Supporting Information

Synthesis of 2-Isoxazolyl-2,3-Dihydrobenzofurans *via* Palladium-Catalyzed Cascade Cyclization of Alkenyl Ethers

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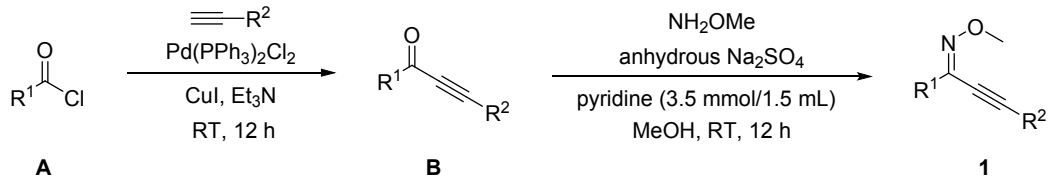
A. General Information

^{1}H and ^{13}C NMR spectra were recorded using Bruker DRX-400 spectrometer or Bruker DRX-500 spectrometer using $CDCl_3$ as solvent. The chemical shifts are referenced to residual ^{1}H and ^{13}C signals of the deuterated solvents respectively (δ_H = 7.26, δ_C = 77.00 for chloroform). Melting points were determined with a Buchi Melting Point B-545 instrument. IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with a Bruker TENSOR 27 spectrometer. The data of HRMS was carried out on a high-resolution mass spectrometer (LCMSIT-TOF). TLC was performed by using commercially prepared 100-400 mesh silica gel plates and visualization was effected at 254 nm. Unless otherwise noted, all reagents and solvents were obtained from commercial suppliers and used without further purification.

B. General Procedure for the Preparation of Alkynyl Oxime Ethers 1

Alkynyl oxime ethers were prepared according to the previously reported procedure.[1]

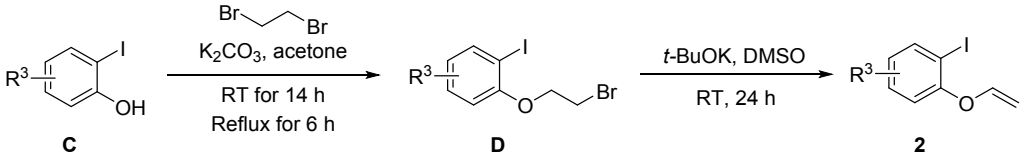


Step 1: $PdCl_2(PPh_3)_2$ (0.02 mmol, 0.4 mol %, 14 mg), CuI (0.1 mmol, 2 mol %, 19 mg), and triethylamine (10 mL) were added to a 50 mL round-bottom flask. The flask was flushed with nitrogen for 3 min, and the terminal acetylene (5.0 mmol) was added to the stirred suspension, followed by immediate dropwise addition of acyl chloride (6.5 mmol). The mixture was stirred at room temperature overnight. After the fully consumption of starting material by TLC detection, the resulting solution was extracted with diethyl ether (3 × 20 mL). The organic layers were combined and dried over anhydrous $MgSO_4$. The solvent was removed under vacuum, and the residue was purified by flash column chromatography on silica gel using PE/EA as the eluent to obtain alkynone **B** (85-90% yields).

Step 2: Alkynone **B** (3.5 mmol), methoxylamine hydrochloride (7.0 mmol, 2.0 equiv, 581 mg), anhydrous Na_2SO_4 (7.0 mmol, 2.0 equiv, 994 mg), pyridine (1 mL), and methanol (10 mL) were added to a 50 mL round-bottom flask. The reaction mixture was stirred at room temperature overnight. The mixture was diluted with saturated NH_4Cl solution (25 mL) and extracted with EtOAc (3 × 25 mL). The organic layers were combined, washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed under vacuum, and the residue was purified by flash column chromatography on silica gel using PE/EA as the eluent to give the desired product **1** (45-85% yields).

C. General Procedure for the Preparation of Alkenyl Ethers 2

Alkenyl ethers were prepared according to the previously reported procedure.[2]



C **D** **2**

Step 1: To a solution of 2-iodophenol (5.0 mmol) and 1,2-dibromoethane (5.0 equiv) in acetone (50 mL) was added K_2CO_3 (2.0 equiv). The resulting mixture was stirred at room temperature for 14 h and then reflux for 6 h. The reaction was quenched with water and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The crude product was purified by a silica gel column chromatography (hexanes/EtOAc = 100: 1) to give **D** (65-70% yields).

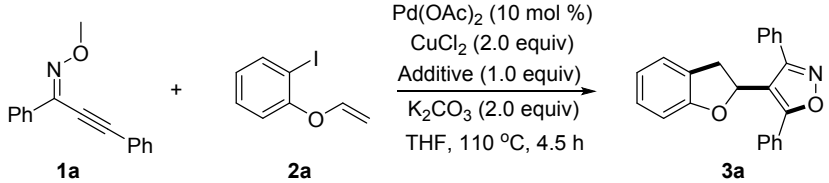
Step 2: To a solution of **D** (3.0 mmol) in DMSO (20 mL) was added *t*-BuOK (1.5 equiv). The resulting mixture was stirred at room temperature for 24 h. The reaction mixture was filtered and washed with CH_2Cl_2. The combined filtrate was concentrated and the residue was purified by a silica gel column chromatography (hexanes/EtOAc = 100: 1) to give the desired products **2** (75-90% yields).

D. General Procedure for the Synthesis of Products 3

To a 25 mL dried reaction tube was added the mixture of $Pd(OAc)_2$ (15 mol %), $CuCl_2$ (2.5 equiv), TBAB (1.0 equiv), K_2CO_3 (2.0 equiv), alkynyl oxime ethers **1** (0.2 mmol) and alkenyl ethers **2** (0.4 mmol) in THF (2.5 mL) successively. The mixture was stirred at 60 °C for 12 h under air atmosphere. After the reaction was completed, the mixture was cooled to room temperature and diluted with H_2O (15 mL), and extracted with EtOAc (3 × 10 mL). Collected organic layers were dried over anhydrous $MgSO_4$ and concentrated in vacuum. The resulting crude was purified by flash column chromatography on silica gel with petroleum ether/ethyl acetate (150: 1~50:1) to give the desired products **3**.

E. Optimization of the Reaction Conditions

I. Screening of Additives



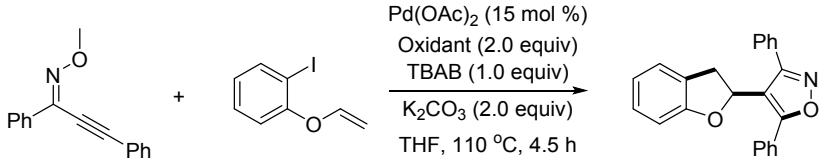
1a **2a** **3a**

Entry	Additive (equiv)	Yield of **3a** (%)[b]
1	**TBAB**	**64**
2	TBAI	27

3	TBAC	46
4	TBAF	23
5	TEBAC	42
6	$TBABR_3$	31
7	TBAB (0.5)	56
8	TBAB (1.5)	64
9	TBAB (2.0)	60

[a]Reaction conditions: **1a** (0.20 mmol), **2a** (0.40 mmol), $Pd(OAc)_2$ (10 mol %), $CuCl_2$ (2.0 equiv), additive (1.0 equiv), K_2CO_3 (2.0 equiv), THF (2.5 mL) stirred at 110 °C for 4.5 h in sealed tube. [b]Detected by NMR using CH_2Br_2 as internal standard.

II. Screening of Oxidants

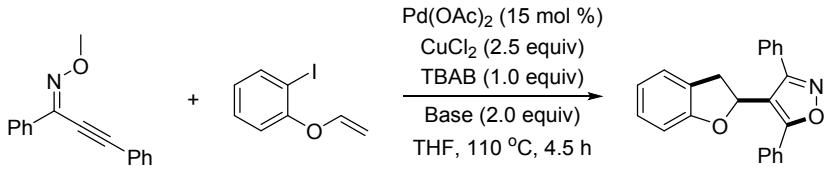


1a **2a** **3a**

Entry	Oxidant (equiv)	Yield of **3a** (%)[b]
1	$CuCl_2{\cdot}2H_2O$	62
2	$CuCl_2$	72
3	$CuSO_4$	35
4	$CuBr_2$	52
5	CuF_2	trace
6	CuO	29
7	$Cu(OAc)_2$	trace
8	$Cu(OH)_2$	n.d.
9	CuBr	trace
10	CuCl	9
11	AgOAc	n.d.
12	Ag_2O	n.d.
13	BQ	trace
14	DMBQ	trace
15	DTBP	n.d.
16	H_2O_2	n.d.
17	TBHP	n.d.
18	$PhI(OAc)_2$	n.d.
19	$CuCl_2$ (1.0)	51
20	$CuCl_2$ (1.5)	63
21	**$CuCl_2$ (2.5)**	**74**
22	$CuCl_2$ (3.0)	73

[a]Reaction conditions: **1a** (0.20 mmol), **2a** (0.40 mmol), $Pd(OAc)_2$ (15 mol %), TBAB (1.0 equiv), K_2CO_3 (2.0 equiv), THF (2.5 mL) stirred at 110 °C for 4.5 h in sealed tube. [b]Detected by NMR using CH_2Br_2 as internal standard.

III. Screening of Bases



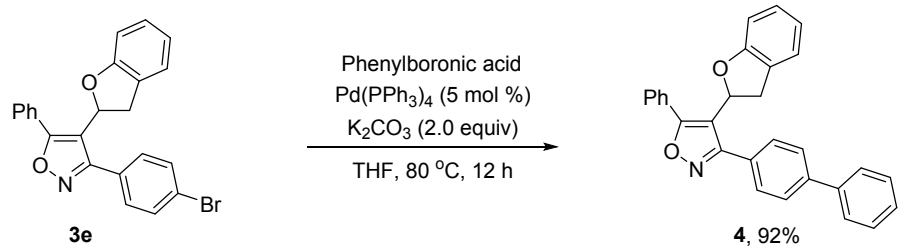
1a + **2a** → **3a**

Entry	Base (equiv)	Yield of **3a** (%)[b]
1	**K_2CO_3**	**74**
2	$KHCO_3$	62
3	Na_2CO_3	55
4	$NaHCO_3$	68
5	Cs_2CO_3	59
6	Li_2CO_3	71
7	KOAc	41
8	NaOAc	55
9	pyridine	trace
10	Et_3N	58
11	K_2CO_3 (3.0)	73
12	K_2CO_3 (4.0)	72

[a]Reaction conditions: **1a** (0.20 mmol), **2a** (0.40 mmol), $Pd(OAc)_2$ (15 mol %), $CuCl_2$ (2.5 equiv), TBAB (1.0 equiv), THF (2.5 mL) stirred at 110 °C for 4.5 h in sealed tube. [b]Detected by NMR using CH_2Br_2 as internal standard.

F. Synthetic Applications

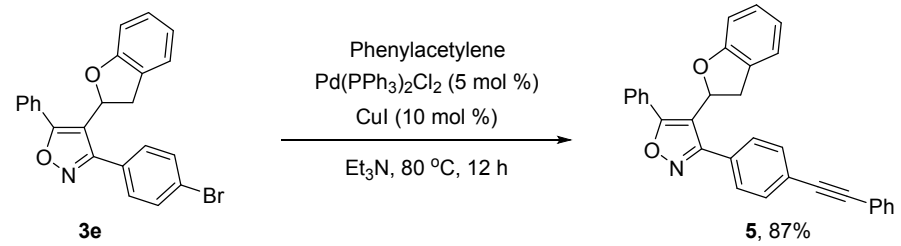
I. Synthetic Procedure for 4



3e → **4**, 92%

To a resealable Schlenk tube was added **3e** (0.2 mmol), phenylboronic acid (1.5 equiv), $Pd(PPh_3)_4$ (5 mol %), K_2CO_3 (2.0 equiv), THF (3.0 mL) and a stir bar. The reaction vessel was fitted with a rubber septum, which was evacuated and back-filled with nitrogen. The reaction tube was sealed and immersed in a preheated oil bath at 80 °C for 12 h and the solution was stirred with the aid of a magnetic stirrer. After the reaction was completed (monitored by TLC), the resulting mixture was cooled to room temperature and extracted with ethyl acetate. The combined organic layers were evaporated under vacuum. The desired product **4** was obtained in 92% yield after purified by column chromatography on silica gel with a mixture of petroleum ether/ethyl acetate (v/v = 50/1).

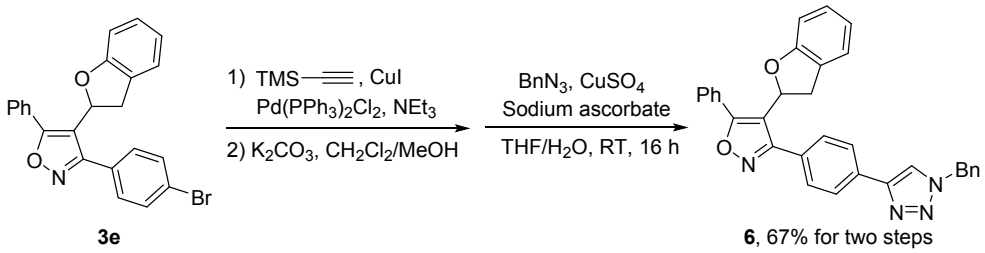
II. Synthetic Procedure for 5



3e **5**, 87%

3-(4-Bromophenyl)-4-(2,3-dihydrobenzofuran-2-yl)-5-phenylisoxazole (**3e**, 0.20 mmol), phenylacetylene (2.0 equiv), $Pd(PPh_3)_2Cl_2$ (5 mol %), CuI (10 mol %) and Et_3N (3.0 mL) were added in a Schlenk tube under nitrogen atmosphere and stirred at 80 °C for 12 h. Aftre the reaction was completed (monitored by TLC), the resulting mixture was cooled to room temperature and extracted with ethyl acetate. The combined organic layers were evaporated under vacuum. The desired product **5** was obtained in 87% yield after purified by column chromatography on silica gel with a mixture of petroleum ether/ethyl acetate (v/v = 100/1).

III. Synthetic Procedure for 6



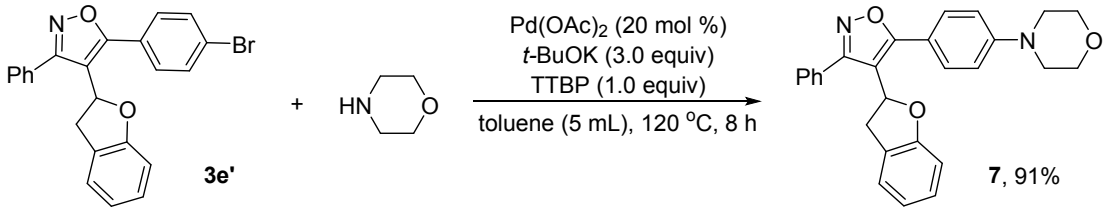
3e **6**, 67% for two steps

Step 1: To a resealable Schlenk tube was added **3e** (1 mmol), $Pd(PPh_3)_2Cl_2$ (5 mol %), CuI (5 mol %), Et_3N (5.0 mL) and a stir bar. The reaction vessel was fitted with a rubber septum, which was evacuated and back-filled with nitrogen and then stirred for 5 min. After trimethylsilylacetylene was added (1.4 equiv), the reaction tube was immersed in a preheated oil bath at 40 °C for 10 h and the solution was stirred with the aid of a magnetic stirrer. The resulting mixture was cooled to room temperature and extracted with dichloromethane. After the reaction solution was vacuumed, potassium carbonate (3.0 mmol) was added. The mixed solution of dichloromethane and methanol (1/1) was used as solvent stirred at room temperature for 2 h. After the reaction was completed (monitored by TLC), the resulting mixture was extracted with ethyl acetate. The combined organic layers were evaporated under vacuum. The terminal alkyne product was obtained in 78% yield after purified by column chromatography on silica gel with a mixture of petroleum ether/ethyl acetate (v/v = 80/1).

Step 2: To a test tube was added the terminal alkyne product (0.15 mmol), benzyl azide (0.1 mmol) and 25% THF aqueous solution and a stir bar. After stirring at room temperature for 10 min, the mixture was added $CuSO_4$ (0.05 mmol) and sodium ascorbate (0.05 mmol). The reaction tube was stirred at room temperature for 12 h. After the reaction was completed (monitored by TLC), the resulting mixture was

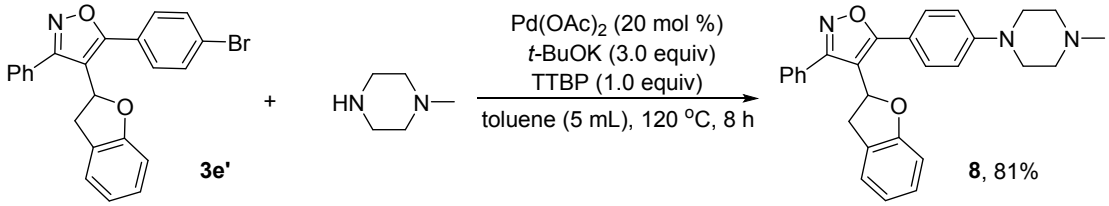
extracted with ethyl acetate and combined organic layers were evaporated under vacuum. The desired product **6** was obtained in 87% yield after purified by column chromatography on silica gel with a mixture of petroleum ether/ethyl acetate (v/v = 50/1).

IV. Synthetic Procedure for 7



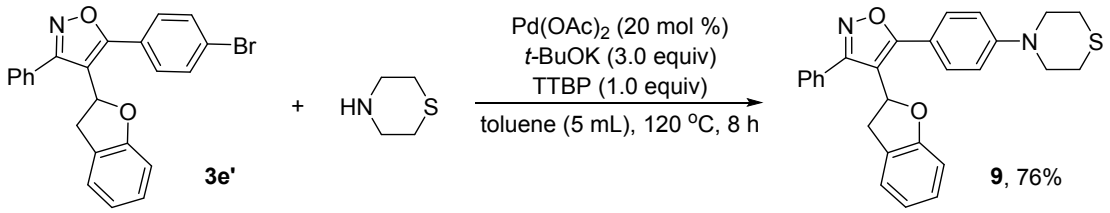
To a resealable Schlenk tube was added **3e'** (0.1 mmol), morpholine (1.2 equiv), $Pd(OAc)_2$ (20 mol %), *t*-BuOK(3.0 equiv), toluene (5.0 mL) and a stir bar. The reaction vessel was fitted with a rubber septum, which was evacuated and back-filled with nitrogen and then stirred for 5 min. After tri-*tert*-butylphosphine (TTBP, 1.0 equiv) was added dropwise, the reaction tube was immersed in a preheated oil bath at 120 °C for 8 h and the solution was stirred with the aid of a magnetic stirrer. The resulting mixture was cooled to room temperature and extracted with ethyl acetate. The combined organic layers were evaporated under vacuum. The product was obtained in 91% yield after purified by column chromatography on silica gel with a mixture of petroleum ether/ethyl acetate (v/v = 50/1).

V. Synthetic Procedure for 8



To a resealable Schlenk tube was added **3e'** (0.1 mmol), 1-methylpiperazine (1.2 equiv), $Pd(OAc)_2$ (20 mol %), *t*-BuOK (3.0 equiv), toluene (5.0 mL) and a stir bar. The reaction vessel was fitted with a rubber septum, which was evacuated and back-filled with nitrogen, and then stirred for 5 min. After TTBP (1.0 equiv) was added dropwise, the reaction tube was immersed in a preheated oil bath at 120 °C for 8 h and the solution was stirred with the aid of a magnetic stirrer. The resulting mixture was cooled to room temperature and extracted with ethyl acetate. The combined organic layers were evaporated under vacuum. The product was obtained in 81% yield after purified by column chromatography on silica gel with a mixture of ethyl acetate/ethanol (v/v = 20/1).

VI. Synthetic Procedure for 9

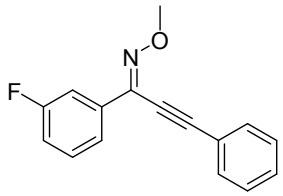


To a resealable Schlenk tube were added **3e'** (0.1 mmol), thiomorpholine (1.2 equiv), $Pd(OAc)_2$ (20 mol %), *t*-BuOK(3.0 equiv), toluene (5.0 mL) and a stir bar. The reaction vessel was fitted with a rubber septum, which was evacuated and back-filled with nitrogen and then stirred for 5 min. After TTBP (1.0 equiv) was added drop by dropwise, the reaction tube was immersed in a preheated oil bath at 120 °C for 8 h and the solution was stirred with the aid of a magnetic stirrer. The resulting mixture was cooled to room temperature and extracted with ethyl acetate. The combined organic layers were evaporated under vacuum. The product was obtained in 76% yield after purified by column chromatography on silica gel with a mixture of petroleum ether/ethyl acetate (v/v = 30/1).

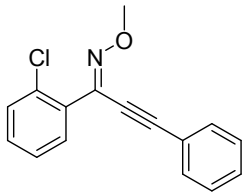
G. Analytical Data for All Compounds

1aa-1ah, **1al-1an**, **1ba-1b and 2ag-2ai** are known compounds and the NMR data are in good agreement with the literature[1, 3, 4]. **1ai**, **1aj** and **1ak** are unknown compounds and the corresponding NMR spectra data are shown as bellow.

(*Z*)-1-(3-Fluorophenyl)-3-phenylprop-2-yn-1-one *O*-Methyl Oxime (1i): Yield: 607 mg (48%), red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.60 (m, 4 H), 7.42 (m, 4 H), 7.16 (m, 1H), 4.22 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6 (d, J = 244.2 Hz), 138.6 (d, J = 3.1 Hz), 135.6 (d, J = 8.0 Hz), 132.0, 129.8 (d, J = 8.2 Hz), 129.5, 128.3, 122.1 (d, J = 2.9 Hz), 121.4, 116.4 (d, J = 21.3 Hz), 113.1(d, J = 23.6 Hz), 101.4, 78.9, 63.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -98.29 – -120.95 (m) ppm; IR (KBr)$\tilde{\nu}_{max}$ 3070, 2937, 2814, 2205, 1602, 1439, 1332, 1240, 1166, 1046, 893, 796, 686, 520 cm^{-1}; HRMS (ESI) Calcd for $C_{16}H_{13}FNO$, $[M+H]^+$: 254.0976, found 254.0978.



(*E*)-1-(2-Chlorophenyl)-3-phenylprop-2-yn-1-one *O*-Methyl Oxime (1j): Yield: 605 mg (45%), red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (m, 3 H), 7.49 (d, J = 6.4 Hz, 1H), 7.37 (m, 5H), 4.21 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 133.1, 131.9, 130.8, 130.2, 129.4, 128.2, 126.7, 121.6, 101.7, 80.0, 62.9 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3592, 3068, 2935, 2202, 1956, 1810, 1563, 1445, 1330, 1216, 1037, 903, 810, 692, 543, 453 cm^{-1}; HRMS (ESI) Calcd for $C_{16}H_{13}ClNO$, $[M+H]^+$: 270.0680, found 270.0685.



(*Z*)-1-(Naphthalen-2-yl)-3-phenylprop-2-yn-1-one *O*-Methyl Oxime (1k): Yield: 576 mg (40%), white solid. M.p.: 115-116 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.13 (d, J = 8.8 Hz, 1H), 8.02 – 7.82 (m, 3H), 7.80 – 7.68 (m, 2H), 7.54 (m, 2H), 7.48 – 7.39 (m, 3H), 4.24 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 140.0, 133.9, 133.0, 132.1, 131.1, 129.5, 128.6, 128.4, 128.1, 127.7, 127.1, 126.8, 126.4, 123.0, 121.8, 101.2, 79.4, 63.2 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3059, 2936, 2817, 2207, 1958, 1601, 1446, 1331, 1250, 1178, 1049, 909, 814, 753, 684, 592, 469 cm^{-1}; HRMS (ESI) Calcd for $C_{20}H_{16}NO$, $[M+H]^+$: 286.1226, found 286.1228.

2-Iodo-4-methyl-1-(vinyloxy)benzene (2aa): Yield: 867 mg (67%), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.14 (d, J = 8.4 Hz, 1H), 6.90 (d, J = 8.2 Hz, 1H), 6.60 (m, 1H), 4.76 (d, J = 13.8 Hz, 1H), 4.51 (d, J = 5.8 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4, 148.4, 139.7, 134.7, 129.9, 117.1, 94.8, 87.3, 20.0 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3042, 2929, 1783, 1631, 1479, 1384, 1240, 1143, 1044, 953, 693, 537 cm^{-1}; HRMS (ESI) Calcd for $C_9H_{10}IO$, $[M+H]^+$: 261.9849, found 261.9853.

4-Bromo-2-iodo-1-(vinyloxy)benzene (2ab): Yield: 949 mg (58%), brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 2.2 Hz, 1H), 7.42 (m, 1H), 6.84 (d, J = 8.8 Hz, 1H), 6.53 (m, 1 H), 4.79 (m, 1H), 4.55 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 147.6, 141.5, 132.4, 118.1, 116.5, 96.6, 88.1 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3481, 3073, 2930, 1734, 1640, 1553, 1368, 1231, 1132, 1036, 811, 691 cm^{-1}; HRMS (ESI) Calcd for C_8H_7BrIO, $[M+H]^+$: 324.8719, found 324.8710.

2-Iodo-4-(trifluoromethyl)-1-(vinyloxy)benzene (2ac): Yield: 813 mg (52%), brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H), 4.90 (d, J = 13.6 Hz, 2H), 4.59 (d, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 146.8, 127.1 (q, J = 3.7 Hz), 125.5, 125.3, 124.9, 122.8, 116.7, 97.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -61.85 ppm; IR (KBr)$\tilde{\nu}_{max}$ 2936, 2417, 1725, 1614, 1518, 1325, 1239, 1131, 937, 815, 696 cm^{-1}; HRMS (ESI) Calcd for $C_9H_7F_3IO$, $[M+H]^+$: 314.9410, found 314.9415.

4-(*tert*-Butyl)-2-iodo-1-(vinyloxy)benzene (2ad): Yield: 906 mg (60%), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 2.0 Hz, 1H), 7.33 (dd, J = 8.6, 2.0 Hz, 1H), 6.91 (d, J = 8.6 Hz, 1H), 6.62 – 6.52 (m, 1H), 4.74 (dd, J = 13.8, 1.2 Hz, 1H), 4.59 – 4.26 (m, 1H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 148.4, 136.6, 126.6, 116.9, 95.2, 87.4, 34.2, 31.3 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3060, 2955, 1745, 1635, 1481, 1380, 1249, 1148, 1040, 952, 835, 693, 604 cm^{-1}; HRMS (ESI) Calcd for $C_{12}H_{16}IO$, $[M+H]^+$: 303.0240, found 303.0235.

4-Chloro-1-iodo-2-(vinyloxy)benzene (2ae): Yield: 599 mg (43%), brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.4 Hz, 1H), 6.96 (d, J = 2.4 Hz, 1H), 6.85 (dd, J = 8.4, 2.2 Hz, 1H), 6.55 (dd, J = 13.6, 6.0 Hz, 1H), 4.86 (dd, J = 13.6, 2.0 Hz, 1H), 4.61 (dd, J = 6.0, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 147.2, 140.1, 135.2, 125.1, 117.3, 97.5, 84.4 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3580, 3497, 3413, 3062, 2253, 1732, 1641, 1562, 1461, 1382, 1236, 1135, 960, 856, 676, 525 cm^{-1}; HRMS (ESI) Calcd for C_8H_7ClIO, $[M+H]^+$: 280.9225, found 280.9221.

4-(2,3-Dihydrobenzofuran-2-yl)-3,5-diphenylisoxazole (3a): Yield: 54 mg (81%), colorless solid. M.p.: 130.2 – 131.1 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 7.0 Hz, 2H), 7.65 (d, J = 7.4 Hz, 2H), 7.53 – 7.43 (m, 3H), 7.39 (t, J = 7.2 Hz, 1H), 7.33 (t, J = 7.3 Hz, 2H), 7.17 (t, J = 7.7 Hz, 1H), 6.96 (d, J = 7.2 Hz, 1H), 6.85 (m ,2H), 5.85 (t, J = 10.1 Hz, 1H), 3.13 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 163.7, 158.7, 130.5, 129.6, 129.0, 128.9, 128.8, 128.5, 128.4, 128.3, 127.5, 126.8, 124.5, 120.8, 112.8, 109.5, 75.5, 34.8 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3359, 3056, 2926, 1604, 1460, 1230, 1017, 910, 726, 496 cm^{-1}; HRMS (ESI) Calcd for $C_{23}H_{18}NO_2$, $[M+H]^+$: 340.1332, found 340.1331.

4-(2,3-Dihydrobenzofuran-2-yl)-5-phenyl-3-(*p*-tolyl)isoxazole (3b): Yield: 56 mg (80%), colorless solid. M.p.: 139.5 – 140.3 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 7.0 Hz, 2H), 7.56 (d, J = 7.7 Hz, 2H), 7.46 (m, 3H), 7.17 (m, 3H), 6.98 (d, J = 7.2 Hz, 1H), 6.86 (m, 2H), 5.84 (t, J = 10.1 Hz, 1H), 3.52 – 2.94 (m, 2H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, 163.6, 158.7, 139.7, 130.4, 129.2, 128.8, 128.7, 128.4, 128.3, 127.5, 126.9, 126.0, 124.6, 120.8, 112.5, 109.5, 75.6, 34.6, 21.3 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3432, 3050, 2931, 1613, 1461, 1327, 1228, 1021, 913, 827, 744, 592, 503 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{20}NO_2$, $[M+H]^+$: 354.1489, found 354.1484.

4-(2,3-Dihydrobenzofuran-2-yl)-3-(4-fluorophenyl)-5-phenylisoxazole (3c): Yield: 61 mg (87%), colorless solid. M.p.: 126.7 – 127.8 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 7.0 Hz, 2H), 7.68 – 7.59 (m, 2H), 7.56 – 7.39 (m, 3H), 7.18 (t, J = 8.0 Hz, 1H), 6.99 (m, 3H), 6.85 (t, J = 8.0 Hz, 2H), 5.84 (t, J = 10.0 Hz, 1H), 3.13 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 163.6 (d, J = 248.3 Hz), 162.8, 158.6, 130.8 (d, J = 8.3 Hz), 130.6, 128.9, 128.4, 128.3, 126.9 (d, J = 83.4 Hz), 125.1 (d, J = 3.1 Hz), 124.6, 120.9, 115.7, 115.5, 112.8, 109.5, 75.4, 34.8; ^{19}F NMR (470 MHz, $CDCl_3$) δ -109.05 – -115.69 (m) ppm; IR (KBr)$\tilde{\nu}_{max}$ 3058, 2934, 1604, 1457, 1333, 1230, 920, 844, 742, 595 cm^{-1}; HRMS (ESI) Calcd for $C_{23}H_{16}FNNaO_2$, $[M+Na]^+$: 380.1057, found 380.1066.

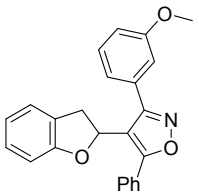
3-(4-Chlorophenyl)-4-(2,3-dihydrobenzofuran-2-yl)-5-phenylisoxazole (3d): Yield: 61 mg (83%), colorless solid. M.p.: 105.3 – 106.2 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 6.8 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 6.6 Hz, 3H), 7.31 (d, J = 8.0 Hz, 2H), 7.21 (t, J = 7.6 Hz, 1H), 7.01 (d, J = 7.2 Hz, 1H), 6.89 (t, J = 6.4 Hz, 2H), 5.86 (t, J = 10.0 Hz, 1H), 3.23 (m, 1H), 3.08 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 162.6, 158.6, 135.9, 130.6, 130.2, 128.9, 128.7, 128.5, 128.4, 127.5, 127.2, 126.6, 124.6, 121.0, 112.8, 109.5, 75.3, 34.8 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3057, 2930, 1597, 1460, 1328, 1229, 1092, 1012, 917, 833, 747, 510 cm^{-1}; HRMS (ESI) Calcd for $C_{23}H_{16}ClNNaO_2$, $[M+Na]^+$: 396.0762, found 396.0762.

3-(4-Bromophenyl)-4-(2,3-dihydrobenzofuran-2-yl)-5-phenylisoxazole (3e): Yield: 65 mg (78%), colorless solid. M.p.: 119.7 – 120.5 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, J = 7.1 Hz, 2H), 7.48 (m, 7H), 7.19 (t, J = 7.6 Hz, 1H), 6.99 (d, J = 7.1 Hz, 1H), 6.86 (t, J = 8.0 Hz, 2H), 5.84 (t, J = 10.0 Hz, 1H), 3.14 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 162.6, 158.5, 131.7, 130.6, 130.4, 128.8, 128.4, 128.3, 128.0, 127.2, 126.5, 124.6, 124.2, 121.0, 112.7, 109.5, 75.3, 34.8 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3359, 2925, 1623, 1461, 1231, 1084, 1008, 917, 837, 751, 500 cm^{-1}; HRMS (ESI) Calcd for $C_{23}H_{16}BrNNaO_2$, $[M+Na]^+$: 440.0257, found 440.0259.

4-(2,3-Dihydrobenzofuran-2-yl)-5-phenyl-3-(4-(trifluoromethyl)phenyl)isoxazole (3f): Yield: 60 mg (74%), colorless solid. M.p.: 133.1 – 134.3 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (t, J = 7.6 Hz, 4H), 7.53 (m, 5H), 7.18 (t, J = 7.6 Hz, 1H), 6.96 (d, J = 7.2 Hz, 1H), 6.85 (t, J = 7.8 Hz, 2H), 5.85 (t, J = 10.0 Hz, 1H), 3.14 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 162.5, 158.5, 132.6, 131.7, 131.3, 130.7, 129.1 (d, J = 37.4 Hz), 128.5, 128.4, 127.1, 126.4, 125.4 (q, J = 3.6 Hz), 124.5, 123.7 (d, J = 270.8 Hz), 121.0, 113.2, 109.5,75.1, 35.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.86 ppm; IR (KBr)$\tilde{\nu}_{max}$ 2937, 1605, 1466, 1323, 1236, 1136, 923, 845, 753, 592, 487 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{16}F_3NNaO_2$, $[M+Na]^+$: 430.1025, found 430.1033.

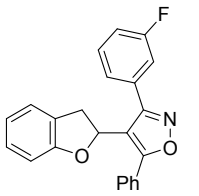
4-(2,3-Dihydrobenzofuran-2-yl)-5-phenyl-3-(4-((trifluoromethyl)thio)phenyl)isoxazole (3g) Yield: 67 mg (77%), colorless solid. M.p.: 160.2 – 161.3 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 6.8 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H), 7.58 (d, J = 8.0 Hz, 2H), 7.51 (m, 3H), 7.18 (t, J = 7.6 Hz, 1H), 6.95 (d, J = 7.2 Hz, 1H), 6.85 (t, J = 7.2 Hz, 2H), 5.86 (t, J = 10.0 Hz, 1H), 3.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 162.5, 158.5, 136.1, 131.7, 130.7, 129.9, 129.3 (d, J = 306.5 Hz), 128.9, 128.5, 128.4, 127.1, 126.4, 126.0 (q, J = 2.0 Hz), 124.5, 121.1, 113.3, 109.5, 75.1, 35.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -42.23 ppm; IR (KBr)$\tilde{\nu}_{max}$ 2935, 1610, 1464, 1238, 1126, 1010, 923, 838, 749, 514 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{16}F_3NNaO_2S$, $[M+Na]^+$: 462.0746, found 462.0752.

