Supporting Information

Regioselective conjugate addition of isoxazol-5-ones to ethenesulfonyl fluoride

Dong-yu Zhu, Yuan Chen, Xue-jing Zhang*, Ming Yan*

Guangdong Provincial Key Laboratory of Chiral Molecules and Drug Discovery, School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou 510006, China

E-mail: yanming@mail.sysu.edu.cn

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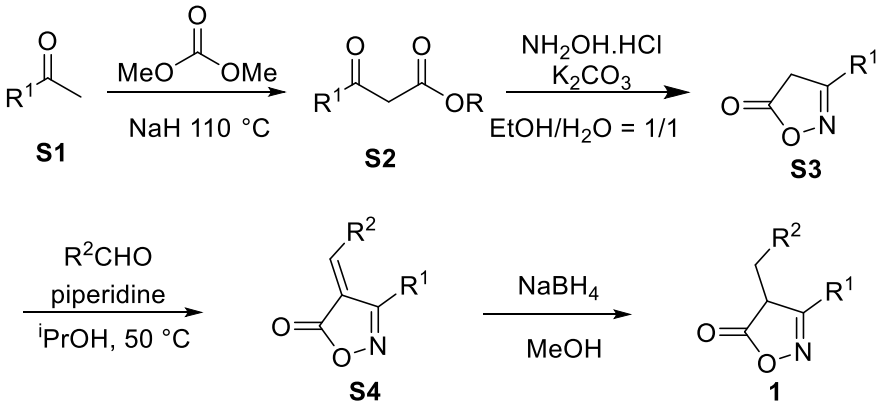
1. General Information

^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker 400 MHz or 500 MHz spectrometer in $CDCl_3$ or DMSO-d_6 with tetramethylsilane (TMS) as the internal standard. Chemical shifts of protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CDCl_3$: δ 7.26; DMSO-d_6: δ 2.50). Chemical shifts of carbon are referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.0; DMSO-d_6: δ 39.5). Peaks are labelled as singlet (s), broad singlet (br), doublet (d), triplet (t), double doublet (dd), multiplet (m). Copies of their ^{1}H NMR and ^{13}C NMR spectra were provided. Melting points were measured on a WRS-2A melting point apparatus and are uncorrected. High-resolution mass spectra (HRMS) were acquired using an electron spray ionization time-of flight (ESI-TOF) mass spectrometer in positive mode. All reagents were used as received from commercial suppliers without further purification unless otherwise noted. All solvents were dried and distilled prior to use according to the standard protocols. Isoxazol-5-ones **1** were synthesized according to the previously reported methods.[1]

2. General Procedure

2.1 Preparation of substituted isoxazol-5-ones 1



A round bottom flask was charged with NaH (2.8 equiv.), dimethyl carbonate (2.0 equiv.) and toluene (0.67 M in respect to the methylketone); and was heated to reflux (110 °C). Next, the methylketone **S1** (1.0 equiv.) was added and the reaction was stirred at 110 °C overnight. Then, the reaction mixture was allowed to cool down to room temperature, and was quenched with an aqueous saturated solution of NH_4Cl. The mixture was extracted with AcOEt (2 x 50 mL). The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography to afford the corresponding *β*-ketoester **S2**.

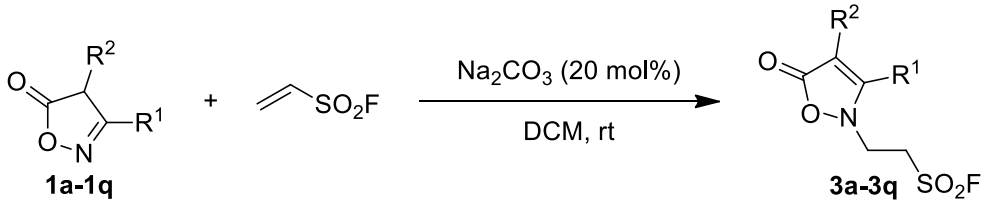
To a solution of hydroxylamine hydrochloride (0.70 g, 10.0 mmol, 1.0 equiv.) and potassium carbonate (0.70 g, 5.0 mmol, 0.5 equiv.) in EtOH/H_2O (v/v 1/1, 20 mL). The mixture was allowed to stir at room temperature for 5 min, then *β*-ketoester **S2** was added. The reaction was stirred at room temperature overnight. The precipitate was filtered and washed with water to give **S3**.

To a solution of **S3** (5.0 mmol, 1.0 equiv.) and piperidine (0.1 equiv.) in ^{i}PrOH (0.4 M) was added the aromatic aldehyde (1.2 equiv.). The reaction mixture was heated at 50 °C for 2~6 h. The precipitate was filtered off, washed with water to give **S4**.

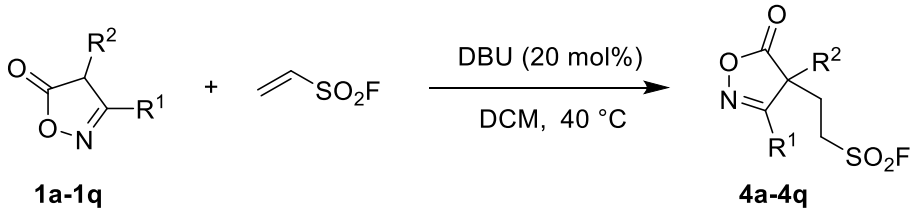
The crude solid **S4** was dissolved in MeOH (0.1 M) and cooled to 0 °C. Then, the sodium borohydride (3.0 equiv.) was added. After all the gas was discharged, the mixture was heated to room temperature and stirred for 6 h. The solution was adjusted to acidity with hydrochloric acid (1.0 M) and was extracted with CH_2Cl_2. The organic layer was dried over sodium sulfate,

filtered and evaporated. After recrystallization from ethanol, the isoxazol-5-one **1** was obtained.

2.2 General procedure for conjugate addition of isoxazole-5-ones 1a-1q with ethylenesulfonyl fluoride

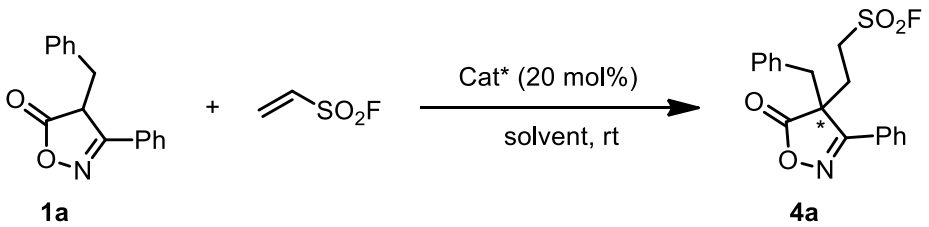


A solution of isoxazole-5-one **1** (0.1 mmol), ESF (0.1 mmol) and Na_2CO_3 (2.12 mg, 0.02 mmol) in CH_2Cl_2 (1.0 mL) was stirred at room temperature. After the raw materials are consumed, the solvent was evaporated under vacuum, and the residue was purified by flash column chromatography over silica gel (petroleum ether/ethyl acetate) to afford the product **3**.



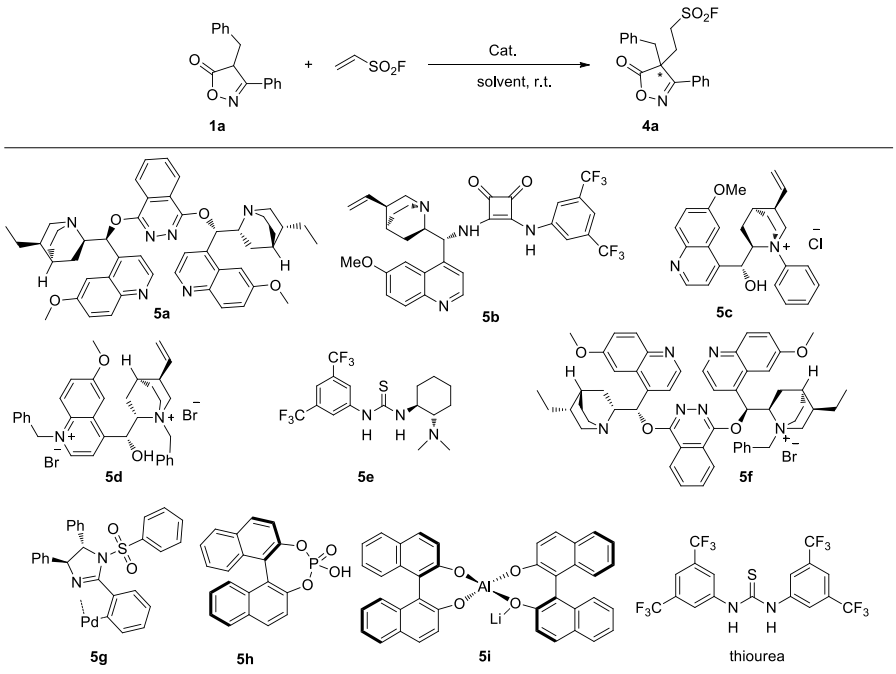
A solution of isoxazolone **1** (0.1 mmol), ESF (0.1 mmol) and DBU (3.04 mg, 0.02 mmol) in CH_2Cl_2 (1.0 mL) was stirred at 40 °C. After the raw materials were consumed, the solvent was evaporated under vacuum, and the residue was purified by flash column chromatography over silica gel (petroleum ether/ethyl acetate) to afford the product **4**.

2.3 General procedure for asymmetric conjugate addition of isoxazolone 1a with ethylenesulfonyl fluoride



A solution of isoxazole-5-one **1a** (0.1 mmol), ESF (0.1 mmol) and catalyst (0.02 mmol) in solvent (1.0 mL) was stirred at rt. After the raw materials were consumed, the solvent was evaporated under vacuum, and the residue was purified by flash column chromatography over silica gel (petroleum ether/ethyl acetate) to afford the chiral product **4a**.

Table S1. Screening of the catalysts for the asymmetric transformation to 4a.

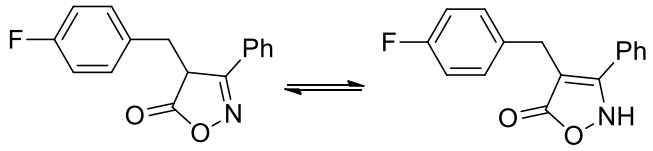


entry	Cat	Additive	solvent	T/°C	**4a** (yield%)[b]	**ee** (%)[c]
1	**5a**	-	DCM	r.t.	40	41
2[e]	**5a**	Thiourea	DCM	r.t.	32	27
3[e]	**5a**	DABCO	DCM	r.t.	50	27
4[e]	**5a**	Na_2CO_3	DCM	r.t.	45	6
5[e]	**5a**	K_3PO_4	DCM	r.t.	68	8
6	**5a**	-	tol	r.t.	38	7
7	**5a**	-	$CHCl_3$	r.t.	35	28
8	**5a**	-	Et_2O	r.t.	17	8
9	**5a**	-	MeCN	r.t.	86	6
10	**5a**	-	Acetone	r.t.	95	0
11	**5a**	-	DCM	40	78	20
12	**5b**	-	DCM	r.t.	15	32
13[f]	**5c**	Cs_2CO_3	THF	r.t.	89	0
14[f]	**5c**	Na_2CO_3	THF	r.t.	90	4
15[f]	**5c**	$NaHCO_3$	THF	r.t.	90	4
16[f]	**5c**	KF	THF	r.t.	91	6
17[f]	**5c**	KF	THF/H_2O	r.t.	88	6
18[f]	**5d**	Na_2CO_3	THF	r.t.	78	4
19	**5e**	-	DCM	r.t.	30	0
20[f]	**5f**	Na_2CO_3	THF	r.t.	86	0
21	**5g**	-	DCM	r.t.	n.d[g]	-
22	**5g**	-	MeCN	r.t.	88	0
23	**5h**	-	DCM	r.t.	n.d[g]	-
24	**5i**	-	THF	r.t.	82	0

[a]The reactions were conducted with **1a** (0.10 mmol), **ESF** (0.10 mmol), and Catalyst (0.02 mmol) in solvent (1.0 mL) for 24 h. [b]Isolated yield. [c]Determined by chiral HPLC analysis. [e]Additive (0.02 mmol). [f] Additive (0.10 mmol). [g]Not detected.

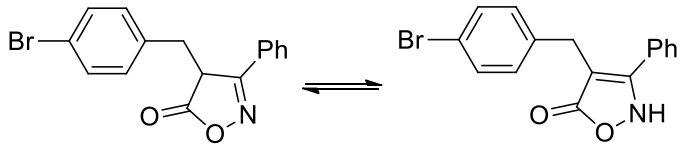
3. Characterization Data

4-(4-Fluorobenzyl)-3-phenylisoxazol-5(4H)-one (1d)



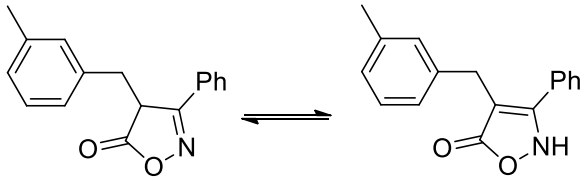
The crude product was purified by recrystallization with ethanol. The ratio of CH:NH tautomers was 5:4. White solid (847.4 mg, 63% yield); m.p. 138.8–139.8 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61–7.55 (m, 3H, ArH), 7.53–7.43 (m, 4H, ArH), 7.19–7.17 (m, 1H, ArH), 6.95–6.92 (m, 1H, ArH), 6.87–6.81 (m, 4H, ArH), 4.15–4.13 (m, 1H$_{imine}$, C*H*), 3.72 (s, 1H$_{enamine}$, C*H*$_2$Ar), 3.35 (dd, *J* = 14.2, 4.6 Hz, 1H$_{imine}$, C*H*$_2$Ar), 3.26 (dd, *J* = 14.2, 5.5 Hz, 1H$_{imine}$, C*H*$_2$Ar); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.5, 165.6, 162.3 (d, *J* = 198.0 Hz), 162.8, 161.6 (d, *J* = 195.9 Hz), 134.4 (d, *J* = 3.2 Hz), 132.0, 131.6, 130.8 (d, *J* = 8.2 Hz), 130.0 (d, *J* = 3.3 Hz), 129.6 (d, *J* = 7.9 Hz), 129.4 (d, *J* = 11.2 Hz), 127.6 (d, *J* = 11.6 Hz), 126.9, 115.7, 115.5, 115.3, 102.1, 46.57, 33.9, 27.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -114.41, -116.67; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{16}H_{13}FNO_2$ 270.0972, found 270.0963.

4-(4-Bromobenzyl)-3-phenylisoxazol-5(4H)-one (1f)



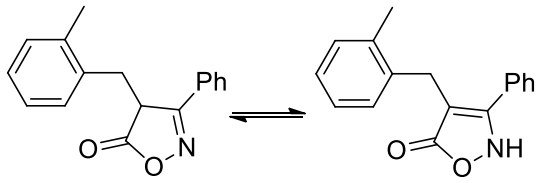
The crude product was purified by recrystallization with ethanol. The ratio of CH:NH tautomers was 10:7. White solid (937.7 mg, 57% yield); m.p. 130.9–131.9 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65–7.57 (m, 3H, ArH), 7.57–7.48 (m, 4H, ArH), 7.43–7.41 (m, 1H, ArH), 7.34–7.28 (m, 2H), 7.16–7.15 (m, 1H), 6.78–6.75 (m, 2H), 4.21–4.14 (m, 1H$_{imine}$, C*H*), 3.75 (s, 1H$_{enamine}$, C*H*$_2$Ar), 3.37 (dd, *J* = 14.1, 4.6 Hz, 1H$_{imine}$, C*H*$_2$Ar), 3.27 (dd, *J* = 14.1, 5.6 Hz, 1H$_{imine}$, C*H*$_2$Ar); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.4, 173.7, 165.5, 162.9, 137.8, 133.2, 132.1, 131.91, 131.70, 131.41, 130.8, 129.8, 129.4, 127.6, 127.6, 127.0, 121.9, 120.3, 101.3, 46.3, 34.0, 27.6; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{16}H_{13}BrNO_2$ 331.1031, found 331.1034.

4-(3-Methylbenzyl)-3-phenylisoxazol-5(4H)-one (1g)



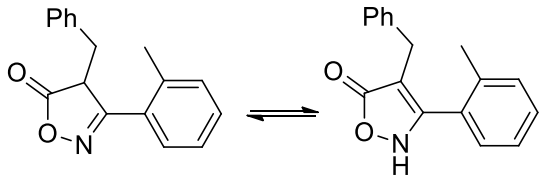
The crude product was purified by recrystallization with ethanol. The ratio of CH:NH tautomers was 10:3. White solid (331.3 mg, 25% yield); m.p. 100.5–101.5 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62–7.56 (m, 3H, ArH), 7.54–7.45 (m, 4H, ArH), 7.21–7.17 (m, 1H, ArH), 7.11–7.02 (m, 3H, ArH), 6.72–6.64 (m, 2H, ArH), 4.17–4.14 (m, 1H$_{imine}$, C*H*), 3.76 (s, 1H$_{enamine}$, C*H*$_2$Ar), 3.34 (dd, J = 14.1, 4.7 Hz, 1H$_{imine}$, C*H*$_2$Ar), 3.27 (dd, J = 14.0, 5.6 Hz, 1H$_{imine}$, C*H*$_2$Ar), 2.32 (s, 1H$_{enamine}$, C*H*$_3$), 2.21 (s, 3H$_{imine}$, C*H*$_3$); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.7, 173.7, 166.0, 162.8, 138.6, 138.3, 134.2, 131.8, 131.5, 129.9, 129.3, 128.9, 128.5, 128.4, 127.9, 127.6, 127.3, 127.0, 126.0, 125.1, 102.9, 46.6, 34.6, 28.0, 21.5, 21.3; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{17}H_{16}NO_2$ 266.1176, found 266.1172.

4-(2-Methylbenzyl)-3-phenylisoxazol-5(4H)-one (1h)



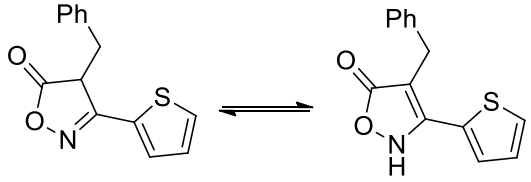
The crude product was purified by recrystallization with ethanol. The ratio of CH:NH tautomers was 15:13. White solid (397.5 mg, 30% yield); m.p. 115.5–116.5 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53–7.35 (m, 11H, ArH), 7.19–7.04 (m, 8H, ArH), 6.98–6.96 (m, 1H, ArH), 4.13–4.10 (m, 1H$_{imine}$, C*H*), 3.70 (s, 2H$_{enamine}$, C*H*$_2$Ar), 3.38–3.21 (m, 2H$_{imine}$, C*H*$_2$Ar), 2.28 (s, 3H$_{enamine}$, C*H*$_3$), 2.14 (s, 3H$_{imine}$, C*H*$_3$); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.6, 174.1, 166.8, 163.1, 136.5, 136.1, 133.4, 131.7, 131.4, 130.7, 130.2, 129.6, 129.3, 129.1, 127.7, 127.5 127.4, 127.2, 126.5, 126.2, 126.2, 100.4, 45.5, 32.2, 25.5, 19.7, 19.4; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{17}H_{16}NO_2$ 266.1176, found 266.1181.

4-Benzyl-3-(*o*-tolyl)isoxazol-5(4H)-one (1i)



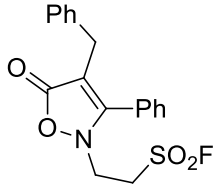
The crude product was purified by recrystallization with ethanol. The ratio of CH:NH tautomers was 2:1. White solid (198.8 mg, 15% yield); m.p. 141.6–142.6 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50–7.48 (m, 2H), 7.40–7.38 (m, 1H), 7.31–7.24 (m, 4H), 7.24–7.13 (m, 4H), 6.91–6.85 (m, 2H), 4.13–4.11 (m, $1H_{imine}$, C*H*), 3.77 (s, $1H_{enamine}$, CH_2Ar), 3.37 (dd, J = 14.0, 4.7 Hz, $1H_{imine}$, CH_2Ar), 3.28 (dd, J = 14.1, 5.6 Hz, $1H_{imine}$, CH_2Ar), 2.44 (s, $3H_{imine}$, CH_3), 2.40 (s, $1H_{enamine}$, CH_3); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.7, 165.6, 142.5, 134.4, 130.0, 129.1, 128.6, 128.1, 127.7, 127.4, 126.9, 126.5, 125.0, 102.9, 100.0, 46.6, 34.8, 28.2, 21.6; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{17}H_{16}NO_2$ 266.1176, found 266.1171..

4-Benzyl-3-(thiophen-2-yl)isoxazol-5(4H)-one (1q)



The crude product was purified by recrystallization with ethanol. The ratio of CH:NH tautomers was 5:4. White solid (321.3 mg, 25% yield); m.p. 96.7–98.7 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.63–7.62 (m, 2H), 7.58–7.53 (m, 2H), 7.52–7.45 (m, 3H), 7.11–7.08 (m, 1H), 6.89–6.87 (m, 1H), 6.84–6.80 (m, 1H), 6.62–6.61 (m, 1H), 4.14–4.12 (m, $1H_{imine}$, C*H*), 3.89 (s, $1H_{enamine}$, CH_2Ar), 3.61 (dd, J = 15.2, 4.4 Hz, $1H_{imine}$, CH_2Ar), 3.50 (dd, J = 15.2, 5.3 Hz, $1H_{imine}$, CH_2Ar); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 177.3, 173.3, 165.6, 162.6, 141.5, 135.4, 132.0, 131.6, 129.4, 127.6, 127.5, 127.3, 127.2, 127.1, 125.3, 125.1, 123.9, 101.5, 46.7, 28.8, 22.9; **HRMS (ESI)** m/z: $[M+Na]^+$ calculated for $C_{14}H_{11}NO_2SNa$ 280.0403, found 280.0407.

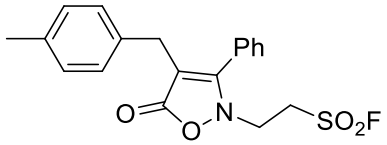
2-(4-Benzyl-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3a)



Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (34.3 mg, 95% yield); m.p. 133.1–134.1 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59–7.50 (m, 3H), 7.42 (dd, *J* = 8.1, 1.4 Hz, 2H), 7.26 (d, *J* = 7.3 Hz, 2H), 7.21 (dd, *J* = 10.1, 4.4 Hz, 3H), 3.81–3.71 (m, 4H), 3.67 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.8, 165.1, 138.3, 131.8, 129.7, 128.8, 128.4, 128.2, 126.7, 126.6, 107.4, 48.4, 47.5 (d, $J_{C\text{-}F}$ = 17.8 Hz), 28.44 (s); **^{19}F**

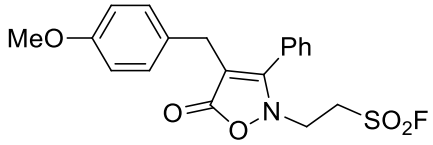
NMR (471 MHz, $CDCl_3$) δ 58.79; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{18}H_{17}FNO_4S$ 362.0857, found 362.0855.

2-(4-(4-Methylbenzyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3b)



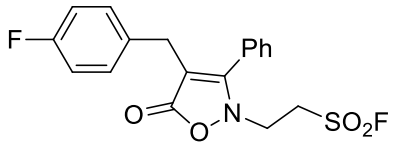
Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (36.0 mg, 96% yield); m.p. 133.6–134.6 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65–7.49 (m, 3H), 7.44–7.42 (m, 2H), 7.09–7.07 (m, 4H), 3.83–3.69 (m, 4H), 3.62–3.60 (m, 2H), 2.30 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.8, 165.0, 136.3, 135.3, 131.8, 129.7, 129.5, 128.4, 128.0, 126.7, 107.7, 48.4, 47.5 (d, J_{C-F} = 17.7 Hz), 28.0, 21.0; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.78; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{19}H_{19}FNO_4S$ 376.1013, found 376.1014.

2-(4-(4-Methoxybenzyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3c)



Petroleum ether/ethyl acetate = 6/1 was used as the eluent for column chromatography. White solid (37.5 mg, 96% yield); m.p. 124.4–125.4 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65–7.52 (m, 3H), 7.46–7.44 (m, 2H), 7.15–7.13 (m, 2H), 6.85–6.83 (m, 2H), 3.84–3.71 (m, 7H), 3.63 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.8, 164.8, 159.4, 132.7, 130.4, 129.9, 127.2, 126.5, 124.1, 114.1, 56.1, 55.2, 46.13 (d, J_{C-F} = 19.6 Hz), 41.5, 29.5; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.76; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{19}H_{19}FNO_5S$ 392.0962, found 392.0960.

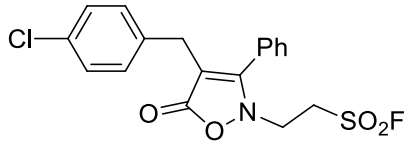
2-(4-(4-Fluorobenzyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3d)



Petroleum ether/ethyl acetate = 6/1 was used as the eluent for column chromatography. White solid (35.6 mg, 94% yield); m.p. 158.0–159.0 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60–7.50 (m, 3H), 7.43–7.36 (m, 2H), 7.16–7.13 (m, 2H), 6.97–6.93 (m, 2H), 3.80–3.74 (m, 4H), 3.63 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.6, 165.1, 161.7 (d, J_{C-F} = 245.0 Hz), 133.9 (d, J_{C-F} = 3.1 Hz), 131.9, 129.7, 129.7 (d, J_{C-F} = 8.1 Hz), 128.3, 126.5, 115.5 (d, J_{C-F} = 21.4 Hz), 107.2,

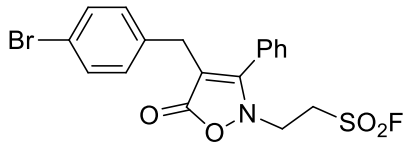
48.3, 47.6 (d, $J_{C\text{-}F}$ = 17.9 Hz), 27.7; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.78, -116.24; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{18}H_{16}F_2NO_4S$ 380.0763, found 380.0768.

2-(4-(4-Chlorobenzyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3e)



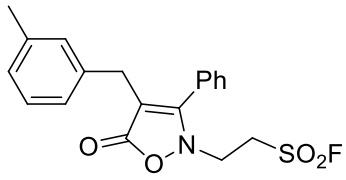
Petroleum ether/ethyl acetate = 6/1 was used as the eluent for column chromatography. White solid (37.1 mg, 94% yield); m.p. 154.1–155.1 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61–7.52 (m, 3H), 7.44–7.37 (m, 2H), 7.26–7.23 (m, 2H), 7.13–7.11 (m, 2H), 3.80–3.74 (m, 4H), 3.63 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.6, 165.2, 136.8, 132.6, 131.9, 129.8, 129.5, 128.9, 128.3, 126.4, 106.8, 48.3, 47.6 (d, $J_{C\text{-}F}$ = 18.0 Hz), 27.9; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 58.85; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{18}H_{16}ClFNO_4S$ 396.0467, found 396.0464.

2-(4-(4-Bromobenzyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3f)



Petroleum ether/ethyl acetate = 6/1 was used as the eluent for column chromatography. White solid (41.4 mg, 94% yield); m.p. 140.3–141.3 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68–7.66 (m, 2H), 7.32–7.26 (m, 4H), 7.24–7.22 (m, 1H), 7.19–7.17 (m, 2H), 3.83–3.79 (m, 2H), 3.72–3.69 (m, 2H), 3.65 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.6, 165.2, 137.3, 131.9, 129.8, 128.3, 126.4, 120.6, 106.7, 48.3, 47.56 (d, $J_{C\text{-}F}$ = 17.9 Hz), 27.9; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 58.83; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{18}H_{16}BrFNO_4S$ 439.9962, found 439.9970.

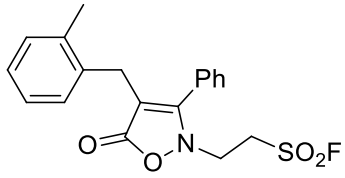
2-(4-(3-Methylbenzyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3g)



Petroleum ether/ethyl acetate = 6/1 was used as the eluent for column chromatography. White solid (35.3 mg, 94% yield); m.p. 127.9–128.9 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63–7.51 (m, 3H), 7.48–7.41 (m, 2H), 7.21–7.17 (m, 1H), 7.06–7.04 (m, 2H), 7.01–6.99 (m, 1H), 3.85–3.72 (m, 4H), 3.66 (s, 2H), 2.33 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.8, 164.9, 138.5, 132.7,

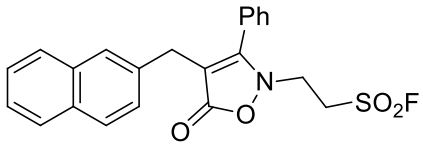
132.1, 130.1, 129.8, 129.0, 128.6, 127.3, 126.5, 126.2, 55.9, 46.1 (d, $J_{C\text{-}F}$ = 19.6 Hz), 42.1, 29.7, 21.3; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 58.85; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{19}H_{19}FNO_4S$ 376.1013, found 376.1010.

2-(4-(2-Methylbenzyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3h)



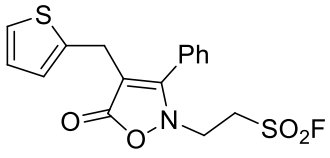
Petroleum ether/ethyl acetate = 6/1 was used as the eluent for column chromatography. White solid (34.9 mg, 93% yield); m.p. 135.8–136.8 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55–7.45 (m, 3H), 7.38–7.33 (m, 2H), 7.14–7.07 (m, 3H), 7.06–7.00 (m, 1H), 3.83–3.75 (m, 4H), 3.63 (s, 2H), 2.19 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.7, 165.5, 136.1, 136.0, 131.8, 130.4, 129.7, 128.2, 127.6, 126.7, 126.7, 126.2, 106.7, 48.5, 47.6 (d, $J_{C\text{-}F}$ = 17.8 Hz), 25.8, 19.6; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 58.77; **HRMS (ESI)** m/z: $[M+Na]^+$ calculated for $C_{19}H_{19}FNO_4S$ 376.1013, found 376.1013.

2-(4-(Naphthalen-2-ylmethyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3i)



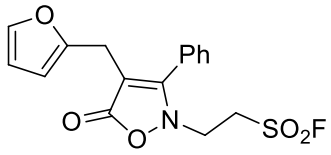
Petroleum ether/ethyl acetate = 6/1 was used as the eluent for column chromatography. White solid (37.8 mg, 92% yield); m.p. 110.4–111.4 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.74 (m, 3H), 7.60 (s, 1H), 7.58–7.48 (m, 3H), 7.47–7.40 (m, 4H), 7.33 (dd, J = 8.5, 1.6 Hz, 1H), 3.82 (s, 2H), 3.80–3.72 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.8, 165.3, 135.9, 133.6, 132.3, 131.8, 129.7, 128.5, 127.7, 126.6, 126.3, 125.7, 107.2, 48.4, 47.6 (d, $J_{C\text{-}F}$ = 17.9 Hz), 28.6; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 58.84; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{22}H_{19}FNO_4S$ 412.1013, found 412.1016.

2-(5-Oxo-3-phenyl-4-(thiophen-2-ylmethyl)isoxazol-2(5H)-yl)ethanesulfonyl fluoride (3j)



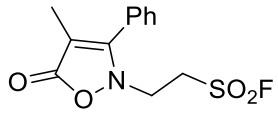
Petroleum ether/ethyl acetate = 6/1 was used as the eluent for column chromatography. White solid (34.1mg, 93% yield); m.p. 101.7–102.7 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61–7.53 (m, 3H), 7.49 (dd, J = 8.0, 1.4 Hz, 2H), 7.14 (dd, J = 5.1, 1.0 Hz, 1H), 6.92 (dd, J = 5.0, 3.5 Hz, 1H), 6.90–6.82 (m, 1H), 3.83 (s, 2H), 3.78 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.2, 165.0, 140.7, 132.0, 129.8, 128.4, 127.2, 126.4, 125.4, 124.1, 106.9, 48.3, 47.4 (d, $J_{C\text{-}F}$ = 17.8 Hz), 23.1; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 58.78; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{16}H_{15}FNO_4S_2$ 368.0421, found 368.0421.

2-(4-(Furan-2-ylmethyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3k)



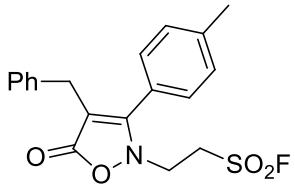
Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (32.3 mg, 92% yield); m.p. 97.3–98.3 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61–7.54 (m, 5H), 7.32–7.31 (m, 1H), 6.35–6.26 (m, 1H), 6.15–6.14 (m, 1H), 3.82–3.75 (m, 4H), 3.66 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.1, 165.4, 151.0, 141.8, 131.9, 129.7, 128.4, 126.4, 110.6, 106.9, 104.6, 48.3, 47.5 (d, $J_{C\text{-}F}$ = 17.8 Hz), 21.9; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 58.76; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{16}H_{15}FNO_5S$ 352.0649, found 352.0642.

2-(4-Methyl-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3l)



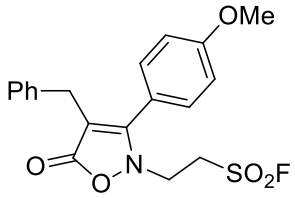
Petroleum ether/ethyl acetate = 6/1 was used as the eluent for column chromatography. White solid (25.1 mg, 88% yield); m.p. 107.1–108.1 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62–7.54 (m, 3H), 7.49–7.47 (m, 2H), 3.81–3.75 (m, 2H), 3.75–3.70 (m, 2H), 1.97 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.3, 164.2, 131.6, 129.6, 128.3, 127.0, 104.6, 48.6, 47.5 (d, $J_{C\text{-}F}$ = 17.8 Hz), 7.9; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 58.68; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{12}H_{13}FNO_4S$ 286.0544, found 286.0548.

2-(4-Benzyl-5-oxo-3-(p-tolyl)isoxazol-2(5H)-yl)ethanesulfonyl fluoride (3m)



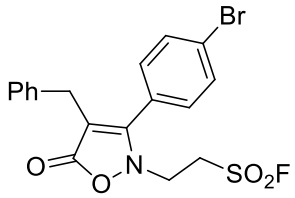
Petroleum ether/ethyl acetate = 6/1 was used as the eluent for column chromatography. White solid (34.9 mg, 93% yield); m.p. 142.1–143.1 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37–7.28 (m, 6H), 7.24 (dd, J = 6.9, 3.6 Hz, 3H), 3.84–3.73 (m, 4H), 3.69 (s, 2H), 2.46 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.9, 165.4, 142.5, 138.5, 130.4, 128.7, 128.2, 126.7, 123.7, 106.9, 48.4, 47.5 (d, $J_{C\text{-}F}$ = 17.7 Hz), 28.5, 21.6; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 58.69,; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{19}H_{19}FNO_4S$ 376.1013, found 376.1009.

2-(4-Benzyl-3-(4-methoxyphenyl)-5-oxoisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3n)



Petroleum ether/ethyl acetate = 6/1 was used as the eluent for column chromatography. White solid (36.4 mg, 93% yield); m.p. 152.1–153.1 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 (d, J = 8.7 Hz, 2H), 7.31–7.26 (m, 2H), 7.24–7.17 (m, 3H), 7.02 (d, J = 8.7 Hz, 2H), 3.87 (s, 3H), 3.81–3.72 (m, 4H), 3.67 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.0, 165.3, 162.3, 138.5, 130.0, 128.8, 128.1, 126.7, 118.6, 115.1, 106.4, 55.6, 48.7, 47.5 (d, $J_{C\text{-}F}$ = 17.8 Hz), 28.5; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 58.79; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{19}H_{19}FNO_5S$ 392.0962, found 392.0958.

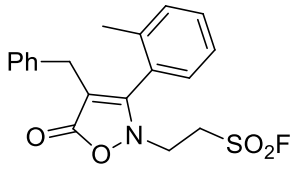
2-(4-Benzyl-3-(4-bromophenyl)-5-oxoisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3o)



Petroleum ether/ethyl acetate = 6/1 was used as the eluent for column chromatography. White solid (37.0 mg, 84% yield); m.p. 154.1–155.1 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.3 Hz, 2H), 7.32–7.26 (m, 4H), 7.23 (d, J = 7.0 Hz, 1H), 7.18 (d, J = 7.4 Hz, 2H), 3.81 (dd, J = 10.5, 5.5 Hz, 2H), 3.72–3.69 (t, J = 6.0 Hz, 2H), 3.65 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.5, 164.0, 138.1, 133.0, 129.8, 128.9, 128.1, 126.9, 126.6, 125.4, 108.0, 48.6, 47.6 (d, $J_{C\text{-}}$

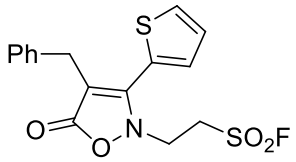
$_F$ = 17.8 Hz), 28.5; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 59.28,; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{18}H_{16}BrFNO_4S$ 439.9962, found 439.9965.

2-(4-Benzyl-5-oxo-3-(o-tolyl)isoxazol-2(5H)-yl)ethanesulfonyl fluoride (3p)



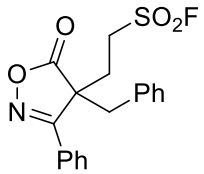
Petroleum ether/ethyl acetate = 6/1 was used as the eluent for column chromatography. White solid (32.6 mg, 87% yield); m.p. 148.5–149.5 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54–7.46 (m, 1H), 7.37–7.28 (m, 2H), 7.24–7.15 (m, 4H), 7.06 (d, J = 6.6 Hz, 2H), 3.84–3.69 (m, 3H), 3.63–3.43 (m, 3H), 2.21 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.5, 164.8, 138.0 , 137.1, 131.4, 129.1, 128.5, 128.4, 128.3, 126.7, 126.6, 125.8, 107.8, 47.6 (d, $J_{C\text{-}F}$ = 17.8 Hz), 46.8, 28.5, 19.5; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 58.37; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{19}H_{19}FNO_4S$ 376.1013, found 376.1010.

2-(4-Benzyl-5-oxo-3-(thiophen-2-yl)isoxazol-2(5H)-yl)ethanesulfonyl fluoride (3q)



Petroleum ether/ethyl acetate = 6/1 was used as the eluent for column chromatography. White solid (33.4 mg, 91% yield); m.p. 122.5–123.5 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (dd, J = 5.0, 1.1 Hz, 1H), 7.40 (dd, J = 3.7, 1.1 Hz, 1H), 7.35–7.30 (m, 2H), 7.28–7.22 (m, 4H), 3.92–3.83 (m, 4H), 3.81 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.2, 165.0, 140.7, 132.0, 129.8, 128.4, 127.2, 126.4, 125.4, 124.1, 106.9, 48.3, 47.4 (d, $J_{C\text{-}F}$ = 17.8 Hz), 23.1; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 58.79; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{16}H_{15}FNO_4S_2$ 368.0421, found 368.0429.

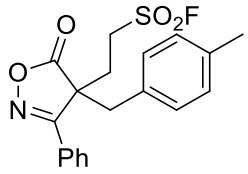
2-(4-Benzyl-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4a)



Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (33.6 mg, 93% yield); m.p. 136.2–137.2 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84–7.72 (m,

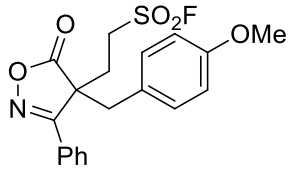
2H), 7.65–7.61 (m, 1H), 7.58–7.55 (m, 2H), 7.25–7.08 (m, 3H), 6.87 (d, *J* = 7.3 Hz, 2H), 3.44–3.27 (m, 3H), 3.26–3.14 (m, 1H), 2.87–2.76 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.7, 164.8, 132.7, 132.2, 129.9, 129.2, 128.8, 128.3, 127.2, 126.5, 55.9, 46.9 (d, $J_{C\text{-}F}$ = 19.6 Hz), 42.2, 29.7; **^{19}F NMR** (376 MHz, $CDCl_3$) δ 53.81; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{18}H_{17}FNO_4S$ 362.0857, found 362.0851.

2-(4-(4-Methylbenzyl)-5-oxo-3-phenyl-4,5**-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4b)**



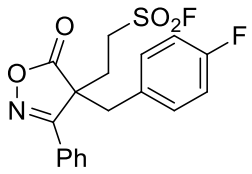
Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (34.5 mg, 92% yield); m.p. 136.2–137.2 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84–7.74 (m, 2H), 7.62 (d, *J* = 7.3 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 2H), 6.96 (d, *J* = 7.9 Hz, 2H), 6.75 (d, *J* = 8.0 Hz, 2H), 3.40–3.26 (m, 3H), 3.25–3.14 (m, 1H), 2.85–2.74 (m, 2H), 2.25 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.8, 164.8, 138.1, 132.7, 129.8, 129.5, 129.1, 129.0(8), 127.2, 126.5, 56.0, 46.1 (d, $J_{C\text{-}F}$ = 19.6 Hz), 41.84, 29.58, 21.08; **^{19}F NMR** (376 MHz, $CDCl_3$) δ 53.75; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{19}H_{19}FNO_4S$ 376.1013, found 376.1013.

2-(4-(4-Methoxybenzyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4c)



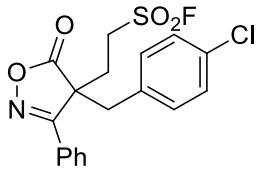
Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (35.8 mg, 91% yield); m.p. 170.3–171.3 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88–7.75 (m, 2H), 7.65 (d, *J* = 7.3 Hz, 1H), 7.61–7.57 (m, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 6.71 (d, *J* = 8.7 Hz, 2H), 3.75 (s, 3H), 3.42–3.27 (m, 3H), 3.26–3.18 (m, 1H), 2.81 (dd, *J* = 9.5, 7.6 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.8, 164.8, 159.4, 132.7, 130.4, 129.9, 127.2, 126.5, 124.1, 114.1, 56.1, 55.2, 46.1 (d, $J_{C\text{-}F}$ = 19.6 Hz), 41.5, 29.6; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.76; **HRMS (ESI)** m/z: $[M+Na]^+$ calculated for $C_{19}H_{18}FNO_5SNa$ 414.0782, found 414.0791.

2-(4-(4-Fluorobenzyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4d)



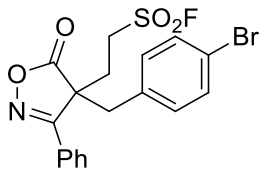
Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (33.4 mg, 88% yield); m.p. 128.3–129.3 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83–7.76 (m, 2H), 7.66–7.63 (m, 1H), 7.59–7.56 (m, 2H), 6.92–6.74 (m, 4H), 3.42–3.26 (m, 3H), 3.25–3.15 (m, 1H), 2.86–2.76 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.6, 164.6, 162.6 (d, $J_{C\text{-}F}$ = 247.8 Hz), 132.9, 131.0 (d, $J_{C\text{-}F}$ = 8.3 Hz), 130.0, 128.0 (d, $J_{C\text{-}F}$ = 3.3 Hz), 127.0, 126.4, 115.8 (d, $J_{C\text{-}F}$ = 21.5 Hz), 56.0, 46.1 (d, $J_{C\text{-}F}$ = 19.7 Hz), 41.3, 29.6; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.86, -113.21; **HRMS (ESI)** m/z: $[M+Na]^+$calculated for $C_{18}H_{15}F_2NO_4SNa$ 402.0582, found 402.0578.

2-(4-(4-Chlorobenzyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4e)



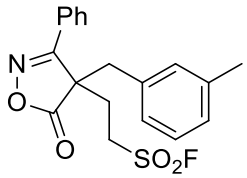
Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (34.8 mg, 88% yield); m.p. 151.9–152.9 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90–7.78 (m, 2H), 7.69–7.66 (m, 1H), 7.62–7.58 (m, 2H), 7.18–7.16 (m, 2H), 6.83–6.81 (m, 2H), 3.43–3.28 (m, 3H), 3.26–3.18 (m, 1H), 2.90–2.77 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.5, 164.5, 134.5, 132.9, 130.7, 130.6, 130.0, 129.1, 127.0, 126.4, 55.8, 46.0 (d, $J_{C\text{-}F}$ = 19.7 Hz), 41.4, 29.7; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.91; **HRMS (ESI)** m/z: $[M+NH_4]^+$ calculated for $C_{18}H_{19}ClFN_2O_4S$ 413.0733, found 413.0727.

2-(4-(4-Bromobenzyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4f)



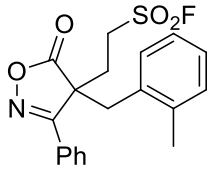
Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (39.6 mg, 90% yield); m.p. 145.3–146.3 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79–7.78 (m, 2H), 7.65–7.63 (m, 1H), 7.60–7.56 (m, 2H), 7.31–7.29 (m, 2H), 6.74–6.72 (m, 2H), 3.39–3.25 (m, 3H), 3.24–3.16 (m, 1H), 2.83–2.77 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.5, 164.5, 132.9, 132.0, 131.2, 130.9, 130.0, 127.0, 126.4, 122.6, 55.7, 46.0 (d, J_{C-F} = 19.8 Hz), 41.4, 29.7; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.92; **HRMS (ESI)** m/z: $[M+Na]^+$ calculated for $C_{18}H_{15}BrFNO_4SNa$ 461.9781, found 461.9777.

2-(4-(3-Methylbenzyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4g)



Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (34.5 mg, 92% yield); m.p. 139.3–140.3 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81–7.72 (m, 2H), 7.65–7.61 (m, 1H), 7.58–7.54 (m, 2H), 7.07–6.98 (m, 2H), 6.68–6.57 (m, 2H), 3.37–3.27 (m, 3H), 3.26–3.17 (m, 1H), 2.86–2.76 (m, 2H), 2.17 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.8, 165.0, 138.5, 132.7, 132.1, 130.1, 129.8, 129.0, 128.6, 127.3, 126.5, 126.2, 55.9, 46.1 (d, J_{C-F} = 19.6 Hz), 42.1, 29.7, 21.3; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.80; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{19}H_{19}FNO_4S$ 376.1013, found 376.1011.

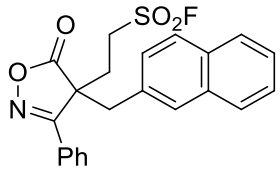
2-(4-(2-Methylbenzyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4h)



Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (34.61mg, 91% yield); m.p. 142.1–143.1 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73–7.71 (m, 2H), 7.62–7.58 (m, 1H), 7.56–7.47 (m, 2H), 7.15–7.09 (m, 1H), 7.08–6.98 (m, 2H), 6.86–6.84 (m, 1H), 3.47–3.26 (m, 3H), 3.23–3.14 (m, 1H), 2.92–2.78 (m, 2H), 2.07 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.8, 165.3, 136.9, 132.7, 131.2, 130.9, 129.8, 129.3, 128.2, 127.3,

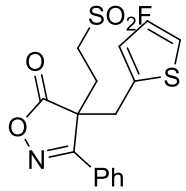
126.5, 126.2, 55.2, 46.1 (d, $J_{C\text{-}F}$ = 19.6 Hz), 38.0, 30.0, 19.6; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.88; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{19}H_{19}FNO_4S$ 376.1013, found 376.1013.

2-(4-(Naphthalen-2-ylmethyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4i)



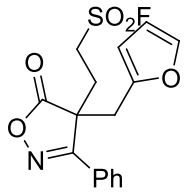
Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (36.6 mg, 89% yield); m.p. 89.7–90.7 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82–7.70 (m, 3H), 7.67–7.61 (m, 2H), 7.61–7.52 (m, 3H), 7.48–7.37 (m, 2H), 7.30–7.29 (m, 1H), 6.96–6.95 (m, 1H), 3.58–3.45 (m, 2H), 3.39–3.30 (m, 1H), 3.28–3.19 (m, 1H), 2.93–2.80 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.8, 164.8, 133.1, 132.8, 132.7, 129.9, 129.7, 128.7, 128.6, 127.8, 127.7, 127.3, 126.6, 126.6, 126.5, 126.4, 56.0, 46.1 (d, $J_{C\text{-}F}$ = 19.6 Hz), 42.2, 29.8; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.90; **HRMS (ESI)** m/z: $[M+Na]^+$ calculated for $C_{22}H_{18}FNO_4SNa$ 434.0833, found 434.0835.

2-(5-Oxo-3-phenyl-4-(thiophen-2-ylmethyl)-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4j)



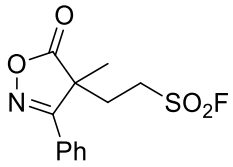
Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (33.8 mg, 92% yield); m.p. 110.3–111.3 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.78 (m, 2H), 7.67–7.60 (m, 1H), 7.60–7.52 (m, 2H), 7.11–7.09 (m, 1H), 6.85–6.83 (m, 1H), 6.67–6.66 (m, 1H), 3.66–3.55 (m, 2H), 3.37–3.28 (m, 1H), 3.27–3.18 (m, 1H), 2.81–2.71 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.5, 164.9, 133.2, 132.8, 129.9, 128.0, 127.3, 126.9, 126.5, 125.9, 56.0, 46.0 (d, $J_{C\text{-}F}$ = 19.7 Hz), 36.0, 29.4; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.87; **HRMS (ESI)** m/z: $[M+Na]^+$ calculated for $C_{16}H_{14}FNO_4S_2Na$ 390.0240, found 390.0231.

2-(4-(Furan-2-ylmethyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4k)



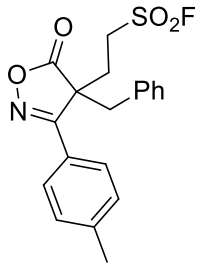
Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (31.6 mg, 90% yield); m.p. 103.1–104.1 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78–7.67 (m, 2H), 7.66–7.57 (m, 1H), 7.55–7.51 (m, 2H), 7.22–7.21 (m, 1H), 6.21–6.19 (m, 1H), 5.99 (d, J = 3.2 Hz, 1H), 3.49–3.39 (m, 2H), 3.36–3.27 (m, 1H), 3.27–3.15 (m, 1H), 2.75–2.62 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.3, 165.6, 146.7, 143.0, 132.5, 129.7, 126.9, 126.7, 110.6, 109.2, 54.0, 45.9 (d, $J_{C\text{-}F}$ = 19.7 Hz), 34.6, 29.1; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.85; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{16}H_{15}FNO_5S$ 352.0649, found 352.0643.

2-(4-Methyl-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4l)



Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (24.8 mg, 87% yield); m.p. 120.4–121.4 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76–7.74 (m, 2H), 7.65–7.48 (m, 3H), 3.37–3.23 (m, 2H), 2.65–2.50 (m, 2H), 1.74 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.4, 167.1, 132.7, 129.8, 126.6, 126.5, 48.5, 45.9 (d, $J_{C\text{-}F}$ = 19.7 Hz), 29.8, 22.0; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.70; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{12}H_{13}FNO_4S$ 286.0544, found 286.0551.

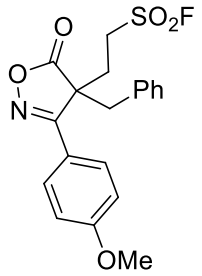
2-(4-Benzyl-5-oxo-3-(p-tolyl)-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4m)



Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (33.8 mg, 90% yield); m.p. 151.0–152.0 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73–7.71 (m, 2H), 7.40–7.38 (m, 2H), 7.28–7.17 (m, 3H), 6.92–6.90 (m, 2H), 3.46–3.29 (m, 3H), 3.26–3.17 (m, 1H), 2.84–2.79 (m, 2H), 2.50 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.8, 164.6, 143.6,

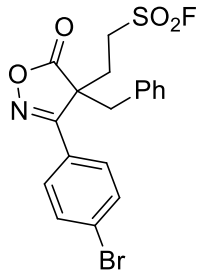
132.3, 130.6, 129.3, 128.8, 128.3, 126.4, 124.3, 56.0, 46.12 (d, $J_{C\text{-}F}$ = 19.5 Hz), 42.2, 29.7, 21.7; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.74; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{19}H_{19}FNO_4S$ 376.1013, found 376.1005.

