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Supporting Information

Tert-butyl nitrite triggered radical cascade reaction for synthesizing isoxazoles by one-pot multicomponent strategy

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Contents:

1. General Remarks

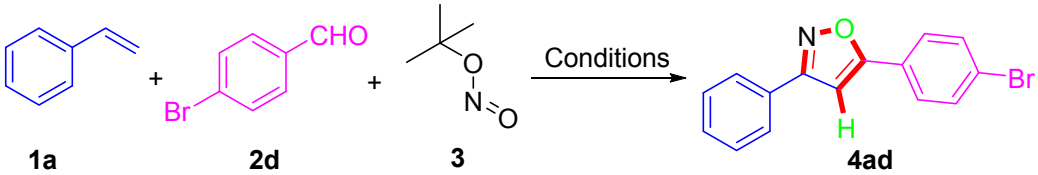
All substrates were purchased commercially without further purification. The yields were determined based on aldehydes. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-300 FT spectrometer at 400 MHz and 100 MHz, an Agilent *VNMRS-600* spectrometer at 600 MHz and 151 MHz, and a Bruker-500 MHz spectrometer at 500 MHz and 126 MHz, respectively, with tetramethylsilane as an internal reference. Chemical shifts (δ) and coupling constants (*J*) were expressed in ppm and Hz, respectively. High resolution mass spectra (HRMS) of products were recorded on a Xevo G2-XS QTOF/MS detector. Melting point was investigated on SGW® X-4B. GC-MS data were measured by Bruker GC-MS 456-Scion.

2. Typical Procedure for the Synthesis of 3,5-Disubstituted Isoxazoles

A mixture of aldehyde (0.25 mmol), alkene (0.75 mmol), TBN (0.75 mmol), sodium persulfate (0.0625 mmol), and glacial acetic acid (0.625 mmol) in 0.5 mL DMF/H_2O (v:v = 4:1) was put into a Schlenk tube at 100 °C for 12 h under air with magnetic stirring. After the reaction was completed, the mixture was extracted with EtOAc (3 × 5 mL) and then the combined organic extracts were washed with brine (10 mL), dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/dichlormethane = 2:1) to give products **4**.

3. Optimization of the reaction conditions

Table S1 Optimization of the reaction conditions [a,b]

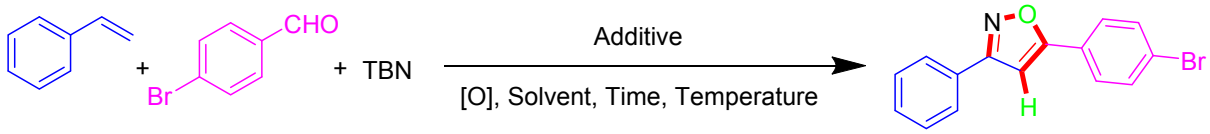


1a **2d** **3** **4ad**

Entry	Solvent	Oxidant	Additive	Time	T/°C	Yield[%][b]
1	H_2O	–	–	8.0 h	100	5
2	THF	–	–	8.0 h	100	trace
3	DMF	–	–	8.0 h	100	15
4	DMF/H_2O(v/v=4:1)	–	–	8.0 h	100	25
5	DMF/H_2O(v/v=4:1)	$Na_2S_2O_8$	–	8.0 h	100	47
6	DMF/H_2O(v/v=4:1)	DTBP	–	8.0 h	100	18
7	DMF/H_2O(v/v=4:1)	$Na_2S_2O_8$	–	8.0 h	110	42
8	DMF/H_2O(v/v=4:1)	$Na_2S_2O_8$	–	8.0 h	80	40
9	DMF/H_2O(v/v=4:1)	$Na_2S_2O_8$	AcOH	8.0 h	100	56
10	DMF/H_2O(v/v=4:1)	$Na_2S_2O_8$	AcOH	5.0 h	100	43
11	DMF/H_2O(v/v=4:1)	$Na_2S_2O_8$	AcOH	12 h	100	62
12[d]	DMF/H_2O(v/v=4:1)	$Na_2S_2O_8$	AcOH	8.0 h	100	22
13[e]	DMF/H_2O(v/v=4:1)	$Na_2S_2O_8$	AcOH	8.0 h	100	71(68)[c]

[a] Reaction conditions:**1a** (0.5 mmol), **2d** (0.25 mmol), **3** (0.5 mmol), Oxidant(0.0625 mmol), Addition (0.625 mmol), Na_2SO_4 (0.5 mmol), solvent (0.5 mL), air.
[b] Yields were calculated by GC-MS using benzophenone as the internal standard (IS).
[c] Isolated yields based on **2d** after chromatography.
[d] 1**a** (0.25 mmol), **2d** (0.5 mmol).
[e] 1**a** (0.75 mmol), **3** (0.75 mmol).

Table S2 Optimization reaction using different conditions



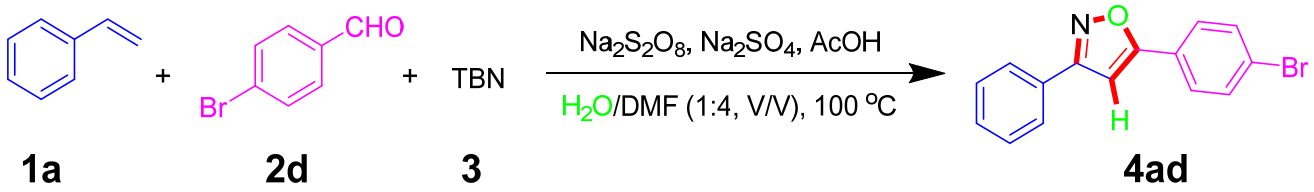
1a **2d** **3** **4ad**

Entry	Solvent	Acid/Base	Oxidant	Additive	[NO] sources	Metal catalysis	T/°C	Time	Yield[%][b]
1	H_2O						80	8h	5
2	THF						80	8h	trace
3	DMF						80	8h	15
4	CH_3CH_2OH						80	8h	9
5	CH_3CN						80	8h	5
6	DMF/H_2O(v/v=4:1)	-					80	8h	25
7	DMF/H_2O(v/v=4:1)	K_2CHO_3					80	8h	12
8	DMF/H_2O(v/v=4:1)	NaOAc					80	8h	15
9	DMF/H_2O(v/v=4:1)	AcOH					80	8h	30
10	DMF/H_2O(v/v=4:1)	HBF_4					80	8h	20
11	DMF/H_2O(v/v=4:1)	HCl					80	8h	19
12	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$				80	8h	47
13	DMF/H_2O(v/v=4:1)	AcOH	TBHP				80	8h	26
14	DMF/H_2O(v/v=4:1)	AcOH	$PhI(OAc)_2$				80	8h	22
15	DMF/H_2O(v/v=4:1)	AcOH	H_2O_2				80	8h	trace
16	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			80	8h	52
17	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			90	8h	55
18	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			100	8h	56
19	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			110	8h	54
20	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			120	8h	45
21	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			100	3h	32
22	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			100	6h	44
23	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			100	10h	59
24	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			100	12h	62
25	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			100	24h	62
26[d]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			100	12h	22
27[e]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			100	12h	55
28[f]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			100	12h	67
29[g]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			100	12h	**71**
30[g]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4			100	12h	**68**[c]
31[h]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4	TBN		100	12h	61
32[h]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4	$CH_3(CH)_2CH_2ONO$		100	12h	48
33[h]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4	$(CH_3)_2CHCH_2ONO$		100	12h	2
34[h]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4	$(CH_3)_2CHCH_2CH_2ONO$		100	12h	40
35[h]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4	TBN	$FeSO_4$	100	12h	58
36[h]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4	TBN	$Co(OAc)_2$	100	12h	47
37[h]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4	TBN	$Ni(OAc)_2$	100	12h	44
38[h]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4	TBN	$Cu(OAc)_2$	100	12h	trace
39[i]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4	TBN		100	12h	63
40[j]	DMF/H_2O(v/v=4:1)	AcOH	$Na_2S_2O_8$	Na_2SO_4	TBN		100	12h	61

[a] Reaction conditions:**1a** (0.5 mmol), **2d** (0.25 mmol), **3** (0.5 mmol), Oxidant(0.0625 mmol), Additive (0.625 mmol), solvent (0.5 mL), air.
[b] Yields were calculated by GC-MS using benzophenone as the internal standard (IS).
[c] Isolated yields based on **2d** after chromatography.
[d] 1**a** (0.25 mmol), **2d** (0.5 mmol).
[e] 1**a** (0.75 mmol), **3** (0.75 mmol).
[f] 1**a** (0.75 mmol), **3** (0.75 mmol).
[g] 1**a** (0.75 mmol), **3** (0.75 mmol).
[h] 1**a** (0.75 mmol), **2a** (0.25 mmol), **3** (0.75 mmol), Oxidant(0.0625 mmol), Additive (0.625 mmol), solvent (0.5 mL), air.
[i] 1**a** (0.875 mmol), **2a** (0.25 mmol), **3** (0.75 mmol), Oxidant(0.0625 mmol), Additive (0.625 mmol), solvent (0.5 mL), air.
[j] 1**a** (1.0 mmol), **2a** (0.25 mmol), **3** (0.75 mmol), Oxidant(0.0625 mmol), Additive (0.625 mmol), solvent (0.5 mL), air.

4. Synthetic Applications

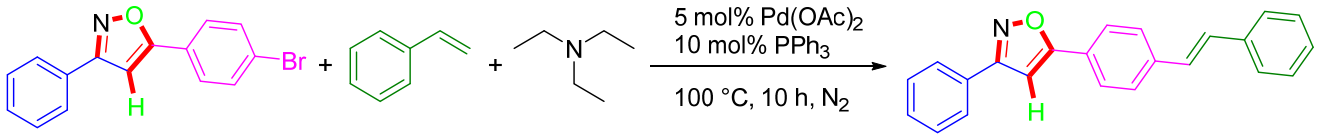
4.1 Scale-up Reaction



1a **2d** **3** **4ad**

The scale-up reaction: **1a** (12 mmol), **2d** (4 mmol), **3** (12 mmol), AcOH (10 mmol), $Na_2S_2O_8$ (1 mmol) and Na_2SO_4 (8 mmol) in 10 mL DMF/water (v:v = 4:1), 100 ℃, under air, 12 h. Product **4ad** was purified by flash chromatography on silica gel to give 65% yield.

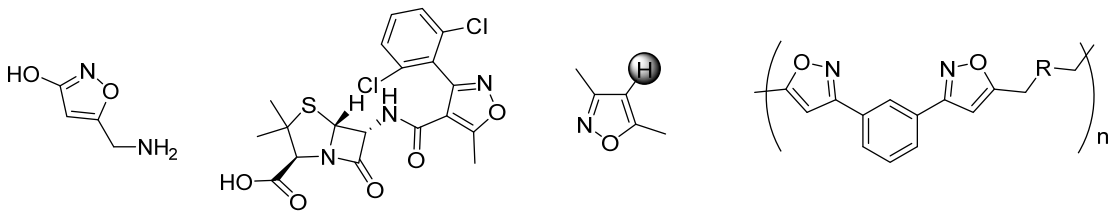
4.2 Transformation of product 4ad



4ad **5**

The transformation reaction of product **4ad** was performed based on the previously reported procedure.[1] A sealed tube was loaded with **4ad** (0.2 mmol), $Pd(OAc)_2$ (0.01 mmol), PPh_3 (0.02 mmol), styrene (0.4 mmol), triethylamine (0.2 mmol) and acetonitrile (0.5 mL). Under nitrogen atmosphere, the reaction mixture was stirred at 100 ℃ for 10 h. The mixture was cooled to room temperature and subsequently extracted with EtOAc three times. The organic layer was dried with anhydrous Na_2SO_4. The solvent was concentrated, and the residue was purified by flash chromatography on silica gel to give the targeted **5** in 85% yield.

4.3 Examples of Bearing Isoxazoles



Muscimol (Natural product)

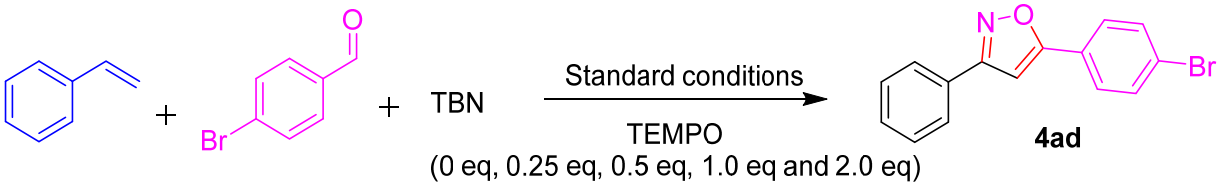
Dicloxacillin Marketed drug

3,5-Dimethylisoxazole Precursor

Polyisoxazole Functional material

5. Mechanistic Studies

5.1 Radical experiment



According to the established method, to add the TEMPO of 0, 0.25, 0.5, 1.0 and 2.0 eq into the reaction system under the standard conditions, respectively. After the reaction being completed, the peak area of **4ad** was determined by GC-MS using benzophenone as the internal standard (IS) as shown in **Figure S1** and the relative yields were further analyzed as displayed in **Figure S2**. In addition, two adducts containing TEMPO **7a** and **7b** were successfully captured by HRMS technique and showed in **Figure S3.**

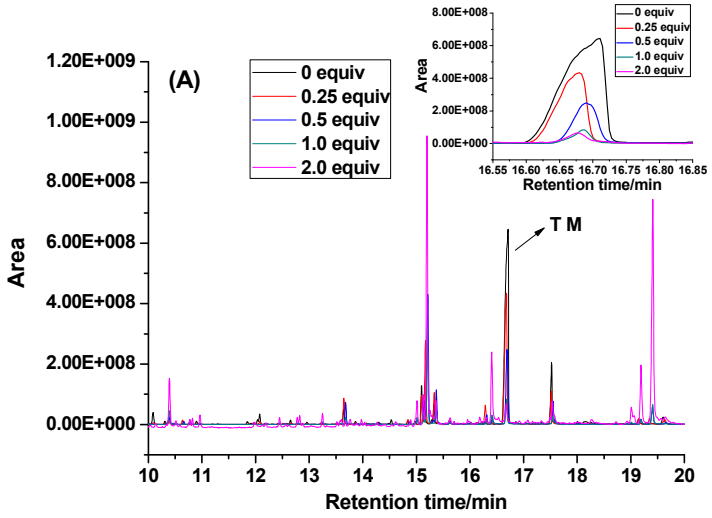


Figure S1 The GC-MS profile of TEMPO experiments

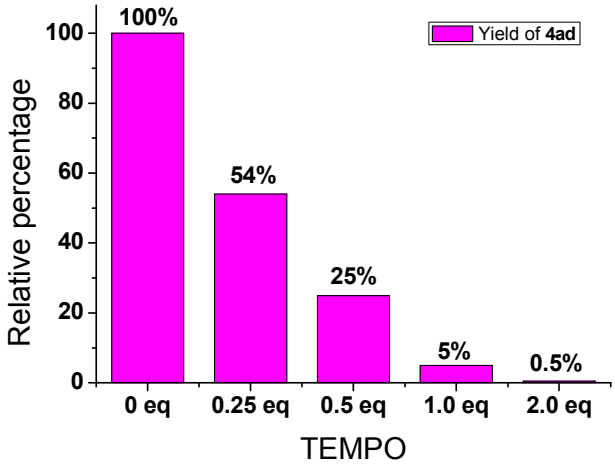


Figure S2 The effect of the different amounts of TEMPO on the relative yield of **4ad**

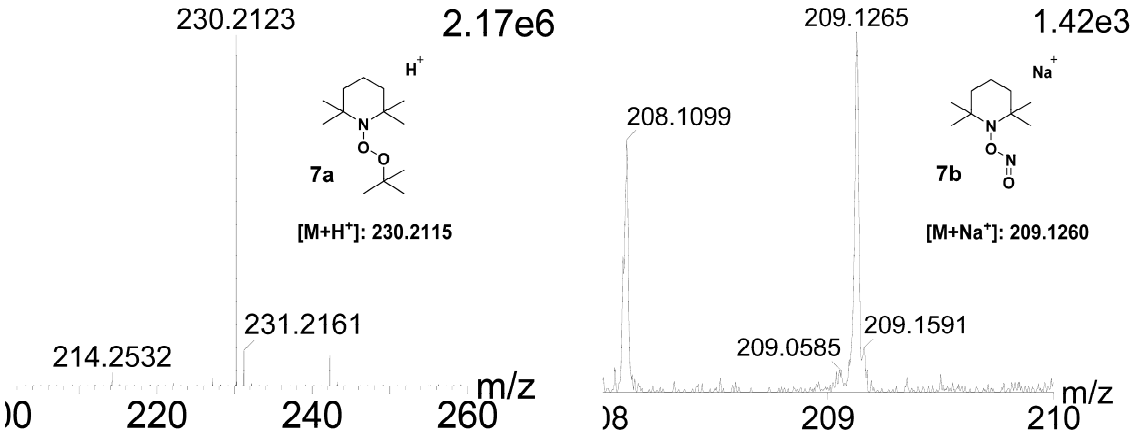
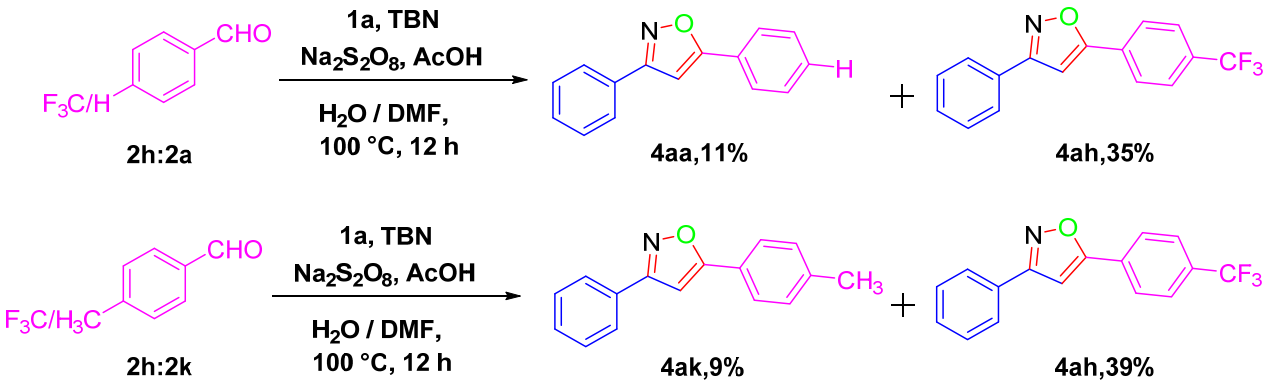


Figure S3 The HRMS data of adducts **7a** and **7b**

5.2 Intermolecular Competition Experiments



A mixture of aldehyde **2a** and **2h** (the molar ratio being 1:1) (0.25 mmol), alkene (0.75 mmol), TBN (0.75 mmol), sodium persulfate (0.0625 mmol), and glacial acetic acid (0.625 mmol) in 0.5 mL DMF/H_2O (v:v = 4:1) was put into a Schlenk tube at 100 °C for 12 h under air with magnetic stirring. After the reaction being completed, the peak areas of **4aa** and **4ah** were determined by GC-MS with diphenylmethanone as an internal standard, and corresponding results were shown in **Figure S4**.

A mixture of aldehyde **2h** and **2k** (the molar ratio being 1:1) (0.25 mmol), alkene (0.75 mmol), TBN (0.75 mmol), sodium persulfate (0.0625 mmol), and glacial acetic acid (0.625 mmol) in 0.5 mL DMF/H_2O (v:v = 4:1) was put into a Schlenk tube at 100 °C for 12 h under air with magnetic stirring. After the reaction being completed, the peak areas of **4ah** and **4ak** were determined by GC-MS with diphenylmethanone as an internal standard, and corresponding results were shown in **Figure S4**.

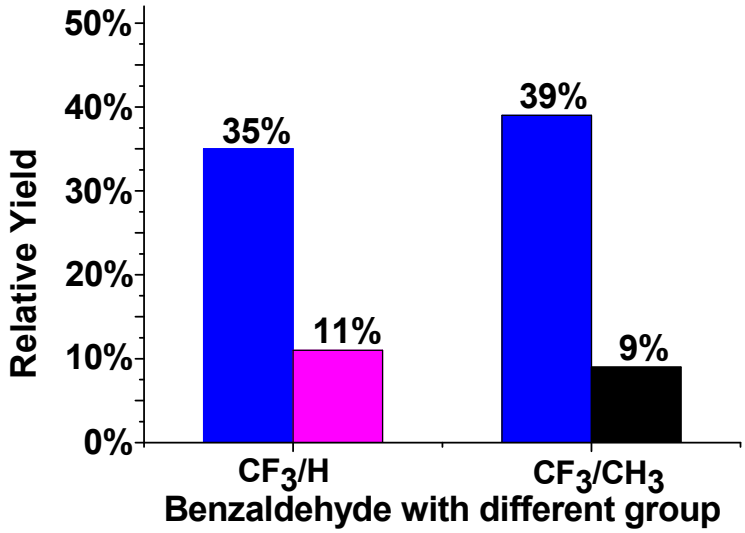


Figure S4 The results of intermolecular competition experiments

5.3 Hammett Correlation Analysis

A series of reactions was performed with electronically differentiated substrate **2** under standard reaction condition. Purification by column chromatography on silica gel (n-hexane/CH_2Cl_2:2/1) afforded the desired products **4**. The Hammett correlation was listed in **Table S1**, and corresponding result of the Hammett plot was showed in **Figure S5**.

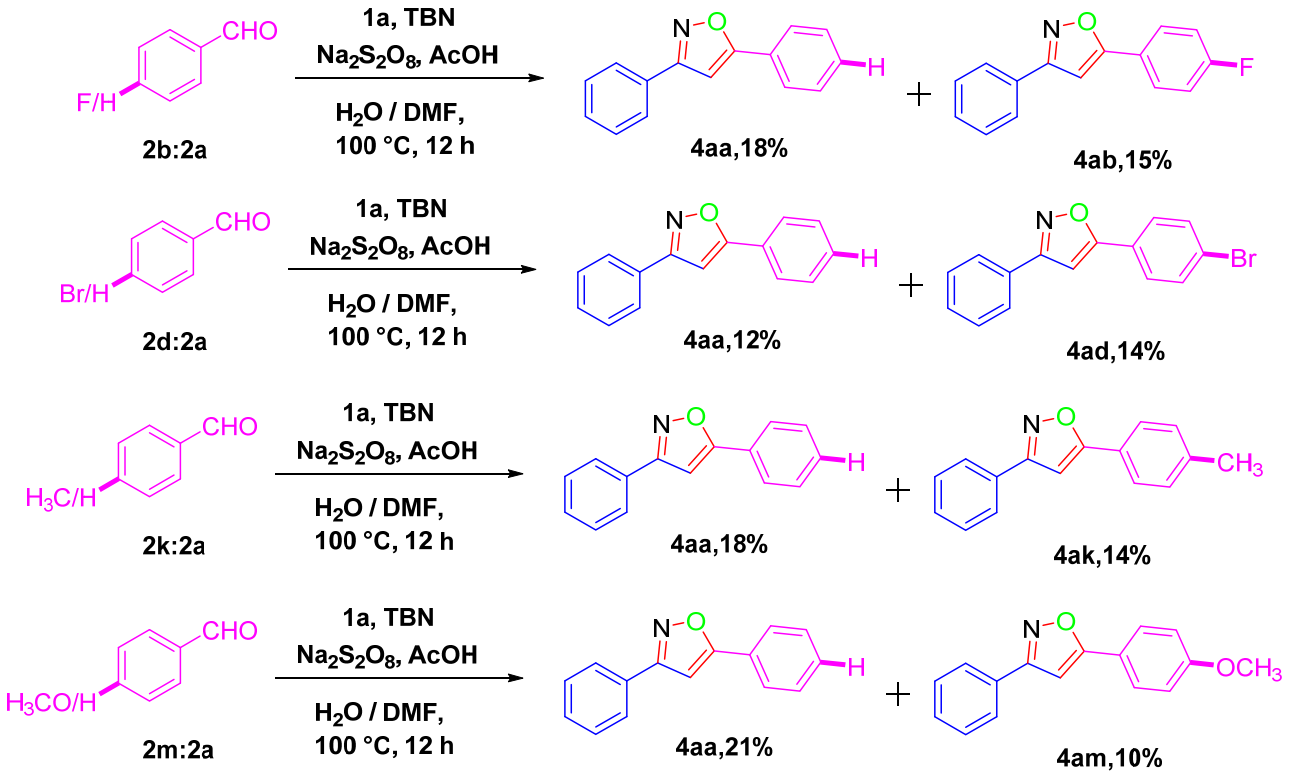


Table S1 Hammett correlation

R_{meta}	k/k_0	$\log(k/k_0)$	σ_{meta}
F	0.8126	-0.0901	0.062
Br	1.1638	0.0659	0.232
CH_3	0.7609	-0.2088	-0.17
OCH_3	0.4486	-0.4911	-0.268

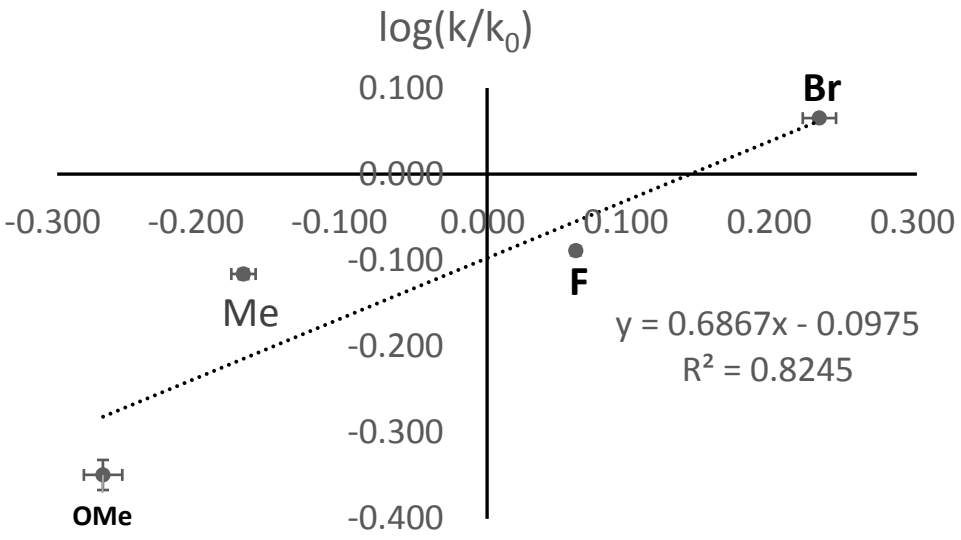


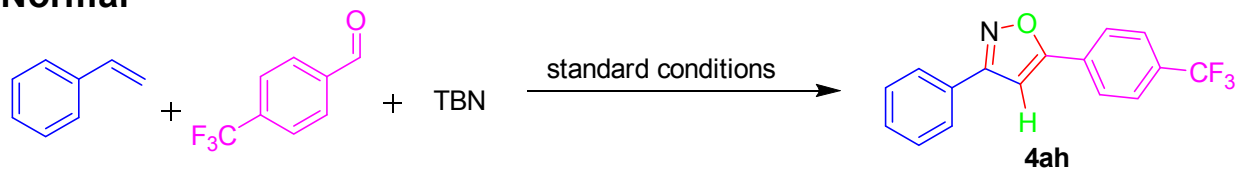
Figure S5 The Hammett plot

A positive ρ value (ρ = 0.69, R^2 = 0.82 using σmeta) from the Hammett correlation suggested that negative charge was formed in the product-determining step, concluding that electrophilic mechanism occurred in the C–H bond scission step.

5.4 Isotope experiments

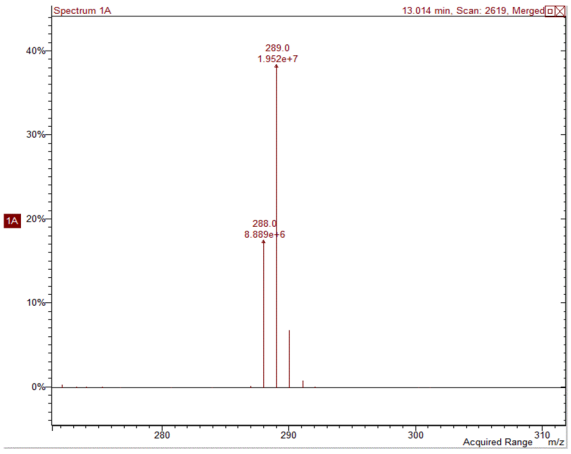
Analysis by GC-MS:

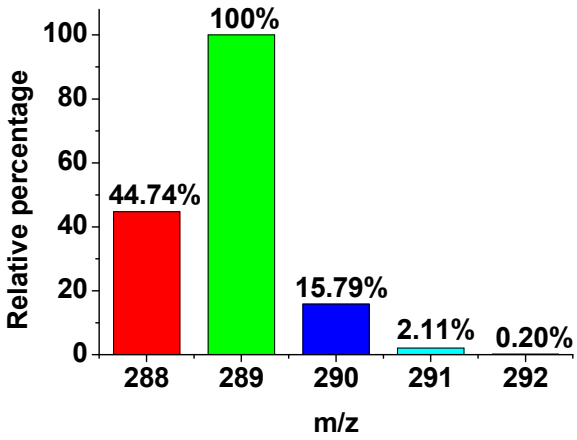
a. Normal



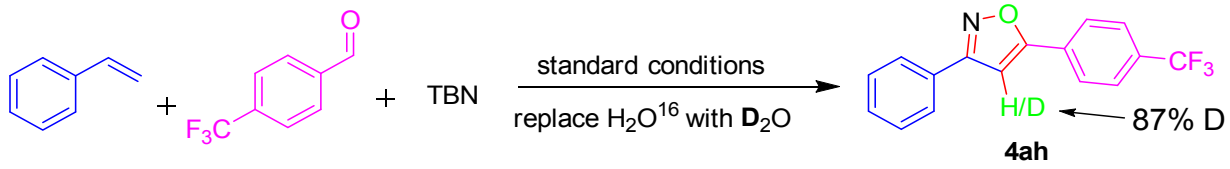
4ah

A mixture of aldehyde **2h** (0.25 mmol), styrene (0.75 mmol), TBN (0.75 mmol), sodium persulfate (0.0625 mmol), and glacial acetic acid (0.625 mmol) in 0.5 mL DMF/H_2O (v:v = 4:1) was put into a Schlenk tube at 100 °C under magnetic stirring for 12 h under air. After cooling to ambient temperature, the mixture was concentrated in vacuo. The reaction solution including product **4ah** was diluted with EtOAc to desired concentrations and passed through a 0.22 μm Millipore membrane filter prior to GC-MS analysis.

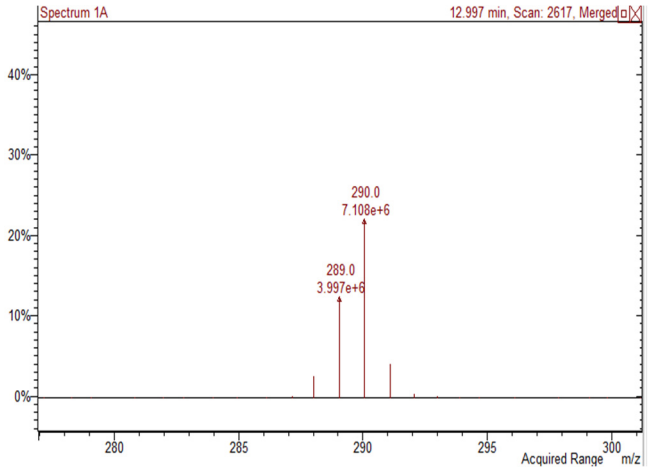


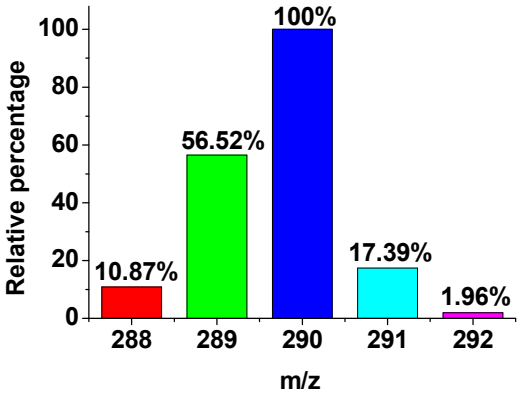


b. Replace H_2O with D_2O

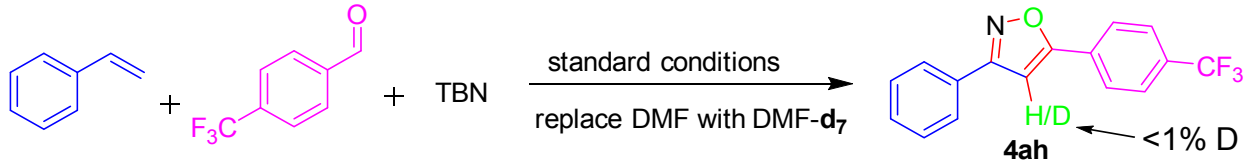


A mixture of aldehyde **2h** (0.25 mmol), styrene (0.75 mmol), TBN (0.75 mmol), sodium persulfate (0.0625 mmol), and glacial acetic acid (0.625 mmol) in 0.5 mL DMF/D_2O (v:v = 4:1) was put into a Schlenk tube at 100 °C under magnetic stirring for 12 h under air. After cooling to ambient temperature, the mixture was concentrated in vacuo. The reaction solution including product **4ah** was diluted with EtOAc to desired concentrations and passed through a 0.22 μm Millipore membrane filter prior to GC-MS analysis.

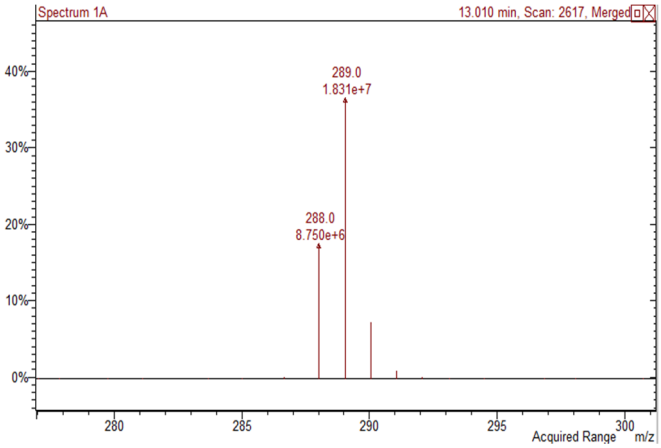


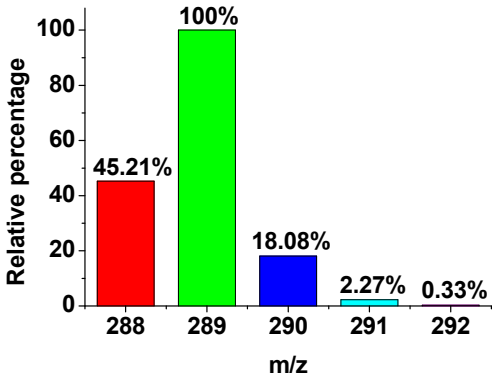


c. Replace DMF with DMF-d_7

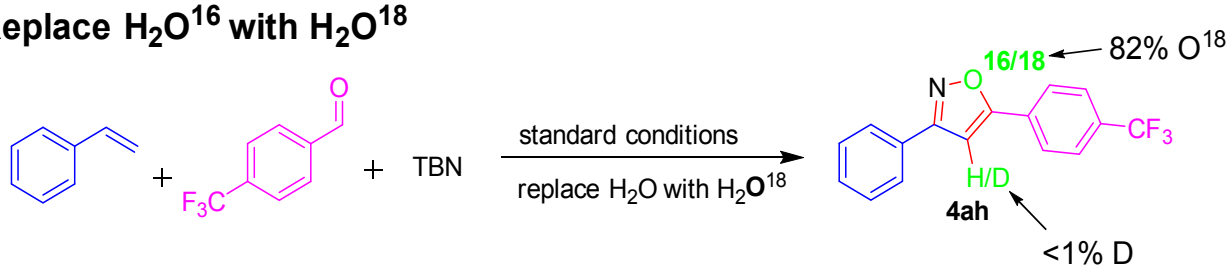


A mixture of aldehyde **2h** (0.25 mmol), styrene (0.75 mmol), TBN (0.75 mmol), sodium persulfate (0.0625 mmol), and glacial acetic acid (0.625 mmol) in 0.5 mL DMF-d_7/H_2O (v:v = 4:1) was put into a Schlenk tube at 100 °C under magnetic stirring for 12 h under air. After cooling to ambient temperature, the mixture was concentrated in vacuo. The reaction solution including product **4ah** was diluted with EtOAc to desired concentrations and passed through a 0.22 μm Millipore membrane filter prior to GC-MS analysis.

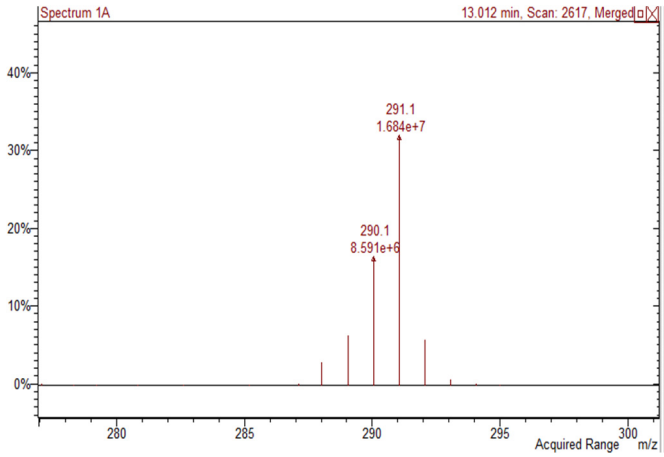


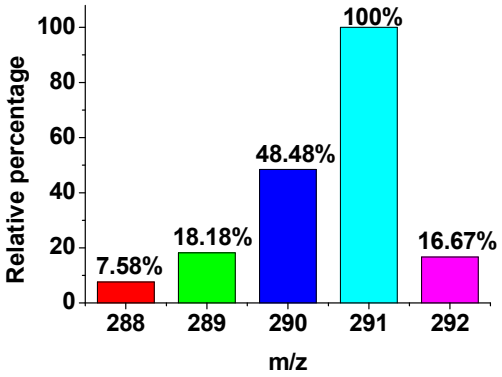


d. Replace H_2O^{16} with H_2O^{18}

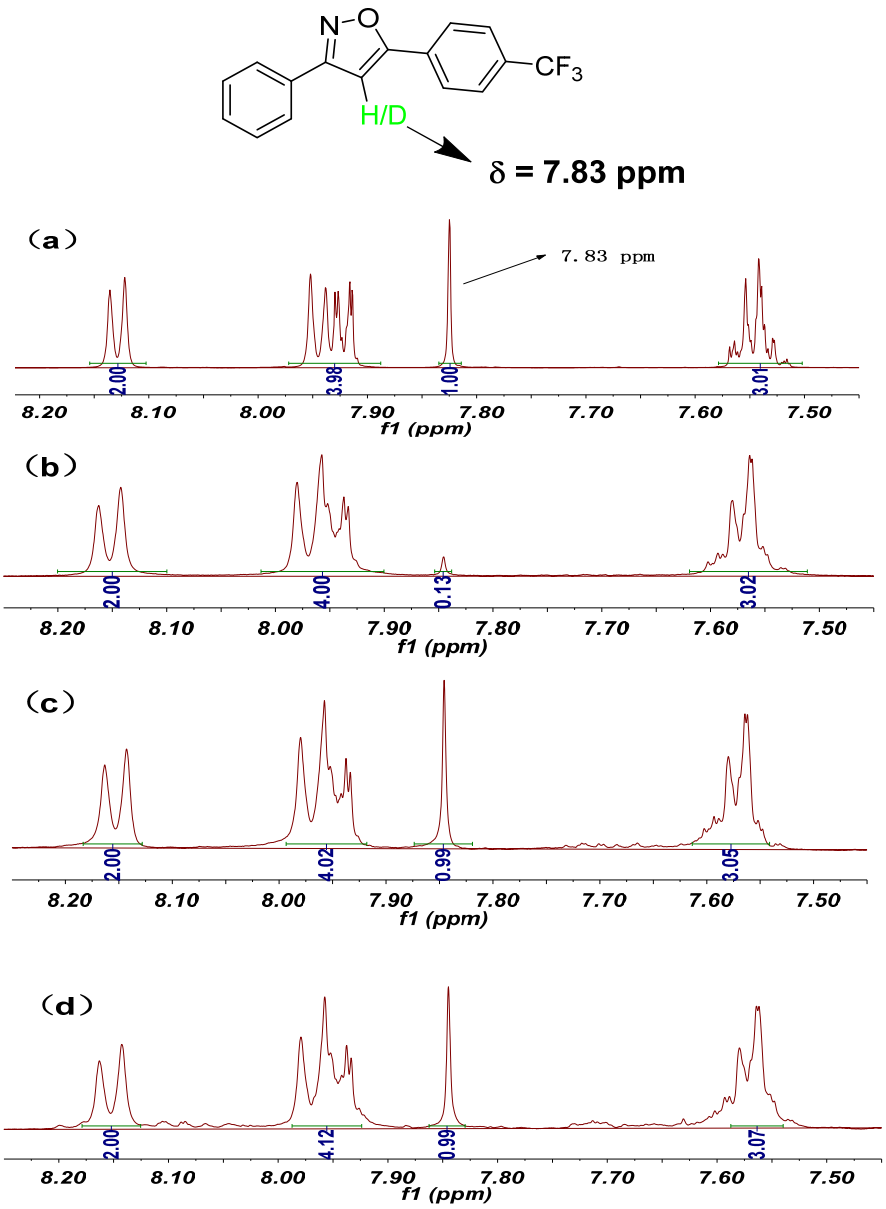


A mixture of aldehyde **2h** (0.25 mmol), styrene (0.75 mmol), TBN (0.75 mmol), sodium persulfate (0.0625 mmol), and glacial acetic acid (0.625 mmol) in 0.5 mL DMF/H_2O^{18} (v:v = 4:1) was put into a Schlenk tube at 100 °C under magnetic stirring for 12 h under air. After cooling to ambient temperature, the mixture was concentrated in vacuo. The reaction solution including product **4ah** was diluted with EtOAc to desired concentrations and passed through a 0.22 μm Millipore membrane filter prior to GC-MS analysis.