4-(2,3-Dihydrobenzofuran-2-yl)-3-(3-methoxyphenyl)-5-phenylisoxazole (3h):



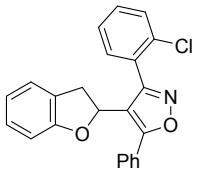
Yield: 57 mg (78%), colorless solid. M.p.: 144.5 – 145.6 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 6.6 Hz, 2H), 7.51 (d, J = 5.2 Hz, 3H), 7.31 (m, 2H), 7.21 (m, 2H), 7.01 (m , 2H), 6.90 (m, 2H), 5.91 (t, J = 10.2 Hz, 1H), 3.58 (s, 3H), 3.19 (d, J = 10.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 163.4, 159.5, 158.6, 130.4, 130.2, 129.6, 128.8, 128.3, 128.2, 127.3, 126.9, 124.6, 121.1, 120.9, 116.6, 113.1, 112.2, 109.5, 75.5, 54.8, 34.4 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3488, 3059, 2937, 2840, 1594, 1467, 1309, 1232, 1163, 1034, 903, 750, 694, 528, 451 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{20}NO_3$, $[M+H]^+$: 370.1438, found 370.1445.

4-(2,3-Dihydrobenzofuran-2-yl)-3-(3-fluorophenyl)-5-phenylisoxazole (3i):



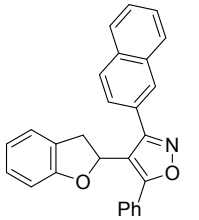
Yield: 57 mg (81%), colorless solid. M.p.: 144.1 – 144.9 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 6.8 Hz, 2H), 7.58 – 7.38 (m, 5H), 7.31 (m, 1H), 7.21 (t, J = 8.0 Hz, 1H), 7.11 (t, J = 8.4 Hz, 1H), 7.01 (d, J = 7.2 Hz, 1H), 6.88 (m, 2H), 5.88 (t, J = 10.0 Hz, 1H), 3.18 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 162.6 (d, J = 2.3 Hz), 162.5 (d, J = 245.7 Hz), 158.5, 130.9 (d, J = 8.3 Hz), 130.6, 130.1 (d, J = 8.2 Hz), 128.8, 128.4, 128.3, 127.2 126.5 124.7 (d, J = 3.0 Hz), 124.5, 120.9, 116.6 (d, J = 20.9 Hz), 116.0 (d, J = 23.1 Hz), 112.9, 109.5, 75.2, 34.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.11 (dd, J = 14.8, 9.0 Hz) ppm; IR (KBr)$\tilde{\nu}_{max}$ 3060, 2936, 1594, 1465, 1229, 895, 752, 507 cm^{-1}; HRMS (ESI) Calcd for $C_{23}H_{16}FNNaO_2$, $[M+Na]^+$: 380.1057, found 380.1063.

3-(2-Chlorophenyl)-4-(2,3-dihydrobenzofuran-2-yl)-5-phenylisoxazole (3j):



Yield: 50 mg (68%), colorless solid. M.p.: 102.8 – 103.7 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (m, 2H), 7.57 – 7.45 (m, 3H), 7.39 (m, 2H), 7.34 – 7.25 (m, 1H), 7.19 (m, 1H), 7.07 (t, J = 7.6Hz, 1H), 6.93 (d, J = 7.2 Hz, 1H), 6.77 (t, J = 7.4 Hz, 1H), 6.66 (d, J = 8.0 Hz, 1H), 6.10 – 5.59 (t, J = 9.2, 1H), 3.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 161.4, 158.6, 133.6, 131.8, 130.7, 130.4, 129.4, 128.8, 128.3, 128.2, 128.1, 127.3, 126.4, 126.1, 124.3, 120.6, 115.0, 109.2, 75.1, 35.3 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3583, 3490, 3385, 3284, 3050, 2936, 2845, 2549, 2417, 2255, 1589, 1448, 1222, 1033, 910, 730, 497 cm^{-1}; HRMS (ESI) Calcd for $C_{23}H_{16}ClNNaO_2$, $[M+Na]^+$: 396.0762, found 396.0765.

4-(2,3-Dihydrobenzofuran-2-yl)-3-(naphthalen-2-yl)-5-phenylisoxazole (3k):



Yield: 56 mg (78%), colorless solid. M.p.: 161.4 – 162.5 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.82 (m, 5H), 7.52 (m, 5H), 7.49 – 7.38 (m, 1H), 7.24 (t, J = 7.8 Hz, 1H), 6.95 (q, J = 8.0 Hz, 2H), 6.84 (t, J = 7.4 Hz, 1H), 5.97 (t, J = 10.0 Hz, 1H), 3.41 – 2.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 163.5, 158.7, 133.6, 132.9, 130.5, 129.0, 128.9, 128.5, 128.4, 128.3, 127.5, 127.4, 126.9, 126.3, 125.7, 124.7, 120.9, 112.7, 109.6, 75.6, 34.7 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3411, 3223, 3053, 2938, 2251, 1594, 1460, 1228, 917, 750, 579, 480 cm^{-1}; HRMS (ESI) Calcd for $C_{27}H_{19}NNaO_2$, $[M+Na]^+$: 412.1308, found 412.1313.

4-(2,3-Dihydrobenzofuran-2-yl)-3-(furan-2-yl)-5-phenylisoxazole (3l): Yield: 48 mg (75%), colorless solid. M.p.: 105.1 – 106.1 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.2 Hz, 2H), 7.53 – 7.39 (m, 3H), 7.33 (s, 1H), 7.17 (m, 2H), 7.00 – 6.70 (m, 3H), 6.43 (s, 1H), 6.04 (t, J = 10.0 Hz, 1H), 3.64 – 3.06 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 159.0, 154.2, 144.1, 143.4, 130.5, 128.7, 128.4, 128.3, 127.1, 126.8, 124.6, 120.8, 112.3, 111.8, 111.5, 109.5, 75.3, 35.8 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3138, 3052, 2930, 1598, 1468, 1327, 1229, 1159, 1084, 1010, 906, 826, 749, 589 cm^{-1}; HRMS (ESI) Calcd for $C_{21}H_{15}NNaO_3$, $[M+Na]^+$: 352.0944, found 352.0945.

3-Cyclohexyl-4-(2,3-dihydrobenzofuran-2-yl)-5-phenylisoxazole (3m): Yield: 35 mg (51%), red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (m, 2H), 7.42 (d, J = 6.0 Hz, 3H), 7.18 (t, J = 8.0 Hz, 2H), 7.02 – 6.65 (m, 2H), 5.87 (t, J = 9.6 Hz, 1H), 3.38 (m, 2 H), 2.57 (t, J = 11.6 Hz, 1H), 2.01 (m, 2H), 1.84 – 1.44 (m, 6H), 1.41 – 1.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 167.0, 159.0, 130.0, 128.7, 128.5, 128.1, 127.8, 126.2, 124.6, 120.9, 113.4, 109.4, 75.3, 36.3, 36.2, 32.6, 31.7, 26.4, 26.2, 25.8 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3420, 3049, 2930, 1614, 1461, 1231,952, 750, 502 cm^{-1}; HRMS (ESI) Calcd for $C_{23}H_{23}NNaO_2$, $[M+Na]^+$: 368.1621, found 368.1625.

4-(2,3-Dihydrobenzofuran-2-yl)-3-phenyl-5-(*p*-tolyl)isoxazole (3n): Yield: 55 mg (79%), colorless solid. M.p.: 138.7 – 139.6 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (m, 4H), 7.39 (m, 3H), 7.29 (d, J = 7.6 Hz, 2H), 7.21 (t, J = 7.6 Hz, 1H), 7.00 (d, J = 7.2 Hz, 1H), 6.88 (m, 2H), 5.87 (t, J = 10.0 Hz, 1H), 3.52 – 2.81 (m, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 163.7 158.7, 140.9, 129.6, 129.5, 129.1, 128.9, 128.5, 128.3, 128.2, 126.9, 124.7, 124.6, 120.8, 112.2, 109.6, 75.6, 34.6, 21.5 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3049, 2932, 2850, 1607, 1464, 1318, 1229, 1097, 1021, 911, 825, 746, 506 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{20}NO_2$, $[M+H]^+$: 354.1489, found 354.1484.

4-(2,3-Dihydrobenzofuran-2-yl)-5-(4-methoxyphenyl)-3-phenylisoxazole (3o): Yield: 54 mg (74%), colorless solid. M.p.: 135.2 – 136.3 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.57 (m, 4H), 7.48 – 7.28 (m, 3H), 7.18 (t, J = 7.8 Hz, 1H), 6.97 (t, J = 7.6 Hz, 3H), 6.85 (m, 2H), 5.82 (t, J = 10..2 Hz, 1H), 3.84 (s, 3H), 3.27 – 2.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 163.6, 161.3, 158.7, 129.9, 129.5, 129.1, 128.8, 128.5, 128.3, 126.9, 124.6, 120.7, 120.0, 114.2, 111.6, 109.5, 75.7, 55.3, 34.5 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3591, 3442, 3228, 2935, 2838, 2248, 1622, 1459, 1248, 1170, 1100, 1026, 910, 835, 529, 449 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{20}NO_3$, $[M+H]^+$: 370.1438, found 370.1441.

5-(4-Chlorophenyl)-4-(2,3-dihydrobenzofuran-2-yl)-3-phenylisoxazole (3p): Yield: 60 mg (81%), red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (m, 4H), 7.39 (m, 5H), 7.19 (t, J = 7.6 Hz, 1H), 6.98 (d, J = 7.2 Hz, 1H), 6.86 (m, 2H), 5.80 (t, J = 10.0 Hz, 1H), 3.14 (m, 2H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 168.3, 163.8, 158.6, 136.8, 129.7, 129.6, 129.1, 128.9, 128.7, 128.6, 128.5, 126.7, 126.0, 124.6, 121.0, 113.2, 109.6, 75.3, 34.8 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3582, 3472, 3058, 2931, 1606, 1472, 1318, 1230, 1161, 1094, 1017, 918, 832, 747, 507 cm^{-1}; HRMS (ESI) Calcd for $C_{23}H_{16}ClNNaO_2$, $[M+Na]^+$: 396.0762, found 396.0765.

4-(2,3-Dihydrobenzofuran-2-yl)-3-phenyl-5-(*m*-tolyl)isoxazole (3q): Yield: 52 mg (75%), colorless solid. M.p.: 130.3 – 131.3 ºC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 7.6 Hz, 2H), 7.54 (d, J = 7.6 Hz, 1H), 7.50 (s, 1H), 7.37 (m, 4H), 7.28 (s, 1H), 7.18 (t, J = 7.8 Hz, 1H), 6.97 (d, J = 7.2 Hz, 1H), 6.86 (m,2H), 5.84 (t, J = 10.0 Hz, 1H), 3.19 (m, 1H), 3.09 (m, 1H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 163.7, 158.8, 138.7, 131.2, 129.6, 129.1, 129.0, 128.9, 128.7, 128.6, 128.4, 127.5, 127.0, 125.4, 124.5, 120.8, 112.8, 109.6, 75.4, 34.8, 21.2 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3557, 3468, 3188, 3036, 2930, 2852, 2717, 2546, 2428, 1622, 1464, 1317, 1229, 1091, 908, 749, 582, 483 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{20}NO_2$, $[M+H]^+$: 354.1489, found 354.1486.

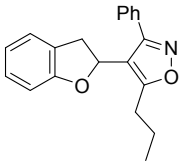
4-(2,3-Dihydrobenzofuran-2-yl)-5-(2-fluorophenyl)-3-phenylisoxazole (3r): Yield: 48 mg (68%), red oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.47 (m, 4H), 7.45 – 7.19 (m, 5H), 7.13 (t, J = 7.4 Hz, 1H), 6.97 (d, J = 6.8 Hz, 1H), 6.88 – 6.64 (m, 2H), 5.79 (t, J = 9.6 Hz, 1H), 3.19 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (d, J = 93.2 Hz), 159.5 (d, J = 250.5 Hz), 158.7, 132.6 (d, J = 8.3 Hz), 131.3, 129.6, 128.9, 128.8, 128.5, 128.2, 126.5, 124.5, 120.7, 116.4, 116.2, 115.9, 115.8, 115.6, 109.4, 75.3, 35.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.09 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3058, 2934, 1602, 1468, 1321, 1229, 1093, 1020, 919, 750, 613, 533 cm^{-1}; HRMS (ESI) Calcd for $C_{23}H_{16}FNNaO_2$, $[M+Na]^+$: 380.1057, found 380.1060.

4-(2,3-Dihydrobenzofuran-2-yl)-3-phenyl-5-(4'-propyl-[1,1'-biphenyl]-4-yl)isoxazole (3s): Yield: 74 mg (81%), colorless solid. M.p.: 148.1 – 149.3 ºC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 7.8 Hz, 4H), 7.55 (d, J = 8.0 Hz, 2H), 7.38 (m, 3H), 7.29 (d, J = 8.0 Hz, 2H), 7.20 (t, J = 7.6 Hz, 1H), 6.99 (d, J = 6.8 Hz, 1H), 6.95 – 6.79 (m, 2H), 5.90 (t, J = 10.0 Hz, 1H), 3.34 – 2.98 (m, 2H), 2.66 (t, J = 7.6 Hz, 2H), 1.72 (m, 2H), 1.00 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 163.7, 158.7, 143.2, 142.7, 137.2, 129.6, 129.0, 128.9, 128.7, 128.5, 128.3, 127.2, 126.9, 126.8, 125.9, 124.6, 120.8, 112.7, 109.5, 75.5, 37.6, 34.7, 24.4, 13.8 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3485, 3387, 3049, 2935, 1610, 1489, 1319, 1229, 1097, 1016, 916, 826, 741, 515 cm^{-1}; HRMS (ESI) Calcd for $C_{32}H_{27}NNaO_2$, $[M+Na]^+$: 480.1934, found 480.1933.

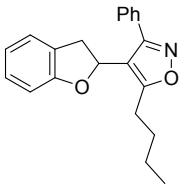
4-(2,3-Dihydrobenzofuran-2-yl)-3-phenyl-5-(thiophen-3-yl)isoxazole (3t): Yield: 48 mg (70%), colorless solid. M.p.: 124.6 – 125.4 ºC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 1.8 Hz, 1H), 7.62 (d, J = 6.8 Hz, 2H),

7.48 (d, J = 5.0 Hz, 1H), 7.44 – 7.30 (m, 4H), 7.19 (t, J = 7.6 Hz, 1H), 7.03 (d, J = 7.2 Hz, 1H), 6.87 (t, J = 6.4 Hz, 2H), 5.86 (t, J = 10.4 Hz, 1H), 3.31 – 2.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 163.5, 158.7, 129.6, 128.9, 128.8, 128.6, 128.4, 128.2, 126.9, 126.8, 126.7, 126.6, 124.6, 121.0, 112.1, 109.6, 75.5, 34.8 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3550, 3093, 2931, 1706, 1601, 1460, 1349, 1227, 900, 742 cm^{-1}; HRMS (ESI) Calcd for $C_{21}H_{15}NNaO_2S$, $[M+Na]^+$: 368.0716, found 368.0718.

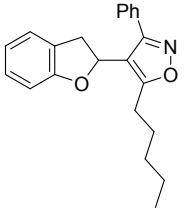
4-(2,3-Dihydrobenzofuran-2-yl)-3-phenyl-5-propylisoxazole (3u): Yield: 27 mg (45%), red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.48 (m, 2H), 7.42 – 7.31 (m, 3H), 7.16 (t, J = 7.6 Hz, 1H), 7.08 (d, J = 7.2 Hz, 1H), 6.91 – 6.76 (m, 2H), 5.72 (t, J = 9.6 Hz, 1H), 3.39 (m, 1H), 3.18 – 2.96 (m, 1H), 2.78 (m, 2 H), 1.74 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 162.3, 158.9, 129.5, 129.2, 128.7, 128.6, 128.4, 126.3, 124.6, 120.9, 113.6, 109.4, 75.5, 36.6, 28.3, 21.4, 13.8 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3499, 3396, 3299, 3054, 2932, 2682, 2590, 2499, 1693, 1588, 1454, 1329, 1224, 901, 746 cm^{-1}; HRMS (ESI) Calcd for $C_{20}H_{19}NNaO_2$, $[M+Na]^+$: 328.1308, found 328.1309.



5-Butyl-4-(2,3-dihydrobenzofuran-2-yl)-3-phenylisoxazole (3v): Yield: 36 mg (57%), red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.4 Hz, 2H), 7.44 – 7.31 (m, 3H), 7.16 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 7.6 Hz, 1H), 6.85 (m, 2H), 5.73 (t, J = 9.4 Hz, 1H), 3.40 (m, 1H), 3.12 (m, 1H), 2.80 (m, 2H), 1.68 (m, 2H), 1.44 – 1.25 (m, 2H), 0.90 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 162.3, 158.9, 129.5, 129.1, 128.7, 128.6, 128.4, 126.3, 124.6, 120.8, 113.5, 109.4, 75.4, 36.5, 30.0, 26.1, 22.3, 13.6 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3357, 3451, 3056, 2944, 1695, 1605, 1462, 1326, 1231, 1089, 913, 750 cm^{-1}; HRMS (ESI) Calcd for $C_{21}H_{21}NNaO_2$, $[M+Na]^+$: 342.1464, found 342.1468.



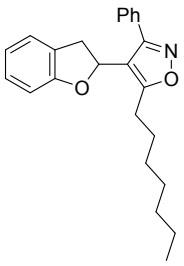
4-(2,3-Dihydrobenzofuran-2-yl)-5-pentyl-3-phenylisoxazole (3w): Yield: 36 mg (56%), red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.53 (m, 2H), 7.42 – 7.31 (m, 3H), 7.16 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 7.4 Hz, 1H), 6.91 – 6.71 (m, 2H), 5.72 (t, J = 9.6 Hz, 1H), 3.39 (m,1H), 3.26 – 3.02 (m, 1H), 2.79 (m, 2H), 1.78 – 1.52 (m, 2H), 1.40 – 1.16 (m, 4H), 0.90 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 162.3, 158.9, 129.5, 129.2, 128.7, 128.6, 128.4, 126.3, 124.6, 120.9, 113.5, 109.4, 75.5, 36.6, 31.3, 27.7, 26.4, 22.2, 13.9 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3424, 3058, 2938, 1705, 1602, 1460, 1320, 1231, 1152, 915, 750 cm^{-1}; HRMS (ESI) Calcd for $C_{22}H_{23}NNaO_2$, $[M+Na]^+$: 356.1621, found 356.1619.



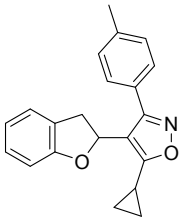
4-(2,3-Dihydrobenzofuran-2-yl)-5-hexyl-3-phenylisoxazole (3x): Yield: 35 mg (51%), red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (m, 2H), 7.42 – 7.30 (m, 3H), 7.16 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 7.2 Hz, 1H), 6.90 – 6.75 (m, 2H), 5.72 (t, J = 9.2 Hz, 1H), 3.39 (m, 1H), 3.23 – 2.95 (m,

1H), 2.91 – 2.46 (m, 2H), 1.78 – 1.60 (m, 2H), 1.29 (m, 6H), 0.88 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 162.3, 158.9, 129.5, 129.2, 128.7, 128.6, 128.4, 126.3, 124.6, 120.9, 113.5, 109.4, 75.5, 36.6, 31.3, 28.9, 27.9, 26.5, 22.4, 13.9 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3561, 3055, 2935, 1693, 1596, 1462, 1330, 1231, 1088, 914, 749, 516 cm^{-1}; HRMS (ESI) Calcd for $C_{23}H_{26}NO_2$, $[M+H]^+$: 348.1958, found 348.1956.

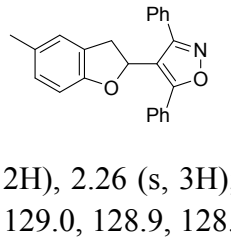
4-(2,3-Dihydrobenzofuran-2-yl)-5-heptyl-3-phenylisoxazole (3y): Yield: 37 mg (52%), red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.0 Hz, 2H), 7.43 – 7.31 (m, 3H), 7.16 (t, J = 7.6 Hz, 1H), 7.09 (d, J = 7.6 Hz, 1H), 6.93 – 6.75 (m, 2H), 5.73 (t, J = 9.6 Hz, 1H), 3.40 (m, 1H), 3.12 (m, 1H), 2.79 (m, 2H), 1.69 (m, 2H), 1.40 – 1.15 (m, 8H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 162.2, 158.9, 129.4, 129.1, 128.6, 128.5, 128.3, 126.2, 124.6, 120.8, 113.4, 109.3, 75.4, 36.5, 31.6, 29.1, 28.7, 28.0, 26.4, 22.5, 14.0 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3281, 3056, 2933, 2862, 1693, 1600, 1462, 1334, 1231, 914, 749, 524 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{27}NNaO_2$, $[M+Na]^+$: 384.1934, found 384.1939.



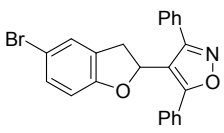
5-Cyclopropyl-4-(5-methyl-2,3-dihydrobenzofuran-2-yl)-3-phenylisoxazole (3z): Yield: 34 mg (54%), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.41 (m, 2H), 7.20 – 7.06 (m, 4H), 6.90 – 6.78 (m, 2H), 5.77 (t, J = 9.6 Hz, 1H), 3.46 – 3.18 (m, 2H), 2.33 (s, 3H), 2.10 – 1.83 (m, 1H), 1.33 – 1.09 (m, 2H), 1.06 – 0.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 162.7, 159.1, 139.6, 129.4, 128.6, 128.4, 126.6, 126.1, 124.7, 120.8, 113.3, 109.4, 75.6, 36.3, 21.3, 8.5, 8.1, 8.0 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3574, 3489, 3334, 3178, 3049, 2932, 2851, 2421, 1712, 1589, 1449, 1215, 1020, 903, 728, 626, 532, 451 cm^{-1}; HRMS (ESI) Calcd for $C_{21}H_{20}NO_2$, $[M+H]^+$: 318.1489, found 318.1484.



4-(5-Methyl-2,3-dihydrobenzofuran-2-yl)-3,5-diphenylisoxazole (3aa): Yield: 33 mg (47%), colorless solid. M.p.: 124.8 – 125.5 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.2 Hz, 2H), 7.66 (d, J = 7.4 Hz, 2H), 7.46 (d, J = 6.6 Hz, 3H), 7.36 (m,3H), 6.97 (d, J = 8.0 Hz, 1H), 6.81 – 6.68 (m, 2H), 5.81 (t, J = 10.0 Hz, 1H), 3.09 (q, J = 15.6 Hz, 2H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 156.6, 130.4, 130.1, 129.6, 129.0, 128.9, 128.8, 128.6, 128.5, 128.4, 127.5, 126.8, 125.1, 112.7, 109.0, 99.9, 75.6, 34.8, 20.7 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3504, 3232, 3163, 3062, 2927, 2848, 2762,2678, 2421, 2256, 2081, 1964, 1876, 1622, 1477, 1215, 1117, 1016, 910, 807, 714, 616, 525, 438 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{20}NO_2$, $[M+H]^+$: 354.1489, found 354.1490.

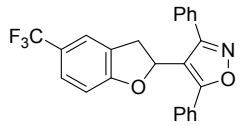


4-(5-Bromo-2,3-dihydrobenzofuran-2-yl)-3,5-diphenylisoxazole (3ab): Yield: 43 mg (52%), red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.2 Hz, 2H), 7.60 (d, J = 7.6 Hz, 2H), 7.41 (m, 6H), 7.27 (d, J = 7.6 Hz, 1H), 7.04 (s, 1H), 6.73 (d, J = 8.4 Hz, 1H), 5.85 (t, J = 10.0 Hz, 1H), 3.11 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 163.6, 157.9, 131.2, 130.7, 129.8, 129.3, 129.0, 128.9, 128.6, 128.4, 127.5, 127.3, 112.6, 112.4, 111.1, 76.2, 34.6 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3573, 3469, 3365, 3202, 2924, 2846, 2419, 1630, 1462, 1231, 1160, 1008, 905, 912, 708, 532, 453 cm^{-1}; HRMS (ESI)



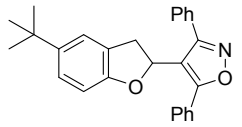
Calcd for $C_{23}H_{16}BrNNaO_2$, $[M+Na]^+$: 440.0257, found 440.0259.

3,5-Diphenyl-4-(5-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)isoxazole (3ac):



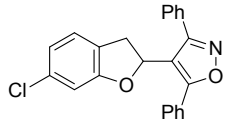
Yield: 32 mg (41%), colorless solid. M.p.: 114.4 – 115.2 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 5.2 Hz, 2H), 7.67 (d, J = 6.0 Hz, 2H), 7.55 (m, 5H), 7.42 (d, J = 8.4 Hz, 2H), 6.73 (d, J = 8.4 Hz, 2H), 5.59 (t, J = 6.8 Hz, 1H), 3.67 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 163.1, 158.9, 130.7 (d, J = 85.9 Hz), 129.2, 129.1, 128.9, 128.4, 127.8 (d, J = 121.0 Hz), 127.1 (q, J = 3.6 Hz), 125.3, 124.8, 124.5, 124.1, 123.8, 122.7, 116.2, 110.8, 71.9, 31.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -61.78 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3508, 3386, 3059, 2922, 2847, 1611, 1511, 1416, 1323, 1242, 1119, 989, 913, 836, 748, 700, 615, 518, 449 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{16}F_3NNaO_2$, $[M+Na]^+$: 430.1025, found 430.1026.

4-(5-(*tert*-Butyl)-2,3-dihydrobenzofuran-2-yl)-3,5-diphenylisoxazole (3ad):



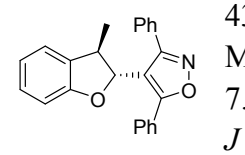
Yield: 44 mg (56%), colorless solid. M.p.: 163.1 – 164.2 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (m, 4H), 7.58 – 7.32 (m, 6H), 7.24 (d, J = 8.0 Hz, 1H), 7.03 (s, 1H), 6.84 (d, J = 8.0 Hz, 1H), 5.98 – 5.58 (t, J = 10.0 Hz, 1H), 3.16 (m, 2H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 163.7, 156.5, 143.9, 130.4, 129.5, 129.0, 128.9, 128.8, 128.5, 128.4, 127.5, 126.5, 125.0, 121.5, 113.0, 108.7, 75.6, 34.9, 34.2, 31.6 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3058, 2952, 1604, 1481, 1237, 1126, 915, 814, 702, 594, 501 cm^{-1}; HRMS (ESI) Calcd for $C_{27}H_{26}NO_2$, $[M+H]^+$: 396.1958, found 396.1949.

4-(6-Chloro-2,3-dihydrobenzofuran-2-yl)-3,5-diphenylisoxazole (3ae):



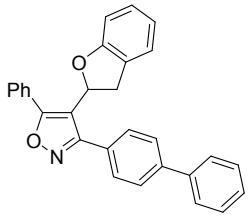
Yield: 38 mg (51%), red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.2 Hz, 2H), 7.61 (d, J = 7.6 Hz, 2H), 7.40 (m, 6H), 6.83 (m, 3H), 5.87 (t, J = 10.0 Hz, 1H), 3.08 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 163.6, 159.6, 133.6, 130.7, 129.7, 129.0, 128.9, 128.6, 128.4, 127.3, 125.6, 125.1, 120.9, 112.4, 110.3, 34.2 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3481, 3418, 3256, 3059, 2925, 2758, 2418, 2259, 1969, 1613, 1470, 1323, 1148, 1065, 918, 839, 705, 601, 516, 439 cm^{-1}; HRMS (ESI) Calcd for $C_{23}H_{17}ClNO_2$, $[M+H]^+$: 374.0942, found 374.0941.

***anti*-4-(3-Methyl-2,3-dihydrobenzofuran-2-yl)-3,5-diphenylisoxazole (3ag):**



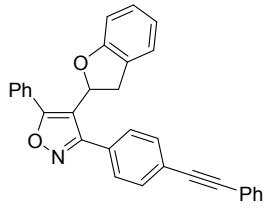
Yield: 43 mg (62%), colorless solid. M.p.: 173.3 – 174.1 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 6.5 Hz, 2H), 7.70 (d, J = 7.0 Hz, 2H), 7.56 – 7.32 (m, 6H), 7.20 (t, J = 7.5 Hz, 1H), 6.91 (m, 3H), 5.30 (d, J = 10.0 Hz, 1H), 3.57 – 3.02 (m, 1H), 1.14 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 164.0, 158.3, 132.0, 130.5, 129.6, 129.0, 128.9 128.8, 128.6, 128.5, 128.3, 127.5, 123.4, 121.0, 111.7, 109.7, 83.4, 40.8, 17.6 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3059, 2915, 1901, 1697, 1597, 1459, 1304, 1224, 1096, 1023, 934, 846, 711, 592, 500 cm^{-1}; HRMS (ESI) Calcd for $C_{24}H_{20}NO_2$, $[M+H]^+$: 354.1489, found 354.1481.

3-([1,1'-Biphenyl]-4-yl)-4-(2,3-dihydrobenzofuran-2-yl)-5-phenylisoxazole (4):



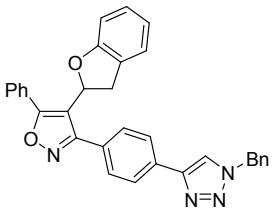
Yield: 76 mg (92%), colorless solid. M.p.: 150.2 – 151.1 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (s, 4H), 7.64 – 7.33 (m, 10H), 7.20 (s, 1H), 6.98 (s, 1H), 6.94 – 6.70 (m, 2H), 5.90 (s, 1H), 3.19 (dd, J = 18.0, 10.0 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.7, 163.4, 158.7, 142.4, 140.2, 130.5, 129.3, 128.9, 128.8, 128.4, 128.3, 127.9, 127.7, 127.5, 127.2, 127.1, 126.9, 124.6, 120.9, 112.8, 109.6, 75.5, 34.8 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3049, 2931, 2847, 1690, 1599, 1463, 1319, 1226, 1013, 911, 845, 698, 577, 499 cm^{-1}; HRMS (ESI) Calcd for $C_{29}H_{22}NO_2$, $[M+H]^+$: 416.1645, found 416.1635.

4-(2,3-Dihydrobenzofuran-2-yl)-5-phenyl-3-(4-(phenylethynyl)phenyl)isoxazole



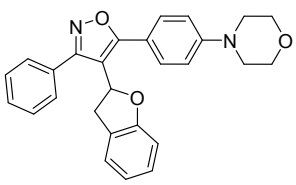
(5): Yield: 76 mg (87%), colorless solid. M.p.: 162.6 – 163.5 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, J = 5.5 Hz, 2H), 7.67 (d, J = 7.5 Hz, 2H), 7.52 (dd, J = 20.9, 4.6 Hz, 7H), 7.36 (s, 3H), 7.21 (t, J = 7.1 Hz, 1H), 7.01 (d, J = 6.6 Hz, 1H), 6.89 (dd, J = 12.3, 7.2 Hz, 2H), 5.87 (t, J = 9.9 Hz, 1H), 3.16 (dt, J = 25.8, 15.3 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.9, 163.1, 158.6, 131.7, 131.6, 130.6, 128.8, 128.7, 128.5, 128.5, 128.4, 128.3, 127.3, 126.7, 124.7, 124.6, 122.9, 121.0, 112.7, 109.6, 90.9, 88.8, 75.5, 34.8 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3055, 2932, 2215, 1894, 1696, 1602, 1459, 1325, 1228, 1019, 916, 843, 741 cm^{-1}; HRMS (ESI) Calcd for $C_{31}H_{22}NO_2$, $[M+H]^+$: 440.1645, found 440.1634.

3-(4-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)phenyl)-4-(2,3-dihydrobenzofuran-2-yl)-5-ph



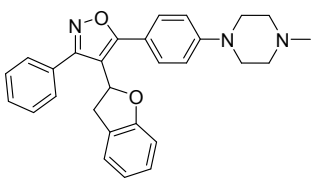
enylisoxazole (6): Yield: 43 mg (87%), colorless solid. M.p.:175.4 – 176.5 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.63 (m, 7H), 7.55 – 7.43 (m, 3H), 7.42 – 7.35 (m, 3H), 7.31 (dd, J = 7.4, 2.2 Hz, 2H), 7.16 (t, J = 7.8, 1H), 6.99 – 6.93 (m, 1H), 6.89 – 6.78 (m, 2H), 5.85 (t, J = 10.2 Hz, 1H), 5.56 (s, 2H), 3.14 (t, J = 9.8 Hz, 2H); ^{13}C NMR (100 Hz, $CDCl_3$) δ 169.8, 163.2, 158.6, 147.4, 134.5, 131.8, 130.6, 129.4, 129.1, 128.9, 128.8, 128.7, 128.5, 128.4, 128.1, 127.4, 126.8, 125.7, 124.7, 120.9, 119.9, 112.6, 109.6, 75.6, 54.2, 34.7; IR (KBr)$\tilde{\nu}_{max}$ 3052, 2926, 2848, 1601, 1454, 1351, 1228, 1043, 909, 840, 735, 458 cm^{-1}; HRMS (ESSI) Calcd for $C_{32}N_4O_2H_{25}$, $[M+H]^+$: 497.1972, found 496.1972.

4-(4-(4-(2,3-Dihydrobenzofuran-2-yl)-3-phenylisoxazol-5-yl)phenyl)morpholine



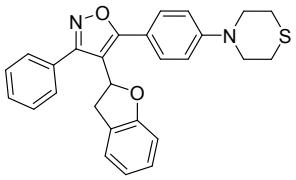
(7): Yield: 38 mg (91%), brown solid. M.p.:156.3 – 157.1 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (t, J = 7.4 Hz, 4H), 7.35 (m, 3H), 7.17 (t, J = 7.6 Hz, 1H), 7.05 – 6.74 (m, 5H), 5.82 (t, J = 10.0 Hz, 1H), 3.86 (t, J = 4.7 Hz, 4H), 3.24 (t, J = 4.8 Hz, 4H), 3.13 (d, J = 10.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 163.7, 158.8, 152.4, 129.5, 129.4, 129.2, 128.9, 128.5, 128.3, 127.1, 124.6, 120.7, 118.2, 114.6, 111.0, 109.6, 75.9, 66.6, 48.0, 34.5 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3201, 3055, 2963, 2921, 2854, 1610, 1516, 1453, 1417, 1361, 1304, 1234, 1120, 977,928, 897, 749, 644, 525 cm^{-1}; HRMS (ESI) Calcd for $C_{27}H_{25}N_2O_3$, $[M+H]^+$: 425.1860, found 425.1855.

4-(2,3-Dihydrobenzofuran-2-yl)-5-(4-(4-methylpiperazin-1-yl)phenyl)-3-



phenyliso xazole (8): Yield: 35 mg (81%), brown solid. M.p.:162.7 – 163.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, 4H), 7.50 – 7.29 (m, 3H), 7.17 (t, J = 7.8 Hz, 1H), 7.04 – 6.70 (m, 5H), 5.82 (t, J = 10.0 Hz, 1H), 3.30 (t, J = 5.0 Hz, 4H), 3.13 (d, J = 10.0 Hz, 2H), 2.56 (t, J = 5.0 Hz, 4H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 163.7, 158.79, 152.3, 129.5, 129.4, 129.2, 128.9, 128.5, 128.2, 127.1, 124.6, 120.7, 117.6, 114.8, 110.8, 109.5, 75.9, 54.8, 47.7, 46.1, 34.4 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3523, 3449, 3403, 3277, 2987, 2903, 2044, 1764, 1672, 1603, 1477, 1430, 1373, 1247, 1052, 1005, 931, 857, 804, 749, 650, 613, 512, 466 cm^{-1}; HRMS (ESI) Calcd for $C_{28}H_{28}N_3O_2$, $[M+H]^+$: 438.2176, found 438.2171.

