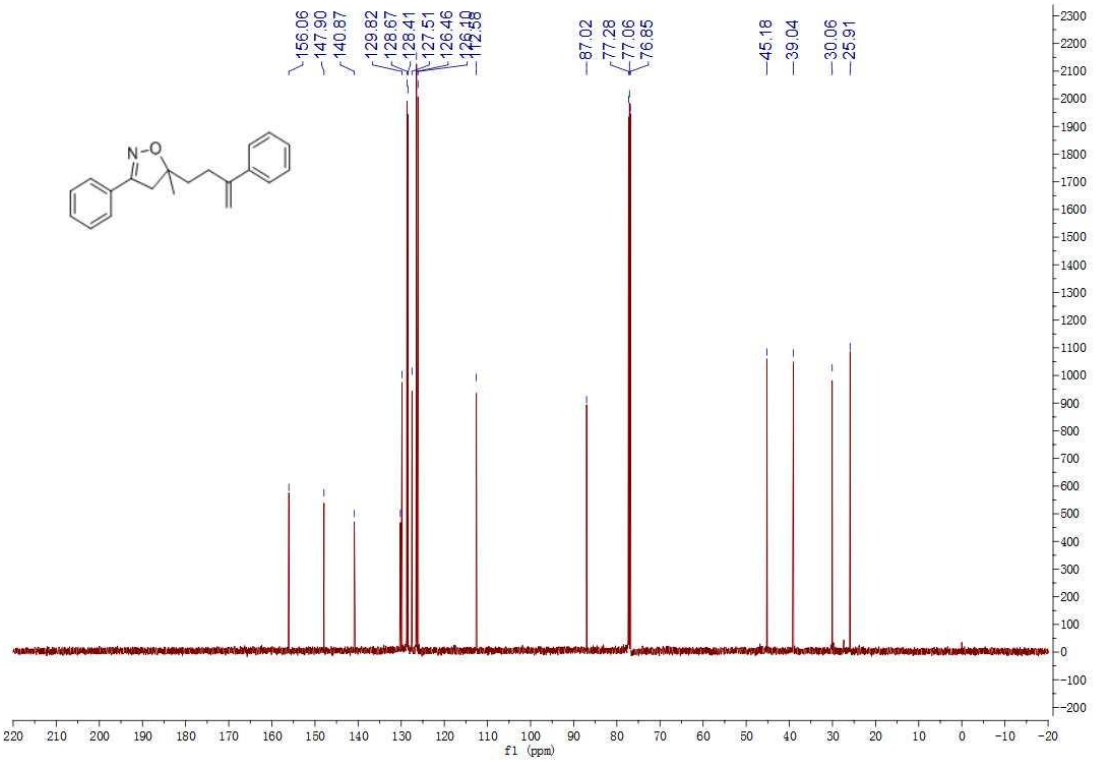
5-methyl-3-phenyl-5-(3-phenylbut-3-en-1-yl)-4,5-dihydroisoxazole(3o)





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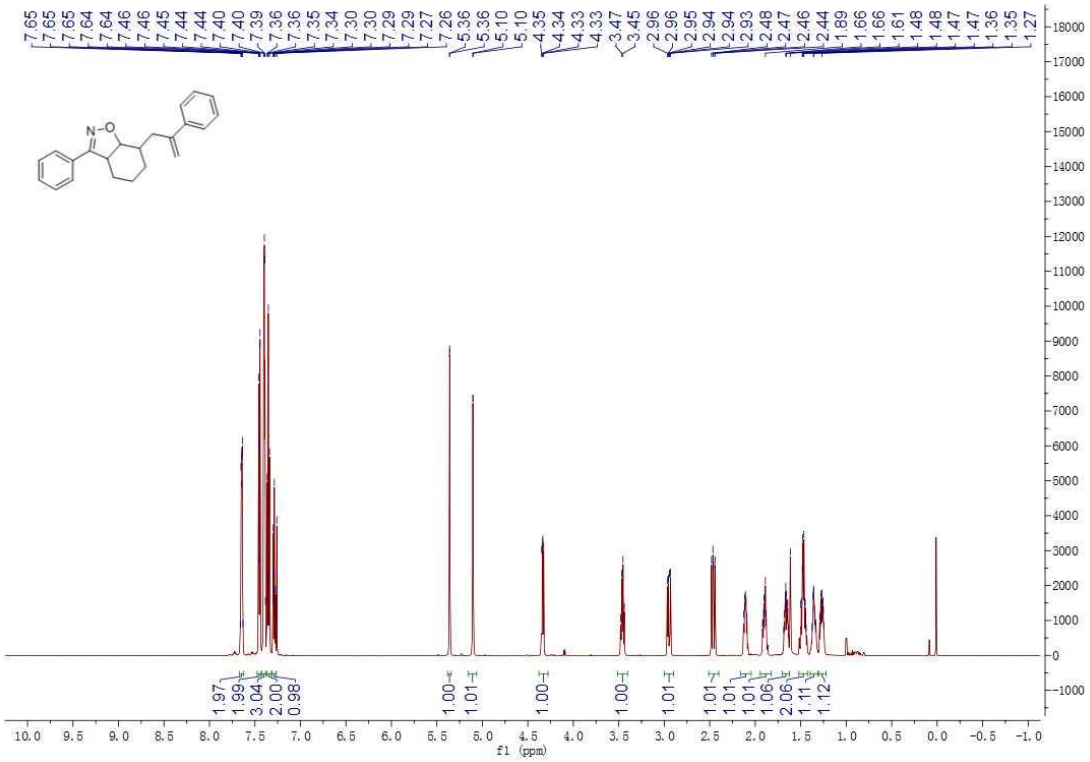
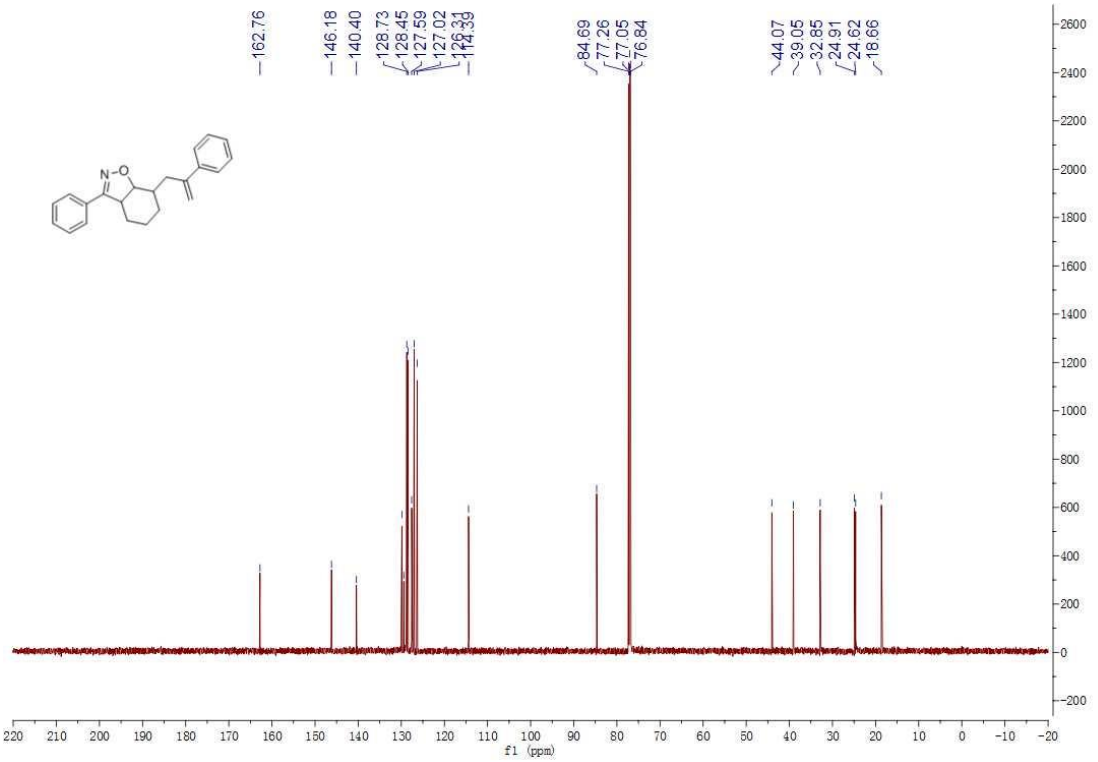
3-phenyl-7-(2-phenylallyl)-3a,4,5,6,7,7a-hexahydrobenzo[d]isoxazole (3p)

