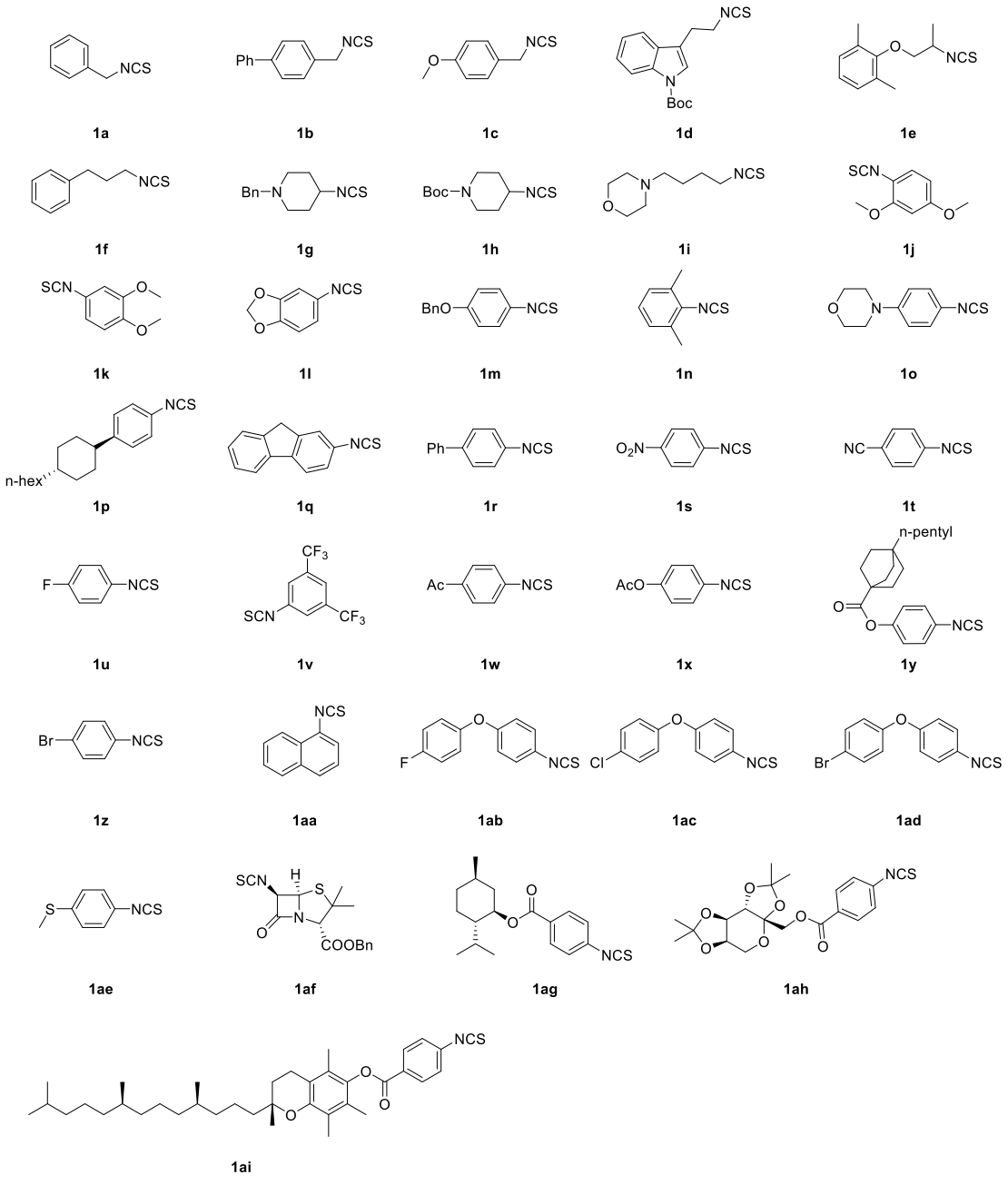
Contents

General information

Commercial reagents were used as supplied. Anhydrous solvents were used as supplied. NMR Spectra were recorded on a Bruker AV 400 spectrometer at 400 MHz (^{1}H NMR), 101 MHz (^{13}C NMR), 376 MHz (^{19}F NMR) or on a Bruker AV 300 spectrometer at 300 MHz (^{1}H NMR), 282 MHz (^{19}F NMR). Multiplicities are indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), p (quintet), sext (sextet), m (multiplet), b (broad). All coupling constants were reported in Hz. HR-MS measurements were performed on a Bruker MicrOTOFQ II (ESI) and an Agilent 7200 GC/Q-TOF (EI) mass spectrometers.

General procedure for the synthesis of isothiocyanates

Prepared starting materials (R-NCS): compounds **1a, 1c, 1i, 1j, 1k, 1n, 1p, 1s, 1t, 1u, 1v, 1w, 1y, 1z, 1aa, 1ae** are commercially available and were used without further purification.



General procedure A for the synthesis of isothiocyanates (adapted from reported literature procedure[1]):

To a 25 mL flask were sequentially added primary amine or ammonium salt (5.0 mmol, 1.0 equiv.), water (5 mL), CS_2 (0.9 mL, 12.5 mmol, 2.5 equiv.), and potassium carbonate (1.38 g, 10.0 mmol, 2.0 equiv.). The mixture was stirred at room temperature overnight, followed by the addition of sodium persulfate (1.19 g, 5.0 mmol, 1.0 equiv.), potassium carbonate (690 mg, 5.0 mmol, 1.0 equiv.), and water (5.0 mL). The mixture was stirred at room temperature for 1 h. After completion,

brine was added (2.0 mL) and the mixture was extracted with ethyl acetate (3×30 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude material obtained was then purified by column chromatography on silica gel.

General procedure B for the synthesis of isothiocyanates (adapted from reported literature procedure[2]):
A 100 mL round-bottom flask was charged with the amine or ammonium salt (5.0 mmol, 1.0 equiv.), CH_2Cl_2 (25 mL) and saturated aqueous $NaHCO_3$ (25 mL). To the biphasic system under strong stirring was slowly added thiophosgene (460 μL, 6.0 mmol, 1.2 equiv.) at room temperature. After 1 h, the two phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (3×30 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude material obtained was then purified by column chromatography on silica gel.

General procedure C for the synthesis of isothiocyanates (adapted from reported literature procedure[2]):
A 50 mL round-bottom flask was charged with the amine (5.0 mmol, 1.0 equiv.) and CH_2Cl_2 (15 mL). To the reaction mixture was added in one portion 1,1'-thiocarbonyldiimidazole (1.07 g, 6.0 mmol, 1.2 equiv.) at room temperature. After 1 h, water was added, and the two layers were separated. The aqueous layer was extracted with ethyl acetate (3×30 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude material obtained was then purified by column chromatography on silica gel.

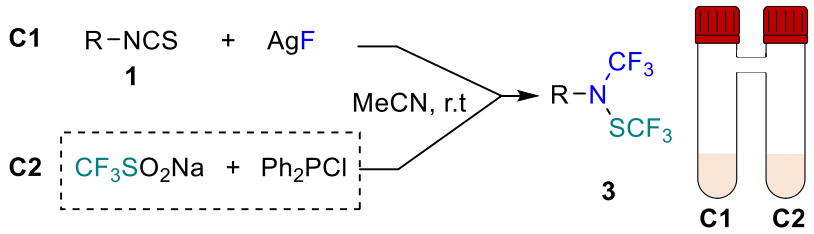
General procedure D for the synthesis of anilines (adapted from reported literature procedure[3])**:**
A flame-dried 100 mL round-bottom equipped with a magnetic stir bar was charged with phenols (10.0 mmol, 1.0 equiv.), 4-nitrobenzoyl chloride (12.0 mmol, 1.2 equiv.), and DMAP (1.0 mmol, 10 mol%), before DCM (25 mL) was added. To the resulting solution, Et_3N (15.0 mmol,1.5 equiv.) was added dropwise at 0 °C (ice bath). Then the reaction was allowed to warm up to room temperature and stirred for an additional 12 h. After the reaction was complete, HCl (1M, aq., 30 mL) was added to reaction mixture. The mixture was then extracted using DCM (3×30 mL) and the layers were separated. The organic layers were combined, washed with brine (25 mL), dried over anhydrous sodium sulfate, filtered, and concentrated with the aid of a rotary evaporator. The solvent was removed under reduced pressure with the aid of a rotary evaporator. The crude product was directly used in the next step without further purification.
To the methanol (10 mL) and THF (10 mL) solution of nitro compounds, 10% palladium on active carbon (202 mg) was added under Argon atmosphere. Hydrogen gas was bubbled into the suspension with stirring at room temperature for 15 h. After the palladium on carbon was removed by filtration, the solvent was removed under reduced pressure, to afford the corresponding anilines.

General information of Stability studies

Solution of **3r** (10 mmol/L, 5 mL) and internal standard ((trifluoromethyl)benzene, 0.23 mmol/L, 14.4 μL) in deuterated acetonitrile was prepared. In an NMR tube, 0.25 mL of the solution with 0.25 mL of respective aqueous solutions or solvents. Remaining of the **3r** was determined based on ^{19}F NMR analysis at room temperature. ^{19}F NMR analysis were Performed at 1 hour, 5 hours, 10 hours, 15 hours, 24 hours and 48 hours respectively.

pH 4.00 (sigma-aldrich, B5020), pH 7.00 (sigma-aldrich, B4770), and pH 10.00 (sigma-aldrich, B4895) buffers and saline (sigma-aldrich, 806544) were commercially available. Hydrochloric acid solution with concentration of 1 mol/L (initial pH 1) and sodium hydroxide solution with concentration of 1 mol/L (initial pH 14) were prepared in the lab. The water was deionized. Anhydrous dimethyl sulfoxide and acetonitrile were purchased from sigma-aldrich.

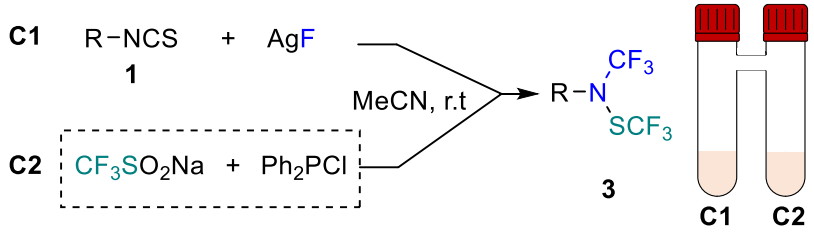
Optimization of the Reaction Conditions (Method with H-tube)



Chamber 1					Chamber 2					Yields[a]
1r/mmol	AgF/mmol	additive	MeCN/mL	Temperature/°C	Ph_2PCl/mmol	CF_3SO_2Na/mmol	additive	MeCN/mL	Temperature/°C	
0.2	0.8	\	1	r.t	0.6	0.6	\	1	r.t	60%
0.2	0.8	\	1	r.t	1.2	0.6	\	1	r.t	80%
0.2	0.8	\	2	r.t	1.2	0.6	\	1	r.t	65%
0.2	0.8	\	0.5	r.t	1.2	0.6	\	1	r.t	55%
0.2	0.8	\	1	r.t	2.4	1.2	\	1	r.t	80%
0.2	0.8	\	1	r.t	1.8	0.9	\	1	r.t	80%
0.2	1	\	1	r.t	1.2	0.6	\	1	r.t	80%
0.2	0.6	\	1	r.t	1.2	0.6	\	1	r.t	55%
0.2	1.2	\	1	r.t	1.2	0.6	\	1	r.t	55%
0.2	0.8	\	1	r.t	1.2	0.6	\	1	35	70%
0.2	0.8	CsF (0.2 mmol)	1	r.t	1.2	0.6	\	1	r.t	35%

[a] reaction with standard condition was performed for 16 hours with: Chamber 1 (C1): **1r** (0.2 mmol, 1 equiv.), AgF (0.8 mmol, 4 equiv.) in MeCN (1 mL); Chamber 2 (C2): CF_3SO_2Na (1.2 mmol, 6 equiv.), Ph_2PCl (0.6 mmol, 3 equiv.) in MeCN (1 mL), Yield determined by ^{19}F NMR spectroscopy with $PhCF_3$ as an internal standard.

Optimization of the Solvents (Method H-tube)

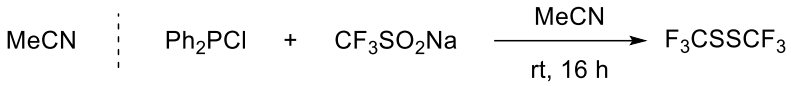


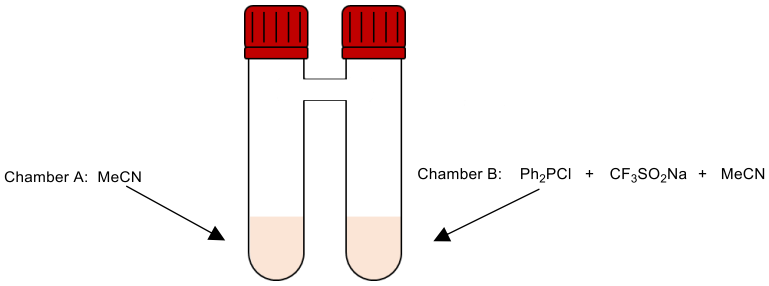
Chamber 1				Chamber 2				Yields[a]
1r/mmol	AgF/mmol	Solvents/1 mL	Temperature/°C	Ph_2PCl/mmol	CF_3SO_2Na/mmol	Solvents/1 mL	Temperature/°C	
0.2	0.8	MeCN	r.t	1.2	0.6	MeCN	r.t	80%
0.2	0.8	THF	r.t	1.2	0.6	MeCN	r.t	8%
0.2	0.8	DMF	r.t	1.2	0.6	MeCN	r.t	55%
0.2	0.8	Toluene	r.t	1.2	0.6	MeCN	r.t	11%
0.2	0.8	DCM	r.t	1.2	0.6	MeCN	r.t	8%
0.2	0.8	Et_2O	r.t	1.2	0.6	MeCN	r.t	30%
0.2	0.8	1,4-Dioxane	r.t	1.2	0.6	MeCN	r.t	20%
0.2	0.8	MeCN	r.t	1.2	0.6	THF	r.t	51%
0.2	0.8	MeCN	r.t	1.2	0.6	DMF	r.t	43%
0.2	0.8	MeCN	r.t	1.2	0.6	Toluene	r.t	69%
0.2	0.8	MeCN	r.t	1.2	0.6	DCM	r.t	46%
0.2	0.8	MeCN	r.t	1.2	0.6	Et_2O	r.t	72%
0.2	0.8	MeCN	r.t	1.2	0.6	1,4-Dioxane	r.t	55%

[a] reaction with standard condition was performed for 16 hours with: Chamber 1 (C1): **1r** (0.2 mmol, 1 equiv.), AgF (0.8 mmol, 4 equiv.) in MeCN (1 mL); Chamber 2 (C2): CF_3SO_2Na (1.2 mmol, 6 equiv.), Ph_2PCl (0.6 mmol, 3 equiv.) in MeCN (1 mL), Yield determined by ^{19}F NMR spectroscopy with $PhCF_3$ as an internal standard.

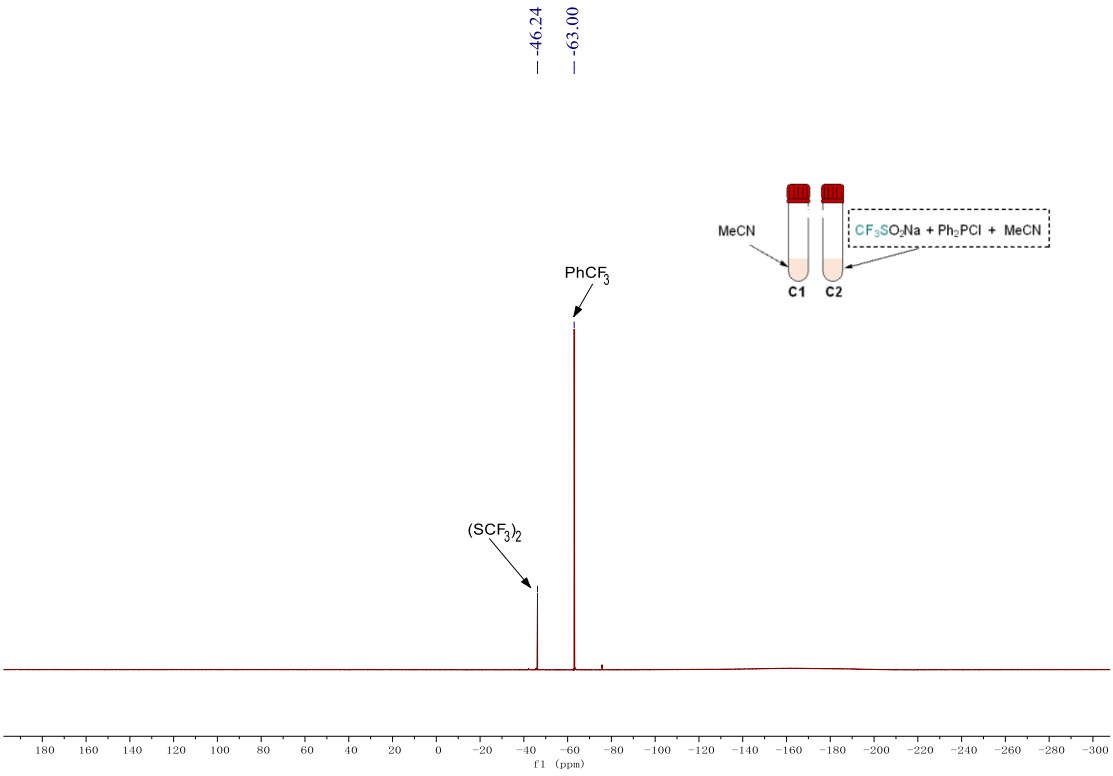
Mechanism Investigation

General procedure for the synthesis trifluoro((trifluoromethyl)sulfinothioyl)methane:



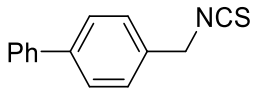


To a H-tube were sequentially added acetonitrile (1 mL) to chamber A. Then sodium triflate (0.6 mmol, 3.0 equiv.) and acetonitrile (1 mL) were added to chamber B. After sealing the H-tube, chlorodiphenylphosphine (1.2 mmol, 3.0 equiv.) was added to chamber B by syringe. The mixture was stirred at room temperature overnight. After completion, the internal standard (trifluoromethyl)benzene (30 μL, 0.244 mmol) was added, and the ^{19}F-NMR spectra is shown as follow:



Characterization of starting materials

4-(isothiocyanatomethyl)-1,1'-biphenyl (1b)

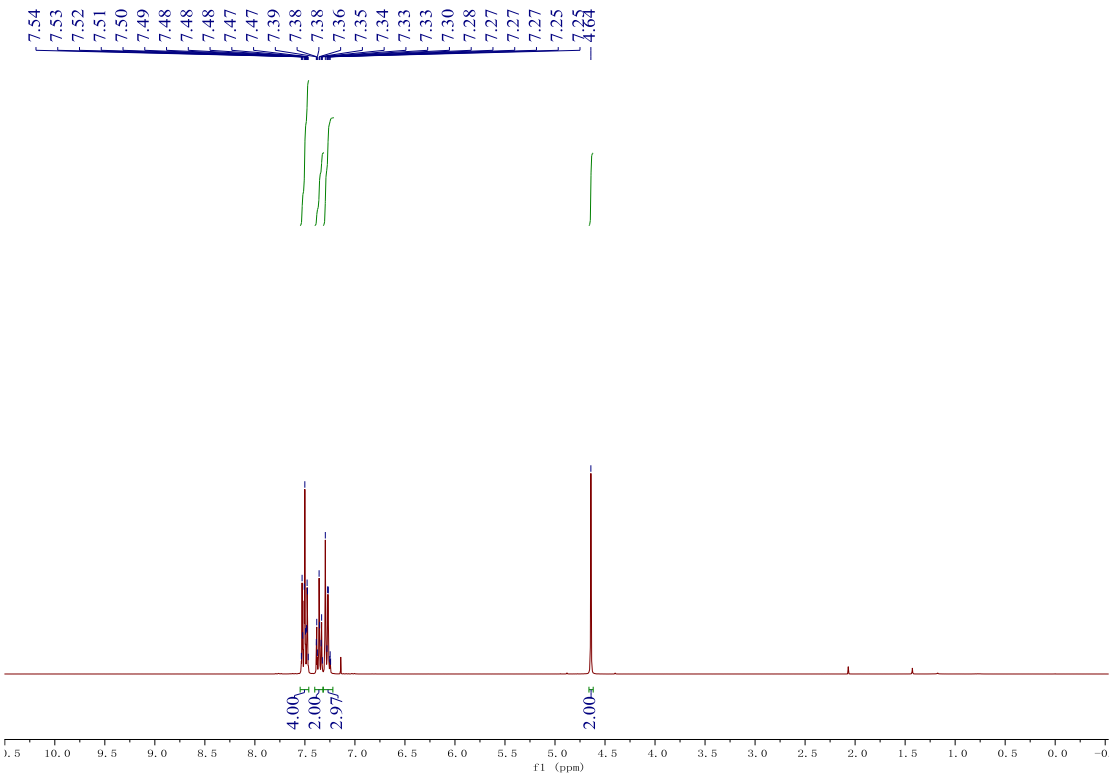


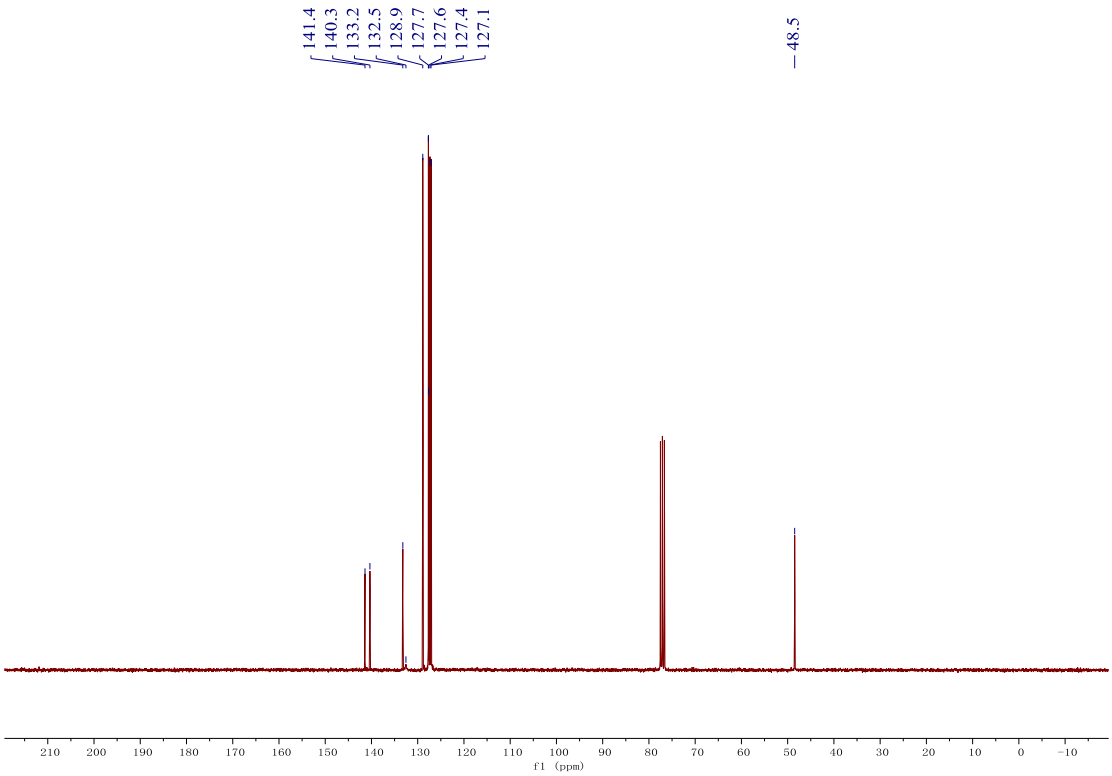
The compound **1b** was obtained as a white solid in 63% yield using [1,1'-biphenyl]-4-ylmethanamine following the general procedure A after column chromatography on silica gel with pentane.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.55 – 7.46 (m, 4H), 7.40 – 7.32 (m, 2H), 7.32 – 7.22 (m, 3H), 4.64 (s, 2H).

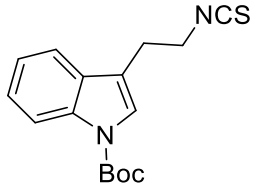
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 141.4, 140.3, 133.2, 132.5, 128.9, 127.7, 127.6, 127.4, 127.1, 48.5.

Characterization data matched that reported in the literature[4]





tert-butyl 3-(2-isothiocyanatoethyl)-1H-indole-1-carboxylate (1d)



3-(2-Isothiocyanatoethyl)-1H-indole was obtained as a colorless oil in 82% yield using 2-(1H-indol-3-yl)ethan-1-amine following the general procedure C after column chromatography on silica gel with cyclohexane/ethyl acetate (5/1).

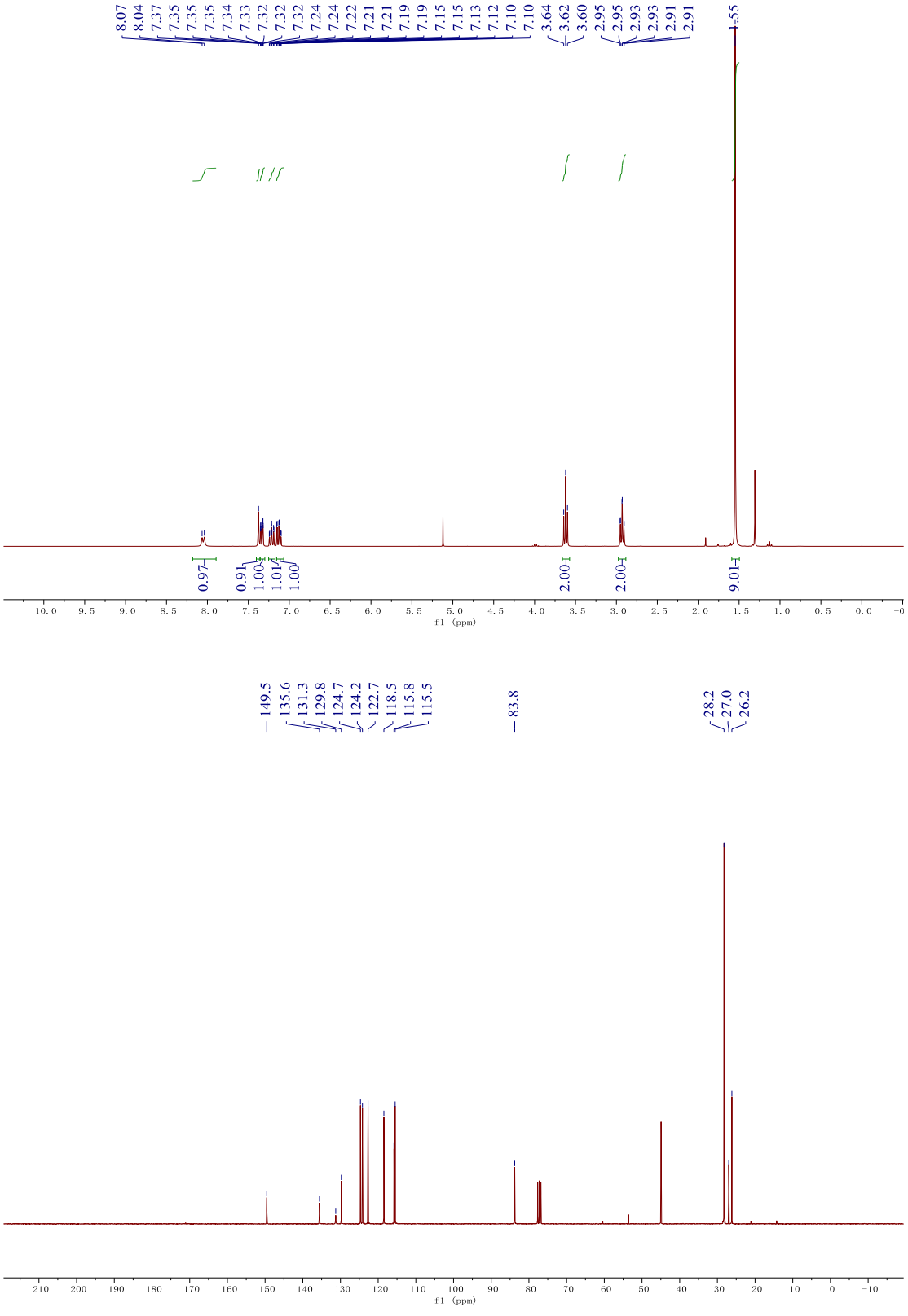
The compound **1d** was obtained as a colorless oil in 70% yield following literature's procedure[5]: 3-(2-isothiocyanatoethyl)-1H-indole (808 mg, 1.0 equiv.) was added to a reaction tube and dissolved in DCM (2.0 mL). Triethylamine (0.66 mL, 1.2 equiv.) and 4- dimethylaminopyridine (48 mg, 0.1 equiv.) were added to the reaction tube. Boc anhydride (1.05 g, 2.4 equiv.) was dissolved in DCM (4 mL) and added to the reaction tube. The mixture was stirred in the sealed tube at rt for 10 h. The reaction mixture was extracted with a saturated solution of NH_4Cl (5.0 mL), water (5.0 mL) and a saturated solution of NaCl (5.0 mL). The combined organic layers were dried over Na_2SO_4 and the volatiles were removed under reduced pressure. The residue was purified by column chromatography on silica gel with cyclohexane/ethyl acetate (50/1).

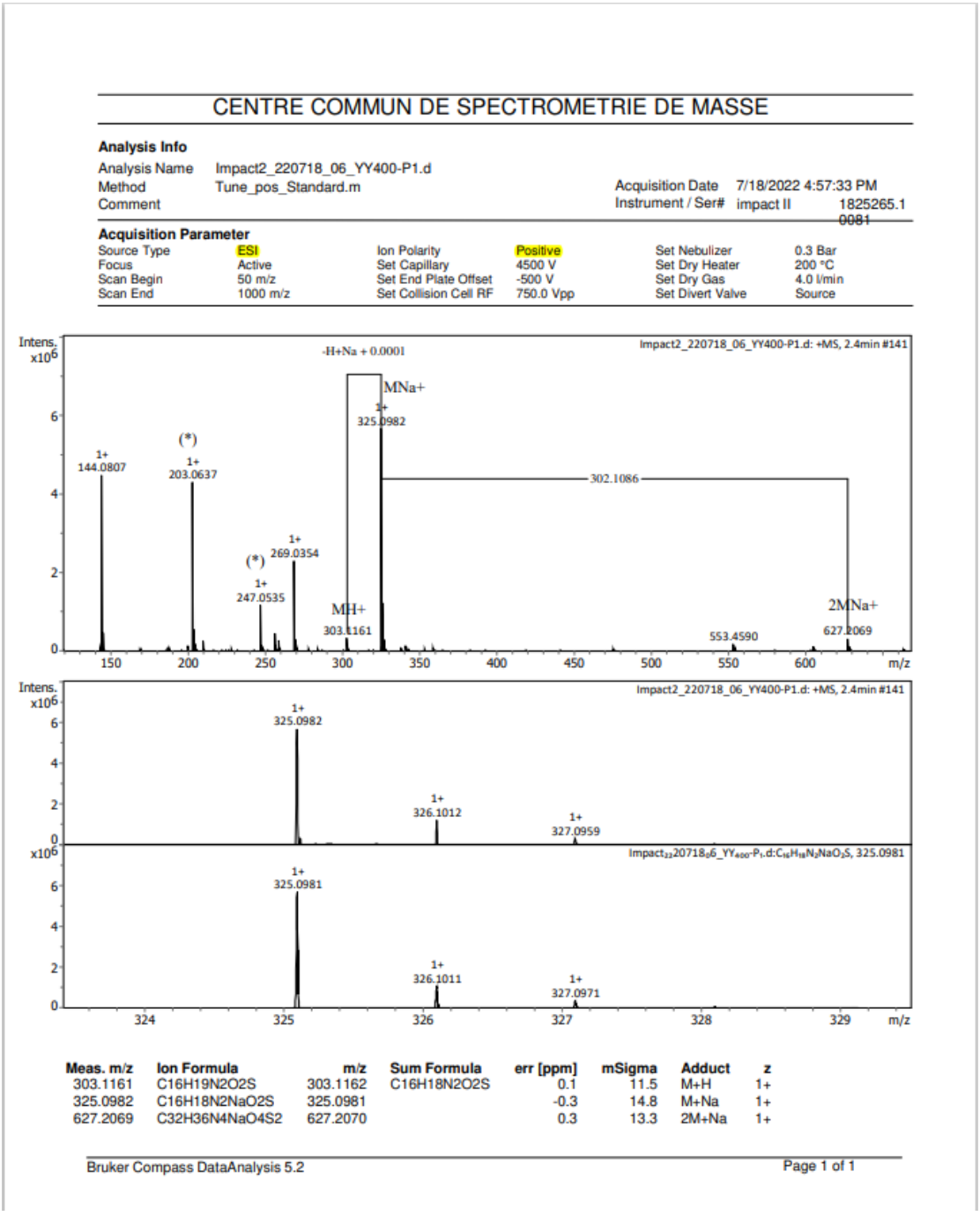
^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.05 (d, *J* = 8.2 Hz, 1H), 7.37 (s, 1H), 7.35 – 7.32 (m, 1H), 7.24 – 7.19 (m, 1H), 7.15 – 7.10 (m, 1H), 3.62 (t, *J* = 6.9 Hz, 2H), 2.93 (t, *J* = 6.8 Hz, 2H), 1.55 (s, 9H).

^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 149.5, 135.6, 131.1, 129.8, 124.7, 124.2, 122.7, 118.5,

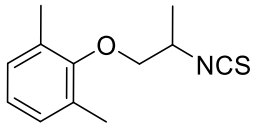
115.8, 115.5, 83.8, 28.2, 27.0, 26.2.

HRMS (ESI) calculated for $C_{16}H_{19}N_2O_2S$: 303.1162 $[M+H]^+$, Found: 303.1161.





2-(2-isothiocyanatopropoxy)-1,3-dimethylbenzene (1e)



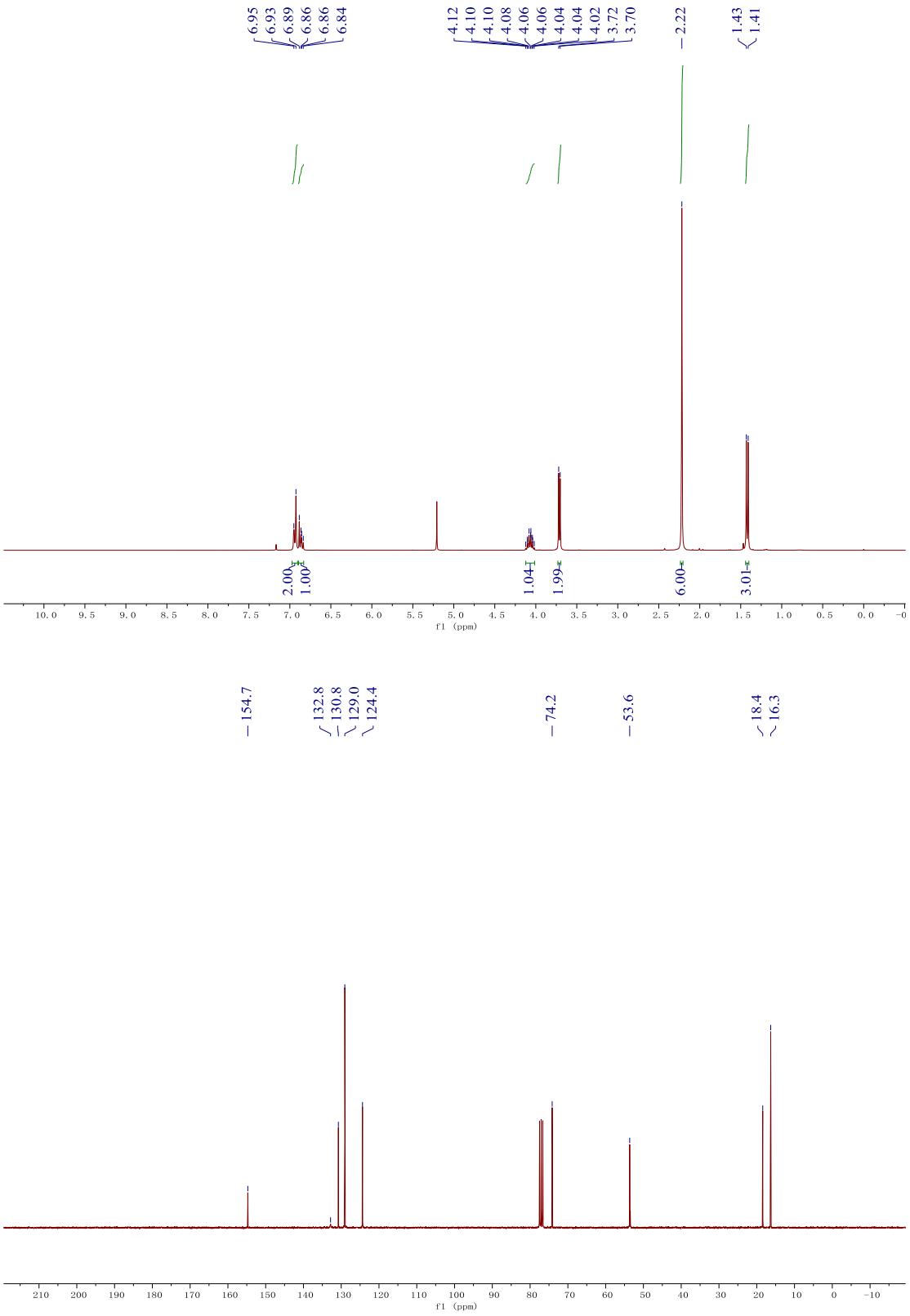
The compound **1e** was obtained as a colorless oil in 74% yield using 1-(2,6-dimethylphenoxy) propan-2-amine hydrochloride following the general procedure A after column chromatography on silica gel with pentane.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 6.95 – 6.92 (m, 2H), 6.89 – 6.84 (m, 1H), 4.12 – 4.01 (m, 1H),

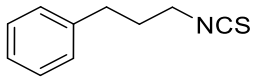
3.71 (d, *J* = 5.5 Hz, 2H), 2.22 (s, 6H), 1.42 (d, *J* = 6.7 Hz, 3H).

$^{13}C\{^{1}H\}$ NMR (75 MHz, Chloroform-*d*) δ 154.7, 132.8, 130.78, 129.0, 124.4, 74.2, 53.6, 18.4, 16.3.

Characterization data matched that reported in the literature[2]



(3-isothiocyanatopropyl)benzene (1f)

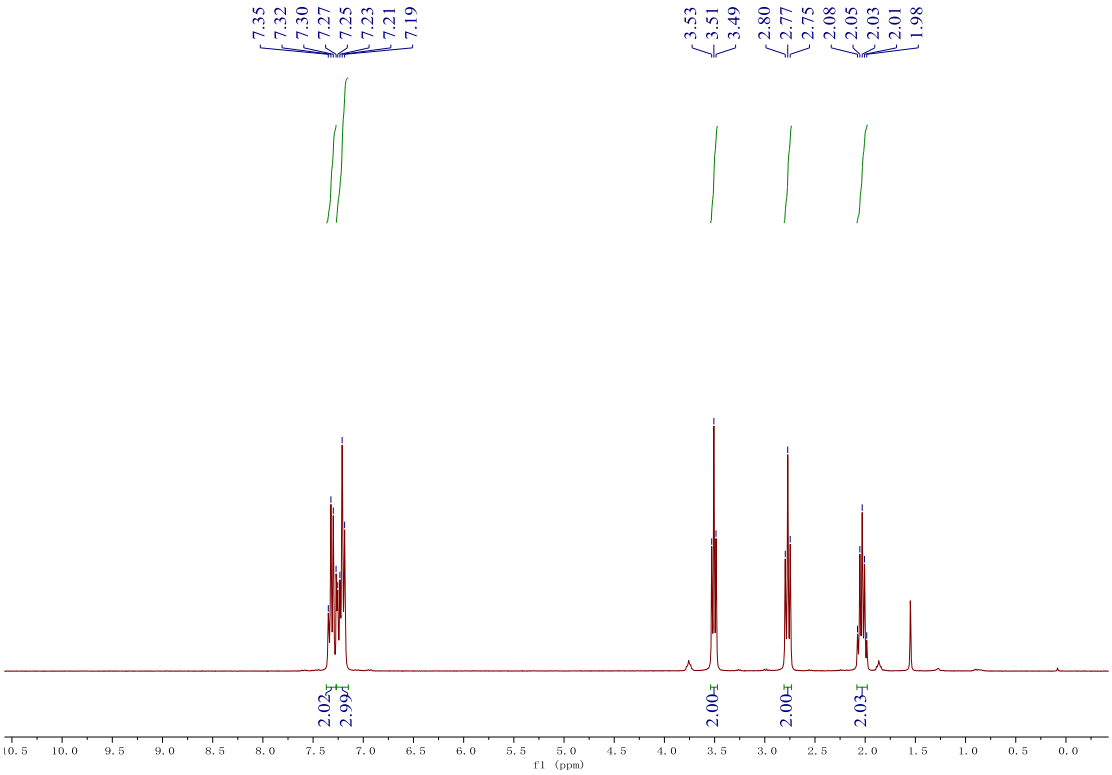


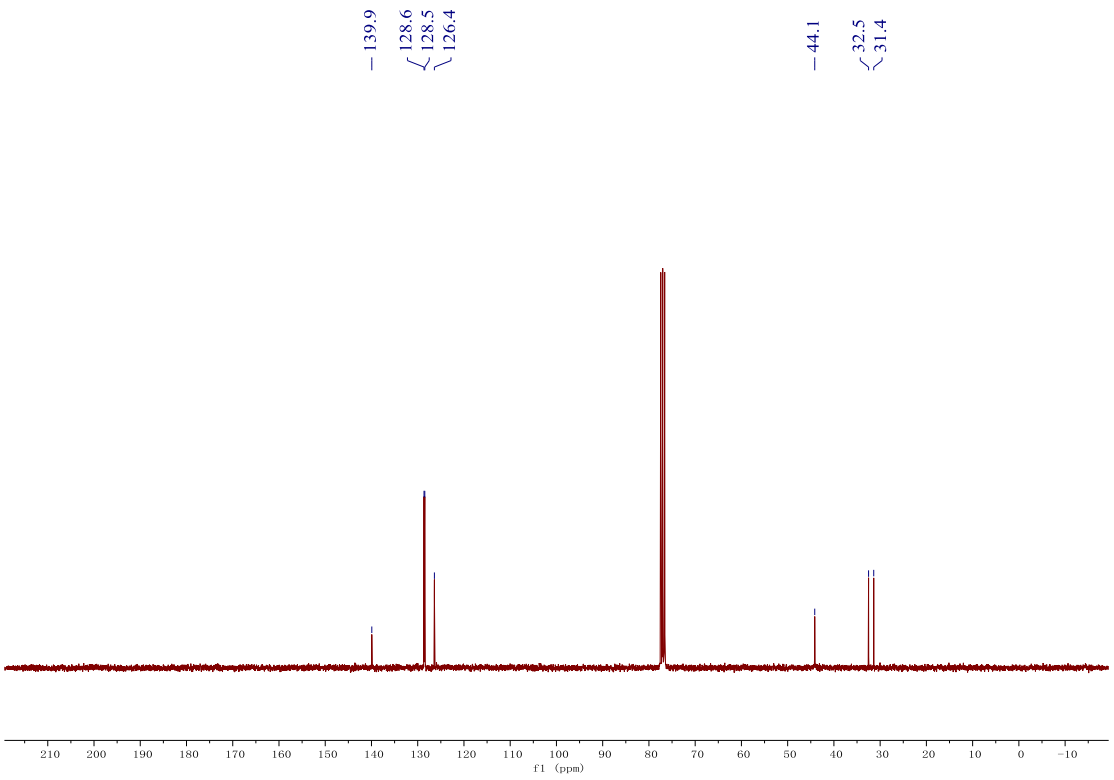
The compound **1f** was obtained as a colorless oil in 99% yield using 3-phenylpropan-1-amine following the general procedure A after column chromatography on silica gel with cyclohexane.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.35 – 7.30 (m, 2H), 7.27 – 7.15 (m, 3H), 3.51 (t, *J* = 6.5 Hz, 2H), 2.77 (t, *J* = 7.4 Hz, 2H), 2.08 – 1.98 (m, 2H).

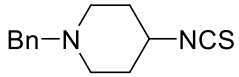
^{13}C{^{1}H} NMR (75 MHz, Chloroform-d) δ 139.9, 128.6, 128.8, 126.4, 44.1, 32.5, 31.4.

Characterization data matched that reported in the literature[6]





1-benzyl-4-isothiocyanatopiperidine (1g)

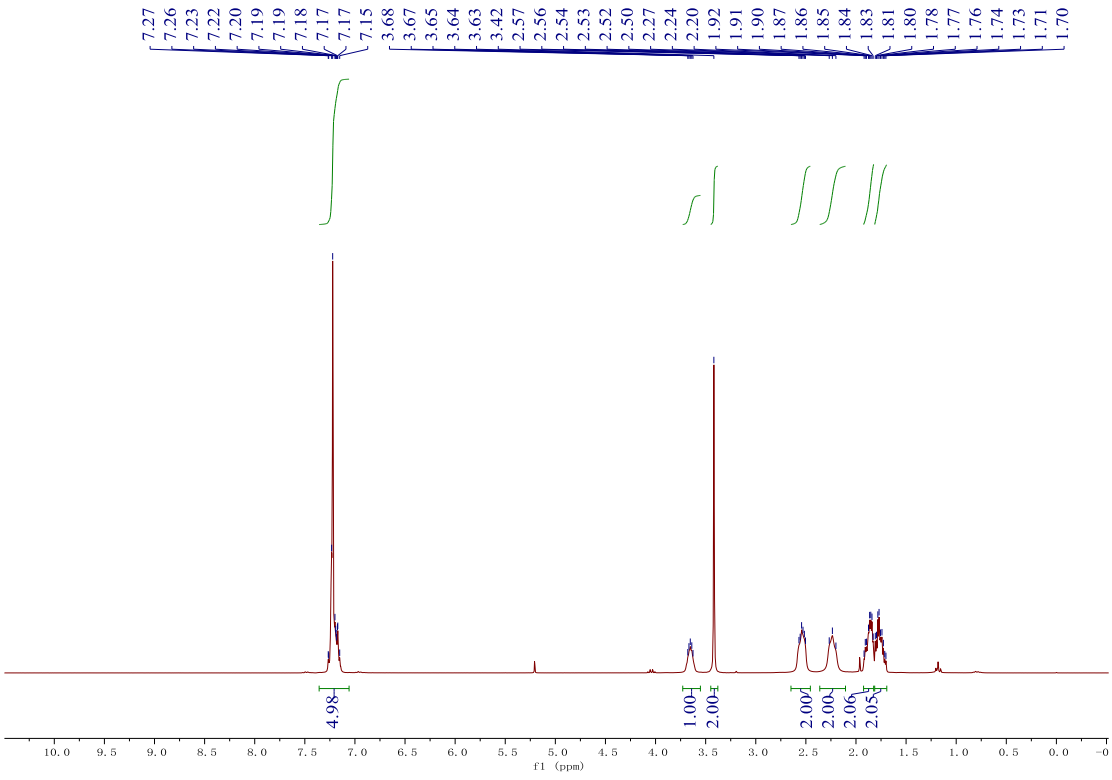


The compound **1g** was obtained as a yellow oil in 40% yield using 1-benzylpiperidin-4-amine following the general procedure A after column chromatography on silica gel with pentane/ethyl acetate (10/1).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.36 – 7.06 (m, 5H), 3.68 – 3.63(m, 1H), 3.42 (s, 2H), 2.57 – 2.50 (m, 2H), 2.27 – 2.20 (m, 2H), 1.92 – 1.83 (m, 2H), 1.81 – 1.70 (m, 2H).

^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 138.2, 131.0, 129.0, 128.3, 127.2, 63.0, 53.4, 50.3, 32.5.

HRMS (ESI) calculated for $C_{13}H_{17}N_2S$: 233.1107 $[M+H]^+$, Found: 233.1110


7.27
7.26
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7.19
7.18
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7.17
7.15
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3.65
3.64
3.63
3.42
2.57
2.56
2.54
2.53
2.52
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2.20
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1.91
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1.87
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1.85
1.84
1.83
1.81
1.80
1.78
1.77
1.76
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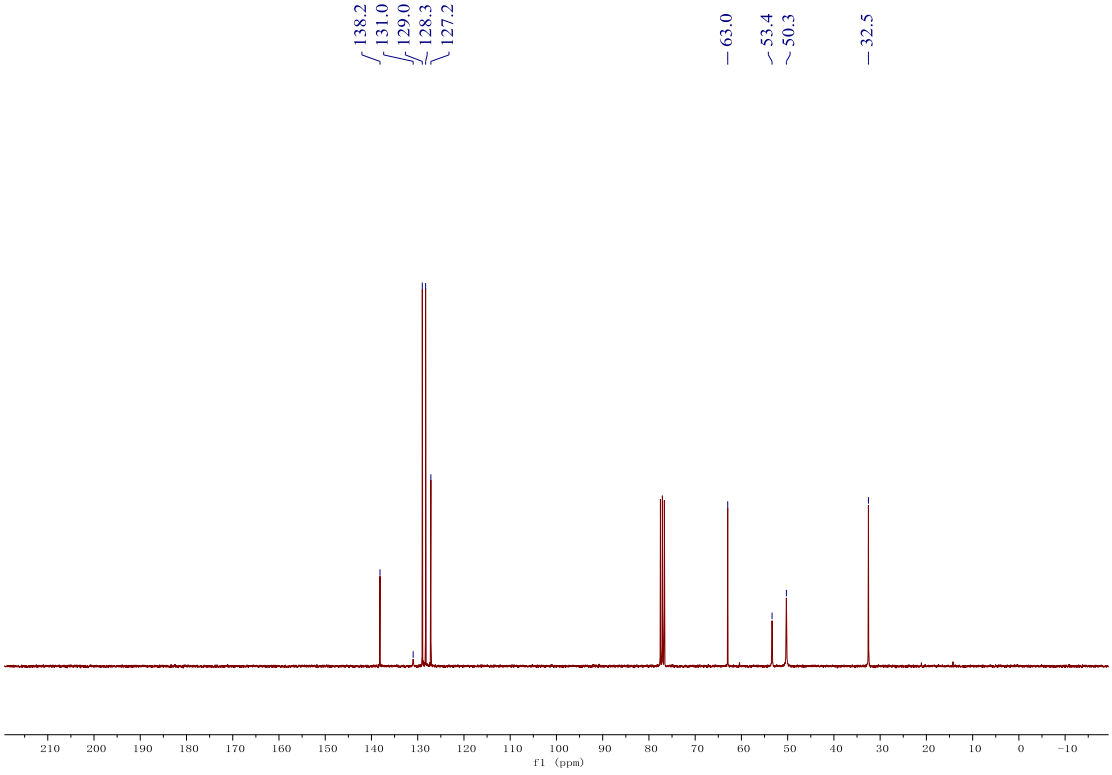
2.00
2.00
2.06
2.05
f1 (ppm)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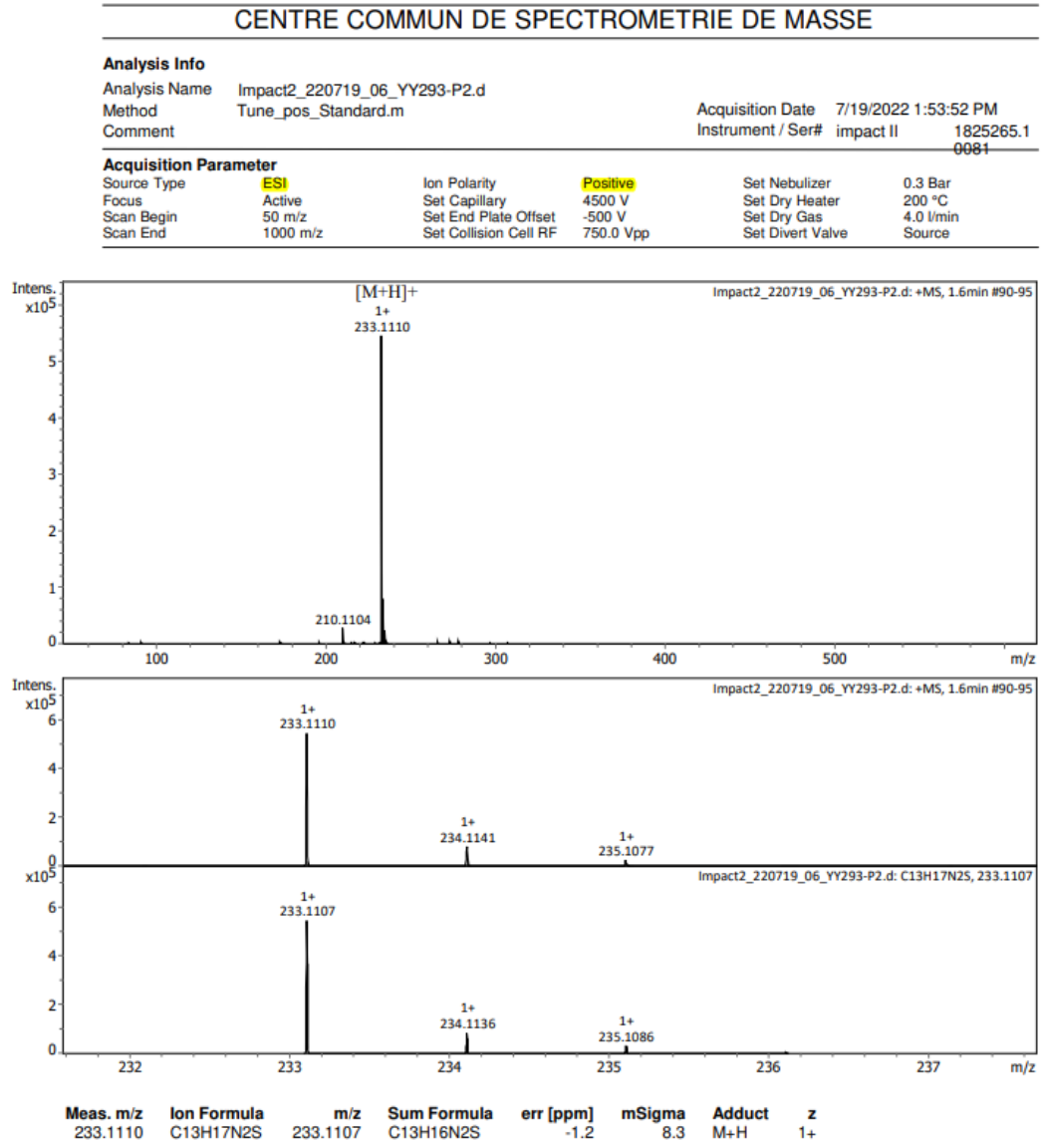
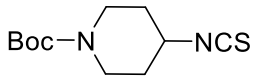
128.3
127.2
63.0
53.4
50.3
32.5
f1 (ppm)



***tert*-butyl 4-isothiocyanatopiperidine-1-carboxylate (1h)**

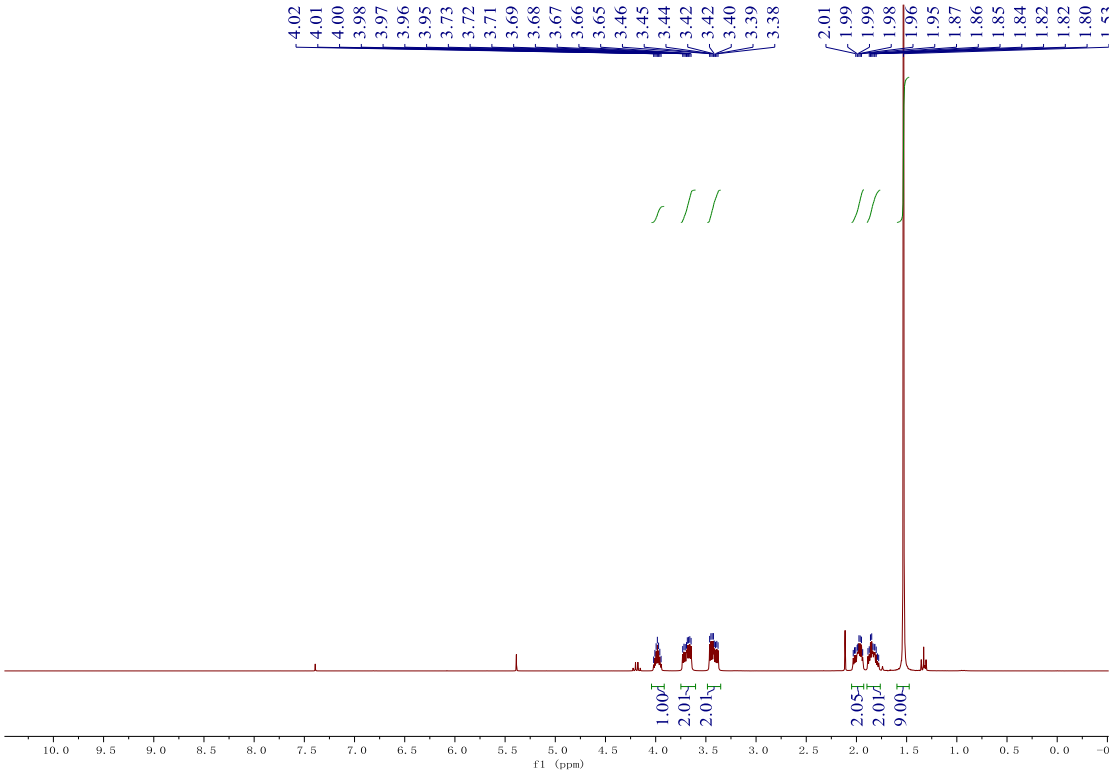


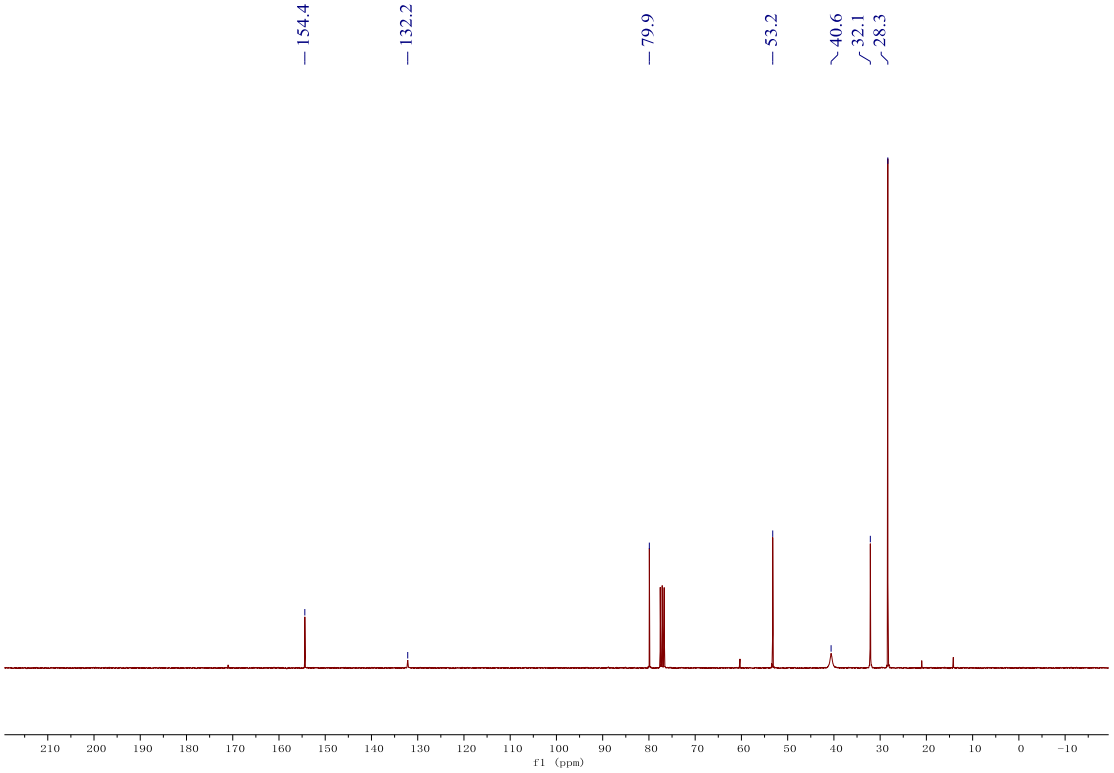
The compound **1h** was obtained as a colorless oil in 91% yield using tert-butyl 4-aminopiperidine-1-carboxylate following the general procedure A after column chromatography on silica gel with pentane/ethyl acetate (20/1).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 3.98 (sept, *J* = 7.4, 3.8 Hz, 1H), 3.73 – 3.65 (m, 2H), 3.46 – 3.38 (m, 2H), 2.03 – 1.94 (m, 2H), 1.89 – 1.78 (m, 2H), 1.53 (s, 9H).

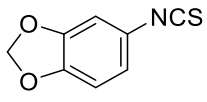
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 154.4, 132.2, 79.9, 53.2, 40.6, 32.1, 28.3.

Characterization data matched that reported in the literature[2]





5-isothiocyanatobenzo[d][1,3]dioxole (1l)

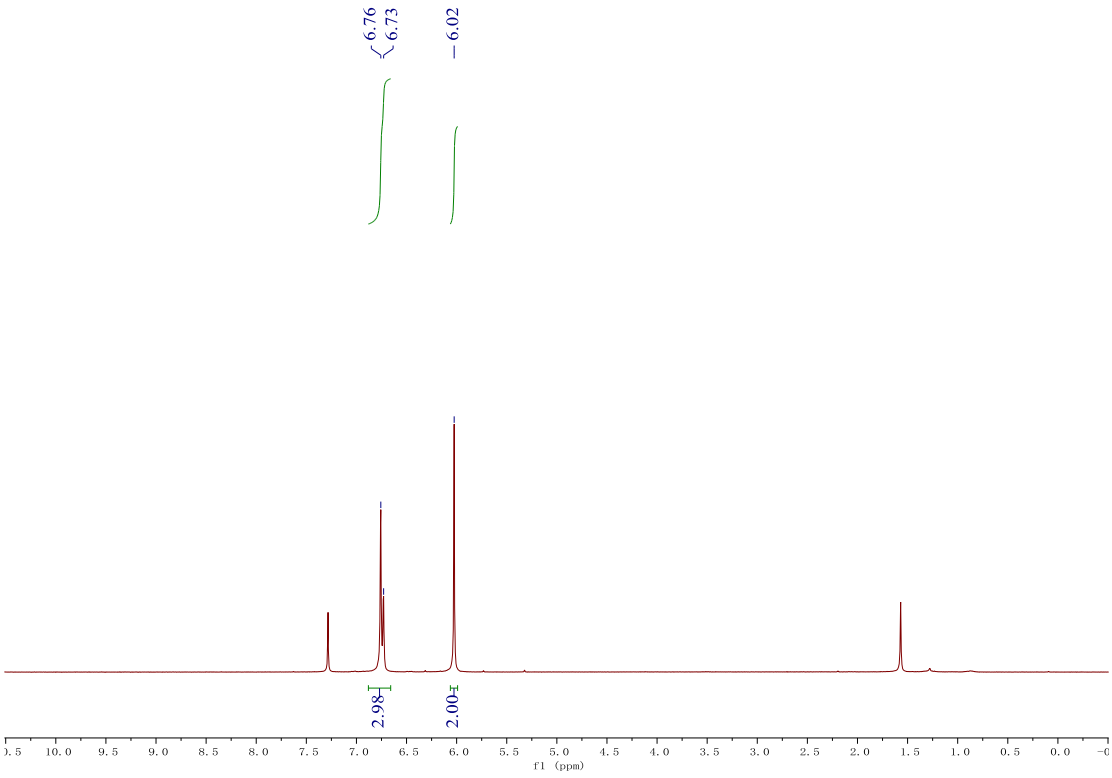


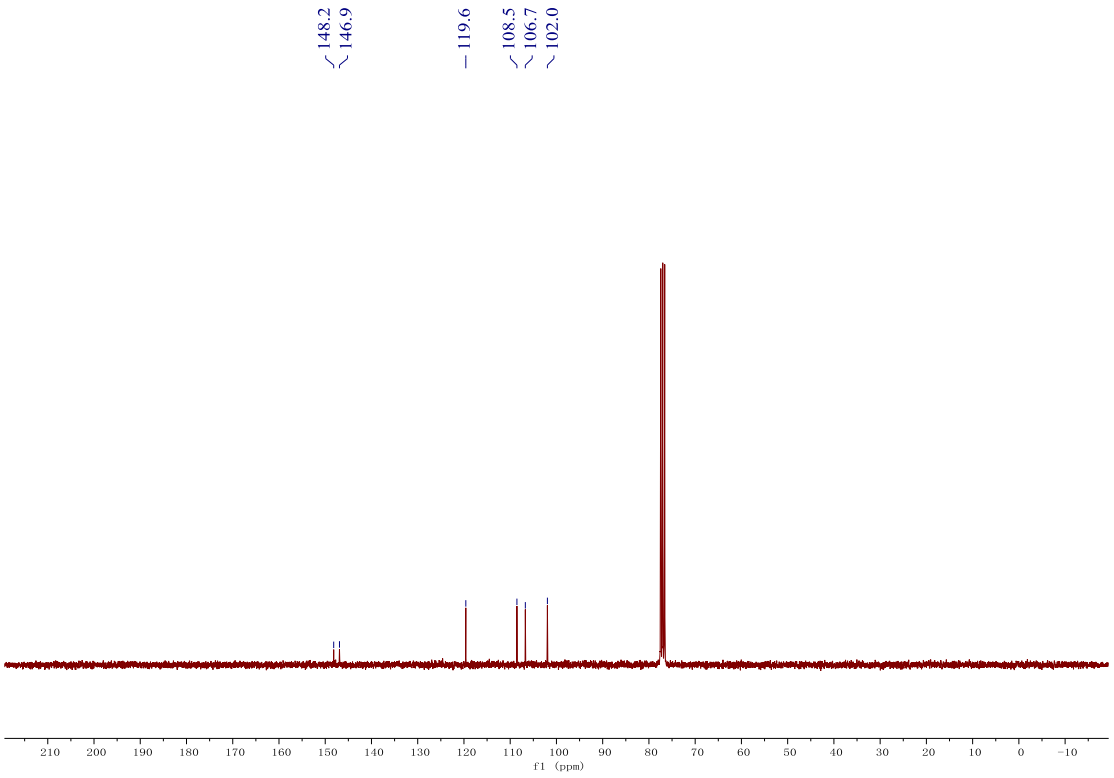
The compound **1l** was obtained as a white solid in 77% yield using benzo[d][1,3]dioxol-5-amine following the general procedure A after column chromatography on silica gel with cyclohexane.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 6.76-6.73 (m, 3H), 6.02 (s, 2H).

^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 148.2, 146.9, 119.6, 108.5, 106.7, 102.0.

Characterization data matched that reported in the literature[7]





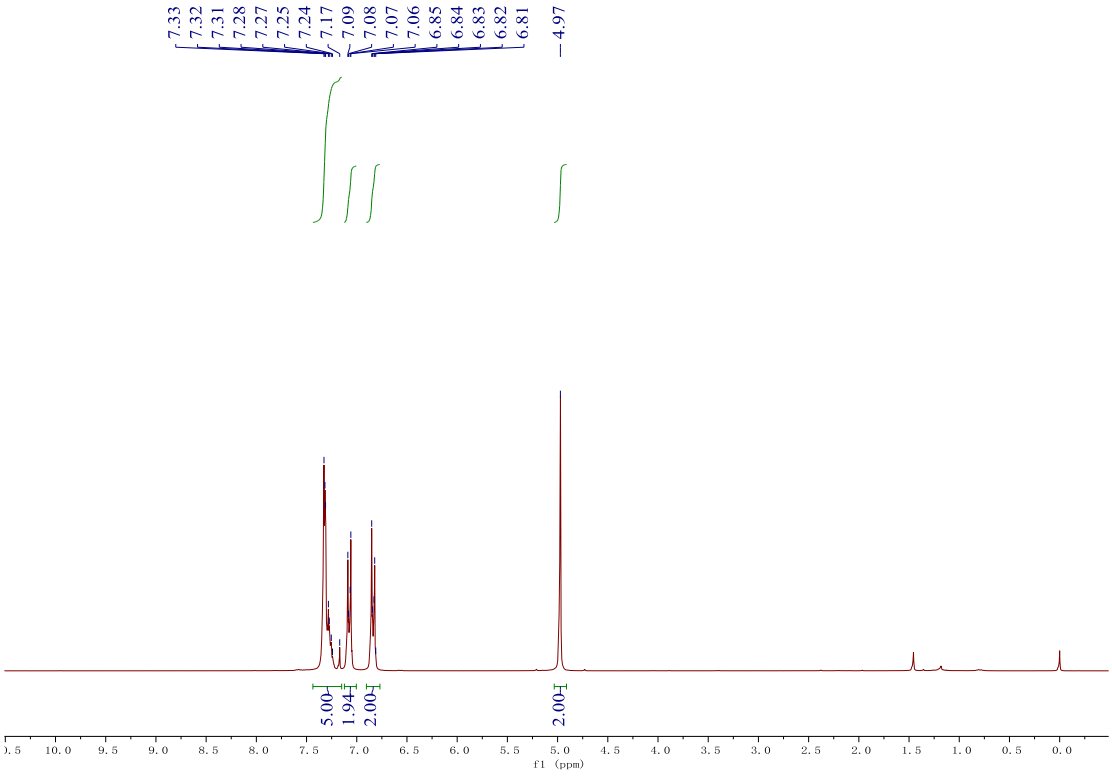
1-(benzyloxy)-4-isothiocyanatobenzene (1m)

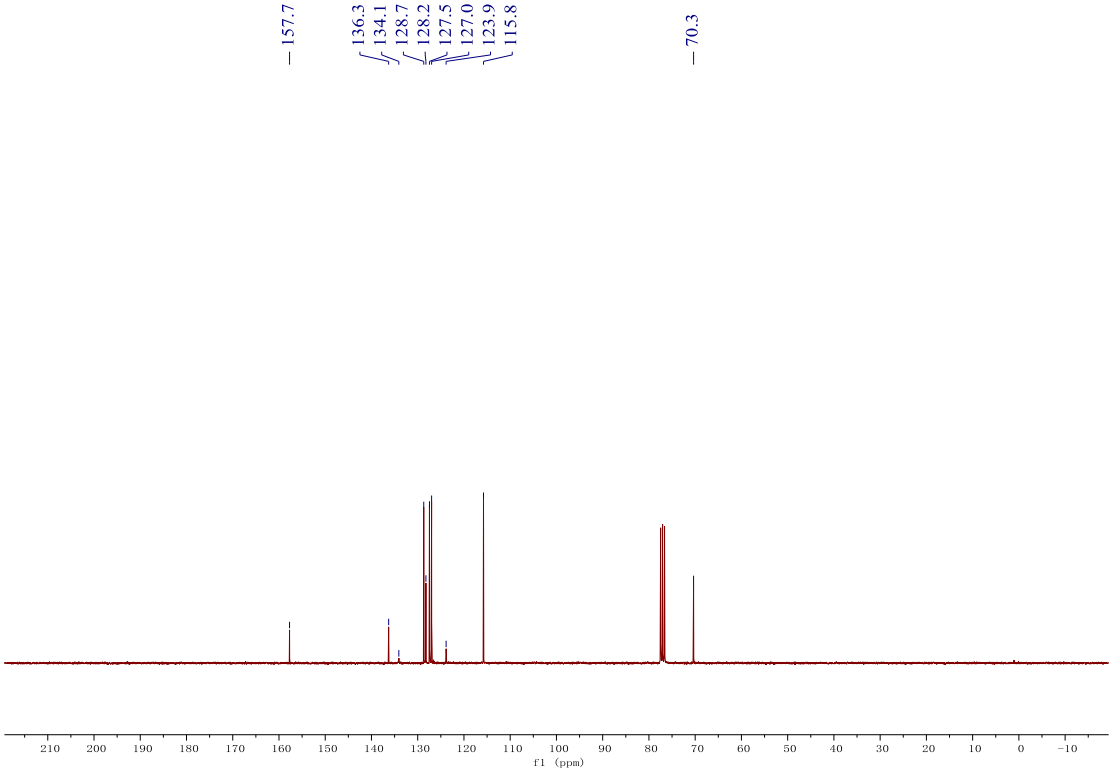
The compound **1m** was obtained as a white solid in 75% yield using 4-(benzyloxy)aniline following the general procedure A after column chromatography on silica gel with pentane.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.44 – 7.15 (m, 5H), 7.12 – 7.00 (m, 2H), 6.90 – 6.77 (m, 2H), 4.97 (s, 2H).

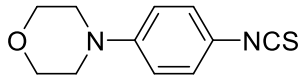
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 157.7, 136.3, 134.1, 128.7, 128.2, 127.5, 127.0, 123.9, 115.8, 70.3.