4-(2,3-Dihydrobenzofuran-2-yl)-3-phenyl-5-(4-thiomorpholinophenyl)isoxazole



(9): Yield: 33 mg (76%), brown solid. M.p.:169.8 – 170.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.57 (m, 4H), 7.48 – 7.29 (m, 3H), 7.20 – 7.10 (m, 1H), 6.98 (d, J = 7.2 Hz, 1H), 6.93 – 6.77 (m, 4H), 5.82 (t, J = 10.2 Hz, 1H), 3.81 – 3.52 (m, 4H), 3.14 (d, J = 10.2 Hz, 2H), 2.82 – 2.60 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 163.7, 158.8, 151.5, 129.7, 129.5, 129.2, 128.9, 128.5, 128.3, 127.1, 124.6, 120.7, 117.4, 115.3, 110.8, 109.6, 75.9, 50.7, 34.5, 26.1 ppm; IR (KBr)$\tilde{\nu}_{max}$ 3049, 2919, 2851, 1608, 1515, 1416, 1385, 1359, 1286, 1226, 1193, 1100, 1018, 949, 895, 858, 822, 749, 699, 526, 453, 421 cm^{-1}; HRMS (ESI) Calcd for $C_{27}H_{25}N_2O_2S$, $[M+H]^+$: 441.1630, found 441.1630.

H. References

(1) Li, C.; Li, J.; Zhou, F.; Li, C.; Wu, W. *J. Org. Chem*. **2019**, *84*, 11958.

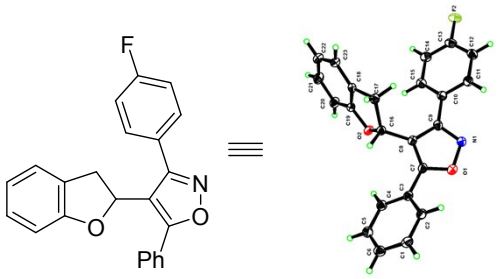
(2) Wu, W.; Yi, S.; Huang, W.; Luo, D.; Jiang, H. *Org. Lett*. **2017**, *19*, 2825.

(3) (a)Wu, W.; Li, C.; Zhou, F.; Li, J.; Xu, X.; Jiang, H. *Adv. Synth. Catal*. **2019**, *361*, 3813. (b) She, Z.; Niu, D.; Chen, L.; Gunawan, M.; Shanja, X.; Hersh, W.; Chen, Y. *J. Org. Chem.* **2012**, *77*, 3627. (c) Li, J.; Hu, M.; Li, C.; Li, C.; Li, J.; Wu, W.; Jiang, H. *Adv. Synth. Catal.* **2018**, *360*, 2707.

(4) Chen, C.; Lai, Y.; Wu, R.; Liu, Y.; Lin, Y. *ChemCatChem* **2016**, *8*, 2193. (b) Zhou, L.; Shi, Y.; Zhu, X.; Zhang, P. *Tetrahedron Lett*. **2019**, *60*, 2005.

I. X-ray Crystallographic Analysis

I. X-ray Crystallographic Analysis for 3c

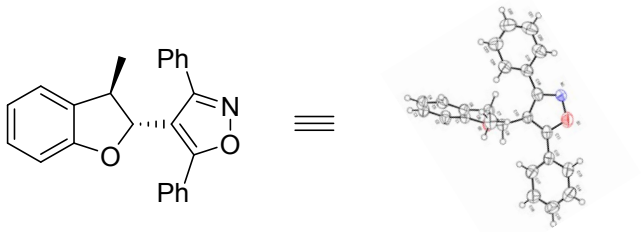


3c CCDC: 2000121

Table S1. Crystal data and structure refinement for **3c**

Empirical formula	$C_{23}H_{16}FNO_2$
Formula weight	357.37
Temperature	170 K
Wavelength	0.71073 Å
Crystal system	triclinic
Space group	P -1
Unit cell dimensions	a = 5.7119(3) Å, α = 72.075(2) °
	b = 11.2727(7) Å, β = 83.916(2) °
	c = 14.3335(8) Å, γ = 83.801(2)°
Density (calculated)	1.364
Absorption coefficient	0.094 mm^{-1}
F(000)	372.0
Crystal size	0.15 × 0.08 × 0.02
Theta range for data collection	5.508 to 52.78
Index ranges	$-6 \le h \le 7$, $-14 \le k \le 14$, $-17 \le l \le 17$
Reflections collected	9745
Independent reflections	3517 [R_{int} = 0.0368, R_{sigma} = 0.0472]
Completeness to theta = 26.390	1.66/0.91
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3517/0/253
Goodness-of-fit on F^2	1.077
Final R indices [$I > 2sigma(I)$]	R_1 = 0.0526, wR_2 = 0.1046
Final R indices (all data)	R_1 = 0.0863, wR_2 = 0.1204

II. X-ray Crystallographic Analysis for 3ag



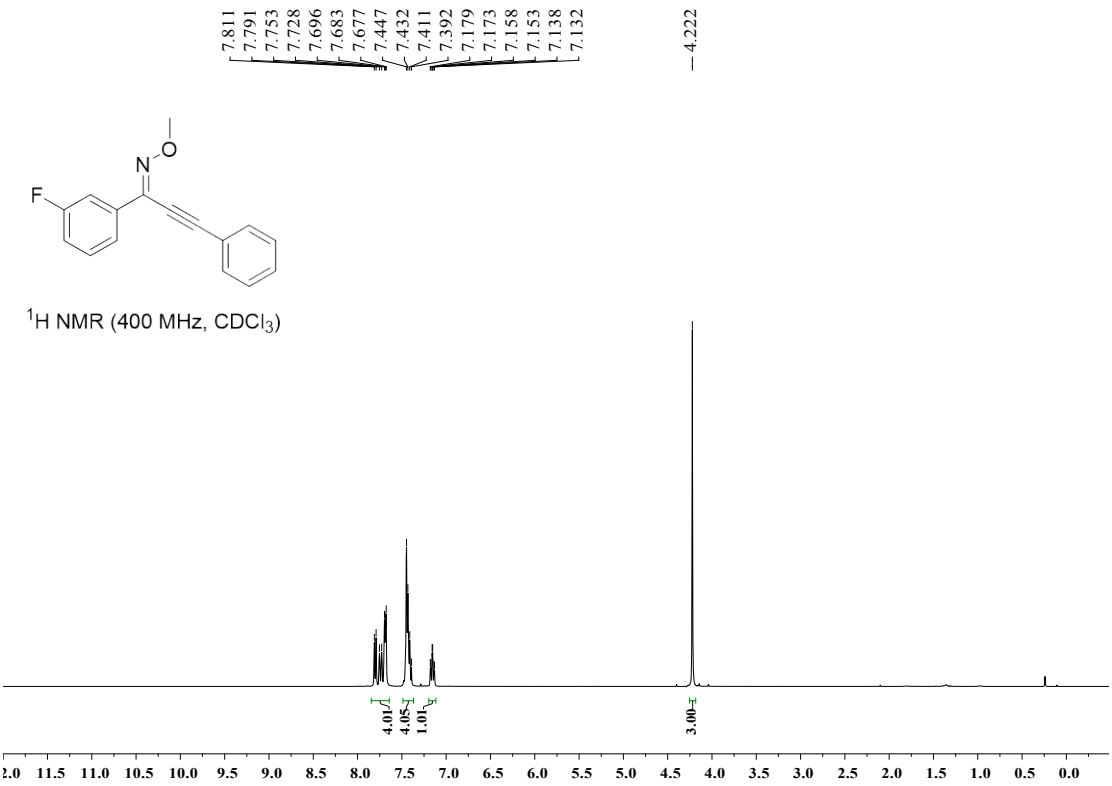
3ag CCDC: 2053026

Table S2. Crystal data and structure refinement for **3ag**

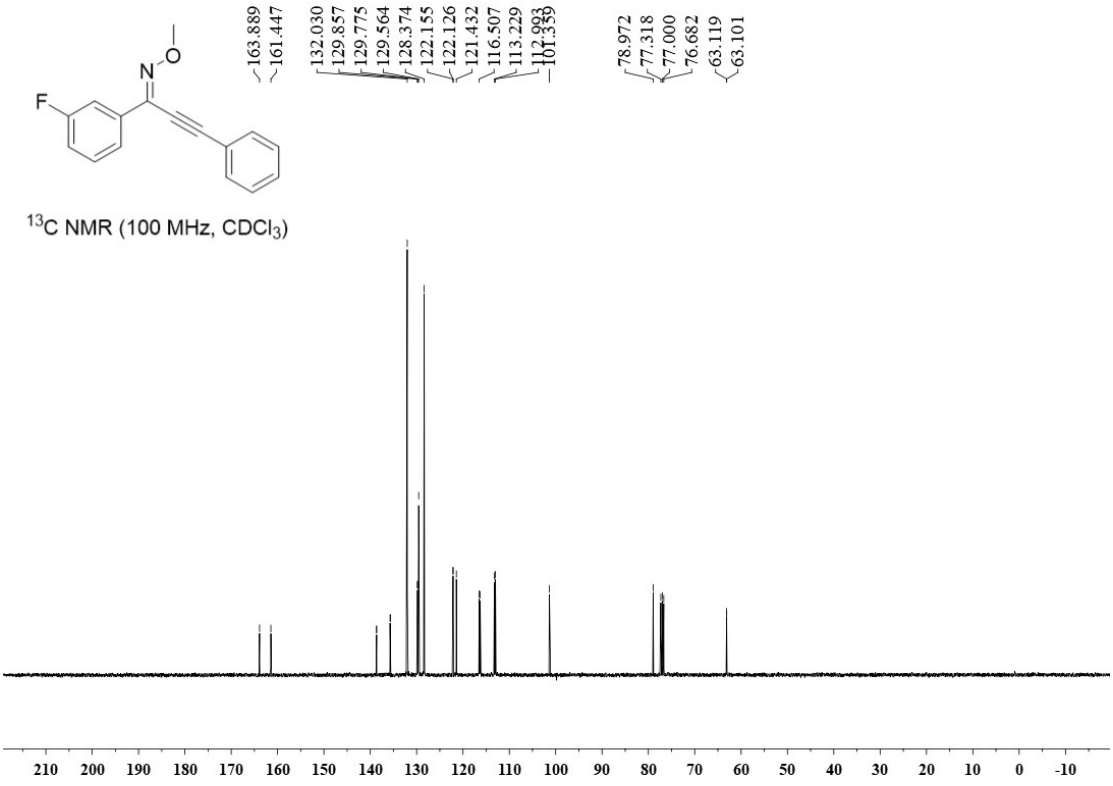
Empirical formula	$C_{24}H_{19}NO_2$
Formula weight	353.40
Temperature	298 K
Wavelength	0.71073Å
Crystal system	monoclinic
Space group	$P2_1/n$
Unit cell dimensions	a = 5.8481(5) Å, α = 90 °
	b = 20.1032 (17) Å, β = 99.844 °
	c = 15.8952 (16) Å, γ = 90 °
Density (calculated)	1.275
Absorption coefficient	0.081 mm^{-1}
F(000)	744.0
Crystal size	0.12 × 0.08 × 0.05
Theta range for data collection	5.508 to 52.78
Index ranges	$-7 \le h \le 6$, $-24 \le k \le 24$, $-16 \le l \le 19$
Reflections collected	14808
Independent reflections	3350 [R_{int} = 0.1022, R_{sigma} = 0.1017]
Completeness to theta = 25.348	0.16/-0.30
Refinement method	Goodness-of-fit on F^2
Data/restraints/parameters	3350/0/245
Goodness-of-fit on F^2	1.057
Final R indices [$I > 2sigma(I)$]	R_1 = 0.0633, wR_2 = 0.1145
Final R indices (all data)	R_1 = 0.1600, wR_2 = 0.1535

J. NMR Spectra for All the Compounds

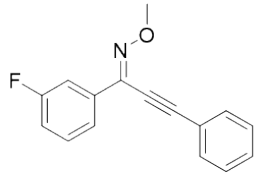
(*Z*)-1-(3-Fluorophenyl)-3-phenylprop-2-yn-1-one *O*-Methyl Oxime (1i)



^{1}H NMR (400 MHz, $CDCl_3$)

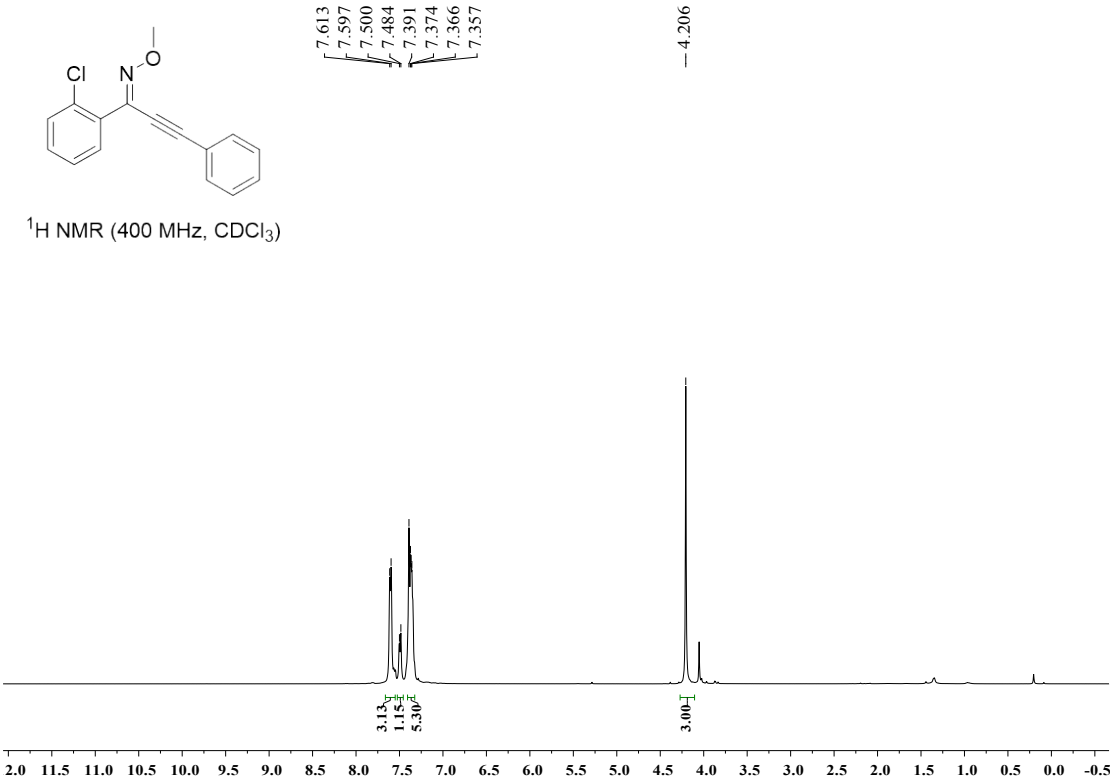


^{13}C NMR (100 MHz, $CDCl_3$)

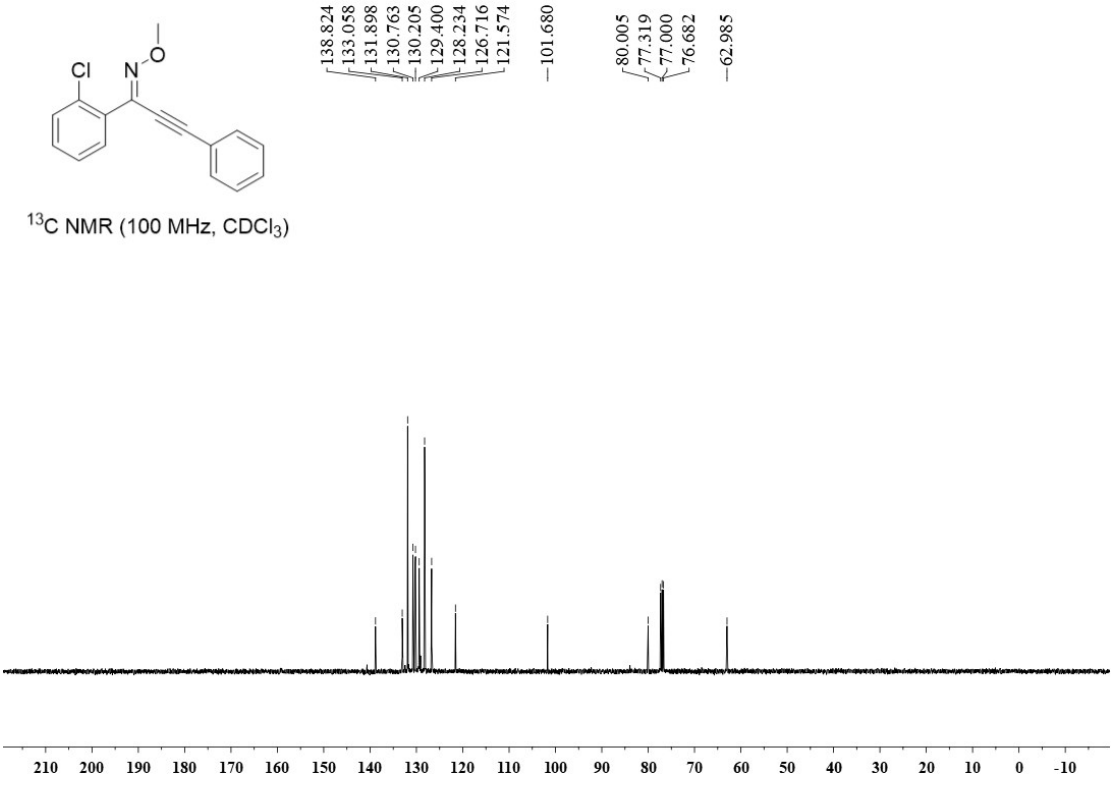


^{19}F NMR (376 MHz, $CDCl_3$)

(*E*)-1-(2-Chlorophenyl)-3-phenylprop-2-yn-1-one *O*-Methyl Oxime (1j)

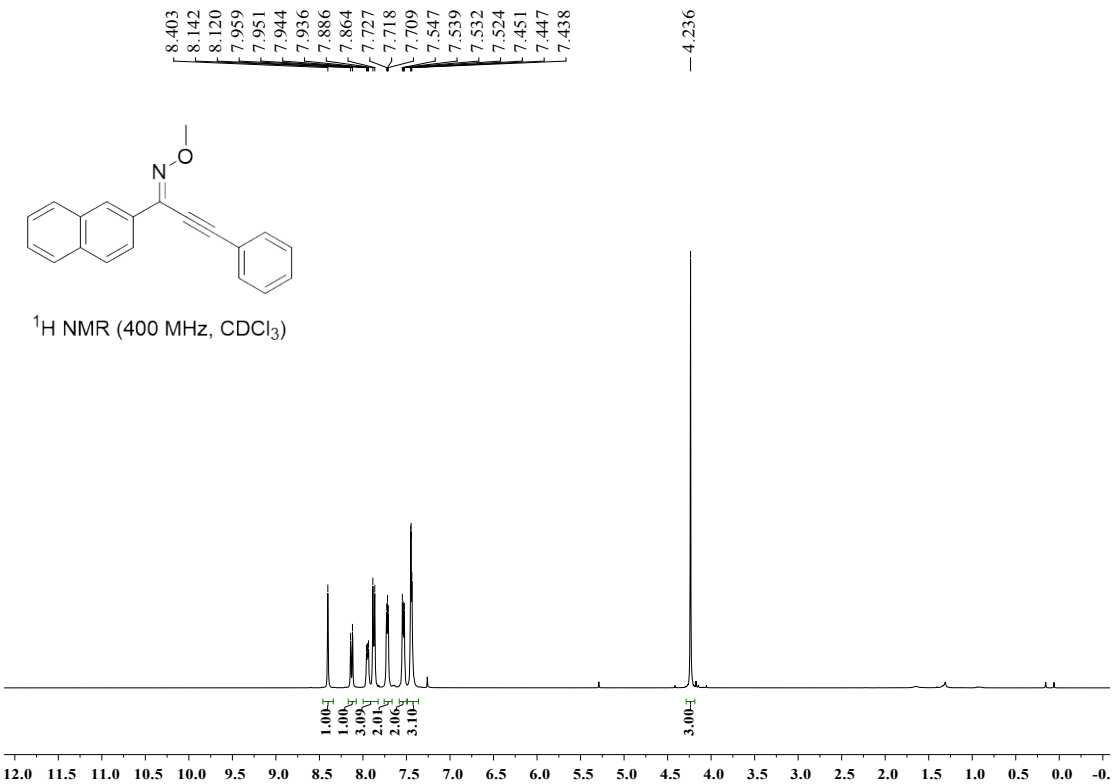


^{1}H NMR (400 MHz, $CDCl_3$)

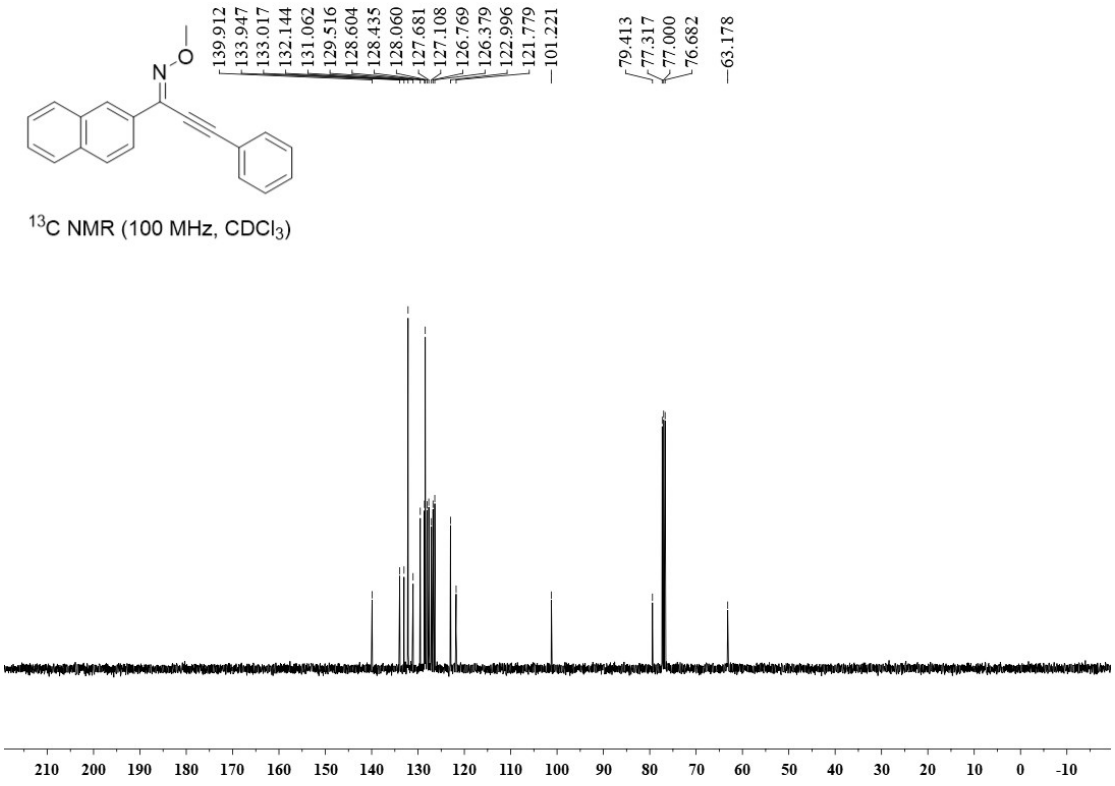


^{13}C NMR (100 MHz, $CDCl_3$)

(Z)-1-(Naphthalen-2-yl)-3-phenylprop-2-yn-1-one *O*-Methyl Oxime (1k)

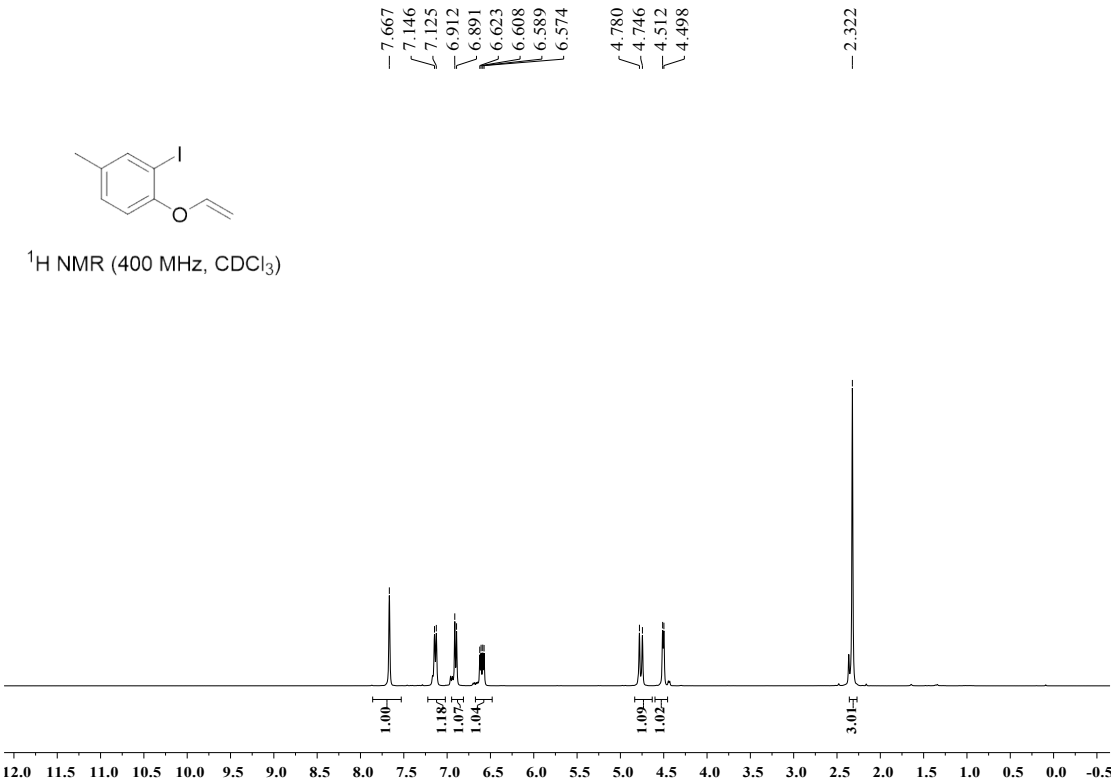


^{1}H NMR (400 MHz, $CDCl_3$)

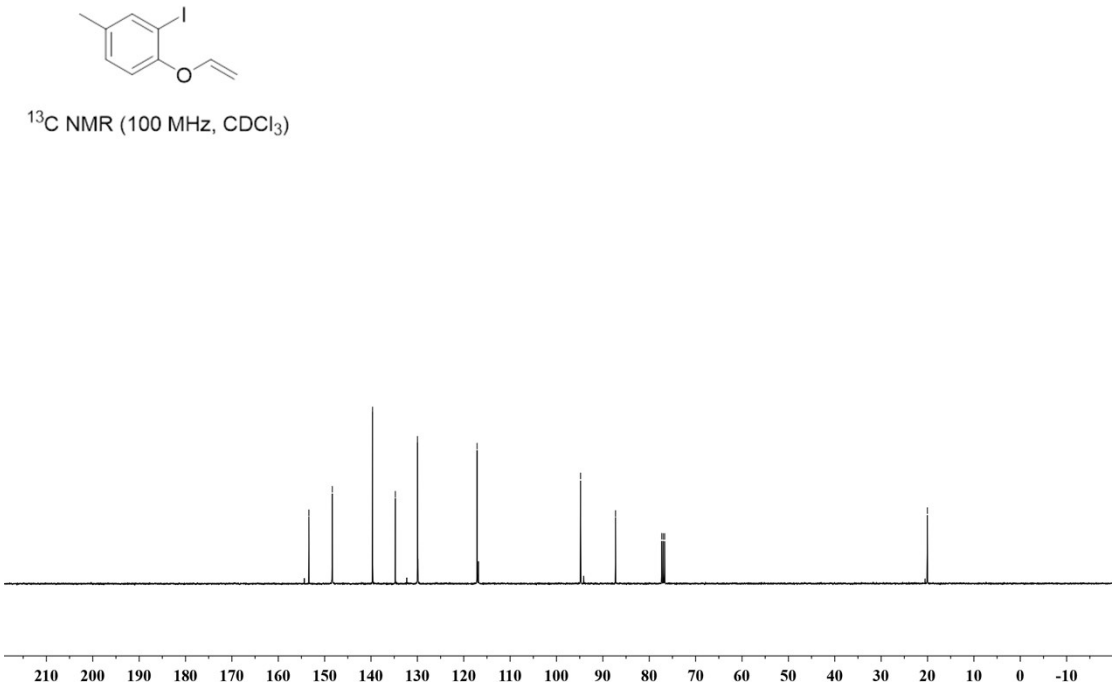


^{13}C NMR (100 MHz, $CDCl_3$)

2-Iodo-4-methyl-1-(vinyloxy)benzene (2aa)

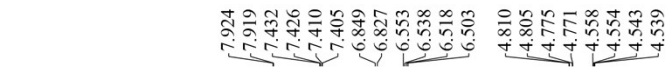


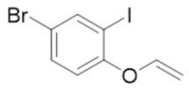
^{1}H NMR (400 MHz, $CDCl_3$)



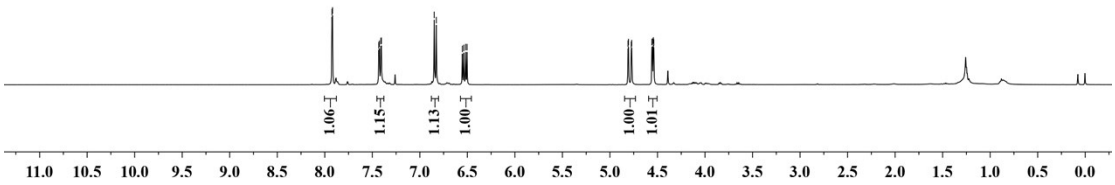
^{13}C NMR (100 MHz, $CDCl_3$)

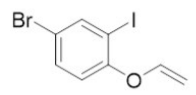
4-Bromo-2-iodo-1-(vinyloxy)benzene (2ab)



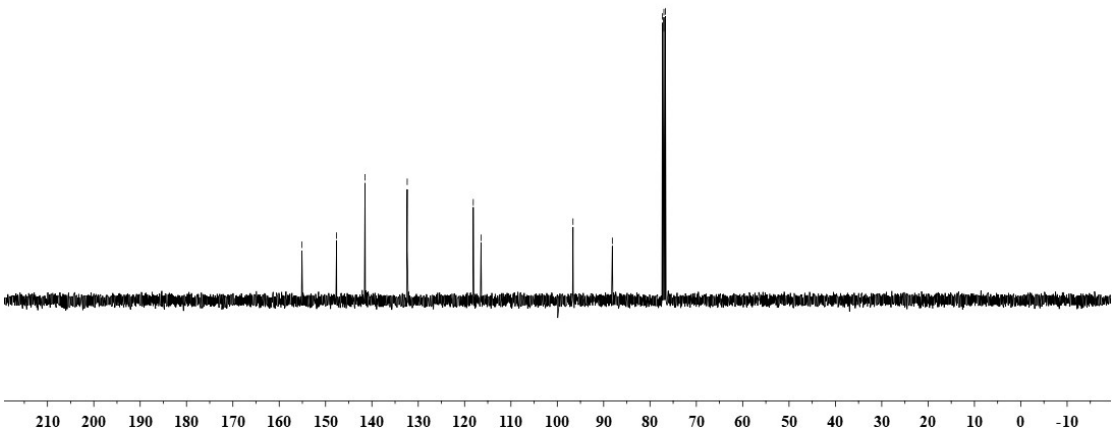


^{1}H NMR (400 MHz, $CDCl_3$)

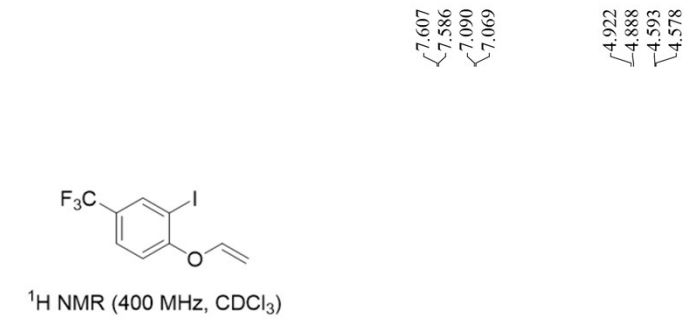


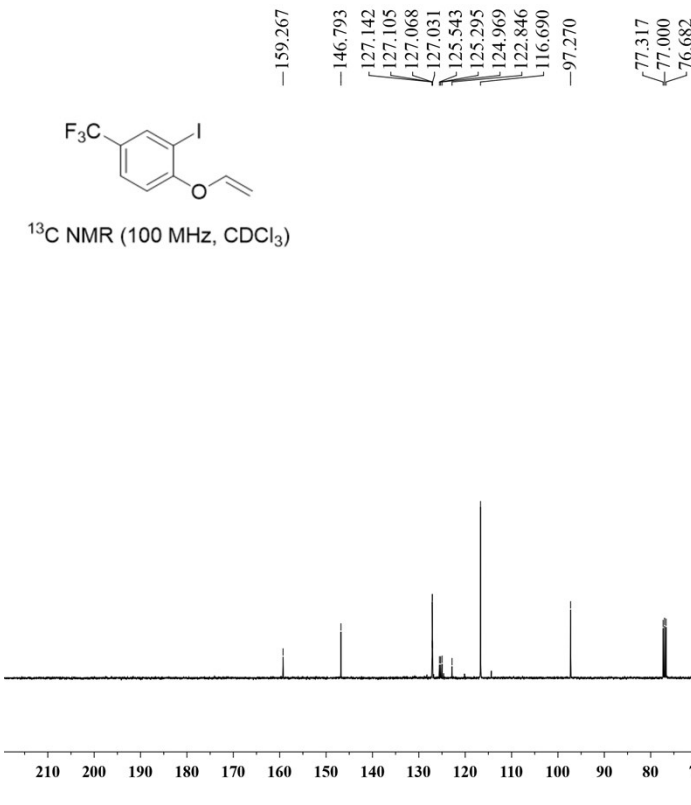


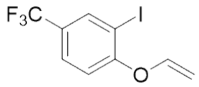
^{13}C NMR (100 MHz, $CDCl_3$)



2-Iodo-4-(trifluoromethyl)-1-(vinyloxy)benzene (2ac)



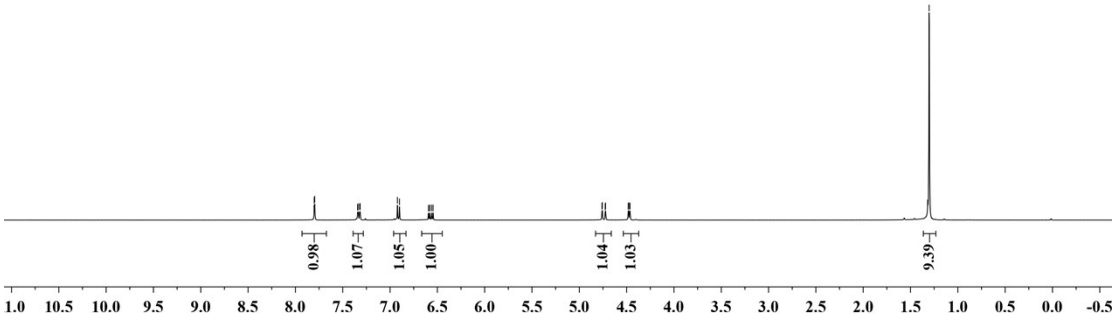


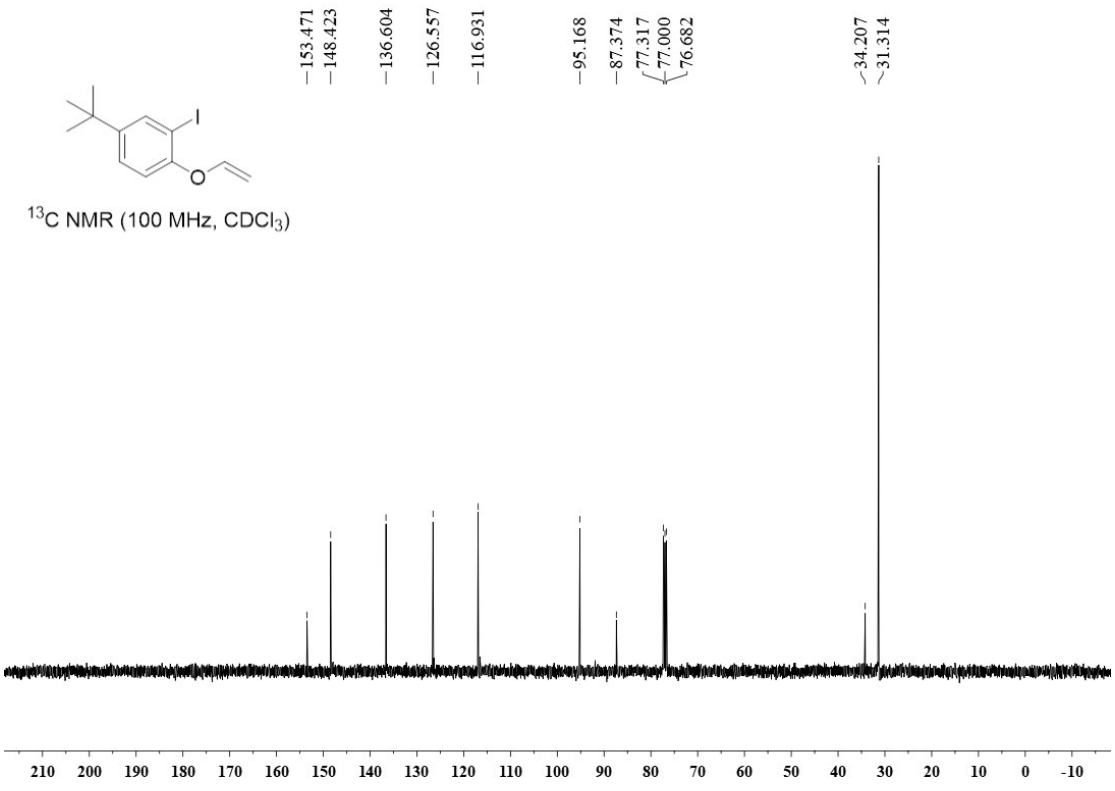


^{19}F NMR (376 MHz, $CDCl_3$)

