Electronic Supplementary Material (ESI) for Chemical Science.

SuFEx-Enabled, Chemoselective Synthesis of Triflates, Triflamides and Triflimidates

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2. General Information

^{1}H NMR spectra
^{1}H NMR spectra were recorded on a Bruker Avance III HD 400 (at 400 MHz) spectrometer. Samples were dissolved in $CDCl_3$ (residual solvent peak at 7.26 ppm, singlet) or DMSO-d_6 (2.50 ppm, quintet) or methanol-d_4 (3.35 ppm, quintet; 4.78 ppm, singlet). The spectra were measured at room temperature and calibrated using tetramethylsilane as an internal standard in $CDCl_3$ and DMSO-d_6. The δ-values are expressed in ppm. Small amounts of solvent traces (H_2O, EtOAc or Heptane) might be visible in some of the reported spectra. In the case of the presence of more significant amounts of solvent (indicated at the respective spectra), this was considered in the reported isolated yields. For those compounds, further purification was not performed due to volatile properties.

^{13}C NMR spectra
^{13}C NMR spectra were recorded on Bruker Avance III HD 400 (working at 101 MHz) spectrometer. The spectra were measured at room temperature and calibrated using the deuterated solvents as internal standard (for $CDCl_3$ a triplet at 77.00 ppm and for DMSO-d_6 a quintet at 39.52 ppm methanol-d_4:). The δ-values are expressed in ppm.

^{19}F NMR spectra
^{19}F NMR spectra were recorded on Bruker Avance III HD 400 (working at 377 MHz) spectrometer or Bruker Avance III HD 500 (working at 471 MHz) spectrometer. Samples were dissolved in $CDCl_3$ or DMSO-d_6 or methanol-d_4. The spectra were measured at room temperature and calibrated with trichlorofluoromethane as an internal standard. The δ-values are expressed in ppm.

IR spectra
FT-IR spectra of unreported products were measured on a Bruker Alpha-T FT-IR spectrometer with universal sampling module. Data were acquired using Bruker OPUS 7.5 and analyzed using ACD/Spectrus Processor 2016.1.1 software. The band frequencies are given to the nearest 1 cm^{-1} and their intensity is provided (very strong (vs), strong (s), medium (m), weak (w), broad (br)).

Melting points
Melting points of unreported products were measured on an Electrothermal IA 9300 melting point apparatus (serial no. R209000150) at a heating rate of 5.0 °C/min at the first time and 0.5°C/min at the second time.

CHN analysis
CHN (carbon, hydrogen, nitrogen) elemental analyses of unreported products were obtained with the aid of a Thermo Scientific Interscience Flash 2000 Elemental analyser.

HRMS analysis
Spectra were acquired on a quadrupole orthogonal acceleration time-of-flight mass spectrometer (Synapt G2 HDMS, Waters, Milford, MA). Samples were infused at 3uL/min and spectra were obtained in positive (or: negative) ionization mode with a resolution of 15000 (FWHM) using leucine enkephalin as lock mass.

APCI spectra were obtained by infusion on a quadrupole/time-of-flight mass spectrometer (Synapt G2, Waters, Milford, MA).

HPLC analysis
The enantiomeric excess of the product was determined by chiral HPLC using an LC instrument on Chiralpak AD-3 column.

Chromatography
TLC analysis was performed using Sigma-Aldrich 20 x 20 cm precoated glass TLC plates with fluorescent indicator at 254 nm (article number 99571: layer thickness 250 µm, particle size 8.0-12.0 µm, average pore diameter 60 Å). Visualization of the products and their fluorescence features were achieved by UV-radiation at 254 nm.

Manual column chromatography was performed by using MP silica 40-60 micrometer (average pore diameter 60 Å).

Flash column chromatography (MPLC) was performed using a Büchi Sepacore® flash system, consisting of a Büchi C-660 Fraction Collector, a Büchi C-615 Pump Manager, a Knauer WellChrom K-2501 spectrophotometer (working at 254 nm), two Büchi C-605 Pump Modules and a Linseis D120S plotter. Büchi PP cartridges (12/150 mm) were filled with 8 g of Acros ultra-pure silica gel for column chromatography (article number 360050300: particle size 40-60 µm, average pore diameter 60 Å) using a Büchi C-670 Cartridger.

Materials
All chemicals were obtained from commercially available sources and were used without any further purification. Reactions were magnetically stirred. Solvents were evaporated with a rotary evaporator at a temperature of 50 °C.

3. Optimization study

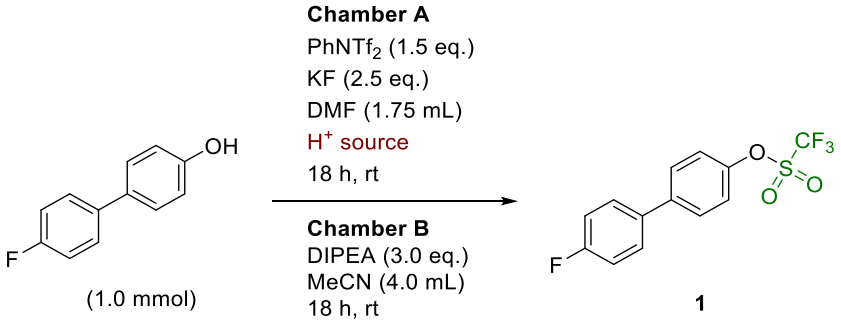
3.1 *N*-Phenyl-bis(trifluoromethanesulfonimide) as Precursor

A. First Solvent Screen in Chamber A

Figure S1. Small two-chamber reactor. Inner volume = 20 mL. Invented by the Skrydstrup group.[1]

Chamber A of a 20 mL small two-chamber reactor (**Figure S1**) was filled with *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 546.8 mg, 1.5 mmol, 1.5 eq.) and potassium fluoride (KF, 99 wt%, 197.2 mg, 2.5 mmol, 2.5 eq.). Next, chamber B was charged with 192.0 mg of 4-fluoro-4'-hydroxybiphenyl (98 wt%, 1.0 mmol, 1.0 eq.). After putting the reactor in a cold water bath, acetonitrile (MeCN, 4.0 mL, 0.25 M), *N*,*N*-diisopropylethylamine (DIPEA, 0.52 mL, 3.0 mmol, 3.0 eq.) and trifluorotoluene (99 wt%, 124 μL, 1.0 mmol) as an internal standard were added to chamber B. Then, dimethylformamide (DMF, 1.75 mL, 0.86 M) was added to chamber A. Finally, the vessel was closed, and the appropriate solvent was added by injection through the septum in chamber A. The reaction was stirred for 18 hours at room temperature. The reaction mixture was analyzed by ^{19}F NMR. (**Table S1.** H+ Source screen in chamber A for the fluorosulfation of 4-fluoro-4'-hydroxybiphenyl with trifluoromethanesulfonyl fluoride gas from PhNTf2.)

Table S1. H^+ Source screen in chamber A for the fluorosulfation of 4-fluoro-4'-hydroxybiphenyl with trifluoromethanesulfonyl fluoride gas from $PhNTf_2$.



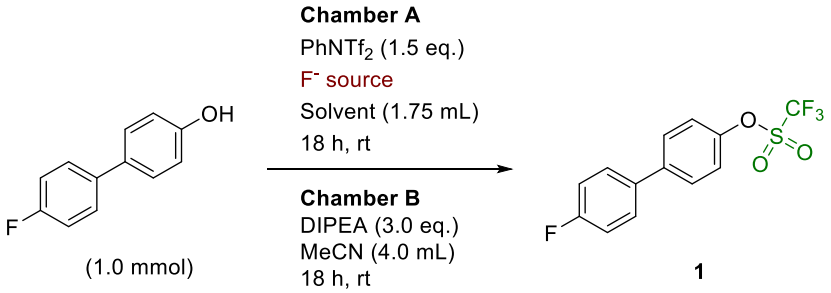
Entry	H^+ source	Volume of H^+ Source (mL)	Conversion (%)	Yield[a] (%)	Final Ratio **1a:2a**
1[b]	TFA	1 mL	49	1.5	97:3
2[b] [c]	TFA	1 mL	11	trace	99.9:0.1
3	0.1 M H_2SO_4	0.75 mL	92	85	8:92
4	0.1 M K_2SO_4	0.75 mL	82	29	38:62
5	0.3 M K_2SO_4	0.75 mL	100	47	0:100
6	0.5 M K_2SO_4	0.75 mL	99	45	3:97
7	H_2O	0.75 mL	75	68	27:73
8	-	-	**95**	**89**	**6:94**

[a] Determined by ^{19}F NMR using trifluorotoluene as an internal standard. $PhNTf_2$ = *N*-phenyltrifluoromethanesulfonimide, KF = potassium fluoride, DMF = dimethylformamide, MeCN = acetonitrile. DIPEA = *N*,*N*-diisopropylethylamine, TFA = trifluoroacetic acid. [b] Chamber A without DMF as solvent. [c] 6.0 eq. KF.

B. F^- Source and Solvent Screen in Chamber A

Chamber A of a 20 mL small two-chamber reactor (**Figure S1**) was filled with *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 546.8 mg, 1.5 mmol, 1.5 eq.) and appropriate F^- source. Next, chamber B was charged with 192.0 mg of 4-fluoro-4'-hydroxybiphenyl (98 wt%, 1.0 mmol, 1.0 eq.). After putting the reactor in a cold water bath, acetonitrile (MeCN, 0.25 M, 4.0 mL), *N*,*N*-diisopropylethylamine (DIPEA, 0.52 mL, 3.0 mmol, 3.0 eq.) and trifluorotoluene (99 wt%, 124 μL, 1.0 mmol) as an internal standard were added to chamber B. Finally, the vessel was closed and 1.75 mL solvent was added by injection through the septum in chamber A. The reaction was stirred for 18 hours at room temperature. The reaction mixture was analyzed through ^{19}F NMR. (**Table S2**)

Table S2. F^- Source and solvent screen in chamber A for the fluorosulfation of 4-fluoro-4'-hydroxybiphenyl with trifluoromethanesulfonyl fluoride gas from $PhNTf_2$.



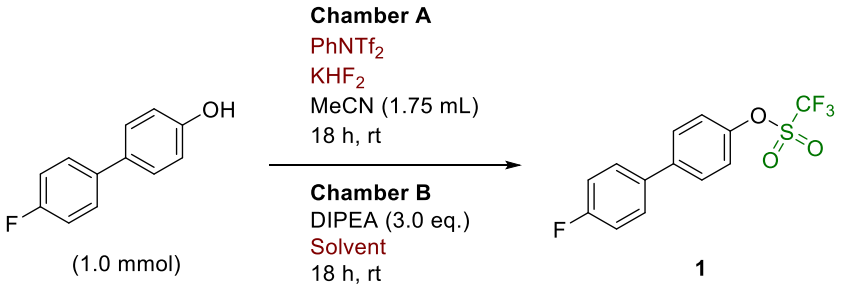
Entry	F^- Source	Amount of F^- Source	Solvent in Chamber A	Conversion (%)	Yield[a] (%)	Final Ratio **1a:2a**
Table S1 Entry 8	KF	2.5 eq.	DMF	95	89	6:94
1	KF	2.5 eq.	Anhydrous DMF	100	91	0:100
2	KF	2.5 eq.	Anhydrous MeCN	99	99	1:99
3	KF (sat.)	0.75 mL	DMF	32	27	72:28
4	KHF_2 (sat.)	0.75 mL	DMF	92	83	8:92
5	KHF_2 (sat.)	1.5 mL	None	89	75	12:88
6	KHF_2	2.5eq.	DMF	100	99	0:100
7	**KHF_2**	**2.5eq.**	**MeCN**	**100**	**>99**	**0:100**

[a] Determined by ^{19}F NMR using trifluorotoluene as an internal standard. $PhNTf_2$ = *N*-phenyltrifluoromethanesulfonimide, KF = potassium fluoride, KHF_2 = potassium bifluoride, DMF = dimethylformamide, MeCN = acetonitrile. DIPEA = *N*,*N*-diisopropylethylamine.

C. Amount of $PhNTf_2$ and KF·HF Optimization in chamber A and Solvent Screen in Chamber B

Chamber A of a 20 mL small two-chamber reactor (**Figure S1**) was filled with the appropriate amount of *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%) and potassium bifluoride (KHF_2, 99+ wt%). Next, chamber B was charged with 192.0 mg of 4-fluoro-4'-hydroxybiphenyl (98 wt%, 1.0 mmol, 1.0 eq.). After putting the reactor in a cold water bath, the appropriate solvent, *N*,*N*-diisopropylethylamine (DIPEA, 0.52 mL, 3.0 mmol, 3.0 eq.) and trifluorotoluene (99 wt%, 124 μL, 1.0 mmol) as an internal standard were added to chamber B. Finally, the vessel was closed, and acetonitrile (MeCN, 1.75 mL) was added by injection through the septum in chamber A. The reaction was stirred for 18 hours at room temperature. The reaction mixture was analyzed by ^{19}F NMR. (**Table S3**)

Table S3. Amount of $PhNTf_2$ and KF·HF optimization in chamber A and solvent screen in Chamber B.



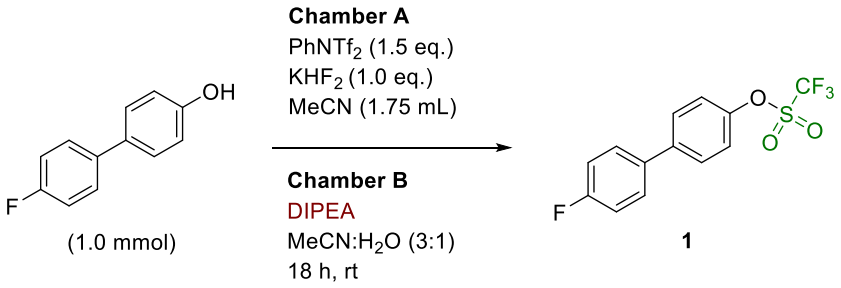
Entry	Amount of $PhNTf_2$ (Eq.)	Amount of KHF_2 (Eq.)	Solvent in Chamber B (mL)	Conversion Rates (%)	Yield[a] (%)	Final Ratio **1a:2a**
Table S2 Entry 7	1.5	2.5	MeCN (4)	100	99	0:100
1	1.5	2.5	MeCN:H_2O = 3:1	100	>99	0:100
2	1.3	2.5	MeCN:H_2O = 3:1	99	89	1:99
3	1.5	2.0	MeCN:H_2O = 3:1	100	>99	0:100
4	1.5	1.5	MeCN:H_2O = 3:1	100	>99	0:100
5	**1.5**	**1.0**	**MeCN:H_2O = 3:1**	**100**	**>99**	**0:100**
6	1.5	0.5	MeCN:H_2O = 3:1	85	85	15:85

[a] Determined by ^{19}F NMR using trifluorotoluene as an internal standard. $PhNTf_2$ = *N*-phenyltrifluoromethanesulfonimide, KHF_2 = potassium bifluoride, MeCN = acetonitrile. DIPEA = *N*,*N*-diisopropylethylamine.

D. Optimization of the Amount of DIPEA in chamber B and Screening of the Reaction Time

Chamber A of a 20 mL small two-chamber reactor (**Figure S1**) was filled with *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 546.8 mg, 1.5 mmol, 1.5 eq.) and potassium bifluoride (KHF_2, 99+ wt%, 78.9 mg, 1.0 mmol, 1.0 eq.). Next, chamber B was charged with 192.0 mg of 4-fluoro-4'-hydroxybiphenyl (98 wt%, 1.0 mmol, 1.0 eq.). After putting the reactor in a cold water bath, the acetonitrile (MeCN) (3.0 mL), H_2O (1.0 mL), appropriate amount of *N*,*N*-diisopropylethylamine (DIPEA) and trifluorotoluene (99 wt%, 124 μL, 1.0 mmol) as an internal standard were added to chamber B. Finally, the vessel was closed, and the acetonitrile (MeCN, 1.75 mL) was added by injection through the septum in chamber A. The reaction was stirred for the appropriate amount of time at room temperature. The reaction mixture was analyzed by ^{19}F NMR (**Table S4**).

Table S4. Optimization of the amount of DIPEA in chamber B and screening of the reaction time.



Entry	Amount of DIPEA (Eq.)	Reaction Time (h)	Conversion (%)	Yield[a] (%)	Final Ratio **1a:2a**
Table S3 Entry 5	3.0	18	100	>99	0:100
1	2.5	18	100	99	0:100
2	2.0	18	100	>99	0:100
3	1.5	18	100	>99	0:100
4	1.0	18	87	84	17:83
5	1.5	1	29	13	84:16
6	1.5	2	91	72	11:89
7	1.5	3	100	91	0.5:99.5
8	**1.5**	**4**	**100**	**>99**	**0:100**
9[b]	1.5	5	100	>99	0:100

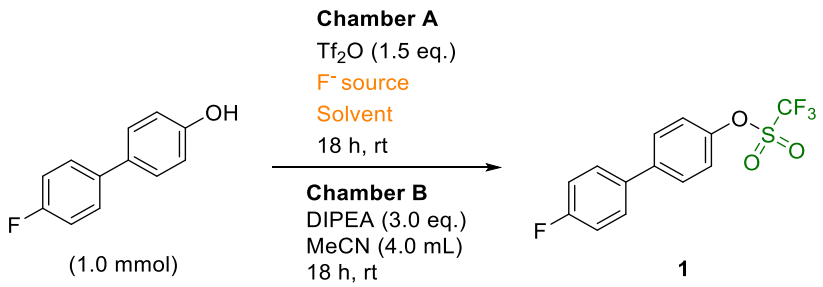
[a] Determined by ^{19}F NMR using trifluorotoluene as an internal standard. $PhNTf_2$ = *N*-phenyltrifluoromethanesulfonimide, KHF_2 = potassium bifluoride, MeCN = acetonitrile. DIPEA = *N*,*N*-diisopropylethylamine. [b] The reactor was not put in a cold water bath, but was directly exposed in the room temperature at the beginning.

3.2. Triflic Anhydride as Precursor

Small optimization of F^- Source and Solvent Screen in Chamber A

Chamber A of a flame-dried small two-chamber reactor (**Figure S1**) was filled with the appropriate F^- source. Next, chamber B was charged with 4-fluoro-4'-hydroxybiphenyl (98 wt%, 0.192 g, 1.0 mmol, 1.0 eq.). After closing the reactor firmly, it was purged with N_2 and put in a cold-water bath. Subsequently, acetonitrile (MeCN, 0.25 M, 4.0 mL) and *N*,*N*-diisopropylethylamine (DIPEA, 0.26 mL, 1.5 mmol, 1.5 eq.) were added to chamber B. Finally, chamber A was charged with trifluoromethanesulfonic anhydride (Tf_2O, 0.25 mL, 1.5 mmol, 1.5 eq.) and the appropriate anhydrous solvent in this particular order by injection through the septum. The reaction was stirred for 16 hours at room temperature. The reaction mixture was analyzed by ^{19}F NMR (**Table S5**).

Table S5. F^- Source and solvent screen in chamber A for the triflylation of 4-fluoro-4'-hydroxybiphenyl with trifluoromethanesulfonyl fluoride gas from Tf_2O.



Entry	F^- source	Amount of F^- Source (mmol)	Solvent in chamber A	Amount of solvent in chamber A (mL)	Conversion (%)	Yield[a] (%)	Final Ratio of **1a:2a**
1	KF	2.5	TFA	1.0	100	70	0:100
2	KF	4.0	TFA	1.0	100	43	0:100
3	KF	6.0	TFA	1.0	>99	42	1:99
4	KF	2.25	H_2O	0.25	98	97	2:98
5	KF	4.0	H_2O	0.25	>99	98	1:99
6	KF	6.0	H_2O	0.25	100	100	0:100
7	KF	6.0	H_2O	0.75	99	73	1:99
8[b]	KF	6.0	H_2O	0.75	66	28	54:46
9[b]	**KHF_2**	**1.0**	**Anhydrous MeCN**	**1.75**	**100**	**100**	**0:100**

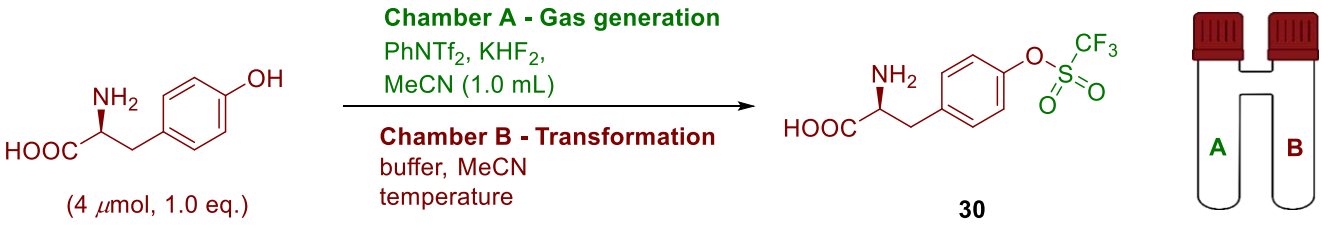
[a] Determined by ^{19}F NMR using trifluorotoluene as an internal standard. Tf_2O= triflic anhydride, KF = potassium fluoride, KHF_2 = potassium bifluoride, MeCN = acetonitrile, DIPEA = *N*,*N*-diisopropylethylamine. [b] The solvent in chamber B is altered to a biphasic solvent mixture of MeCN: H_2O (3.0 mL: 1.0 mL).

3.3 Optimization study of peptide triflation

Chamber A of a 20 mL small two-chamber reactor (**Figure S1**) was filled with *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%) and potassium bifluoride (KHF_2, 99+ wt%) to generate the FSO_2CF_3 gas. Next, chamber B was charged with *L*-tyrosine (4 μmol, 1.0 eq. Then the appropriate buffer was added to chamber B. Finally, the vessel was closed and acetonitrile (MeCN, 1.0 mL) was added by injection through the septum in chamber A. The reaction was stirred for several hours at the appropriate temperature. The cap on chamber B was carefully removed to release the residual pressure. The reaction was stirred for another 5 minutes to ensure that all trifluoromethanesulfonyl fluoride gas was extracted out of the fume hood. (**Table S5**).

After checking 12 experiments to optimize the conditions, we found that under pH = 9.0, the triflation of *L*-tyrosine could go up to 93.4 %AUC in the room temperature (table S6, entry 7 & 8). Besides, the improvement of the gas amount to 50 eq. (table S6, entry 11 & 12), the concentration of starting material in Chamber B (table S6, entry 10 &12), temperature to 37 ℃ (table S6, entry 4, 5 & 6) and longer the reaction time to 24 h, or even to 72 h (table S6, entry 1–6 & 9) cannot make the assay yield improve obviously. Also, changing the pH value to 8.0 and 10.0 could reduce the assay yield (table S6, entry 1, 2 & 3).

Table S6. Optimization study of peptide triflation using *L*-tyrosine as starting material



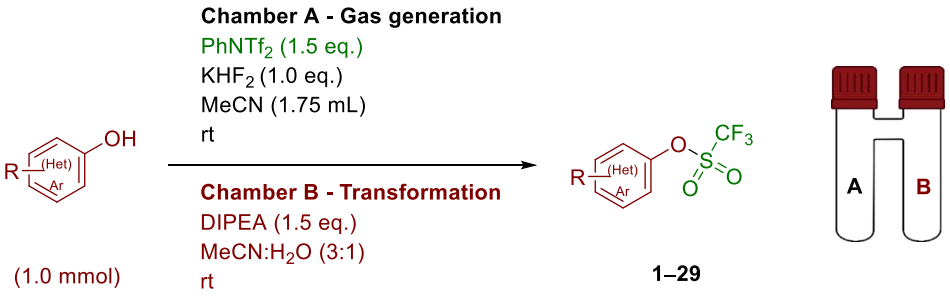
Entry[a]	Gas equivalent in Chamber A[b] (eq.)	pH[c]	Solvent volume in chamber B[d] (mL)	Temperature (℃)	Reaction time (h)	Assay Yield[e] (%AUC)
1	25	8.0	2+2	25	72	82.2
2	25	9.0	2+2	25	72	92.9
3	25	10.0	2+2	25	72	91.5
4	25	8.0	2+2	37	72	86.0
5	25	9.0	2+2	37	72	92.1
6	25	10.0	2+2	37	72	90.7
7	25	9.0	2+2	25	4	93.4
8[f]	25	9.0	2+2	25	4	93.4
9	25	9.0	2+2	25	24	85.0
10	25	9.0	2 [g]	25	4	94.3
11	50	9.0	2+2	25	4	92.8
12	50	9.0	2 [g]	25	4	94.9

[a] How to add 4 μmol *L*-tyrosine in Chamber B: weighed 3.7 mg *L*-Tyrosine (98 wt%, 20 μmol), and then dissolved in 10 mL MeCN; after sonicating, added into chamber B according to the needy of optimization reaction. [b] The equivalent of gas depends on the amount of $PhNTf_2$, and the ratio of $PhNTf_2$ and KHF_2 always equals to 1.5:1.0. [c] pH 8.0 →100 mL 0.025 M $Na_2B_4O_7.10H_2O$ (borax) + 41.0 mL of 0.1 M HCl; pH 9.0 → 100 mL 0.025 M $Na_2B_4O_7.10H_2O$ (borax) + 9.2 mL of 0.1 M HCl; pH 10.0 → 100 mL 0.05 M $Na_2B_4O_7.10H_2O$ (borax) + 41.0 mL of 0.1 M NaOH. [d] The number means the volume of buffer : the volume of MeCN in which the *L*-Tyrosine was dissolved. [e] Determined by LC-MS, "%AUC" → area under curve. KHF_2 = potassium bifluoride, MeCN = acetonitrile. [f] The duplicated reaction of entry 7. [g] weighed 3.7 mg *L*-Tyrosine (98 wt%, 20 μmol), and then dissolved in 5 mL MeCN and 5 mL 9.0 pH buffer; after sonicating, added into chamber B the mixture 2 mL in total.

4. General Procedure

4.1. General Procedures of Synthesize the Triflates

4.1.1. General procedure A (Synthesis aryl triflates from N-phenyltrifluoromethanesulfonimide)



Scheme S1. Synthesis of aryl trifluoromethanesulfates via *ex situ* generated trifluoromethanesulfonyl fluoride gas in a two-chamber reactor.

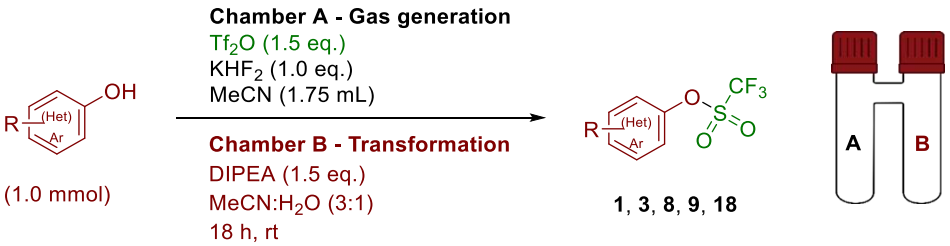
Chamber A of a 20 mL small two-chamber reactor (**Figure S1**) was filled with *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 546.8 mg, 1.5 mmol, 1.5 eq.) and potassium bifluoride (KHF_2, 99+ wt%, 78.9 mg, 1.0 mmol, 1.0 eq.). Next, chamber B was charged with phenol **1** (1.0 mmol, 1.0 eq.). Then the acetonitrile (MeCN, 3.0 mL), H_2O (1.0 mL), trifluorotoluene (99 wt%, 124 μL, 1.0 mmol) as an internal standard and *N*,*N*-diisopropylethylamine (DIPEA, 0.26 mL, 1.5 mmol, 1.5 eq.) were added to chamber B. Finally, the vessel was closed and acetonitrile (MeCN, 1.75 mL) was added by injection through the septum in chamber A (**Scheme S1**). The reaction was monitored by ^{19}F NMR. The cap on chamber B was carefully removed to release the residual pressure. The reaction was stirred for another 5 minutes to ensure that all trifluoromethanesulfonyl fluoride gas was extracted out of the fume hood. The content of chamber B was transferred to a 100 mL separatory funnel. Chamber B was rinsed five times with 5 mL of ethyl acetate (EtOAc); the fractions were collected in the same funnel. The mixture was washed with saturated NH_4Cl (1 x 20 mL). Then the water phase was re-extracted by ethyl acetate (EtOAc) (2 x 10 mL). The combined organic layers were washed with brine (1 x 20 mL), dried over anhydrous Na_2SO_4 and then concentrated *in vacuo* to give the crude product. Further purification is reported in the respective experimental data.

Caution!

1) After reaction, chamber A was quenched with NaOH (1M) to neutralize trifluoroacetic acid and the in situ formed HF. The alkaline solution was discarded in basic waste. Etching of the glassware of Chamber A was seen after multiple experiments.

2) The maximally allowed pressure in the two-chamber vessel is 5 bar. In order not to exceed this pressure in the small 20-mL two-chamber vessel, the amount of generated gas should be calculated based on the rest inner volume of reactor (20 mL total minus the volume of solvent) at room temperature before setting up the experiment.

4.1.2. General procedure B (Synthesis aryl triflates from trifluoromethanesulfonic anhydride)



Scheme S2. Synthesis of aryl trifluoromethanesulfonates via *ex situ* generated trifluoromethanesulfonyl fluoride gas in a two-chamber reactor.

Chamber A of a small flame-dried two-chamber reactor (**Figure S1**) was charged with potassium bifluoride (KHF_2, 99+% wt, 78.9 mg, 1.0 mmol, 1.0 eq.). Next, chamber B was filled with phenol (1.0 mmol, 1.0 eq.). The two-chamber reactor was closed and was purged 3x with Argon. Diisopropylethylamine (DIPEA, 0.26 mL, 1.5 mmol, 1.5 eq.), acetonitrile (CH_3CN, 3.0 mL) and water (H_2O, 1.0 mL) were added to chamber B. Trifluoromethanesulfonic anhydride (Tf_2O, 0.25 mL, 1.5 mmol, 1.5 eq.) was added to chamber A. Finally, 1.75 mL of anhydrous acetonitrile (MeCN, 1.75 mL) was added to chamber A. The reaction was stirred, for 5 min in a cold- water bath and subsequent at room temperature for about 18 hours (**Scheme S1**). The reaction was monitored with TLC and ^{19}F NMR. After completion, the cap on chamber B was carefully removed to release the residual pressure. The reaction was stirred for another 10 minutes to ensure that all trifluoromethanesulfonyl fluoride gas is extracted out of the fume hood. The content of chamber B was transferred to a 250 mL separatory funnel. Chamber B was rinsed five times with 3 mL of ethyl acetate (EtOAc); the fractions were collected in the same funnel. The mixture was washed with saturated NH_4Cl (3 x 50 mL). Then the water phase was re-extracted by EtOAc (2 x 10 mL). The combined organic layers were washed with brine (1 x 50 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give the crude product. Further purification is reported in the respective experimental data.

4.1.3. General procedures C, D and E of Benchmark methods (Parallel Experiments Between Published Methods)

General procedure C: Aryl triflates were prepared using the triflic anhydride

Under argon, phenol (1.0 mmol, 1.0 eq.), anhydrous dichloromethane (2.0 mL) and analytical grade triethylamine (99 wt%, 0.28 mL, 2.0 mmol, 2.0 eq.) were added successively into a 25-mL Schlenk flask containing a magnetic stirring bar. After the solution was chilled to 0 °C in an ice/water bath, triflic anhydride (99 wt%, 0.2 mL, 1.2 mmol, 1.2 eq.) was added dropwise over 2 minutes. The resulting mixture was slowly warmed up to room temperature and kept stirring for 18 hours. At the end of the reaction (monitored by ^{19}F NMR), the mixture was concentrated on a rotary evaporator under reduced pressure and the residue was directly subjected to flash chromatography to afford the desired aryl triflates. This procedure is set up on the reference[2].

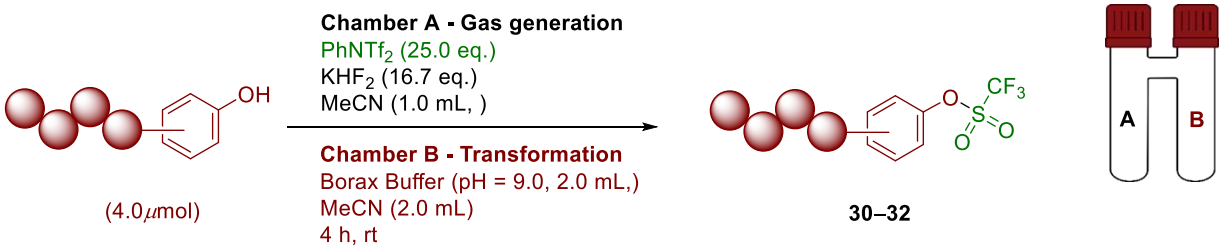
General procedure D: Aryl triflates were prepared using the triflic anhydride under aqueous conditions

Reactions conducted at 0 °C with slow addition of Tf_2O (99 wt%, 0.2 mL, 1.2 mmol, 1.2 eq.) to a toluene (2.1 mL)/30% (w/v) aqueous K_3PO_4 (2.1 mL, 3.0 mmol, 3.0 eq.) biphasic mixture of phenol (1.0 mmol, 1.0 eq.) followed by warming to room temperature for 30 min. At the end of the reaction (monitored by ^{19}F NMR). The content of 25-mL round bottle was transferred to a 100 mL separatory funnel and the bottle was rinsed five times with 5 mL of methyl *tert*-butyl ether (MTBE); the fractions were collected in the same funnel. The mixture was washed with saturated NH_4Cl (1 x 20 mL). Then the water phase was re-extracted by MTBE (2 x 10 mL). The combined organic layers were washed with brine (1 x 20 mL), dried over anhydrous Na_2SO_4 and then concentrated *in vacuo* to give the crude product. Further purification is reported in the respective experimental data. This procedure is according to the reference[3].

General procedure E: Aryl triflates could be synthesized adding the N-phenyltrifluoromethanesulfonimide ($PhNTf_2$) directly

Phenol (1 mmol, 1.0 eq.), *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 546.8 mg, 1.5 mmol, 1.5 eq.), DMAP (99 wt%, 12.3 mg, 0.1 mmol, 0.1 eq.) were added to a flame-dried round bottmed flask. The flask was purged with nitrogen. DCM (2 mL, 0.5 M) and Et_3N (99 wt%, 0.42 mL, 3.0 mmol, 3.0 eq.) were added to the mixture and the reaction mixture was stirred at room temperature for 3 h. At the end of the reaction (monitored by ^{19}F NMR). Volatiles were removed under reduced pressure and concentrated *in vacuo* to afford the crude material, which was purified by flash chromatography to afford the desired aryl triflate. This procedure is based on the reference[4].

4.1.4. General Procedure F of Peptide Substrates Triflates Synthesis



Scheme S3. Synthesis of Peptide Substrates Triflates *via* optimized conditions

Chamber A of a 20 mL small two-chamber reactor (**Figure S1**) was filled with 36.5 mg *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 100 μmol, 25.0 eq.) and 5.3 mg potassium bifluoride (KHF_2, 99+ wt%, 66.7 μmol, 16.7 eq.) to generate the FSO_2CF_3 gas. Next, chamber B was charged with the solution of *L*-tyrosine or peptide (4 μmol, 1.0 eq) dissolved in MeCN: pH 9.0 borax buffer (2 mL:2 mL). Finally, the vessel was closed and acetonitrile (MeCN, 1.0 mL) was added by injection through the septum in chamber A. The reaction was stirred for 4 hours at the room temperature. The cap on chamber B was carefully removed to release the residual pressure. The reaction was stirred for another 5 minutes to ensure that all trifluoromethanesulfonyl fluoride gas was extracted out of the fume hood. Then the solvent in Chamber B was token to be checked the assay yield *via* LC-MS (**Scheme S3**).

4.2. General Procedure G of Analysis of Allowed Solvent-Base Combinations

Stock solutions: in 40 mL of solvent, 2-bromophenol (1.730 g, 10 mmol, 0.25 M) and dibenzyl ether as the internal standard (2.203 g, 10 mmol, 0.25 M) were dissolved.
Solvents selected (6 total): MeCN, DMF, DMSO, toluene, THF, 1,4-dioxane
Bases selected (7 total): DIPEA, TMG, DBU, K_2CO_3, $KHCO_3$, K_3PO_4, NaO*t*Bu
Experiment: 4 mL of stock solution, along with 1.5 mmol of the designated base, was brought in the chamber B of a 20 mL two-chamber reactor. Chamber A was charged with $PhNTf_2$ (547 mg, 1.5 mmol) and KFHF (79 mg, 1.0 mmol). Lastly, MeCN (1.75 mL) was added to chamber A and the vessel was quickly closed while stirring at room temperature.
Sampling: After 4 h and 22 h, an aliquot of ±100 μL was taken from chamber B with a needle (without opening the vessel). This was partitioned between 200 μL of water and 1.5 mL of MTBE in a 2 mL sample vial, which was submitted for GC-MS measurement.
Calibration: The starting material (2-bromophenol), the product (2-bromophenyl triflate) and the internal standard (dibenzyl ether) were dissolved in MTBE in a 1:1:1 molar ratio, and a sample of this solution was submitted to GC-MS. The calibration was carried out in

duplicate, and integration of the AUC gave a response factor (RF) of 0.452 of SM relative to IS, and 0.888 of P relative to IS. These corrections were further used for quantification of remaining starting material (RSM) and product yield. (**Table S7**)

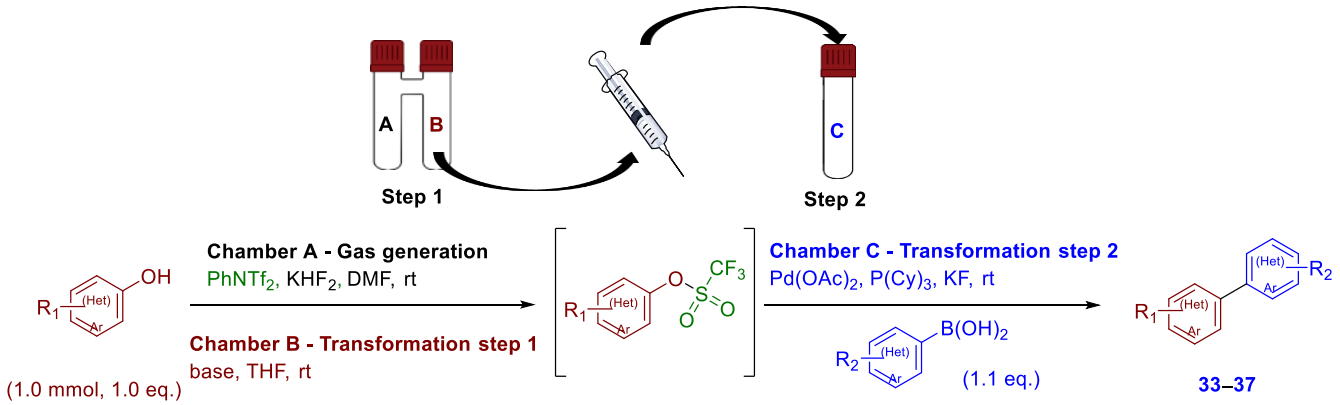
$$RSM = \frac{AUC_{SM}}{AUC_{IS} \times RF_{SM}} \qquad yield_P = \frac{AUC_P}{AUC_{IS} \times RF_P}$$

Table S7. Analysis of Allowed Solvent-Base Combinations

		DIPEA		TMG		DBU		K_2CO_3		$KHCO_3$		K_3PO_4		NaO*t*Bu	
		SM	P	SM	P	SM	P	SM	P	SM	P	SM	P	SM	P
MeCN	**4h**	0.00	0.82	0.06	0.73	0.05	0.81	0.00	0.97	0.00	0.98	0.00	1.04	0.00	0.98
	22h	n.d.	n.d.	0.14	0.67	0.05	0.83	n.d.	n.d.	0.00	0.98	0.27	0.59	0.00	1.01
DMF	**4h**	0.00	0.87	0.06	0.72	0.02	0.89	0.00	0.98	0.00	0.99	0.00	1.02	0.00	0.95
	22h	n.d.	n.d.	0.17	0.58	0.04	0.78	n.d.	n.d.	0.03	0.90	0.03	0.85	n.d.	n.d.
DMSO	**4h**	0.01	0.77	0.18	0.53	0.05	0.77	0.00	0.90	0.00	0.92	0.14	0.64	0.32	0.30
	22h	n.d.	n.d.	0.28	0.46	0.04	0.80	n.d.	n.d.	0.09	0.70	0.12	0.69	0.30	0.45
toluene	**4h**	0.18	0.53	0.00	0.92	0.00	0.90	0.22	0.52	0.61	0.02	0.11	0.68	0.30	0.34
	22h	0.00	0.92	n.d.	n.d.	0.03	0.87	n.d.	n.d.	0.20	0.51	0.01	0.88	0.01	0.89
THF	**4h**	0.20	0.55	0.00	0.92	0.00	0.91	0.03	0.94	0.46	0.16	0.05	0.92	0.21	0.56
	22h	0.00	0.87	0.11	0.70	0.02	0.87	n.d.	n.d.	0.07	0.83	0.03	0.85	0.22	0.61
dioxane	**4h**	n.d.	n.d.	0.03	0.78	0.00	0.86	0.23	0.48	0.53	0.05	0.21	0.58	0.29	0.40
	22h	0.00	0.83	0.13	0.73	0.03	0.95	n.d.	n.d.	0.17	0.65	0.48	0.30	0.33	0.45

(n.d. = not determined)

4.3. General Procedure H of 'One Pot Two Steps' Suzuki Cross Coupling *via* Aryl Trifluoromethanesulfonate



Scheme S4. General procedures of 'one pot two steps' Suzuki cross coupling *via* aryl trifluoromethanesulfonates.

Step 1:
Chamber A of a 20 mL small two-chamber reactor (**Figure S1**) was filled with *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 546.8 mg, 1.5 mmol, 1.5 eq.) and potassium bifluoride (KHF_2, 99+ wt%, 78.9 mg, 1.0 mmol, 1.0 eq.). Next, chamber B was charged with phenol **1** (1.0 mmol, 1.0 eq.). Then 207.4 mg potassium carbonate (K_2CO_3, 99.9 wt%, 1.5 mmol, 1.5 eq.) and anhydrous tetrahydrofuran (THF, 3.0 mL, 0.33 M) were added into chamber B. Finally, the vessel was closed and anhydrous dimethylformamide (DMF, 1.75 mL, 0.86 M) was added by injection through the septum in chamber A and instant gas formation was observed. The reaction was monitored by TLC. The cap on chamber B, which kept closed until the step 2 finished, was carefully removed to release the residual pressure. The reaction was stirred for another 5 minutes to ensure that all trifluoromethanesulfonyl fluoride gas was extracted out of the fume hood.

Step 2:

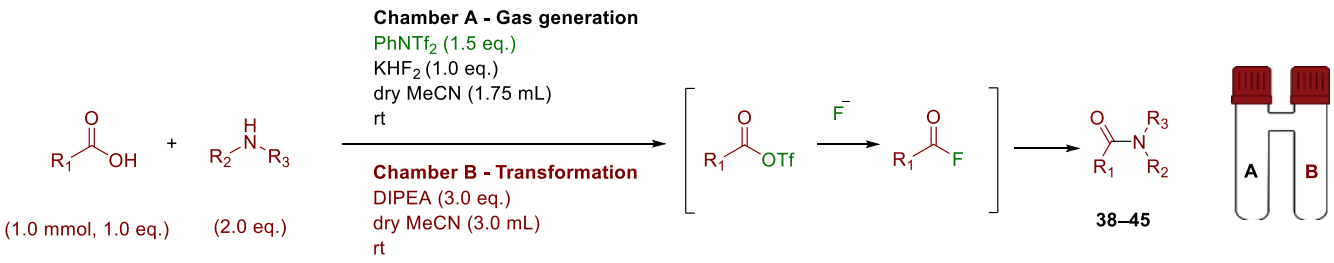
According to the literature[5], step 2 was followed. A 10 mL single chamber tube C (**Error! Reference source not found.**) was charged w ith boronic acid **3** (1.1 mmol, 1.1 eq.), palladium(II) acetate ($Pd(OAc)_2$, 98+ wt%, 2.3 mg, 0.01 mmol, 0.01 eq.), tricyclohexylphosphine (PCy_3, 97 wt%, 3.5 mg, 0.012 mmol, 0.012 eq.) and potassium fluoride (KF, 99.9 wt%, 203.5 mg, 3.5 mmol, 3.5 eq.). Then the vessel was closed. After changing the air in tube C into nitrogen using Schlenk system three times, the content of chamber B was transferred into chamber of tube C using a 3 mL injector through the septum in tube C at the room temperature. The reaction was monitored by TLC. The mixture in tube C was transferred to a 100 mL separatory funnel. Tube C was rinsed five times with 5 mL of methyl *tert*-butyl ether (MTBE); the fractions were collected in the same funnel. The mixture was washed with 1M HCl (20 mL). Then the combined water phase was re-extracted by MTBE (2 x 10 mL). The combined organic layers were washed with brine (1 x 20 mL), dried over anhydrous Na_2SO_4 and then concentrated *in vacuo* to give the crude product. Further purification and the amount of some reagents mentioned above is reported in the respective experimental data.

Caution!

1) Choose 0.90 x70 mm BL/LB needle to transfer the mixture from Chamber B into tube C; otherwise, the base has chance to block the needle.

2) When the mixture in Chamber B was suck out using the injector, keep stirring the magneton in case the base in Chamber B would sink in the bottom, which would cause the transfer procedure hardly.

4.4. General Procedure I of 'One Pot One Step' Amide Synthesis via Acyl Fluoride Intermediate



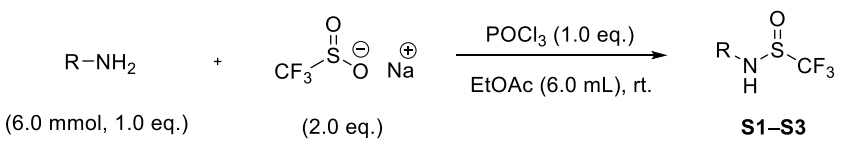
Scheme S5. General procedures of 'one pot one step' amide synthesis *via* acyl fluoride intermediates

Chamber A of a 20 mL oven-dried two-chamber reactor (**Figure S1**) was filled with *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 546.8 mg, 1.5 mmol, 1.5 eq.) and potassium bifluoride (KHF_2, 99+ wt%, 78.9 mg, 1.0 mmol, 1.0 eq.). Next, chamber B was charged with carboxylic acid 5 (1.0 mmol, 1.0 eq.) and amine **6** (2.0 mmol, 2.0 eq.). Then the anhydrous acetonitrile (anhydrous MeCN, 3.0 mL) and *N*,*N*-diisopropylethylamine (DIPEA, 0.52 mL, 3.0 mmol, 3.0 eq.) were added to chamber B. Finally, the vessel was closed and anhydrous acetonitrile (anhydrous MeCN, 1.75 mL, 0.86 M) was added by injection through the septum in chamber A (**Scheme S5**). The reaction was monitored by TLC. The cap on chamber B was carefully removed to release the residual pressure. The reaction was stirred for another 5 minutes to ensure that all trifluoromethanesulfonyl fluoride gas was extracted out of the fume hood. The content of chamber B was transferred to a 100 mL separatory funnel. Chamber B was rinsed five times with 5 mL of ethyl acetate (EtOAc); the fractions were collected in the same funnel. The mixture was washed sequentially with $NaHCO_3$ (sat.) (1 x 20 mL), 1.0 M HCl (1 x 20 mL) and brine (1 x 20 mL). The organic layer was dried over anhydrous Na_2SO_4 and then concentrated *in vacuo* to give the crude product. Further purification is reported in the respective experimental data.

This procedure is modified from the reference[6].

4.5. General Procedure J of Triflimidates Synthesis

4.5.1. General Procedure J1 of the Trifluoromethanesulfinamides Synthesis (First Step of Synthesize the Triflimidates)



Scheme S6. General Procedure J1 of the Trifluoromethanesulfinamides Synthesis

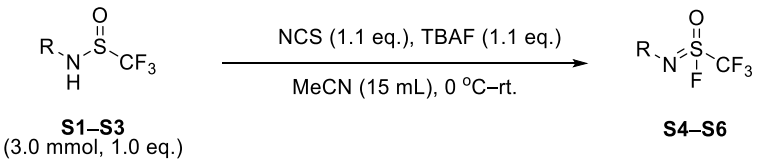
All of the trifluoromethanesulfinamides have been prepared by the following procedure. To a solution of 1.971 g (12 mmol) of sodium trifluoromethanesulfinate (95 wt%, 1.971 g, 12 mmol, 2.0 eq.) in 12 mL of ethyl acetate was added at room temperature 0.555 mL of phosphoryl chloride (99 wt%, 6.0 mmol, 1.0 eq.). The resulting mixture was stirred for 5 mins, then 6 mmol of amine (1.0 eq.) was added dropwise and the reaction mixture was stirred for an additional 30 mins at room temperature. The reaction mixture was then washed with brine (20 mL) and extracted with ethyl acetate (20 mL). The combined ethyl acetate fractions were dried over Na_2SO_4 and

concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford the desired product (**Scheme S6**).

This procedure is modified from the reference[7].

Caution! The trifluoromethanesulfinamides are not stable under Air. Need to seal trifluoromethanesulfinamides under N_2 flush and then put it in the fridge (< 4 °C) for longer storage.

4.5.2. General Procedure J2 of the Sulfonimidoyl Fluoride Synthesis (Sectond Step of Synthesize the Triflimidates)



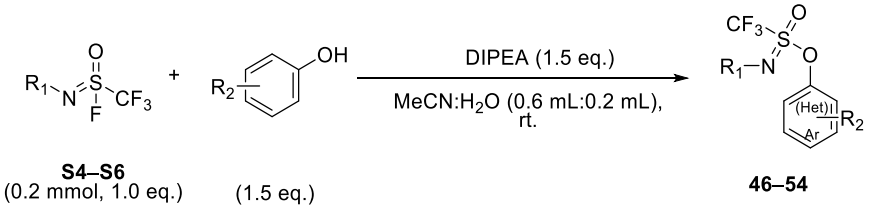
Scheme S7. General Procedure J2 of the Trifluoromethylsulfonimid-amides Synthesis

To a stirred solution of sulfinamide (3.0 mmol) and NCS (98 wt%, 450 mg, 3.3 mmol, 1.1 eq.) in MeCN (15 mL) was added TBAF (1 M in THF, 3.3 mL, 3.3 mmol, 1.1 eq.) in a round-bottomed flask at 0 °C. The reaction mixture was allowed to be warmed to room temperature over 30 mins. Then the reaction mixture was concentrated to dryness in vacuo. Further purification is reported in the respective experimental data (**Scheme S7**).

This procedure is modified from the reference[8].

Caution! The Sulfonimidoyl Fluoride are not stable under room temperature. Need to put it in the fridge (<4°C) for longer storage.

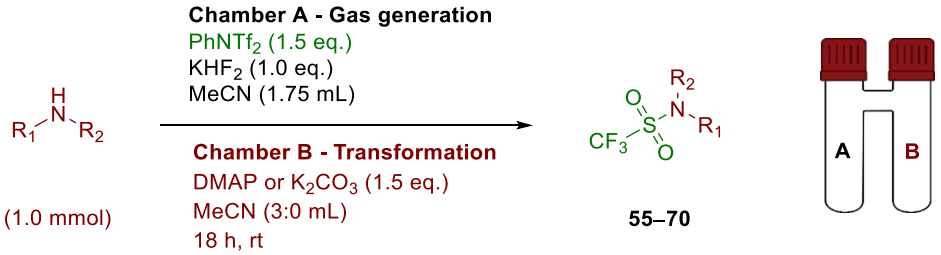
4.5.3. General Procedure J3 of the Triflimidates Synthesis



Scheme S8. General Procedure J2 of the Trifluoromethylsulfonimid-amides Synthesis

A 10 mL small glass tube was filled with sulfonimidoyl fluoride (0.2 mmol, 1.0 eq.) and phenol (0.3 mmol, 1.5 eq.). Then the acetonitrile (MeCN, 0.6 mL), H_2O (0.2 mL), trifluorotoluene (99 wt%, 25 μL, 1.0 mmol) as an internal standard and *N*,*N*-diisopropylethylamine (DIPEA, 99 wt%, 53 μL, 0.3 mmol, 1.5 eq.) as base were followed. Finally, the vessel was closed, and the reaction was monitored by ^{19}F NMR. The content of glass tube was transferred to a baker with anhydrous Na_2SO_4 to dried over directly without extraction to give the crude product. Further purification is reported in the respective experimental data (**Scheme S8**).

4.6. General Procedure K of Triflamides Synthesis

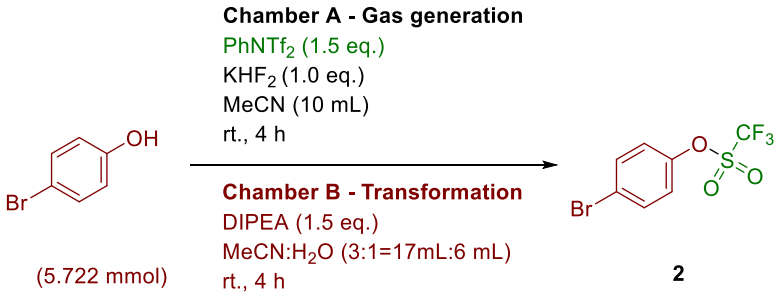


Scheme S9. Synthesis of triflamides via *ex situ* generated trifluoromethanesulfonyl fluoride gas in a two-chamber reactor.

Chamber A of a small two-chamber reactor (**Figure S1**) was charged with *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 546.8 mg, 1.5 mmol, 1.5 eq.) and potassium bifluoride (KHF_2, 99+% wt, 78.9 mg, 1.0 mmol, 1.0 eq.). Next, chamber B was filled with amine derivative (1.0 mmol, 1.0 eq.) and 4-dimethylaminopyridine (DMAP, 99+% wt, 185 mg, 1.5 mmol, 1.5 eq.). The two-chamber reactor was closed, and anhydrous acetonitrile (MeCN, 3.0 mL) was added to chamber B. Finally, 1.75 mL of dry acetonitrile (MeCN, 1.75 mL) was added to chamber A. The reaction was stirred for 18 hours (**Scheme S1)**. The reaction was monitored with TLC and ^{19}F NMR. After completion, the cap on chamber B was carefully removed to release the residual pressure. The reaction was stirred for another

10 minutes to ensure that all trifluoromethanesulfonyl fluoride gas is extracted out of the fume hood. The content of chamber B was transferred to a 250 mL separatory funnel. Chamber B was rinsed five times with 3 mL of ethyl acetate (EtOAc); the fractions were collected in the same funnel. The mixture was extracted with HCl 1M (3 x 25 mL). The combined organic fractions were washed with brine (2 x 50 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give the crude product. Further purification is reported in the respective experimental data.

4.7. Procedure L of Triflate (4-Bromophenyl Trifluoromethanesulfonate) Gram-scale Synthesis



Scheme S10. Gram-scale sythesis of aryl trifluoromethanesulfates via *ex situ* generated trifluoromethanesulfonyl fluoride gas in a large two chamber reactor.

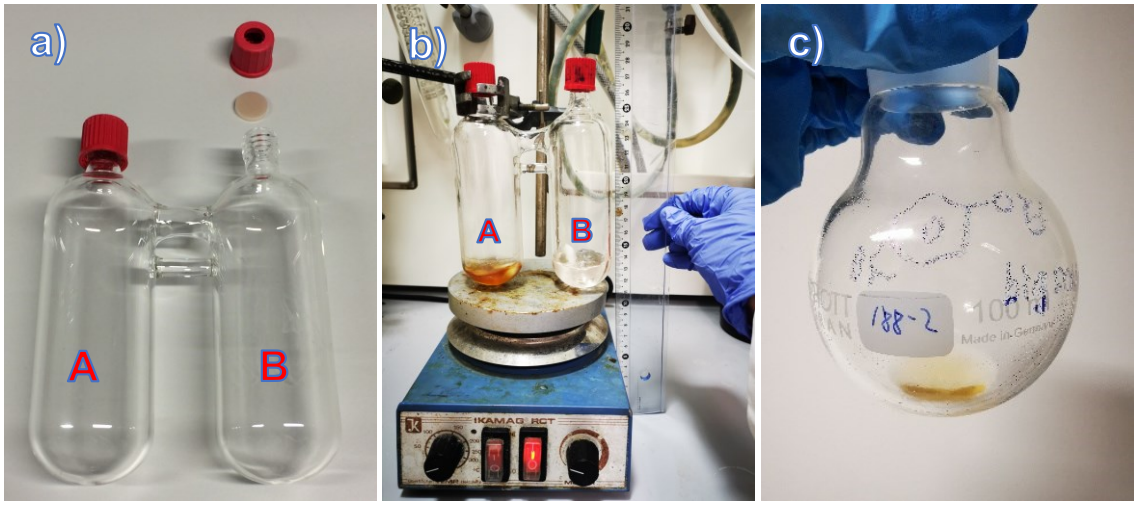


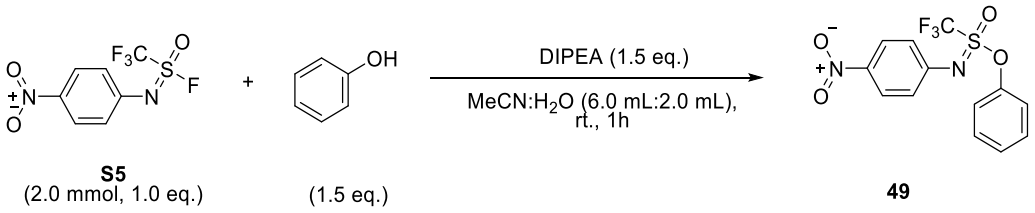
Figure S2. a) Large two-chamber reactor. (Inner volume = 400 mL. Invented by the Skrydstrup group.); b) gram-scale reaction photo; c) the crude product after extraction.

Chamber A (left chamber) of a 400 mL large two-chamber reactor (**Figure S1 S2, a)**) was filled with *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 3.129 g, 8.583 mmol, 1.5 eq.) and potassium bifluoride (KHF_2, 99+ wt%, 0.451 g, 5.722 mmol, 1.0 eq.). Next, chamber B was charged with 1.0 g 4-bromophenol (5.722 mmol, 1.0 eq.). Then the acetonitrile (MeCN, 17.0 mL), H_2O (5.7 mL), trifluorotoluene (99 wt%, 0.071 mL, 0.1 mmol) as an internal standard and *N*,*N*-diisopropylethylamine (DIPEA, 1.5 mL, 8.583 mmol, 1.5 eq.) were added to chamber B. Finally, the vessel was closed, and acetonitrile (MeCN, 10.0 mL) was added by injection through the septum in chamber A (**Scheme S10**). The reaction was monitored by ^{19}F NMR. The cap on chamber B was carefully removed to release the residual pressure. The reaction was stirred for another 10 minutes to ensure that all trifluoromethanesulfonyl fluoride gas was extracted out of the fume hood. The content of chamber B was transferred to a 250 mL separatory funnel. Chamber B was rinsed five times with 30 mL of ethyl acetate (EtOAc); the fractions were collected in the same funnel. The mixture was washed with saturated NH_4Cl (1 x 50 mL), water (1 x 50 mL) and then brine (1 x 50 mL), dried over anhydrous Na_2SO_4 and then concentrated *in vacuo* to give the crude product.

Caution!

For the large two-chamber vessel, the amount of generated gas was limited to 50 mmol at room temperature. This was calculated based on an inner volume of 300 mL (400 mL total minus 100 mL solvent). Pressure measurements revealed that the internal pressure never exceeded 2.8 bar when the general procedure was followed (vide infra).

4.8. Procedure M of Triflimidate (Phenyl Trifluoro-*N*-(4-nitrophenyl)methanesulfonimidate) Large-scale Synthesis



S5
(2.0 mmol, 1.0 eq.)

(1.5 eq.)

49

Scheme S11. Procedure M of the Triflimidates (Phenyl Trifluoro-*N*-(4-nitrophenyl)methanesulfonimidate) Large-scale Synthesis

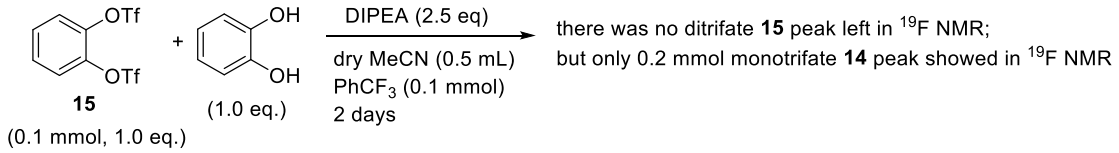
A 25 mL round-bottom flask was filled with 544.9 mg sulfonimidoyl fluoride S5 (2.0 mmol, 1.0 eq.) and phenol (99.0 wt%, 285.2 mg, 3.0 mmol, 1.5 eq.). Then the acetonitrile (MeCN, 6.0 mL), H_2O (2.0 mL), trifluorotoluene (99 wt%, 248 μL, 1.0 mmol) as an internal standard and *N*,*N*-diisopropylethylamine (DIPEA, 99 wt%, 0.53 mL, 3.0 mmol, 1.5 eq.) as base were followed. Finally, the flask was closed, and the reaction was monitored by ^{19}F NMR. After 1h, the flask was rinsed three times with 20 mL of dichloromethane (DCM); the fractions were collected in the same funnel. The mixture was washed with water (1 x 20 mL) and brine (1 x 20 mL), dried over anhydrous Na_2SO_4 and then concentrated *in vacuo* to give the crude product.

5. Additional experiments with bis-nucleophies

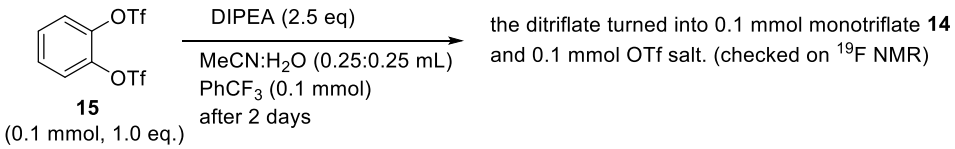
5.1. Stability test of catechol ditriflate (compound 15, cas number: 17763-91-6)

Knowing the ^{19}F NMR chemical shift of catechol ditriflate **15** is -73.6269 ppm; after long time (3 months) storage under N_2 atmosphere and room temperature, the **15** was still pure and the ^{19}F NMR showed the peak was -73.6229 ppm.

1)



2)



Conclusion: *the catechol ditriflate could be stable in the N_2 atmosphere and room temperature for a long time; but is capable of transfering the [SO_2CF_3] group to other nucleophiles such as water or other phenols.*

5.2. Stoichiometry test of 1-(4-hydroxyphenyl)-piperazine triflation

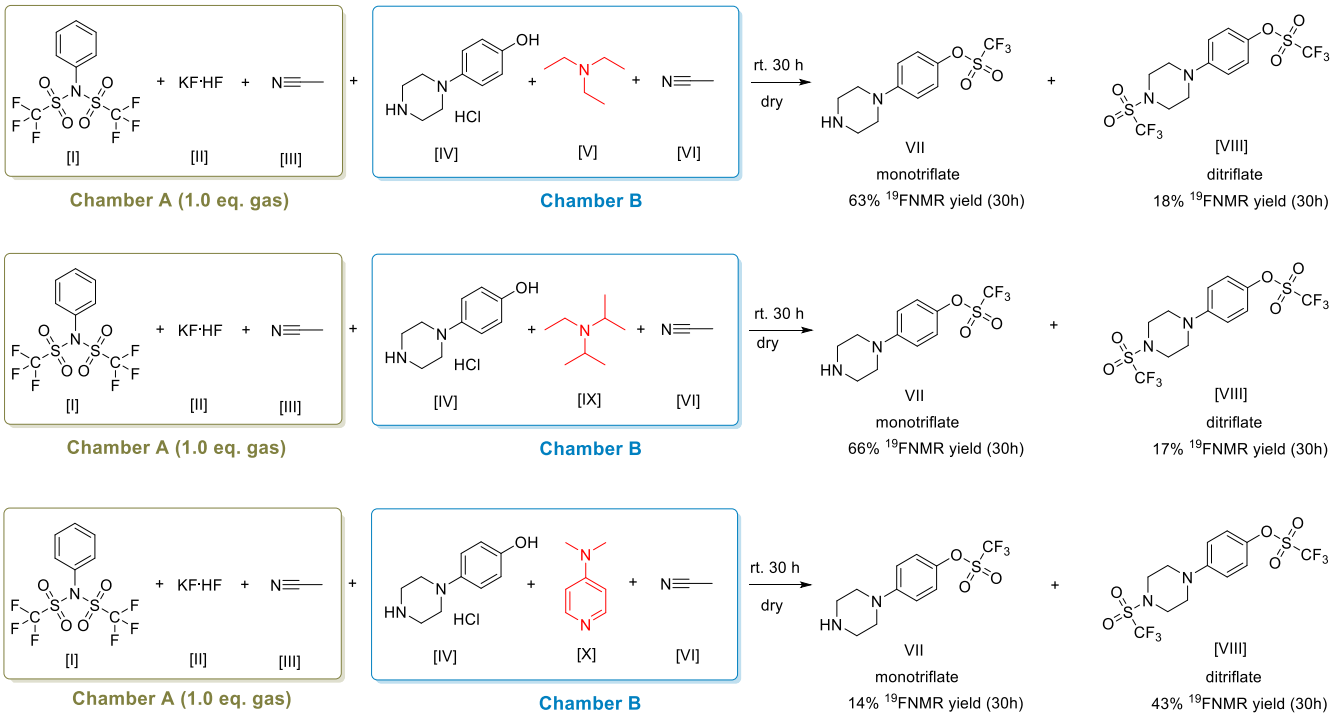
5.2.1. 2.5 Equivalent of CF_3SO_2F Gas Condition to Confirm about the Chemoselectivity:

Chamber A of a 20 mL small two-chamber reactor (**Figure S1**) was filled with *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 911.3 mg, 2.5 mmol, 2.5 eq.) and potassium bifluoride (KHF_2, 99+ wt%, 131.7 mg, 1.67 mmol, 1.67 eq.). Next, chamber B was charged with 221.3 mg of 1-(4-hydroxyphenyl)-piperazine (97 wt%, 1.0 mmol, 1.0 eq.). Then the acetonitrile (MeCN, 3.0 mL), H_2O (1.0 mL), trifluorotoluene (99 wt%, 124 µL, 1.0 mmol) as an internal standard and triethylamine (TEA, 0.35 mL, 2.5 mmol, 2.5 eq.) were added to chamber B. Finally, the vessel was closed and acetonitrile (MeCN, 1.75 mL) was added by injection through the septum in chamber A (**Scheme S1**). The reaction was monitored by ^{19}F NMR.

After 48 hours, the ^{19}F NMR showed the yield of monotriflation product was >99%. Most importantly, there was no N-SO_2CF_3 peak found in the ^{19}F NMR. The cap on chamber B was carefully removed to release the residual pressure. The reaction was stirred for another 5 minutes to ensure that all trifluoromethanesulfonyl fluoride gas was extracted out of the fume hood. The content of chamber B was transferred to a 100 mL separatory funnel. Chamber B was rinsed five times with 5 mL of methyl tert-butyl ether (MTBE); the fractions were collected in the same funnel. The mixture was washed with saturated NH_4Cl (1 x 20 mL). Then the water phase was re-extracted by MTBE (2 x 10 mL). The combined organic layers were washed with brine (1 x 20 mL), dried over anhydrous Na_2SO_4 and then concentrated in vacuo to give the crude product. The extraction yield is 71%.

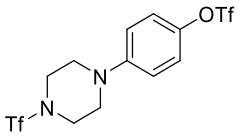
Conclusion: *when there was water in the system, even we used higher amount of CF_3SO_2F gas (2.5 eq.), the N-nucleophile would not undergo triflation.*

5.2.2. 1.0 Equivalent of CF_3SO_2F Gas condition to test the reactivity difference of phenols and amine groups:



Conclusion: *Comparing the reactivity difference of phenols and amine groups, the results showed whatever the base we used, under only 1.0 equivalent of FSO_3CF_3 and anhydrous conditions, the phenols always behaved more reactively than the amine groups after 30 hours.*

5.3. Hydrolytic stability test of 1-(4-hydroxyphenyl)-piperazine ditriflate (compound 60)



(0.1 mmol, 1.0 eq.)

-73.1783, -75.5426 ppm (MeOD, ^{19}F NMR)

DIPEA (2.5 eq)

dry MeCN (0.5 mL)

H_2O (0.15 mL)

$PhCF_3$ (0.1 mmol)

48 h

in MeOD ^{19}F NMR:

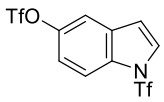
-73.1382 (1.15), -75.5142 (1.16)

(integrate area of $PhCF_3$ is 1)

no hydrolysis

Conclusion: *after 48h, the 1-(4-hydroxyphenyl)-piperazine ditriflate was still not hydrolyzed under the same condition of synthesizing 1-(4-hydroxyphenyl)-piperazine monotriflate; which means, there was no possibility that we got ditrifate first and then in situ it was hydrolyzed to monotriflate.*

5.4. Hydrolytic stability test of indole ditriflate (compound 70)



(0.1 mmol, 1.0 eq.)

(-73.0219, -75.5304 ppm MeOD ^{19}F NMR)

DIPEA (2.5 eq)

dry MeCN (0.5 mL)

H_2O (0.15 mL)

$PhCF_3$ (0.1 mmol)

48 h

-72.9847(1.13), -75.5051(1.15)

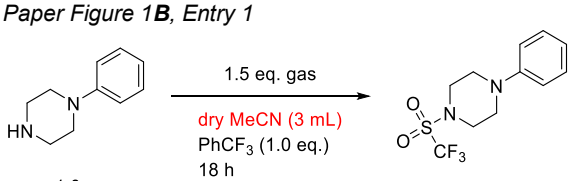
-73.1642(0.10, monotrifate), -78.4071(0.12 OTf salt)

(integrate area of $PhCF_3$ is 1.0)

Conclusion: *Seems around 9% indole ditrifate hydrolyzed into monotriflate after 48 h. which means, when we synthesized the monotriflate, it is unlikely that synthesizing the ditriflate first and then in situ totally hydrolysized into monotrifate in 18 h.*

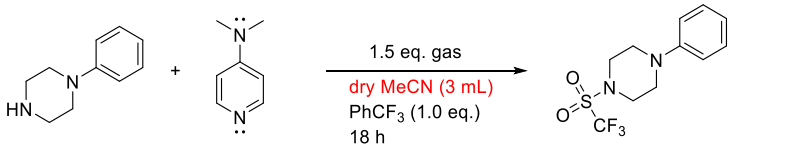
6. Experimental studies of Piperidine to complement the *in silico* findings

*Paper Figure 1**B**, Entry 1*



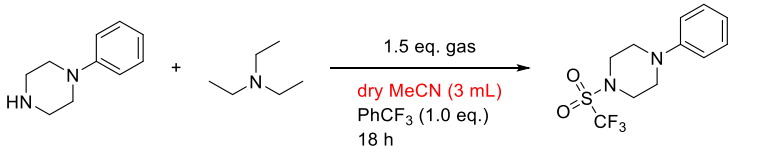
-62.84 (1.0; $PhCF_3$) -75.74 (0.57; product)

*Paper figure **1B**, Entry 2 (Blank control experiment)*



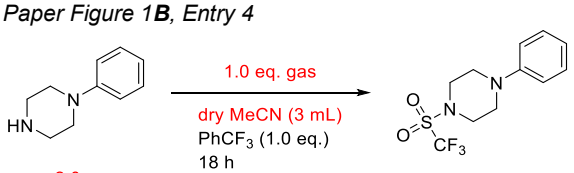
-61.85 (1.0; $PhCF_3$) -75.70 (1.07; product)

*Paper Figure 1**B**, Entry 3*



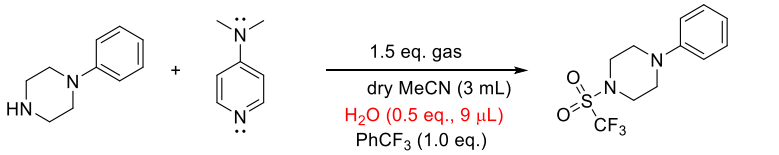
-62.95 (1.0; $PhCF_3$) -75.97 (1.07; product)

*Paper Figure 1**B**, Entry 4*



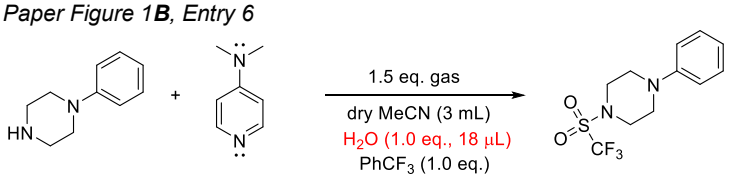
-62.82 (1.0; $PhCF_3$) -75.72 (0.82; product)

*Paper Figure 1**B**, Entry 5*



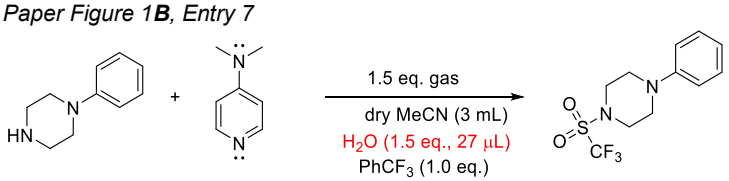
-63.17 (1.0) -75.76 (1.01)

*Paper Figure 1**B**, Entry 6*



-63.16 (1.0) -75.76 (0.46)

*Paper Figure 1**B**, Entry 7*

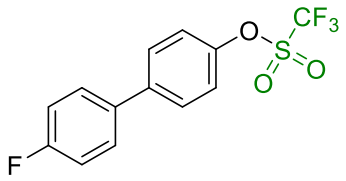


-63.17 (1.0) -75.76 (0.02)

7. Experimental Data

7.1. Experimental Data of Synthesized Aryl Triflates (precursor $PhNTf_2$)

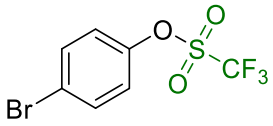
4'-fluoro-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (compound 1, cas number: 2377919-62-3)



Chemical Formula: $C_{13}H_8F_4O_3S$
Exact Mass: 320.0130

General procedure A was followed using 192.0 mg of 4-fluoro-4'-hydroxybiphenyl (98 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 4 hours (>99% yield determined by ^{19}F NMR). The extraction yield is 97%. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.40, *n*-heptane/ethyl acetate = 200/1). The title compound was obtained as colorless oil (272.2 mg, 85%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.4 Hz, 2H), 7.48–7.44 (m, 2H), 7.30 (d, *J* = 8.3 Hz, 2H), 7.10 (t, *J* = 8.3 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 162.89 (d, $^1J_{CF}$ = 248.7 Hz), 148.93, 140.64, 135.38, 128.77 (d, $^3J_{CF}$ = 8.2 Hz) 128.66, 121.65, 118.84 (q, $^1J_{CF}$ = 322.0 Hz), 115.86 (d, $^2J_{CF}$ = 21.7 Hz) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.30 (d, $^{12}J_{FF}$ = 2.1 Hz, 3F), -114.81 (s, F) ppm. These data are in agreement with literature data[9].

4-bromophenyl trifluoromethanesulfonate (compound 2, cas number: 66107-30-0)

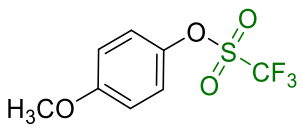


Chemical Formula: $C_7H_4BrF_3O_3S$
Exact Mass: 303.9017

General procedure A was followed using 174.8 mg of 4-bromophenol (99 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 4 hours (>99% yield determined by ^{19}F NMR). The title compound was obtained after extraction as yellowish oil (292.9 mg, 96%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.56 (dt, *J* = 9.8, 2.8 Hz, 2H), 7.15 (dt, *J* = 9.7, 2.7 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 148.45, 133.34, 123.00, 118.67 (q, $^1J_{CF}$ = 321.9 Hz) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.20 (s, 3F) ppm. Spectral data are consistent with those previously reported[10].

Gram-scale reaction: procedure L was followed using 1.0 g of 4-bromophenol (99 wt%, 5.722 mmol, 1.0 eq.). The reaction was stirred at room temperature for 4 hours (97% yield determined by ^{19}F NMR). The title compound was obtained after extraction as yellowish oil (1.2998 g, 75%).

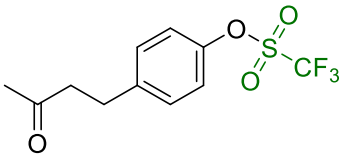
4-methoxyphenyl trifluoromethanesulfonate (compound 3, cas number: 66107-29-7)



Chemical Formula: $C_8H_7F_3O_4S$
Exact Mass: 256.0017

General procedure A was followed using 125.4 mg of 4-methoxyphenol (99 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 18 hours (>99% yield determined by ^{19}F NMR). The extraction yield is 84%. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.35, *n*-heptane/ethyl acetate = 19/1). The title compound was obtained as yellowish oil (192.3 mg, 75%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.18 (dt, *J* = 10.3, 3.1 Hz, 2H), 6.90 (dt, *J* = 10.3, 3.1 Hz, 2H), 3.78 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 159.13, 143.02, 122.26, 118.78 (q, $^1J_{CF}$ = 322.0 Hz), 114.97, 55.50 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.28 (s, 3F) ppm. These data are in agreement with literature data[11].

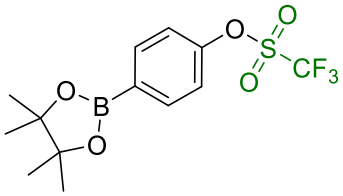
4-(3-oxobutyl)phenyl trifluoromethanesulfonate (compound 4, cas number: 261157-51-1)



Chemical Formula: $C_{11}H_{11}F_3O_4S$
Exact Mass: 296.0330

General procedure A was followed using 165.9 mg of 4-(4-hydroxyphenyl)-2-butanone (raspberry ketone, 99+ wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 18 hours (>99% yield determined by ^{19}F NMR). The extraction yield is 98%. The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.4, DCM). The title compound was obtained as yellowish oil (229.9 mg, 78%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.29–7.25 (m, 2H), 7.17 (dt, *J* = 8.9, 2.4 Hz, 2H), 2.92 (t, *J* = 7.4 Hz, 2H), 2.77 (t, *J* = 7.4 Hz, 2H), 2.14 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 206.95, 147.82, 141.69, 130.04, 121.12, 118.63 (q, $^1J_{CF}$ = 322.0 Hz), 44.45, 29.82, 28.70 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.40 (s, 3F) ppm. These data are in agreement with literature data[12].

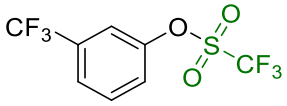
4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl trifluoromethanesulfonate (compound 5, cas number: 1027059-48-8)



Chemical Formula: $C_{13}H_{16}BF_3O_5S$
Exact Mass: 352.0764

General procedure A in which changing the solvent in two chambers into anhydrous MeCN was followed using 144.3 mg of 4-hydroxyphenylboronic acid (97 wt%, 1.0 mmol, 1.0 eq.) and 0.44 mL DIPEA (2.5 mmol, 2.5 eq.). The reaction was stirred at room temperature for 12 hours (86% yield determined by ^{19}F NMR). The crude reaction mixture was evaporated directly and then was transferred into a 25 mL round bottle and reacted with 143.23 mg of pinacol (99 wt%, 1.2 mmol, 1.2 eq.) in 10 mL DCM for 12 hours. The crude reaction mixture purified by short column chromatography on silica gel (R_f = 0.50, *n*-heptane/ethyl acetate = 9/1). The title compound was obtained as white crystal (271.1 mg, 77%). **Melting point** = 88.0–89.5 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.90 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 2H), 1.34 (s, 12H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 151.80, 136.87, 123.52, 120.53, 118.74 (q, $^1J_{CF}$ = 321.8 Hz), 84.29, 24.78 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.39 (s, 3F) ppm. These data are in agreement with literature data[13].

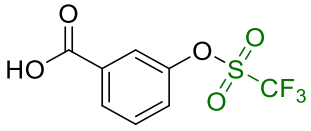
3-(trifluoromethyl)phenyl trifluoromethanesulfonate (compound 6, cas number: 199188-30-2)



Chemical Formula: $C_8H_4F_6O_3S$
Exact Mass: 293.9785

General procedure A was followed using 165.4 mg of 3-(trifluoromethyl)phenol (98 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 1.5 hours (>99% yield determined by ^{19}F NMR). The title compound was obtained after extraction and low pressure vacuuming as yellowish oil (261.8 mg, 89%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 7.8 Hz, 1H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.55 (s, 1H), 7.50–7.48 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 149.47, 133.11 (q, $^2J_{CF}$ = 34.0 Hz), 131.12, 125.34 (q, $^3J_{CF}$ = 3.7 Hz), 124.96, 122.95 (q, $^1J_{CF}$ = 273.6 Hz), 118.82 (q, $^3J_{CF}$ = 3.9 Hz), 118.80 (q, $^1J_{CF}$ = 321.7 Hz) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -63.40 (s, 3F, CF_3), -73.19 (s, 3F, OTf) ppm. These data are in agreement with literature data[13].

3-(((trifluoromethyl)sulfonyl)oxy)benzoic acid (compound 7, cas number: 32578-33-9)

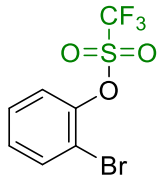


Chemical Formula: $C_8H_5F_3O_5S$
Exact Mass: 269.9810

General procedure A was followed using 138.1 mg of 3-Hydroxybenzoic Acid (99 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 18 hours (99+% yield determined by ^{19}F NMR). The title compound was obtained after extraction and vacuuming

as white solid (257.3 mg, 95%)). **Melting point** = 92.5–93.5 °C. **^{1}H NMR** (400 MHz, DMSO-d_6): δ 13.59 (br s, 1H), 8.08 (dt, J = 7.6, 1.3 Hz, 1H), 7.93–7.92 (m, 1H), 7.82–7.79 (m, 1H), 7.74 (t, J = 8.0, 1H) ppm. **^{13}C NMR** (101 MHz, DMSO-d_6): δ 165.61, 149.11, 133.54, 131.34 129.69, 125.89, 121.79, 118.25 (q, J = 322.1 Hz) ppm. **^{19}F NMR** (377 MHz, DMSO-d_6): δ -72.29 (s, 3H) ppm. **IR** (neat) $\tilde{\nu}$ = 2954 (br, carboxylic acid O-H stretching), 1686 (s, carboxylic acid C=O stretching), 1414 (s, S=O stretching), 1214 (vs, C-F stretching), 1079 (m, S=O stretching) cm^{-1}. **HRMS** (ESI) *m/z*: Calcd for $C_8H_4F_3O_5S$ [*M*-H]$^-$: 268.9737, found: 268.9827.

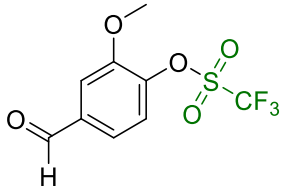
2-bromophenyl trifluoromethanesulfonate (compound 8, cas number: 129112-25-0)



Chemical Formula: $C_7H_4BrF_3O_3S$
Exact Mass: 303.9017

General procedure A was followed using 176.5 mg of 2-bromophenol (98 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 4 hours (>99% yield determined by ^{19}F NMR). The title compound was obtained after extraction as yellowish oil (280.7 mg, 92%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.65 (dd, J = 8.0, 1.5 Hz, 1H), 7.39–7.32 (m, 2H), 7.25–7.21 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 147.01, 134.40, 129.45, 129.07, 122.82, 118.63 (q, $^1J_{CF}$ = 321.6 Hz),115.89 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.87 (s, 3F) ppm. These data are in agreement with literature data[10].

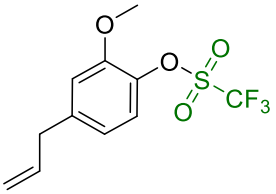
4-formyl-2-methoxyphenyl trifluoromethanesulfonate ((Vanillin Triflate, compound 9, cas number: 194018-68-3)



Chemical Formula: $C_9H_7F_3O_5S$
Exact Mass: 283.9966

General procedure A was followed using 153.7 mg of vanillin (99 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 12 hours (>99% yield determined by ^{19}F NMR). The extraction yield is 98%. The crude reaction mixture was purified by column chromatography on silica gel (**R$_f$** = 0.40, *n*-heptane/ethyl acetate = 6/1). The title compound was obtained as colorless oil (222.2 mg, 78%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.99 (s, 1H), 7.57 (d, J = 1.8 Hz, 1H), 7.52 (dd, J = 8.2, 1.8 Hz, 1H), 7.42 (d, J = 8.2 Hz, 1H), 4.00 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 190.29, 152.17, 142.65, 136.76, 123.98, 123.14, 118.63 (q, $^1J_{CF}$ = 321.7 Hz), 111.76, 56.43 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -74.21 (s, 3F) ppm. These data are in agreement with literature data[14].

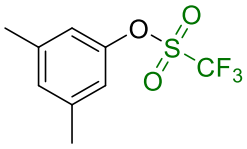
4-allyl-2-methoxyphenyl trifluoromethanesulfonate (compound 10, cas number: 1073426-46-6)



Chemical Formula: $C_{11}H_{11}F_3O_4S$
Exact Mass: 296.0330

General procedure A was followed using 167.6 mg of eugenol (98 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 22 hours (93% yield determined by ^{19}F NMR). The extraction yield is 88%. The crude reaction mixture was purified by column chromatography on silica gel (**R$_f$** = 0.4, *n*-heptane/ethyl acetate = 15/1). The title compound was obtained as yellowish oil (211.2 mg, 72%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.12 (d, J = 8.2 Hz, 1H), 6.85 (d, J = 1.8 Hz, 1H), 6.79 (dd, J = 8.3, 1.9 Hz, 1H), 5.99–5.89 (m, 1H), 5.14 (t, J = 1.3 Hz, 1H), 5.11–5.09 (m, 1H), 3.89 (s, 3H), 3.40 (s, 1H), 3.38 (s, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 151.16, 141.78, 137.09, 136.25, 122.12, 120.77, 118.74 (q, $^1J_{CF}$ = 321.6 Hz), 116.77, 113.31, 56.04, 39.97 ppm. **^{19}F NMR** (377MHz, $CDCl_3$): δ -74.42 (s, 3F) ppm. These data are in agreement with literature data[15].

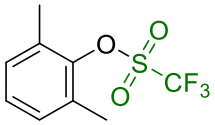
3,5-dimethylphenyl trifluoromethanesulfonate (compound 11, cas number: 219667-41-1)



Chemical Formula: $C_9H_9F_3O_3S$
Exact Mass: 254.0224

General procedure A was followed using 123.4 mg of 3,5-dimethylphenol (99+ wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 18 hours (>99% yield determined by ^{19}F NMR). The extraction yield is 87%. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.5, *n*-heptane/ethyl acetate = 25/1). The title compound was obtained as yellowish oil (203.1 mg, 80%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.98 (s, 1H), 6.87 (s, 2H), 2.32 (s, 6H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 149.54, 140.41, 129.95, 118.78 (q, $^{1}J_{CF}$ = 321.7 Hz), 118.67, 21.00 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.57 (s, 3F) ppm. These data are in agreement with literature data[16].

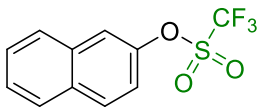
2,6-dimethylphenyl trifluoromethanesulfonate (compound 12, cas number: 86364-02-5)



Chemical Formula: $C_9H_9F_3O_3S$
Exact Mass: 254.0224

General procedure A was followed using 123.4 mg of 2,6-dimethylphenol (99 wt%, 1.0 mmol, 1.0 eq.) and 3 mL MeCN in chamber B rather than MeCN: H_2O. The reaction was stirred at room temperature for 18 hours (>99% yield determined by ^{19}F NMR). The mixture in chamber B was concentrated *in vacuo* to give the crude product directly. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.3, *n*-heptane/ethyl acetate = 100/1). The title compound was obtained as colorless oil (203.4 mg, 80%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.15–7.09 (m, 3H), 2.37 (s, 6H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 146.90, 131.47, 129.86, 127.95, 118.64 (q, $^{1}J_{CF}$ = 320.8 Hz), 17.08 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -74.08 (s, 3F) ppm. These data are in agreement with literature data[14].

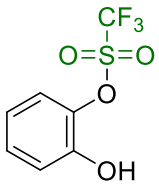
naphthalen-2-yl trifluoromethanesulfonate (compound 13, cas number: 3857-83-8)



Chemical Formula: $C_{11}H_7F_3O_3S$
Exact Mass: 276.0068

General procedure A was followed using 145.6 mg of 2-naphthol (99+ wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 6 hours (>99% yield determined by ^{19}F NMR). The title compound was obtained after extraction as yellow oil (270.7 mg, 98%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76–7.69 (m, 3H), 7.65 (d, *J* = 2.4 Hz, 1H), 7.46–7.42 (m, 2H), 7.27 (dd, *J* = 9.0, 2.5 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 147.02, 133.23, 132.26, 130.50, 127.85, 127.77, 127.42, 127.06, 119.34, 119.10,118.88 (q, $^{1}J_{CF}$ = 321.9 Hz) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.30 (s, 3F) ppm. These data are in agreement with literature data[11].

2-hydroxyphenyl trifluoromethanesulfonate (compound 14, cas number: 133617-36-4)

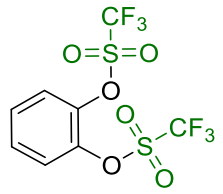


Chemical Formula: $C_7H_5F_3O_4S$
Exact Mass: 241,9861

General procedure A was followed using 111.2 mg of catechol (99 wt%, 1.0 mmol, 1.0 eq.) and 0.44 mL DIPEA (2.5 mmol, 2.5 eq.). In camber A, using *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 911.3 mg, 2.5 mmol, 2.5 eq.) and potassium bifluoride (KHF_2, 99+ wt%, 131.7 mg, 1.67 mmol, 1.67 eq.) to generate 2.5 eq. trifluoromethanesulfonyl fluoride gas. The reaction was stirred at room temperature for 4 days (>99% yield determined by ^{19}F NMR). The extraction yield is 95%. The crude reaction mixture was purified by

short column chromatography on silica gel ($\mathbf{R_f}$ = 0.3, *n*-heptane/ethyl acetate = 4/1). The title compound was obtained as yellow oil (207.0 mg, 86%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.23–7.18 (m, 2H), 7.00–6.97 (m, 1H), 6.96–6.92 (m, 1H), 5.48 (s, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 147.43, 137.51, 129.40, 122.33, 121.50, 118.64 (q, $^1J_{CF}$ = 321.6 Hz), 118.17 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.95 (s, 3F) ppm. **IR** (neat) $\tilde{\nu}$ = 3530 (m, O-H stretching, free), 3307 (br, O–H stretching, intermolecular bonded), 2992 (w, O-H stretching, intermolecular bonded), 1702 (m, aromatic C=C bending), 1463 (s, aromatic C=C stretching), 1418 (s, S=O stretching), 1203 (vs, C-F stretching), 1036 (m, S=O stretching) cm^{-1}.

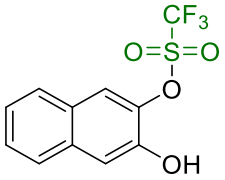
1,2-phenylene bis(trifluoromethanesulfonate) (compound 15, cas number: 17763-91-6)



Chemical Formula: $C_8H_4F_6O_6S_2$
Exact Mass: 373.9353

Chamber A of a 20 mL small two-chamber reactor (Figure S1) was filled with *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 911.3 mg, 2.5 mmol, 2.5 eq.) and potassium bifluoride (KHF_2, 99+ wt%, 131.7 mg, 1.67 mmol, 1.67 eq.). The vessel was closed and air switching to Argon atmosphere was required. Next, chamber B was charged with 111.2 mg of catechol (99 wt%, 1.0 mmol, 1.0 eq.). Then the anhydrous acetonitrile (MeCN, 3.0 mL), trifluorotoluene (99 wt%, 124 μL, 1.0 mmol) as an internal standard and *N*,*N*-diisopropylethylamine (DIPEA, 99 wt%, 0.44 mL, 2.5 mmol, 2.5 eq.) were added to chamber B. Finally, anhydrous acetonitrile (MeCN, 1.75 mL) was added by injection through the septum in chamber A and instant gas formation was observed (Scheme S1). The reaction was stirred at room temperature for 6 hours (85% yield determined by ^{19}F NMR). The mixture in chamber B was concentrated *in vacuo* to give the crude product directly. The crude reaction mixture was purified by a very short column chromatography on silica gel ($\mathbf{R_f}$ = 0.5, *n*-heptane/ethyl acetate = 9/1). The title compound was obtained as yellowish oil (207 mg, 55%, storage under N_2 atmosphere). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.49 (s, 4H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 147.51, 140.48, 129.63, 129.35, 123.76, 122.41, 119.65 (q, $^1J_{CF}$ = 328.9 Hz), 118.57 (q, $^1J_{CF}$ = 321.9 Hz) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.63 (s, 3F) ppm. **IR** (neat) $\tilde{\nu}$ = 1492 (m, aromatic C=C stretching), 1429 (s, S=O stretching), 1207 (vs, C–F stretching), 1036 (m, S=O stretching) cm^{-1}.

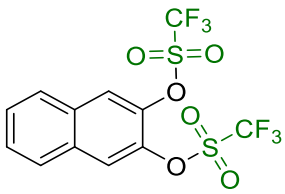
3-(trifluoromethylsulfonyl)naphth-2-ol (compound 16, cas number: 342890-35-1)



Chemical Formula: $C_{11}H_7F_3O_4S$
Exact Mass: 292.0017

General procedure A was followed using 108.3 mg of 2,3-naphthalenediol (98 wt%, 1.0 mmol, 1.0 eq.) and 0.44 mL DIPEA (2.5 mmol, 2.5 eq.). In camber A, using *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 911.3 mg, 2.5 mmol, 2.5 eq.) and potassium bifluoride (KHF_2, 99+ wt%, 131.7 mg, 1.67 mmol, 1.67 eq.) to generate 2.5 eq. trifluoromethanesulfonyl fluoride gas. The reaction was stirred at room temperature for 48 hours (>99% yield determined by ^{19}F NMR). The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.25, *n*-heptane/ethyl acetate = 6/1). The title compound was obtained as a white solid (272.0 mg, 92%). **Melting point** = 68.0–69.0 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.1 Hz, 1H), 7.70 (s, 1H), 7.60 (d, *J* = 8.2 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.26 (s, 1H), 5.97 (br s, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 145.25, 138.09, 133.24, 128.08, 127.73, 127.56, 126.28, 125.13, 120.68, 118.72 (q, $^1J_{CF}$ = 321.8 Hz), 113.01 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.82 (s, 3F) ppm. These data are in agreement with literature data[17].

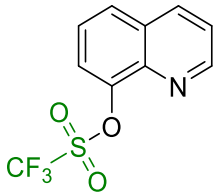
naphthalene-2,3-diyl Bis(trifluoromethanesulfonate (compound 17, cas number: 125261-31-6)



Chemical Formula: $C_{12}H_6F_6O_6S_2$
Exact Mass: 423.9510

General procedure A was followed using 108.3 mg of 2,3-naphthalenediol (98 wt%, 1.0 mmol, 1.0 eq.) and 0.44 mL DIPEA (2.5 mmol, 2.5 eq.). In camber A, using *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 911.3 mg, 2.5 mmol, 2.5 eq.) and potassium bifluoride (KHF_2, 99+ wt%, 131.7 mg, 1.67 mmol, 1.67 eq.) to generate 2.5 eq. trifluoromethanesulfonyl fluoride gas. The reaction was stirred at room temperature for 1.5 hours (70% yield determined by ^{19}F NMR). The extraction yield is 61%. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.3, *n*-heptane/ethyl acetate = 8/1). The title compound was obtained as white solid (221.0 mg, 52%). **Melting point** = 83.0–83.5 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.92 (s, 2H), 7.91–7.89 (m, 2H), 7.67–7.64 (m, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 137.98, 131.79, 128.72, 128.06, 122.18, 118.67 (q, $^1J_{CF}$ = 322.0 Hz) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.46 (s, 3F) ppm. These data are in agreement with literature data[17].

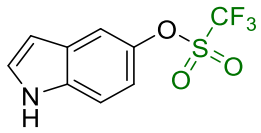
8-quinolinyl trifluoromethanesulfonate (compound 18, cas number: 108530-08-1)



Chemical Formula: $C_{10}H_6F_3NO_3S$
Exact Mass: 277.0020

General procedure A was followed using 146.6 mg of 8-hydroxyquinoline (99+ wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 18 hours (99% yield determined by ^{19}F NMR). The title compound was obtained after extraction as white crystal (252.3 mg, 91%). **Melting point** = 57.5–65.2 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.00 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.16 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.81 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.60 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.52 (t, *J* = 8.1 Hz, 1H), 7.47 (q, *J* = 4.19 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 151.52, 145.90, 140.84, 135.72, 129.65, 128.22, 125.81, 122.54, 120.85, 118.86 (q, $^1J_{CF}$ = 321.5 Hz) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -74.51 (s, 3F) ppm. These data are in agreement with literature data[2].

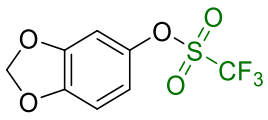
1H-indol-5-yl trifluoromethanesulfonate (compound 19, cas number: 128373-13-7)



Chemical Formula: $C_9H_6F_3NO_3S$
Exact Mass: 265.0020

General procedure A was followed using 137.3 mg of 5-hydroxyindole (97 wt%, 1.0 mmol, 1.0 eq.) and 0.44 mL DIPEA (2.5 mmol, 2.5 eq.). In camber A, using *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 911.3 mg, 2.5 mmol, 2.5 eq.) and potassium bifluoride (KHF_2, 99+ wt%, 131.7 mg, 1.67 mmol, 1.67 eq.) to generate 2.5 eq. trifluoromethanesulfonyl fluoride gas. The reaction was stirred at room temperature for 18 hours (>99% yield determined by ^{19}F NMR). The extraction yield is 80%. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.3, *n*-heptane/ethyl acetate = 8/1). The title compound was obtained as yellow solid (221.0 mg, 71%). **Melting point** = 48.5–49.0 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.24 (s, 1H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.20 (d, *J* = 8.9 Hz, 1H), 7.16 (t, *J* = 2.8 Hz, 1H), 7.00 (dd, *J* = 8.9, 2.4 Hz, 1H), 6.50–6.49 (m, 1H), ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 143.56, 134.54, 127.99, 126.85, 118.85 (q, $^1J_{CF}$ = 322.0 Hz), 114.82, 112.80, 112.02, 103.10 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.30 (s, 3F) ppm. These data are in agreement with literature data[16].

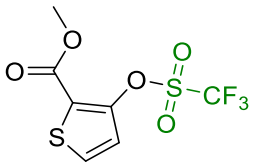
benzo[d][1,3]dioxol-5-yl trifluoromethanesulfonate (compound 20, cas number: 109586-40-5)



Chemical Formula: $C_8H_5F_3O_5S$
Exact Mass: 269.9810

General procedure A was followed using 140.9 mg of sesamol (98 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 4 hours (99% yield determined by ^{19}F NMR). The title compound was obtained after extraction as yellowish oil (295.6 mg, 84%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.79 (d, *J* = 8.4 Hz, 1H), 6.73 (td, *J* = 7.4, 2.4 Hz, 1H), 6.02 (d, *J* = 1.3 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 148.53, 147.45, 143.47, 118.71 (q, $^1J_{CF}$ = 322.1 Hz), 114.37, 108.17, 103.35, 102.46 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.21 (s, 3F) ppm. These data are in agreement with literature data[11].

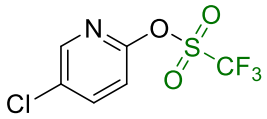
methyl 3-(((trifluoromethyl)sulfonyl)oxy)thiophene-2-carboxylate (compound 21, cas number: 313697-13-1)



Chemical Formula: $C_7H_5F_3O_5S_2$
Exact Mass: 289.9530

General procedure A was followed using 163.1 mg of methyl 3-hydroxythiophene-2-carboxylate (97 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 18 hours (>99% yield determined by ^{19}F NMR). The extraction yield is 82%. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.3, *n*-heptane/ethyl acetate = 9/1). The title compound was obtained as yellow oil (208.3 mg, 72%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.57 (d, *J* = 5.5 Hz, 1H), 7.02 (d, *J* = 5.5 Hz, 1H), 3.93 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 159.94, 145.39, 130.47, 122.39, 122.04, 118.63 (q, $^{1}J_{CF}$ = 322.0 Hz), 52.42 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.99 (s, 3F) ppm. These data are in agreement with literature data[18].

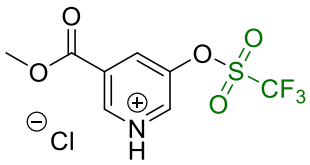
5-chloropyridin-2-yl trifluoromethanesulfonate (compound 22, cas number: 87412-10-0)



Chemical Formula: $C_6H_3ClF_3NO_3S$
Exact Mass: 260.9474

General procedure A was followed using 133.6 mg of 5-chloro-2-hydroxypyridine (97 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 6 hours (>99% yield determined by ^{19}F NMR). The mixture was washed with saturated $NaHCO_3$ (3 x 20 mL) and the extraction yield is 80%. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.40, *n*-heptane/ethyl acetate = 10/1). The title compound was obtained as colorless oil (198.8 mg, 76%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.37–8.35 (m, 1H), 7.88 (dt, *J* = 8.6, 2.9 Hz, 1H), 7.18 (dd, *J* = 8.6, 2.0 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 153.86, 147.30, 140.61, 132.41,118.54 (q, $^{1}J_{CF}$ = 321.7 Hz), 116.24 ppm. **^{19}F NMR** (377MHz, $CDCl_3$): δ -73.43 (s, 3 F) ppm. These data are in agreement with literature data[19].

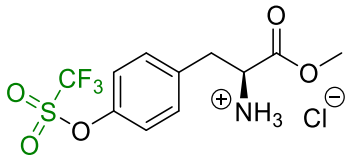
3-(methoxycarbonyl)-5-(((trifluoromethyl)sulfonyl)oxy)pyridin-1-ium chloride (compound 23)



Chemical Formula: $C_8H_7ClF_3NO_5S$
Exact Mass: 320.9686
Elemental Analysis:
C, 29.87; H, 2.19; Cl, 11.02; F, 17.72; N, 4.35; O, 24.87; S, 9.97

General procedure A was followed using 156.3 mg of methyl 5-hydroxynicotinate (98 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 6 hours (>99% yield determined by ^{19}F NMR). The mixture was washed with saturated $NaHCO_3$ (3 x 20 mL) and the extraction yield is 99%. The title compound was obtained as white solid after salt formation with 2N HCl solution in diethyl ether (315.2 mg, 98%). **Melting point** = 48.8–49.8 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.25 (d, *J* = 1.5 Hz, 1H), 8.77 (d, *J* = 2.7 Hz, 1H), 7.18 (dd, *J* = 2.7, 1.7 Hz, 1H), 4.01 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 163.83, 150.27, 146.43, 146.38, 129.80, 127.66, 118.67 (q, $^{1}J_{CF}$ = 322.1 Hz), 52.97 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -72.94(s, 3F) ppm. **CHN**: calculated for $C_8H_7ClF_3NO_5S$: C 29.87%, H 2.19%, N 4.35%; found: C 28.05%, H 2.28%, N 1.67% (average number based on three run rounds). **IR** (neat) $\tilde{\nu}$ = 2922 (br, amine salt N–H stretching), 1722 (s, ester C=O stretching), 1385 (s, S=O stretching), 1207 (vs, C–F stretching), 1066 (m, S=O stretching) cm^{-1}. **HRMS** (ESI) *m/z*: Calcd for $C_8H_7F_3NO_5S$ $[M+H]^+$: 285.9992, found: 285.9982.

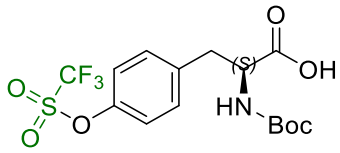
(S)-1-methoxy-1-oxo-3-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)propan-2-aminium chloride (compound 24, cas number: 2253981-98-3)



Chemical Formula: $C_{11}H_{13}ClF_3NO_5S$
Exact Mass: 363.0155
Elemental Analysis:
C, 36.32; H, 3.60; Cl, 9.75; F, 15.67; N, 3.85; O, 21.99; S, 8.81

General procedure A was followed using 236.4 mg of *L*-tyrosine methyl ester hydrochloride (98 wt%, 1.0 mmol, 1.0 eq.) and 0.44 mL DIPEA (2.5 mmol, 2.5 eq.). The reaction was stirred at room temperature for 6 hours (>99% yield determined by ^{19}F NMR). The mixture was washed with saturated $NaHCO_3$ (3 x 20 mL) and the extraction yield is 98%. The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.30, *n*-heptane/ethyl acetate/TEA = 20/80/1, 317.5 mg, 97%, little yellow oil). The title compound was obtained as white solid after salt formation with 2N HCl solution in diethyl ether (331.0 mg, 91%). **Melting point** = 162.5–164.0 °C. **^{1}H NMR** (400 MHz, Methanol-d_4): δ 7.37 (dt, *J* = 9.2, 2.3 Hz, 2H), 7.28 (dt, *J* = 9.3, 2.3 Hz, 2H), 4.76 (br s, 3 H), 4.29 (t, *J* = 6.9 Hz, 1H), 3.70 (s, 3 H), 3.26–3.14 (m, 2H) ppm. **^{13}C NMR** (101 MHz, Methanol-d_4): δ 170.17, 150.60, 136.62,132.76,123.07,120.15 (q, $^1J_{CF}$ = 320.3 Hz), 54.90, 53.66, 36.57 ppm. **^{19}F NMR** (377 MHz, Methanol-d_4): δ -73.24 (s, 3F) ppm. **CHN**: calculated for $C_{11}H_{13}ClF_3NO_5S$: C 36.32%, H 3.60%, N 3.85%; found: C 36.36%, H 3.63%, N 1.79% (average number based on three run rounds). **IR** (neat) ṽ = 2800 (br, amine salt N–H stretching), 1743 (s, ester C=O stretching), 1382 (s, S=O stretching), 1204 (vs, C–F stretching), 1052 (m, S=O stretching) cm^{-1}. **HRMS** (ESI) *m/z*: Calcd for $C_{11}H_{13}F_3NO_5S$ [*M*+H]$^+$: 328.0461, found: 328.0463.

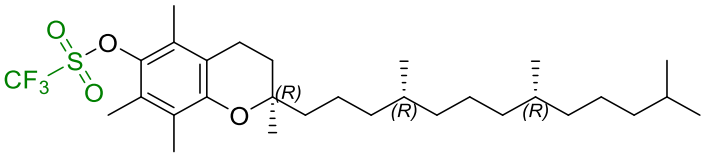
(S)-2-((tert-butoxycarbonyl)amino)-3-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)propanoic acid (compound 25, cas number: 2093022-49-0)



Chemical Formula: $C_{15}H_{18}F_3NO_7S$
Exact Mass: 413.0756

General procedure A was followed using 287.0 mg of Boc-Tyr-OH (98 wt%, 1.0 mmol, 1.0 eq.) and 0.44 mL DIPEA (2.5 mmol, 2.5 eq.). The reaction was stirred at room temperature for 18 hours (>99% yield determined by ^{19}F NMR). The title compound was obtained as yellowish oil after the extraction (379.8 mg, 92%). **^{1}H NMR** (400 MHz, DMSO-d_6): δ 12.54 (br s, 1H), 7.45–7.39 (m, 4H), 7.16 (d, *J* = 8.6 Hz, 1H, NH), 4.18–4.03 (m, 1H), 3.10 (dd, *J* = 13.8, 4.4 Hz, 1H), 2.86 (dd, *J* = 13.7, 10.9 Hz, 1H), 1.33–1.25 (m, 9H) ppm. **^{13}C NMR** (101 MHz, DMSO-d_6): δ 173.28, 172.02, 155.40, 147.87, 139.26, 131.36, 120.99, 118.26 (q, $^1J_{CF}$ = 322.1 Hz), 78.09, 54.90, 54.67, 35.77, 28.07 ppm. **^{19}F NMR** (377 MHz, DMSO-d_6): δ -73.40 (s, 3F) ppm. **HPLC** enantiomeric ratio 99.5:0.5 (details, see Section 10) **IR** (neat) ṽ = 3420 (w, N–H stretching), 2982 (br, carboxylic acid O–H stretching), 1713 (s, carboxylic acid C=O stretching), 1419 (s, S=O stretching), 1209 (vs, C–F stretching), 1054 (m, S=O stretching) cm^{-1}. **HRMS** (ESI) *m/z*: Calcd for $C_{15}H_{18}F_3NNaO_7S$ [*M*+Na]$^+$: 436.0648, found: 436.0643.

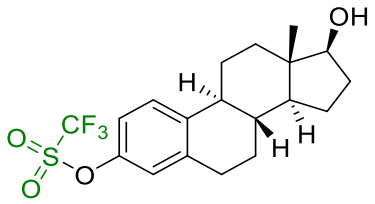
(R)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl trifluoromethanesulfonate (compound 26, cas number: 261929-85-5)



Chemical Formula: $C_{30}H_{49}F_3O_4S$
Exact Mass: 562.3304

General procedure A was followed using 444.0 mg of D-alpha-Tocopherol (97 wt%, 1.0 mmol, 1.0 eq.) and 3 mL MeCN in chamber B rather than MeCN: H_2O. The reaction was stirred at room temperature for 48 hours (97% yield determined by ^{19}F NMR). The extraction yield is 88%. The title compound was obtained after extraction as sticky yellow oil (495.4 mg, 88%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.58 (t, *J* = 6.5 Hz, 2H), 2.21 (s, 3H), 2.18 (s, 3H), 2.10 (s, 3H), 1.81–1.74 (m, 2H), 1.58–1.48 (m, 3H), 1.46–1.03 (m, 21H), 0.88–0.84 (m, 12H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 150.92, 139.66, 128.06, 126.67, 124.34, 118.74 (q, $^1J_{CF}$ = 321.0 Hz), 118.40, 75.58, 39.95, 39.42, 37.49, 37.42, 37.33, 32.82, 32.67, 30.87, 27.99, 24.85, 24.47, 23.73, 22.66, 22.73, 20.97, 20.67, 19.69, 19.59, 13.89, 13.07, 11.88 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -74.11 (s, 3F) ppm. These data are in agreement with literature data[20].

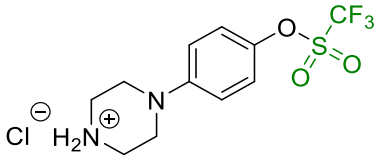
(8R,9S,13S,14S,17S)-17-hydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl trifluoromethanesulfonate (compound 27, cas number: 167845-80-9)



Chemical Formula: $C_{19}H_{23}F_3O_4S$
Exact Mass: 404.1269

General procedure A was followed using 280.8 mg of beta-estradiol (97+ wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 48 hours (>99% yield determined by ^{19}F NMR). The extraction yield is 95%. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R}_f$ = 0.3, *n*-heptane/ethyl acetate = 7/3). The title compound was obtained as yellowish oil (303.3 mg, 75%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.33 (d, *J* = 8.6 Hz, 1H), 7.01 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.96 (d, *J* = 2.6 Hz, 1H), 3.73 (t, *J* = 8.5 Hz, 1H), 2.89–2.86 (m, 2H), 2.34–2.28 (m, 1H), 2.25–2.18 (m, 1H), 2.16–2.05 (m, 1H), 1.99–1.88 (m, 3H), 1.75–1.67 (m, 1H), 1.57–1.25 (m, 6H), 1.23–1.15 (m, 1H), 0.78 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 147.36, 140.81, 139.43, 127.05, 121.00, 118.65 (q, $^1J_{CF}$ = 322.0 Hz),117.97, 81.55, 49.92, 43.97, 43.04, 38.11, 36.48, 30.33, 29.38, 26.66, 25.97, 22.98, 10.92 ppm. **^{19}F NMR** (377 MHz, Methanol-*d*$_4$): δ -73.32 (s, 3F) ppm. These data are in agreement with literature data[21].

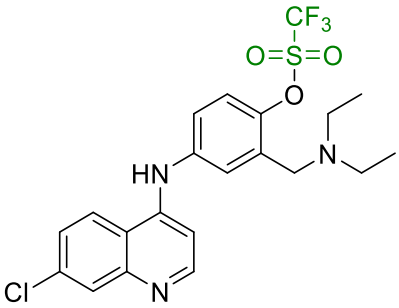
4-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)piperazin-1-ium chloride (compound 28)



Chemical Formula: $C_{11}H_{14}ClF_3N_2O_3S$
Exact Mass: 346,03658
Elemental Analysis: C, 38.10; H, 4.07; Cl, 10.22; F, 16.44; N, 8.08; O, 13.84; S, 9.25

General procedure A was followed using 221.3 mg of 1-(4-hydroxyphenyl)-piperazine (97 wt%, 1.0 mmol, 1.0 eq.) and 0.44 mL DIPEA (2.5 mmol, 2.5 eq.). The reaction was stirred at room temperature for 4 hours (>99% yield determined by ^{19}F NMR). The mixture was washed with saturated $NaHCO_3$ (3 x 20 mL) and the extraction yield is 95%. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R}_f$ = 0.40, *n*-heptane/ethyl acetate = 100/1, 251.1 mg, 81%). The title compound was obtained as yellowish solid after salt formation with 2N HCl solution in diethyl ether (221.9 mg, 64%). **Melting point** = 158.7–159.5 °C. **^{1}H NMR** (400 MHz, Methanol-*d*$_4$): δ 7.16 (dt, *J* = 10.2, 3.0 Hz, 2H), 7.02 (dt, *J* = 10.2, 3.0 Hz, 2H), 3.36–3.34 (m, 4H), 3.25–3.20 (m, 4H) ppm. **^{13}C NMR** (101 MHz, Methanol-*d*$_4$): δ 151.69, 144.48, 123.18, 120.18 (q, $^1J_{CF}$ = 321.1 Hz), 118.70, 47.64, 44.75 ppm. **^{19}F NMR** (377 MHz, Methanol-*d*$_4$): δ -73.17 (s, 3F) ppm. **CHN**: calculated for $C_{11}H_{14}ClF_3N_2O_3S$: C 38.10%, H 4.07%, N 8.08%; found: C 34.03%, H 4.01%, N 4.86% (average number based on three run rounds). **IR** (neat) $\tilde{\nu}$ = 3080 (br, amine salt N–H stretching), 1433 (s, S=O stretching), 1345 (m, aromatic amine C–N stretching), 1251 (m, C–N stretching), 1206 (vs, C–F stretching), 1050 (m, S=O stretching) cm^{-1}. **HRMS** (ESI) *m/z*: Calcd for $C_{11}H_{14}F_3N_2O_3S$ $[M+H]^+$: 311.0672, found: 311.0669.

4-((7-chloroquinolin-4-yl)amino)-2-((diethylamino)methyl)phenyl trifluoromethanesulfonate (compound 29)



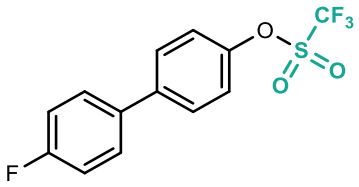
Chemical Formula: $C_{21}H_{21}ClF_3N_3O_3S$
Exact Mass: 487.0944

General procedure A was followed using 474.3 mg of amodiaquin dihydrochloride dihydrate (98 wt%, 1.0 mmol, 1.0 eq.) and 0.49 mL *N*,*N*-Diethylethanamine (TEA, 3.5 mmol, 3.5 equiv.) and DMSO (0.25 M, 4.0 mL). The reaction was stirred at room temperature for 18 h (>99% yield determined by ^{19}F NMR). The mixture was washed with saturated $NaHCO_3$ (3 x 20 mL). The crude reaction mixture was purified by short column chromatography on silica gel ($\mathbf{R}_f$ = 0.3, *n*-heptane/ethyl acetate = 1/1). The title compound was obtained as white solid (401.6 mg, 82%). **Melting point** = 187.3 – 187.7 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.57 (d, *J* = 5.3 Hz, 1H), 8.00 (d, *J* = 2.1 Hz, 1H), 7.95 (d, *J* = 9.0 Hz, 1H), 7.60 (d, *J* = 2.4 Hz, 1H), 7.40 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.34 (br s, 1H), 7.27–7.20 (m, 2H), 7.02 (d, *J*

= 5.3 Hz, 1H), 3.64 (s, 2H), 2.54 (q, *J* = 7.1 Hz, 4H), 1.01 (t, *J* = 7.1 Hz, 6H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 151.72, 149.62, 147.16, 134.94, 139.81, 135.67, 135.52, 128.70, 126.30, 124.01, 122.36, 121.64, 121.13, 118.57 (q, $^1J_{CF}$ = 321.5 Hz), 188.42, 103.10, 51.56, 46.97, 11.59 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -74.20 (s, 3F) ppm. **IR** (neat) ṽ = 3049 (br, N–H stretching), 1372 (s, S=O stretching), 1265 (s, aromatic amine C–N stretching), 1203 (vs, C–F stretching), 1141 (s, S=O stretching), 1080 (w, C–N stretching), 870 (s, C–Cl stretching) cm^{-1}. **HRMS** (ESI) *m/z*: Calcd for $C_{21}H_{22}ClF_3N_3O_3S$ [*M*+H]$^+$: 488.1017, found: 488.1010.

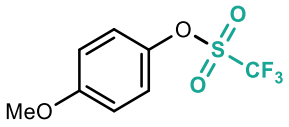
7.2. Experimental Data of Synthesized Aryl Triflates (precursor Tf_2O)

4'-fluoro-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (compound 1(B))



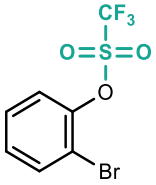
General procedure B was followed using 192.0 mg of 4-fluoro-4'-hydroxybiphenyl (98 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 16 hours (>99% yield determined by ^{19}F NMR). The title compound was obtained as yellow oil (286 mg, 89%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65–7.60 (m, 2H), 7.57–7.51 (m, 2H), 7.39–7.34 (m, 2H), 7.21–7.14 (m, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.9 (d, $^1J_{CF}$ = 247.3 Hz), 148.9, 140.7, 135.4 (d, $^3J_{CF}$ = 3.2 Hz, 2C), 128.9, 128.8, 128.8 (d, $^4J_{CF}$ = 0.8 Hz), 121.7 (2C), 118.8 (q, $^1J_{CF}$ = 320.5 Hz), 115.9 (d, $^2J_{CF}$ = 21.6 Hz, 2C) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -72.8 (s, 3F), -114.3 (s, 1F) ppm. These data are in agreement with literature data.[9]

4-methoxyphenyl trifluoromethanesulfonate (compound 3(B))



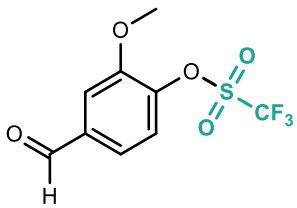
General procedure B was followed using 127 mg of 4-methoxyphenol (98 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 18 hours (>99% yield determined by ^{19}F NMR). The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.35, *n*-heptane/ethyl acetate (95/5)). The title compound was obtained as colorless oil (58 mg, 23%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.24–7.19 (m, 2H), 6.97–6.92(m, 2H), 3.84 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 159.1, 143.1, 122.3, 118.8 (q, $^1J_{CF}$ = 321 Hz), 115.1, 55.7 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -72.8 (s, 3F) ppm. These data are in agreement with literature data.[11]

2-bromophenyl trifluoromethanesulfonate (compound 8(B))



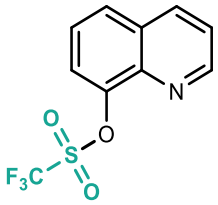
General procedure B was followed using 177 mg of 2-bromophenol (98 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 18 hours (97% yield determined by ^{19}F NMR). The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.22, *n*-heptane (100%)). The title compound was obtained as colorless oil (102 mg, 34%).**^{1}H NMR** (400 MHz, DMSO-d_6): δ 7.92 (app ddd, *J* = 7.9, 1.3, 0.4 Hz, 1H), 7.64–7.57 (m, 2H), 7.50–7.43 (m, 1H) ppm. **^{13}C NMR** (101 MHz, DMSO-d_6) δ 146.4, 134.6, 130.7, 130.2, 123.3, 118.1 (q, $^1J_{CF}$ = 321.4 Hz), 115.2 ppm. **^{19}F NMR** (377 MHz, DMSO-d_6): δ -73.25 (s, 3F) ppm. These data are in agreement with literature data.[10]

4-formyl-2-methoxyphenyl trifluoromethanesulfonate ((Vanillin Triflate, compound 9(B)))



General procedure B was followed using 155 mg of vanillin **(**98 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 18 hours (>99% yield determined by ^{19}F NMR). The crude reaction mixture was purified by column chromatography on silica gel (**R_f** = 0.26, *n*-heptane/ethyl acetate (85/15)). The title compound was obtained as off-white crystalline solid (143 mg, 50%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 10.01 (s, 1H), 7.60 (app d, *J* = 1.8 Hz, 1H), 7.54 (app dd, *J* = 8.2, 1.8 Hz ,1H), 7.44 (app d, *J* = 8.1 Hz, 1H), 4.03 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 190.3, 152.3, 142.8, 136.8, 124.1, 123.2, 118.7 (q, $^1J_{CF}$ = 320.1 Hz), 111.8, 56.5 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.68 (s, 3F) ppm. These data are in agreement with literature data.[14]

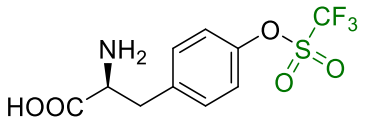
8-Quinolinyl trifluoromethanesulfonate (compound 18(B))



General procedure B was followed using 148 mg of 8-hydroxyquinoline (98 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 48 hours (82% yield determined by ^{19}F NMR). The title compound was obtained after preparative TLC (rf: 0.25, *n*-heptane/ethyl acetate/Et_3N (85/15/0.1)) as yellow oil (107 mg, 39%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.09 (app dd, *J* = 4.2, 1.6 Hz, 1H), 8.26 (app ddd, *J* = 8.3, 1.7, 0.3 Hz, 1H), 7.89 (app dd, *J* = 8.0, 1.5 Hz, 1H), 7.67–7.64 (m, 1H), 7.61 (app d, *J* = 8 Hz, 1H), 7.58–7.55 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.7, 146.1, 141.1, 135.8, 129.8, 128.3, 126.0, 122.7, 121.0, 118.9 (q, $^1J_{CF}$ = 320.53 Hz) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -73.76 (s, 3F) ppm. These data are in agreement with literature data.[2]

7.3. Experimental Data of Synthesized Peptides Substrate Scope

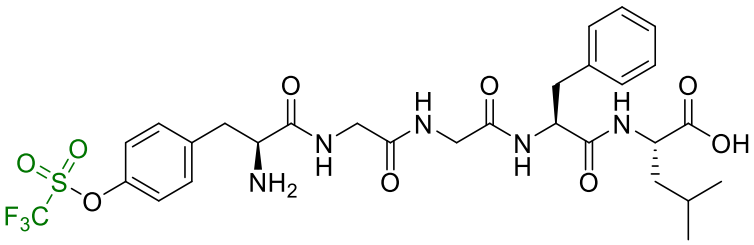
(S)-2-amino-3-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)propanoic acid (compound 30)



Chemical Formula: $C_{10}H_{10}F_3NO_5S$
Exact Mass: 313.02318

General procedure F was followed using 4 mL in-advance prepared solution of 1 mM *L*-Tyrosine in MeCN:pH 9.0 borax buffer = 1:1 (4 μmol *L*-Tyrosine in total, 1.0 eq.). The reaction was stirred at room temperature for 4 hours. The assay yield is 93.4% (average over two runs, standard deviation = 0.032), defined by dividing the [M+132] peak area by the total AUC of the HPLC-MS TIC chromatogram (Method: DA-40-40-70-100_20-40-2MIN_+.M; D = MeOH; A = H_2O + 0.1% HCOOH).

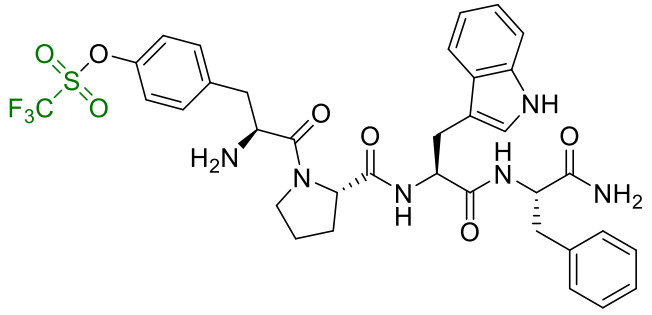
((S)-2-amino-3-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)propanoyl)glycylglycyl-L-phenylalanyl-L-leucine (compound 31)



Chemical Formula: $C_{29}H_{36}F_3N_5O_9S$
Exact Mass: 687.2186

General procedure F was followed using 2.3 mg Leucine Enkephalin acetate salt hydrate (95 wt%, 4 μmol, 1.0 eq.) in MeCN:pH 9.0 borax buffer = 2 mL:2mL. The reaction was stirred at room temperature for 4 hours. The assay yield is 71.3% (average over two runs, standard deviation = 0.862), defined by dividing the [M+132] peak area by the total AUC of the HPLC-MS TIC chromatogram (Method: DA-40-40-70-100_20-40-2MIN_+.M; D = MeOH; A = H_2O + 0.1% HCOOH).

4-((S)-2-amino-3-((S)-2-(((S)-1-(((S)-1-amino-1-oxo-3-phenylpropan-2-yl)amino)-3-(1H-indol-3-yl)-1-oxopropan-2-yl)carbamoyl)pyrrolidin-1-yl)-3-oxopropyl)phenyl trifluoromethanesulfonate (compound 32)

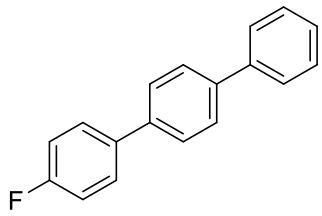


Chemical Formula: $C_{35}H_{37}F_3N_6O_7S$
Exact Mass: 742.2397

General procedure F was followed using 2.6 mg Endomorphin-1 (95 wt%, 4 μmol, 1.0 eq.) in MeCN:pH 9.0 borax buffer = 2 mL:2mL. The reaction was stirred at room temperature for 4 hours. The assay yield is 85.4% (average over two runs, standard deviation = 0.103), defined by dividing the [M+132] peak area by the total AUC of the HPLC-MS TIC chromatogram (Method: DA-20-60-60-100_20-10-5MIN_+.M; D = MeOH; A = H_2O + 0.1% HCOOH).

7.4. Experimental Data of Synthesized Suzuki Cross-Coupling compounds *via* Aryl Trifluoromethanesulfonate

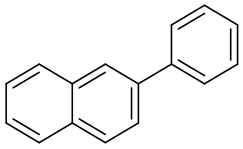
4-fluoro-1,1':4',1''-terphenyl (compound 33, cas number: 3799-84-6)



Chemical Formula: $C_{18}H_{13}F$
Exact Mass: 248.1001

General procedure H was followed using 192.0 mg of 4-Fluoro-4-hydroxybiphenyl (98 wt%, 1.0 mmol, 1.0 eq.) in Chamber B. Reaction of step 1 was stirred at room temperature for 4 hours. Then step 2 was following 136.9 mg phenylboronic acid (98+ wt%, 1.1 mmol, 1.1 eq.) and then stirred at room temperature for 18 hours. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R}_f$ = 0.3, *n*-heptane). The title compound was obtained as white solid (216.0 mg, 87%). **Melting point** = 208.0–214.5 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68–7.64 (m, 3H), 7.63–7.56 (m, 5H), 7.48–7.44 (m, 2H), 7.38–7.34 (m, 1H), 7.17–7.11 (m, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.51 (d, $^1J_{CF}$ = 247.4 Hz), 140.58, 140.13, 139.13, 136.81 (d, $^4J_{CF}$ = 3.3 Hz), 128.82, 128.56 (d, $^3J_{CF}$ = 8.1 Hz), 127.54, 127.48, 127.39, 127.34, 127.02, 115.67 (d, $^2J_{CF}$ = 21.5 Hz) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -116.16 (s, F) ppm. These data are in agreement with literature data[22].

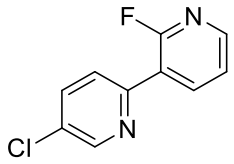
2-phenylnaphthalene (compound 34, cas number: 612-94-2)



Chemical Formula: $C_{16}H_{12}$
Exact Mass: 204.0939

General procedure H was followed using 145.6 mg of 2-naphthol (99+ wt%, 1.0 mmol, 1.0 eq.) in Chamber B. Reaction of step 1 was stirred at room temperature for 6 hours. Then step 2 was following 136.9 mg phenylboronic acid (98+ wt%, 1.1 mmol, 1.1 eq.) and then stirred at room temperature for 18 hours. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R}_f$ = 0.3, *n*-heptane/ethyl acetate = 100/1). The title compound was obtained as white solid (186.5 mg, 91%). **Melting point** = 101.5 – 102.0 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.89–7.83 (m, 3H), 7.73–7.69 (m, 3H), 7.47–7.44 (m, 4H), 7.37–7.34 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.09, 138.52, 133.66, 132.59, 128.82, 128.38, 128.17, 127.61, 127.40, 127.31, 126.25, 125.89, 125.77, 125.56 ppm. These data are in agreement with literature data[23].

5-chloro-2'-fluoro-2,3'-bipyridine (compound 35, cas number: 942206-10-2)

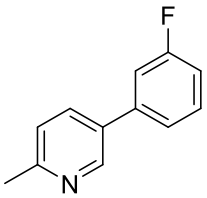


Chemical Formula: $C_{10}H_6ClFN_2$
Exact Mass: 208.0204

Chamber A of a 20 mL small two-chamber reactor (**Figure S1**) was filled with *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 546.8 mg, 1.5 mmol, 1.5 eq.) and potassium bifluoride (KHF_2, 99+ wt%, 78.9 mg, 1.0 mmol, 1.0 eq.). Next, chamber B was charged with 133.6 mg of 5-chloro-2-hydroxypyridine (97 wt%, 1.0 mmol, 1.0 eq.). Then 126.1 mg sodium bicarbonate ($NaHCO_3$, 99.9 wt%, 1.5 mmol, 1.5 eq.) and 1,4-dioxane/H_2O (2.5 mL/0.5 mL) were added into chamber B. Finally, the vessel was closed and anhydrous dimethylformamide (DMF, 1.75 mL, 0.86 M) was added by injection through the septum in chamber A. The reaction was monitored by TLC. After 48 h, the cap on chamber B was carefully removed to release the residual pressure. The reaction was stirred for another 5 minutes to ensure that all trifluoromethanesulfonyl fluoride gas was extracted out of the fume hood. According to the literature[5], step 2 was followed. An 8 mL single chamber tube C was charged with 158.2 mg 2-fluoropyridine-3-boronic acid (98 wt%, 1.1 mmol, 1.1 eq.), 4.5 mg palladium(II) acetate ($Pd(OAc)_2$, 98+ wt%, 0.02 mmol, 0.02 eq.), 6.9 mg tricyclohexylphosphine (PCy_3, 97 wt%, 0.024 mmol, 0.024 eq.) and 185.0 mg sodium bicarbonate ($NaHCO_3$, 99.9 wt%, 2.2 mmol, 2.2 eq.). Then the vessel was closed. After changing the air in tube C into nitrogen using Schlenk system three times, the content of chamber B was transferred into chamber of tube C using a 3 mL injector through the septum in tube C at the room temperature and then was hearted into 80°C for 2 h. The reaction was monitored by TLC. The mixture in tube C was transferred to a 100 mL separatory funnel. Tube C was rinsed five times with 5 mL of methyl *tert*-butyl ether (MTBE); the fractions were collected in the same funnel. The mixture was washed with $NaHCO_3$ (aq., 20 mL). Then the combined water phase was re-extracted by MTBE (2 x 10 mL). The combined organic layers were washed with brine (1 x 20 mL), dried over anhydrous Na_2SO_4 and then concentrated *in vacuo* to give the crude product.

The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R}_f$ = 0.2, *n*-heptane/ethyl acetate = 12/1). The title compound was obtained as beige solid (131.5 mg, 63%). **Melting point** = 99.0 – 100.0 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.68 (dd, *J* = 2.4, 0.6 Hz, 1H), 8.54 (ddd, *J* = 9.8, 7.7, 2.1 Hz, 1H), 8.27 (ddd, *J* = 4.8, 1.9, 1.4 Hz, 1H), 7.88 (ddd, *J* = 8.5, 1.7, 0.7 Hz, 1H), 7.35 (ddd, *J* = 7.5, 4.8, 2.0 Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.55 (d, $^1J_{CF}$ = 241.5 Hz), 149.27 (d, $^3J_{CF}$ = 7.1 Hz), 148.81, 147.88 (d, $^3J_{CF}$ = 15.2 Hz), 141.26 (d, $^4J_{CF}$ = 3.5 Hz), 136.41, 131.64, 124.66 (d, $^3J_{CF}$ = 11.5 Hz), 122.07 (d, $^4J_{CF}$ = 4.4 Hz), 121.10 (d, $^2J_{CF}$ = 26.5 Hz) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -69.48 (s, F) ppm. These data are in agreement with literature data[24].

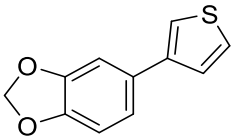
5-(3-fluorophenyl)-2-methylpyridine (compound 36, cas number: 713143-67-0)



Chemical Formula: $C_{12}H_{10}FN$
Exact Mass: 187.0797

General procedure H was followed using 110.2 mg of 6-methyl-3-pyridinol (99 wt%, 1.0 mmol, 1.0 eq.) in Chamber B. Reaction of step 1 was stirred at room temperature for 24 hours. Then step 2 was following 158.7 mg 3-fluorophenylboronic acid (97 wt%, 1.1 mmol, 1.1 eq.), 4.5 mg palladium(II) acetate ($Pd(OAc)_2$, 98+ wt%, 0.02 mmol, 0.02 eq.), 6.9 mg tricyclohexylphosphine (PCy_3, 97 wt%, 0.024 mmol, 0.024 eq.) and then stirred at room temperature for 3 days. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R}_f$ = 0.25, *n*-heptane/ethyl acetate = 7/1). The title compound was obtained as yellowish oil (149.6 mg, 80%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.70 (d, *J* = 2.1 Hz, 1H), 7.70 (dd, *J* = 8.0, 2.4 Hz, 1H), 7.37 (td, *J* = 7.9, 5.9 Hz, 1H), 7.30 (dt, *J* = 7.7, 2.6 Hz, 1H), 7.22 (dt, *J* = 10.0, 2.1 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.06–7.00 (m, 1H), 2.58 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.04 (d, $^1J_{CF}$ = 247.2 Hz), 157.68, 147.18, 139.96 (d, $^3J_{CF}$ = 7.8 Hz), 134.36, 132.26 (d, $^4J_{CF}$ = 2.2 Hz), 130.32 (d, $^3J_{CF}$ = 8.3 Hz), 122.96, 122.33 (d, $^4J_{CF}$ = 2.9 Hz), 114.36 (d, $^2J_{CF}$ = 21.3 Hz), 113.59 (d, $^2J_{CF}$ = 22.2 Hz), 23.86 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -112.79 (s, 1F) ppm. These data are in agreement with literature data[25].

5-(thiophen-3-yl)benzo[d][1,3]dioxole (compound 37, cas number: 740804-24-4)

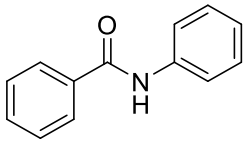


Chemical Formula: $C_{11}H_8O_2S$
Exact Mass: 204.0245

General procedure H was followed using 140.9 mg of sesamol (98 wt%, 1.0 mmol, 1.0 eq.) in Chamber B. Reaction of step 1 was stirred at room temperature for 4 hours. Then step 2 was following 145.1 mg 3-thienylboronic acid (97 wt%, 1.1 mmol, 1.1 eq.), 4.5 mg palladium(II) acetate ($Pd(OAc)_2$, 98+ wt%, 0.02 mmol, 0.02 eq.), 6.4 mg tricyclohexylphosphine (PCy_3, 97 wt%, 0.022 mmol, 0.022 eq.) and then stirred at room temperature for 3 hours. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R}_f$ = 0.35, *n*-heptane/ethyl acetate = 20/1). The title compound was obtained as yellowish solid (202.2 mg, 99%). **Melting point** = 69.5–70.5 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34–7.32 (m, 1H), 7.30–7.27 (m, 2H), 7.06–7.04 (m, 2H), 6.83–6.80 (m, 1H), 5.95 (s, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.00, 146.74, 141.99, 130.24, 126.25, 126.06, 119.86, 119.31, 108.50, 107.02, 101.03 ppm. These data are in agreement with literature data[26].

7.5. Experimental Data of Synthesized Amides *via* Acyl Fluoride Intermediate

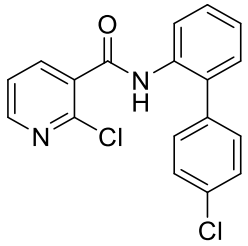
N-phenylbenzamide (compound 38, cas number: 93-98-1)



Chemical Formula: $C_{13}H_{11}NO$
Exact Mass: 197.0841

General procedure I was followed using 122.7 mg of benzoic acid (99.5+ wt%, 1.0 mmol, 1.0 eq.) and 0.18 mL aniline (99.8 wt%, 186.mg, 2.0 mmol, 2.0 eq.) in Chamber B. Reaction was stirred at room temperature for 5 hours. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R}_f$ = 0.25, DCM/TEA = 100/1). The title compound was obtained as white solid (180.0 mg, 91%). **Melting point** = 162.5 – 163.5 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.23 (s, 1H), 7.97 (d, *J* = 7.2 Hz, 2H), 7.80 (d, *J* = 7.7 Hz, 2H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.53 (t, *J* = 7.3 Hz, 2H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.11 (t, *J* = 7.3 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, DMSO-d_6) δ 165.51, 139.14, 134.97, 131.44, 128.52, 128.29, 127.58, 123.58, 120.35 ppm. These data are in agreement with literature data[27].

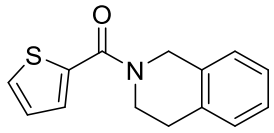
2-chloro-N-(4'-chloro-[1,1'-biphenyl]-2-yl)nicotinamide (compound 39, cas number: 188425-85-6)



Chemical Formula: $C_{18}H_{12}Cl_2N_2O$
Exact Mass: 342.0327

General procedure I was followed using 159.1 mg of 2-chloronicotinic acid (99 wt%, 1.0 mmol, 1.0 eq.) and 428.8 mg 2-amino-4'-chlorobiphenyl (95 wt%, 2.0 mmol, 2.0 eq.) in Chamber B. Reaction was stirred at room temperature for 18 hours. Without extraction, the crude reaction mixture was purified by column chromatography on silica gel directly ($\mathbf{R}_f$ = 0.20, *n*-heptane/ethyl acetate = 2/1). The title compound was obtained as yellowish solid (238.6 mg, 70%). **Melting point** = 143.0–143.6 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 (dd, *J* = 4.7, 1.9 Hz, 1H), 8.31 (d, *J* = 8.2 Hz, 1H), 8.22 (s, 1H), 8.03 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.44–7.38 (m, 3H), 7.33–7.24 (m, 5H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.50, 151.00, 146.58, 139.70, 136.25, 134.19, 134.15, 132.46, 131.05, 130.65, 130.11, 129.07, 128.69, 125.33, 122.67, 122.38 ppm. These data are in agreement with literature data[27].

(3,4-dihydroisoquinolin-2(1H)-yl)(thiophen-2-yl)methanone (compound 40, cas number: 349097-64-9)

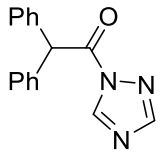


Chemical Formula: $C_{14}H_{13}NOS$

Exact Mass: 243.0718

General procedure I was followed using 129.4 mg of 2-thiophenecarboxylic acid (99 wt%, 1.0 mmol, 1.0 eq.) and 280.4 mg 1,2,3,4-tetrahydroisoquinoline (95 wt%, 2.0 mmol, 2.0 eq.) in Chamber B. Reaction was stirred at room temperature for 5 hours. During extraction procedure, the mixture was washed sequentially with NH_4Cl (sat.) (1 x 20 mL) and brine (1 x 20 mL). The crude reaction mixture was purified by column chromatography on silica gel directly ($\mathbf{R}_f$ = 0.35, *n*-heptane/ethyl acetate = 2/1). The title compound was obtained as yellowish oil (183.8 mg, 76%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44–7.42 (m, 1H), 7.37–7.36 (m, 1H), 7.19–7.13 (m, 3H), 7.09 (br s, 1H), 7.07–7.04 (m, 1H), 4.85 (s, 2H), 3.93–3.89 (m, 2H), 2.93 (t, *J* = 5.9 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.65, 137.40, 134.27, 132.80, 128.71, 128.66, 128.49, 126.62, 126.36, 126.21, 47.33 (br s), 43.76 (br s), 28.97 ppm. These data are in agreement with literature data[28].

2,2-diphenyl-1-(1H-1,2,4-triazol-1-yl)ethan-1-one (compound 41, cas number: 80928-24-1)

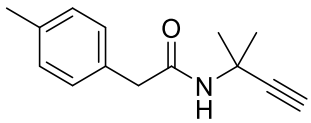


Chemical Formula: $C_{16}H_{13}N_3O$

Exact Mass: 263.1059

General procedure I was followed using 216.6 mg of diphenylacetic acid (98+ wt%, 1.0 mmol, 1.0 eq.) and 138.8 mg 1,2,4-triazole (99.5 wt%, 2.0 mmol, 2.0 eq.) in Chamber B. Reaction was stirred at room temperature for 5 hours. During extraction procedure, the mixture was washed sequentially with NH_4Cl (sat.) (1 x 20 mL) and brine (1 x 20 mL). The crude reaction mixture was purified by column chromatography on silica gel directly ($\mathbf{R}_f$ = 0.35, *n*-heptane/ethyl acetate = 2/1). Then the product was extracted with $NaHCO_3$ (sat.) (1 x 20 mL) and ethyl acetate (1 x 20 mL). The title compound was obtained as white solid (217.3 mg, 83%). **Melting point** = 75.0–78.0 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.91 (s, 1H), 7.96 (s, 1H), 7.39–7.37 (m, 4H), 7.33–7.29 (m, 4H), 7.27–7.23 (m, 2H), 6.36 (s, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.53, 152.90, 143.99, 136.80, 128.76, 128.74, 128.61, 128.42 127.69, 127.05, 54.93 ppm. These data are in agreement with literature data[6].

N-(2-methylbut-3-yn-2-yl)-2-(p-tolyl)acetamide (compound 42, cas number: 1488858-94-1)

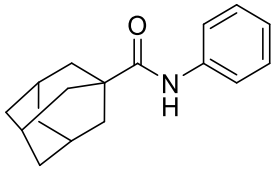


Chemical Formula: $C_{14}H_{17}NO$

Exact Mass: 215.1310

General procedure I was followed using 151.7 mg of *p*-tolylacetic acid (99 wt%, 1.0 mmol, 1.0 eq.) and 0.22 mL 2-methyl-3-butyn-2-amine (95 wt%, 175.0 mg, 2.0 mmol, 2.0 eq.) in Chamber B. Reaction was stirred at room temperature for 18 hours. During extraction procedure, the mixture was washed sequentially with 1 M HCl (1 x 20 mL), $NaHCO_3$ (sat.) (1 x 20 mL) and brine (1 x 20 mL). The crude reaction mixture was purified by column chromatography on silica gel directly ($\mathbf{R}_f$ = 0.15, *n*-heptane/ethyl acetate = 2/1). The title compound was obtained as white solid (141.8 mg, 66%). **Melting point** = 115.0–123.5 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.16–7.11 (m, 4H), 5.59 (br s, 1H), 3.49 (s, 2H), 2.34 (s, 3H), 2.30 (s, 1 H), 1.56 (s, 6 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.21, 136.81, 131.72, 129.58, 129.36, 129.25, 129.12, 86.97, 69.02, 47.46, 43.87, 28.75, 21.00 ppm. These data are in agreement with literature data[6].

(3r,5r,7r)-N-phenyladamantane-1-carboxamide (compound 43, cas number: 3796-79-0)



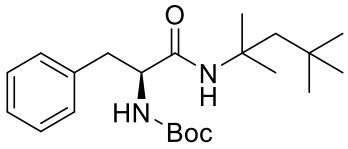
Chemical Formula: $C_{17}H_{21}NO$

Exact Mass: 255.1623

General procedure I was followed using 180.3 mg of 1-adamantanecarboxylic acid (99 wt%, 1.0 mmol, 1.0 eq.) and 0.18 mL aniline (99 wt%, 186.6 mg, 2.0 mmol, 2.0 eq.) in Chamber B. Reaction was stirred at room temperature for 5 hours. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R}_f$ = 0.30, *n*-heptane/ethyl acetate = 10/1). The title compound was obtained as white solid (235 mg, 92%). **Melting point** = 183.0–186.0 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54–7.51 (m, 2H), 7.34 (br s, 1H), 7.32–

7.27 (m, 2H), 7.10–7.05 (m, 1H), 2.09 (s, 3H), 1.96 (d, *J* = 2.7 Hz, 6H), 1.79–1.71 (m, 6H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.98, 138.05, 128.83, 124.00, 119.95, 41.43, 39.22, 36.39, 28.11 ppm. These data are in agreement with literature data[27].

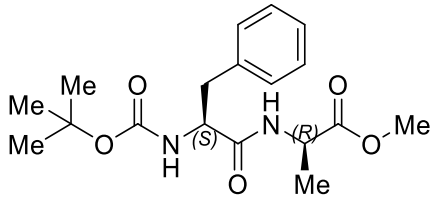
tert-butyl (S)-(1-oxo-3-phenyl-1-((2,4,4-trimethylpentan-2-yl)amino)propan-2-yl)carbamate (compound 44, new compound)



Chemical Formula: $C_{22}H_{36}N_2O_3$
Exact Mass: 376.2726

General procedure I was followed using 268.0 mg of Boc-Ph-OH (99 wt%, 1.0 mmol, 1.0 eq.) and 0.32 mL tert-octylamine (99 wt%, 261.1 mg, 2.0 mmol, 2.0 eq.) in Chamber B. Reaction was stirred at room temperature for 18 hours. Without extraction, the crude reaction mixture was purified by column chromatography on silica gel directly (R_f = 0.30, *n*-heptane/ethyl acetate = 5/1). The title compound was obtained as white solid (316.3 mg, 84%). **Melting point** = 128.0–129.0 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30–7.20 (m, 5H), 5.63 (br s, 1H), 5.22 (t, *J* = 8.2 Hz, 1H), 4.18 (q, *J* = 7.0 Hz, 1H), 3.05–2.97 (m, 2H), 1.67 (d, *J* = 14.8 Hz, 1H), 1.47 (s, 1H), 1.41 (s, 9H), 1.31 (s, 3H), 1.26 (s, 3H), 0.90 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.66, 155.27, 137.10, 129.35, 128.47, 126.68, 79.77, 56.54, 55.09, 52.16, 38.56, 31.39, 31.27, 28.54, 28.47, 28.18 ppm. **IR** (neat) $\tilde{\nu}$ = 3305 (m, N–H stretching) , 2974 (m, N–H stretching), 1687(s, C=O stretching), 1655(s, C=O stretching) cm^{-1}. **HRMS** (ESI) *m/z*: Calcd for $C_{22}H_{37}N_2O_3$ $[M+H]^+$: 377.2799, found: 377.2804. **Chiral-HPLC** (Daicel Chiralpak AD-3_n-hexane/iPrOH = 95:5, flow rate 1.0 mL/min, detection at 250 nm and 273 nm): t_R = 13.0 min, t_R = 26.3 min; 40% ee was detected.

methyl (tert-butoxycarbonyl)-L-phenylalanyl-D-alaninate (compound 45, cas number: 15136-30-8)

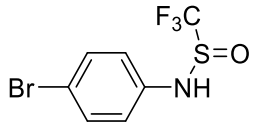


Chemical Formula: $C_{18}H_{26}N_2O_5$
Exact Mass: 350.1842

General procedure I was followed using 268 mg of Boc-*L*-phenylalanine (99.0 wt%, 1.0 mmol, 1.0 eq.) and 285 mg *D*-Alanine methyl ester hydrochloride (98 wt%, 2.0 mmol, 2.0 eq.) in Chamber B. Reaction was stirred at room temperature for 24 hours. The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.25, *n*-heptane/ethyl acetate = 3/1). The title compound was obtained as white solid (345mg, 98%). **Melting point** = 88.5–89.0 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29–7.20 (m, 5H), 6.81 (br s, 0.0682 H, NH), 6.63 (br s, 0.8950 H, NH) (according to the ratio of integration area, the *dr.* value would be 92:8), 5.35 (d, *J* = 8.1 Hz, 1H), 4.55–4.47 (m, 1H), 4.44 (s, 1H), 3.69 (s, 3H), 3.06 (d, *J* = 5.5 Hz, 2H), 1.39 (d, *J* = 1.6 Hz, 9H), 1.34 (d, *J* = 7.1 Hz, 0.2888 H), 1.24 (d, *J* = 6.6 Hz, 2.9733 H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.90, 170.71, 155.26, 126.63, 129.25, 129.20, 128.39, 126.67, 79.82, 55.51, 52.22, 47.88, 47.72, 38.62, 38.29, 28.09, 17.95, 17.83 ppm. These data are in agreement with literature data[29]

7.6. Experimental Data of Synthesized Trifluoromethanesulfinamides, Sulfonimidoyl Fluoride and Triflimidates

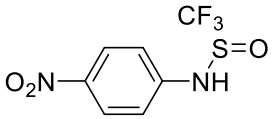
N-(4-bromophenyl)-1,1,1-trifluoromethanesulfinamide (compound S1) (cas number: 868395-08-8)



Chemical Formula: $C_7H_5BrF_3NOS$
Exact Mass: 286.9227

General procedure J1 was followed using 1.053 g of 4-bromoaniline (98 wt%, 6.0 mmol, 1.0 eq.). Reaction was stirred at room temperature for 1 h. The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.30, n-heptane/ethyl acetate = 7/1). The title compound was obtained as yellowish solid (987.7 mg, 57%). **Melting point** = 95.8–96.6 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 11.8 Hz, 2H), 7.01 (d, *J* = 11.7 Hz, 2H), 6.32 (br s, 1H, amine) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.04, 132.91, 122.14, 120.41 (q, $^1J_{CF}$ = 322.3 Hz, CF_3), 118.73 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -78.19 (s, 3F) ppm. These data are in agreement with literature data[8]

1,1,1-trifluoro-N-(4-nitrophenyl)methanesulfinamide (compound S2) (new compound)

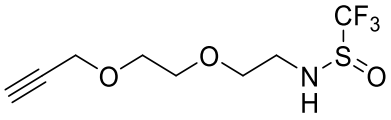


Chemical Formula: $C_7H_5F_3N_2O_3S$

Exact Mass: 253.9973

General procedure J1 was followed using 0.846 g of 4-nitroaniline (98 wt%, 6.0 mmol, 1.0 eq.). Reaction was stirred at room temperature for 30 min. The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.30, n-heptane/ethyl acetate = 3/1). The title compound was obtained as yellow solid (1.220 g, 80%). **Melting point** = 105.0–106.5 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.01 (s, 1H), 8.24 (dt, *J* = 10.2, 2.7 Hz, 2H), 7.39 (dt, *J* = 10.2, 2.7 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, DMSO-d_6) δ 146.34, 142.57, 125.70, 123.92 (q, $^1J_{CF}$ = 338.4 Hz, CF_3), 117.52 ppm. **^{19}F NMR** (377 MHz, DMSO-d_6) δ -75.51 (s, 3F) ppm. **IR** (neat) $\tilde{\nu}$ = 3407 (br, N–H stretching), 1148 (vs, C–F stretching), 1053 (vs, S=O stretching) cm^{-1}. **HRMS** (APCI) *m/z*: Calcd for $C_7H_4F_3N_2O_3S$ [*M*-H]$^+$: 252.9900, found: 252.9911.

1,1,1-trifluoro-N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)methanesulfinamide (compound S3) (new compound)



Chemical Formula: $C_8H_{12}F_3NO_3S$

Exact Mass: 259.0490

General procedure A was followed using 0.877 g of 2-[2-(2-propynyloxy)ethoxy]ethylamine (6.0 mmol, 1.0 equiv). Reaction was stirred for 1 h at room temperature. The crude reaction mixture was purified by column chromatography on silica gel (n-heptane/ethyl acetate = 1/1). The title compound was obtained as yellow oil (0.683 g, 44%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.30 (s, 1H, NH), 4.21 (d, *J* = 2.4 Hz, 2H, CH_2), 3.72–3.59 (m, 6H, CH_2), 3.55–3.3.47 (m, 1H), 3.37–3.30 (m, 1H), 2.48 (t, *J* = 4.4 Hz, 1H, C≡CH) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 123.63 (q, $^1J_{CF}$ = 336.30 Hz, CF_3), 79.24, 74.73, 70.27, 70.06, 68.87, 58.23, 41.47 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -77.55 (s, 3F) ppm. **IR** (neat) $\tilde{\nu}$ = 3253 (br, N–H stretching), 2117 (w, C≡C stretching), 1172 (vs, C–F stretching), 1154 (s, aliphatic ether C–O stretching), 1136 (s, aliphatic ether C–O stretching), 1072 (s, S=O stretching) cm^{-1}. **HRMS** (ESI) m/z: Calcd for $C_8H_{12}F_3NNaO_3S$ [*M*+Na]$^+$: 282.0382, found: 282.0381.

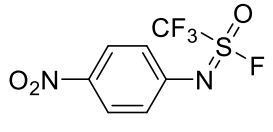
N-(4-bromophenyl)-1,1,1-trifluoromethanesulfonimidoyl fluoride (compound S4) (cas number: 2273795-55-2)

Chemical Formula: $C_7H_4BrF_4NOS$

Exact Mass: 304.9133

General procedure J2 was followed using 0.9154 g of N-(4-bromophenyl)-triflinamide (>99 wt%, 3.2 mmol, 1.0 eq.), 0.467 g N-chlorosuccinimide (NCS, 98 wt%, 3.5 mmol, 1.1 eq.) and 3.50 mL tetra-n-butylammonium fluoride (TBAF, 1 M in THF, 3.5 mmol, 1.1 eq.). Reaction was stirred at room temperature for 30 min. The crude reaction mixture was purified by column chromatography on silica gel (**R_f** = 0.30, n-heptane/ethyl acetate = 20/1). The title compound was obtained as orange oil (0.743 g, 76%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 11.3 Hz, 2H, ArH), 7.02 (d, *J* = 11.0 Hz, 2H, ArH) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 134.87 (d, $^3J_{CF}$ = 8.9 Hz), 132.69 (d, $^6J_{CF}$ = 1.2 Hz), 125.35 (d, $^4J_{CF}$ = 6.7 Hz), 119.21 (d, $^5J_{CF}$ = 2.6 Hz), 118.00 (qd, *J* = 372.3, 76.6 Hz, CF_3) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ 60.04 (q, *J* = 16.2 Hz, 1F), -72.91 (d, *J* = 16.2 Hz, 3F) ppm. **IR** (neat) $\tilde{\nu}$ = 1217 (vs, C–F stretching), 1067 (S=O stretching), 643 (s, C–Br stretching) cm^{-1}. **HRMS** (APCI) *m/z*: Calcd for $C_7H_5BrF_4NOS$ [*M*+H]$^+$: 305.9206 found 306.1361.

1,1,1-trifluoro-N-(4-nitrophenyl)methanesulfonimidoyl fluoride (compound S5) (new compound)



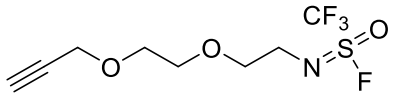
Chemical Formula: $C_7H_4F_4N_2O_3S$

Exact Mass: 271.9879

General procedure J2 was followed using 1.220 g of N-(4-nitrophenyl)-triflinamide (>99 wt%, 4.8 mmol, 1.0 eq.), 0.719 g N-chlorosuccinimide (NCS, 98 wt%, 5.28 mmol, 1.1 eq.) and 5.28 mL tetra-n-butylammonium fluoride (TBAF, 1 M in THF, 5.28 mmol, 1.1 eq.). Reaction was stirred at room temperature for 15 min. The crude reaction mixture was purified by column chromatography on silica gel (**R_f** = 0.30, n-heptane/ethyl acetate = 20/1). The title compound was obtained as orange oil (0.682 g, 52%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.26–8.22 (m, 2H, ArH), 7.32–7.28 (m, 2H, ArH) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.38, 141.82 (d, $^3J_{CF}$ = 6.3 Hz), 125.31 (d, $^5J_{CF}$ = 1.1 Hz), 124.37 (d, $^4J_{CF}$ = 4.9 Hz), 118.00 (qd, $^1J_{CF}$ = 319.11, 61.45 Hz, CF_3) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ 58.98 (q, *J*

= 16.4 Hz, 1F), -72.76 (d, *J* = 16.4 Hz, 3F) ppm. **IR** (neat) ṽ = 1521 (s, nitro compound N–O stretching), 1218 (vs, C–F stretching), 1078 (S=O stretching) cm^{-1}. **HRMS** (APCI) m/z: Calcd for $C_7H_5F_4N_2O_3S$ [*M*+H]$^+$: 272.9951, found: 272.9938.

1,1,1-trifluoro-N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)methanesulfonimidoyl fluoride (compound S6, new compound)

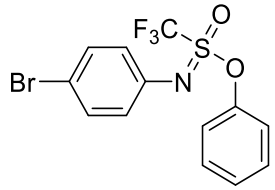


Chemical Formula: $C_8H_{11}F_4NO_3S$

Exact Mass: 277.0396

General procedure J2 was followed using 1.220 g of N-(4-nitrophenyl)-triflinamide (>99 wt%, 4.8 mmol, 1.0 eq.), 0.719 g N-chlorosuccinimide (NCS, 98 wt%, 5.28 mmol, 1.1 eq.) and 5.28 mL tetra-n-butylammonium fluoride (TBAF, 1 M in THF, 5.28 mmol, 1.1 eq.). Reaction was stirred at room temperature for 15 min. The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.30, n-heptane/ethyl acetate = 20/1). The title compound was obtained as yellowish oil (0.682 g, 52%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.21 (d, *J* = 2.3 Hz, 2H), 4.21–3.49 (m, 8H), 2.44 (t, *J* = 2.2 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 117.84 (dq, *J* = 318.7, 67.3 Hz, CF_3), 79.49, 74.44, 70.27, 69.94 (d, $^3J_{CF}$ = 6.6 Hz), 69.02, 58.40, 44.59 (d, $^4J_{CF}$ = 4.9 Hz) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ 64.88 (q, *J* = 16.7 Hz, 1F), -74.10 (d, *J* = 16.7 Hz, 3F) ppm. **IR** (neat) ṽ = 2118 (w, C≡C stretching), 1210 (vs, C–F stretching), 1137 (s, aliphatic ether C–O stretching), 1104 (s, aliphatic ether C–O stretching), 1034 (S=O stretching) cm^{-1}. **HRMS** (ESI) m/z: Calcd for $C_8H_{11}F_4NNaO_3S$ [*M*+Na]$^+$: 300.0288, found: 300.0284.

phenyl N-(4-bromophenyl)trifluoromethanesulfonimidate (compound 46, new compound)

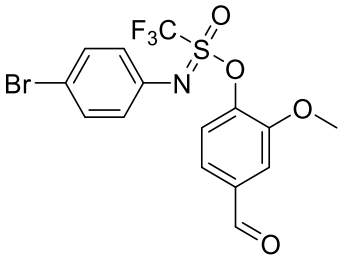


Chemical Formula: $C_{13}H_9BrF_3NO_2S$

Exact Mass: 378.9489

General procedure J3 was followed using 63 mg of *N*-(4-bromophenyl)-triflimidoyl fluoride (>99.5 wt%, 0.2 mmol, 1.0 eq.) and 29 mg phenol (99 wt%, 0.3 mmol, 1.5 eq.). Reaction was stirred at room temperature for 1 h. The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.35, n-heptane/MTBE = 50/1). The title compound was obtained as yellow oil (58.3 mg, 77%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44–7.32 (m, 5H, ArH), 7.25–7.22 (m, 2H, ArH), 6.90–6.87 (m, 2H, ArH) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.11, 137.71, 132.29, 130.09, 127.96, 125.40, 122.15, 117.60, 119.19 (q, $^1J_{CF}$ = 324.1 Hz, CF_3) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -74.07 (s, 3F) ppm. **IR** (neat) ṽ = 1202 (vs, C–F stretching), 1079 (m, S=O stretching), 686 (s, C–Br stretching) cm^{-1}. **HRMS** (APCI) m/z: Calcd for $C_{13}H_8BrF_3NNa_2O_2S$ [*M*+2Na-H]$^+$: 423.9202, found 424.4567.

4-formyl-2-methoxyphenyl N-(4-bromophenyl)trifluoromethanesulfonimidate (compound 47, new compound)



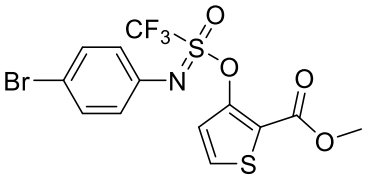
Chemical Formula: $C_{15}H_{11}BrF_3NO_4S$

Exact Mass: 436.9544

General procedure J3 was followed using 68.5 mg of *N*-(4-bromophenyl)-triflimidoyl fluoride (>99.5 wt%, 0.22 mmol, 1.0 eq.) and 36.5 mg vanillin (99 wt%, 0.24 mmol, 1.1 eq.). Reaction was stirred at room temperature for 1 h. The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.28, *iso*-hexane/ethyl acetate = 4/1). The title compound was obtained as brown oil (64.7 mg, 67%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.96 (s, 1H, carbonyl), 7.50 (dd, *J* = 8.1, 1.8 Hz, 1H, aromatic), 7.43 (d, *J* = 1.8 Hz, 1H, aromatic), 7.40–7.35 (m, 3H, aromatic), 6.95–6.91 (m, 2H, aromatic), 3.65 (s, 3H, methyl) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.54 (C=O), 171.21, 152.50, 143.51, 137.56, 136.31, 132.12, 125.54, 124.37, 123.54, 117.68, 111.13, 118.93 (q, $^1J_{CF}$ = 322.0 Hz, CF_3), 55.96 (CH_3) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -74.82 (s, 3F) ppm. **IR** (neat) ṽ = 1705 (s, aldehyde C=O stretching), 1275 (s, alkyl aryl ether C–O stretching), 1204 (vs, C–F stretching), 1078 (m, S=O stretching), 689 (s, C–Br stretching) cm^{-1}. **HRMS** (APCI) m/z: Calcd for $C_{15}H_9BrF_3NO_4S$ [*M*-2H]$^{2-}$: 217.4700 found 217.9114.

**Note: solvent are present in the ^{1}H NMR spectra, this is taken into account when determining the reported isolated yield and is left as such as the compound is rather small scale and unstable.*

methyl 3-((N-(4-bromophenyl)-S-(trifluoromethyl)sulfonimidoyl)oxy)thiophene-2-carboxylate (compound 48, new compoound)

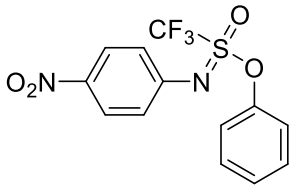


Chemical Formula: $C_{13}H_9BrF_3NO_4S_2$

Exact Mass: 442.9108

General procedure J3 was followed using 61 mg of *N*-(4-bromophenyl)-triflimidoyl fluoride (>99.5 wt%, 0.2 mmol, 1.0 eq.) and 38 mg phenol (99 wt%, 0.24 mmol, 1.2 eq.). Reaction was stirred at room temperature for 3 h (60% yield determined by ^{19}F NMR). The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.23, *iso*-hexane/ethyl acetate = 10/1). The title compound was obtained as brown oil (44.5 mg, 50%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 5.5 Hz, 1H, aromatic), 7.39–7.35 (m, 2H, aromatic), 7.00 (d, *J* = 5.5 Hz, 1H, aromatic), 6.92–6.89 (m, 2H, aromatic), 3.66 (s, 3H, CH_3) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.16 (C=O), 160.30, 146.73, 137.27, 132.22, 130.22, 125.46, 123.06, 122.52,119.18, 117.82, 119.08 (q, $^1J_{CF}$ = 323.2 Hz, CF_3), 52.25 (methyl) ppm. ^{19}F NMR (377 MHz, $CDCl_3$) δ -74.23 (s, 3F) ppm. **IR** (neat) ṽ = 1714 (s, ester C=O stretching), 1210 (vs, C–F stretching), 1158 (s, ester C–O stretching), 1064 (s, S=O stretching), 652 (s, C–Br stretching) cm^{-1}. **HRMS** (APCI) m/z: Calcd for $C_{13}H_9BrF_3NNaO_4S_2$ [*M*+Na]$^+$: 465.9001, found: 466.1741.

phenyl trifluoro-N-(4-nitrophenyl)methanesulfonimidate (compound 49, new compound)



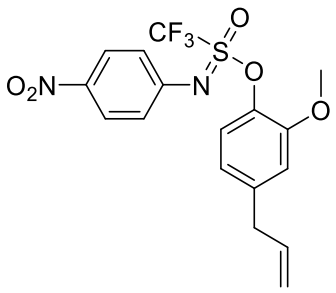
Chemical Formula: $C_{13}H_9F_3N_2O_4S$

Exact Mass: 346.0235

General procedure J3 was followed using 54.5 mg of *N*-(4-nitrophenyl)-triflimidoyl fluoride (>99.5 wt%, 0.2 mmol, 1.0 eq.) and 28.5 mg phenol (99 wt%, 0.3 mmol, 1.5 eq.). Reaction was stirred at room temperature for 1 h (96% yield determined by ^{19}F NMR). The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.30, n-heptane/ethyl acetate = 20/1). The title compound was obtained as yellow oil (65.1 mg, 94%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14–8.12 (m, 2H), 7.46–7.42 (m, 2H), 7.40–7.36 (m, 1H), 7.28–7.25 (m, 2H), 7.12 (dt, *J* = 9.6, 2.6 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.78, 145.28, 144.23, 130.25, 128.32, 125.04, 123.90, 122.03,119.20 (q, $^1J_{CF}$ = 329.8 Hz) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -74.08 (s, 3F) ppm. **IR** (neat) ṽ = 1516 (s, nitro compound N–O stretching), 1202 (vs, C–F stretching), 1067 (m, S=O stretching) cm^{-1}. **HRMS** (APCI) m/z: Calcd for $C_{13}H_{10}F_3N_2O_4S$ [*M*+H]$^+$: 347.0308, found: 347.0311.