2-(4-Benzyl-3-(4-methoxyphenyl)-5-oxo-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4n)



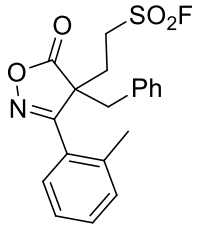
Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (34.4 mg, 88% yield); m.p. 156.2–157.2 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76–7.74 (m, 2H), 7.24–7.13 (m, 3H), 7.06–7.04 (m, 2H), 6.89–6.87 (m, 2H), 3.90 (s, 3H), 3.42–3.25 (m, 3H), 3.23–3.14 (m, 1H), 2.85–2.71 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.9, 164.1, 162.9, 132.4, 129.3, 128.8, 128.3, 128.2, 119.3, 115.3, 56.0, 55.6, 46.1 (d, $J_{C\text{-}F}$ = 19.5 Hz), 42.3, 29.7; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.74; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{19}H_{19}FNO_5S$ 392.0962, found 392.0964.

2-(4-Benzyl-3-(4-bromophenyl)-5-oxo-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4o)



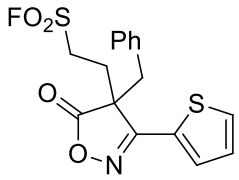
Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (35.2 mg, 80% yield); m.p. 158.9–159.9 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76–7.64 (m, 4H), 7.29–7.18 (m, 3H), 6.89–6.88 (m, 2H), 3.45–3.31 (m, 3H), 3.27–3.16 (m, 1H), 2.88–2.72 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.5, 164.1, 133.2, 132.1, 129.1, 128.9, 128.5, 127.8, 127.6, 126.0, 55.7, 46.0 (d, $J_{C\text{-}F}$ = 19.7 Hz), 42.1, 29.5; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.97; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{18}H_{16}BrFNO_4S$ 439.9962, found 439.9946.

2-(4-Benzyl-5-oxo-3-(o-tolyl)-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4p)



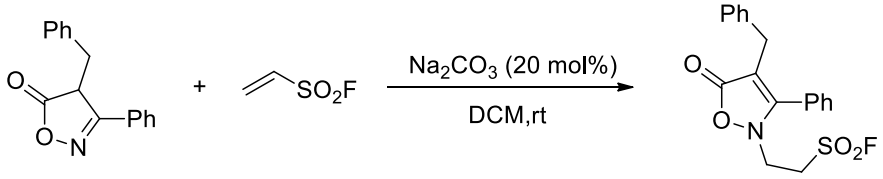
Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (31.9 mg, 85% yield); m.p. 153.1–154.1 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73–7.71 (m, 2H), 7.62–7.58 (m, 1H), 7.56–7.47 (m, 2H), 7.15–7.09 (m, 1H), 7.08–6.98 (m, 2H), 6.86–6.84 (m, 1H), 3.47–3.26 (m, 3H), 3.23–3.14 (m, 1H), 2.92–2.78 (m, 2H), 2.07 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.6, 165.4, 140.0, 133.3, 132.6, 131.6, 129.1, 128.9, 128.2, 126.7, 126.5, 126.4, 56.8, 46.0 (d, $J_{C\text{-}F}$ = 19.5 Hz), 41.5, 30.6, 22.8; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.99; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{19}H_{19}FNO_4S$ 376.1013, found 376.1019.

2-(4-Benzyl-5-oxo-3-(thiophen-2-yl)-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4q)



Petroleum ether/ethyl acetate = 20/1 was used as the eluent for column chromatography. White solid (32.3 mg, 88% yield); m.p. 103.1–104.1 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.78 (m, 2H), 7.67–7.60 (m, 1H), 7.60–7.52 (m, 2H), 7.11–7.09 (m, 1H), 6.85–6.83 (m, 1H), 6.67–6.66 (m, 1H), 3.66–3.55 (m, 2H), 3.37–3.28 (m, 1H), 3.25–3.21 (m, 1H), 2.81 – 2.71 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.0, 161.1, 132.1, 131.4, 129.4, 129.3, 129.2, 128.9, 128.7, 128.4, 56.1, 46.1 (d, $J_{C\text{-}F}$ = 19.6 Hz), 42.3, 29.6; **^{19}F NMR** (471 MHz, $CDCl_3$) δ 53.86; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{16}H_{15}FNO_4S_2$ 368.0421, found 368.0422.

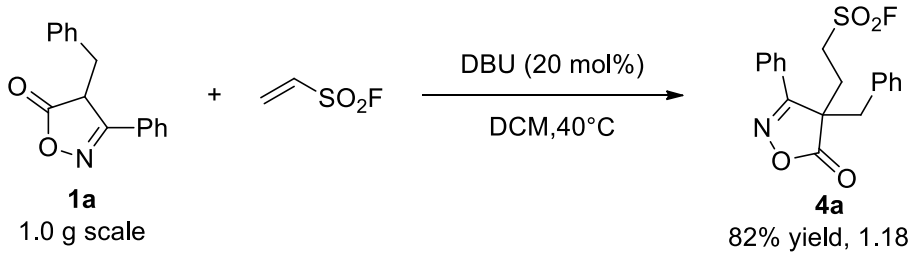
4. Scale-up experiments and tansformations of the product 4a



1a
1.0 g scale

3a
79% yield, 1.14g

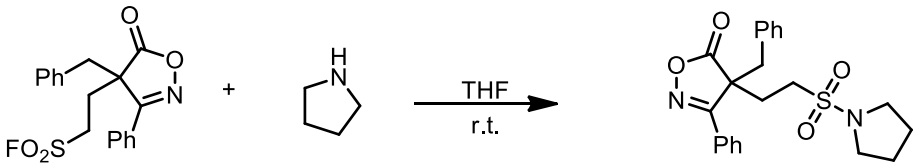
A solution of isoxazolone **1a** (4.0 mmol), ESF (4.0 mmol), and Na_2CO_3 (84.8 mg, 0.8 mmol) in CH_2Cl_2 (40 mL) was stirred at room temperature. After the raw materials are consumed, the solvent was evaporated under vacuum, and the residue was purified by flash column chromatography over silica gel (petroleum ether/ethyl acetate) to afford the product **3a**.



1a
1.0 g scale

4a
82% yield, 1.18 g

A solution of isoxazolone **1a** (4.0 mmol), ESF (4.0 mmol), and DBU (121.6 mg, 0.8 mmol), in CH_2Cl_2 (40 mL), was stirred at 40 °C. After the raw materials were consumed, the solvent was evaporated under vacuum, and the residue was purified by flash column chromatography over silica gel (petroleum ether/ethyl acetate) to afford the product **4a**.



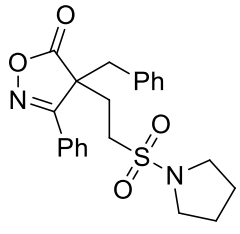
4a

1.5 equiv.

6, 95%

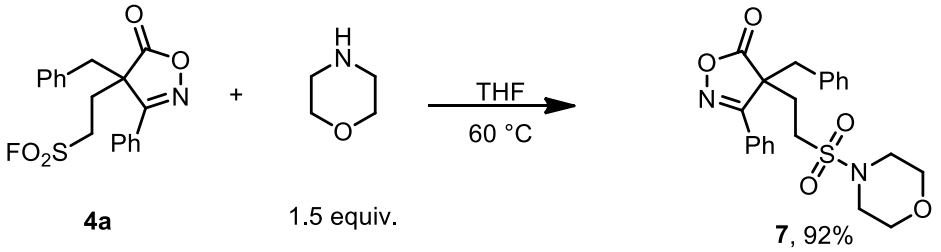
To a solution of **4a** (0.2 mmol) in THF (2 mL) was added pyrrolidine (0.3 mmol). [(2)] The mixture was stirred at room temperature for 12 h. After the reaction was finished, the solvent was removed under vacuum. The residue was then purified by silica gel chromatography (PE:AcOEt = 2:1) to afford **6** with 95% yield.

4-Benzyl-3-phenyl-4-(2-(pyrrolidin-1-ylsulfonyl)ethyl)isoxazol-5(4H)-one (6)



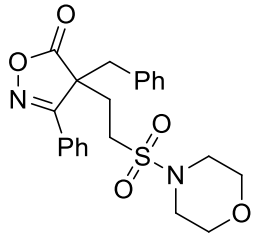
Petroleum ether/ethyl acetate = 2/1 was used as the eluent for column chromatography. White solid (78.3 mg, 95% yield); m.p. 145.8–146.8 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81–7.72 (m, 2H), 7.62–7.50 (m, 3H), 7.23–7.14 (m, 3H), 6.85 (d, J = 7.1 Hz, 2H), 3.28 (dd, J = 15.4, 9.1 Hz, 6H), 2.93–2.83 (m, 1H), 2.81–2.65 (m, 3H), 1.95–1.84 (m, 4H); **^{13}C NMR** (101 MHz,

$CDCl_3$) δ 179.4, 165.7, 132.9, 132.4, 129.7, 129.3, 128.7, 128.1, 127.6, 126.7, 56.6, 47.8, 44.7, 42.2, 30.1, 25.8; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{22}H_{25}N_2O_4S$ 413.1530, found 413.1536.

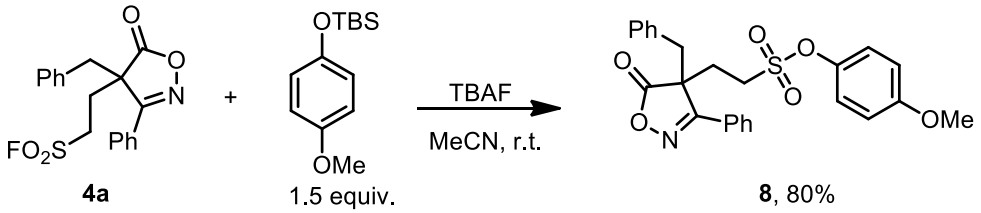


To a solution of **4a** (0.2 mmol) in THF (2 mL) was added morpholine (0.3 mmol). The mixture was stirred at 60℃ for 12 h. The solvent was then removed under vacuum. The residue was purified by silica gel chromatography (PE:AcOEt = 1:1) to afford **7** with 92% yield.

4-Benzyl-4-(2-(morpholinosulfonyl)ethyl)-3-phenylisoxazol-5(4H)-one (7)

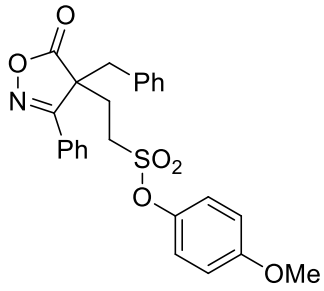


Petroleum ether/ethyl acetate = 1/1 was used as the eluent for column chromatography. White solid (78.8 mg, 92% yield); m.p. 153.6–154.6 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81–7.74 (m, 2H), 7.64–7.51 (m, 3H), 7.23–7.14 (m, 3H), 6.85 (d, J = 7.1 Hz, 2H), 3.75–3.65 (m, 4H), 3.37–3.28 (m, 2H), 3.23–3.13 (m, 4H), 2.87–2.65 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.3, 165.5, 132.7, 132.5, 129.7, 129.2, 128.7, 128.1, 127.6, 126.7, 66.4, 56.5, 45.7, 44.3, 42.2, 29.8; **HRMS (ESI)** m/z: $[M+H]^+$ calculated for $C_{22}H_{25}N_2O_5S$ 429.1479, found 429.1474.



To a solution of **4a** (0.2 mmol), tetrabutylammonium fluoride (TBAF) (0.02 mmol) in THF (2 mL) was added *p*-methoxyphenyl TBS ether (0.3 mmol). [(3)] The mixture was stirred at room temperature for 6 h. The solvent was removed under vacuum. The residue was then purified by silica gel chromatography (PE:AcOEt = 15:1) to afford **8** with 80% yield.

4-Methoxyphenyl 2-(4-benzyl-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonate (8)

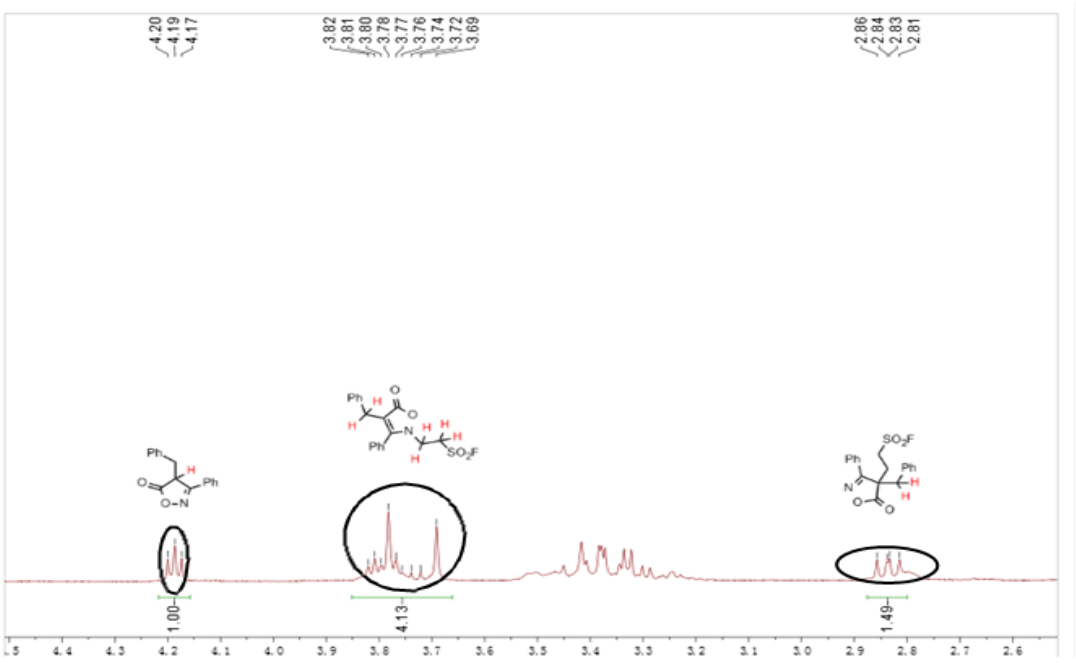


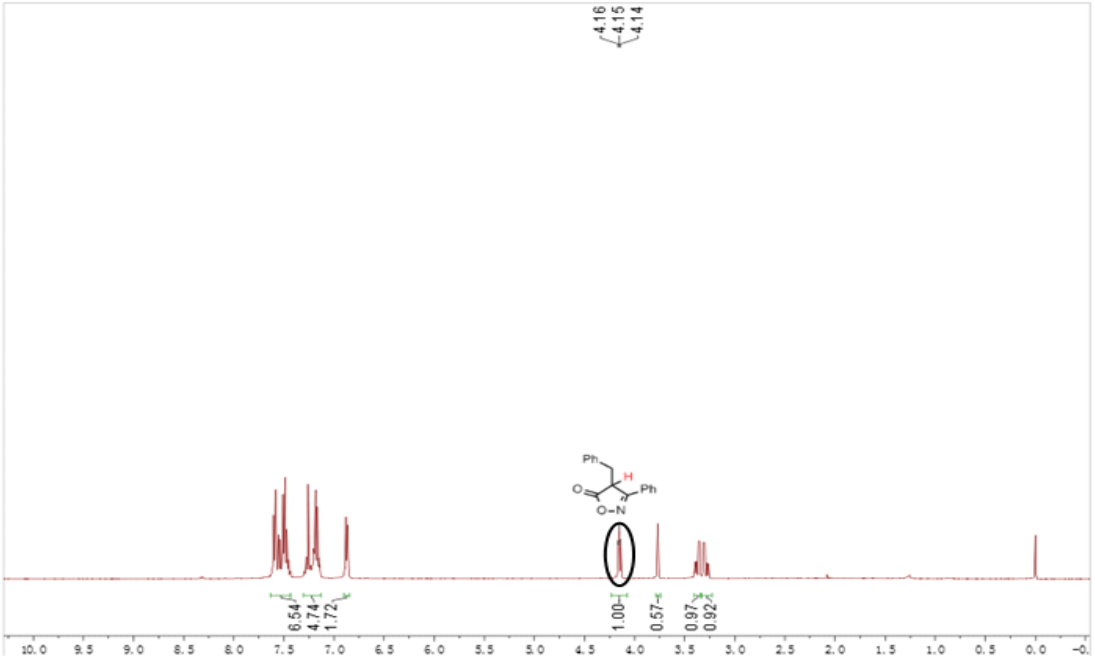
Petroleum ether/ethyl acetate = 15/1 was used as the eluent for column chromatography. White solid (74.4 mg, 80% yield); m.p. 153.6–154.6 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92–7.69 (m, 2H), 7.64–7.61 (m, 1H), 7.58–7.54 (m, 2H), 7.24–7.13 (m, 3H), 7.12–7.01 (m, 2H), 6.95–6.74 (m, 4H), 3.80 (s, 3H), 3.38 (q, J = 13.7 Hz, 2H), 3.19–3.07 (m, 1H), 3.06–2.94 (m, 1H), 2.93–2.79 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 179.1, 165.0, 158.6, 142.2, 132.6, 132.5, 129.8, 129.2, 128.7, 128.2, 127.4, 126.6, 122.9, 115.0, 56.3, 55.7, 45.0, 42.3, 30.2; **HRMS (ESI)** m/z: $[M+Na]^+$ calculated for $C_{25}H_{23}NO_6SNa$ 488.1138, found 488.1133.

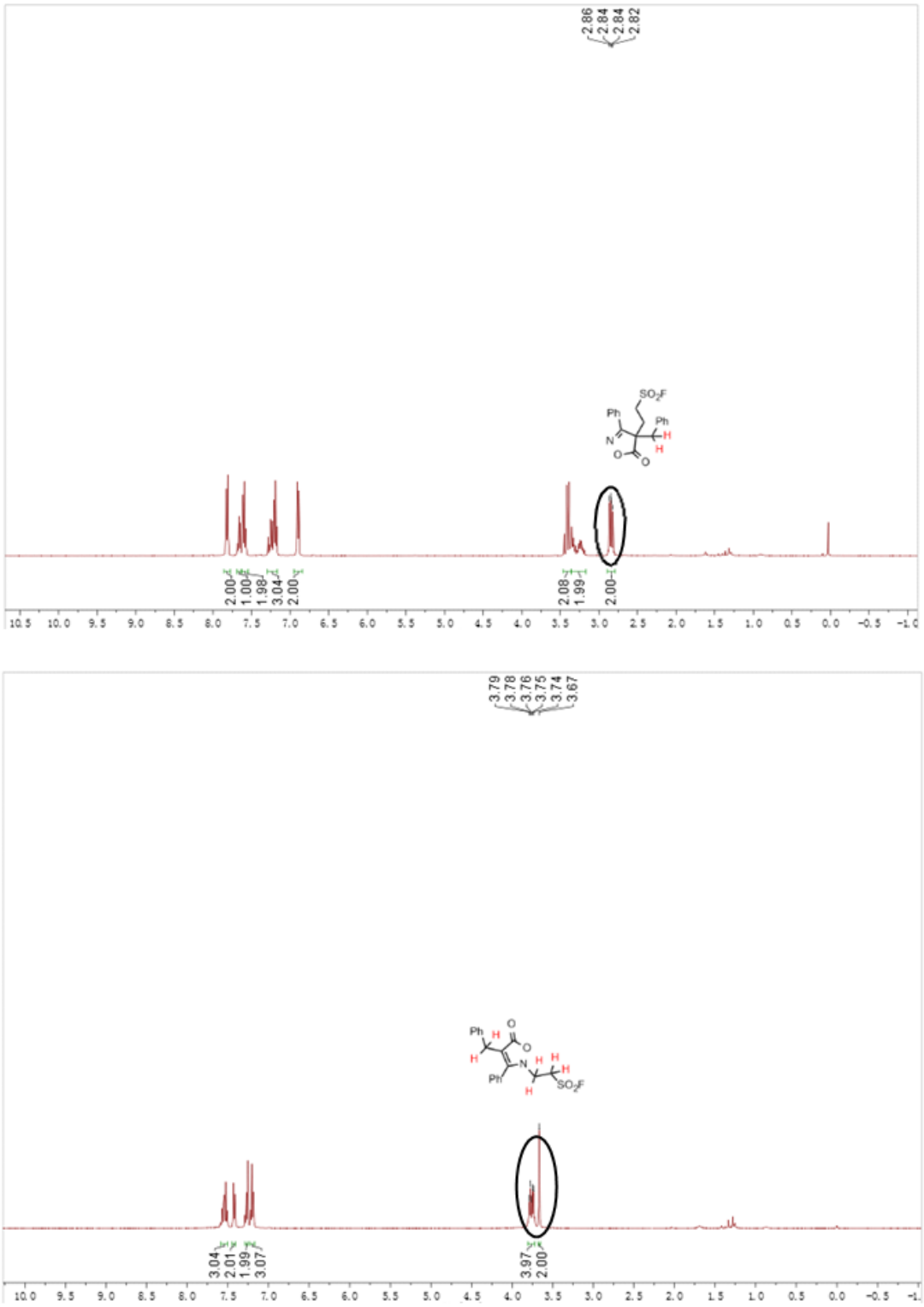
5. Experiments for Mechanism

5.1 Verification experiments of reverse aza-Michael addition

A solution of **3a** (0.1 mmol) and DBU (0.02 mmol) in CH_2Cl_2 (1.0 mL) was stirred at room temperature. After 1.5 h, the reaction mixture was neutralized by HCl (1 M). Starting material **1a** and product **4a** were detected from TLC. The signals of the hydrogens of **1a**, **3a** and **4a** were found by **^{1}H NMR** (400 MHz, $CDCl_3$) analysis (as indicated by the red marks).



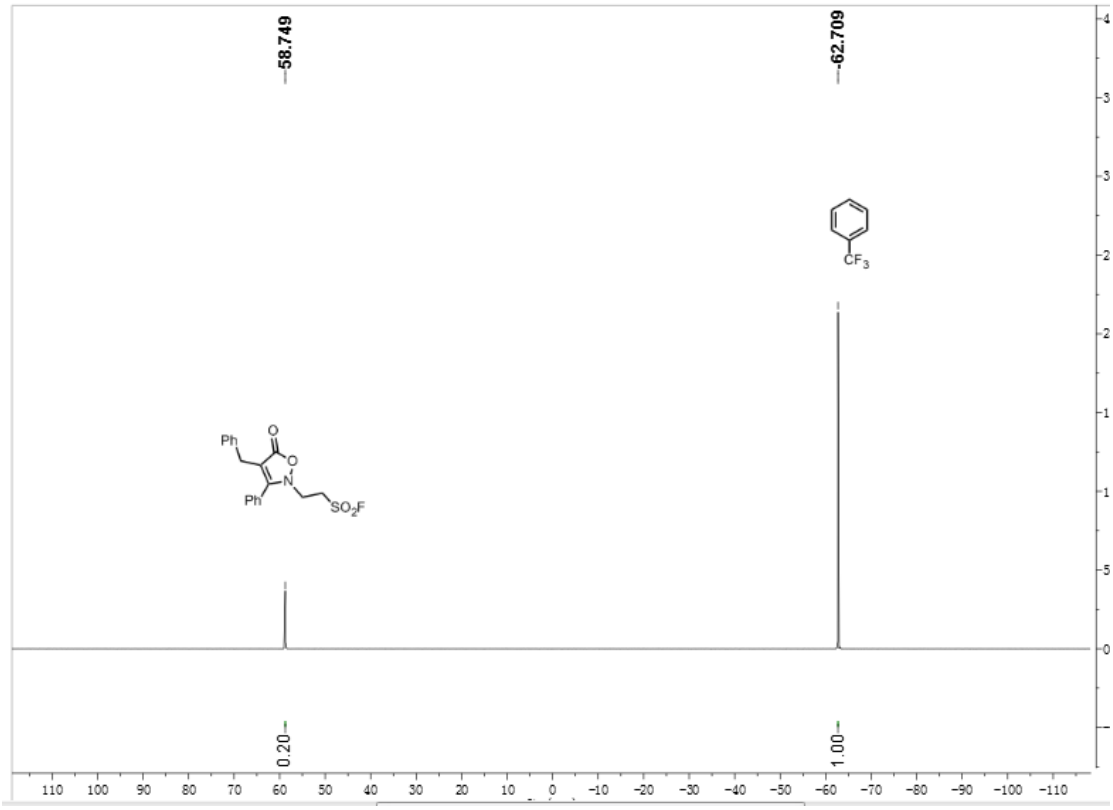




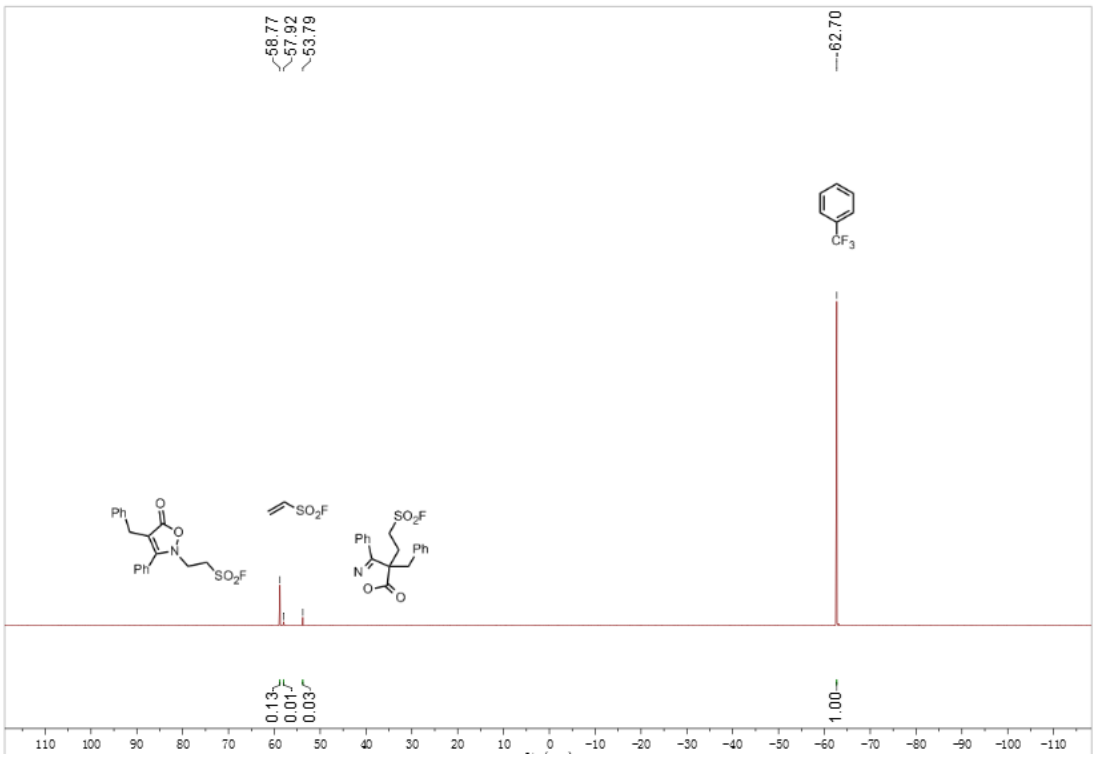
5.2 Kinetic experiments

Using trifluorotoluene as the internal standard, the conversion rate of **3a** to **4a** was determined by ^{19}F NMR spectroscopy. The F signals of **3a** and **4a** together with a small amount of ESF were detected. The reaction was determined to be first order in **3a**.

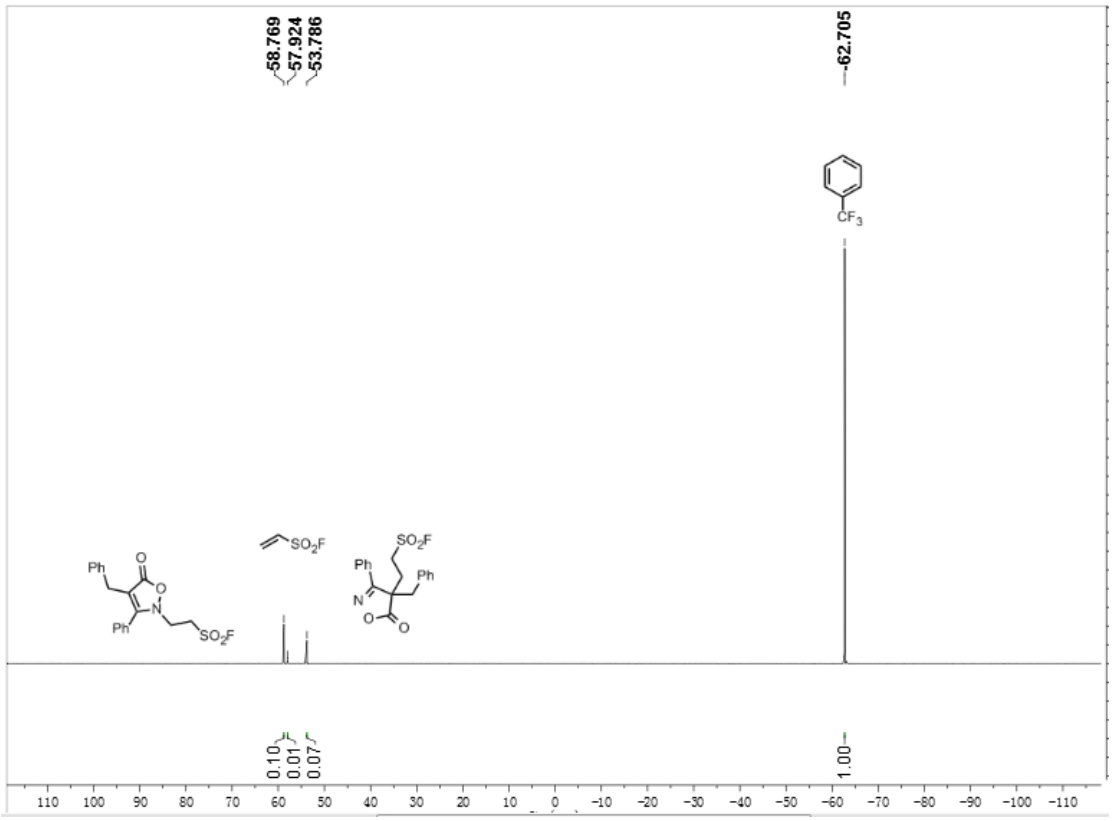
0 min:


-58.749
-62.709
Ph
O
O
N
Ph
SO2F
CF3
0.20
1.00

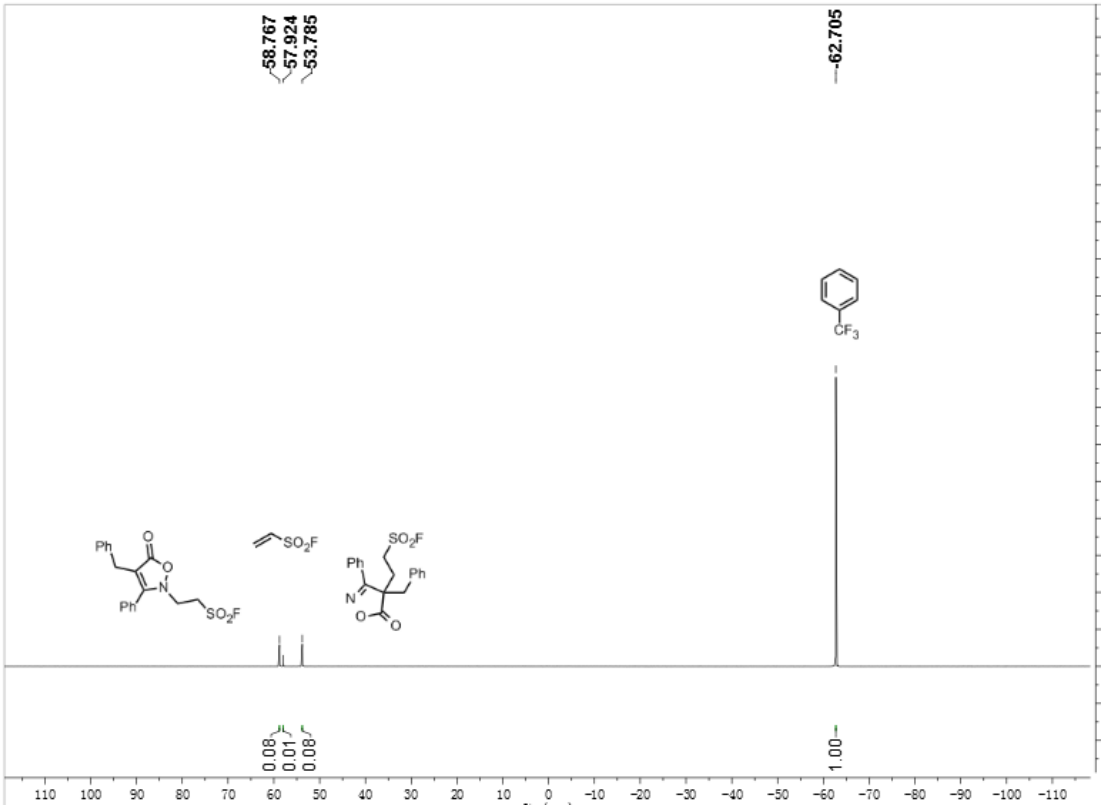
5 min:


-58.77
-57.92
-53.79
-62.70
Ph
O
O
N
Ph
SO2F
SO2F
SO2F
Ph
Ph
N
O
O
CF3
0.13
0.01
0.03
1.00

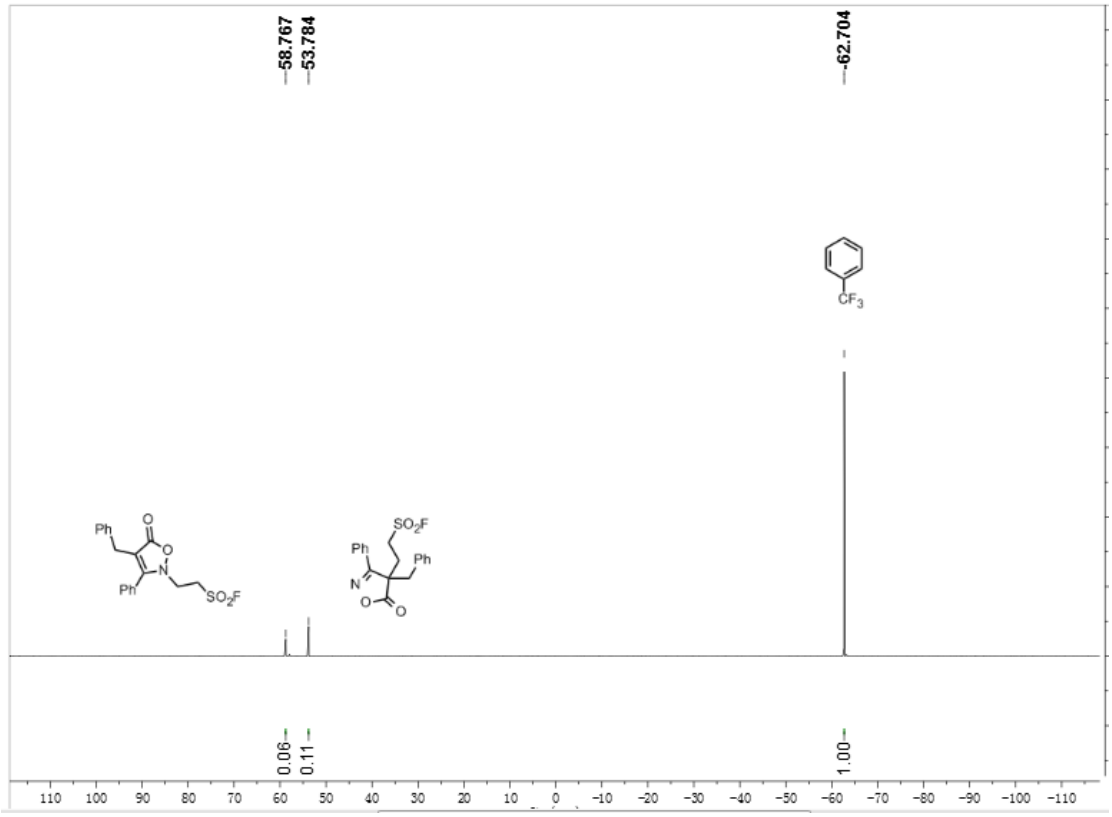
10 min:


-58.769
-57.924
-53.786
-62.705
0.10
0.01
0.07
1.00

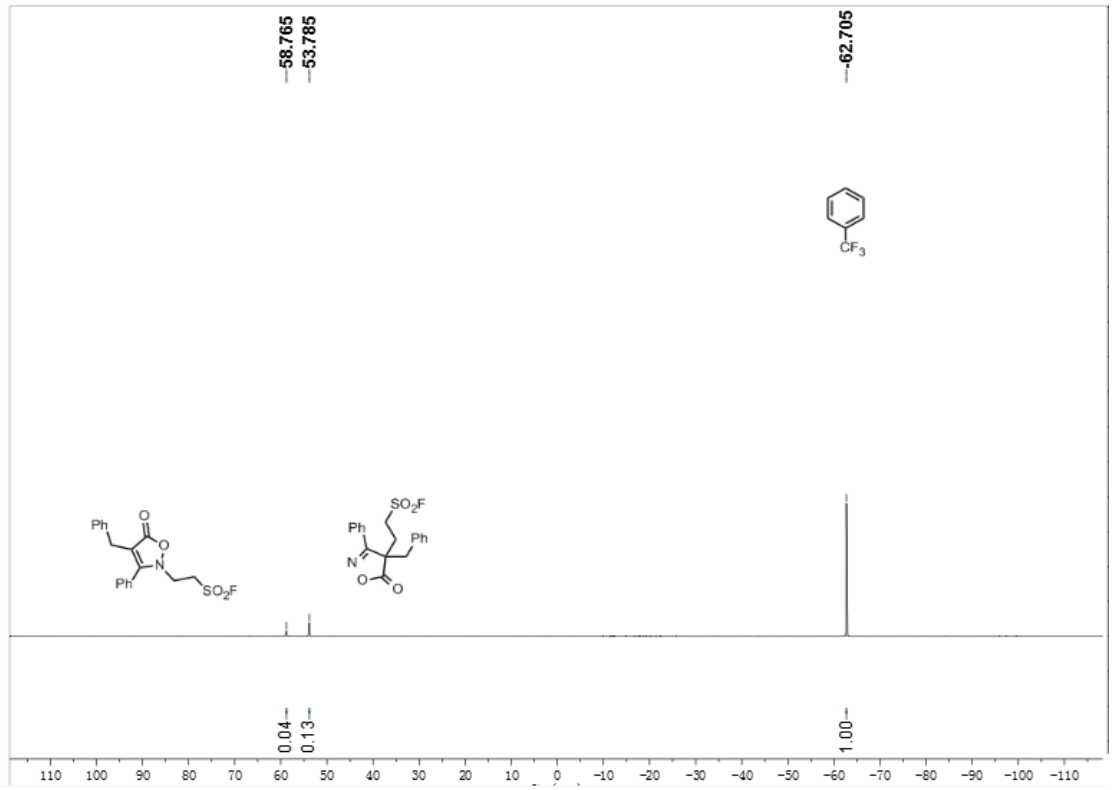
15 min:


-58.767
-57.924
-53.785
-62.705
0.08
0.01
0.08
1.00

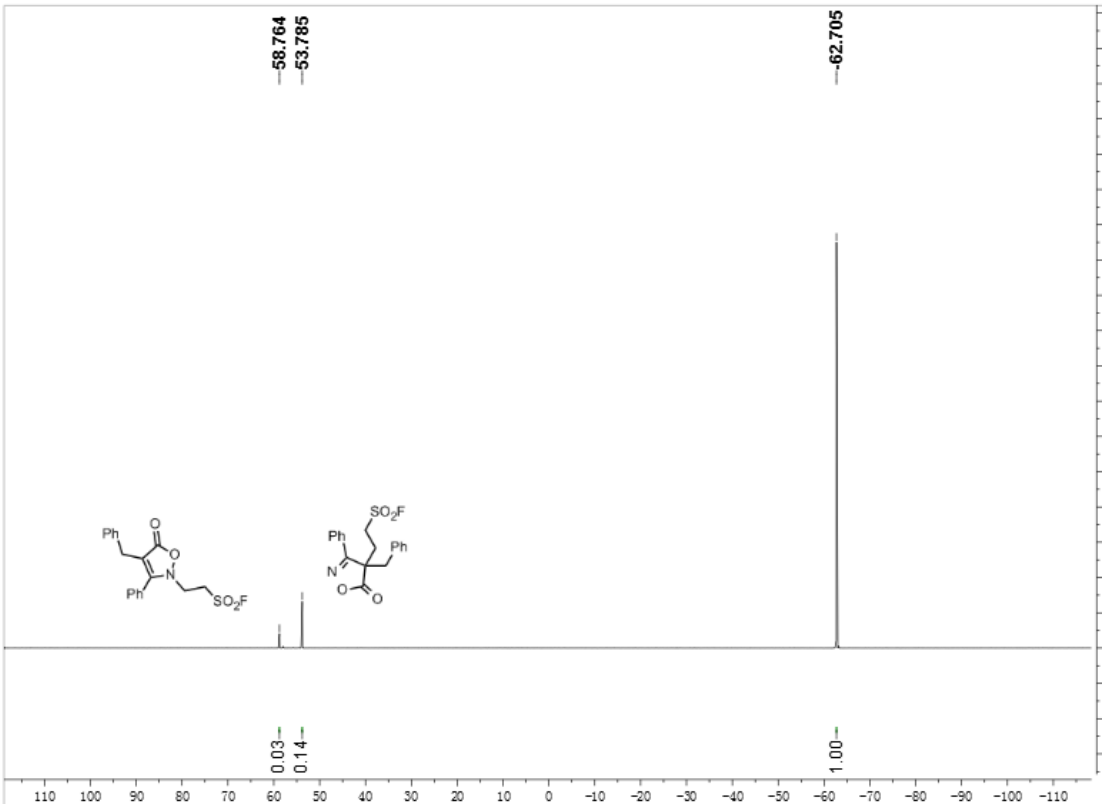
20 min:


-58.767
-53.784
-62.704
CF3
Ph
O
O
N
Ph
SO2F
SO2F
Ph
Ph
N
O
O
0.06
0.11
1.00
110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110

25 min:


-58.765
-53.785
-62.705
CF3
Ph
O
O
N
Ph
SO2F
SO2F
Ph
Ph
N
O
O
0.04
0.13
1.00
110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110

30 min:



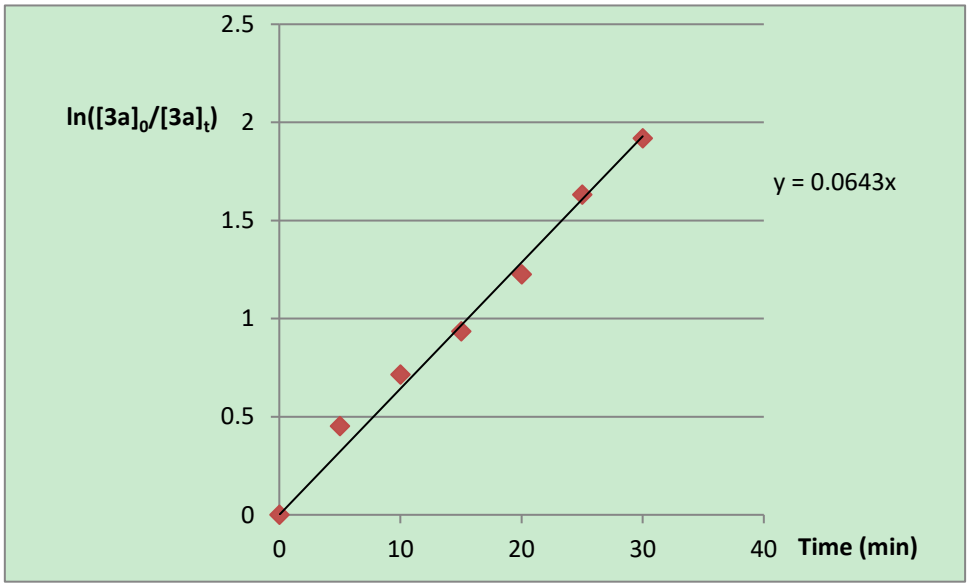


Figure S1: First-order kinetics

6. References

(1) Hellmuth, T.; Frey, W.; Peters, R. Regioselective catalytic asymmetric C-alkylation of isoxazolinones by a base-free palladacycle-catalyzed direct 1,4-addition. *Angew. Chem. Int. Ed. Engl.* **2015**, 54, 2788-2791.

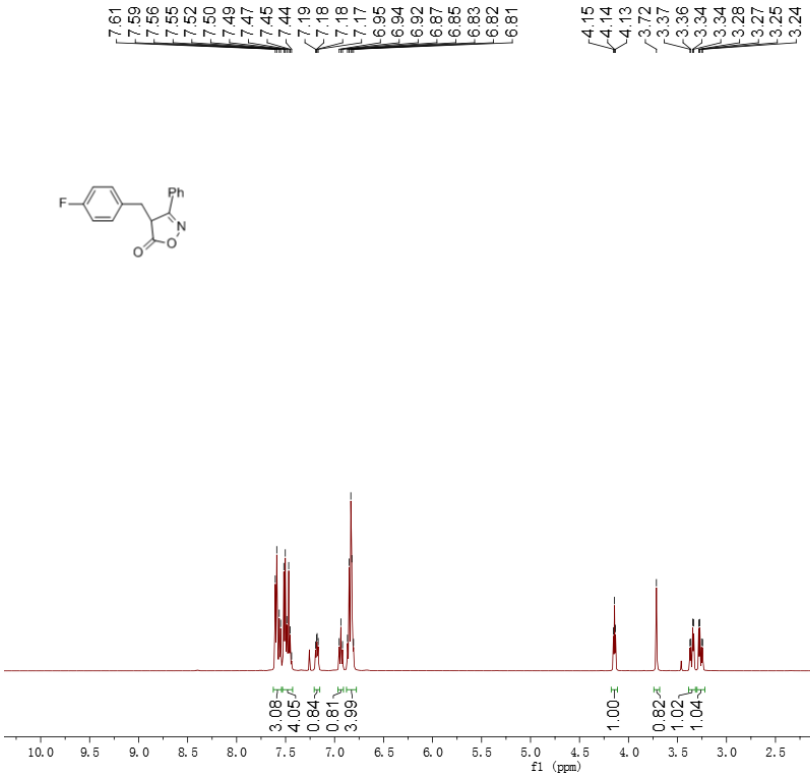
(2) Zhu, D. Y.; Zhang, X. J.; Yan, M. Enantioselective Addition of Azlactones to Ethylene Sulfonyl Fluoride via Dual Catalysis. *Org. Lett.* **2021**, 23, 4228-4232.

(3) Chen, J.; Huang, B. Q.; Wang, Z. Q.; Zhang, X. J.; Yan, M. Asymmetric Conjugate Addition of Ethylene Sulfonyl Fluorides to 3-Amido-2-oxindoles: Synthesis of Chiral Spirocyclic Oxindole Sultams. *Org. Lett.* **2019**, 21, 9742-9746.