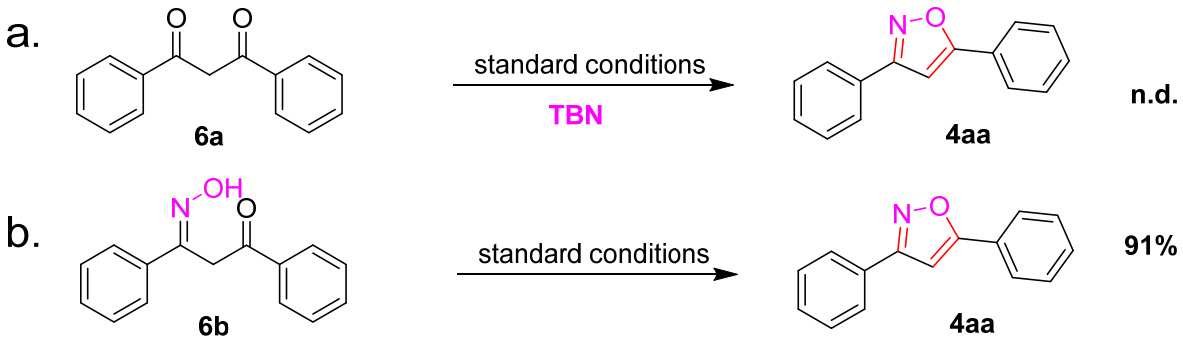


Analysis by ^{1}H NMR spectroscopy:



Spectra related to the ^{1}H NMR experiment in (a) H_2O, the singlet at 7.83 ppm is the peak of hydrogen atom at the 4 position on isoxazole skeleton; (b) Replacing H_2O with D_2O; (c) Replacing DMF with DMF-d_7; (d) Replace H_2O with H_2O^{18}.

5.5 Intermediate experiments

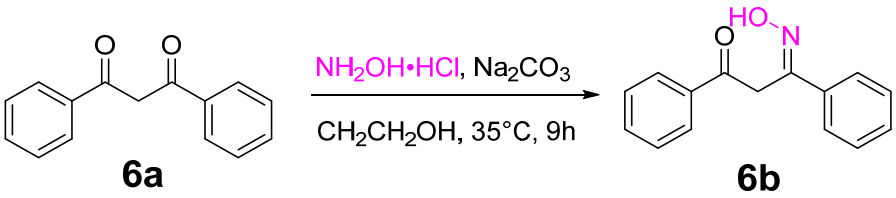


Reaction **a**: A mixture of **6a** (0.25 mmol), TBN (0.75 mmol), sodium persulfate (0.0625 mmol), and glacial acetic acid (0.625 mmol) in 0.5 mL DMF/H_2O (v:v = 4:1) was put into a Schlenk tube at 100 °C under magnetic stirring for 12 h under air. After cooling to ambient temperature, the mixture was concentrated in vacuo. Purification by column chromatography on silica gel (n-hexane/CH_2Cl_2:2/1) afforded the desired products **4aa** in 0% yield.

Reaction **b**: A mixture of **6b** (0.25 mmol), sodium persulfate (0.0625 mmol), and glacial acetic acid (0.625 mmol) in 0.5 mL DMF/H_2O (v:v = 4:1) was put into a Schlenk tube at 100 °C under magnetic stirring for 12 h under air. After cooling to ambient temperature, the mixture was concentrated in vacuo. Purification by column chromatography on silica gel (n-hexane/CH_2Cl_2:2/1) afforded the desired products **4aa** in 91% yield.

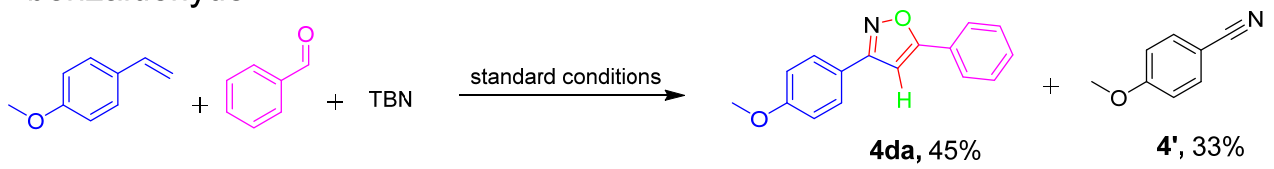
Synthetic Procedure for Intermediate 6b:

To an oven-dried Schlenk bottle (10 mL) with a magnetic bar was added dibenzoylmethane (2.5 mmol), $NH_2OH{\cdot}HCl$ (2 mmol), Na_2CO_3 (2 mmol) and ethanol (2 mL). The mixture was stirred at 35 ℃ for 9 h. After cooling to room temperature, the mixture was extracted with EtOAc. The organic phase dried over Na_2SO_4. The solvent was evaporated, and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate) to afford the corresponding products **6b**.

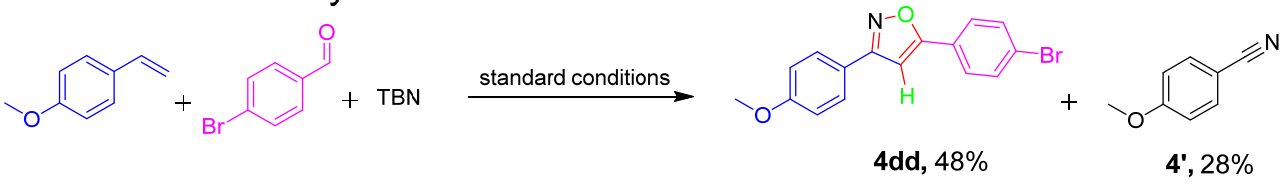


5.6 By-product experiments

a. benzaldehyde



b. 4-bromobenzaldehyde



Reaction a: A mixture of 4-methoxy styrene **1d** (0.75 mmol), benzaldehyde **2a** (0.25 mmol), TBN (0.75 mmol), sodium persulfate (0.0625 mmol), and glacial acetic acid (0.625 mmol) in 0.5 mL DMF/H_2O (v:v = 4:1) was put into a Schlenk tube at 100 °C under magnetic stirring for 12 h under air. After cooling to ambient temperature, the mixture was concentrated in vacuo. Purification by column chromatography on silica gel (n-hexane/CH_2Cl_2:2/1) afforded the desired products **4da** in 45% and **4'** in 33% yield, respectively.

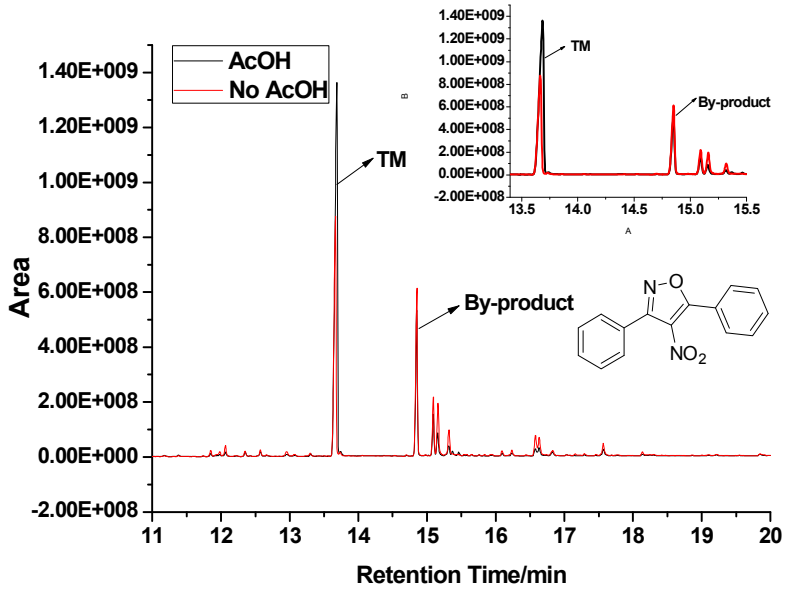
Reaction b: A mixture of 4-methoxy styrene **1d** (0.75 mmol), 4-bromobenzaldehyde **2d** (0.25 mmol), TBN (0.75 mmol), sodium persulfate (0.0625 mmol), and glacial acetic acid (0.625 mmol) in 0.5 mL DMF/H_2O (v:v = 4:1) was put into a Schlenk tube at 100 °C under magnetic stirring for 12 h under air. After cooling to ambient temperature, the mixture was concentrated in vacuo. Purification by column chromatography on silica gel (n-hexane/CH_2Cl_2:2/1) afforded the desired products **4dd** in 48% and **4'** in 28% yield, respectively.

5.7 The roles of AcOH and $Na_2S_2O_8$

A mixture of styrene **1a** (0.75 mmol), benzaldehyde **2a** (0.25 mmol), TBN (0.75 mmol), sodium persulfate (0.0625 mmol), and acetic acid (0, and 0.625 mmol) in 0.5 mL DMF/H_2O (v:v = 4:1) was put into a Schlenk tube at 100 °C under magnetic stirring for 12 h under air. After cooling to ambient temperature, the mixture was concentrated in vacuo. Purification by column chromatography on silica gel (n-hexane/CH_2Cl_2:2/1) afforded the desired products **4aa**.

The effects of the acetic acid on yield of product **4aa**

Entry	Acid/Base	Solvent	Additive	Yield(%)
1	-	DMF/H_2O(v/v=4:1)	Na_2SO_4	31
2	AcOH	DMF/H_2O(v/v=4:1)	Na_2SO_4	61



A mixture of styrene **1a** (0.75 mmol), benzaldehyde **2a** (0.25 mmol), TBN (0.75 mmol), sodium persulfate (0, 0.0625, 0.125, 0.25, and 0.5 mmol), and acetic acid (0.625 mmol) in 0.5 mL DMF/H_2O (v:v = 4:1) was put into a Schlenk tube at 100 °C under magnetic stirring for 12 h under air. After cooling to ambient temperature, the mixture was concentrated in vacuo. Purification by column chromatography on silica gel (n-hexane/CH_2Cl_2:2/1) afforded the desired products **4aa**.

The effects of the $Na_2S_2O_8$ on yield of product **4aa**

Entry	Acid/Base	[NO]sources	Oxidant	Yield(%)
1	AcOH	TBN	-	<5
2	AcOH	TBN	0.25 eq $Na_2S_2O_8$	61
3	AcOH	TBN	0.5 eq $Na_2S_2O_8$	45
4	AcOH	TBN	1.0 eq $Na_2S_2O_8$	26
5	AcOH	TBN	2.0 eq $Na_2S_2O_8$	32

5.8 Possible mechanism

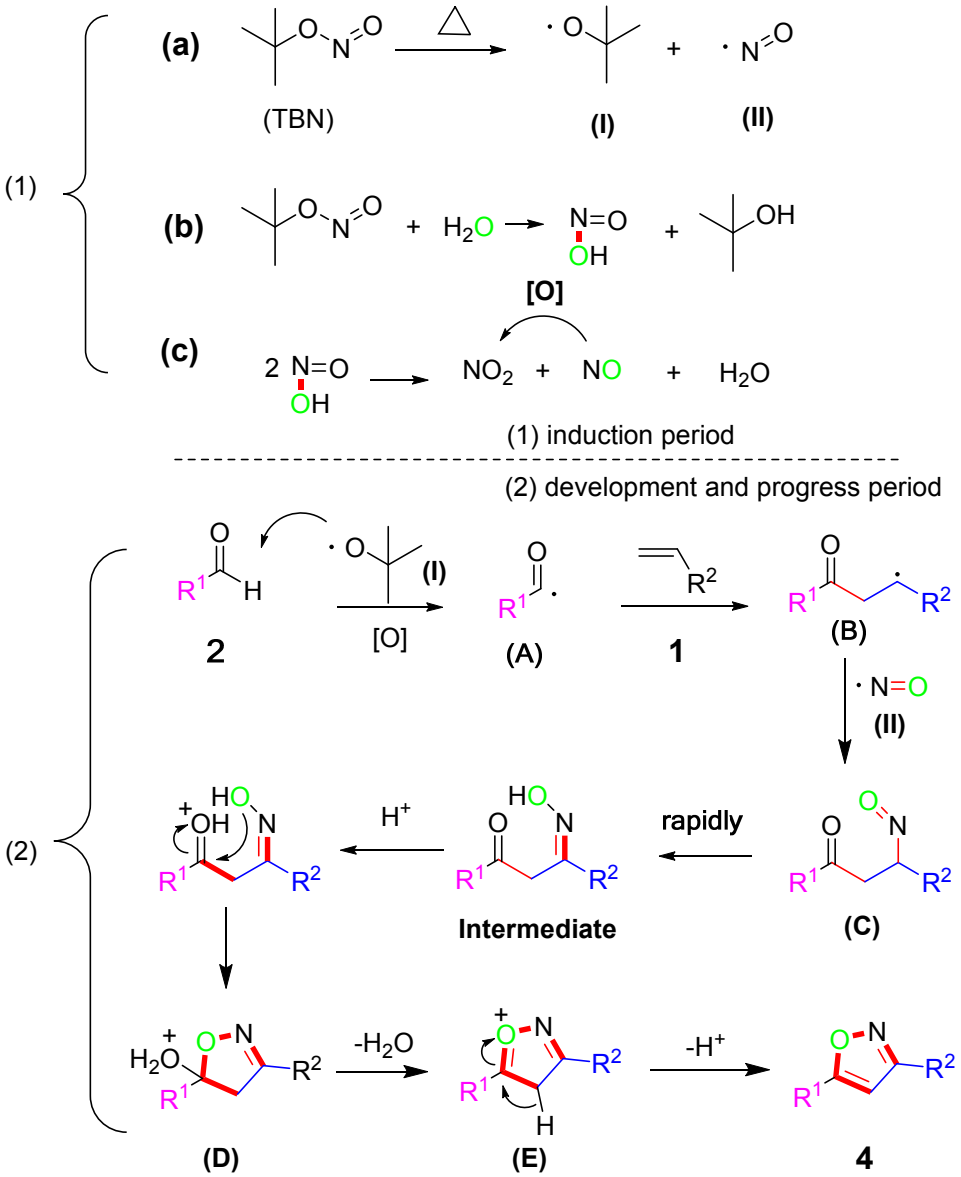
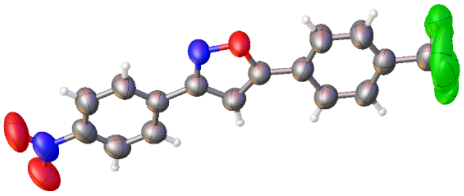


Figure S6 Possible mechanism

6. X-ray Crystal data

Crystallographic data for compound **4ih** (CCDC-2123693) has been deposited with the Cambridge Crystallographic Data Centre, Copies of the data can be obtained, free of charge, on application to CCDC (Email:deposit@ccdc.cam.ac.uk).



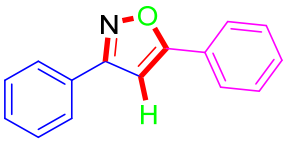
Bond precision:	C-C = 0.0040 A	Wavelength=1.54184	
Cell:	a=21.1543(5)	b=14.2842(3)	c=30.5779(7)
	alpha=90	beta=105.722(2)	gamma=90
Temperature:	293 K		
	Calculated		Reported
Volume	8894.1(4)		8894.1(4)
Space group	C 2/c		C 1 2/c 1
Hall group	-C 2yc		-C 2yc
Moiety formula	C16 H9 F3 N2 O3		C16 H9 F3 N2 O3
Sum formula	C16 H9 F3 N2 O3		C16 H9 F3 N2 O3
Mr	334.25		334.25
Dx, g cm-3	1.498		1.498
Z	24		24
Mu (mm-1)	1.132		1.132
F000	4080.0		4080.0
F000’	4096.56		
h,k,lmax	26,17,37		26,17,37
Nref	8905		8678
Tmin,Tmax	0.762,0.788		0.780,1.000
Tmin’	0.762		

Correction method= # Reported T Limits: Tmin=0.780 Tmax=1.000

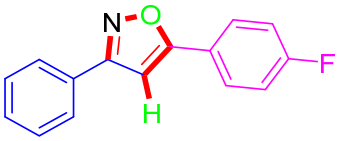
AbsCorr = MULTI-SCAN

Data completeness= 0.975	Theta(max)= 73.057
R(reflections)= 0.0703(6235)	wR2(reflections)= 0.2115(8678)
S = 1.073 Npar = 730	

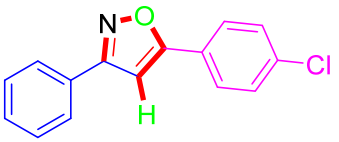
7. Characterization Data of Products



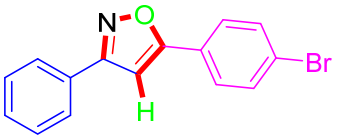
3,5-diphenylisoxazole (4aa). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 61% yield; m.p. = 133–134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.77 (m, 4H), 7.58 – 7.38 (m, 6H), 6.84 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 163.0, 130.2, 130.0, 129.1, 129.0, 128.9, 127.4, 126.8, 125.8, 97.5; HRMS[M+H]$^+$ calcd for $C_{15}H_{11}NO$: 222.0913, found 222.0909.



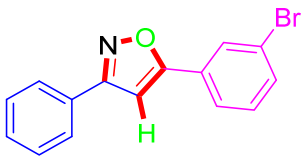
5-(4-fluorophenyl)-3-phenylisoxazole (4ab). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 65% yield; m.p. = 163–164 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 – 7.80 (m, 4H), 7.52 – 7.44 (m, 3H), 7.22 – 7.15 (m, 2H), 6.78 (s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.4, 163.8 (d, $^{1}J_{CF}$ = 249.9 Hz), 163.0, 130.1, 129.0, 127.9 (d, $^{3}J_{CF}$ = 8.6 Hz) , 127.8, 126.8, 123.8 (d, $^{4}J_{CF}$ = 3.3 Hz), 116.2 (d, $^{2}J_{CF}$ = 22.1 Hz), 97.3; ^{19}F NMR (564 MHz, $CDCl_3$) δ -109.44 – -109.48 (m). HRMS[M+H]$^+$ calcd for $C_{15}H_{10}FNO$: 240.0819, found 240.0828.



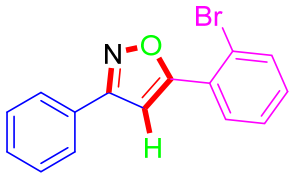
5-(4-chlorophenyl)-3-phenylisoxazole (4ac). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 71% yield; m.p.= 166– 168; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 – 7.83 (m, 2H), 7.80 – 7.75 (m, 2H), 7.51 – 7.44 (m, 5H), 6.82 (s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.2, 163.0, 136.2, 130.1, 129.3, 128.9, 128.9, 127.0, 126.7, 125.9, 97.7. HRMS[M+H]$^+$ calcd for $C_{15}H_{10}ClNO$: 256.0529, found 256.0536.



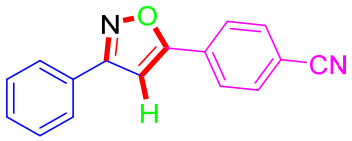
5-(4-bromophenyl)-3-phenylisoxazole (4ad). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 68% yield; m.p. = 177–179 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 – 7.79 (m, 2H), 7.67 (dd, *J* = 40.6, 8.4 Hz, 4H), 7.48 (d, *J* = 5.5 Hz, 3H), 6.84 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.3, 163.1, 132.3, 130.1, 129.0, 128.9, 127.3, 126.8, 126.3, 124.6, 97.9; HRMS[M+H]$^+$ calcd for $C_{15}H_{10}BrNO$: 300.0019, found 300.0024.



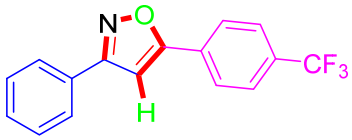
5-(3-bromophenyl)-3-phenylisoxazole (4ae). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a light blue solid: 73% yield; m.p. = 124–126 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.86 (dd, *J* = 7.4, 2.1 Hz, 2H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.58 (dd, *J* = 8.0, 0.7 Hz, 1H), 7.52 – 7.43 (m, 3H), 7.36 (t, *J* = 7.9 Hz, 1H), 6.85 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.7, 163.0, 133.1, 130.6, 130.2, 129.2, 129.0, 128.8, 128.8, 126.8, 124.3, 123.1, 98.32; HRMS[M+H]$^+$ calcd for $C_{15}H_{10}BrNO$: 300.0019, found 300.0024.



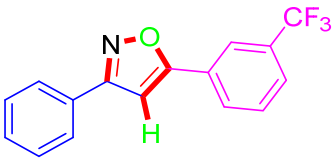
5-(2-bromophenyl)-3-phenylisoxazole (4af). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a light yellow solid: 64% yield; m.p. = 107– 108 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 – 7.87 (m, 3H), 7.73 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.52 – 7.43 (m, 4H), 7.33 – 7.27 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.9, 162.7, 134.2, 131.0, 130.11, 130.0, 129.0, 128.9, 128.3, 127.7, 126.8, 121.1, 102.3; HRMS[M+H]$^+$ calcd for $C_{15}H_{10}BrNO$: 300.0019, found 300.0024.



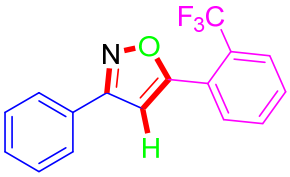
4-(3-phenylisoxazol-5-yl)benzonitrile (4ag). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a light purple solid: 85% yield; m.p. =196– 197 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 – 7.74 (m, 6H), 7.49 (s, 3H), 6.96 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.1, 163.2, 132.8, 131.1, 130.4, 129.0, 128.5, 126.8, 126.2, 118.1, 113.6, 99.67 ; HRMS[M+H]$^+$ calcd for $C_{16}H_{10}N_2O$: 247.0866, found 247.0863.



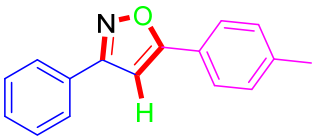
3-phenyl-5-(4-(trifluoromethyl)phenyl)isoxazole (4ah). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a green solid: 83% yield; m.p. =185– 187 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.13 (d, *J* = 8.2 Hz, 2H), 7.97 – 7.90 (m, 4H), 7.82 (s, 1H), 7.58 – 7.50 (m, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.7, 163.2, 130.3, 129.6 (d, $^{1}J_{CF}$ = 272.9 Hz), 129.0, 128.7, 126.8, 126.1, 126.1, 126.1, 126.0, 98.9; ^{19}F NMR (564 MHz, $CDCl_3$) δ -62.94 (s). HRMS[M+H]$^+$ calcd for $C_{16}H_{10}F_3NO$: 290.0787, found 290.0779.



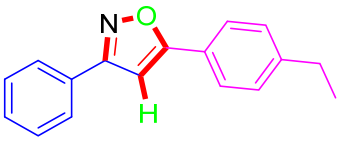
3-phenyl-5-(3-(trifluoromethyl)phenyl)isoxazole (4ai). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a blue solid: 72% yield; m.p. = 128– 130 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 (s, 1H), 8.04 (d, *J* = 7.8 Hz, 1H), 7.91 – 7.86 (m, 2H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 7.53 – 7.47 (m, 3H), 6.93 (s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.9, 163.3, 131.8 (d, $^{2}J_{CF}$ = 32 Hz), 130.4, 129.8, 129.1, 129.0 (d, $^{5}J_{CF}$ = 0.9 Hz), 128.9, 128.3, 127.0, 126.9 (dd, $^{4}J_{CF}$ = 3.6 Hz), 124.7, 122.8 (dd, $^{3}J_{CF}$ = 3.9 Hz), 98.7; ^{19}F NMR (564 MHz, $CDCl_3$) δ -62.93 (s). HRMS[M+H]$^{+}$ calcd for $C_{16}H_{10}F_3NO$: 290.0787, found 290.0779.



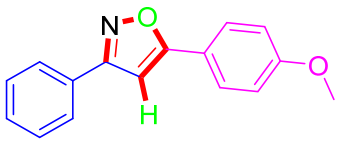
3-phenyl-5-(2-(trifluoromethyl)phenyl)isoxazole (4aj). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow oily substance: 60% yield; m.p. = 194– 196 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.81 (m, 4H), 7.65 (dt, *J* = 33.1, 7.5 Hz, 2H), 7.54 – 7.42 (m, 3H), 6.87 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 162.8, 132.1, 131.0, 130.2 (d, J_{CF} = 6.2 Hz), 129.0, 128.8, 128.0 (d, J_{CF} = 46.7 Hz), 126.9, 126.7(dd, J_{CF} = 8.1 Hz), 126.3 (d, J_{CF} = 3 Hz) 124.9, 122.2, 102.4 (dd, J_{CF} = 5.4 Hz); ^{19}F NMR (564 MHz, $CDCl_3$) δ -59.19 (s). HRMS[M+H]$^{+}$ calcd for $C_{16}H_{10}F_3NO$: 290.0787, found 290.0779.



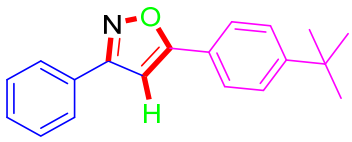
3-phenyl-5-(p-tolyl)isoxazole (4ak). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a light yellow solid: 53% yield; m.p. = 126– 128 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 – 7.84 (m, 2H), 7.73 (d, *J* = 8.1 Hz, 2H), 7.52 – 7.43 (m, 3H), 7.29 (d, *J* = 7.9 Hz, 2H), 6.78 (s, 1H), 2.41 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.6, 162.9, 140.5, 123.0, 129.6, 129.2, 128.9, 126.8, 125.8, 124.7, 96.9, 21.5; HRMS[M+H]$^{+}$ calcd for $C_{16}H_{13}NO$: 236.1070, found 236.1075.



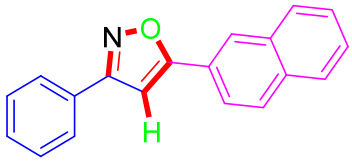
5-(4-ethylphenyl)-3-phenylisoxazole (4al). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 51% yield; m.p. = 82– 83 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 7.7, 1.4 Hz, 2H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.50 – 7.46 (m, 3H), 7.32 (d, *J* = 8.1 Hz, 2H), 6.79 (s, 1H), 2.71 (q, *J* = 7.6 Hz, 2H), 1.28 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.6, 162.9, 146.8, 129.9, 129.2, 128.9, 128.5, 126.8, 125.9, 125.0, 96.9, 28.8, 15.4; HRMS[M+H]$^{+}$ calcd for $C_{17}H_{15}NO$: 250.1226, found 250.1224.



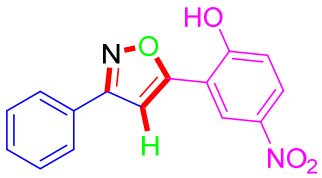
5-(4-methoxyphenyl)-3-phenylisoxazole (4am). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 45% yield; m.p. = 119– 121 °C; ^{1}H NMR (600 MHz, d_2o) δ 7.86 (dd, *J* = 7.8, 1.5 Hz, 2H), 7.78 (d, *J* = 8.8 Hz, 2H), 7.51 – 7.44 (m, 3H), 7.00 (d, *J* = 8.8 Hz, 2H), 6.71 (s, 1H), 3.87 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.3, 162.9, 161.1, 129.9, 129.2, 128.8, 127.4, 126.7, 120.3, 114.3, 96.1, 55.4; HRMS[M+H]$^+$ calcd for $C_{16}H_{14}NO_2$: 252.1019, found 252.1030. This compound was known.[2]



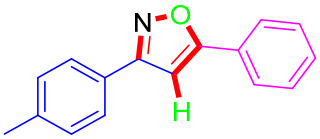
5-(4-(tert-butyl)phenyl)-3-phenylisoxazole (4an). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 42% yield; m.p. = 88– 89 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 – 7.86 (m, 2H), 7.80 – 7.76 (m, 2H), 7.53 – 7.45 (m, 5H), 6.79 (s, 1H), 1.36 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.5, 162.9, 153.6, 129.9, 129.2, 128.8, 126.8, 125.9, 125.6, 124.7, 96.9, 34.9, 31.1; HRMS[M+H]$^+$ calcd for $C_{19}H_{19}NO$: 278.1539, found 278.1548.



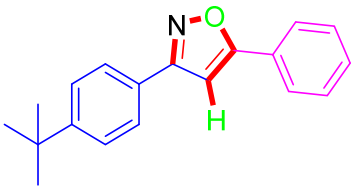
5-(naphthalen-2-yl)-3-phenylisoxazole (4ao). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 45% yield; m.p. = 160–161 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.98 – 7.85 (m, 6H), 7.59 – 7.46 (m, 5H), 6.95 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.4, 163.1, 133.9, 133.1, 130.0, 128.9, 128.9, 128.7, 127.9, 127.3, 126.9, 126.8, 125.6, 122.9, 97.8; HRMS[M+H]$^+$ calcd for $C_{19}H_{13}NO$: 272.1070, found 272.1064.



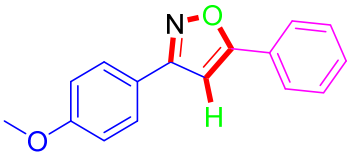
4-nitro-2-(3-phenylisoxazol-5-yl)phenol (4ap). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 46% yield; m.p. = 171-172 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.47 (d, *J* = 2.4 Hz, 1H), 8.28 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.97 – 7.82 (m, 2H), 7.56 – 7.43 (m, 3H), 7.01 (d, *J* = 9.0 Hz, 1H), 6.62 (d, *J* = 8.3 Hz, 1H), 6.36 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.3, 154.3, 143.3, 131.2, 129.4, 128.5, 127.6, 127.5, 126.3, 123.4, 111.5, 92.7, 84.3; HRMS[M+H]$^+$ calcd for $C_{15}H_{10}N_2O_4$: 283.0713, found 283.0709.



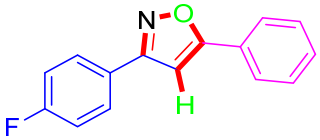
5-phenyl-3-(p-tolyl)isoxazole (4ba). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 65% yield; m.p. = 128-129 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 – 7.81 (m, 2H), 7.77 (d, *J* = 8.1 Hz, 2H), 7.51 – 7.41 (m, 3H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.81 (s, 1H), 2.42 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.3, 163.0, 130.2, 129.7, 129.1, 127.6, 126.8, 126.3, 125.9, 97.5, 21.5; HRMS[M+H]$^+$ calcd for $C_{16}H_{13}NO$: 236.1070, found 236.1075.



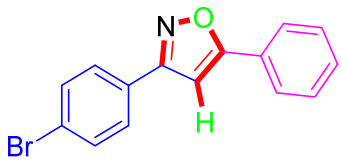
3-(4-(tert-butyl)phenyl)-5-phenylisoxazole (4ca). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 69% yield; m.p. = 111-113 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 – 7.78 (m, 4H), 7.53 – 7.42 (m, 5H), 6.82 (s, 1H), 1.37 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.1, 162.8, 153.3, 130.1, 128.9, 127.5, 126.5, 126.2, 125.8, 125.8, 97.4, 34.8, 31.2; HRMS[M+H]$^+$ calcd for $C_{19}H_{19}NO$: 278.1545, found 278.1535.



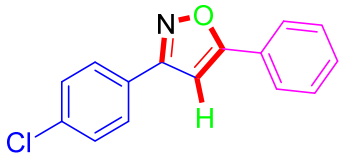
3-(4-methoxyphenyl)-5-phenylisoxazole (4da). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 45% yield; mp = 114-115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.78 (m, 4H), 7.52 – 7.41 (m, 3H), 7.03 – 6.95 (m, 2H), 6.78 (s, 1H), 3.86 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 162.6, 161.0, 130.1, 129.0, 128.2, 127.5, 125.8, 121.6, 114.3, 97.2, 55.4. HRMS[M+H]$^+$ calcd for $C_{16}H_{14}NO_2$: 252.1019, found 252.1030.



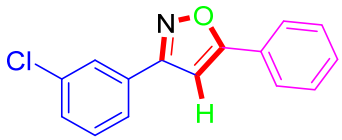
3-(4-fluorophenyl)-5-phenylisoxazole (4ea). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 52% yield; mp = 166-167 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 – 7.81 (m, 4H), 7.55 – 7.42 (m, 3H), 7.17 (t, *J* = 8.6 Hz, 2H), 6.79 (s, 1H) ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.7, 164.0 (d, $^{1}J_{CF}$ = 248.7 Hz), 162.2, 130.5, 129.2, 128.8 (d, $^{3}J_{CF}$ = 8.3 Hz), 127.5, 126.0, 125.5 (d, $^{4}J_{CF}$ = 3.3 Hz), 116.2 (d, $^{2}J_{CF}$ = 21.8 Hz), 97.4; ^{19}F NMR (564 MHz, $CDCl_3$) δ -110.56 - -110.61 (m). HRMS[M+H]$^+$ calcd for $C_{15}H_{10}FNO$: 240.0819, found 240.0828.



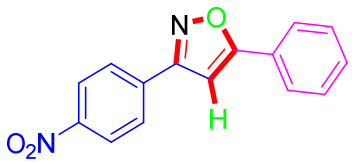
3-(4-bromophenyl)-5-phenylisoxazole (4fa). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 51% yield; m.p. = 175-177 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 – 7.44 (m, 9H), 6.80 (s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.6, 162.0, 132.1, 130.3, 129.0, 128.2, 127.2, 125.8, 124.3, 97.2, 77.2; HRMS[M+H]$^{+}$ calcd for $C_{15}H_{10}BrNO$: 300.0019, found 301.0024.



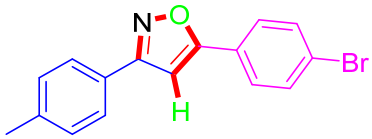
3-(4-chlorophenyl)-5-phenylisoxazole (4ga). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 51% yield; m.p. = 173-174 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.77 (m, 4H), 7.56 – 7.41 (m, 5H), 6.80 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 162.0, 136.0, 130.4, 129.2, 129.0, 128.1, 127.6, 127.2, 125.8, 97.3; HRMS[M+H]$^{+}$ calcd for $C_{15}H_{10}ClNO$: 256.0529, found 256.0536. This compound was known.[3]



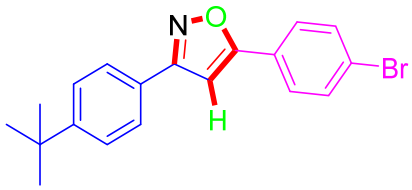
3-(3-chlorophenyl)-5-phenylisoxazole (4ha). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 41 % yield; m.p. = 168-170 ^{o}C; ^{1}H NMR (400 MHz, DMSO) δ 11.90 (s, 1H), 7.65 (dd, 8.8, 2.8Hz, 4H), 7.41 (d, 8.8Hz,2H), 7.06 (d, 8.8Hz, 2H), 4.91 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.8, 145.5, 134.2, 133.9, 131.4, 130.7, 128.7, 128.6, 114.7, 56.2, 51.8. HRMS[M+H]$^{+}$ calcd for $C_{15}H_{10}ClNO$: 256.0529, found 256.0536.



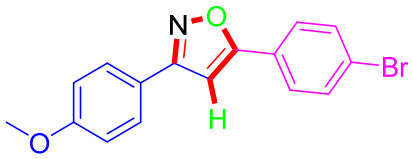
3-(4-nitrophenyl)-5-phenylisoxazole (4ia). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a light yellow solid: 46% yield; m.p. = 186-188 ^{o}C; ^{1}H NMR (600 MHz, DMSO) δ 8.39 (d, *J* = 8.8 Hz, 2H), 8.19 (d, *J* = 8.8 Hz, 2H), 7.95 – 7.89 (m, 2H), 7.77 (s, 1H), 7.61 – 7.53 (m, 3H); ^{13}C NMR (151 MHz, DMSO) δ 171.0, 161.6, 148.8, 135.0, 131.2, 129.8, 128.3, 126.9, 126.1, 124.8, 99.5; This compound was known.[2]



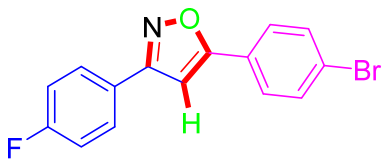
5-(4-bromophenyl)-3-(p-tolyl) isoxazole (4bd). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a deep pink solid: 70% yield; m.p. = 202-203 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.49 (m, 6H), 7.27 (dd, *J* = 13.8, 4.5 Hz, 2H), 6.80 (s, 1H), 2.41 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 163.0, 140.3, 132.3, 129.6, 127.2, 126.7, 126.4, 126.0, 124.5, 97.8, 21.4; HRMS[M+H]$^+$ calcd for $C_{16}H_{12}BrNO$: 314.0175, found 314.0182.



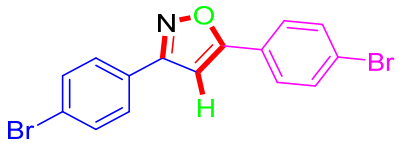
5-(4-bromophenyl)-3-(4-(tert-butyl) phenyl) isoxazole (4cd). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as an orange solid: 73% yield; m.p. = 158-159 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 – 7.76 (m, 2H), 7.74 – 7.68 (m, 2H), 7.63 (d, *J* = 6.9 Hz, 2H), 7.51 (d, *J* = 6.8 Hz, 2H), 6.82 (d, *J* = 1.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 163.0, 153.5, 132.2, 127.3, 126.5, 126.4, 126.0, 125.9, 124.5, 97.8; HRMS[M+H]$^+$ calcd for $C_{19}H_{18}BrNO$: 356.0645, found 356.0638.



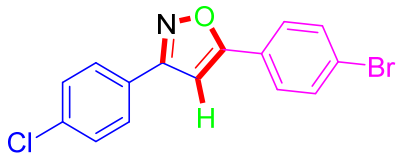
5-(4-bromophenyl)-3-(4-methoxyphenyl) isoxazole (4dd). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 48% yield; m.p. = 196-197 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 – 7.60 (m, 6H), 7.02 – 6.97 (m, 2H), 6.78 (s, 1H), 3.87 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.0, 162.6, 161.0, 132.2, 128.1, 127.2, 126.4, 124.4, 121.3, 114.3, 97.6, 55.3; HRMS[M+H]$^+$ calcd for $C_{16}H_{12}BrNO_2$: 330.0124, found 330.0123.



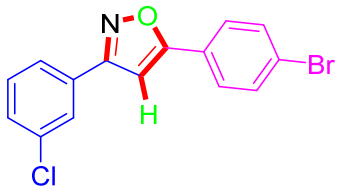
5-(4-bromophenyl)-3-(4-fluorophenyl) isoxazole (4ed) This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a light yellow solid: 60% yield; m.p. = 169-170 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 – 7.82 (m, 2H), 7.70 (d, *J* = 8.5 Hz, 2H), 7.63 (d, *J* = 8.5 Hz, 2H), 7.17 (t, *J* = 8.6 Hz, 2H), 6.79 (s, 1H) ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.5, 163.9 (d, $^{1}J_{CF}$ = 249 Hz), 162.2 132.3, 128.7 (d, $^{3}J_{CF}$ = 8.4 Hz), 127.3, 126.2, 125.1(d, $^{4}J_{CF}$ =3.5 Hz), 124.7, 116.1 (d, $^{2}J_{CF}$ = 21.8 Hz) 97.7; ^{19}F NMR (564 MHz, $CDCl_3$) δ -110.29 (s). HRMS[M+H]$^+$ calcd for $C_{15}H_9BrFNO$: 319.9904, found 319.9895.



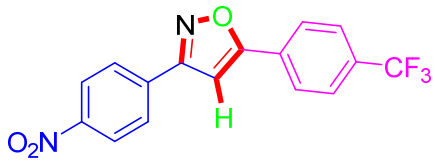
3,5-bis(4-bromophenyl) isoxazole (4fd). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow solid: 57% yield; mp = 212-213 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 – 7.69 (m, 4H), 7.64 – 7.61 (m, 4H), 6.81 (s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.6, 162.2, 132.3, 132.2, 128.3, 127.8, 127.3, 126.1, 124.8, 124.5, 97.6; HRMS[M+H]$^{+}$ calcd for $C_{15}H_9Br_2NO$: 379.9103, found 379.9113.



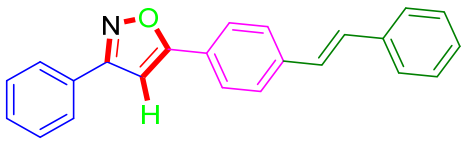
5-(4-bromophenyl)-3-(4-chlorophenyl) isoxazole (4gd). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a red solid: 56% yield; m.p. = 197-198 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.5 Hz, 2H), 7.70 (d, *J* = 8.5 Hz, 2H), 7.63 (d, *J* = 8.5 Hz, 2H), 7.46 (d, *J* = 8.5 Hz, 2H), 6.80 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.6, 162.1, 136.2, 132.3, 129.2, 128.0, 127.3, 127.3, 126.1, 124.7, 97.7; HRMS[M+H]$^{+}$ calcd for $C_{15}H_9BrClNO$: 335.9608, found 335.9605.



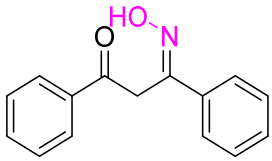
5-(4-bromophenyl)-3-(3-chlorophenyl) isoxazole (4hd). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a light pink solid: 50% yield; m.p. = 118-119 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 – 7.80 (m, 3H), 7.76 (dt, *J* = 7.0, 1.6 Hz, 1H), 7.51 – 7.40 (m, 5H), 6.81 (s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.7, 161.8, 134.9, 130.8, 130.3, 130.2, 130.0, 129.0, 126.9, 125.8, 124.9, 97.3, 77.2; HRMS[M+H]$^{+}$ calcd for $C_{15}H_9BrClNO$: 335.9608, found 335.9605.



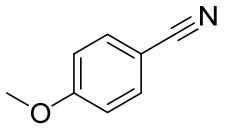
3-(4-nitrophenyl)-5-(4-(trifluoromethyl)phenyl)isoxazole (4ih). This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow solid: 52% yield; m.p. = 194-196 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.38 – 8.35 (m, 2H), 8.08 – 8.05 (m, 2H), 7.98 (d, *J* = 8.1 Hz, 2H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.01 (s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.9, 161.5, 149.0, 134.9, 132.5 (d, $^{2}J_{CF}$ = 32 Hz) 130.1, 127.9, 126.4 (d, $^{3}J_{CF}$ = 3.9), 126.3, 124.5, 123.3, 99.1; ^{19}F NMR (564 MHz, $CDCl_3$) δ -63.01 (s). HRMS[M+H]$^{+}$ calcd for $C_{16}H_9F_3N_2O_3$: 335.0638, found 335.0647.



(E)-3-phenyl-5-(4-styrylphenyl)isoxazole (5). White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.80 (m, 4H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.60 – 7.42 (m, 6H), 7.38 (q, *J* = 7.3 Hz, 2H), 7.31 (d, *J* = 7.3 Hz, 1H), 7.14 (d, *J* = 16.4 Hz, 1H), 6.85 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 163.0, 139.2, 136.9, 130.3, 130.0, 129.1, 128.9, 128.8, 128.1, 127.6, 127.0, 126.8, 126.7, 126.3, 126.2, 97.4.



(E)-3-(hydroxyimino)-1,3-diphenylpropan-1-one (6b). White solid. ^{1}H NMR (600 MHz, DMSO) δ 7.74 – 7.68 (m, 2H), 7.58 – 7.54 (m, 2H), 7.51 – 7.42 (m, 4H), 7.41 – 7.37 (m, 2H), 7.35 (dt, *J* = 9.5, 4.3 Hz, 1H), 3.55 (d, *J* = 0.6 Hz, 2H); ^{13}C NMR (151 MHz, DMSO) δ 157.0, 142.2, 130.5, 130.1, 129.2, 128.6, 128.5, 126.9, 126.2, 108.0, 48.9. This compound was known.[4]



4-methoxybenzonitrile (4'). White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.54 (m, 2H), 6.99 – 6.91 (m, 2H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8 (s), 134.0 (s), 119.2 (s), 114.7 (s), 103.9 (s), 55.5 (s).

