Electronic Supporting Information

Newly Synthesized 3-Sulfenylindole Derivatives from 4-Hydroxydithiocoumarin using Oxidative Cross Dehydrogenative Coupling Reaction (OCDCR): Potential Lead Molecules for Antiproliferative Activity[1]

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1. General Information and Methods

^{1}H and ^{13}C NMR spectra were recorded on 600 MHz and 400 MHz spectrometers, TMS as internal reference; chemical shifts (δ scale) are reported in parts per million (ppm). ^{1}H NMR spectra are reported in the order: multiplicity, coupling constant (*J* value) in hertz (Hz) and number of protons; signals were characterized as s (singlet), d (doublet), t (triplet) and m (multiplet). IR spectra were recorded in KBr. HRMS spectra were recorded using ESI mode. The X-ray crystal structures were determined with a diffractometer. Complete crystallographic data of **3a** (CCDC no. 1887551), **5a** (CCDC no. 1887550) for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

2. Molecular Docking Study against DNA

In order to study the interaction between DNA and the synthesized compounds molecular docking was performed using AutoDock vina software. The three dimensional structure of the compounds were generated using BUILDER option in Pymol software and the energy minimization of the compounds was performed using sculpt option in Pymol. To dock the compounds with DNA, the three dimensional structure of B-DNA was obtained from Protein Data Bank (PBD ID- 1BNA).[1,2] All the water molecules from DNA were removed and the polar hydrogens were added using AutoDock tool (MGLTools 1.5.6). A grid box was created in order to encompass the entire DNA fragment. Finally, molecular docking was performed using AutoDock vina to estimate the DNA-ligand binding affinity. Based on the binding affinity of the DNA-ligand interaction, 11 compounds were selected and the intermolecular interactions were determined using Pymol.

To determine the anti-proliferative activity of the compounds, it was imperative to identify the potential cellular target of the synthesized compounds. DNA holds huge impetus as an important class of target for potential anti-proliferative agents. Anti-proliferative agents targeting DNA have shown significant clinical as well as commercial success.[3,4] Thus, in the present study molecular docking was performed to determine any possible interactions between the sulfone derivatives and DNA. The relative binding energy of the compound-DNA interactions determined by using AutoDockVina was found to be in the range of -6.4kcal mol^{-1} to -9.3 kcal mol^{-1}, as illustrated in Table S1. Based on the binding affinity a total of 11 compounds (namely **3k, 3l, 3m, 3r, 4b, 5a, 5d, 5c, 5d, 5e, 5g**) were selected to further determine their mode of interaction with the DNA. The docking conformation using pymol depicts that the compounds interact with the DNA via hydrogen bonds with the guanine (G) or cytosine (C) bases of the DNA (Table S2). This shows that the compounds preferentially bind to the GC rich region of the DNA. Typically, binding of small aromatic molecules to the GC rich region of the DNA is

indicative of intercalative mode of binding.[5,6] Thus, the compounds potentially act as DNA intercalators as depicted in Figure S1.

Table S1. Binding energies of the compound-DNA interaction using AutoDockVina

Sl. No.	Compound Name	Binding Affinity (kcal/mol)
1	3a	-6.7
2	3b	-7.4
3	3c	-7.9
4	3d	-7.7
5	3e	-8.4
6	3f	-8.0
7	3g	-7.3
8	3h	-8.4
9	3i	-7.1
10	3j	-8.5
11	3k	-8.7
12	3l	-9.0
13	3m	-7.8
14	3n	-7.8
15	3o	-7.9
16	3p	-7.9
17	3q	-7.8
18	3r	-8.4
19	3s	-7.6
20	3t	-7.1
21	3u	-8.1
22	3v	-7.0
23	4a	-7.1
24	4b	-7.4
25	4c	-6.5
26	4d	-7.4
27	4e	-6.9
28	5a	-8.2
29	5b	-8.1
30	5c	-8.3
31	5d	-8.1
32	5e	-8.8

33	5f	-7.6
34	5g	-8.6
35	5h	-9.2
36	5i	-9.2
37	5j	-7.5
38	5k	-8.5
39	5l	-9.3
40	5m	-8.3
41	5n	-8.3
42	5o	-8.4
43	5p	-8.0
44	5q	-8.1
45	5r	-8.5
46	5s	-8.3

Table S2. Interaction parameters between the compounds and DNA (1BNA)

Sl No	**Compound name**	**From**	**To**	**Bond length (A^0)**
1	3k	DG-16:H3	3k:O01	2.4
		DG-10:H21	3k:O01	2.1
2	3l	DC-15:02	3l:H03	2.1
		DG-16:H22	3l:O01	2.0
		DC-11:H21	3l:O01	2.5
3	3m	DG-04:O4’	3m:H03	2.1
4	3r	DC-15:02	3R:H03	2.1
		DG-16:H22	3R:O01	2.1
		DG-10:H21	3R:O01	2.5
		DG-10:H3	3R:O01	2.4
		DG-10:H21	3k:O01	2.1
5	4b	DA-5:H3	4B:O01	1.9
6	5a	DG-22:H3	5A:O03	2.5
		DG-4:H22	5A:O03	2.5
7	5b	DC-23:O4’	5B:H03	2.6
8	5c	DC-23:04’	5C:H03	2.3
		DG-4:H22	5C:O02	2.3
		DA-5:H3	5C:O02	2.3
9	5d	DG-4:O4’	5D:H03	2.3

		DG-22:H3	5D:O01	2.0
10	5e	DG-22:H3	5E:O03	2.5
		DG-4:H22	5E:O03	2.5
11	5h	DC-9:O2	5H:O01	2.6
		DG-16:H22	5H:O01	2.1
		DG-10:H3	5H:O01	2.5
12	5l	DC-9:O2	5L:H03	2.4
		DG-10:H3	5L:O01	2.7
		DG-10:H21	5L:O01	2.0
		DG-16:H22	5L:O03	2.1
		DC-9:O2	5L:H03	2.4

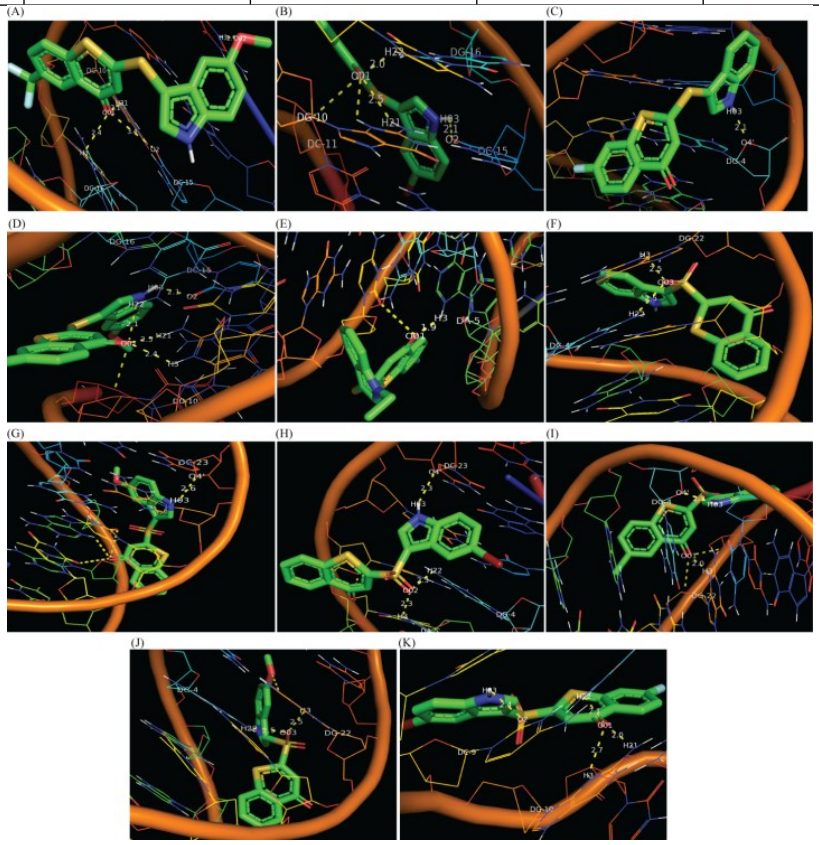


Figure S1. (A-K) Molecular docking of the DNA (1BNA) with the compounds 3**k**, **3l**, **3m**, **3r**, **4b**, **5a**, **5b**, **5c**, **5d**, **5e** and **5g**, respectively. The yellow dotted line depicts the hydrogen bond between the compounds and the GC bases of the DNA.

PI based flow cytometry data:

Propidium iodide (PI) is a non-permeable DNA binding dye, which can enter only membrane compromised cells. Thus, PI is commonly used to distinguish between viable cells and membrane compromised cells. MCF-7 cells were treated with compounds **3k, 3l, 5a, 5b, 5d** and **5e** which led to reduction in cell viability as determined by MTT assay. The probable reason could be disruption of membrane integrity by the compounds. To determine the same PI based propidium assay was performed. Experiment was carried out in 6 well plates. Compounds were added at their IC_{50} concentration for 48 hours. Following incubation, media cell suspension was collected in microcentrifuge tube. The cell in the plates were washed with PBS and then trypsinized. Following trypsinization, cells were again washed with the media cell suspension that was previously collected. These cells were then further centrifuged at 650 RCF for 10 min and re-suspended in 400 µl PBS. To the cell suspension, 5µl of the 1mg/ml of PI staining solution was added and centrifuged at 650 RCF for 5 min. Cells were again re-suspended in 400 µl PBS. PI binds to the double stranded DNA of the membrane compromised cells by intercalating between base pairs. PI fluorescence was determined by flow cytometry using Beckman coulter at 488 nm excitation. Treatment with the compounds displayed significant increase in the percentage of compromised cells upon 48 h incubation, which indicates that the compounds are biologically active and impart their anti-proliferative activity by inducing membrane damage of the cancer cells (Figure 2). Untreated and DMSO treated cells did not show any significant effect as shown in Figure S2. The percentage of compromised cells and their respective flow cytometry data is presented in Table 3 and Figure S3, respectively.

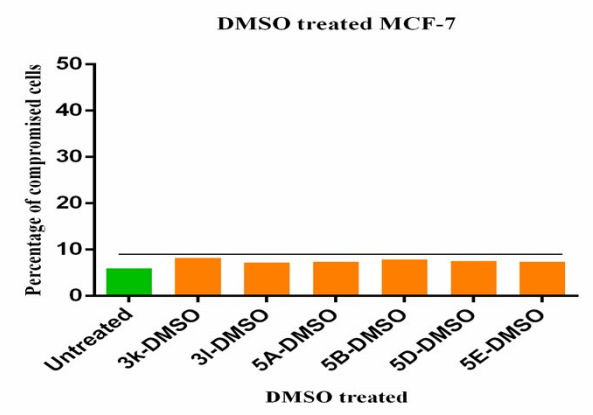


Figure S2. Percentage of compromised cells for untreated and DMSO treated MCF 7 cells

Table S3. Percentage of compromised cells when treated by IC_{50} concentration of different compounds

Sl No	Compounds	% of Dead cells
1	Control	2.750±0.55
2	3k	22.40±1.105
3	3l	20.54±0.965
4	5a	27.37±0.98
5	5b	28.97±1.1
6	5d	27.04±3.04
7	5e	28.16±0.505

Sl No	DMSO	% of Dead cells
1	Control	5.92
2	3k	7.8
3	3l	7.9
4	5a	7.5
5	5b	7.4
6	5d	8.3
7	5e	7.2

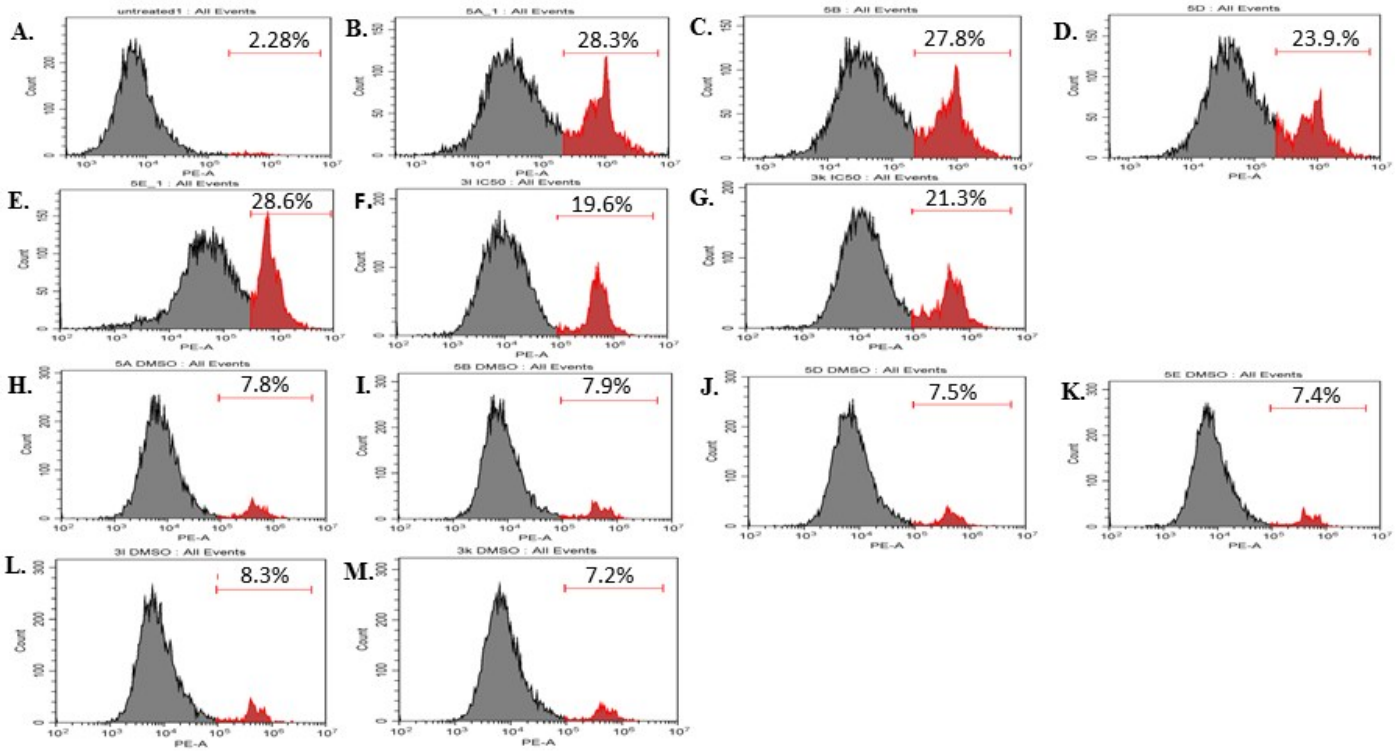


Figure S3. PI based flow cytometry data of (A) Untreated cells (B-G) Upon treatment with compounds 5a, 5b, 5d, 5e, 3l, 3k, respectively (H-M) DMSO treated cells, corresponding to controls for compounds 5a, 5b, 5d, 5e, 3l, 3k, respectively.

3. Dual staining with Ethidium bromide (EtBr) and Acridine Orange:

MCF-7 cells were seeded in 96 well plate and treated with c the compounds by their respective IC_{50} for 24 h. After that cells were washed with 1X PBS pH 7.4 buffer and stained with 4 µM acridine orange for half an hour and then again cell was washed with 1X PBS pH 7.4 buffer and incubated with 2µM EtBr for 15 min. After washing with 1X PBS pH 7.4 buffer cell imaging was done by Zeiss LSM 880 confocal microscope.

Cell membrane is permeable to acridine orange, but not EtBr. Treatment of the cells with the compounds showed double staining under excitation of green and red laser, emitting slight orange colour, which confirmed the rupture of cell membrane. However, the untreated control cells did not show double staining or EtBr staining, which conferred membrane integrity.

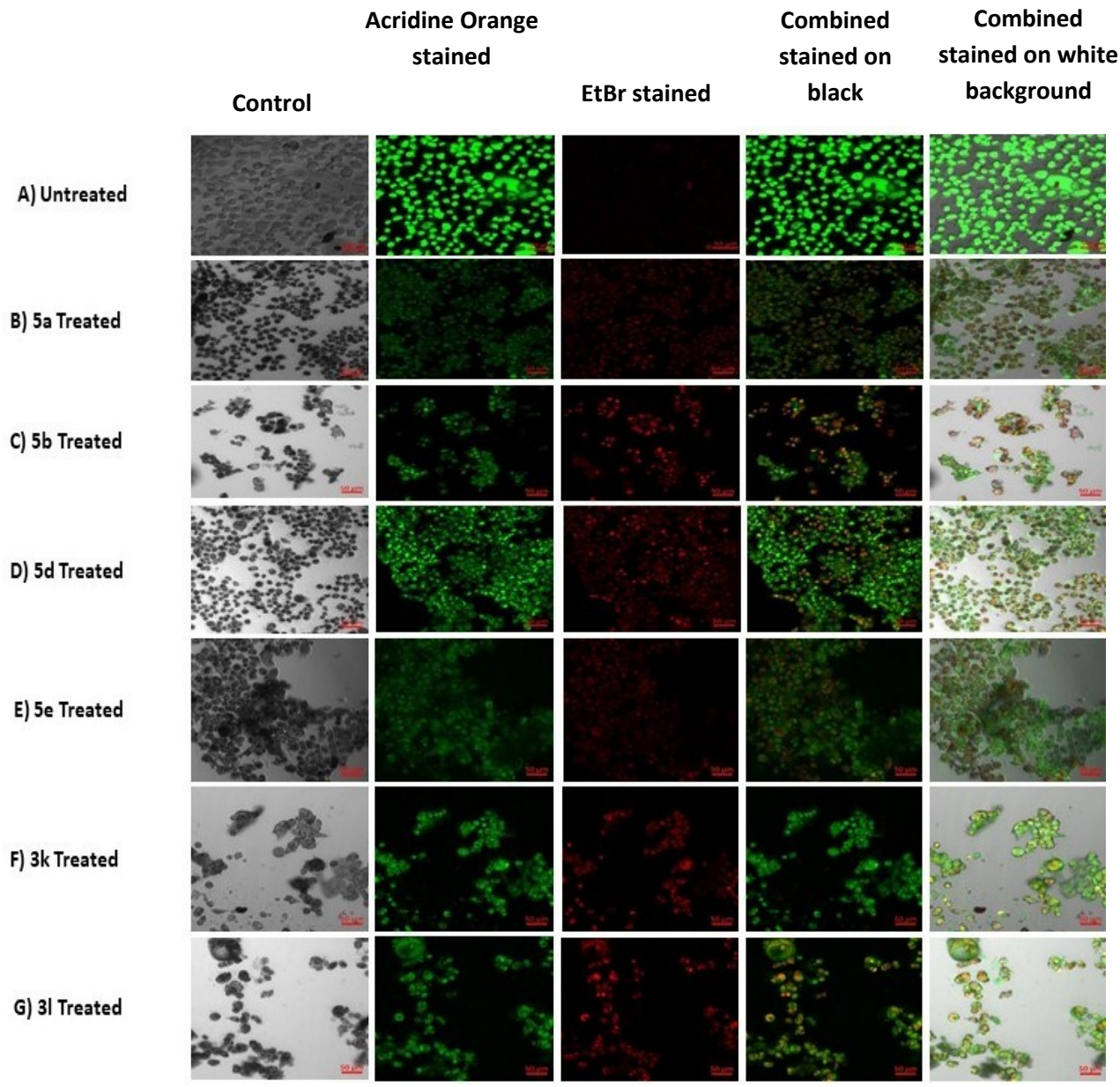
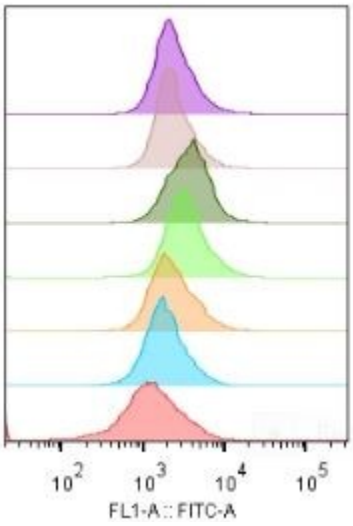


Figure S4: Dual staining with EtBr and acridine of MCF-7 cells upon treatment with the compounds.

4. Cellular Reactive Oxygen Species (ROS) Detection assay:

ROS assay was performed using cell permeant reagent 2', 7' dichlorofluorescin diacetate (DCFDA), a fluorogenic dye that measures hydroxyl, peroxyl and other ROS activity within the

cell. The MCF-7 cells were treated with IC_{50} concentration of the compounds. After 6 h of treatment, DCF-DA was added and incubated at 37 °C for 30 min. After the incubation, dye was removed and washed with PBS and fluorescence was measured using Cytoflex Beckman coulter instrument. Fluorescence peak shifts was observed upon treatment.

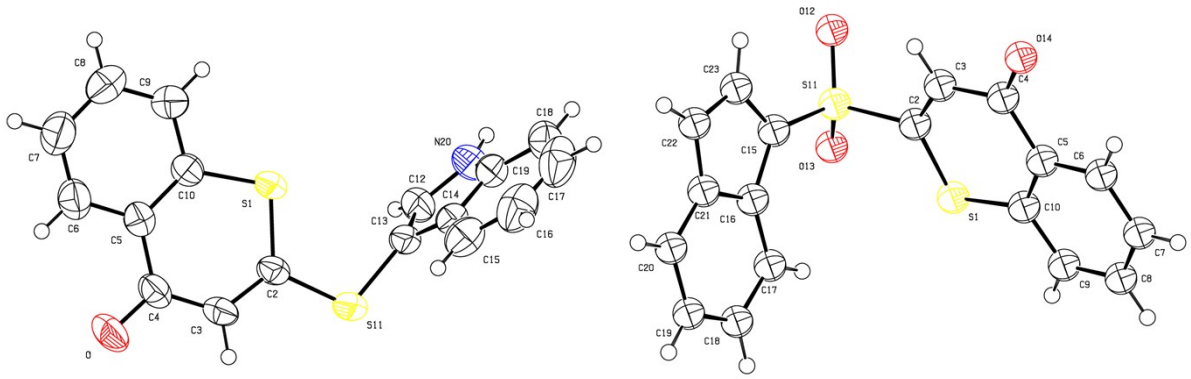


	Sample Name	Subset Name	Count	Mean : FL1-H	Mean : FL1-A
	3l_1.fcs	Ungated	10000	1862	3028
	3k_1.fcs	Ungated	10000	2017	3591
	5e_1.fcs	Ungated	10000	2617	4333
	5d_1.fcs	Ungated	10000	2301	4107
	5b_1.fcs	Ungated	10000	1831	3062
	5a_1.fcs	Ungated	10000	1652	2363
	UNTR_9.fcs	Ungated	10000	1673	2311

Table S4: Showing mean value of fluorescence intensity for the respective compounds

Figure S5: Fluorescence peak shift in flow cytometry studies

5. X-ray Structure of Compounds 3a, 5a



3a **5a**

Figure S6. ORTEP diagram of compound 3a and compound 5a.

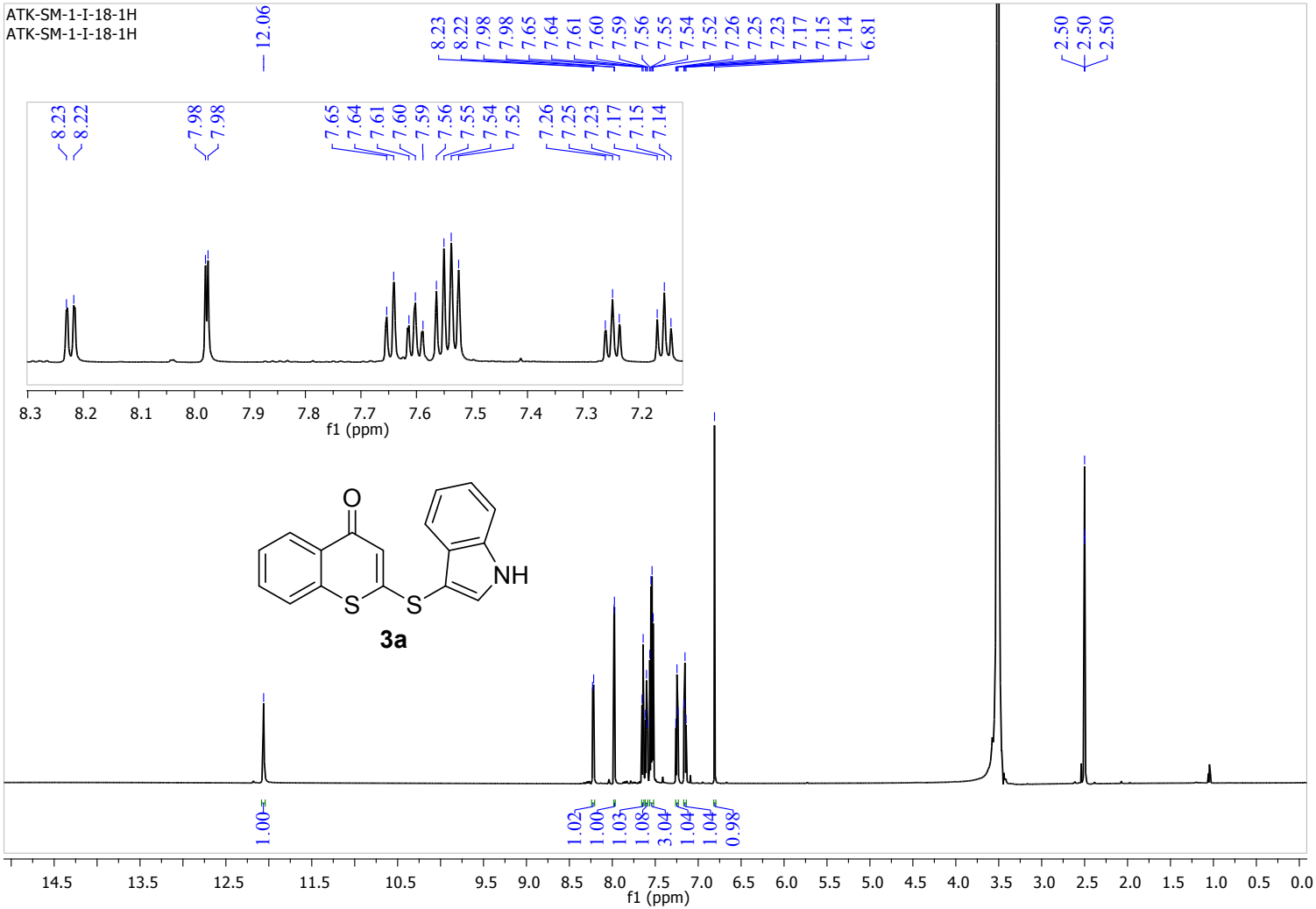
6. Crystal Data and Structure Refinement for Compounds 3a, 5a

Table S5. Crystal data and structure refinement for compound **3a** and **5a**.

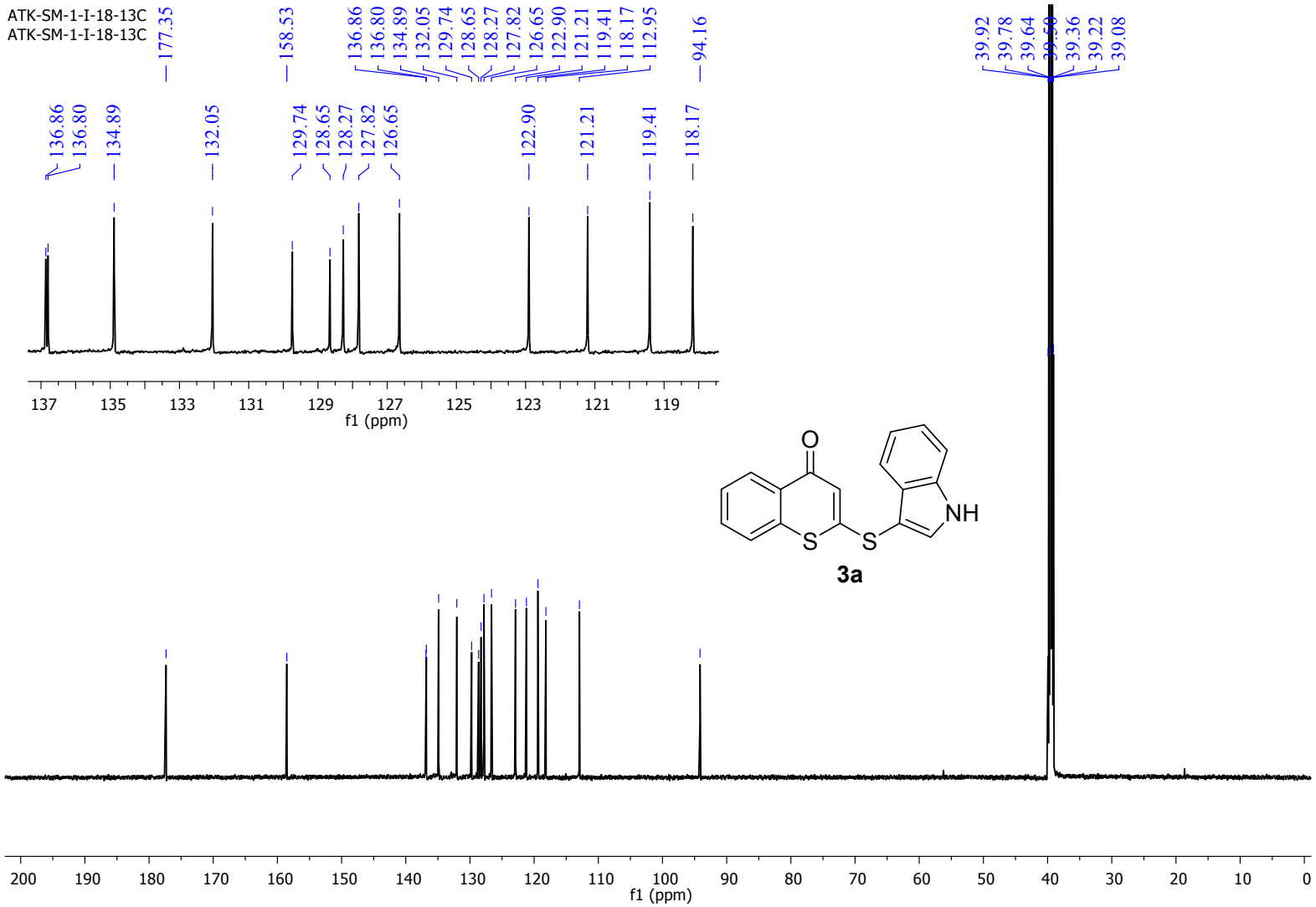
Entry	Identification code	Compound 3a	Compound 5a
01	Empirical formula	C17H11NOS2	C17 H11 N O3 S2
02	Formula weight	309.39	341.39
03	Temperature	293 K	293 K
04	Wavelength	0.71073	0.71073
05	Radiation type	Mo K\a	Mo K\a
06	Radiation source	Fine-focus sealed tube	Fine-focus sealed tube
07	Crystal system	Monoclinic	Orthorhombic
08	Space group	C 2/ c	P 21 21 21
09	Cell length	a 17.5086(10) b 11.7781(8) c 13.9721(9)	a 6.4978(4) b 14.5164(14) c 16.2262(14)
10	Cell Angle	α 90 β 92.716(6) δ 90	α 90 β 90 δ 90
11	Cell Volume	2878.1(3)	1530.5 (2)
12	Density	1.428	1.482
13	Completeness to theta	25°/ 99.7%	25°/ 99.73%
14	Absorption correction	multi-scan	multi-scan
15	Refinement method	Full-matrix least-squares on F2	Full-matrix least-squares on F2
16	Index ranges	-23<=h<=22, -15<=k<=15, -17<=l<=17	-8<=h<=8, -10<=k<=18, -12<=l<=21
17	Reflection number	6700	5606
18	R(reflections)	0.0458(2015)	0.0580(1799)
19	wR2(reflections)	0.1324(2550)	0.0975(2644)
20	gooF (S)	1.022	1.066
21	Theta range	2.9190- 28.7886	2.8762- 28.6975
22	Cell formula units Z	8	4
23	CCDC no	1887551	1887550