4-(*tert*-Butyl)-2-iodo-1-(vinyloxy)benzene (2ad)

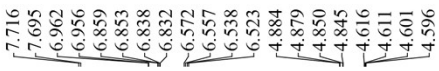
^{1}H NMR (400 MHz, $CDCl_3$)

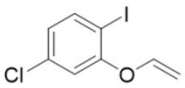




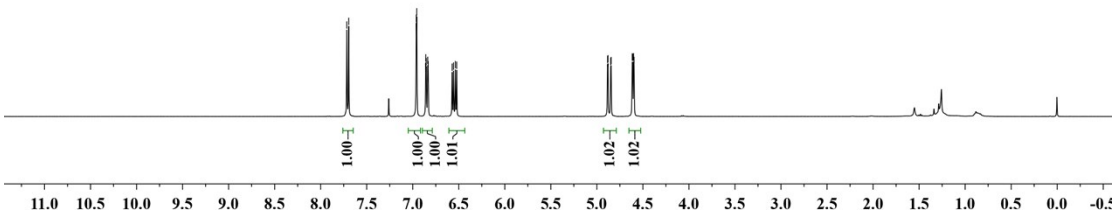
^{13}C NMR (100 MHz, $CDCl_3$)

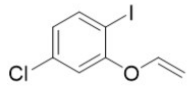
4-Chloro-1-iodo-2-(vinyloxy)benzene (2ae)



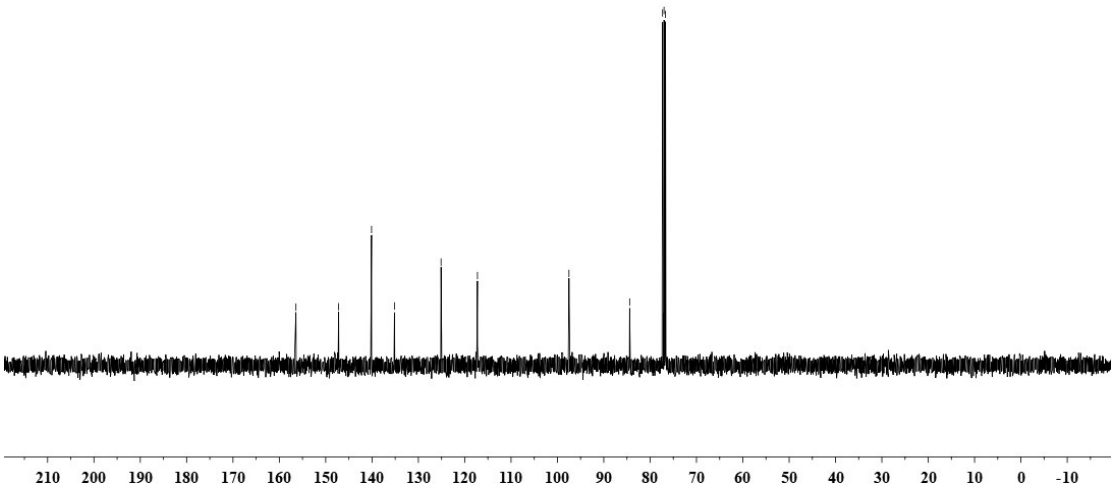


^{1}H NMR (100 MHz, $CDCl_3$)

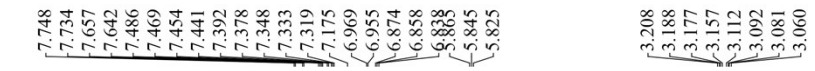


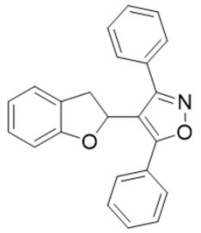


^{13}C NMR (400 MHz, $CDCl_3$)

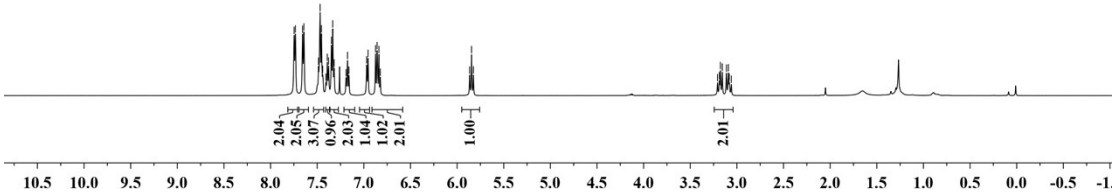


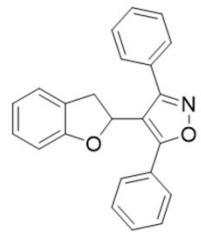
4-(2,3-Dihydrobenzofuran-2-yl)-3,5-diphenylisoxazole (3a)



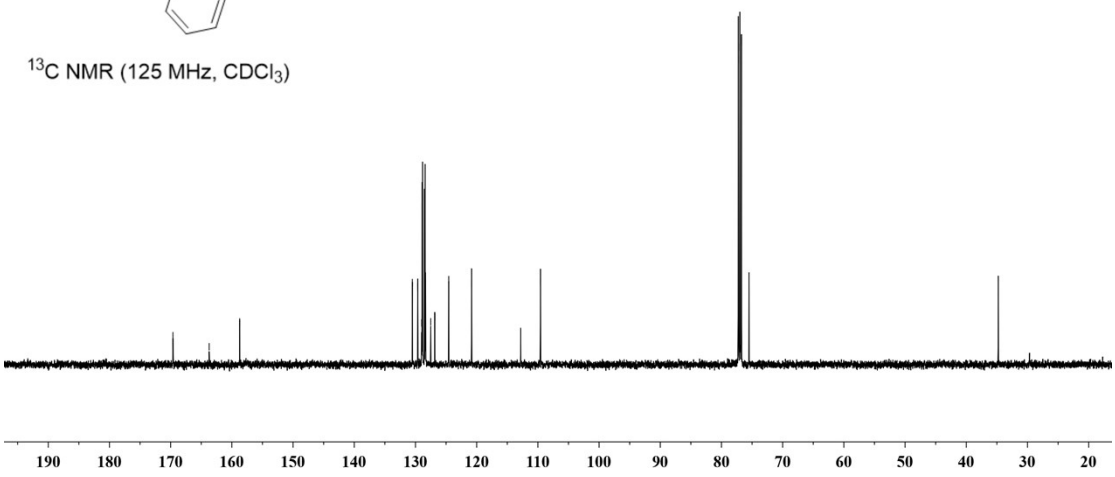


^{1}H NMR (500 MHz, $CDCl_3$)

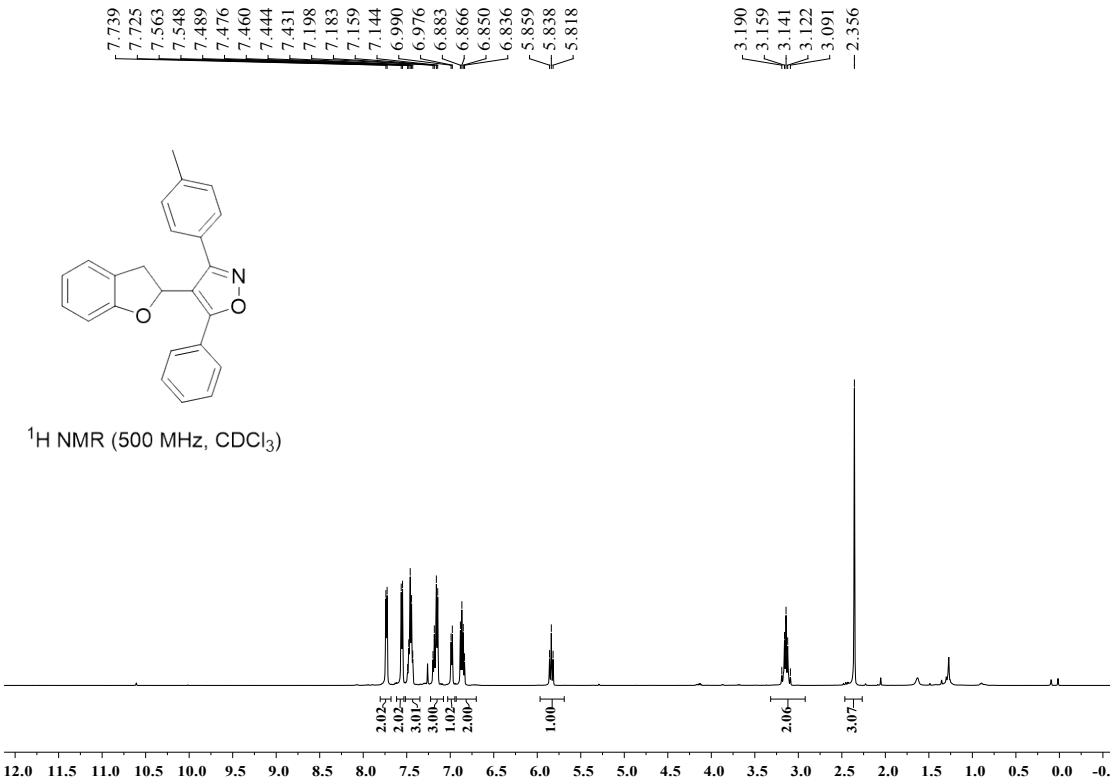


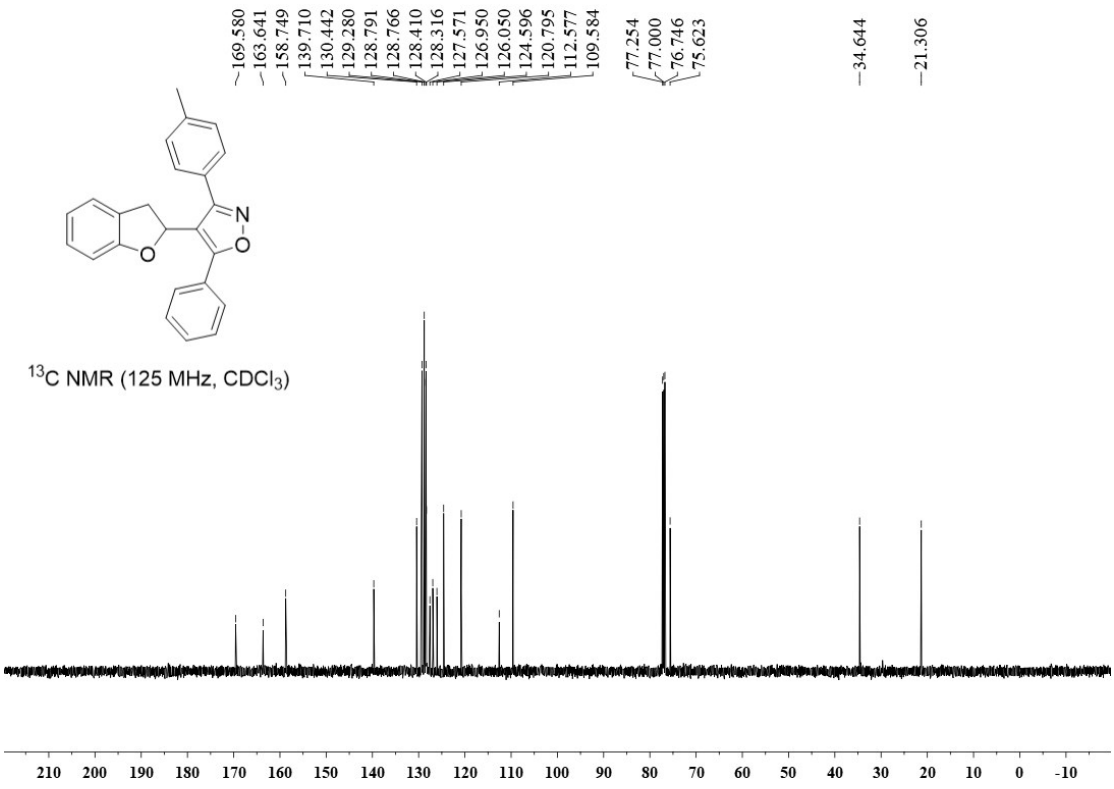


^{13}C NMR (125 MHz, $CDCl_3$)

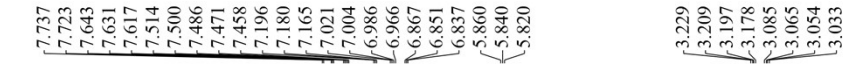


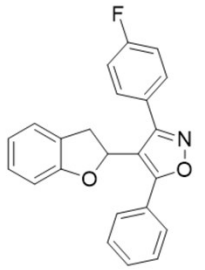
4-(2,3-Dihydrobenzofuran-2-yl)-5-phenyl-3-(p-tolyl)isoxazole (3b)



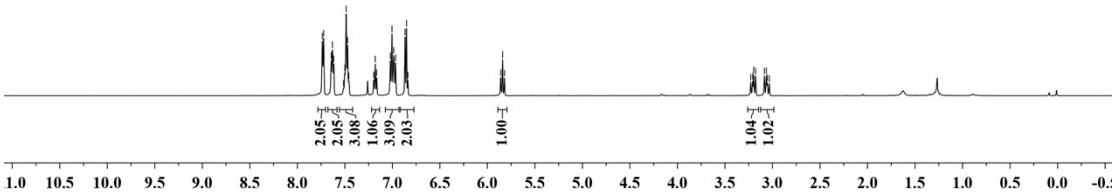


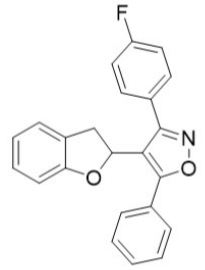
4-(2,3-Dihydrobenzofuran-2-yl)-3-(4-fluorophenyl)-5-phenylisoxazole (3c)



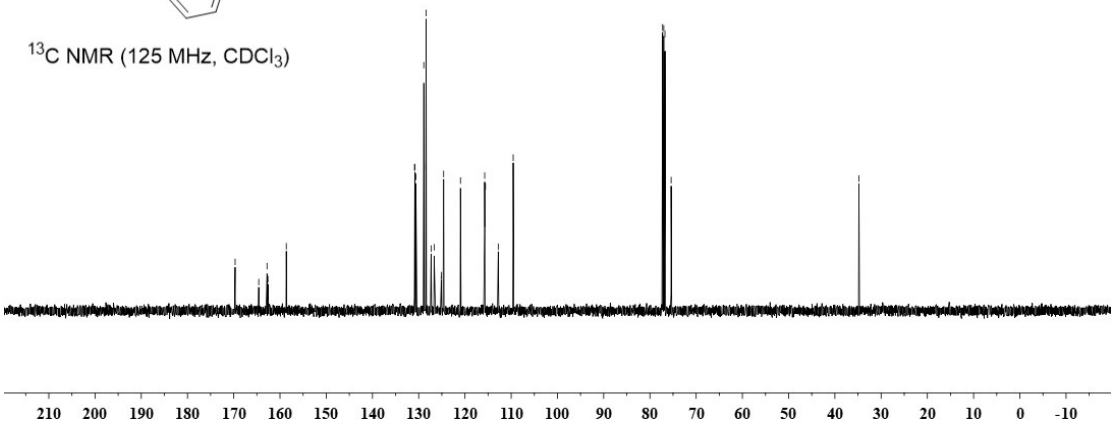


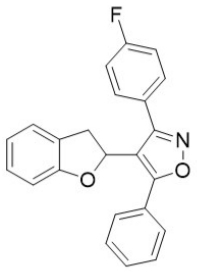
^{1}H NMR (500 MHz, $CDCl_3$)

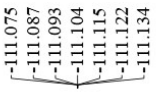




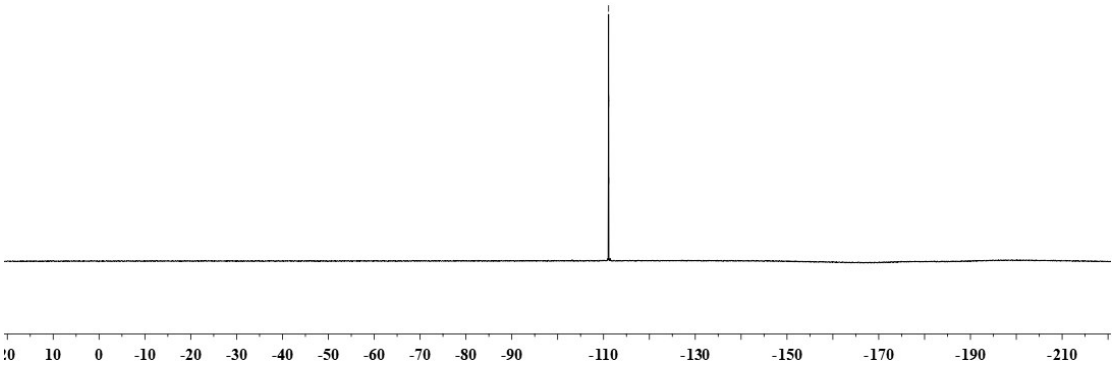
^{13}C NMR (125 MHz, $CDCl_3$)



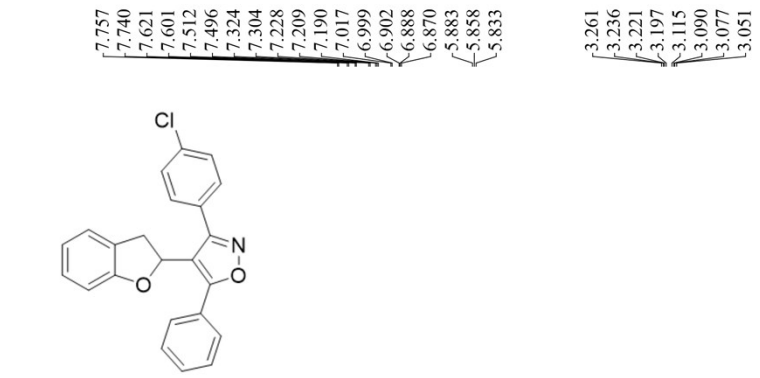




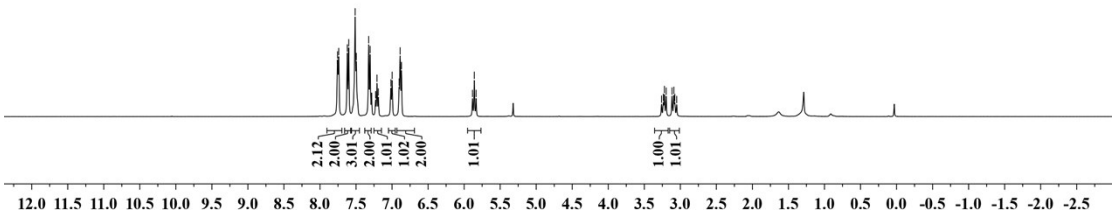
^{19}F NMR (470 MHz, $CDCl_3$)

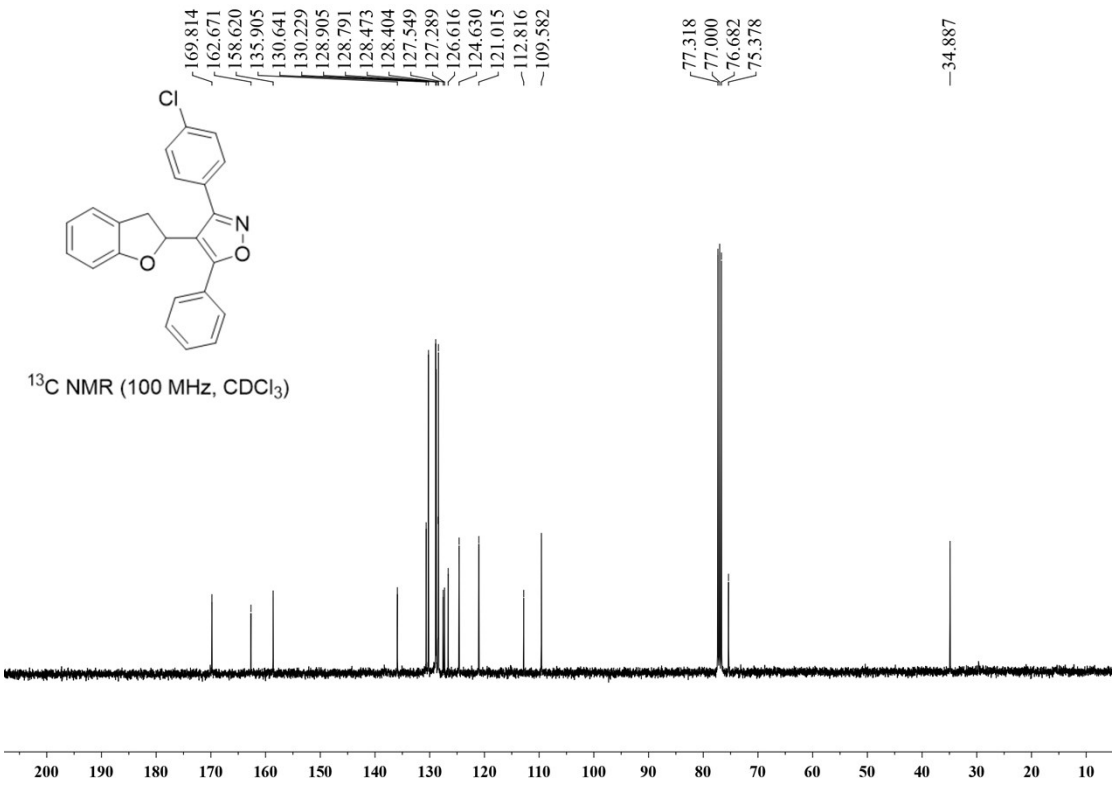


3-(4-Chlorophenyl)-4-(2,3-dihydrobenzofuran-2-yl)-5-phenylisoxazole (3d)



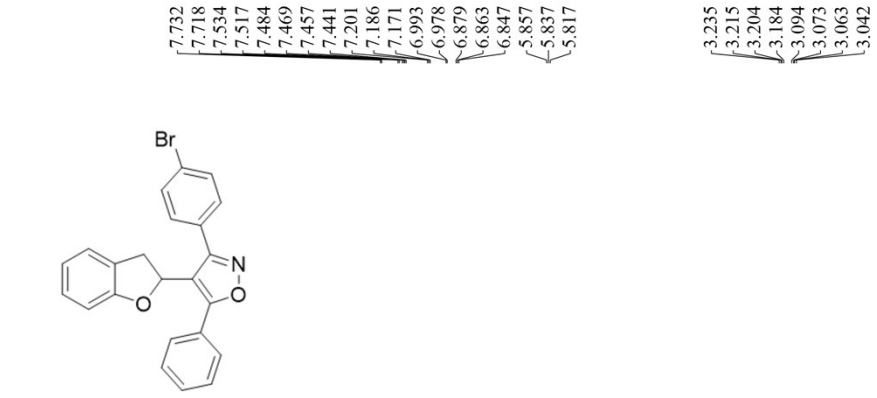
^{1}H NMR (400 MHz, $CDCl_3$)



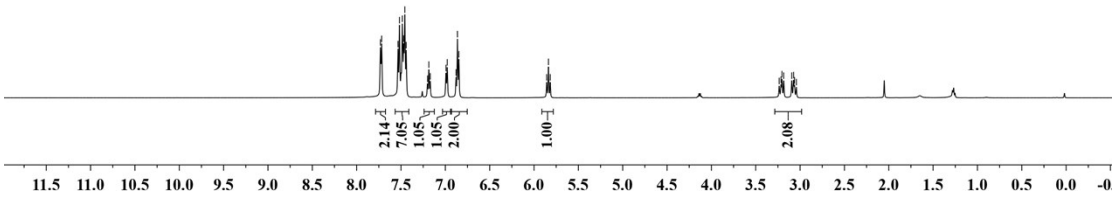


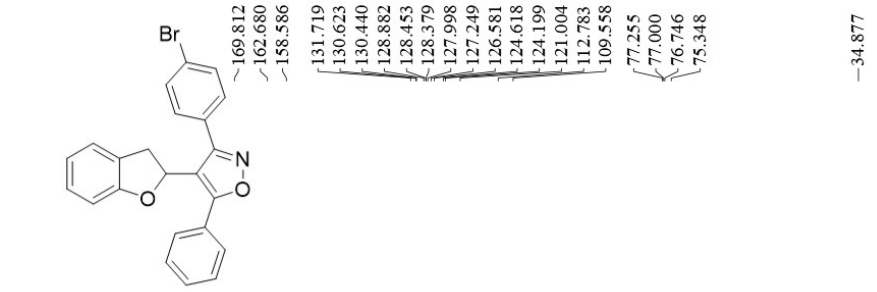
^{13}C NMR (100 MHz, $CDCl_3$)

3-(4-Bromophenyl)-4-(2,3-dihydrobenzofuran-2-yl)-5-phenylisoxazole (3e)

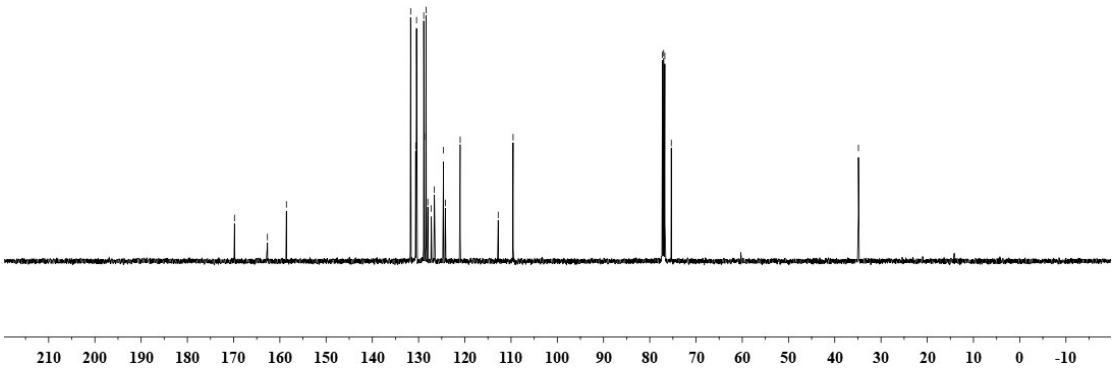


^{1}H NMR (500 MHz, $CDCl_3$)

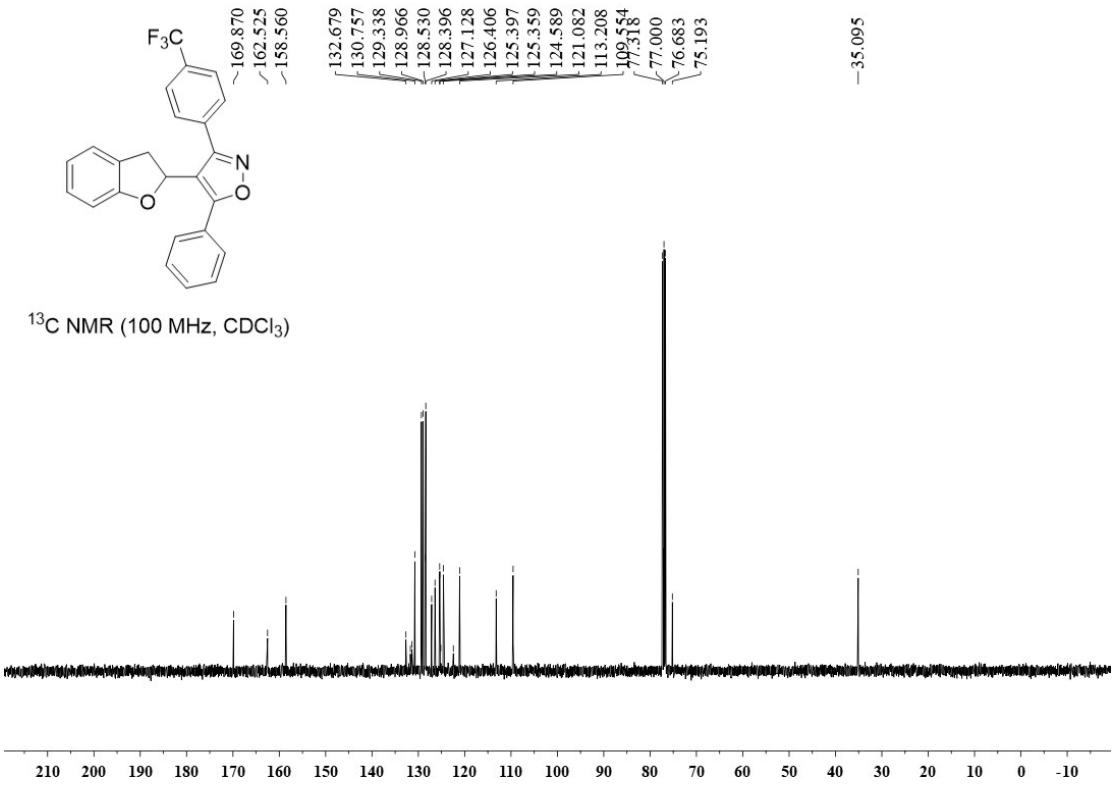


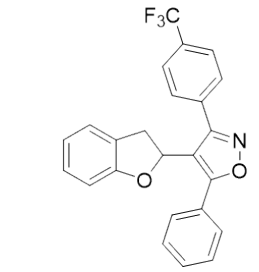


^{13}C NMR (125 MHz, $CDCl_3$)



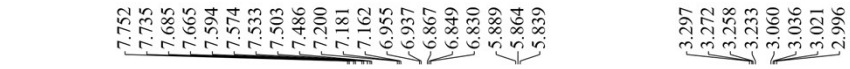
4-(2,3-Dihydrobenzofuran-2-yl)-5-phenyl-3-(4-(trifluoromethyl)phenyl)isoxazole (3f)

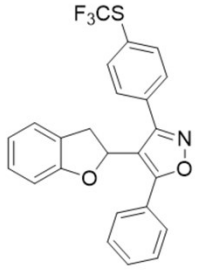




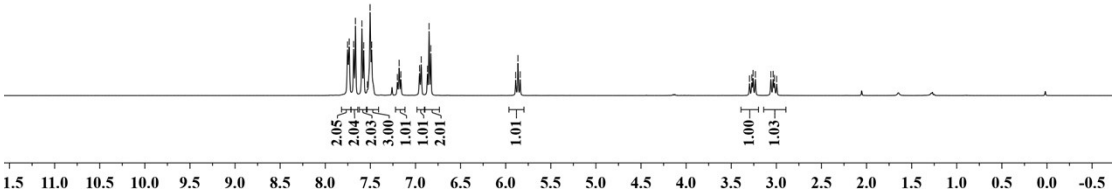
^{19}F NMR (376 MHz, $CDCl_3$)

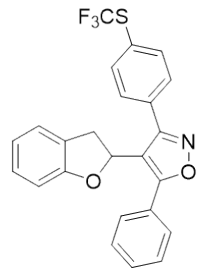
4-(2,3-Dihydrobenzofuran-2-yl)-5-phenyl-3-(4-((trifluoromethyl)thio)phenyl)isoxazole (3g)



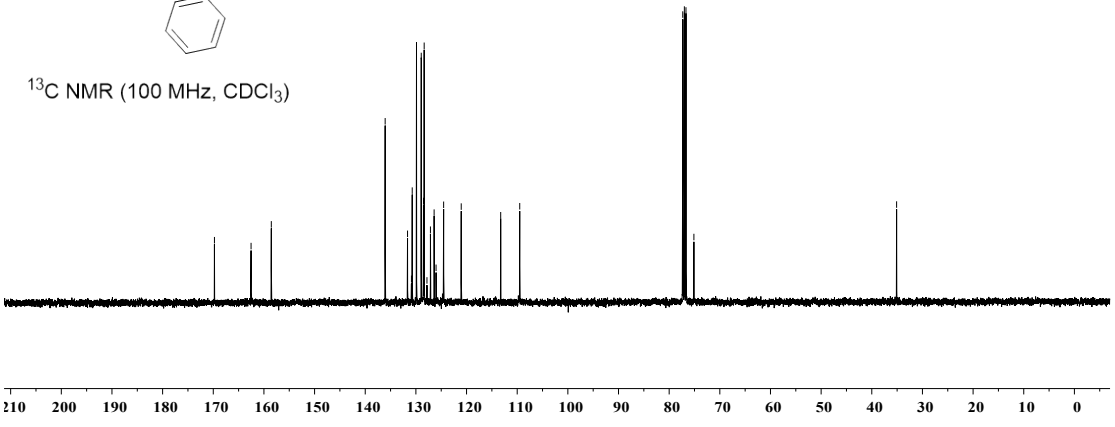


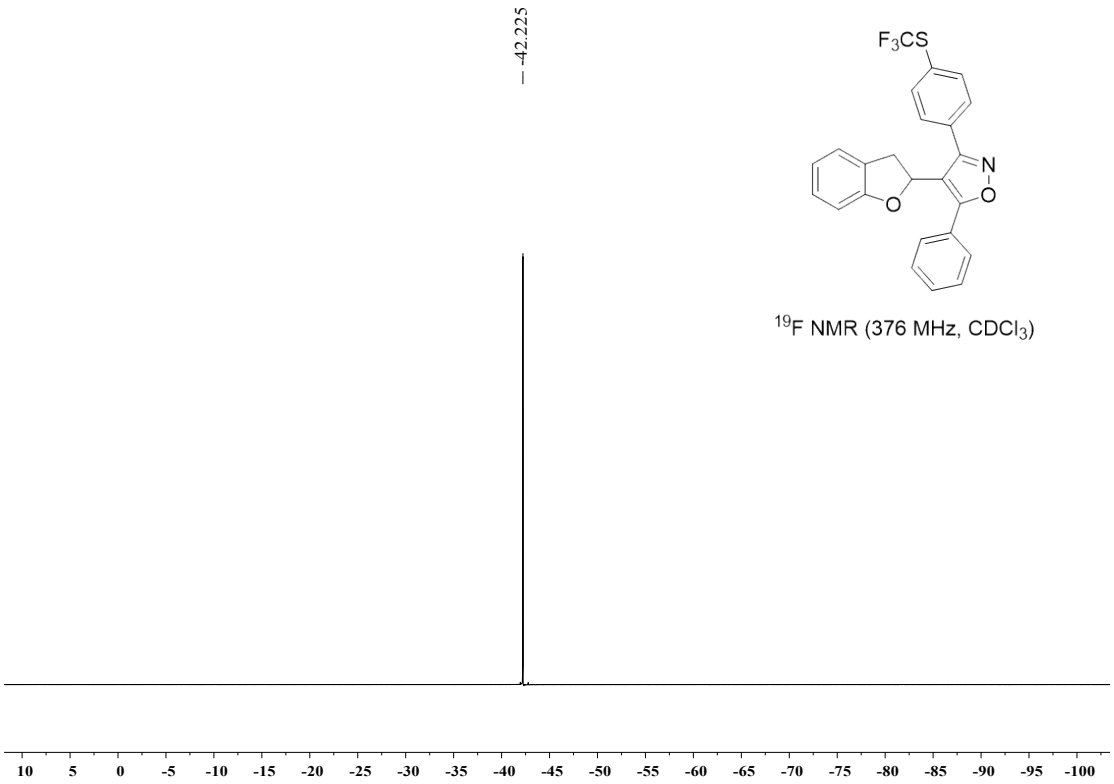
^{1}H NMR (400 MHz, $CDCl_3$)