Characterization data matched that reported in the literature[8]





4-(4-isothiocyanatophenyl)morpholine (1o)



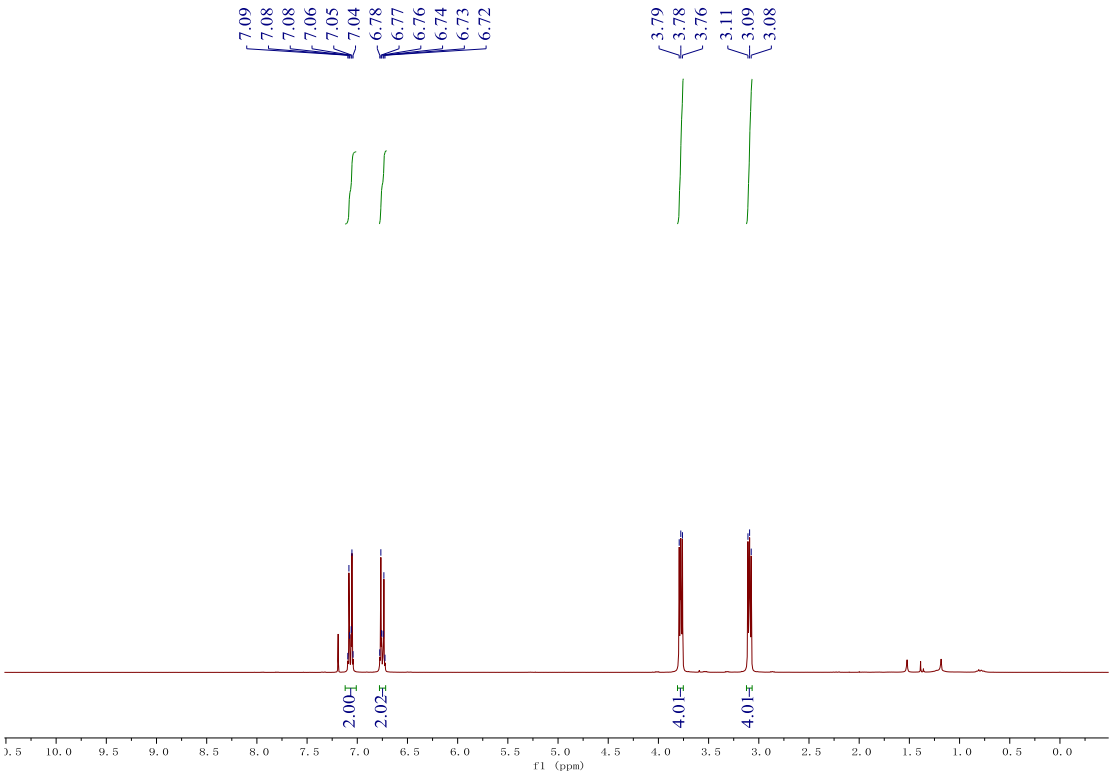
The compound **1o** was obtained as a white solid in 83% yield using 4-morpholinoaniline following

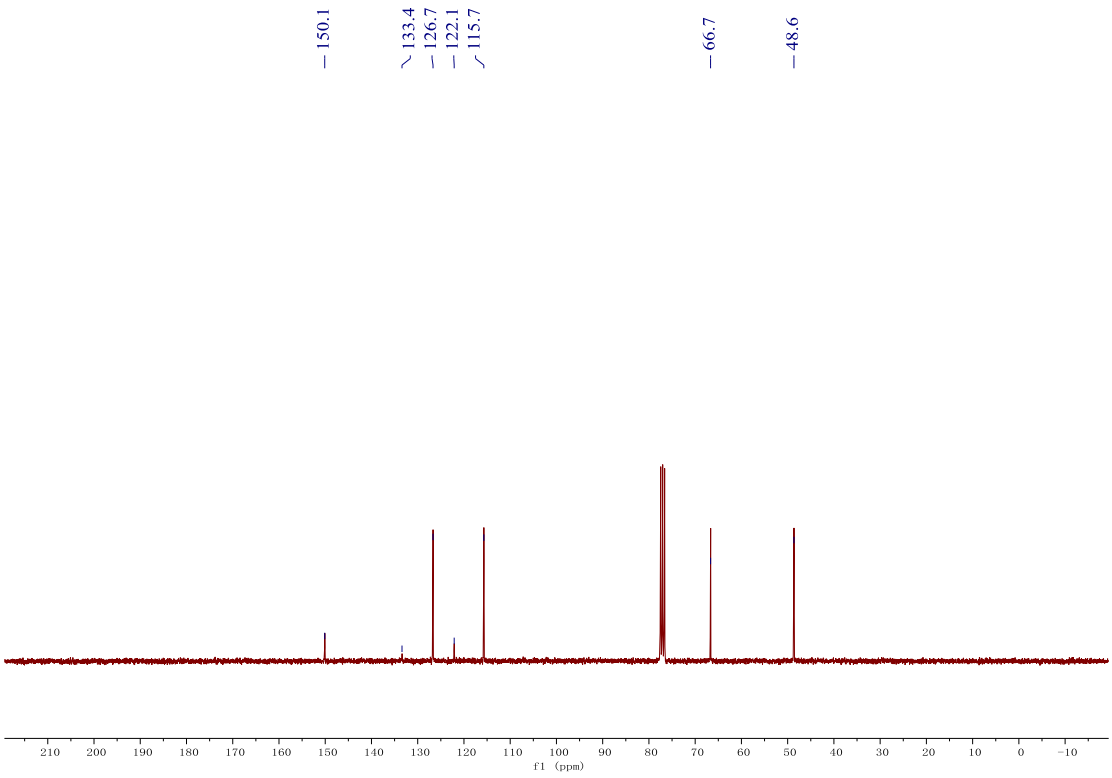
the general procedure A after column chromatography on silica gel with pentane/ethyl acetate (8/1).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.12 – 7.01 (m, 2H), 6.78 – 6.72 (m, 2H), 3.81 – 3.75 (m, 4H), 3.12 – 3.07 (m, 4H).

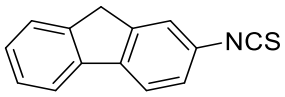
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 150.1, 133.4, 126.7, 122.1, 115.7, 66.7, 48.6.

Characterization data matched that reported in the literature[9]





2-isothiocyanato-9H-fluorene (1q)

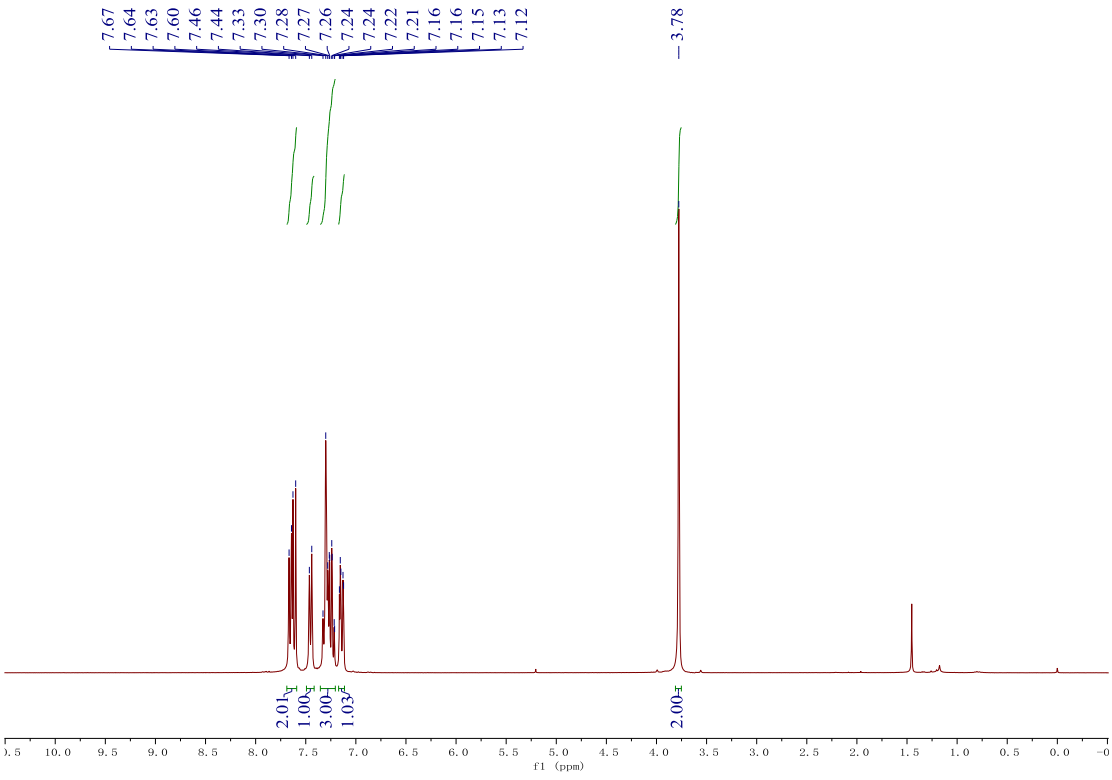


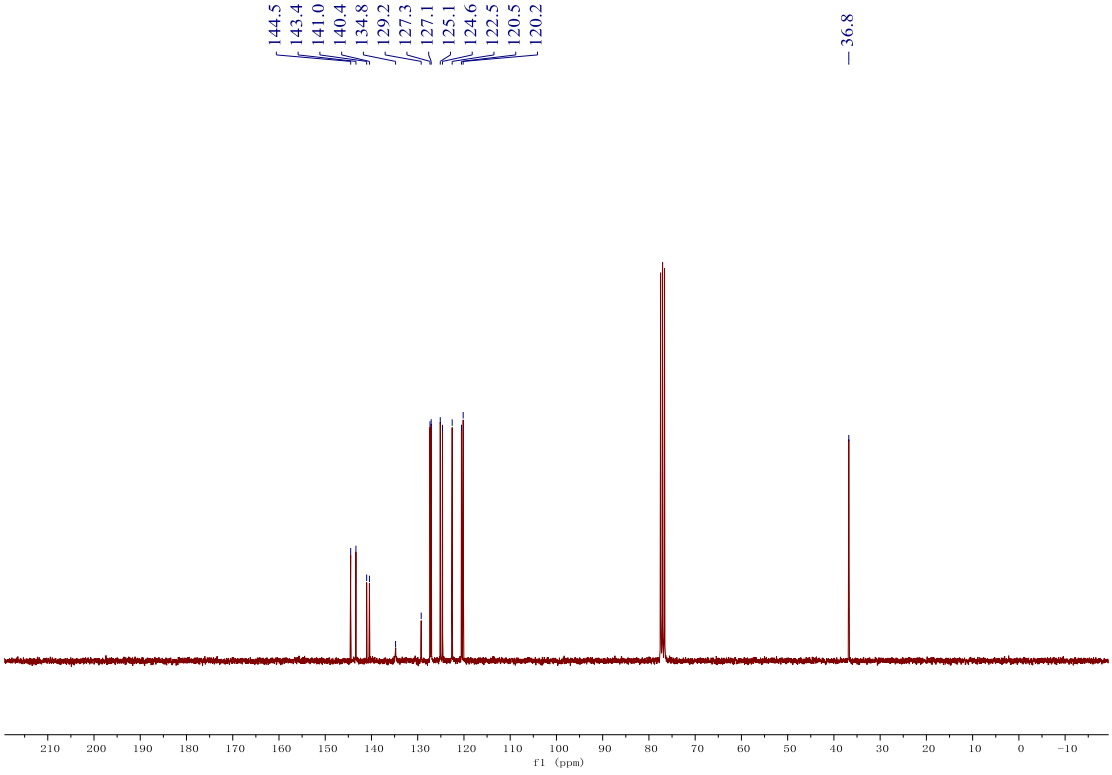
The compound **1q** was obtained as a yellow solid in 50% yield using 9H-fluoren-2-amine following the general procedure A after column chromatography on silica gel with pentane/ethyl acetate (20/1).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.67 – 7.67 (m, 2H), 7.45 (d, *J* = 7.2 Hz, 1H), 7.35 – 7.20 (m, 3H), 7.17 – 7.11 (m, 1H), 3.78 (s, 2H).

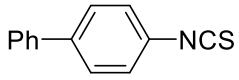
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 144.5, 143.4, 141.0, 140.4, 134.8, 129.2, 127.3, 127.1, 125.1, 124.6, 122.5, 120.5, 120.2, 36.8.

Characterization data matched that reported in the literature[2]





4-isothiocyanato-1,1'-biphenyl (1r)



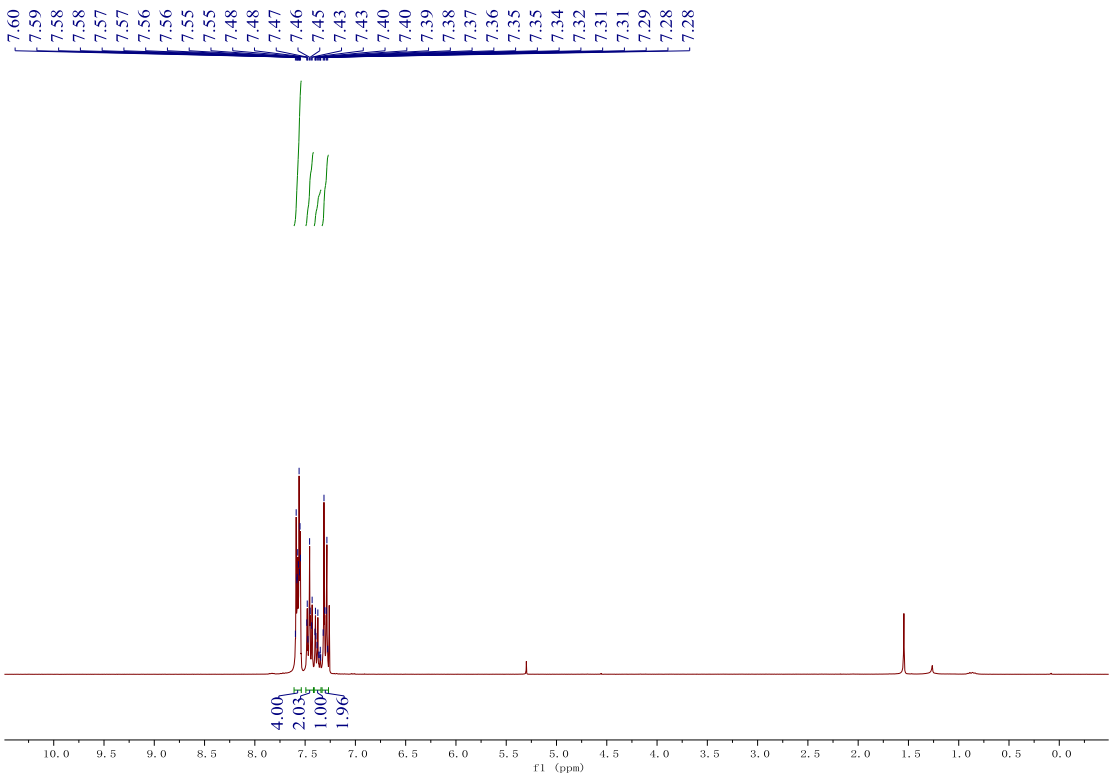
The compound **1r** was obtained as a white solid in 75% yield using 4-(benzyloxy)aniline following

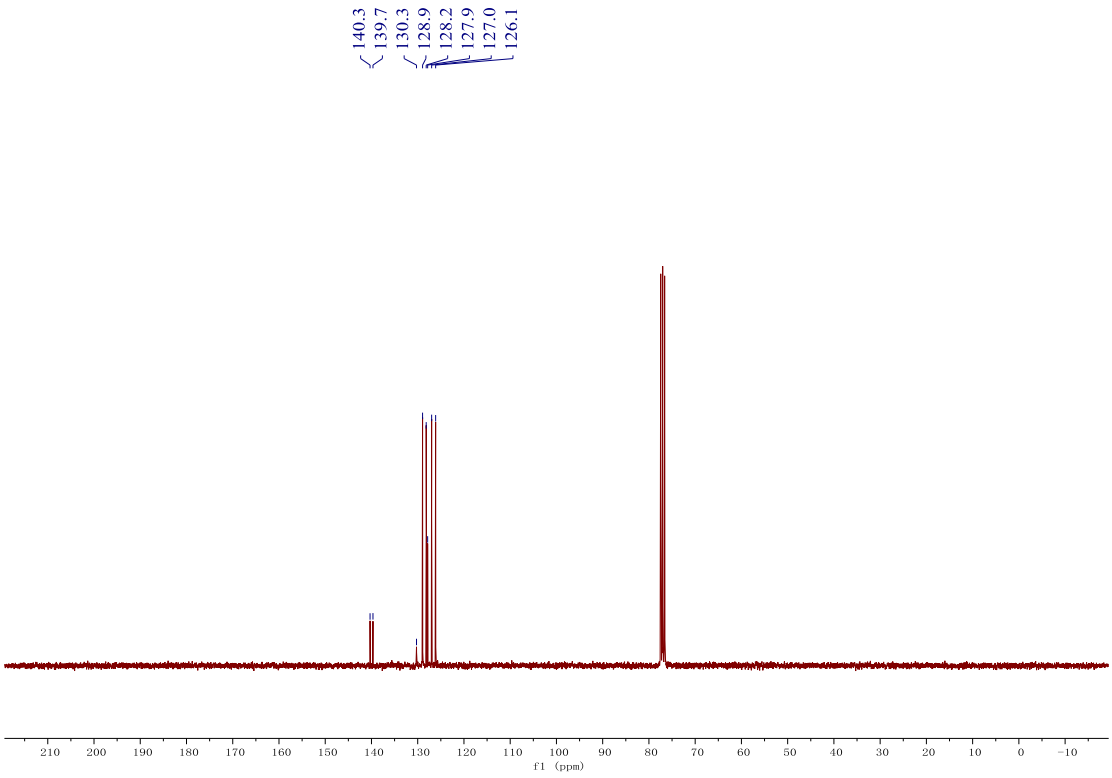
the general procedure A after column chromatography on silica gel with pentane.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.61 – 7.54 (m, 4H), 7.49 – 7.42 (m, 2H), 7.41 – 7.34 (m, 1H), 7.33 – 7.27 (m, 2H).

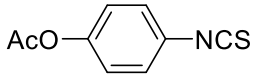
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 140.3, 139.7, 130.3, 128.9, 128.2, 127.9, 127.0, 126.1.

Characterization data matched that reported in the literature[6]





4-isothiocyanatophenyl acetate (1x)



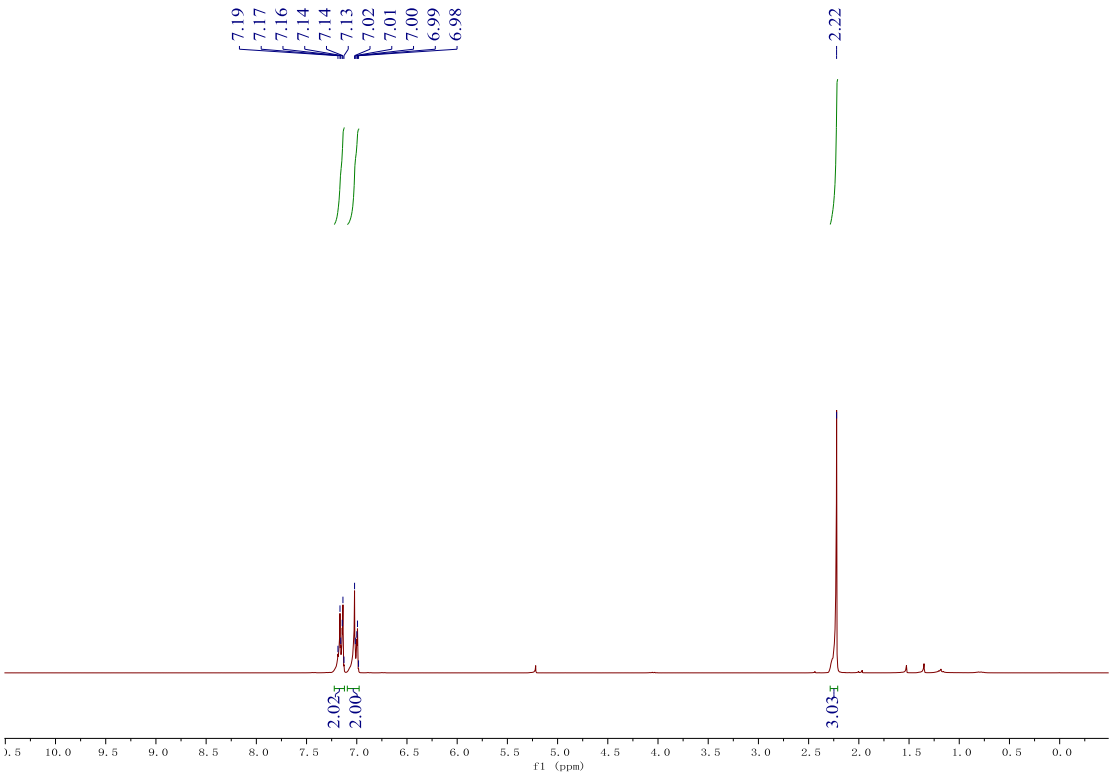
4-Isothiocyanatophenol was obtained as a yellowish oil in 80% yield using 4-aminophenol following the general procedure A after column chromatography on silica gel with cyclohexane/ethyl acetate (20/1).

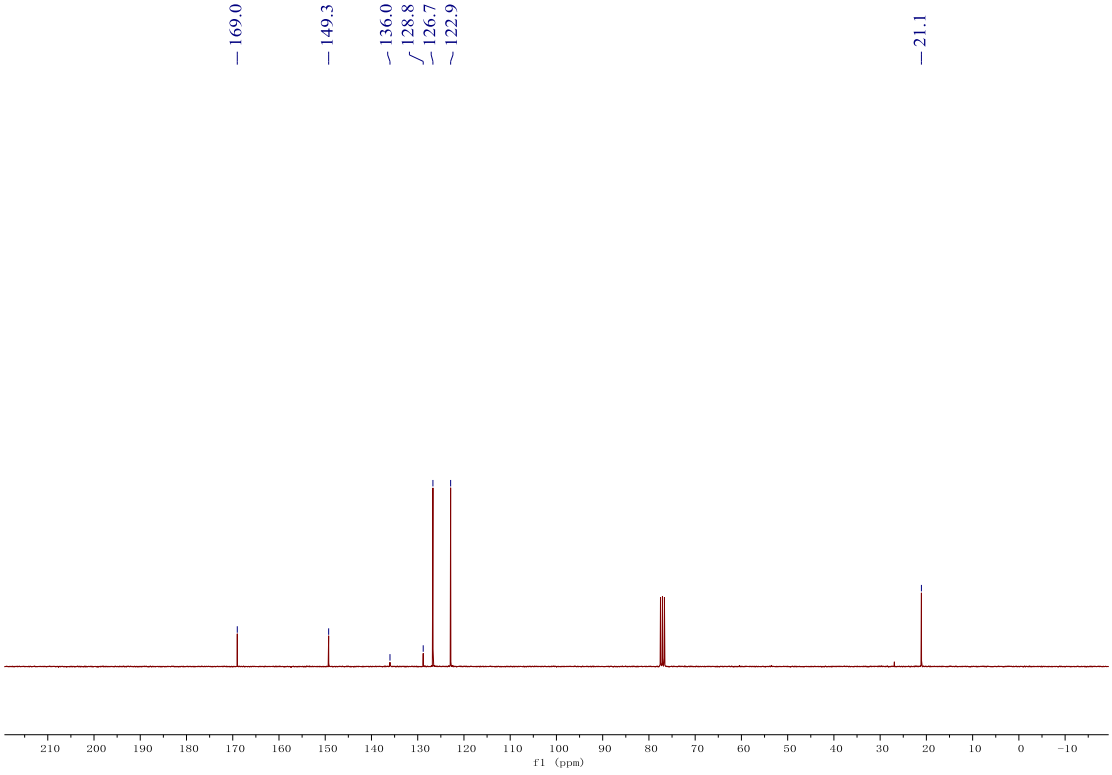
The compound **1x** was obtained as a yellow solid in 81% yield following literature's procedure[10]: Acetic anhydride (0.95 mL, 2.0 equiv.), DIPEA (1.23 mL, 1.4 equiv.), and DMAP (61.1 mg, 0.1 equiv.) were added to a solution of the 4-isothiocyanatophenol (755 mg, 1.0 equiv.) in Acetonitrile (5 mL). The mixture was stirred at room temperature until starting material is consumed. The reaction was poured into water (10 mL), and the mixture was stirred vigorously for 30 min. The aqueous phase was extracted with ethyl acetate (3×10 mL). The combined organic layers were washed with 1 M aq. HCl (10 mL), saturated aq. $NaHCO_3$ (10 mL), water (10 mL) and brine (10 mL), and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced and vacuum to give the compound **1x** without further purification.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.22 – 7.12 (m, 2H), 7.09 – 6.98 (m, 2H), 2.22 (s, 3H).

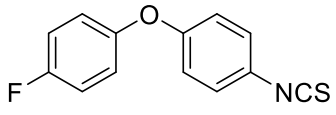
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 169.0, 149.3, 136.0, 128.8, 126.7, 122.9, 21.1.

Characterization data matched that reported in the literature[2]





1-fluoro-4-(4-isothiocyanatophenoxy)benzene (1ab)



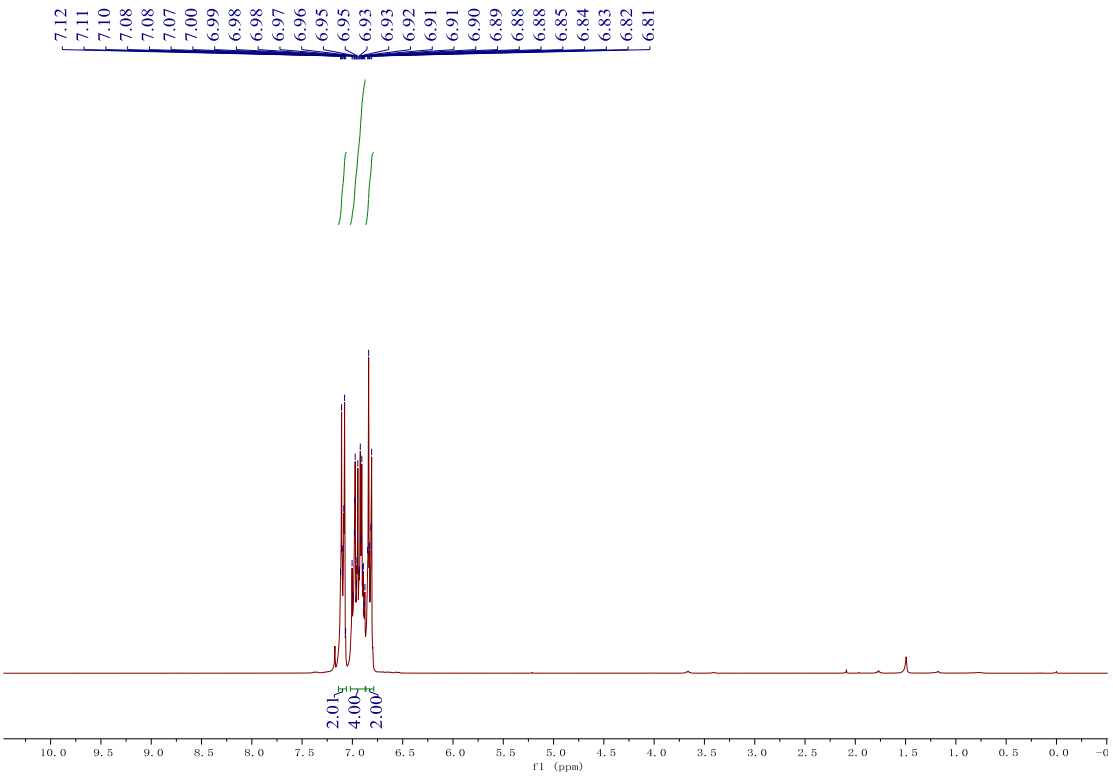
The compound **1ab** was obtained as a colorless oil in 89% yield using 4-(4-fluorophenoxy)aniline following the general procedure A after column chromatography on silica gel with pentane.

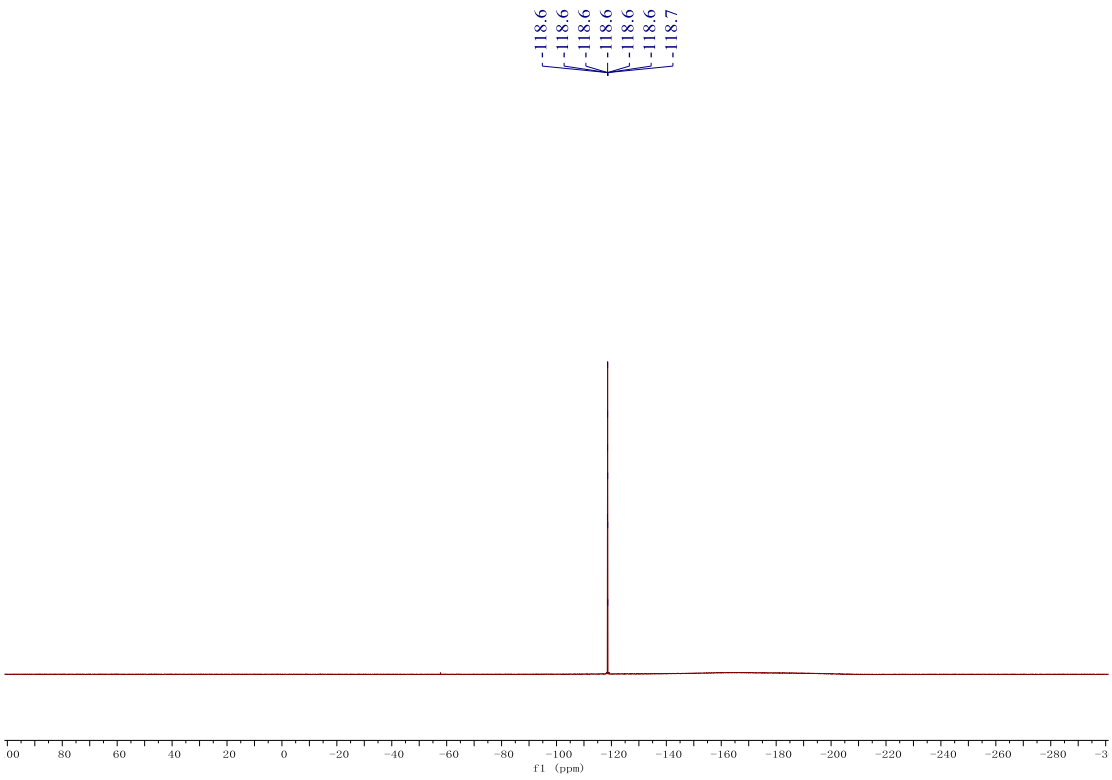
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.12 – 7.07 (m, 2H), 7.00 – 6.88 (m, 4H), 6.87 – 6.79 (m, 2H).

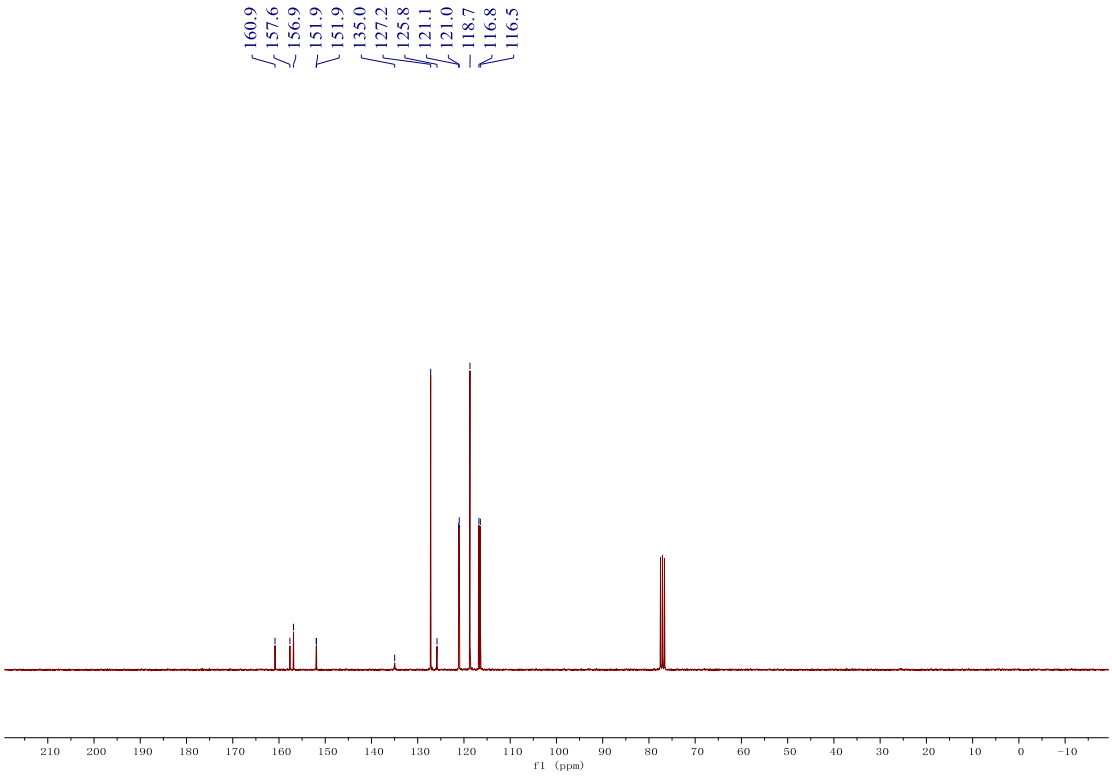
^{19}F NMR (282 MHz, Chloroform-*d*) δ -118.6 – -118.7 (m).

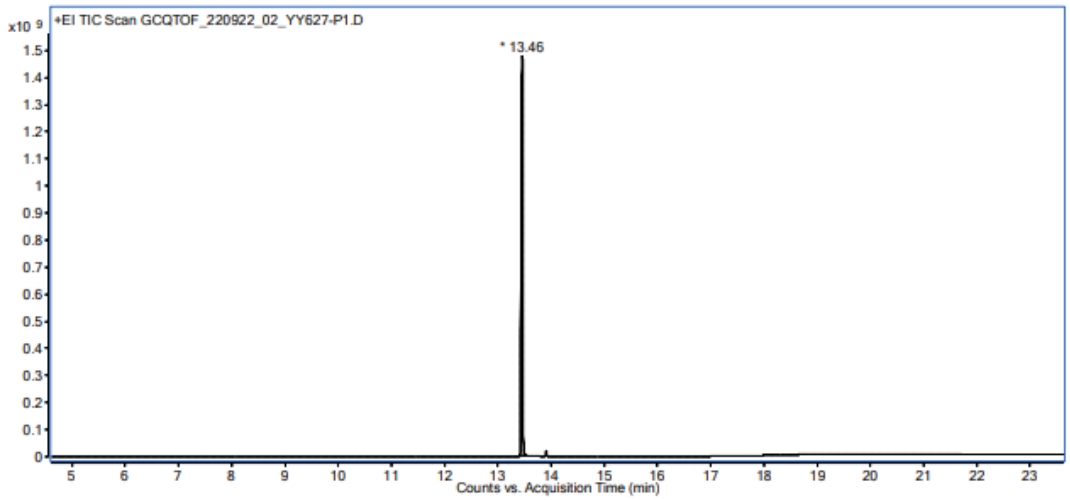
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 159.3 (d, J = 242.9 Hz), 156.9, 151.9 (d, J = 2.7 Hz), 135.0, 127.2, 125.8, 121.1 (d, J = 8.3 Hz), 118.7, 116.6 (d, J = 23.4 Hz).

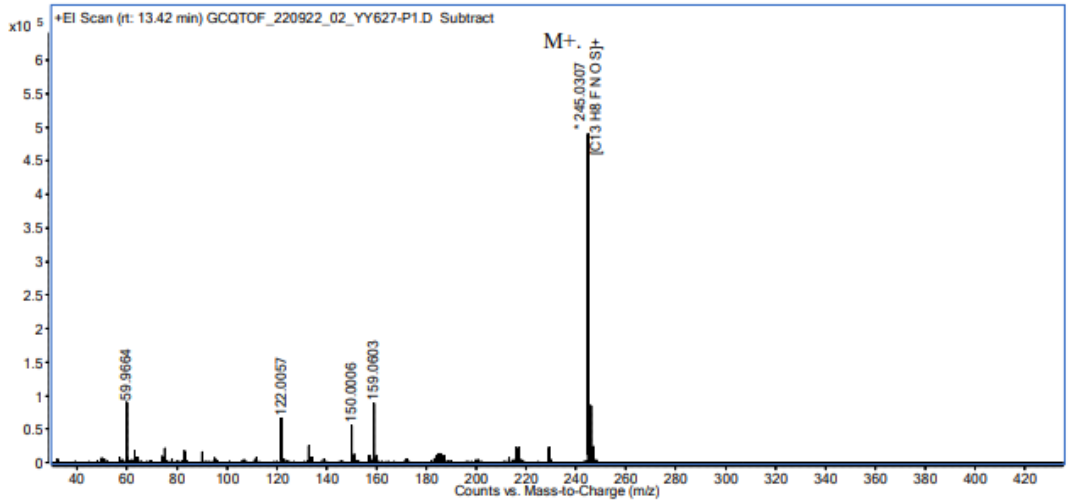
HRMS (EI) calculated for $C_{13}H_8FNOS$: 245.0305 $[M]^+$, Found: 245.0307.

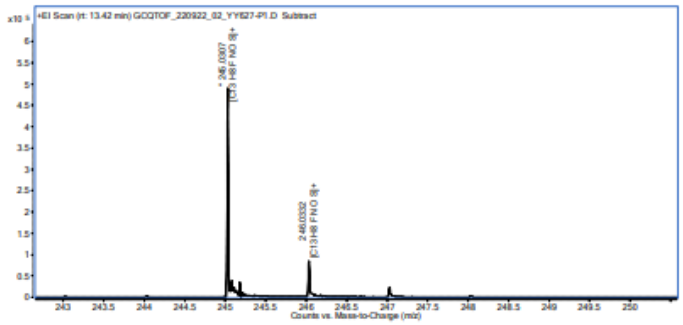



-118.6
-118.6
-118.6
-118.6
-118.6
-118.6
-118.7
f1 (ppm)


160.9
157.6
156.9
151.9
151.9
135.0
127.2
125.8
121.1
121.0
118.7
116.8
116.5
f1 (ppm)

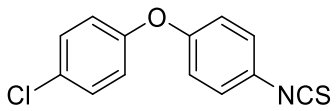






m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
245.0307	C3H8FNOS	245.0305	0.8	$[M]^{+\cdot}$

1-chloro-4-(4-isothiocyanatophenoxy)benzene (1ac)



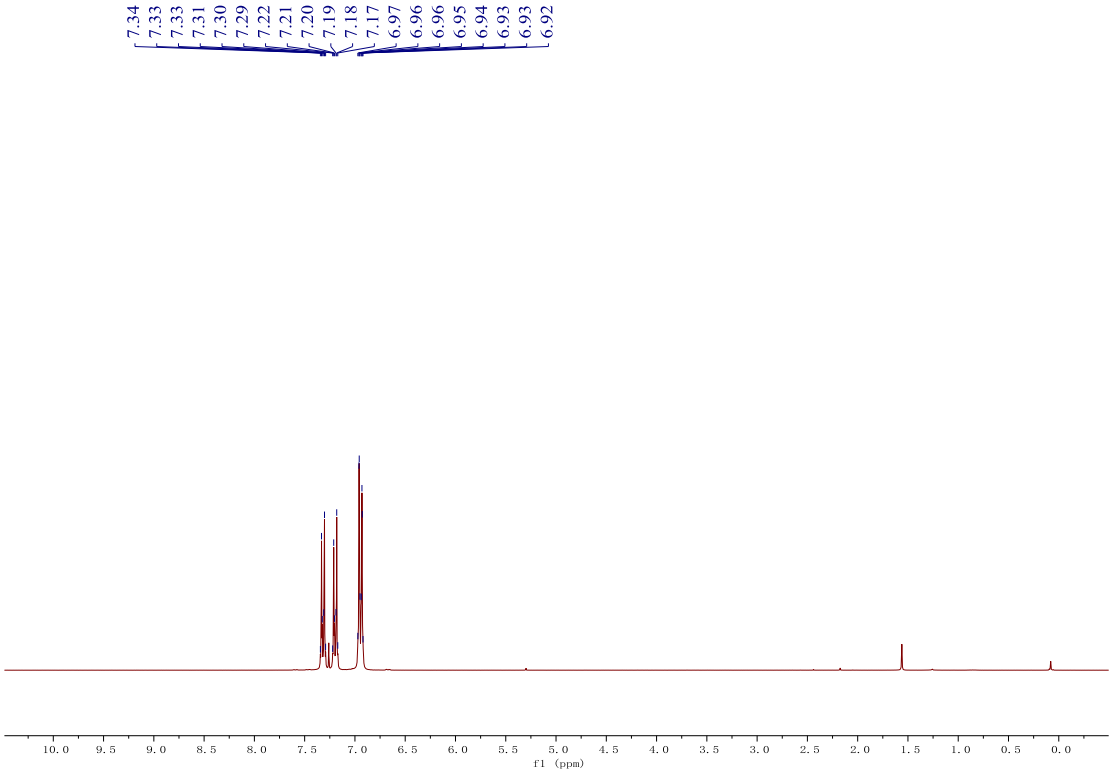
The compound **1ac** was obtained as a colorless oil in 80% yield using 4-(4-chlorophenoxy)aniline following the general procedure C after column chromatography on silica gel with pentane.

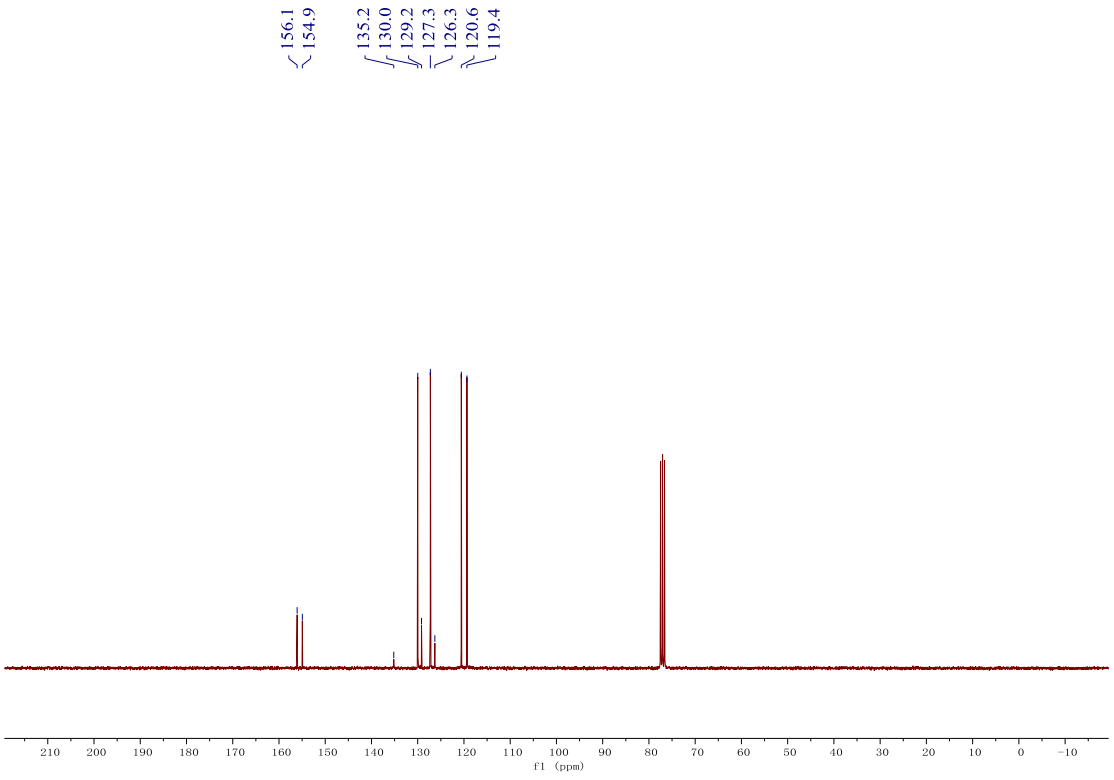
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.49 – 7.42 (m, 2H), 7.23 – 7.17 (m, 2H), 6.97 – 6.92 (m, 2H),

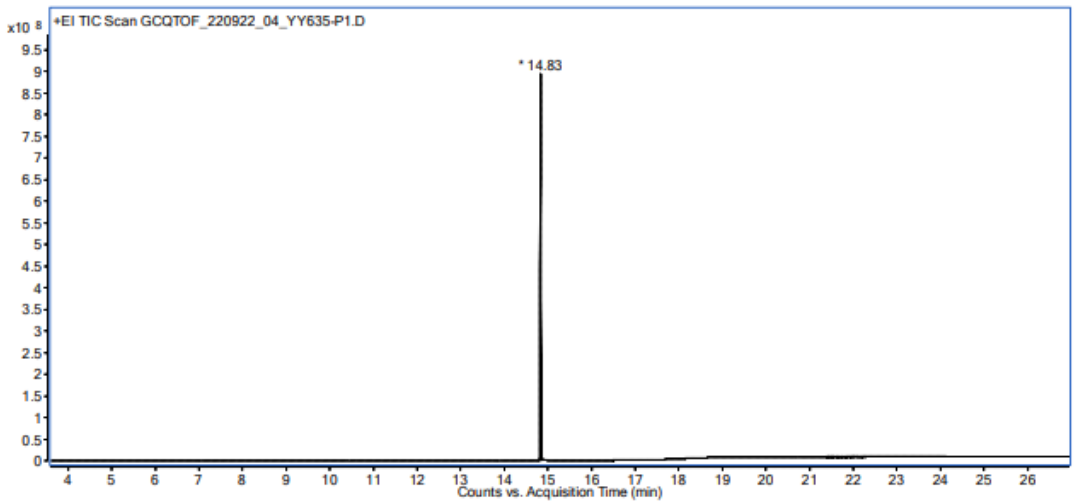
6.92 – 6.86 (m, 2H).

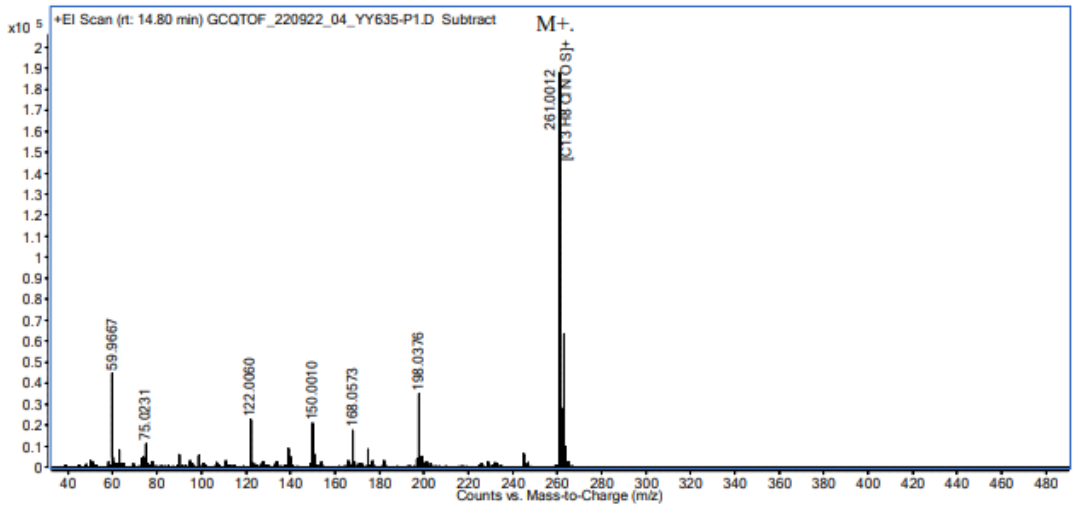
$^{13}C\{^{1}H\}$ NMR (75 MHz, Chloroform-*d*) δ 156.1, 154.9, 135.2, 130.0, 129.2, 127.3, 126.3, 120.6, 119.4.

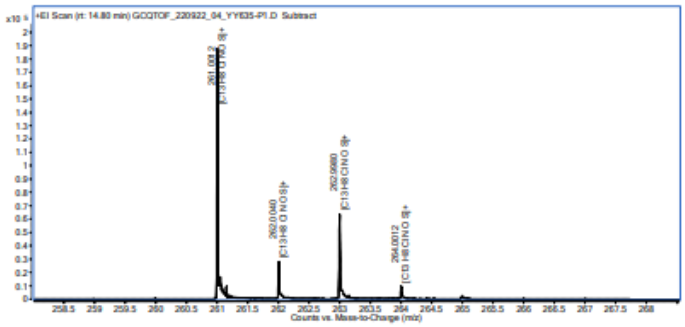
HRMS (EI) calculated for $C_{13}H_8ClNOS$: 261.0010 $[M]^+$, Found: 261.0012.




156.1
154.9
135.2
130.0
129.2
127.3
126.3
120.6
119.4
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)

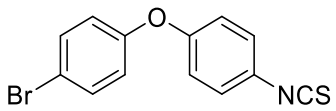






m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
261.0012	C13H8ClNOS	261.0010	0.8	$[M]^{+\cdot}$

1-bromo-4-(4-isothiocyanatophenoxy)benzene (1ad)

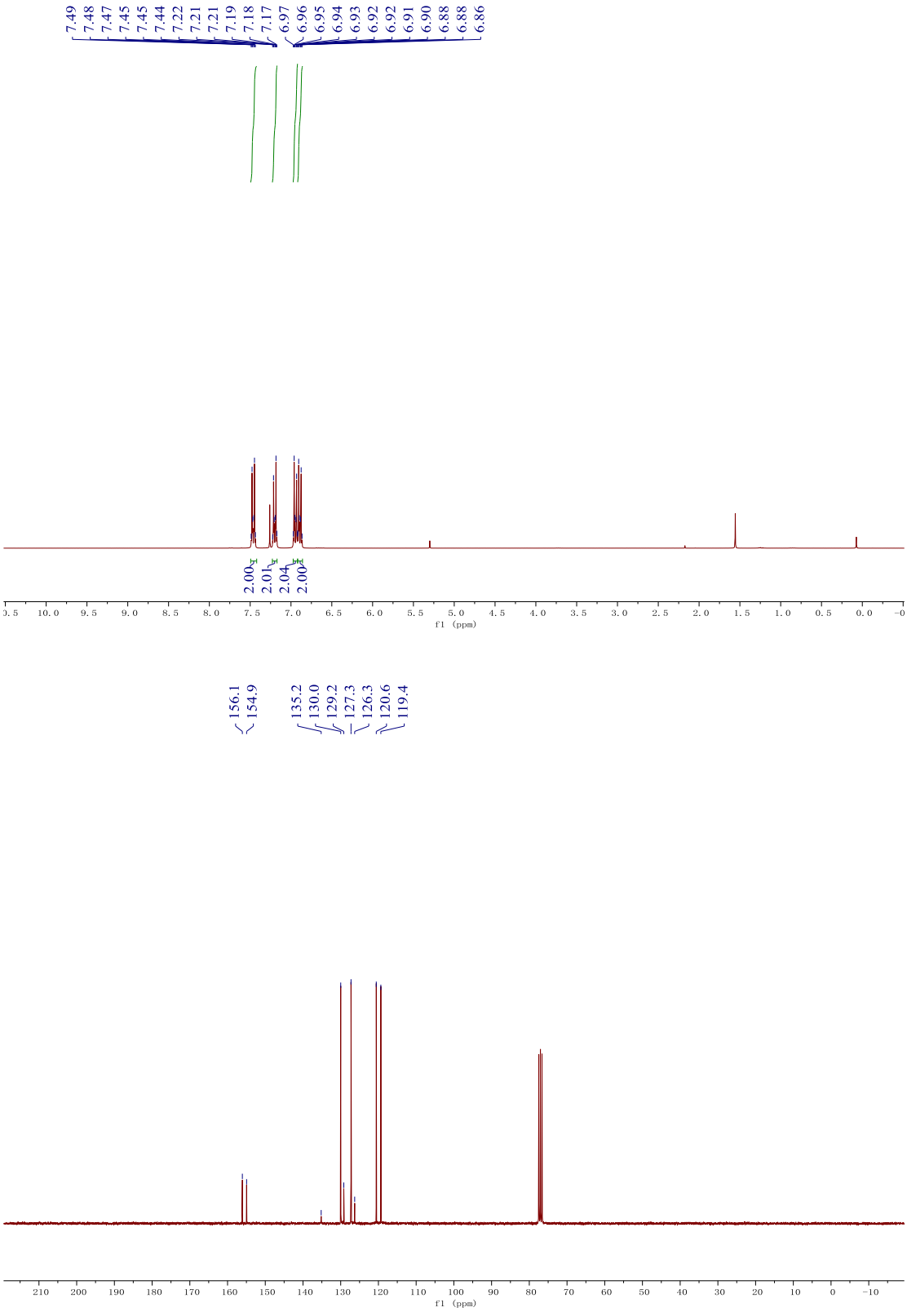


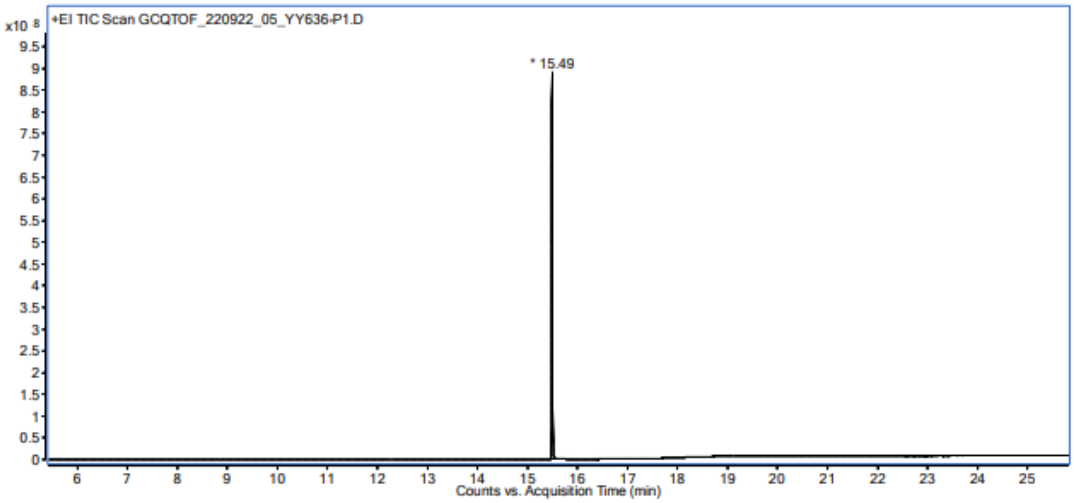
The compound **1ad** was obtained as a colorless oil in 95% yield using 4-(4-bromophenoxy)aniline following the general procedure C after column chromatography on silica gel with pentane.

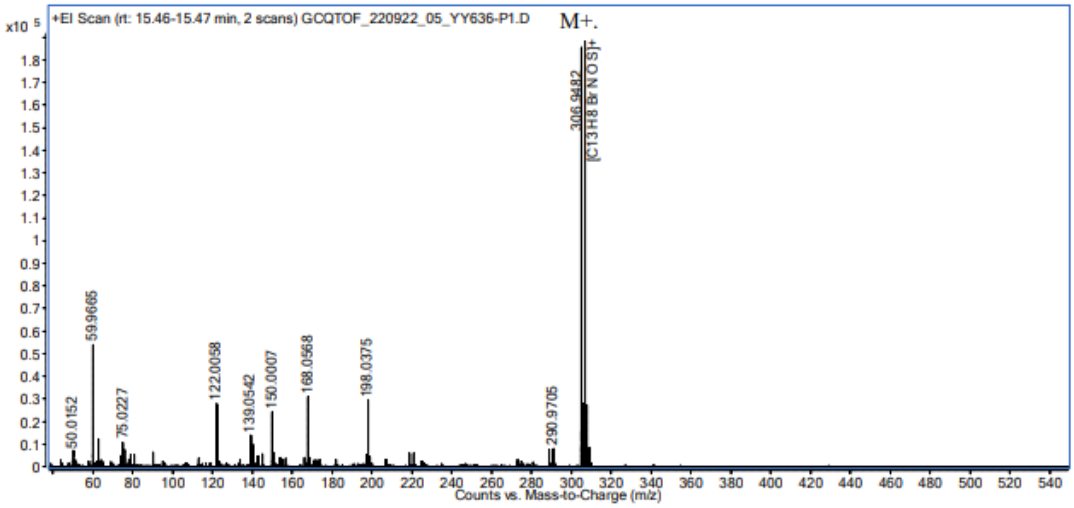
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.38 – 7.26 (m, 1H), 7.25 – 7.14 (m, 1H), 7.00 – 6.89 (m, 3H).

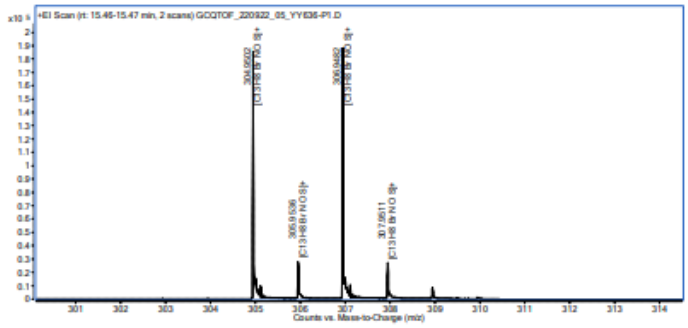
$^{13}C\{^{1}H\}$ NMR (75 MHz, Chloroform-*d*) δ 156.1, 154.9, 130.0, 129.2, 127.3, 126.3, 120.8, 119.4.

HRMS (EI) calculated for $C_{13}H_8BrNOS$: 304.9504 $[M]^+$, Found: 304.9502.



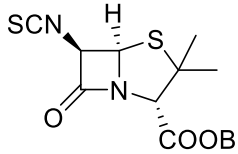






m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
304.9502	C13H8BrNOS	304.9504	-0.7	$[M]^{+\cdot}$

benzyl (2S,5R,6R)-6-isothiocyanato-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate (1af)



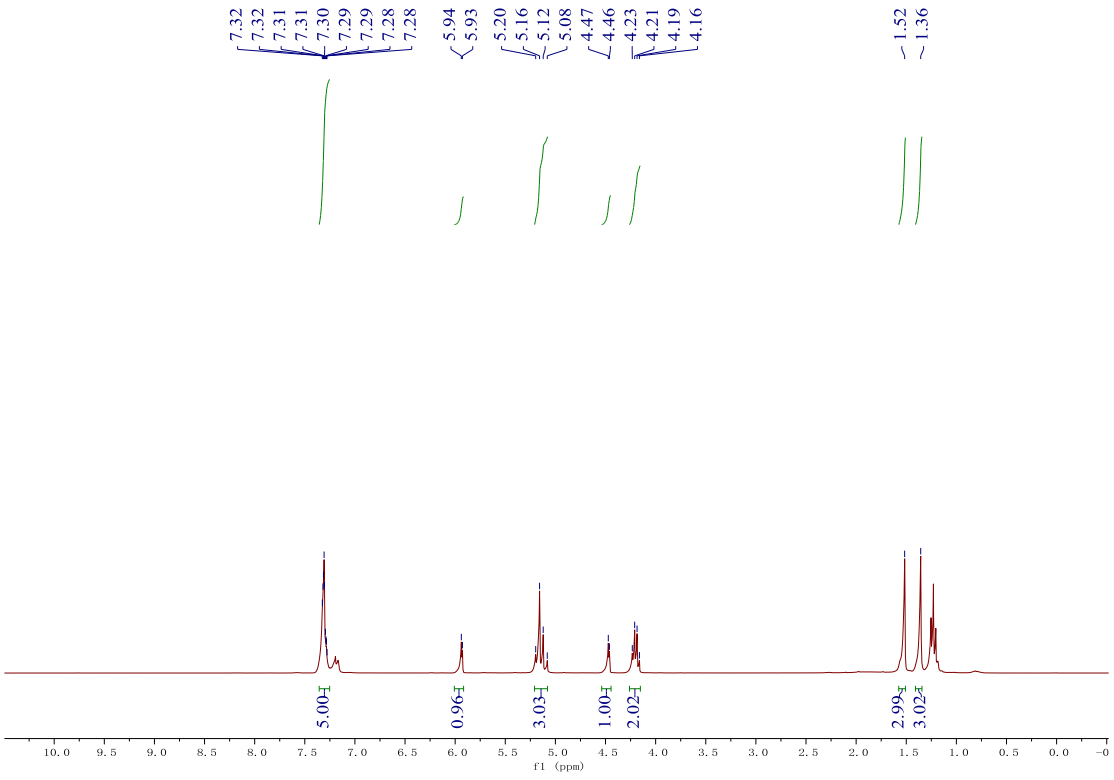
The compound **1af** was obtained as a yellow solid in 95% yield using (2S,5R,6R)-2-((benzyloxy)carbonyl)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptan-6-aminium

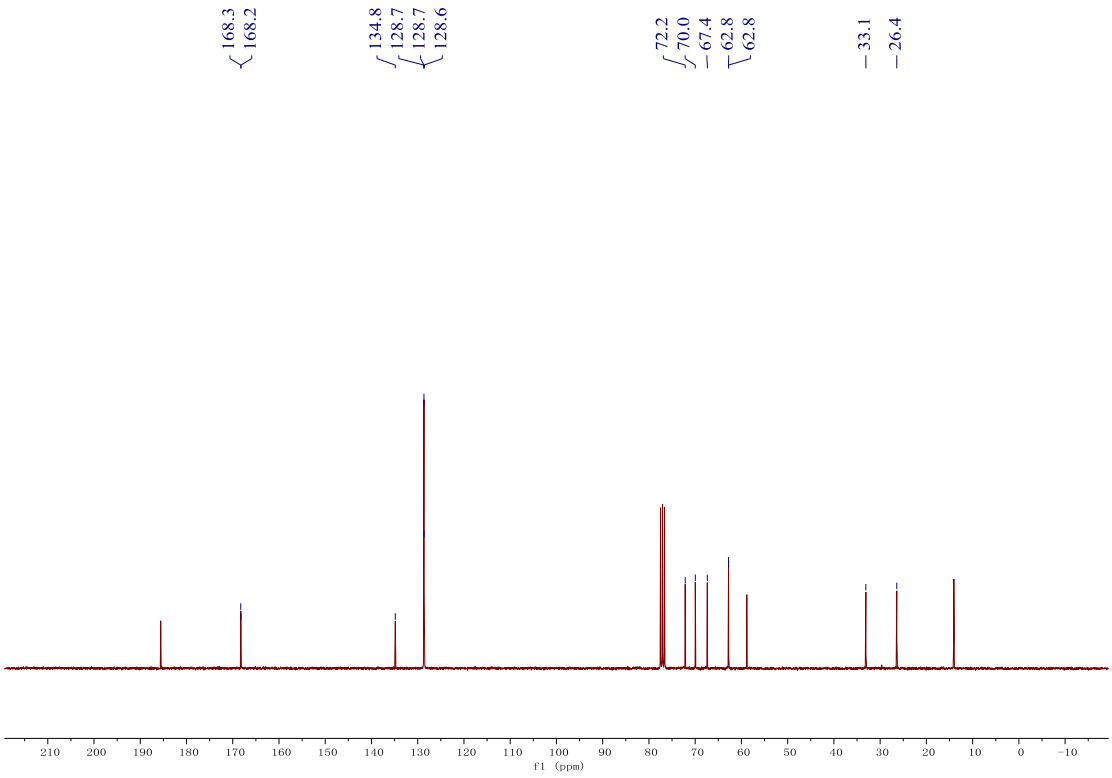
trifluoromethanesulfonate following the general procedure B without further purification.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.36 – 7.25 (m, 5H), 5.93 (d, *J* = 3.3 Hz, 1H), 5.20 – 5.08 (m, 3H), 4.47 (d, *J* = 3.4 Hz, 1H), 1.52 (s, 3H), 1.36 (s, 3H).

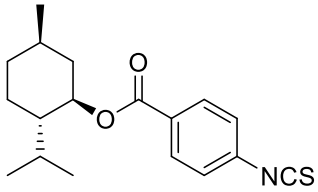
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 168.3, 168.2, 134.8, 128.7, 128.7, 128.6, 72.2, 70.0, 67.4, 62.8, 62.8, 33.1, 26.4.

Characterization data matched that reported in the literature[2]





(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 4-isothiocyanatobenzoate (1ag)



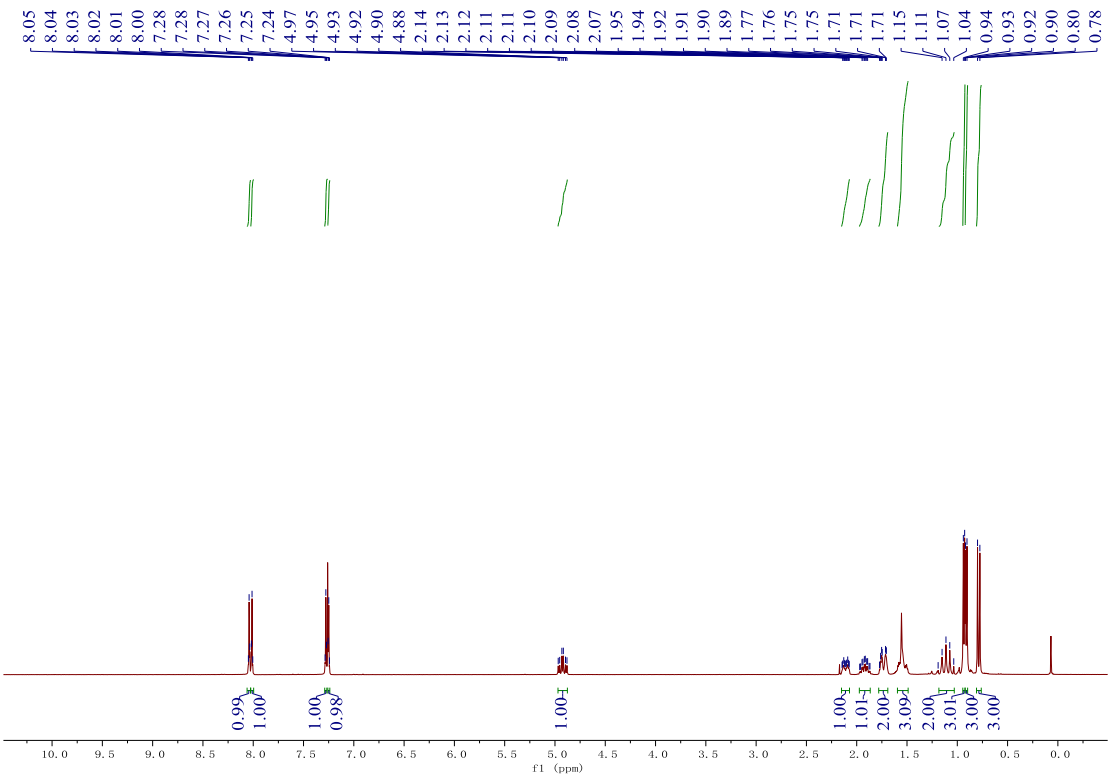
(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 4-aminobenzoate was obtained as a white solid in 99% yield using 4-aminobenzoyl chloride and (1R,2S,5R)-2-isopropyl-5-methylcyclohexan-1-ol following the general procedure D.

The compound **1ag** was obtained as a white solid in 35% yield using (1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 4-aminobenzoate following the general procedure C after column chromatography on silica gel with pentane.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.05 – 8.03 (m, 1H), 8.02 – 8.00 (m, 1H), 7.28 – 7.27 (m, 1H), 7.26 – 7.24 (m, 1H), 4.97 – 4.88 (m, 1H), 2.15 – 2.07 (m, 1H), 1.97 – 1.87 (m, 1H), 1.78 – 1.69 (m, 2H), 1.59 – 1.49 (m, 3H), 1.09 (q, *J* = 11.8 Hz, 2H), 0.93 (d, *J* = 3.9 Hz, 3H), 0.91 (d, *J* = 4.4 Hz, 3H), 0.79 (d, *J* = 6.9 Hz, 3H).

^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 164.9, 137.6, 135.4, 131.0, 129.4, 125.6, 75.4, 47.2, 40.9, 34.3, 31.4, 26.6, 23.6, 22.0, 20.7, 16.5.