8. Reference

[1] J. E. Plevyak, J. E. Dickerson and R. F. Heck, *J. Org. Chem.*, 1979, **44**, 4078.

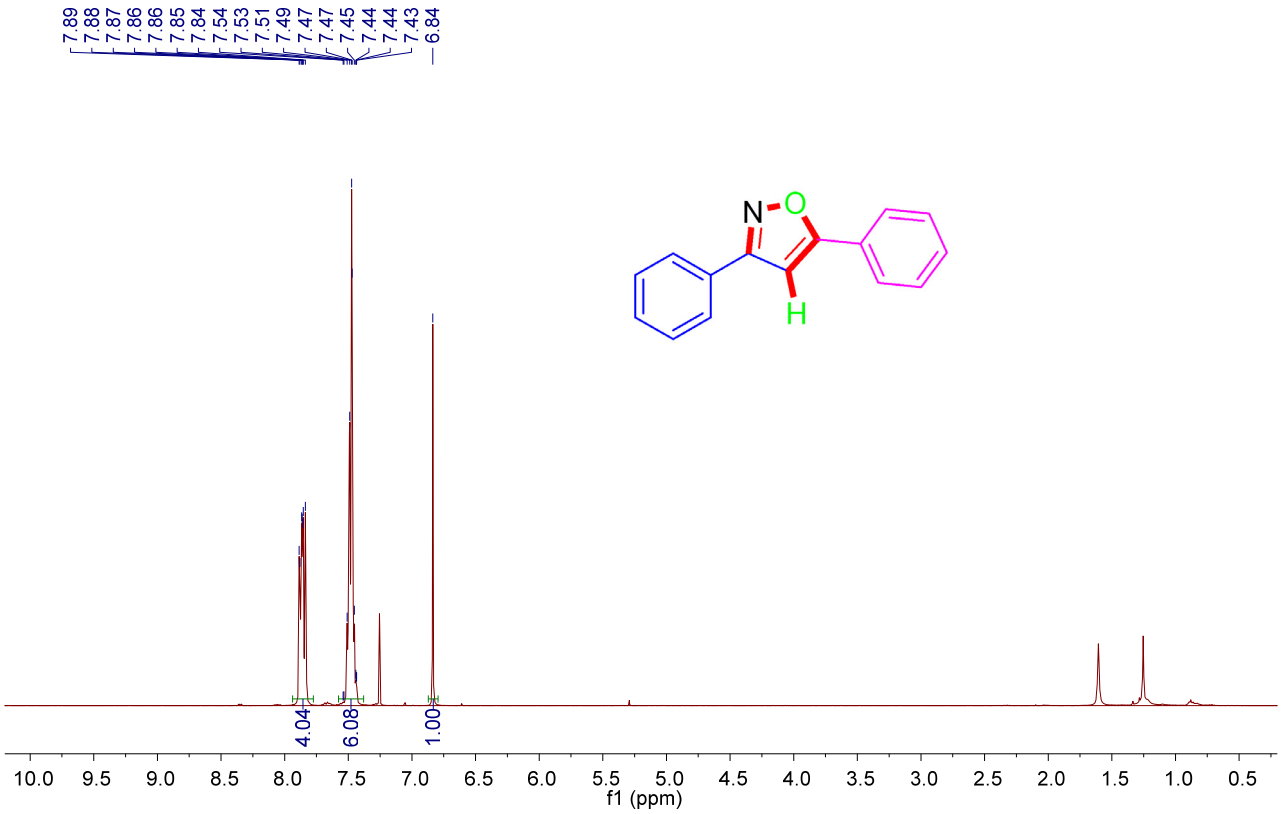
[2] A. M. Jawalekar, E. Reubsaet, F. P. J. T. Rutjes, F. L. van Delft, *Chem Comm.*, 2011, **47**, 3198.

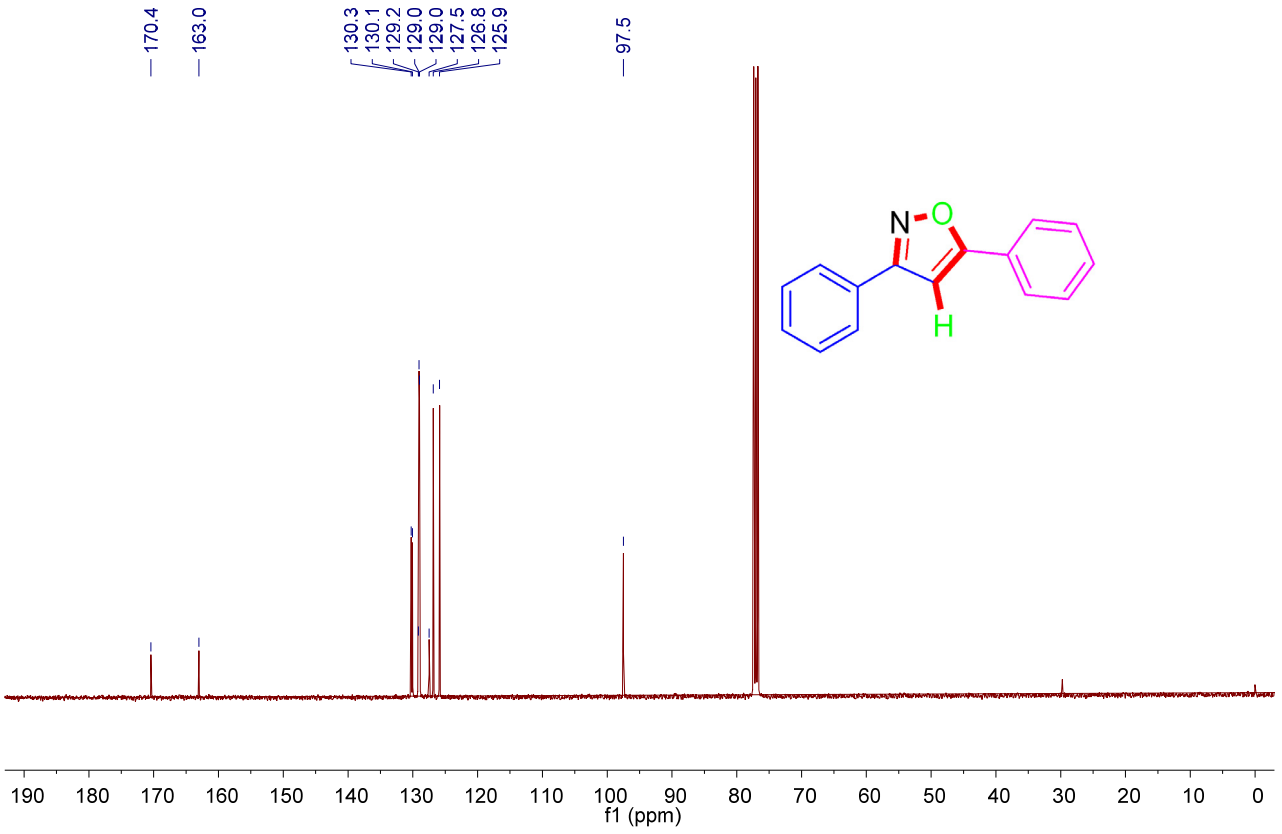
[3] A. Yoshimura, K. R. Middleton, A. D. Todora, B. J. Kastern, S. R. Koski, A. V. Maskaev, V. V. Zhdankin, *Org. Lett.*, 2013, **15**,3805.

[4], T. M. V. D. Pinho e Melo, *Curr. Org. Chem.*, 2005, **9**, 925.

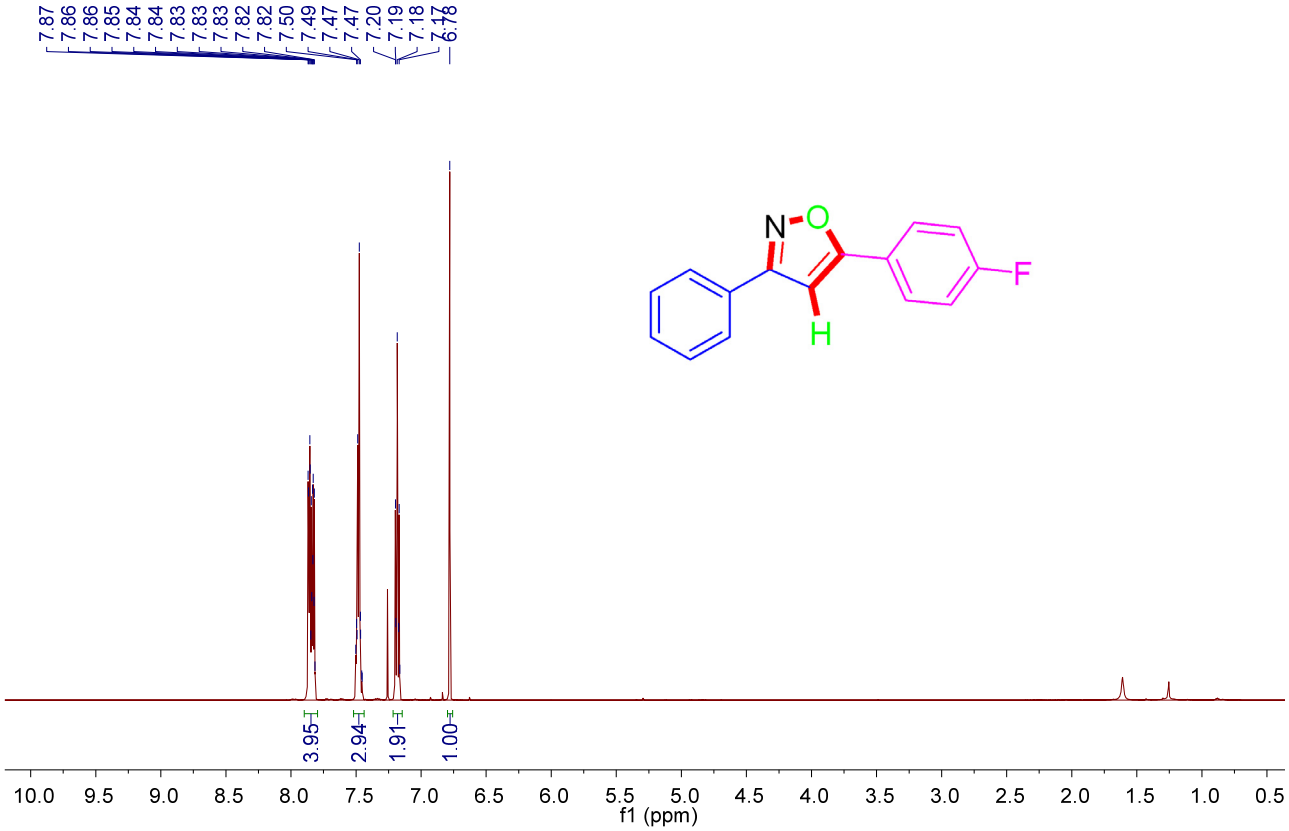
9. The ^{1}H NMR and ^{13}C NMR Spectra of products

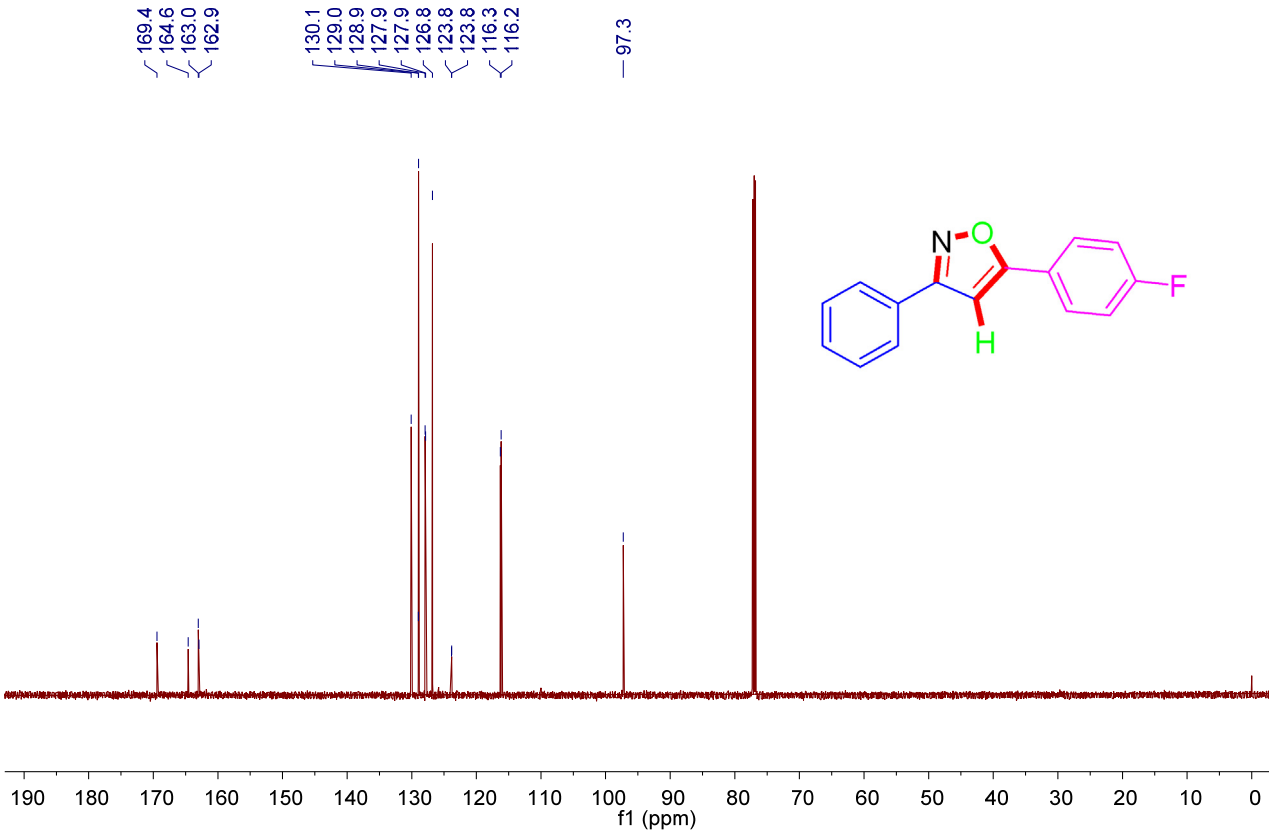
3,5-diphenylisoxazole (4aa).

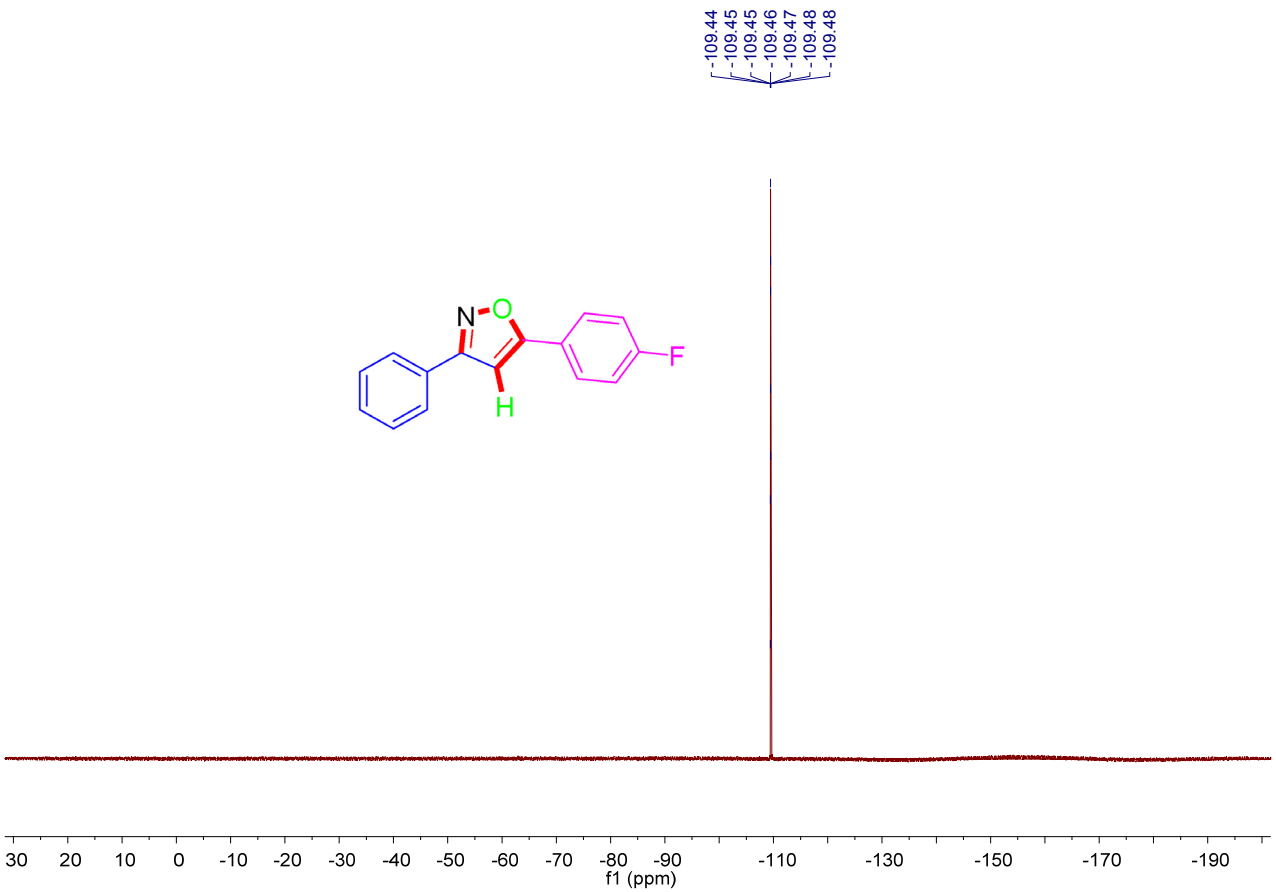




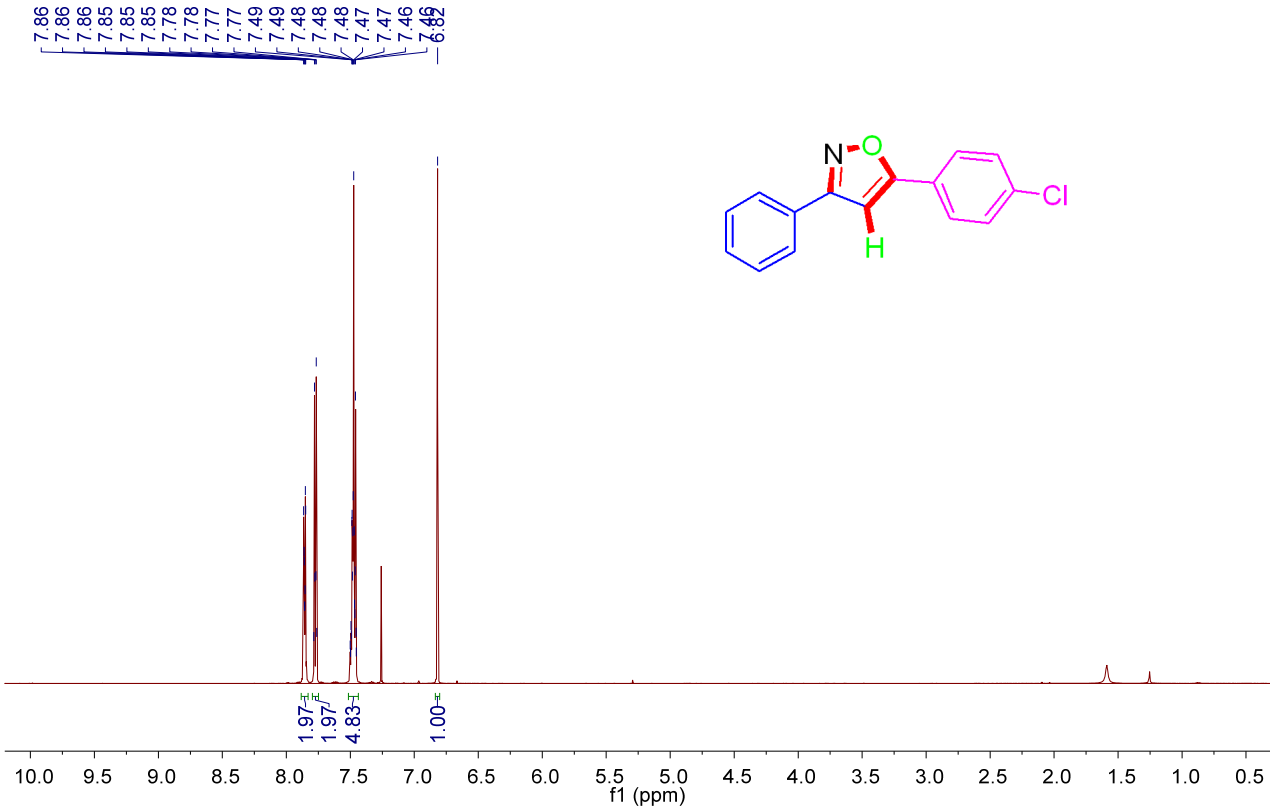
5-(4-fluorophenyl)-3-phenylisoxazole (4ab).

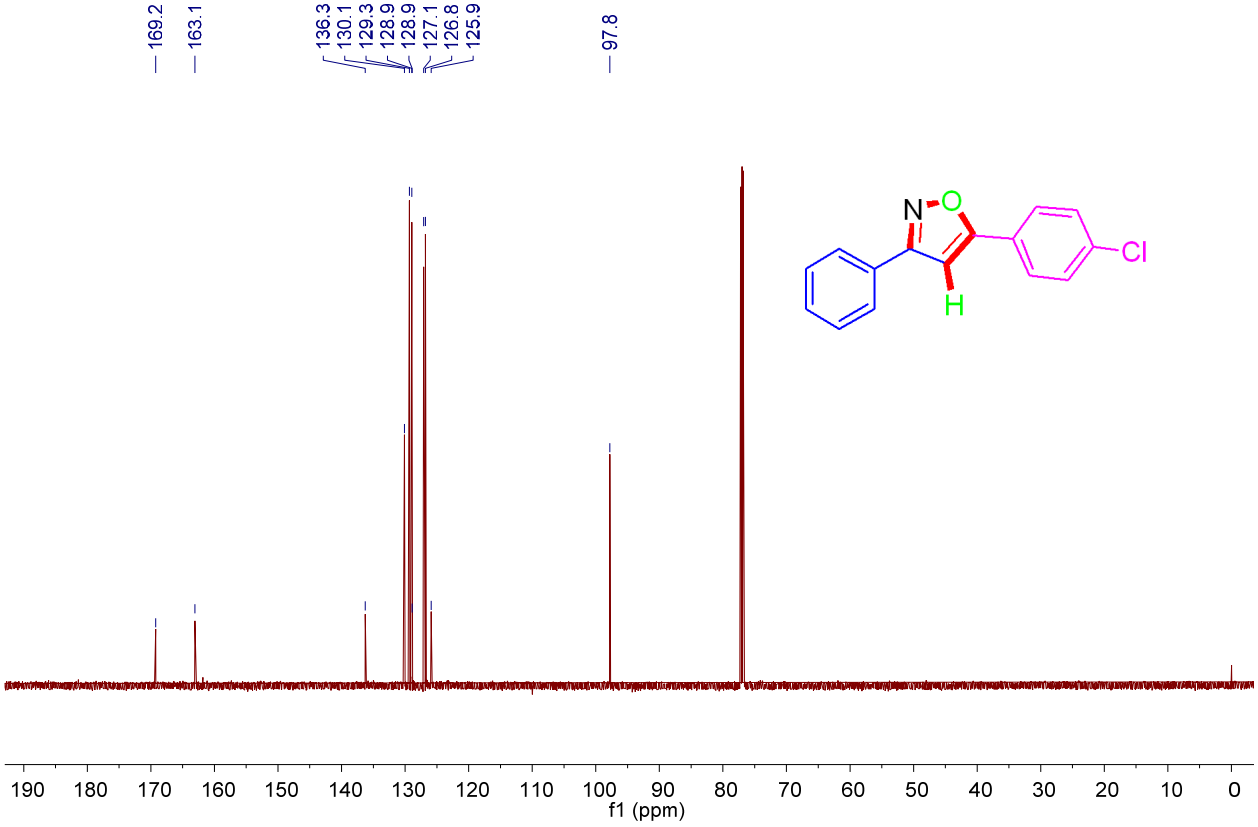




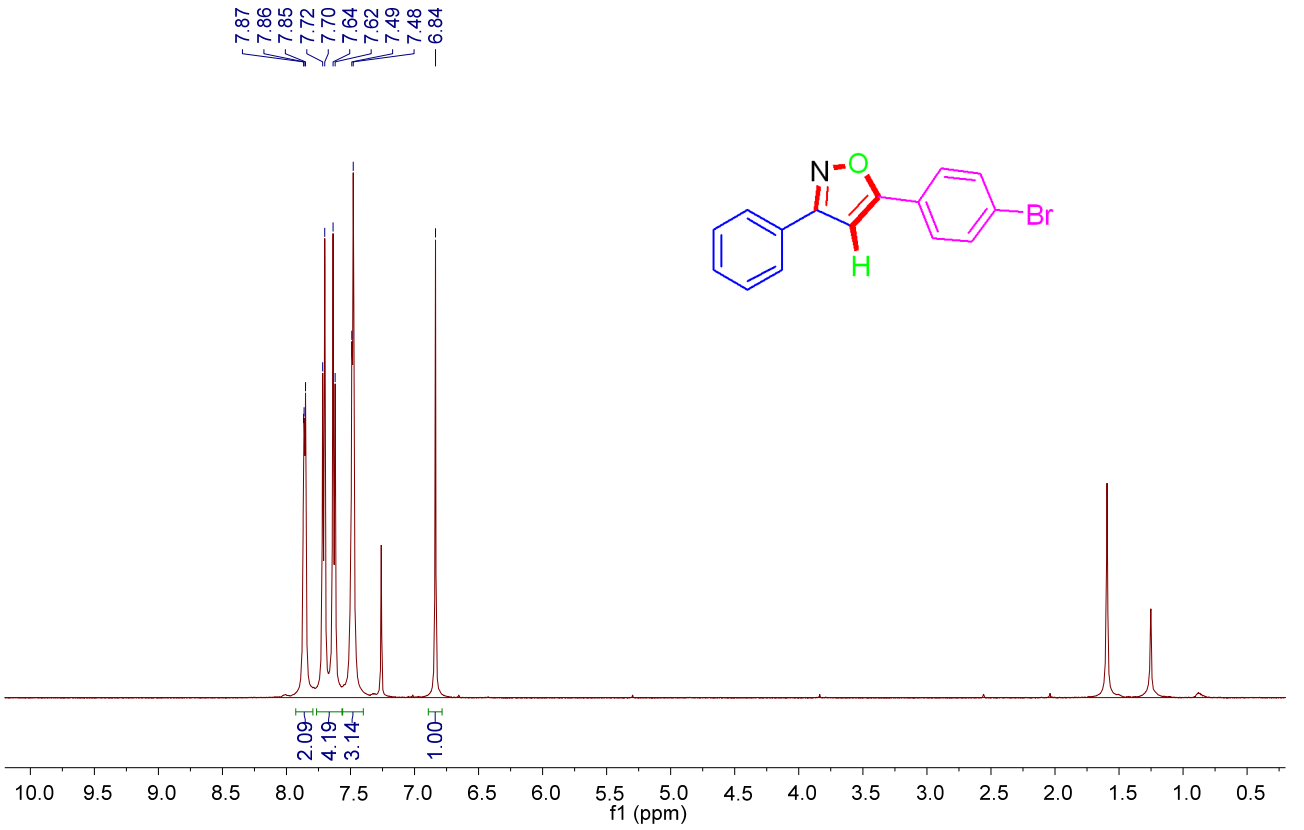

-109.44
-109.45
-109.45
-109.46
-109.47
-109.48
-109.48
N
O
F
H
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-130
-150
-170
-190
f1 (ppm)

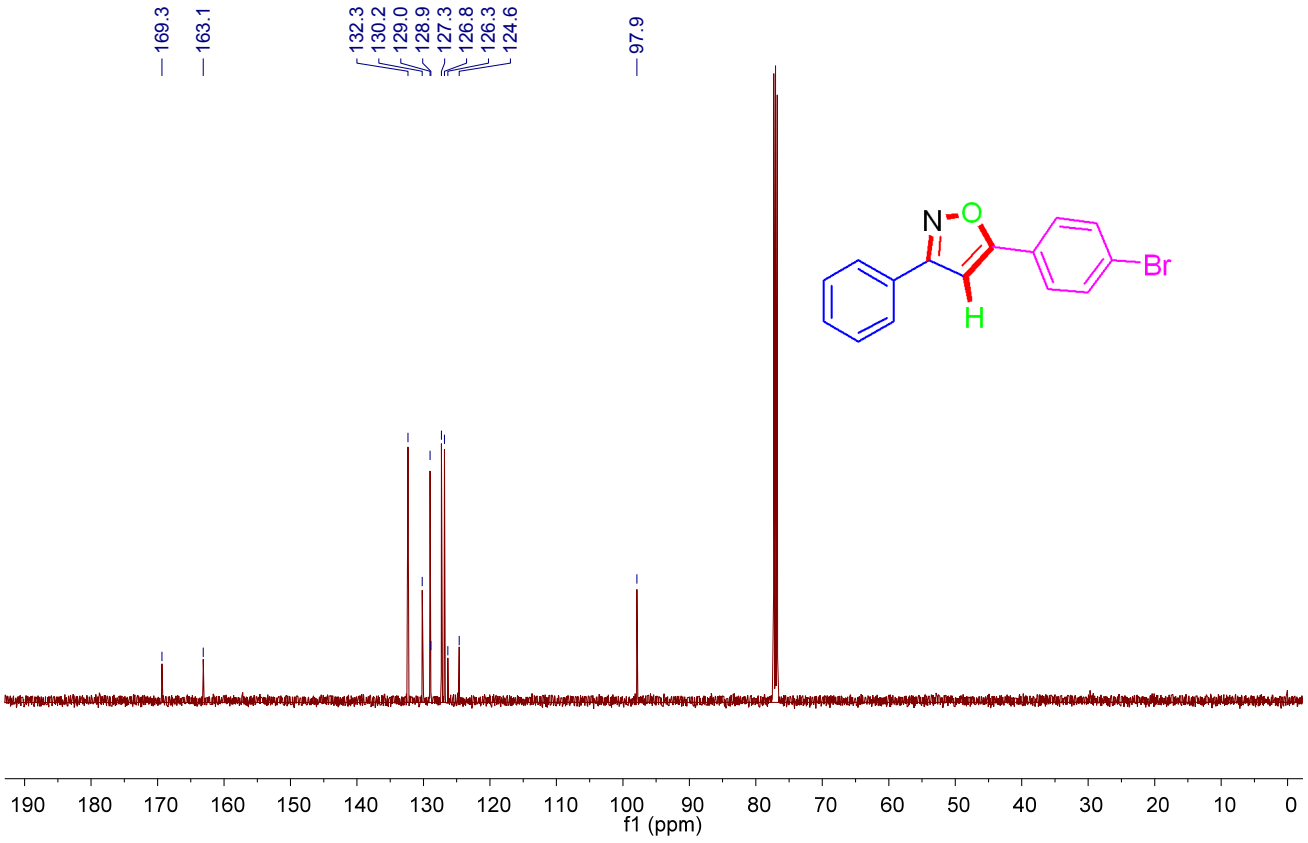
5-(4-chlorophenyl)-3-phenylisoxazole(4ac).



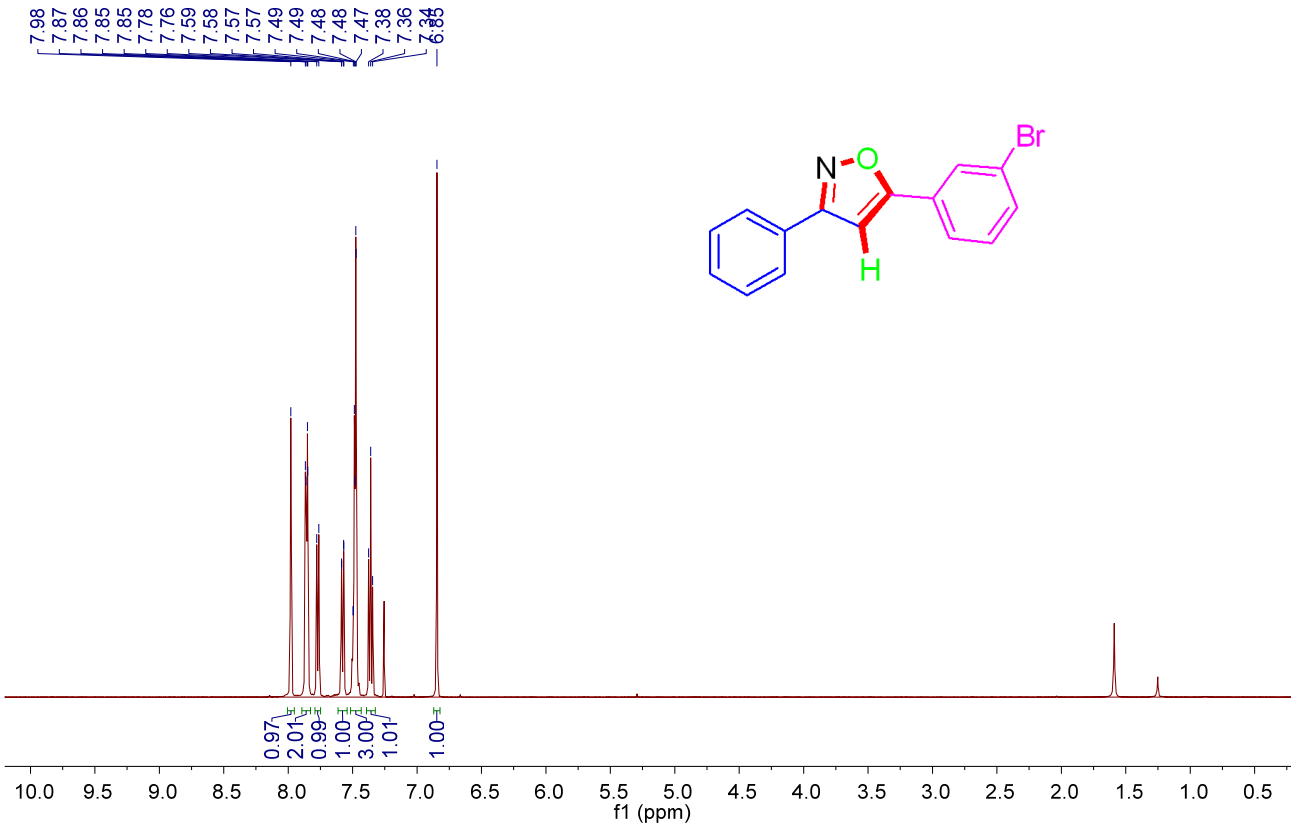


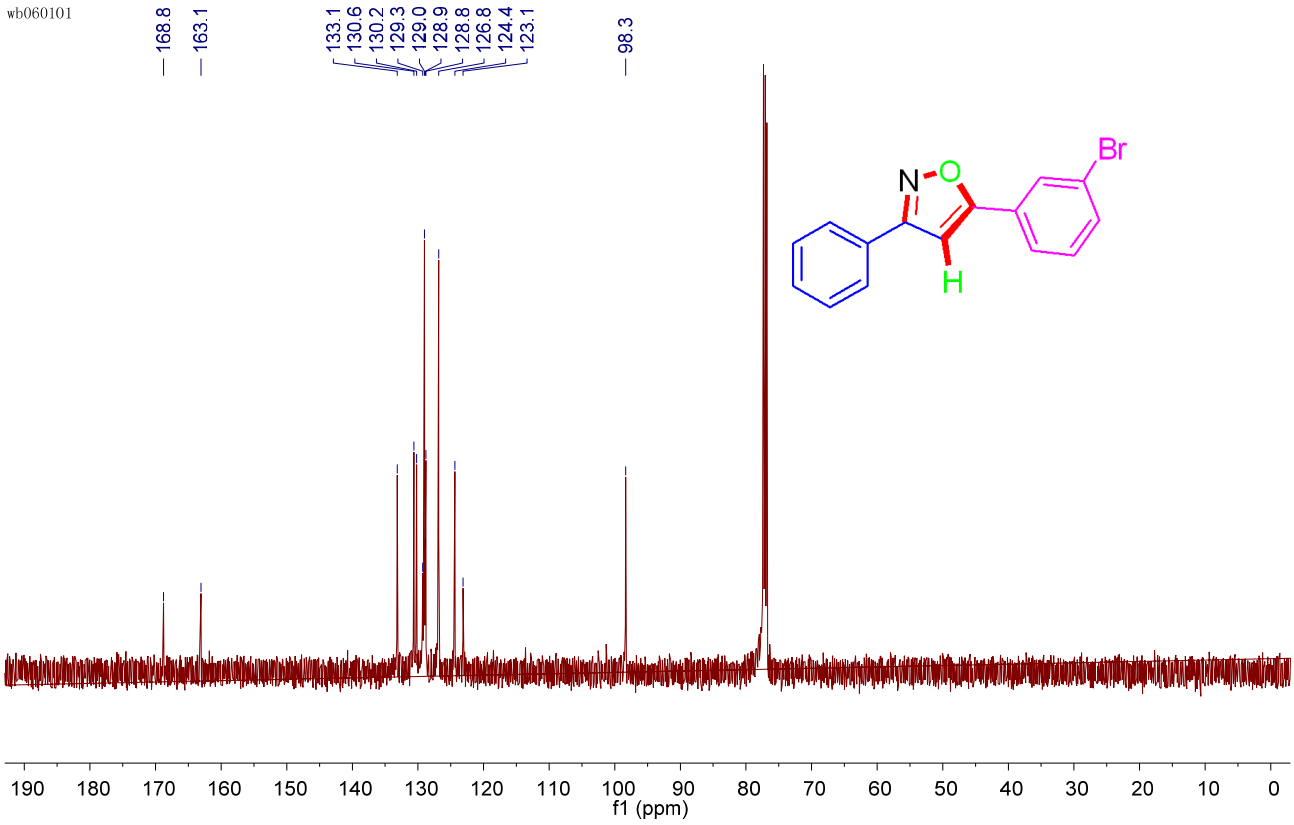
5-(4-bromophenyl)-3-phenylisoxazole (4ad).



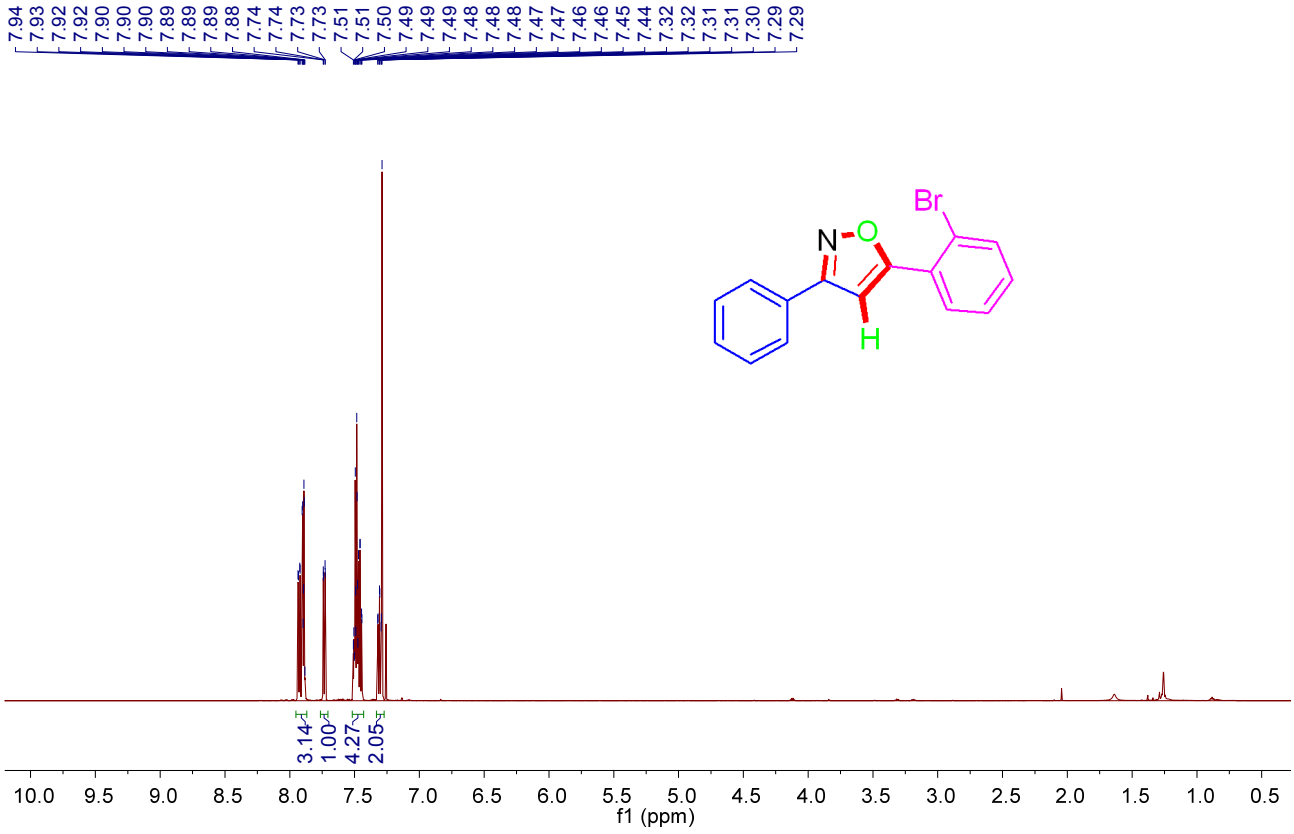


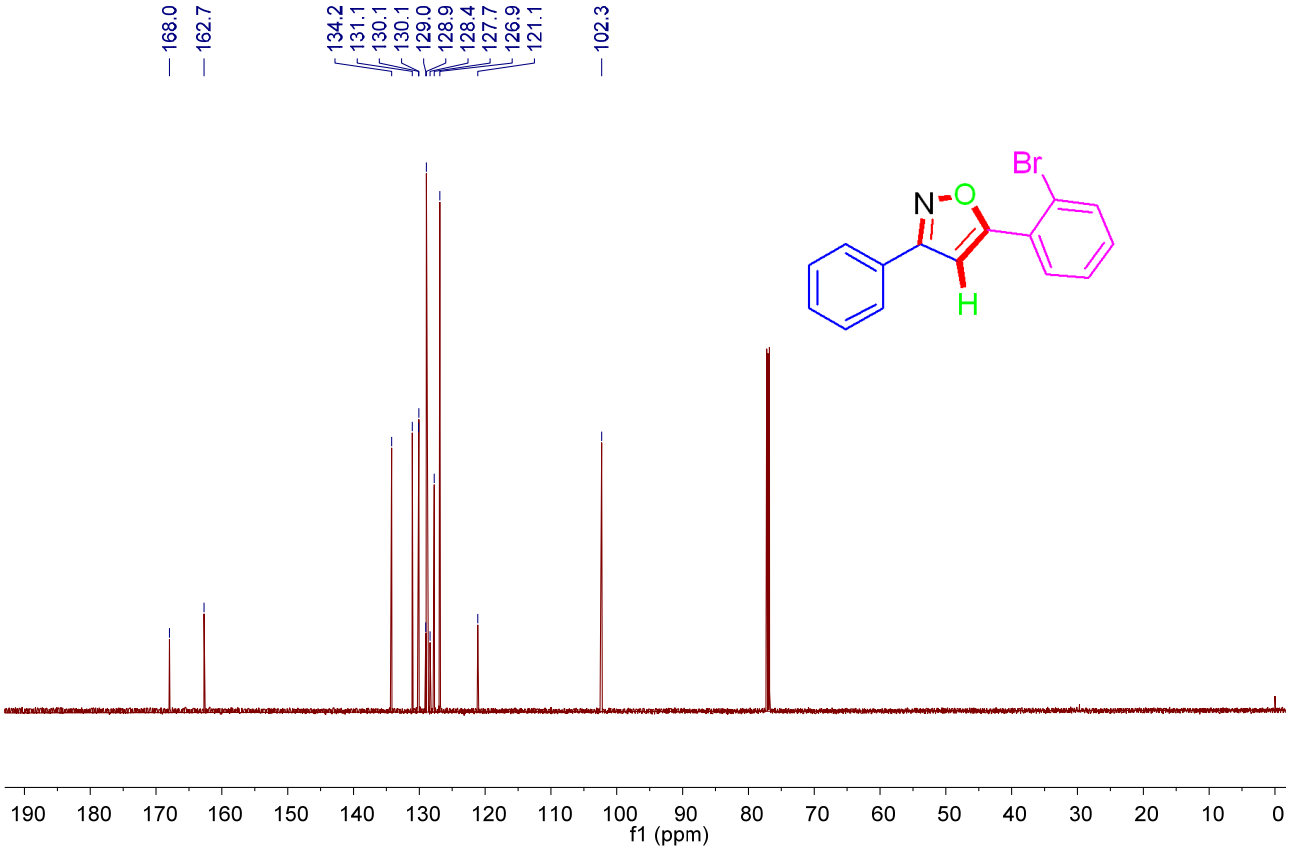
5-(3-bromophenyl)-3-phenylisoxazole (4ae).