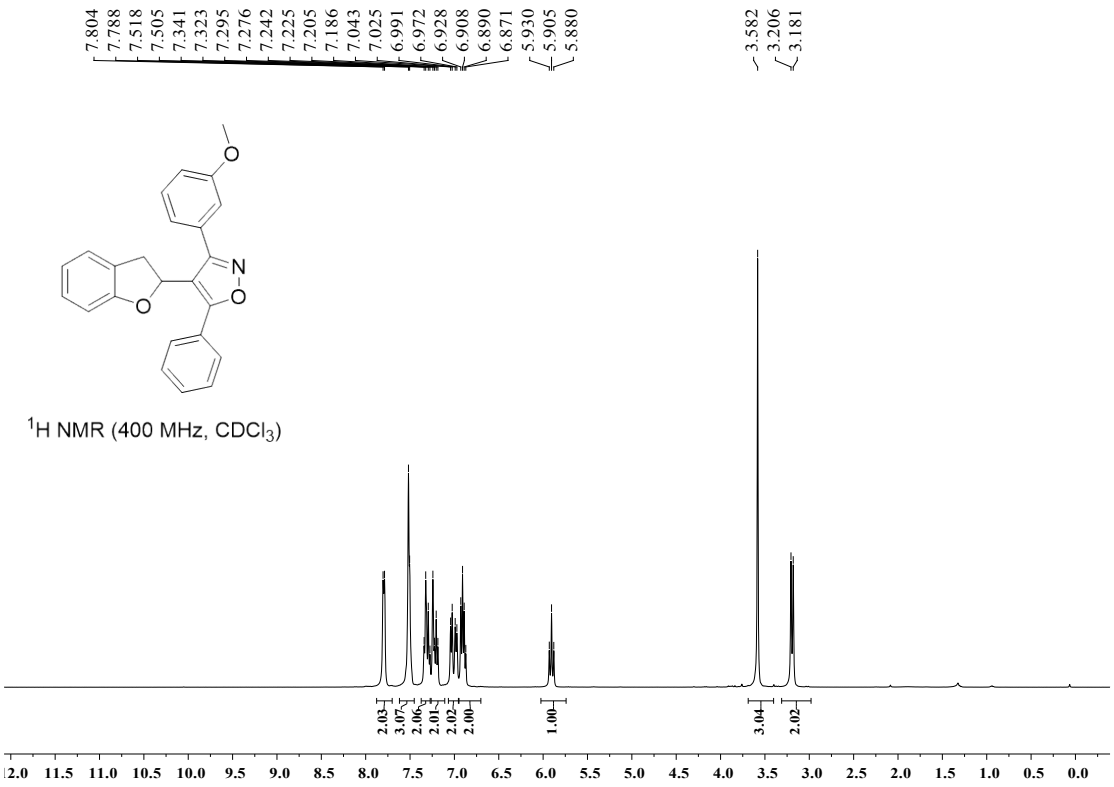
^{13}C NMR (100 MHz, $CDCl_3$)

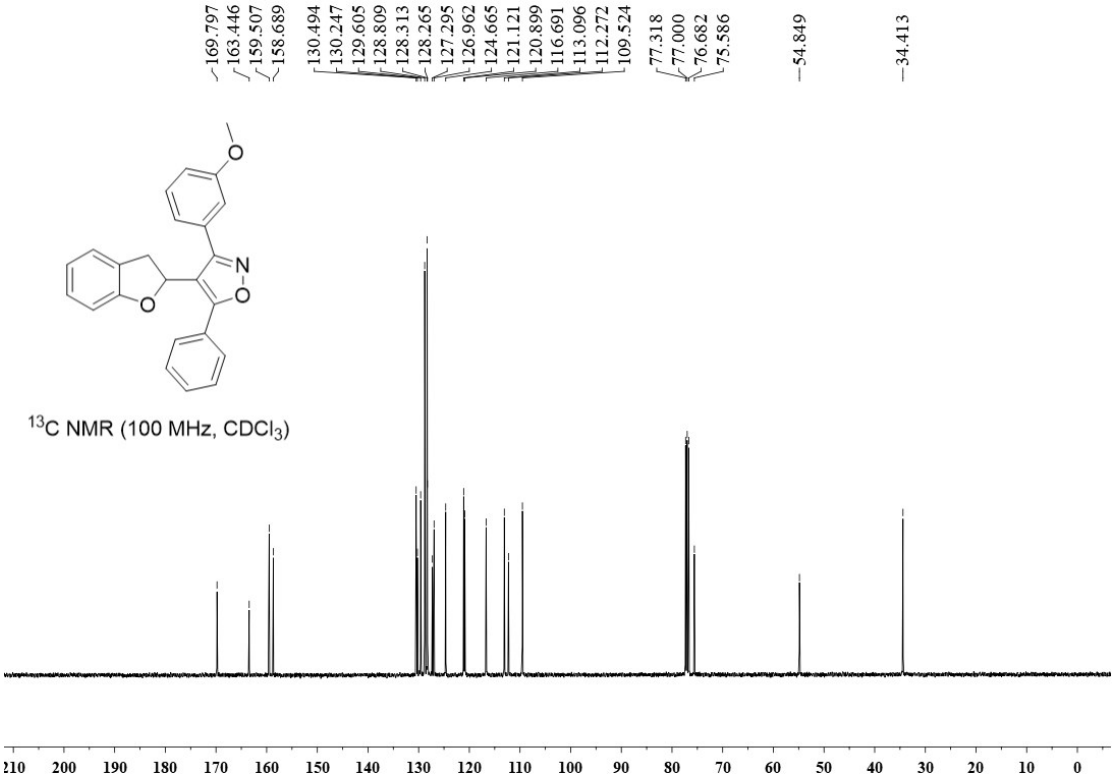




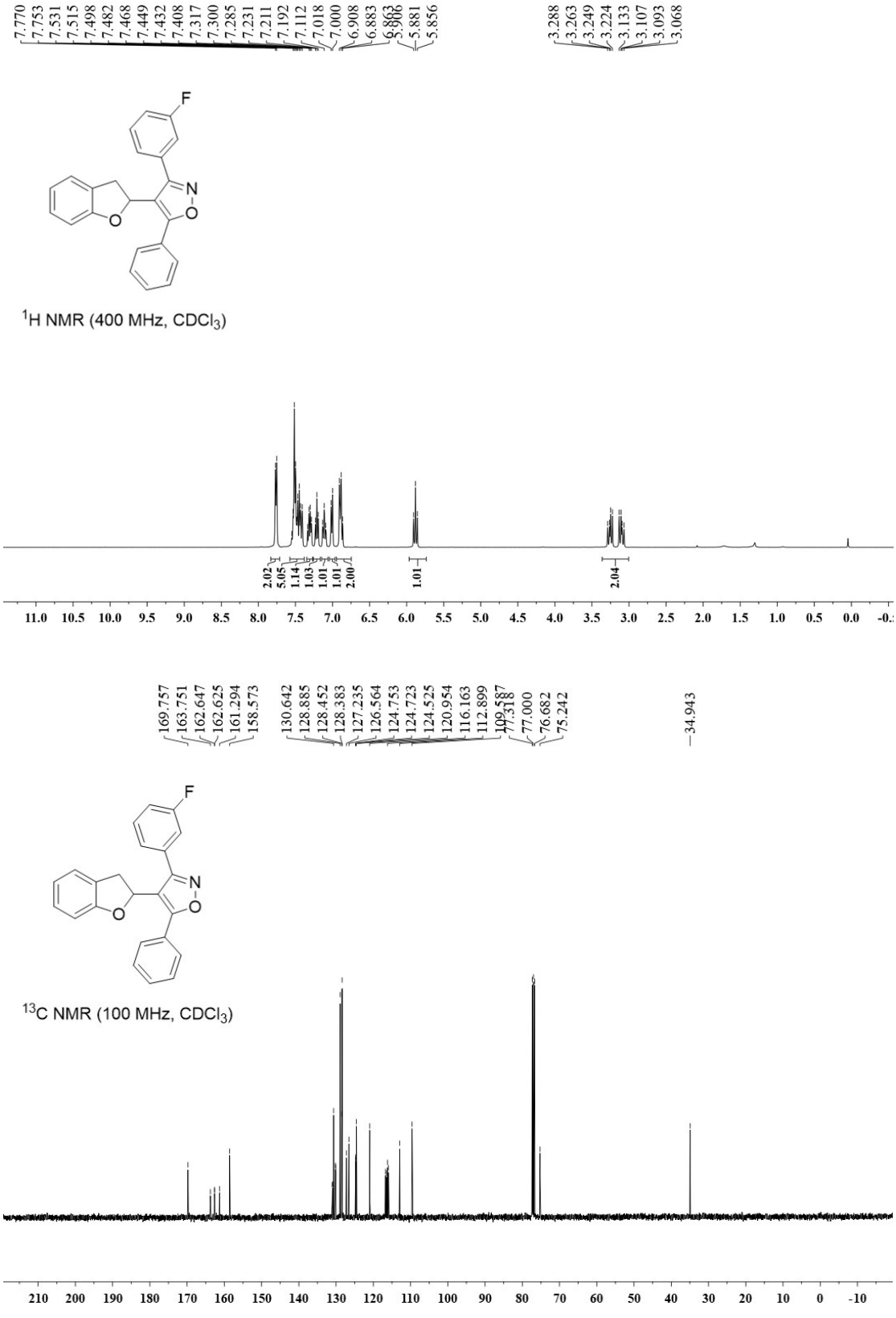
^{19}F NMR (376 MHz, $CDCl_3$)

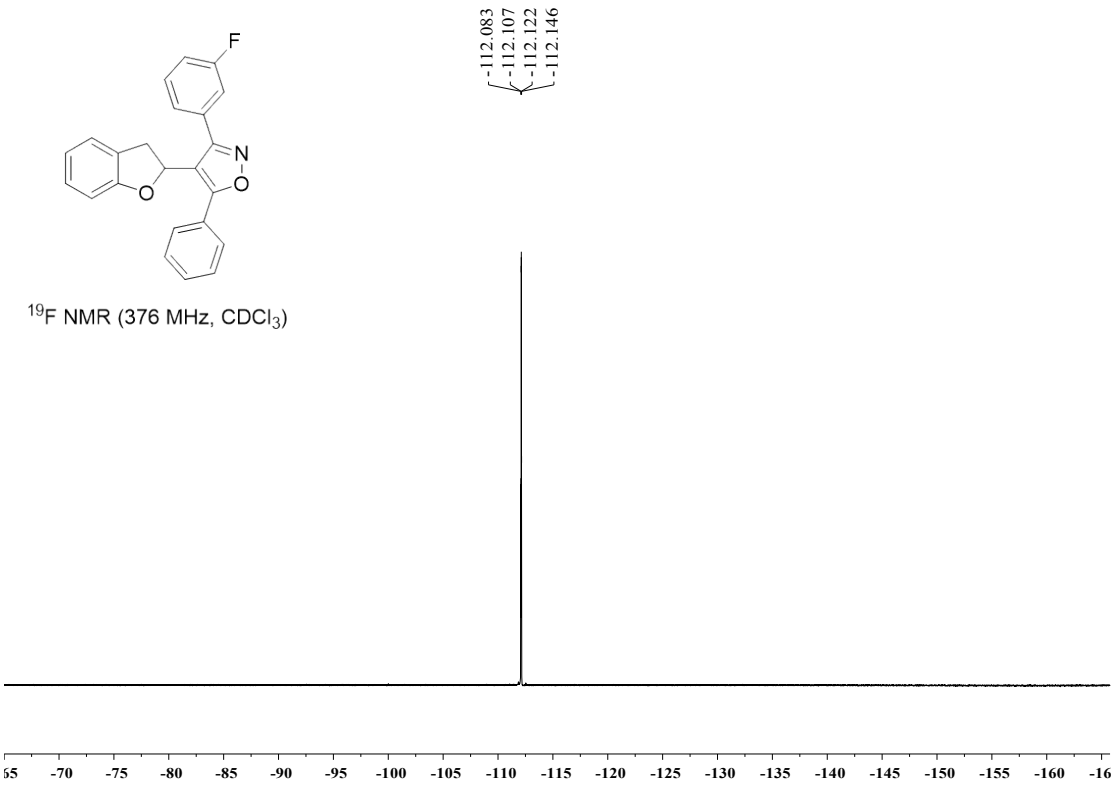
4-(2,3-Dihydrobenzofuran-2-yl)-3-(3-methoxyphenyl)-5-phenylisoxazole (3h)



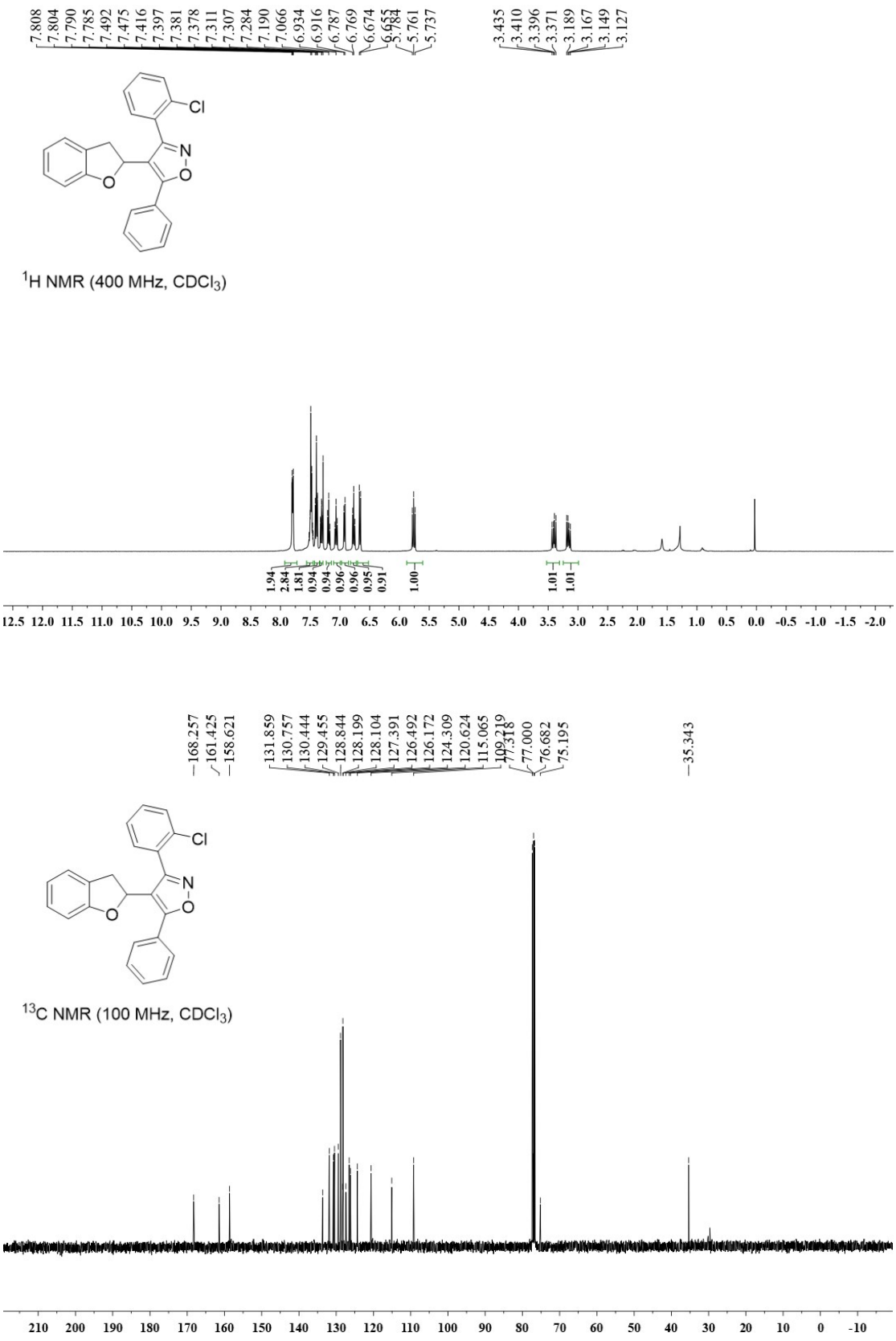


4-(2,3-Dihydrobenzofuran-2-yl)-3-(3-fluorophenyl)-5-phenylisoxazole (3i)

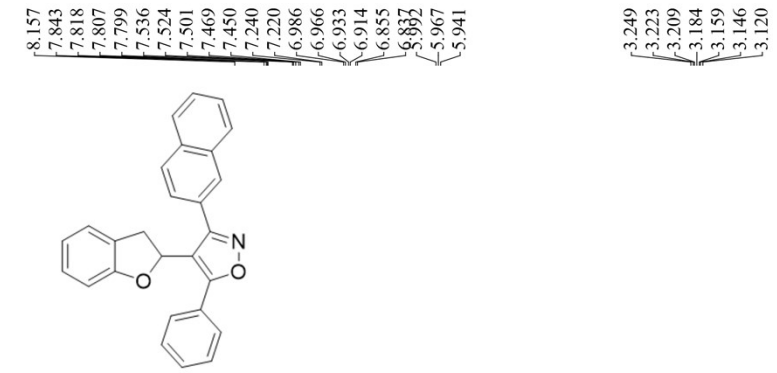



F
N
O
O
-112.083
-112.107
-112.122
-112.146
^{19}F NMR (376 MHz, CDCl$_3$)
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160

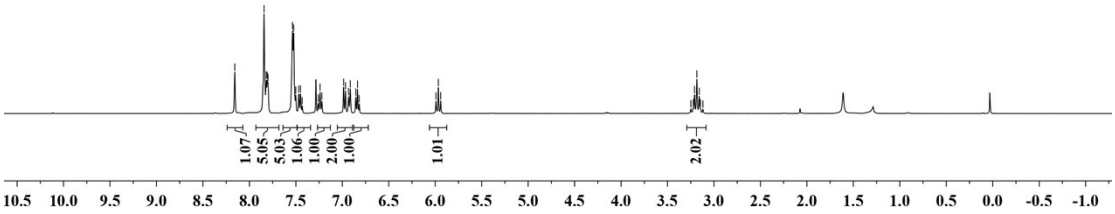
3-(2-Chlorophenyl)-4-(2,3-dihydrobenzofuran-2-yl)-5-phenylisoxazole (3j)

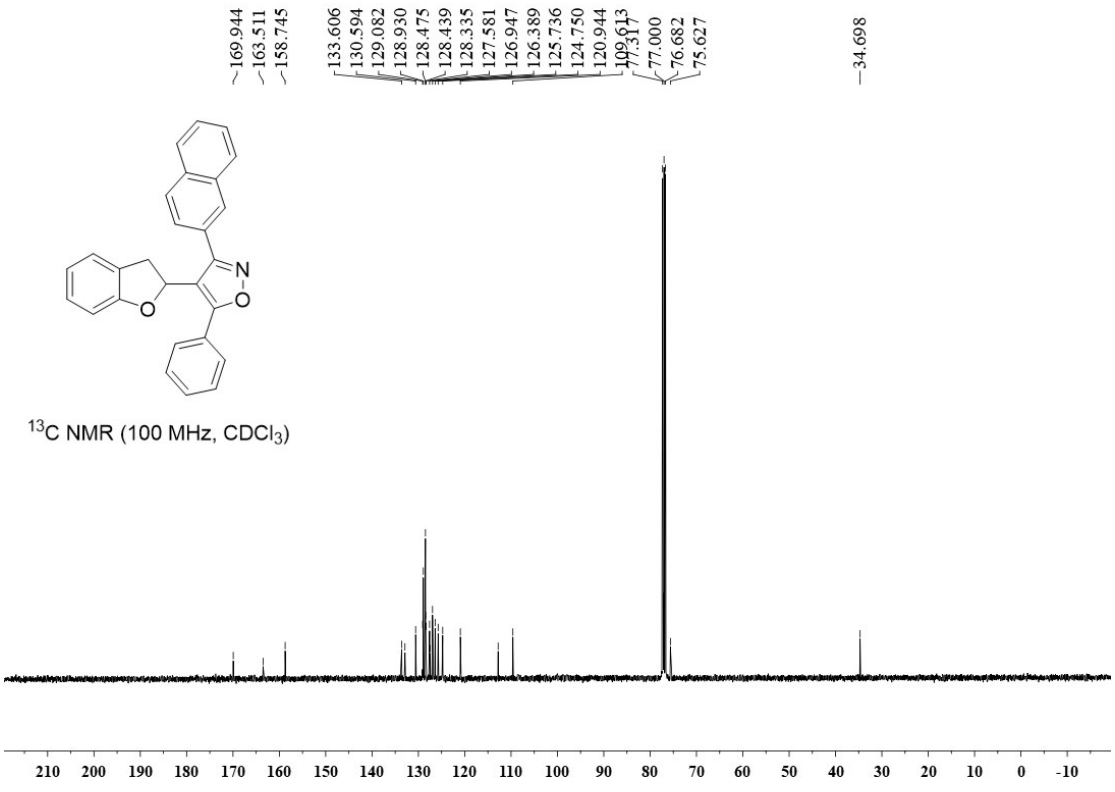


4-(2,3-Dihydrobenzofuran-2-yl)-3-(naphthalen-2-yl)-5-phenylisoxazole (3k)



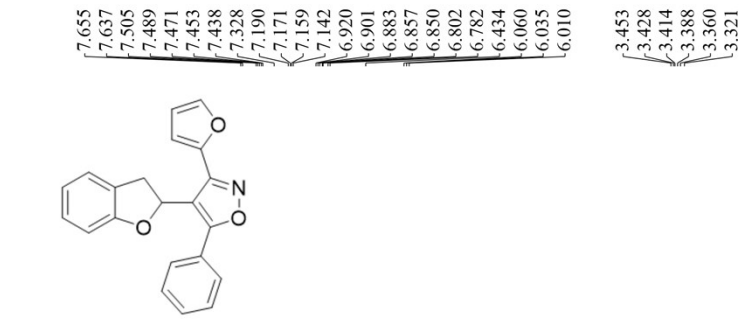
^{1}H NMR (400 MHz, $CDCl_3$)



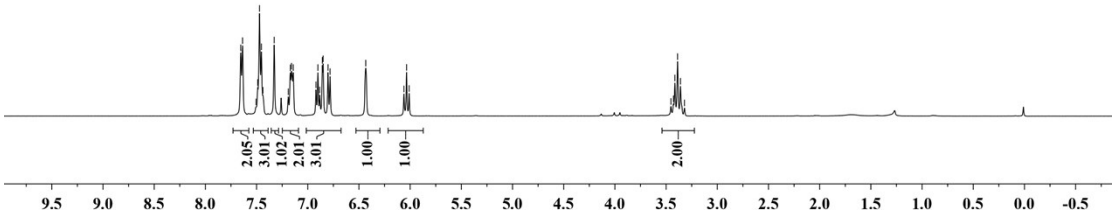


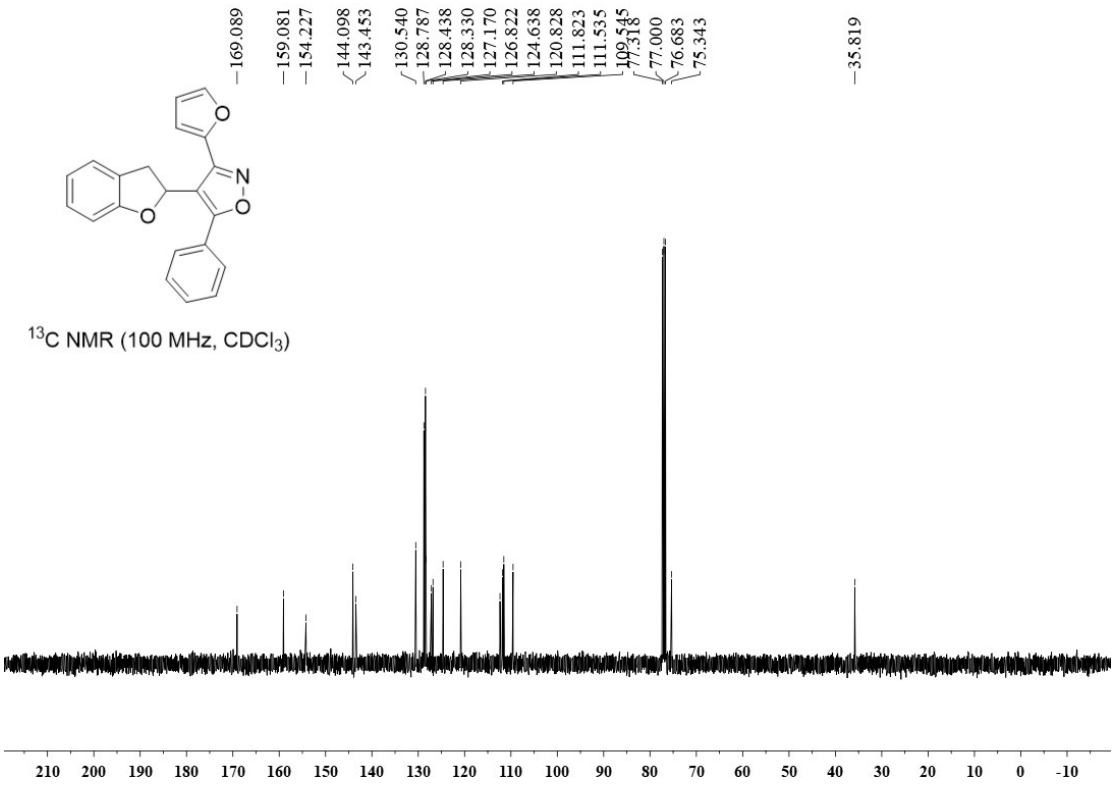
^{13}C NMR (100 MHz, $CDCl_3$)

4-(2,3-Dihydrobenzofuran-2-yl)-3-(furan-2-yl)-5-phenylisoxazole (3l)



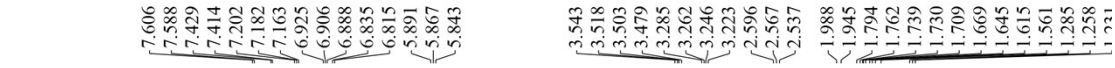
^{1}H NMR (400 MHz, $CDCl_3$)

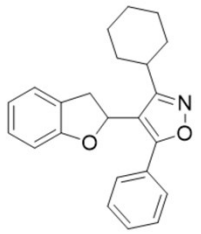




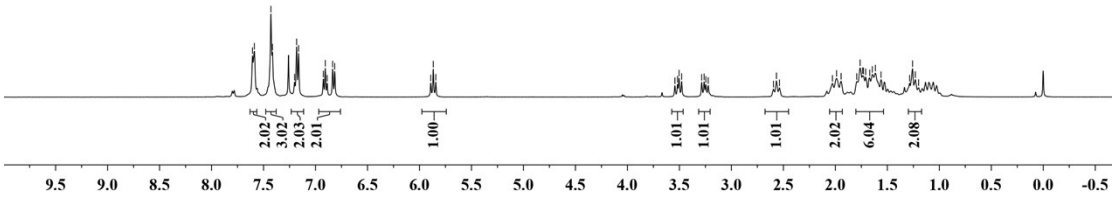
^{13}C NMR (100 MHz, $CDCl_3$)

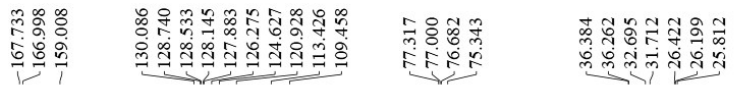
3-Cyclohexyl-4-(2,3-dihydrobenzofuran-2-yl)-5-phenylisoxazole (3m)

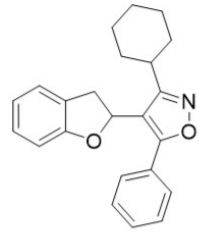




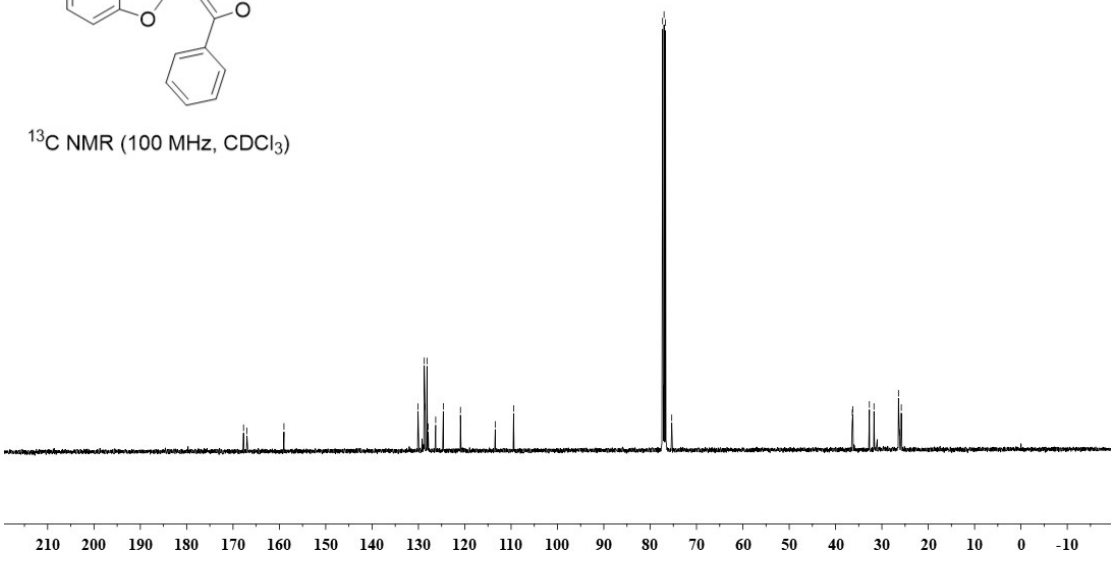
^{1}H NMR (400 MHz, $CDCl_3$)



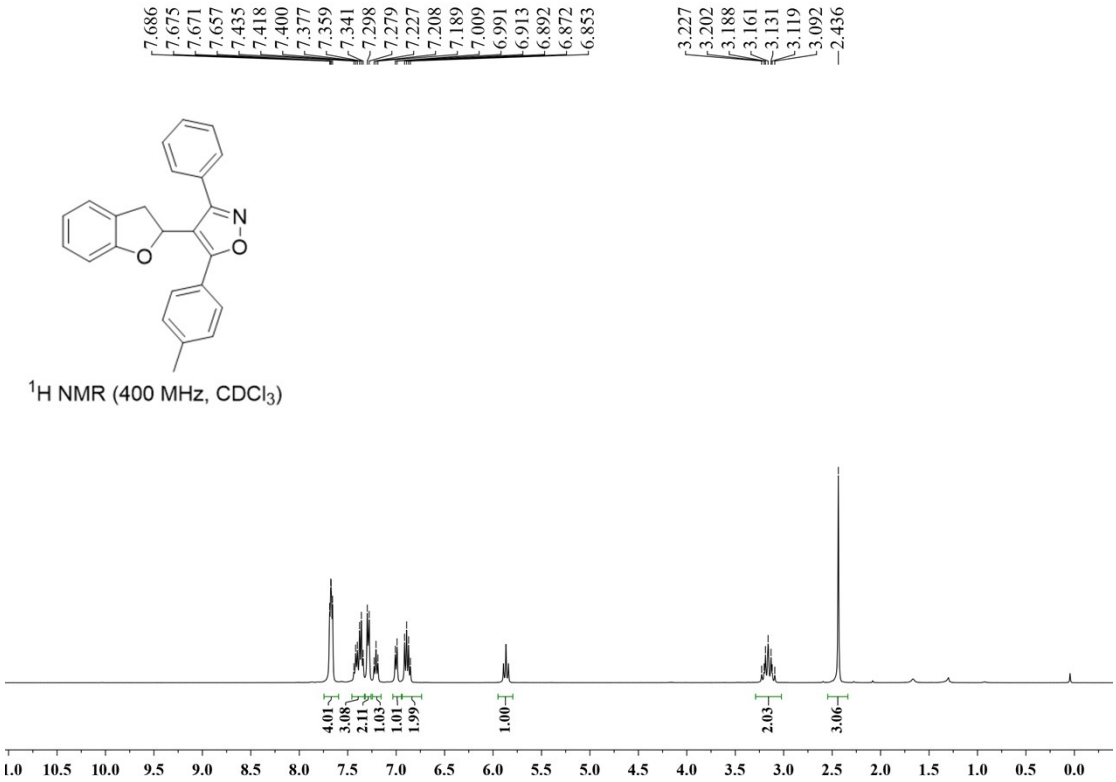


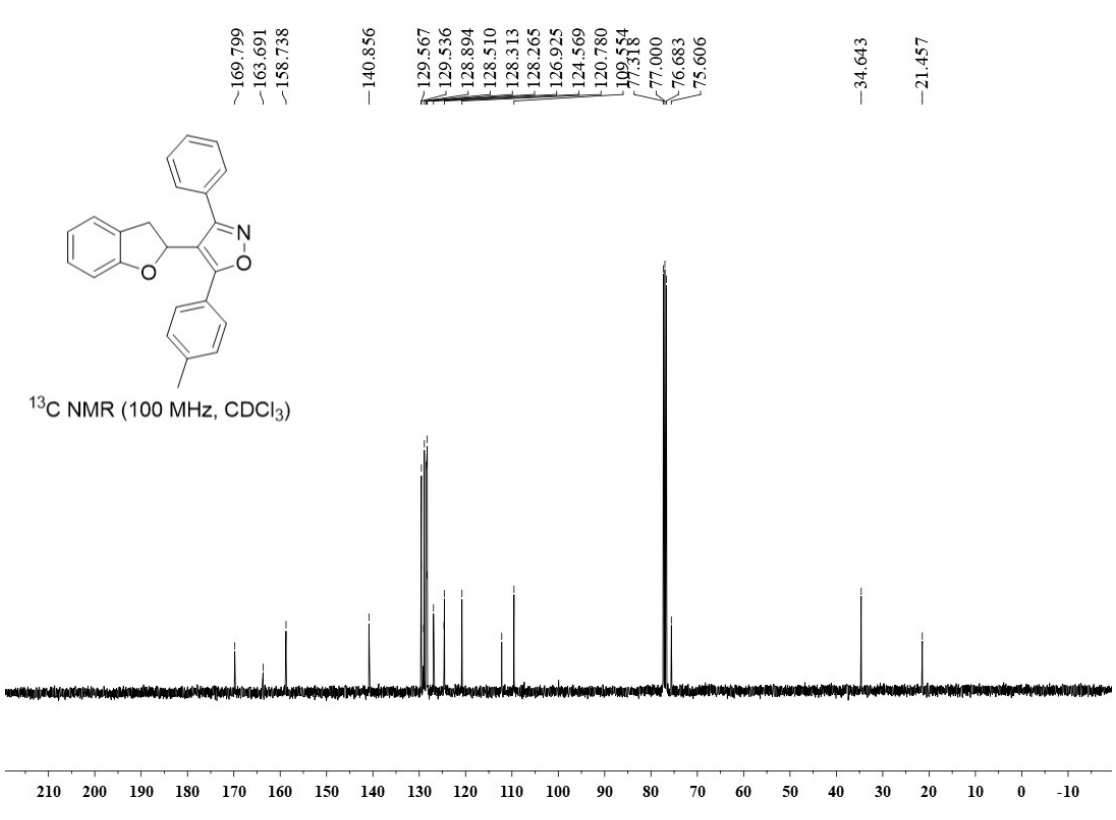


^{13}C NMR (100 MHz, $CDCl_3$)