HRMS (ESI) calculated for $C_{18}H_{24}NO_2S$: 318.1522 $[M+H]^+$, Found: 318.1526.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8.02
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7.26
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7.24
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4.95
4.93
4.92
4.90
4.88
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2.11
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1.94
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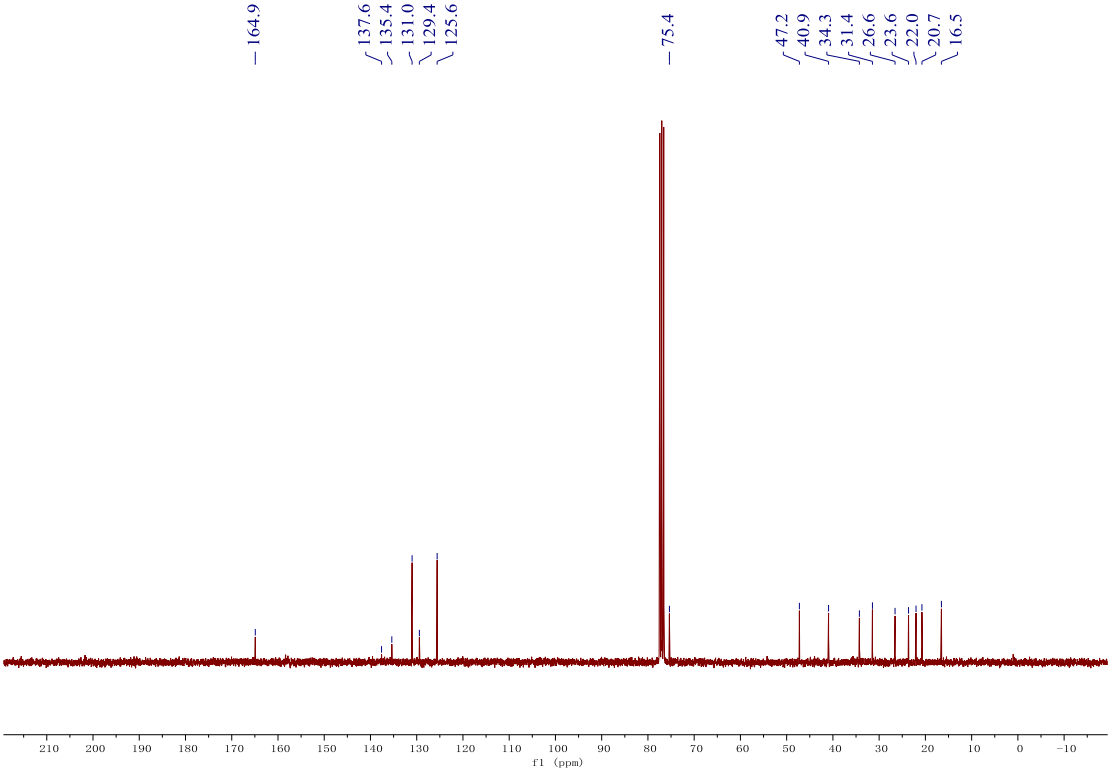
1.75
1.75
1.71
1.71
1.71
1.15
1.11
1.07
1.04
0.94
0.93
0.92
0.90
0.80
0.78

0.99
1.00
1.00
0.98
1.00
1.00
1.01
2.00
3.09
2.00
3.01
3.00
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


164.9
137.6
135.4
131.0
129.4
125.6
75.4
47.2
40.9
34.3
31.4
26.6
23.6
22.0
20.7
16.5
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)

CENTRE COMMUN DE SPECTROMETRIE DE MASSE

Analysis Info

Analysis Name	Impact2_220912_01_YY617-P1.d		
Method	Tune_pos_Standard.m	Acquisition Date	9/12/2022 10:29:27 AM
Comment		Instrument / Ser#	impact II 1825265.10081

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
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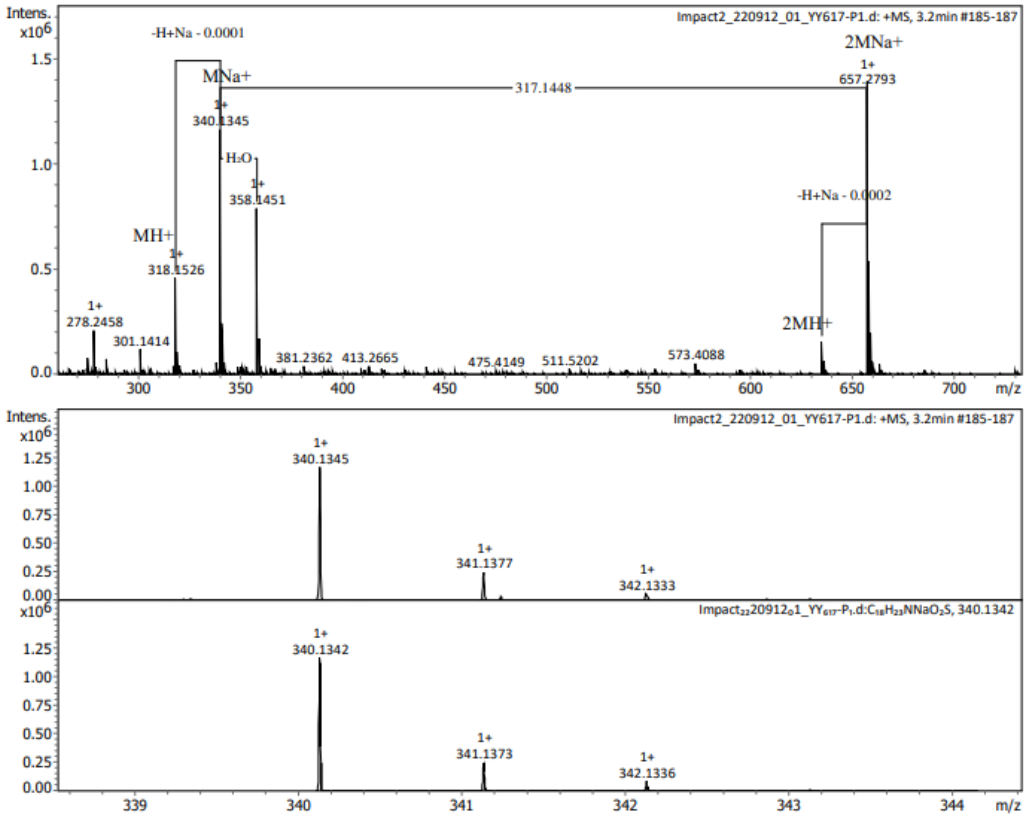
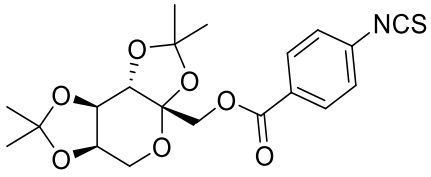
Scan End	1000 m/z	Set Collision Cell RF	1500.0 Vpp	Set Divert Valve	Source



Meas. m/z	Ion Formula	m/z	Sum Formula	err [ppm]	mSigma	Adduct	z
318.1526	C18H24NO2S	318.1522	C18H23NO2S	-1.2	15.4	M+H	1+
340.1345	C18H23NNaO2S	340.1342		-0.9	12.3	M+Na	1+
635.2976	C36H47N2O4S2	635.2972		-0.6	12.9	2M+H	1+
657.2793	C36H46N2NaO4S2	657.2791		-0.3	19.9	2M+Na	1+

((3aS,5aR,8aR,8bS)-2,2,7,7-tetramethyltetrahydro-3aH-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-3a-yl)methyl 4-isothiocyanatobenzoate (1ah)



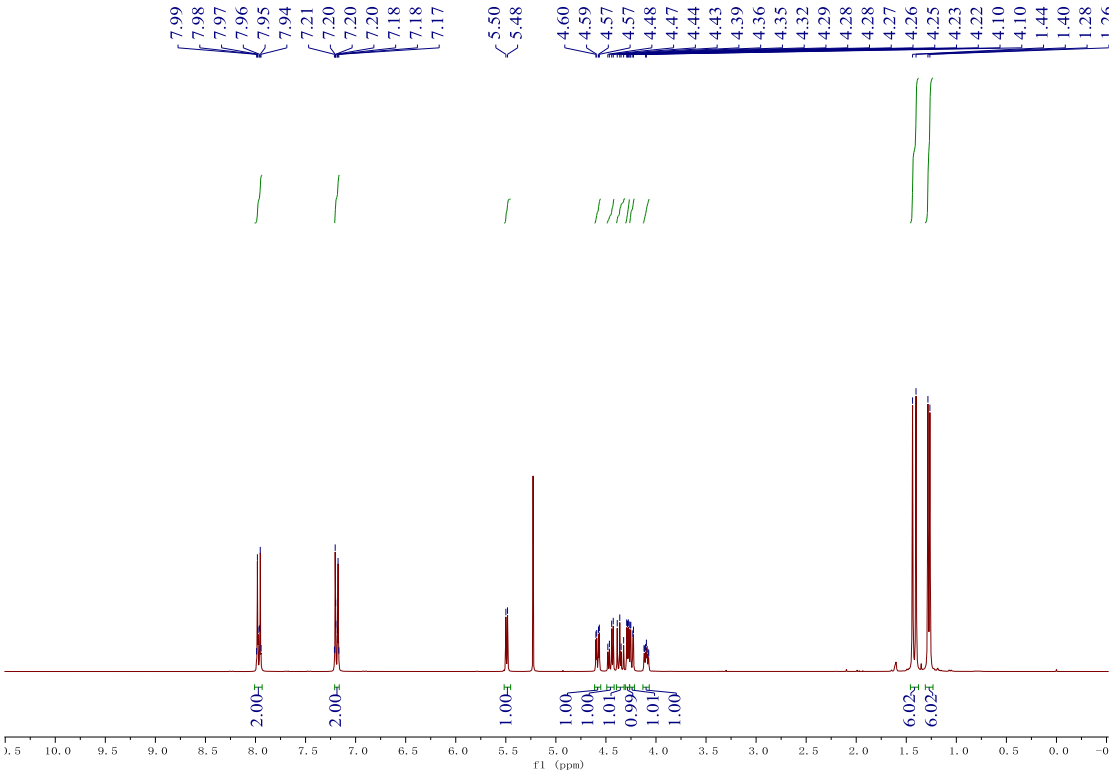
((3aS,5aR,8aR,8bS)-2,2,7,7-tetramethyltetrahydro-3aH-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-3a-yl)methyl 4-aminobenzoate was obtained as a white solid in 99% yield using 4-aminobenzoyl chloride and ((3aS,5aR,8aR,8bS)-2,2,7,7-tetramethyltetrahydro-3aH-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-3a-yl)methanol following the general procedure D.

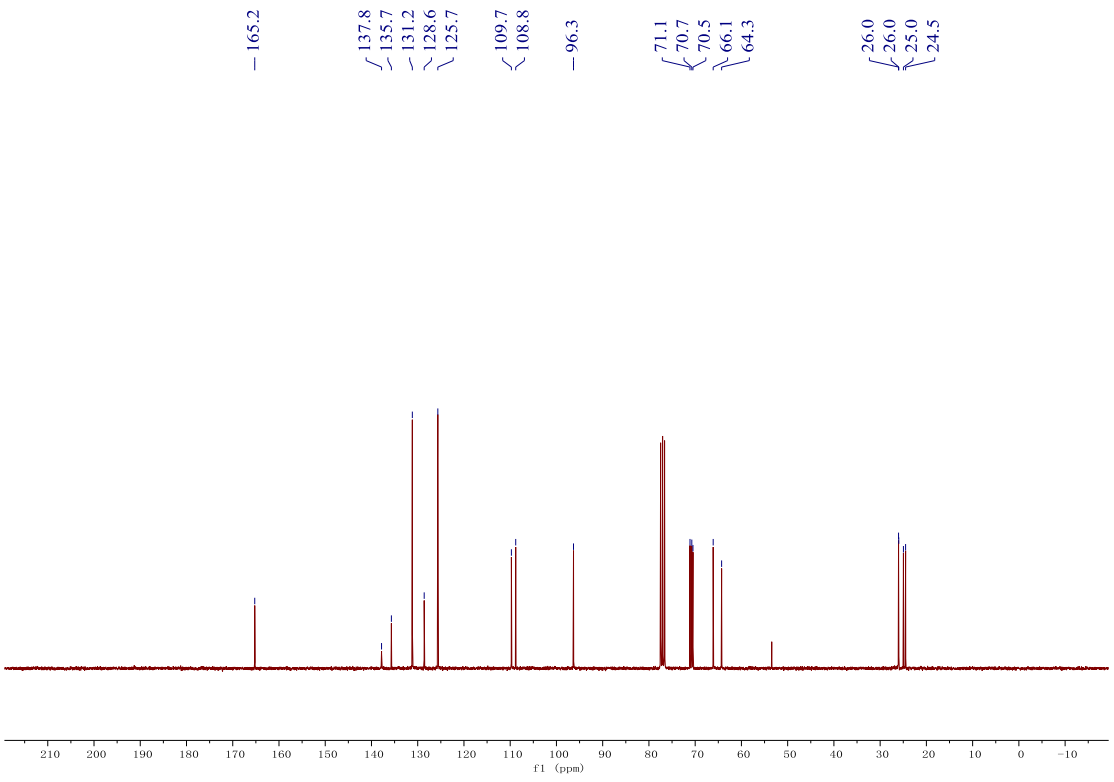
The compound **1ah** was obtained as a colorless oil in 48% yield using ((3aS,5aR,8aR,8bS)-2,2,7,7-tetramethyltetrahydro-3aH-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-3a-yl)methyl 4-aminobenzoate following the general procedure C after column chromatography on silica gel with pentane/ethyl acetate (9/1).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.01 – 7.93 (m, 2H), 7.21 – 7.16 (m, 2H), 5.49 (d, *J* = 4.9 Hz, 1H), 4.60 – 4.57 (m, 1H), 4.48 – 4.43 (m, 1H), 4.39 – 4.32 (m, 1H), 4.29 – 4.27 (m, 1H), 4.26 – 4.22 (m, 1H), 4.12 – 4.07 (m, 1H), 1.42 (d, *J* = 10.3 Hz, 6H), 1.27 (d, *J* = 5.9 Hz, 6H).

^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 165.2, 137.8, 135.7, 131.7, 128.6, 125.7, 109.7, 108.8, 96.3, 71.1, 70.7, 70.5, 66.1, 64.3, 26.0, 26.0, 25.0, 24.5.

HRMS (EI) calculated for $C_{20}H_{24}NO_7S$: 422.1276 $[M+H]^+$, Found: 422.1268.




165.2
137.8
135.7
131.2
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125.7
109.7
108.8
96.3
71.1
70.7
70.5
66.1
64.3
26.0
26.0
25.0
24.5
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)

CENTRE COMMUN DE SPECTROMETRIE DE MASSE

Analysis Info

Analysis Name	Impact2_220929_02_YY643-P1.d		
Method	Tune_pos_Standard.m	Acquisition Date	9/29/2022 5:11:51 PM
Comment		Instrument / Ser#	impact II 1825265.10081

Acquisition Parameter

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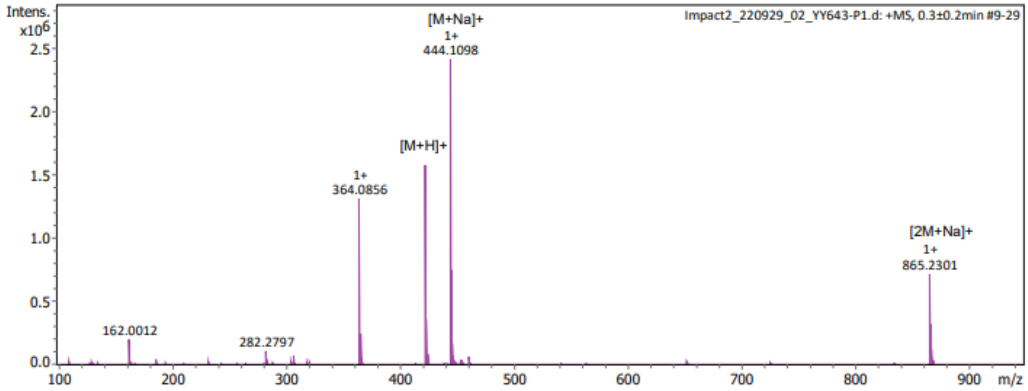
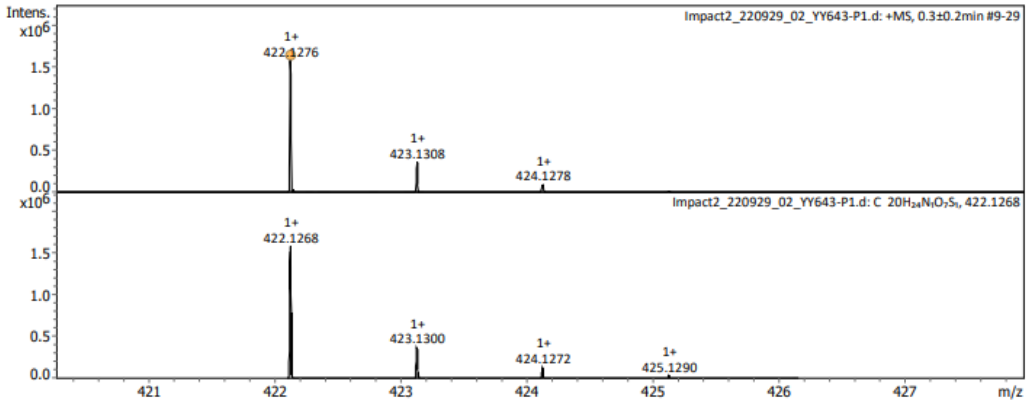
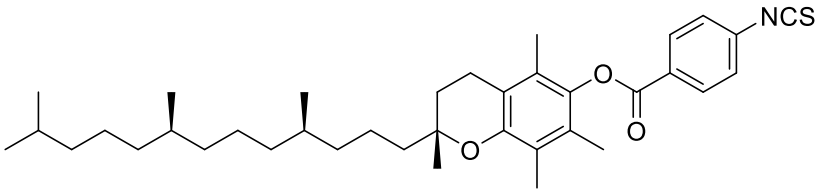
Scan End	1000 m/z	Set Collision Cell RF	750.0 Vpp	Set Divert Valve	Source





Meas. m/z	Ion Formula	m/z	Sum Formula	err [ppm]	mSigma	Adduct	z
422.1276	C20H24NO7S	422.1268	C20H23NO7S	-2.0	16.1	M+H	1+
444.1098	C20H23NNaO7S	444.1087		-2.3	39.8	M+Na	1+
865.2301	C40H46N2NaO14S2	865.2283		-2.1	25.0	2M+Na	1+

(R)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl 4-isothiocyanatobenzoate (1ai)



(R)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl 4-aminobenzoate was obtained as a white solid in 99% yield using 4-aminobenzoyl chloride and (R)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-ol following the general procedure D.

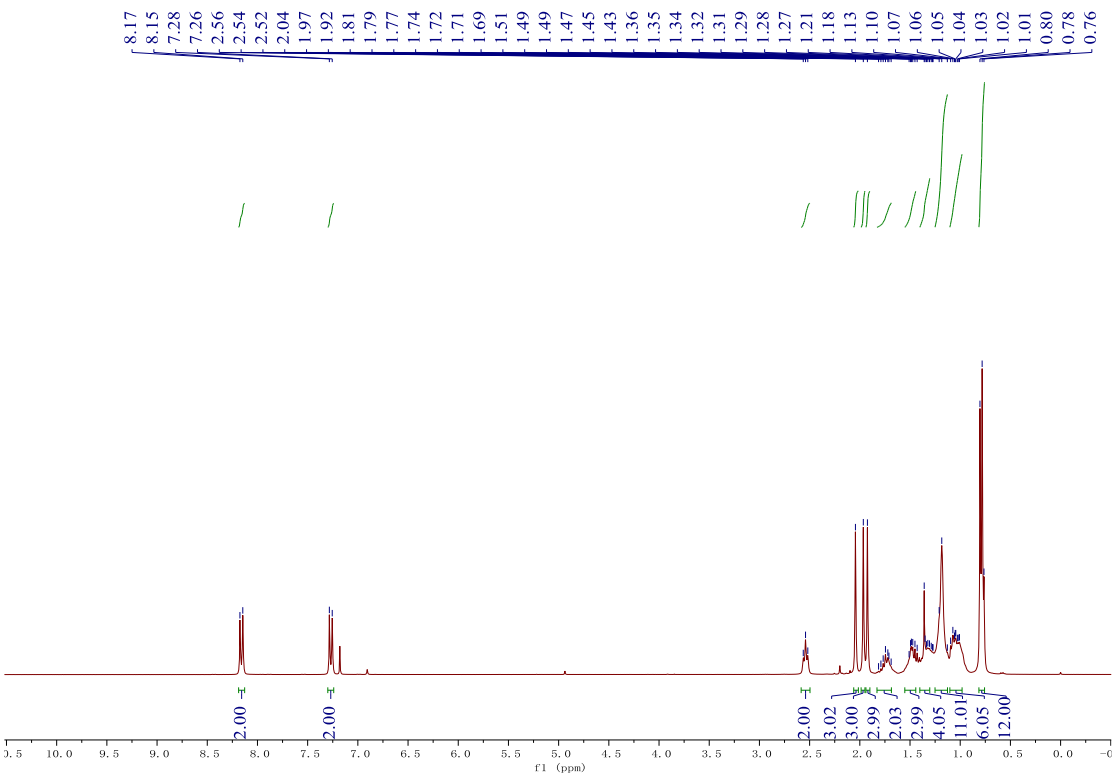
The compound **1ai** was obtained as a yellow oil in 56% yield using(R)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl 4-aminobenzoate following the general procedure

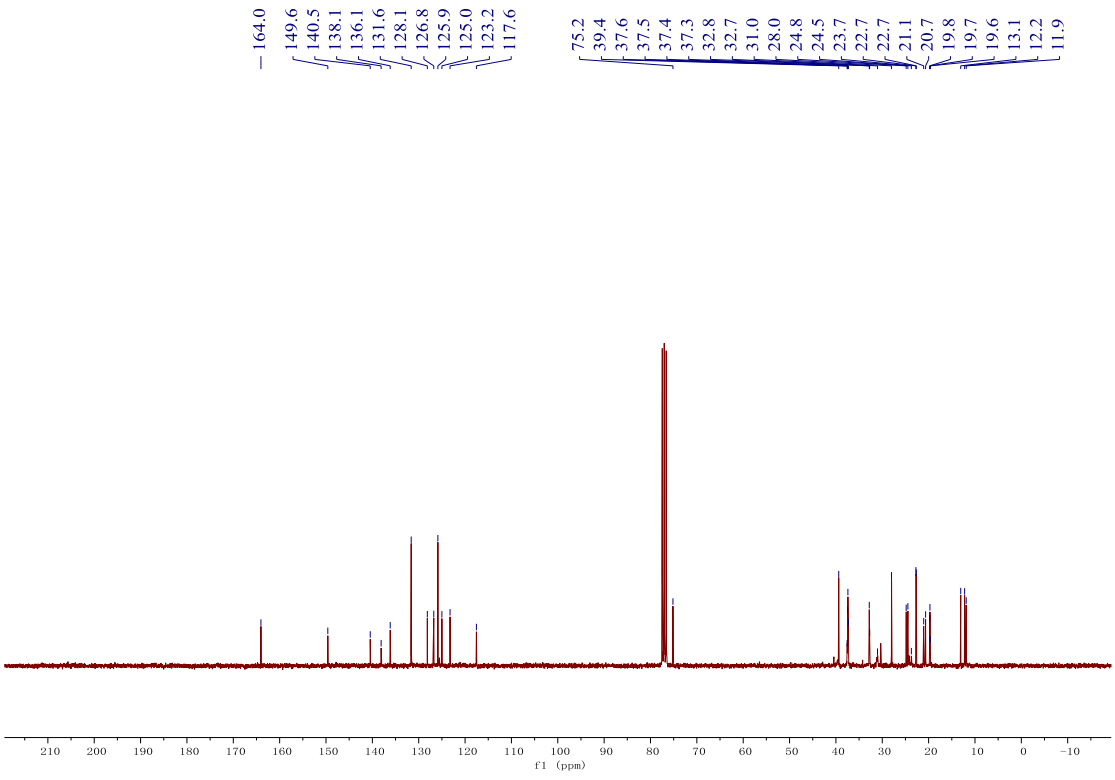
C after column chromatography on silica gel with pentane/ethyl acetate (50/1).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.16 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 8.6 Hz, 2H), 2.54 (t, *J* = 6.8 Hz, 2H), 2.04 (s, 3H), 1.97 (s, 3H), 1.92 (s, 3H), 1.81 – 1.69 (m, 2H), 1.55 – 1.44 (m, 3H), 1.40 – 1.30 (m, 4H), 1.27 – 1.13 (m, 11H), 1.10 – 0.98 (m, 6H), 0.80 – 0.76 (m, 12H).

^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 164.04, 149.61, 140.46, 138.11, 136.15, 131.62, 128.14, 126.75, 125.87, 125.00, 123.24, 117.55, 75.15, 39.39, 37.58, 37.48, 37.41, 37.31, 32.80, 32.72, 31.02, 28.00, 24.84, 24.47, 22.75, 22.65, 21.06, 20.65, 19.78, 19.71, 19.63, 13.08, 12.23, 11.89.

HRMS (EI) calculated for $C_{37}H_{54}NO_3S$: 592.3819 $[M+H]^+$, Found: 592.3823.




164.0
149.6
140.5
138.1
136.1
131.6
128.1
126.8
125.9
125.0
123.2
117.6
75.2
39.4
37.6
37.5
37.4
37.3
32.8
32.7
31.0
28.0
24.8
24.5
23.7
22.7
22.7
21.1
20.7
19.8
19.7
19.6
13.1
12.2
11.9
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)

CENTRE COMMUN DE SPECTROMETRIE DE MASSE

Analysis Info

Analysis Name	Impact2_220929_04_YY647-P1.d		
Method	Tune_pos_Standard.m	Acquisition Date	9/29/2022 5:25:06 PM
Comment		Instrument / Ser#	impact II 1825265.10081

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
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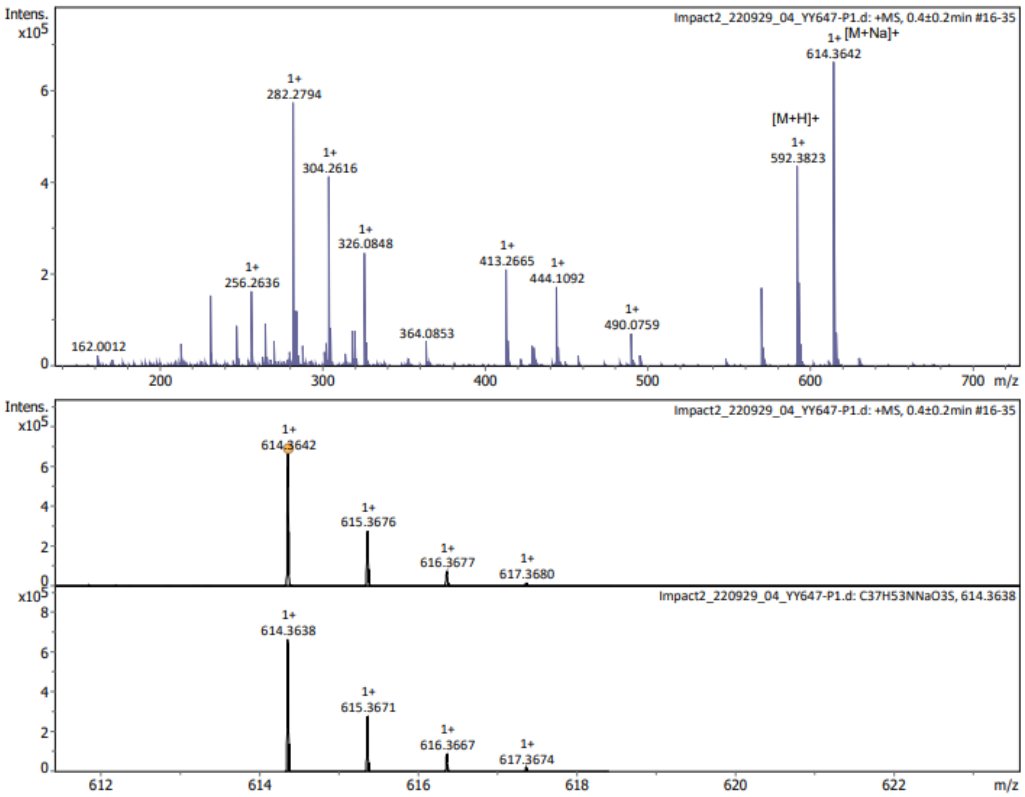
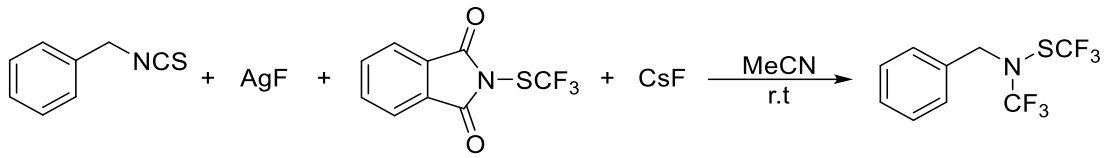
Scan End	1000 m/z	Set Collision Cell RF	1500.0 Vpp	Set Divert Valve	Source



Meas. m/z	Ion Formula	m/z	Sum Formula	err [ppm]	mSigma	Adduct	z
592.3823	C37H54NO3S	592.3819	C37H53NO3S	-0.7	13.9	M+H	1+
614.3642	C37H53NNaO3S	614.3638		-0.6	14.3	M+Na	1+

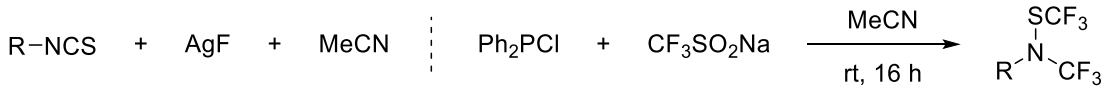
General procedure for the synthesis of N, S-bis(trifluoromethyl) thiohydroxylamine

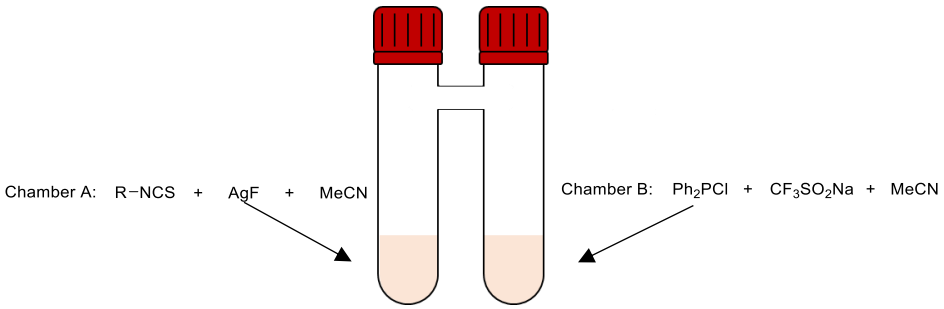
General procedure E for the synthesis of N, S-bis(trifluoromethyl)thiohydroxylamine:



To a 10 mL tube were sequentially added isothiocyanates (0.2 mmol, 1 equiv.), silver fluoride (0.6 mmol, 3.0 equiv.), 2-((trifluoromethyl)thio)isoindoline-1,3-dione (0.2 mmol, 1.0 equiv.), cesium fluoride (0.2 mmol, 1.0 equiv.), and acetonitrile (1 mL). The reaction mixture was stirred at room temperature overnight. After completion, the mixture was filtered through a celite pad, then extracted with ethyl acetate (3×10 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude material obtained was then purified by column chromatography on silica gel.

General procedure F for the synthesis of N, S-bis(trifluoromethyl)thiohydroxylamine:





To a H-tube were sequentially added isothiocyanate (0.2 mmol, 1.0 equiv.), silver fluoride (0.8 mmol, 4.0 equiv.), and acetonitrile (1 mL) to chamber A. Then sodium triflate (0.6 mmol, 3.0 equiv.) and acetonitrile (1 mL) were added to chamber B. After sealing the H-tube, chlorodiphenylphosphine (1.2 mmol, 3.0 equiv.) was added to chamber B by syringe. The mixture was stirred at room temperature overnight. After completion, the mixture in chamber A was filtered through a celite pad, then extracted with ethyl acetate (3×10 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude material obtained was then purified by column chromatography on silica gel.

General procedure G for the synthesis of N, S-bis(trifluoromethyl)thiohydroxylamine in large scale (2 g scale):

To a 400 mL H-tube were sequentially added isothiocyanate (10.0 mmol, 1.0 equiv.), silver fluoride (40.0 mmol, 4.0 equiv.), and acetonitrile (50 mL) to chamber A. Then sodium triflate (30.0 mmol, 3.0 equiv.) and acetonitrile (50 mL) was added to chamber B. After sealing the H-tube,

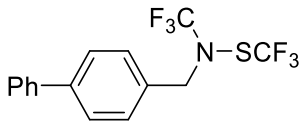
chlorodiphenylphosphine (60.0 mmol, 6.0 equiv.) was slowly added to chamber B slowly syringe. The mixture was stirred at room temperature for 24 hours. The reaction process was monitored by ^{19}F-NMR. After completion, the mixture in chamber A was filtered through a celite pad, then extracted with ethyl acetate (3×30 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude material obtained was then purified by column chromatography on silica gel.

General procedure H for the synthesis of N, S-bis(trifluoromethyl)thiohydroxylamine in large scale (4 g scale):

To a 400 mL H-tube were sequentially added isothiocyanate (20.0 mmol, 1.0 equiv.), silver fluoride (80.0 mmol, 4.0 equiv.), and acetonitrile (100 mL) to chamber A. Then sodium triflate (60.0 mmol, 3.0 equiv.) and acetonitrile (100 mL) was added to chamber B. After sealing the H-tube, chlorodiphenylphosphine (120.0 mmol, 6.0 equiv.) was slowly added to chamber B slowly syringe at 0 ℃ (ice bath). The mixture was then stirred at room temperature for 24 hours. The reaction process was monitored by ^{19}F-NMR. After completion, the mixture in chamber A was filtered through a celite pad, then extracted with ethyl acetate (3×30 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude material obtained was then purified by column chromatography on silica gel.

Characterization of N, S-bis(trifluoromethyl)thiohydroxylamine

N-([1,1'-biphenyl]-4-ylmethyl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3b)



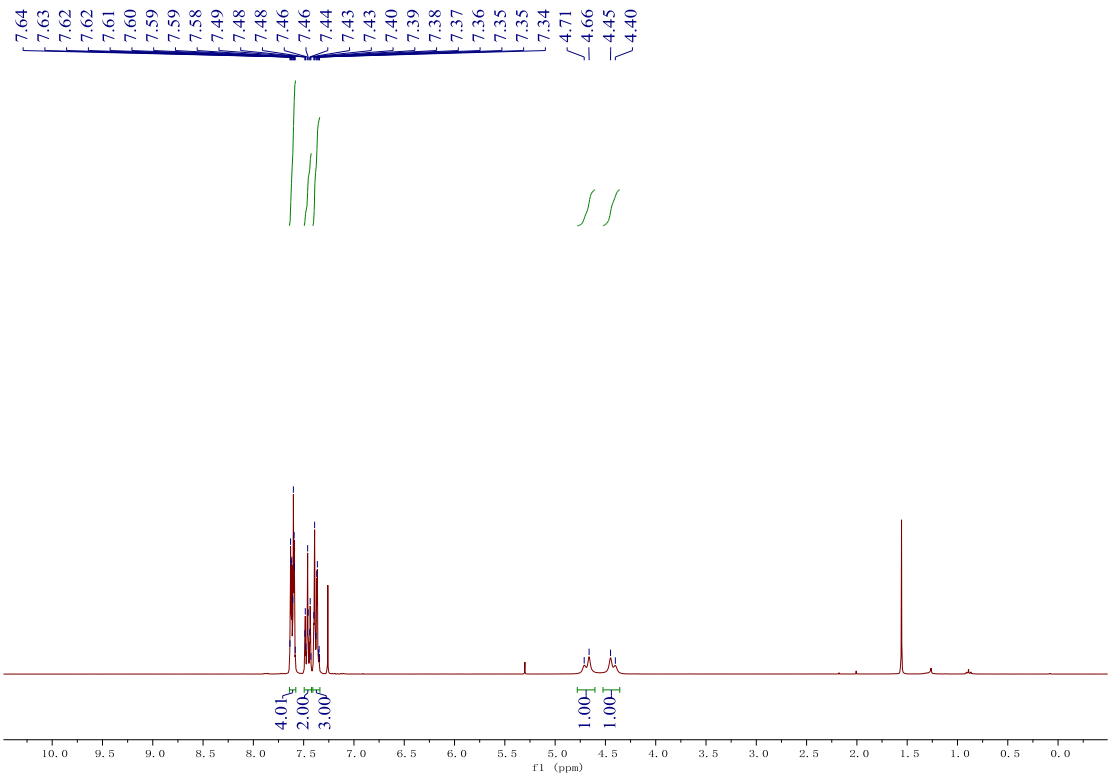
The compound **3b** was obtained as a colorless oil in 57% yield using 4-(isothiocyanatomethyl)-1,1'-biphenyl following the general procedure E after column chromatography on silica gel with pentane.

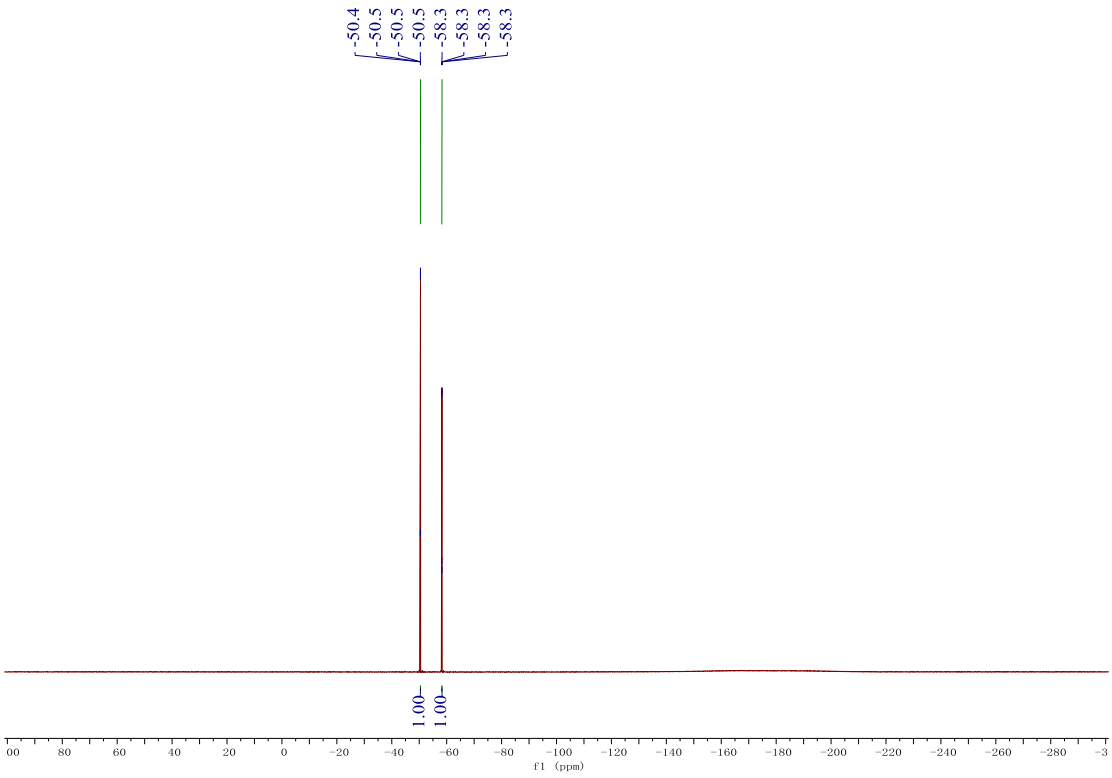
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.64 – 7.58 (m, 4H), 7.49 – 7.42 (m, 2H), 7.41 – 7.34 (m, 3H), 4.69 (d, *J* = 14.3 Hz, 1H), 4.43 (d, *J* = 14.3 Hz, 1H).

^{19}F NMR (282 MHz, Chloroform-*d*) δ -50.5 (q, *J* = 3.4 Hz), -58.3 (q, *J* = 3.4 Hz).

^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 141.6, 140.4, 133.8, 129.2, 128.8 (q, *J* = 315.2 Hz), 128.8, 127.6, 127.5, 127.1, 123.1 (q, *J* = 260.4 Hz), 56.2.

HRMS (EI) calculated for $C_{15}H_{11}F_6NS$: 351.0511 $[M]^+$, Found: 351.0516.

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-50.5
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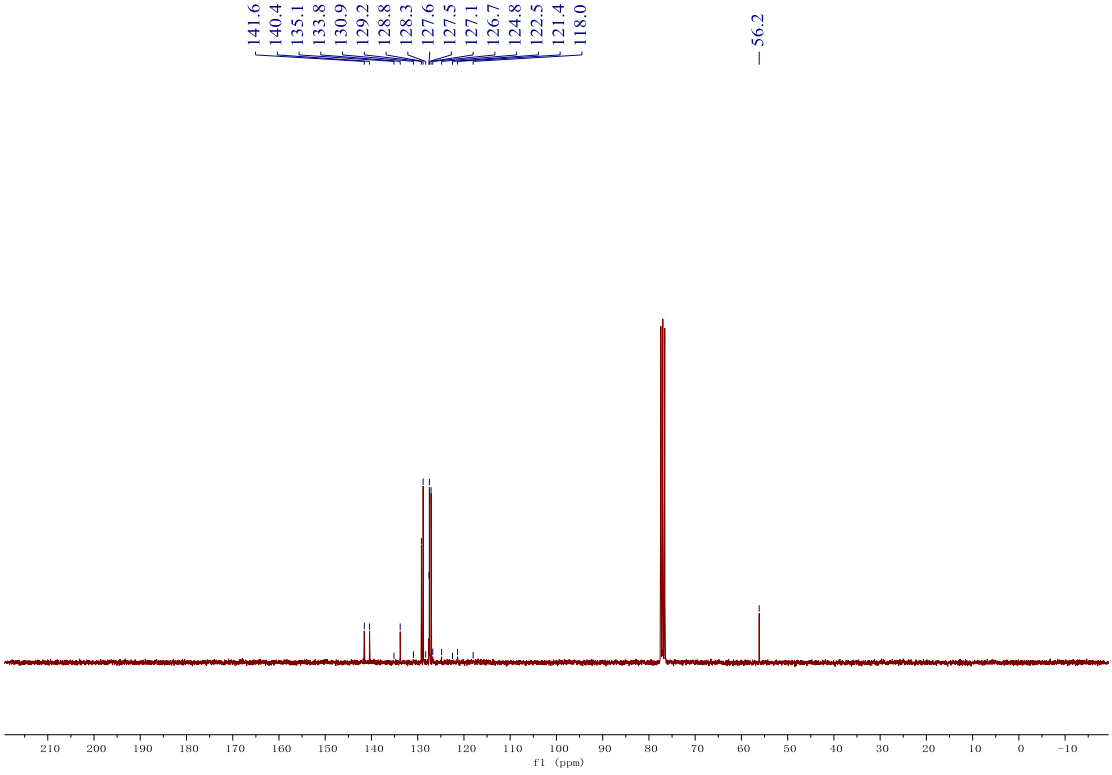
-58.3
-58.3
-58.3
1.00
1.00
f1 (ppm)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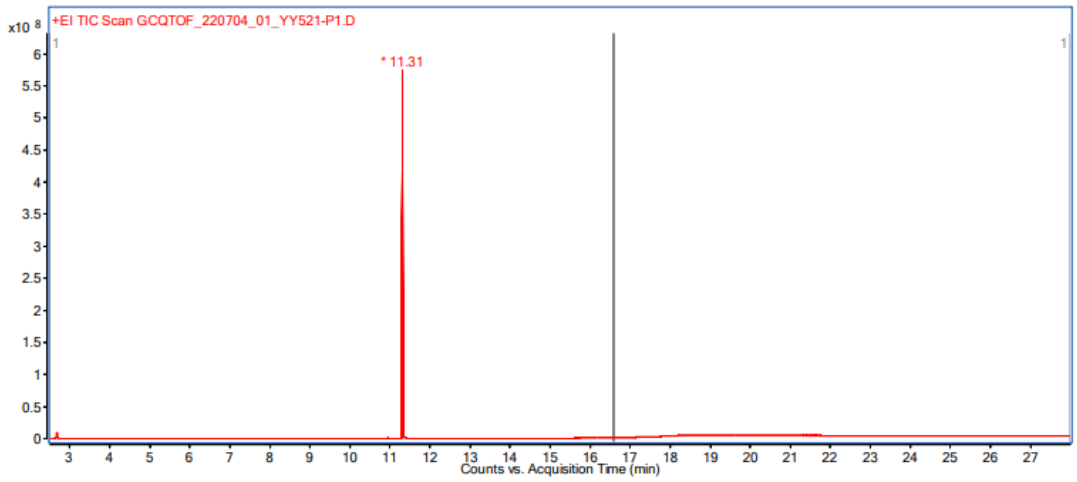
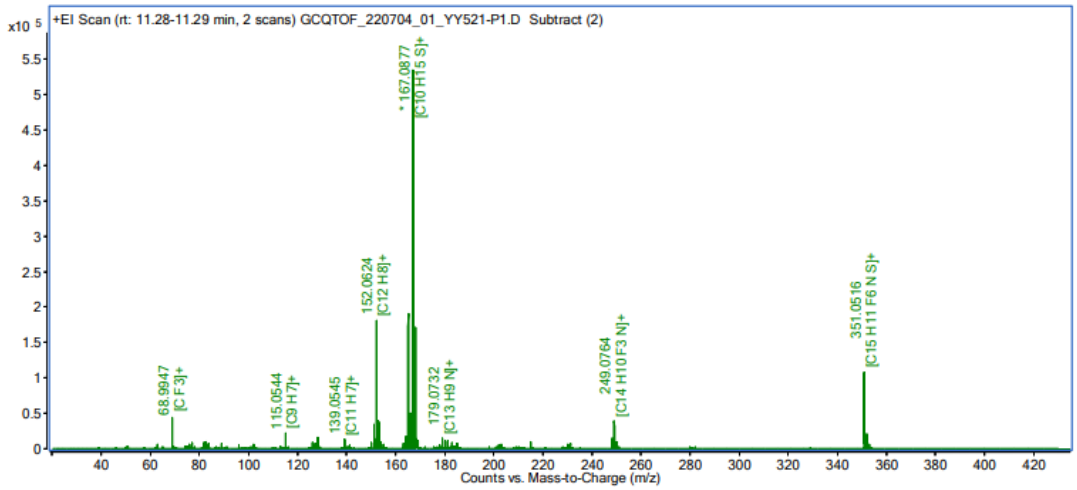
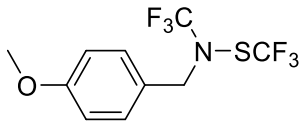
133.8
130.9
129.2
128.8
128.3
127.6
127.5
127.1
126.7
124.8
122.5
121.4
118.0
56.2
f1 (ppm)





m/z	Ion Formula	m/z (Calc)	Diff (ppm)	
351.0516	C15H11F6NS	351.0511	1.4	$[M]^{+\cdot}$

N-(4-methoxybenzyl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3c)



The compound **3c** was obtained as a colorless oil in 30% yield using 1-(isothiocyanatomethyl)-4-methoxybenzene following the general procedure E after column chromatography on silica gel with pentane.

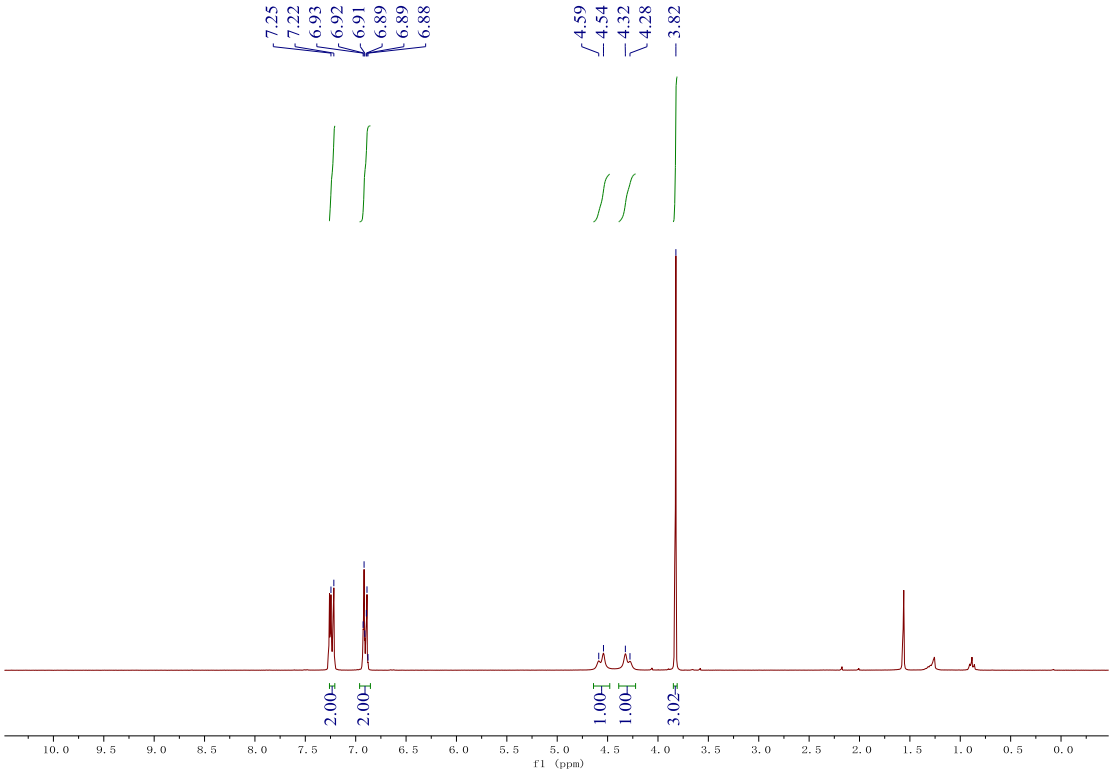
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.25 – 7.22 (m, 2H), 6.92 – 6.88 (m, 2H), 4.56 (d, *J* = 14.1 Hz, 1H), 4.30 (d, *J* = 13.7 Hz, 1H), 3.82 (s, 3H).

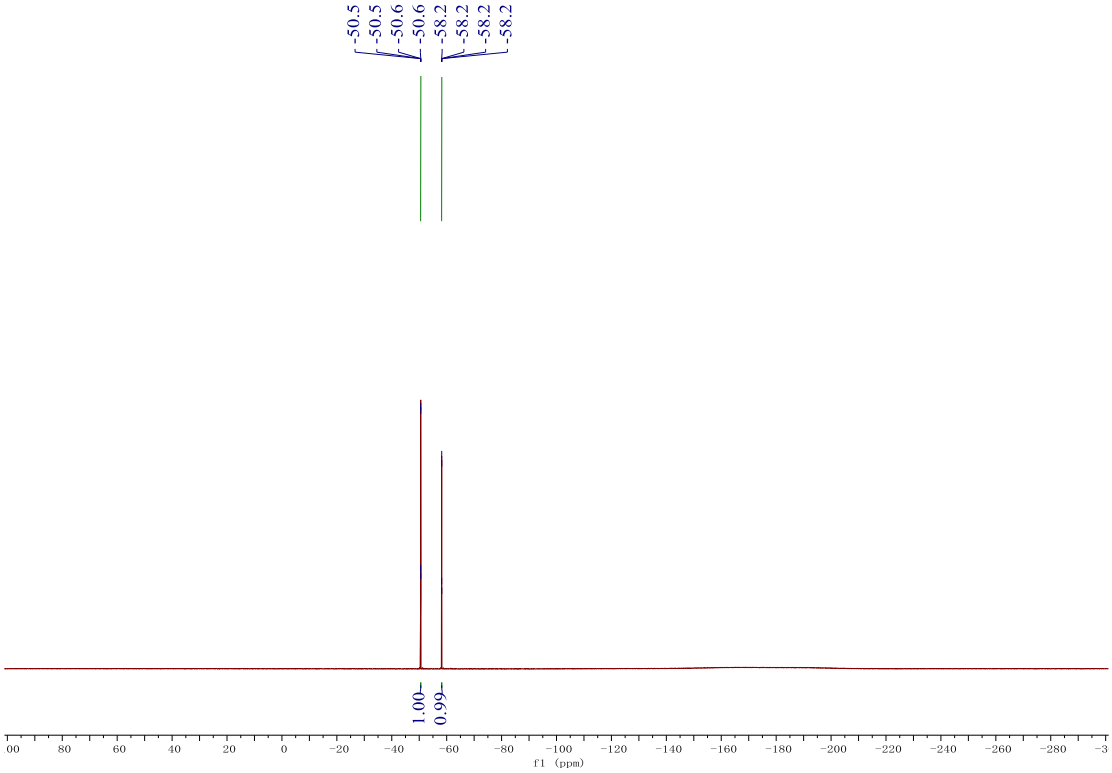
^{19}F NMR (282 MHz, Chloroform-*d*) δ -50.5 (q, *J* = 3.4 Hz), -58.2 (q, *J* = 3.4 Hz).

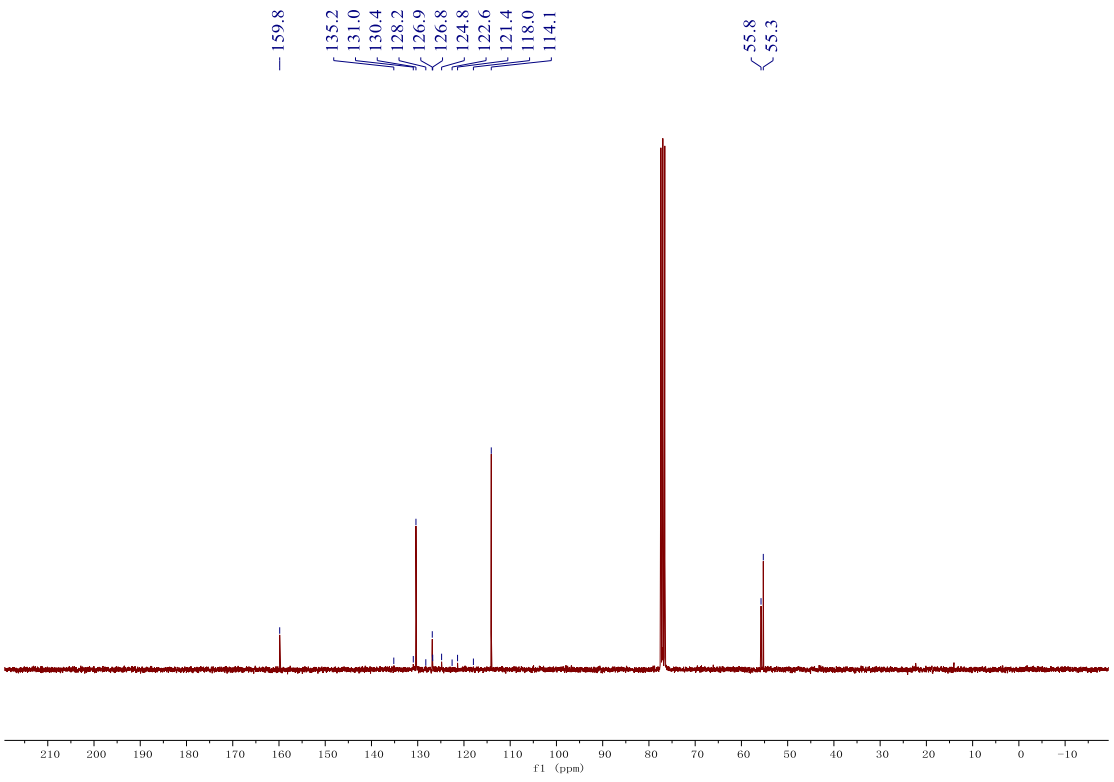
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 159.8, 130.4, 128.9 (q, *J* = 316.9 Hz), 126.8, 123.1 (q, *J*

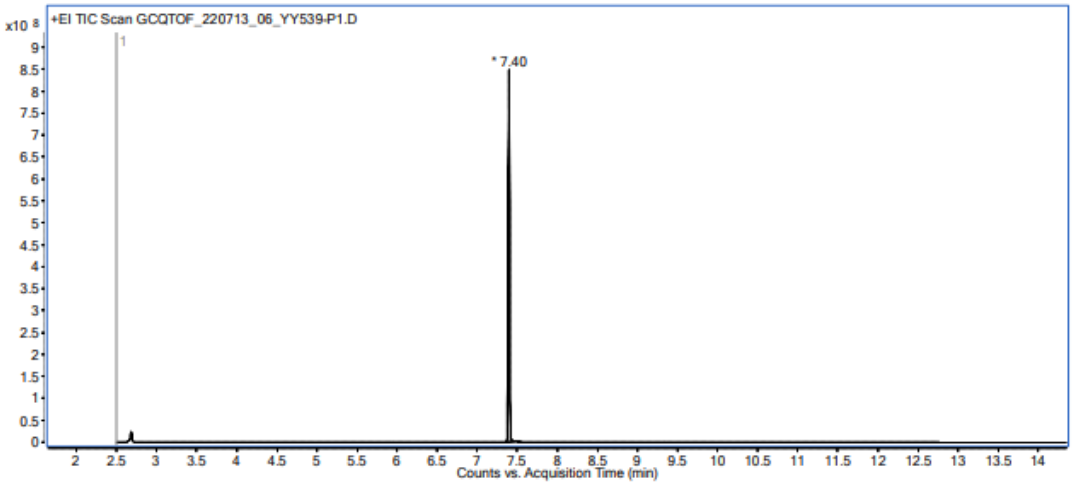
= 260.4 Hz), 114.1, 55.8, 55.3.

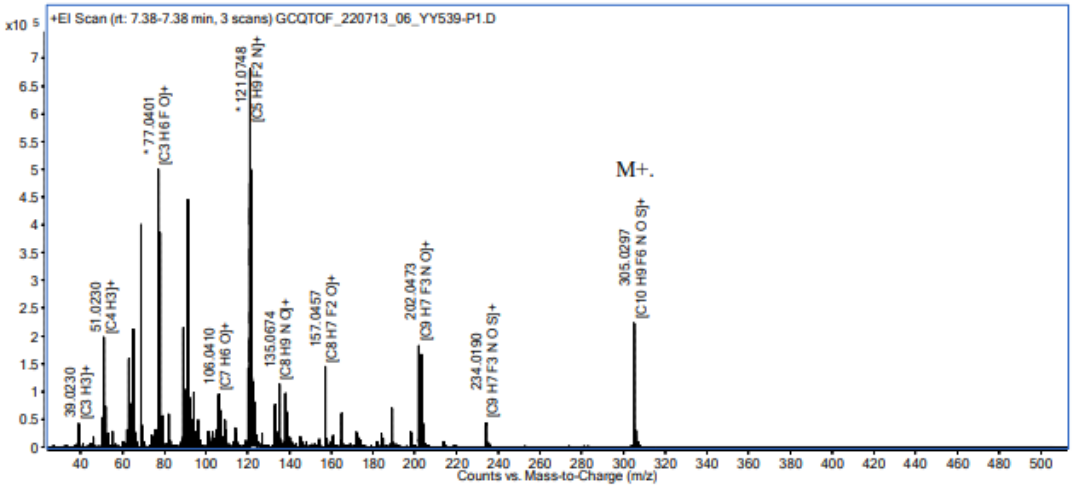
HRMS (EI) calculated for $C_{10}H_9F_6NOS$: 305.0304 $[M]^+$, Found: 305.0297.

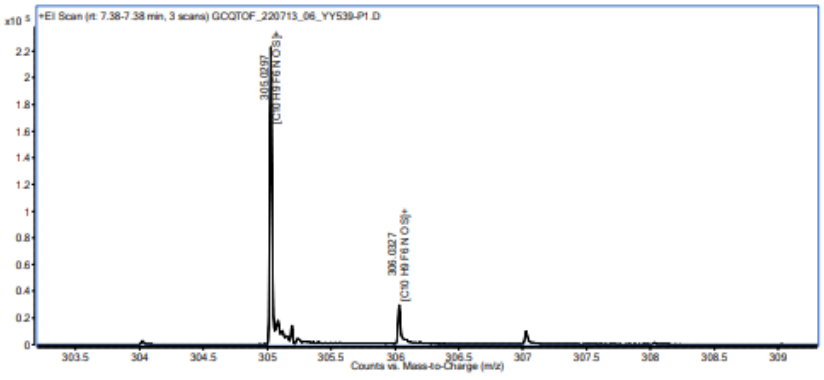





159.8
135.2
131.0
130.4
128.2
126.9
126.8
124.8
122.6
121.4
118.0
114.1
55.8
55.3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

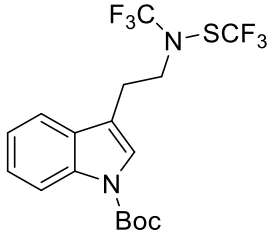






m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
305.0297	C10H9F6NOS	305.0304	-2.3	$[M]^{+\cdot}$

***tert*-butyl 3-(2-((trifluoromethyl)((trifluoromethyl)thio)amino)ethyl)-1H-indole-1-arboxylate (3d)**



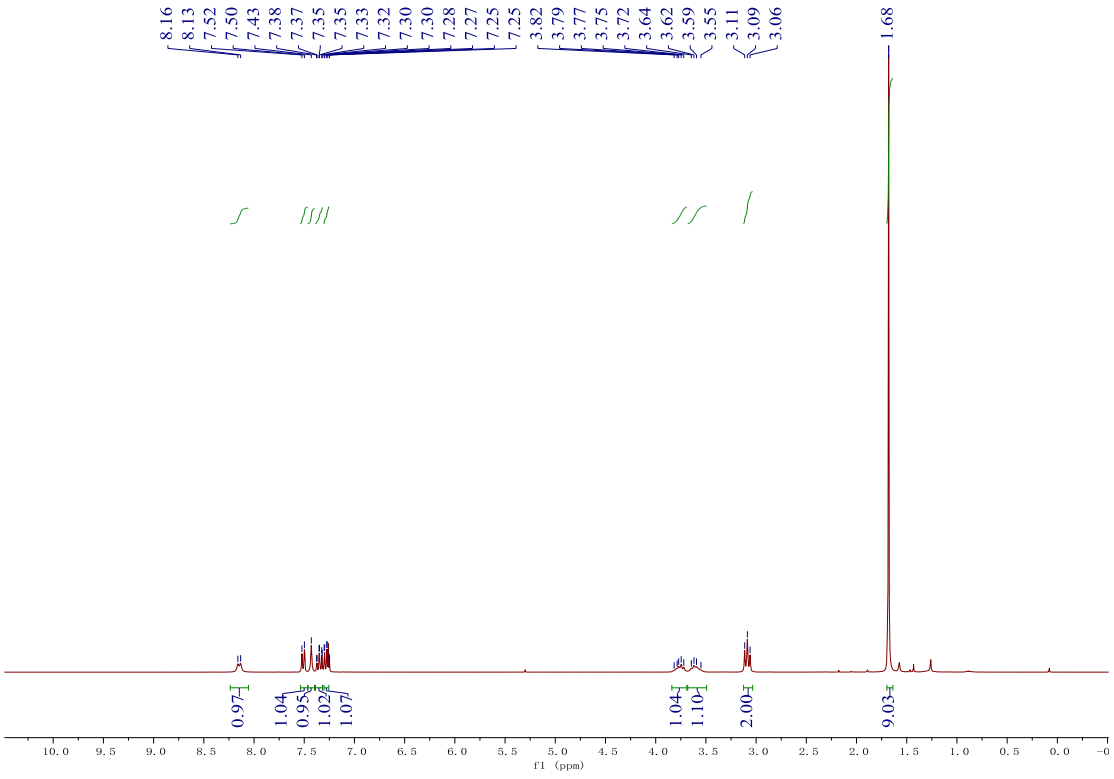
The compound **3d** was obtained as a colorless oil in 35% yield using tert-butyl 3-(2-isothiocyanatoethyl)-1H-indole-1-carboxylate following the general procedure E after column chromatography on silica gel with pentane.

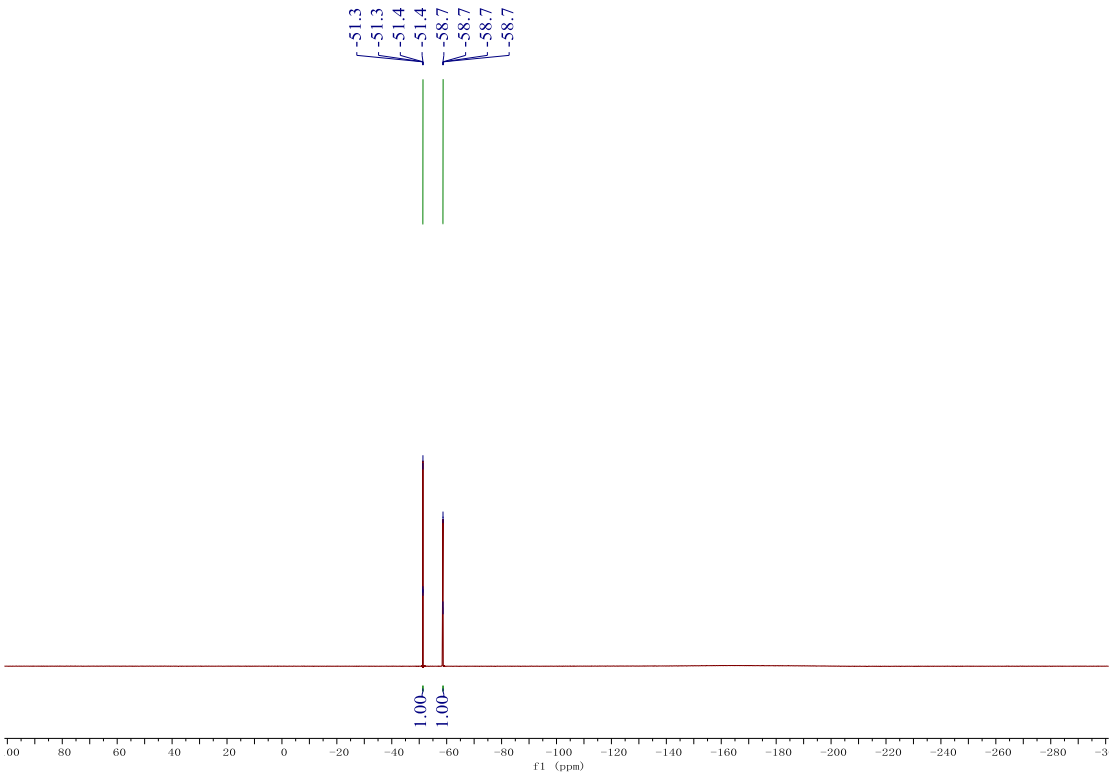
^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 8.1 Hz, 1H), 7.51 (d, *J* = 7.4 Hz, 1H), 7.43 (s, 1H), 7.39 – 7.32 (m, 1H), 7.30 – 7.25 (m, 1H), 3.82 – 3.75 (m, 1H), 3.64 – 3.55 (m, 1H), 3.09 (t, *J* = 8.0 Hz, 2H), 1.68 (s, 9H).

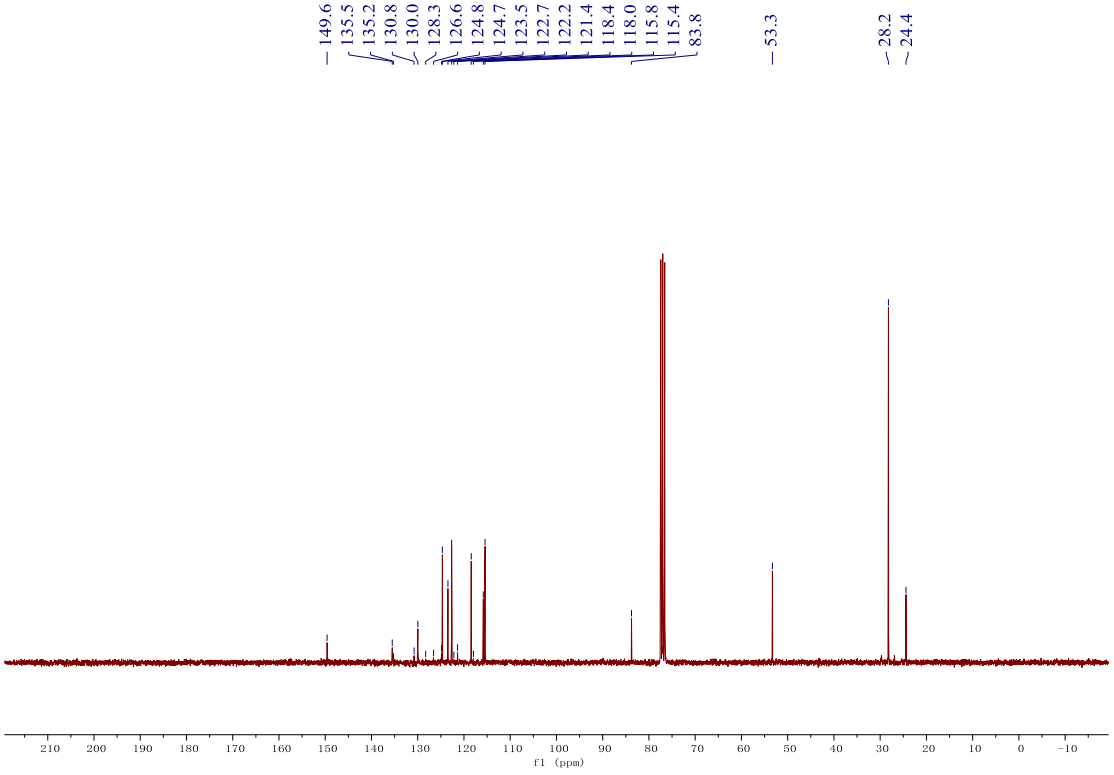
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.3 (q, *J* = 3.4 Hz), -58.7 (q, *J* = 3.4 Hz).

^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 149.6, 135.5, 130.0, 128.7 (q, *J* = 318.1 Hz), 124.7, 123.5, 123.1 (q, *J* = 259.8 Hz), 122.7, 118.4, 115.8, 115.4, 83.8, 53.3, 28.2, 24.4.

HRMS (ESI) calculated for $C_{17}H_{19}F_6N_2O_2S$: 429.1066 $[M+H]^+$, Found: 429.1066.




-51.3
-51.3
-51.4
-51.4
-58.7
-58.7
-58.7
-58.7
1.00
1.00
f1 (ppm)


149.6
135.5
135.2
130.8
130.0
128.3
126.6
124.8
124.7
123.5
122.7
122.2
121.4
118.4
118.0
115.8
115.4
83.8
53.3
28.2
24.4
f1 (ppm)

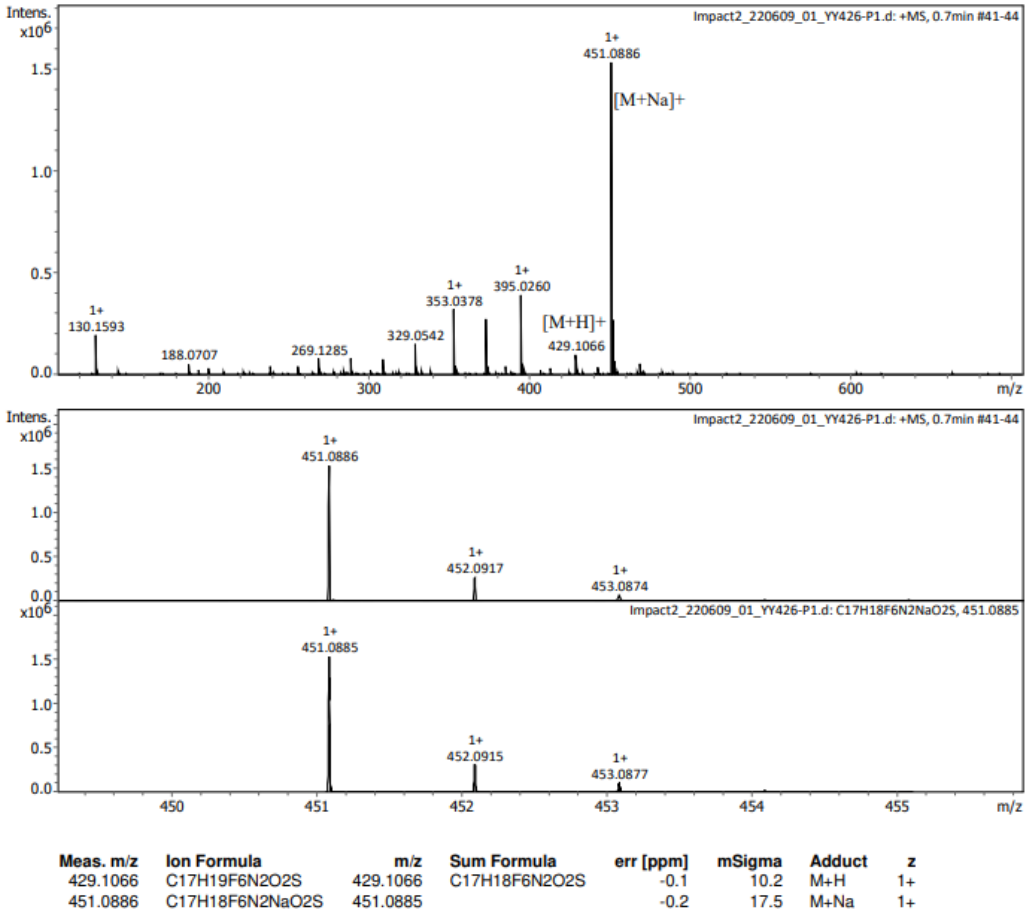
CENTRE COMMUN DE SPECTROMETRIE DE MASSE

Analysis Info

Analysis Name	Impact2_220609_01_YY426-P1.d		
Method	Tune_pos_Standard.m	Acquisition Date	6/9/2022 9:00:18 AM
Comment		Instrument / Ser#	impact II 1825265.10081

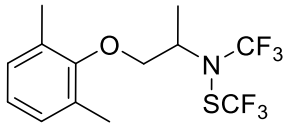
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	2500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	750.0 Vpp	Set Divert Valve	Source



Meas. m/z	Ion Formula	m/z	Sum Formula	err [ppm]	mSigma	Adduct	z
429.1066	C17H19F6N2O2S	429.1066	C17H18F6N2O2S	-0.1	10.2	M+H	1+
451.0886	C17H18F6N2NaO2S	451.0885		-0.2	17.5	M+Na	1+

N-(1-(2,6-dimethylphenoxy)propan-2-yl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3e)



The compound **3e** was obtained as a colorless oil in 49% yield using 4-(4-isothiocyanatobutyl)morpholine following the general procedure E after column chromatography on silica gel with pentane/ether (3/4).

Isomer A:

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.00 (s, 2H), 6.96 – 6.94 (m, 1H), 4.20 – 4.07 (m, 1H), 3.92 – 3.87 (m, 1H), 3.67 – 3.62 (m, 1H), 2.27 (s, 6H), 1.44 (d, *J* = 6.8 Hz, 3H).

^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.4 (q, *J* = 3.4 Hz), -57.3 (q, *J* = 3.4 Hz).

