Supplementary Information for

Synthesis of α-trifluoromethoxy-sulfide through the Pummerer rearrangement

Mingxin Zhao, Ziyang Zhou and Pingping Tang*

*To whom correspondence should be addressed. E-mail: ptang@nankai.edu.cn

Table of Contents

Supplementary Notes

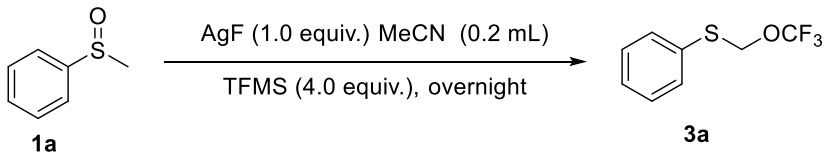
All reactions were conducted in oven-dried glassware under an atmosphere of nitrogen unless otherwise noted. EA, Acetone, DCE, 1, 4-dioxane, Et_2O, DMSO and DCM were dried by distillation over CaH_2. DMA used in reactions were dried by stirring over CaH_2 (5%w/v) overnight, and fractional distillation, then bubbled in argon balloon for 0.5 h, THF, dioxane and toluene were dried by distillation over sodium/benzophenone. $CDCl_3$, CD_3CN was purchased from Sigma-Aldrich. AgF (Cat 7775-41-9) was purchased from Leyan, Shanghai, China. OCF_3 reagents were prepared according to the reported literatures.[1] TLC was performed on silica gel Huanghai HSGF254 plates and visualized by quenching of UV fluorescence (λ_{max}= 254 nm). 200-300 mesh silica gel was purchased from Qingdao Haiyang Chemical Co., China. Unless otherwise noted, all other reagents and starting materials were purchased from commercial sources and used without further purification. The data for NMR spectra (^{1}H NMR, ^{13}C NMR and ^{19}F NMR) were recorded at 293 K on a Bruker AVANCE AV 400 (400 MHz, 101 MHz and 376 MHz) and chemical shifts were recorded relative to the solvent resonance. Signal positions were recorded in ppm and the following abbreviations are used singularly or in combination to indicate the multiplicity of signals: s singlet, d doublet, t triplet, q quartet, m multiplet, Hz Hertz. For ^{1}H NMR: $CDCl_3$ = δ 7.26 ppm. For ^{13}C NMR: $CDCl_3$ = δ 77.16 ppm. Mass spectra were obtained on Agilent 6520 Q-TOF LC/MS and Aligent 7890/5975C-GS/MSD. HRMS were obtained on VG ZAB-HS(ESI), Thermo Fisher Q-Exactive Orbitrap(ESI) and GCT Premier(EI). GCMS analysis was performed on an Aligent 7890/5975C-GS/MSD. HRMS were obtained on VG ZAB-HS(ESI), Thermo Fisher Q-Exactive Orbitrap(ESI) and GCT Premier(EI). GCMS analysis was performed on an Aligent 7890/5975C-GS/MSD. ^{19}F NMR spectrometer used standard pulse sequences with 16 scans and an optimized relaxation delays (d_1= 20 s for ^{19}F NMR).

Supplementary Discussion

Effect of temperature on the reaction

In a nitrogen-filled glovebox, methyl sulfoxide substrate **1** (0.05 mmol, 1.0 equiv.) and AgF (6.1 mg, 0.05 mmol, 1.0 equiv.) were charged into a 2.00 mL sealed vial. Subsequently, acetonitrile (0.2 mL) and trifluoromethyl 4-fluorobenzenesulfonate (TFMS, 32.0 µL, 0.2 mmol, 4.0 equiv.) were added sequentially. The reaction was stirred overnight at different temperatures. The yield of **3a** was determined by comparing the integration of the ^{19}F NMR resonance of **3a** (-59.8 ppm) with that of benzotrifluoride (-62.8 ppm). Yields are reported in Supplementary Table 1.

Supplementary Table 1: Effect of temperature on the reaction



1a **3a**

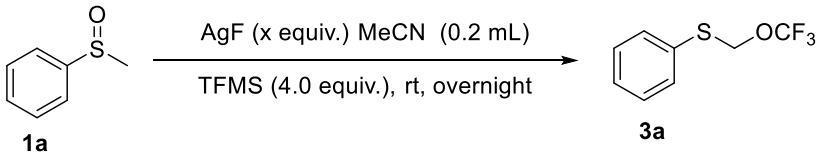
entry	T	^{19}F NMR yield of **A**
1	-20 °C	trace
2	0 °C	10%
3	10 °C	22%
4	rt	28%
5	30 °C	27%
6	40 °C	27%
7	60 °C	9%
8	80 °C	trace

Effect of the equivalent of AgF and other fluorine salts on the reaction

In a nitrogen-filled glovebox, methyl sulfoxide substrate **1** (0.05 mmol, 1.0 equiv.) and AgF or

other fluorine salts were charged into a 2.00 mL sealed vial. Subsequently, acetonitrile (0.2 mL) and trifluoromethyl 4-fluorobenzenesulfonate (TFMS, 32.0 μL, 0.2 mmol, 4.0 equiv.) were added sequentially. The reaction was stirred overnight at different temperatures. The yield of **3a** was determined by comparing the integration of the ^{19}F NMR resonance of **3a** (-59.8 ppm) with that of benzotrifluoride (-62.8 ppm). Yields are reported in Supplementary Table 2.

Supplementary Table 2: Effect of the equivalent of AgF and other fluorine salts on the reaction



1a **3a**

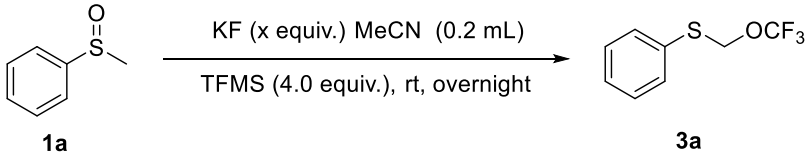
entry	F salt	^{19}F NMR yield of **3a**
1	AgF 1.0 equiv.	27%
2	AgF 0.8 equiv.	n.d.
3	AgF 0.6 equiv.	30%
4	AgF 0.4 equiv.	31%
5	AgF 0.2 equiv.	28%
6	KF (1.0 equiv.)	34%
7	CsF (1.0 equiv.)	32%
8	LiF (1.0 equiv.)	n.d.
9	NaF (1.0 equiv.)	n.d.
10	w/o AgF	n.d.
11	NBu_4BF_4 (1.0 equiv.)	n.d.

Effect of the equivalent of KF on the reaction

In a nitrogen-filled glovebox, methyl sulfoxide substrate **1** (0.05 mmol, 1.0 equiv.) and KF were charged into a 2.00 mL sealed vial. Subsequently, acetonitrile (0.2 mL) and trifluoromethyl 4-

fluorobenzenesulfonate (TFMS, 32.0 μL, 0.2 mmol, 4.0 equiv.) were added sequentially. The reaction was stirred overnight at different temperatures. The yield of **3a** was determined by comparing the integration of the ^{19}F NMR resonance of **3a** (-59.8 ppm) with that of benzotrifluoride (-62.8 ppm). Yields are reported in Supplementary Table 3.

Supplementary Table 3: Effect of the equivalent of KF on the reaction



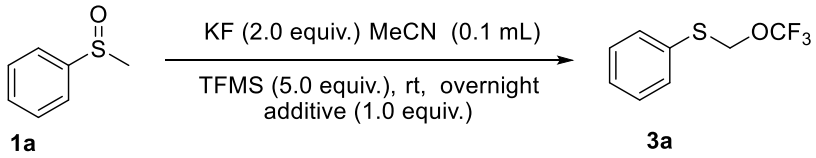
1a **3a**

entry	KF	other	^{19}F NMR yield of **3-3a**
1	1.0 equiv.	-	34%
2	0.5 equiv.	-	16%
3	0.2 equiv.	-	n.d.
4	1.5 equiv.	-	36%
5	2.0 equiv.	-	37%
6	3.0 equiv.	-	29%
7	1.0 equiv.	TFMS (5.0 equiv.)	40%

Effect of additive on the reaction

In a nitrogen-filled glovebox, methyl sulfoxide substrate **1** (0.05 mmol, 1.0 equiv.), KF (5.8 mg, 0.10 mmol, 2.0 equiv.) and additives (0.05 mmol, 1.0 equiv.) were charged into a 2.00 mL sealed vial. Subsequently, acetonitrile (0.2 mL) and trifluoromethyl 4-fluorobenzenesulfonate (TFMS, 32.0 μL, 0.2 mmol, 4.0 equiv.) were added sequentially. The reaction was stirred overnight at different temperatures. The yield of **3a** was determined by comparing the integration of the ^{19}F NMR resonance of **3a** (-59.8 ppm) with that of benzotrifluoride (-62.8 ppm). Yields are reported in Supplementary Table 4.

Supplementary Table 4: Effect of additive on the reaction



1a **3a**

entry	additive	^{19}F NMR yield of **3a**
1	Benzo-18-crown-6	35%
2	-	33%
3	TMABr	17%
4	TEABr	19%
5	Benzo-15-crown-7	31%
6	18-crown-6	28%
7	TBABr	16%
8	TPABr	24%
9	TMACl	28%
10	TMAF	29%
11	MMC	25%
12	4Å molecular sieve (5.0 mg)	35%
13	5Å molecular sieve (5.0 mg)	34%
14	4Å molecular sieve (5.0 mg) Benzo-18-crown-6	41%

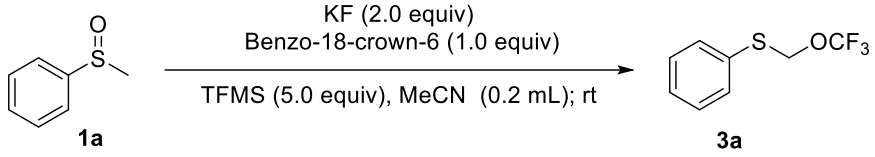
MMC = (Methoxymethyl)triphenylphosphonium chloride

Effect of reaction time on the reaction and additives

In a nitrogen-filled glovebox, methyl sulfoxide substrate **1** (0.05 mmol, 1.0 equiv.), KF (5.8 mg, 0.10 mmol, 2.0 equiv.) and benzo-18-crown-6 (15.6 mg, 0.05 mmol, 1.0 equiv.) were charged into a 2.00 mL sealed vial. Subsequently, acetonitrile (0.2 mL) and trifluoromethyl 4-fluorobenzenesulfonate (TFMS, 32.0 µL, 0.2 mmol, 4.0 equiv.) were added sequentially. The

yield of **3a** was determined by comparing the integration of the ^{19}F NMR resonance of **3a** (-59.8 ppm) with that of benzotrifluoride (-62.8 ppm). Yields are reported in Supplementary Table 5.

Supplementary Table 5: Effect of reaction time on the reaction and additives



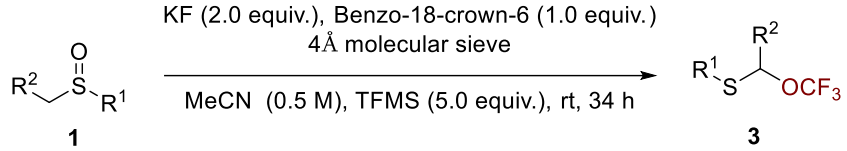
1a **3a**

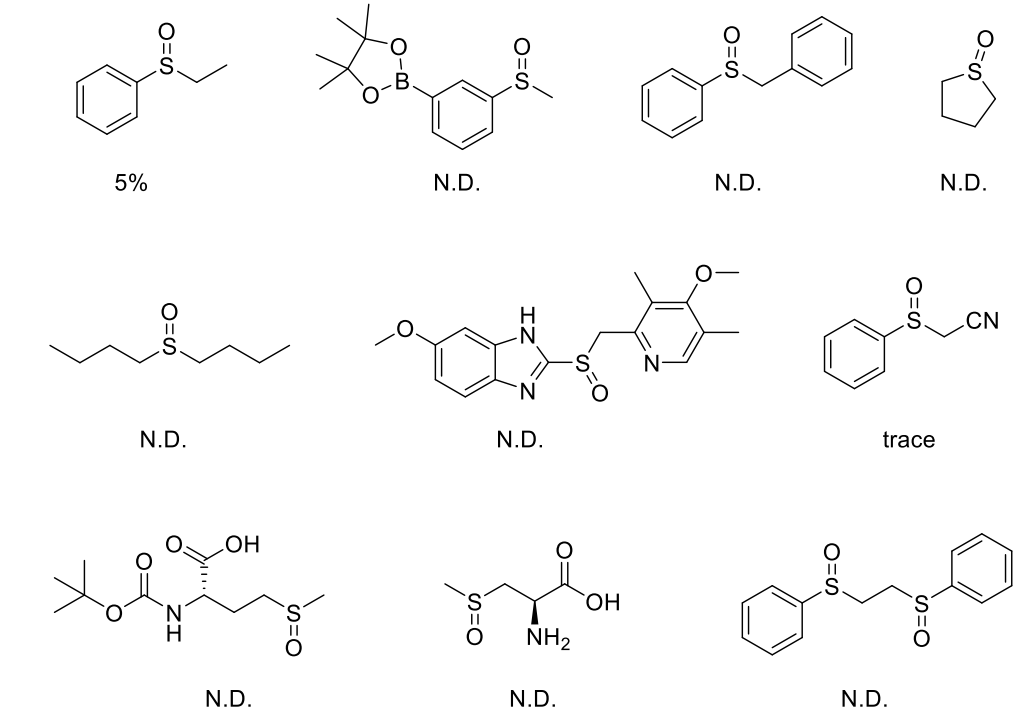
entry	other	*T*/h	^{19}F NMR yield of **3-3a**
1	-	4	24%
2	-	8	26%
3	-	12	34%
4	-	22	49%
5	-	28	53%
6	-	34	55%
7	-	40	55%
8	4Å molecular sieve (5.0 mg)	28	58%
9	4Å molecular sieve (5.0 mg)	34	65%
10	H_2O (1.0 equiv)	34	38%
11	H_2O (4.0 equiv)	34	trace

Substrates for conversion failure

In a nitrogen-filled glovebox, methyl sulfoxide substrate **1** (0.05 mmol, 1.0 equiv.), KF (5.8 mg, 0.10 mmol, 2.0 equiv.) 4Å molecular sieve (5.0 mg), and benzo-18-crown-6 (15.6 mg, 0.05 mmol, 1.0 equiv.) were charged into a 2.00 mL sealed vial. Subsequently, acetonitrile (0.2 mL) and trifluoromethyl 4-fluorobenzenesulfonate (TFMS, 32.0 µL, 0.2 mmol, 4.0 equiv.) were added sequentially. Yields were determined by ^{19}F NMR with benzotrifluoride as a standard. Yields are reported in Supplementary Scheme 1. We hypothesized that the presence of KF

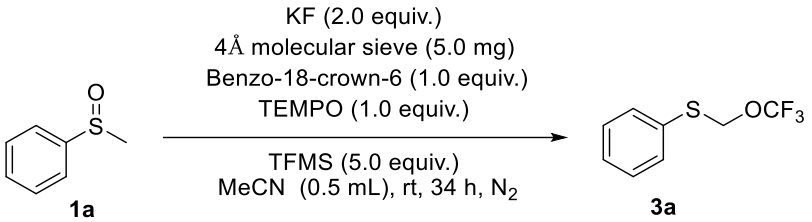
preferentially drives E1 elimination over nucleophilic trapping at the secondary carbocation stage, accounting for the diminished yield.





Supplementary Scheme 1: Substrates for conversion failure

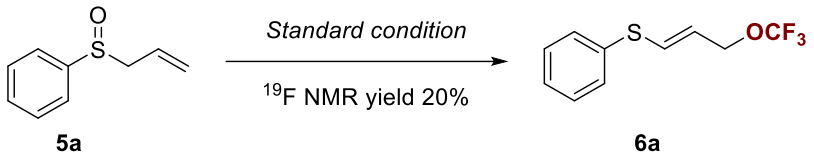
TEMPEO inhibition experiments



Under a nitrogen atmosphere in a glovebox, methyl sulfoxide substrate **1a** (0.25 mmol, 1.00 equiv.) was combined with KF (29.1 mg, 0.50 mmol, 2.00 equiv.) and benzo-18-crown-6 (78.0 mg, 0.25 mmol, 1.00 equiv.) in a 4.00 mL sealed vial. Acetonitrile (0.5 mL) and trifluoromethyl 4-fluorobenzenesulfonate (TFMS) (200.0 μL, 1.25 mmol, 5.0 equiv.) were subsequently added to the reaction mixture. The sealed vial was then transferred out of the glovebox, and the

mixture was stirred at ambient temperature for 34 hours. After completion, the reaction system was diluted with dichloromethane (1.0 mL). The ^{19}F NMR yield of product **3a** was determined to be 61% through integration comparison between the characteristic resonance of **3a** (-59.5 ppm) and trifluorotoluene (-62.8 ppm) as an internal standard, following TEMPO addition.

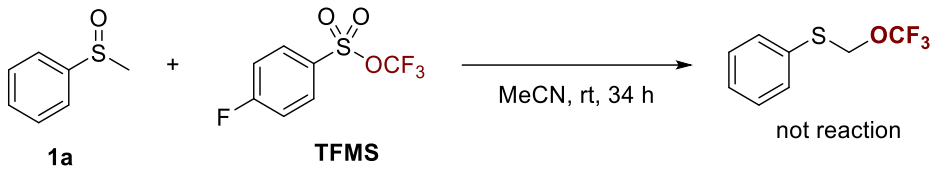
Double bond migration experiment



5a **6a**

Under a nitrogen atmosphere in a glovebox, (allylsulfinyl)benzene **5a** (0.25 mmol, 1.00 equiv.) was combined with KF (29.1 mg, 0.50 mmol, 2.00 equiv.) and benzo-18-crown-6 (78.0 mg, 0.25 mmol, 1.00 equiv.) in a 4.00 mL sealed vial. Acetonitrile (0.5 mL) and trifluoromethyl 4-fluorobenzenesulfonate (TFMS) (200.0 μL, 1.25 mmol, 5.0 equiv.) were subsequently added to the reaction mixture. The sealed vial was then transferred out of the glovebox, and the mixture was stirred at ambient temperature for 34 hours. After completion, the reaction system was diluted with dichloromethane (1.0 mL). The ^{19}F NMR yield of product **6a** was determined to be 20% through integration comparison between the characteristic resonance of **6a** (-60.0 ppm) and trifluorotoluene (-62.8 ppm) as an internal standard. HRMS-EI (*m/z*): Calcd for $C_{10}H_9F_3OS^+$ $[M]^+$, 234.0321. Found, 234.0321.

1a Reaction with TFMS

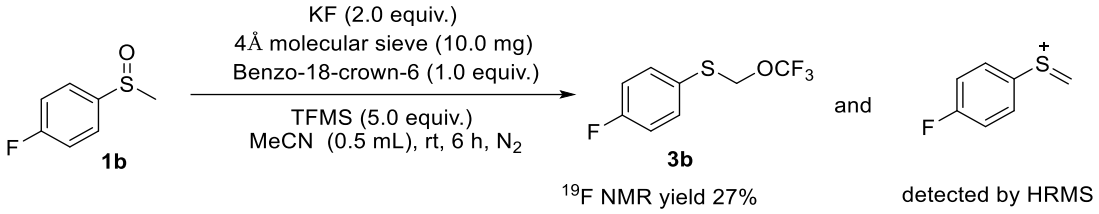


1a **TFMS**

Under a nitrogen atmosphere in a glovebox, methyl sulfoxide substrate **1a** (0.25 mmol, 1.00 equiv.) was combined in a 4.00 mL sealed vial. Acetonitrile (0.5 mL) and trifluoromethyl 4-fluorobenzenesulfonate (TFMS) (200.0 μL, 1.25 mmol, 5.0 equiv.) were subsequently added to the reaction mixture. The sealed vial was then transferred out of the glovebox, and the mixture

was stirred at ambient temperature for 34 hours. After completion, the reaction system was diluted with dichloromethane (1.0 mL). The GC-MS analysis revealed no reaction between **1a** and TFMS, indicating that the TFMS reagent fails to activate the sulfinyl group.

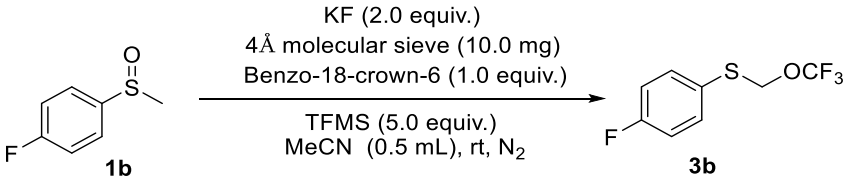
HRMS for identifying intermediate I-2



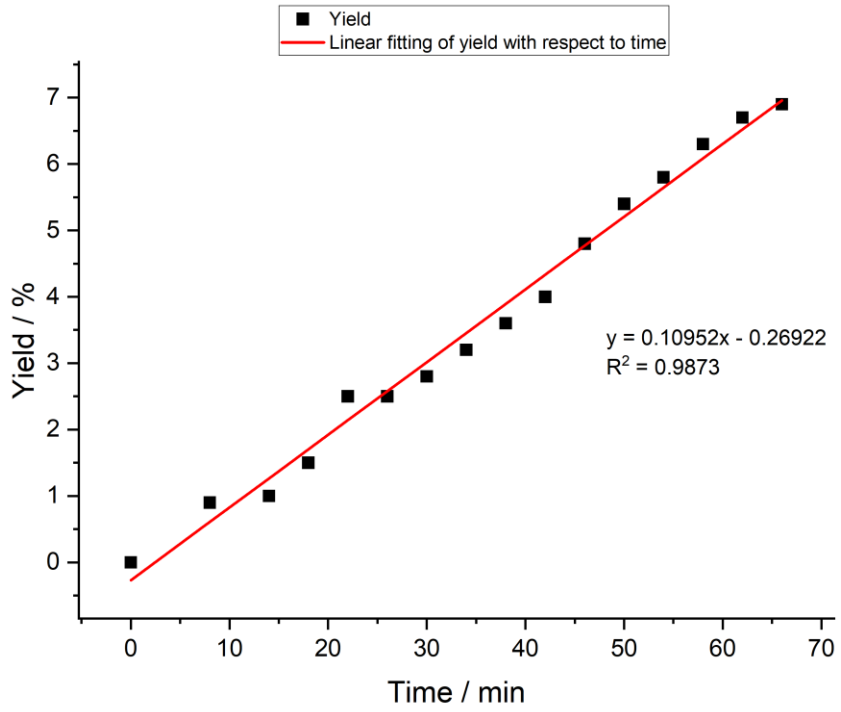
Under a nitrogen atmosphere in a glovebox, methyl sulfoxide substrate **1b** (15.8 mg, 0.10 mmol, 1.00 equiv.) was combined with KF (11.6 mg, 0.20 mmol, 2.00 equiv.) and benzo-18-crown-6 (31.2 mg, 0.10 mmol, 1.00 equiv.) in a 2.00 mL sealed vial. Acetonitrile (0.2 mL) and trifluoromethyl 4-fluorobenzenesulfonate (TFMS) (80.0 μL, 0.5 mmol, 5.0 equiv.) were subsequently added to the reaction mixture. The sealed vial was then transferred out of the glovebox, and the mixture was stirred at ambient temperature for 6 hours. HRMS-EI (*m/z*): Calcd for $C_7H_6FS^+$ $[M]^+$, 141.0169. Found, 141.0167.

Kinetic studies

Under a nitrogen atmosphere in a glovebox, methyl sulfoxide substrate **1b** (15.8 mg, 0.10 mmol, 1.00 equiv.) was combined with KF (11.6 mg, 0.20 mmol, 2.00 equiv.) and benzo-18-crown-6 (31.2 mg, 0.10 mmol, 1.00 equiv.) in a J-Young NMR tube. Acetonitrile (0.4 mL), trifluorotoluene (12 μL, 0.10 mmol, 1.00 equiv.) and trifluoromethyl 4-fluorobenzenesulfonate (TFMS) (80.0 μL, 0.5 mmol, 5.0 equiv.) were subsequently added to the reaction mixture. Monitor the reaction process through ^{19}F NMR.



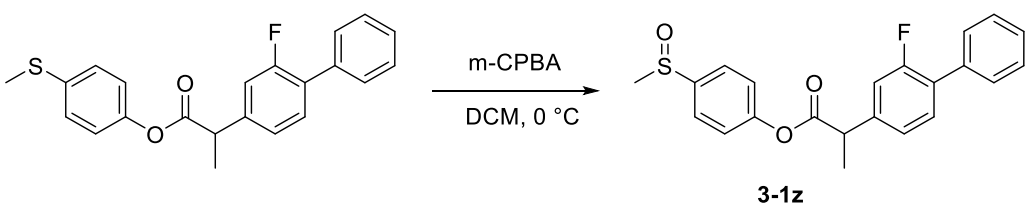
Time / min	Yield / %	Time / min	Yield / %	Time / min	Yield / %
8	0.9	30	2.8	50	5.4
14	1	34	3.2	54	5.8
18	1.5	38	3.6	58	6.3
22	2.5	42	4.0	62	6.7
26	2.5	46	4.8	66	6.9



Supplementary Scheme 2: Linear fitting of yield with respect to time

Supplementary Methods

Flurbiprofen derivatives (1z)

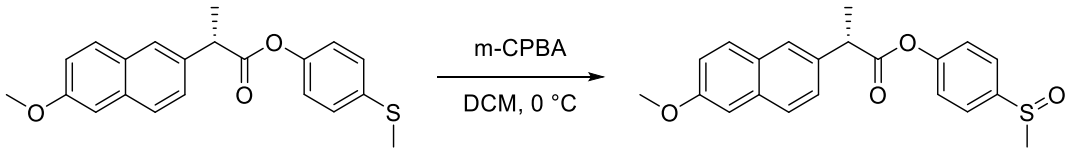


3-1z

A 50 mL round-bottom flask was charged with flurbiprofen derivative (366.5 mg, 1.0 mmol, 1.0 equiv.) under 0 °C conditions, followed by sequential addition of dichloromethane (12 mL) and m-chloroperbenzoic acid (m-CPBA) (103.5 mg, 0.6 mmol, 0.6 equiv.). The reaction mixture was stirred at 0 °C for 2 h, after which an additional portion of m-CPBA (86.3 mg, 0.5 mmol, 0.5 equiv.) was introduced. Following 4 h of continuous stirring at 0 °C, the reaction was quenched with saturated aqueous sodium thiosulfate solution (0.1 mL). The organic layer was successively washed with saturated aqueous sodium carbonate solution (10 mL × 3), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. Purification via flash column chromatography (eluent: hexanes/ethyl acetate) afforded 240.6 mg of pale yellow solid **1z**, representing a 63% yield.

R_f = 0.20 [*n*-hexane : EA = 1 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 – 7.63 (m, 2H), 7.59 – 7.52 (m, 2H), 7.47 (td, *J* = 6.8, 6.3, 3.6 Hz, 3H), 7.44 – 7.37 (m, 1H), 7.30 – 7.14 (m, 4H), 4.04 (q, *J* = 7.1 Hz, 1H), 2.73 (s, 3H), 1.69 (dd, *J* = 7.2, 1.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.2, 159.9 (d, *J* = 249.0 Hz), 152.9, 143.2, 140.92 (d, *J* = 7.6 Hz), 135.4, 131.25 (d, *J* = 4.2 Hz), 129.06 (d, *J* = 3.0 Hz), 128.6, 127.9, 125.0, 125.0, 123.68 (d, *J* = 3.4 Hz), 122.7, 115.6, 115.3, 45.2, 44.3, 18.5. HRMS-ESI (*m/z*): Calcd for $C_{22}H_{19}FNaO_3S^+$ $[M+Na]^+$, 405.0931. Found, 405.0929.

Naproxen derivatives (1aa)



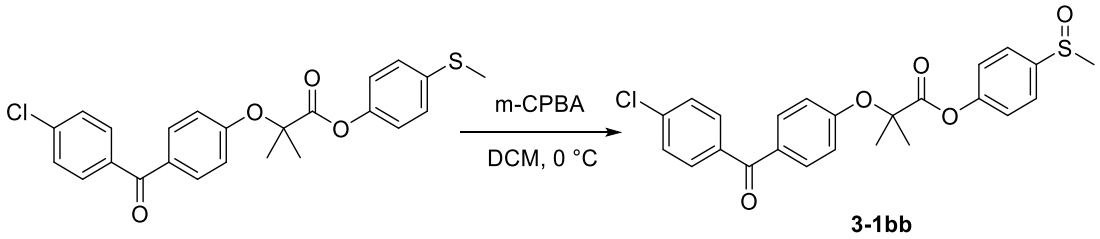
3-1aa

A 50 mL round-bottom flask was charged with Naproxen derivatives (352.4 mg, 1.0 mmol, 1.0 equiv.) under 0 °C conditions, followed by sequential addition of dichloromethane (12 mL) and m-chloroperbenzoic acid (m-CPBA) (103.5 mg, 0.6 mmol, 0.6 equiv.). The reaction mixture was stirred at 0 °C for 2 h, after which an additional portion of m-CPBA (86.3 mg, 0.5 mmol, 0.5 equiv.) was introduced. Following 4 h of continuous stirring at 0 °C, the reaction was quenched with saturated aqueous sodium thiosulfate solution (0.1 mL). The organic layer was successively washed with saturated aqueous sodium carbonate solution (10 mL × 3), dried over

anhydrous sodium sulfate, and concentrated under reduced pressure. Purification via flash column chromatography (eluent: hexanes/ethyl acetate) afforded 184.4 mg of pale yellow solid **1aa**, representing a 50% yield.

R_f = 0.20 [*n*-hexane : EA = 1 : 2 (v/v)]. NMR Spectroscopy: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 – 7.71 (m, 3H), 7.66 – 7.58 (m, 2H), 7.49 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.22 – 7.12 (m, 4H), 4.11 (q, *J* = 7.1 Hz, 1H), 3.93 (s, 3H), 2.69 (s, 3H), 1.70 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 157.9, 152.9, 142.8, 134.7, 133.9, 129.3, 129.0, 127.5, 126.2, 126.0, 124.9, 122.6, 119.3, 105.6, 55.4, 45.6, 44.1, 18.4. HRMS-ESI (*m/z*): Calcd for $C_{21}H_{20}NaO_4S^+$ $[M+Na]^+$, 391.0975. Found, 391.0969.