7. Copies of ^{1}H NMR, ^{13}C NMR and HRMS spectra of all Compounds

^{1}H NMR spectra of compound: 3a



^{13}C NMR spectra of compound: 3a



HRMS spectra of compound: 3a

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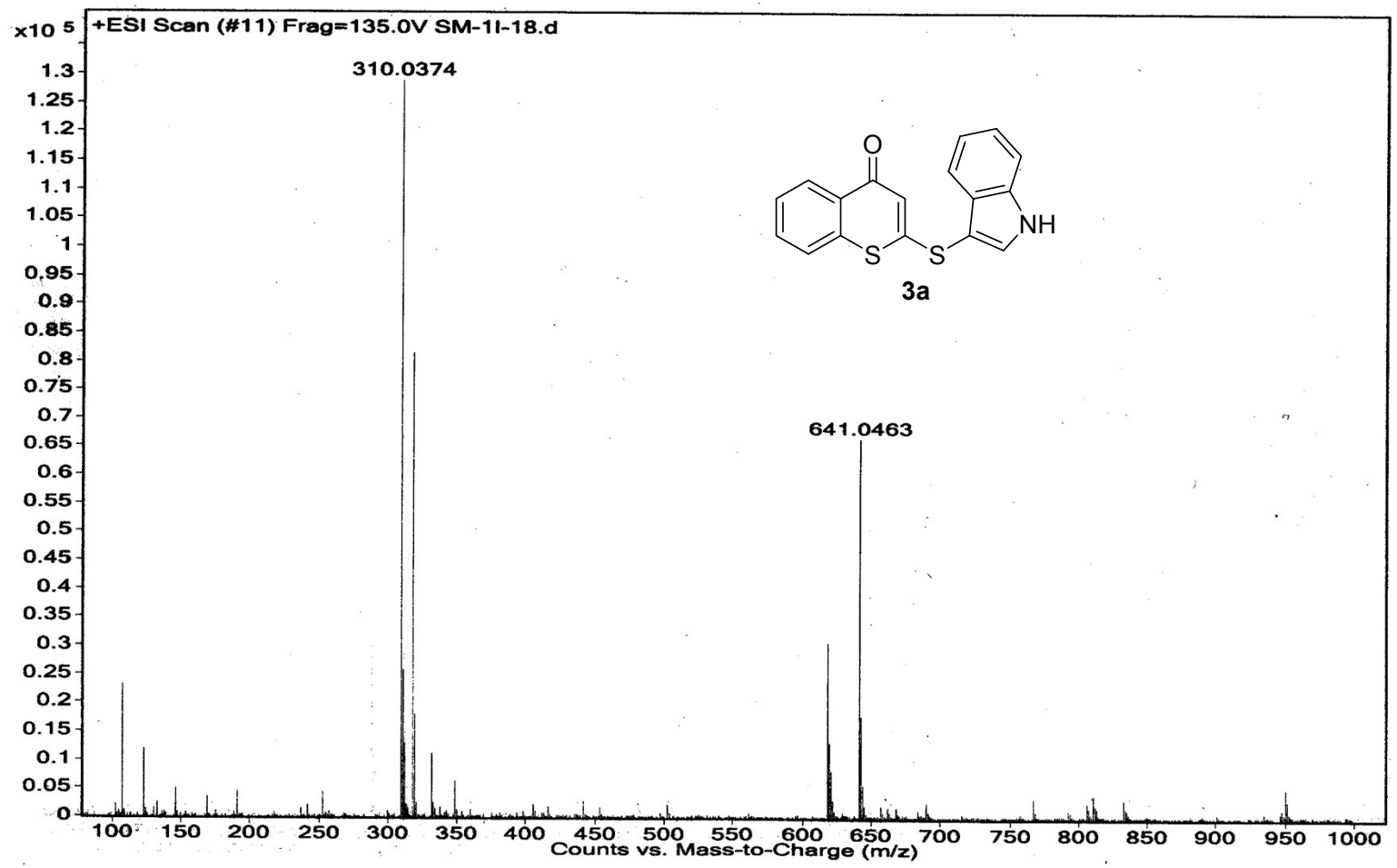
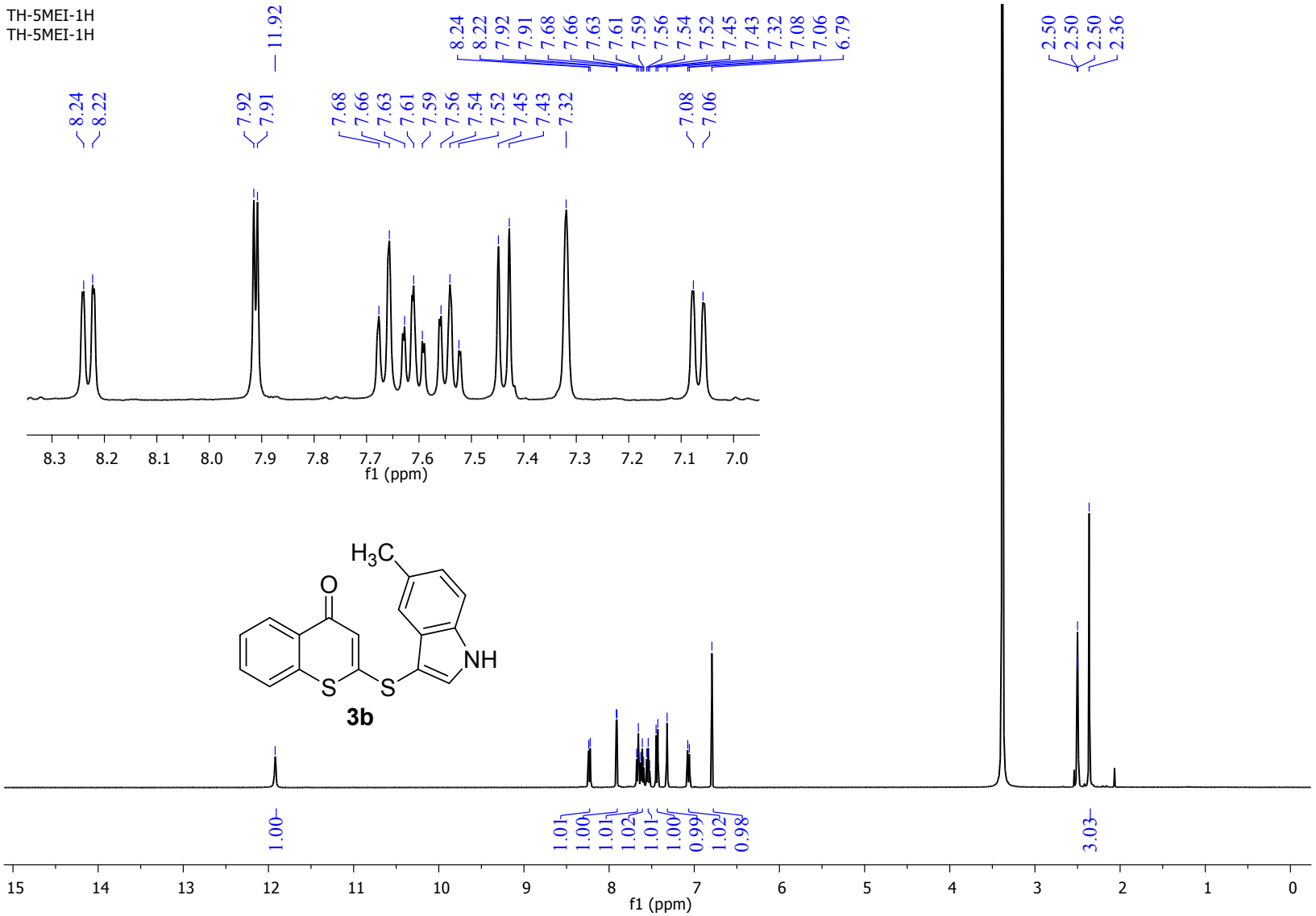
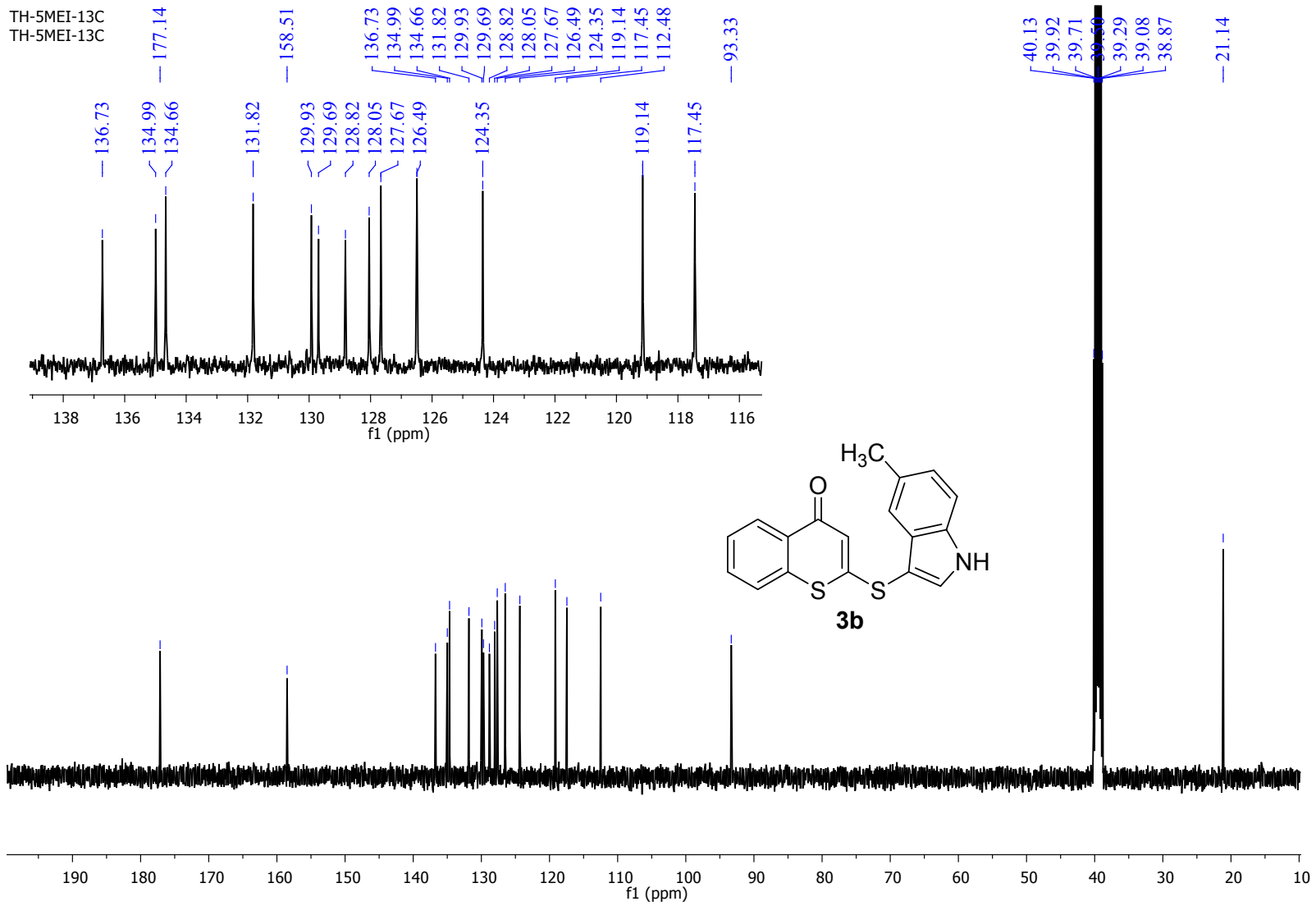


^{1}H NMR spectra of compound: 3b



^{13}C NMR spectra of compound: 3b



HRMS spectra of compound: 3b

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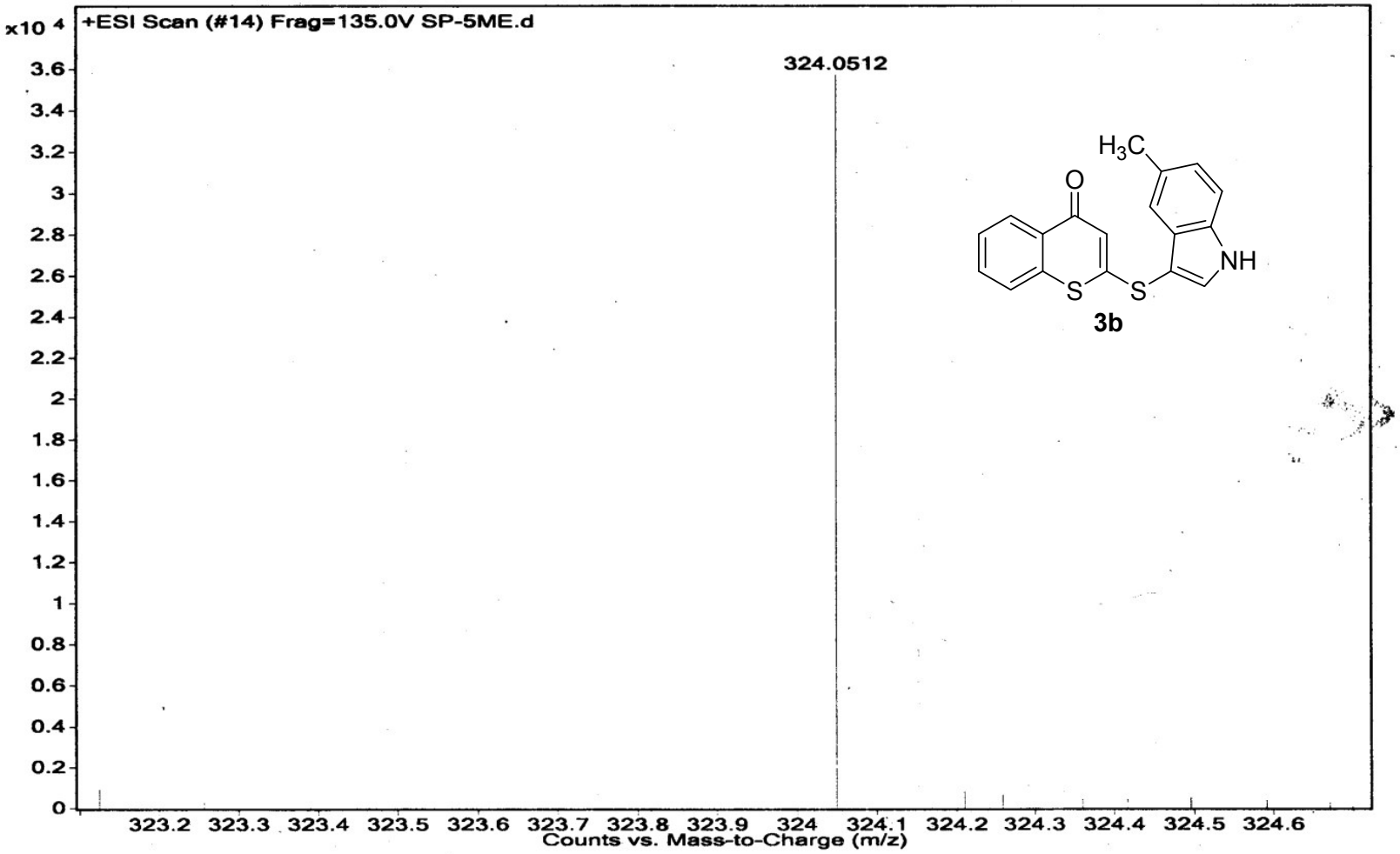
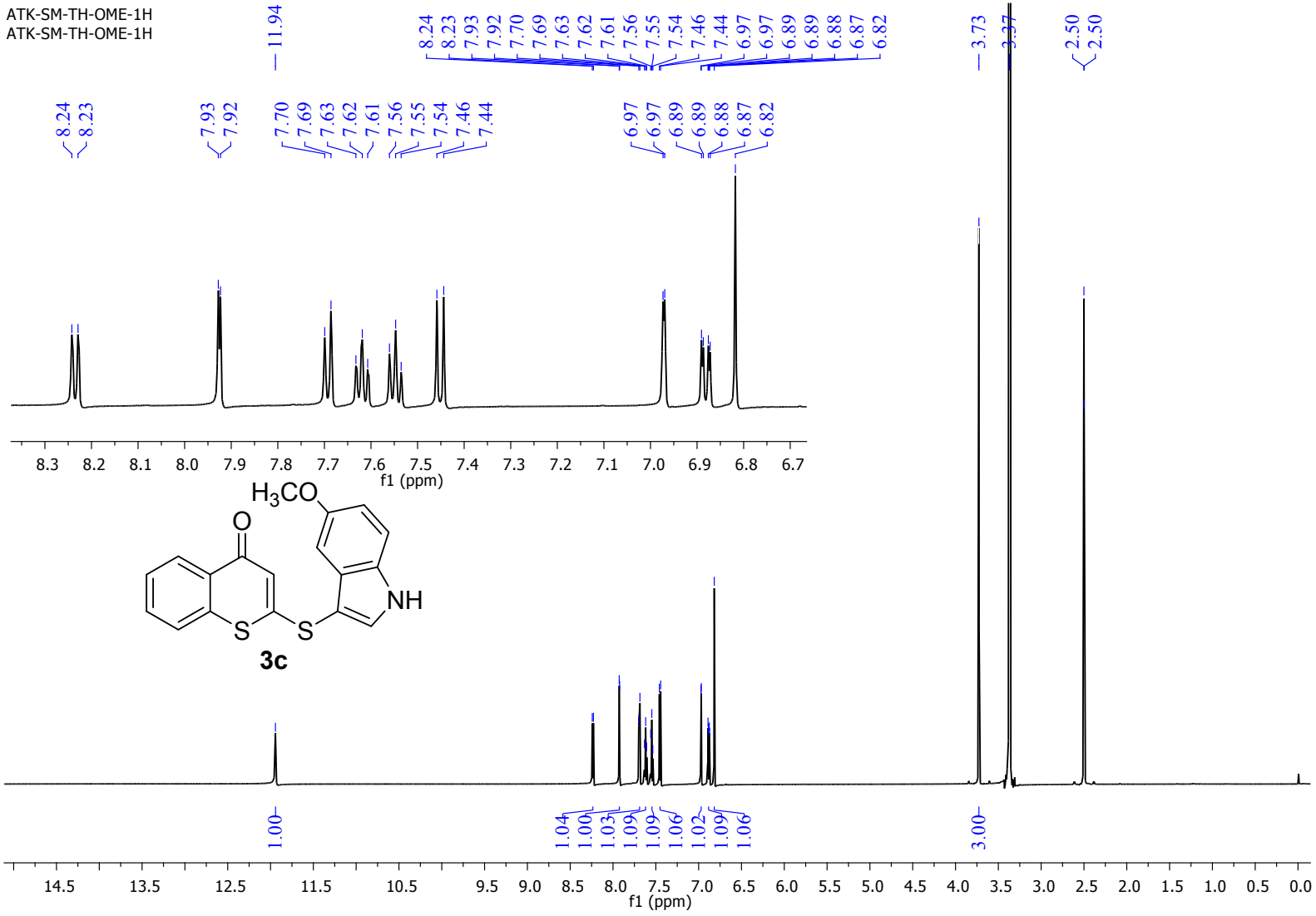
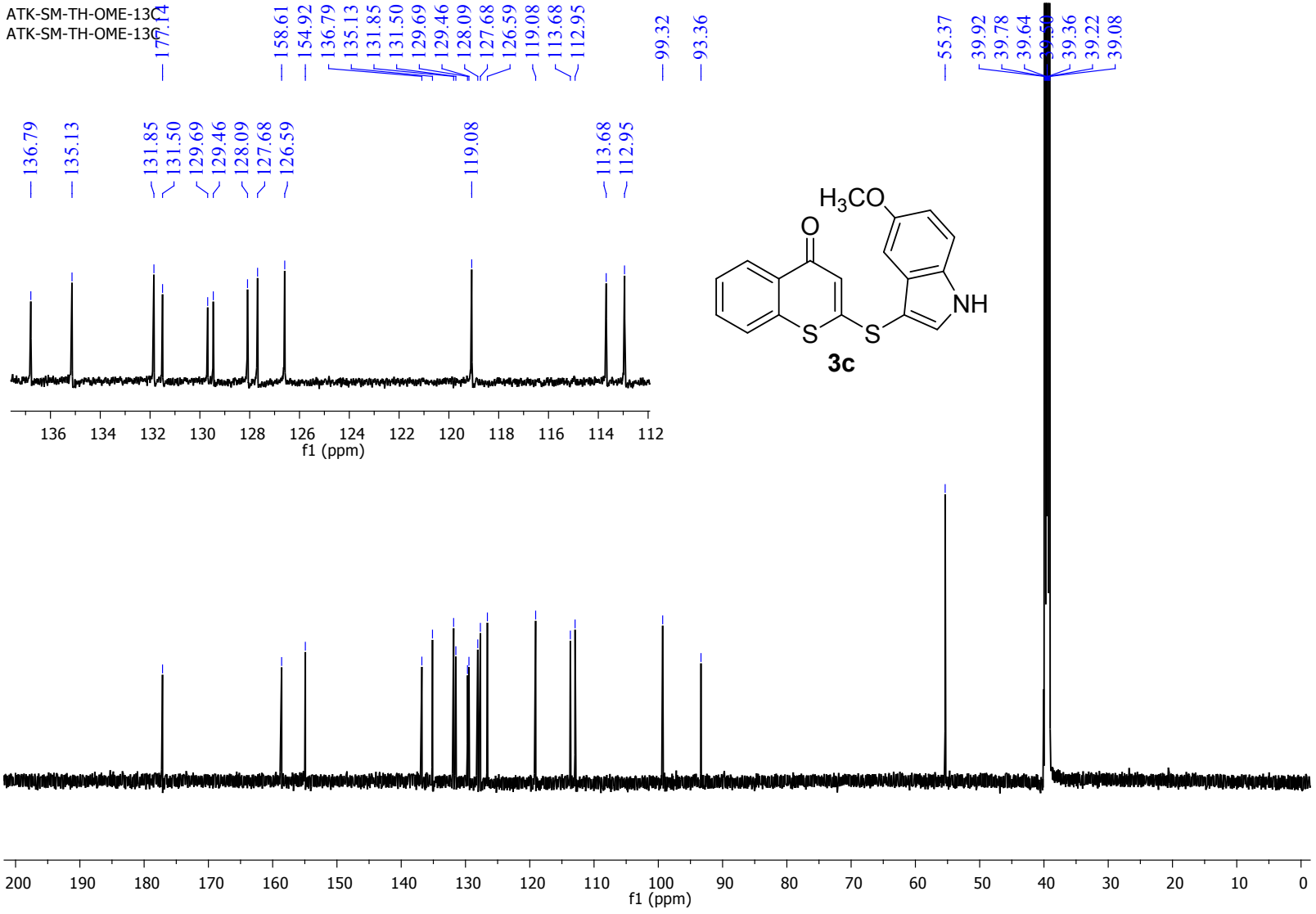


^{1}H NMR spectra of compound: 3c



^{13}C NMR spectra of compound: 3c



HRMS spectra of compound: 3c

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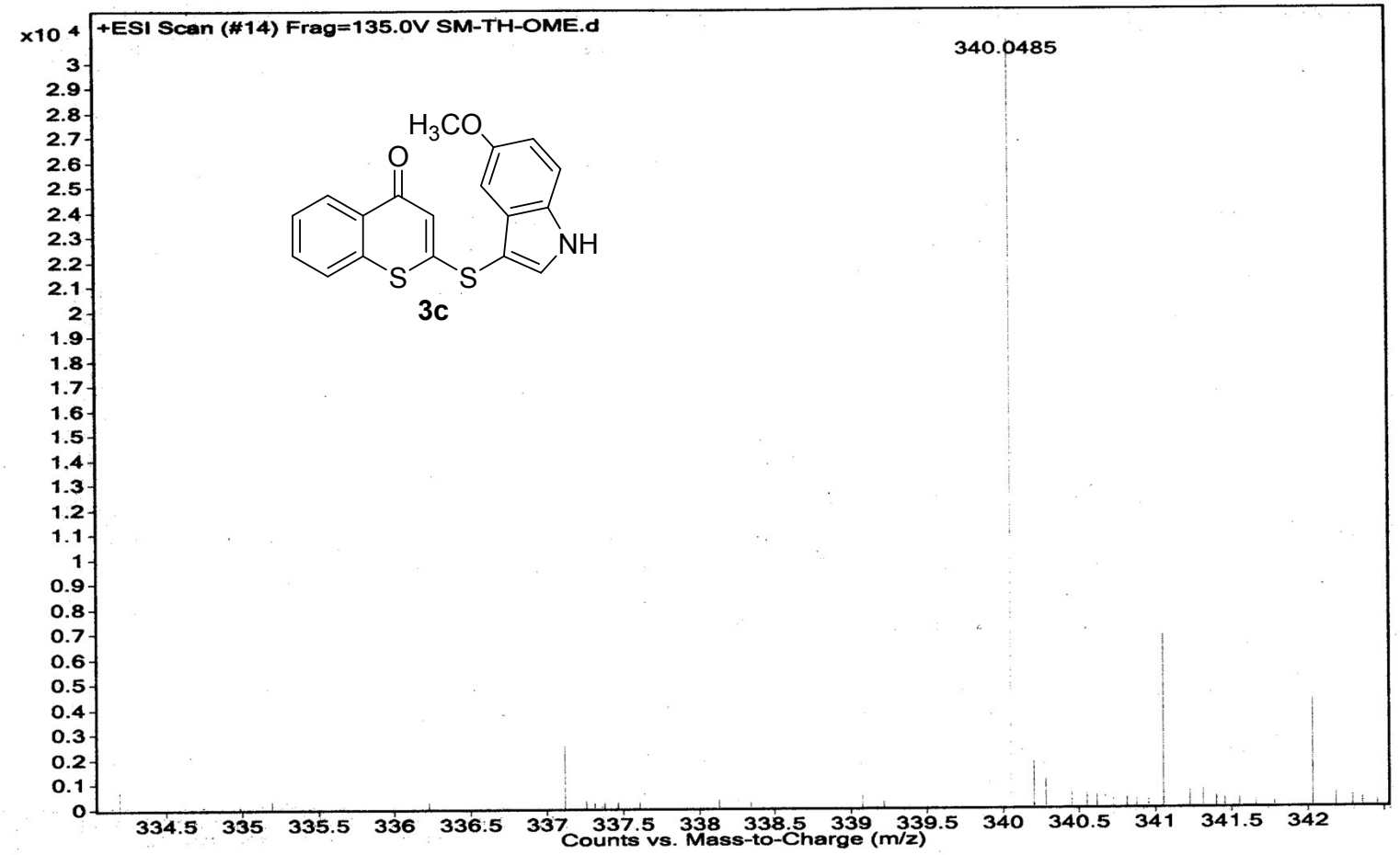
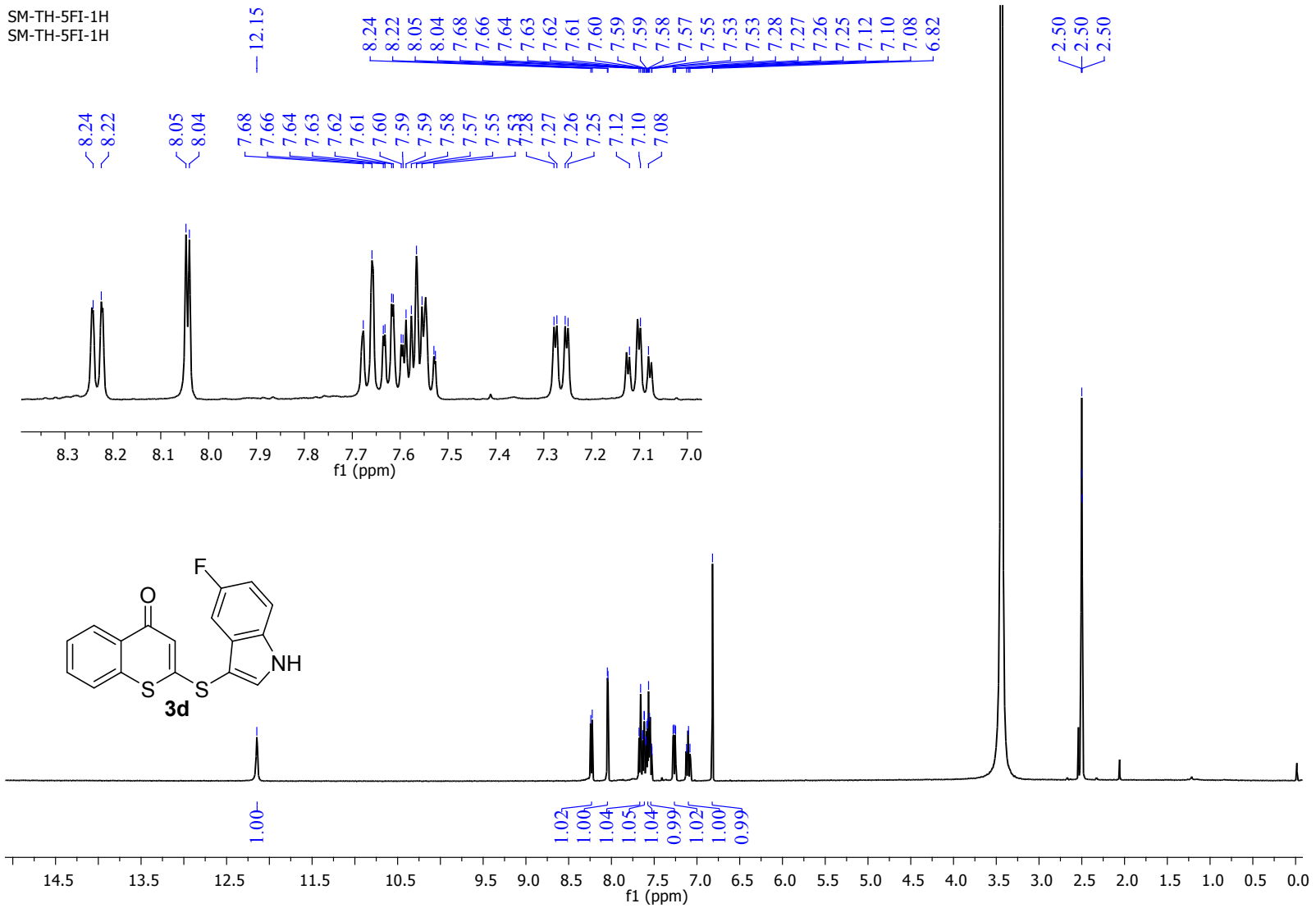
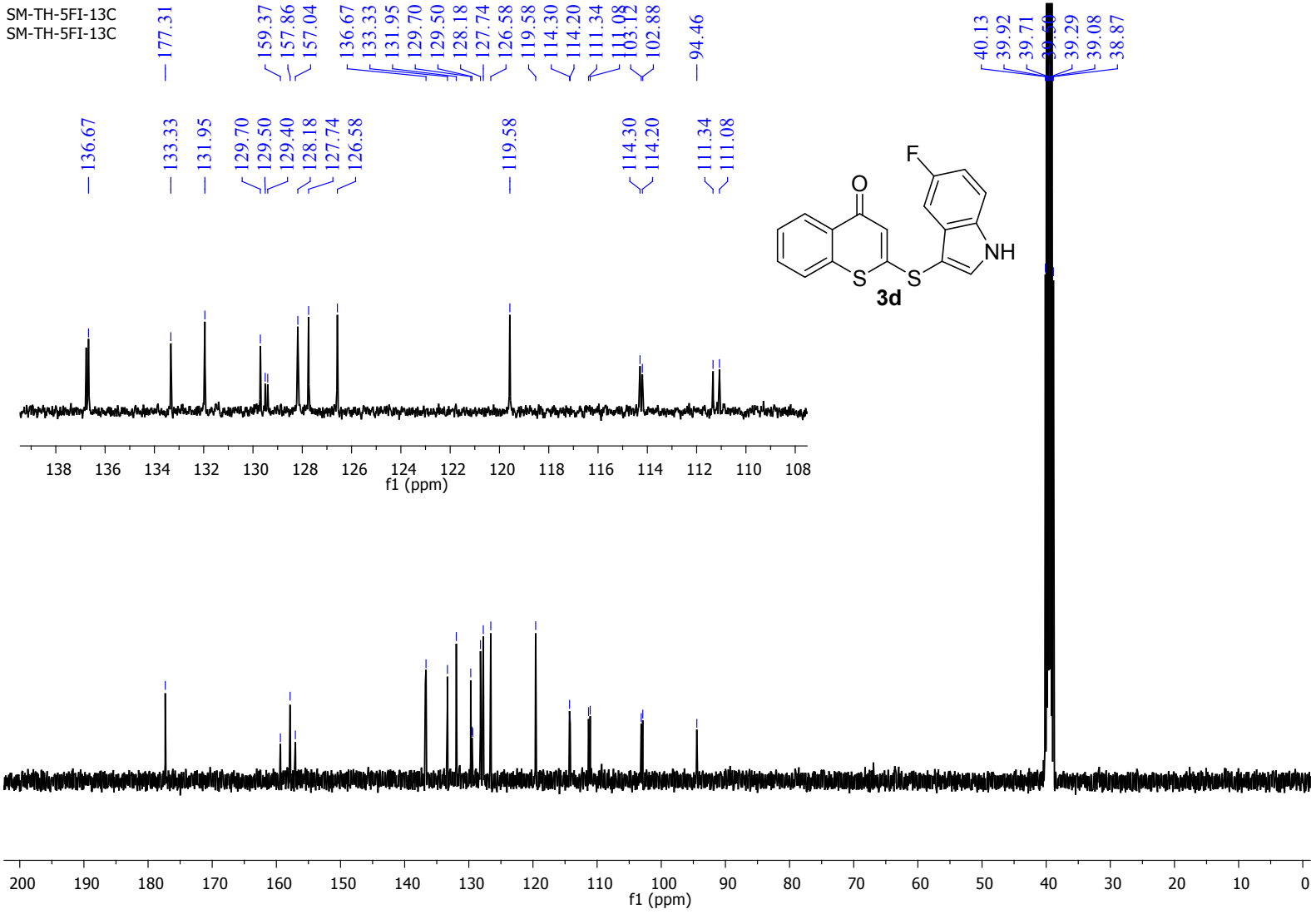