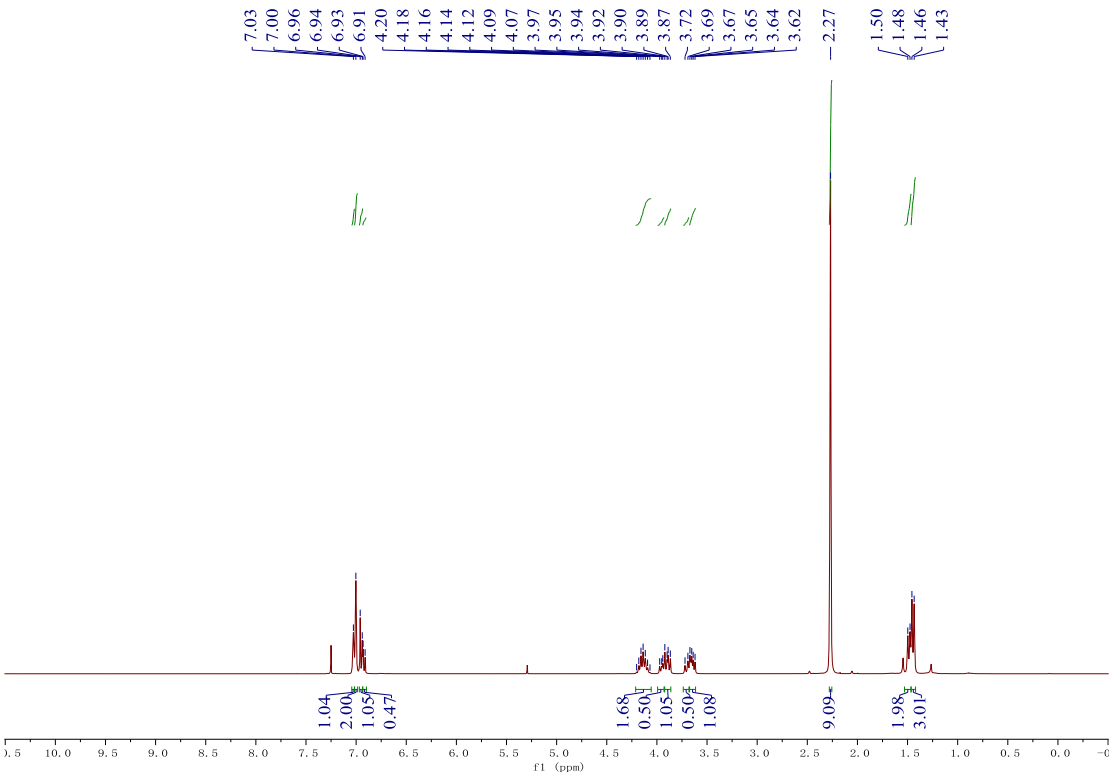
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 154.9, 130.7, 129.0, 128.1 (d, *J* = 314.1 Hz), 124.3, 123.3 (q, *J* = 260.9 Hz), 72.2, 55.7, 16.4, 16.2

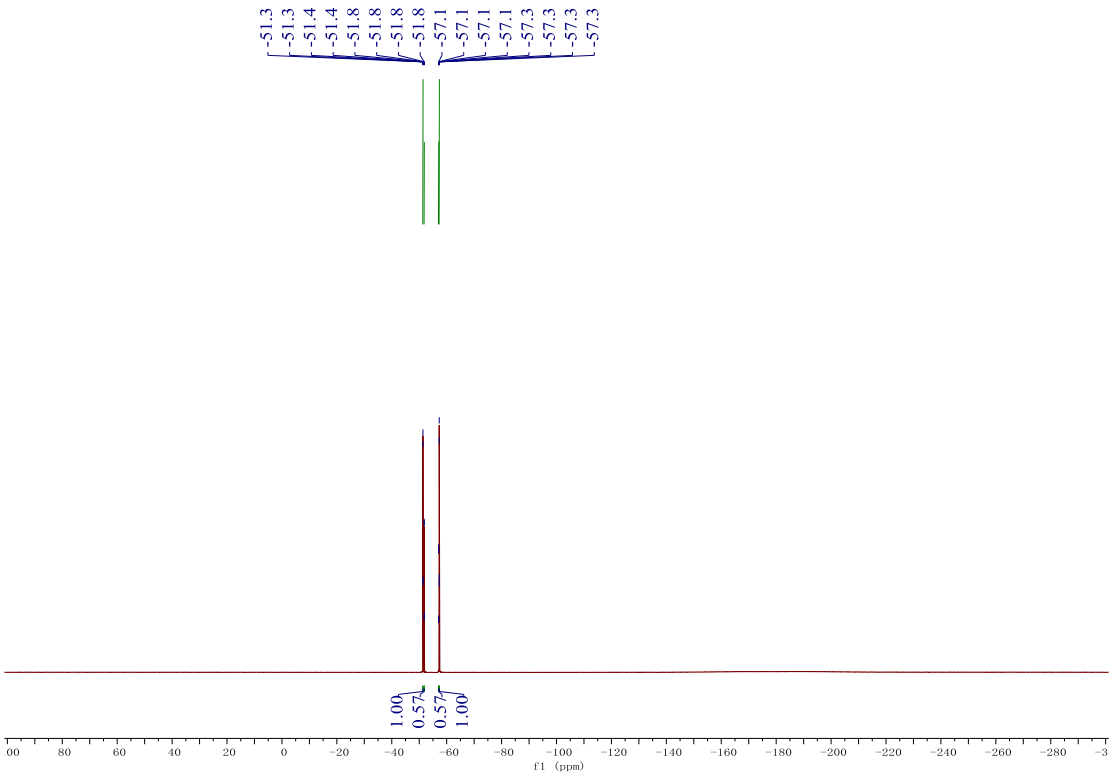
Isomer B:
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.03 (s, 2H), 6.93 – 6.91 (m, 1H), 4.20 – 4.07 (m, 1H), 3.97 – 3.94 (m, 1H), 3.72 – 3.69 (m, 1H), 2.27 (s, 6H), 1.49 (d, *J* = 6.8 Hz, 3H).

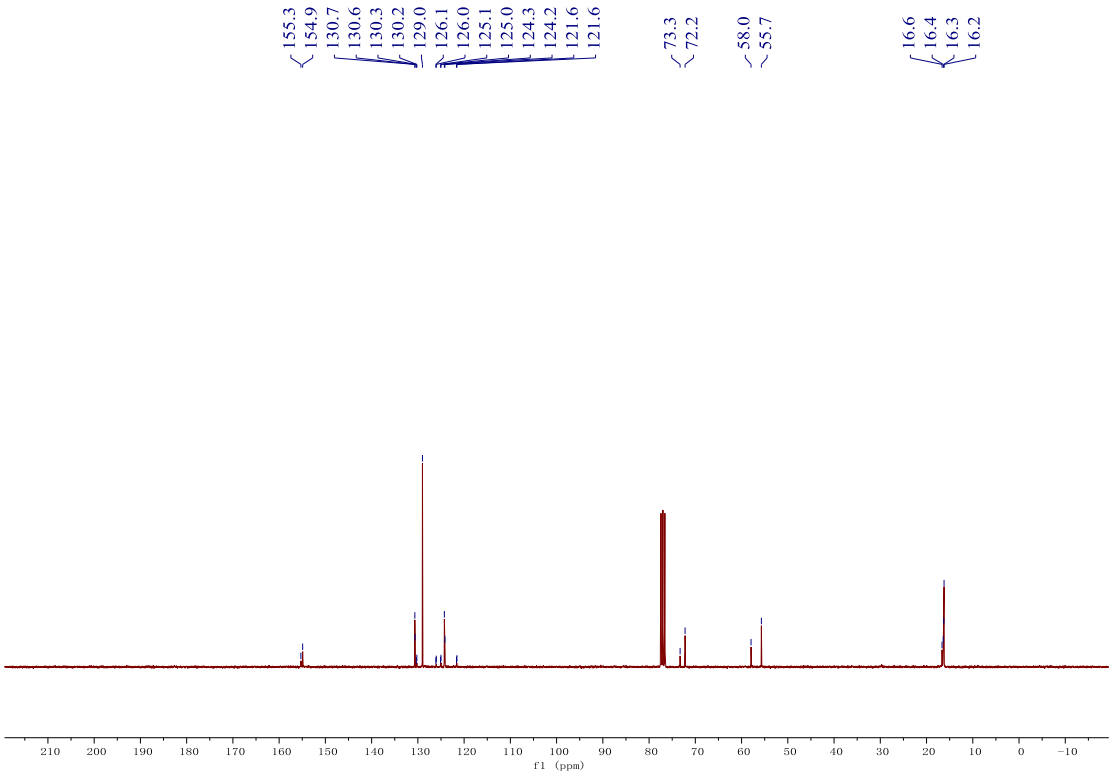
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.8 (q, J = 3.4 Hz), -57.1 (q, J = 3.4 Hz).

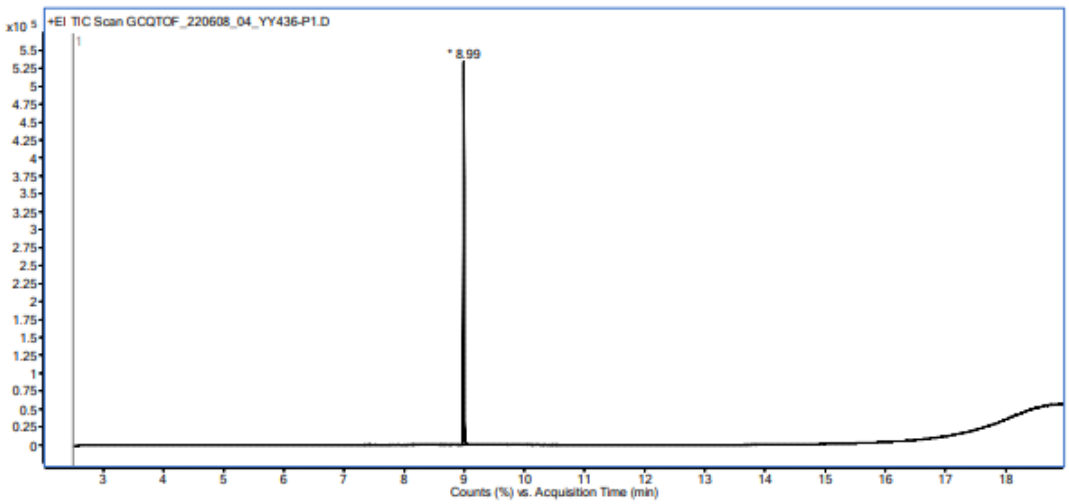
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 155.3, 130.6, 129.0, 128.2 (d, *J* = 314.1 Hz), 124.2, 123.3 (q, *J* = 260.9 Hz), 73.3, 58.0, 16.6, 16.3.

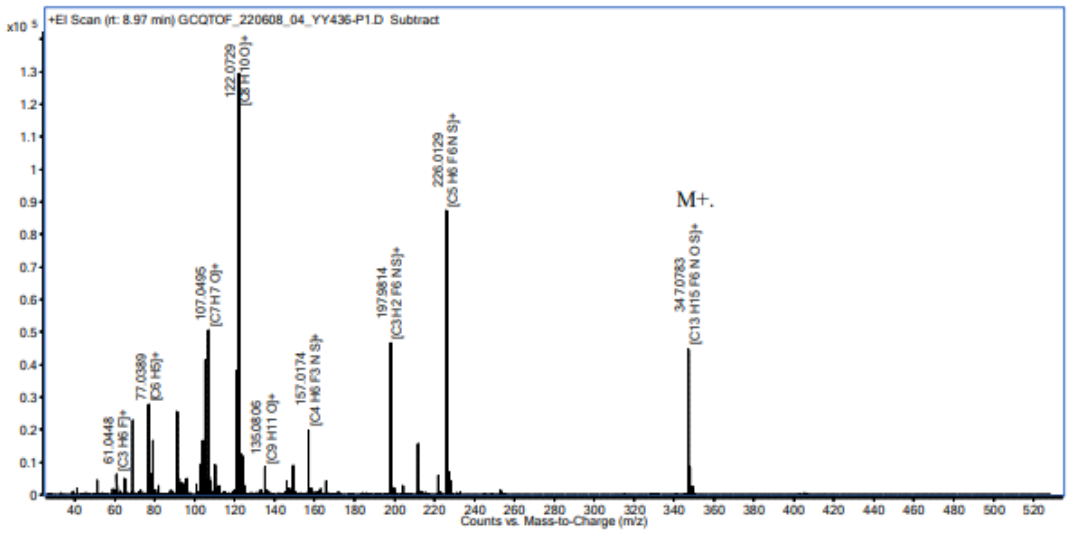
HRMS (EI) calculated for $C_{13}H_{15}F_6NOS$: 347.0773 $[M]^+$, Found: 347.0783.

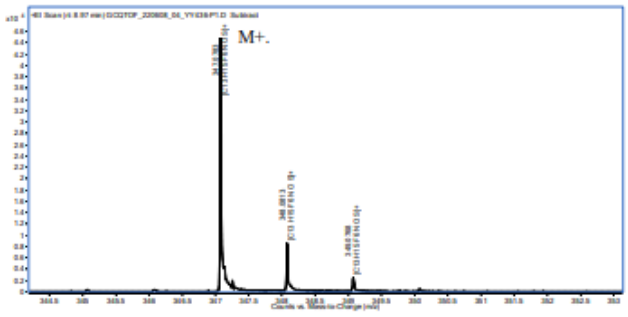



-51.3
-51.3
-51.4
-51.4
-51.8
-51.8
-51.8
-51.8
-57.1
-57.1
-57.1
-57.1
-57.3
-57.3
-57.3
-57.3
1.00
0.57
0.57
1.00
f1 (ppm)


155.3
154.9
130.7
130.6
130.3
130.2
129.0
126.1
126.0
125.1
125.0
124.3
124.2
121.6
121.6
73.3
72.2
58.0
55.7
16.6
16.4
16.3
16.2
f1 (ppm)

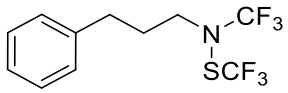






Meas. m/z	Ion Formula	m/z (Calc)	err (ppm)	
347.0783	C13H15F6NOS	347.0773	2.9	$[M]^{+\cdot}$

N-(3-phenylpropyl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3f)



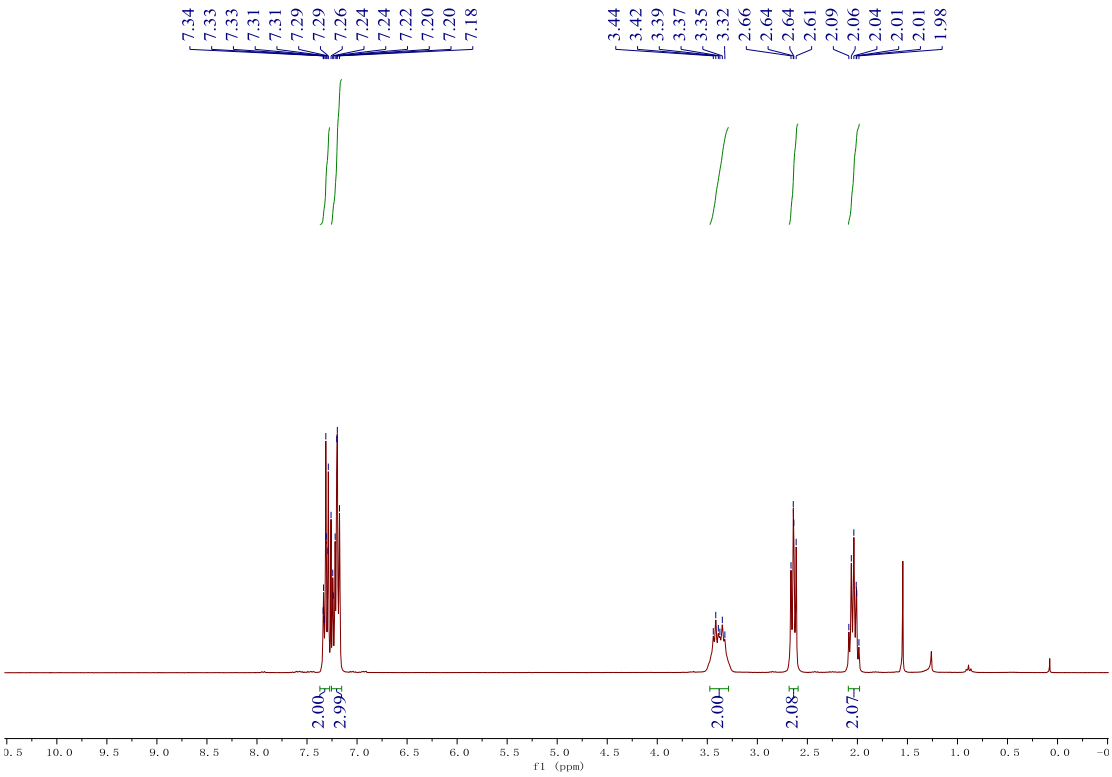
The compound **3f** was obtained as a colorless oil in 67% yield using (3-isothiocyanatopropyl)benzene following the general procedure E after column chromatography on silica gel with pentane.

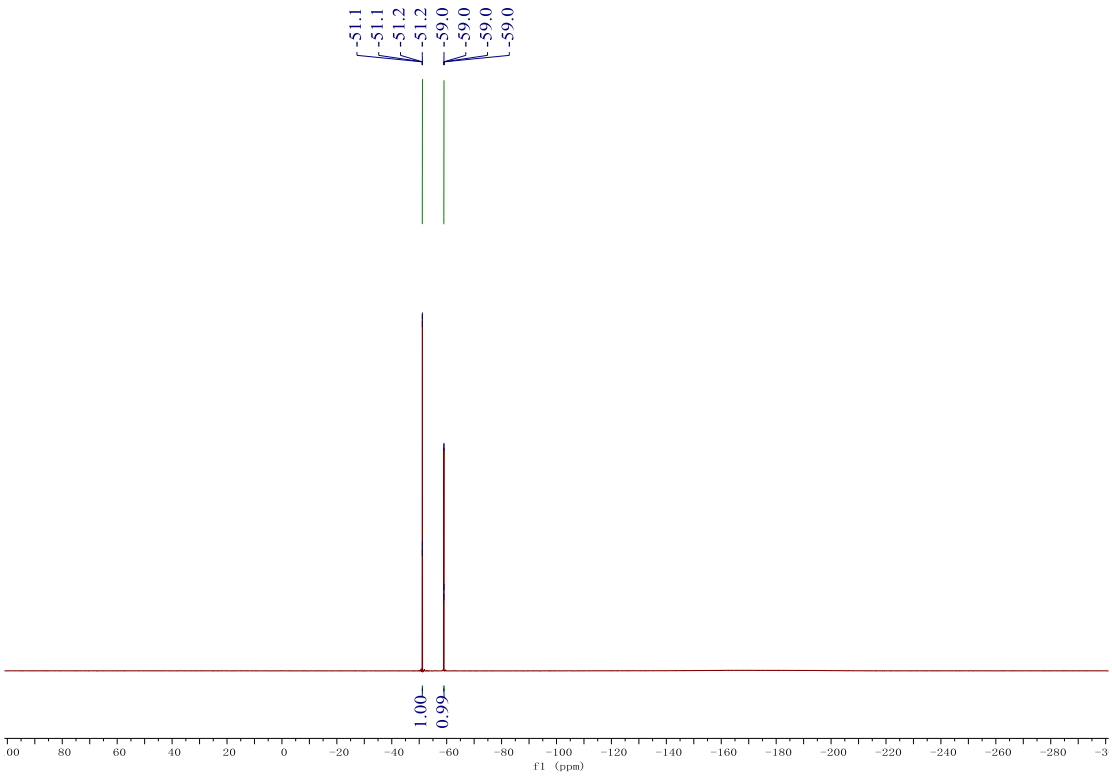
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.34 – 7.29 (m, 2H), 7.26 – 7.15 (m, 3H), 3.44 – 3.32 (m, 2H), 2.68 – 2.59 (m, 2H), 2.09 – 1.98 (m, 2H).

^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.1 (q, *J* = 3.4 Hz), -59.0 (q, *J* = 3.4 Hz).

^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 140.6, 128.7 (q, *J* = 314.9 Hz), 128.5, 128.2, 126.2, 123.1 (q, *J* = 259.7 Hz), 52.9, 32.4, 29.6.

HRMS (EI) calculated for $C_{11}H_{11}F_6NS$: 303.0511 $[M]^+$, Found: 303.0500.




-51.1
-51.1
-51.2
-51.2
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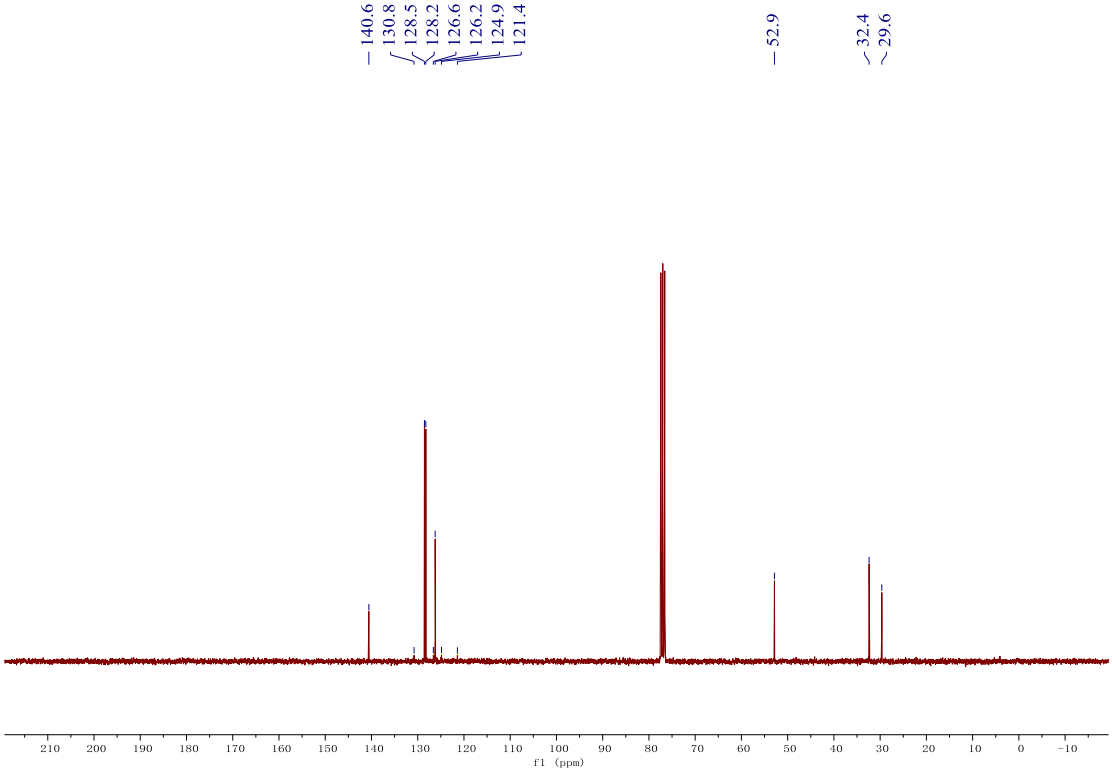
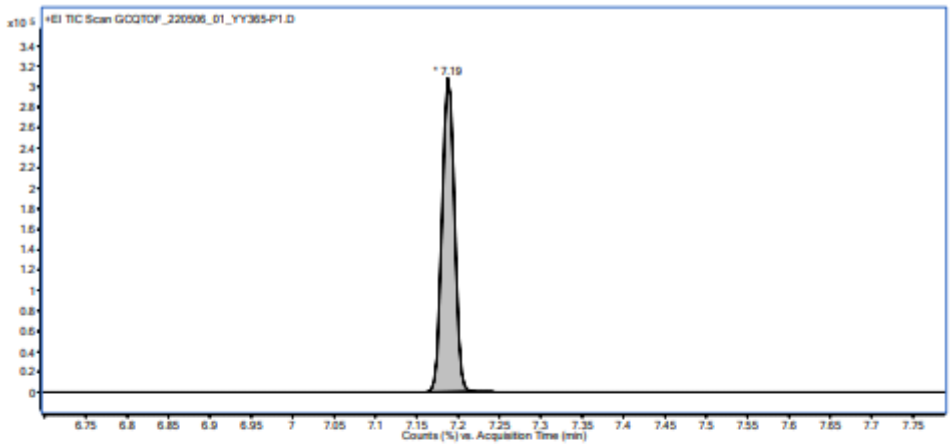
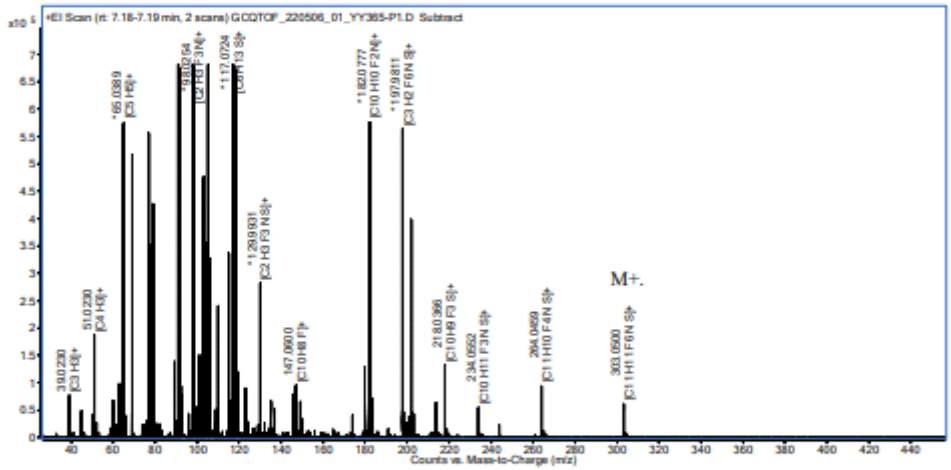
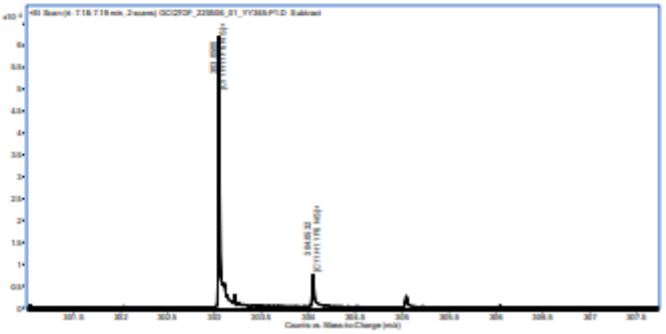
1.00
0.99
f1 (ppm)


140.6
130.8
128.5
128.2
126.6
126.2
124.9
121.4
52.9
32.4
29.6
f1 (ppm)

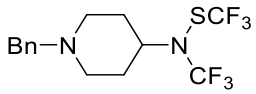






m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
303.0500	C11H11F6NS	303.0511	-3.6	$[M]^{+\cdot}$

N-(1-benzylpiperidin-4-yl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3g)



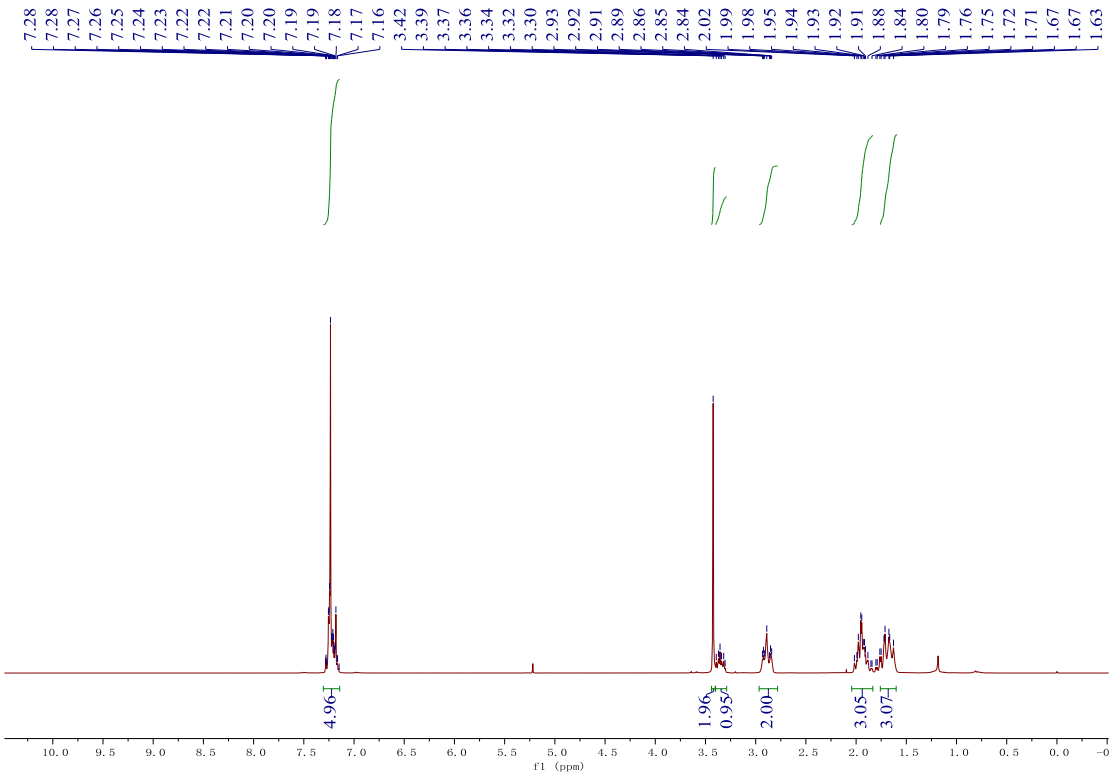
The compound **3g** was obtained as a colorless oil in 63% yield using 1-benzyl-4-isothiocyanatopiperidine following the general procedure E after column chromatography on silica gel with pentane.

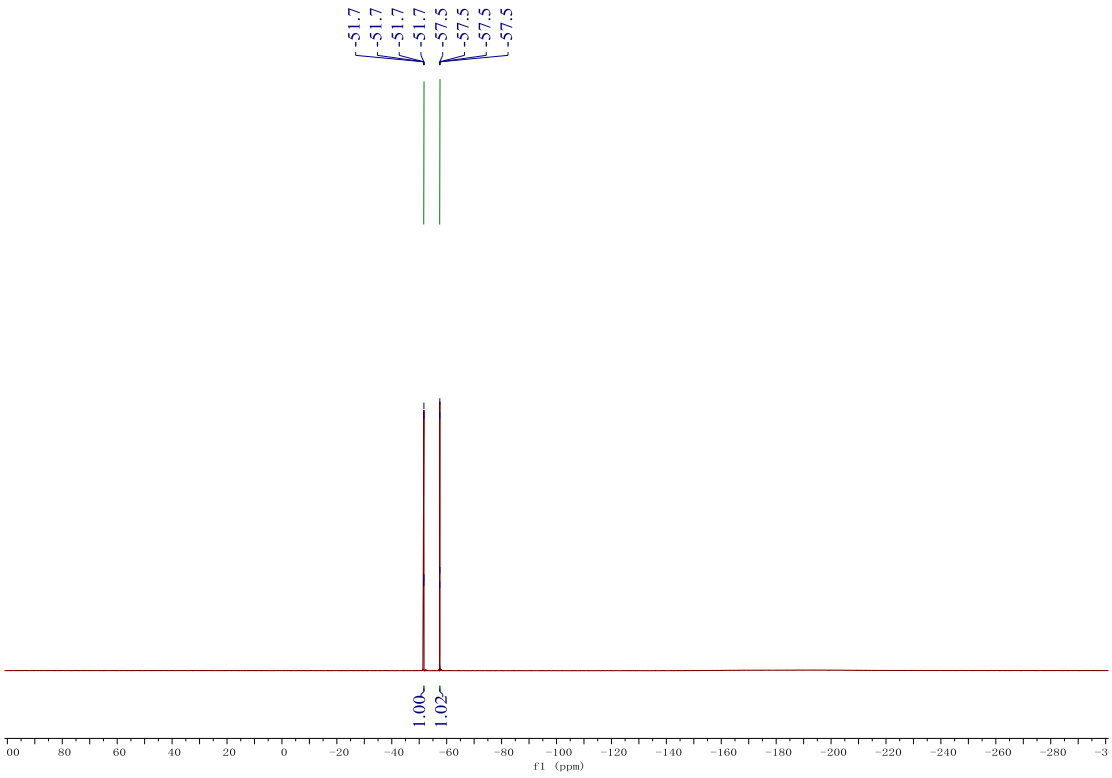
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.31 – 7.14 (m, 5H), 3.42 (s, 2H), 3.39 – 3.30 (m, 1H), 2.97 – 2.78 (m, 2H), 2.02 – 1.84 (m, 3H), 1.76 – 1.60 (m, 3H).

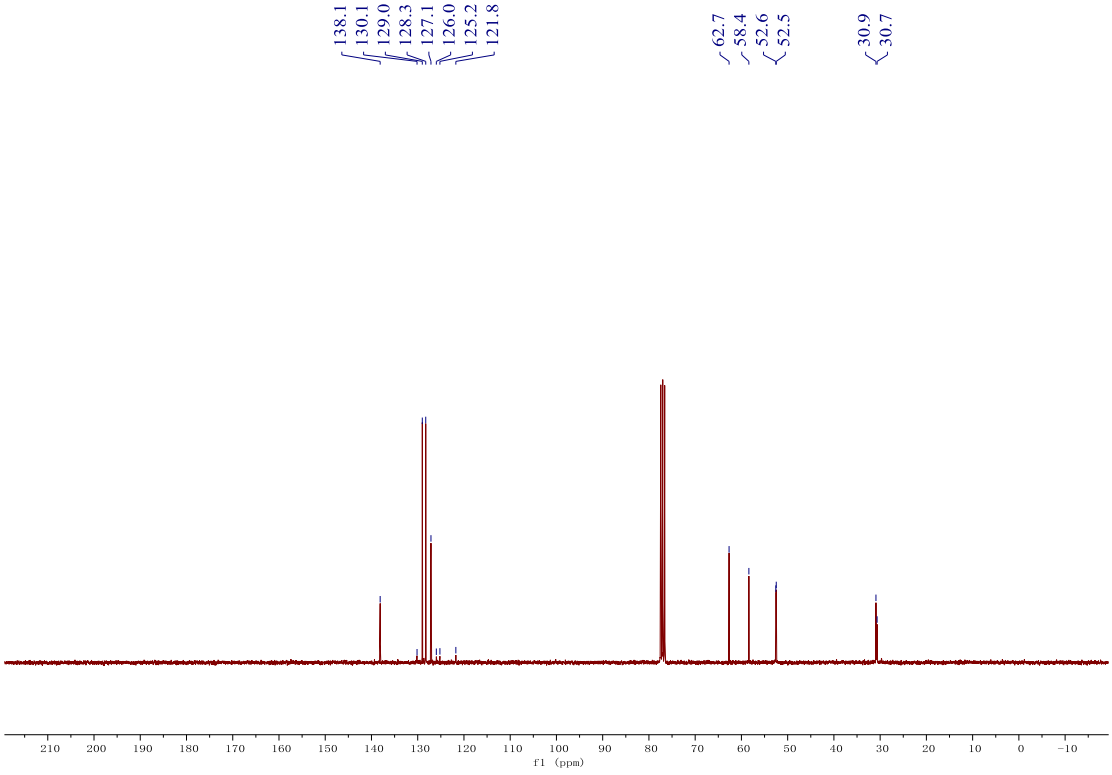
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.7 (q, *J* = 3.4 Hz), -57.5 (q, *J* = 3.4 Hz).

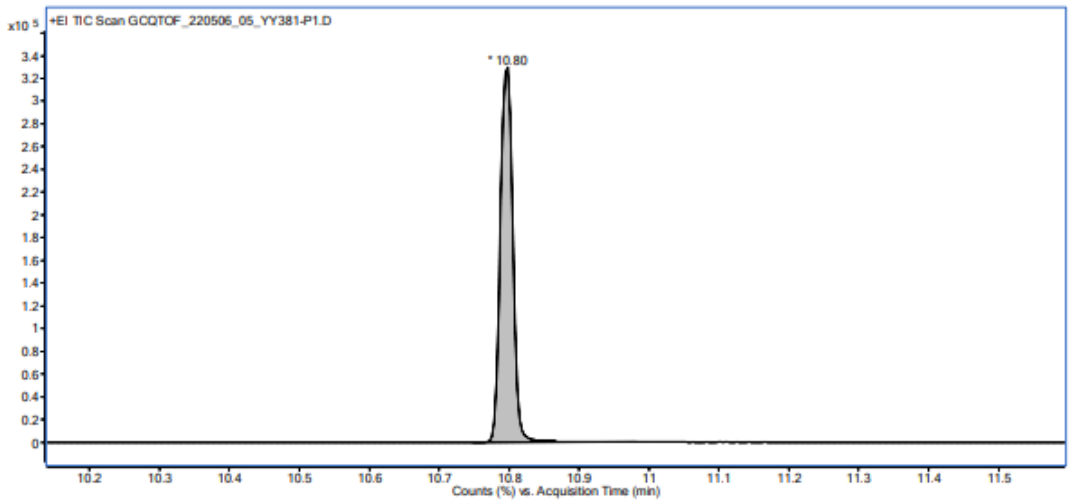
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 138.1, 129.0, 128.3, 128.0 (q, *J* = 314.8 Hz), 127.1, 123.5 (q, *J* = 259.9 Hz), 62.7, 58.4, 52.6, 52.5, 30.9, 30.7.

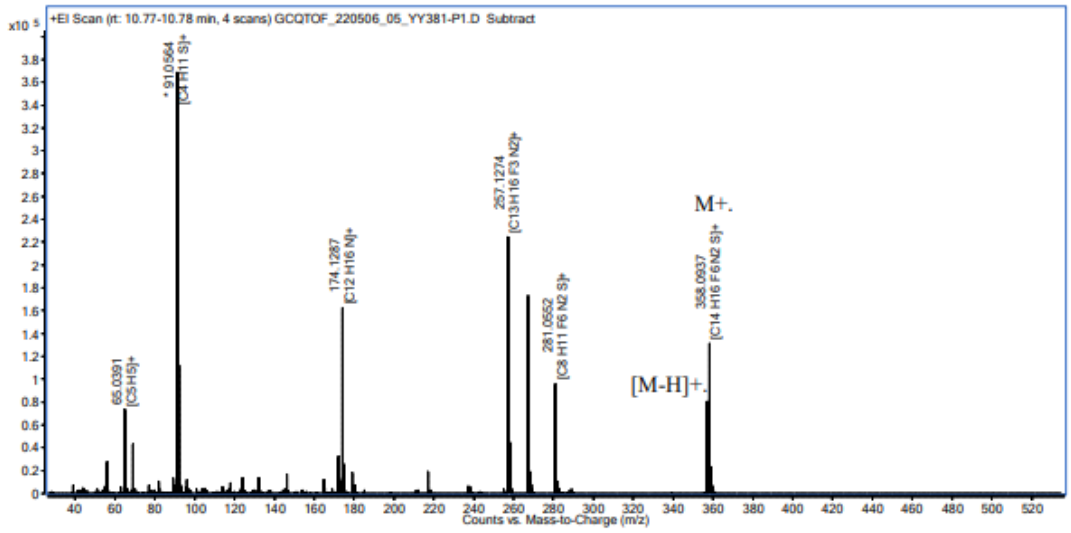
HRMS (EI) calculated for $C_{14}H_{16}F_6N_2S$: 358.0933 $[M]^+$, Found: 358.0937.

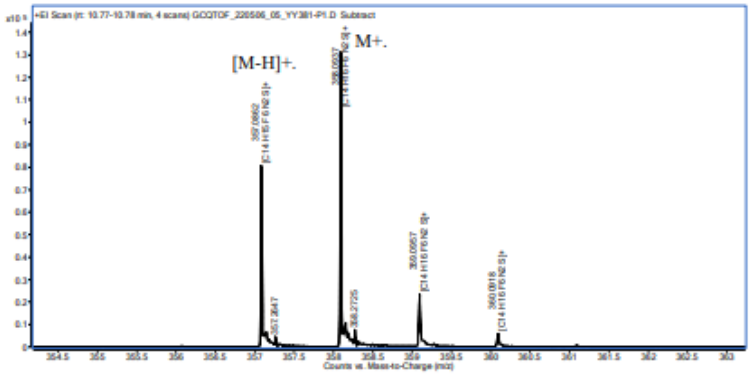



-51.7
-51.7
-51.7
-51.7
-57.5
-57.5
-57.5
-57.5
1.00
1.02
f1 (ppm)


138.1
130.1
129.0
128.3
127.1
126.0
125.2
121.8
62.7
58.4
52.6
52.5
30.9
30.7
f1 (ppm)

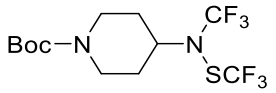






m/z	Ion Formula	Sum Formula	m/z (Calc)	Diff (ppm)	
357.0862	C14H15F6N2S	C14H16F6N2S	357.0855	2.0	$[M-H]^{+\cdot}$
358.0937	C14H16F6N2S		358.0933	1.1	$[M]^{+\cdot}$

tert-butyl 4-((trifluoromethyl)((trifluoromethyl)thio)amino)piperidine-1-carboxylate (3h)



The compound **3h** was obtained as a colorless oil in 54% yield using tert-butyl 4-isothiocyanatopiperidine-1-carboxylate following the general procedure E after column

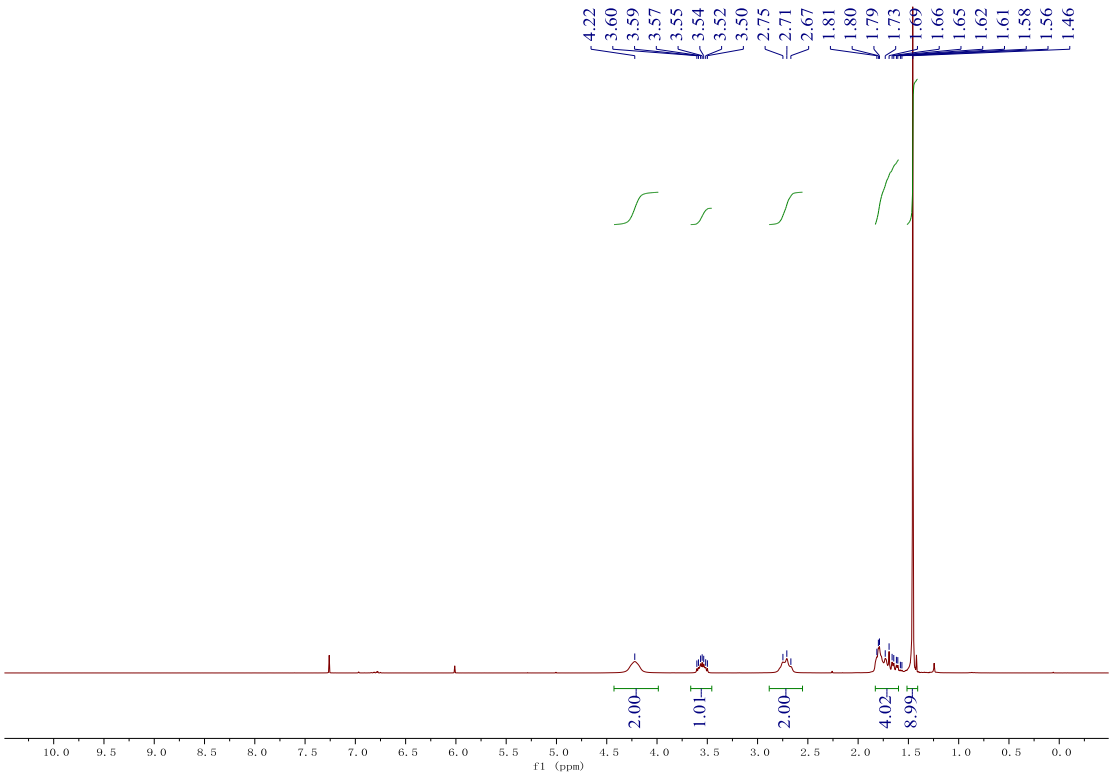
chromatography on silica gel with pentane/ether (10/1).

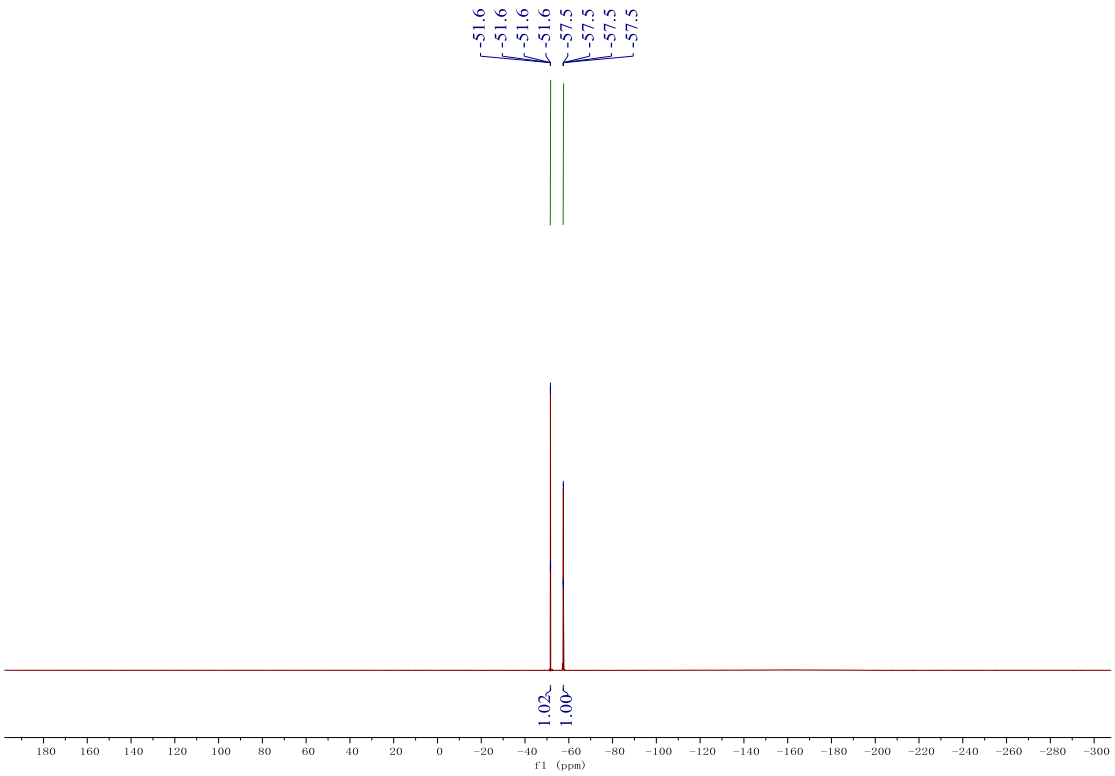
^{1}H NMR (300 MHz, Chloroform-*d*) δ 4.22 (s, 2H), 3.60 – 3.50 (m, 1H), 2.75 – 2.67 (m, 2H), 1.83 – 1.60 (m, 4H), 1.46 (s, 9H).

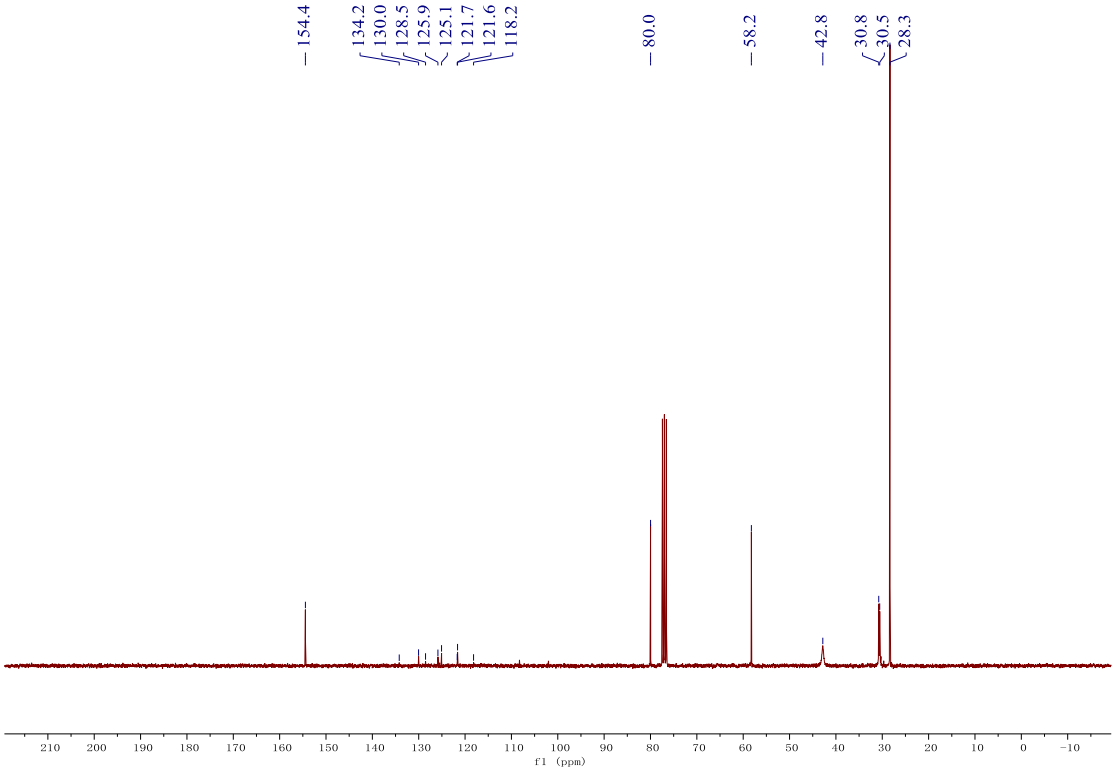
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.6 (q, J = 3.4 Hz), -57.5 (q, J = 3.4 Hz).

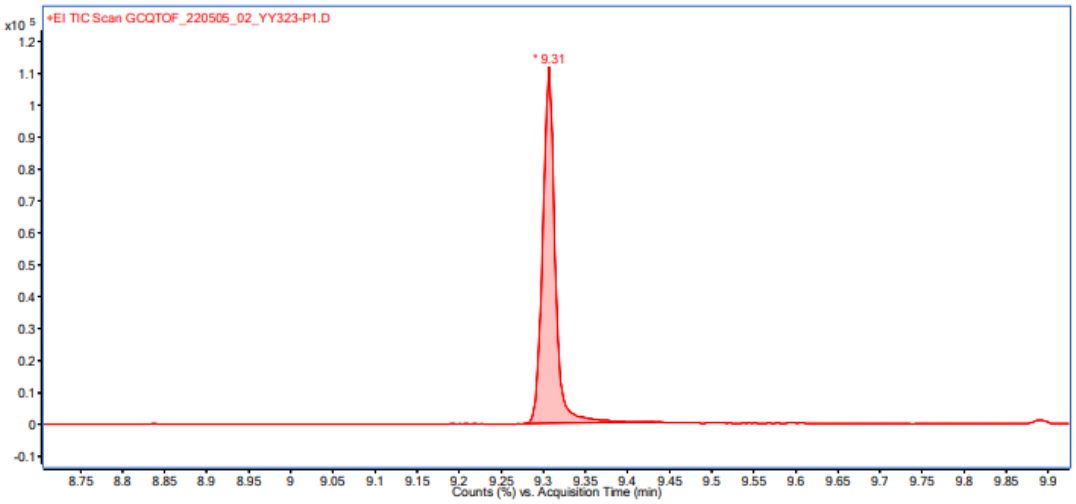
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 154.4, 127.9 (q, *J* = 315.2 Hz), 123.3 (q, *J* = 260.5 Hz), 80.0, 58.2, 42.8, 30.8, 30.5, 28.3.

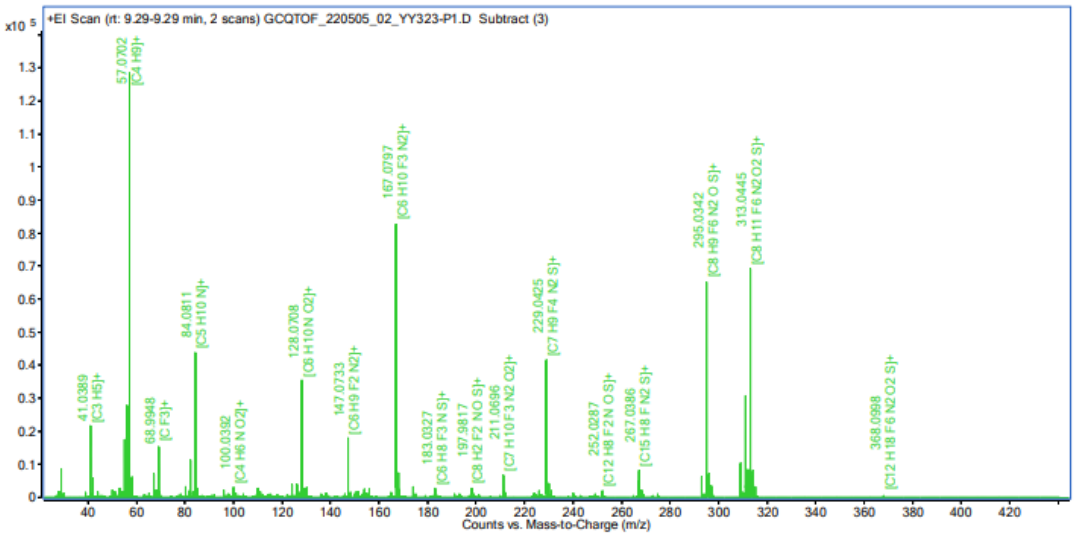
HRMS (EI) calculated for $C_{12}H_{18}F_6N_2O_2S$: 368.0988 $[M]^+$, Found: 368.0998.




-51.6
-51.6
-51.6
-51.6
-57.5
-57.5
-57.5
-57.5
1.02
1.00
f1 (ppm)

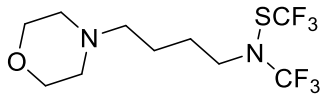

154.4
134.2
130.0
128.5
125.9
125.1
121.7
121.6
118.2
80.0
58.2
42.8
30.8
30.5
28.3
f1 (ppm)





m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
368.0998	C12H18F6N2O2S	368.0988	2.7	$[M]^{+\cdot}$

N-(4-morpholinobutyl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3i)



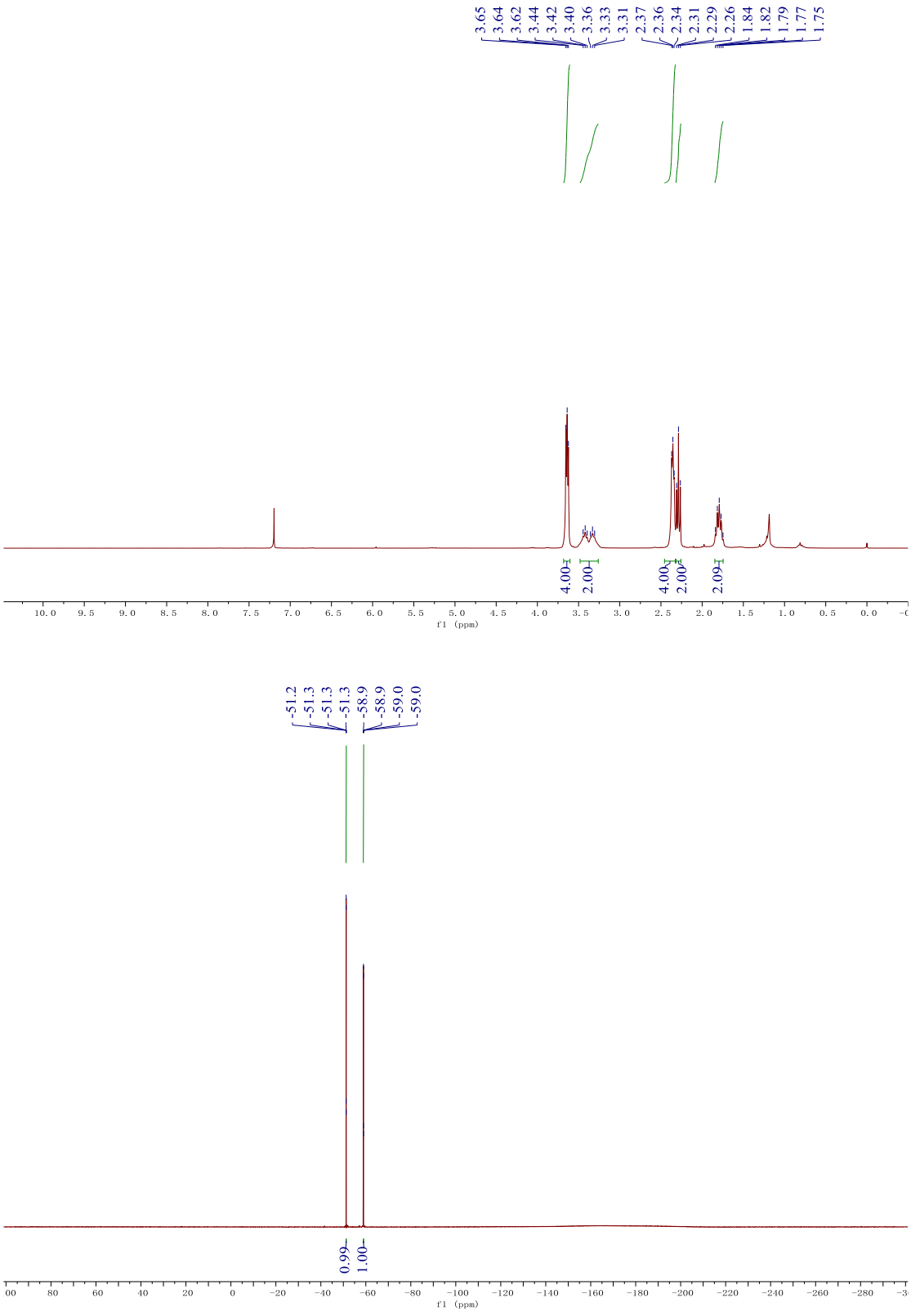
The compound **3i** was obtained as a colorless oil in 56% yield using 4-(4-isothiocyanatobutyl)morpholine following the general procedure E after column chromatography on silica gel with pentane/ether (3/4).

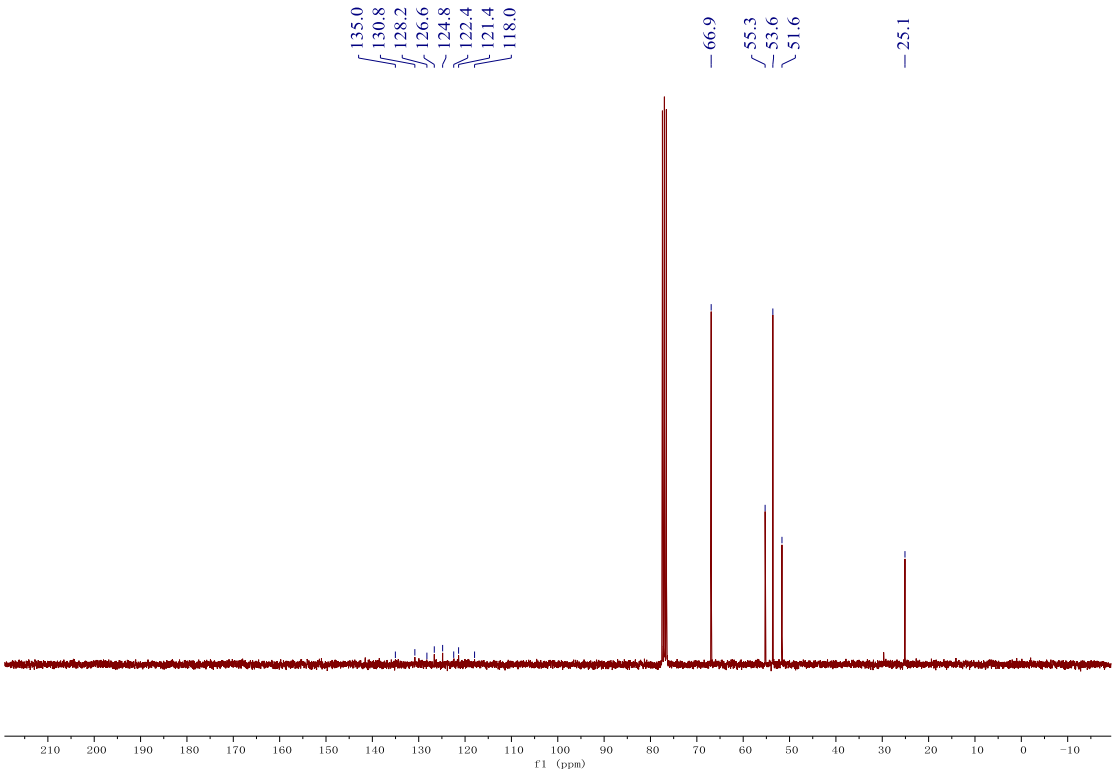
^{1}H NMR (300 MHz, Chloroform-*d*) δ 3.68 – 3.60 (m, 4H), 3.38 (dt, *J* = 27.3, 7.6 Hz, 2H), 2.46 – 2.33 (m, 4H), 2.29 (t, *J* = 6.9 Hz, 2H), 1.79 (p, *J* = 6.8 Hz, 2H).

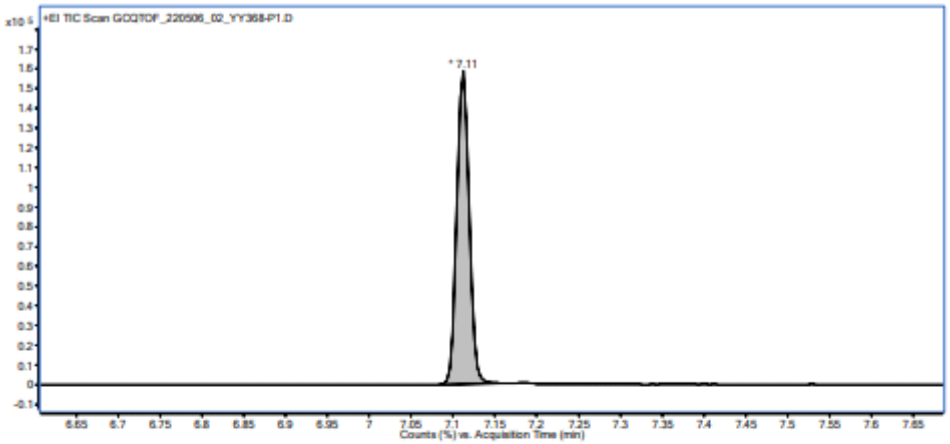
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.4 (q, *J* = 3.4 Hz), -58.9 (q, *J* = 3.4 Hz).

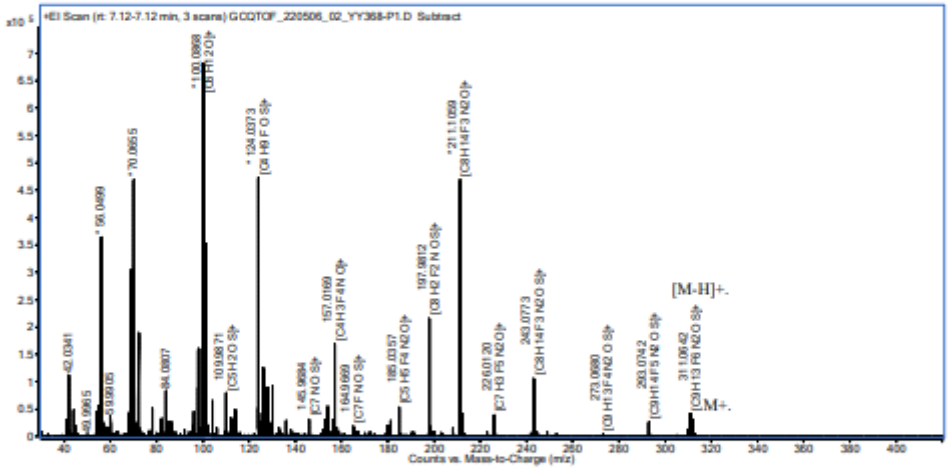
$^{13}C\{^{1}H\}$ NMR (75 MHz, Chloroform-*d*) δ 141.7, 141.1, 139.7, 128.9, 128.5 (d, *J* = 314.1 Hz), 128.2, 127.9, 127.3, 127.2, 122.1 (q, *J* = 260.9 Hz).

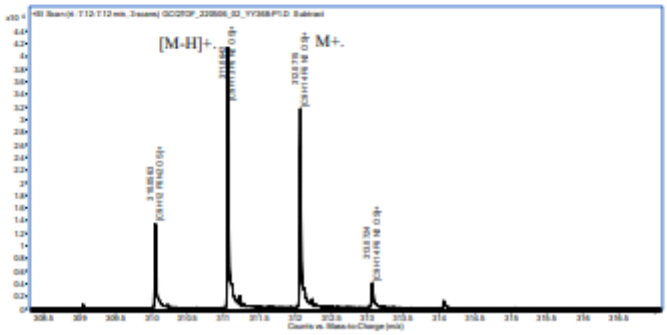
HRMS (EI) calculated for $C_9H_{14}F_6N_2OS$: 312.0726 $[M]^+$, Found: 312.0715.




135.0
130.8
128.2
126.6
124.8
122.4
121.4
118.0
66.9
55.3
53.6
51.6
25.1
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)

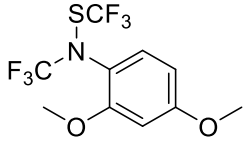






m/z	Ion Formula	Sum Formula	m/z (Calc)	Diff (ppm)	
311.0642	C9H13F6N2OS	C9H14F6N2OS	311.0647	-1.6	$[M-H]^{+\cdot}$
312.0715	C9H14F6N2OS		312.0726	-3.5	$[M]^{+\cdot}$

N-(2,4-dimethoxyphenyl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3j)



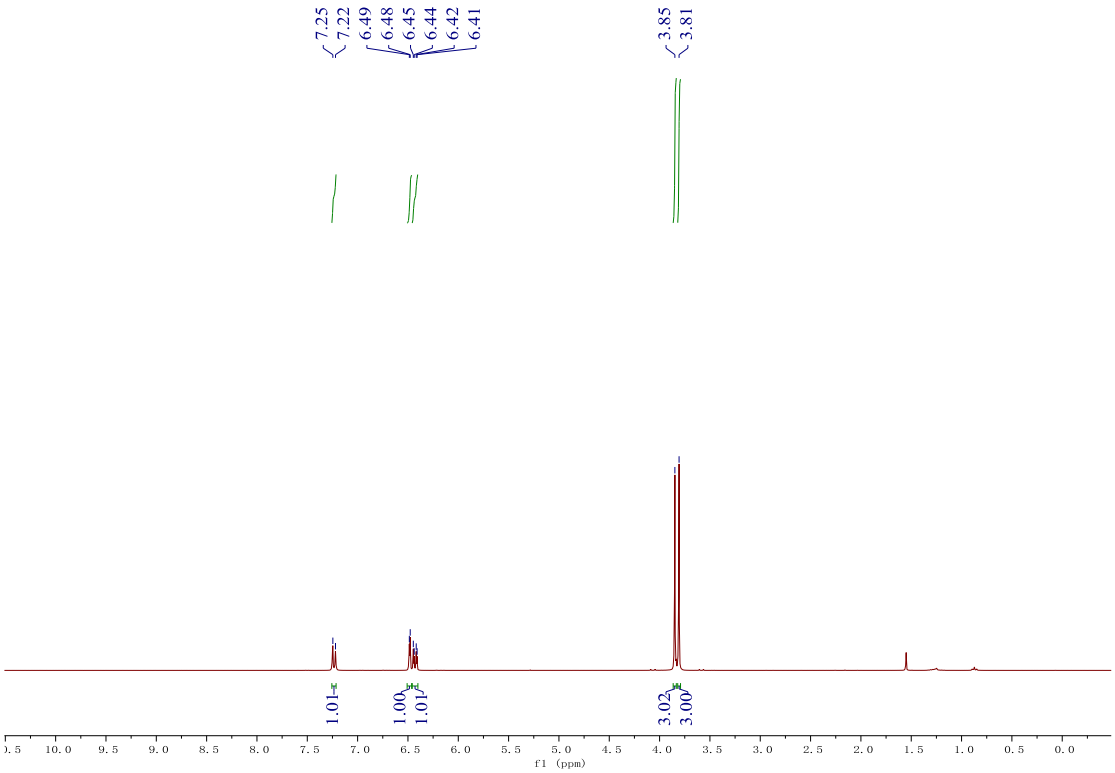
The compound **3j** was obtained as a colorless oil in 70% yield using 1-isothiocyanato-2,4-dimethoxybenzene following the general procedure F after column chromatography on silica gel with pentane.

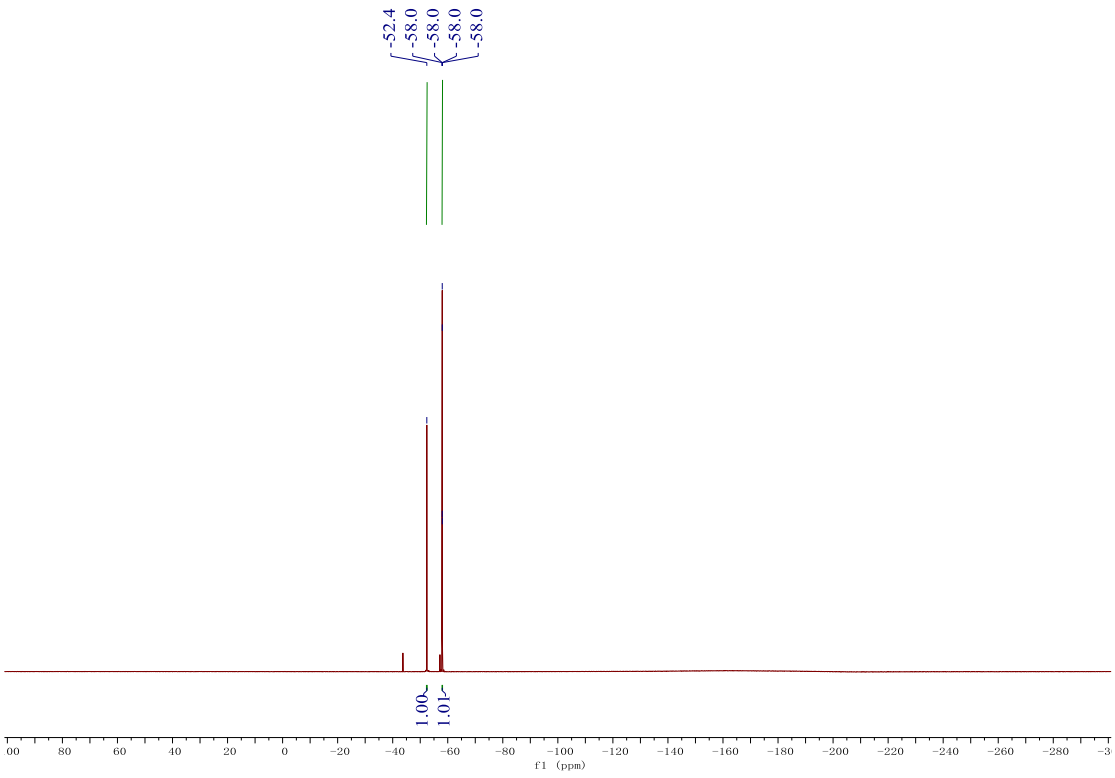
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.23 (d, *J* = 7.8 Hz, 1H), 6.48 (d, *J* = 2.6 Hz, 1H), 6.43 (dd, *J* = 8.7, 2.7 Hz, 1H), 3.85 (s, 3H), 3.81 (s, 3H).

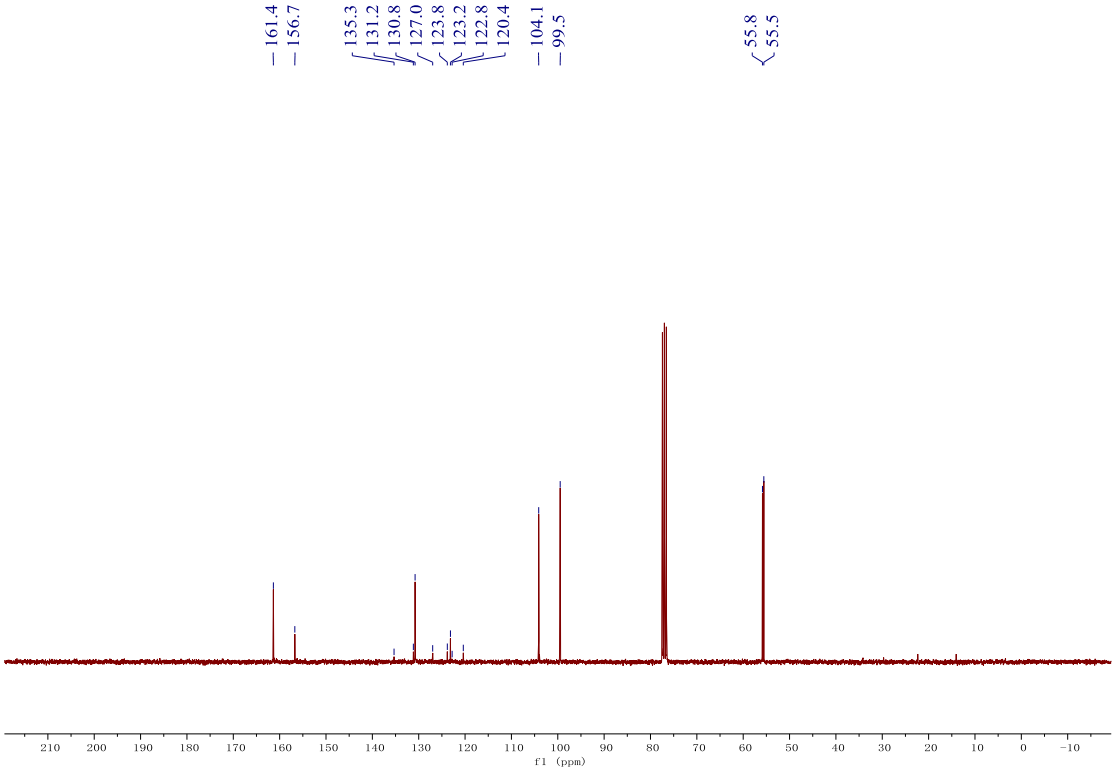
^{19}F NMR (282 MHz, Chloroform-*d*) δ -52.40, -58.01 (q, *J* = 3.4 Hz).

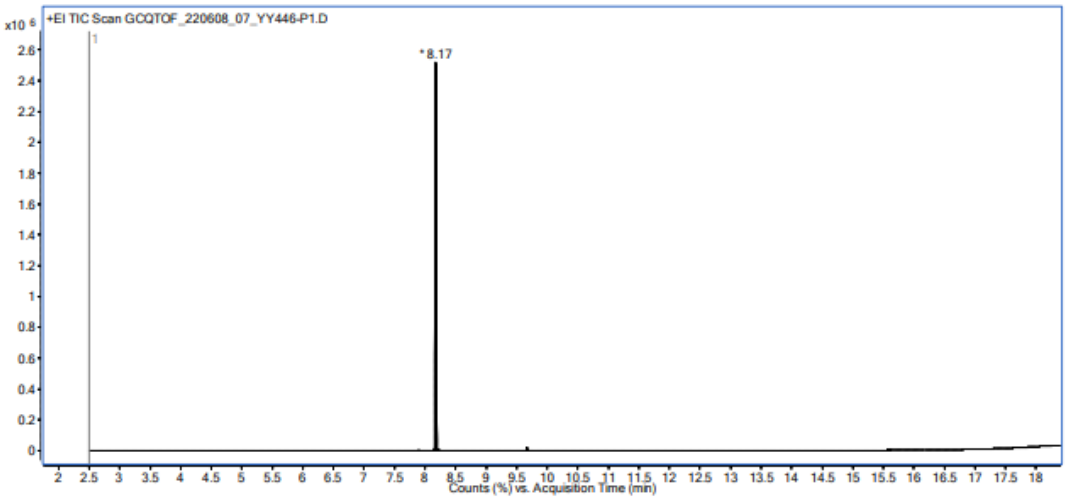
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 161.4, 156.7, 130.8, 129.1 (q, *J* = 314.7 Hz), 123.2, 122.1 (q, *J* = 260.1 Hz), 104.1, 99.5, 55.8, 55.5.