Fenofibrate derivatives (1bb)

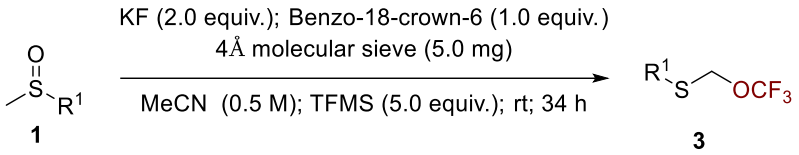


A 50 mL round-bottom flask was charged with Fenofibrate derivatives (440.9 mg, 1.0 mmol, 1.0 equiv.) under 0 °C conditions, followed by sequential addition of dichloromethane (12 mL) and m-chloroperbenzoic acid (m-CPBA) (103.5 mg, 0.6 mmol, 0.6 equiv.). The reaction mixture was stirred at 0 °C for 2 h, after which an additional portion of m-CPBA (86.3 mg, 0.5 mmol, 0.5 equiv.) was introduced. Following 4 h of continuous stirring at 0 °C, the reaction was quenched with saturated aqueous sodium thiosulfate solution (0.1 mL). The organic layer was successively washed with saturated aqueous sodium carbonate solution (10 mL × 3), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. Purification via flash column chromatography (eluent: hexanes/ethyl acetate) afforded 242.0 mg of pale yellow solid **1bb**, representing a 53% yield.

R_f = 0.20 [*n*-hexane : EA = 1 : 2 (v/v)]. NMR Spectroscopy: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 – 7.76 (m, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 8.7 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.20 – 7.12 (m, 2H), 7.02 – 6.95 (m, 2H), 2.71 (s, 3H), 1.84 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.3, 172.3, 159.5, 152.5, 143.7, 138.7, 136.3, 132.3, 131.3, 131.0,

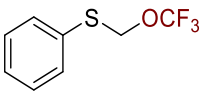
128.7, 125.2, 122.5, 117.4, 79.5, 44.3, 25.6, 25.5. HRMS-ESI (*m/z*): Calcd for $C_{24}H_{21}ClNaO_5S^+$ $[M+Na]^+$, 479.0690. Found, 479.0686.

General Procedure A



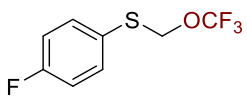
In a nitrogen-filled glovebox, methyl sulfoxide substrate **1** (0.25 mmol, 1.0 equiv.), KF (29.1 mg, 0.50 mmol, 2.0 equiv.), and benzo-18-crown-6 (78.0 mg, 0.25 mmol, 1.0 equiv.) were charged into a 4.00 mL sealed vial. Subsequently, acetonitrile (0.5 mL) and trifluoromethyl 4-fluorobenzenesulfonate (TFMS, 200.0 µL, 1.25 mmol, 5.0 equiv.) were added sequentially. The sealed vial was then removed from the glovebox, and the reaction mixture was stirred at room temperature for 34 hours. Upon completion, the crude mixture was directly concentrated under reduced pressure. The resulting residue was purified by flash column chromatography using a hexane/ethyl acetate gradient eluent system.

Phenyl((trifluoromethoxy)methyl)sulfane (3a)



According to General Procedure A, methyl phenyl sulfoxide **1a** (35.0 mg, 0.25 mmol, 1.0 equiv.) was employed. The ^{19}F NMR yield of **3a** was determined to be 65% by comparative integration of its resonance signal at -59.8 ppm with that of trifluorotoluene (-62.8 ppm) in ^{19}F NMR analysis. HRMS-EI (*m/z*): Calcd for $C_8H_7F_3OS^+$ $[M]^+$, 208.0164. Found, 208.0164.

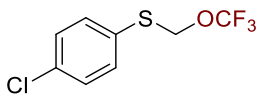
(4-fluorophenyl)((trifluoromethoxy)methyl)sulfane (3b)



Following the general synthetic procedure A, methyl(4-fluorophenyl)sulfoxide **1b** (39.5

mg, 0.25 mmol, 1.0 equiv.) was employed as the starting material. The ^{19}F NMR yield of **3b** was determined to be 61% by comparing the integration values of its characteristic resonance at δ −59.9 ppm with that of trifluorotoluene (δ −62.8 ppm) as an internal standard. HRMS-EI (*m/z*): Calcd for $C_8H_6F_4OS^+$ $[M]^+$, 226.0070. Found, 226.0067.

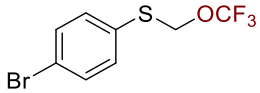
(4-chlorophenyl)((trifluoromethoxy)methyl)sulfane (3c)



Following General Procedure A, methyl (4-chlorophenyl) sulfoxide **1c** (43.6 mg, 0.25 mmol, 1.0 equiv.) was employed as the starting material. The crude product was purified by flash column chromatography using an n-hexane/ethyl acetate gradient eluent, affording compound **3c** as a colorless oily liquid (36.2 mg, 60% yield).

R_f = 0.50 [*n*-hexane : EA = 200 : 1(v/v)]. NMR Spectroscopy: ^1H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.40 (m, 2H), 7.35 – 7.30 (m, 2H), 5.24 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.8, 133.0, 131.7, 129.6, 121.4 (q, *J* = 258.3 Hz), 72.7 (q, *J* = 3.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.2. HRMS-EI (*m/z*): Calcd for $C_8H_6ClF_3OS^+$ $[M]^+$, 241.9775. Found, 241.9770.

(4-bromophenyl)((trifluoromethoxy)methyl)sulfane (3d)

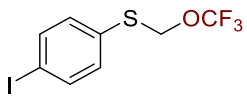


Following the general synthetic procedure A, methyl (4-bromophenyl) sulfoxide **1d** (54.8 mg, 0.25 mmol, 1.0 equiv.) was employed as the starting material. Purification by flash column chromatography using n-hexane/ethyl acetate as eluent afforded the target compound **3d** as a colorless oily liquid (34.5 mg, 48% yield).

R_f = 0.50 [*n*-hexane : EA = 200 : 1(v/v)]. NMR Spectroscopy: ^1H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.40 (m, 2H), 7.35 – 7.30 (m, 2H), 5.24 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.8, 133.0, 131.7, 129.6, 121.4 (q, *J* = 258.3 Hz), 72.7 (q, *J* = 3.5 Hz); ^{19}F NMR

(376 MHz, $CDCl_3$) δ -59.2. HRMS-ESI (*m/z*): Calcd for C8H6ClF3OS$^+$ $[M]^+$, 241.9775. Found, 241.9770. HRMS-ESI (*m/z*): Calcd for $C_8H_6BrF_3OS^+$ $[M]^+$, 285.9269. Found, 285.9269.

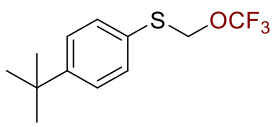
(4-iodophenyl)((trifluoromethoxy)methyl)sulfane (3e)



According to the general synthetic procedure A, methyl(4-iodophenyl)sulfoxide **1e** (66.5 mg, 0.25 mmol, 1.0 equiv.) was employed. Purification via flash column chromatography using a hexane/ethyl acetate gradient system afforded compound **3e** as a colorless oily liquid (44.2 mg, 53% yield).

R_f = 0.45 [*n*-hexane : EA = 200 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 5.25 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4, 133.2, 132.9, 121.3 (d, *J* = 258.2 Hz), 94.0, 72.2 (q, *J* = 3.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.1. HRMS-ESI (*m/z*): Calcd for $C_8H_6F_3IOS^+$ $[M]^+$, 333.9131. Found, 333.9130.

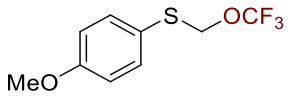
(4-(*tert*-butyl)phenyl)((trifluoromethoxy)methyl)sulfane (3f)



Following the general synthetic procedure A, methyl(4-tert-butylphenyl)sulfoxide **1f** (49.1 mg, 0.25 mmol, 1.0 equiv.) was employed. Purification via flash column chromatography using n-hexane/ethyl acetate as the eluent afforded compound **3f** as a colorless oily liquid (51.0 mg, 85% yield).

R_f = 0.40 [*n*-hexane : EA = 200 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 – 7.41 (m, 2H), 7.40 – 7.36 (m, 2H), 5.25 (s, 2H), 1.32 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.4, 130.8, 126.4, 126.1, 121.4 (d, *J* = 258.1 Hz), 73.1 (q, *J* = 3.4 Hz), 41.4, 31.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.4. HRMS-EI (*m/z*): Calcd for $C_{12}H_{15}F_3OS^+$ $[M]^+$, 264.0790. Found, 264.0792.

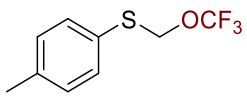
(4-methoxyphenyl)((trifluoromethoxy)methyl)sulfane (3g)



According to the general synthetic procedure A, methyl(4-methoxyphenyl)sulfoxide **1g** (42.5 mg, 0.25 mmol, 1.0 equiv.) was employed as the starting material. Purification via flash column chromatography using n-hexane/ethyl acetate as eluent afforded the desired product **3g** as a colorless oily liquid (59.1 mg, 99% isolated yield).

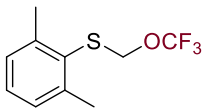
R_f = 0.20 [*n*-hexane : EA = 100 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 – 7.43 (m, 2H), 6.95 – 6.84 (m, 2H), 5.16 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 134.9, 123.5, 121.5 (q, J = 257.6 Hz), 115.0, 74.2 (q, J = 3.4 Hz), 55.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.7. HRMS-EI (*m/z*): Calcd for $C_9H_9F_3O_2S^+$ $[M]^+$, 238.0270. Found, 238.0269.

***p*-tolyl((trifluoromethoxy)methyl)sulfane (3h)**



According to the general synthetic procedure A, methyl(4-methylphenyl)sulfoxide **1h** (38.5 mg, 0.25 mmol, 1.0 equiv.) was employed as the starting material. The ^{19}F NMR yield of **3h** was determined to be 78% by comparing the integration values of its characteristic resonance at -59.9 ppm with that of trifluorotoluene (-62.8 ppm) as an internal standard. HRMS-EI (*m/z*): Calcd for $C_9H_9F_3OS^+$ $[M]^+$, 222.0321. Found, 222.0317.

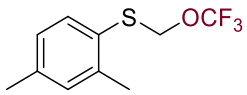
(2,6-dimethylphenyl)((trifluoromethoxy)methyl)sulfane (3i)



According to the general synthetic procedure A, methyl(2,6-dimethylphenyl)sulfoxide **1i** (42.1 mg, 0.25 mmol, 1.0 equiv.) was employed as the starting material. The ^{19}F NMR yield of **3i** was determined to be 85% by comparative integration analysis

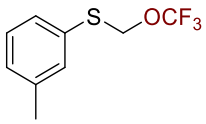
between its characteristic resonance at -60.0 ppm and the reference signal of trifluorotoluene (-62.8 ppm) in the ^{19}F NMR spectrum. HRMS-EI (*m/z*): Calcd for $C_{10}H_{11}F_3OS^+$ $[M]^+$, 236.0477. Found, 236.0476.

(2,4-dimethylphenyl)((trifluoromethoxy)methyl)sulfane (3j)



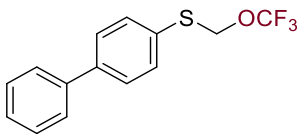
The compound methyl(2,4-dimethylphenyl)sulfoxide **1j** (38.5 mg, 0.25 mmol, 1.0 equiv.) was employed according to General Procedure A. The ^{19}F NMR yield of **3j** was determined to be 80% through comparative integration analysis of its characteristic resonance at -59.9 ppm and the reference signal of trifluorotoluene at -62.8 ppm in the ^{19}F NMR spectrum. HRMS-EI (*m/z*): Calcd for $C_{10}H_{11}F_3OS^+$ $[M]^+$, 236.0477. Found, 236.0477.

***m*-tolyl((trifluoromethoxy)methyl)sulfane (3k)**



According to the general synthetic procedure A, methyl(4-methylphenyl)sulfoxide **1k** (38.5 mg, 0.25 mmol, 1.0 equiv.) was employed. The ^{19}F NMR yield of **3k** was determined to be 69% by comparing the integral values of its ^{19}F NMR resonance signal at -59.9 ppm with that of trifluorotoluene (-62.8 ppm). HRMS-EI (*m/z*): Calcd for $C_9H_9F_3OS^+$ $[M]^+$, 222.0321. Found, 222.0319.

[1,1'-biphenyl]-4-yl((trifluoromethoxy)methyl)sulfane (3l)

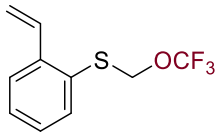


Following the general synthetic procedure A, methyl(4-phenylphenyl)sulfoxide **1l** (54.0 mg, 0.25 mmol, 1.0 equiv.) was employed as the starting material. Purification by flash column

chromatography using a hexane/ethyl acetate mixture as eluent afforded the desired product **3l** as a white solid (39.8 mg, 56% yield).

R_f = 0.30 [*n*-hexane : EA = 200 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 – 7.56 (m, 6H), 7.49 – 7.44 (m, 2H), 7.42 – 7.35 (m, 1H), 5.32 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.3, 140.1, 132.1, 131.7, 128.9, 128.0, 128.0, 127.7, 127.1, 121.4 (q, *J* = 258.3 Hz), 72.7 (q, *J* = 3.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.0. HRMS-EI (*m/z*): Calcd for $C_{14}H_{11}F_3OS^+$ $[M]^+$, 284.0477. Found, 236.0478.

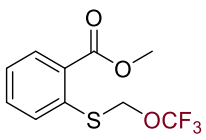
((trifluoromethoxy)methyl)(2-vinylphenyl)sulfane (3m)



According to the general synthetic procedure A, methyl(2-vinylphenyl)sulfoxide **1m** (41.6 mg, 0.25 mmol, 1.0 equiv.) was employed as the starting material. Purification by flash column chromatography using n-hexane/ethyl acetate as eluent afforded **3m** as a colorless oily liquid (43.9 mg, 75% yield).

R_f = 0.40 [*n*-hexane : EA = 200 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (dd, *J* = 7.4, 4.8 Hz, 2H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.36 – 7.27 (m, 2H), 5.76 (d, *J* = 17.4 Hz, 1H), 5.42 (d, *J* = 11.0 Hz, 1H), 5.25 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.9, 134.5, 134.4, 133.4, 131.2, 129.0, 129.0, 128.5, 126.4, 125.2, 121.4 (q, *J* = 258.0 Hz), 116.8, 72.6 (q, *J* = 3.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.6. HRMS-EI (*m/z*): Calcd for $C_{10}H_9F_3OS^+$ $[M]^+$, 234.0321. Found, 234.0324.

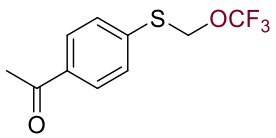
Methyl 2-(((trifluoromethoxy)methyl)thio)benzoate (3n)



Following the general synthetic procedure A, methyl (2-methoxycarbonylphenyl)sulfoxide 3-1n (49.6 mg, 0.25 mmol, 1.0 equiv.) was employed. Purification by flash column chromatography using hexane/ethyl acetate as eluent afforded compound 3-3n as a colorless oily liquid (39.2 mg, 59% yield).

R_f = 0.50 [*n*-hexane : EA = 50 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.97 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.63 – 7.48 (m, 2H), 7.32 – 7.27 (m, 1H), 5.36 (s, 2H), 3.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 138.0, 133.1, 131.3, 127.4, 126.3, 121.5 (q, *J* = 258.1 Hz), 70.2 (q, *J* = 3.5 Hz).52.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.7. HRMS-EI (*m/z*): Calcd for $C_{10}H_9F_3O_3S^+$ $[M]^+$, 266.0219. Found, 266.0220.

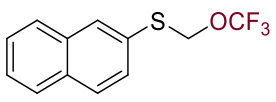
1-(4-(((trifluoromethoxy)methyl)thio)phenyl)ethan-1-one (3o)



According to the general synthetic procedure A, methyl(4-acetylphenyl)sulfoxide **1o** (45.6 mg, 0.25 mmol, 1.0 equiv.) was employed as the starting material. Purification via flash column chromatography using a hexane/ethyl acetate eluent system afforded the desired compound **3o** as a colorless oily liquid (19.4 mg, 31% yield).

R_f = 0.40 [*n*-hexane : EA = 100 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (400 MHz, Acetonitrile-d_3) δ 7.94 (d, *J* = 8.2 Hz, 2H), 7.56 (d, *J* = 8.3 Hz, 2H), 5.57 (s, 2H), 2.55 (s, 3H); ^{13}C NMR (151 MHz, CD_3CN) δ 198.1, 140.5, 136.9, 130.0, 129.5, 122.4 (q, *J* = 256.6 Hz), 72.1 (q, *J* = 3.5 Hz). 26.9; ^{19}F NMR (376 MHz, CD_3CN) δ -60.0. HRMS-EI (*m/z*): Calcd for $C_{10}H_9F_3O_2S^+$ $[M]^+$, 250.0270. Found, 250.0268.

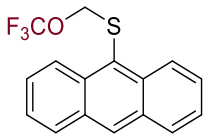
Naphthalen-2-yl((trifluoromethoxy)methyl)sulfane (3p)



Following the general synthetic procedure A, methyl(2-naphthyl)sulfoxide **1p** (47.6 mg, 0.25 mmol, 1.0 equiv.) was employed. Purification via flash column chromatography using n-hexane/ethyl acetate as the eluent afforded **3p** as a colorless oily liquid (43.2 mg, 67% yield).

R_f = 0.40 [*n*-hexane : EA = 200 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 – 7.95 (m, 1H), 7.87 – 7.79 (m, 3H), 7.59 – 7.49 (m, 3H), 5.38 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.6, 132.7, 130.5, 130.5, 129.1, 128.3, 127.8, 127.7, 126.9, 126.7, 121.4 (q, *J* = 258.2 Hz), 72.7 (q, *J* = 3.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.4. HRMS-EI (*m/z*): Calcd for $C_{12}H_9F_3OS^+$ $[M]^+$, 258.0321. Found, 258.0322.

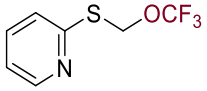
Anthracen-9-yl((trifluoromethoxy)methyl)sulfane (3q)



According to General Procedure A, methyl(9-anthryl)sulfoxide **1q** (60.1 mg, 0.25 mmol, 1.0 equiv.) was employed as the starting material. Purification via flash column chromatography using n-hexane/ethyl acetate as eluent afforded compound **3q** as a colorless oily liquid (51.0 mg, 66% yield).

R_f = 0.30 [*n*-hexane : EA = 200 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.87 (d, *J* = 9.0 Hz, 2H), 8.56 (s, 1H), 8.04 (d, *J* = 8.5 Hz, 2H), 7.64 (t, *J* = 7.7 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 2H), 5.27 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 134.8, 131.9, 130.6, 129.1, 127.3, 126.6, 125.7, 125.7, 121.4 (q, *J* = 257.9 Hz), 74.4 (q, *J* = 3.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.8. HRMS-EI (*m/z*): Calcd for $C_{16}H_{11}F_3OS^+$ $[M]^+$, 308.0477. Found, 308.0477.

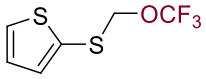
2-(((trifluoromethoxy)methyl)thio)pyridine (3r)



According to General Procedure A, methyl(2-pyridyl)sulfoxide **1r** (35.3 mg, 0.25 mmol, 1.0 equiv.) was employed. Purification by flash column chromatography (eluent: n-hexane/ethyl acetate) afforded the target compound **3r** as a colorless oily liquid (26.1 mg, 50% yield).

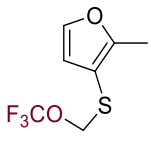
R_f = 0.30 [*n*-hexane : EA = 100 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (400 MHz, Acetonitrile-d_3) δ 8.49 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.68 (td, *J* = 7.8, 1.9 Hz, 1H), 7.34 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.19 (ddd, *J* = 7.4, 4.9, 1.1 Hz, 1H), 5.87 (s, 2H); ^{13}C NMR (151 MHz, CD_3CN) δ 155.0, 150.7, 138.3, 123.6, 122.5 (q, *J* = 256.1 Hz), 122.3, 68.6 (q, *J* = 3.5 Hz); ^{19}F NMR (376 MHz, CD_3CN) δ -58.9. HRMS-EI (*m/z*): Calcd for $C_7H_6F_3NOS^+$ $[M]^+$, 209.0117. Found, 209.0114.

2-(((trifluoromethoxy)methyl)thio)thiophene (3s)



According to the general synthetic procedure A, methyl(2-thienyl)sulfoxide **1s** (36.5 mg, 0.25 mmol, 1.0 equiv.) was employed. The ^{19}F NMR yield of **3s** was determined to be 71% through comparative integration analysis between its characteristic resonance at -59.4 ppm and the reference signal of trifluorotoluene (-62.8 ppm). HRMS-EI (*m/z*): Calcd for $C_6H_5F_3OS_2^+$ $[M]^+$, 213.9728. Found, 213.9727.

2-methyl-3-(((trifluoromethoxy)methyl)thio)furan (3t)

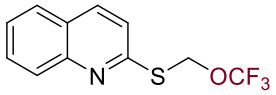


Following the general synthetic procedure A, methyl(2-(2-methylfuryl)) sulfoxide **1t** (36.1 mg, 0.25 mmol, 1.0 equiv.) was treated as described. Purification by flash column chromatography using hexanes/EtOAc as eluent afforded colorless oily liquid **3t** (47.6 mg, 80% yield).

R_f = 0.40 [*n*-hexane : EA = 200 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.34 – 7.27 (m, 1H), 6.42 – 6.38 (m, 1H), 5.00 (s, 2H), 2.37 (s, 3H); ^{13}C NMR

(151 MHz, $CDCl_3$) δ 156.6, 141.1, 114.9, 107.9, 121.5 (q, J = 257.7 Hz) , 73.7 (t, J = 3.4 Hz), 11.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.0. HRMS-EI (*m/z*): Calcd for $C_7H_7F_3O_2S^+$ $[M]^+$, 212.0113. Found, 212.0112.

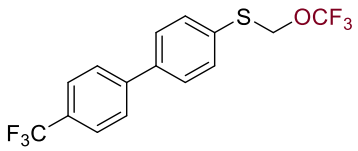
2-(((trifluoromethoxy)methyl)thio)quinoline (3u)



Following the general synthetic procedure A, methyl(2-(2-methylfuryl)) sulfoxide **1t** (36.1 mg, 0.25 mmol, 1.0 equiv.) was treated as described. Purification by flash column chromatography using hexanes/EtOAc as eluent afforded colorless oily liquid **3t** (47.6 mg, 80% yield).

R_f = 0.30 [*n*-hexane : EA = 100 : 1(v/v)]. NMR Spectroscopy: ^1H NMR (600 MHz, Chloroform-*d*) δ 8.01 (d, J = 8.4 Hz, 2H), 7.77 (d, J = 8.1 Hz, 1H), 7.71 (t, J = 7.7 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.31 – 7.26 (m, 1H), 6.00 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 154.2, 148.2, 136.8, 130.2, 128.6, 127.8, 126.7, 126.2, 121.8 (q, J = 257.9 Hz), 120.7, 66.4 (q, J = 3.7 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.8. HRMS-EI (*m/z*): Calcd for $C_{11}H_8F_3NOS^+$ $[M]^+$, 259.0273. Found, 259.0273.

((trifluoromethoxy)methyl)(4'-(trifluoromethyl)-[1,1'-biphenyl]-3-yl)sulfane (3v)

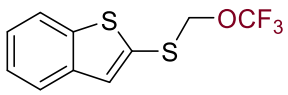


Following the general procedure A, methyl(4-(4-(trifluoromethyl)phenyl)phenyl)sulfoxide **1v** (71.1 mg, 0.25 mmol, 1.0 equiv.) was employed. Purification by flash column chromatography using hexanes/ethyl acetate as eluent afforded compound **3v** as a white solid (30.9 mg, 38% yield).

R_f = 0.30 [*n*-hexane : EA = 100 : 1(v/v)]. NMR Spectroscopy: ^1H NMR (400 MHz, Chloroform-*d*) δ 7.75 – 7.66 (m, 4H), 7.59 (s, 4H), 5.33 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 139.8, 133.6, 131.7, 128.2, 127.5, 126.0 (q, J = 3.7 Hz), 124.4 (q, J = 272.0 Hz), 121.5

(q, J = 258.2 Hz), 72.5 (q, J = 3.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.5 (s, 3F), -62.5 (s, 3F). HRMS-EI (*m/z*): Calcd for $C_{15}H_{10}F_6OS^+$ $[M]^+$, 352.0351. Found, 352.0352.

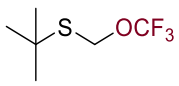
2-(((trifluoromethoxy)methyl)thio)benzo[*b*]thiophene (3w)



Following the general procedure A, methyl(2-benzothienyl)sulfoxide **1w** (49.1 mg, 0.25 mmol, 1.0 equiv.) was employed. Purification by flash column chromatography using n-hexane/ethyl acetate as eluent afforded the desired product **3w** as a white solid (29.0 mg, 44% yield).

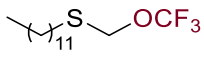
R_f = 0.40 [*n*-hexane : EA = 200 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 – 7.69 (m, 2H), 7.51 (s, 1H), 7.41 – 7.34 (m, 2H), 5.23 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.5, 139.4, 131.9, 131.6, 125.3, 124.8, 123.8, 122.0, 121.3 (q, J = 258.6 Hz), 73.6 (q, J = 3.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.4. HRMS-EI (*m/z*): Calcd for $C_{10}H_7F_3OS_2^+$ $[M]^+$, 263.9885. Found, 263.9886.

***tert*-butyl((trifluoromethoxy)methyl)sulfane (3x)**



According to the general synthetic procedure A, methyl tert-butyl sulfoxide **1x** (30.1 mg, 0.25 mmol, 1.0 equiv.) was employed. The ^{19}F NMR yield of **3x** was determined to be 78% through comparative integration of its characteristic resonance at -59.3 ppm with that of trifluorotoluene (-62.8 ppm) as an internal standard. HRMS-EI (*m/z*): Calcd for $C_6H_{11}F_3OS^+$ $[M]^+$, 188.0477. Found, 188.0476.

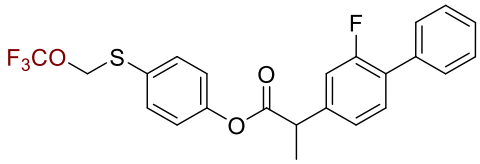
Dodecyl((trifluoromethoxy)methyl)sulfane (3y)



According to the general synthetic procedure A, methyl(1-dodecyl)sulfoxide **1y** (58.1 mg, 0.25 mmol, 1.0 equiv.) was employed. Purification via flash column chromatography using hexane/ethyl acetate as eluent afforded the desired product **3y** as a white solid (49.7 mg, 66% yield).

R_f = 0.50 [*n*-hexane : EA = 200 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.04 (s, 2H), 2.69 (t, *J* = 7.4 Hz, 2H), 1.73 – 1.57 (m, 2H), 1.43 – 1.18 (m, 21H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 121.3 (d, *J* = 257.5 Hz), 71.0 (q, *J* = 3.4 Hz).32.0, 31.9, 29.6, 29.6, 29.5, 29.3, 29.3, 29.1, 28.6, 22.7, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.7. HRMS-EI (*m/z*): Calcd for $C_{12}H_{25}S^+$ $[M\text{-}CH_2OCF_3]^+$, 201.1671. Found, 201.1669.

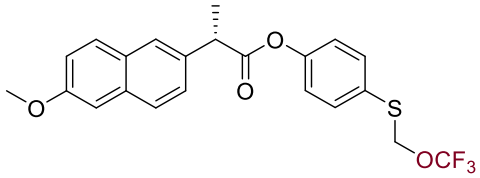
Flurbiprofen derivatives (3z)



According to the general synthetic procedure A, flurbiprofen derivative **1z** (95.6 mg, 0.25 mmol, 1.0 equiv.) was subjected to the reaction. The crude product was purified by flash column chromatography using a hexane/ethyl acetate eluent system to afford compound **3z** as a white solid (68.5 mg, 61% yield).

R_f = 0.40 [*n*-hexane : EA = 5 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 7.7 Hz, 2H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.49 – 7.44 (m, 3H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.30 – 7.18 (m, 2H), 7.07 (d, *J* = 8.3 Hz, 2H), 5.24 (s, 2H), 4.15 (q, *J* = 7.2 Hz, 1H), 1.68 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.3, 159.9 (d, *J* = 248.8 Hz), 151.0, 141.1 (d, *J* = 7.7 Hz), 135.4, 133.1, 131.2 (d, *J* = 4.1 Hz), , 130.5, 129.1 (d, *J* = 2.9 Hz), 128.6, 127.9, 123.7 (d, *J* = 3.2 Hz),122.4, 121.4 (q, *J* = 258.2 Hz), 115.5, 115.3, 73.0 (q, *J* = 3.6 Hz), 45.2, 18.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.4 (s, 3F), -117.0 (s, 1F). HRMS-ESI (*m/z*): Calcd for $C_{23}H_{18}F_4NaO_3S^+$ $[M+Na]^+$, 473.0805. Found, 473.0797.

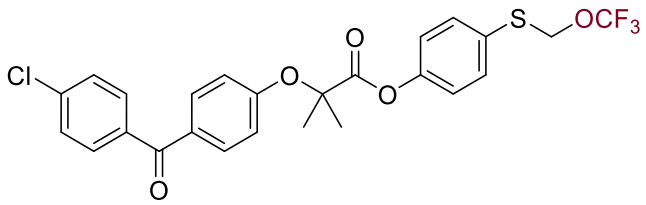
Naproxen derivatives (3aa)



According to the general procedure A, the naproxen derivative **1aa** (92.1 mg, 0.25 mmol, 1.0 equiv.) was employed. Purification by flash column chromatography using hexanes/ethyl acetate as eluent afforded the desired product **3aa** as a white solid (36.2 mg, 33% yield).

R_f = 0.20 [*n*-hexane : EA = 5 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.80 – 7.72 (m, 3H), 7.56 – 7.44 (m, 3H), 7.20 – 7.11 (m, 2H), 7.00 (d, *J* = 8.2 Hz, 2H), 5.21 (s, 2H), 4.10 (q, *J* = 7.3 Hz, 1H), 3.93 (s, 3H), 1.70 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.9, 157.8, 151.1, 134.9, 133.9, 133.0, 130.2, 129.3, 129.0, 127.5, 126.2, 126.0, 122.4, 121.3 (q, *J* = 258.1 Hz), 119.2, 105.6, 72.98 (q, *J* = 3.5 Hz), 55.3, 45.6, 18.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.5. HRMS-ESI (*m/z*): Calcd for $C_{22}H_{19}F_3NaO_4S^+$ $[M+Na]^+$, 459.0848. Found, 459.0844.

Fenofibrate derivatives (3bb)



Following the general synthetic procedure A, fenofibrate derivative **1bb** (92.1 mg, 0.25 mmol, 1.0 equiv.) was employed as the starting material. Purification by flash column chromatography using n-hexane/ethyl acetate as the eluent system afforded the desired product **3bb** as a white solid (45.8 mg, 35% yield).