Large-scale reaction: procedure M was followed using 573.0 mg of *N*-(4-nitrophenyl)-triflimidoyl fluoride (99.9 wt%, 2.0 mmol, 1.0 eq.) and 285.2 mg phenol (99 wt%, 3.0 mmol, 1.5 eq.). Reaction was stirred at room temperature for 1 h (96% yield determined by ^{19}F NMR). The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.30, n-heptane/ethyl acetate = 20/1). The title compound was obtained as yellow oil (564.8 mg, 82%).

4-allyl-2-methoxyphenyl trifluoro-N-(4-nitrophenyl)methanesulfonimidate (compound 50, new compound)



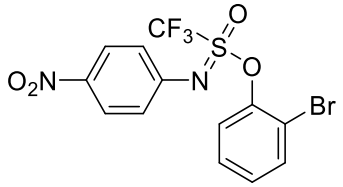
Chemical Formula: $C_{17}H_{15}F_3N_2O_5S$

Exact Mass: 416.0654

General procedure J3 was followed using 54.5 mg of *N*-(4-nitrophenyl)-triflimidoyl fluoride (>99.5 wt%, 0.2 mmol, 1.0 eq.) and 49.8 mg eugenol (99 wt%, 0.3 mmol, 1.5 eq.). Reaction was stirred at room temperature for 1 h (80% yield determined by ^{19}F NMR). The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.15, n-heptane/ethyl acetate = 30/1). The title compound was obtained as brown oil (59.9 mg, 72%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 (dt, *J* = 9.7, 2.6 Hz, 2H), 7.17 (dt, *J* = 9.7, 2.6 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 1H), 6.80 (dd, *J* = 8.2, 1.9 Hz, 1H), 6.74 (d, *J* = 1.8 Hz, 1H), 5.96–5.88 (m, 1H), 5.14–5.07 (m, 2H), 3.61 (s, 3H), 3.38 (d, *J* = 6.7 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.24, 145.73, 143.98, 141.57, 137.07, 136.27, 124.73, 124.11, 122.49, 120.95, 118.97 (q, $^1J_{CF}$ = 322.5 Hz), 116.72, 112.90, 55.61, 39.95 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -74.96 (s, 3F) ppm. **IR** (neat) ṽ =

1602 (m, C=C stretching), 1515 (s, nitro compound N–O stretching), 1203 (vs, C–F stretching), 1177 (s, C–O stretching), 1067 (m, S=O stretching) cm^{-1}. **HRMS** (ESI) m/z: Calcd for $C_{17}H_{16}F_3N_2O_5S$ [*M*+H]$^+$: 417.0727, found: 417.0733.

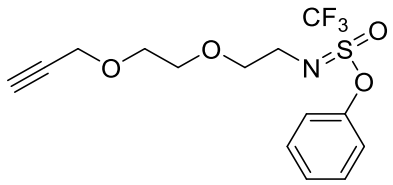
2-bromophenyl trifluoro-N-(4-nitrophenyl)methanesulfonimidate (compound 51, new compound)



Chemical Formula: $C_{13}H_8BrF_3N_2O_4S$
Exact Mass: 423.9340

General procedure J3 was followed using 54.5 mg of *N*-(4-nitrophenyl)-triflimidoyl fluoride (>99.5 wt%, 0.2 mmol, 1.0 eq.) and 53.0 mg 2-bromophenol (98 wt%, 0.3 mmol, 1.5 eq.). Reaction was stirred at room temperature for 1 h (>99% yield determined by ^{19}F NMR). The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.2, n-heptane/ethyl acetate = 50/1). The title compound was obtained as yellow oil (68.4 mg, 80%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.6 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.42–7.36 (m, 2H), 7.27–7.22 (m, 1H), 7.13 (dt, *J* = 9.6, 2.4 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 146.73, 144.81, 144.39, 134.34, 129.33, 129.07, 124.93, 124.16, 123.60, 119.04 (q, $^1J_{CF}$ = 323.7 Hz), 116.69 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -74.29 (s, 3F) ppm. **IR** (neat) $\tilde{\nu}$ = 1516 (s, nitro compound N–O stretching), 1204 (vs, C–F stretching), 1069 (m, S=O stretching), 698 (s, C–Br stretching) cm^{-1}. **HRMS** (ESI) m/z: Calcd for $C_{13}H_9BrF_3N_2O_4S$ [*M*+H]$^+$: 424,9413, found: 424.9460.

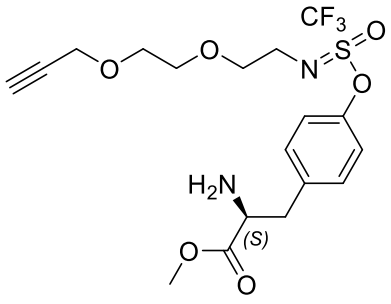
phenyl trifluoro-N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)methanesulfonimidate (compound 52, new compound)



Chemical Formula: $C_{14}H_{16}F_3NO_4S$
Exact Mass: 351.0752

A 10 mL small glass tube was filled with 55.4 mg 2-[2-(2-propyn-1-yloxy)ethoxy]ethyl-triflimidoyl fluoride (>99.5 wt%, 0.2 mmol, 1.0 eq.) and 28.5 mg phenol (0.3 mmol, 1.5 eq.). Then the acetonitrile (MeCN, 0.6 mL), H_2O (0.2 mL), trifluorotoluene (99 wt%, 25 μL, 1.0 mmol) as an internal standard and 46.4 mg 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU, 98 wt%, 0.3 mmol, 1.5 eq.) as base were followed. Finally, the vessel was closed and was stirred at 50 °C for 1 h (96% yield determined by ^{19}F NMR). The content was transferred to a 25 mL separatory funnel. The glass tube was rinsed five times with 5 mL of EtOAc; the fractions were collected in the same funnel. The mixture was extracted with H_2O (1 x 5 mL) and EtOAc (3 x 5 mL). The combined organic layers were washed with brine (1 x 5 mL), dried over anhydrous Na_2SO_4 and then concentrated *in vacuo* to give the crude product. The crude reaction mixture was purified by column chromatography on silica gel ($\mathbf{R_f}$ = 0.15, n-heptane/ethyl acetate = 20/1). The title compound was obtained as yellowish oil (52.1 mg, 74%).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43–7.39 (m, 2H), 7.33–7.30 (m, 1H), 7.28–7.26 (m, 2H), 4.18 (d, *J* = 2.4 Hz, 2H), 3.67–3.59 (m, 4H), 3.56–3.47 (m, 4H), 2.42 (t, *J* = 2.4 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.13, 129.80, 129.51, 122.23, 119.24 (q, $^1J_{CF}$ = 324.5 Hz), 79.55, 74.46, 71.12, 70.15, 69.00, 58.34, 44.25 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -74.75 (s, 3F) ppm. **IR** (neat) $\tilde{\nu}$ = 2118 (w, C≡C stretching), 1194 (vs, C–F stretching), 1137(s, aliphatic ether C–O stretching), 1102 (s, aliphatic ether C–O stretching), 1025 (m, S=O stretching) cm^{-1}. **HRMS** (APCI) m/z: Calcd for $C_{14}H_{17}F_3NO_4S$ [*M*+H]$^+$: 352.0825, found: 352.0817.

methyl (2S)-2-amino-3-(4-((N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)-S-(trifluoromethyl)sulfonimidoyl)oxy)phenyl)propanoate (compound 53, new compound)

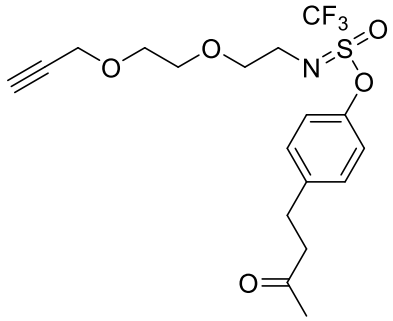


Chemical Formula: $C_{18}H_{23}F_3N_2O_6S$
Exact Mass: 452.1229

A 10 mL small glass tube was filled with 55.4 mg 2-[2-(2-propyn-1-yloxy)ethoxy]ethyl-triflimidoyl fluoride (>99.5 wt%, 0.2 mmol, 1.0 eq.) and 59.7 mg *L*-tyrosine methyl ester (0.3 mmol, 1.5 eq.). Then the acetonitrile (MeCN, 0.6 mL), H_2O (0.2 mL), trifluorotoluene (99 wt%, 25 μL, 1.0 mmol) as an internal standard and 46.4 mg 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU, 98 wt%, 0.3 mmol, 1.5 eq.) as base

were followed. Finally, the vessel was closed and was stirred at 50 °C for 1 h (81% yield determined by ^{19}F NMR). The content of glass tube was transferred to a baker with anhydrous Na_2SO_4 to dried over directly without extraction to give the crude product. The crude reaction mixture was purified by column chromatography on silica gel (**R_f** = 0.25, ethyl acetate). The title compound was obtained as yellow oil (57.2 mg, 61%).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28–7.17 (m, 4H), 4.18 (d, *J* = 2.4 Hz, 2H), 3.74–3.71 (m, 4H), 3.68–3.60 (m, 4H), 3.55–3.48 (m, 4H), 3.08 (dd, *J* = 13.6, 5.3 Hz, 1H), 2.89 (dd, *J* = 13.7, 7.8 Hz, 1H), 2.44 (t, *J* = 2.3 Hz, 1H), 1.75 (br s, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.10,148.03, 148.02, 136.75, 130.60, 122.24, 119.22 (q, $^1J_{CF}$ = 324.6 Hz), 115.54, 79.55, 74.50, 71.09, 70.14, 69.00, 58.33, 55.59, 51.99, 44.24, 40.28 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -74.6402 (s, 3F, one of enantiomers), -74.6451 (s, 3F, one of enantiomers) ppm. **IR** (neat) ṽ = 3293 (br, N–H stretching), 2110 (w, C≡C stretching), 1736 (s, ester C=O stretching), 1193 (vs, C–F stretching), 1138 (s, aliphatic ether C–O stretching), 1101 (s, aliphatic ether C–O stretching), 1030 (m, S=O stretching) cm^{-1}. **HRMS** (ESI) m/z: Calcd for $C_{18}H_{24}F_3N_2O_6S$ [*M*+H]$^+$: 453.1302, found: 453.1288.

4-(3-oxobutyl)phenyl trifluoro-N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)methanesulfonimidate (compound 54, new compound)



Chemical Formula: $C_{18}H_{22}F_3NO_5S$
Exact Mass: 421.1171

A 10 mL small glass tube was filled with 55.4 mg 2-[2-(2-propyn-1-yloxy)ethoxy]ethyl-triflimidoyl fluoride (>99.5 wt%, 0.2 mmol, 1.0 eq.) and 50.3 mg 4-(4-hydroxyphenyl)-2-butanone (0.3 mmol, 1.5 eq.). Then the acetonitrile (MeCN, 0.6 mL), H_2O (0.2 mL), trifluorotoluene (99 wt%, 25 μL, 1.0 mmol) as an internal standard and 46.4 mg 1,8-Diazabicyclo[5,4,0]undec-7-ene (DBU, 98 wt%, 0.3 mmol, 1.5 eq.) as base were followed. Finally, the vessel was closed and was stirred at 50 °C for 1 h (89% yield determined by ^{19}F NMR). The content of glass tube was transferred to a baker with anhydrous Na_2SO_4 to dried over directly without extraction to give the crude product. The crude reaction mixture was purified by column chromatography on silica gel (**R_f** = 0.2, n-heptane/ethyl acetate = 2/1). The title compound was obtained as yellow oil (68.7 mg, 81%).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23–7.16 (m, 4H), 4.18 (d, *J* = 2.4 Hz, 2H), 3.68–3.60 (m, 4H), 3.55–3.47 (m, 4H), 2.90 (t, *J* = 7.4 Hz, 2H), 2.76 (t, *J* = 7.4 Hz, 2H), 2.43 (t, *J* = 2.4 Hz, 1H), 2.15 (s, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.32, 147.41, 140.45, 129.66, 129.31, 122.18, 119.25 (q, $^1J_{CF}$ = 324.6 Hz), 115.29, 79.56, 74.50, 71.14, 70.17, 69.02, 58.36, 44.78, 44.24, 30.03, 28.88 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -74.66 (s, 3F) ppm. **IR** (neat) ṽ = 2115 (w, C≡C stretching), 1715 (s, C=O stretching), 1193 (vs, C–F stretching), 1138 (s, aliphatic ether C–O stretching), 1102 (s, aliphatic ether C–O stretching), 1035 (m, S=O stretching) cm^{-1}. **HRMS** (ESI) m/z: Calcd for $C_{18}H_{23}F_3NO_5S$ [*M*+H]$^+$: 422.1243, found: 422.1250.

Unsuccessful substrates:

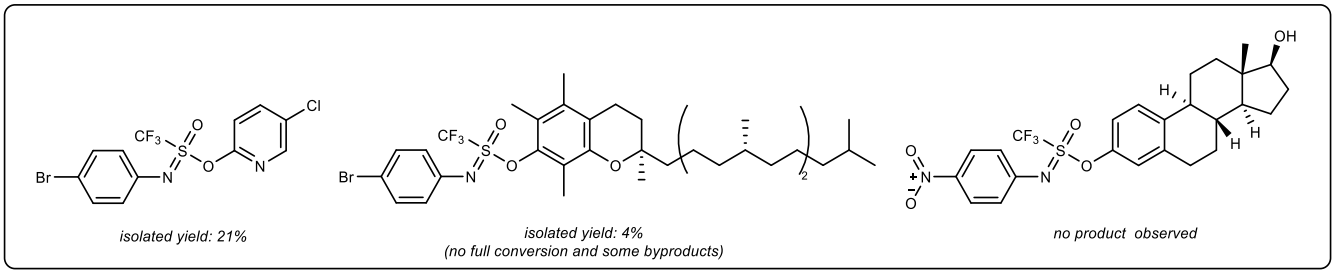
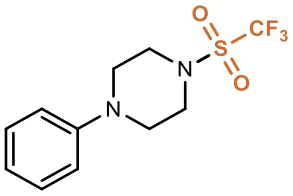


Figure S3. Unsuccessful targeted products

7.7. Experimental Data of Synthesized Triflamides

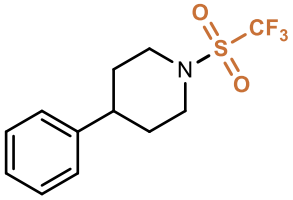
1-phenyl-4-((trifluoromethyl)sulfonyl)piperazine (compound 55, new compound)



Chemical Formula: $C_{11}H_{13}F_3N_2O_2S$
Exact Mass: 294,06498

General procedure K was followed using 166 mg of 1-phenylpiperazine (97 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 18 hours (>99% yield determined by ^{19}F NMR). The crude reaction mixture was concentrated in vacuo over a longer period of ±5h. The title compound was obtained as taupe solid (234 mg, 80%). **Melting point:** 85.0–87.0 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.36–7.30 (m, 2H), 7.01–6.94 (m, 2H), 3.77–3.60 (m, 4H), 3.37–3.21 (m, 4H) ppm.**^{13}C NMR** (101 MHz, $CDCl_3$): δ 150.5, 129.4, 121.5, 120.1 (q, $^1J_{CF}$ = 323.6Hz), 117.3, 49.9, 46.5 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -75.21 (s, 3F) ppm. **IR** (neat) ṽ = 1599 (m, aromatic), 1580 (w, aromatic), 1495 (m, aromatic), 1447 (w, aromatic) 1391 (s, S=O stretching), 1226 (vs, C–F stretching), 1144 (s, S=O stretching) cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{11}H_{14}F_3N_2O_2S$ $[M+H]^+$: 295.0723, found 295.0718.

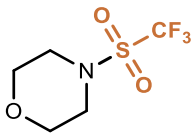
4-phenyl-1-((trifluoromethyl)sulfonyl)piperidine (compound 56, new compound)



Chemical Formula: $C_{12}H_{14}F_3NO_2S$
Exact Mass: 293,06973

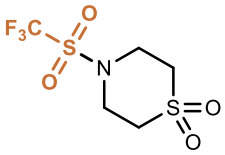
General procedure K was followed using 165 mg of 1-phenylpiperidine **(**97 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 72 hours (>99% yield determined by ^{19}F NMR). The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.37, *n*-heptane/ethyl acetate (87/13)). The title compound was obtained as white solid (191 mg, 65%). **Melting point:** 40–44 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.40–7.34 (m, 2H), 7.31–7.21 (m, 3H), 4.12 (dqui, J = 13.2, 2.28 Hz, 2H), 3.19 (t, *J* = 12.58 Hz, 2H), 2.74 (tt, *J* = 12.22, 3.63 Hz, 1H), 2.05–1.97 (m, 2H), 1.91-1.78 (m, 2H) ppm.**^{13}C NMR** (101 MHz, $CDCl_3$): δ 144.2, 128.8, 126.9, 126.6, 120.2 (q, $^1J_{CF}$ = 324.9 Hz), 47.4, 41.7, 33.0 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -75.35 (brs, 3F) ppm. **IR** (neat) ṽ = 1601 (m, aromatic), 1494 (m, aromatic), 1466 (m, aromatic), 1452 (m, aromatic), 1380 (s, S=O stretching), 1224 (vs, C–F stretching), 1176 (S=O stretching) cm^{-1}. **HRMS** (APCI) m/z calcd for $C_{12}H_{13}F_3K_2NO_2S$ $[M+2K-H]^+$: 369.9888, found 370.0765; **MS** ($ASAP^+$) m/z calcd for $C_{12}H_{15}F_3NO_2S$ $[M+H]^+$: 294.08, found 294.0.

4-((trifluoromethyl)sulfonyl)morpholine (compound 57)



General procedure K was followed using 89 mg of morpholine **(**98 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 18 hours (>99% yield determined by ^{19}F NMR). The title compound was obtained after extraction as yellow oil (194 mg, 89%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.8 (t, *J* = 4.7 Hz, 4H), 3.56–3.48 (m, 4H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 120.1 (q, $^1J_{CF}$ = 323.5 Hz), 66.4, 46.5 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -75.13 (s, 3F) ppm. These data are in agreement with literature data.[30]

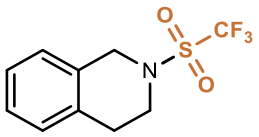
4-((trifluoromethyl)sulfonyl)thiomorpholine 1,1-dioxide (compound 58)



General procedure K was followed using 0.175 mg of thiomorpholine 1,1-dioxide HCl **(**98 wt%, 1.0 mmol, 1.0 eq.) and 367 mg DMAP (99wt%, 3.0 mmol,3.0 eq.). The reaction was stirred at room temperature for 48 hours (98% yield determined by ^{19}F NMR). After extraction of the crude mixture, the organic phase was concentrated under vacuo for a longer period of time (± 4h) to remove all traces of solvent. The title compound was obtained as white powder (164 mg, 61%). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 3.93 (m, 4H), 3.39 (m,

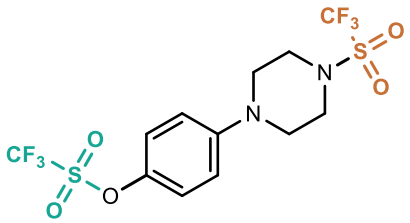
4H) ppm; traces of H_2O (3.34 ppm) and $CDCl_3$ (8.32 ppm). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 124.6 (q, $^1J_{CF}$ = 322.8 Hz), 56.0, 50.8 ppm. **^{19}F NMR** (377 MHz, DMSO-d_6) δ -76.05 (s, 3F) ppm. These data are in agreement with literature data.[30]

2-((trifluoromethyl)sulfonyl)-1,2,3,4-tetrahydroisoquinoline (compound 59)



General procedure K was followed using 0.13 mL of 1,2,3,4-tetrahydroisoquinoline **(**98 wt%, 136 mg, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 48 hours (>99% yield determined by ^{19}F NMR). The crude reaction mixture was purified by column chromatography on silica gel (**R_f** = 0.41, *n*-heptane/ethyl acetate (95/5)). The title compound was obtained as colourless oil (152 mg, 54%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28–7.24 (m, 2H), 7.23–7.18 (m, 1H), 7.14–7.09 (m, 1H), 4.69 (brs, 2H), 3.8 (brs, 2H), 3.02 (t, *J* = 5.8 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 132.6, 130.7, 129.2, 127.4, 126.9, 126.0, 120.1 (q, $^1J_{CF}$ = 322.9 Hz), 47.55, 44.4, 28.9 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -75.51 (s, 3F) ppm. These data are in agreement with literature data.[31]

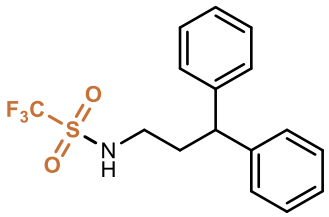
4-(4-((trifluoromethyl)sulfonyl)piperazin-1-yl)phenyl trifluoromethanesulfonate (compound 60, new compound)



Chemical Formula: $C_{12}H_{12}F_6N_2O_5S_2$
Exact Mass: 442.0092

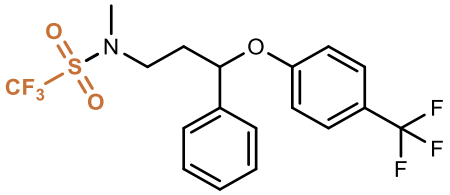
General procedure K was followed using 221.3 mg of 1-(4-hydroxyphenyl)-piperazine (97 wt%, 1.0 mmol, 1.0 eq.) and 431.9 mg DMAP (99wt%, 3.5 mmol, 3.5 eq.) in chamber B and 911.3 mg of *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 2.5 mmol, 2.5 eq.) and 131.7 mg of potassium bifluoride (KHF_2, 99+ wt%, 1.67 mmol, 1.67 eq.) in chamber A to generate 2.5 eq. trifluoromethanesulfonyl fluoride gas. The reaction was stirred at room temperature for 30 hours (>99% yield determined by ^{19}F NMR). After extraction the crude reaction mixture was purified by column chromatography on silica gel (**R_f** = 0.5, *n*-heptane/ethyl acetate = 8:2). The title compound was obtained as white solid (357.1 mg, 85%). **Melting point** = 82.0–82.5 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.19 (dt, *J* = 10.2, 3.0 Hz, 2H), 6.93 (dt, *J* = 10.2, 3.0 Hz, 2H), 3.65 (s, 4H), 3.28 (s, 4H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 150.20, 143.25, 122.22, 120.04 (q, $^1J_{CF}$ = 324.4 Hz), 118.76 (q, $^1J_{CF}$ = 322.1 Hz), 117.93, 49.43, 46.29 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.34 (s, 3F), -75.82 (s, 3F) ppm. **IR** (neat) $\tilde{\nu}$ = 1384 (s, S=O stretching), 1201 (vs, C–F stretching), 1181 (vs, C–F stretching), 1065 (s, S=O stretching) cm^{-1}. **HRMS** (ESI) *m/z*: Calcd for $C_{12}H_{13}F_6N_2O_5S_2$ $[M+H]^+$: 443.0164, found: 433.0160.

N-(3,3-diphenylpropyl)-1,1,1-trifluoromethanesulfonamide (compound 61)



General procedure K was followed using 222 mg of 3,3-diphenylpropylamine **(**95 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 18 hours (>99% yield determined by ^{19}F NMR). The title compound was obtained after extraction as yellow oil (278 mg, 81%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.37–7.31 (m, 4H), 7.28–7.21 (m, 6H), 4.7 (brs, 1H), 4.02 (t, *J* = 7.8 Hz, 1H), 3.32 (app. t, *J* = 6.5 Hz, 2H), 2.44–2.38 (m, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 143.14, 128.9, 127.6, 126.9, 119.6 (q, $^1J_{CF}$ = 320.86 Hz), 48.5, 43.3, 36.1 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -77.27 (s, 3F) ppm. These data are in agreement with literature data.[32]

N-(((1S,2R,5S)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl)methyl)-1,1,1-trifluoromethanesulfonamide (compound 62, new compound)

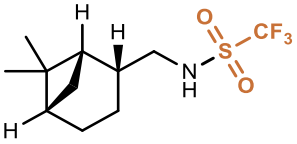


Chemical Formula: $C_{18}H_{17}F_6NO_3S$
Exact Mass: 441,08333

General procedure K was followed using 353 mg of fluoxetine HCl (98 wt%, 1.0 mmol, 1.0 eq.) and 368 mg of DMAP (99wt%, 3.0 mmol, 3.0 eq.). The reaction was stirred at room temperature for 18 hours (92% yield determined by ^{19}F NMR). The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.35, *n*-heptane/ethyl acetate (85/15)). The title compound was obtained as colourless oil (280 mg, 61%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49–7.44 (m, 2H), 7.42–7.30 (m, 5H), 6.93–6.89 (m, 2H), 5.26 (dd, *J* = 9.0 Hz, 3.7 Hz, 1H), 3.80–3.44 (m, 2H), 3.08 (app q, $^4J_{HF}$ = 1.2 Hz, 3H), 2.41–2.29 (m, 1H), 2.26-2.16 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.9 (q, $^5J_{CF3}$ = *1.2* Hz; M1*)*, 139.8, 129.1 (2C), 128.4 (2C), 126.9 (q, $^3J_{CF3}$ = 3.8 Hz, 2C; M2),125.6, 123.4 (q, $^1J_{CF3}$ = 271.2 Hz*; M5), 123.3 (q, $^2J_{CF3}$ = 32.9 Hz; M3), 120.2 (q, $^1J_{CF(SO2)}$ = 323.9 Hz; M4), 115.8, 77.21, 48.0, 37.2, 35.7 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -61.66 (s, 3F), -74.86 (s, 3F) ppm. **IR** (neat) ῡ = 2954-2898 (alkyl), 1614 (m, aromatic), 1591 (w, aromatic), 1517 (m, aromatic), 1495 (w, aromatic), 1455 (w, methyl), 1387 (s, S=O stretching), 1325 (vs, phenyl-CF_3), 1247 (vs, C–F stretching), 1225 (vs, alkyl-aryl ether), 1178 (s, phenyl-CF_3), 1158 (s, S=O stretching), 1108 (s, phenyl-CF_3), 1009 (m, ether) cm^{-1}. **HRMS** (ESI and APCI) no conclusion;

**note: part of the quartet lies underneath other Carbon signals.*

N-(((1S,2R,5S)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl)methyl)-1,1,1-trifluoromethanesulfonamide (compound 63, new compound)

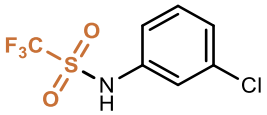


Chemical Formula: $C_{11}H_{18}F_3NO_2S$
Exact Mass: 285,10103

General procedure K was followed using 156 mg of (-)-cis-myrtanylamine **(**98 wt%, 1.0 mmol, 1.0 eq.) and 368 mg of DMAP (99wt%, 3.0 mmol, 3.0 eq.) in chamber B and 714 mg of *N*-phenyltrifluoromethanesulfonimide (PhNTf$_2$, 98 wt,% 2.0 mmol, 2.0 eq.) and 105 mg of potassium bifluoride (KHF_2, 99+% wt, 1.34 mmol, 1.34 eq.) in chamber A to generate 2.0 eq. trifluoromethanesulfonyl fluoride gas. The reaction was stirred at room temperature for 48 hours (96% yield determined by ^{19}F NMR). The crude reaction mixture was washed with Isohexane to precipitate the remaining starting material. The isohexane solution was transferred to another flask and was concentrated under vacuo. The title compound was obtained as orange/brown oil (267 mg, 94%*). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.84 (brs, 1H), 3.39–3.24 (m, 2H), 2.50–2.35 (m, 1H), 2.34–2.19 (m, 1H), 2.06–1.88 (m, 5H), 1.57–1.42 (m, 1H), 1.24 (s, 3H), 1.02 (s, 3H), 0.97–0.93 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 119.7 (q, $^1J_{CF}$ = 321.9 Hz), 49.7, 43.0, 41.7, 41.2, 38.6, 33.0, 27.8, 25.7, 23.1, 19.3 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -77.20 (s, 3F) ppm. **IR** (neat) ῡ = 3316-3291 (br, NH stretching), 2911-2871 (alkyl), 1366 (s, S=O stretching), 1229 (vs, C–F stretching), 1143 (s, S=O stretching) cm^{-1}. **HRMS** (ESI) *m/z*: Calcd for $C_{11}H_{17}F_3NO_2S$ [*M*-H]$^-$: 284.0937, found 284.0897.

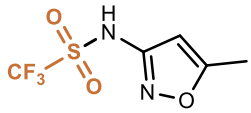
**Note: solvent traces are present in the ^{1}H NMR spectra, this is taken into account when determining the reported isolated yield and is left as such as the compound is rather volatile.*

N-(3-chlorophenyl)-1,1,1-trifluoromethanesulfonamide (compound 64)



General procedure K was followed using 0.11 mL of 3-chloroaniline **(**95 wt%, 128 mg, 1.0 mmol, 1.0 eq.), 368 mg of DMAP (99wt%, 3.0 mmol, 3.0 eq.) in chamber B and 714 mg of *N*-phenyltrifluoromethanesulfonimide (PhNTf$_2$, 98 wt,% 2.0 mmol,2.0 eq.) and 105 mg of potassium bifluoride (KHF_2, 99+% wt, 1.34 mmol, 1.34 eq.) in chamber A to generate 2.0 eq. trifluoromethanesulfonyl fluoride gas. The reaction was stirred at 50 °C for 18 hours (>99% yield determined by ^{19}F NMR). The title compound was obtained as brown/orange crystalline solid (228 mg, 88%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39–7.30 (m, 3H), 7.22–7.18 (m, 1H), 6.94 (brs, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 135.4, 134.8, 130.7, 127.8, 123.4, 121.3, 119.6 (q, $^1J_{CF}$ = 322.6 Hz) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -75.30 (s, 3F) ppm. These data are in agreement with literature data.[33]

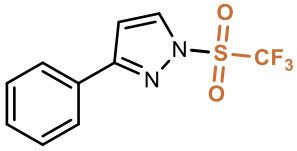
1,1,1-trifluoro-N-(3-methylisoxazol-5-yl)methanesulfonamide (compound 65, new compound)



Chemical Formula: $C_5H_5F_3N_2O_3S$
Exact Mass: 229,99730

General procedure K was followed using of 3-amino-5-methylisoxazole (97 wt%, 101 mg, 1.0 mmol, 1.0 eq.) 368 mg of DMAP (99wt%, 3.0 mmol, 3.0 eq.) in chamber B and 714 mg of *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt,% 2.0 mmol,2.0 eq.) and 105 mg of potassium bifluoride (KHF_2, 99+% wt, 1.34 mmol, 1.34 eq.) in chamber A to generate 2.0 eq. trifluoromethanesulfonyl fluoride gas. The reaction was stirred at 50 °C for 48 hours (>99% yield determined by ^{19}F NMR). The title compound was obtained as off-white solid (160 mg, 70%). **Melting point:** 140.4–142.7 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.17 (brs, 1H), 6.31 (app q, $^4J_{HH}$ = 0.8 Hz, 1H), 2.47 (d, $^4J_{HH}$ = 0.8 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.1, 156.6, 119.4 (q, $^1J_{CF}$ = 321.3 Hz), 95.3, 12.8 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -76.54 (s, 3F) ppm. **IR** (neat) ῡ = 3180 (br, N–H stretching), 3087 (w, 5-membered heterocycle), 3012 (w, 5-membered heterocycle), 2990 (w, 5-membered heterocycle), 1373 (s, S=O stretching), 1266 (vs, C–F stretching), 1138 (s, S=O stretching) cm^{-1}. **HRMS** (ESI) *m/z*: Calcd for $C_5H_4F_3N_2O_3S$ $[M\text{-}H]^-$: 228.9900, found 228.9892.

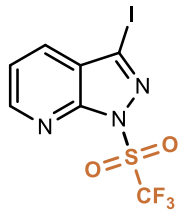
3-phenyl-1-((trifluoromethyl)sulfonyl)-1H-pyrazole (compound 66, new compound)



Chemical Formula: $C_{10}H_7F_3N_2O_2S$
Exact Mass: 276,01803

General procedure K was followed using 147 mg of 3-phenyl-1H-pyrazole (98 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 48 hours (>99% yield determined by ^{19}F NMR). The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.31, *n*-heptane/ethyl acetate/triethylamine (9/1/0.05)) The title compound was obtained as white crystalline solid (195 mg, 71%). **Melting point:** 91.7–92.7 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13 (app d, J = 3.0 Hz, 1H), 7.96–7.90 (m, 2H), 7.53–7.46 (m, 3H), 6.89 (app d, *J* = 3.0 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.7, 135.0, 130.3, 130.1, 129.0 (2C), 126.8 (2C), 119.1 (q, $^1J_{CF}$ = 323.2 Hz), 109.5 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -74.24 (s, 3F) ppm. **IR** (neat) ῡ = 3156.16 (w, 5 membered heterocycle), 3133 (w, 5-membered heterocycle), 3078 (w, 5-membered heterocycle), 1605.23 (w, aromatic), 1545.36 (m, aromatic), 1507 (w, aromatic), 1455 (m, aromatic), 1385 (s, S=O stretching), 1229 (vs, C–F stretching), 1168 (S=O stretchings,) cm^{-1}. **HRMS** (APCI) *m/z*: Calcd for $C_{10}H_8F_3N_2O_2S$ $[M+H]^+$: 277.0253, found 277.0257.

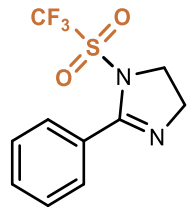
3-iodo-1-((trifluoromethyl)sulfonyl)-1H-pyrazolo[3,4-b]pyridine (compound 67, new compound)



Chemical Formula: $C_7H_3F_3IN_3O_2S$
Exact Mass: 376,89427

General procedure K was followed using 258 mg of 3-iodo-1H-pyrazolo-[3,4-b]pyridine (95 wt%, 1.0 mmol, 1.0 eq.) and anhydrous potassium carbonate (anh. K_2CO_3, 99% wt, 209 mg, 1.5 mmol, 1.5 eq.) rather than DMAP as base in chamber B and 714 mg of *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt,% 2.0 mmol, 2.0 eq.) and 105 mg of potassium bifluoride (KHF_2, 99+% wt, 1.34 mmol, 1.34 eq.) in chamber A to generate 2.0 eq. trifluoromethanesulfonyl fluoride gas. The reaction was stirred at room temperature for 72 hours (>99% yield determined by ^{19}F NMR). After extraction of the crude reaction mixture the organic fraction is partly crystallized. The crystals (pure product) are separated from the liquid phase (impure product mixture). The liquid fraction was purified by column chromatography on silica gel (R_f = 0.31, Isohexane/ethyl acetate/triethylamine (8/2//0.15)). Purification of the compound seems rather difficult, partly mixed fractions are obtained from the column chromatography. Subsequently, the mixed fractions where purified through preparative TLC in the same solvent mixture. The title compound was obtained as beige crystalline solid (95 mg, 25%). **Melting point:** 126.3–127.6 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.85 (app dd, *J* = 4.7, 1.6 Hz, 1H), 7.99 (app. dd, *J* = 8.1 Hz, 1.6 Hz, 1H), 7.56 (dd, *J* = 8.1 Hz, 4.7 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.7, 152.3, 132.3, 123.2, 122.0, 119.2 (q, $^1J_{CF}$ = 324.0 Hz), 105.3 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -73.99 (s, 3F) ppm. **IR** (neat) ῡ = 1592 (w, C=C aromatic), 1574 (m, C=C aromatic), 1482 (w, C=C aromatic), 1387 (m, S=O stretching), 1210 (vs, C–F stretching), 1132 (s, S=O stretching) cm^{-1}. **HRMS** (ESI) *m/z*: Calcd for $C_7H_4F_3N_3O_2S$ $[M+H]^+$: 377.9017, found 377.9015.

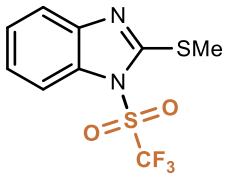
2-phenyl-1-((trifluoromethyl)sulfonyl)-4,5-dihydro-1H-imidazole (compound 68, new compound)



Chemical Formula: $C_{10}H_9F_3N_2O_2S$
Exact Mass: 278,03368

General procedure K was followed using 149 mg of 2-phenyl-2-imidazoline (98 wt%, 1.0 mmol, 1.0 eq.). The reaction was stirred at room temperature for 18 hours (>99% yield determined by ^{19}F NMR). The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.2, isohexane/ethyl acetate/ triethylamine (85/15/1)) The title compound was obtained as white crystalline solid (149 mg, 54%). **Melting point:** 91–92.2 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69-7.63 (m, 2H), 7.56-7.50 (m, 1H), 7.47–7.41 (m, 2H), 4.27–4.20 (m, 2H), 4.17–4.10 (m, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.5, 131.4, 129.2, 128.8, 128.7, 128.0, 127.0, 119.8 (q, $^1J_{CF}$ = 324.3 Hz), 54.4, 50.6 (q, $^4J_{CF}$ = 0.9 Hz) ppm. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -74.73 (s, 3F) ppm. **IR** (neat) ṽ = 3065-2920 (br, 5-membered heterocycle), 1651 (m, aromatic), 1599 (w, aromatic), 1494 (w, aromatic), 1401 (s, S=O Stretching), 1195 (vs, C–F stretching) cm^{-1}. **HRMS** (ESI) *m/z*: Calcd for $C_{10}H_{10}F_3N_2O_2S$ $[M+H]^+$: 279.0410, found 279.0413.

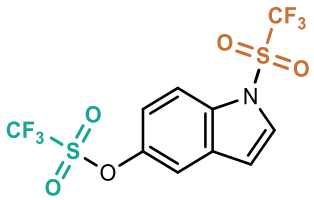
2-phenyl-1-((trifluoromethyl)sulfonyl)-4,5-dihydro-1H-imidazole (compound 69, new compound)



Chemical Formula: $C_9H_7F_3N_2O_2S_2$
Exact Mass: 295,99010

General procedure K was followed using 168 mg of 2-(methylmercapto)benzimidazole (98 wt%, 1.0 mmol, 1.0 eq.) and anhydrous potassium carbonate (anh. K_2CO_3, 99% wt, 209 mg, 1.5 mmol, 1.5 eq.) rather than DMAP as base in Chamber B. The reaction was stirred at room temperature for 36 hours (>99% yield determined by ^{19}F NMR). The title compound was obtained as a off-white crystalline solid (251 mg, 85%). **Melting point:** 101.5–102.8 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.78–7.75 (m, 1H), 7.75–7.72 (m, 1H), 7.52–7.42 (m, 2H), 2.78 (s, 3H) ppm. **^{13}C NMR** (101 MHz, DMSO-d_6) δ 155.1, 142.8, 133.6, 127.1, 125.8, 119.8, 119.6 (q, $^1J_{CF}$ = 325.2 Hz), 113.1, 15.8 ppm. **^{19}F NMR** (377 MHz, DMSO-d_6) δ -74.12 (s, 3F) ppm. **IR** (neat) ṽ = 3067 (w, 5-membered heterocycle), 3025 (w, 5-membered heterocycle), 2929 (w, 5-membered heterocycle), 2852 (w, 5-membered heterocycle), 1416 (s, S=O stretching), 1217 (vs, C–F stretching), 1195 (s, S=O stretching) cm^{-1}. **HRMS** (ESI) *m/z*: Calcd for $C_9H_8F_3N_2O_2S_2$ $[M+H]^+$: 296.9974 found 296.9940.

1-((trifluoromethyl)sulfonyl)-1H-indol-5-yl trifluoromethanesulfonate (compound 70, new compound)



Chemical Formula: $C_{10}H_5F_6NO_5S_2$
Exact Mass: 396,95133

General procedure K was followed using 137.3 mg of 5-hydroxyindole (97 wt%, 1.0 mmol, 1.0 eq.) and 308.5 mg DMAP (99wt%, 2.5 mmol, 2.5 eq.) in chamber B and using 911.3 mg *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 98 wt%, 2.5 mmol, 2.5 eq.) and 131.7 mg potassium bifluoride (KHF_2, 99+ wt%,1.67 mmol, 1.67 eq.) in chamber A to generate 2.5 eq. trifluoromethanesulfonyl fluoride gas. The reaction was stirred at room temperature for 4 hours (95% yield determined by ^{19}F NMR). The mixture in chamber B was concentrated *in vacuo* to give the crude product directly. The crude reaction mixture was purified by column chromatography on silica gel (R_f = 0.5, *n*-heptane/ethyl acetate = 5/1). The title compound was obtained as yellow oil (295.6 mg, 74%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.01 (app d, *J* = 9.2 Hz, 1H), 7.63–7.60 (m, 1H), 7.53 (app d, *J* = 3.8 Hz, 1H), 7.35 (dd, *J* = 9.12, 2.22 Hz, 1H), 6.88 (d, *J* = 3.8 Hz, 1H), ppm. **^{13}C NMR** (101 MHz, $CDCl_3$): δ 146.67, 134.21, 131.87, 128.65, 119.46 (q, $^1J_{CF}$ = 324.5 Hz), 118.94, 118.81 (q, $^1J_{CF}$ = 321.8 Hz), 115.17, 114.73, 111.25 ppm. **^{19}F NMR** (377 MHz, $CDCl_3$): δ -73.16 (s, 3F), -75.81 (s, 3F) ppm. **IR** (neat) ṽ =1454 (s, S=O stretching), 1417 (s, S=O stretching), 1197 (vs, C–F stretching), 1138 (s, S=O stretching), 745 (s, C=C bending) cm^{-1}. **HRMS** (ESI) *m/z*: Calcd for $C_{10}H_6F_6NO_5S_2$ $[M+H]^+$: 397.9586 found 397.9566.

Unsuccessful substrates:

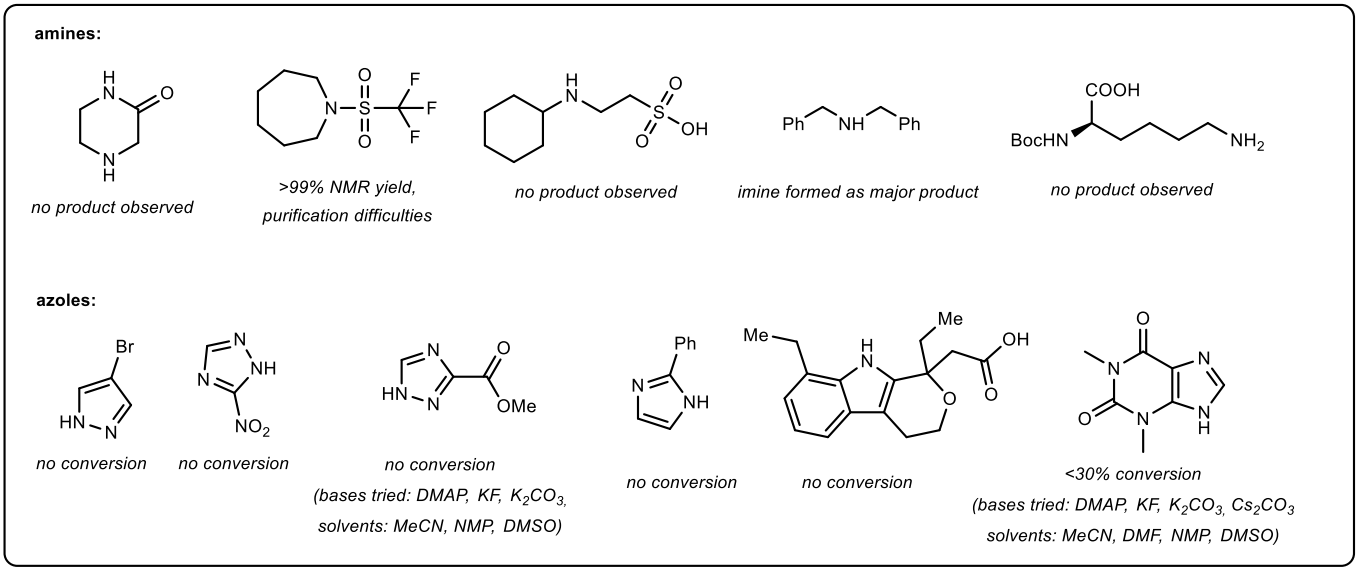
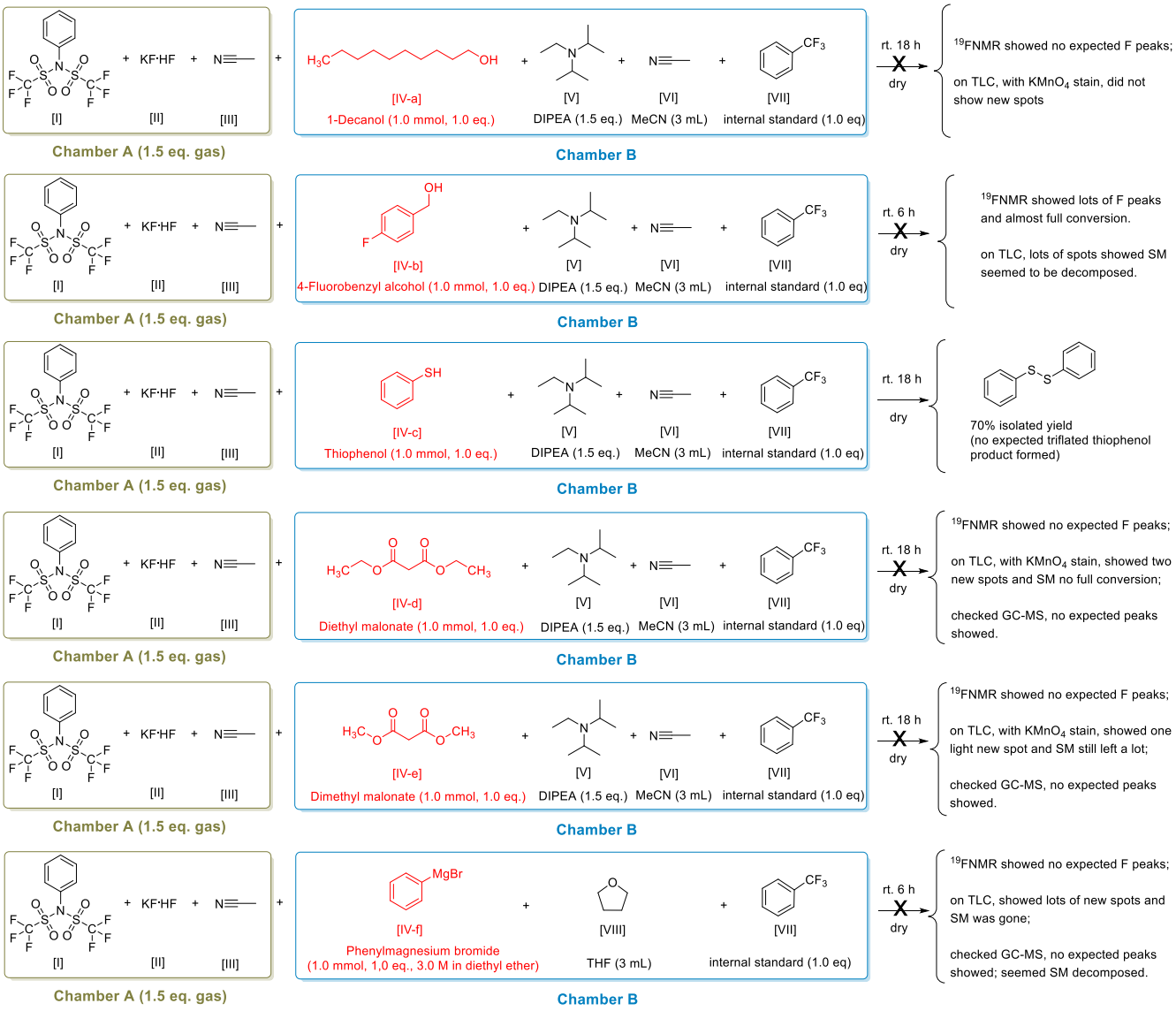


Figure S4. Unsuccessful Substrates of Amines and Azoles

7.8. Experimental Data of other common nucleophiles



8. Computational details

8.1. Metadynamics simulations

Input preparation

Simulating chemical reactions using *ab-initio* molecular dynamics (AIMD) is usually an insurmountable task due to the limited timescale (order of picoseconds) that is currently available to these computationally demanding simulations. With metadynamics, the sampling efficiency is enhanced by placing a number of artificial Gaussian potentials along a predetermined set of collective variables (CVs) that describe the reaction coordinate.[34] Doing so, effectively flattens the potential energy surface which enables the *ab-initio* dynamic simulation of a chemical reaction. In this work, all *ab-initio* simulations were performed using the open-source CP2K code (Version 6.1) with the Quickstep implementation.[35] Forces driving the simulations were calculated on the fly at the DFT level using the PBE GGA functional[36] including Grimme's D3 long-range dispersion corrections[37] and the DZVP-MOLOPT-GTH plane wave basis set[38] with the grid level cut-off set at 350 Ry and the relative cut-off set at 50 Ry.

The choice of functional was based on its accuracy in describing the interactions between an amine and triflylfluoride, which were the key reactants in this study. To benchmark the performance of different DFT methods, a DMAP-triflylfluoride complex was constructed and its geometry was optimized at the 6-31+G(d)/B3LYP-D3 level of theory with acetonitrile included as a solvent using the SMD implicit solvation model.[39] To ensure the complex corresponded to an actual minima on the potential energy surface, a vibrational analysis was performed. Next, using the same method, a relaxed scan starting from the optimized complex was initiated where the $|N_{DMAP}\text{-}S_{triflyl}|$ distance was varied from 1.75 Å to 3.75 Å in steps of 0.25 Å resulting in 9 additional structures. The optimization and frequency calculations were performed using the Gaussian software (Revision 16.A).[40] Next, for these 10 structures, single point energy calculations were performed at the cc-pVTZ/DLPNO-CCSD(T) level of theory at the normal accuracy level (normal PNO cut-off scheme: $T_{CutPairs} = 10^{-4}$, $T_{CutPNO} = 3.33 \times 10^{-7}$, $T_{CutMKN} = 10^{-3}$).[41] Latter calculations were performed using the open-source Orca package (version 4.1) and the energy values served as benchmarking reference.[42] Using the exact same geometries of the 10 structures, single point energy calculations were performed using the DZVP-MOLOPT-GTH plane wave basis set and a set of DFT functionals available in the CP2K code and computationally tractable to perform the simulations. The functionals considered in our benchmark were: LDA[43], PBE-D3[36], revPBE-D3[44] and BLYP-D3[39c]. From the results of the benchmark study, it becomes clear that the PBE-D3 functional describes the energetics associated to the amine-triflylfluoride interactions most accurately, based on the root-mean-square deviations (RMSDs) with respect to the relative energies computed at the cc-pVTZ/DLPNO-CCSD(T) level of theory. Besides the lowest RMSD, PBE-D3 and cc-pVTZ/DLPNO-CCSD(T) methods provide similar variation of the energy as a function of the $|N_{DMAP}\text{-}S_{triflyl}|$ distance, *i.e.* the energy minimum corresponds to the same structure. (**Table S8** and **Figure S5**).

Table S8. Benchmark study using relative energies of different triflyl fluoride-DMAP complexes computed at different levels of theories. cc-pVTZ/DLPNO-CCSD(T) relative energies served as benchmarking reference. All DFT computations were performed with the DZVP-MOLOPT-GTH plane wave basis set and the functional mentioned.

$\|N_{DMAP}\text{-}S_{triflyl}\|$ distance (Å)	**cc-PVTZ/DLPNO-** CCSD(T) (kcal mol^{-1})	**LDA** (kcal mol^{-1})	**BLYP-D3** (kcal mol^{-1})	**PBE-D3** (kcal mol^{-1})	**revPBE-D3** (kcal mol^{-1})
1.75	113.99	74.64	68.88	71.54	70.01
2.00	17.26	3.76	13.15	11.20	15.06
2.04[a]	15.52	2.58	12.96	9.58	13.46
2.25	10.33	0.51	6.44	5.66	8.55
2.50	6.03	0.34	4.14	3.25	5.27
2.75	2.90	0.99	3.93	1.84	2.82
3.00	0.00	0.00	0.00	0.00	0.48
3.25	0.51	1.70	1.43	0.31	0.08
3.50	1.26	3.09	1.83	1.01	0.09
3.75	1.94	4.00	3.73	1.24	0.00
MAD (kcal mol^{-1})	N.A.	8.83	6.19	6.41	5.49
RMSD (kcal mol^{-1})	N.A.	14.28	14.43	13.80	13.97

[a] $|N_{DMAP}\text{-}S_{triflyl}|$ distance for optimized complex at the 6-31+G(d)/B3LYP-D3 level of theory including acetonitrile as a solvent implicitly using the SMD solvent model.

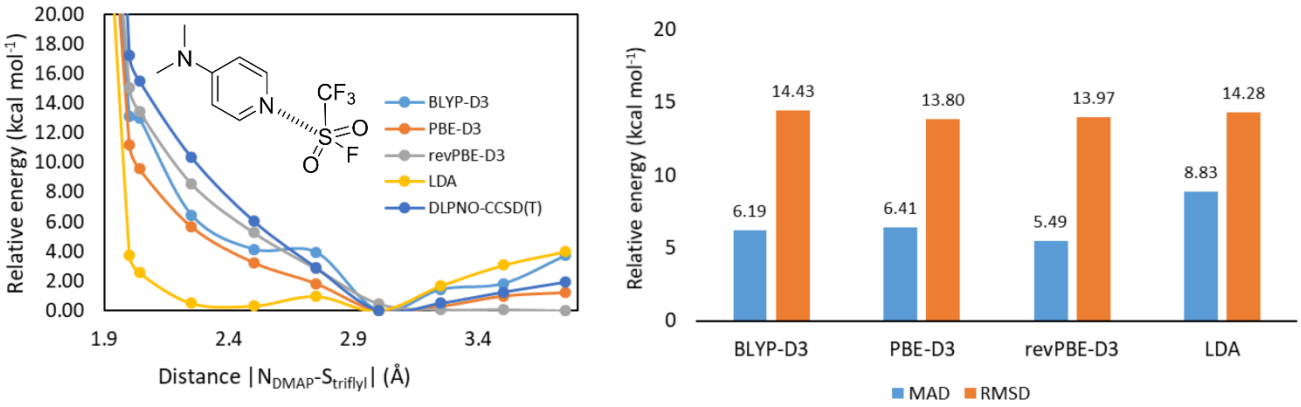


Figure S5. Left: evolution of the relative energies as a function of the $|N_{DMAP}\text{-}S_{triflyl}|$ distance at different levels of theory. Right: mean absolute deviation (MAD) and root-mean-square deviation (RMSD) of the relative energies obtained with different DFT functionals, computed with respect to the relative energies obtained with the cc-pVTZ/DLPNO-CCSD(T) method.

All simulations were performed in an NVT ensemble with the temperature controlled by the CSVR thermostat using a time constant of 1 fs. For all simulations, the temperature was set at 298 K to match the experimental ambient conditions. Moreover, each system underwent an equilibration phase by performing non-biased AIMD simulations for 5 ps, with a timestep of 1 fs. After this equilibration, Gaussian potentials were added every 25 steps along 2 CVs with a hill height of 2.0 kJ mol^{-1} and a width scale of 0.02. CVs were defined as coordination numbers (CN) describing the bonding between two atoms in the molecular system using the following mathematical expression.

$$CN = \sum_{i,j} \frac{1-\left(\frac{r_{ij}}{r_0}\right)^6}{1-\left(\frac{r_{ij}}{r_0}\right)^{12}} \quad (1)$$

Here r_{ij} represents the distance between atom *i* and *j*, while r_0 is a preset reference distance. Details concerning the choice of CN and reference distance for each system are listed in **Table S9** to **S12**.

Reactants together with the solvent (acetonitrile) were randomly placed in a cubic, periodic simulation box using the packmol software.[45] Additionally, the mass of all hydrogens was set to the mass of tritium to dampen excessive proton fluctuations at the 1 fs timestep, which would cause the simulation to be unstable. For each reactive system, simulations were ran in triplicate to ensure statistical relevance of the results. Below the details are presented for each system concerning the simulation box settings, coordination number choice, as well as an example input file.

Entry I

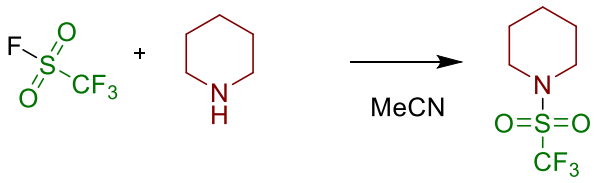


Table S9. Details simulation box settings and collective variables for reactive system 1.

Species	Box edge (Å)	CV1 (CN1) / r_0^1 (Å) [a]	CV2 (CN2) / r_0^2 (Å)
1 x triflylfluoride 1 x piperidine 18 x acetonitrile	12.00	$N_{pip}S_{triflyl}$ / 2.1 Å	$S_{triflyl}F_{triflyl}$ / 1.8 Å

[a] A half harmonic bias potential was added to CN1 at a value of 0.015 and force constant K = 300.0 a.u. to reduce the sampling region to a relevant chemical space.

Input file

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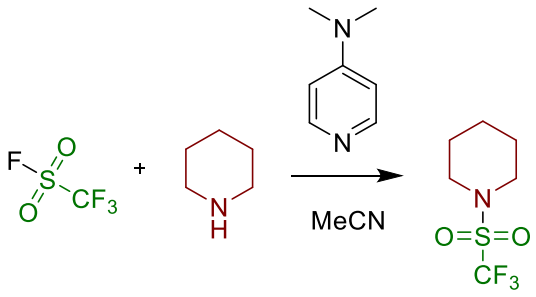

Table S10. Details simulation box settings and collective variables for reactive system 2.

Species	Box edge (Å)	CV1 (CN1) / r_0^1 (Å) [a]	CV2 (CN2) / r_0^2 (Å) [a]
1 x triflylfluoride 1 x piperidine 1 x DMAP 17 x acetonitrile	11.97	$N_{pip}S_{triflyl}$ / 2.1 Å	$N_{DMAP}H_{pip}$ / 1.2 Å

[a] A half harmonic bias potential was added to CN1 and CN2 at a value of 0.015 and force constant K = 300.0 a.u. to reduce the sampling region to a relevant chemical space.

Input file

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C	7.477365	6.425646	2.829372
N	8.037654	6.903337	1.915010
C	6.534297	6.040054	3.876111
H	6.660950	6.652391	4.777855
H	5.517729	6.284197	3.549657
H	6.570025	4.993254	4.163317
C	6.980525	2.629902	3.000723
N	6.401453	2.458918	3.987962
C	7.352665	2.823087	1.607502
H	7.337122	1.848169	1.103363
H	6.580978	3.444584	1.140831
H	8.245975	3.380614	1.614291
C	2.829024	-3.519210	6.045402
N	1.855029	-4.161135	6.177692
C	3.949093	-2.618602	5.837183
H	4.379137	-2.769871	4.821928
H	3.567817	-1.582583	5.869565
H	4.704113	-2.800372	6.599709
C	11.913247	5.016756	7.878115
N	11.073402	5.742813	7.502837
C	12.817278	3.978285	8.347314
H	13.000216	4.146582	9.418089
H	12.325281	3.004451	8.176419
H	13.808784	3.951325	7.815299
C	6.107713	1.416504	9.116746
N	6.555378	1.612770	10.178702
C	5.399747	1.415058	7.861273
H	6.128652	1.245825	7.071492
H	4.624576	0.617827	7.782760
H	4.847362	2.375220	7.707562
C	5.453580	6.598743	8.582206
N	5.361427	6.064452	7.548914
C	5.835372	7.402372	9.728687
H	5.073566	7.442362	10.504933

```
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 H        6.104831       8.435732       9.394727
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  &END COLVAR
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  &COLVAR
    &COORDINATION
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  &END COLVAR
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    POTENTIAL GTH-PBE-q4
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  &KIND H
    MASS 3
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  &KIND O
    BASIS_SET DZVP-MOLOPT-GTH
    POTENTIAL GTH-PBE-q6
  &END KIND
  &KIND F
    BASIS_SET DZVP-MOLOPT-GTH
    POTENTIAL GTH-PBE-q7
  &END KIND
  &KIND N
    BASIS_SET DZVP-MOLOPT-GTH
    POTENTIAL GTH-PBE-q5
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  &KIND S
    BASIS_SET DZVP-MOLOPT-GTH
    POTENTIAL GTH-PBE-q6
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 &END SUBSYS
&END FORCE_EVAL
&GLOBAL
 PRINT_LEVEL LOW
 PROJECT md
 RUN_TYPE MD
&END GLOBAL
&MOTION
 &PRINT
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    MD 2000
   &END EACH
  &END RESTART_HISTORY
  &TRAJECTORY
   &EACH
    MD 2
   &END EACH
   FORMAT DCD
  &END TRAJECTORY
 &END PRINT
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  ENSEMBLE NVT
  STEPS 20000
  TIMESTEP 1.0
  TEMPERATURE 298
  &THERMOSTAT
   TYPE CSVR
   &CSVR
    TIMECON 1
   &END CSVR
  &END THERMOSTAT
 &END MD
 &FREE_ENERGY
  &METADYN
   DO_HILLS TRUE
   NT_HILLS 25
   WW [kjmol] 2.0
   &METAVAR
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   SCALE 0.02
     &WALL
      TYPE QUADRATIC
      POSITION 0.015
      &QUADRATIC
       DIRECTION WALL_MINUS
       K 300.0
      &END QUADRATIC
     &END WALL
   &END METAVAR
   &METAVAR 2
   COLVAR 2
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      &WALL
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      POSITION 0.015
      &QUADRATIC
        DIRECTION WALL_MINUS
        K 300.0
      &END QUADRATIC
    &END WALL
   &END METAVAR
   &PRINT
    &COLVAR
     COMMON_ITERATION_LEVELS 2
     &EACH
      MD 1
     &END
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   &END PRINT
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 &END FREE_ENERGY
&END MOTION
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Entry III

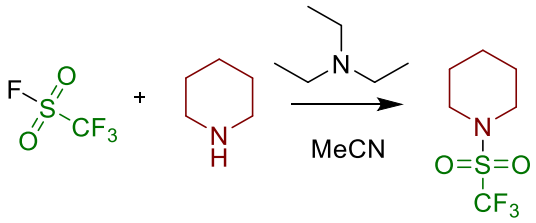

Table S11. Details simulation box settings and collective variables for reactive system 3.

Species	Box edge (Å)	CV1 (CN1) / r_0^1 (Å) [a]	CV2 (CN2) / r_0^2 (Å) [a]
1 x triflylfluoride 1 x piperidine 1 x Et_3N 17 x acetonitrile	12.07	$N_{pip}S_{triflyl}$ / 2.1 Å	$N_{Et3N}H_{pip}$ / 1.2 Å

[a] A half harmonic bias potential was added to CN1 and CN2 at a value of 0.015 and force constant K = 300.0 a.u. to reduce the sampling region to a relevant chemical space.

Input file

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   PERIODIC XYZ
   POISSON_SOLVER PERIODIC
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  POTENTIAL_FILE_NAME GTH_POTENTIALS
  CHARGE 0
  &QS
  &END QS
  &XC
   &XC_FUNCTIONAL PBE
   &END XC_FUNCTIONAL
   &VDW_POTENTIAL
    POTENTIAL_TYPE PAIR_POTENTIAL
    &PAIR_POTENTIAL
     TYPE DFTD3
     PARAMETER_FILE_NAME dftd3.dat
     REFERENCE_FUNCTIONAL PBE
    &END PAIR_POTENTIAL
   &END VDW_POTENTIAL
  &END XC
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   EPS_SCF 1.0E-5
   SCF_GUESS RESTART
   &OT
    MINIMIZER DIIS
    PRECONDITIONER FULL_SINGLE_INVERSE
   &END OT
  &END SCF
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     CUTOFF 350
REL_CUTOFF 50
     COMMENSURATE TRUE
  &END MGRID
 &END DFT
 &SUBSYS
  &COORD
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C       5.992160      2.005014      3.785798
C       6.840715      2.962659      2.827489
C       5.820229      3.771362      2.027900
C       4.796566      4.497311      3.028573
```

H	6.670540	1.376033	4.394112
H	3.301294	2.938944	3.540131
H	3.586729	4.077532	4.786963
H	7.550456	3.657769	3.248689
H	7.508082	2.394092	2.177129
H	6.158296	4.539728	1.287457
H	5.238120	3.061930	1.352854
H	5.289555	5.310678	3.617431
H	3.980805	5.003874	2.421625
H	5.461685	1.362350	3.061431
N	5.059791	2.656090	4.737198
H	5.468462	3.097242	5.549720
S	4.861614	10.736803	5.990763
O	4.321216	12.059902	6.186564
O	5.087132	9.728153	6.970517
F	6.163249	11.054392	5.226888
C	3.932101	9.929647	4.580654
F	2.654765	9.783926	4.831275
F	4.512561	8.760236	4.405681
F	4.053052	10.711175	3.544467
N	6.314659	4.128718	7.440911
C	6.573823	2.801198	7.940093
H	6.983270	2.928310	8.932170
H	5.584611	2.352102	8.104869
C	7.444236	1.823982	7.118434
H	7.689904	0.952212	7.743247
H	6.974607	1.608678	6.151634
H	8.447971	2.294556	6.953101
C	7.520094	4.942463	7.312474
H	8.152663	4.849921	8.241922
H	8.080442	4.453817	6.552335
C	7.358193	6.462956	7.154315
H	6.911293	6.912514	8.044519
H	8.402329	6.770316	7.036697
H	6.711912	6.840436	6.326670
C	5.316345	4.708197	8.298883
H	5.483813	4.540665	9.390173
H	5.327093	5.773566	8.068854
C	3.867487	4.308334	7.886336
H	3.641419	3.247401	7.768680
H	3.101745	4.710783	8.598541
H	3.720513	4.866362	6.909191
C	-0.215858	3.308584	2.884695
N	0.639239	4.014514	3.258445
C	-1.294215	2.453173	2.456906
H	-1.123516	1.386368	2.688322
H	-2.228017	2.716486	3.001996
H	-1.549217	2.496126	1.412873
C	4.709079	8.772830	1.083135
N	3.962962	9.325430	0.379768
C	5.747320	8.039178	1.713077
H	6.289599	7.329230	1.090515
H	6.446650	8.766595	2.144780
H	5.378639	7.415460	2.543342
C	-0.156560	1.563434	5.563012
N	-1.192566	1.185610	5.157477
C	1.215770	1.924440	6.034227
H	1.930731	1.356584	5.397585
H	1.465569	2.989817	5.921985
H	1.309417	1.573374	7.067946
C	0.822171	2.524448	10.959881
N	0.109755	1.650618	11.285711
C	1.843617	3.527419	10.819172
H	2.738598	3.114130	10.298077
H	1.593279	4.452615	10.318274
H	2.165056	3.779429	11.848279
C	9.655453	2.719948	10.138179
N	10.221321	2.172585	9.264832
C	9.085463	3.508894	11.234900
H	9.756232	3.614951	12.093555
H	8.816519	4.510515	10.835502
H	8.138342	2.978228	11.545267
C	1.279062	6.514456	7.165761
N	2.316633	6.974463	6.882674
C	0.174454	5.647966	7.563350
H	-0.133661	5.829963	8.599991
H	-0.683508	5.895744	6.931312
H	0.483122	4.608275	7.379455
C	0.703767	6.821584	4.163784
N	-0.432809	6.777296	4.460202
C	2.120375	6.845085	3.966477
H	2.410108	7.873737	3.784030
H	2.563695	6.565544	4.925342
H	2.445882	6.164813	3.171623
C	13.640765	-1.373751	9.780894
N	13.367281	-1.662653	10.881573
C	13.628284	-1.187445	8.315217
H	13.507323	-0.127034	8.020322
H	14.411819	-1.731445	7.743372
H	12.719180	-1.705106	7.977020
C	8.239760	-1.261762	1.523515
N	9.156588	-1.963510	1.779937
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H	7.006460	-0.365101	0.023801
H	6.157321	-0.595158	1.429994
H	7.424874	0.750936	1.273466
C	10.015972	10.018031	6.436351
N	11.068404	10.016360	6.937438
C	8.749126	10.199007	5.772560
H	8.083315	9.415887	6.148534

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N        1.244951       6.870263      11.439066
C       -0.812020       7.220511      12.928065
H       -1.030181       8.300664      13.166518
H       -1.616480       6.733807      12.410617
H       -0.765588       6.729711      13.882380
C        9.203043      -0.844605      10.125943
N        8.316342      -0.575131       9.394676
C       10.572054      -1.027057      10.755845
H       10.558370      -1.414555      11.796541
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H        4.310199      -0.781159       9.439727
C        4.441815       7.011096      10.665546
N        5.301915       6.360164      11.130526
C        3.708932       7.995519       9.885563
H        3.280506       7.594010       8.960701
H        2.903511       8.417525      10.466520
H        4.438692       8.772842       9.612021
C        8.939732       7.446051      10.156876
N        9.895276       6.971910       9.665688
C        7.706943       8.084124      10.548912
H        7.020201       7.356226      11.020710
H        7.941255       8.867526      11.269759
H        7.294148       8.557913       9.667638
C        8.596780       6.187665      14.506143
N        8.809230       6.030110      13.380333
C        8.406658       6.574331      15.874677
H        8.913926       7.543956      15.951632
H        7.334269       6.558093      16.150288
H        8.934890       5.925872      16.566988
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    PERIODIC XYZ
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  &END COLVAR
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  &END COLVAR
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  &END TOPOLOGY
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  &END KIND
  &KIND H
    MASS 3
    BASIS_SET DZVP-MOLOPT-GTH
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  &END KIND
  &KIND O
    BASIS_SET DZVP-MOLOPT-GTH
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    POTENTIAL GTH-PBE-q5
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    POTENTIAL GTH-PBE-q6
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 RUN_TYPE MD
&END GLOBAL
&MOTION
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  &END RESTART_HISTORY
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  &END THERMOSTAT
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     &END QUADRATIC
    &END WALL
   &END METAVAR
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   COLVAR 2
   SCALE 0.02
    &WALL
     TYPE QUADRATIC
     POSITION 0.015
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      DIRECTION WALL_MINUS
      K 300.0
     &END QUADRATIC
    &END WALL
   &END METAVAR
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  &END METADYN
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&END MOTION
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Entry IV

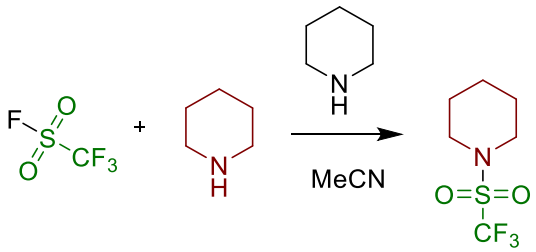

Table S12. Details simulation box settings and collective variables for entry IV.

Species	Box edge (Å)	CV1 (CN1) / r_0^1 (Å) [a]	CV2 (CN2) / r_0^2 (Å) [a]
1 x triflylfluoride 2 x piperidine 17 x acetonitrile	11.92	$N_{pip1}S_{triflyl}$ / 2.1 Å	$N_{pip2}H_{pip1}$ / 1.2 Å

[a] A half harmonic bias potential was added to CN1 and CN2 at a value of 0.015 and force constant K = 300.0 a.u. to reduce the sampling region to a relevant chemical space.