major isomer





minor isomer

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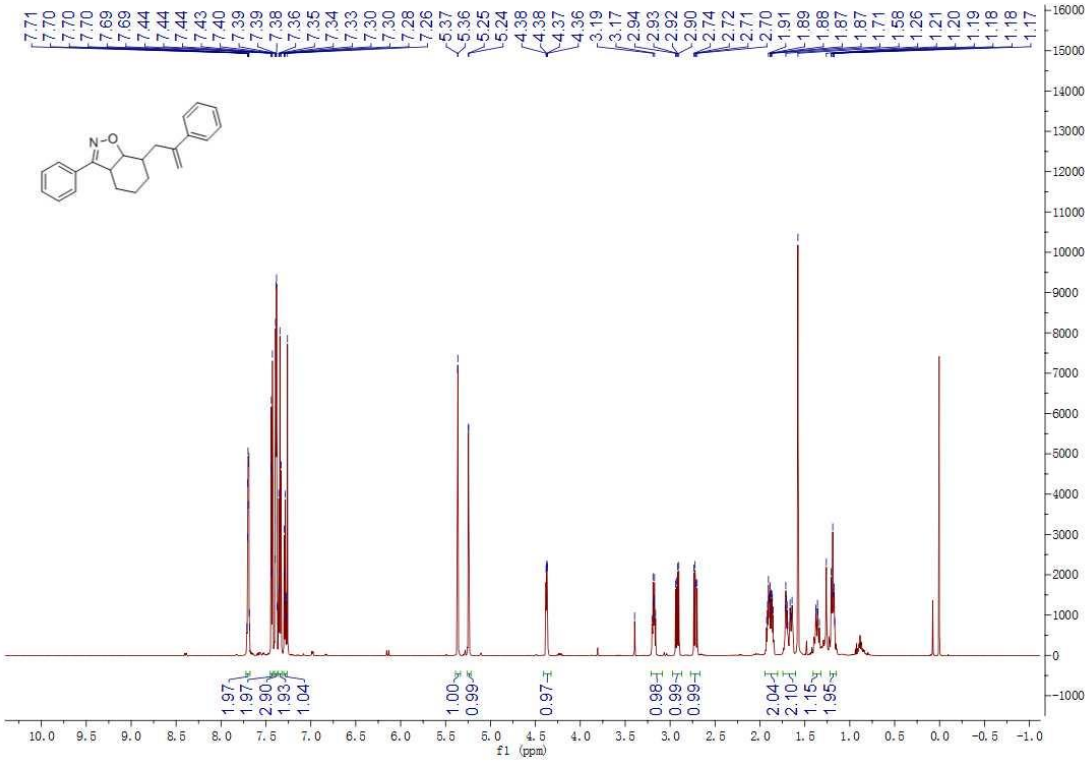
7.71
7.70
7.70
7.70
7.69
7.69
7.44
7.44
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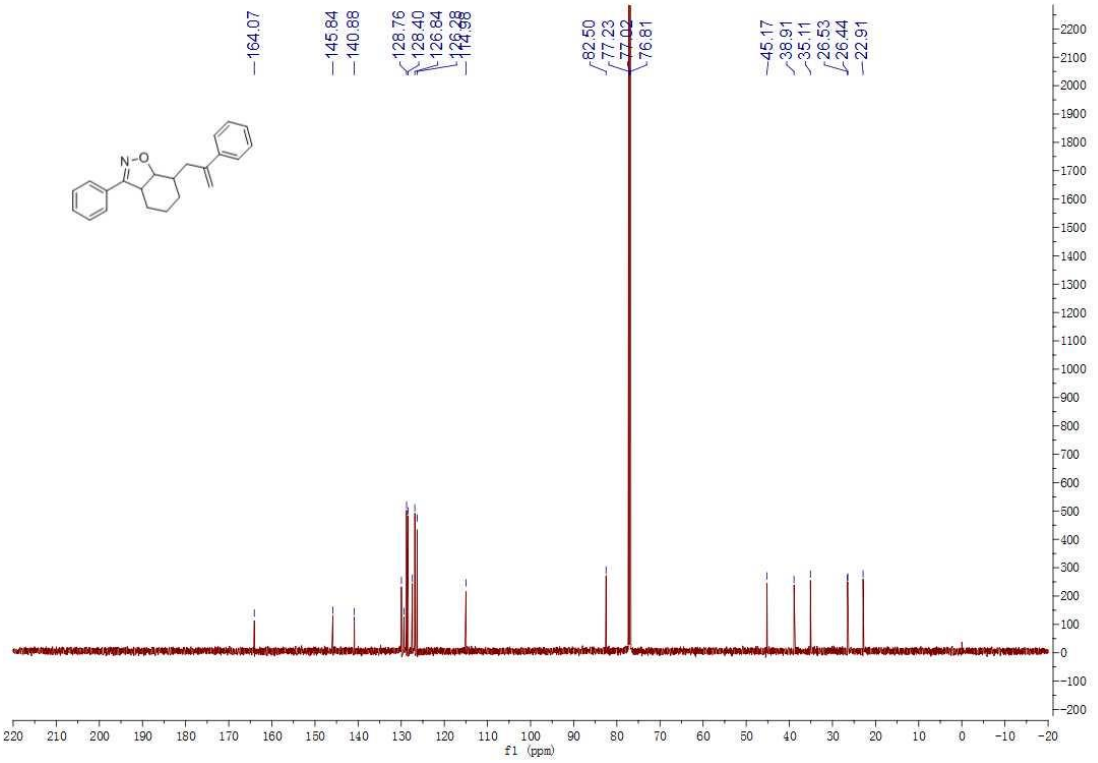