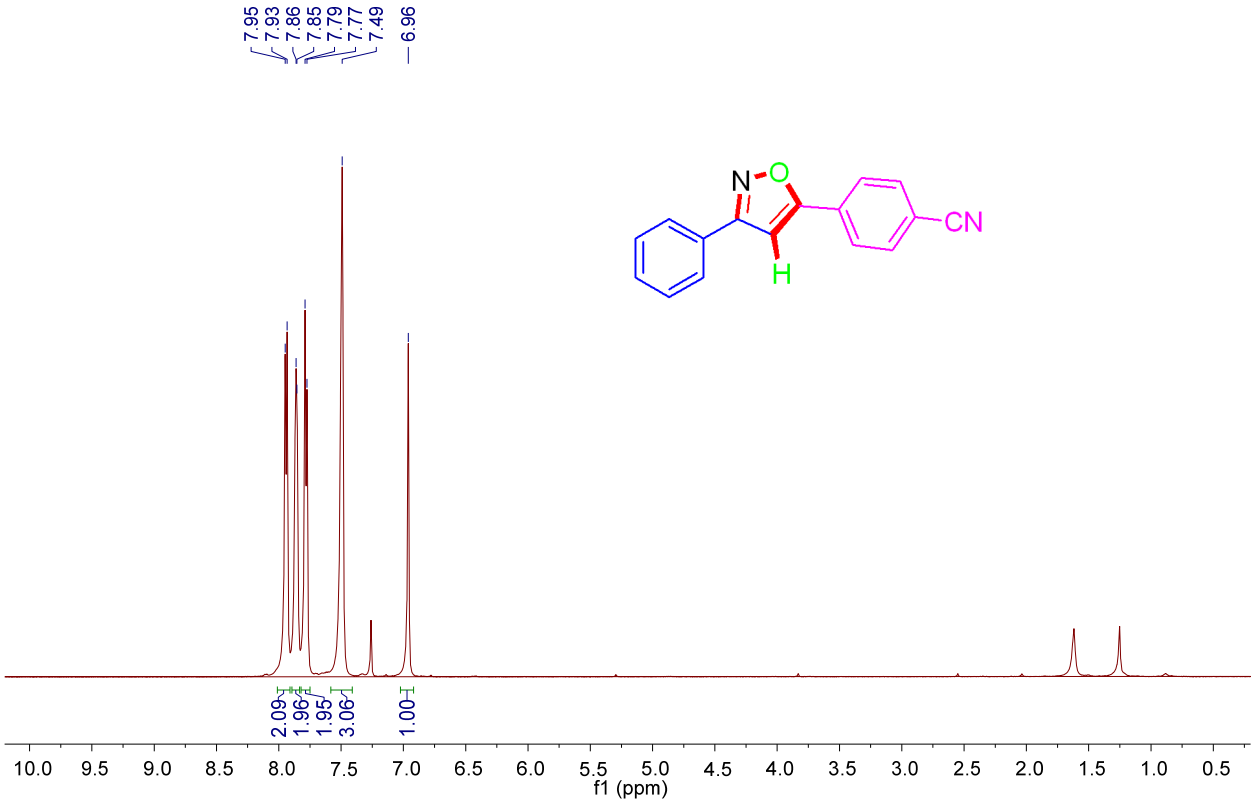


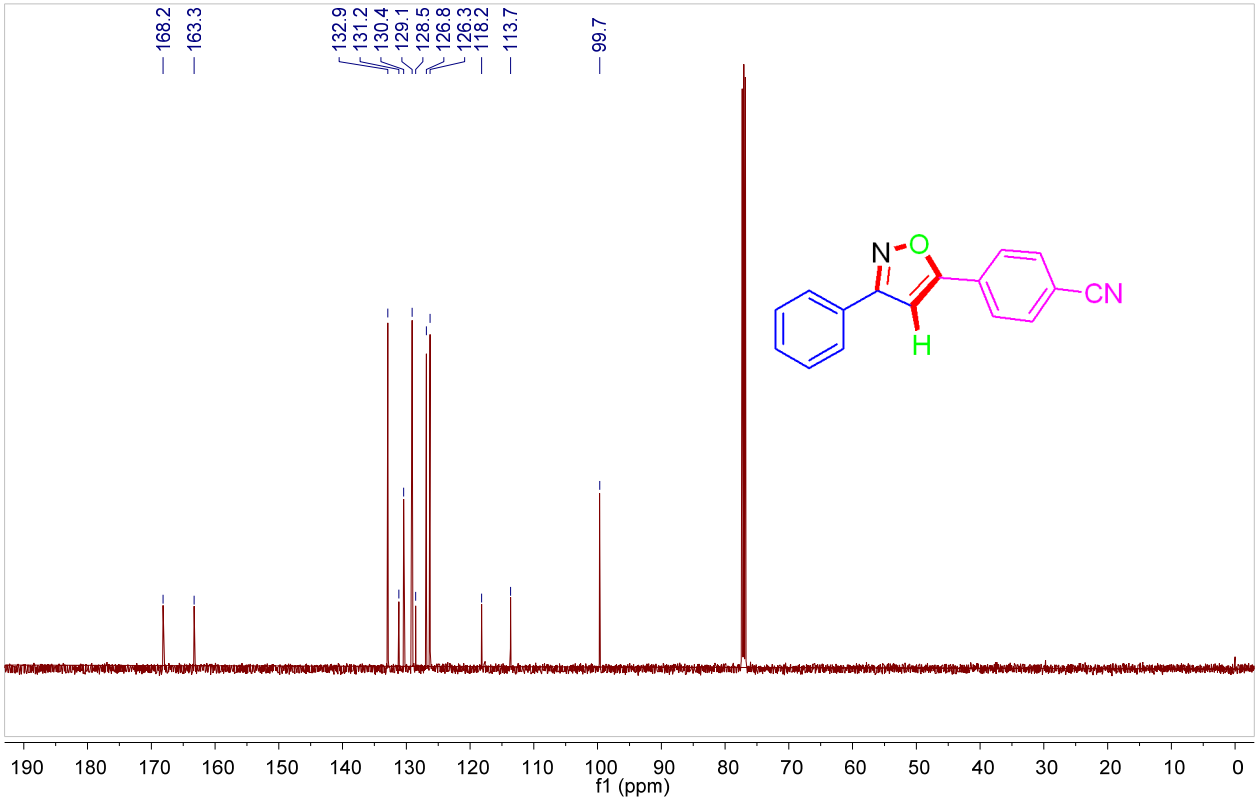
5-(2-bromophenyl)-3-phenylisoxazole (4af).



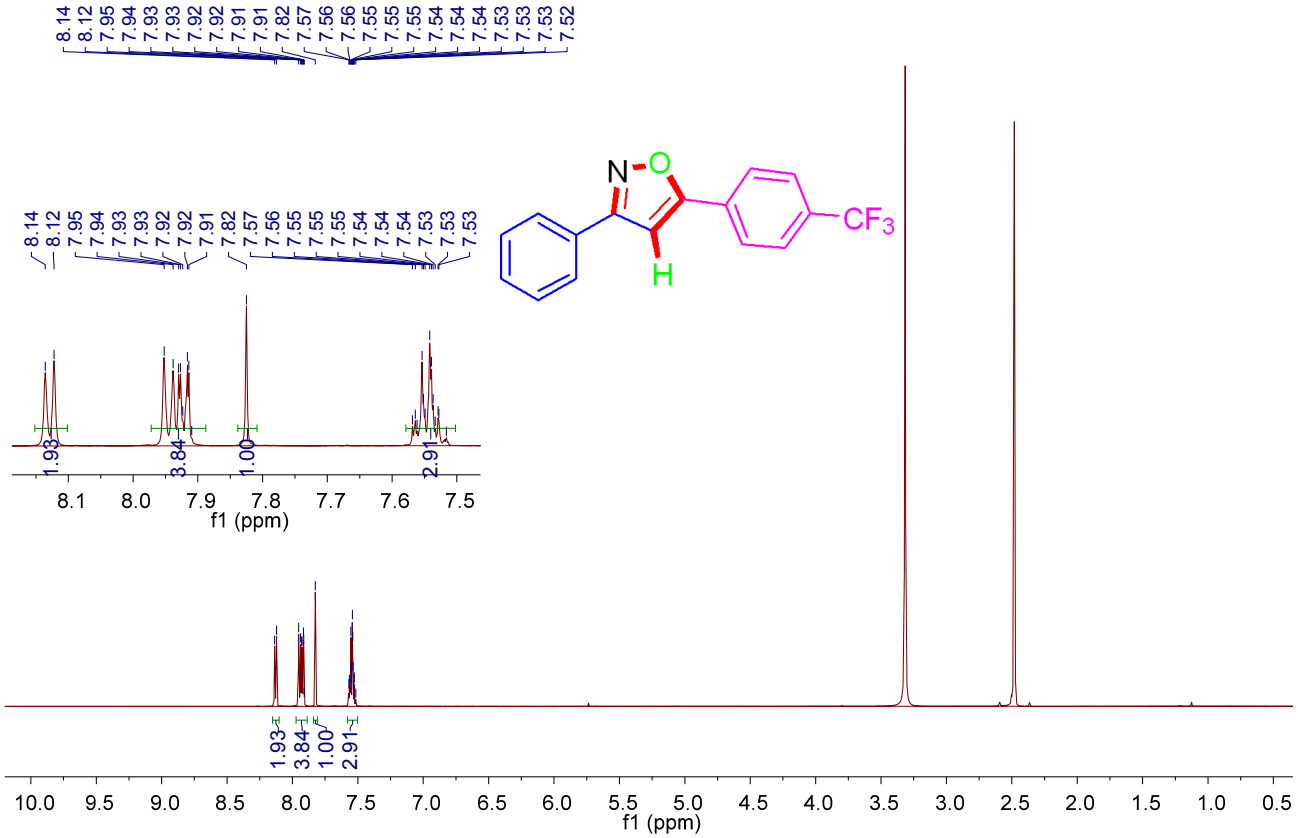


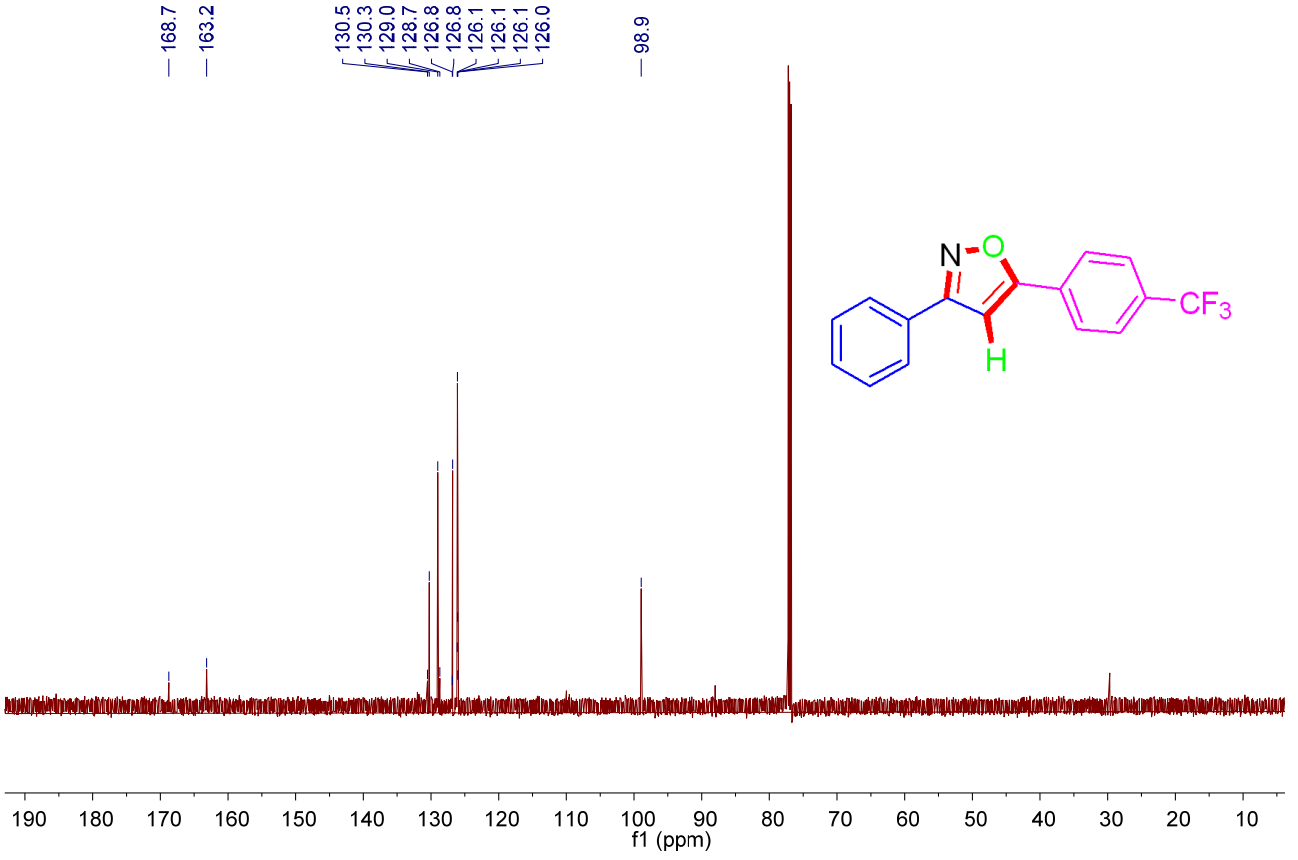
4-(3-phenylisoxazol-5-yl)benzonitrile (4ag).

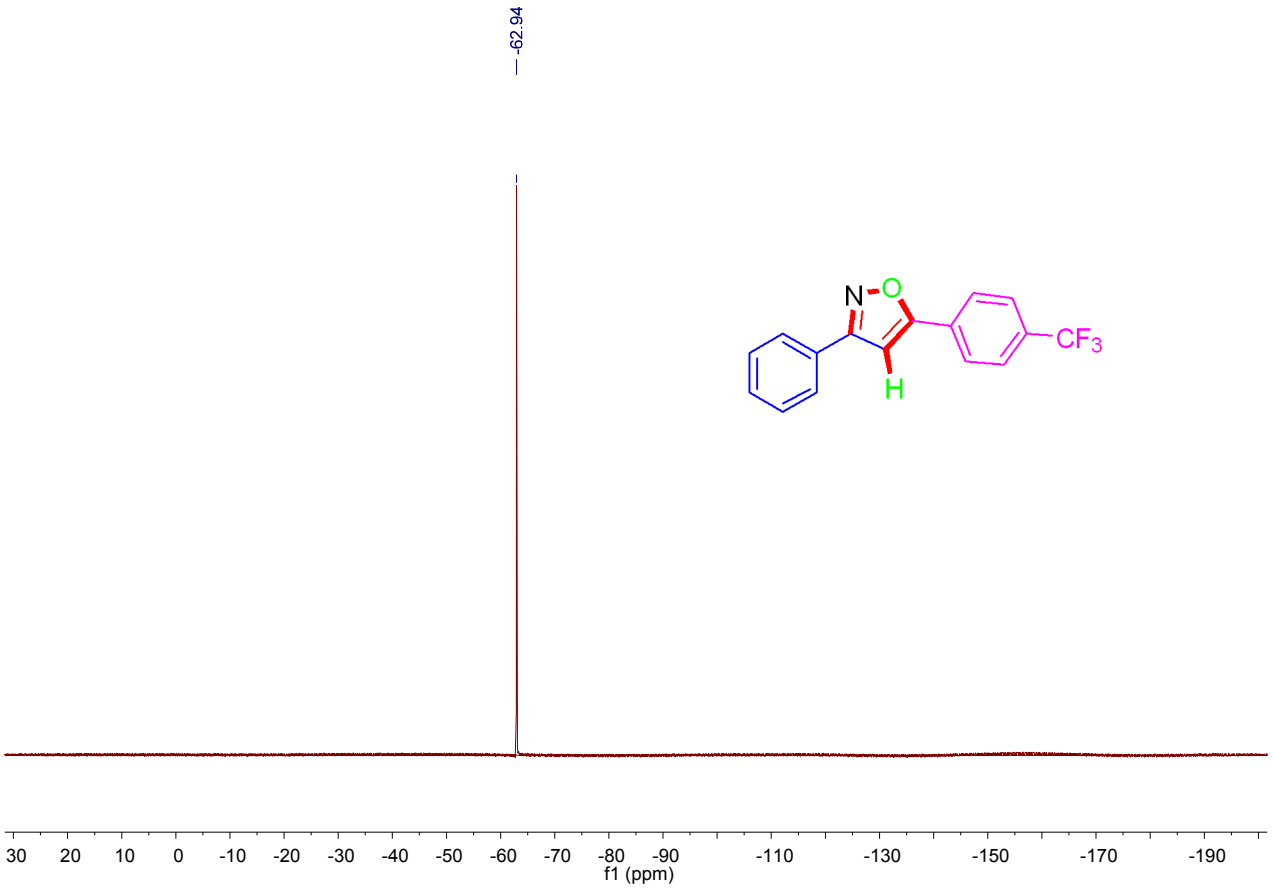




3-phenyl-5-(4-(trifluoromethyl)phenyl)isoxazole (4ah).



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-40
-50
-60
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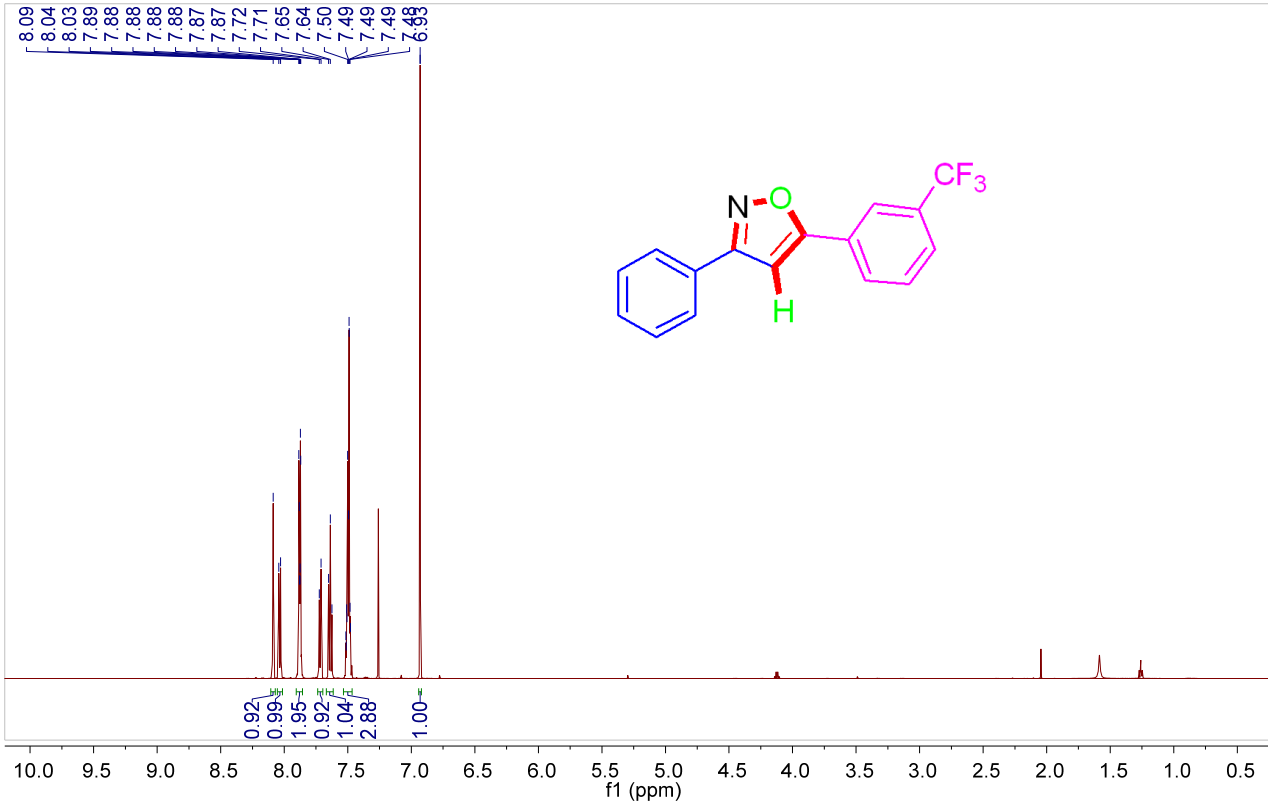
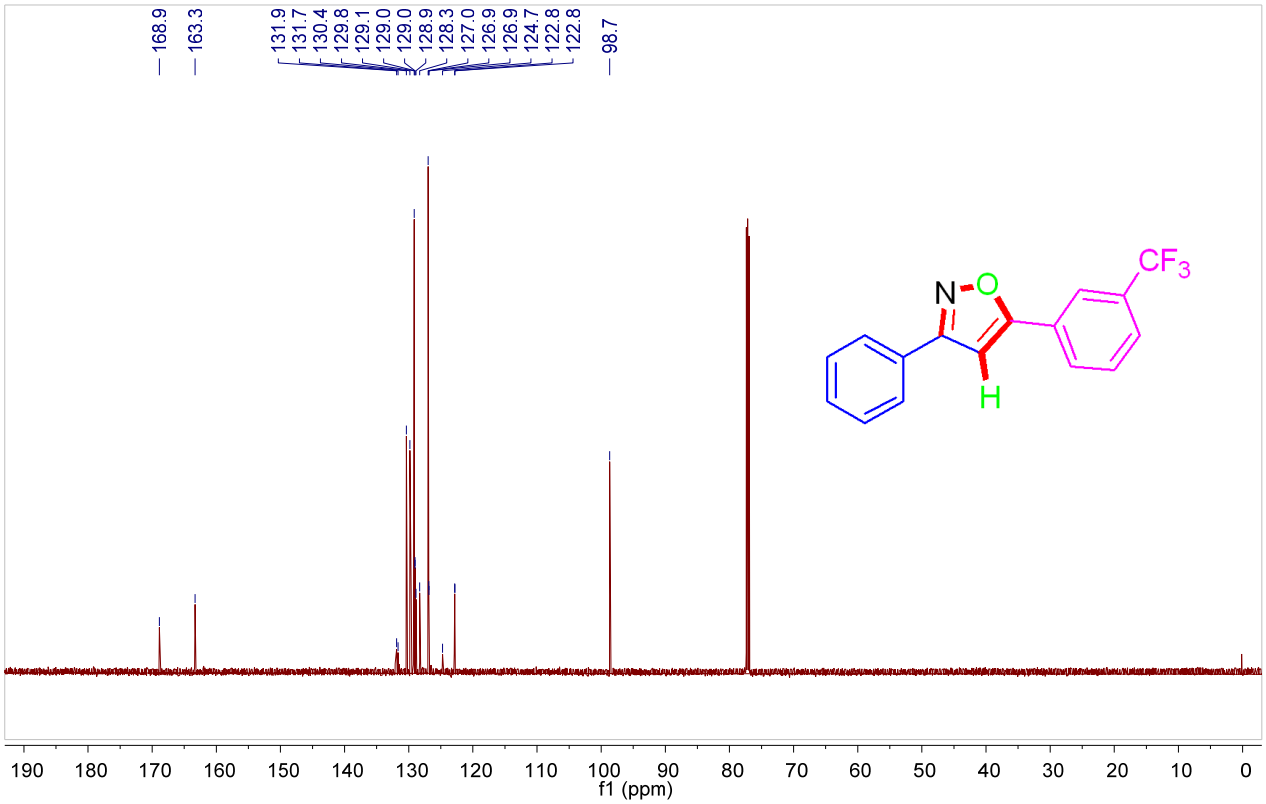
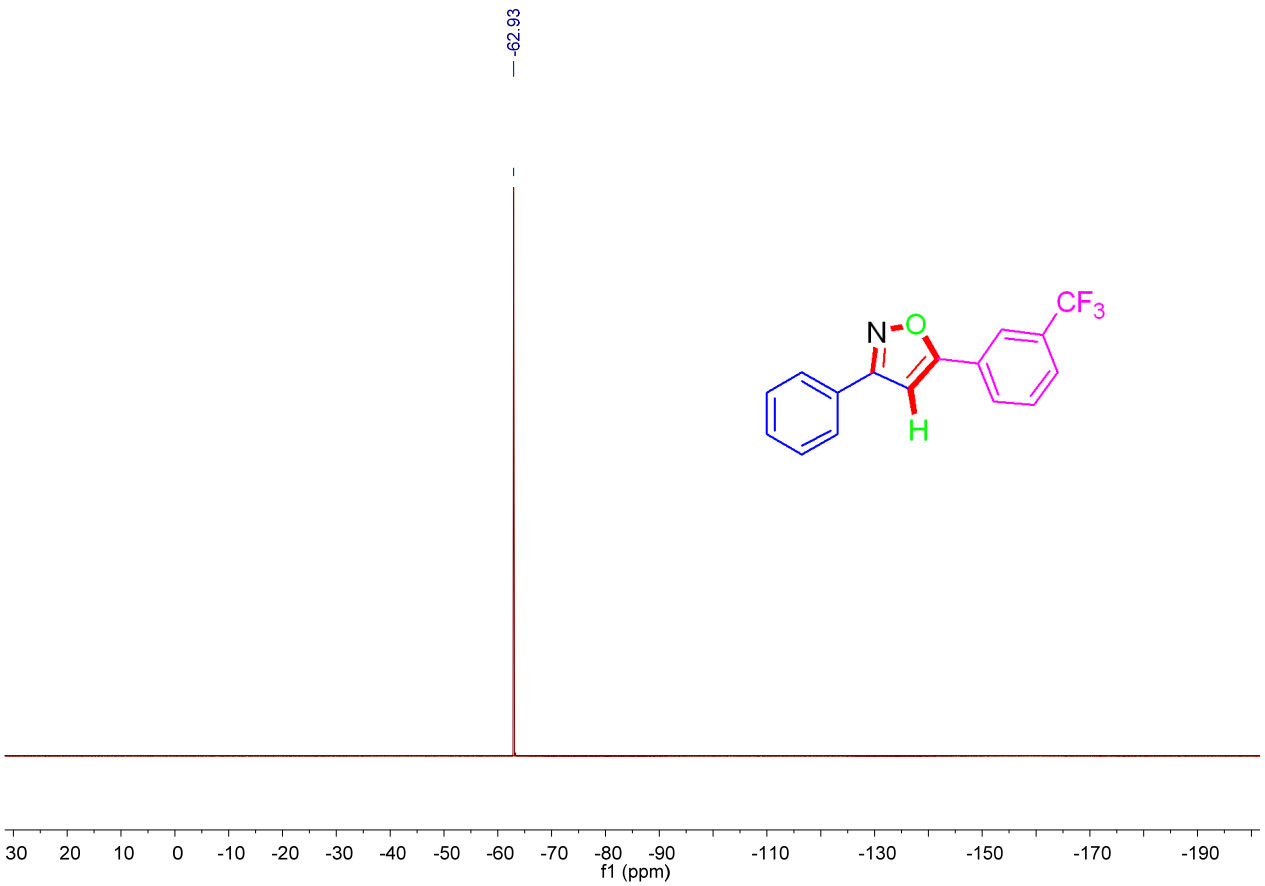
-150
-170
-190
f1 (ppm)

3-phenyl-5-(3-(trifluoromethyl)phenyl)isoxazole (4ai).



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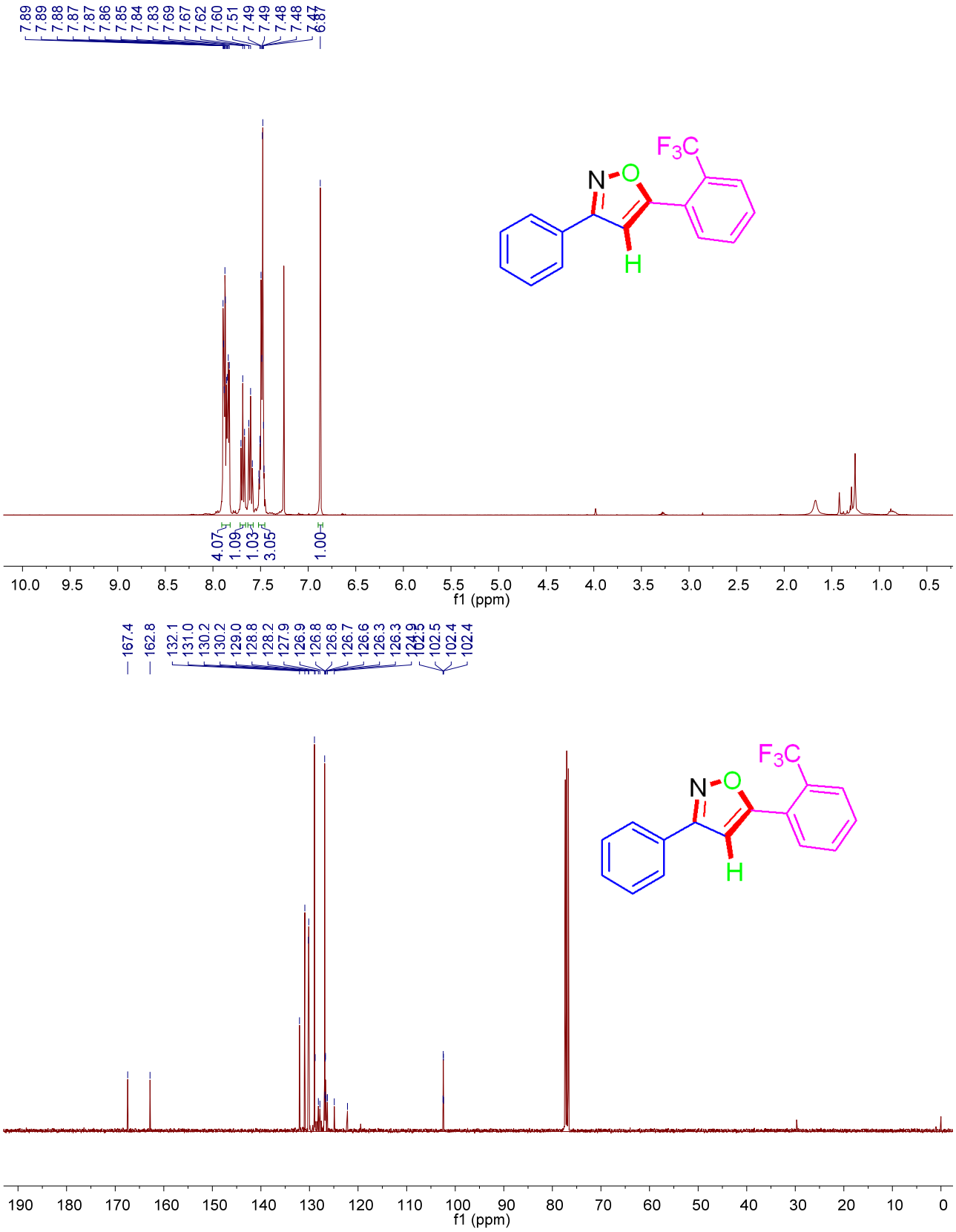
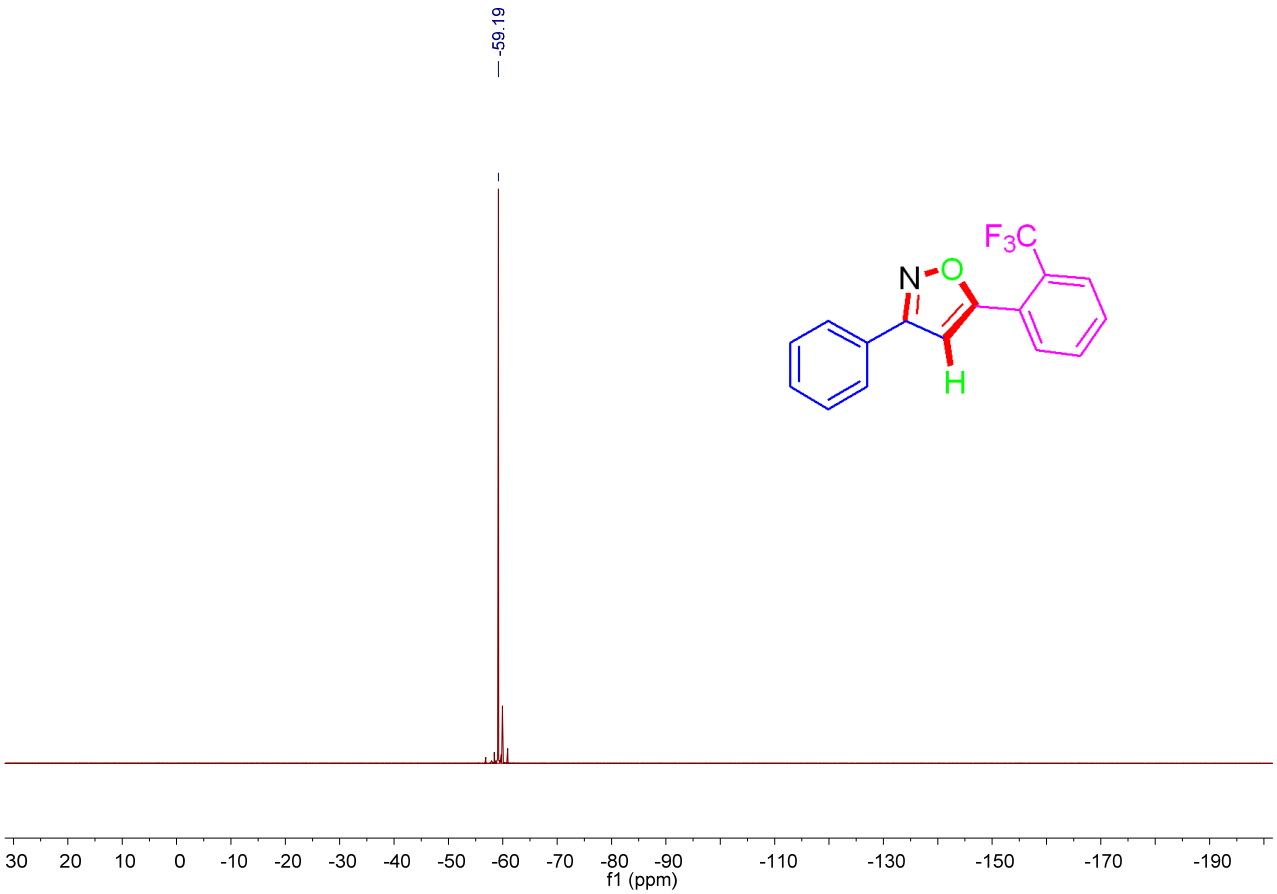
f1 (ppm)

3-phenyl-5-(2-(trifluoromethyl)phenyl)isoxazole (4aj).