^{1}H NMR spectra of compound: 3d



^{13}C NMR spectra of compound: 3d



HRMS spectra of compound: 3d

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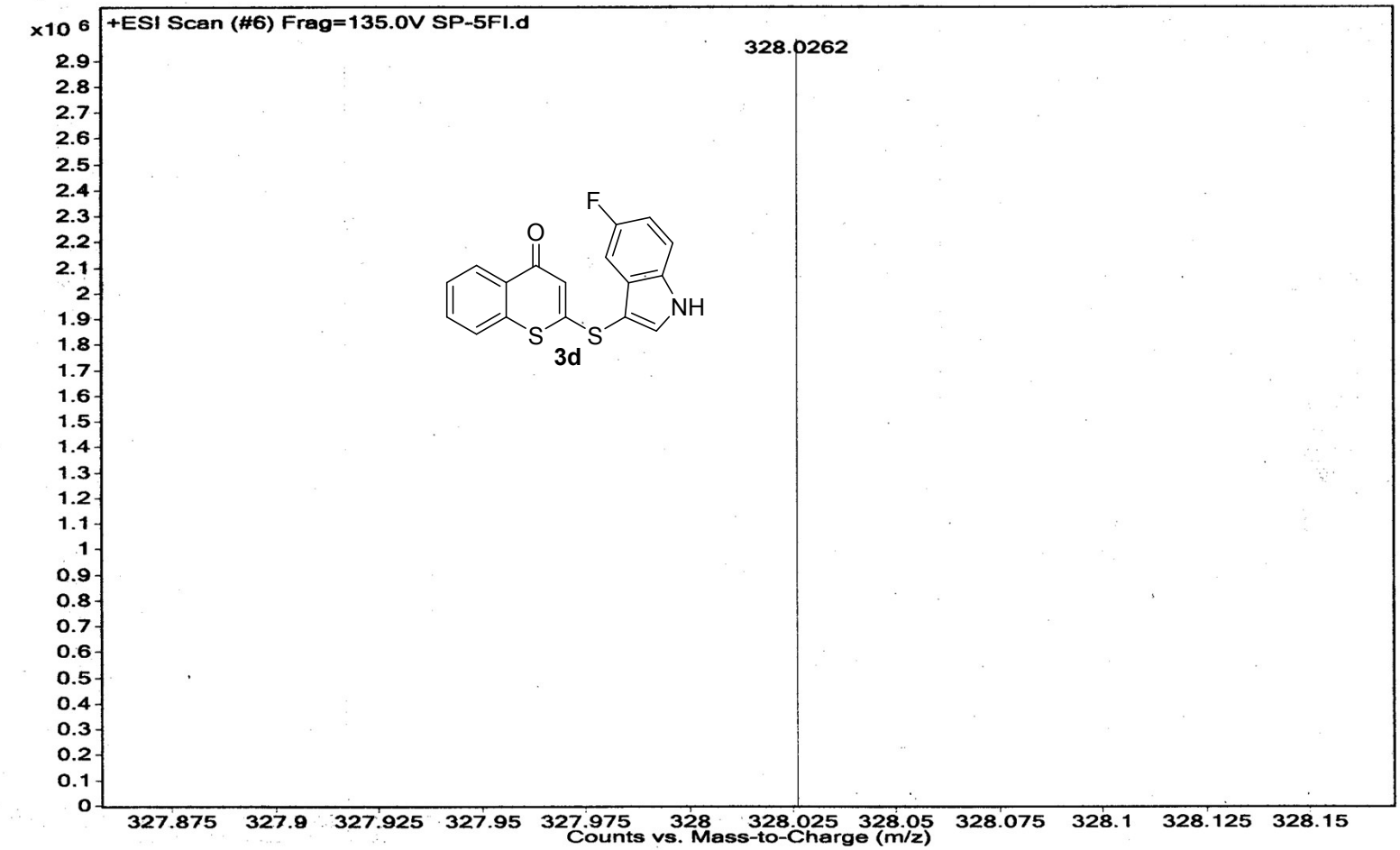
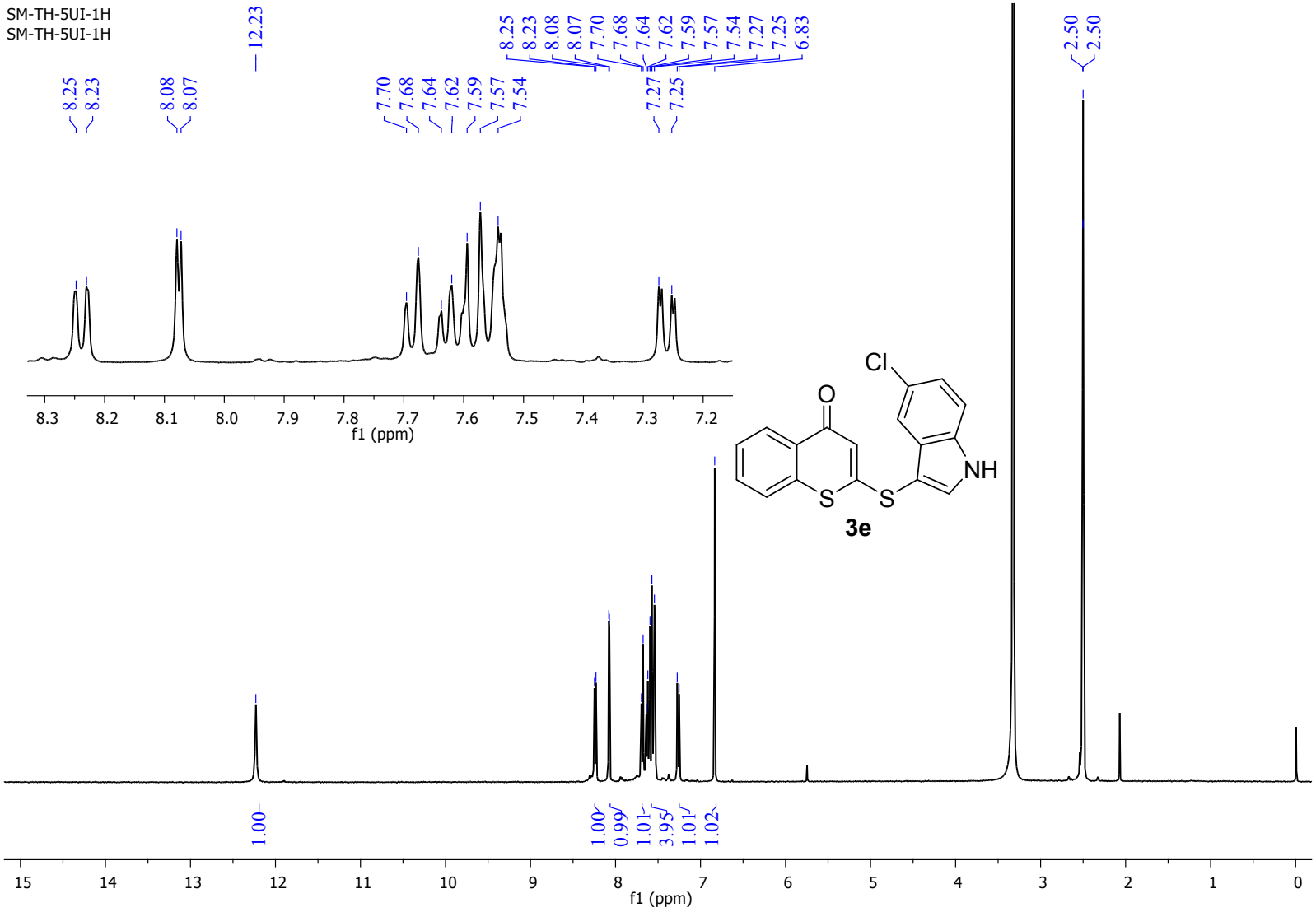
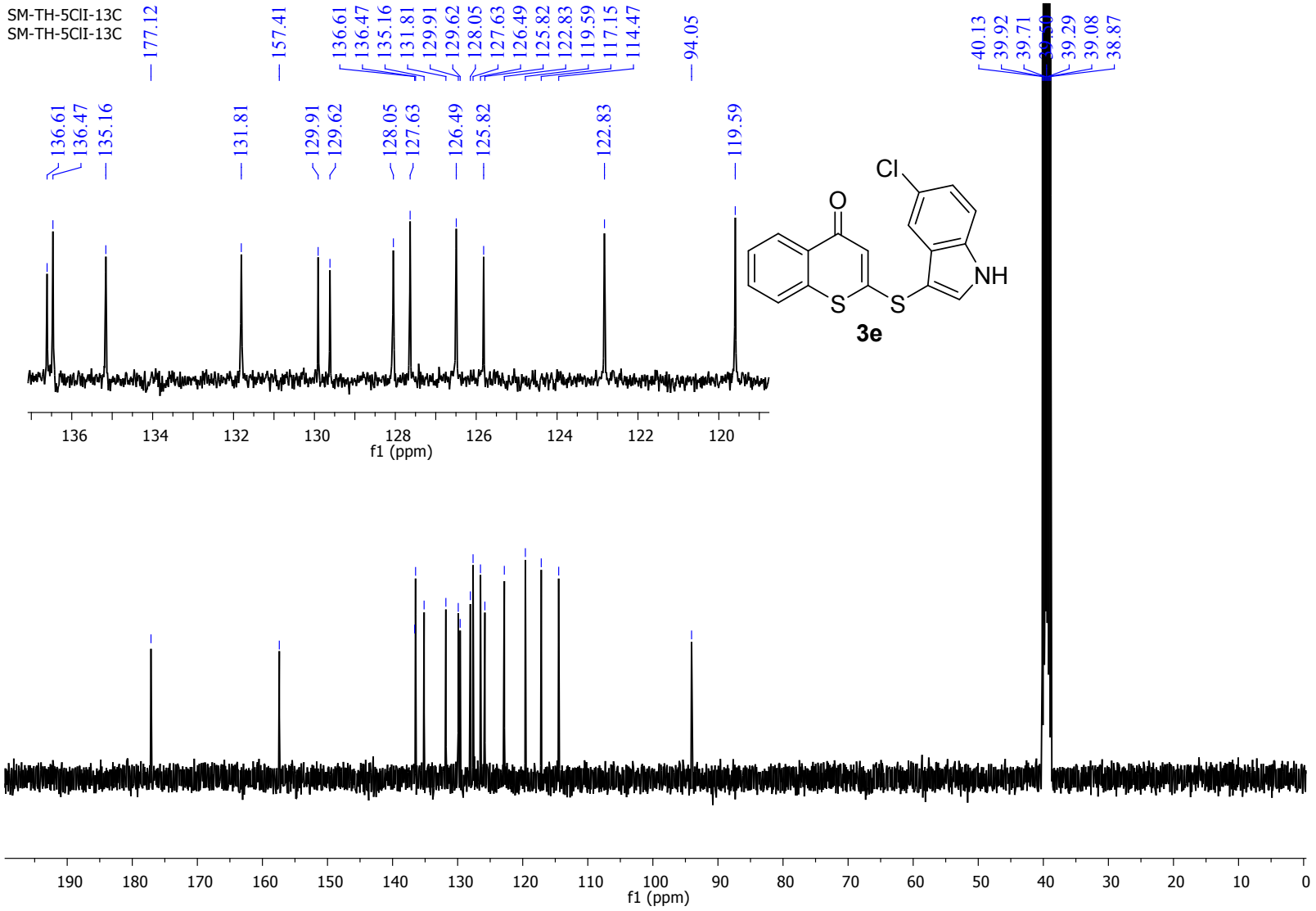


^{1}H NMR spectra of compound: 3e



^{13}C NMR spectra of compound: 3e



HRMS spectra of compound: 3e

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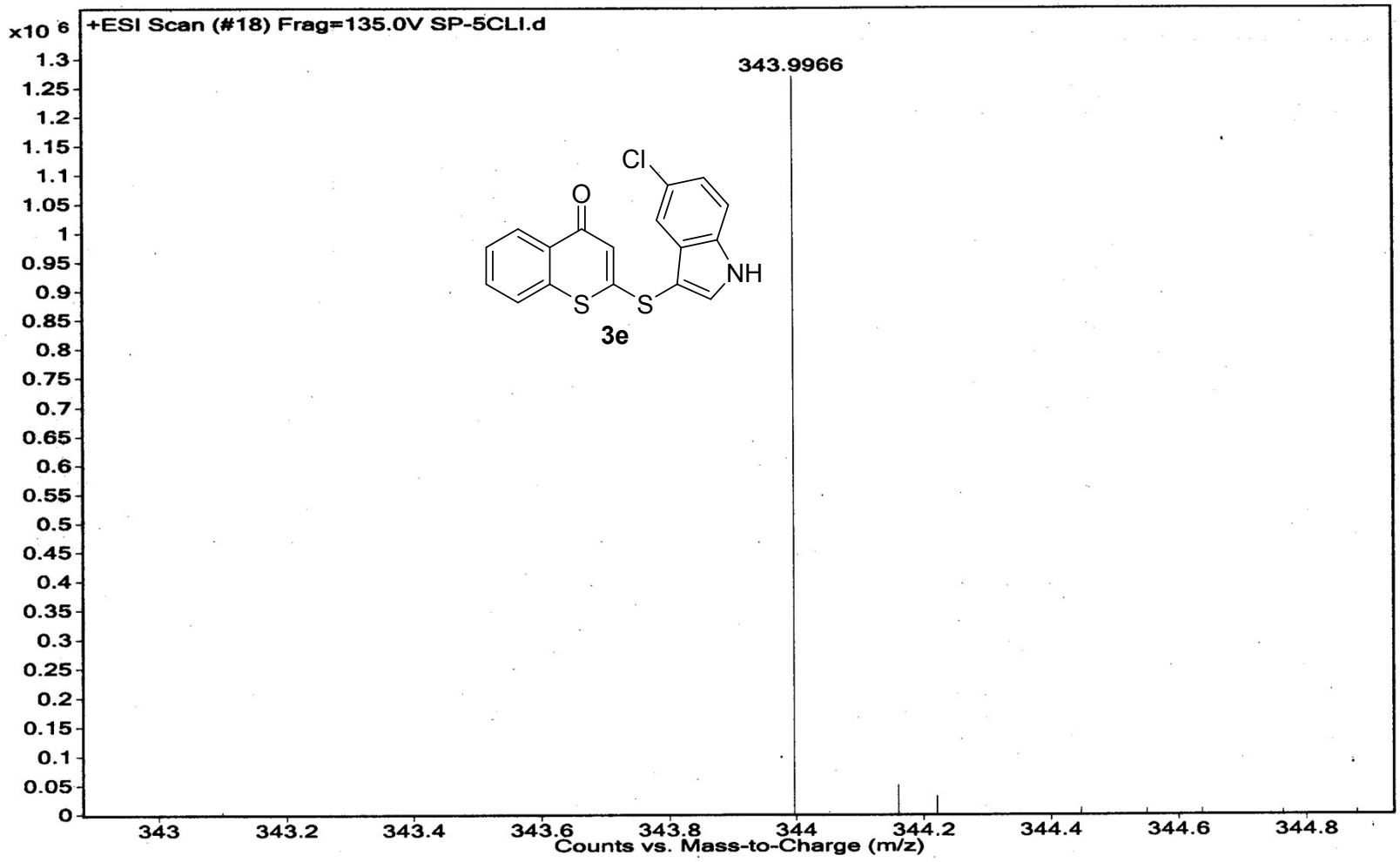
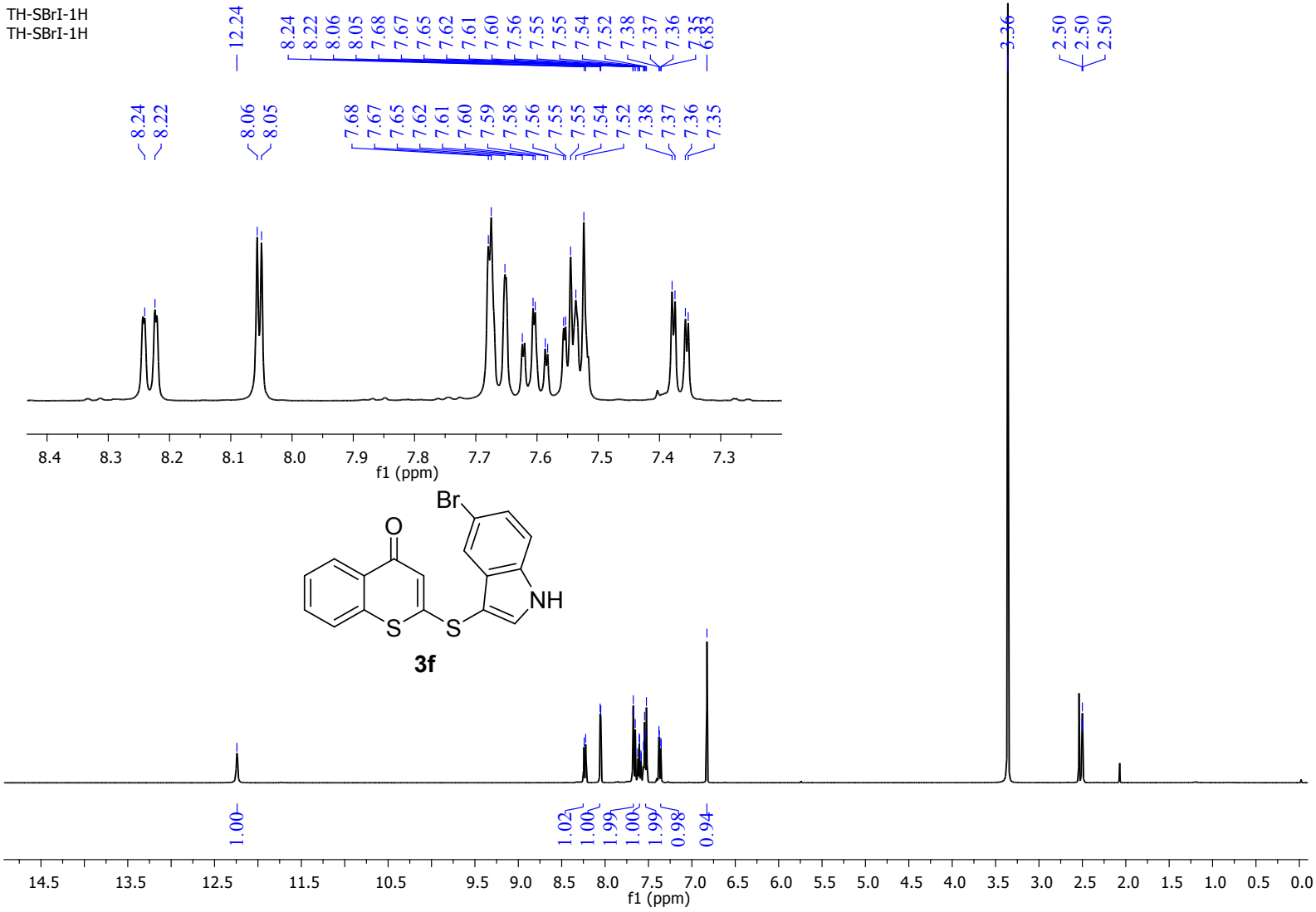
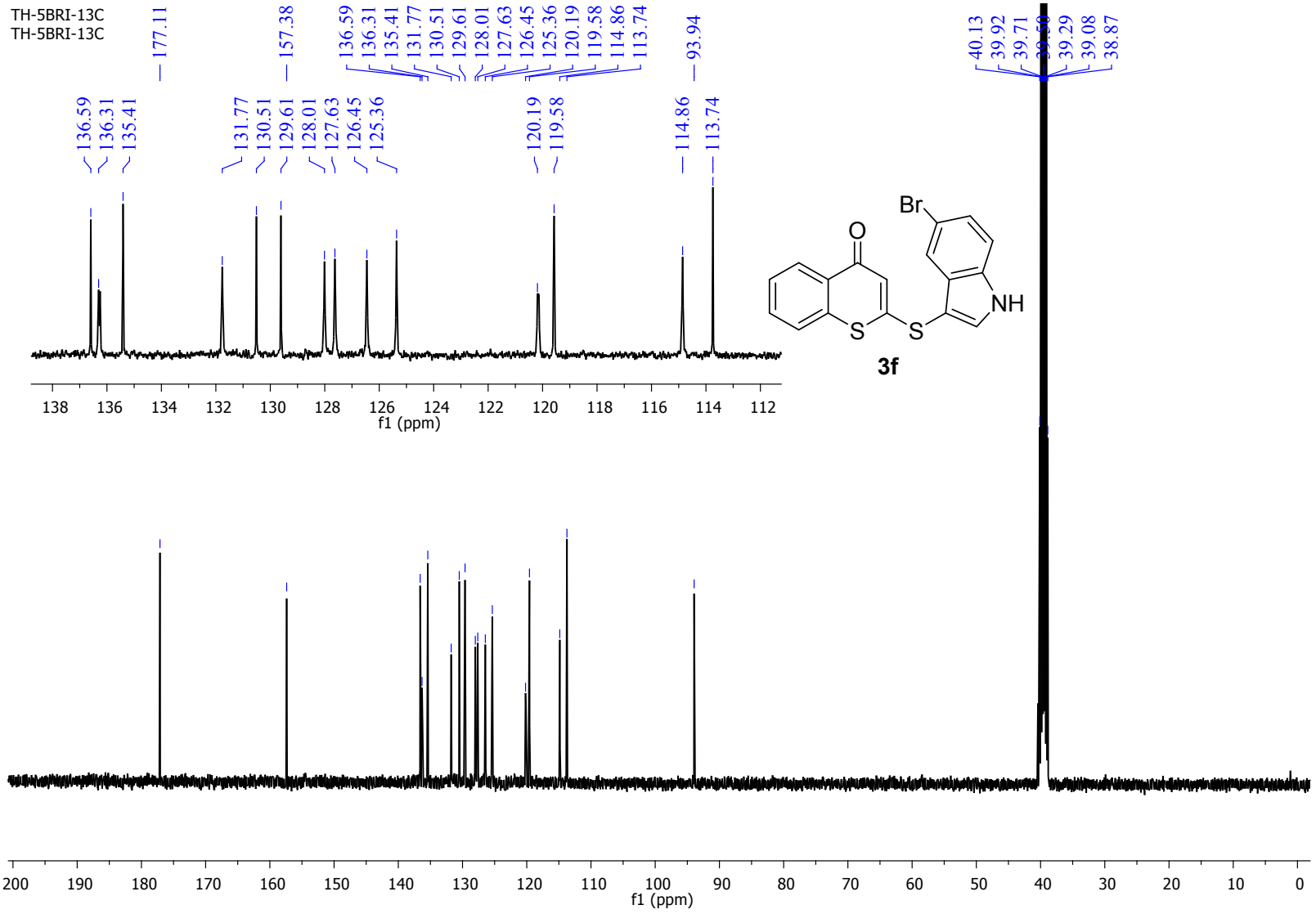


^{1}H NMR spectra of compound: 3f



^{13}C NMR spectra of compound: 3f



HRMS spectra of compound: 3f

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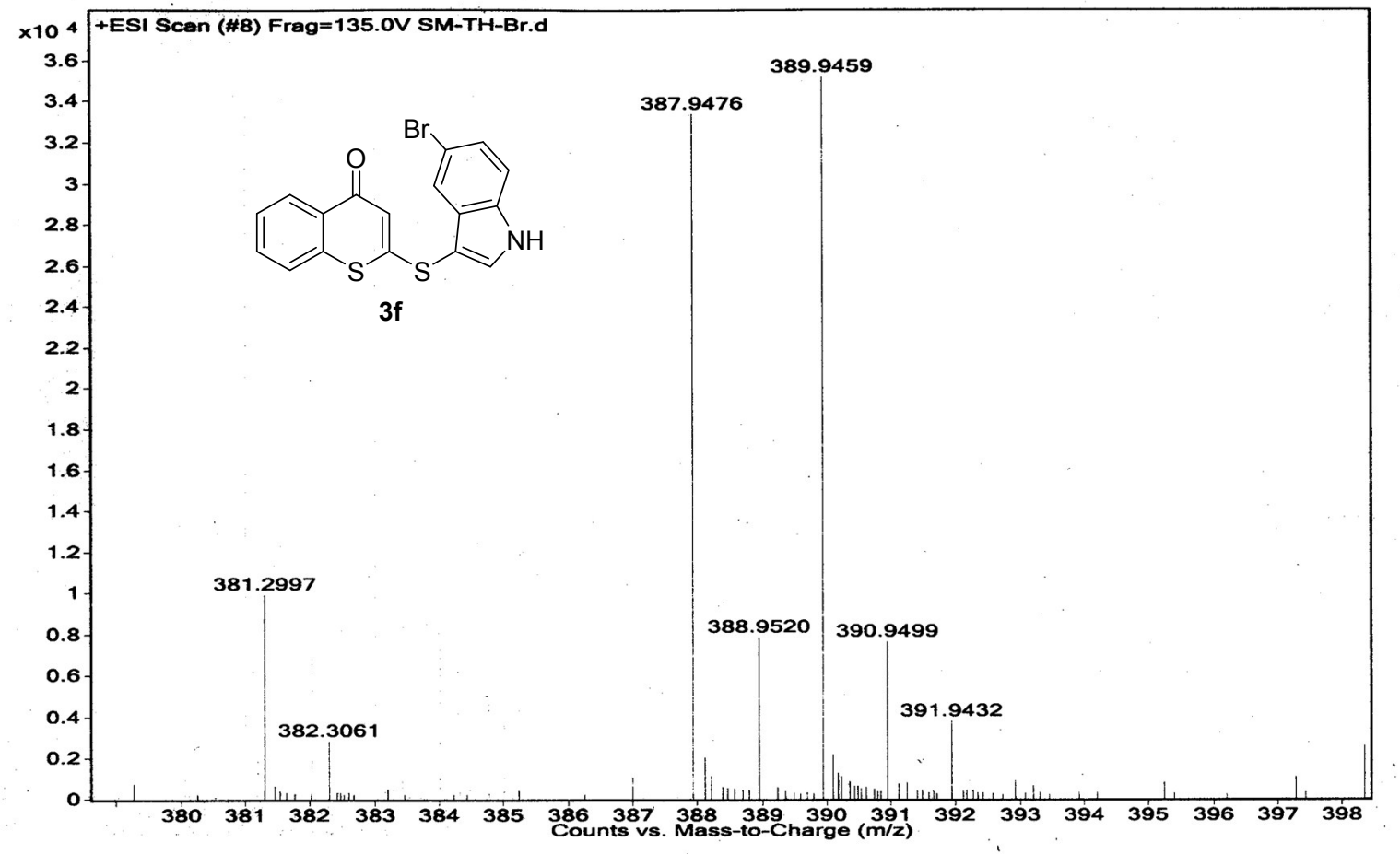
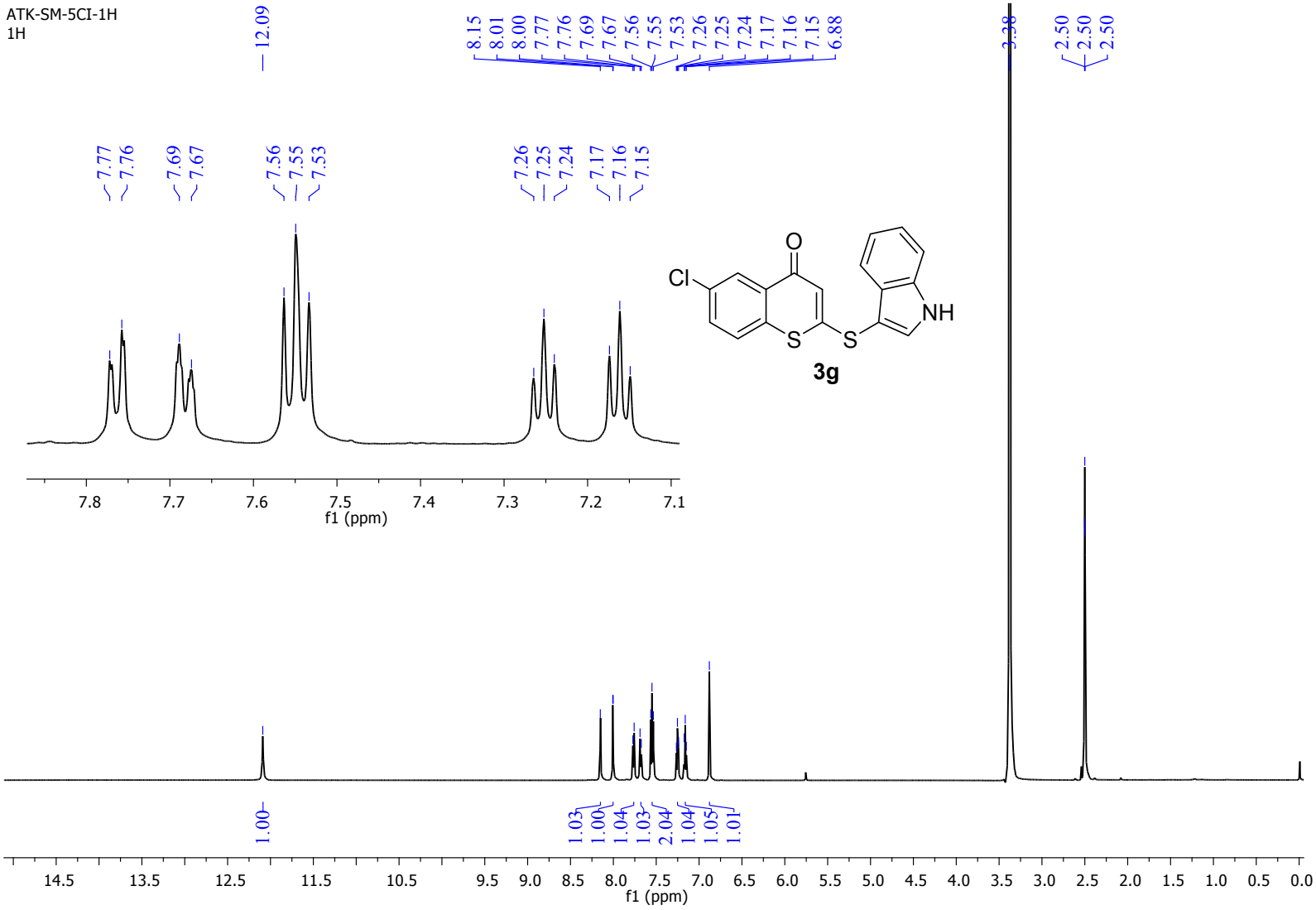
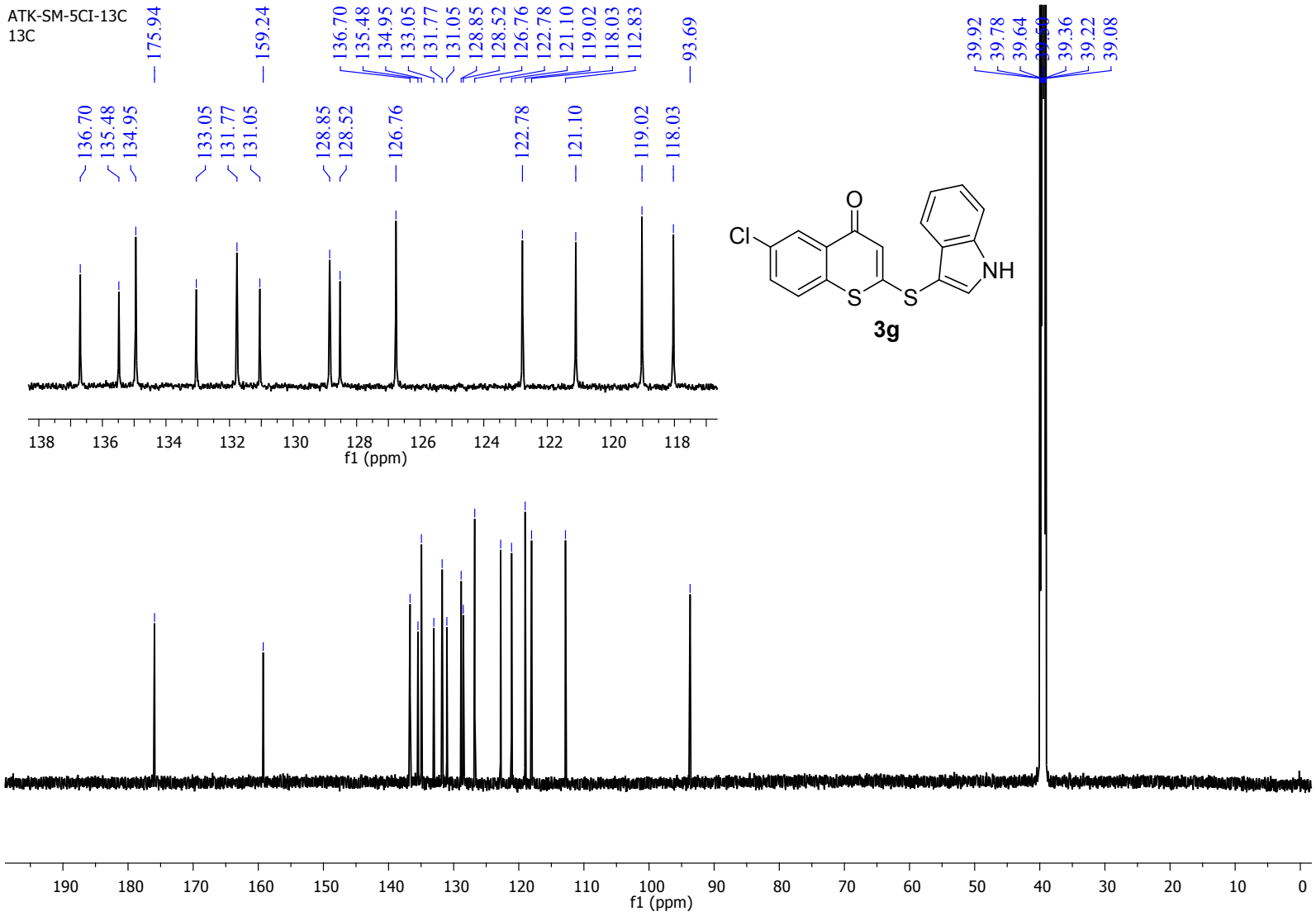