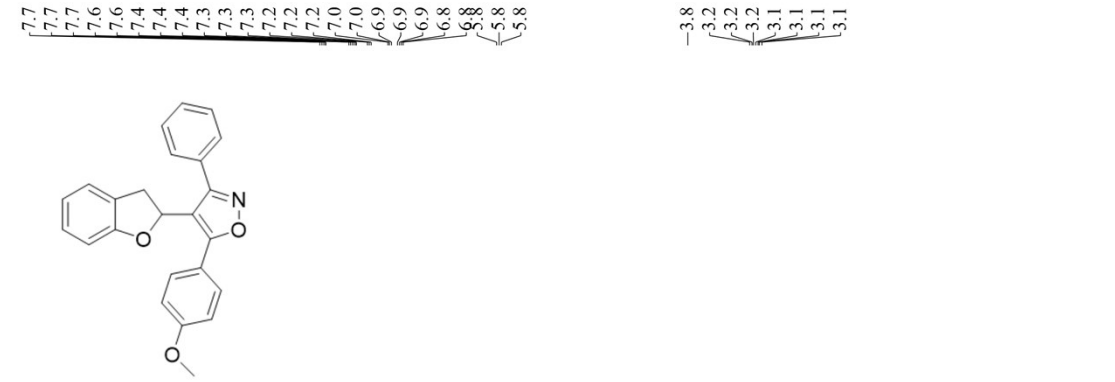


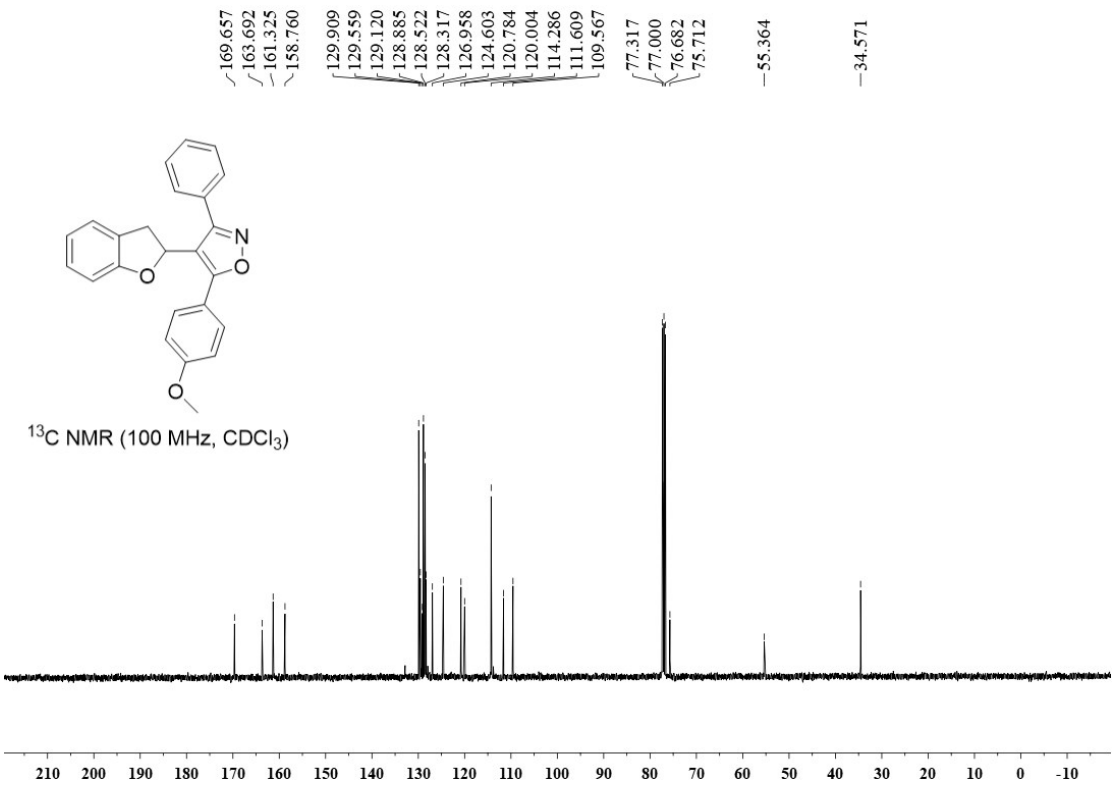
4-(2,3-Dihydrobenzofuran-2-yl)-3-phenyl-5-(p-tolyl)isoxazole (3n)



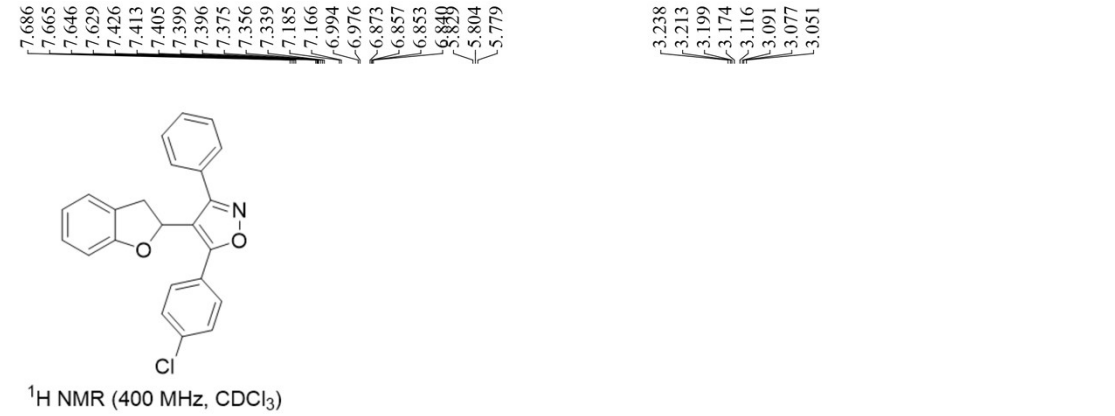


4-(2,3-Dihydrobenzofuran-2-yl)-5-(4-methoxyphenyl)-3-phenylisoxazole (3o)

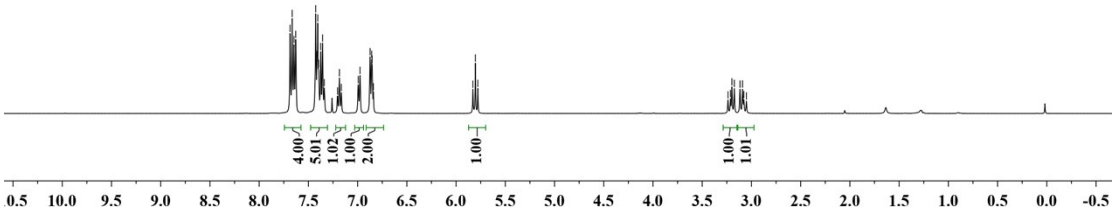


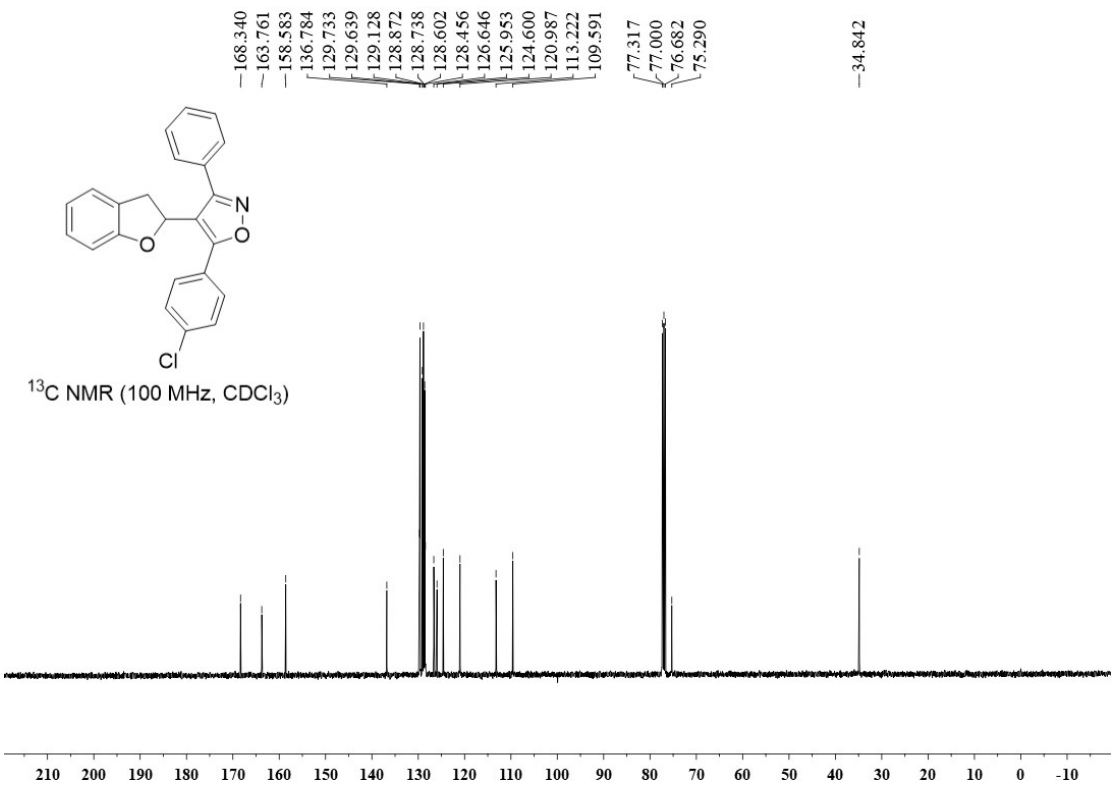


5-(4-Chlorophenyl)-4-(2,3-dihydrobenzofuran-2-yl)-3-phenylisoxazole (3p)



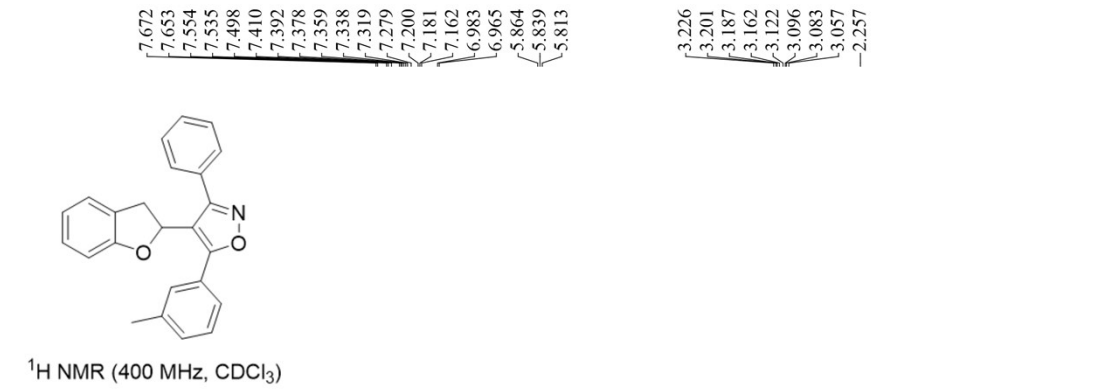
^{1}H NMR (400 MHz, $CDCl_3$)



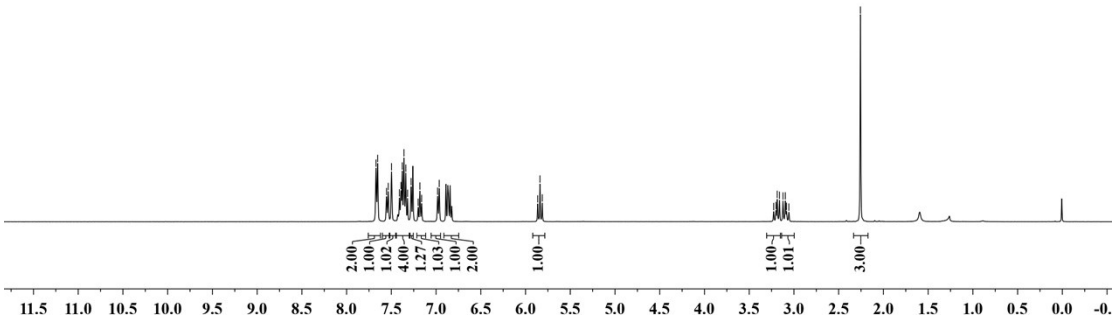


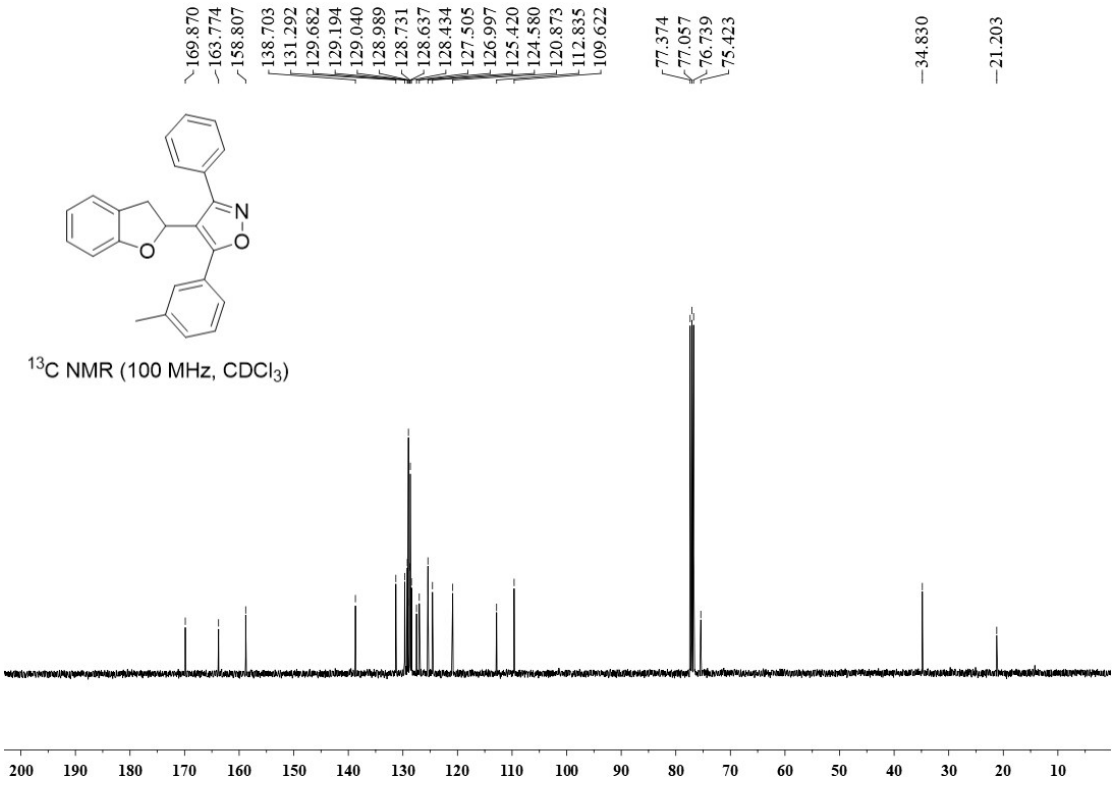
^{13}C NMR (100 MHz, $CDCl_3$)

4-(2,3-Dihydrobenzofuran-2-yl)-3-phenyl-5-(m-tolyl)isoxazole (3q)



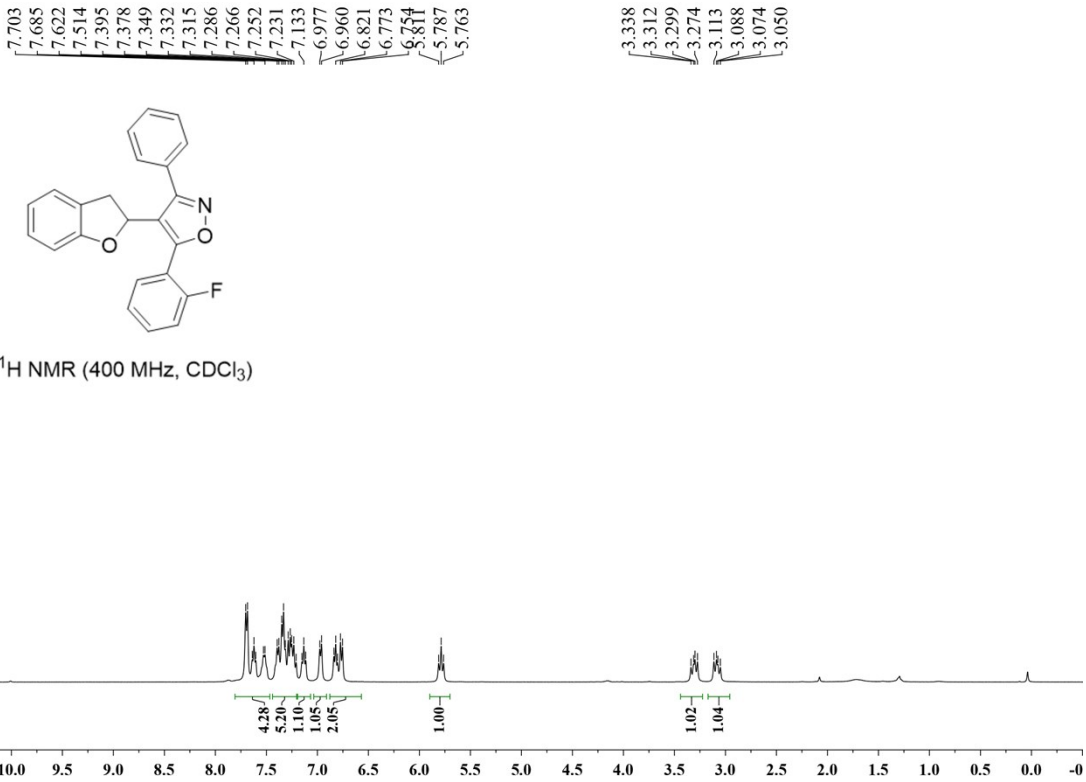
^{1}H NMR (400 MHz, $CDCl_3$)

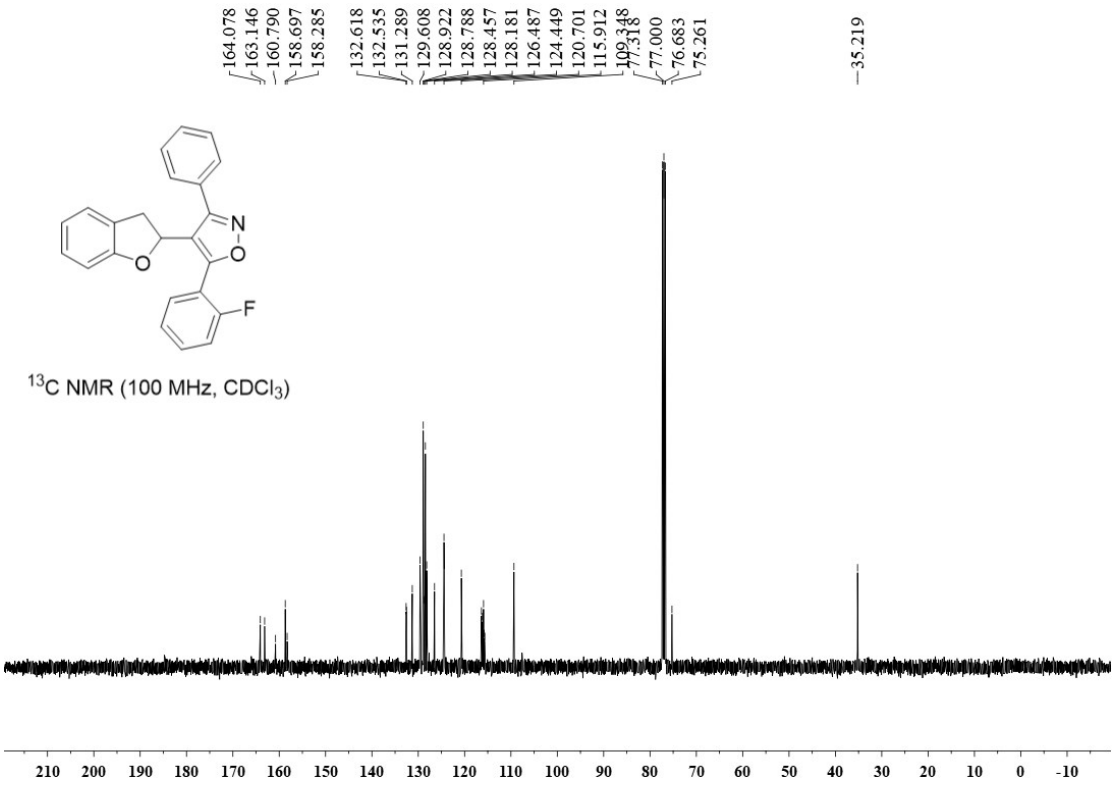


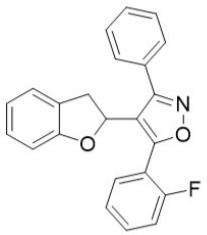


^{13}C NMR (100 MHz, $CDCl_3$)

4-(2,3-Dihydrobenzofuran-2-yl)-5-(2-fluorophenyl)-3-phenylisoxazole (3r)

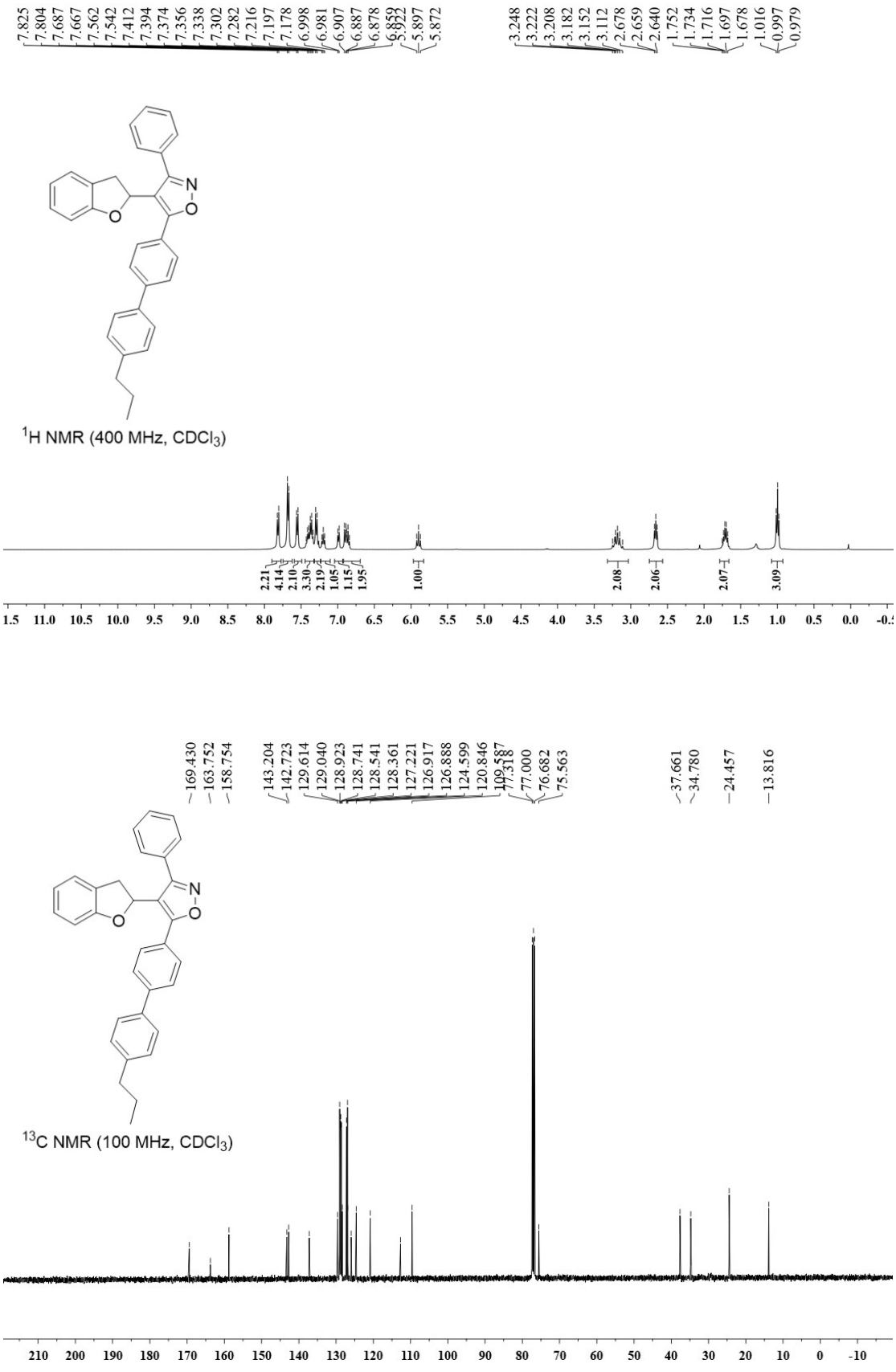




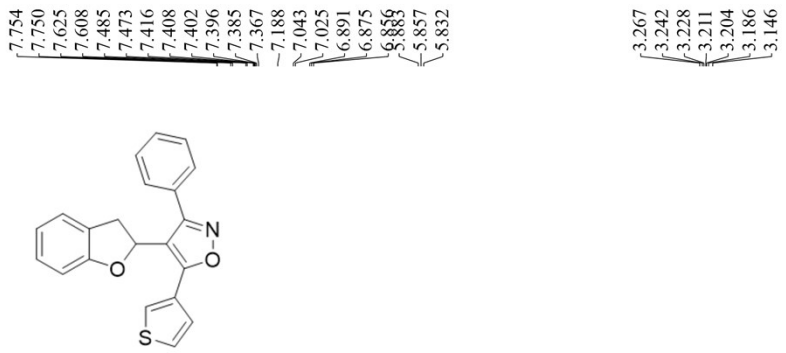


^{19}F NMR (376 MHz, $CDCl_3$)

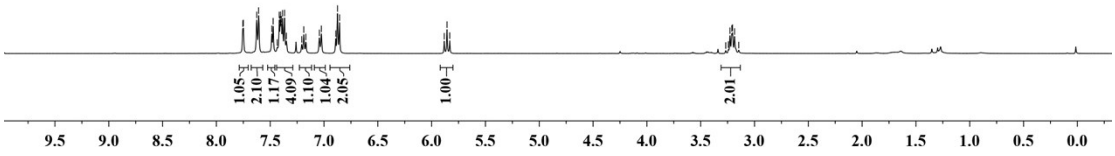
4-(2,3-Dihydrobenzofuran-2-yl)-3-phenyl-5-(4'-propyl-[1,1'-biphenyl]-4-yl)isoxazole (3s)

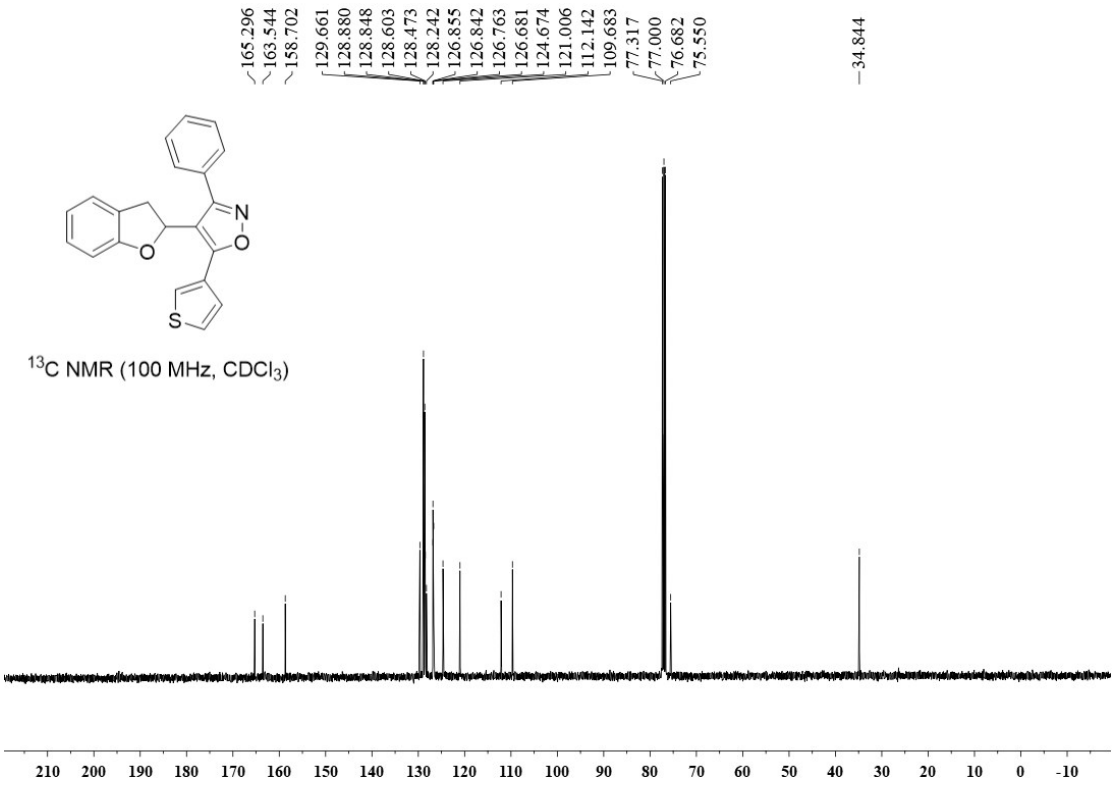


4-(2,3-Dihydrobenzofuran-2-yl)-3-phenyl-5-(thiophen-3-yl)isoxazole (3t)



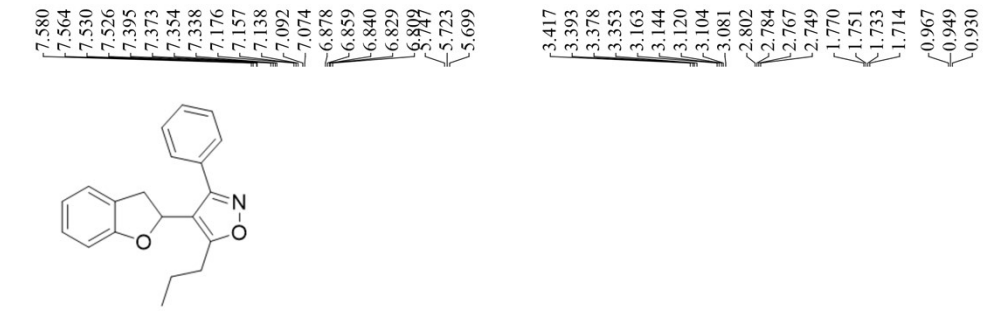
^{1}H NMR (400 MHz, $CDCl_3$)



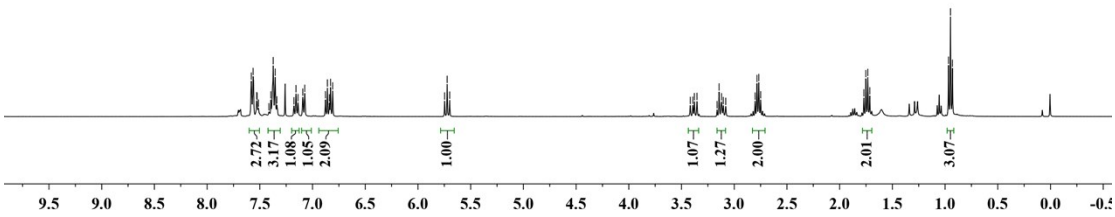


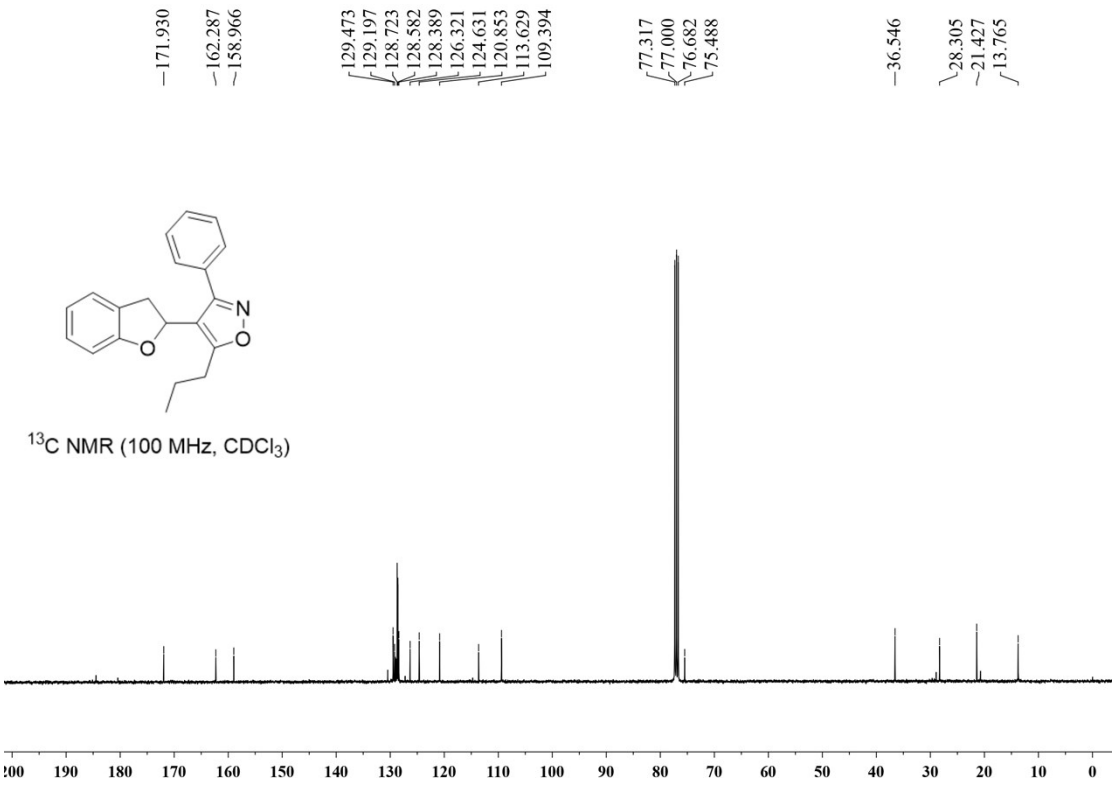
^{13}C NMR (100 MHz, $CDCl_3$)

4-(2,3-Dihydrobenzofuran-2-yl)-3-phenyl-5-propylisoxazole (3u)



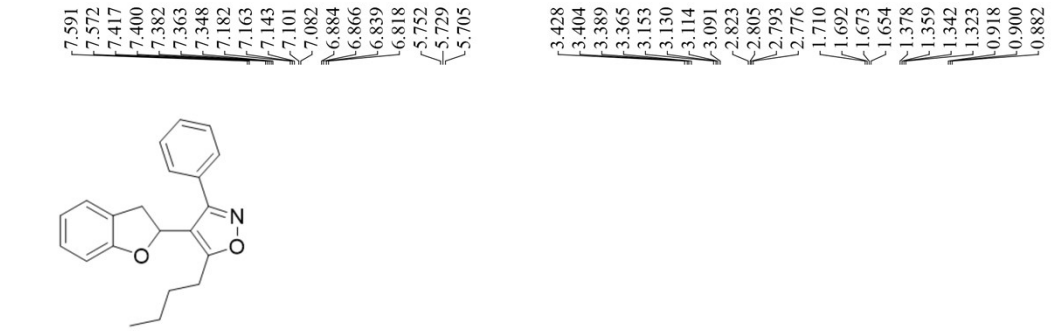
^{1}H NMR (400 MHz, $CDCl_3$)