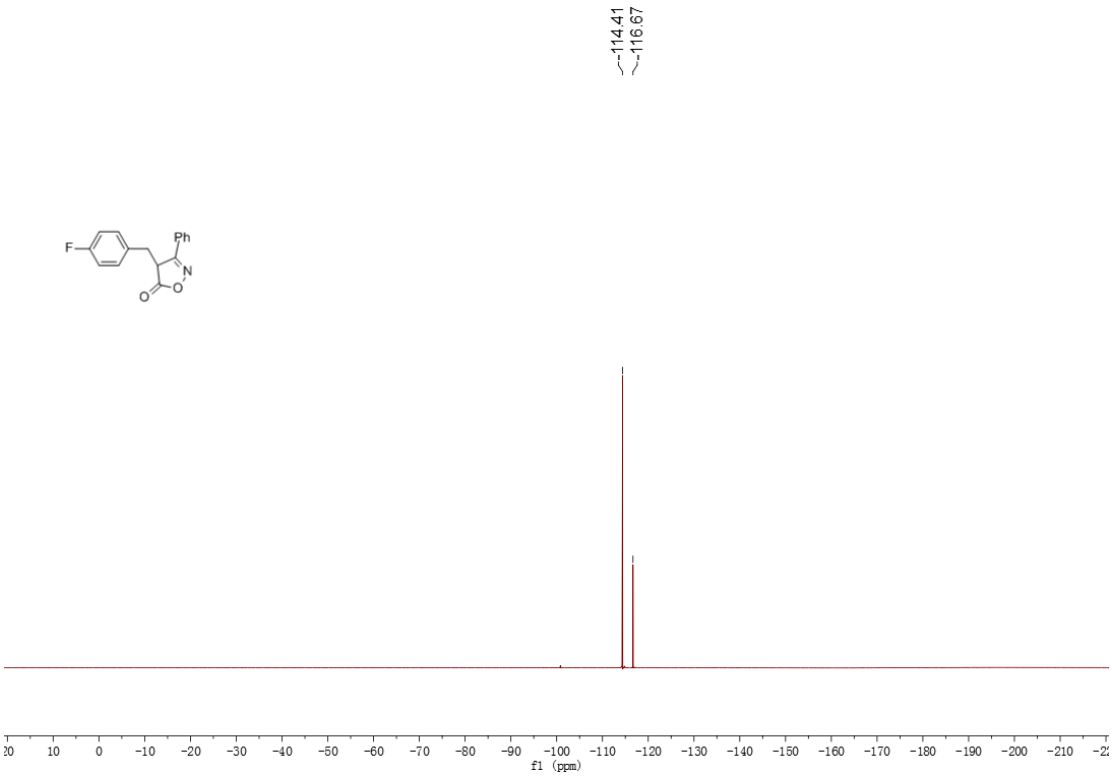
7. NMR Spectra

4-(4-Fluorobenzyl)-3-phenylisoxazol-5(4H)-one (1d)

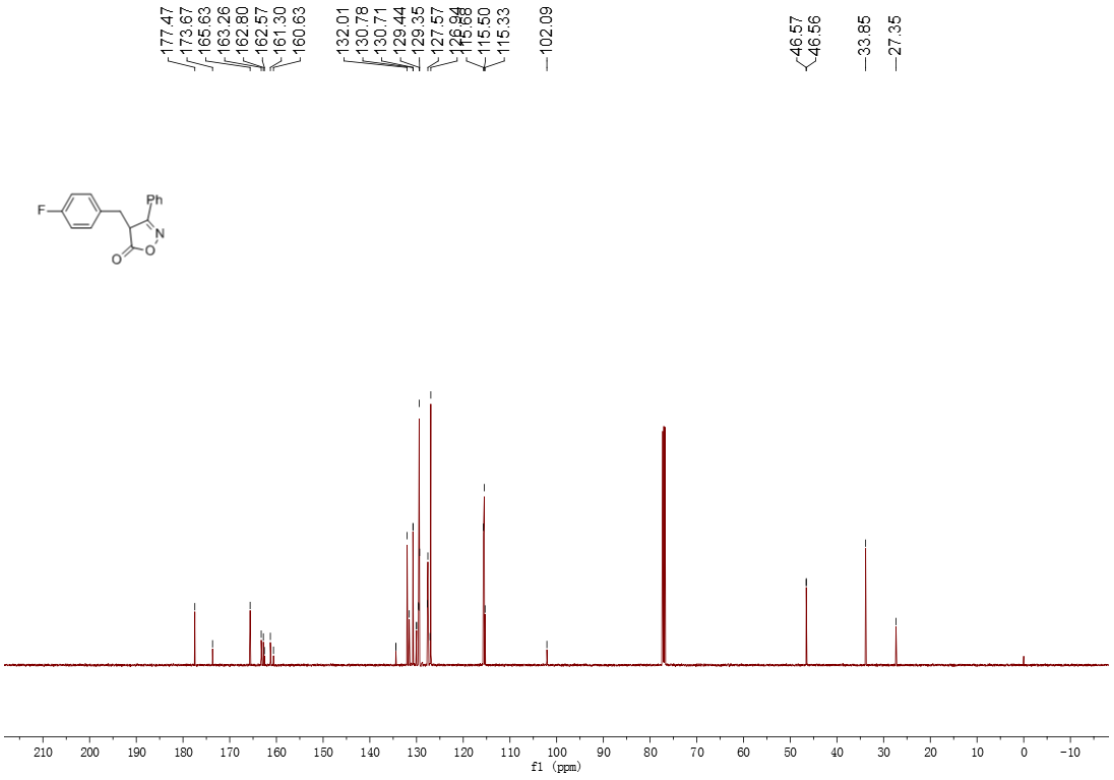
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

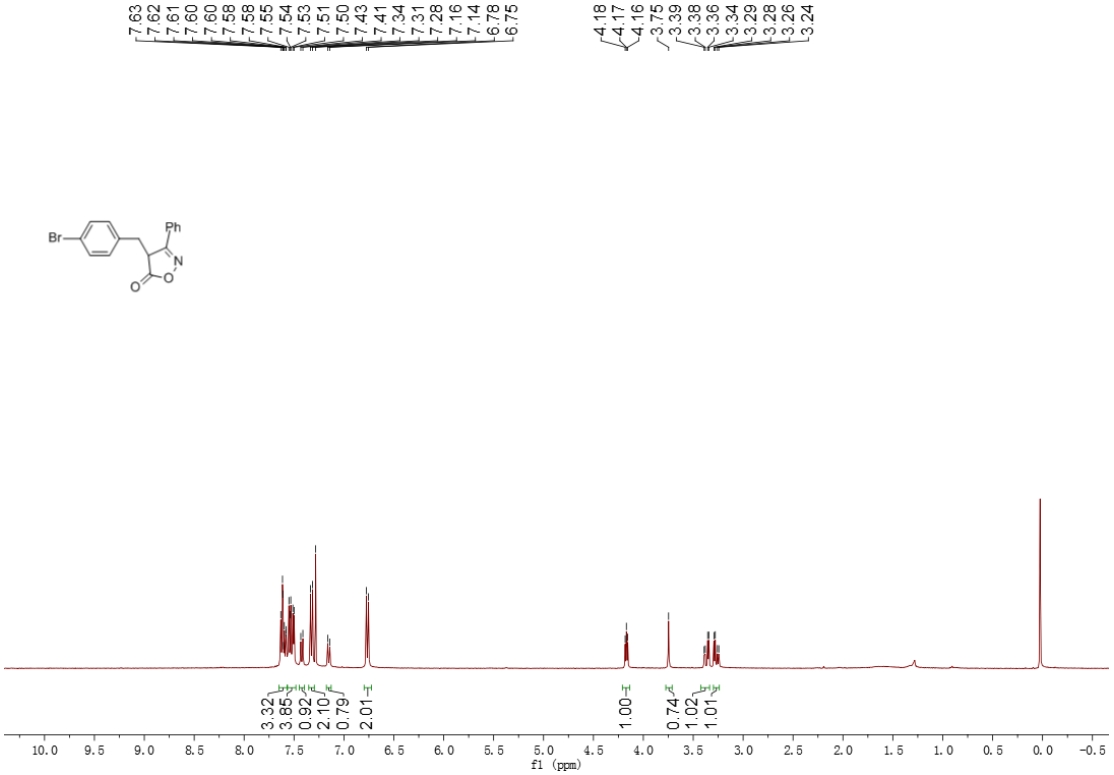


^{13}C NMR (101 MHz, $CDCl_3$)

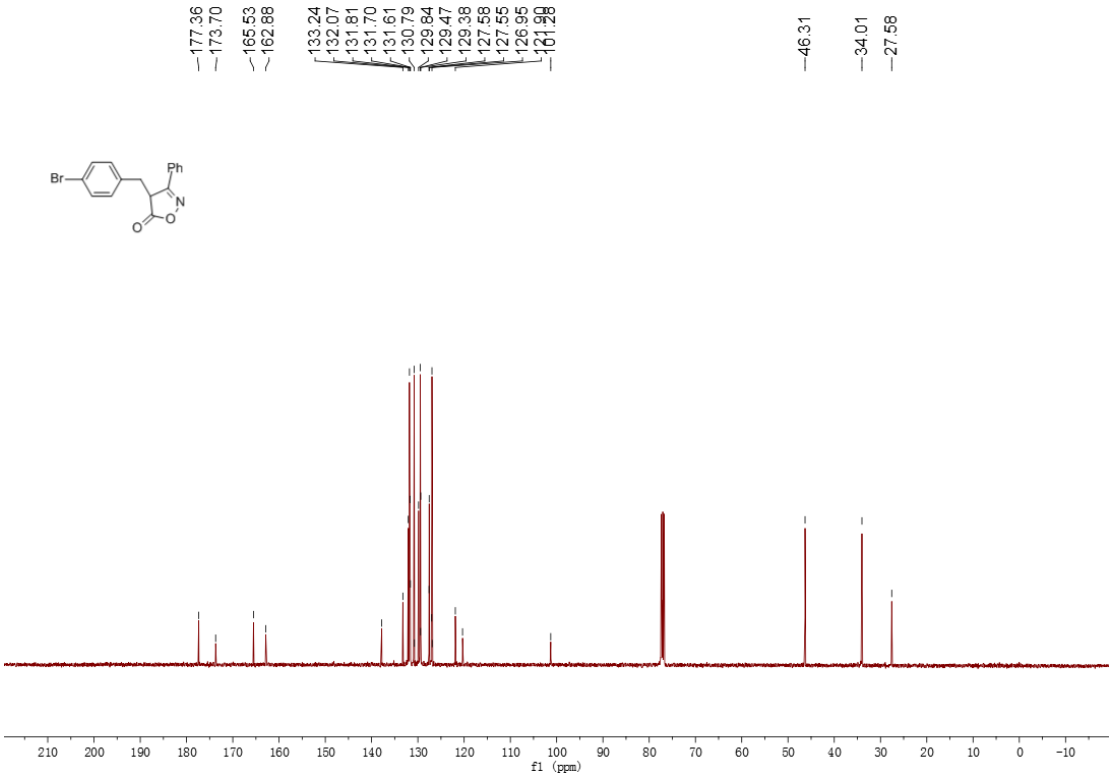


4-(4-Bromobenzyl)-3-phenylisoxazol-5(4H)-one (1f)

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

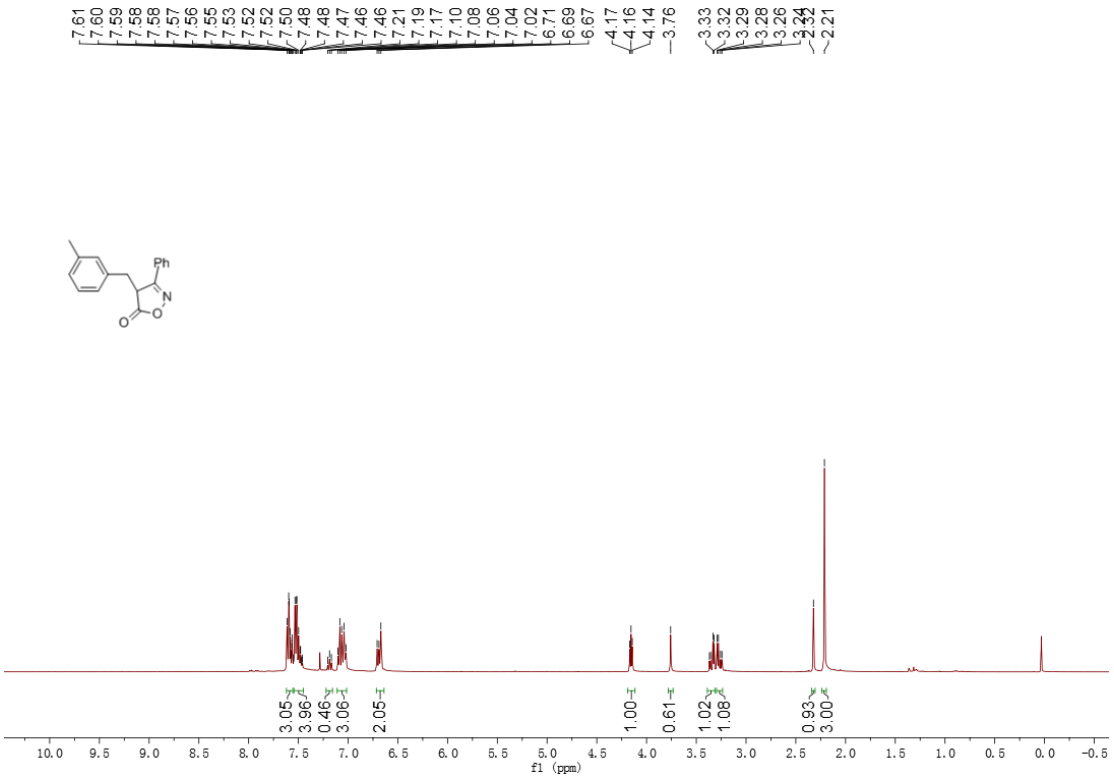


^{13}C NMR (101 MHz, $CDCl_3$)

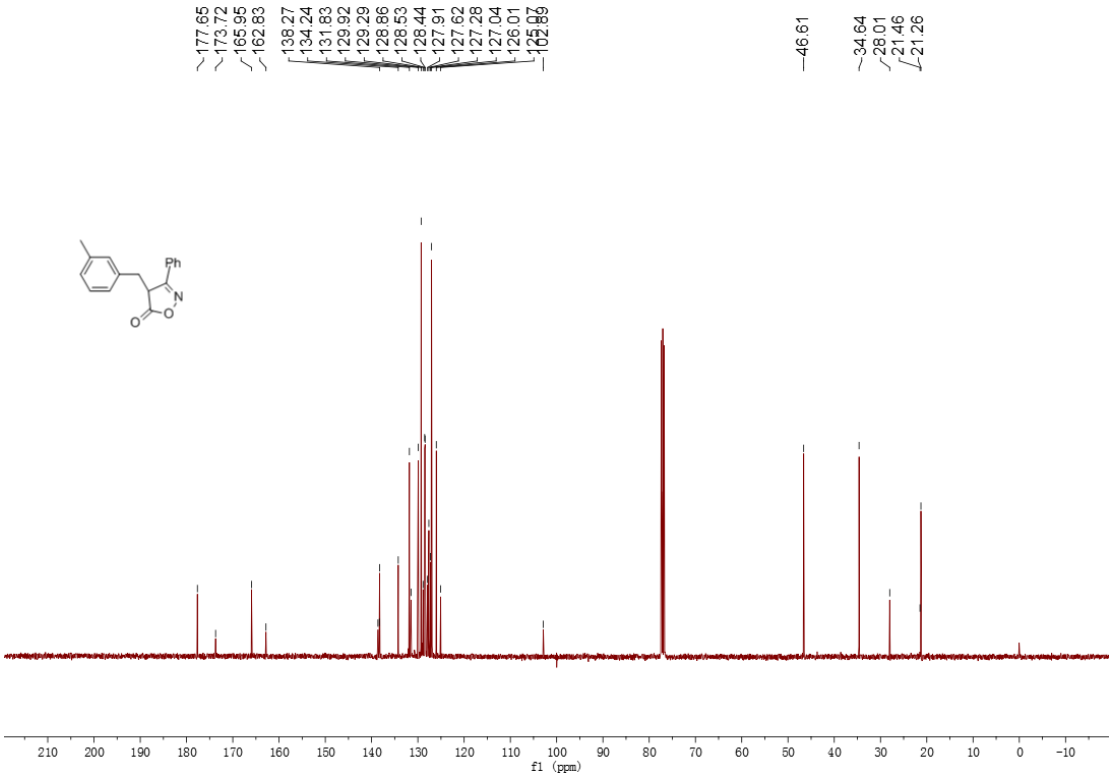


4-(3-Methylbenzyl)-3-phenylisoxazol-5(4H)-one (1g)

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

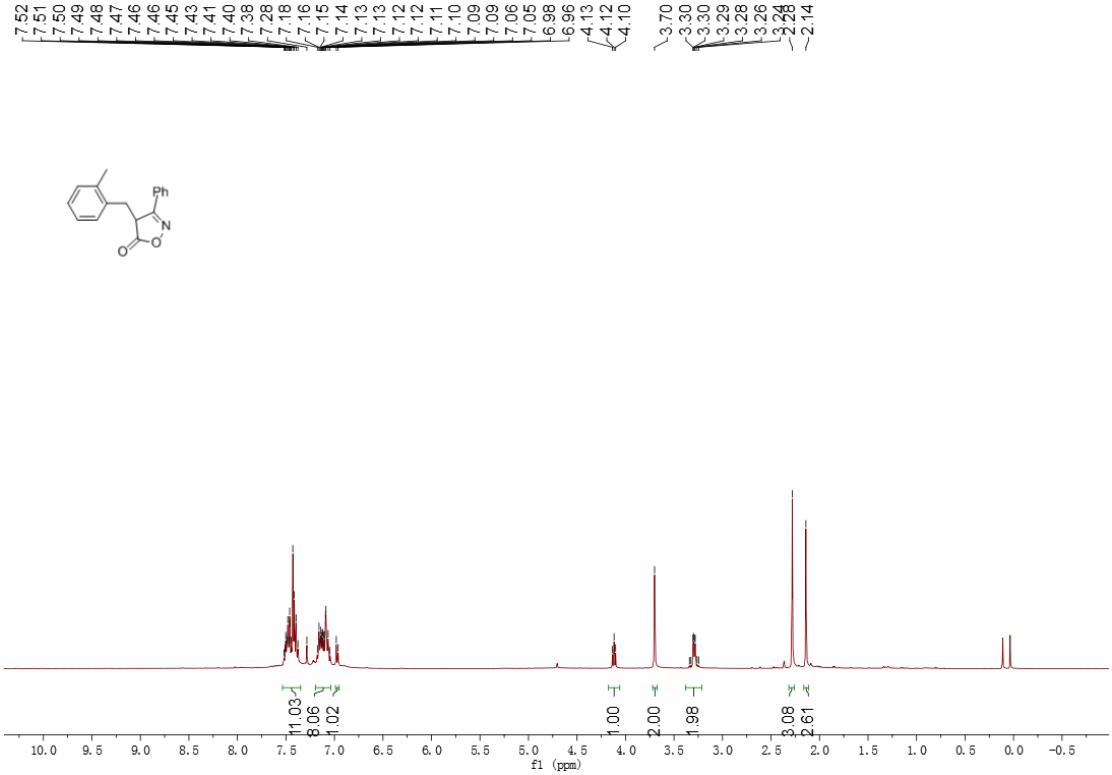


^{13}C NMR (101 MHz, $CDCl_3$)

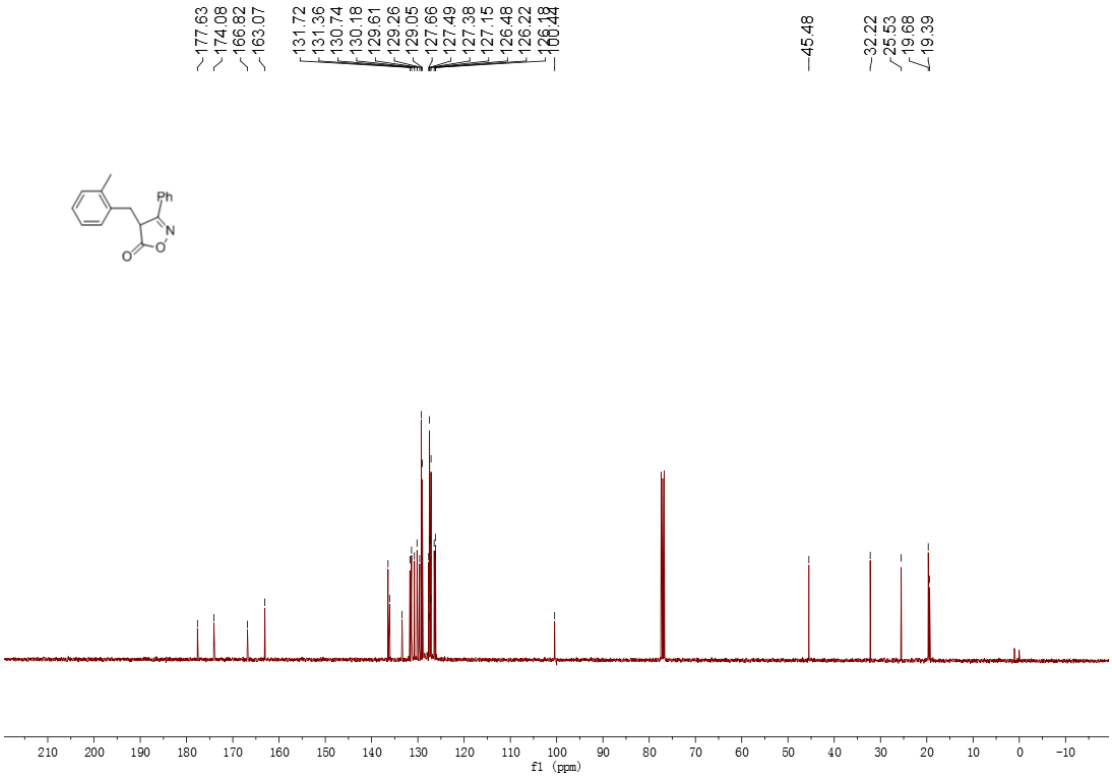


4-(2-Methylbenzyl)-3-phenylisoxazol-5(4H)-one (1h)

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

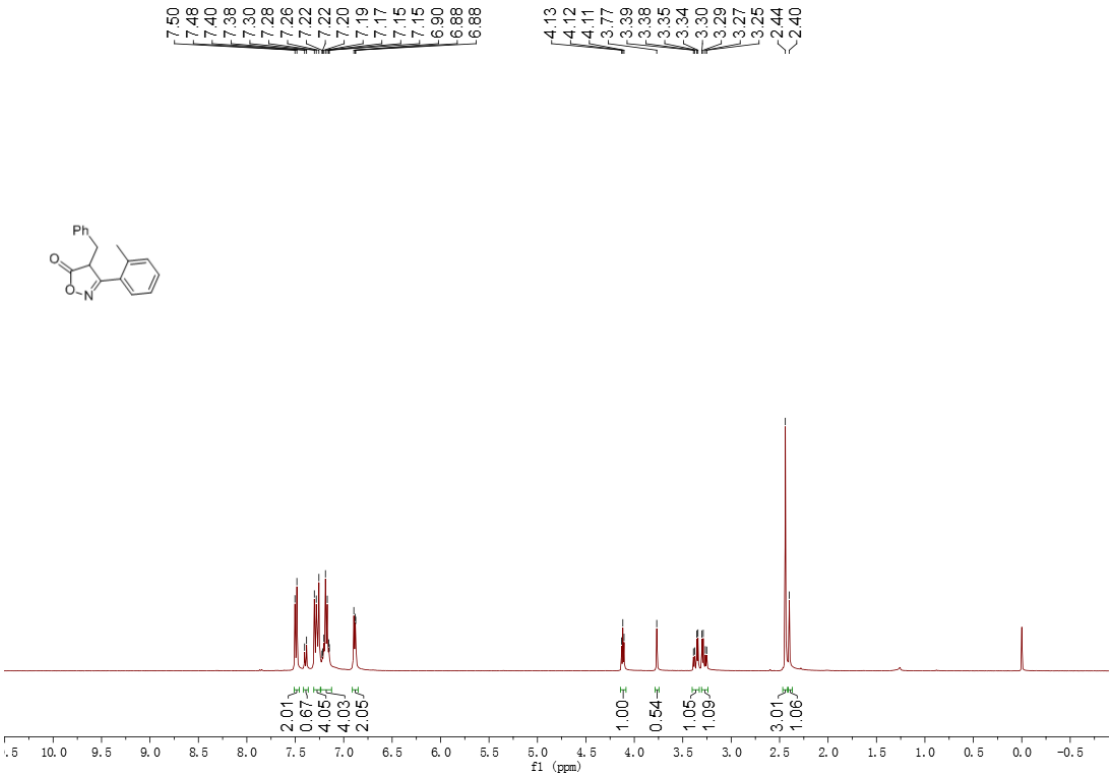


^{13}C NMR (101 MHz, $CDCl_3$)

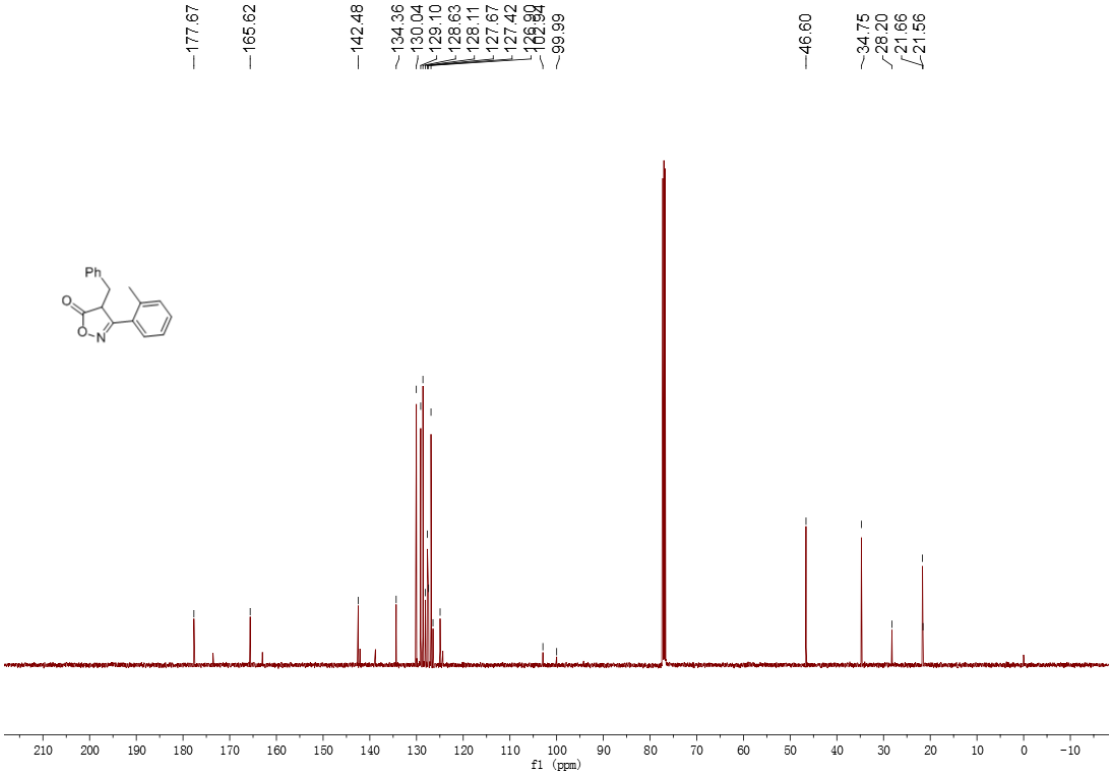


4-Benzyl-3-(o-tolyl)isoxazol-5(4H)-one (1i)

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

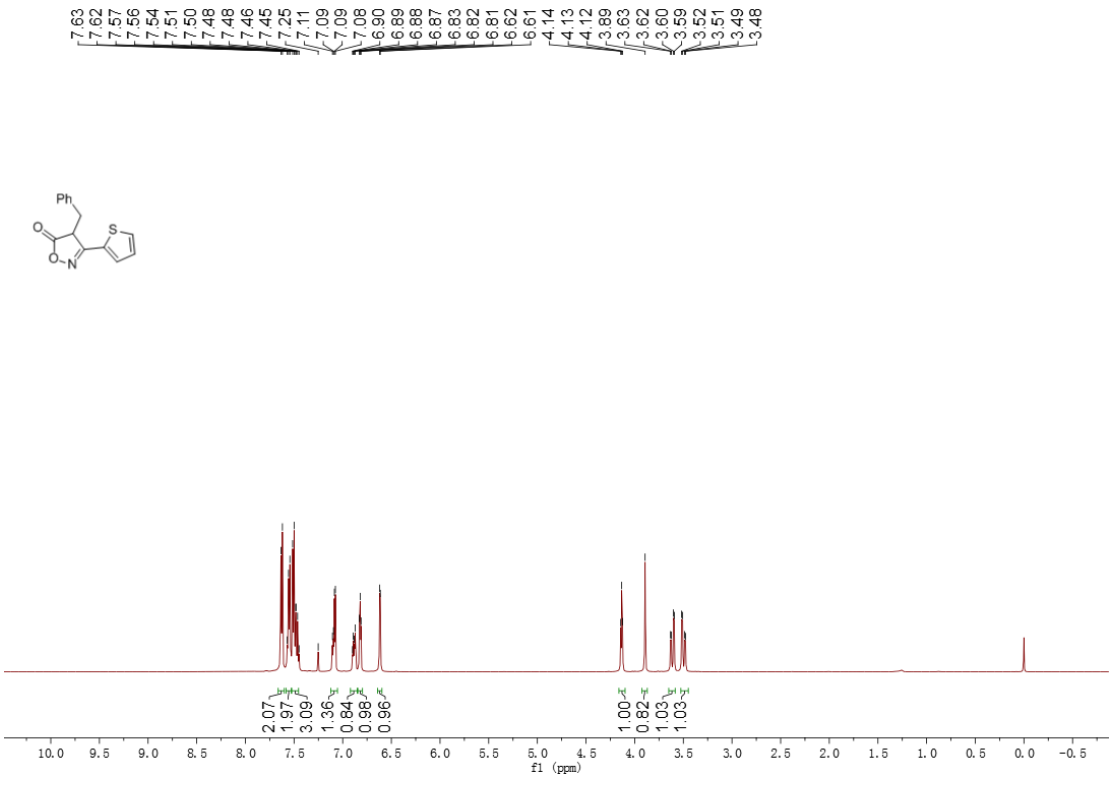


^{13}C NMR (101 MHz, $CDCl_3$)

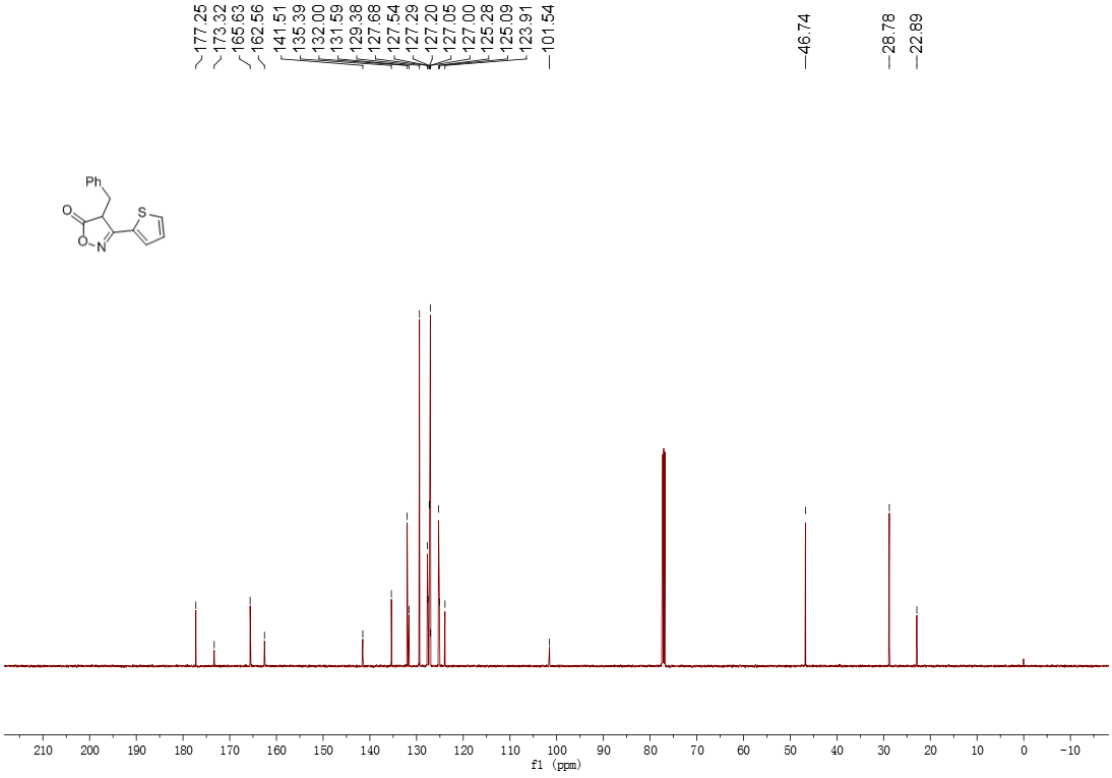


4-Benzyl-3-(thiophen-2-yl)isoxazol-5(4H)-one (1q)

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

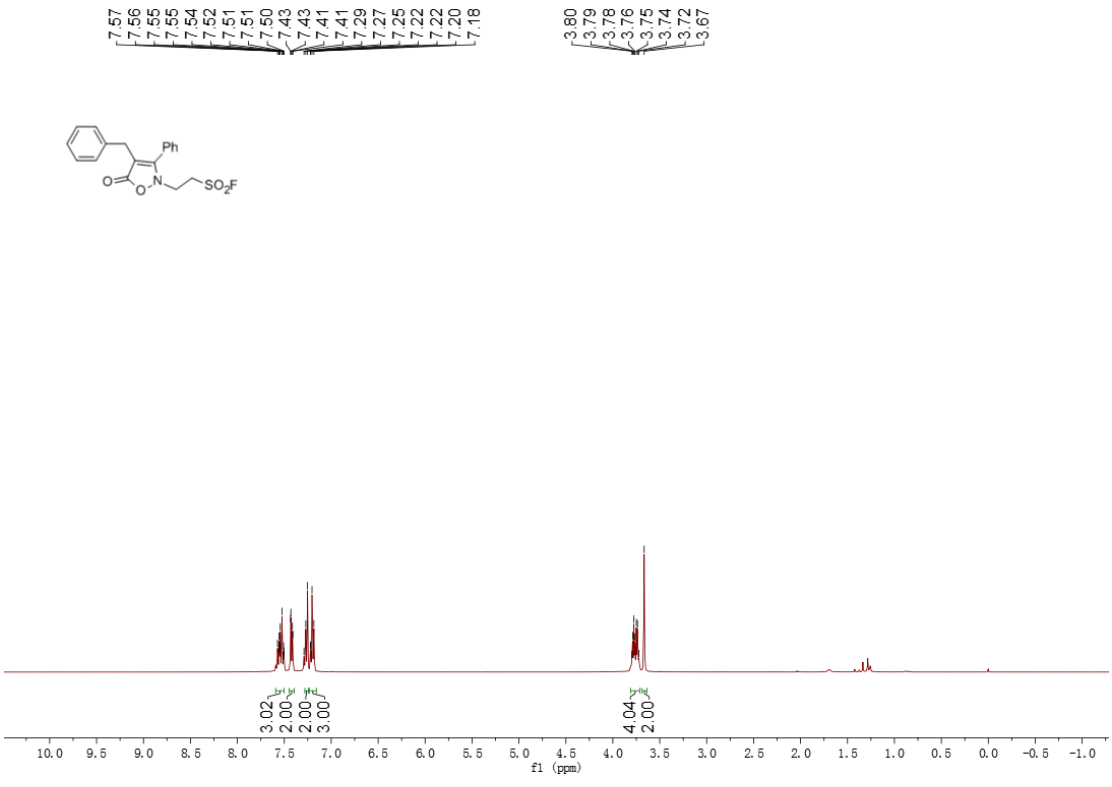


^{13}C NMR (101 MHz, $CDCl_3$)

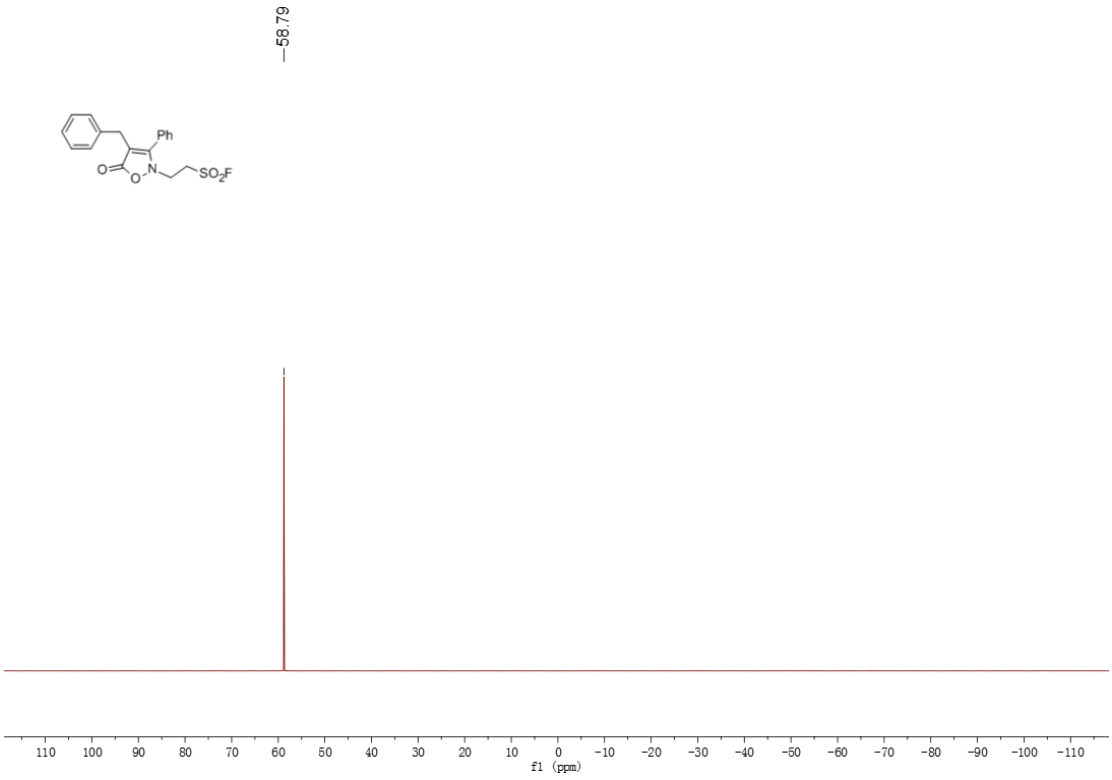


2-(4-Benzyl-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3a)

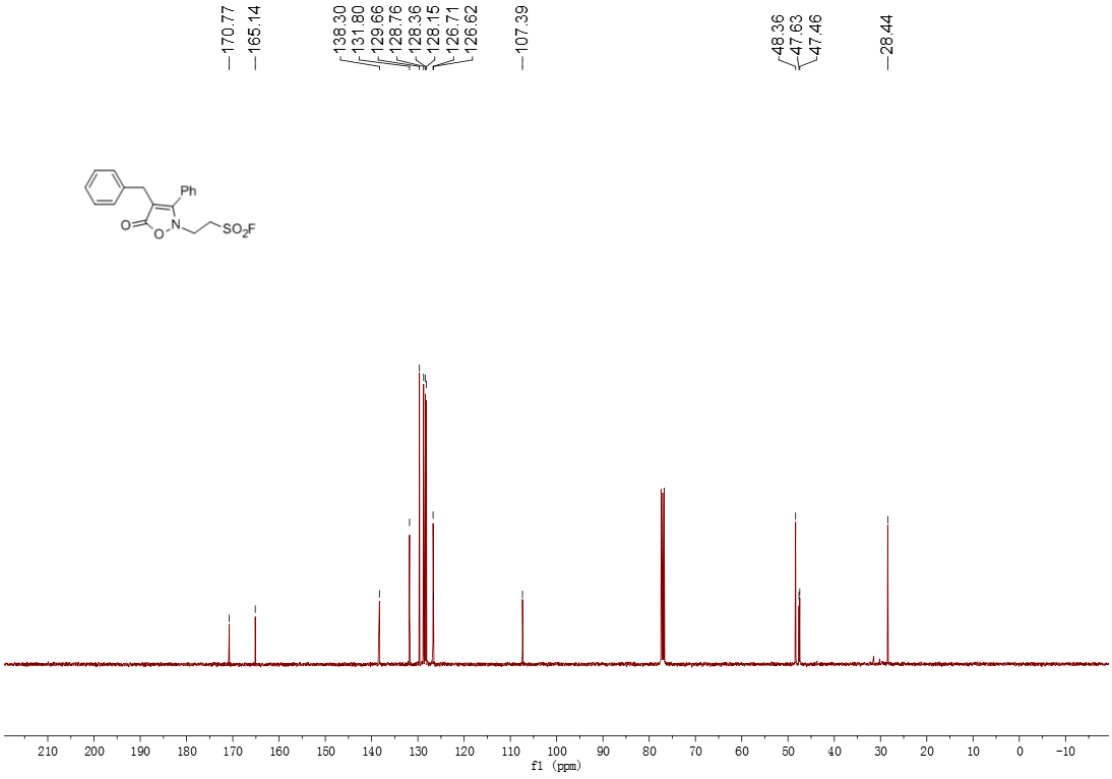
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

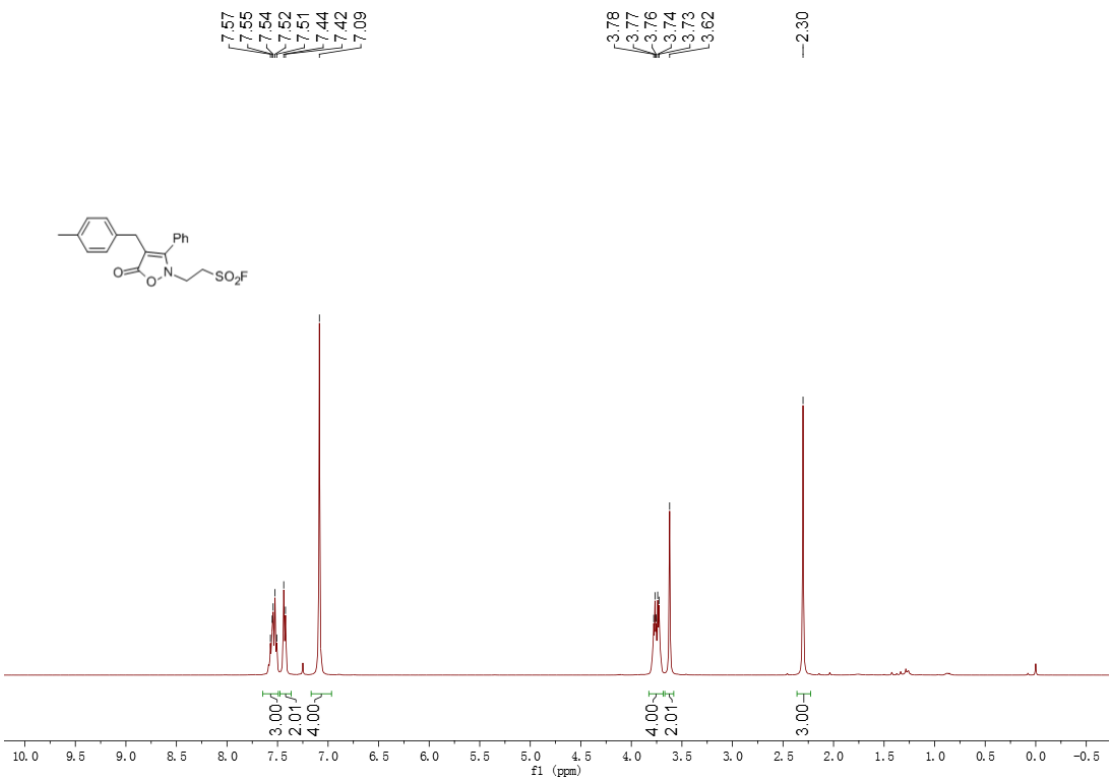


^{13}C NMR (101 MHz, $CDCl_3$)

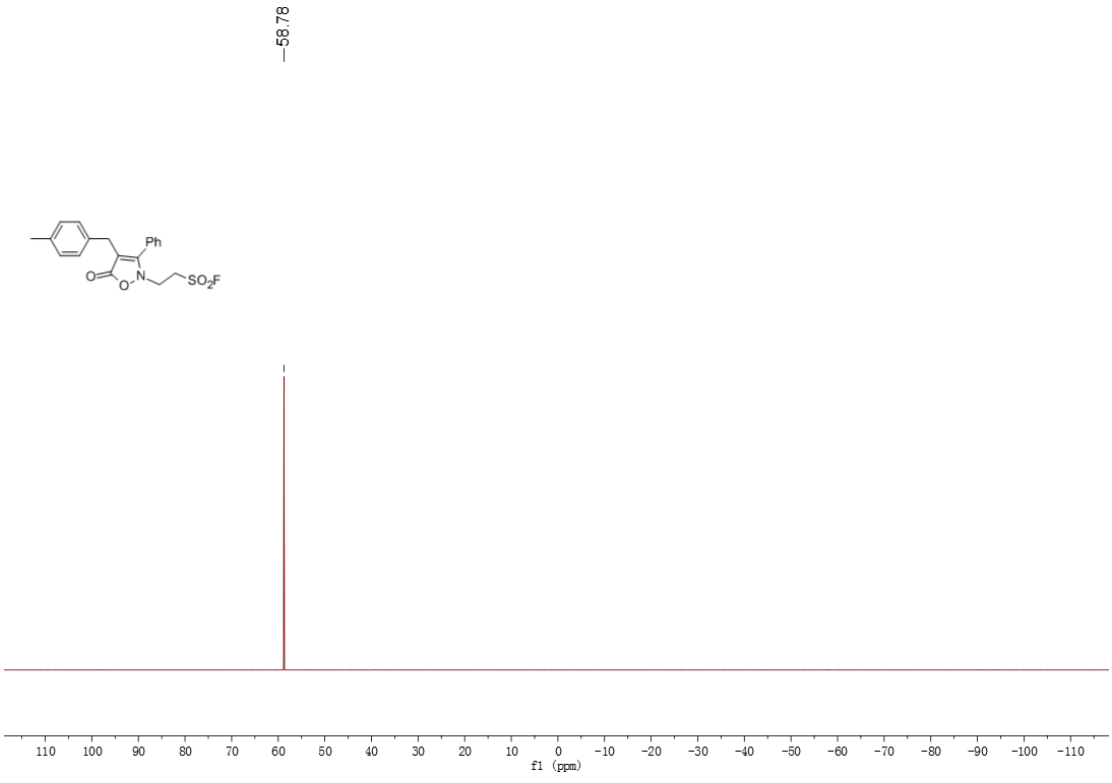


2-(4-(4-Methylbenzyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3b)

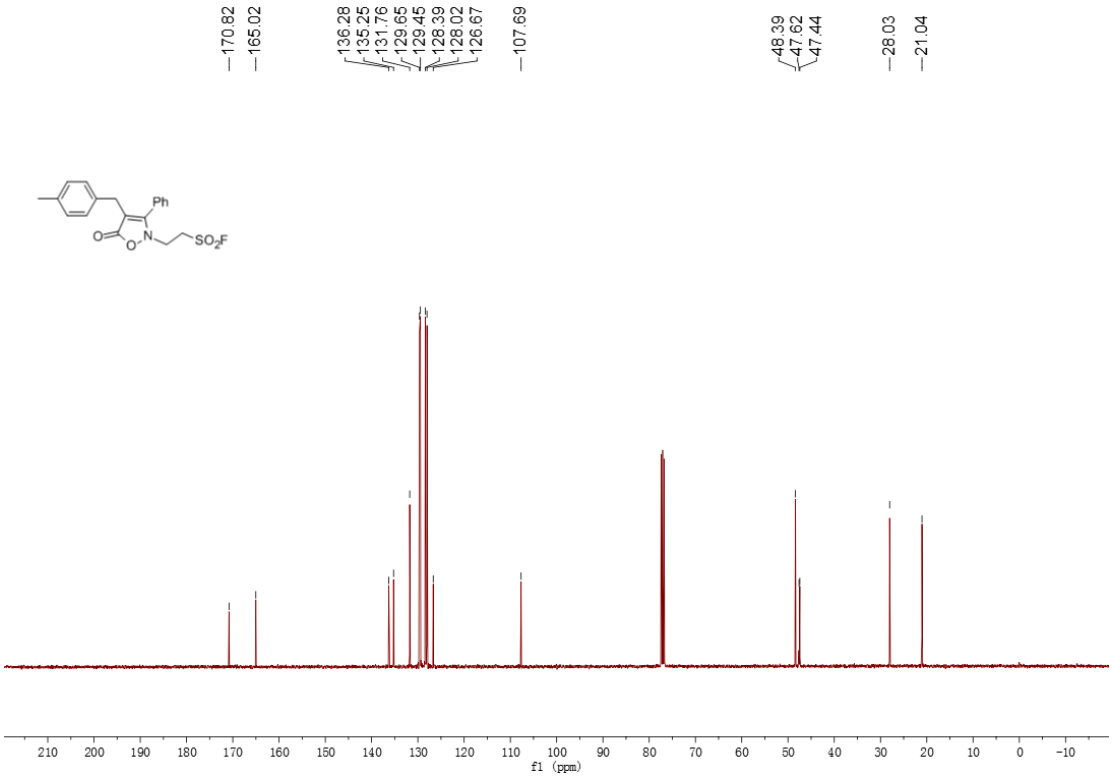
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

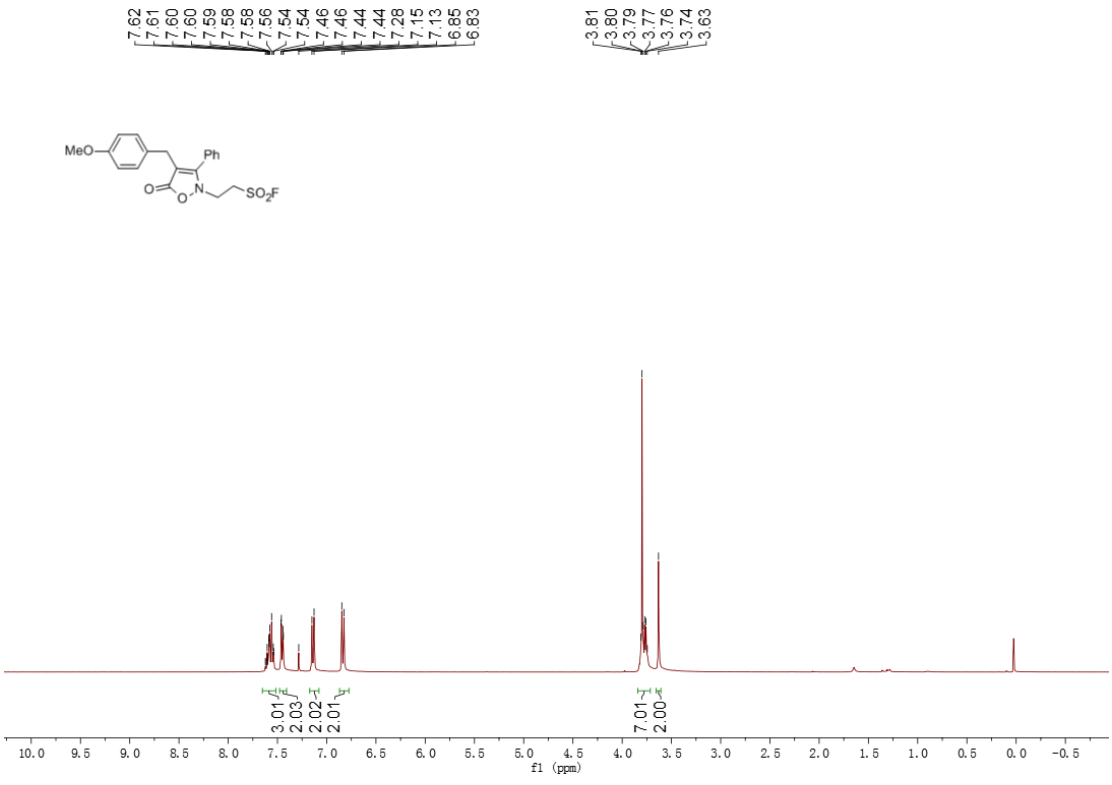


^{13}C NMR (101 MHz, $CDCl_3$)

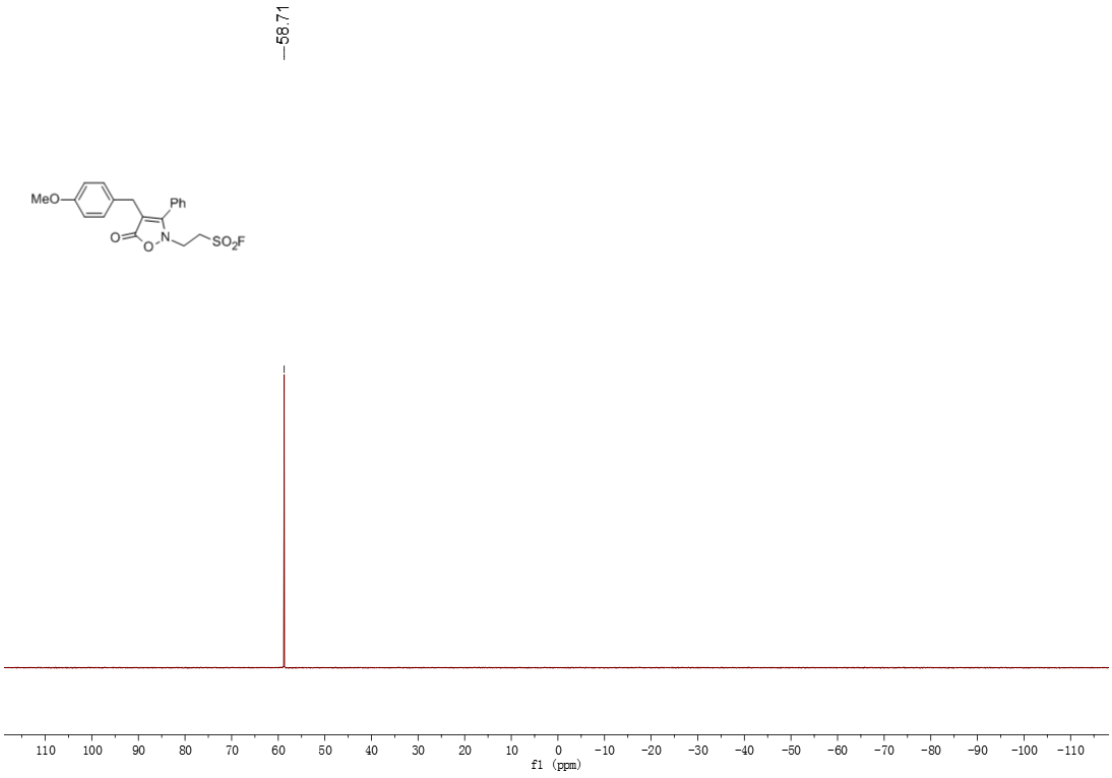


2-(4-(4-Methoxybenzyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3c)