^{1}H NMR spectra of compound: 3g

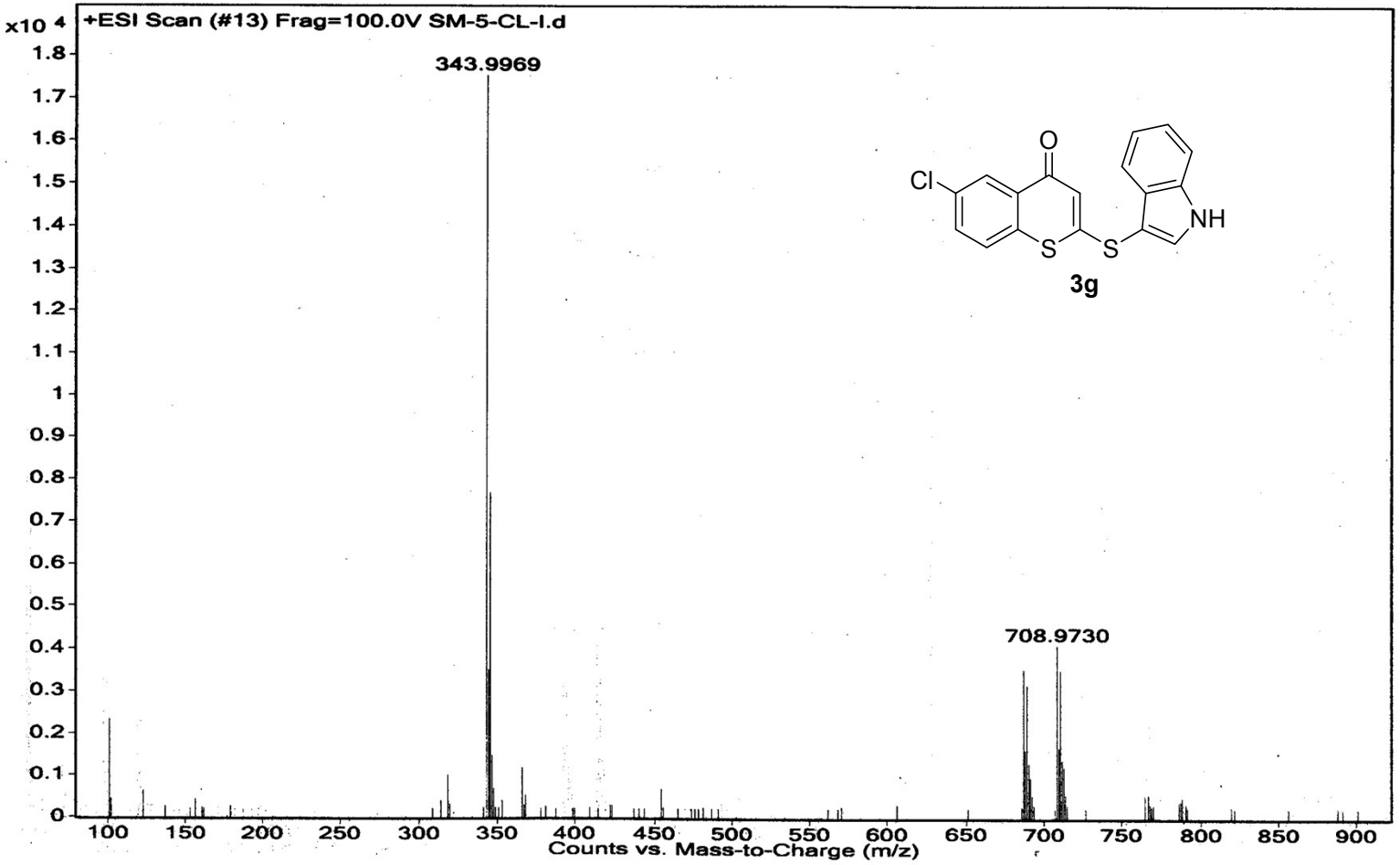


^{13}C NMR spectra of compound: 3g

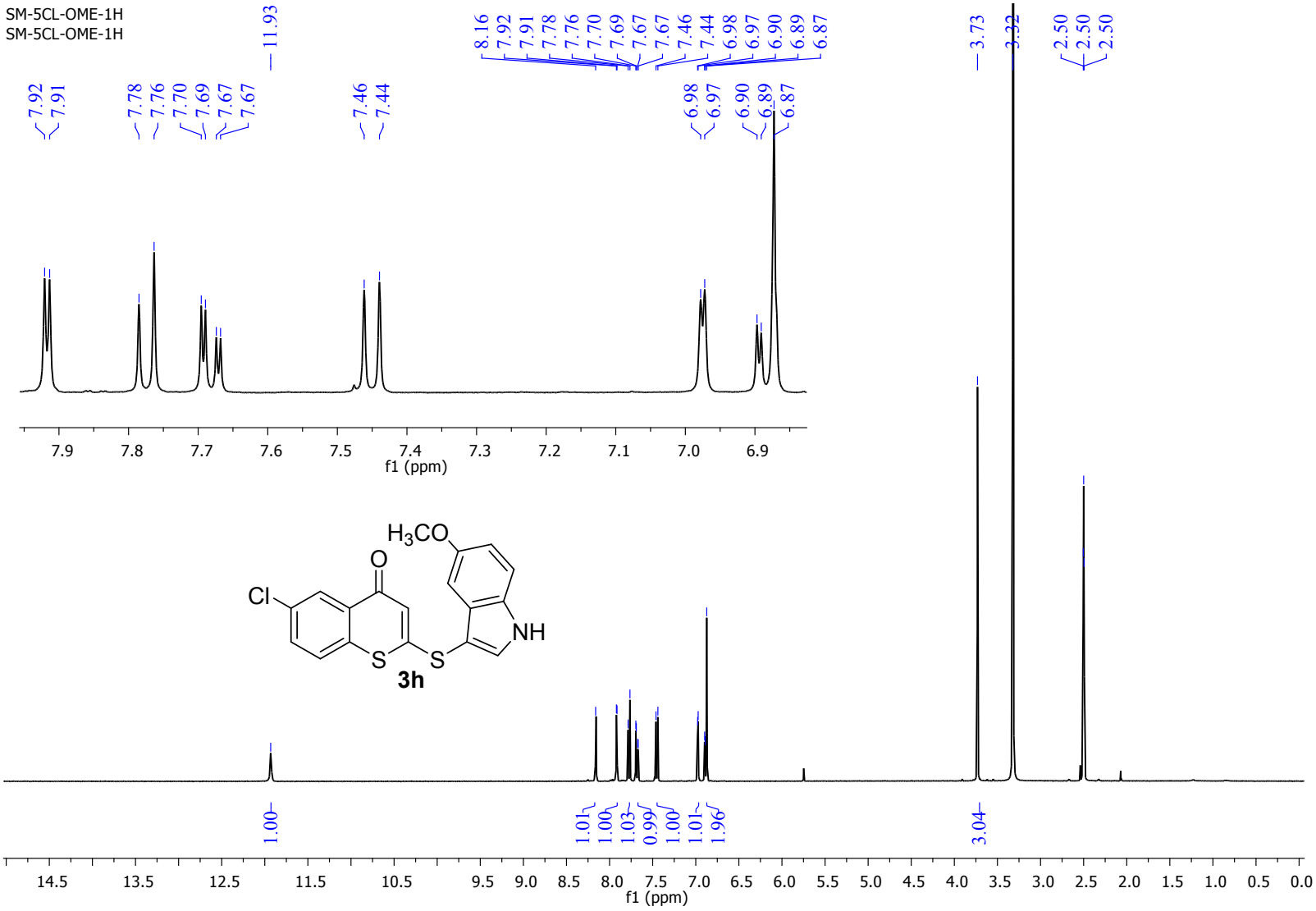


HRMS spectra of compound: 3g

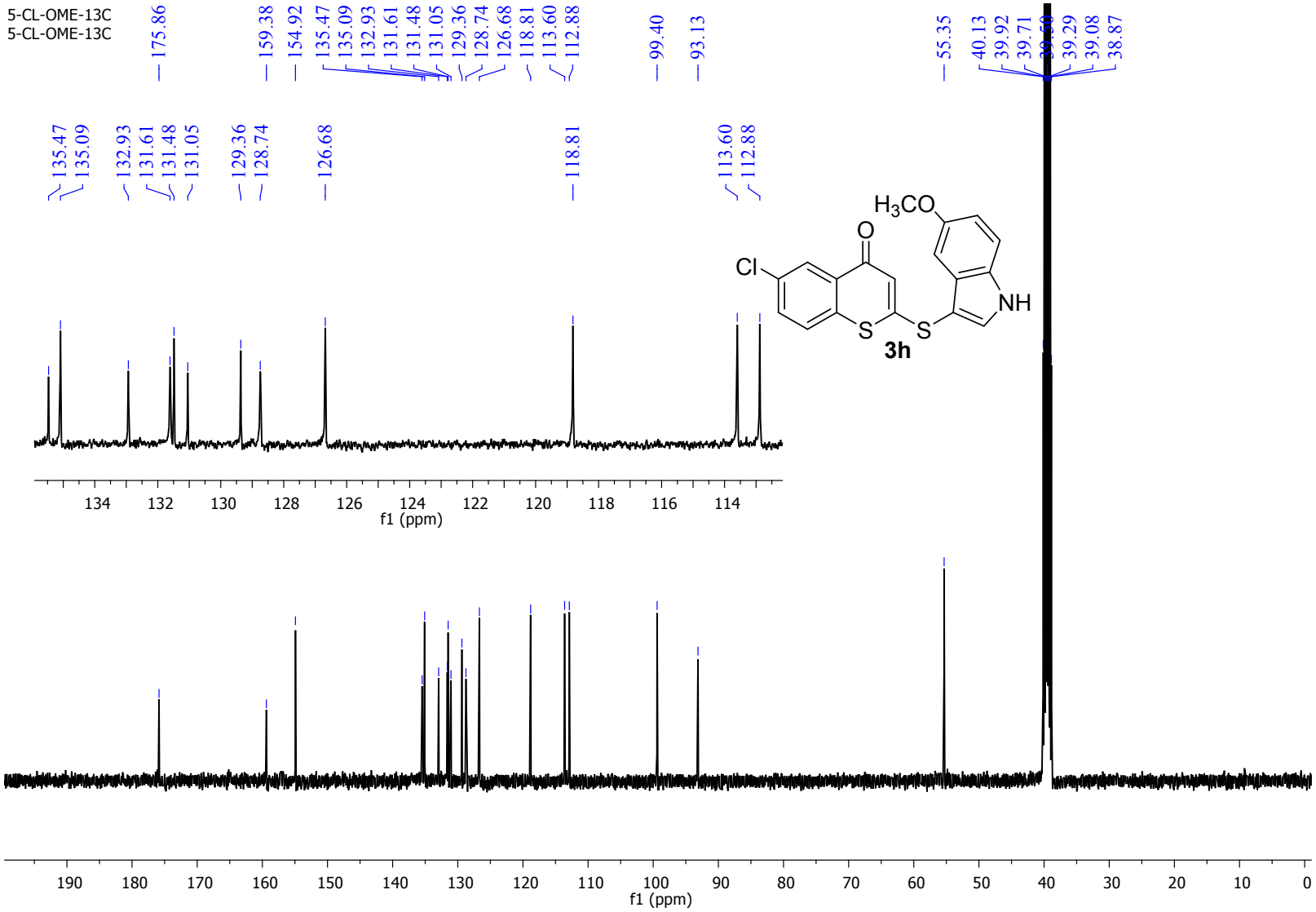
Sample Name	SM-5-CL-I	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-5-CL-I.d	**ACQ Method**		**Comment**		**Acquired Time**	7/31/2018 11:04:38 AM



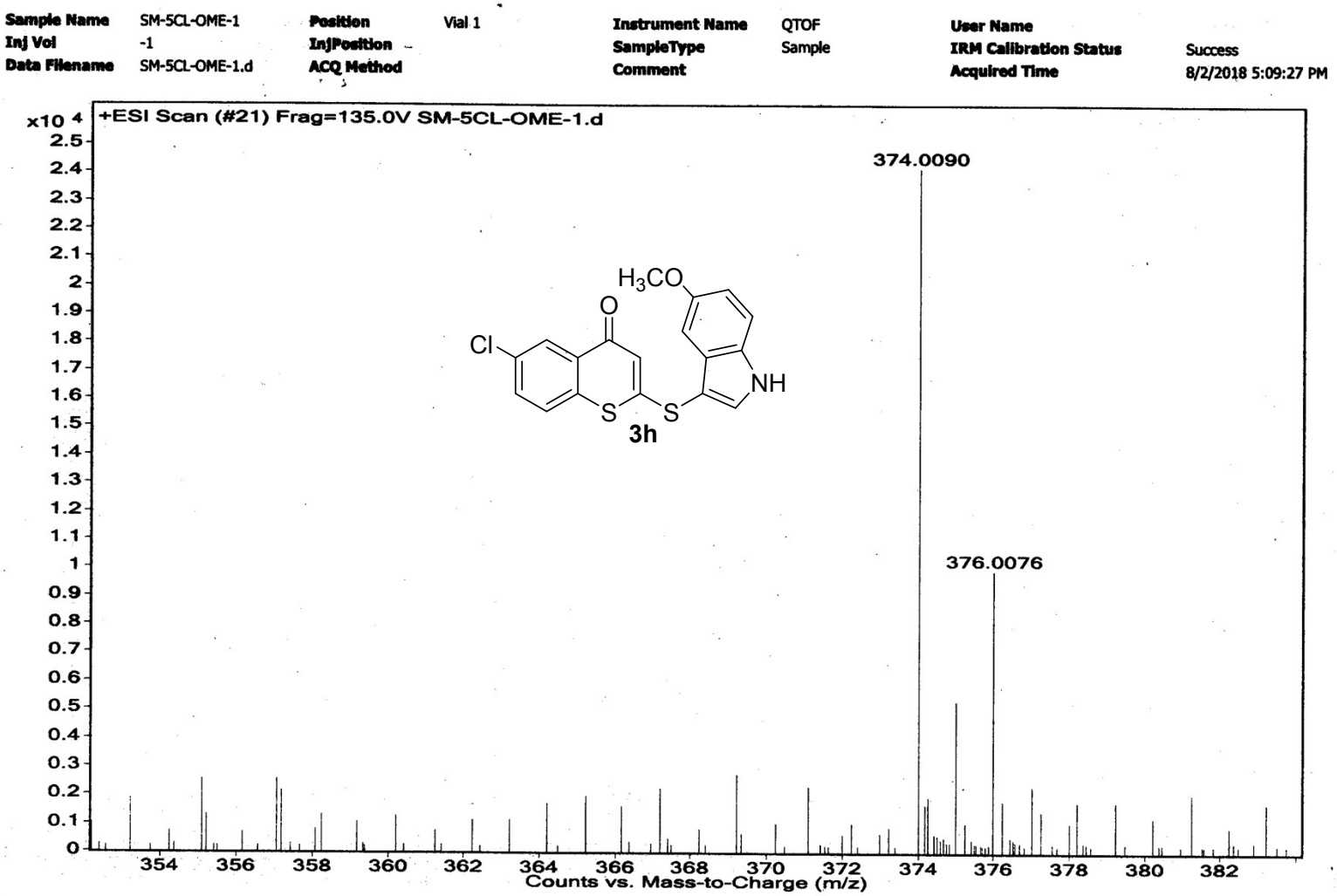
^{1}H NMR spectra of compound: 3h



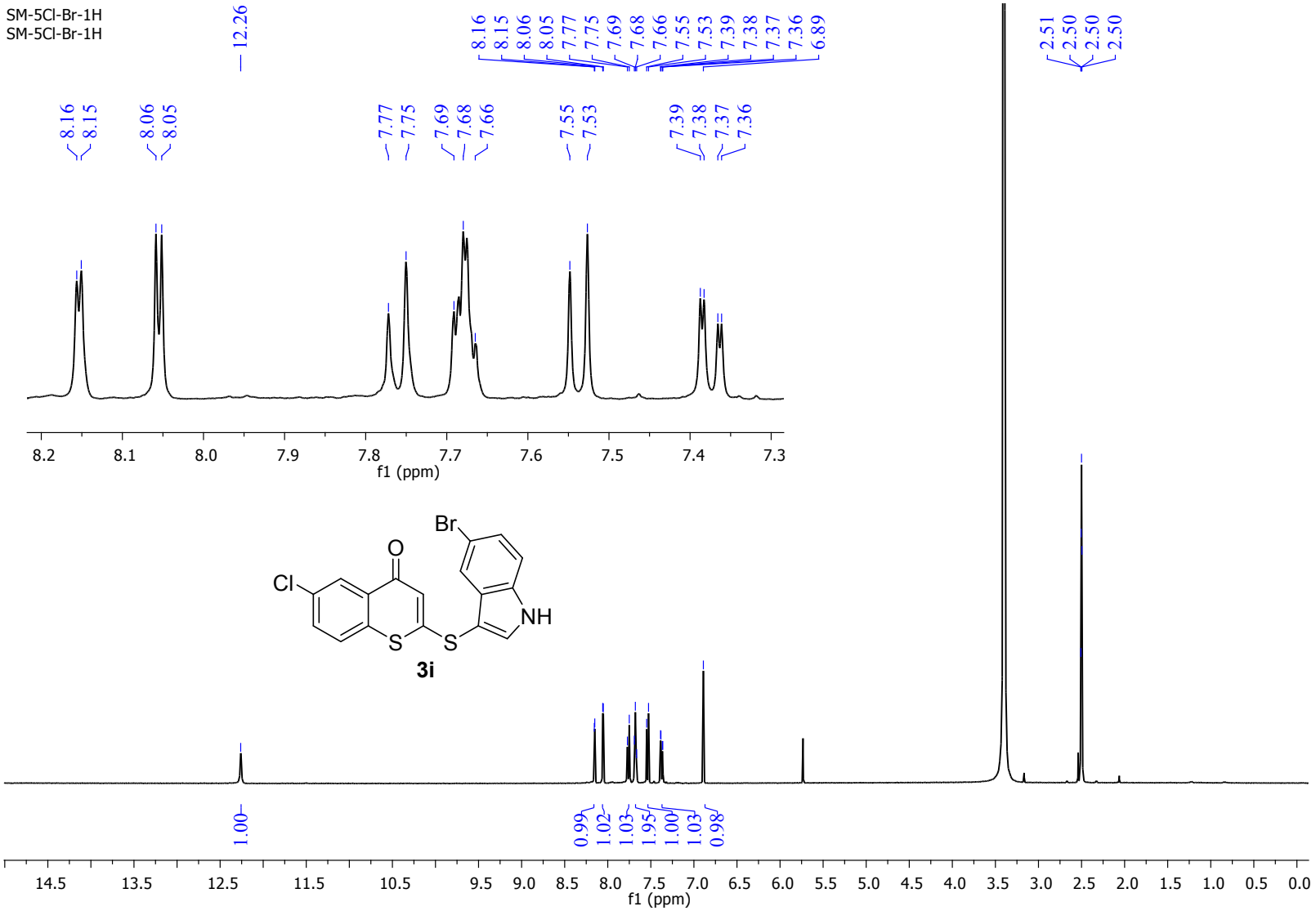
^{13}C NMR spectra of compound: 3h



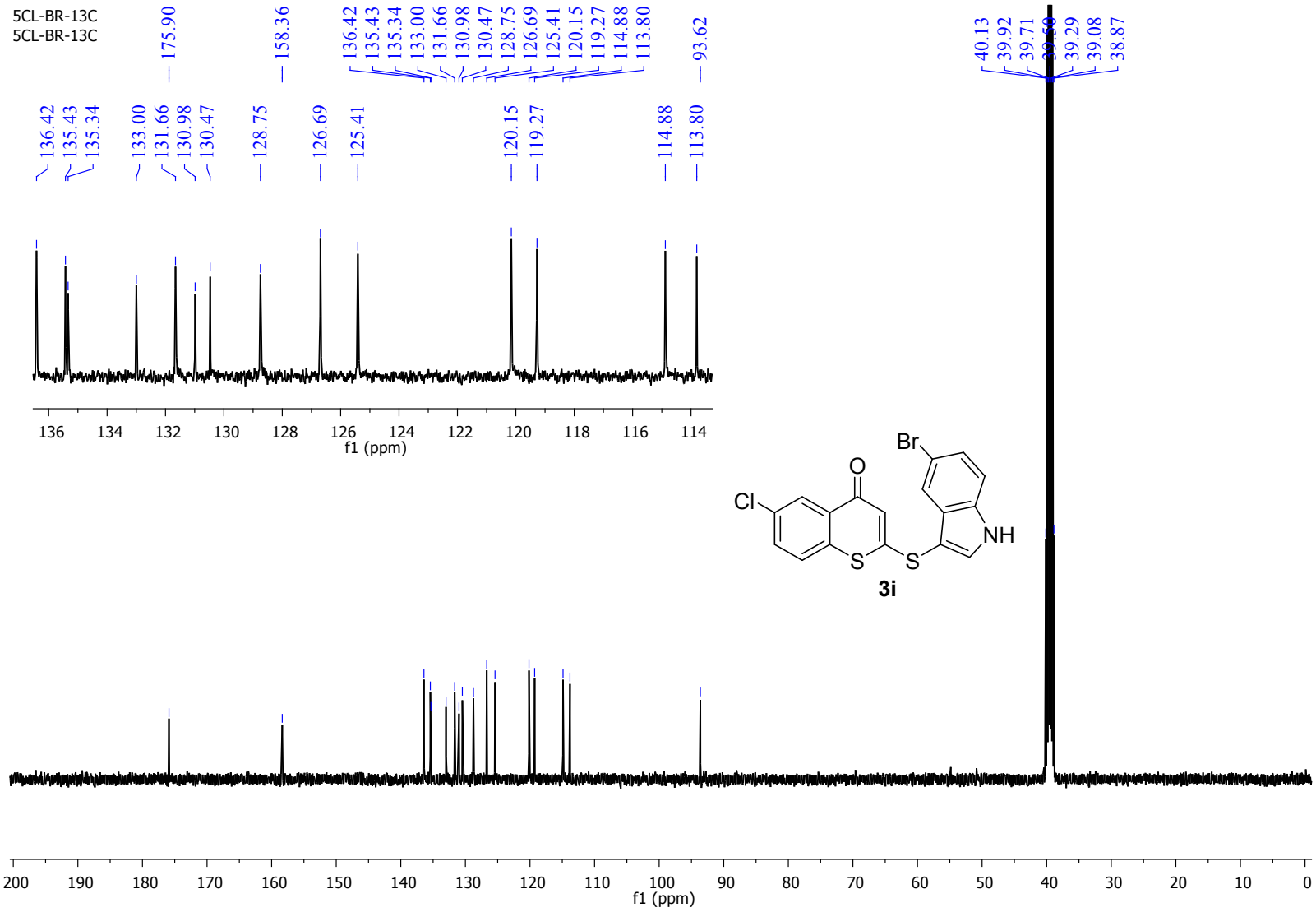
HRMS spectra of compound: 3h



^{1}H NMR spectra of compound: 3i

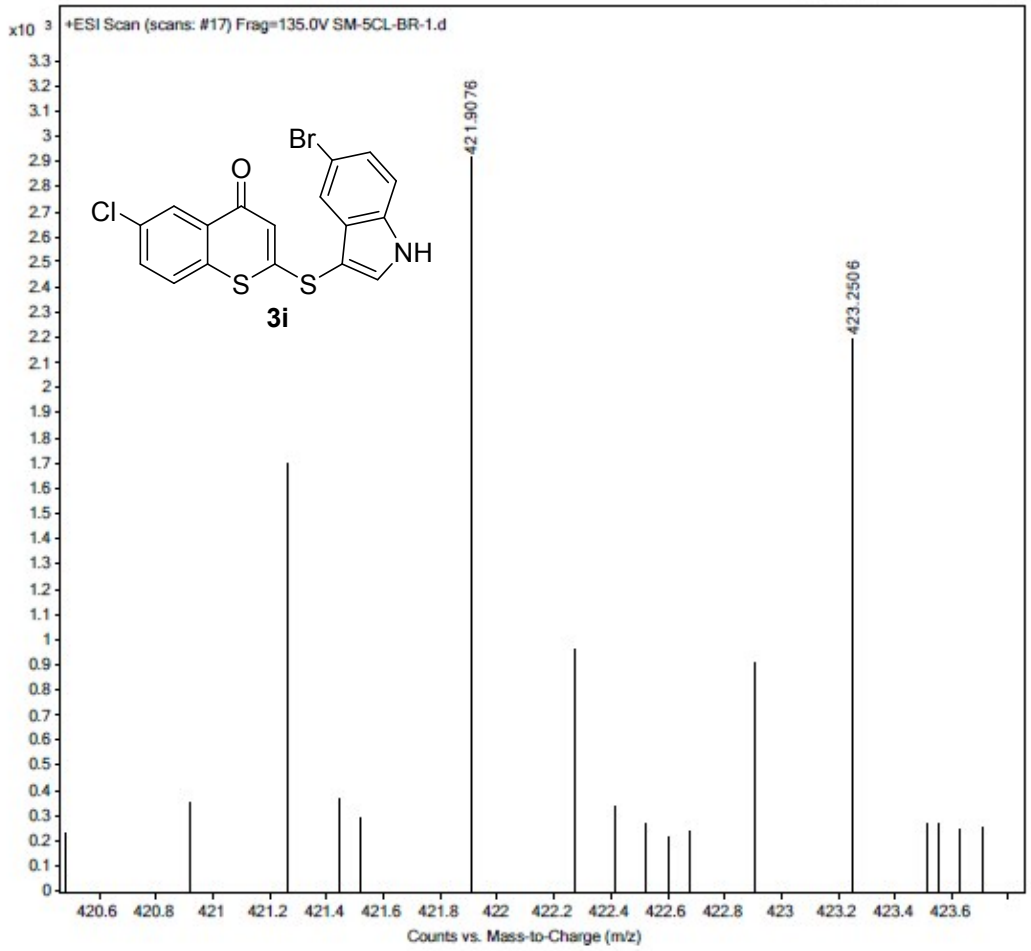


^{13}C NMR spectra of compound: 3i

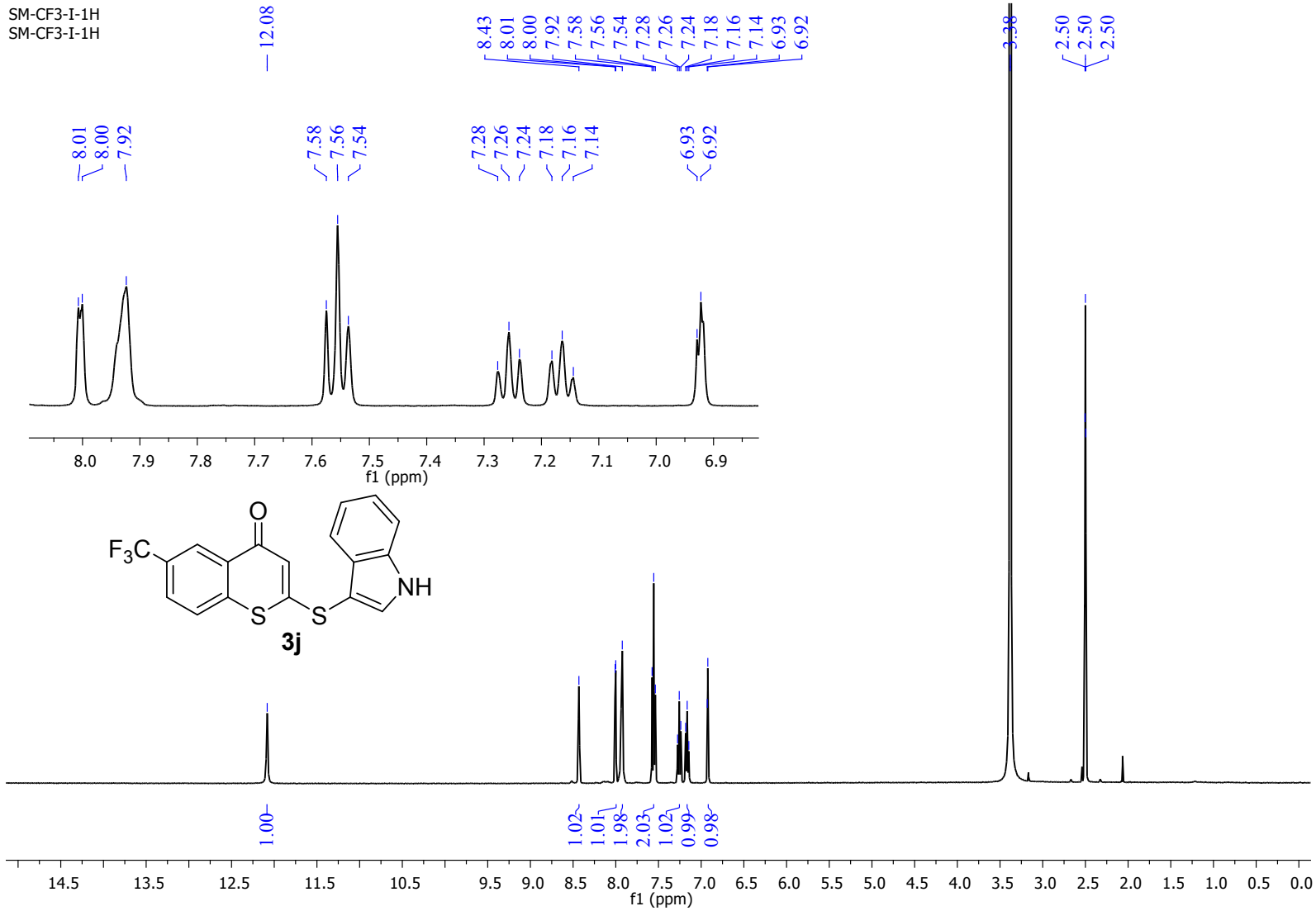


HRMS spectra of compound: 3i

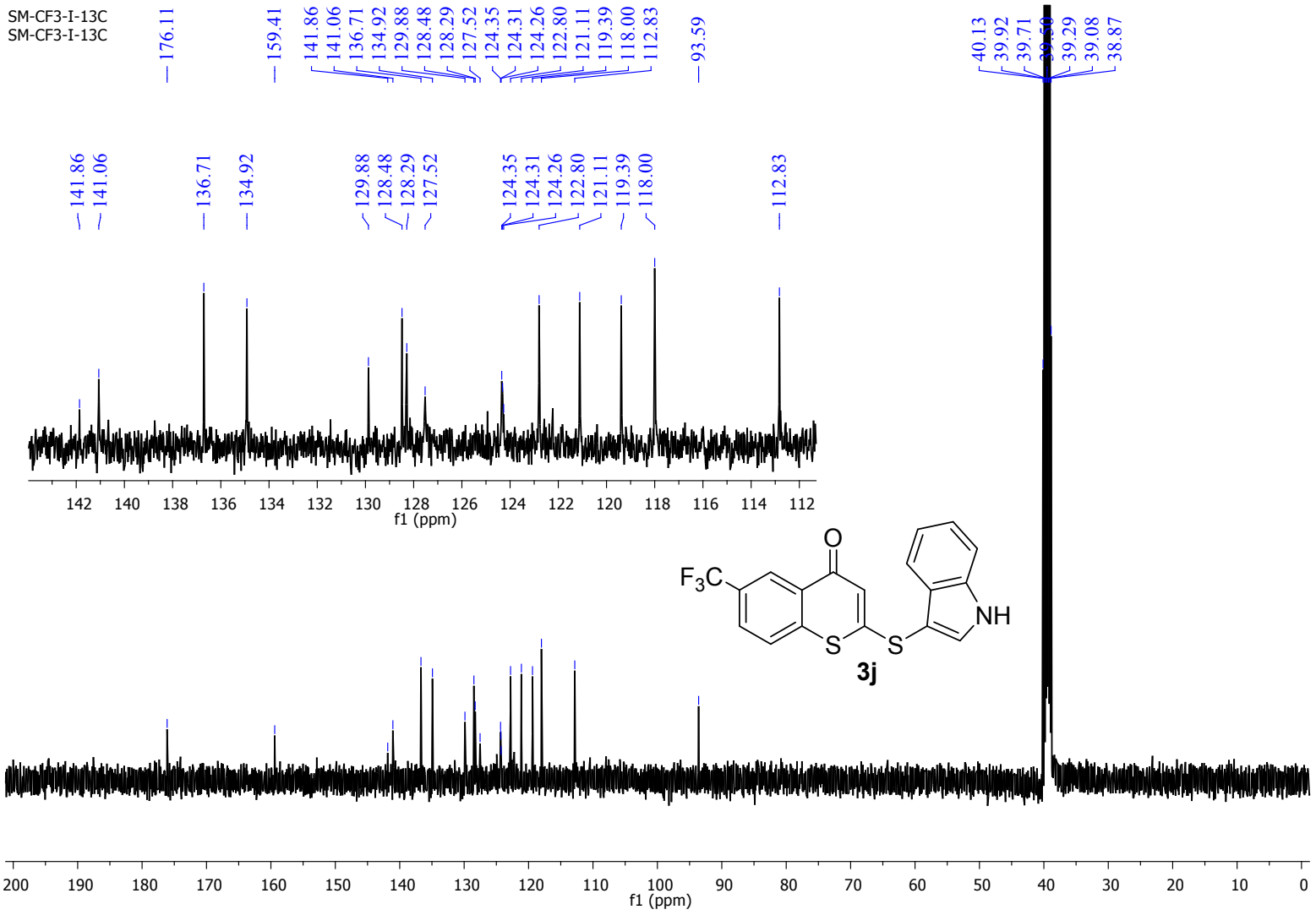
Sample Name	SM-5CL-BR-1	**Position**	Vial 1	**Instrument Name**	QTOF
User Name		**Inj Vol**	-1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	SM-5CL-BR-1.d
ACQ Method		**Comment**		**Acquired Time**	02-08-2018 17:07:37 (UTC+05:30)