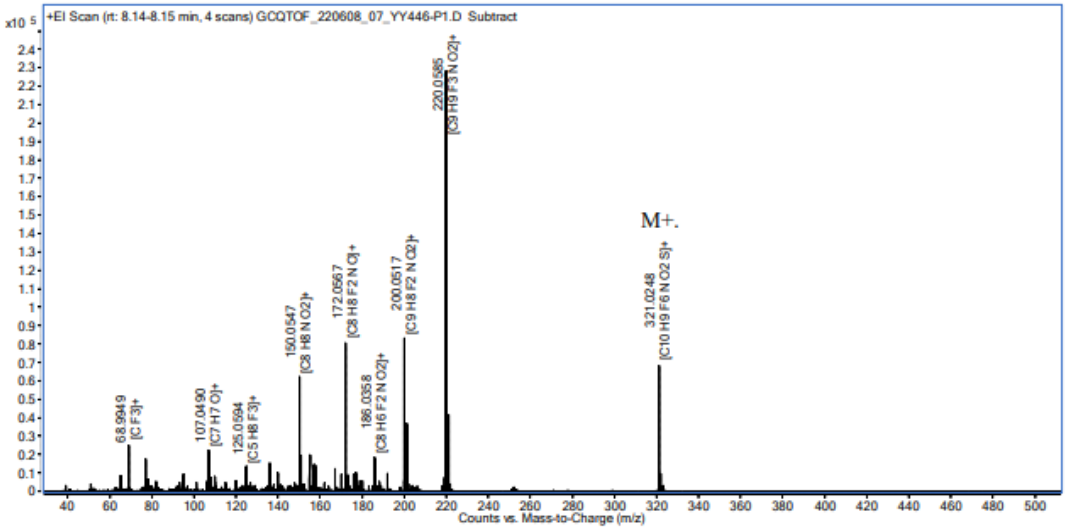
HRMS (EI) calculated for $C_{10}H_9F_6NO_2S$: 321.0253 $[M]^+$, Found: 321.0248.

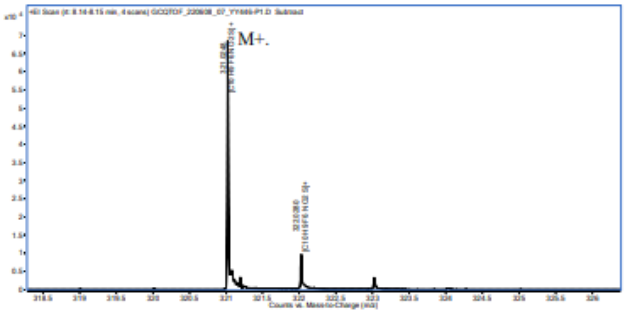



-52.4
-58.0
-58.0
-58.0
-58.0
1.00
1.01
f1 (ppm)


161.4
156.7
135.3
131.2
130.8
127.0
123.8
123.2
122.8
120.4
104.1
99.5
55.8
55.5
f1 (ppm)







Meas. m/z	Ion Formula	m/z (Calc)	err (ppm)	
321.0248	C10H9F6NO2S	321.0253	-1.6	$[M]^{+\cdot}$

N-(3,4-dimethoxyphenyl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3k)

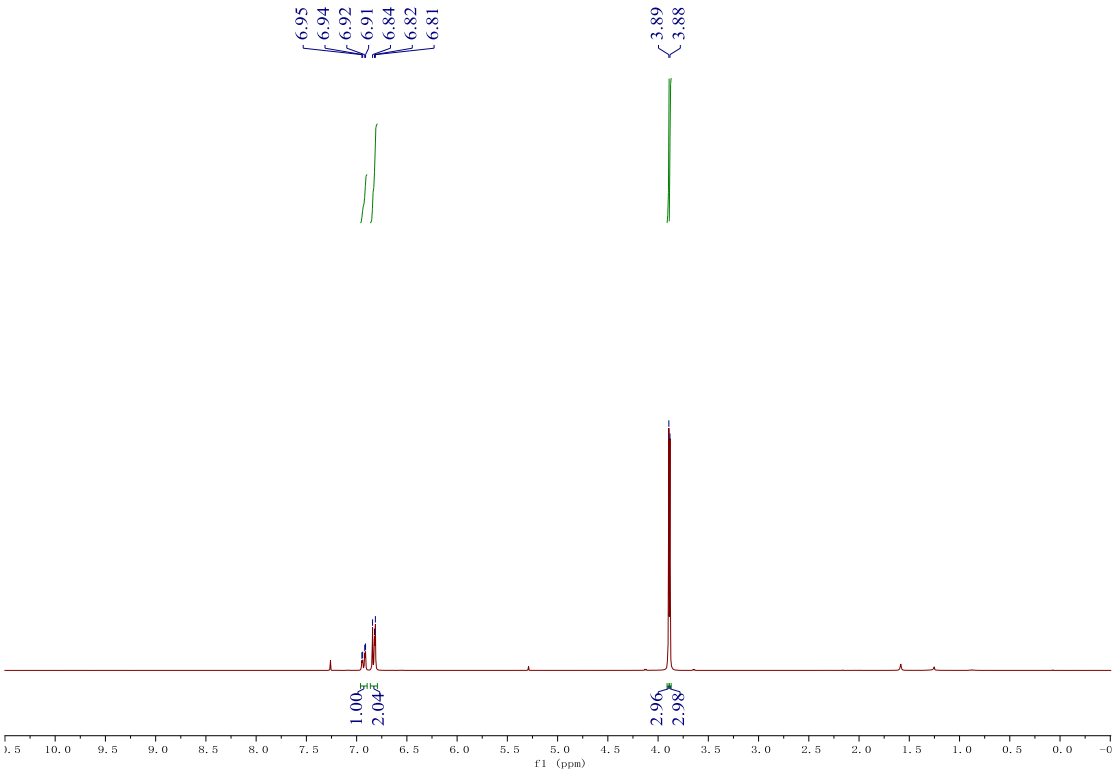
The compound **3l'** was obtained as a colorless oil in 73% yield using 4-isothiocyanato-1,2-dimethoxybenzene following the general procedure F after column chromatography on silica gel with pentane.

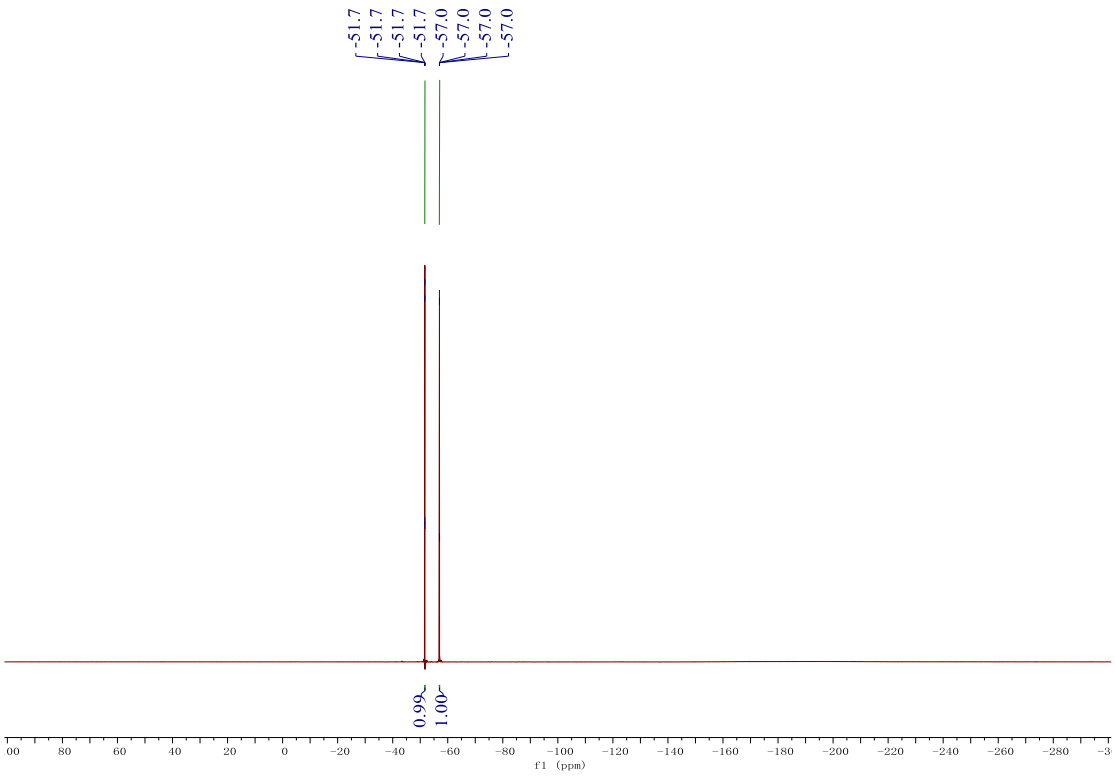
^{1}H NMR (300 MHz, Chloroform-*d*) δ 6.95 – 6.91 (m, 1H), 6.86 – 6.79 (m, 2H), 3.89 (s, 3H), 3.88 (s, 3H).

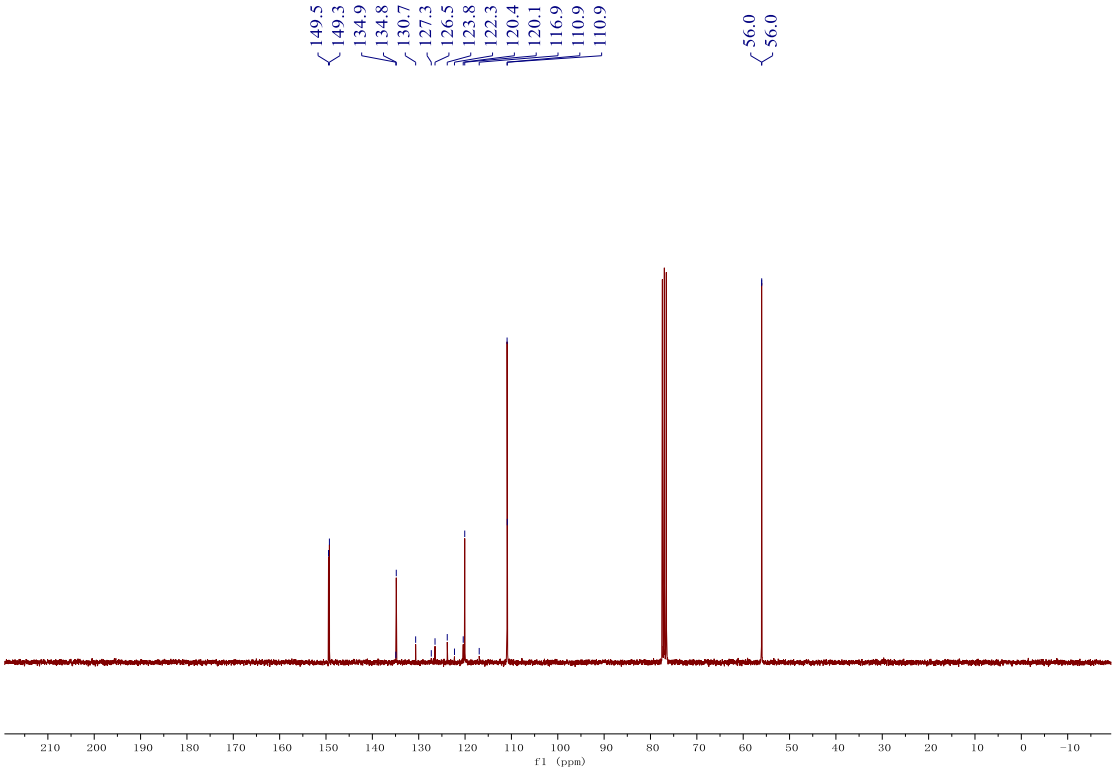
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.7 (q, *J* = 3.4 Hz), -57.0 (q, *J* = 3.4 Hz).

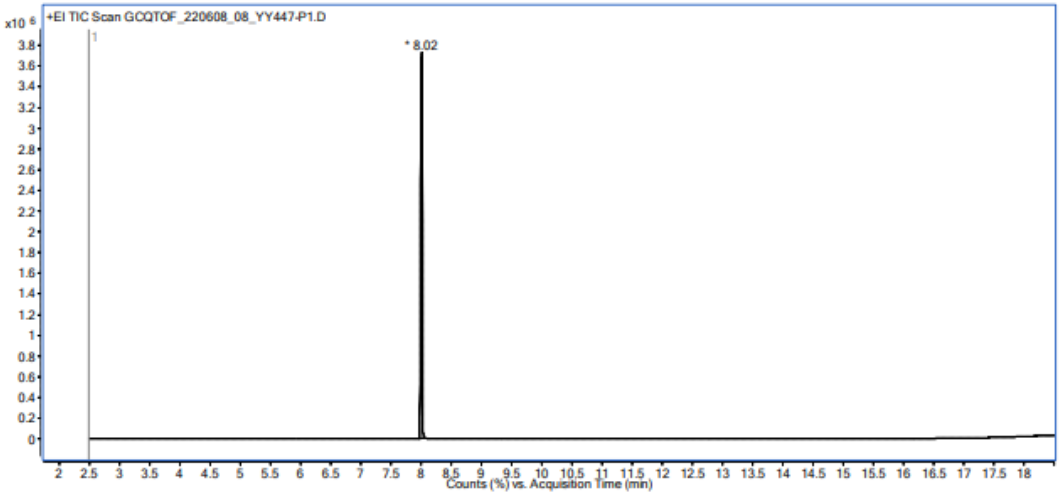
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 149.5, 149.3, 134.8, 128.6 (q, *J* = 315.5 Hz), 122.1 (q, *J* = 259.9 Hz), 120.1, 110.9, 110.9, 56.0, 56.0.

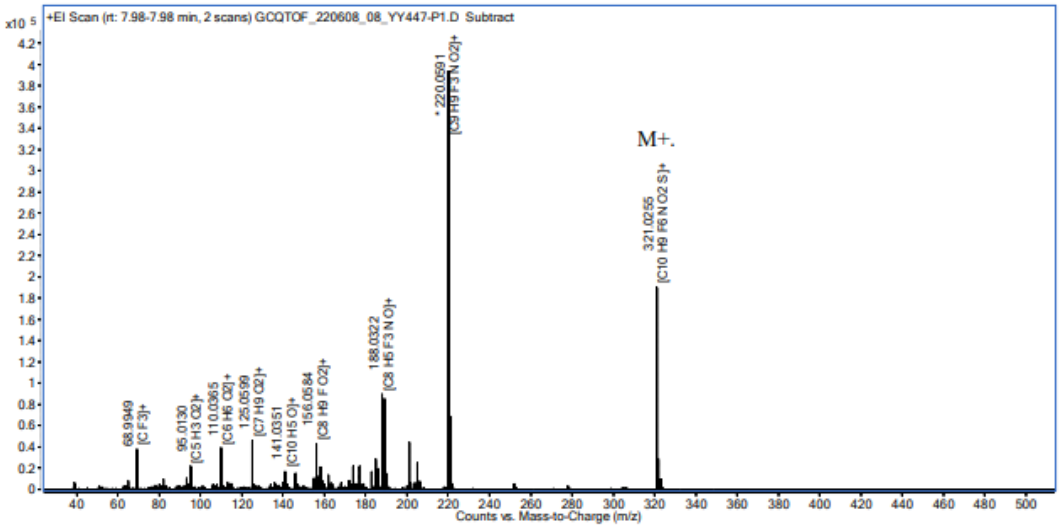
HRMS (EI) calculated for $C_{10}H_9F_6NO_2S$: 321.0253 $[M]^+$, Found: 321.0255.

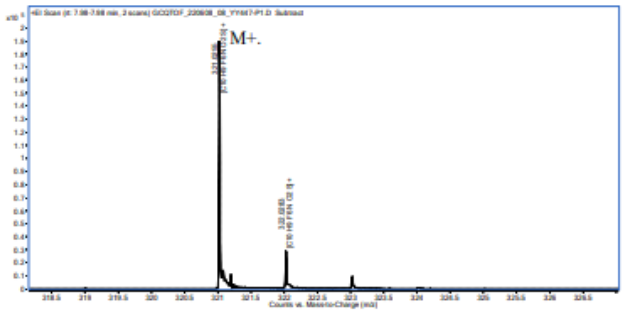



-51.7
-51.7
-51.7
-51.7
-57.0
-57.0
-57.0
-57.0
0.99
1.00
f1 (ppm)


149.5
149.3
134.9
134.8
130.7
127.3
126.5
123.8
122.3
120.4
120.1
116.9
110.9
110.9
56.0
56.0
f1 (ppm)

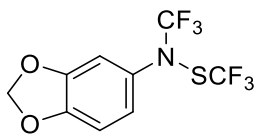






Meas. m/z	Ion Formula	m/z (Calc)	err (ppm)	
321.0255	C10H9F6NO2S	321.0253	0.6	$[M]^{+\cdot}$

N-(benzo[d][1,3]dioxol-5-yl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3l)



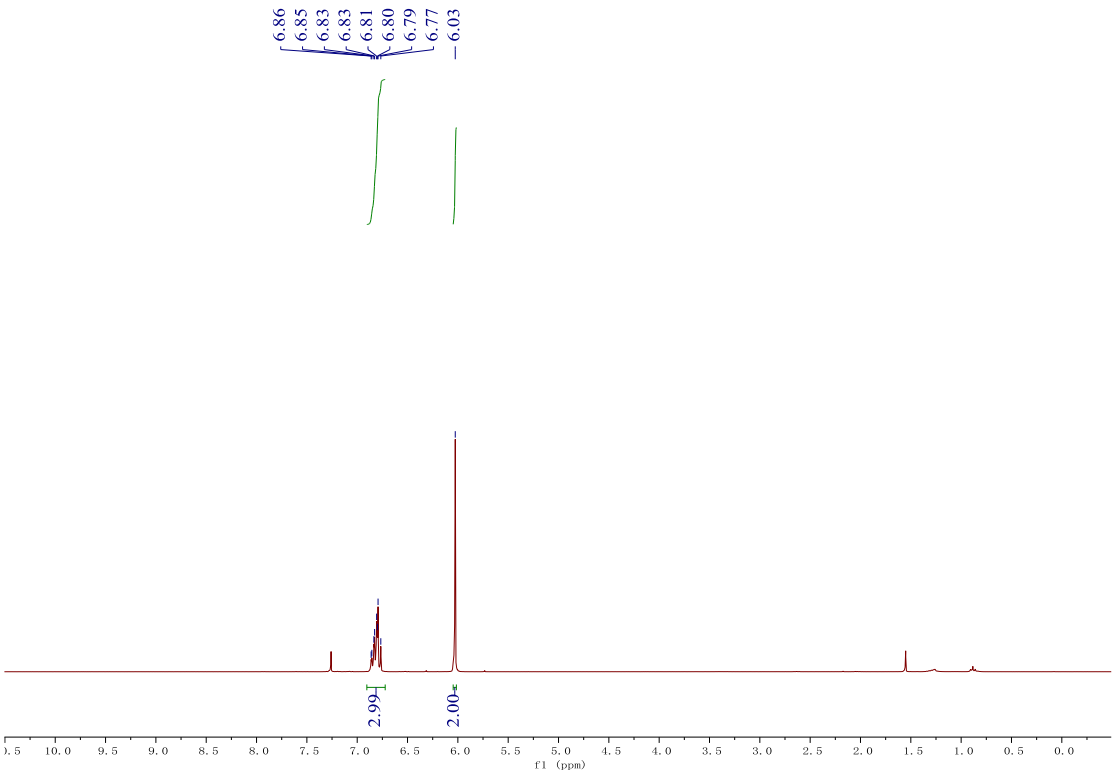
The compound **3l** was obtained as a colorless oil in 65% yield using 5-isothiocyanatobenzo[d][1,3]dioxole following the general procedure E after column chromatography on silica gel with pentane.

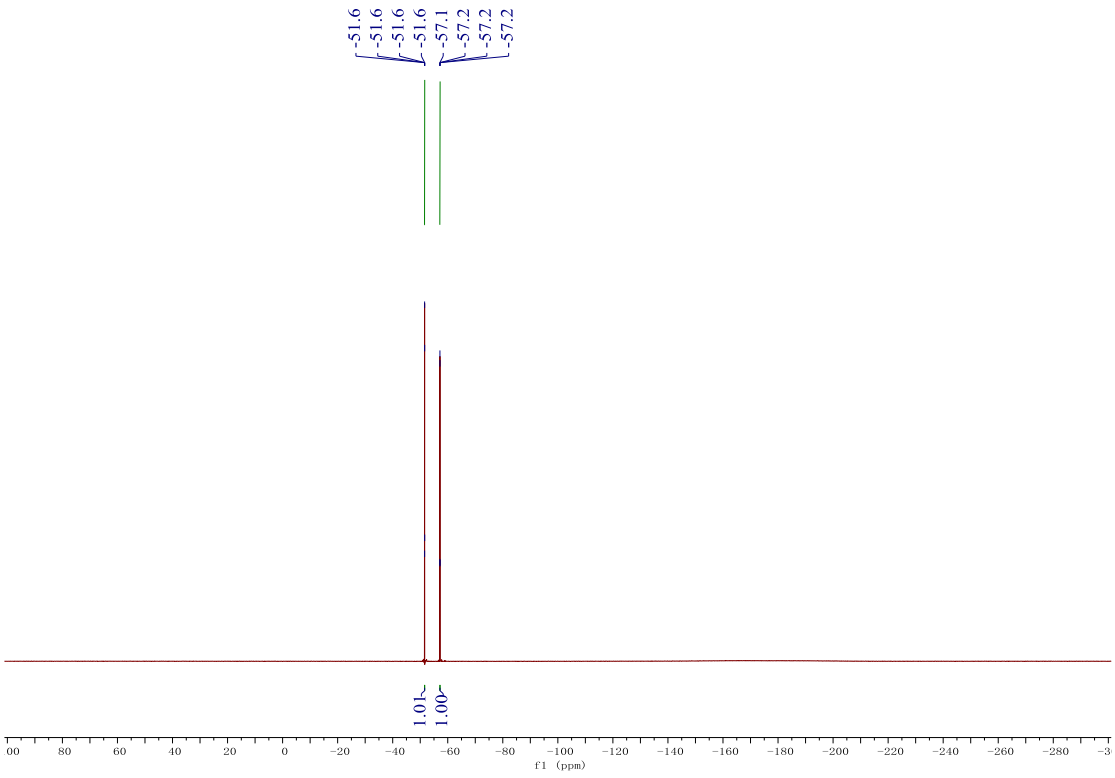
^{1}H NMR (300 MHz, Chloroform-*d*) δ 6.90 – 6.72 (m, 3H), 6.03 (s, 2H).

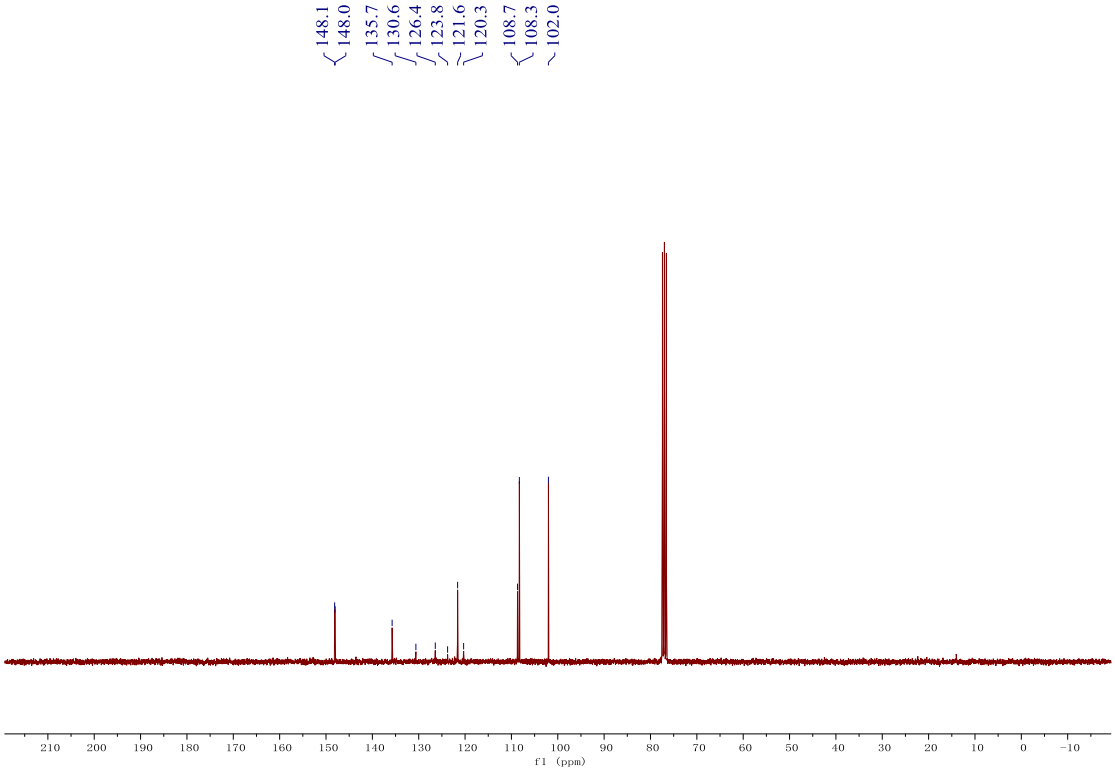
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.6 (q, *J* = 3.4 Hz), -57.2 (q, *J* = 3.4 Hz).

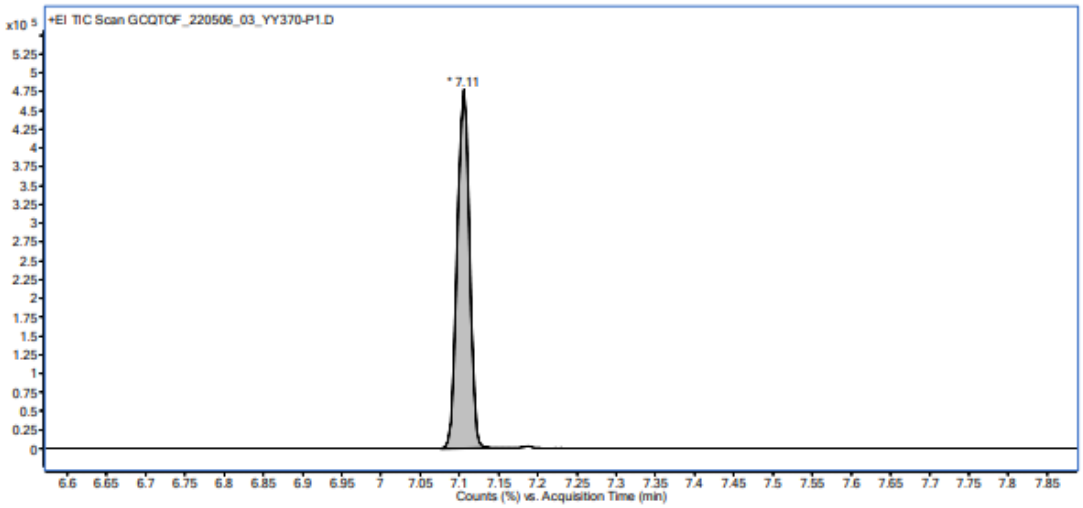
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 148.1, 148.0, 135.7, 128.5 (q, *J* = 315.6 Hz), 122.0 (q, *J* = 260.9 Hz), 121.6, 108.7, 108.3, 102.0.

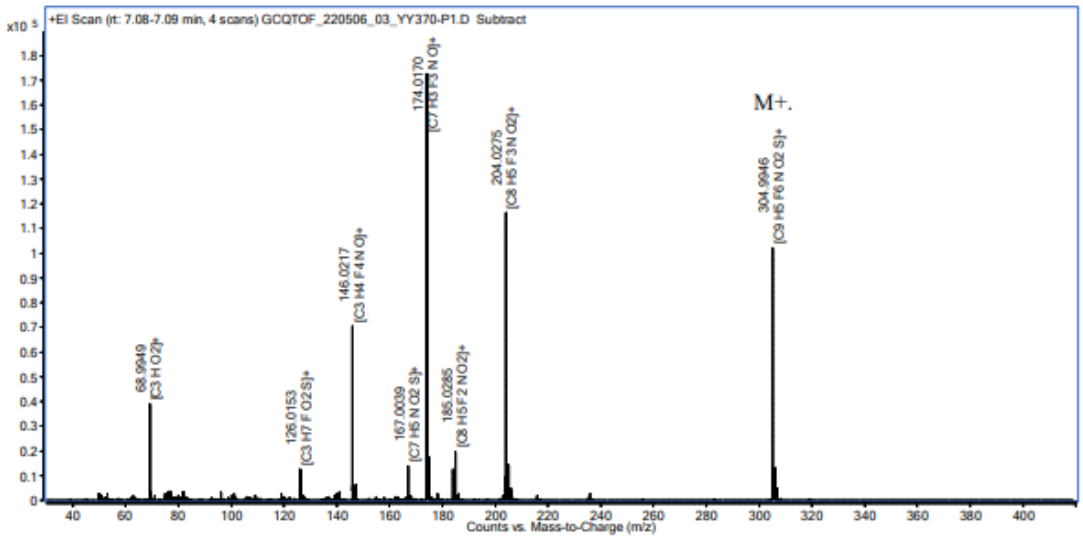
HRMS (EI) calculated for $C_9H_5F_6NO_2S$: 304.9940 $[M]^+$, Found: 304.9946.

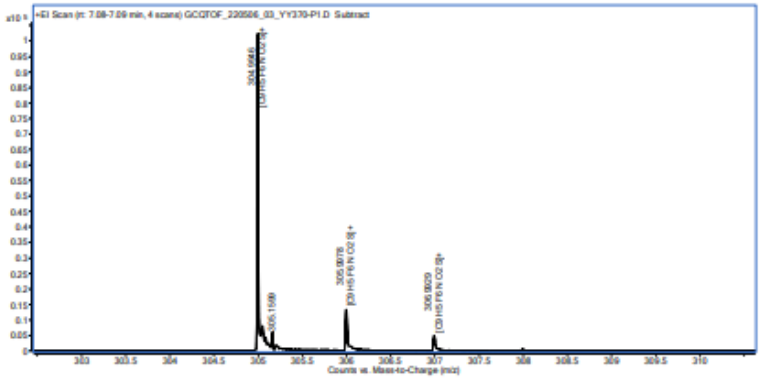



-51.6
-51.6
-51.6
-51.6
-57.1
-57.2
-57.2
-57.2
1.01
1.00
f1 (ppm)


148.1
148.0
135.7
130.6
126.4
123.8
121.6
120.3
108.7
108.3
102.0
f1 (ppm)

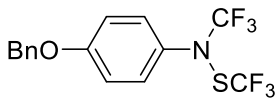






m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
304.9946	C9H5F6NO2S	304.9940	2.0	$[M]^{+\cdot}$

N-(4-(benzyloxy)phenyl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3m)



The compound **3h** was obtained as a white solid in 57% yield using 1-(benzyloxy)-4-

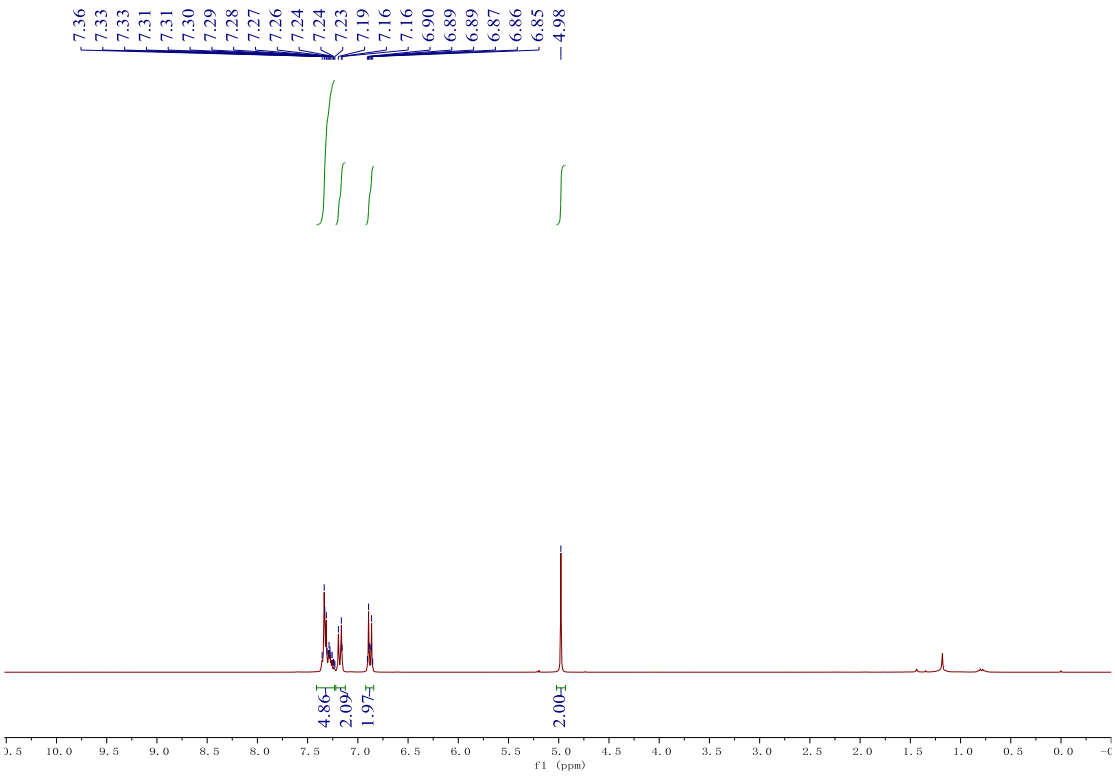
isothiocyanatobenzene following the general procedure E after column chromatography on silica gel with pentane.

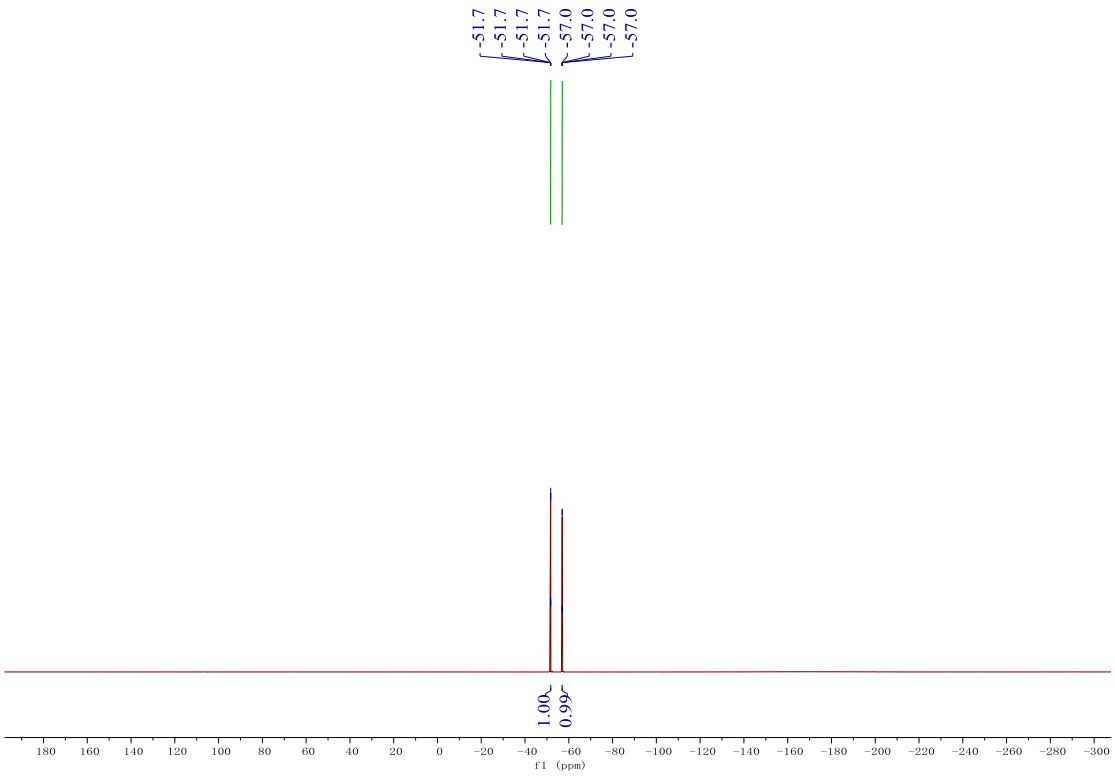
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.41 – 7.23 (m, 5H), 7.22 – 7.12 (m, 2H), 6.92 – 6.84 (m, 2H), 4.98 (s, 2H).

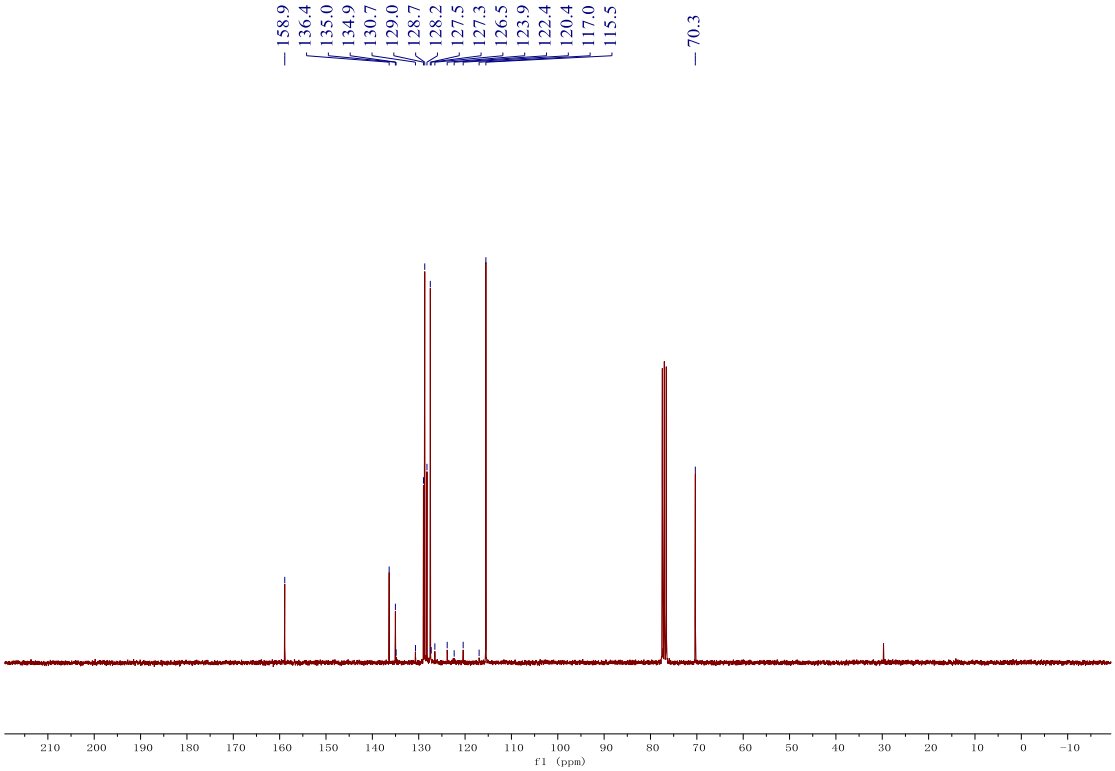
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.7 (q, *J* = 3.4 Hz), -57.0 (q, *J* = 3.4 Hz).

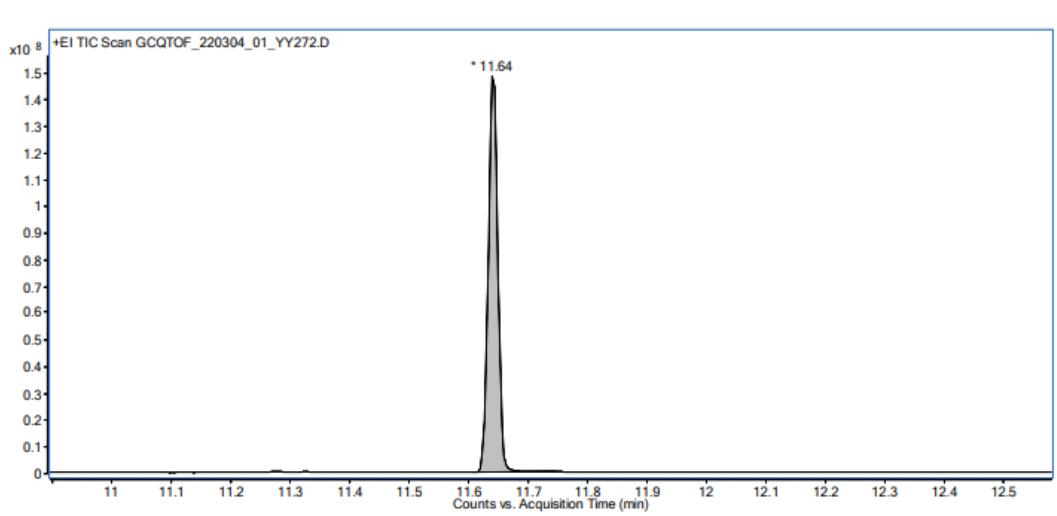
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 158.9, 136.4, 135.0, 129.0, 128.7, 128.6 (q, *J* = 315.7 Hz), 128.2, 127.5, 122.1 (q, *J* = 259.9 Hz), 115.5, 70.3.

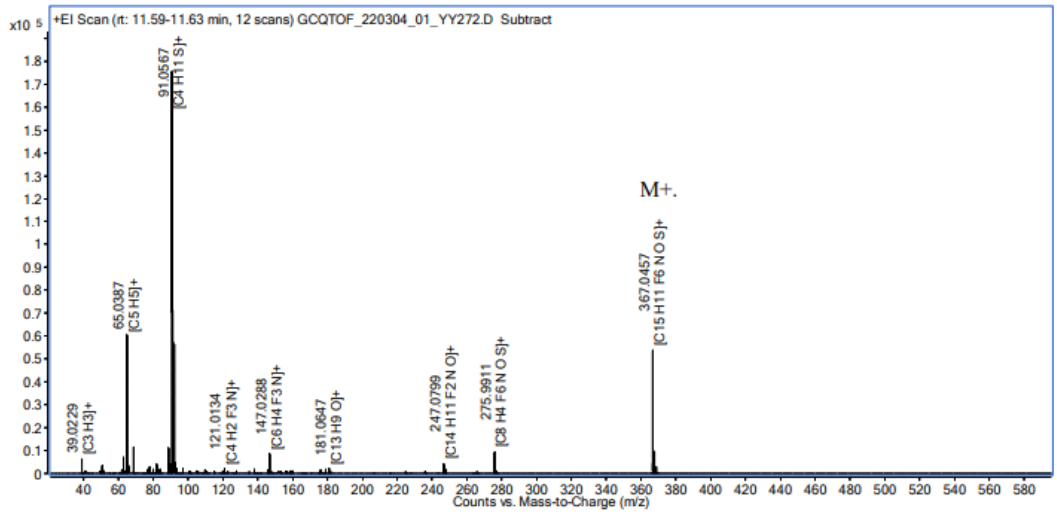
HRMS (EI) calculated for $C_{15}H_{11}F_6NOS$: 367.0460 $[M]^+$, Found: 367.0457.




-51.7
-51.7
-51.7
-51.7
-57.0
-57.0
-57.0
-57.0
1.00
0.99
f1 (ppm)

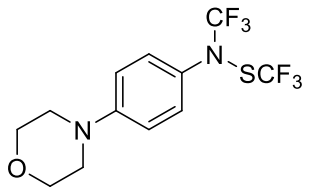

158.9
136.4
135.0
134.9
130.7
129.0
128.7
128.2
127.5
127.3
126.5
123.9
122.4
120.4
117.0
115.5
70.3
f1 (ppm)





m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
367.0457	C15H11F6NOS	367.0460	-0.8	$[M]^{+\cdot}$

N-(4-morpholinophenyl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3o)



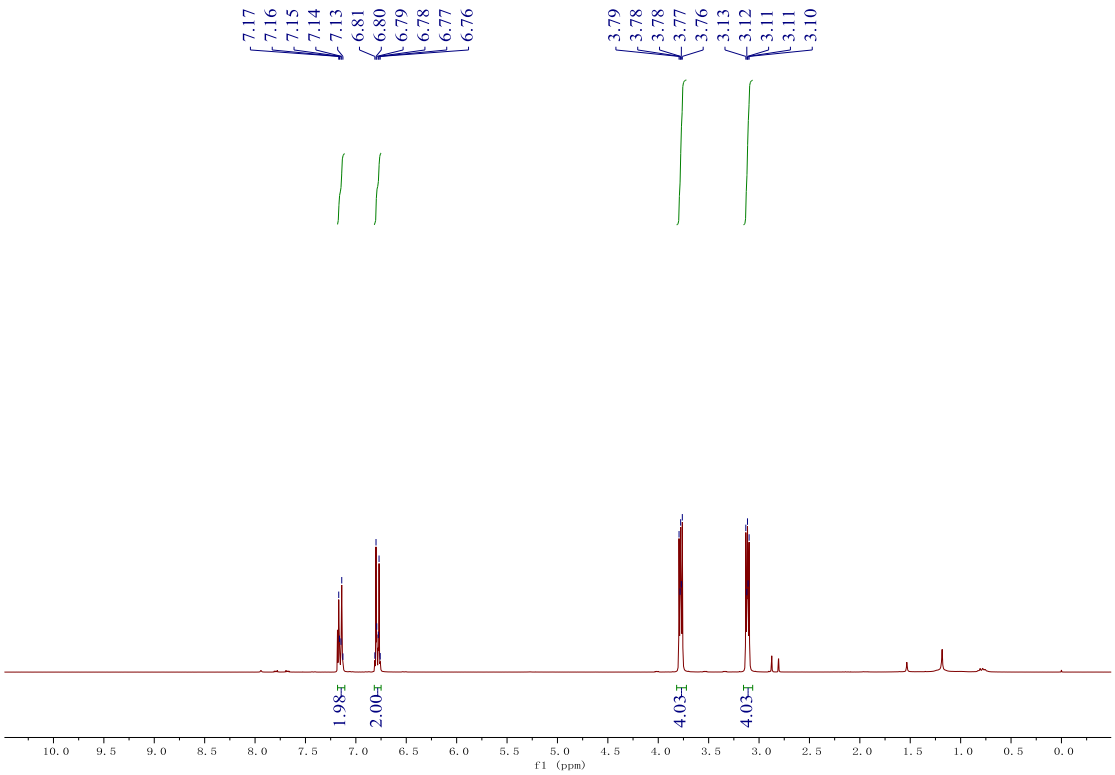
The compound **3o** was obtained as a colorless oil in 78% yield using 4-(4-isothiocyanatophenyl)morpholine following the general procedure E after column chromatography on silica gel with toluene.

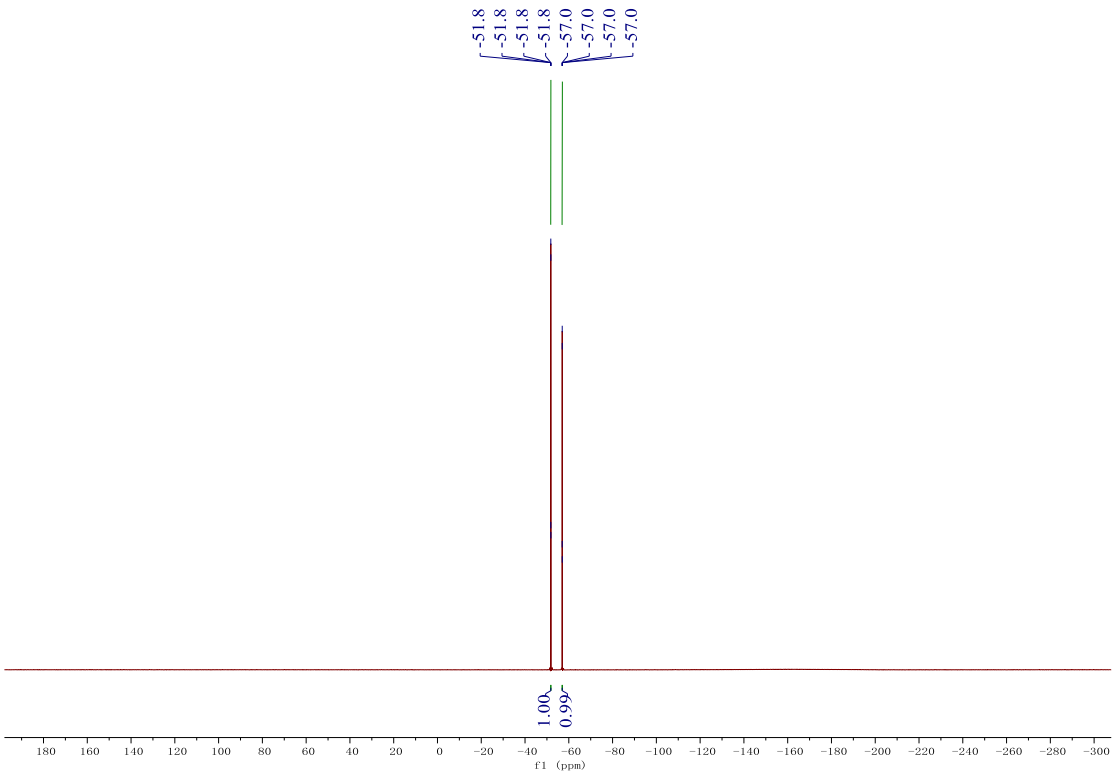
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.18 – 7.11 (m, 2H), 6.82 – 6.75 (m, 2H), 3.82 – 3.72 (m, 4H), 3.15 – 3.06 (m, 4H).

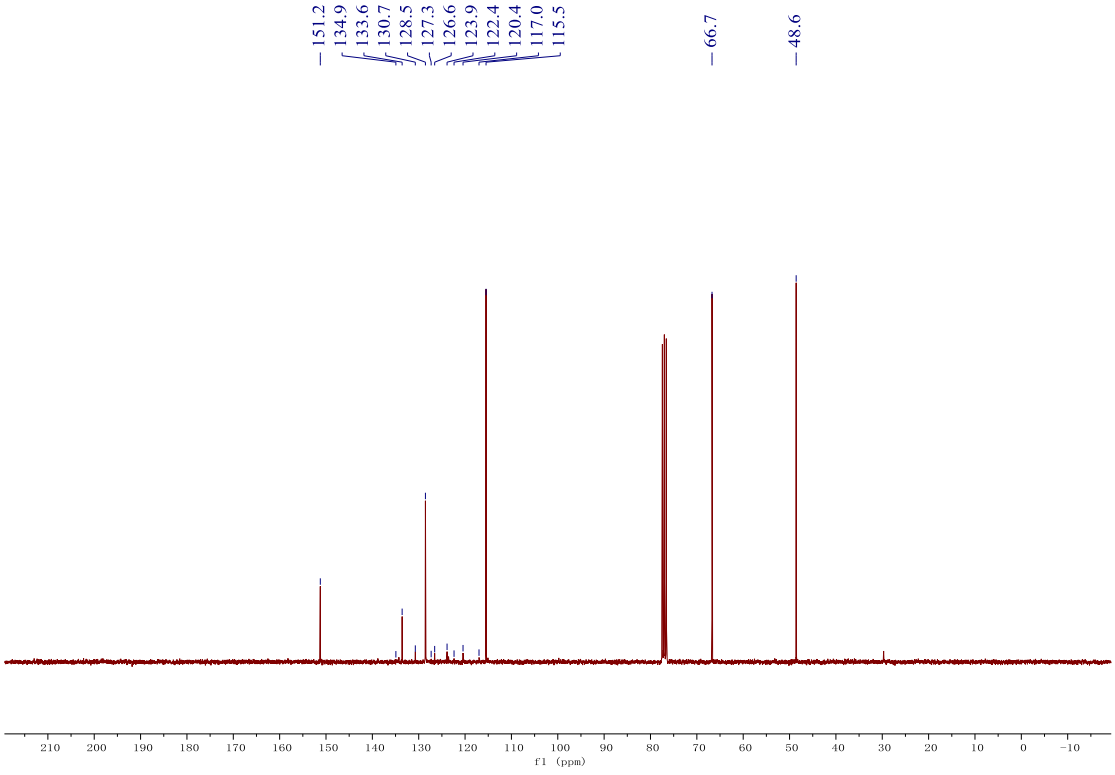
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.8 (q, *J* = 3.4 Hz), -57.0 (q, *J* = 3.4 Hz).

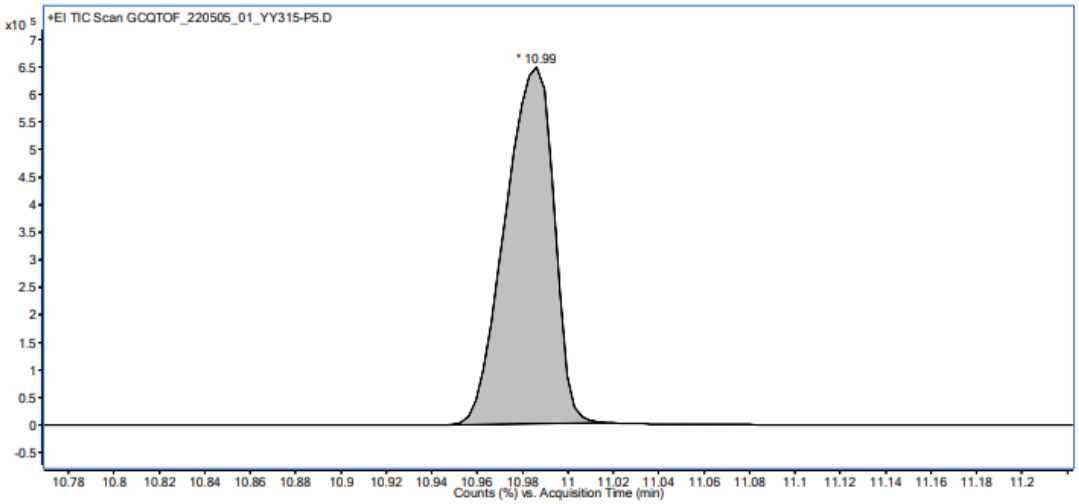
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 151.2, 133.6, 128.5 (q, *J* = 315.2 Hz), 128.5, 122.2 (q, *J* = 259.9 Hz), 115.5, 66.7, 48.6.

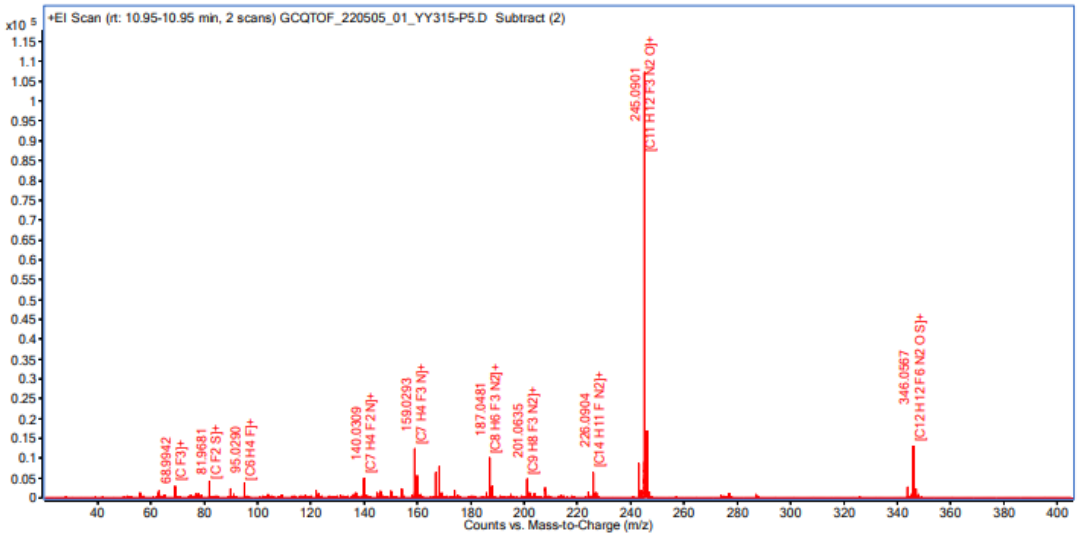
HRMS (EI) calculated for $C_{12}H_{12}F_6N_2OS$: 346.0569 $[M]^+$, Found: 346.0567.




-51.8
-51.8
-51.8
-51.8
-57.0
-57.0
-57.0
-57.0
1.00
0.99
f1 (ppm)

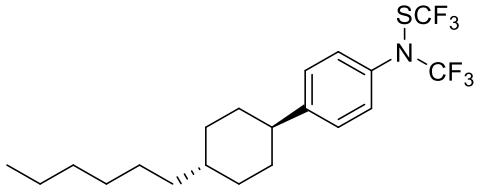

151.2
134.9
133.6
130.7
128.5
127.3
126.6
123.9
122.4
120.4
117.0
115.5
66.7
48.6
f1 (ppm)





m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
346.0567	C12H12F6N2OS	346.0569	-0.6	$[M]^{+\cdot}$

N-(4-((1s,4r)-4-hexylcyclohexyl)phenyl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3p)



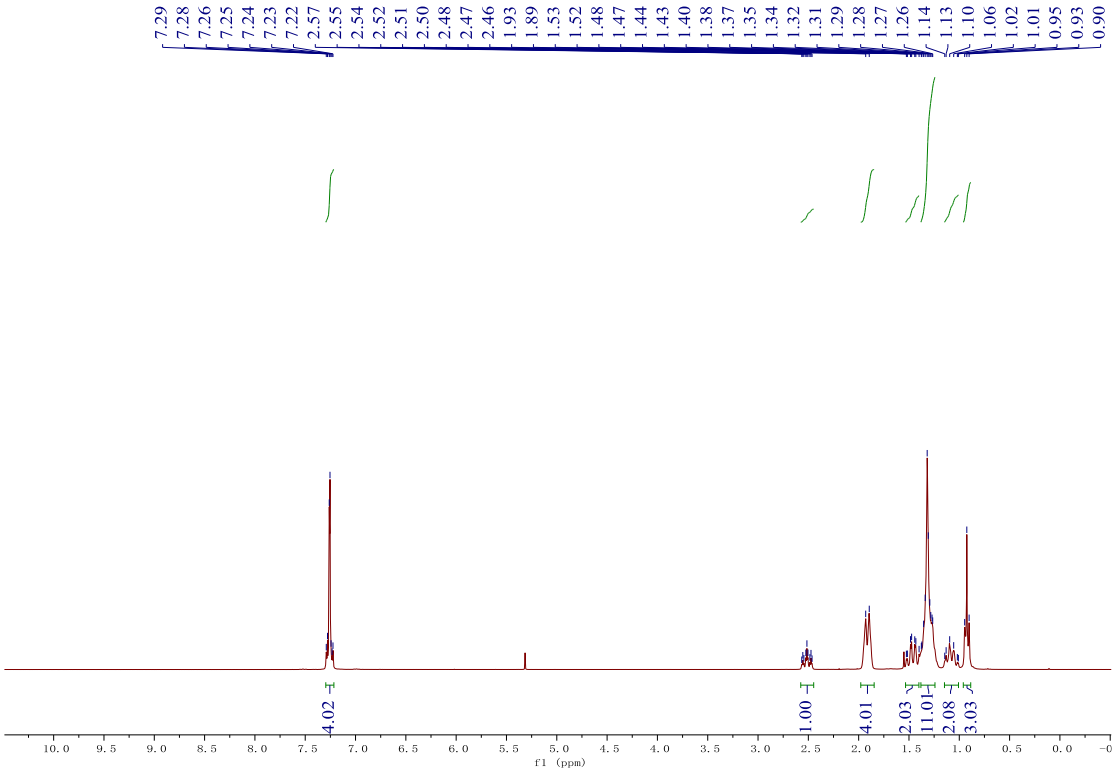
The compound **3p** was obtained as a colorless oil in 36% yield using 1-((1s,4r)-4-hexylcyclohexyl)-4-isothiocyanatobenzene following the general procedure E after column chromatography on silica gel with cyclohexane.

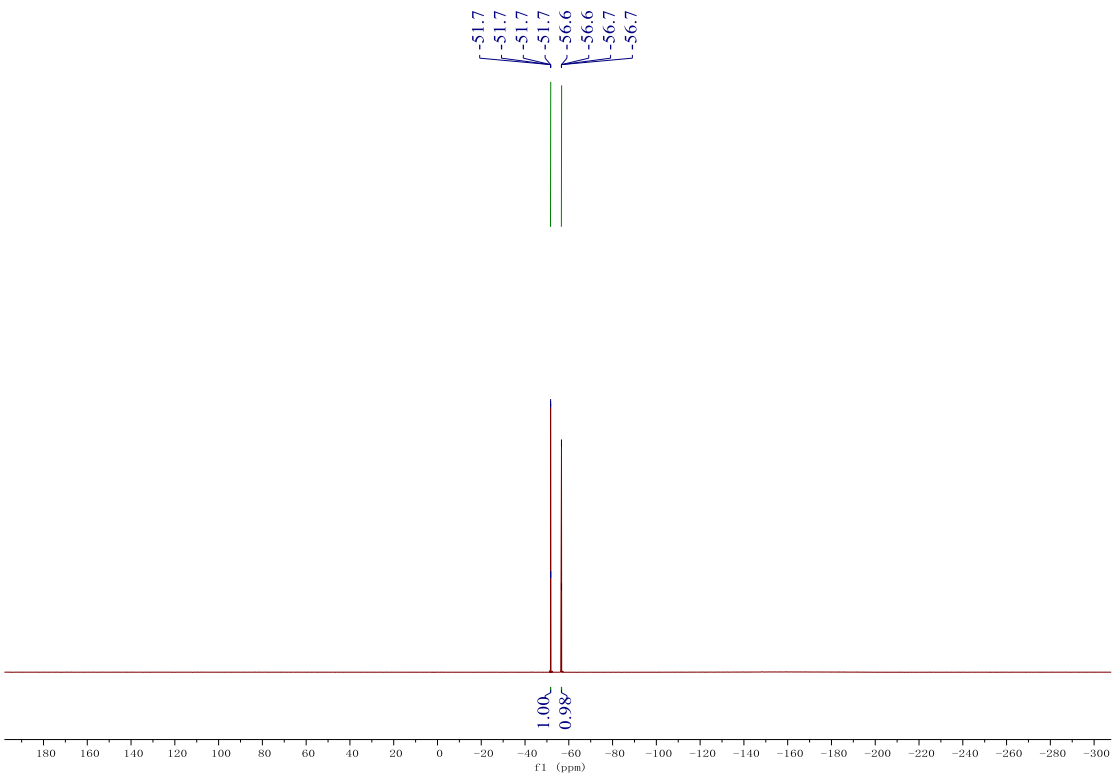
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.30 – 7.22 (m, 4H), 2.51 (tt, *J* = 12.2, 3.2 Hz, 1H), 1.91 (d, *J* = 10.6 Hz, 4H), 1.53 – 1.38 (m, 2H), 1.37 – 1.26 (m, 11H), 1.15 – 1.01 (m, 2H), 0.96 – 0.89 (m, 3H).

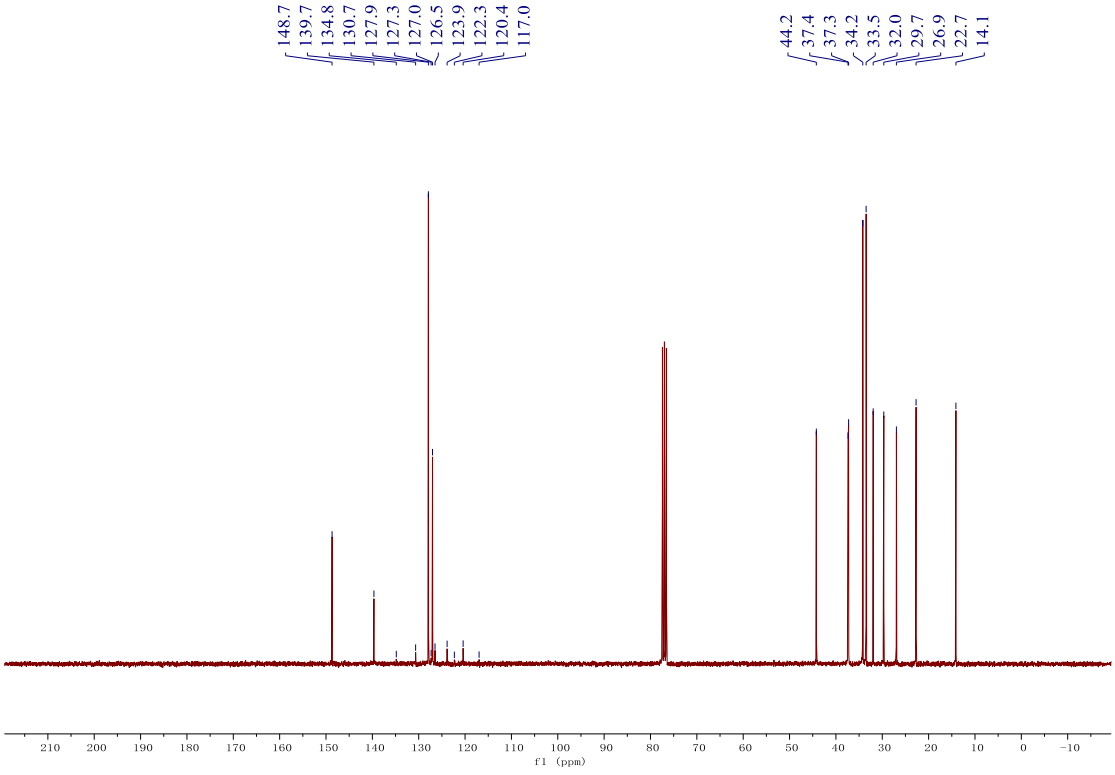
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.7 (q, *J* = 3.4 Hz), -56.7 (q, *J* = 3.4 Hz).

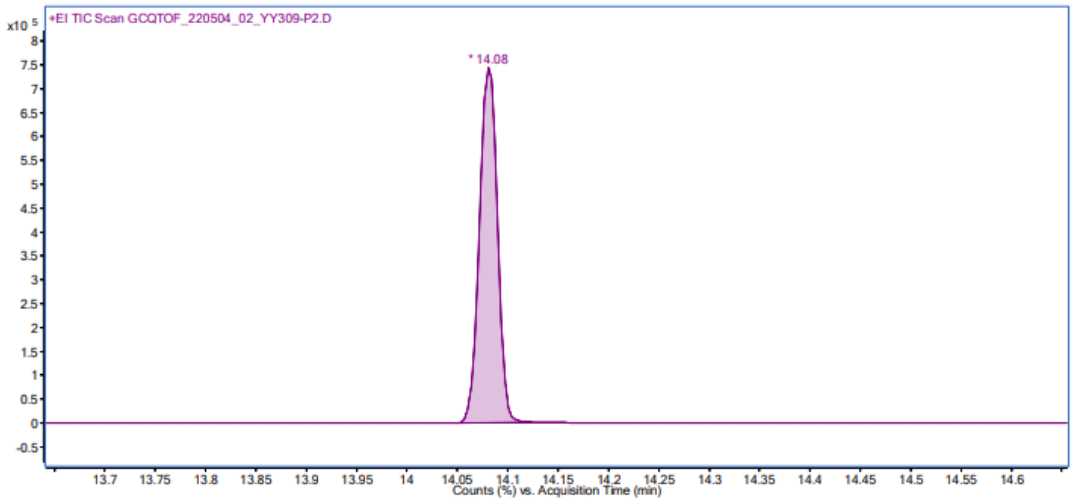
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 148.7, 139.7, 128.6 (q, *J* = 315.9 Hz), 127.9, 127.0, 122.2 (q, *J* = 260.7 Hz), 44.2, 37.4, 37.3, 34.2, 33.5, 32.0, 29.7, 26.9, 22.7, 14.1.

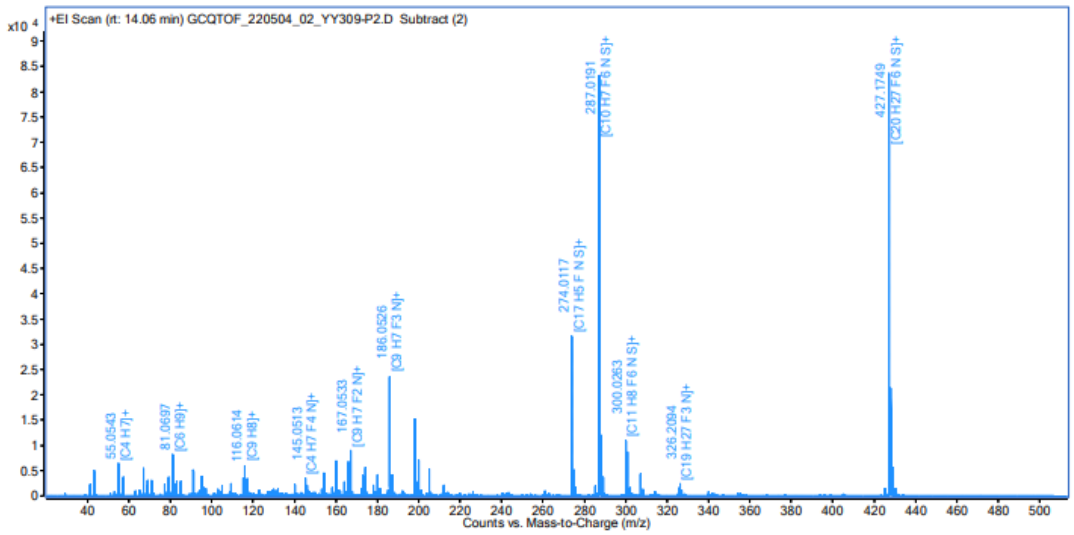
HRMS (EI) calculated for $C_{20}H_{27}F_6NS$: 427.1763 $[M]^+$, Found: 427.1749.




-51.7
-51.7
-51.7
-51.7
-56.6
-56.6
-56.7
-56.7
1.00
0.98
f1 (ppm)

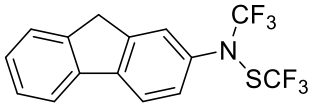

148.7
139.7
134.8
130.7
127.9
127.3
127.0
126.5
123.9
122.3
120.4
117.0
44.2
37.4
37.3
34.2
33.5
32.0
29.7
26.9
22.7
14.1
f1 (ppm)





m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
427.1749	C20H27F6NS	427.1763	-3.3	$[M]^{+\cdot}$

N-(9H-fluoren-2-yl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3q)



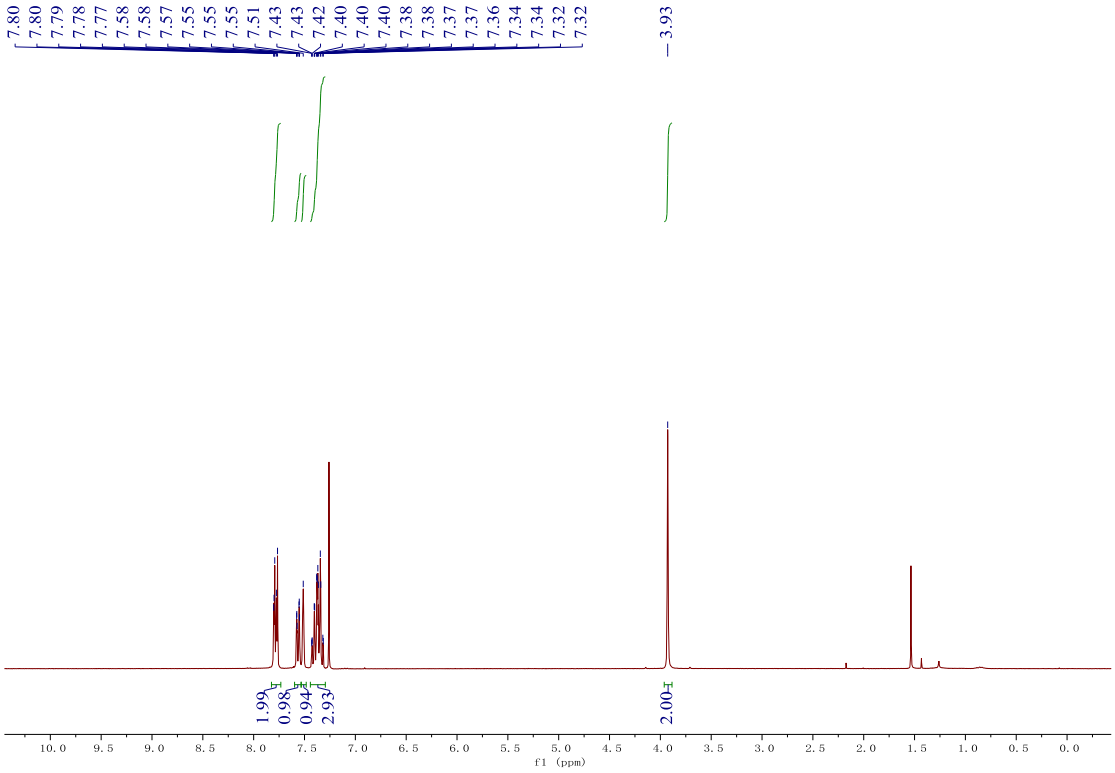
The compound **3q** was obtained as a white solid in 57% yield using 2-isothiocyanato-9H-fluorene following the general procedure E after column chromatography on silica gel with pentane.