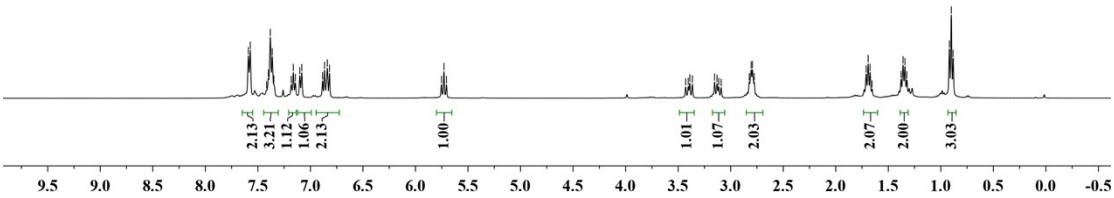


^{13}C NMR (100 MHz, $CDCl_3$)

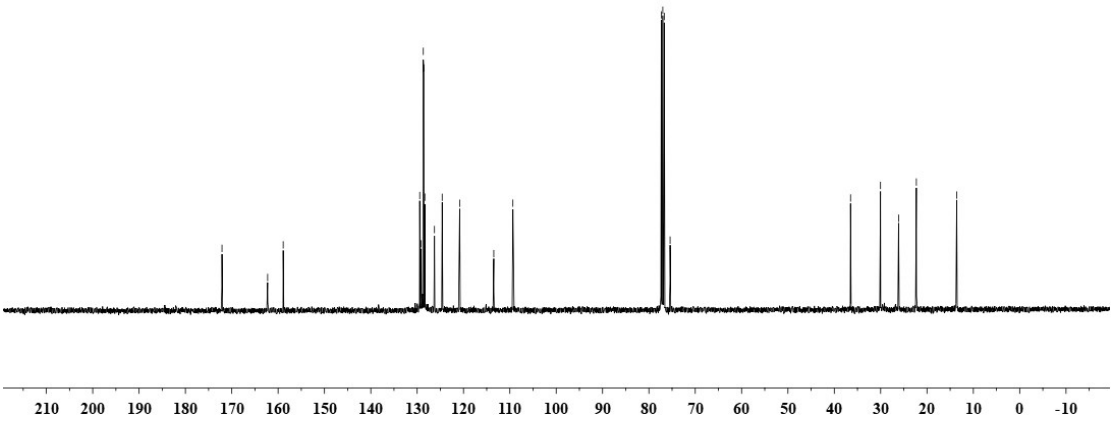
5-Butyl-4-(2,3-dihydrobenzofuran-2-yl)-3-phenylisoxazole (3v)



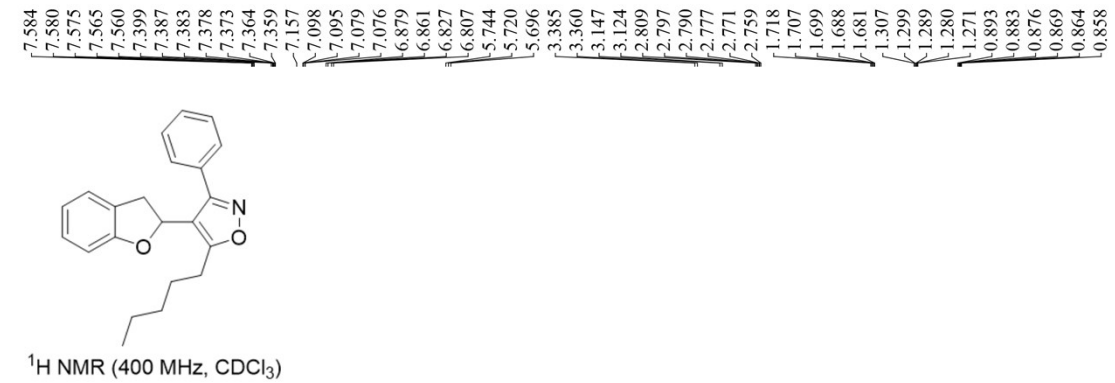
^{1}H NMR (400 MHz, $CDCl_3$)



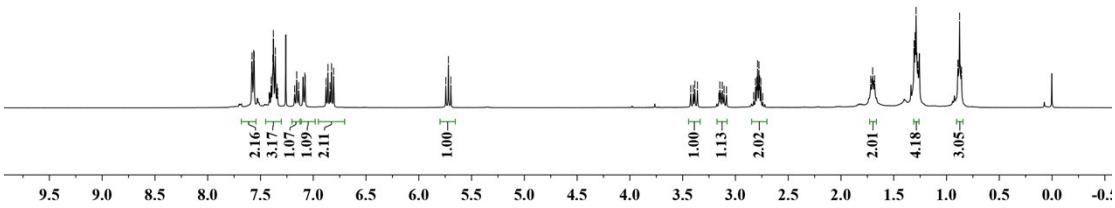
^{13}C NMR (100 MHz, $CDCl_3$)

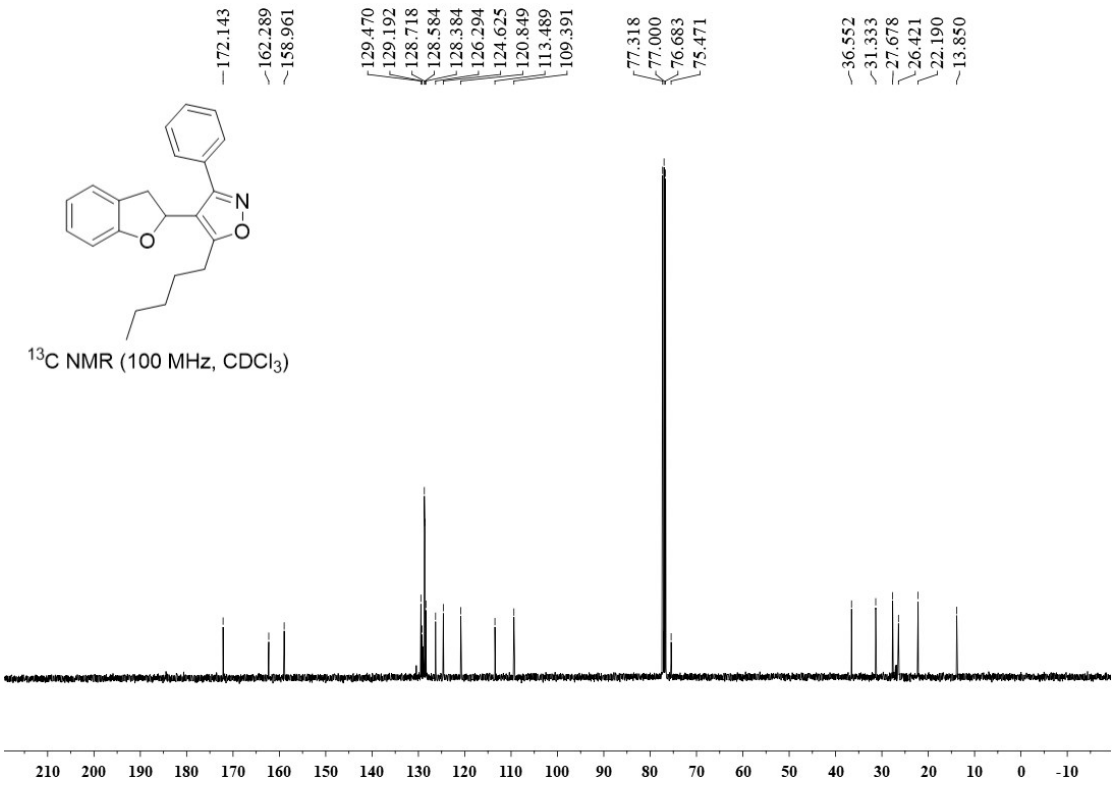


4-(2,3-Dihydrobenzofuran-2-yl)-5-pentyl-3-phenylisoxazole (3w)



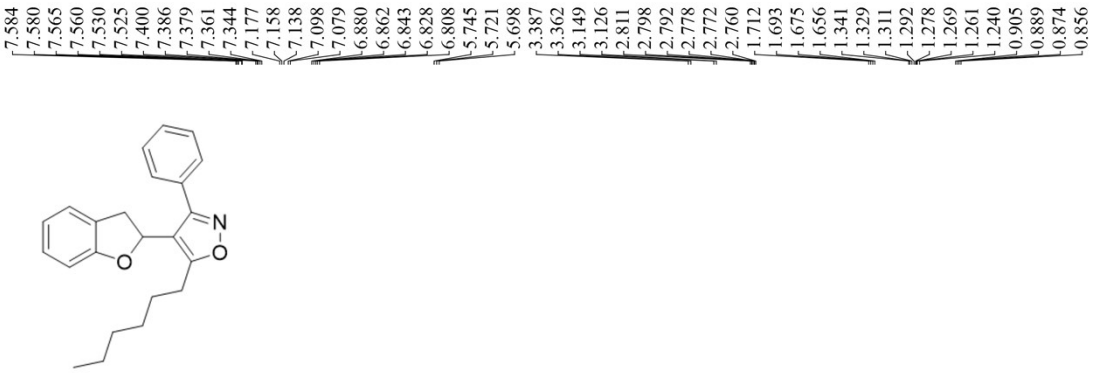
^{1}H NMR (400 MHz, $CDCl_3$)



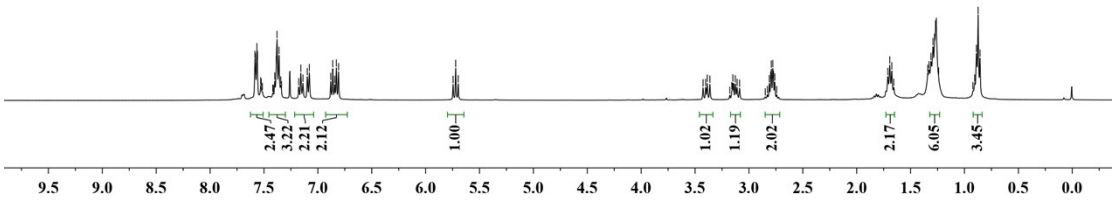


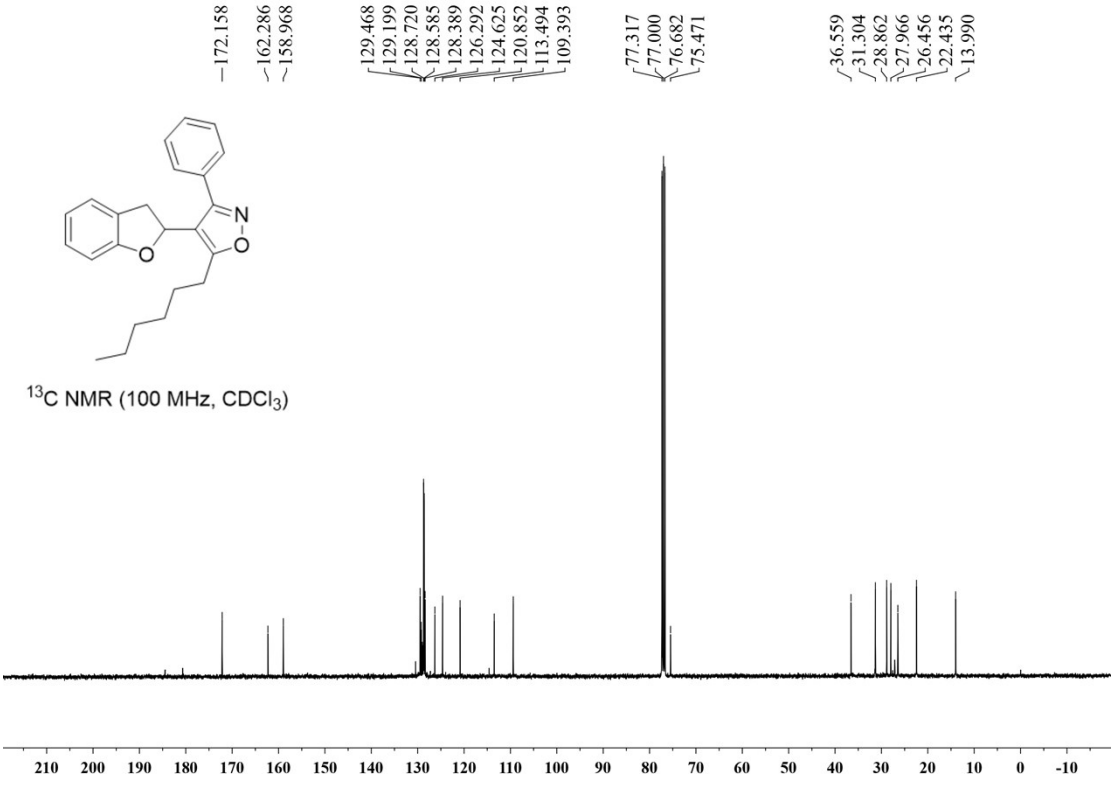
^{13}C NMR (100 MHz, $CDCl_3$)

4-(2,3-Dihydrobenzofuran-2-yl)-5-hexyl-3-phenylisoxazole (3x)



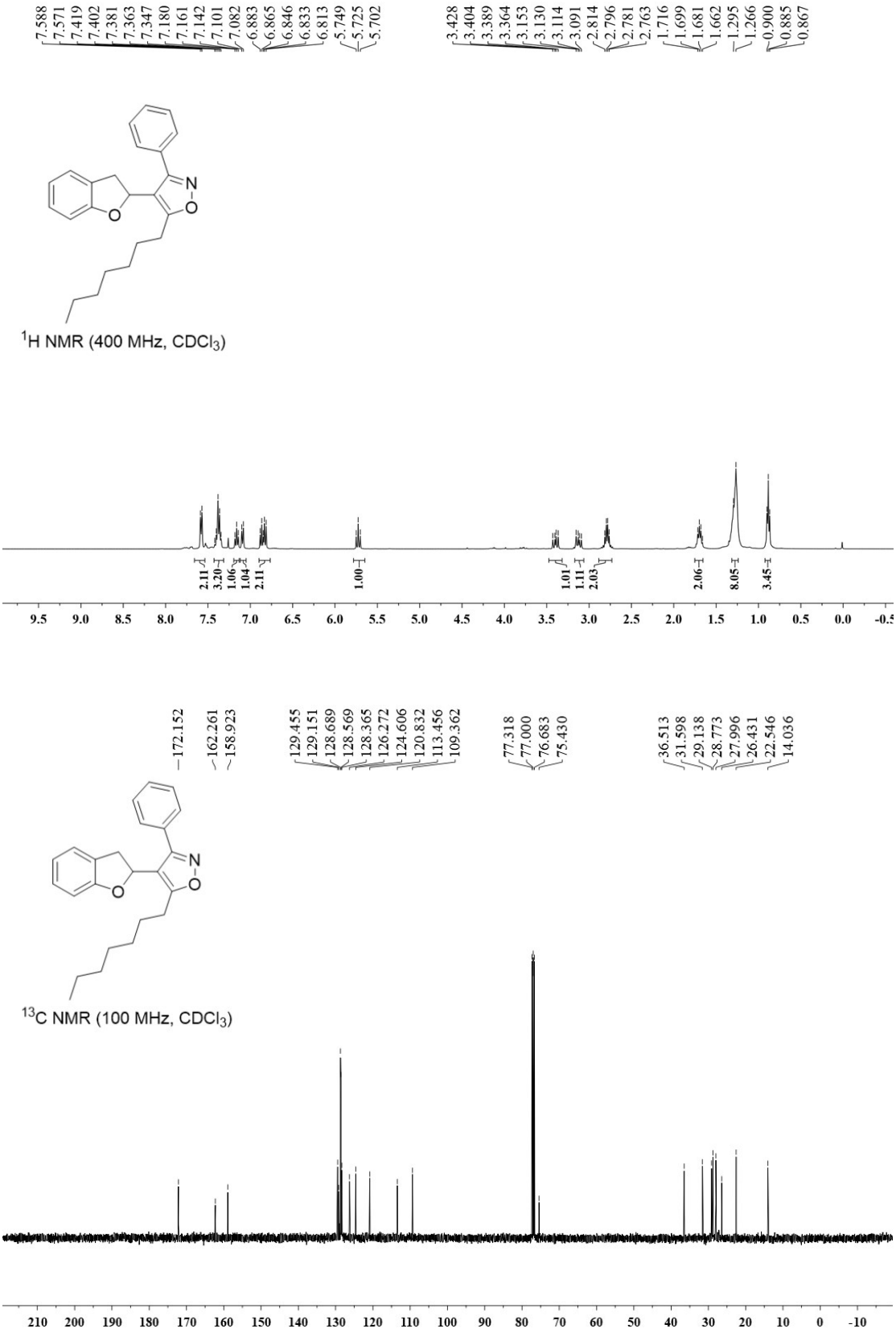
^{1}H NMR (400 MHz, $CDCl_3$)



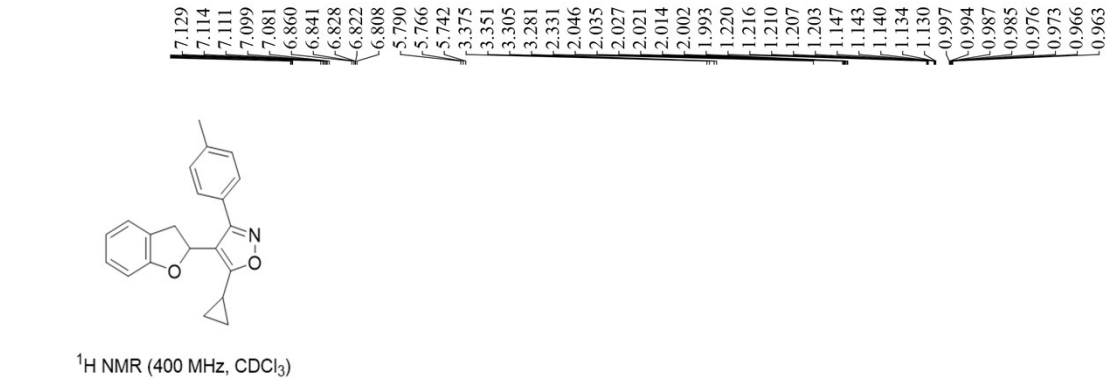


^{13}C NMR (100 MHz, $CDCl_3$)

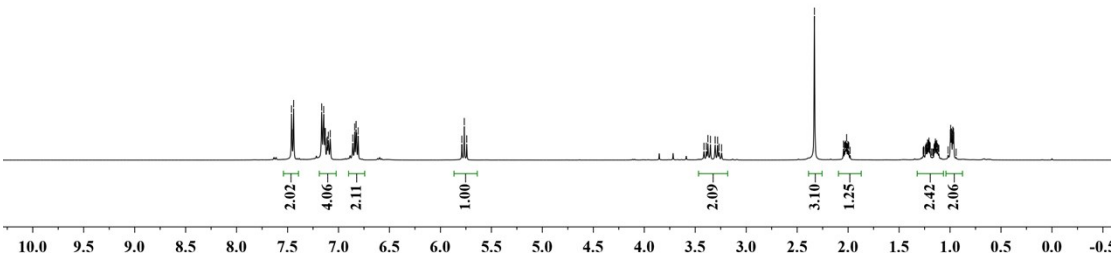
4-(2,3-Dihydrobenzofuran-2-yl)-5-heptyl-3-phenylisoxazole (3y)



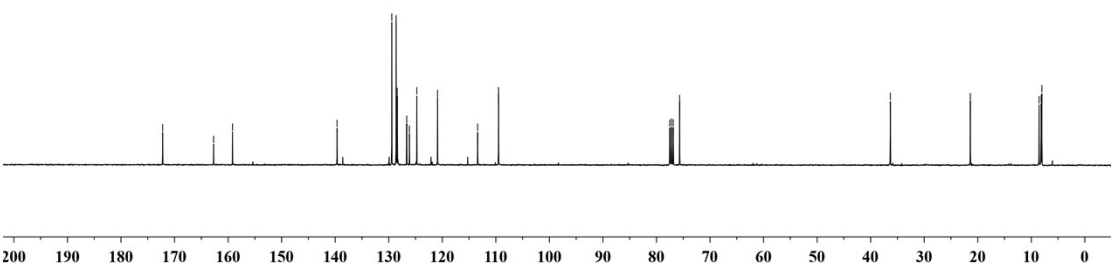
5-Cyclopropyl-4-(5-methyl-2,3-dihydrobenzofuran-2-yl)-3-phenylisoxazole (3z)



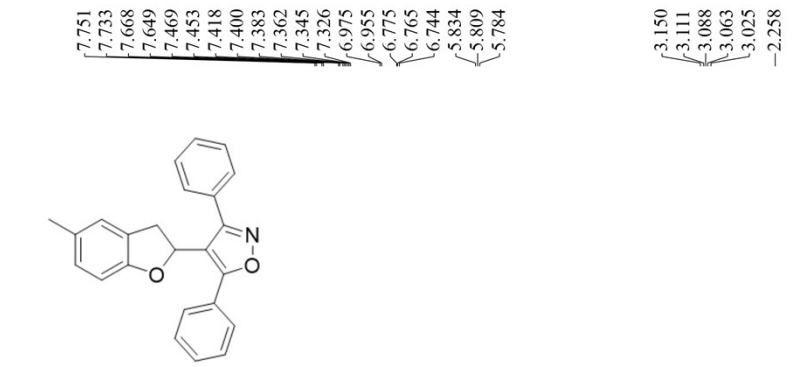
^{1}H NMR (400 MHz, $CDCl_3$)



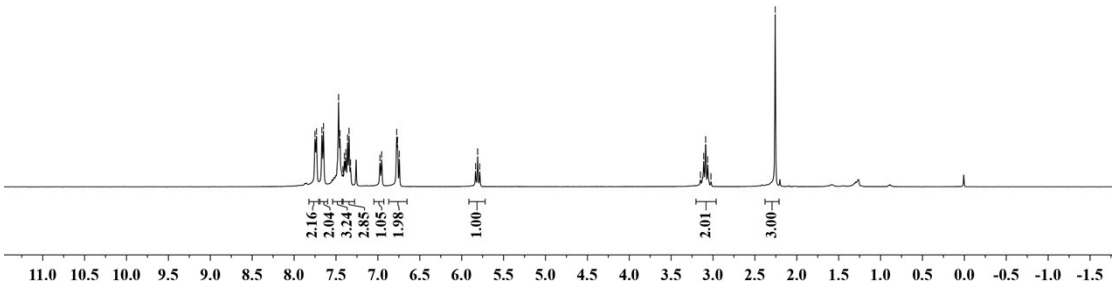
^{13}C NMR (100 MHz, $CDCl_3$)

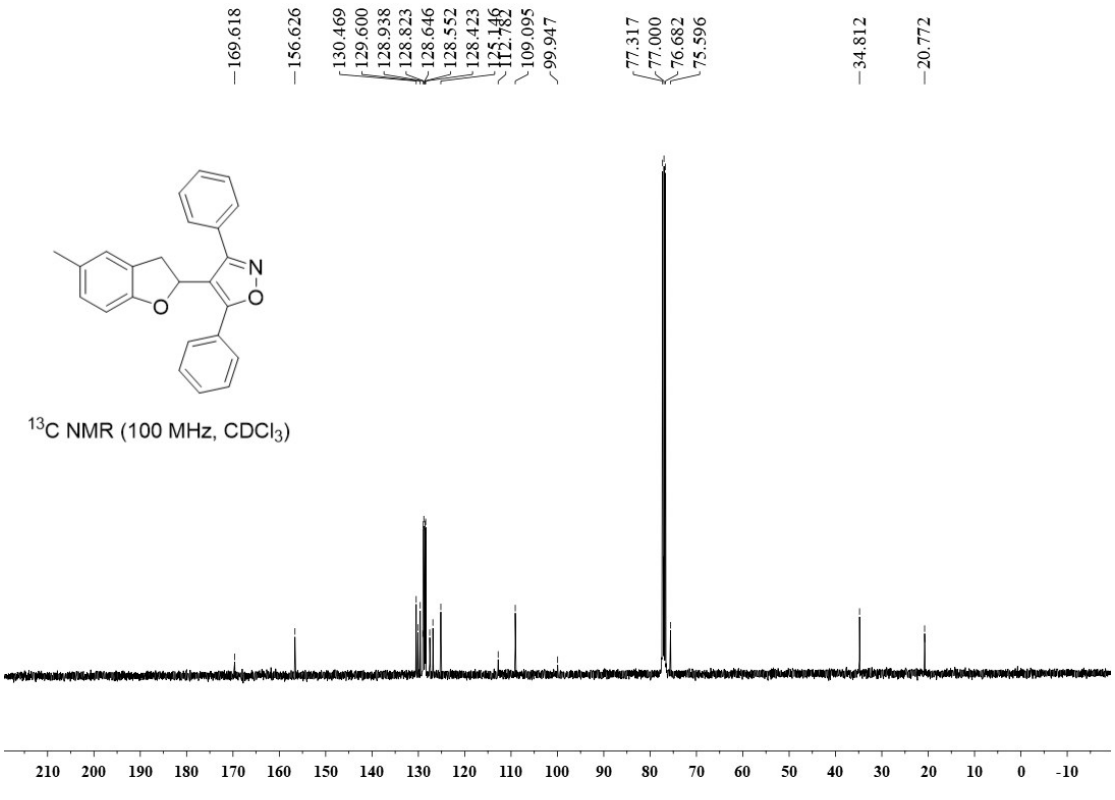


4-(5-Methyl-2,3-dihydrobenzofuran-2-yl)-3,5-diphenylisoxazole (3aa)



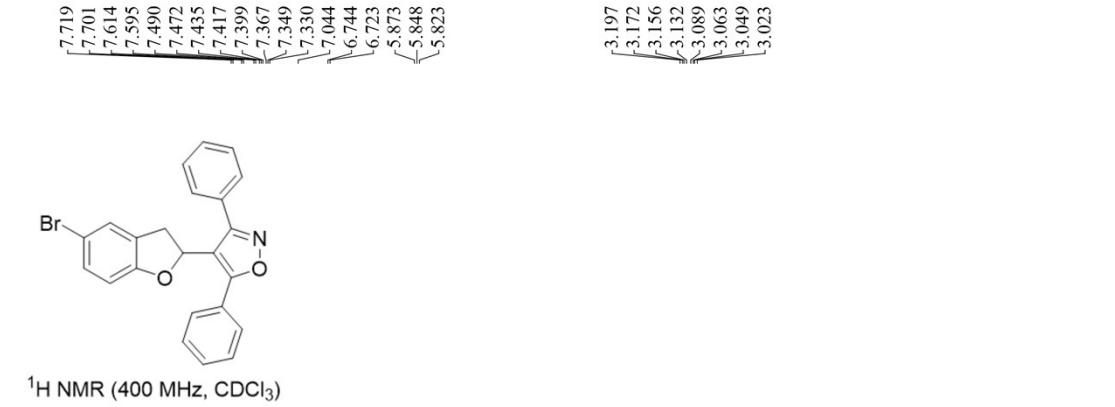
^{1}H NMR (400 MHz, $CDCl_3$)

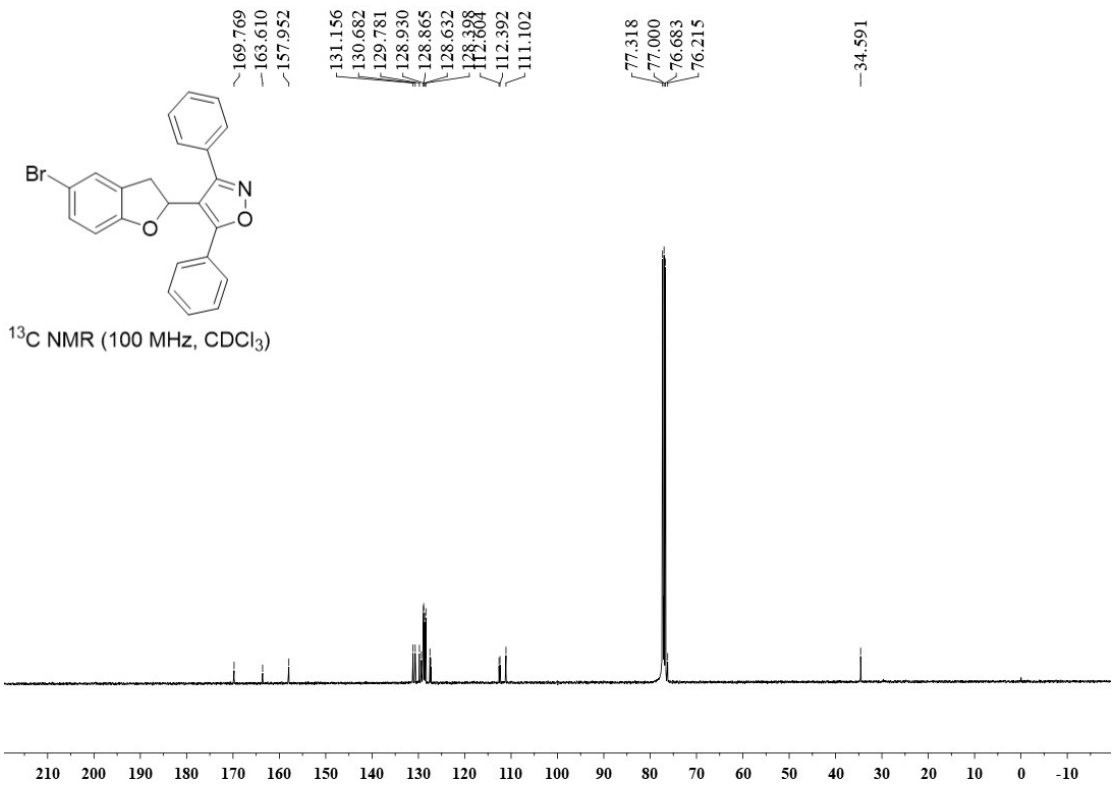




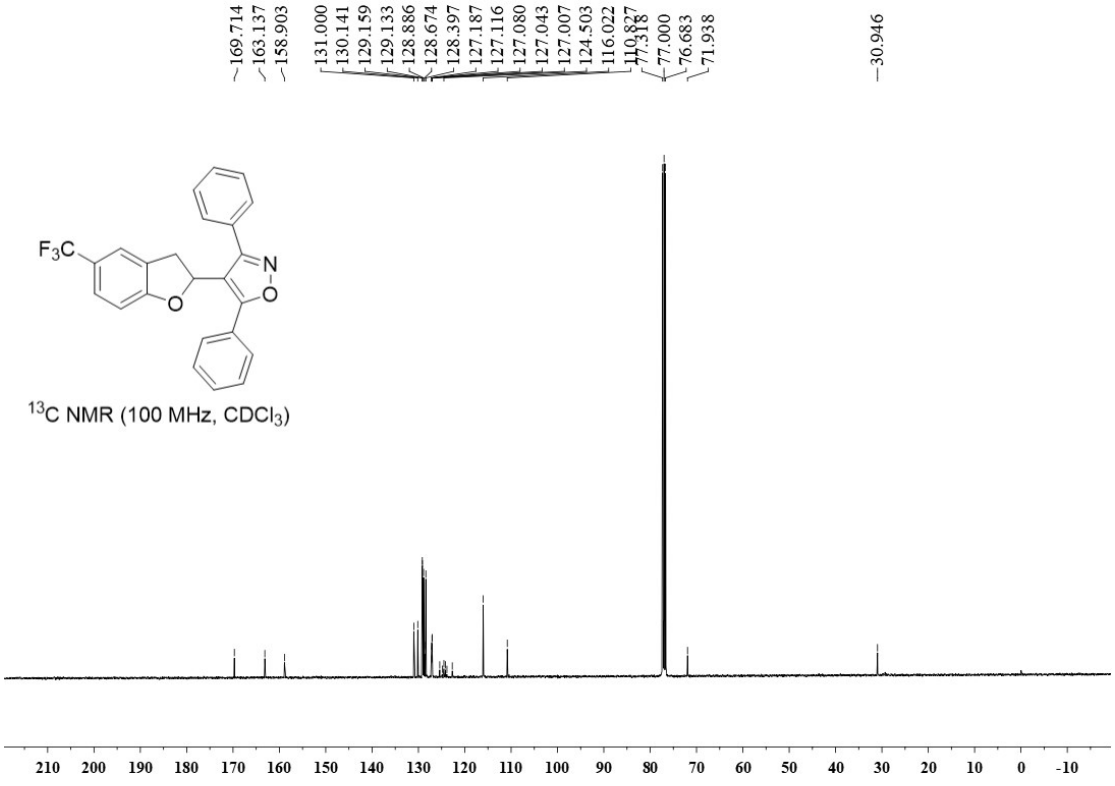
^{13}C NMR (100 MHz, $CDCl_3$)

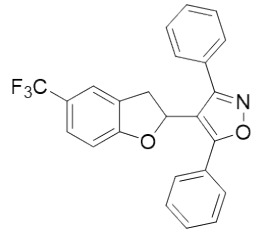
4-(5-Bromo-2,3-dihydrobenzofuran-2-yl)-3,5-diphenylisoxazole (3ab)





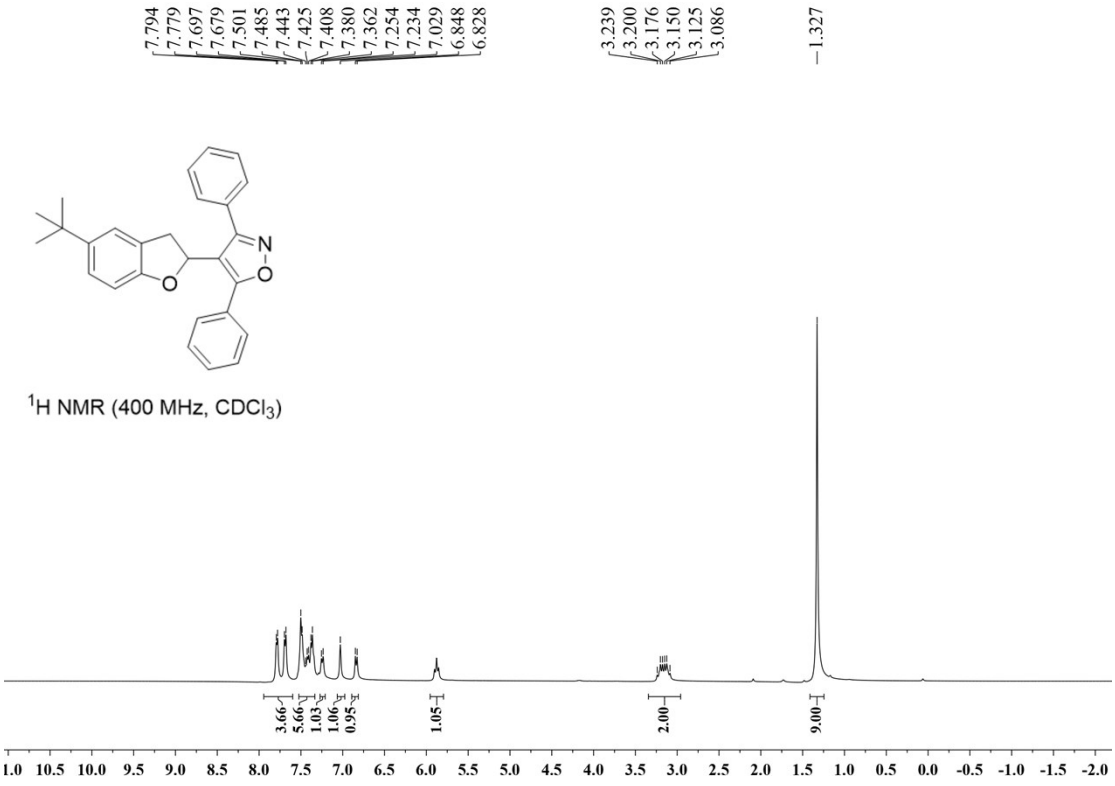
3,5-Diphenyl-4-(5-(trifluoromethyl)-2,3-dihydrobenzofuran-2-yl)isoxazole (3ac)