^{1}H NMR spectra of compound: 3j

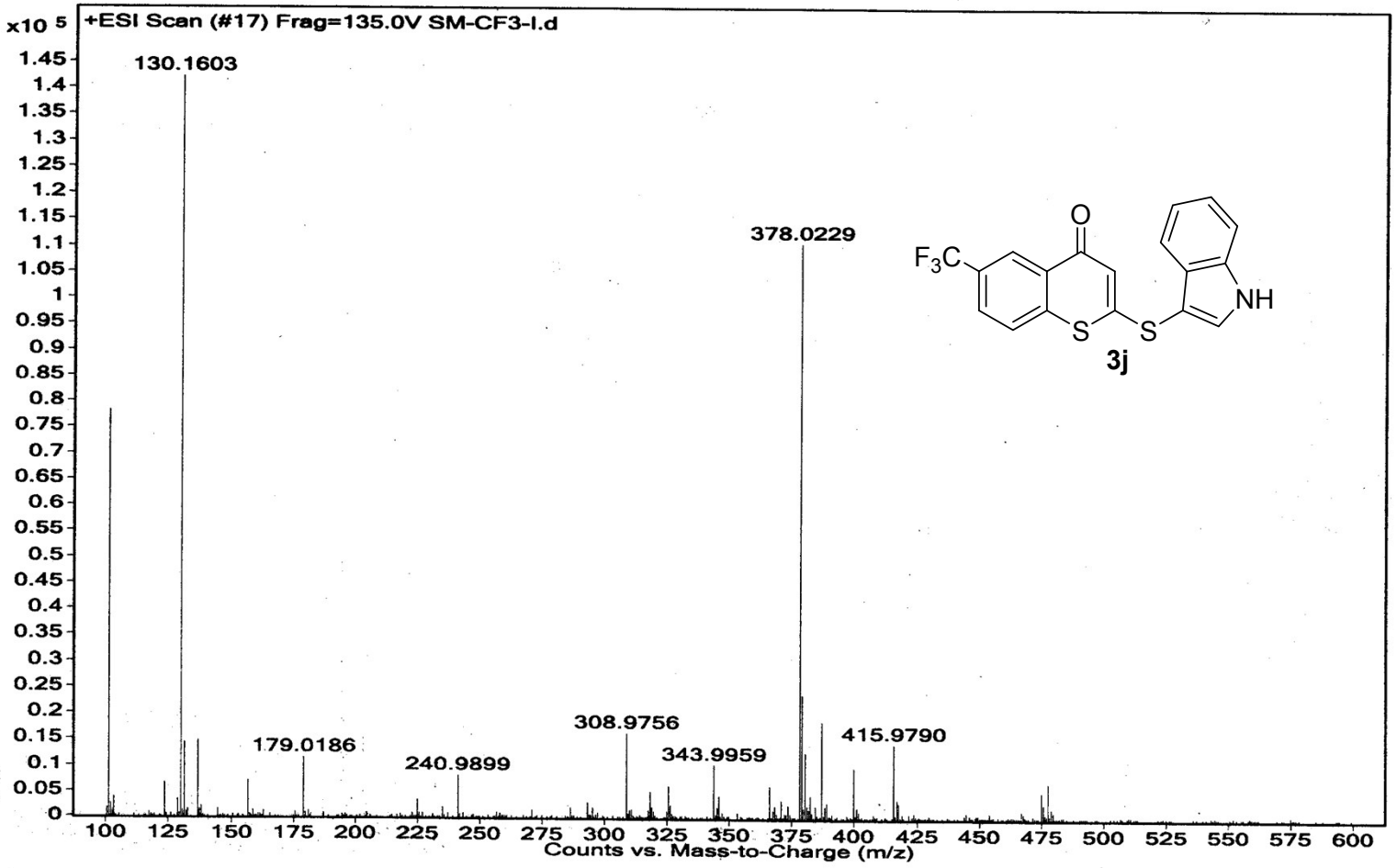


^{13}C NMR spectra of compound: 3j

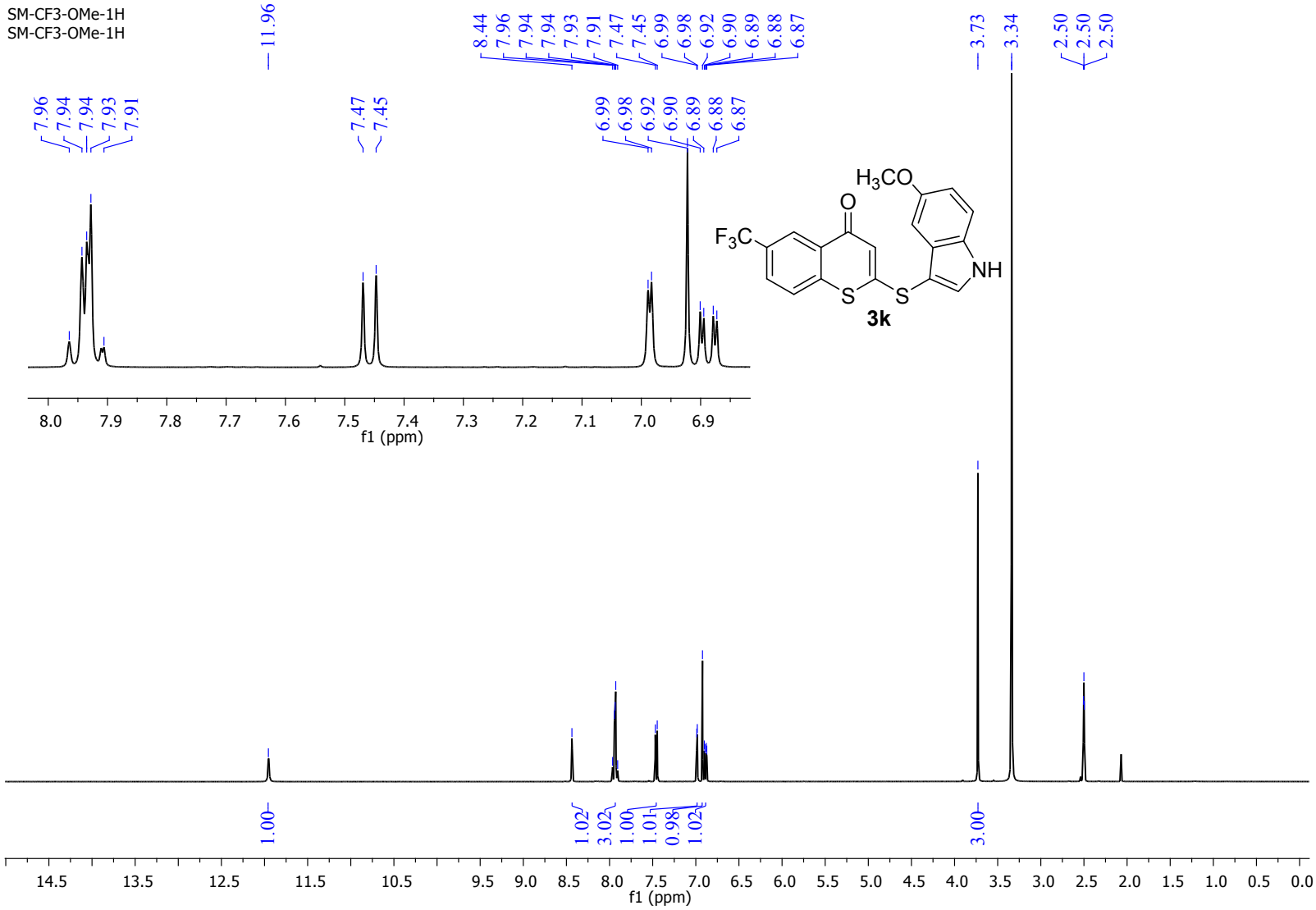


HRMS spectra of compound: 3j

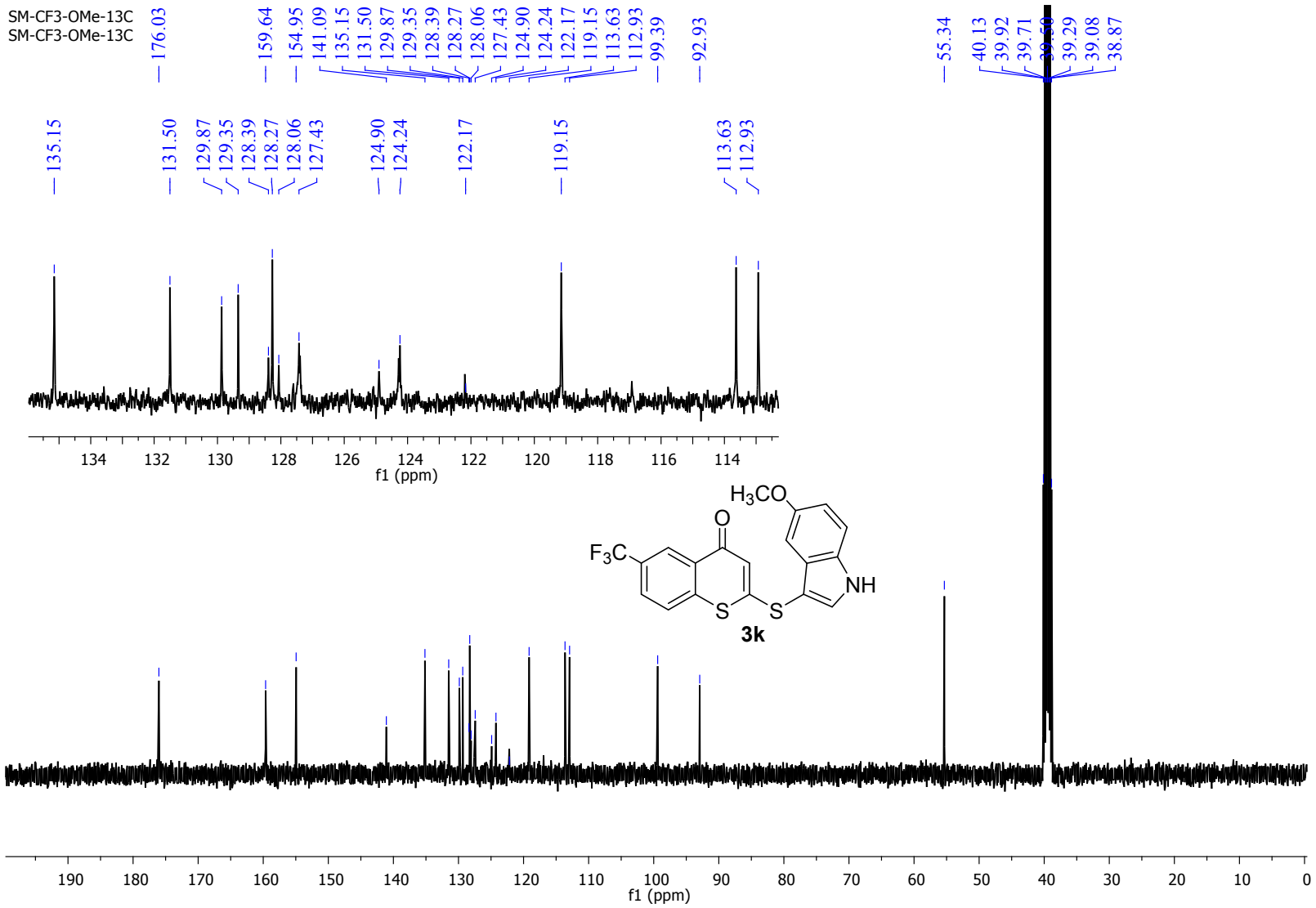
Sample Name	SM-CF3-I	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-CF3-I.d	**ACQ Method**		**Comment**		**Acquired Time**	7/26/2018 4:07:19 PM



^{1}H NMR spectra of compound: 3k

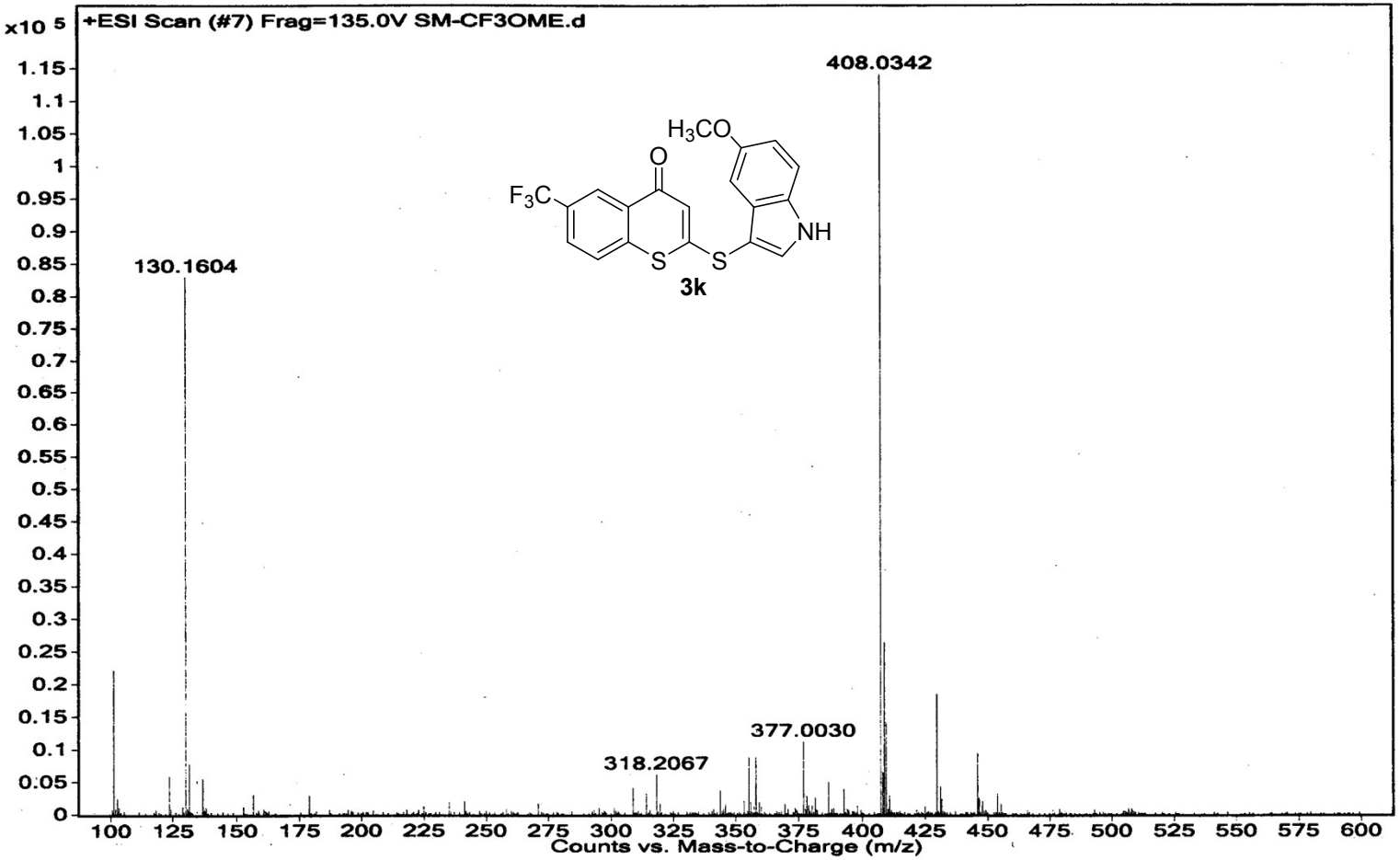


^{13}C NMR spectra of compound: 3k

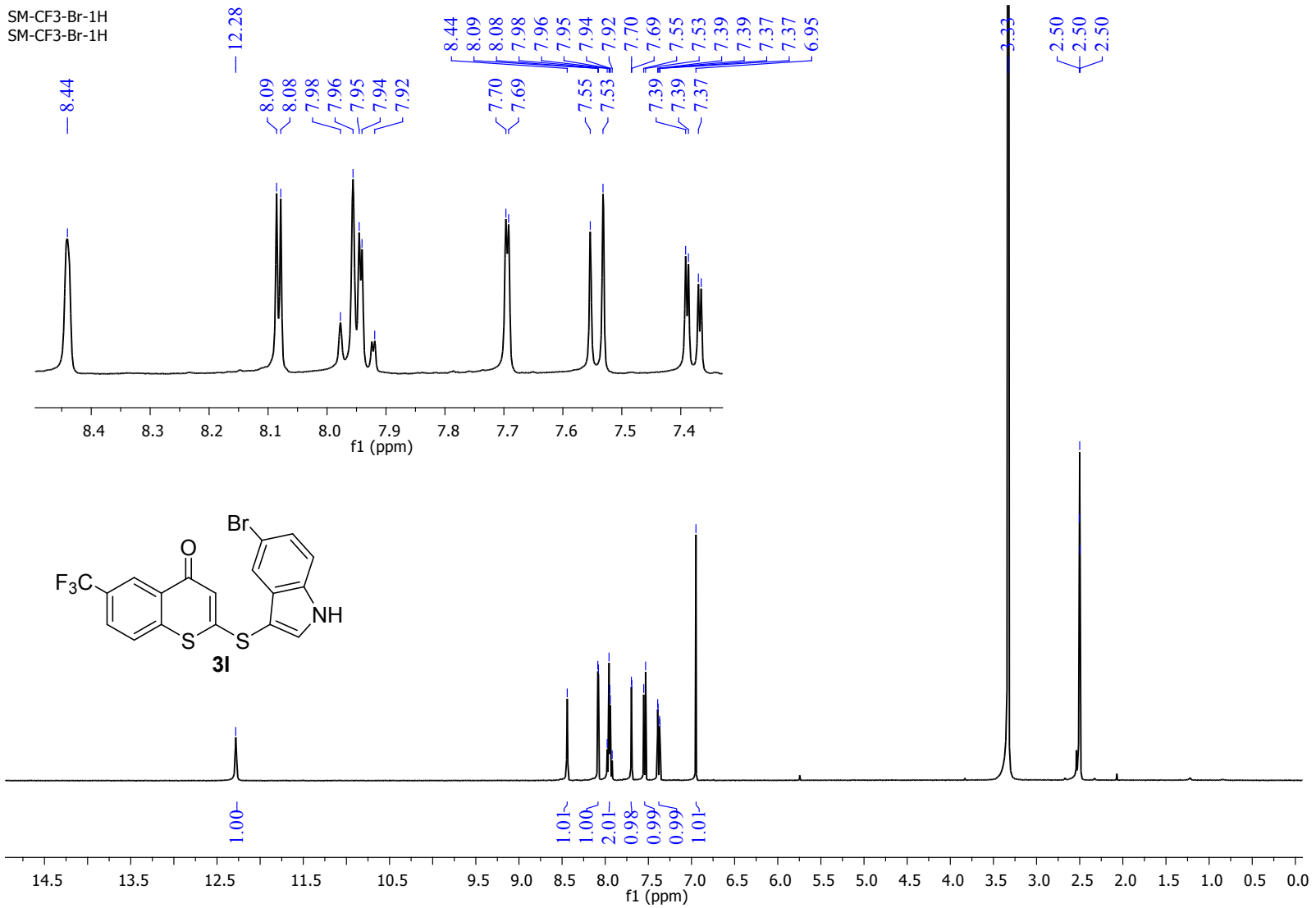


HRMS spectra of compound: 3k

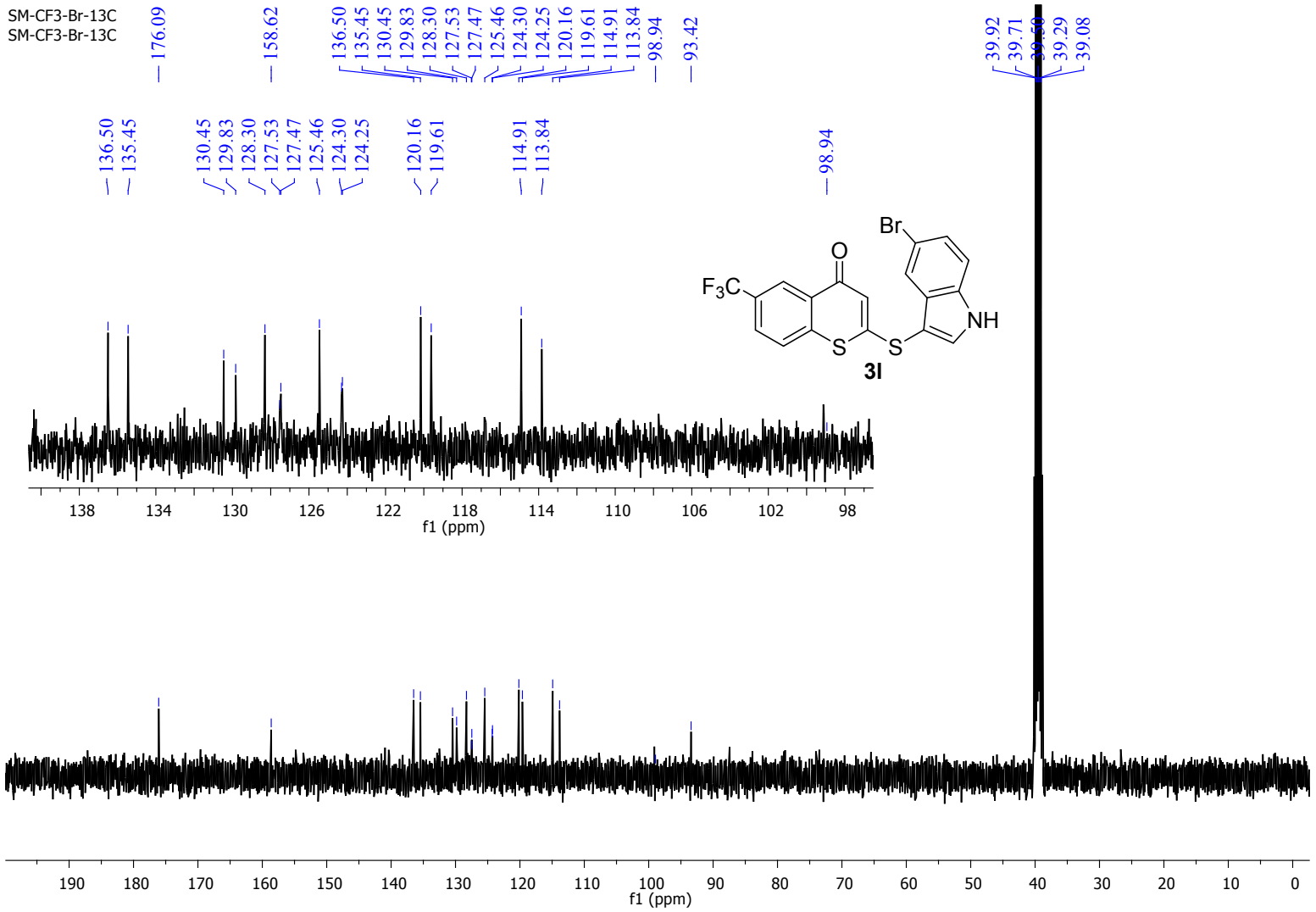
Sample Name	SM-CF3OME	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-CF3OME.d	**ACQ Method**		**Comment**		**Acquired Time**	7/26/2018 4:12:02 PM



^{1}H NMR spectra of compound: 3l

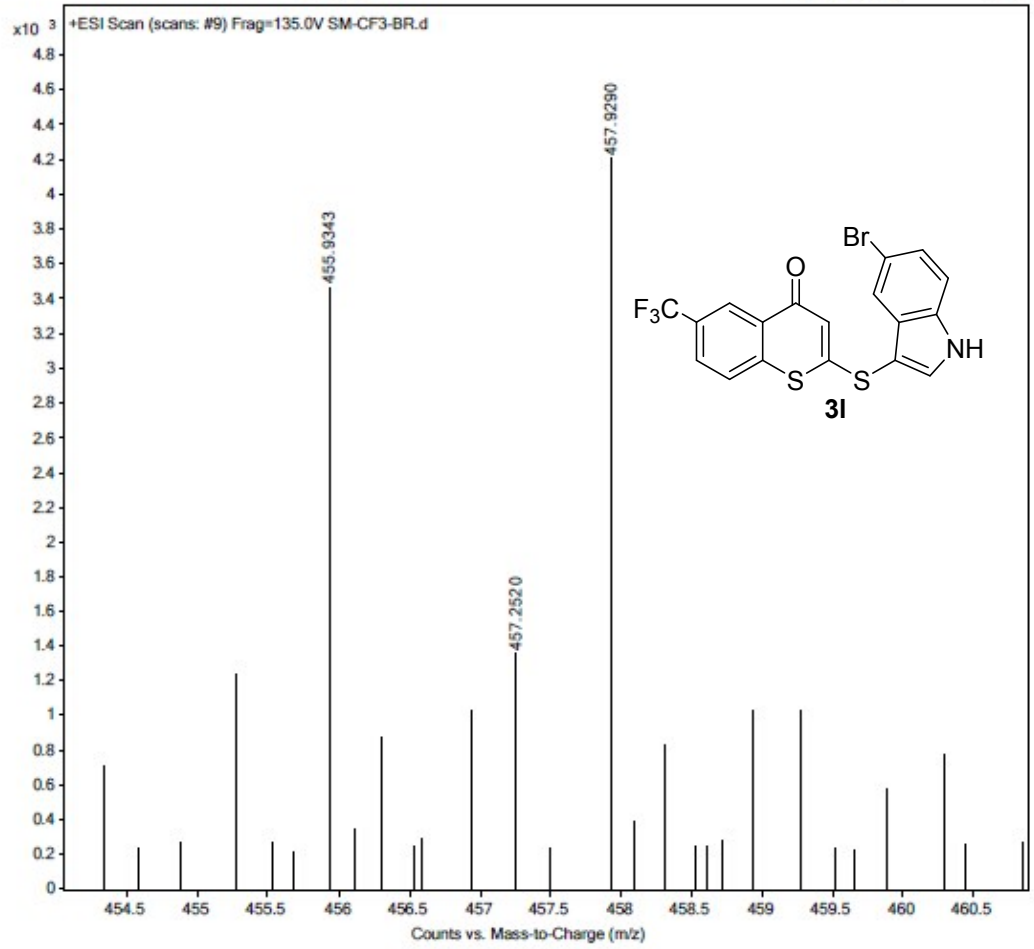


^{13}C NMR spectra of compound: 3l

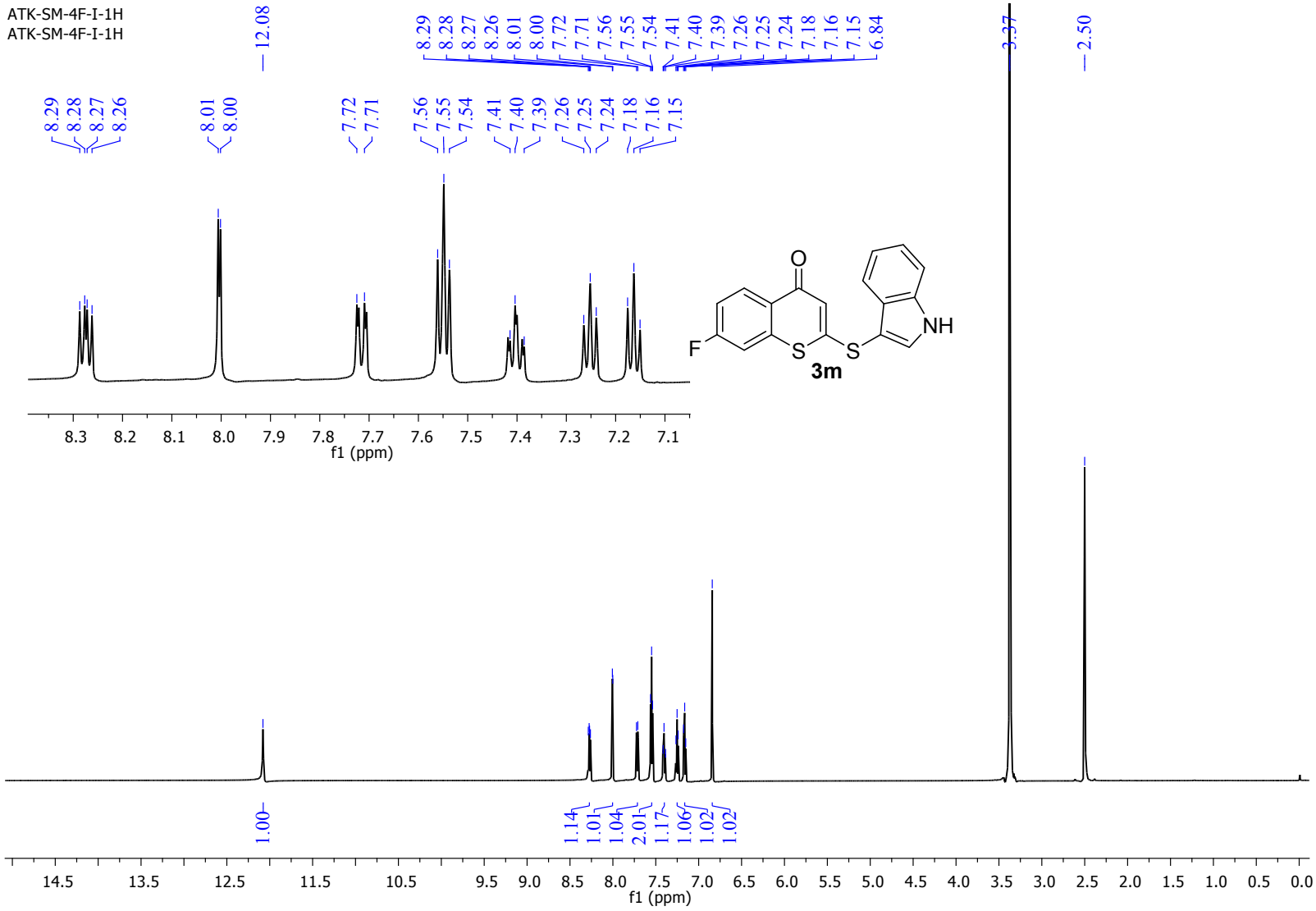


HRMS spectra of compound: 3l

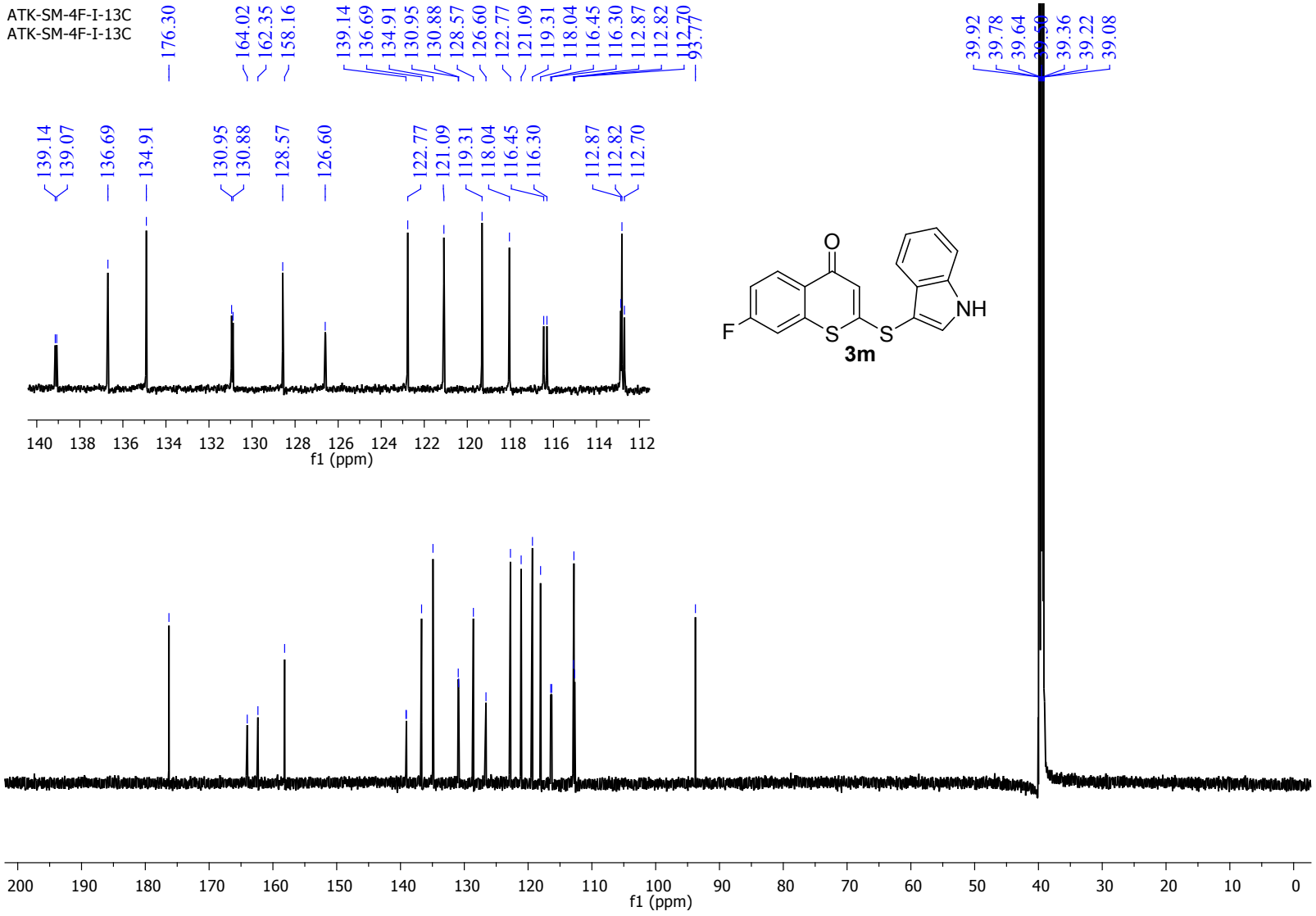
Sample Name	SM-CF3-BR	**Position**	Vial 1	**Instrument Name**	QTOF
User Name		**Inj Vol**	-1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	SM-CF3-BR.d
ACQ Method		**Comment**		**Acquired Time**	06-08-2018 10:40:30 (UTC+05:30)