Input file

```
&FORCE_EVAL
```

```
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     PERIODIC XYZ
     POISSON_SOLVER PERIODIC
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   POTENTIAL_FILE_NAME GTH_POTENTIALS
   CHARGE 0
   &QS
   &END QS
   &XC
    &XC_FUNCTIONAL PBE
    &END XC_FUNCTIONAL
    &VDW_POTENTIAL
      POTENTIAL_TYPE PAIR_POTENTIAL
      &PAIR_POTENTIAL
        TYPE DFTD3
        PARAMETER_FILE_NAME dftd3.dat
        REFERENCE_FUNCTIONAL PBE
      &END PAIR_POTENTIAL
    &END VDW_POTENTIAL
   &END XC
   &SCF
    EPS_SCF 1.0E-5
    SCF_GUESS RESTART
    &OT
      MINIMIZER DIIS
      PRECONDITIONER FULL_SINGLE_INVERSE
    &END OT
   &END SCF
   &MGRID
      CUTOFF 350
         REL_CUTOFF 50
      COMMENSURATE TRUE
   &END MGRID
  &END DFT
  &SUBSYS
   &COORD
S        7.546309       8.390260      10.096187
O        8.191679       7.159264      10.099788
O        8.166866       9.673798      10.008153
F        6.548922       8.590472      11.331284
C        6.046457       8.228096       9.073243
F        5.132298       9.203597       9.356463
F        5.531978       7.067039       9.525965
F        6.279486       8.022781       7.761414
C        6.586982      -0.138470       0.662556
C        6.218906      -1.187535       2.850682
C        4.700763      -0.867766       2.824259
C        4.495899       0.360932       1.854345
C        5.090513       0.109467       0.499389
H        6.469265      -2.091618       3.385600
H        7.048902       0.802222       1.085592
H        7.059616      -0.334789      -0.318388
H        4.202847      -1.764126       2.441844
H        4.241692      -0.711426       3.808471
H        3.424686       0.611722       1.816067
H        5.009948       1.208330       2.302755
H        4.603260      -0.800340       0.111001
H        4.876017       0.965421      -0.189822
H        6.664606      -0.381262       3.459641
N        6.777609      -1.321488       1.533256
H        7.671328      -1.778804       1.488628
C       10.391541       8.208779       0.920854
C        9.058601       7.151638       2.732269
C       10.336389       6.581574       3.347152
C       11.497056       6.421800       2.311685
C       11.734497       7.722281       1.498276
H        8.345546       7.482992       3.484396
H       10.062733       7.555581       0.106188
H       10.560269       9.168246       0.401089
H       10.733927       7.240418       4.167058
H       10.135394       5.610842       3.766040
H       12.363366       6.249510       2.942364
H       11.363294       5.566490       1.680645
H       12.151472       8.414145       2.159422
H       12.372813       7.621624       0.620025
H        8.514190       6.389505       2.162686
N        9.306379       8.328952       1.870132
H        9.534121       9.131644       2.460093
C        3.221008       3.305517      -0.528522
N        2.436827       2.606240       0.034856
C        4.097334       4.273277      -1.145805
H        5.133189       4.074227      -0.878262
H        3.994548       4.274651      -2.243380
H        3.845158       5.275171      -0.728685
C        3.005991       7.847837      -0.203669
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Analysis

From the trajectories obtained, bond length analyses were performed to gain insight into the reaction pathway for each system. The plots shown in **Figure S6**, indicate that all reactions occur through a concerted mechanism, as the S-N bond formation and the S-F bond breaking occurs simultaneously. Furthermore, from this analysis a time-interval of the simulation where the transition state occurs can be defined. Accurate determination of the transition state was established by taking a snapshot at the moment when the system reaches its maximum potential energy. At this point, the partial derivatives of the potential energy with respect to the collective variables is equal to zero, indicating a stationary point in the potential energy surface defined in collective variable space. Having localized the transition state in the simulation, the Helmoltz free energy of activation ($\Delta F^{\ddagger}$) is calculated by equation (2), where k_b denotes the Boltzmann constant, T the temperature, P_{TS} the population at the transition state and P_{sum} the sum of all calculated populations. Activation energies for each simulation is provided in **Table S13**.

$$\Delta F^{\ddagger} = -k_b T \ln \frac{P_{TS}}{P_{sum}} \qquad (2)$$

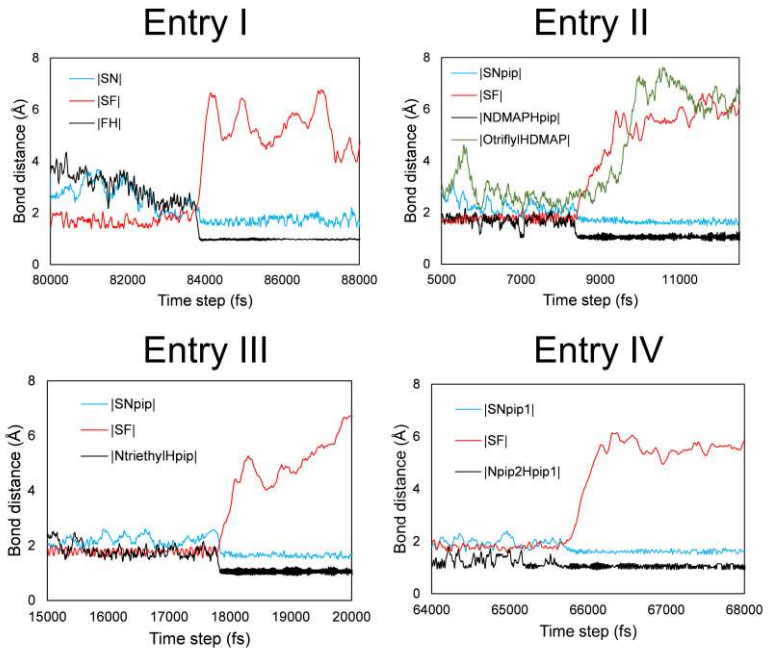

Figure S6. Bond length analyses of the trajectory for a single run for each reactive system. The blue line |SN| and $|SN_{pip}|$ describes the bond distance evolution between the triflylfluoride sulphur and the nucleophilic piperidine nitrogen, the red line |SF| describes the bond distance evolution between the triflylfluoride sulphur and fluor, the black line describes the distance between the triflylfluoride fluor and the piperidine hydrogen |FH| for entry I, DMAP nitrogen and piperidine hydrogen $|N_{DMAP}H_{pip}|$ for entry II, trimethylamine nitrogen and piperidine hydrogen $|N_{triethyl}H_{pip}|$ for entry III and base piperidine nitrogen and nucleophilic piperidine hydrogen for entry IV. The green line for system 2 describes the evolution between a triflylfluoride oxygen and DMAP hydrogen $|O_{triflyl}H_{DMAP}|$ suggesting a non-classical CH•••O hydrogen bond to be formed at the transition state.

Table S13. Helmoltz free energy of activation ($\Delta F^{\ddagger}$) for each metadynamics simulation performed in this work.

entry	**run**	$\Delta F^{\ddagger}$ (in kcal mol^{-1})
1	A	25.288
	B	27.746
	C	32.903
Average		29 ± 4
2	A	12.951
	B	12.129
	C	14.278
Average		13 ± 1
3	A	21.591
	B	22.264
	C	22.481
Average		22.1 ± 0.5

4	A	18.413
	B	21.995
	C	13.385
Average		18 ± 4

8.2. NCI analysis

To elucidate the differences between the DMAP-mediated and the Et_3N-mediated triflylation of piperidine, a Non-Covalent Interaction (NCI) analysis was performed on the transition states of both reactions. Established in 2010, NCI is a method which allows to visualize and quantify both inter- and intramolecular noncovalent interactions in a molecular system or solids based on the relationship between the product of the electron density and the sign of the second eigenvalue of the electron density Hessian matrix (ρsign(λ_2)) and the reduced density gradient (s).[46] The reduced density gradient is defined by equation 3, with ρ being the electron density and $|\nabla\rho|$ its gradient . In this work, the electron density of systems 2 and 3 at the transition states was obtained by performing a single point energy calculation at the 6-31+G(d)/PBE level of theory using the coordinates from the transition state obtained from the metadynamics simulation. Previous studies have shown the robustness of the NCI approach towards the choice of exchange-correlation functional and basis set.[47] As our focus was to single out the interactions between the reactants, we removed the coordinates related to the solvent in this case. Coordinates of the respective transition states in absence of solvent molecules can be found below. The NCIPLOT program version 4.0 was used to run the calculations, while visualization of the isosurfaces in 3D was accomplished by the VMD software version 1.9.3.[48]

$$s = \frac{1}{2(3\pi^2)^{1/3}} \frac{|\nabla\rho|}{\rho^{4/3}} \qquad (3)$$

Transition state system 2

C	1.7989	8.2372	2.4237
C	3.2029	8.1544	0.4636
C	3.9757	9.3564	1.077
C	3.1097	10.3201	1.8609
C	2.4523	9.5661	2.9336
H	3.949	7.5267	-0.0578
H	0.8146	8.6142	2.1728
H	1.5703	7.6425	3.4369
H	4.8784	9.1532	1.5302
H	4.3506	9.8235	0.1211
H	3.909	11.0026	2.3849
H	2.3972	10.8803	1.2349
H	3.2533	9.2866	3.7073
H	1.6537	10.1946	3.461
H	2.3663	8.4418	-0.1377
N	2.5428	7.3155	1.5687
H	3.3662	6.6621	2.3227
S	1.3145	6.0035	0.8668
O	0.7604	5.6798	2.2063
O	0.745	6.7243	-0.3014
F	0.5168	4.4497	0.1165
C	2.7368	4.6954	0.4953
F	3.985	5.323	0.5812
F	2.7769	4.0051	-0.6368
F	2.4918	3.855	1.5009
C	4.5469	4.7237	5.2423
C	3.64	5.3004	4.316
C	5.405	6.6327	3.4369
C	6.353	6.2101	4.3447
C	5.9103	5.1781	5.2236
H	4.2764	3.8294	5.7819
H	2.5686	4.9956	4.2607
H	5.571	7.3299	2.6615
H	7.4129	6.5662	4.1906
N	4.1167	6.1743	3.408
N	6.7553	4.5975	6.0809
C	6.3357	3.4269	7.0224
H	6.6734	3.748	8.0406
H	5.2323	3.4279	7.1024
H	6.8829	2.5495	6.6428
C	8.2544	4.9373	6.0875
H	8.7765	4.6398	7.0052
H	8.5802	4.603	5.0907
H	8.3691	6.07	6.0316

Transition state system 3

C	1.7989	8.2372	2.4237
C	3.2029	8.1544	0.4636
C	3.9757	9.3564	1.077
C	3.1097	10.3201	1.8609
C	2.4523	9.5661	2.9336
H	3.949	7.5267	-0.0578
H	0.8146	8.6142	2.1728
H	1.5703	7.6425	3.4369

H	4.8784	9.1532	1.5302
H	4.3506	9.8235	0.1211
H	3.909	11.0026	2.3849
H	2.3972	10.8803	1.2349
H	3.2533	9.2866	3.7073
H	1.6537	10.1946	3.461
H	2.3663	8.4418	-0.1377
N	2.5428	7.3155	1.5687
H	3.3662	6.6621	2.3227
S	1.3145	6.0035	0.8668
O	0.7604	5.6798	2.2063
O	0.745	6.7243	-0.3014
F	0.5168	4.4497	0.1165
C	2.7368	4.6954	0.4953
F	3.985	5.323	0.5812
F	2.7769	4.0051	-0.6368
F	2.4918	3.855	1.5009
C	4.5469	4.7237	5.2423
C	3.64	5.3004	4.316
C	5.405	6.6327	3.4369
C	6.353	6.2101	4.3447
C	5.9103	5.1781	5.2236
H	4.2764	3.8294	5.7819
H	2.5686	4.9956	4.2607
H	5.571	7.3299	2.6615
H	7.4129	6.5662	4.1906
N	4.1167	6.1743	3.408
N	6.7553	4.5975	6.0809
C	6.3357	3.4269	7.0224
H	6.6734	3.748	8.0406
H	5.2323	3.4279	7.1024
H	6.8829	2.5495	6.6428
C	8.2544	4.9373	6.0875
H	8.7765	4.6398	7.0052
H	8.5802	4.603	5.0907
H	8.3691	6.07	6.0316

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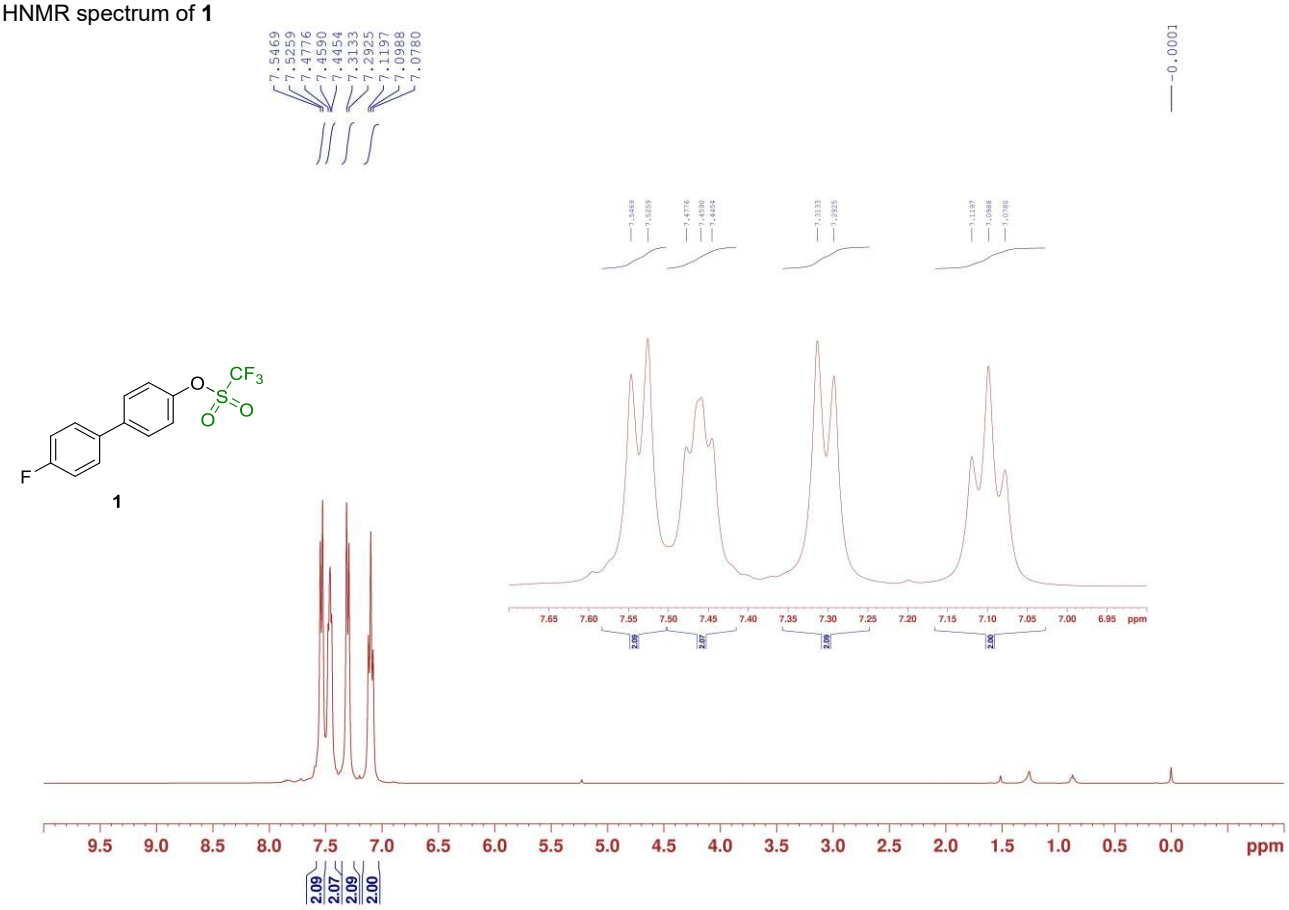

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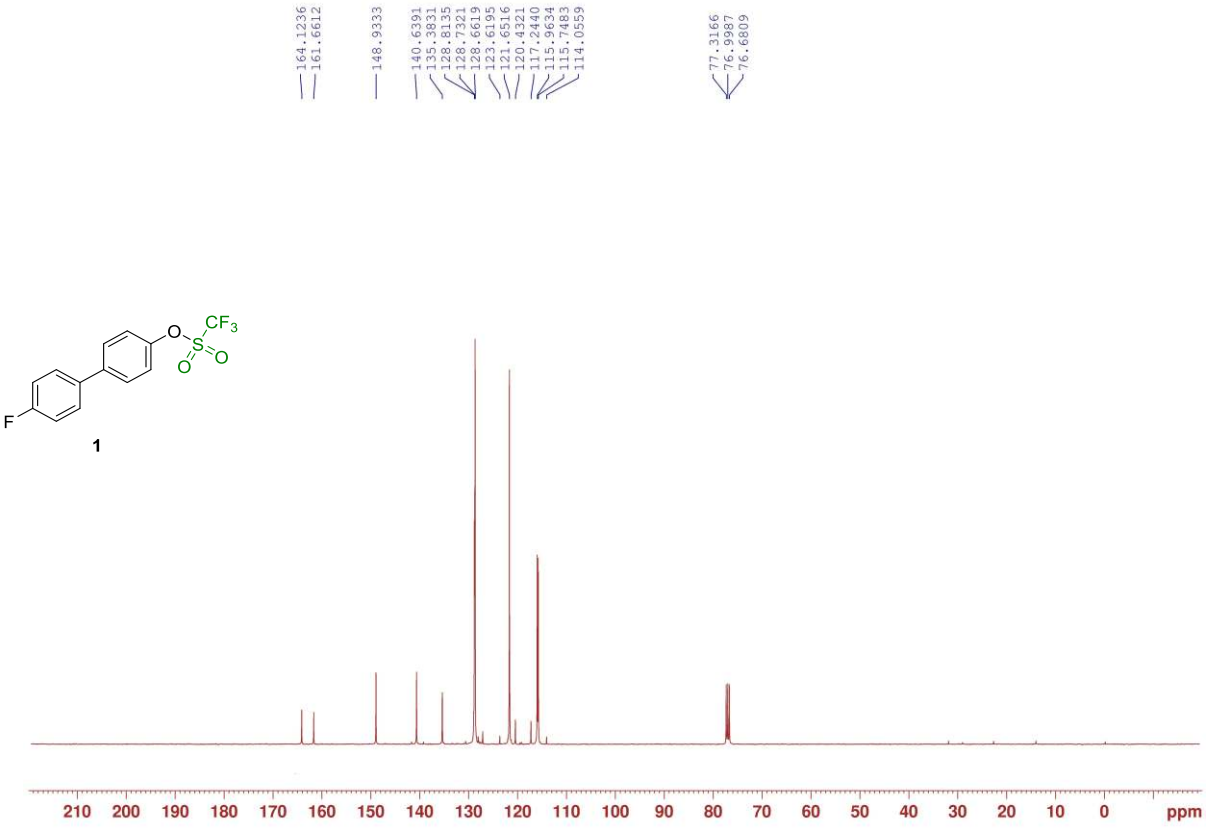

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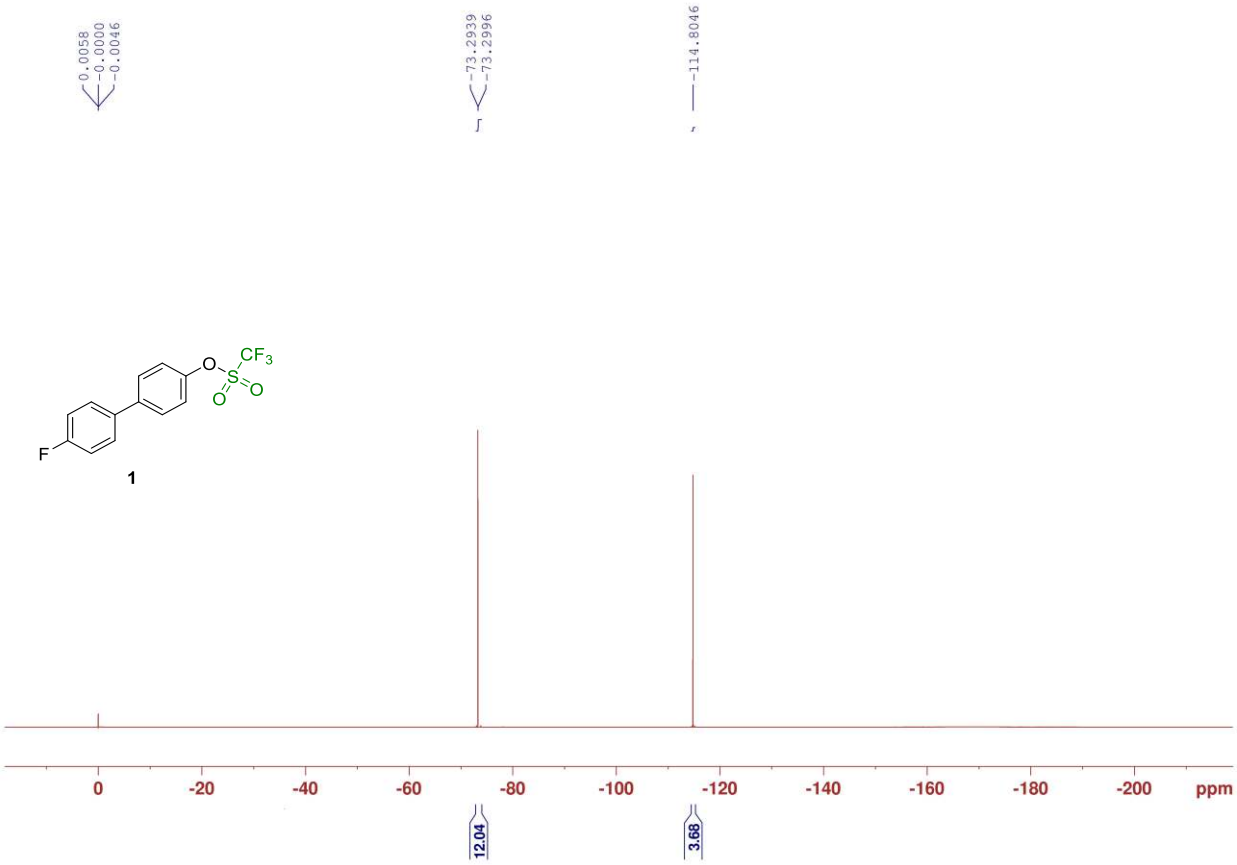

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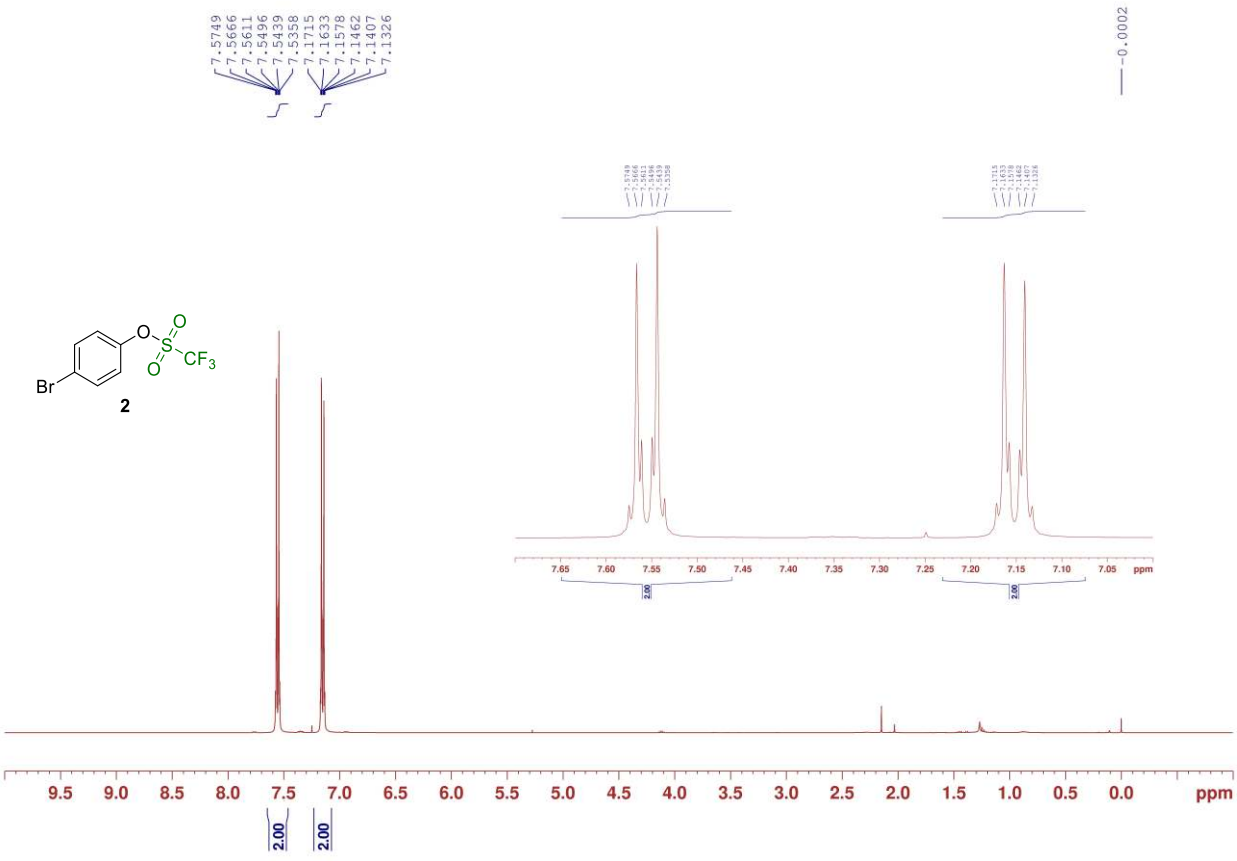

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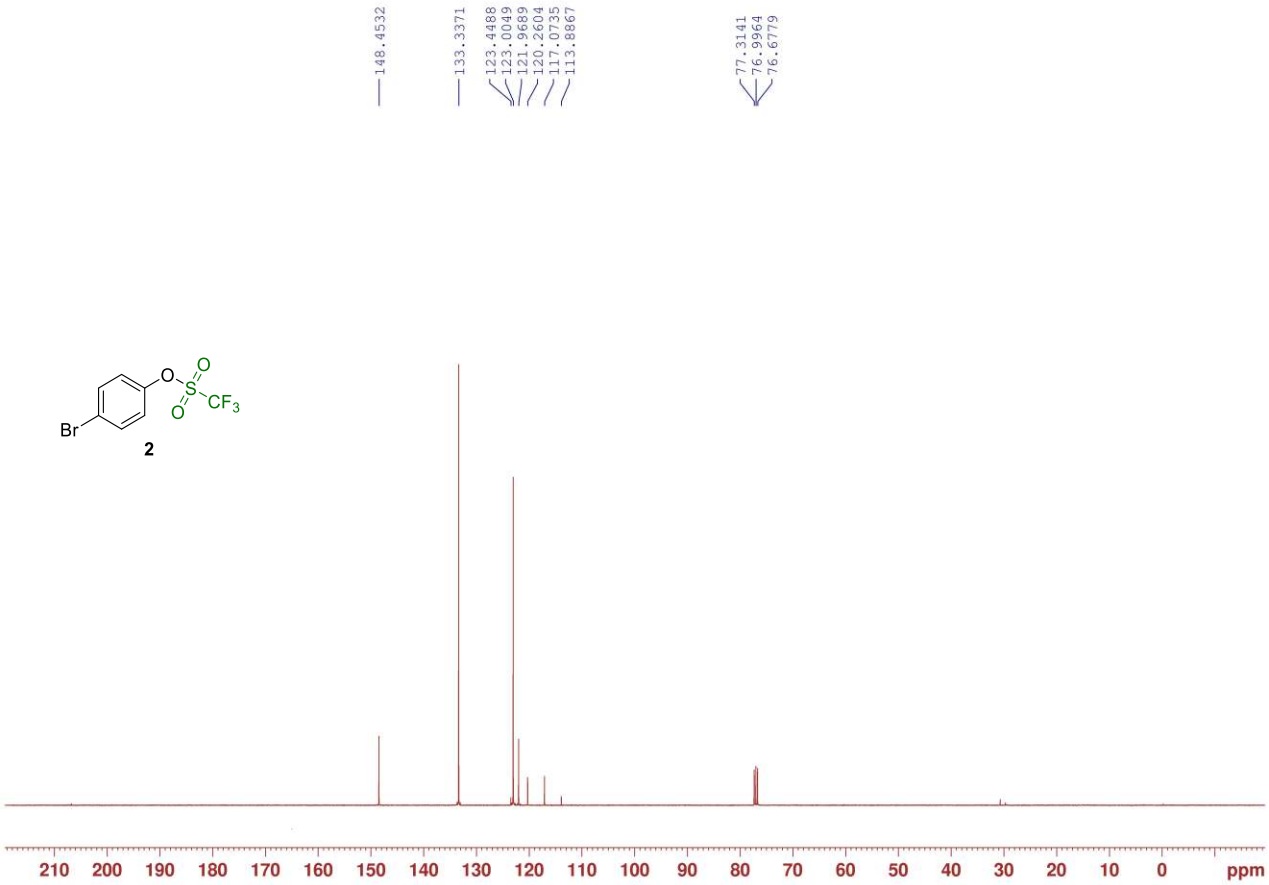

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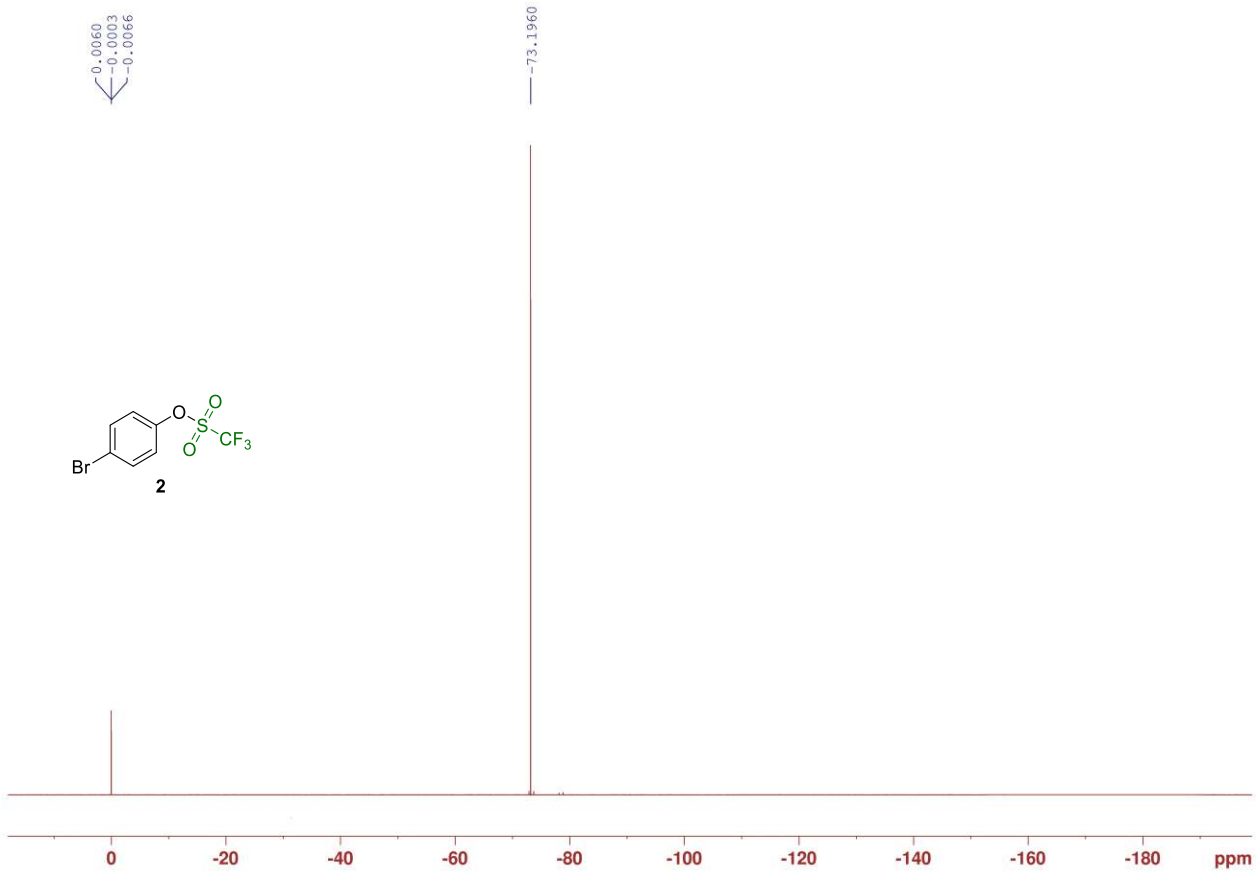

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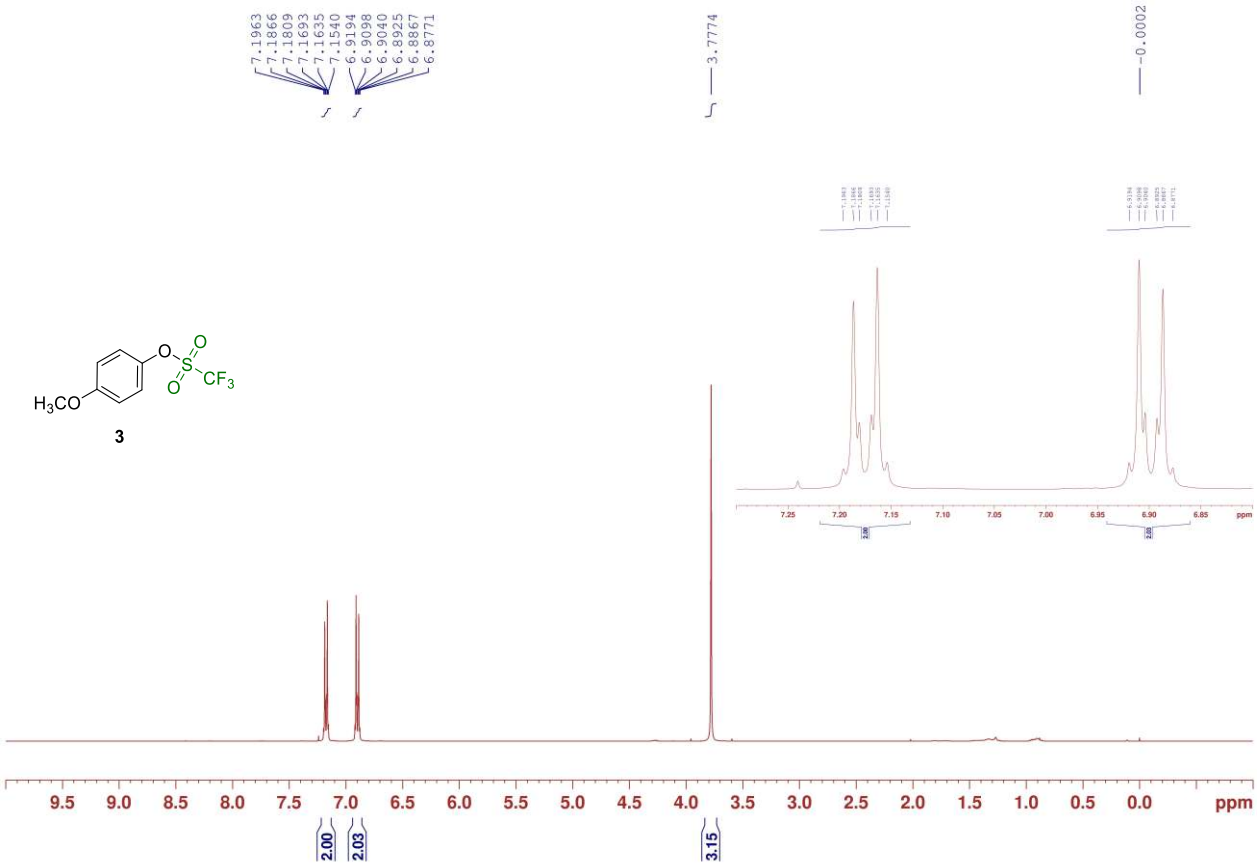

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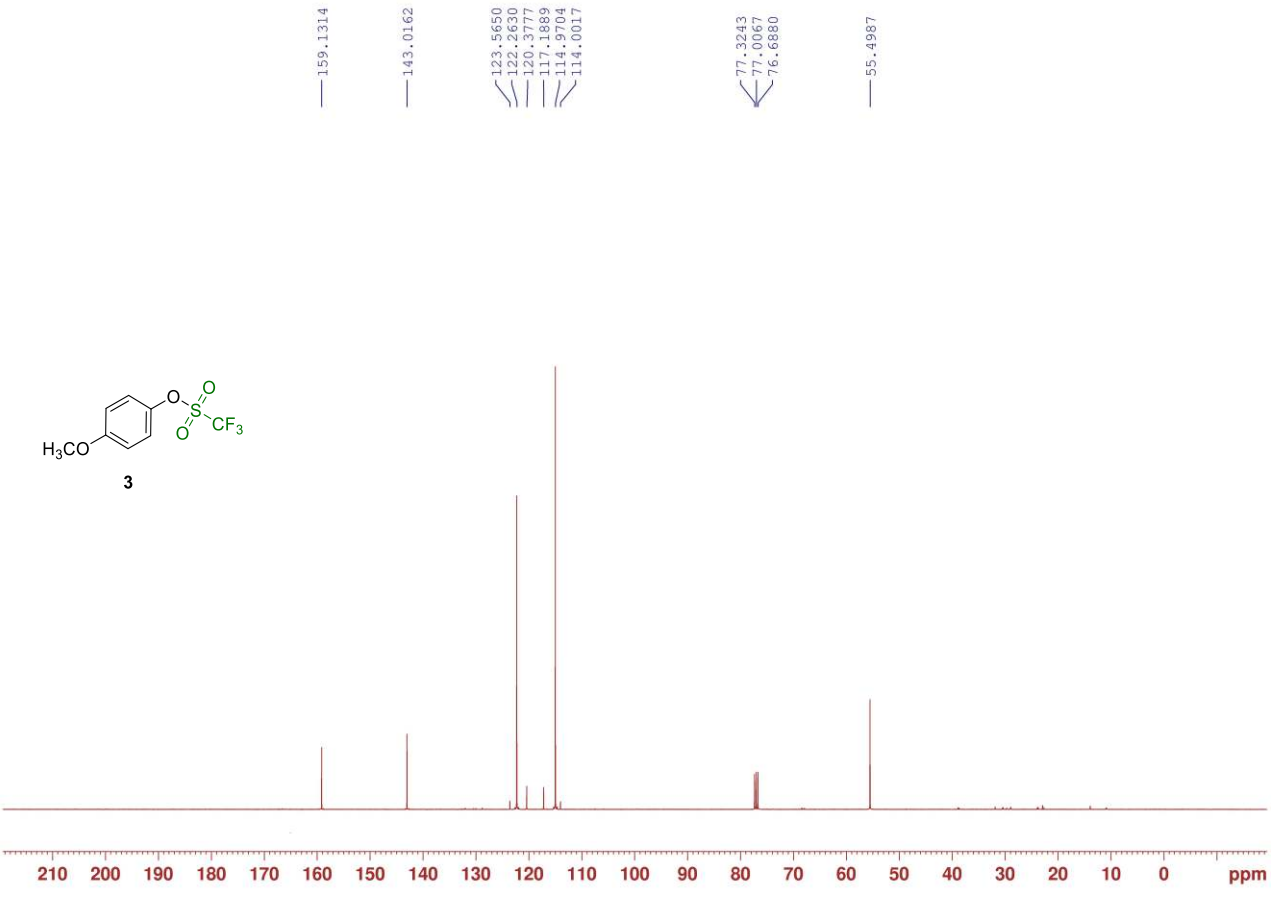

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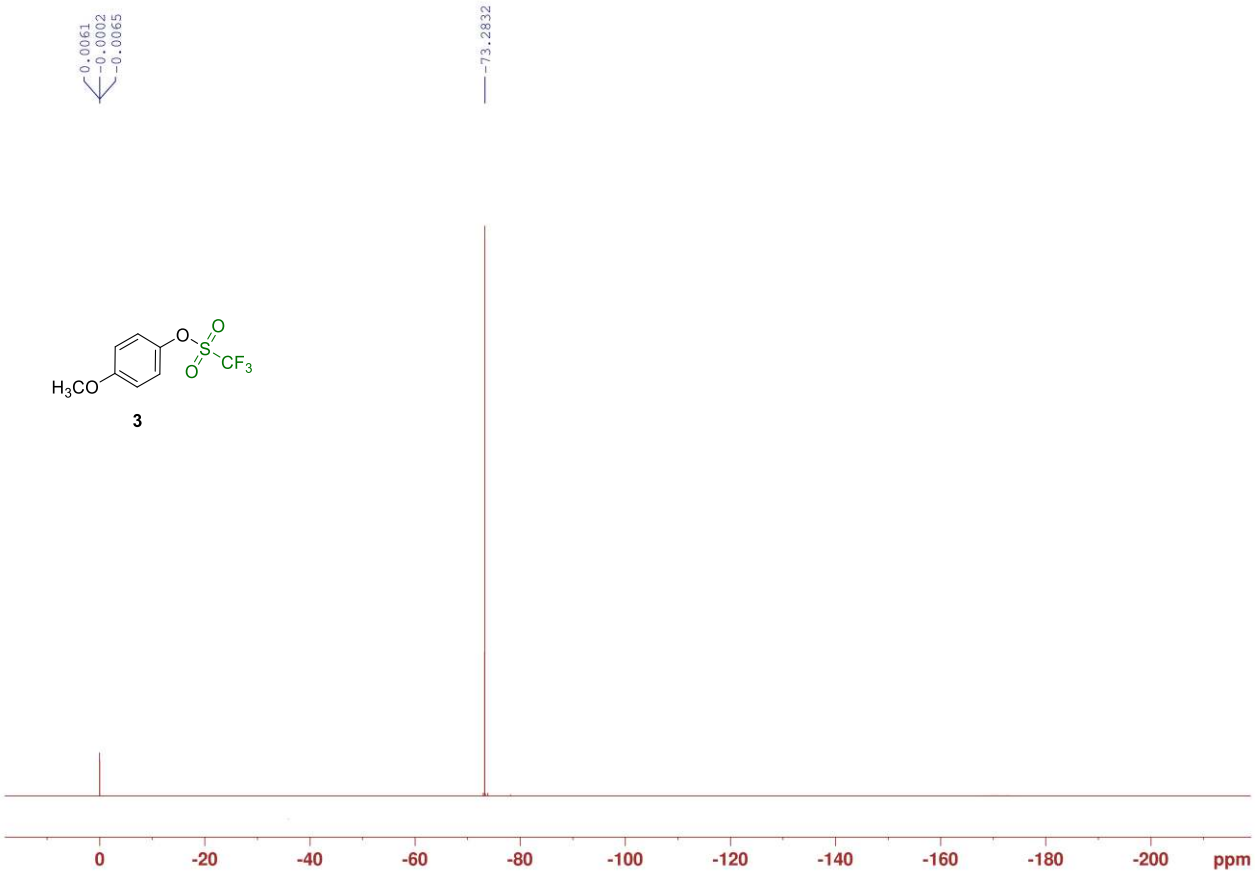

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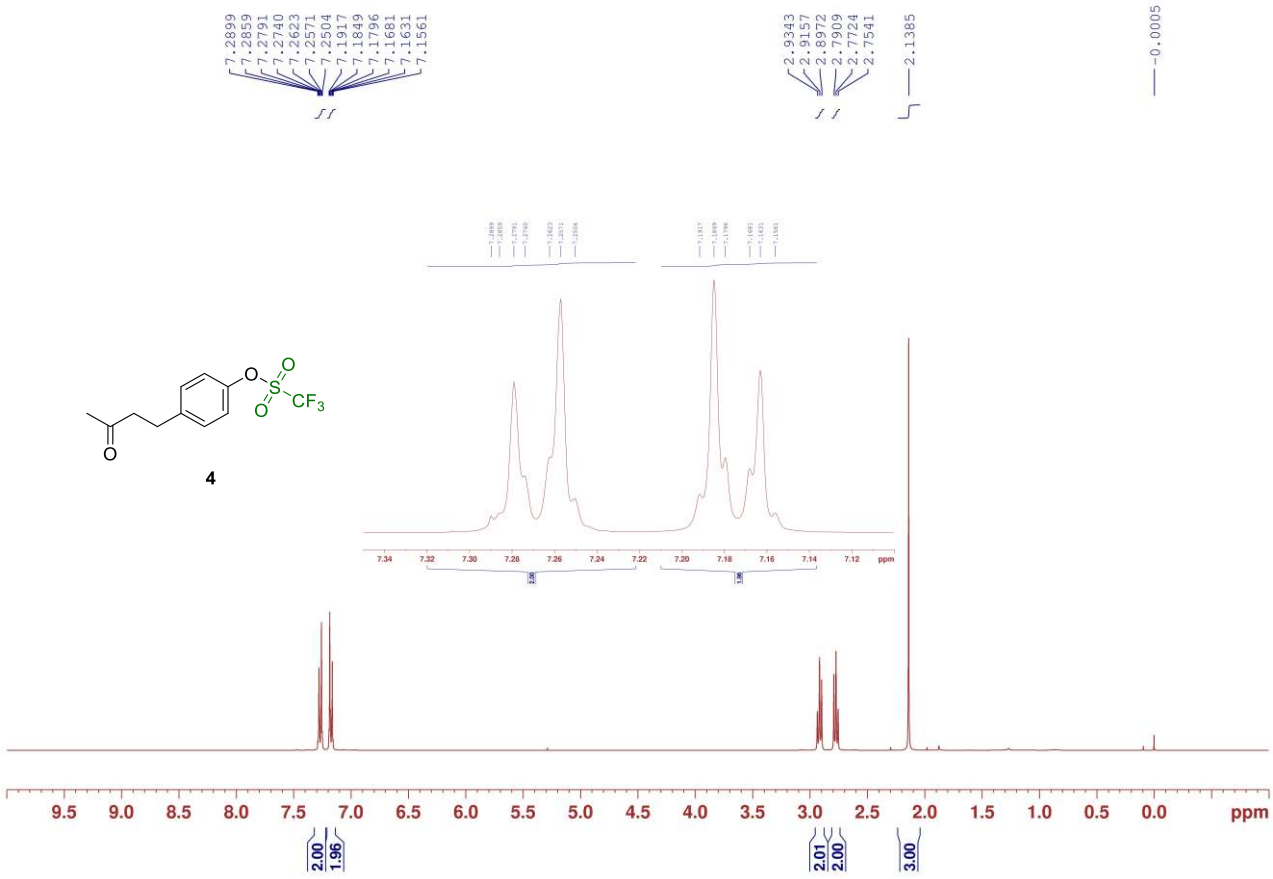

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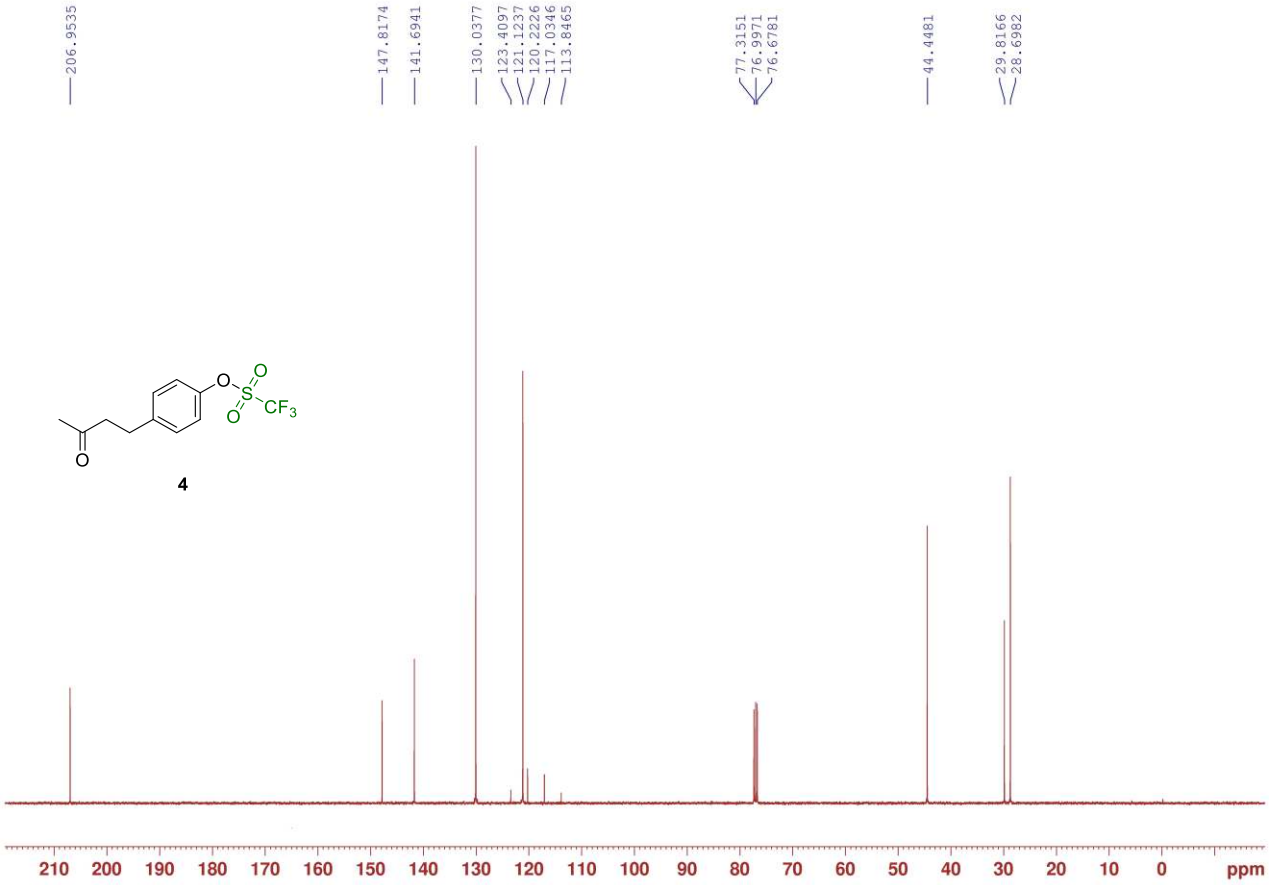

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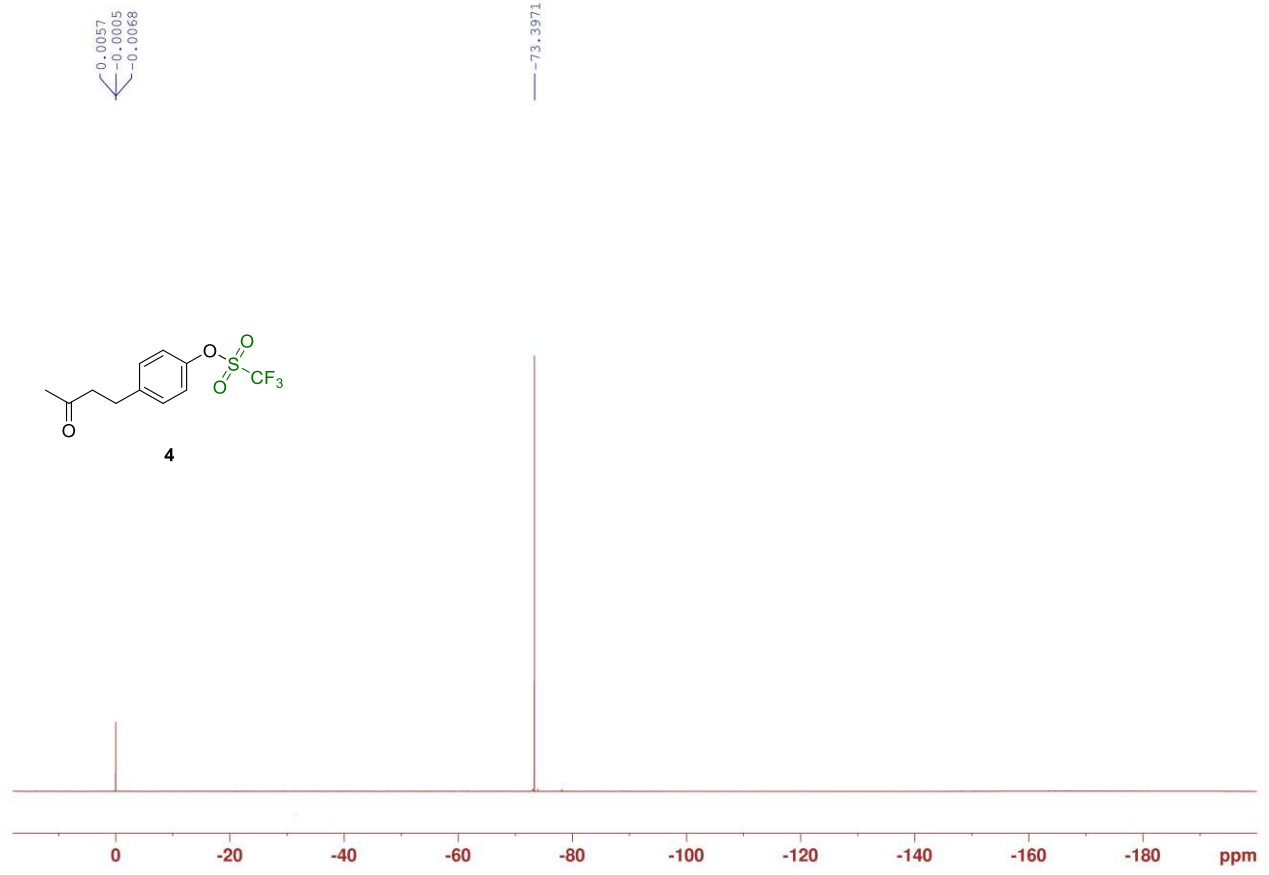

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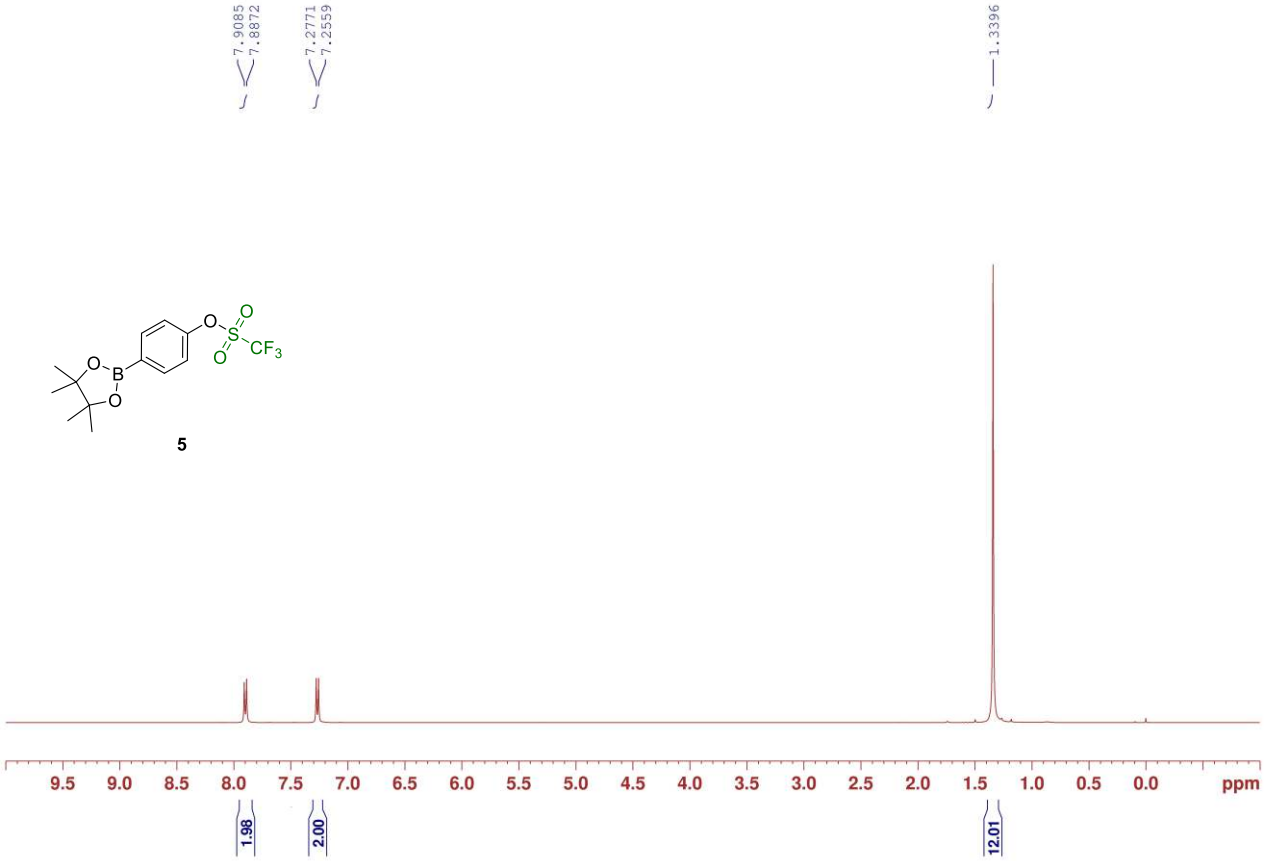

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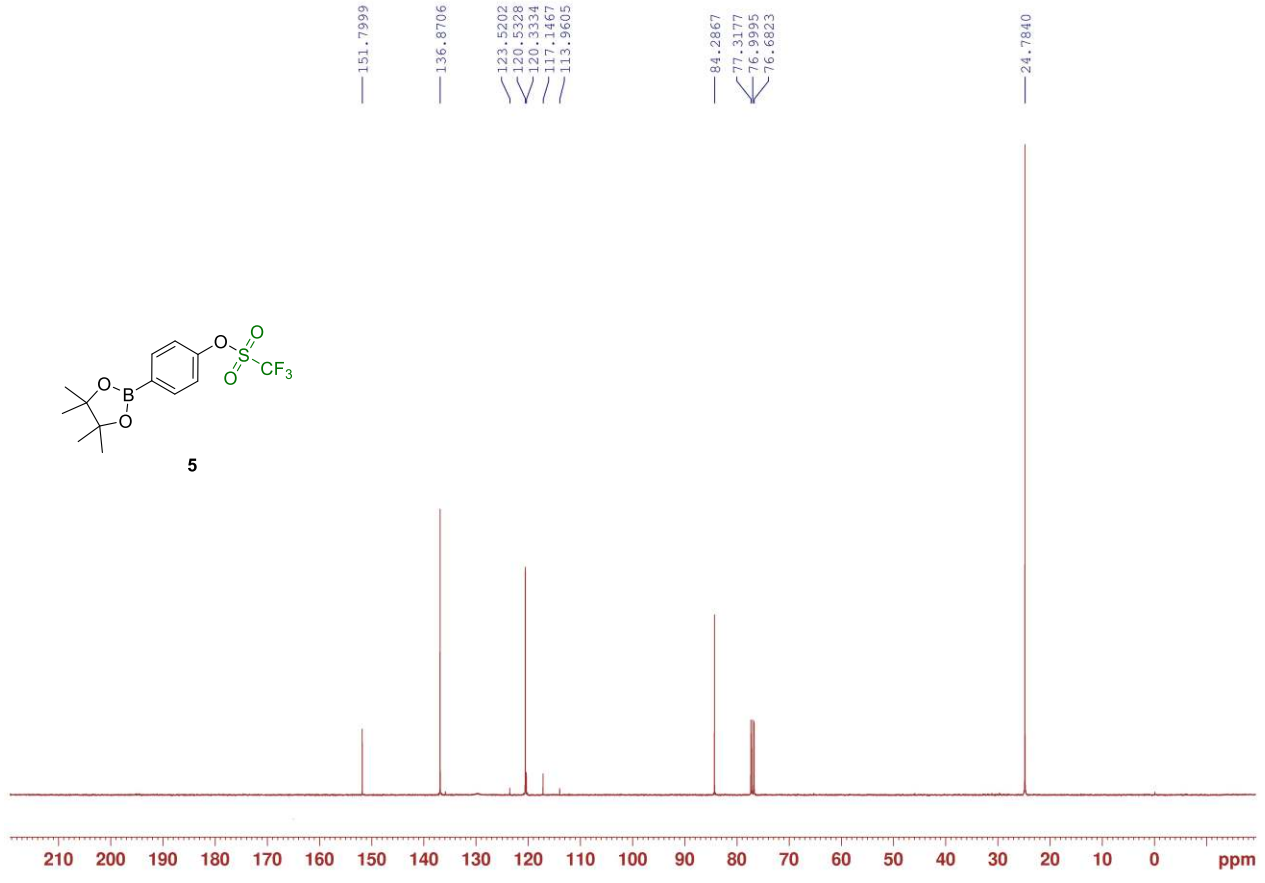

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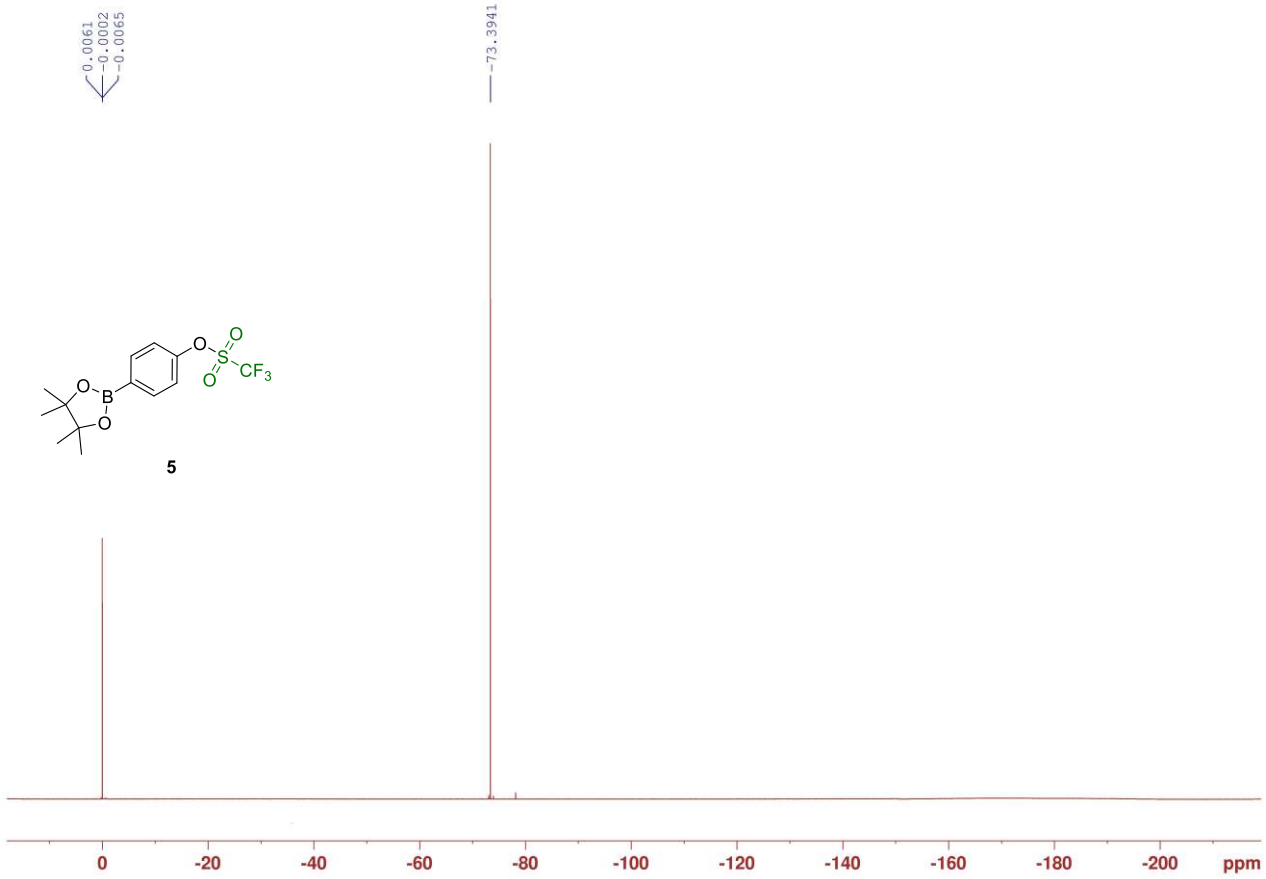

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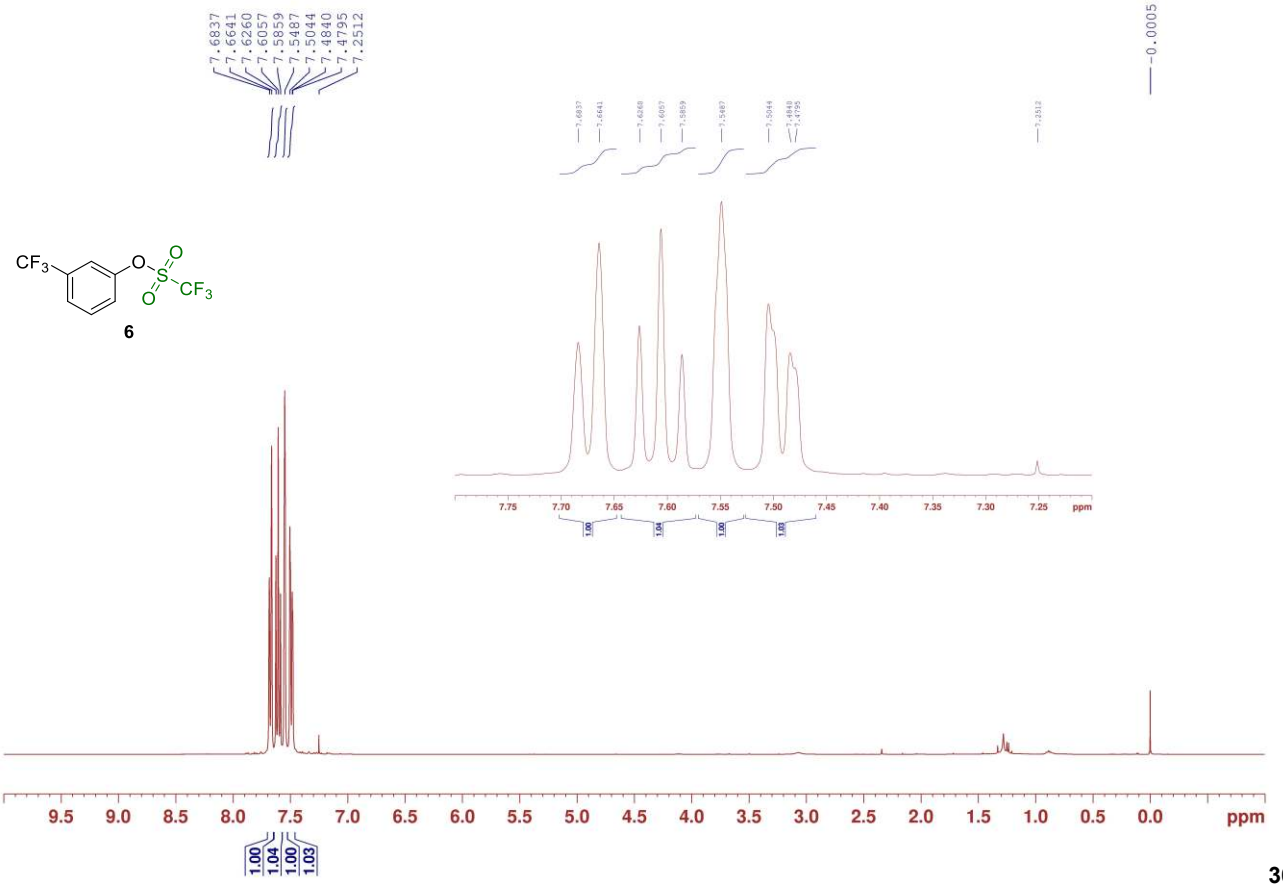

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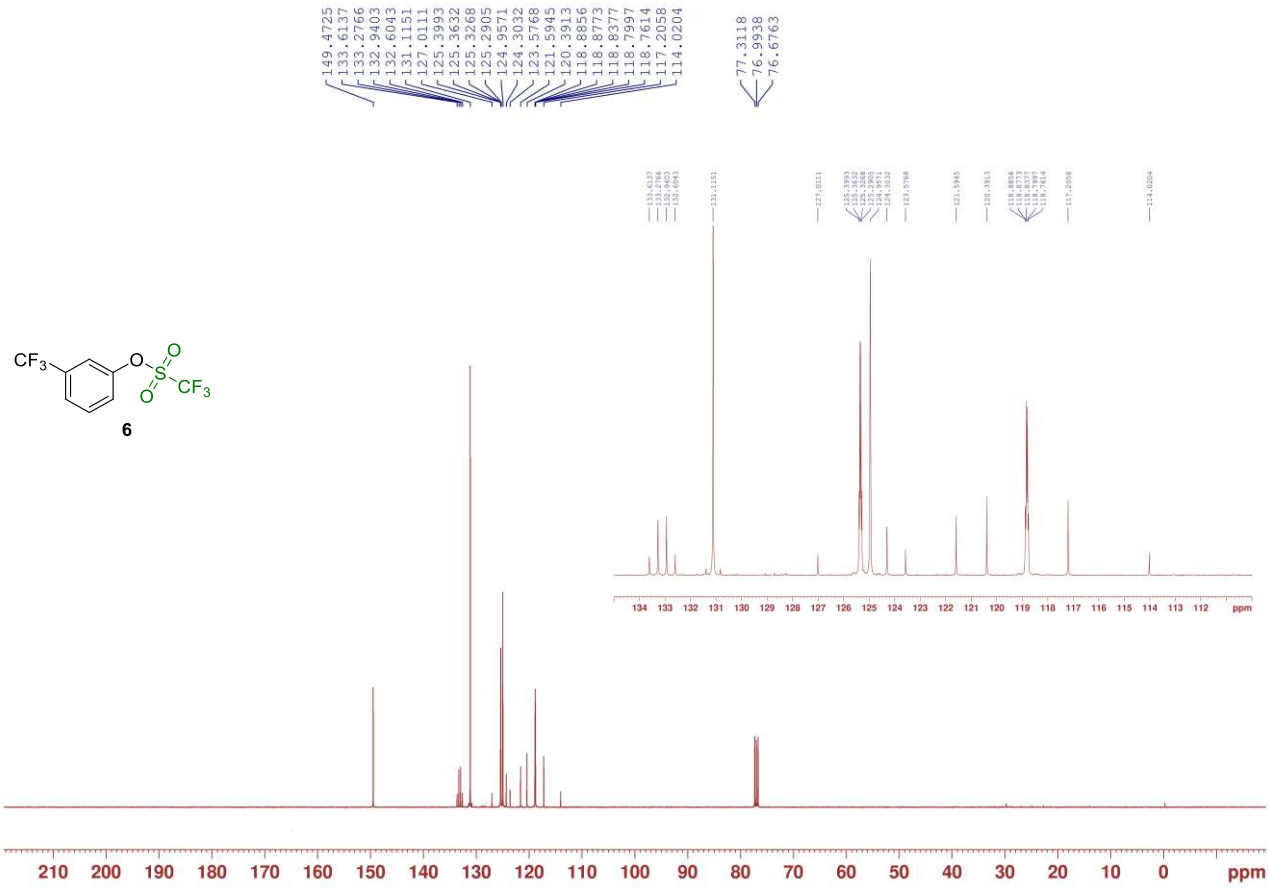
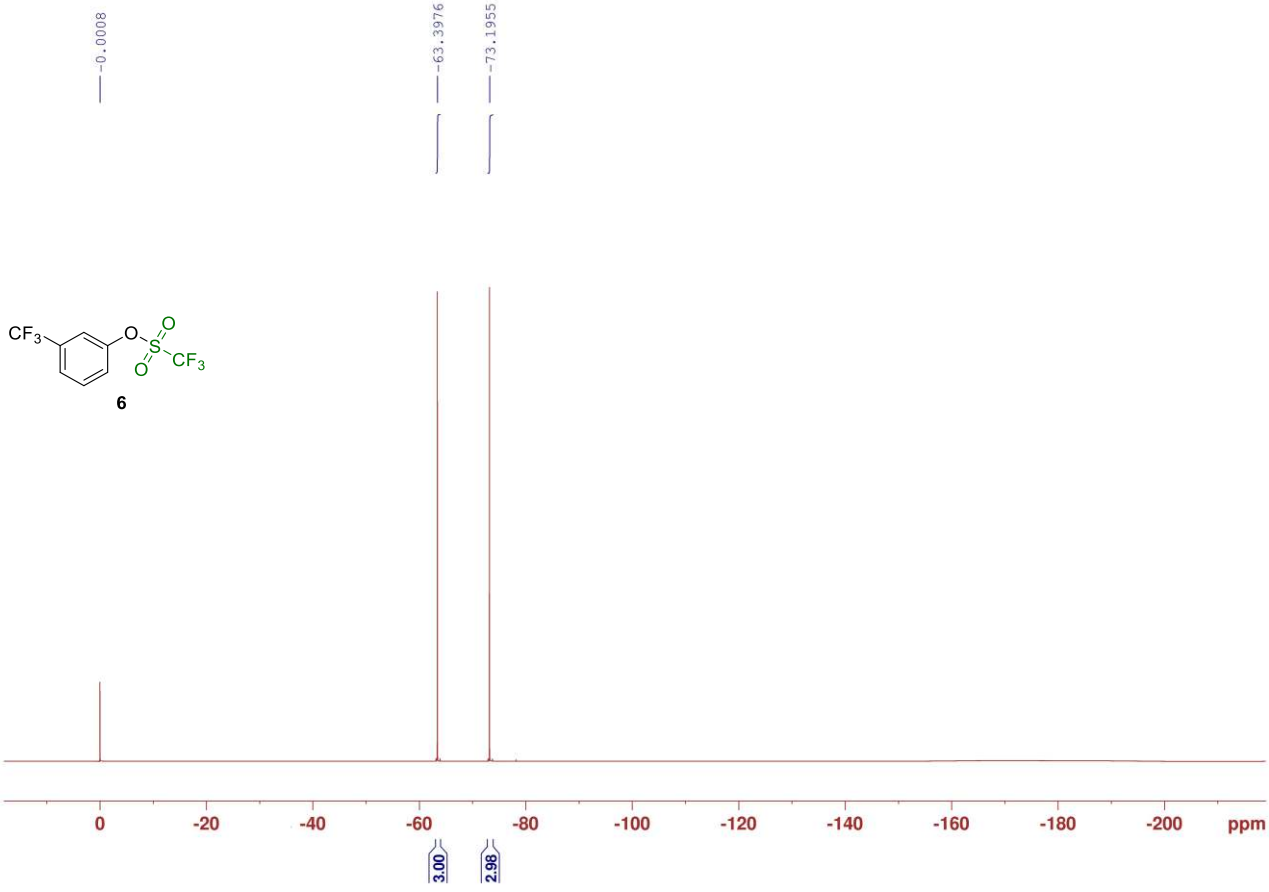
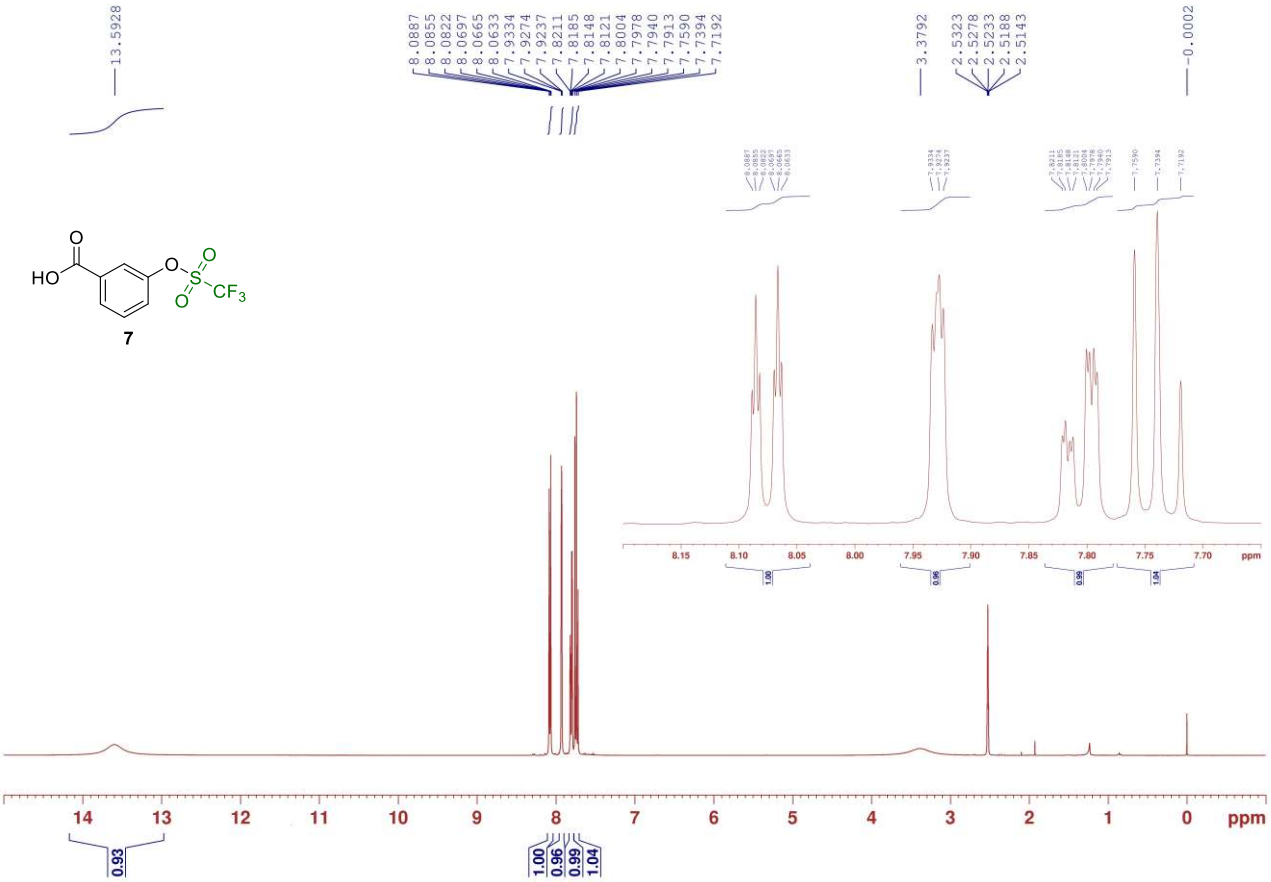


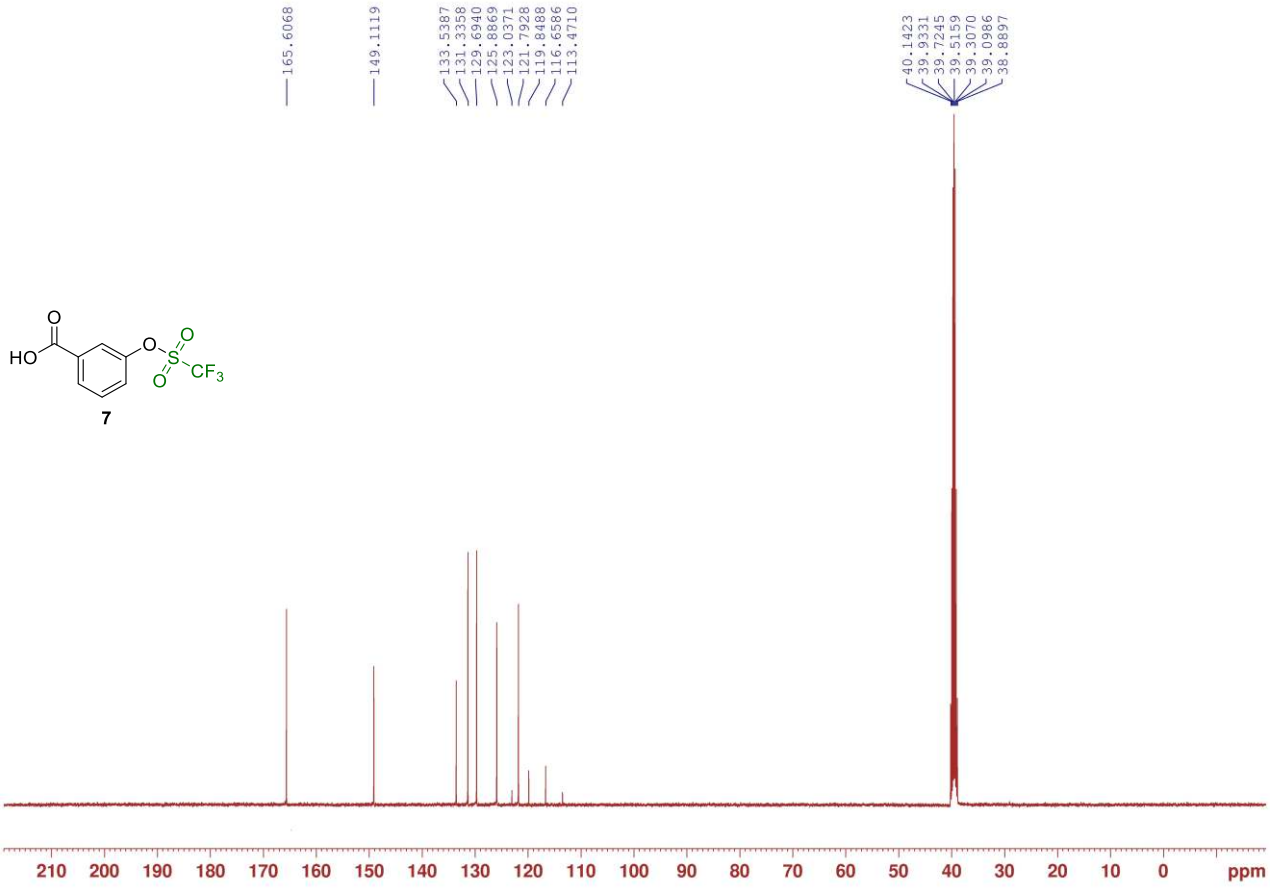
^{19}FNMR spectrum of **6**



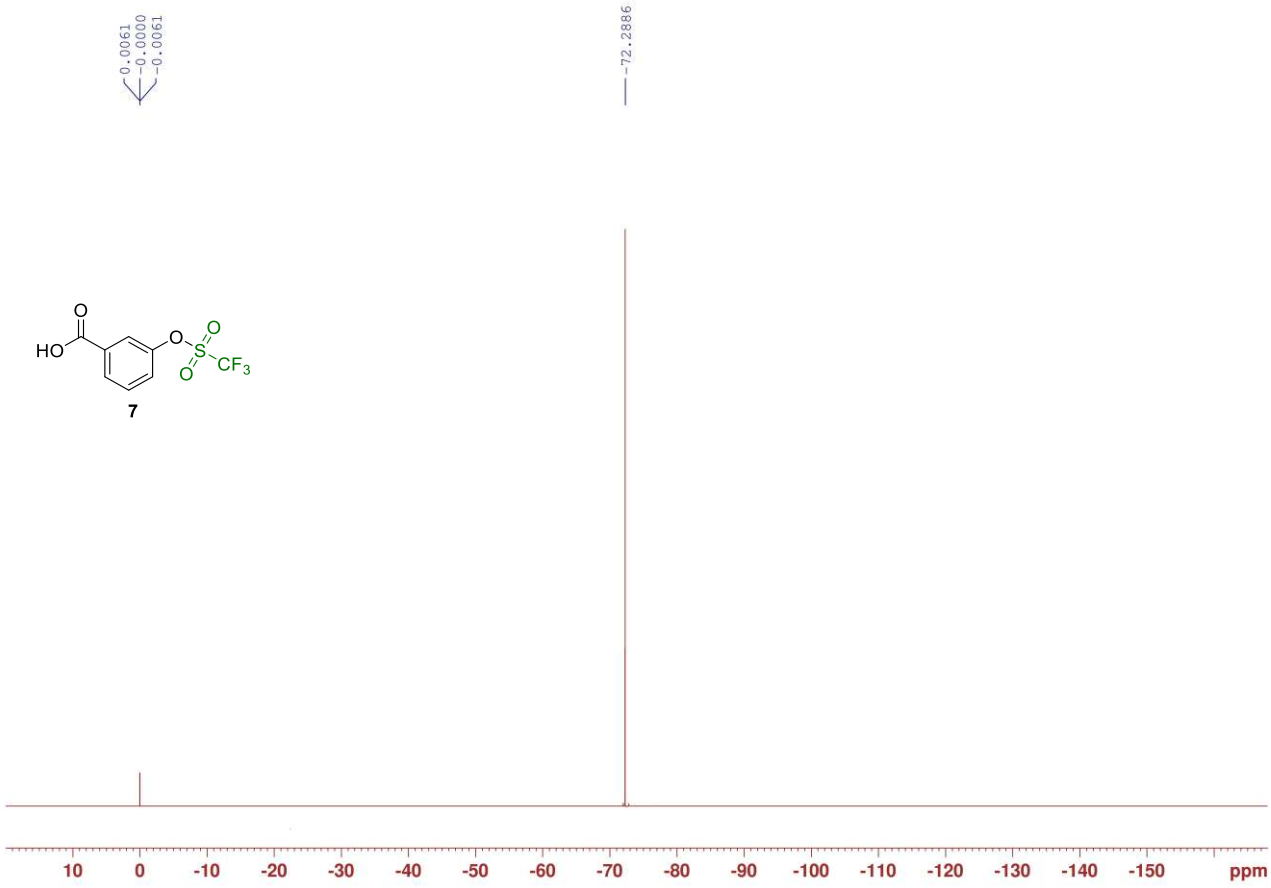
^{1}HNMR spectrum of **7** (DMSO-*d*6)



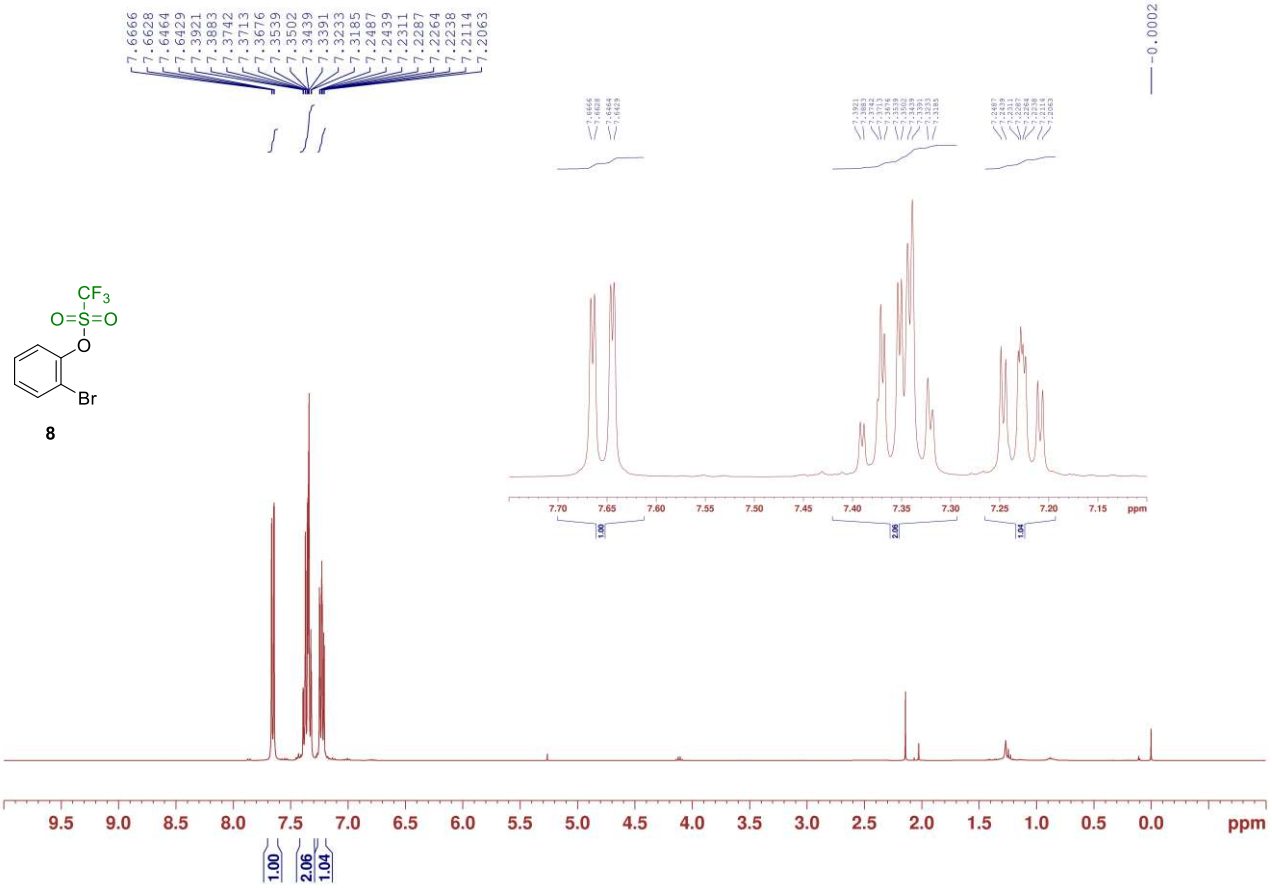
^{13}CNMR spectrum of **7** (DMSO-*d*6)



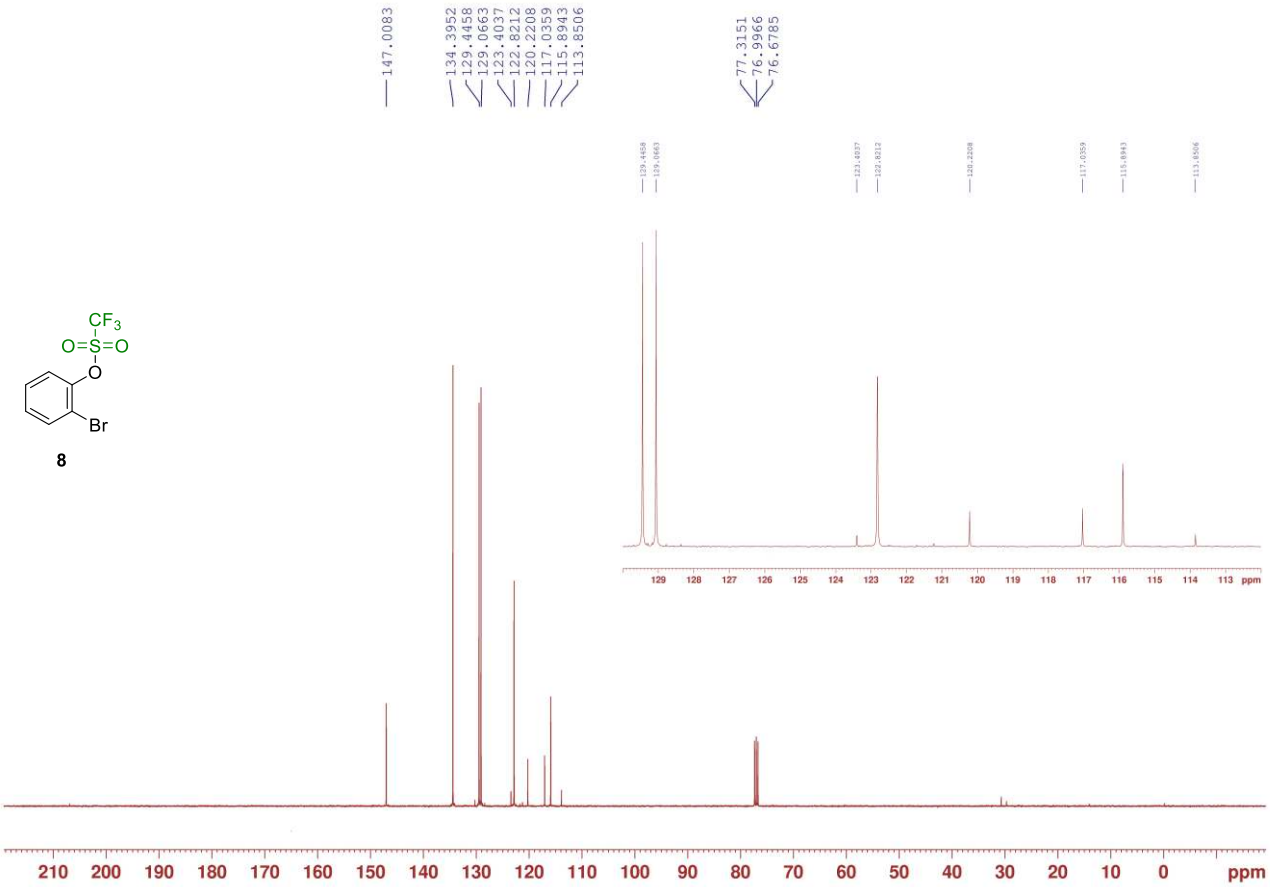
^{19}FNMR spectrum of **7** (DMSO-*d*6)



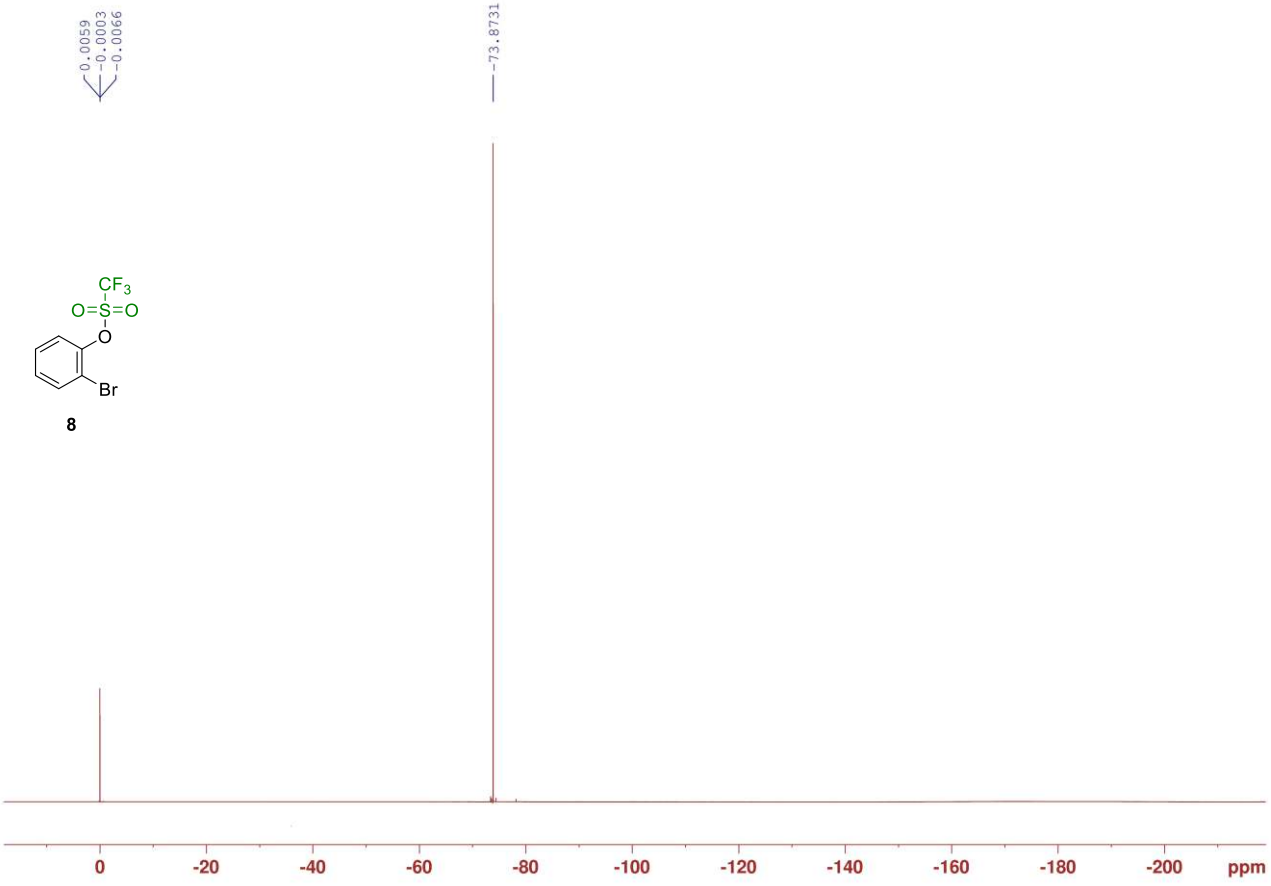
^{1}HNMR spectrum of **8**



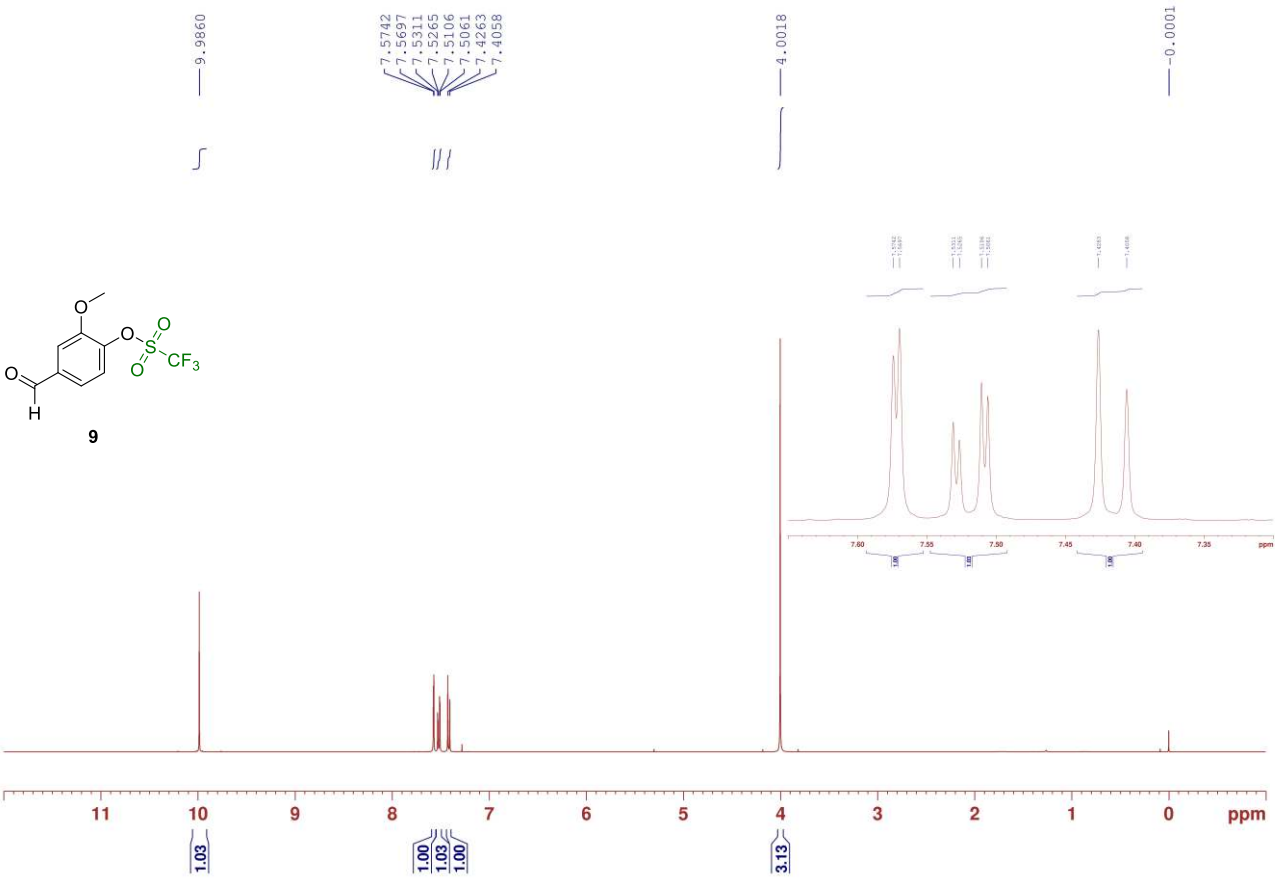
^{13}CNMR spectrum of **8**



^{19}FNMR spectrum of **8**

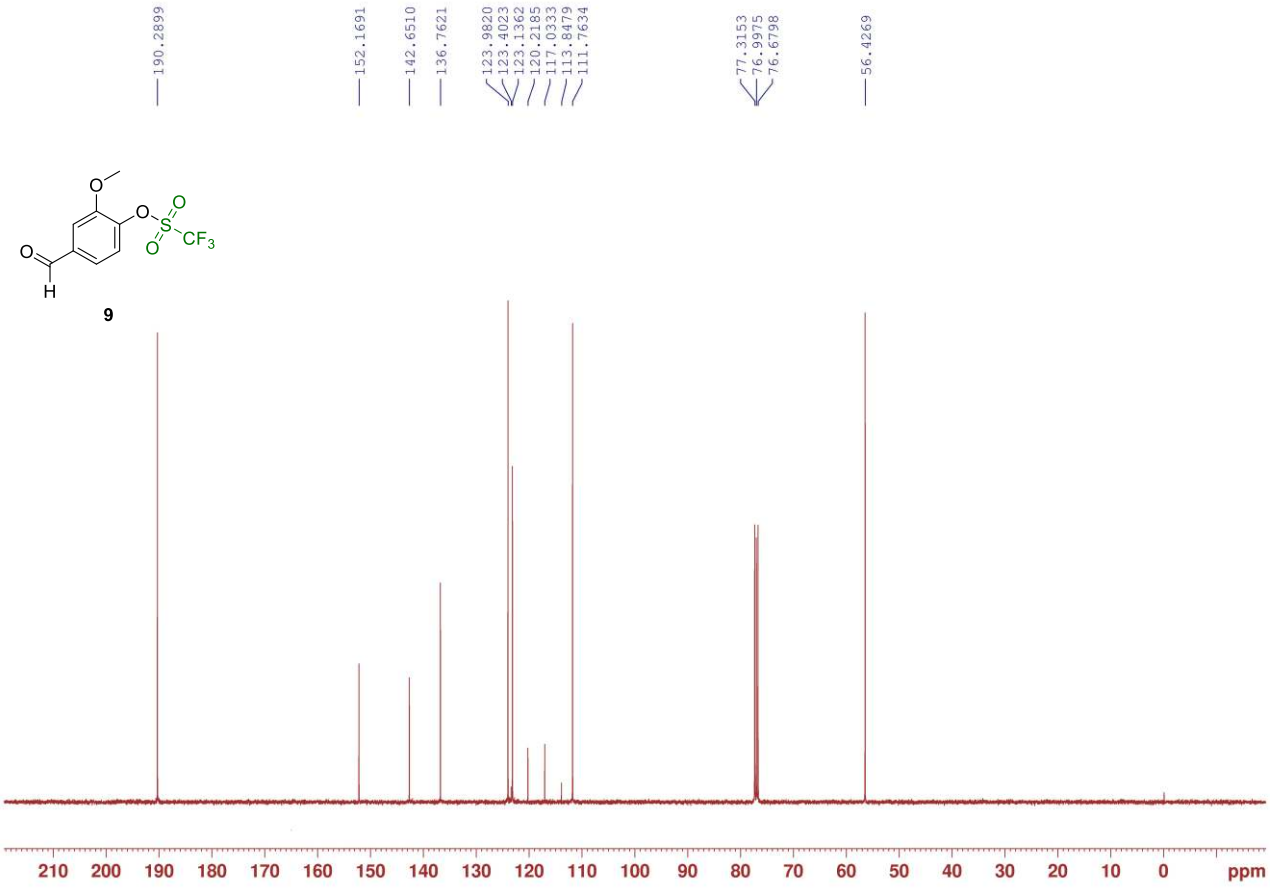


^{1}HNMR spectrum of **9**



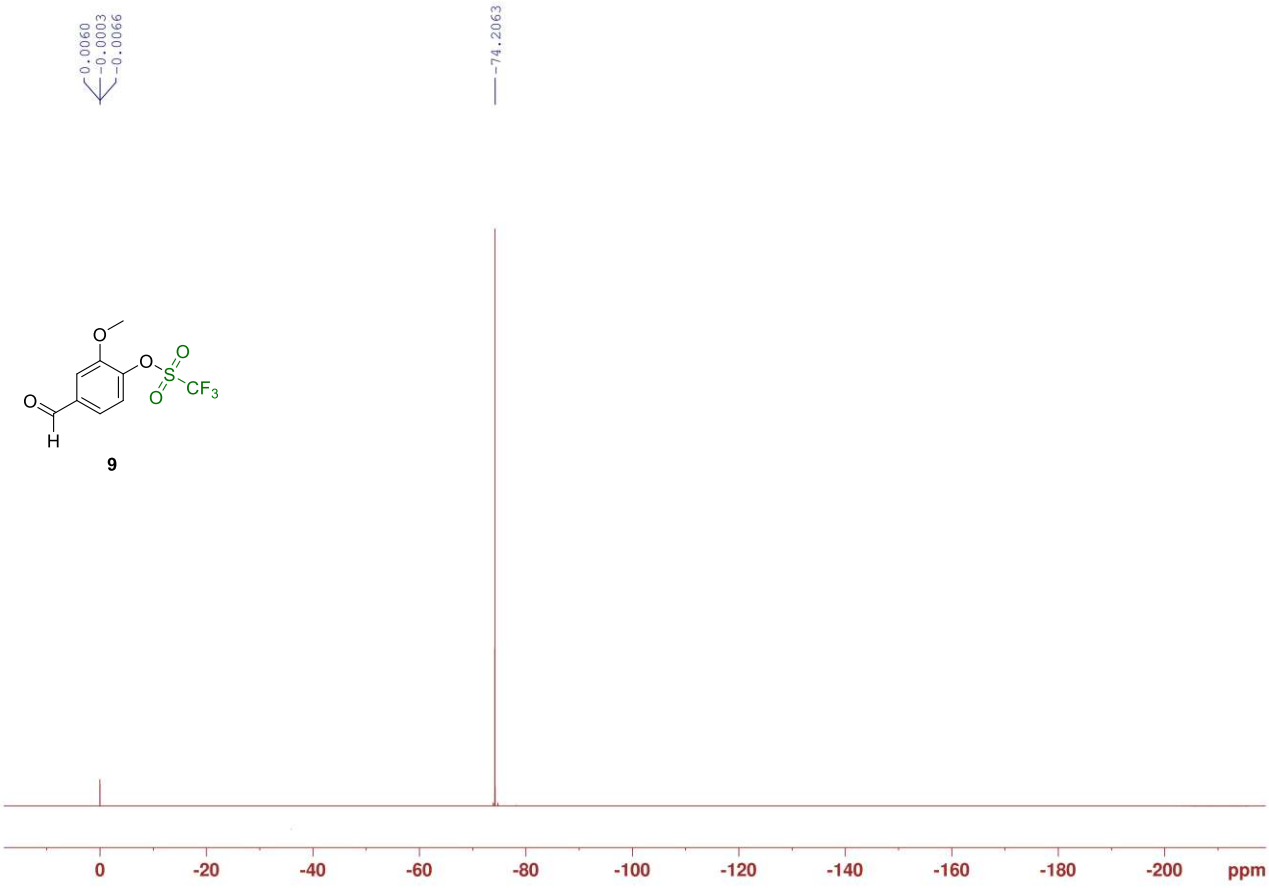
9

^{13}CNMR spectrum of **9**



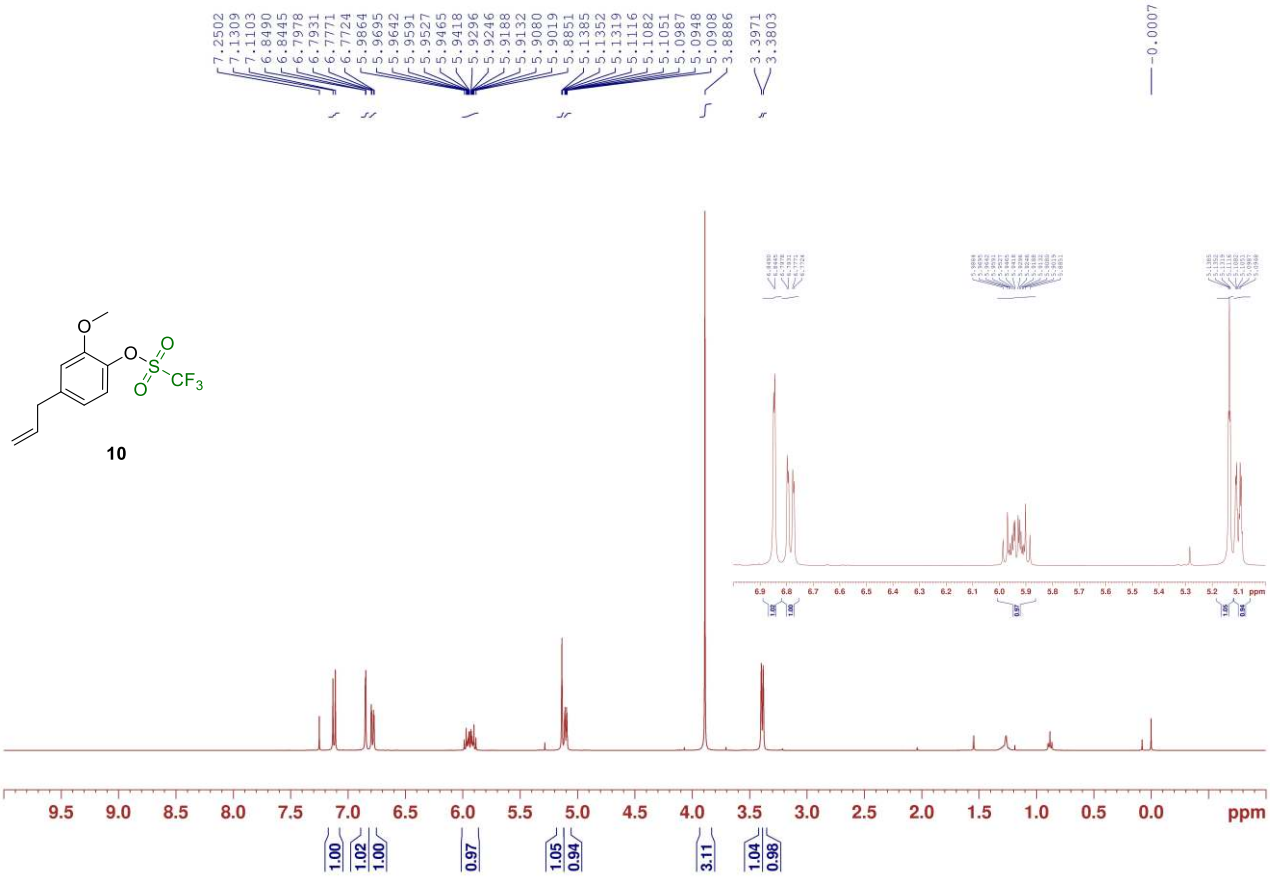
9

^{19}FNMR spectrum of **9**



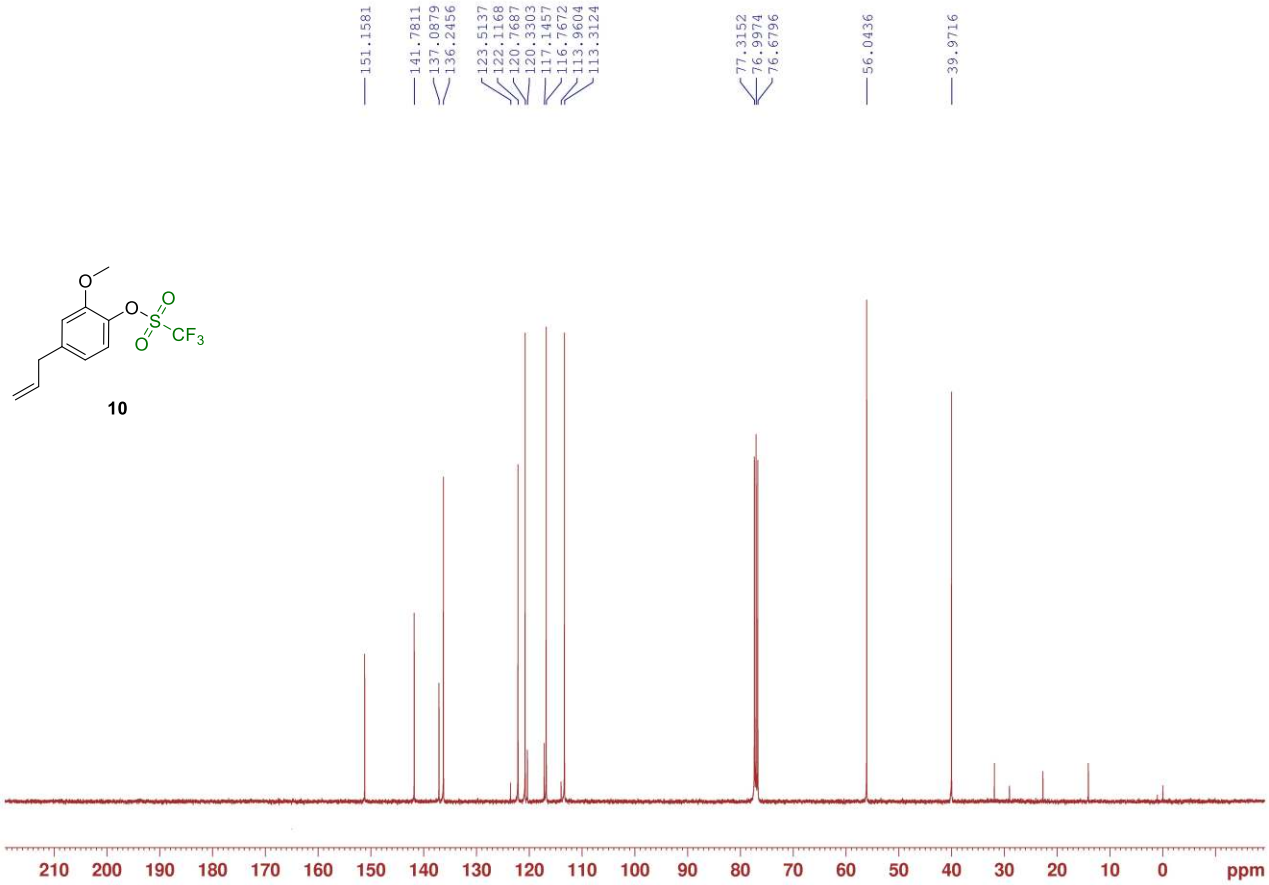
9

^{1}HNMR spectrum of **10**

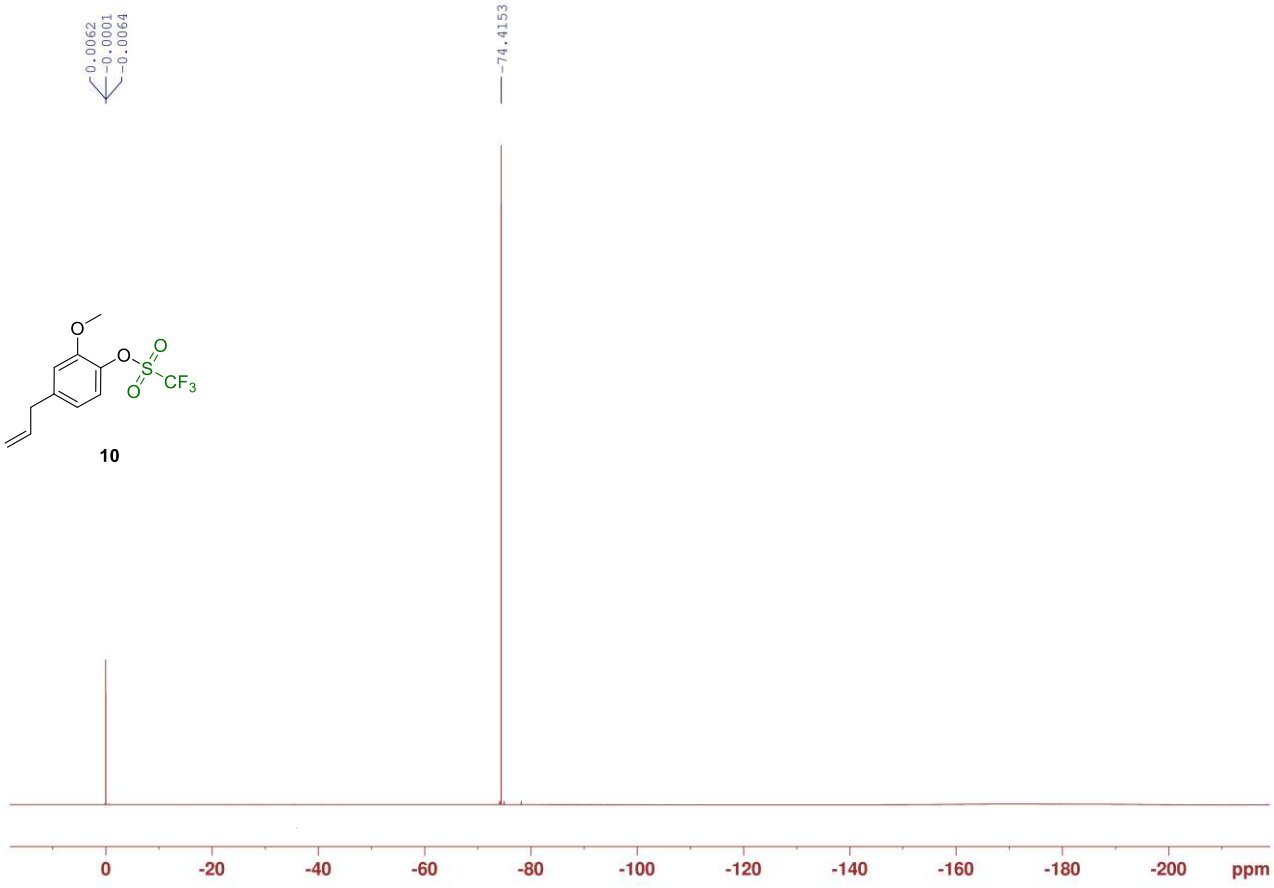


10

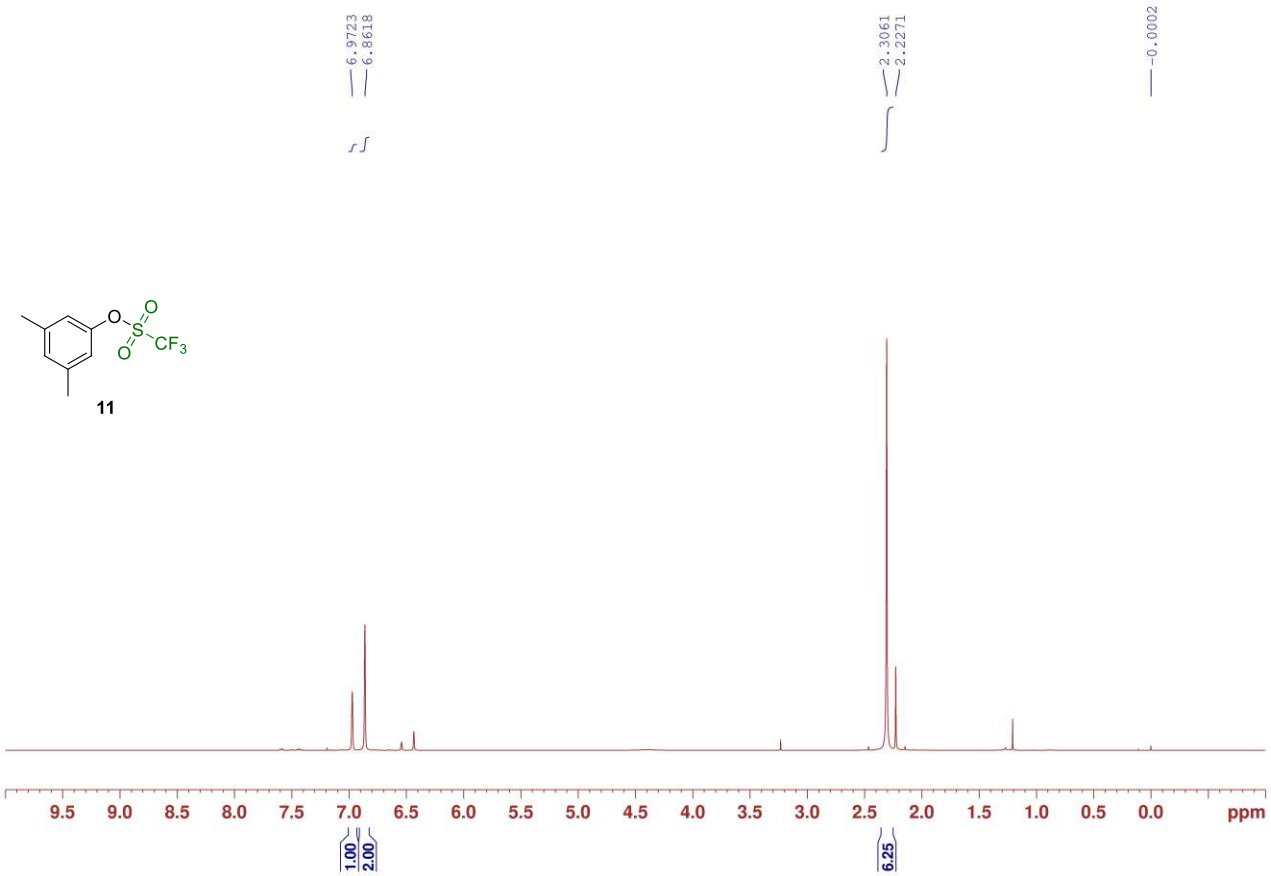
^{13}CNMR spectrum of **10**



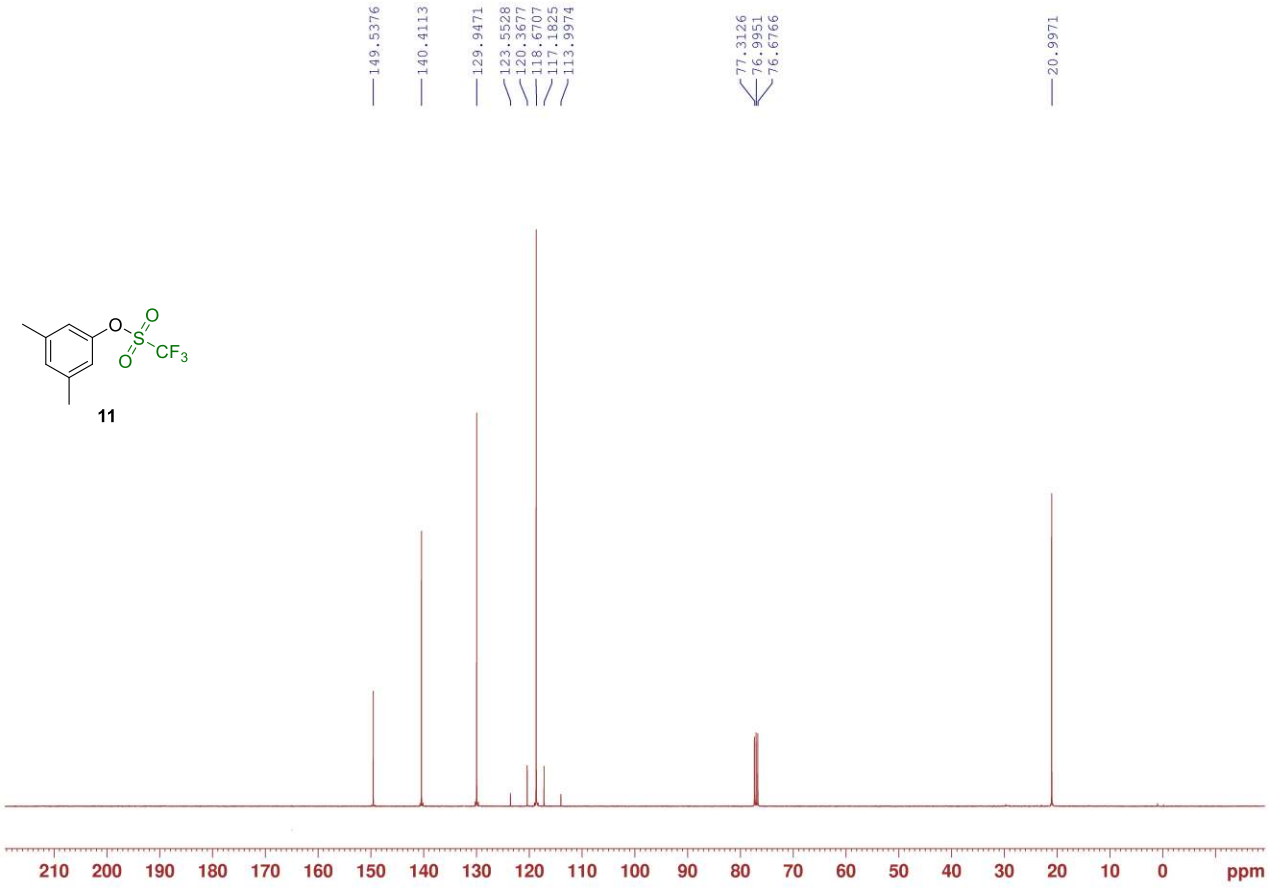
^{19}FNMR spectrum of **10**



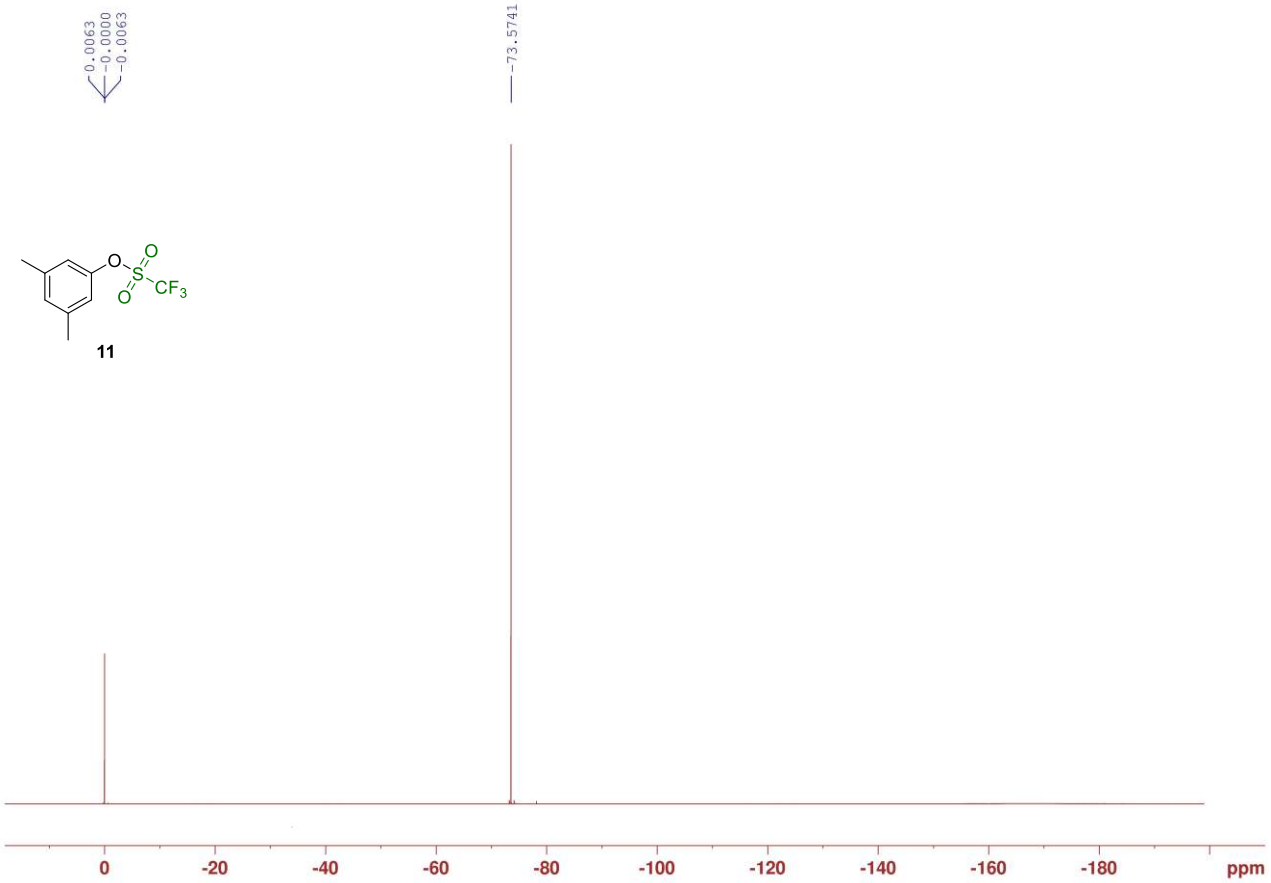
^{1}HNMR spectrum of **11**



^{13}CNMR spectrum of **11**

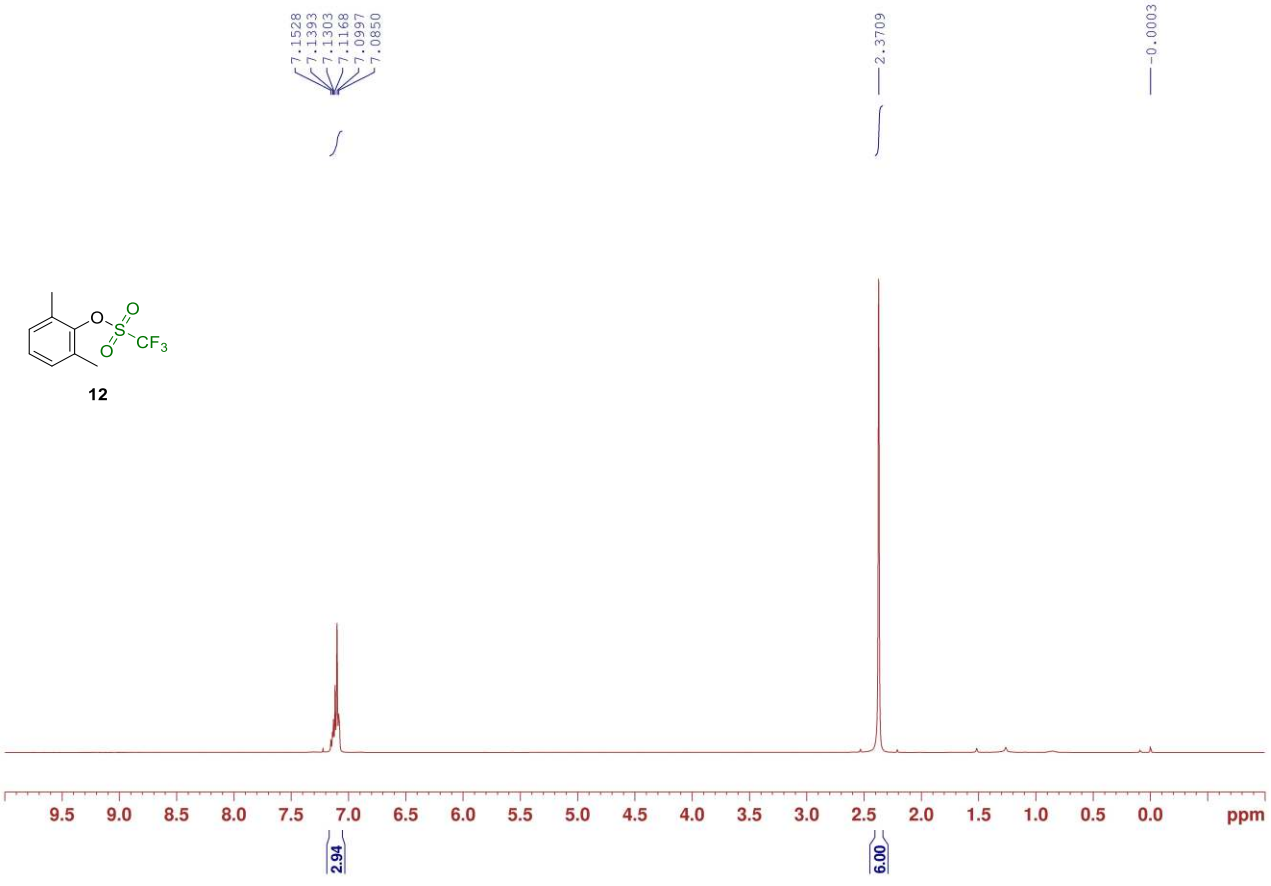


^{19}FNMR spectrum of **11**



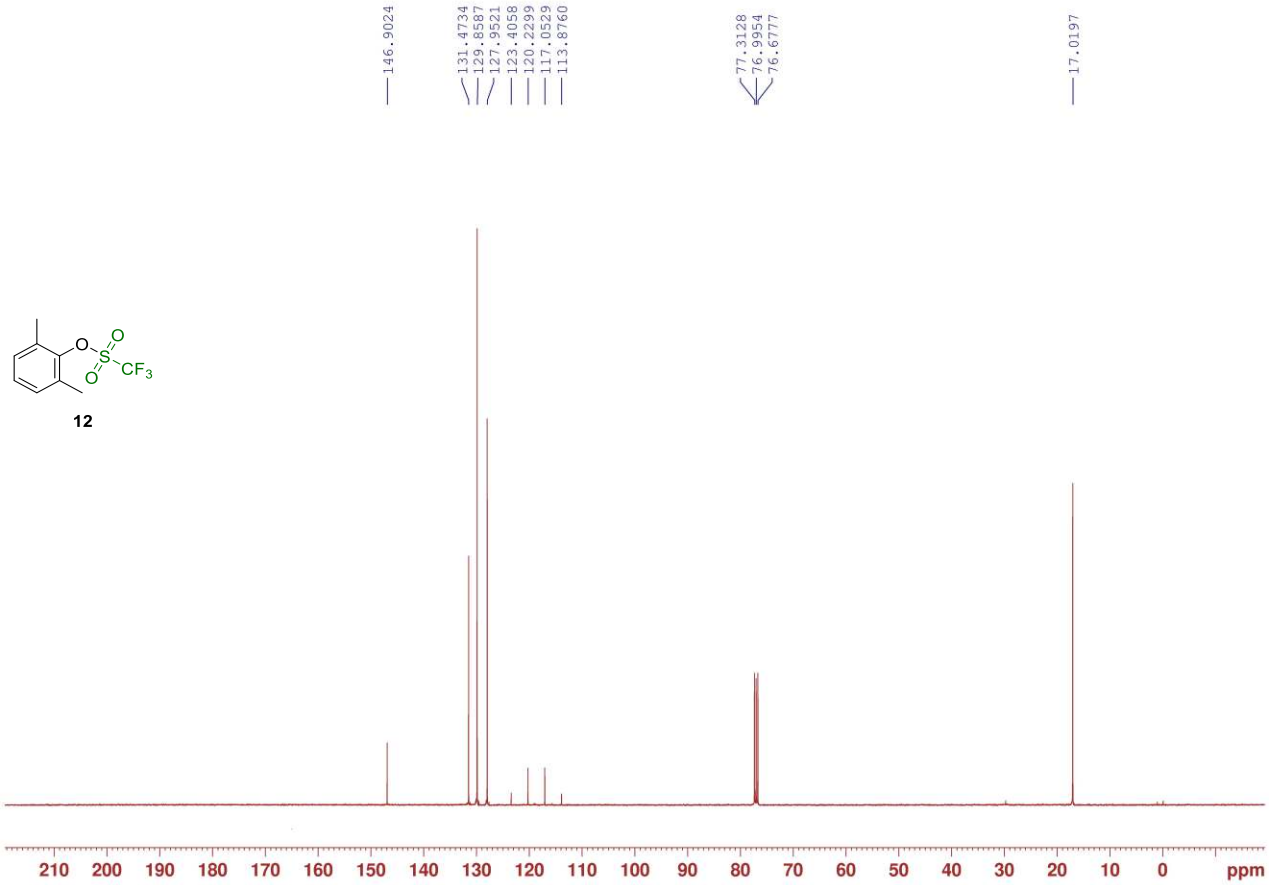
11

^{1}HNMR spectrum of **12**



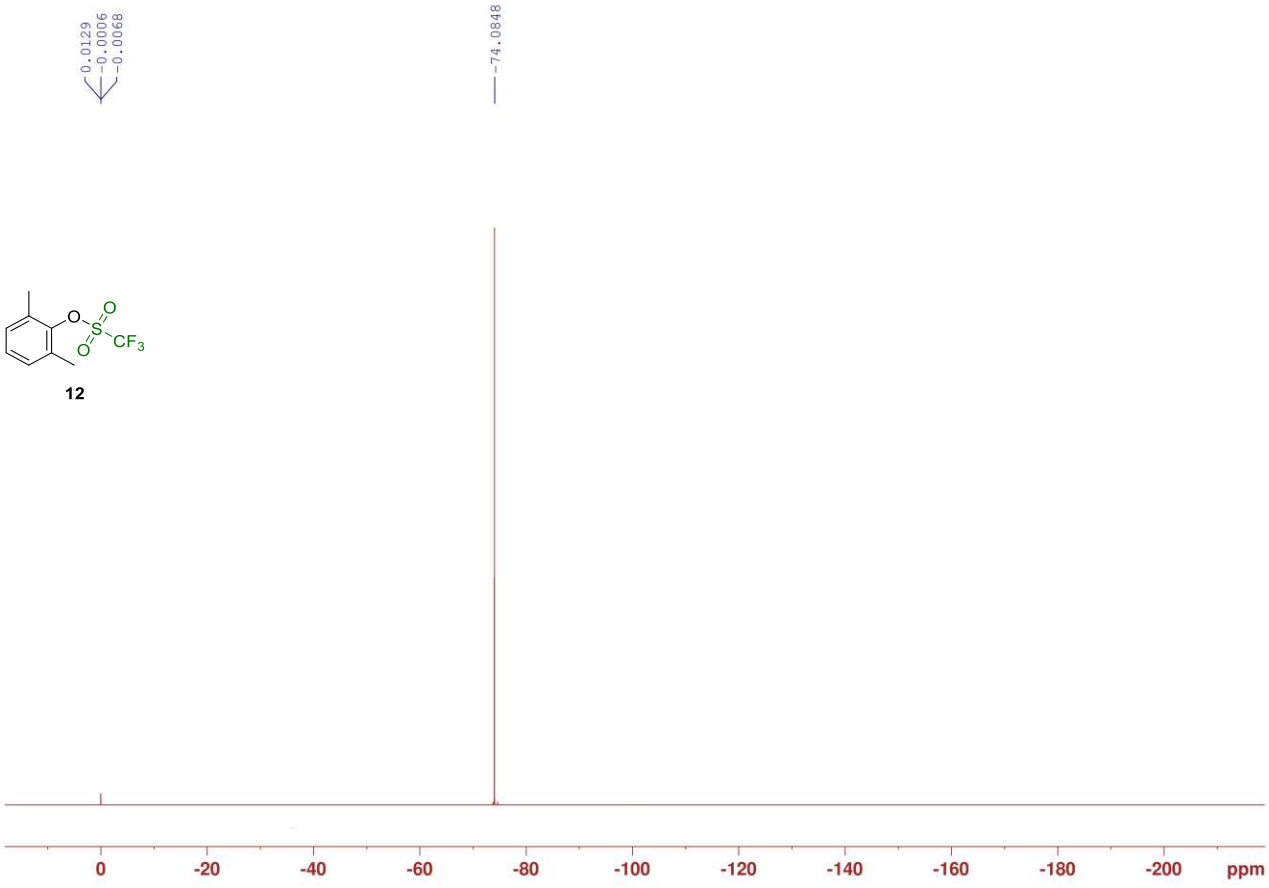
12

^{13}CNMR spectrum of **12**



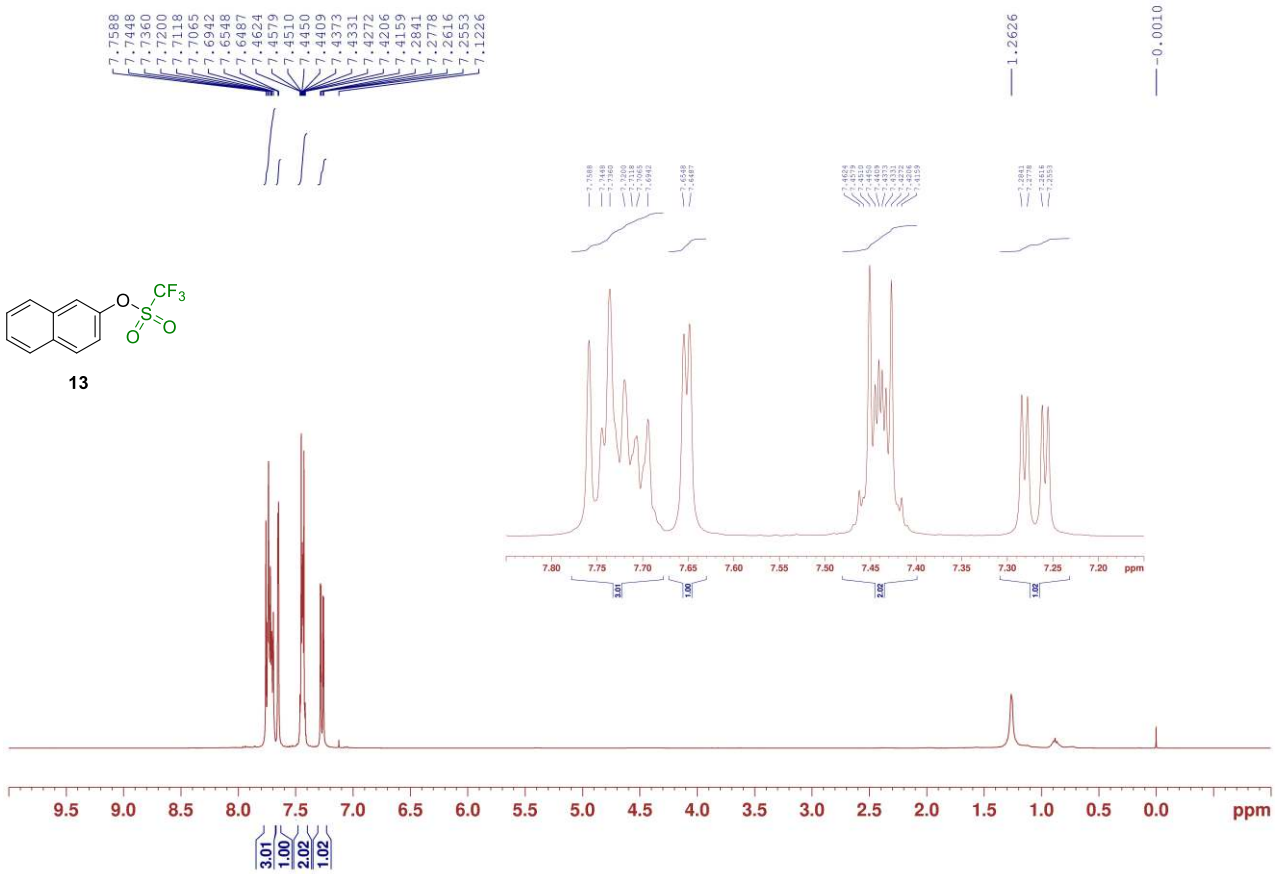
12

^{19}FNMR spectrum of **12**

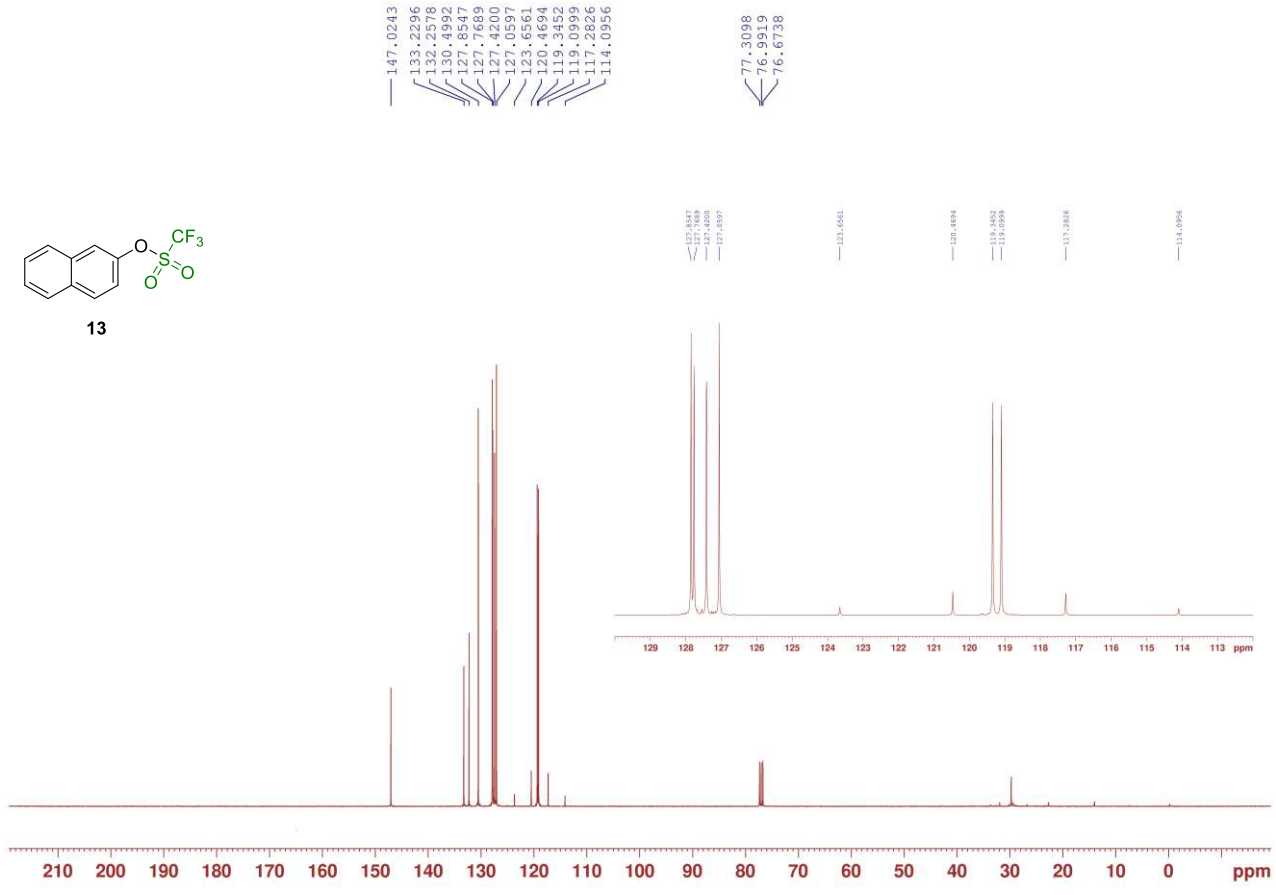


12

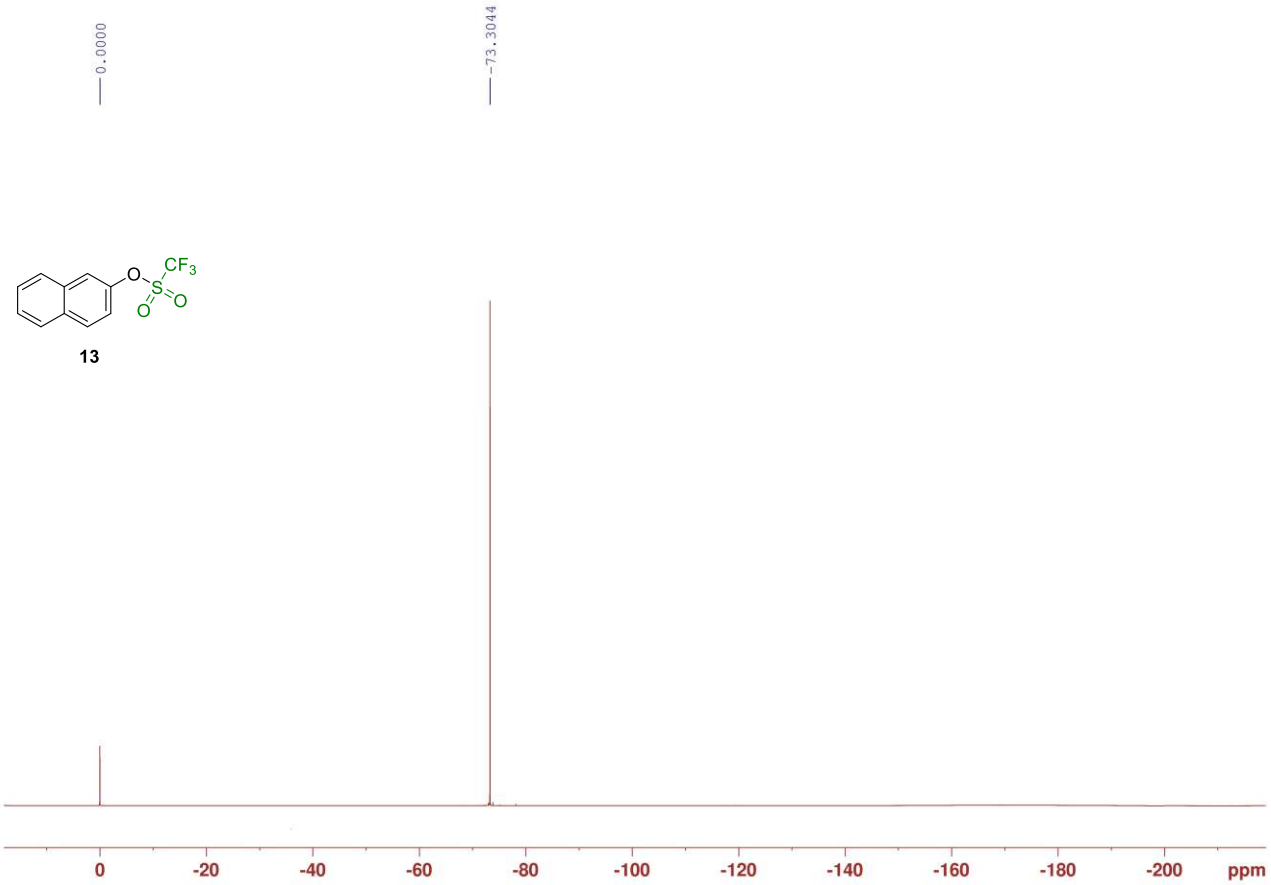
^{1}HNMR spectrum of **13**



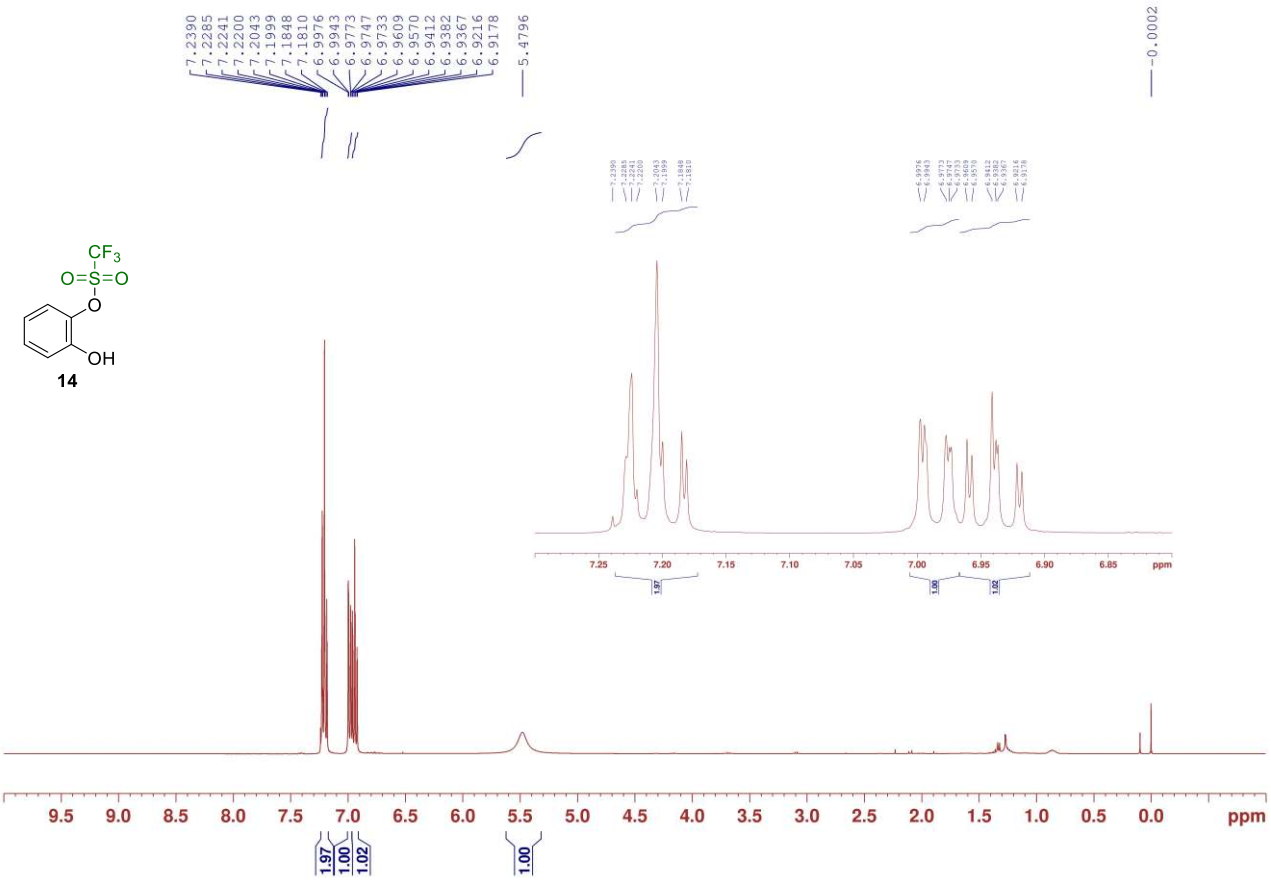
^{13}CNMR spectrum of **13**



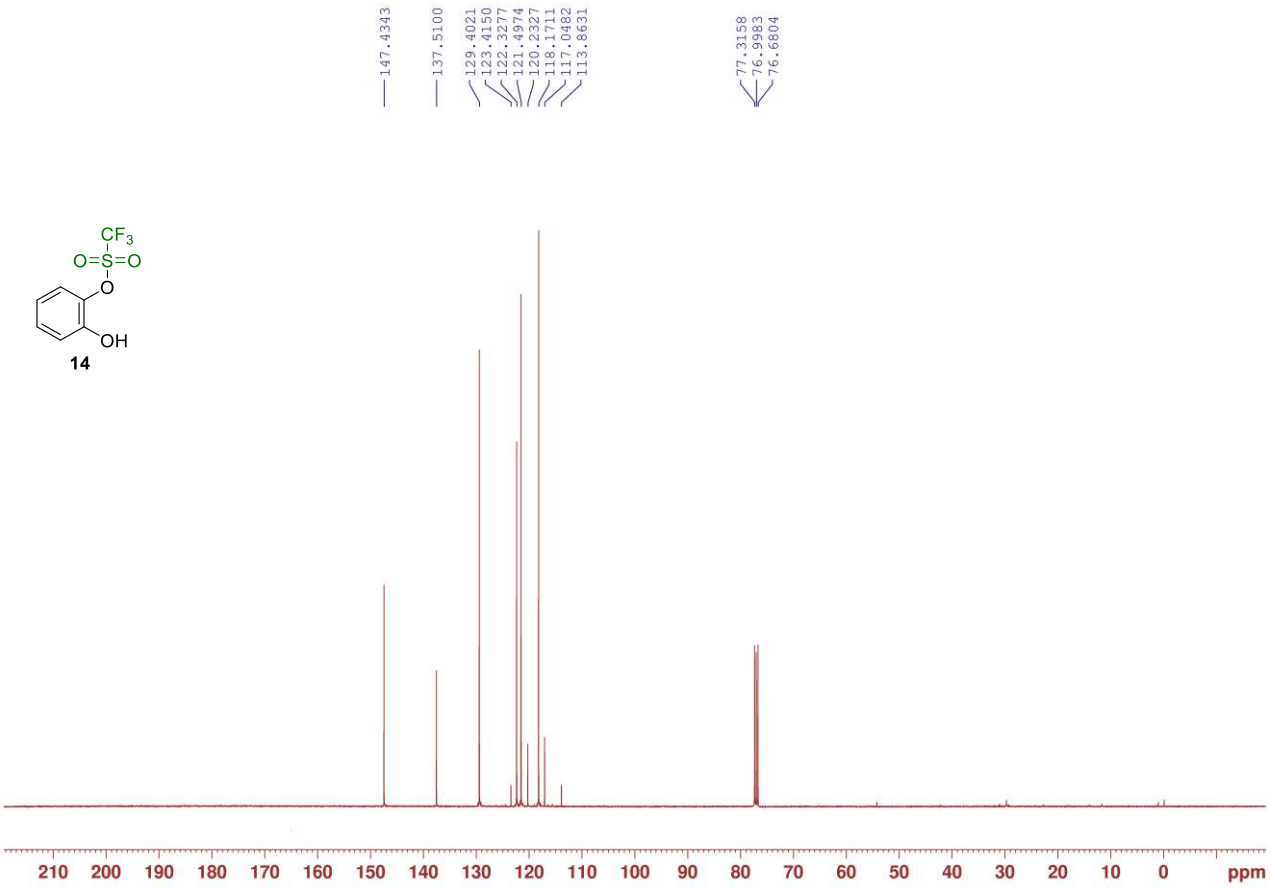
^{19}FNMR spectrum of **13**



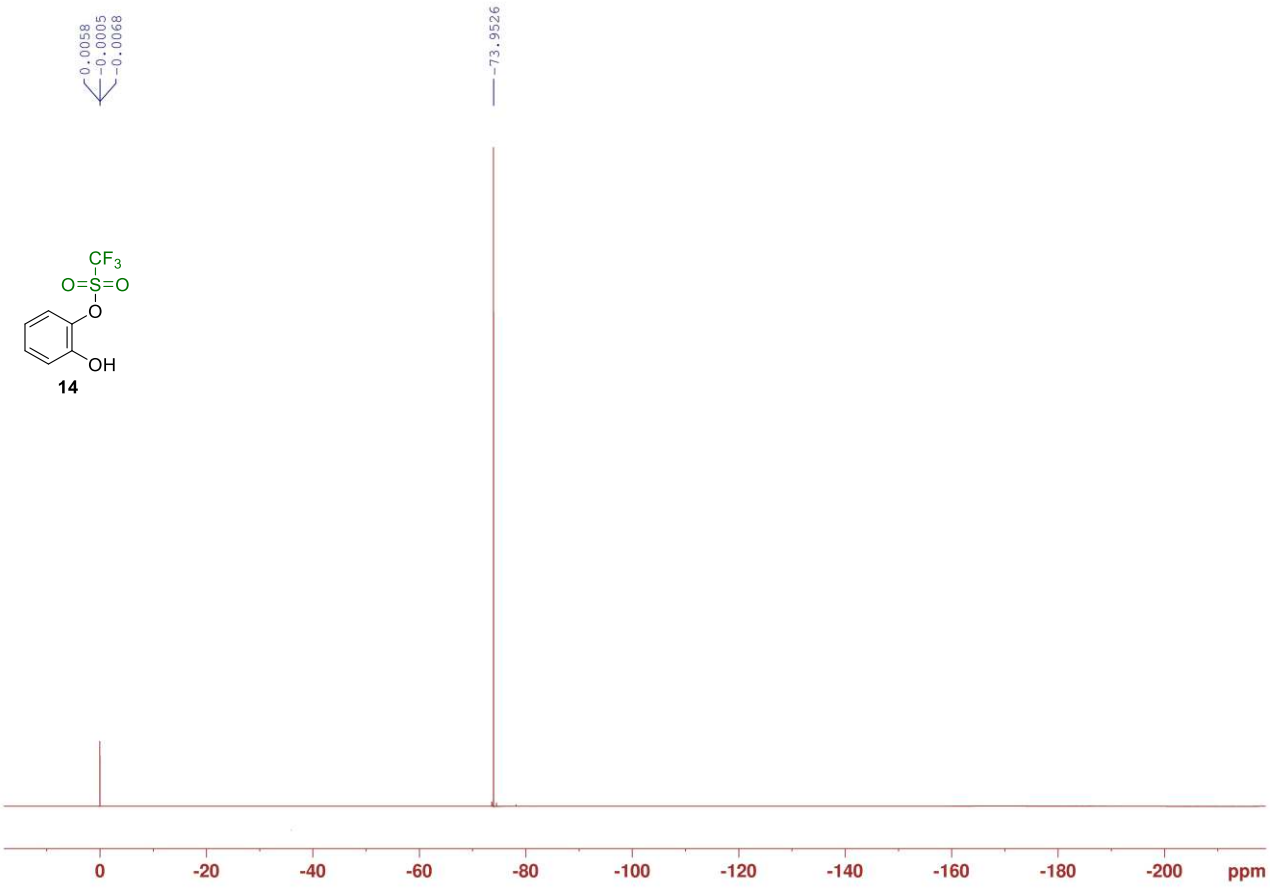
^{1}HNMR spectrum of **14**



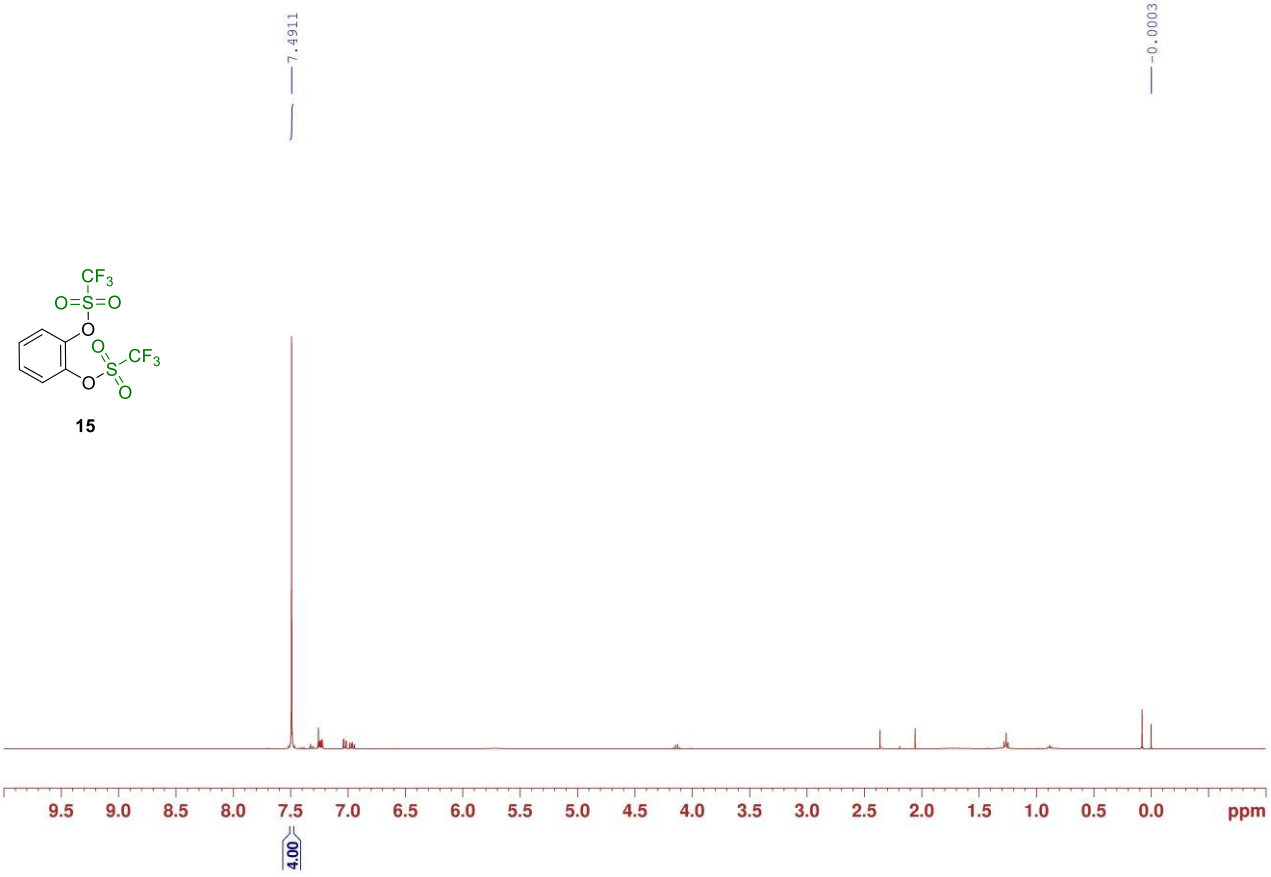
^{13}CNMR spectrum of **14**



^{19}FNMR spectrum of **14**

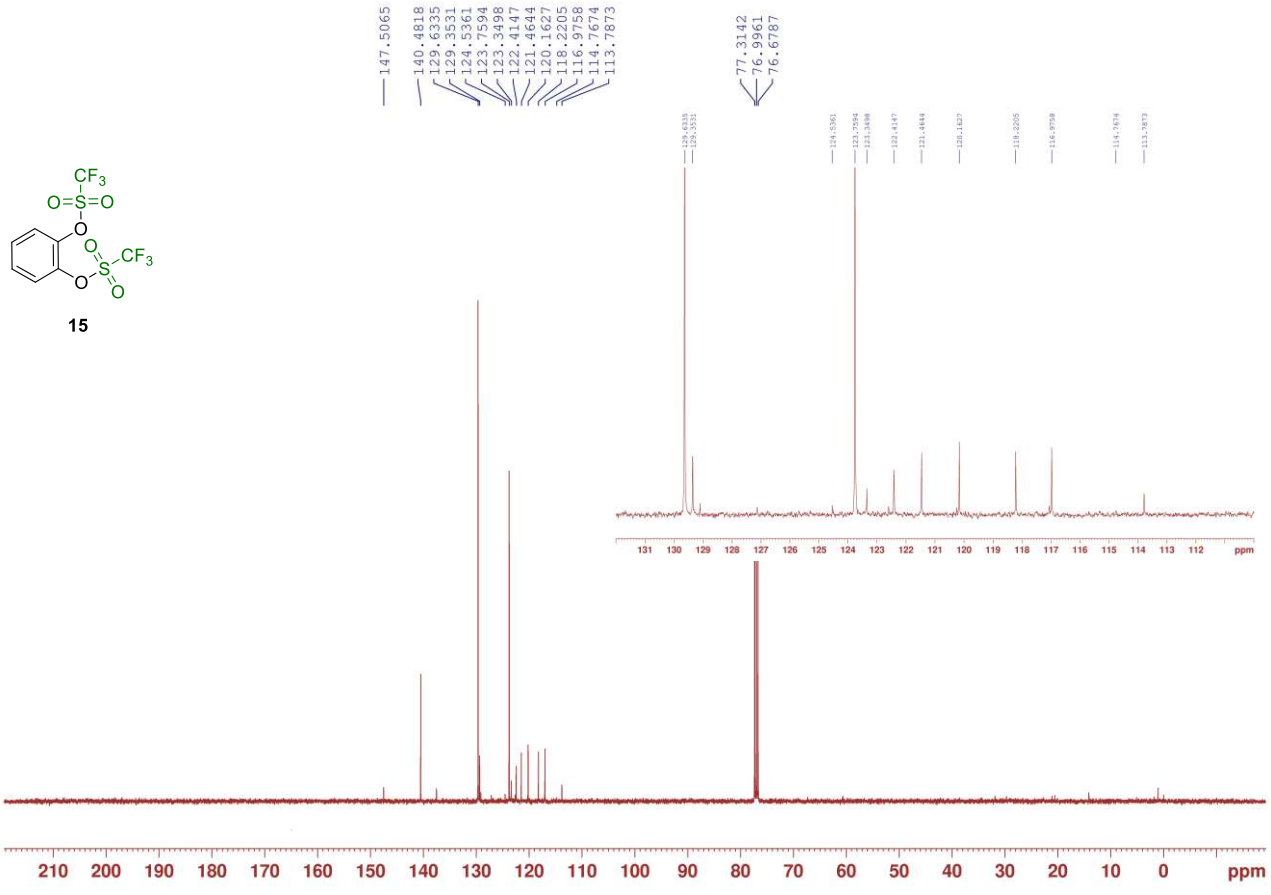


^{1}HNMR spectrum of **15**



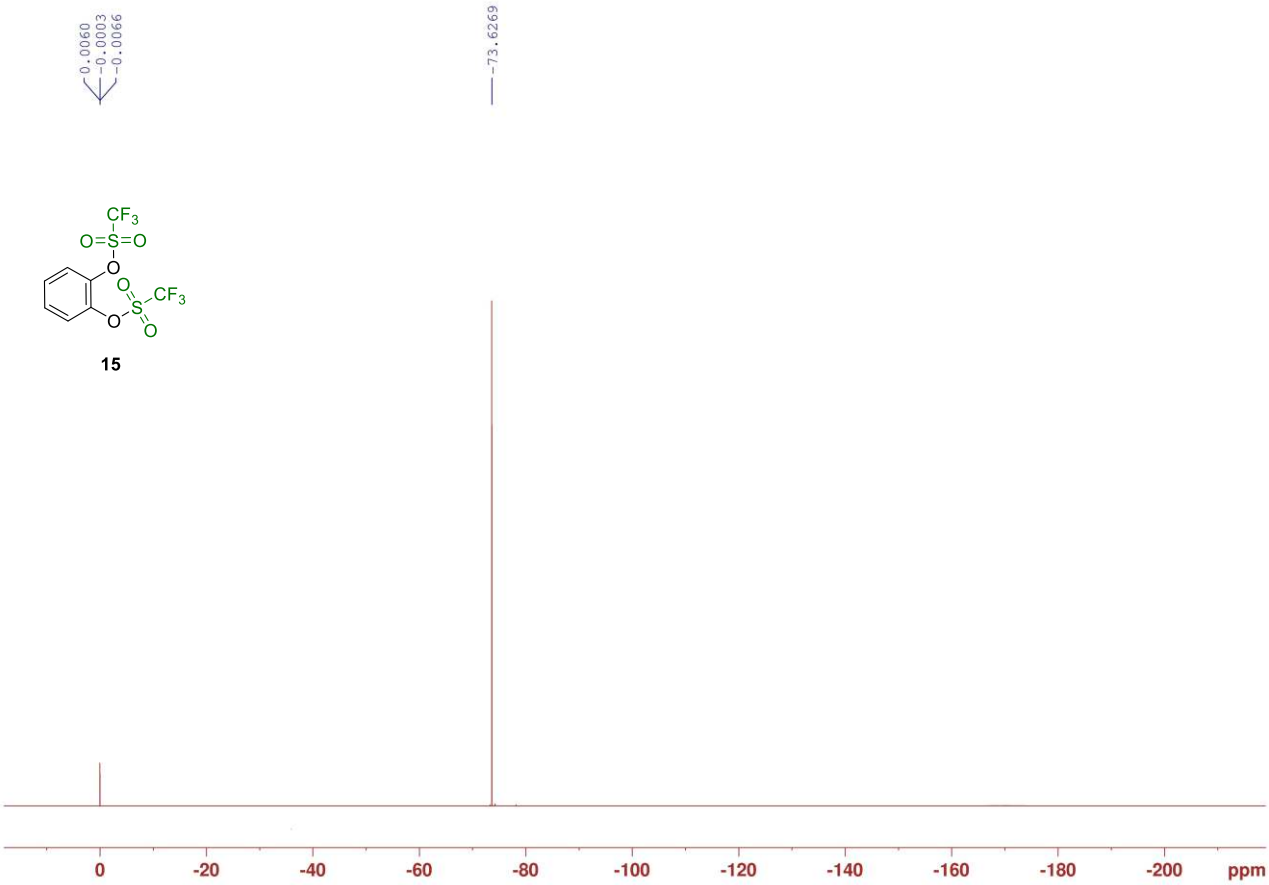
15

^{13}CNMR spectrum of **15**

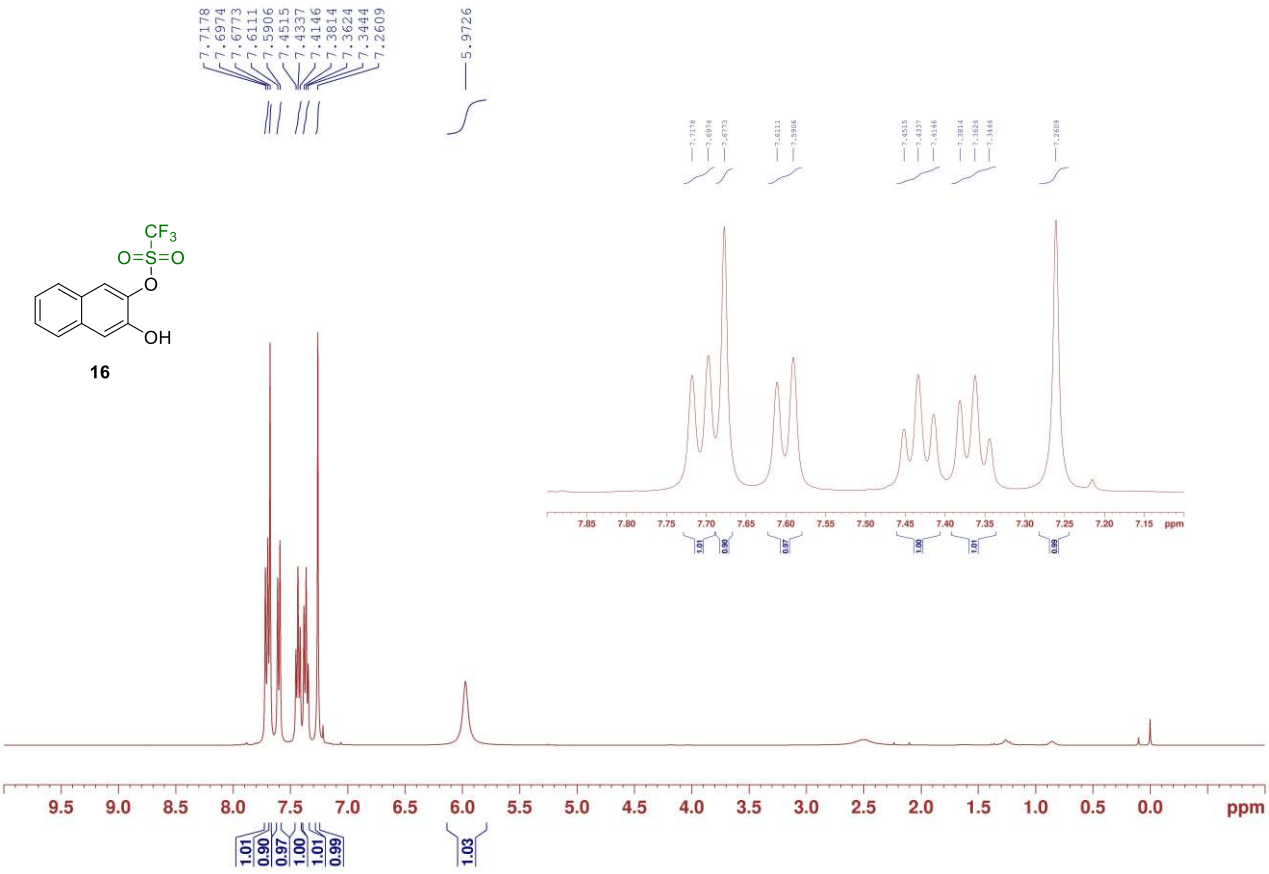


15

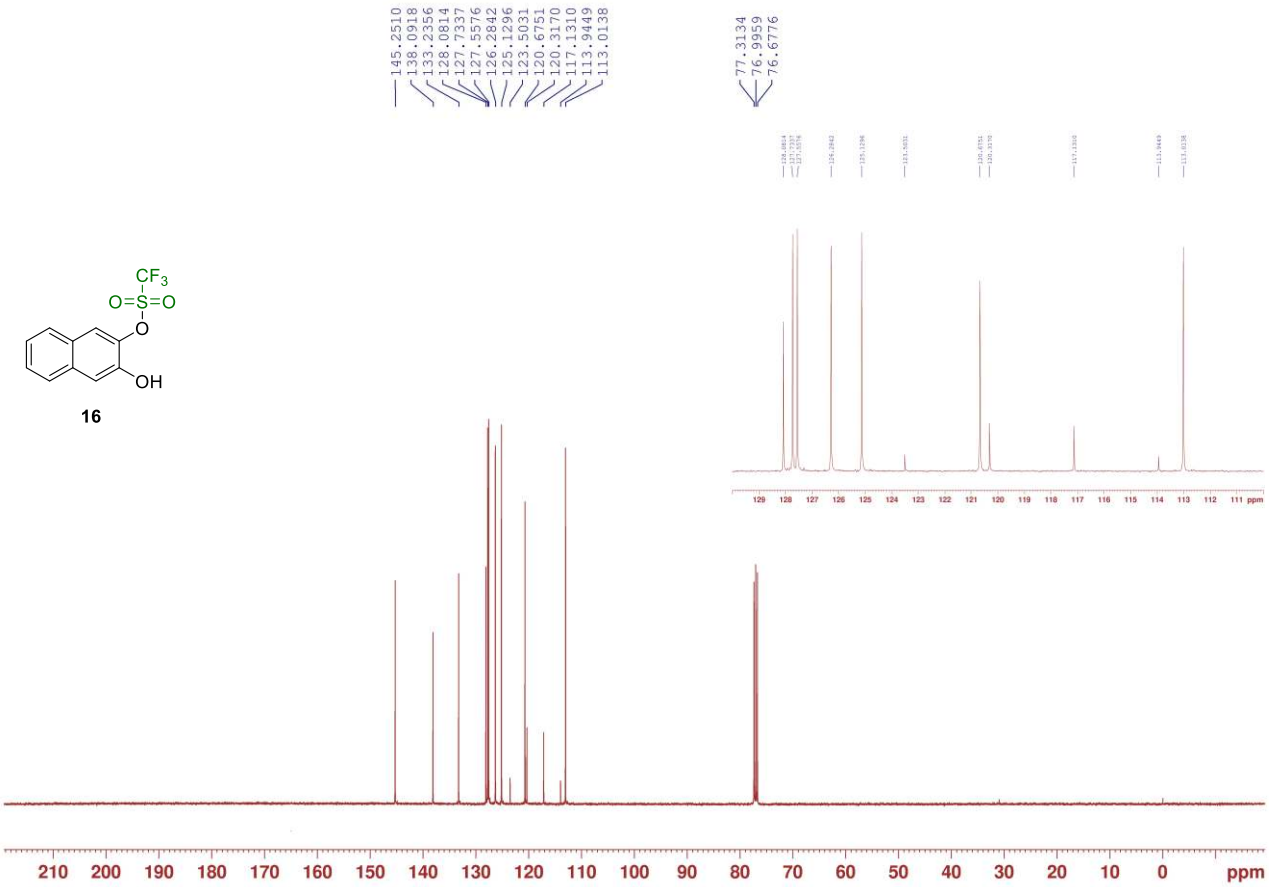
^{19}FNMR spectrum of **15**



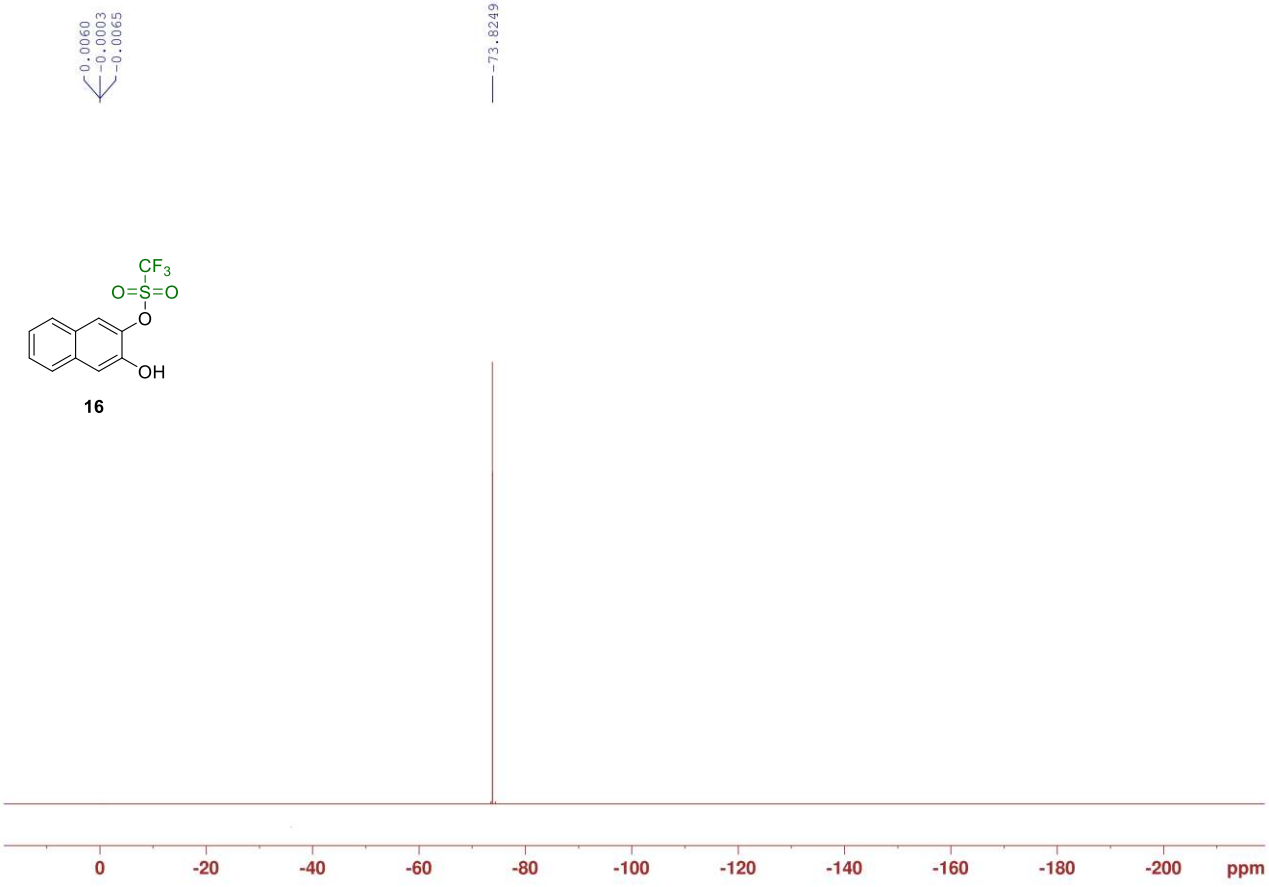
^{1}HNMR spectrum of **16**



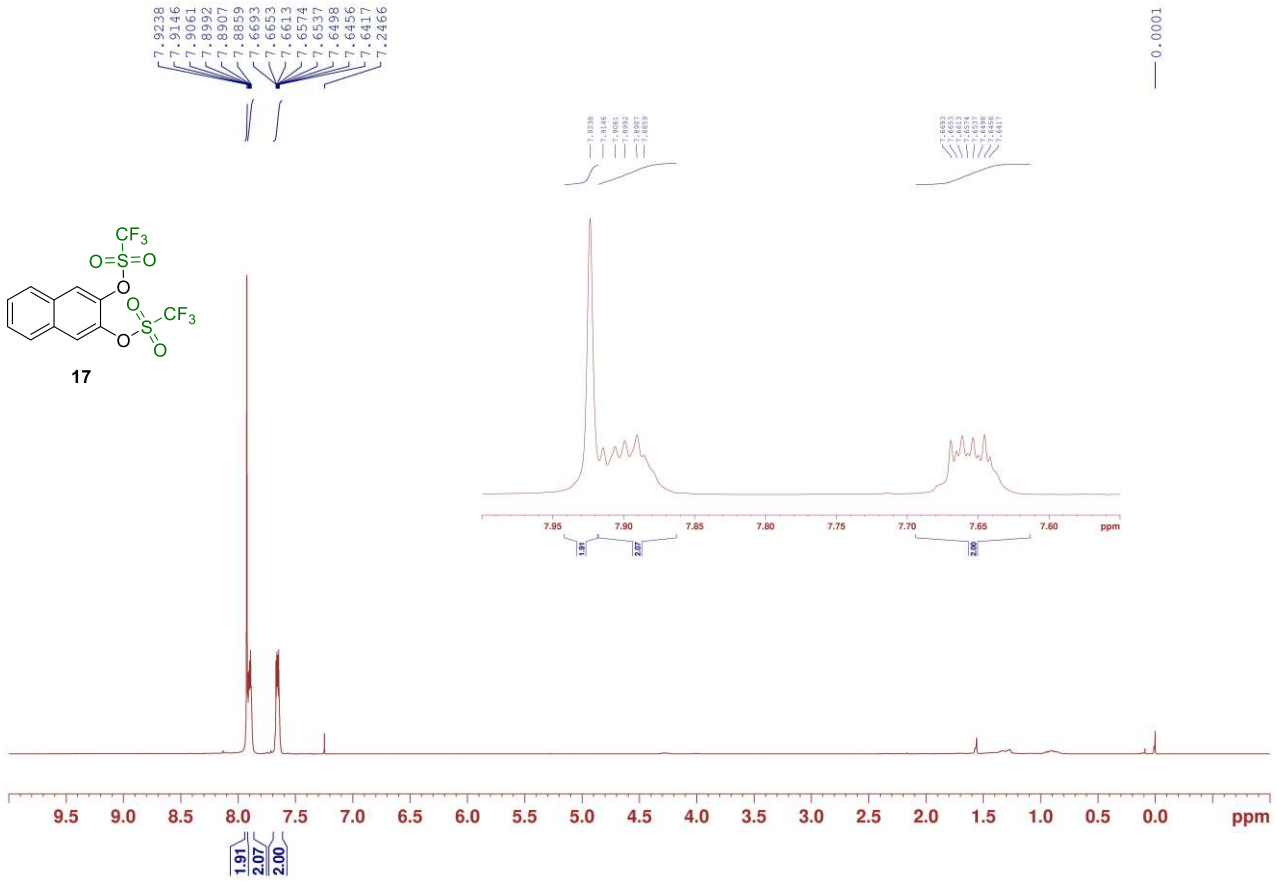
^{13}CNMR spectrum of **16**



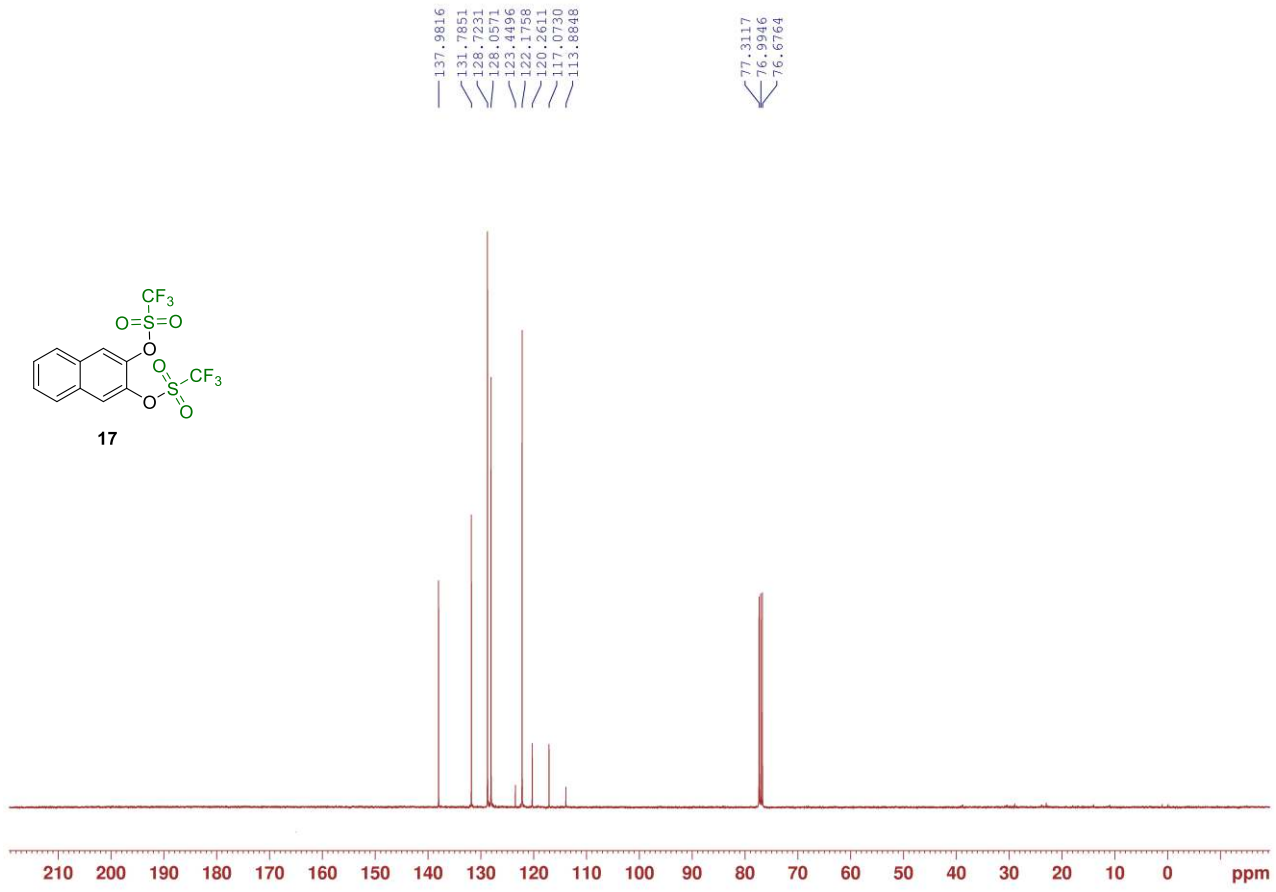
^{19}FNMR spectrum of **16**



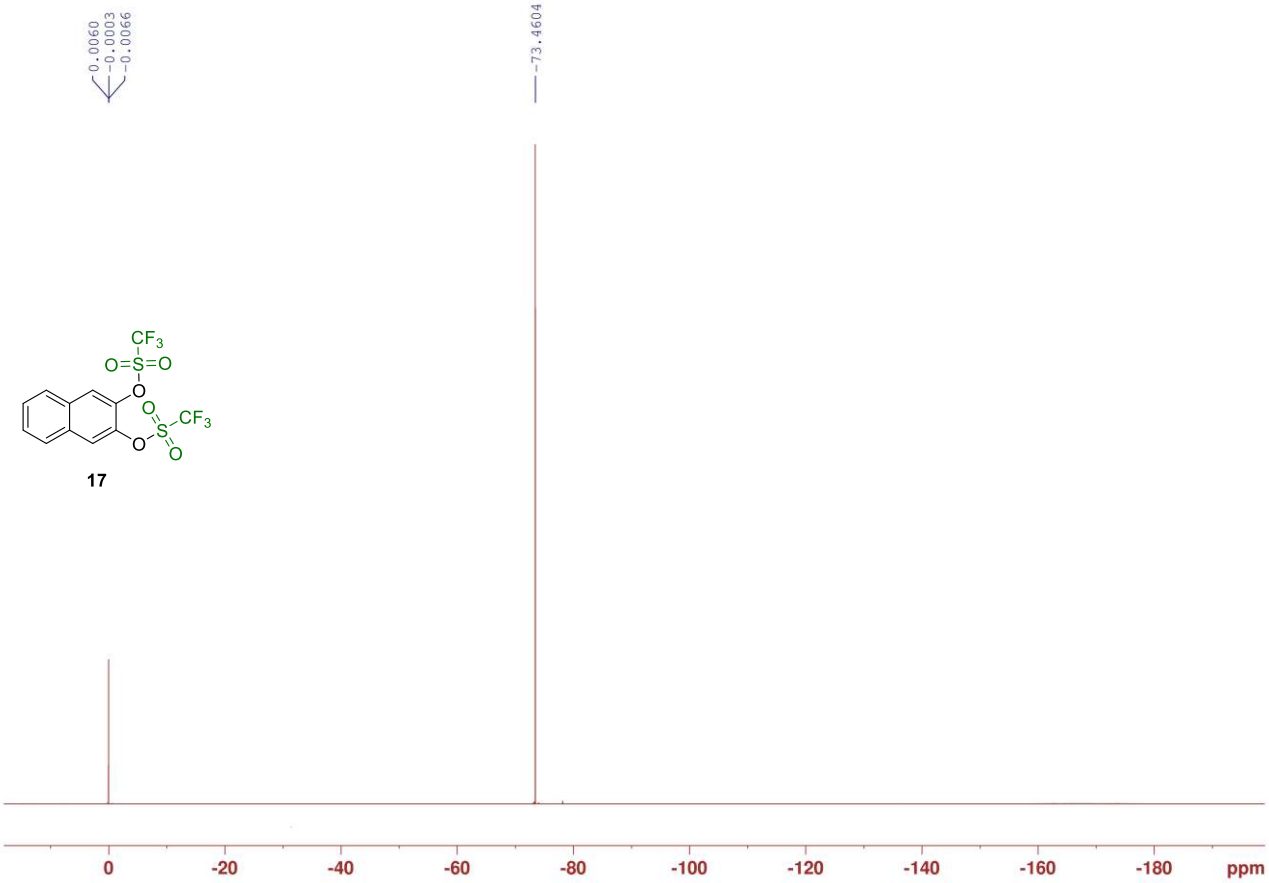
^{1}HNMR spectrum of **17**



^{13}CNMR spectrum of **17**

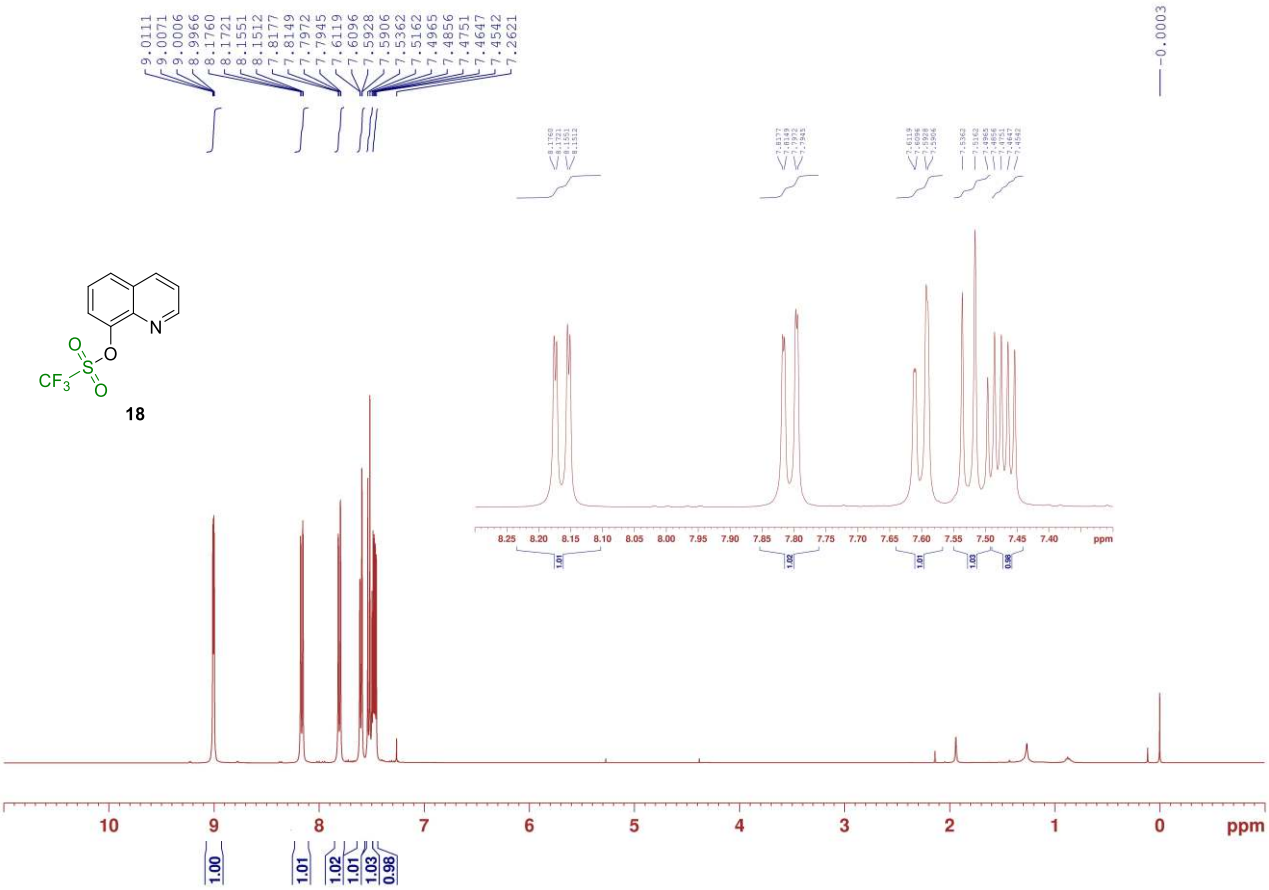


^{19}FNMR spectrum of **17**



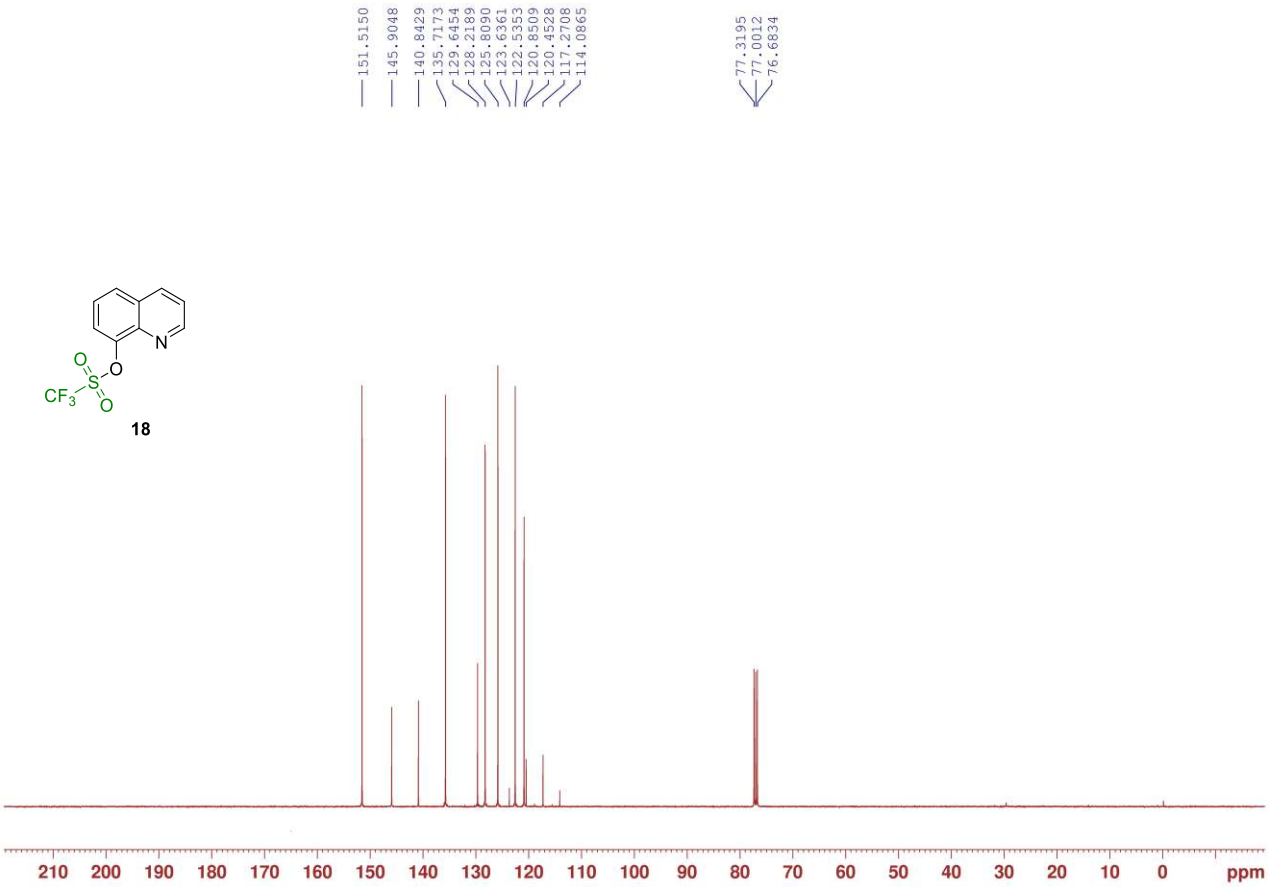
17

^{1}HNMR spectrum of **18**

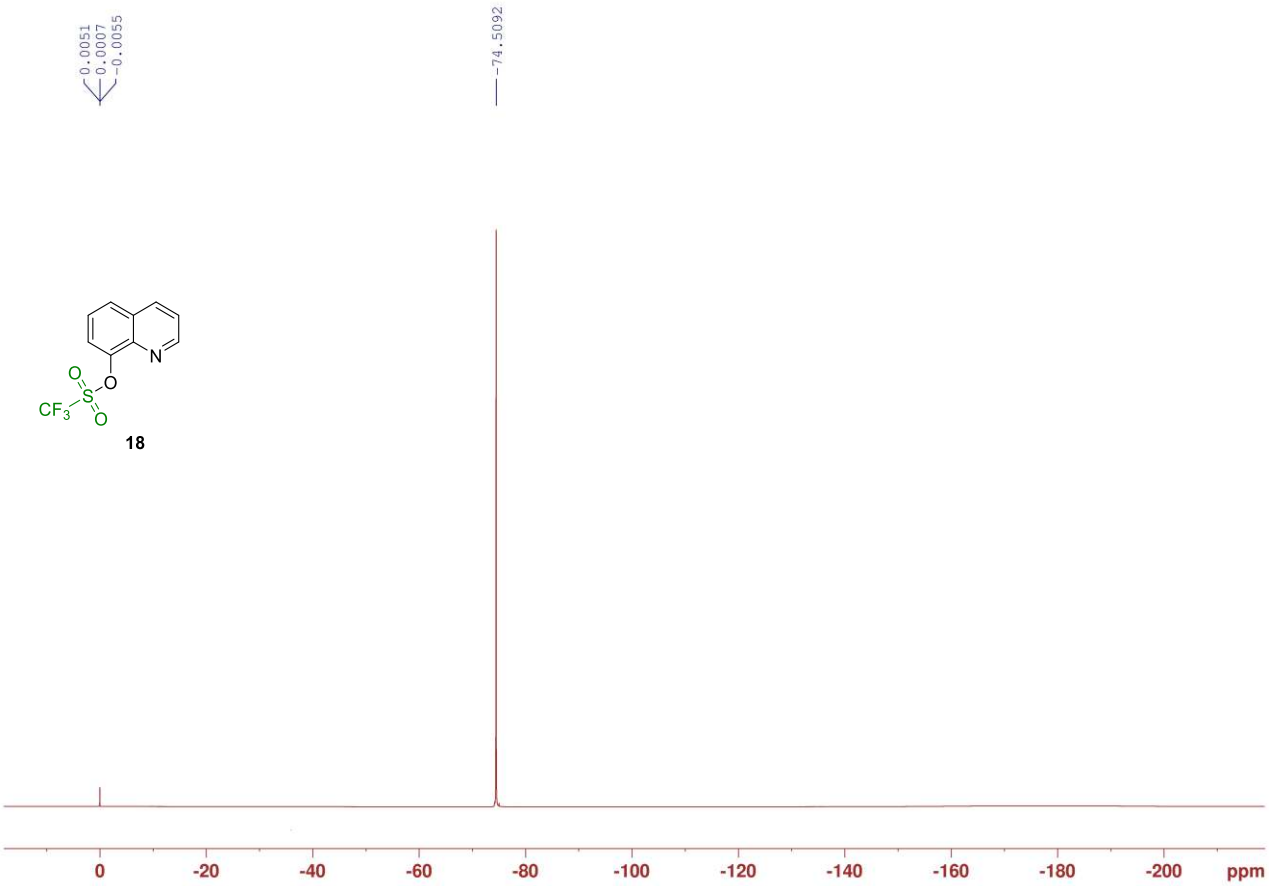


18

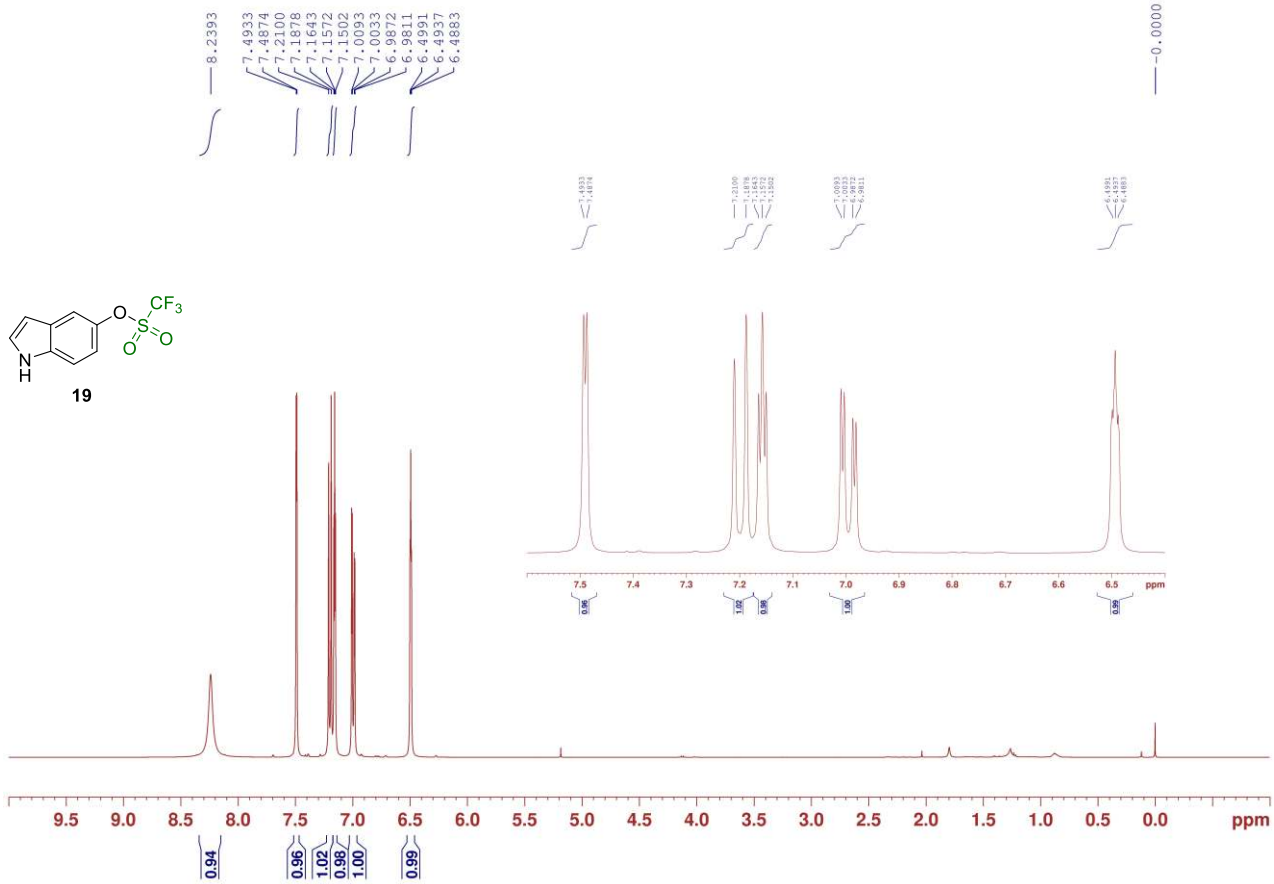
^{13}CNMR spectrum of **18**



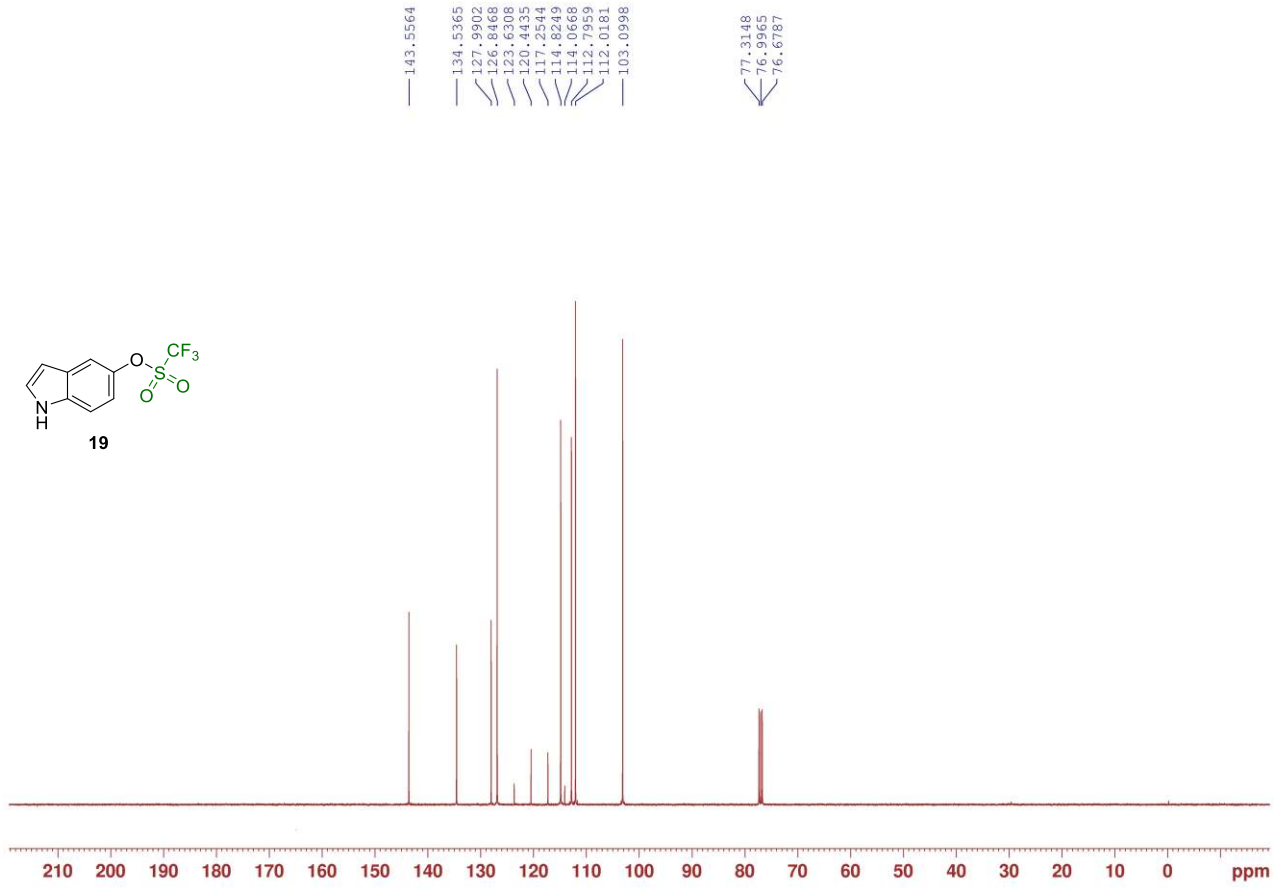
^{19}FNMR spectrum of **18**



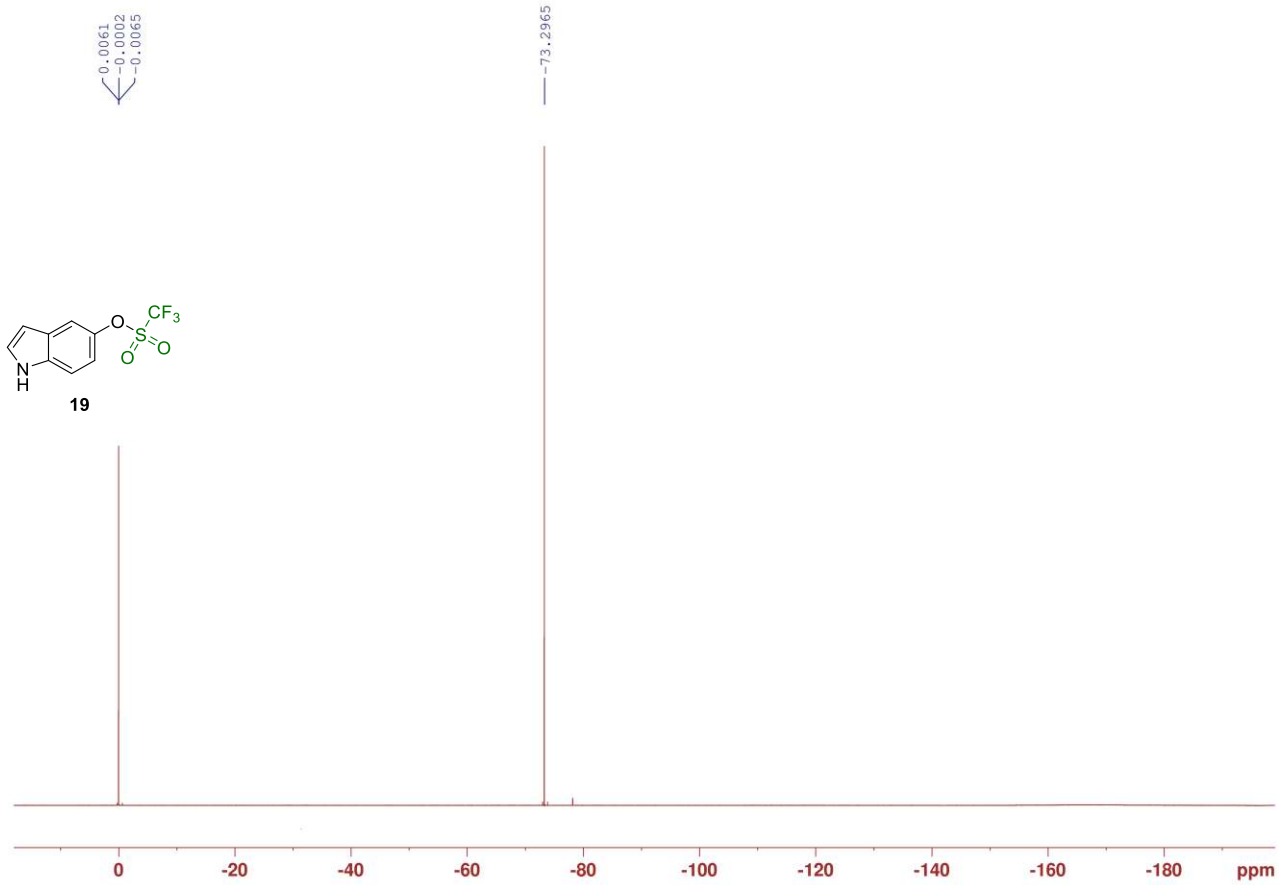
[1]HNMR spectrum of **19**



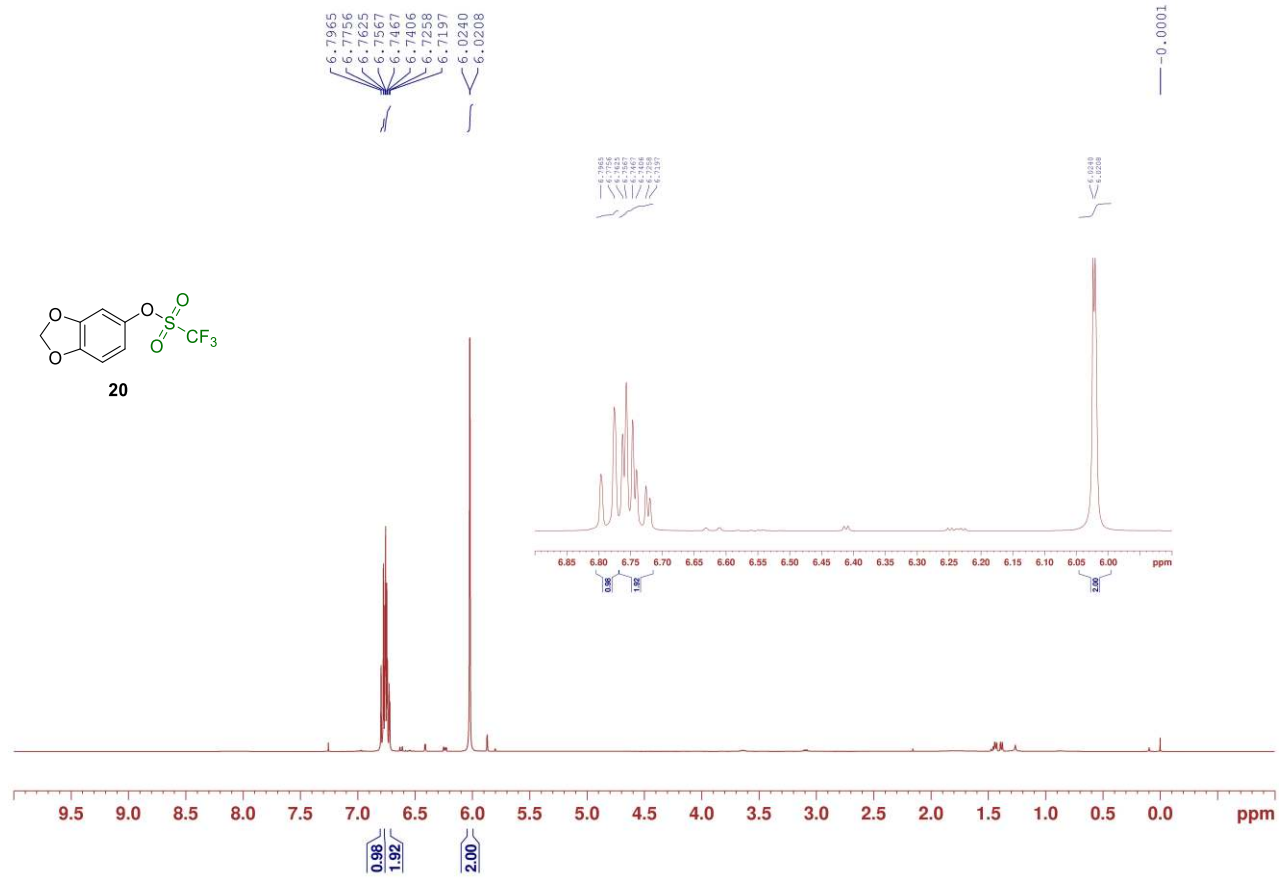
[13]CNMR spectrum of **19**



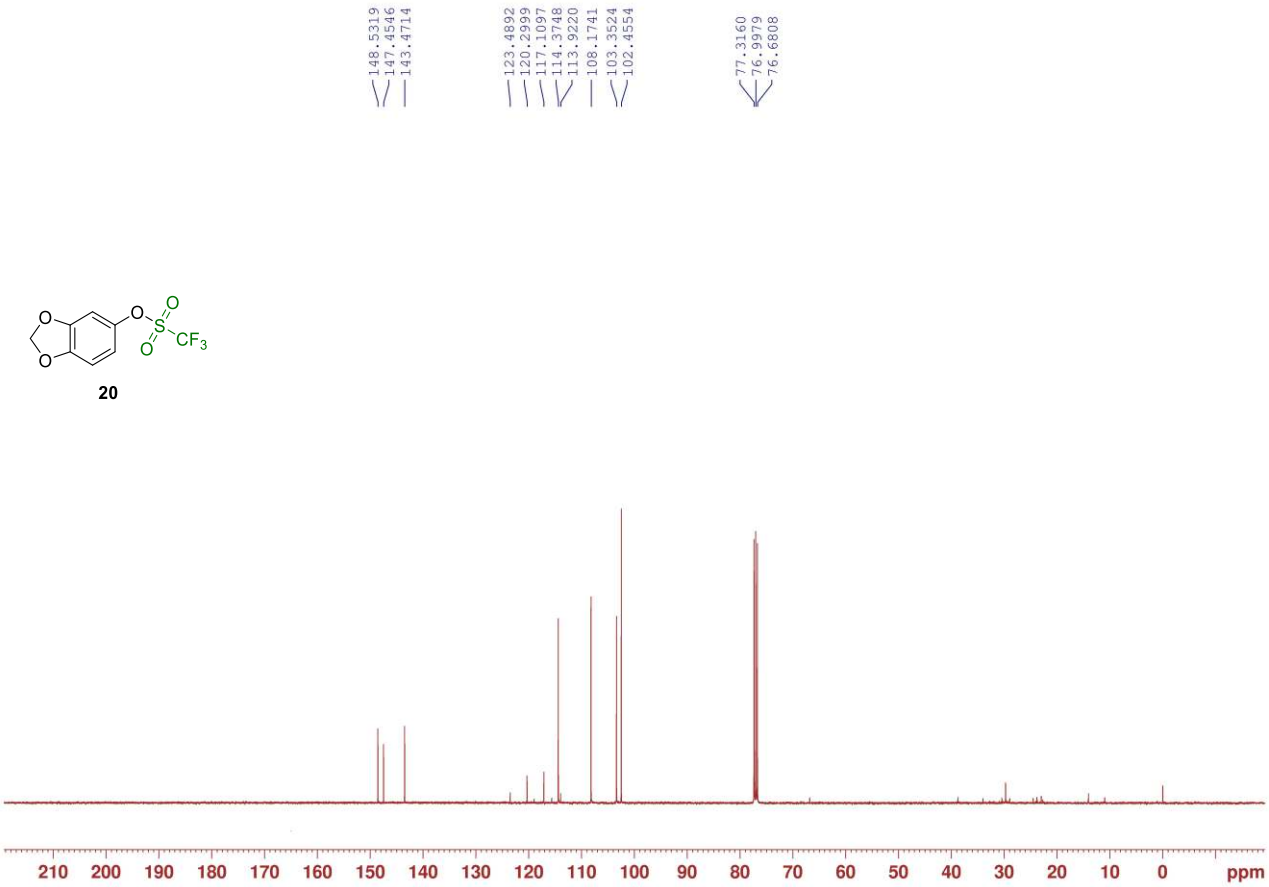
^{19}FNMR spectrum of **19**



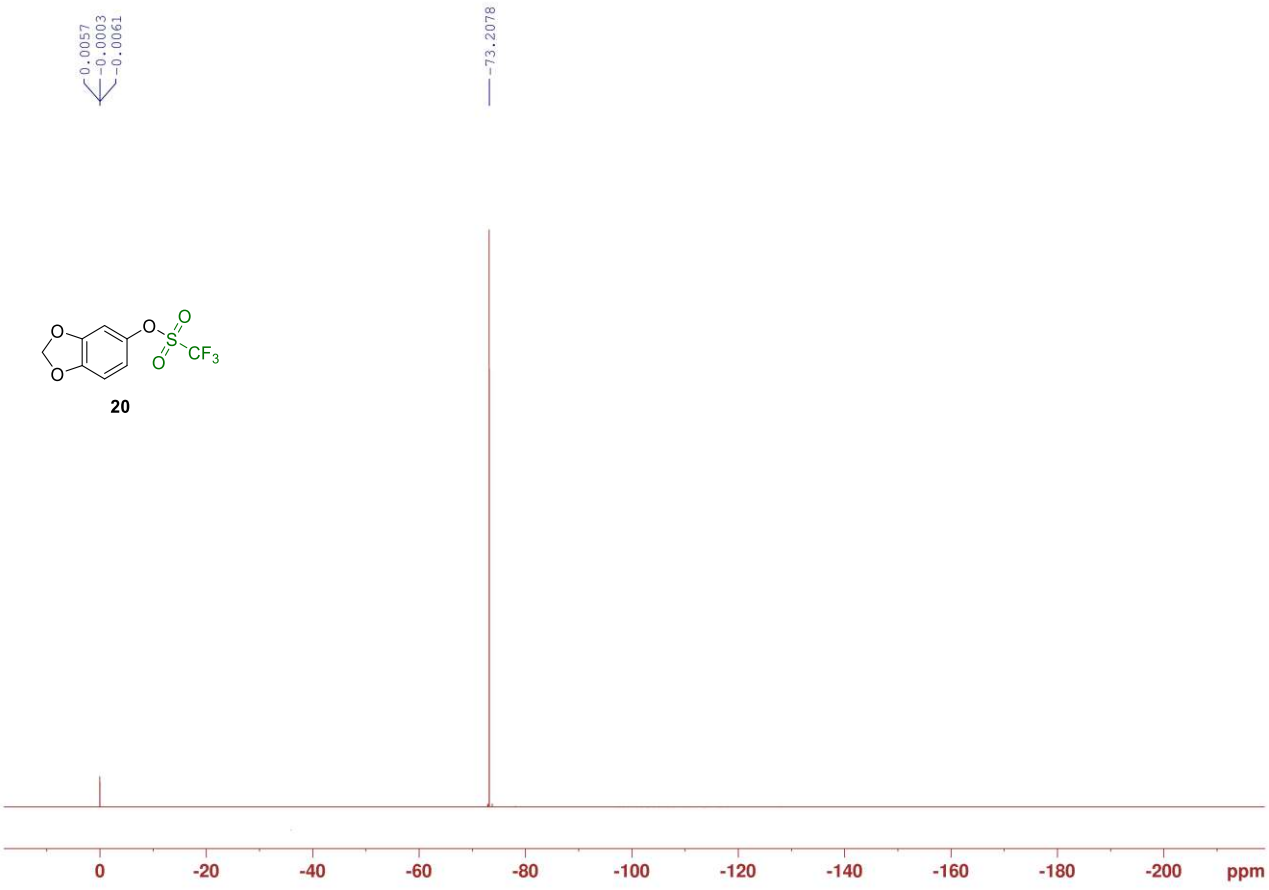
^{1}HNMR spectrum of **20**



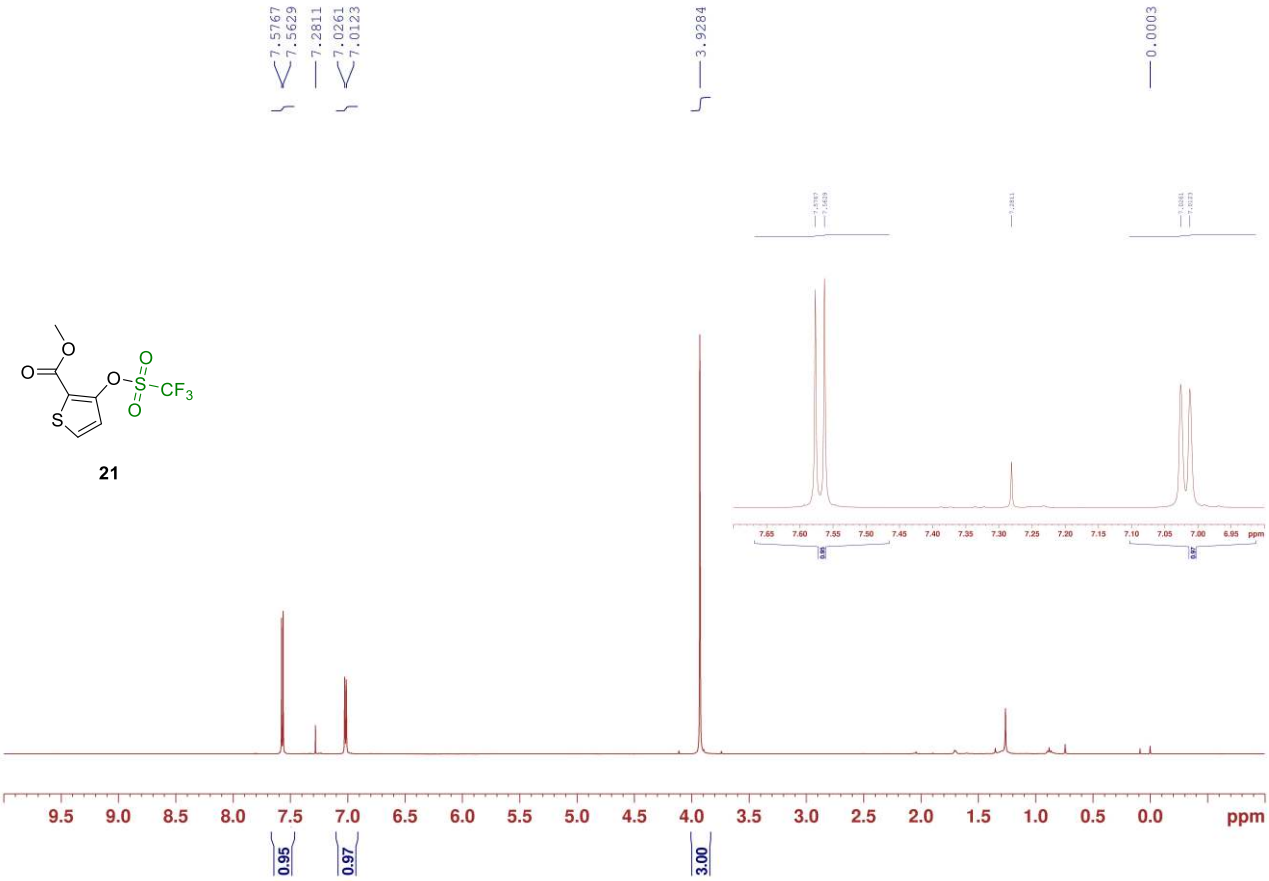
^{13}CNMR spectrum of **20**



^{19}FNMR spectrum of **20**

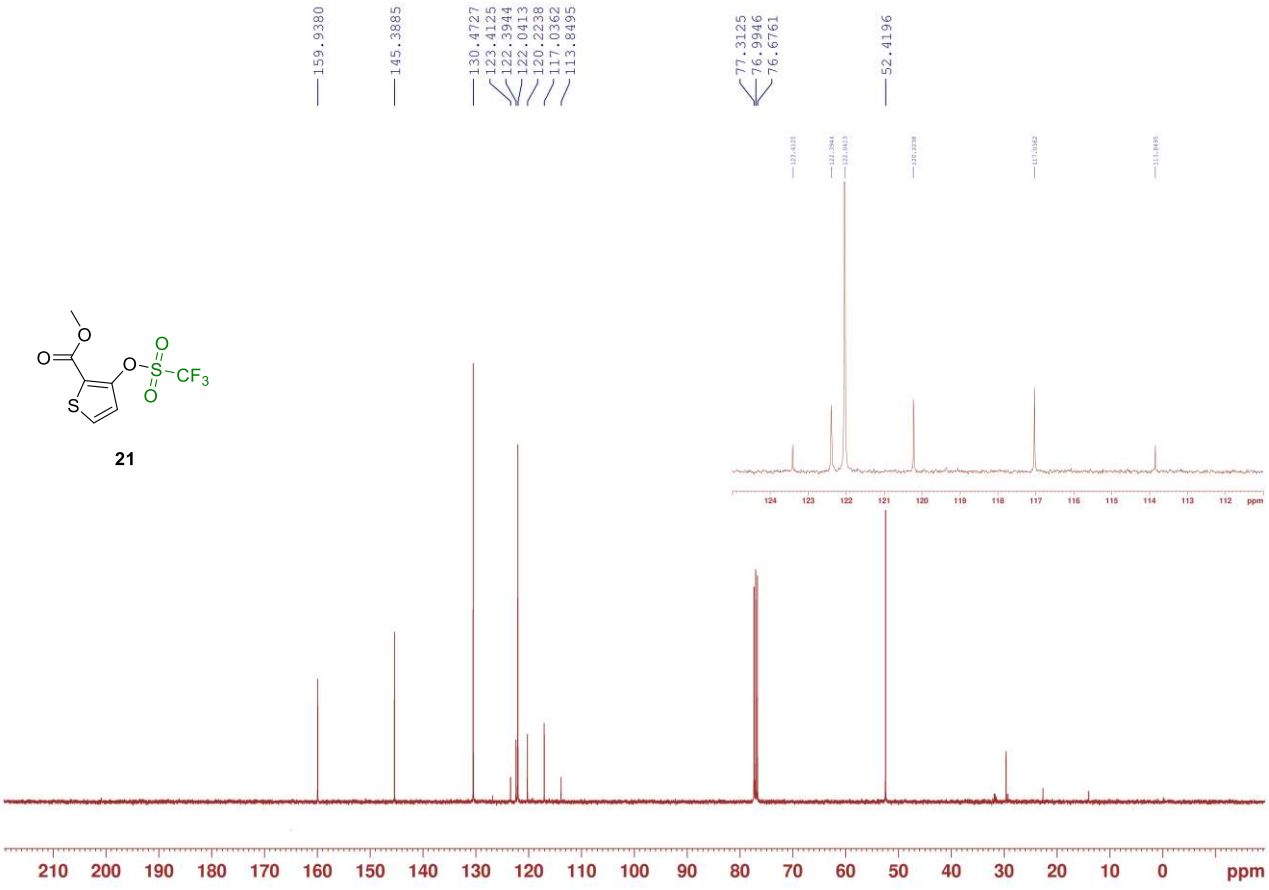


^{1}HNMR spectrum of **21**



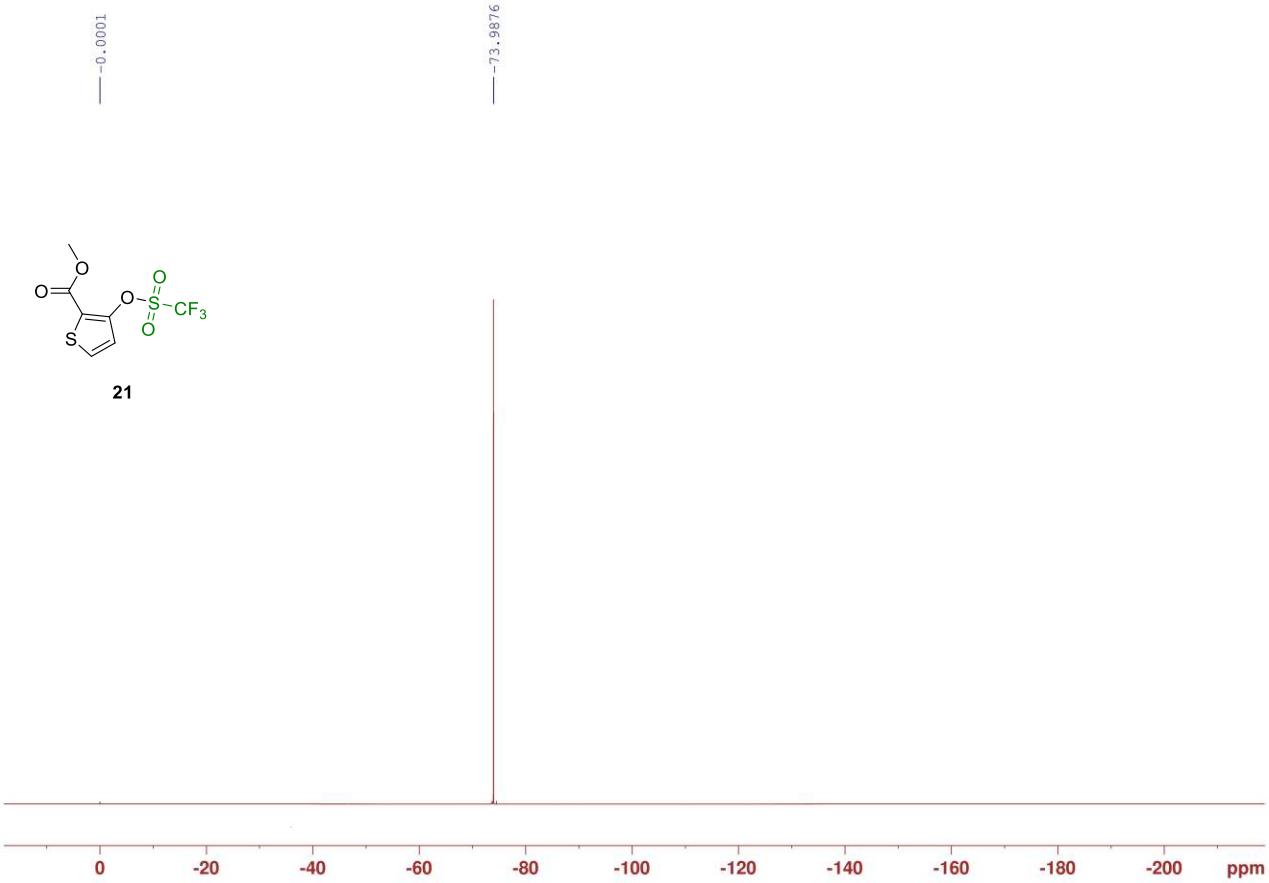
21

^{13}CNMR spectrum of **21**

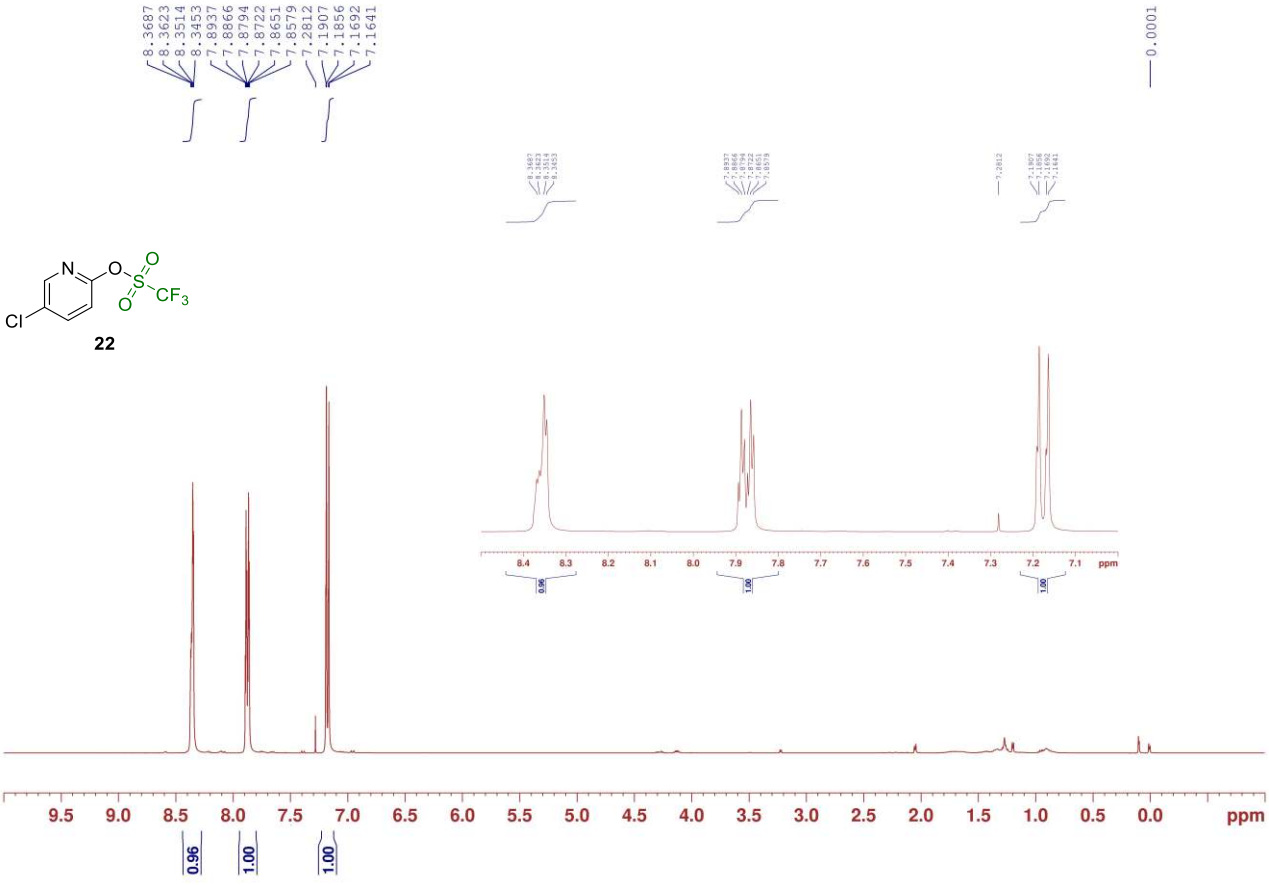


21

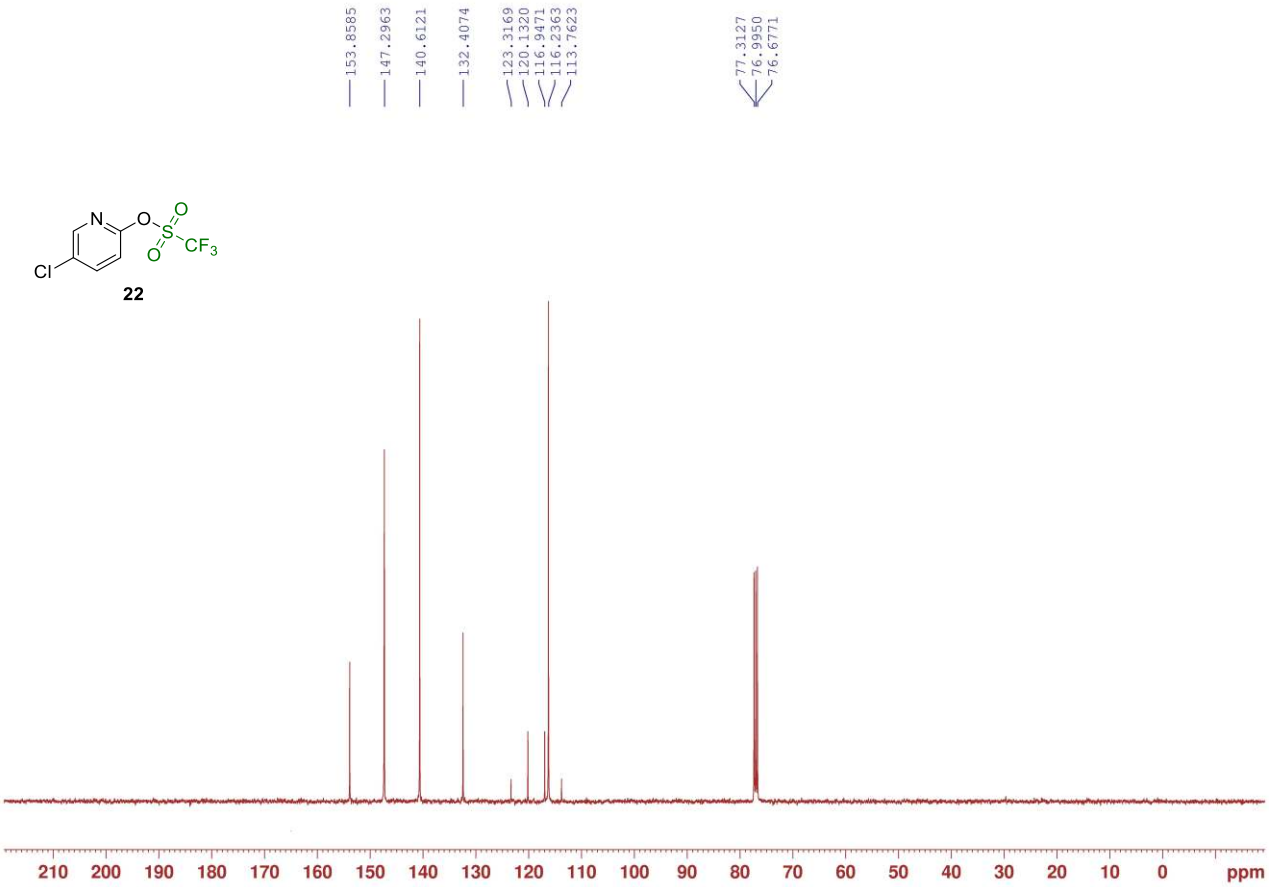
^{19}FNMR spectrum of **21**



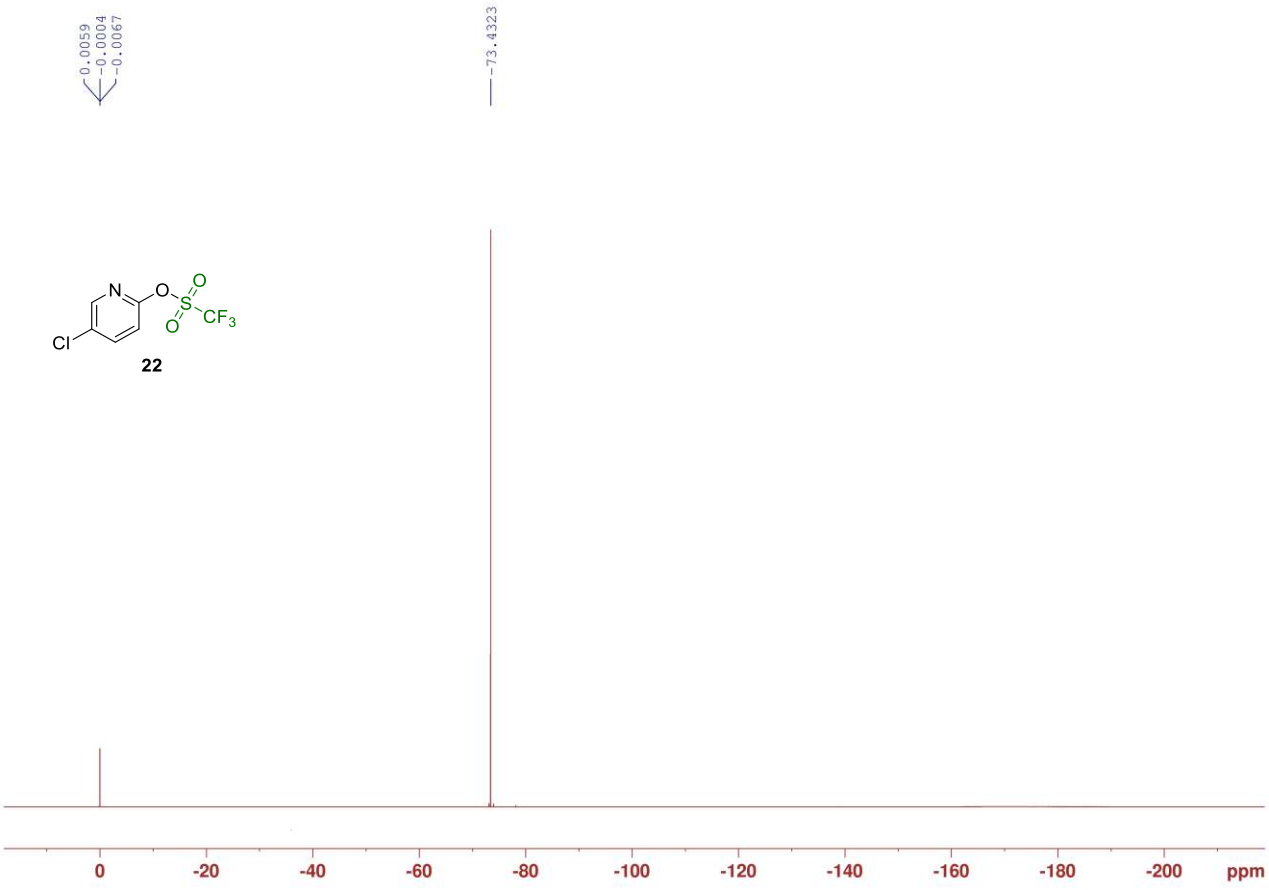
^{1}HNMR spectrum of **22**



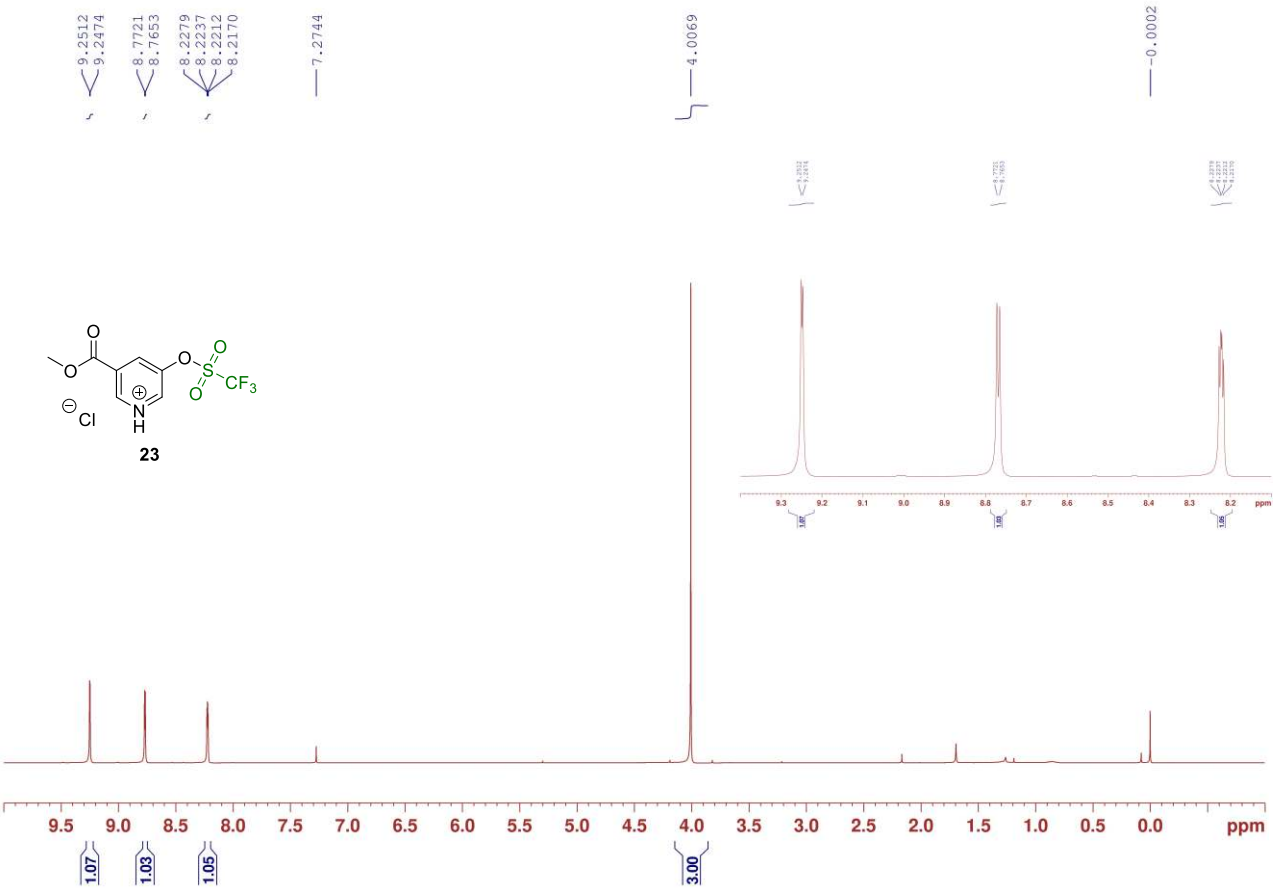
^{13}CNMR spectrum of **22**