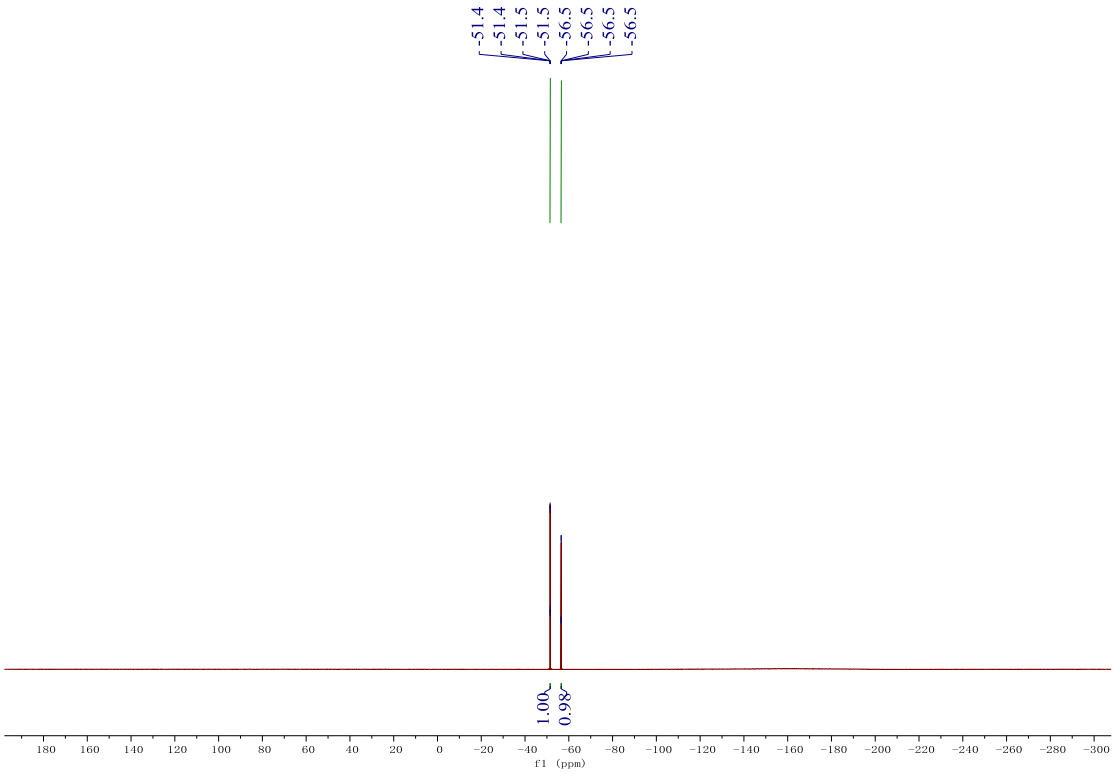
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.82 – 7.73 (m, 2H), 7.60 – 7.53 (m, 1H), 7.51 (s, 1H), 7.44 – 7.30 (m, 3H), 3.93 (s, 2H).

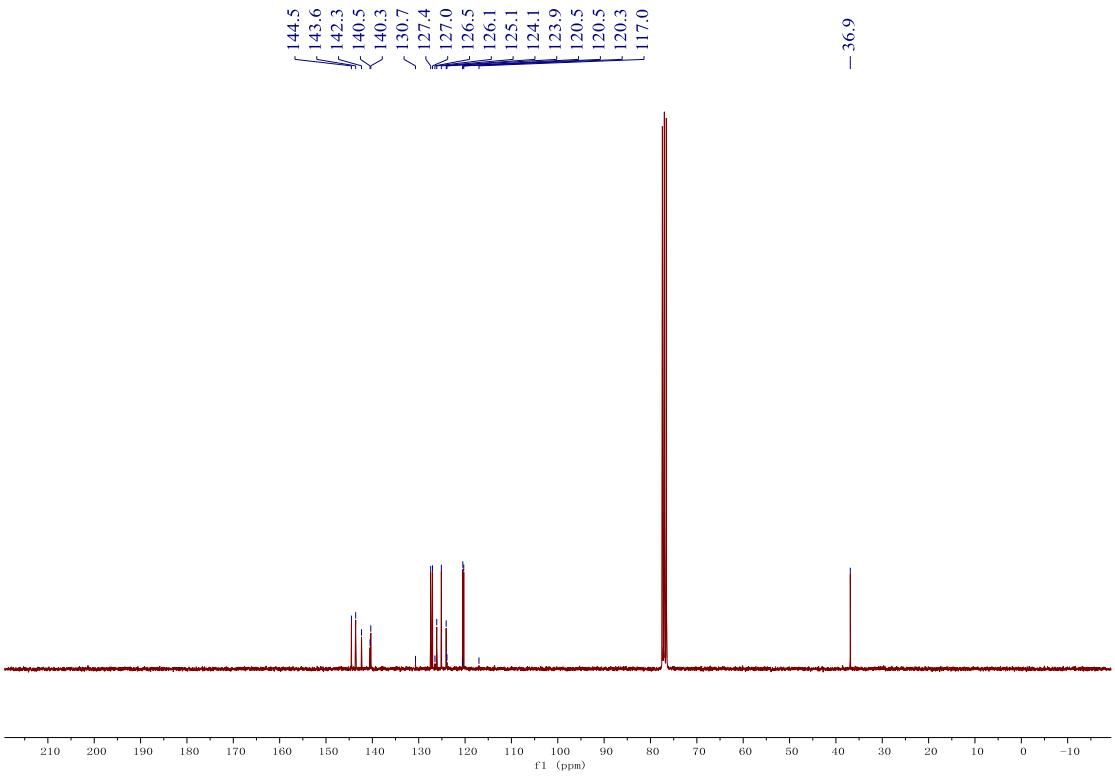
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.5 (q, *J* = 3.4 Hz), -56.5 (q, *J* = 3.4 Hz).

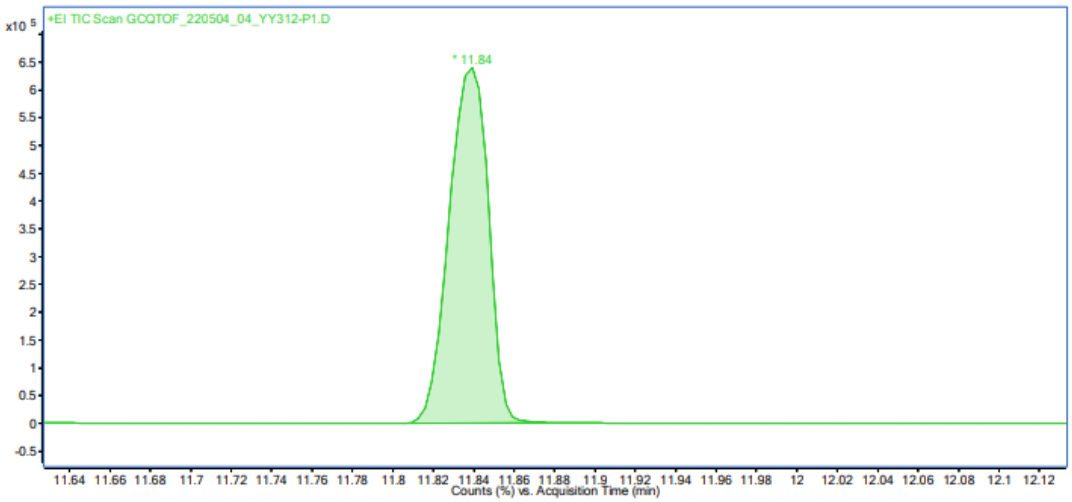
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 144.5, 143.6, 142.3, 140.5, 140.3, 128.6 (d, *J* = 315.8 Hz), 127.4, 127.0, 126.1, 125.1, 124.1, 122.2 (d, *J* = 253.7 Hz), 120.5, 120.3, 36.9.

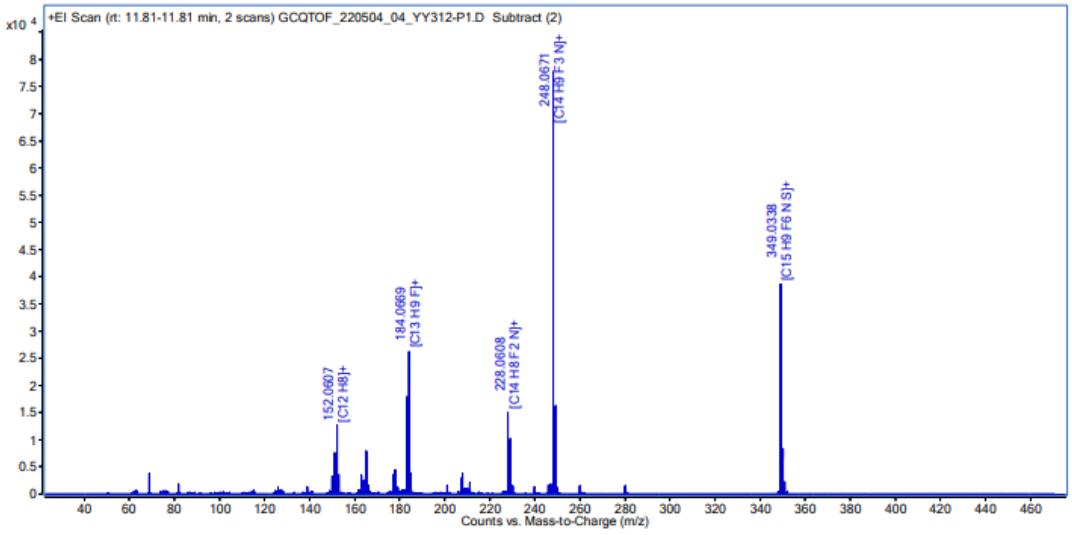
HRMS (EI) calculated for $C_{15}H_9F_6NS$: 349.0354 $[M]^+$, Found: 349.0338.





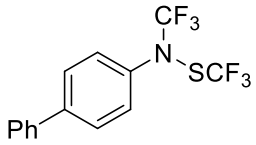

144.5
143.6
142.3
140.5
140.3
130.7
127.4
127.0
126.5
126.1
125.1
124.1
123.9
120.5
120.5
120.3
117.0
36.9
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)





m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
349.0338	C15H9F6NS	349.0354	-4.6	$[M]^{+\cdot}$

N-([1,1'-biphenyl]-4-yl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3r)



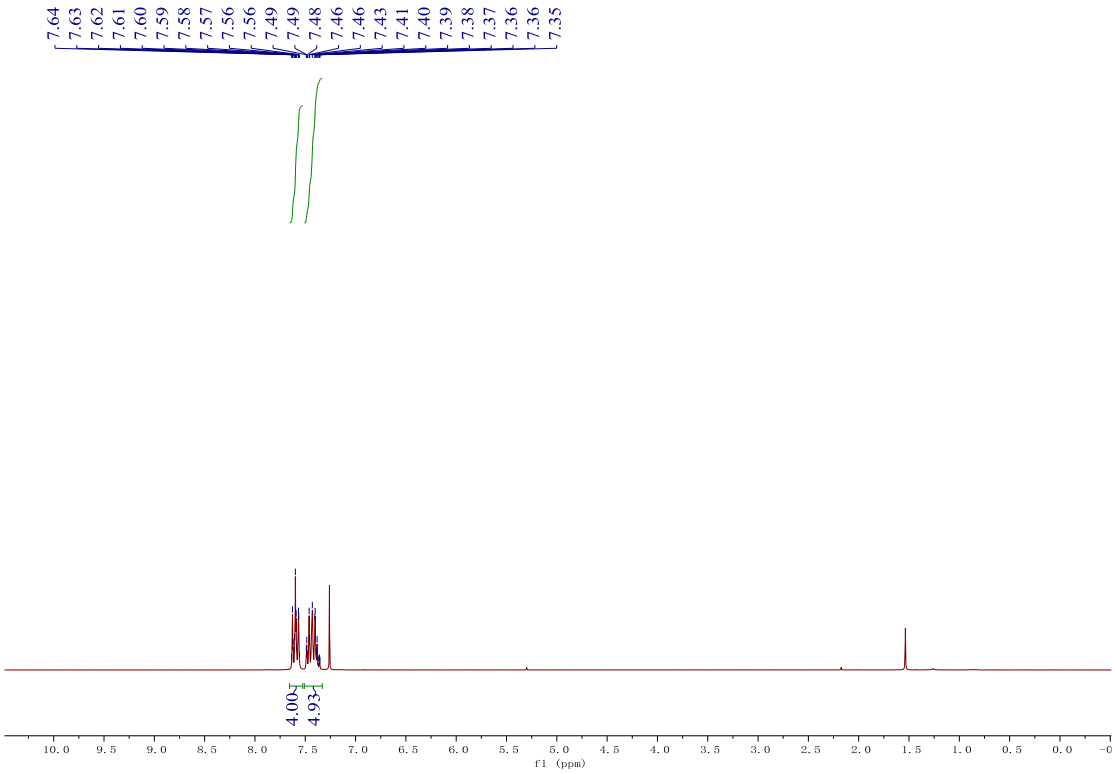
The compound **3r** was obtained as a white solid in 67% yield using 4-isothiocyanato-1,1'-biphenyl following the general procedure E after column chromatography on silica gel with pentane.

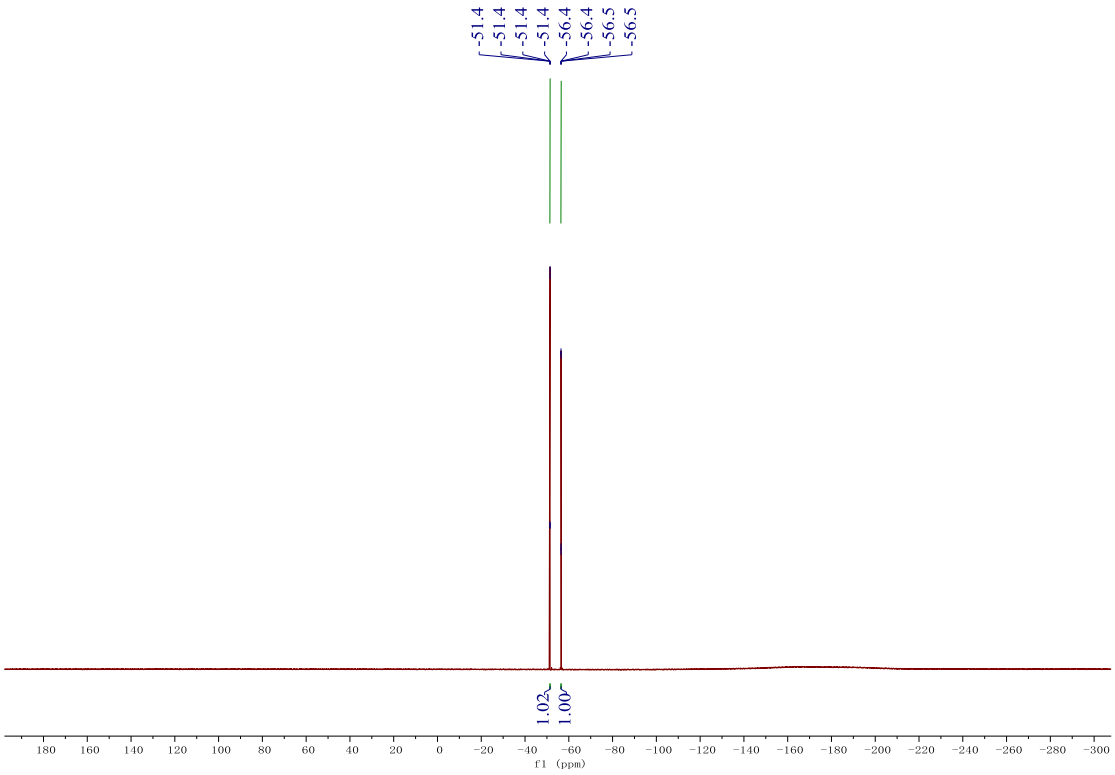
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.66 – 7.52 (m, 4H), 7.51 – 7.33 (m, 5H).

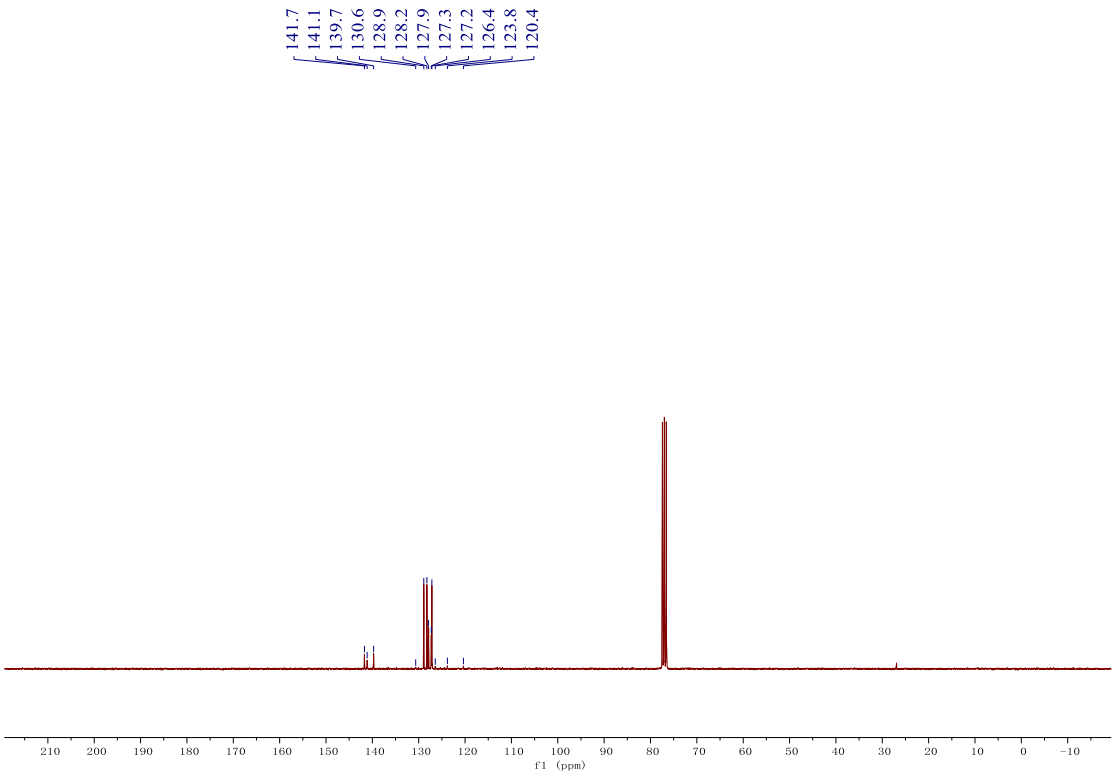
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.4 (q, *J* = 3.4 Hz), -56.5 (q, *J* = 3.4 Hz).

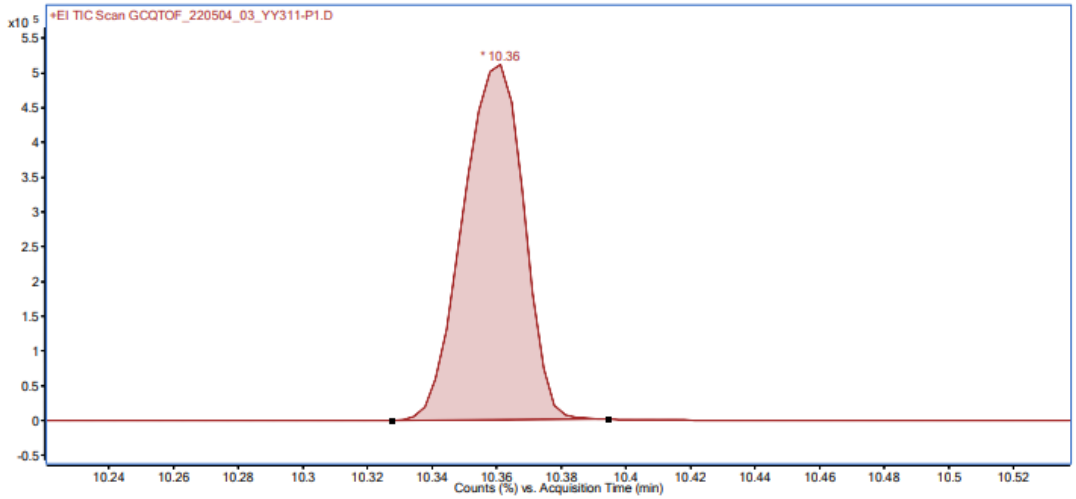
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 141.7, 141.1, 139.7, 128.9, 128.5 (d, *J* = 314.1 Hz), 128.2, 127.9, 127.3, 127.2, 122.1 (q, *J* = 260.9 Hz).

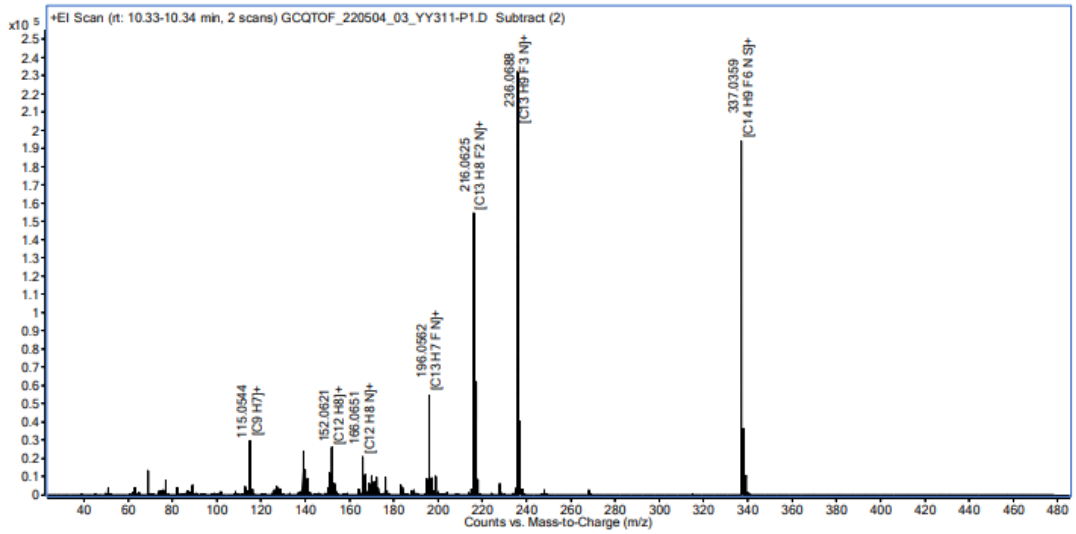
HRMS (EI) calculated for $C_{14}H_9F_6NS$: 337.0353 $[M]^+$, Found: 337.0359.





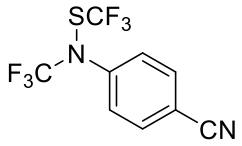

141.7
141.1
139.7
130.6
128.9
128.2
127.9
127.3
127.2
126.4
123.8
120.4
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)





m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
337.0359	C14H9F6NS	337.0353	1.8	$[M]^{+\cdot}$

4-((trifluoromethyl)((trifluoromethyl)thio)amino)benzonitrile (3t)



The compound **3t** was obtained as a colorless oil in 40% yield using 4-isothiocyanatobenzonitrile following the general procedure F after column chromatography on silica gel with pentane.

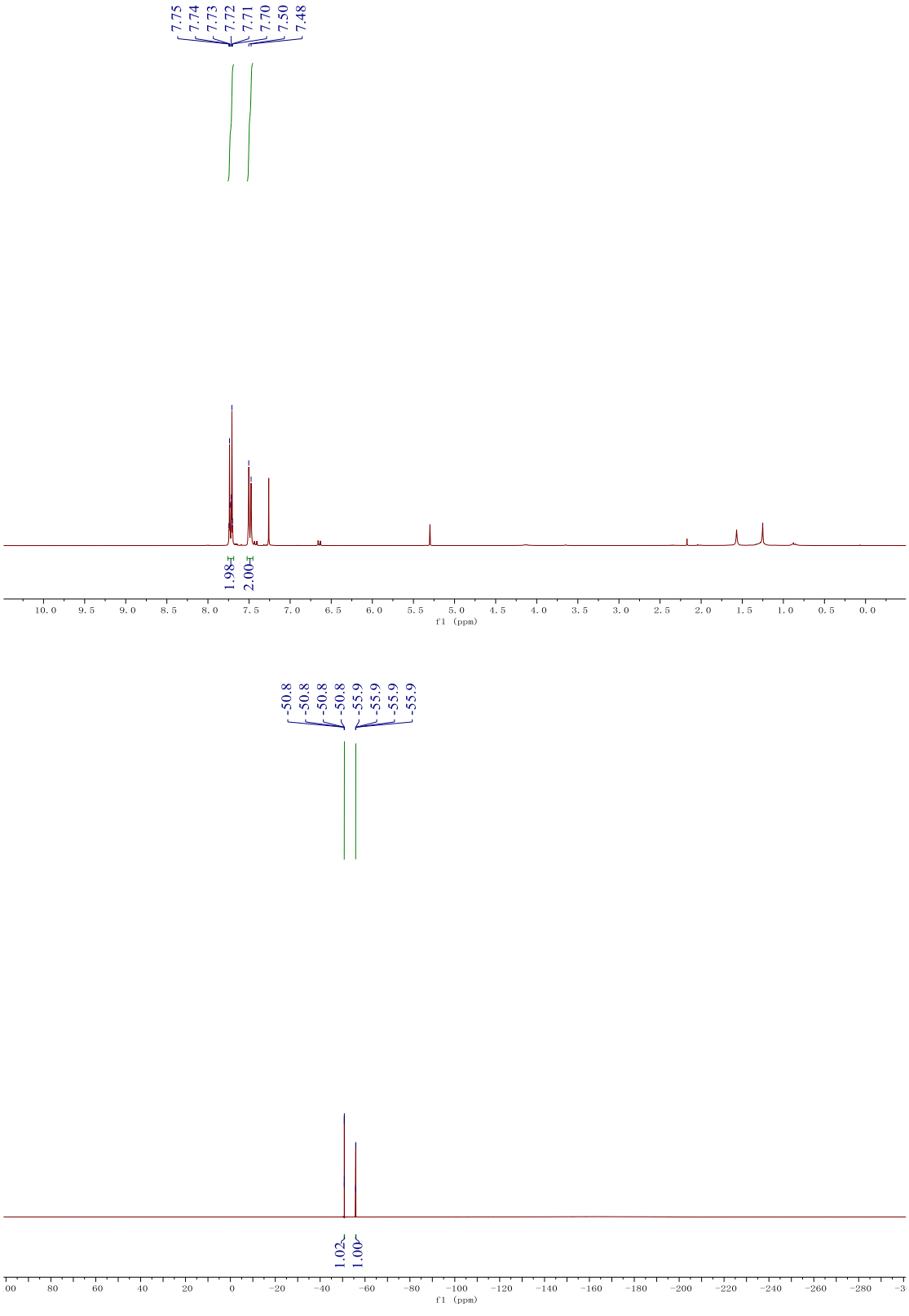
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.75 – 7.69 (m, 2H), 7.49 (d, *J* = 8.4 Hz, 2H).

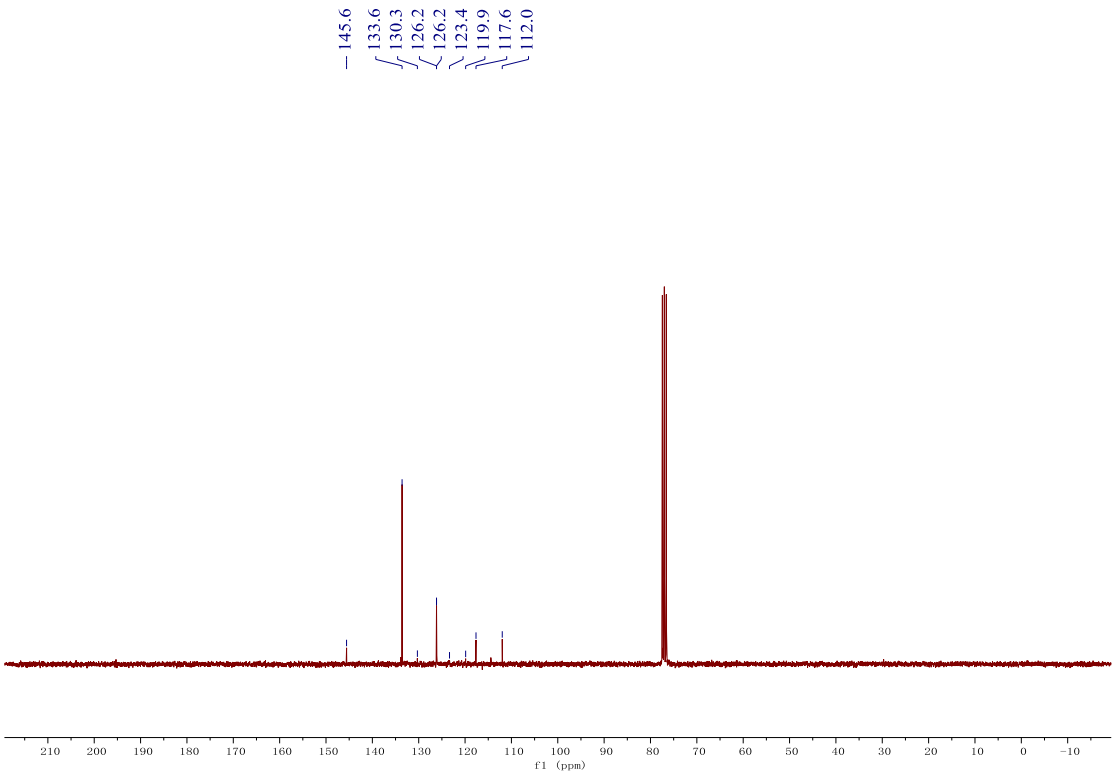
^{19}F NMR (282 MHz, Chloroform-*d*) δ -50.8 (q, *J* = 3.4 Hz), -55.9 (q, *J* = 3.4 Hz).

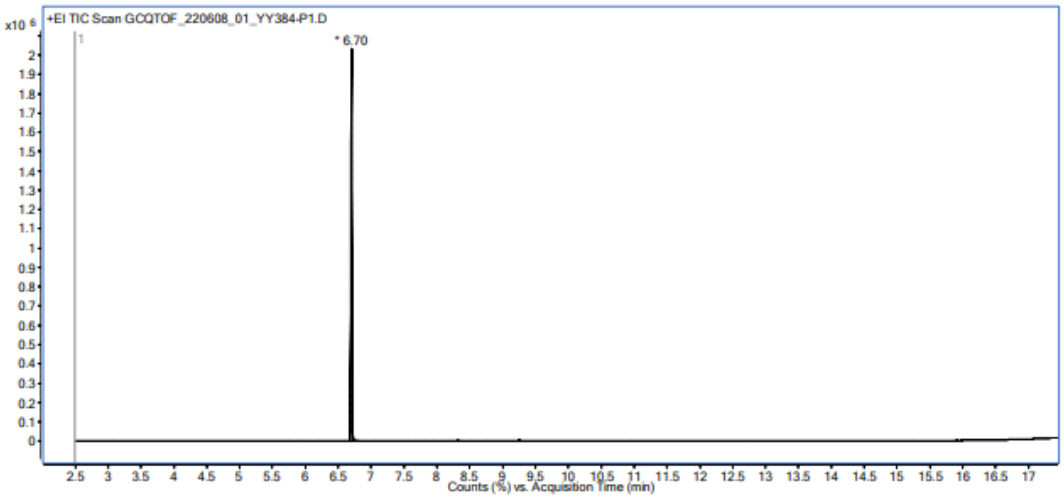
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 145.6, 133.6, 128.2 (q, *J* = 316.8 Hz), 126.2, 121.6 (q, *J*

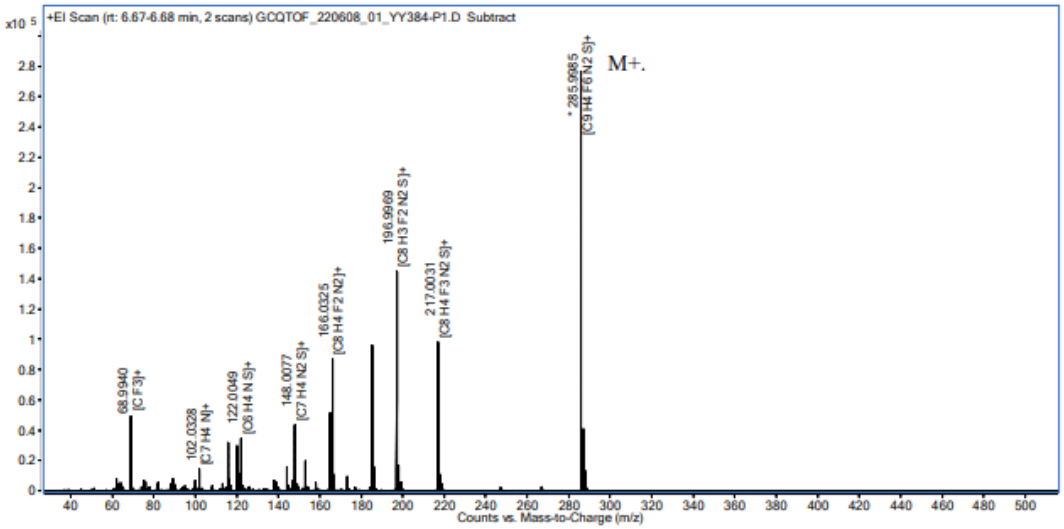
= 262.8 Hz), 117.6, 112.0.

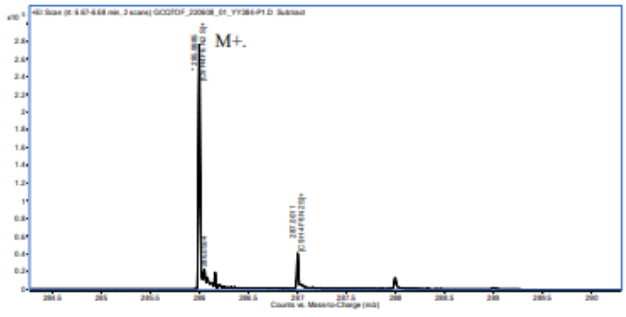
HRMS (EI) calculated for $C_9H_4F_6N_2S$: 285.9994 $[M]^+$, Found: 285.9985.




145.6
133.6
130.3
126.2
126.2
123.4
119.9
117.6
112.0
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)

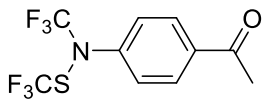






Meas. m/z	Ion Formula	m/z (Calc)	err (ppm)	
285.9985	C9H4F6N2S	285.9994	-3.1	$[M]^{+\cdot}$

1-(4-((trifluoromethyl)((trifluoromethyl)thio)amino)phenyl)ethan-1-one (3w)



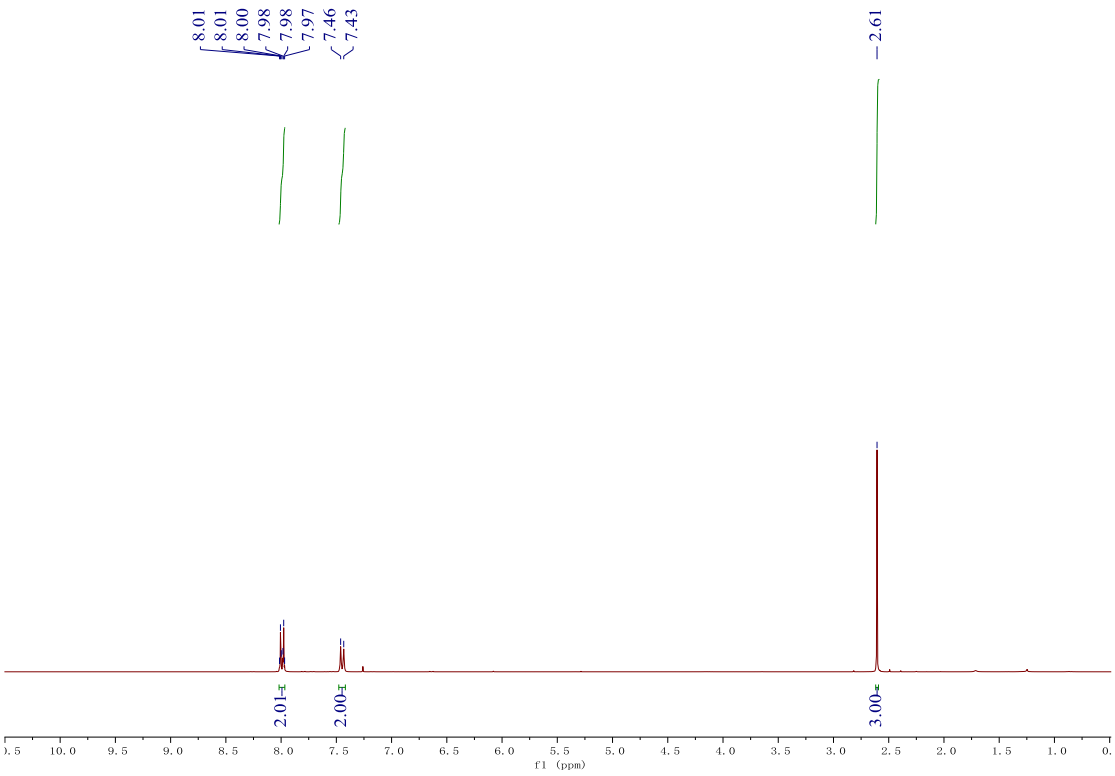
The compound **3w** was obtained as a yellowish oil in 71% yield using 1-(4-isothiocyanatophenyl)ethan-1-one following the general procedure F after column chromatography on silica gel with pentane.

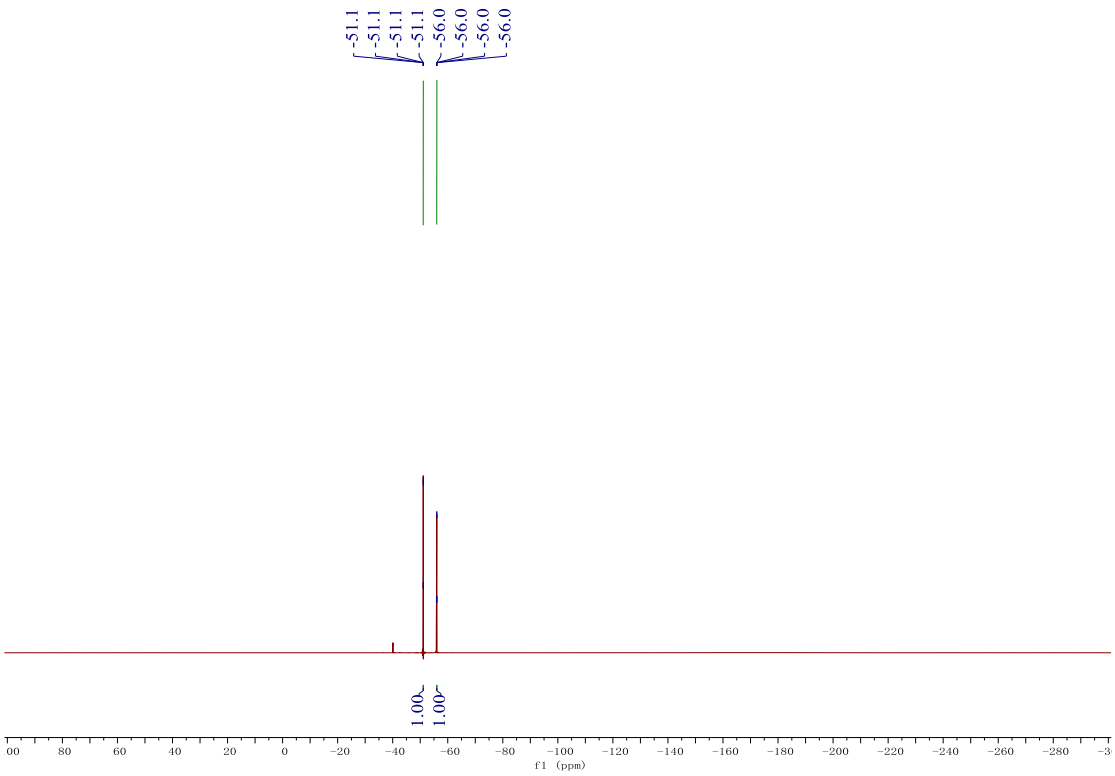
^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.02 – 7.97 (m, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 2.61 (s, 3H).

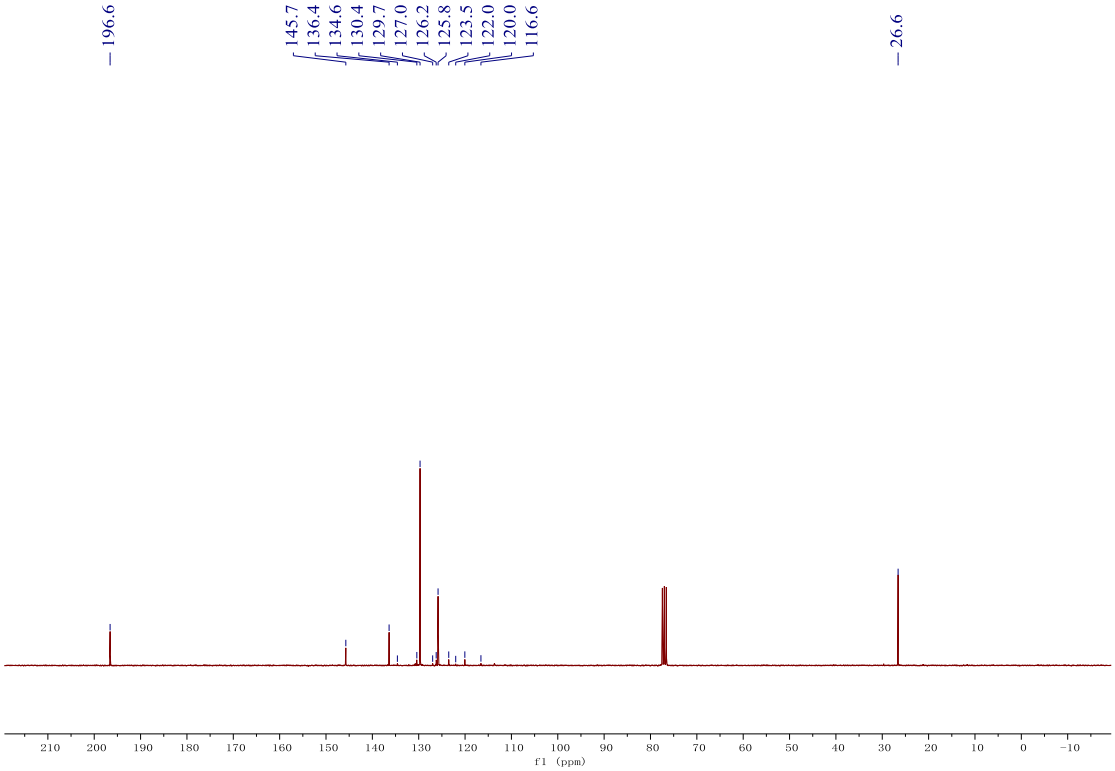
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.1 (q, q, *J* = 3.4 Hz), -56.0 (q, *J* = 3.4 Hz).

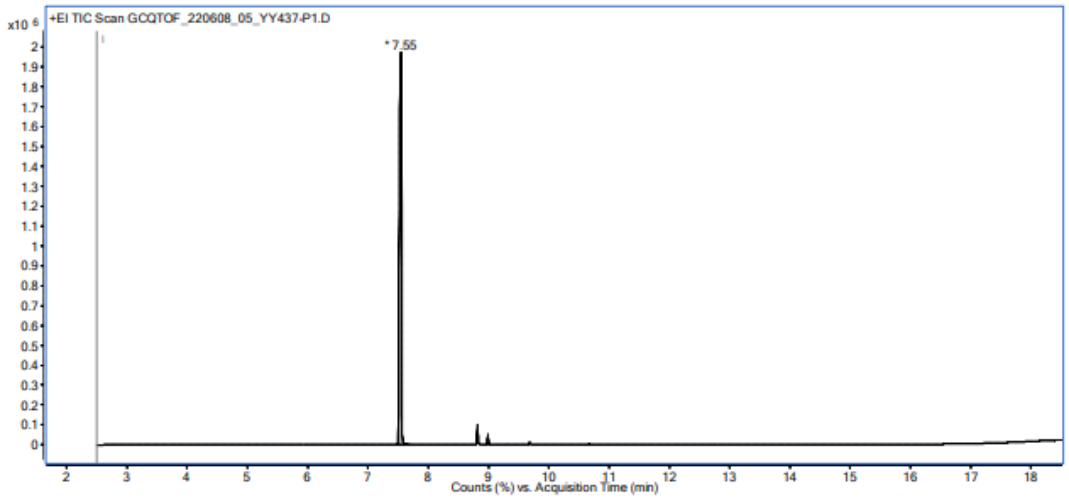
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 196.6, 145.2, 136.4, 129.7, 128.3 (q, *J* = 315.3 Hz), 125.8, 121.8 (q, *J* = 262.0 Hz), 26.6.

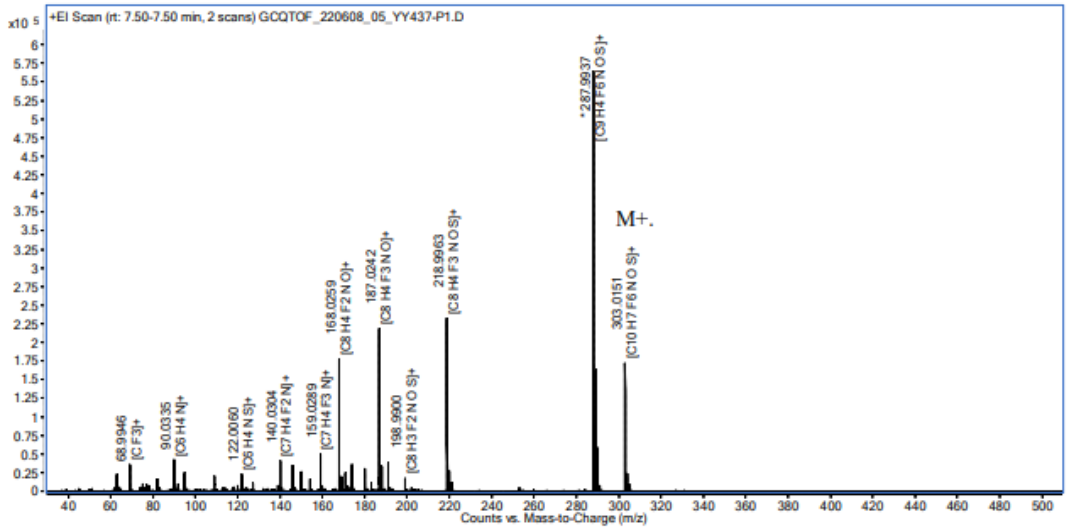
HRMS (EI) calculated for $C_{10}H_7F_6NOS$: 303.0147 $[M]^+$, Found: 303.0151.

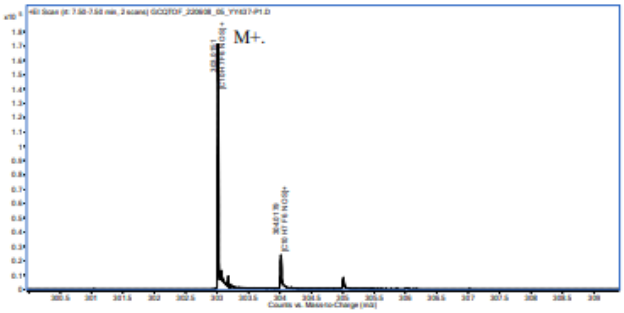



-51.1
-51.1
-51.1
-51.1
-56.0
-56.0
-56.0
-56.0
1.00
1.00
f1 (ppm)


196.6
145.7
136.4
134.6
130.4
129.7
127.0
126.2
125.8
123.5
122.0
120.0
116.6
26.6
f1 (ppm)

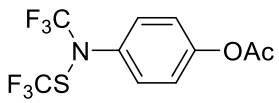






Meas. m/z	Ion Formula	m/z (Calc)	err (ppm)	
303.0151	C10H7F6NOS	303.0147	1.3	$[M]^{+\cdot}$

4-((trifluoromethyl)((trifluoromethyl)thio)amino)phenyl acetate (3x)



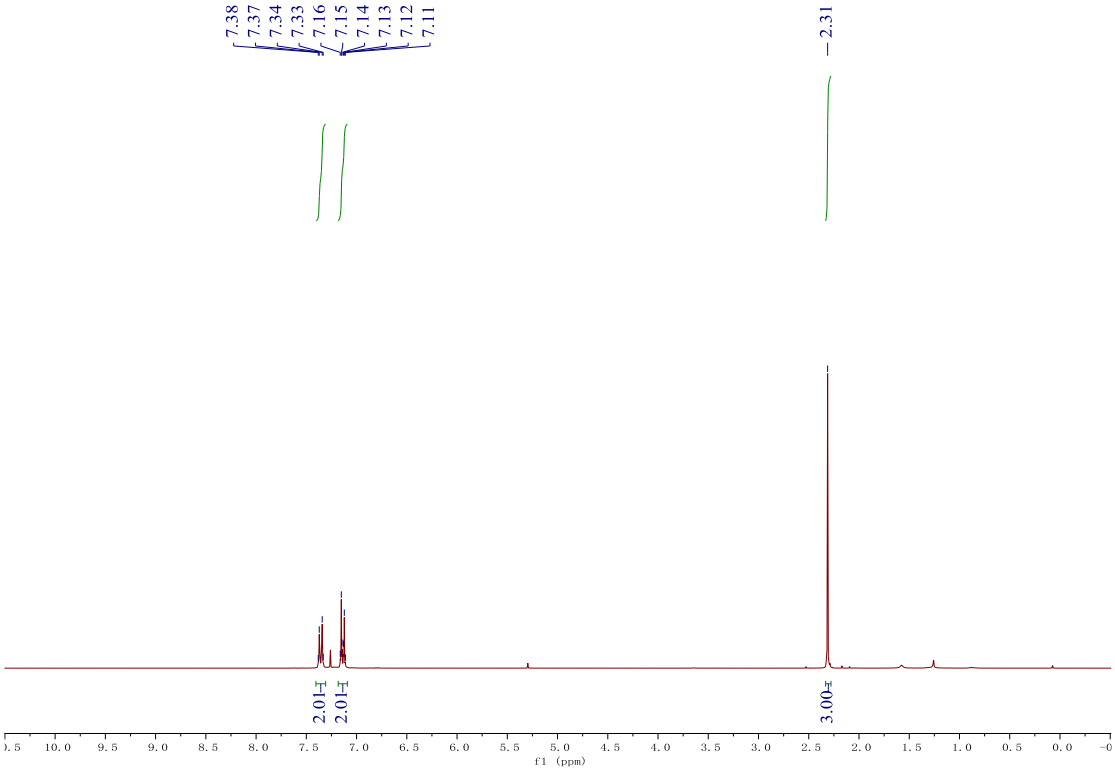
The compound **3x** was obtained as a yellowish oil in 58% yield using 4-isothiocyanatophenyl acetate following the general procedure F after column chromatography on silica gel with pentane.

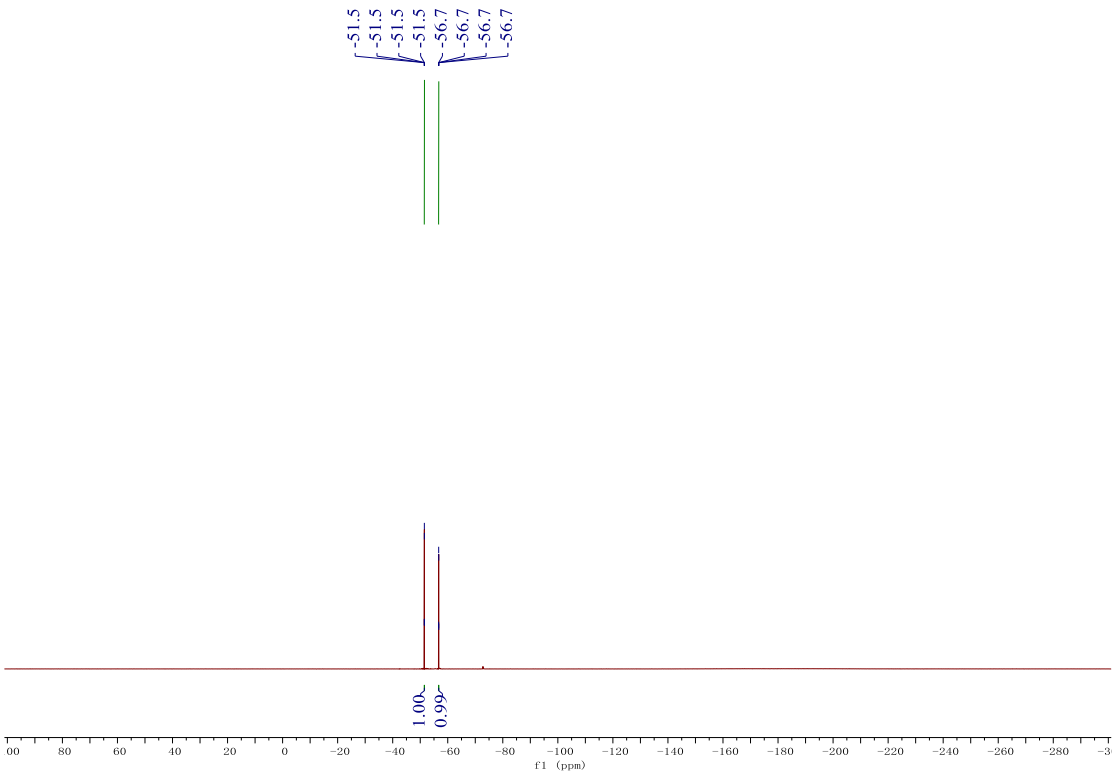
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.40 – 7.31 (m, 2H), 7.18 – 7.09 (m, 2H), 2.31 (s, 3H).

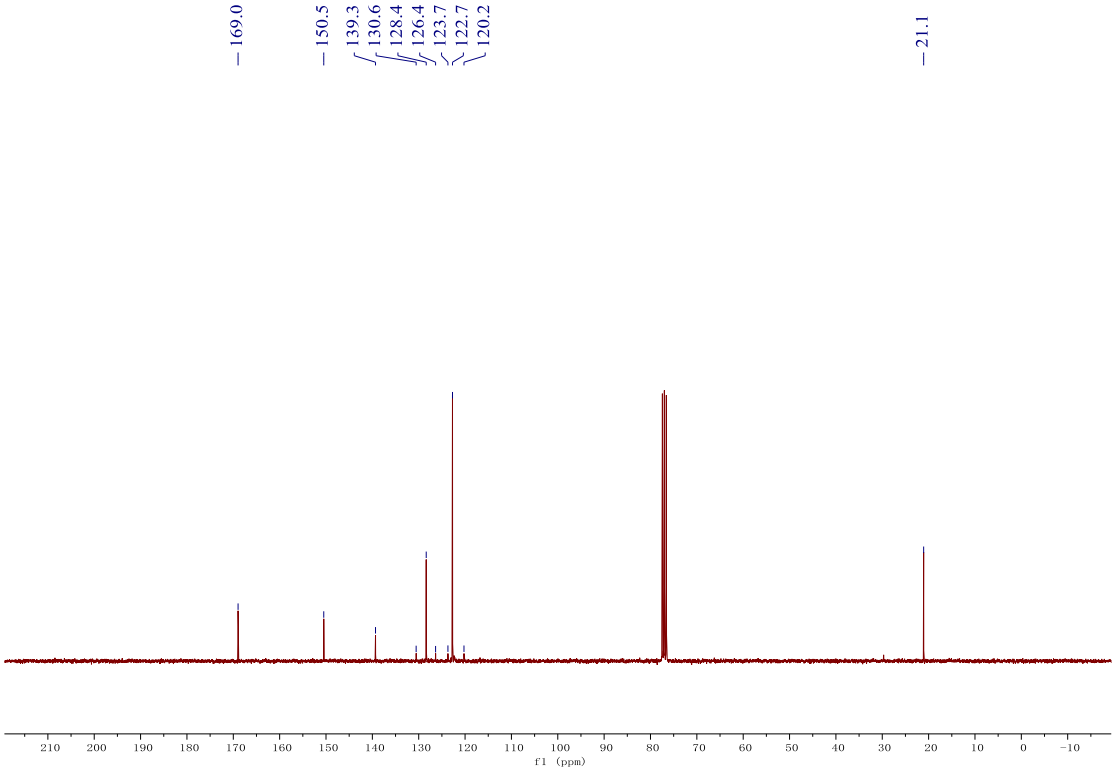
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.5 (q, *J* = 3.4 Hz), -56.7 (q, *J* = 3.4 Hz).

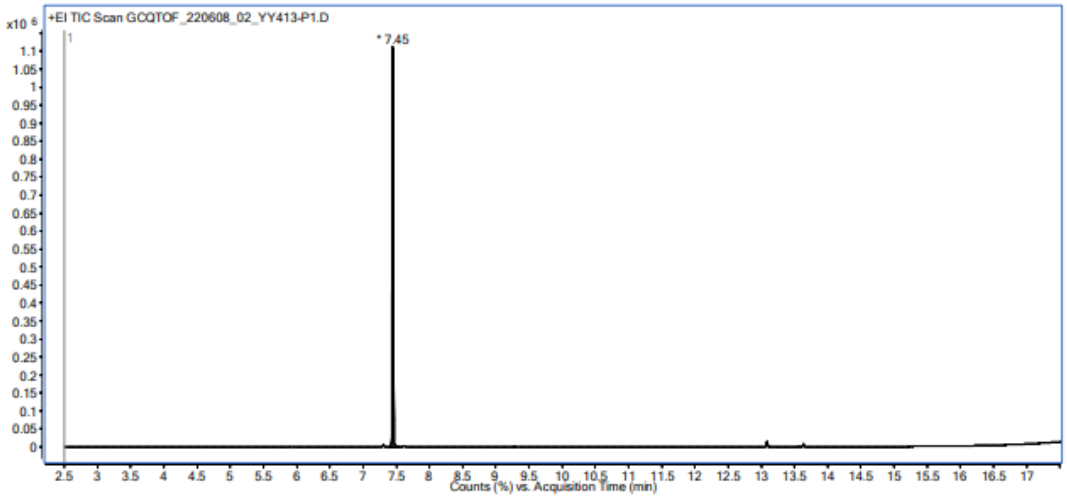
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 169.0, 150.5, 139.3, 128.5 (q, *J* = 316.5 Hz), 128.4, 122.7, 122.0 (q, *J* = 261.2 Hz), 21.1.

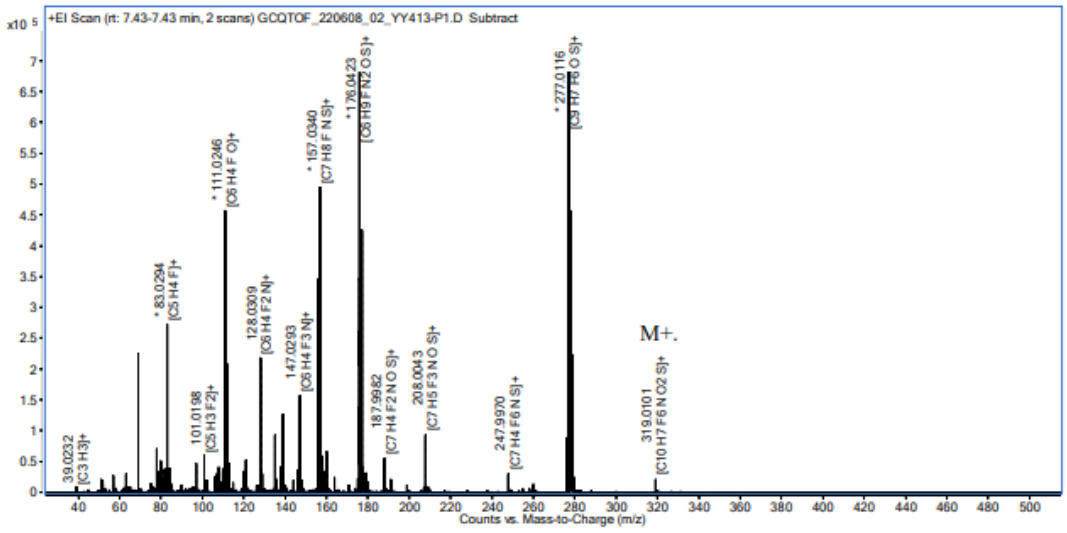
HRMS (EI) calculated for $C_{10}H_7F_6NO_2S$: 319.0096 $[M]^+$, Found: 319.0101.

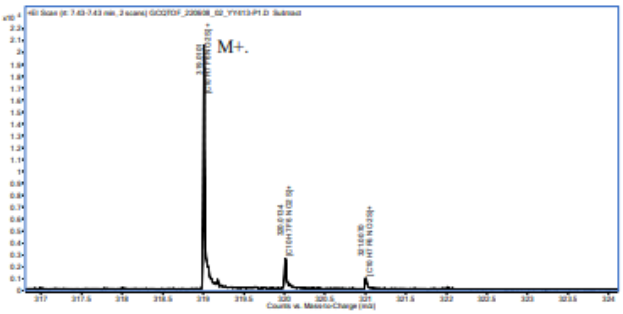



-51.5
-51.5
-51.5
-51.5
-56.7
-56.7
-56.7
-56.7
1.00
0.99
f1 (ppm)


169.0
150.5
139.3
130.6
128.4
126.4
123.7
122.7
120.2
21.1
f1 (ppm)

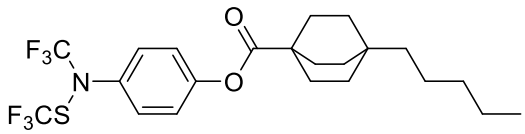






Meas. m/z	Ion Formula	m/z (Calc)	err (ppm)	
319.0101	C10H7F6NO2S	319.0096	1.6	$[M]^{+\cdot}$

4-((trifluoromethyl)((trifluoromethyl)thio)amino)phenyl 4-pentylbicyclo[2.2.2]octane-1-carboxylate (3y)



The compound **3y** was obtained as a colorless oil in 65% yield using 4-isothiocyanatophenyl 4-pentylbicyclo[2.2.2]octane-1-carboxylate following the general procedure F after column

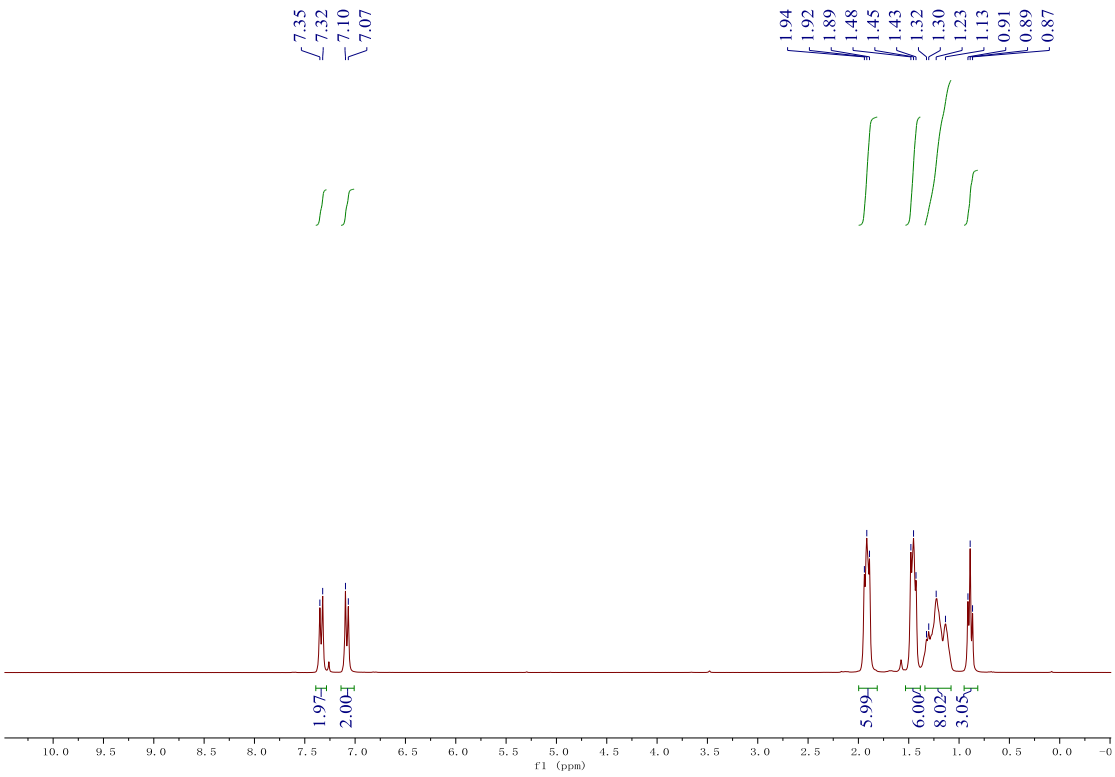
chromatography on silica gel with pentane.

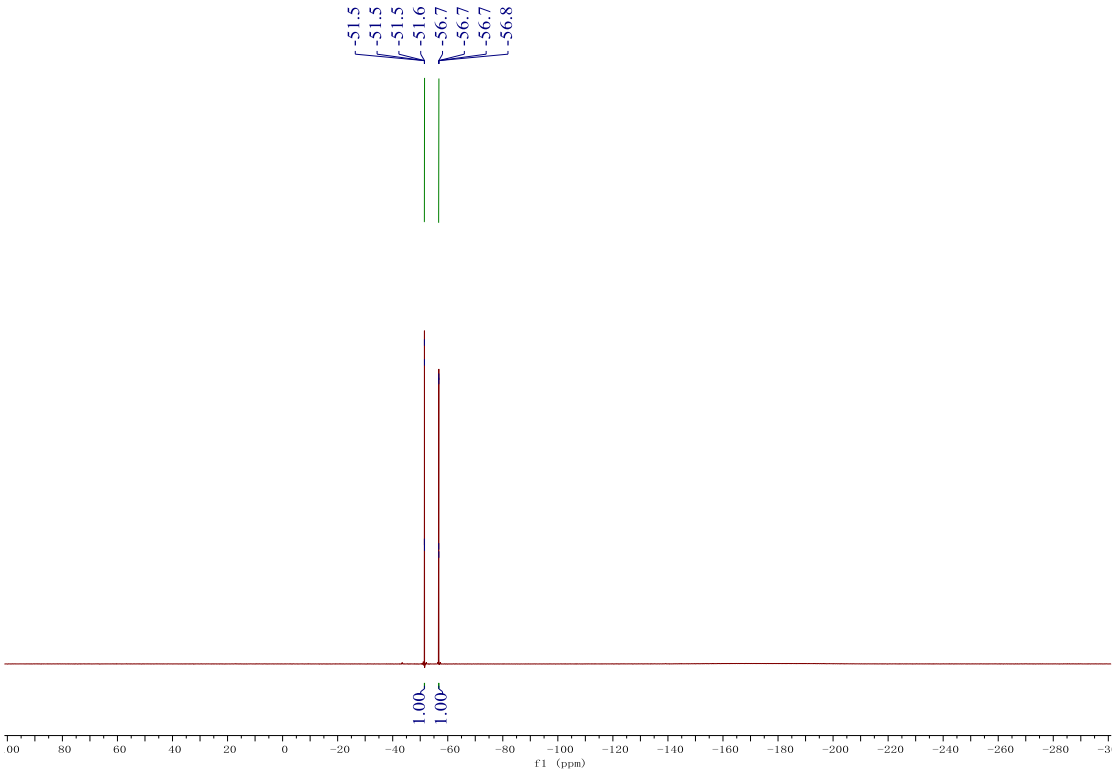
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.34 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.5 Hz, 2H), 2.00 – 1.81 (m, 6H), 1.53 – 1.38 (m, 6H), 1.34 – 1.08 (m, 8H), 0.89 (t, *J* = 6.9 Hz, 3H).

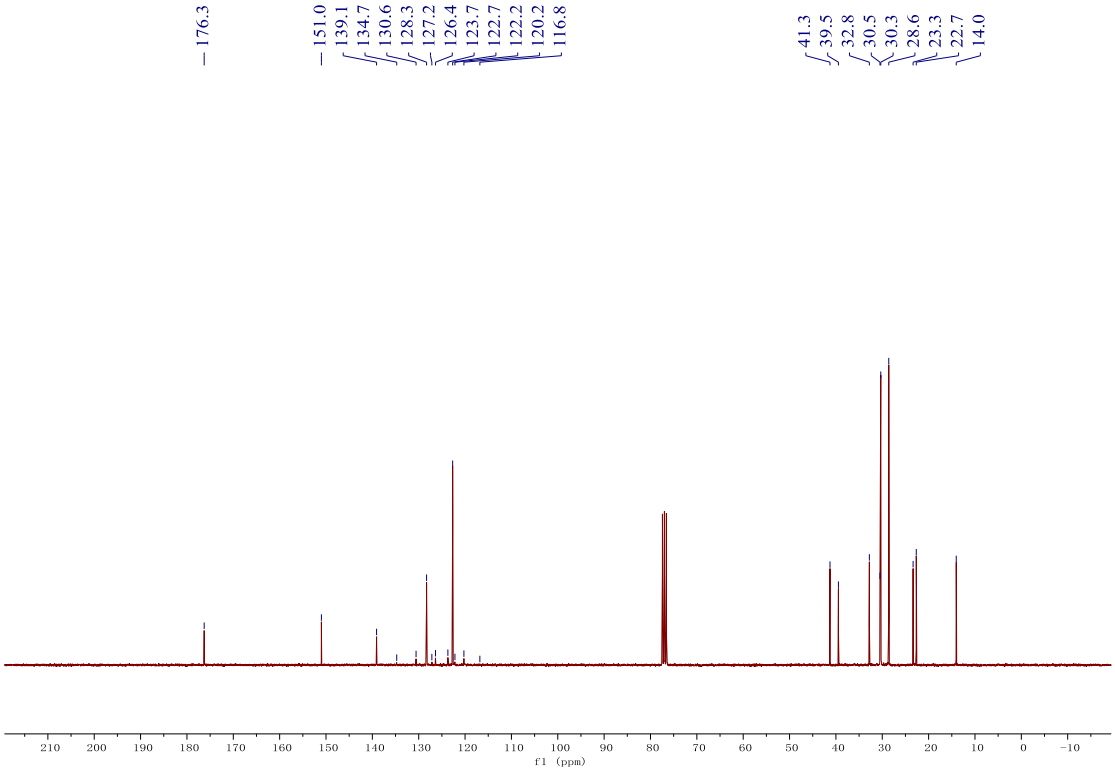
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.5 (q, *J* = 3.4 Hz), -56.7 (q, *J* = 3.4 Hz).

^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 176.3, 151.0, 139.1, 128.5 (q, *J* = 316.8 Hz), 128.3, 122.7, 122.0 (q, *J* = 260.9 Hz), 41.3, 39.5, 32.8, 30.5, 30.3, 28.6, 23.3, 22.7, 14.0.

HRMS (ESI) calculated for $C_{22}H_{28}F_6NO_2S$: 484.1739 $[M+H]^+$, Found: 484.1739.