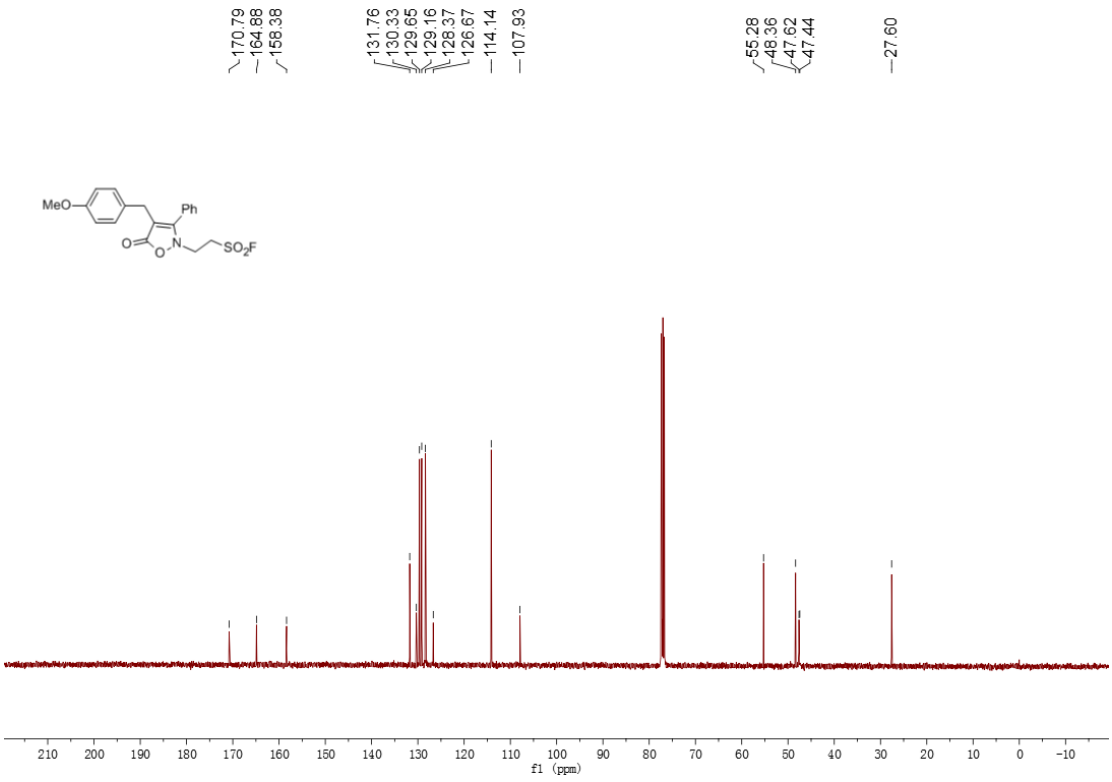
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

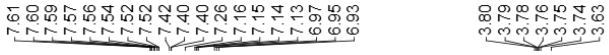


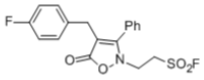
^{13}C NMR (101 MHz, $CDCl_3$)

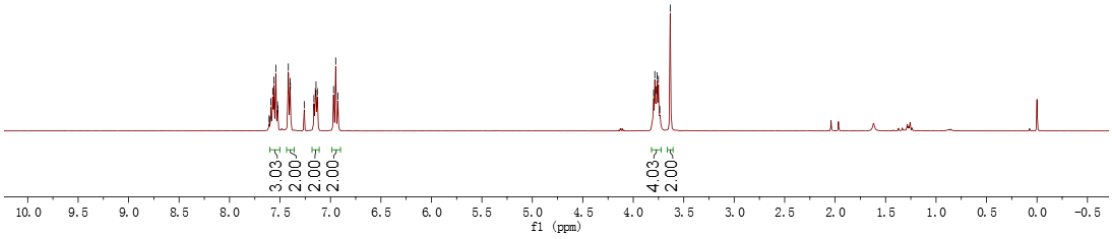


2-(4-(4-Fluorobenzyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3d)

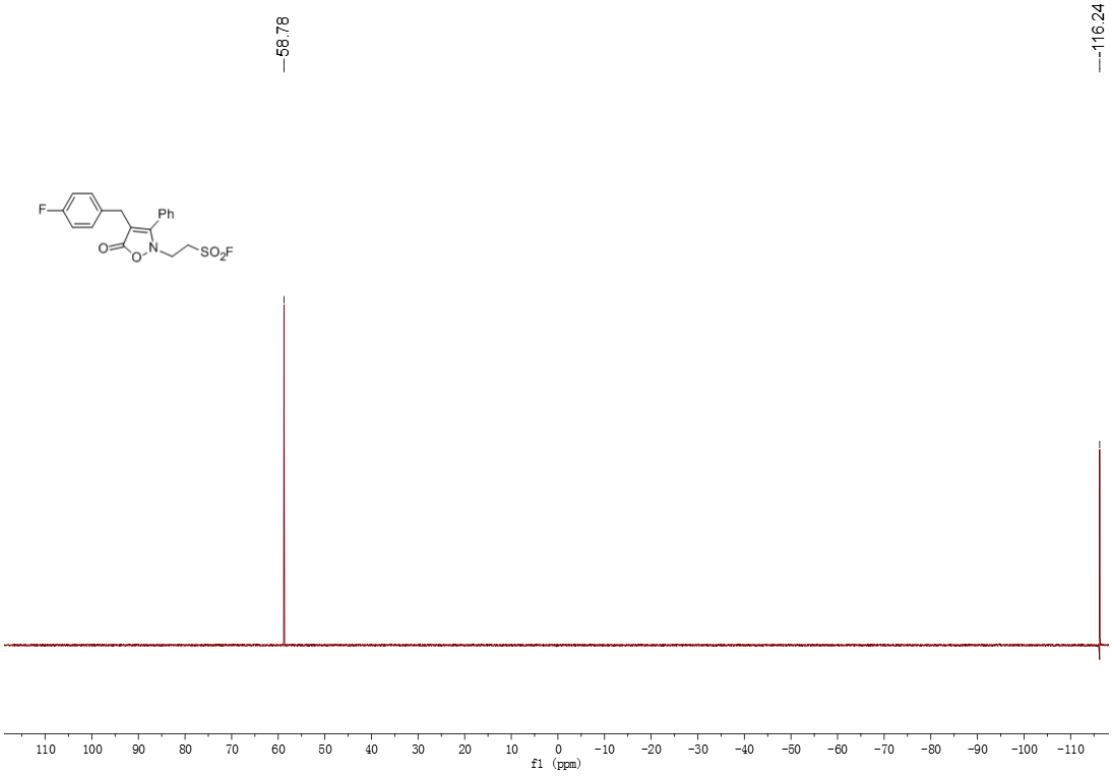
^{1}H NMR (400 MHz, $CDCl_3$)



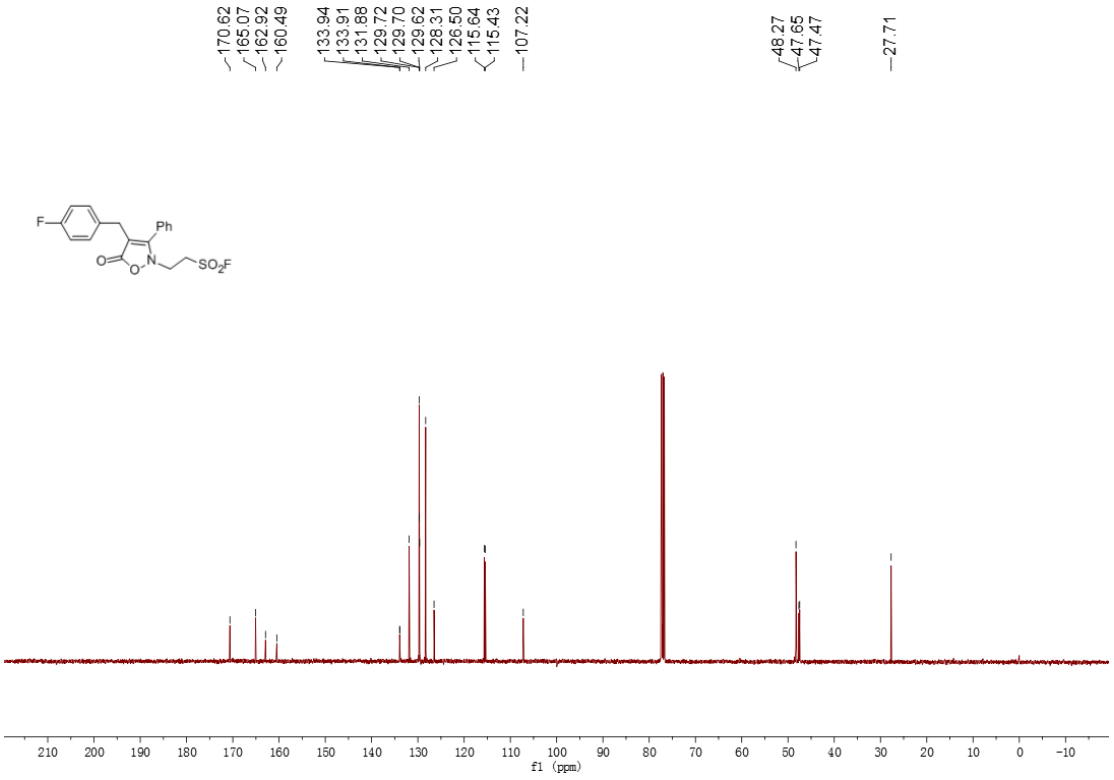




^{19}F NMR (471 MHz, $CDCl_3$)

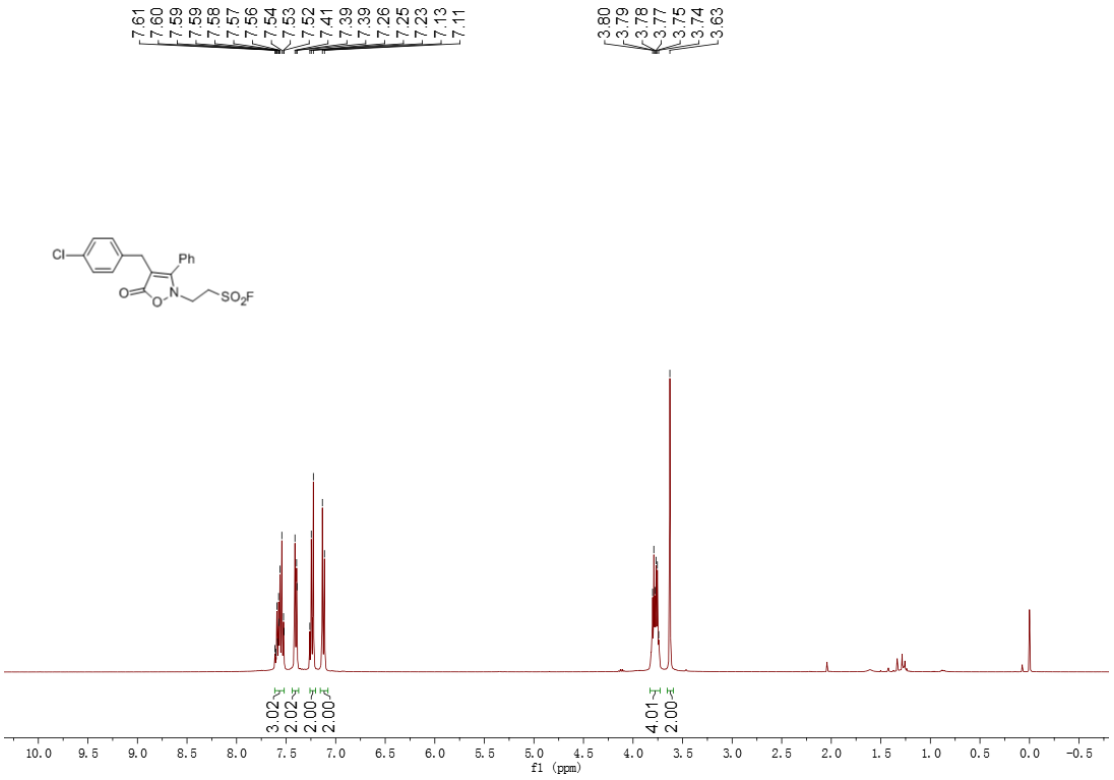


^{13}C NMR (101 MHz, $CDCl_3$)

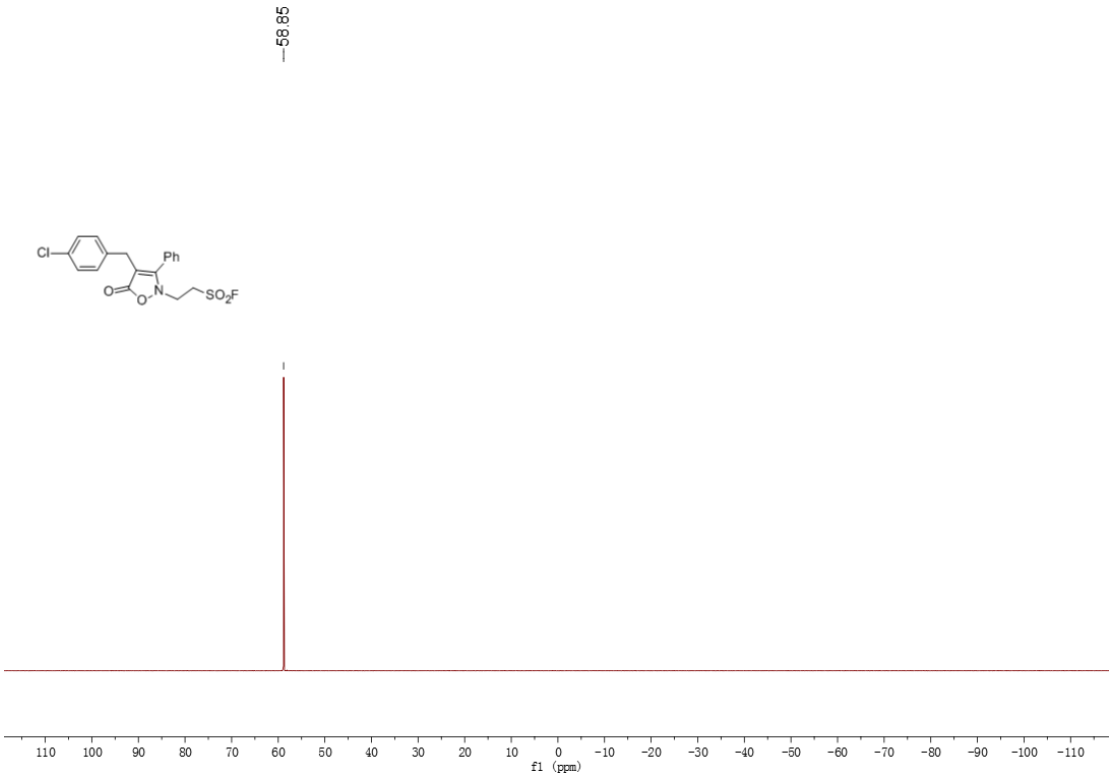


2-(4-(4-Chlorobenzyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3e)

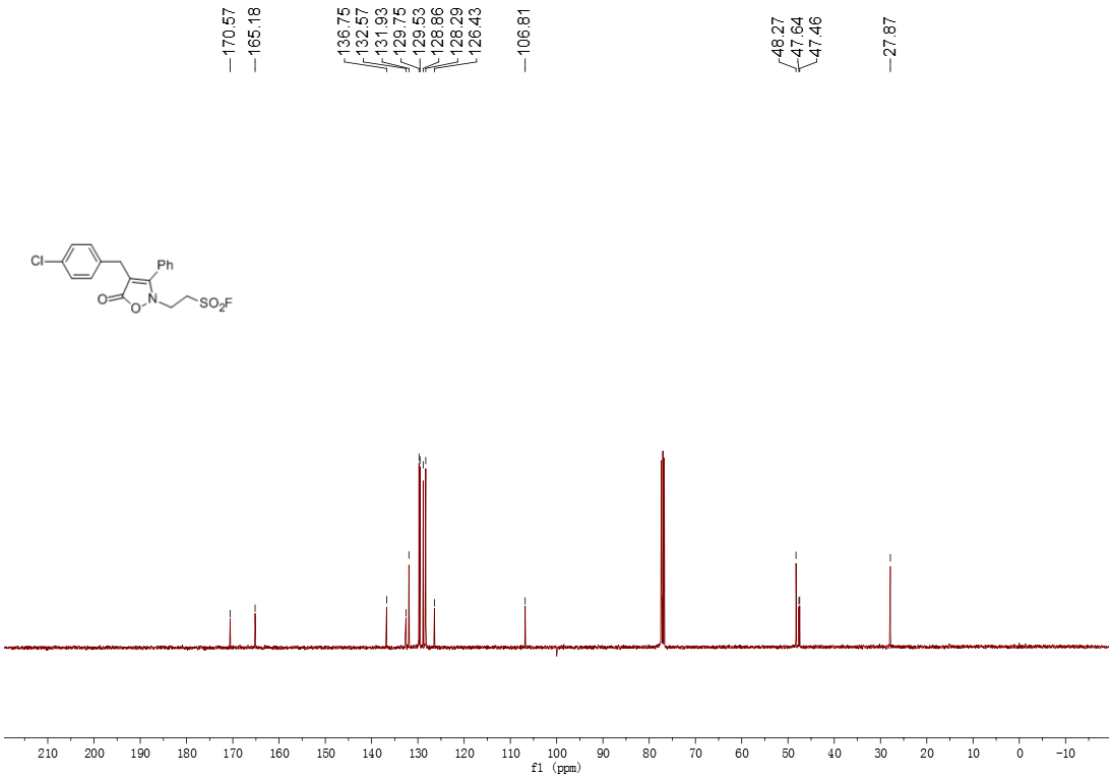
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

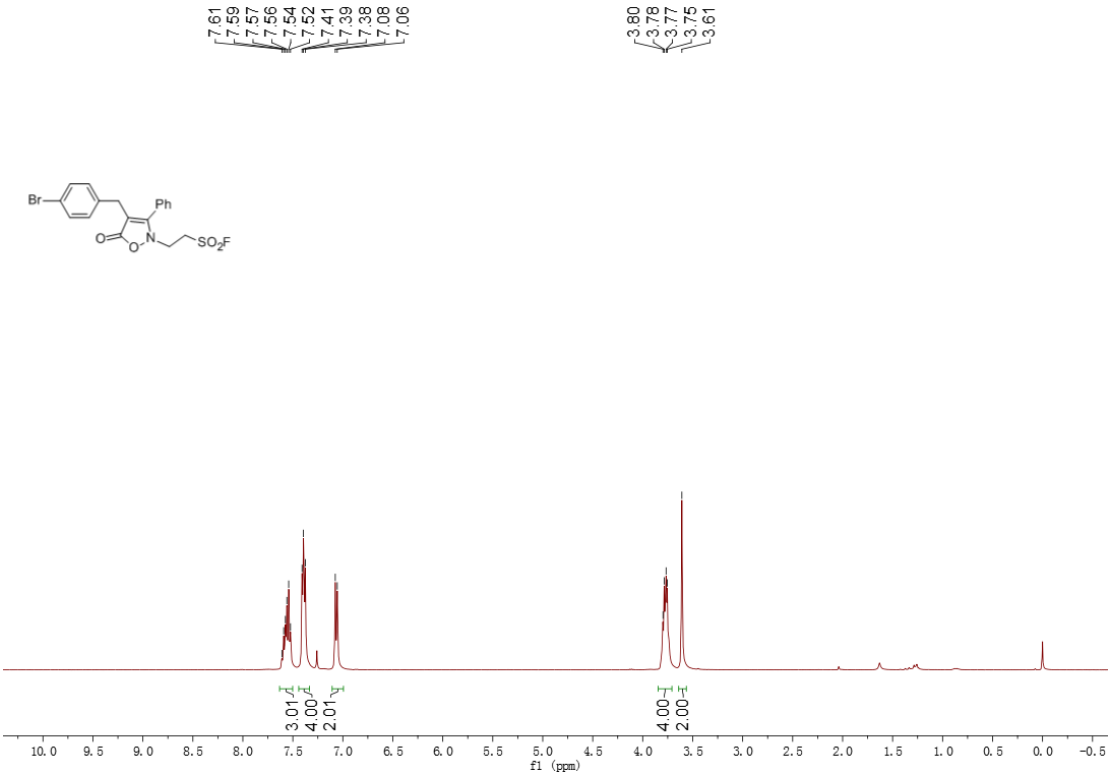


^{13}C NMR (101 MHz, $CDCl_3$)

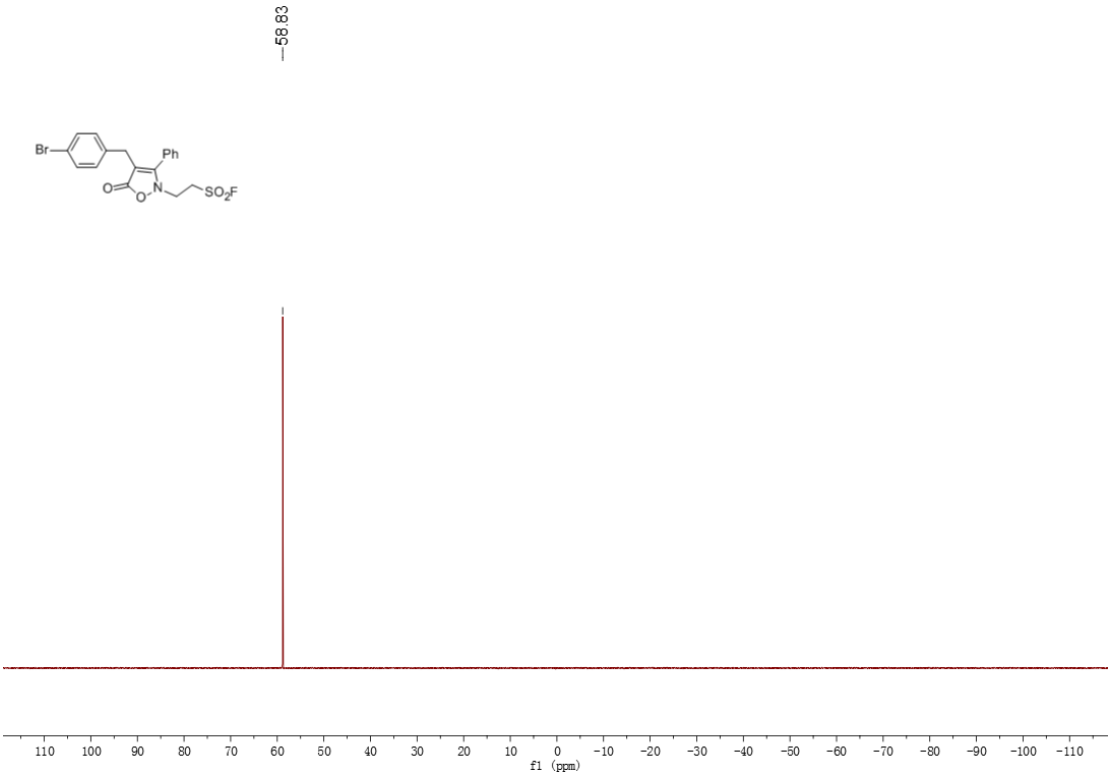


2-(4-(4-Bromobenzyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3f)

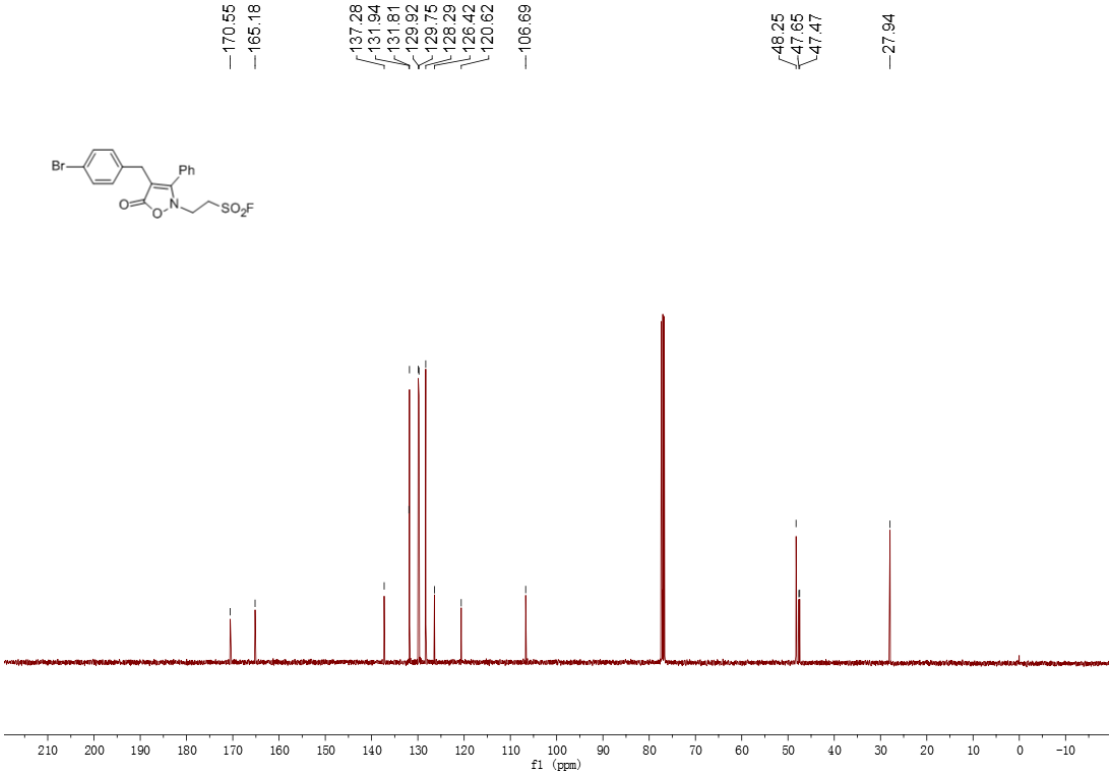
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

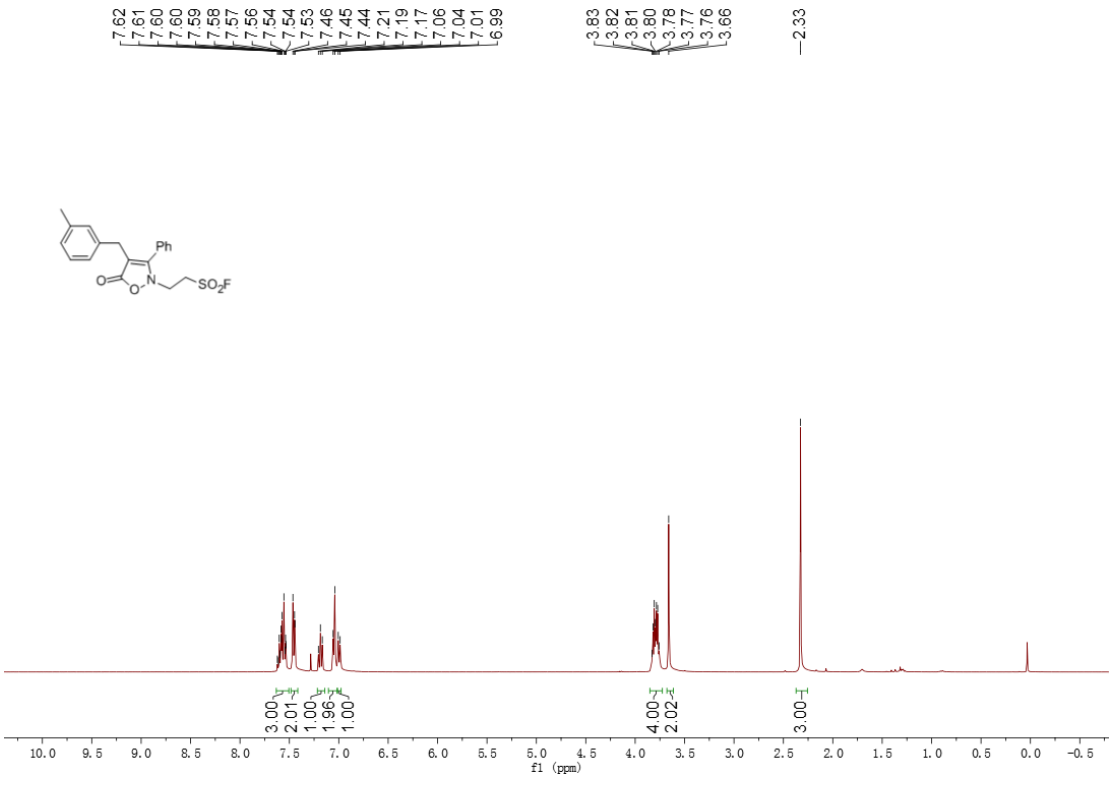


^{13}C NMR (101 MHz, $CDCl_3$)

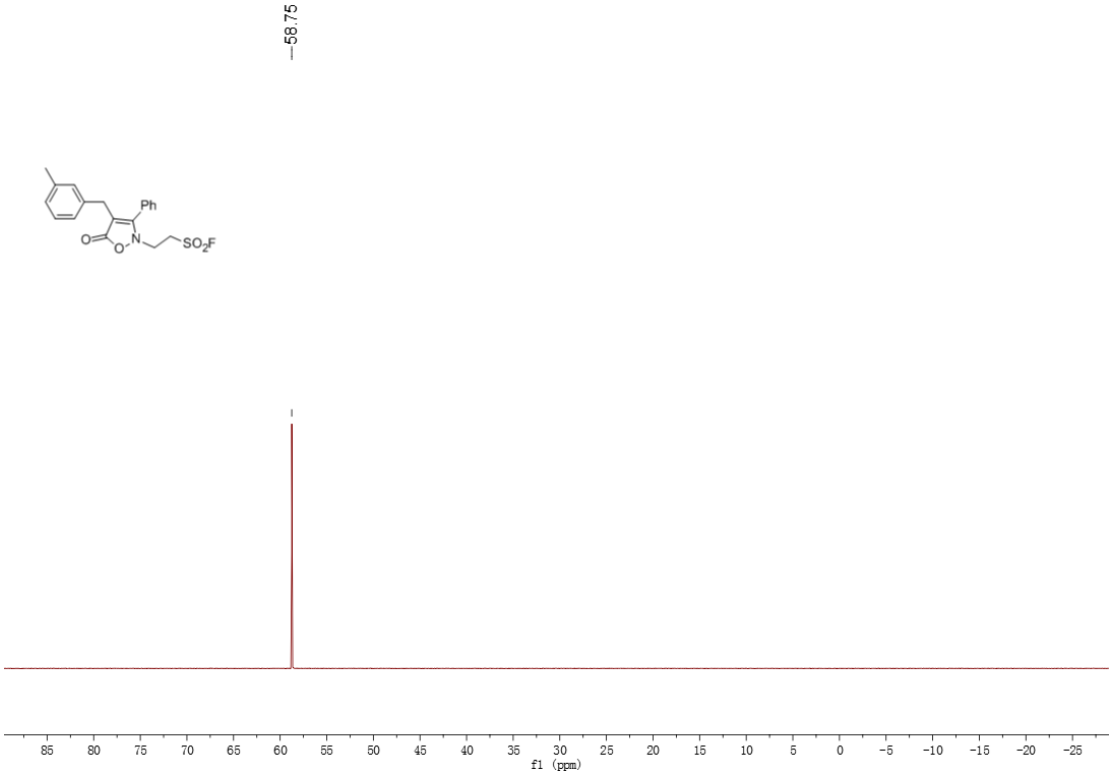


2-(4-(3-Methylbenzyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3g)

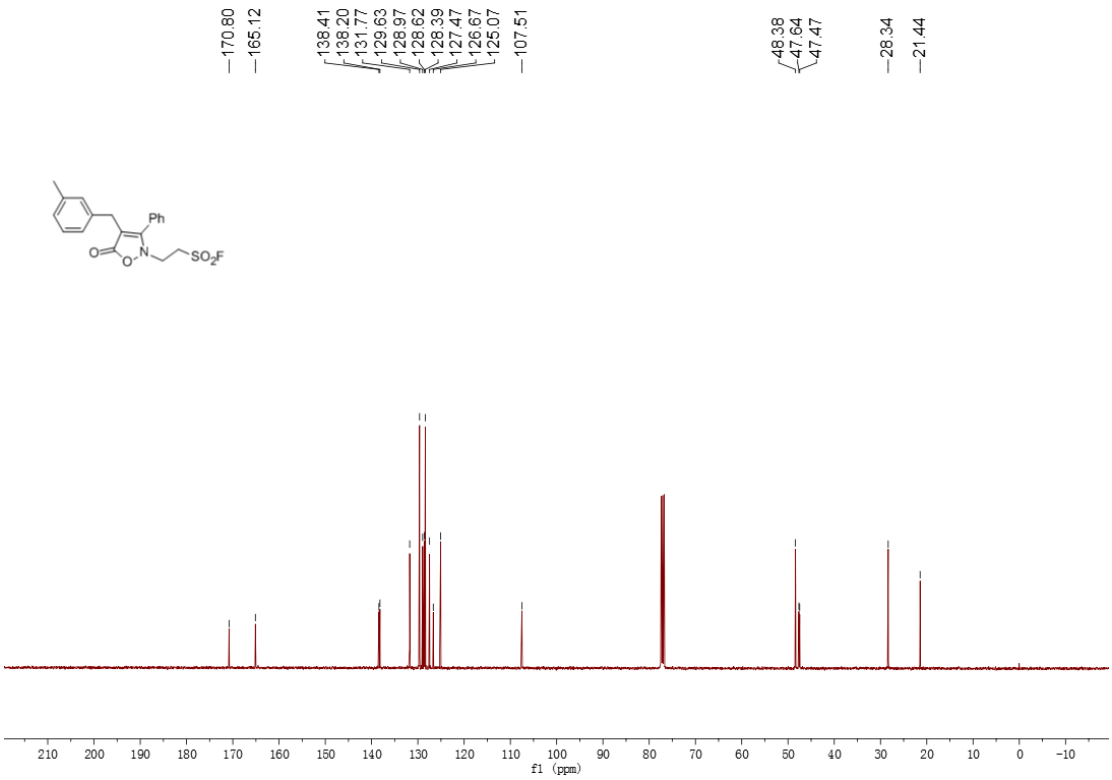
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

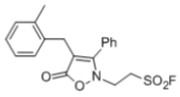


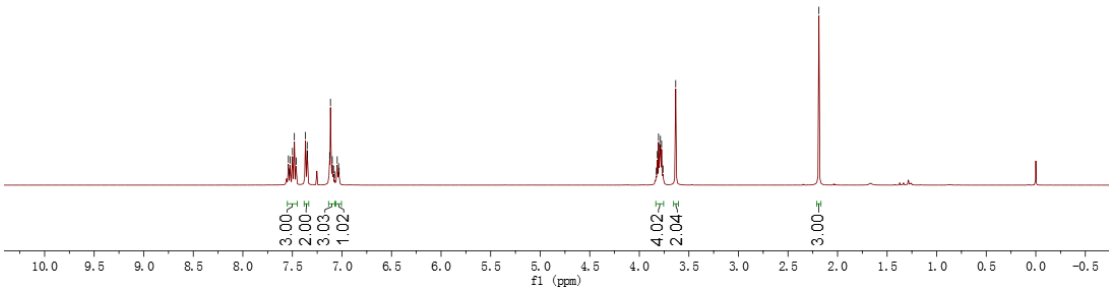
^{13}C NMR (101 MHz, $CDCl_3$)



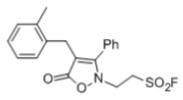
2-(4-(2-Methylbenzyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3h)

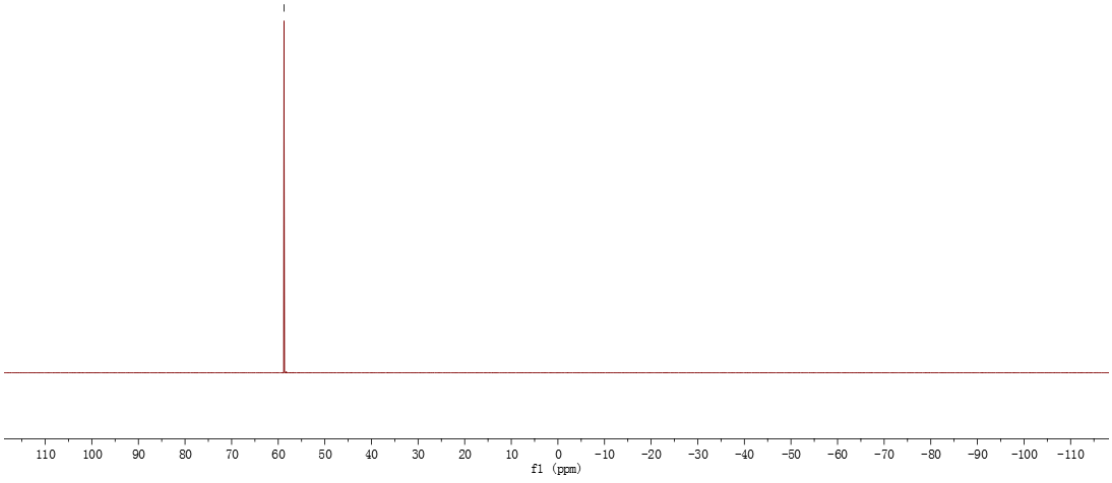
^{1}H NMR (400 MHz, $CDCl_3$)



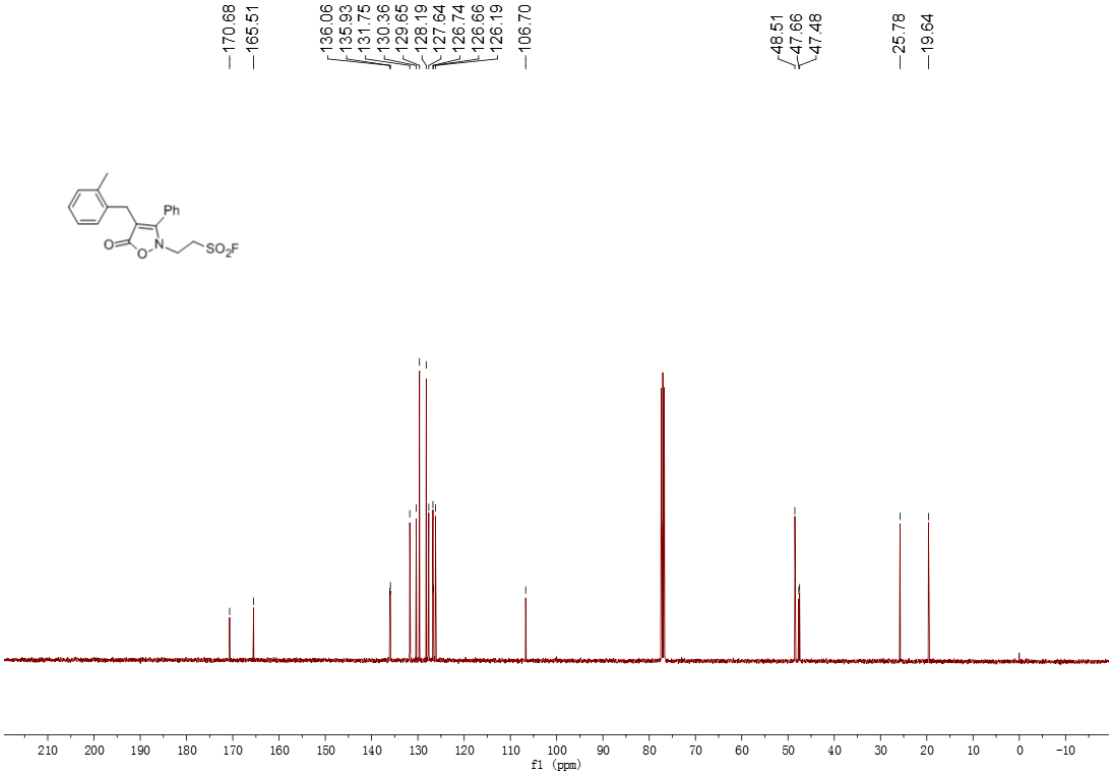


^{19}F NMR (471 MHz, $CDCl_3$)



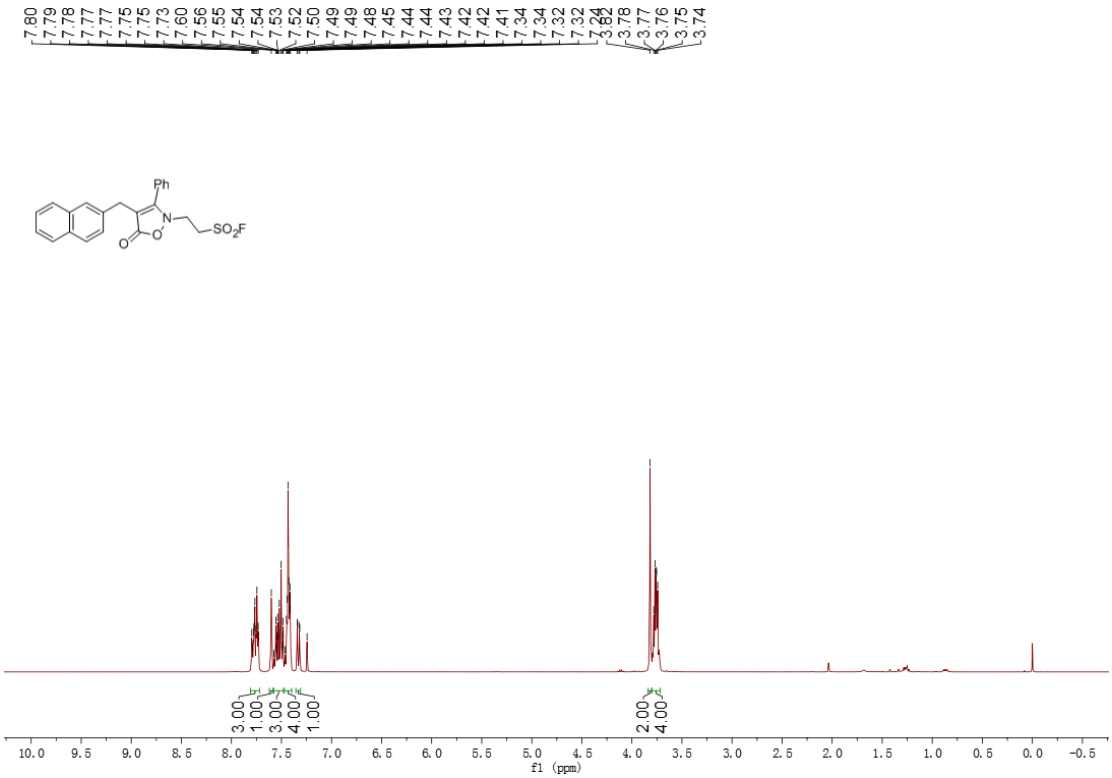


^{13}C NMR (101 MHz, $CDCl_3$)

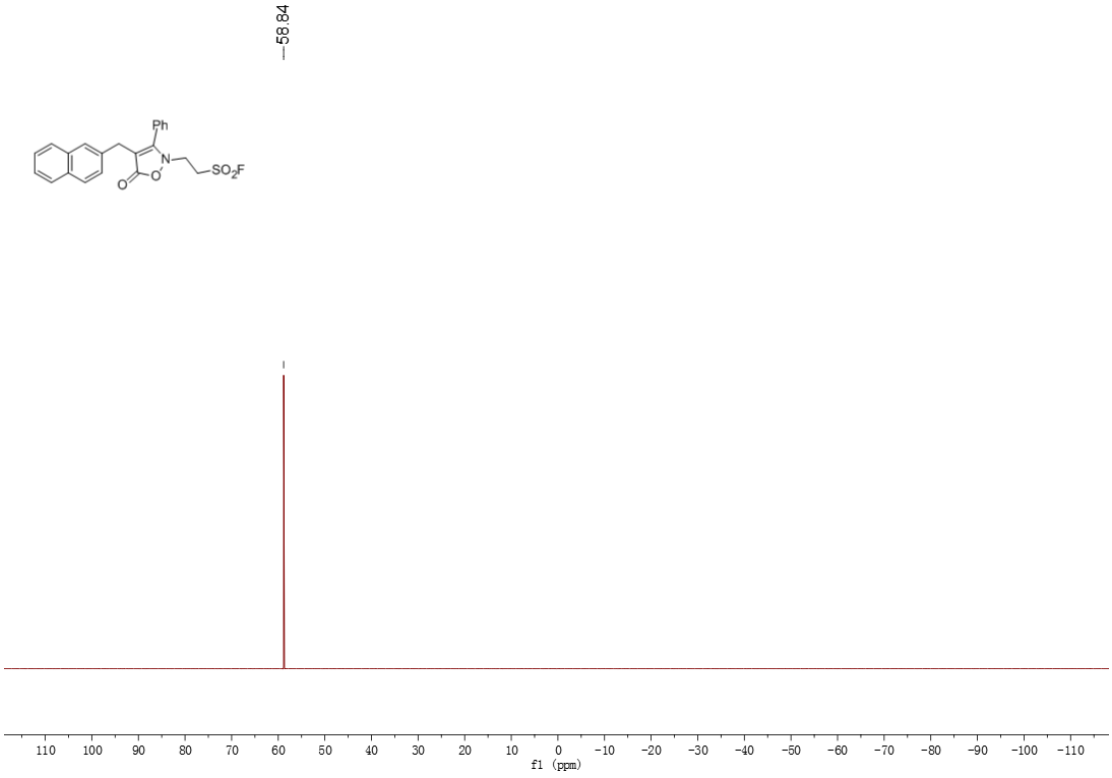


2-(4-(Naphthalen-2-ylmethyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3i)

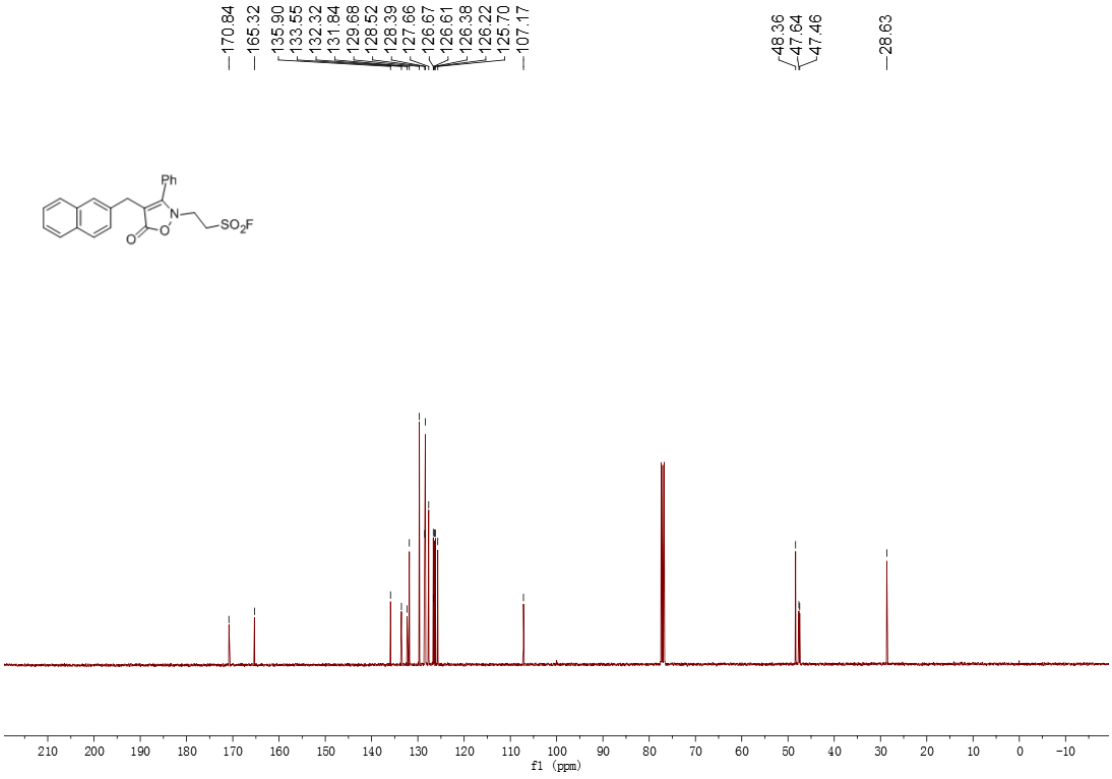
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

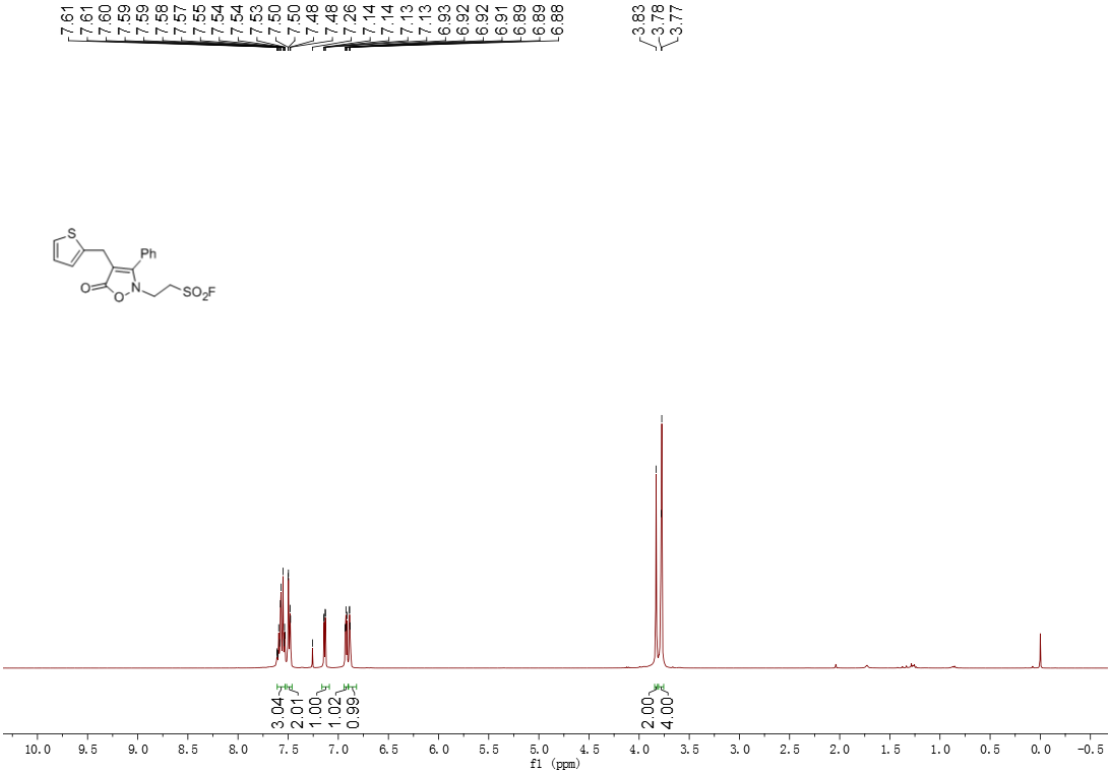


^{13}C NMR (101 MHz, $CDCl_3$)