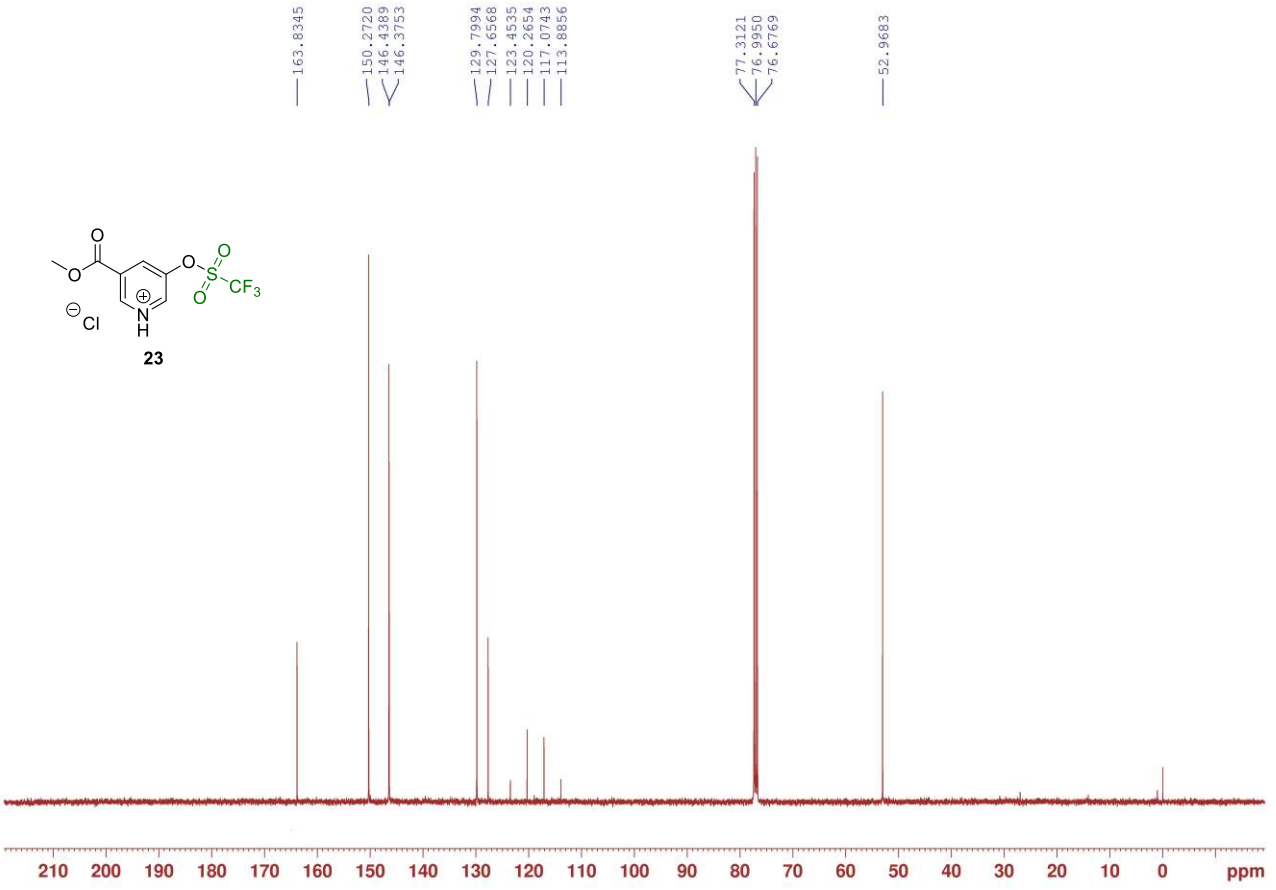
^{19}FNMR spectrum of **22**



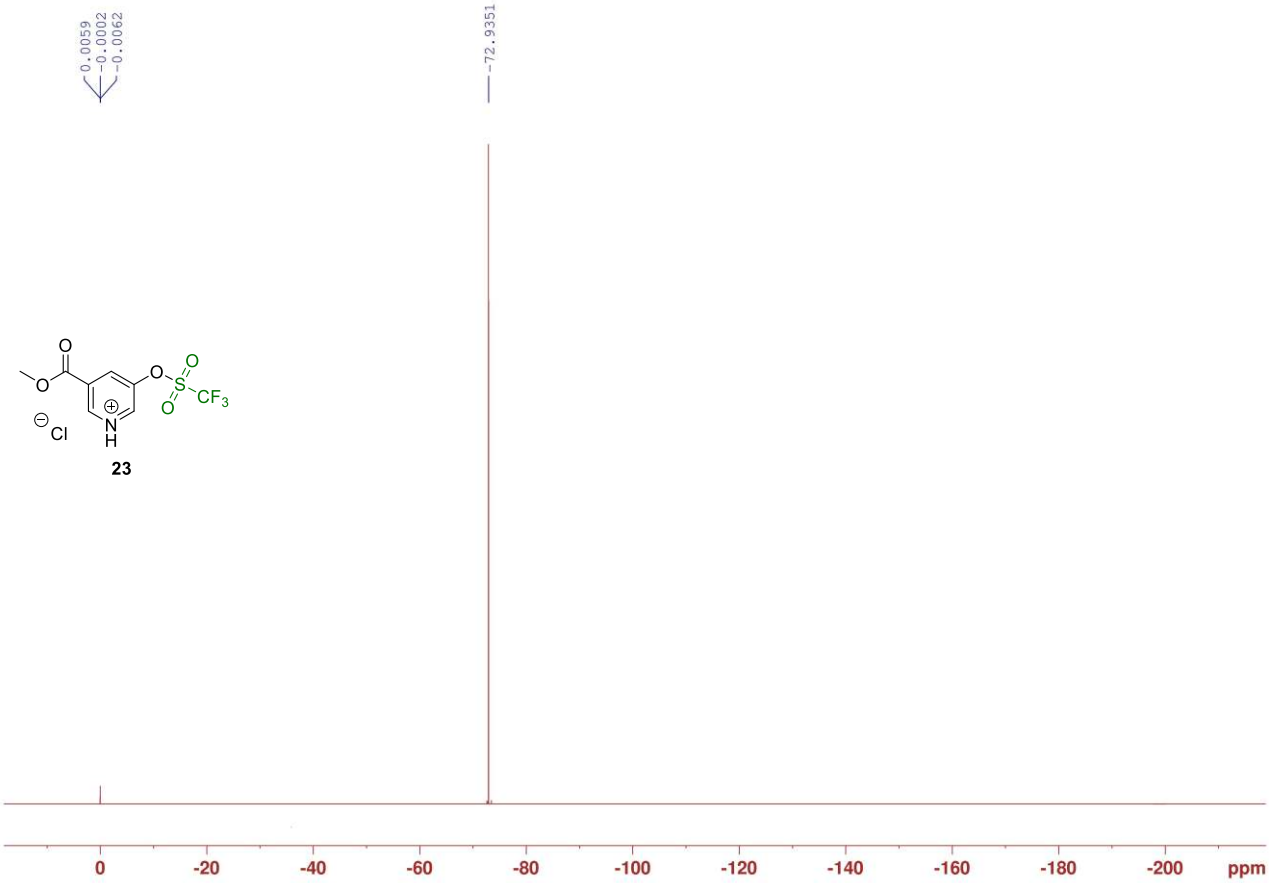
^{1}HNMR spectrum of **23**



^{13}CNMR spectrum of **23**

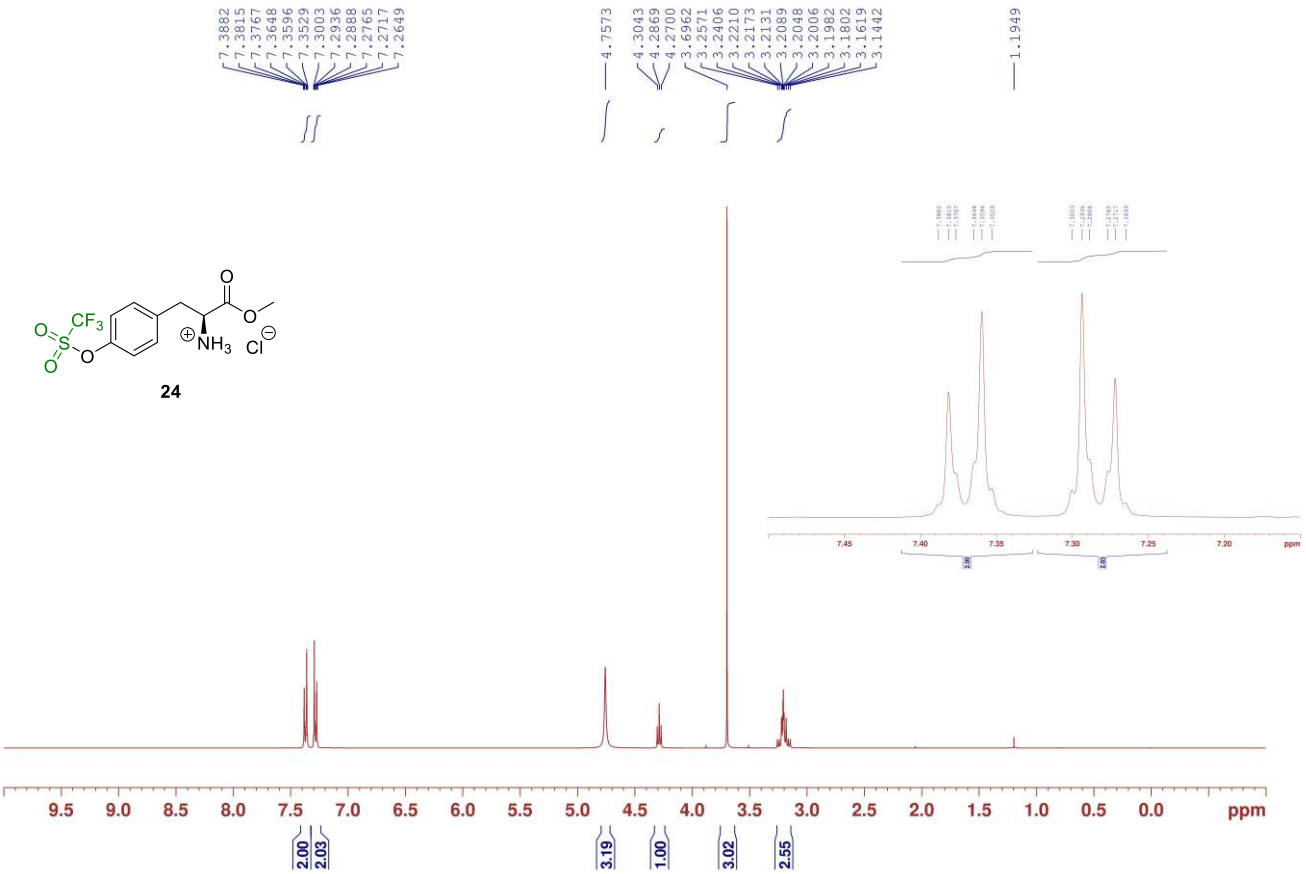


^{19}FNMR spectrum of **23**



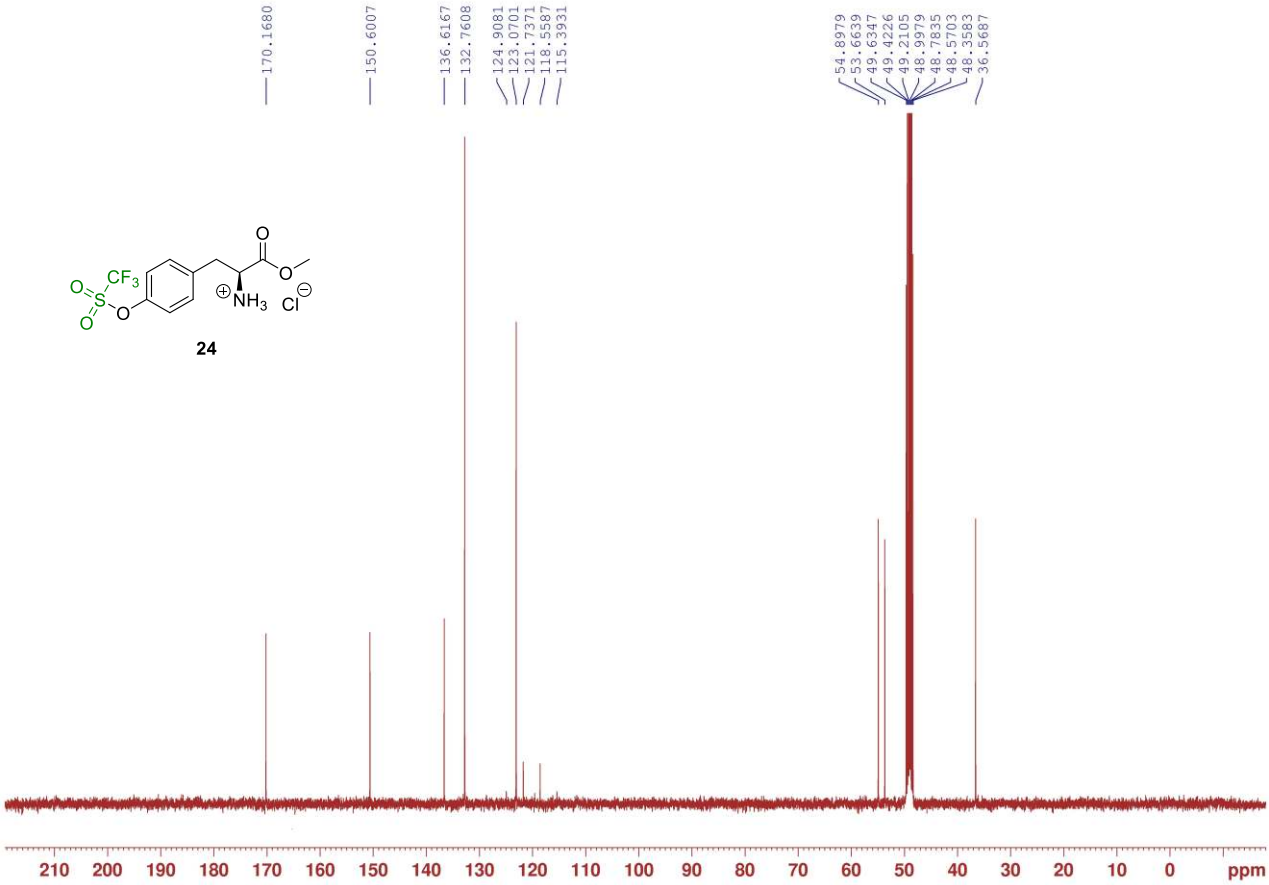
23

^{1}HNMR spectrum of **24** (Methanol-d_4)



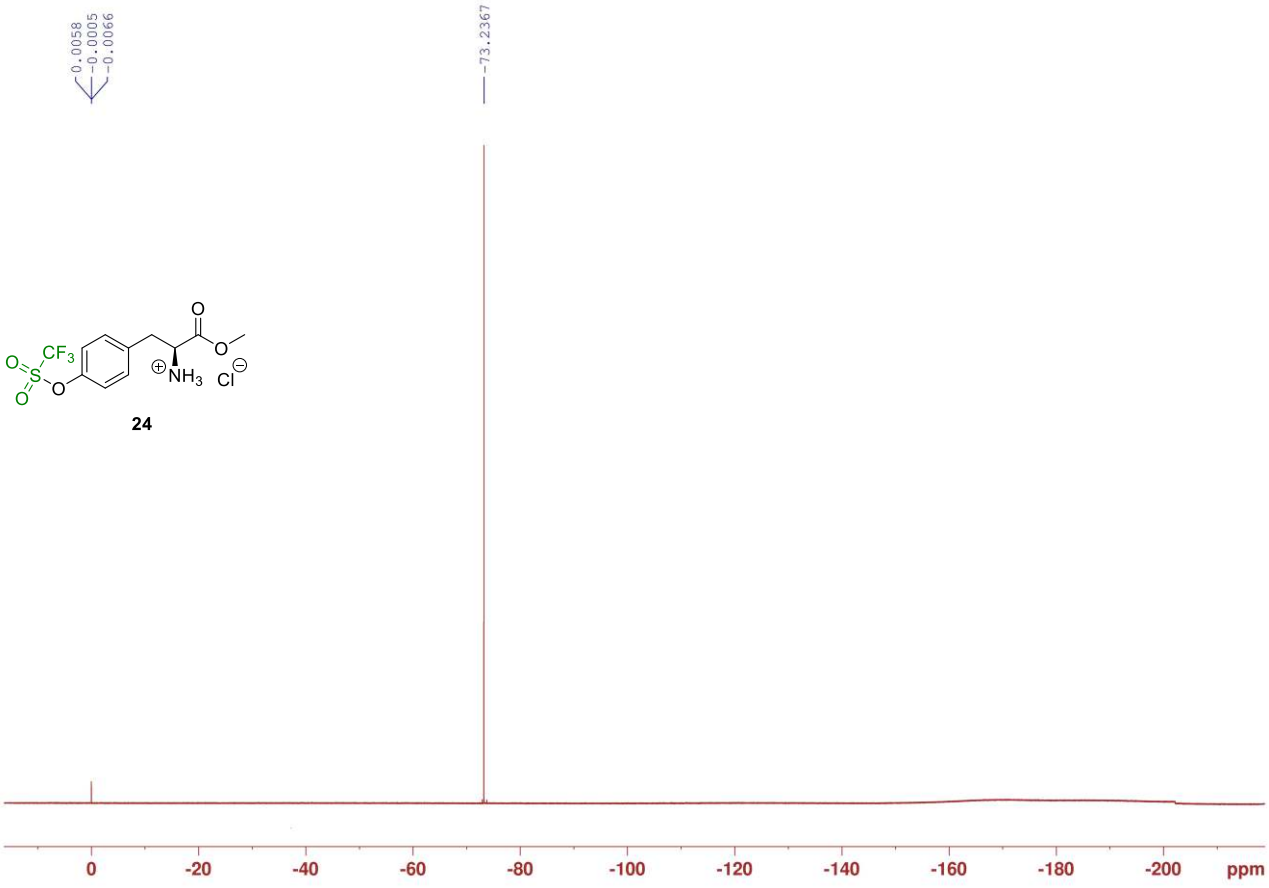
24

^{13}CNMR spectrum of **24** (Methanol-d_4)



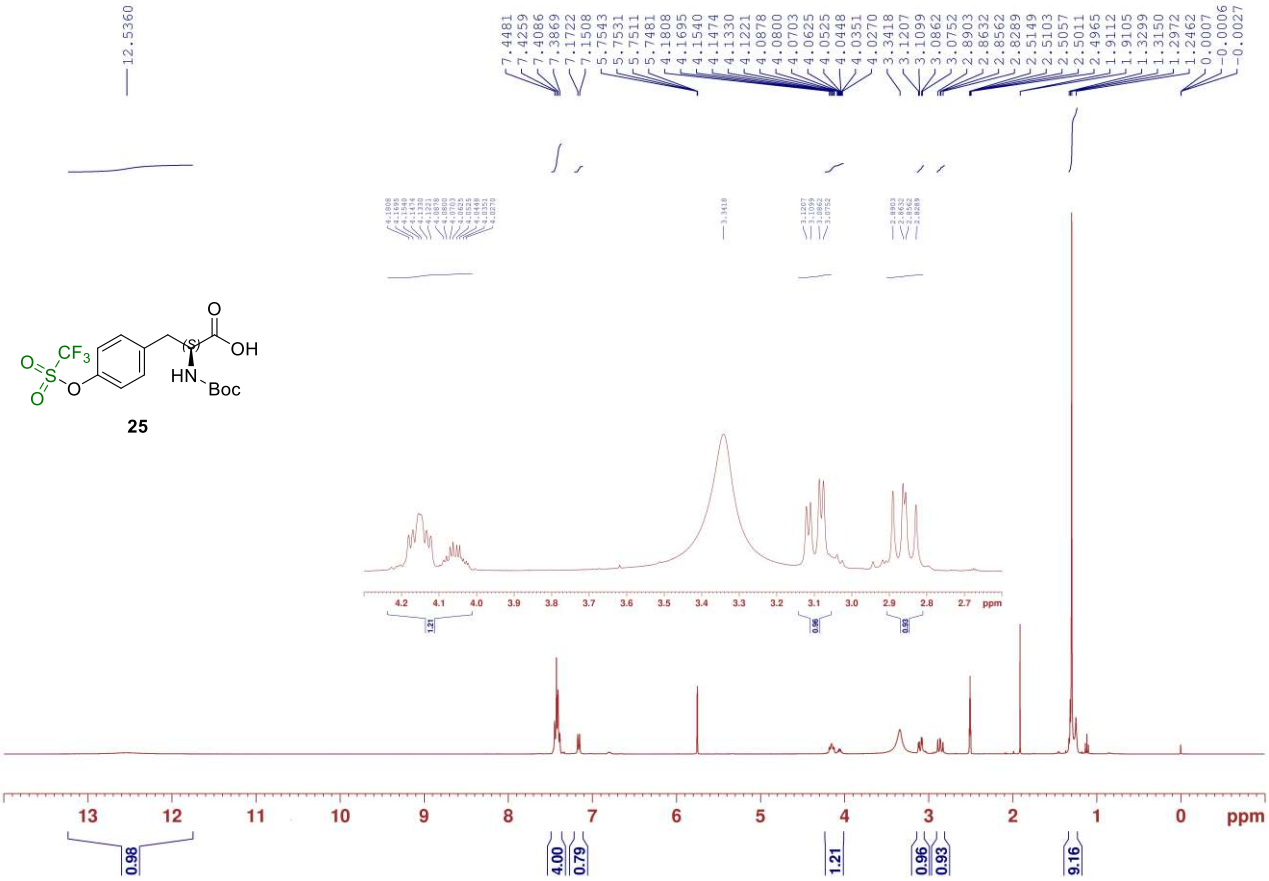
24

^{19}FNMR spectrum of **24** (Methanol-d_4)

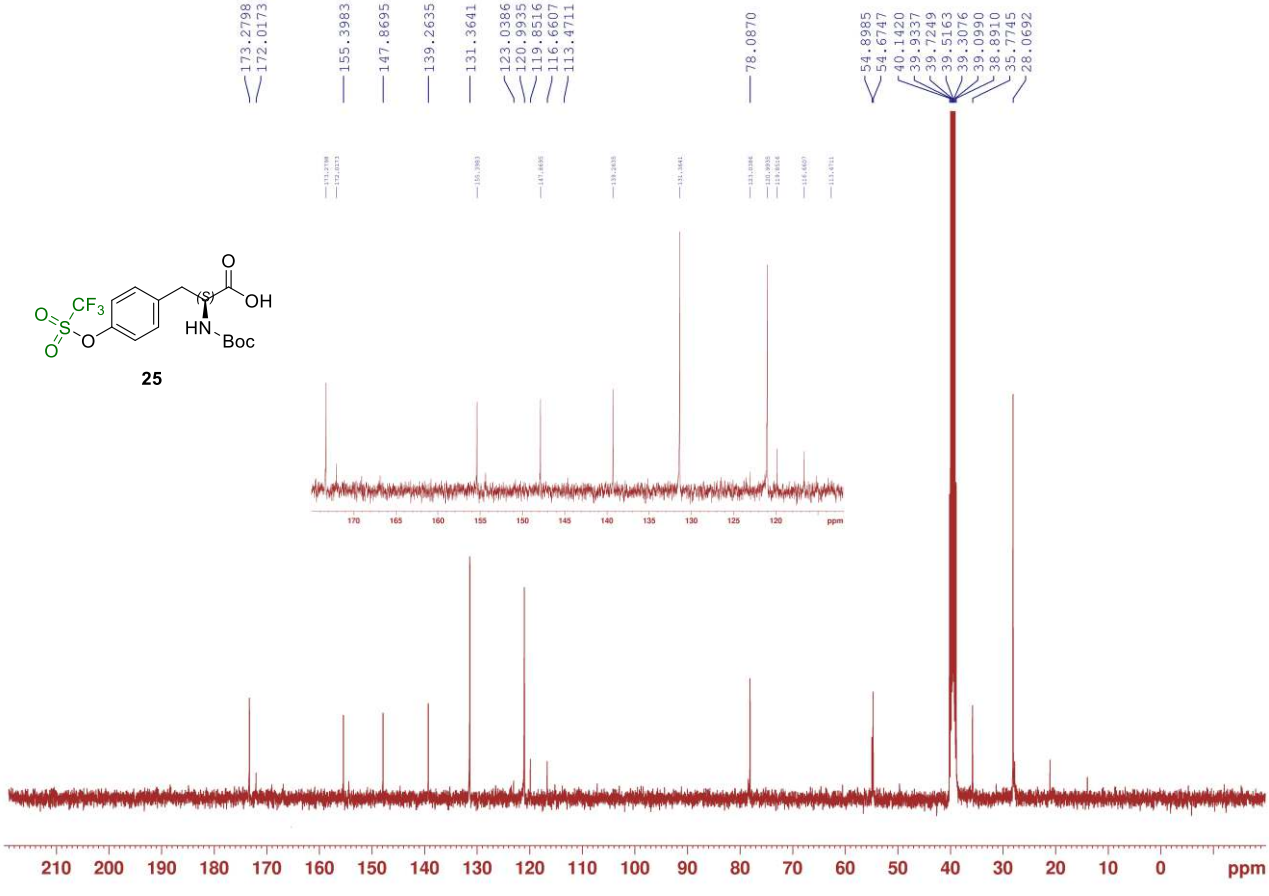


24

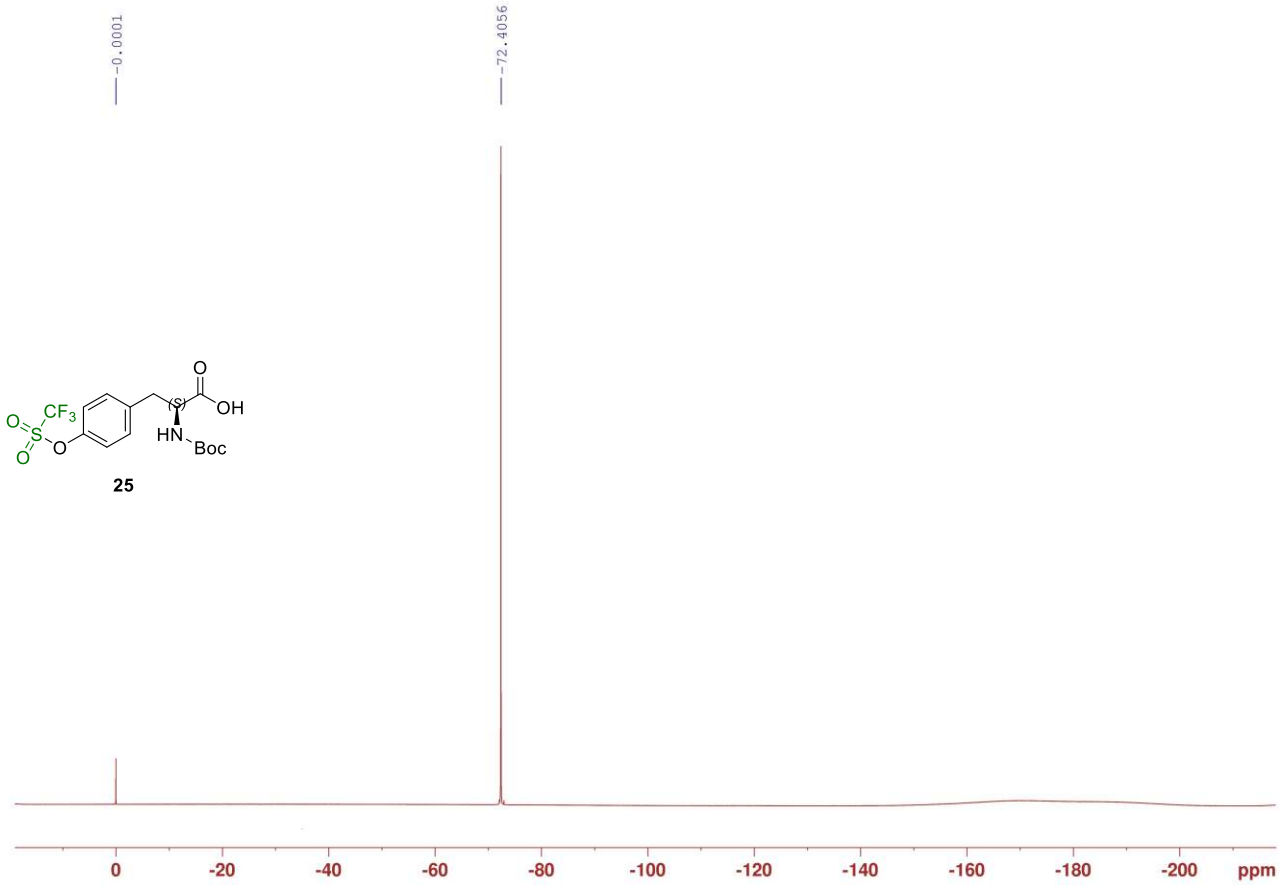
^{1}HNMR spectrum of **25** (in DMSO-*d6*)



^{13}CNMR spectrum of **25** (in DMSO-*d6*)

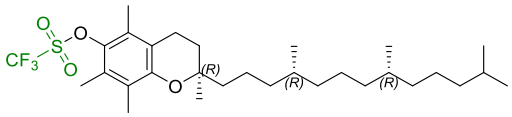


^{19}FNMR spectrum of **25** (in DMSO-*d6*)



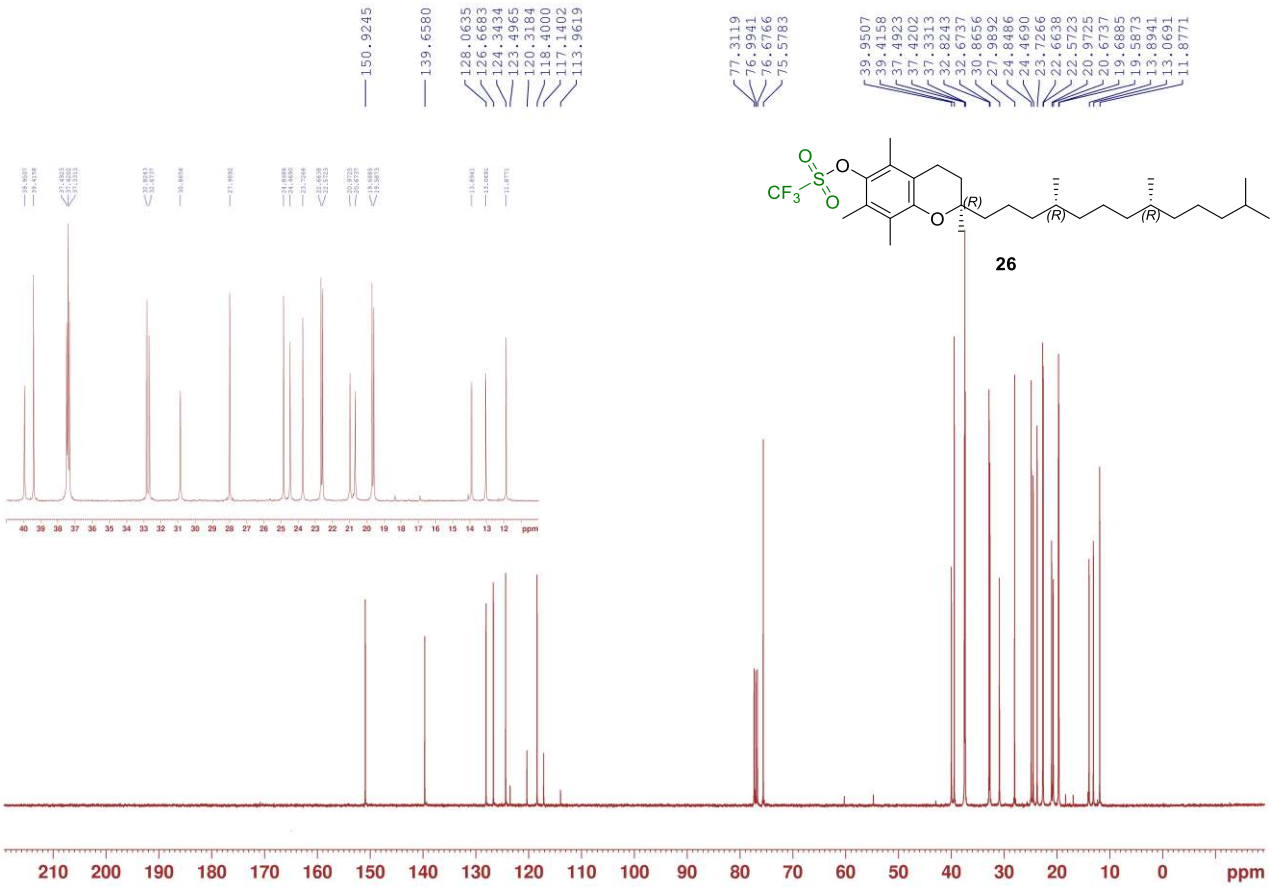
25

^{1}HNMR spectrum of **26**

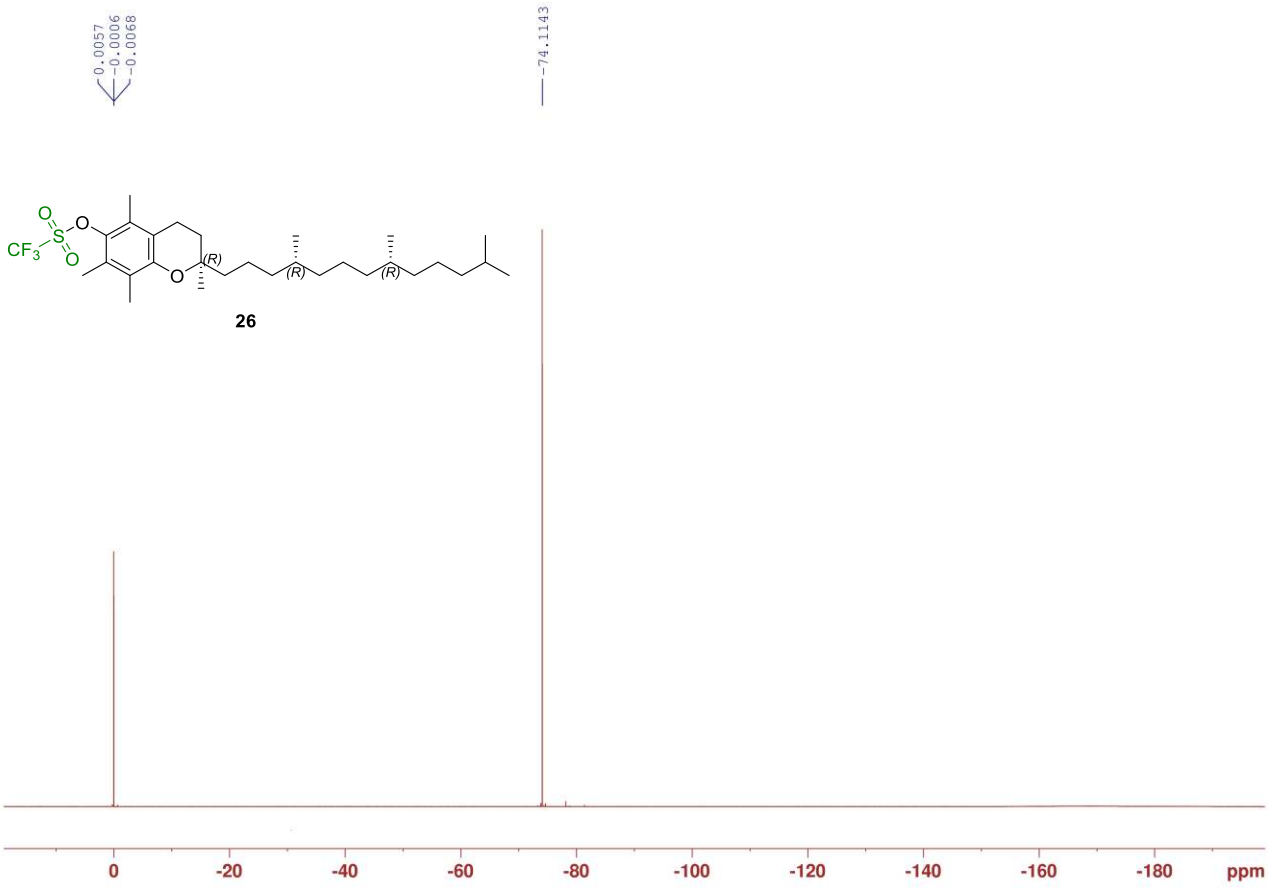


26

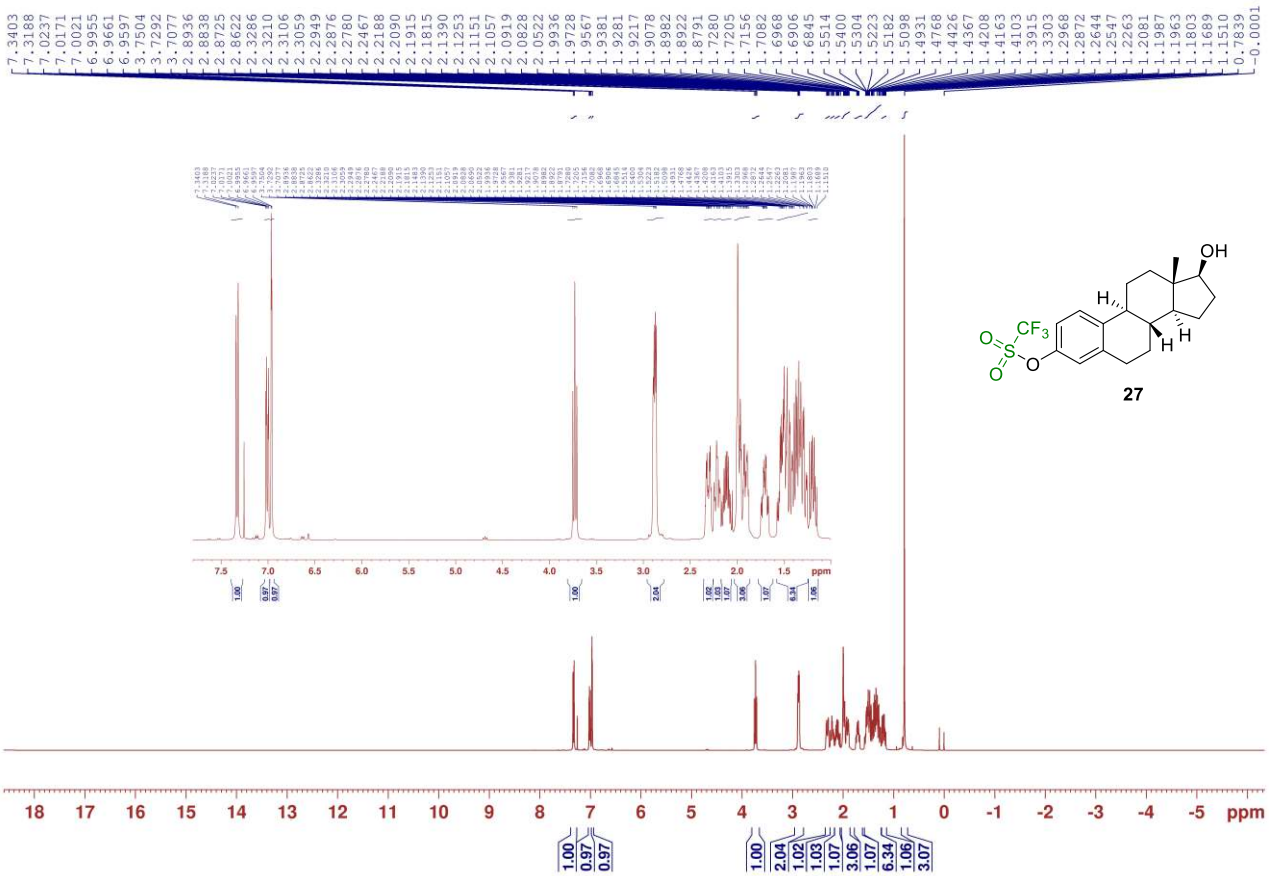
^{13}CNMR spectrum of **26**



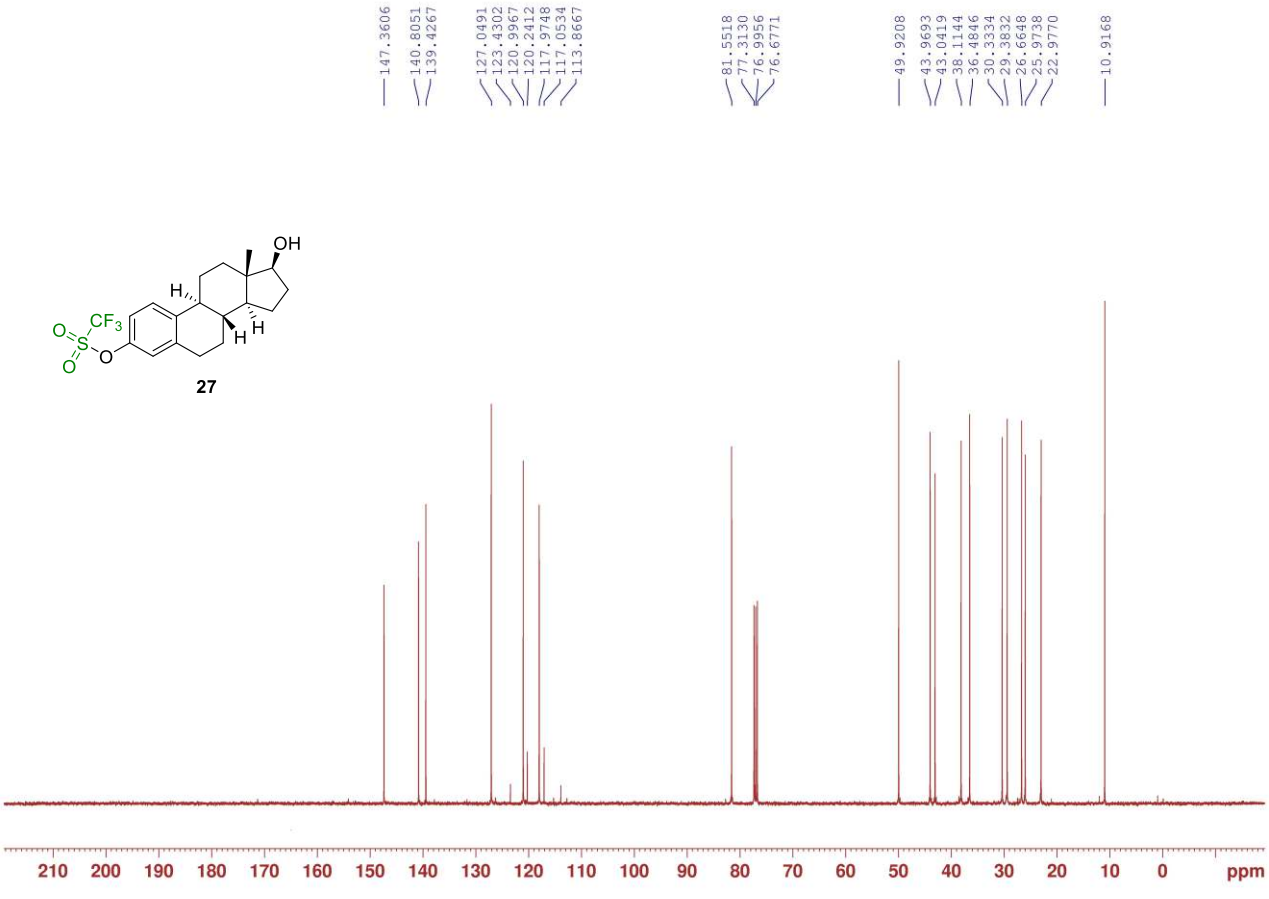
^{19}FNMR spectrum of **26**



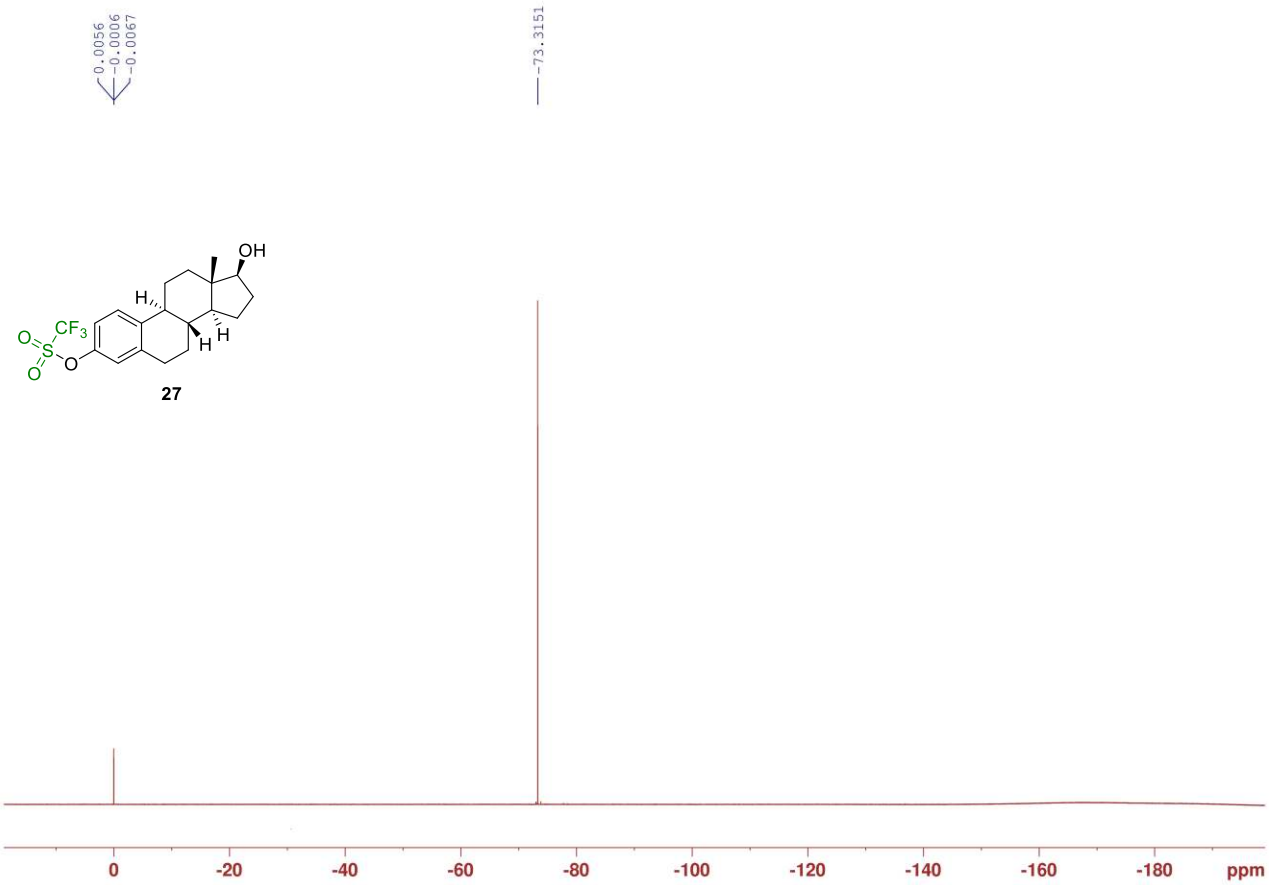
^{1}HNMR spectrum of **27**



^{13}CNMR spectrum of **27**

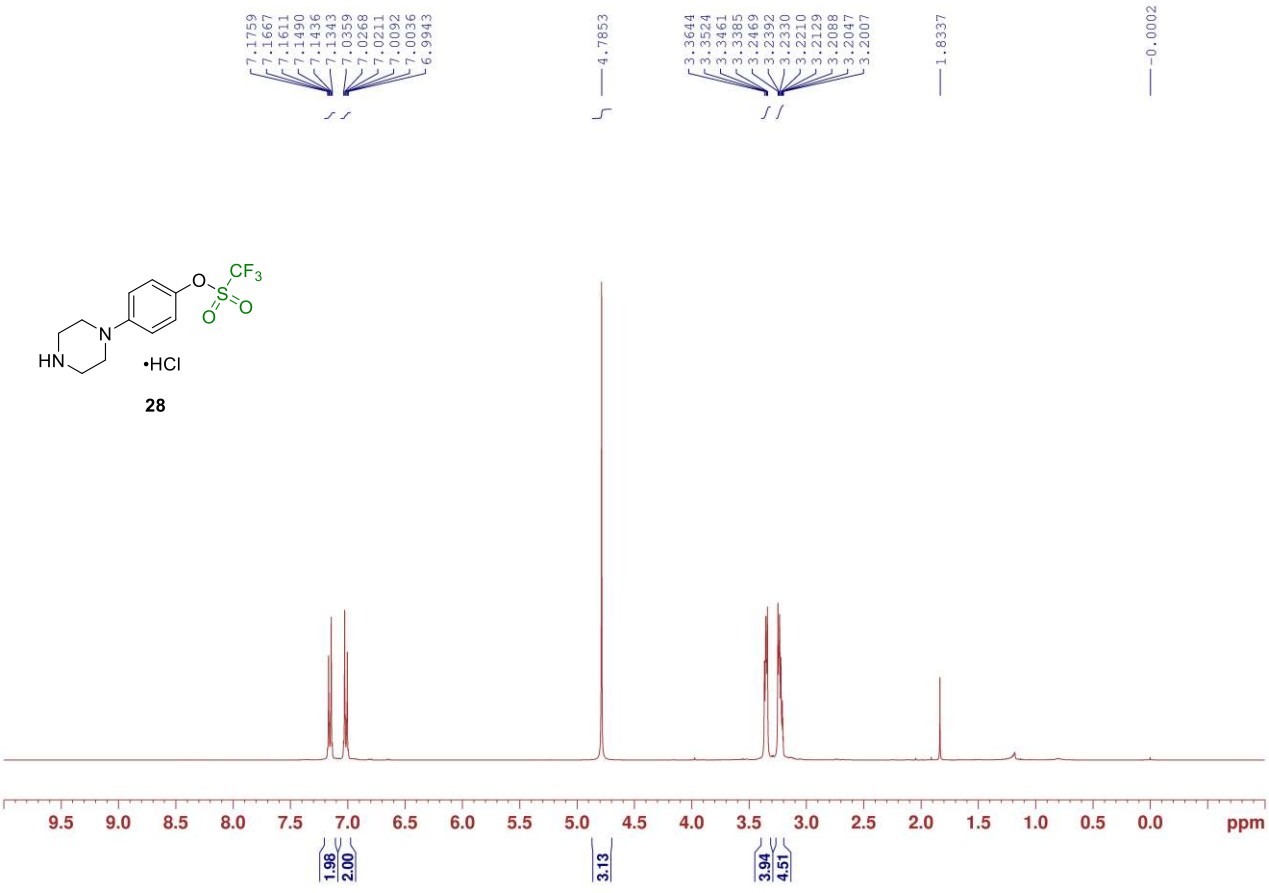


^{19}FNMR spectrum of **27** (Methanol-d_4)



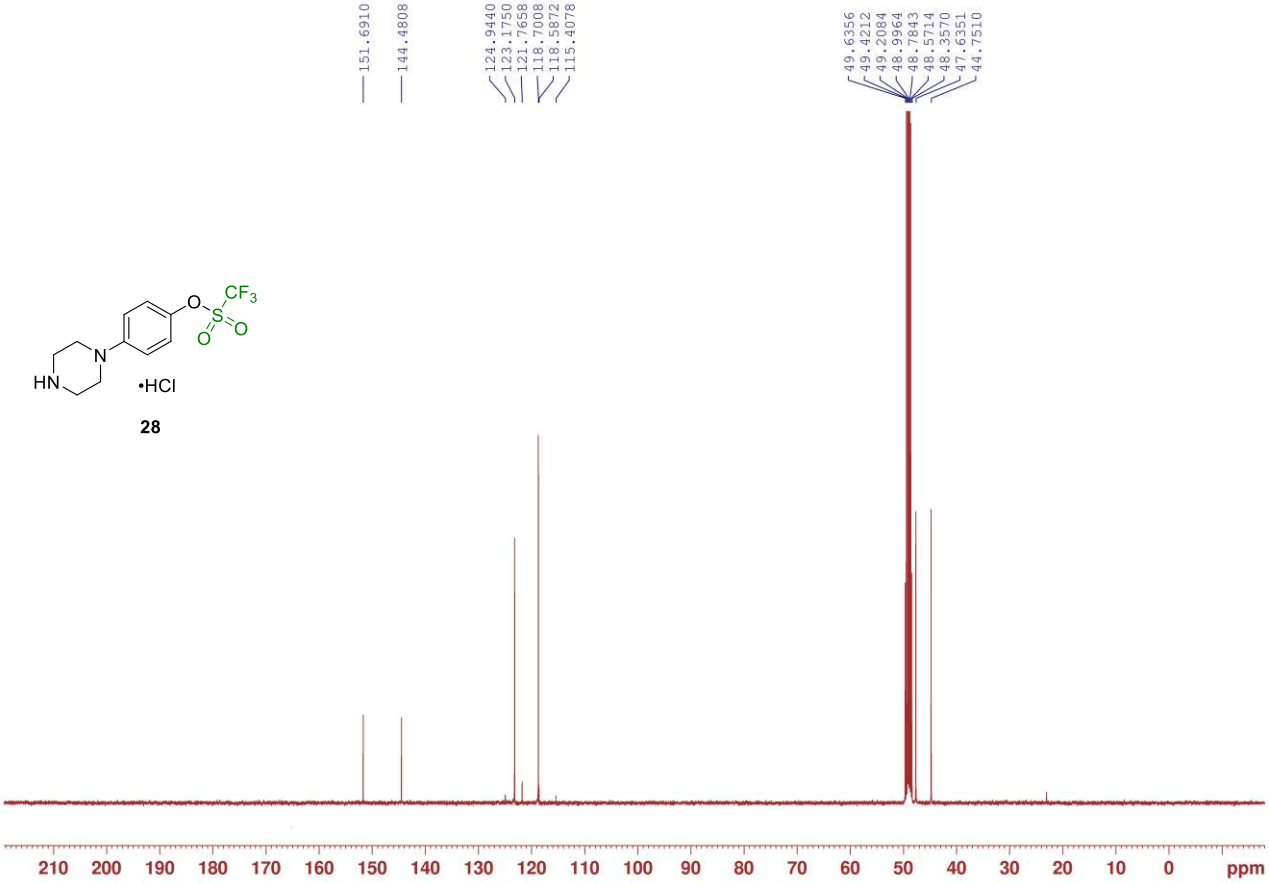
27

^{1}HNMR spectrum of **28** (Methanol-d_4)



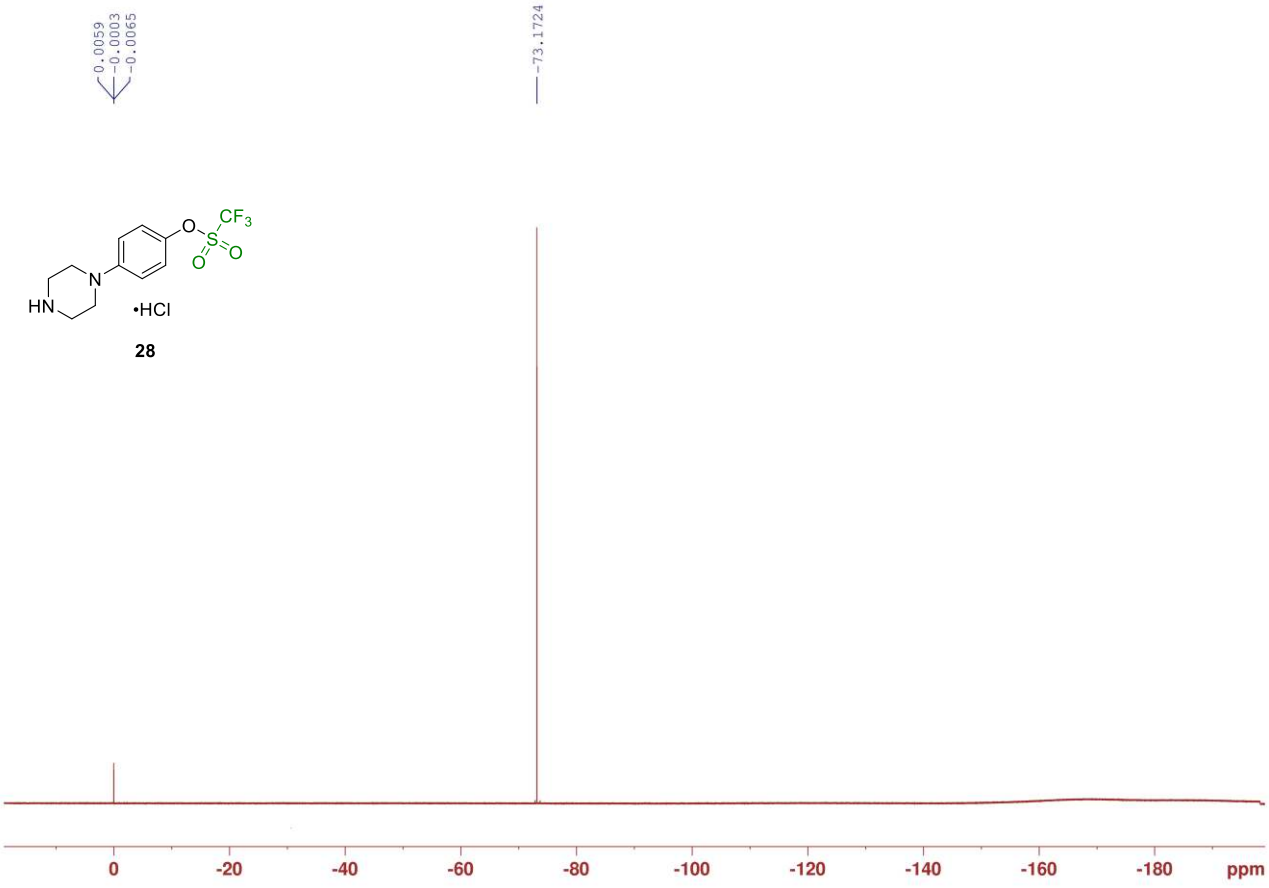
28

^{13}CNMR spectrum of **28** (Methanol-d_4)



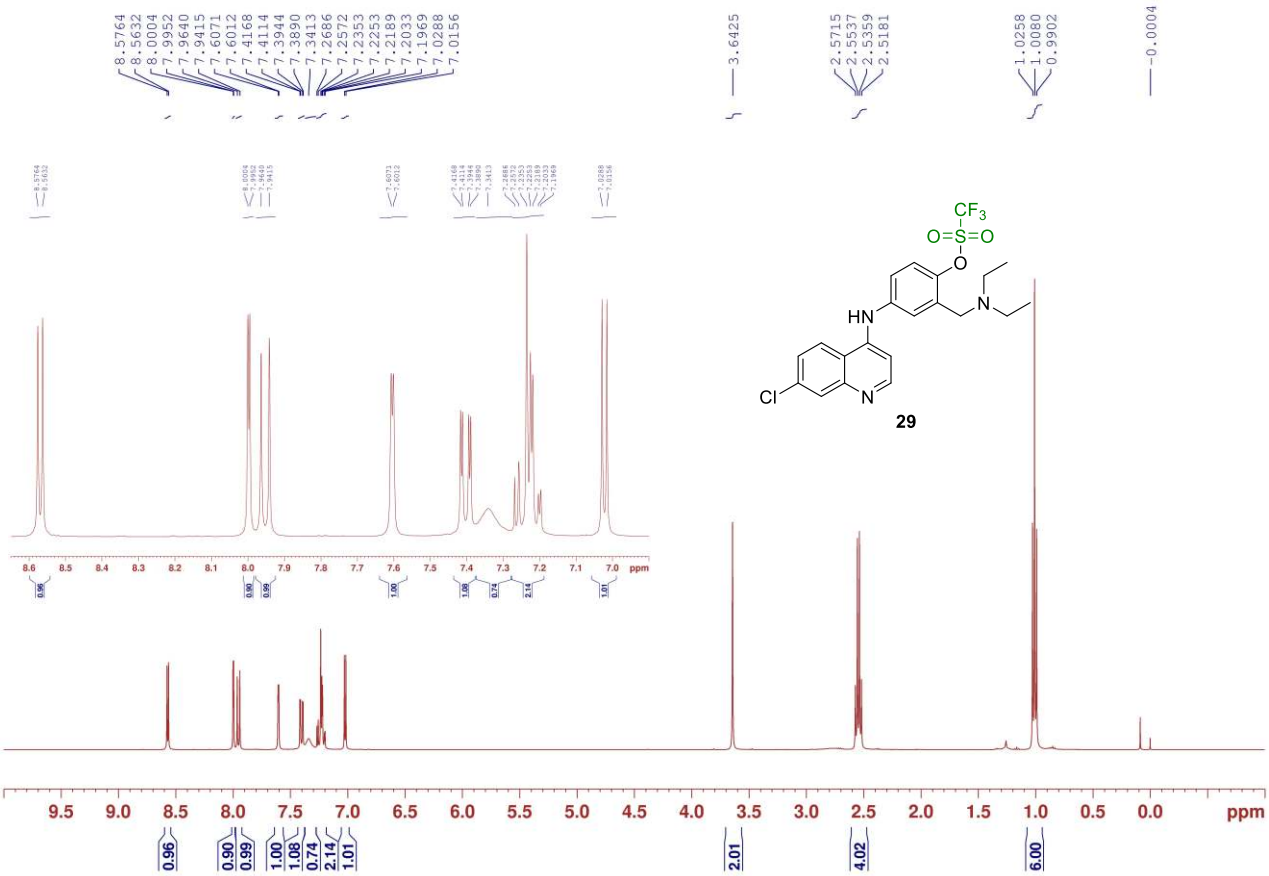
28

^{19}FNMR spectrum of **28** (Methanol-d_4)

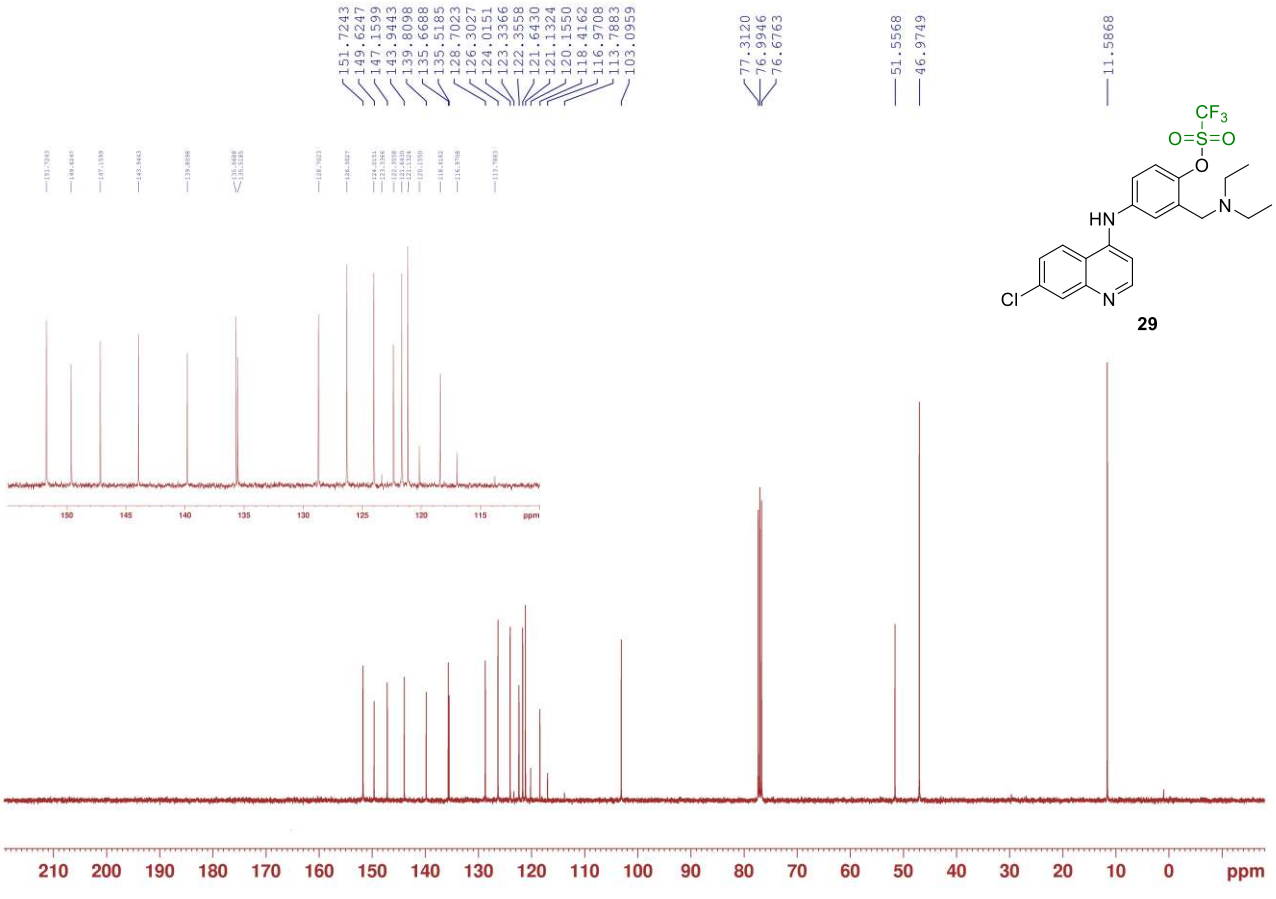


28

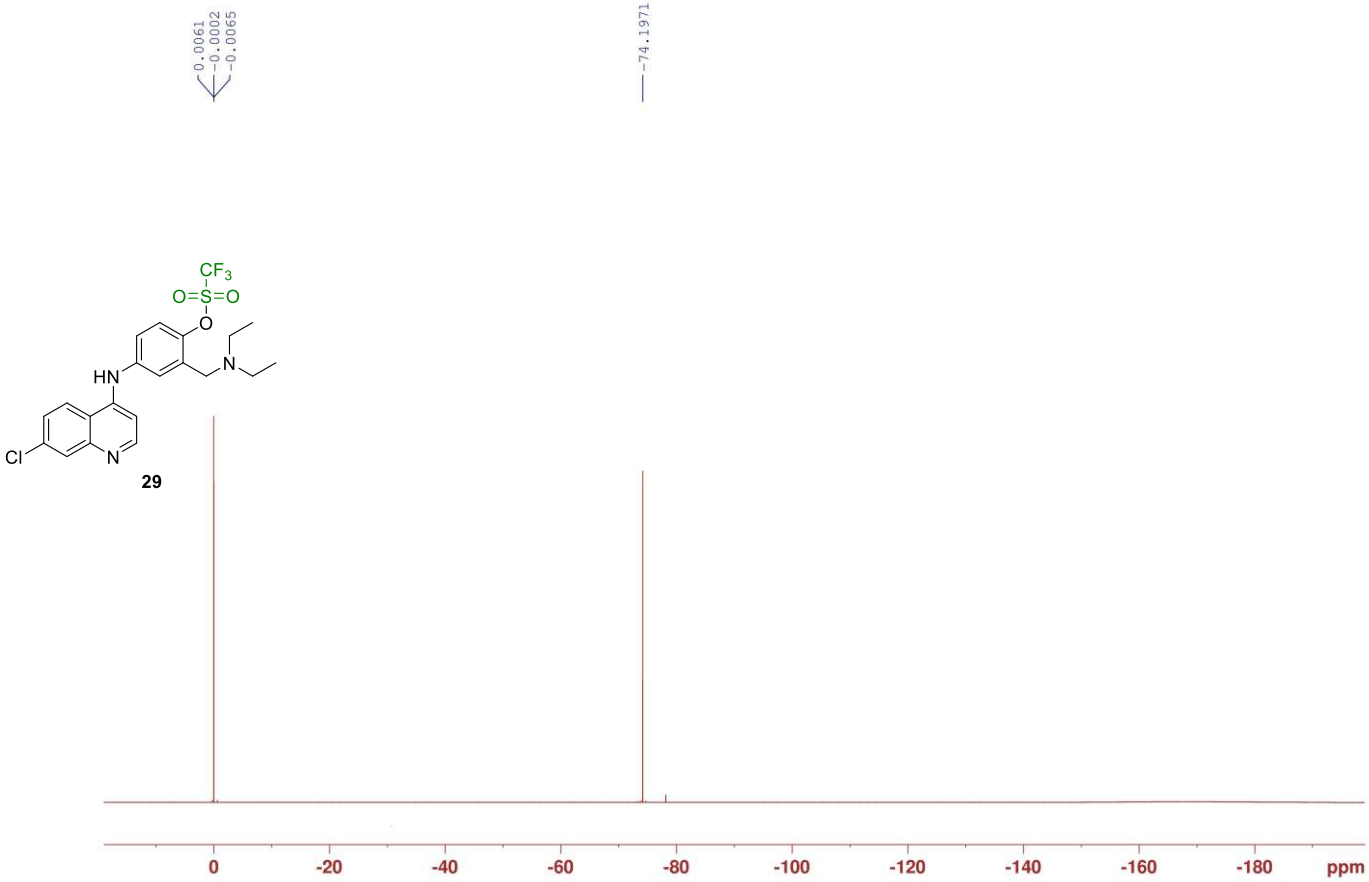
^{1}HNMR spectrum of **29**



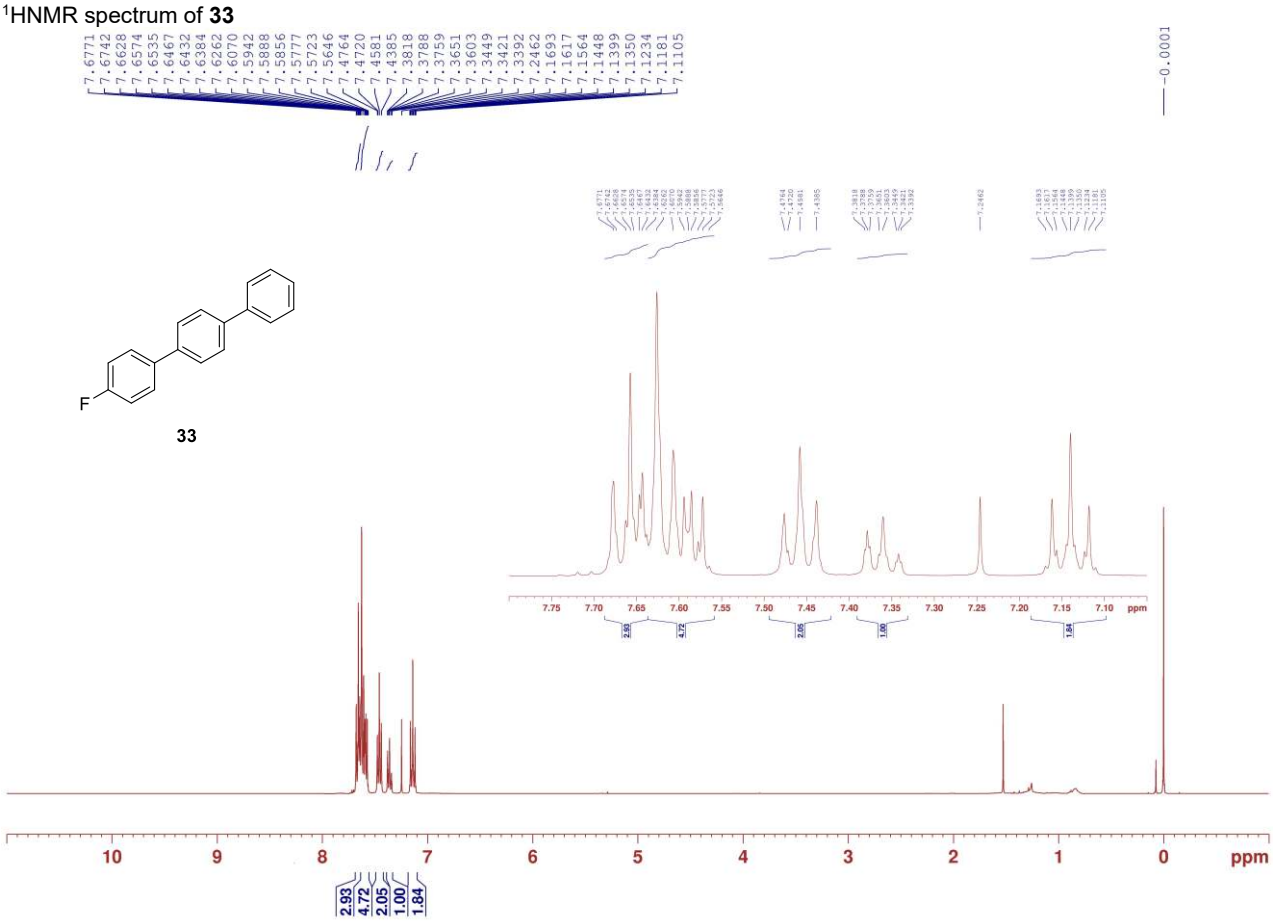
^{13}CNMR spectrum of **29**



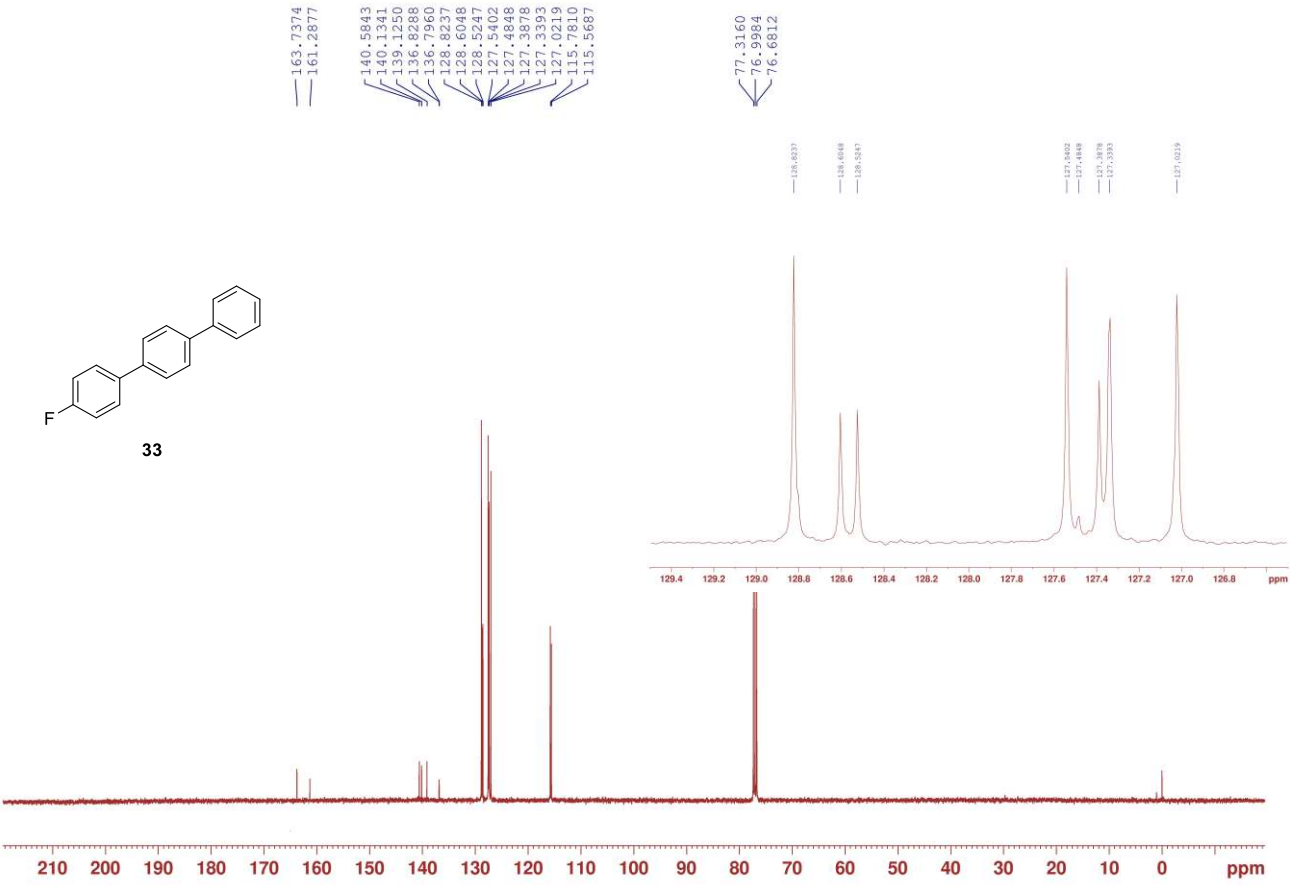
^{19}FNMR spectrum of **29**



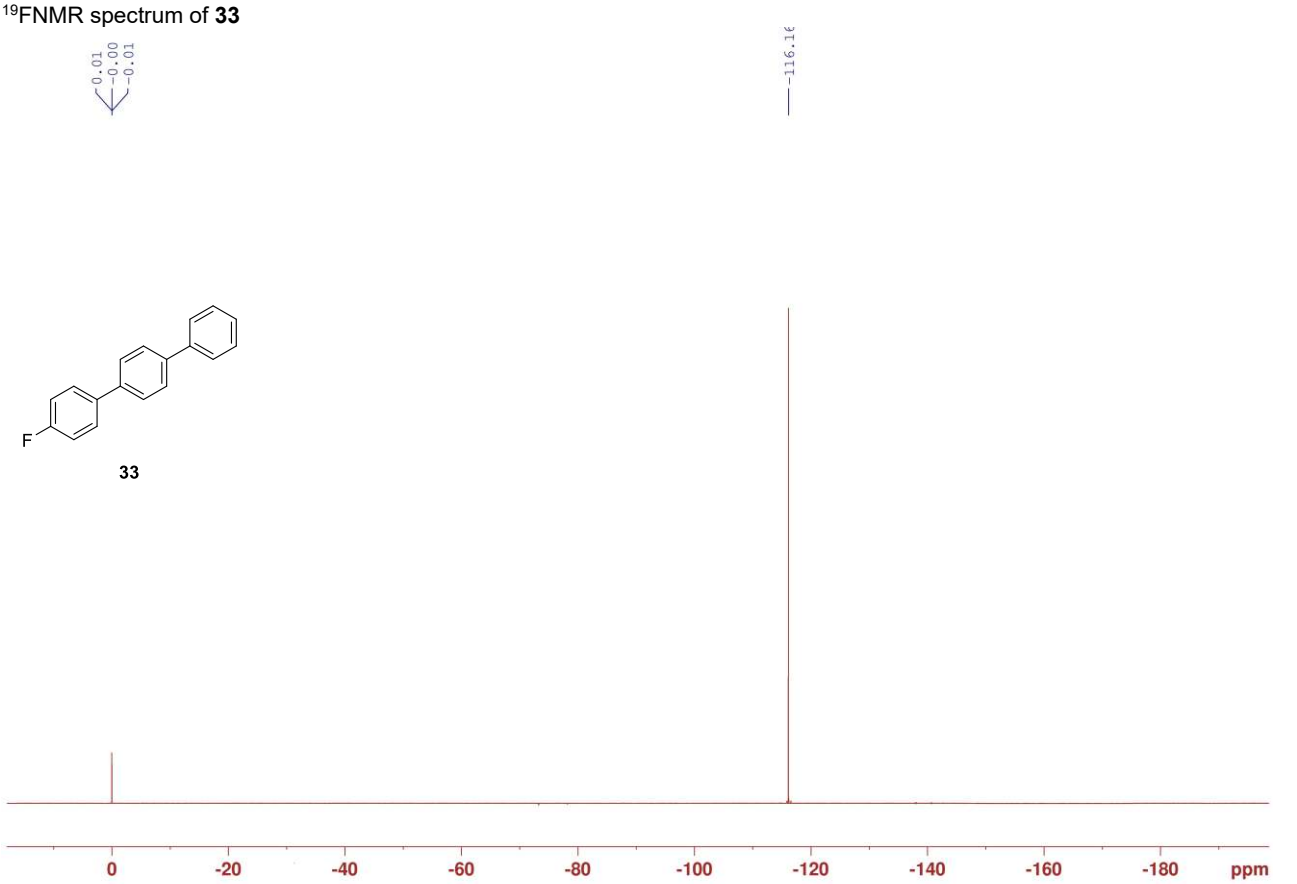
^{1}HNMR spectrum of **33**



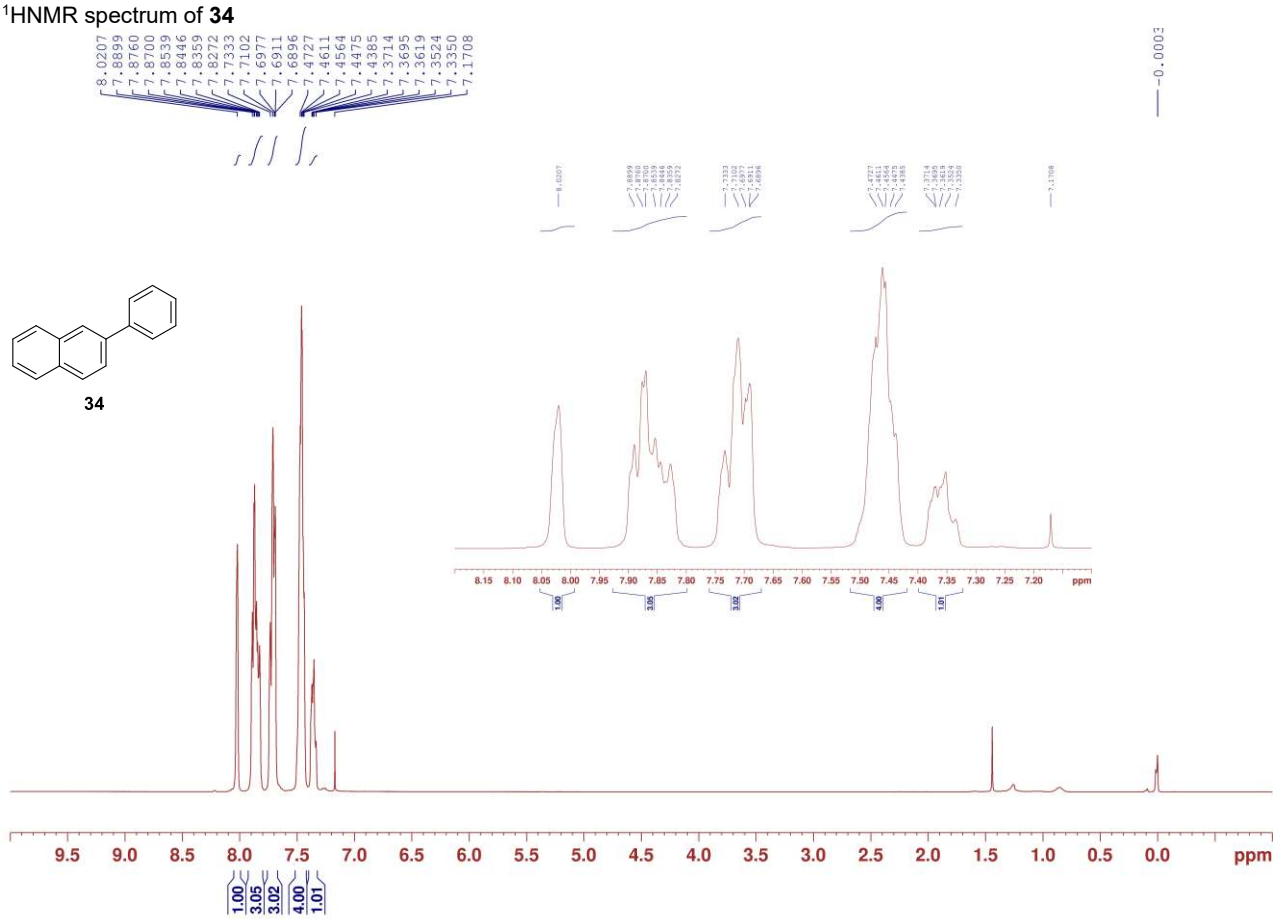
^{13}CNMR spectrum of **33**



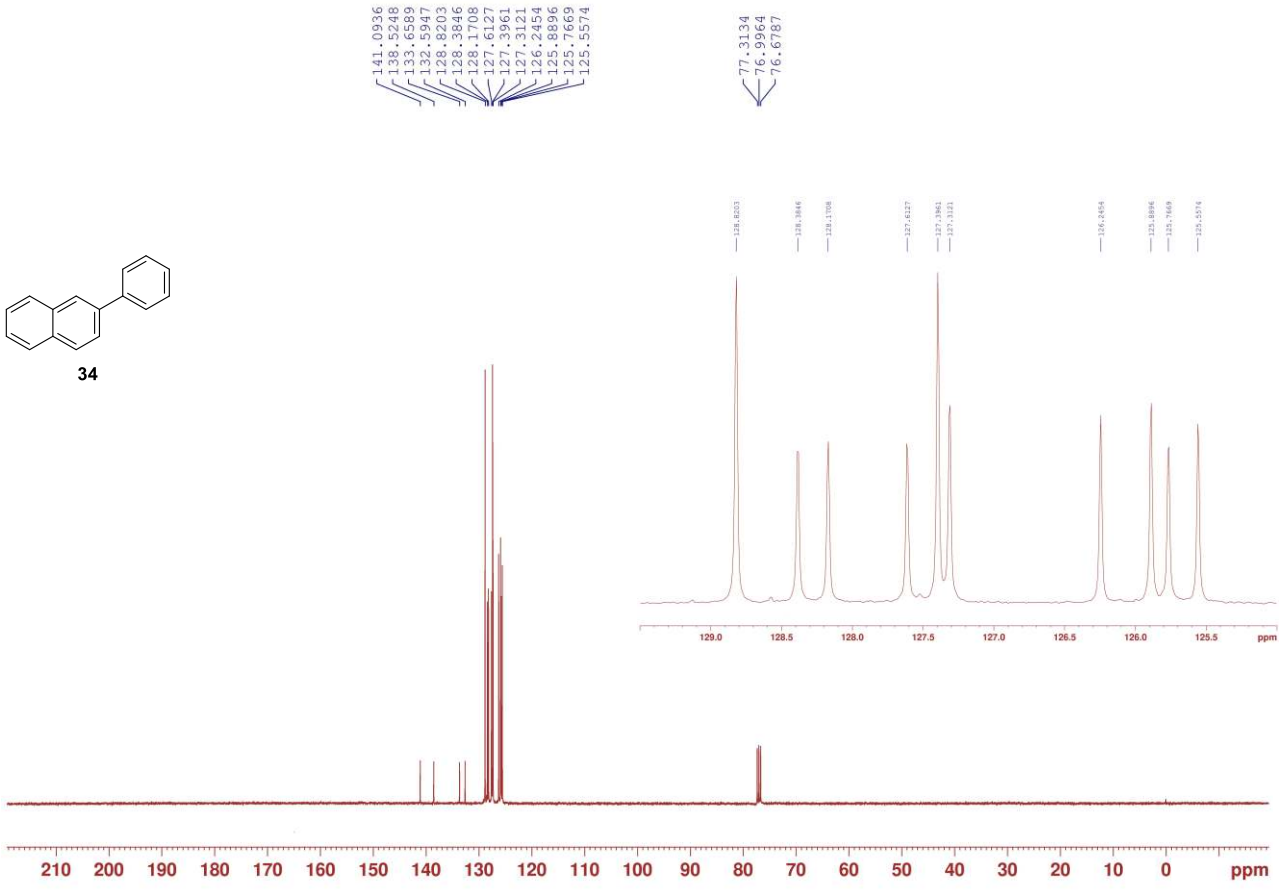
^{19}FNMR spectrum of **33**



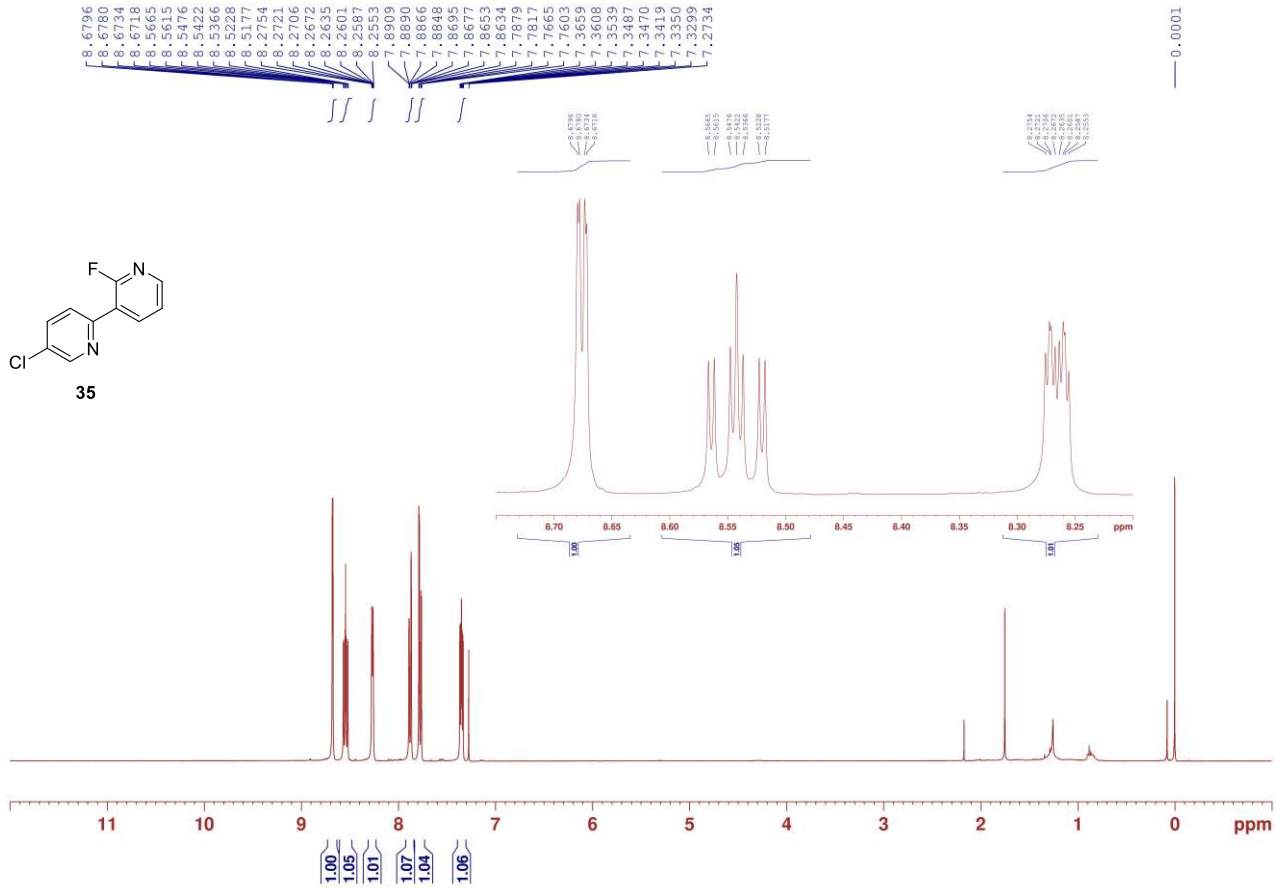
^{1}HNMR spectrum of **34**



^{13}CNMR spectrum of **34**

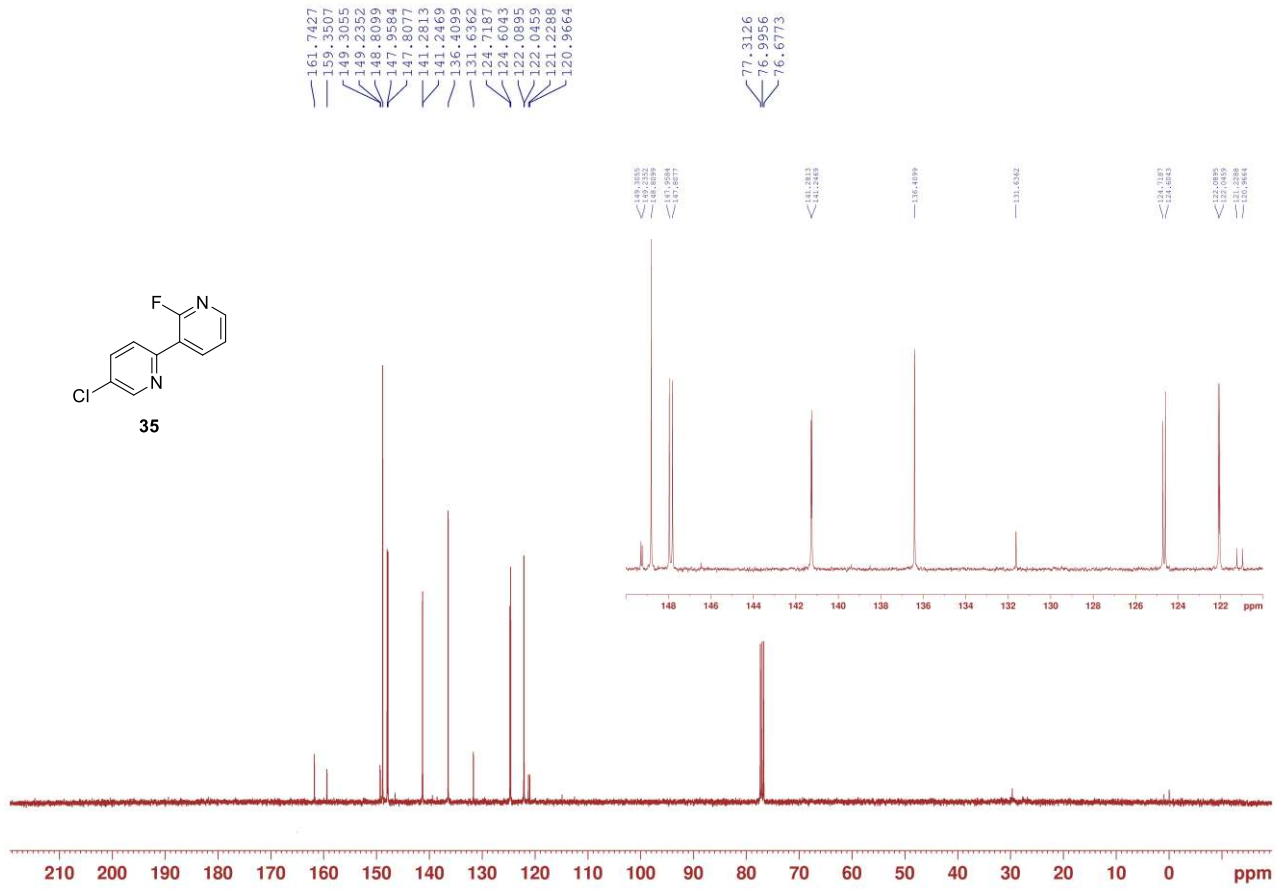


^{1}HNMR spectrum of **35**



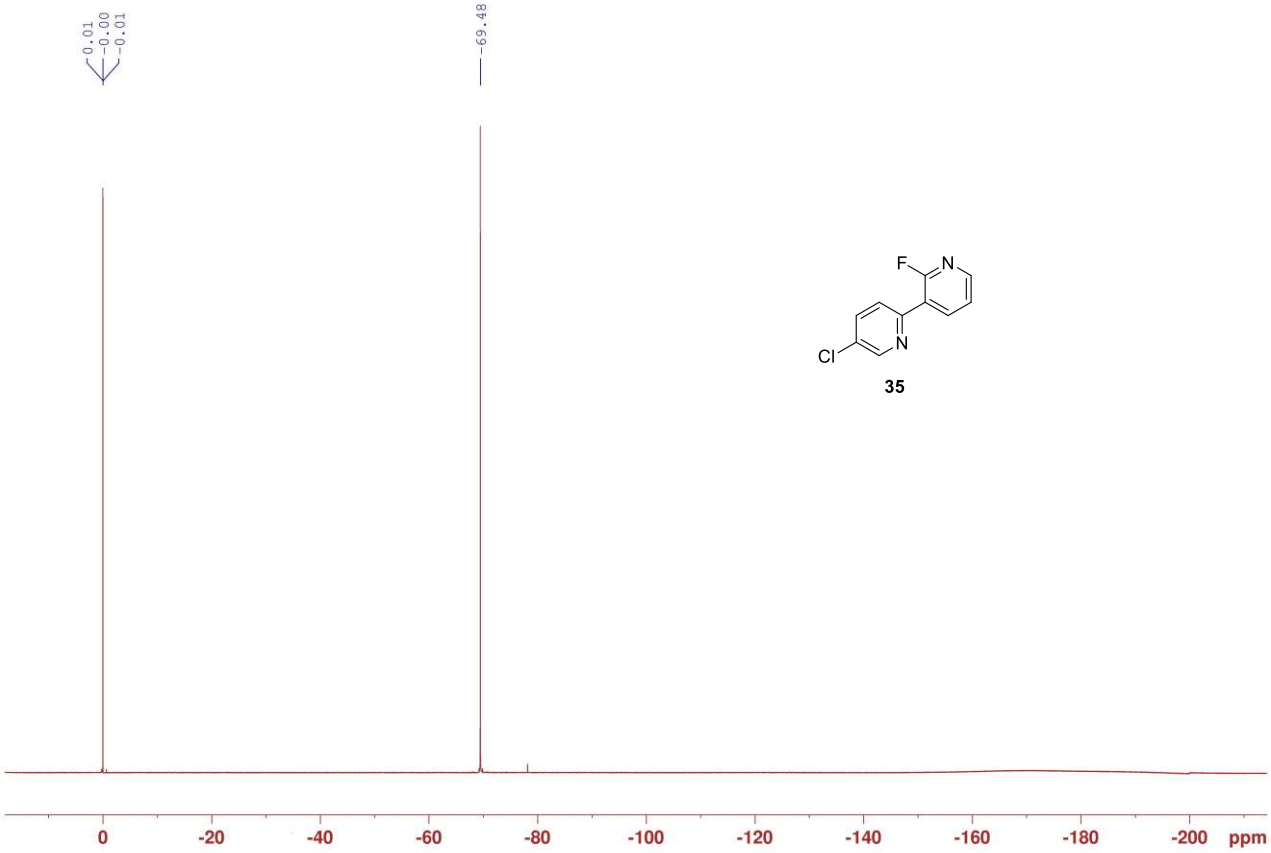
35

^{13}CNMR spectrum of **35**

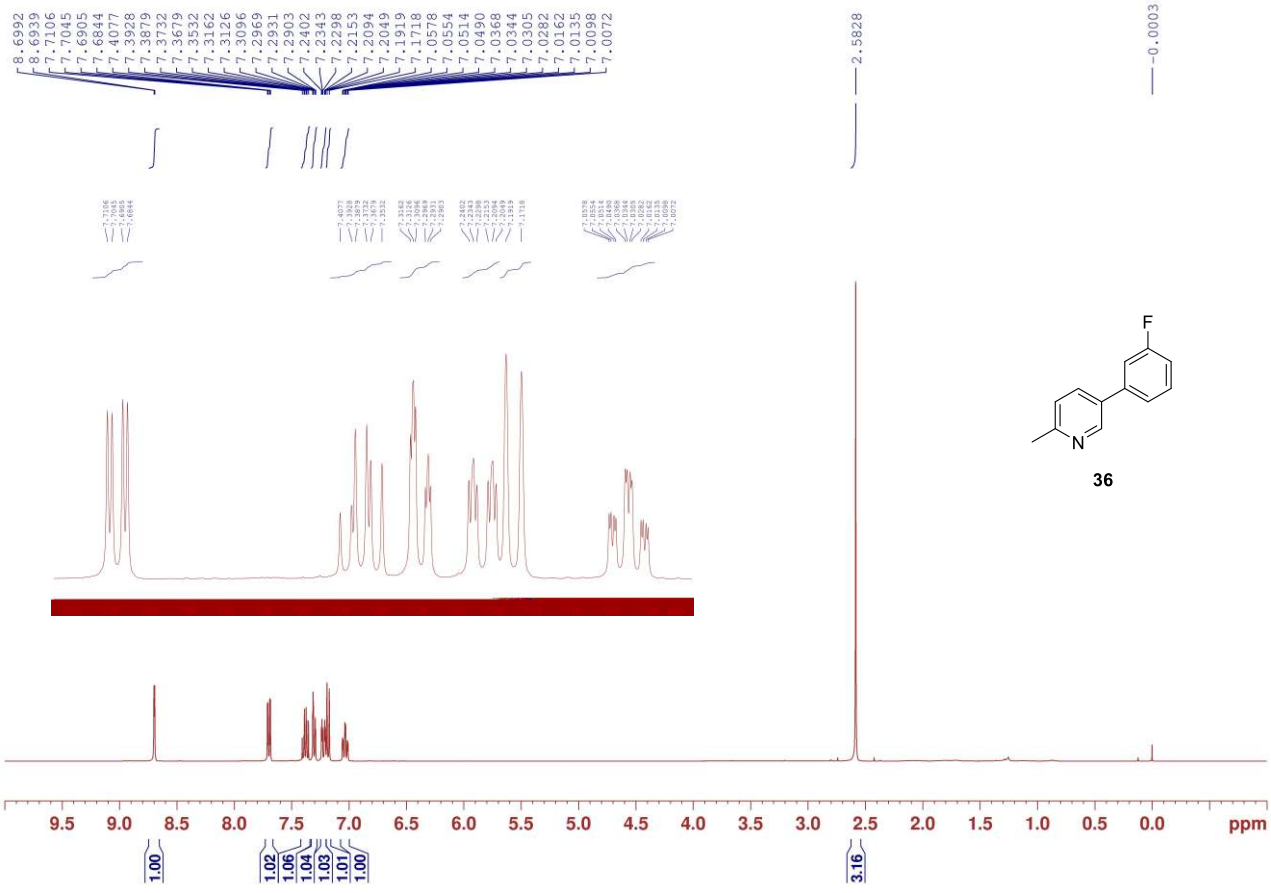


35

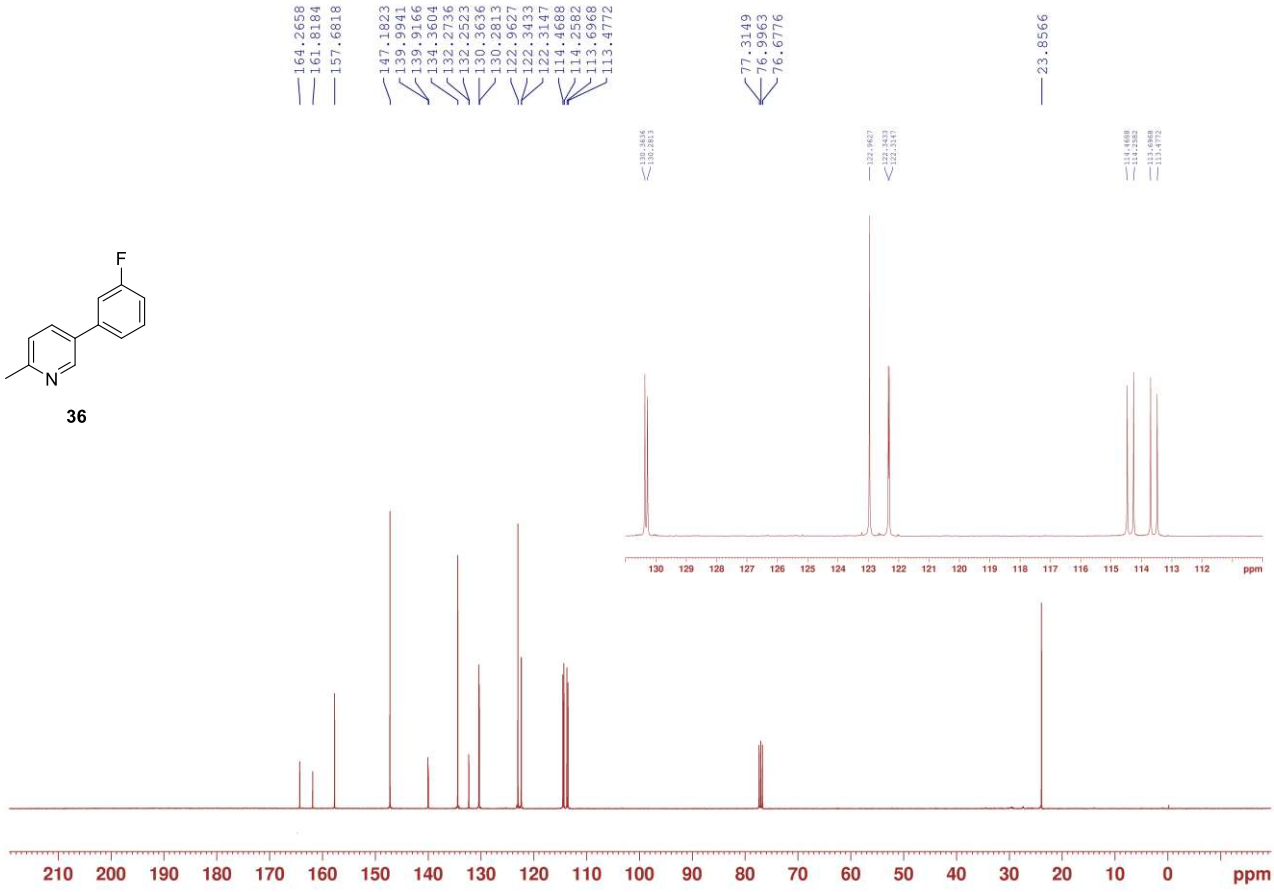
^{19}FNMR spectrum of **35**



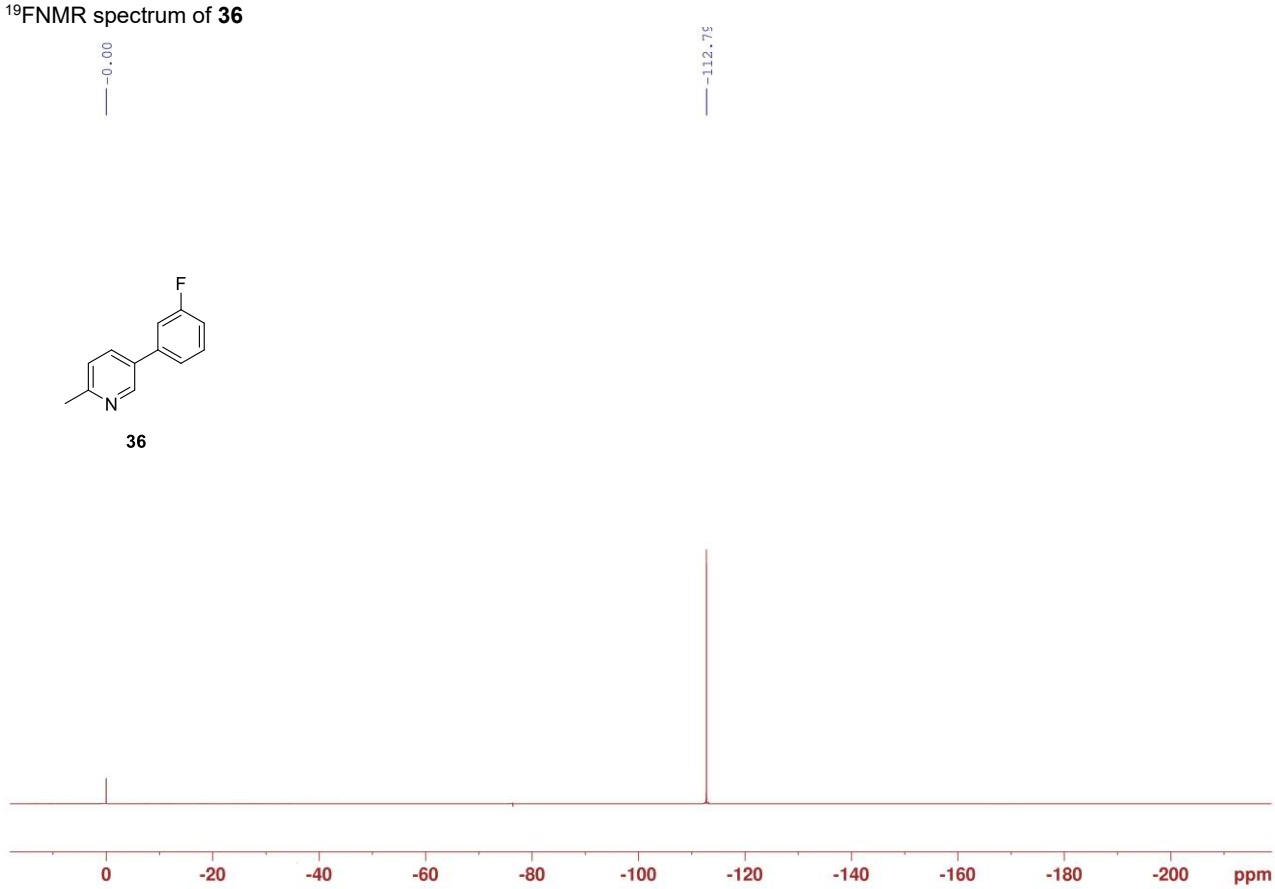
^{1}HNMR spectrum of **36**



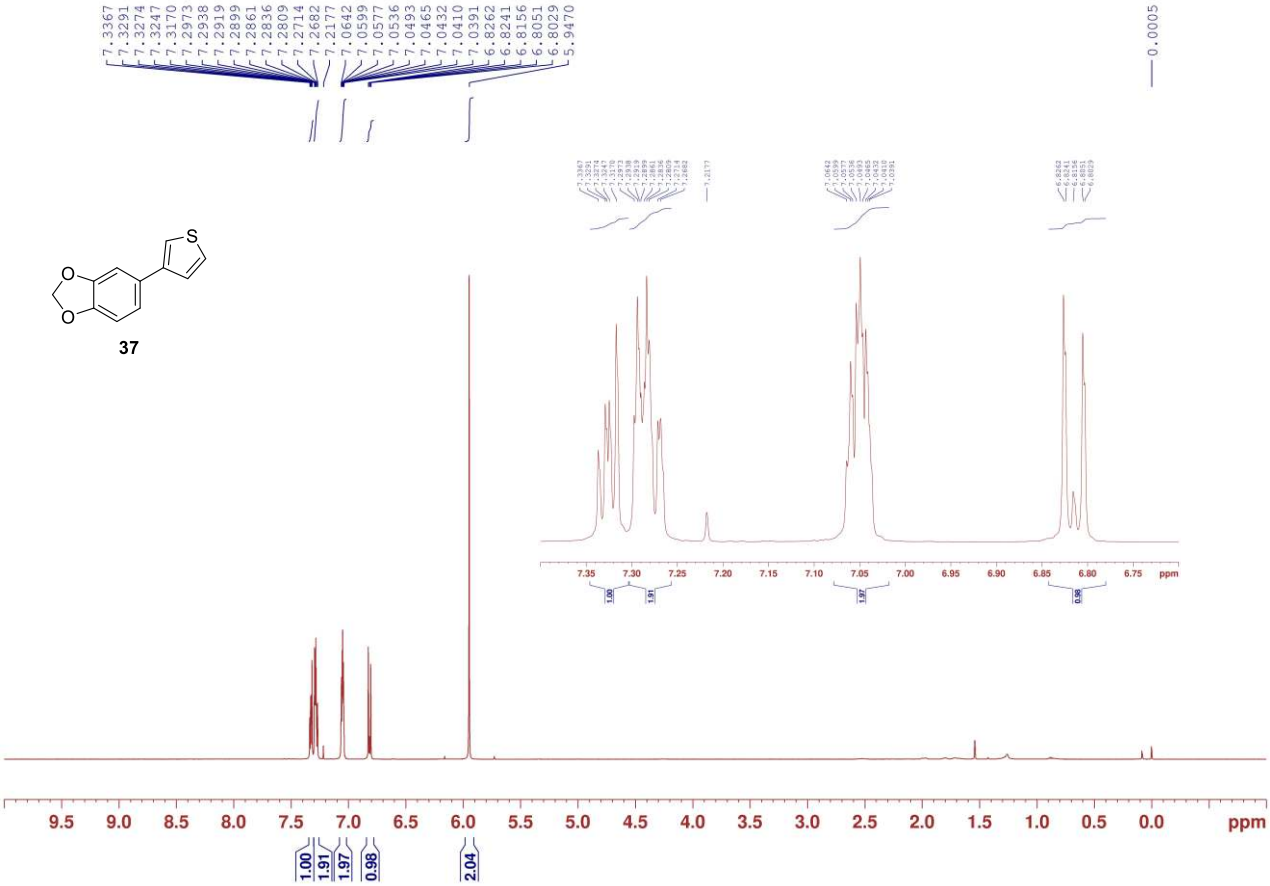
^{13}CNMR spectrum of **36**



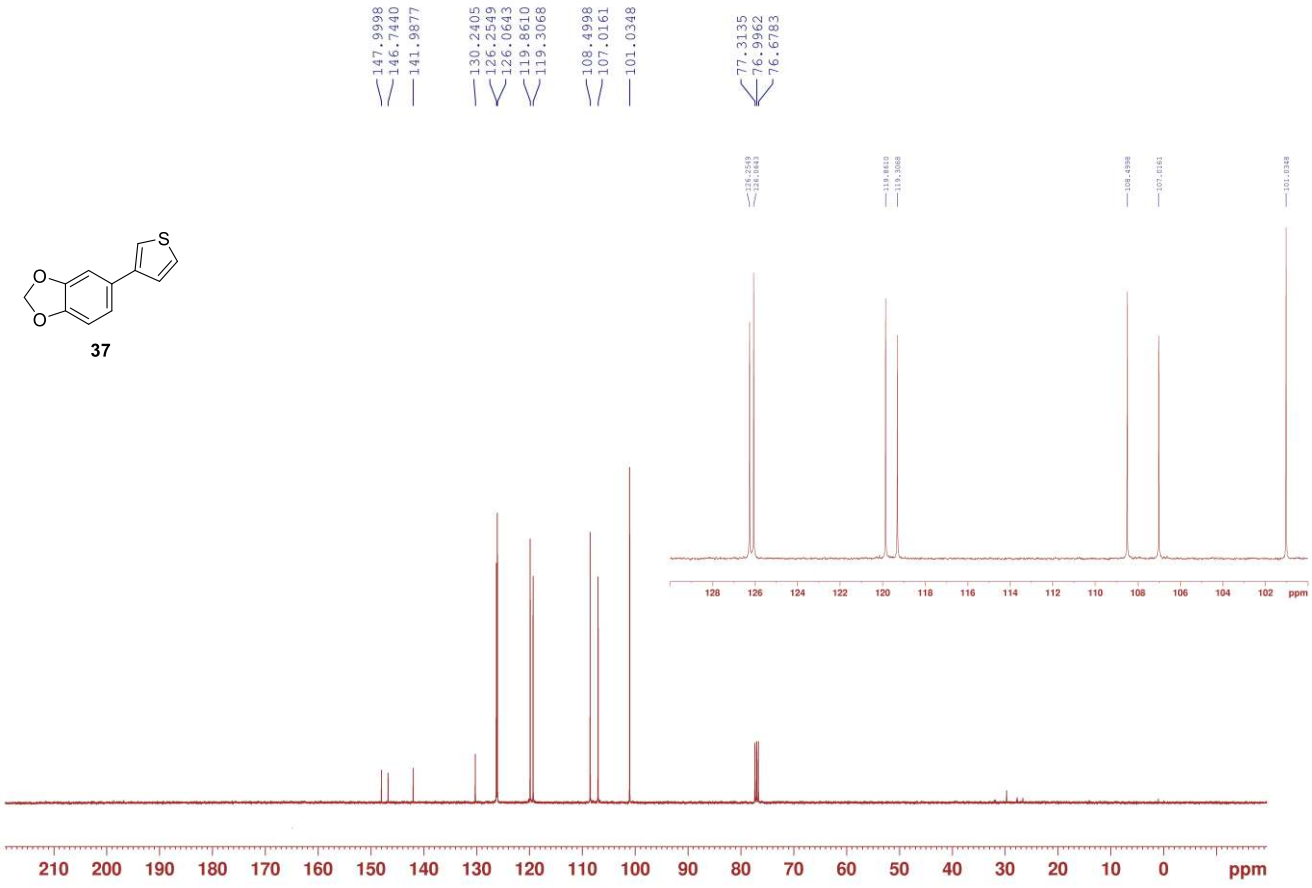
^{19}FNMR spectrum of **36**



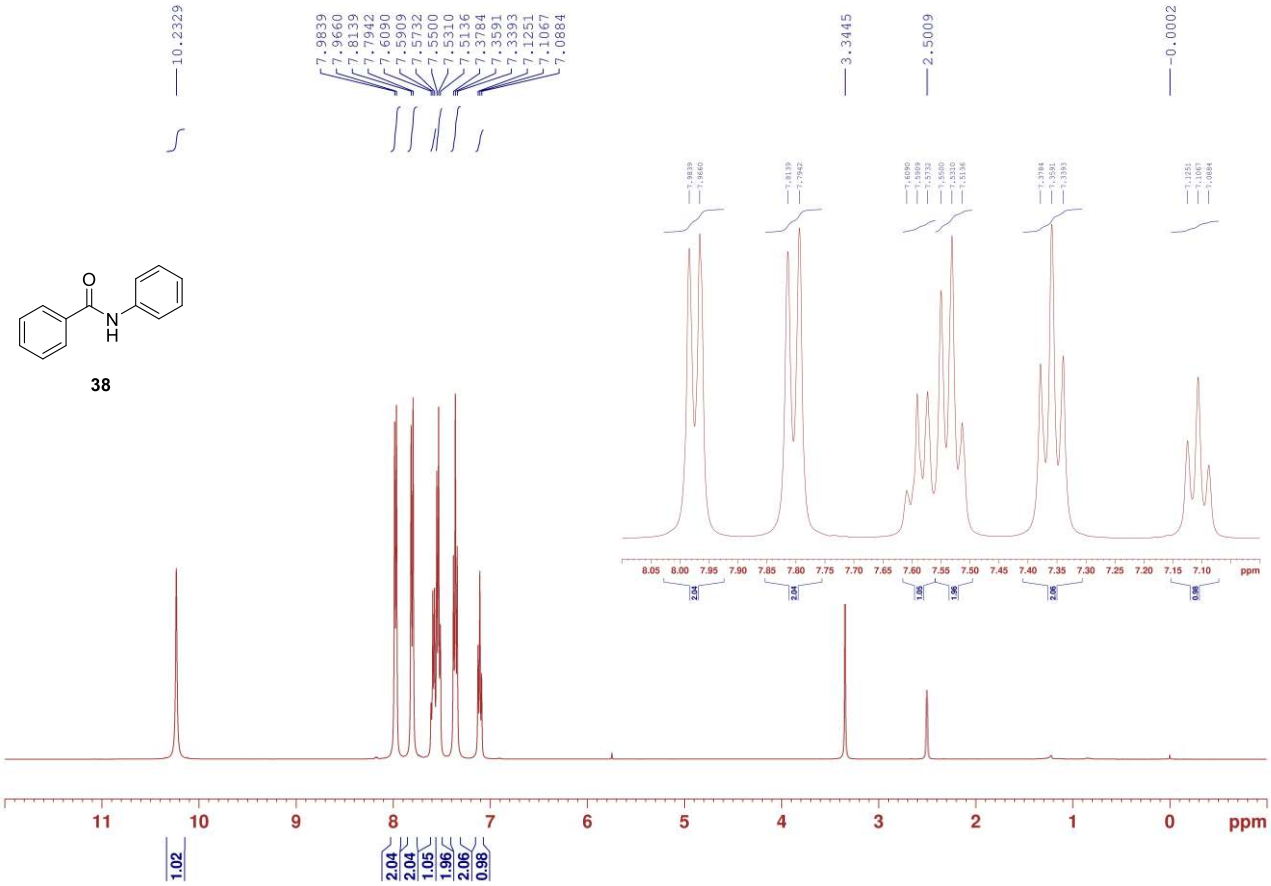
[1]HNMR spectrum of **37**



[13]CNMR spectrum of **37**

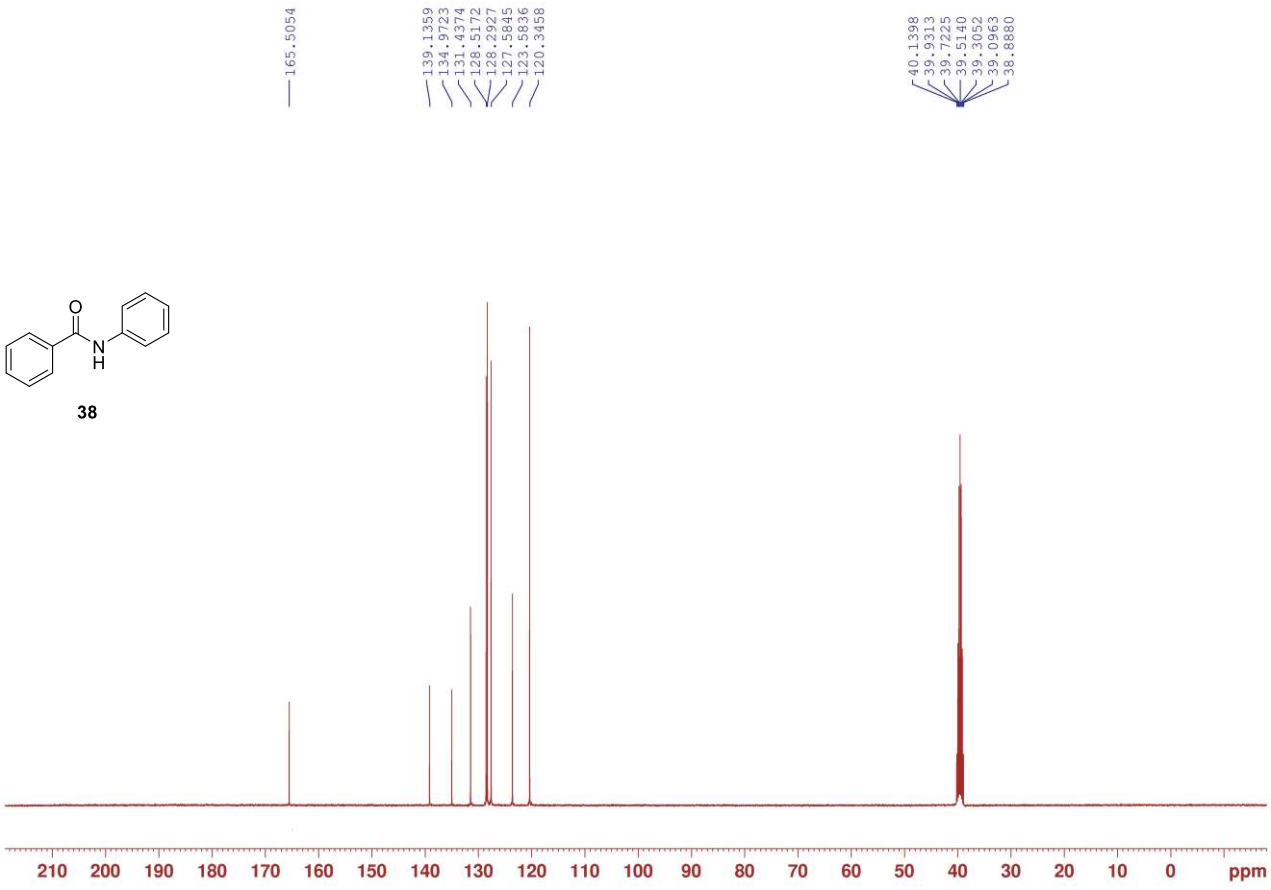


[1]HNMR spectrum of **38** (DMSO-*d6*)



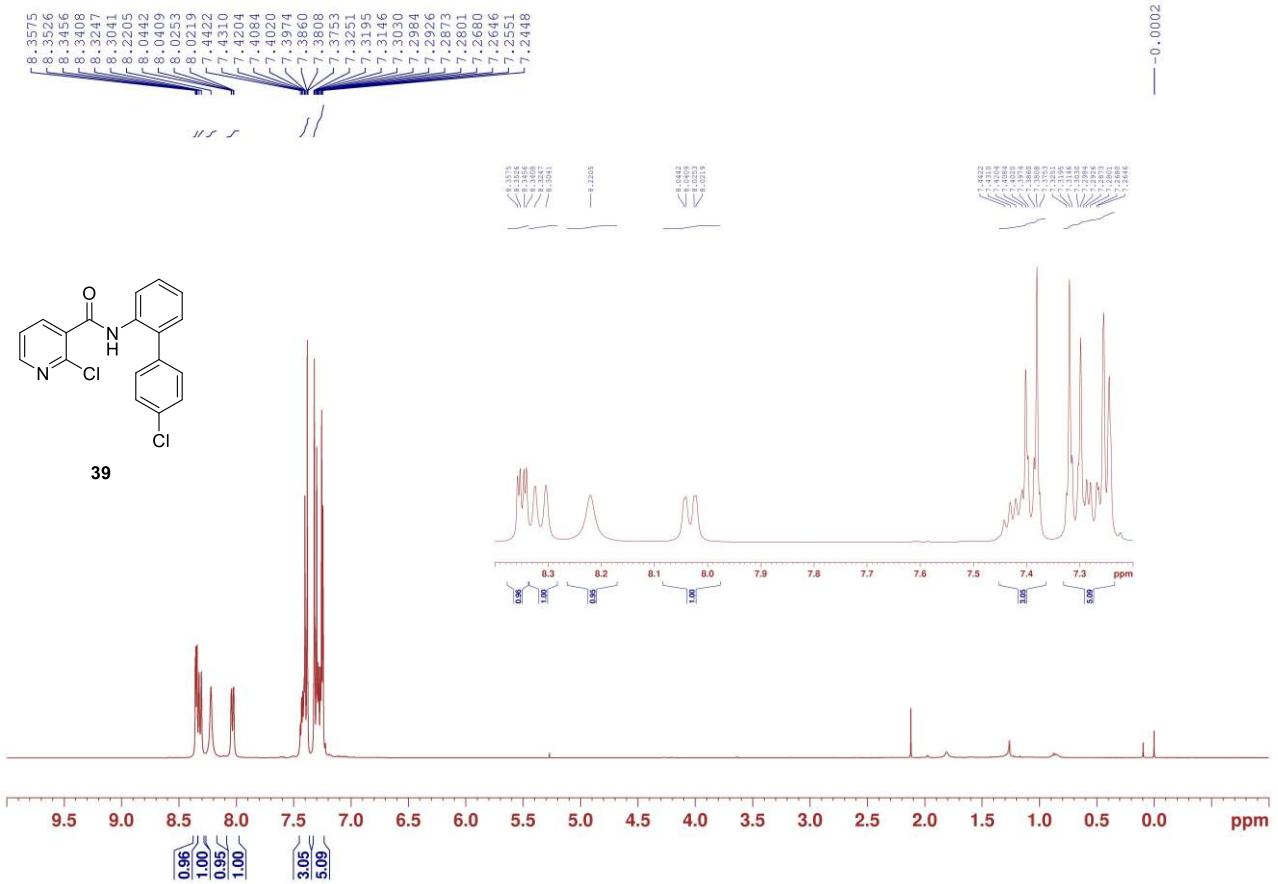
38

[13]CNMR spectrum of **38** (DMSO-*d6*)



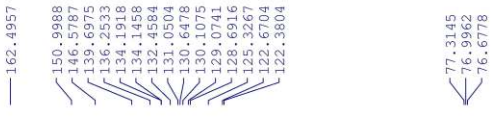
38

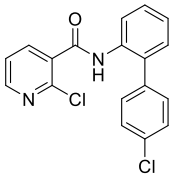
[1]HNMR spectrum of **39**



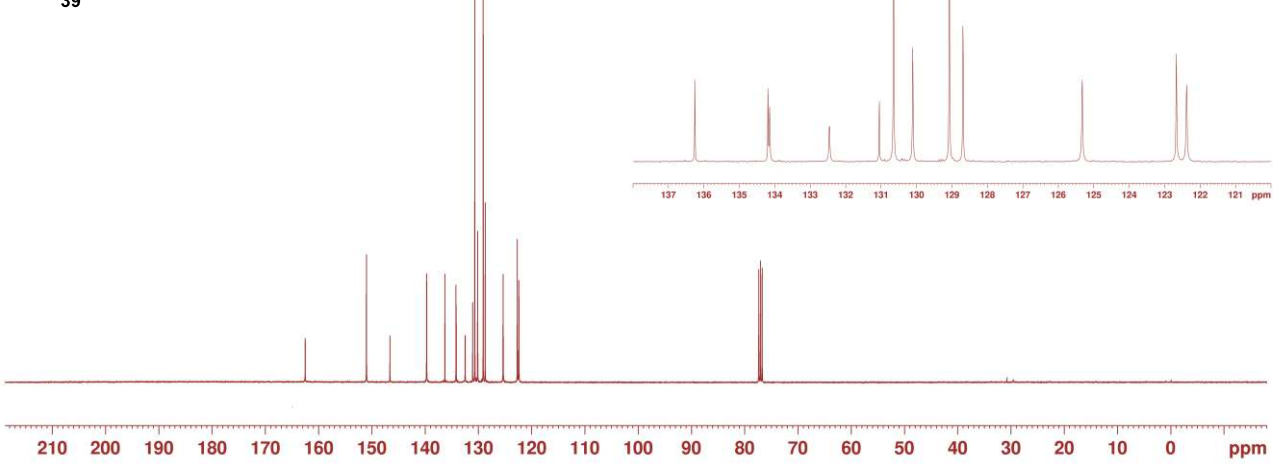
39

[13]CNMR spectrum of **39**

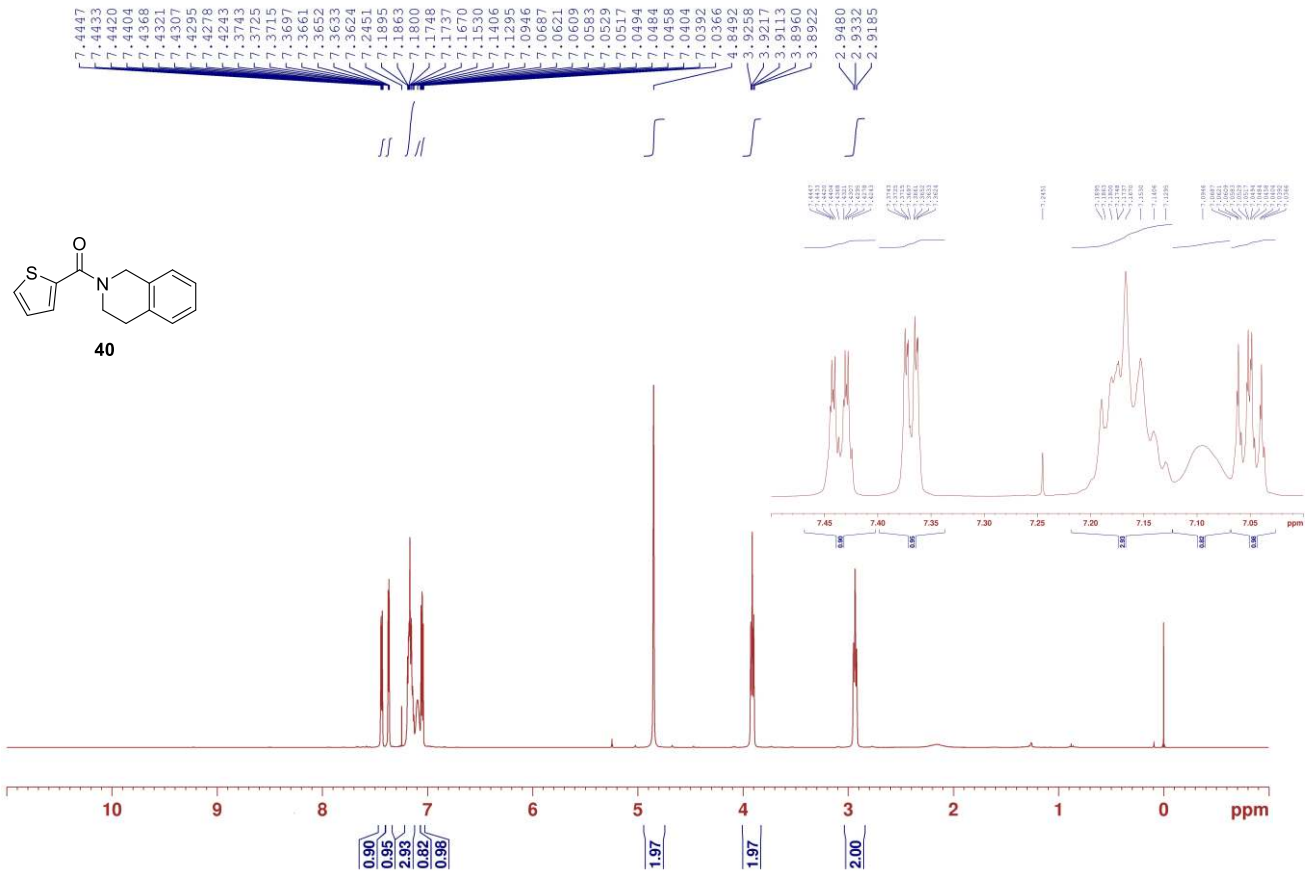




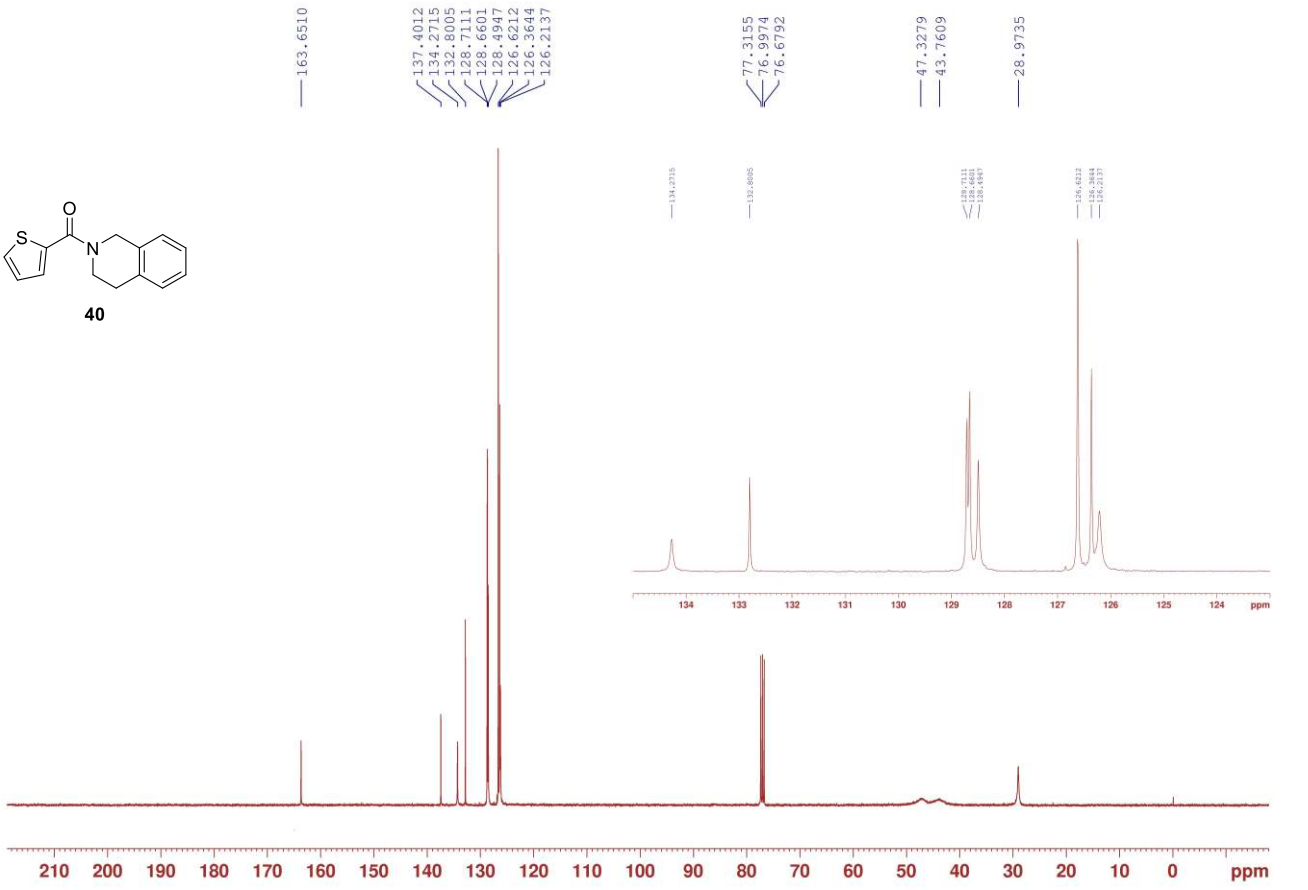
39



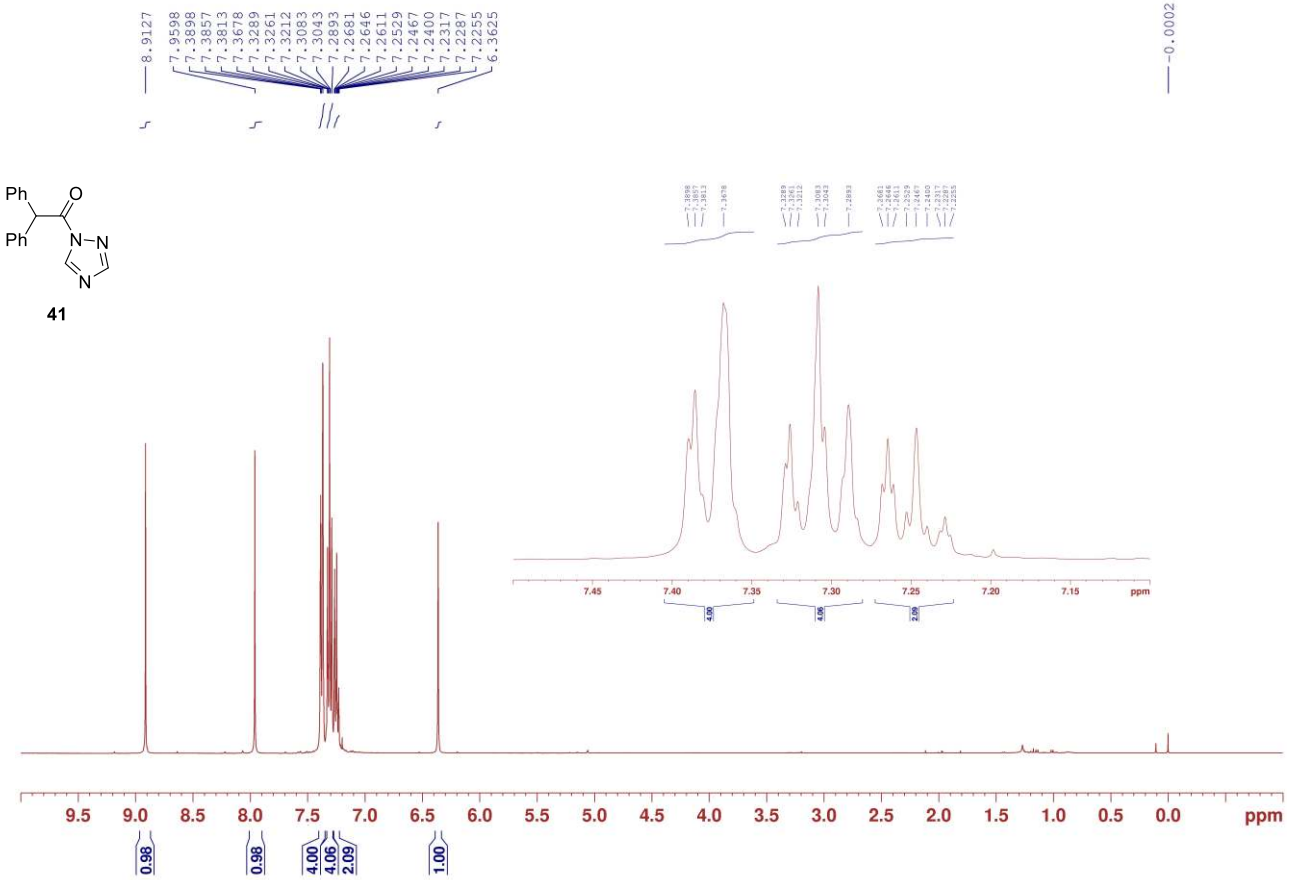
^{1}HNMR spectrum of **40**



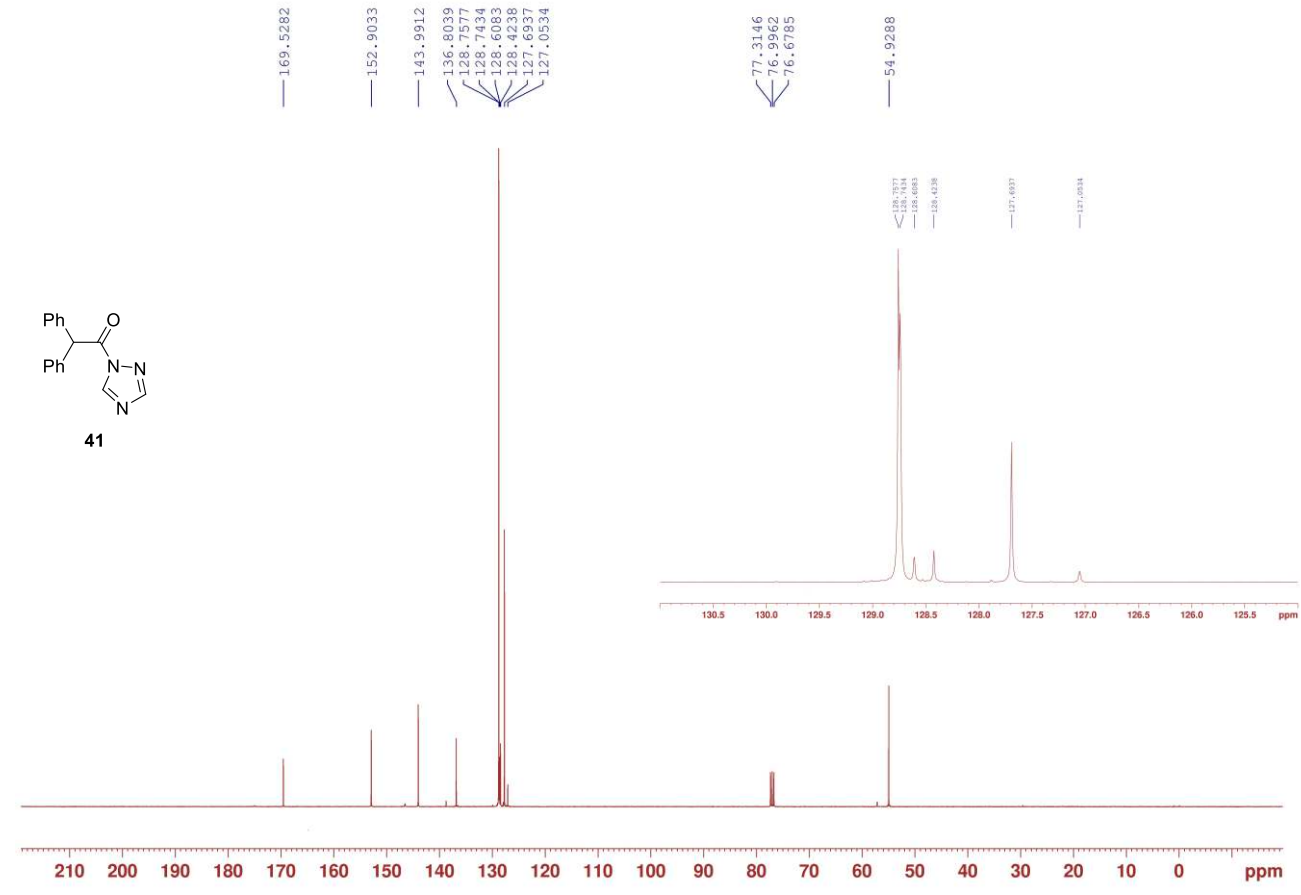
^{13}CNMR spectrum of **40**



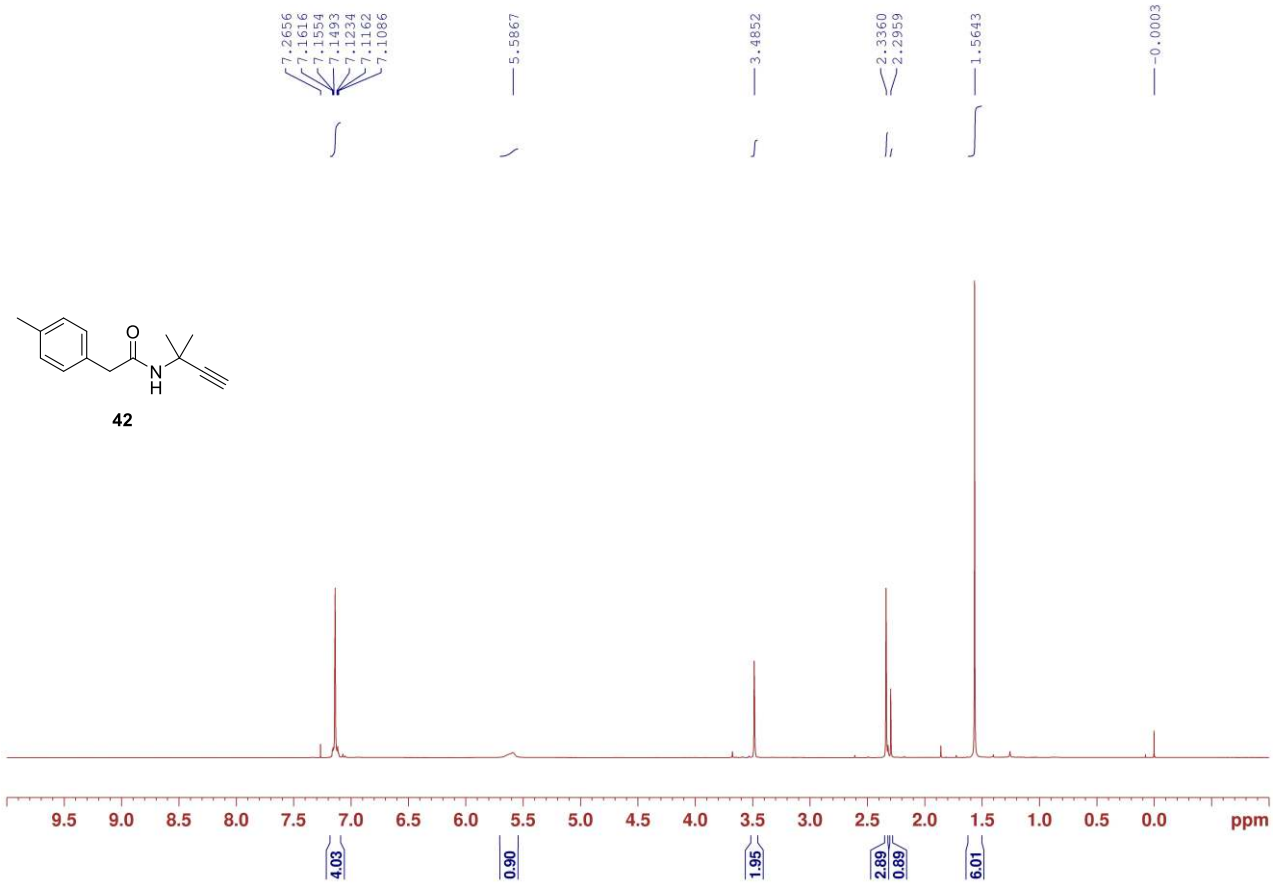
[1]HNMR spectrum of **41**



[13]CNMR spectrum of **41**

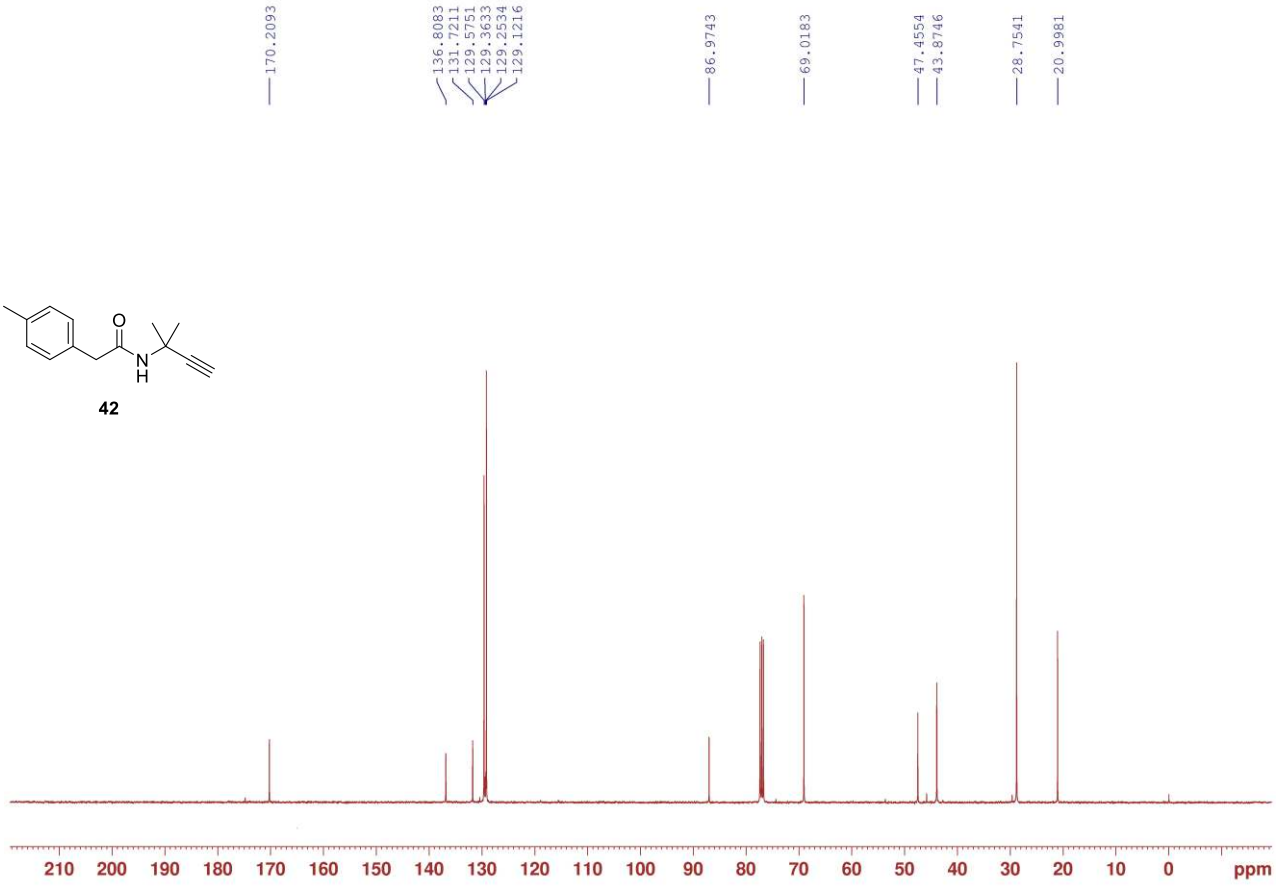


[1]HNMR spectrum of **42**



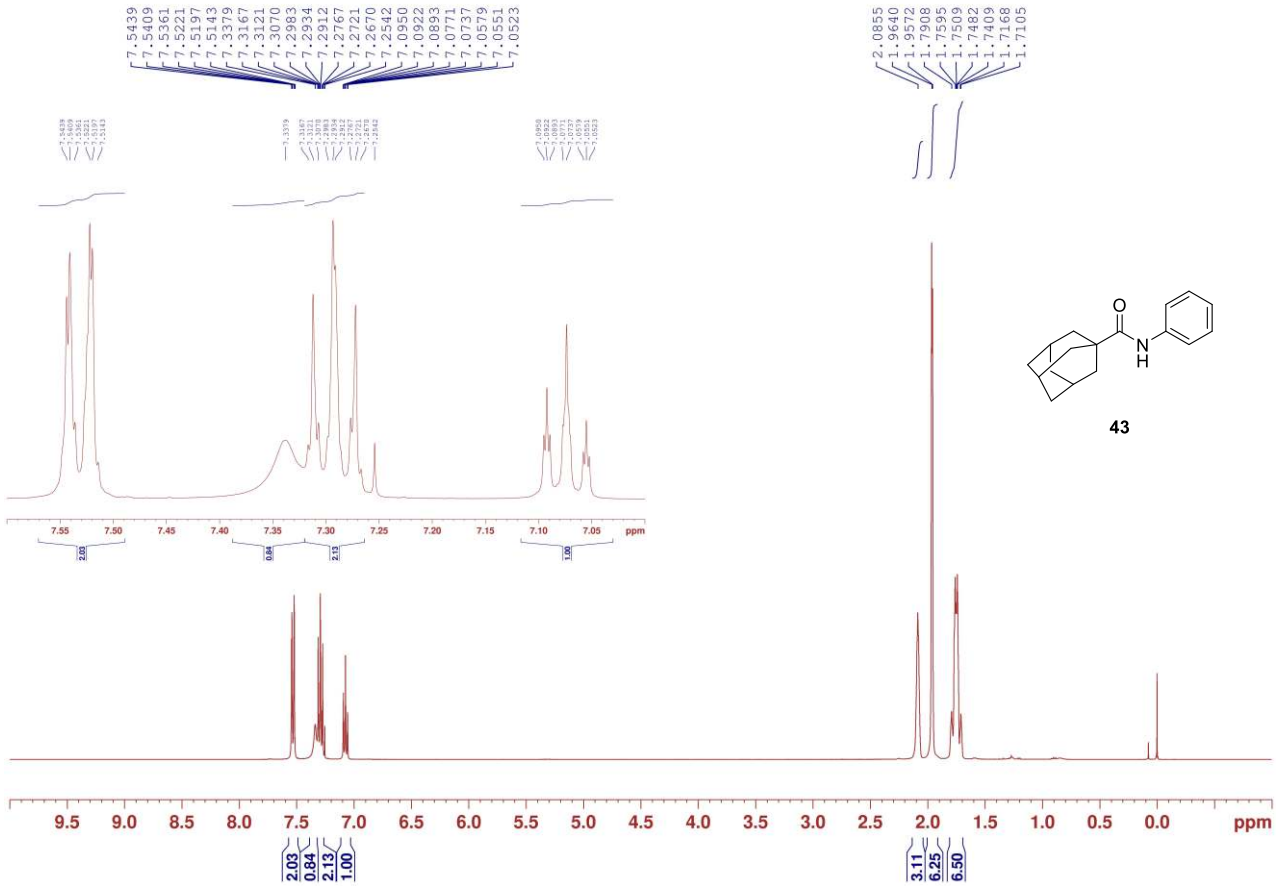
42

[13]CNMR spectrum of **42**



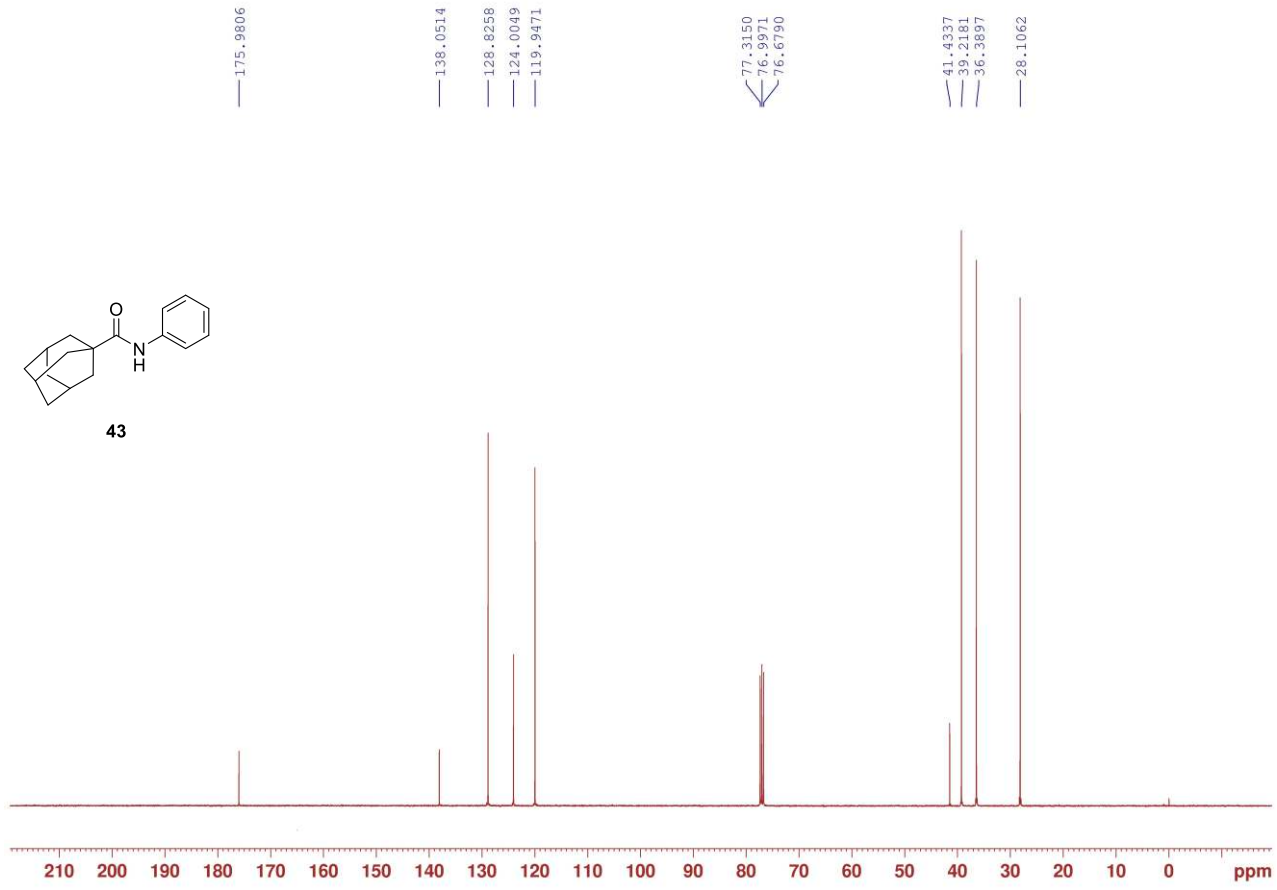
42

^{1}HNMR spectrum of **43**



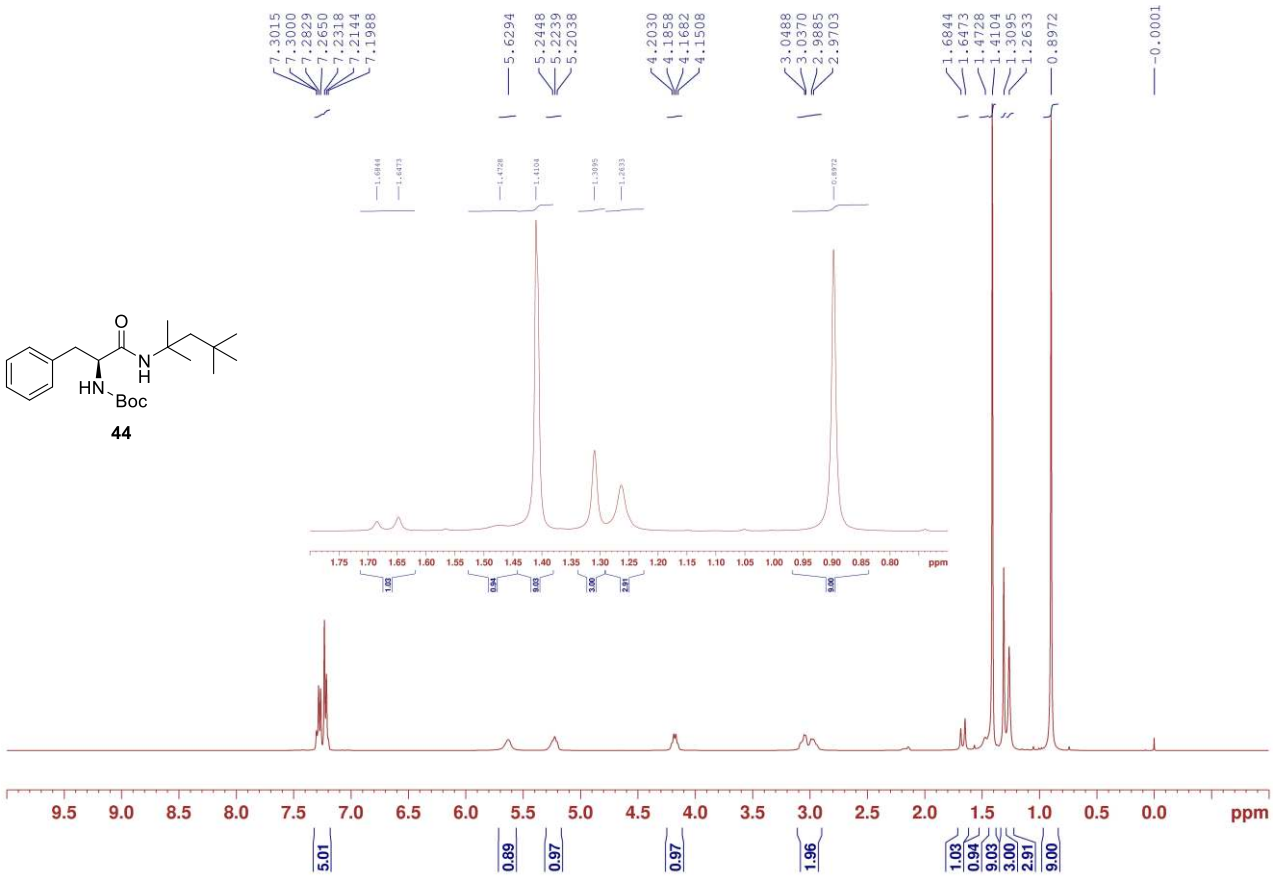
43

^{13}CNMR spectrum of **43**



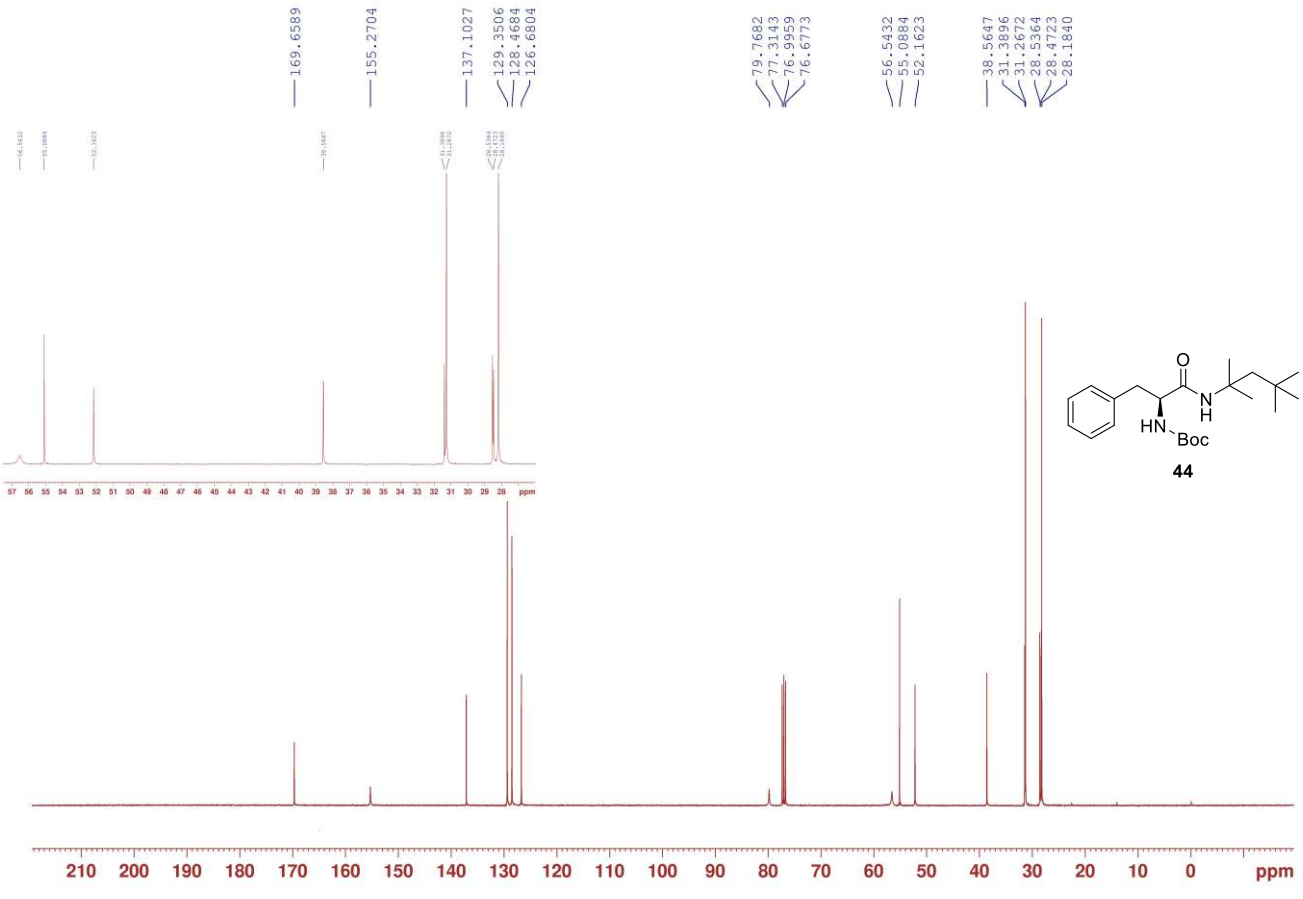
43

[1]HNMR spectrum of **44**



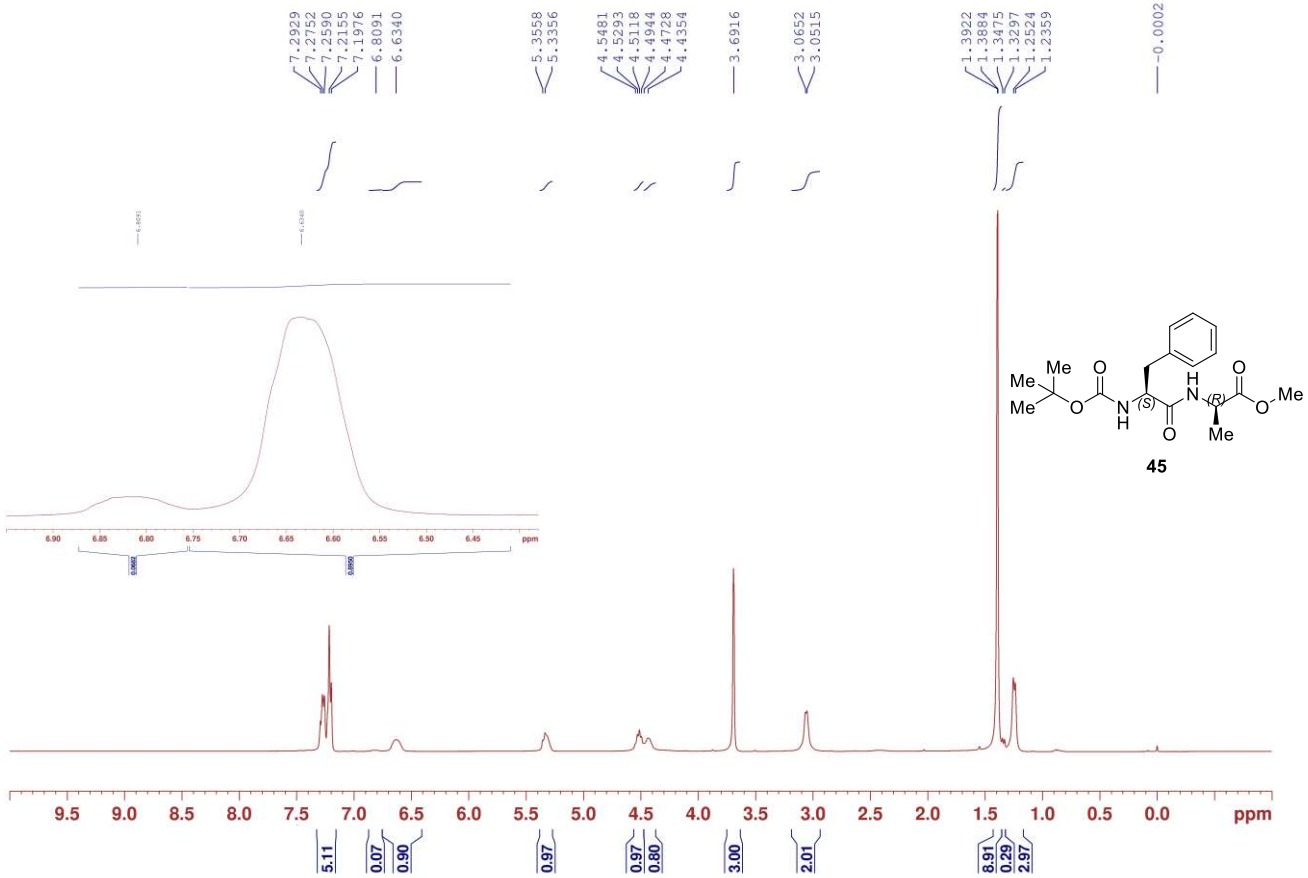
44

[13]CNMR spectrum of **44**



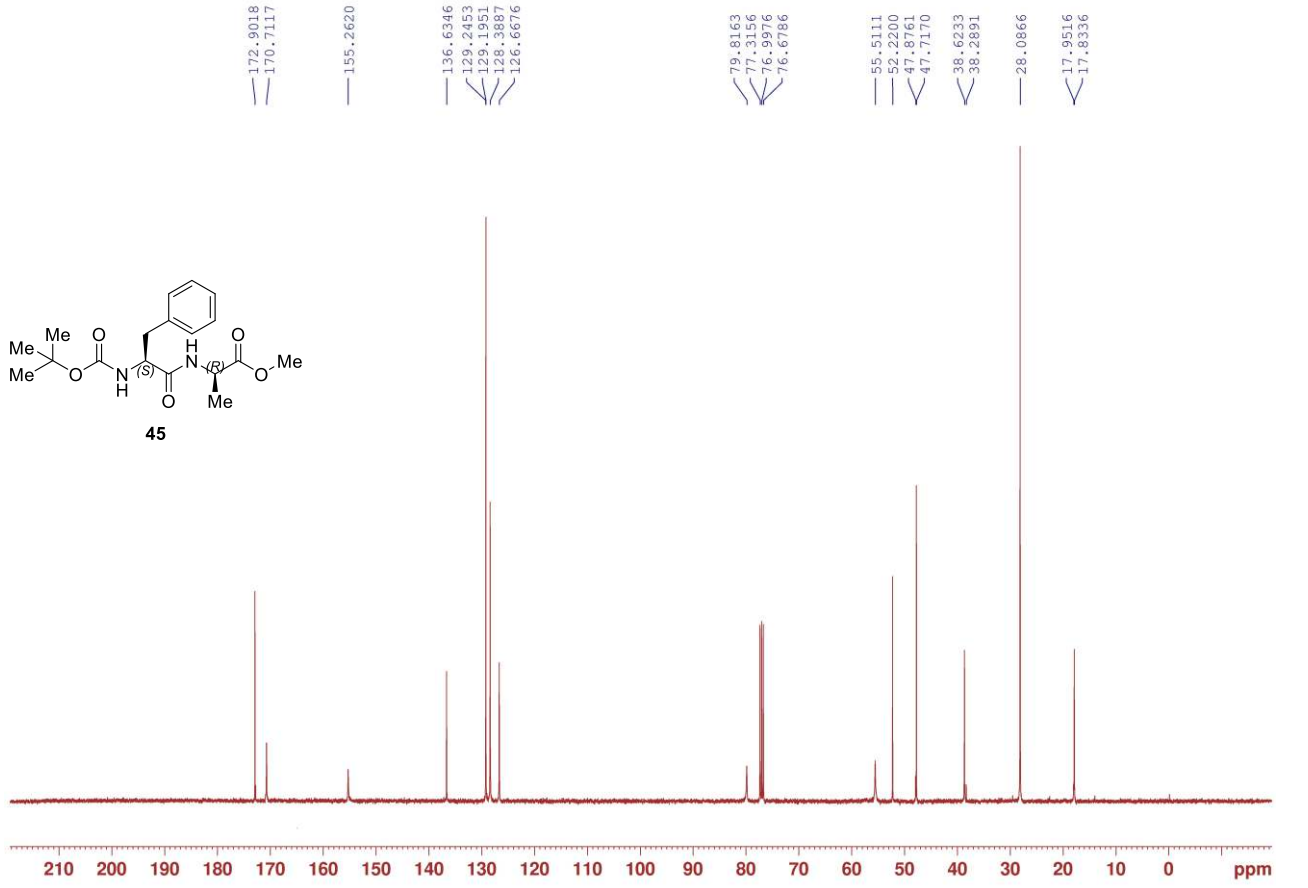
44

^{1}HNMR spectrum of **45**



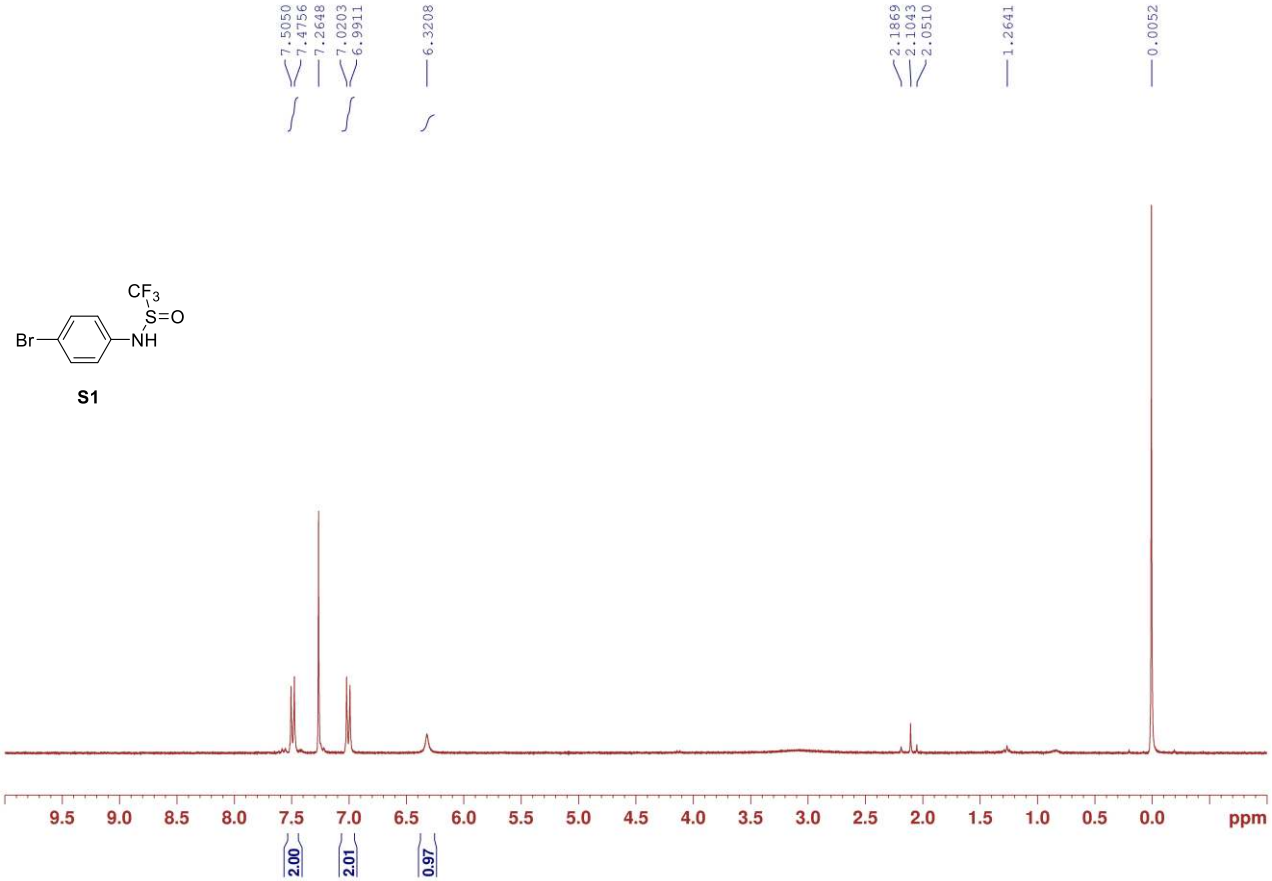
45

^{13}CNMR spectrum of **45**

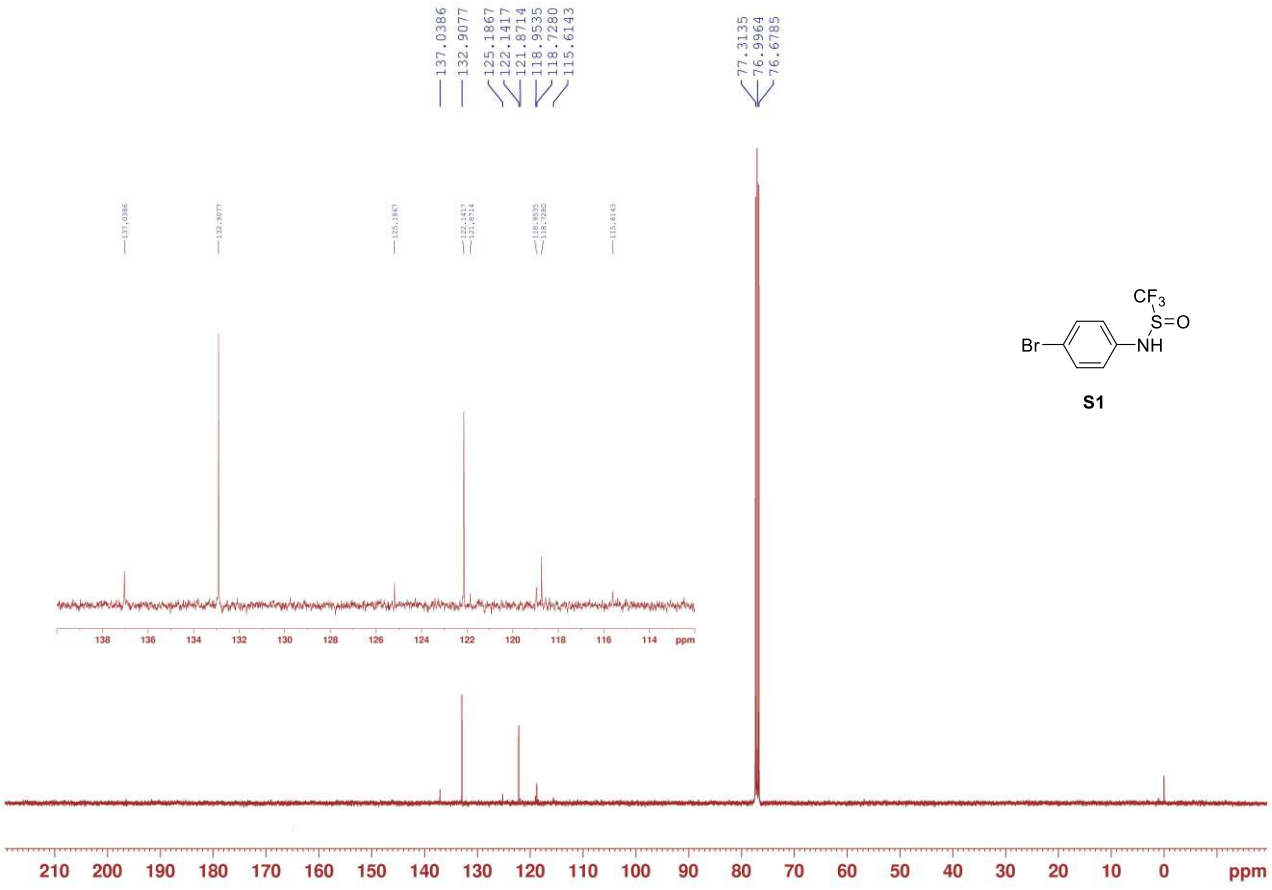


45

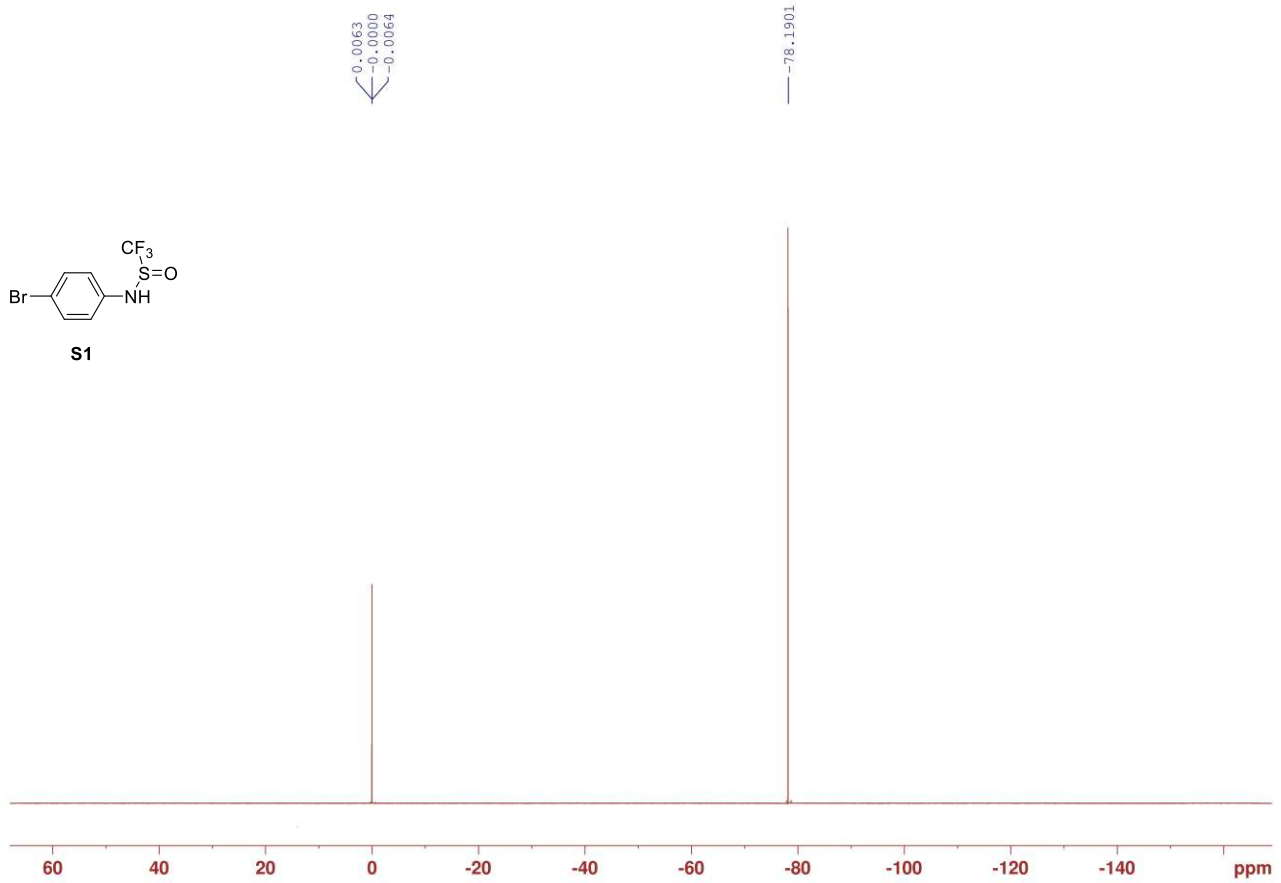
^{1}HNMR spectrum of **S1**



^{13}CNMR spectrum of **S1**

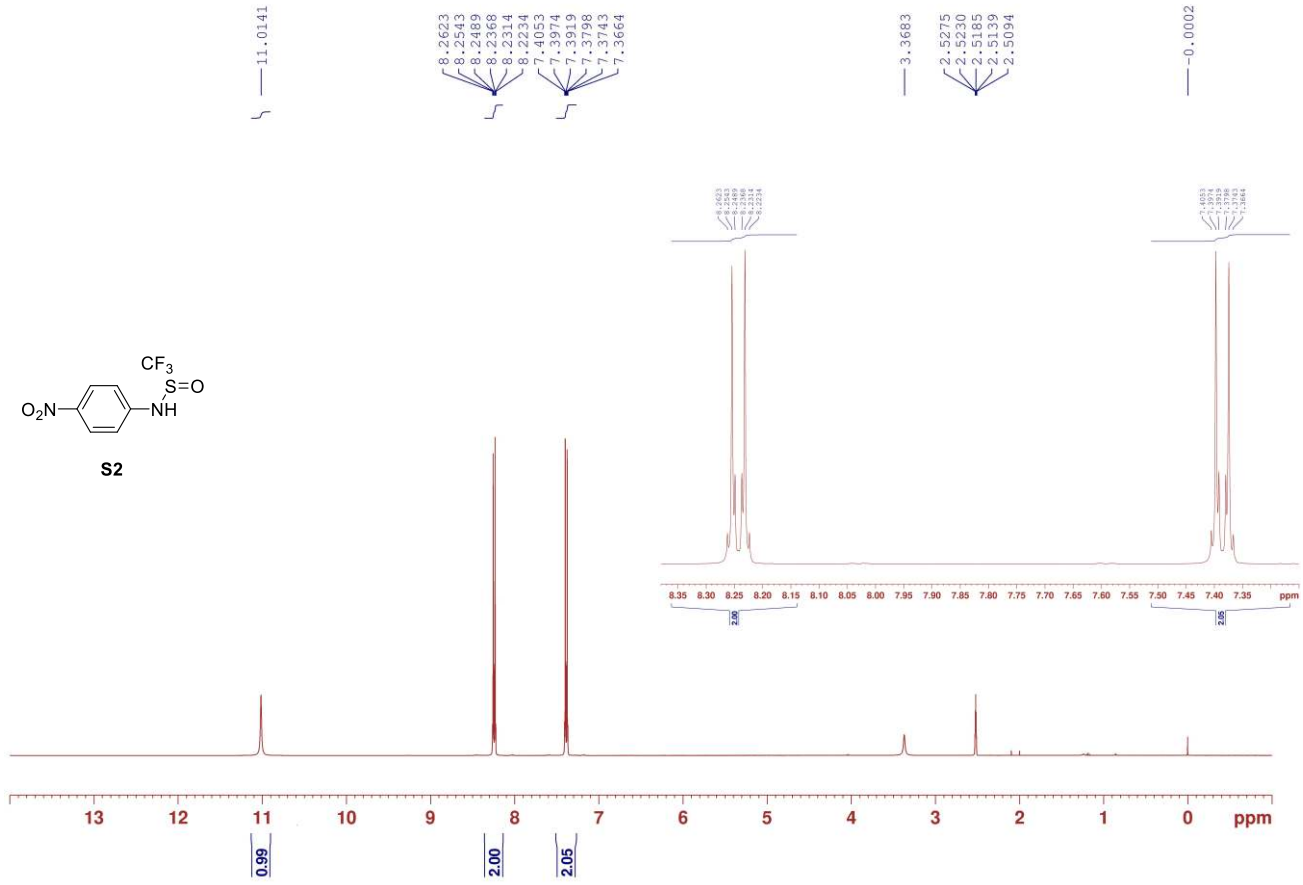


^{19}FNMR spectrum of **S1**



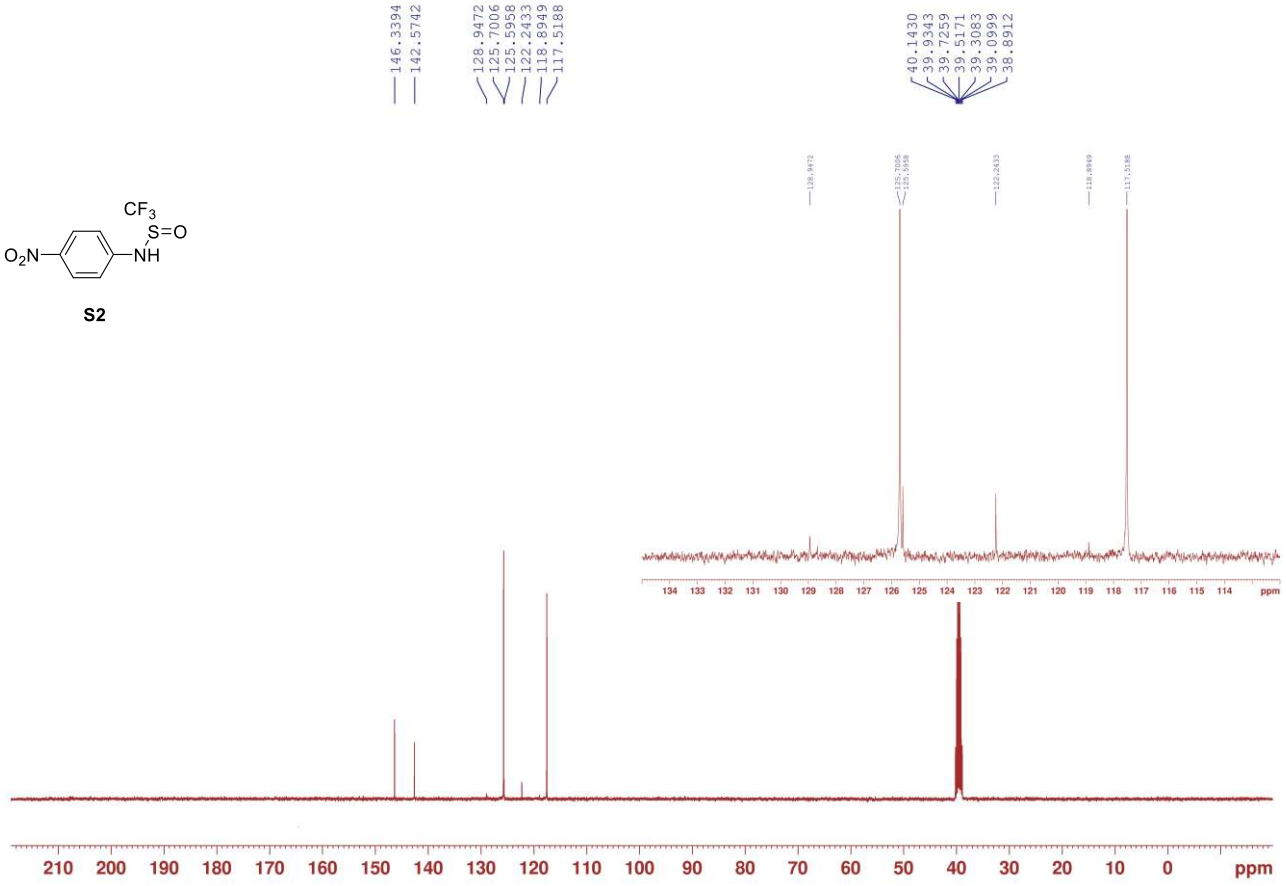
S1

^{1}HNMR spectrum of **S2** (DMSO-*d6*)

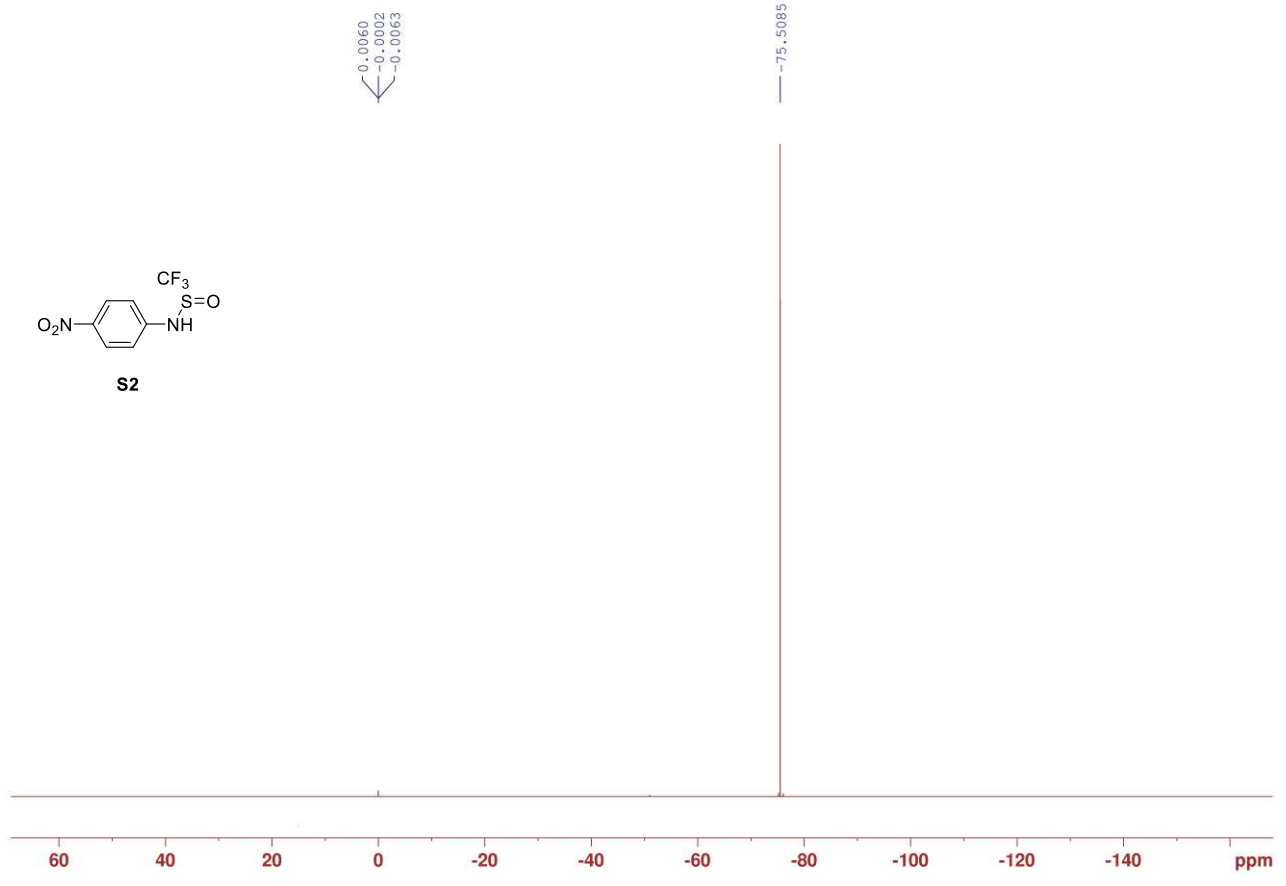


S2

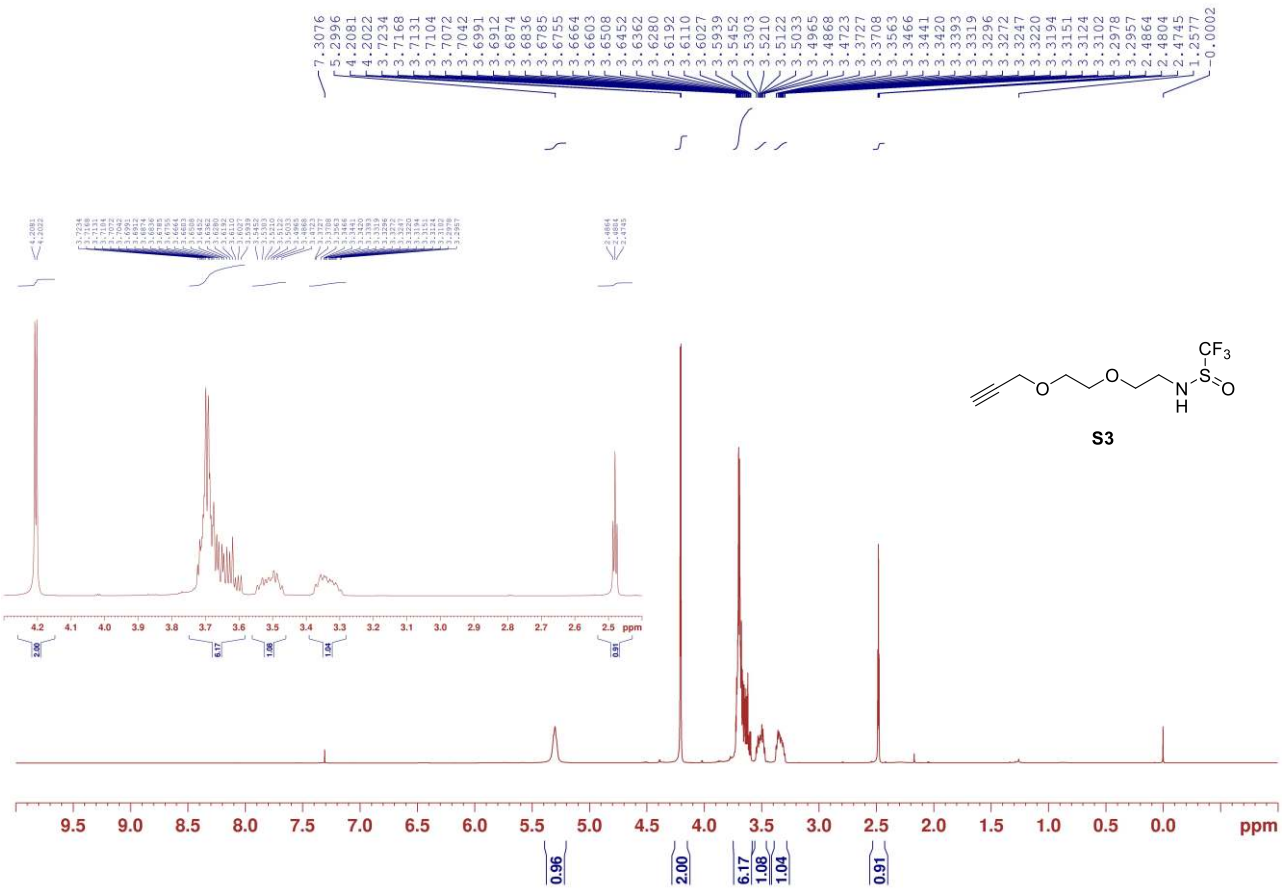
^{13}CNMR spectrum of **S2** (DMSO-*d6*)



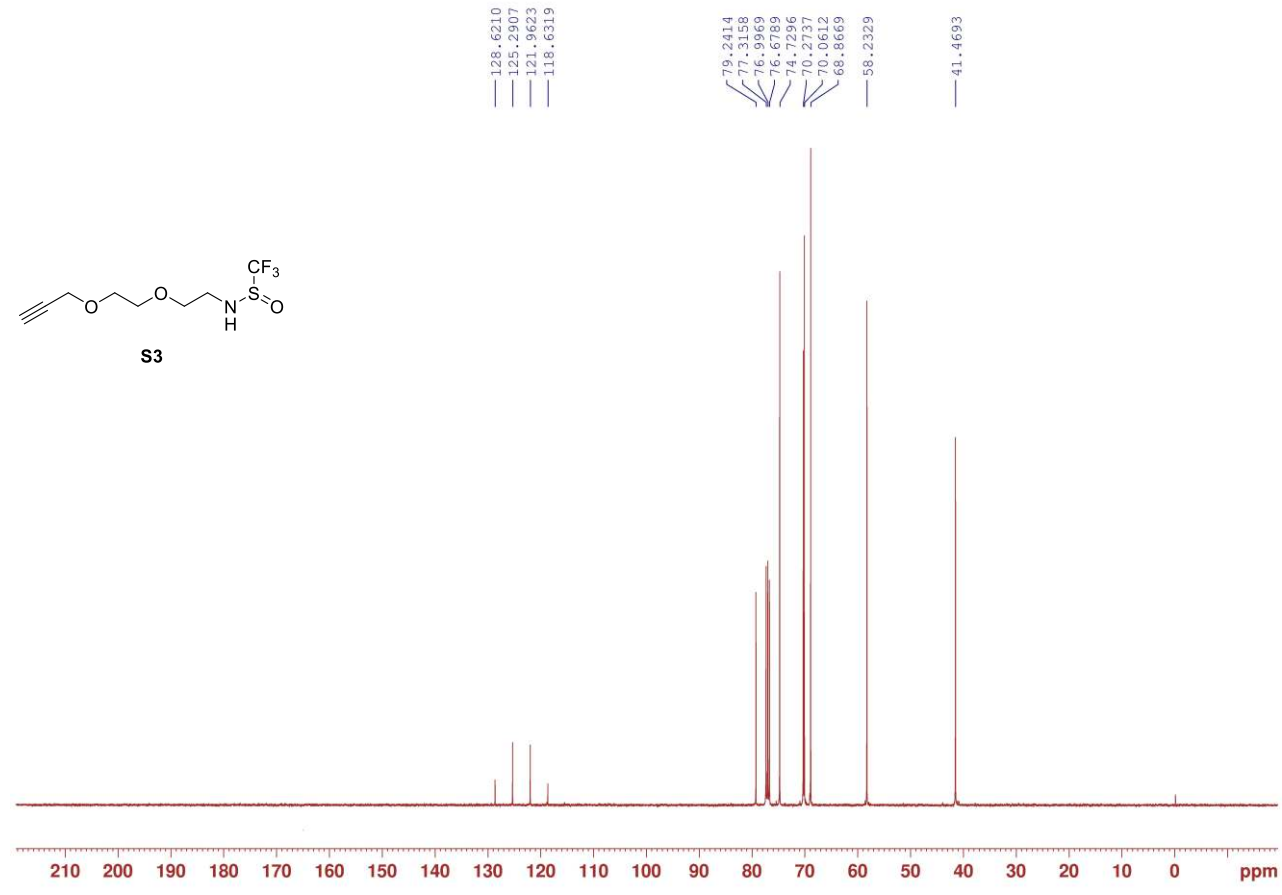
^{19}FNMR spectrum of **S2** (DMSO-*d6*)



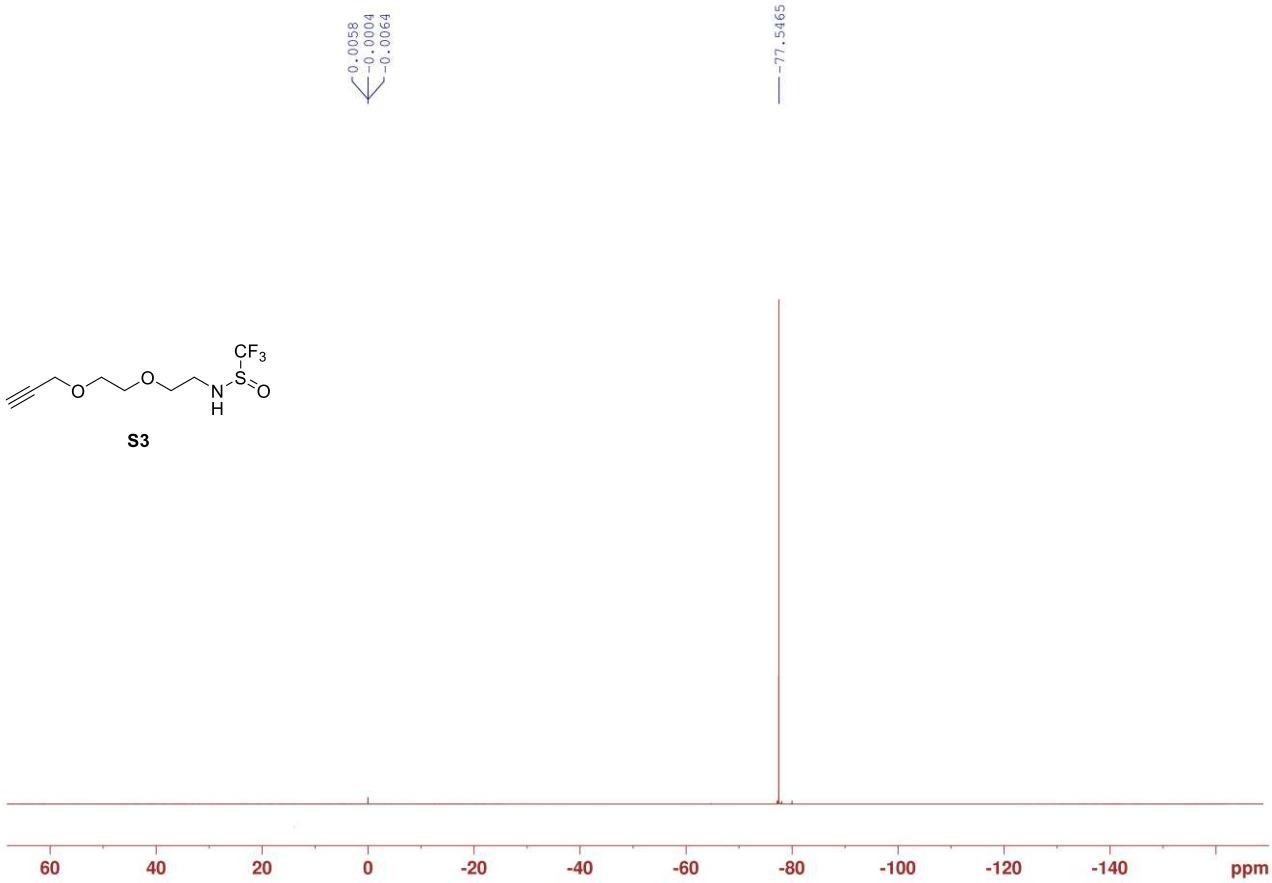
[1]HNMR spectrum of **S3**



[13]CNMR spectrum of **S3**

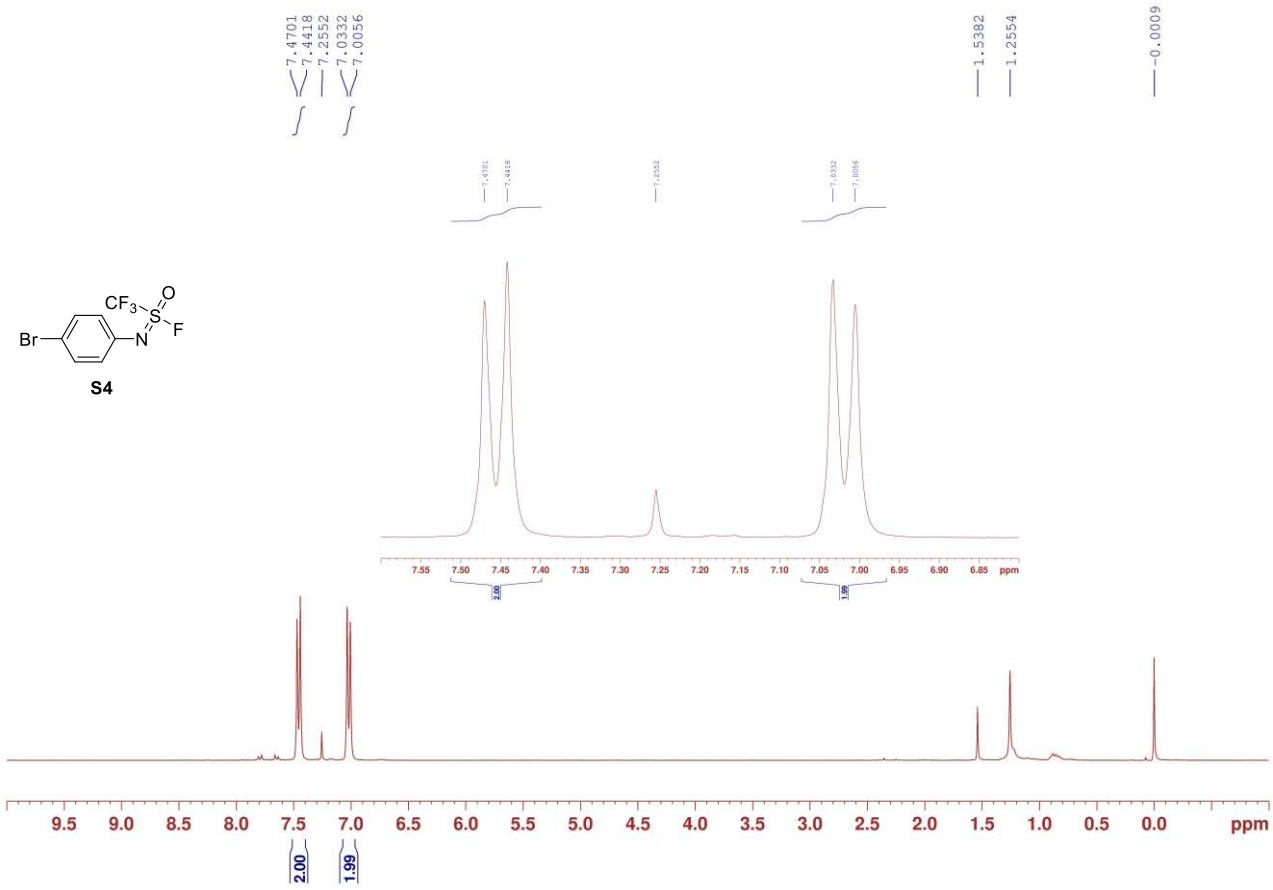


^{19}FNMR spectrum of **S3**



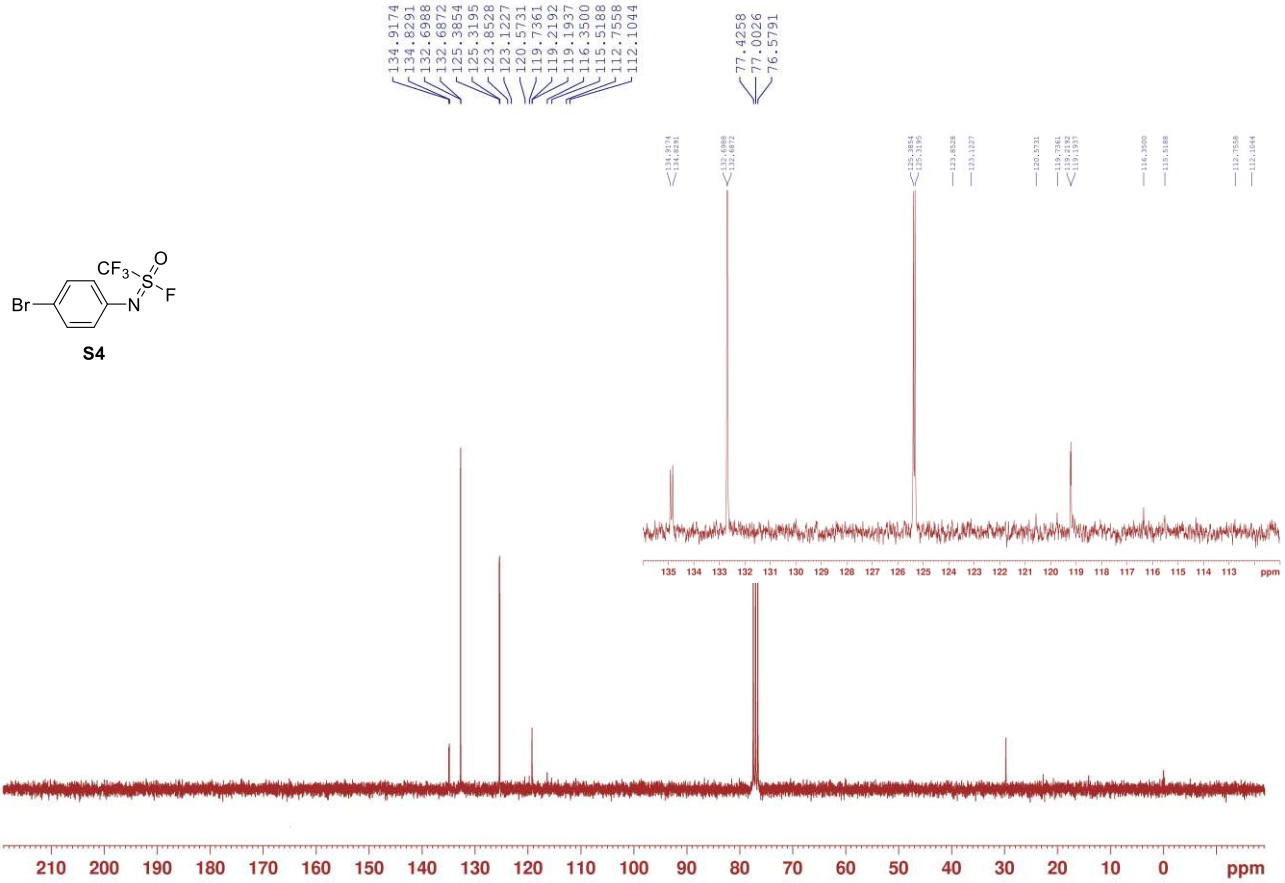
S3

^{1}HNMR spectrum of **S4**

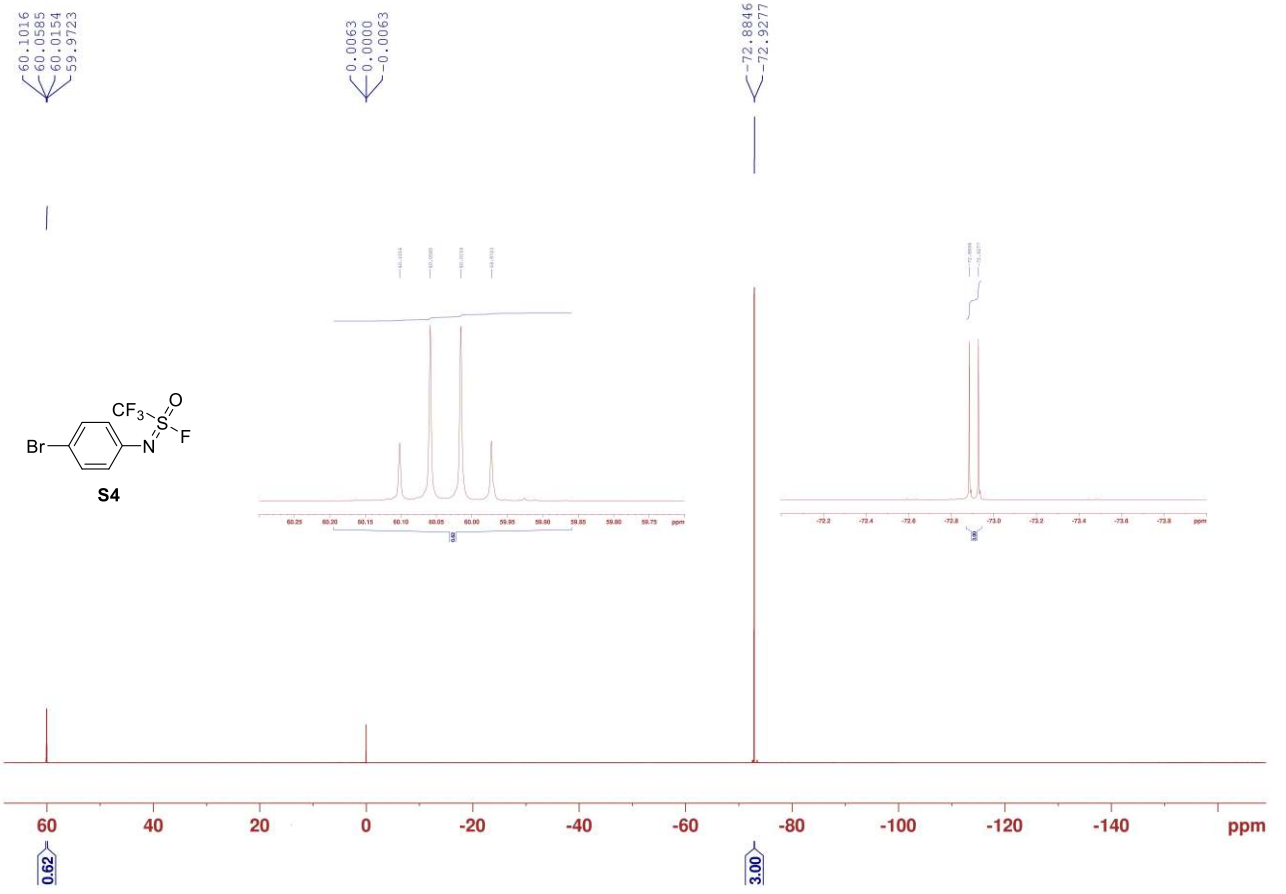


S4

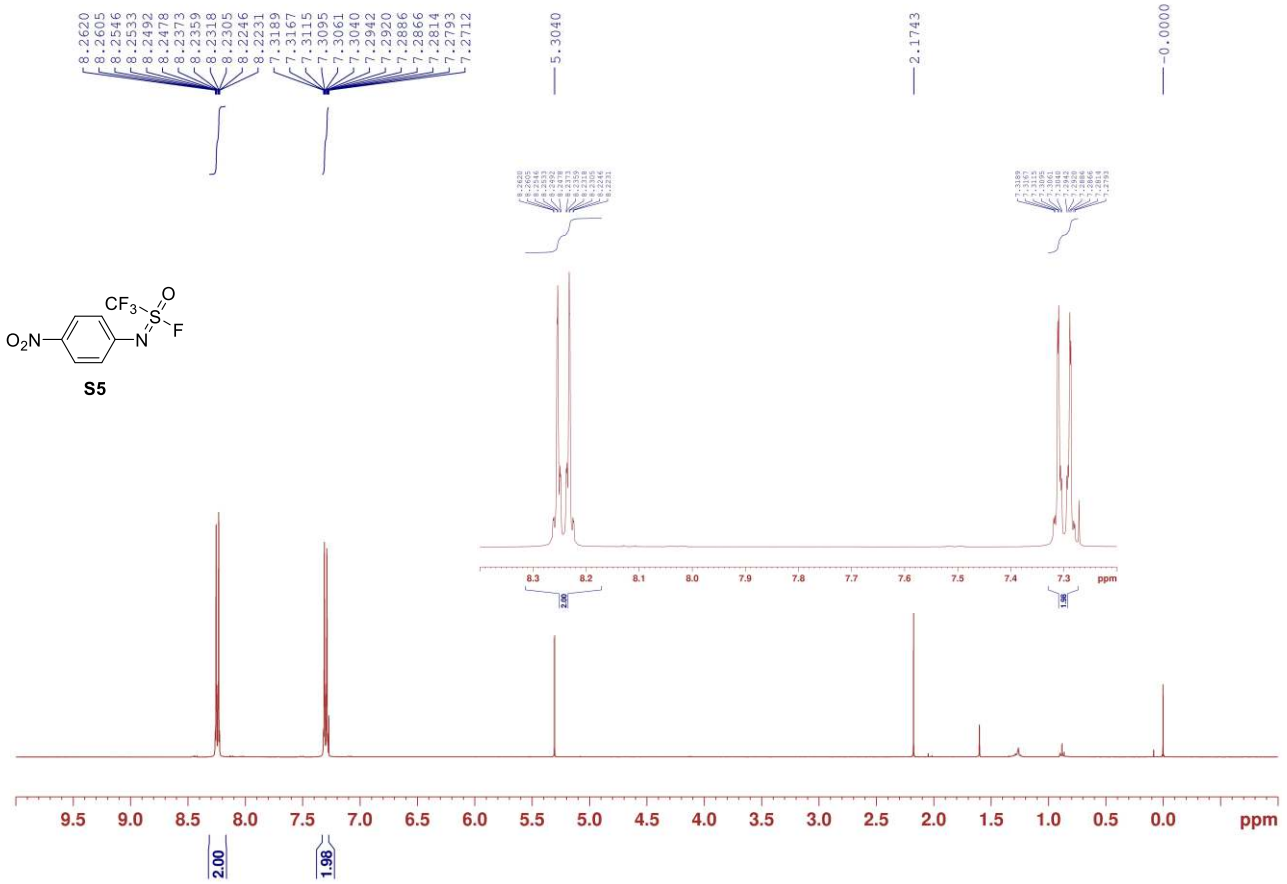
^{13}CNMR spectrum of **S4**



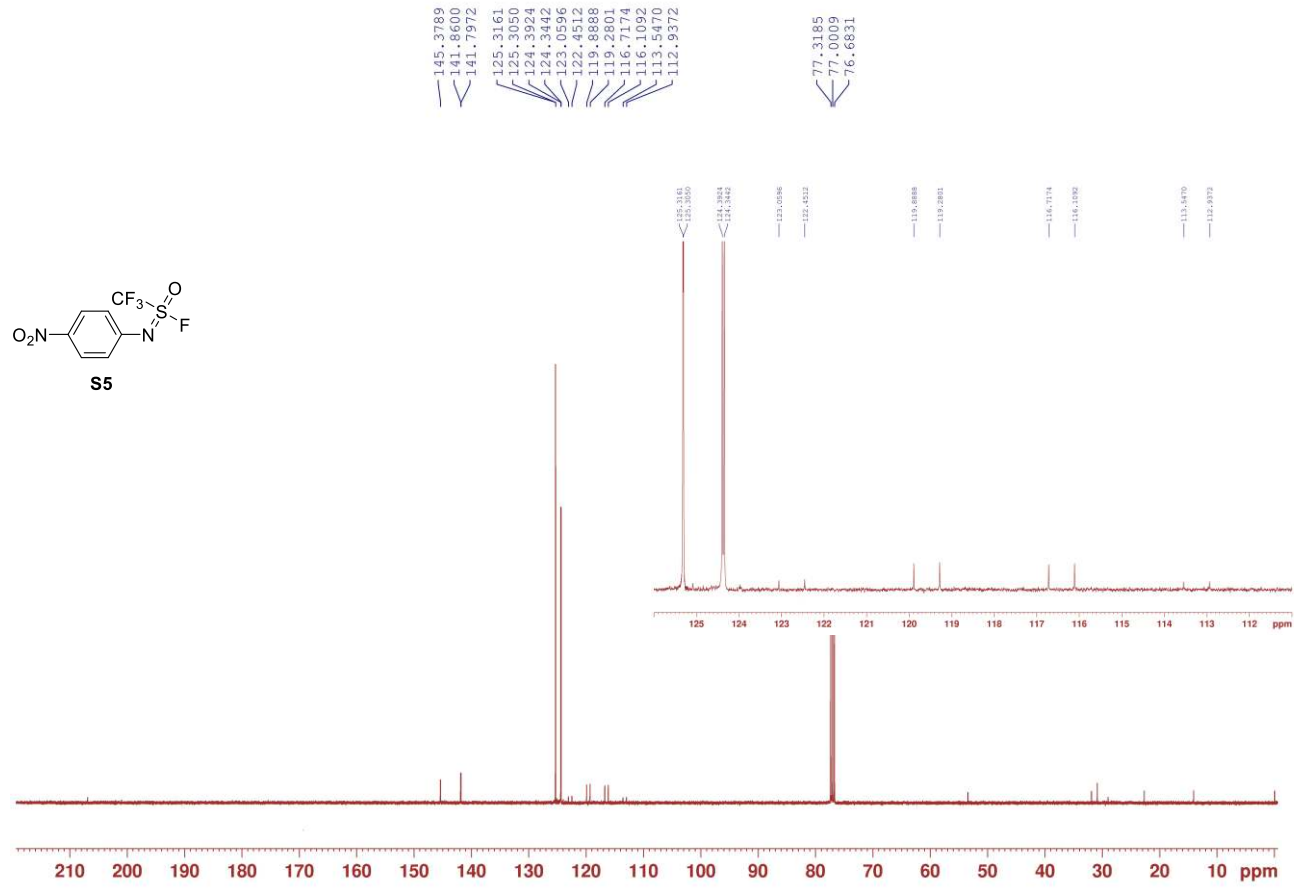
^{19}FNMR spectrum of **S4**



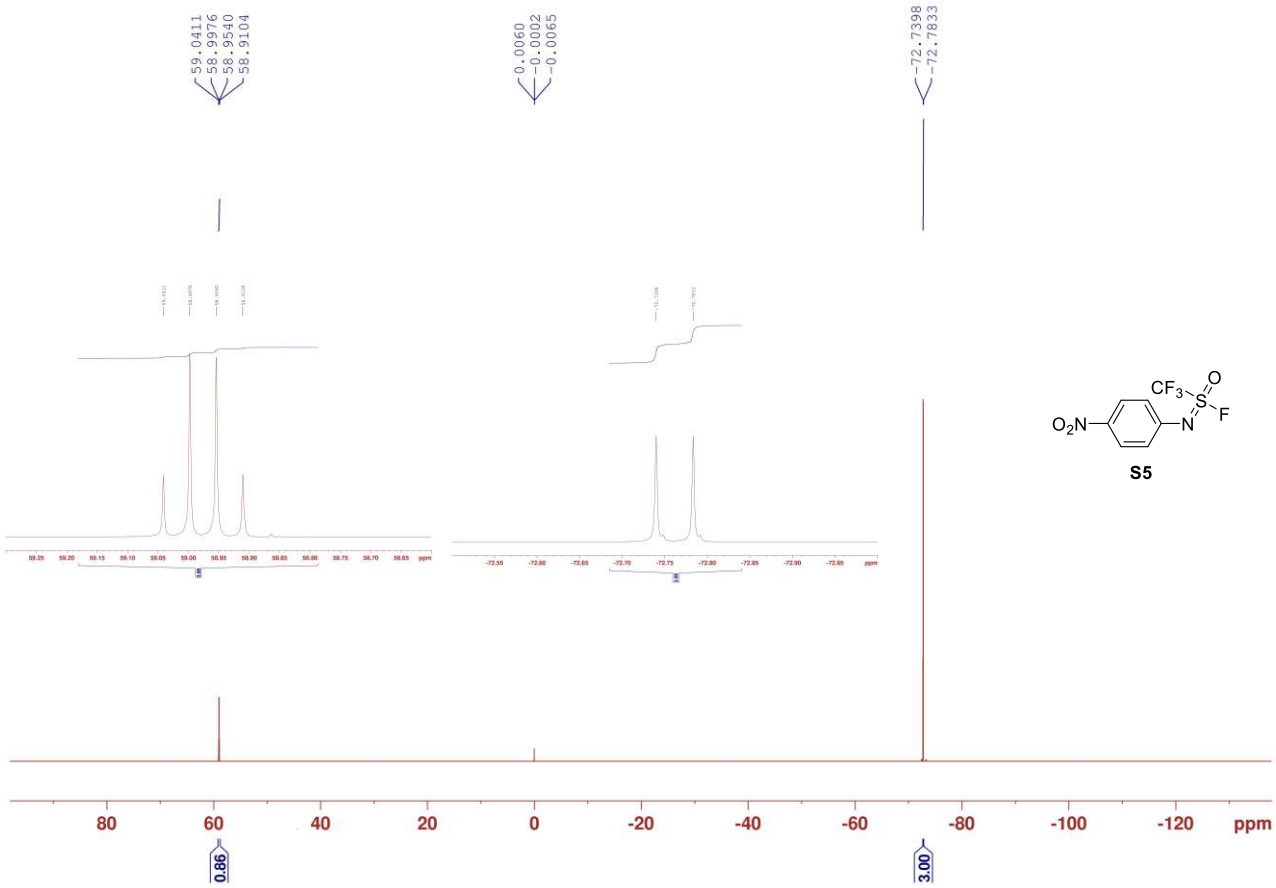
^{1}HNMR spectrum of **S5**



^{13}CNMR spectrum of **S5**

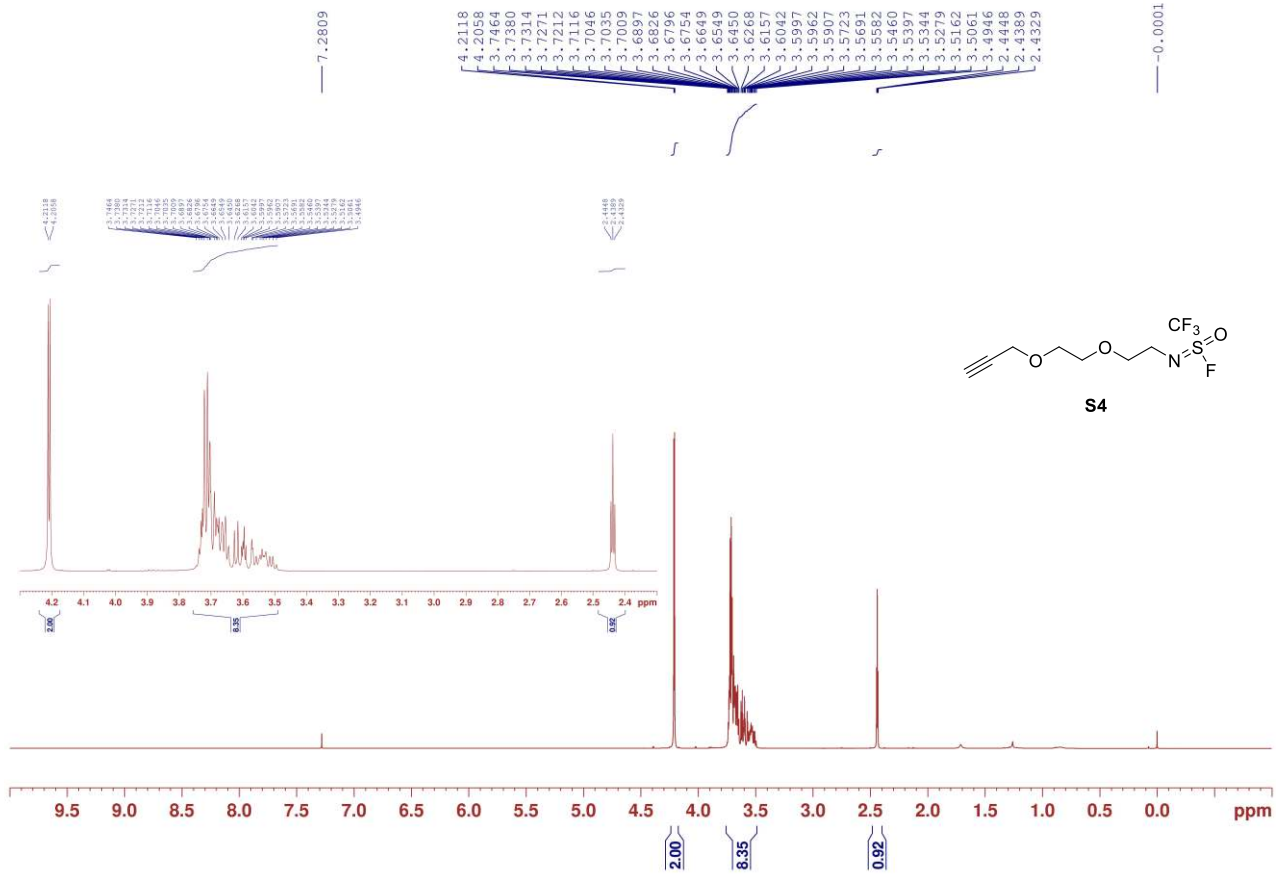


^{19}FNMR spectrum of **S5**



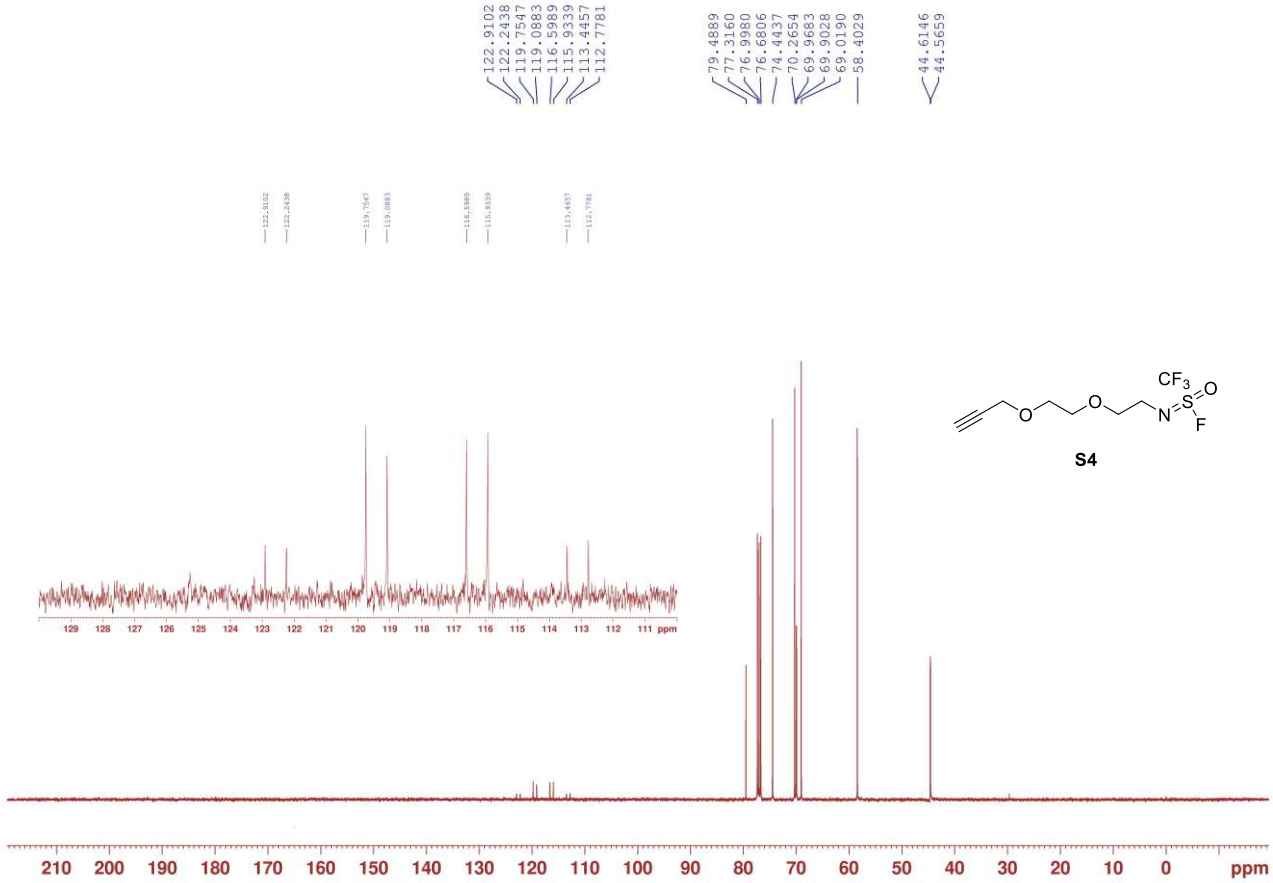
S5

^{1}HNMR spectrum of **S6**

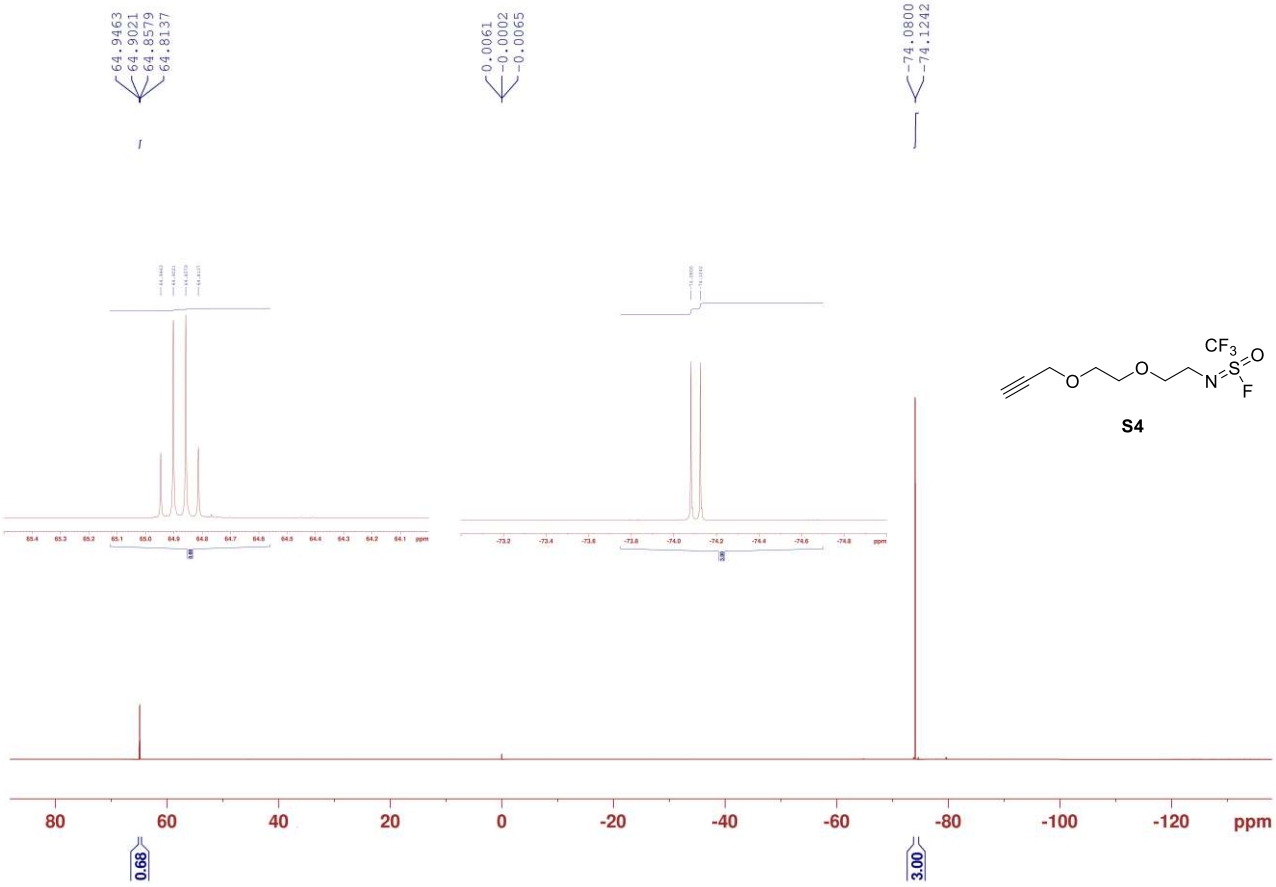


S4

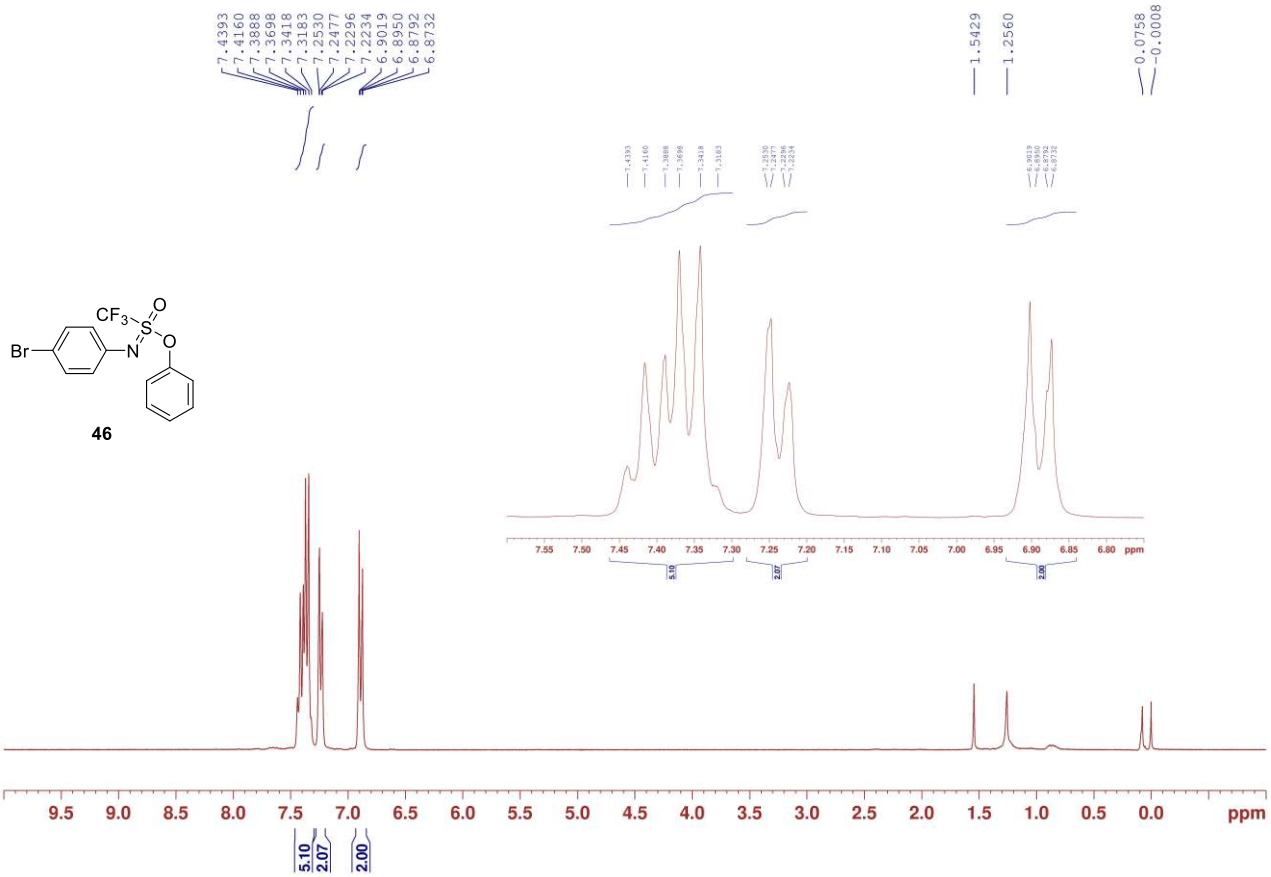
^{13}CNMR spectrum of **S6**



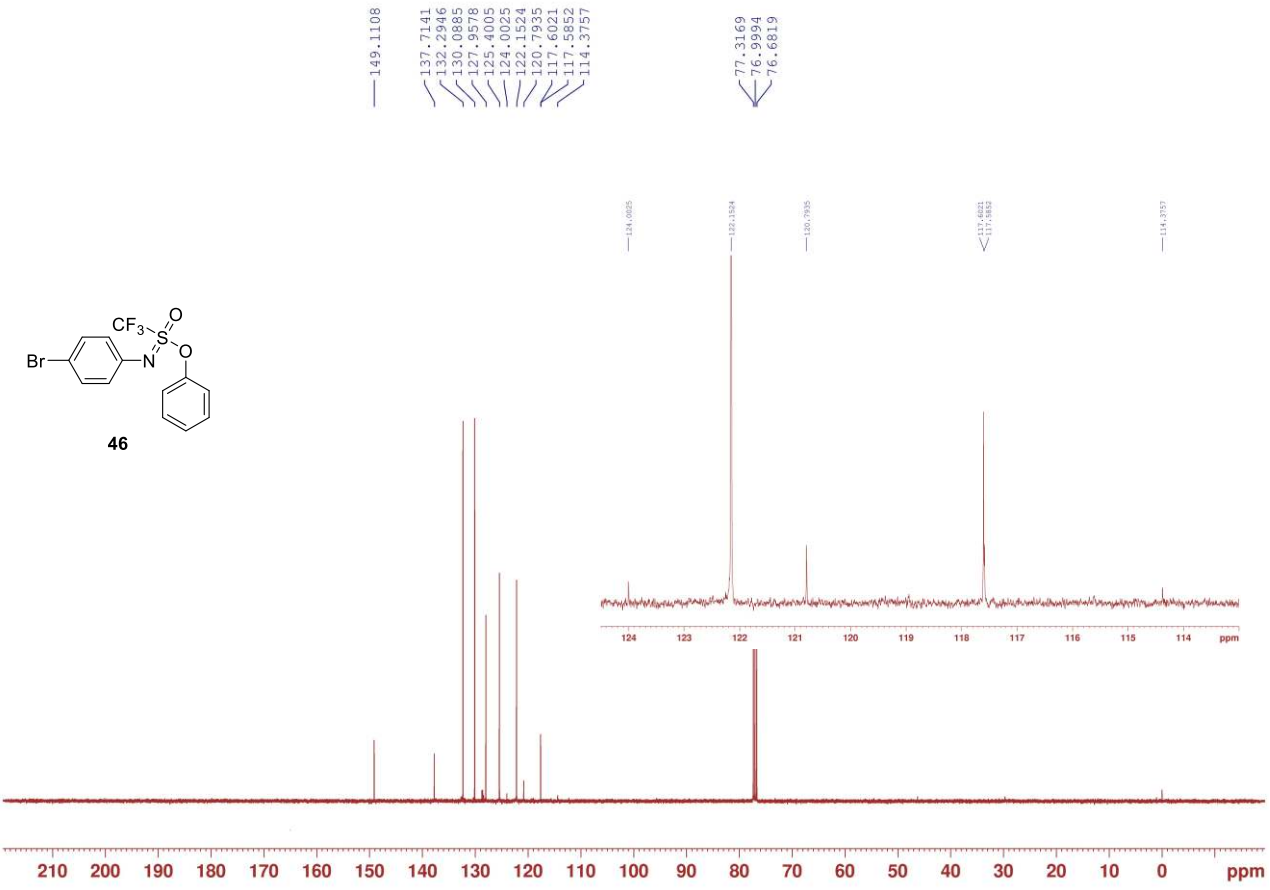
^{19}FNMR spectrum of **S6**



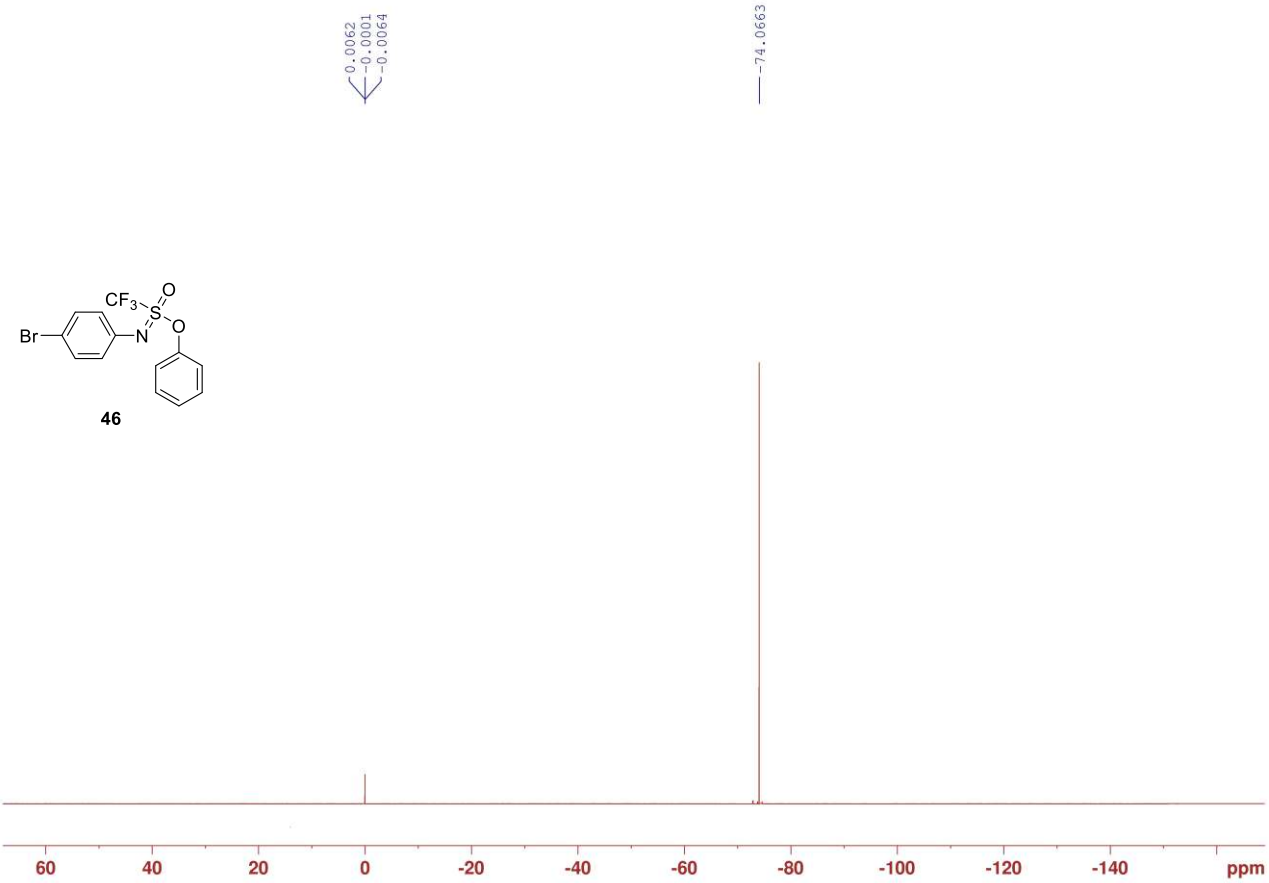
^{1}HNMR spectrum of **46**



^{13}CNMR spectrum of **46**

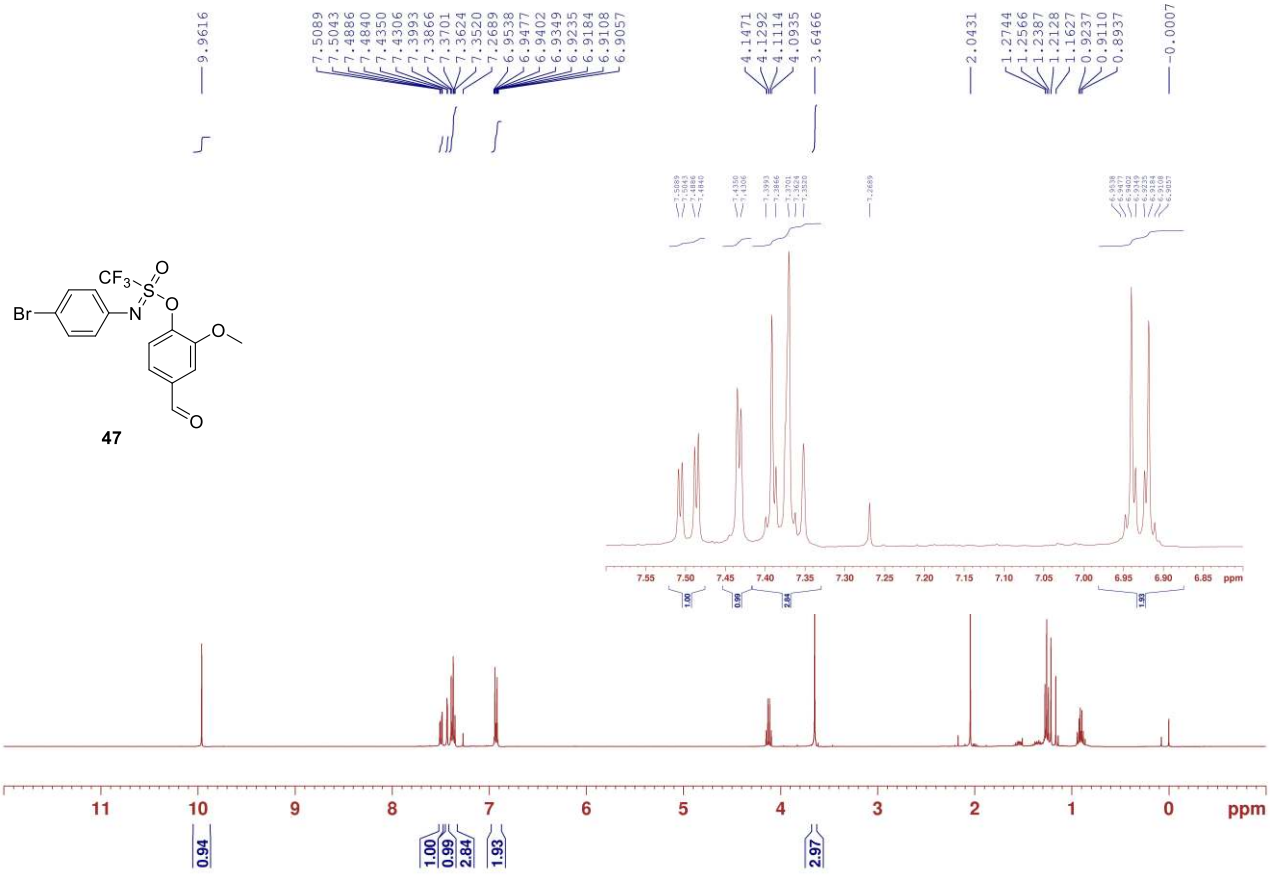


^{19}FNMR spectrum of **46**



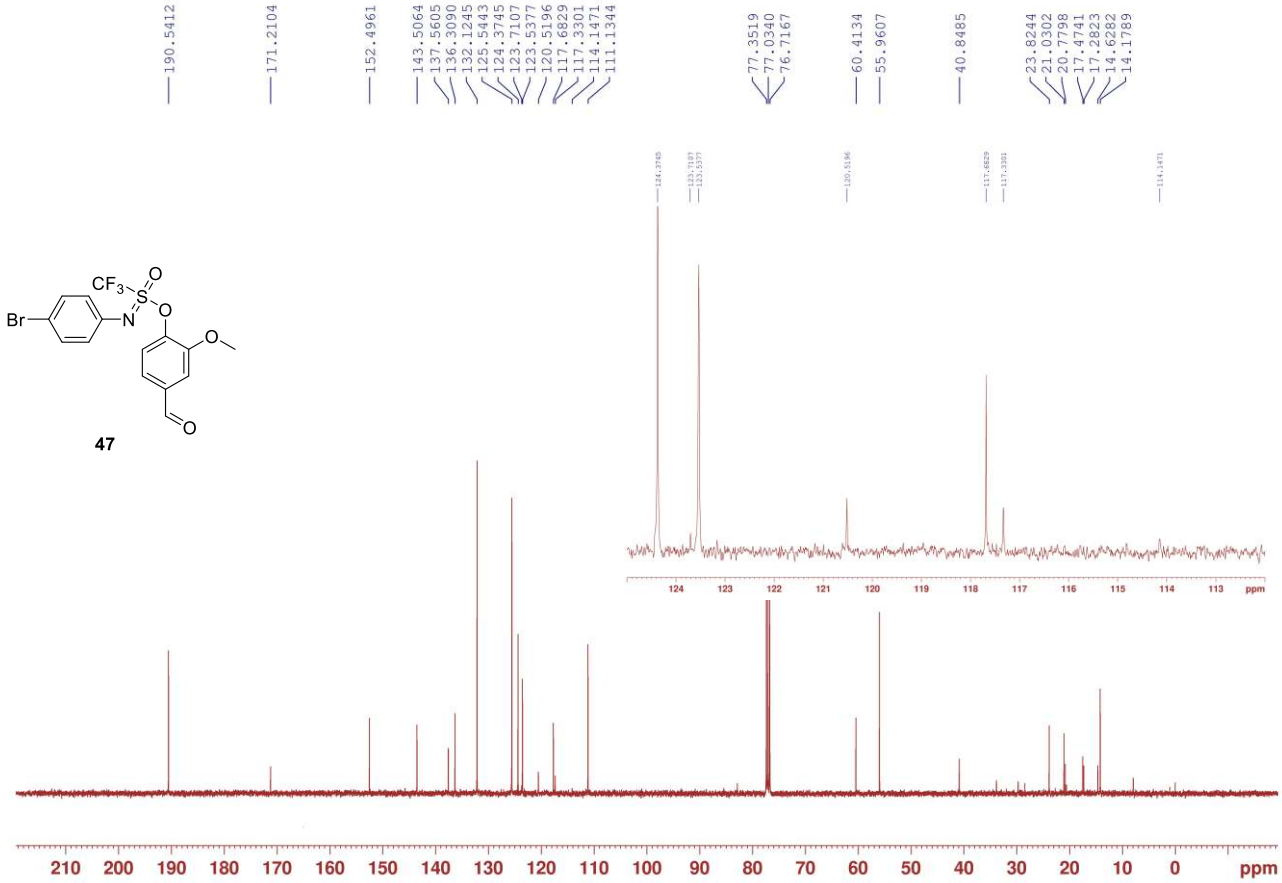
46

^{1}HNMR spectrum of **47**



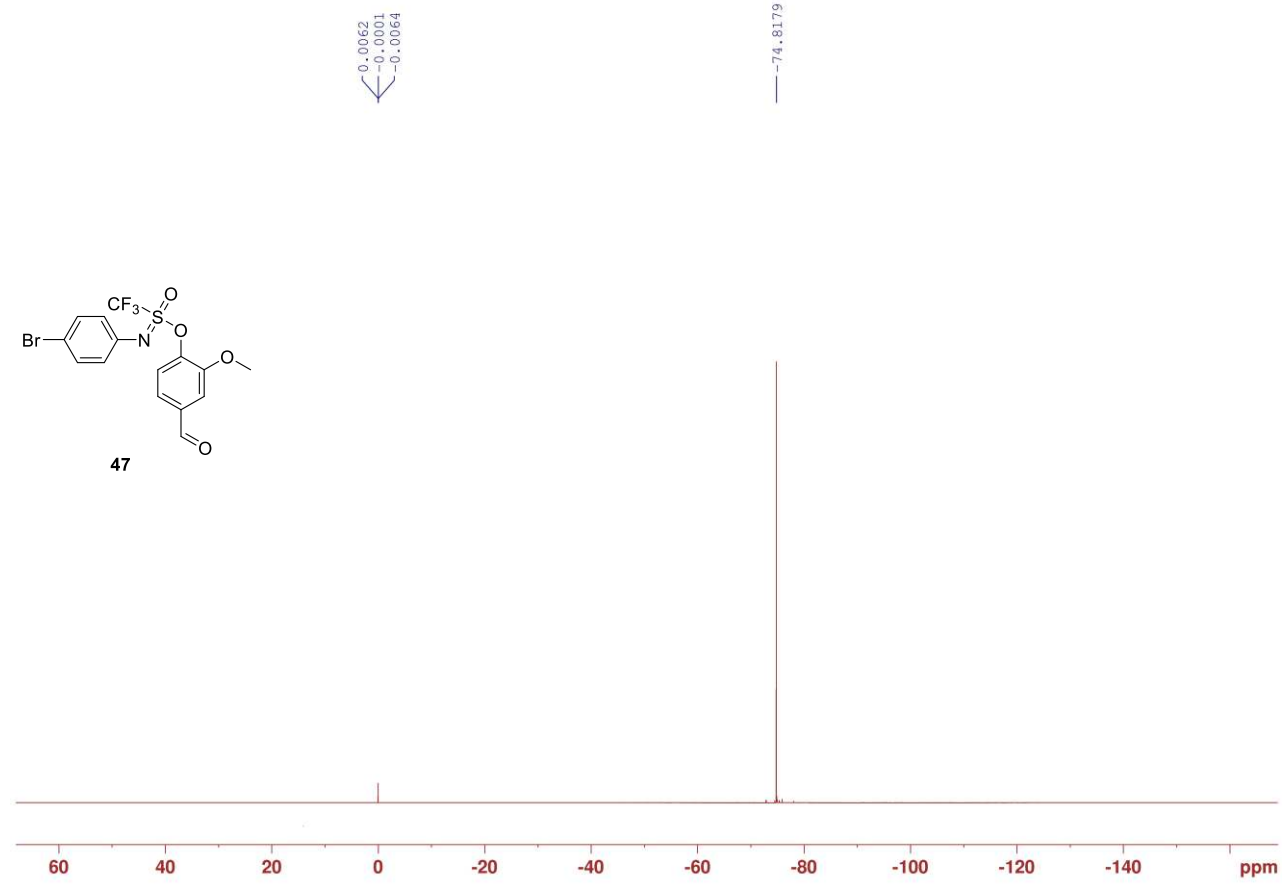
47

^{13}CNMR spectrum of **47**



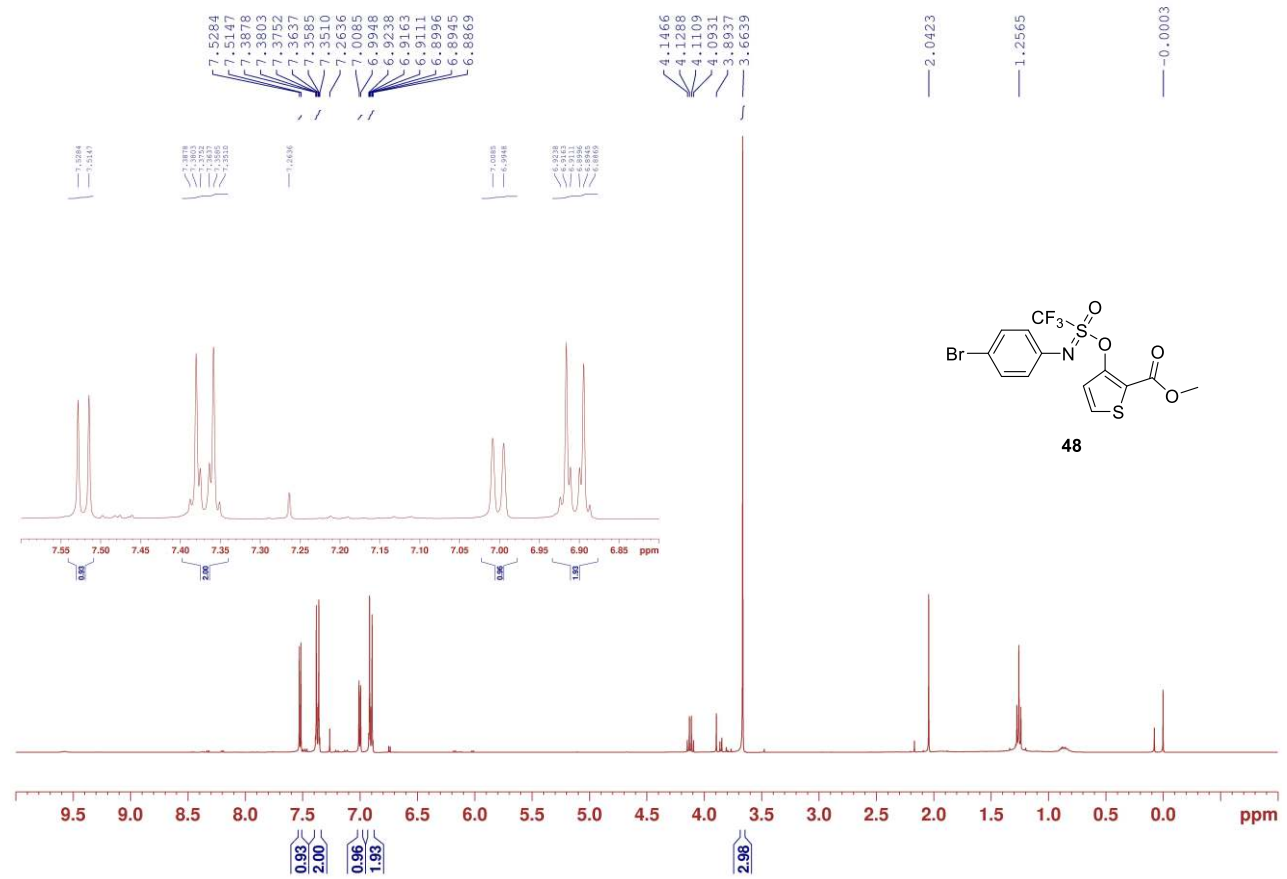
47

^{19}FNMR spectrum of **47**



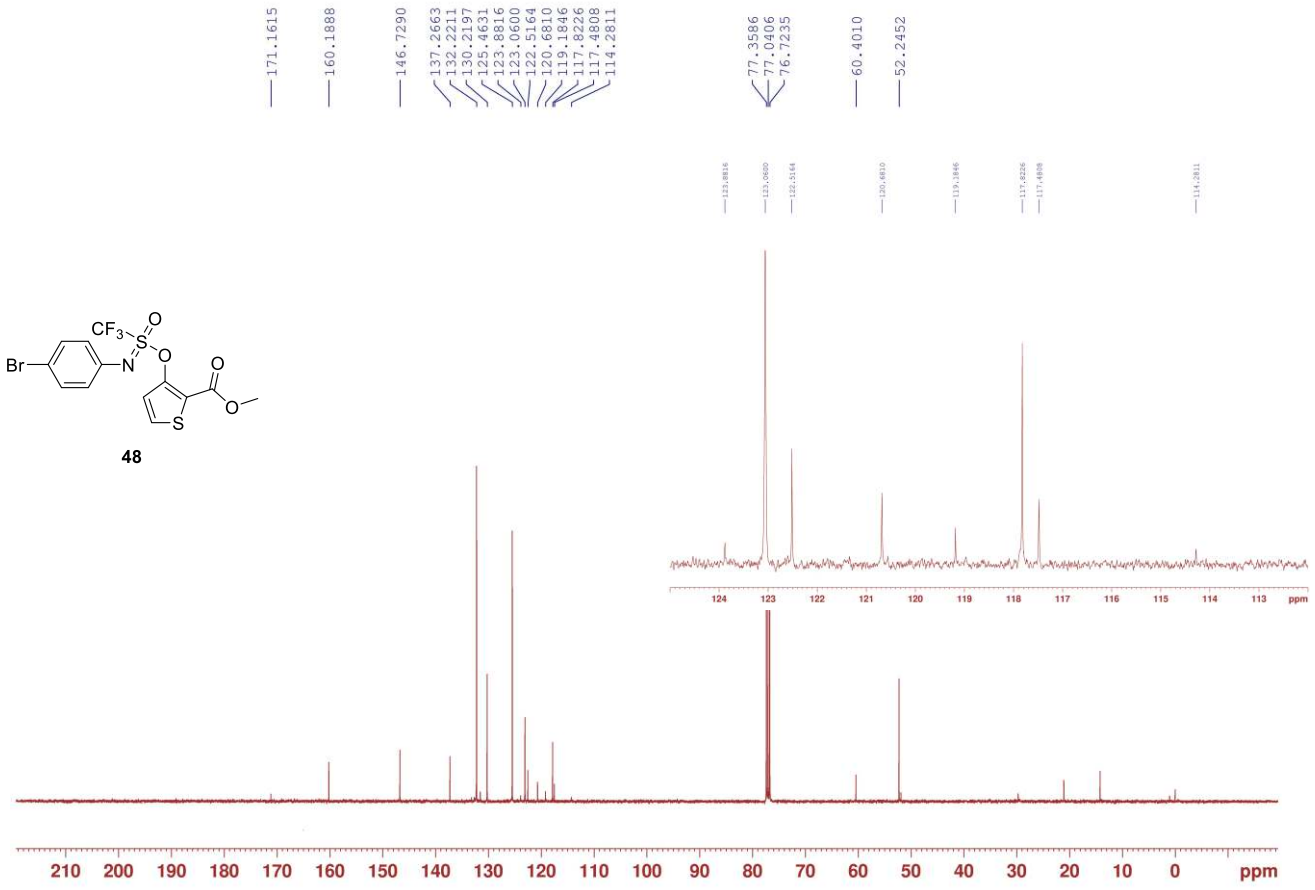
47

^{1}HNMR spectrum of **48**



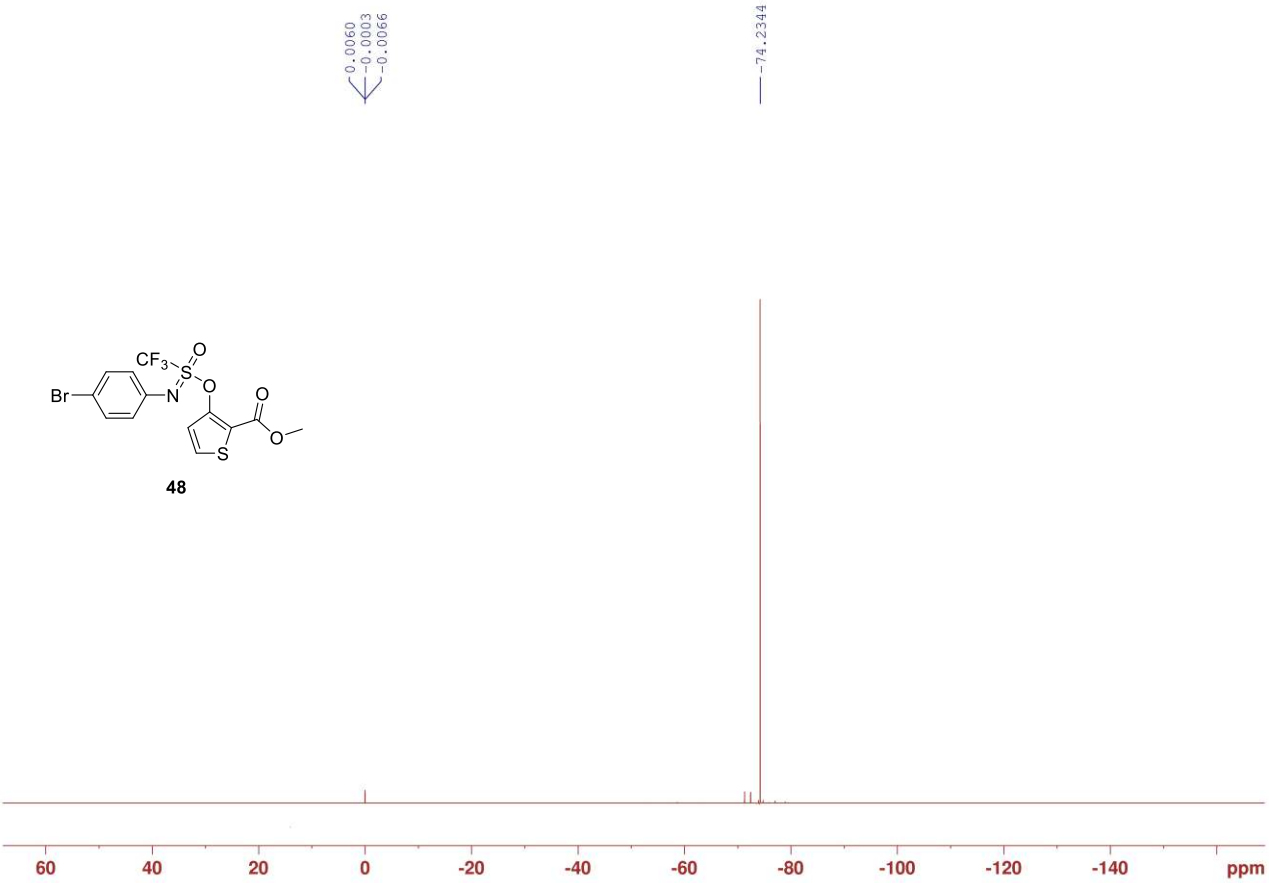
48

^{13}CNMR spectrum of **48**



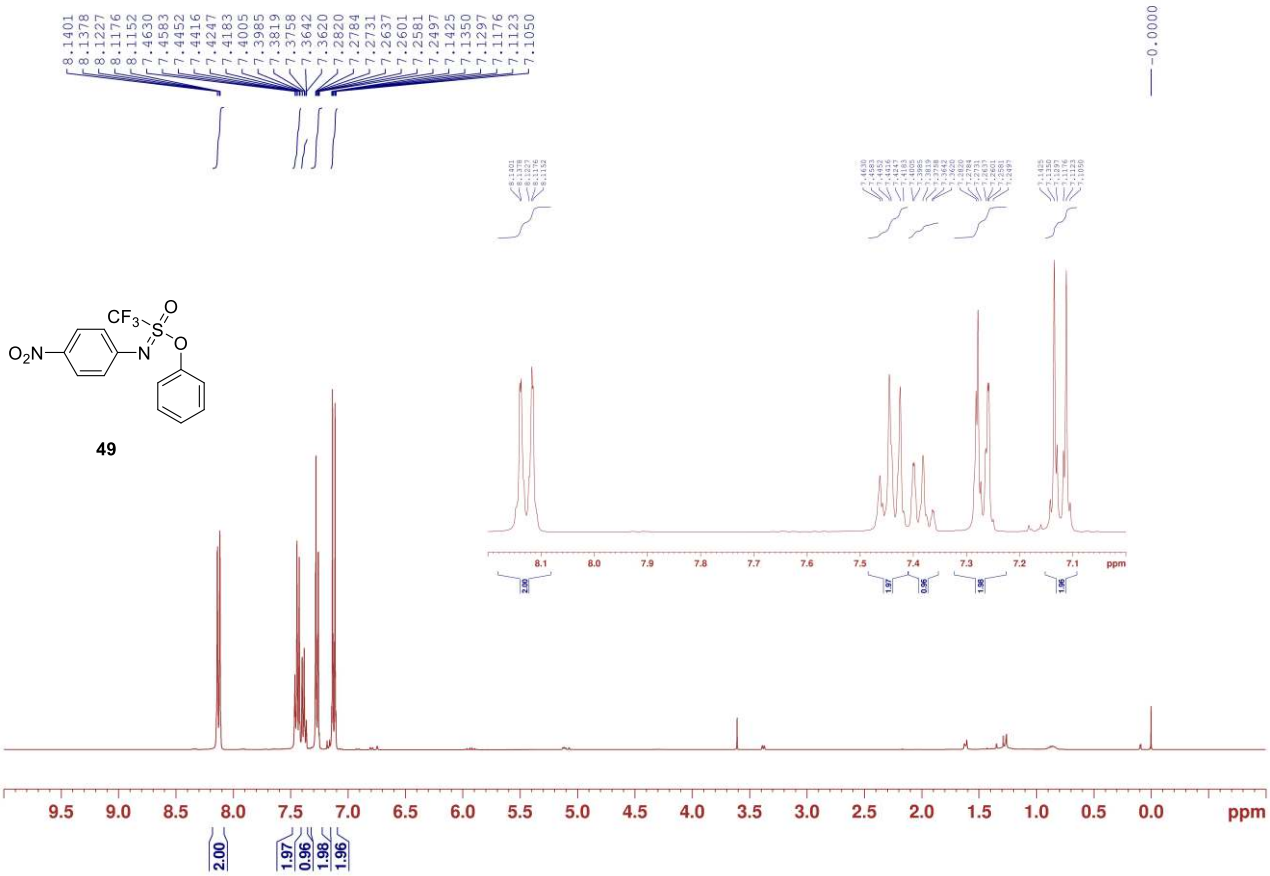
48

^{19}FNMR spectrum of **48**



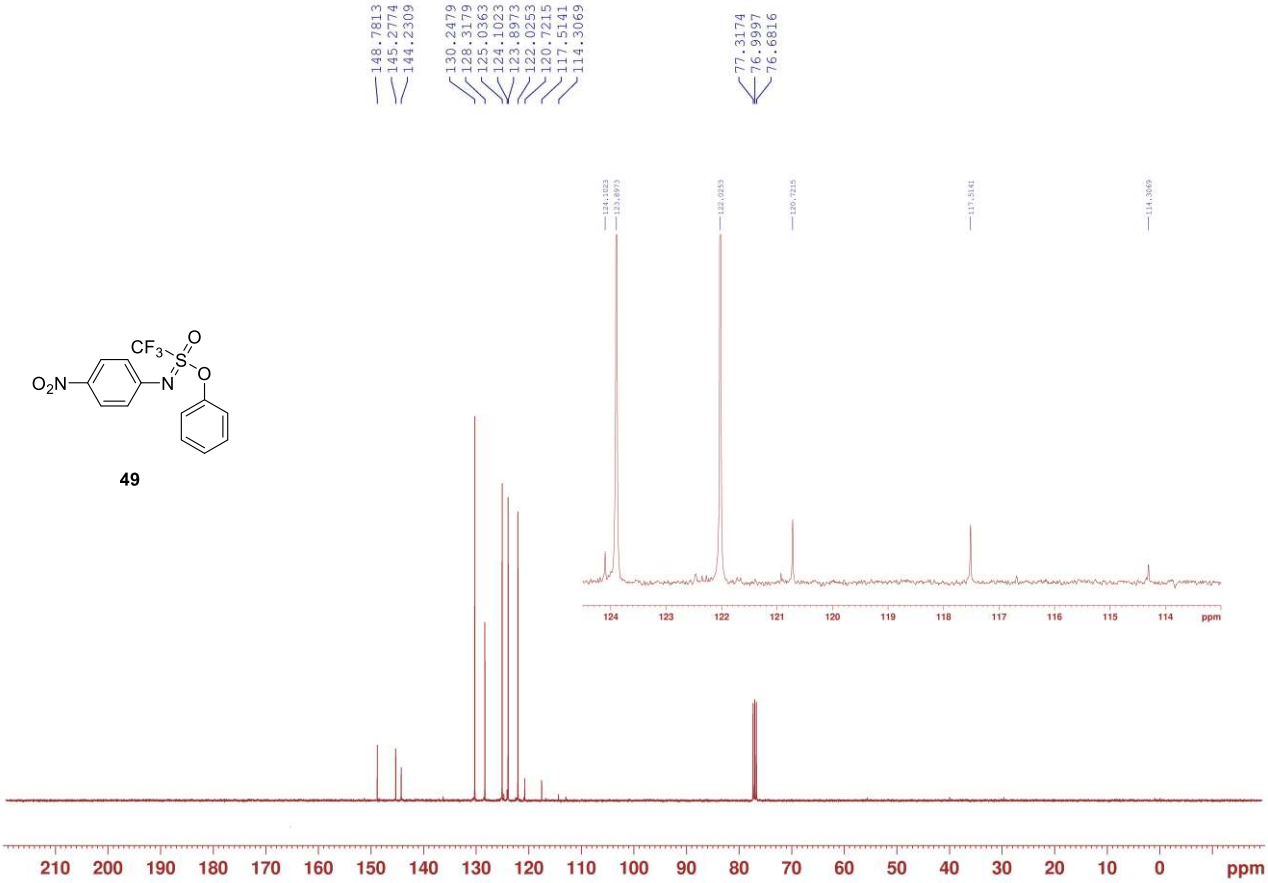
48

^{1}HNMR spectrum of **49**



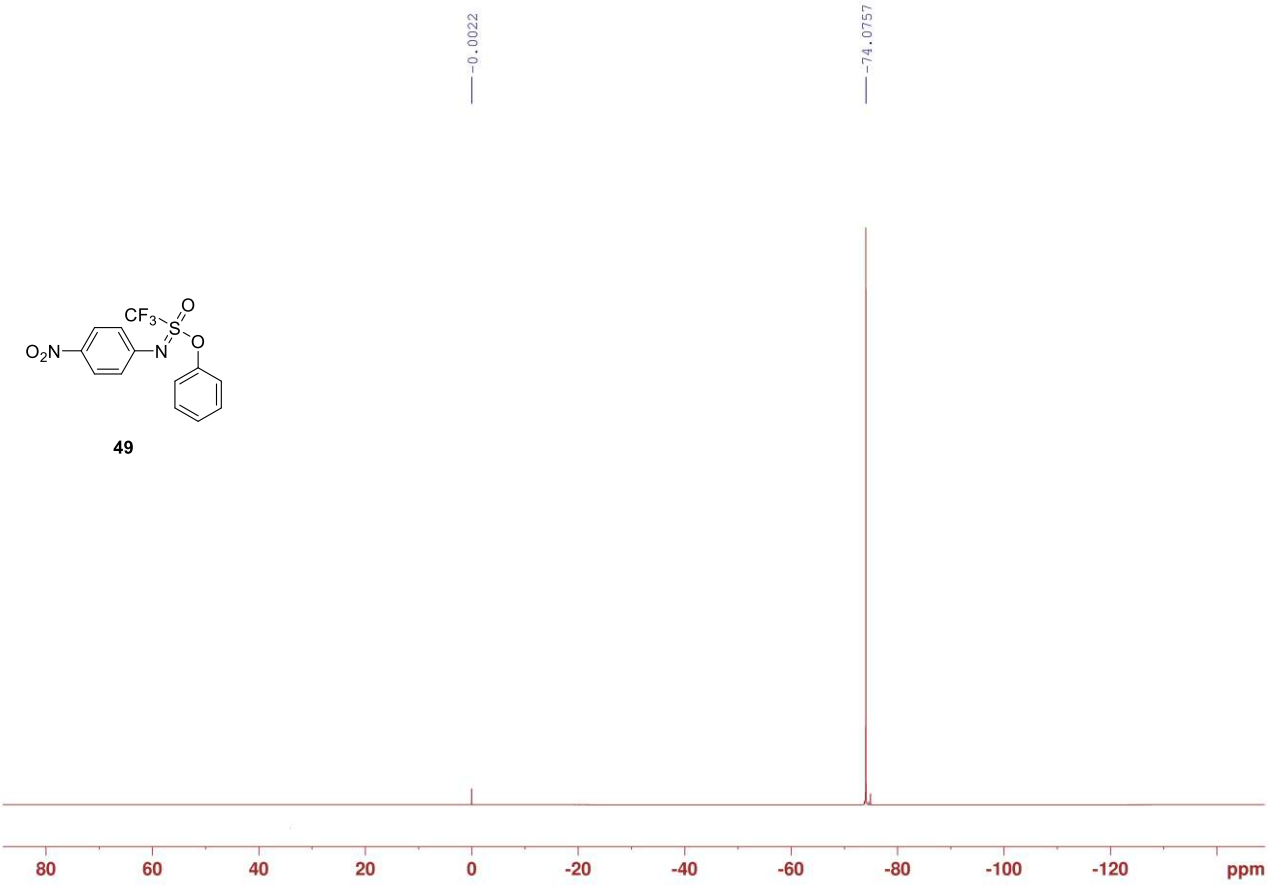
49

^{13}CNMR spectrum of **49**



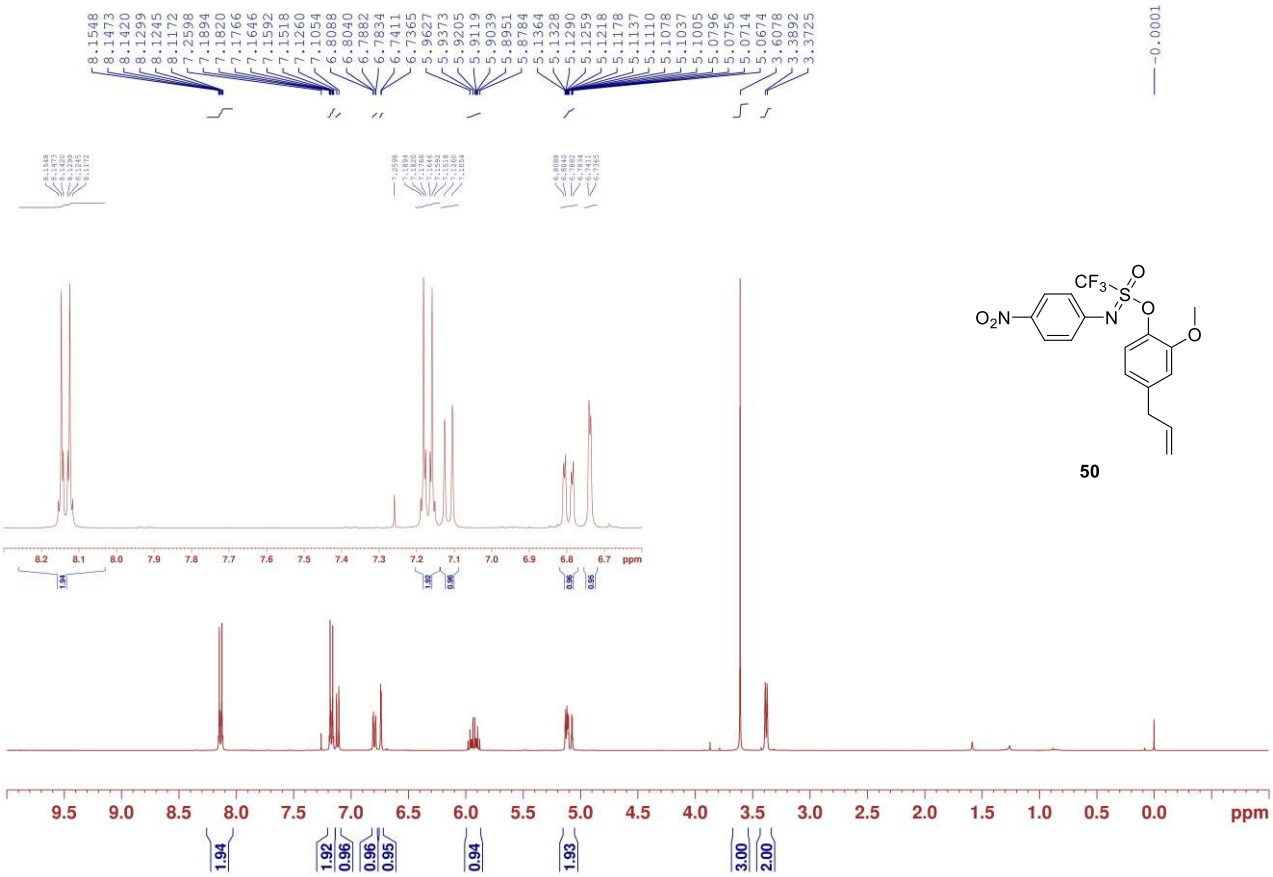
49

^{19}FNMR spectrum of **49**



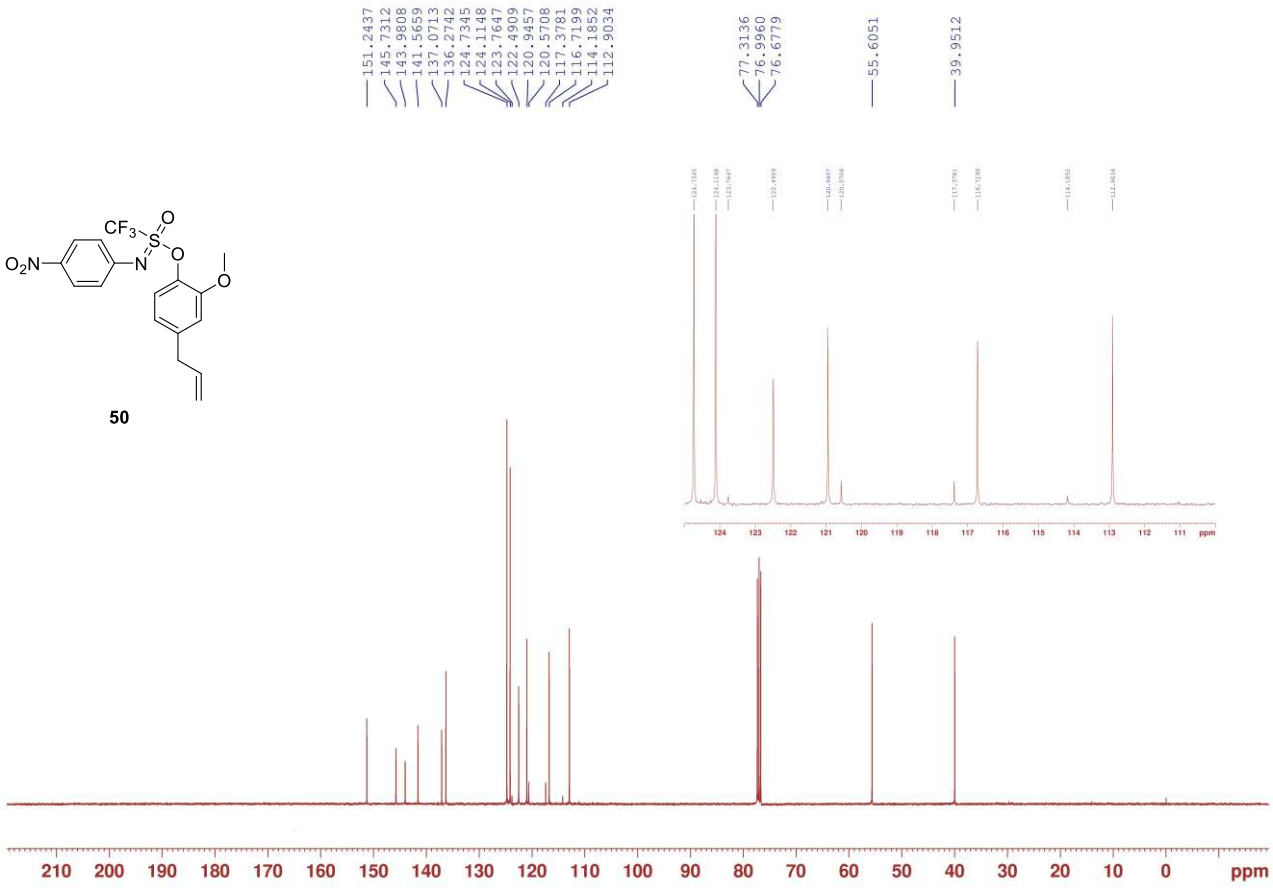
49

^{1}HNMR spectrum of **50**



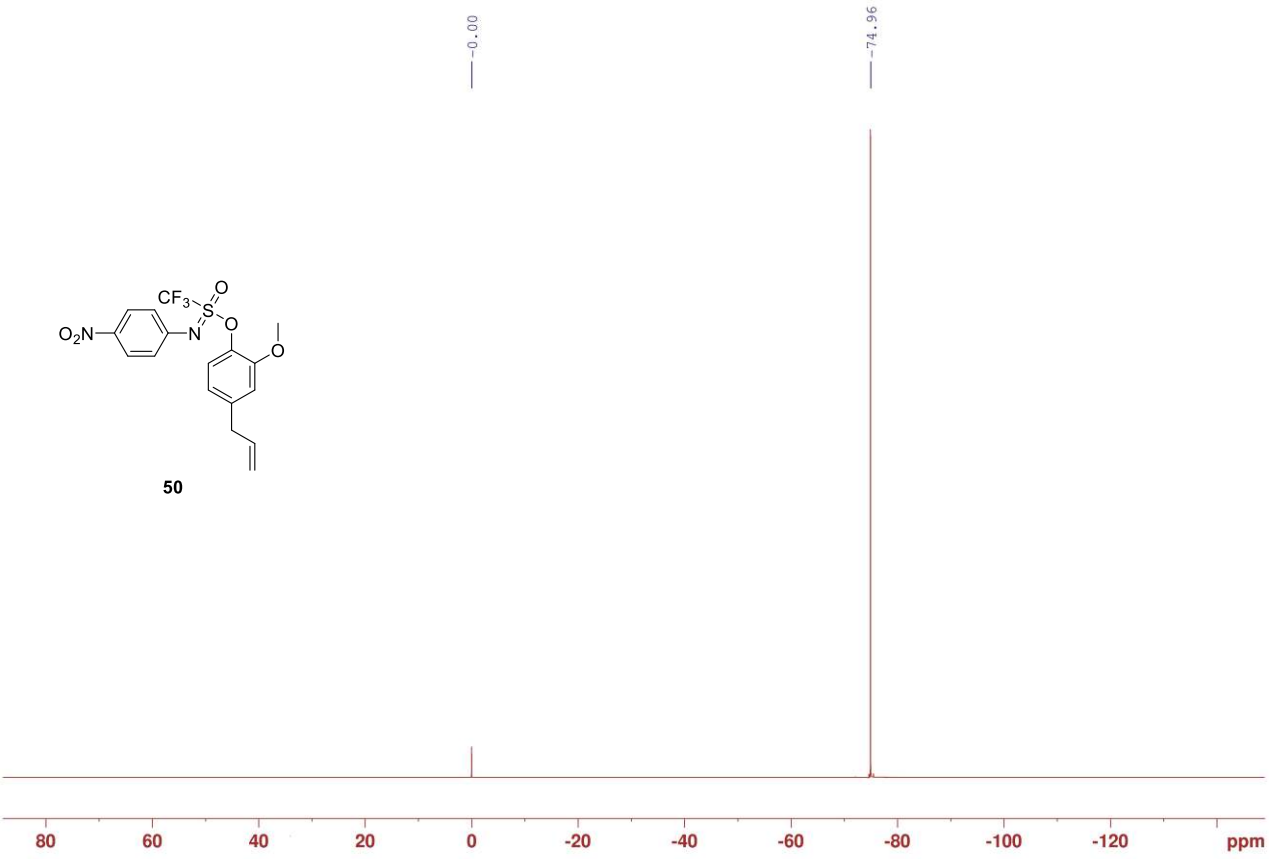
50

^{13}CNMR spectrum of **50**



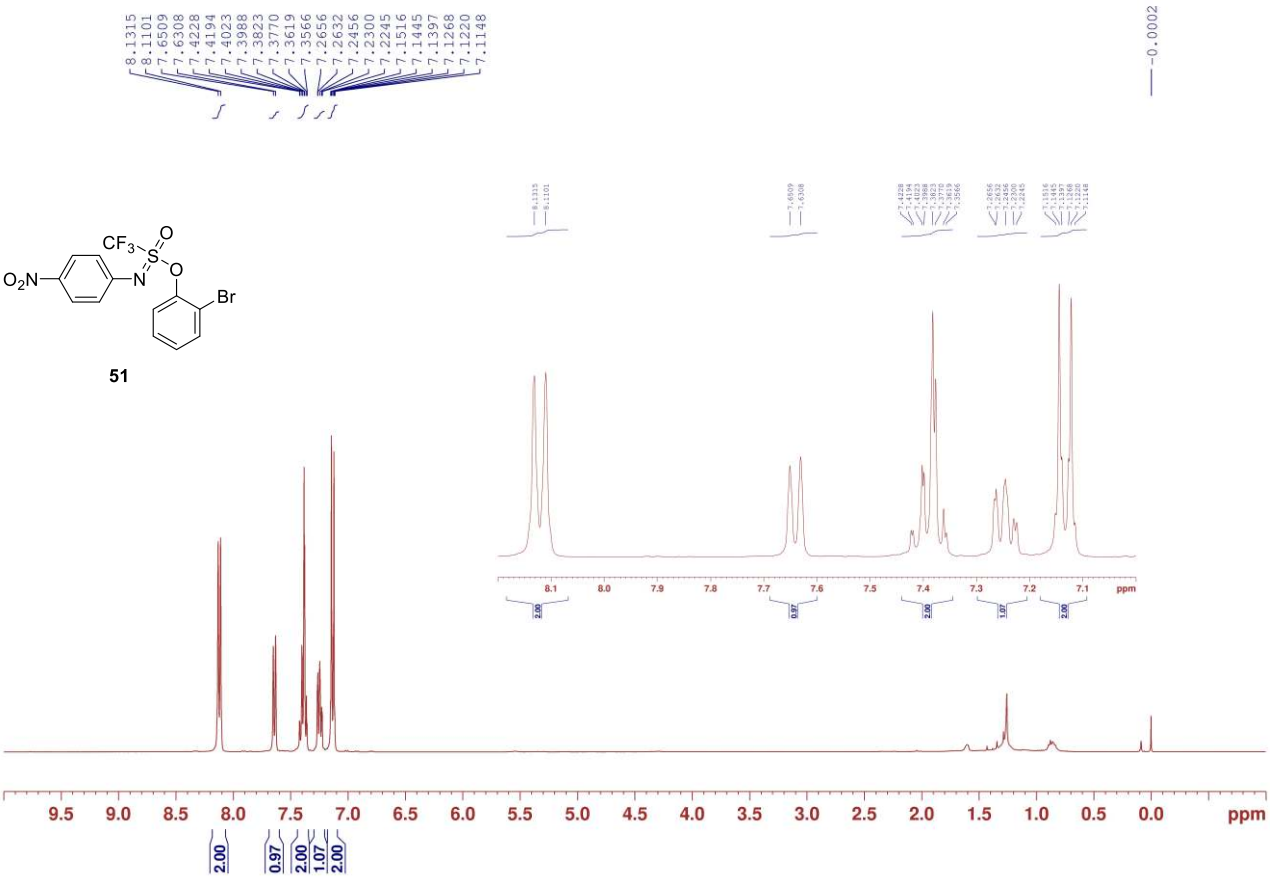
50

^{19}FNMR spectrum of **50**



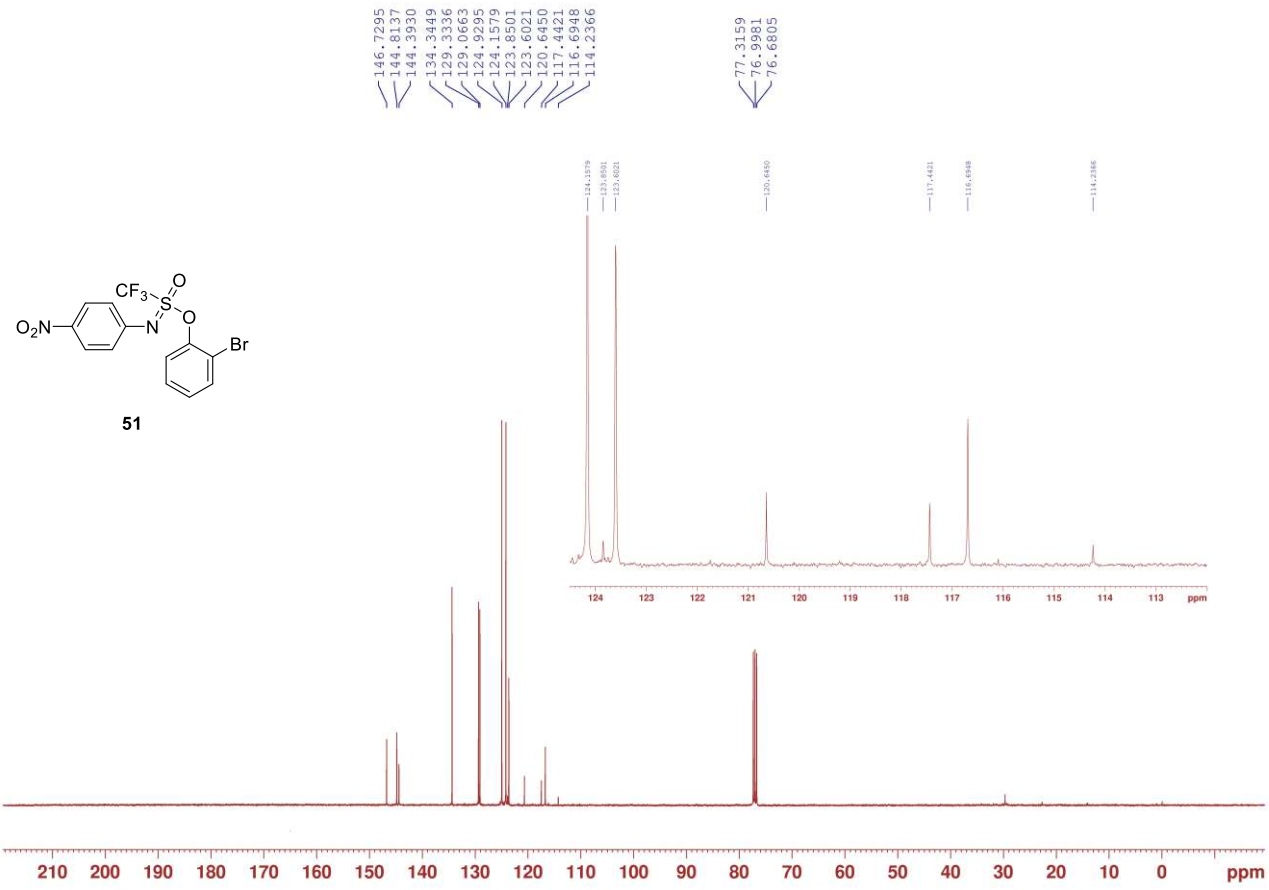
50

^{1}HNMR spectrum of **51**



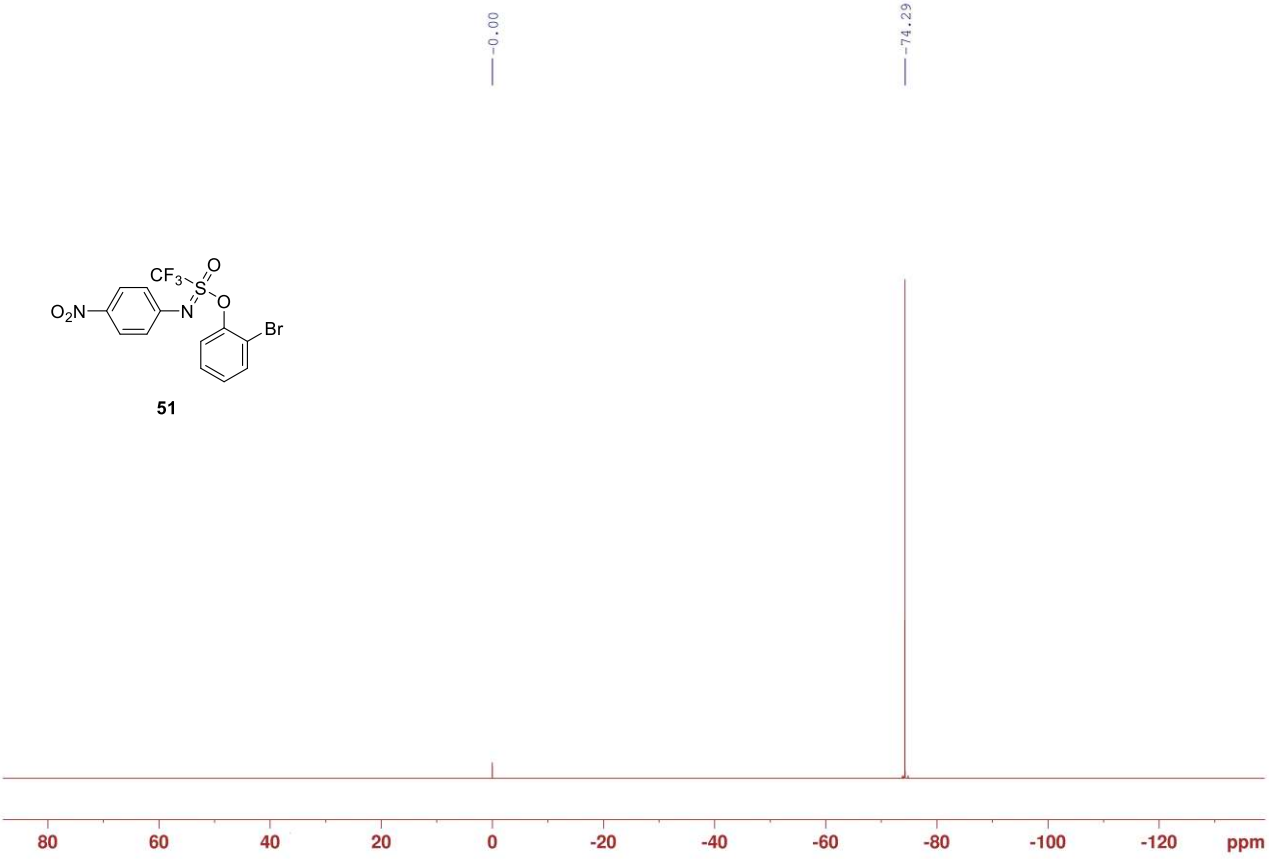
51

^{13}CNMR spectrum of **51**



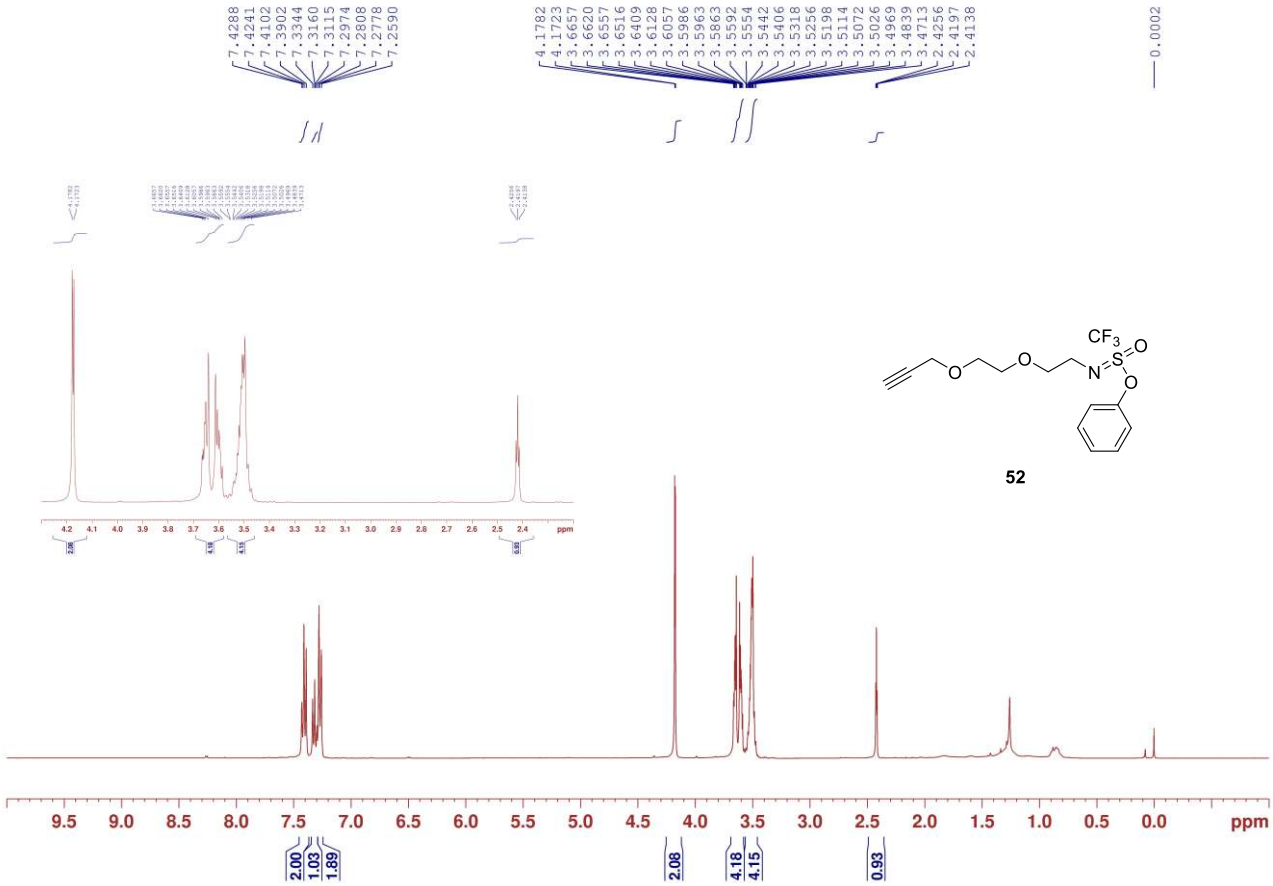
51

^{19}FNMR spectrum of **51**

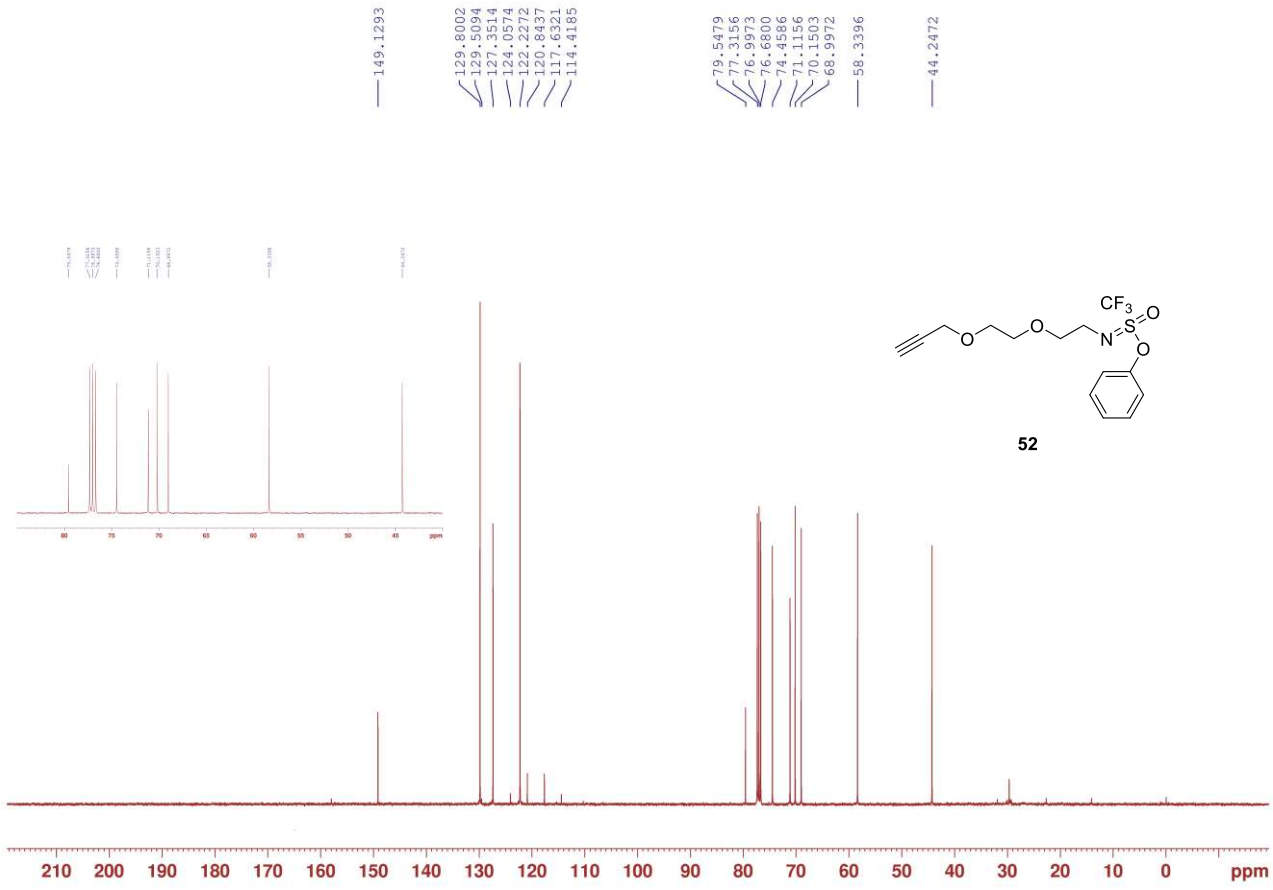


51

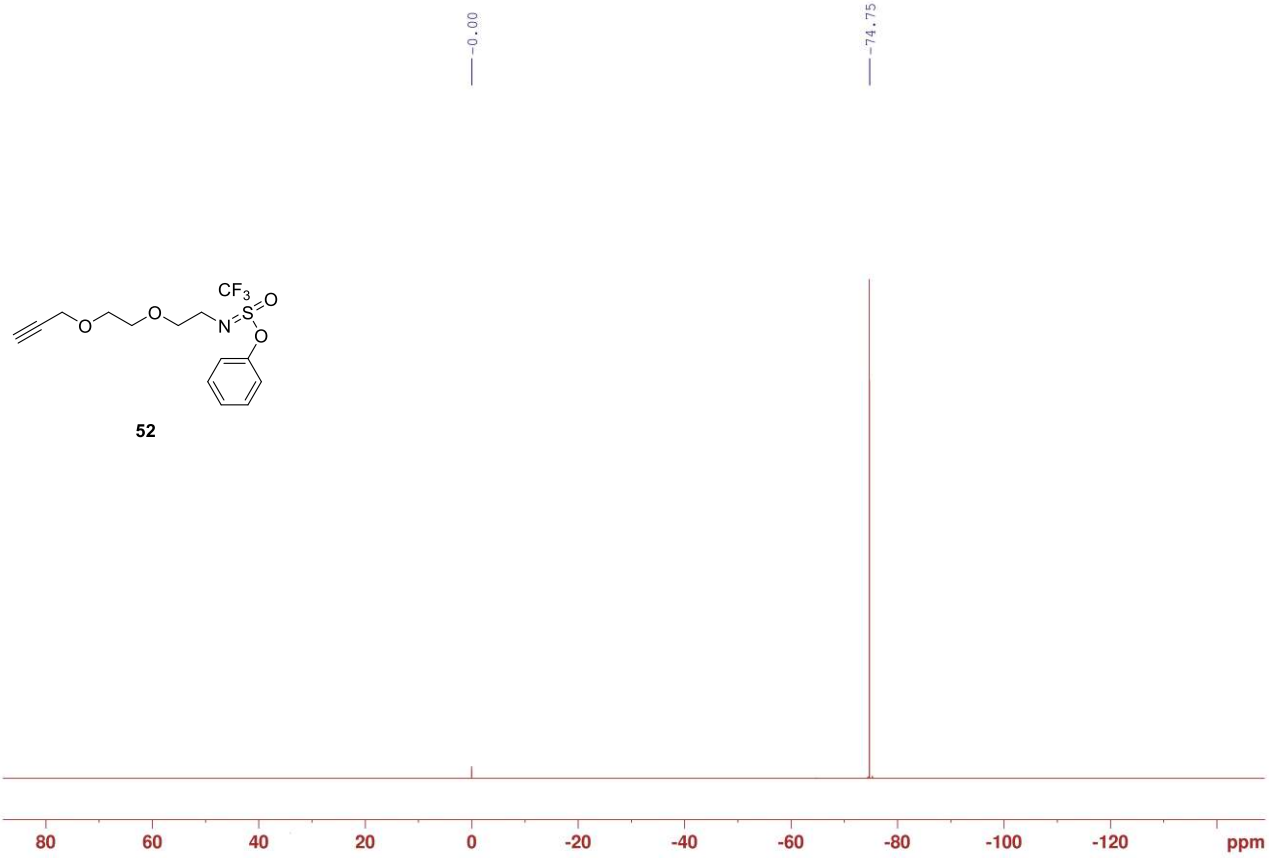
^{1}HNMR spectrum of **52**



^{13}CNMR spectrum of **52**

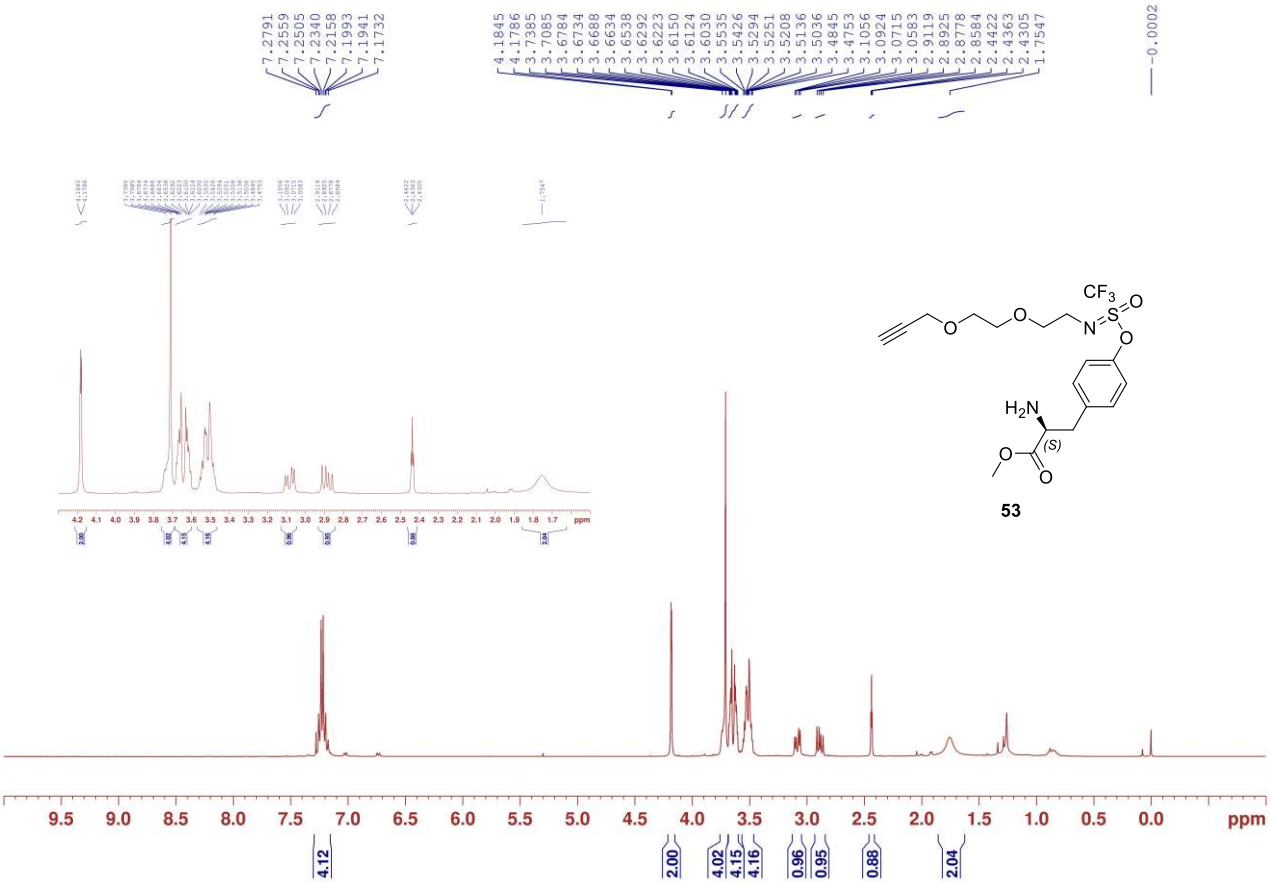


^{19}FNMR spectrum of **52**



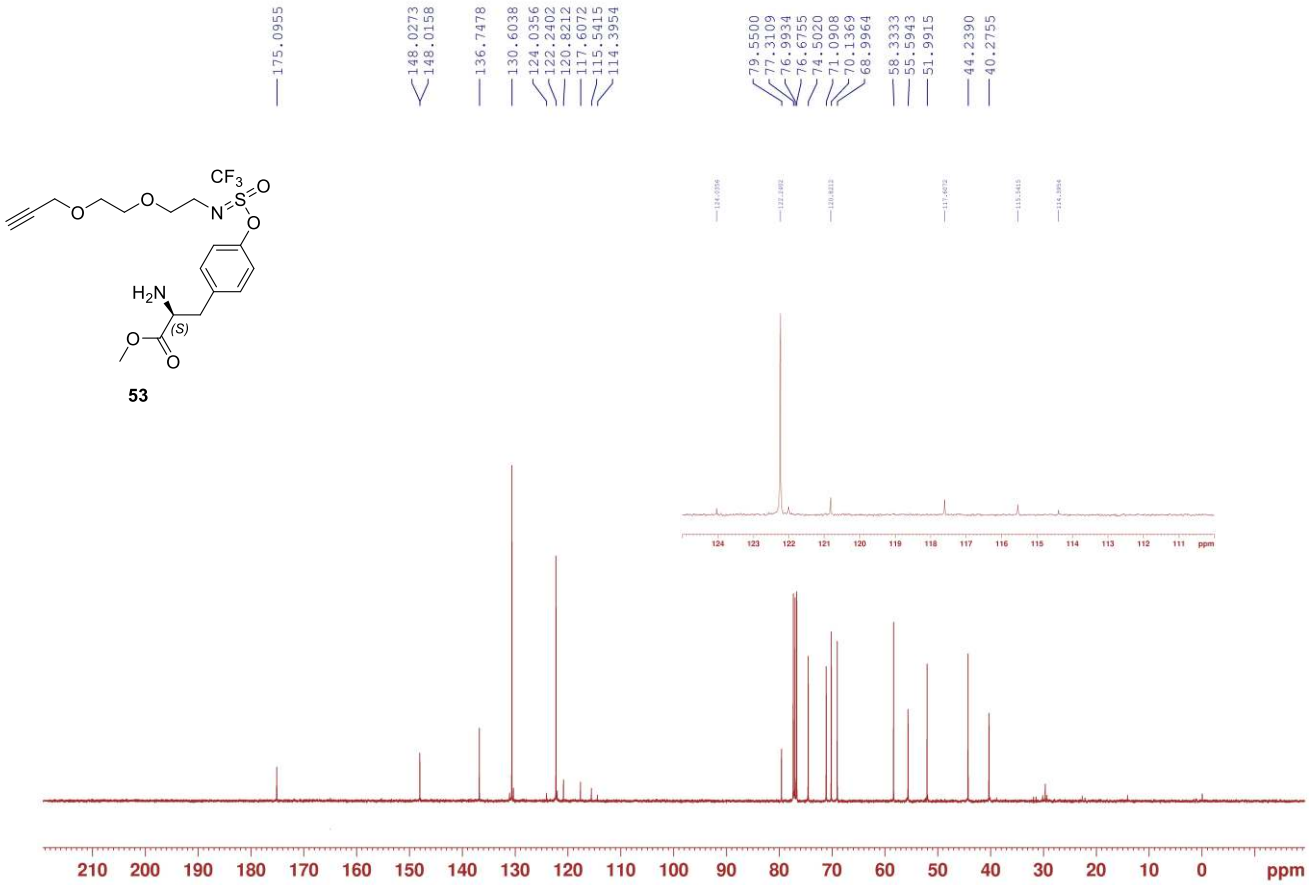
52

^{1}HNMR spectrum of **53**

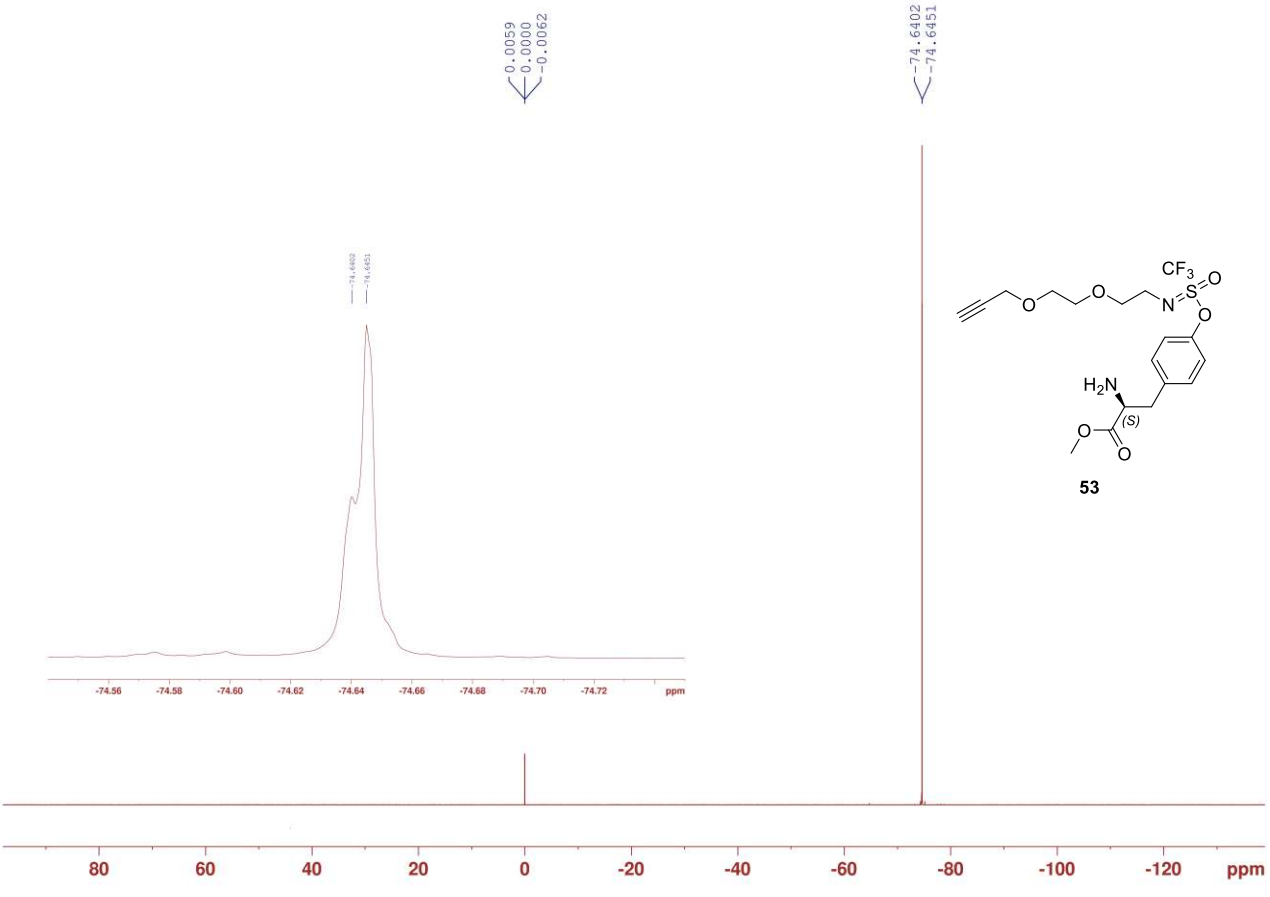


53

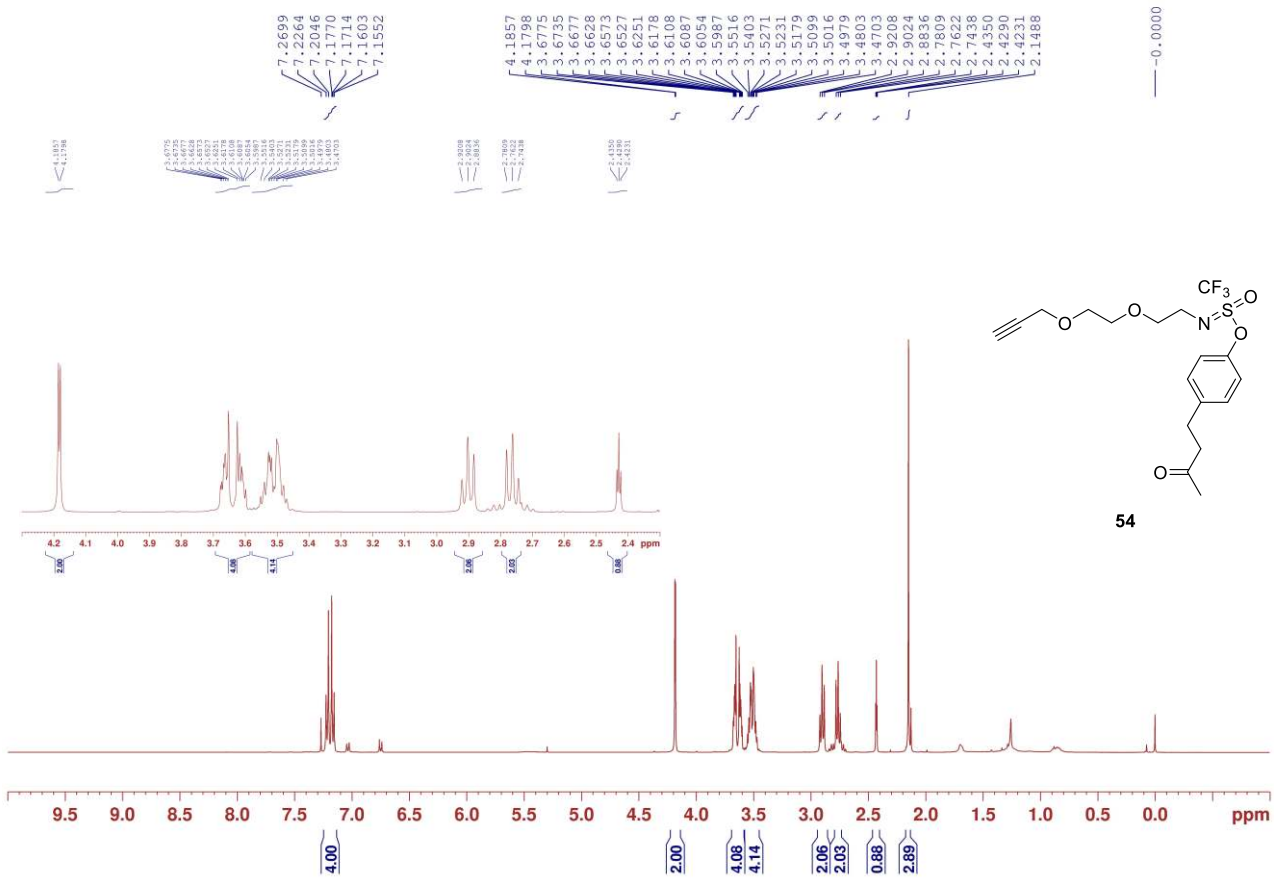
^{13}CNMR spectrum of **53**



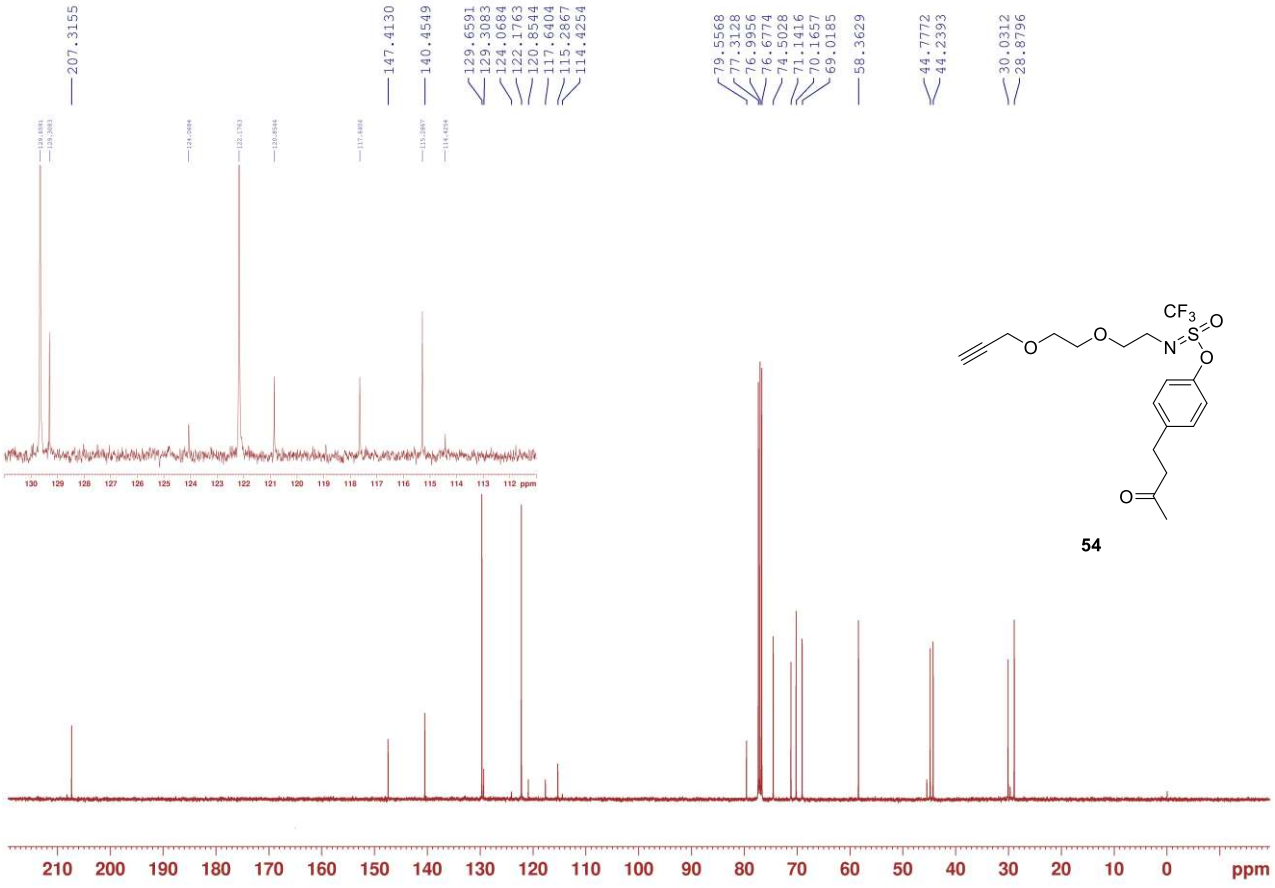
^{19}FNMR spectrum of **53**



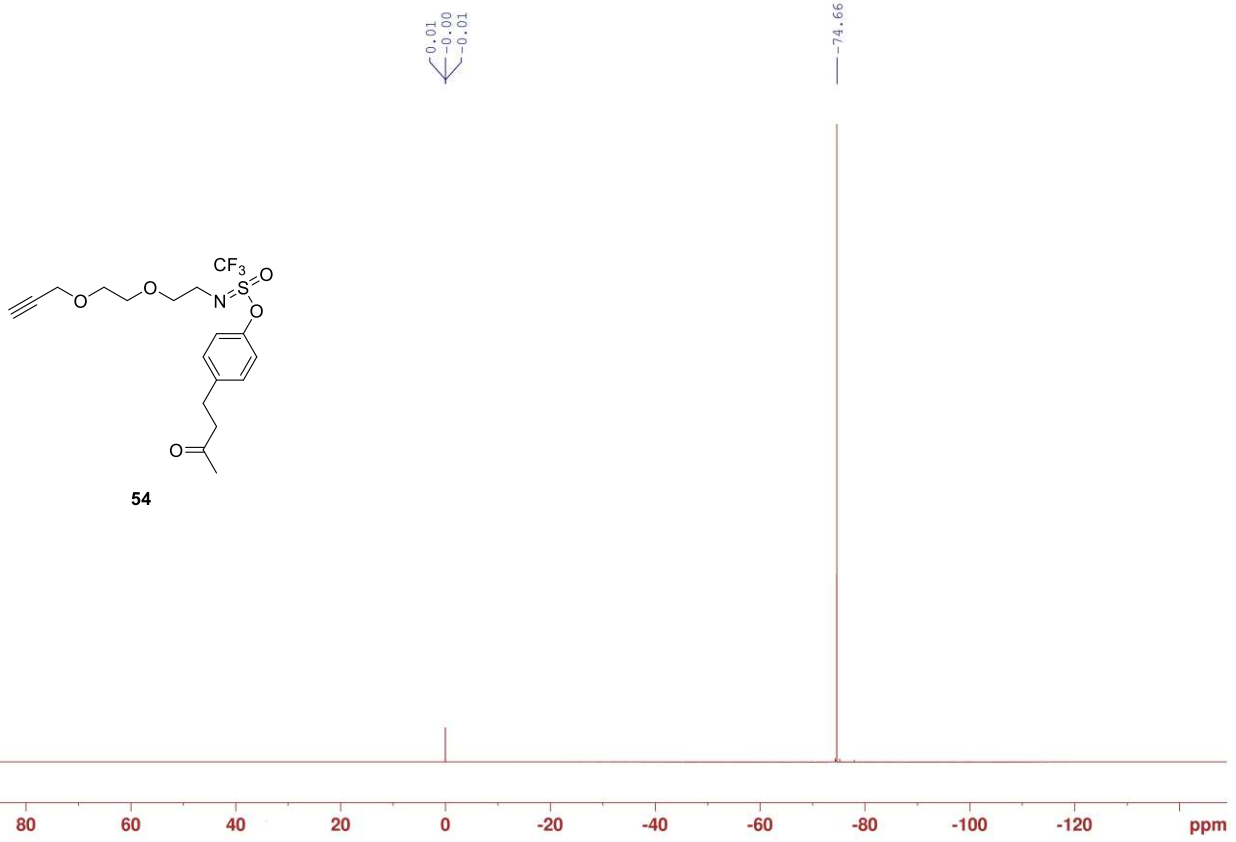
[1]HNMR spectrum of **54**



[13]CNMR spectrum of **54**

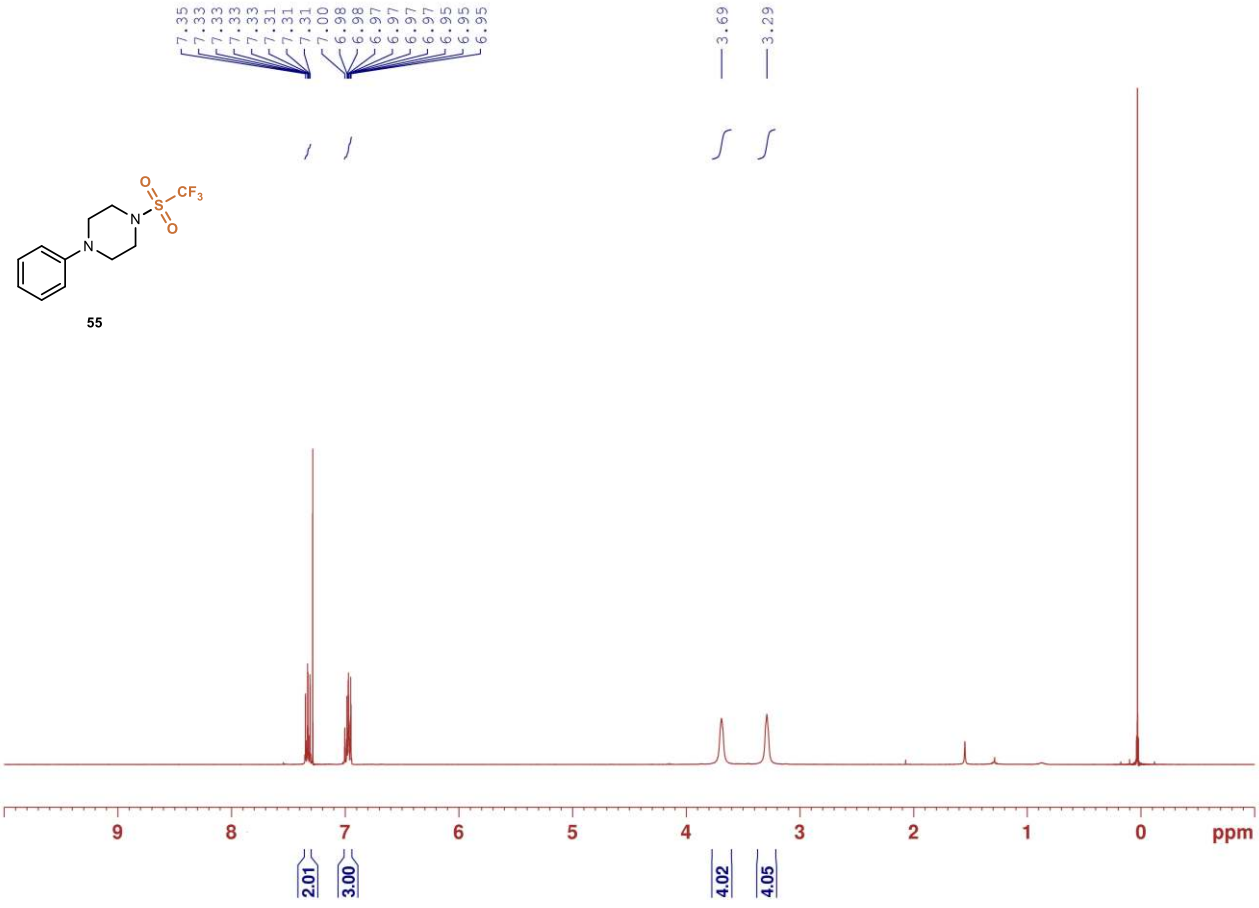


^{19}FNMR spectrum of **54**



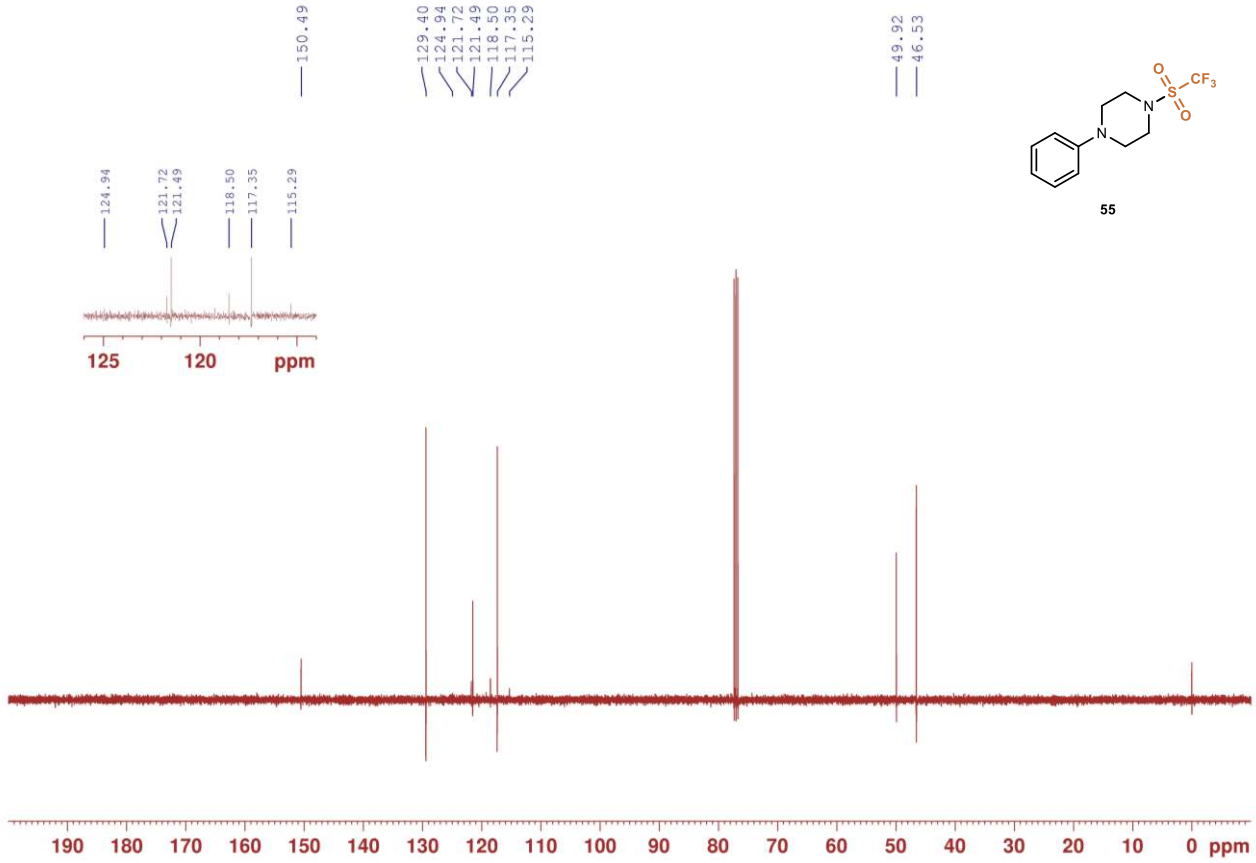
54

^{1}HNMR spectrum of **55**

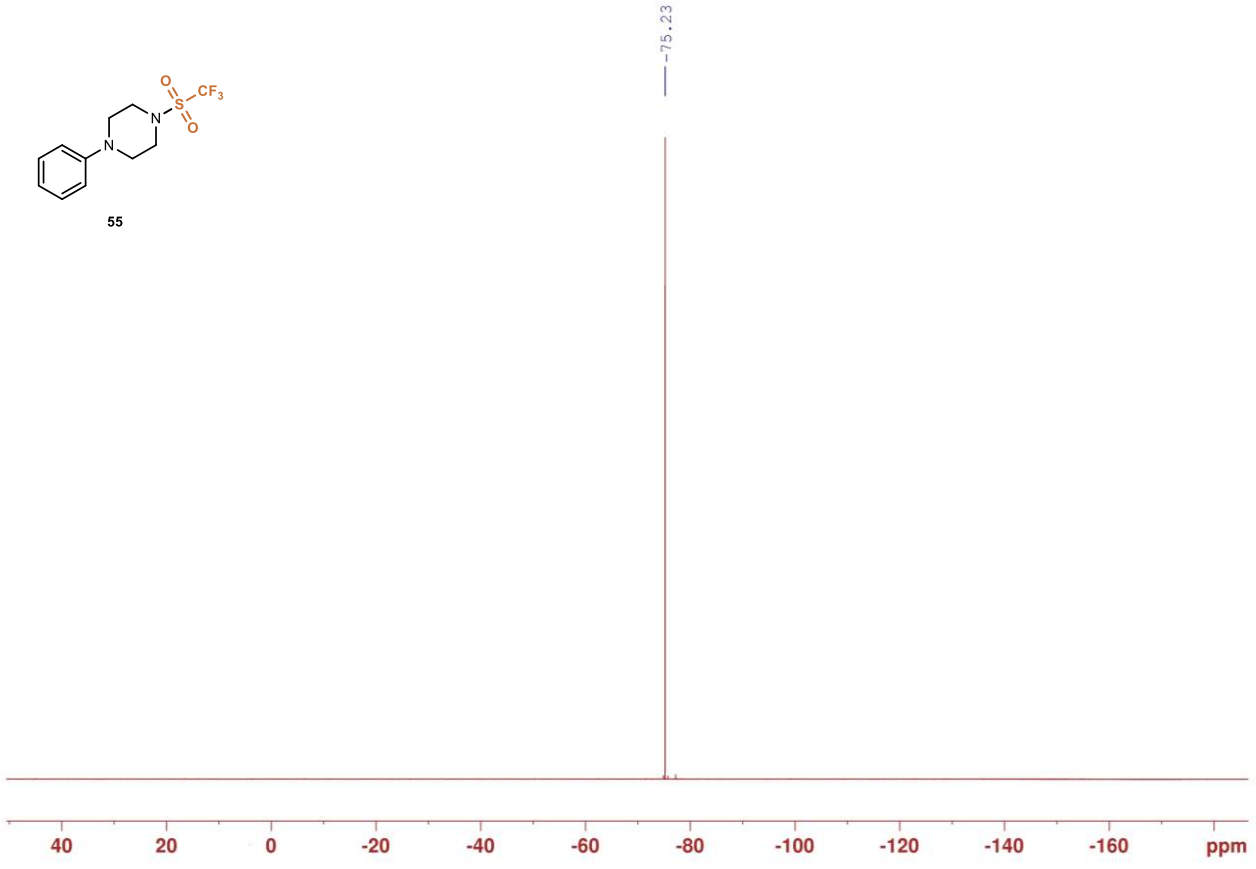


55

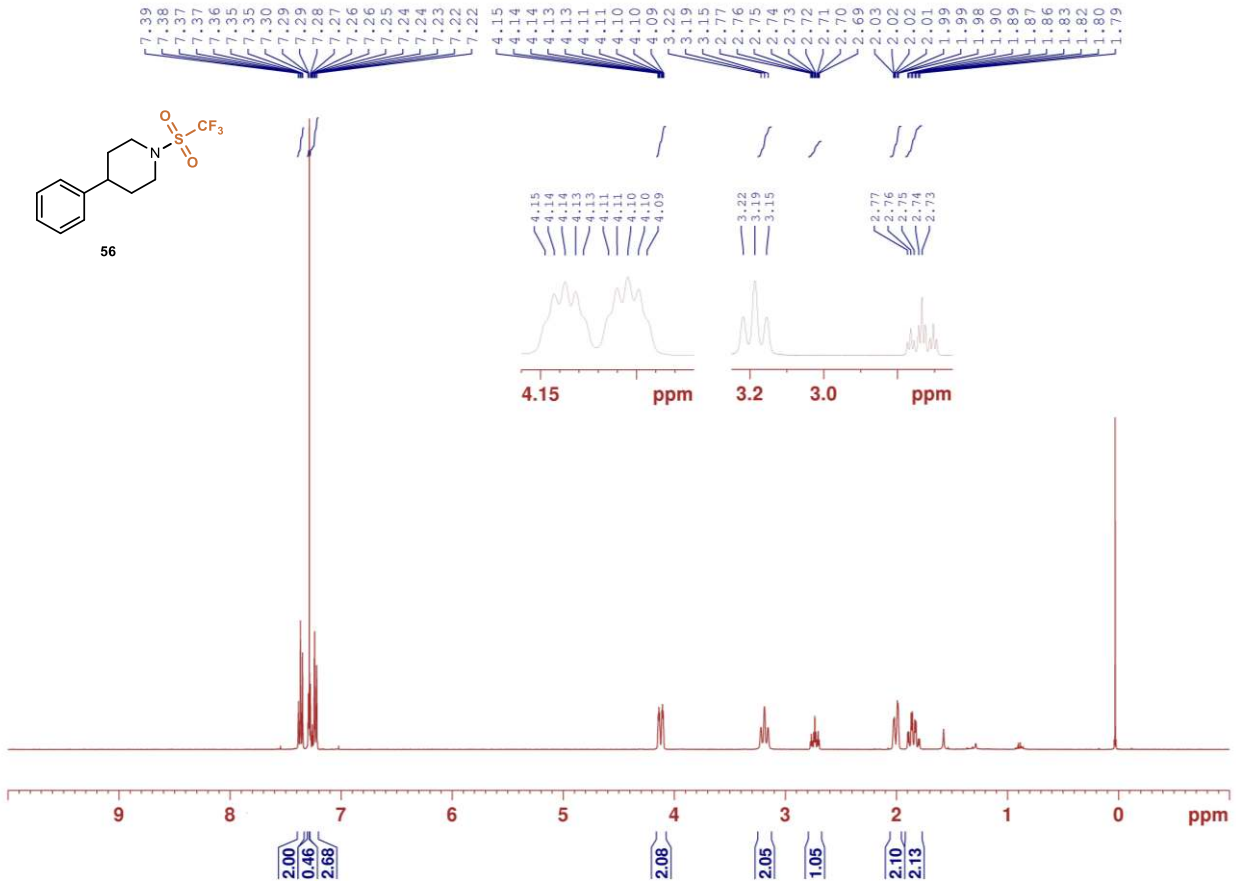
^{13}CNMR spectrum of **55**



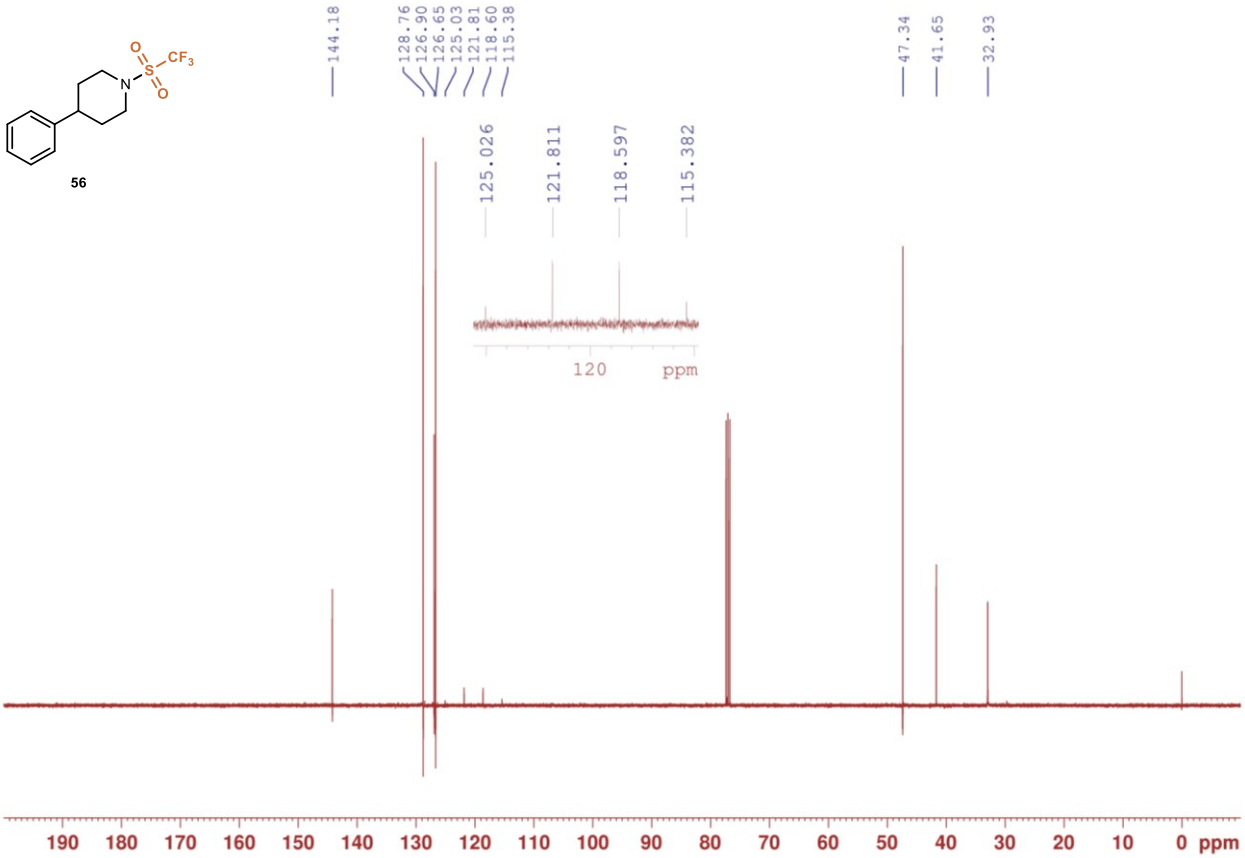
^{19}FNMR spectrum of **55**



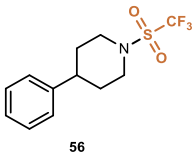
^{1}HNMR spectrum of **56**



^{13}CNMR spectrum of **56**

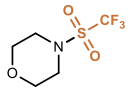


^{19}FNMR spectrum of **56**



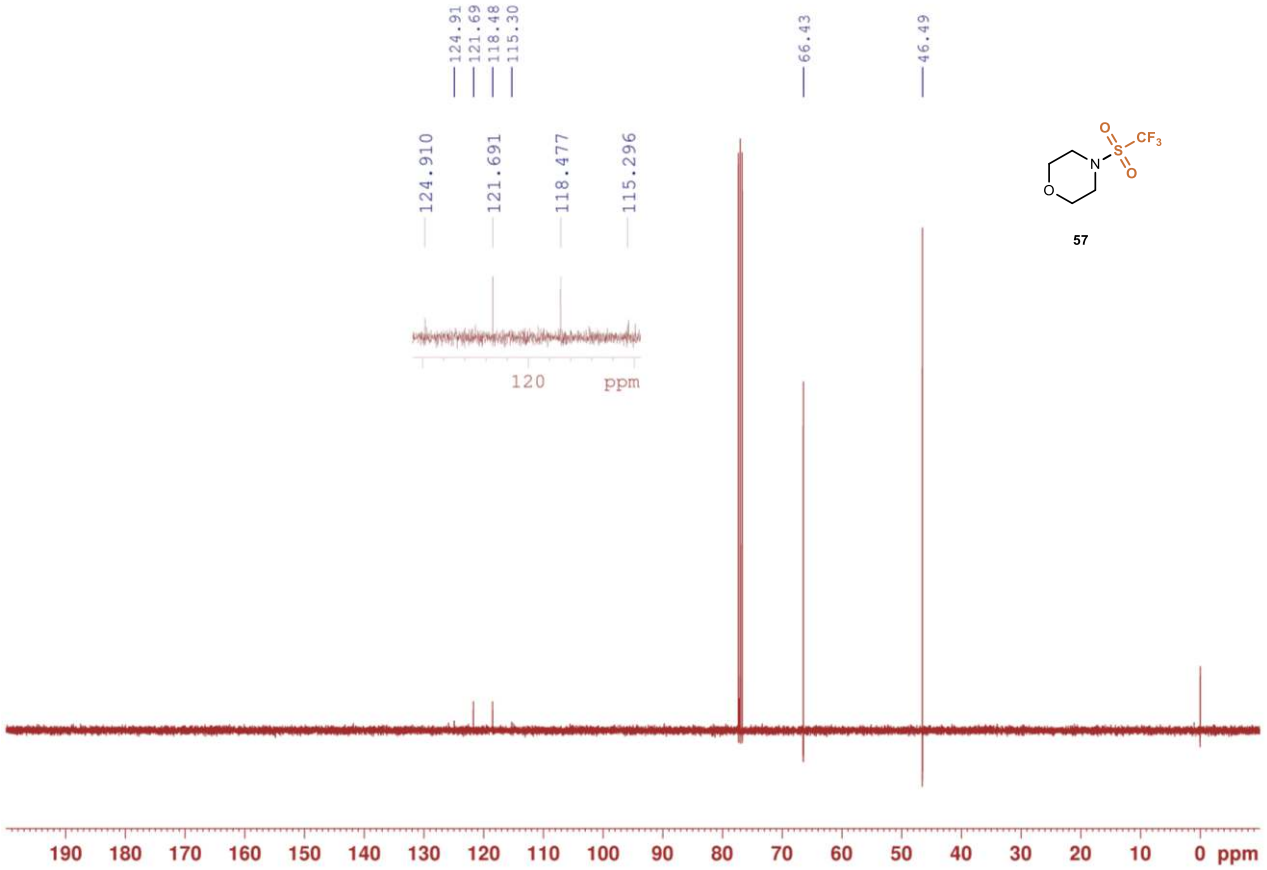
56

^{1}HNMR spectrum of **57**

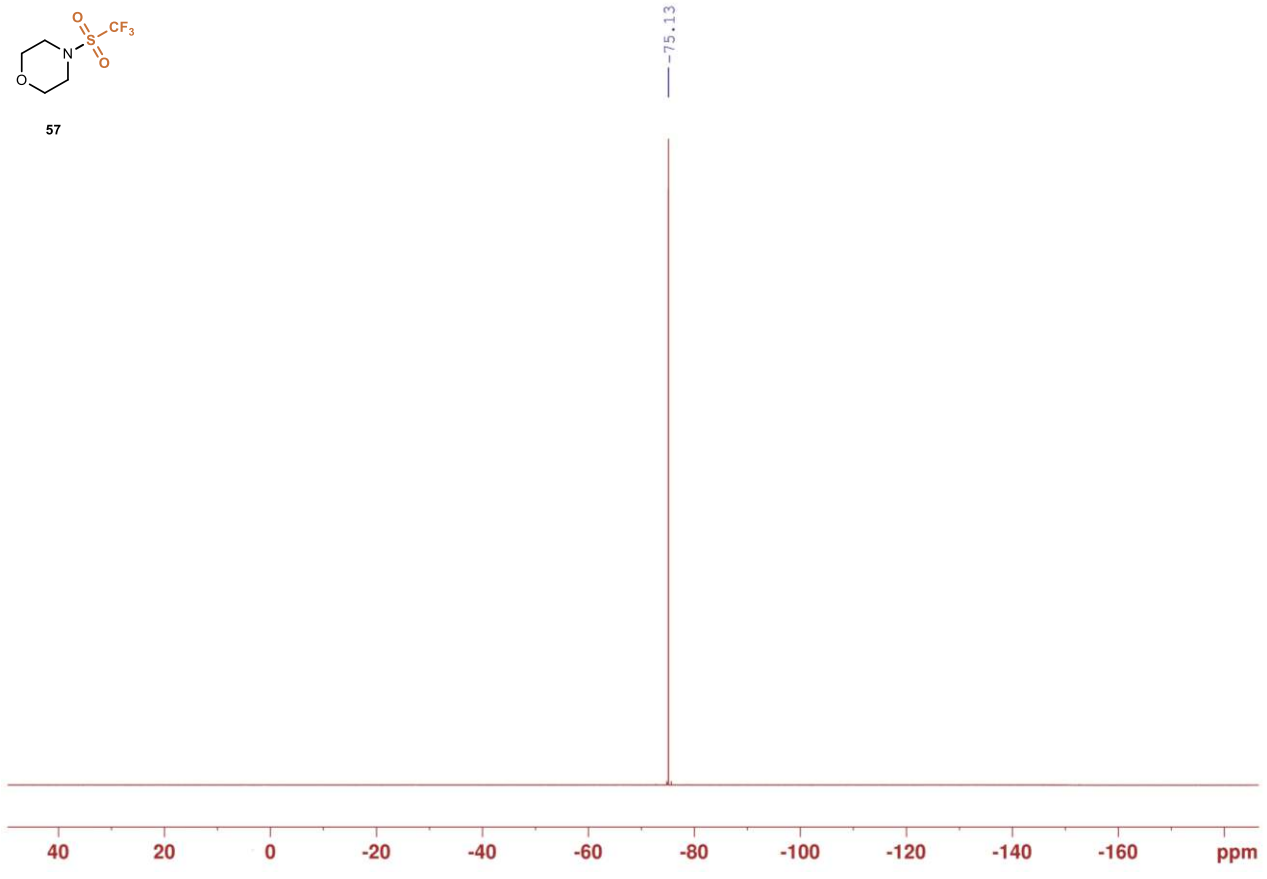


57

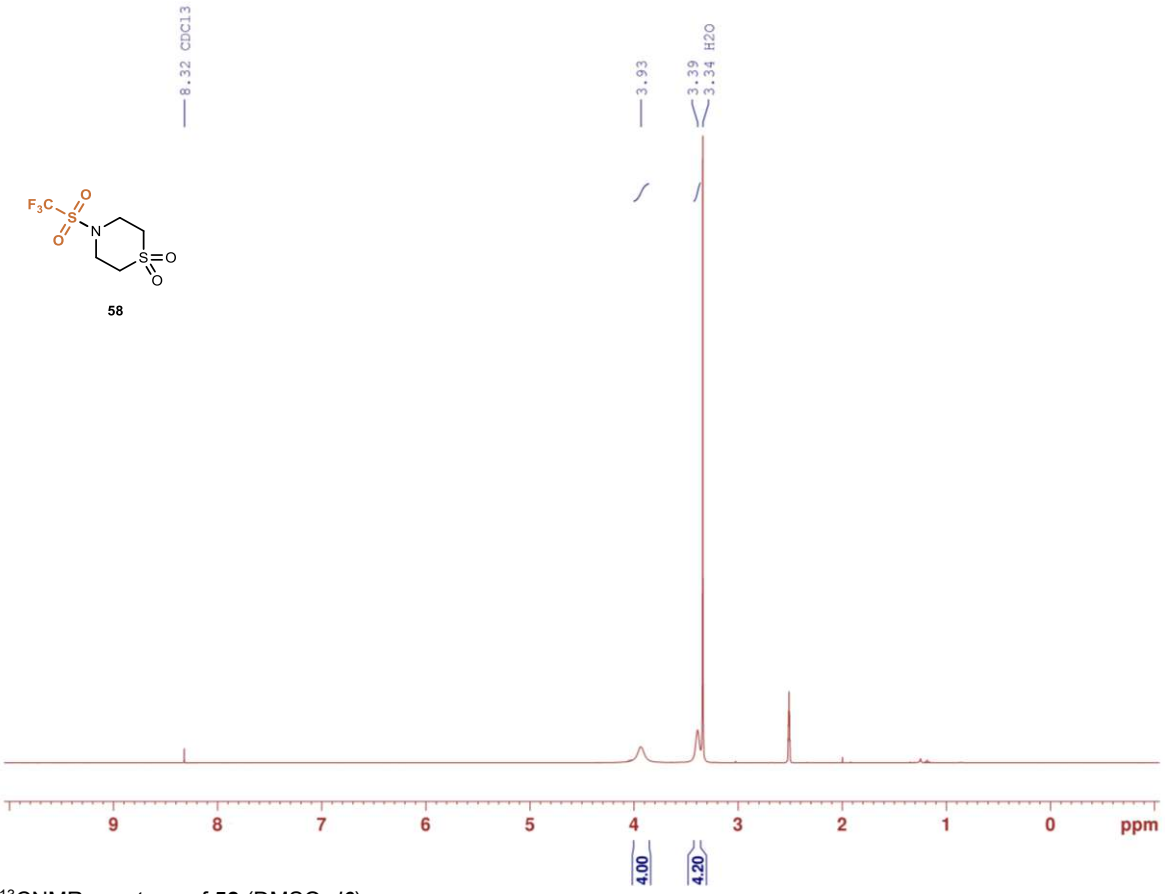
^{13}CNMR spectrum of **57**



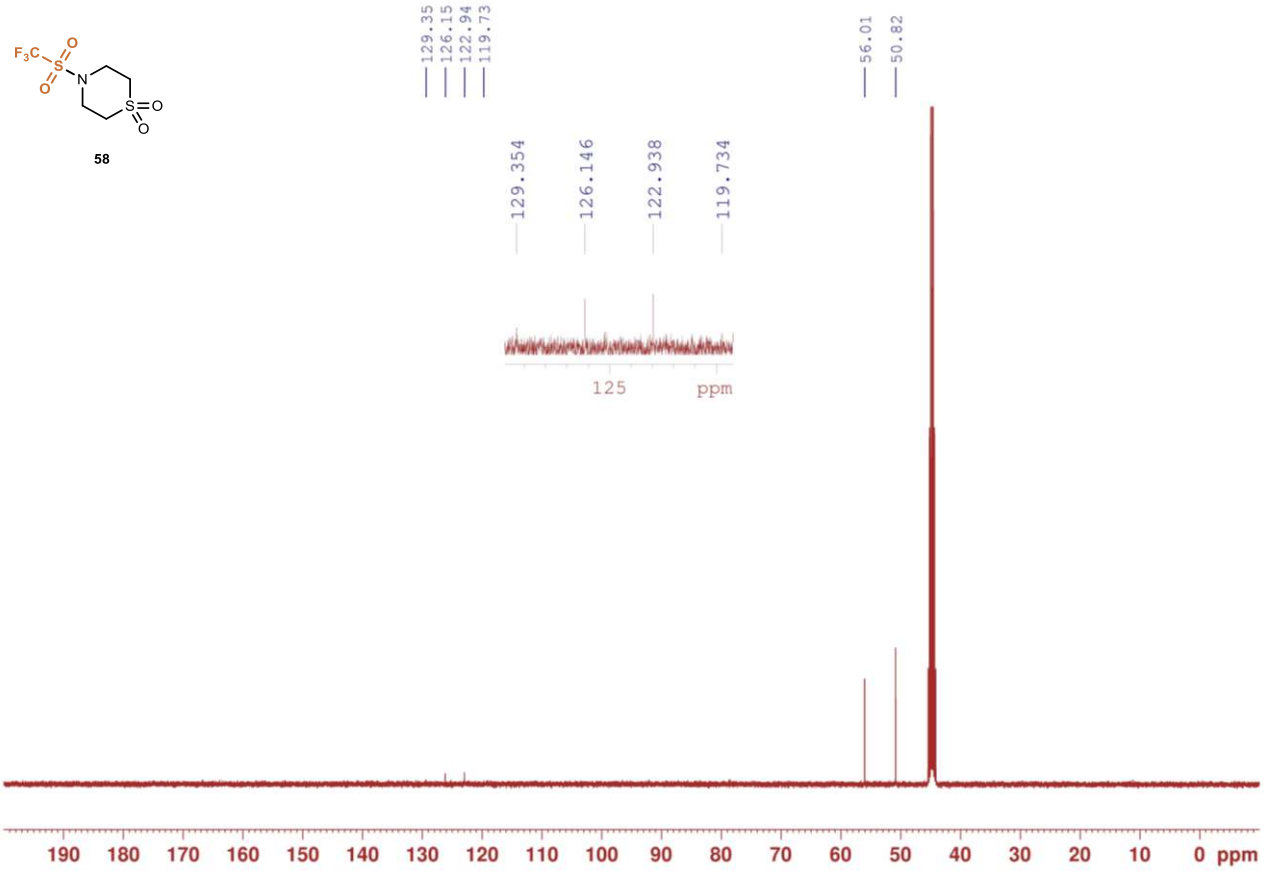
^{19}FNMR spectrum of **57**



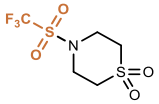
^{1}HNMR spectrum of **58** ($CDCl_3$ and DMSO-*d6*)



^{13}CNMR spectrum of **58** (DMSO-*d6*)

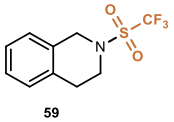


^{19}FNMR spectrum of **58** (DMSO-*d6*)



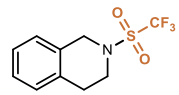
58

^{1}HNMR spectrum of **59**



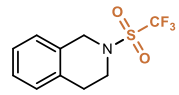
59

^{13}CNMR spectrum of **59**



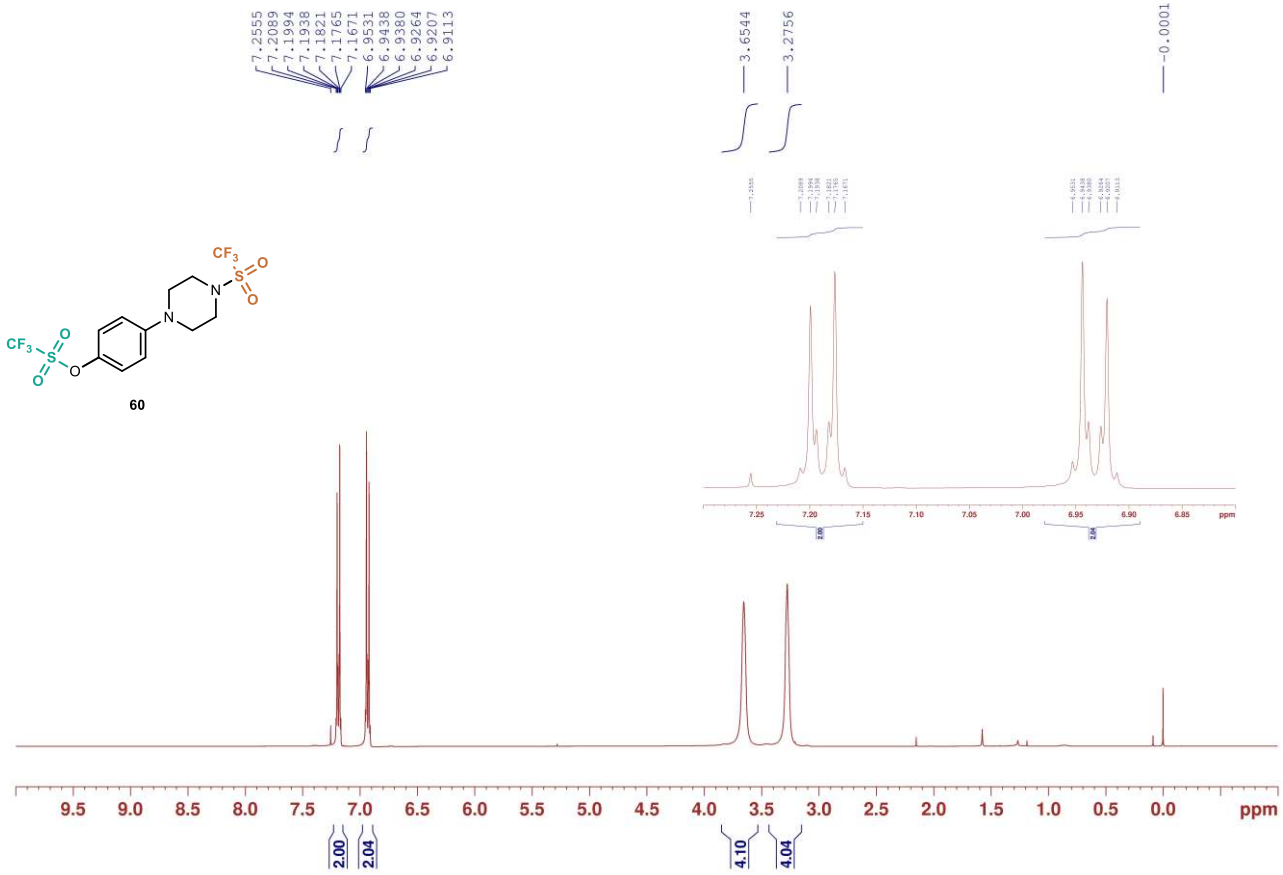
59

^{19}FNMR spectrum of **59**

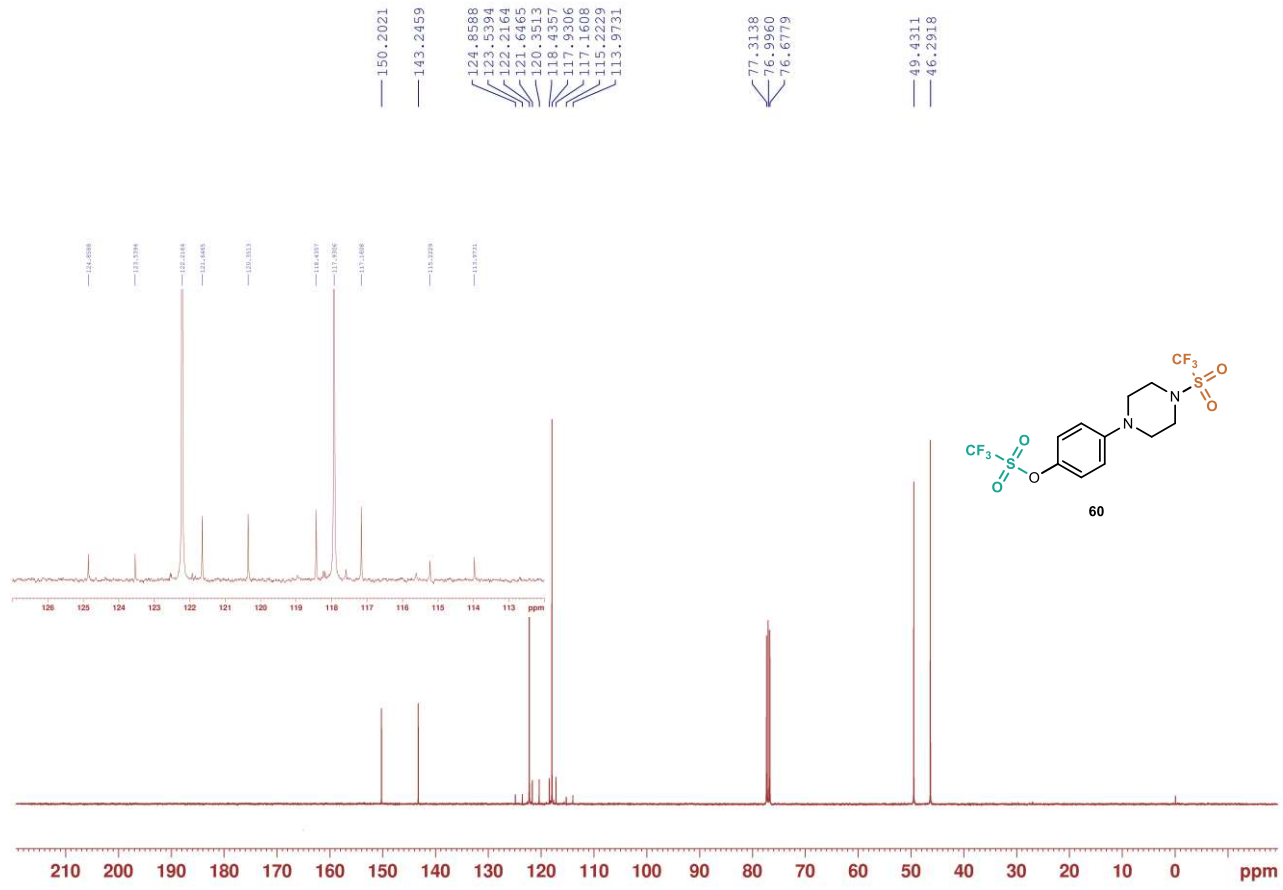


59

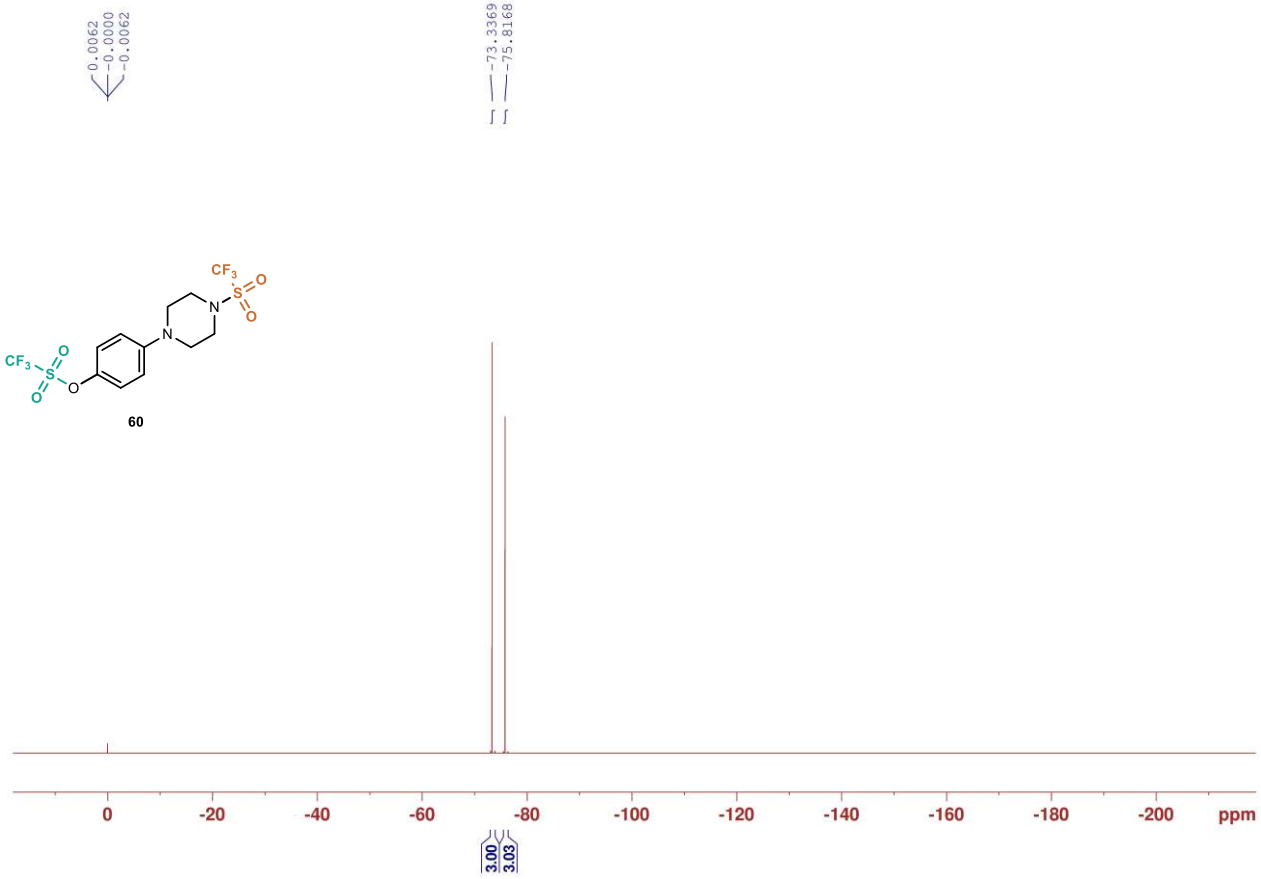
^{1}HNMR spectrum of **60**



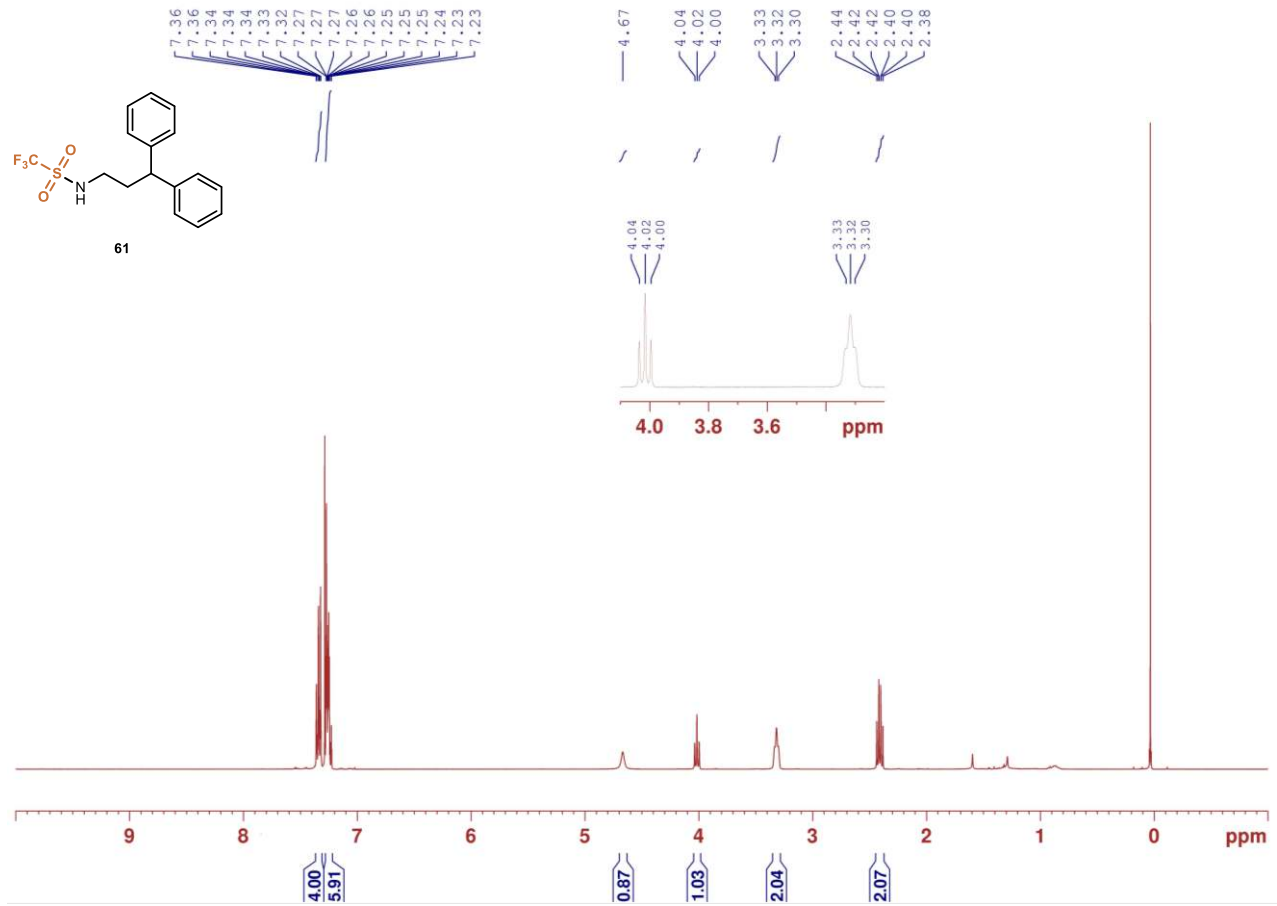
^{13}CNMR spectrum of **60**



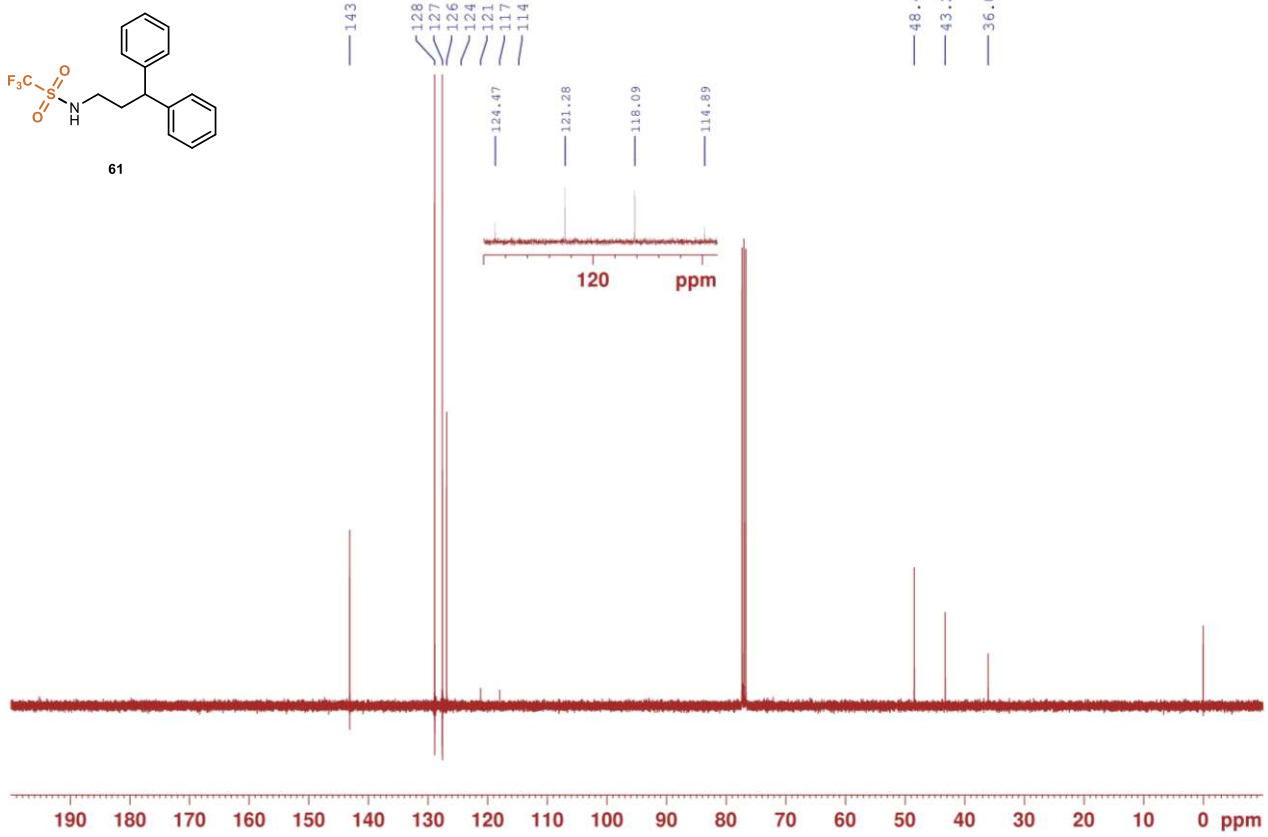
^{19}FNMR spectrum of **60**



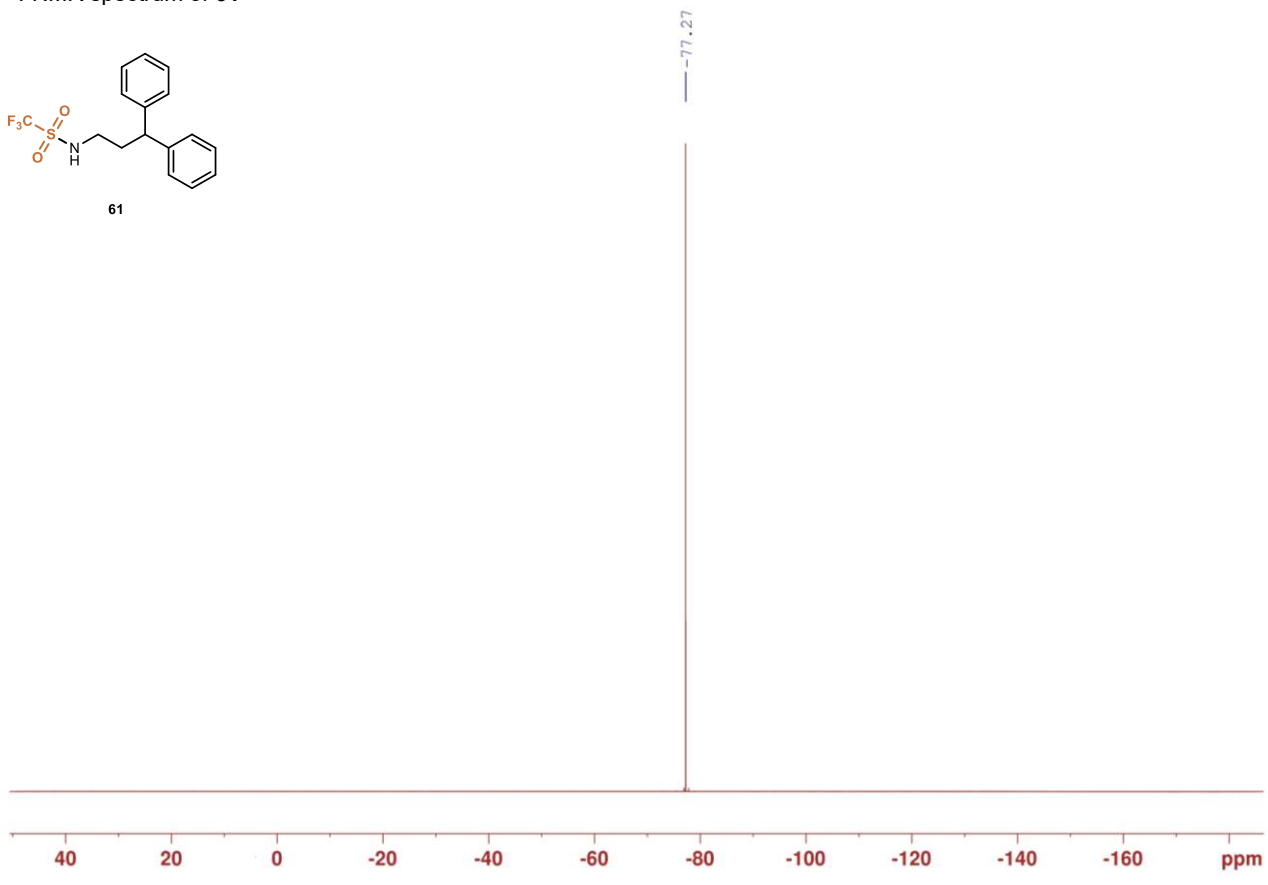
^{1}HNMR spectrum of **61**



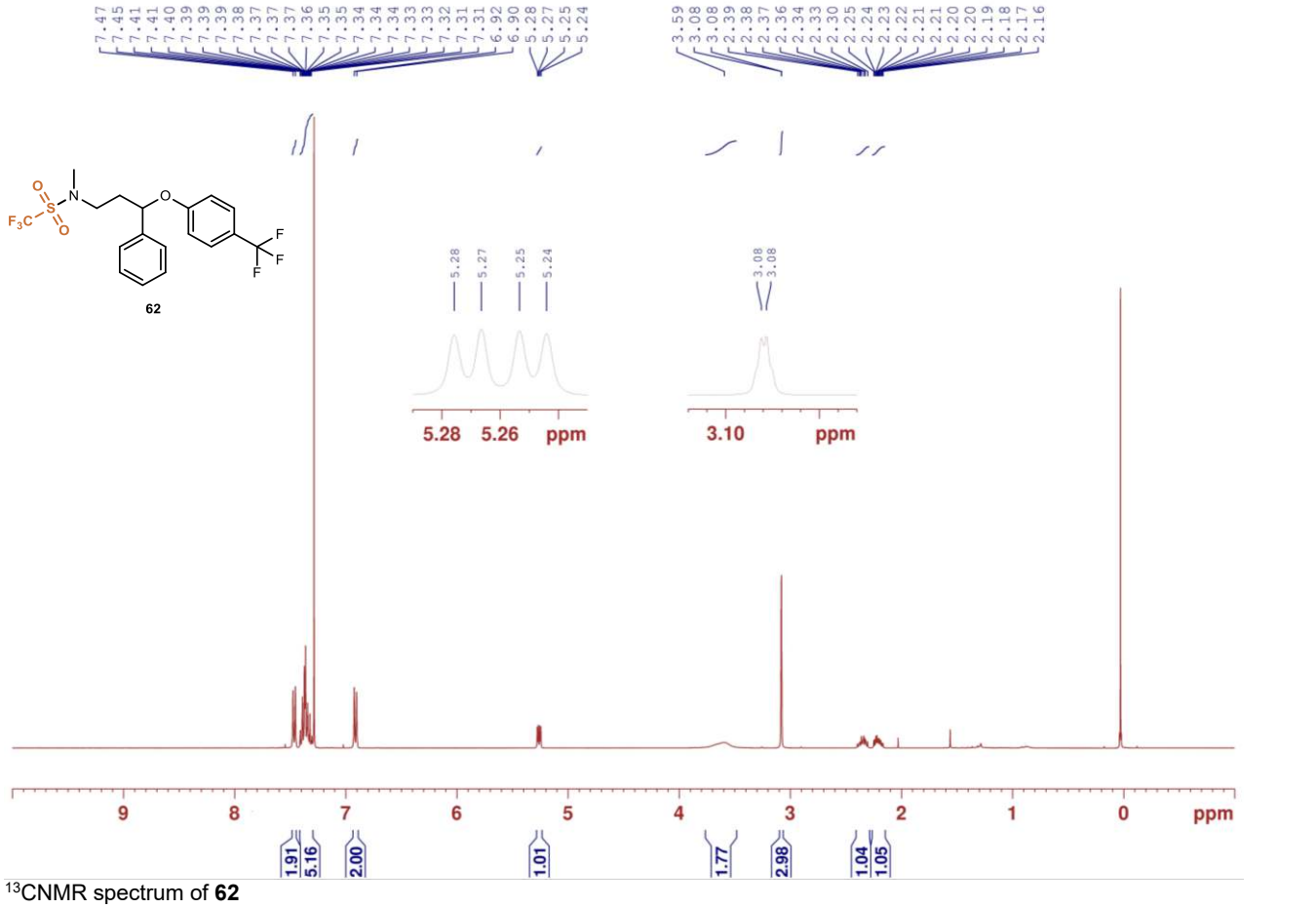
^{13}CNMR spectrum of **61**



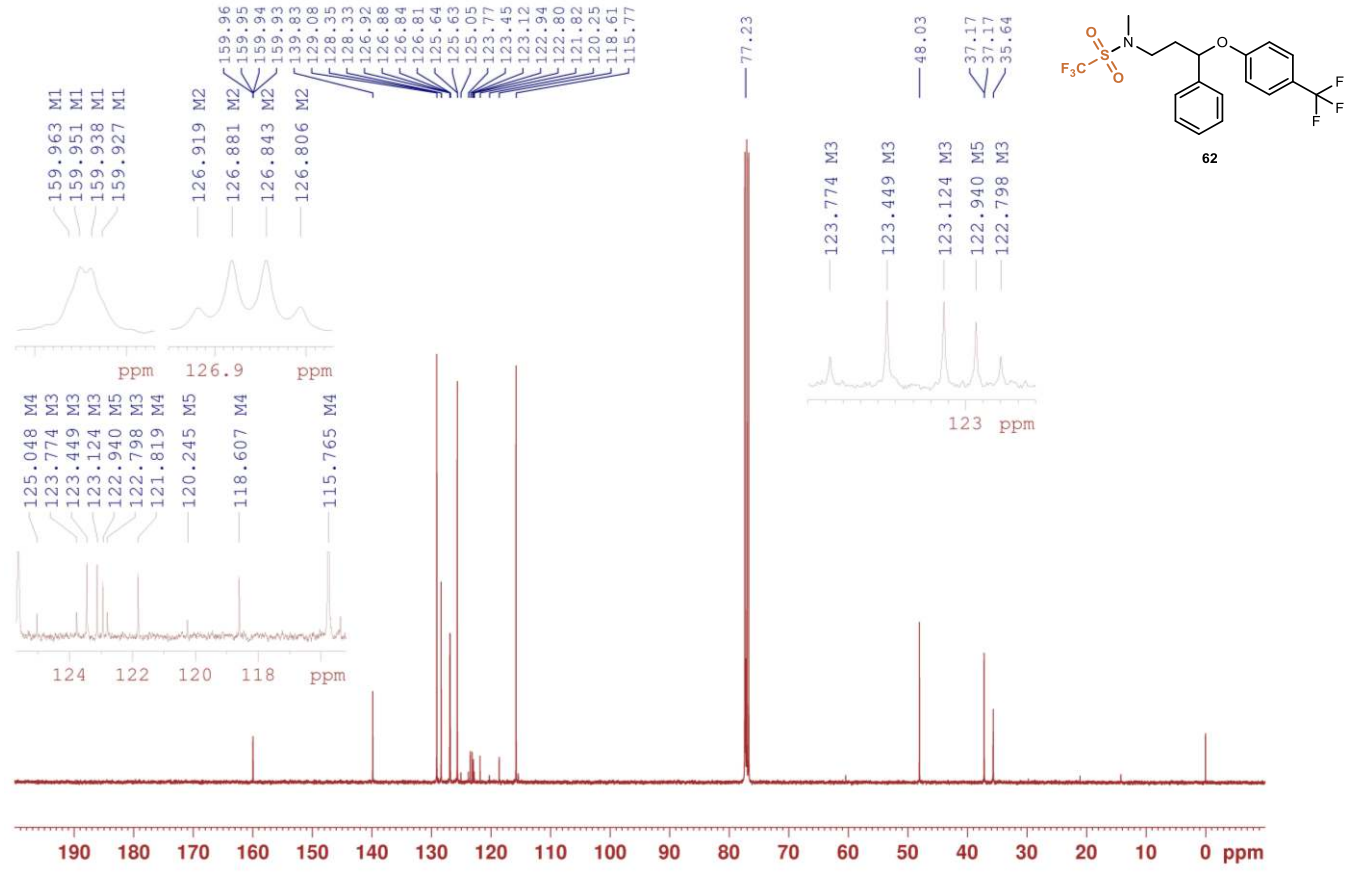
^{19}FNMR spectrum of **61**



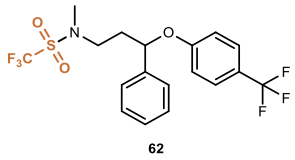
^{1}HNMR spectrum of **62**



^{13}CNMR spectrum of **62**

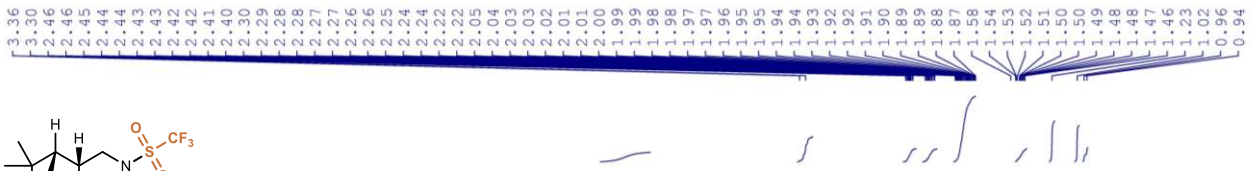


^{19}FNMR spectrum of **62**

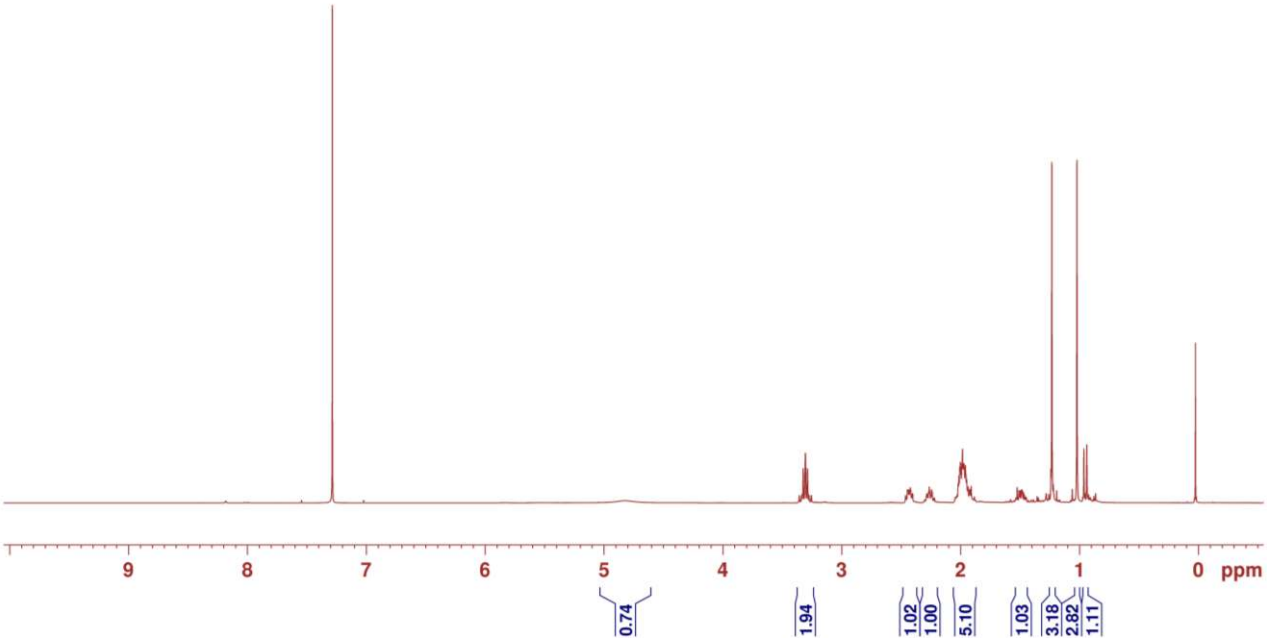


62

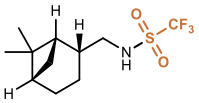
^{1}HNMR spectrum of **63**



63

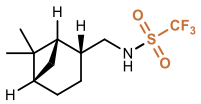


^{13}CNMR spectrum of **63**



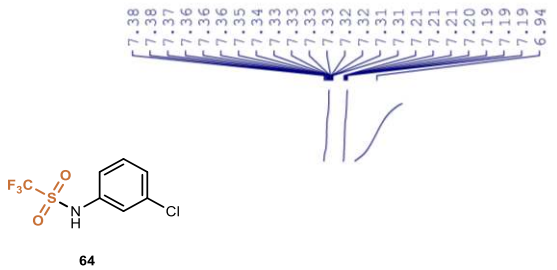
63

^{19}FNMR spectrum of **63**

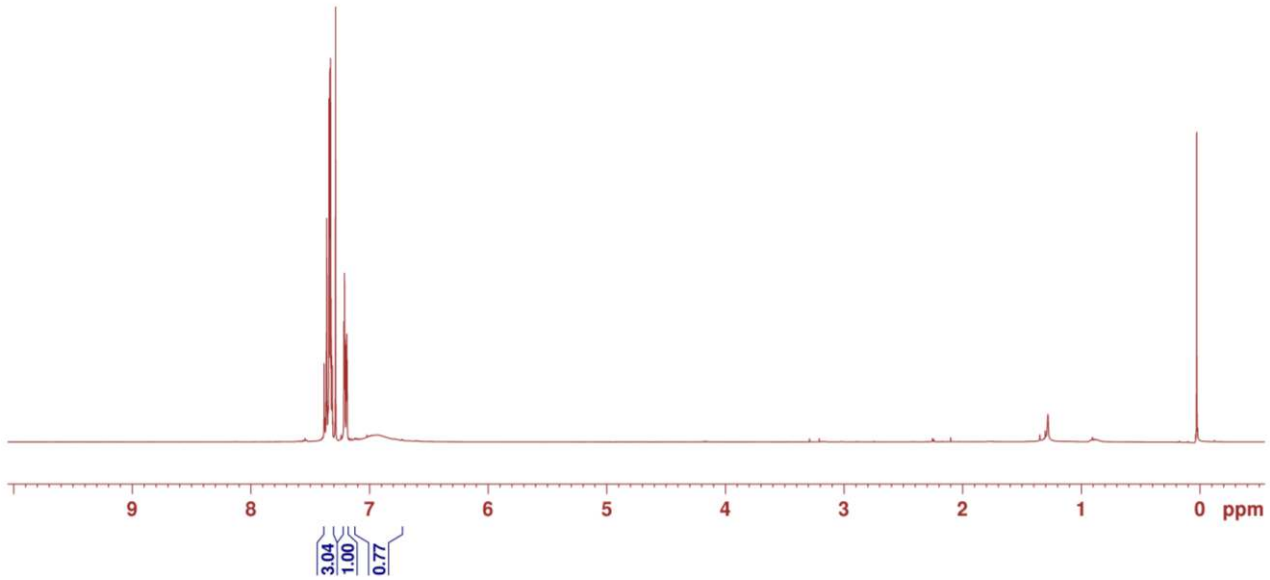


63

^{1}HNMR spectrum of **64**



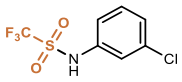
64



^{13}CNMR spectrum of **64**

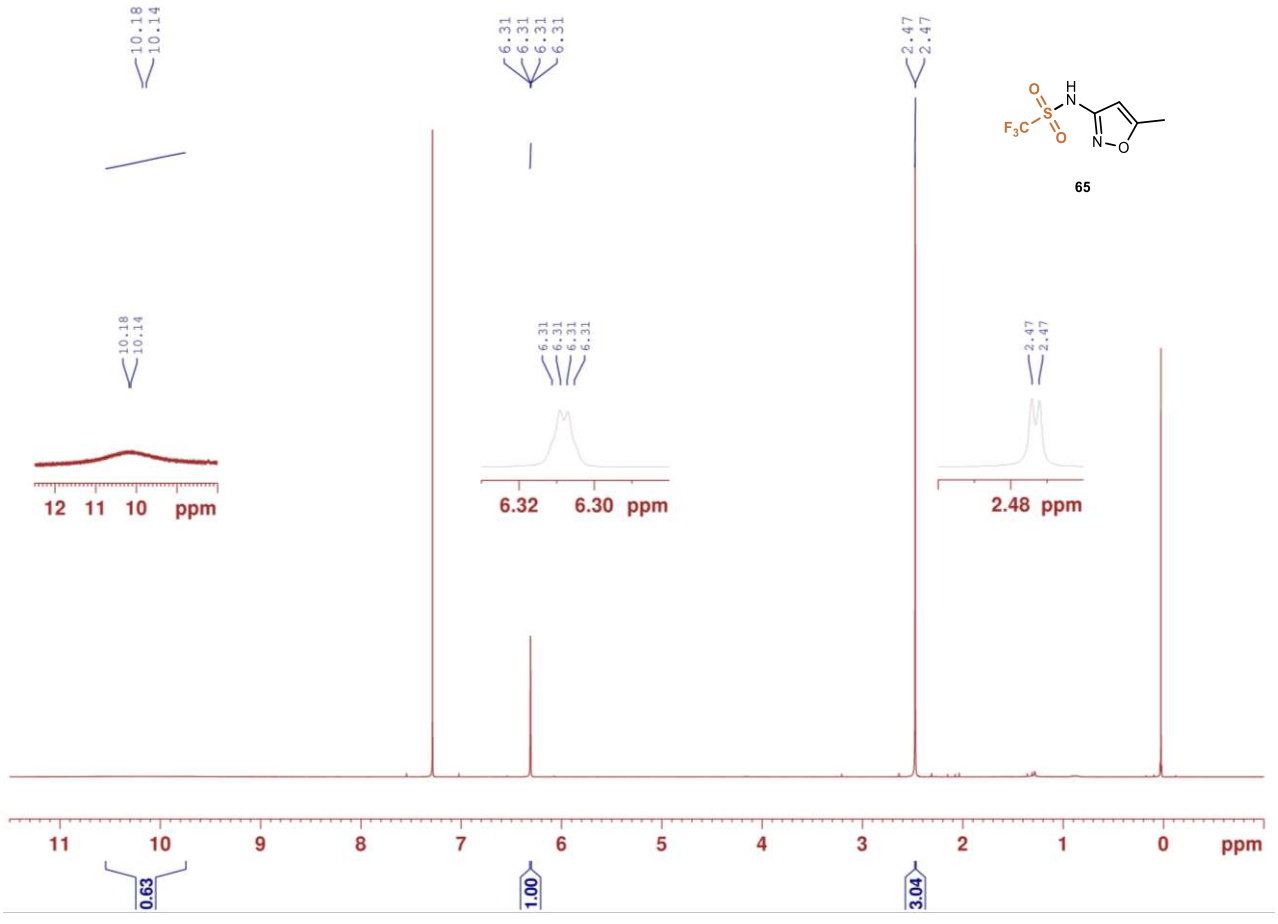
64

^{19}FNMR spectrum of **64**



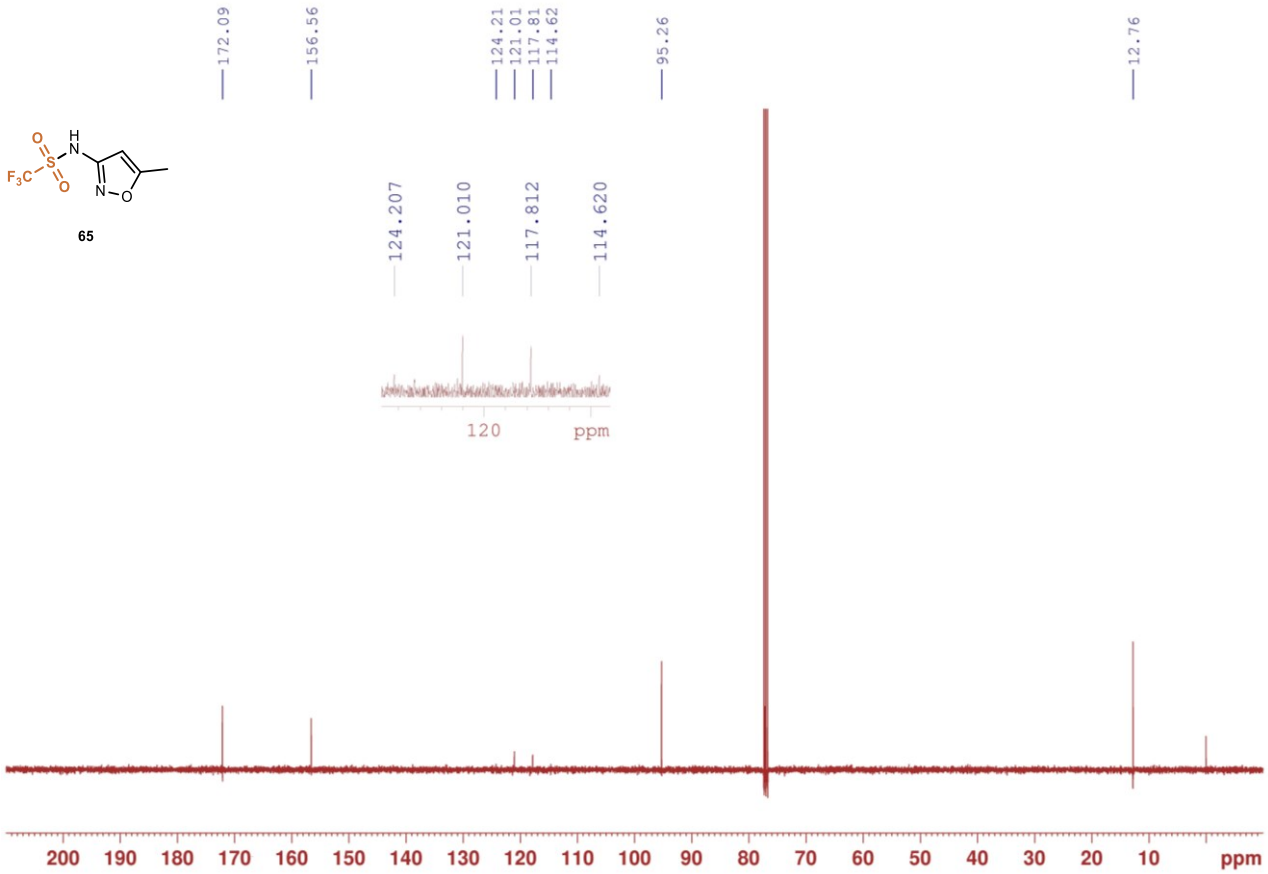
64

^{1}HNMR spectrum of **65**



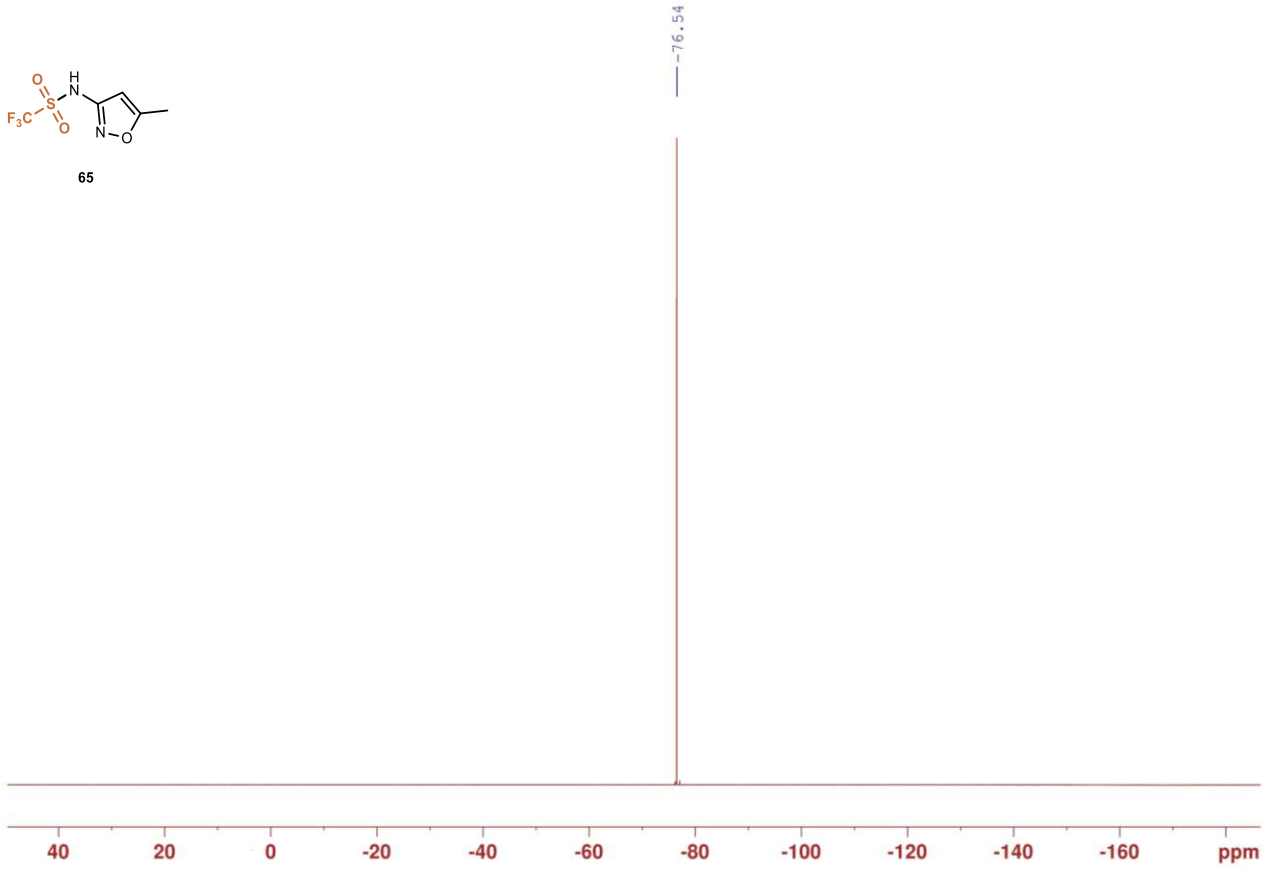
65

^{13}CNMR spectrum of **65**



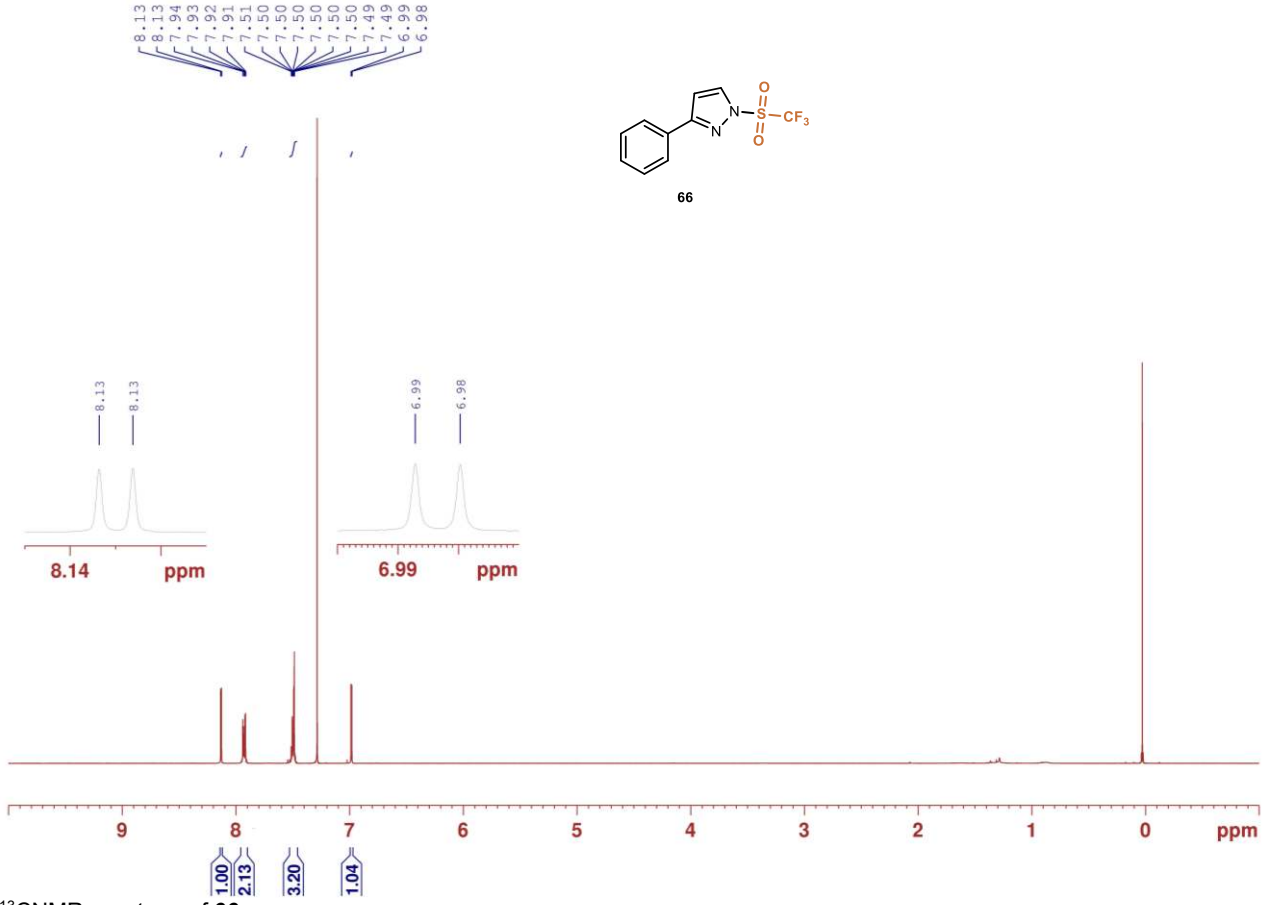
65

^{19}FNMR spectrum of **65**

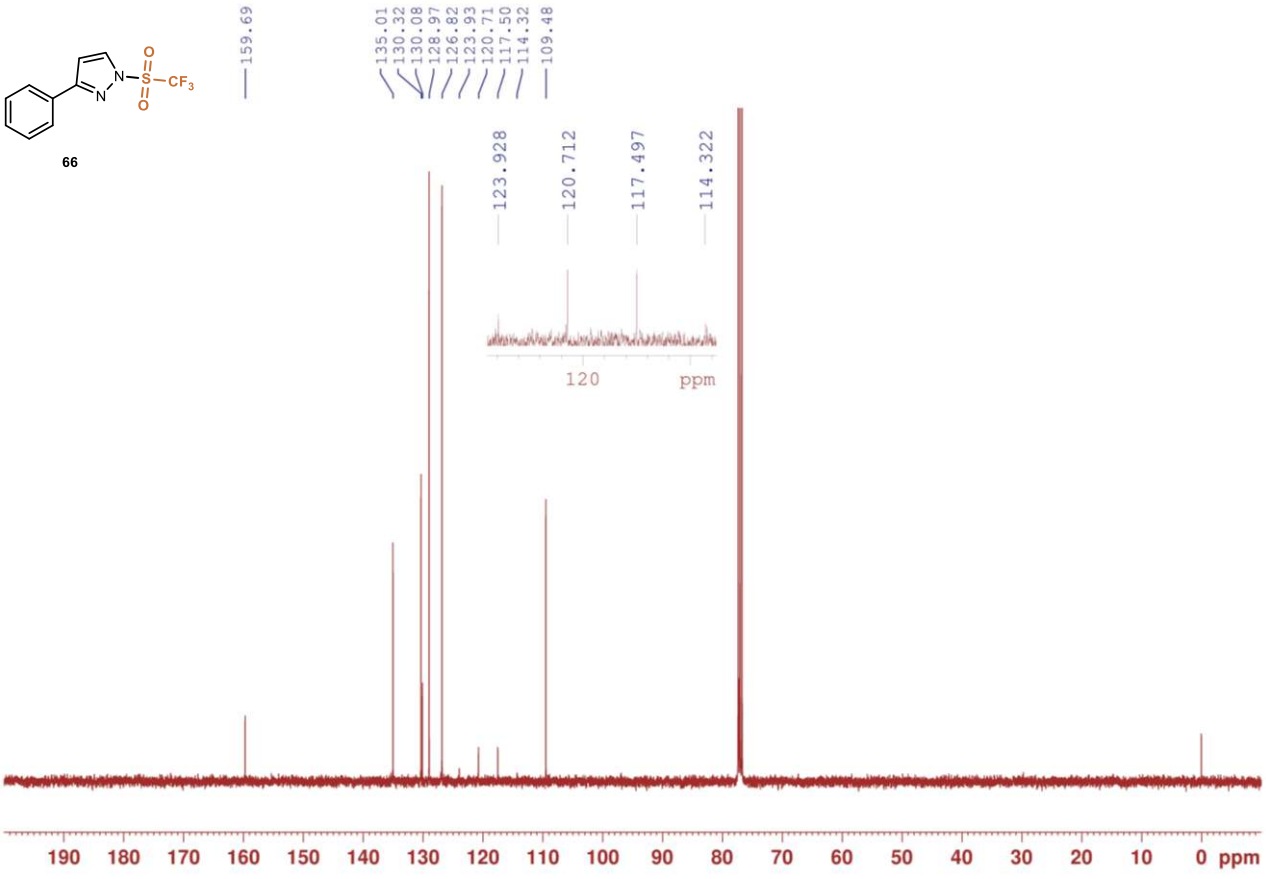


65

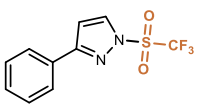
^{1}HNMR spectrum of **66**



^{13}CNMR spectrum of **66**

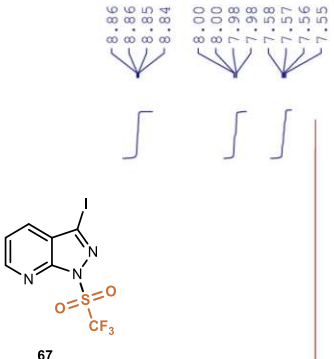


^{19}FNMR spectrum of **66**



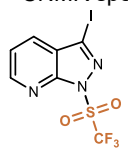
66

^{1}HNMR spectrum of **67**



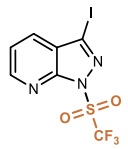
67

^{13}CNMR spectrum of **67**



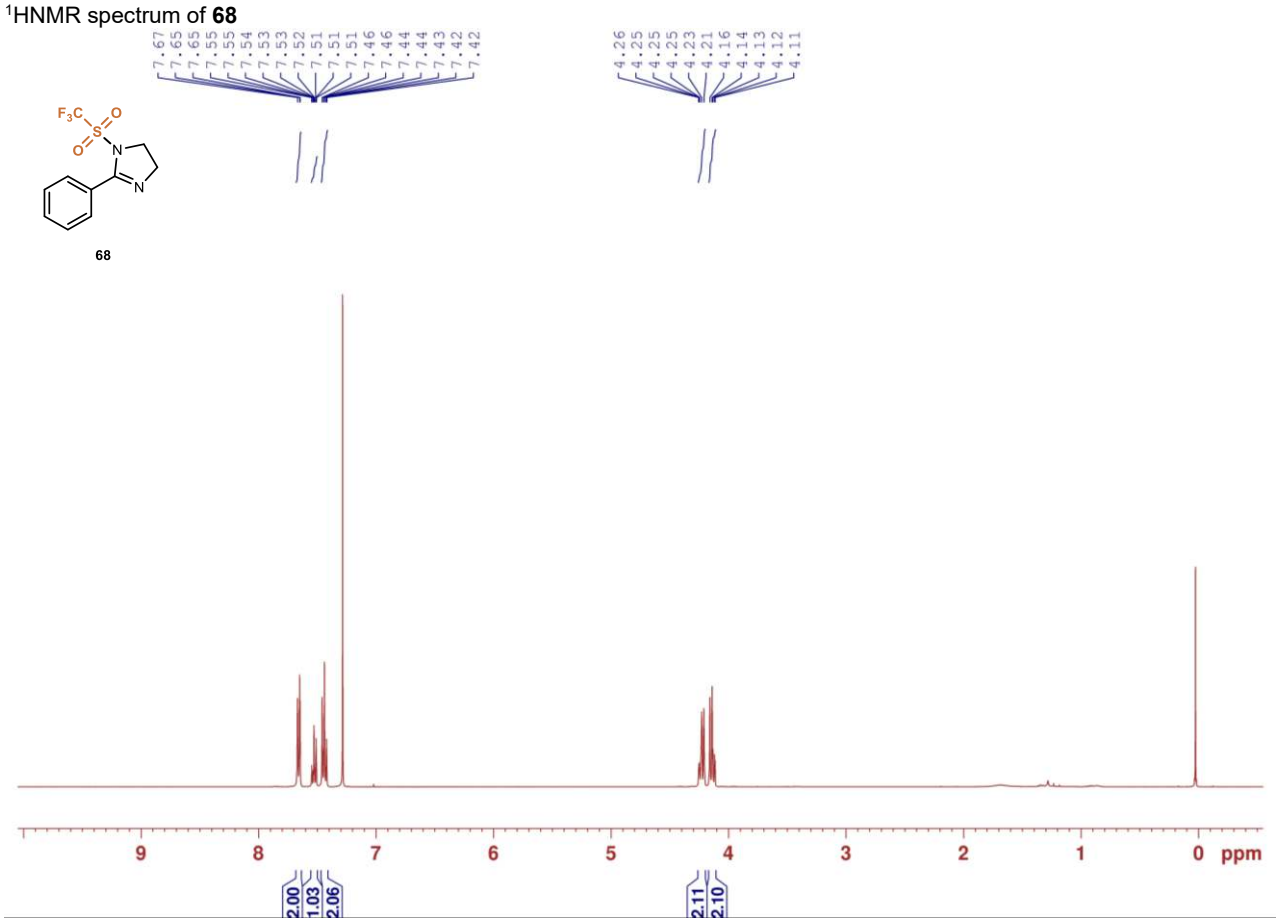
67

^{19}FNMR spectrum of **67**

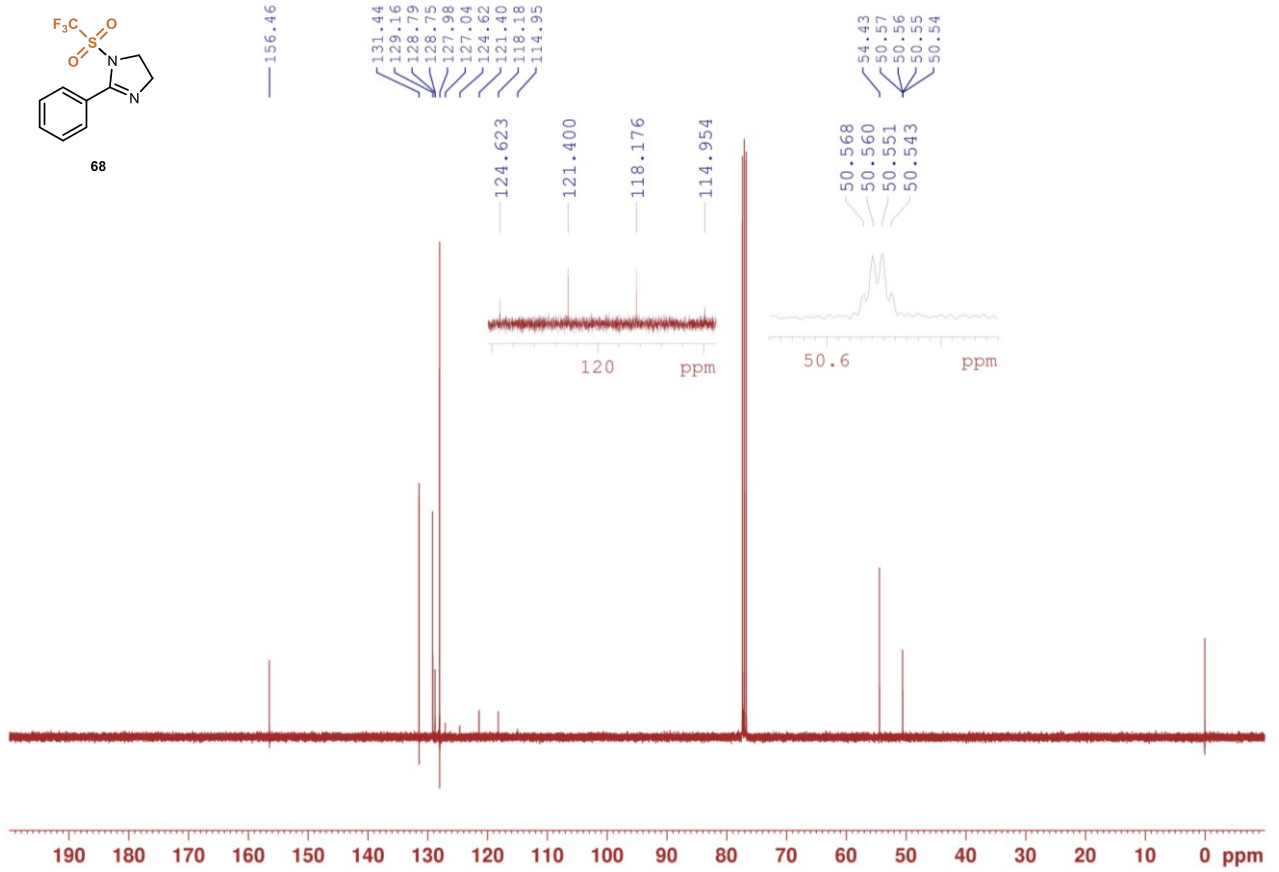


67

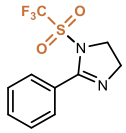
^{1}HNMR spectrum of **68**



^{13}CNMR spectrum of **68**

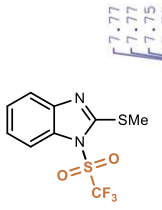


^{19}FNMR spectrum of **68**



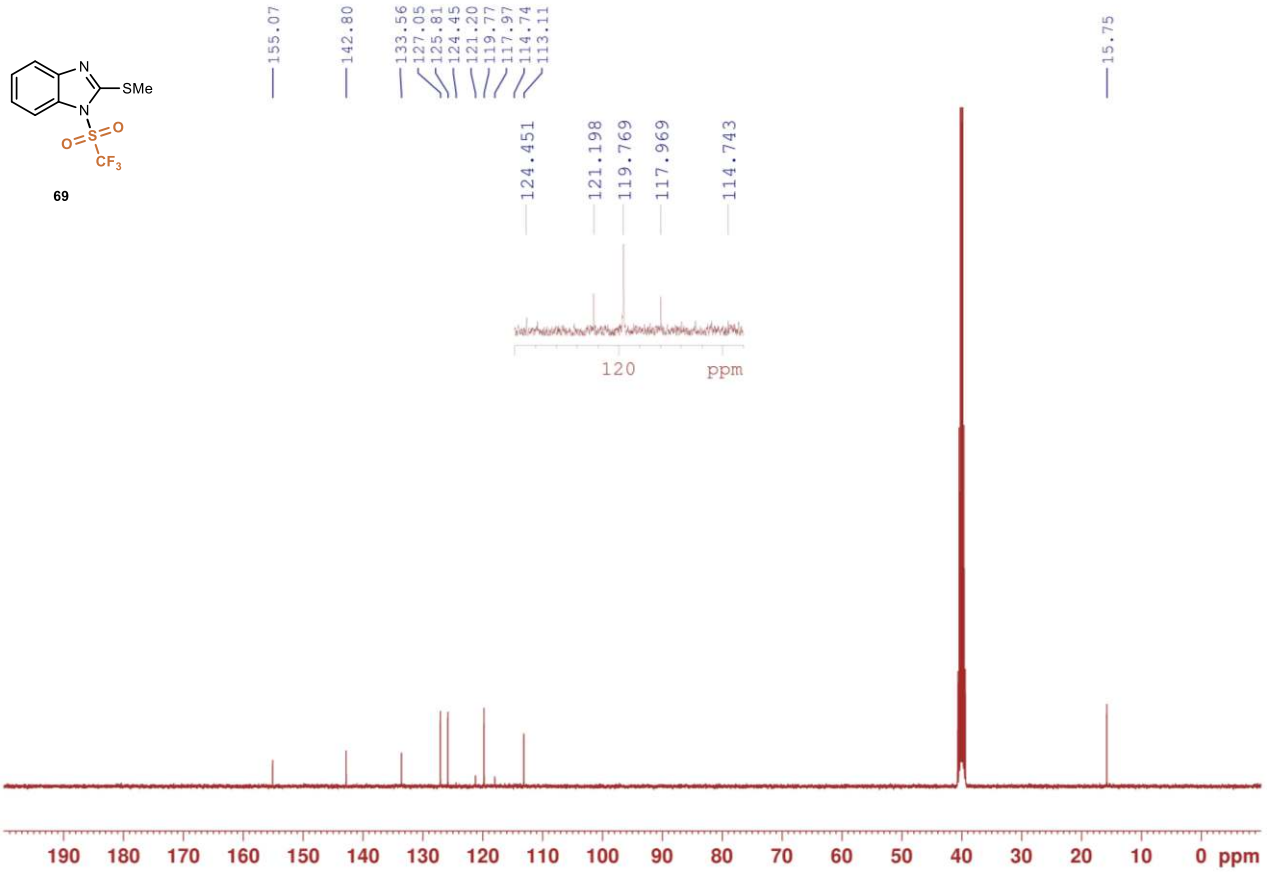
68

^{1}HNMR spectrum of **69** (DMSO-*d6*)

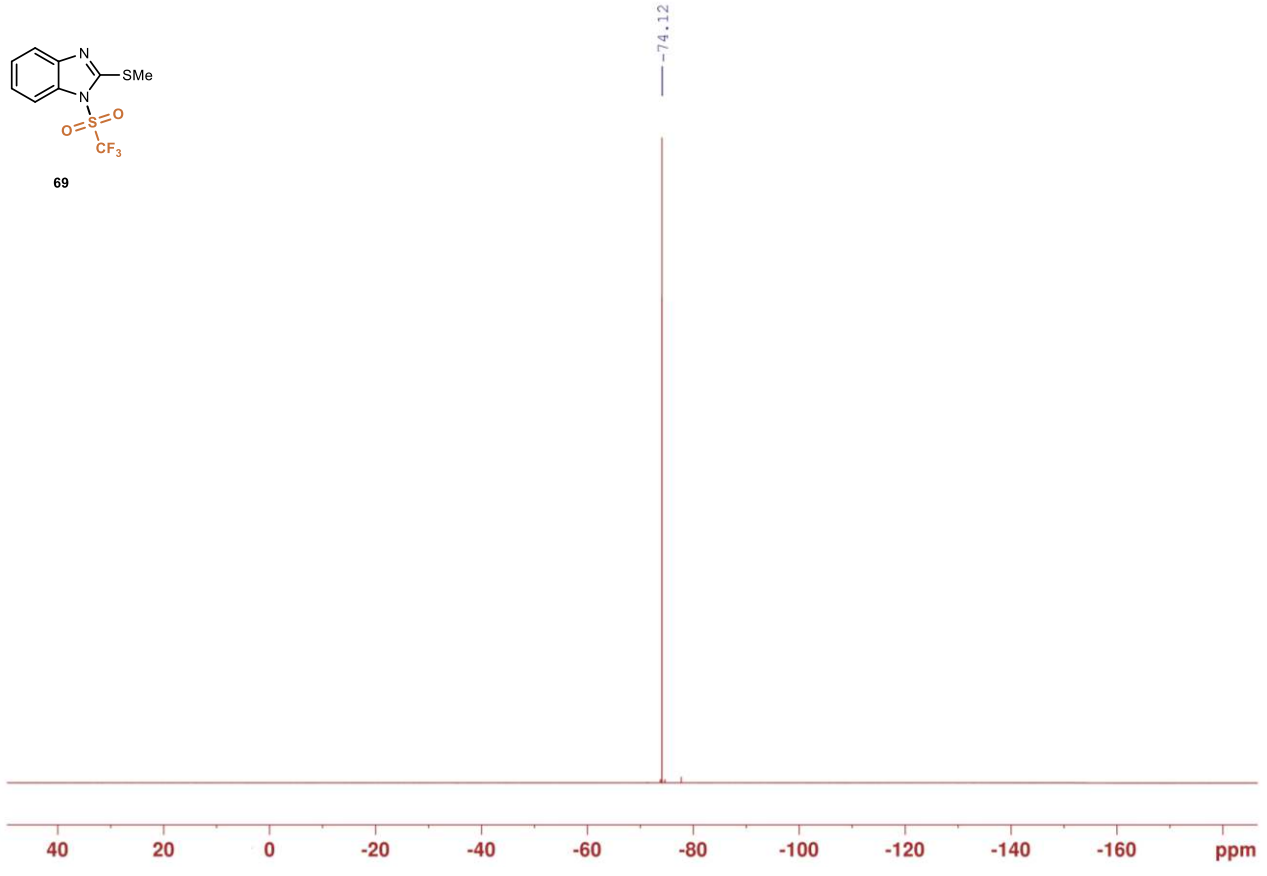


69

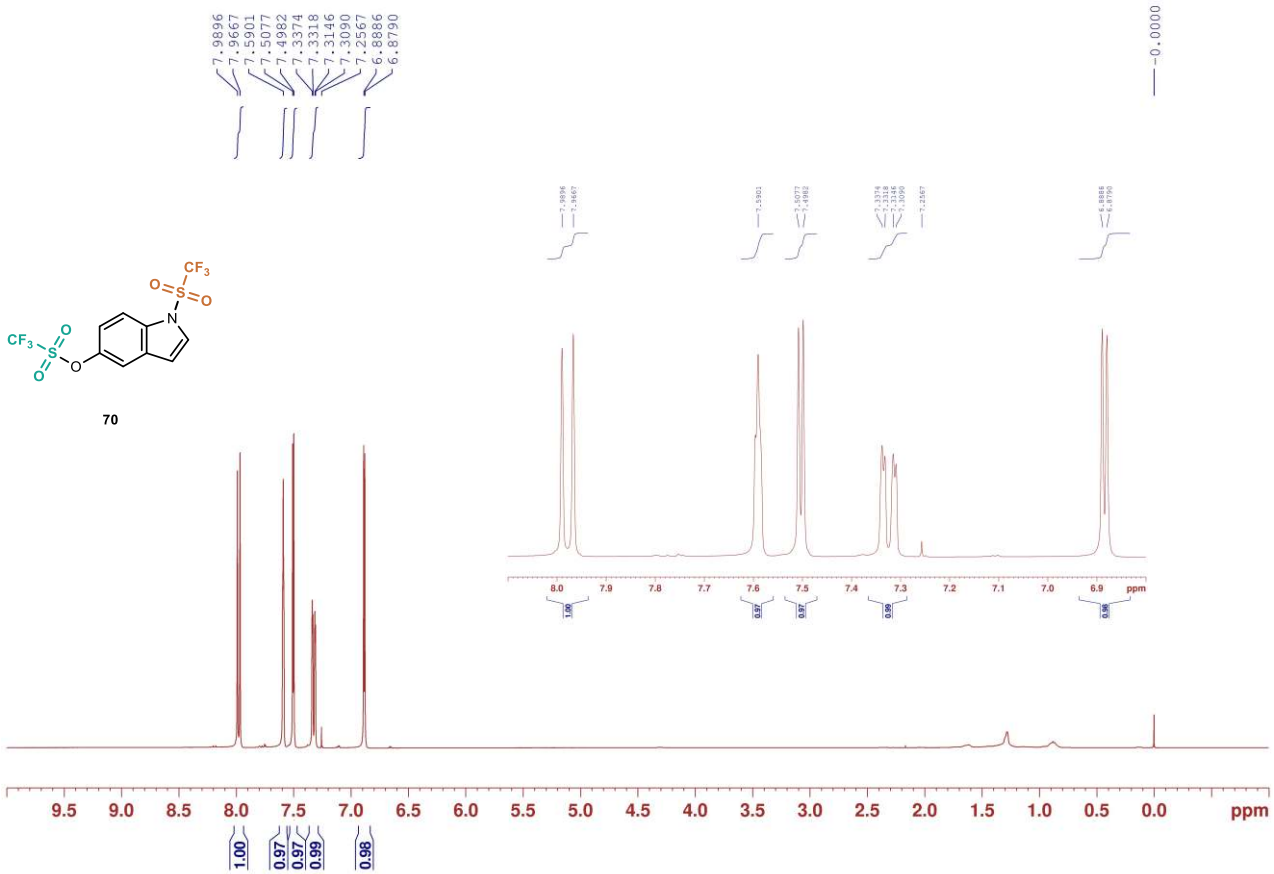
^{13}CNMR spectrum of **69** (DMSO-*d6*)



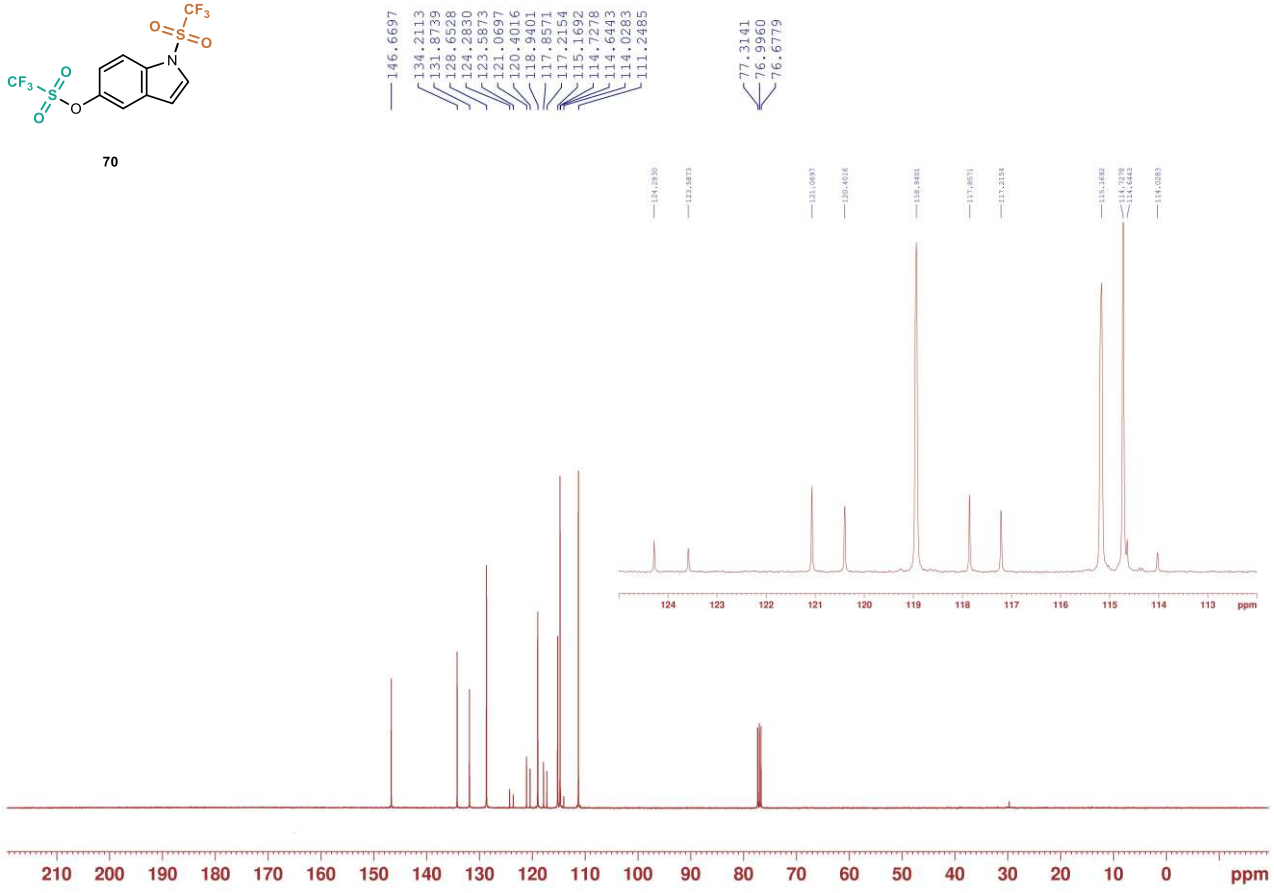
^{19}FNMR spectrum of **69** (DMSO-*d6*)



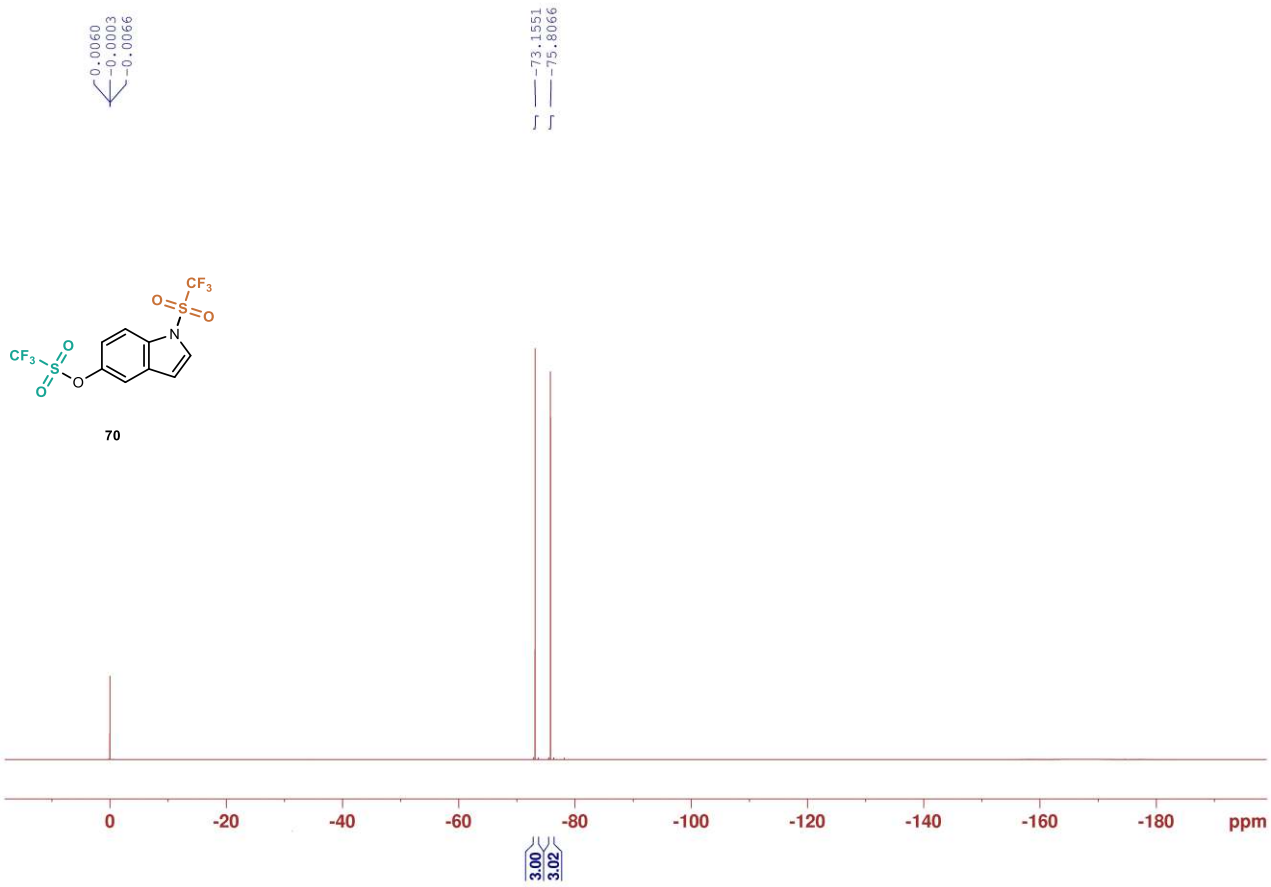
^{1}HNMR spectrum of **70**



^{13}CNMR spectrum of **70**

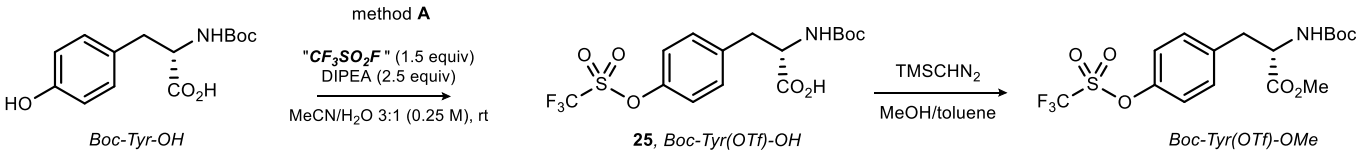


^{19}FNMR spectrum of **70**



10. Copies of the HPLC Spectra

To verify whether racemization had taken place under the triflation conditions of method **A** (**scheme 2** in the paper), tyrosine derivative **25** was subjected to chiral HPLC analysis for the separation of enantiomers. Because the carboxylic acid group of **25** was incompatible with the column, the compound was methylated to give the *N*,*O*-bisprotected derivative Boc-L-Tyr(OTf)-OMe as shown below. Separation conditions: CHIRALPAK® AD-H heptane/*i*PrOH 70:30 0.6 mL/min, (R) and (S)-enantiomers at 8.7 min and 12.4 min, respectively.

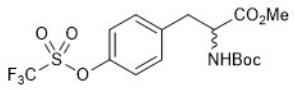


Boc-Tyr-OH **25**, *Boc-Tyr(OTf)-OH* *Boc-Tyr(OTf)-OMe*

Sample Name: jd4-rac
Data File: C:\CHEM32\2\DATA\JDEMAEREL\JD4-RAC-ADH1.D

Sample Info: AD-H, Hep/iPrOH = 70:30, 0.6 mL/min, 20 °C

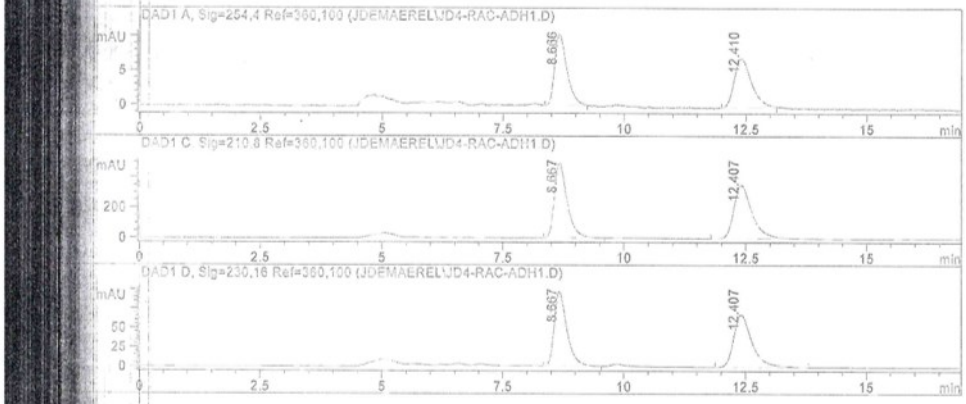
Instrument Name: 1200
Column program: C:\CHEM32\2\METHODS\MF_AD-H.M
Column info:
Operator: Marcus



Injection Time: 13:07:26
Injection Date: 4/12/2021

Injection Volume in µL: 10.0

Instrument Conditions:	At Start	At Stop
Temperature in °C:	26.1	23.0
Pressure in bar:	50.4	50.3
Flow in mL/min:	0.60	0.60



DAD1 A, Sig=254,4 Ref=360,100

Peak #	Ret. Time in min	Width in min	Height in mAU	Area in mAU*s	Area %
1	8.666	0.2924	10.36052	181.79144	50.7978
2	12.410	0.4134	7.05829	176.08147	49.2022
Total				357.87291	100.0000

DAD1 C, Sig=210,8 Ref=360,100

Peak #	Ret. Time in min	Width in min	Height in mAU	Area in mAU*s	Area %
1	8.667	0.2748	498.30981	9088.33496	49.7982
2	12.407	0.3899	351.68182	9162.00977	50.2018
Total				18250.34473	100.0000

DAD1 D, Sig=230,16 Ref=360,100

Peak #	Ret. Time in min	Width in min	Height in mAU	Area in mAU*s	Area %
1	8.667	0.3018	96.71703	1751.30481	49.7088
2	12.407	0.4353	67.84133	1771.82251	50.2912
Total				3523.12732	100.0000

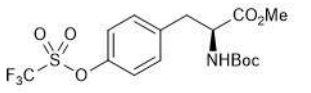
Sample Name: jd3
Data file: C:\CHEM32\2\DATA\JDEMAEREL\JD3-VERD.D

Sample Info: AD-H, Hep/iPrOH = 70:30, 0.6 mL/min, 20 °C

Instrument Name: 1200
Column program: C:\CHEM32\2\METHODS\MF_AD-H.M
Column info:
Operator: Marcus

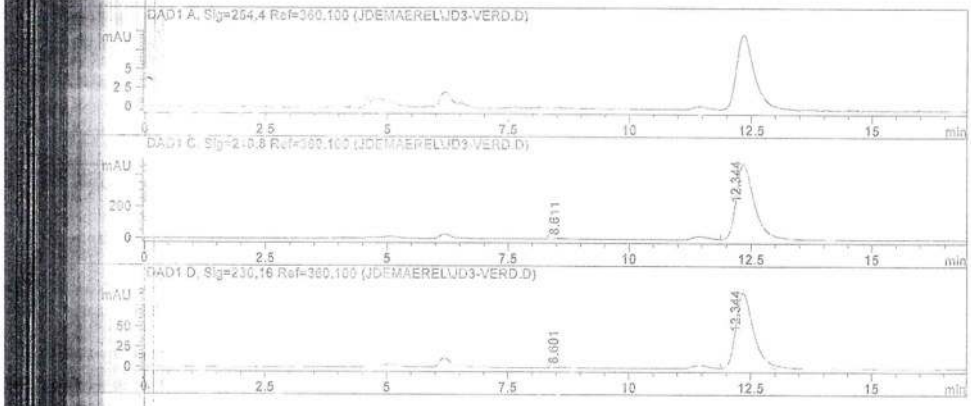
Injection Time: 14:03:01
Injection Date: 4/12/2021

Injection Volume in µL: 10.0



derived from **25** *(Boc-L-Tyr(OTf)-OH)*

Instrument Conditions:	At Start	At Stop
Temperature in °C:	26.4	23.3
Pressure in bar:	49.7	49.9
Flow in mL/min:	0.00	0.60



DAD1 A, Sig=254,4 Ref=360,100

Peak #	Ret. Time in min	Width in min	Height in mAU	Area in mAU*s	Area %
1	8.611	0.2644	3.43695	54.53382	0.4339
2	12.344	0.4340	480.53970	12512.33789	99.5661
Total				12566.87171	100.0000

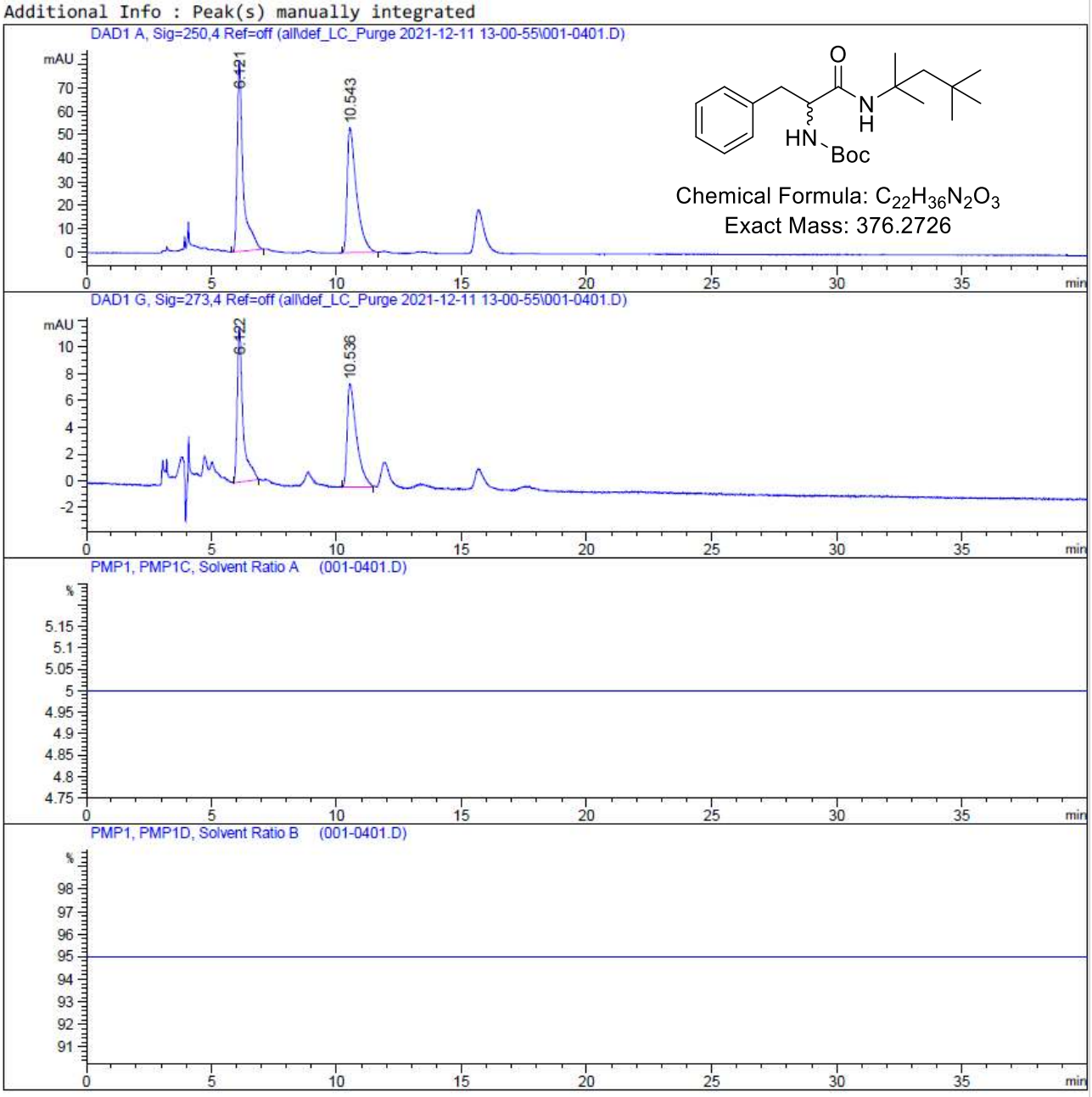
DAD1 D, Sig=230,16 Ref=360,100

Peak #	Ret. Time in min	Width in min	Height in mAU	Area in mAU*s	Area %
1	8.601	0.2438	0.70859	10.36619	0.4277
2	12.344	0.4333	92.83936	2413.57788	99.5723
Total				2423.94407	100.0000

Data File E:\Chem32\1\Data\all\def_LC_Purge 2021-12-11 13-00-55\001-0401.D
Sample Name: ly-71-r-12

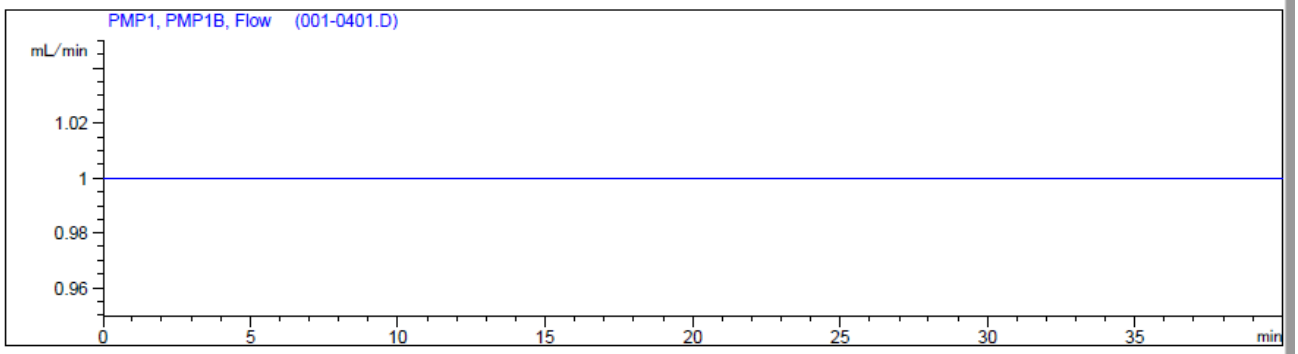
```
==========================================================================
Acq. Operator   : SYSTEM                          Seq. Line :   4
Acq. Instrument : HPLC-2                           Location :   1
Injection Date  : 12/11/2021 1:43:38 PM                Inj :   1
                                                 Inj Volume : 5.000 µl
Different Inj Volume from Sample Entry!  Actual Inj Volume : 8.000 µl
Method          : E:\Chem32\1\Data\all\def_LC_Purge 2021-12-11 13-00-55\AD_hex95_iPrOH5_1.0mL
                  _40min.M (Sequence Method)
Last changed    : 12/11/2021 1:01:01 PM by SYSTEM
Method Info     : Test