^{1}H NMR spectra of compound: 3m

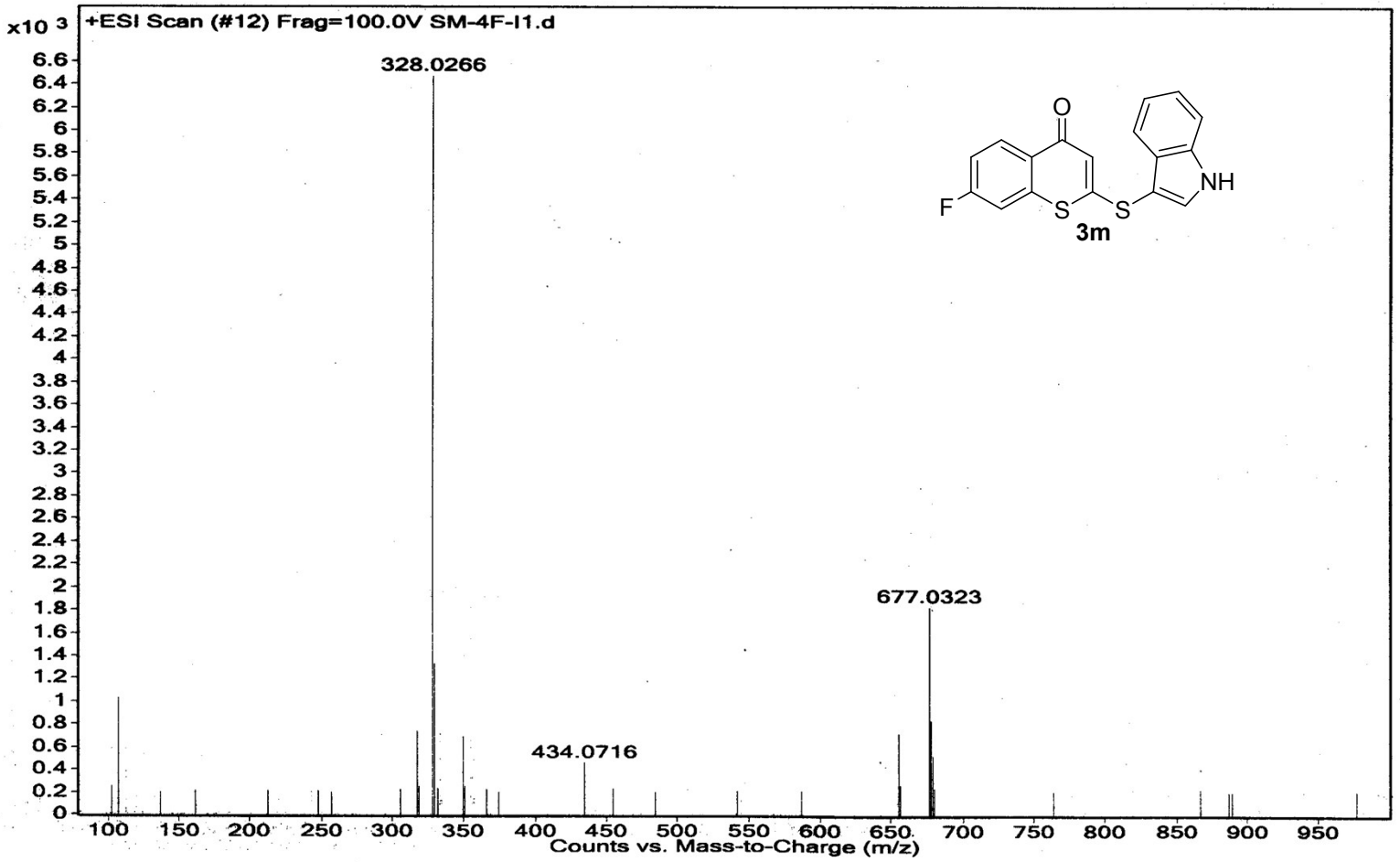


^{13}C NMR spectra of compound: 3m

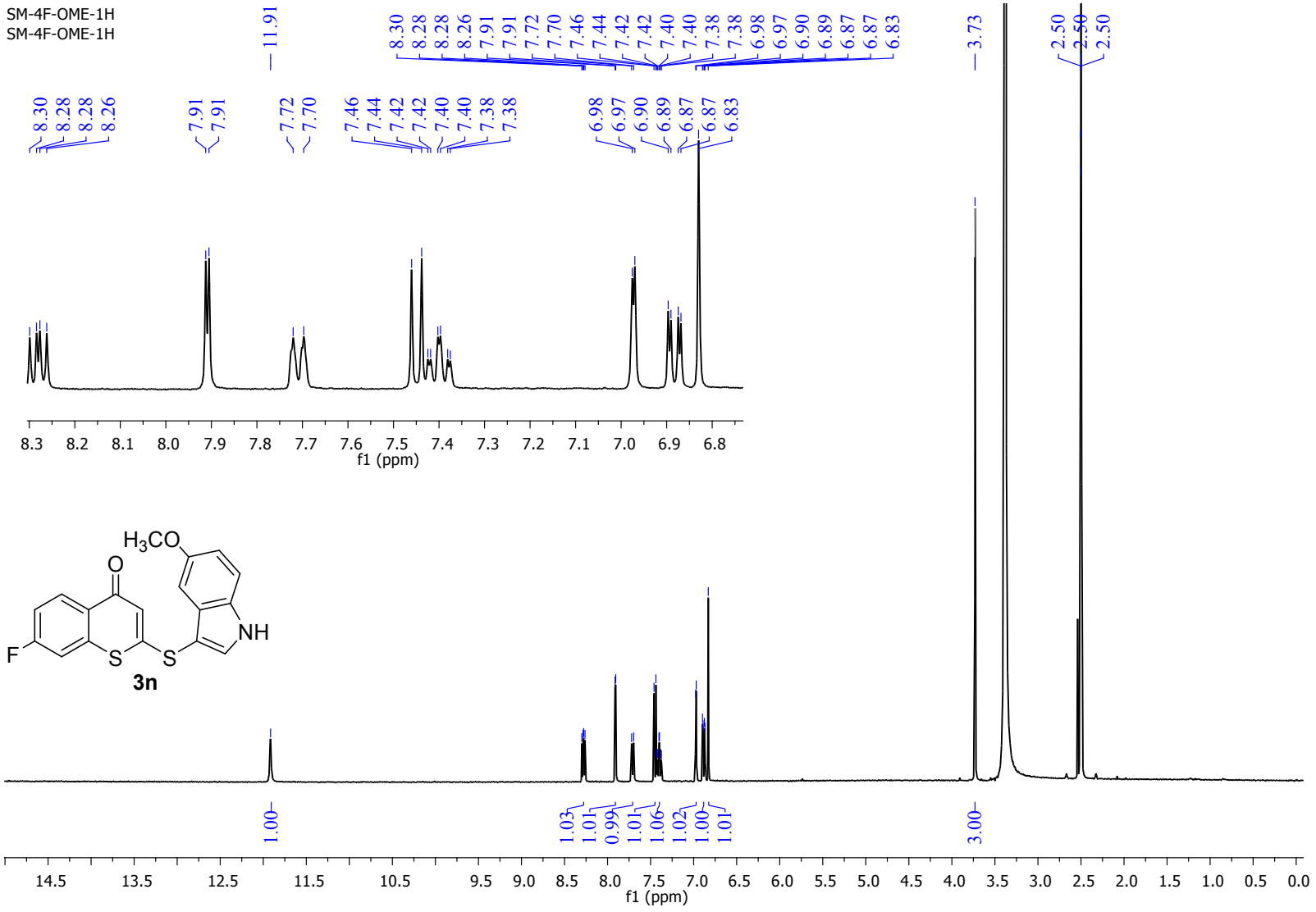


HRMS spectra of compound: 3m

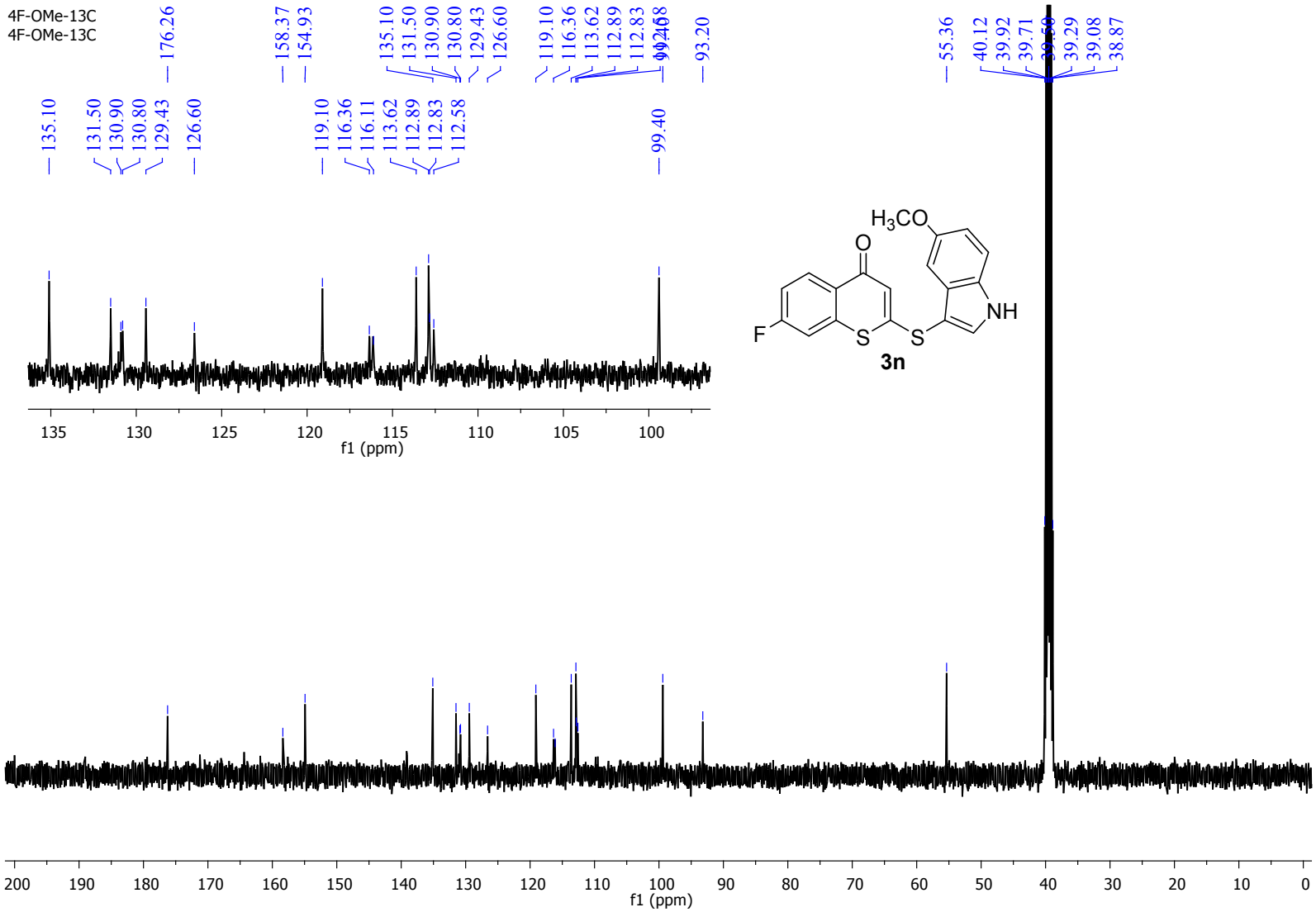
Sample Name	SM-4F-I1	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-4F-I1.d	**ACQ Method**		**Comment**		**Acquired Time**	7/31/2018 10:53:52 AM



^{1}H NMR spectra of compound: 3n

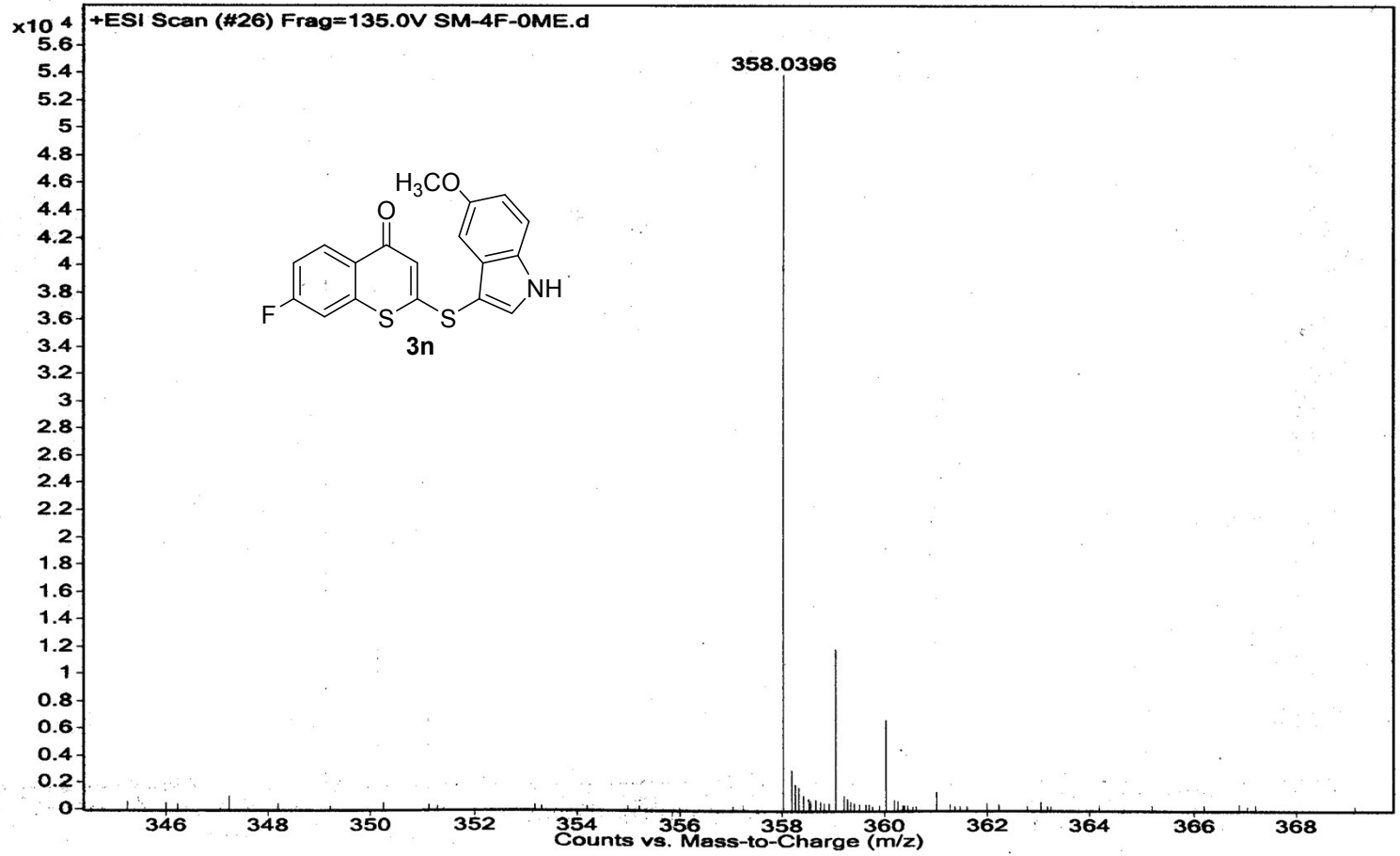


^{13}C NMR spectra of compound: 3n

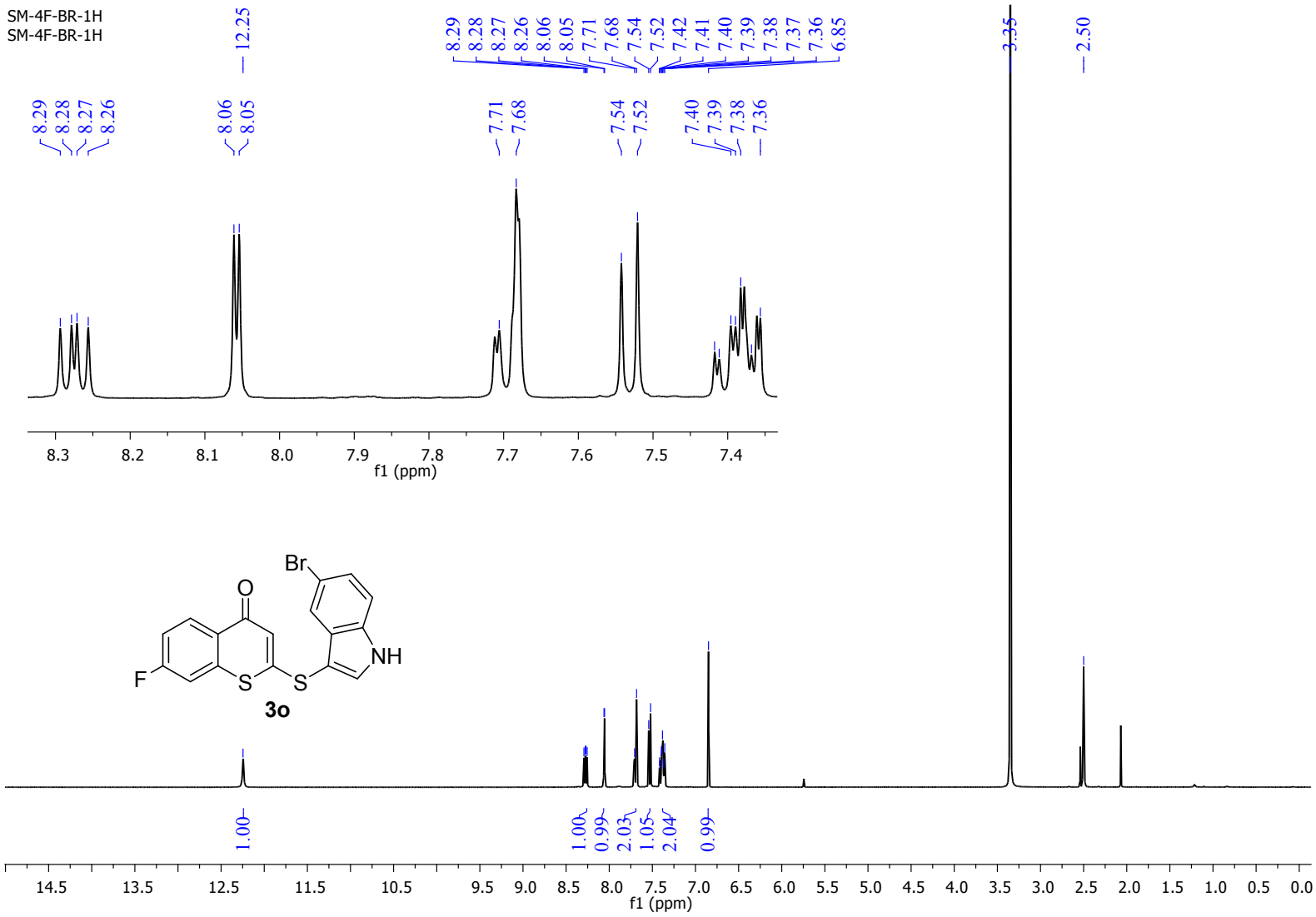


HRMS spectra of compound: 3n

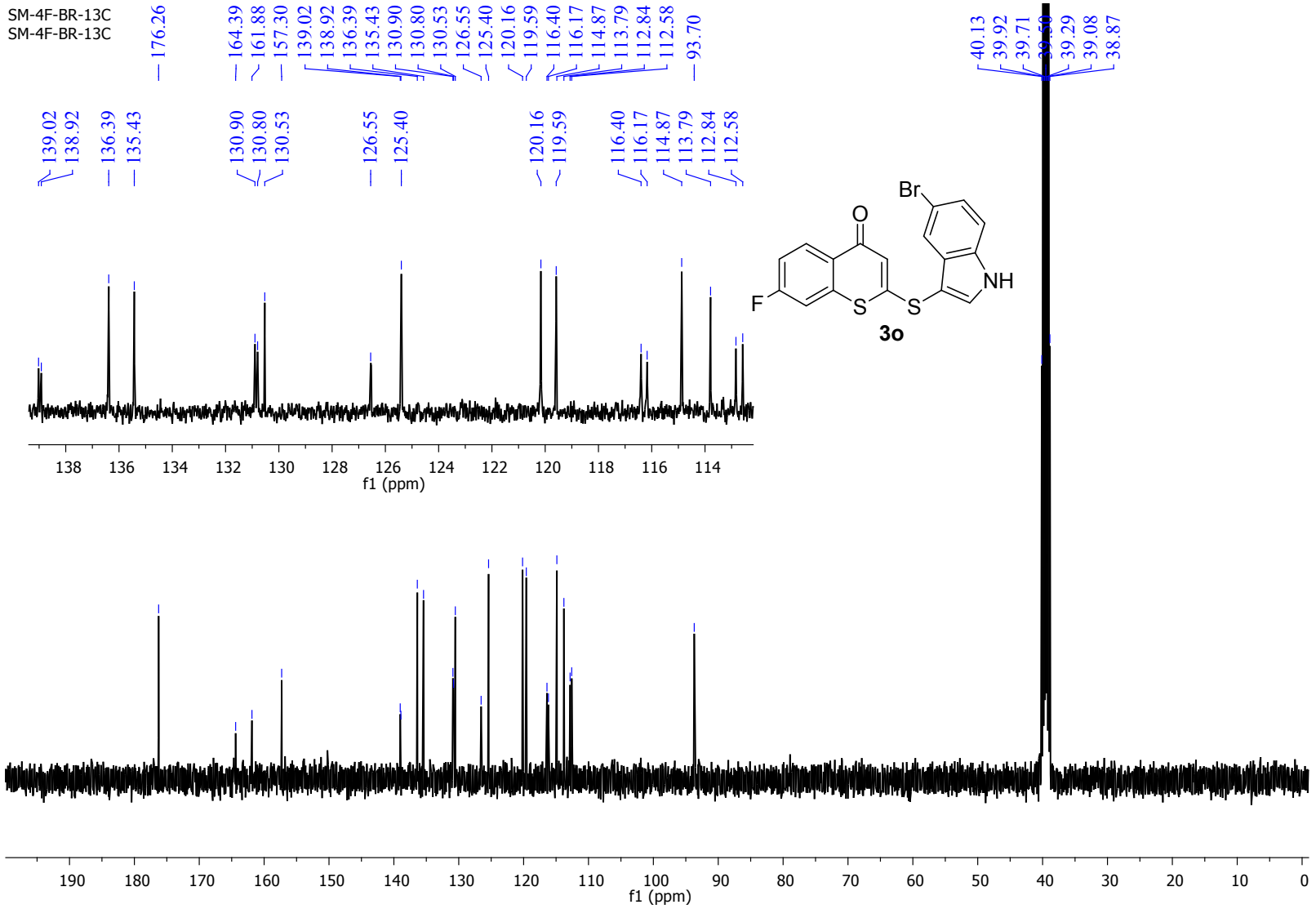
Sample Name	SM-4F-0ME	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-4F-0ME.d	**ACQ Method**		**Comment**		**Acquired Time**	7/27/2018 12:04:45 PM



^{1}H NMR spectra of compound: 3o

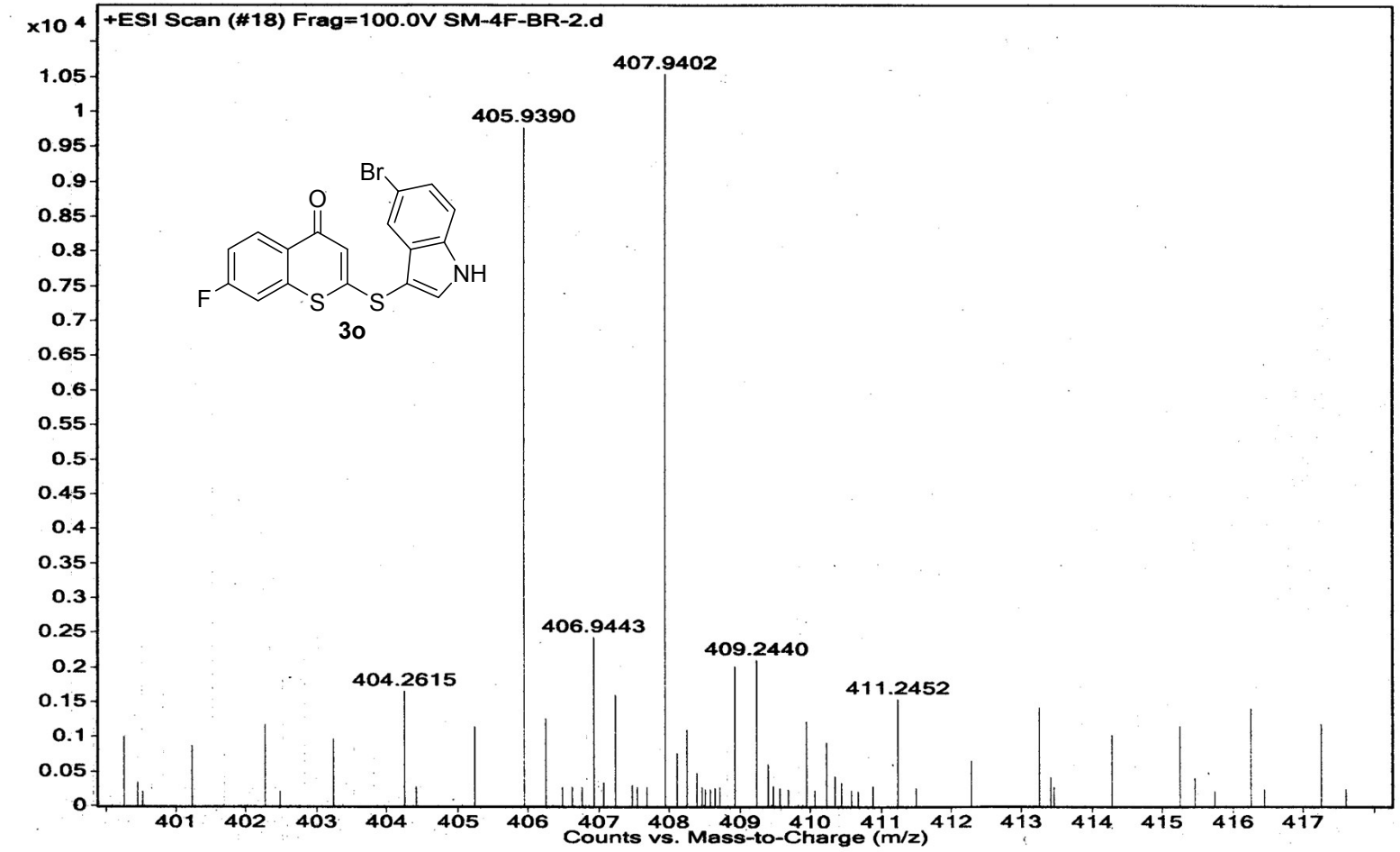


^{13}C NMR spectra of compound: 3o

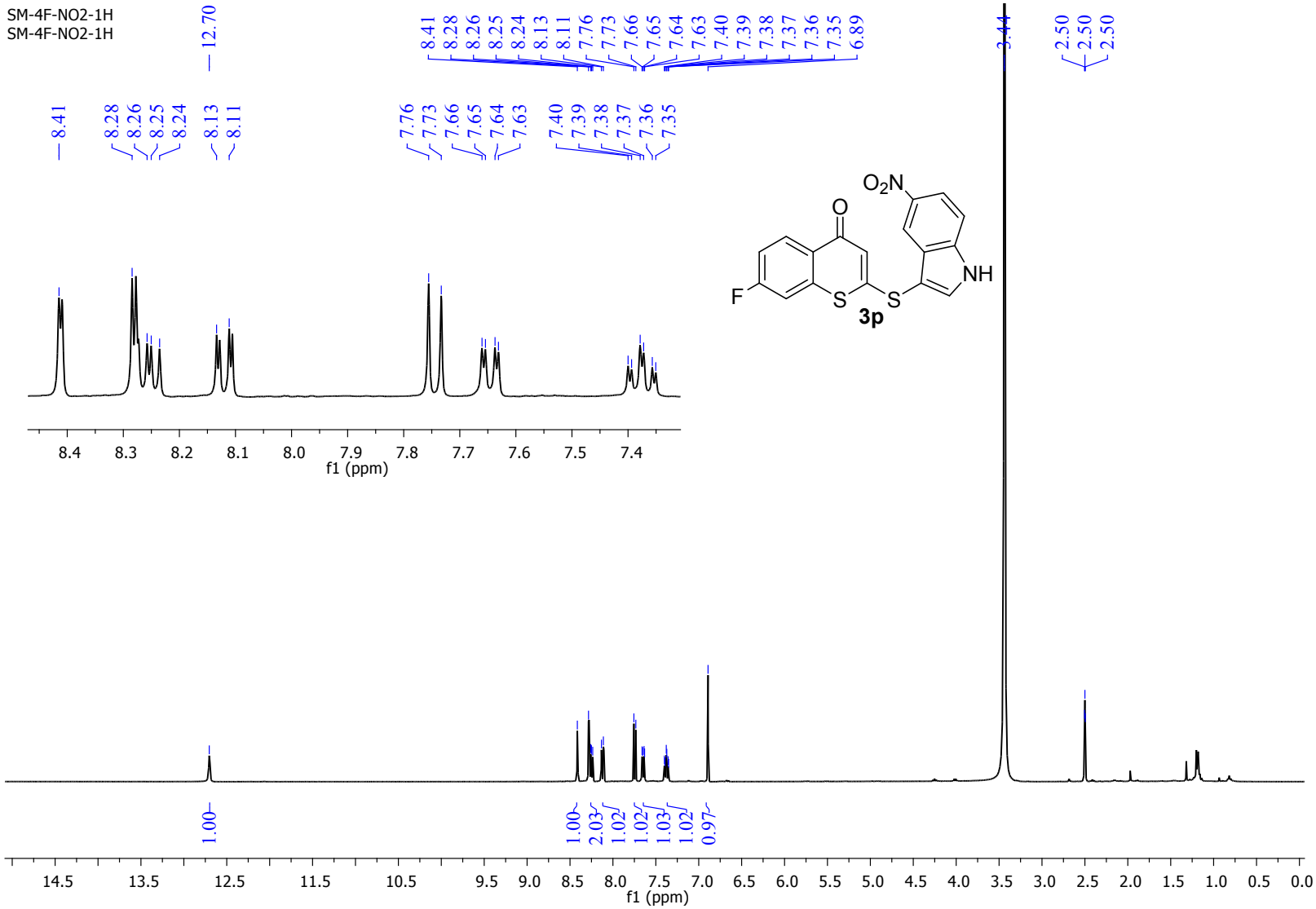


HRMS spectra of compound: 3o

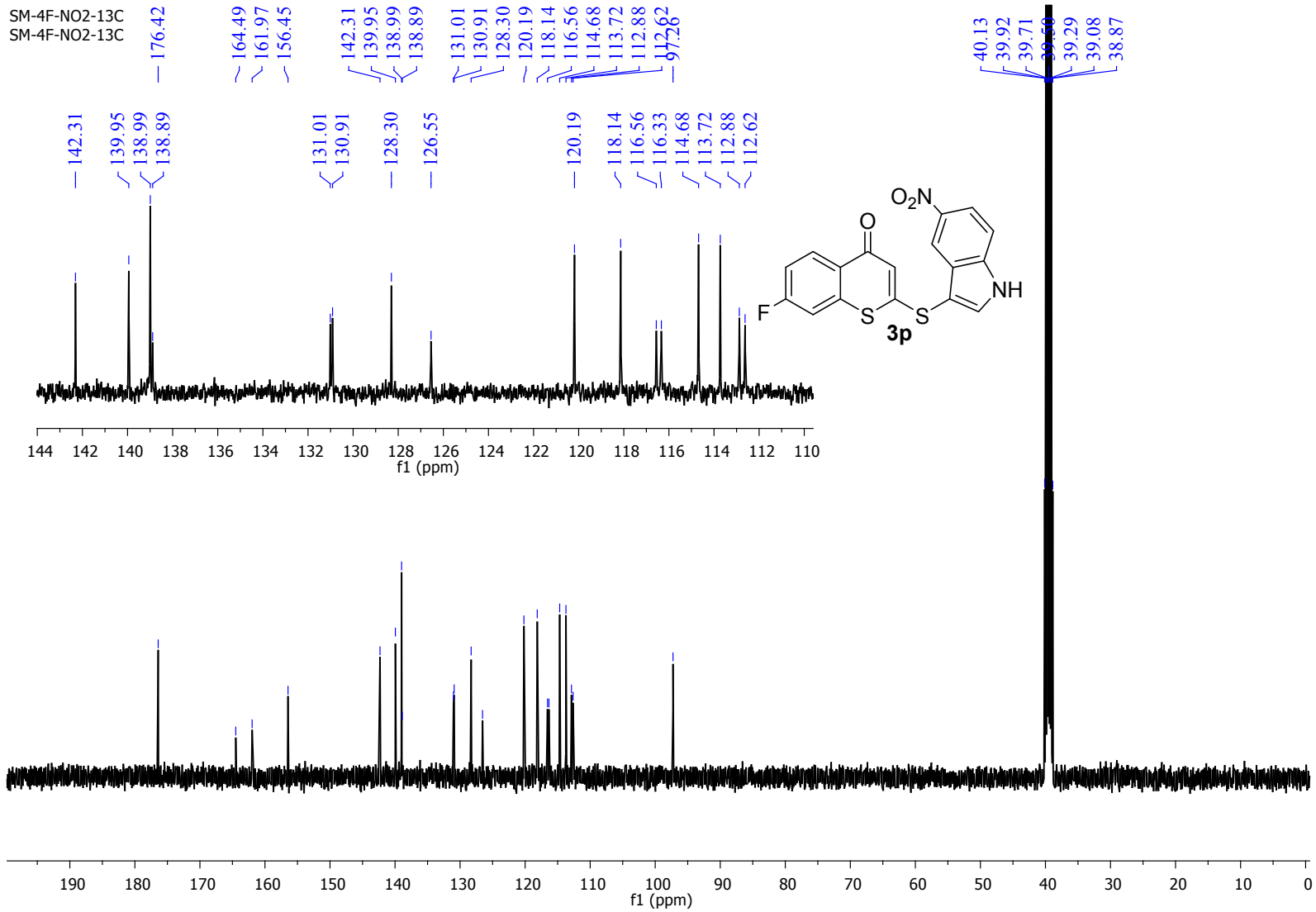
Sample Name	SM-4F-BR-2	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-4F-BR-2.d	**ACQ Method**		**Comment**		**Acquired Time**	8/1/2018 10:51:24 AM