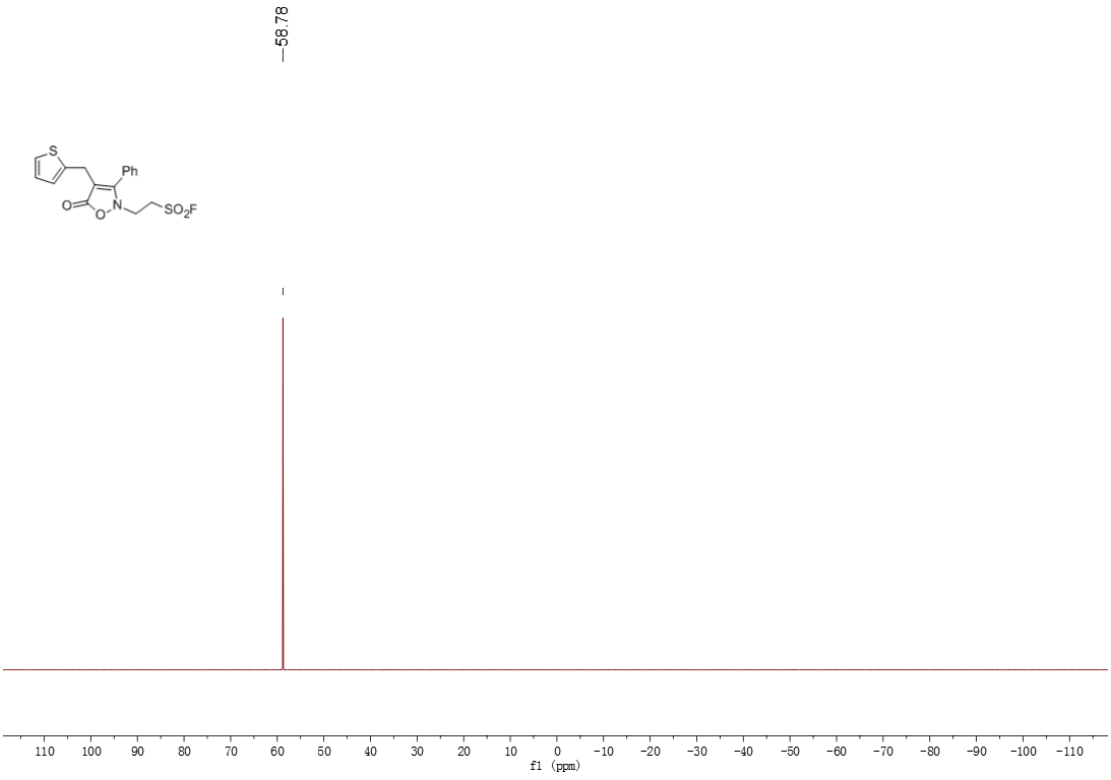


2-(5-Oxo-3-phenyl-4-(thiophen-2-ylmethyl)isoxazol-2(5H)-yl)ethanesulfonyl fluoride (3j)

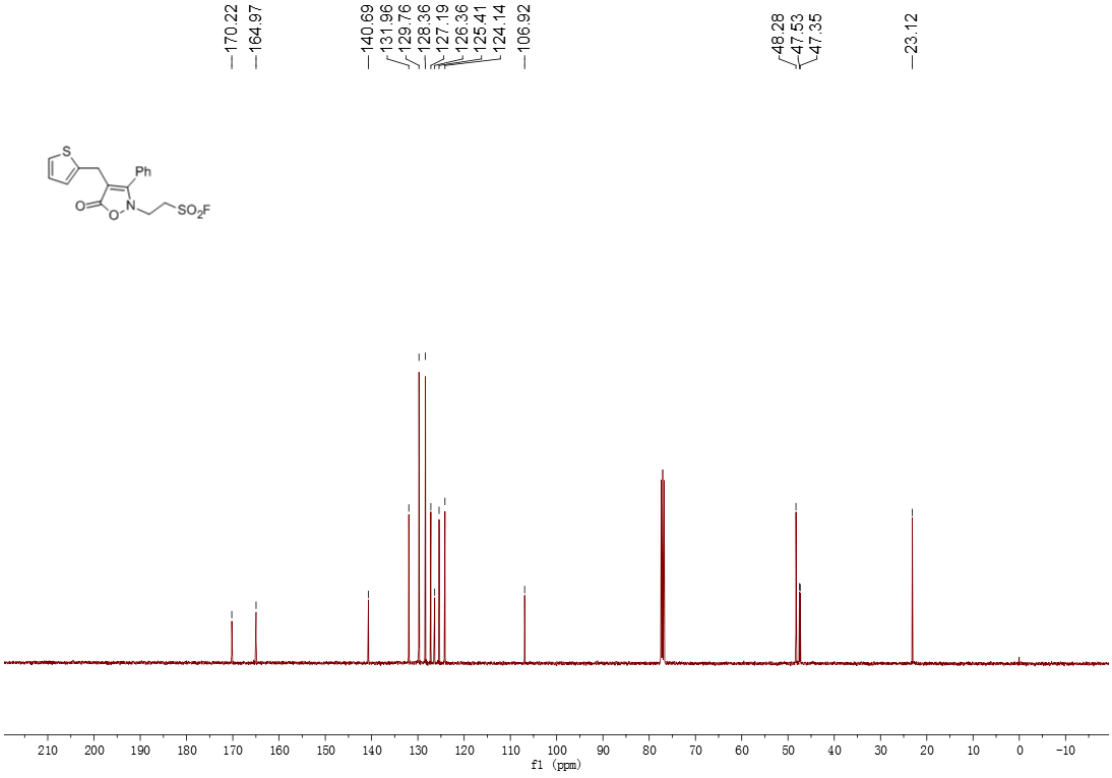
^{1}H NMR (400 MHz, DMSO)



^{19}F NMR (471 MHz, DMSO)

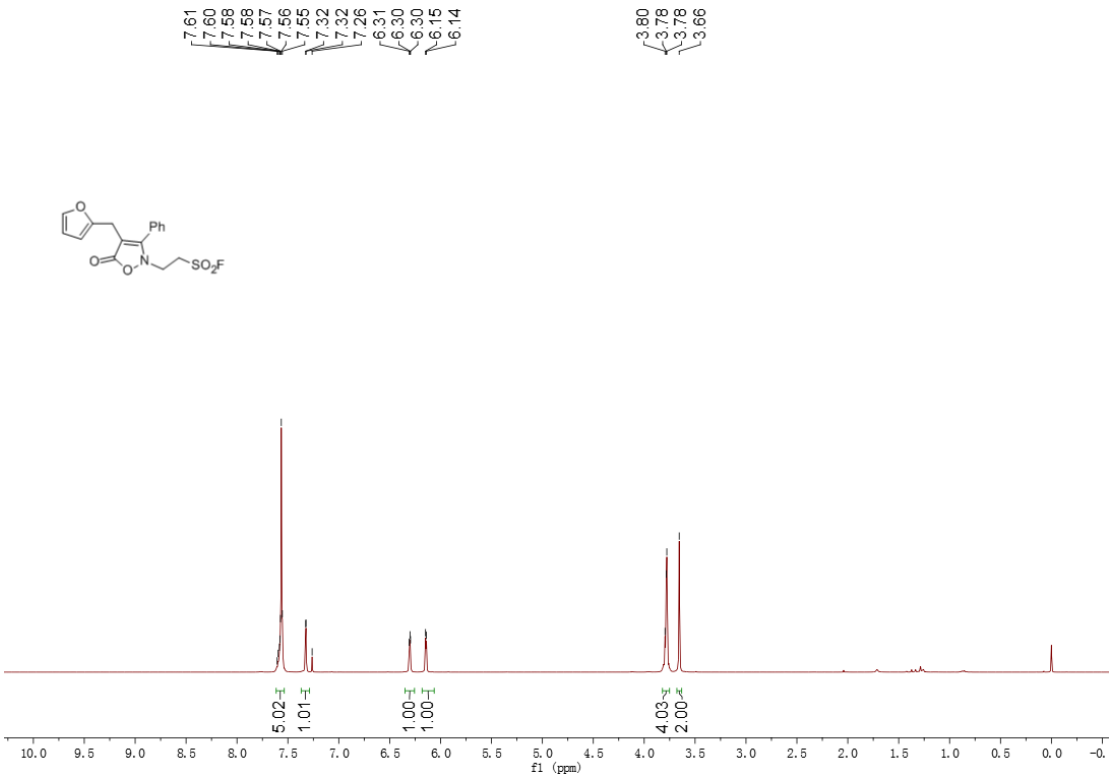


^{13}C NMR (101 MHz, DMSO)

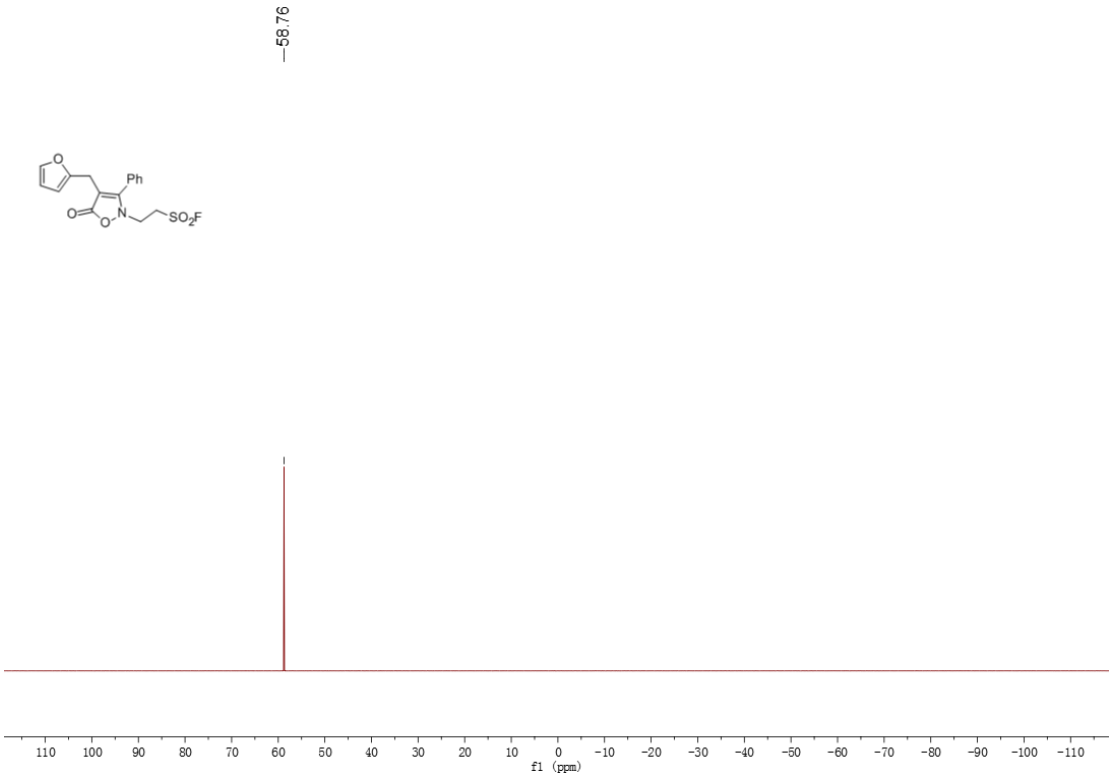


2-(4-(Furan-2-ylmethyl)-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3k)

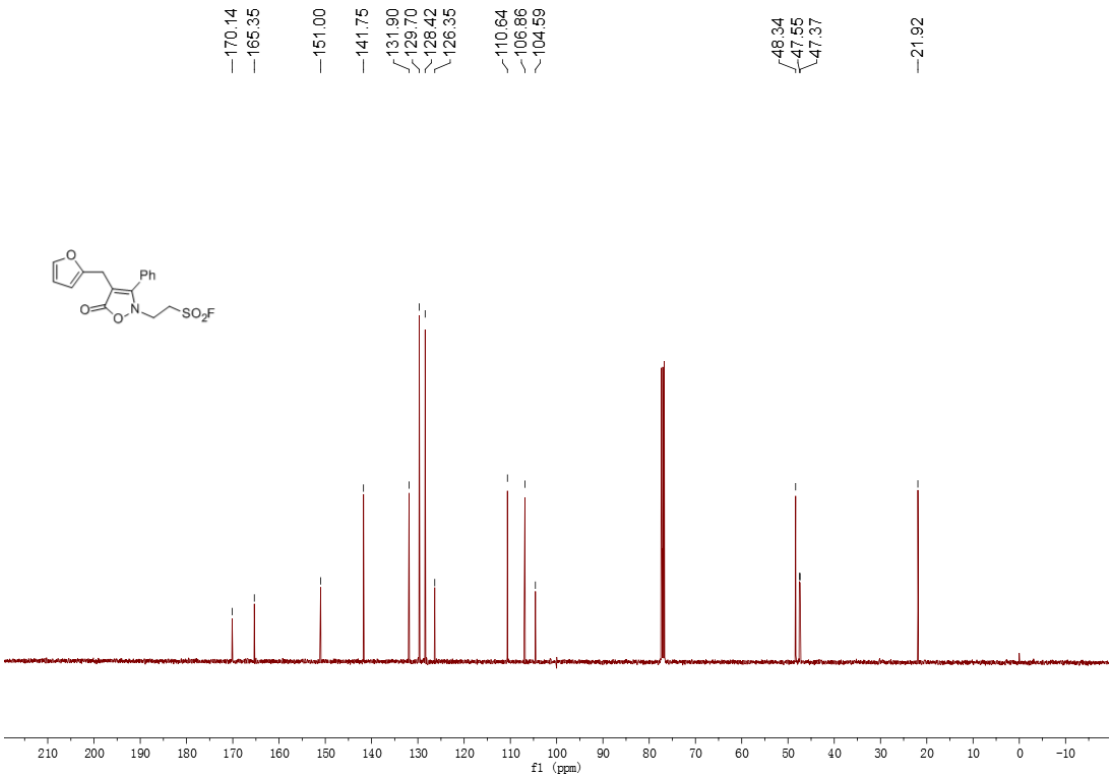
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, DMSO)

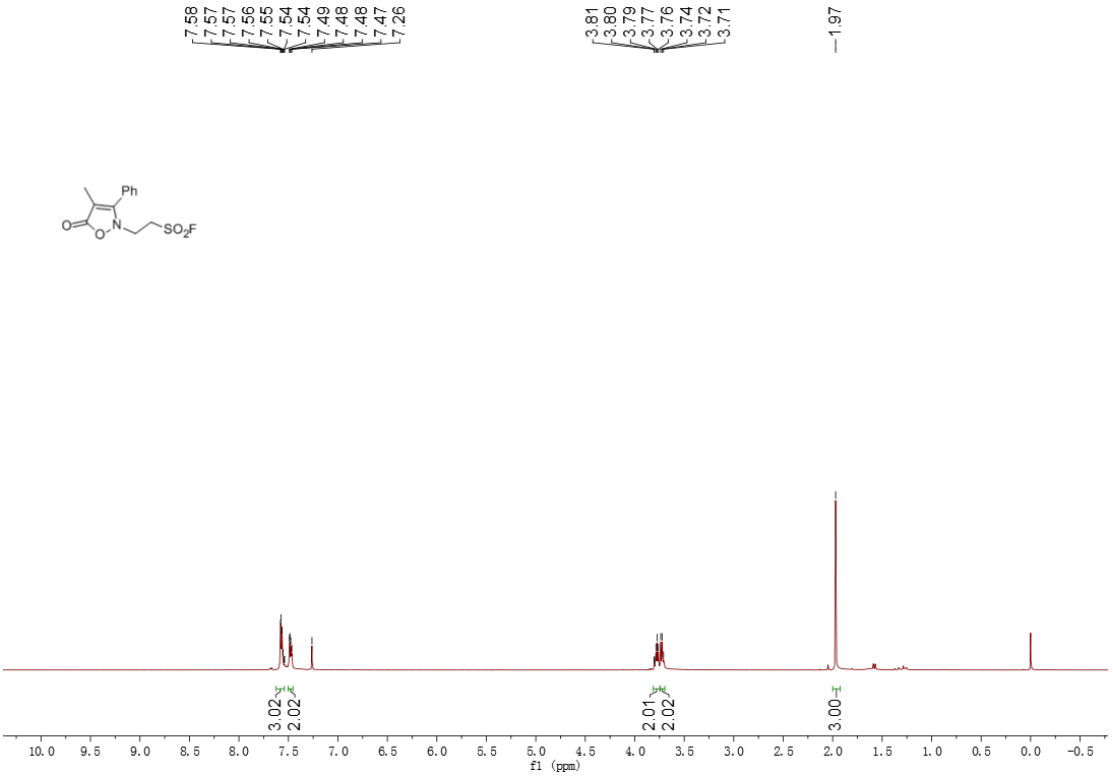


^{13}C NMR (101 MHz, $CDCl_3$)

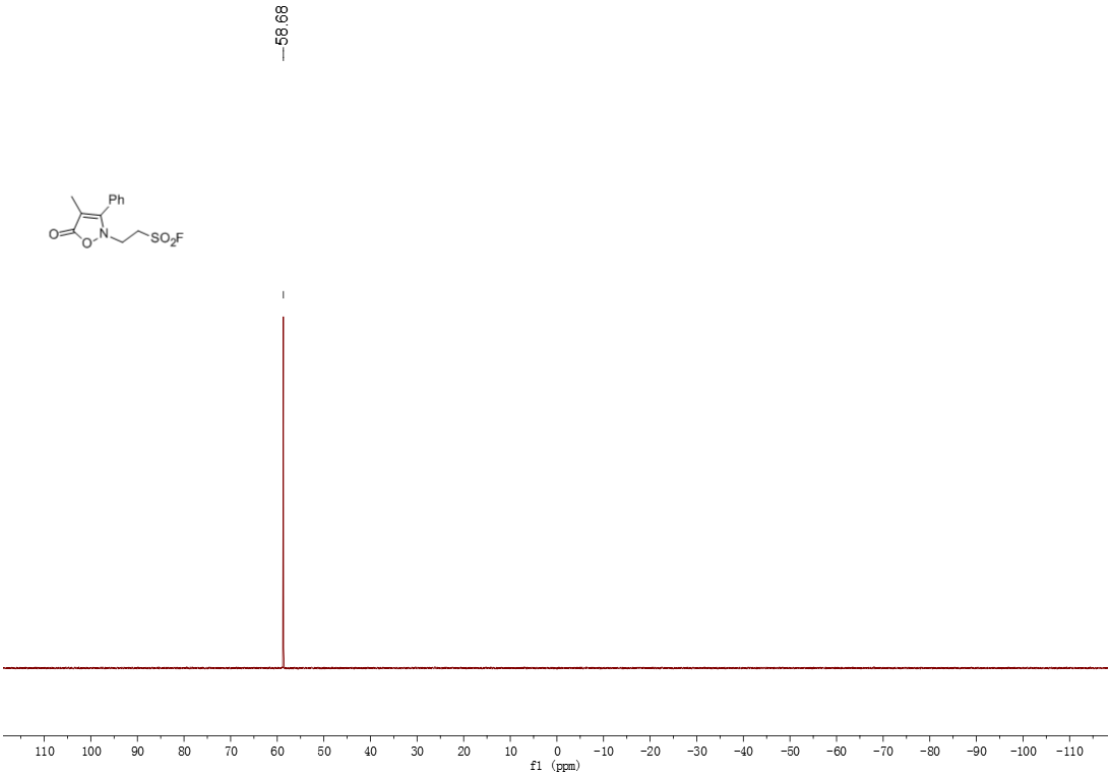


2-(4-Methyl-5-oxo-3-phenylisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3l)

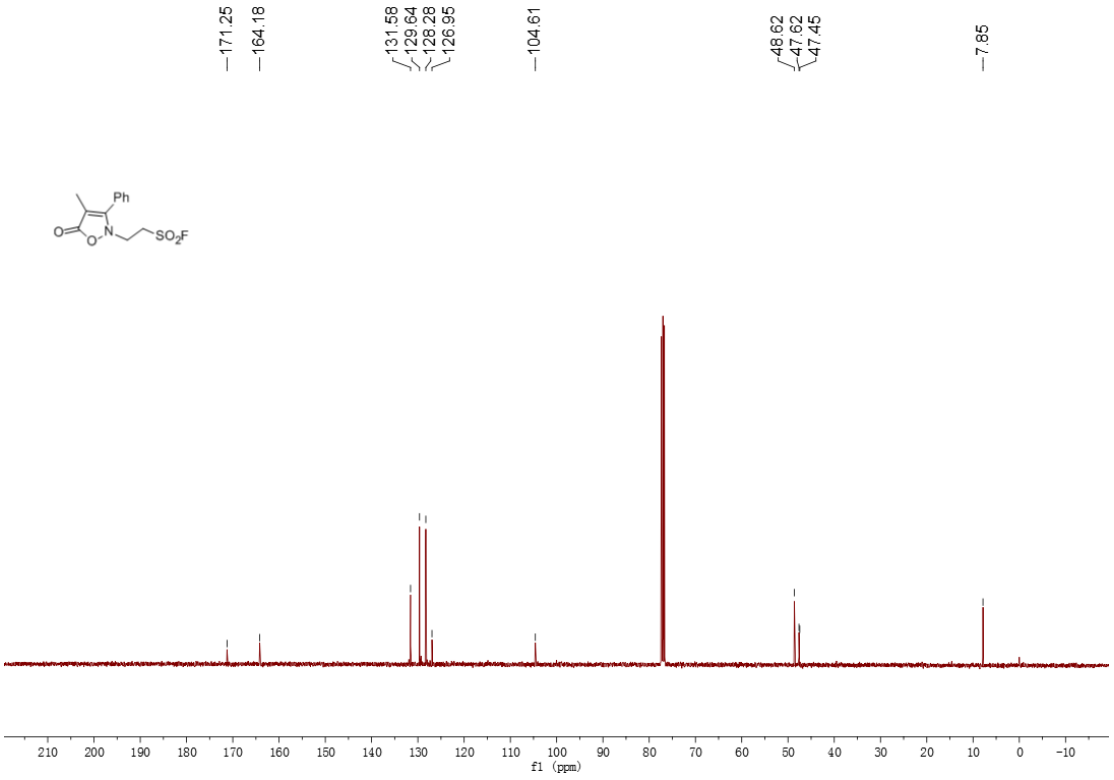
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

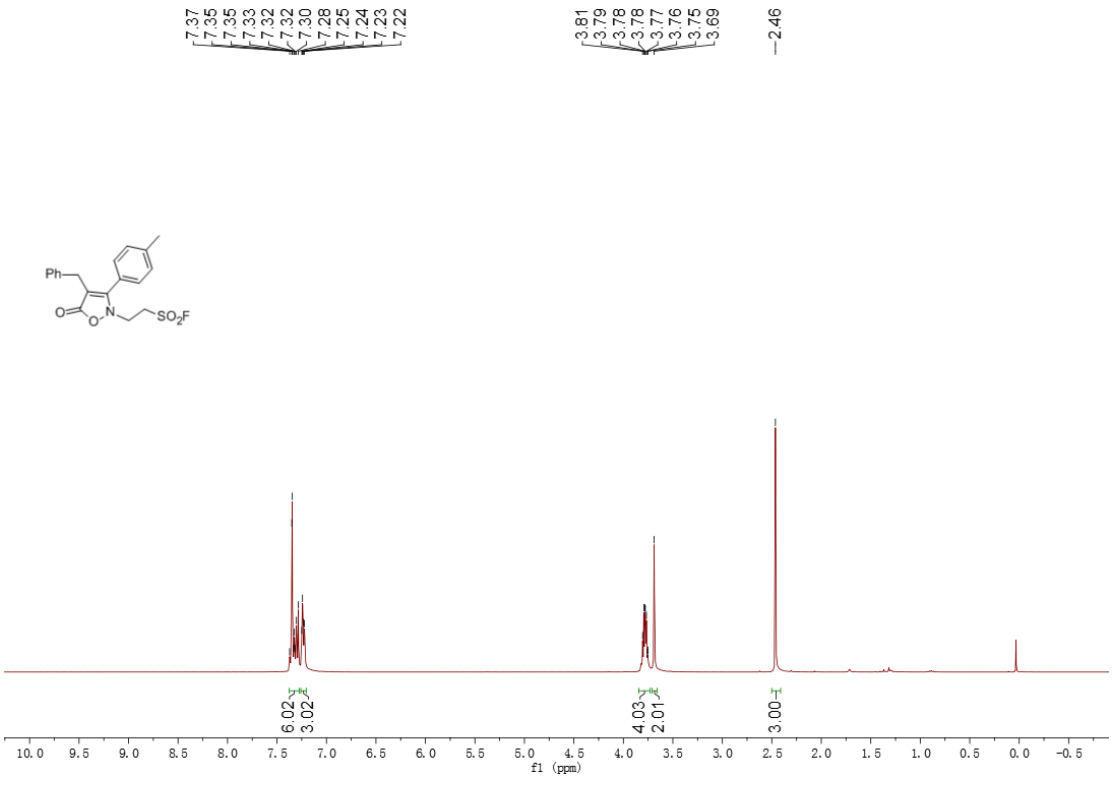


^{13}C NMR (101 MHz, $CDCl_3$)

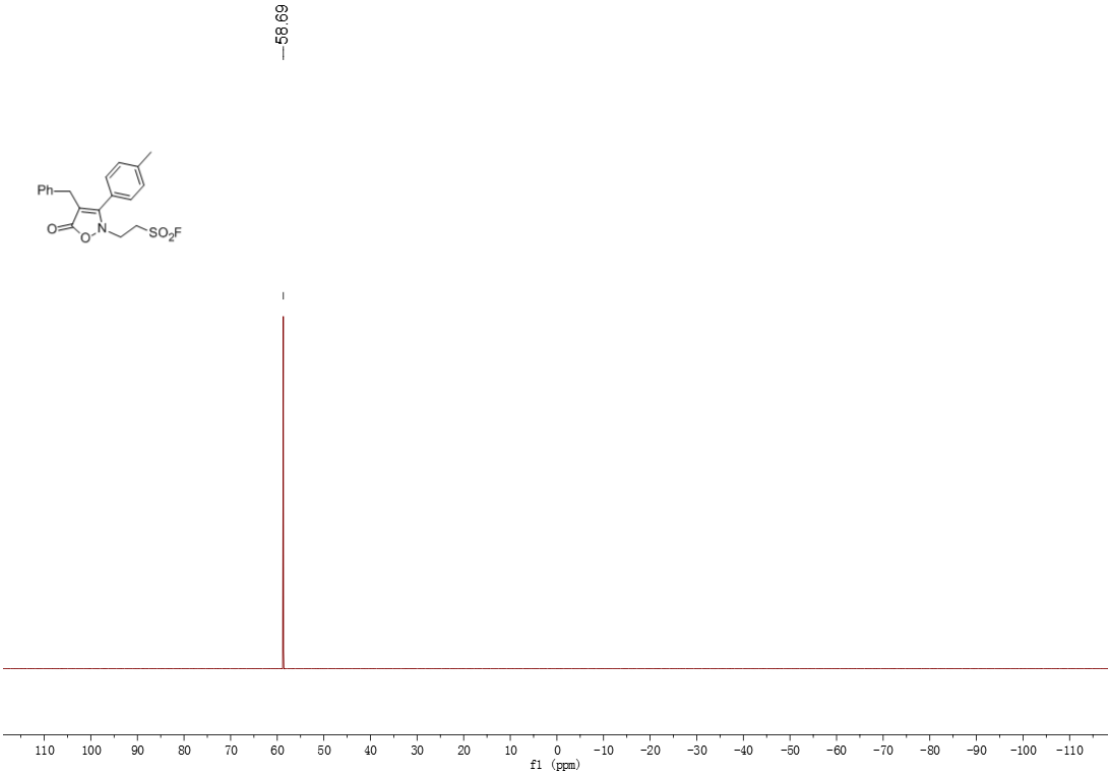


2-(4-Benzyl-5-oxo-3-(p-tolyl)isoxazol-2(5H)-yl)ethanesulfonyl fluoride (3m)

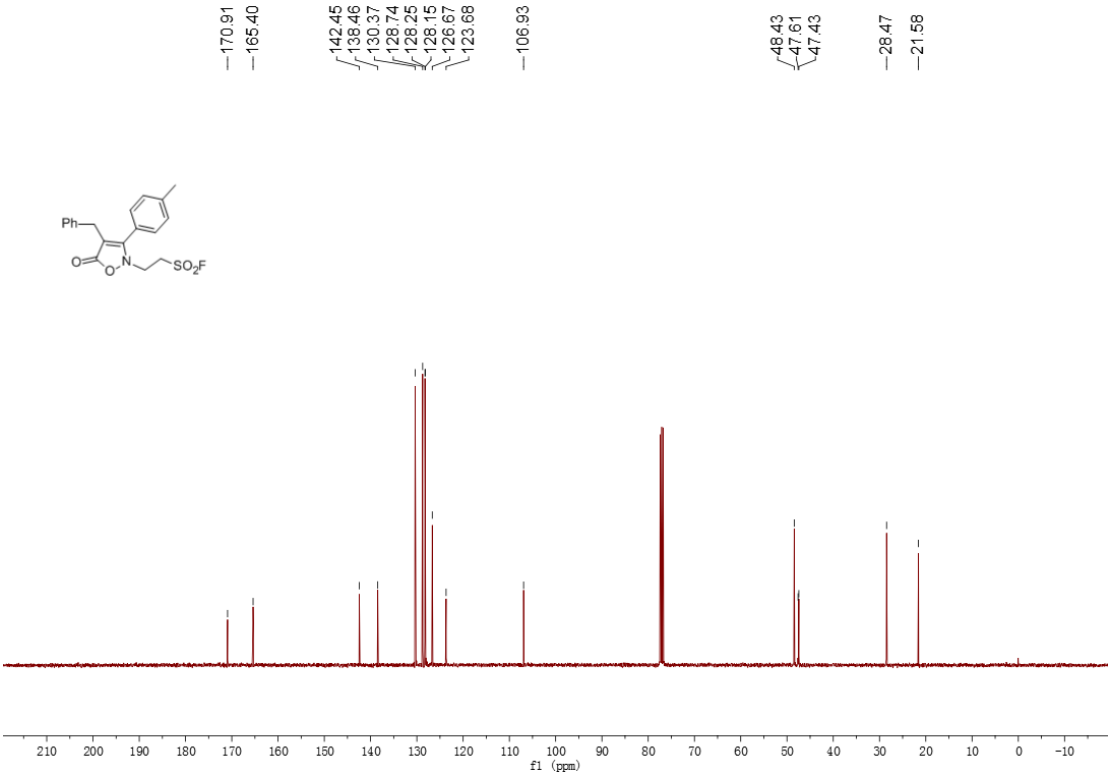
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

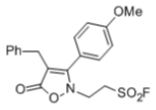


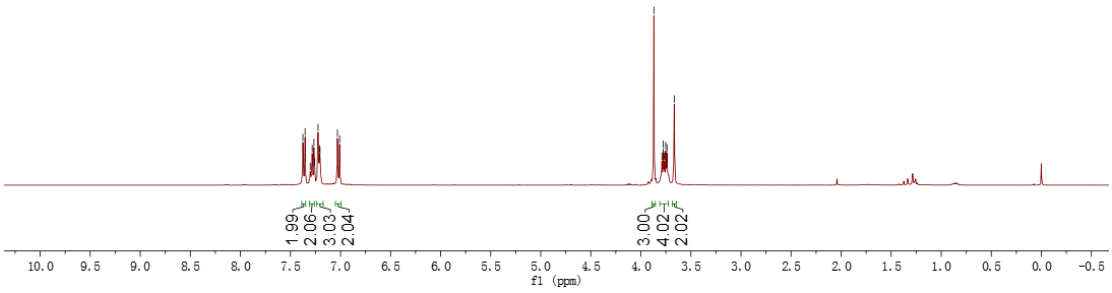
^{13}C NMR (101 MHz, $CDCl_3$)



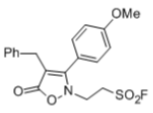
2-(4-Benzyl-3-(4-methoxyphenyl)-5-oxoisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3n)

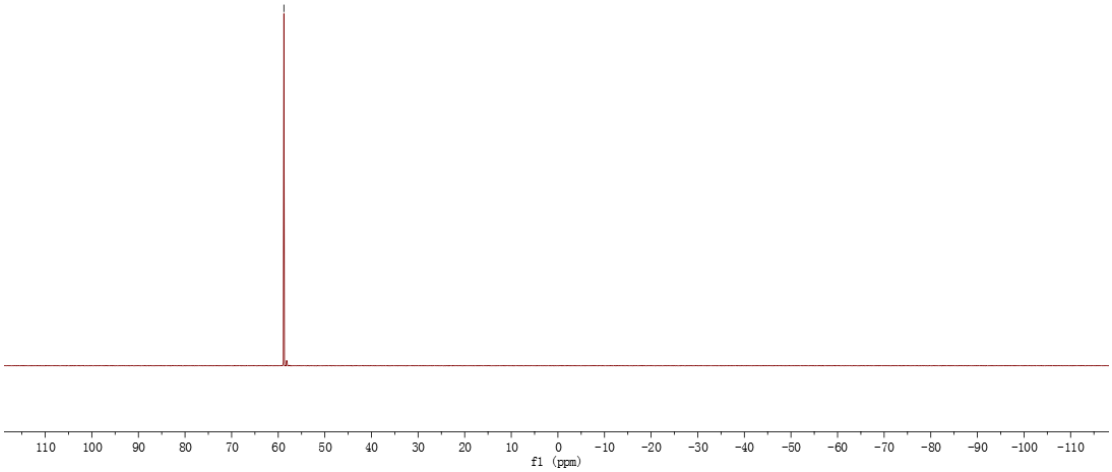
^{1}H NMR (400 MHz, $CDCl_3$)



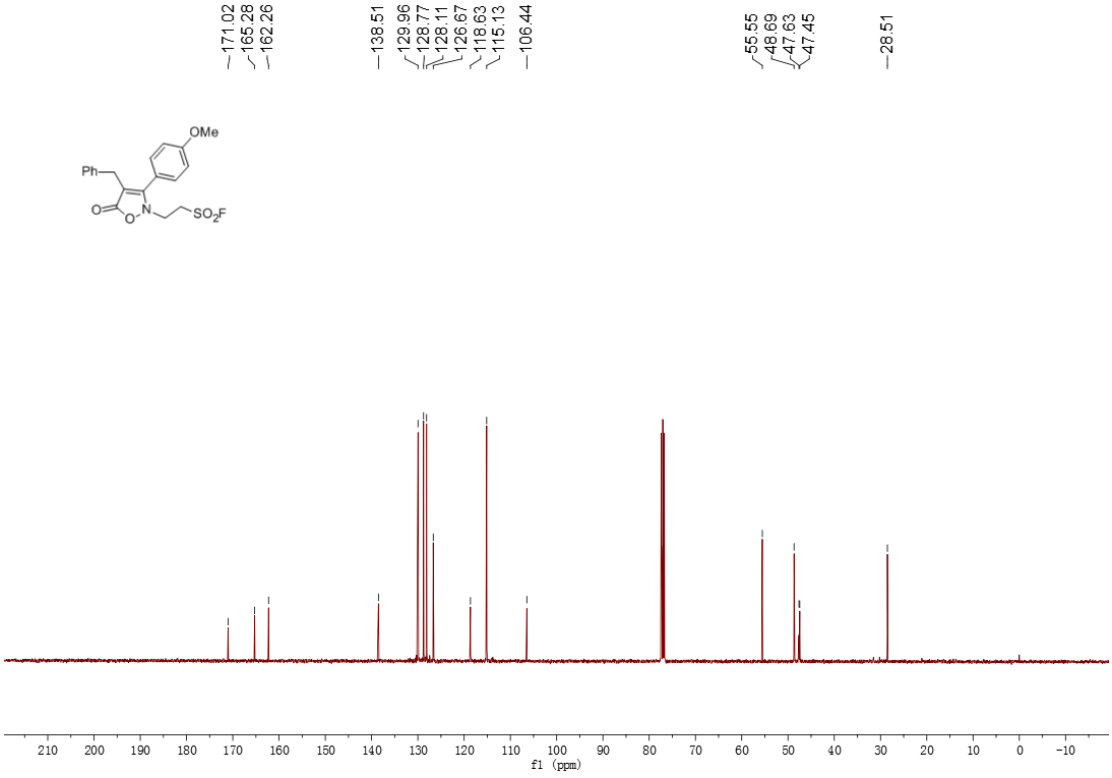


^{19}F NMR (471 MHz, $CDCl_3$)



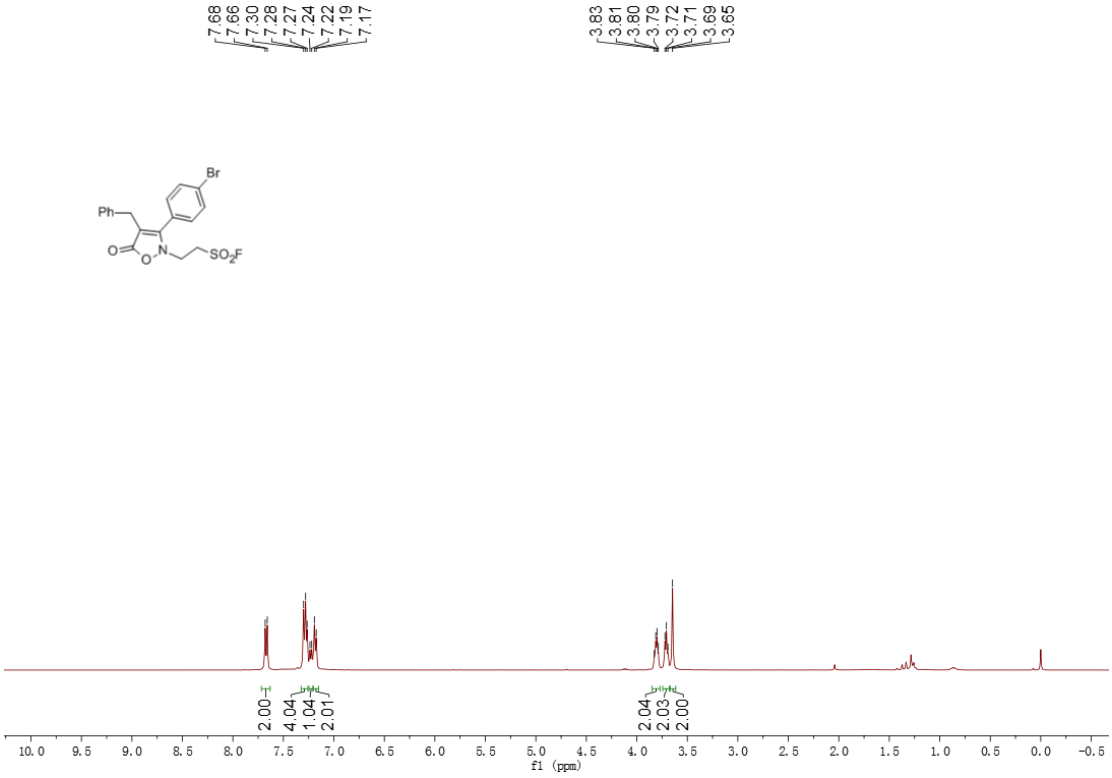


^{13}C NMR (101 MHz, $CDCl_3$)

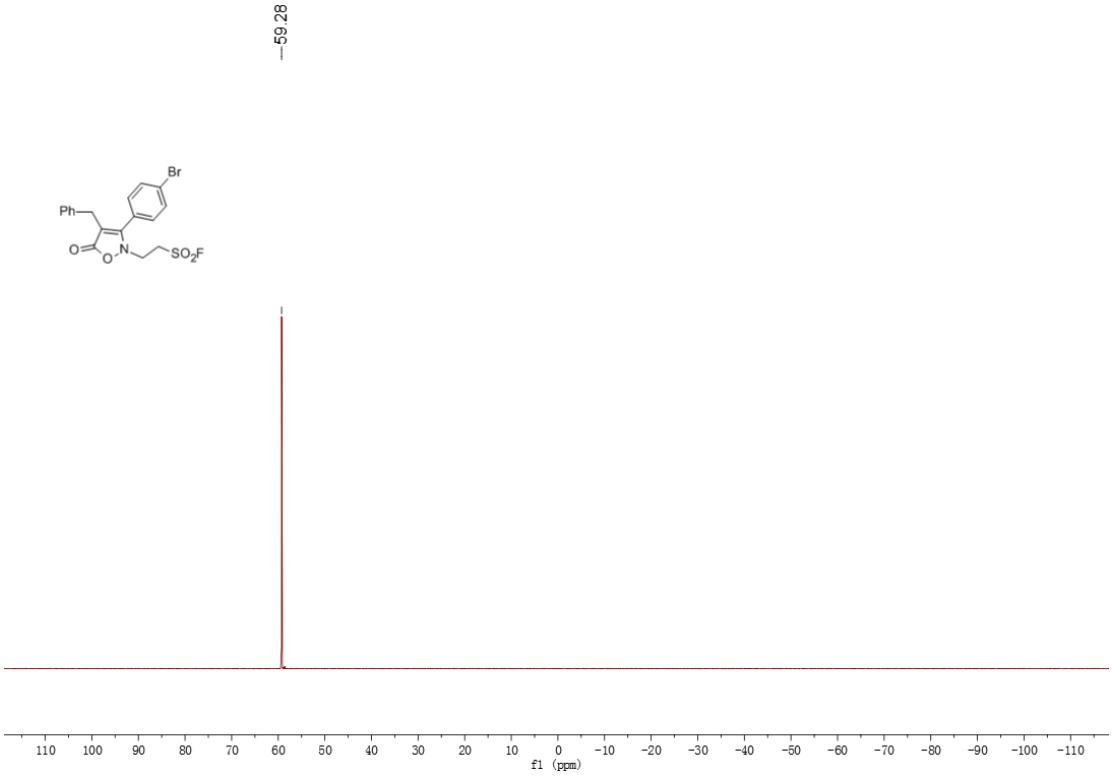


2-(4-Benzyl-3-(4-bromophenyl)-5-oxoisoxazol-2(5H)-yl)ethanesulfonyl fluoride (3o)

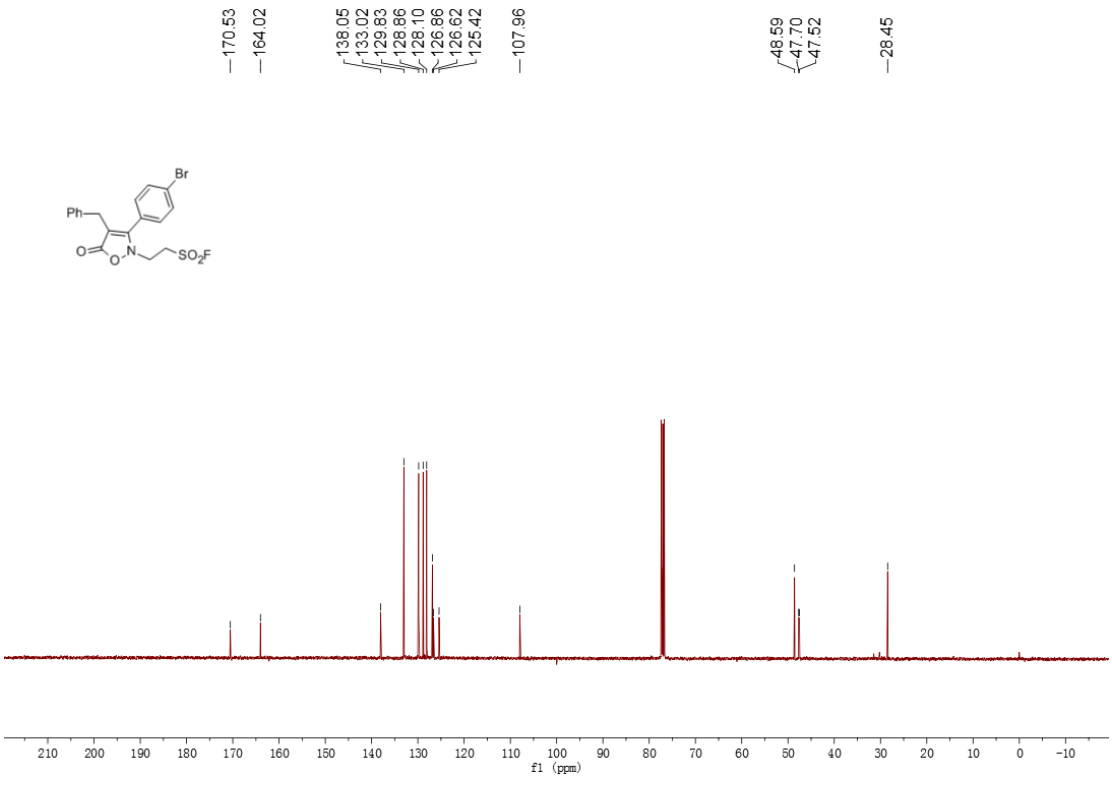
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

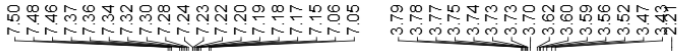


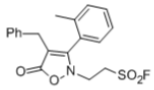
^{13}C NMR (101 MHz, $CDCl_3$)

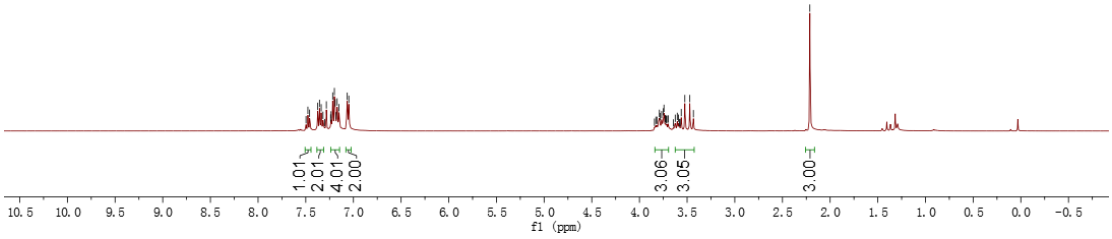


2-(4-Benzyl-5-oxo-3-(o-tolyl)isoxazol-2(5H)-yl)ethanesulfonyl fluoride (3p)

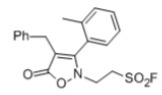
^{1}H NMR (400 MHz, $CDCl_3$)

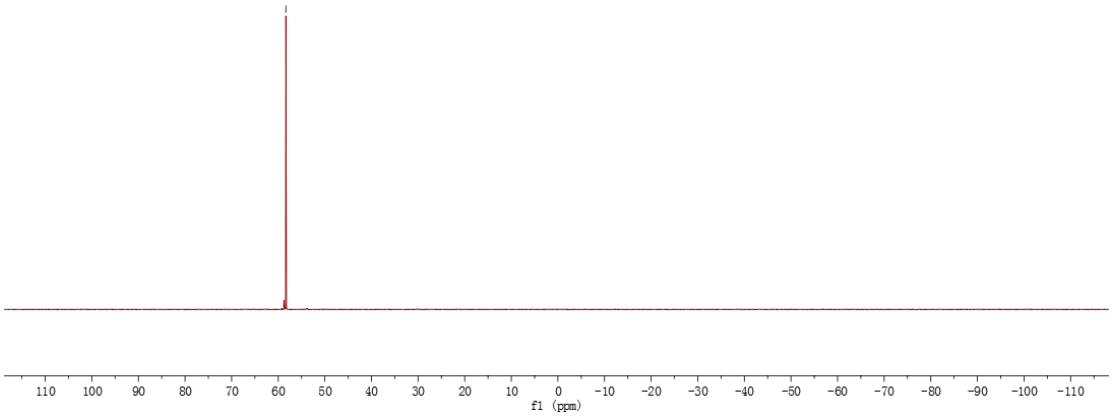




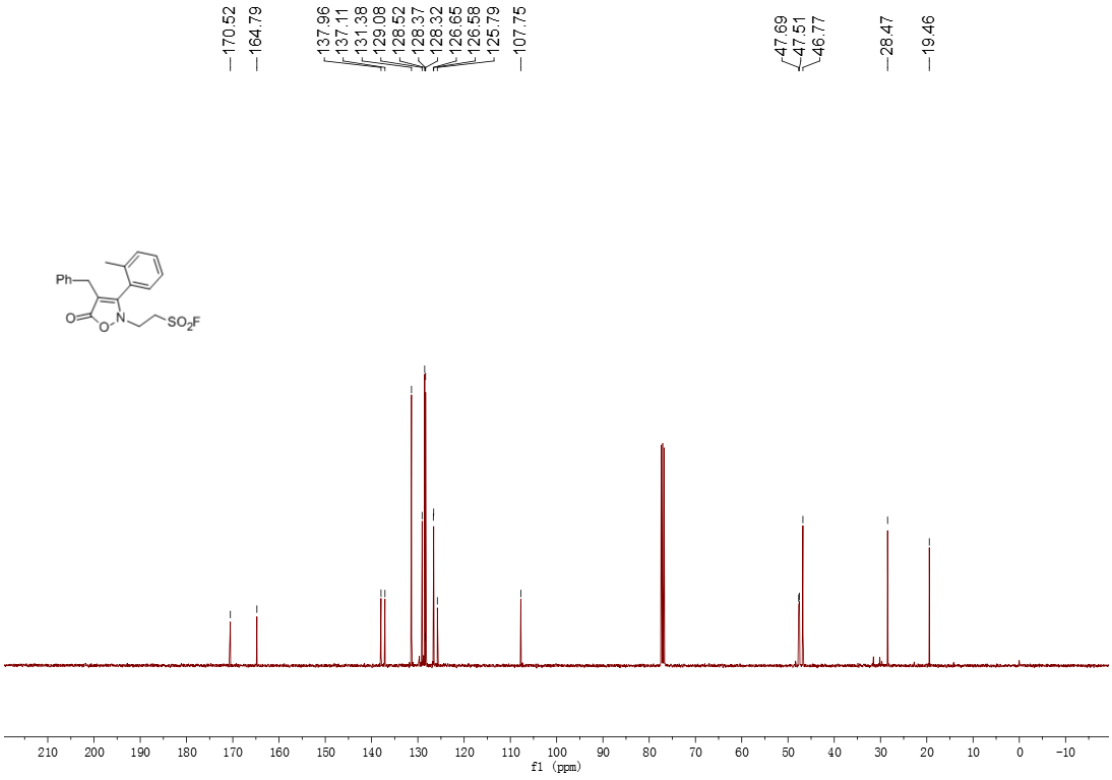


^{19}F NMR (471 MHz, $CDCl_3$)