Additional Info : Peak(s) manually integrated
```



Chemical Formula: $C_{22}H_{36}N_2O_3$
Exact Mass: 376.2726

Data File E:\Chem32\1\Data\all\def_LC_Purge 2021-12-11 13-00-55\001-0401.D
Sample Name: ly-71-r-12



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Area Percent Report

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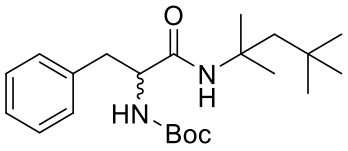
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.121	BB	0.2383	1350.74524	81.09950	49.4625
2	10.543	BB	0.3601	1380.10413	53.12610	50.5375
Totals :				2730.84937	134.22561	



Chemical Formula: $C_{22}H_{36}N_2O_3$
Exact Mass: 376.2726

Signal 2: DAD1 G, Sig=273,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.122	BB	0.2237	187.00113	11.56401	48.6384
2	10.536	BB	0.3155	197.47086	7.64063	51.3616
Totals :				384.47198	19.20464	

==========

*** End of Report ***

Data File E:\Chem32\1\Data\all\def_LC_Purge 2021-12-13 11-22-10\OnlineEdited0.D
Sample Name: ly-71-c-6

```
======================================================================
Acq. Operator   : SYSTEM                        Seq. Line :   5
Acq. Instrument : HPLC-2                         Location :   91
Injection Date  : 12/13/2021 12:35:33 PM              Inj :   1
                                                Inj Volume : 5.000 µl
Different Inj Volume from Sample Entry!  Actual Inj Volume : 8.000 µl
Method          : E:\Chem32\1\Data\all\def_LC_Purge 2021-12-13 11-22-10\AD_hex95_iPrOH5_1.0mL
                  _20min.M (Sequence Method)
Last changed    : 12/13/2021 11:34:57 AM by SYSTEM
Method Info     : Test