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-50
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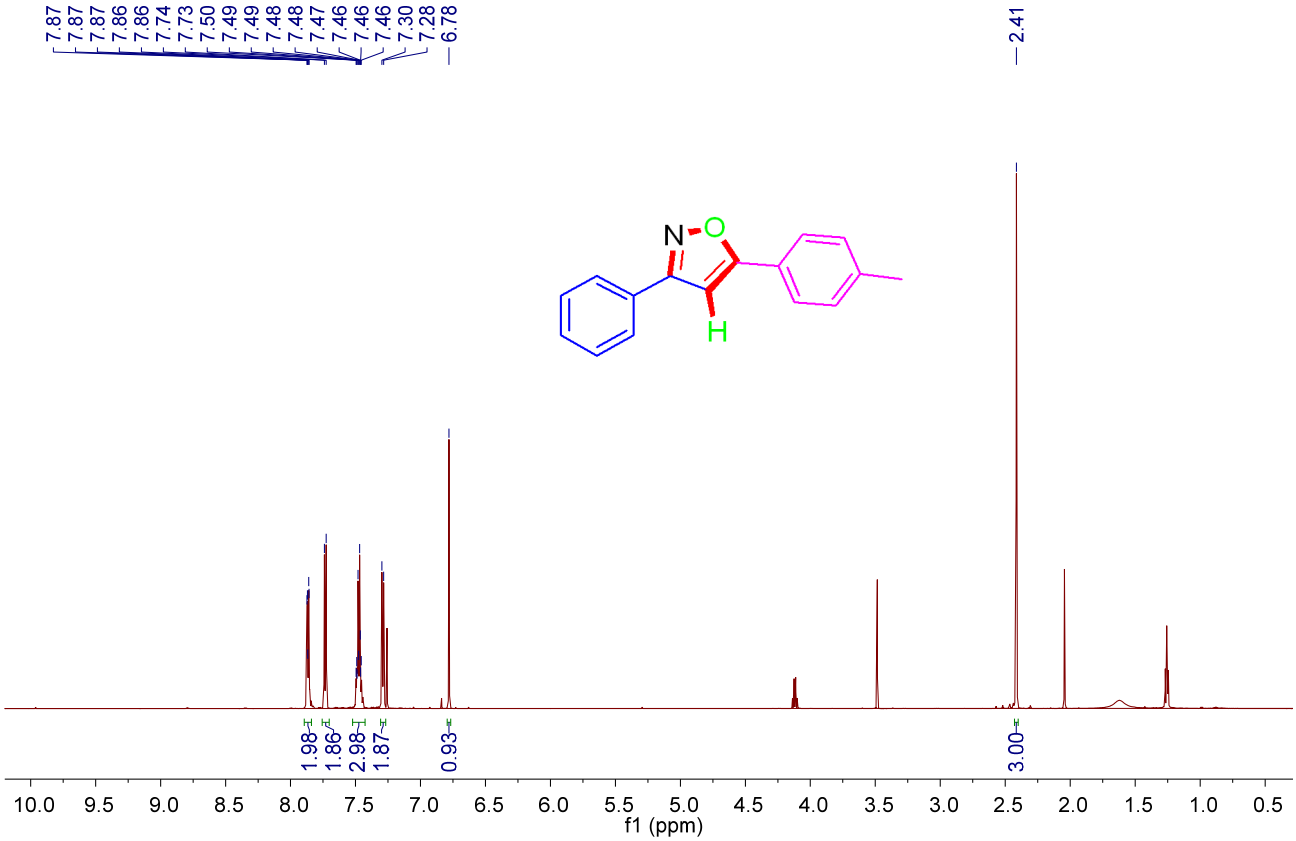
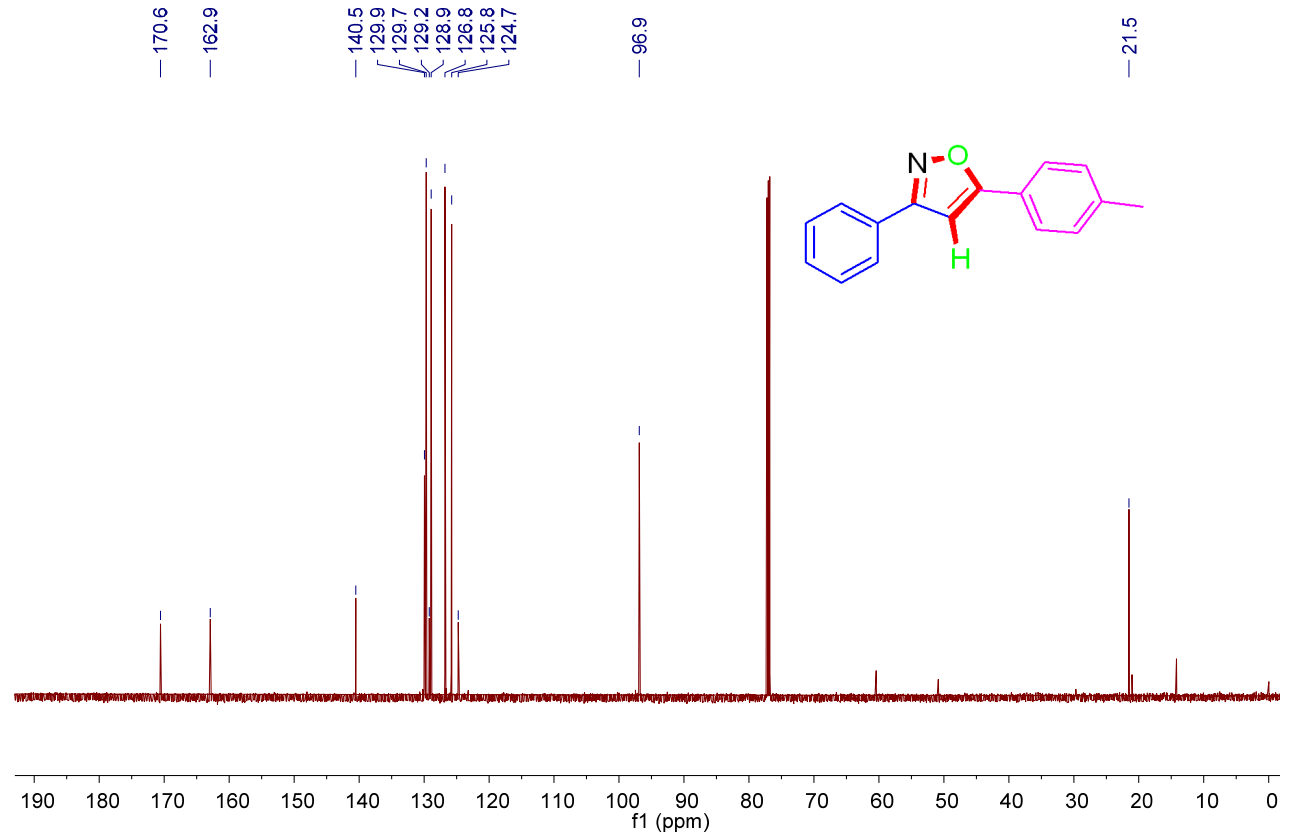
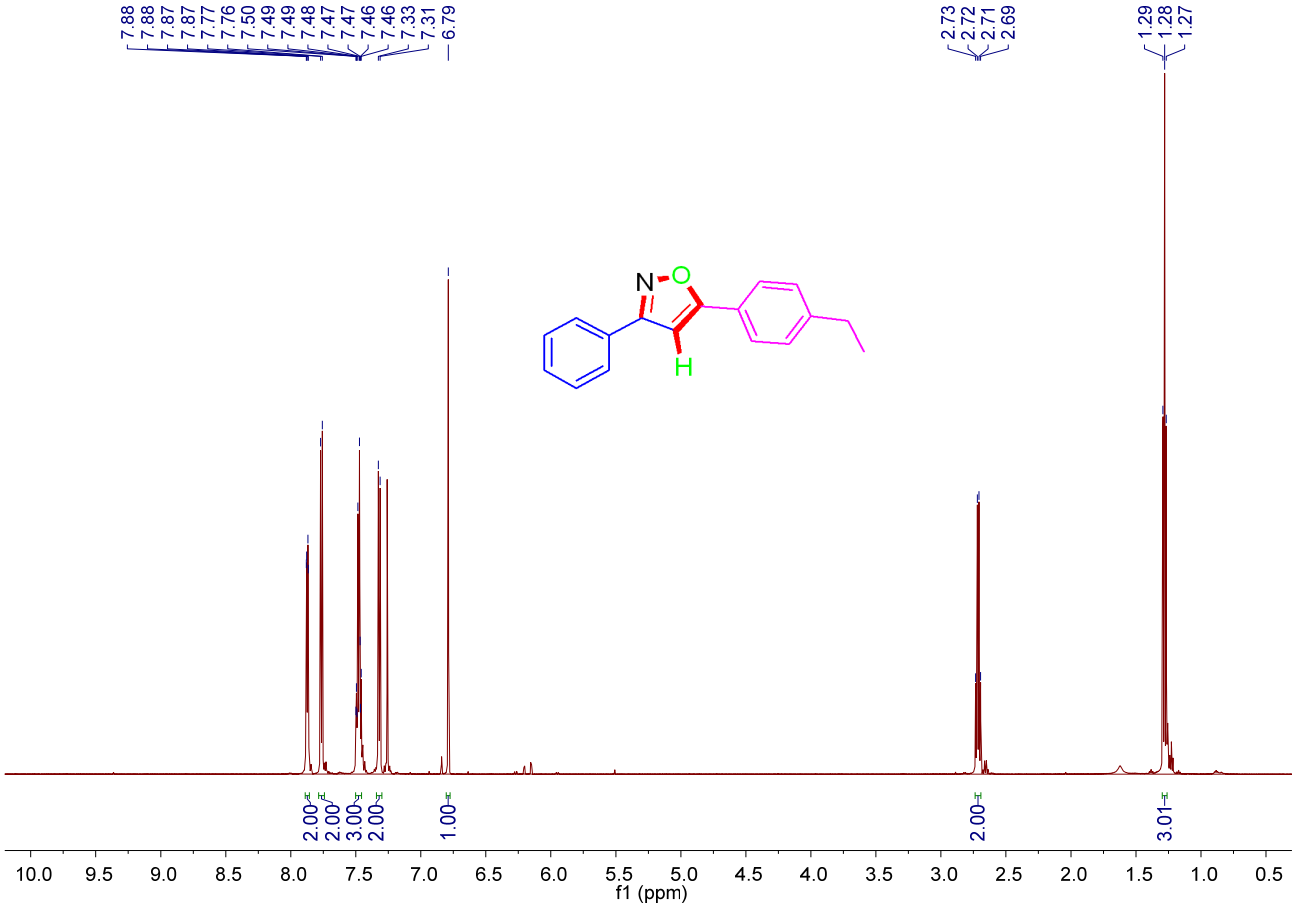
-150
-170
-190
f1 (ppm)

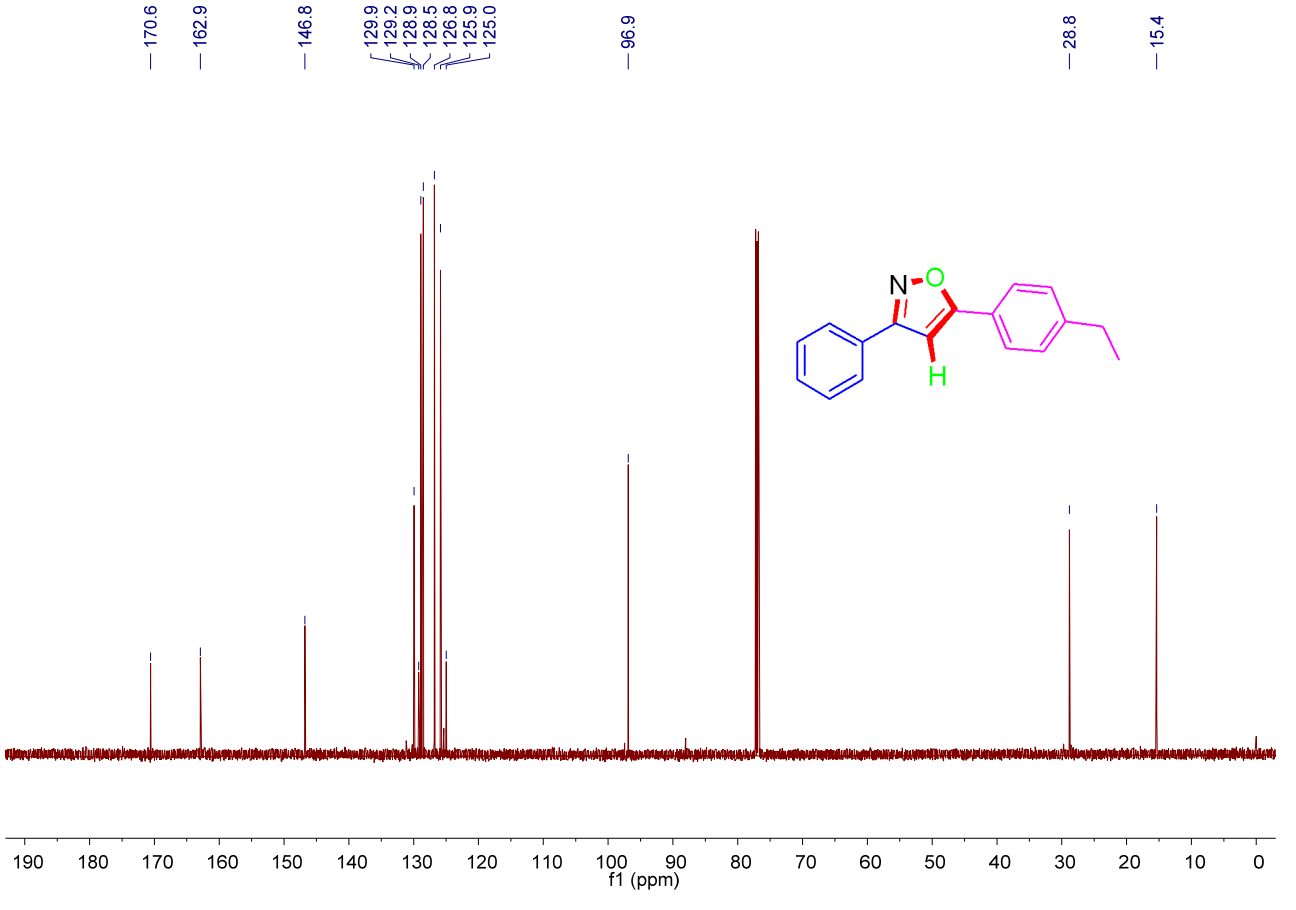
3-phenyl-5-(p-tolyl)isoxazole (4ak).



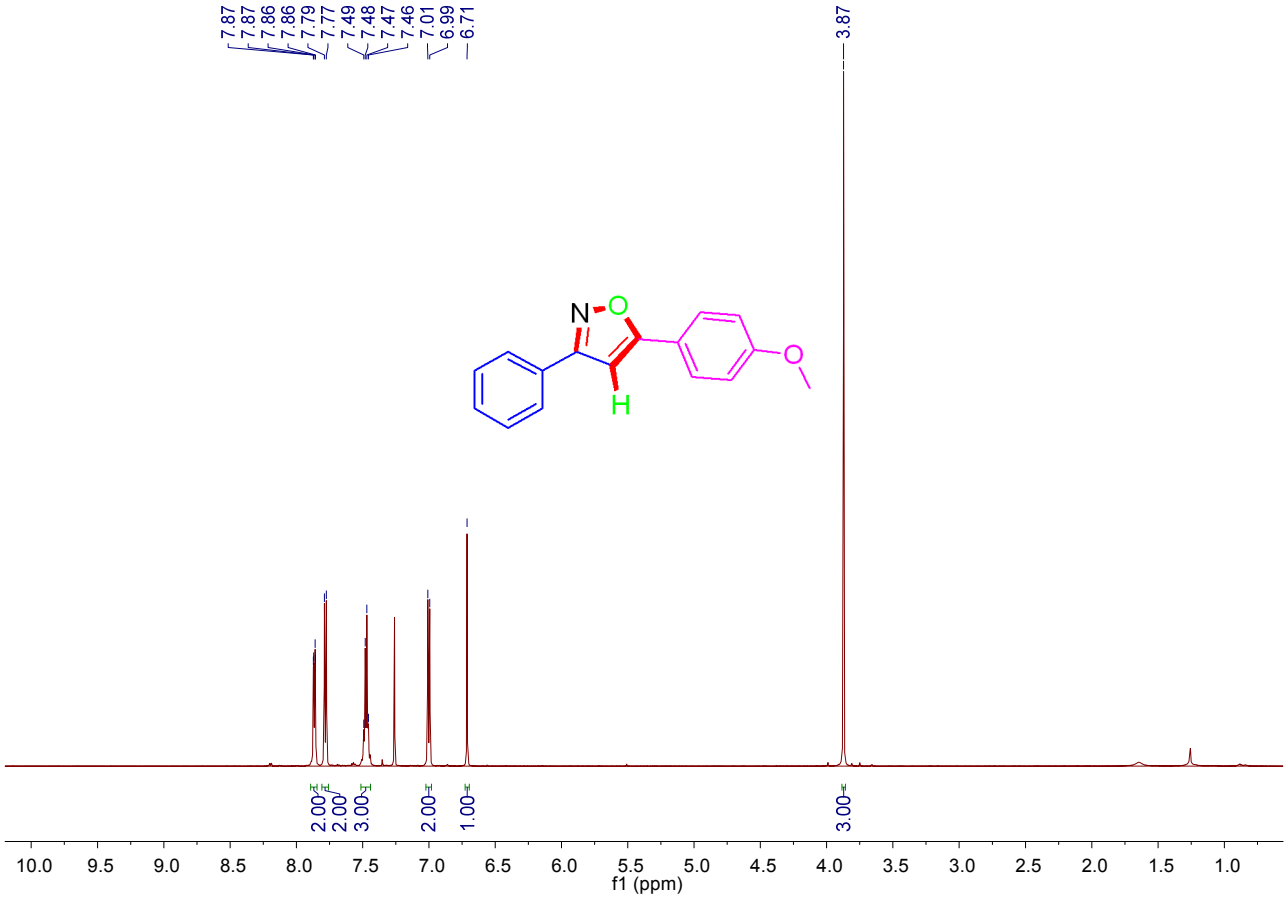


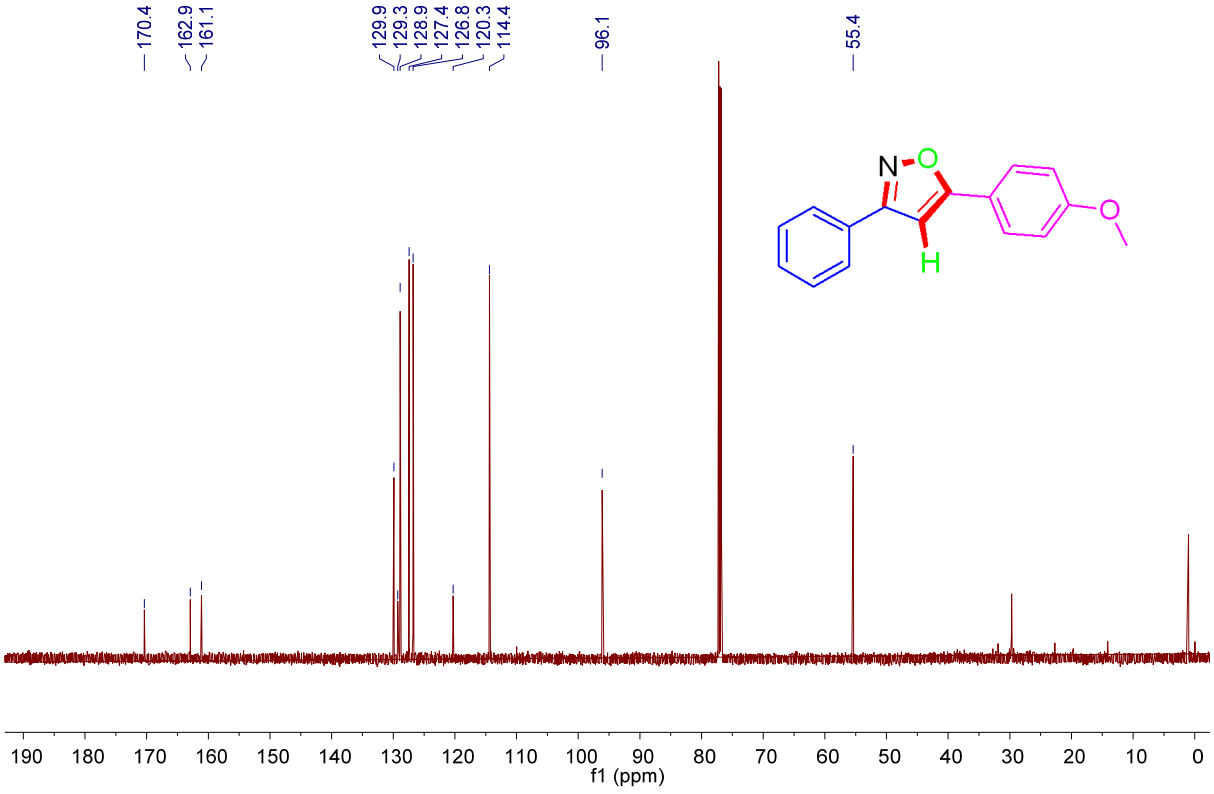
5-(4-ethylphenyl)-3-phenylisoxazole (4al).



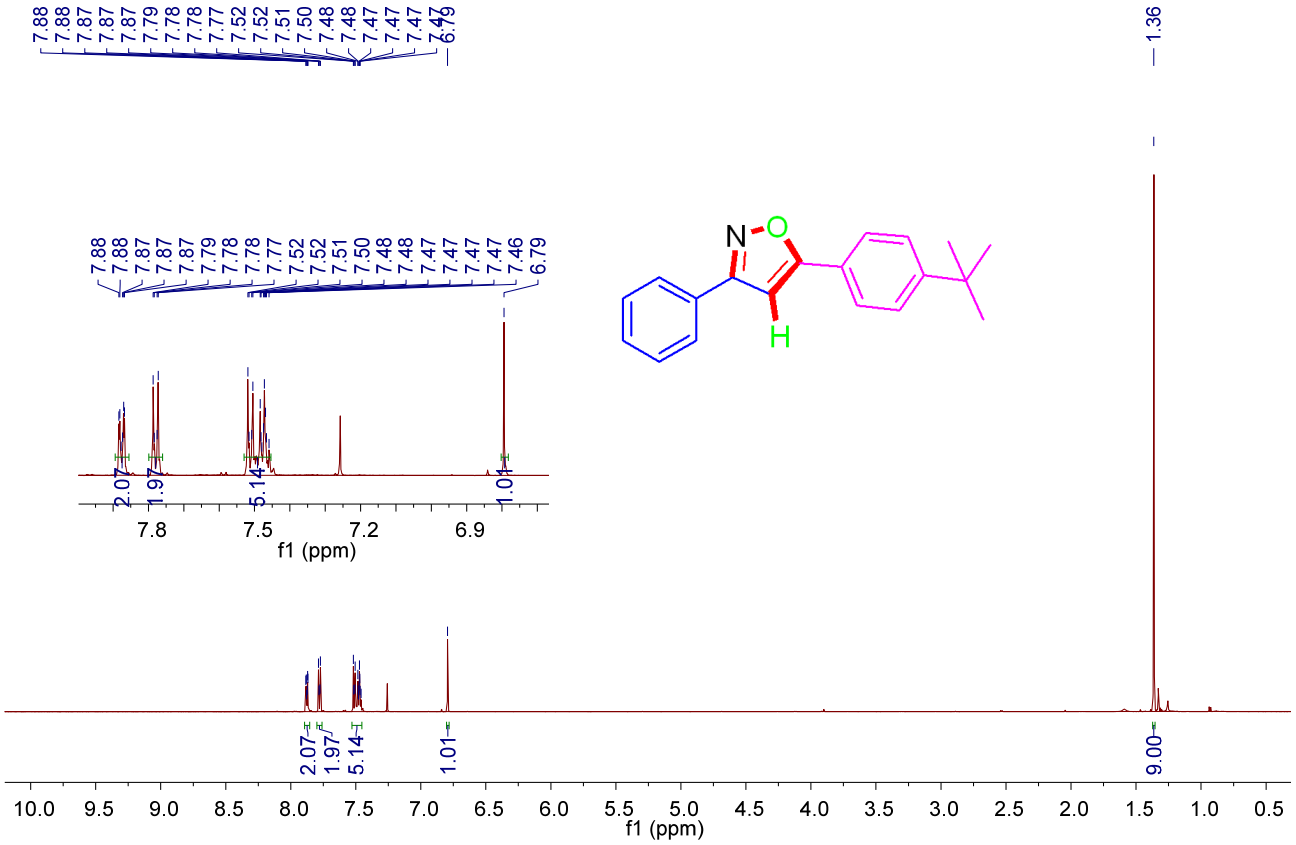


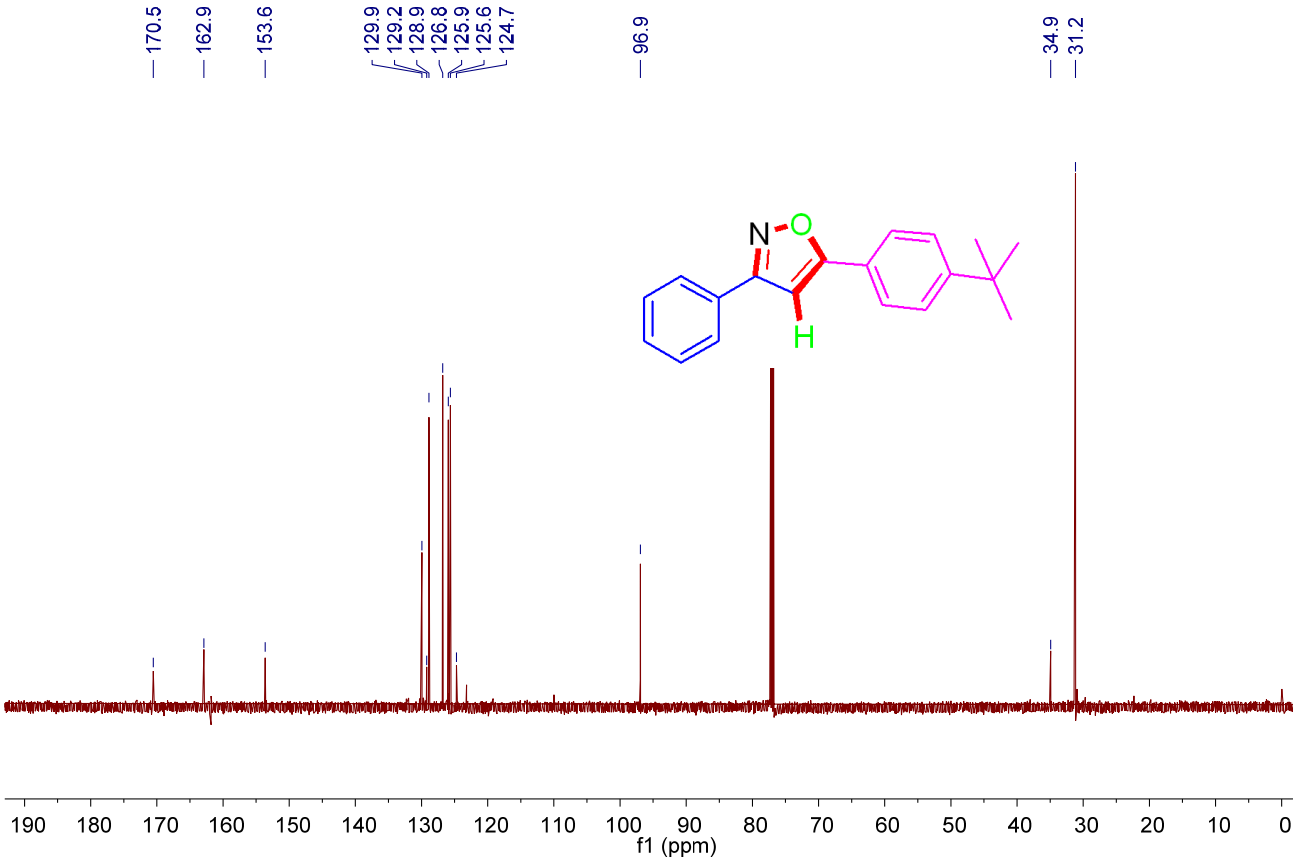
5-(4-methoxyphenyl)-3-phenylisoxazole (4am).



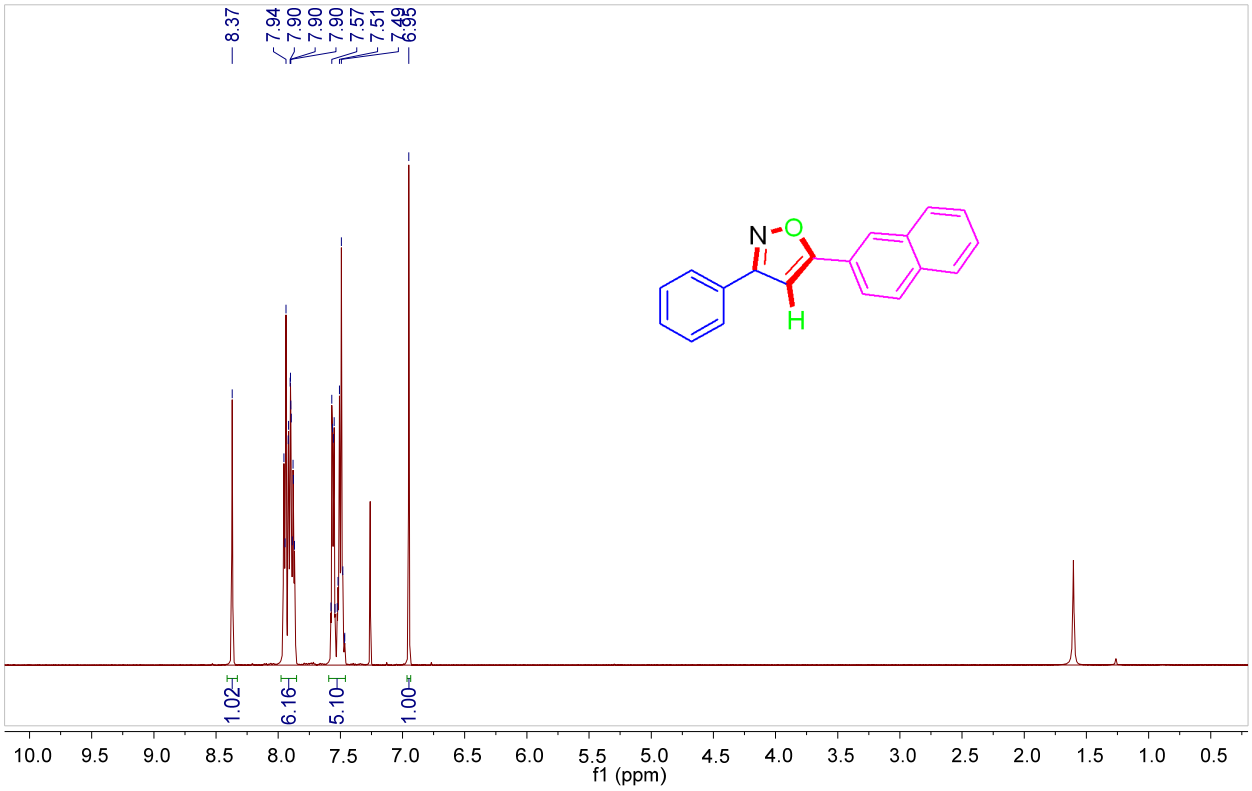


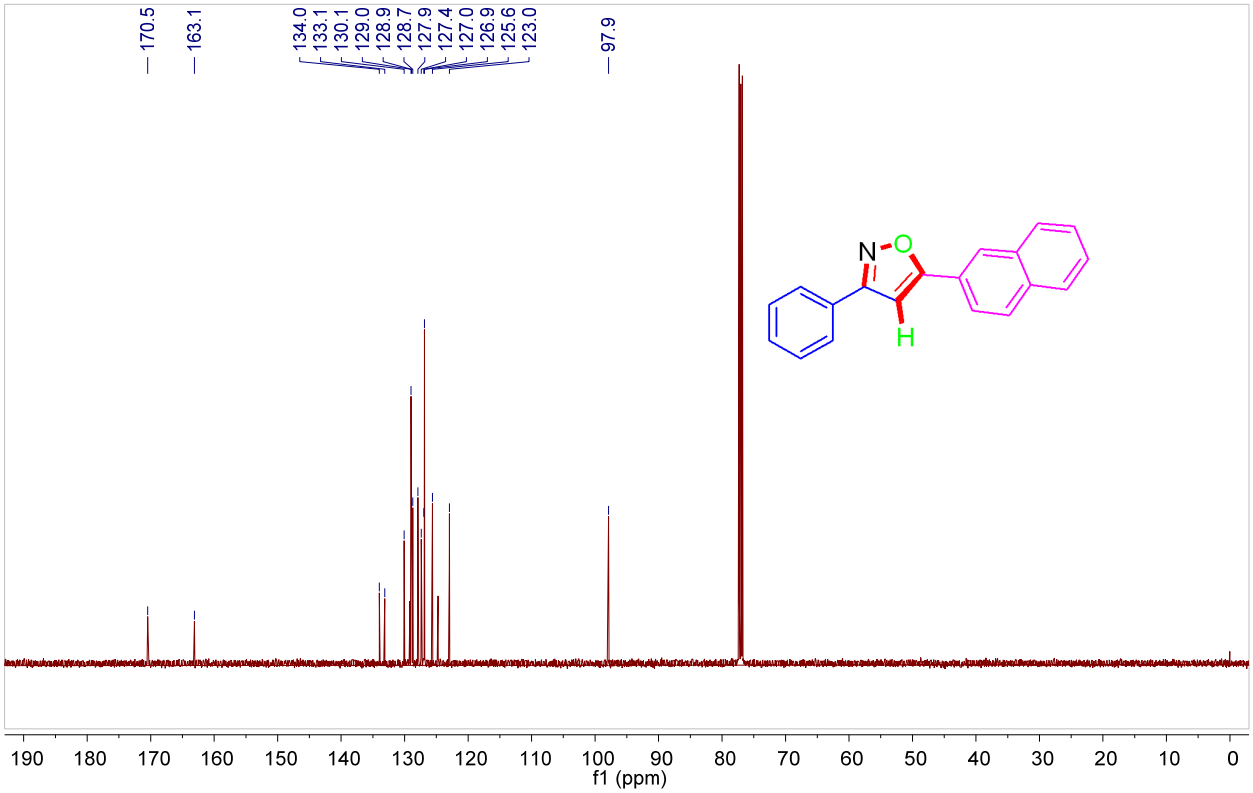
5-(4-(tert-butyl)phenyl)-3-phenylisoxazole (4an).



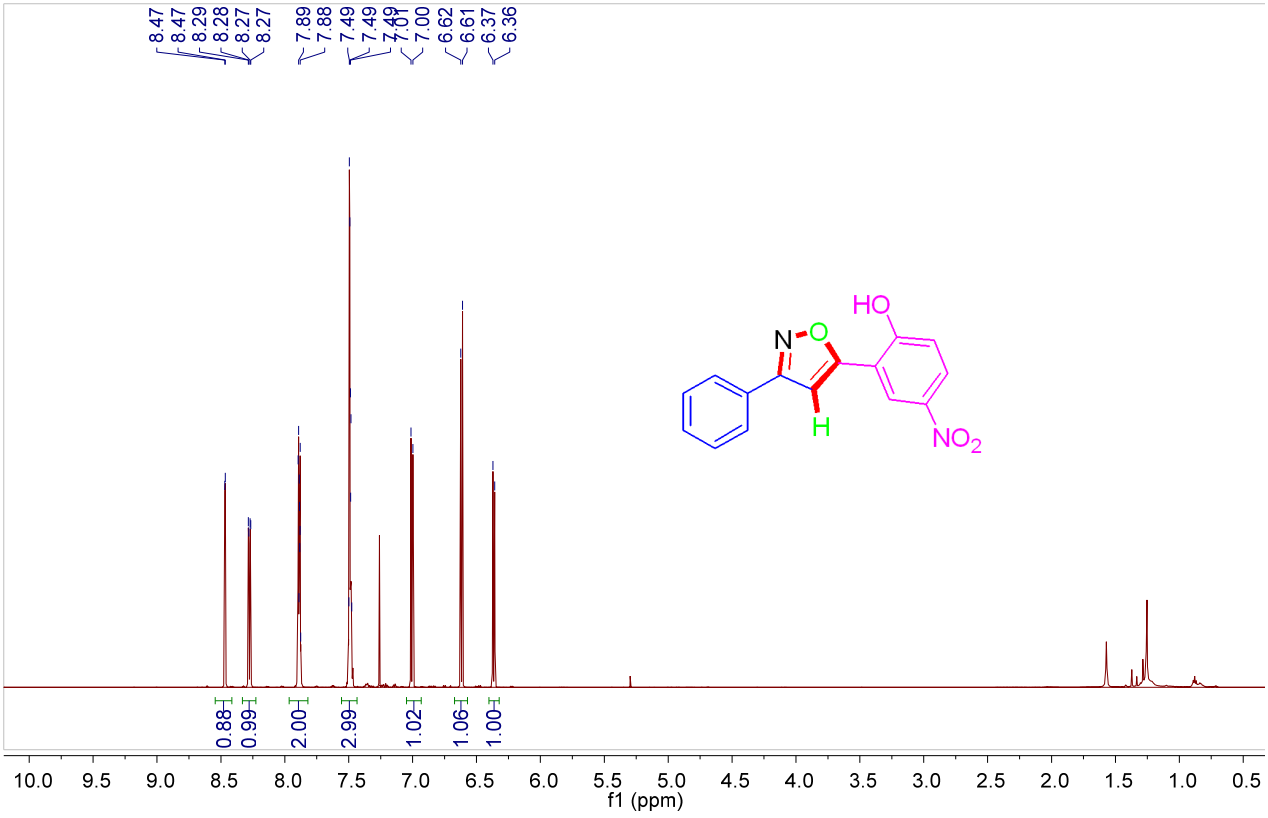


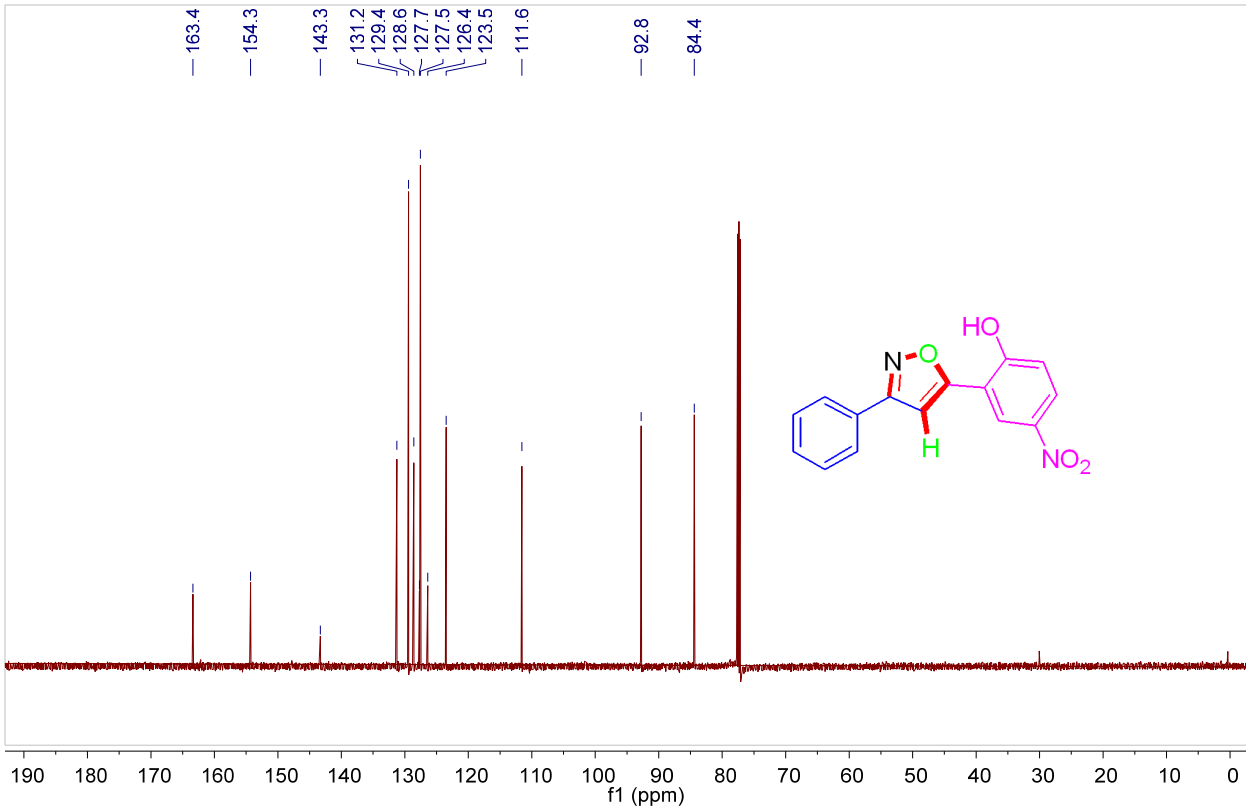
5-(naphthalen-2-yl)-3-phenylisoxazole (4ao).



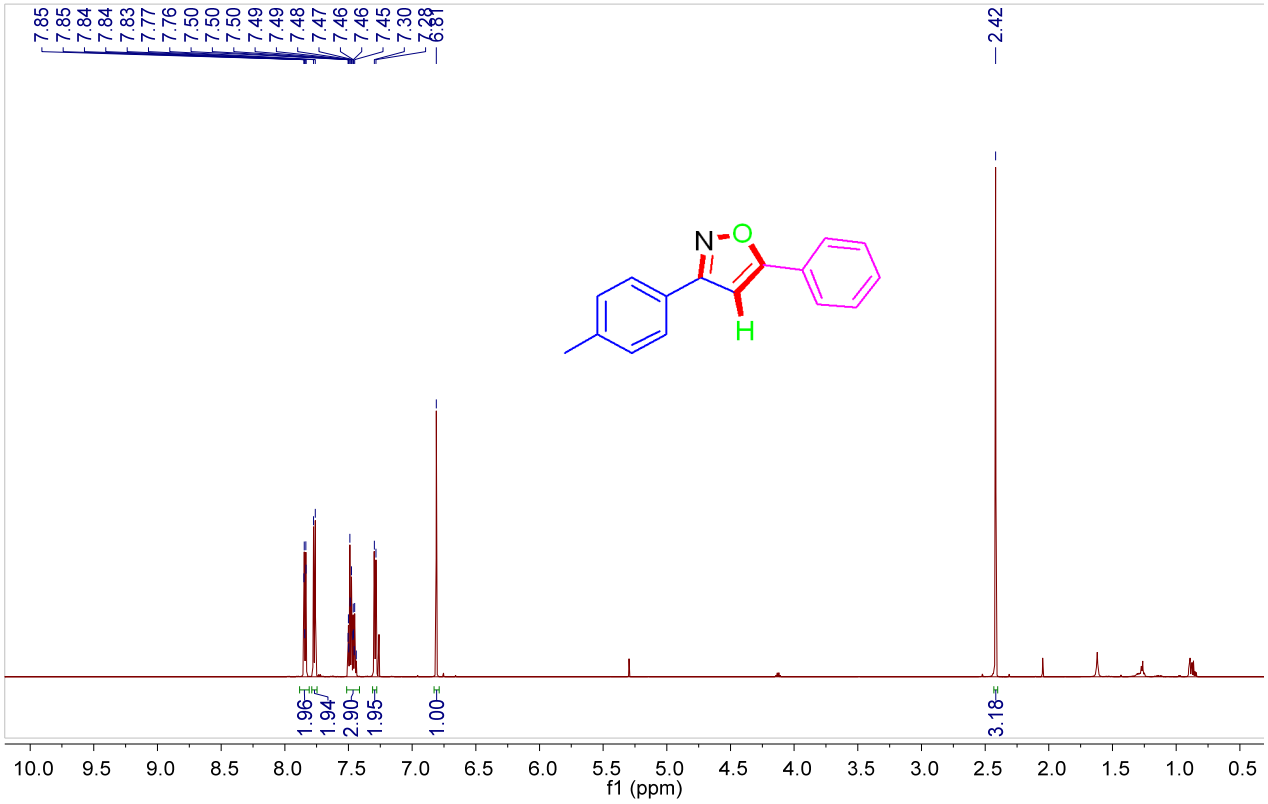


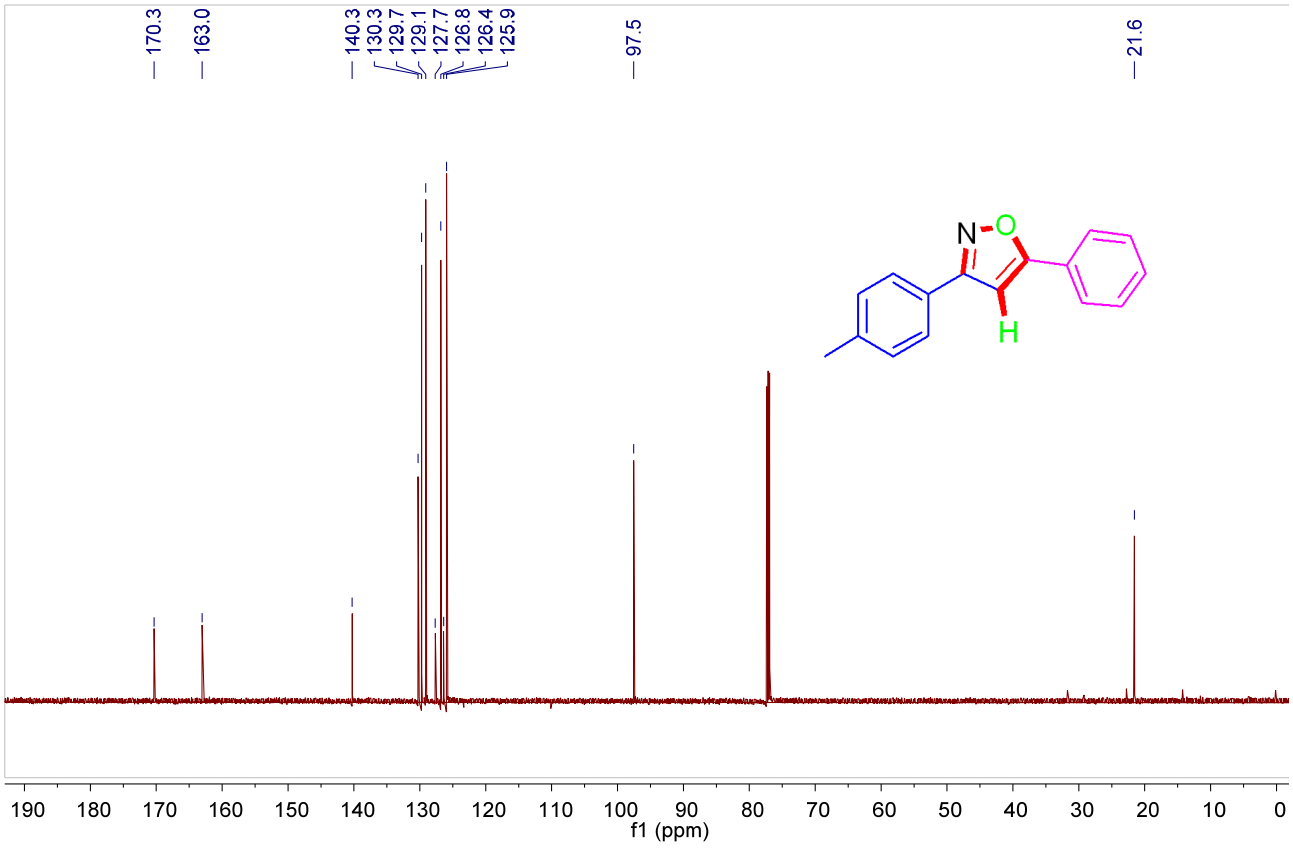
4-nitro-2-(3-phenylisoxazol-5-yl)phenol (4ap).