R_f = 0.35 [*n*-hexane : EA = 5 : 1(v/v)]. NMR Spectroscopy: ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.50 (d, *J* = 8.2 Hz, 2H), 7.45 (d, *J* = 8.1 Hz, 2H), 7.02 – 6.86 (m, 4H), 5.23 (s, 2H), 1.82 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.2, 172.3, 159.5, 150.6, 138.6, 136.4, 133.1, 132.3, 131.3, 131.1, 130.9, 128.7,

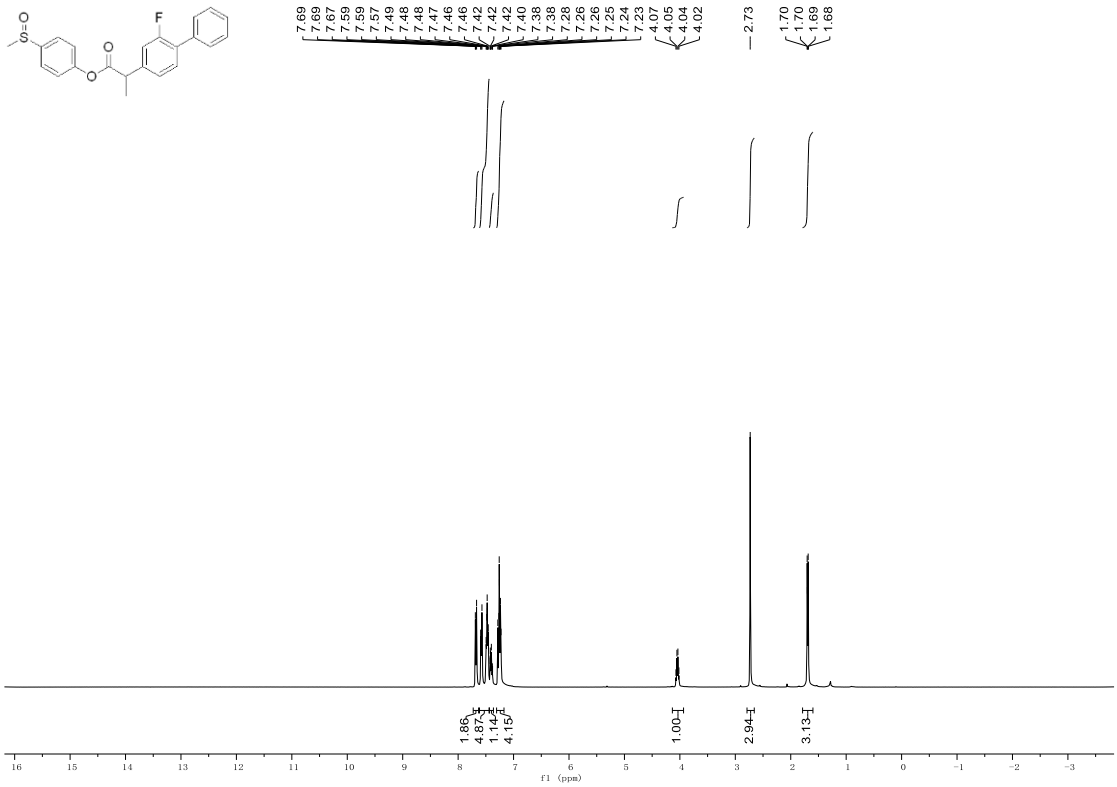
122.3, 121.3 (q, J = 240.4 Hz) 117.4, 79.5, 72.9 (q, J = 3.4 Hz), 25.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.4. HRMS-ESI (*m/z*): Calcd for $C_{25}H_{21}ClF_3O_5S^+$ $[M+H]^+$, 525.0745. Found, 525.0743.

Supplementary References

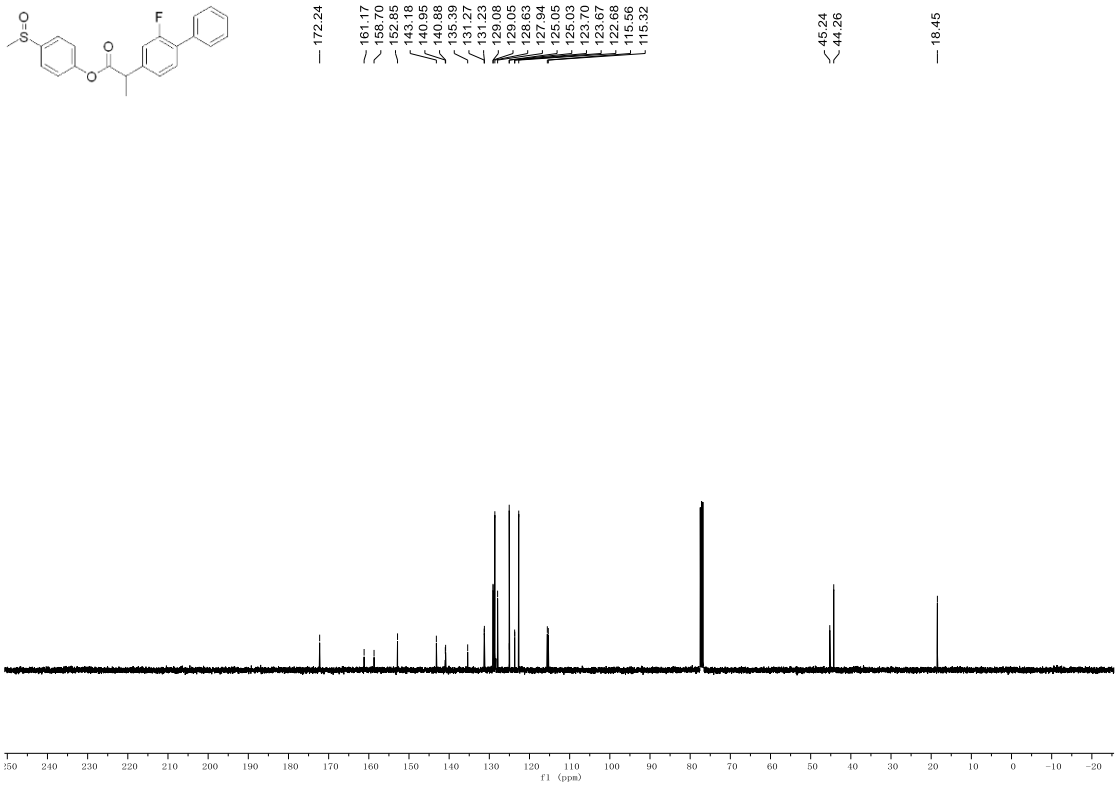
[1] S. Guo, F. Cong, R. Guo, L. Wang and P. Tang, *Nat. Chem.*, 2017, **9**, 546–551.

Spectra Data

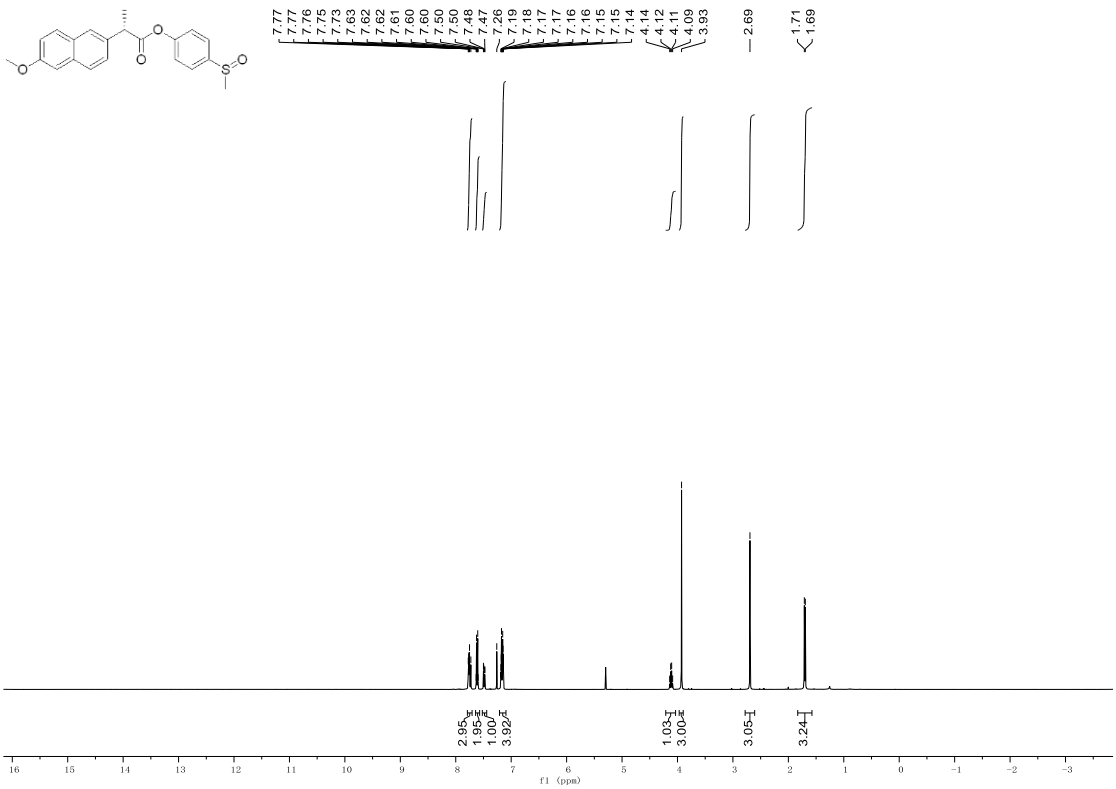
^{1}H NMR, ^{13}C NMR and ^{19}F NMR Spectra



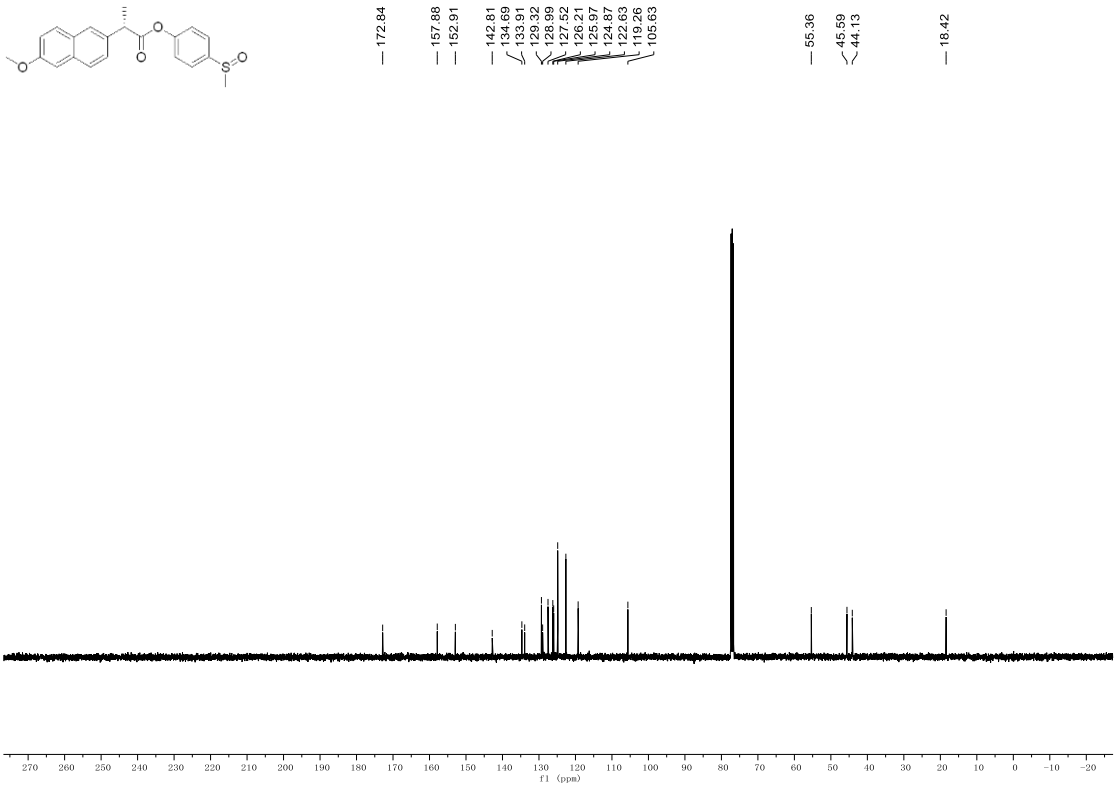
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **1z**



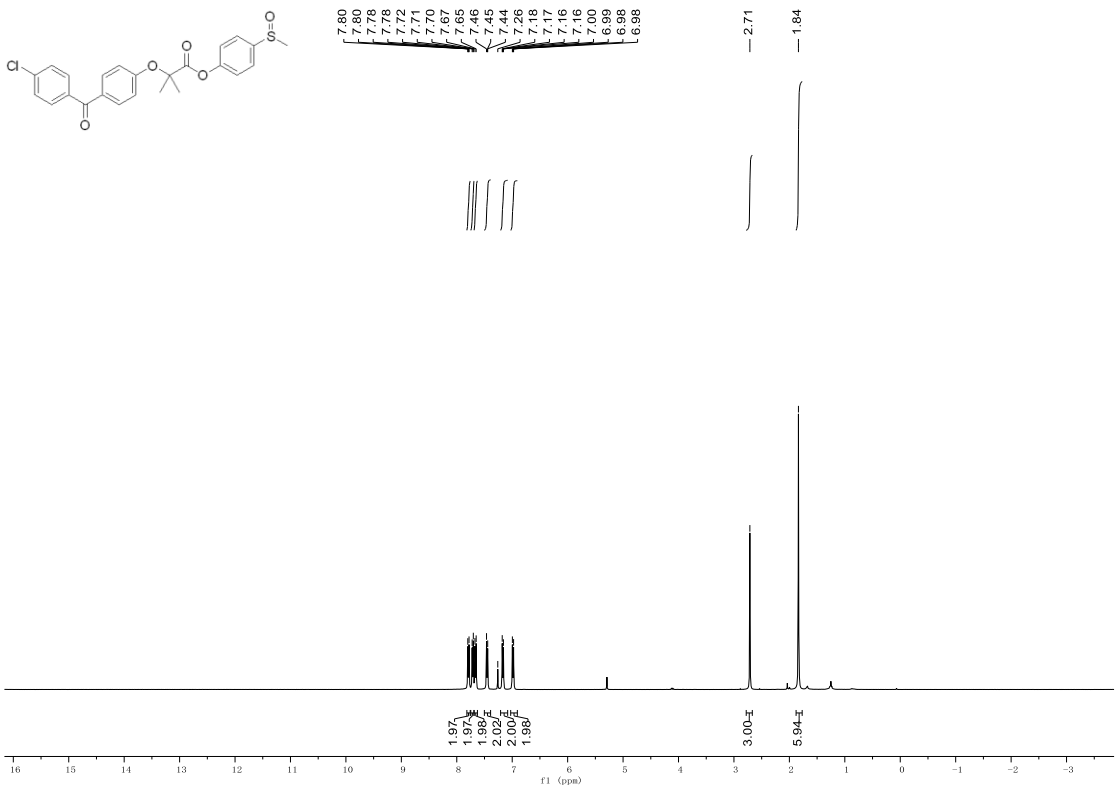
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **1z**



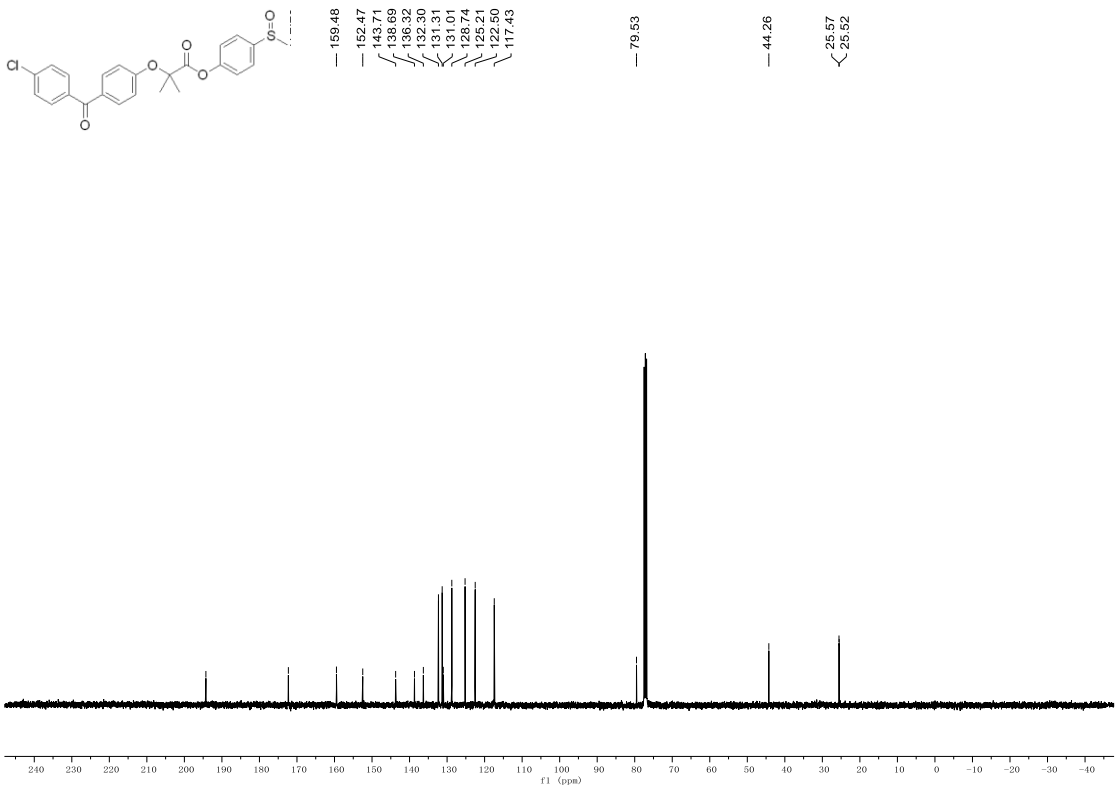
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **1aa**



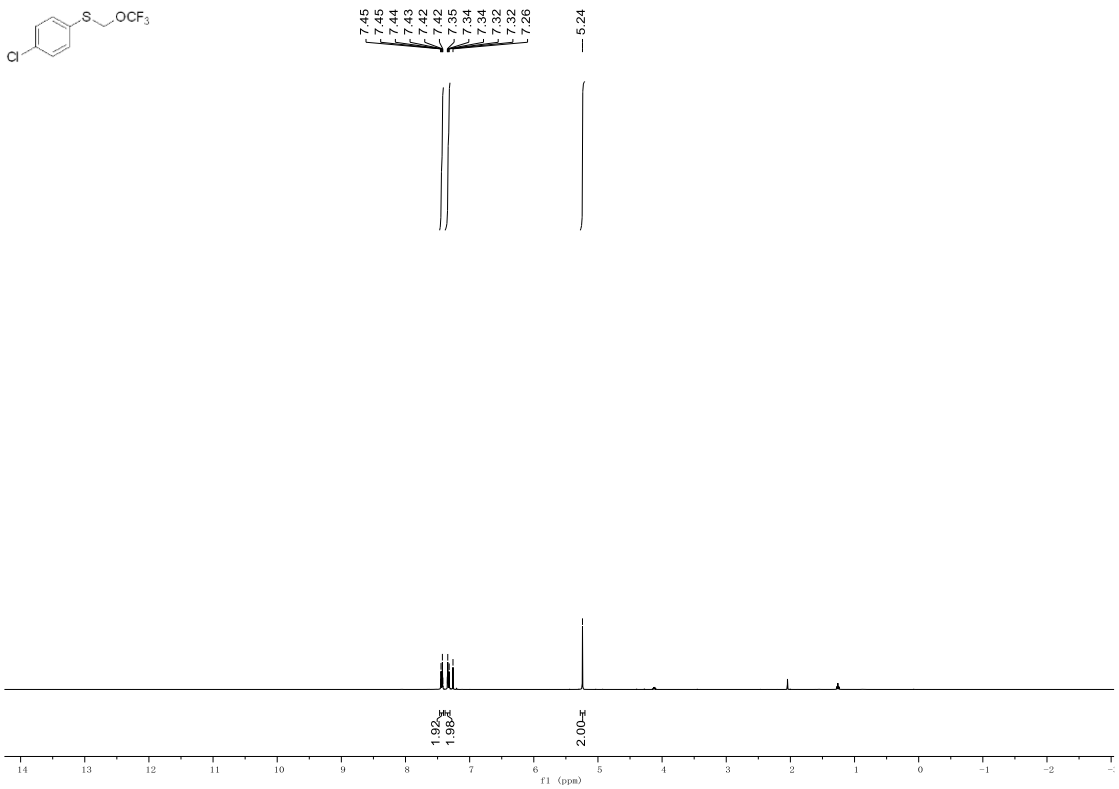
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **1aa**



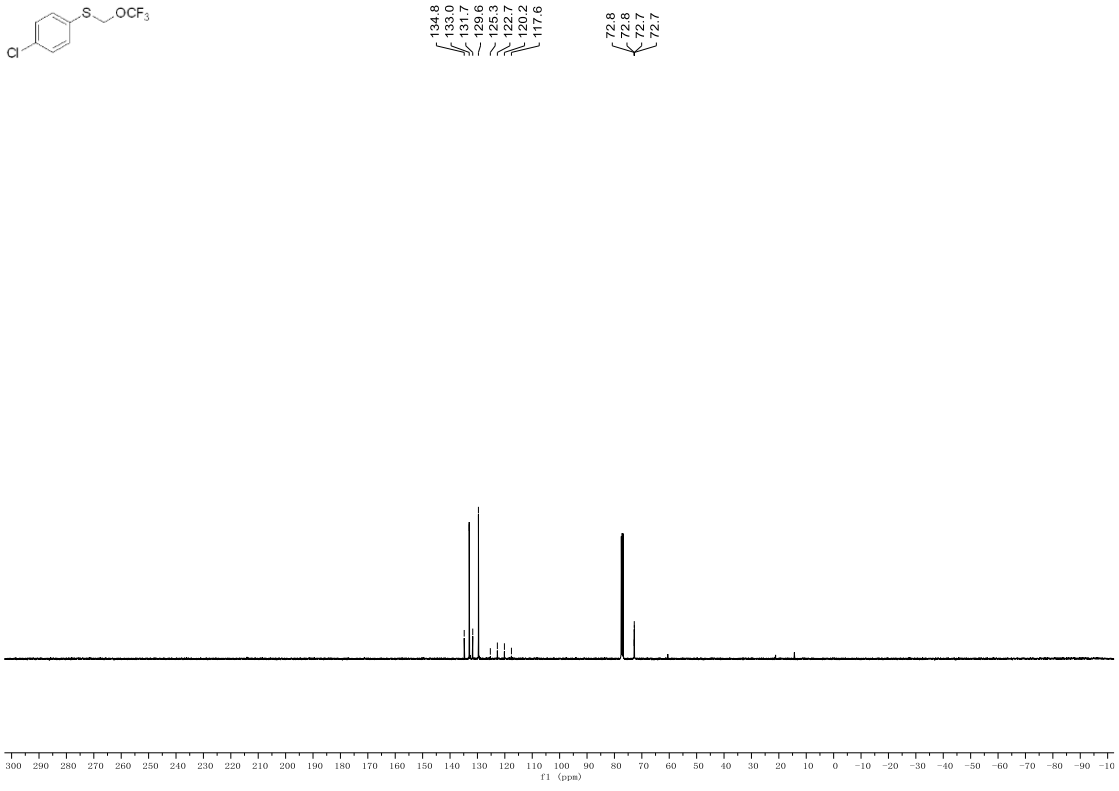
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **1bb**



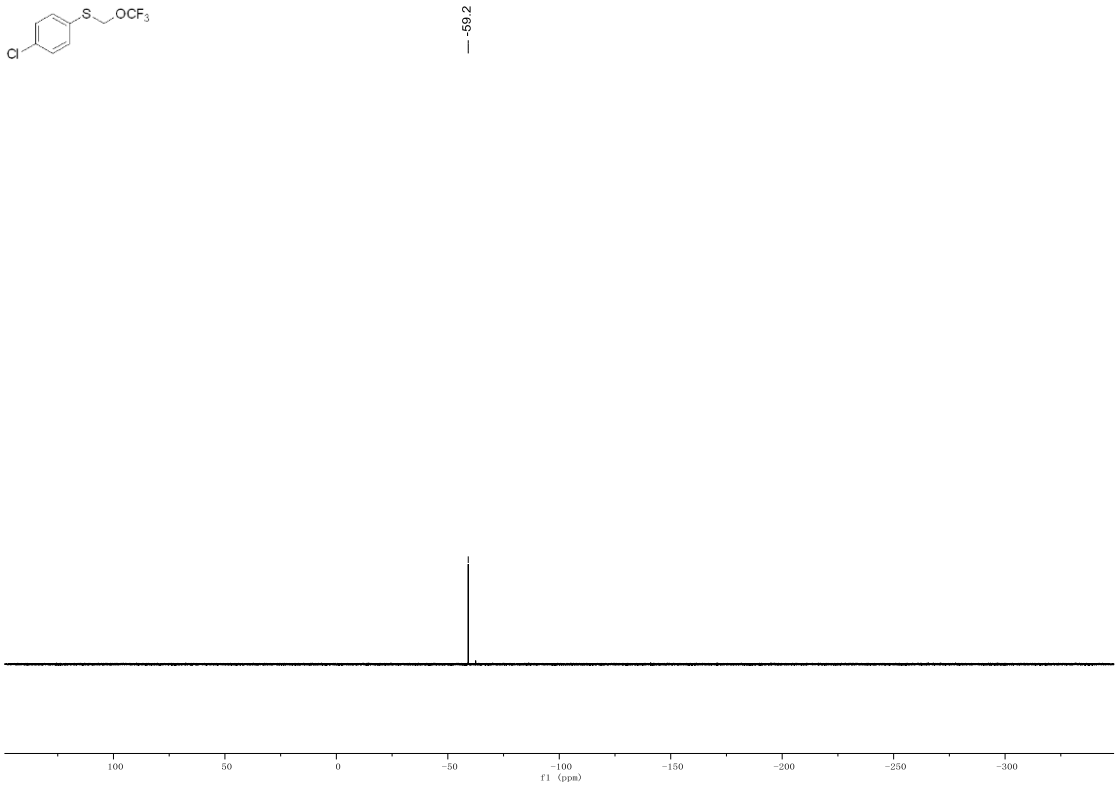
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **1bb**



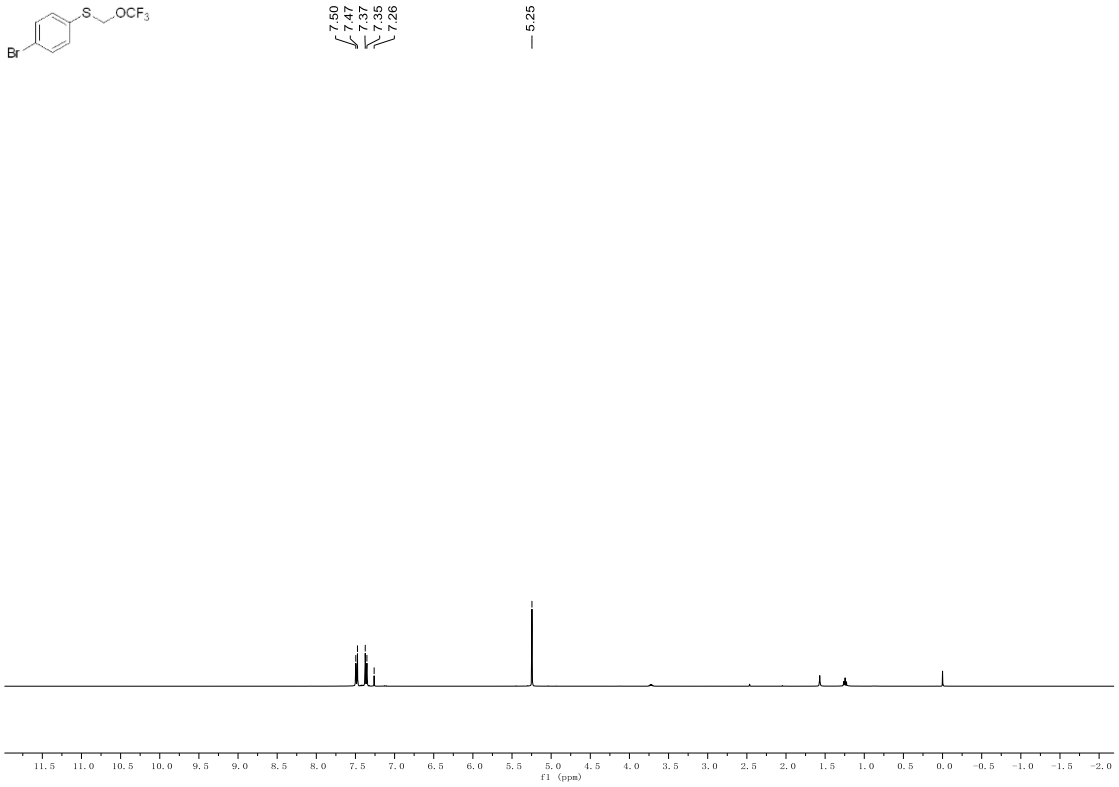
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3c**



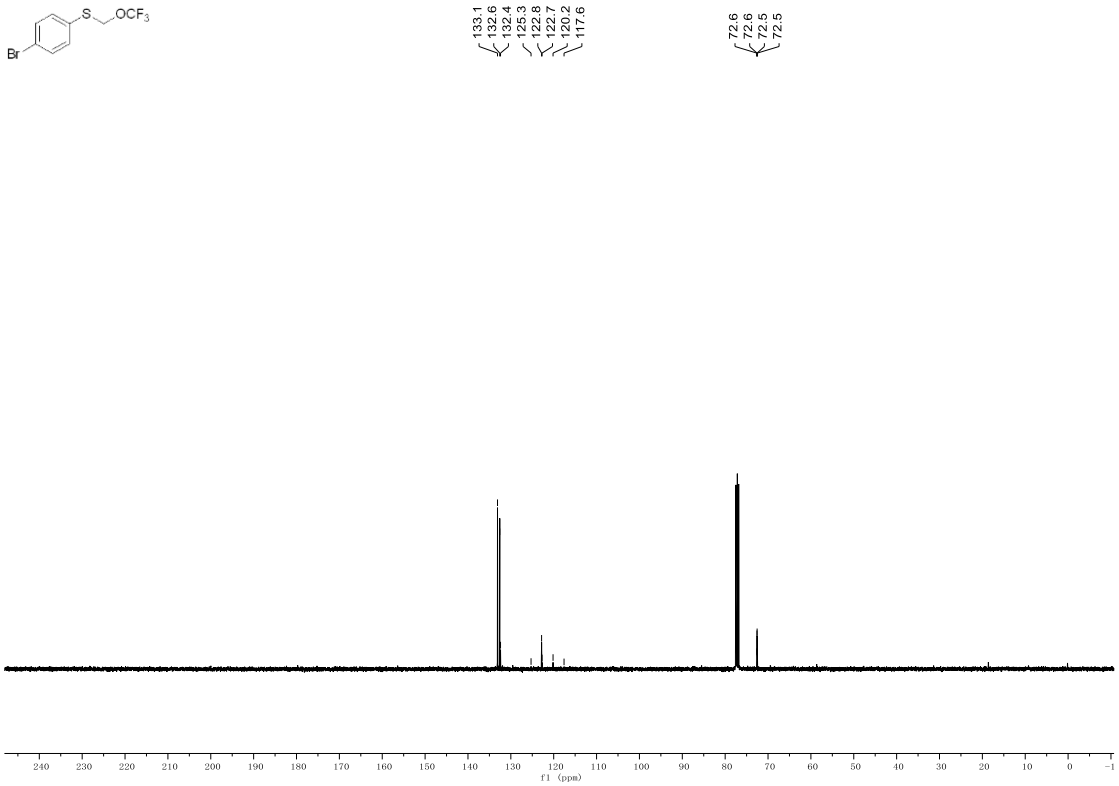
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **3c**