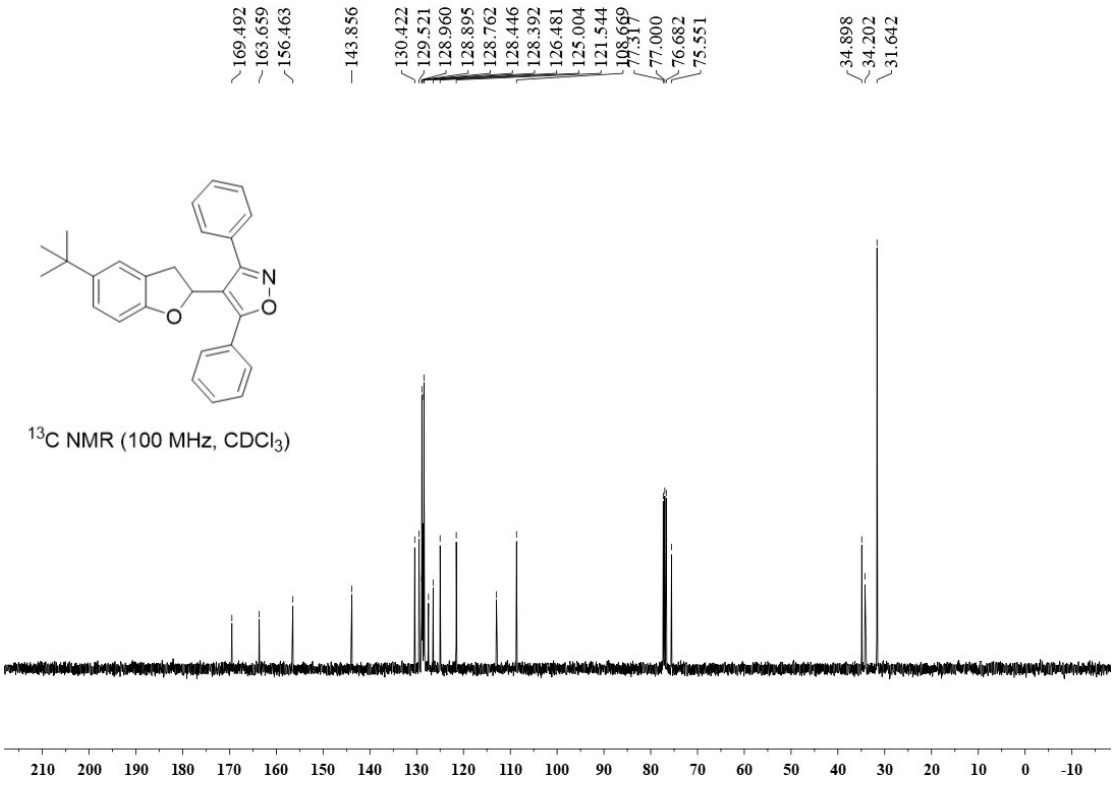




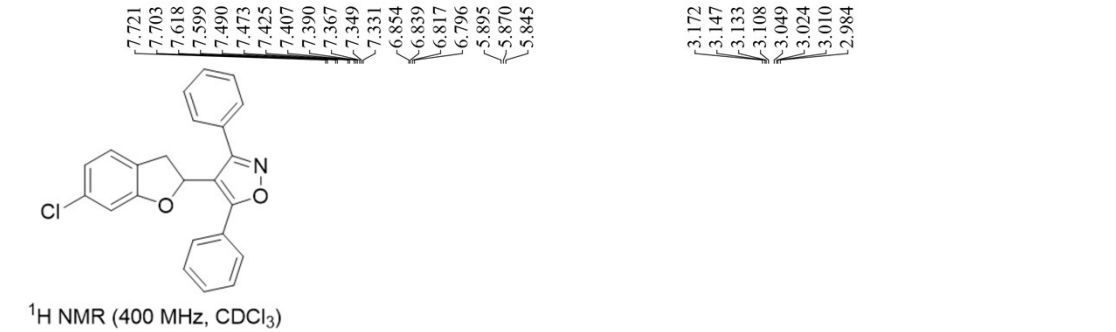
^{19}F NMR (376 MHz, $CDCl_3$)

4-(5-(*tert*-Butyl)-2,3-dihydrobenzofuran-2-yl)-3,5-diphenylisoxazole (3ad)

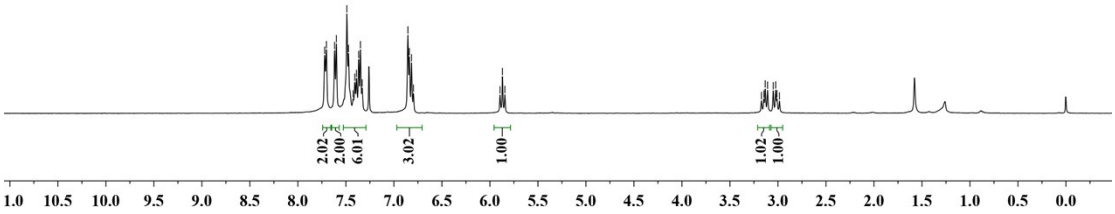


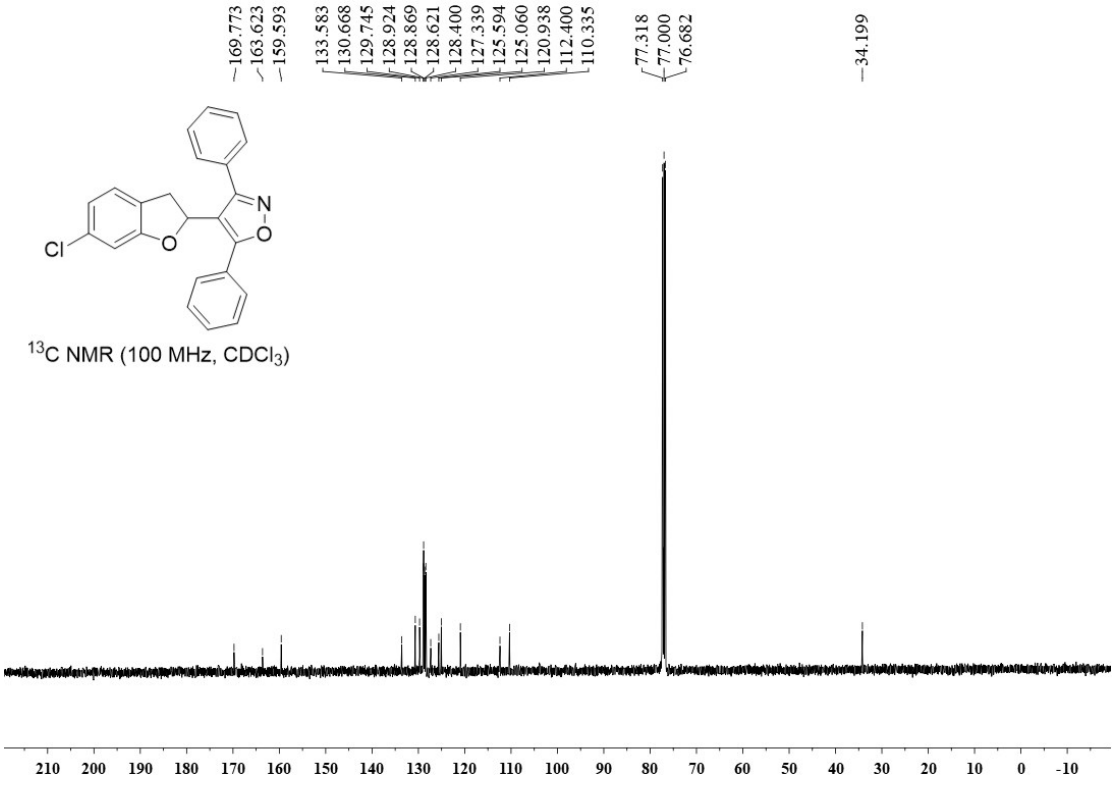


4-(6-Chloro-2,3-dihydrobenzofuran-2-yl)-3,5-diphenylisoxazole (3ae)



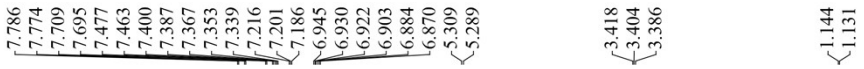
^{1}H NMR (400 MHz, $CDCl_3$)

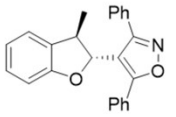




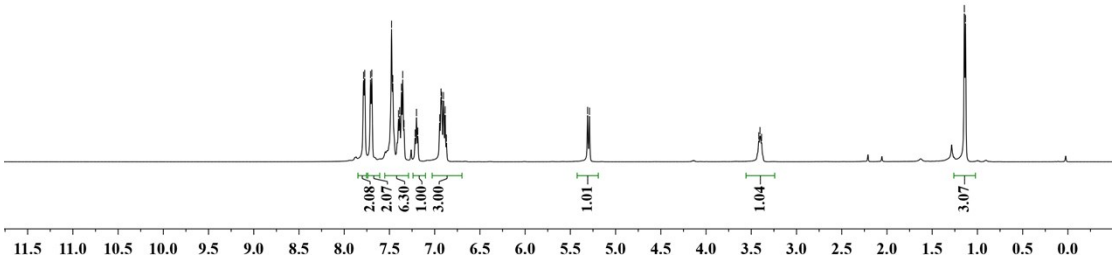
^{13}C NMR (100 MHz, $CDCl_3$)

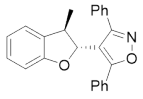
anti-4-(3-Methyl-2,3-dihydrobenzofuran-2-yl)-3,5-diphenylisoxazole (3ag)



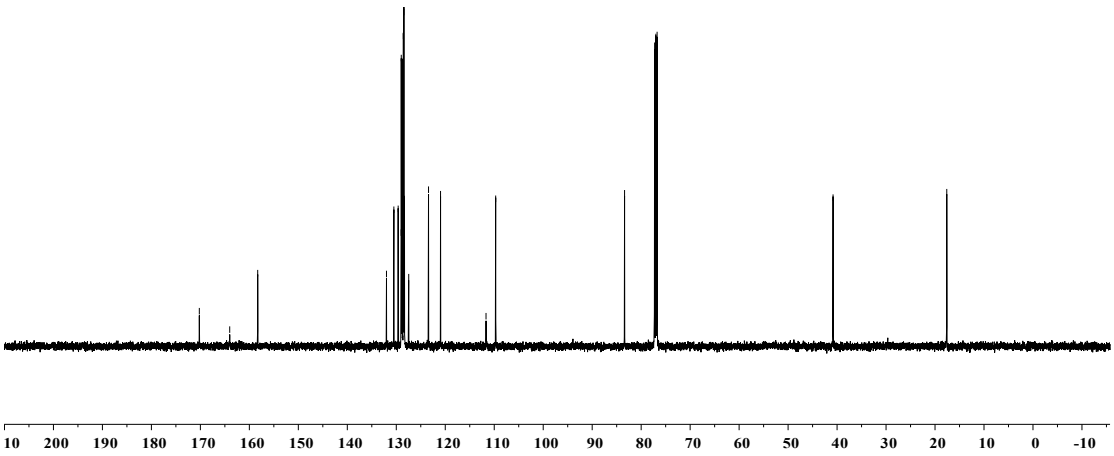


^{1}H NMR (500 MHz, $CDCl_3$)

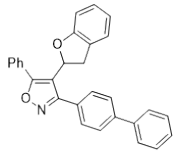




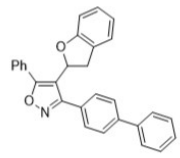
^{13}C NMR (125 MHz, $CDCl_3$)



3-([1,1'-Biphenyl]-4-yl)-4-(2,3-dihydrobenzofuran-2-yl)-5-phenylisoxazole (4)

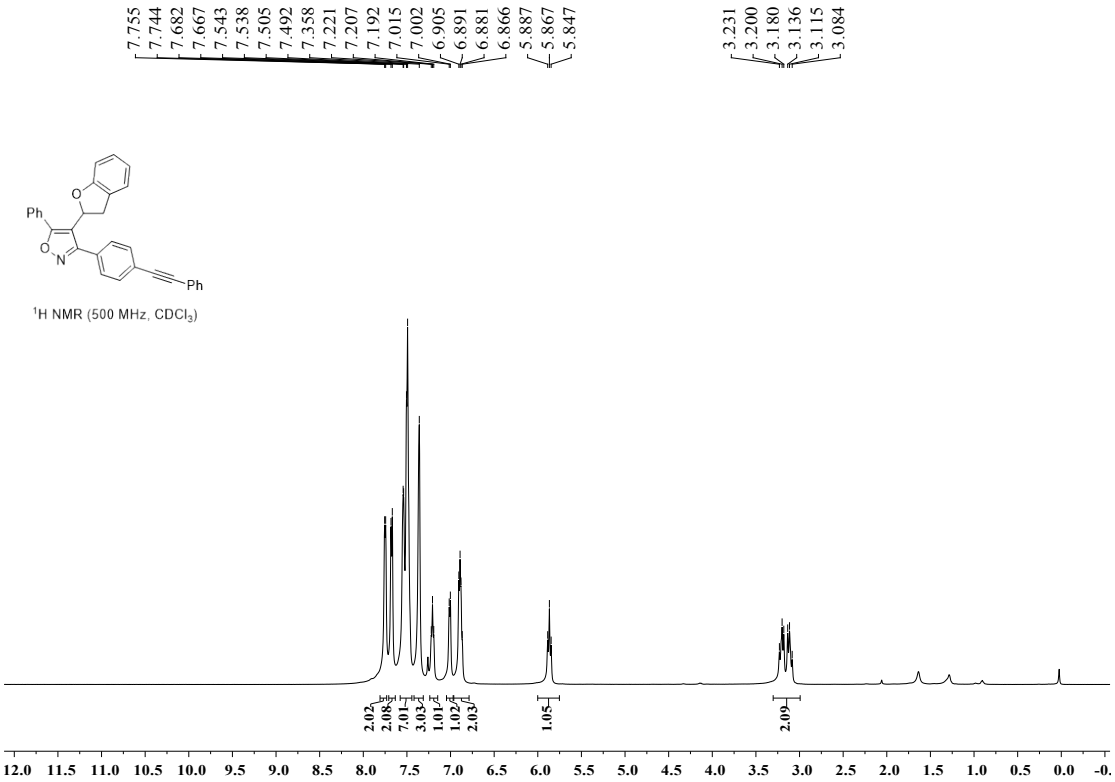


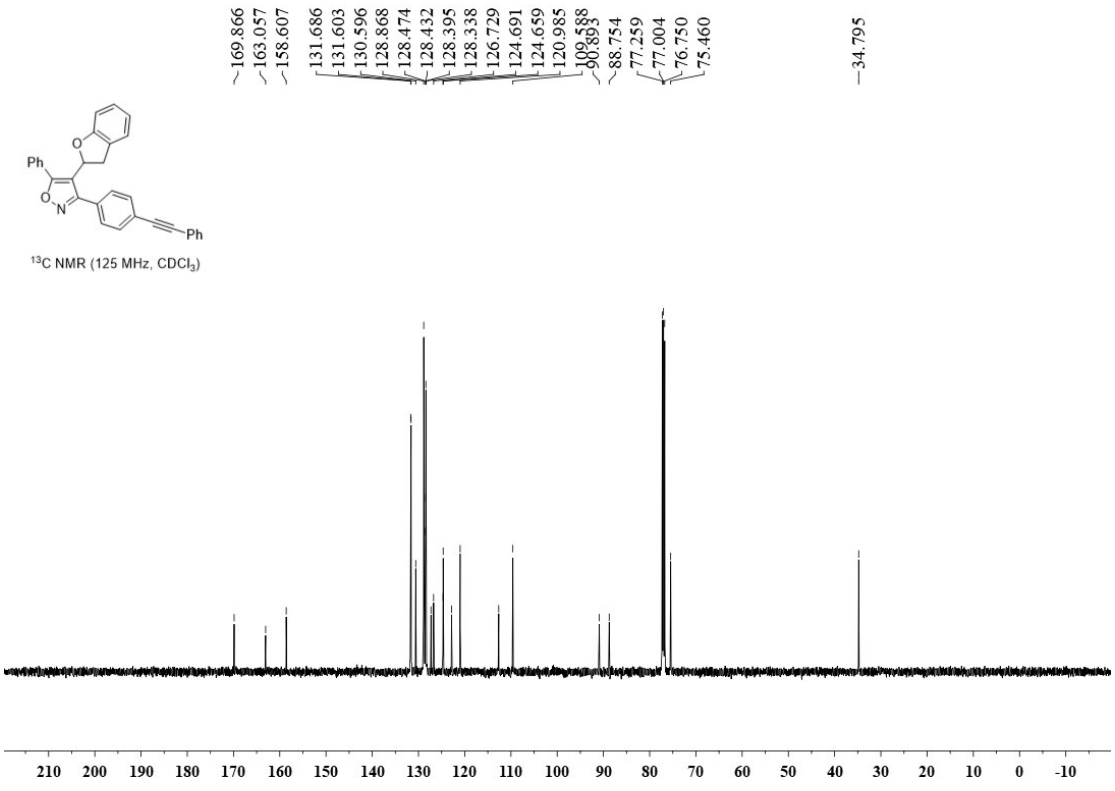
^{1}H NMR (500 MHz, $CDCl_3$)



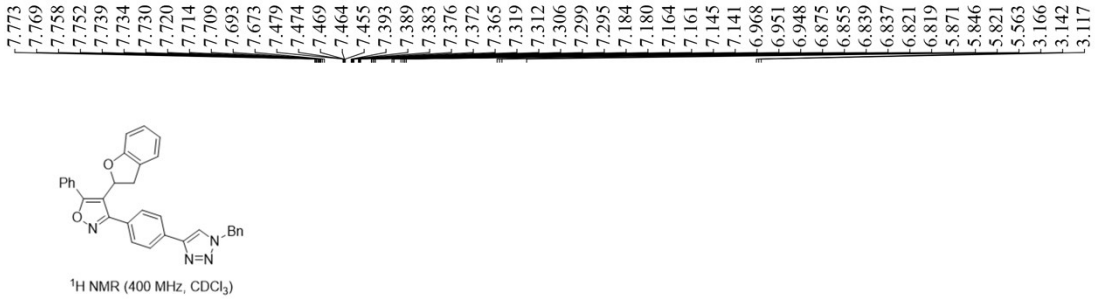
^{13}C NMR (125 MHz, $CDCl_3$)

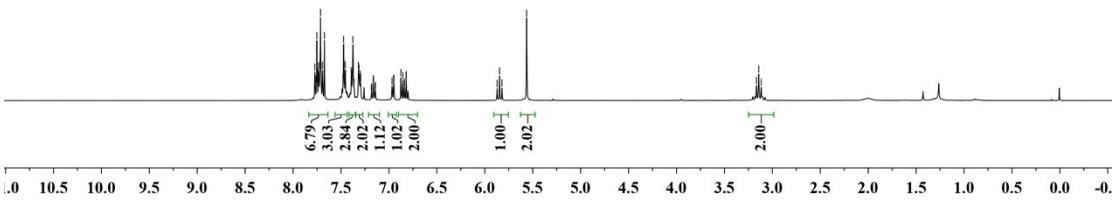
4-(2,3-Dihydrobenzofuran-2-yl)-5-phenyl-3-(4-(phenylethynyl)phenyl)isoxazole (5)

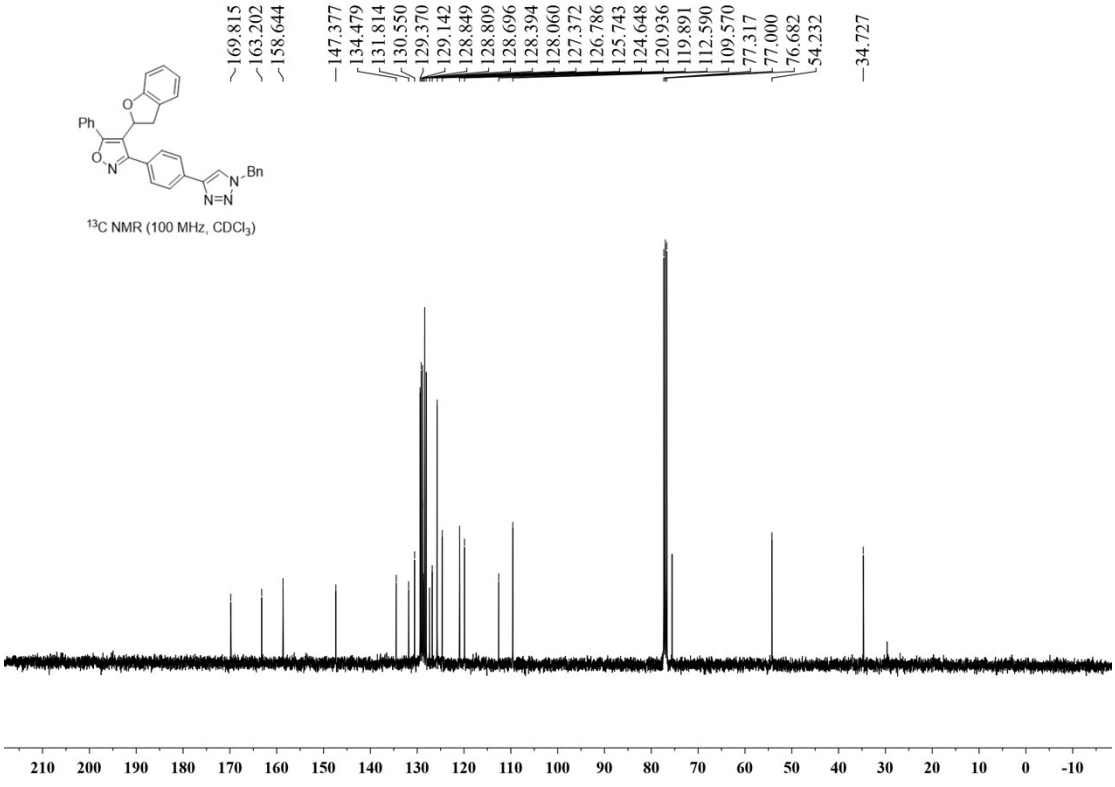




3-(4-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)phenyl)-4-(2,3-dihydrobenzofuran-2-yl)-5-phenylisoxazole (6)

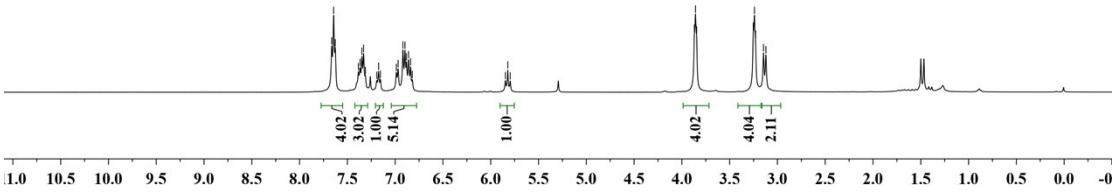


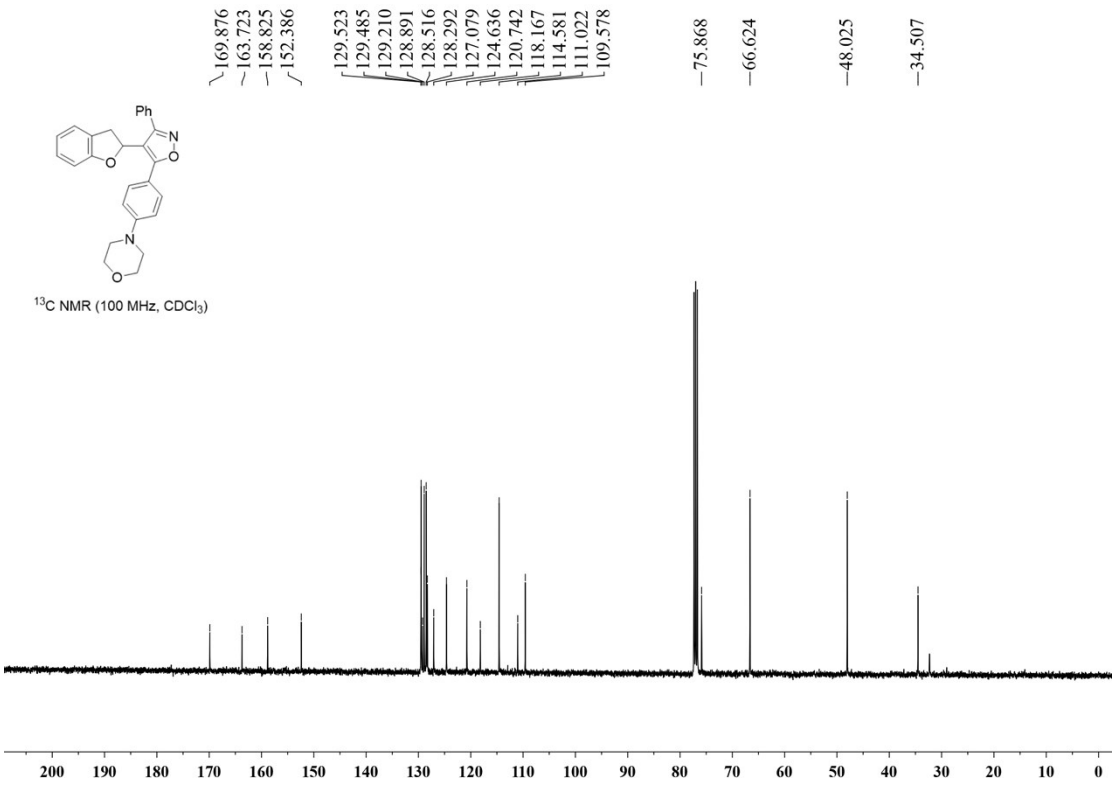




4-(4-(4-(2,3-Dihydrobenzofuran-2-yl)-3-phenylisoxazol-5-yl)phenyl)morpholine (7)

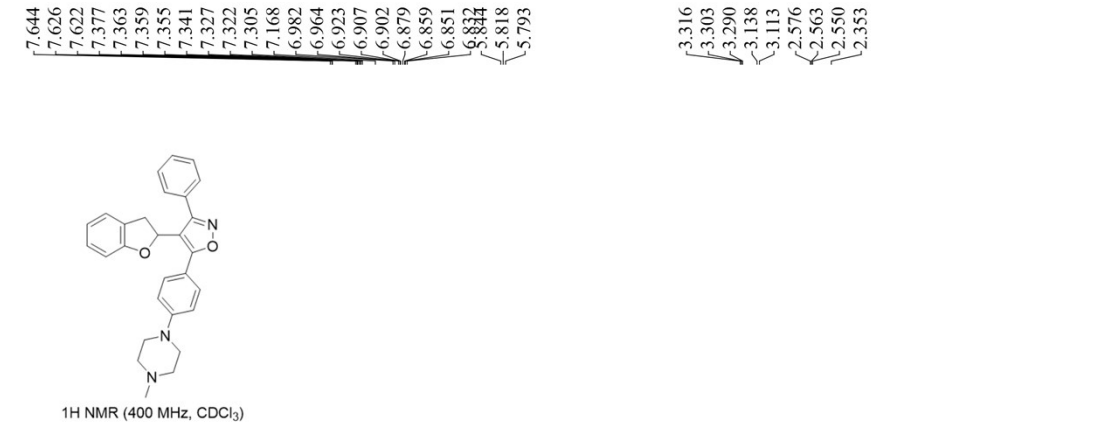
^{1}H NMR (400 MHz, $CDCl_3$)

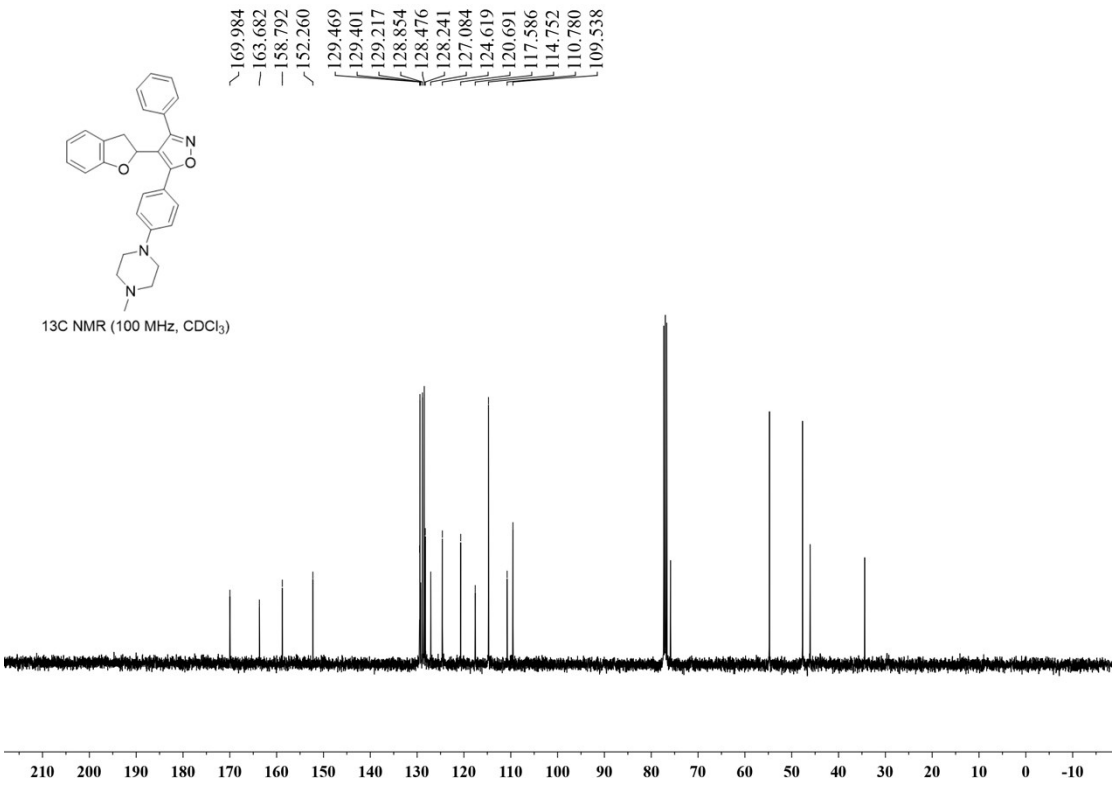




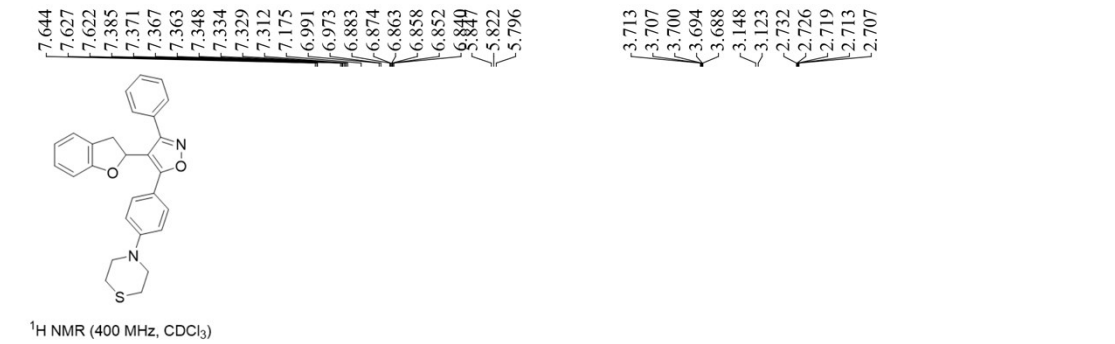
^{13}C NMR (100 MHz, $CDCl_3$)

4-(2,3-Dihydrobenzofuran-2-yl)-5-(4-(4-methylpiperazin-1-yl)phenyl)-3-phenyliso xazole (8)

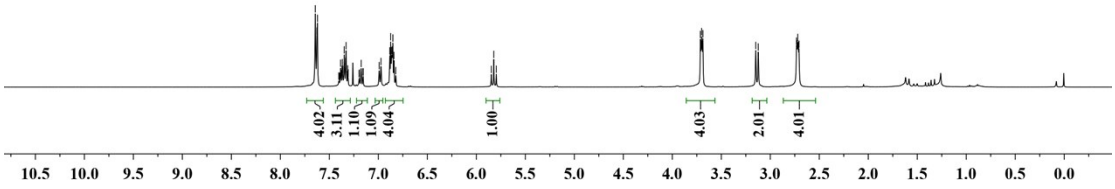


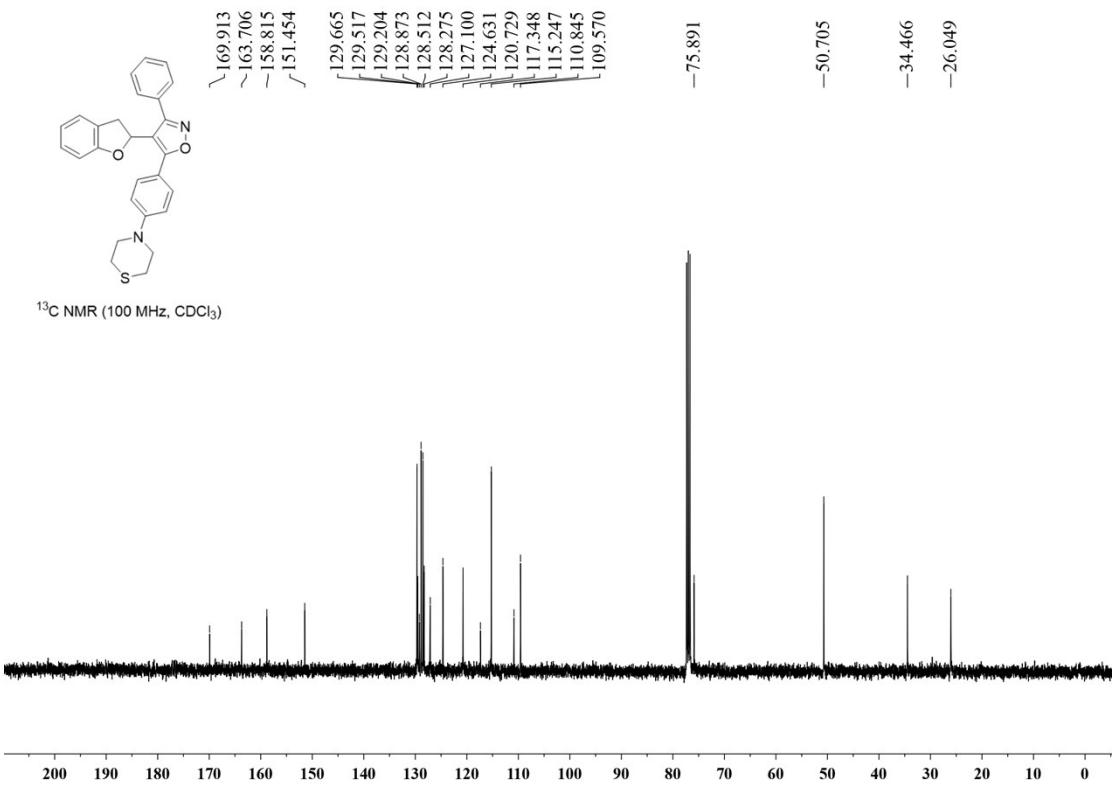


4-(2,3-Dihydrobenzofuran-2-yl)-3-phenyl-5-(4-thiomorpholinophenyl)isoxazole (9)



^{1}H NMR (400 MHz, $CDCl_3$)





^{13}C NMR (100 MHz, $CDCl_3$)