-51.5
-51.5
-51.5
-51.6
-56.7
-56.7
-56.7
-56.8
1.00
1.00
f1 (ppm)


176.3
151.0
139.1
134.7
130.6
128.3
127.2
126.4
123.7
122.7
122.2
120.2
116.8
41.3
39.5
32.8
30.5
30.3
28.6
23.3
22.7
14.0
f1 (ppm)

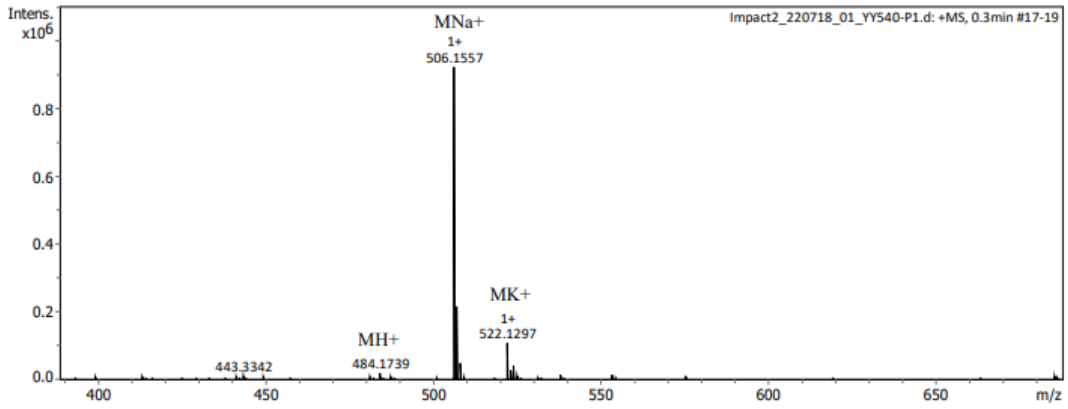
CENTRE COMMUN DE SPECTROMETRIE DE MASSE

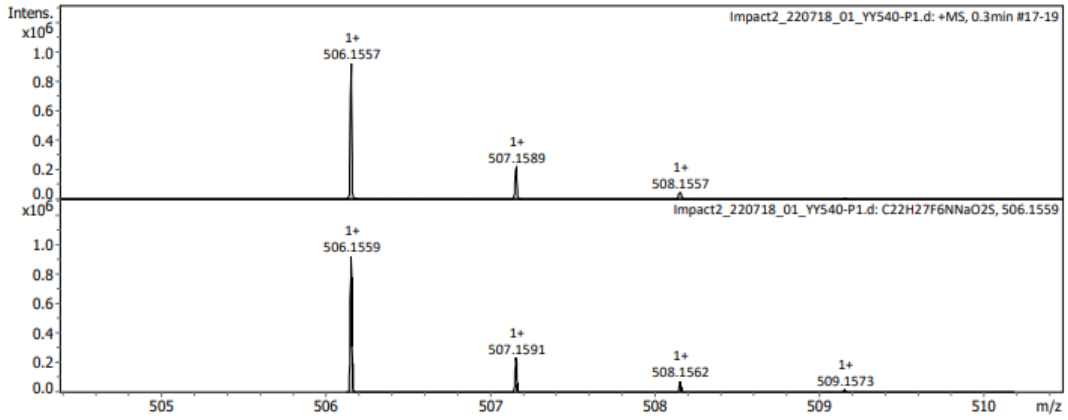
Analysis Info

Analysis Name	Impact2_220718_01_YY540-P1.d		
Method	Tune_pos_Standard.m	Acquisition Date	7/18/2022 11:10:08 AM
Comment		Instrument / Ser#	impact II 1825265.10081

Acquisition Parameter

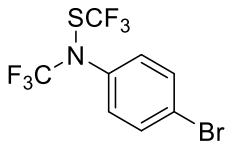
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	1200 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	750.0 Vpp	Set Divert Valve	Source





Meas. m/z	Ion Formula	m/z	Sum Formula	err [ppm]	mSigma	Adduct	z
484.1739	C22H28F6NO2S	484.1739	C22H27F6NO2S	-0.0	11.5	M+H	1+
506.1557	C22H27F6NNaO2S	506.1559		0.3	16.9	M+Na	1+
522.1297	C22H27F6KNO2S	522.1298		0.2	6.5	M+K	1+

N-(4-bromophenyl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3z)



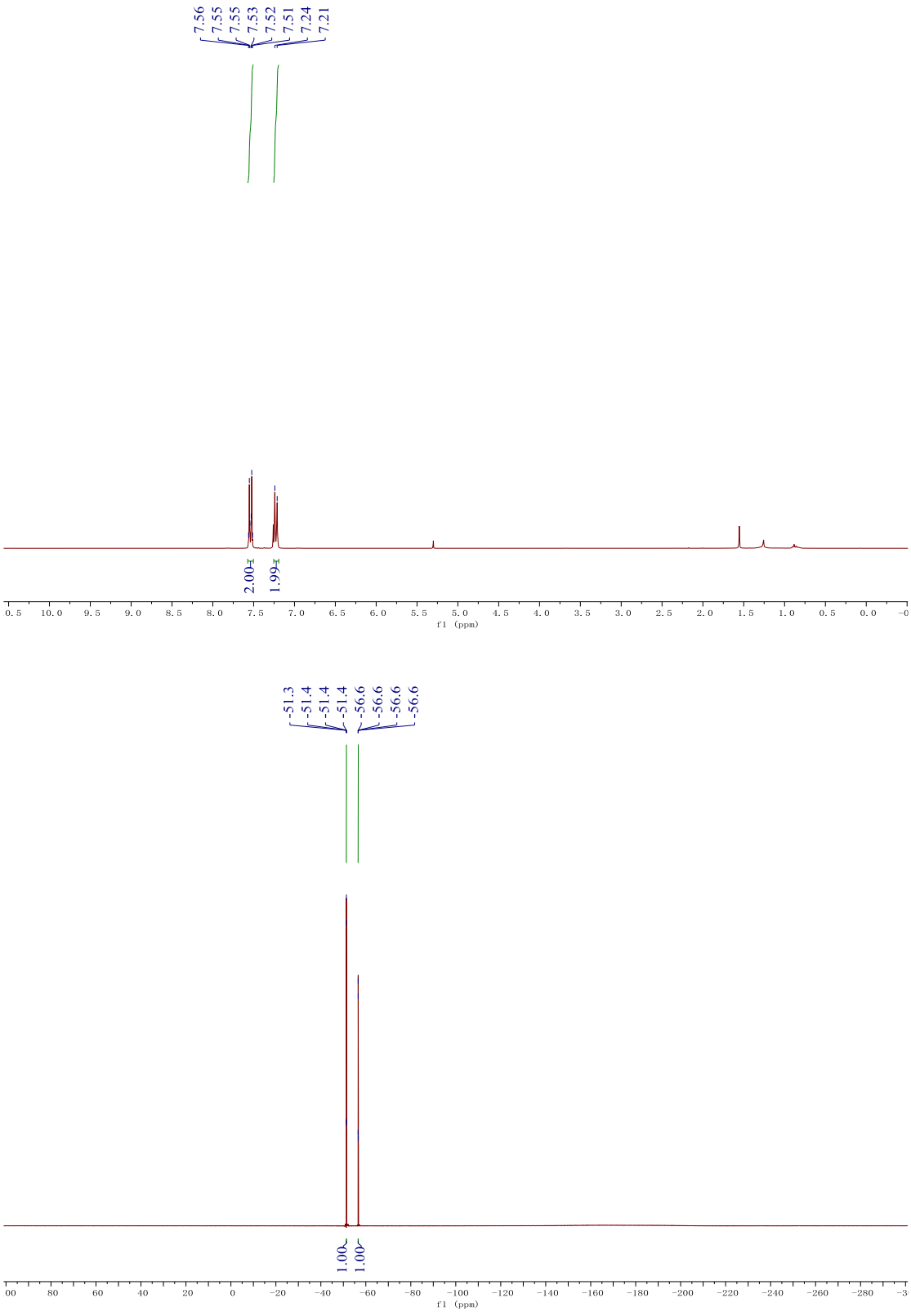
The compound **3z** was obtained as a colorless oil in 70% yield using 1-bromo-4-isothiocyanatobenzene following the general procedure F after column chromatography on silica gel with pentane.

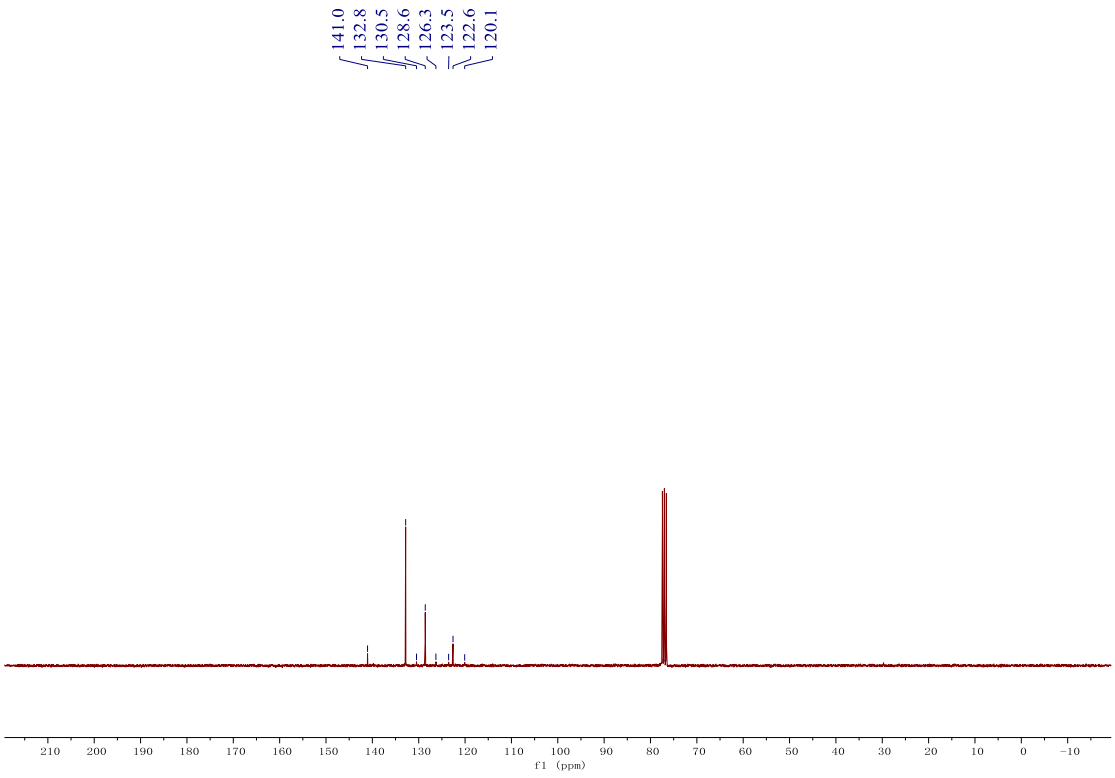
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.57 – 7.50 (m, 2H), 7.23 (d, *J* = 8.7 Hz, 2H).

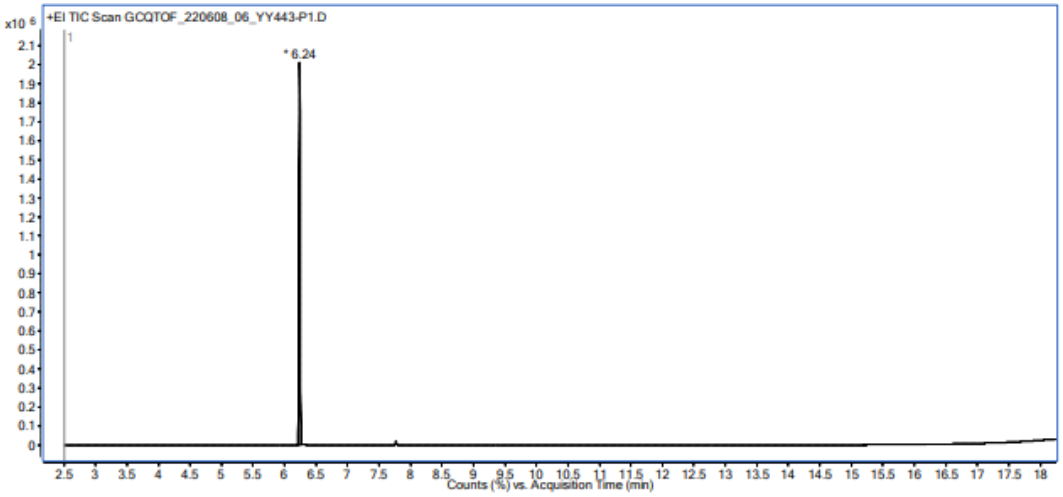
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.4 (q, *J* = 3.4 Hz), -56.6 (q, *J* = 3.4 Hz).

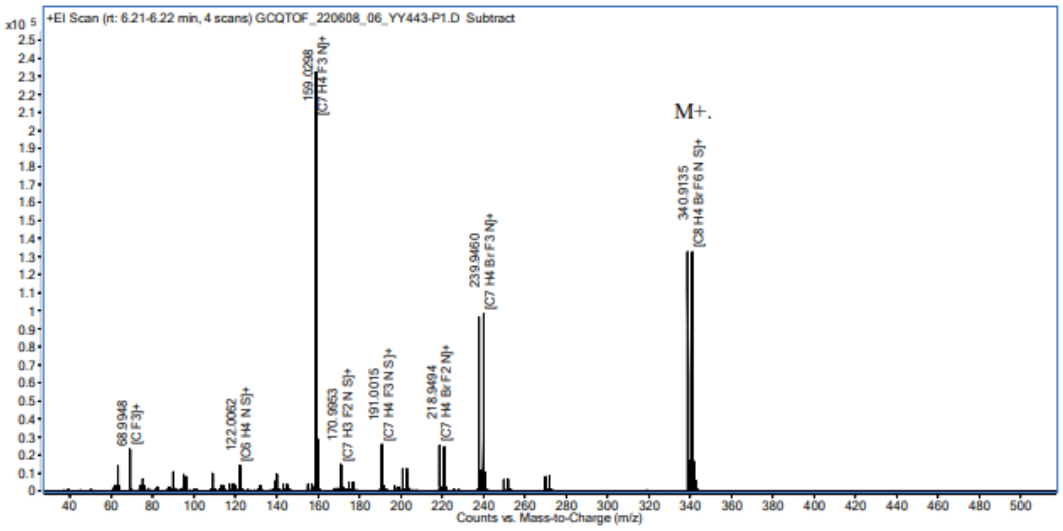
$^{13}C\{^{1}H\}$ NMR (75 MHz, Chloroform-*d*) δ 141.0, 132.8, 128.6, 128.4 (q, *J* = 316.0 Hz), 122.6, 121.8 (q, *J* = 261.5 Hz).

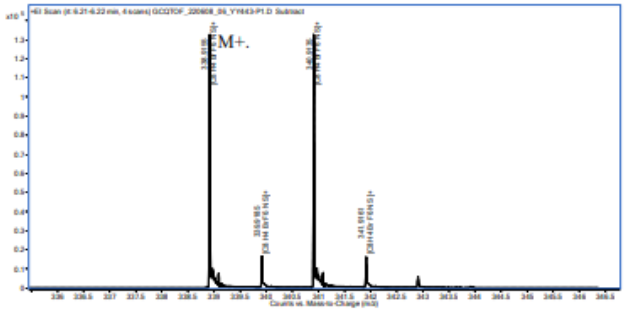
HRMS (EI) calculated for $C_8H_4BrF_6NS$: 338.9147 $[M]^+$, Found: 338.9155.




141.0
132.8
130.5
128.6
126.3
123.5
122.6
120.1
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)

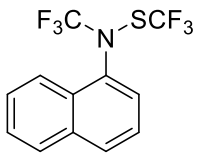






Meas. m/z	Ion Formula	m/z (Calc)	err (ppm)	
338.9155	C8H4BrF6NS	338.9147	2.4	$[M]^{+\cdot}$

N-(naphthalen-1-yl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3aa)



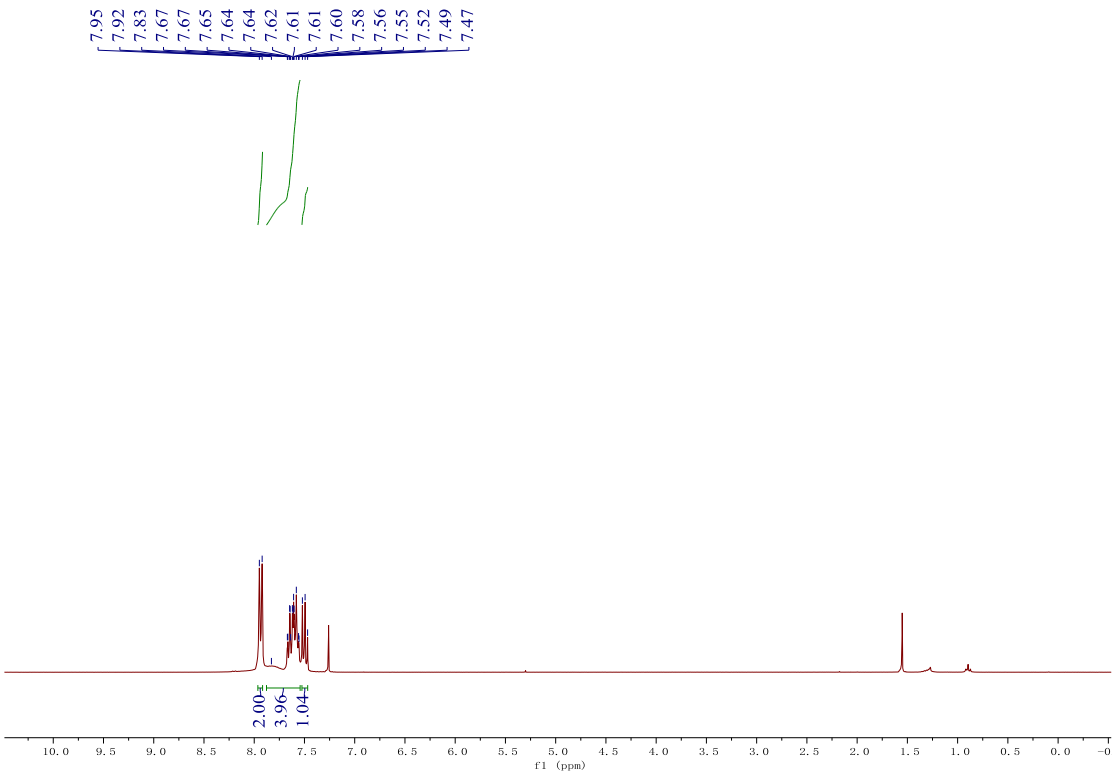
The compound **3aa** was obtained as a colorless oil in 72% yield using 1-isothiocyanatonaphthalene following the general procedure F after column chromatography on silica gel with pentane.

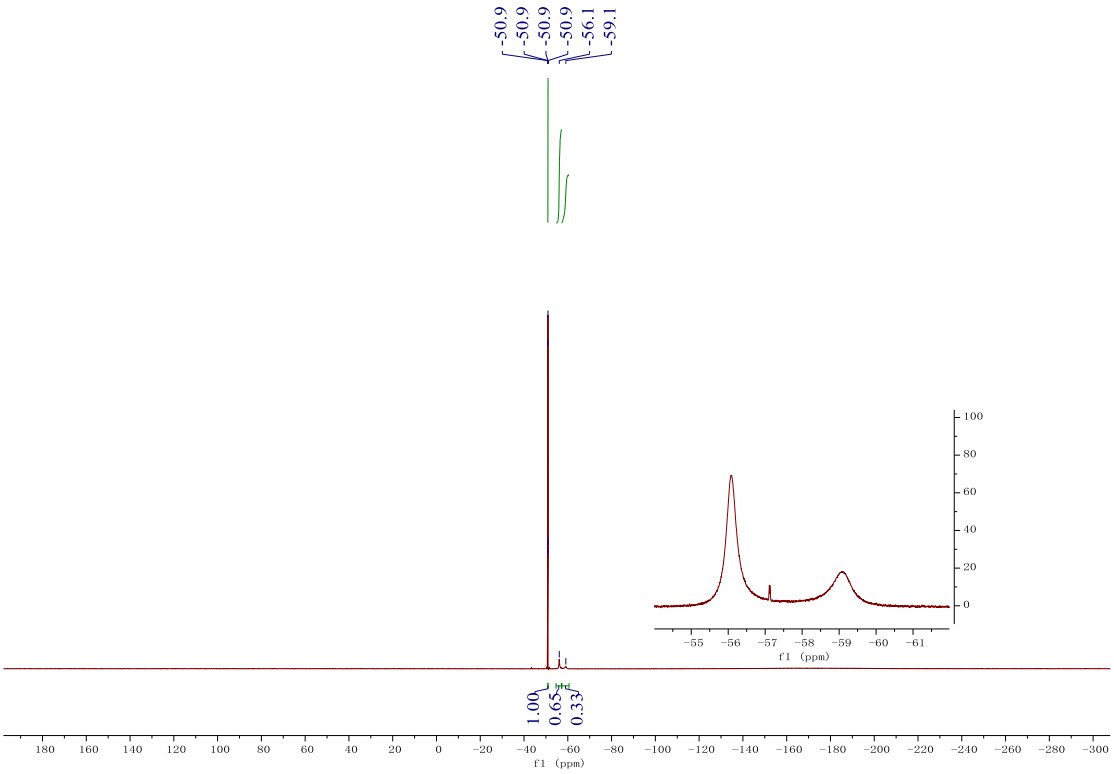
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.94 (d, *J* = 8.3 Hz, 2H), 7.88 – 7.54 (m, 4H), 7.53 – 7.47 (m, 1H).

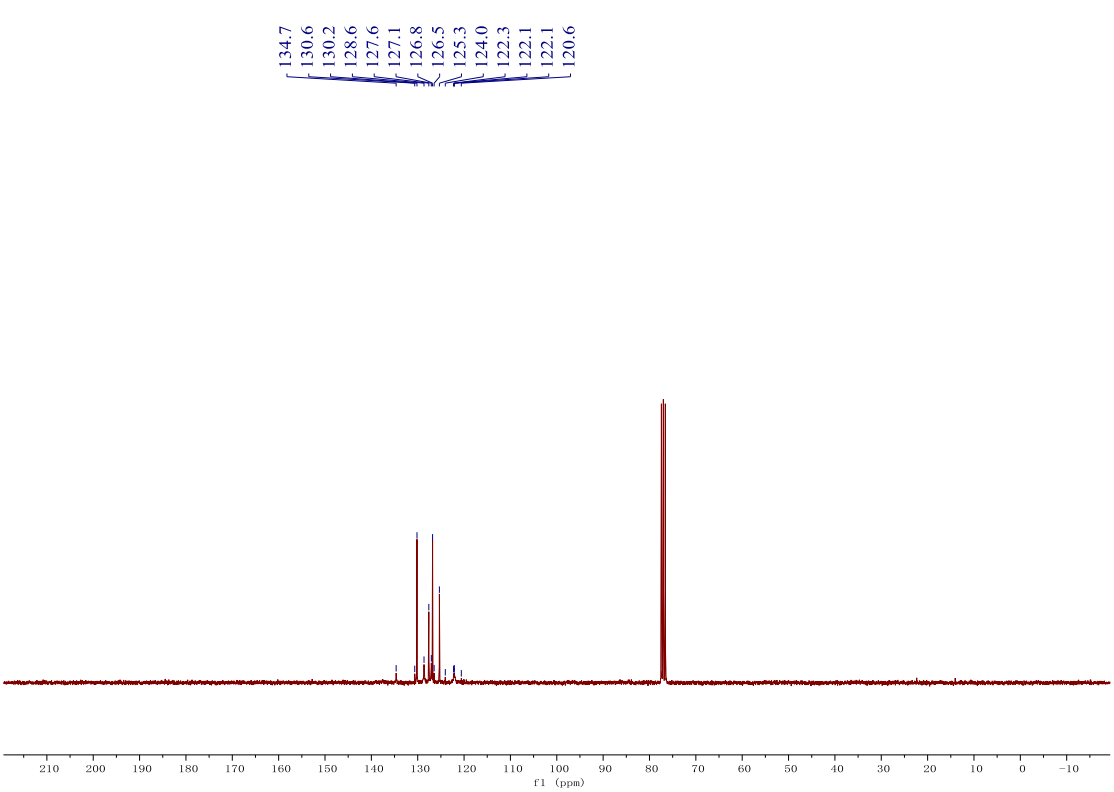
^{19}F NMR (282 MHz, Chloroform-*d*) δ -50.9 (q, *J* = 3.4 Hz), -56.1, -59.1.

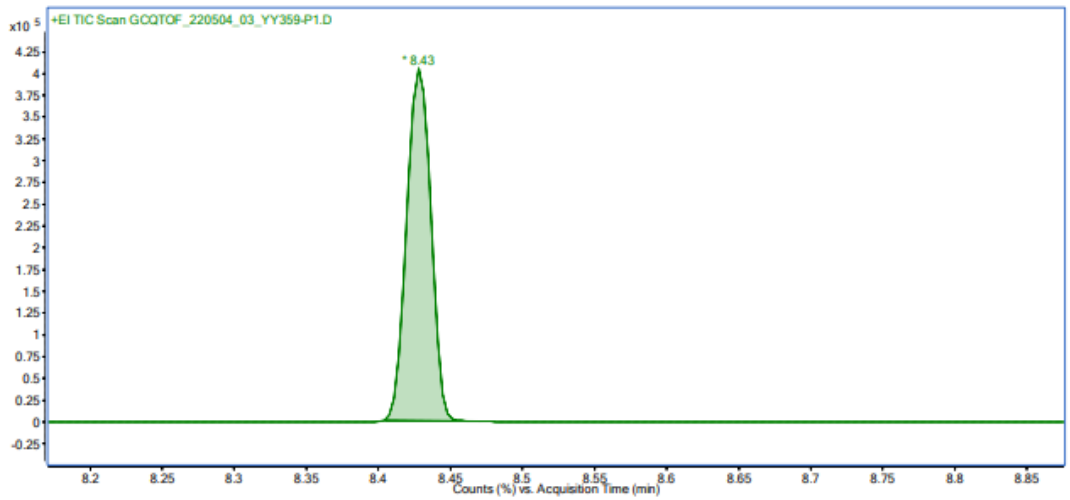
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 134.7, 130.2, 128.6, 128.6 (q, *J* = 315.7 Hz), 127.6, 127.1, 126.8, 125.3, 122.3 (q, *J* = 259.0 Hz), 122.3, 122.1.

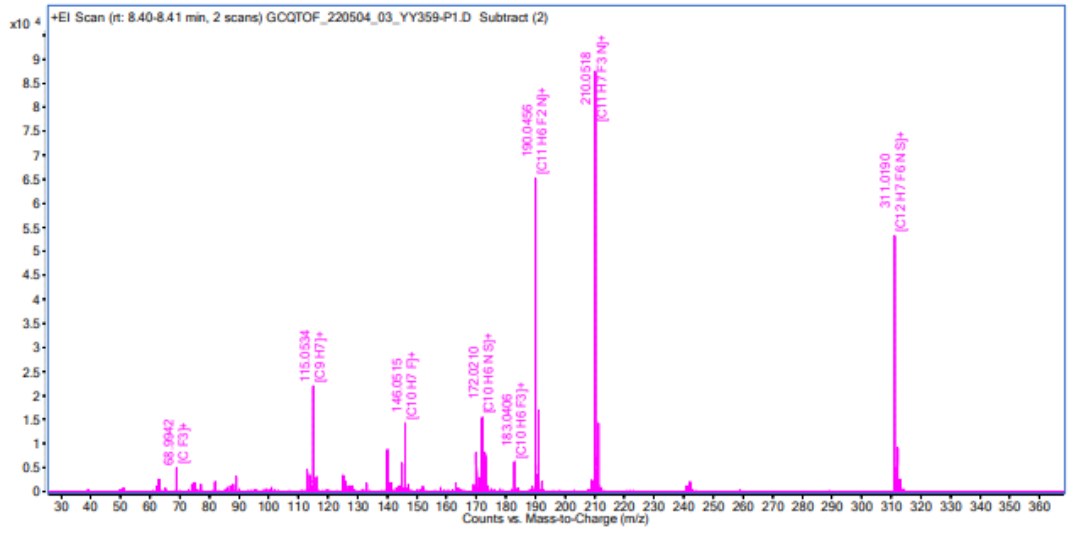
HRMS (EI) calculated for $C_{12}H_7F_6NS$: 311.0198 $[M]^+$, Found: 311.0190.




-50.9
-50.9
-50.9
-50.9
-56.1
-59.1
1.00
0.65
0.33
f1 (ppm)

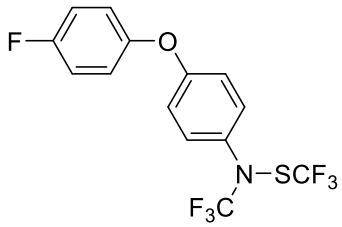

134.7
130.6
130.2
128.6
127.6
127.1
126.8
126.5
125.3
124.0
122.3
122.1
122.1
120.6
f1 (ppm)





m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
311.0190	C12H7F6NS	311.0198	-2.6	$[M]^{+\cdot}$

N-(4-(4-fluorophenoxy)phenyl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3ab)



The compound **3ab** was obtained as a colorless oil in 67% yield using 1-fluoro-4-(4-isothiocyanatophenoxy)benzene following the general procedure F after column chromatography on silica gel with pentane.

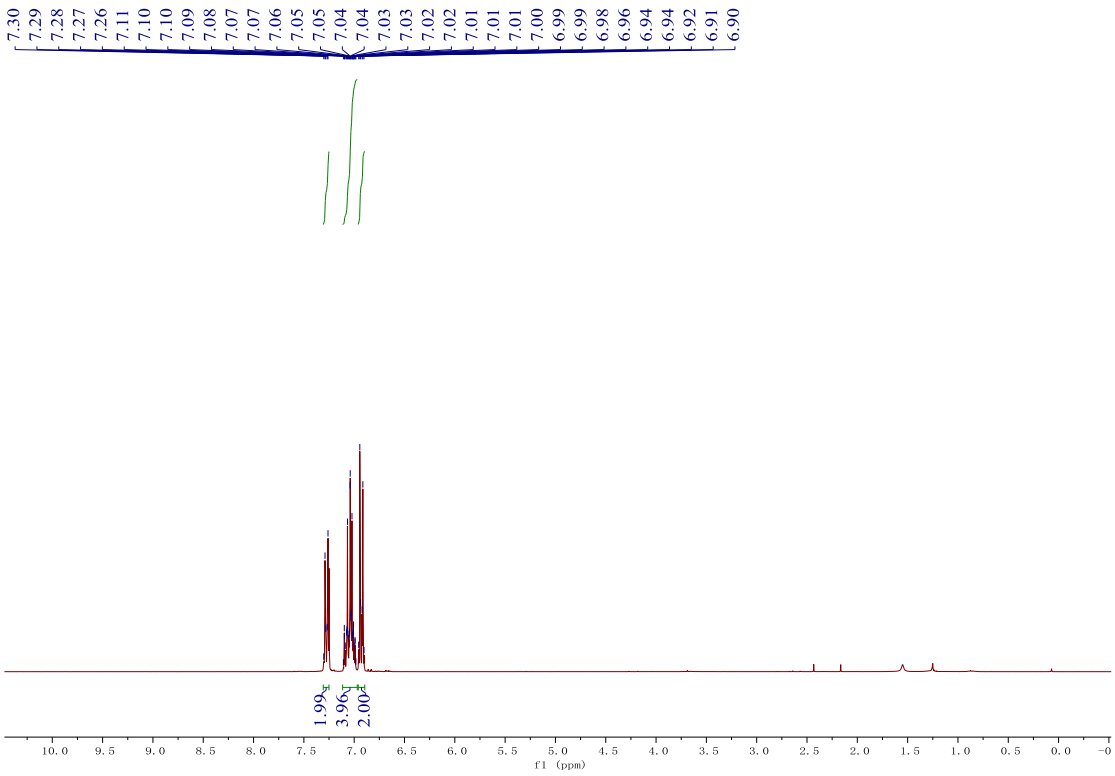
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.31 – 7.25 (m, 2H), 7.11 – 6.97 (m, 4H), 6.96 – 6.89 (m, 2H).

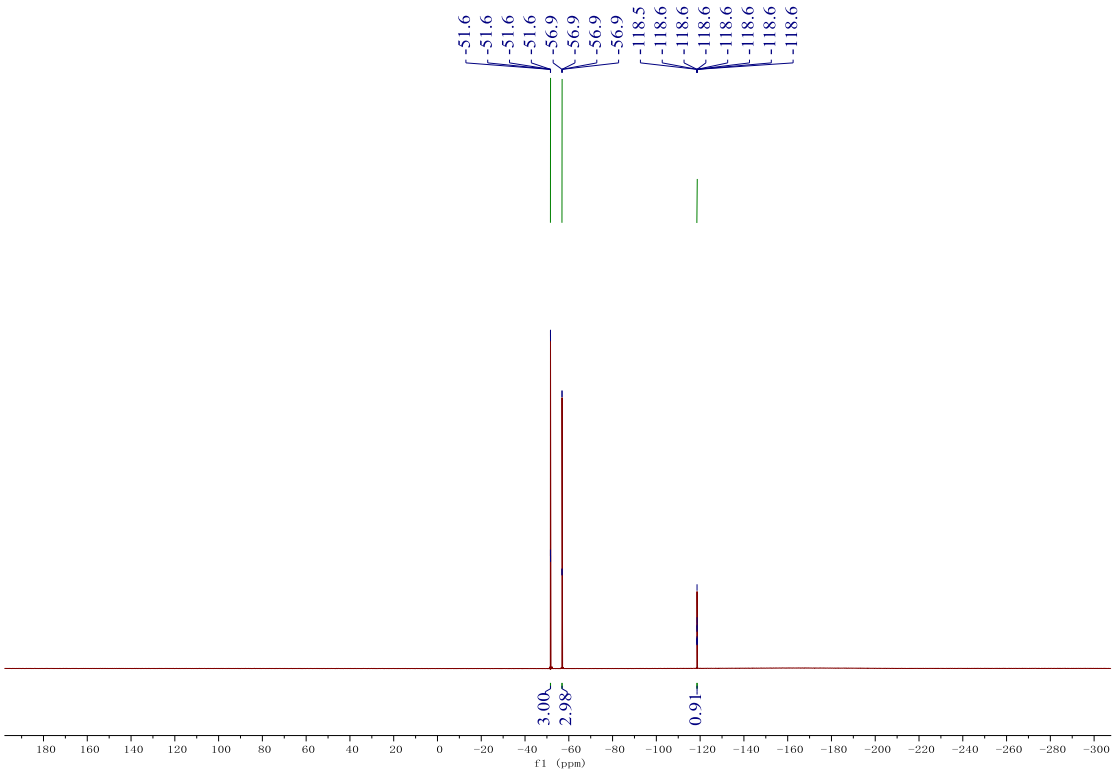
.

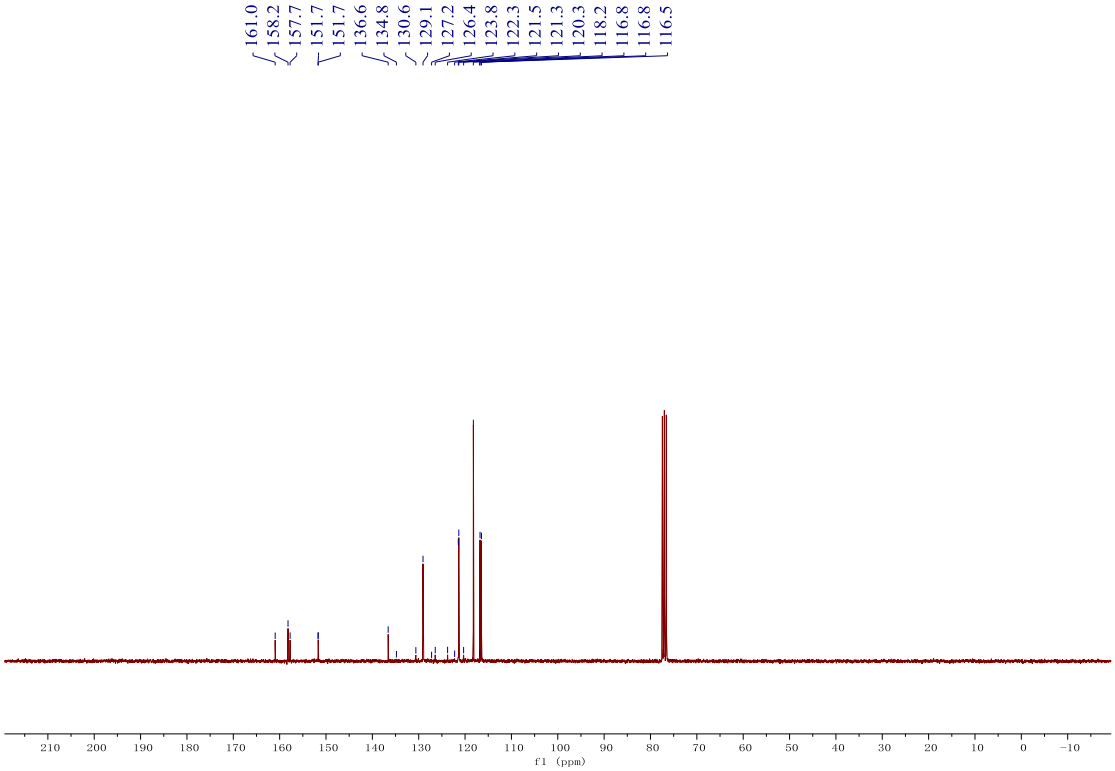
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.6 (q, *J* = 3.4 Hz), -56.9 (q, *J* = 3.4 Hz), -118.5 – -118.7 (m).

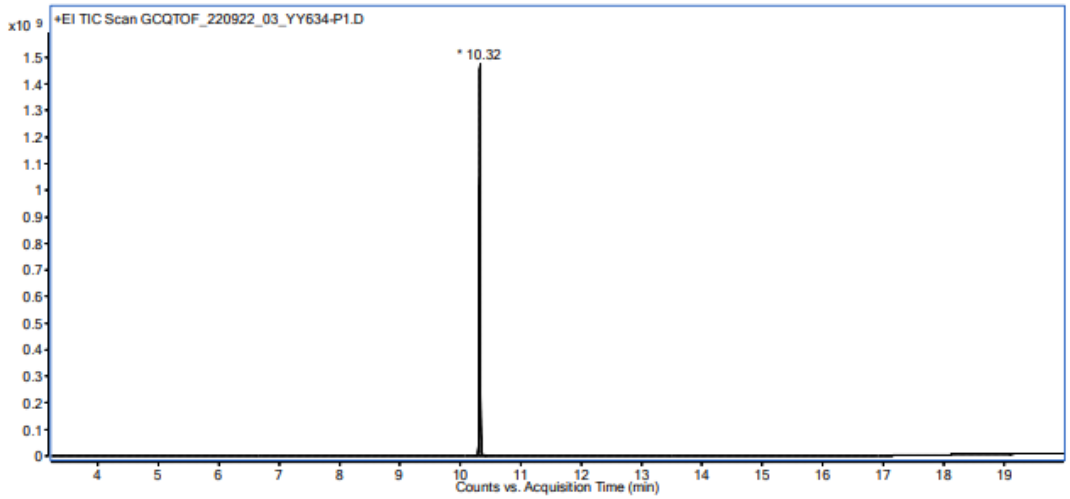
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 159.4 (d, *J* = 243.0 Hz), 158.2, 151.7 (d, *J* = 2.6 Hz), 136.6, 1291, 128.5 (q, *J* = 315.7 Hz), 122.0 (q, *J* = 260.6 Hz), 121.4 (d, *J* = 8.4 Hz), 118.2, 116.6 (d, *J* = 23.4 Hz).

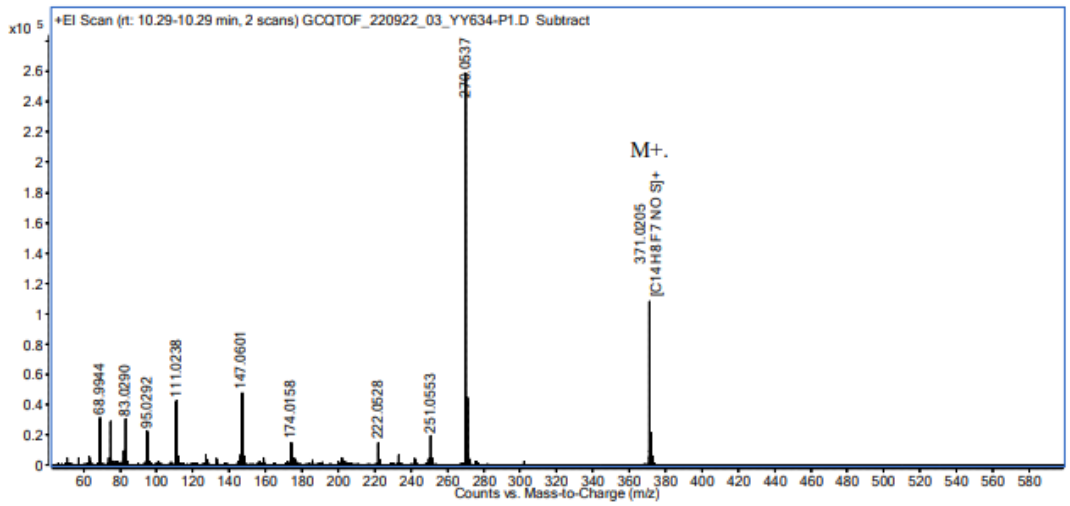
HRMS (EI) calculated for $C_{14}H_8F_7NOS$: 371.0209 $[M]^+$, Found: 371.0205.

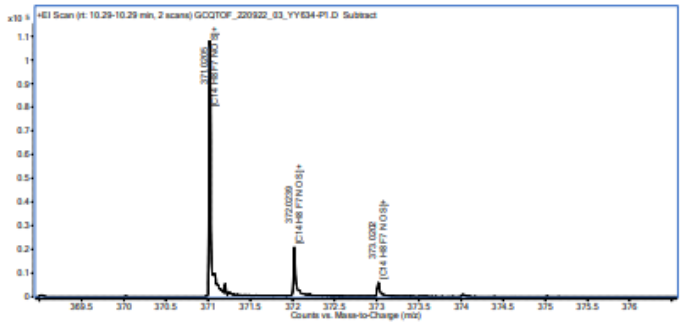



-51.6
-51.6
-51.6
-51.6
-56.9
-56.9
-56.9
-56.9
-118.5
-118.6
-118.6
-118.6
-118.6
-118.6
-118.6
3.00
2.98
0.91
f1 (ppm)


161.0
158.2
157.7
151.7
151.7
136.6
134.8
130.6
129.1
127.2
126.4
123.8
122.3
121.5
121.3
120.3
118.2
116.8
116.8
116.5
f1 (ppm)

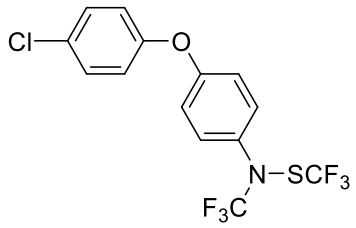






m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
371.0205	C14H8F7NOS	371.0209	-1.1	$[M]^{+\cdot}$

N-(4-(4-chlorophenoxy)phenyl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3ac)



The compound **3ac** was obtained as a colorless oil in 84% yield using 1-chloro-4-(4-

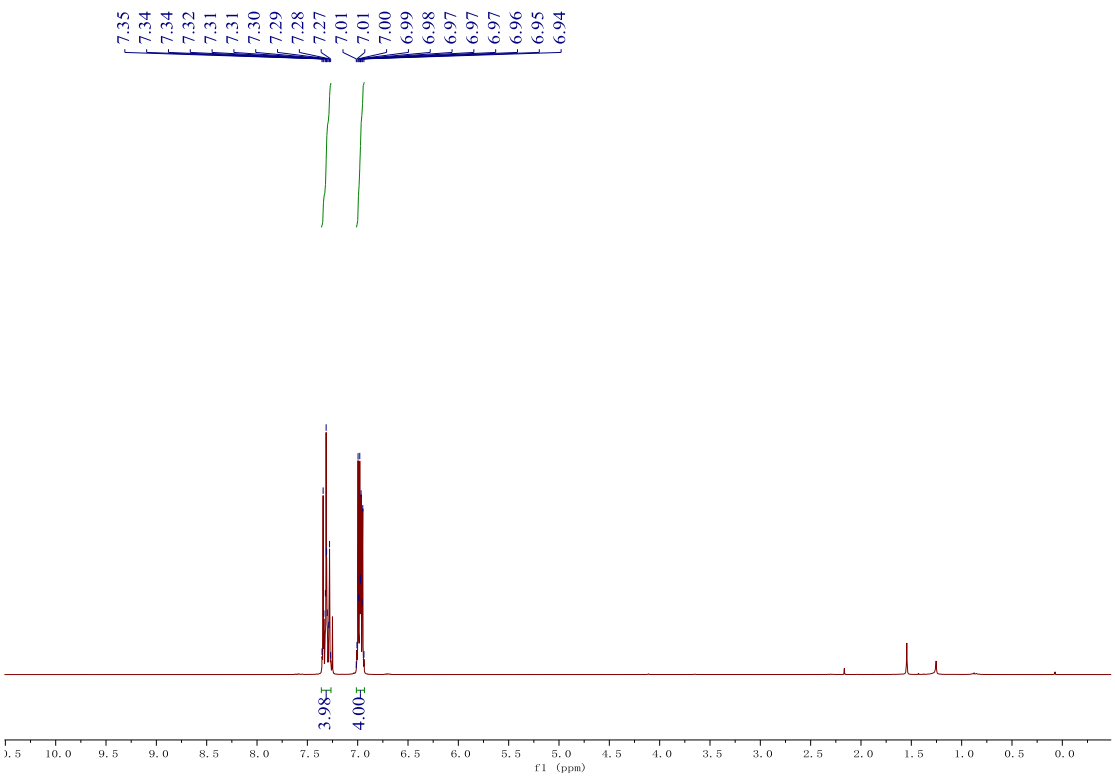
isothiocyanatophenoxy)benzene following the general procedure F after column chromatography on silica gel with pentane.

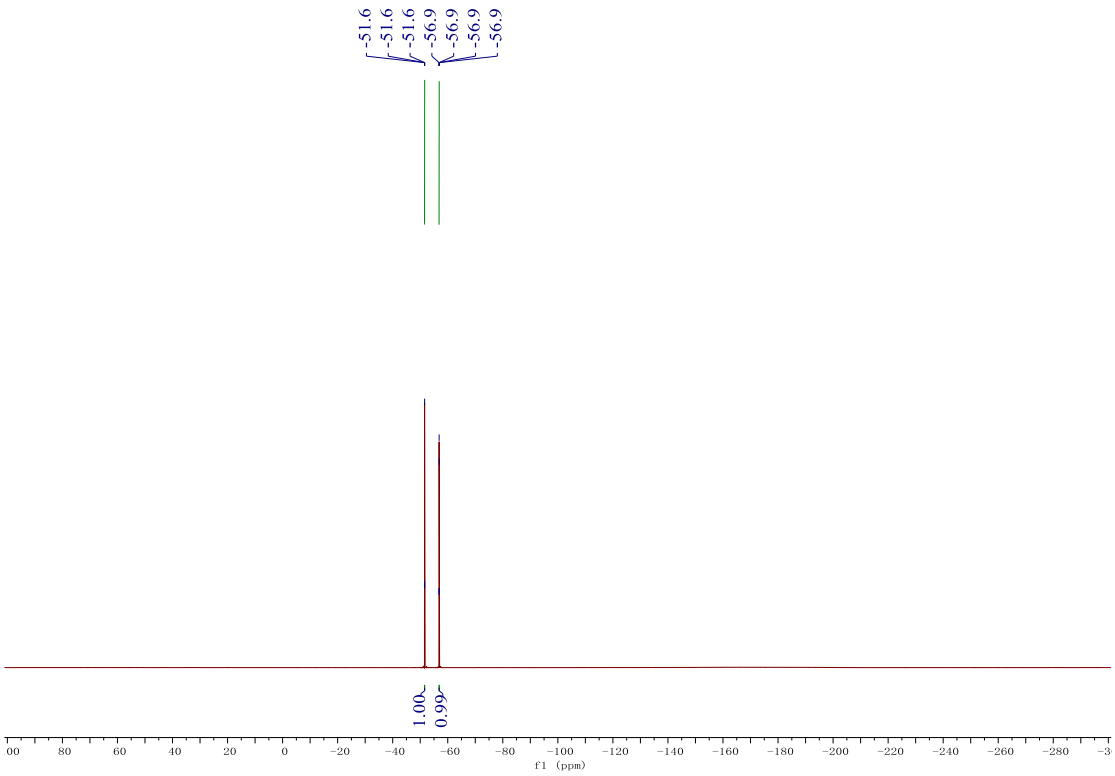
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.36 – 7.27 (m, 4H), 7.01 – 6.93 (m, 4H).

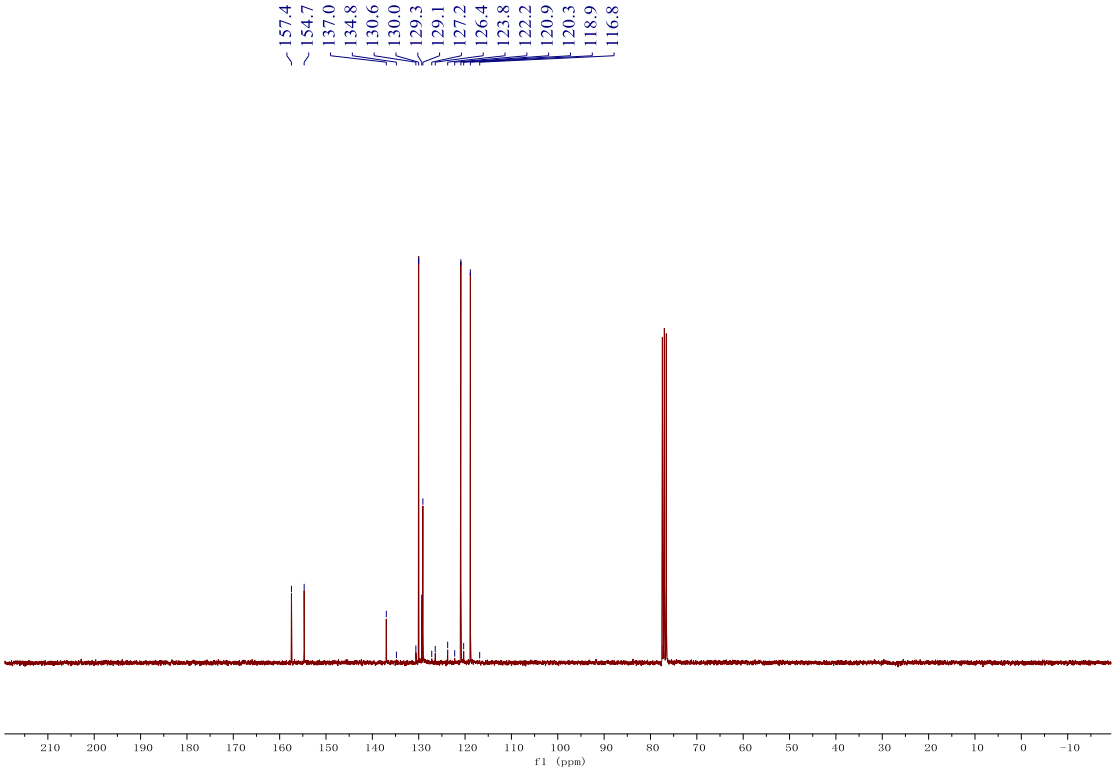
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.6 (q, *J* = 3.4 Hz), -56.9 (q, *J* = 3.4 Hz).

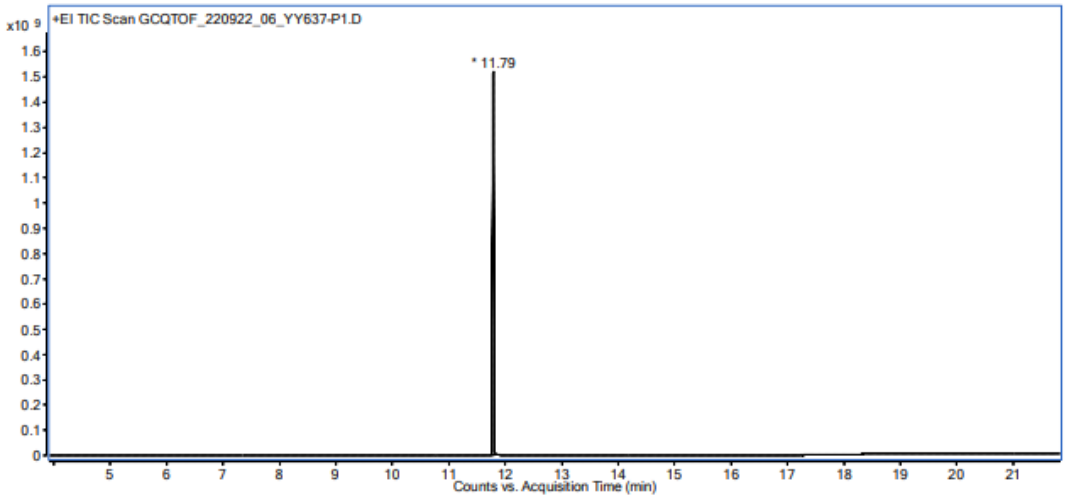
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 157.4, 154.7, 137.0, 130.0, 129.3, 129.1, 128.5 (q, *J* = 315.8 Hz), 122.0 (q, *J* = 260.4 Hz), 120.9, 118.9.

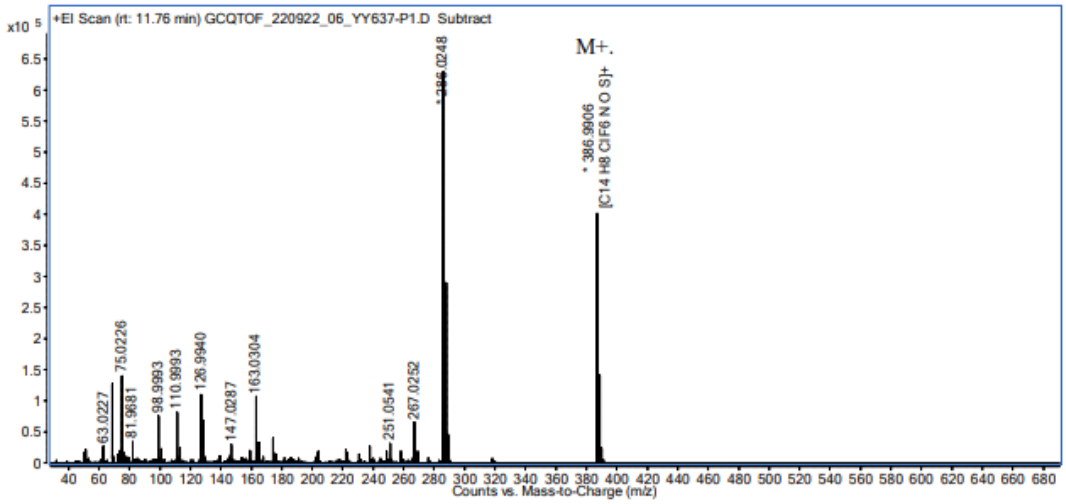
HRMS (EI) calculated for $C_{14}H_8ClF_6NOS$: 386.9914 $[M]^+$, Found: 386.9906.

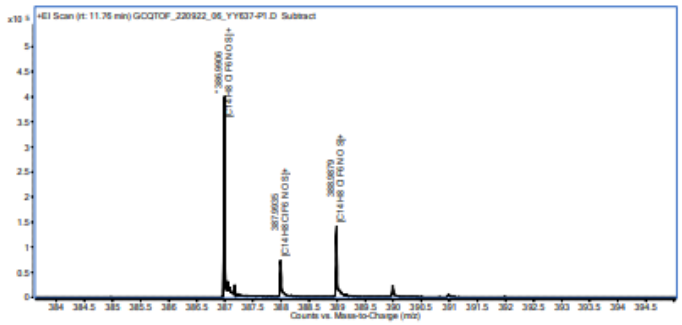



-51.6
-51.6
-51.6
-56.9
-56.9
-56.9
-56.9
1.00
0.99
f1 (ppm)


157.4
154.7
137.0
134.8
130.6
130.0
129.3
129.1
127.2
126.4
123.8
122.2
120.9
120.3
118.9
116.8
f1 (ppm)

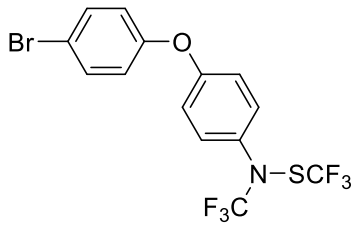






m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
386.9906	C14H8ClF6NOS	386.9914	-2.1	$[M]^{+\cdot}$

N-(4-(4-bromophenoxy)phenyl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3ad)



The compound **3ad** was obtained as a colorless oil in 90% yield using 1-bromo-4-(4-

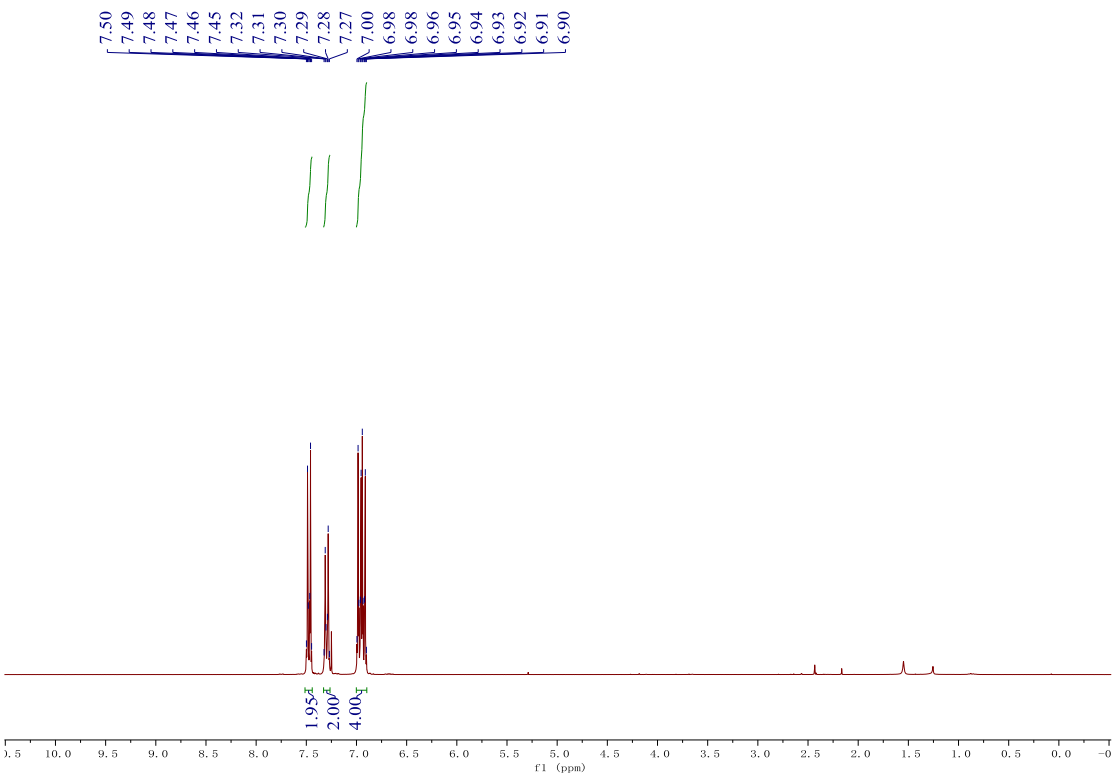
isothiocyanatophenoxy)benzene following the general procedure F after column chromatography on silica gel with pentane.

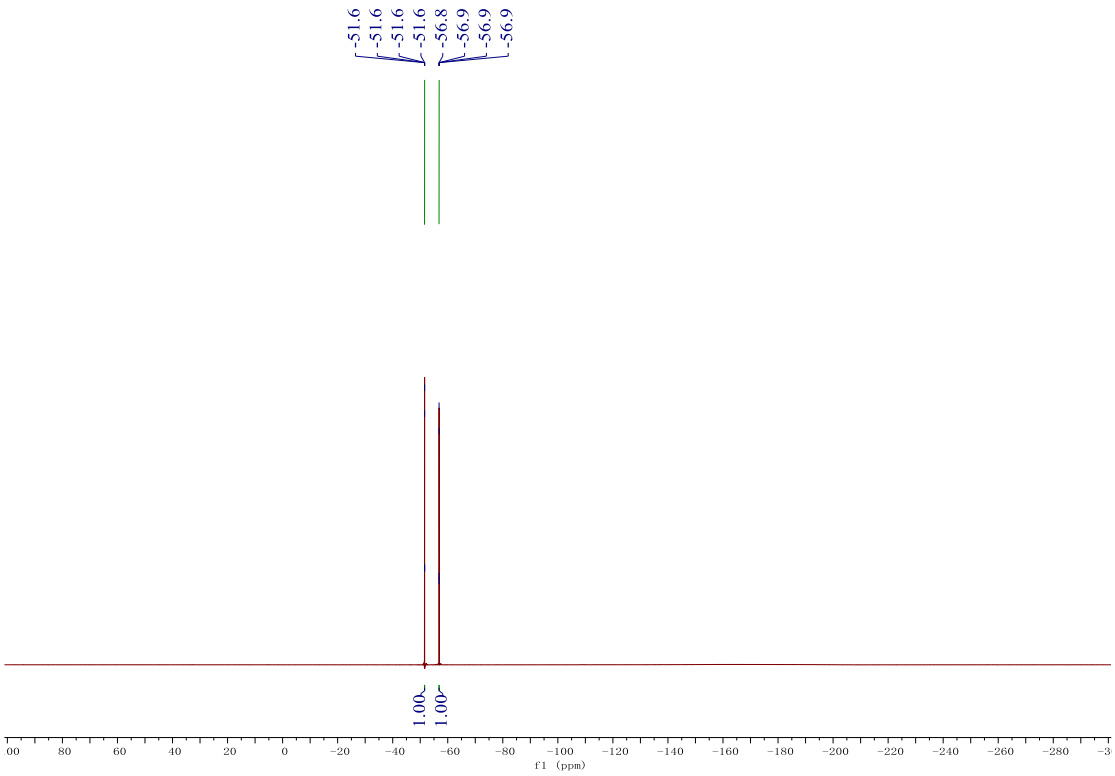
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.51 – 7.44 (m, 2H), 7.33 – 7.26 (m, 2H), 7.00 – 6.90 (m, 4H).

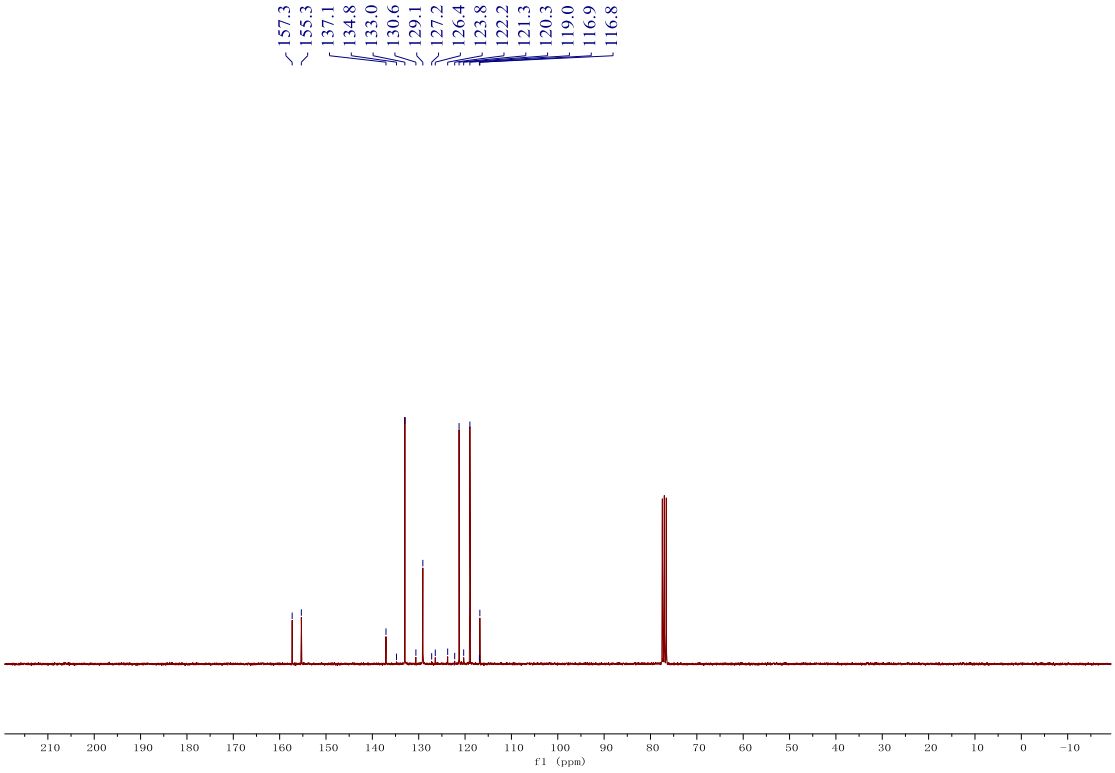
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.6 (q, *J* = 3.4 Hz), -56.9 (q, *J* = 3.4 Hz).

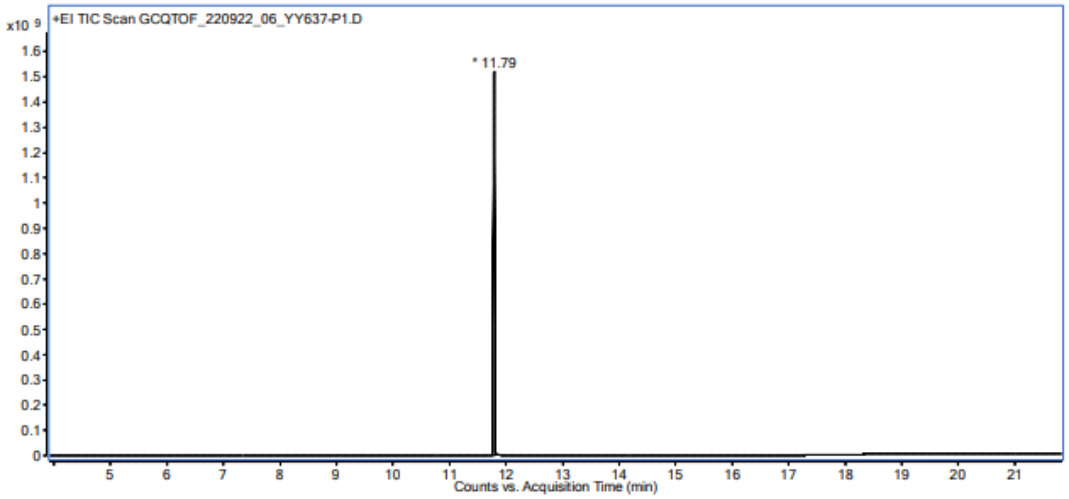
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 157.3, 155.3, 137.1, 133.0, 129.1, 128.5 (q, *J* = 315.8 Hz), 122.0 (q, *J* = 260.5 Hz), 121.3, 119.0, 116.8.

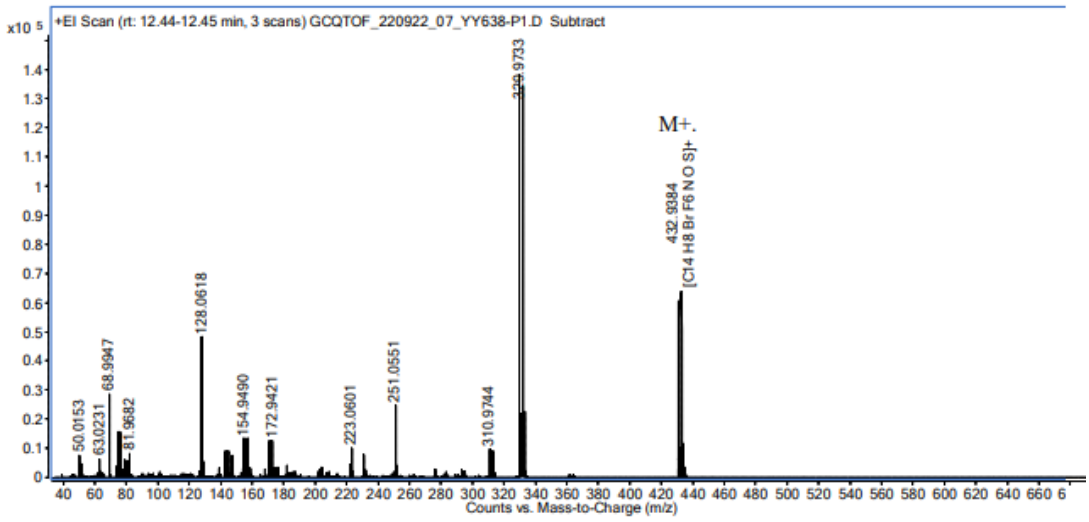
HRMS (EI) calculated for $C_{14}H_8BrF_6NOS$: 430.9409 [M]$^{+}$, Found: 430.9407.

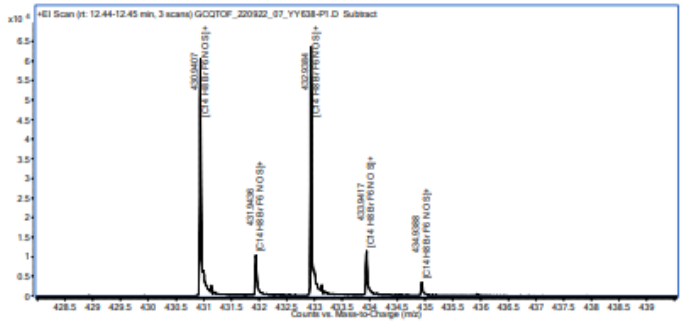



-51.6
-51.6
-51.6
-51.6
-56.8
-56.9
-56.9
-56.9
1.00
1.00
f1 (ppm)


157.3
155.3
137.1
134.8
133.0
130.6
129.1
127.2
126.4
123.8
122.2
121.3
120.3
119.0
116.9
116.8
f1 (ppm)

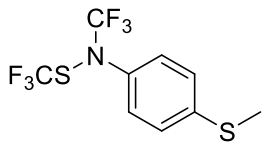






m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
430.9407	C14H8BrF6NOS	430.9409	-0.5	$[M]^{+\cdot}$

N-(4-(methylthio)phenyl)-N,S-bis(trifluoromethyl)thiohydroxylamine (3ae)



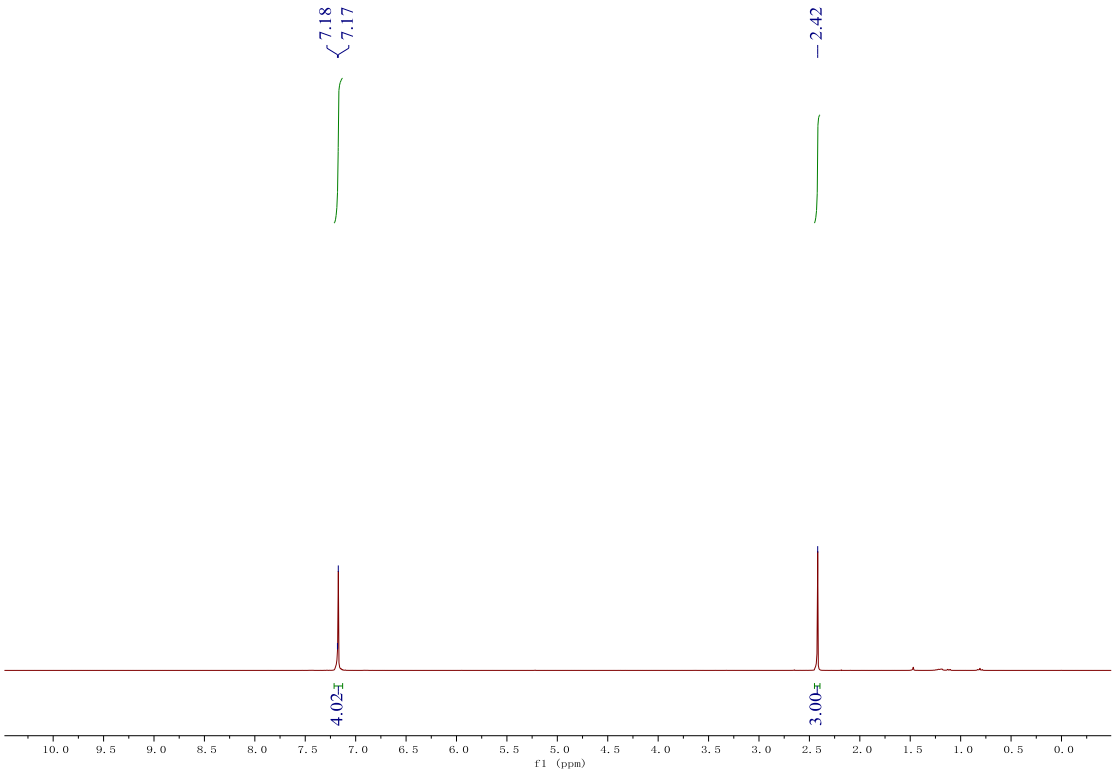
The compound **3ae** was obtained as a colorless oil in 68% yield using (4-isothiocyanatophenyl) (methyl)sulfane following the general procedure F after column chromatography on silica gel with pentane.

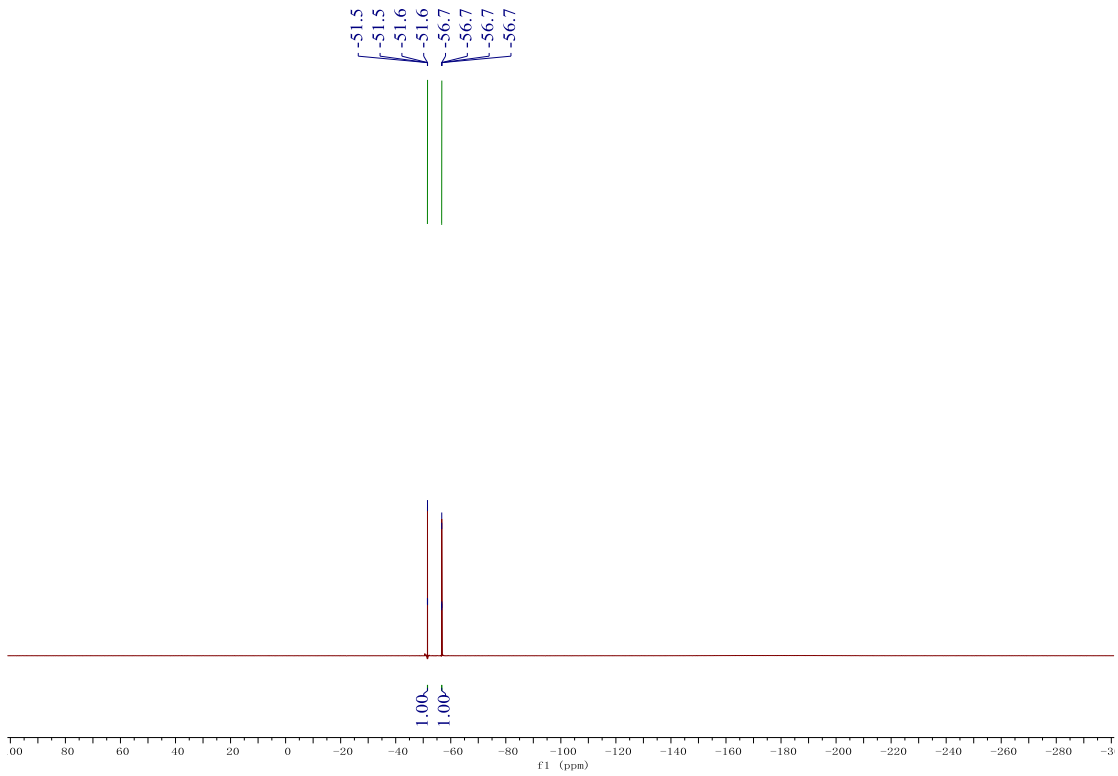
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.18 – 7.17 (m, 4H), 2.42 (s, 3H).