^{1}H NMR spectra of compound: 3p

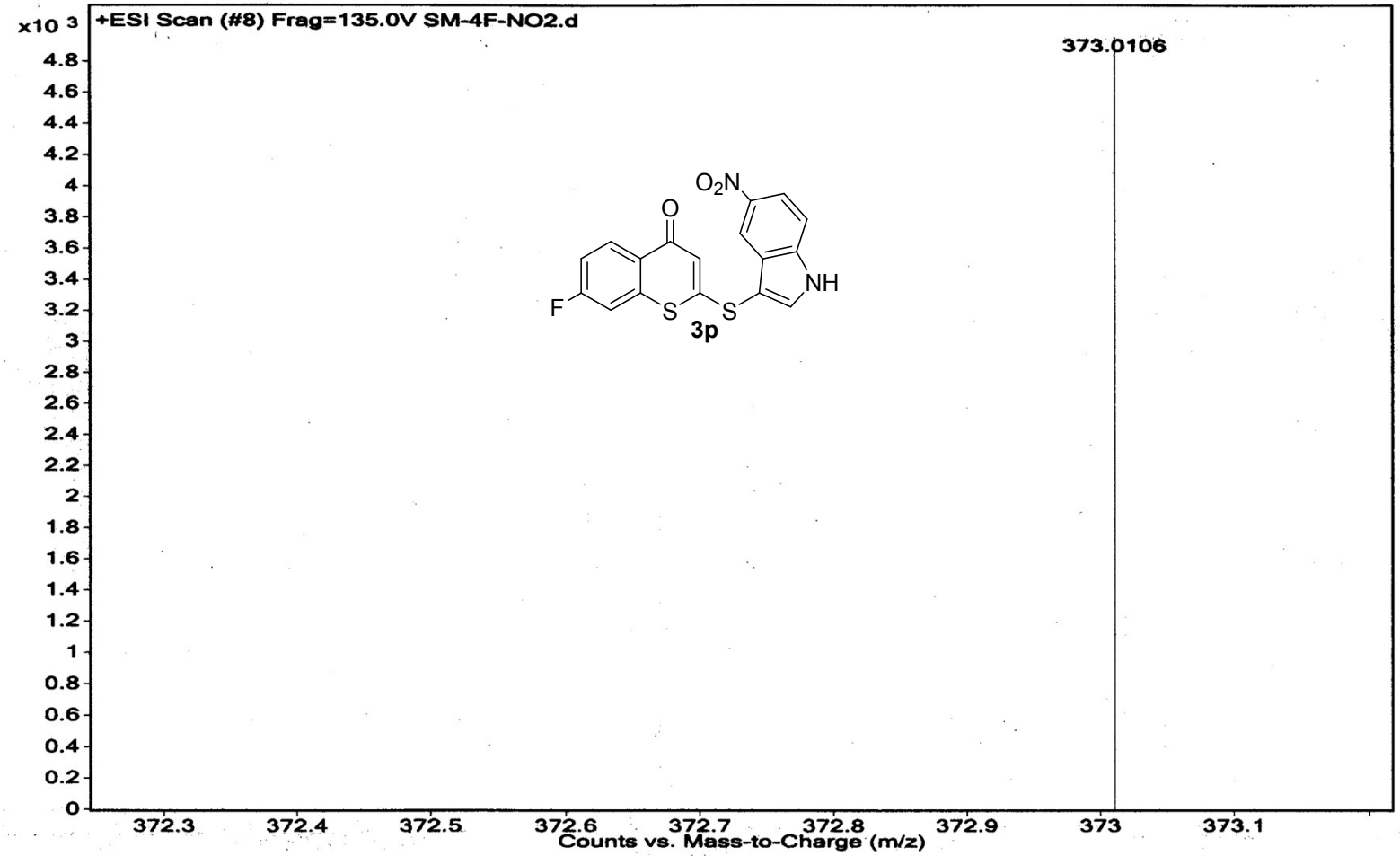


^{13}C NMR spectra of compound: 3p

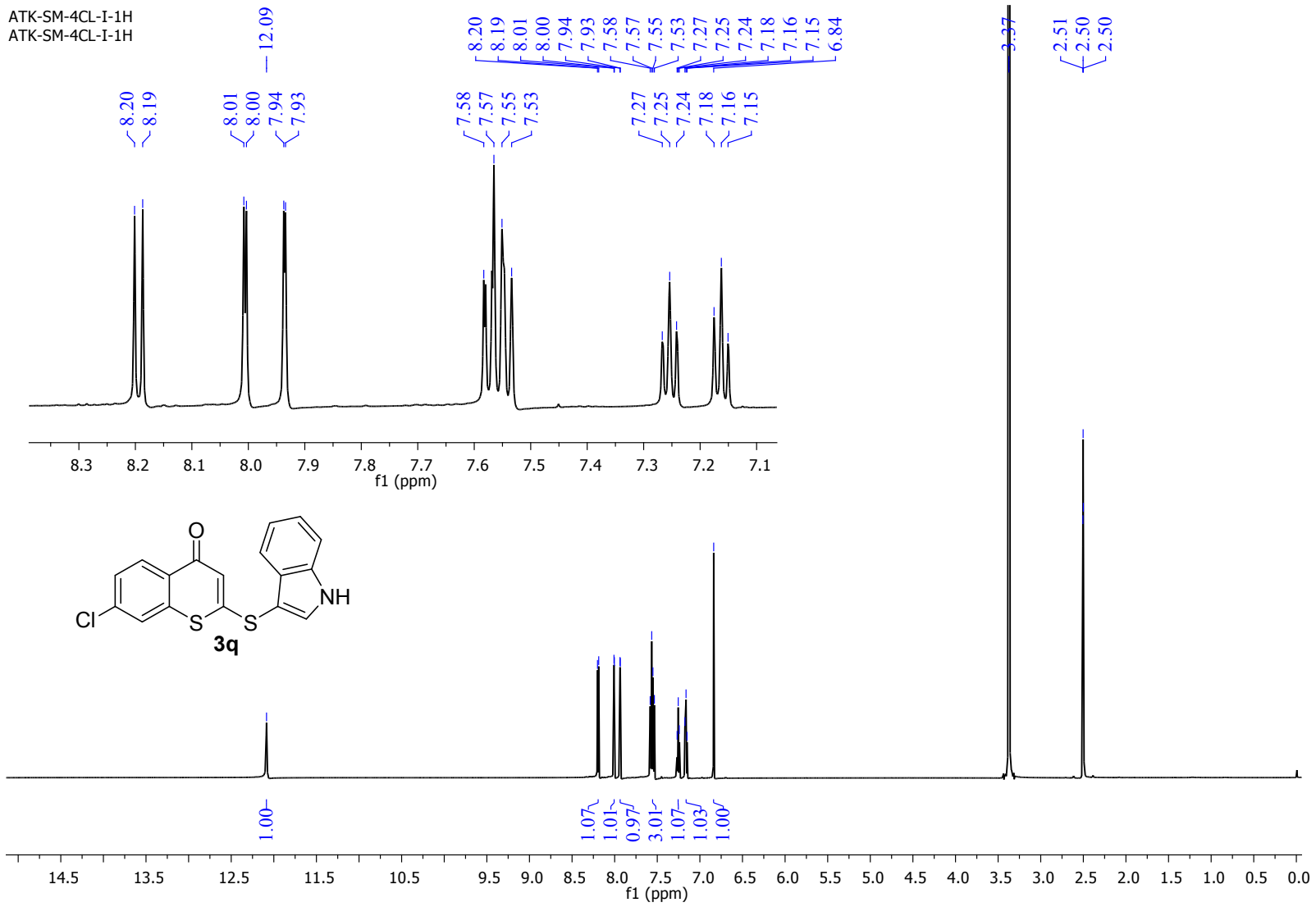


HRMS spectra of compound: 3p

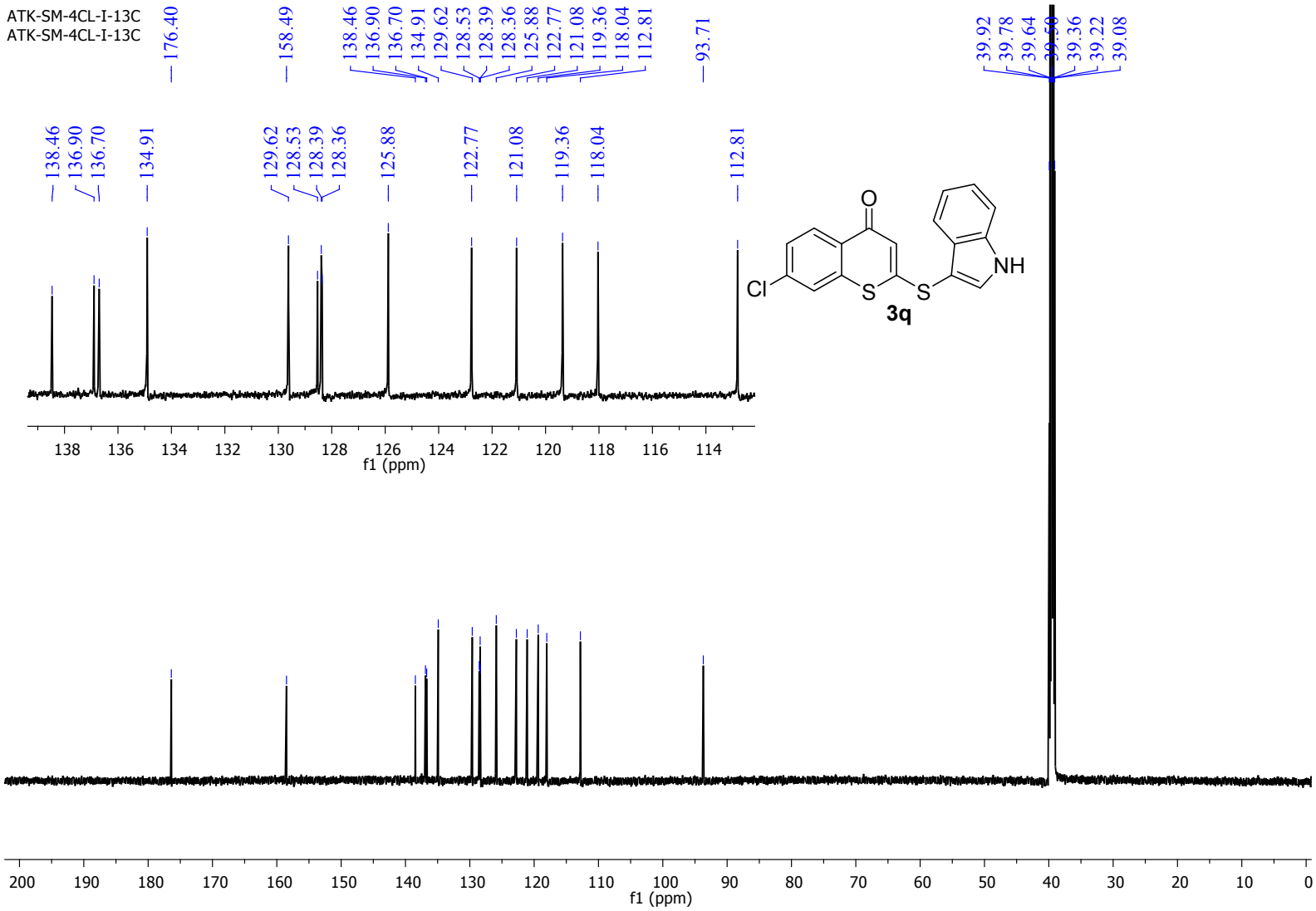
Sample Name	SM-4F-NO2	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-4F-NO2.d	**ACQ Method**		**Comment**		**Acquired Time**	8/6/2018 10:42:15 AM



^{1}H NMR spectra of compound: 3q

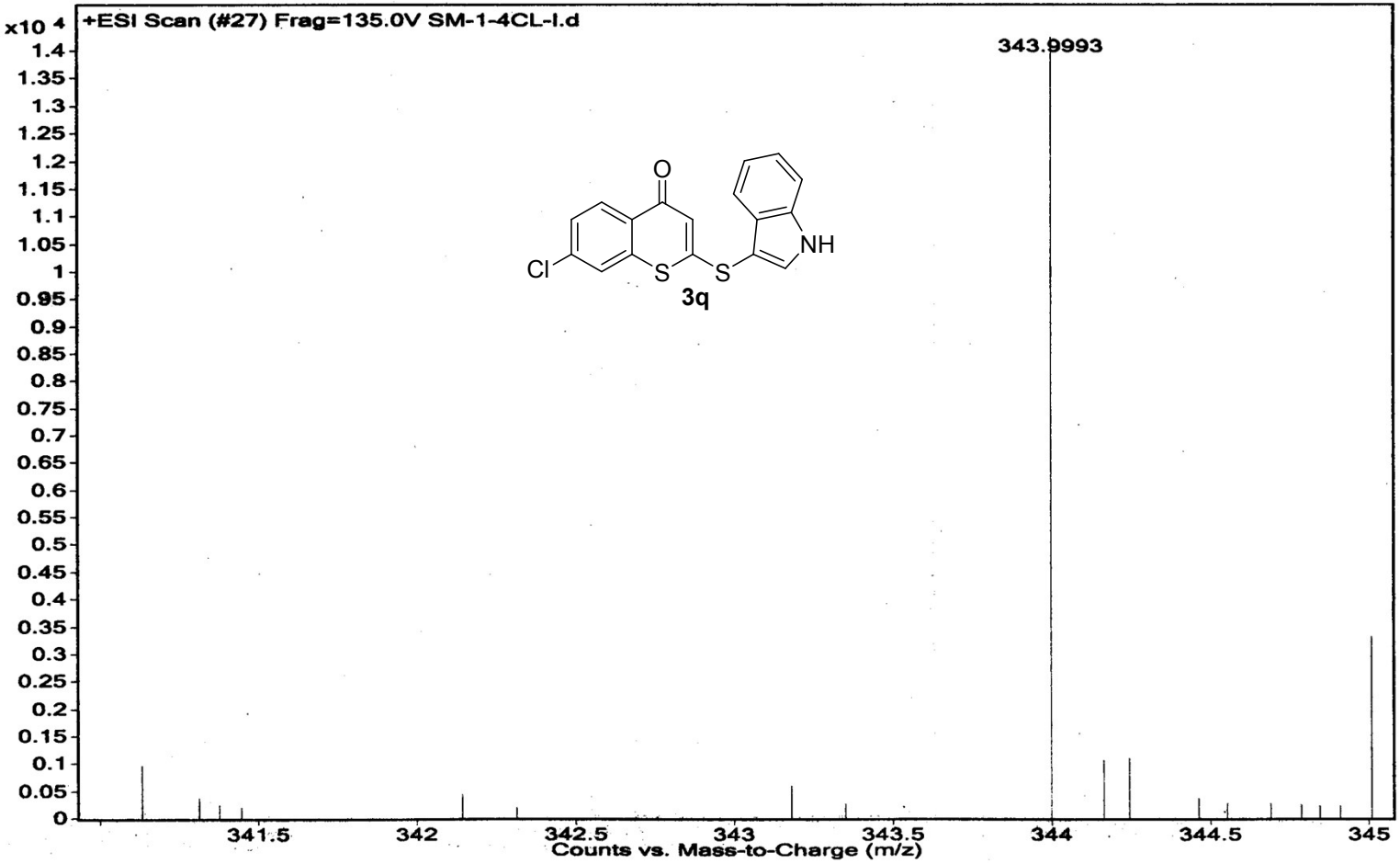


^{13}C NMR spectra of compound: 3q

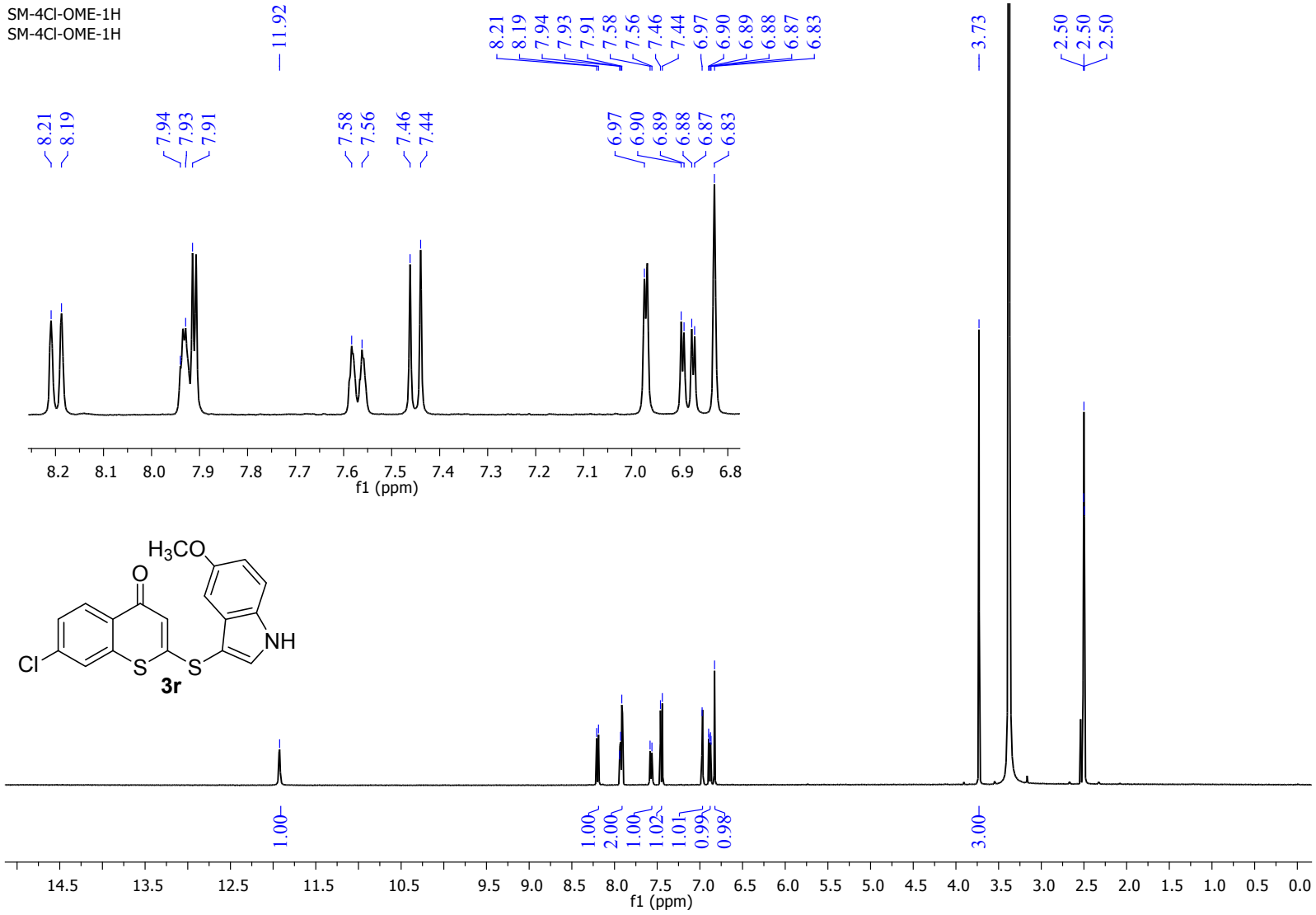


HRMS spectra of compound: 3q

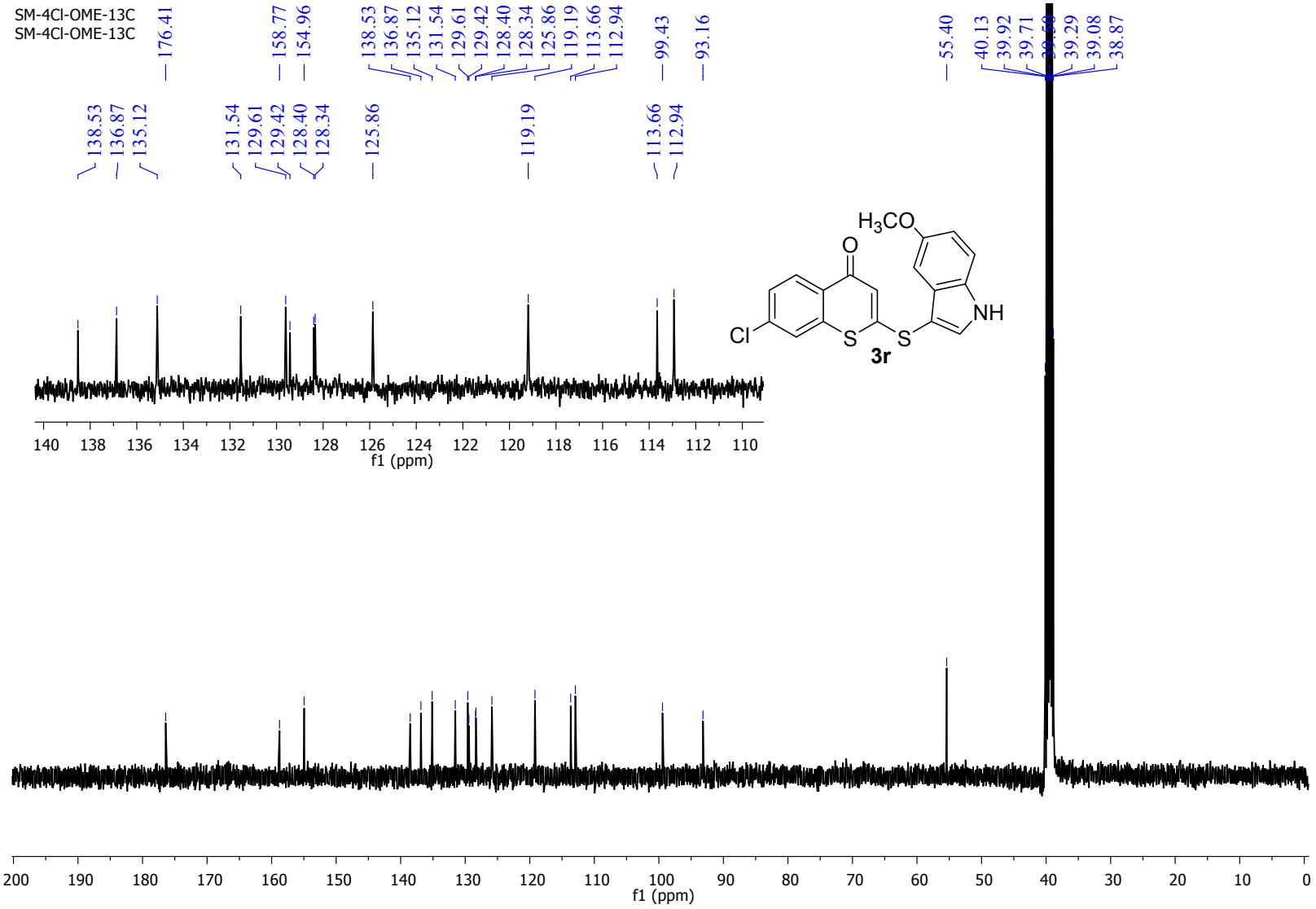
Sample Name	SM-1-4CL-I	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-1-4CL-I.d	**ACQ Method**		**Comment**		**Acquired Time**	7/27/2018 3:27:01 PM



^{1}H NMR spectra of compound: 3r

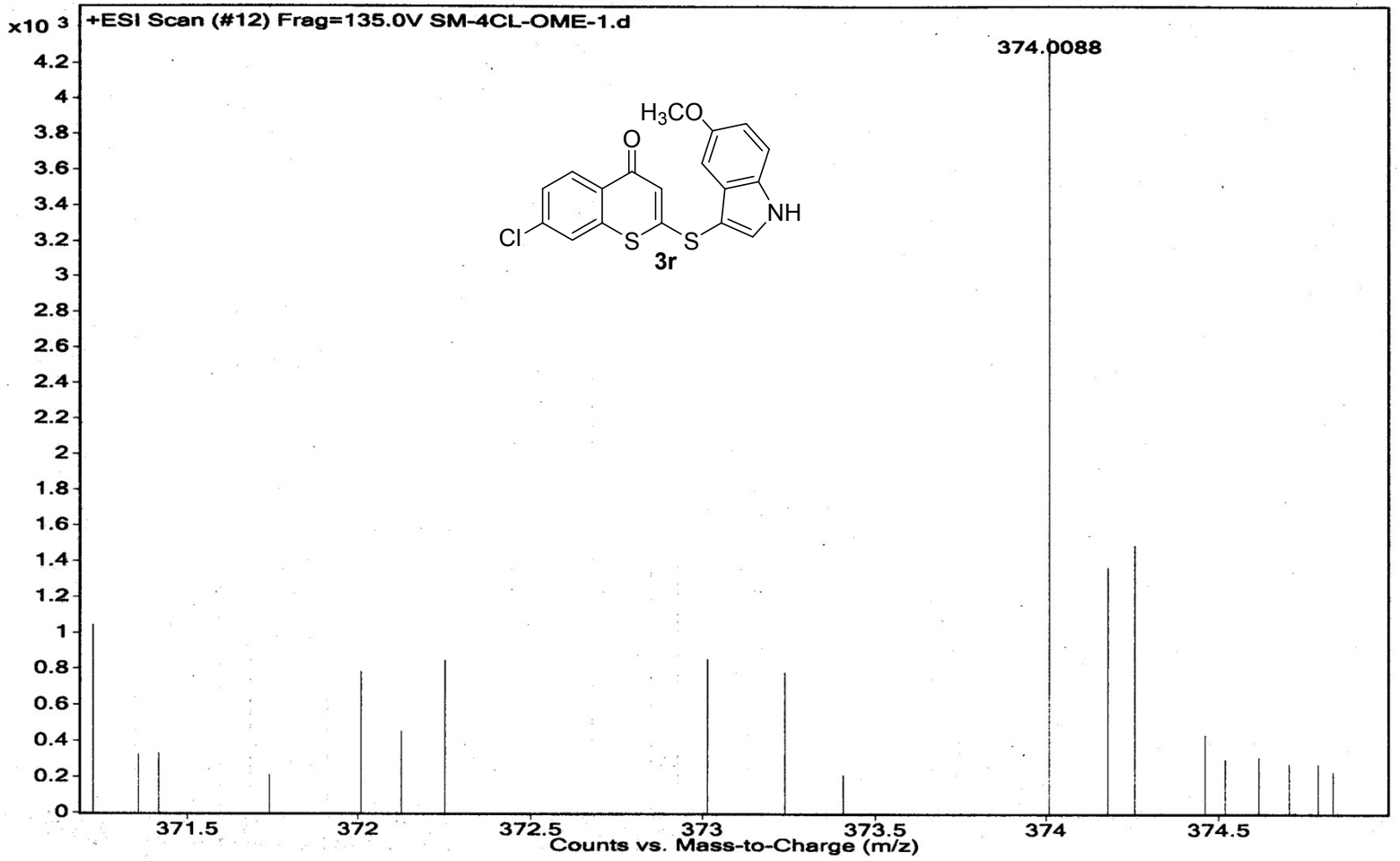


^{13}C NMR spectra of compound: 3r

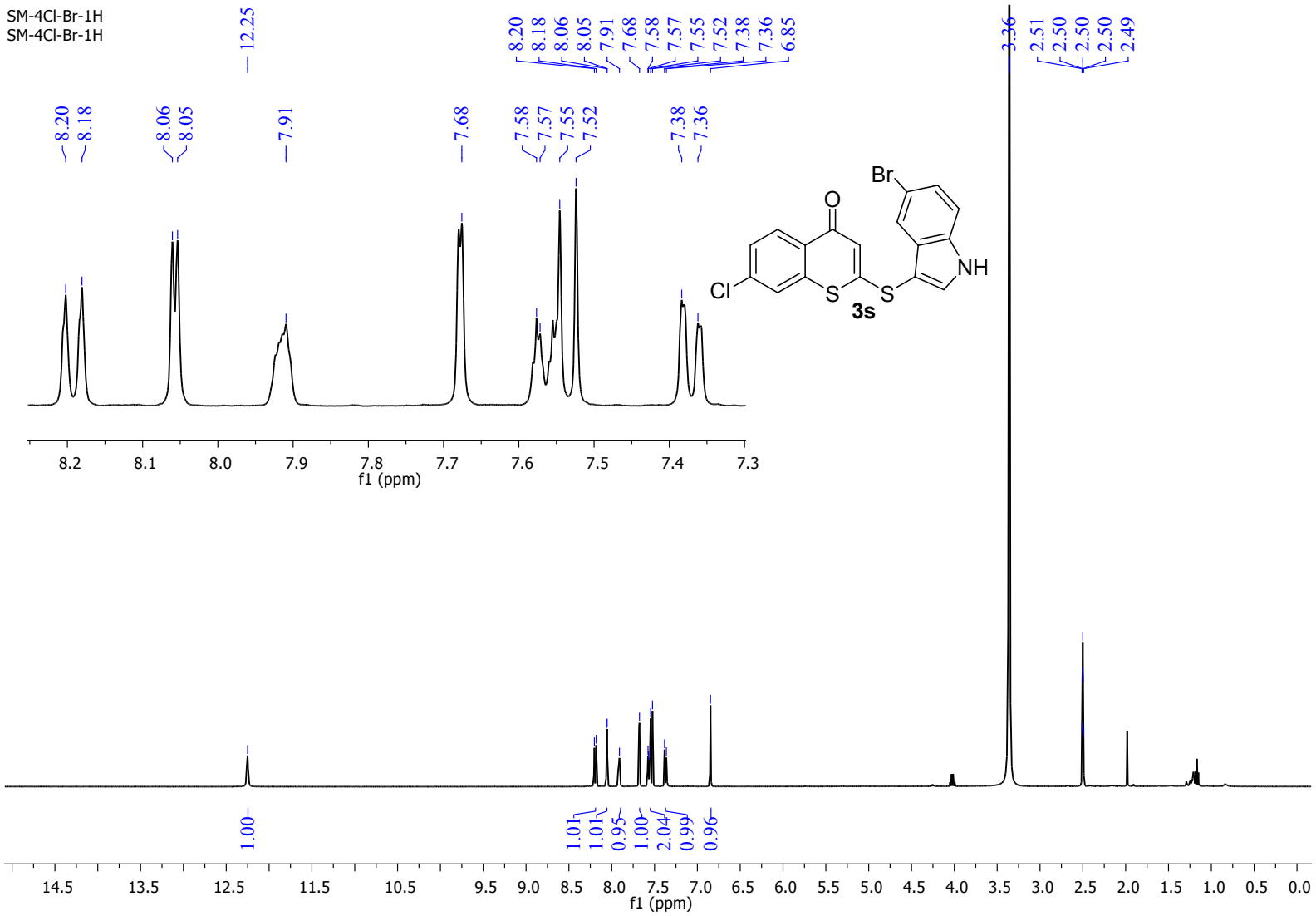


HRMS spectra of compound: 3r

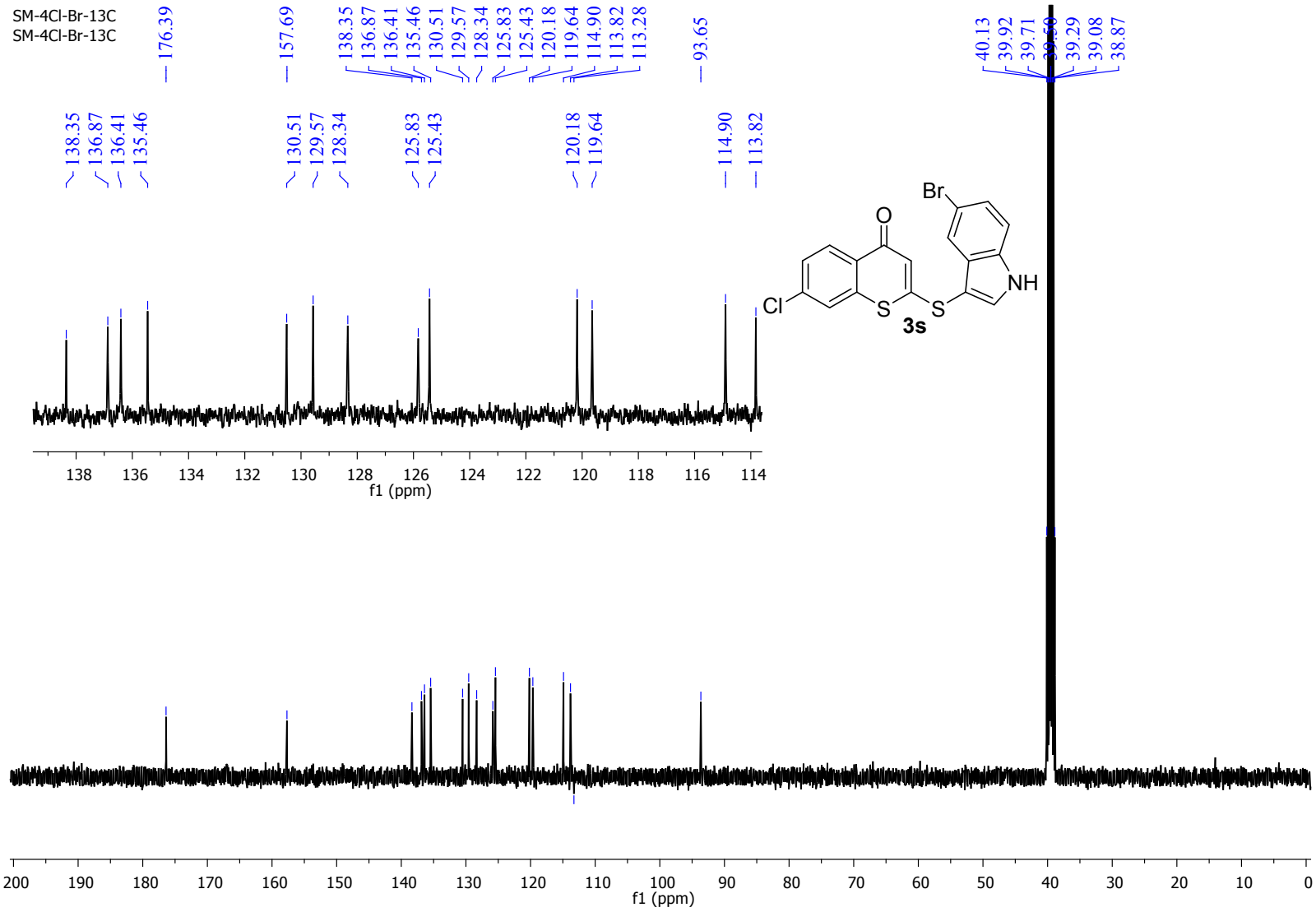
Sample Name	SM-4CL-OME-1	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-4CL-OME-1.d	**ACQ Method**		**Comment**		**Acquired Time**	8/2/2018 5:06:03 PM