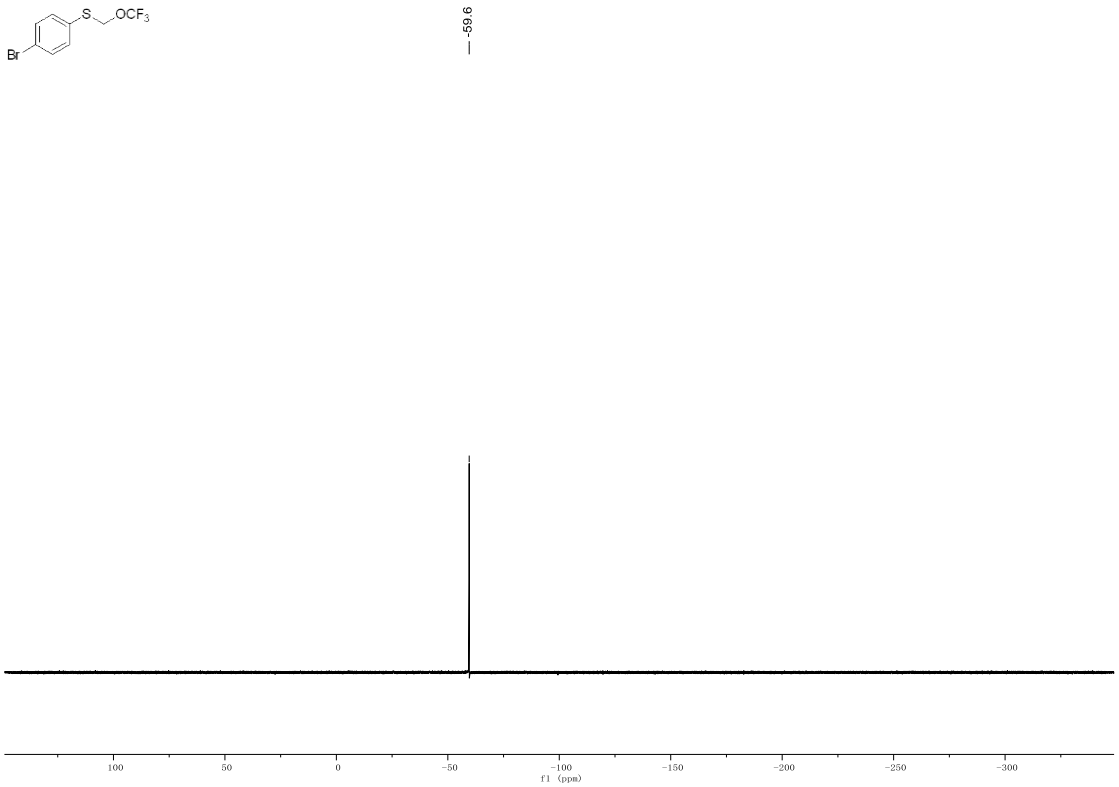
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3c**



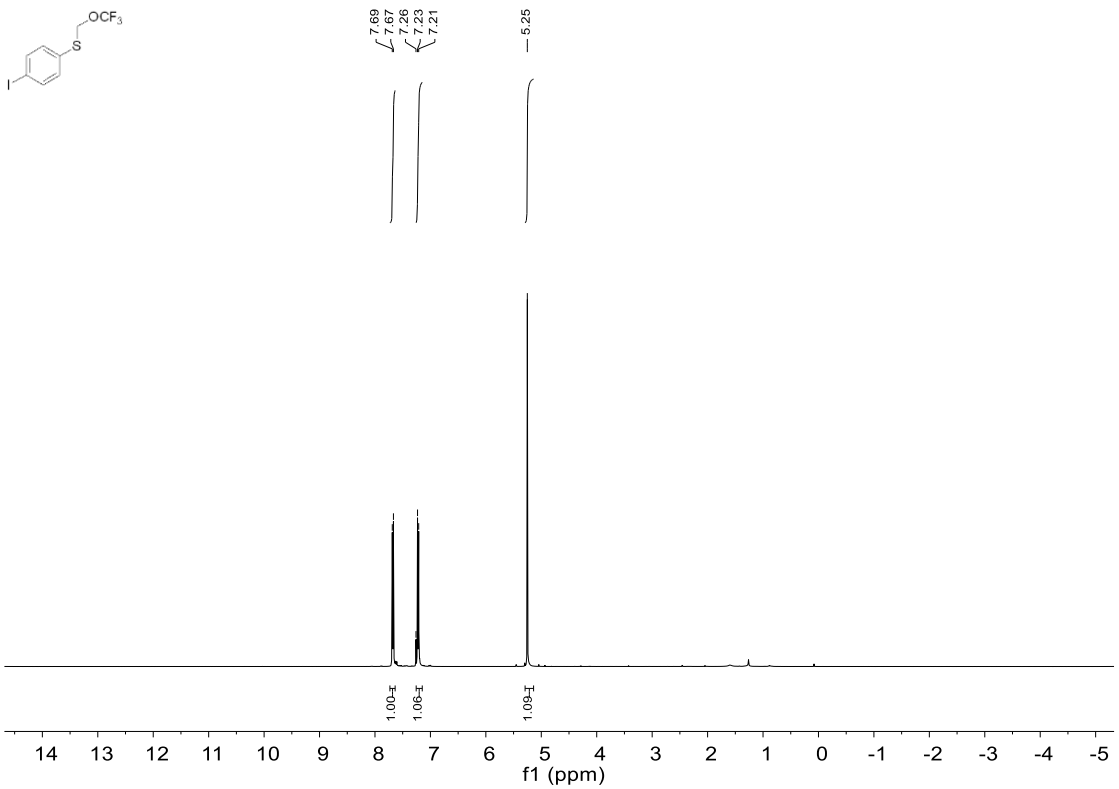
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3d**



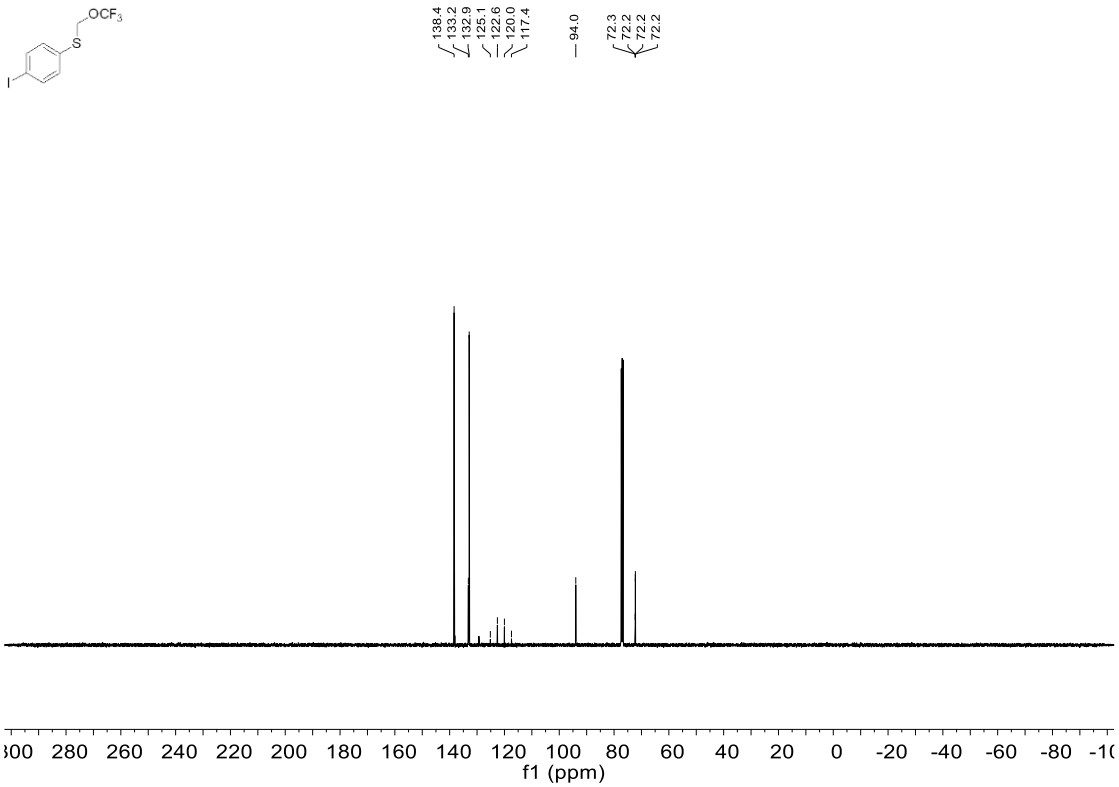
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **3d**



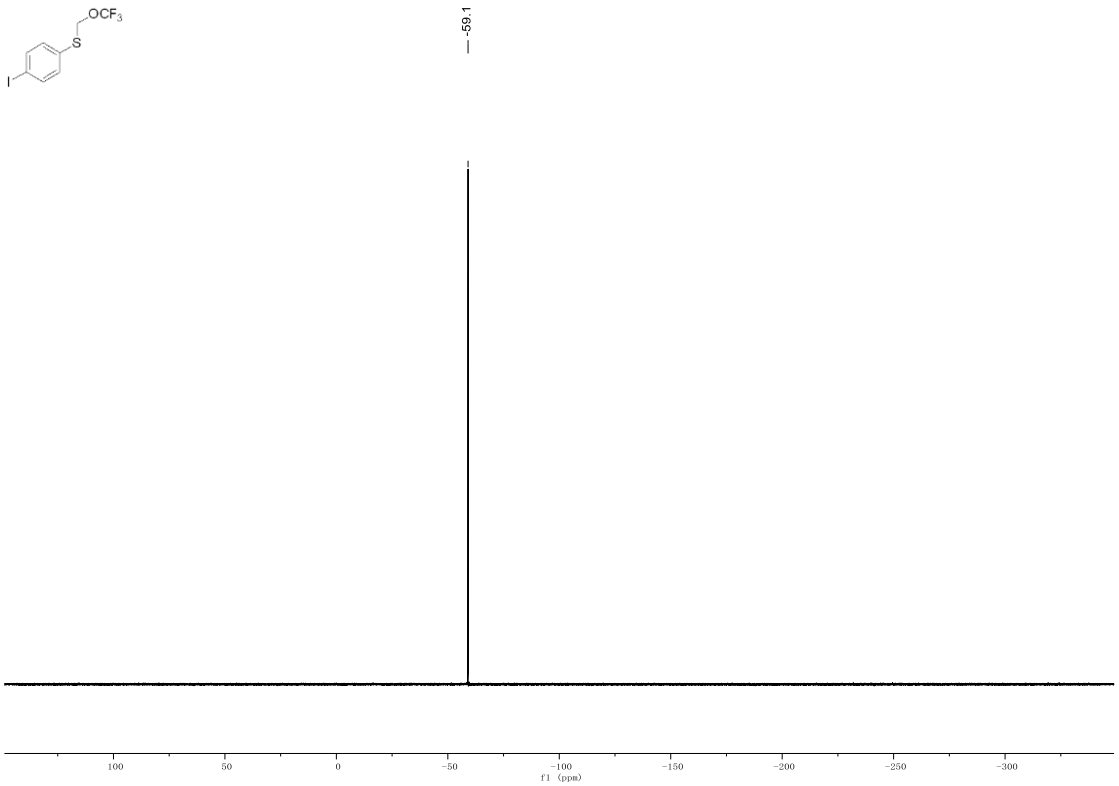
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3d**



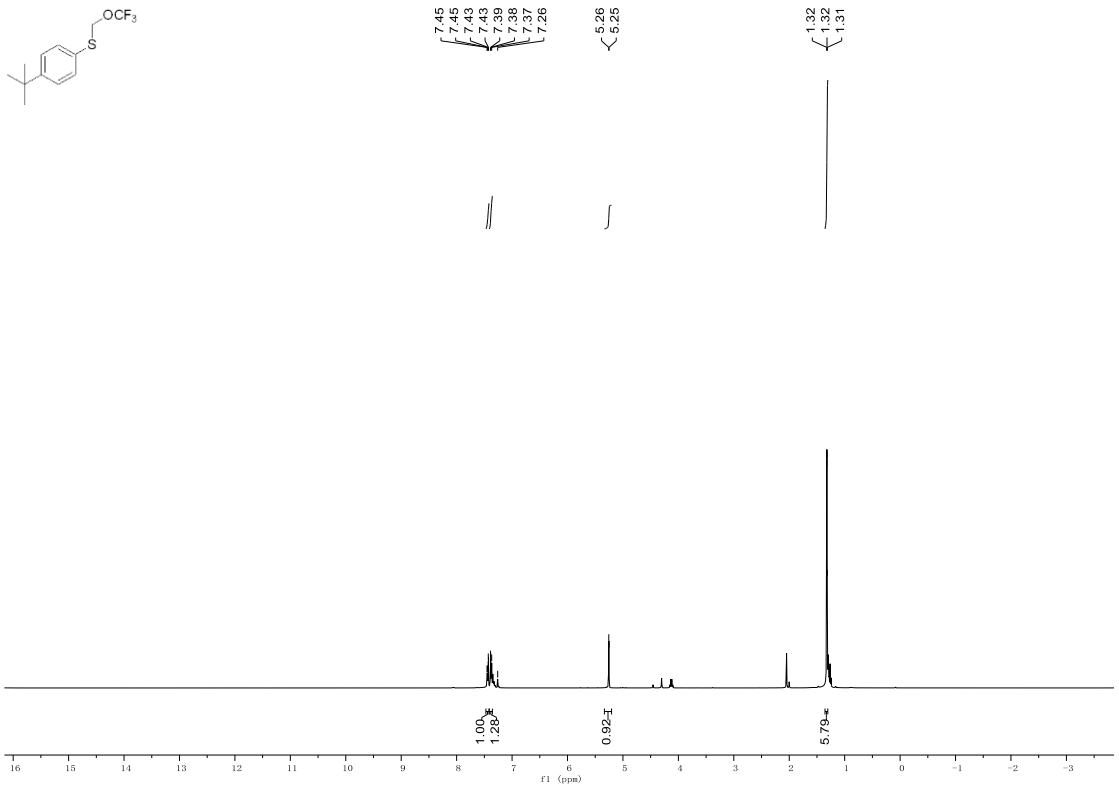
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3e**



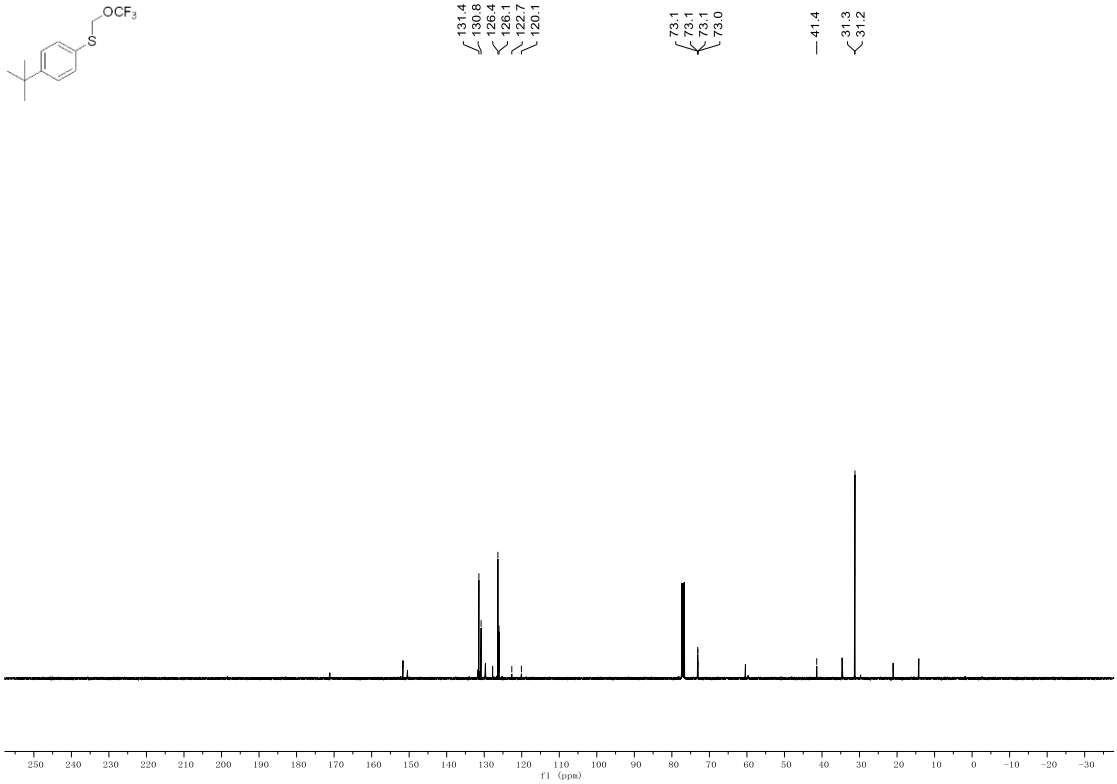
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **3e**



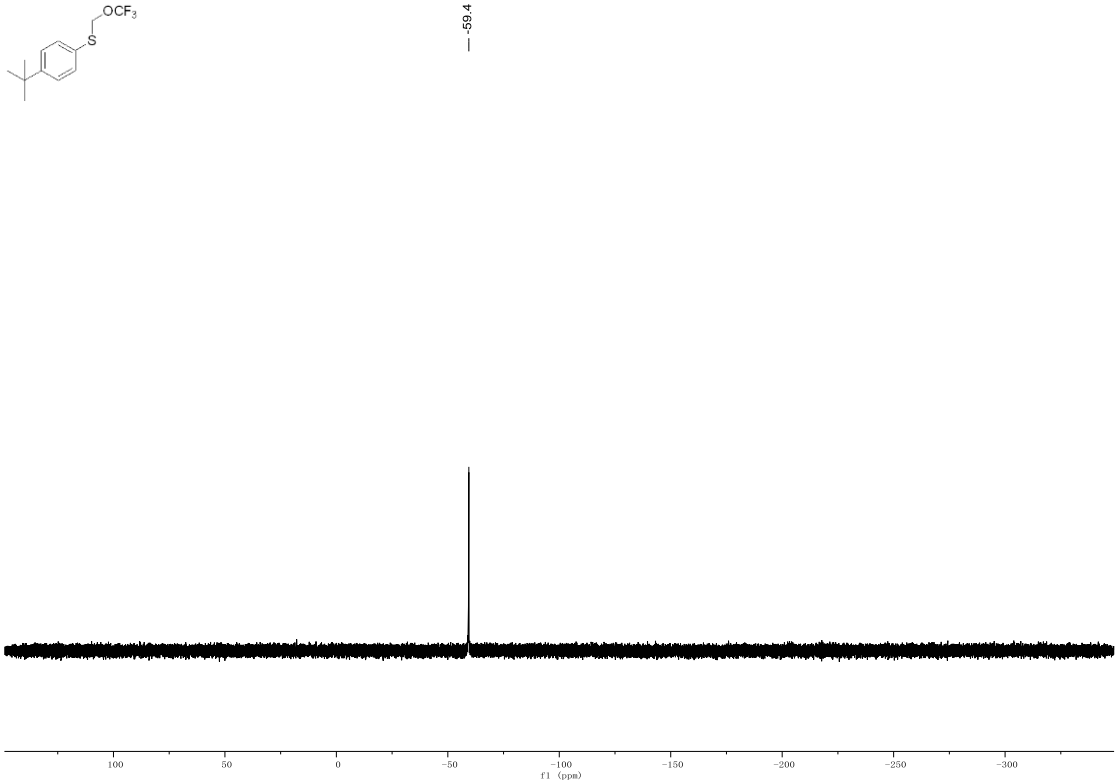
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3e**



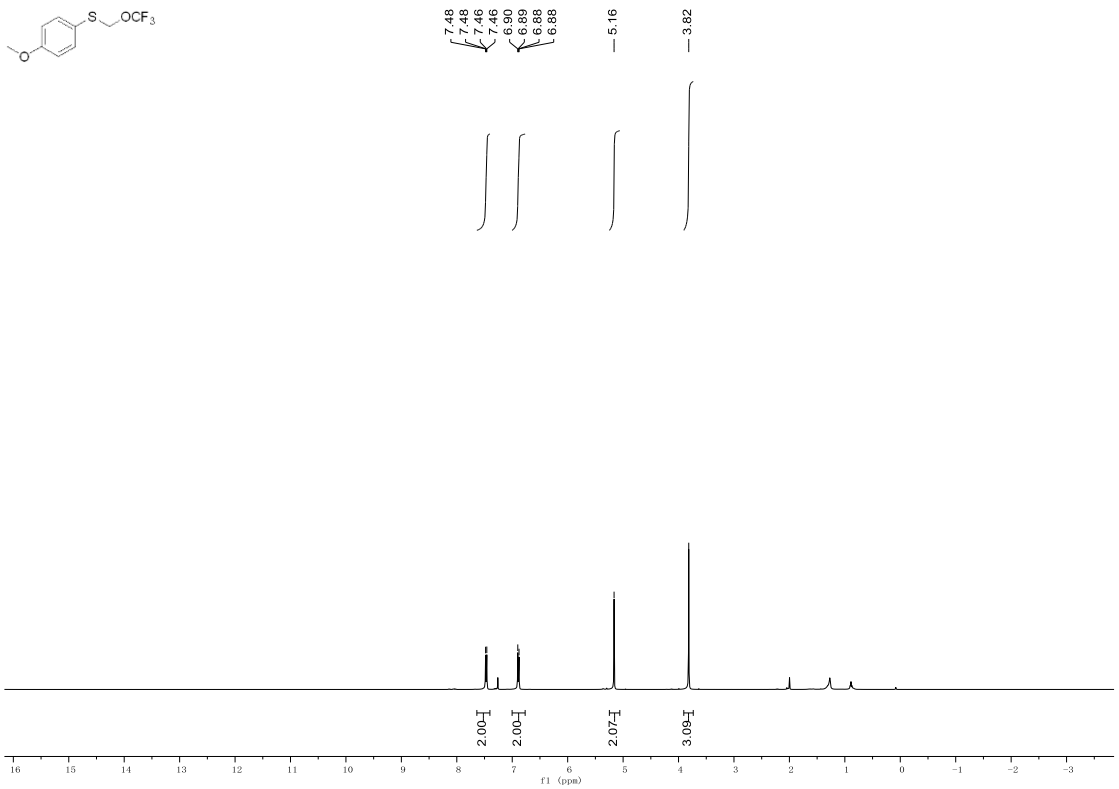
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3f**



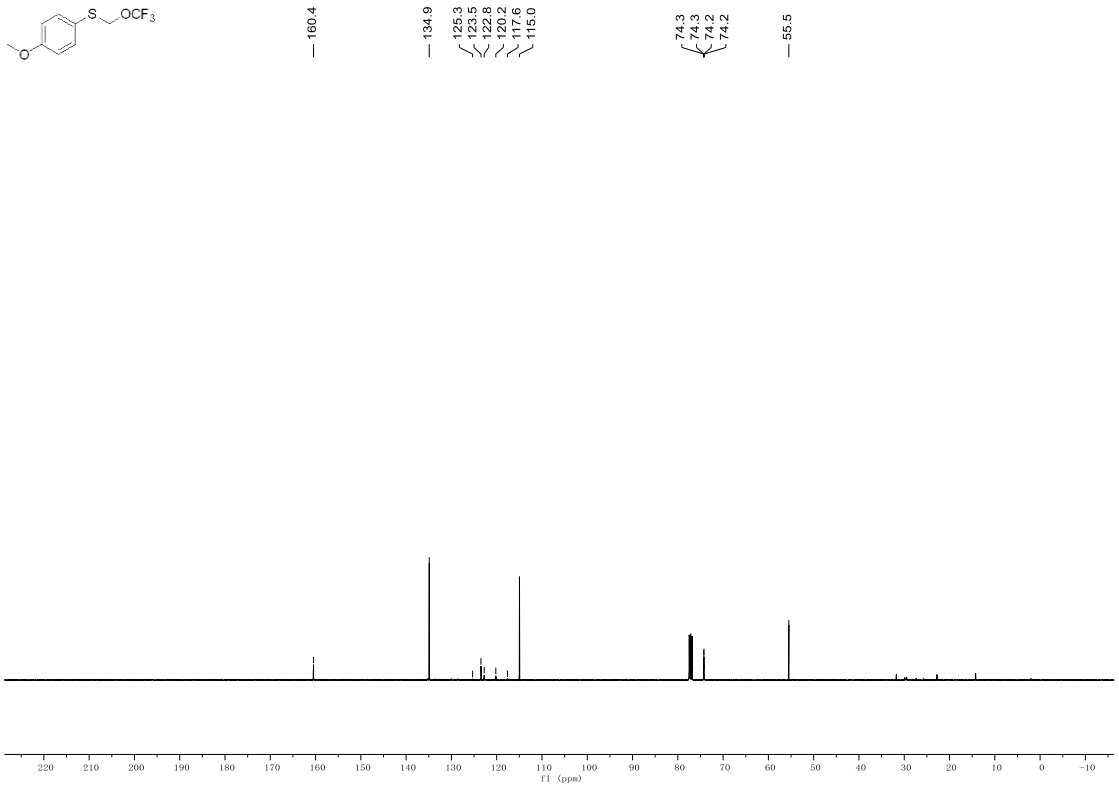
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **3f**



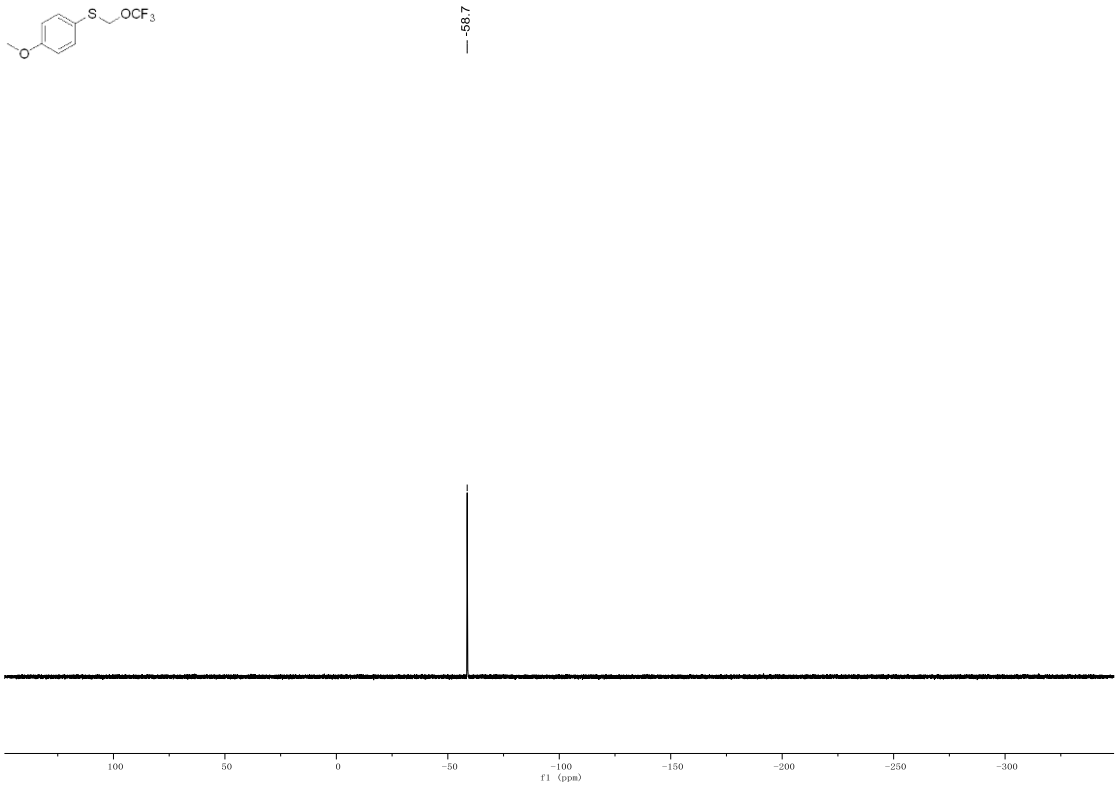
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3f**



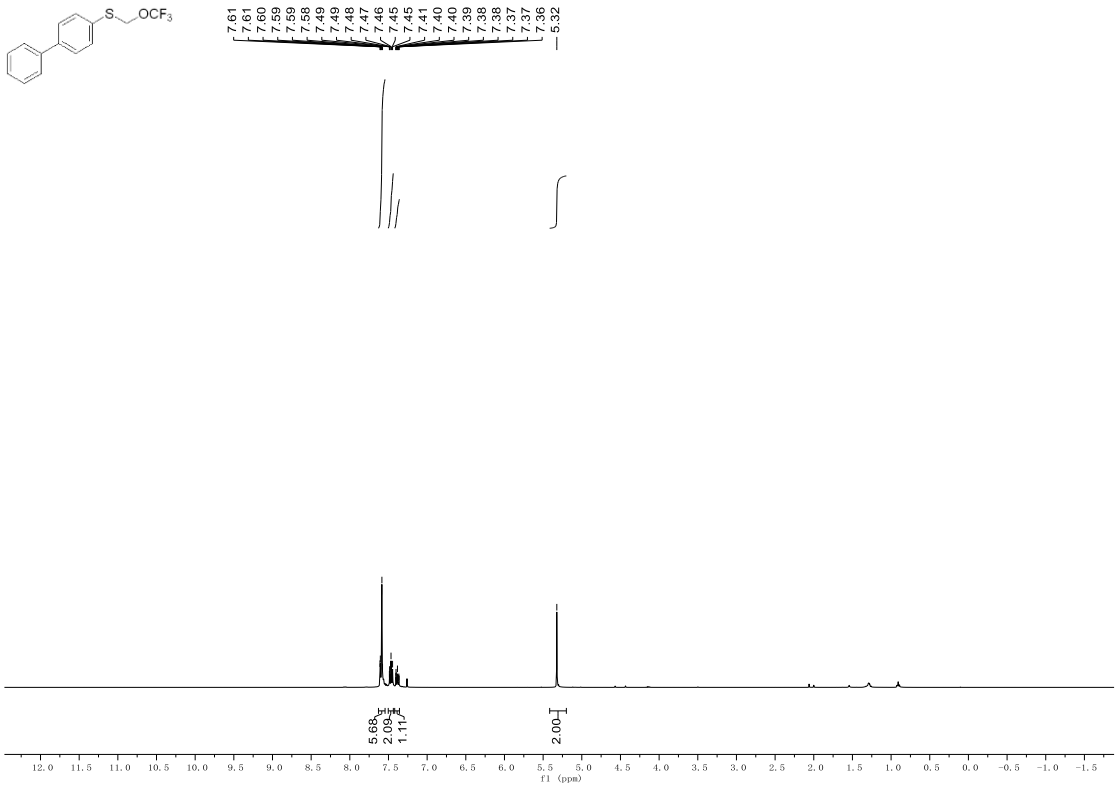
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3g**