7.43
7.40
7.39
7.39
7.38
7.36
7.35
7.34
7.33
7.30
7.30
7.28
7.26
5.37
5.36
5.25
5.24
4.38
4.38
4.37
4.36
3.19
3.17
2.94
2.93
2.92
2.90
2.74
2.72
2.71
2.70
1.91
1.89
1.88
1.87
1.87
1.71
1.58
1.26
1.21
1.20
1.19
1.18
1.18
1.17
1.97
1.97
2.90
1.93
1.04
1.00
0.99
0.97
0.98
0.99
0.99
2.04
2.10
1.15
1.95
f1 (ppm)


164.07
145.84
140.88
128.76
128.40
126.84
82.50
77.23
77.02
76.81
45.17
38.91
35.11
26.53
26.44
22.91
f1 (ppm)

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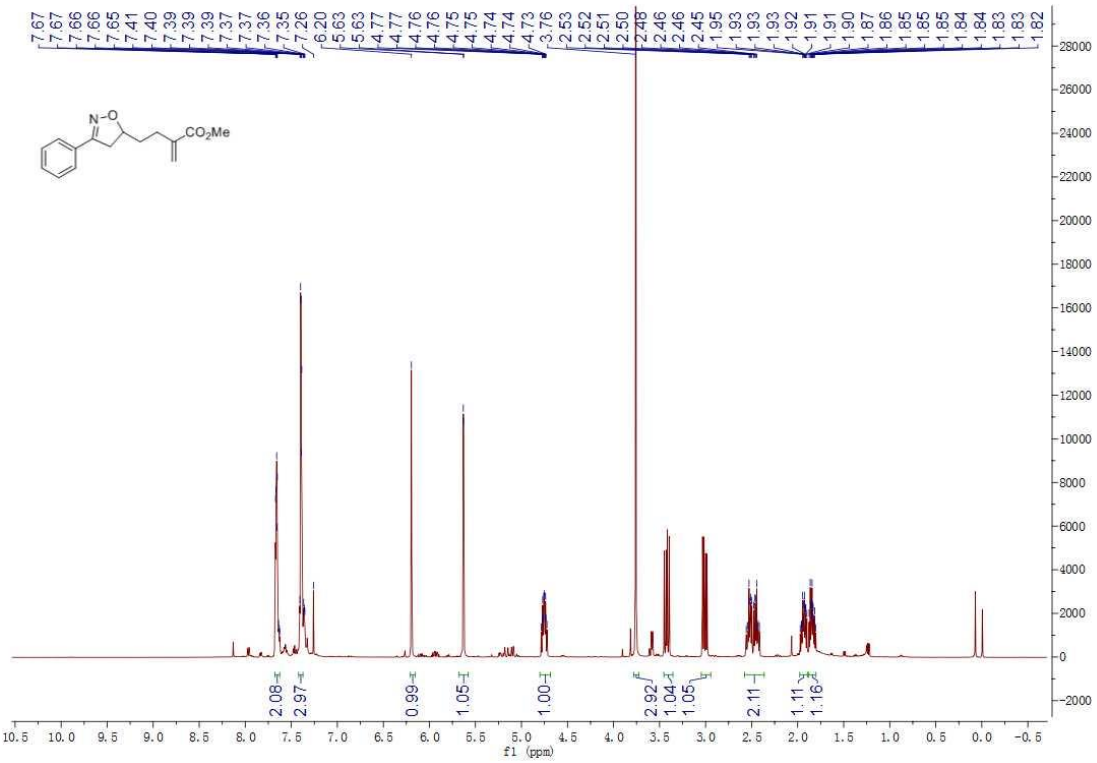
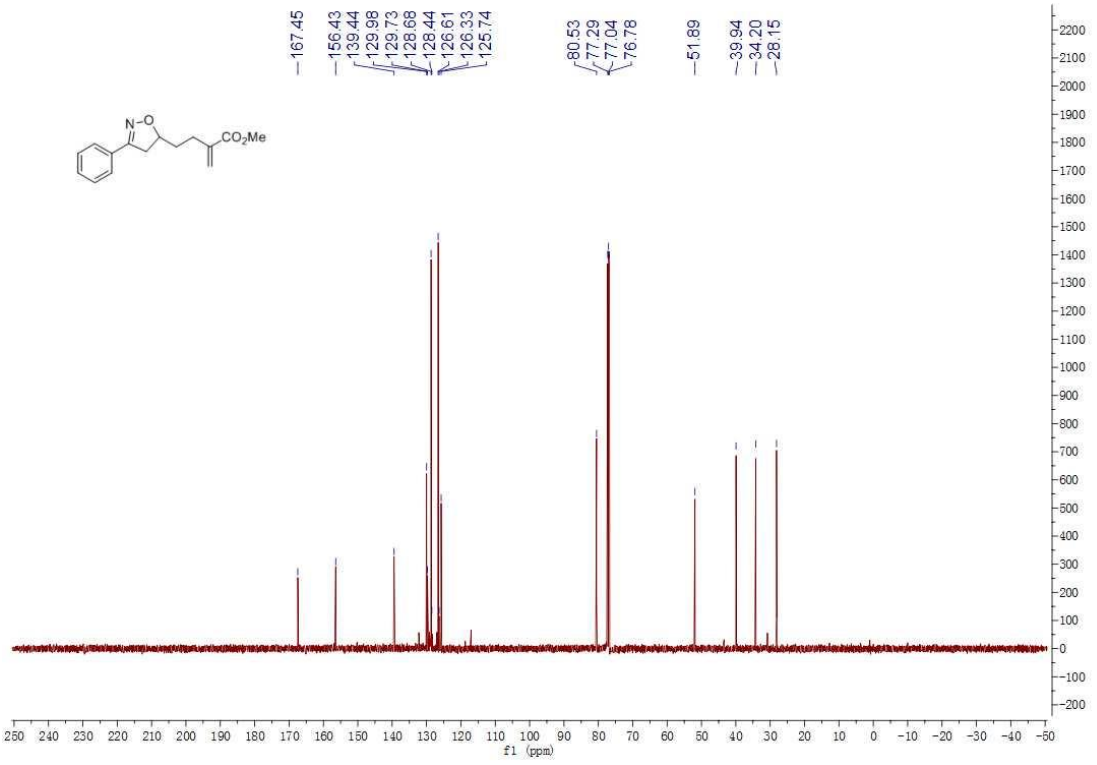