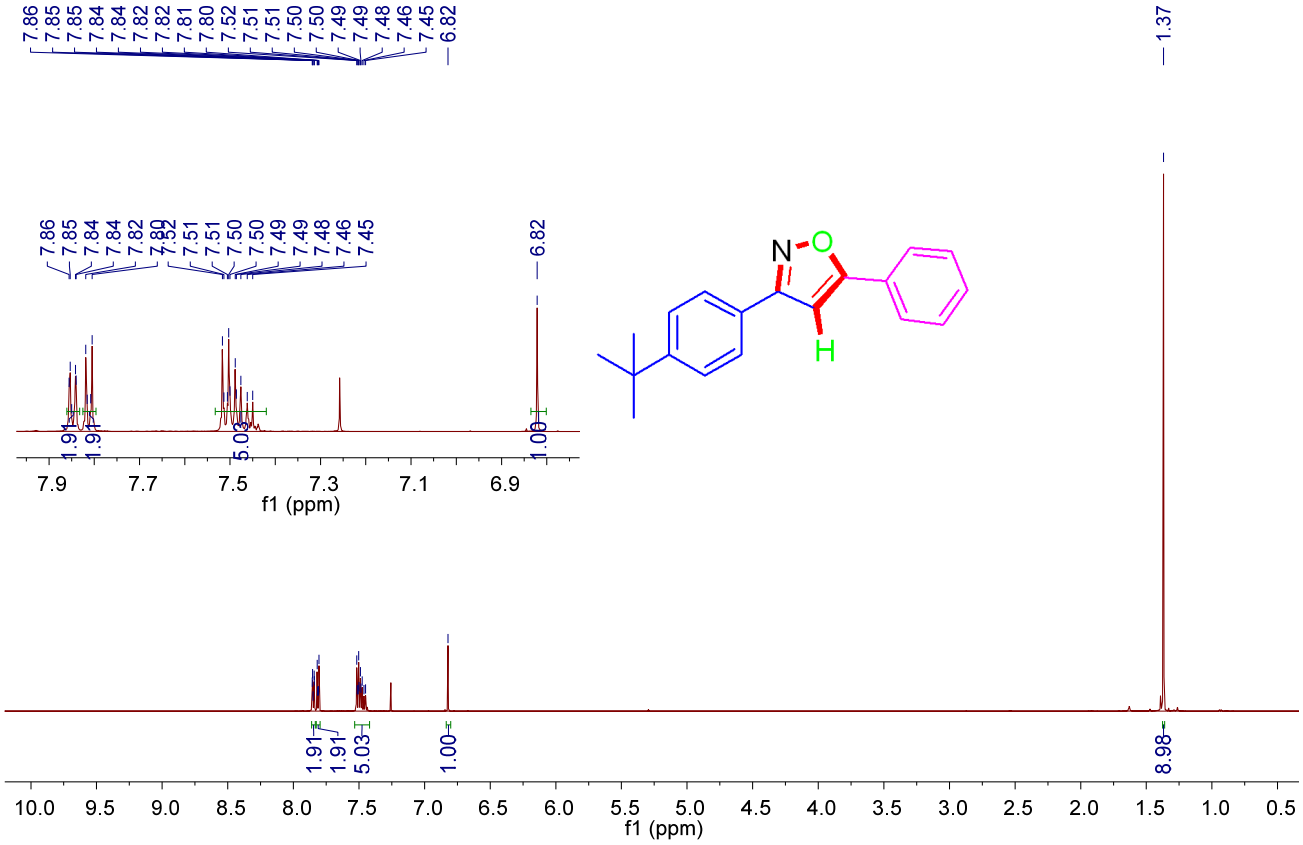


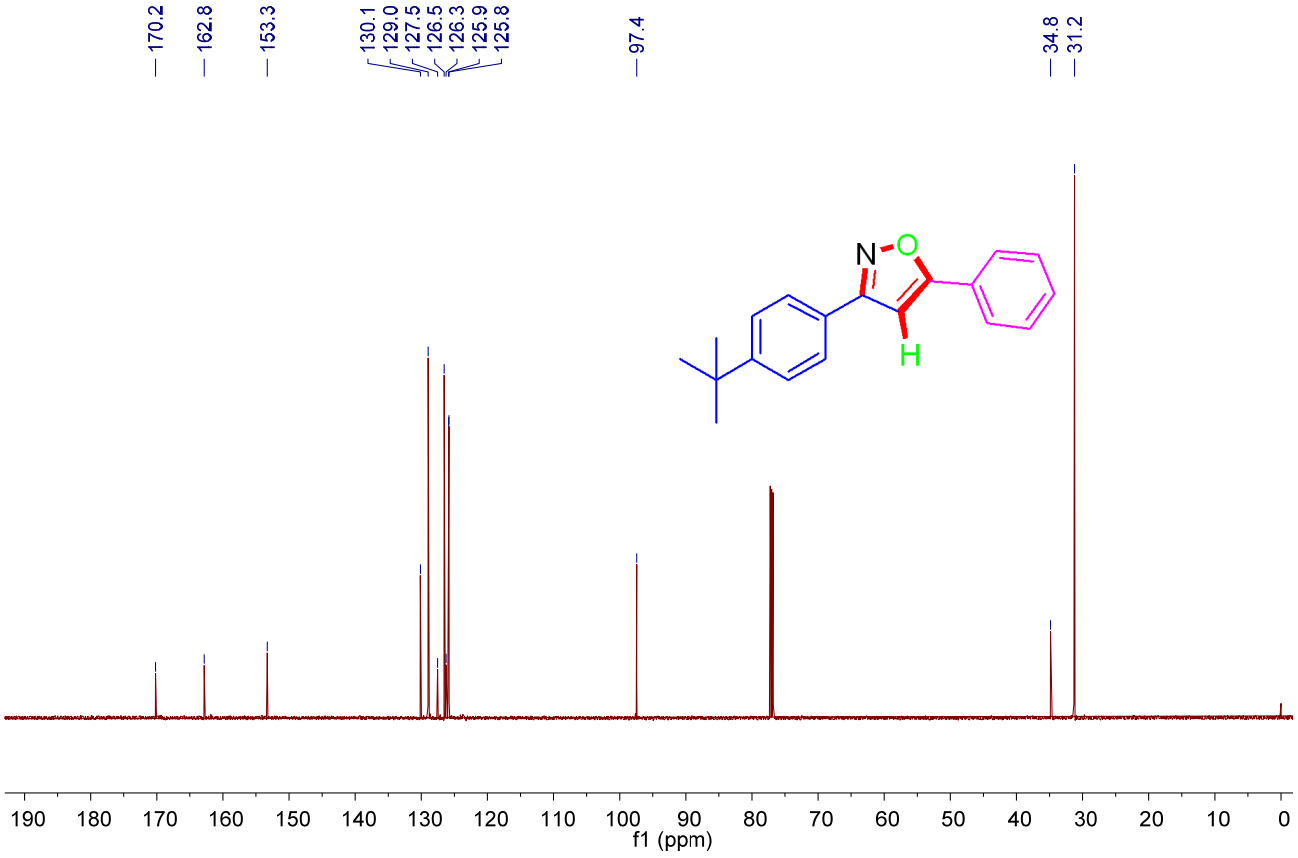
5-phenyl-3-(p-tolyl)isoxazole (4ba).



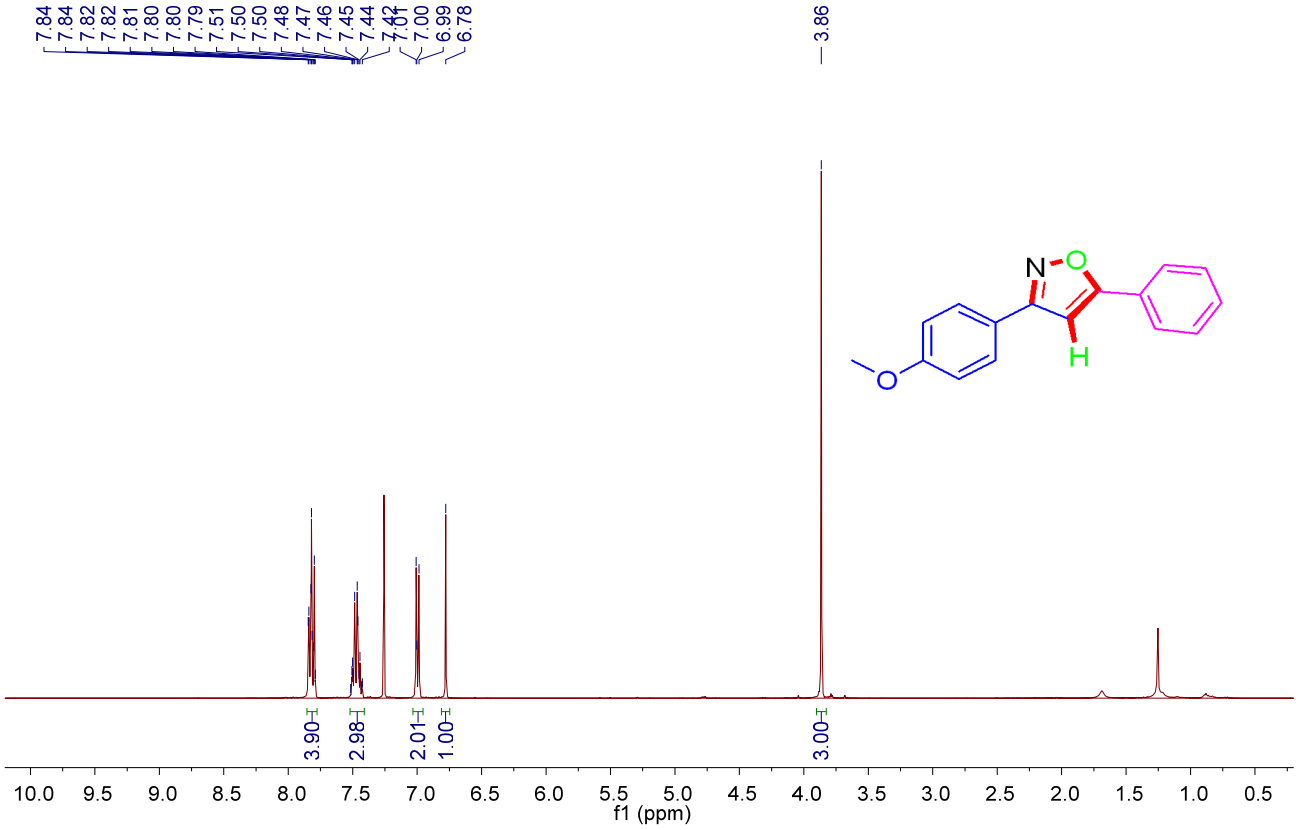


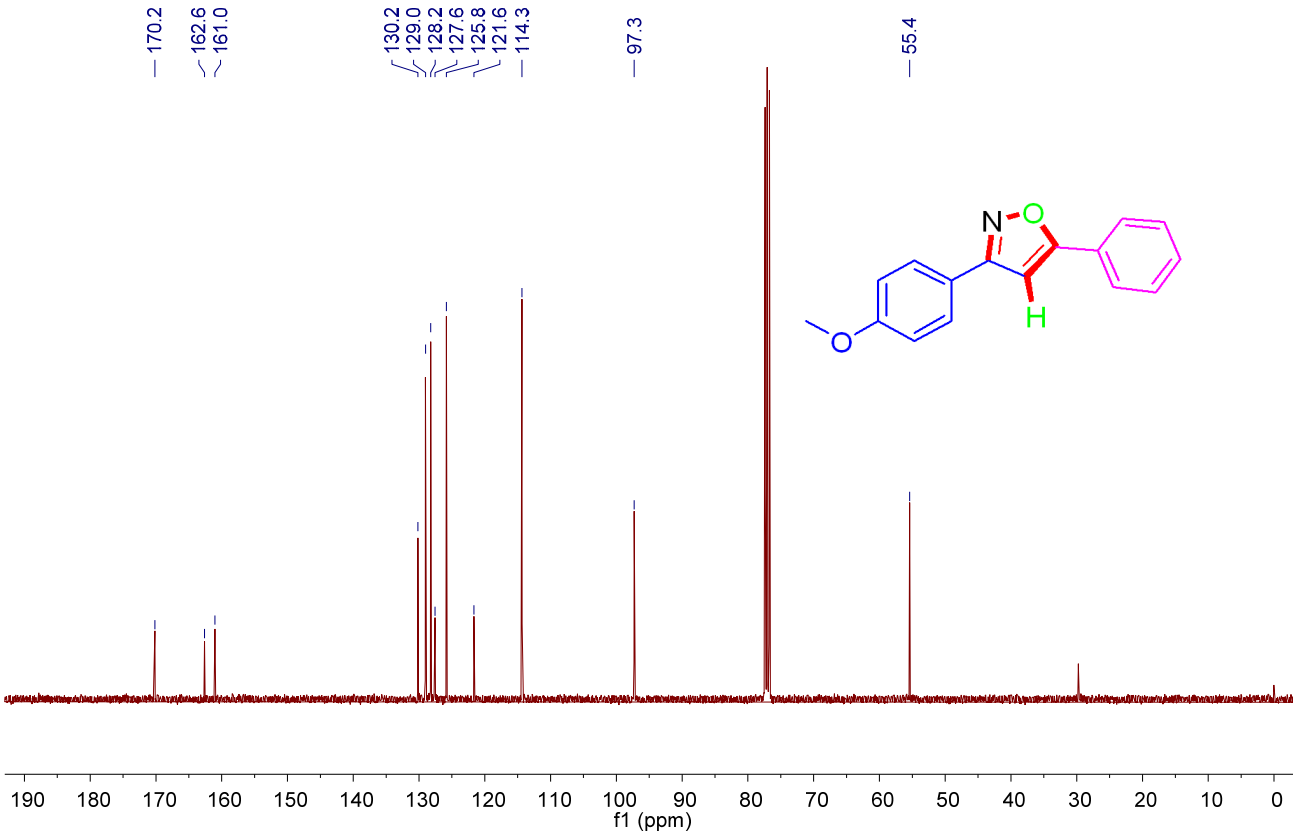
3-(4-(tert-butyl)phenyl)-5-phenylisoxazole (4ca).



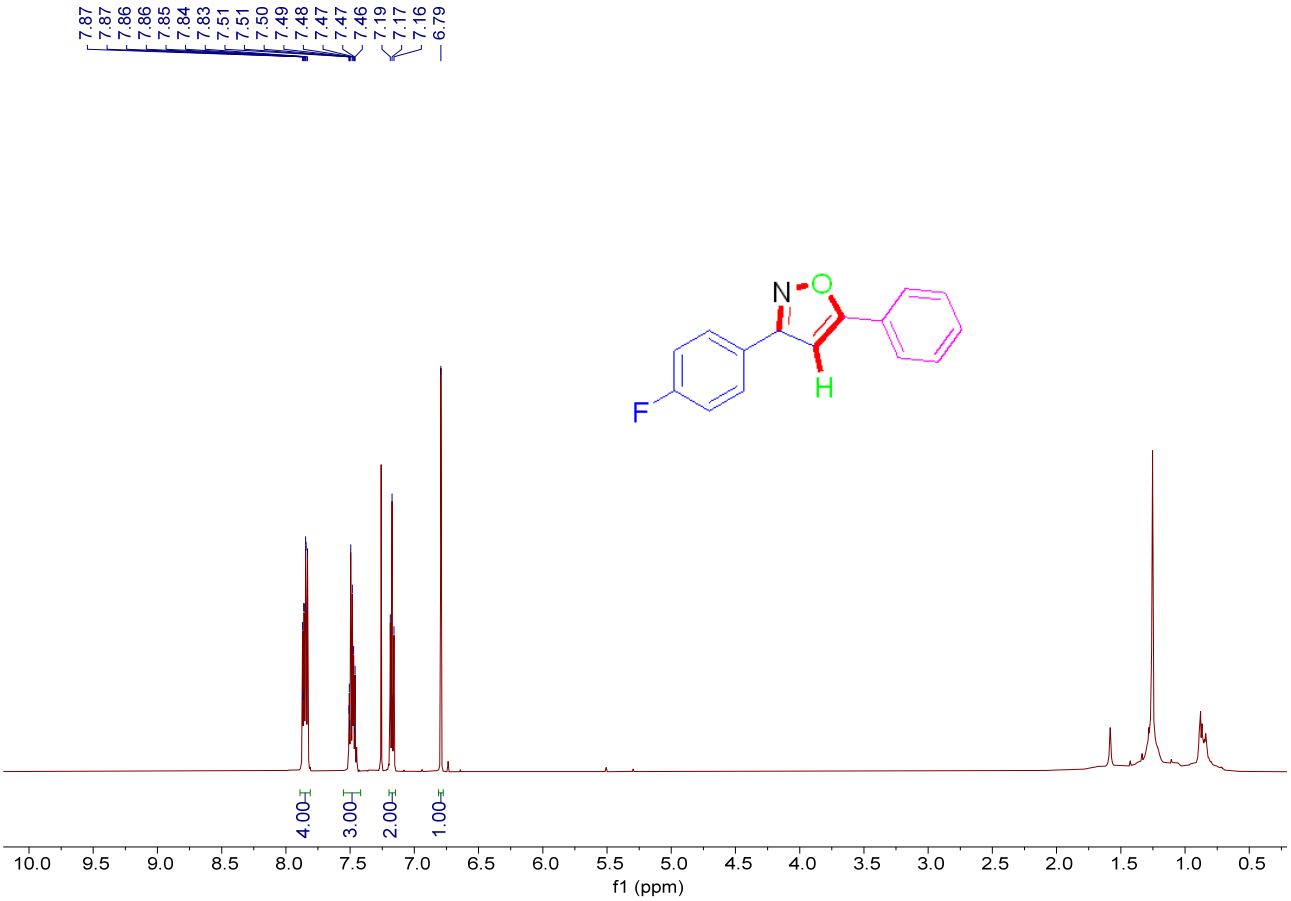


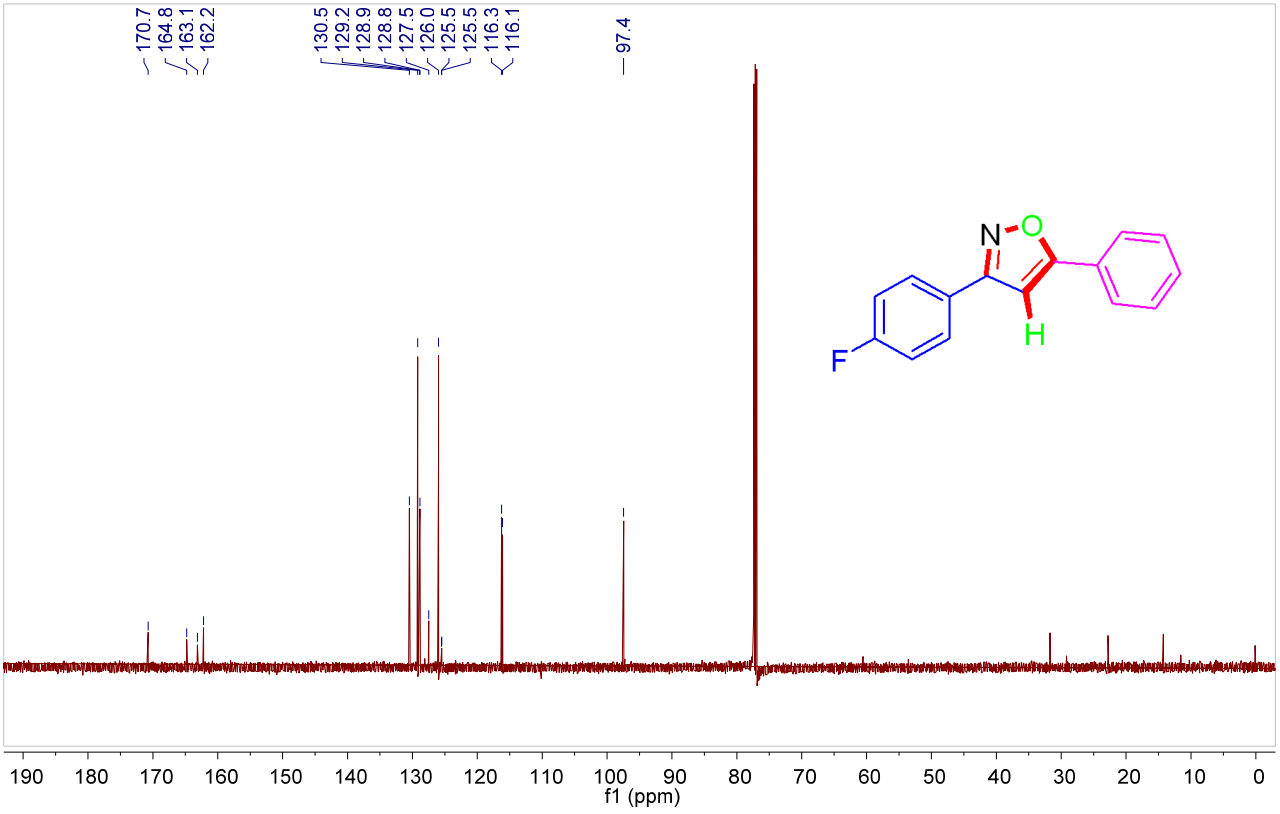
3-(4-methoxyphenyl)-5-phenylisoxazole (4da).

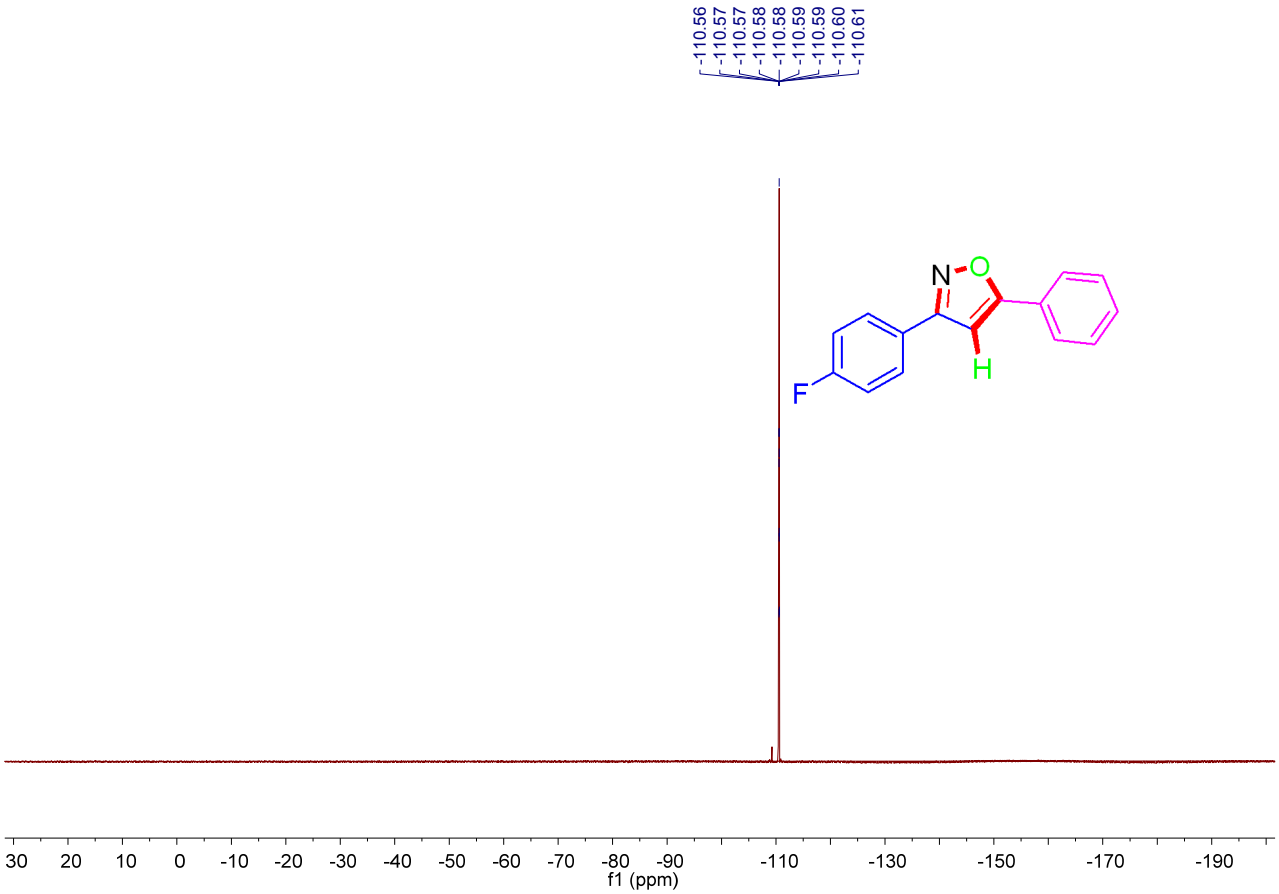




3-(4-fluorophenyl)-5-phenylisoxazole (4ea).



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-110.57
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-110.59
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-110.61
N
O
H
F
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
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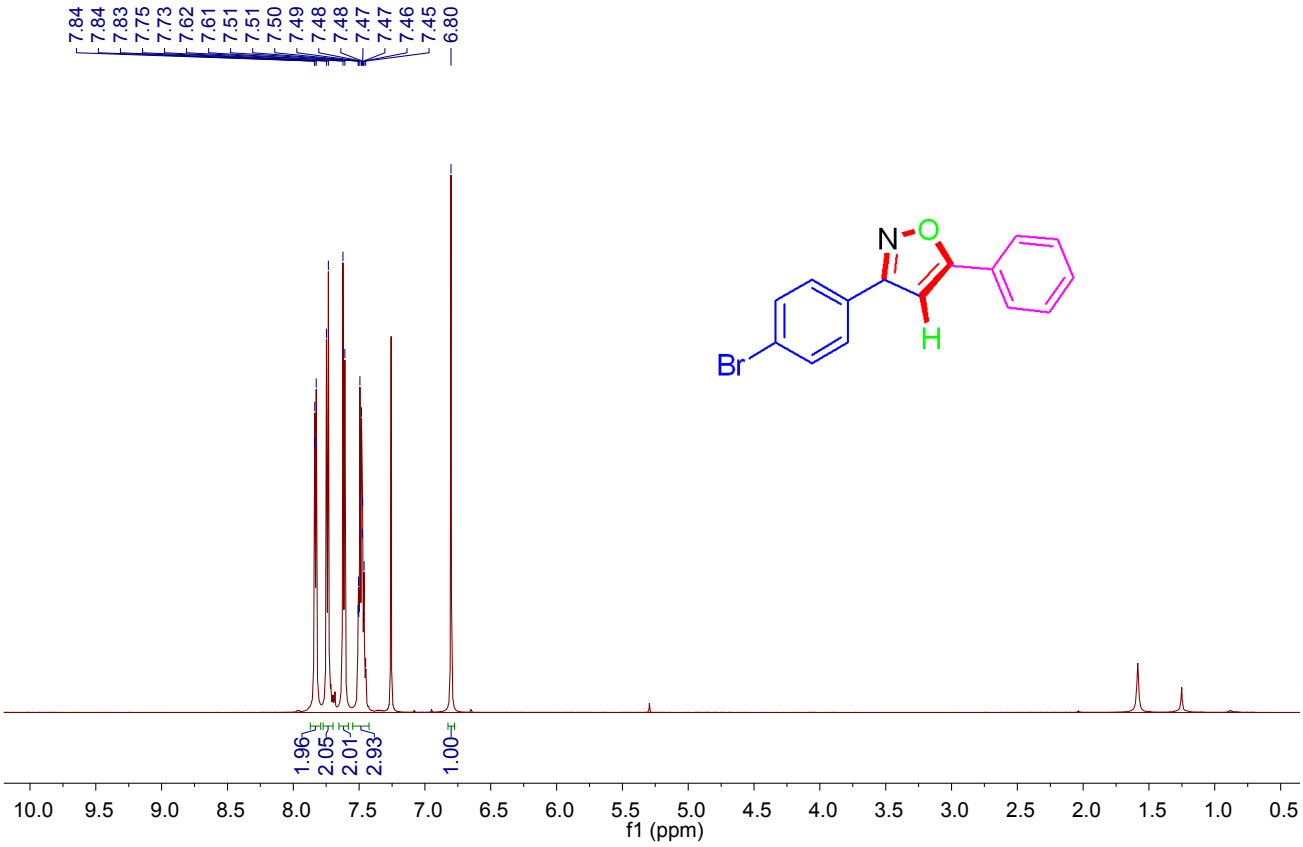
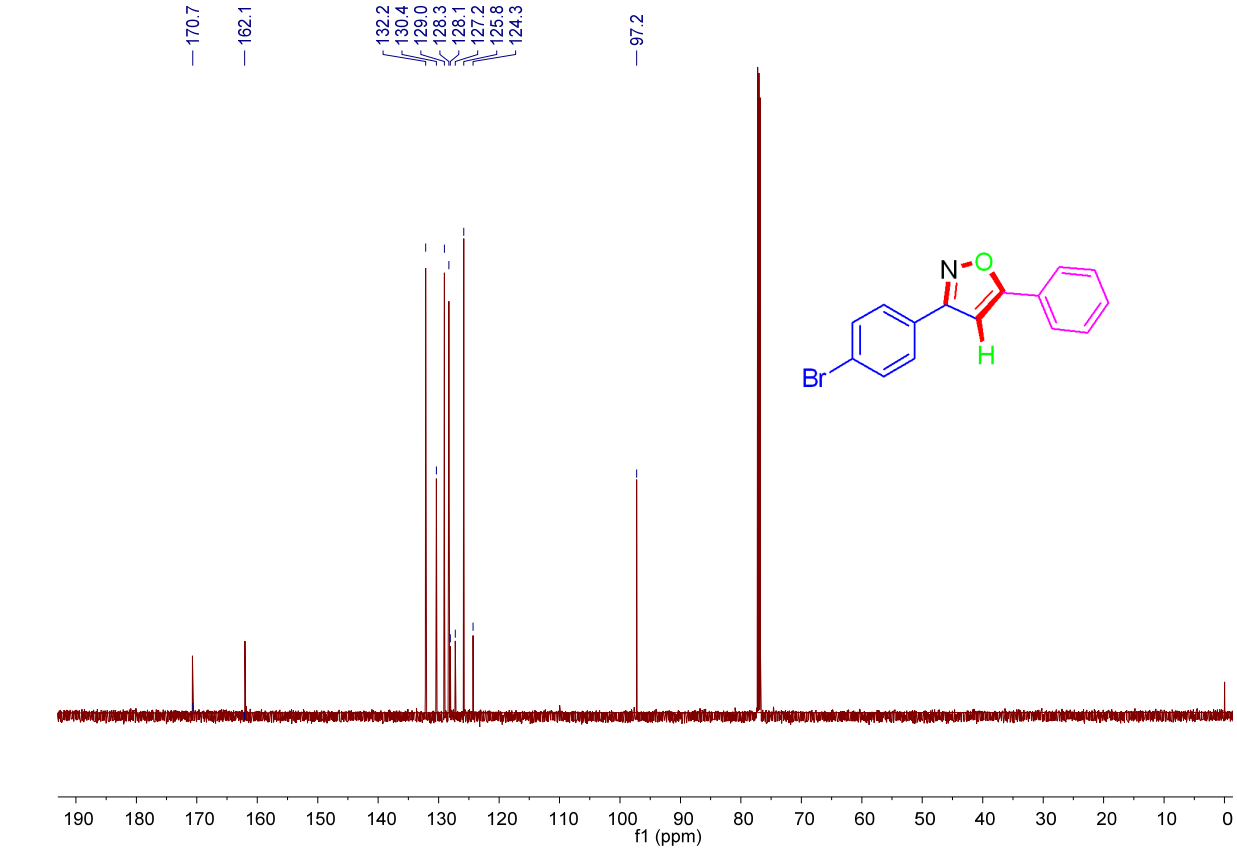
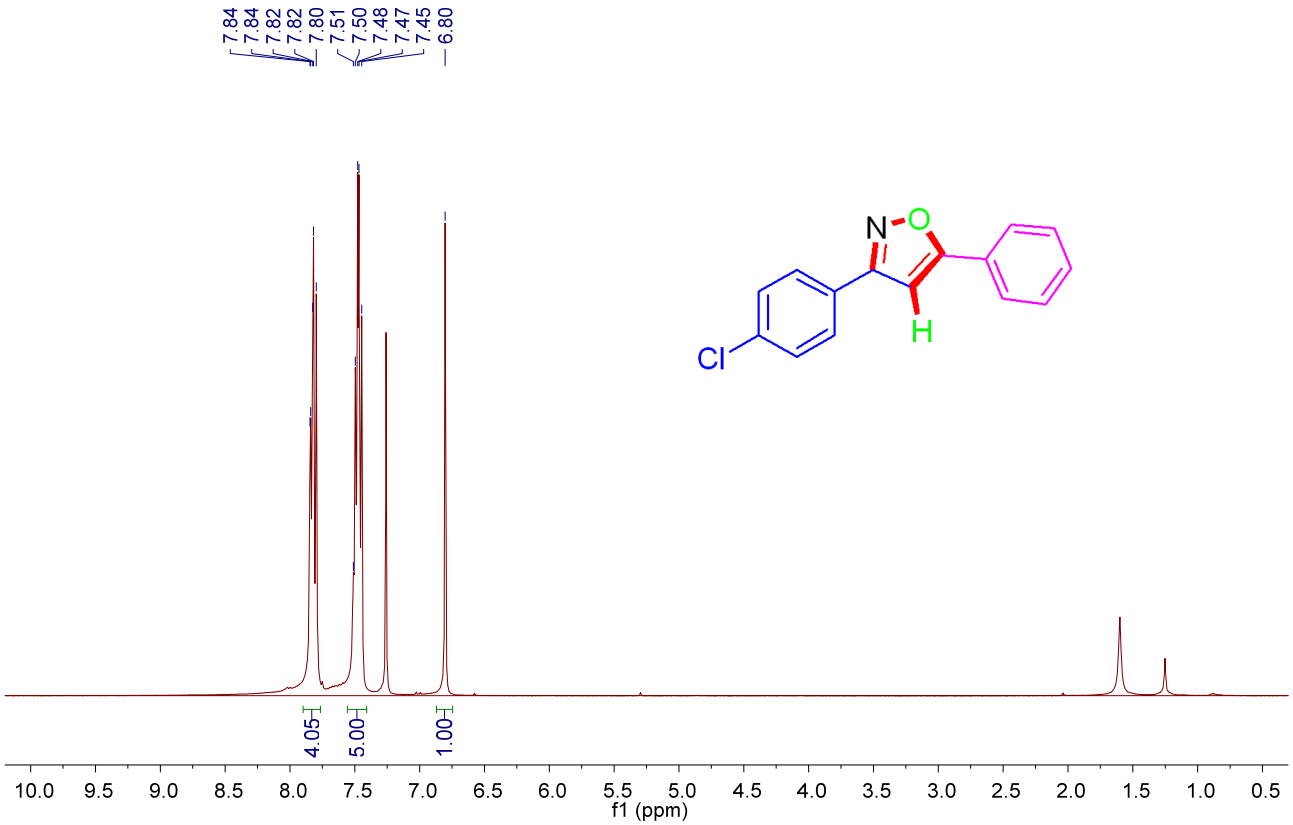
-110
-130
-150
-170
-190
f1 (ppm)

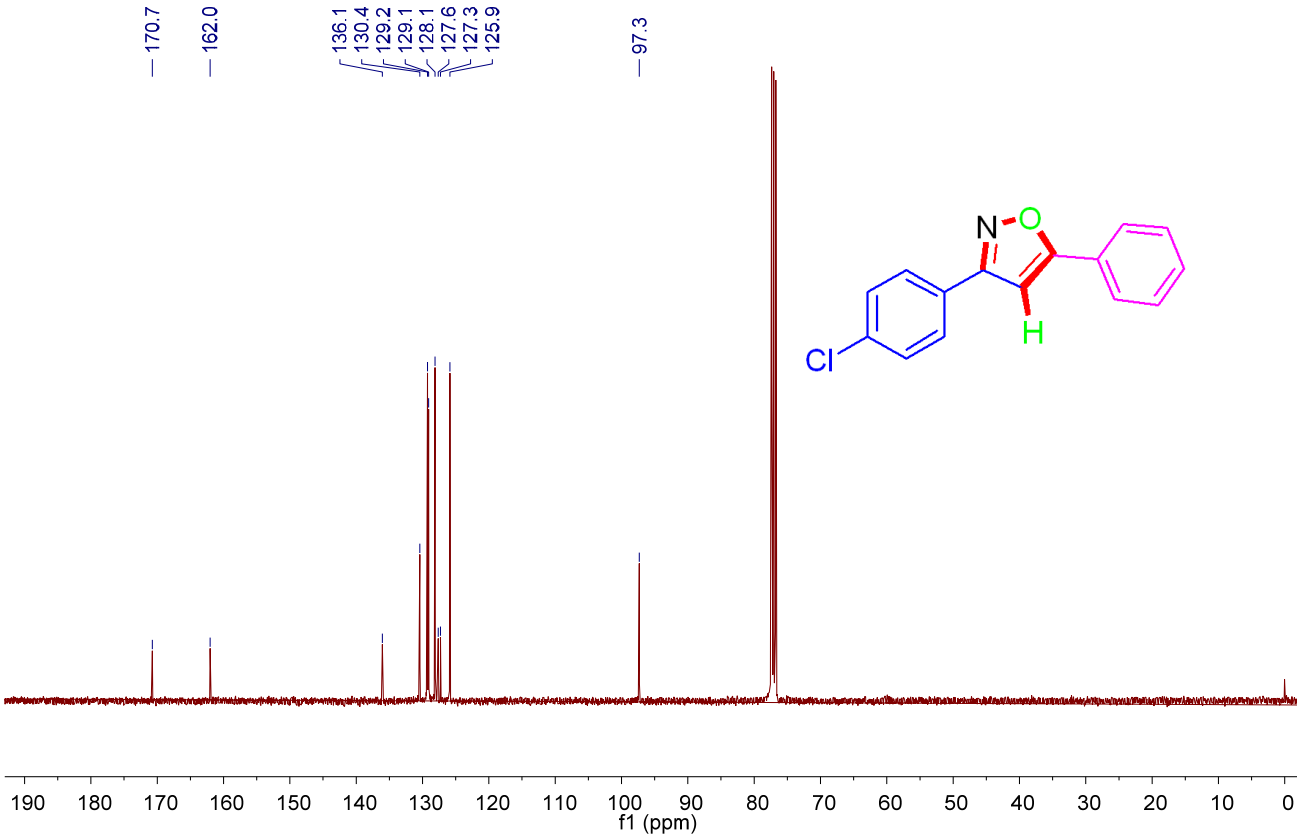
3-(4-bromophenyl)-5-phenylisoxazole (4fa).



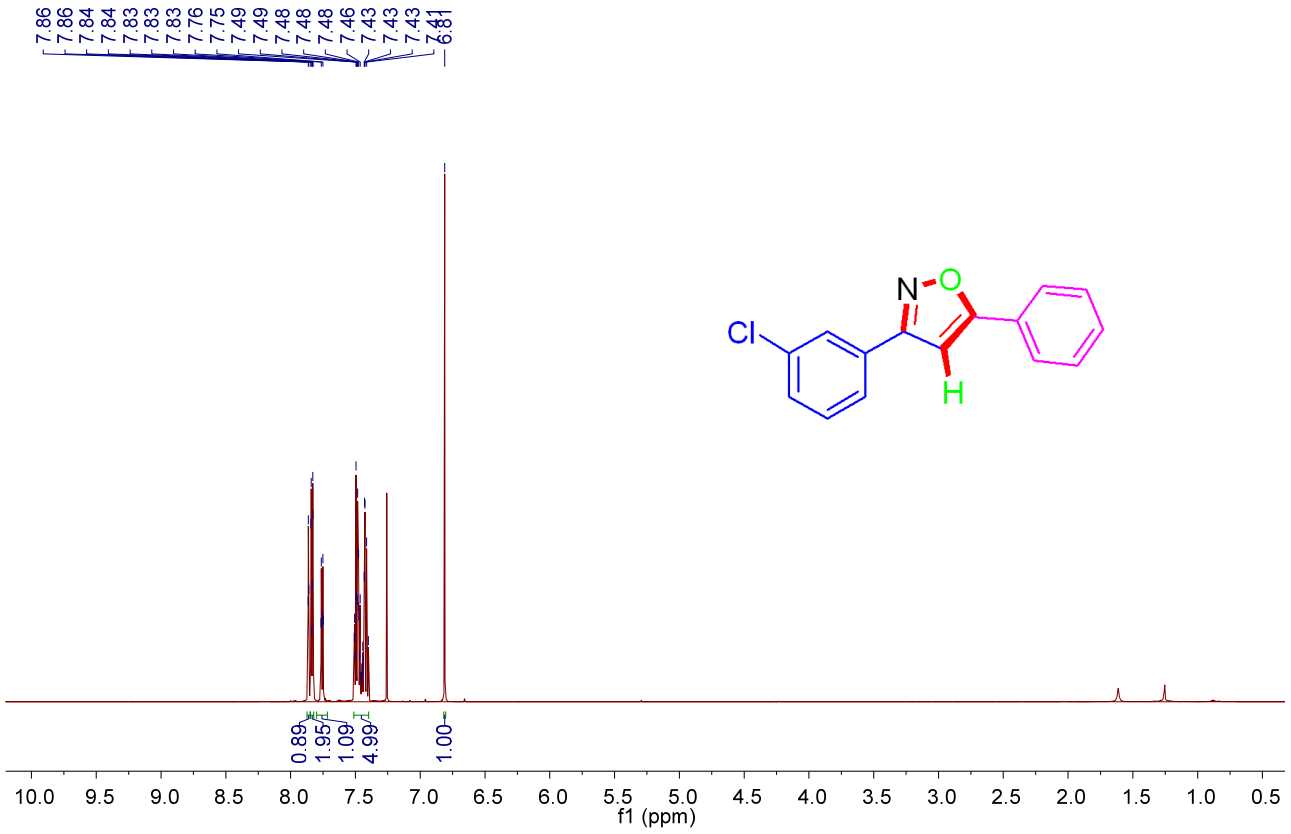


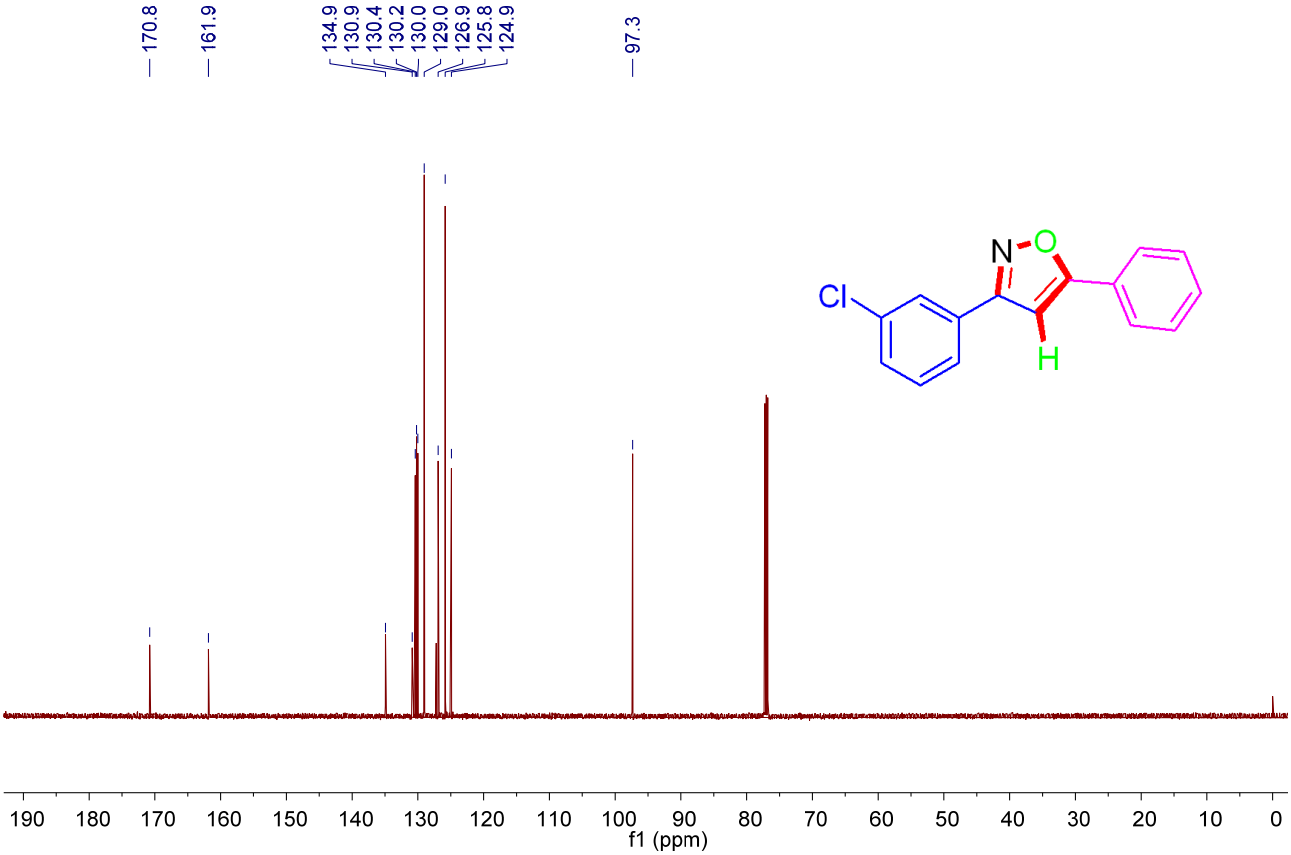
3-(4-chlorophenyl)-5-phenylisoxazole (4ga).