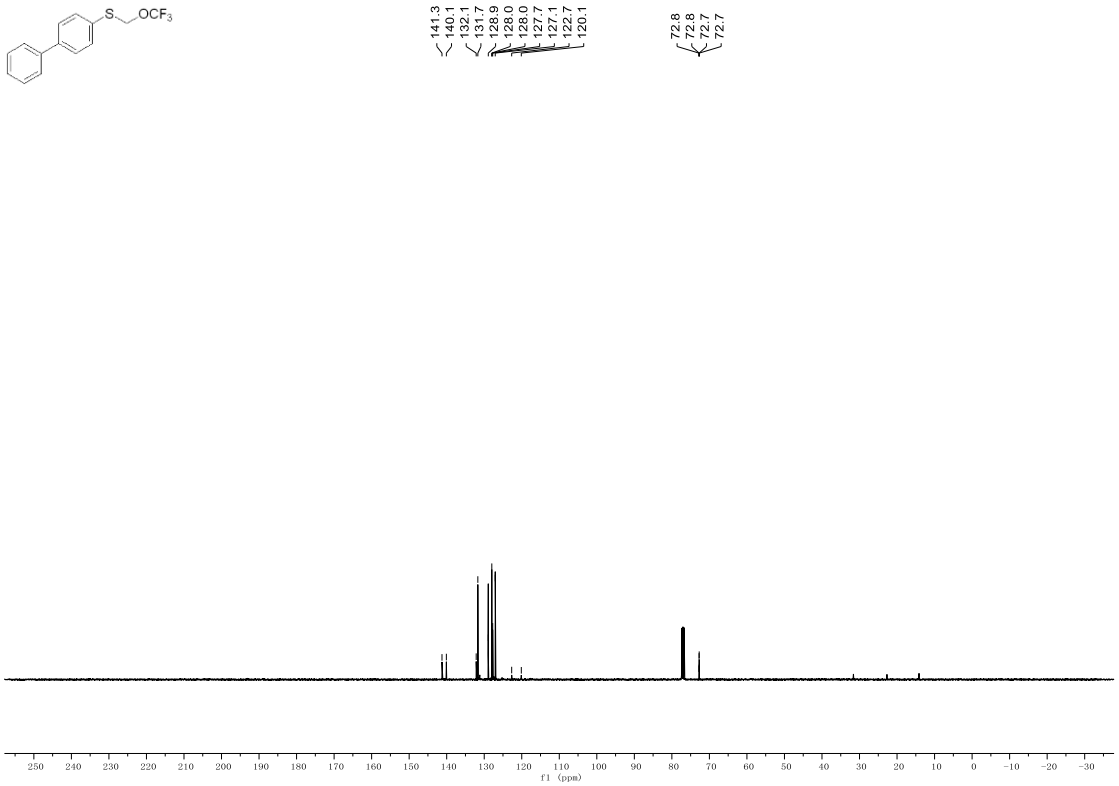
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **3g**



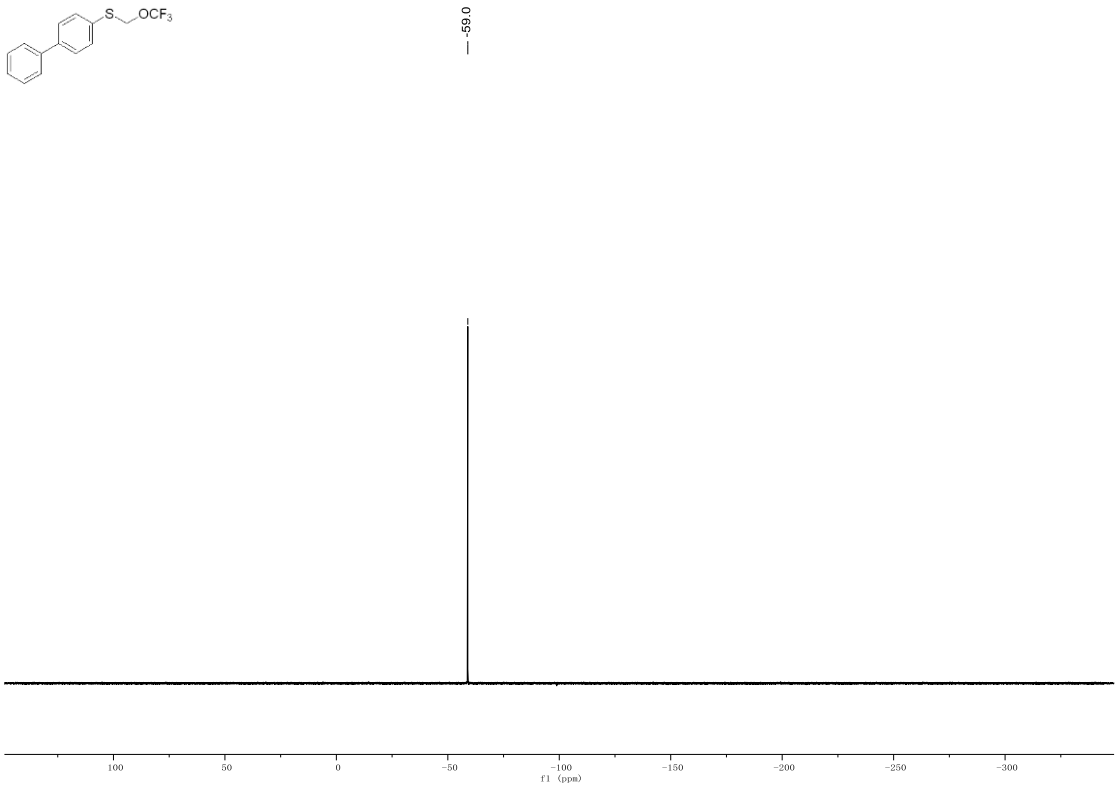
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3g**



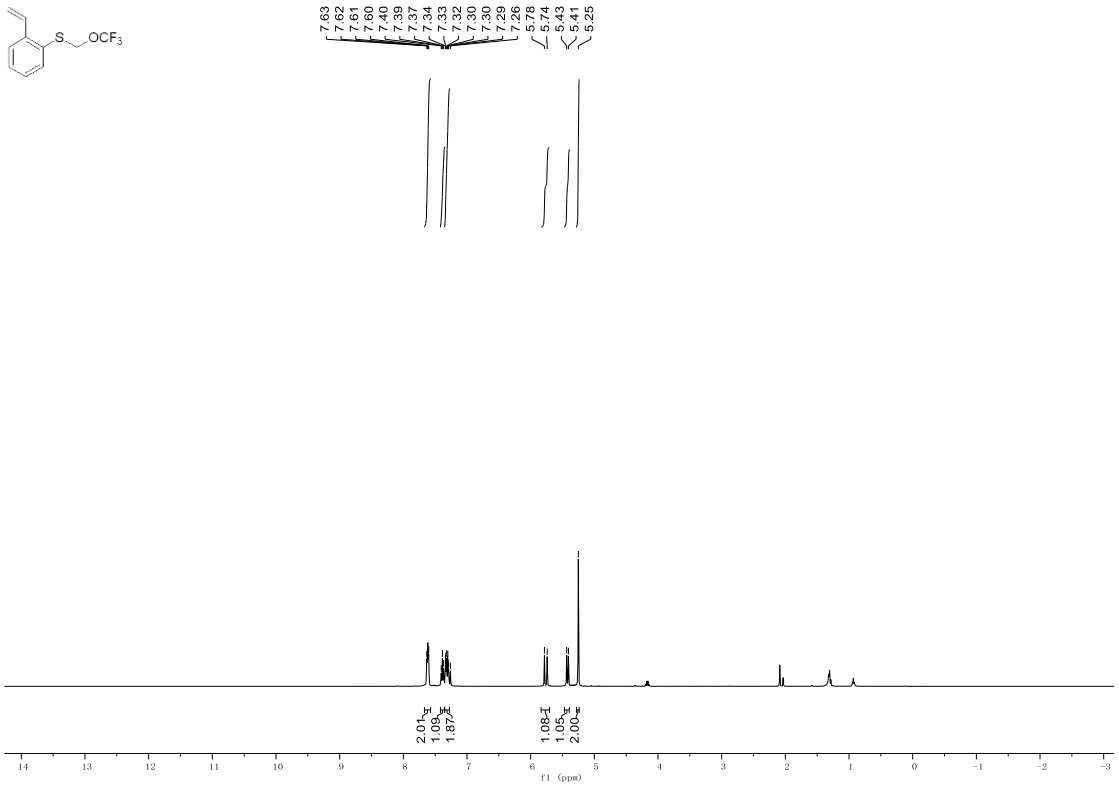
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3l**



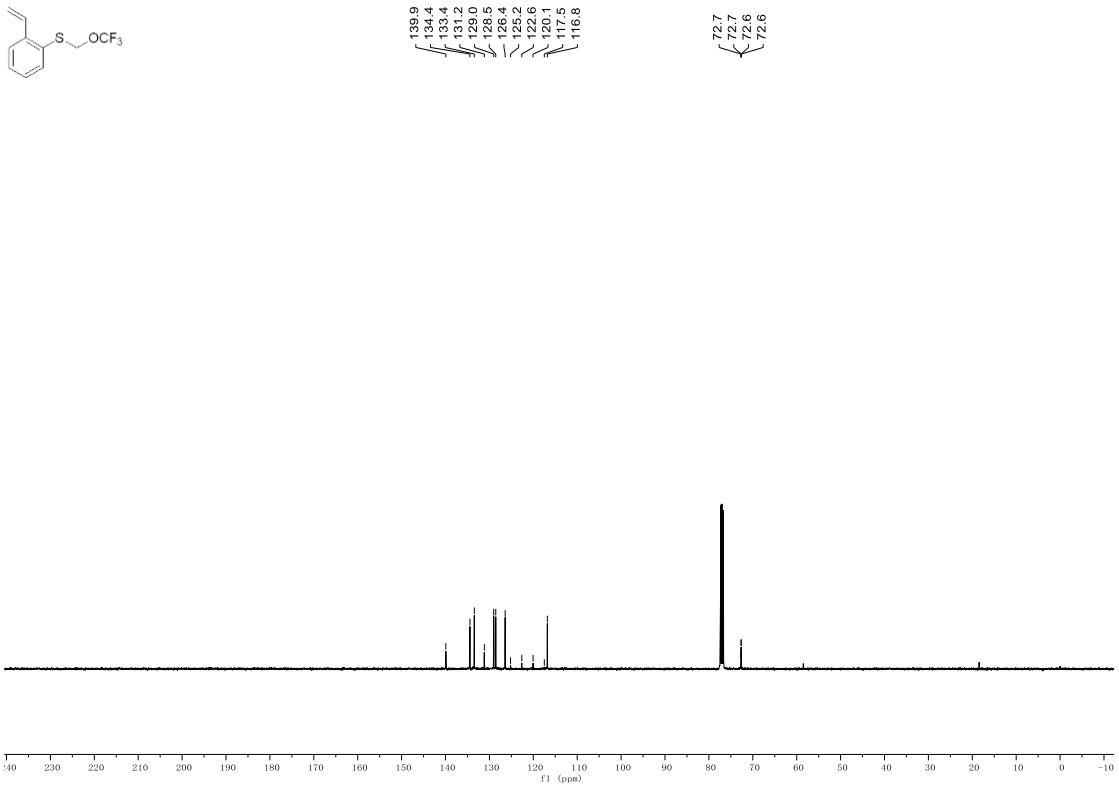
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **3l**



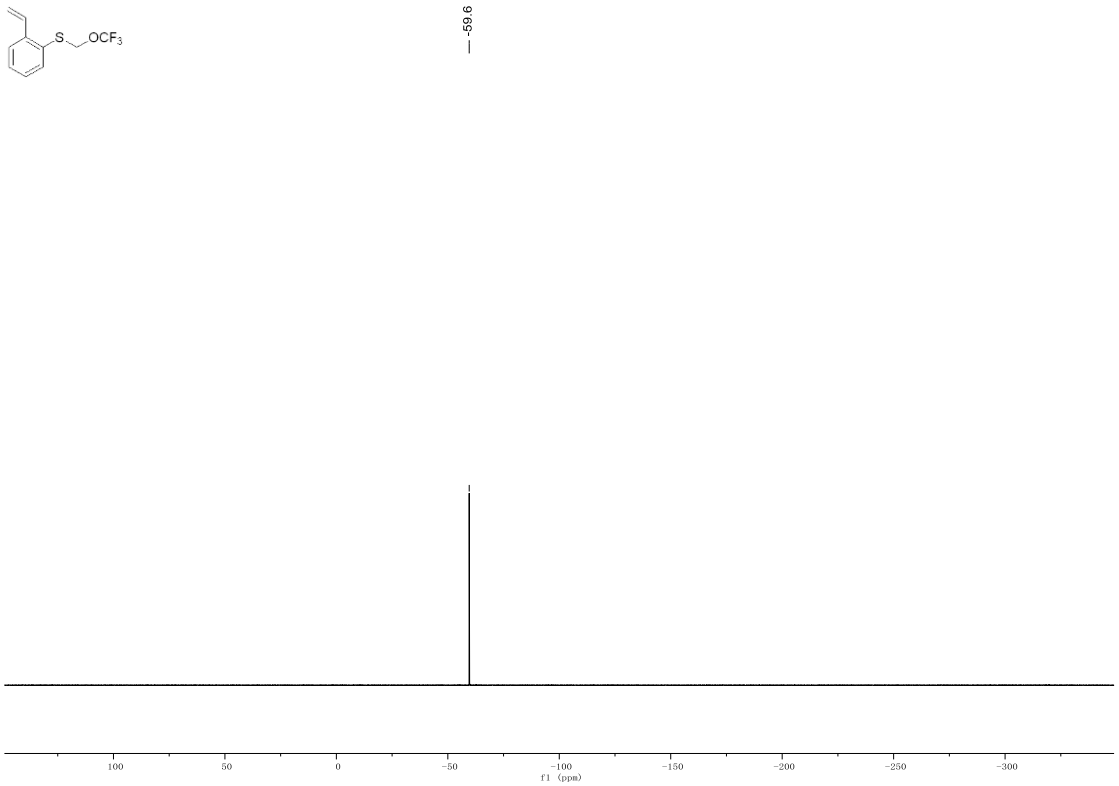
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3l**



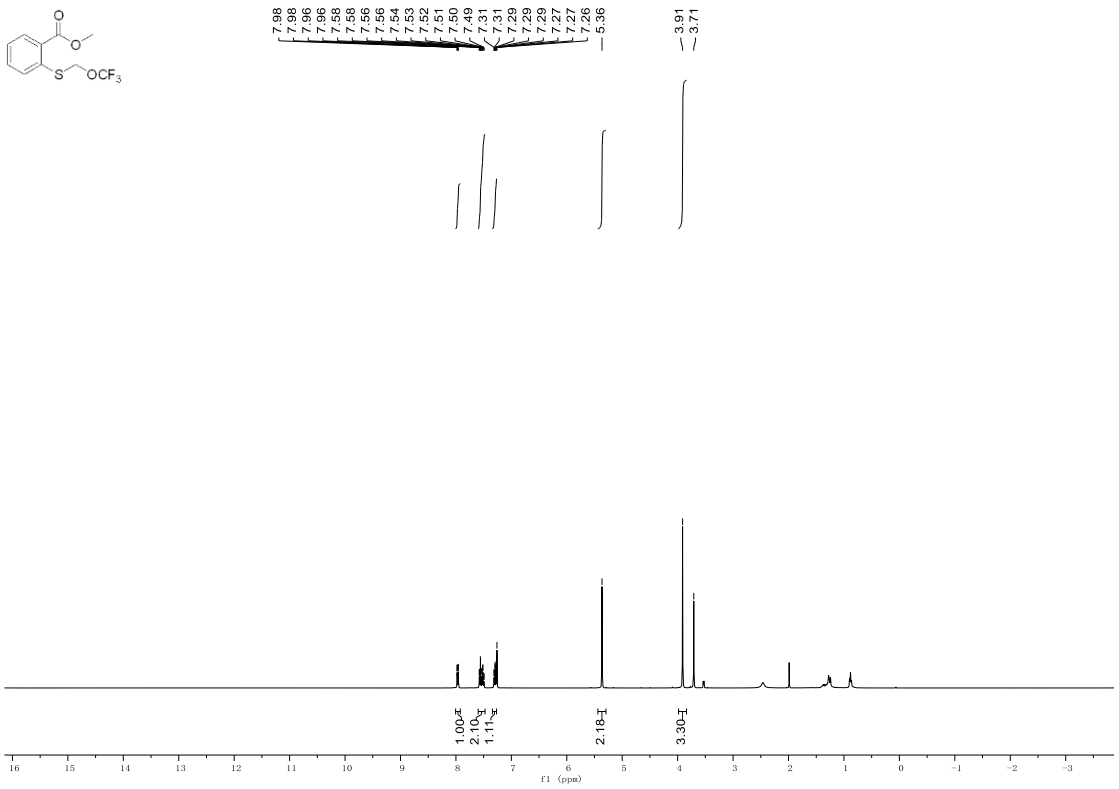
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3m**



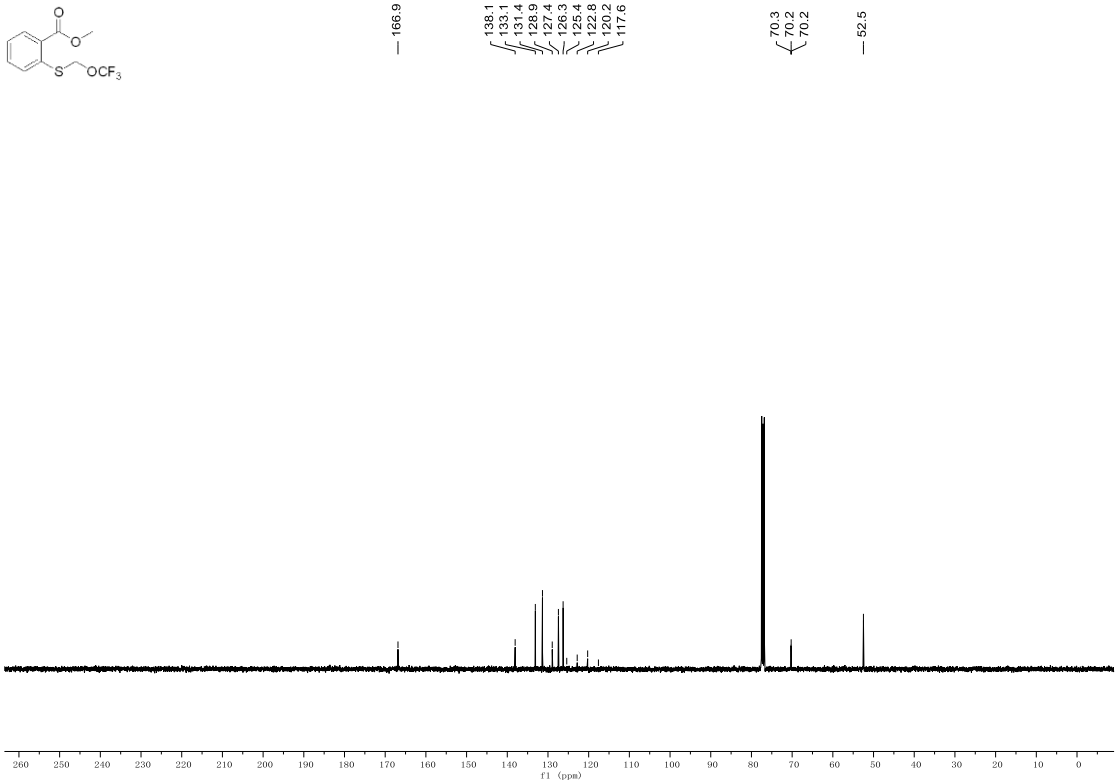
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **3m**



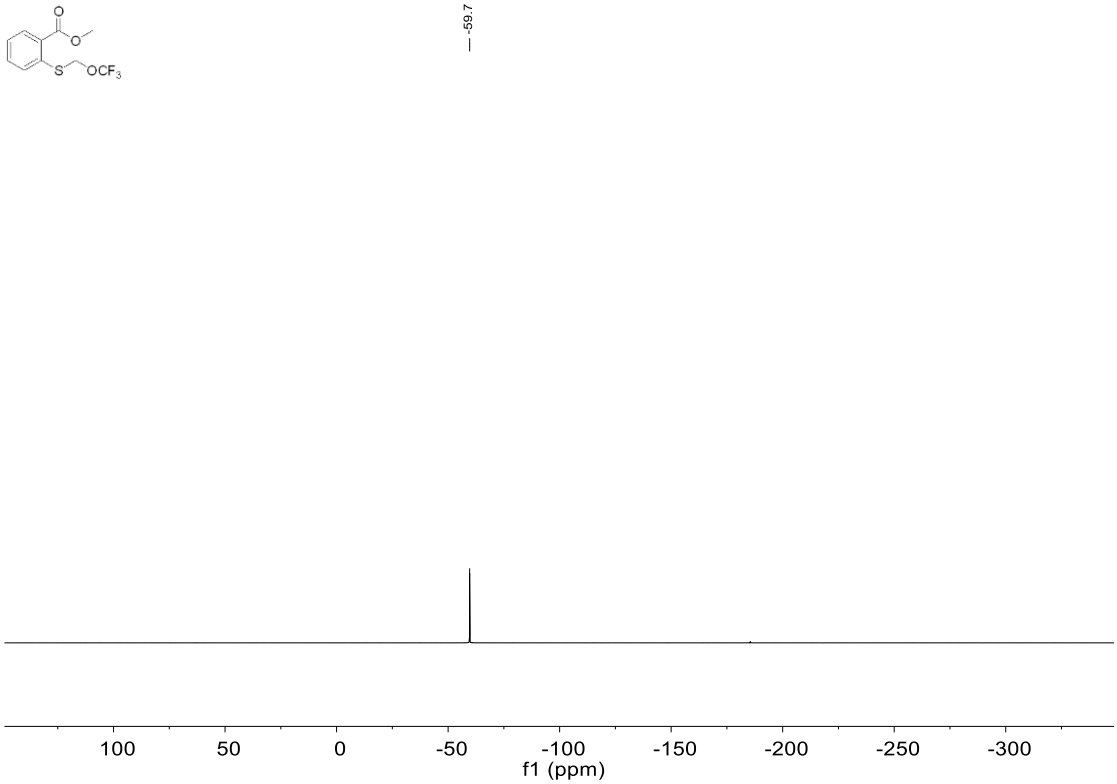
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3m**



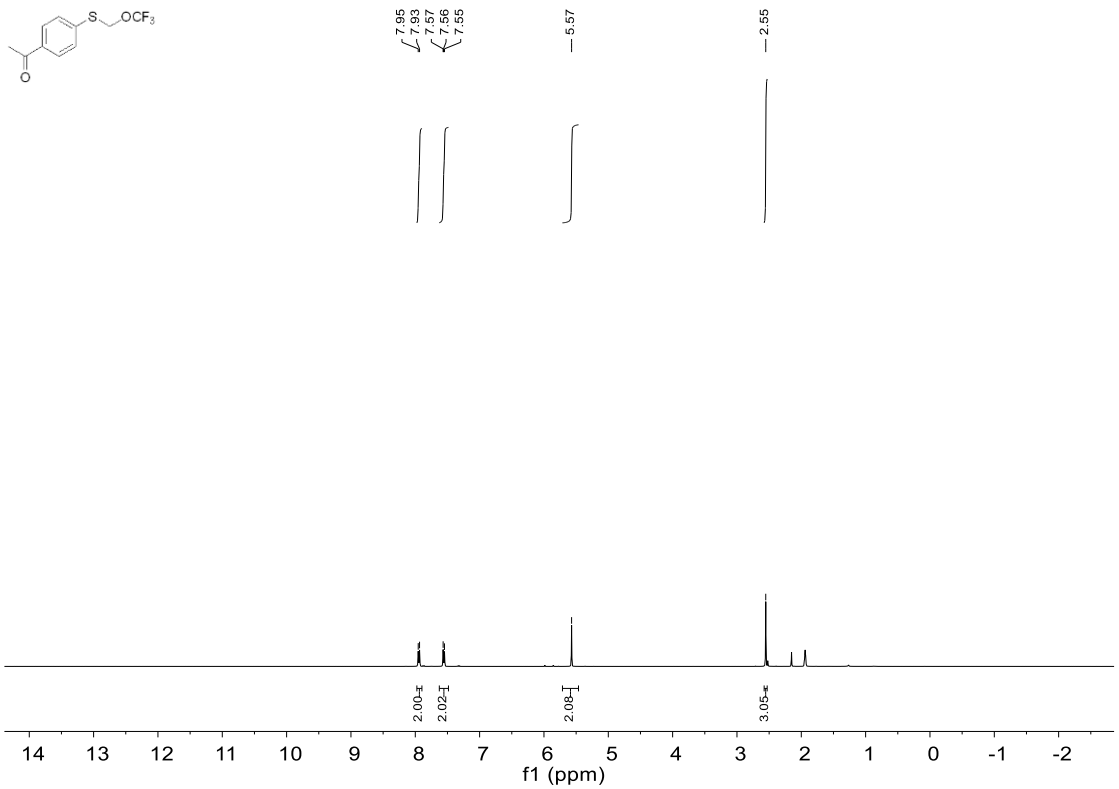
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3n**



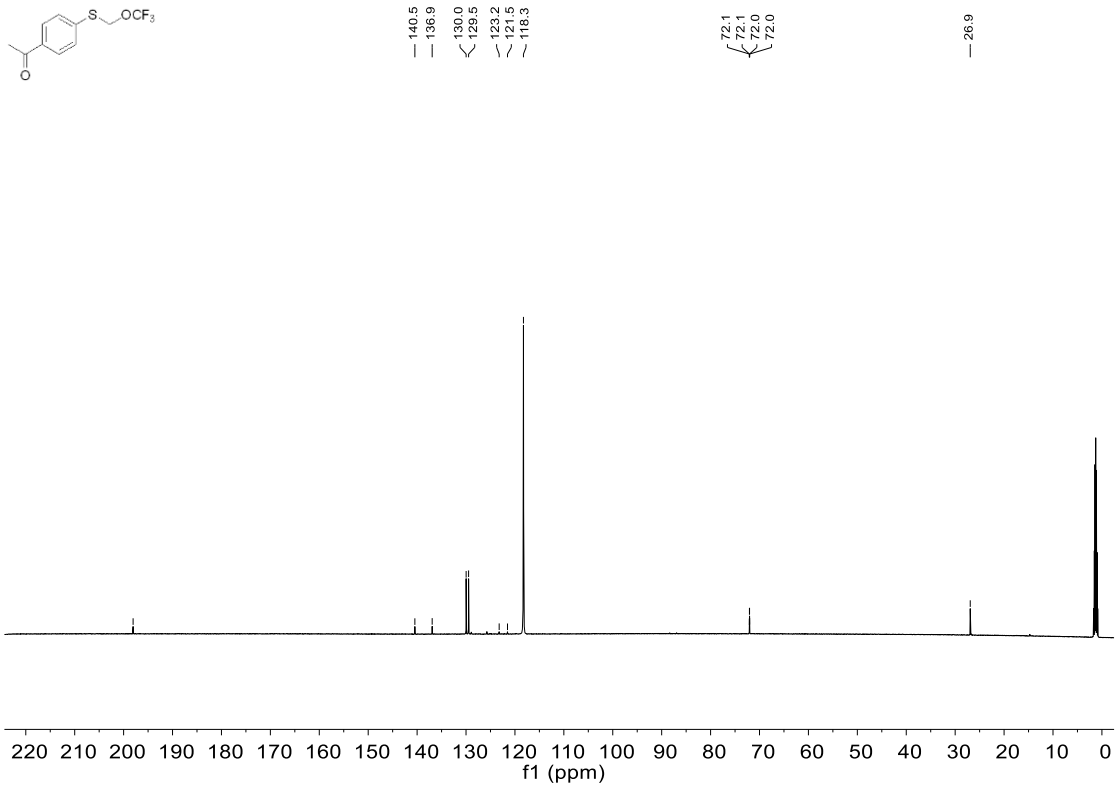
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **3n**



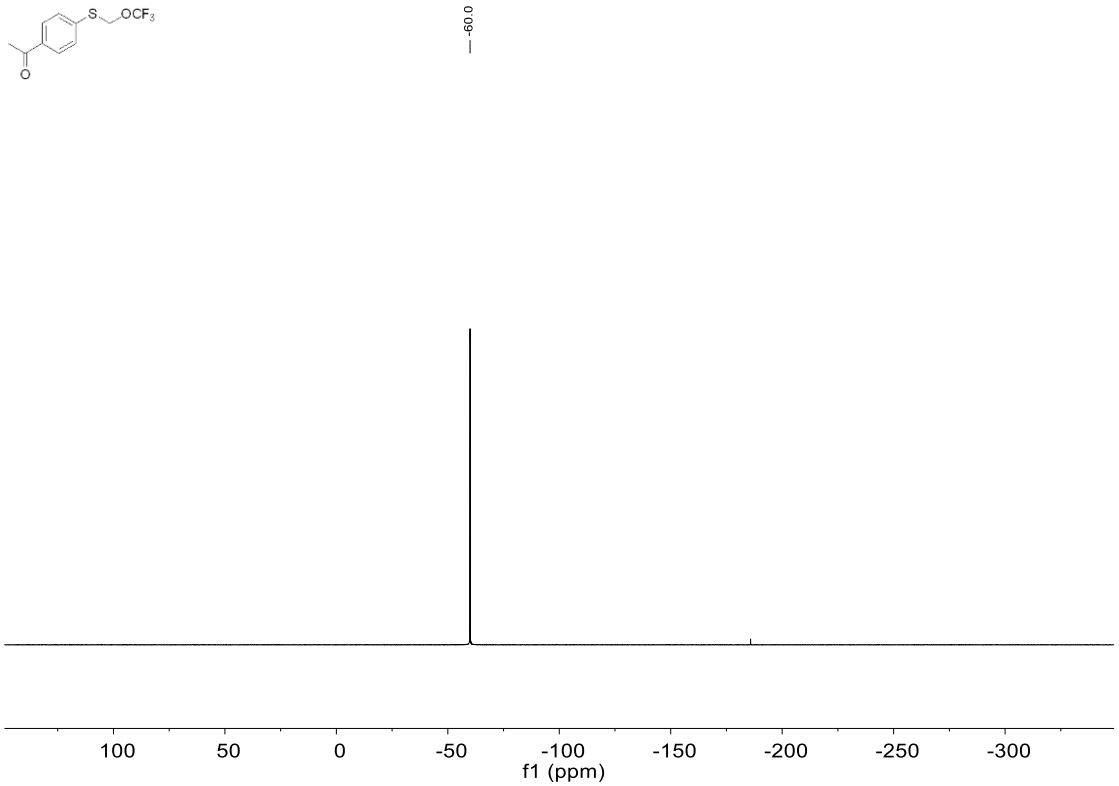
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3n**