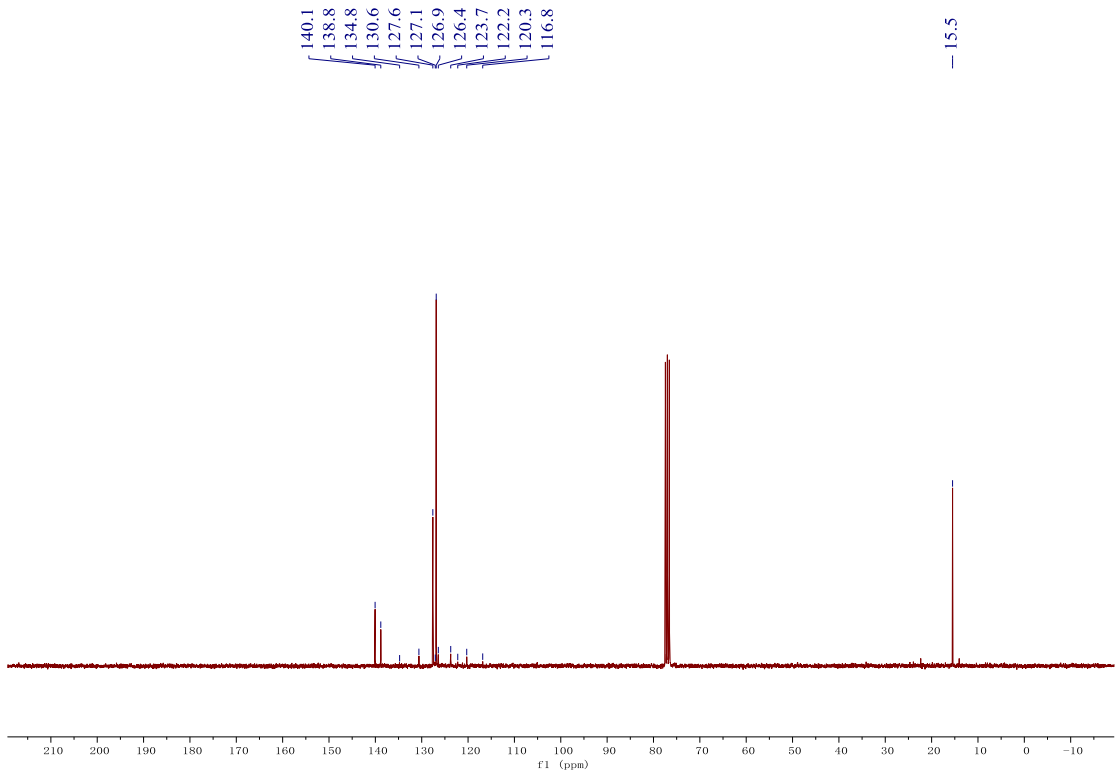
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.5 (q, *J* = 3.4 Hz), -56.7 (q, *J* = 3.4 Hz).

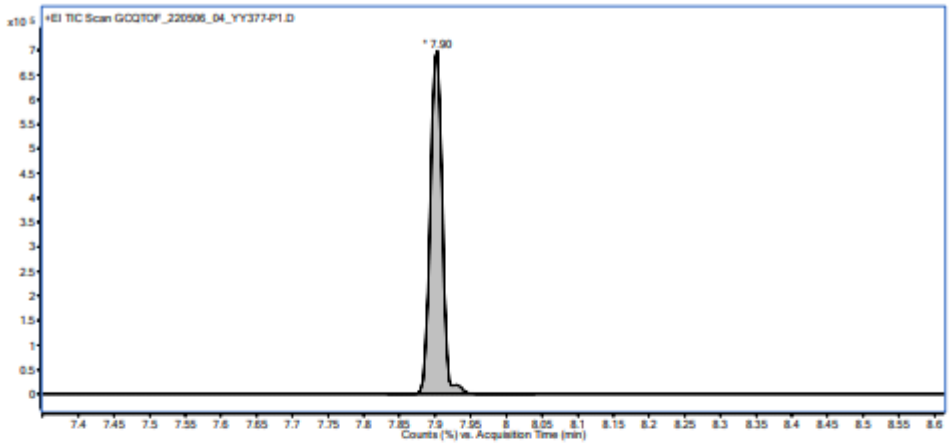
^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 140.1, 138.8, 128.5 (q, *J* = 316.3 Hz), 127.6, 126.9, 122.0 (q, *J* = 260.6 Hz), 15.5.

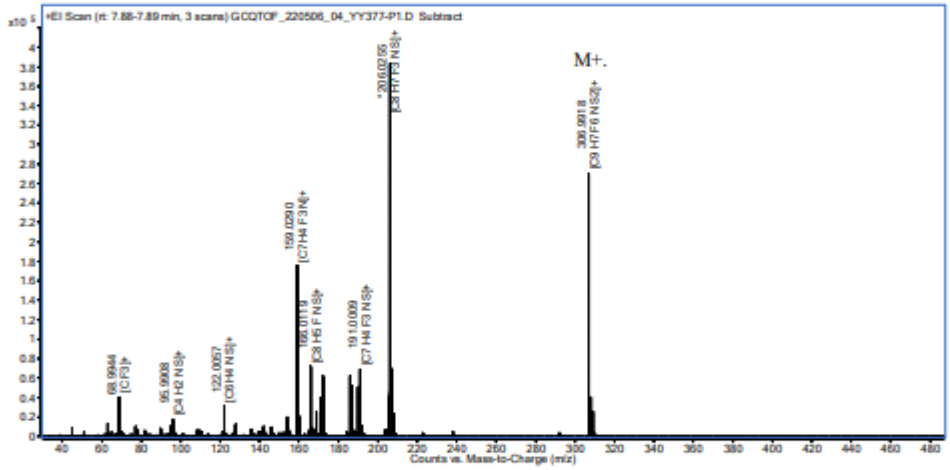
HRMS (EI) calculated for $C_9H_7F_6NS_2$: 306.9919 $[M]^+$, Found: 306.9918.

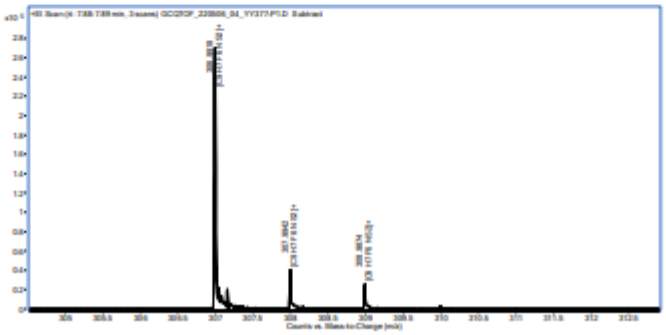



-51.5
-51.5
-51.6
-51.6
-56.7
-56.7
-56.7
-56.7
1.00
1.00
f1 (ppm)


140.1
138.8
134.8
130.6
127.6
127.1
126.9
126.4
123.7
122.2
120.3
116.8
15.5
f1 (ppm)

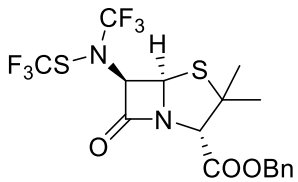






m/z	Formula (M)	m/z (Calc)	Diff (ppm)	
306.9918	C9H7F6NS2	306.9919	-0.3	$[M]^{+\cdot}$

benzyl (2S,5R,6R)-3,3-dimethyl-7-oxo-6-((trifluoromethyl)((trifluoromethyl)thio)amino)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate (3af)



The compound **3af** was obtained as a colorless oil in 33% yield using benzyl (2S,5R,6R)-6-isothiocyanato-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate following the

general procedure F after column chromatography on silica gel with pentane.

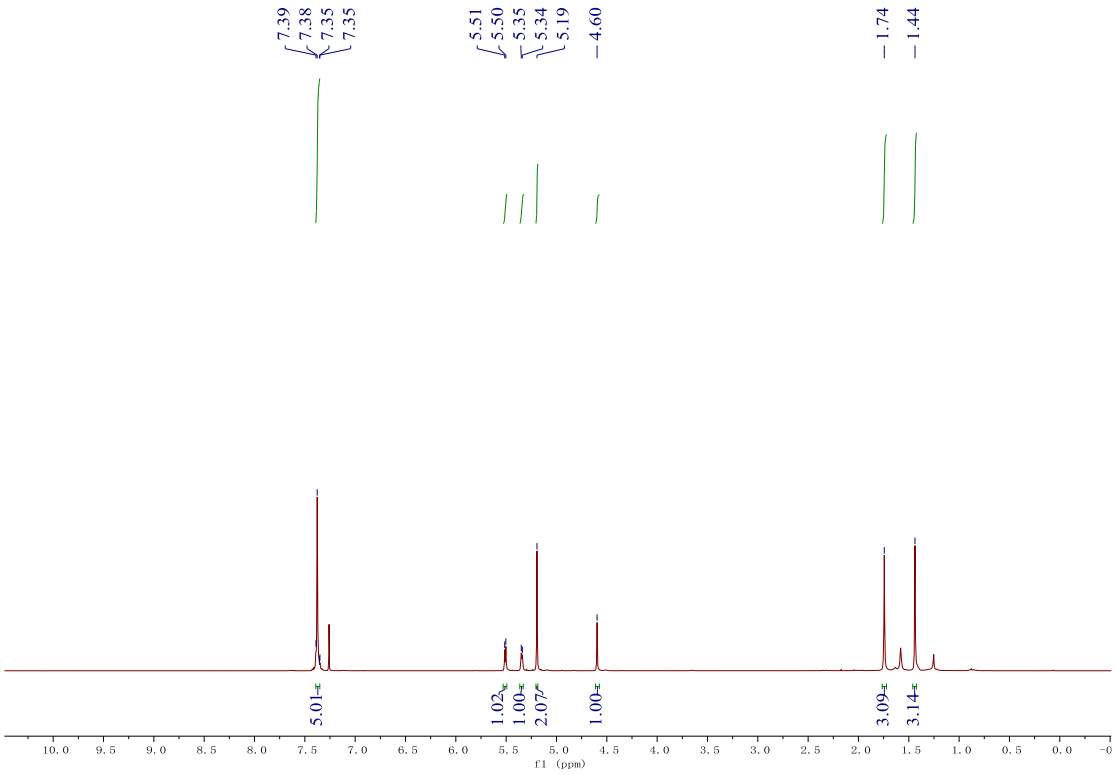
$[\alpha]_D$ = +20.5 (c = 1, $CHCl_3$, 25°C)

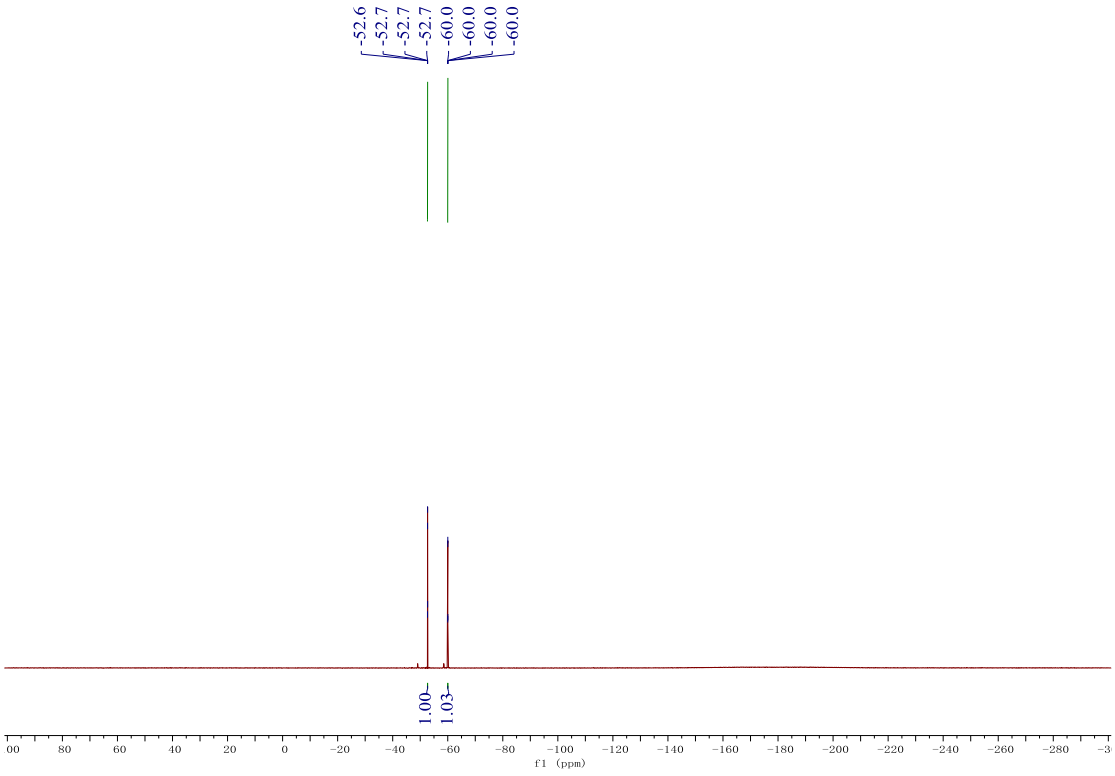
^1H NMR (300 MHz, Chloroform-*d*) δ 7.39 – 7.35 (m, 5H), 5.51 (d, *J* = 3.5 Hz, 1H), 5.34 (d, *J* = 3.2 Hz, 1H), 5.19 (s, 2H), 4.60 (s, 1H), 1.74 (s, 3H), 1.44 (s, 3H).

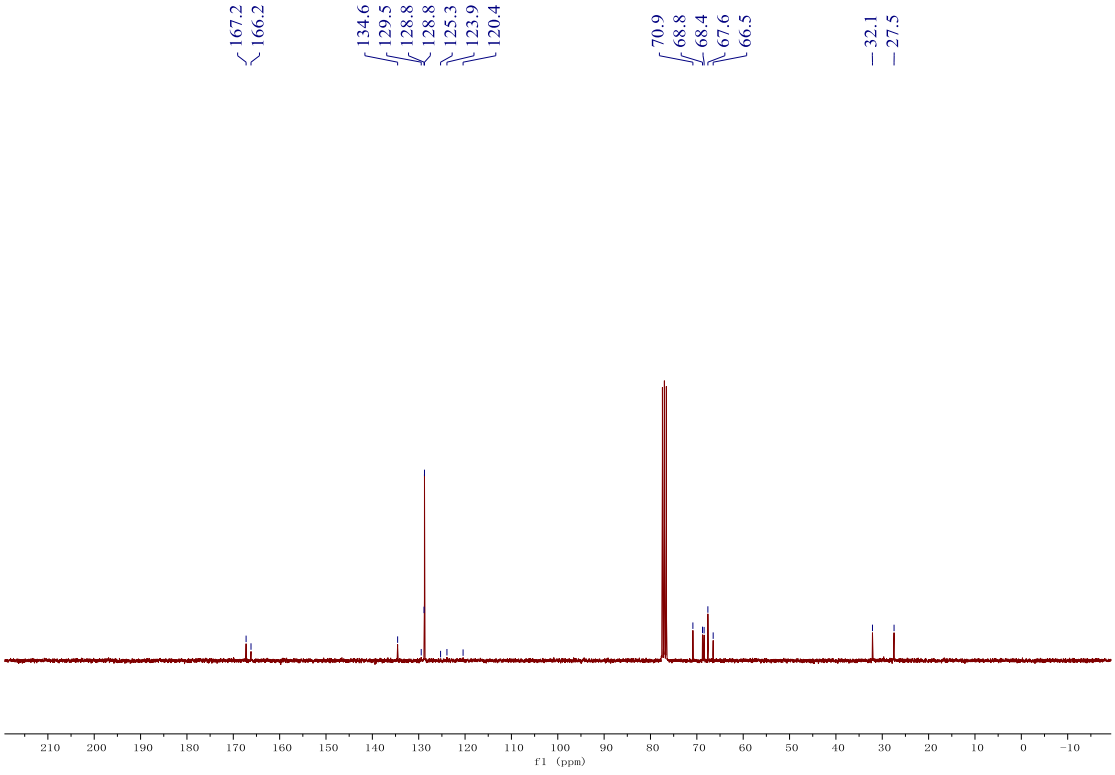
^{19}F NMR (282 MHz, Chloroform-*d*) δ -52. 7 (q, *J* = 3.4 Hz), -60.0 (q, *J* = 3.4 Hz).

$^{13}C\{^1H\}$ NMR (75 MHz, Chloroform-*d*) δ 167.2, 166.2, 134.6, 128.8, 128.8, 127.4 (d, *J* = 315.0 Hz), 122.2 (q, *J* = 262.9 Hz), 70.9, 68.8, 68.4, 67.6, 66.5, 32.1, 27.5.

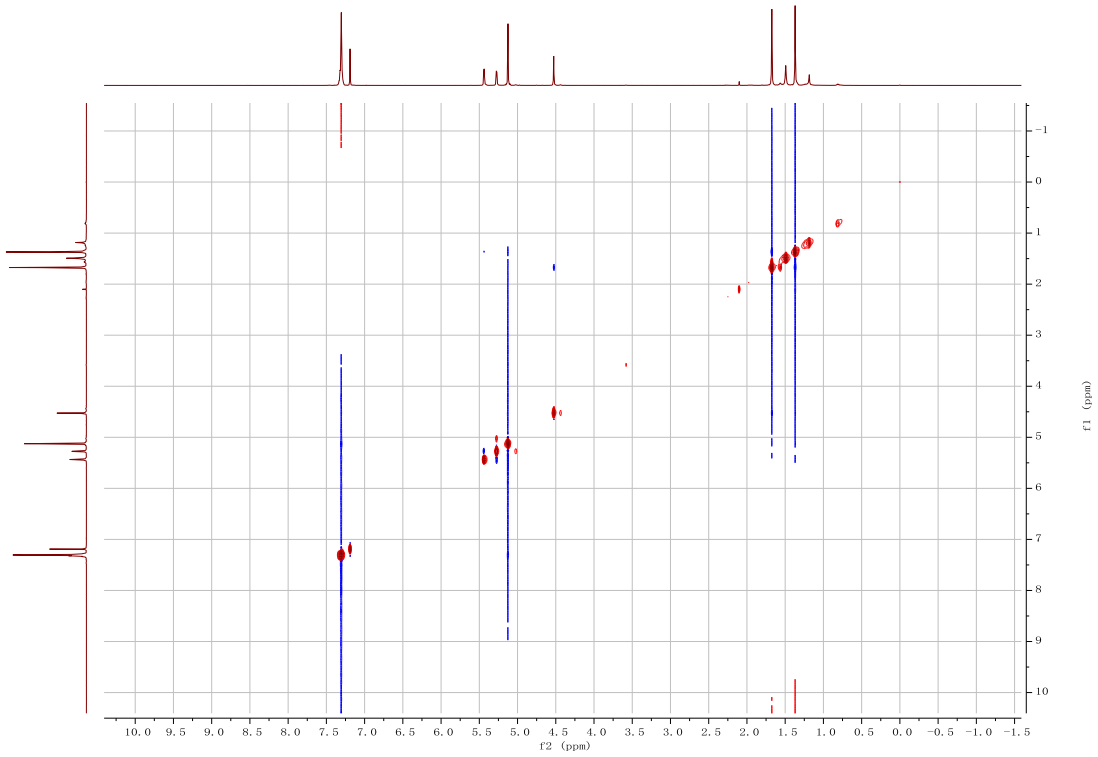
HRMS (ESI) calculated for $C_{17}H_{17}F_6N_2O_3S_2$: 475.0579 $[M+H]^+$, Found: 475.0580.



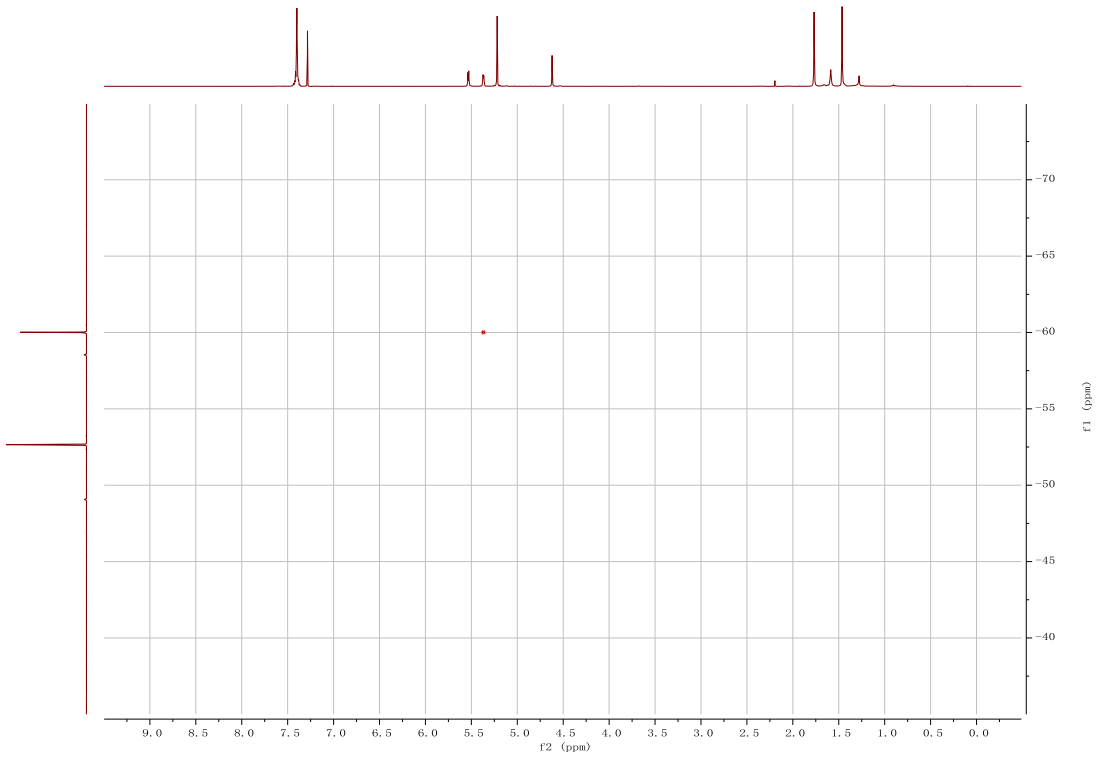

-52.6
-52.7
-52.7
-52.7
-60.0
-60.0
-60.0
-60.0
1.00
1.03
f1 (ppm)


167.2
166.2
134.6
129.5
128.8
128.8
125.3
123.9
120.4
70.9
68.8
68.4
67.6
66.5
32.1
27.5
f1 (ppm)

^{1}H-^{1}H NOESY:



^{1}H-^{19}F NOESY:



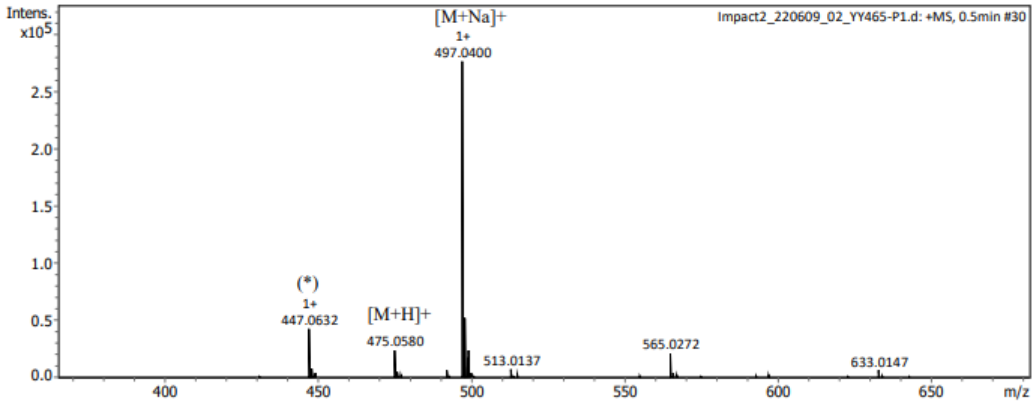
CENTRE COMMUN DE SPECTROMETRIE DE MASSE

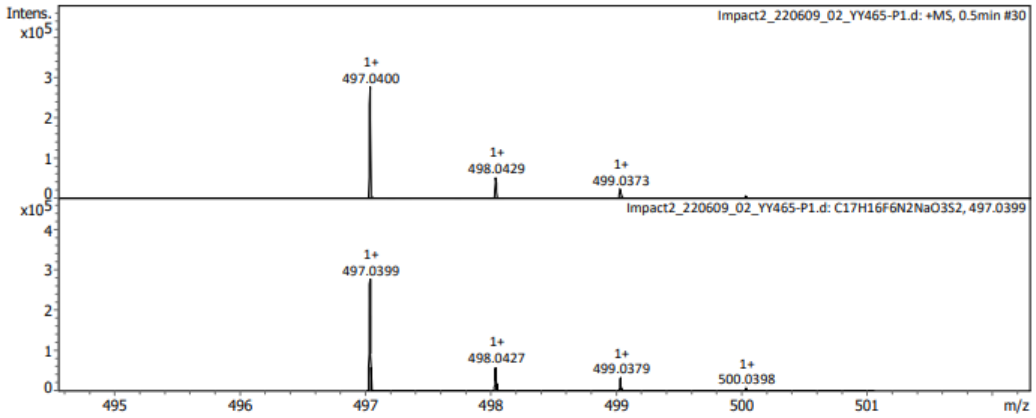
Analysis Info

Analysis Name	Impact2_220609_02_YY465-P1.d		
Method	Tune_pos_Standard.m	Acquisition Date	6/9/2022 10:09:58 AM
Comment		Instrument / Ser#	impact II 1825265.10081

Acquisition Parameter

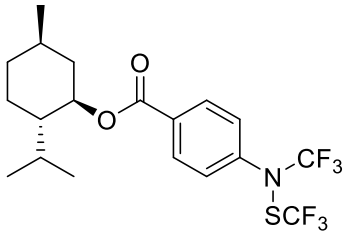
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	2500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	750.0 Vpp	Set Divert Valve	Source





Meas. m/z	Ion Formula	m/z	Sum Formula	err [ppm]	mSigma	Adduct	z
475.0580	C17H17F6N2O3S2	475.0579	C17H16F6N2O3S2	-0.2	10.2	M+H	1+
497.0400	C17H16F6N2NaO3S2	497.0399		-0.2	18.5	M+Na	1+

(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 4-((trifluoromethyl)((trifluoromethyl)thio) amino)benzoate (3ag)



The compound **3ag** was obtained as a colorless oil in 56% yield using (1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 4-isothiocyanatobenzoate following the general procedure F after column chromatography on silica gel with pentane.

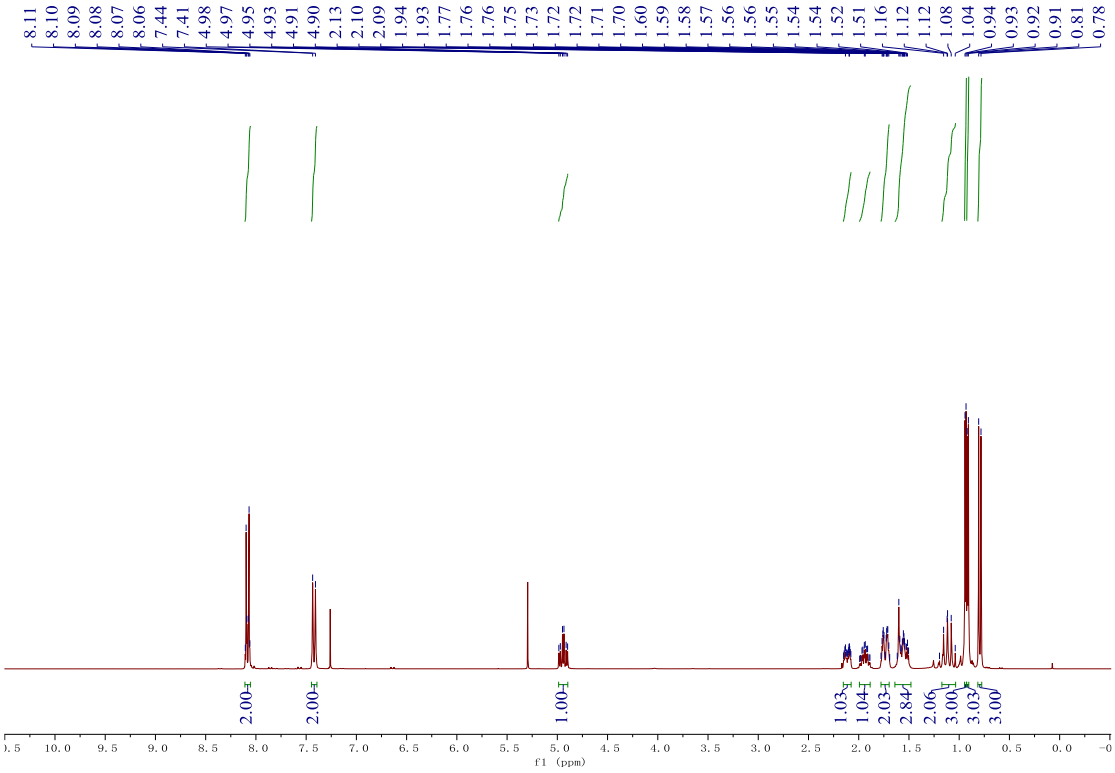
^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.09 – 8.02 (m, 2H), 7.40 (d, *J* = 8.4 Hz, 2H), 4.96 – 4.88 (m, 1H), 2.13 – 2.06 (m, 1H), 1.97 – 1.87 (m, 1H), 1.76 – 1.67 (m, 2H), 1.61 – 1.48 (m, 3H), 1.15 – 1.01 (m, 2H), 0.92 (d, *J* = 3.1 Hz, 3H), 0.89 (d, *J* = 3.6 Hz, 3H), 0.77 (d, *J* = 6.9 Hz, 3H).

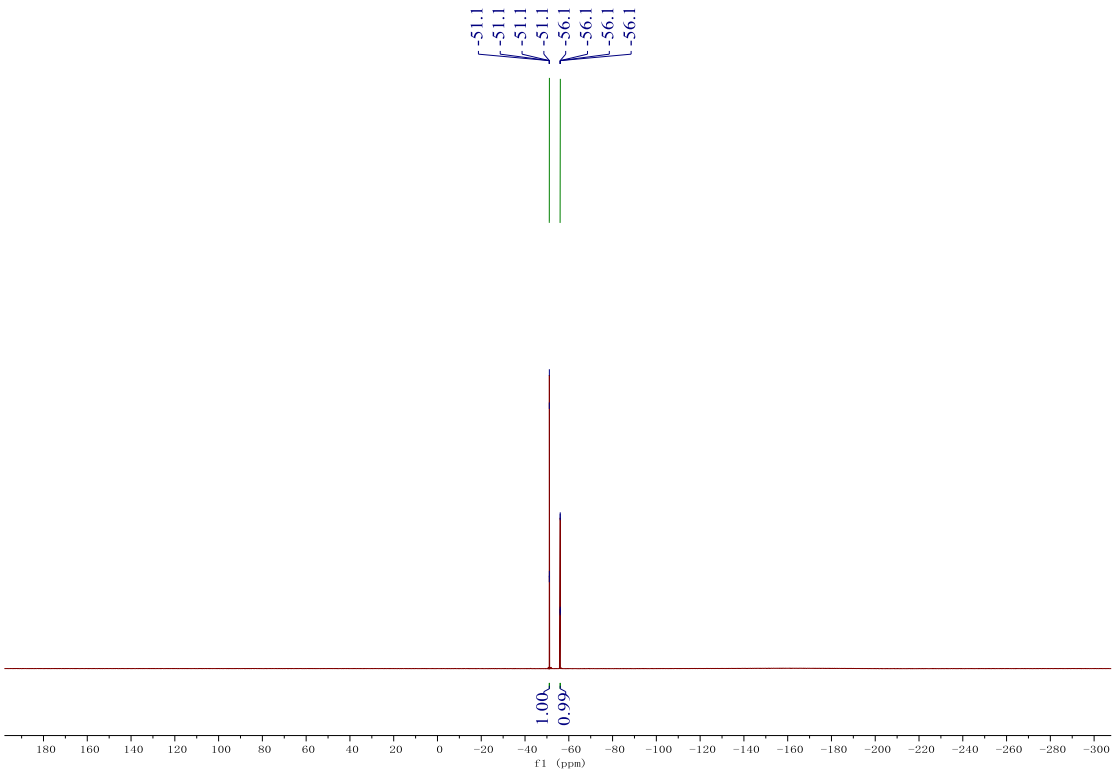
.

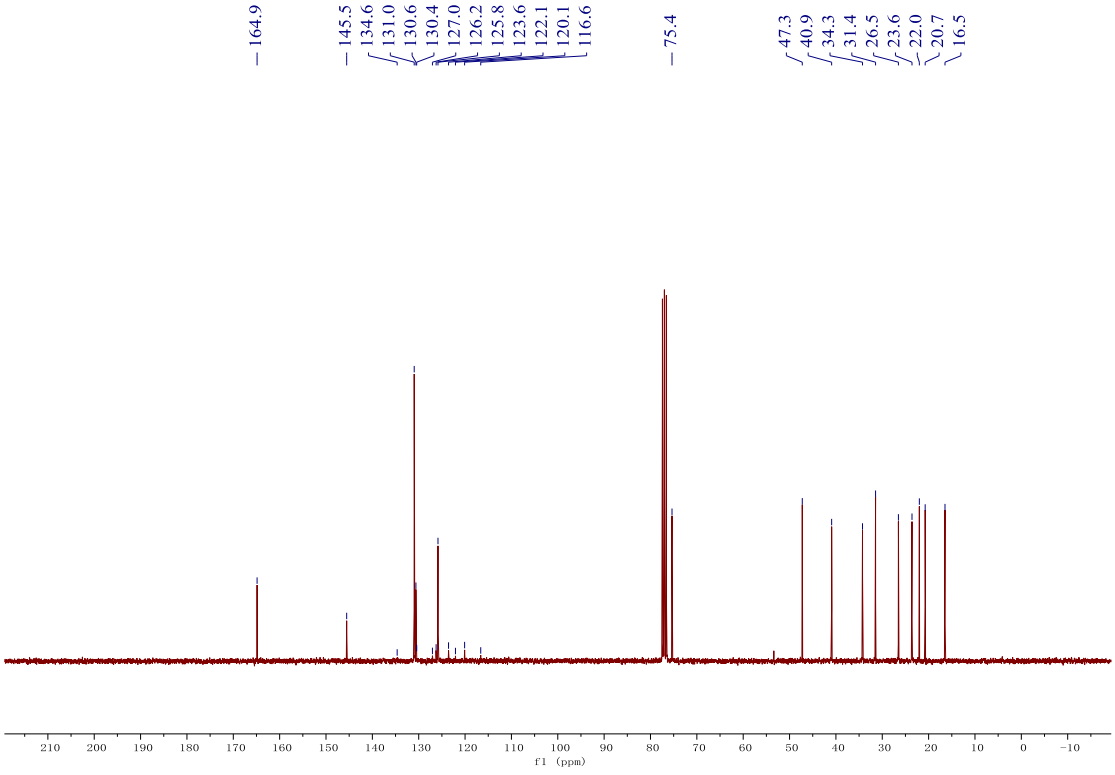
^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.1 (q, *J* = 3.4 Hz), -56.1 (q, *J* = 3.4 Hz).

^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 164.9, 145.5, 131.0, 130.6, 128.4 (q, *J* = 314.2 Hz), 125.8, 121.8 (d, *J* = 261.8 Hz), 75.4, 47.3, 40.9, 34.3, 31.4, 26.5, 23.6, 22.0, 20.7, 16.5.

HRMS (ESI) calculated for $C_{19}H_{23}F_6NO_2S$: 444.1426 $[M+H]^+$, Found: 444.1426.




-51.1
-51.1
-51.1
-51.1
-56.1
-56.1
-56.1
-56.1
1.00
0.99
f1 (ppm)


164.9
145.5
134.6
131.0
130.6
130.4
127.0
126.2
125.8
123.6
122.1
120.1
116.6
75.4
47.3
40.9
34.3
31.4
26.5
23.6
22.0
20.7
16.5
f1 (ppm)

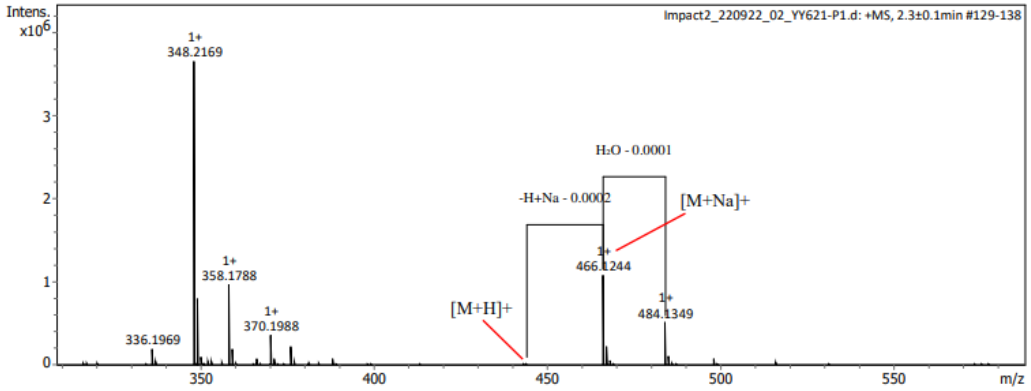
CENTRE COMMUN DE SPECTROMETRIE DE MASSE

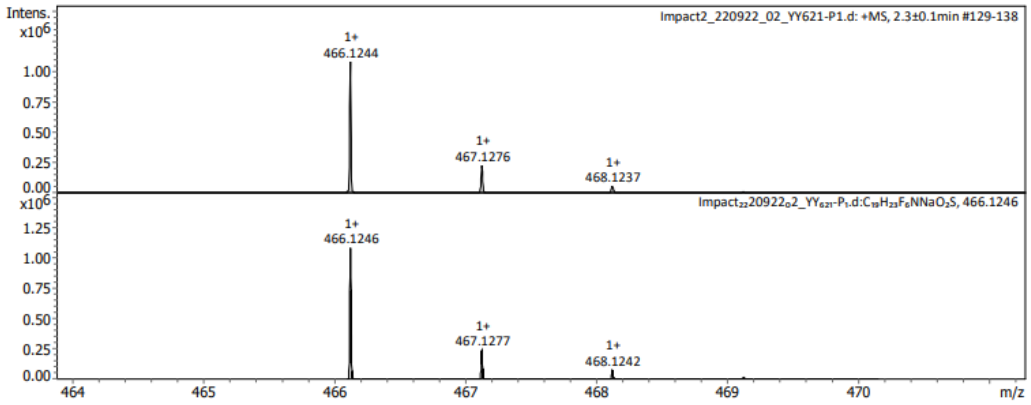
Analysis Info

Analysis Name	Impact2_220922_02_YY621-P1.d		
Method	Tune_pos_Standard.m	Acquisition Date	9/22/2022 2:22:58 PM
Comment		Instrument / Ser#	impact II 1825265.10081

Acquisition Parameter

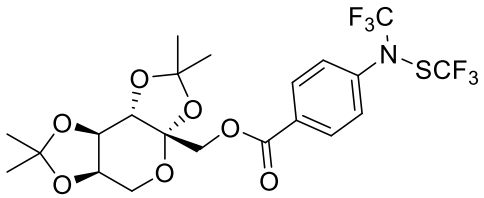
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	1000 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	750.0 Vpp	Set Divert Valve	Source





Meas. m/z	Ion Formula	m/z	Sum Formula	err [ppm]	mSigma	Adduct	z
444.1426	C19H24F6NO2S	444.1426	C19H23F6NO2S	0.1	36.6	M+H	1+
466.1244	C19H23F6NNaO2S	466.1246		0.4	11.7	M+Na	1+

((3aS,5aR,8aR,8bS)-2,2,7,7-tetramethyltetrahydro-3aH-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-3a-yl)methyl 4-((trifluoromethyl)((trifluoromethyl)thio)amino)benzoate (3ah)



The compound **3ah** was obtained as a colorless oil in 69% yield using ((3aS,5aR,8aR,8bS)-2,2,7,7-tetramethyltetrahydro-3aH-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-3a-yl)methyl 4-isothiocyanatobenzoate following the general procedure F after column chromatography on silica gel with pentane/ethyl acetate (15/1).

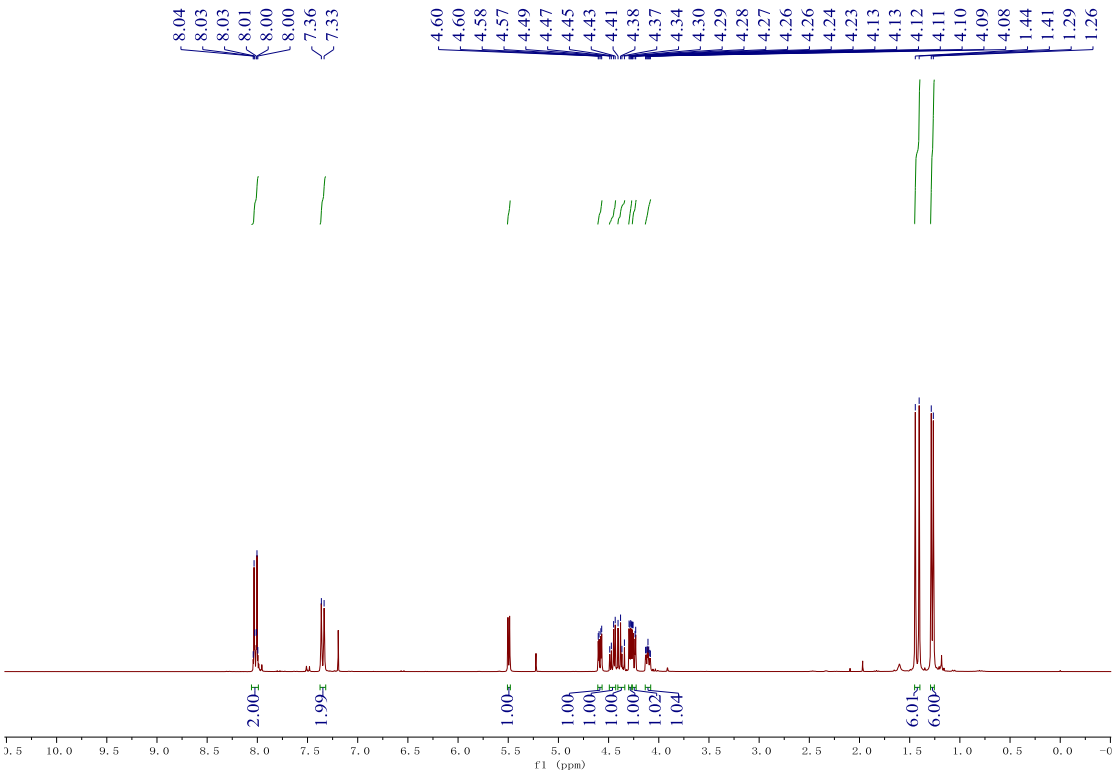
^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.06 – 7.99 (m, 2H), 7.35 (d, *J* = 8.2 Hz, 2H), 5.49 (d, *J* = 4.9 Hz, 1H), 4.60 – 4.57 (m, 1H), 4.49 – 4.43 (m, 1H), 4.41 – 4.34 (m, 1H), 4.30 – 4.27 (m, 1H), 4.26

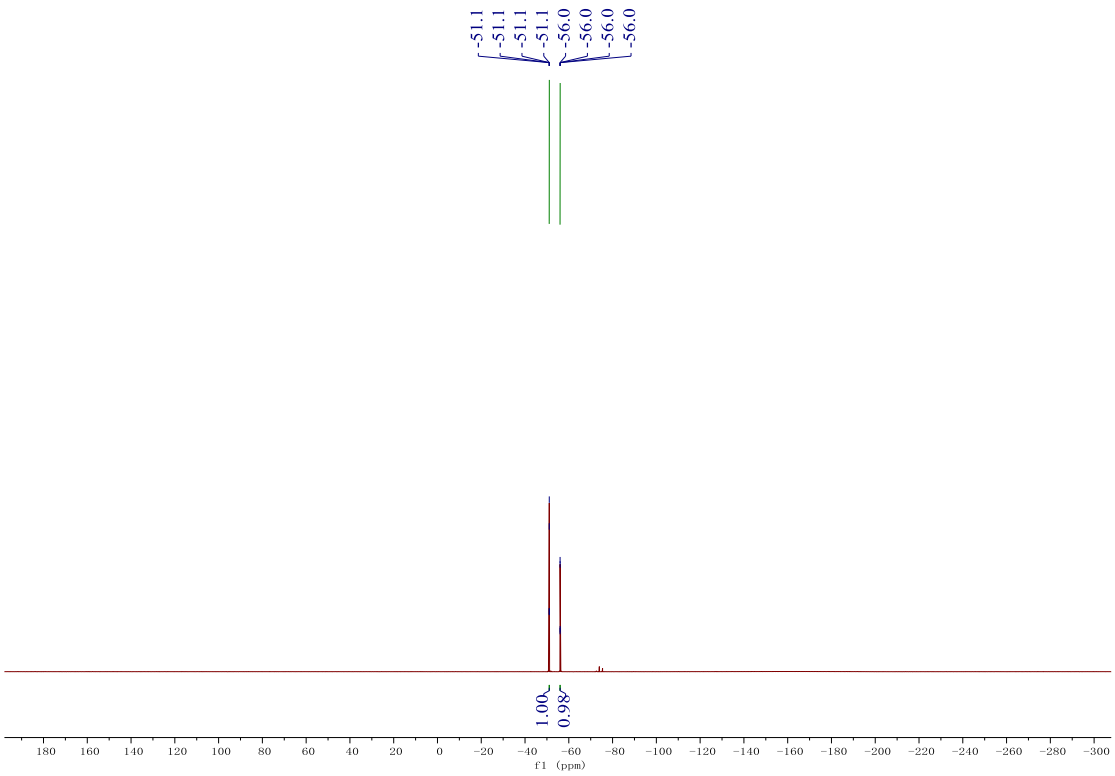
– 4.23 (m, 1H), 4.13 – 4.08 (m, 1H), 1.42 (d, J = 11.6 Hz, 6H), 1.27 (d, J = 6.2 Hz, 6H).

^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.1 (q, J = 3.4 Hz), -56.0 (q, J = 3.4 Hz).

^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 165.2, 145.8, 131.1, 129.7, 128.3 (q, J = 317.6 Hz), 125.7, 121.8 (q, J = 261.8 Hz), 109.7, 108.8, 96.3, 71.1, 70.7, 70.5, 66.1, 64.3, 26.0, 26.0, 24.9, 24.5.

HRMS (EI) calculated for $C_{21}H_{24}F_6NO_7S$: 548.1172 $[M+H]^+$, Found: 548.1178.

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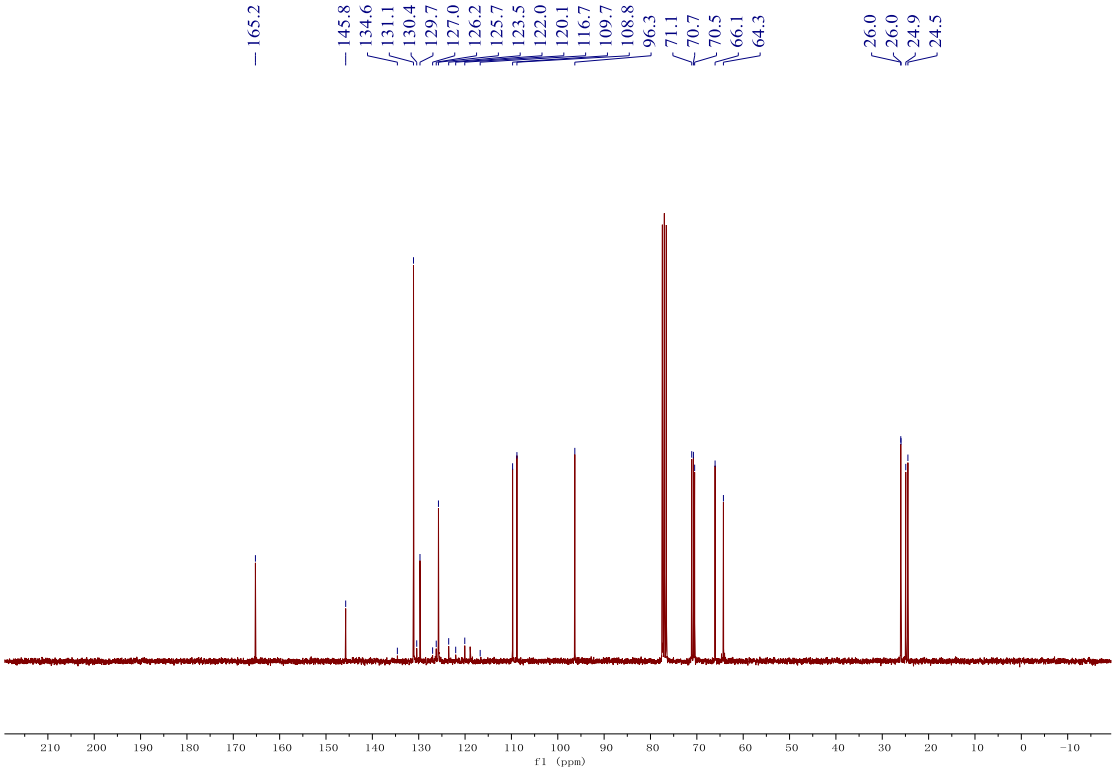
-51.1
-56.0
-56.0
-56.0
-56.0
1.00
0.98
f1 (ppm)


165.2
145.8
134.6
131.1
130.4
129.7
127.0
126.2
125.7
123.5
122.0
120.1
116.7
109.7
108.8
96.3
71.1
70.7
70.5
66.1
64.3
26.0
26.0
24.9
24.5
f1 (ppm)

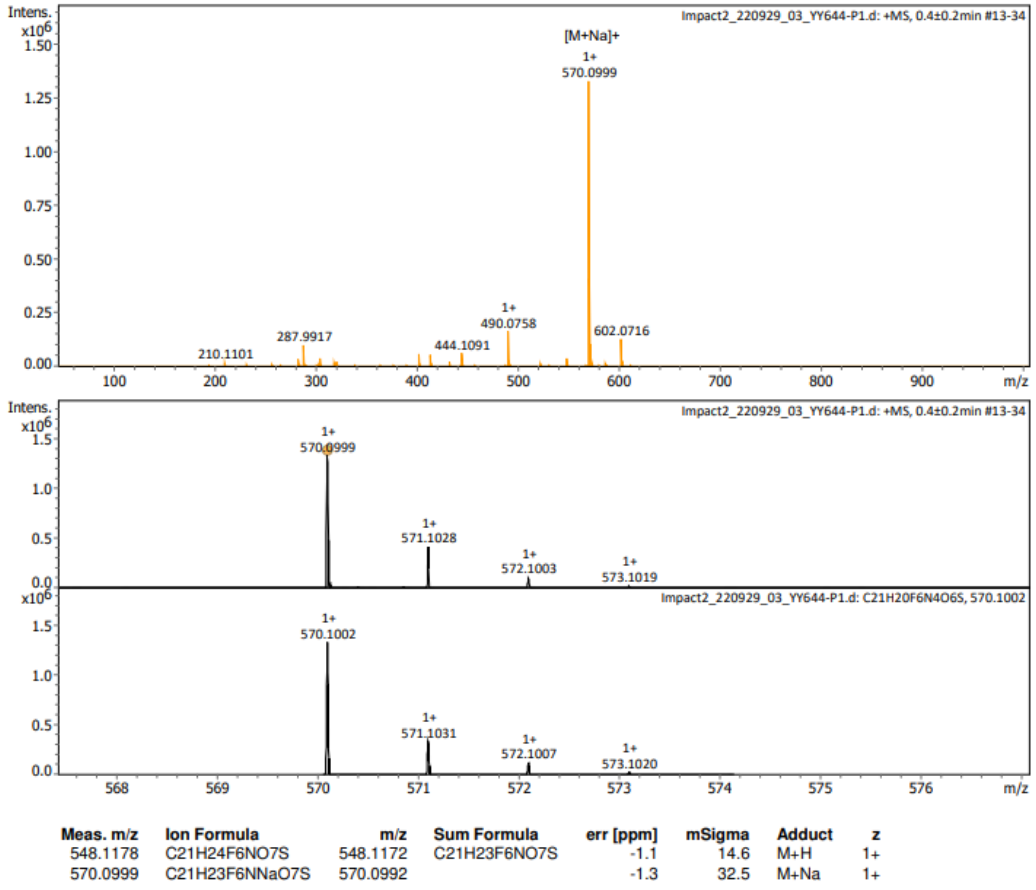
CENTRE COMMUN DE SPECTROMETRIE DE MASSE

Analysis Info

Analysis Name	Impact2_220929_03_YY644-P1.d		
Method	Tune_pos_Standard.m	Acquisition Date	9/29/2022 5:18:17 PM
Comment		Instrument / Ser#	impact II 1825265.10081

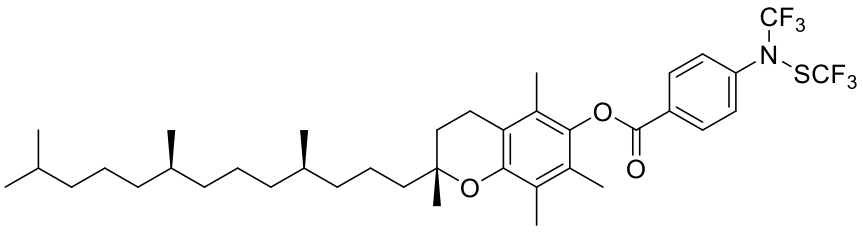
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	1000 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	1500.0 Vpp	Set Divert Valve	Source



Meas. m/z	Ion Formula	m/z	Sum Formula	err [ppm]	mSigma	Adduct	z
548.1178	C21H24F6NO7S	548.1172	C21H23F6NO7S	-1.1	14.6	M+H	1+
570.0999	C21H23F6NNaO7S	570.0992		-1.3	32.5	M+Na	1+

(R)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl 4-((trifluoromethyl)((trifluoromethyl)thio)amino)benzoate (3ai)



The compound **3ai** was obtained as a colorless oil in 83% yield using (R)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl 4-isothiocyanatobenzoate following the general procedure F after column chromatography on silica gel with pentane/ethyl acetate (50/1).

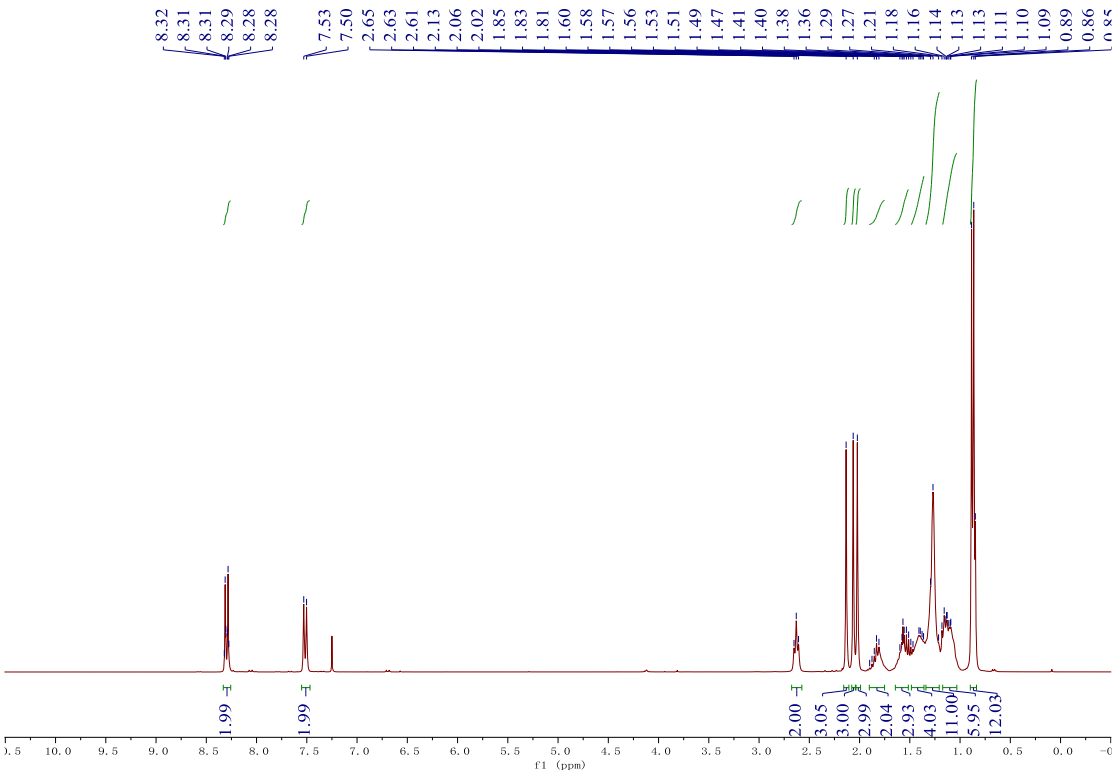
^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.33 – 8.26 (m, 2H), 7.52 (d, *J* = 8.4 Hz, 2H), 2.63 (t, *J* = 6.8

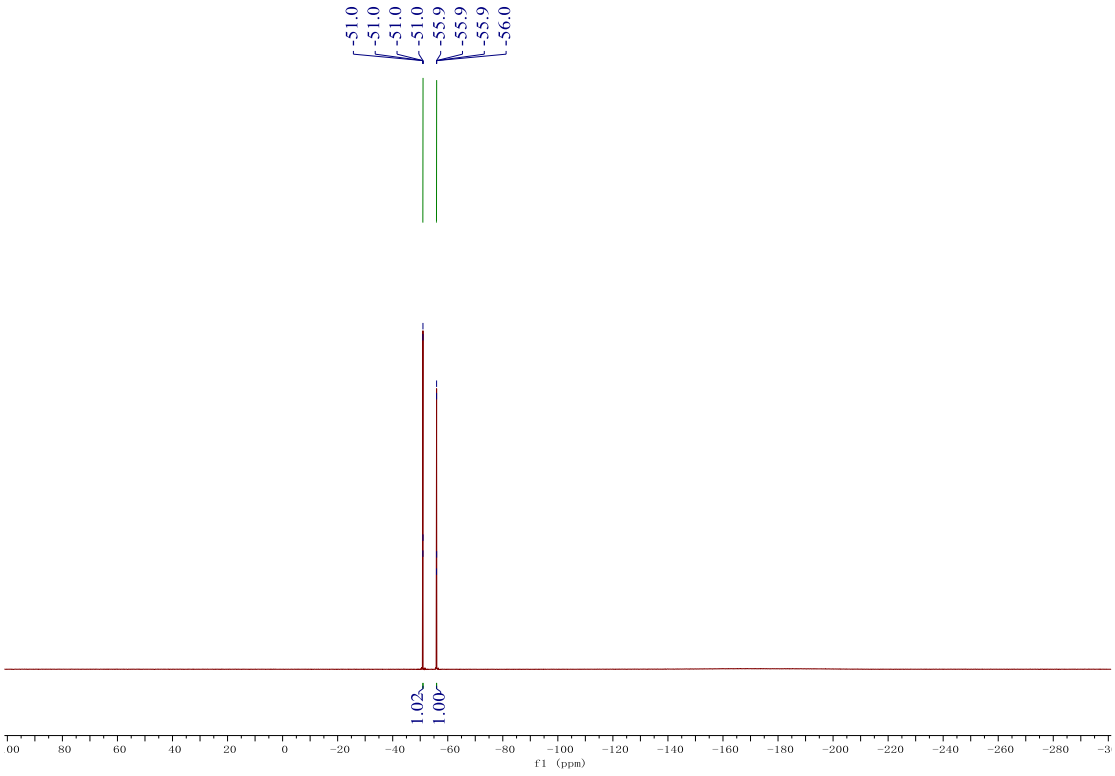
Hz, 2H), 2.13 (s, 3H), 2.06 (s, 3H), 2.02 (s, 3H), 1.90 – 1.87 (m, 2H), 1.60 – 1.51 (m, 3H), 1.48 – 1.36 (m, 4H), 1.30 – 1.21 (m, 11H), 1.17 – 1.03 (m, 6H), 0.90 – 0.84 (m, 12H).

^{19}F NMR (282 MHz, Chloroform-*d*) δ -51.0 (q, *J* = 3.4 Hz), -55.9 (q, *J* = 3.4 Hz).

^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*) δ 164.0, 149.6, 146.1, 140.5, 131.6, 129.3, 128.4 (q, *J* = 317.6 Hz), 126.8, 126.0, 125.0, 123.3, 121.8 (q, *J* = 261.8 Hz), 117.6, 75.2, 39.4, 37.6, 37.5, 37.4, 37.3, 32.8, 32.7, 31.0, 28.0, 24.9, 24.5, 23.7, 22.7, 22.6, 21.1, 20.7, 19.8, 19.7, 19.6, 13.1, 12.2, 11.9.

HRMS (EI) calculated for $C_{38}H_{54}F_6NO_3S$: 718.3723 $[M+H]^+$, Found: 718.3723.

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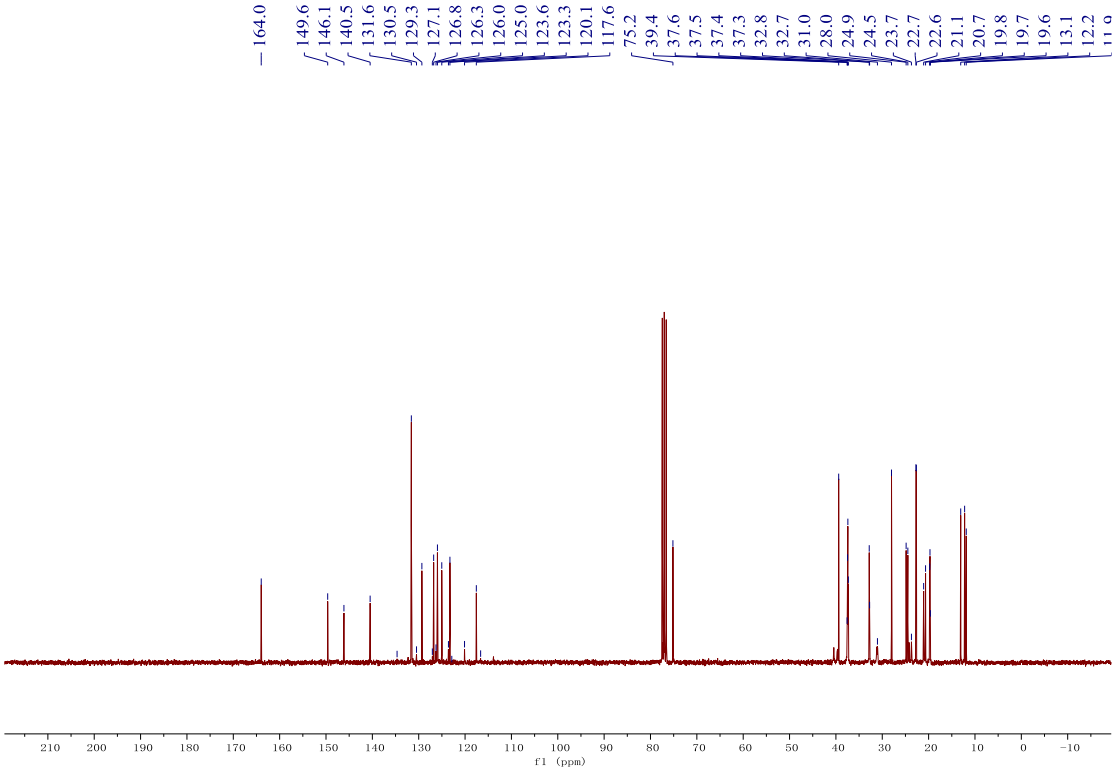
-51.0
-55.9
-55.9
-55.9
-56.0
1.02
1.00
f1 (ppm)


164.0
149.6
146.1
140.5
131.6
130.5
129.3
127.1
126.8
126.3
126.0
125.0
123.6
123.3
120.1
117.6
75.2
39.4
37.6
37.5
37.4
37.3
32.8
32.7
31.0
28.0
24.9
24.5
23.7
22.7
22.6
21.1
20.7
19.8
19.7
19.6
13.1
12.2
f1 (ppm)

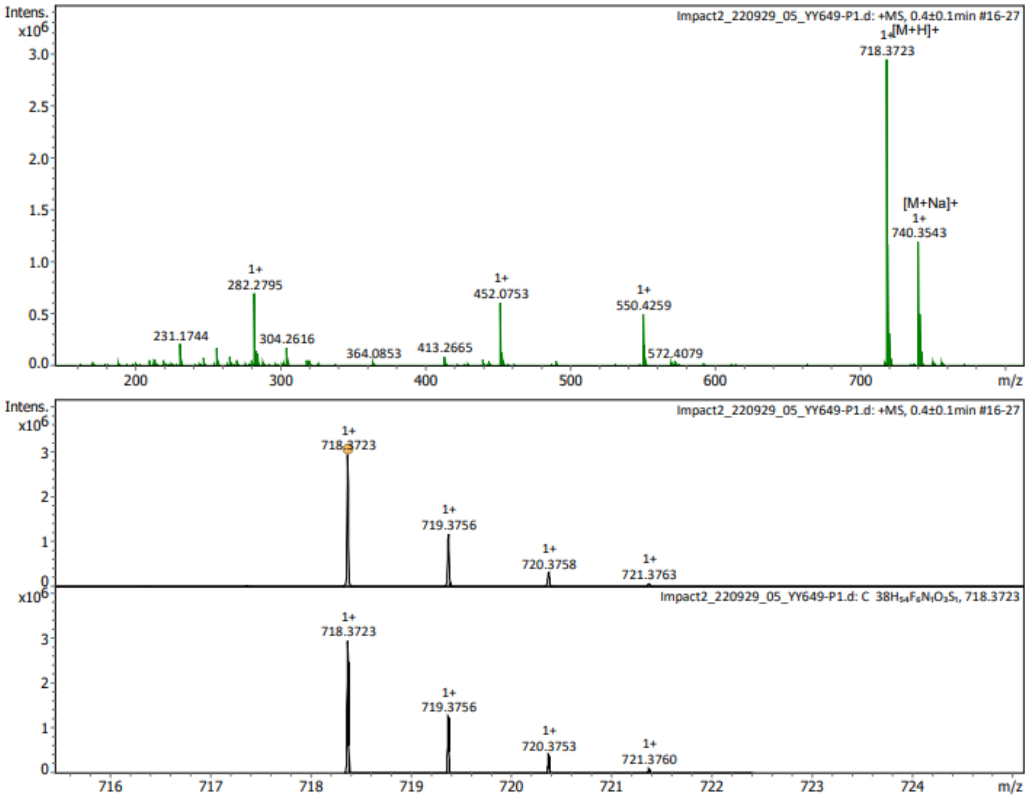
CENTRE COMMUN DE SPECTROMETRIE DE MASSE

Analysis Info

Analysis Name	Impact2_220929_05_YY649-P1.d		
Method	Tune_pos_Standard.m	Acquisition Date	9/29/2022 5:29:18 PM
Comment		Instrument / Ser#	impact II 1825265.10081

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	1500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	1500.0 Vpp	Set Divert Valve	Source



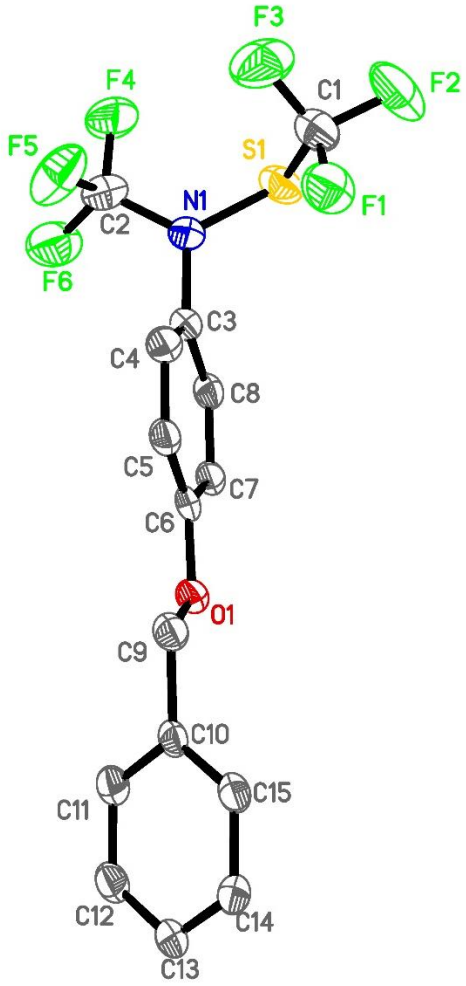
Meas. m/z	Ion Formula	m/z	Sum Formula	err [ppm]	mSigma	Adduct	z
718.3723	C38H54F6NO3S	718.3723	C38H53F6NO3S	0.0	24.1	M+H	1+
740.3543	C38H53F6NNaO3S	740.3543		-0.0	13.9	M+Na	1+

Crystallographic data collection and structure determination:

Single-crystal X-ray diffraction data collection of N(SCF3)(CF3)-amine **3m** was performed at low temperature (193 K) on a Bruker-AXS D8-Venture diffractometer equipped with a Mo Kα sealed tube (λ = 0.71073 Å), a multilayer TRIUMPH X-ray mirror, a Photon III-C14 detector and an Oxford Instruments Cryostream 700+ Series low-temperature device. Phi- and omega- scans were used. The data were indexed and integrated using the SAINT program[11] and an empirical absorption correction with SADABS was applied[12]. The structure was solved by dual space methods (SHELXT)[13] and refined using a least-squares method on F^2[14]. All non-H atoms were refined with anisotropic displacement parameters. Hydrogen atoms were refined isotropically at calculated positions using a riding model with their isotropic displacement parameters constrained to be equal to 1.2 times the equivalent isotropic displacement parameters. The N(SCF3)(CF3)-group is disordered over 2 positions. Several restraints (SAME, SIMU, DELU) were applied to refine this part of the molecule and to avoid the collapse of the structure during the least-squares refinement by the large anisotropic displacement parameters.

CCDC-2211357 (**3m**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via https://www.ccdc.cam.ac.uk/structures/.

Selected data for 3m : $C_{15}H_{11}F_6NOS$, M = 367.31, triclinic, space group $P\ \bar{1}$, a = 6.173(4) Å, b = 7.530(4) Å, c = 17.450(10) Å, α = 99.942(15)°, β = 93.614(16)°, γ = 95.649(16)° V = 792.4(8) Å^3, Z = 2, crystal size 0.25 x 0.06 x 0.02 mm^3, 21071 reflections collected (3248 independent, R*int* = 0.1684), 308 parameters, 365 restraints, $R1$ [I>2σ(I)] = 0.0713, $wR2$ [all data] = 0.2145, largest diff. peak and hole: 0.247 and –0.249 eÅ^{-3}.



Molecular structure of **3m**. Thermal ellipsoids represent 50 % probability. H and disordered atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: N1-C3 1.446(6), N1-C2 1.405(7), N1-S1 1.662(5), S1-C1 1.782(3), C1-F3 1.309(7), C1-F2 1.314(8), C1-F1 1.322(7), C2-F4 1.299(6), C2-F5 1.303(7), C2-F6 1.319(7), C3-N1-C2 117.5(4), C3-N1-S1 120.5(3), C2-N1-S1 121.9(4), N1-S1-C1 102.0(3), C4-C3-N1 121.3(4), C8-C3-N1 119.2(4), F3-C1-F2 106.4(6), F3-C1-F1 106.0(6), F2-C1-F1 106.4(6), F3-C1-S1 114.2(5), F2-C1-S1 109.4(5), F1-C1-S1 113.9(5), F4-C2-F5 106.7(5), F4-C2-F6 108.3(6), F5-C2-F6 104.4(6), F4-C2-N1 113.4(6), F5-C2-N1 112.5(5), F6-C2-N1 111.0(5).

reference

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12. SADABS, Program for data correction, Bruker-AXS.
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14. Sheldrick, G., Crystal structure refinement with SHELXL. *Acta Crystallographica Section C* **2015,** *71* (1), 3-8.