Additional Info : Peak(s) manually integrated
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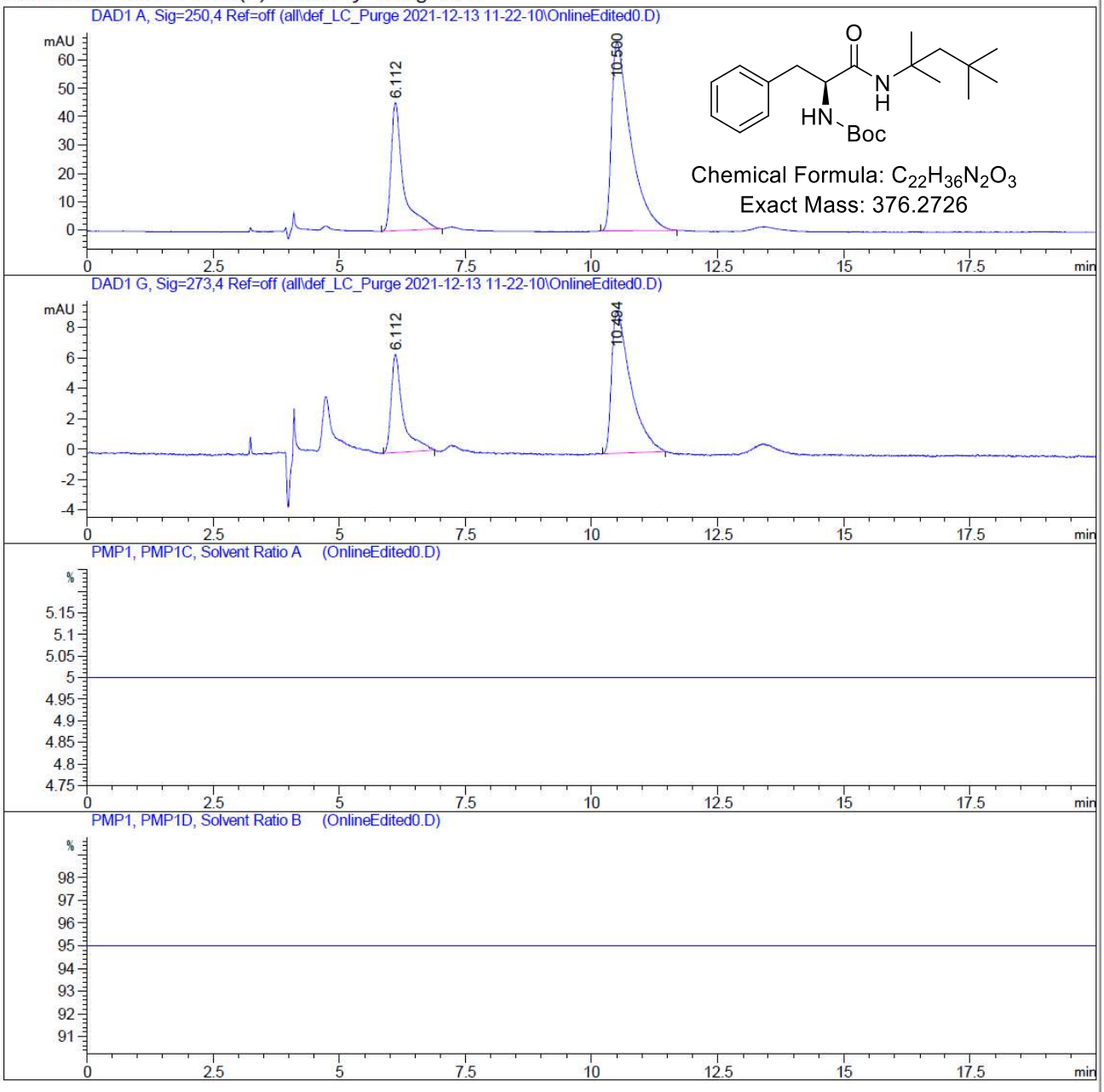
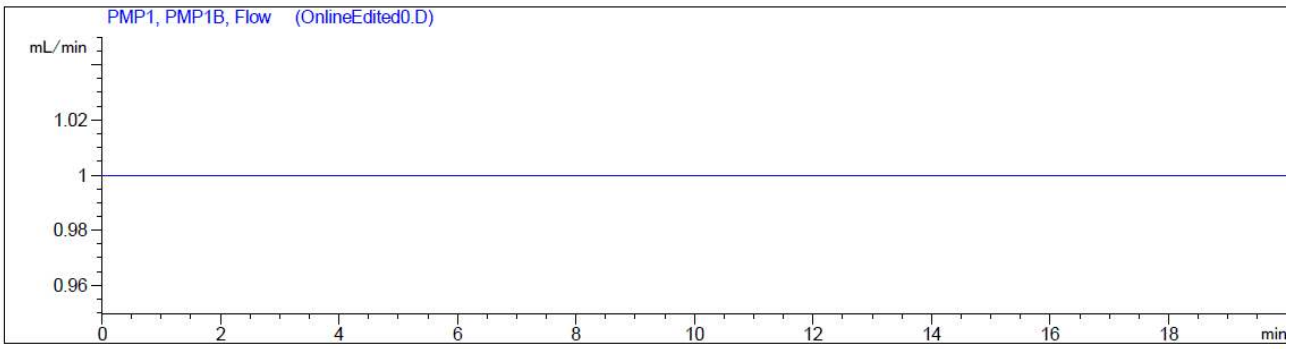


Data File E:\Chem32\1\Data\all\def_LC_Purge 2021-12-13 11-22-10\OnlineEdited0.D
Sample Name: ly-71-c-6



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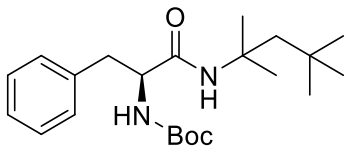
Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs



Chemical Formula: $C_{22}H_{36}N_2O_3$
Exact Mass: 376.2726

Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.112	BB	0.2408	764.91138	45.35095	30.3219
2	10.500	BB	0.3578	1757.72583	66.62794	69.6781
Totals :				2522.63721	111.97889	

Signal 2: DAD1 G, Sig=273,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.112	BB	0.2131	105.79185	6.45851	30.1656
2	10.494	BB	0.3157	244.91148	9.37764	69.8344
Totals :				350.70334	15.83614	

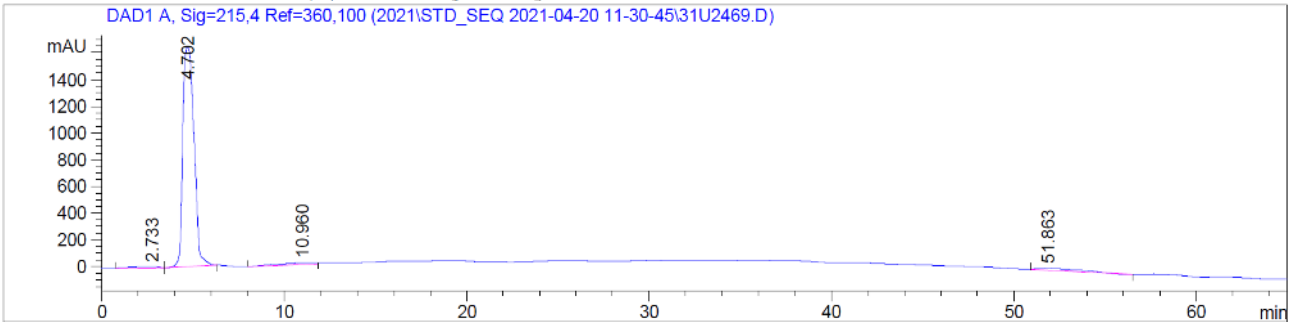
==========

*** End of Report ***

11. Copies of the LC-MS Spectra

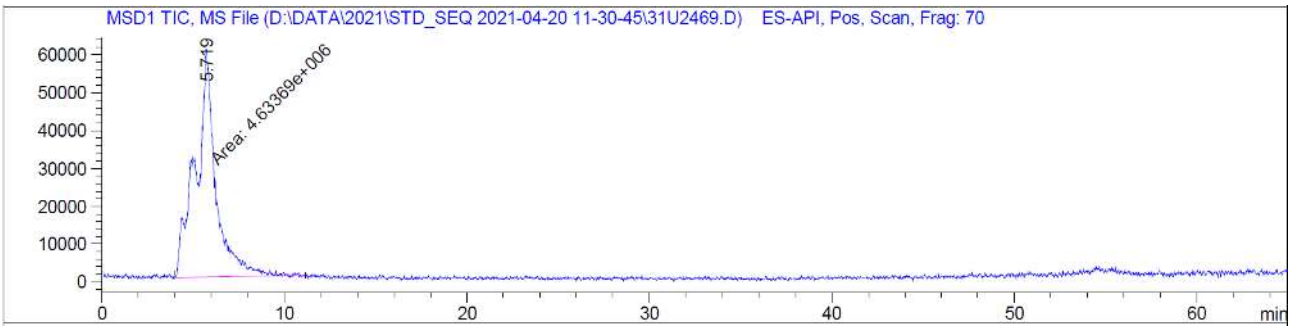
LC-MS spectra of *L*-Tyrosine (starting material of 30)

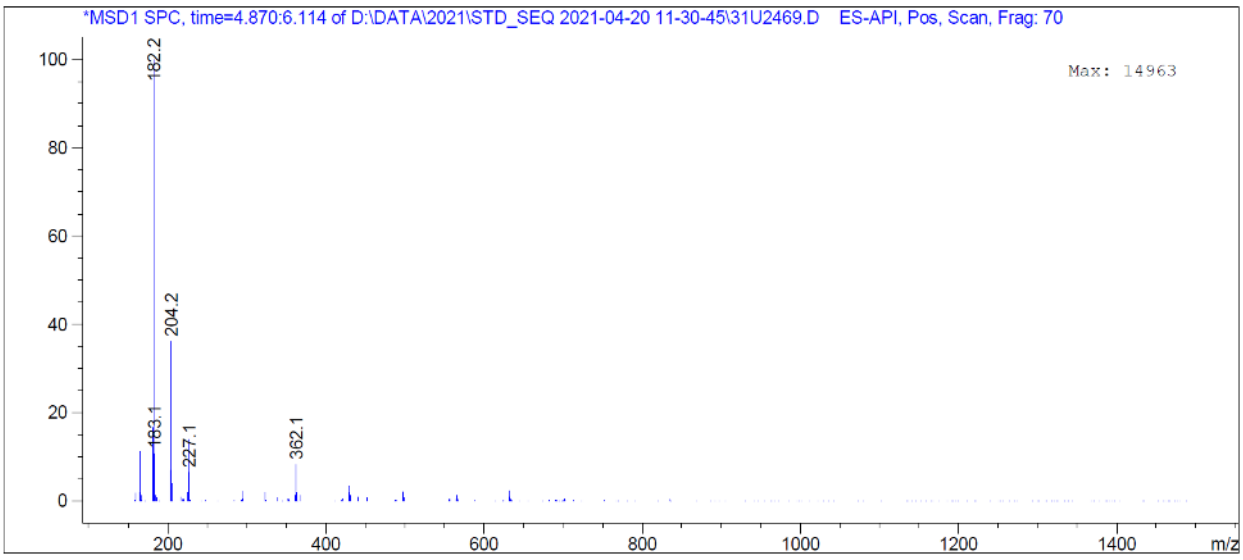
```
======================================================================
Acq. Operator   :                                Seq. Line :  25
Acq. Instrument : Instrument 1                    Location : Vial 31
Injection Date  : 20/04/2021 23:22:14                 Inj :   1
                                                 Inj Volume : 10.0 µl
Acq. Method     : D:\DATA\2021\STD_SEQ 2021-04-20 11-30-45\DA_40-40-70-100_20-
Last changed    : 5/03/2010 15:30:00 by bds
Analysis Method : D:\METHODS\KOLOM 2\PREVAIL3U\DA_0-60_20MIN_+.M
Last changed    : 20/04/2021 11:36:06
Additional Info : Peak(s) manually integrated
```




```
MS Signal: MSD1 TIC, MS File,  ES-API, Pos, Scan, Frag: 70
    Spectra averaged over upper half of peaks.
    Noise Cutoff: 1000 counts.
    Reportable Ion Abundance: > 10%.
```

Retention Time (MS)	MS Area	Mol. Weight or Ion
5.719	4633693	226.20 I
		204.20 I
		183.15 I
		182.20 I
		181.55 I
		165.20 I

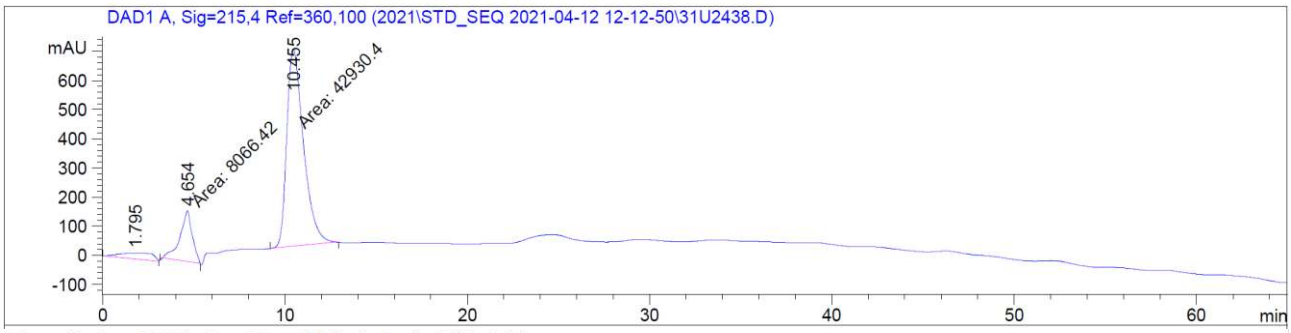




*** End of Report ***

LC-MS spectra of *L*-Tyrosine triflate (30) _first test

```
================================================================================
Acq. Operator   :                                  Seq. Line :  28
Acq. Instrument : Instrument 1                      Location : Vial 39
Injection Date  : 13/04/2021 3:03:02                    Inj :   1
                                                  Inj Volume : 10.0 µl
Acq. Method     : D:\DATA\2021\STD_SEQ 2021-04-12 12-12-50\DA_40-40-70-100_20-
Last changed    : 5/03/2010 15:30:00 by bds
Analysis Method : D:\METHODS\KOLOM 2\PREVAIL3U\BA_0-100-100_40-10MIN_+.M
Last changed    : 13/04/2021 12:41:00
Additional Info : Peak(s) manually integrated
================================================================================
```

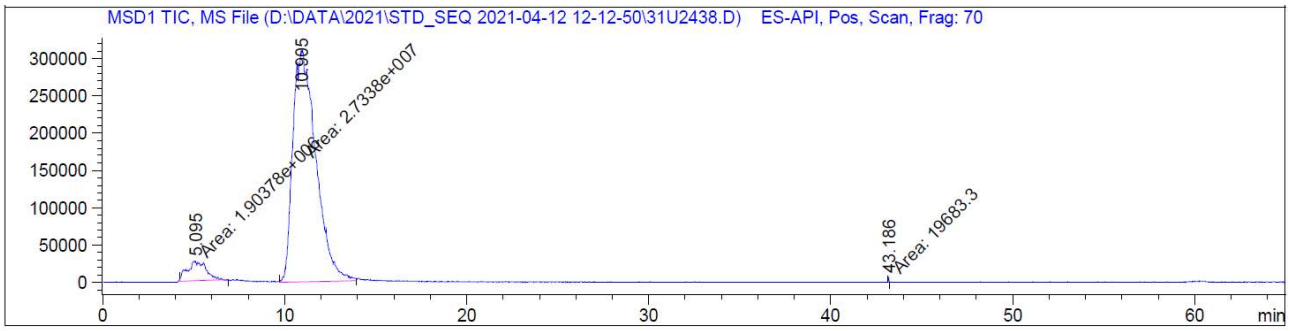


Signal 1: DAD1 A, Sig=215,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.795	BV	1.5395	2757.19385	21.00307	5.1293
2	4.654	MM	0.7729	8066.42334	173.95300	15.0062
3	10.455	MM	1.0579	4.29304e4	676.34216	79.8645

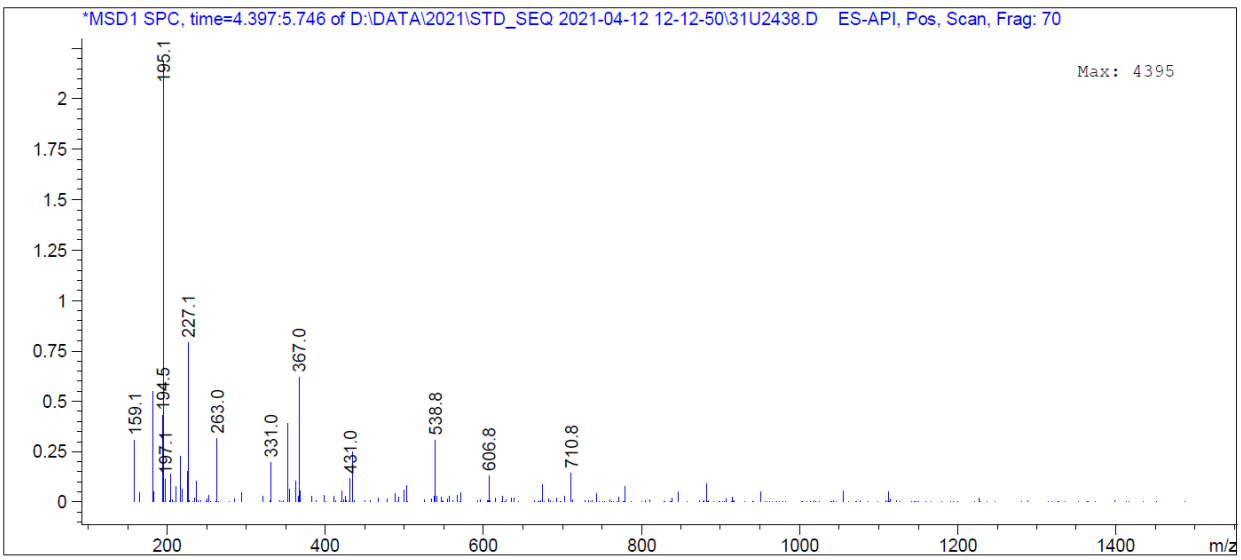
MS Signal: MSD1 TIC, MS File, ES-API, Pos, Scan, Frag: 70
    Spectra averaged over upper half of peaks.
    Noise Cutoff: 1000 counts.
    Reportable Ion Abundance: > 10%.

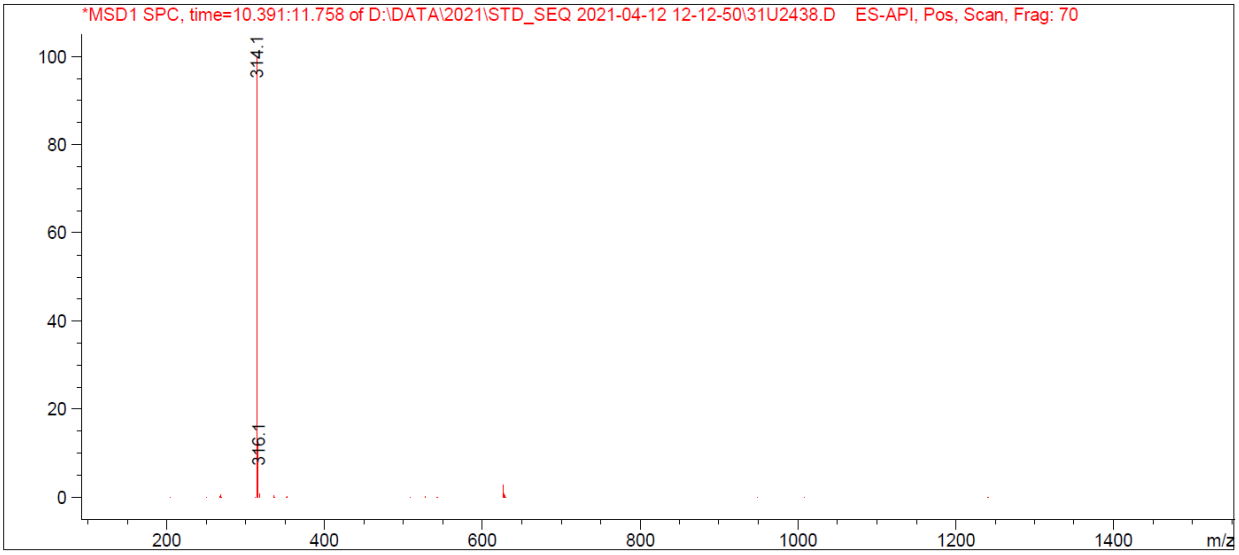
Retention Time (MS)	MS Area	Mol. Weight or Ion
5.095	1903775	366.95 I
		227.10 I
		195.05 I
		182.20 I
10.905	27338038	315.10 I
		314.15 I
43.186	19683	1330.80 I

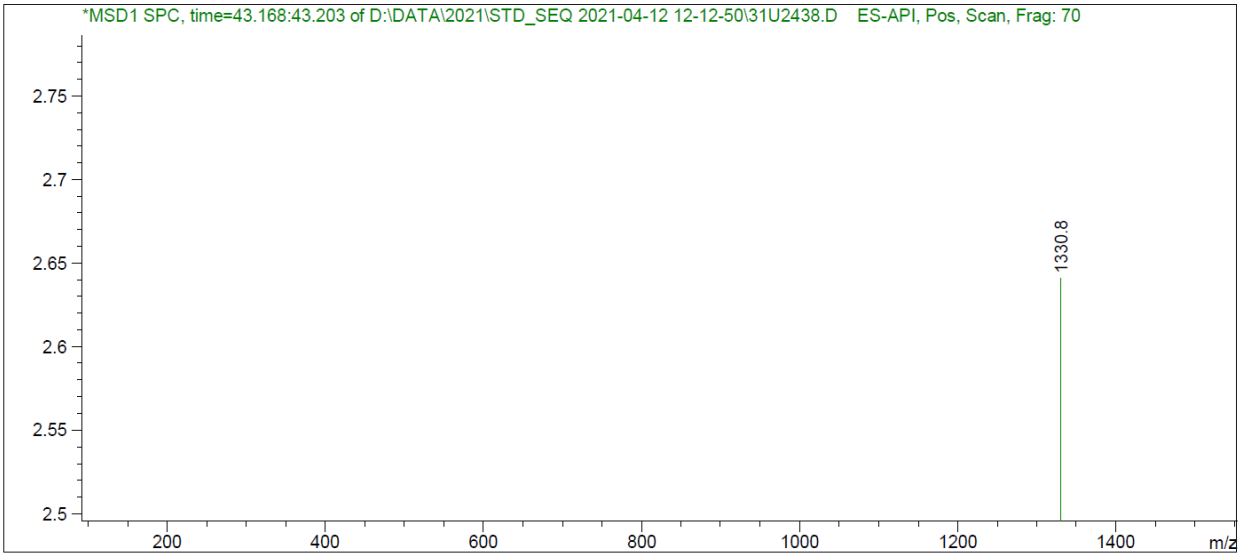


Peak #	RetTime [min]	Type	Width [min]	Area	Height	Area %
1	5.095	MM	1.2092	1.90378e6	2.62392e4	6.5061
2	10.905	MM	1.4598	2.73380e7	3.12131e5	93.4267
3	43.186	MM	0.0491	1.96833e4	6675.27344	0.0673
Totals :				2.92615e7	3.45045e5	

==========



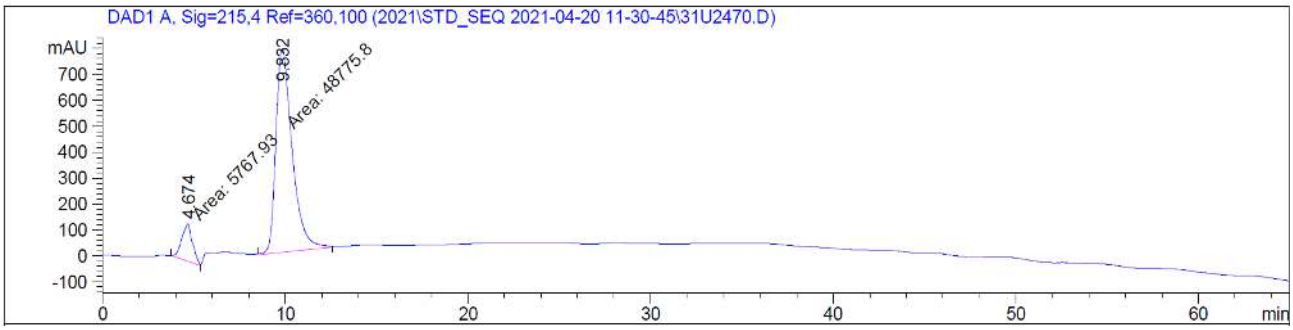




*** End of Report ***

LC-MS spectra of *L*-Tyrosine triflate (30) _second test

```
=====================================================================
Acq. Operator   :                                Seq. Line :  28
Acq. Instrument : Instrument 1                    Location : Vial 32
Injection Date  : 21/04/2021 1:11:12                   Inj :   1
                                                Inj Volume : 10.0 µl
Acq. Method     : D:\DATA\2021\STD_SEQ 2021-04-20 11-30-45\DA_40-40-70-100_20-
Last changed    : 5/03/2010 15:30:00 by bds
Analysis Method : D:\METHODS\KOLOM 2\PREVAIL3U\DA_0-60_20MIN_+.M
Last changed    : 21/04/2021 15:33:41
                  (modified after loading)
Additional Info : Peak(s) manually integrated
```

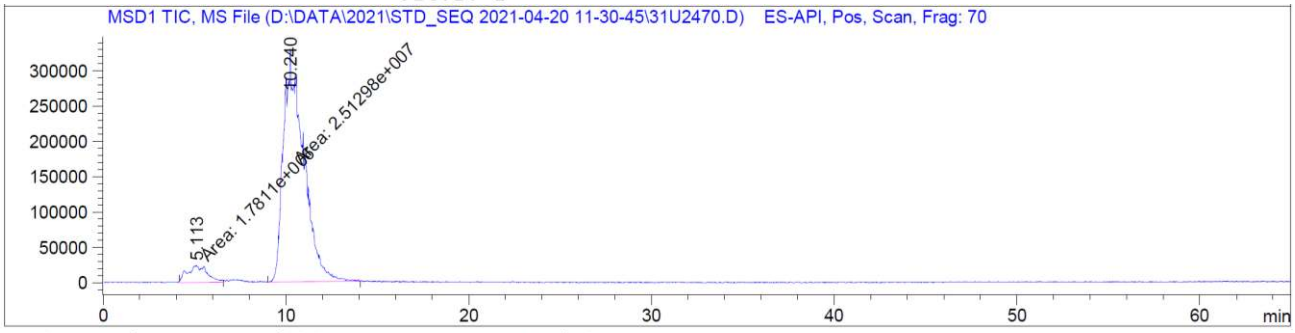


Signal 1: DAD1 A, Sig=215,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.674	MM	0.6636	5767.93066	144.85756	10.5749
2	9.832	MM	1.0359	4.87758e4	784.72253	89.4251
Totals :				5.45437e4	929.58009	

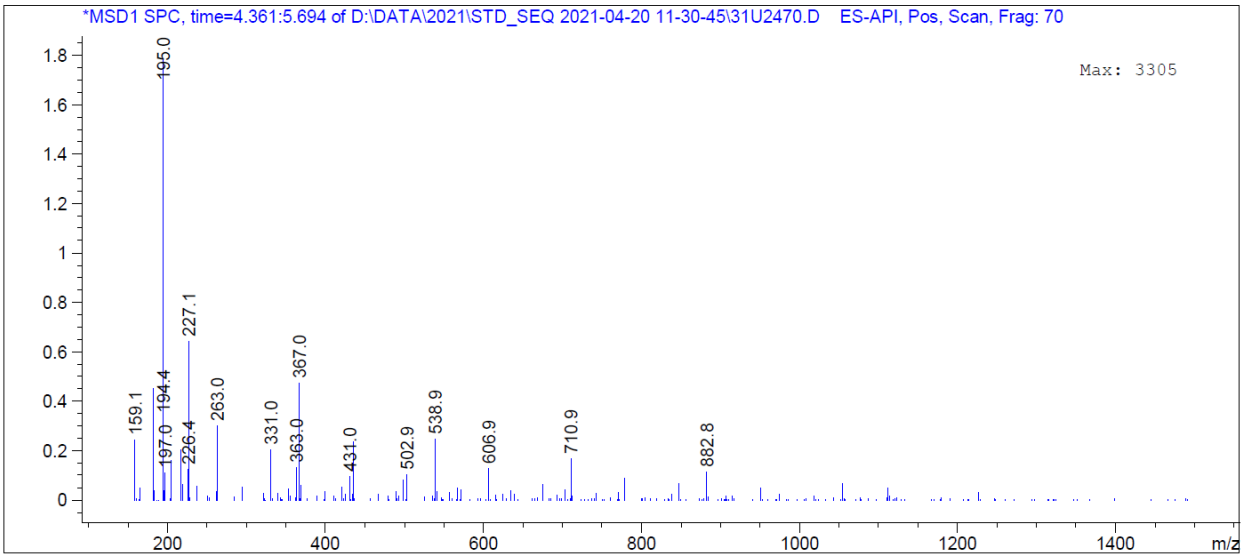
MS Signal: MSD1 TIC, MS File, ES-API, Pos, Scan, Frag: 70
Spectra averaged over upper half of peaks.
Noise Cutoff: 1000 counts.
Reportable Ion Abundance: > 10%.

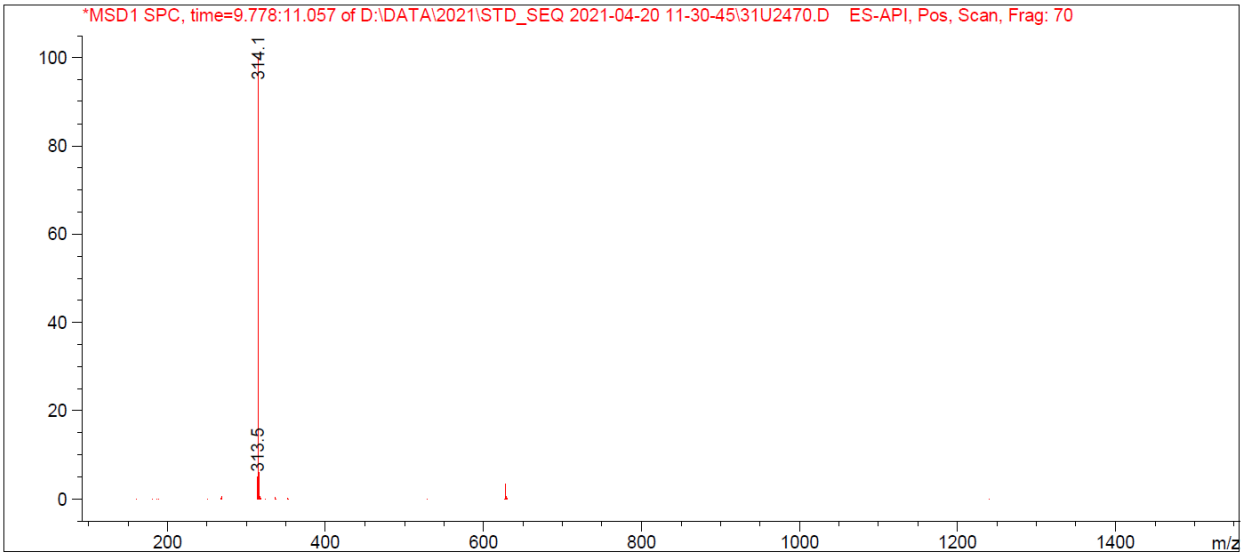
Retention Time (MS)	MS Area	Mol. Weight or Ion
5.113	1781098	227.05 I
		195.00 I
10.240	25129796	315.10 I
		314.10 I



Peak #	RetTime [min]	Type	Width [min]	Area	Height	Area %
1	5.113	MM	1.2359	1.78110e6	2.40197e4	6.6185
2	10.240	MM	1.2469	2.51298e7	3.35909e5	93.3815
Totals :				2.69109e7	3.59929e5	

==========

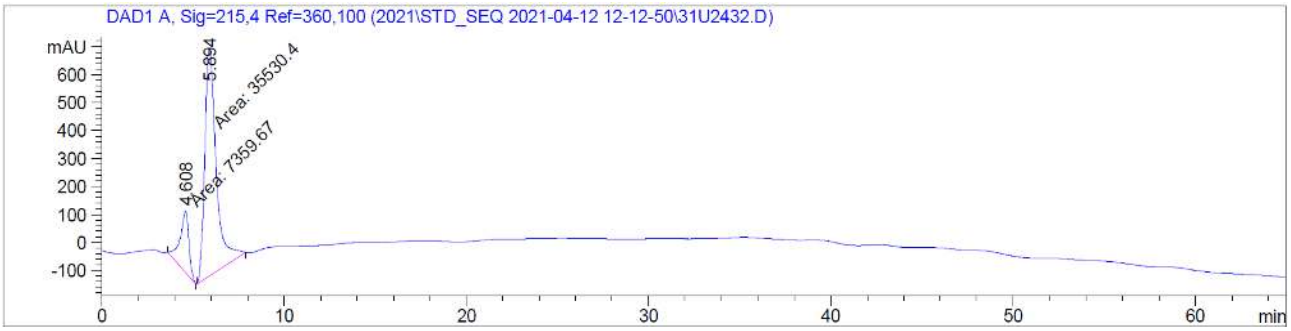




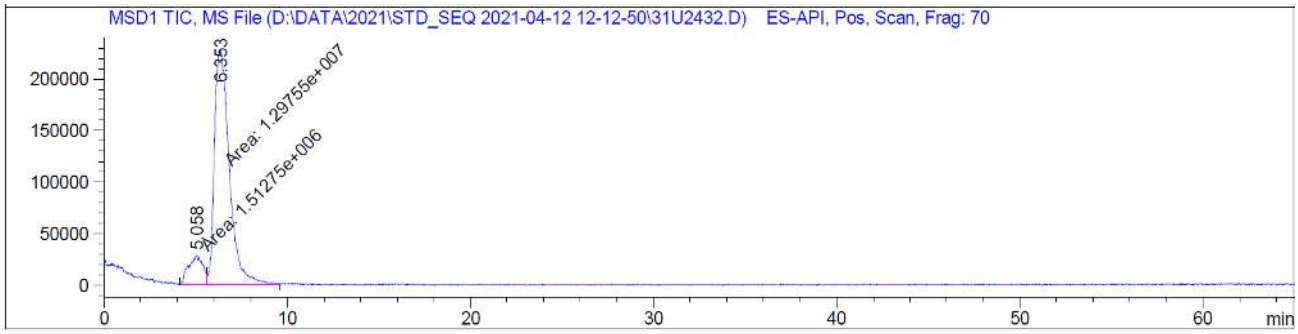
*** End of Report ***

LC-MS spectra of Leu-enkephalin (starting material of 31)

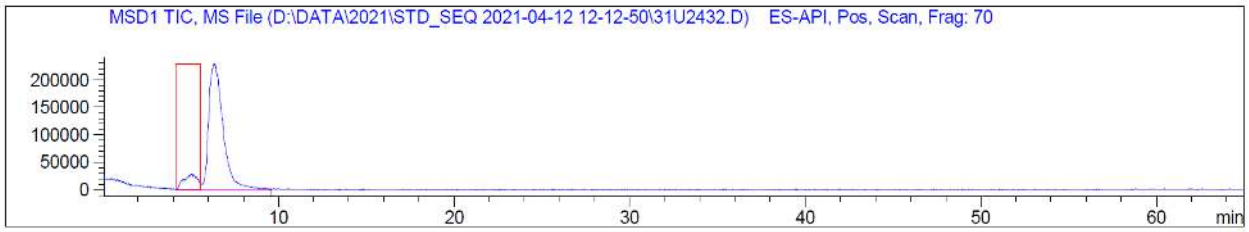
```
==================================================================
Acq. Operator   :                                Seq. Line :   3
Acq. Instrument : Instrument 1                    Location : Vial 35
Injection Date  : 12/04/2021 12:58:04                 Inj :   1
                                                 Inj Volume : 10.0 µl
Acq. Method     : D:\DATA\2021\STD_SEQ 2021-04-12 12-12-50\DA_40-40-70-100_20-
Last changed    : 5/03/2010 15:30:00 by bds
Analysis Method : D:\DATA\2021\STD_SEQ 2021-05-07 10-41-44\BA_STAB0_20MIN_+_SELAM.M
Last changed    : 7/05/2021 15:53:20
                  (modified after loading)
Additional Info : Peak(s) manually integrated
```

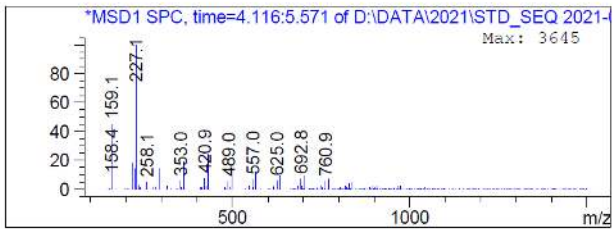


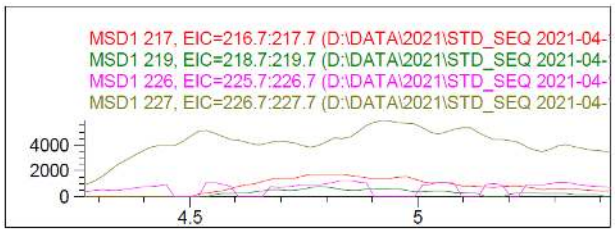

```
Signal 1: DAD1 A, Sig=215,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.608 MM    0.5553 7359.66553  220.89052  17.1594
   2   5.894 MM    0.7283 3.55304e4   813.12646  82.8406

Totals :                  4.28900e4  1034.01698
==================================================================
```



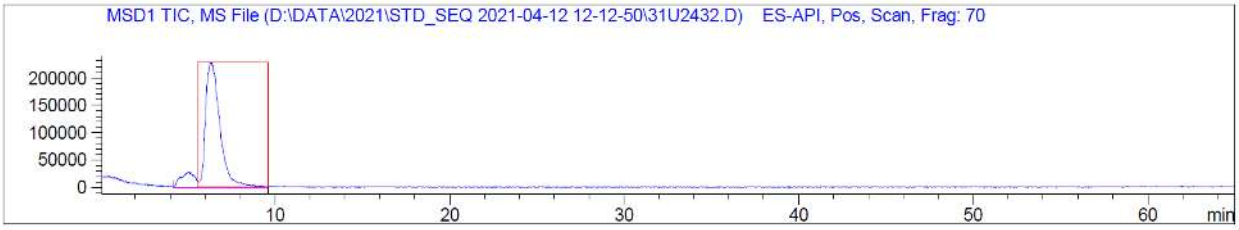

```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]                          %
----|-------|----|-------|----------|----------|--------|
   1   5.058 MF    0.8761 1.51275e6  2.87785e4   10.4412
   2   6.353 FM    0.9465 1.29755e7  2.28488e5   89.5588

Totals :                  1.44883e7  2.57266e5
==================================================================
```

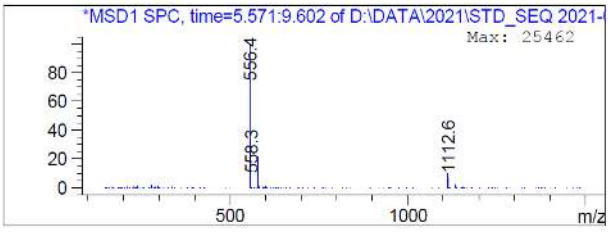


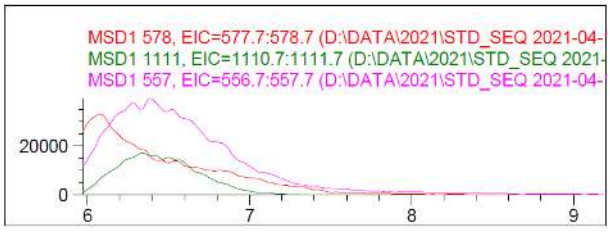




Peak #1 at 5.058 min (4.124 to 5.567 min)





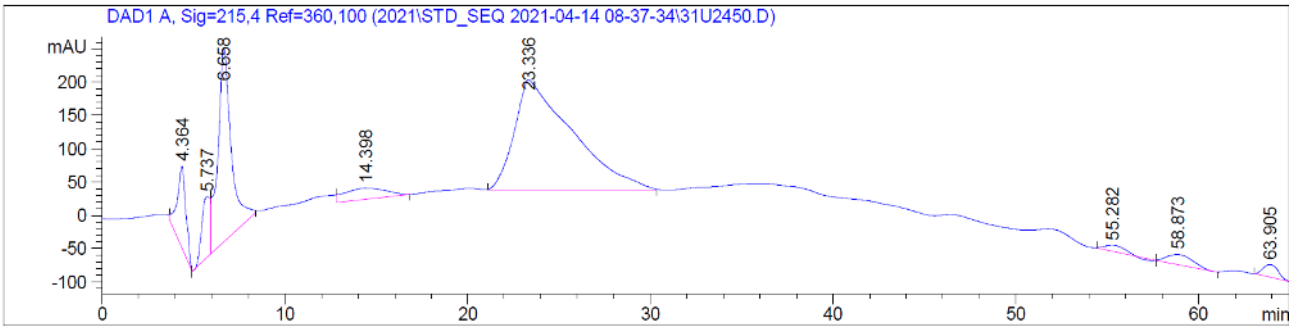


Peak #2 at 6.353 min (5.567 to 9.606 min)

*** End of Report ***

LC-MS spectra of Leu-enkephalin triflate (31) _first test

```
==================================================================
Acq. Operator   :                                Seq. Line :  31
Acq. Instrument : Instrument 1                    Location : Vial 11
Injection Date  : 14/04/2021 23:14:45                  Inj :   1
                                                 Inj Volume : 10.0 µl
Acq. Method     : D:\DATA\2021\STD_SEQ 2021-04-14 08-37-34\DA_40-40-70-100_20-
Last changed    : 5/03/2010 15:30:00 by bds
Analysis Method : D:\DATA\2021\STD_SEQ 2021-05-07 10-41-44\BA_STAB0_20MIN_+_SELAM.M
Last changed    : 7/05/2021 16:05:19
                  (modified after loading)
Additional Info : Peak(s) manually integrated
```



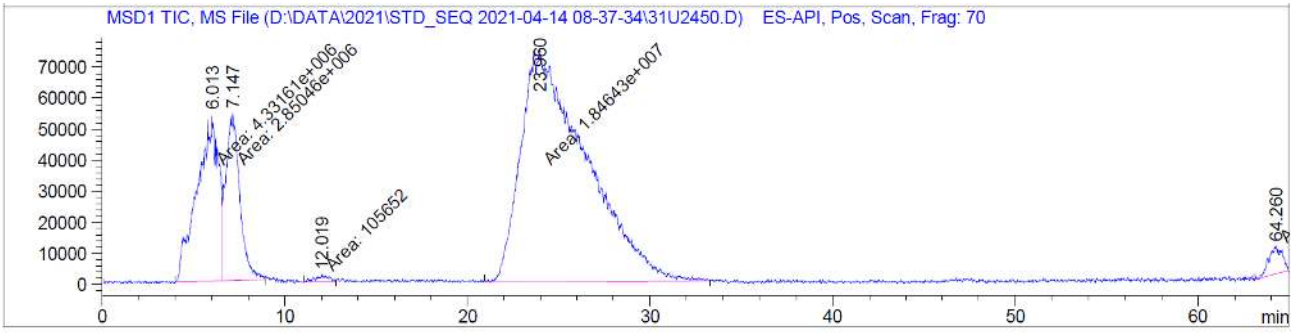

```
Signal 1: DAD1 A, Sig=215,4 Ref=360,100
```

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.364	BV	0.4607	4020.65308	123.21447	6.3293
2	5.737	VV	0.4657	2902.80347	90.61417	4.5696
3	6.658	VB	0.7006	1.47658e4	290.70630	23.2441
4	14.398	BV	1.8187	2575.91650	16.57844	4.0550
5	23.336	BB	2.6258	3.61303e4	165.31367	56.8759
6	55.282	BB	0.7918	576.43280	8.58016	0.9074
7	58.873	BV	1.1495	1459.35693	14.99378	2.2973
8	63.905	BBA	0.6972	1093.51245	18.83832	1.7214
Totals :				6.35247e4	728.83930	

```
==================================================================
```

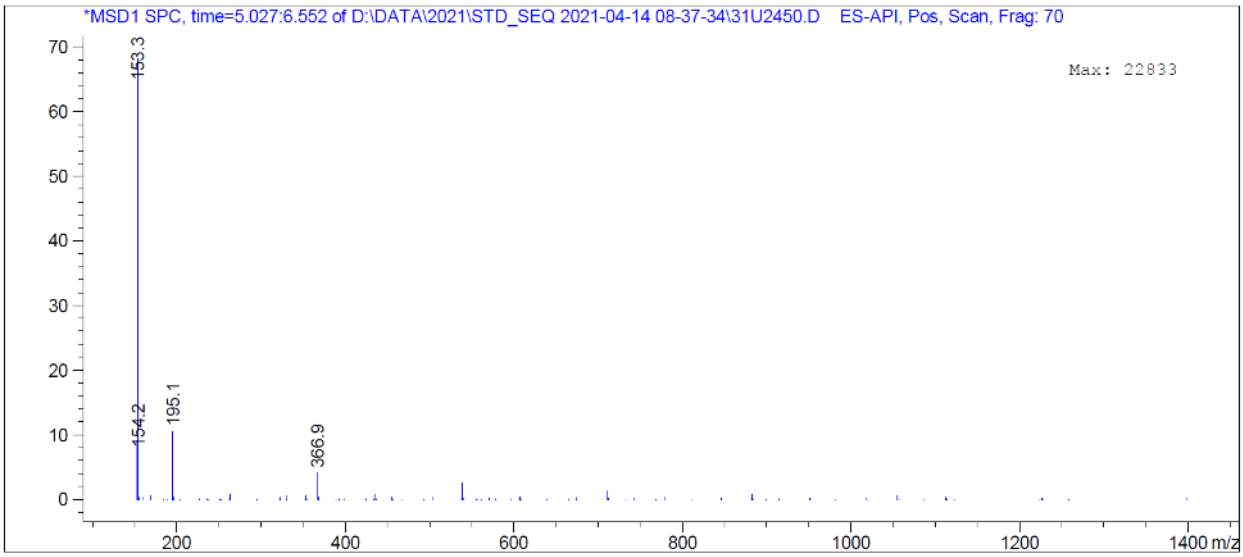
MS Signal: MSD1 TIC, MS File, ES-API, Pos, Scan, Frag: 70
Spectra averaged over upper half of peaks.
Noise Cutoff: 1000 counts.
Reportable Ion Abundance: > 10%.