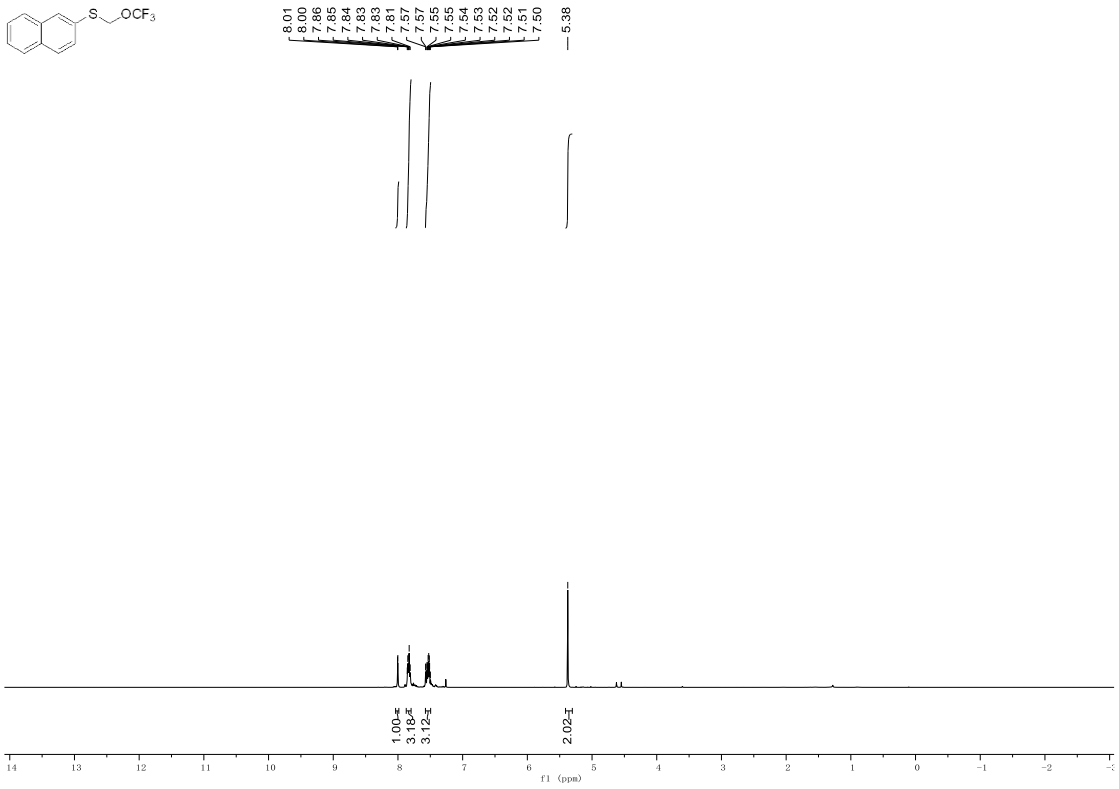
^{1}H NMR spectrum (600 MHz, CD_3CN) of **3o**



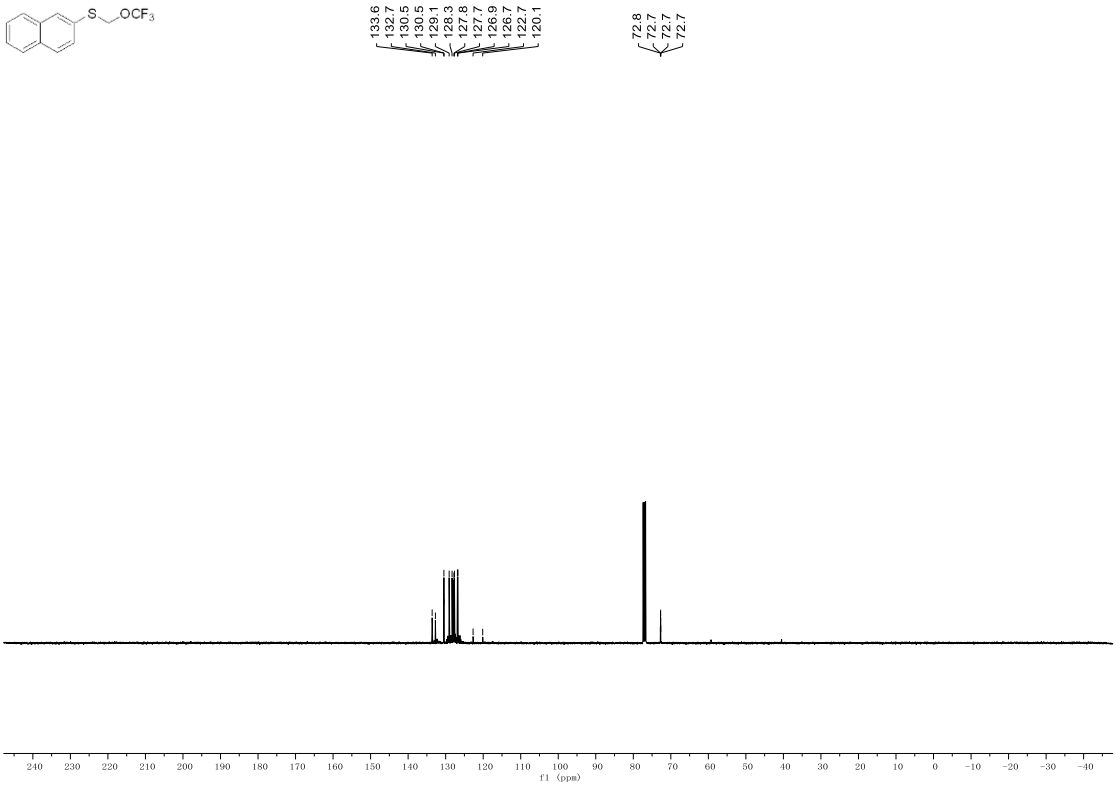
^{13}C NMR spectrum (151 MHz, CD_3CN) of **3o**



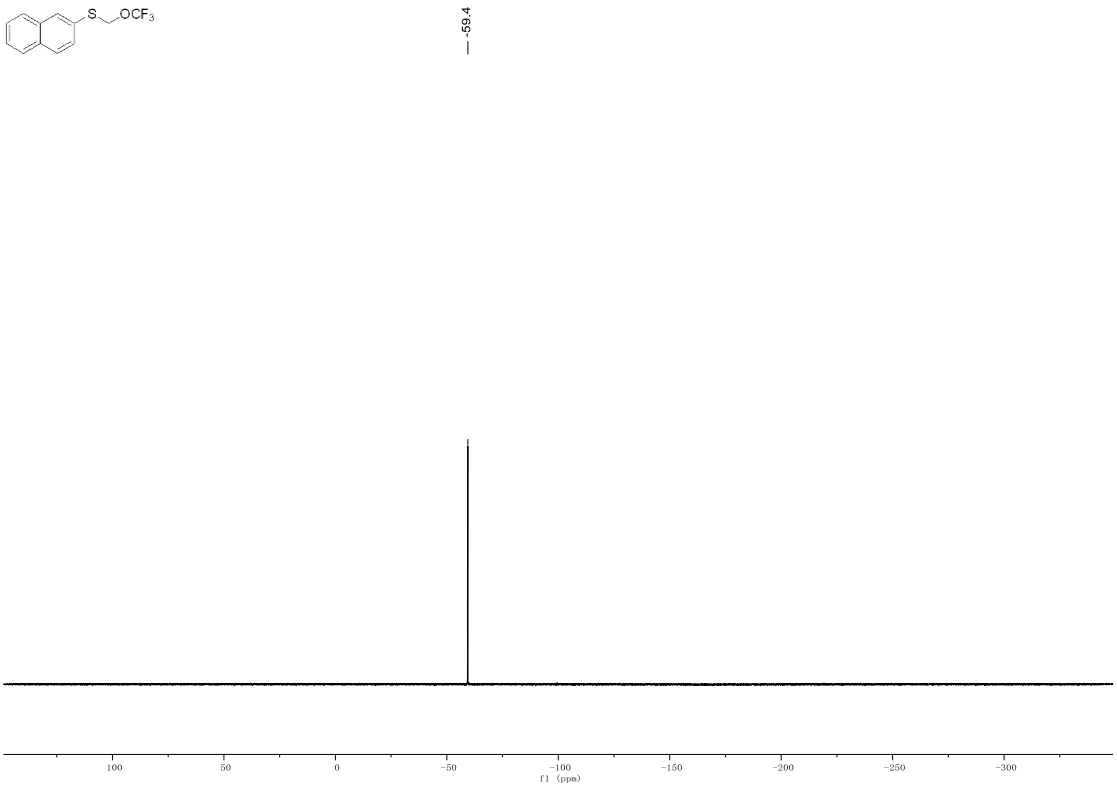
^{19}F NMR spectrum (376 MHz, CD_3CN) of **3o**



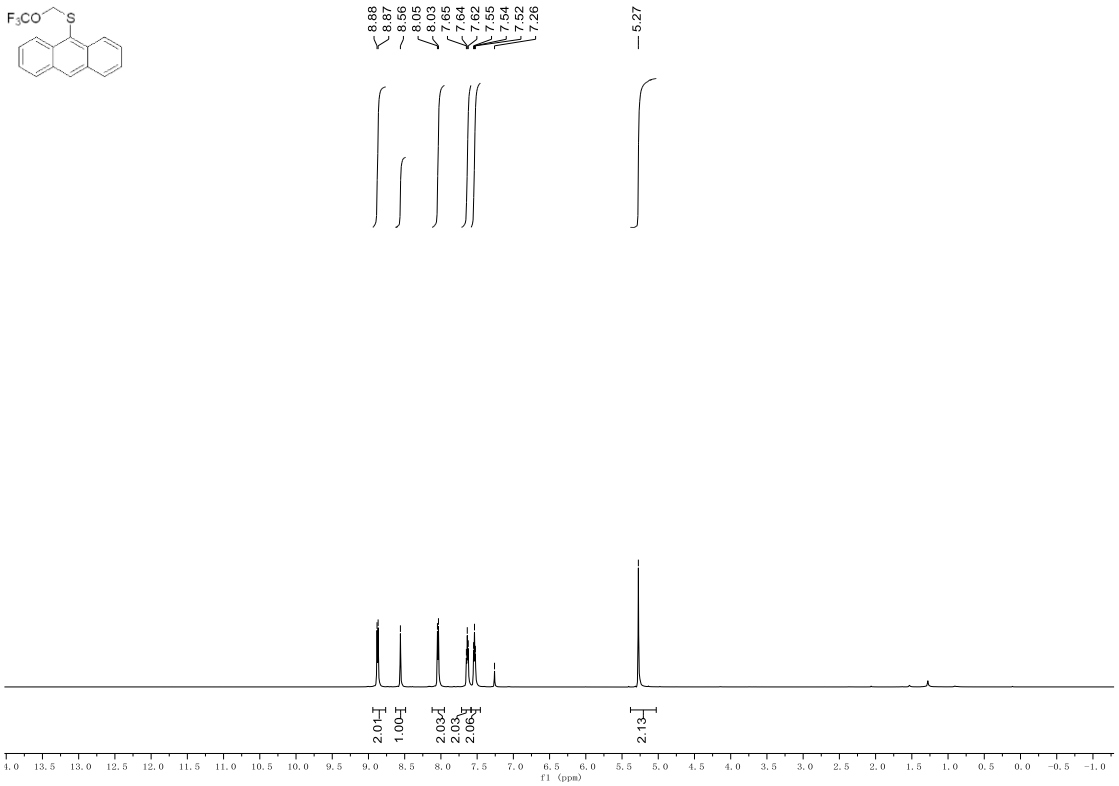
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3p**



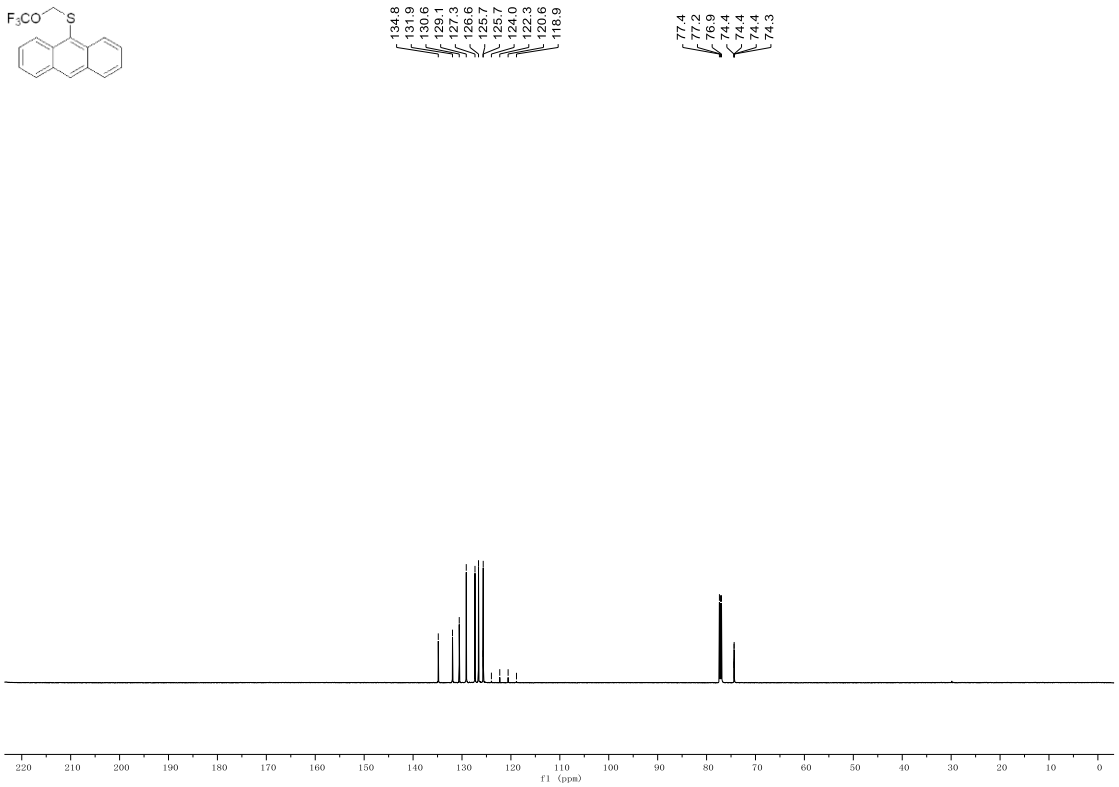
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **3p**



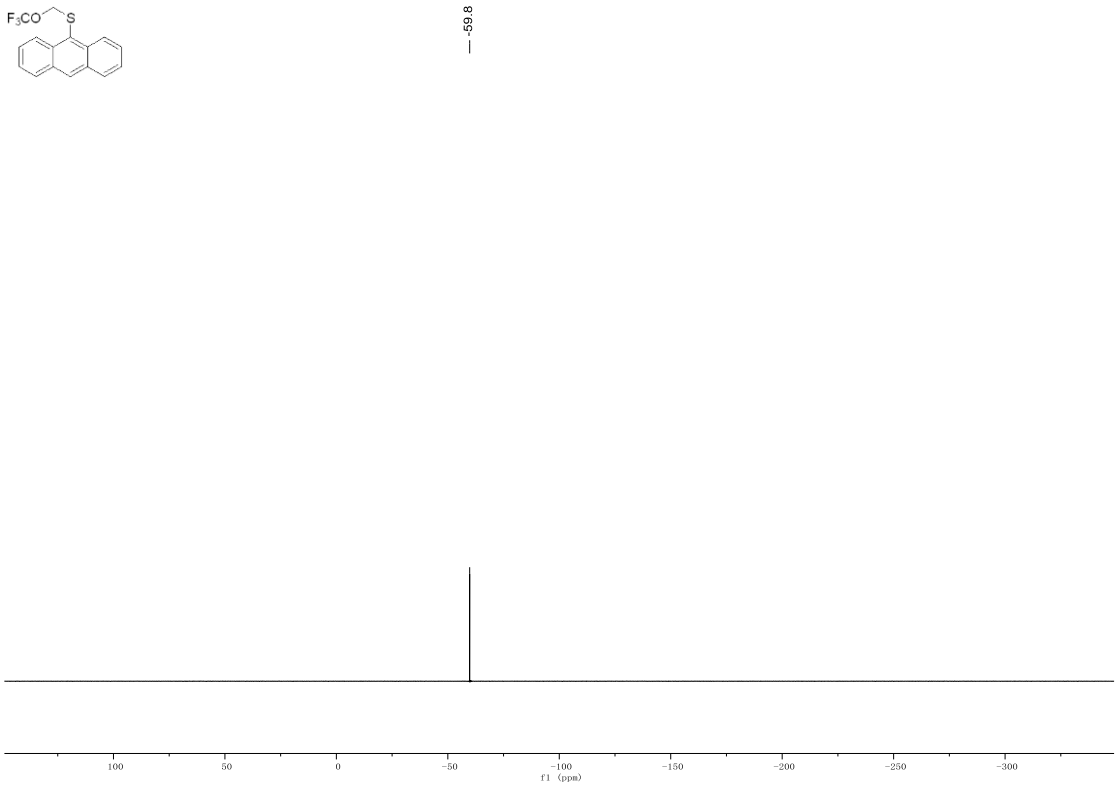
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3p**



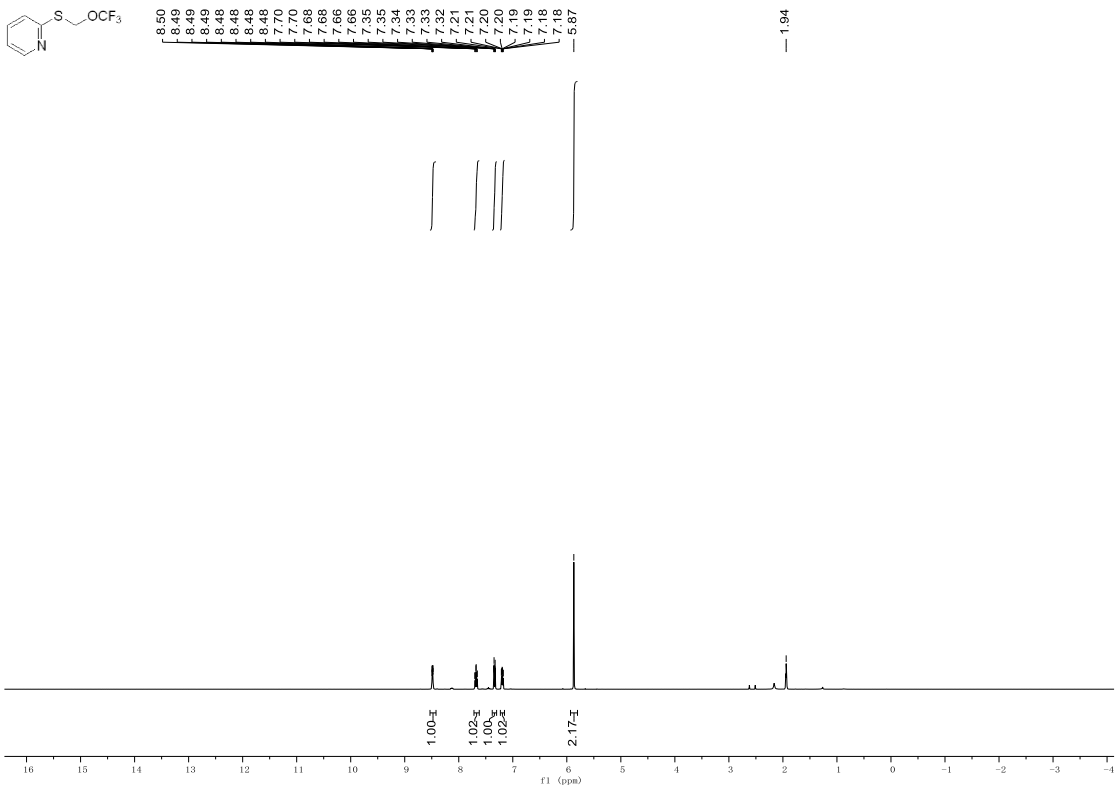
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3q**



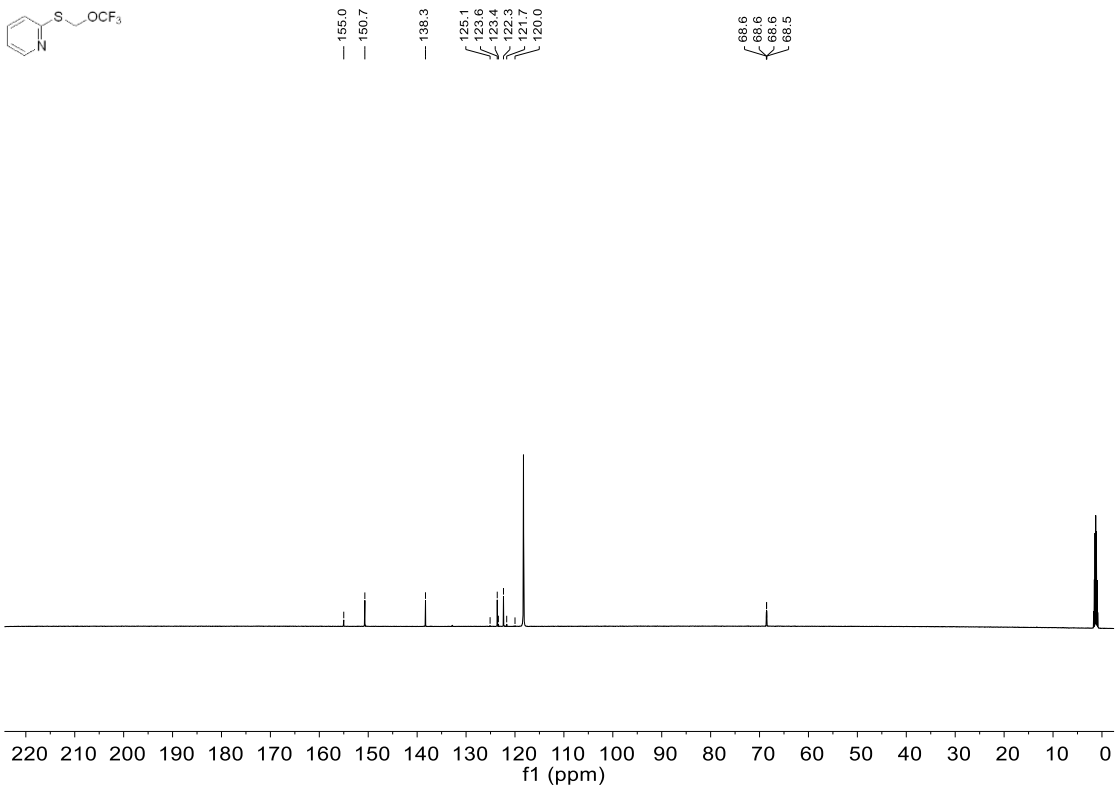
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **3q**



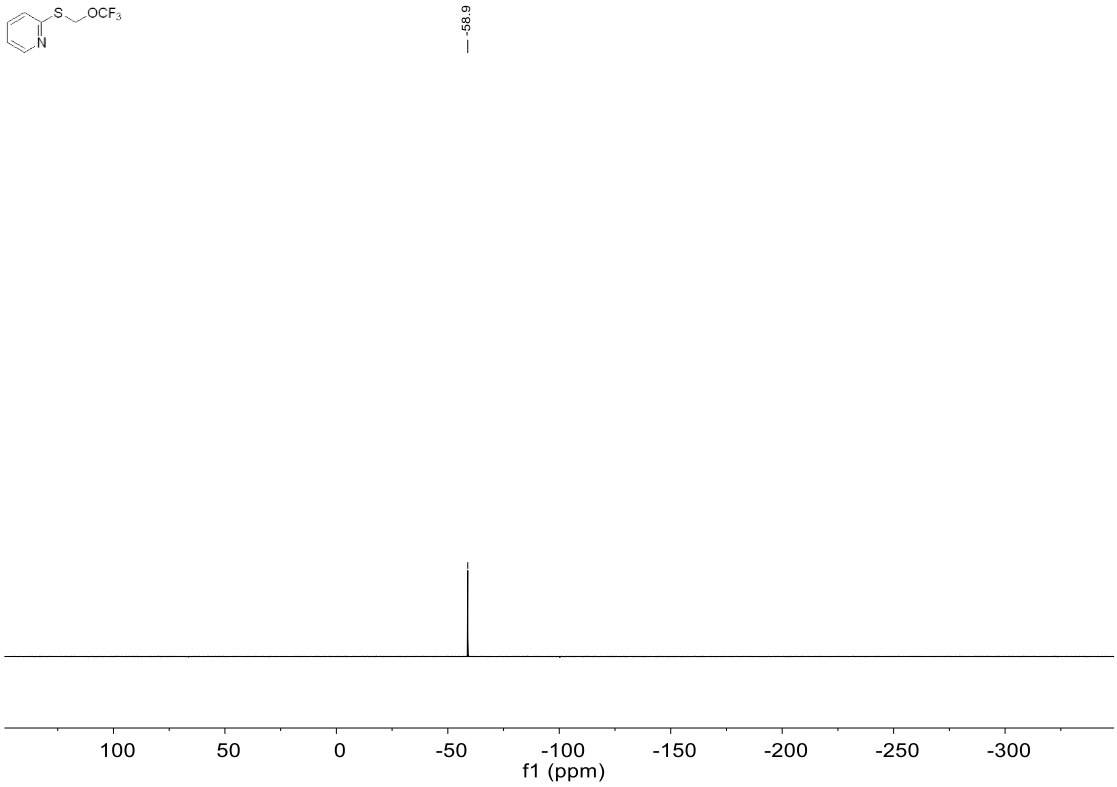
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3q**



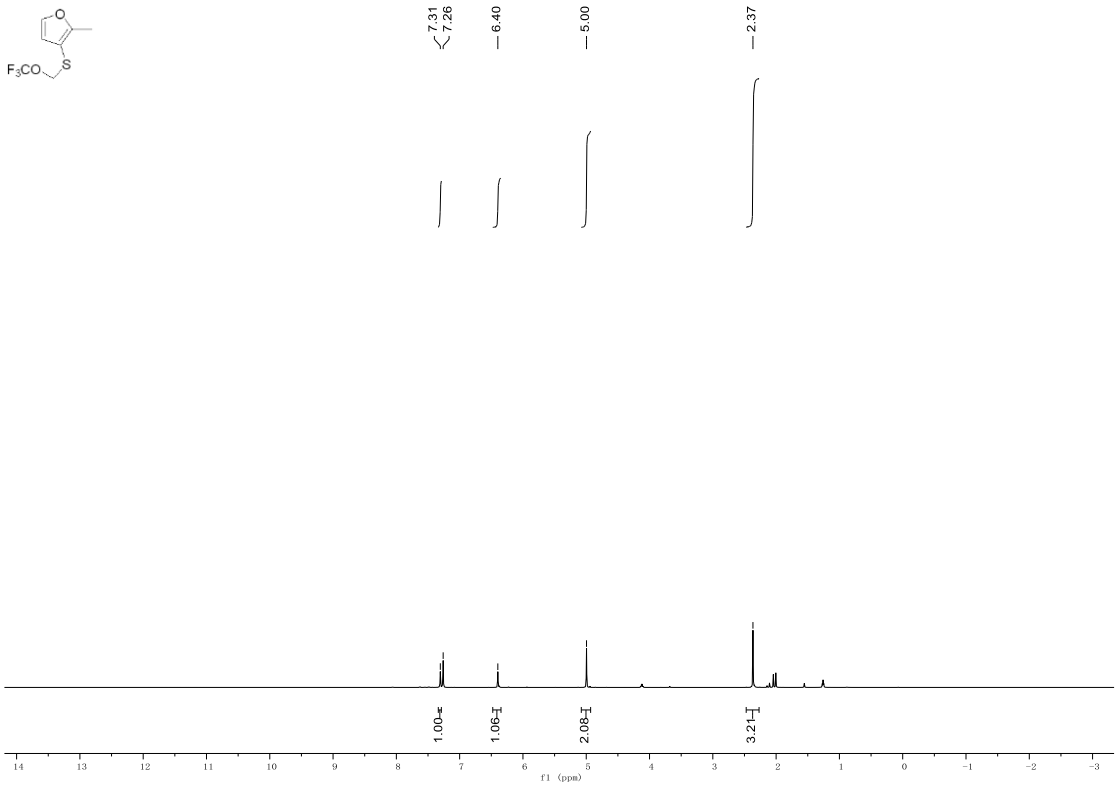
^{1}H NMR spectrum (400 MHz, CD_3CN) of **3r**



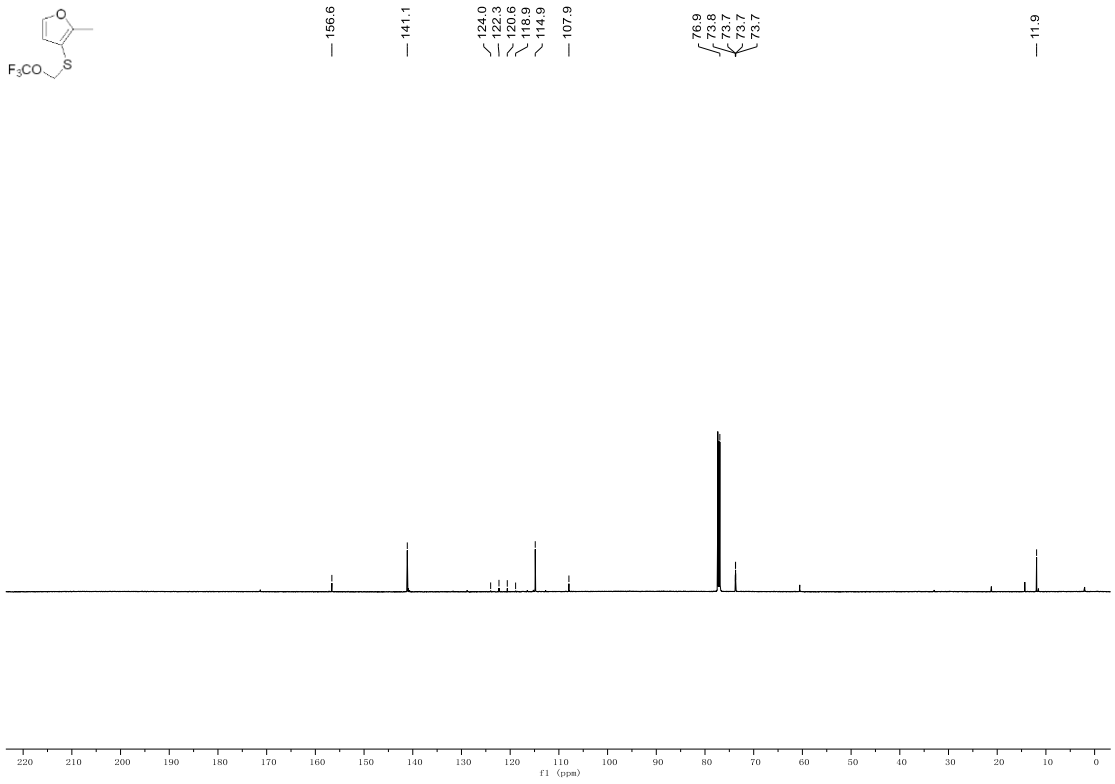
^{13}C NMR spectrum (151 MHz, CD_3CN) of **3r**