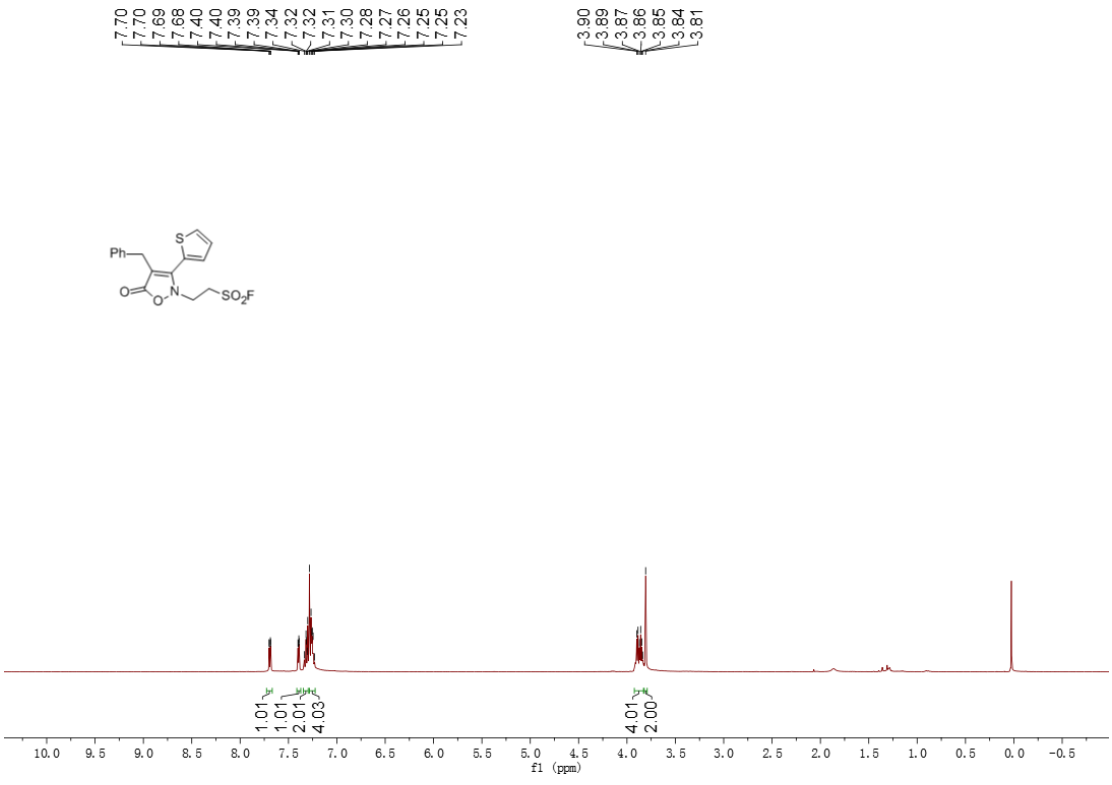


^{13}C NMR (101 MHz, $CDCl_3$)

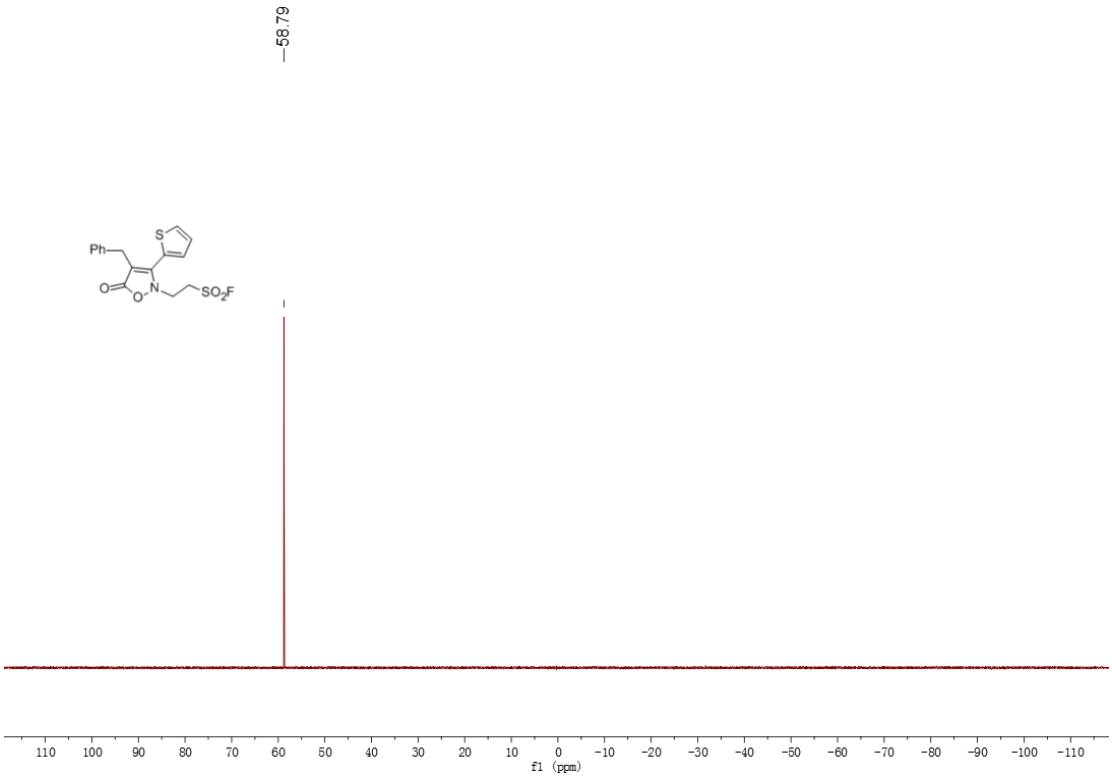


2-(4-Benzyl-5-oxo-3-(thiophen-2-yl)isoxazol-2(5H)-yl)ethanesulfonyl fluoride (3q)

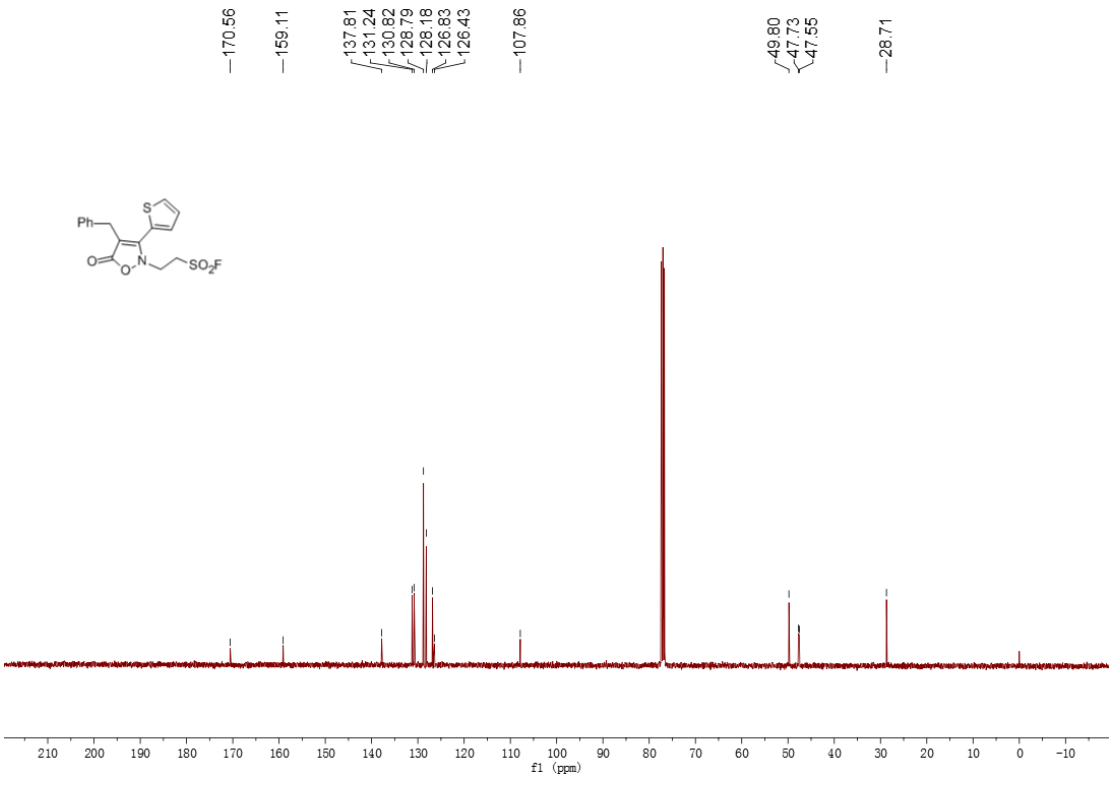
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

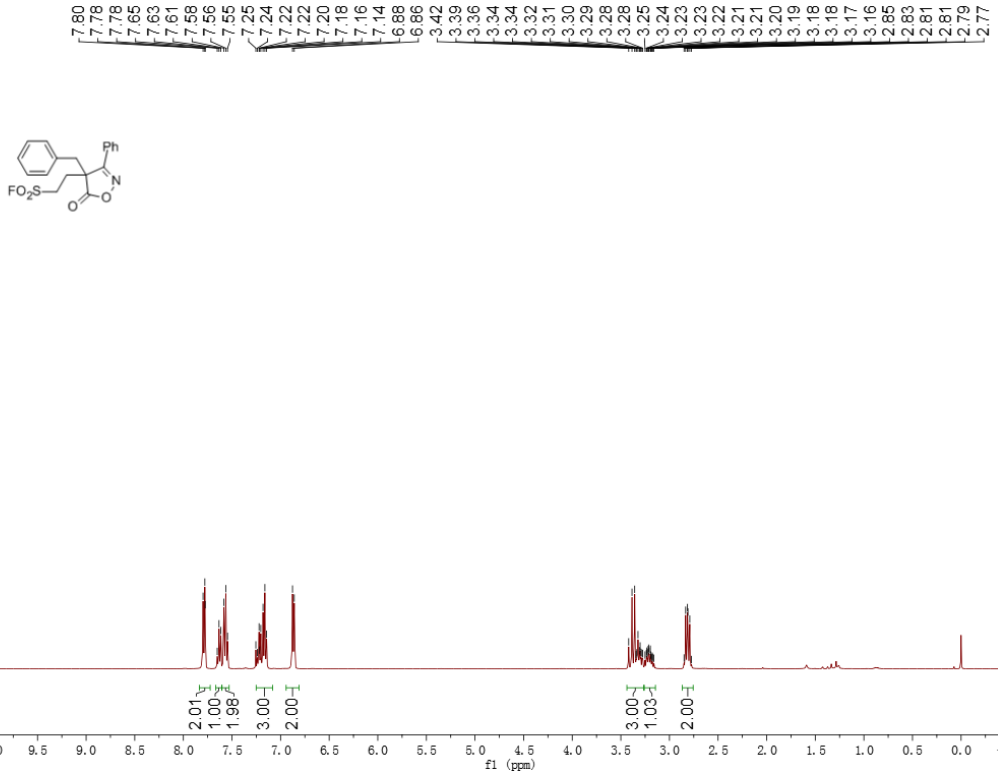


^{13}C NMR (101 MHz, $CDCl_3$)

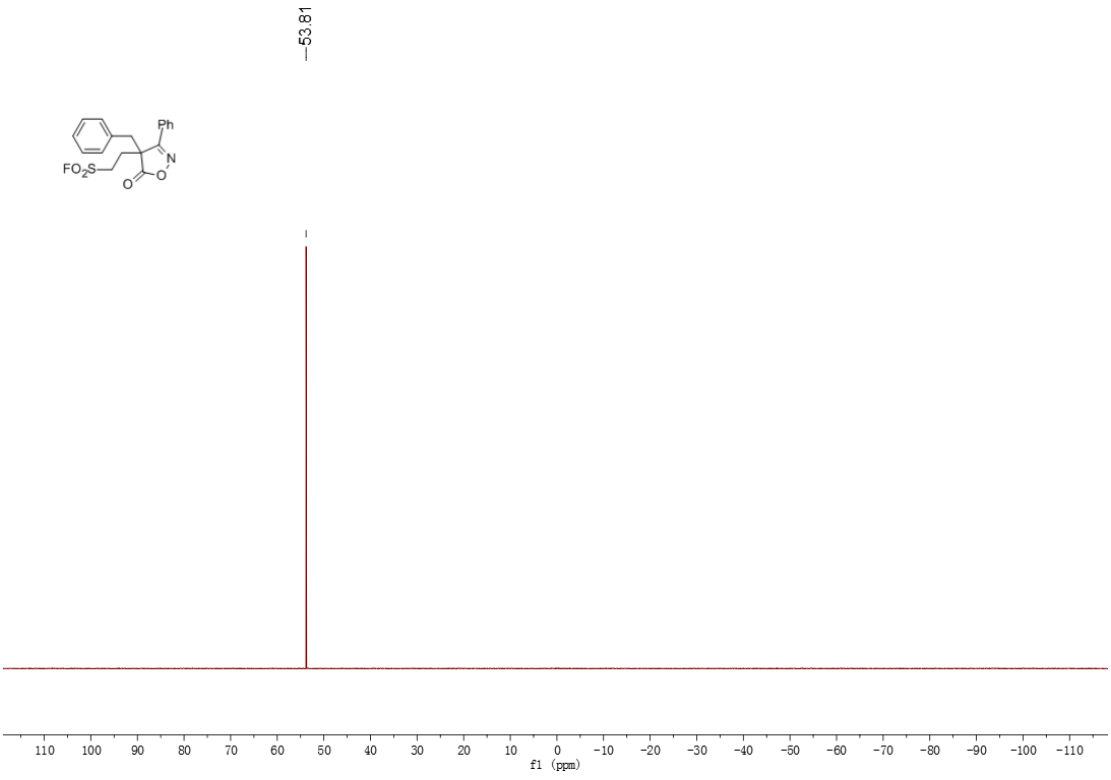


2-(4-Benzyl-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4a)

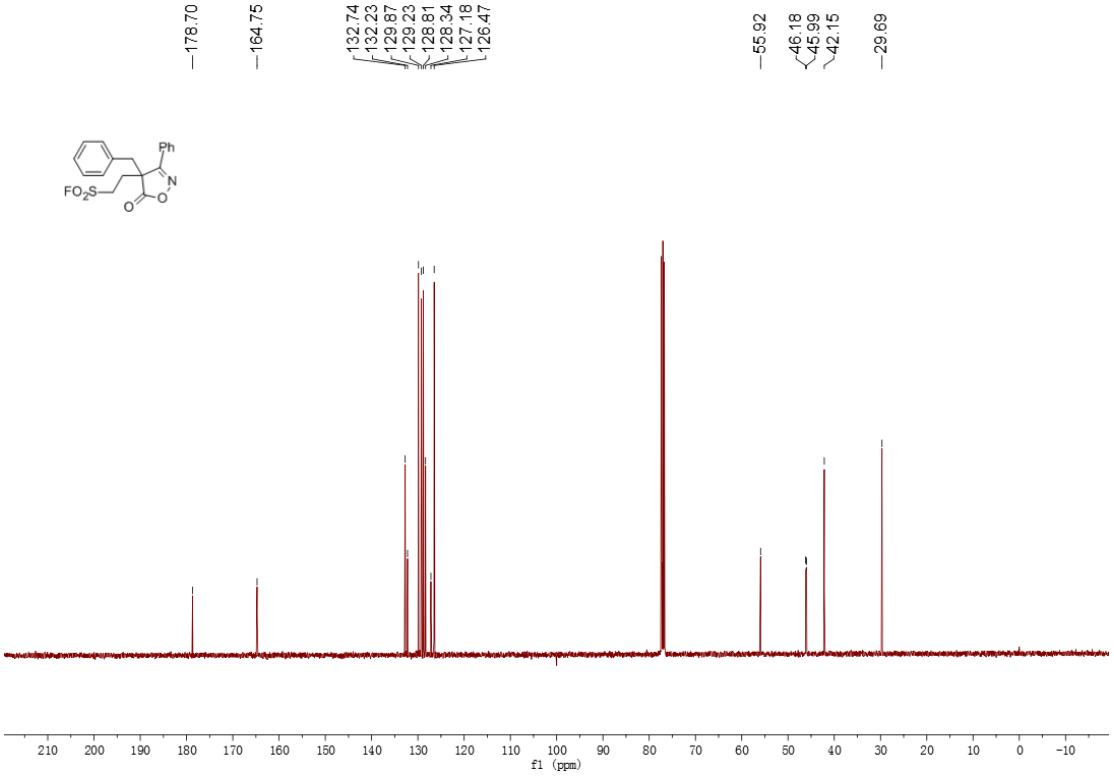
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

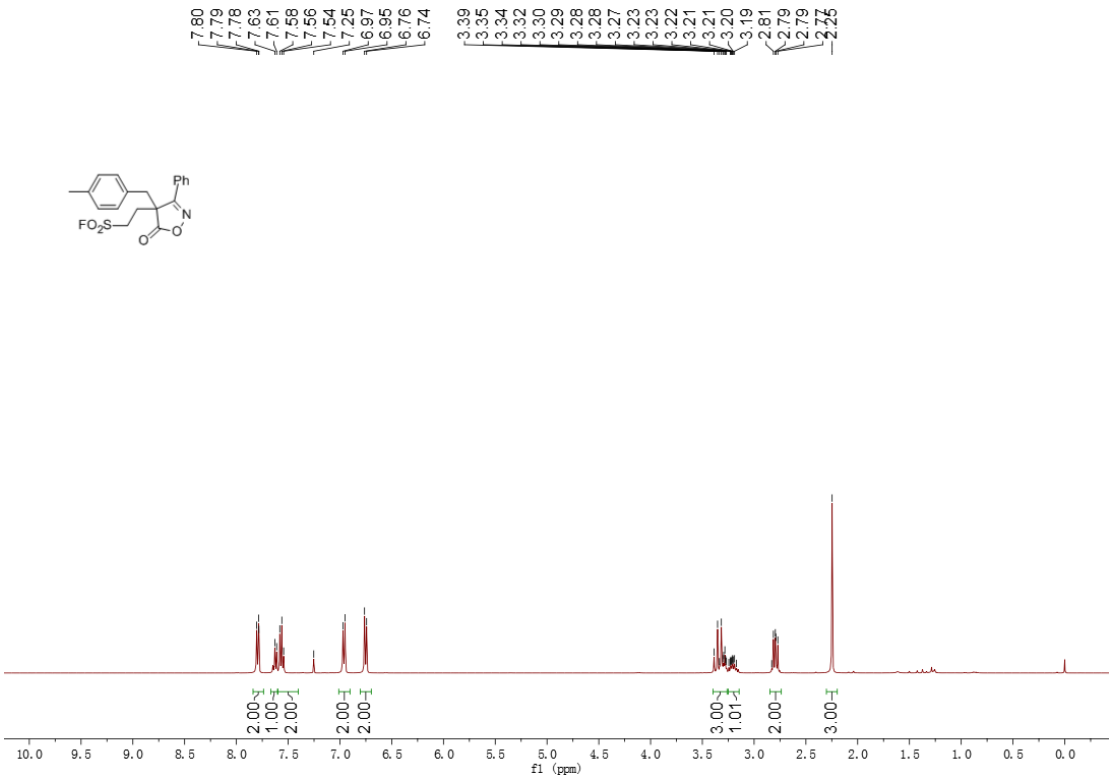


^{13}C NMR (101 MHz, $CDCl_3$)

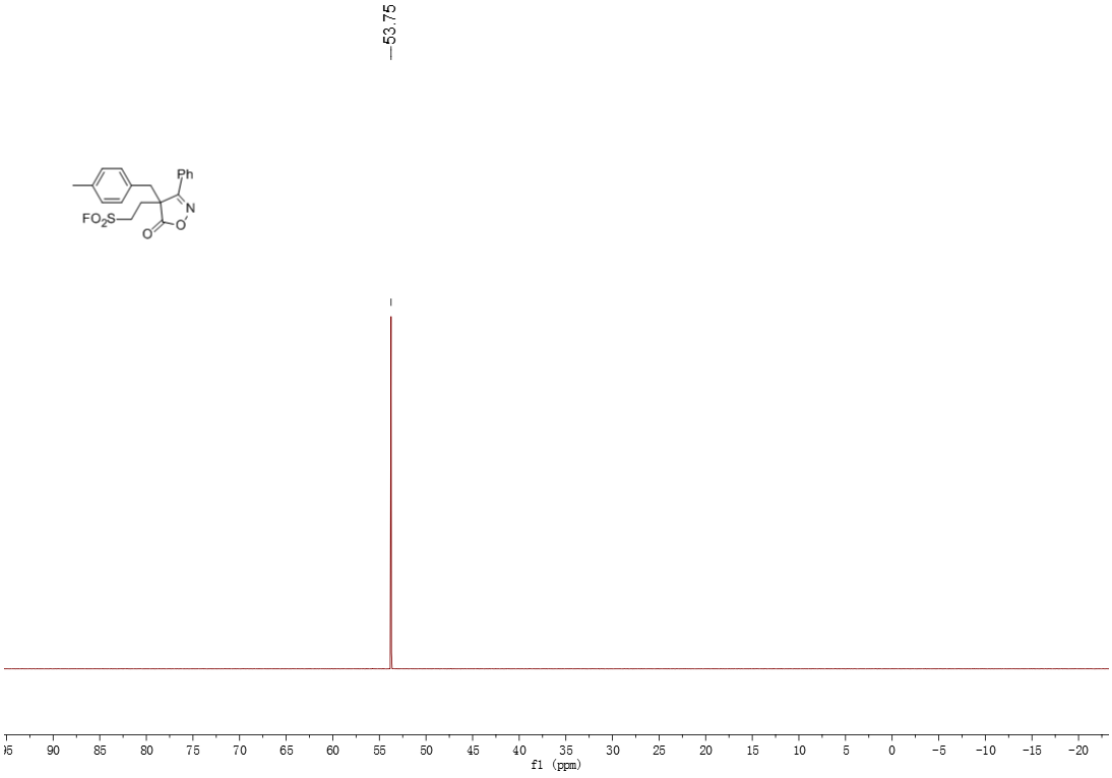


2-(4-(4-Methylbenzyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4b)

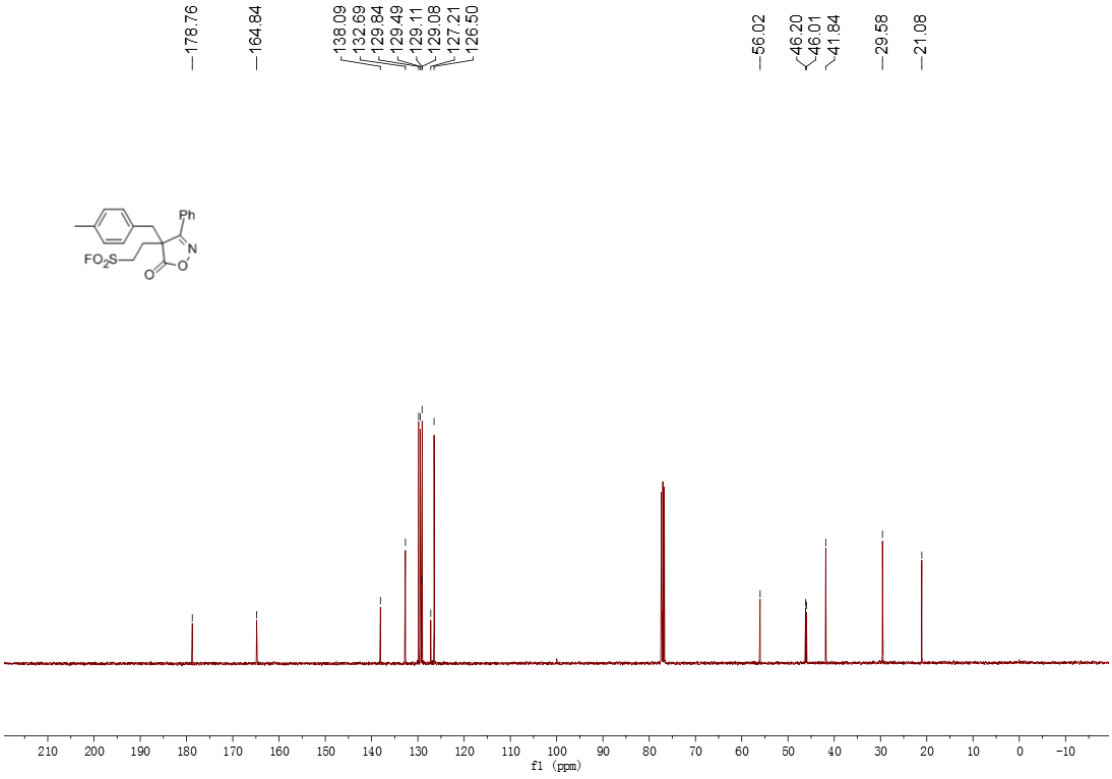
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

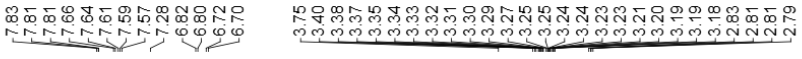


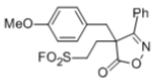
^{13}C NMR (101 MHz, $CDCl_3$)

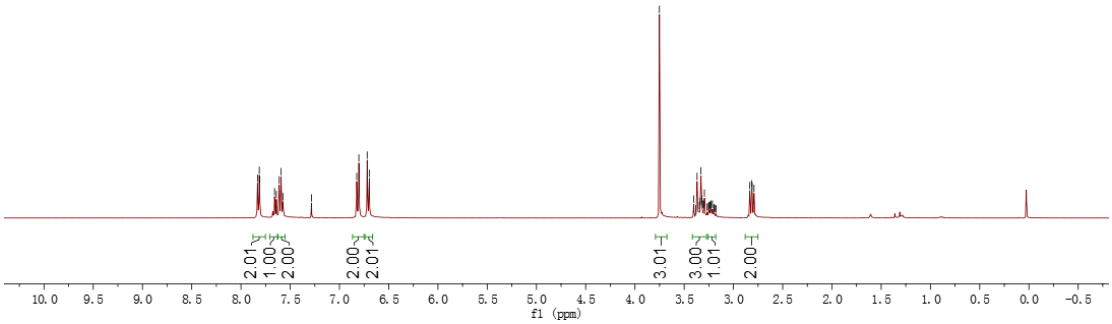


2-(4-(4-Methoxybenzyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4c)

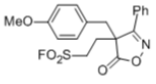
^{1}H NMR (400 MHz, $CDCl_3$)

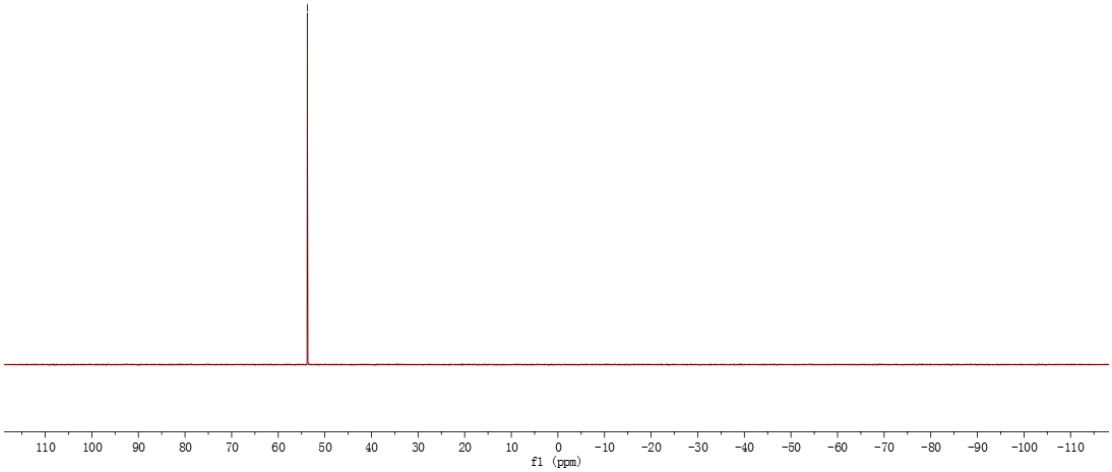




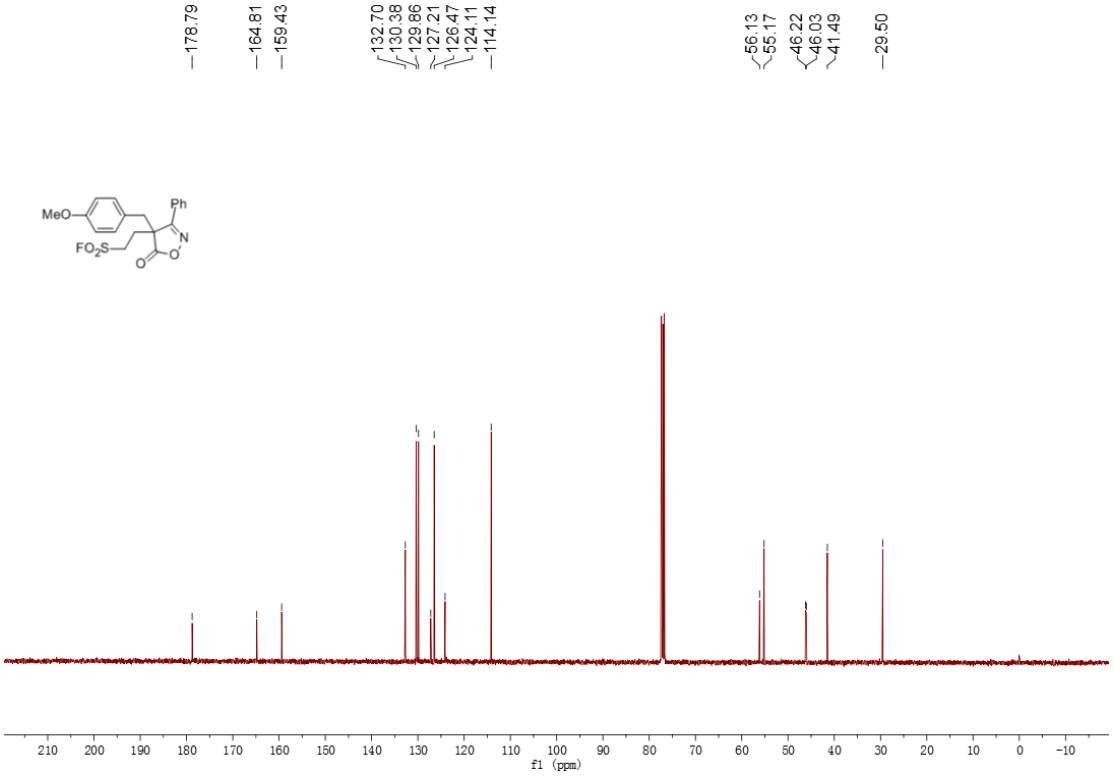


^{19}F NMR (471 MHz, $CDCl_3$)



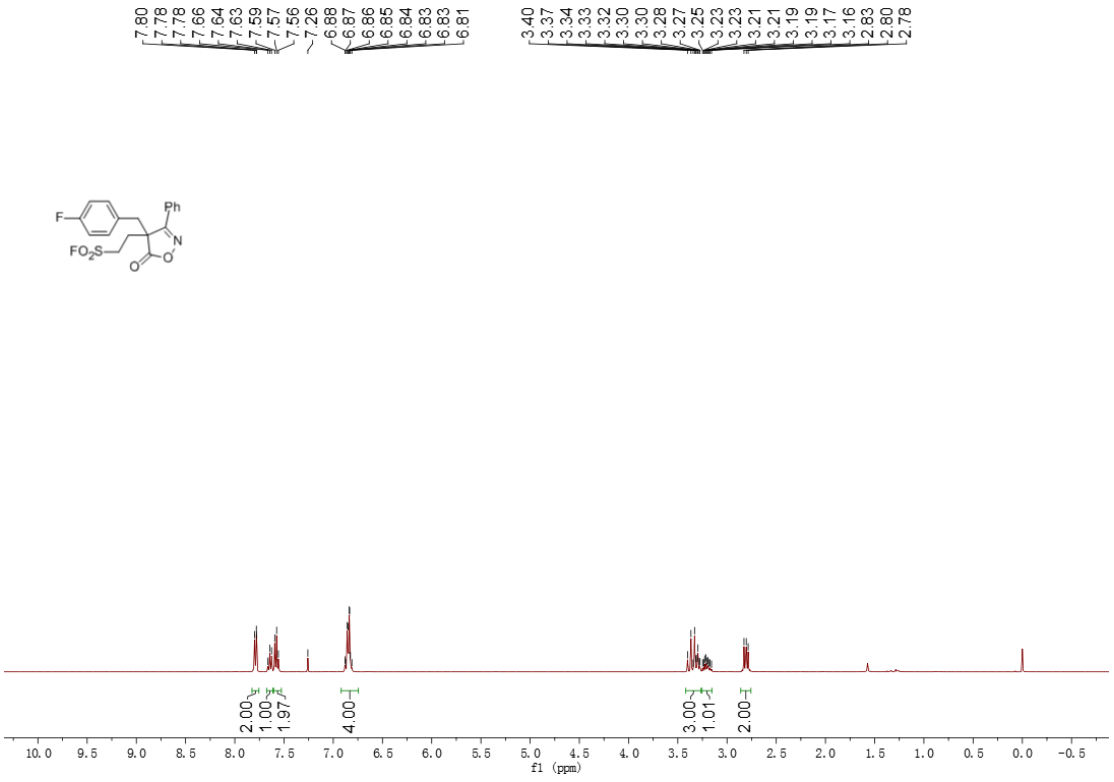


^{13}C NMR (101 MHz, $CDCl_3$)

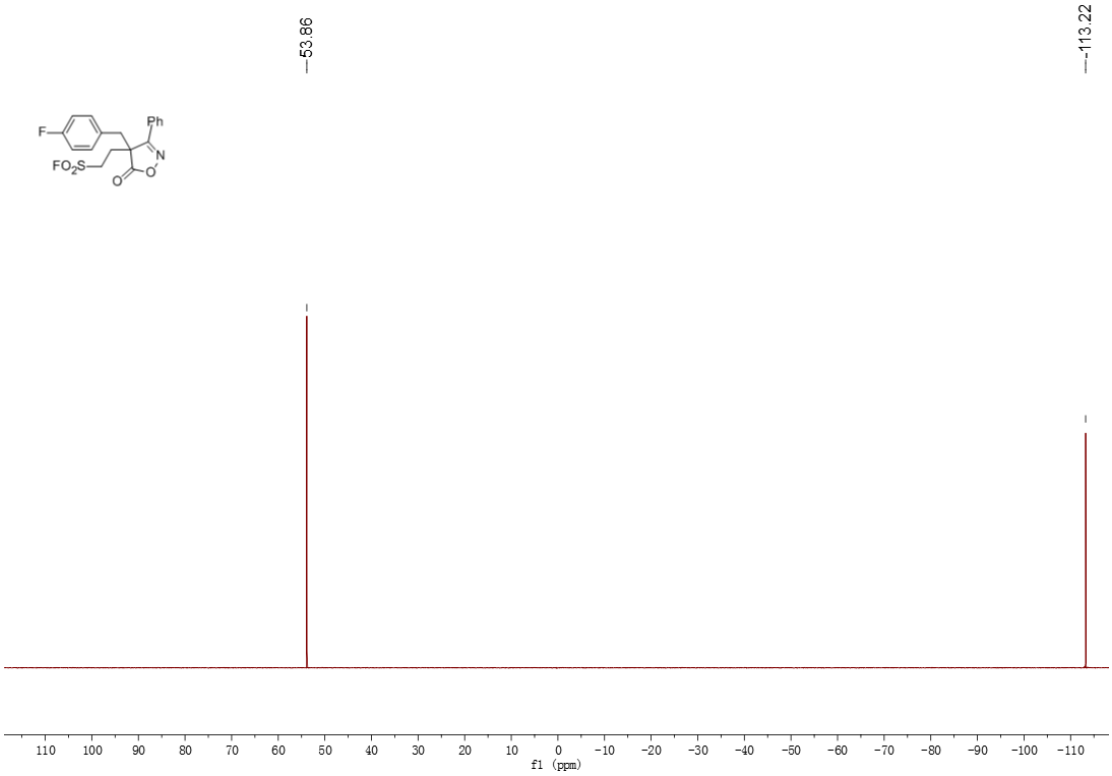


2-(4-(4-Fluorobenzyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4d)

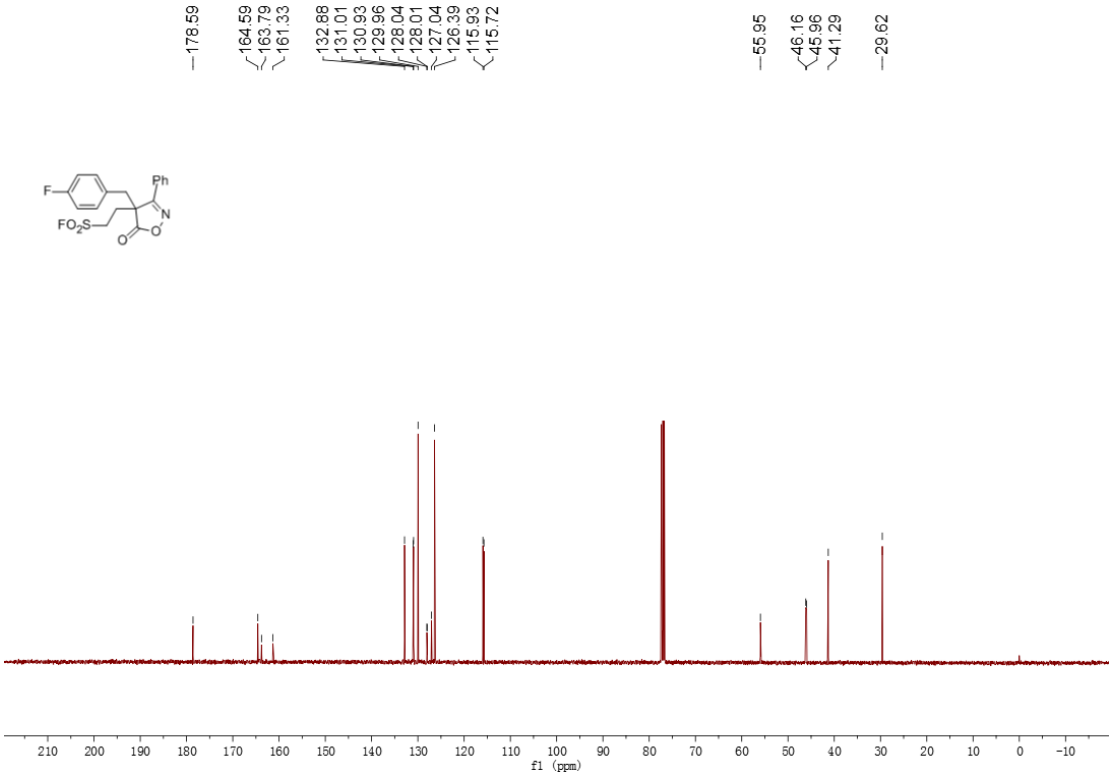
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

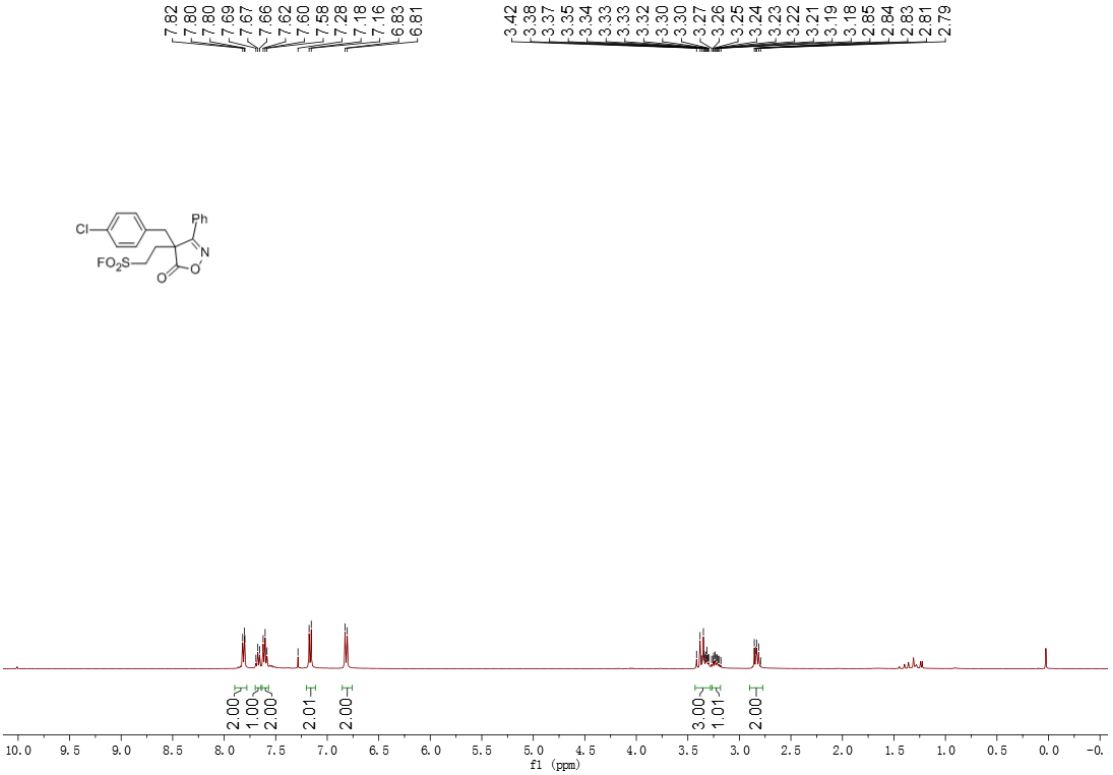


^{13}C NMR (101 MHz, $CDCl_3$)

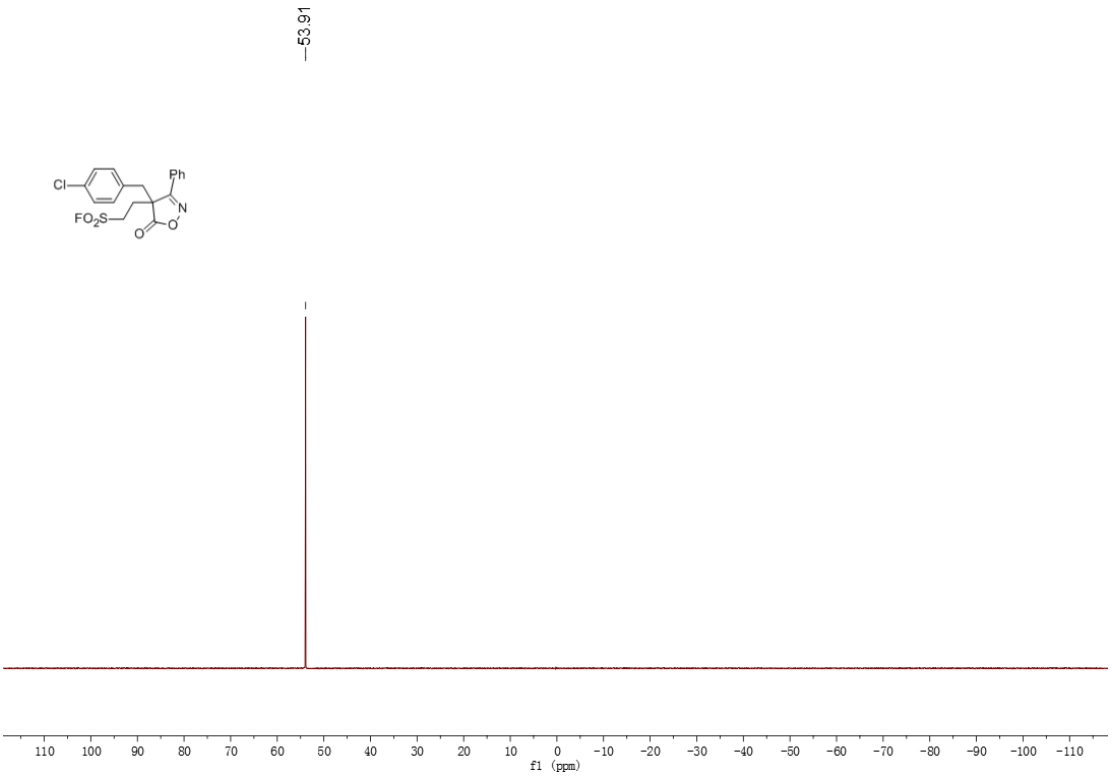


2-(4-(4-Chlorobenzyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4e)

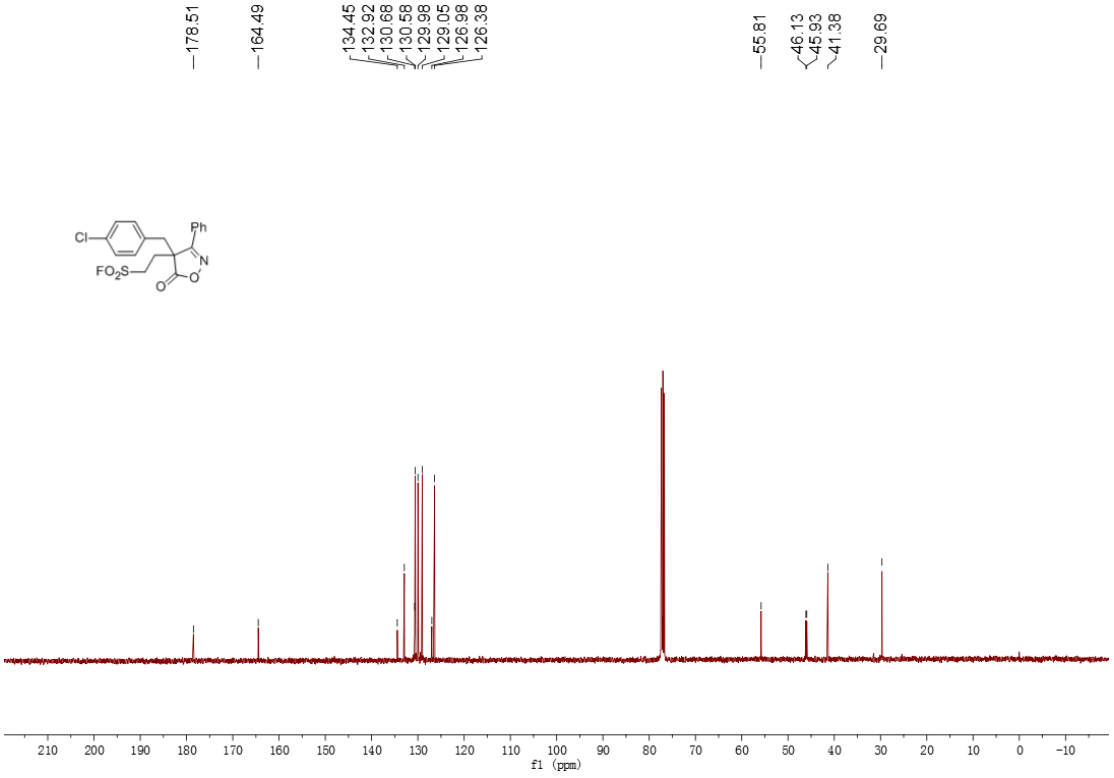
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

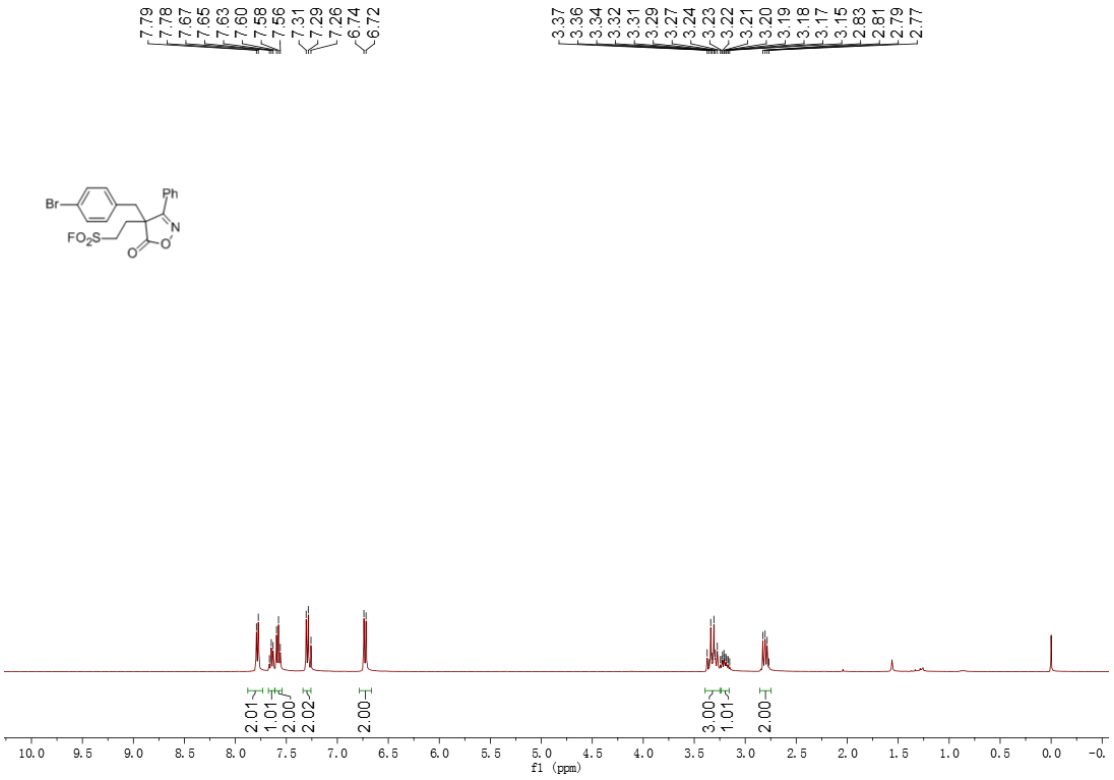


^{13}C NMR (101 MHz, $CDCl_3$)

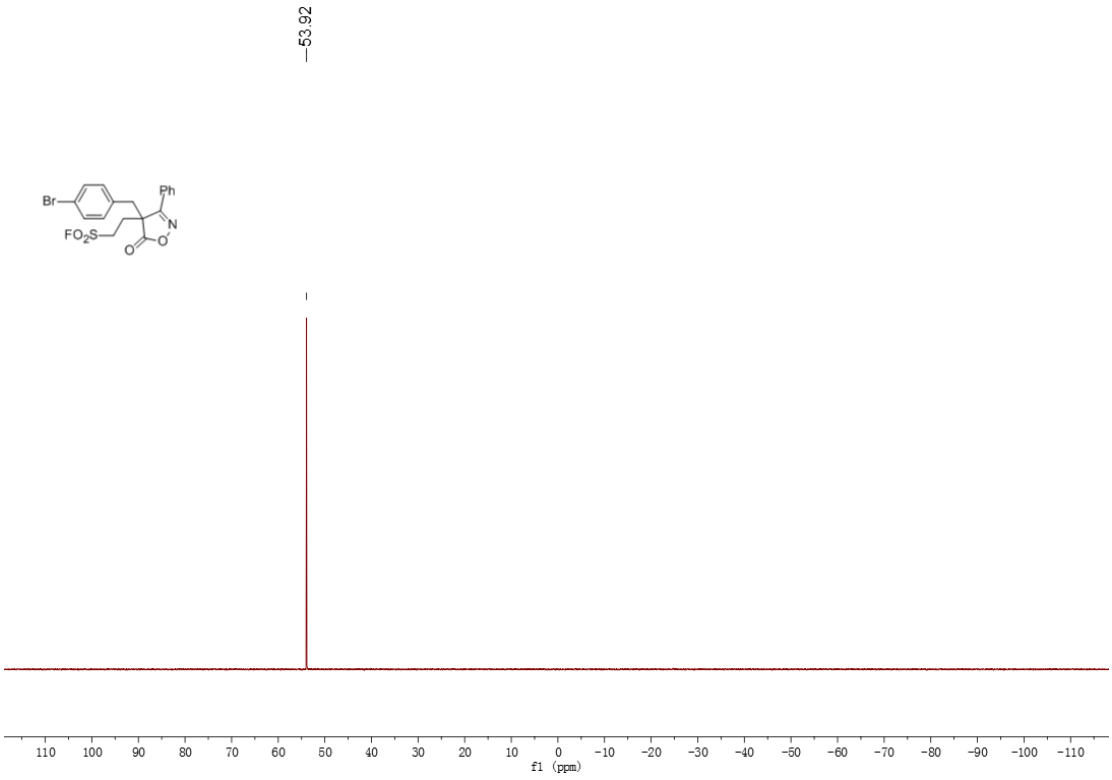


2-(4-(4-Bromobenzyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4f)