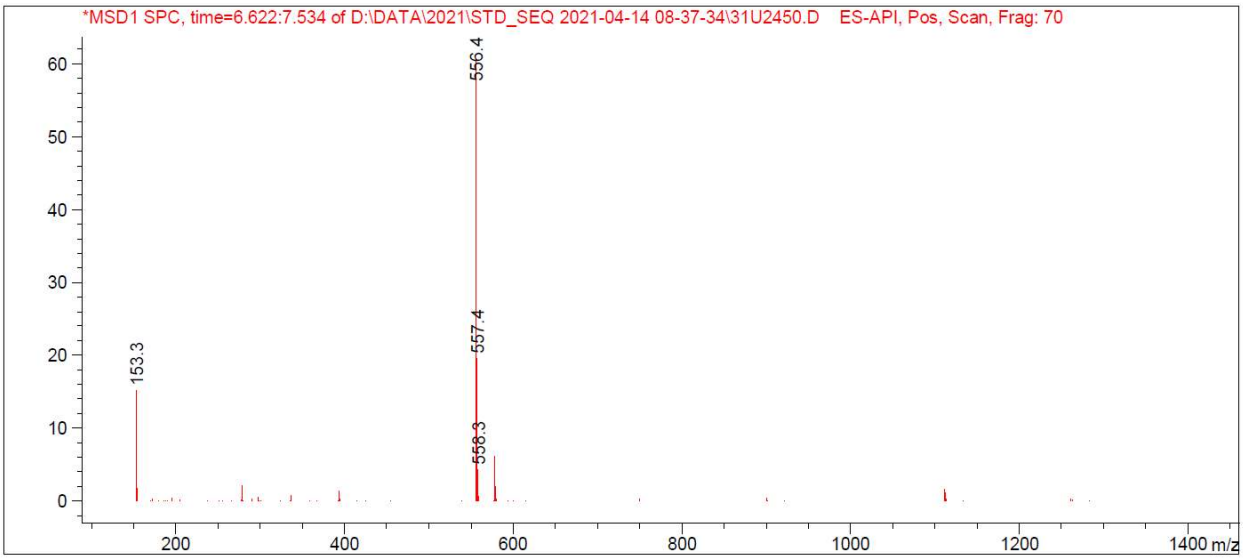
Retention Time (MS)	MS Area	Mol. Weight or Ion
6.013	4331612	195.10 I
		154.20 I
		153.30 I
		152.65 I
7.147	2850464	578.30 I
		557.40 I
		556.40 I
		153.30 I
12.019	105652	
23.960	18464312	690.30 I
		689.30 I
		688.30 I
64.260	449081	692.30 I
		670.25 I

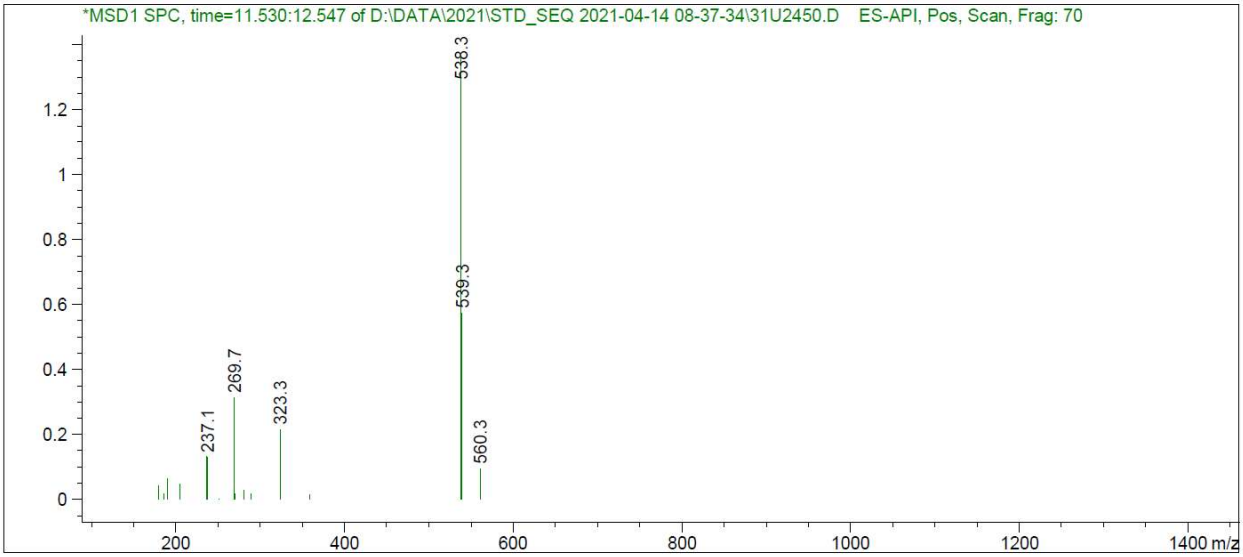


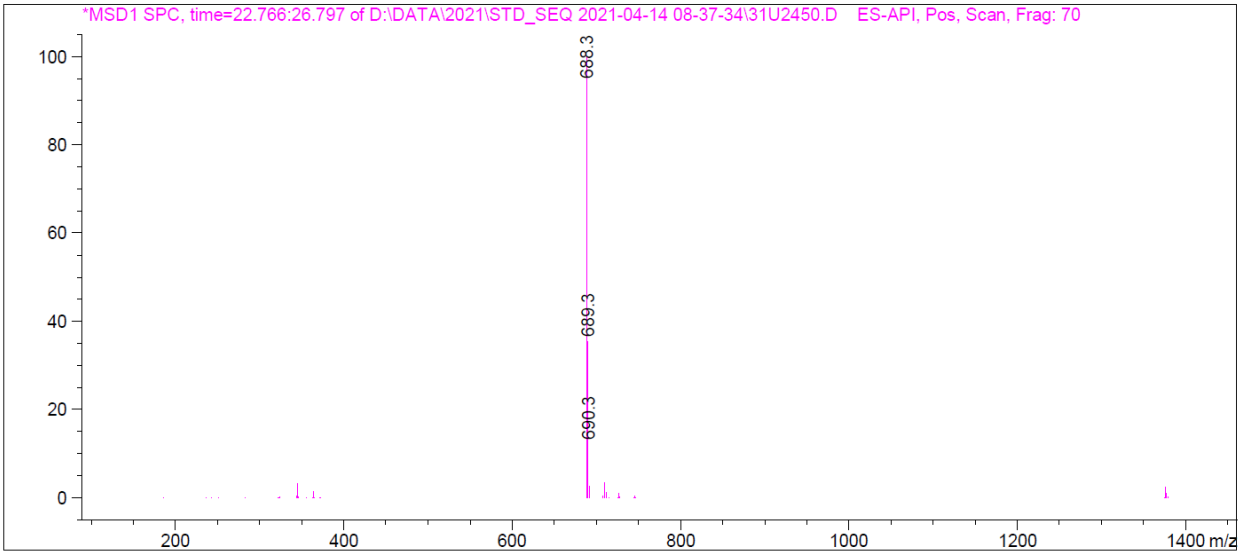
Peak #	RetTime [min]	Type	Width [min]	Area	Height	Area %
1	6.013	MF	1.3466	4.33161e6	5.36108e4	16.5322
2	7.147	FM	0.8829	2.85046e6	5.38094e4	10.8792
3	12.019	MM	0.7941	1.05652e5	2217.47437	0.4032
4	23.960	MM	4.1050	1.84643e7	7.49671e4	70.4715
5	64.260	MM	0.8371	4.49081e5	8941.00879	1.7140
Totals :				2.62011e7	1.93546e5	

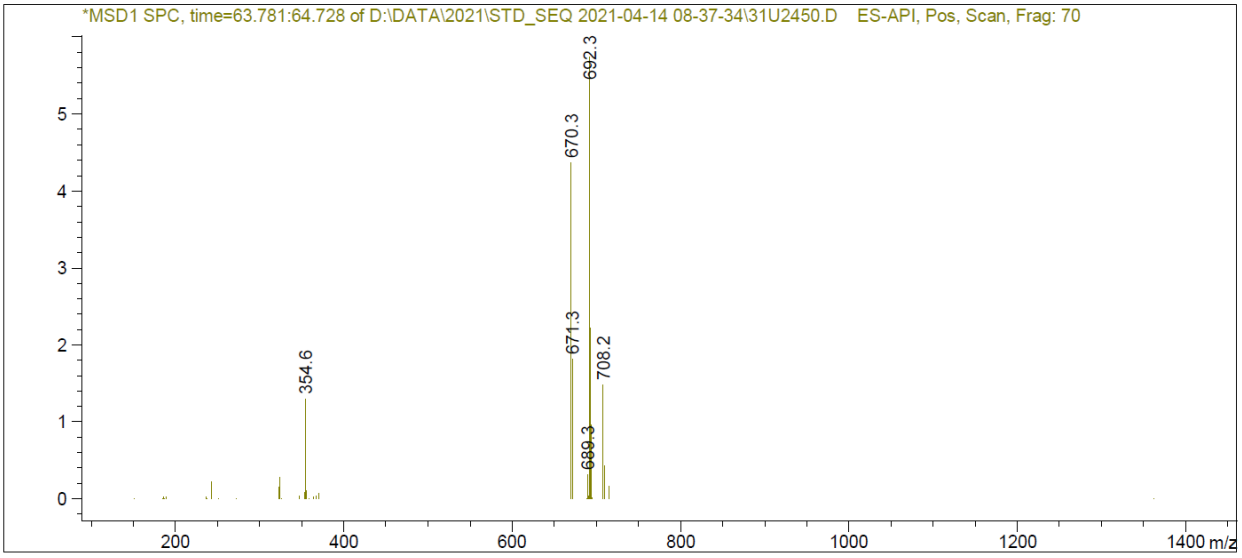
==========


*MSD1 SPC, time=5.027:6.552 of D:\DATA\2021\STD_SEQ 2021-04-14 08-37-34\31U2450.D ES-API, Pos, Scan, Frag: 70
Max: 22833
153.3
154.2
195.1
366.9
m/z


*MSD1 SPC, time=6.622:7.534 of D:\DATA\2021\STD_SEQ 2021-04-14 08-37-34\31U2450.D ES-API, Pos, Scan, Frag: 70
556.4
557.4
558.3
153.3
m/z


*MSD1 SPC, time=11.530:12.547 of D:\DATA\2021\STD_SEQ 2021-04-14 08-37-34\31U2450.D ES-API, Pos, Scan, Frag: 70
538.3
539.3
560.3
269.7
323.3
237.1
m/z

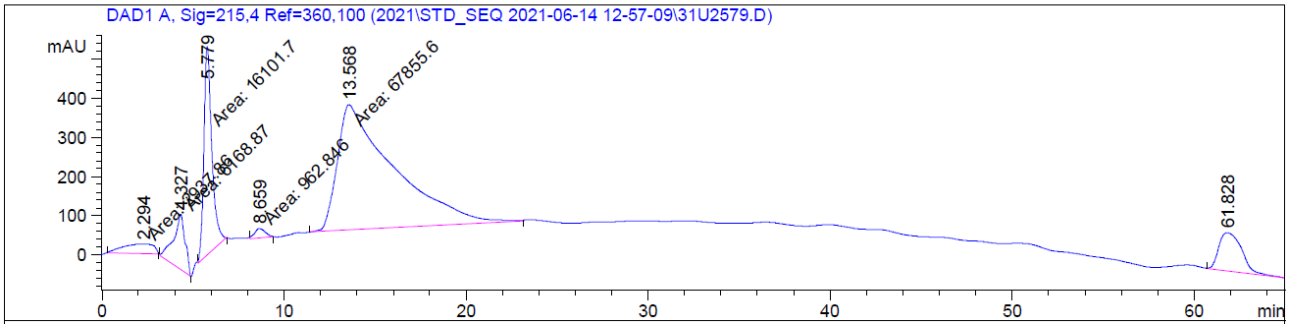




*** End of Report ***

LC-MS spectra of Leu-enkephalin triflate (31) _second test

```
==================================================================
Acq. Operator   :                                Seq. Line :  13
Acq. Instrument : Instrument 1                    Location : Vial 42
Injection Date  : 14/06/2021 20:35:16                  Inj :   1
                                                 Inj Volume : 10.0 µl
Acq. Method     : D:\DATA\2021\STD_SEQ 2021-06-14 12-57-09\DA_40-40-70-100_20-
Last changed    : 5/03/2010 15:30:00 by bds
Analysis Method : D:\METHODS\KOLOM 1\ZORBAX\FLUSH.M
Last changed    : 15/06/2021 15:04:00
                  (modified after loading)
Additional Info : Peak(s) manually integrated
```



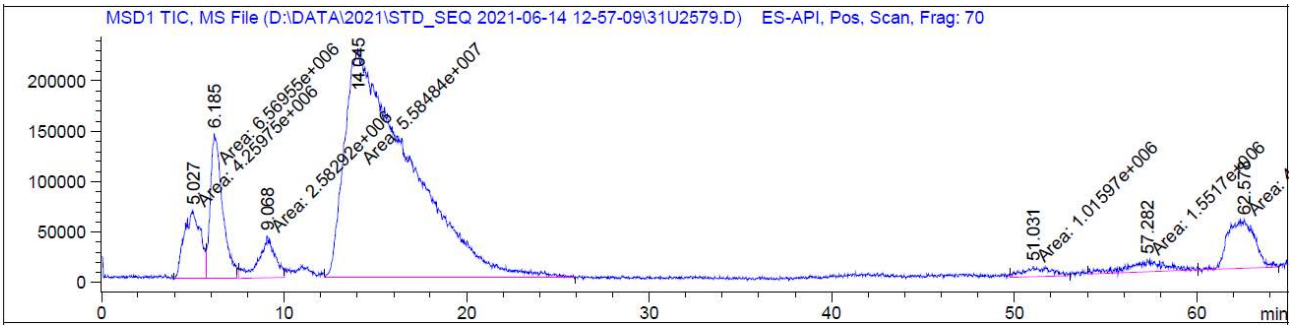

```
Signal 1: DAD1 A, Sig=215,4 Ref=360,100
```

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.294	MM	1.9897	2937.86133	24.60870	2.8654
2	4.327	MM	0.7324	6168.87402	140.37366	6.0168
3	5.779	MM	0.5044	1.61017e4	531.99622	15.7047
4	8.659	MM	0.6656	962.84625	24.10959	0.9391
5	13.568	MM	3.5451	6.78556e4	319.01511	66.1828
6	61.828	BBA	1.0367	8500.72266	96.78464	8.2912
Totals :				1.02528e5	1136.88791	

```
==================================================================
```

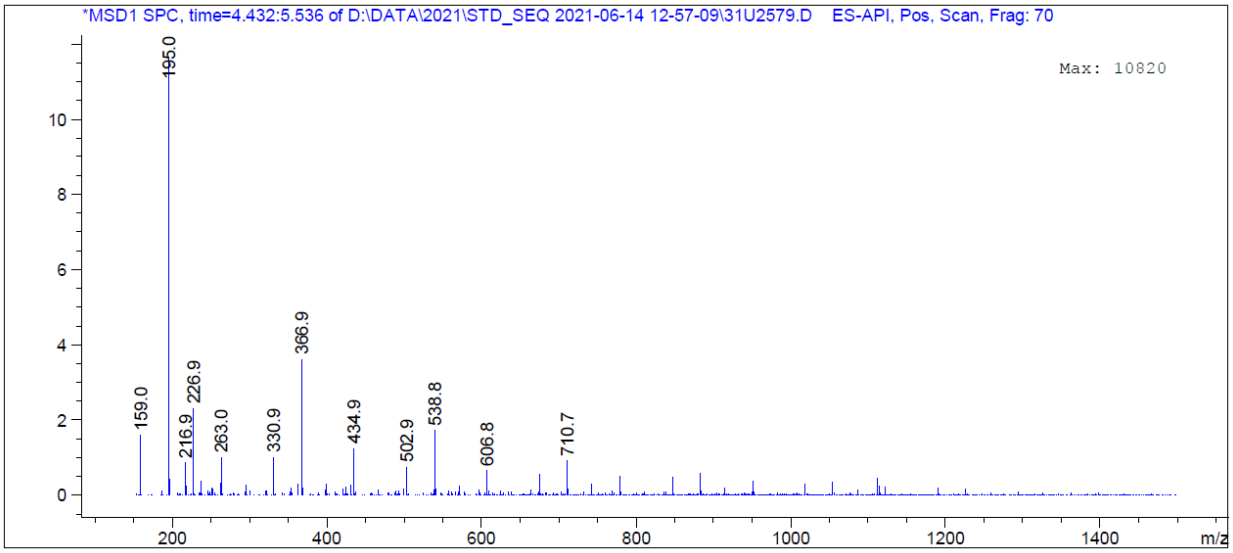
MS Signal: MSD1 TIC, MS File, ES-API, Pos, Scan, Frag: 70
Spectra averaged over upper half of peaks.
Noise Cutoff: 1000 counts.
Reportable Ion Abundance: > 10%.

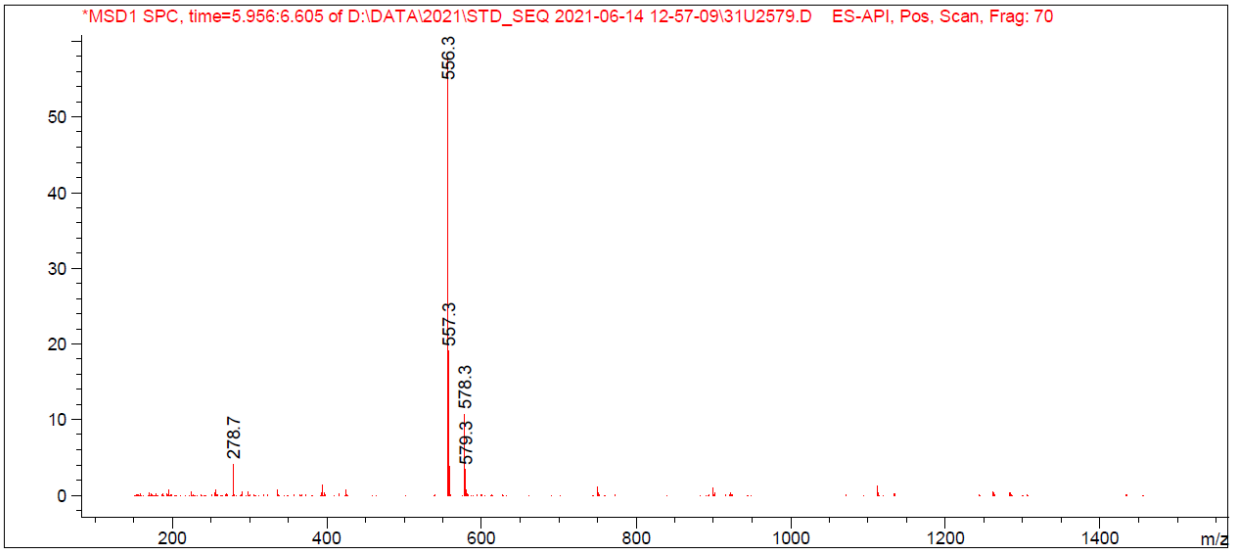
Retention Time (MS)	MS Area	Mol. Weight or Ion
5.027	4259746	538.85 I
		434.85 I
		366.85 I
		226.95 I
		195.00 I
		159.00 I
6.185	6569547	578.25 I
		557.30 I
		556.30 I
9.068	2582919	560.25 I
		539.25 I
		538.30 I
		288.60 I
		236.95 I
14.045	55848376	690.20 I
		689.25 I
		688.20 I
51.031	1015974	
57.282	1551698	
62.578	4997222	708.10 I
		694.20 I
		693.20 I
		692.20 I
		689.20 I
		671.20 I
		670.20 I
		354.70 I
		354.55 I

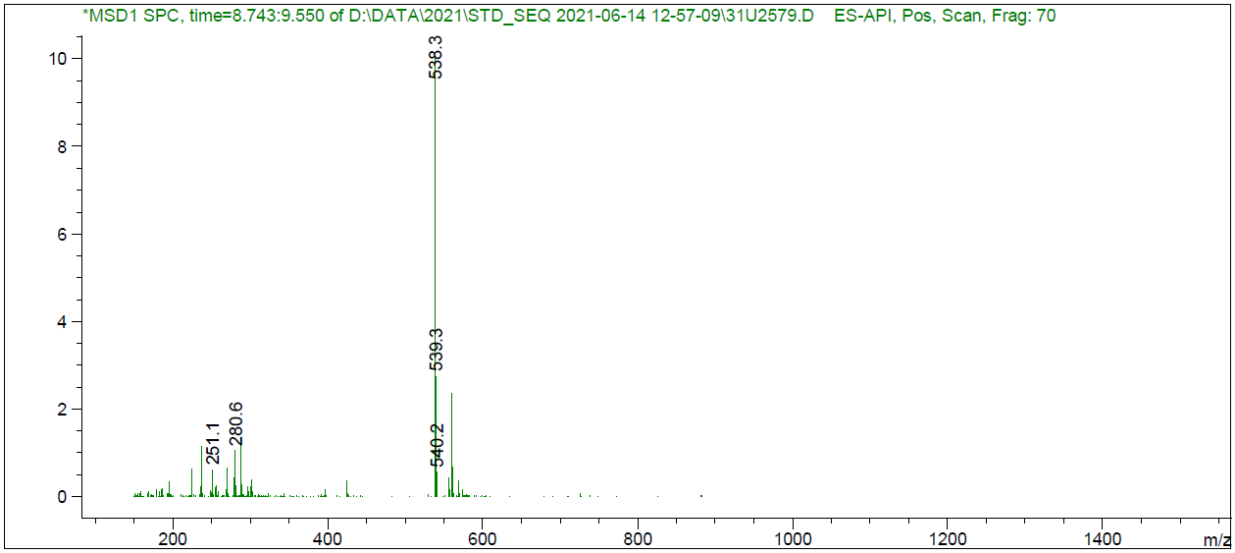


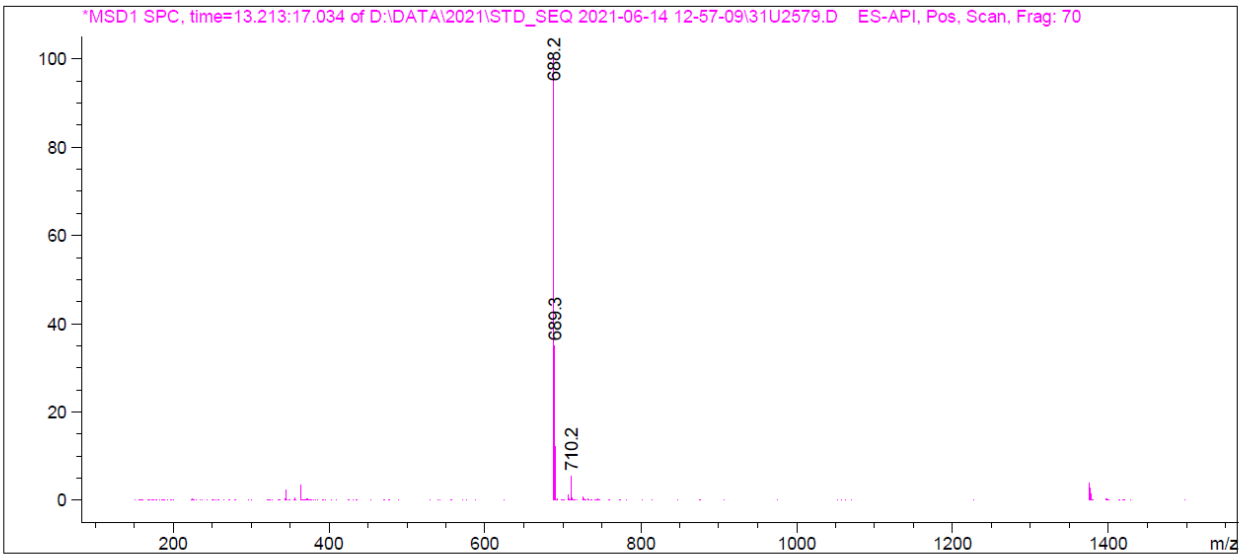
Signal 3: MSD1 TIC, MS File

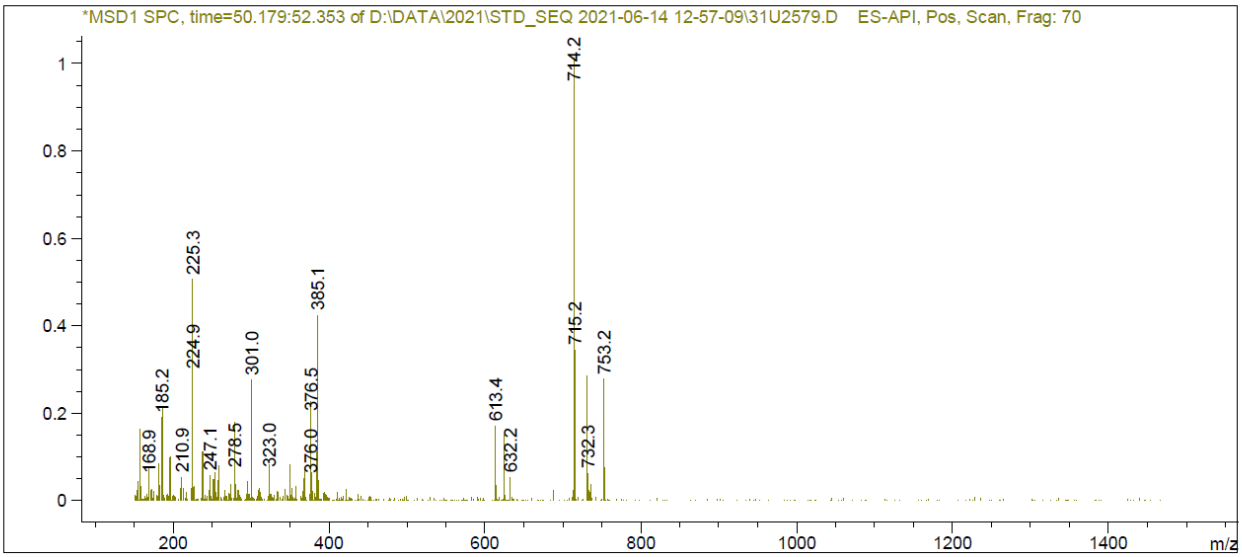
Peak #	RetTime [min]	Type	Width [min]	Area	Height	Area %
1	5.027	MF	1.0519	4.25975e6	6.74906e4	5.5447
2	6.185	FM	0.7593	6.56955e6	1.44207e5	8.5513
3	9.068	MF	1.0311	2.58292e6	4.17503e4	3.3621
4	14.045	FM	4.0891	5.58484e7	2.27630e5	72.6951
5	51.031	MM	1.5807	1.01597e6	1.07121e4	1.3224
6	57.282	MF	2.0455	1.55170e6	1.26434e4	2.0198
7	62.578	FM	1.7172	4.99722e6	4.85008e4	6.5046
Totals :				7.68255e7	5.52934e5	

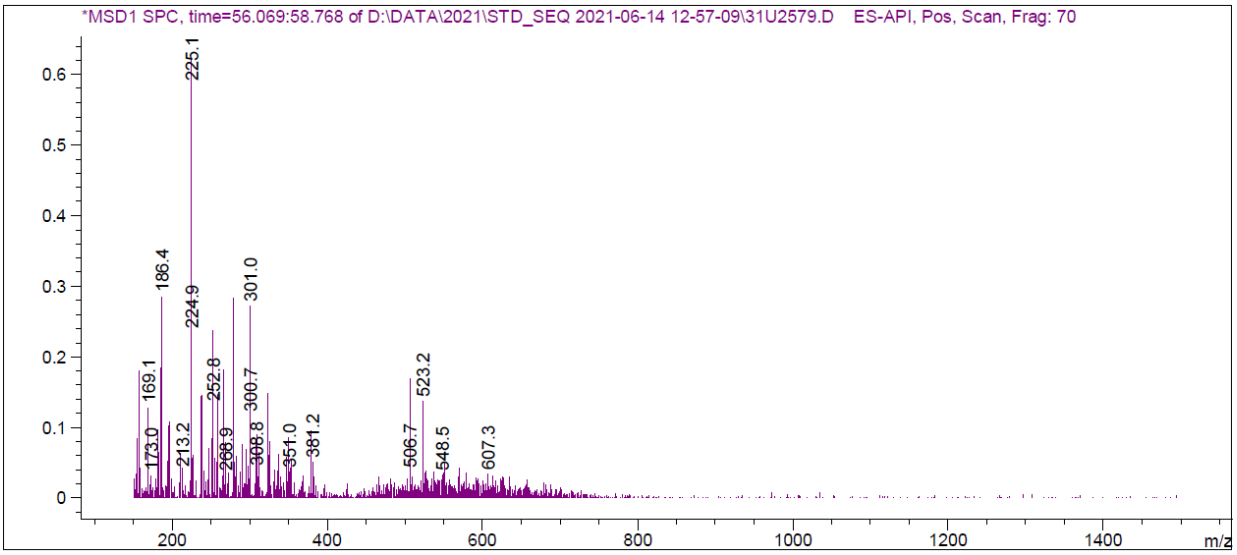

*MSD1 SPC, time=4.432:5.536 of D:\DATA\2021\STD_SEQ 2021-06-14 12-57-09\31U2579.D ES-API, Pos, Scan, Frag: 70
Max: 10820
195.0
159.0
216.9
226.9
263.0
330.9
366.9
434.9
502.9
538.8
606.8
710.7
m/z

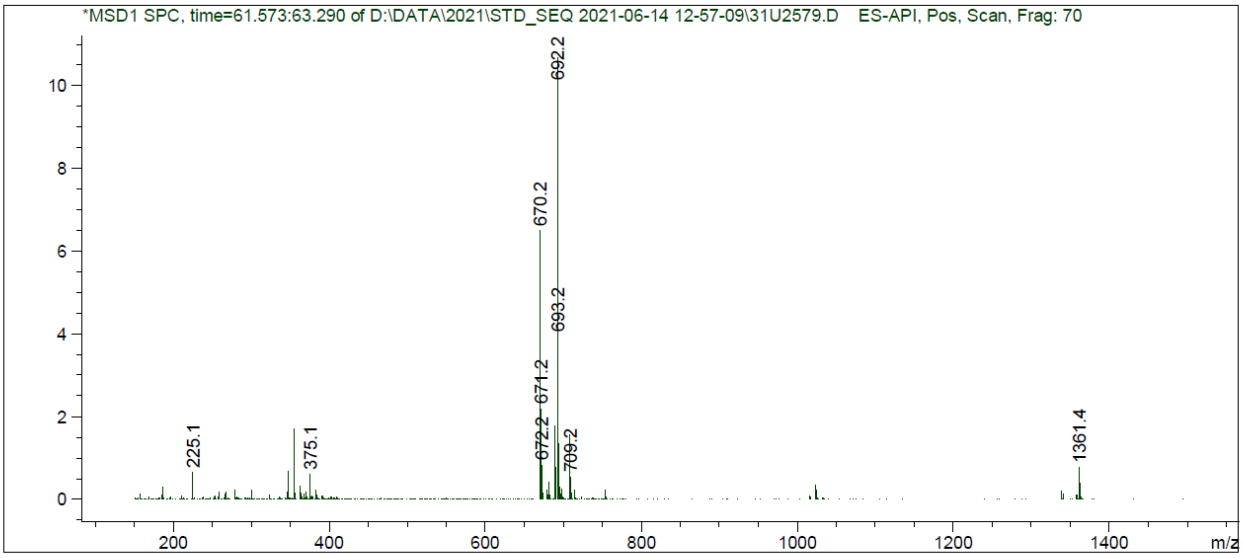

*MSD1 SPC, time=5.956:6.605 of D:\DATA\2021\STD_SEQ 2021-06-14 12-57-09\31U2579.D ES-API, Pos, Scan, Frag: 70
556.3
557.3
578.3
579.3
278.7
m/z


*MSD1 SPC, time=8.743:9.550 of D:\DATA\2021\STD_SEQ 2021-06-14 12-57-09\31U2579.D ES-API, Pos, Scan, Frag: 70
538.3
539.3
540.2
251.1
280.6
m/z


*MSD1 SPC, time=13.213:17.034 of D:\DATA\2021\STD_SEQ 2021-06-14 12-57-09\31U2579.D ES-API, Pos, Scan, Frag: 70
688.2
689.3
710.2
m/z


*MSD1 SPC, time=50.179:52.353 of D:\DATA\2021\STD_SEQ 2021-06-14 12-57-09\31U2579.D ES-API, Pos, Scan, Frag: 70
714.2
225.3
385.1
715.2
753.2
224.9
301.0
185.2
376.5
613.4
168.9
210.9
247.1
278.5
323.0
376.0
632.2
732.3
m/z

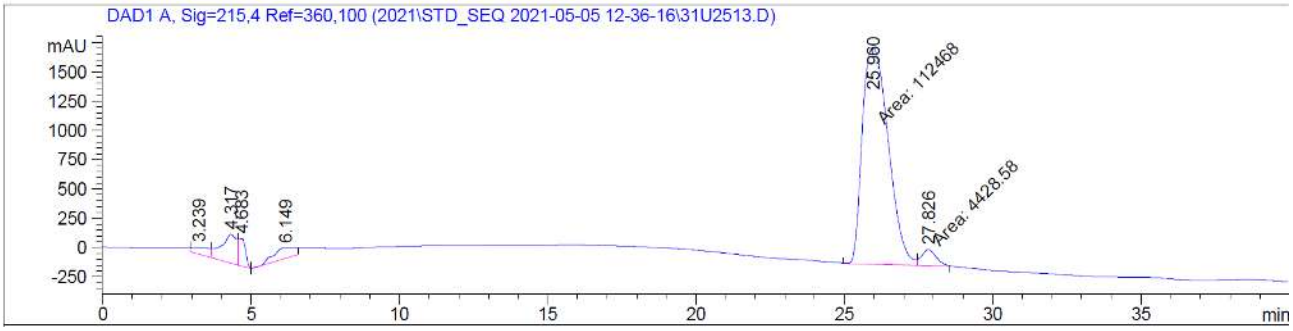

*MSD1 SPC, time=56.069:58.768 of D:\DATA\2021\STD_SEQ 2021-06-14 12-57-09\31U2579.D ES-API, Pos, Scan, Frag: 70
225.1
186.4
301.0
224.9
169.1
252.8
523.2
300.7
213.2
351.0
381.2
506.7
548.5
607.3
m/z



*** End of Report ***

LC-MS spectra of Endomorphin-1 (starting material of 32)

```
==================================================================
Acq. Operator   :                                Seq. Line :  13
Acq. Instrument : Instrument 1                    Location : Vial 33
Injection Date  : 5/05/2021 17:43:34                   Inj :   1
                                                Inj Volume : 10.0 µl
Acq. Method     : D:\DATA\2021\STD_SEQ 2021-05-05 12-36-16\DA_20-60-60-100_20-
Last changed    : 17/03/2010 10:30:31 by bds
Analysis Method : D:\DATA\2021\STD_SEQ 2021-05-07 10-41-44\BA_STAB0_20MIN_+_SELAM.M
Last changed    : 7/05/2021 15:39:50
                  (modified after loading)
Additional Info : Peak(s) manually integrated
```

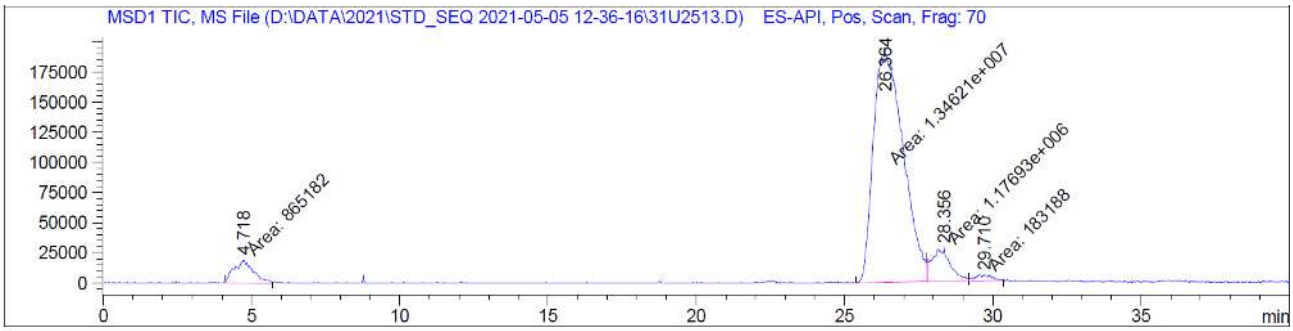



```
Signal 1: DAD1 A, Sig=215,4 Ref=360,100
```

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.239	BV	0.5558	2667.64575	57.23273	1.9496
2	4.317	VV	0.4821	8770.92676	244.71590	6.4101
3	4.683	VV	0.2412	3746.41431	236.03462	2.7380
4	6.149	VV	0.7031	4747.68604	91.54134	3.4698
5	25.960	MF	1.0135	1.12468e5	1849.42041	82.1958
6	27.826	FM	0.5534	4428.57910	133.36894	3.2366
Totals :				1.36829e5	2612.31393	

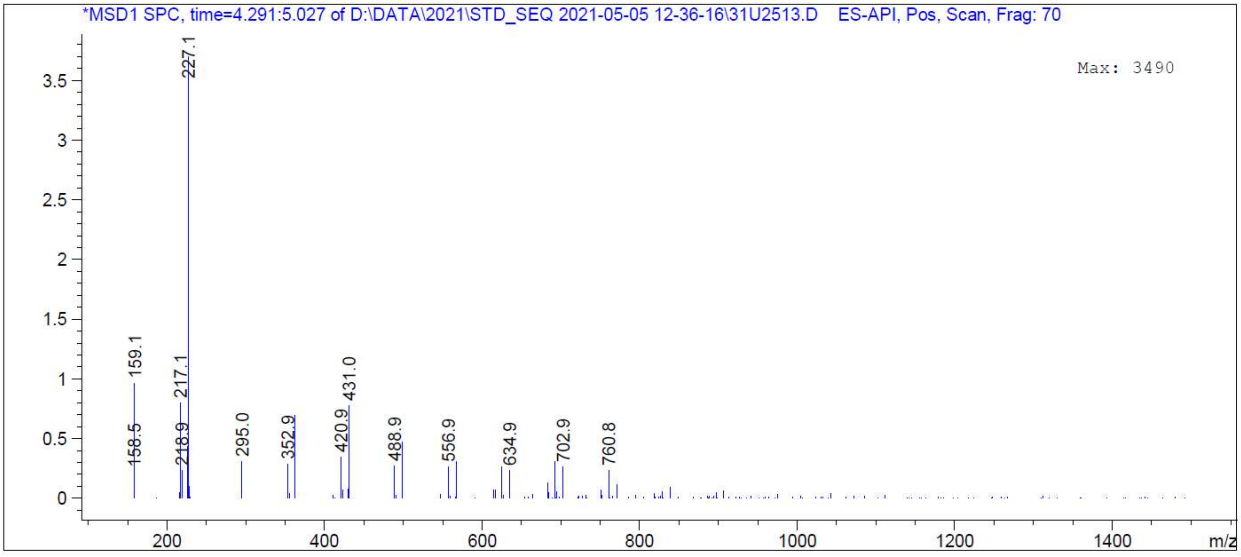
```
==================================================================
MS Signal: MSD1 TIC, MS File,  ES-API, Pos, Scan, Frag: 70
    Spectra averaged over upper half of peaks.
    Noise Cutoff: 1000 counts.
    Reportable Ion Abundance: > 10%.
```

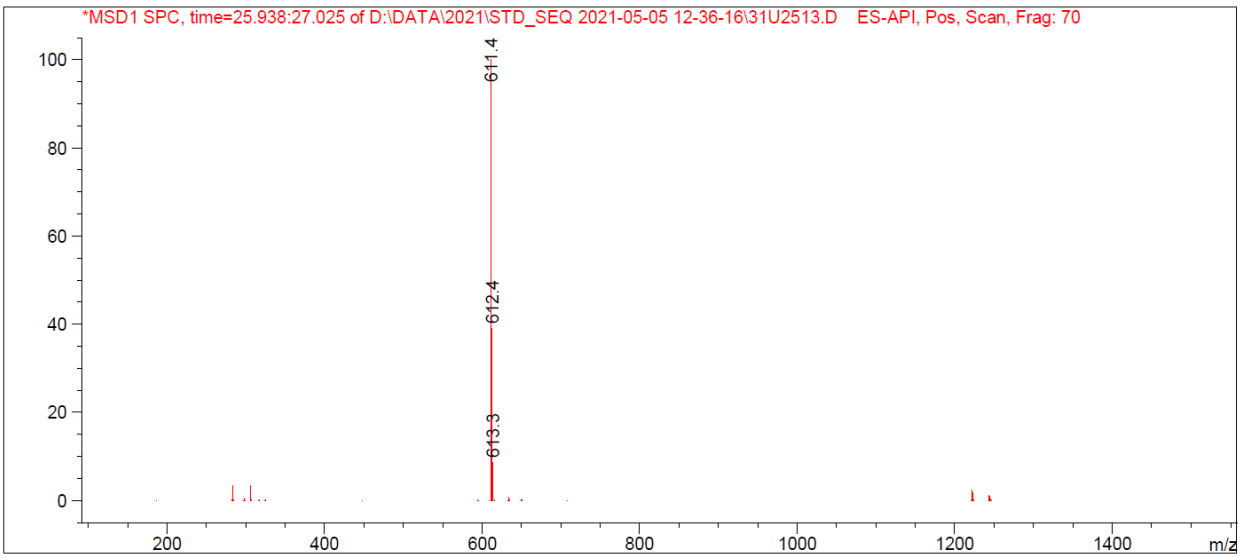
Retention Time (MS)	MS Area	Mol. Weight or Ion
4.718	865182	227.05 I
26.364	13462094	612.40 I
		611.40 I
28.356	1176929	613.35 I
		612.40 I
		611.40 I
29.710	183188	

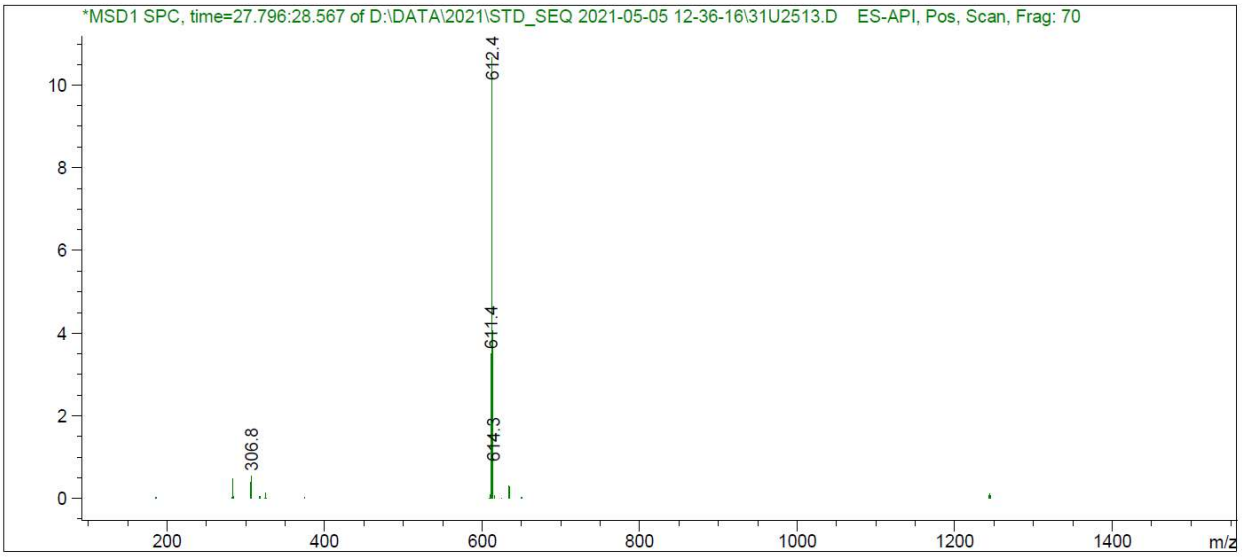


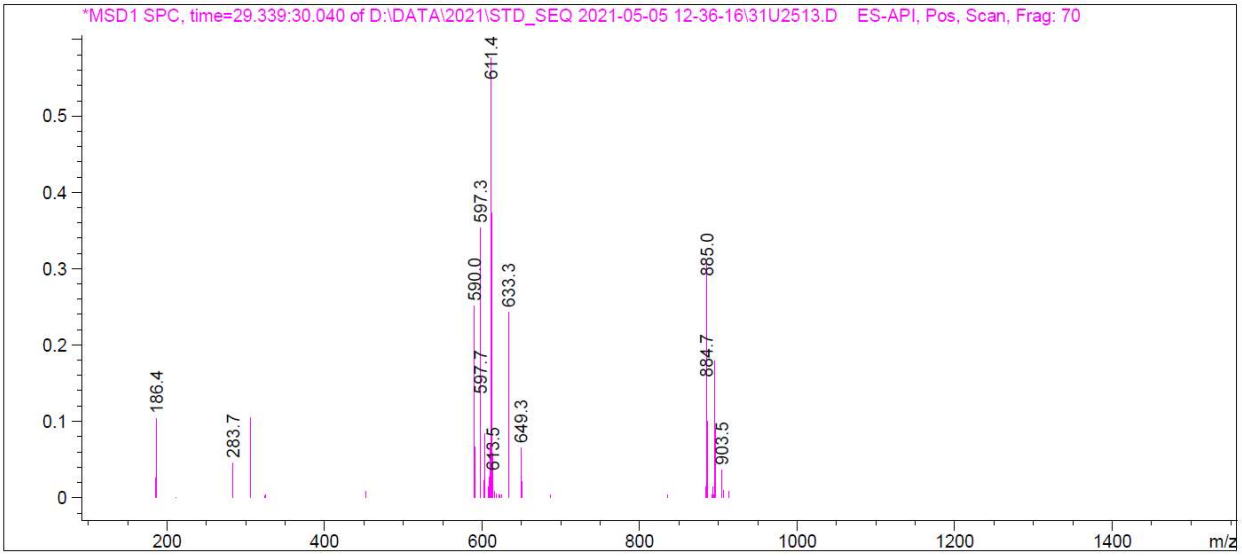
Peak #	RetTime [min]	Type	Width [min]	Area	Height	Area %
1	4.718	MM	0.7468	8.65182e5	1.93076e4	5.5151
2	26.364	MF	1.1563	1.34621e7	1.94037e5	85.8147
3	28.356	MF	0.7196	1.17693e6	2.72573e4	7.5024
4	29.710	FM	0.6275	1.83188e5	4865.77246	1.1677
Totals :				1.56874e7	2.45467e5	

==========





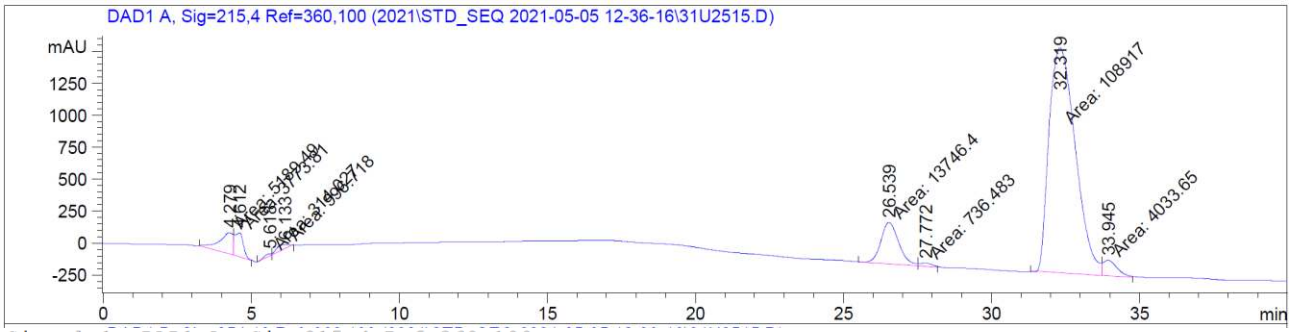




*** End of Report ***

LC-MS spectra of Endomorphin-1 triflate (32)_first test

```
======================================================================
Acq. Operator   :                                Seq. Line :  30
Acq. Instrument : Instrument 1                    Location : Vial 34
Injection Date  : 6/05/2021 2:31:10                    Inj :   1
                                                 Inj Volume : 10.0 µl
Acq. Method     : D:\DATA\2021\STD_SEQ 2021-05-05 12-36-16\DA_20-60-60-100_20-
Last changed    : 17/03/2010 10:30:31 by bds
Analysis Method : D:\DATA\2021\STD_SEQ 2021-05-07 10-41-44\BA_STAB0_20MIN_+_SELAM.M
Last changed    : 7/05/2021 15:39:50
                  (modified after loading)
Additional Info : Peak(s) manually integrated
```



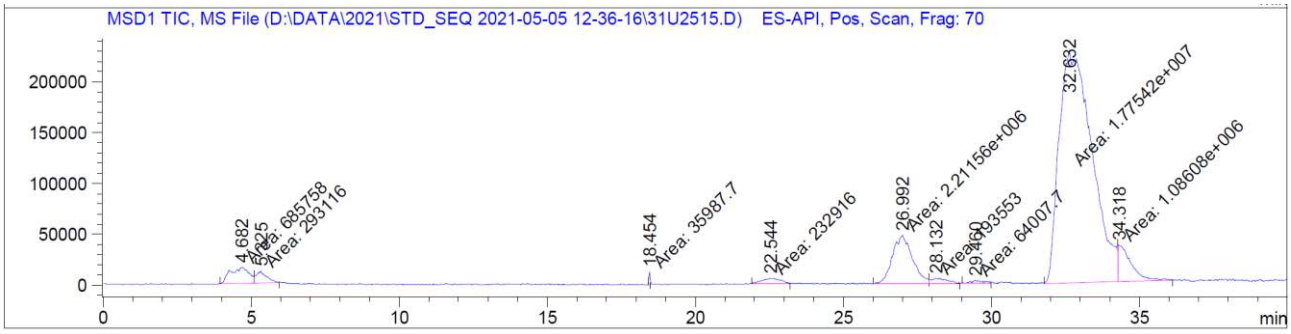

```
Signal 1: DAD1 A, Sig=215,4 Ref=360,100
```

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.279	MF	0.5200	5189.48877	166.31747	3.7685
2	4.612	FM	0.3350	3773.80615	187.72859	2.7405
3	5.618	MF	0.3215	314.02710	16.27930	0.2280
4	6.133	FM	0.5470	996.71771	30.36698	0.7238
5	26.539	MF	0.7051	1.37464e4	324.93195	9.9823
6	27.772	FM	0.4680	736.48254	26.22608	0.5348
7	32.319	MF	1.0328	1.08917e5	1757.66516	79.0929
8	33.945	FM	0.5568	4033.64966	120.74442	2.9291
Totals :				1.37707e5	2630.25995	

```
======================================================================
```

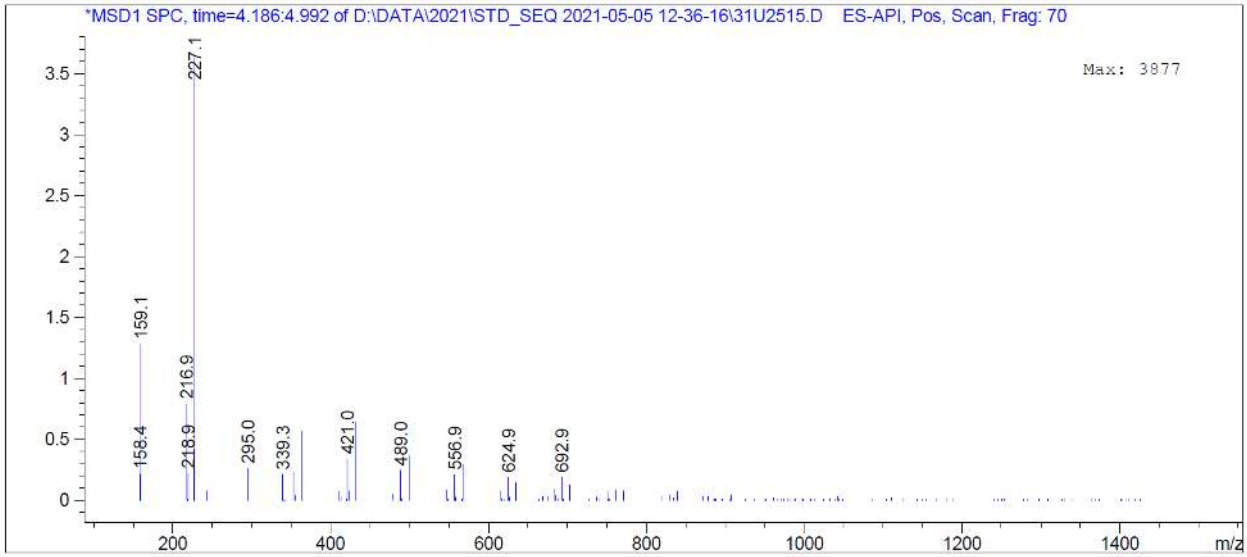
MS Signal: MSD1 TIC, MS File, ES-API, Pos, Scan, Frag: 70
Spectra averaged over upper half of peaks.
Noise Cutoff: 1000 counts.
Reportable Ion Abundance: > 10%.

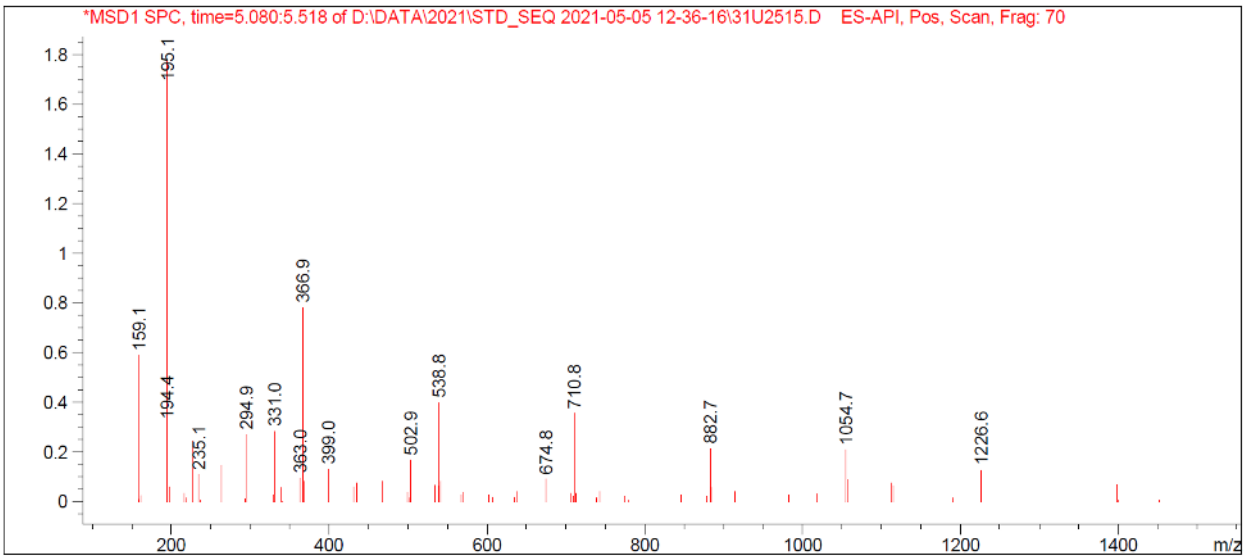
Retention Time (MS)	MS Area	Mol. Weight or Ion
4.682	685758	227.10 I
		159.10 I
5.325	293116	195.05 I
18.454	35988	654.20 I
22.544	232916	
26.992	2211560	612.40 I
		611.40 I
28.132	193553	612.40 I
29.460	64008	
32.632	17754192	745.30 I
		744.30 I
		743.30 I
34.318	1086078	746.25 I
		745.30 I
		744.30 I
		743.35 I

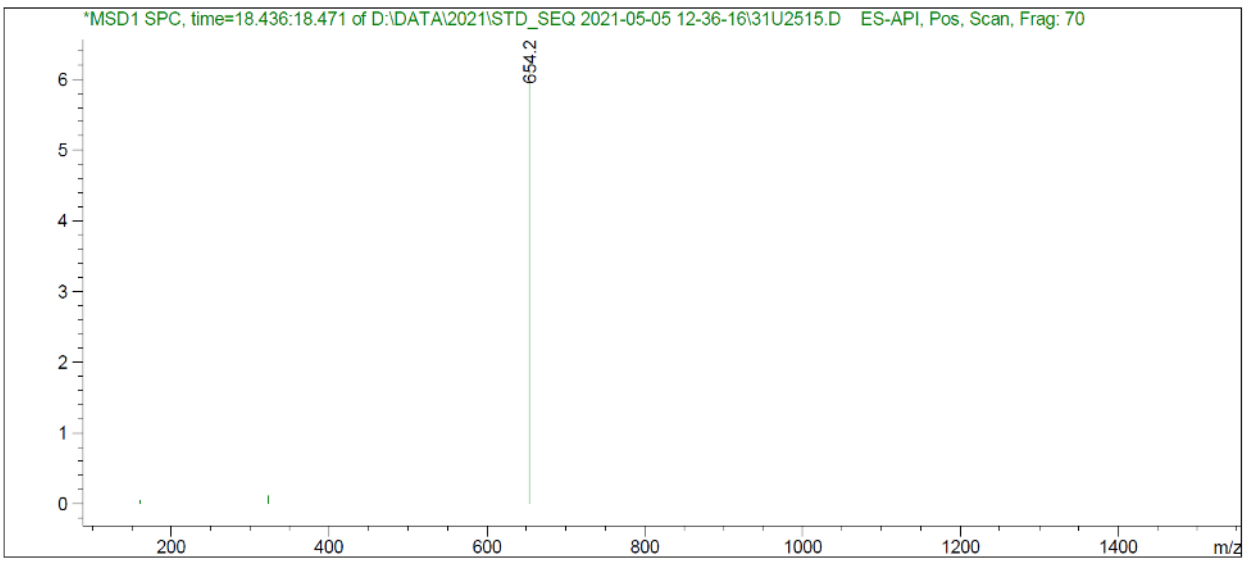


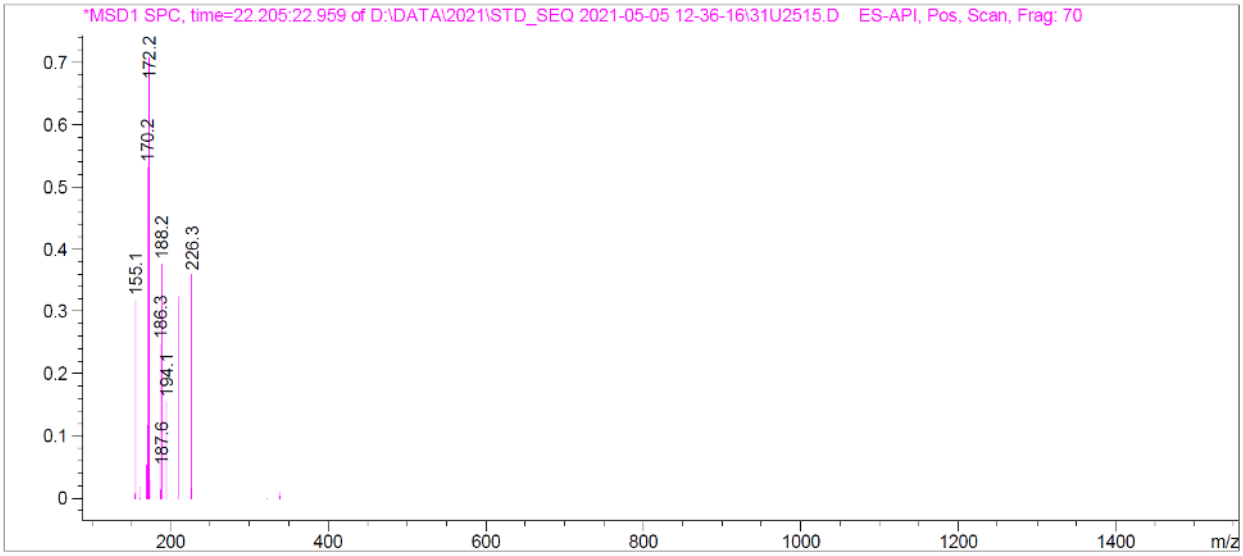
Peak #	RetTime [min]	Type	Width [min]	Area	Height	Area %
1	4.682	MF	0.7133	6.85758e5	1.60224e4	3.0401
2	5.325	FM	0.4173	2.93116e5	1.17082e4	1.2994
3	18.454	MM	0.0469	3.59877e4	1.27772e4	0.1595
4	22.544	MM	0.7298	2.32916e5	5319.23682	1.0326
5	26.992	MF	0.7744	2.21156e6	4.75985e4	9.8042
6	28.132	FM	0.5849	1.93553e5	5515.57471	0.8581
7	29.460	MM	0.4380	6.40077e4	2435.51343	0.2838
8	32.632	MF	1.2913	1.77542e7	2.29155e5	78.7075
9	34.318	FM	0.5019	1.08608e6	3.60683e4	4.8148
Totals :				2.25572e7	3.66600e5	

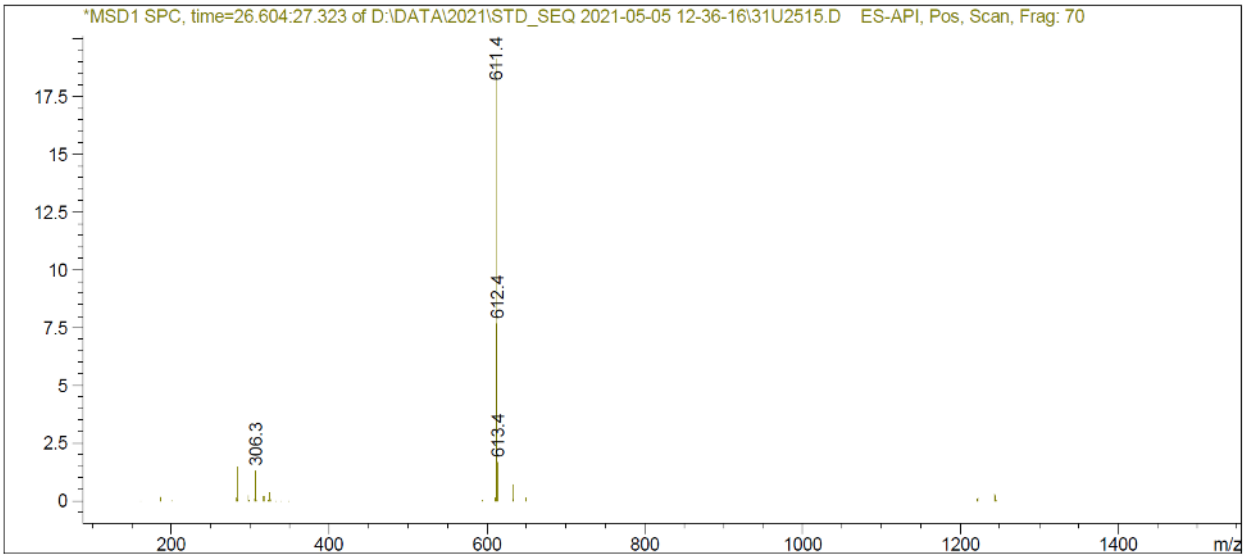
==========

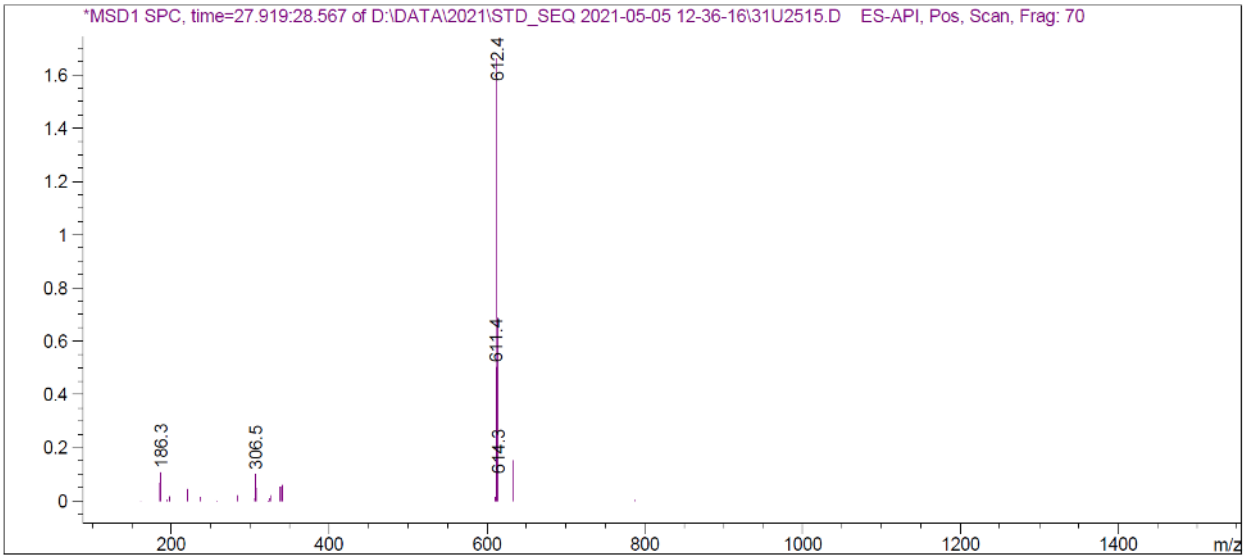

*MSD1 SPC, time=4.186:4.992 of D:\DATA\2021\STD_SEQ 2021-05-05 12-36-16\31U2515.D ES-API, Pos, Scan, Frag: 70
Max: 3877
227.1
159.1
216.9
158.4
218.9
295.0
339.3
421.0
489.0
556.9
624.9
692.9
m/z

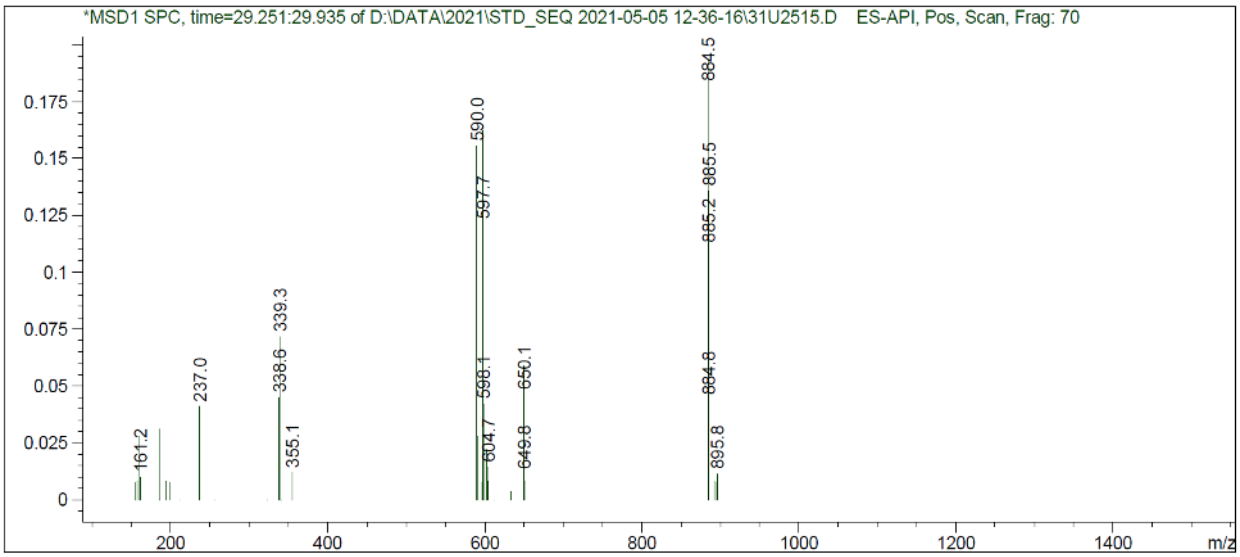

*MSD1 SPC, time=5.080:5.518 of D:\DATA\2021\STD_SEQ 2021-05-05 12-36-16\31U2515.D ES-API, Pos, Scan, Frag: 70
195.1
366.9
159.1
194.4
538.8
294.9
331.0
710.8
235.1
363.0
399.0
502.9
674.8
882.7
1054.7
1226.6
m/z

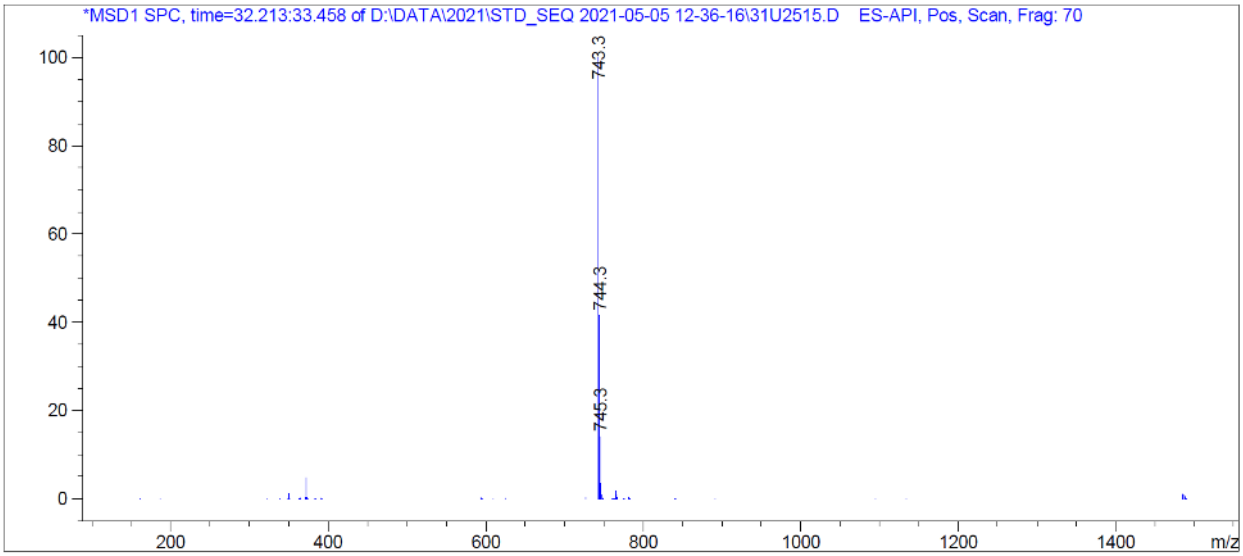

*MSD1 SPC, time=18.436:18.471 of D:\DATA\2021\STD_SEQ 2021-05-05 12-36-16\31U2515.D ES-API, Pos, Scan, Frag: 70
654.2
m/z

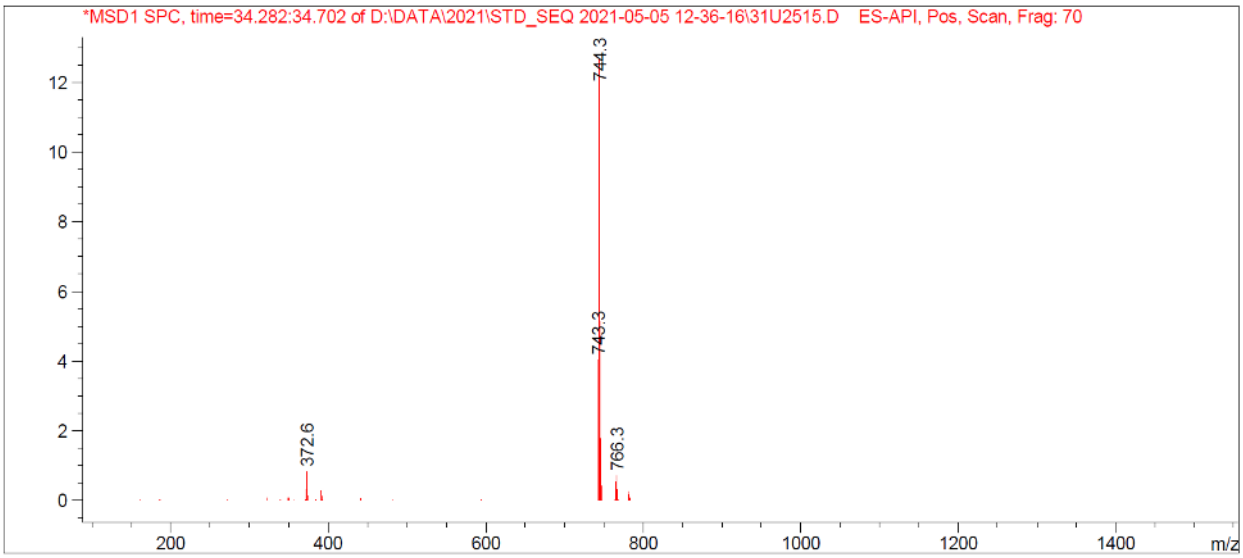

*MSD1 SPC, time=22.205:22.959 of D:\DATA\2021\STD_SEQ 2021-05-05 12-36-16\31U2515.D ES-API, Pos, Scan, Frag: 70
172.2
170.2
188.2
226.3
155.1
186.3
194.1
187.6
m/z


*MSD1 SPC, time=26.604:27.323 of D:\DATA\2021\STD_SEQ 2021-05-05 12-36-16\31U2515.D ES-API, Pos, Scan, Frag: 70
611.4
612.4
613.4
306.3
m/z


*MSD1 SPC, time=27.919:28.567 of D:\DATA\2021\STD_SEQ 2021-05-05 12-36-16\31U2515.D ES-API, Pos, Scan, Frag: 70
612.4
611.4
614.3
186.3
306.5
m/z



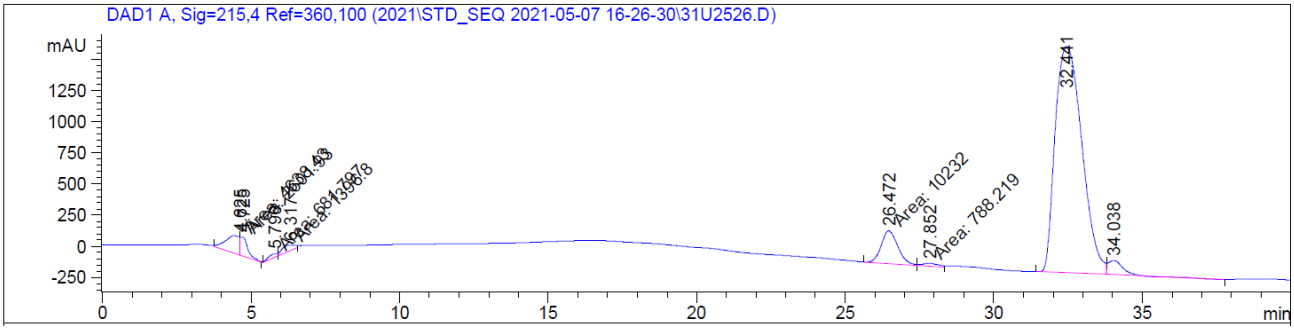




*** End of Report ***

LC-MS spectra of Endomorphin-1 triflate (32)_second test

```
======================================================================
Acq. Operator   :                                Seq. Line :  19
Acq. Instrument : Instrument 1                    Location : Vial 33
Injection Date  : 8/05/2021 4:52:57                    Inj :   1
                                                 Inj Volume : 10.0 µl
Acq. Method     : D:\DATA\2021\STD_SEQ 2021-05-07 16-26-30\DA_20-60-60-100_20-
Last changed    : 17/03/2010 10:30:31 by bds
Analysis Method : D:\DATA\2021\STD_SEQ 2021-05-07 10-41-44\BA_STAB0_20MIN_+_SELAM.M
Last changed    : 10/05/2021 20:05:31
                  (modified after loading)
Additional Info : Peak(s) manually integrated
```



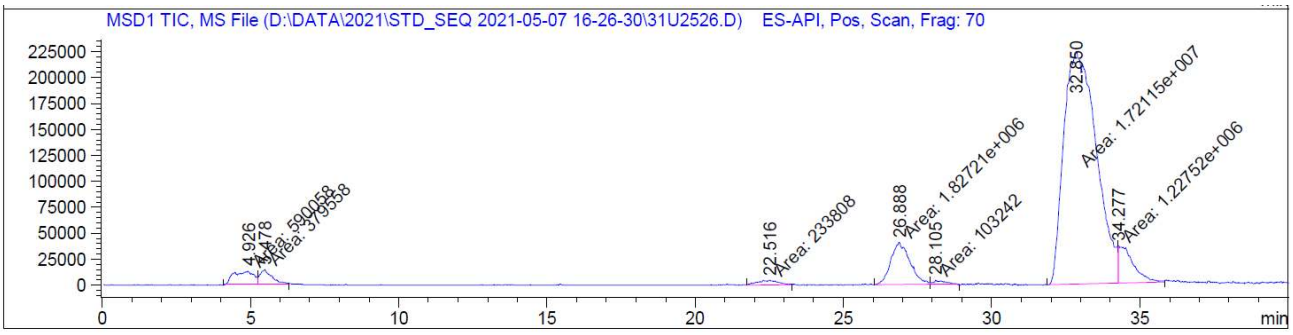
Signal 1: DAD1 A, Sig=215,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.625	MF	0.5324	4638.43213	145.19720	3.3600
2	4.725	FM	0.2865	2601.92578	151.36952	1.8848
3	5.790	MF	0.4007	681.79730	28.35742	0.4939
4	6.317	FM	0.5547	1396.79517	41.97036	1.0118
5	26.472	MF	0.6490	1.02320e4	262.78378	7.4120
6	27.852	FM	0.6168	788.21857	21.29988	0.5710
7	32.441	VV	0.7778	1.13794e5	1814.09998	82.4315
8	34.038	VV	0.5040	3913.45728	115.30743	2.8349
Totals :				1.38047e5	2580.38558	

```
======================================================================
```

MS Signal: MSD1 TIC, MS File, ES-API, Pos, Scan, Frag: 70
    Spectra averaged over upper half of peaks.
    Noise Cutoff: 1000 counts.
    Reportable Ion Abundance: > 10%.

Retention Time (MS)	MS Area	Mol. Weight or Ion
4.926	590058	227.10 I
		159.10 I
5.478	379558	366.95 I
		195.05 I
22.516	233808	
26.888	1827211	612.40 I
		611.40 I
28.105	103242	612.35 I
32.850	17211474	745.30 I
		744.30 I
		743.30 I
34.277	1227517	746.30 I
		745.30 I
		744.30 I
		743.30 I



Peak #	RetTime [min]	Type	Width [min]	Area	Height	Area %
1	4.926	MF	0.7808	5.90058e5	1.25953e4	2.7352
2	5.478	FM	0.4507	3.79558e5	1.40358e4	1.7594
3	22.516	MM	0.8102	2.33808e5	4809.57959	1.0838
4	26.888	MF	0.7489	1.82721e6	4.06665e4	8.4700
5	28.105	FM	0.4190	1.03242e5	4106.37354	0.4786
6	32.850	MF	1.2791	1.72115e7	2.24257e5	79.7830
7	34.277	FM	0.5742	1.22752e6	3.56276e4	5.6901
Totals :				2.15729e7	3.36098e5	

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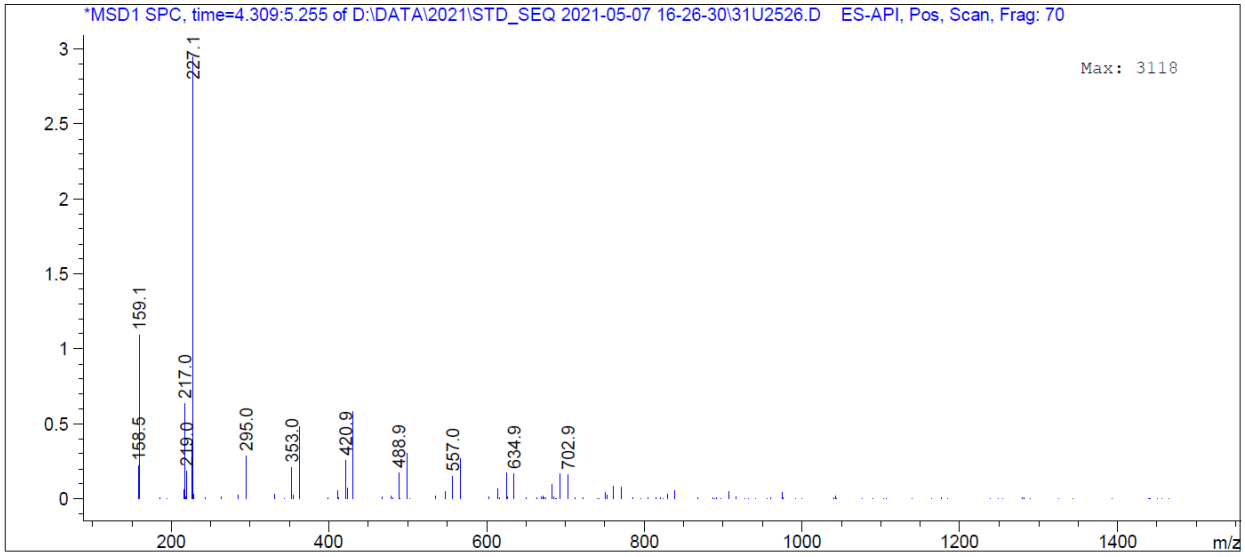
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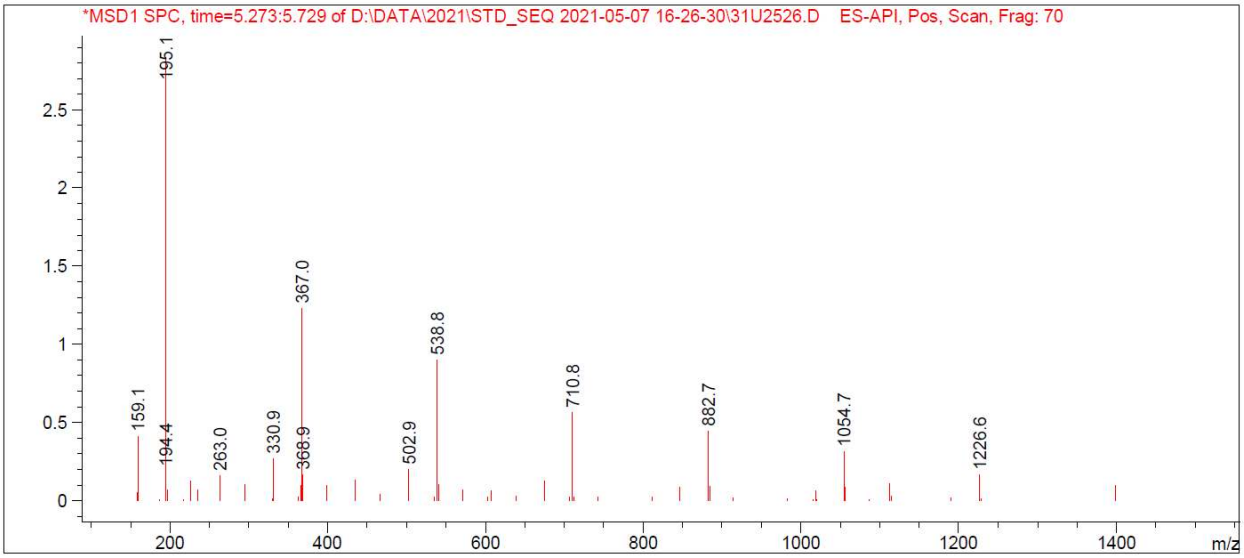
Max: 3118
227.1
159.1
217.0
158.5
219.0
295.0
353.0
420.9
488.9
557.0
634.9
702.9
m/z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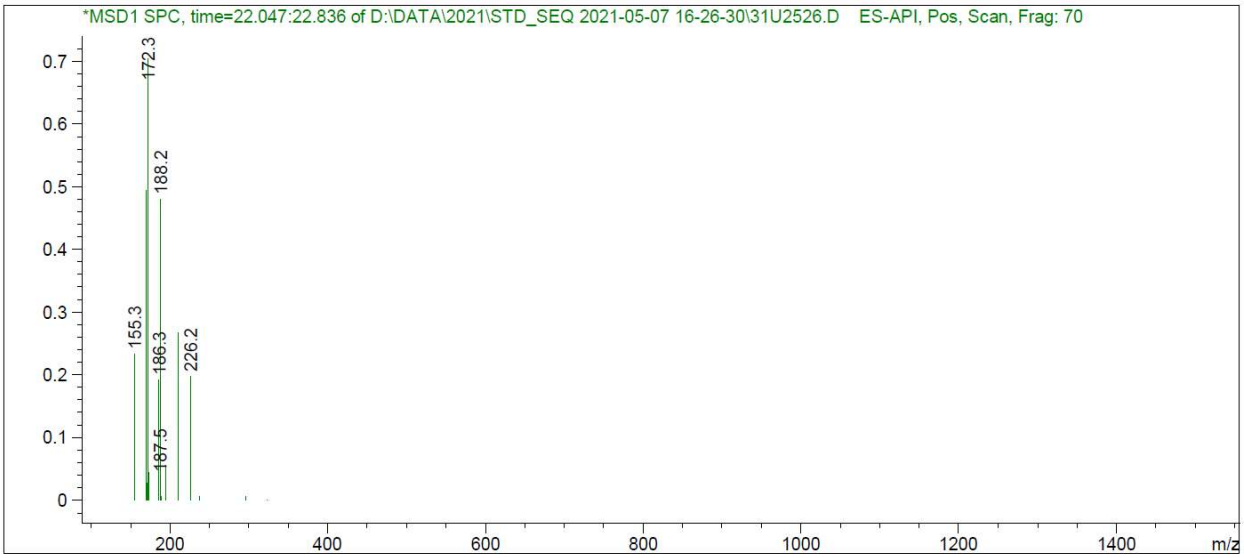
195.1
367.0
538.8
710.8
882.7
1054.7
1226.6
159.1
194.4
263.0
330.9
368.9
502.9
m/z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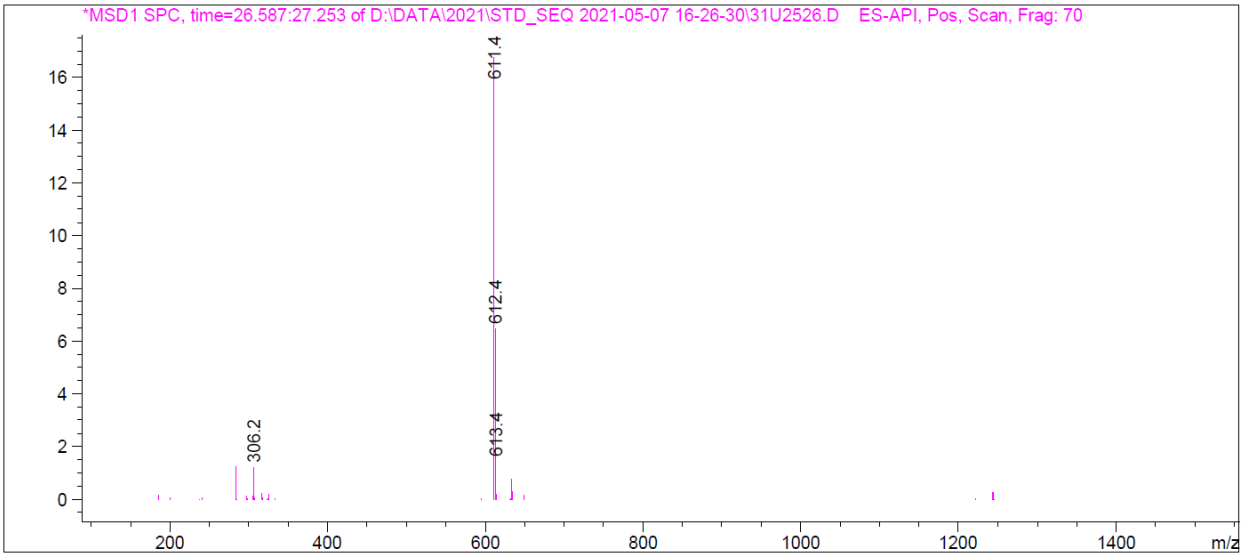
172.3
188.2
155.3
186.3
226.2
187.5
m/z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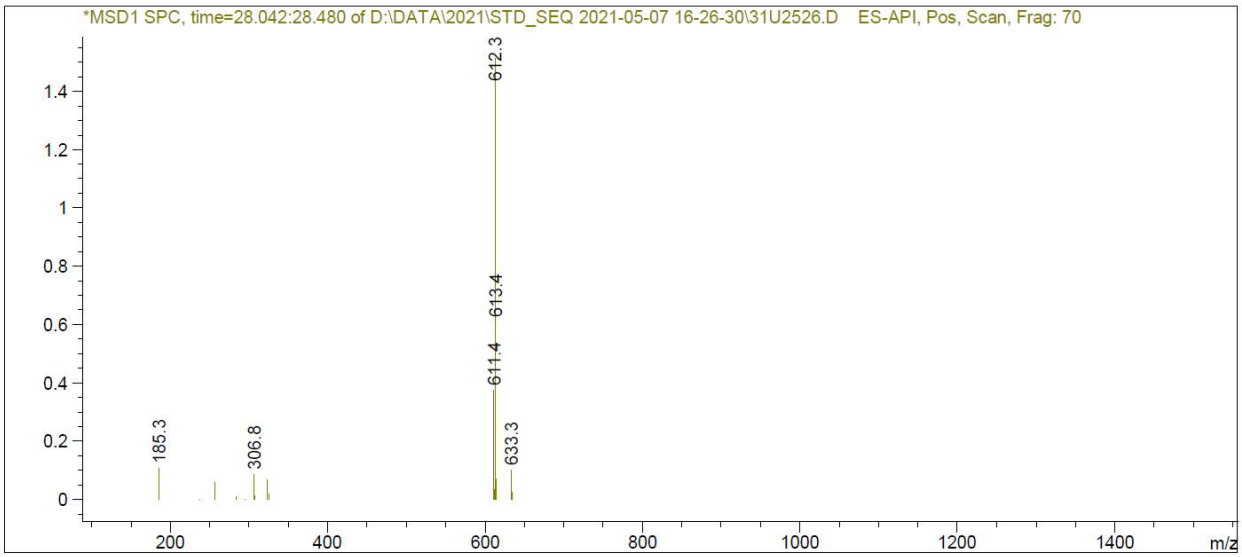
611.4
612.4
613.4
306.2
m/z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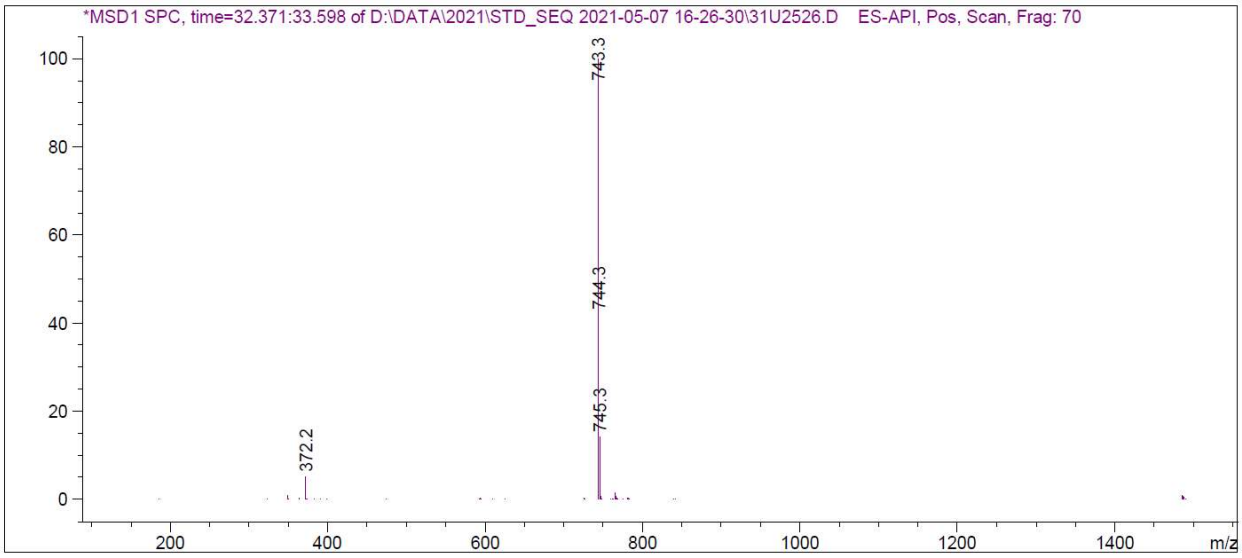
612.3
613.4
611.4
633.3
185.3
306.8
m/z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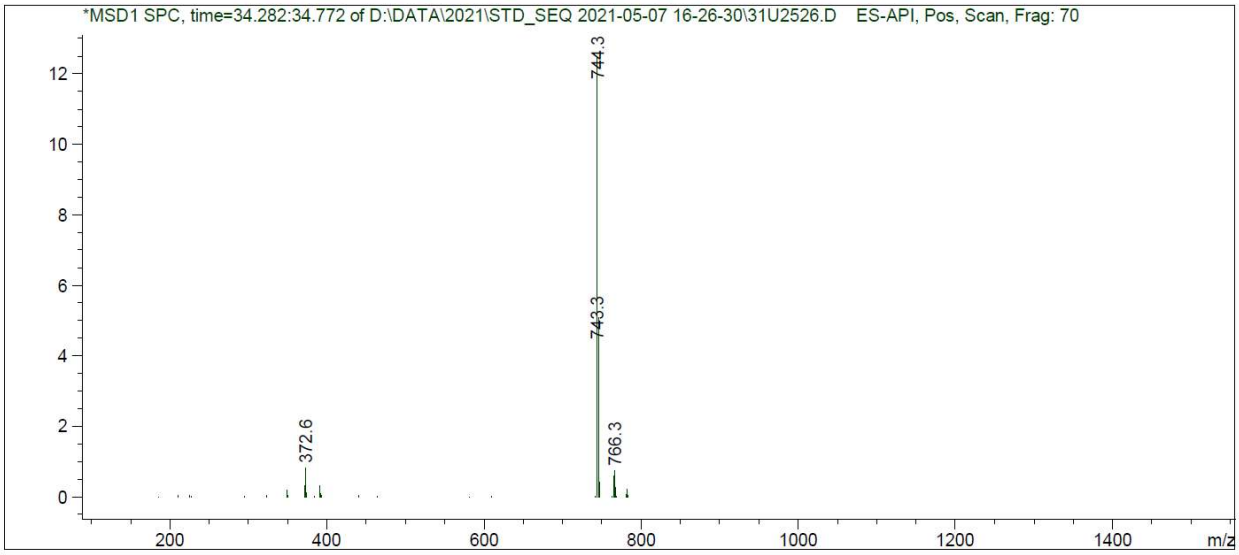
743.3
744.3
745.3
372.2
m/z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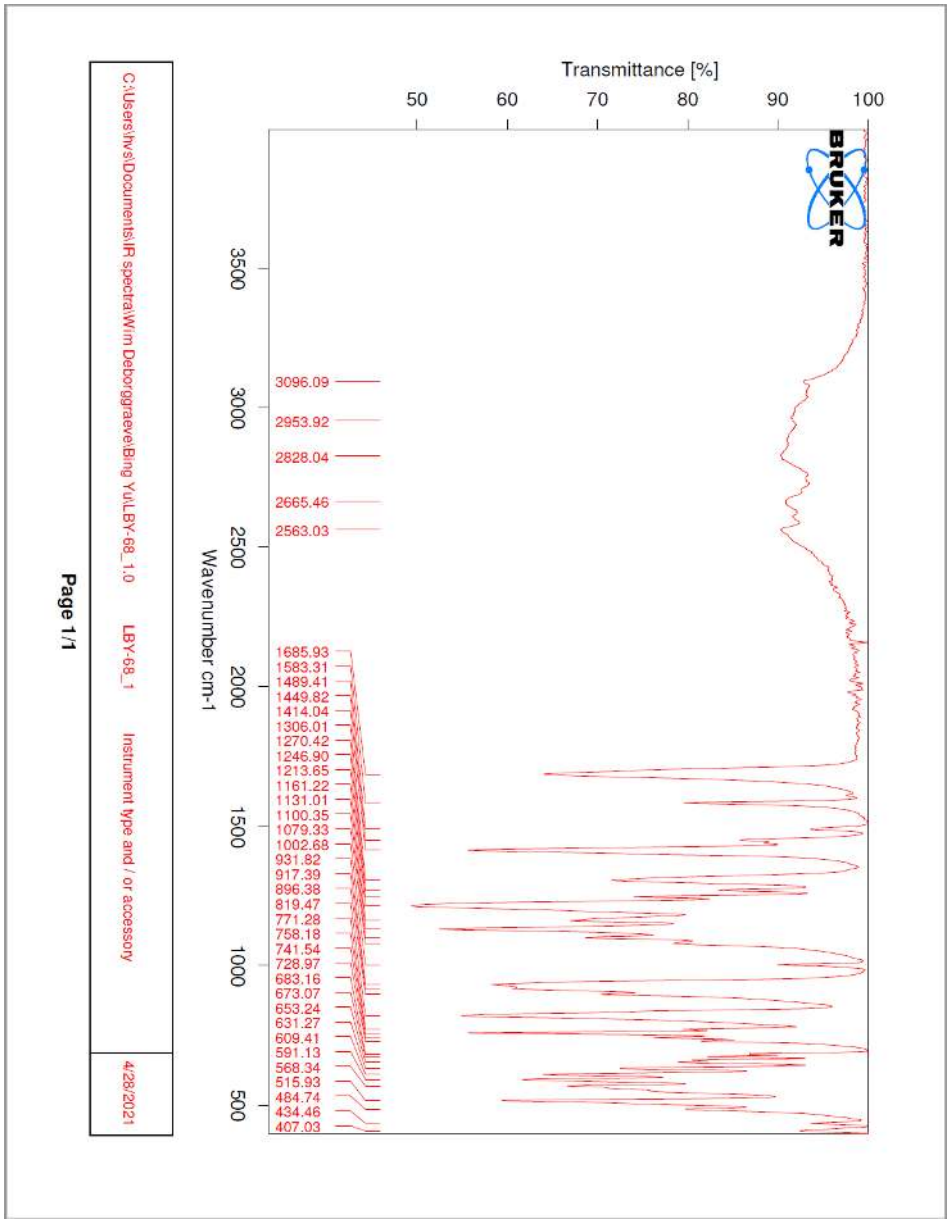
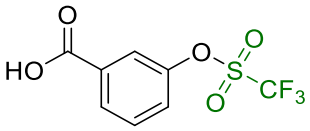
744.3
743.3
372.6
766.3
12
10
8
6
4
2
0
200
400
600
800
1000
1200
1400
m/z

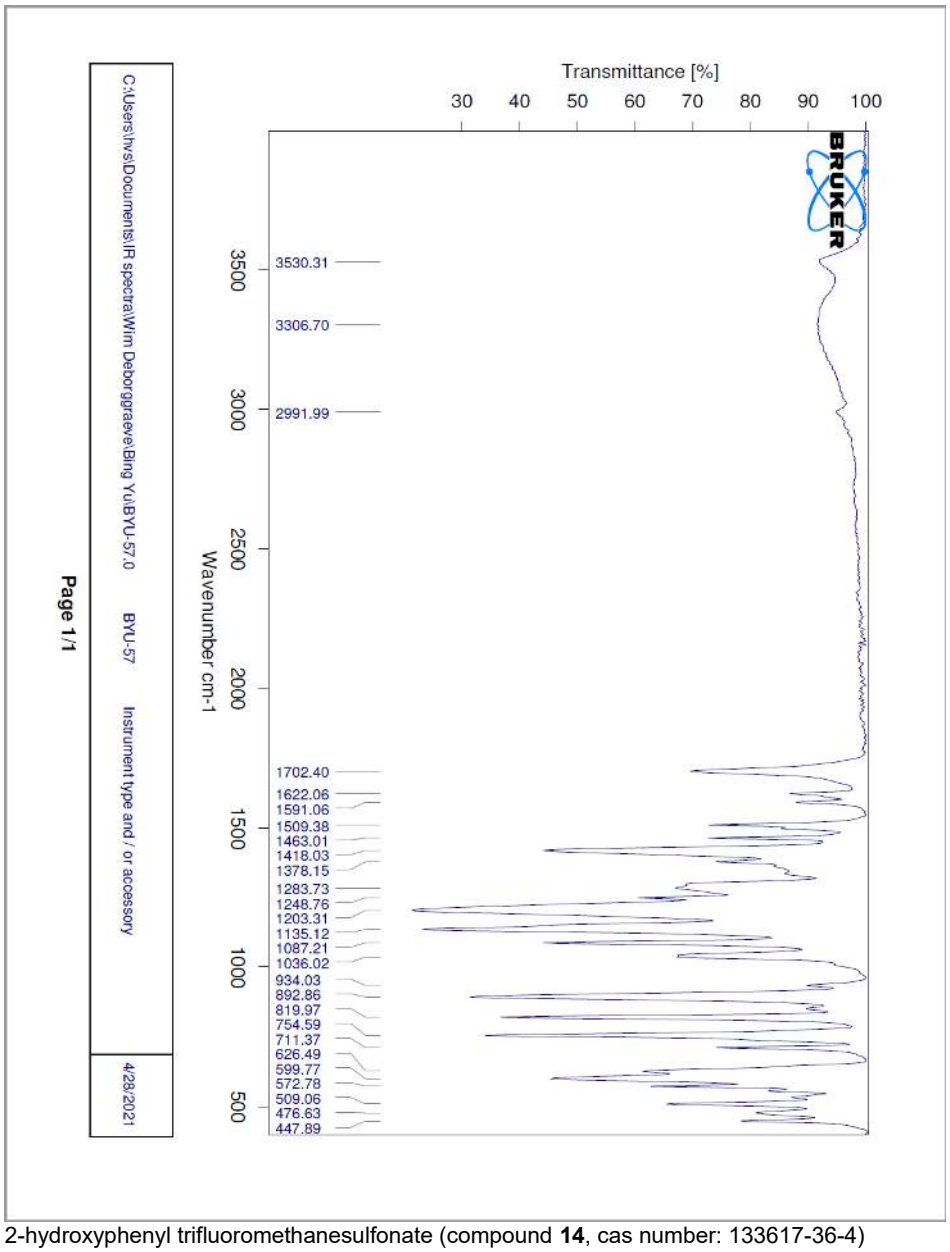
12. Copies of the IR Spectra

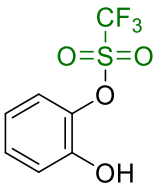




Chemical Formula: $C_8H_5F_3O_5S$
Exact Mass: 269.9810

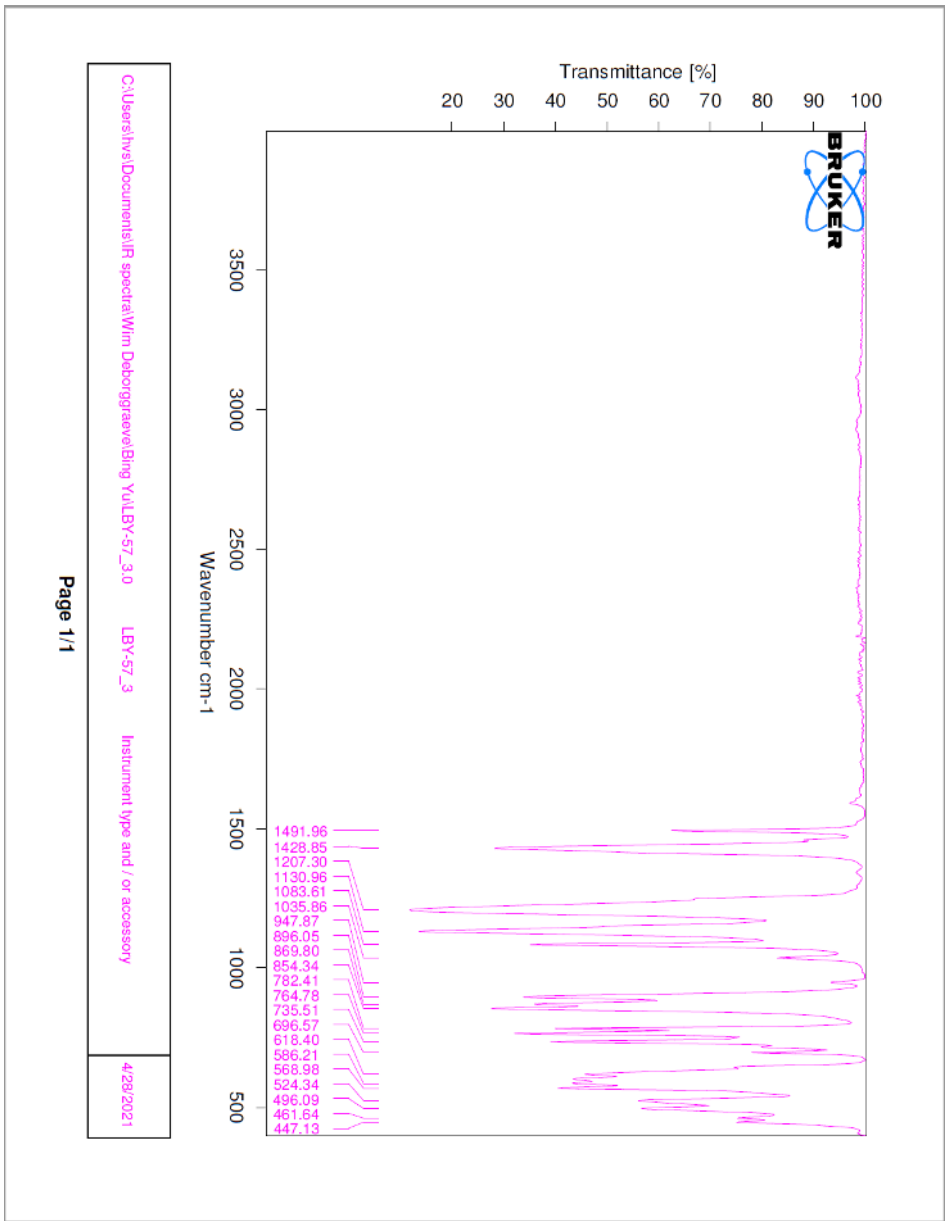
3-(((trifluoromethyl)sulfonyl)oxy)benzoic acid (compound **7**, cas number: 32578-33-9)

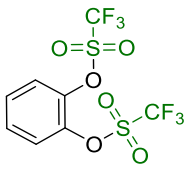




Chemical Formula: $C_7H_5F_3O_4S$
Exact Mass: 241,9861

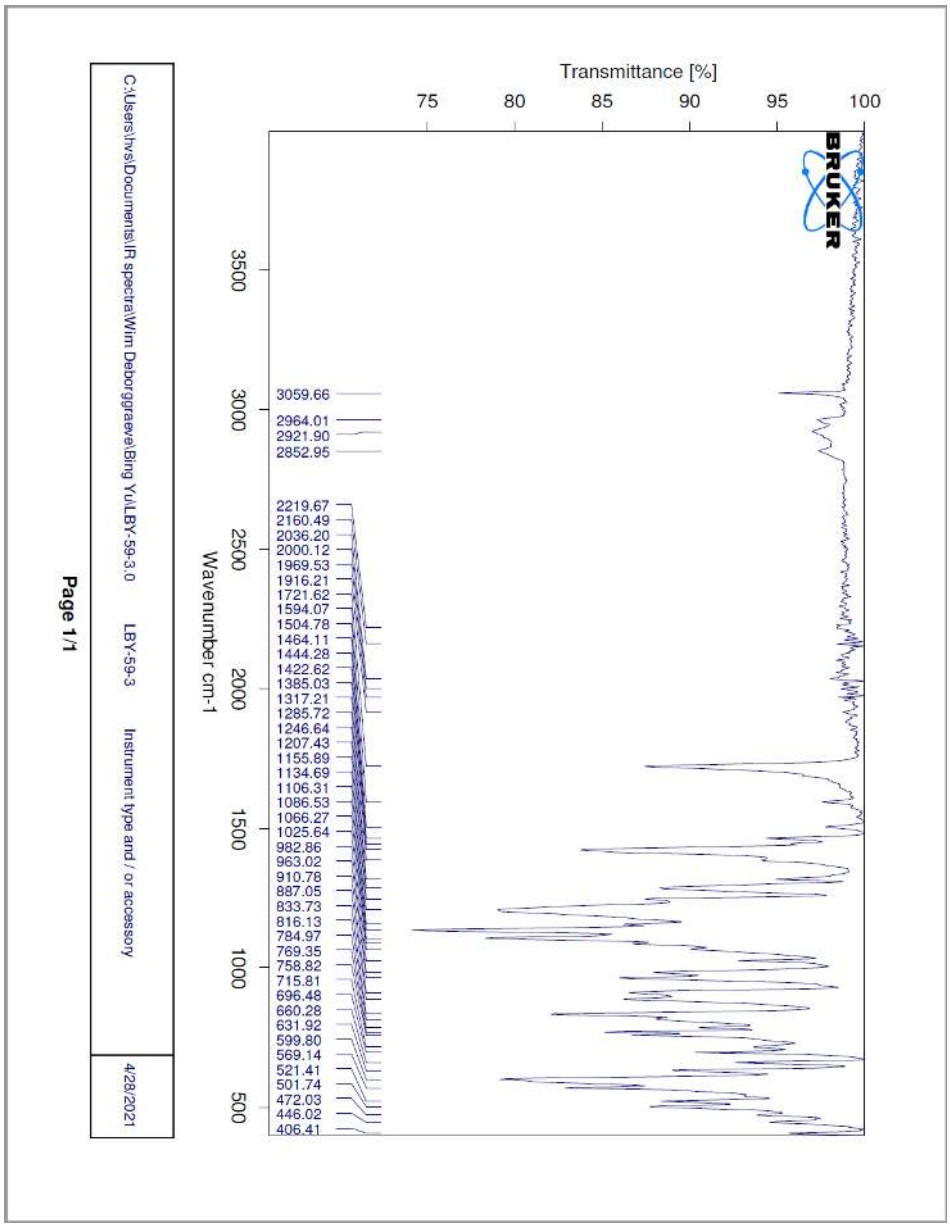
2-hydroxyphenyl trifluoromethanesulfonate (compound **14**, cas number: 133617-36-4)

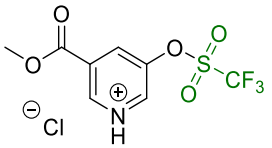




Chemical Formula: $C_8H_4F_6O_6S_2$
Exact Mass: 373.9353

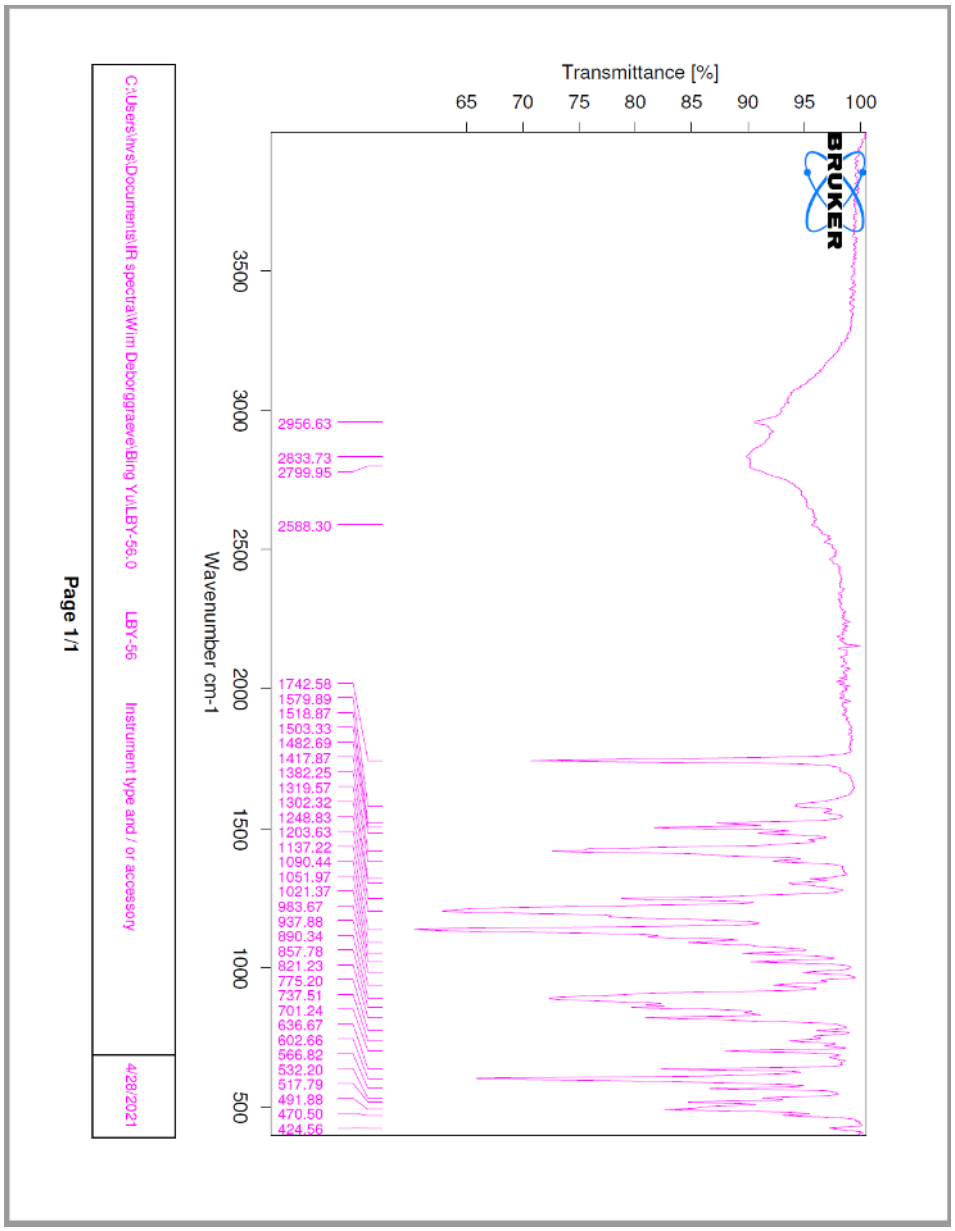
1,2-phenylene bis(trifluoromethanesulfonate) (compound **15**, cas number: 17763-91-6)

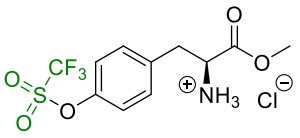




Chemical Formula: $C_8H_7ClF_3NO_5S$
Exact Mass: 320.9686

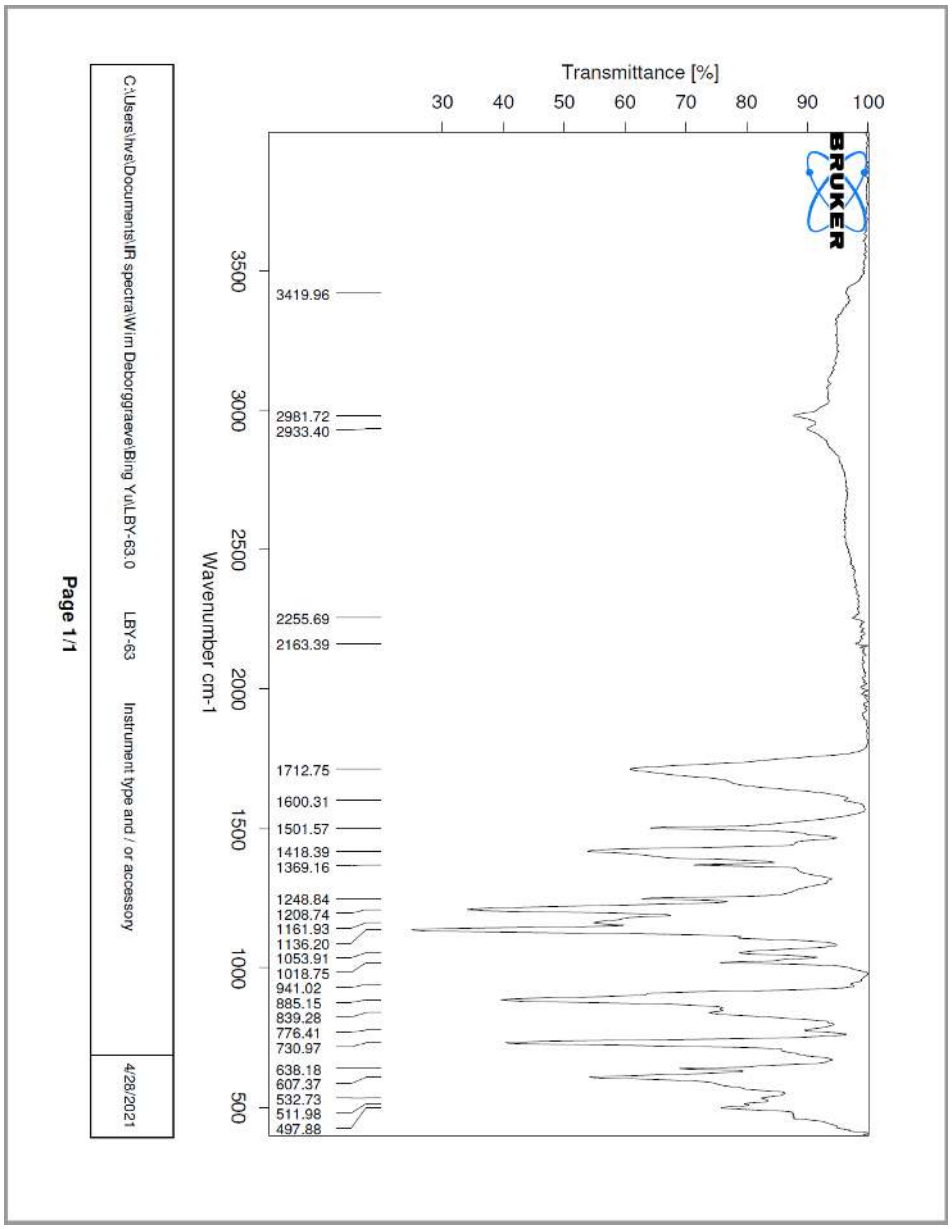
3-(methoxycarbonyl)-5-(((trifluoromethyl)sulfonyl)oxy)pyridin-1-ium chloride (compound **23**)

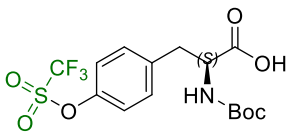




Chemical Formula: $C_{11}H_{13}ClF_3NO_5S$
Exact Mass: 363.0155

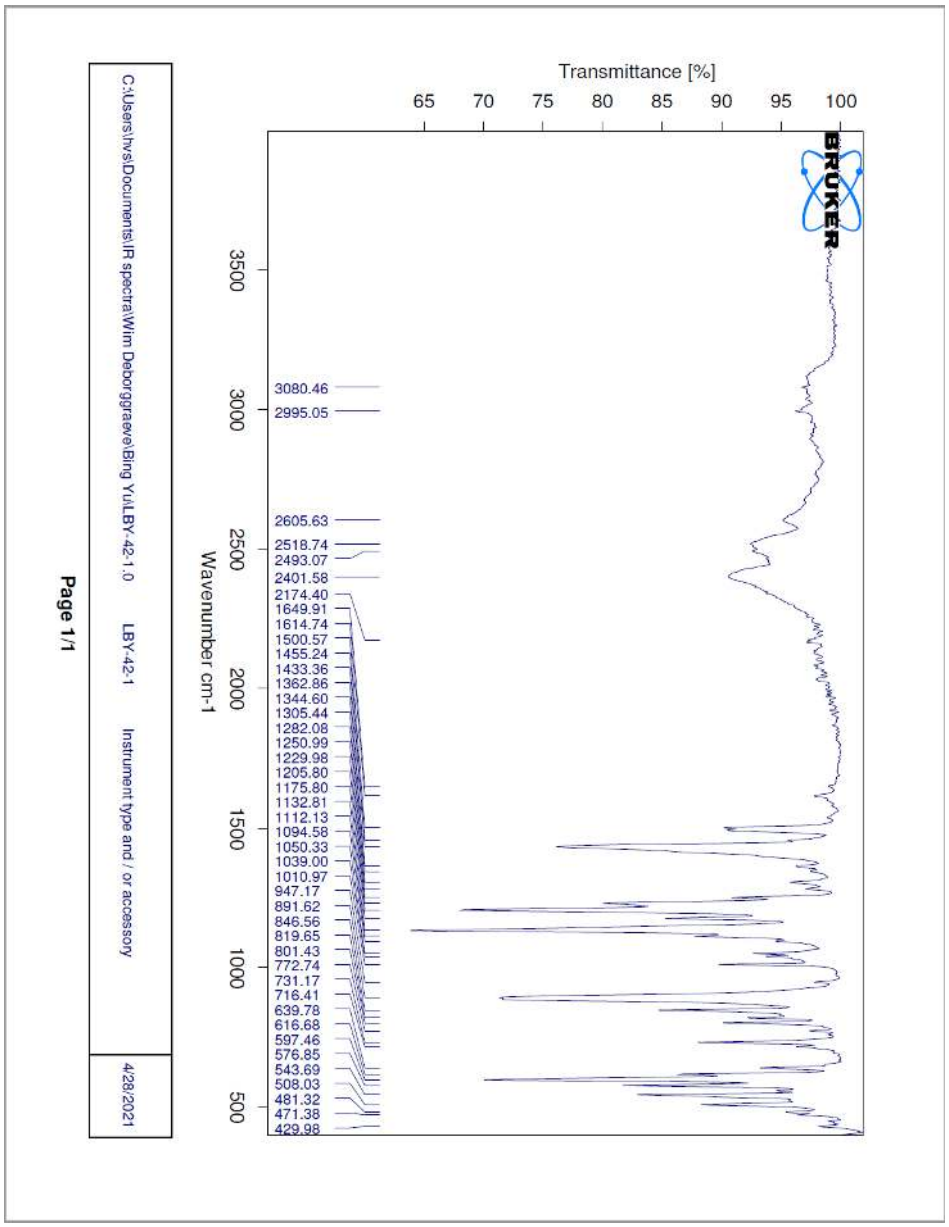
(S)-1-methoxy-1-oxo-3-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)propan-2-aminium chloride (compound **24**, cas number: 2253981-98-3)

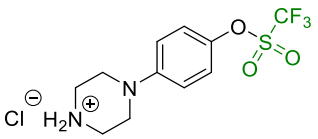




Chemical Formula: $C_{15}H_{18}F_3NO_7S$
Exact Mass: 413.0756

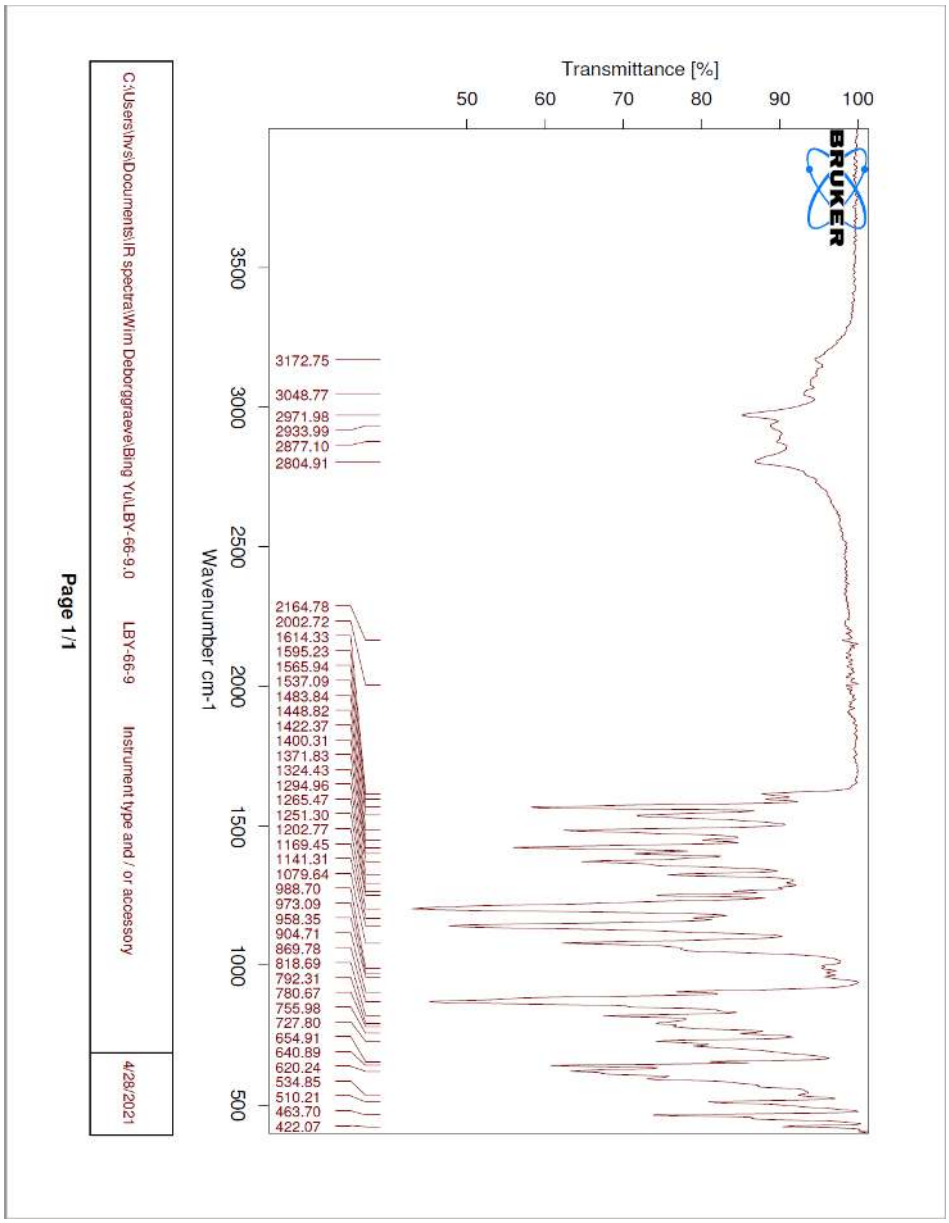
(S)-2-((tert-butoxycarbonyl)amino)-3-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)propanoic acid (compound **25**, cas number: 2093022-49-0)

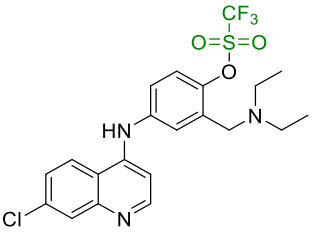




Chemical Formula: $C_{11}H_{14}ClF_3N_2O_3S$
Exact Mass: 346,03658

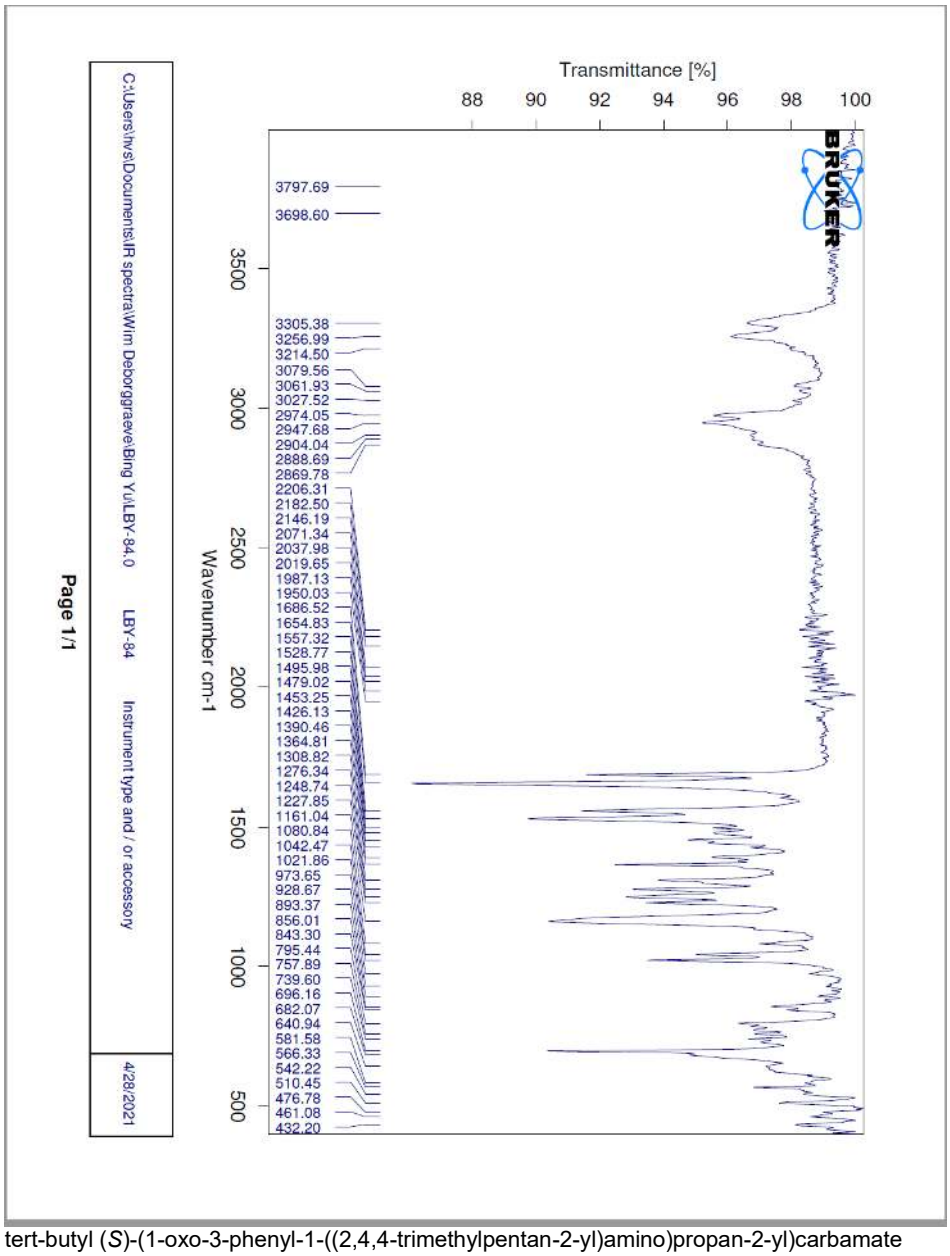
4-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)piperazin-1-ium chloride (compound 28)

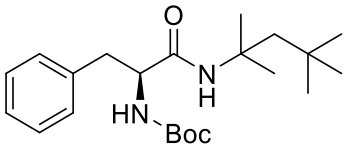




Chemical Formula: $C_{21}H_{21}ClF_3N_3O_3S$
Exact Mass: 487.0944

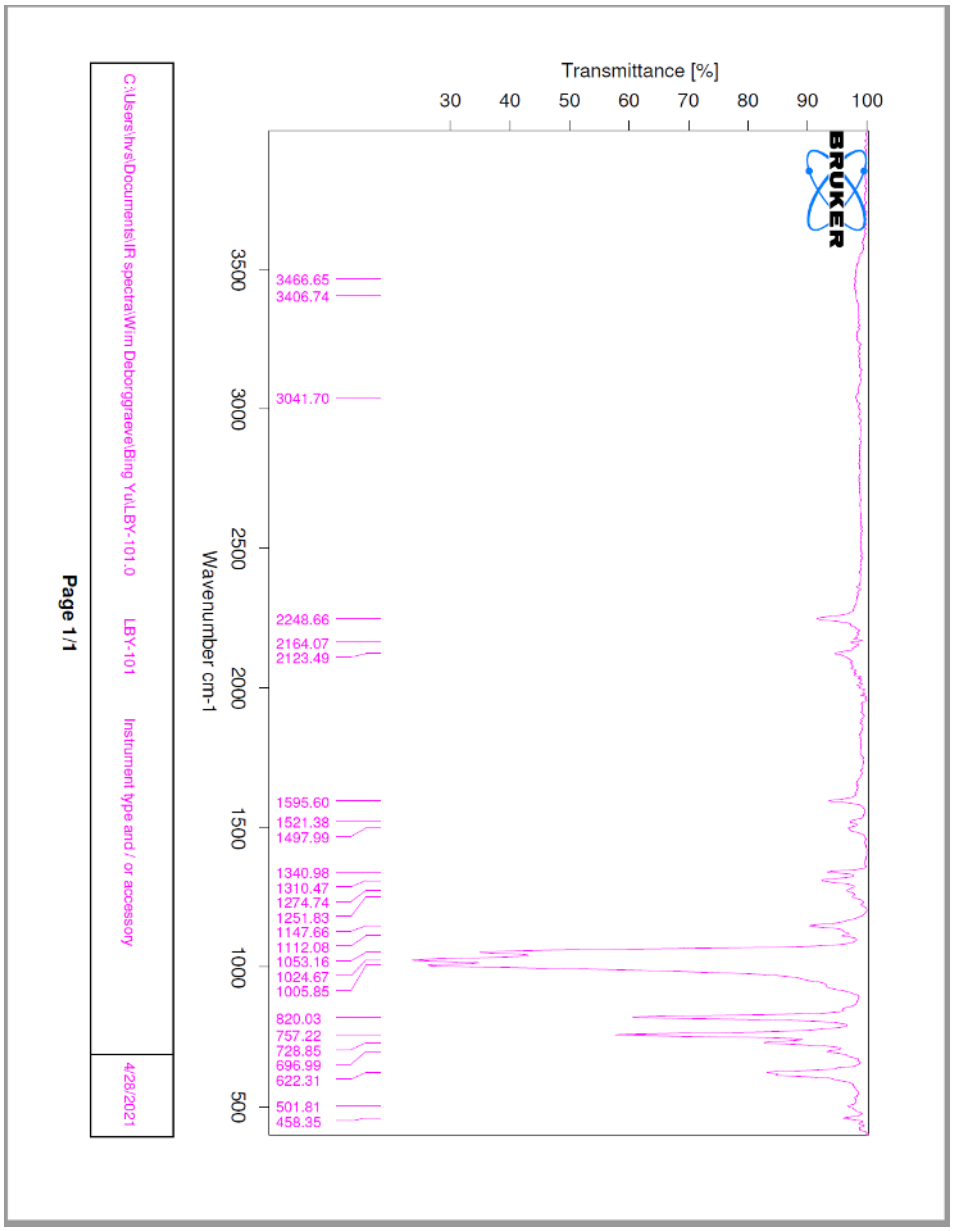
4-((7-chloroquinolin-4-yl)amino)-2-((diethylamino)methyl)phenyl trifluoromethanesulfonate (compound **29**)

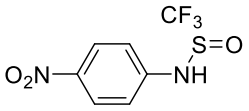




Chemical Formula: $C_{22}H_{36}N_2O_3$
Exact Mass: 376.2726

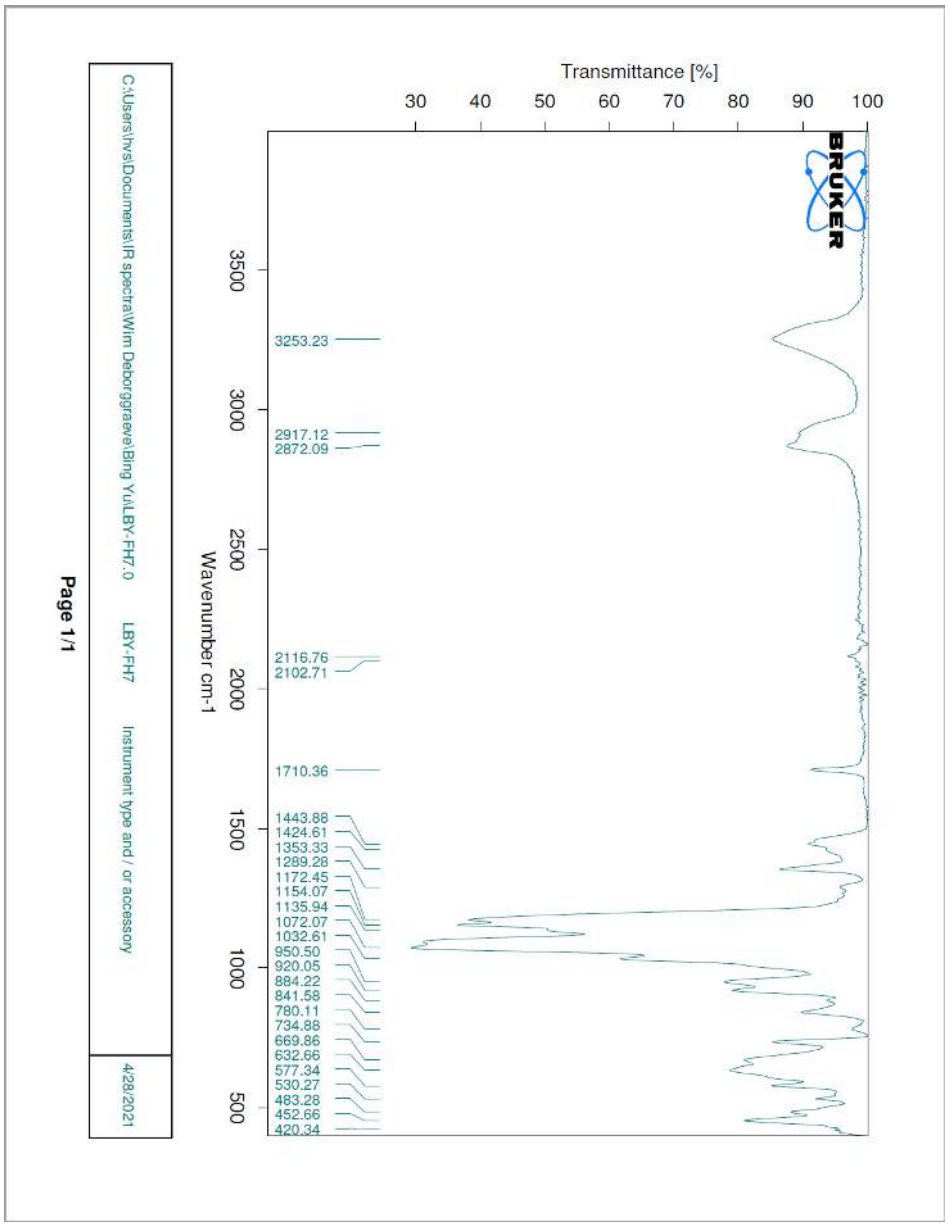
tert-butyl (*S*)-(1-oxo-3-phenyl-1-((2,4,4-trimethylpentan-2-yl)amino)propan-2-yl)carbamate (compound **44**, new compound)

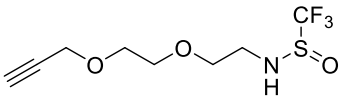




Chemical Formula: $C_7H_5F_3N_2O_3S$
Exact Mass: 253.9973

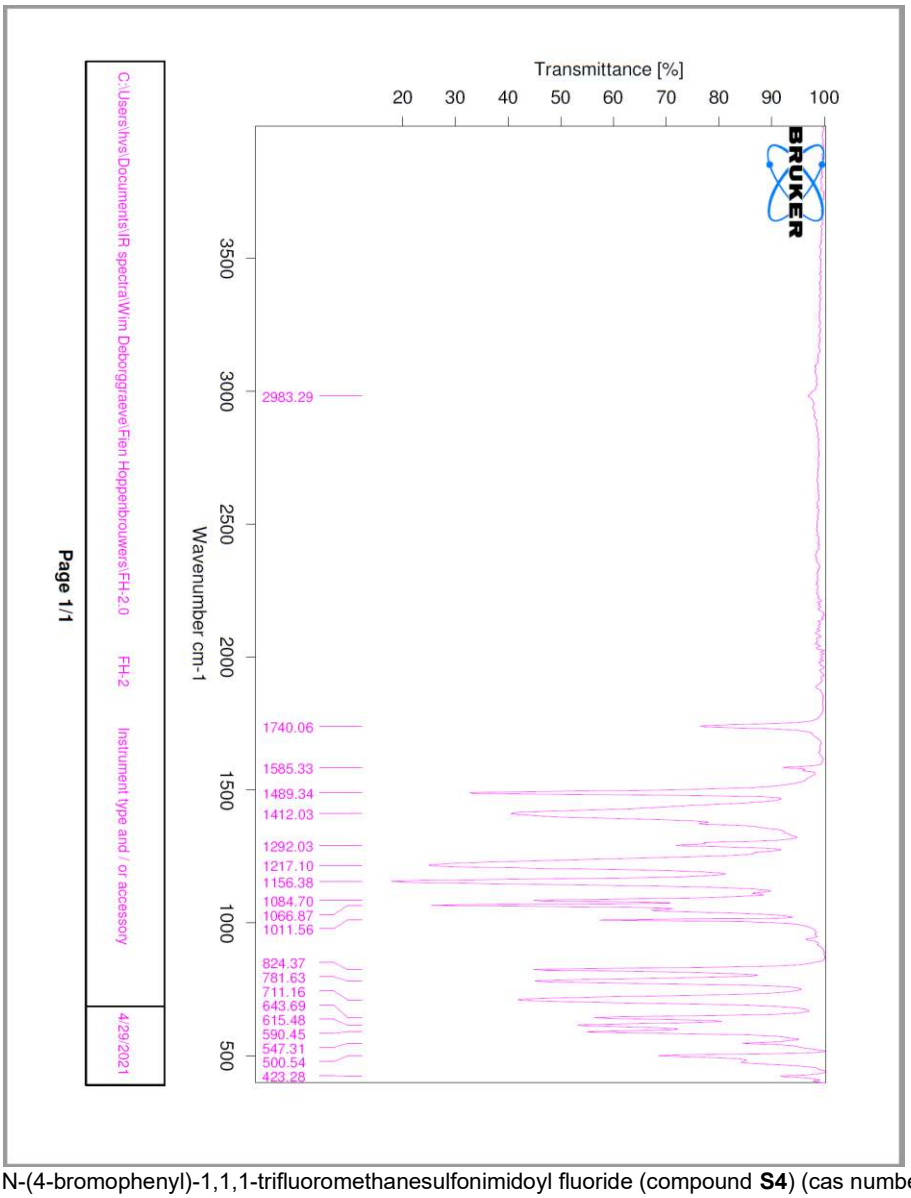
1,1,1-trifluoro-N-(4-nitrophenyl)methanesulfinamide (compound **S2**) (new compound)

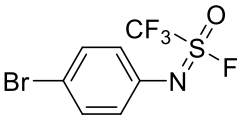




Chemical Formula: $C_8H_{12}F_3NO_3S$
Exact Mass: 259.0490

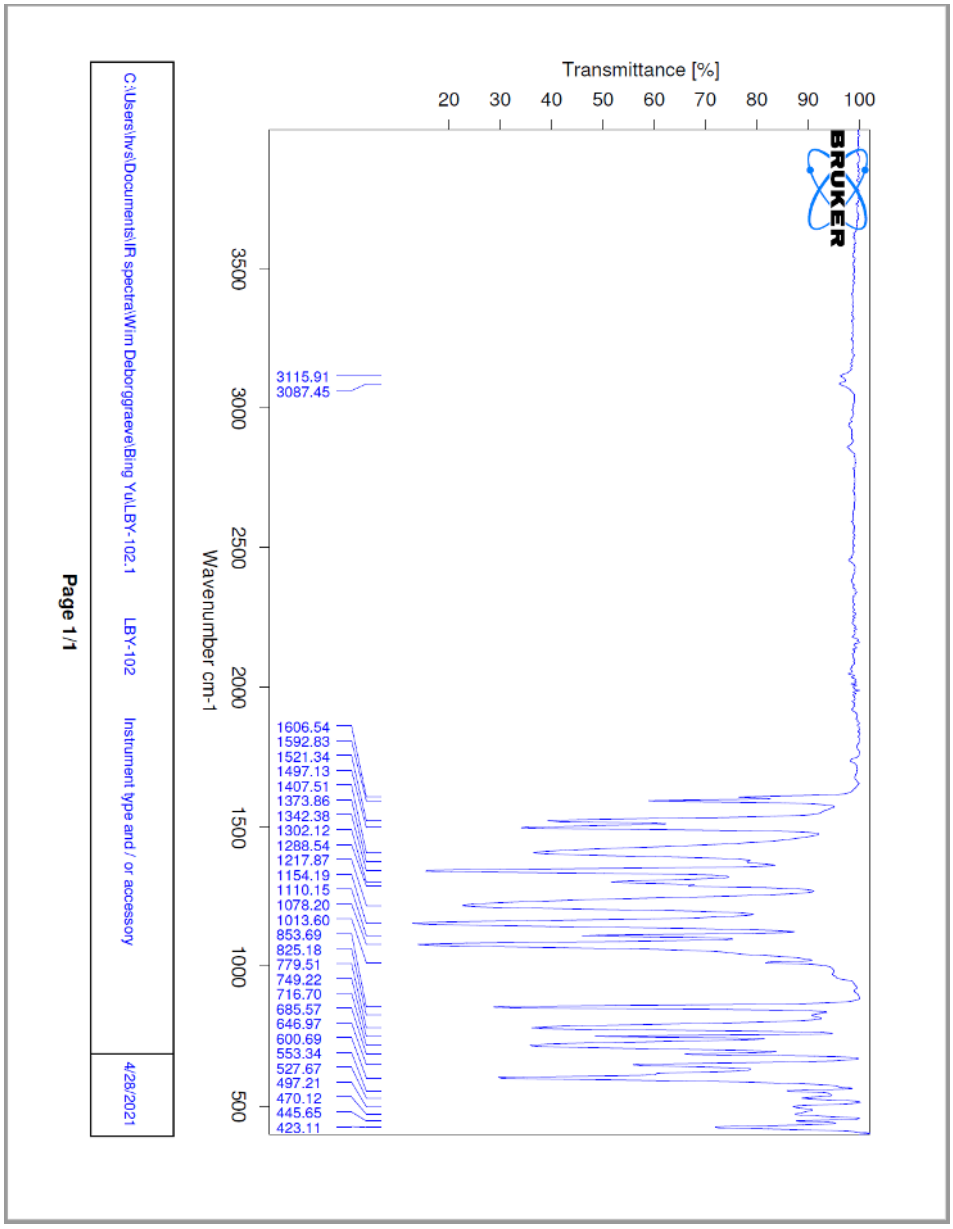
1,1,1-trifluoro-N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)methanesulfinamide (compound **S3**) (new compound)

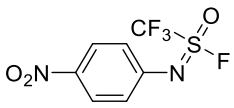




Chemical Formula: $C_7H_4BrF_4NOS$
Exact Mass: 304.9133

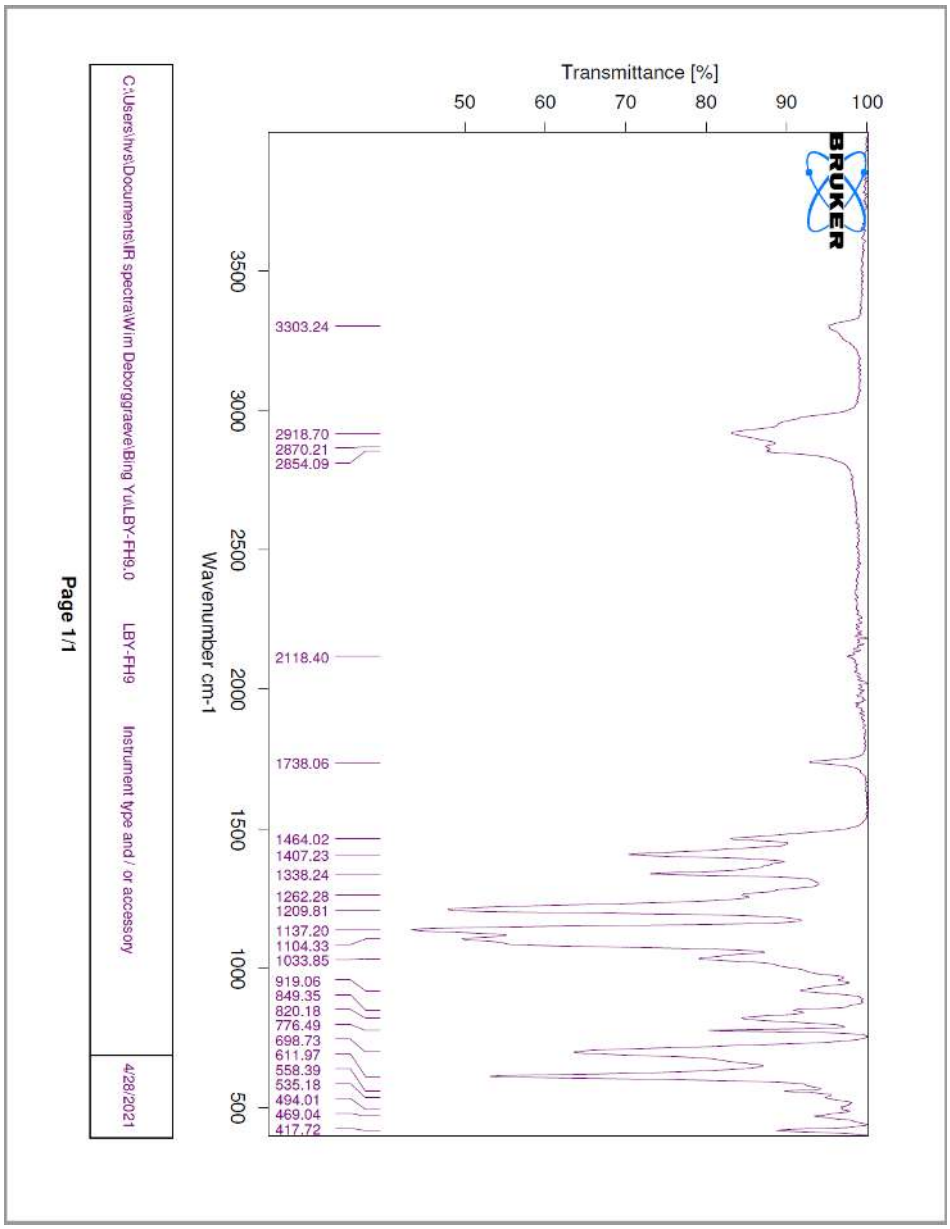
N-(4-bromophenyl)-1,1,1-trifluoromethanesulfonimidoyl fluoride (compound **S4**) (cas number: 2273795-55-2)

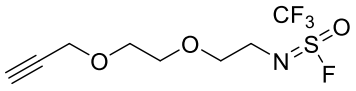




Chemical Formula: $C_7H_4F_4N_2O_3S$
Exact Mass: 271.9879

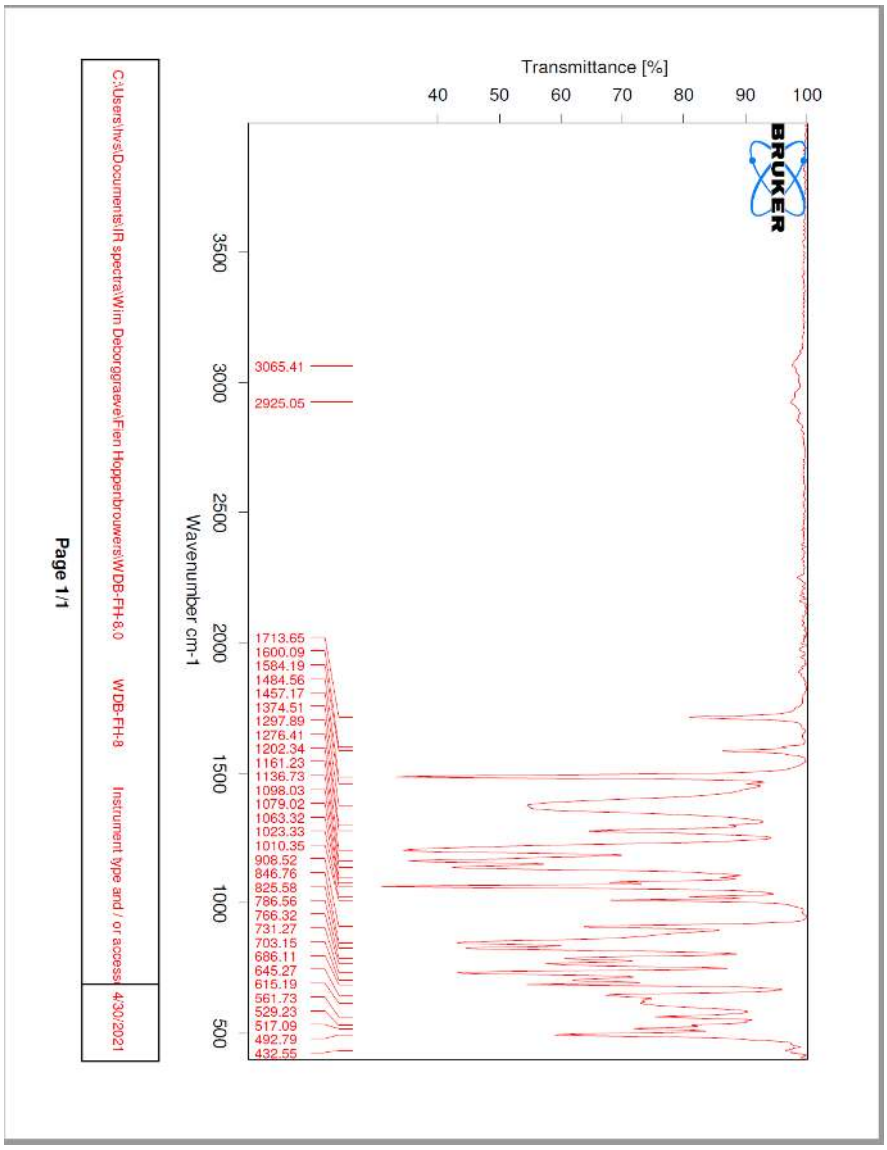
1,1,1-trifluoro-N-(4-nitrophenyl)methanesulfonimidoyl fluoride (compound **S5**) (new compound)

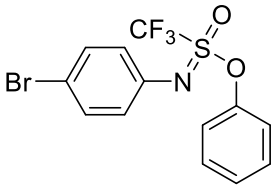




Chemical Formula: $C_8H_{11}F_4NO_3S$
Exact Mass: 277.0396

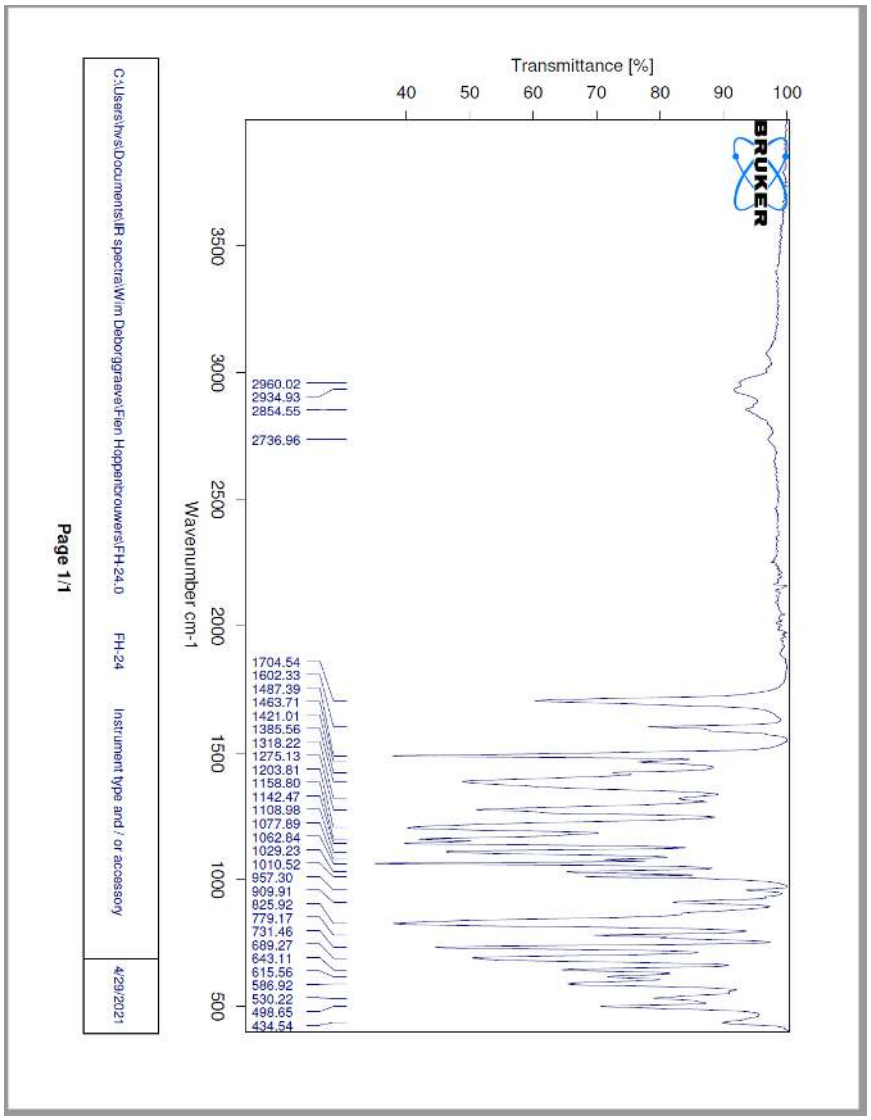
1,1,1-trifluoro-N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)methanesulfonimidoyl fluoride (compound **S6**) (new compound)

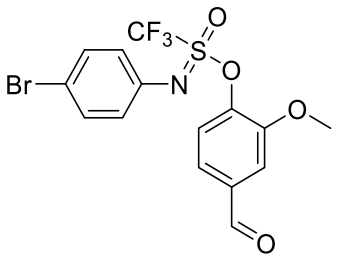




Chemical Formula: $C_{13}H_9BrF_3NO_2S$
Exact Mass: 378.9489

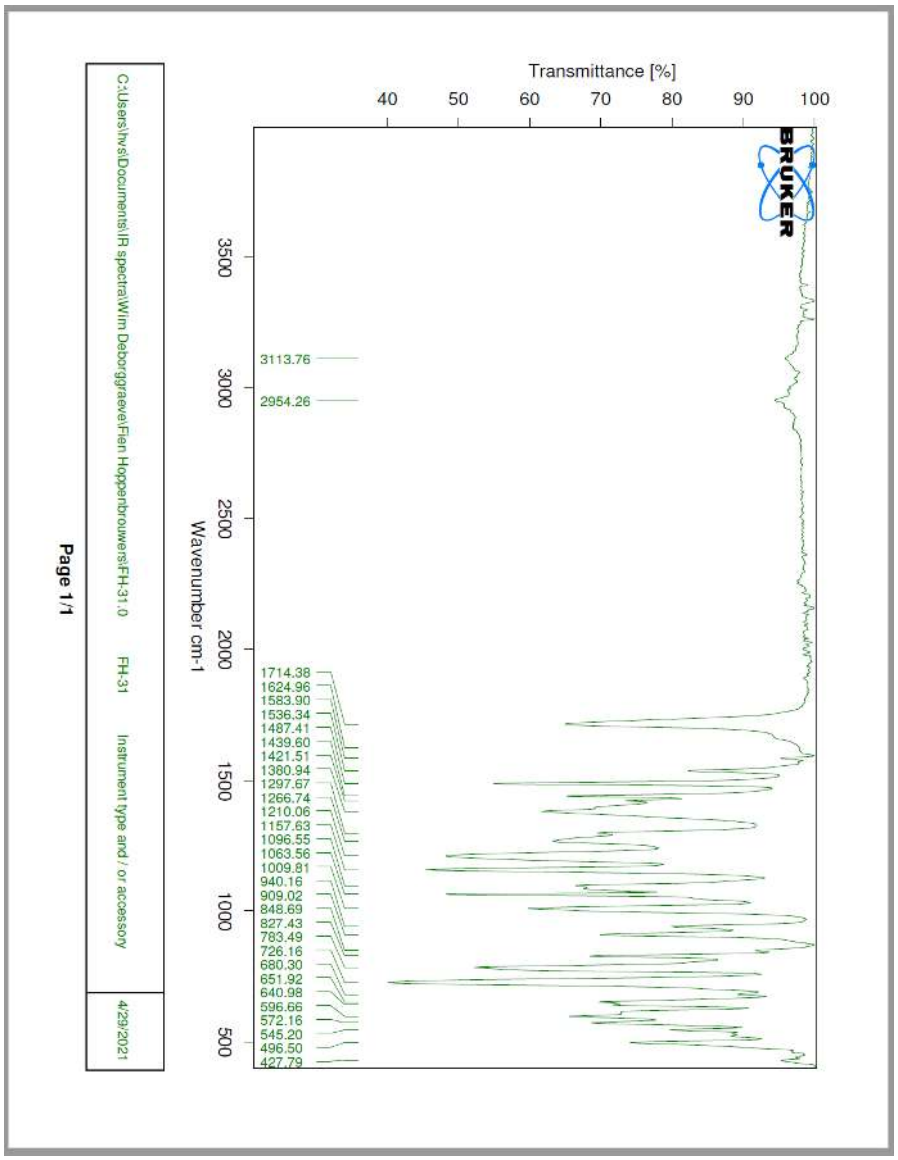
phenyl *N*-(4-bromophenyl)trifluoromethanesulfonimidate (compound **46**)

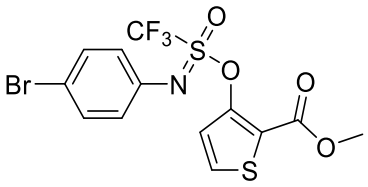




Chemical Formula: $C_{15}H_{11}BrF_3NO_4S$
Exact Mass: 436.9544

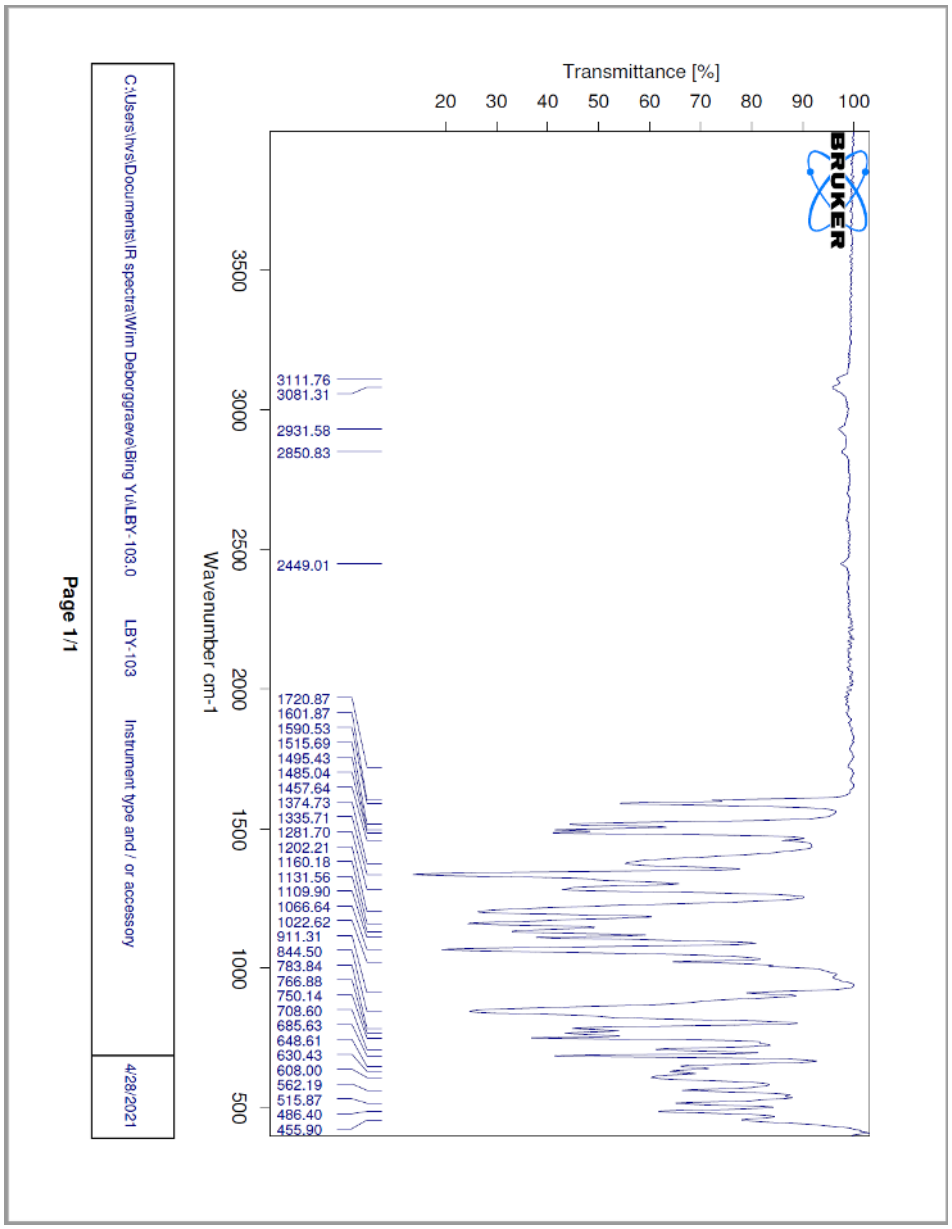
4-formyl-2-methoxyphenyl N-(4-bromophenyl)trifluoromethanesulfonimidate (compound **47**)