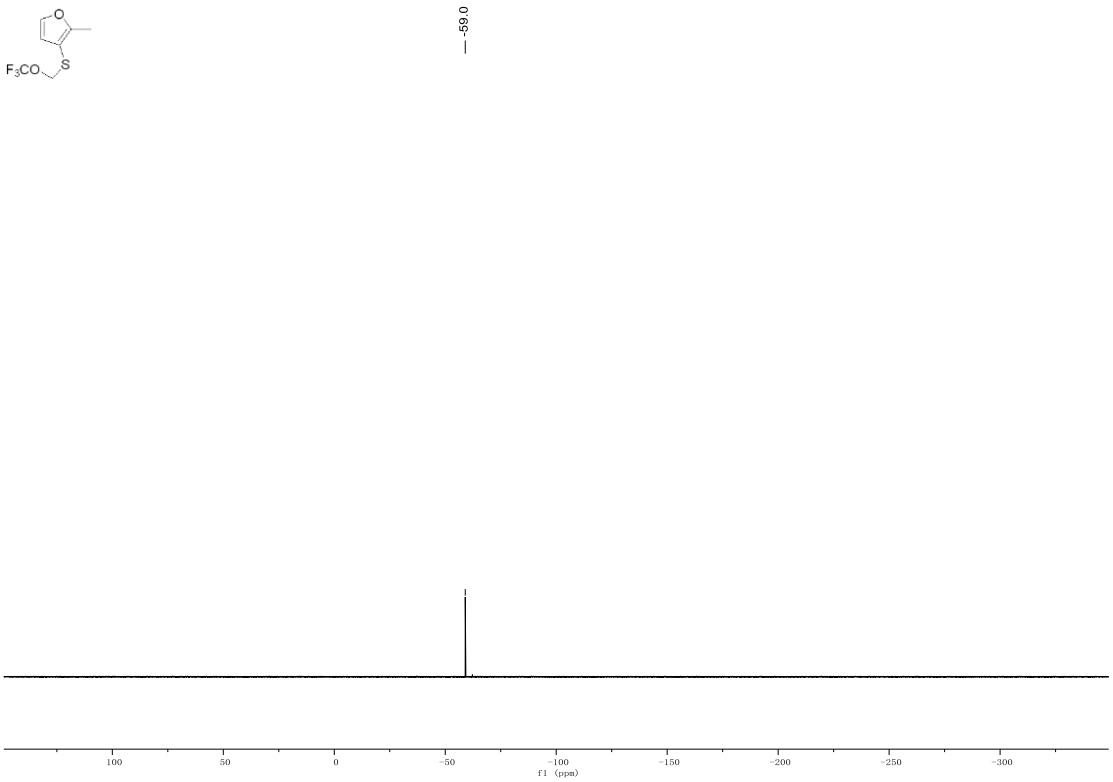
^{19}F NMR spectrum (376 MHz, CD_3CN) of **3r**



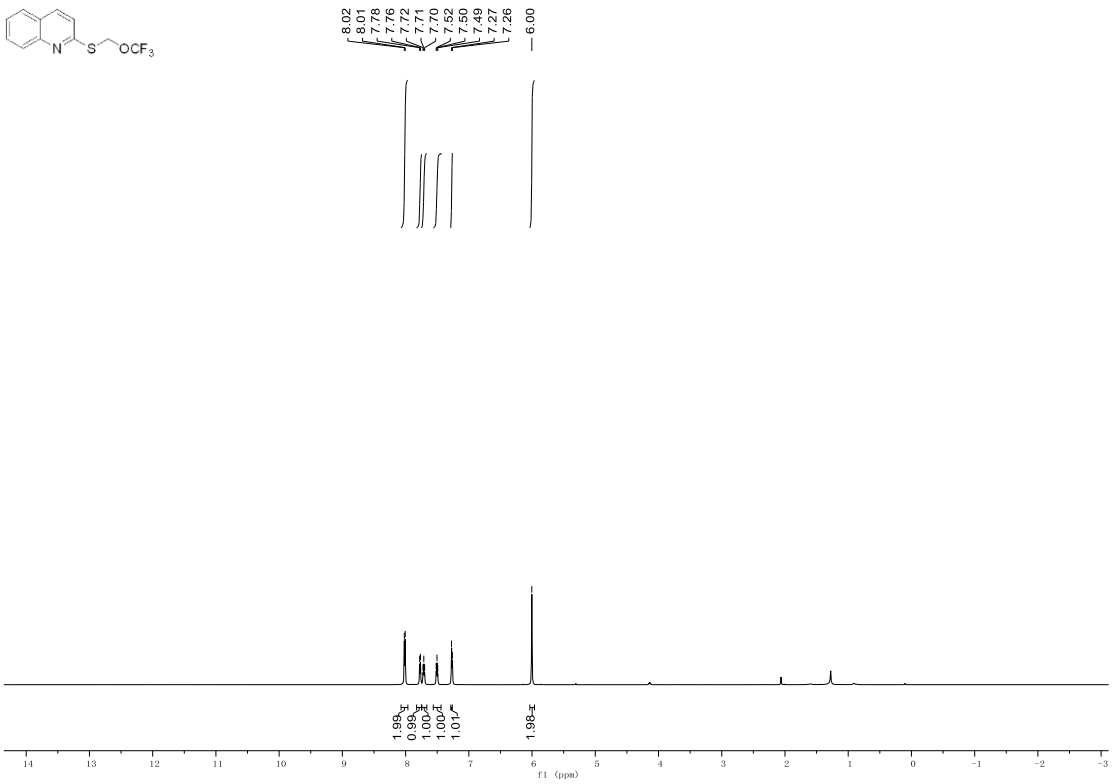
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of **3t**



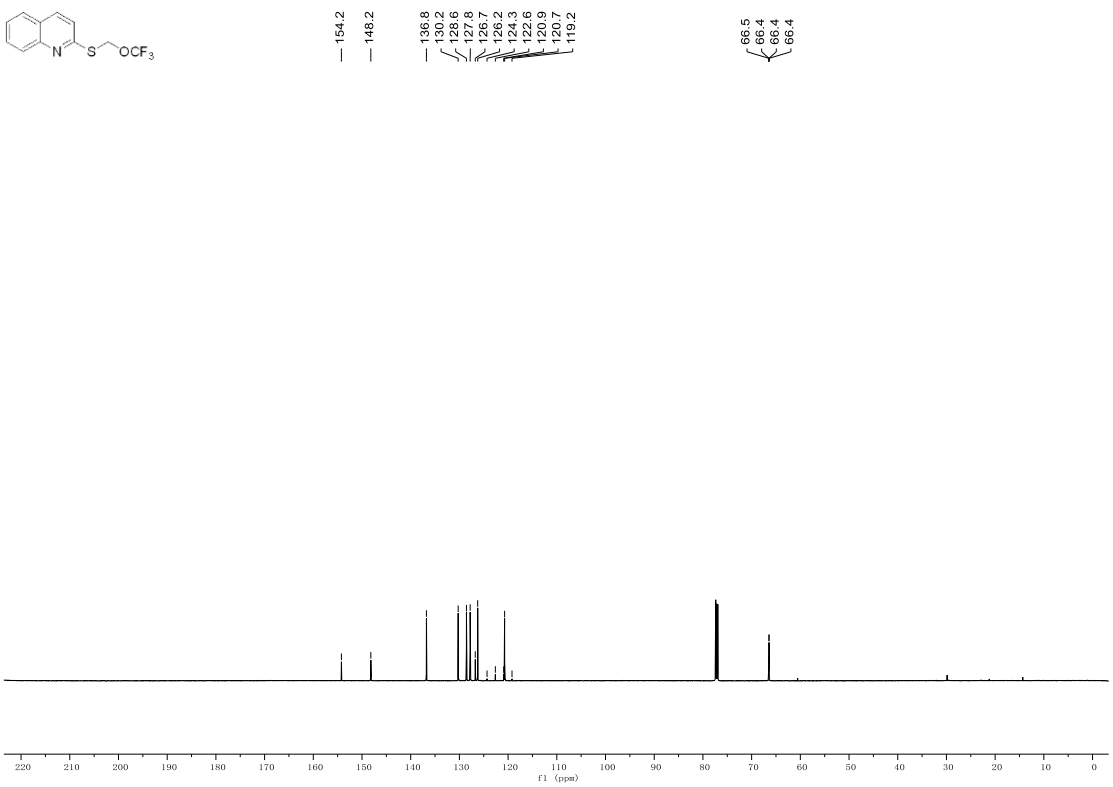
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of **3t**



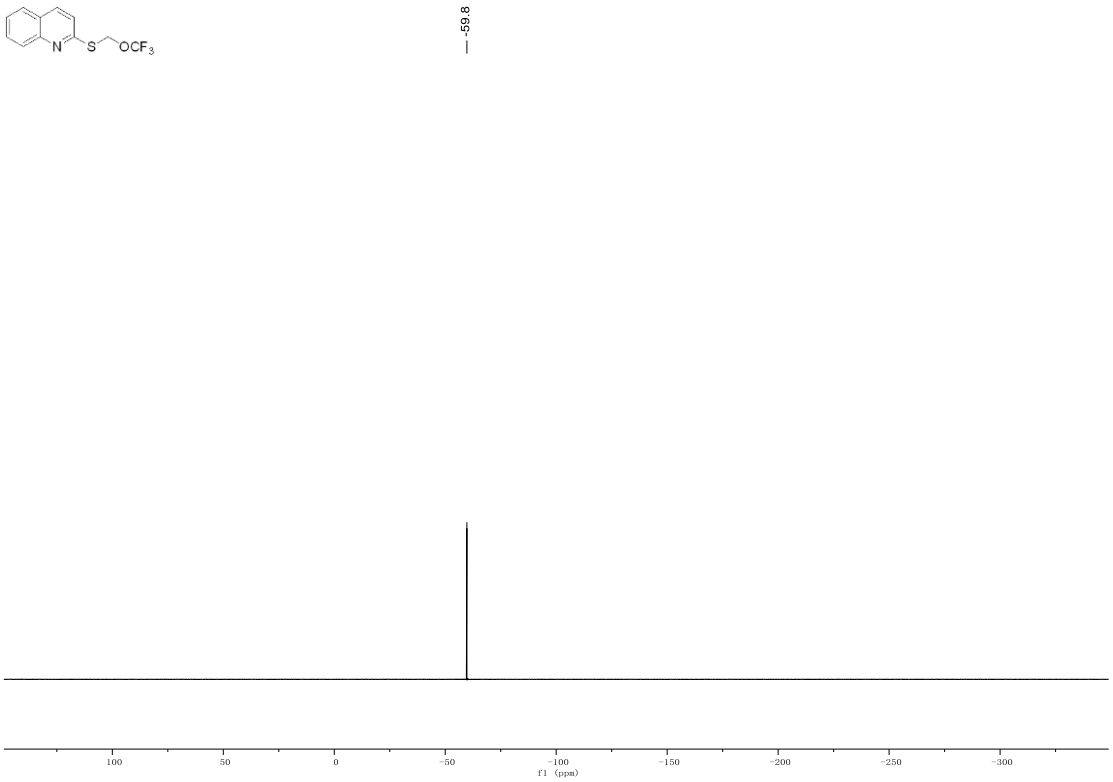
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3t**



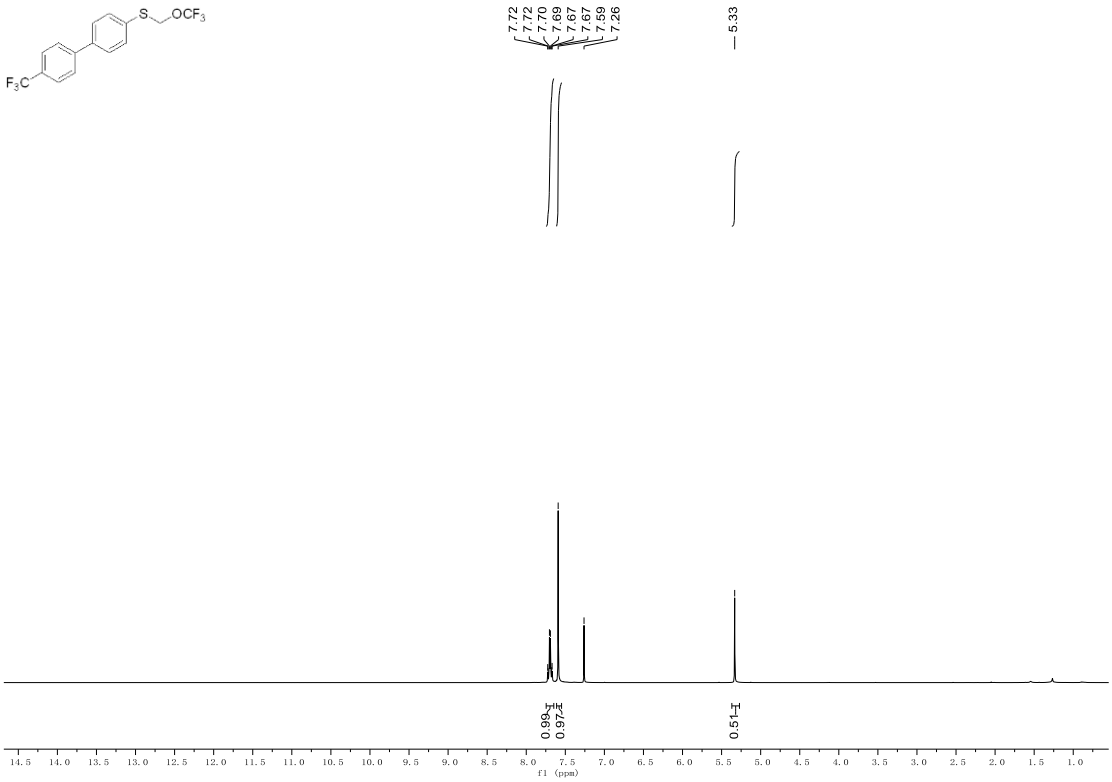
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of **3u**



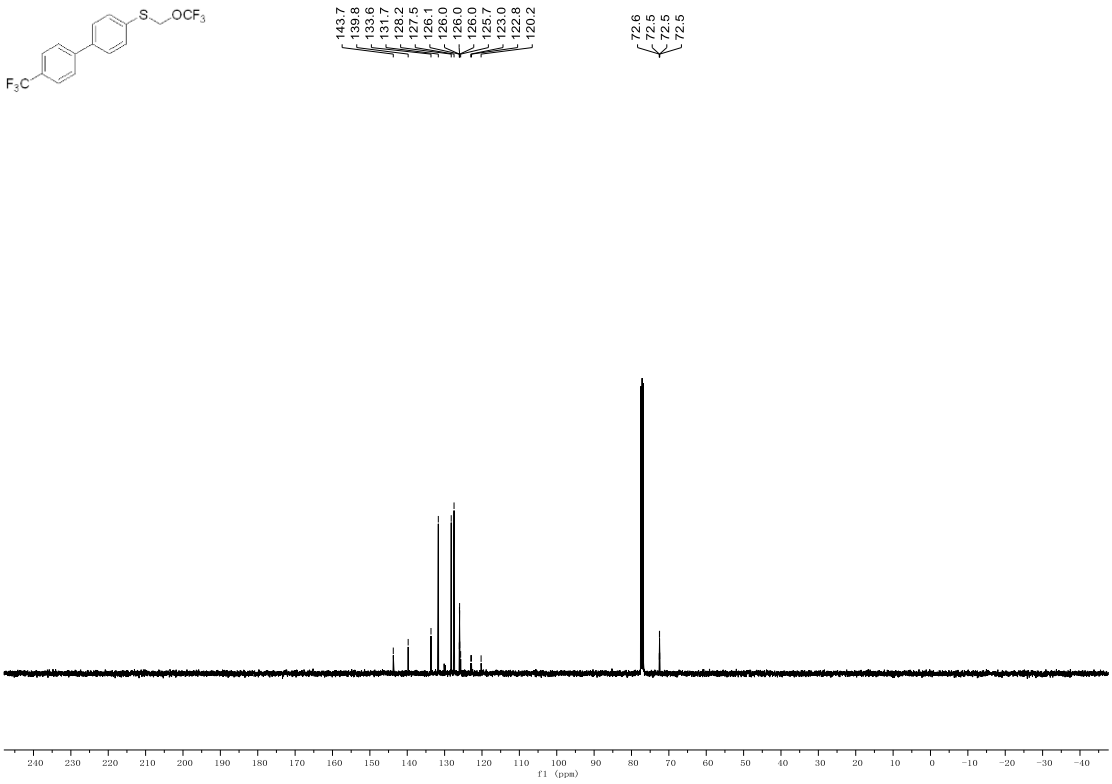
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of **3u**



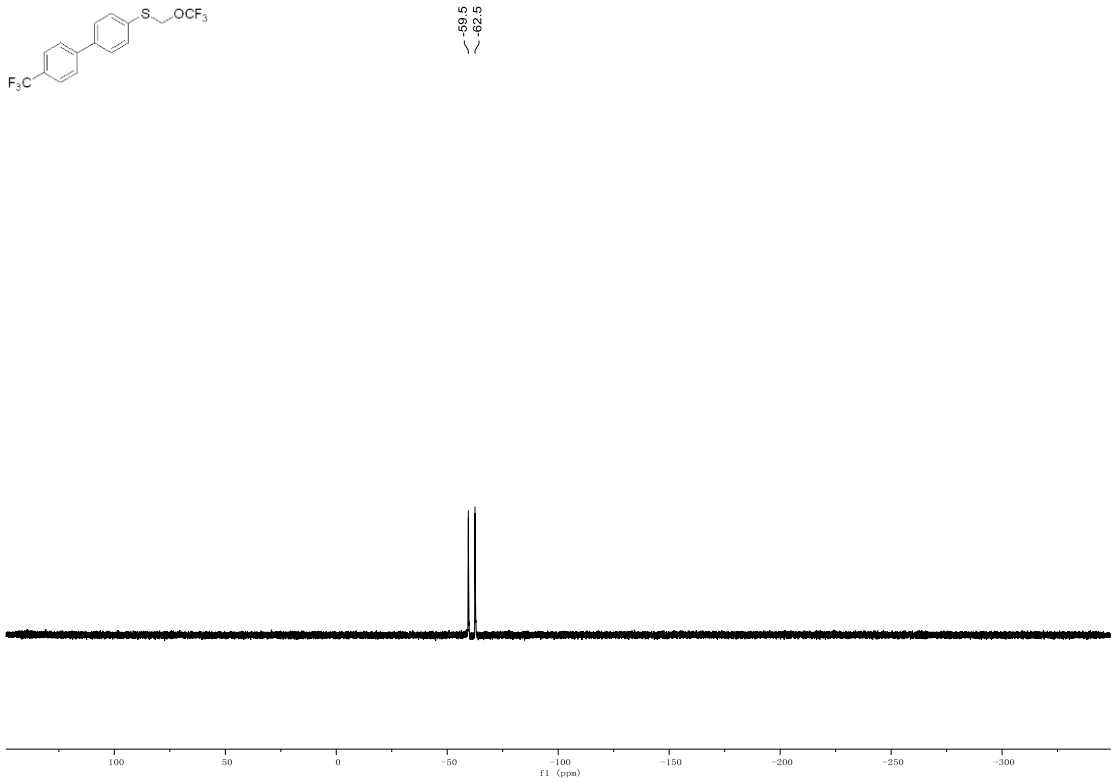
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3u**



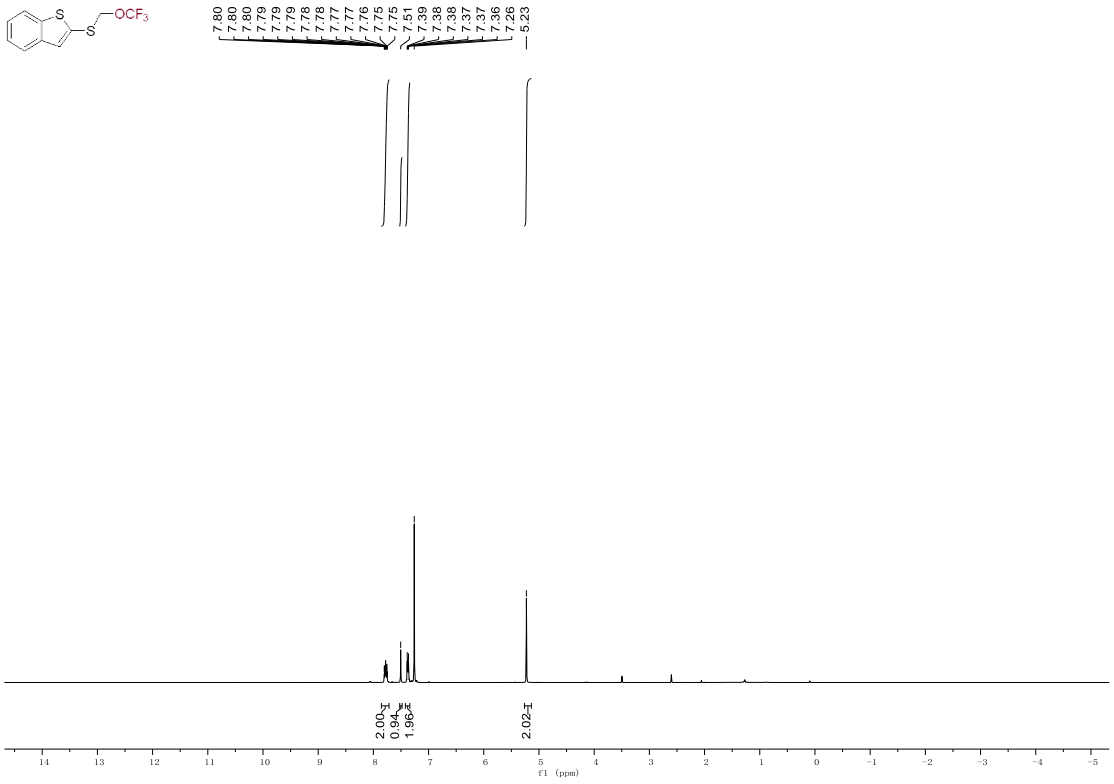
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3v**



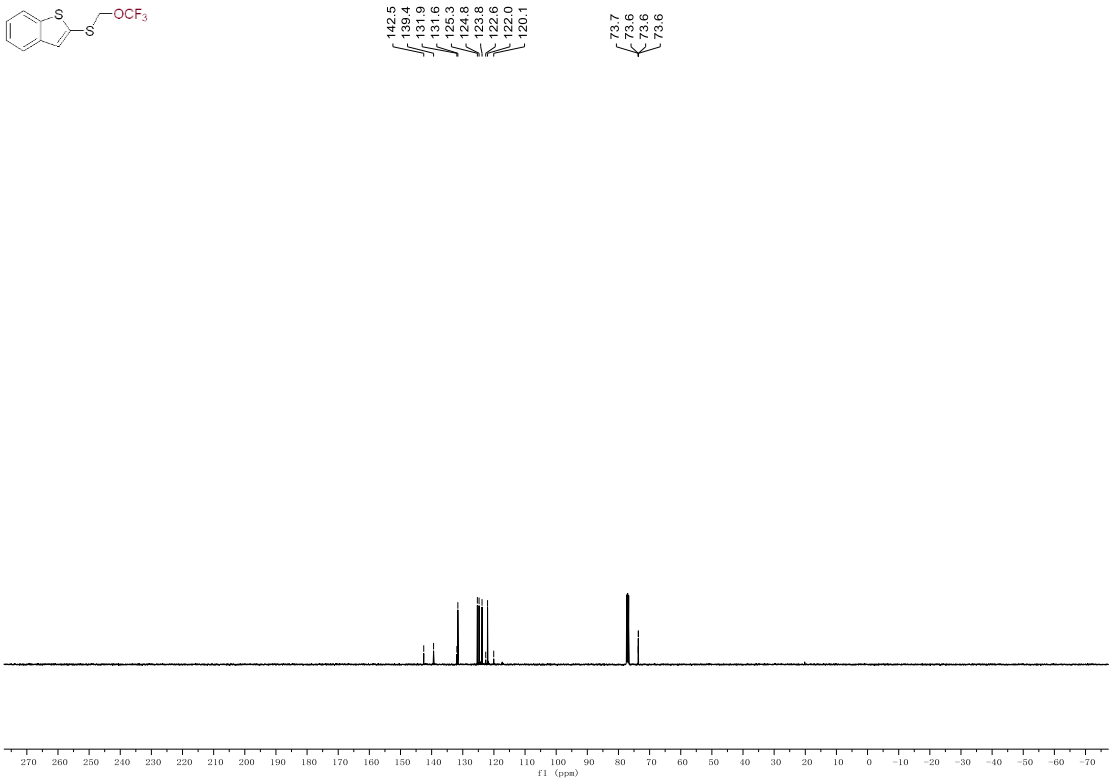
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **3v**



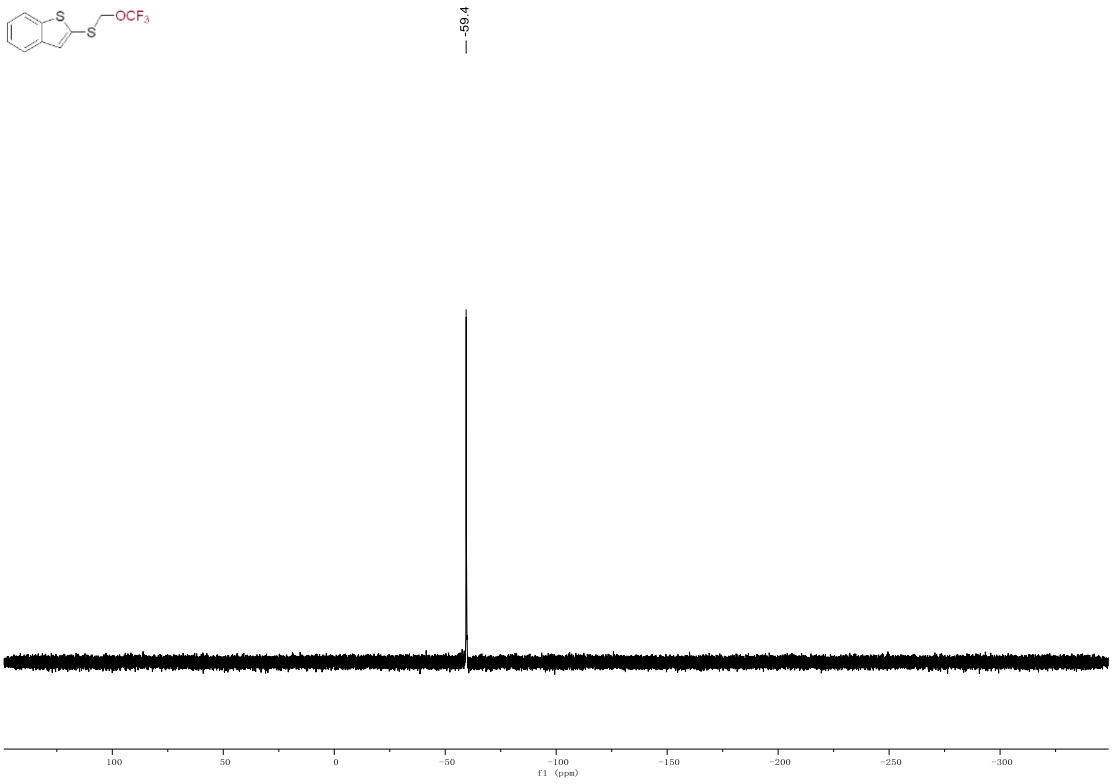
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3v**



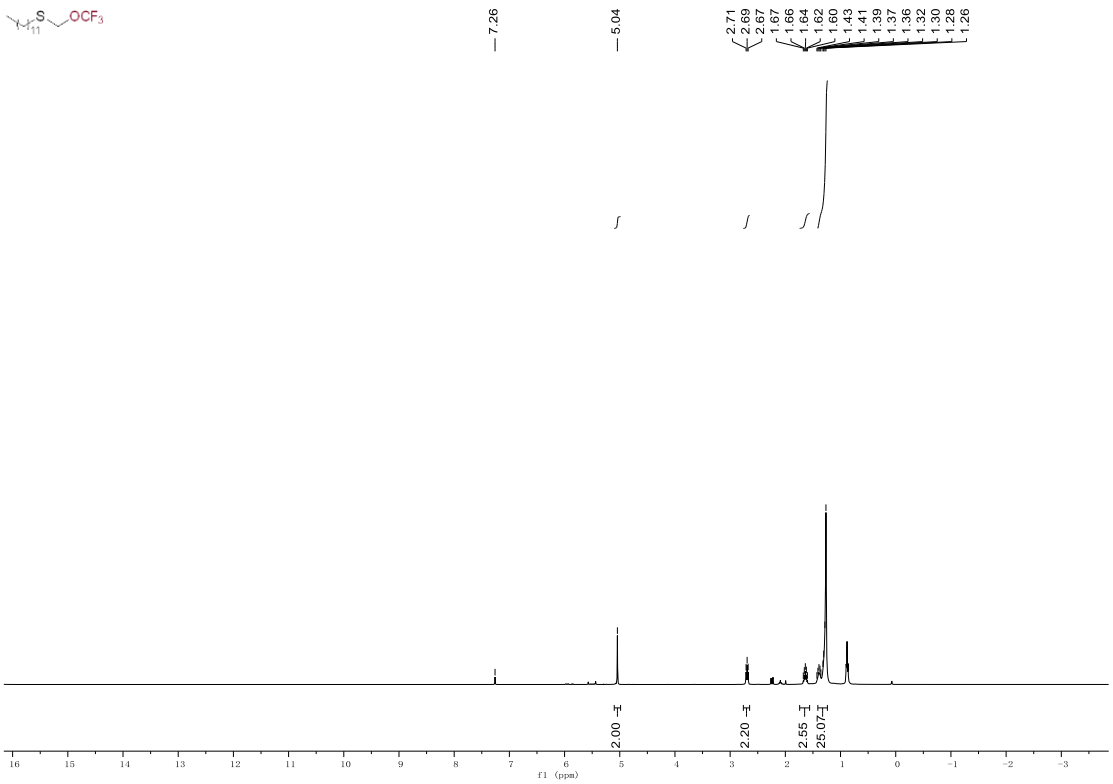
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3w**