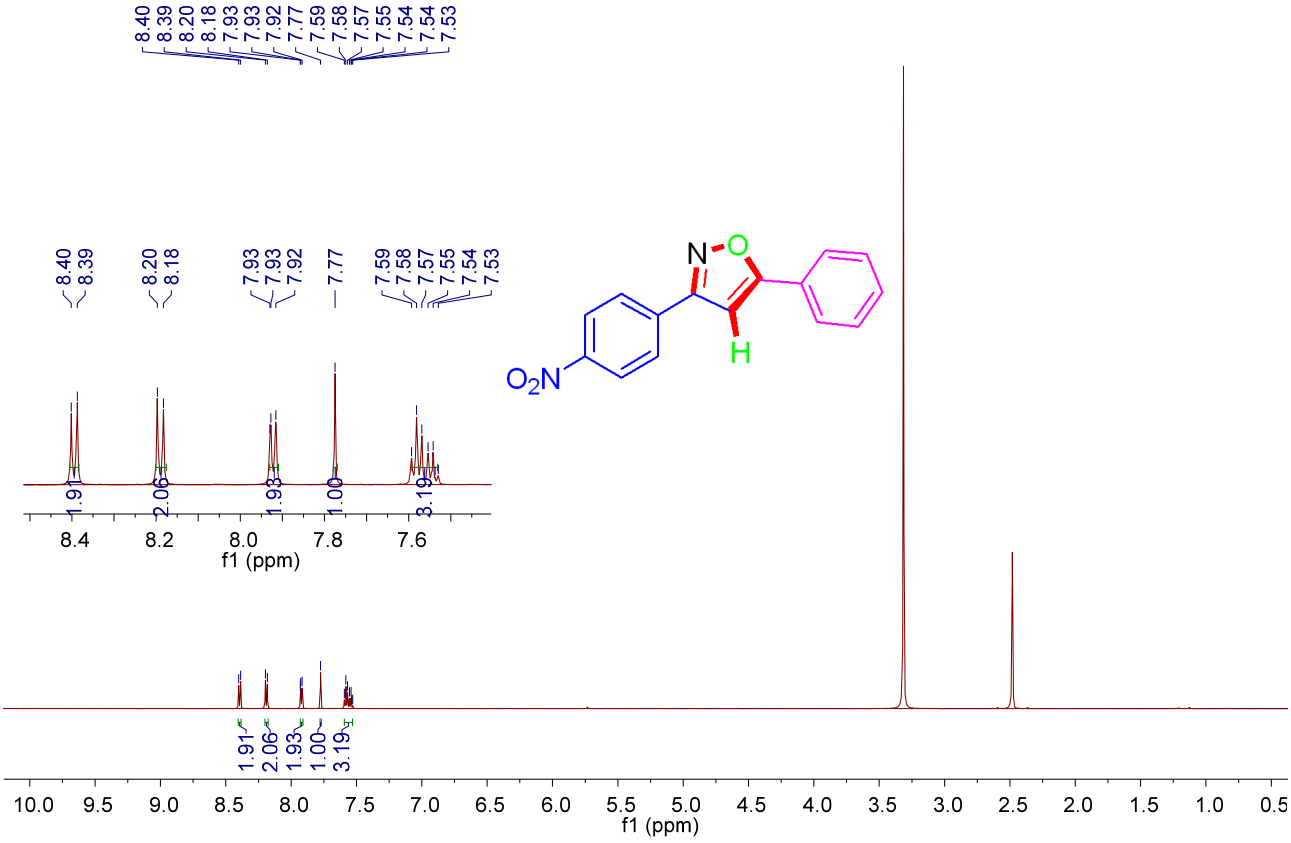


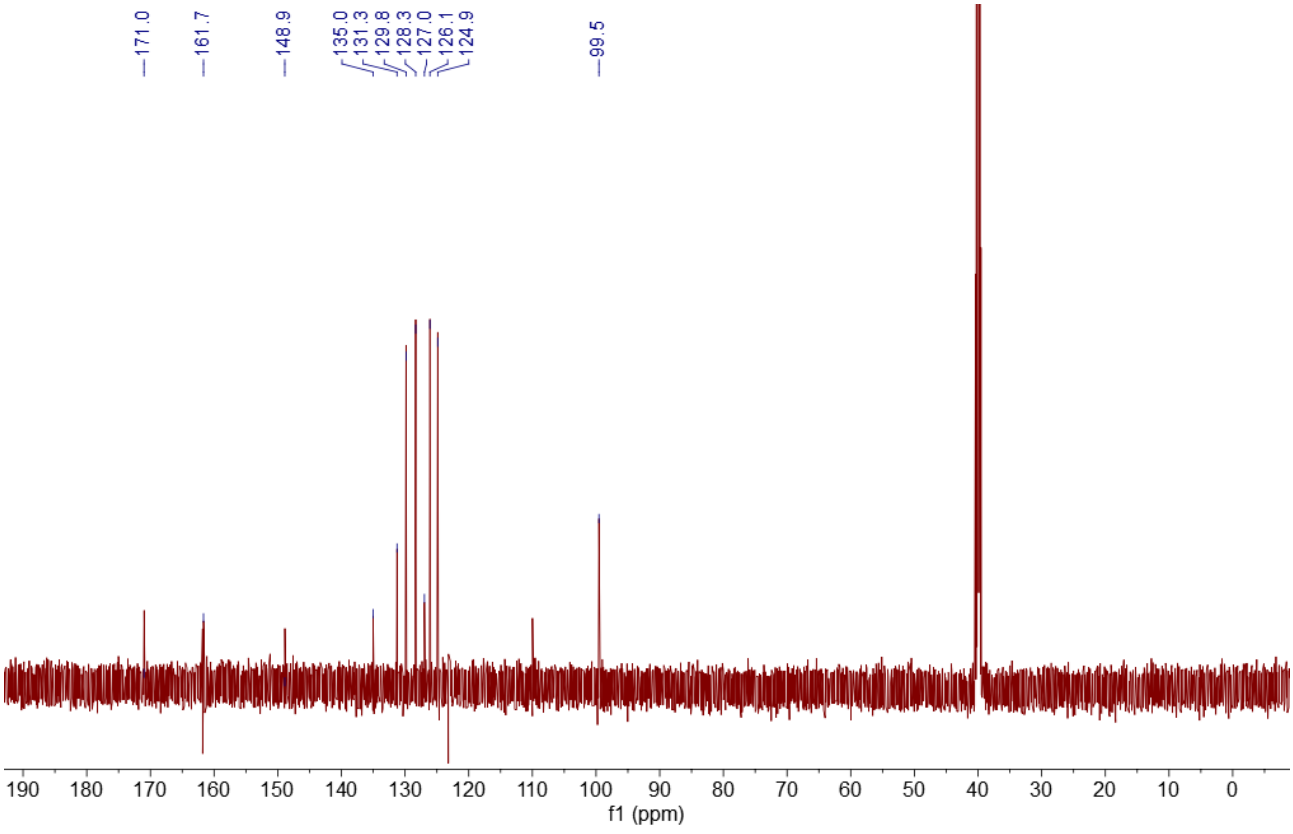
3-(3-chlorophenyl)-5-phenylisoxazole (4ha).



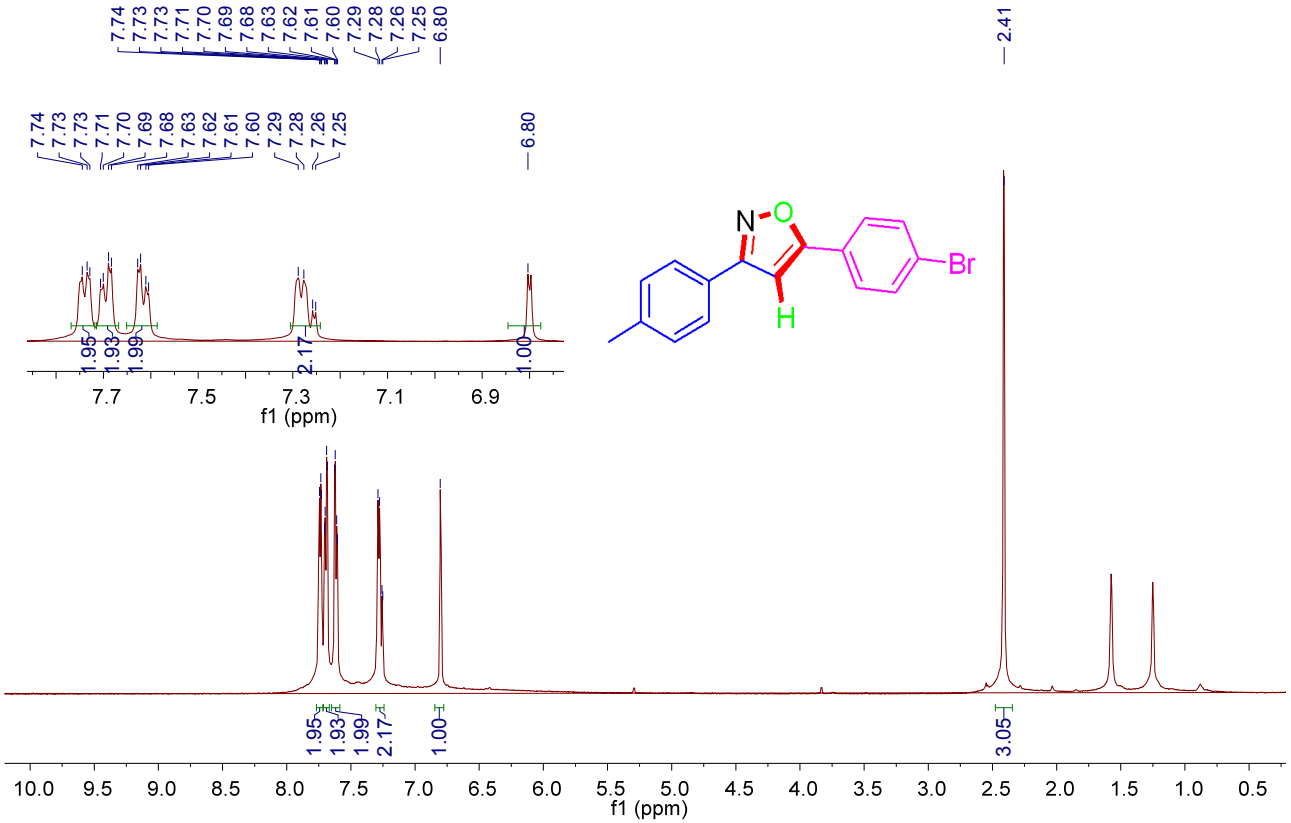


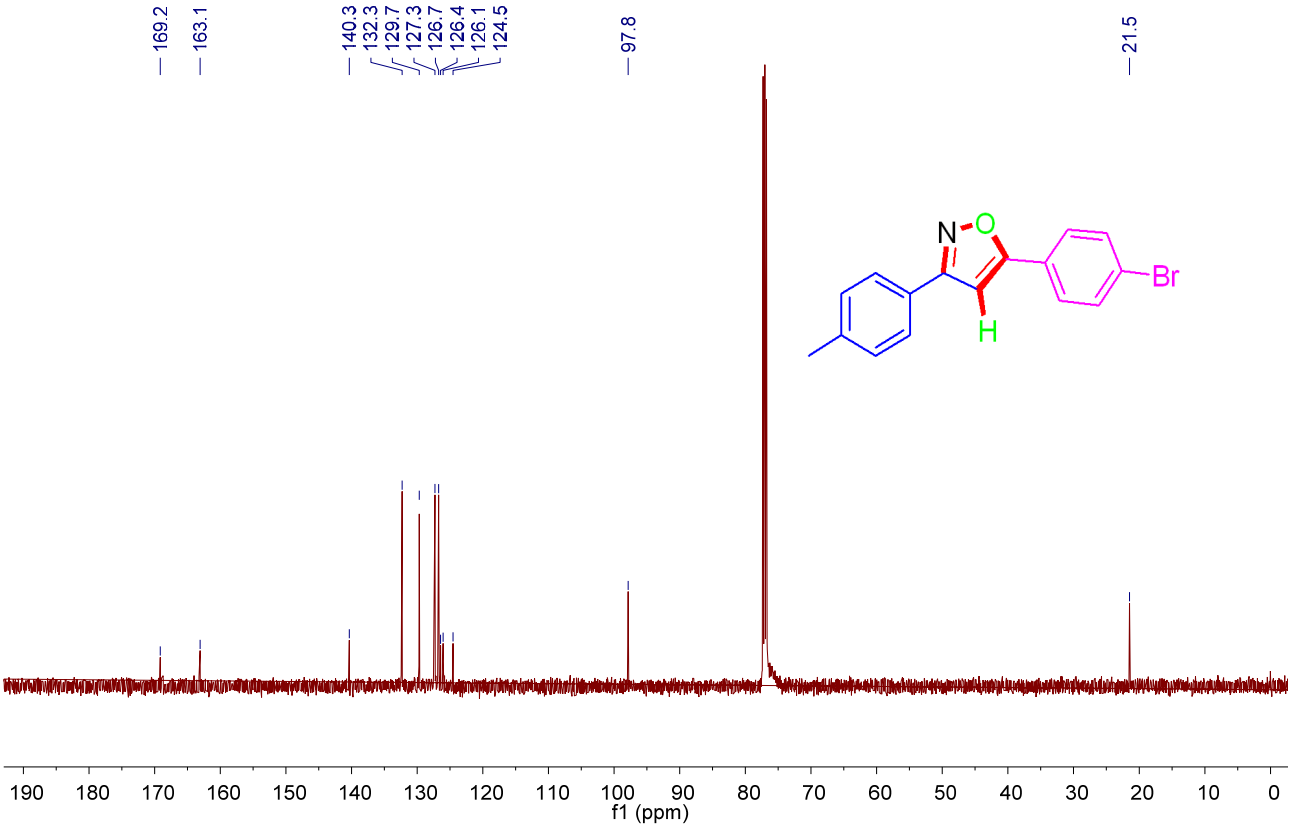
3-(4-nitrophenyl)-5-phenylisoxazole (4ia).



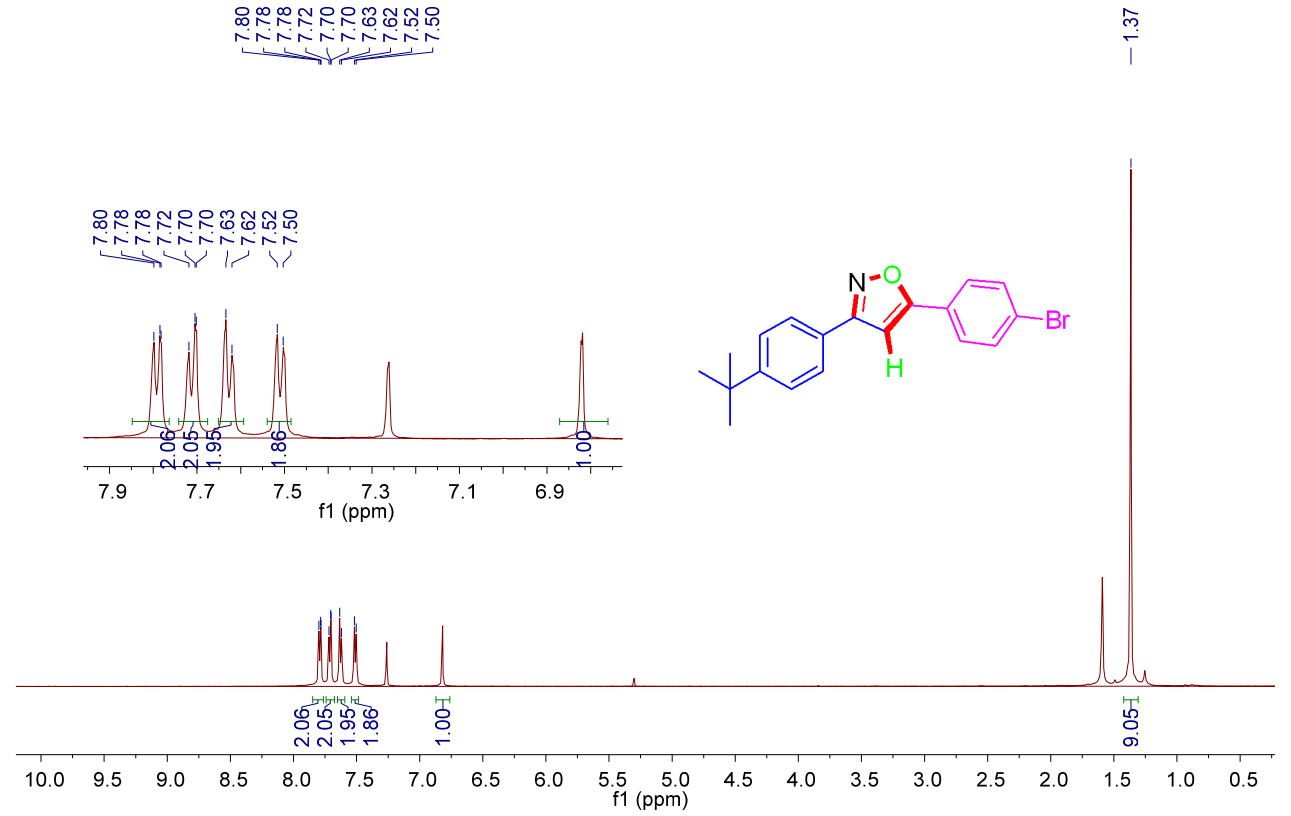


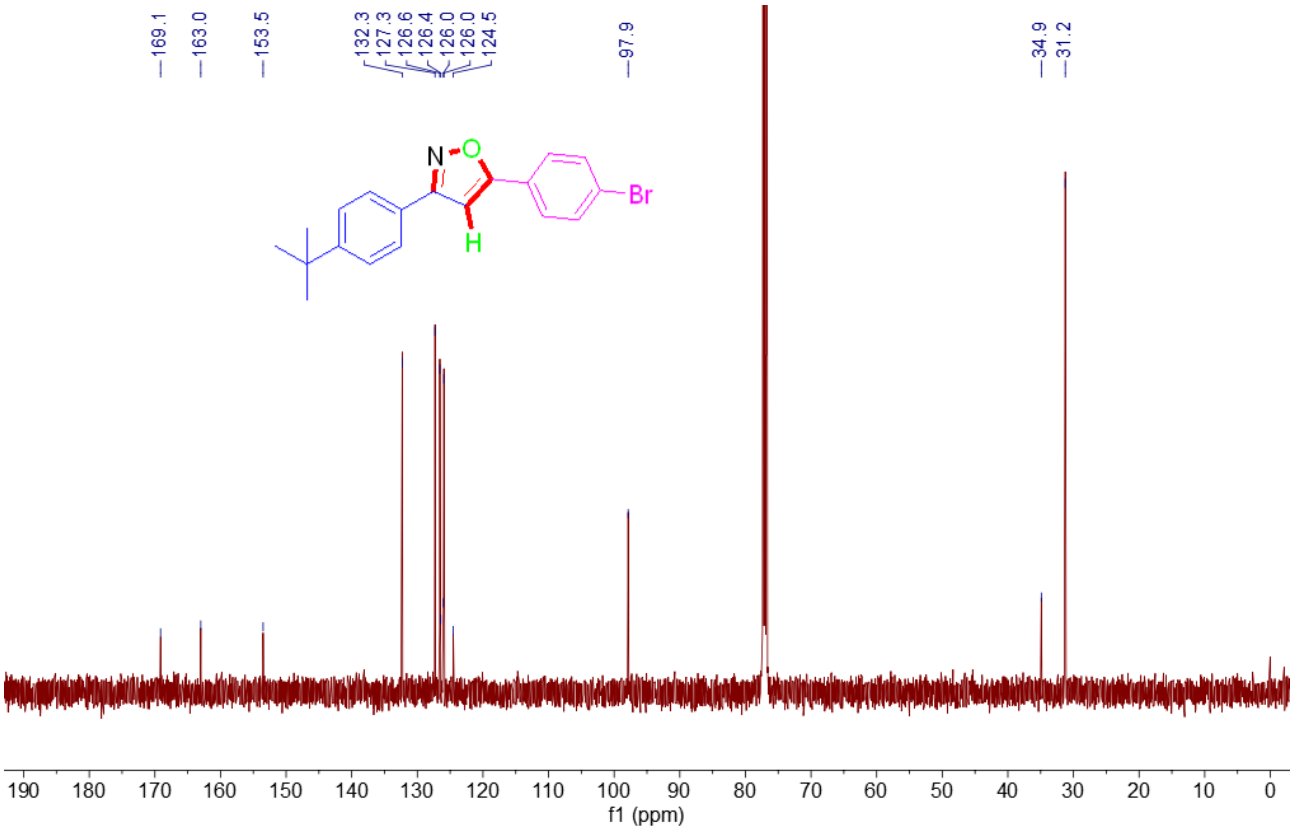
5-(4-bromophenyl)-3-(p-tolyl)isoxazole (4bd).



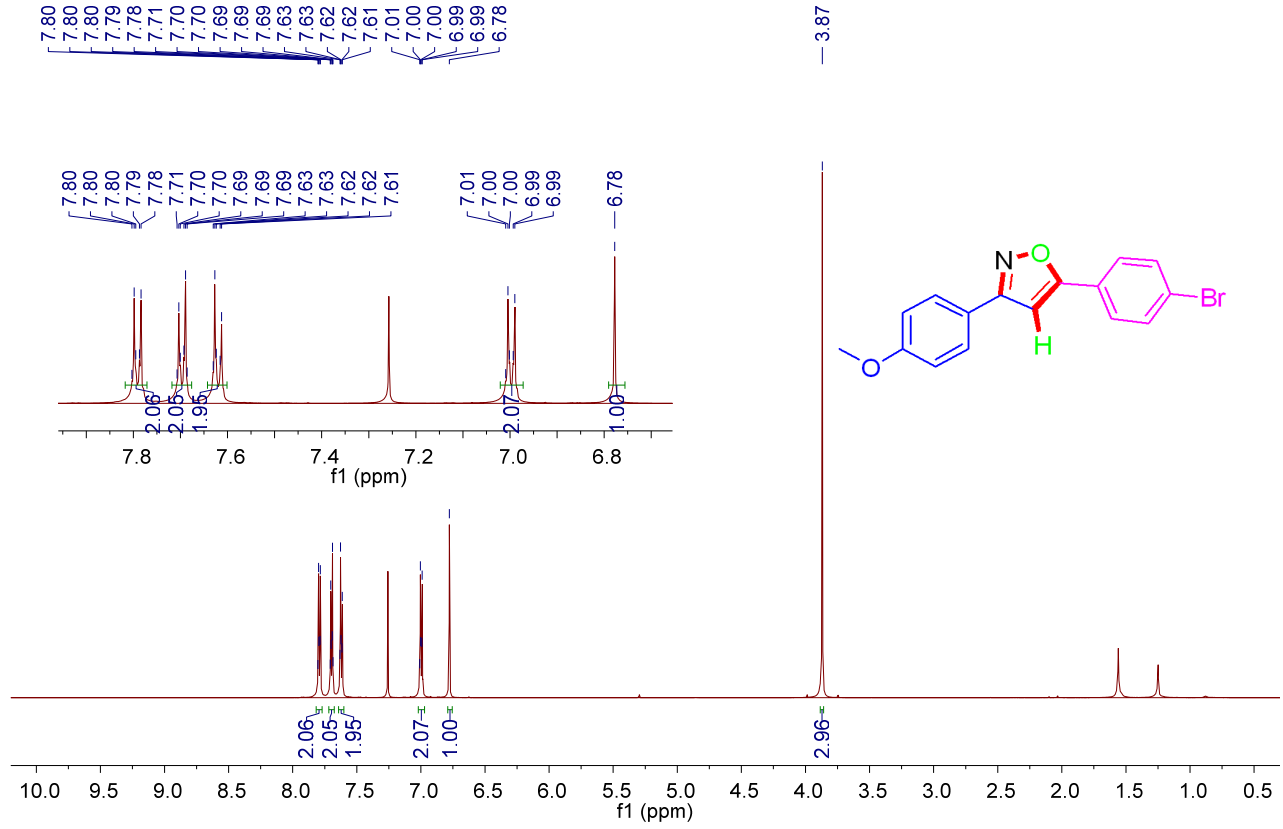


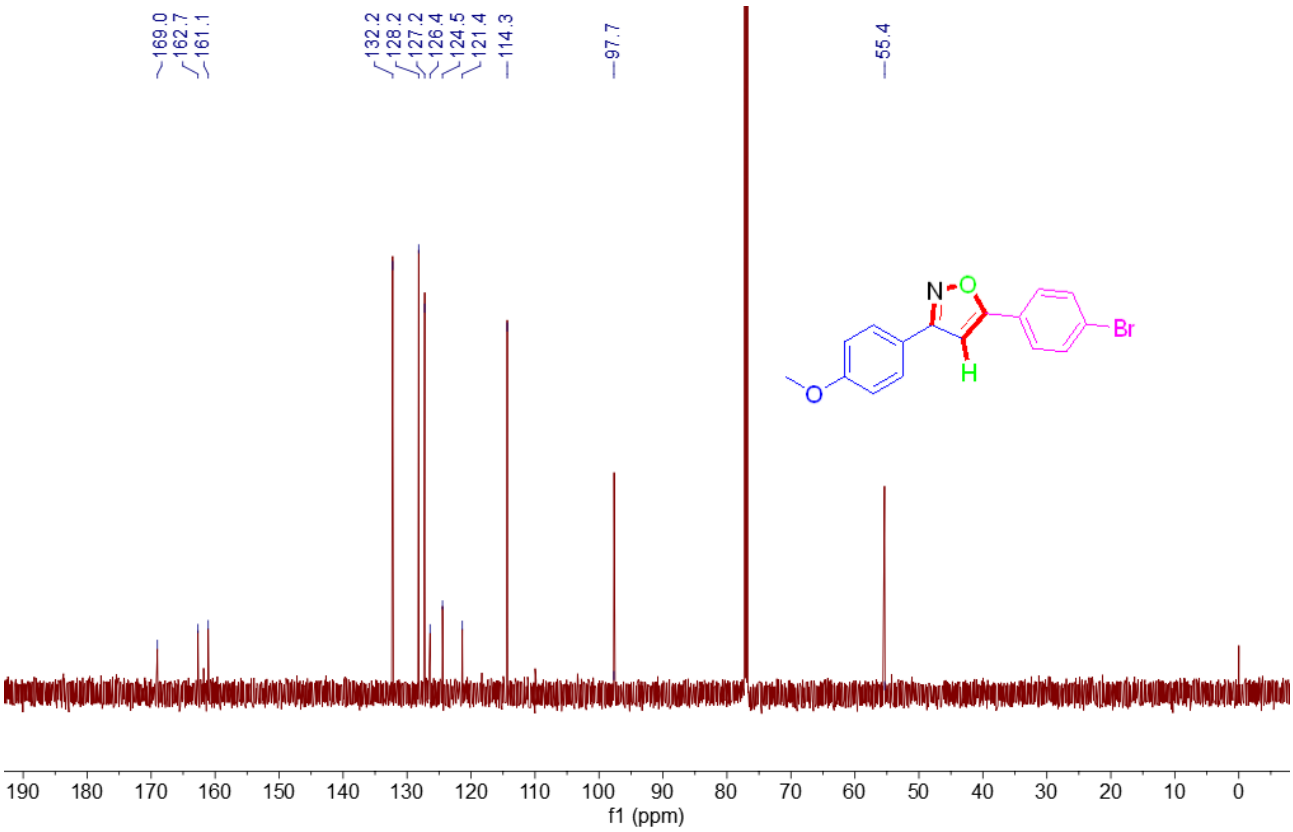
5-(4-bromophenyl)-3-(4-(tert-butyl)phenyl)isoxazole (4cd).



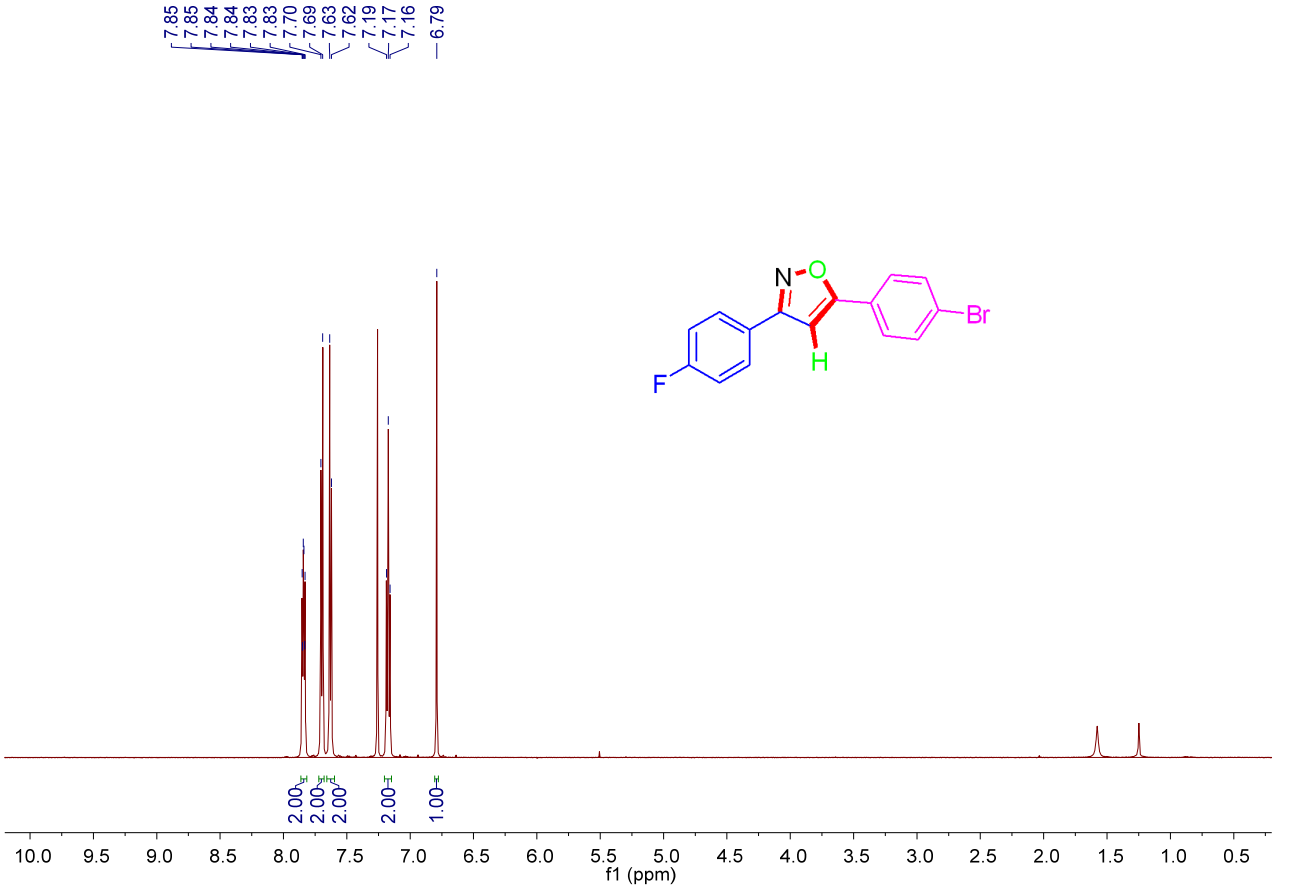


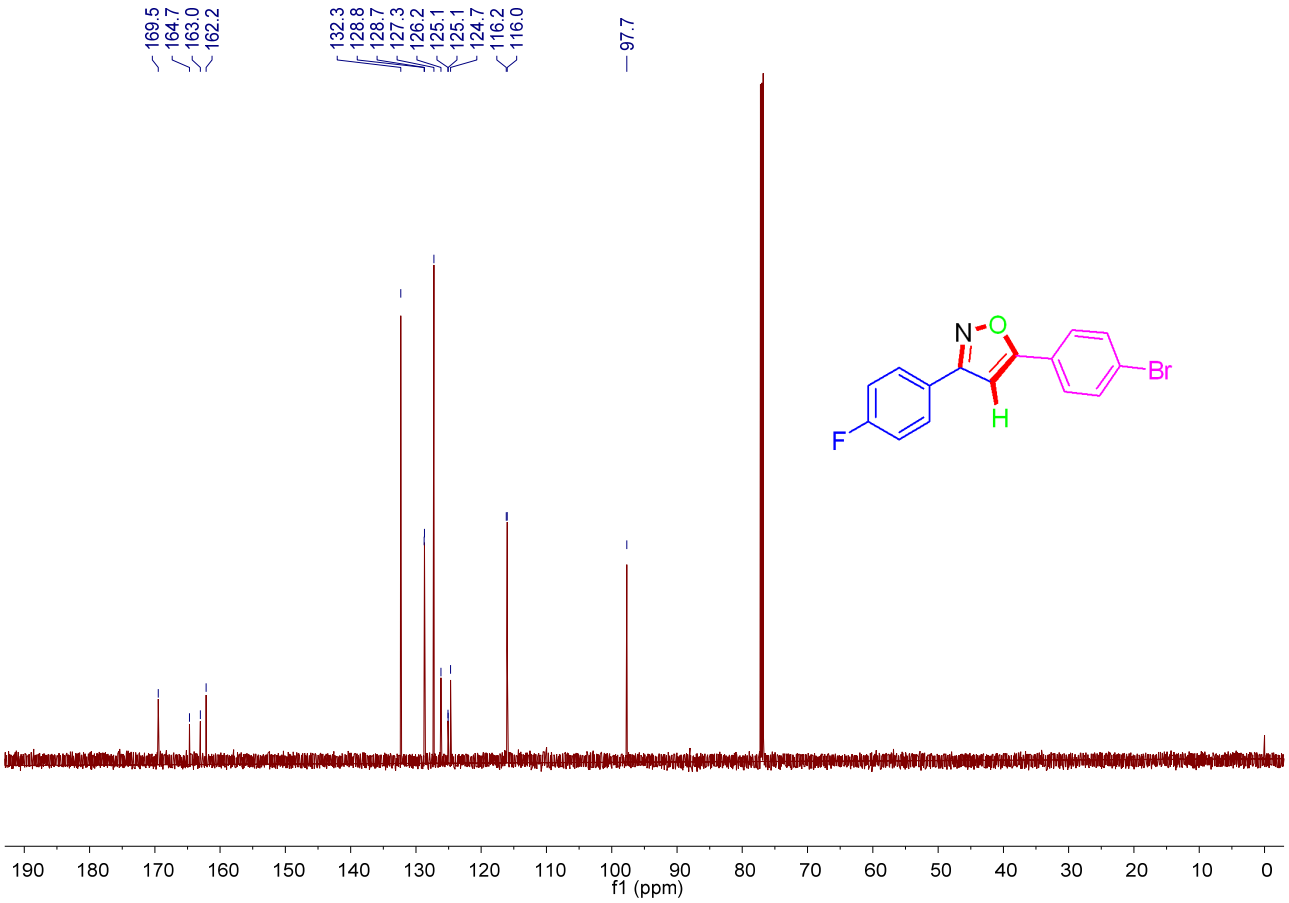
5-(4-bromophenyl)-3-(4-methoxyphenyl)isoxazole (4dd).

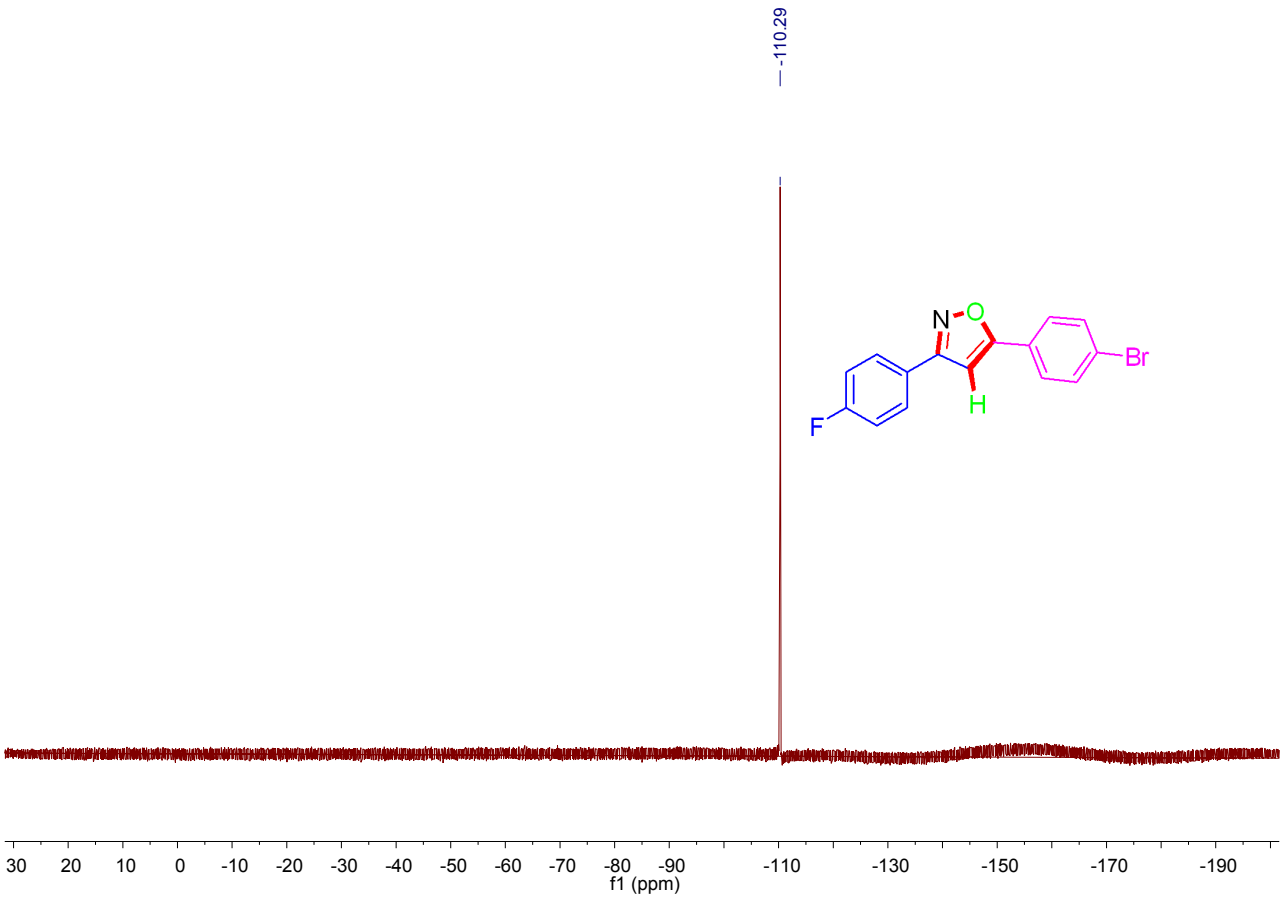




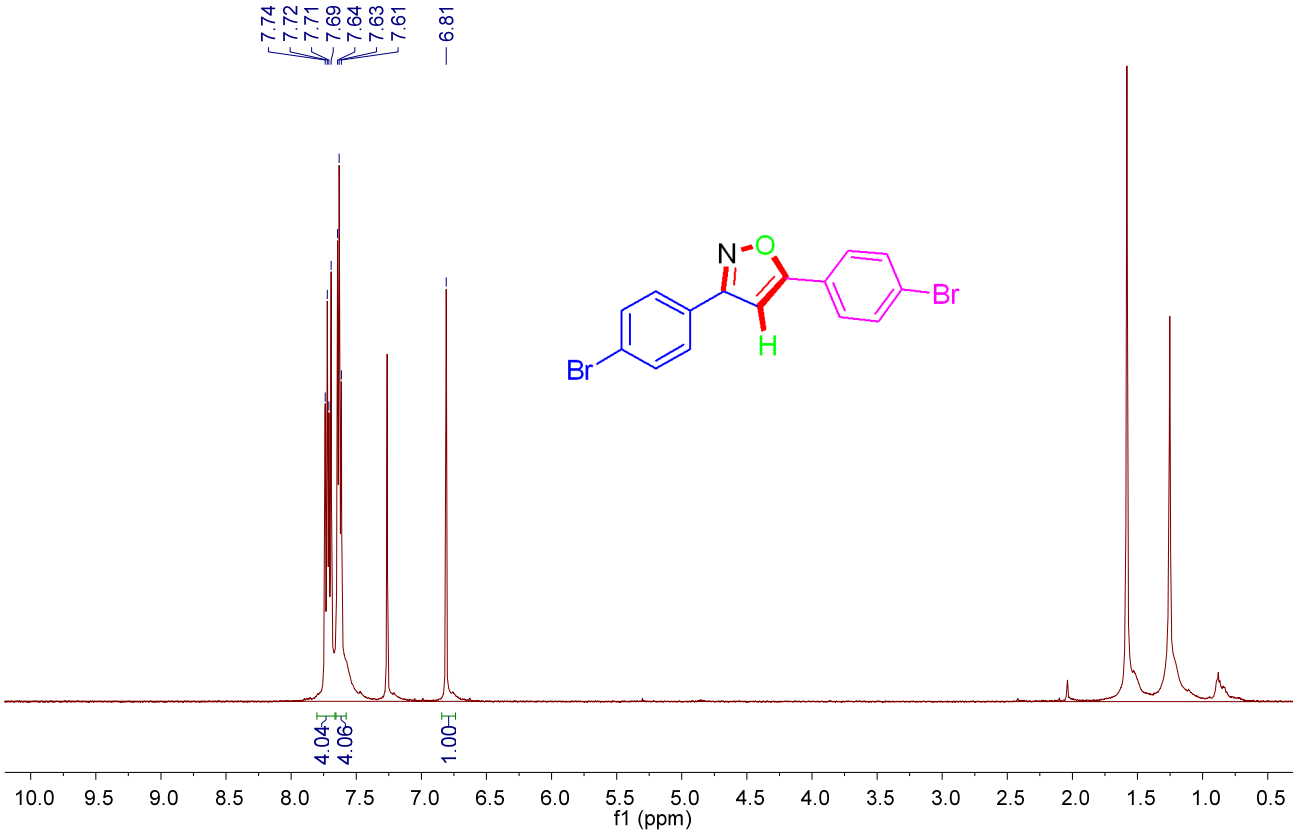
5-(4-bromophenyl)-3-(4-fluorophenyl)isoxazole (4ed).