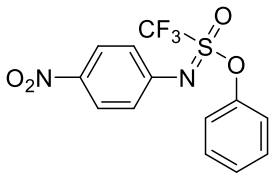




Chemical Formula: $C_{13}H_9BrF_3NO_4S_2$
Exact Mass: 442.9108

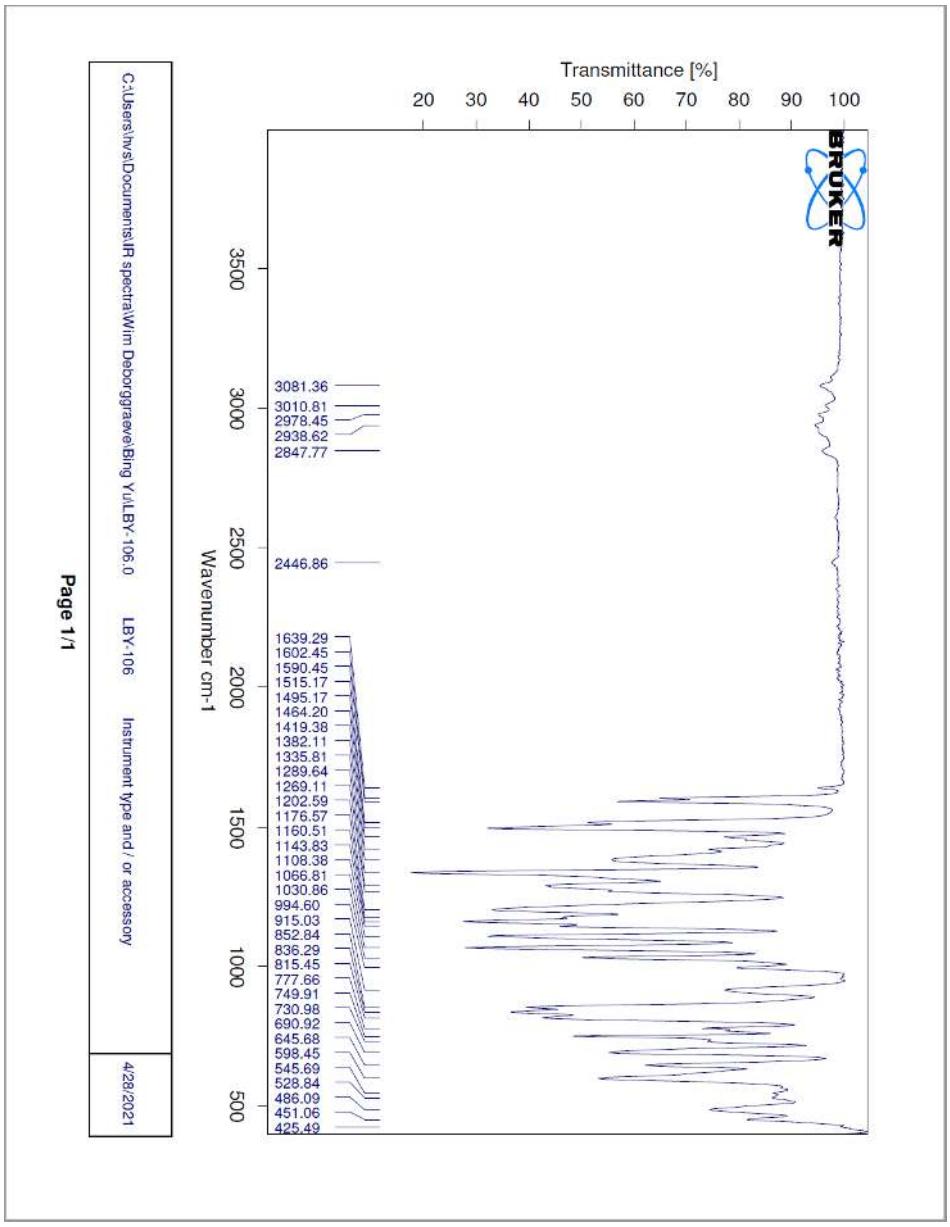
methyl 3-((*N*-(4-bromophenyl)-S-(trifluoromethyl)sulfonimidoyl)oxy)thiophene-2-carboxylate (compound **48**)

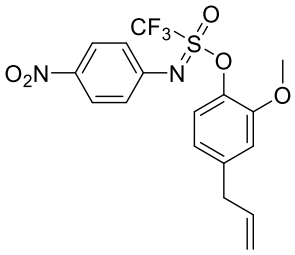




Chemical Formula: $C_{13}H_9F_3N_2O_4S$
Exact Mass: 346.0235

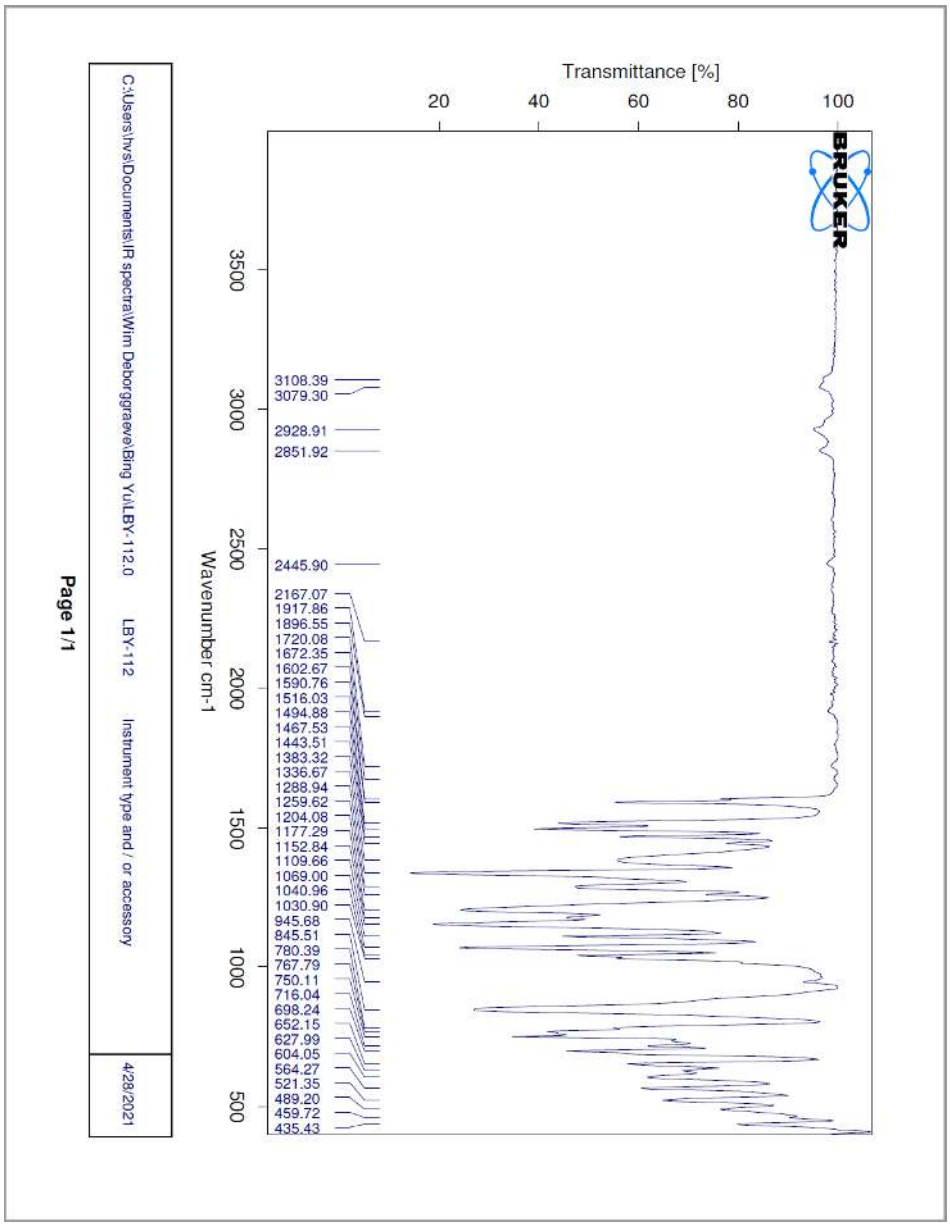
phenyl trifluoro-N-(4-nitrophenyl)methanesulfonimidate (compound **49**, new compound)

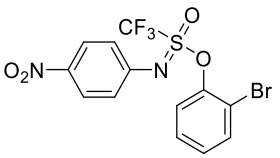




Chemical Formula: $C_{17}H_{15}F_3N_2O_5S$
Exact Mass: 416.0654

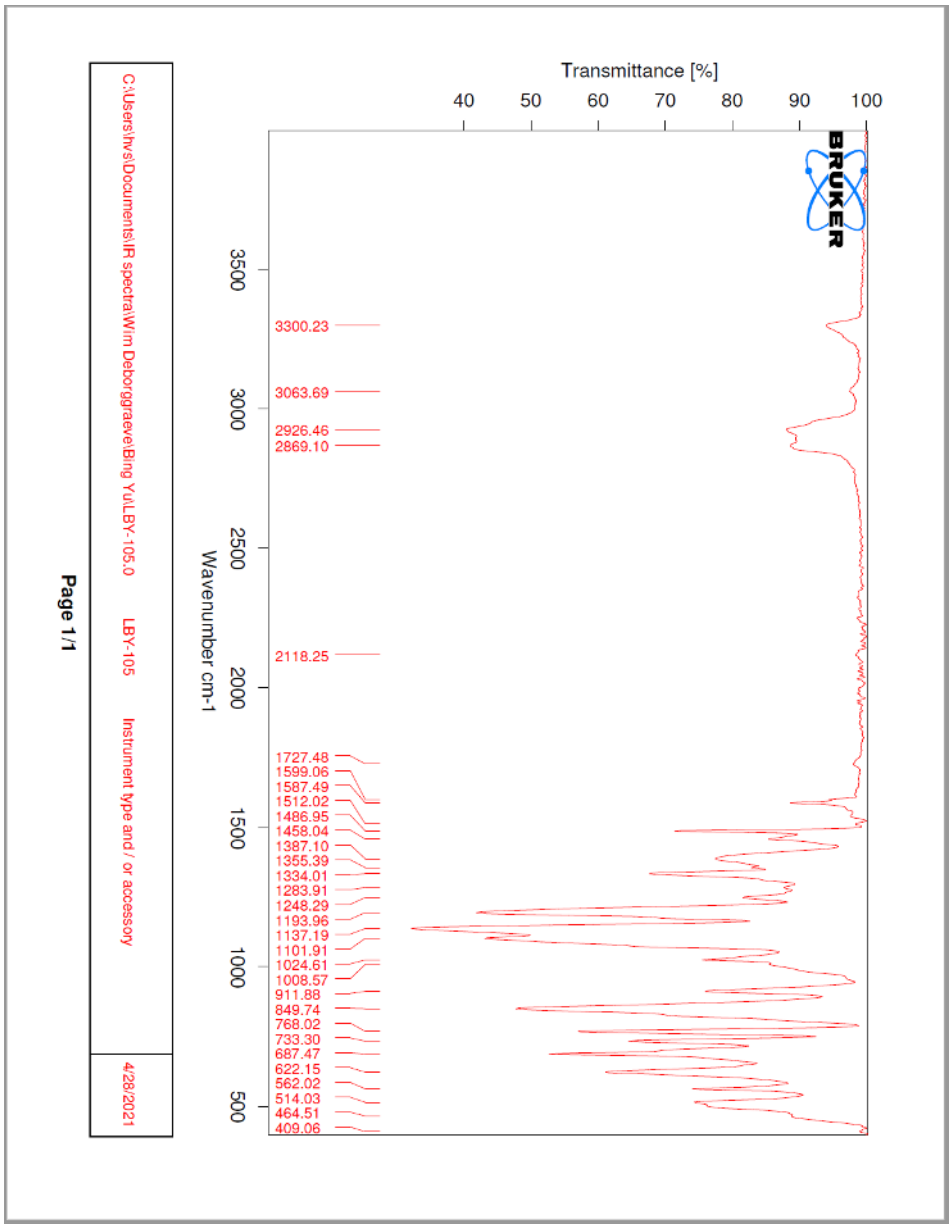
4-allyl-2-methoxyphenyl trifluoro-N-(4-nitrophenyl)methanesulfonimidate (compound **50**, new compound)

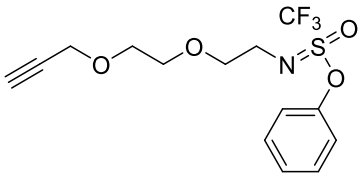




Chemical Formula: $C_{13}H_8BrF_3N_2O_4S$
Exact Mass: 423.9340

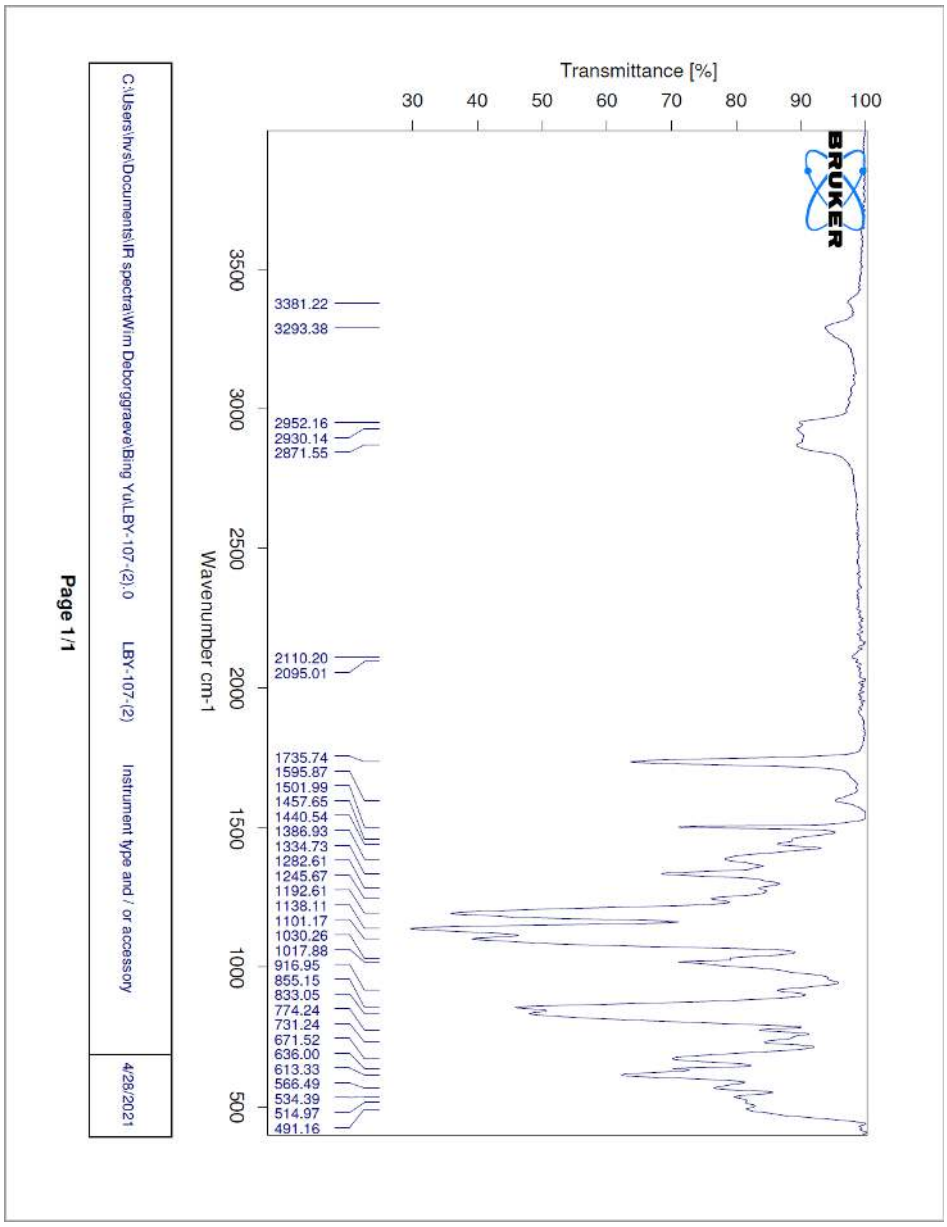
2-bromophenyl trifluoro-N-(4-nitrophenyl)methanesulfonimidate (compound **51**, new compound)

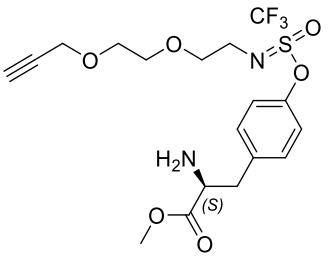




Chemical Formula: $C_{14}H_{16}F_3NO_4S$
Exact Mass: 351.0752

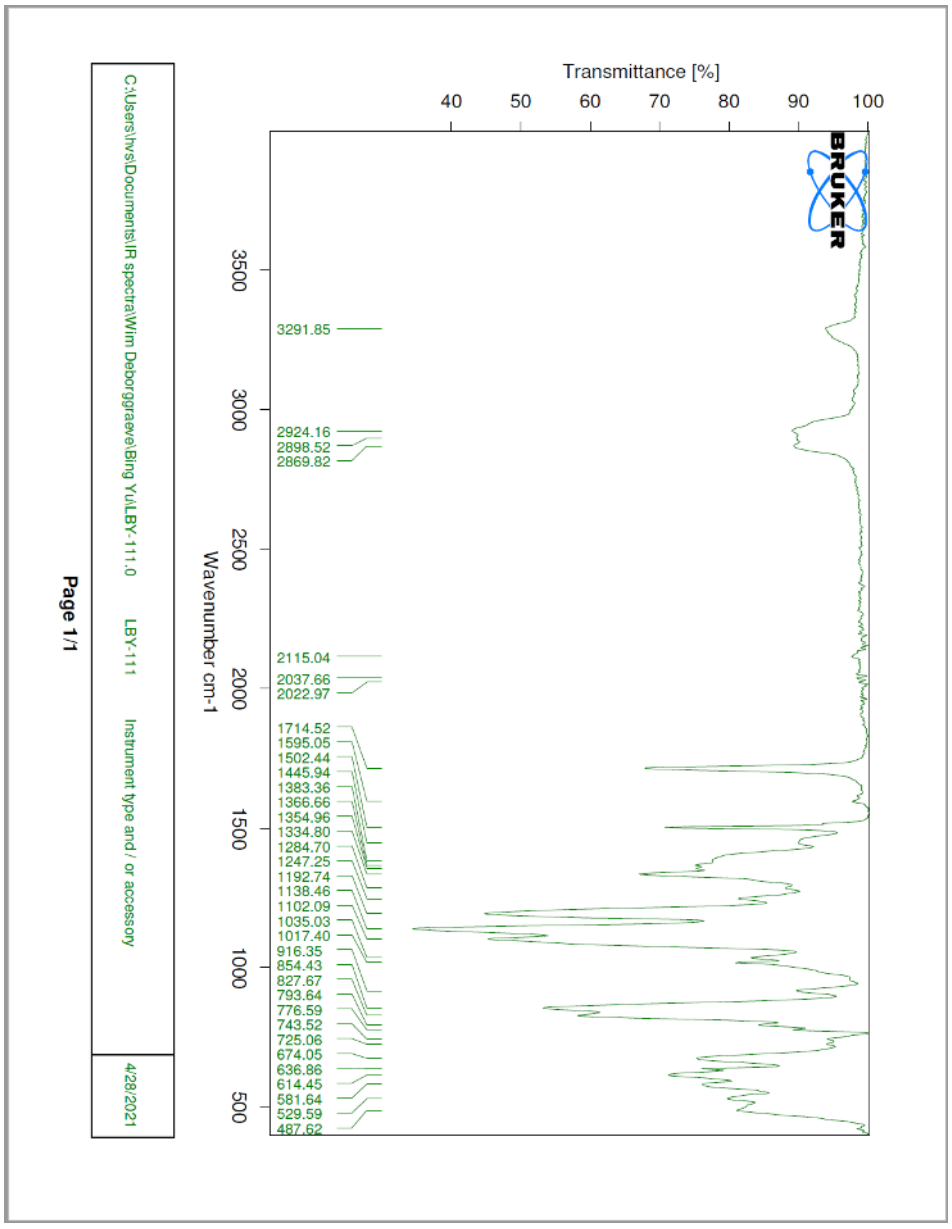
phenyl trifluoro-N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)methanesulfonimidate (compound **52**, new compound)

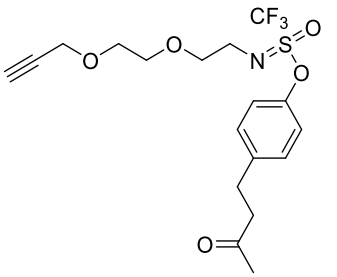




Chemical Formula: $C_{18}H_{23}F_3N_2O_6S$
Exact Mass: 452.1229

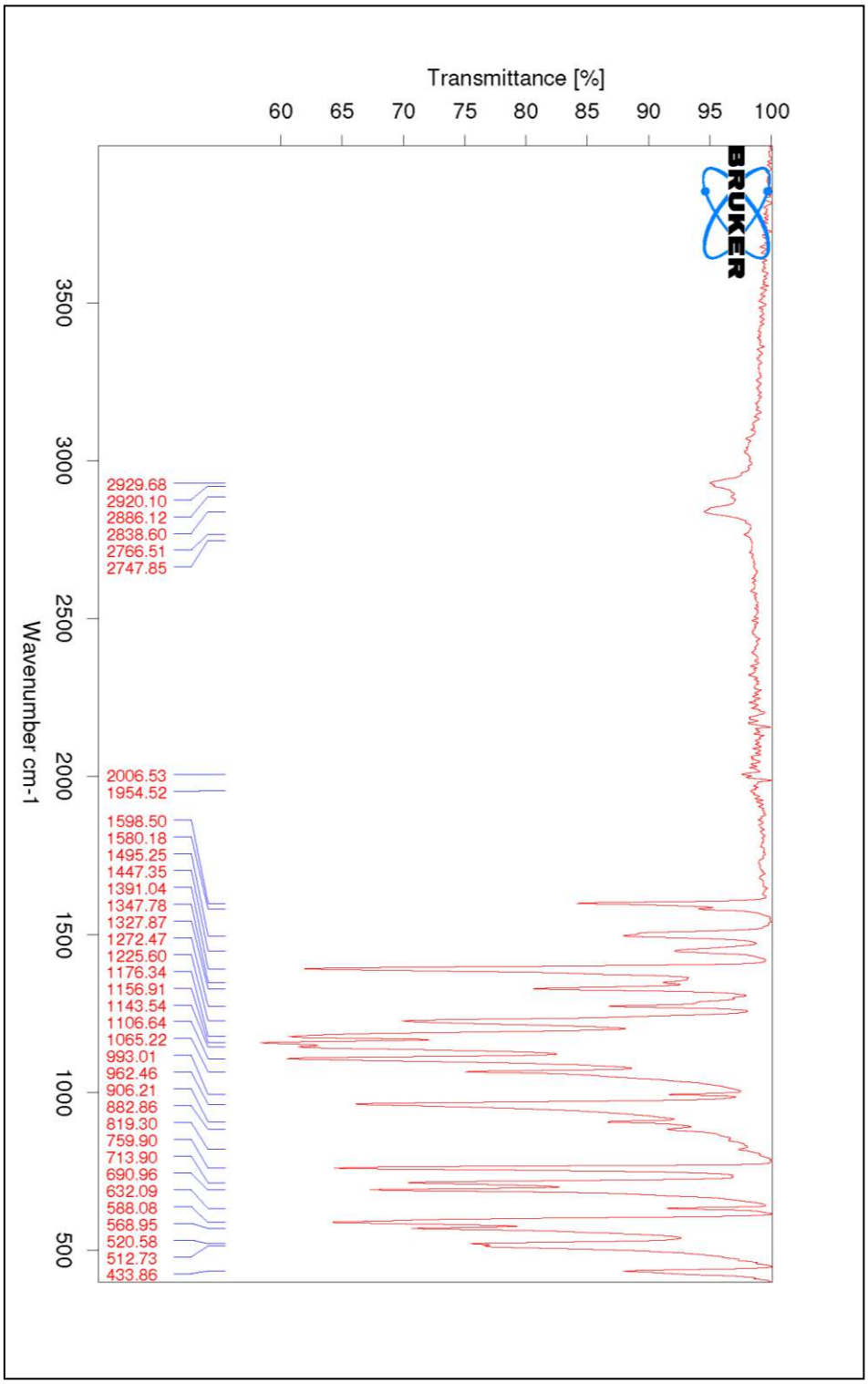
methyl (2*S*)-2-amino-3-(4-((N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)-*S*-(trifluoromethyl)sulfonimidoyl)oxy)phenyl)propanoate (compound **53**, new compound)

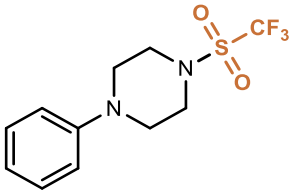




Chemical Formula: $C_{18}H_{22}F_3NO_5S$
Exact Mass: 421.1171

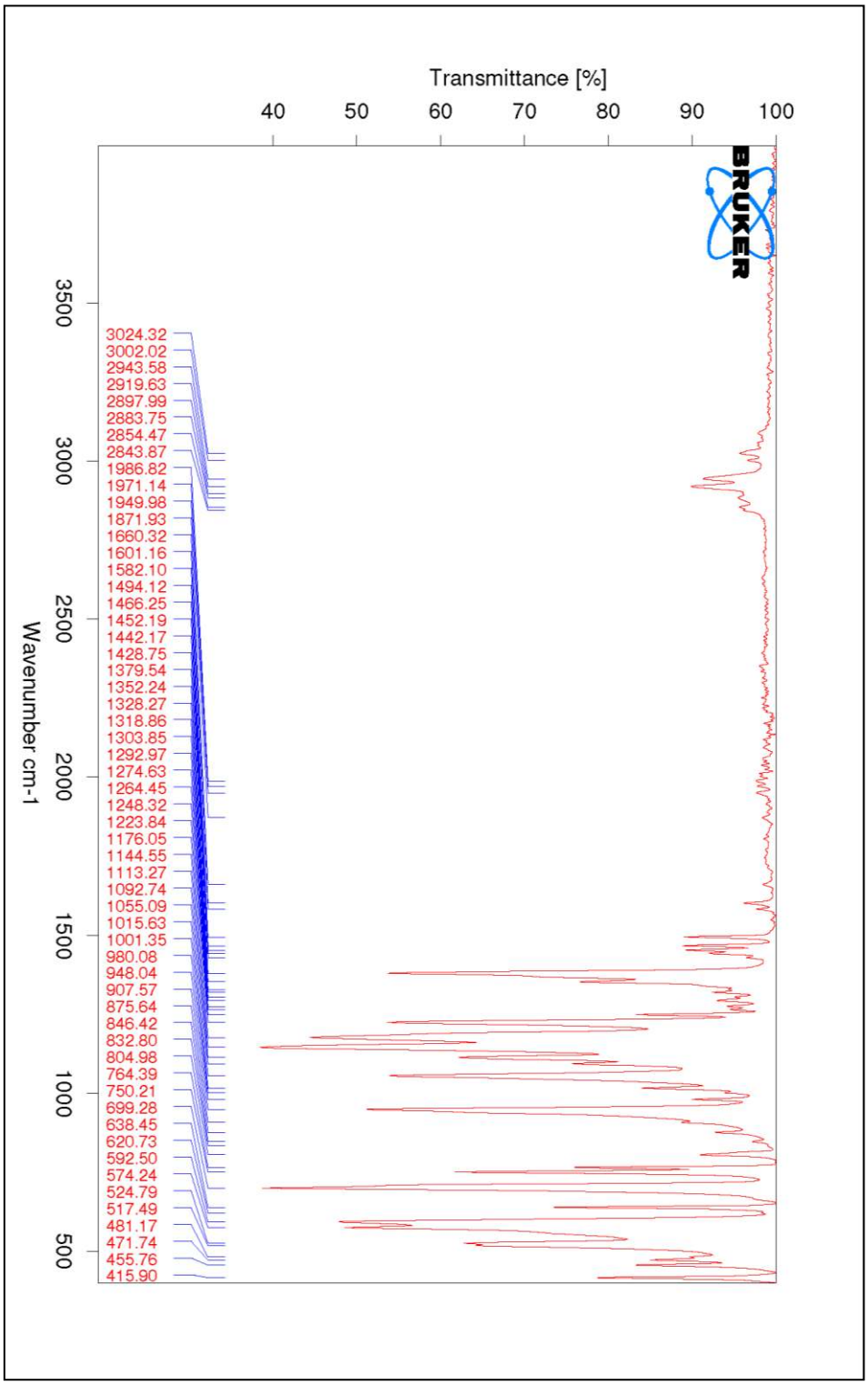
4-(3-oxobutyl)phenyl trifluoro-N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)methanesulfonimidate (compound **54**, new compound)

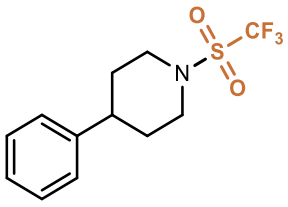




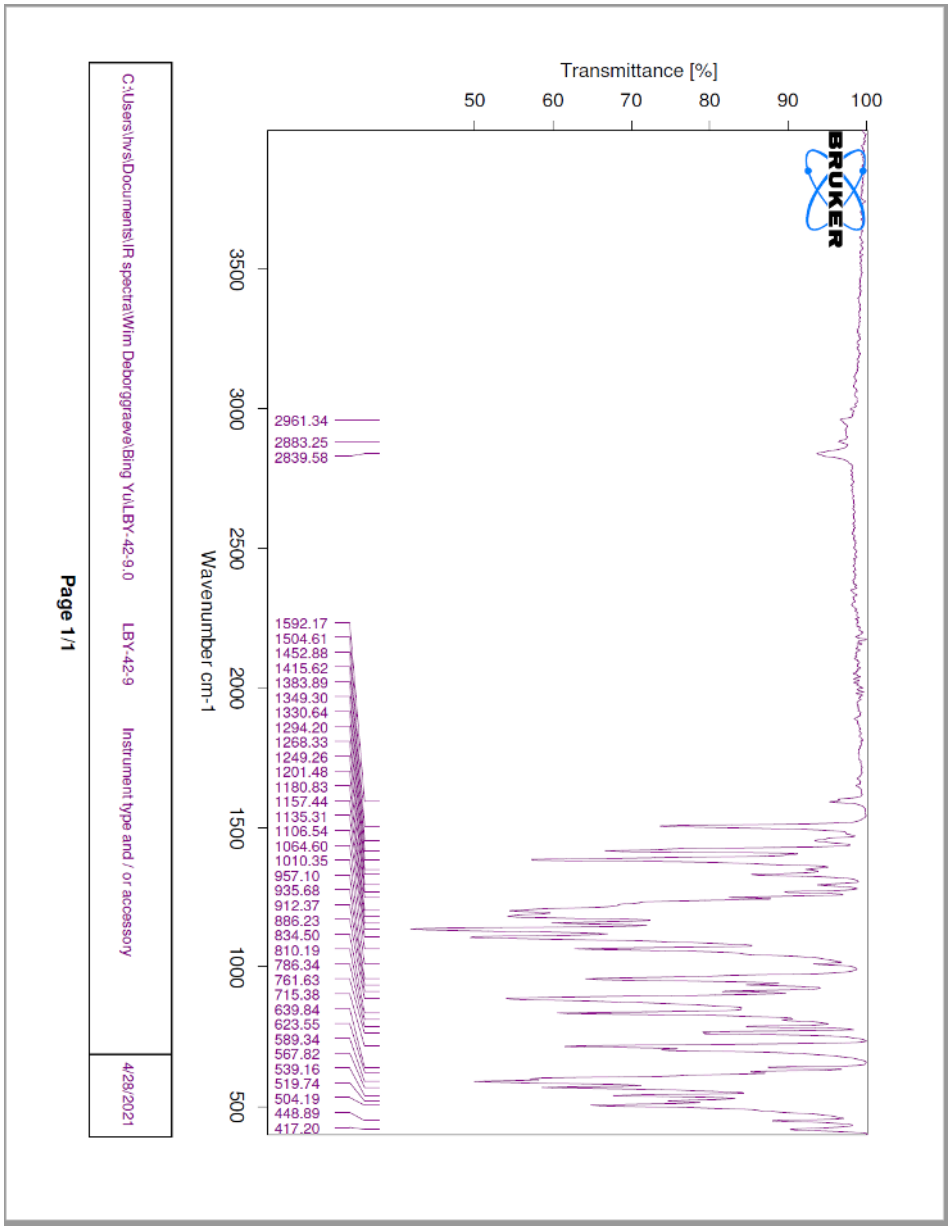
Chemical Formula: $C_{11}H_{13}F_3N_2O_2S$
Exact Mass: 294.06

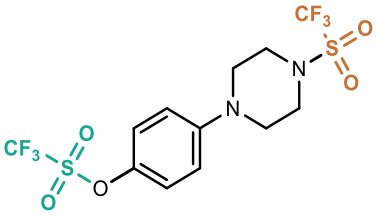
1-phenyl-4-((trifluoromethyl)sulfonyl)piperazine (compound 55)





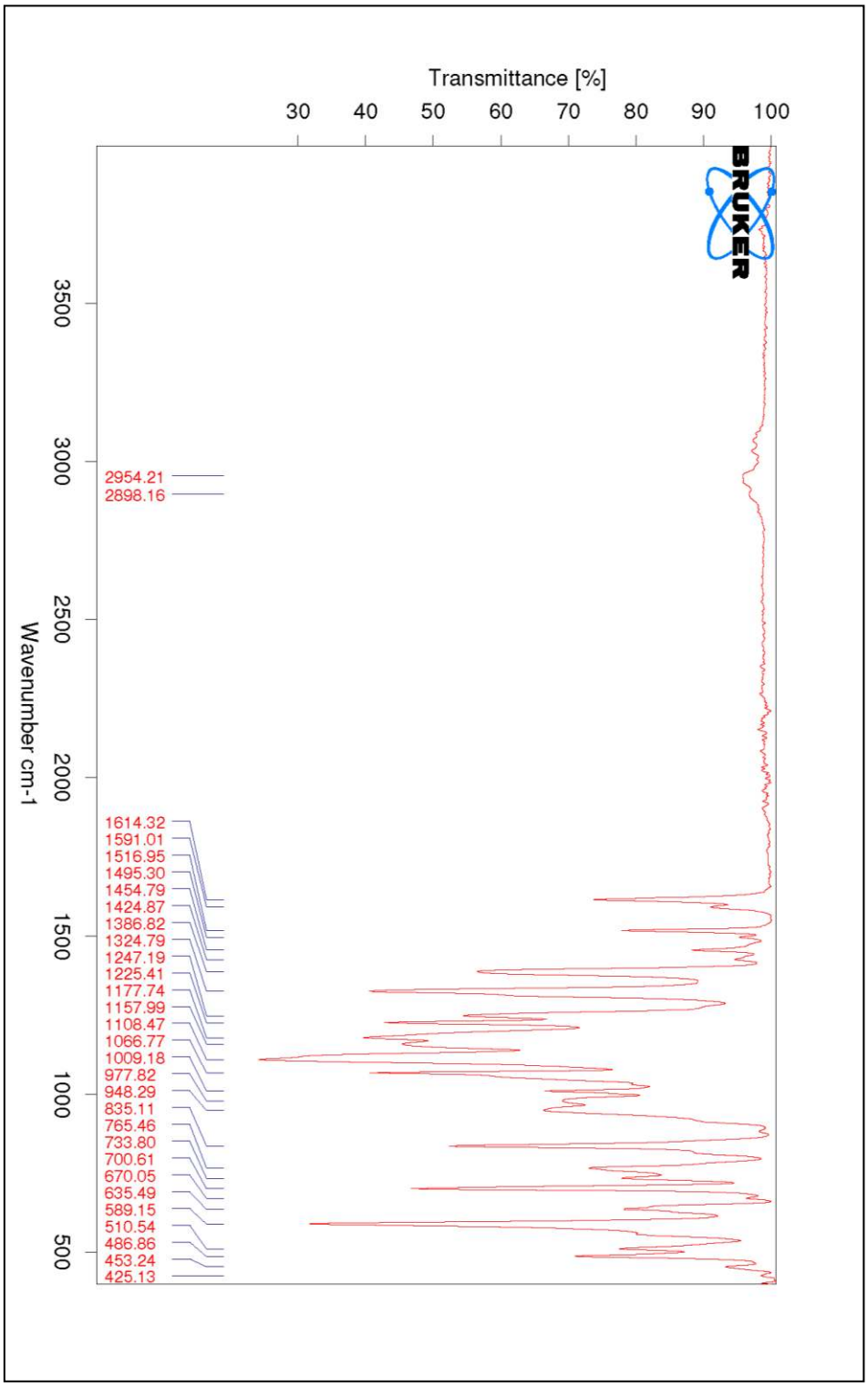
4-phenyl-1-((trifluoromethyl)sulfonyl)piperidine (compound 56)

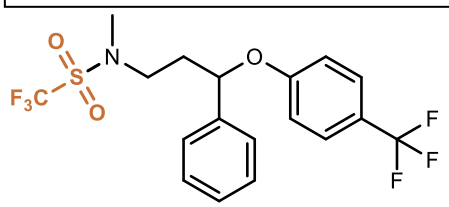




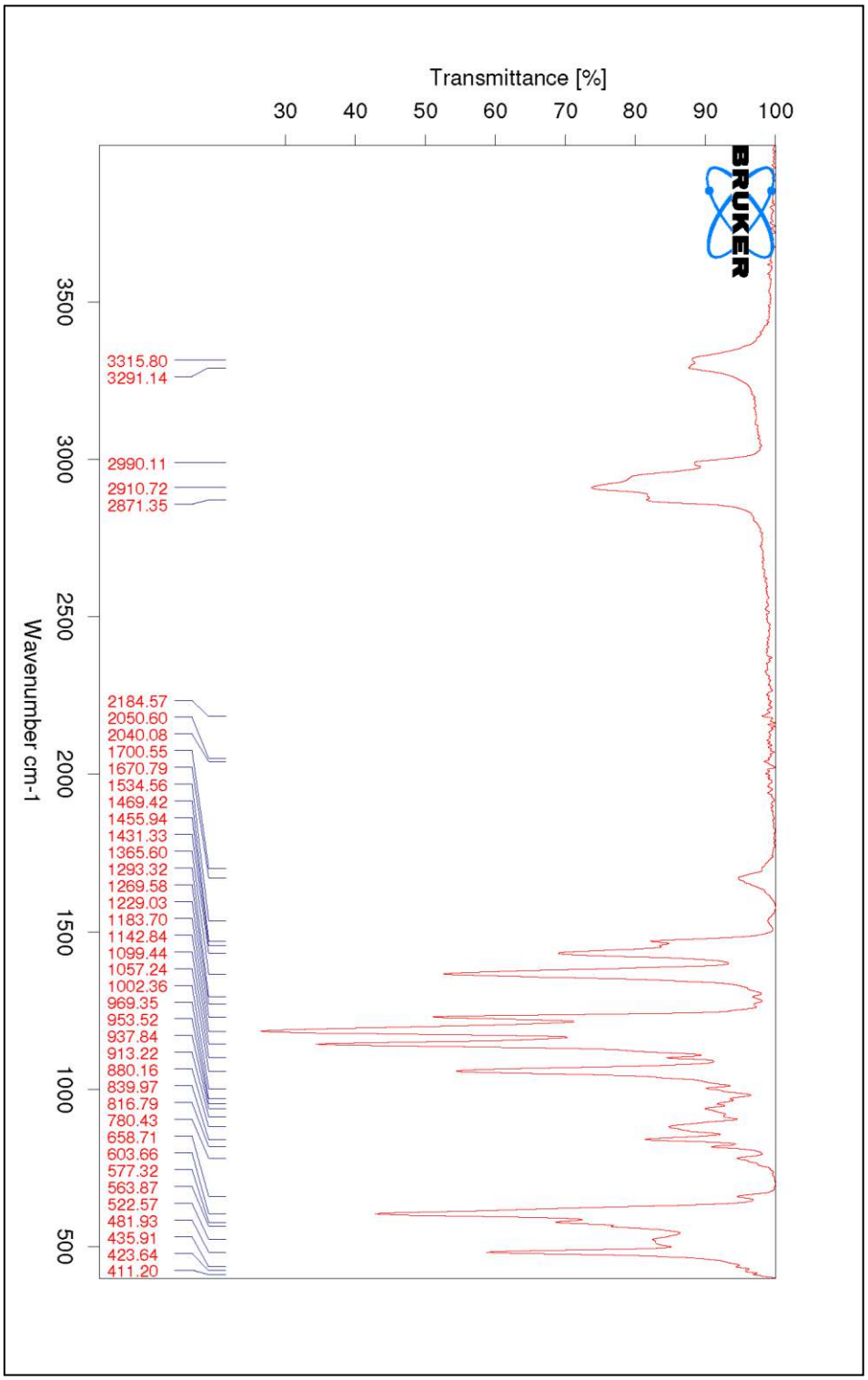
Chemical Formula: $C_{12}H_{12}F_6N_2O_5S_2$
Exact Mass: 442.0092

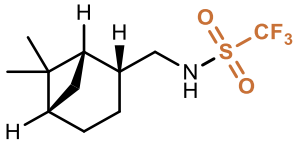
4-(4-((trifluoromethyl)sulfonyl)piperazin-1-yl)phenyl trifluoromethanesulfonate (compound **60**)



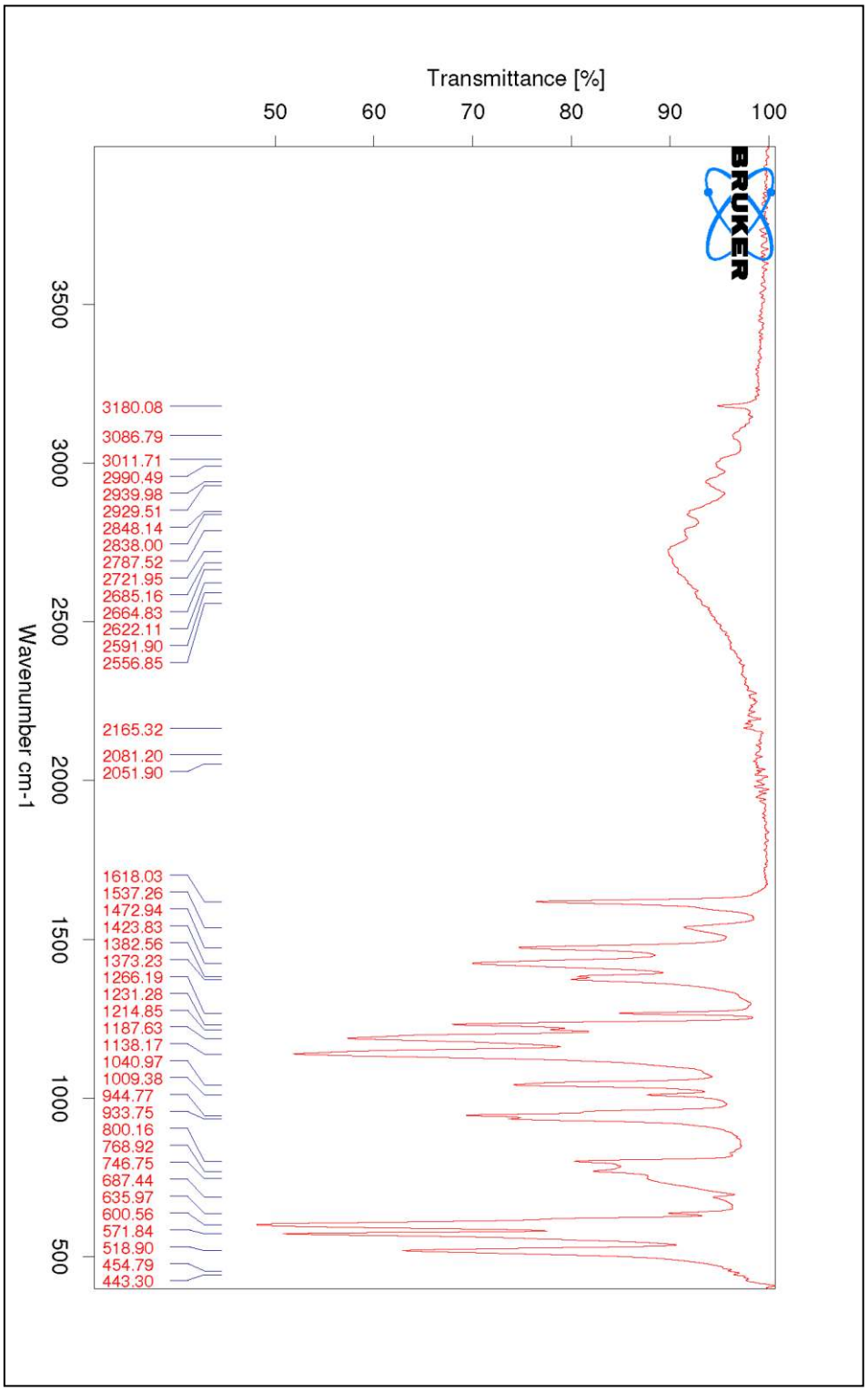


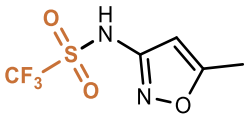
N-(((1S,2R,5S)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl)methyl)-1,1,1-trifluoromethanesulfonamide (compound 62)



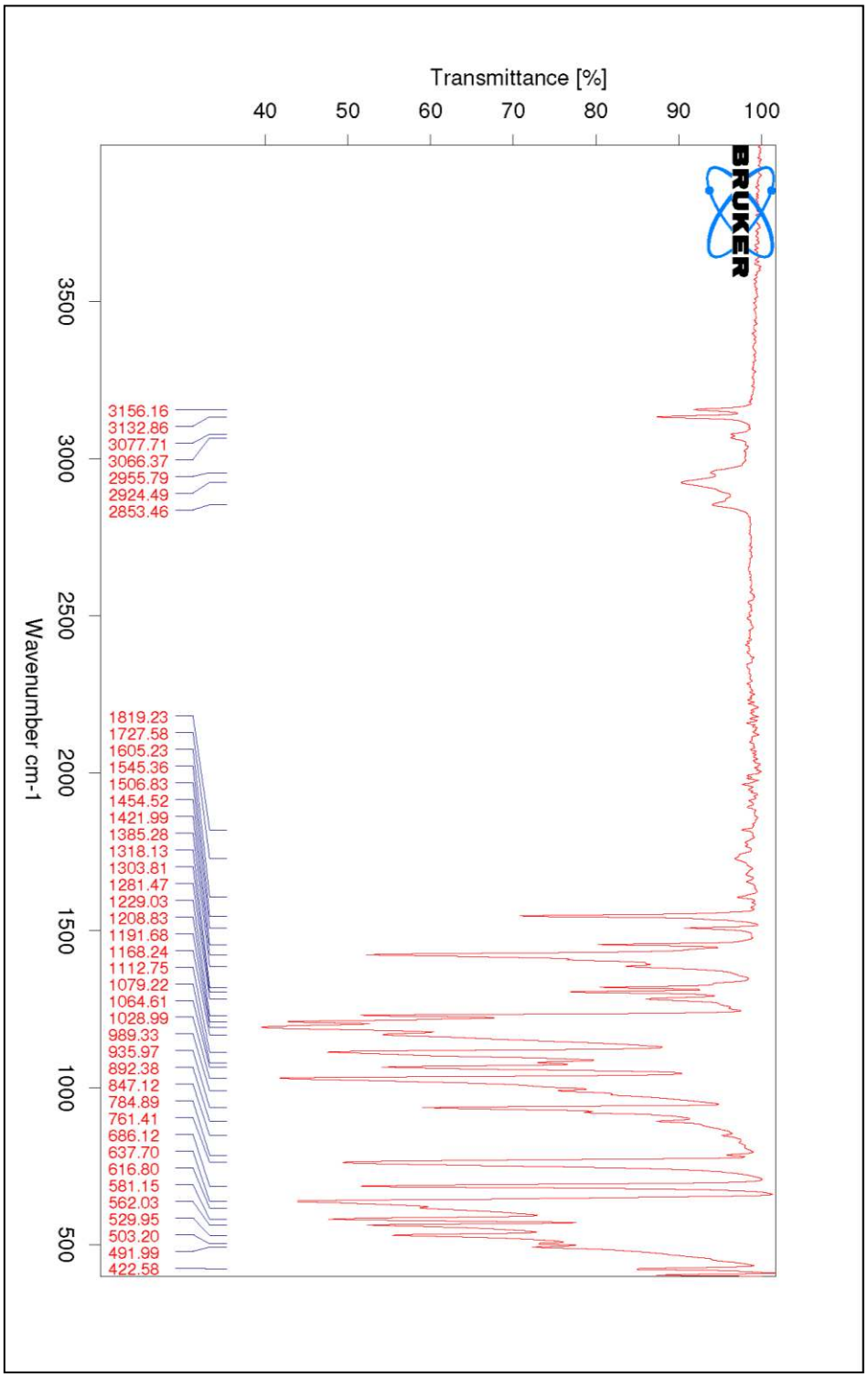


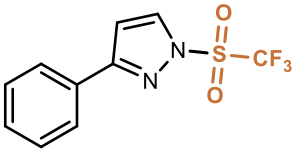
N-(((1S,2R,5S)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl)methyl)-1,1,1-trifluoromethanesulfonamide (compound 63)



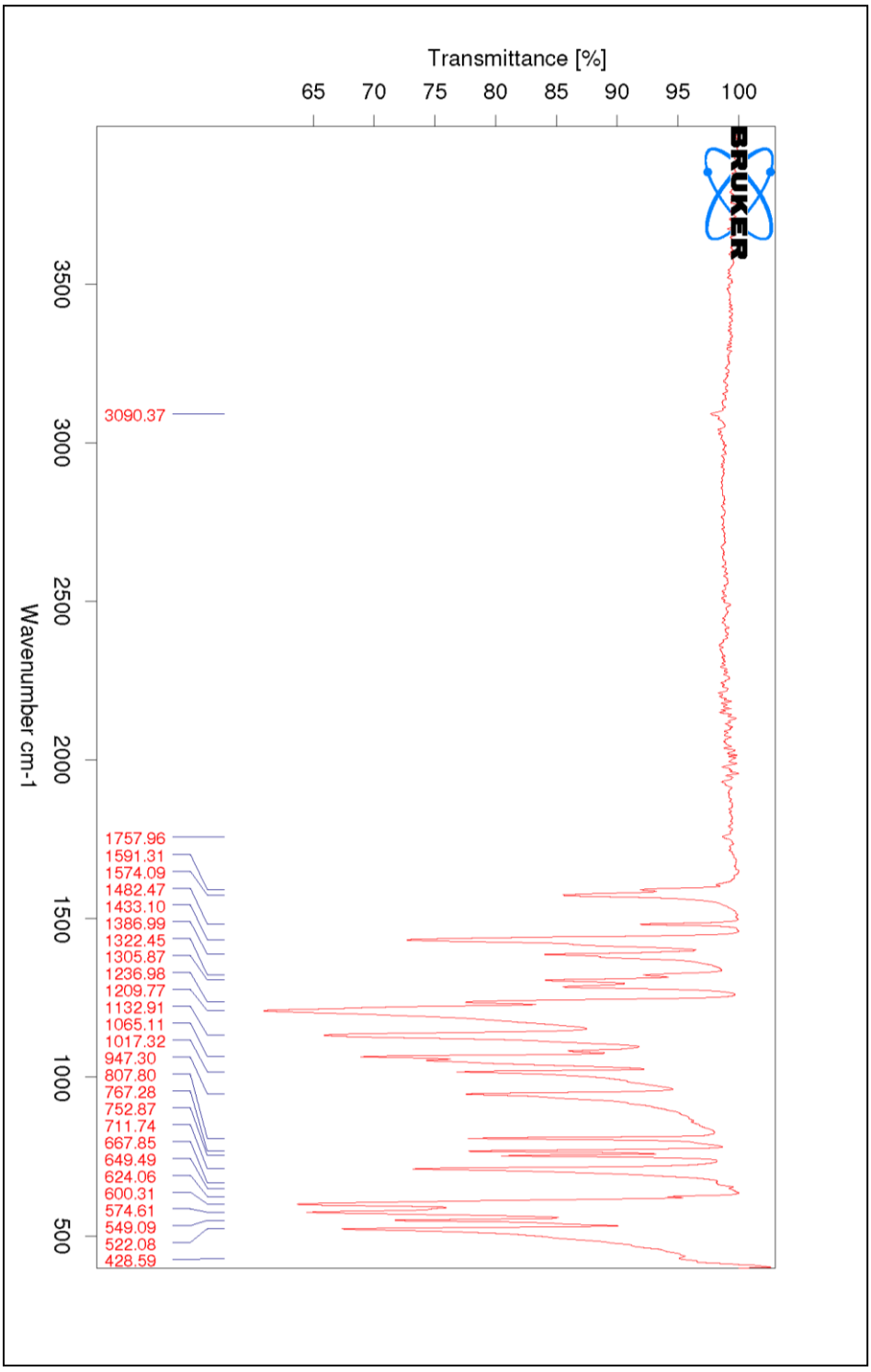


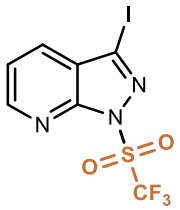
1,1,1-trifluoro-N-(3-methylisoxazol-5-yl)methanesulfonamide (compound 65)



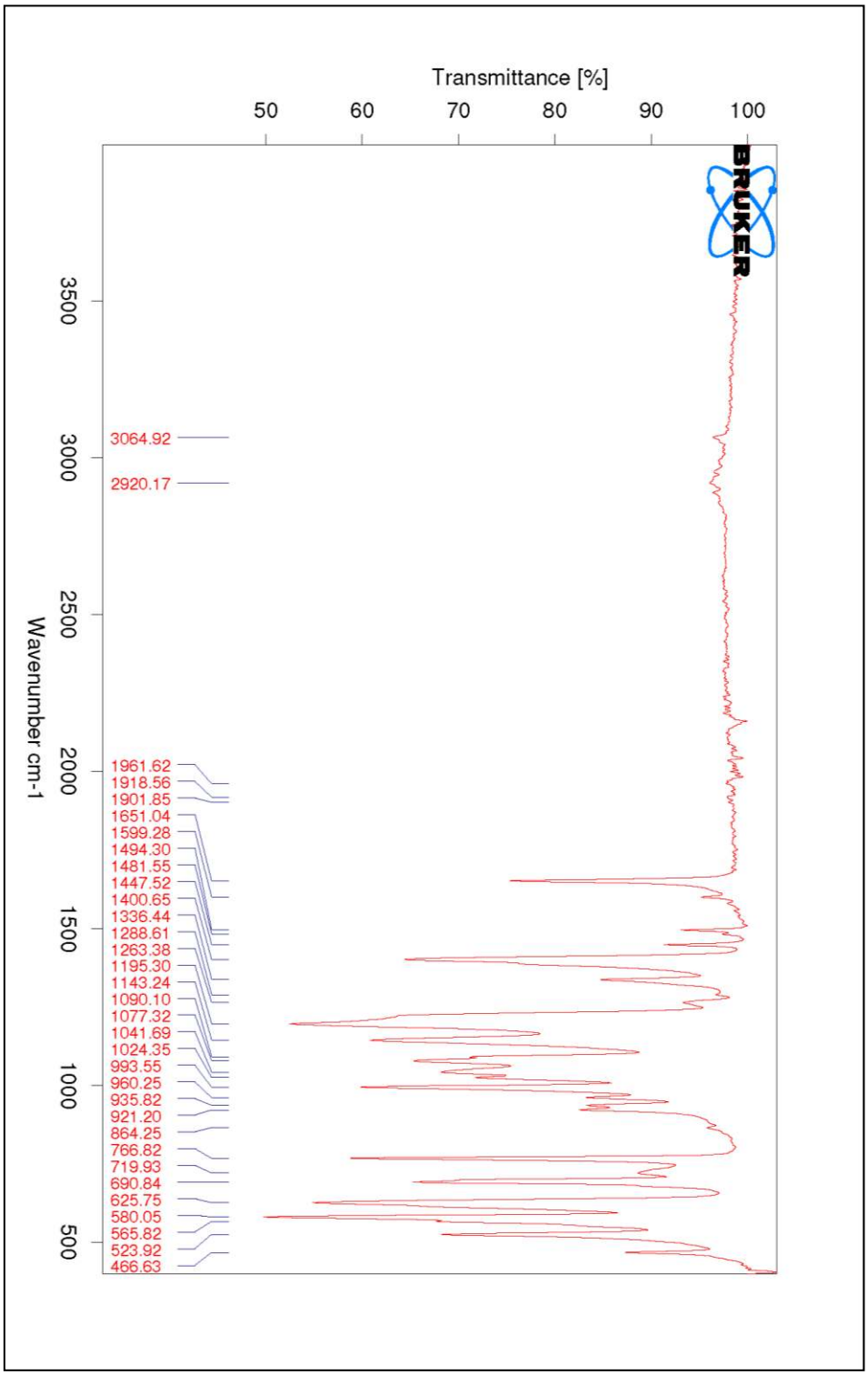


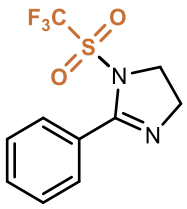
3-phenyl-1-((trifluoromethyl)sulfonyl)-1H-pyrazole (compound 66)



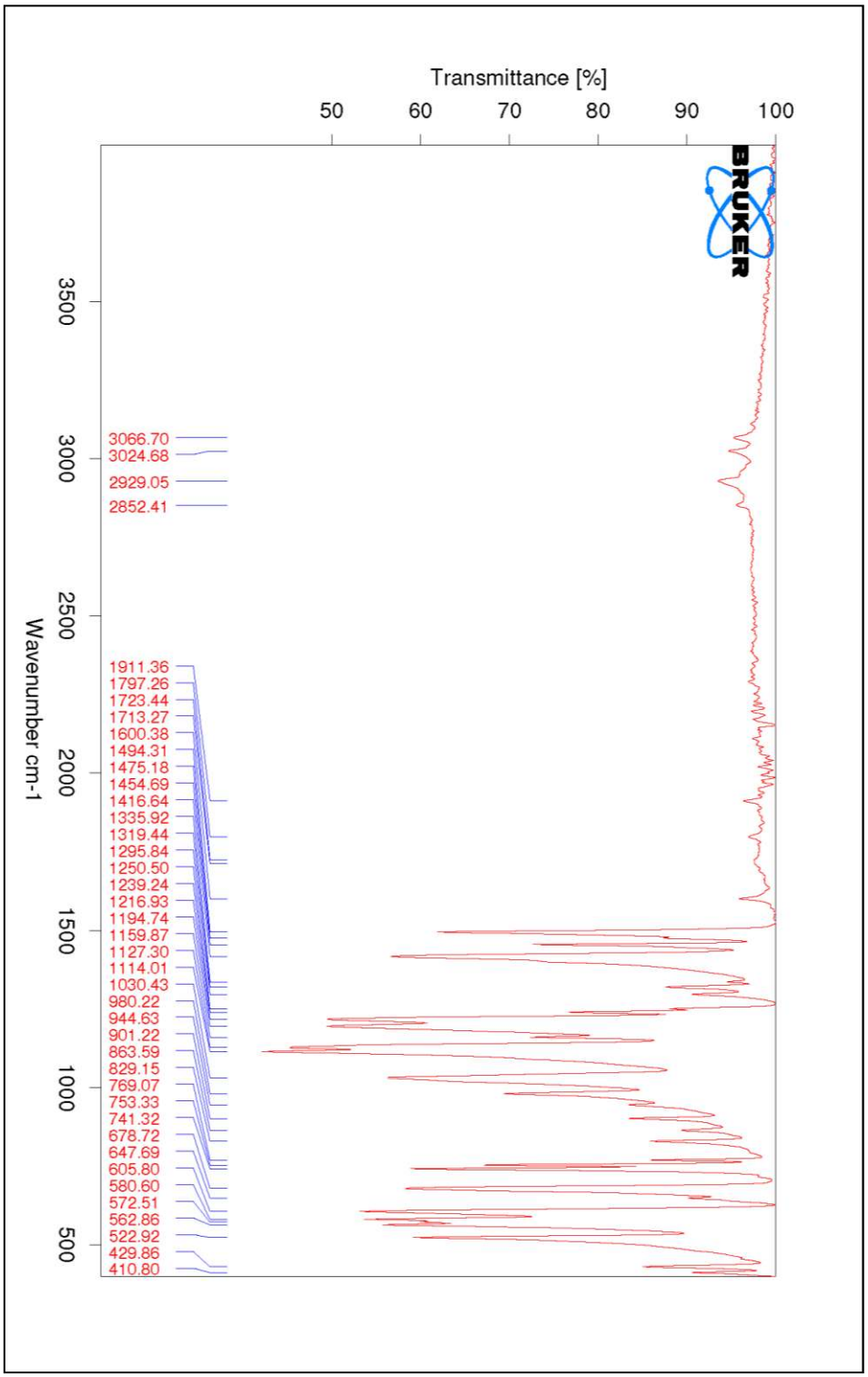


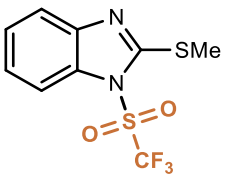
3-iodo-1-((trifluoromethyl)sulfonyl)-1H-pyrazolo[3,4-b]pyridine (compound 67)



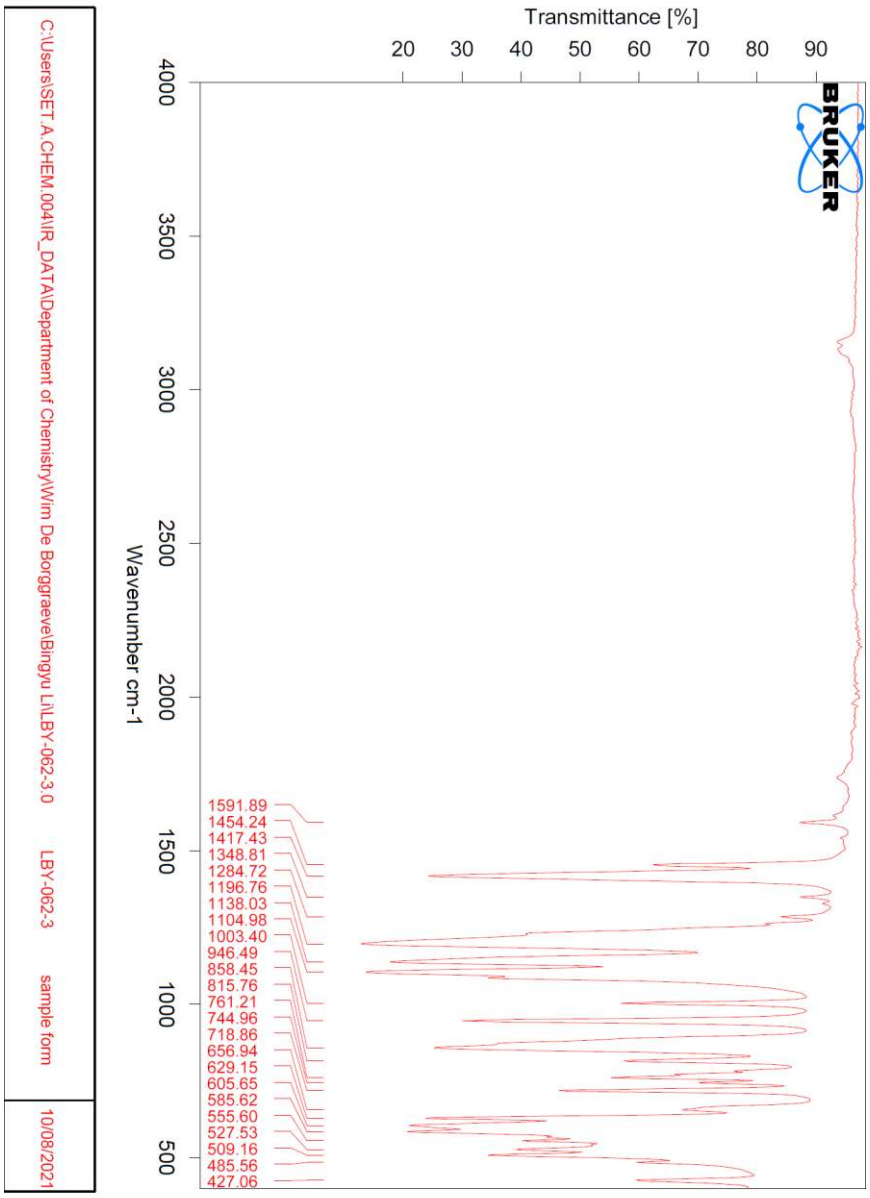


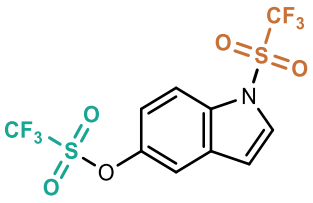
2-phenyl-1-((trifluoromethyl)sulfonyl)-4,5-dihydro-1H-imidazole (compound 68)





2-phenyl-1-((trifluoromethyl)sulfonyl)-4,5-dihydro-1H-imidazole (compound 69)

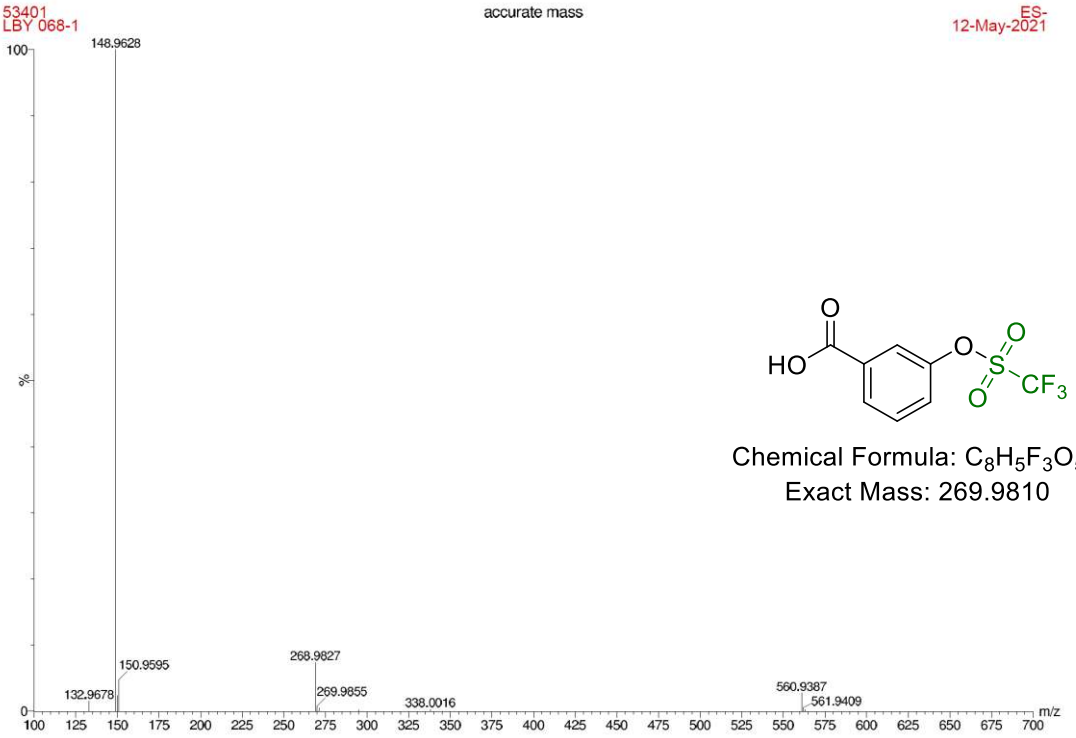




Chemical Formula: $C_{10}H_5F_6NO_5S_2$
Exact Mass: 396,95133

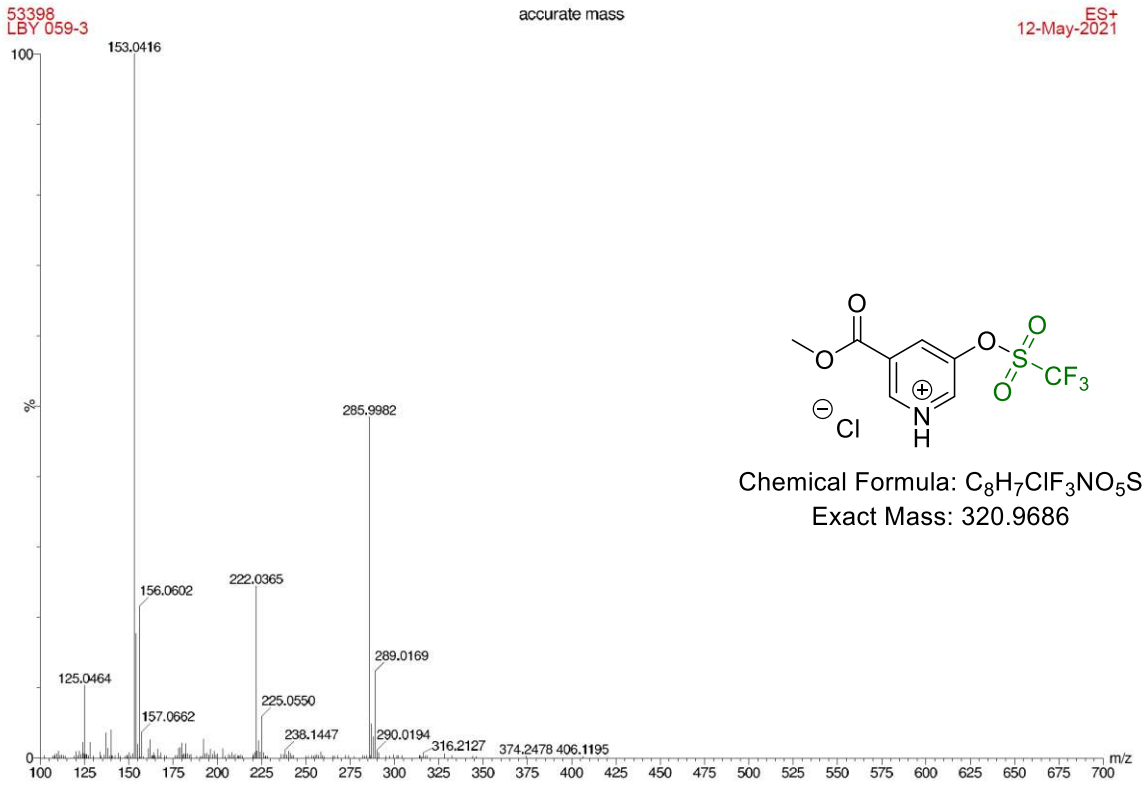
1-((trifluoromethyl)sulfonyl)-1H-indol-5-yl trifluoromethanesulfonate (compound 70, new compound)

13. Copies of the HRMS Spectra



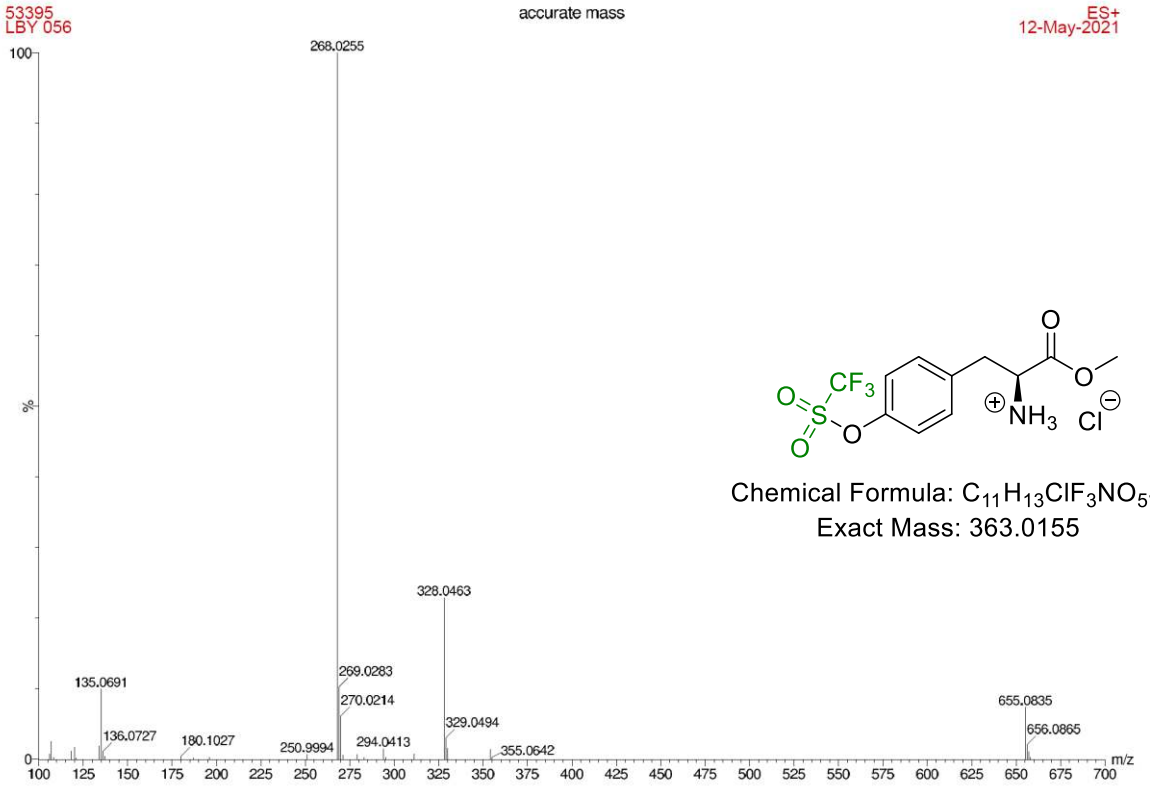
Chemical Formula: $C_8H_5F_3O_5S$
Exact Mass: 269.9810

3-(((trifluoromethyl)sulfonyl)oxy)benzoic acid (compound **7**, cas number: 32578-33-9)

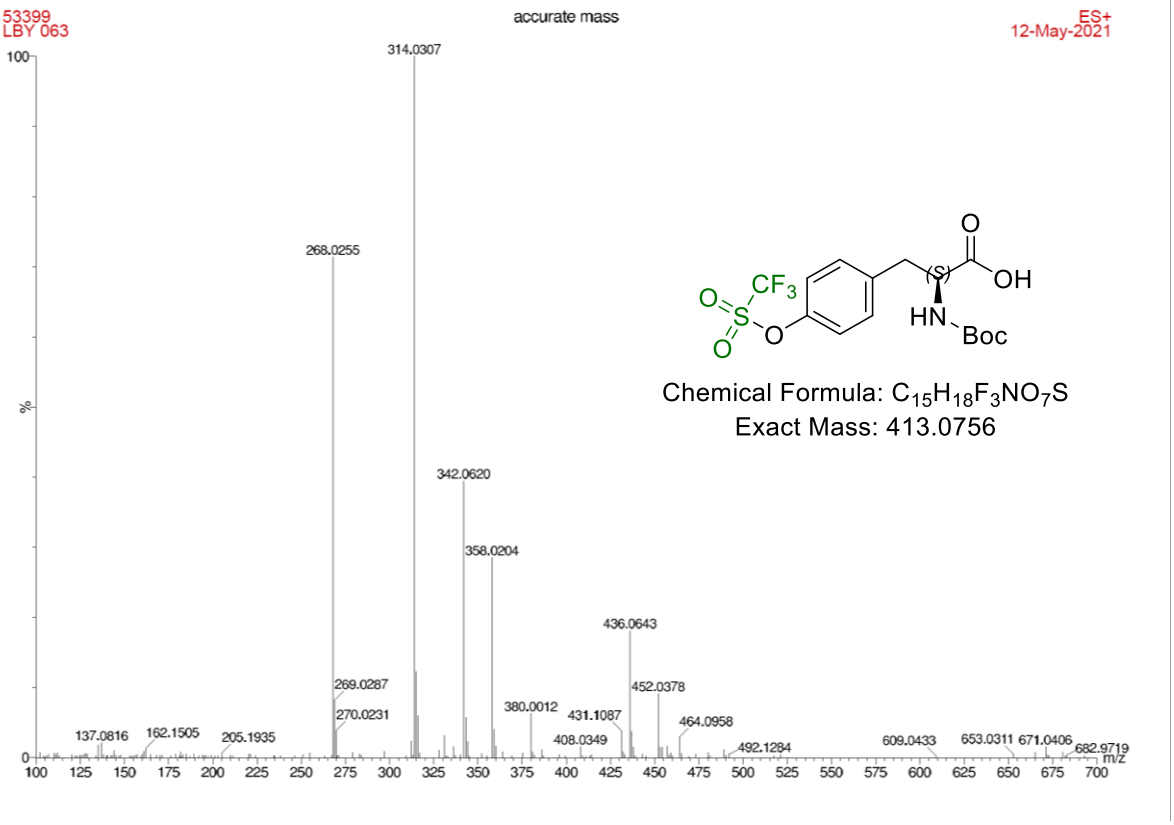


Chemical Formula: $C_8H_7ClF_3NO_5S$
Exact Mass: 320.9686

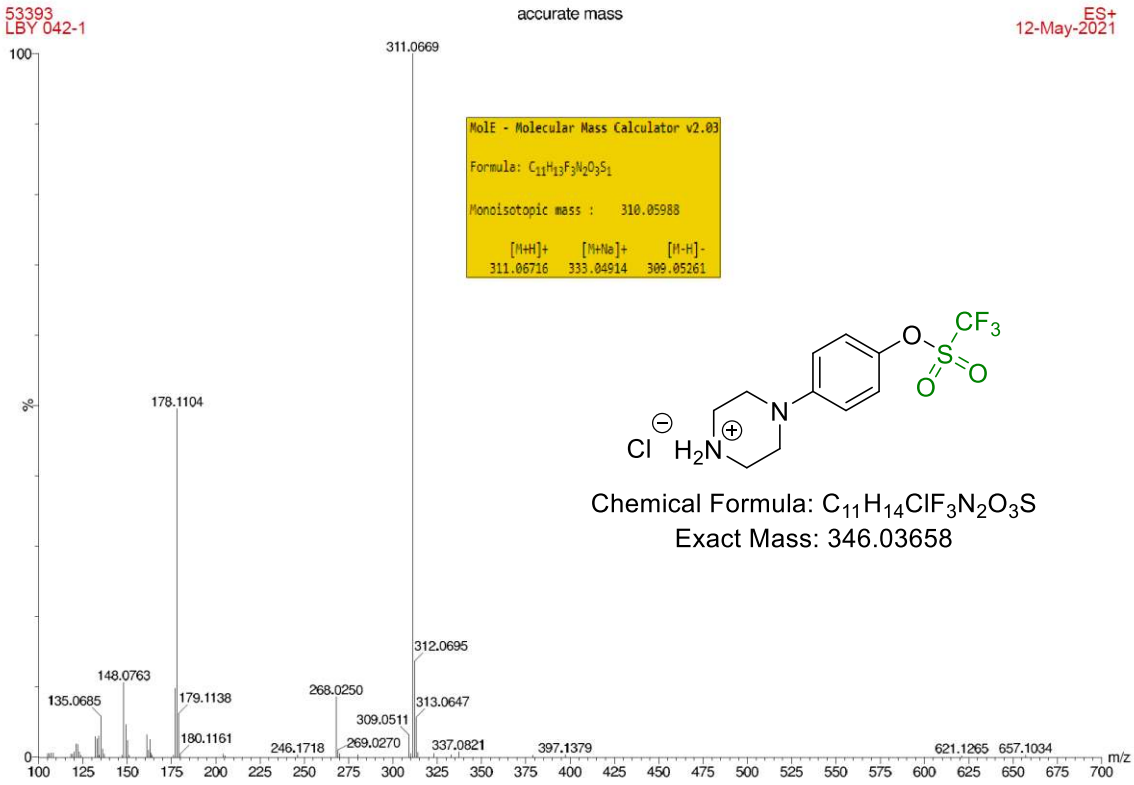
3-(methoxycarbonyl)-5-(((trifluoromethyl)sulfonyl)oxy)pyridin-1-ium chloride (compound **23**)



(S)-1-methoxy-1-oxo-3-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)propan-2-aminium chloride (compound **24**, cas number:2253981-98-3)

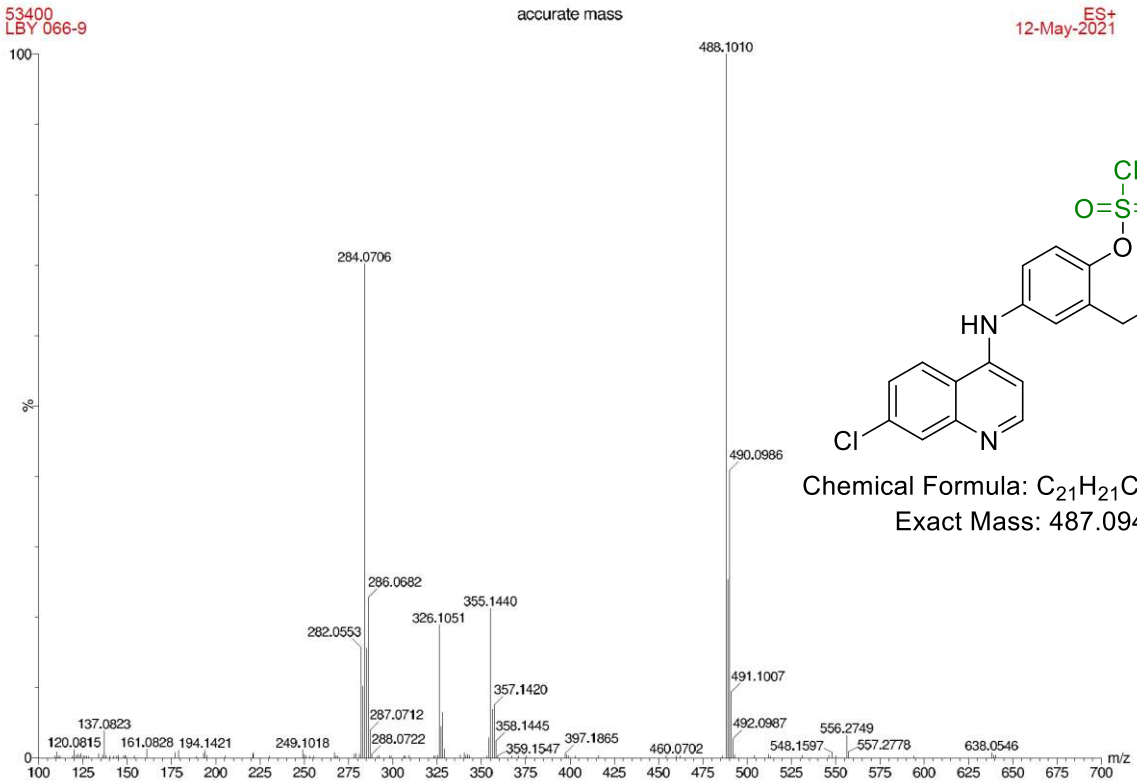


(S)-2-((tert-butoxycarbonyl)amino)-3-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)propanoic acid (compound **25**,cas number2093022-49-0)



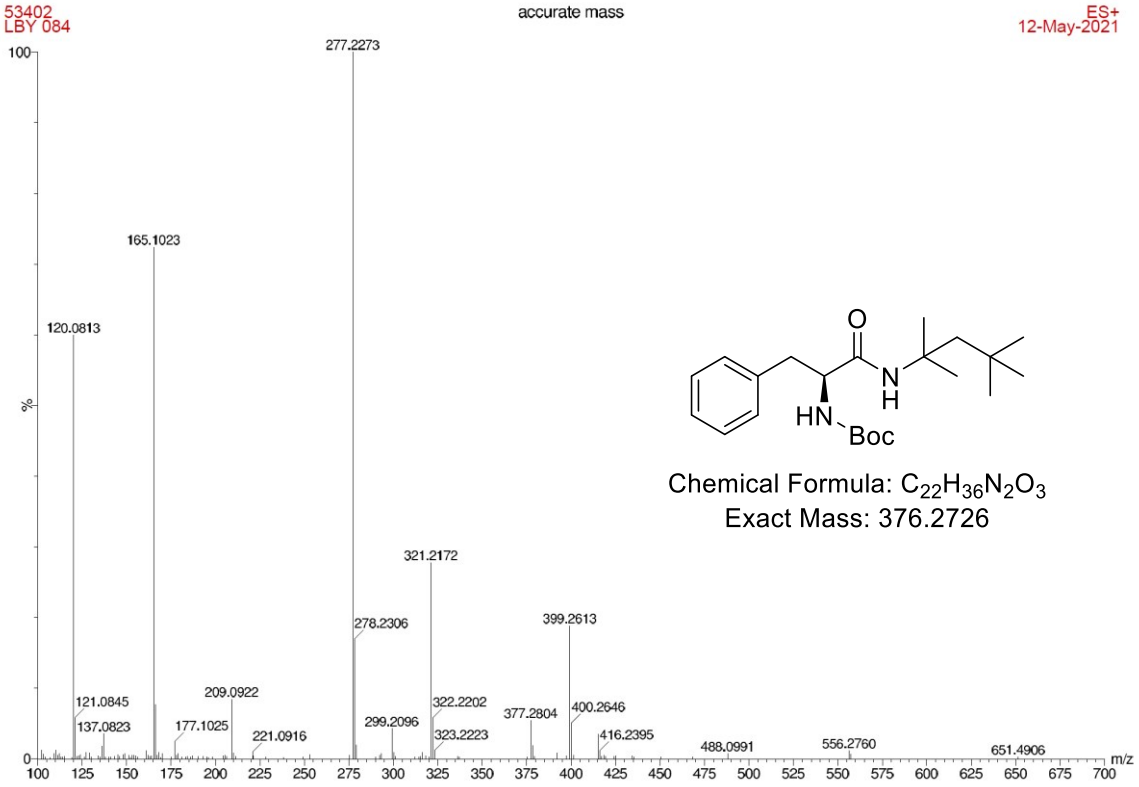
Chemical Formula: $C_{11}H_{14}ClF_3N_2O_3S$
Exact Mass: 346.03658

4-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)piperazin-1-ium chloride (compound **28**)

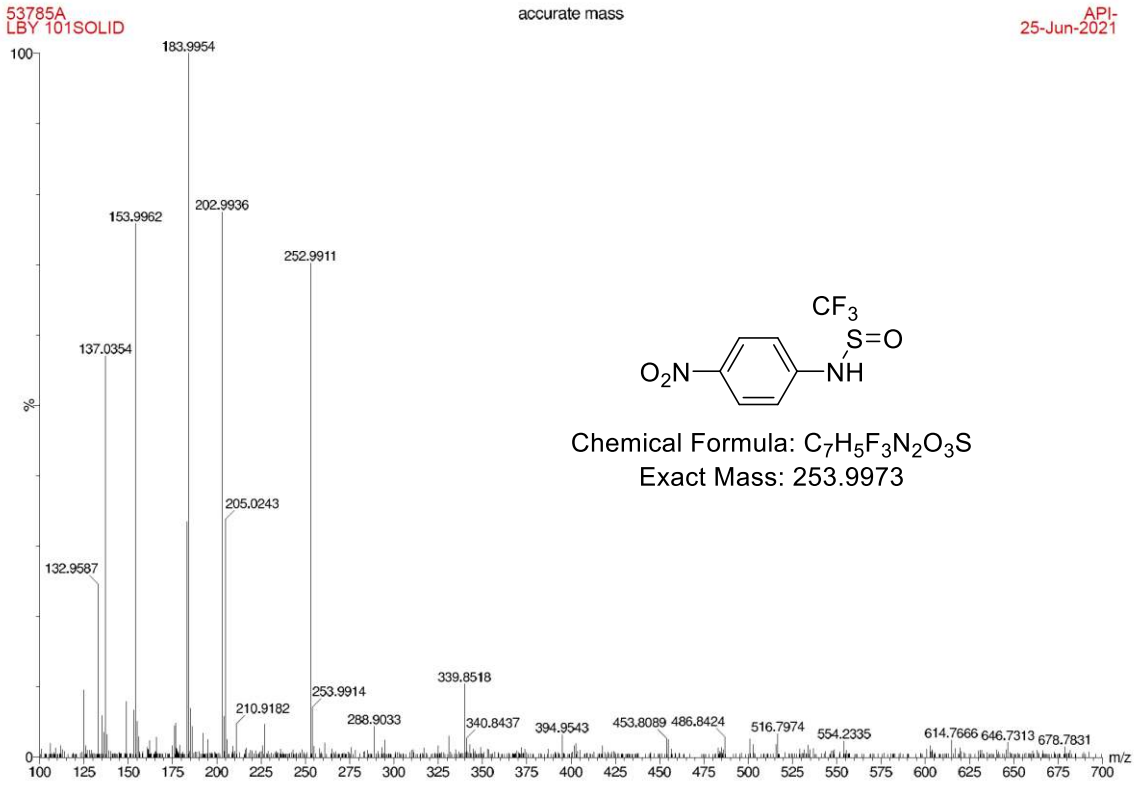


Chemical Formula: $C_{21}H_{21}ClF_3N_3O_3S$
Exact Mass: 487.0944

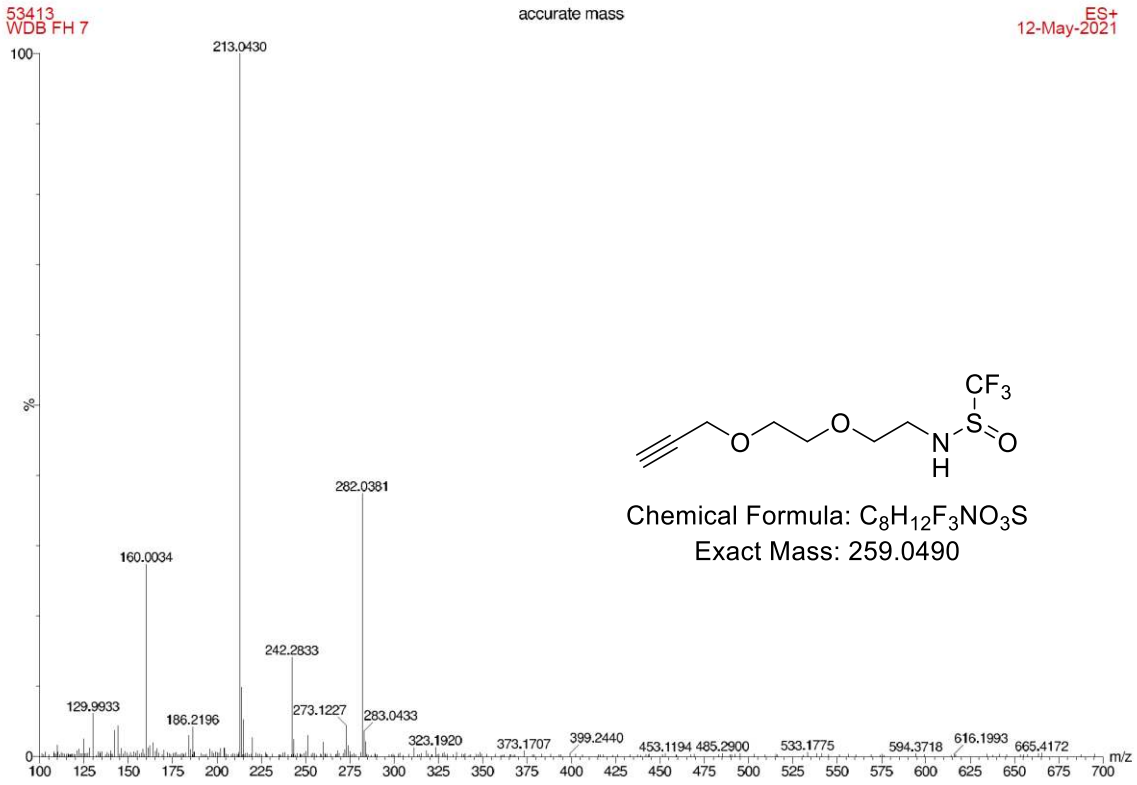
4-((7-chloroquinolin-4-yl)amino)-2-((diethylamino)methyl)phenyl trifluoromethanesulfonate (compound **29**)



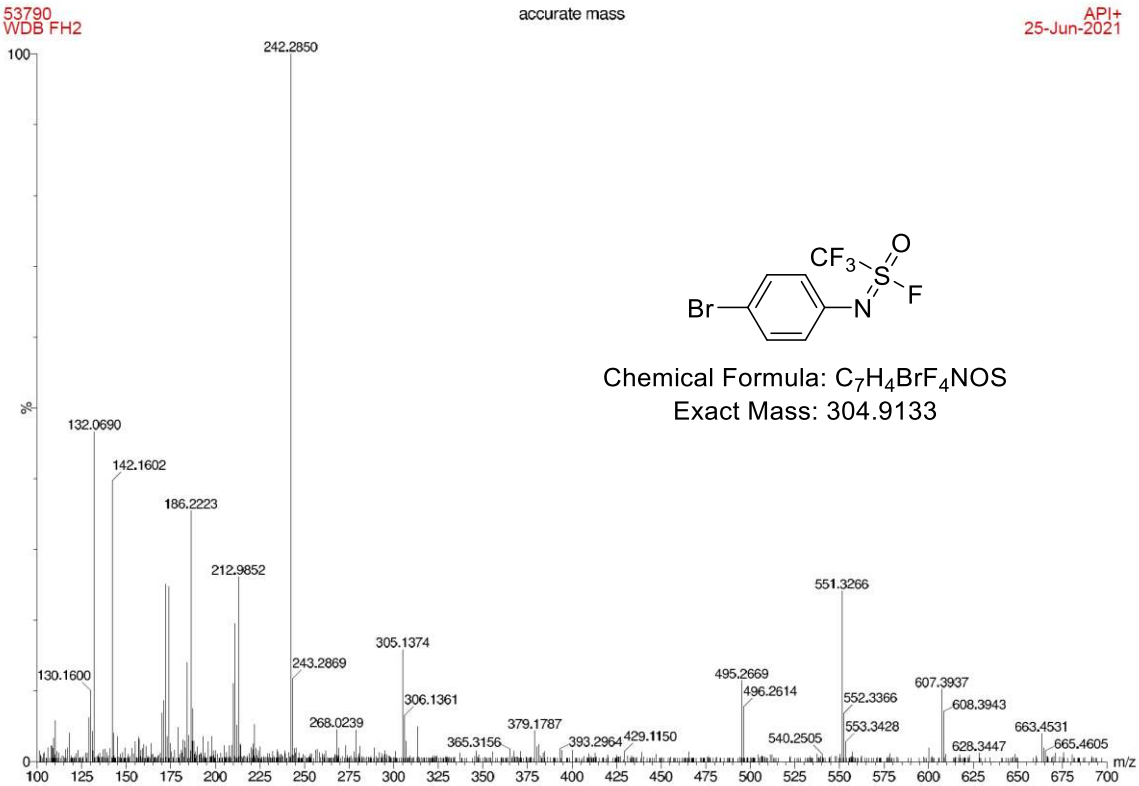
tert-butyl (S)-(1-oxo-3-phenyl-1-((2,4,4-trimethylpentan-2-yl)amino)propan-2-yl)carbamate (compound **44**, new compound)



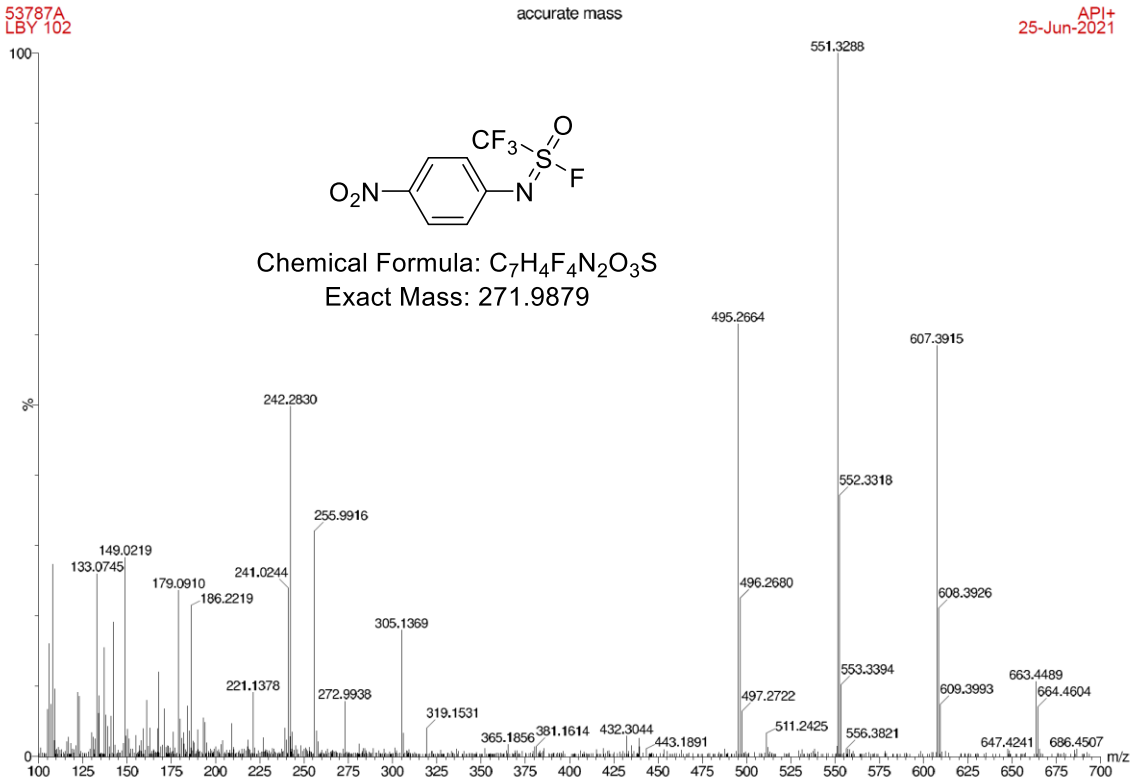
1,1,1-trifluoro-N-(4-nitrophenyl)methanesulfinamide (compound **S2**) (new compound)



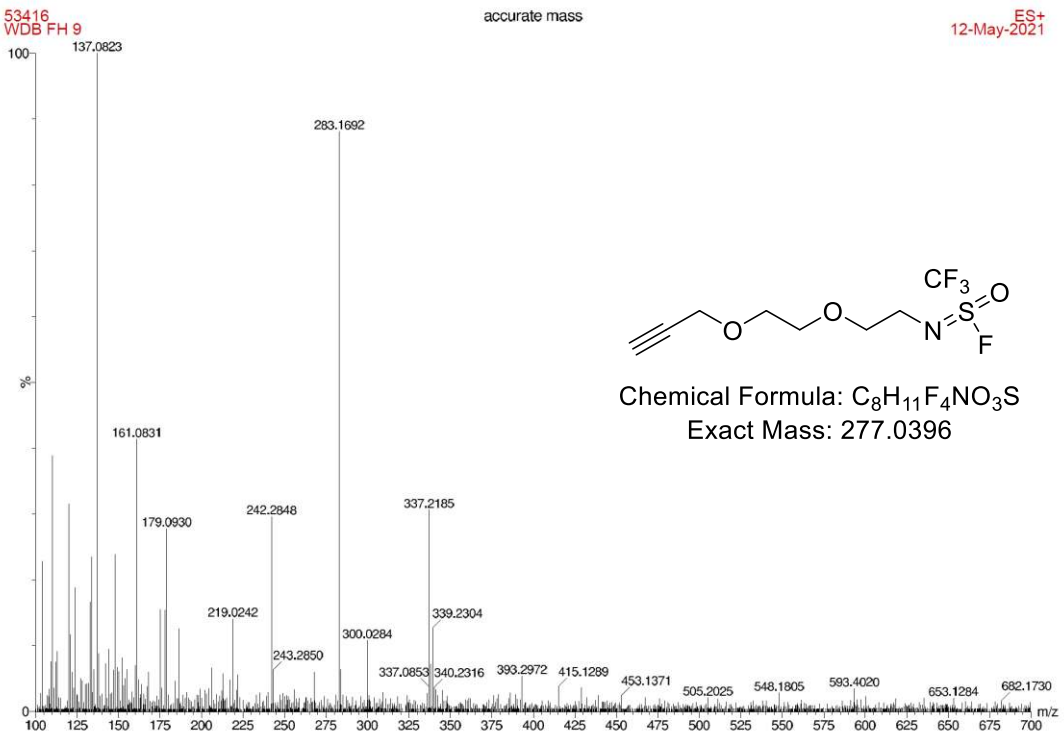
1,1,1-trifluoro-N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)methanesulfinamide (compound **S3**) (new compound)



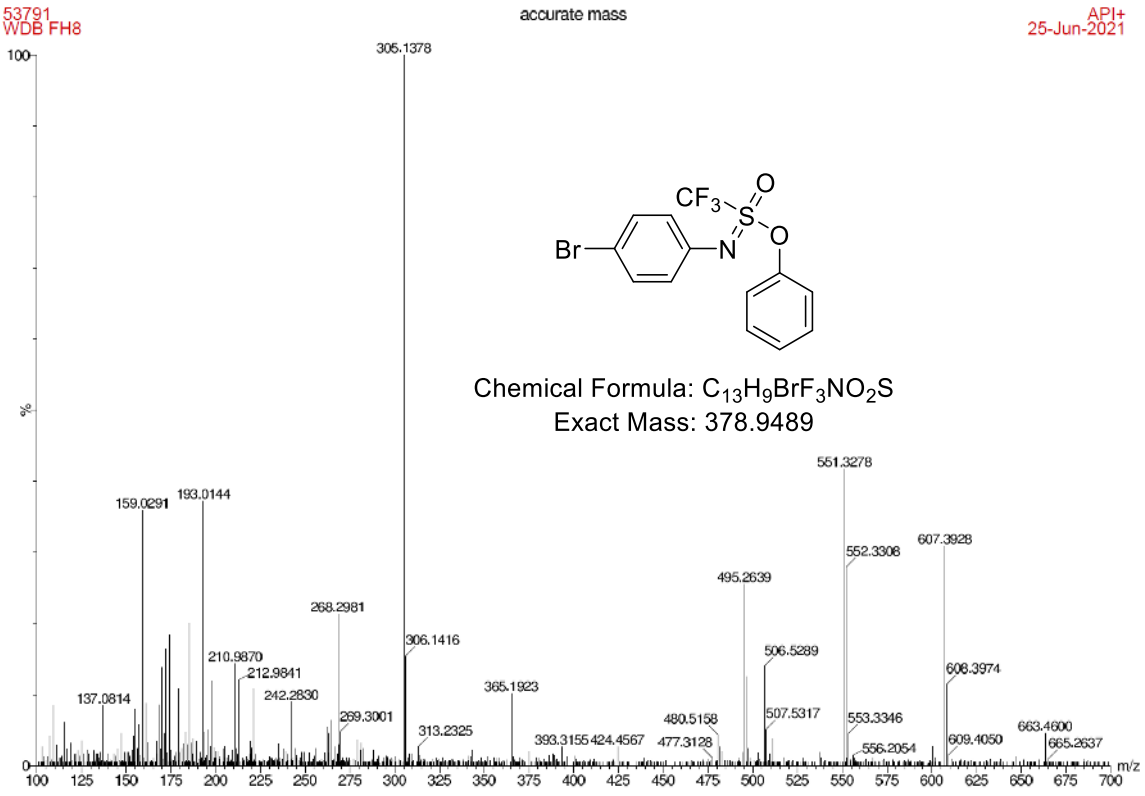
N-(4-bromophenyl)-1,1,1-trifluoromethanesulfonimidoyl fluoride (compound **S4**) (cas number: 2273795-55-2)



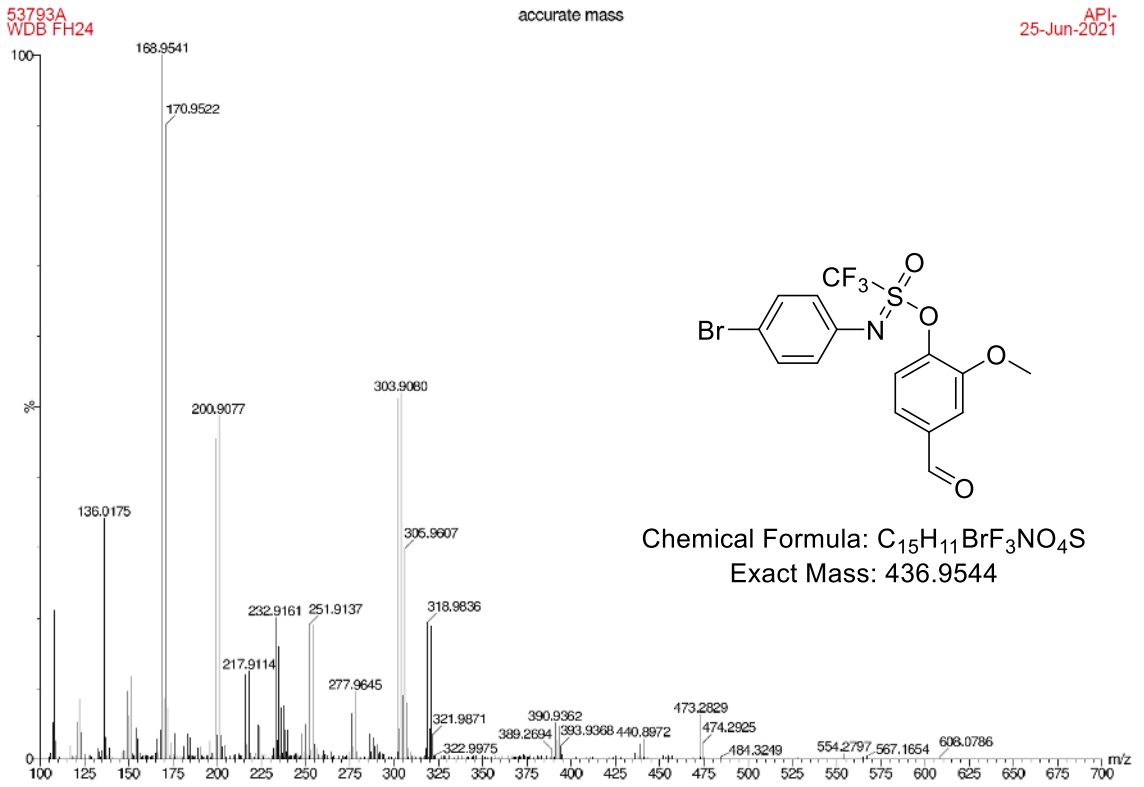
1,1,1-trifluoro-*N*-(4-nitrophenyl)methanesulfonimidoyl fluoride (compound **S5**) (new compound)



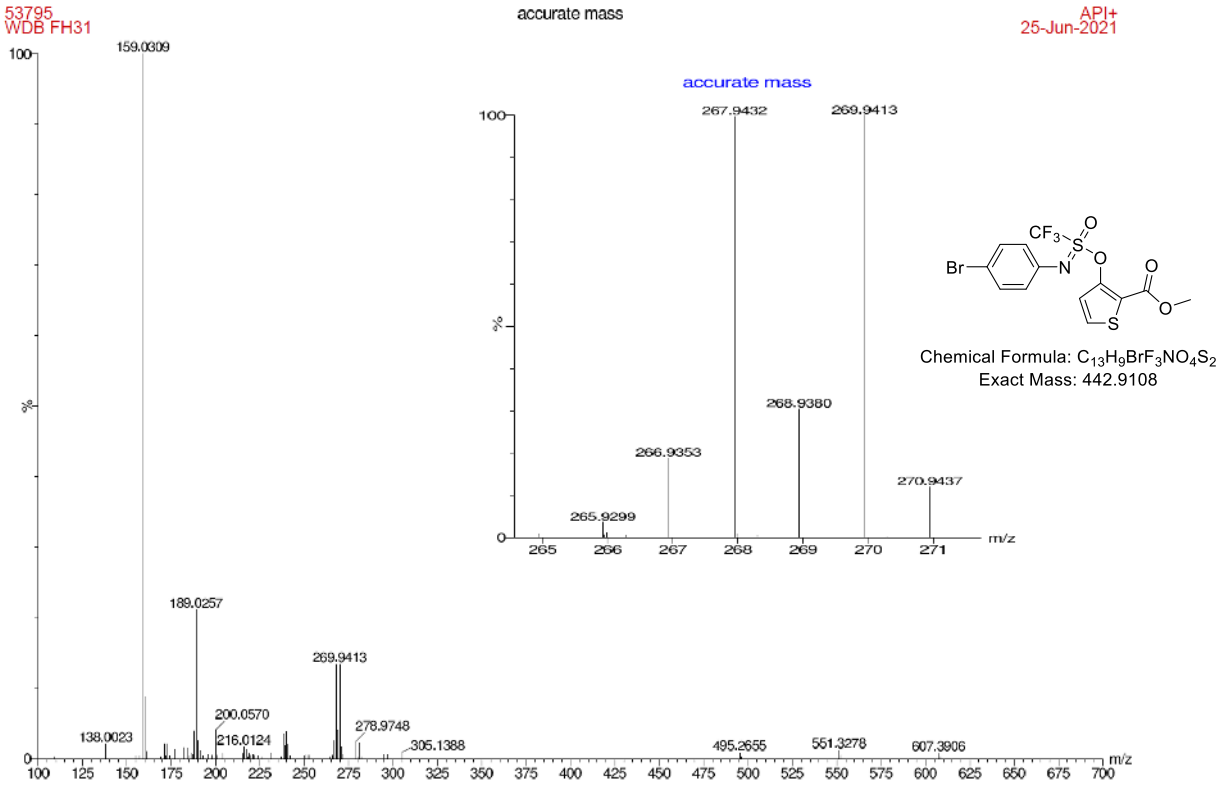
1,1,1-trifluoro-N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)methanesulfonimidoyl fluoride (compound **S6**, new compound)

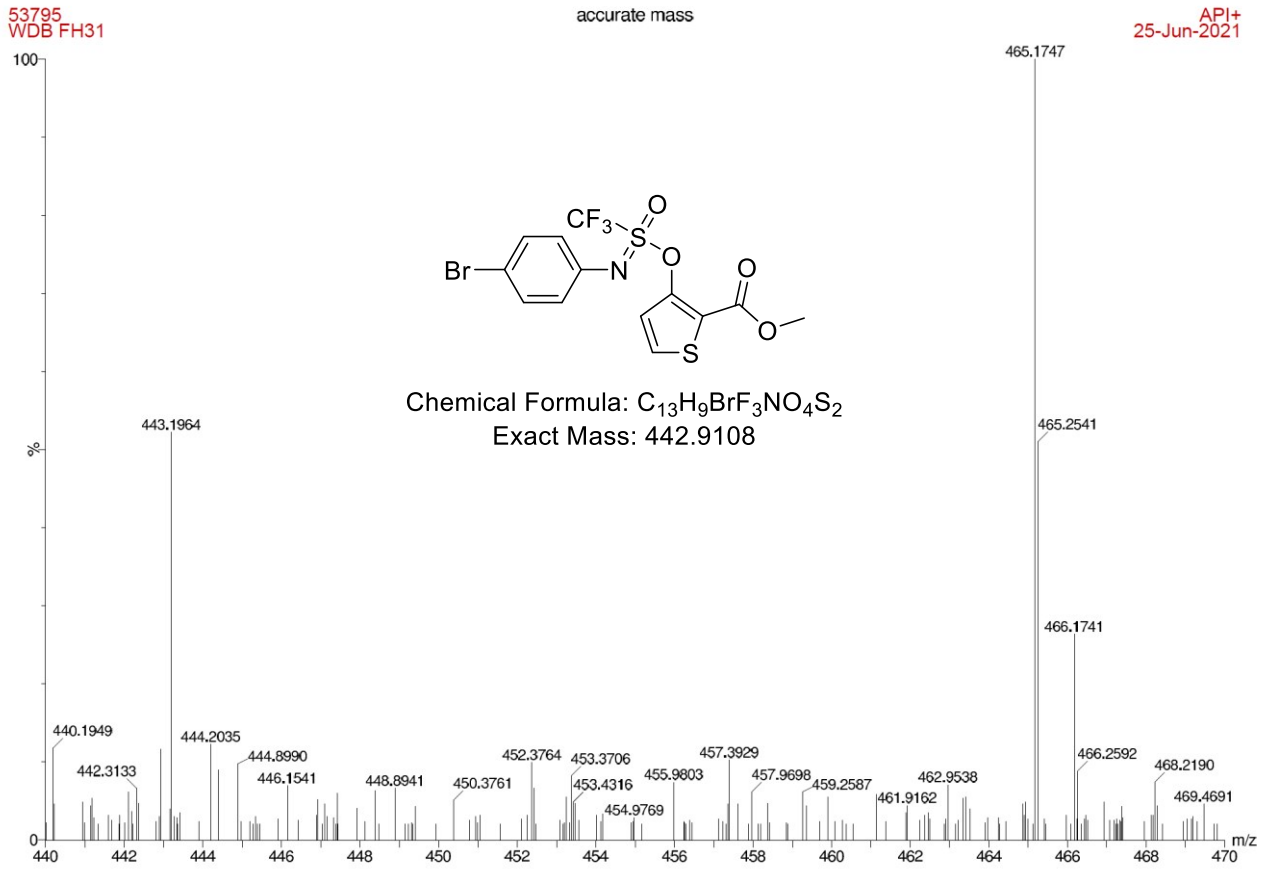


phenyl N-(4-bromophenyl)trifluoromethanesulfonimidate (compound **46**, new compound)

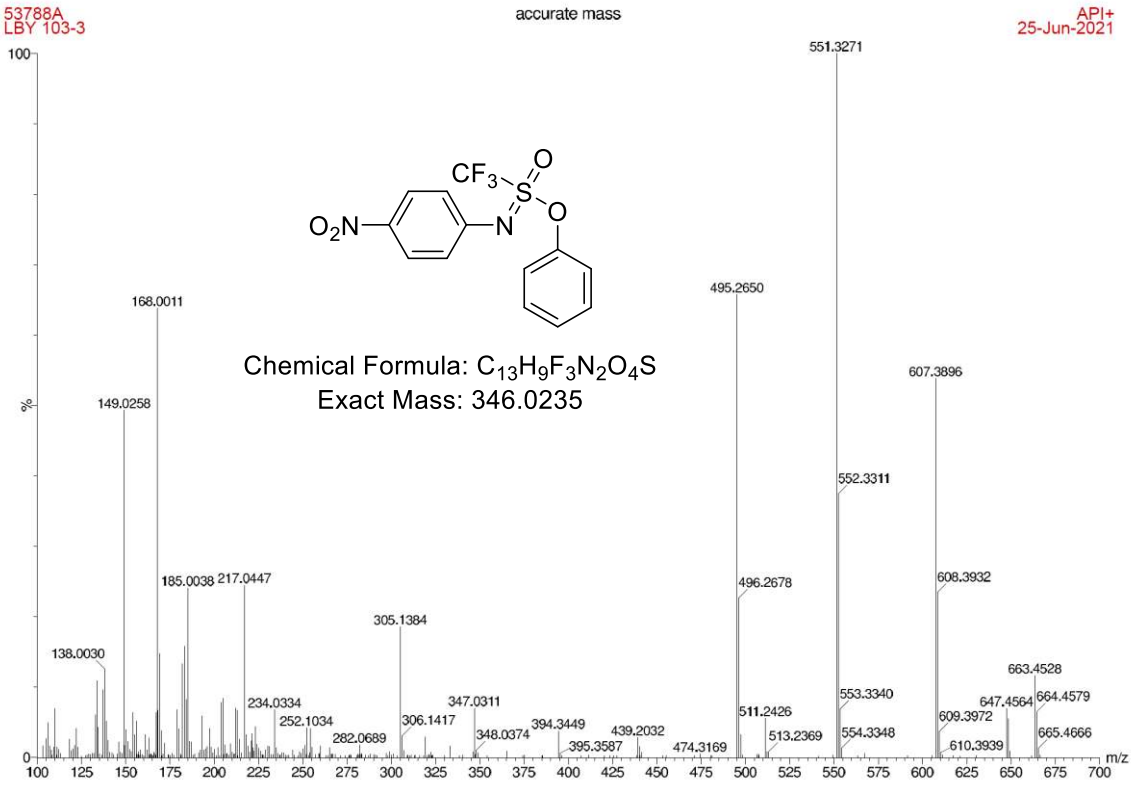


4-formyl-2-methoxyphenyl N-(4-bromophenyl)trifluoromethanesulfonimidate (compound **47**, new compound)

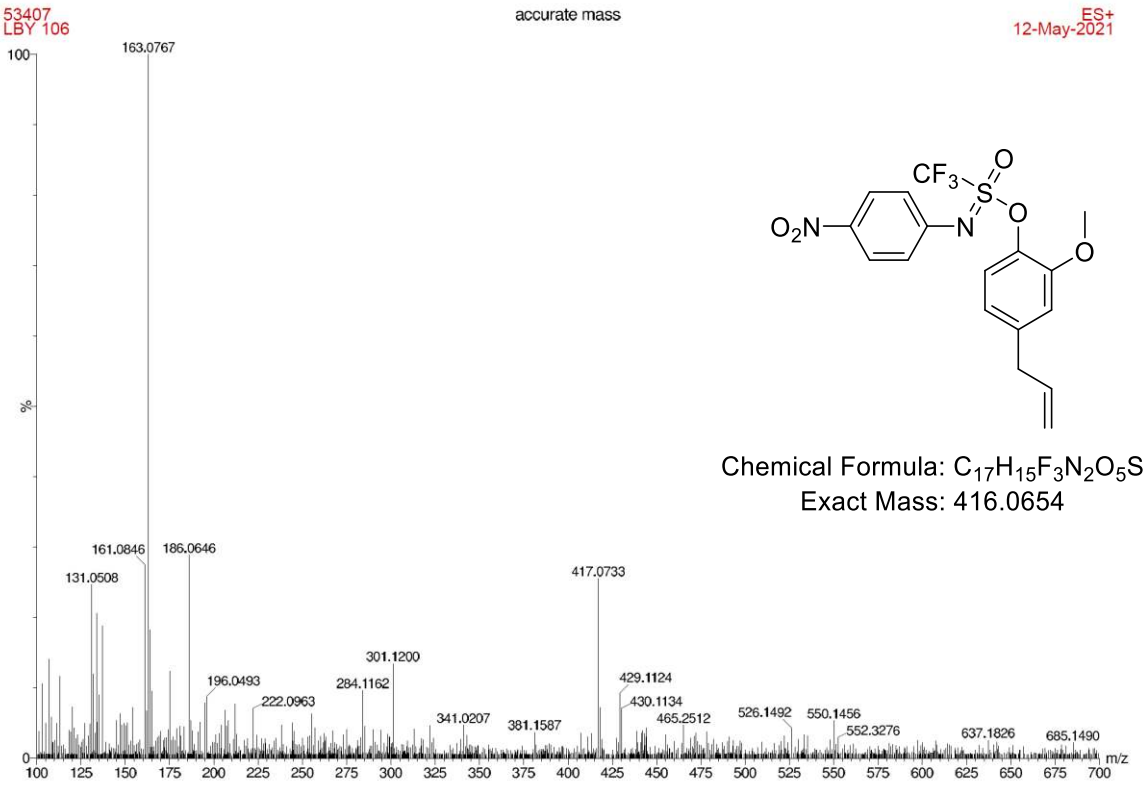




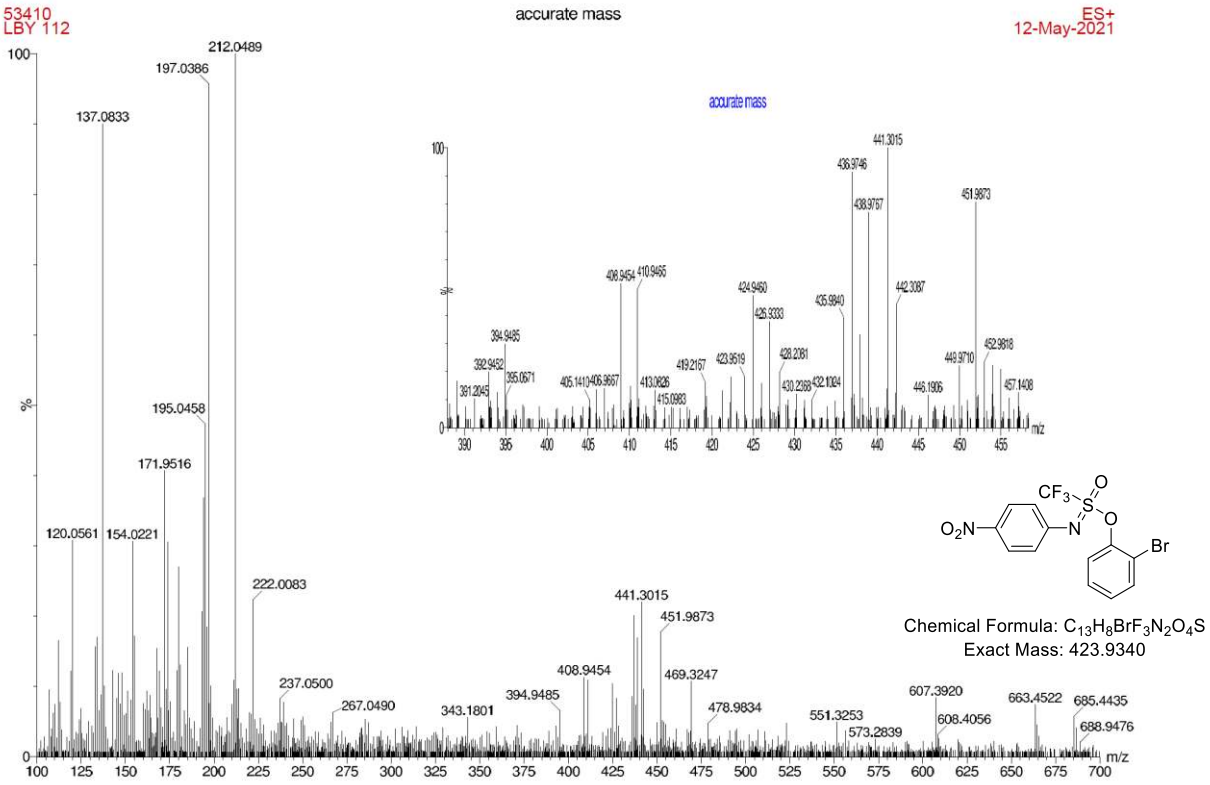
methyl 3-((N-(4-bromophenyl)-S-(trifluoromethyl)sulfonimidoyl)oxy)thiophene-2-carboxylate (compound **48**, new compoound)



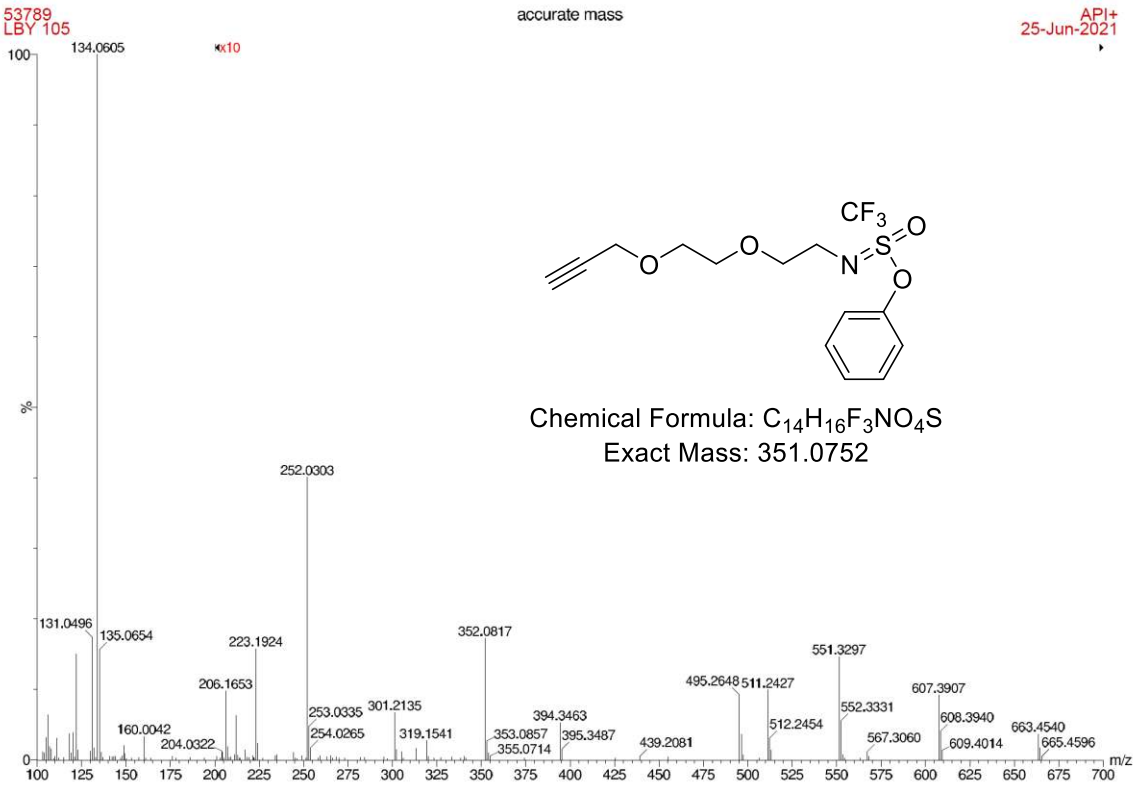
phenyl trifluoro-N-(4-nitrophenyl)methanesulfonimidate (compound **49**, new compound)



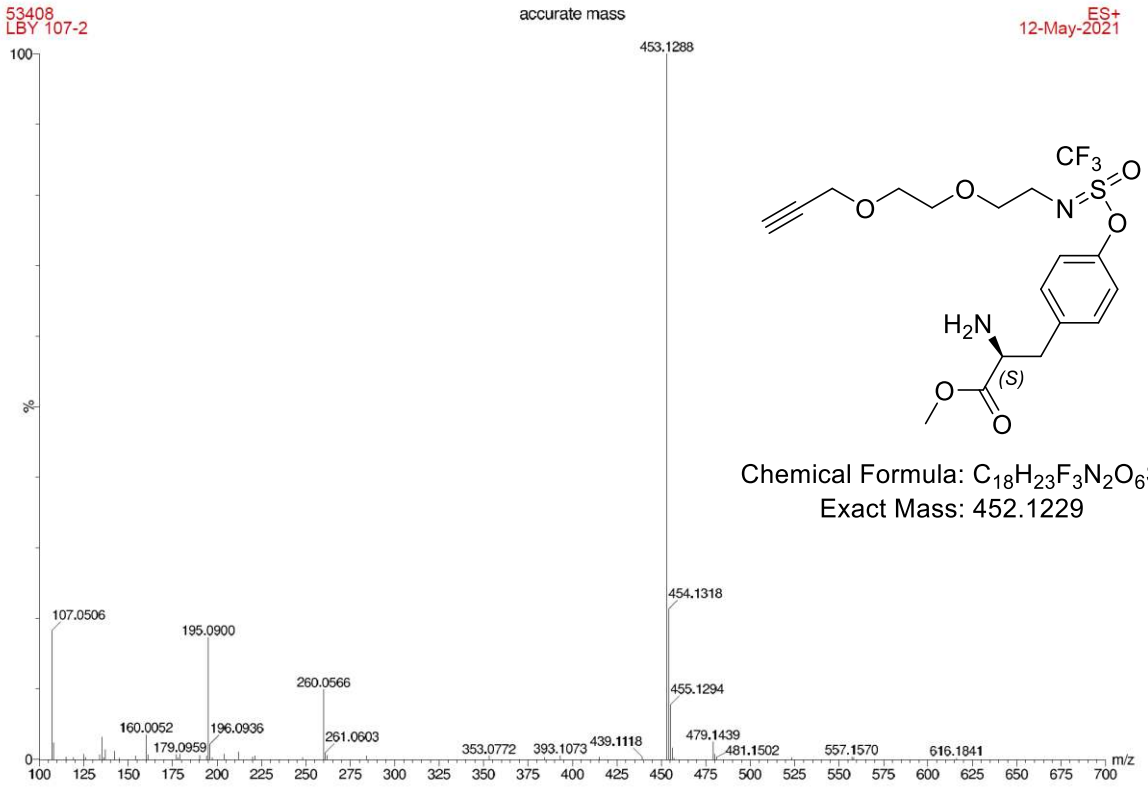
4-allyl-2-methoxyphenyl trifluoro-N-(4-nitrophenyl)methanesulfonimidate (compound **50**, new compound)



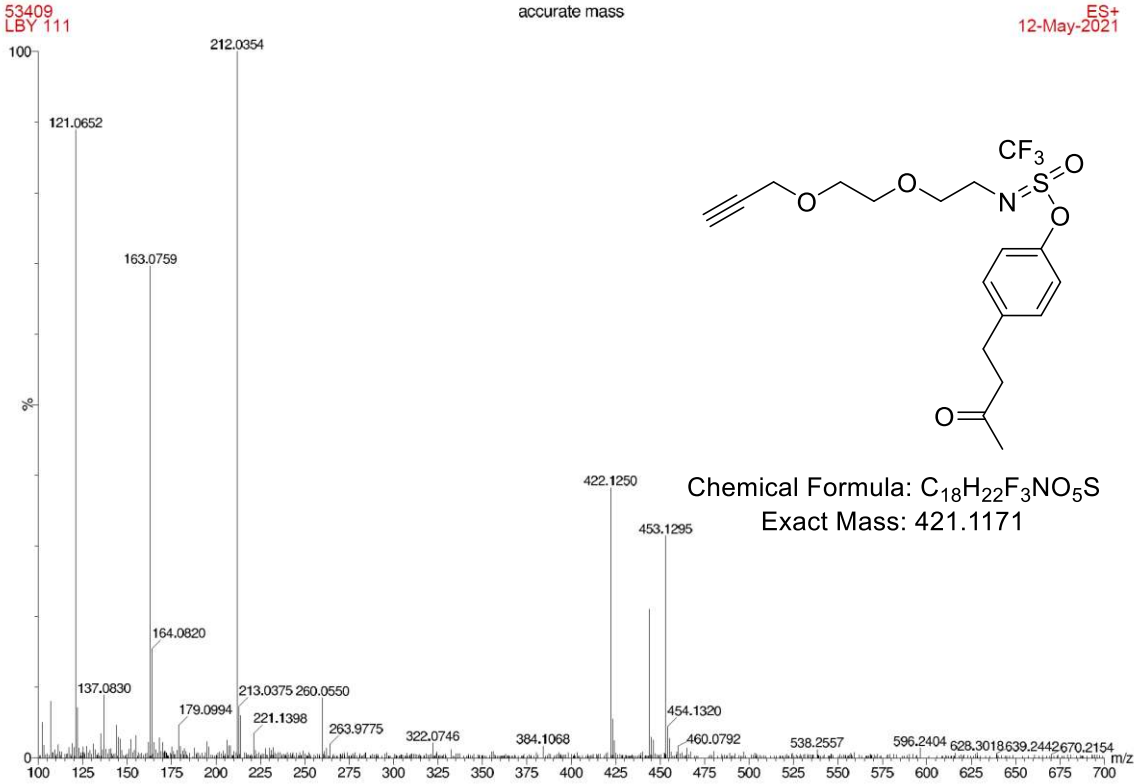
2-bromophenyl trifluoro-N-(4-nitrophenyl)methanesulfonimidate (compound **51**, new compound)



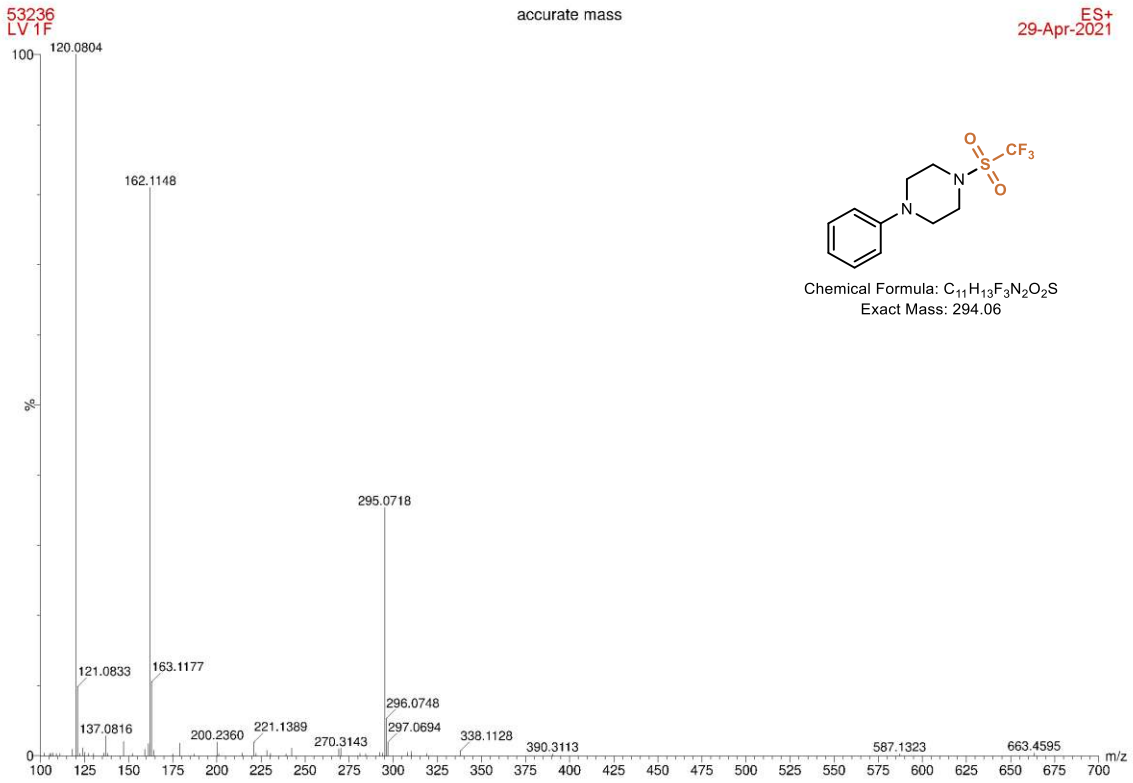
phenyl trifluoro-N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)methanesulfonimidate (compound **52**, new compound)



methyl (2S)-2-amino-3-(4-((N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)-S-(trifluoromethyl)sulfonimidoyl)oxy)phenyl)propanoate (compound **53**, new compound)

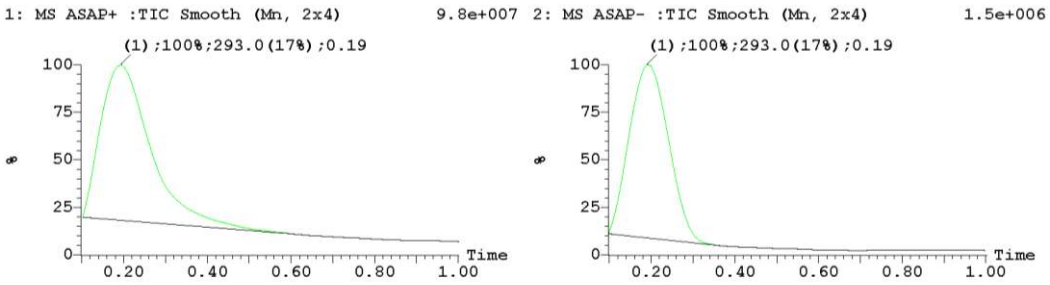


4-(3-oxobutyl)phenyl trifluoro-N-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)methanesulfonimidate (compound **54**, new compound)



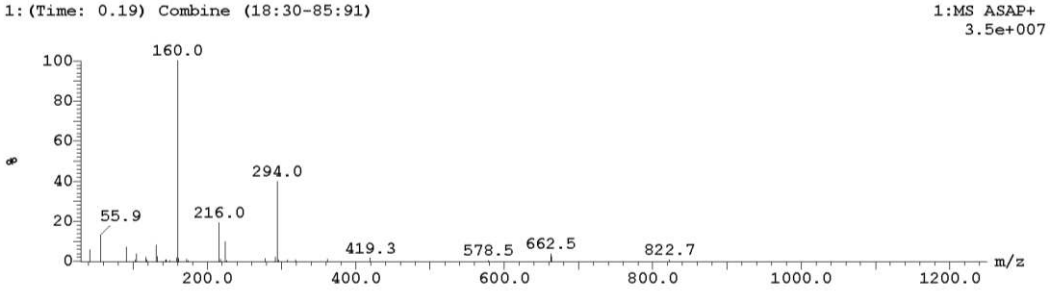
1-phenyl-4-((trifluoromethyl)sulfonyl)piperazine (compound **55**)

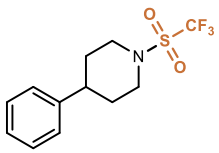
Sample Report:



Peak ID	Compound	Time	Mass Found
1	Tentative	0.19	294

1:(Time: 0.19) Combine (18:30-85:91)

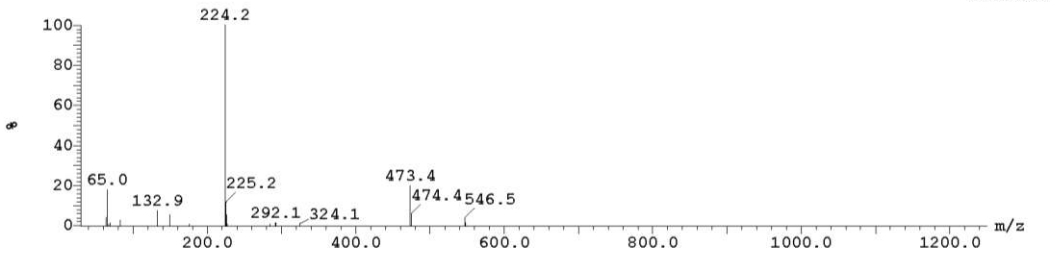


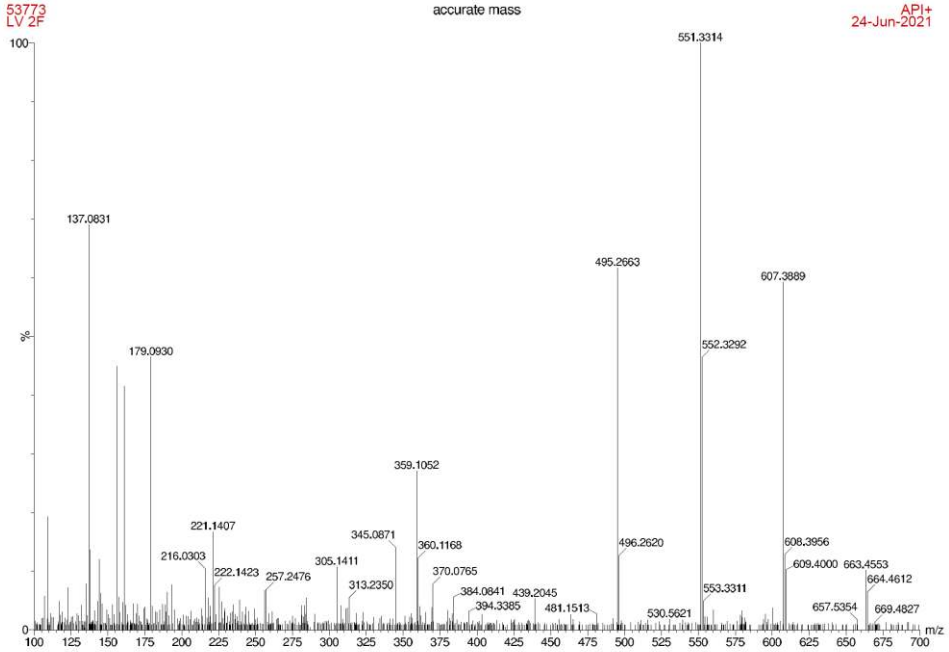


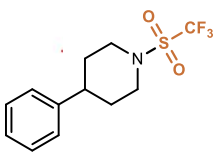
Chemical Formula: $C_{12}H_{14}F_3NO_2S$
Exact Mass: 293,06973

Peak ID	Compound	Time	Mass Found
1		0.19	Not Found

1:(Time: 0.19) Combine (17:29-55:61)

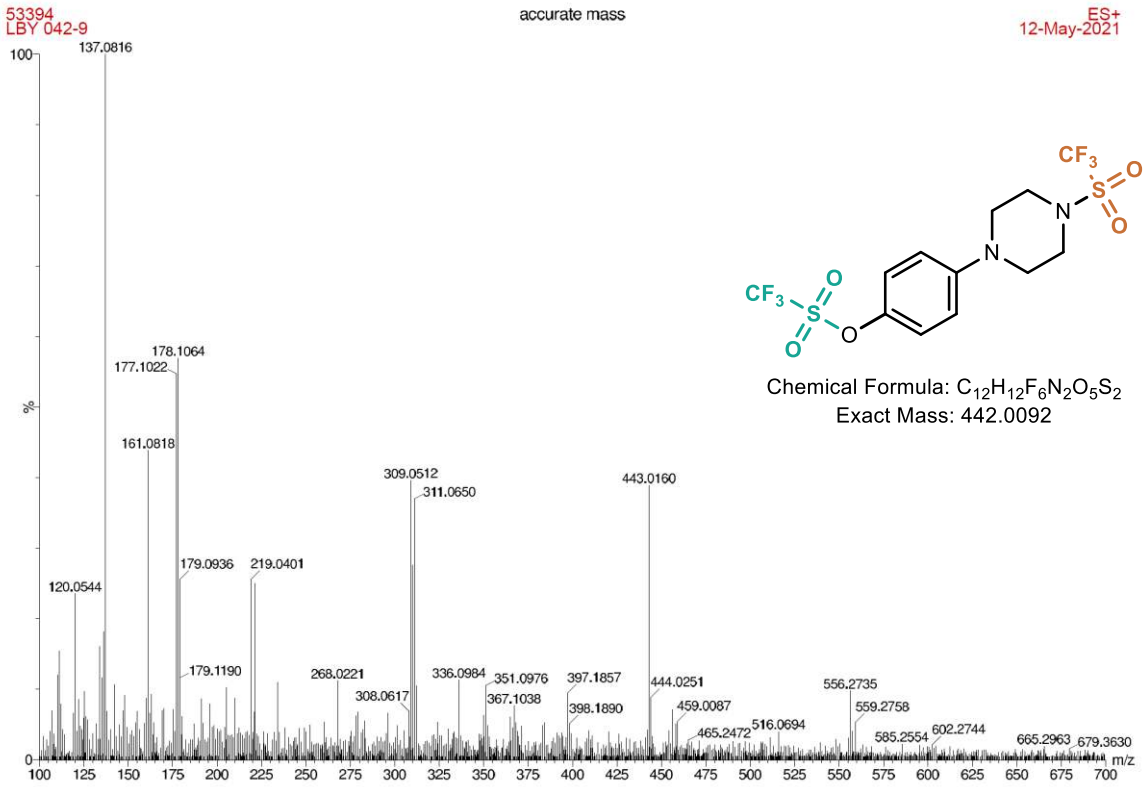






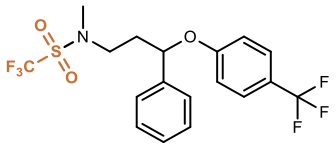
Chemical Formula: $C_{12}H_{14}F_3NO_2S$
Exact Mass: 293,06973

4-phenyl-1-((trifluoromethyl)sulfonyl)piperidine (compound **56**)



Chemical Formula: $C_{12}H_{12}F_6N_2O_5S_2$
Exact Mass: 442.0092

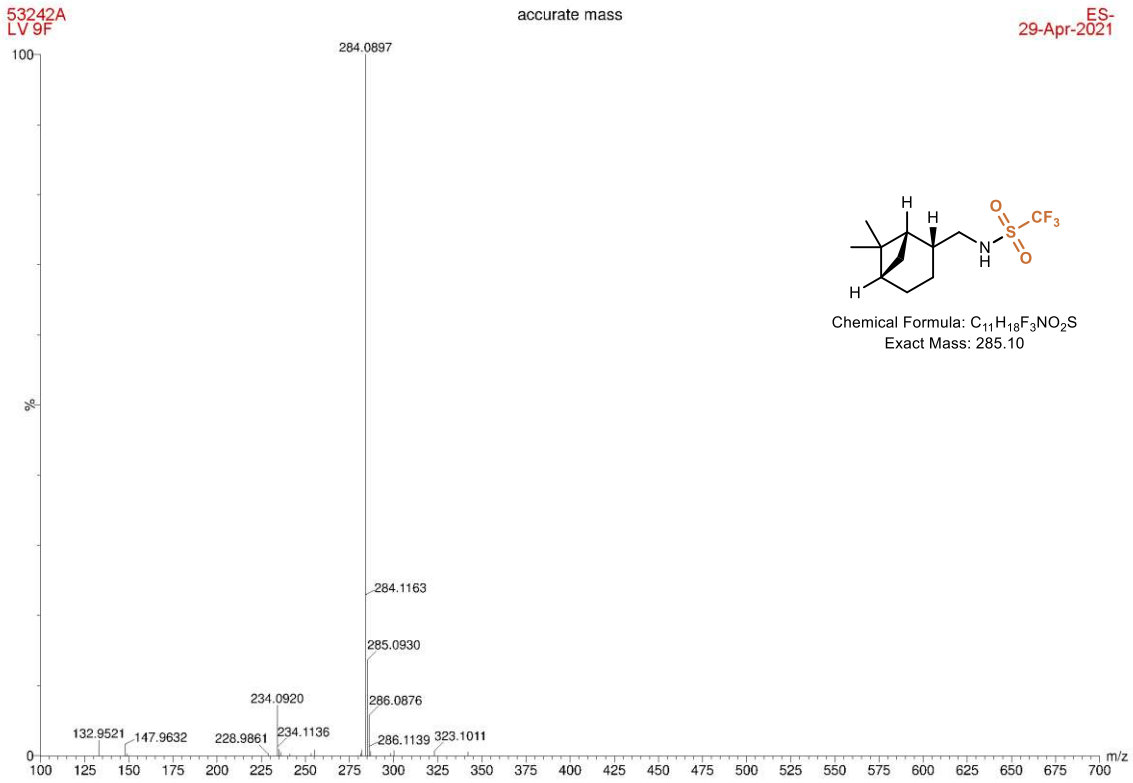
4-(4-((trifluoromethyl)sulfonyl)piperazin-1-yl)phenyl trifluoromethanesulfonate (compound **60**)



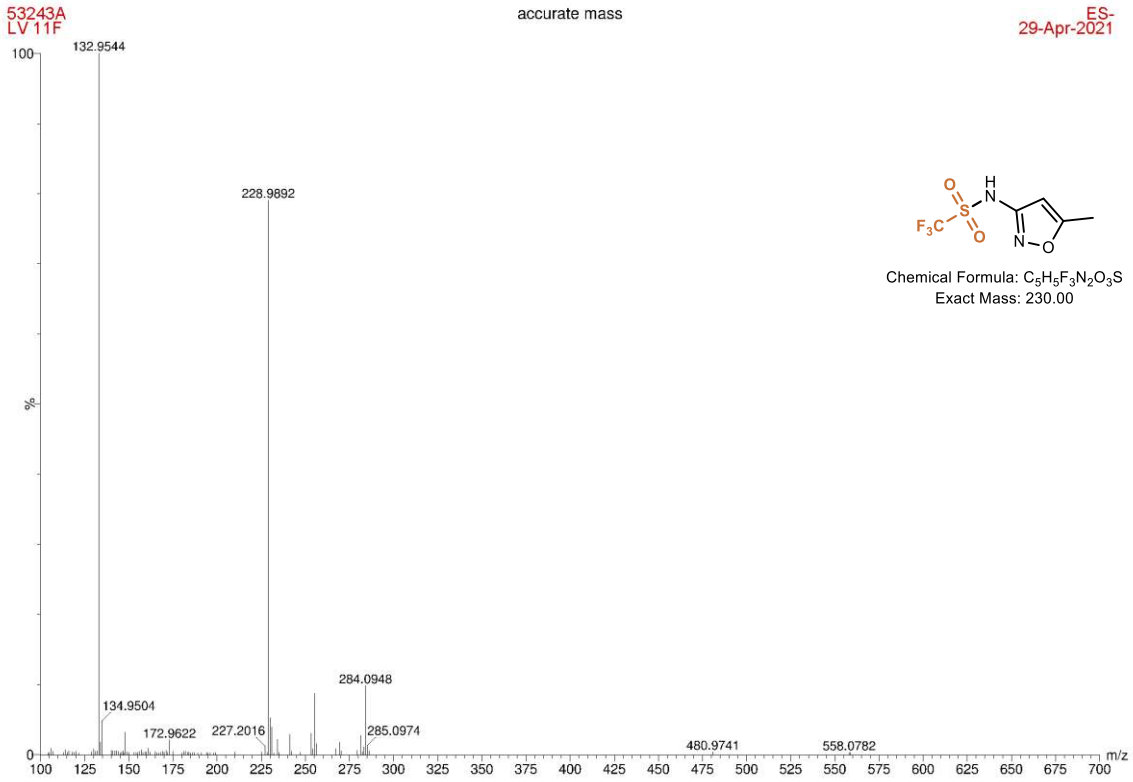
Chemical Formula: $C_{18}H_{17}F_6NO_3S$
Exact Mass: 441.08

No mass corresponding (HRMS, APCI, Water radian)

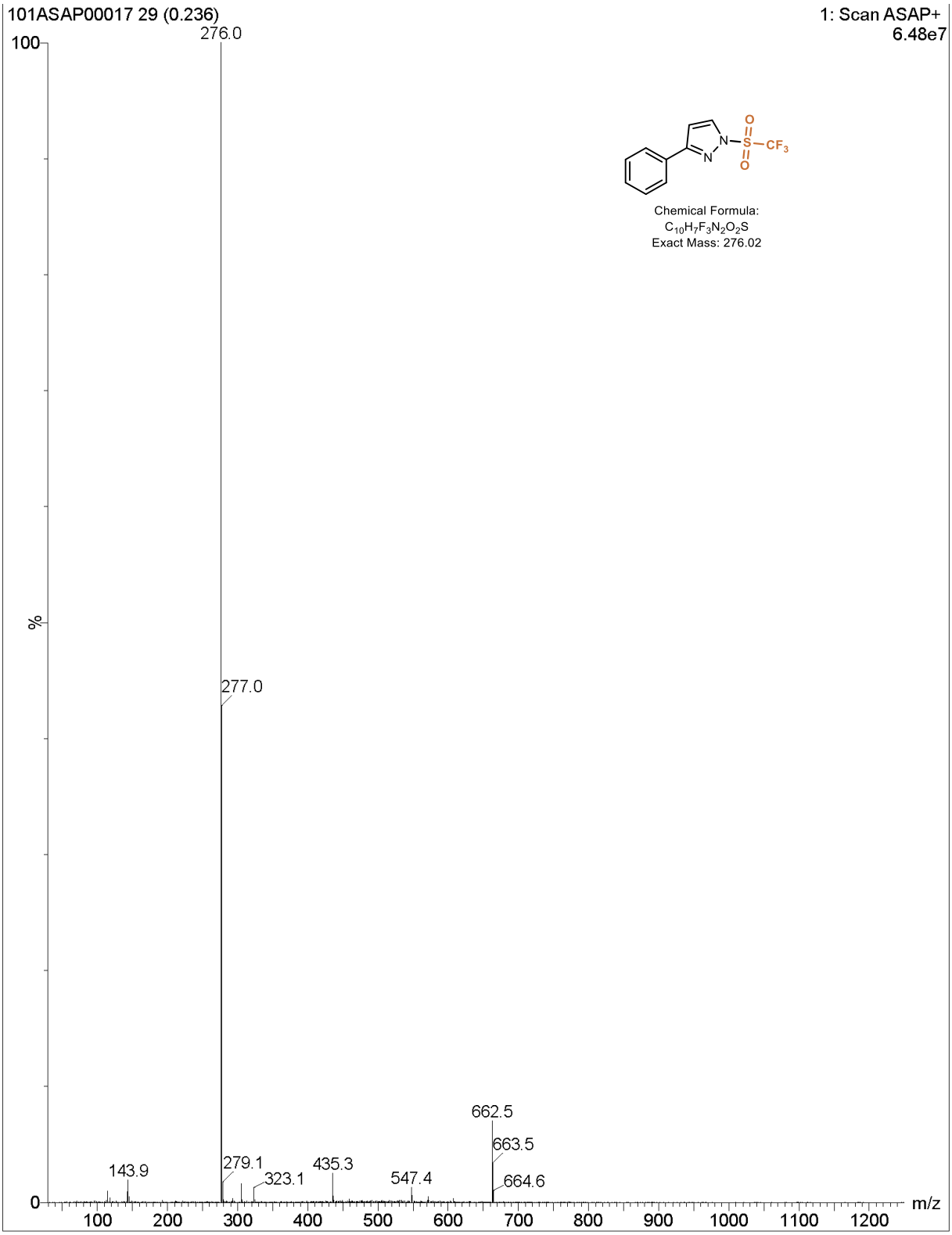
N-(((1S,2R,5S)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl)methyl)-1,1,1-trifluoromethanesulfonamide (compound **62**)



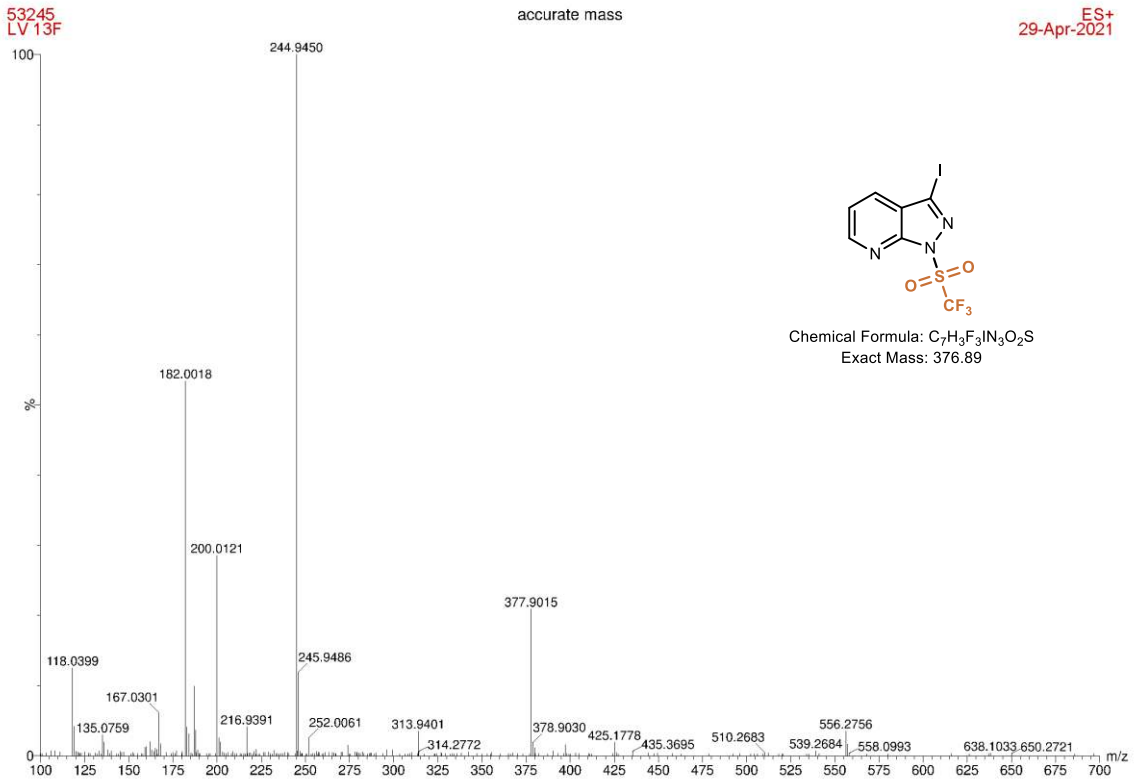
N-(((1S,2R,5S)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl)methyl)-1,1,1-trifluoromethanesulfonamide (compound **63**)



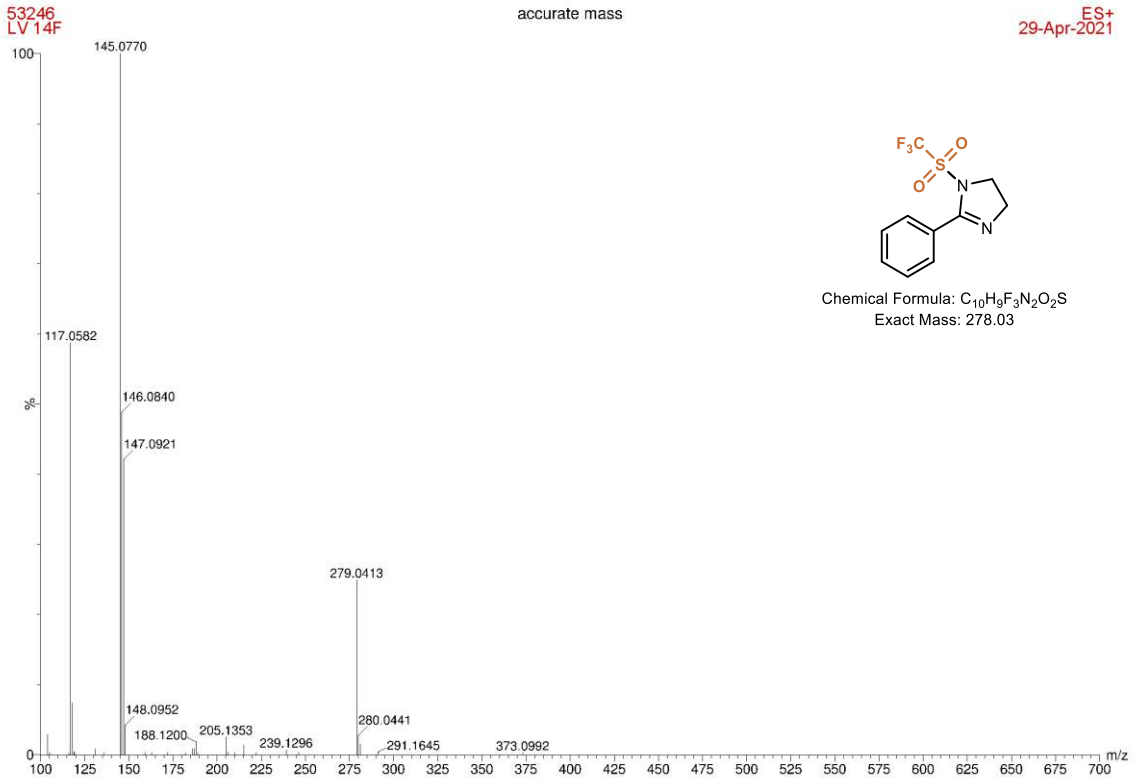
1,1,1-trifluoro-N-(3-methylisoxazol-5-yl)methanesulfonamide (compound **65**)



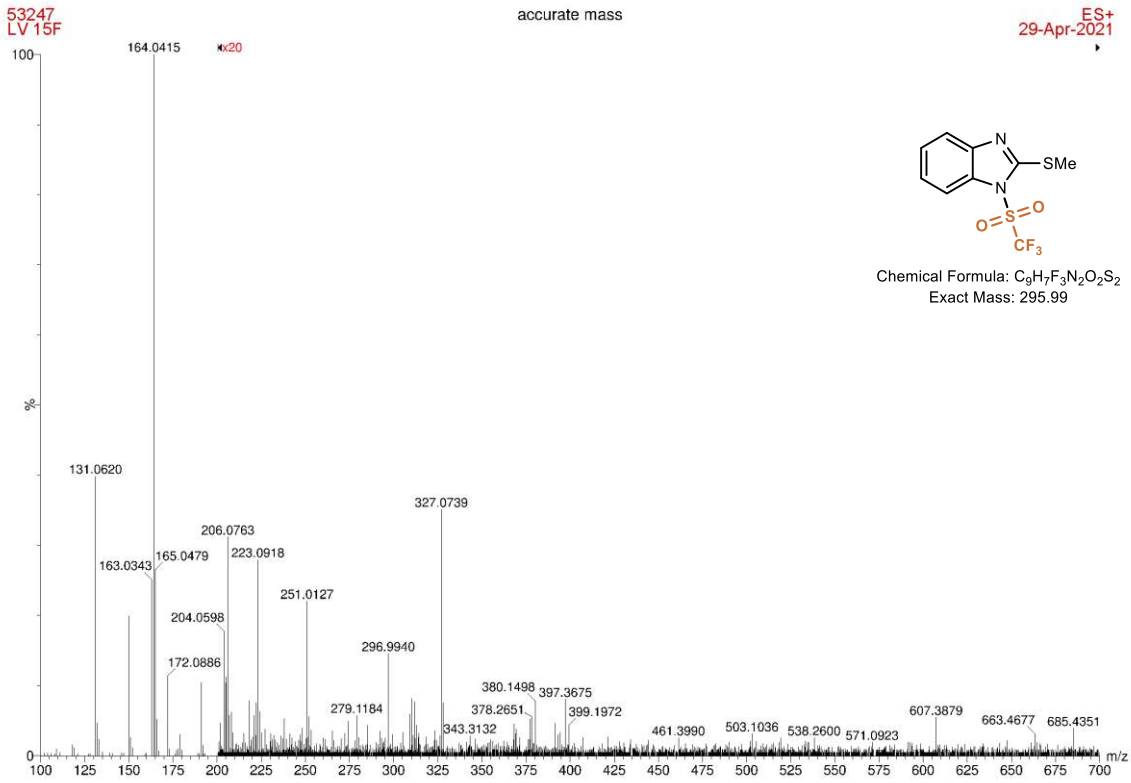
3-phenyl-1-((trifluoromethyl)sulfonyl)-1H-pyrazole (compound **66**)



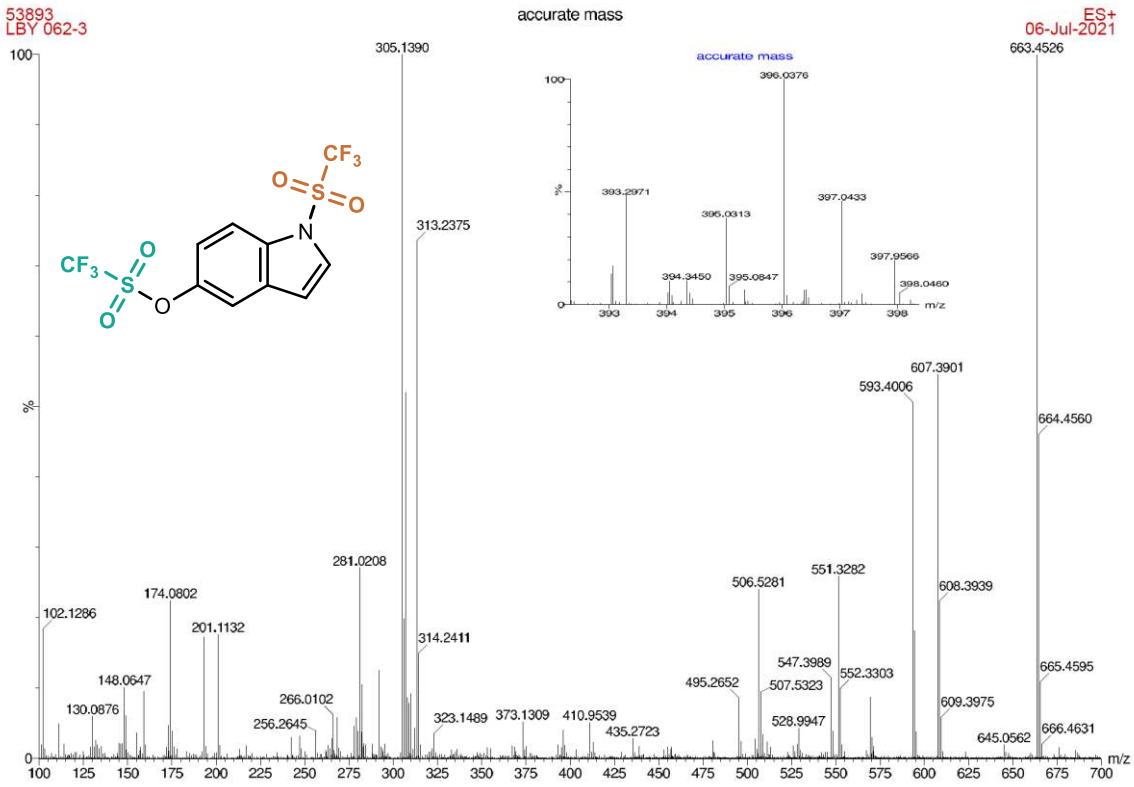
3-iodo-1-((trifluoromethyl)sulfonyl)-1H-pyrazolo[3,4-b]pyridine (compound **67**)



2-phenyl-1-((trifluoromethyl)sulfonyl)-4,5-dihydro-1H-imidazole (compound **68**)



2-phenyl-1-((trifluoromethyl)sulfonyl)-4,5-dihydro-1H-imidazole (compound **69**)



1-((trifluoromethyl)sulfonyl)-1H-indol-5-yl trifluoromethanesulfonate (compound **70**, new compound)

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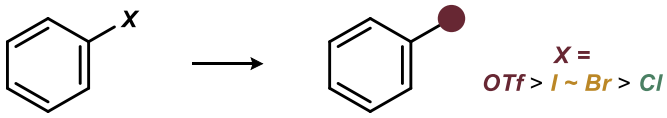
15. Additional literature

- Selected references where the OTf leaving group outperforms the halide series, due to difference of the chemical environment or absence of side reactions:



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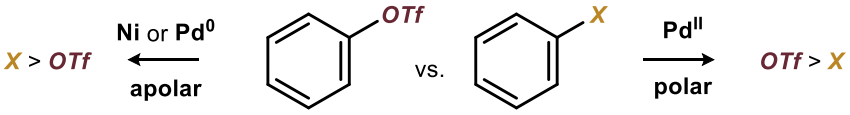
- References that have investigated the role of solvent, metal and ligand on (pseudo)halide selectivity:



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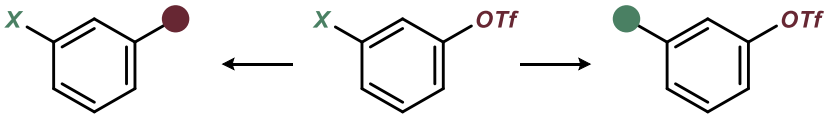
- References that discuss chemodivergence in halophenyl triflates:



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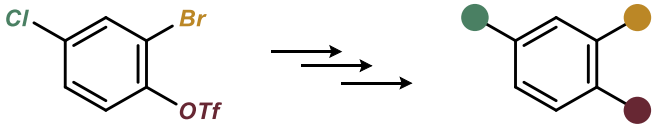
- Iterative cross-coupling of OTf-containing halobenzenes:



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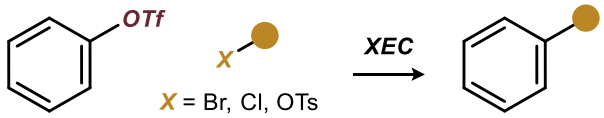

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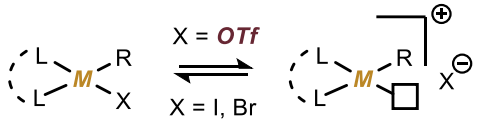

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