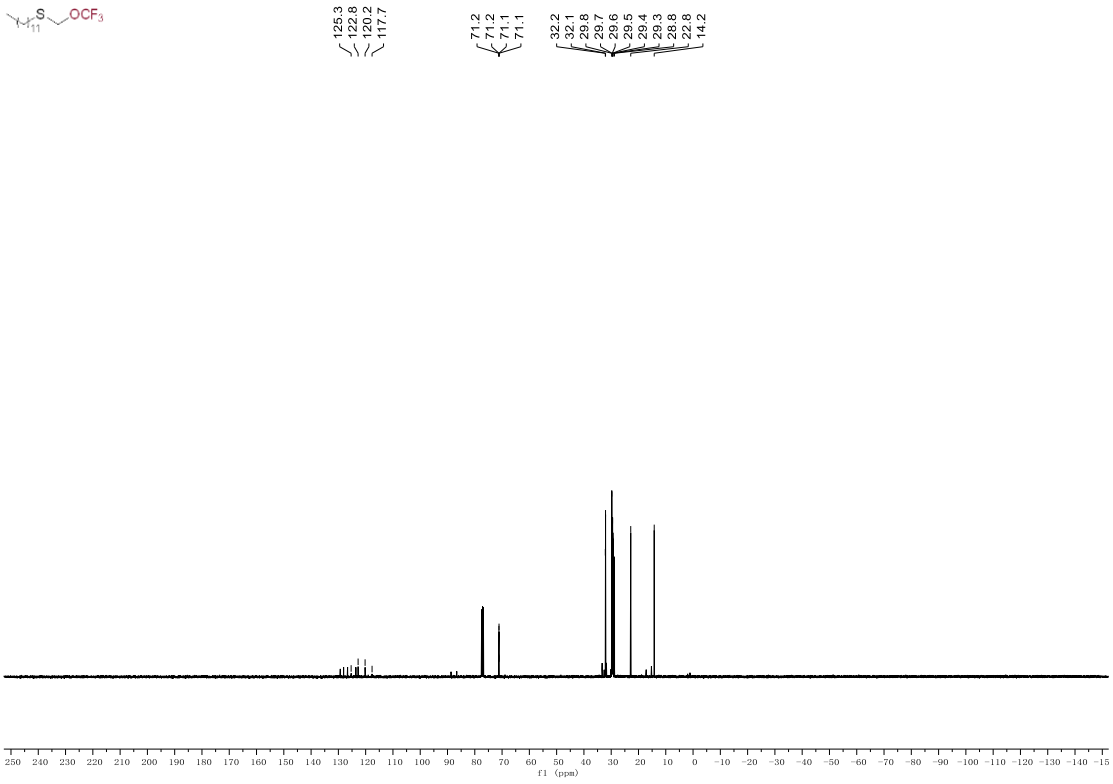
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **3w**



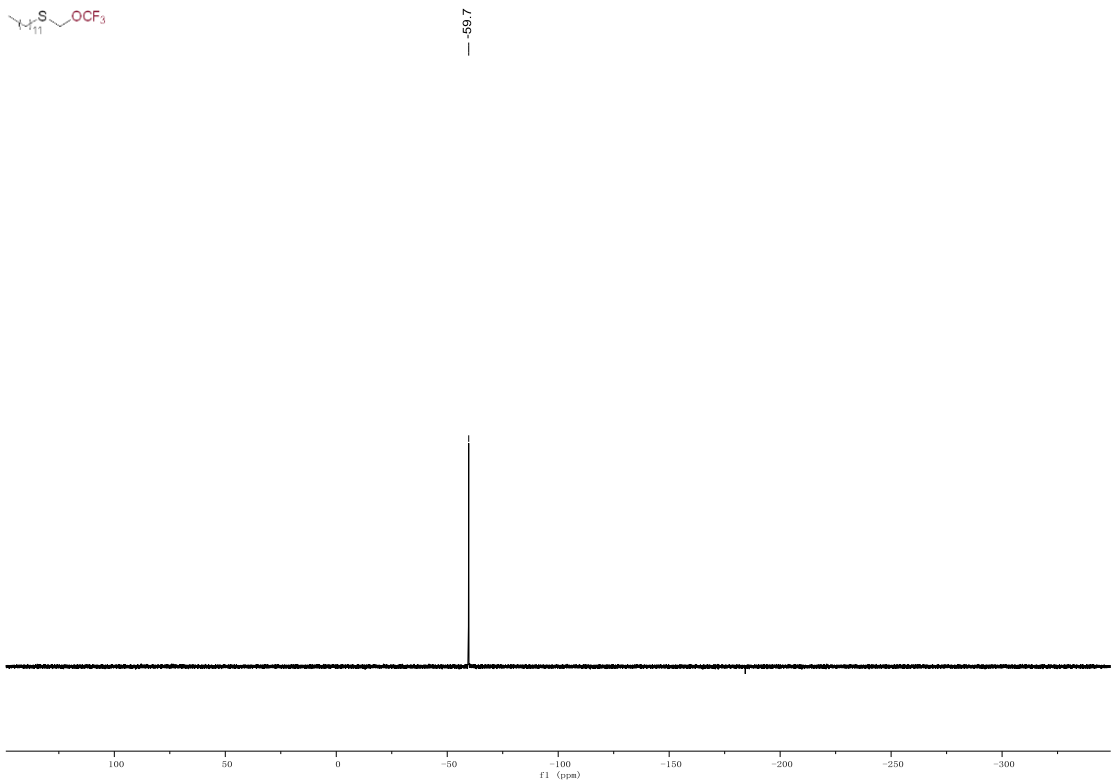
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3w**



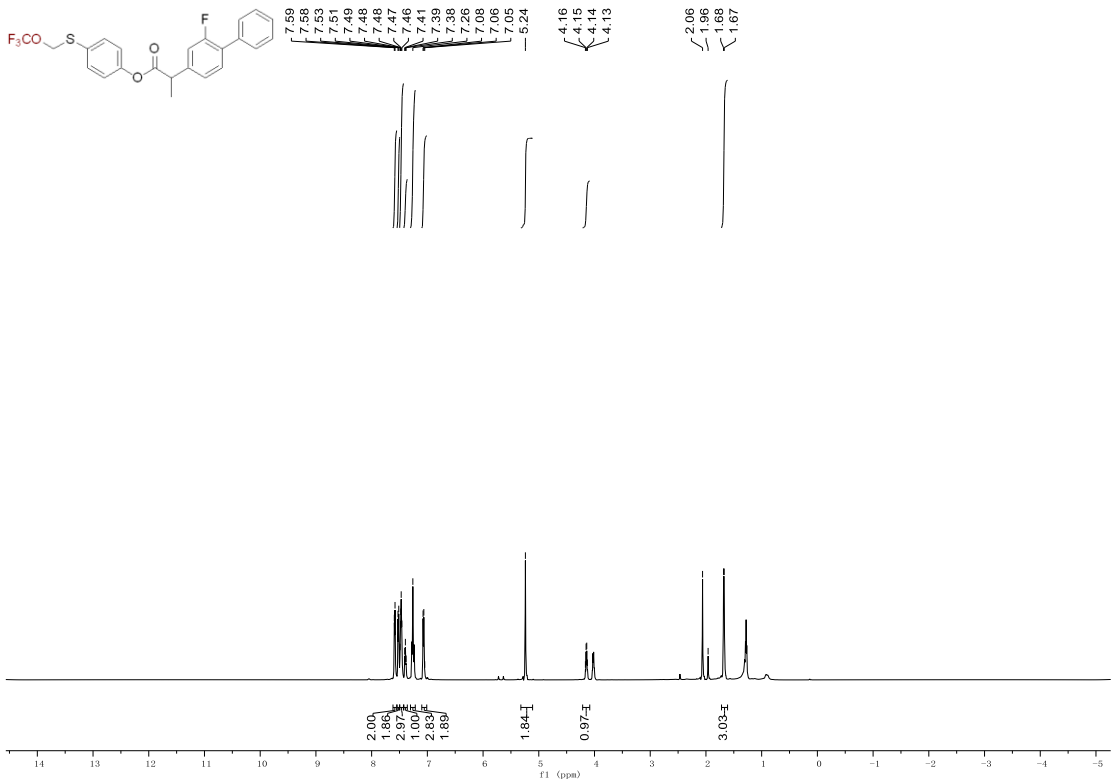
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **3y**



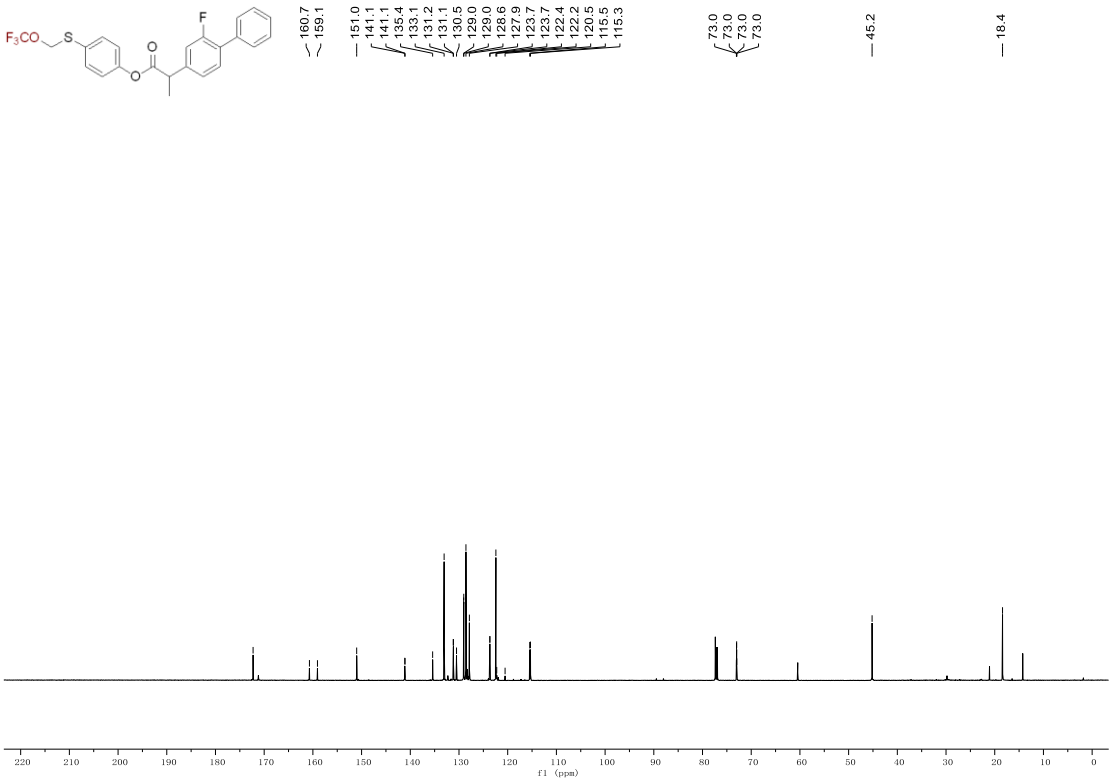
^{13}C NMR spectrum (101 MHz, $CDCl_3$) of **3y**



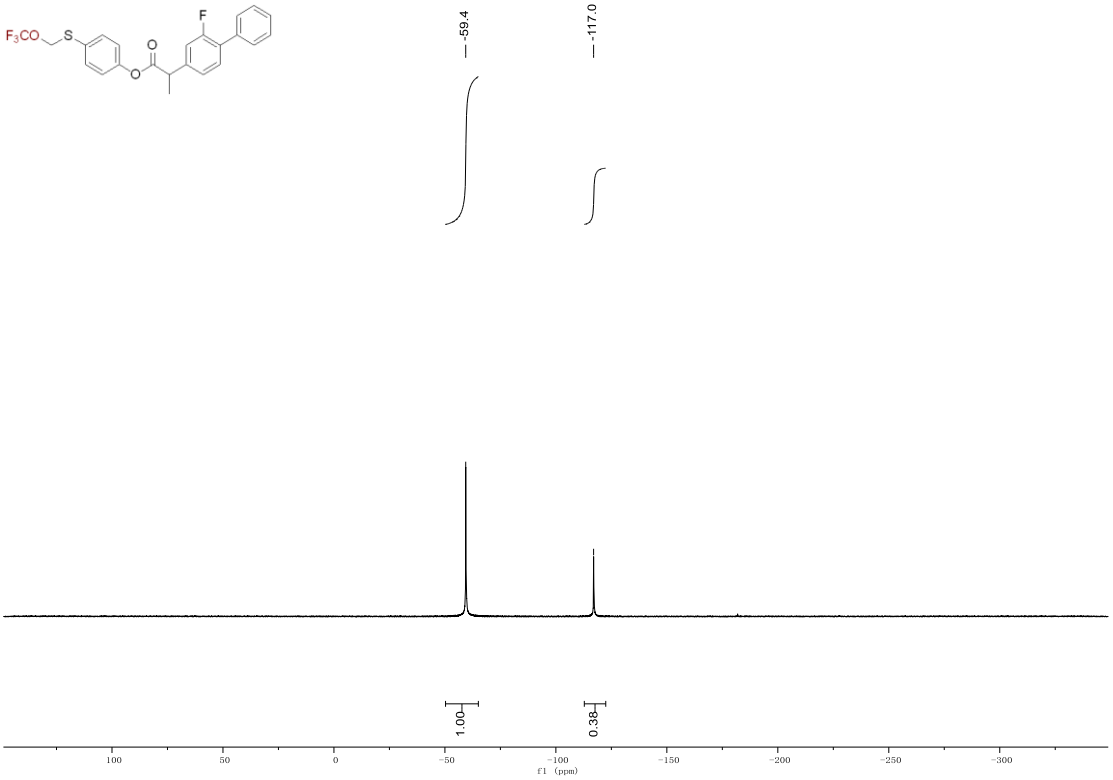
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3y**



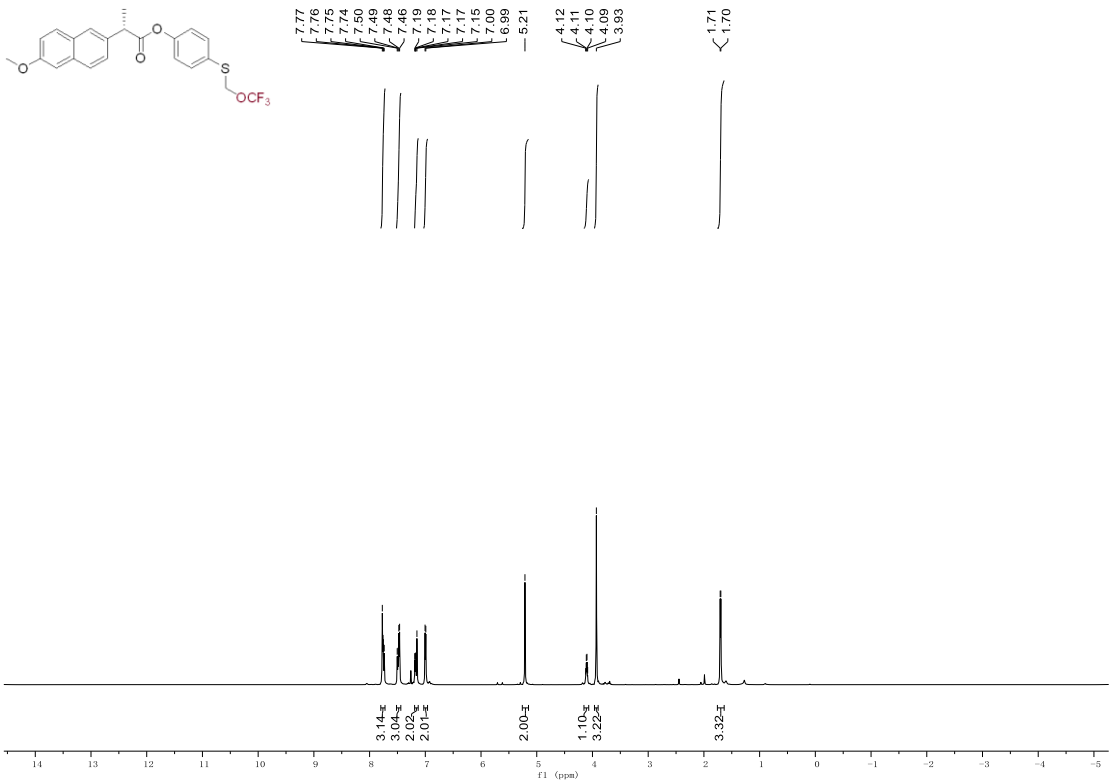
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of **3z**



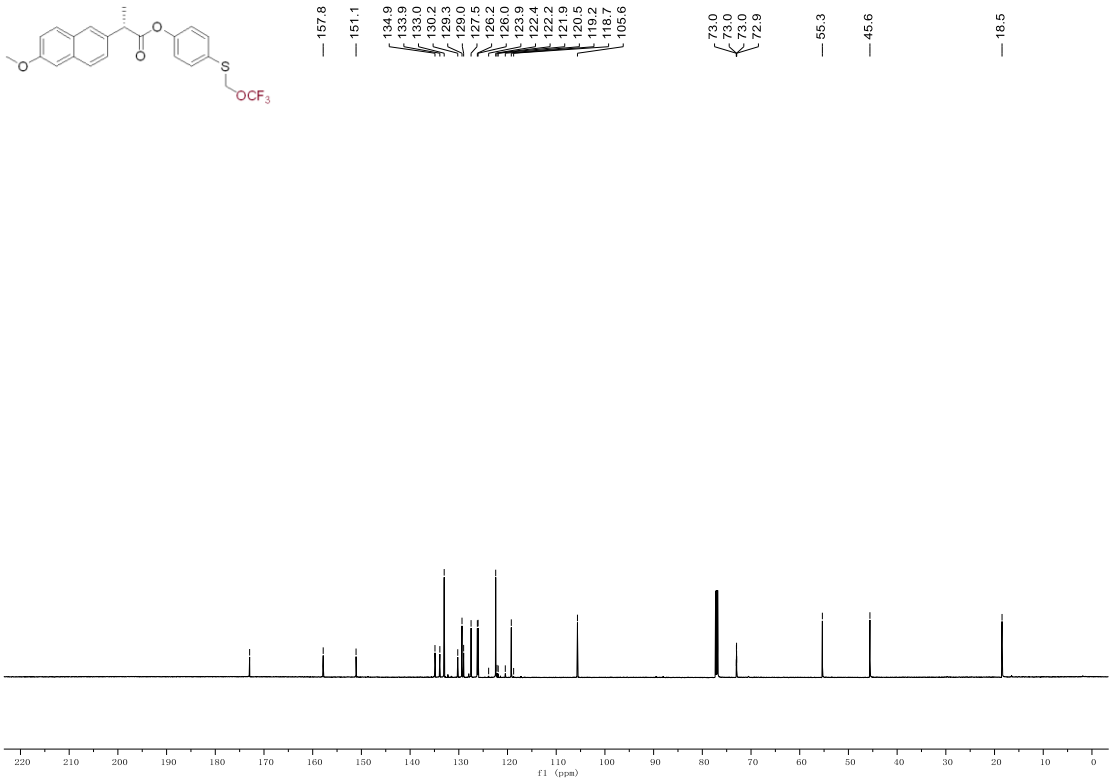
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of **3z**



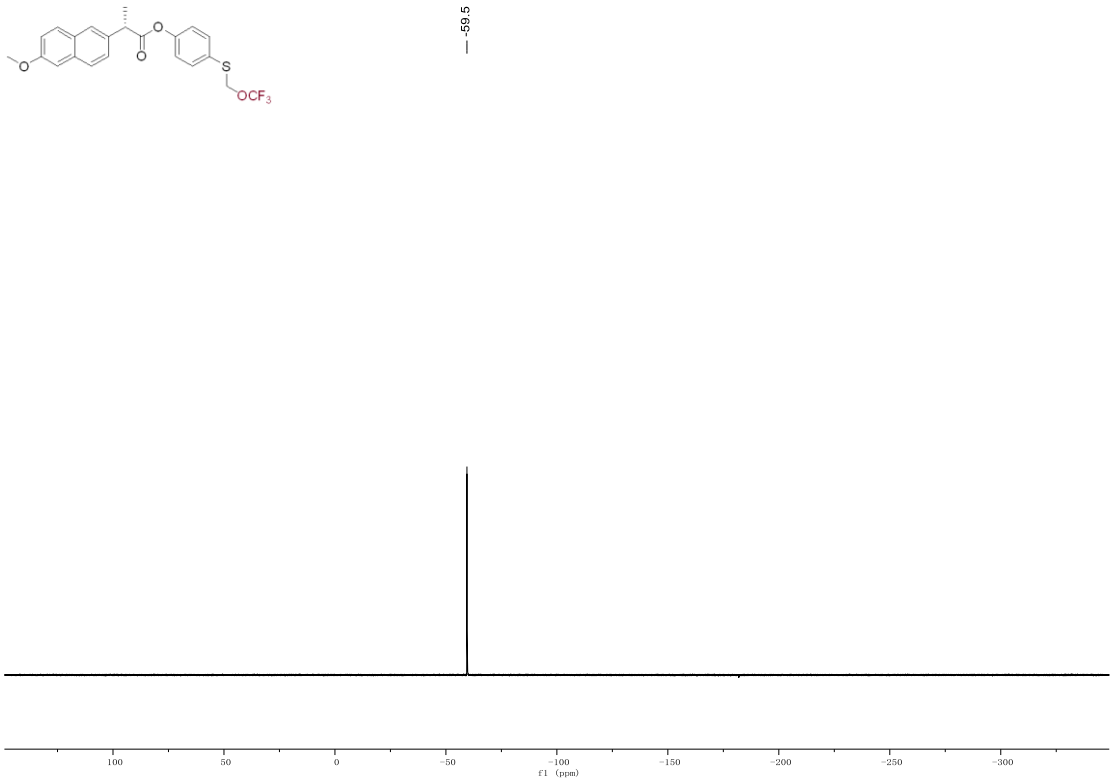
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3z**



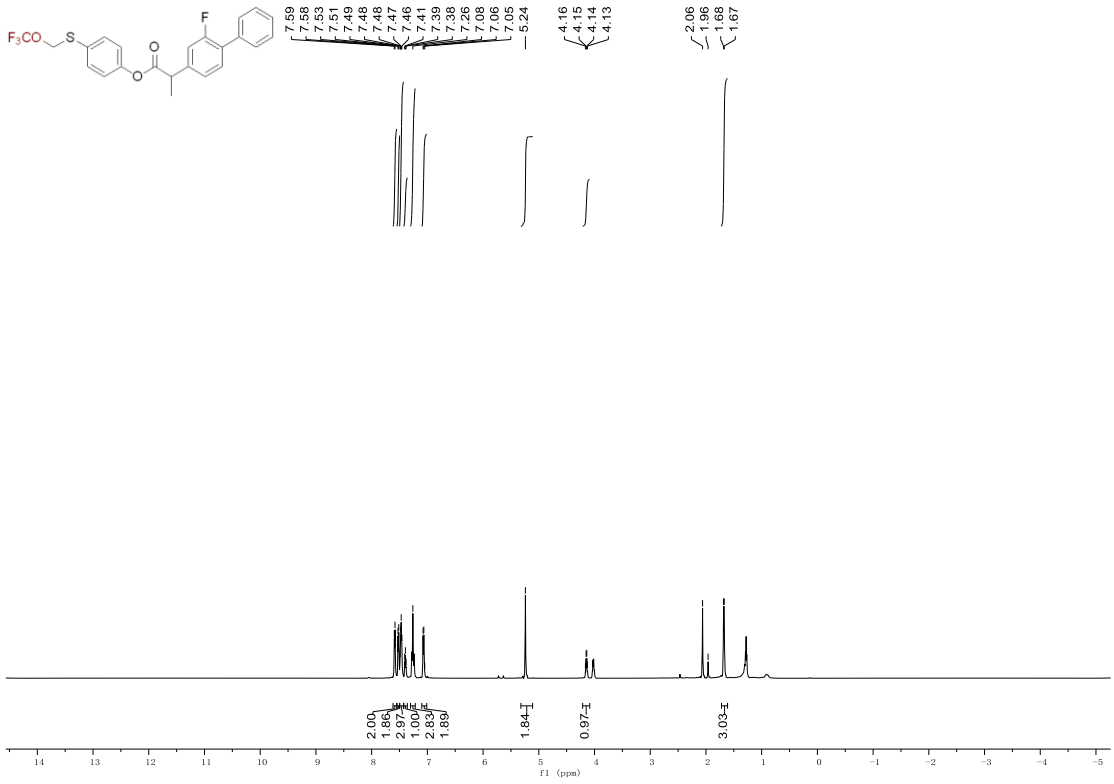
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of **3aa**



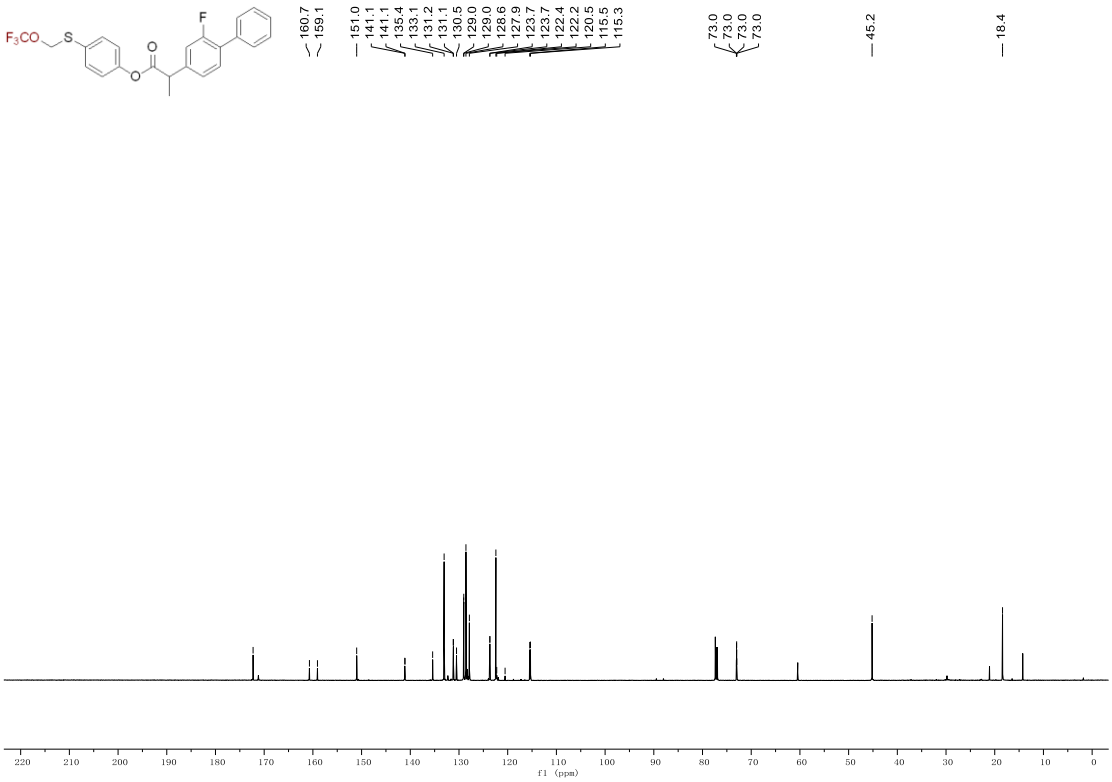
^{13}C NMR spectrum (151 MHz, $CDCl_3$) of **3aa**



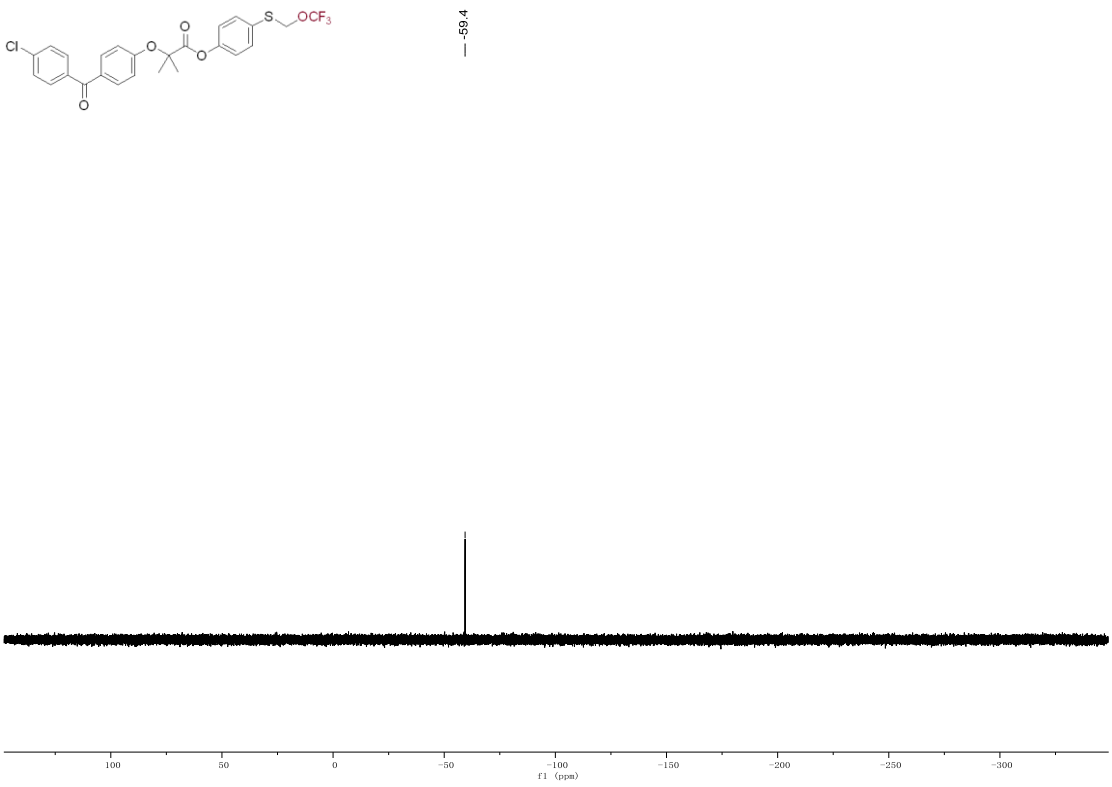
^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3aa**



^{1}H NMR spectrum (600 MHz, $CDCl_3$) of **3bb**



^{13}C NMR spectrum (151 MHz, $CDCl_3$) of **3bb**



^{19}F NMR spectrum (376 MHz, $CDCl_3$) of **3bb**