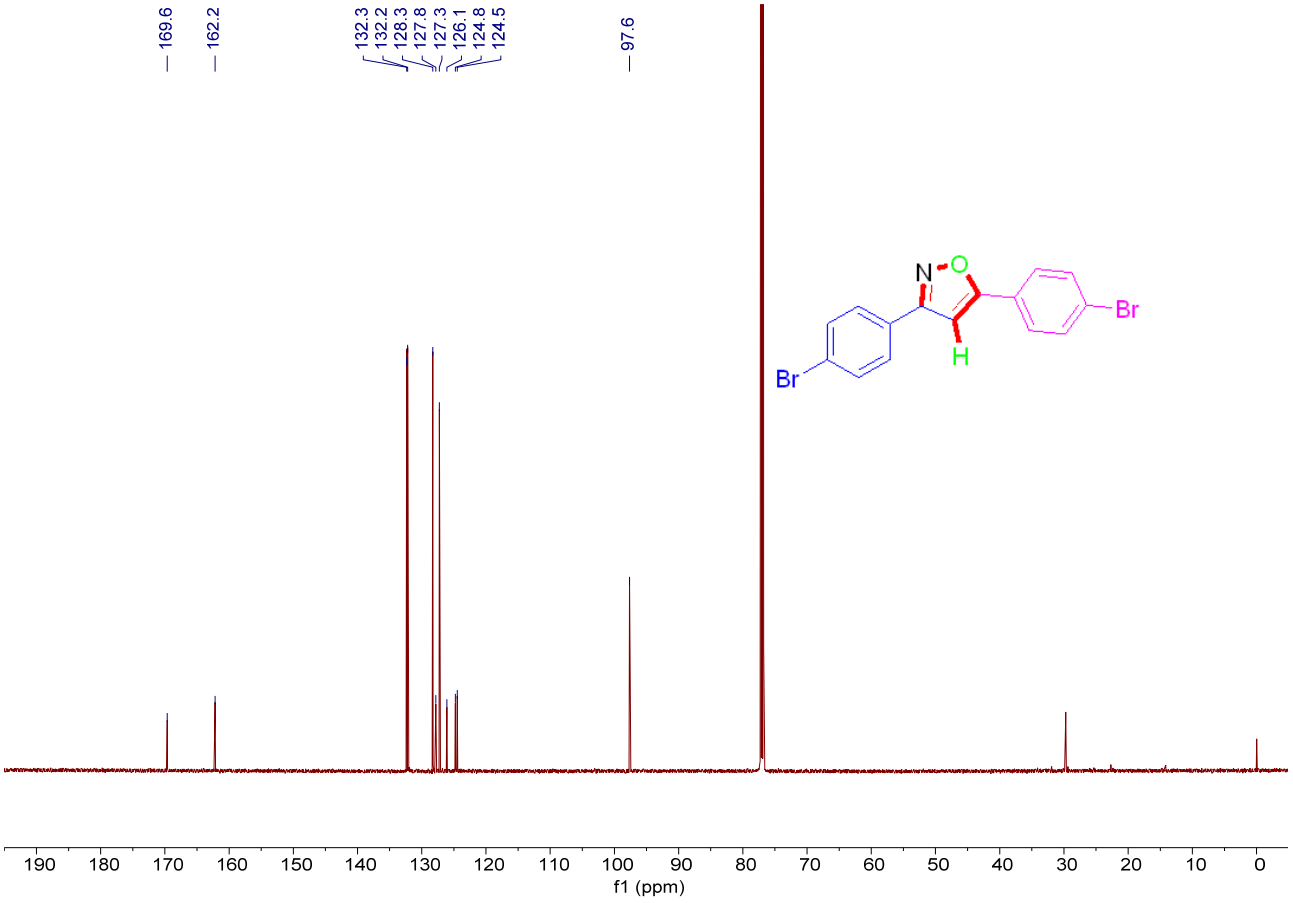




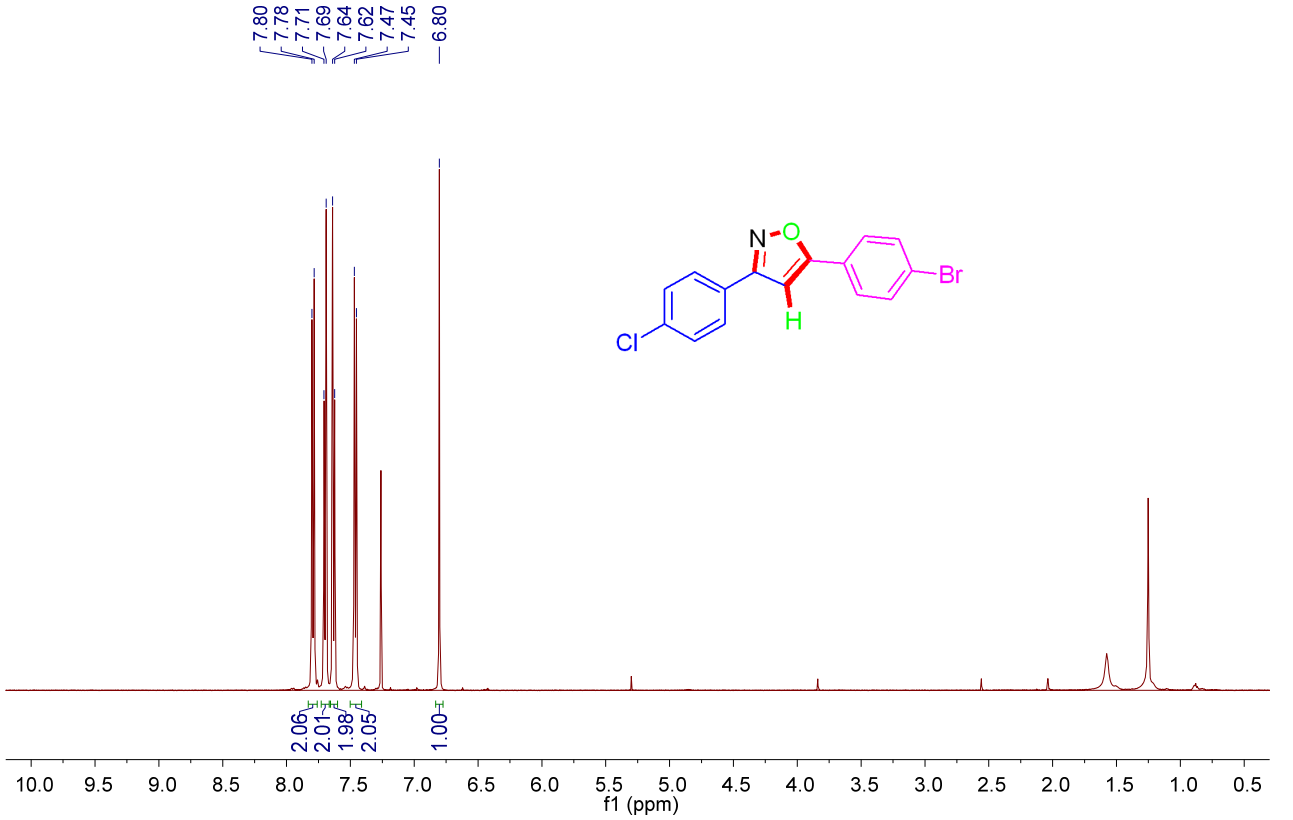

-110.29
N
O
Br
H
F
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-130
-150
-170
-190
f1 (ppm)

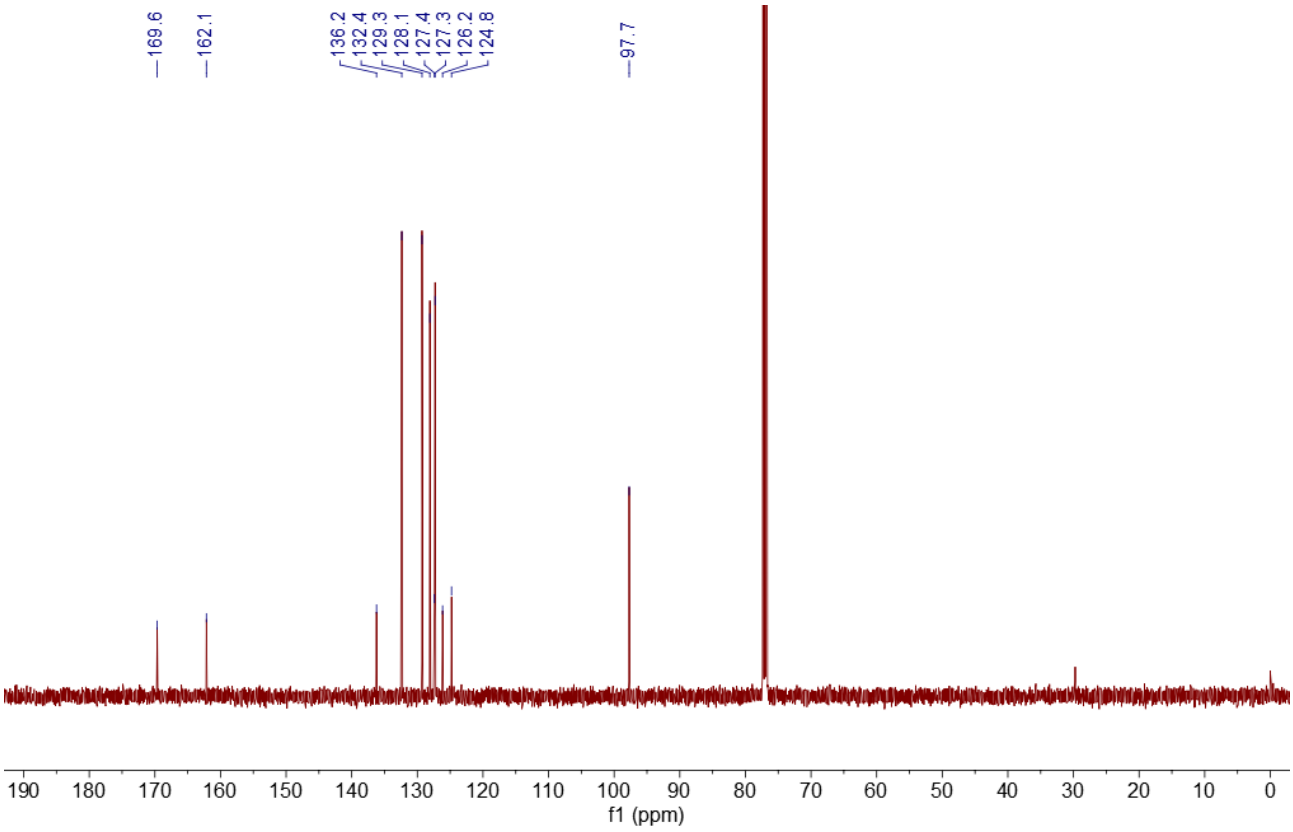
3,5-bis(4-bromophenyl)isoxazole (4fd).



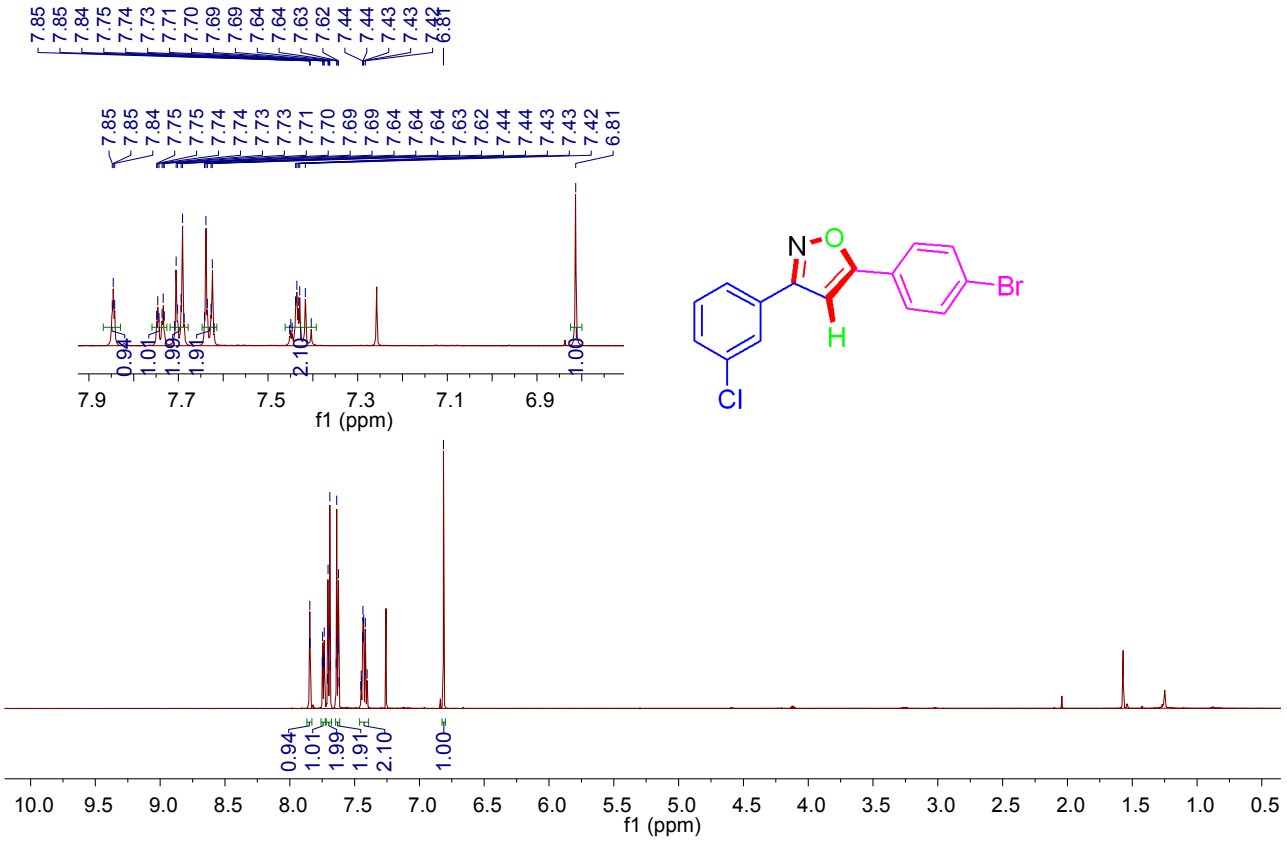


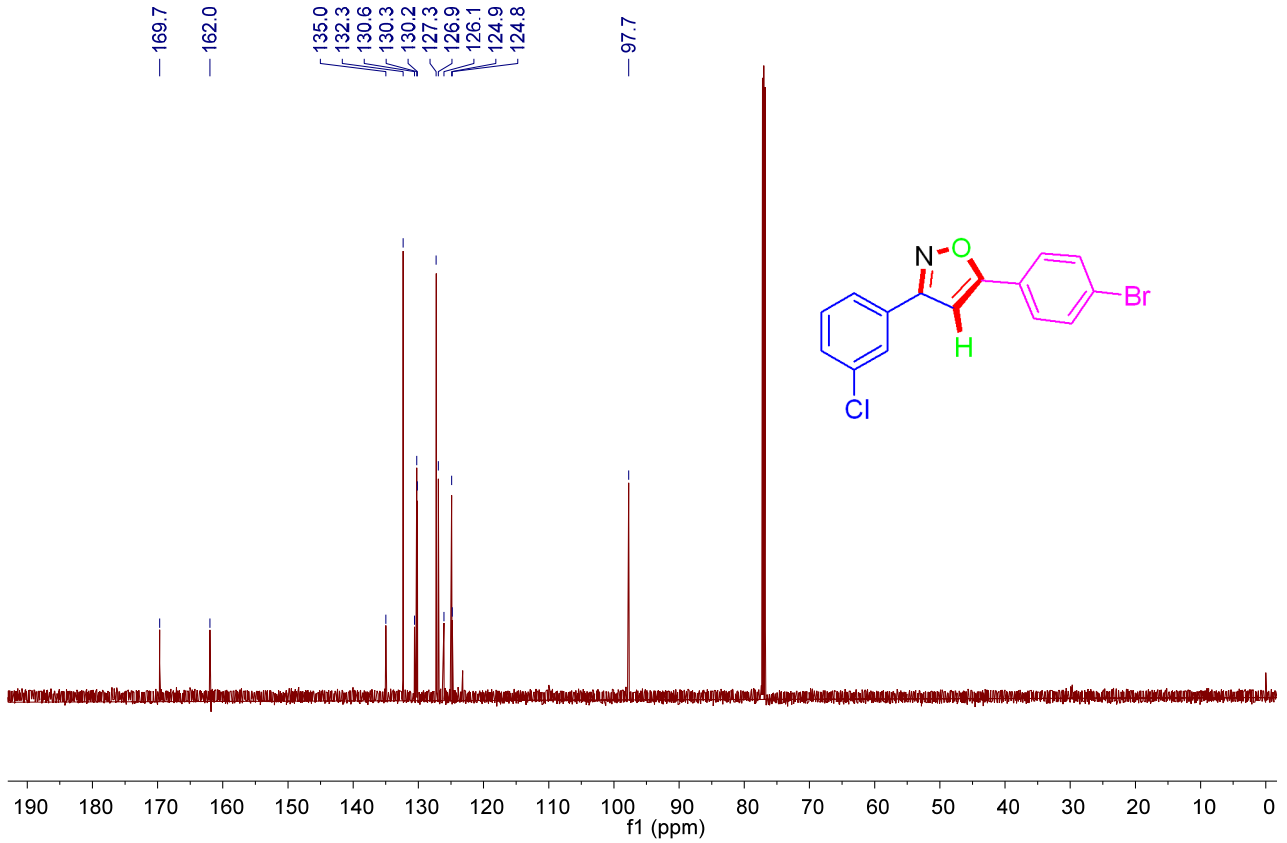
5-(4-bromophenyl)-3-(4-chlorophenyl)isoxazole(4gd).



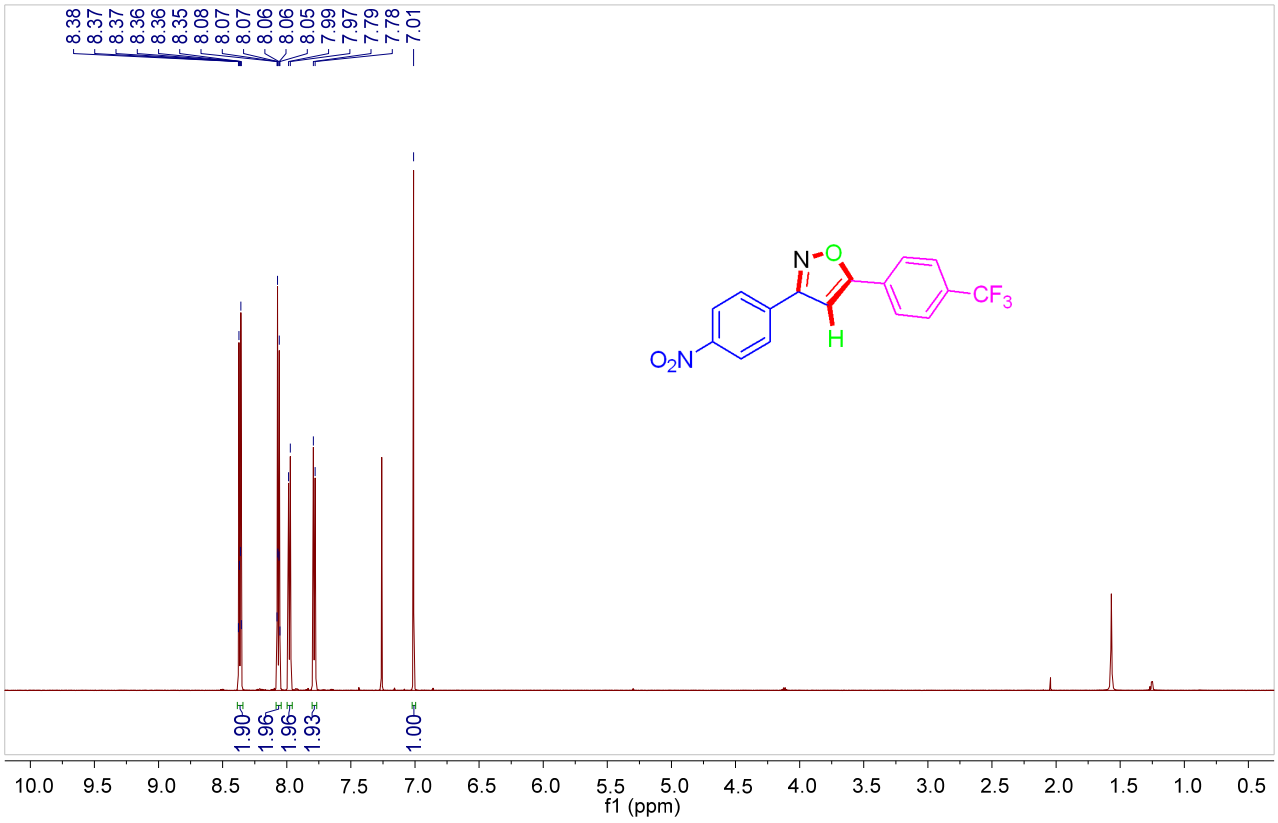


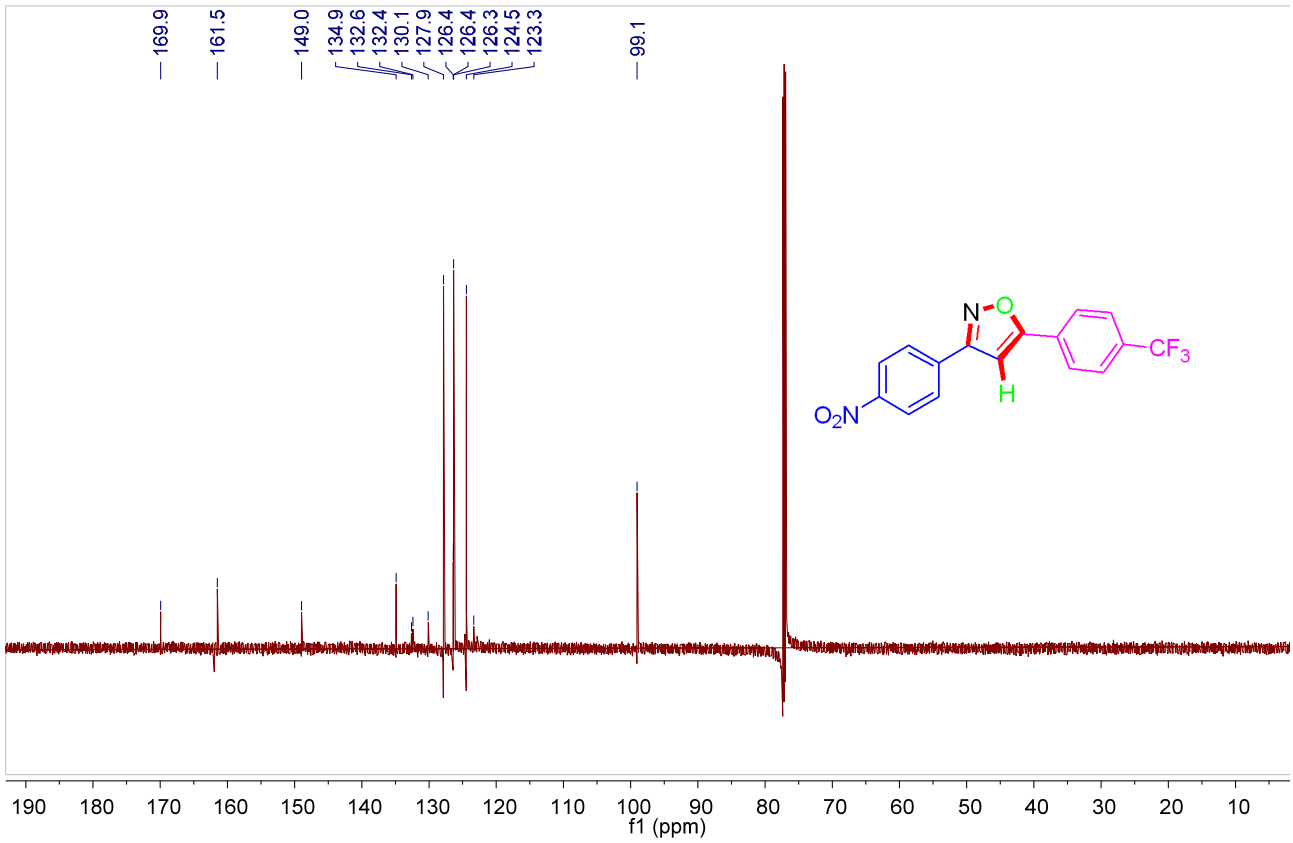
5-(4-bromophenyl)-3-(3-chlorophenyl)isoxazole (4hd).

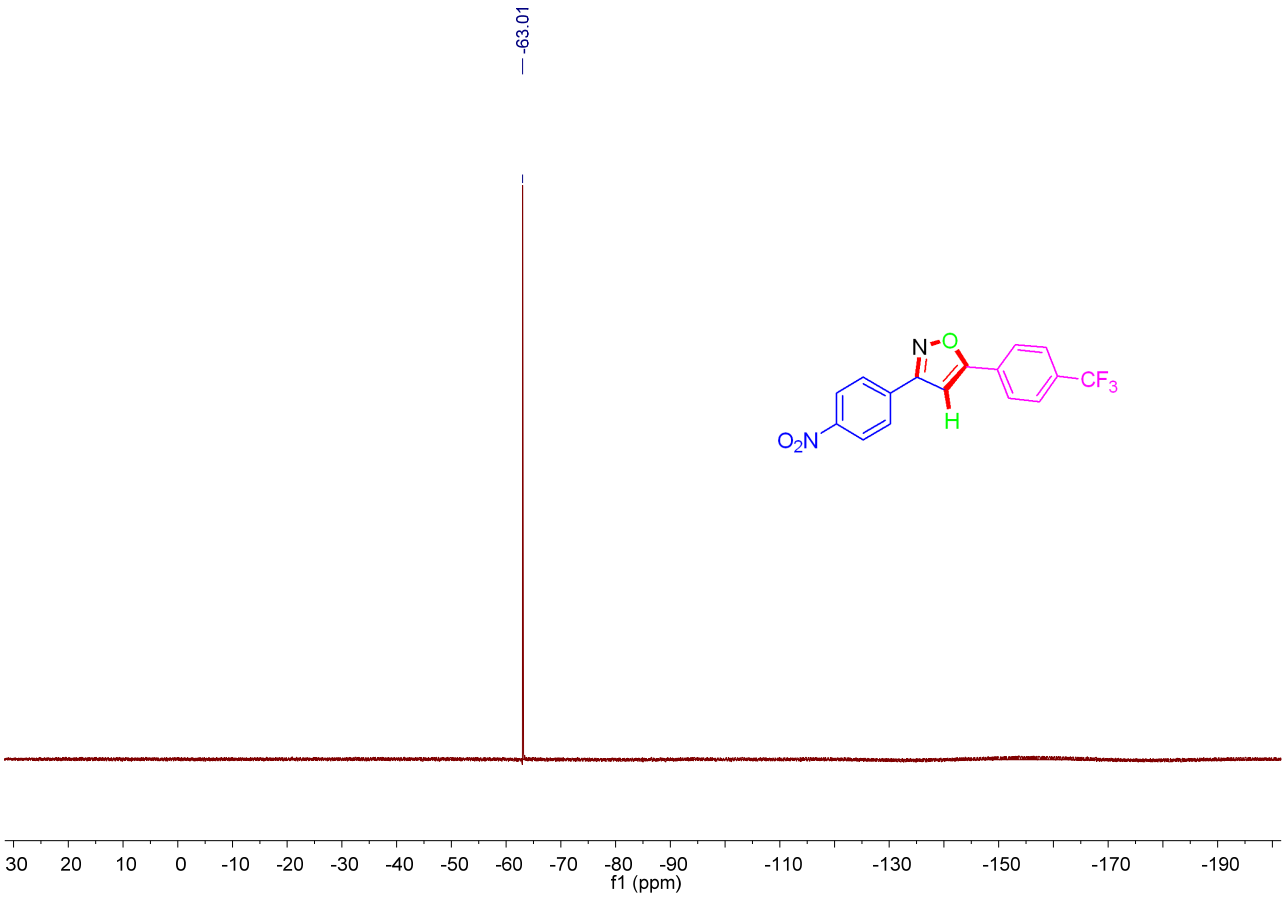




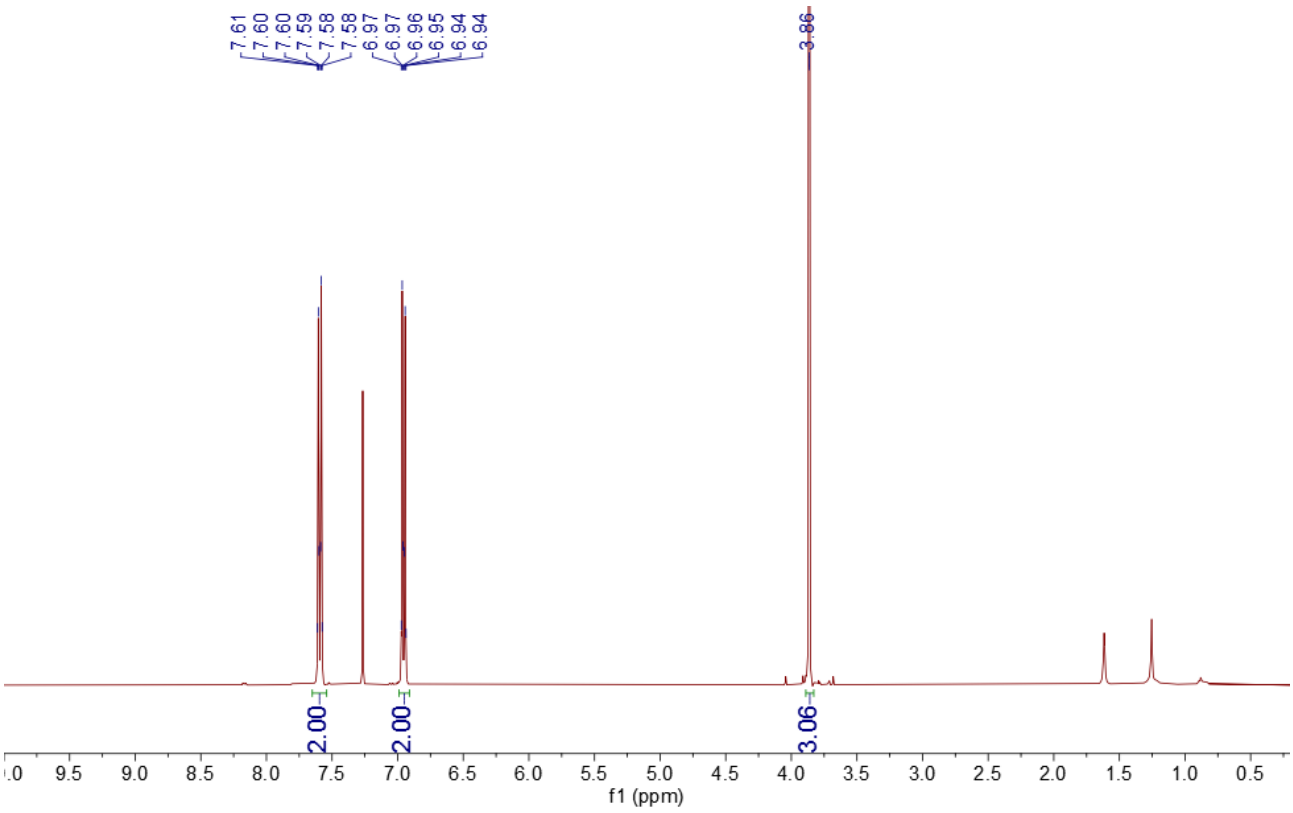
3-(4-nitrophenyl)-5-(4-(trifluoromethyl)phenyl)isoxazole (4ih).

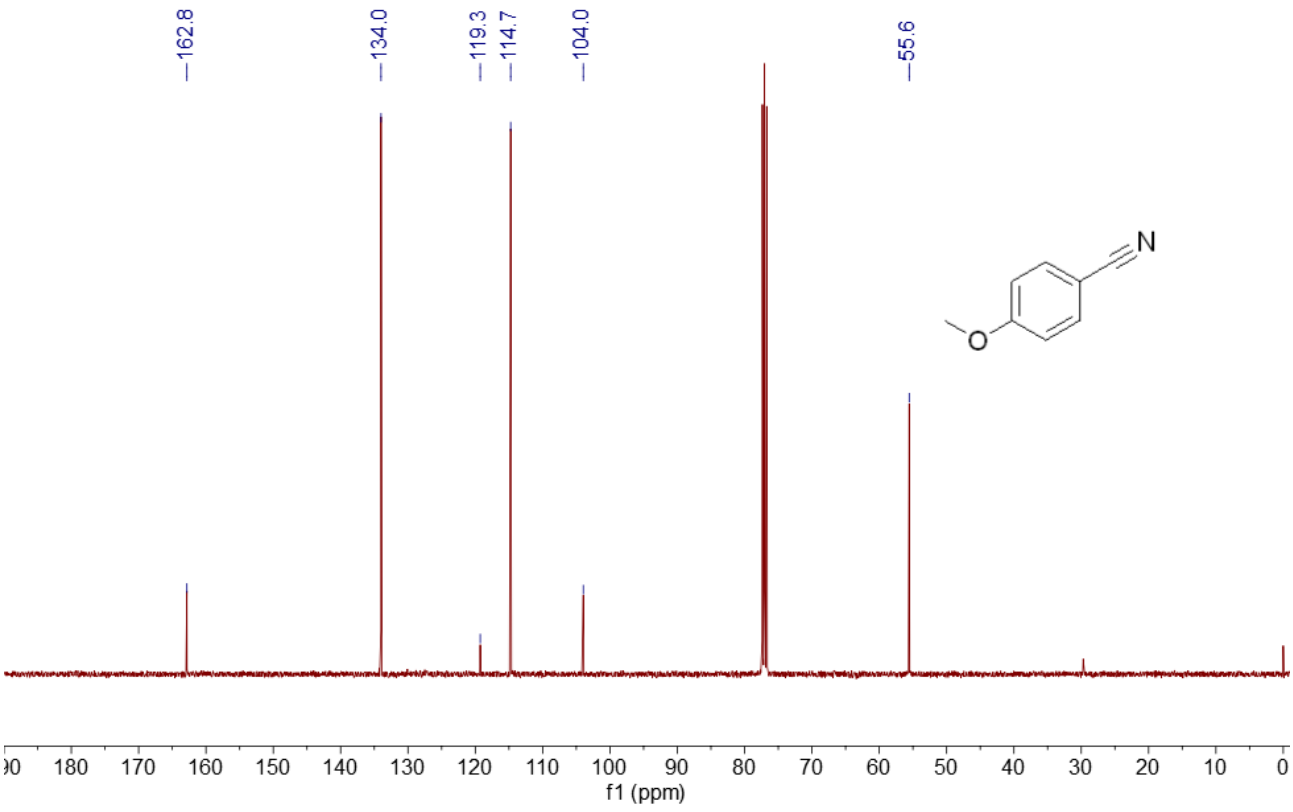




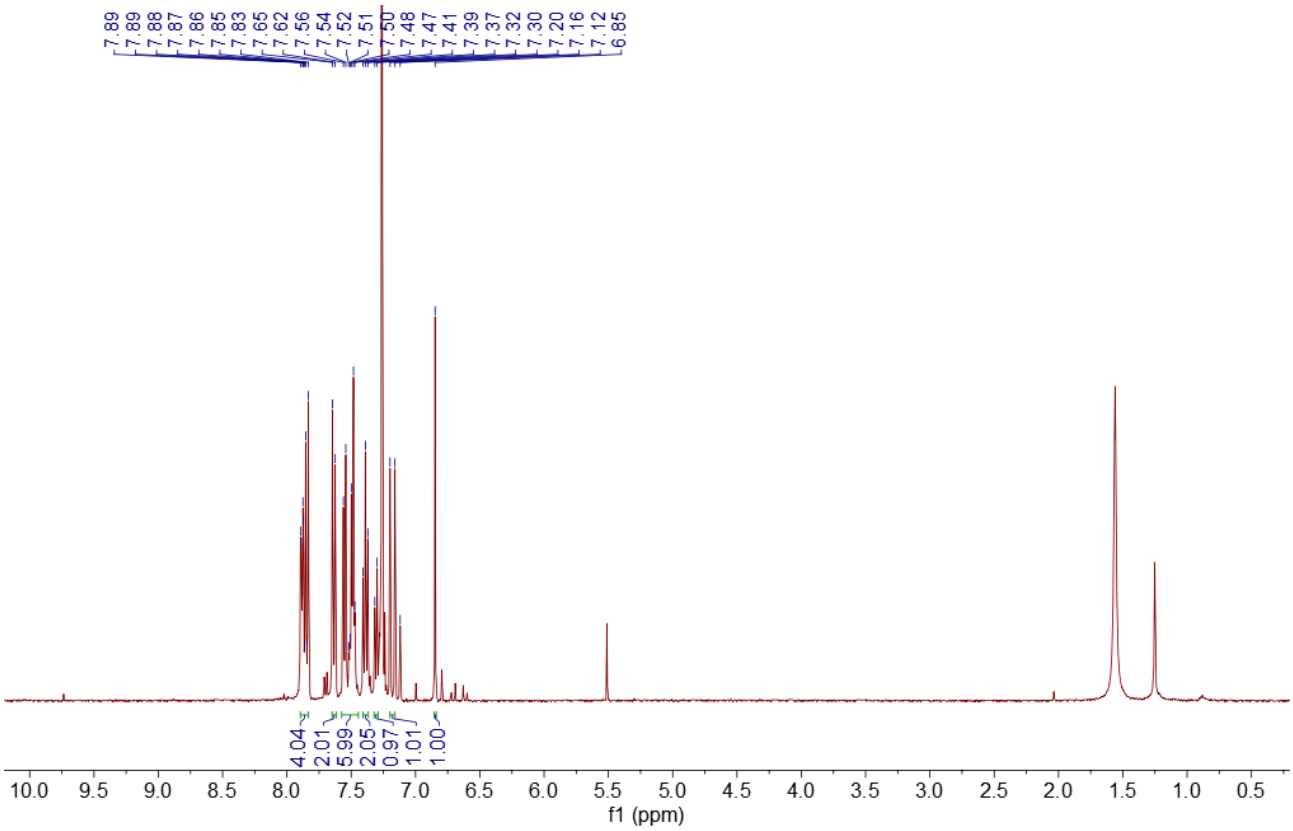

-63.01
N
O
CF3
H
O2N
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-130
-150
-170
-190
f1 (ppm)

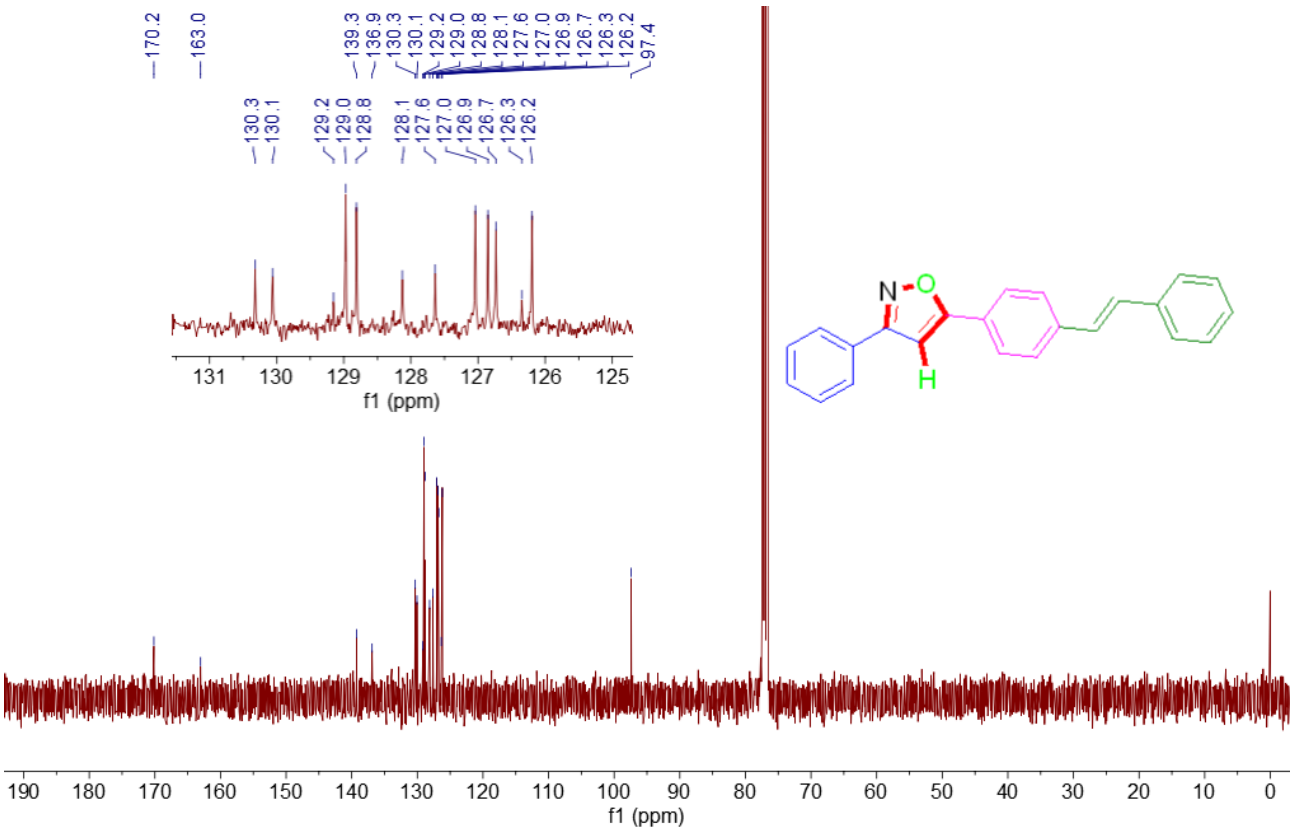
4-methoxybenzonitrile (4').





(E)-3-phenyl-5-(4-styrylphenyl)isoxazole (5).





(E)-3-(hydroxyimino)-1,3-diphenylpropan-1-one (6b)