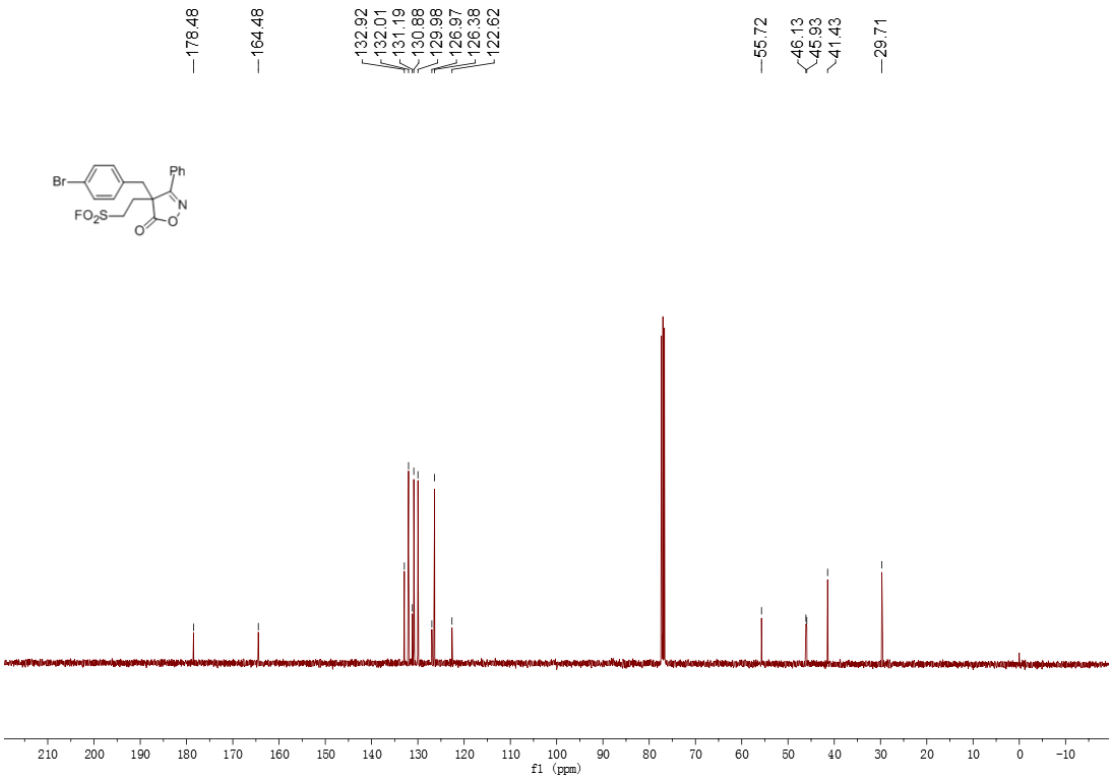
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

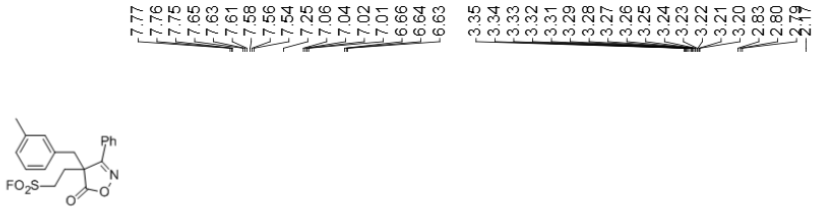


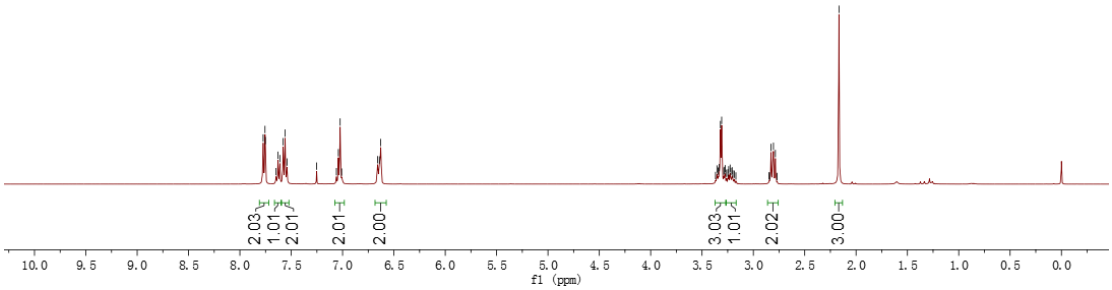
^{13}C NMR (101 MHz, $CDCl_3$)



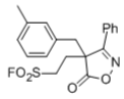
2-(4-(3-Methylbenzyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4g)

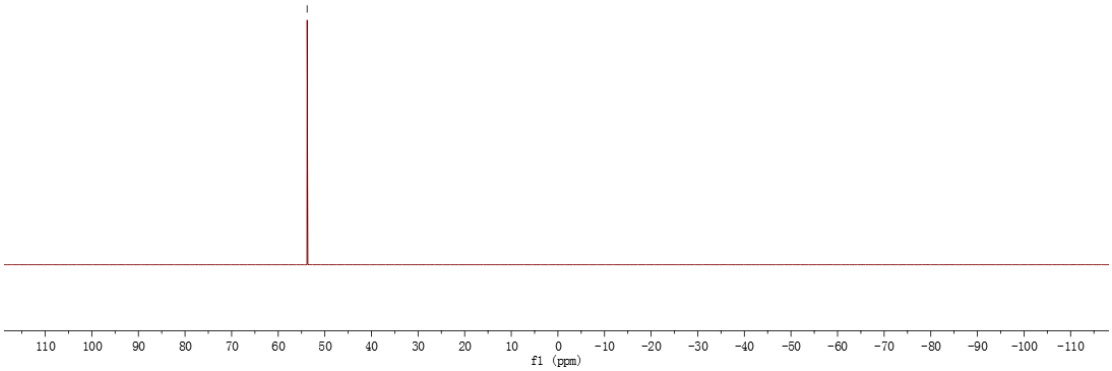
^{1}H NMR (400 MHz, $CDCl_3$)



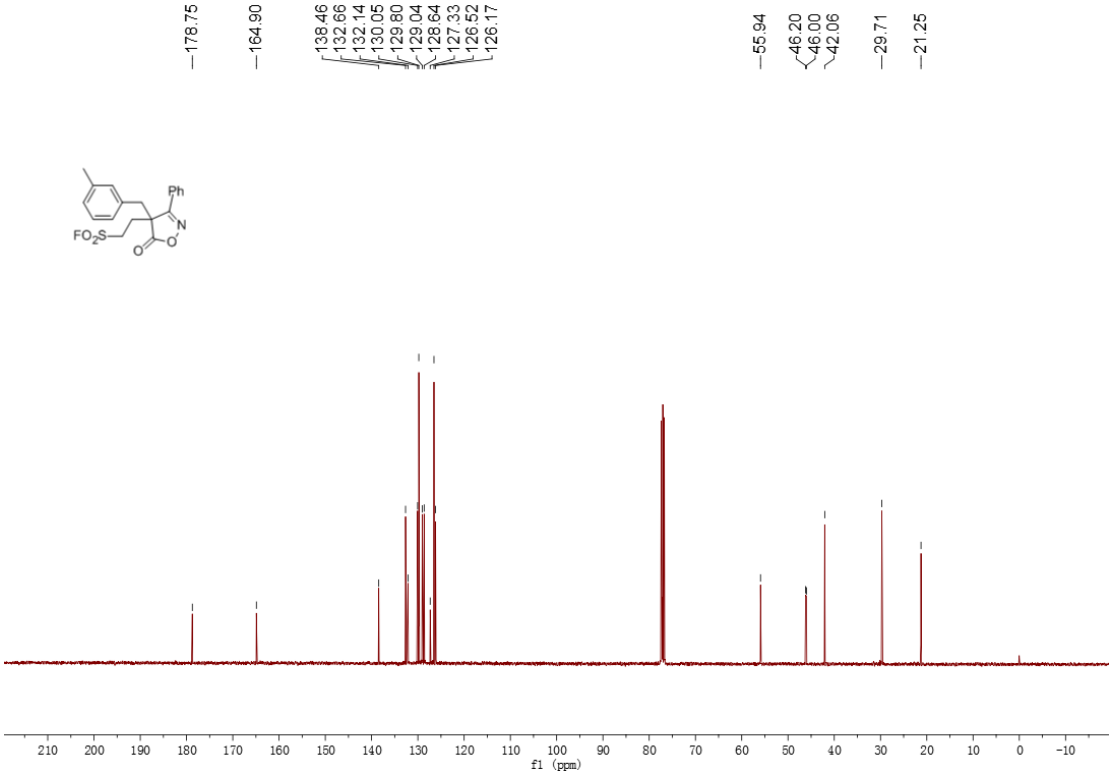


^{19}F NMR (471 MHz, $CDCl_3$)



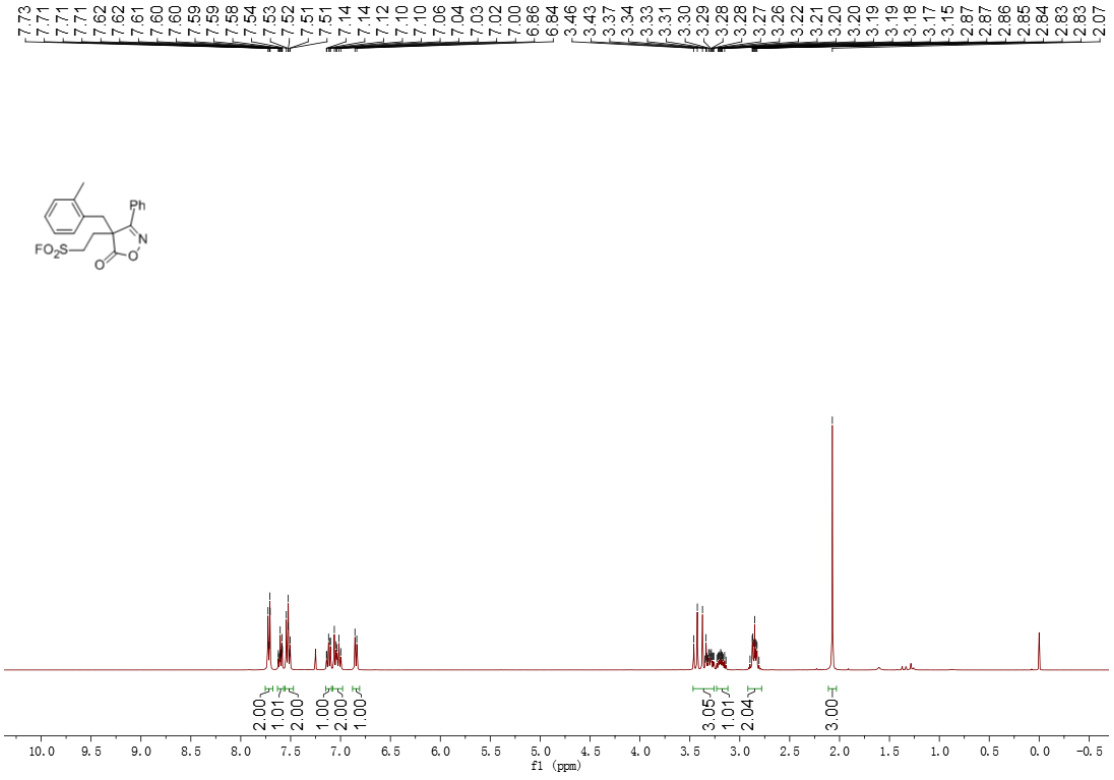


^{13}C NMR (101 MHz, $CDCl_3$)

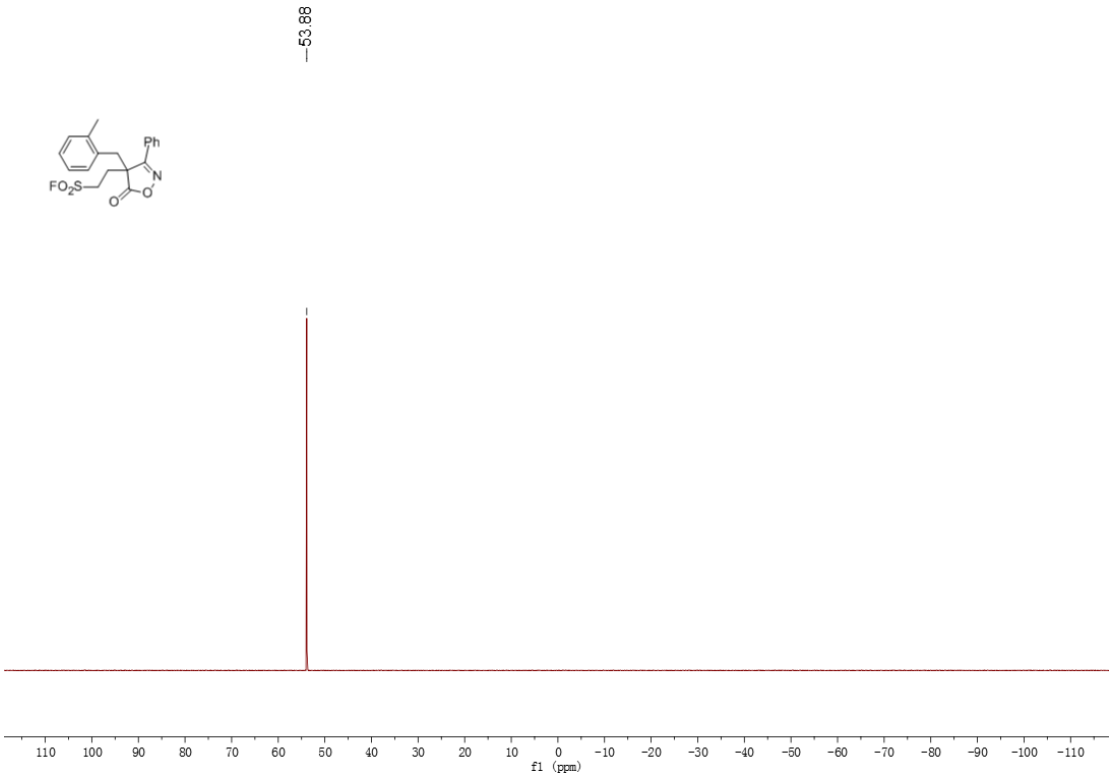


2-(4-(2-Methylbenzyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4h)

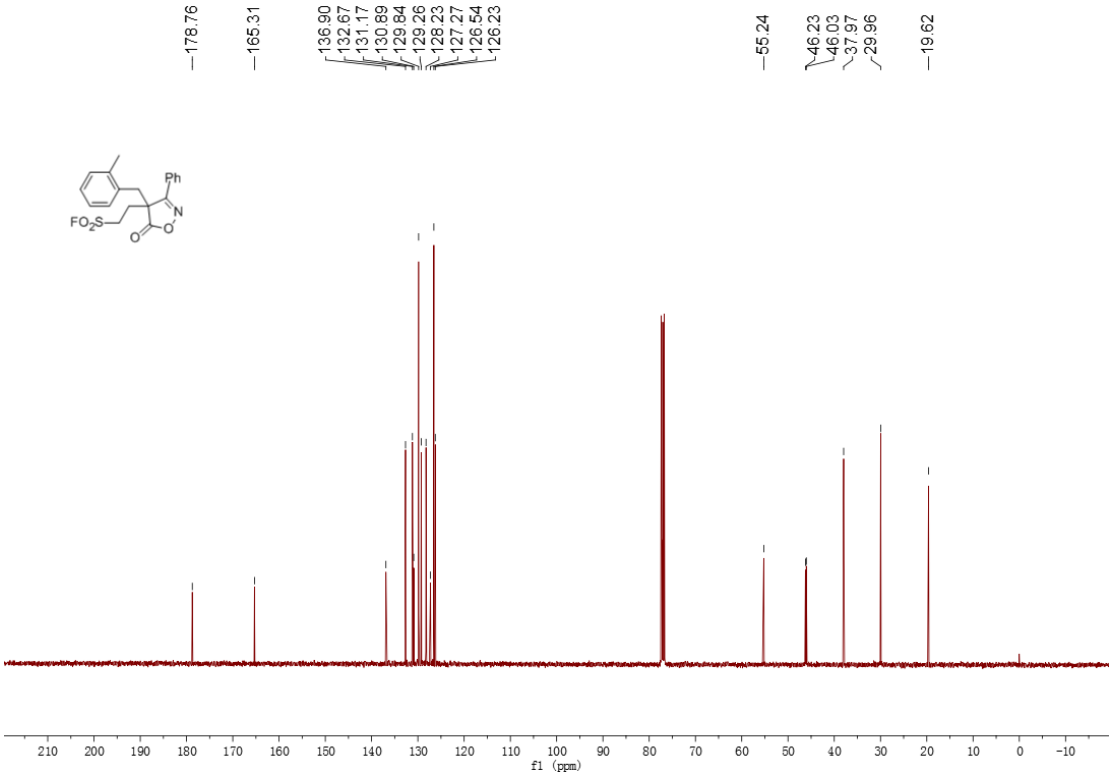
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

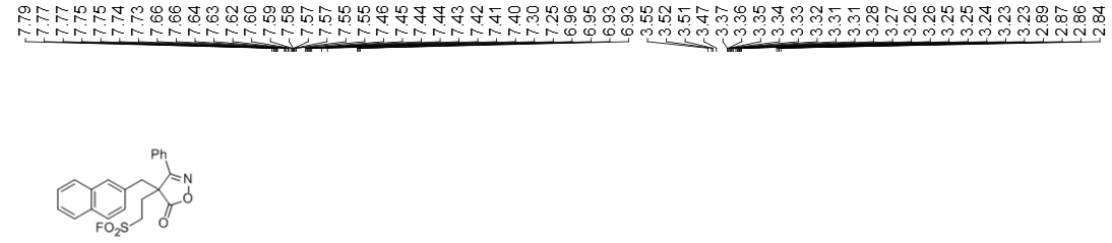


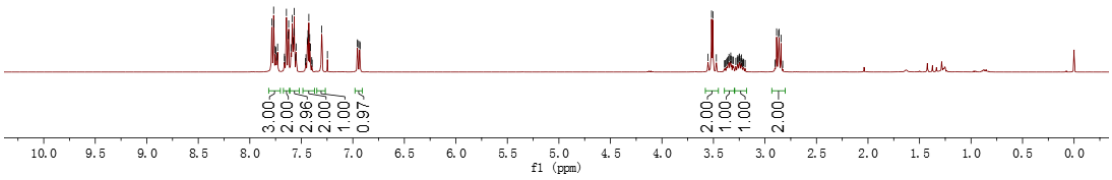
^{13}C NMR (101 MHz, $CDCl_3$)



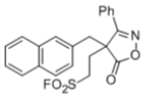
2-(4-(Naphthalen-2-ylmethyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4i)

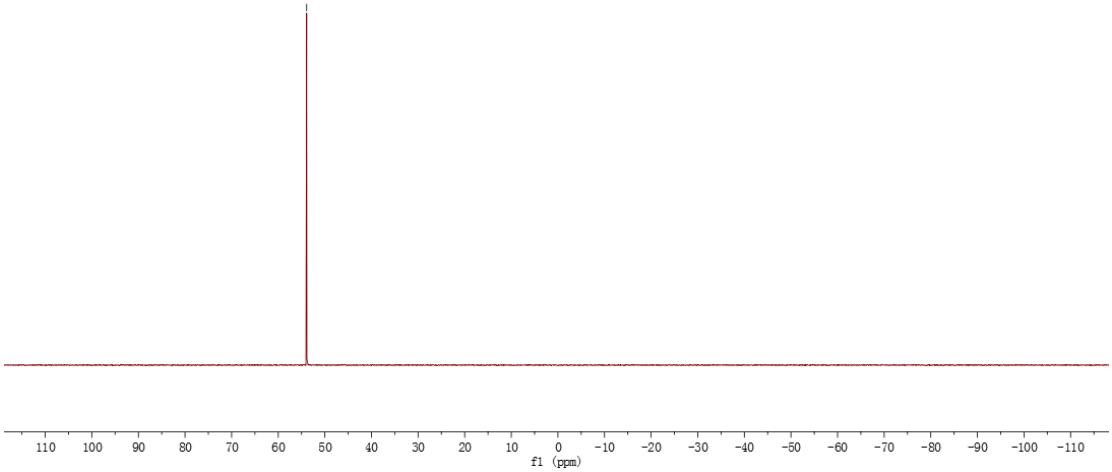
^{1}H NMR (400 MHz, $CDCl_3$)



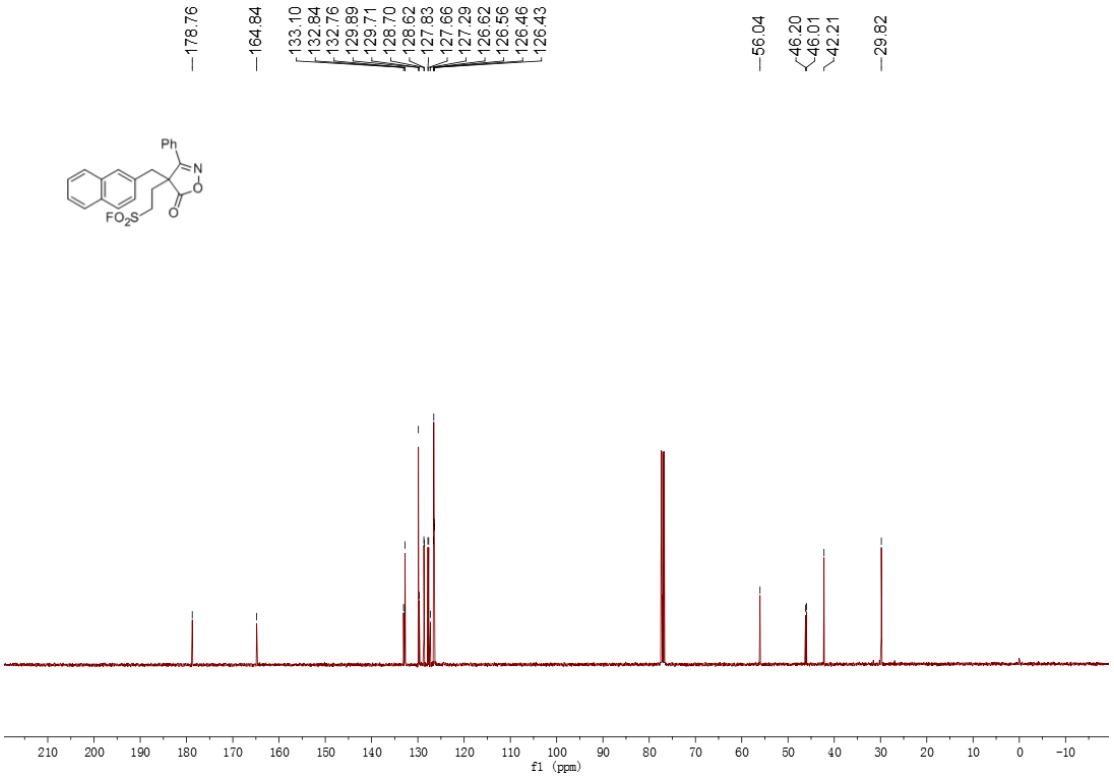


^{19}F NMR (471 MHz, $CDCl_3$)



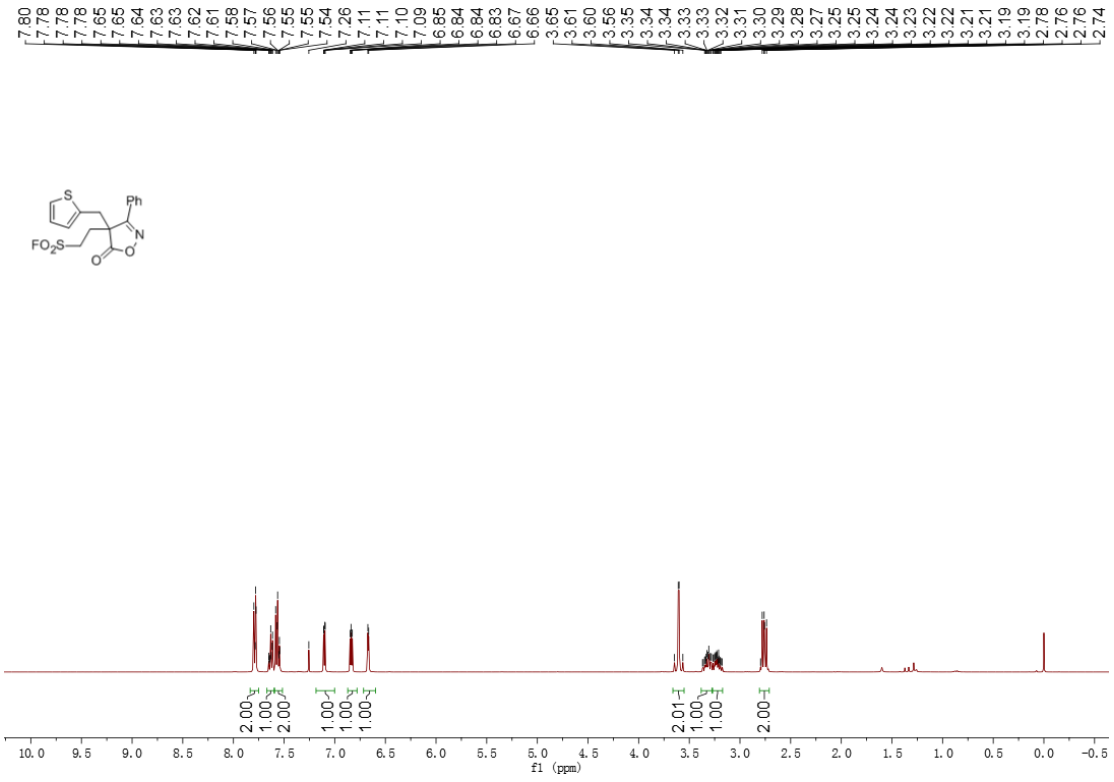


^{13}C NMR (101 MHz, $CDCl_3$)

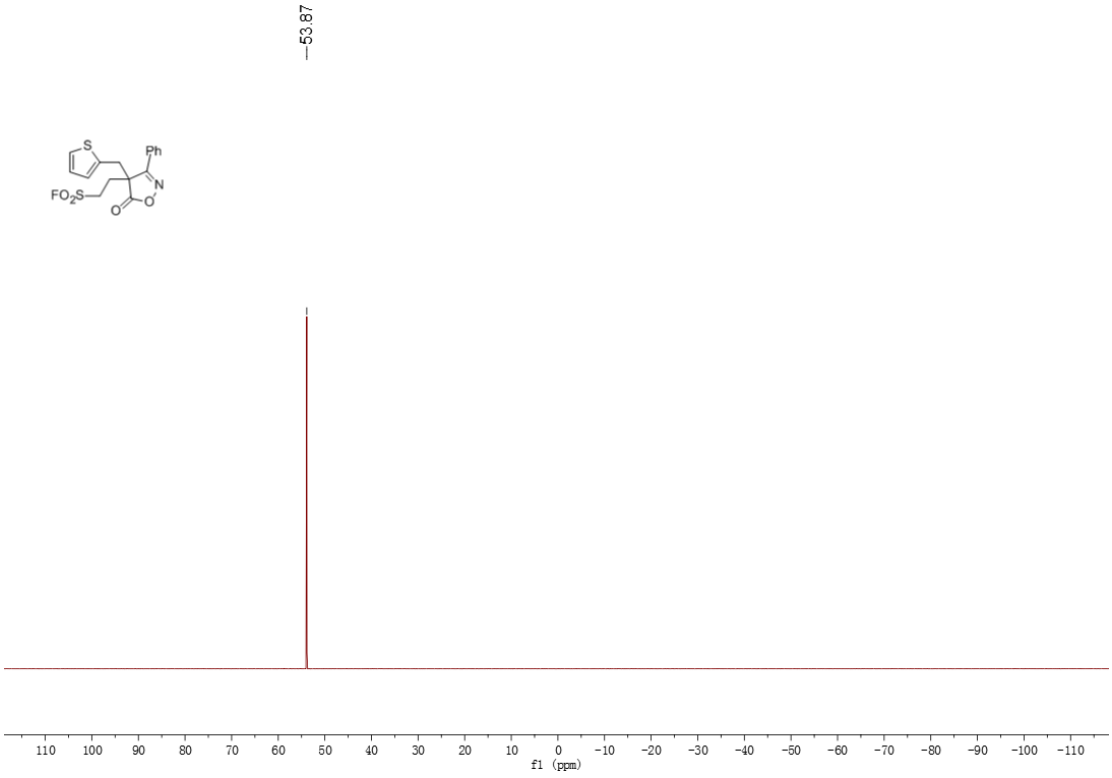


2-(5-Oxo-3-phenyl-4-(thiophen-2-ylmethyl)-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4j)

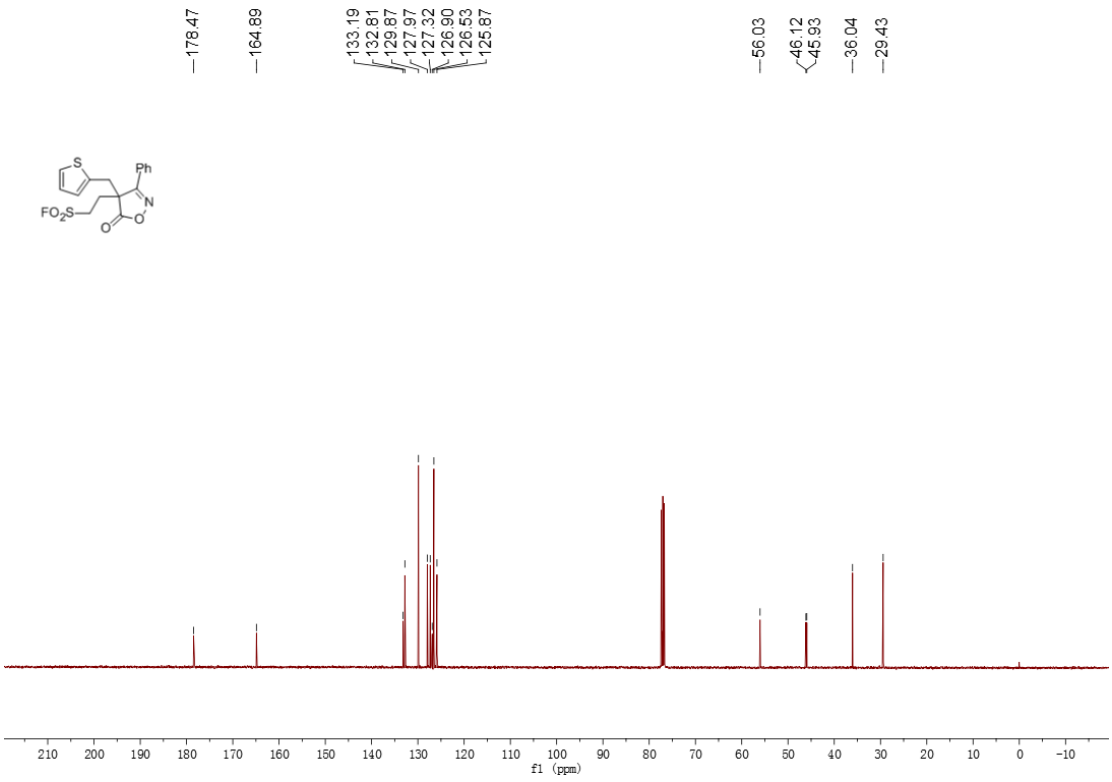
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

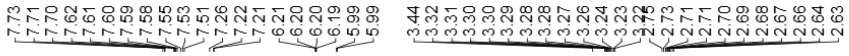


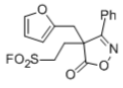
^{13}C NMR (101 MHz, $CDCl_3$)

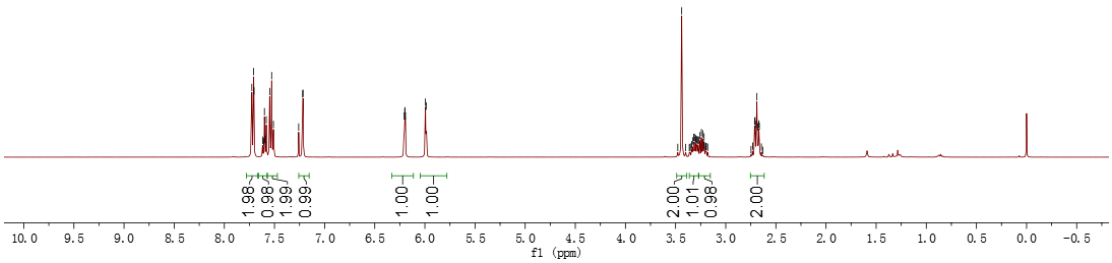


2-(4-(Furan-2-ylmethyl)-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4k)

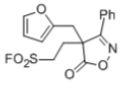
^{1}H NMR (400 MHz, $CDCl_3$)



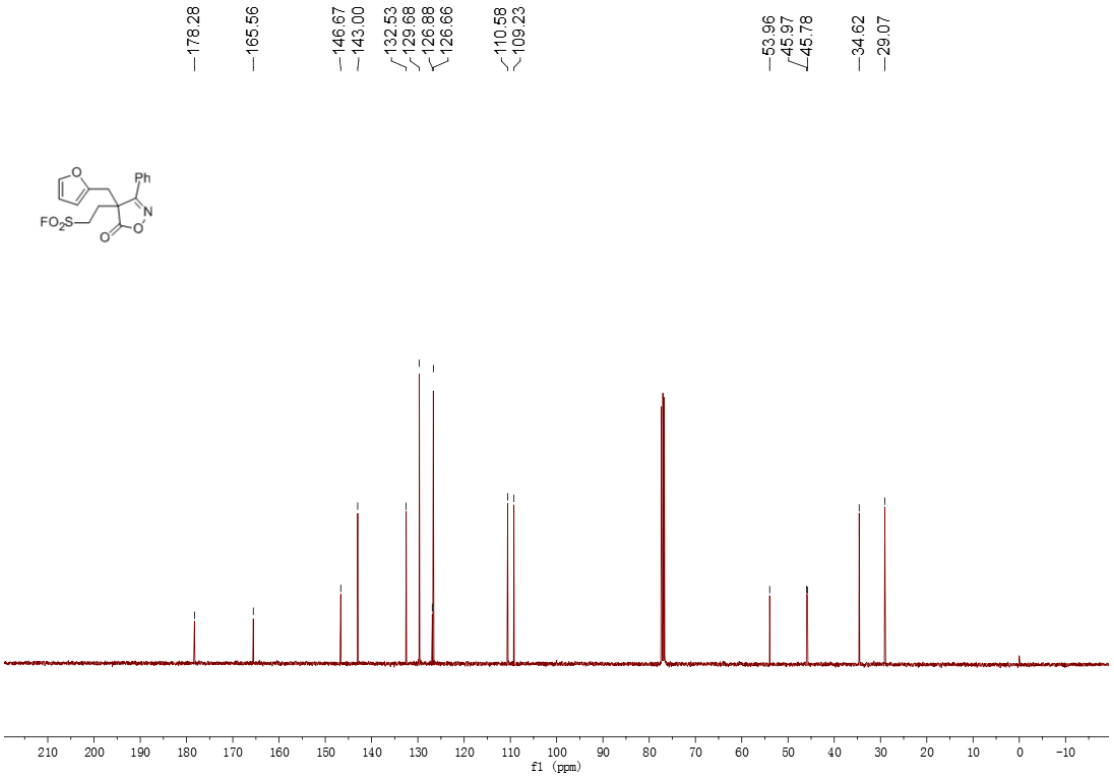




^{19}F NMR (471 MHz, $CDCl_3$)

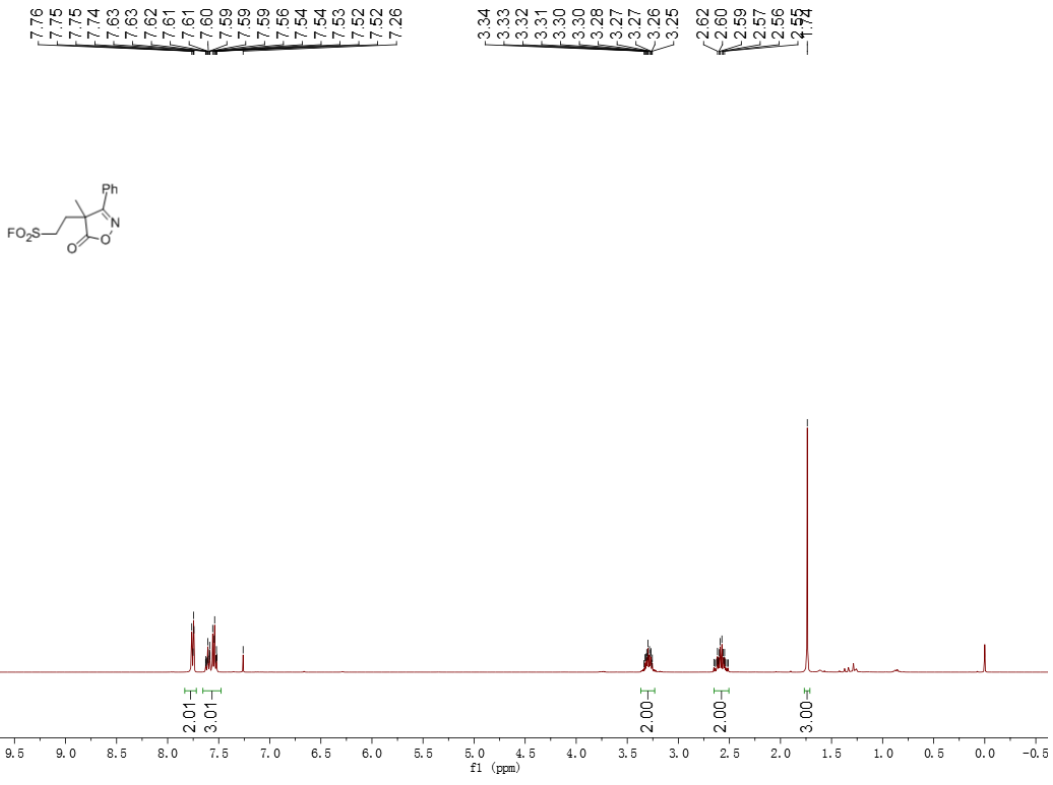


^{13}C NMR (101 MHz, $CDCl_3$)

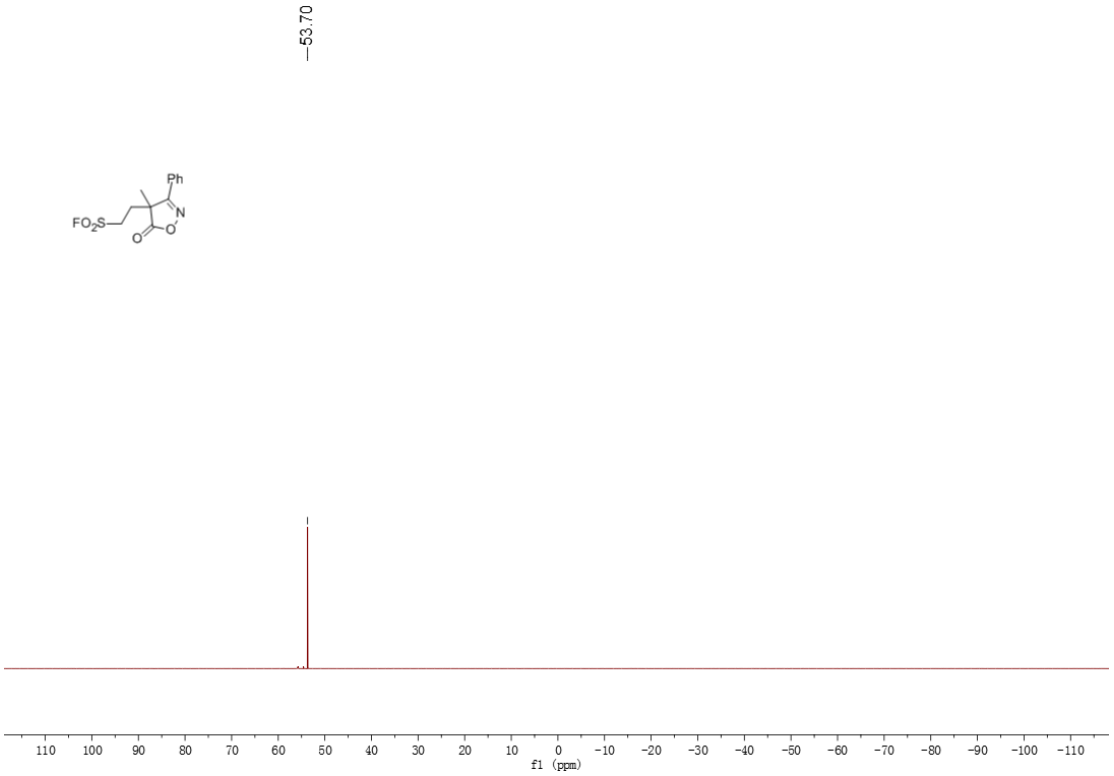


2-(4-Mthyl-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4l)

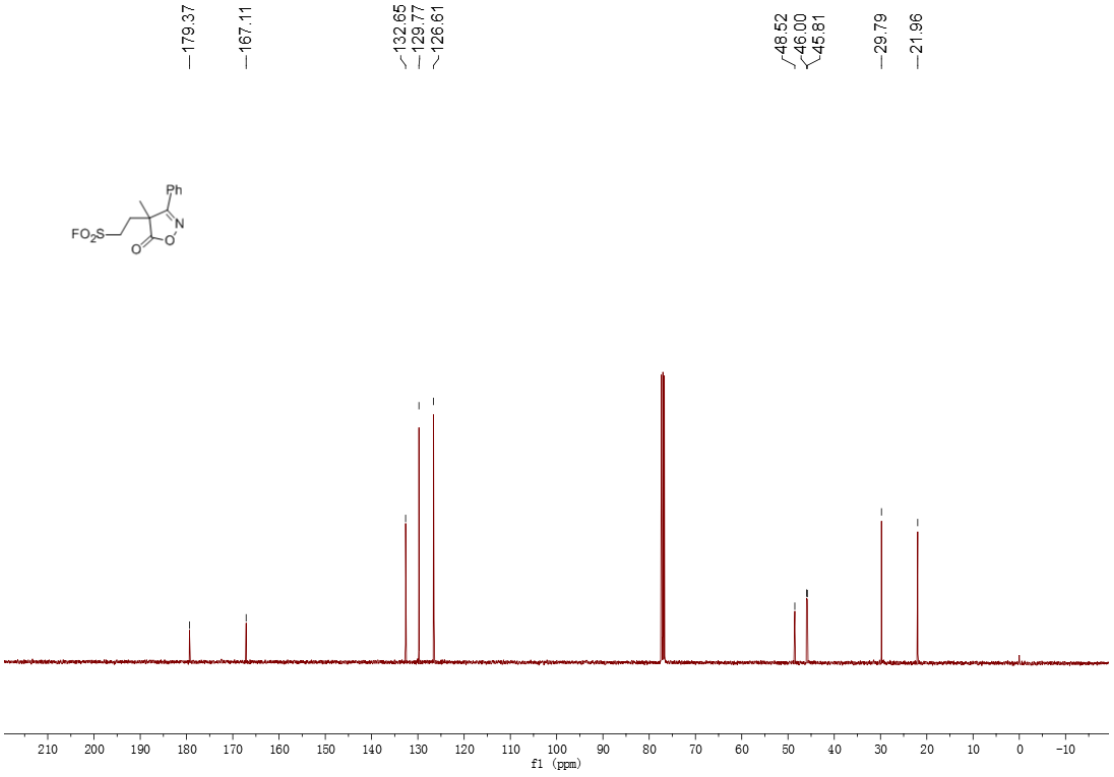
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

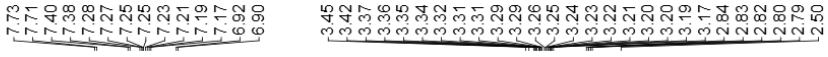


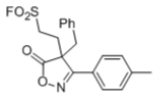
^{13}C NMR (101 MHz, $CDCl_3$)

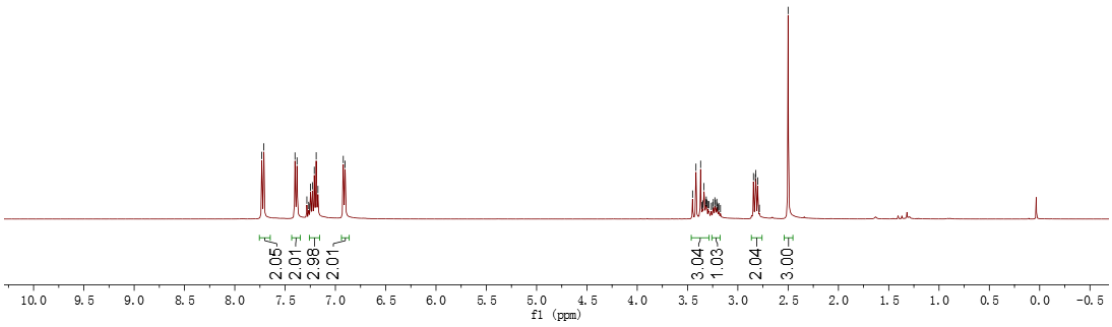


2-(4-Benzyl-5-oxo-3-(p-tolyl)-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4m)

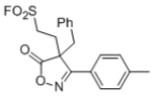
^{1}H NMR (400 MHz, $CDCl_3$)

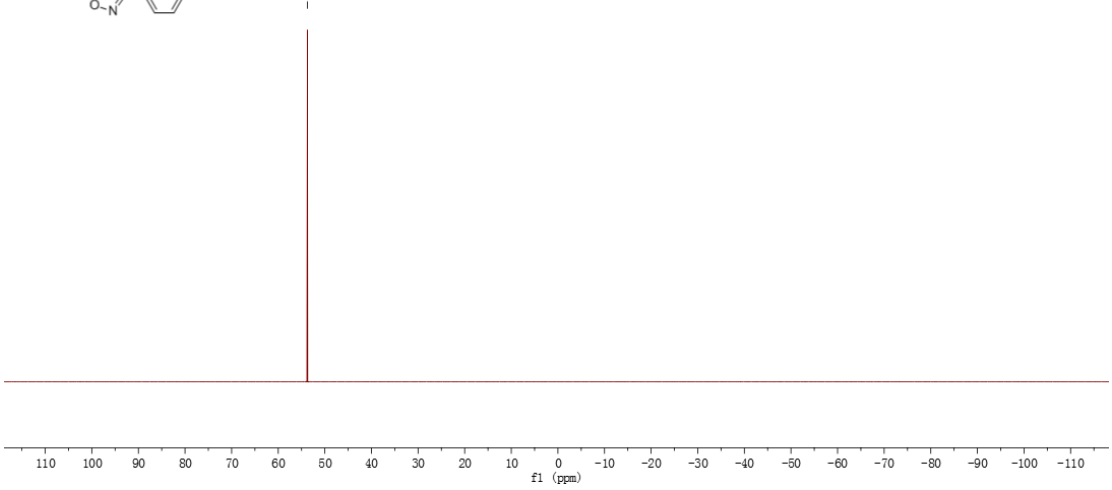




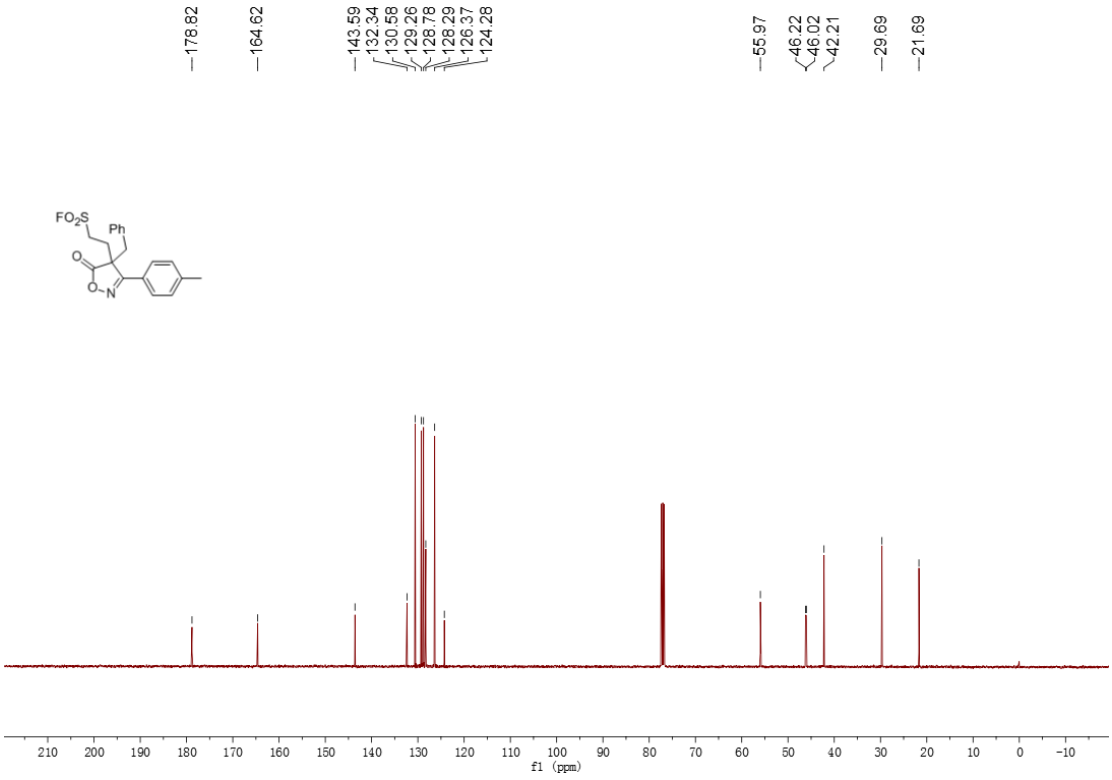


^{19}F NMR (471 MHz, $CDCl_3$)



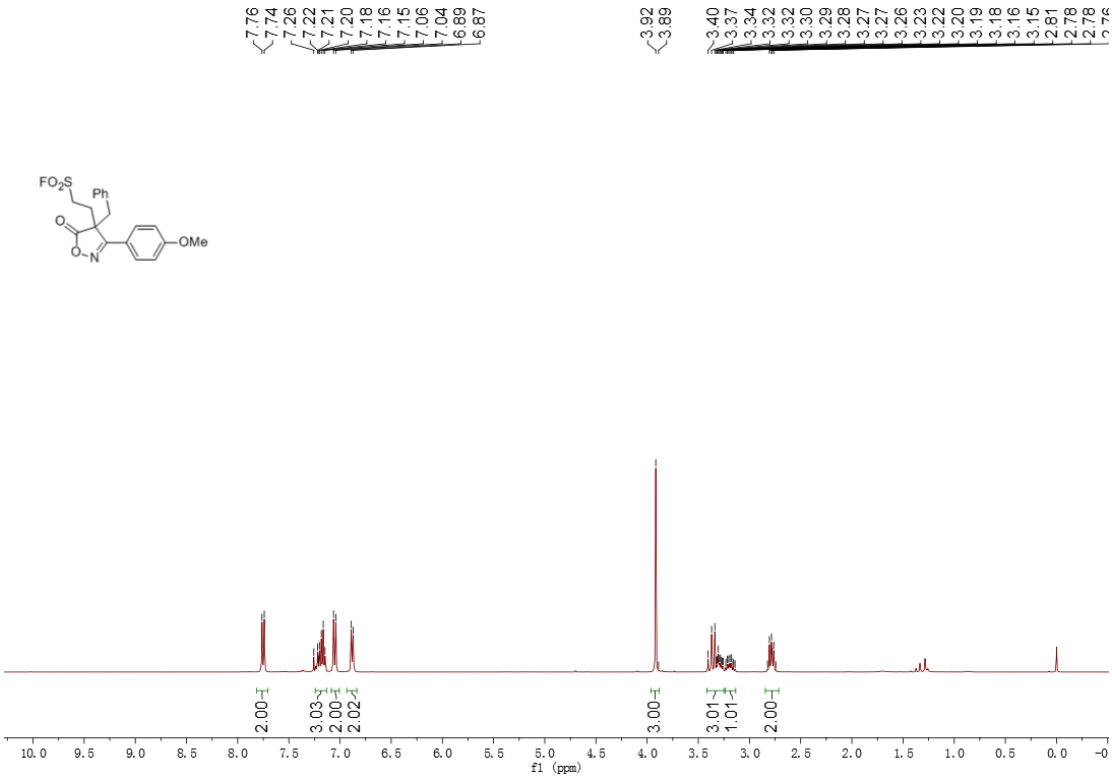


^{13}C NMR (101 MHz, $CDCl_3$)