methyl 2-methylene-4-(3-phenyl-4,5-dihydroisoxazol-5-yl)butanoate (4a)





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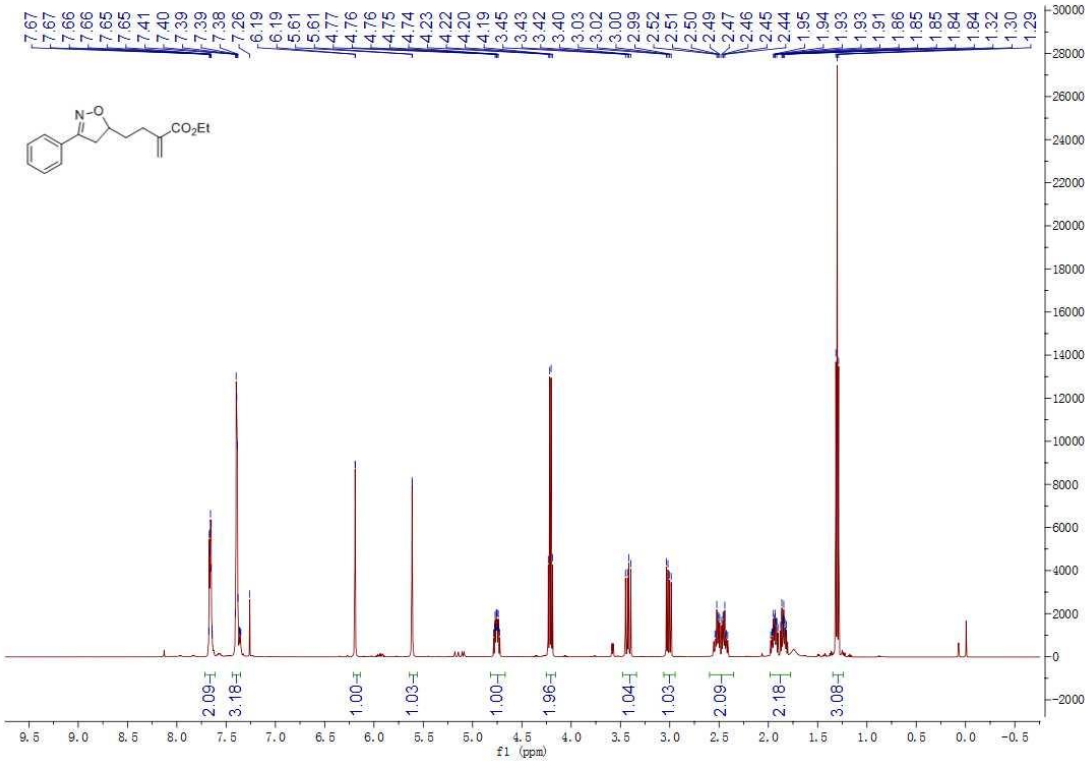
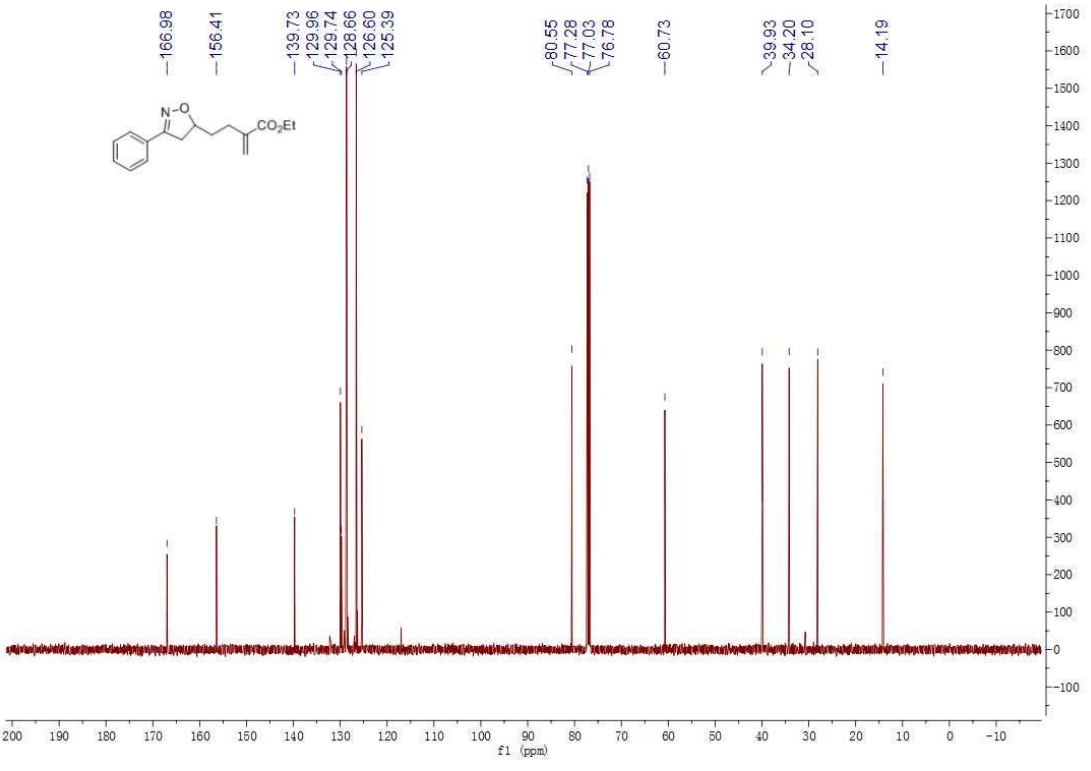
ethyl 2-methylene-4-(3-phenyl-4,5-dihydroisoxazol-5-yl)butanoate(4b)