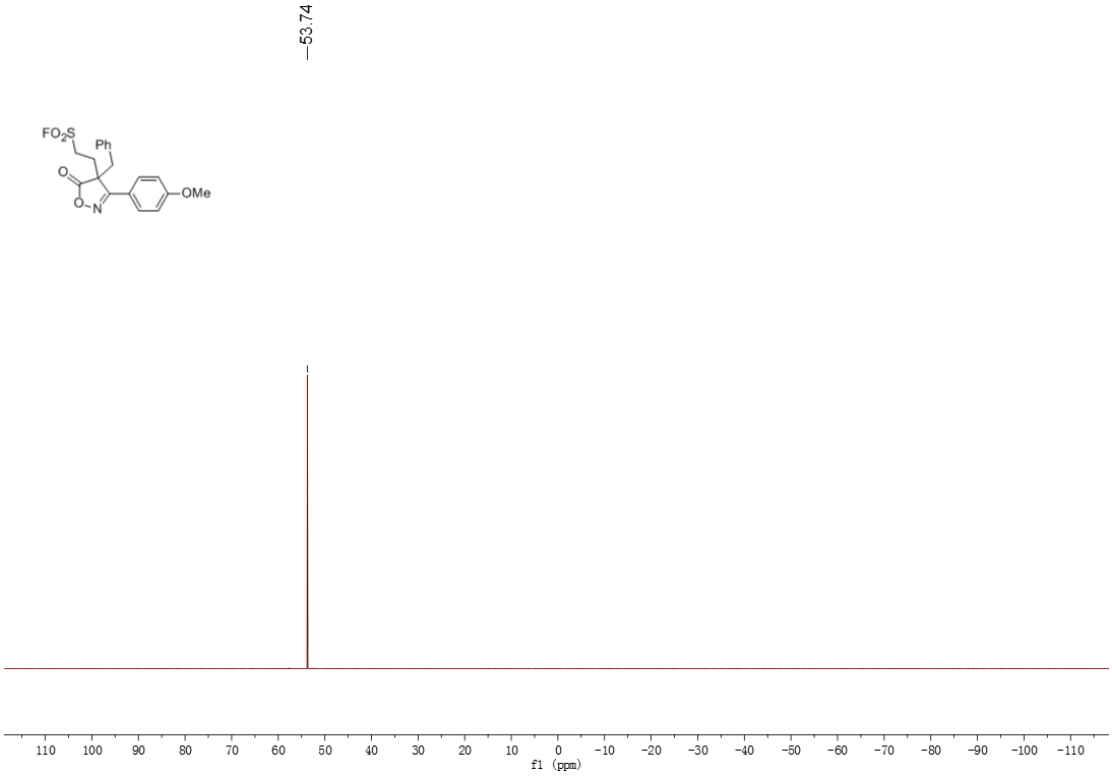


2-(4-Benzyl-3-(4-methoxyphenyl)-5-oxo-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4n)

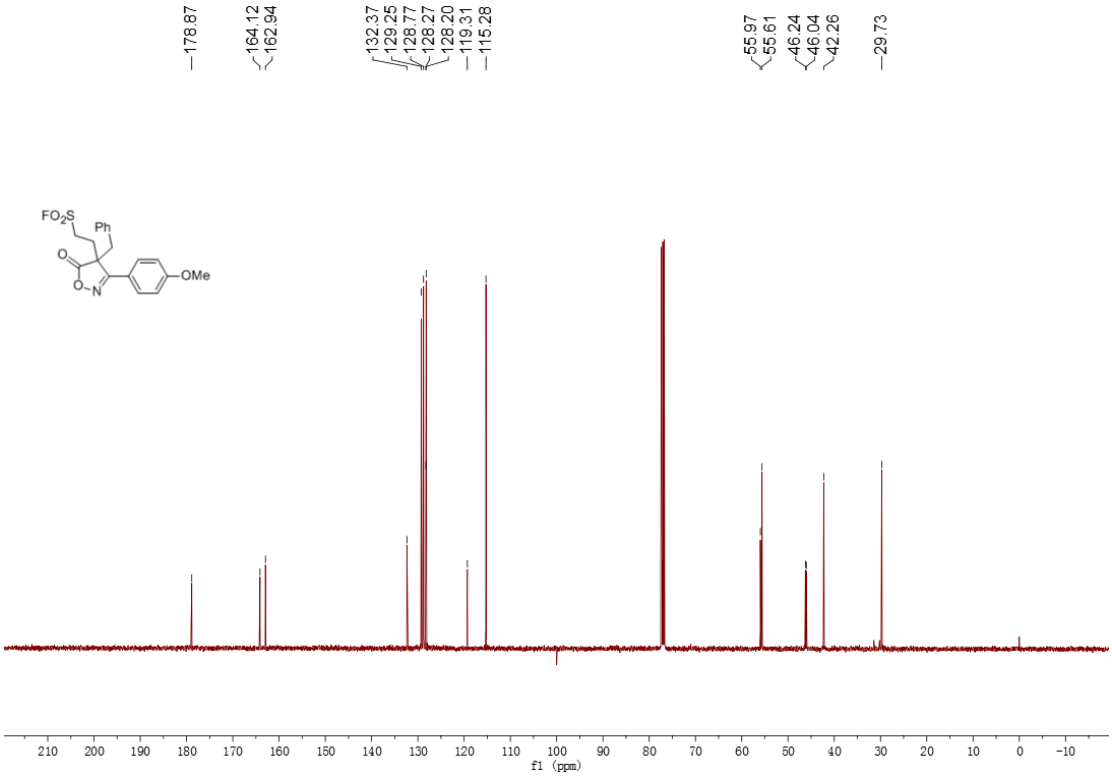
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

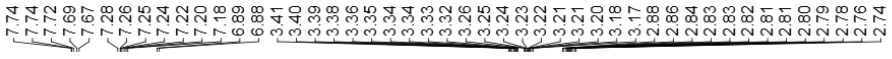


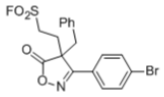
^{13}C NMR (101 MHz, $CDCl_3$)

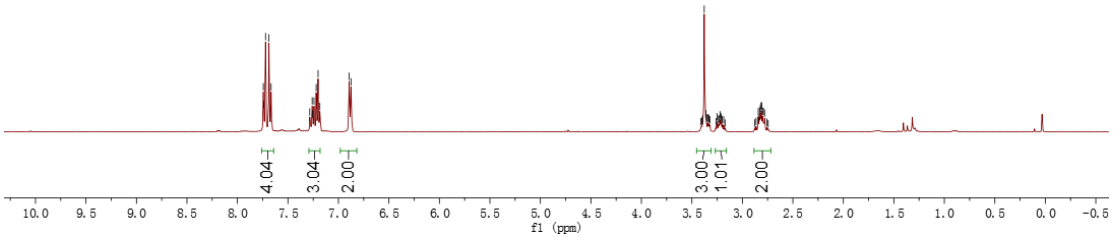


2-(4-Benzyl-3-(4-bromophenyl)-5-oxo-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4o)

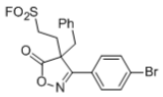
^{1}H NMR (400 MHz, $CDCl_3$)

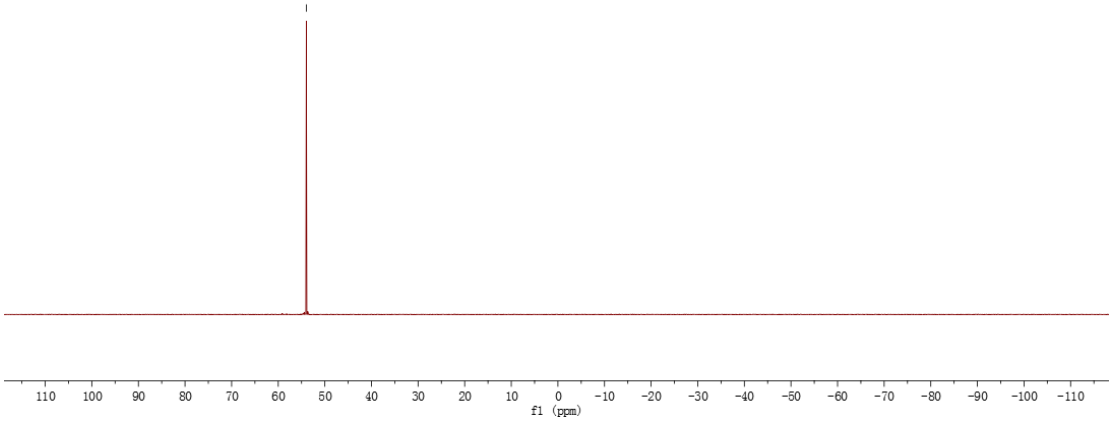




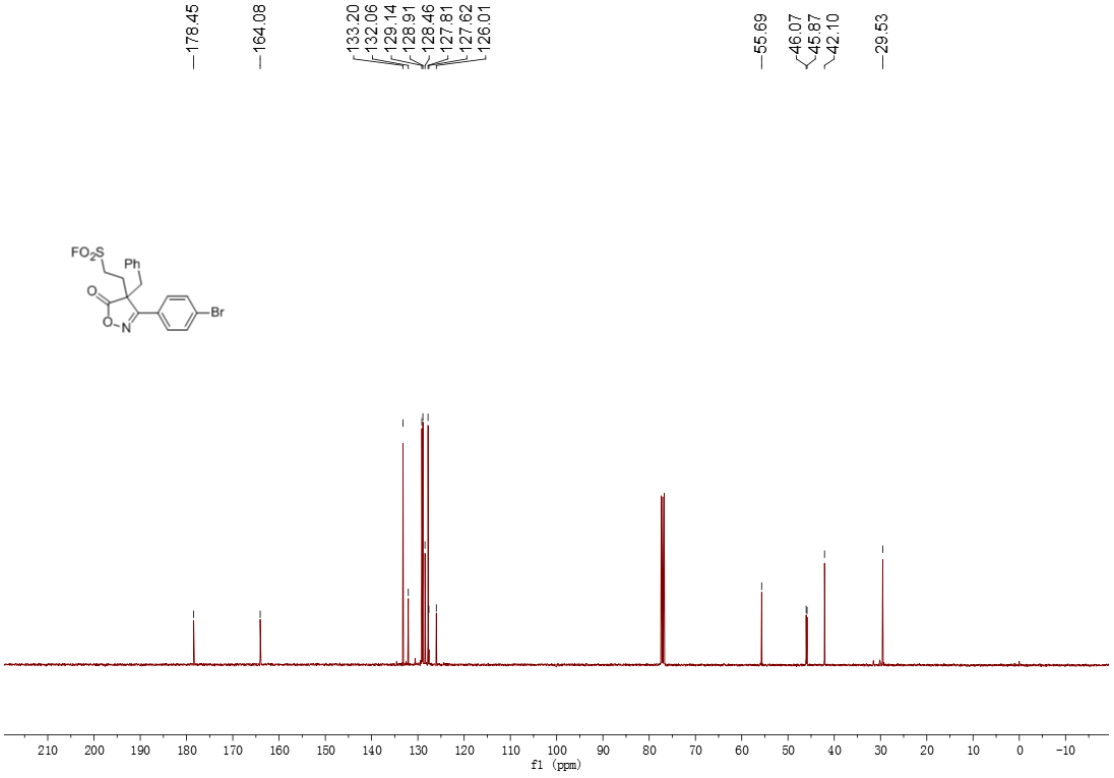


^{19}F NMR (471 MHz, $CDCl_3$)



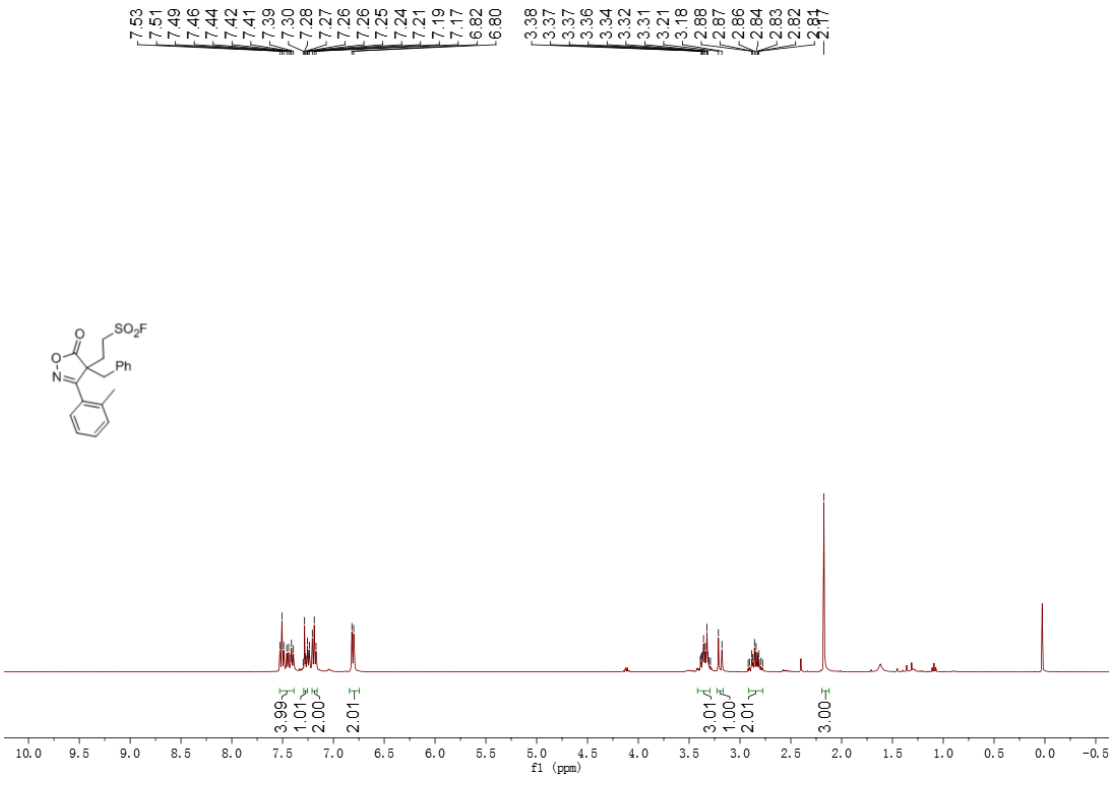


^{13}C NMR (101 MHz, $CDCl_3$)

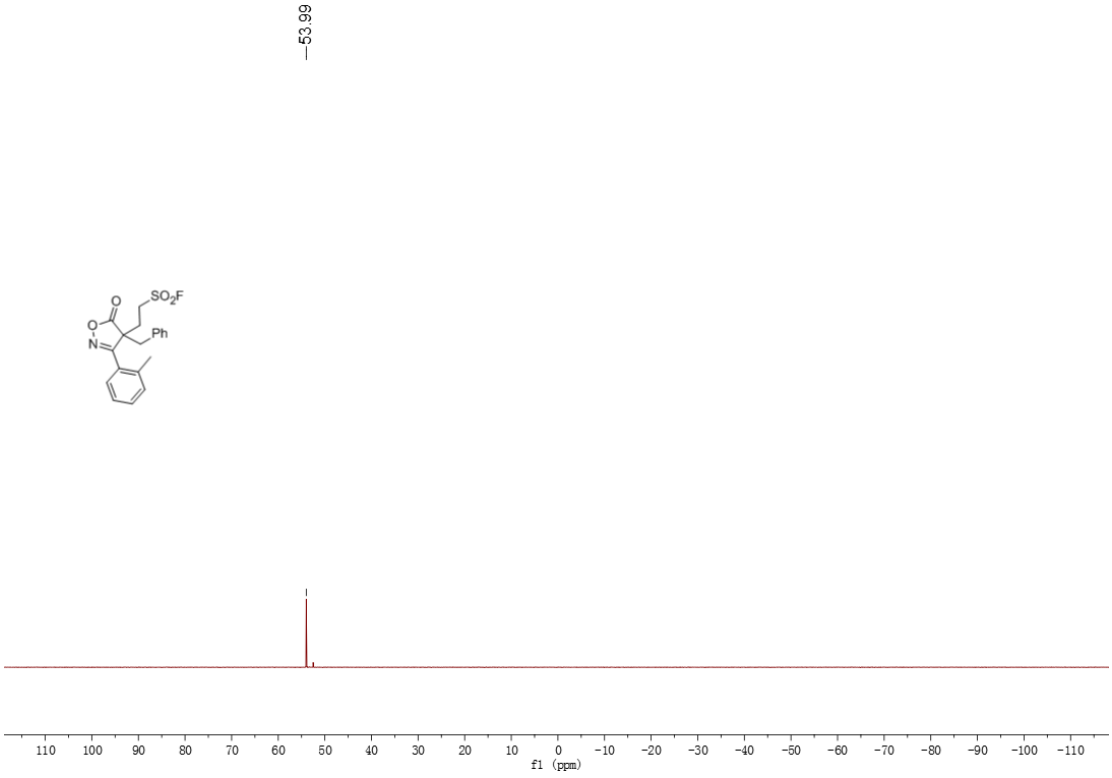


2-(4-Benzyl-5-oxo-3-(o-tolyl)-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4p)

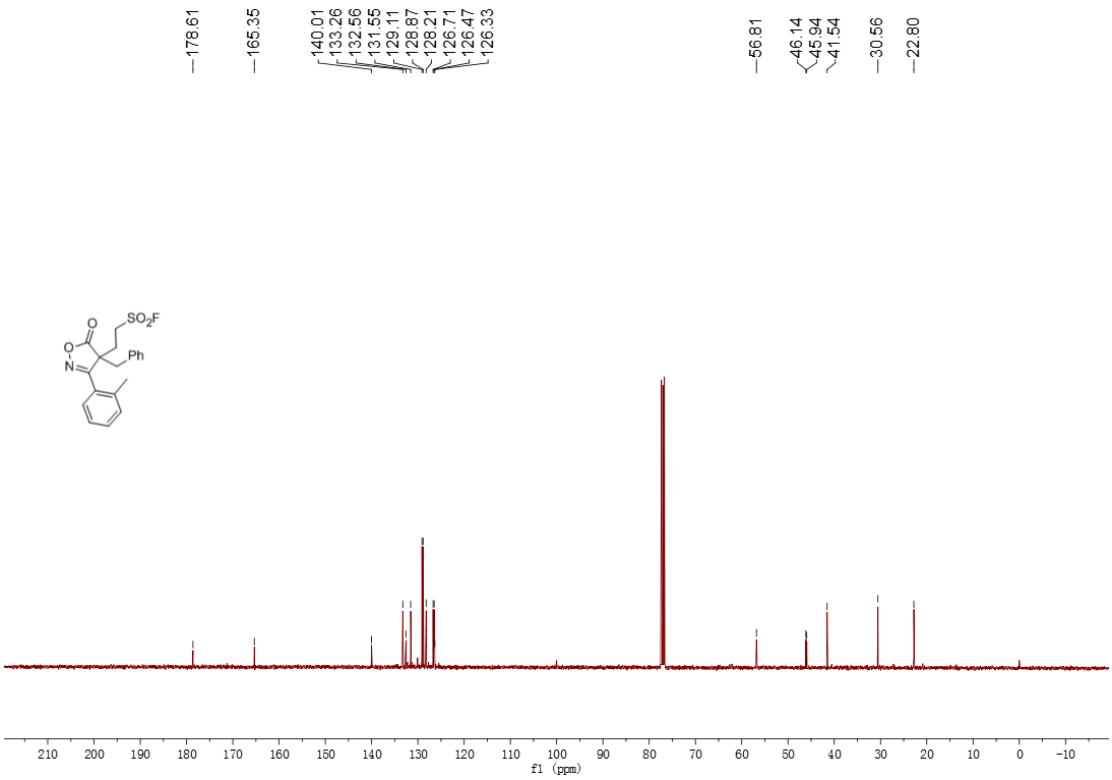
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (471 MHz, $CDCl_3$)

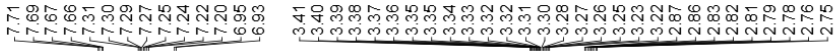


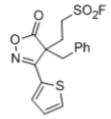
^{13}C NMR (101 MHz, $CDCl_3$)

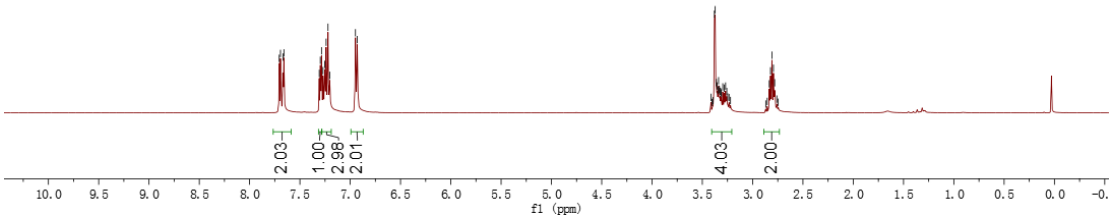


2-(4-Benzyl-5-oxo-3-(thiophen-2-yl)-4,5-dihydroisoxazol-4-yl)ethanesulfonyl fluoride (4q)

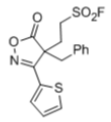
^{1}H NMR (400 MHz, $CDCl_3$)

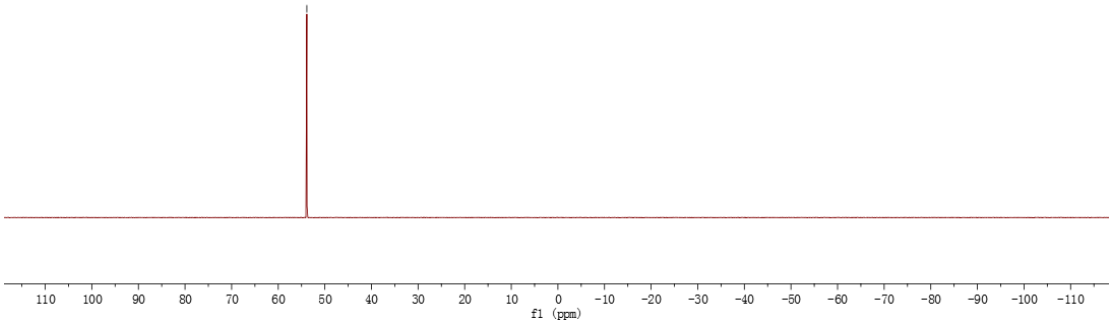




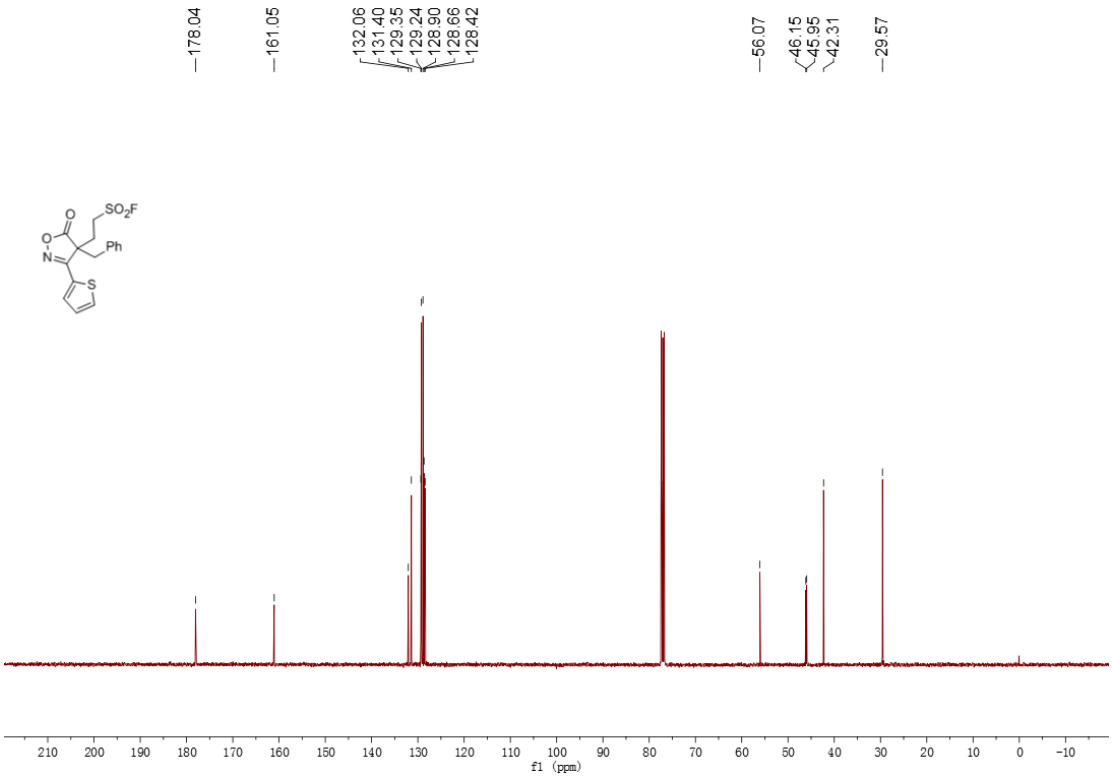


^{19}F NMR (471 MHz, $CDCl_3$)



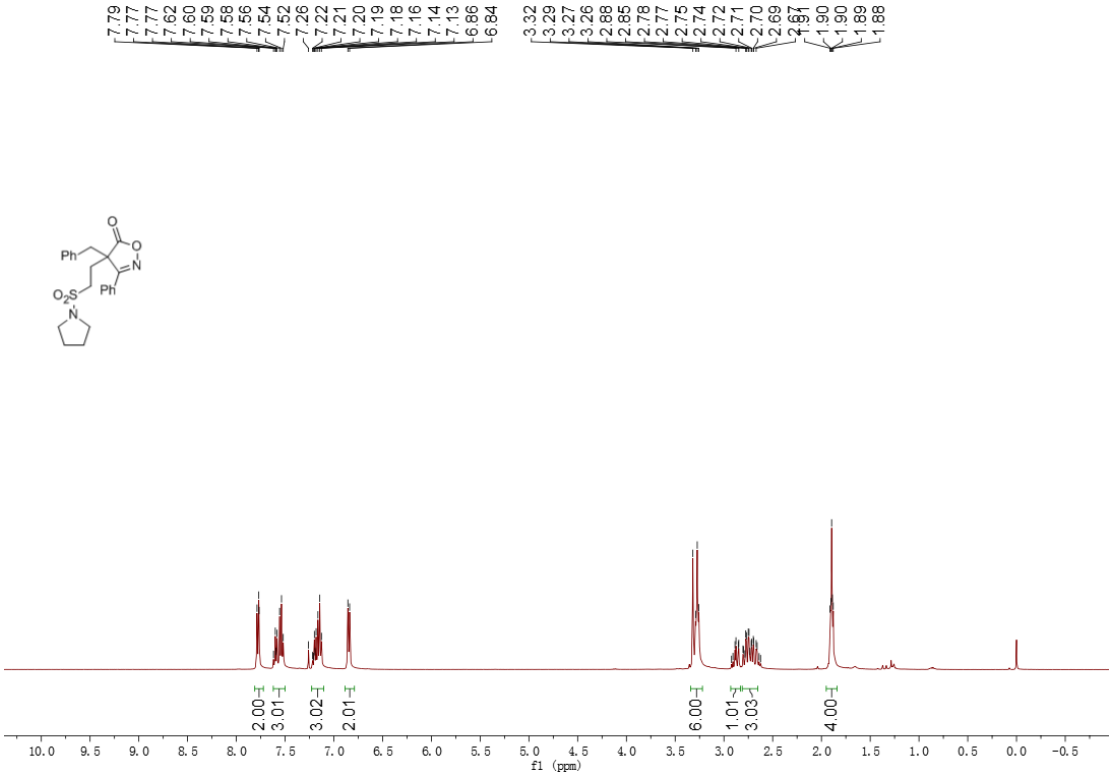


^{13}C NMR (101 MHz, $CDCl_3$)

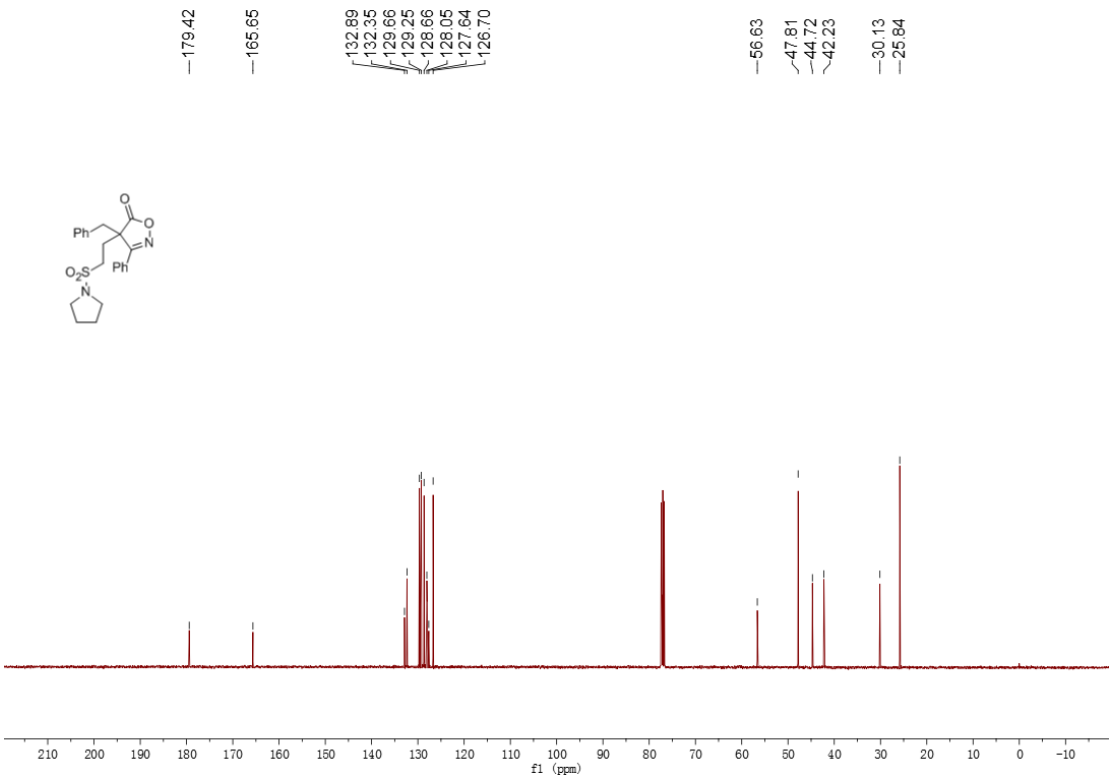


4-Benzyl-3-phenyl-4-(2-(pyrrolidin-1-ylsulfonyl)ethyl)isoxazol-5(4H)-one (6)

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

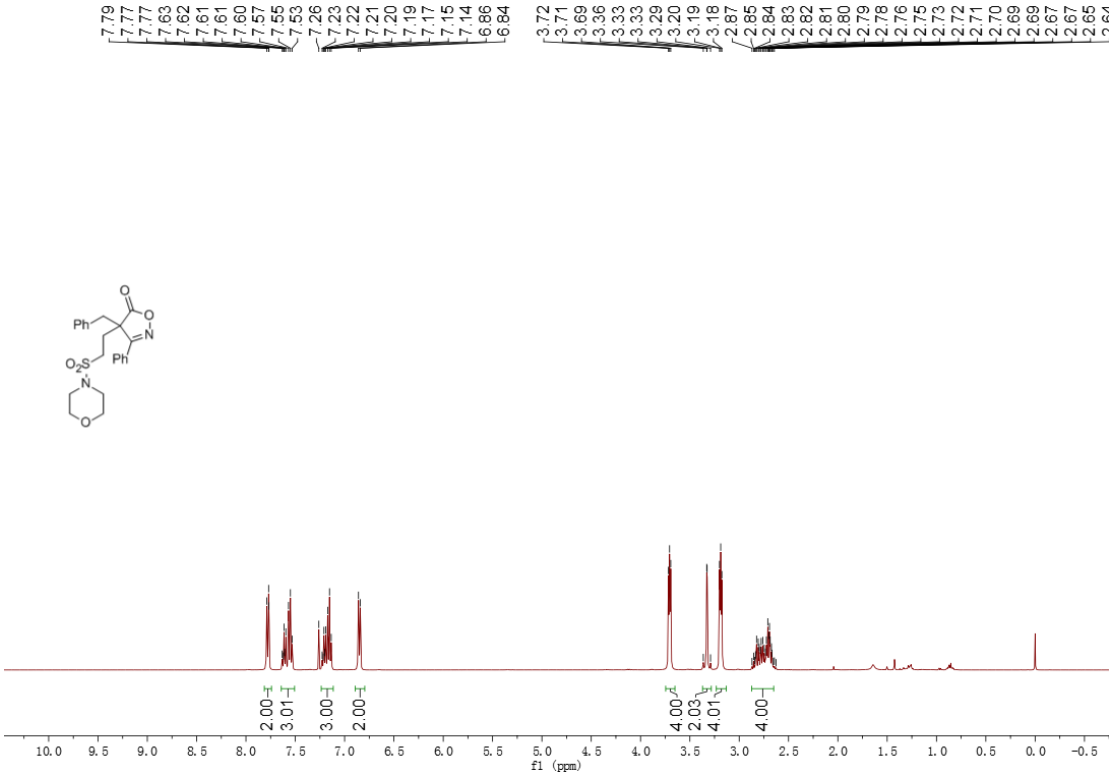


^{13}C NMR (101 MHz, $CDCl_3$)

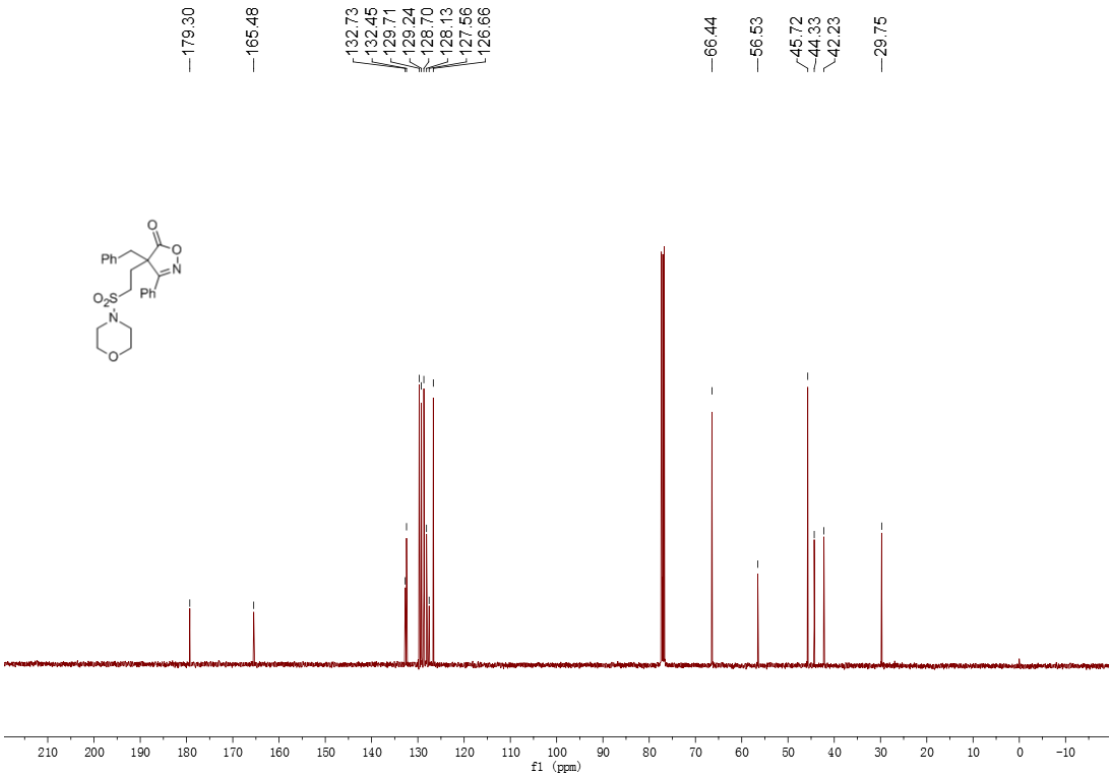


4-Benzyl-4-(2-(morpholinosulfonyl)ethyl)-3-phenylisoxazol-5(4H)-one (7)

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

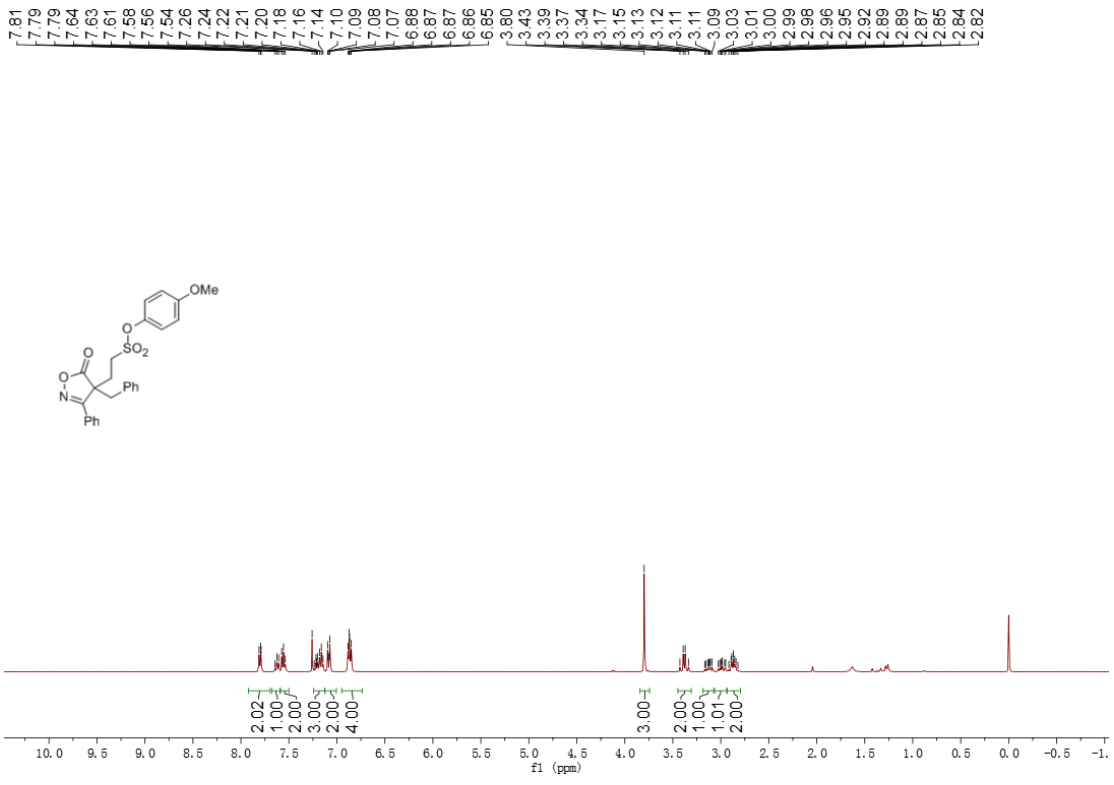


^{13}C NMR (101 MHz, $CDCl_3$)

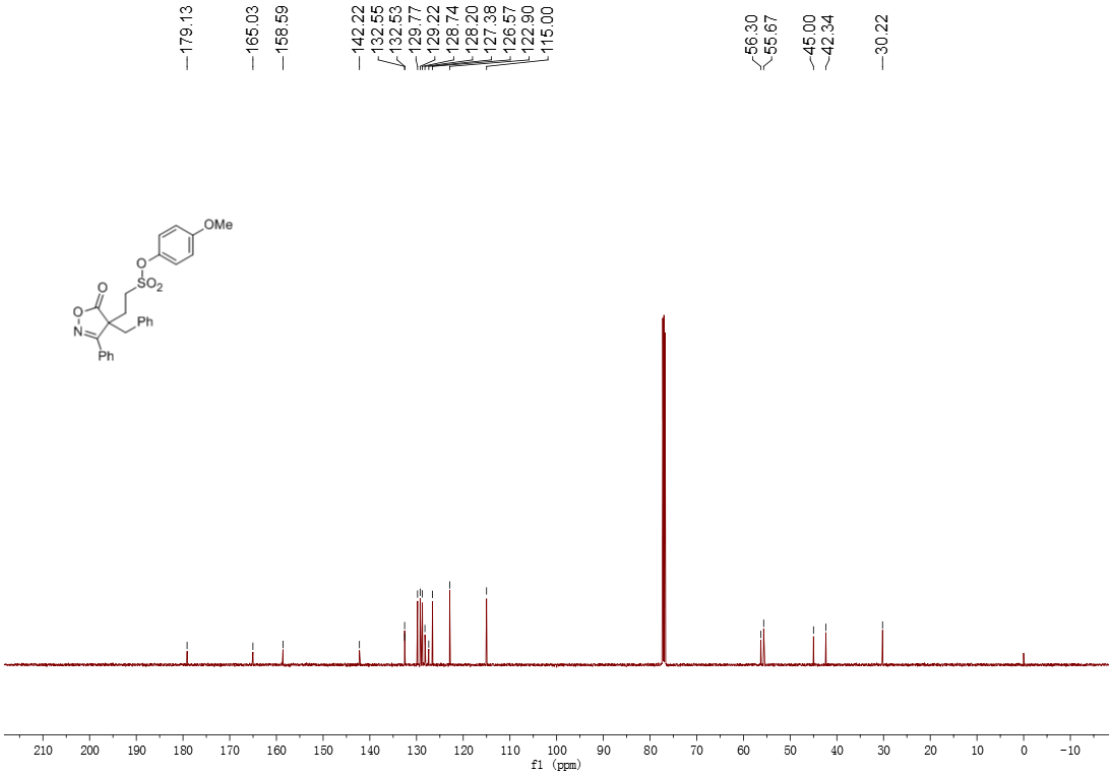


4-Methoxyphenyl 2-(4-benzyl-5-oxo-3-phenyl-4,5-dihydroisoxazol-4-yl)ethanesulfonate (8)

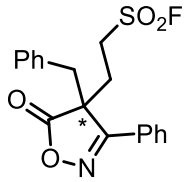
^{1}H NMR (400 MHz, $CDCl_3$)



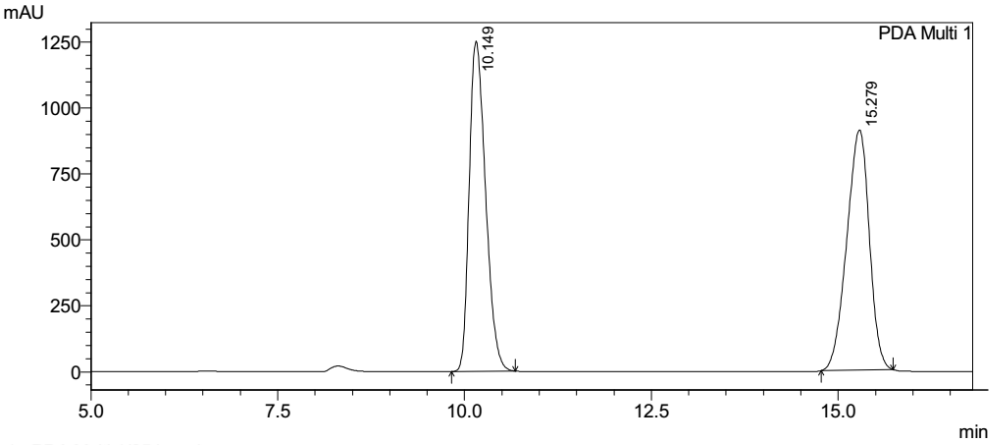
^{13}C NMR (101 MHz, $CDCl_3$)


179.13
165.03
158.59
142.22
132.55
132.53
129.77
129.22
128.74
128.20
127.38
126.57
122.90
115.00
56.30
55.67
45.00
42.34
30.22
OMe
O
SO2
O
O
N
Ph
Ph
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

8. HPLC Spectra



The reaction catalyzed by **5a** gave product **4a** with 41% ee. Chiral HPLC analysis (Chiral pak AD-H, *i*-PrOH/*n*-hexane = 10/90, flow rate = 1.0 mL/min, wave length = 254 nm), t_R (minor) = 15.295 min, t_R (major) = 10.199 min, 41% ee.

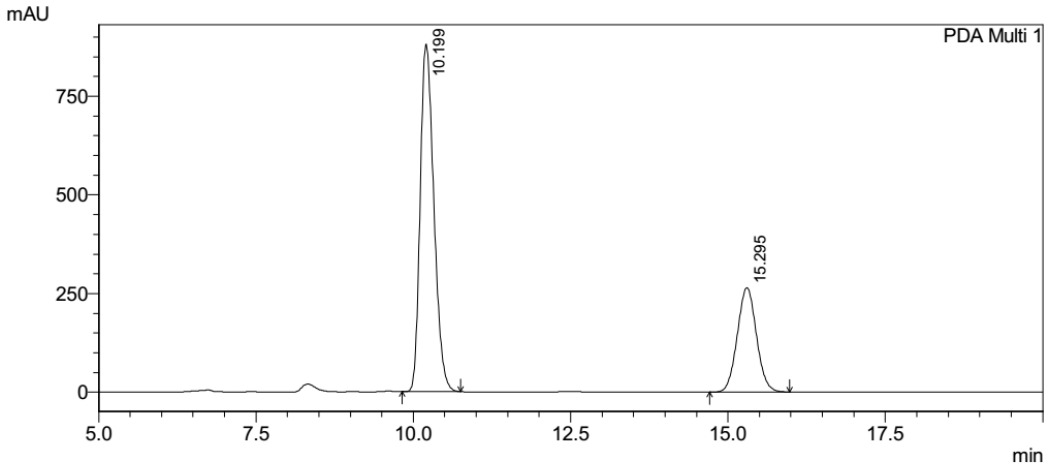


1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %
1	10.149	19091645	1252043	49.949
2	15.279	19130479	911482	50.051
Total		38222124	2163525	100.000



1 PDA Multi 1/254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %
1	10.199	13310900	880021	70.381
2	15.295	5601730	264265	29.619
Total		18912630	1144286	100.000

9. X-Ray Crystallographic Data

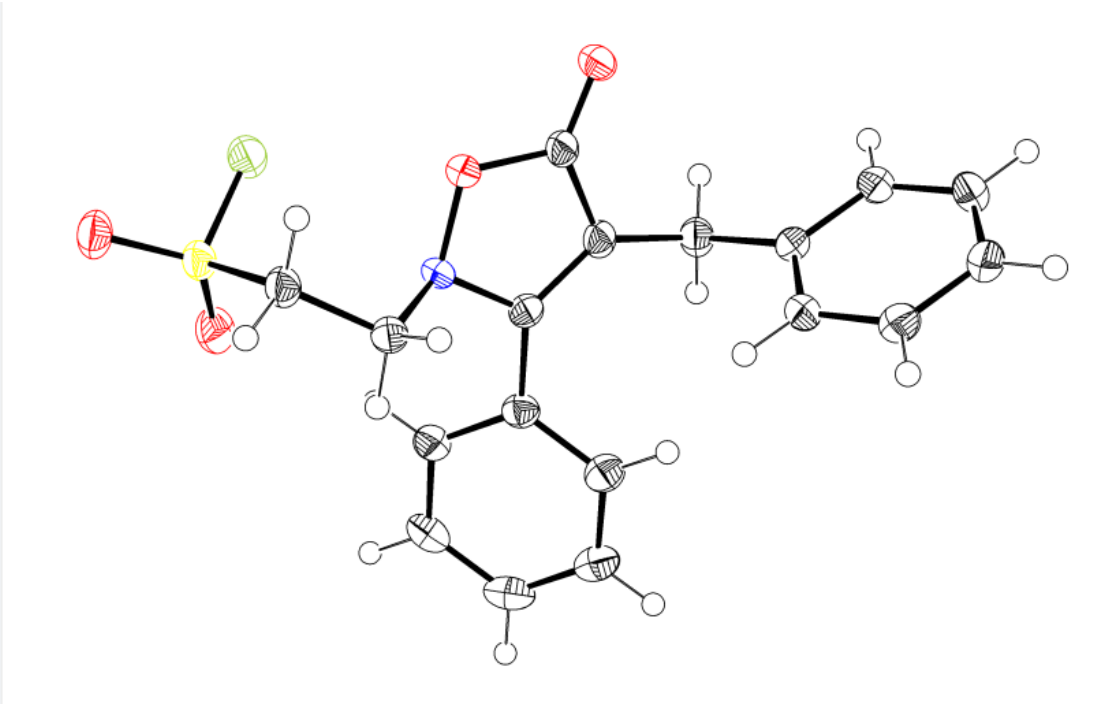
A suitable crystal was selected and mounted on a XtaLAB Synergy R, DW system, HyPix diffractometer. The crystal was kept at 100.00(10) K during data collection

Single crystals of **3a** were obtained by slow evaporation of a solution containing **3a** in the mixture of petroleum ether and dichloromethane at room temperature. A suitable crystal was selected and the crystal data and structure refinement results for compound **3a** are listed below.

X-ray structure of product **3a** (ellipsoid contour at 50% probability).

CCDC 2158101 (**3a**) contain the supplementary crystallo-graphic data for this paper.

These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif



3a CCDC 2158101

Identification code	**3a**
Empirical formula	C18H16FNO4S
Formula weight	361.38
Temperature/K	100.00(10)
Crystal system	monoclinic

Space group	P21/c
a/Å	12.6101(6)
b/Å	13.2345(4)
c/Å	10.6349(5)
α/°	90
β/°	110.857(5)
γ/°	90
Volume/Å3	1658.54(13)
Z	4
ρcalcmg/mm3	1.447
μ/mm-1	2.047
F(000)	752.0
Crystal size/mm3	0.25 × 0.15 × 0.1
2Θ range for data collection	10.05 to 134.148°
Index ranges	-15 ≤ h ≤ 15, -15 ≤ k ≤ 15, -10 ≤ l ≤ 12
Reflections collected	9675
Independent reflections	2927[R(int) = 0.0658]
Data/restraints/parameters	2927/0/226
Goodness-of-fit on F2	1.052
Final R indexes [I>=2σ (I)]	R1 = 0.0482, wR2 = 0.1287
Final R indexes [all data]	R1 = 0.0569, wR2 = 0.1358
Largest diff. peak/hole / e Å-3	0.31/-0.55