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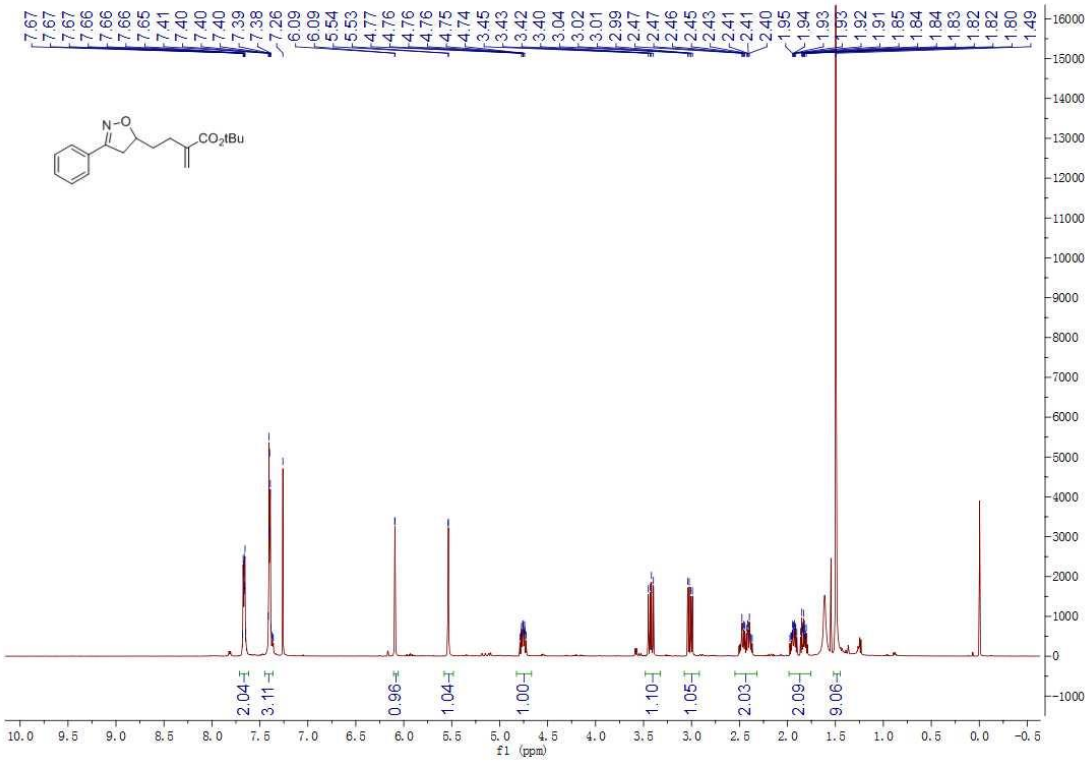
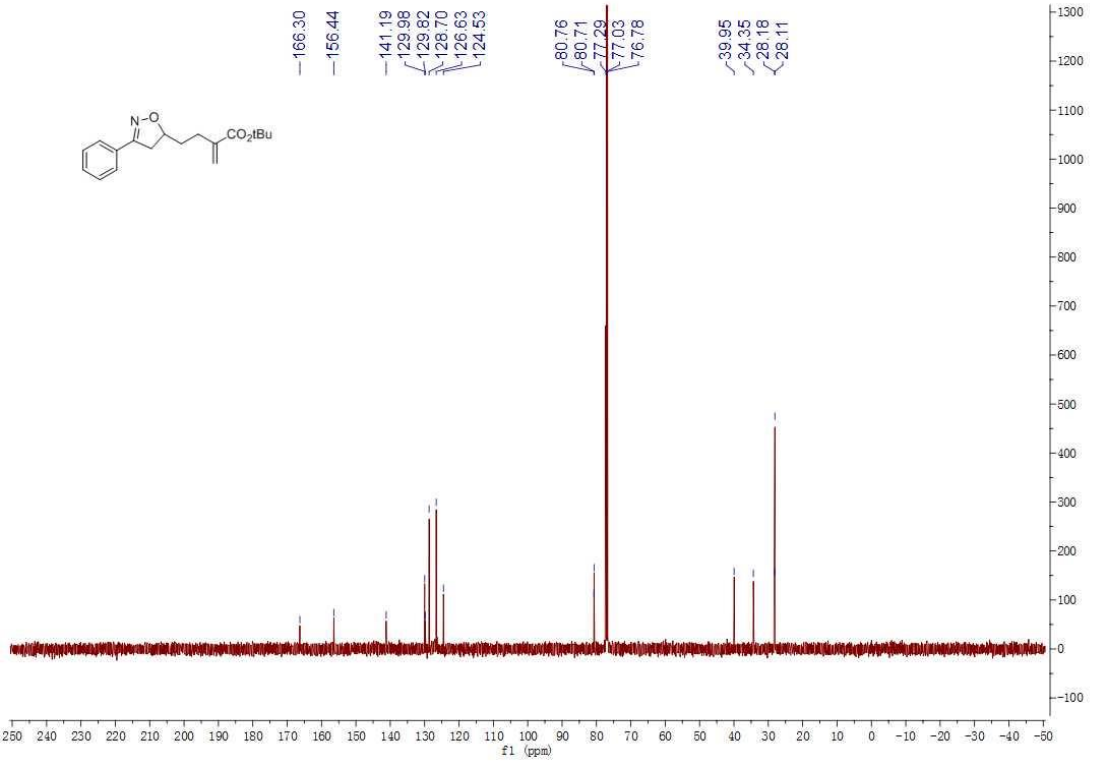
tert-butyl 2-methylene-4-(3-phenyl-4,5-dihydroisoxazol-5-yl)butanoate(4c)





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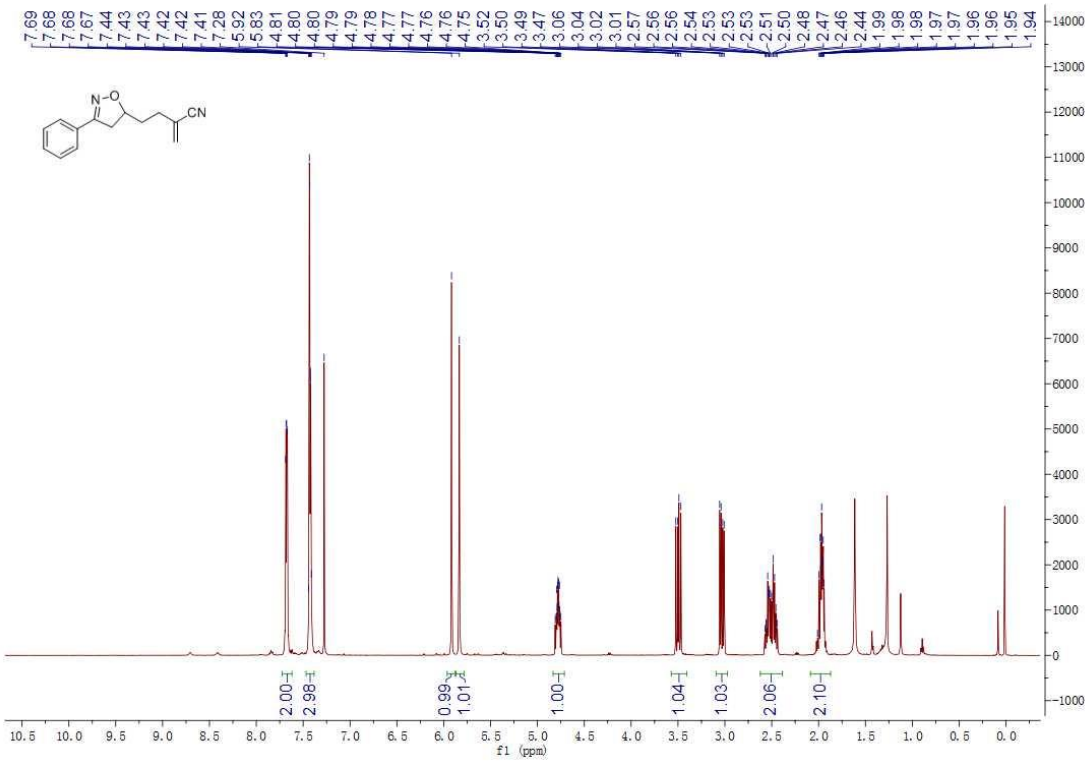
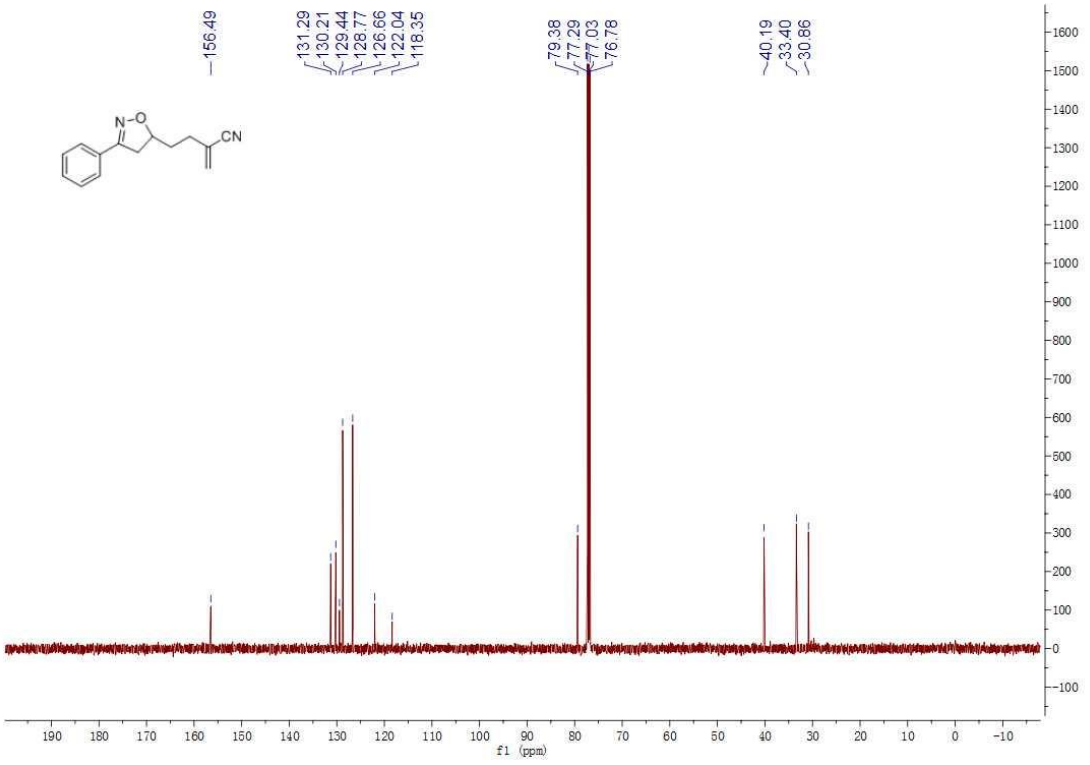
2-methylene-4-(3-phenyl-4,5-dihydroisoxazol-5-yl)butanenitrile(4d)





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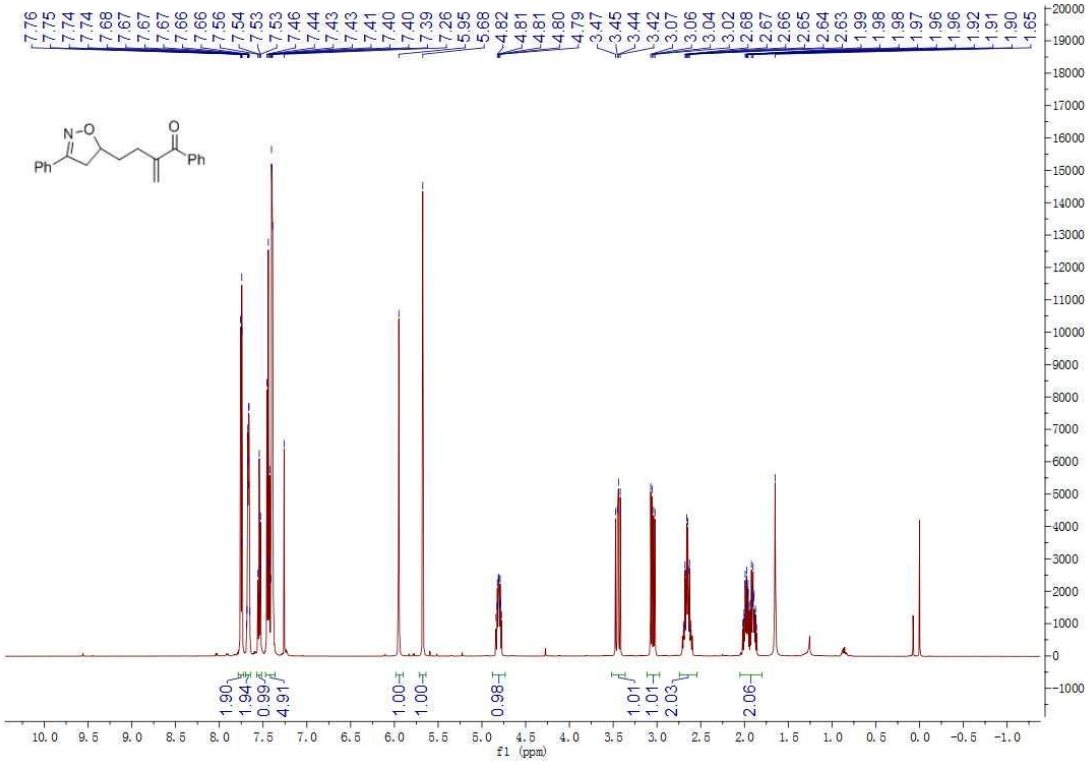
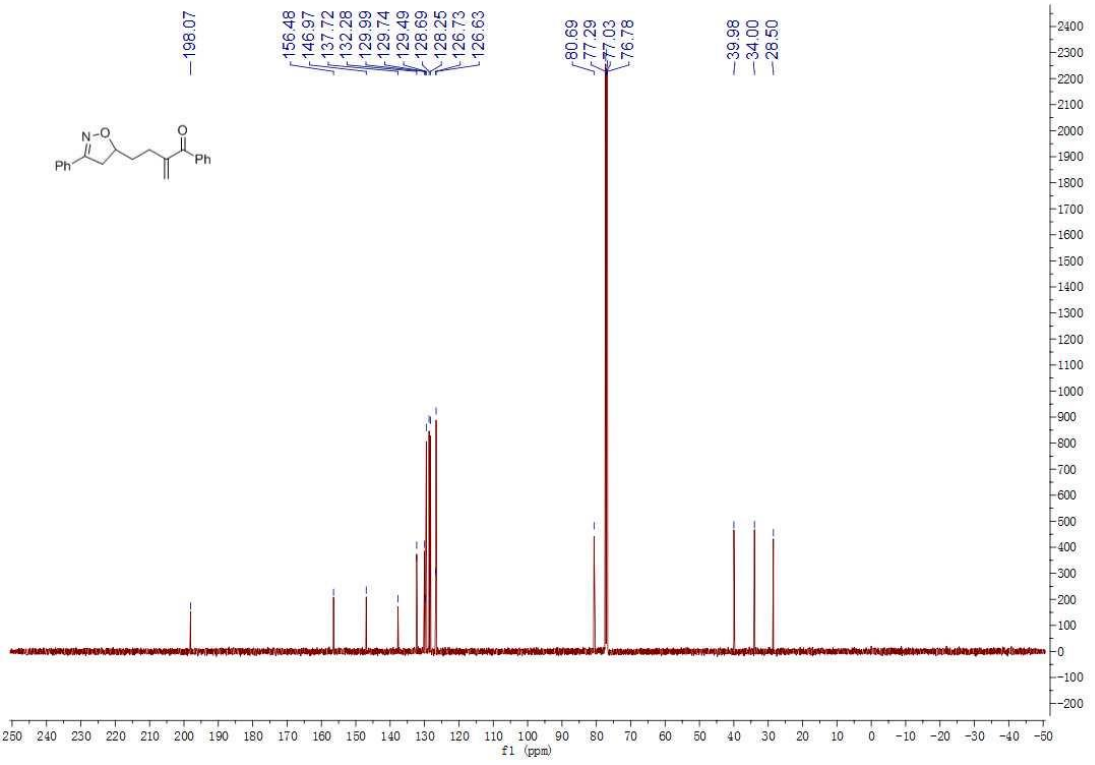
2-methylene-1-phenyl-4-(3-phenyl-4,5-dihydroisoxazol-5-yl)butan-1-one(4e)





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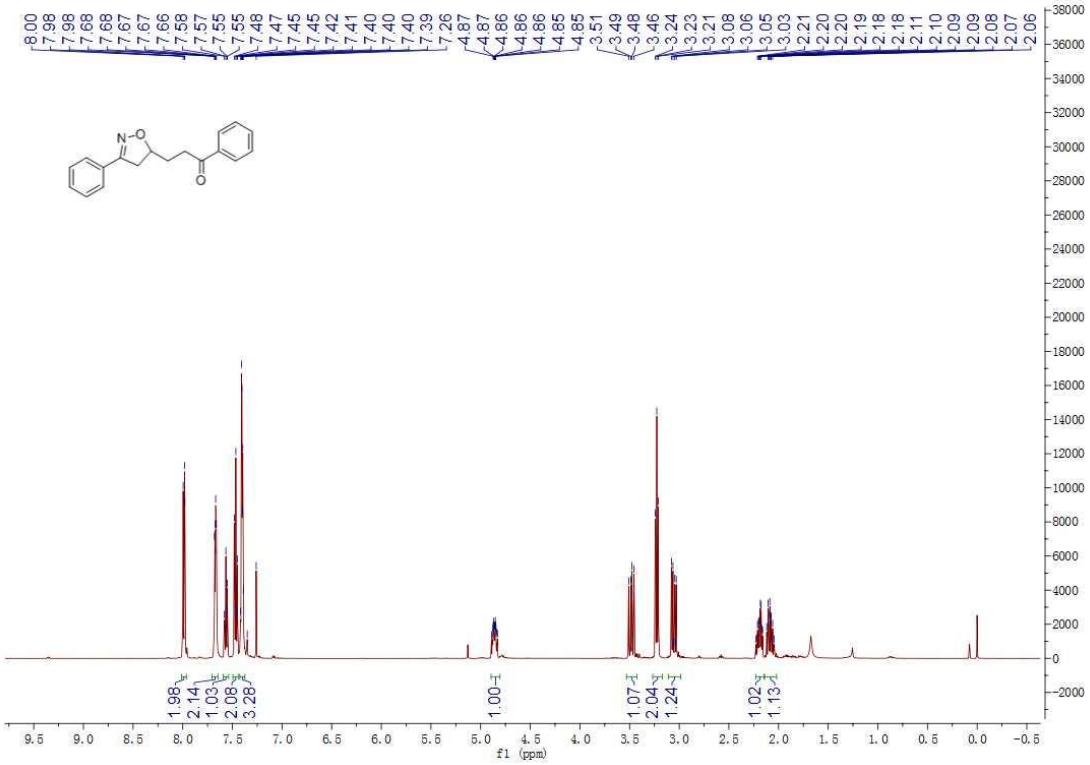
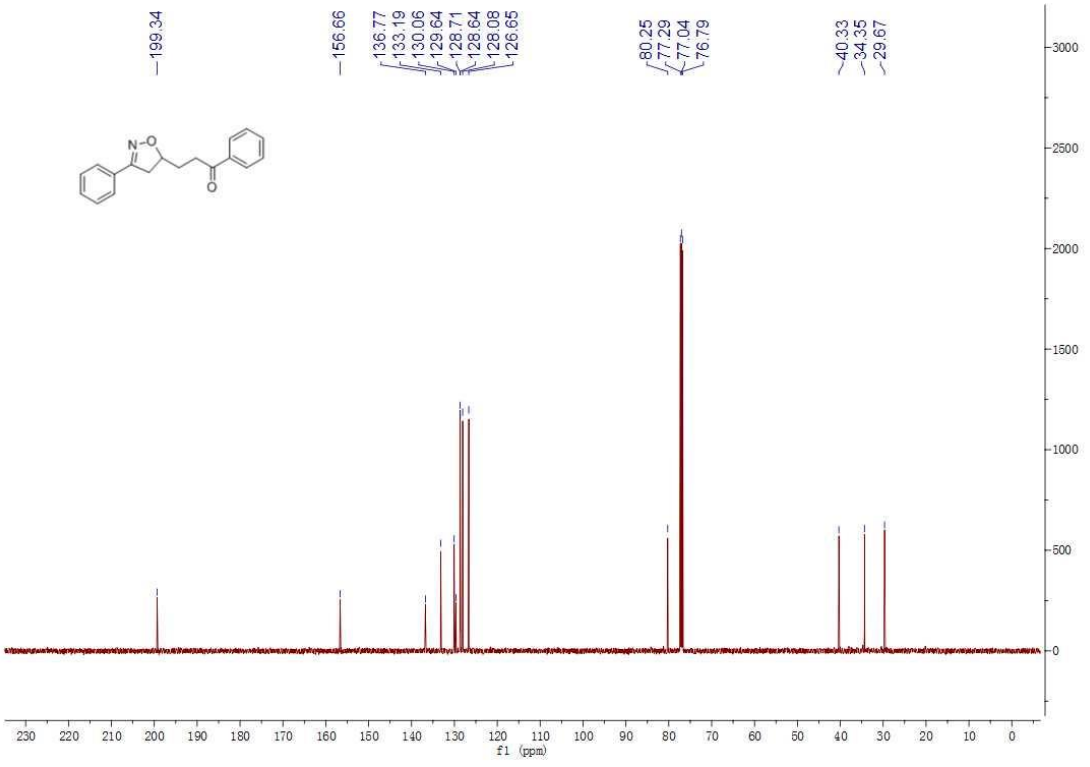
phenyl-3-(3-phenyl-4,5-dihydroisoxazol-5-yl)propan-1-one(5a)





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