^{1}H NMR spectra of compound: 3s

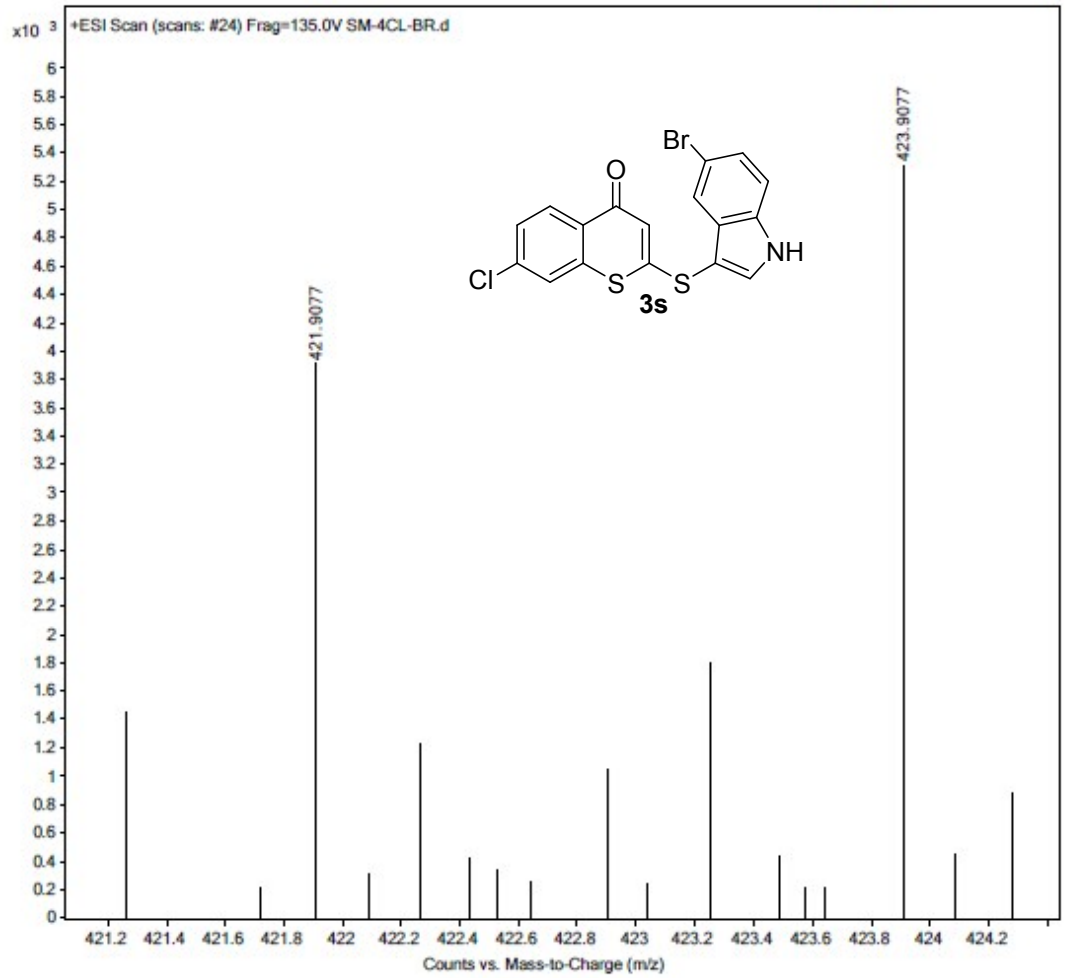


^{13}C NMR spectra of compound: 3s

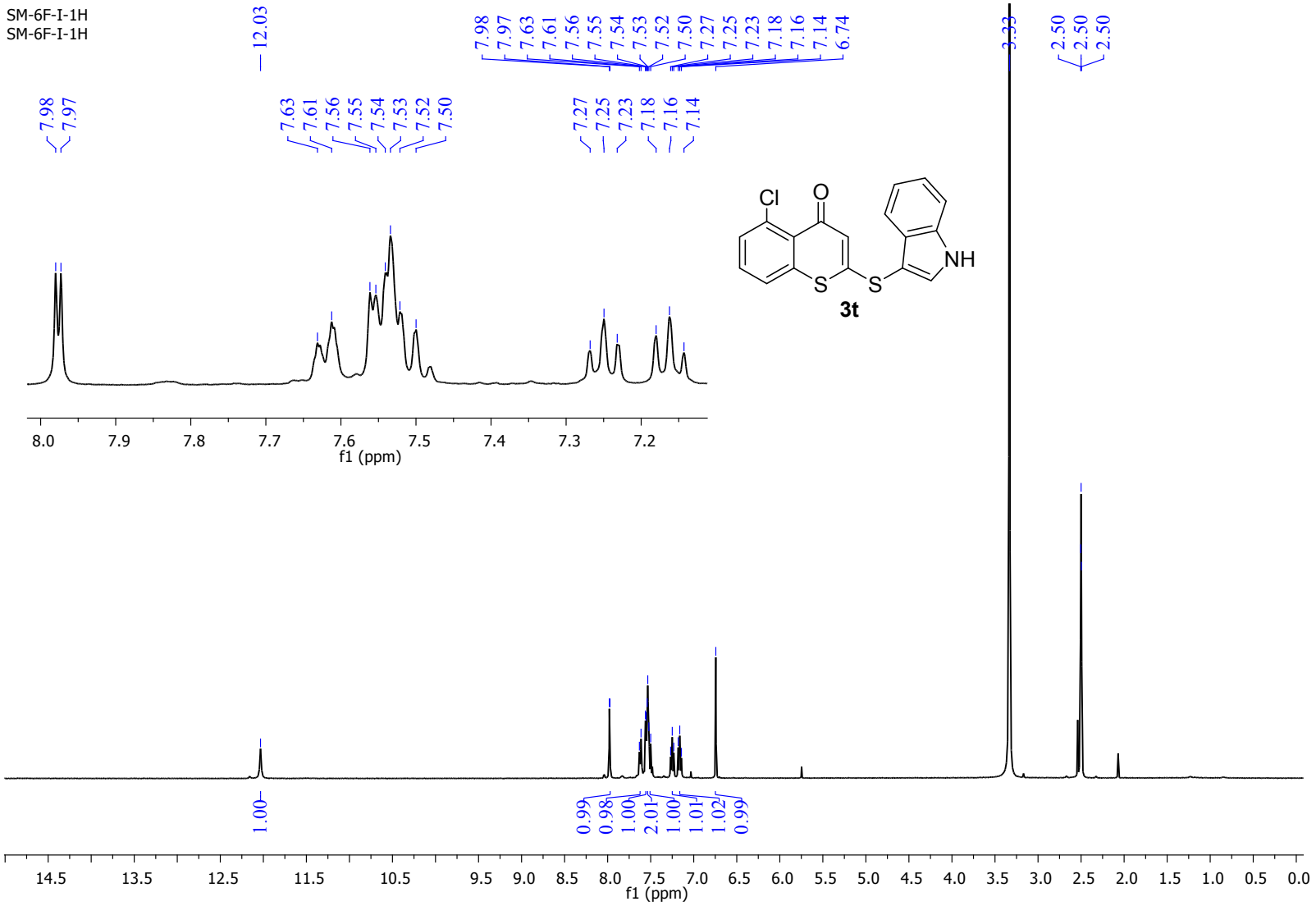


HRMS spectra of compound: 3s

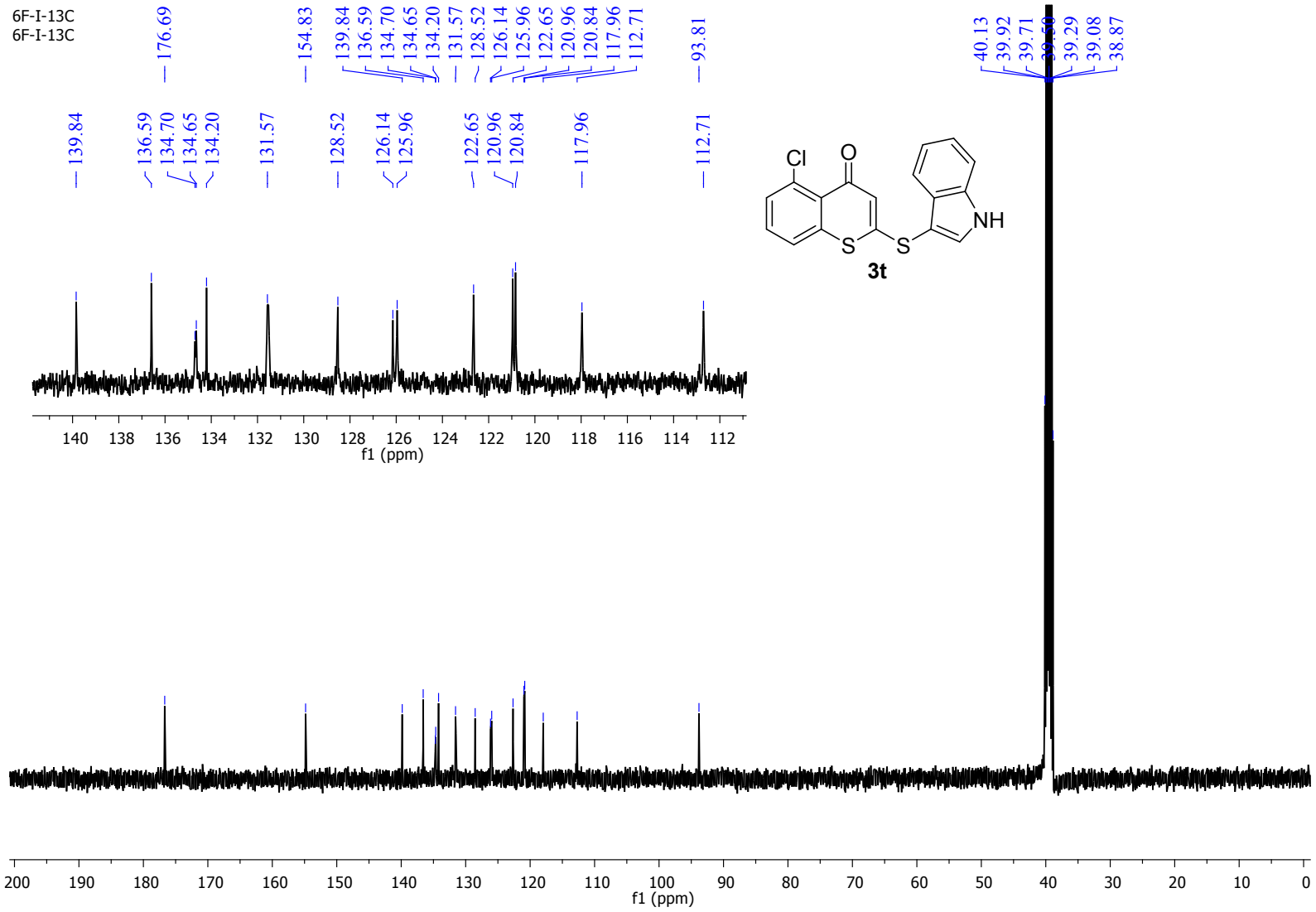
Sample Name	SM-4CL-BR	**Position**	Vial 1	**Instrument Name**	QTOF
User Name		**Inj Vol**	-1	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	SM-4CL-BR.d
ACQ Method		**Comment**		**Acquired Time**	02-08-2018 16:56:17 (UTC+05:30)



^{1}H NMR spectra of compound: 3t

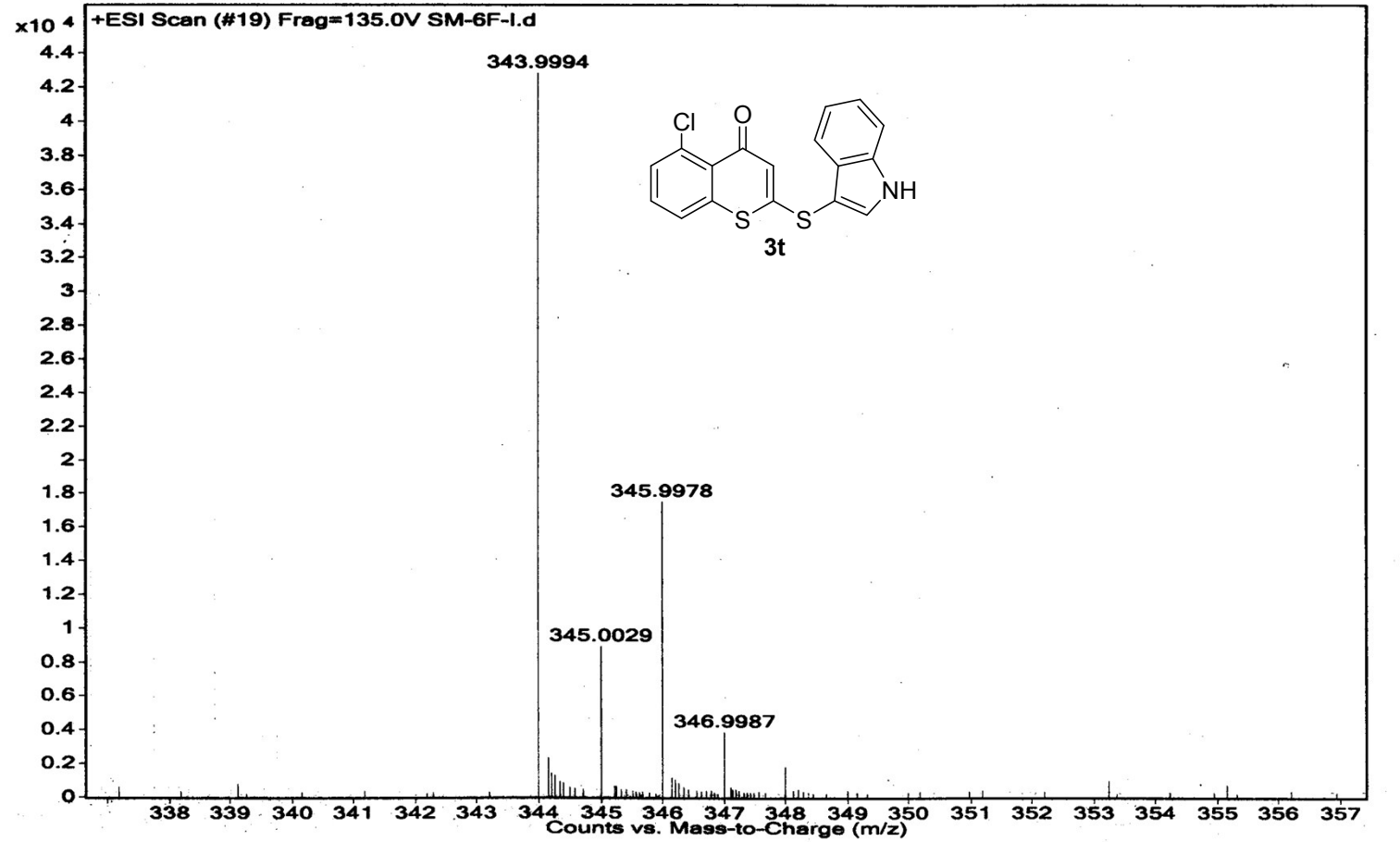


^{13}C NMR spectra of compound: 3t

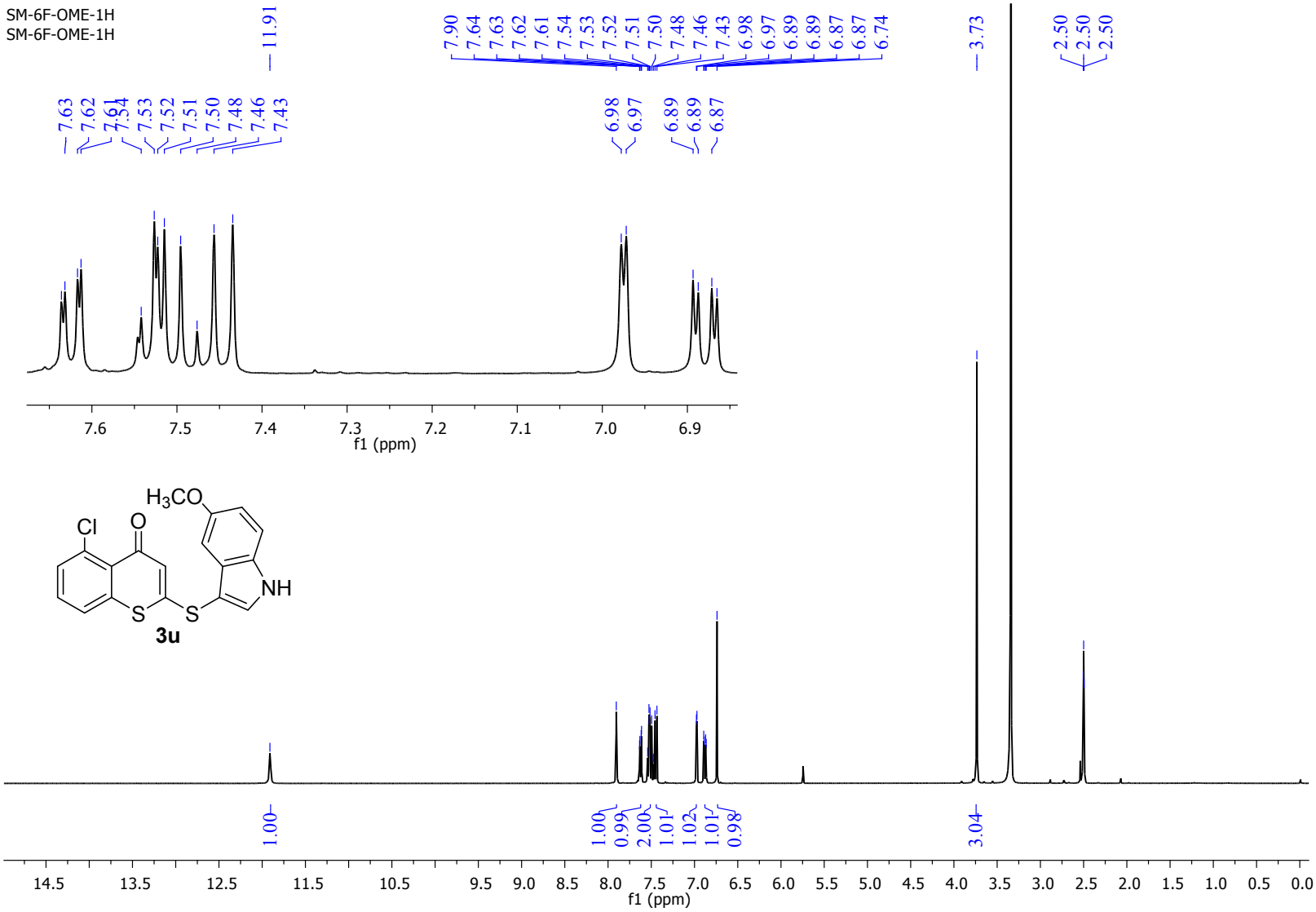


HRMS spectra of compound: 3t

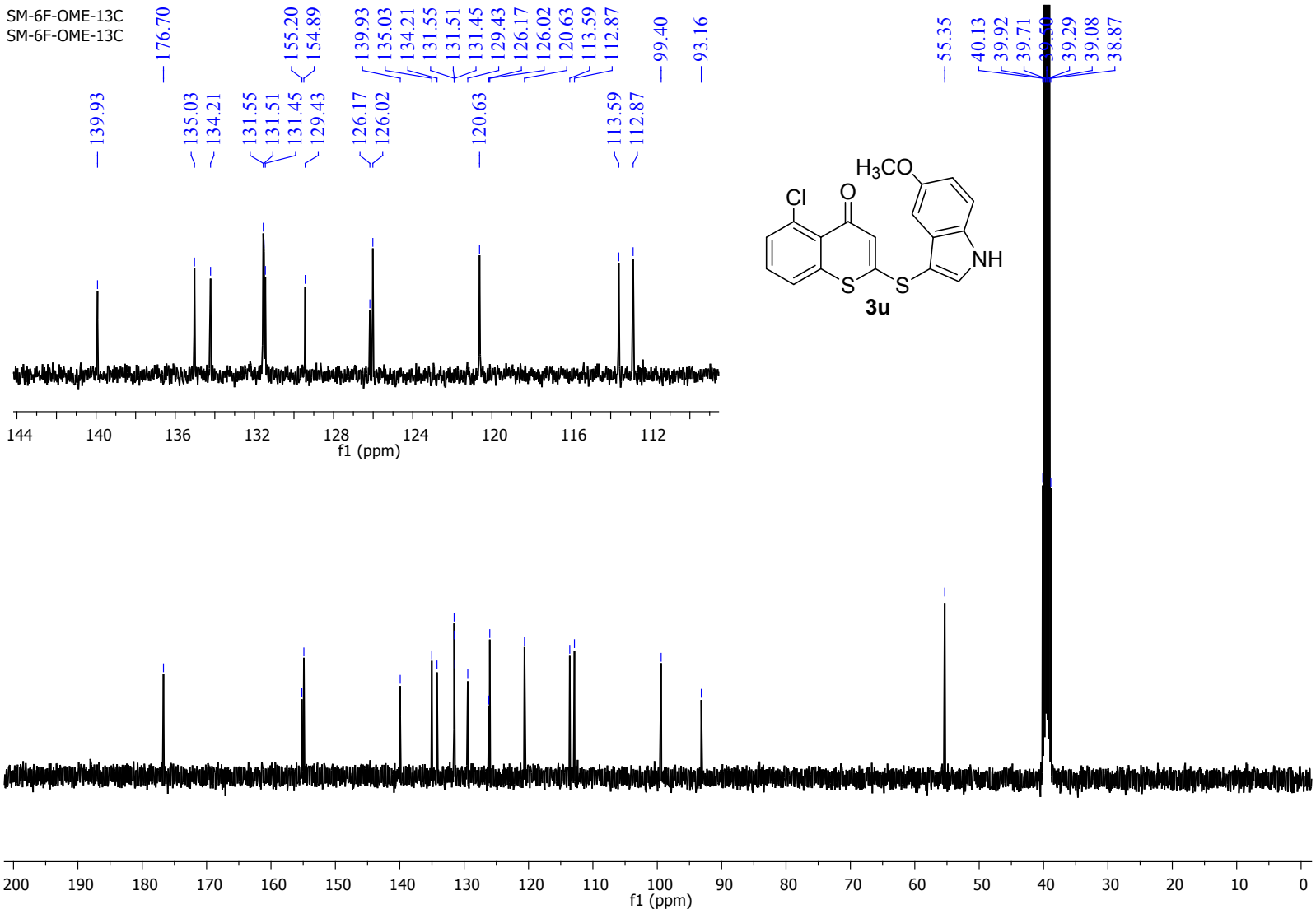
Sample Name	SM-6F-I	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-6F-I.d	**ACQ Method**		**Comment**		**Acquired Time**	7/30/2018 3:47:11 PM



^{1}H NMR spectra of compound: 3u

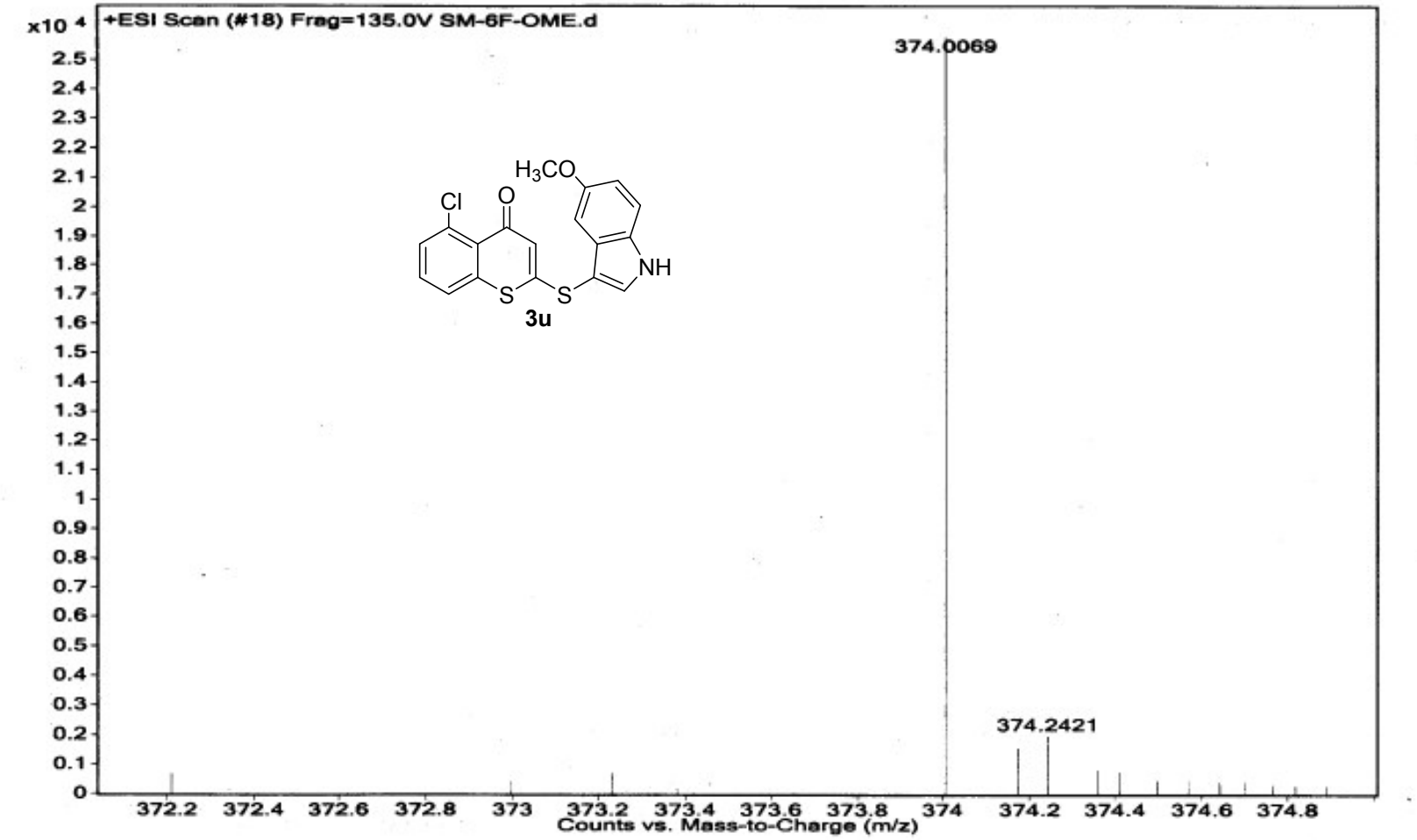


^{13}C NMR spectra of compound: 3u

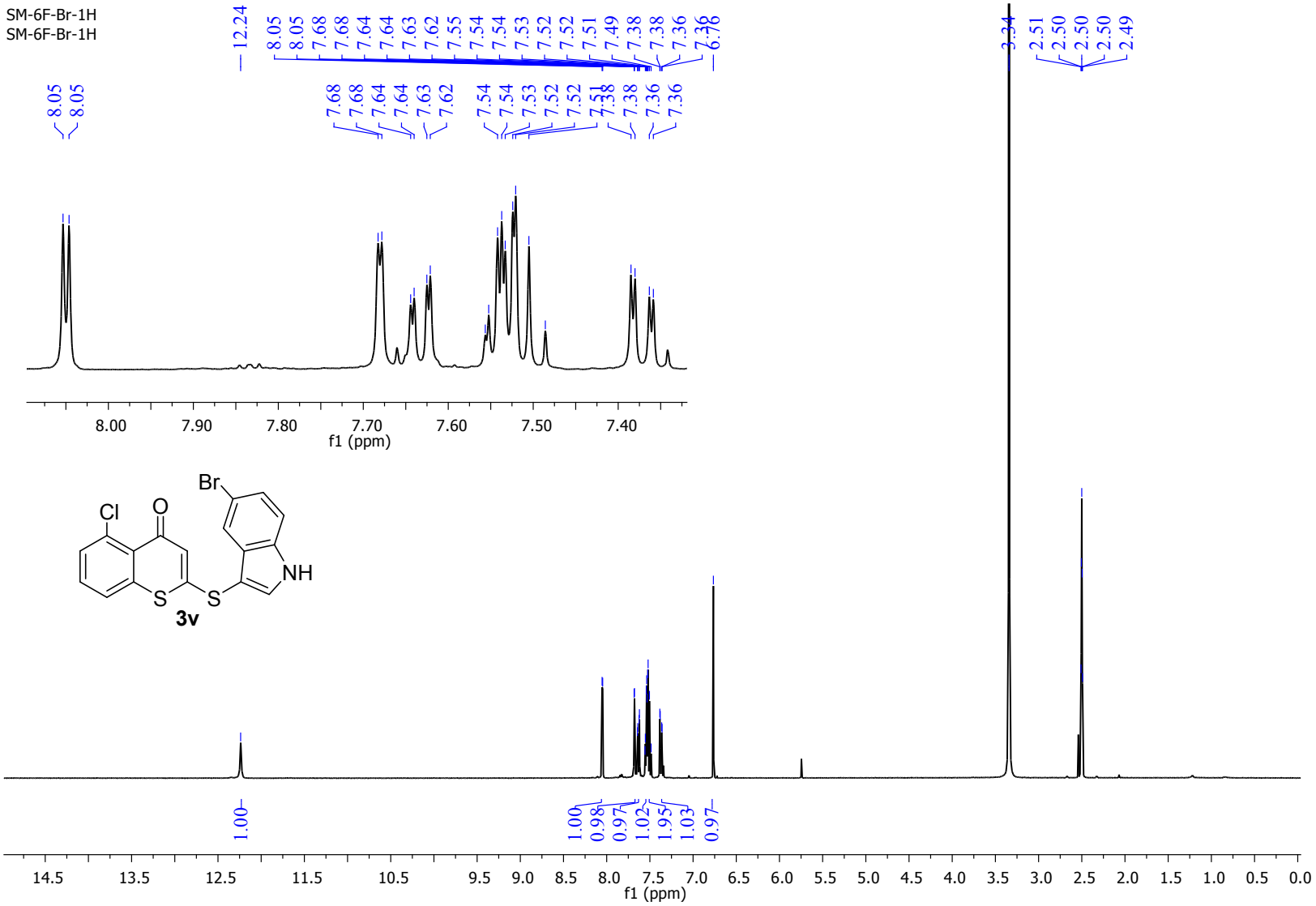


HRMS spectra of compound: 3u

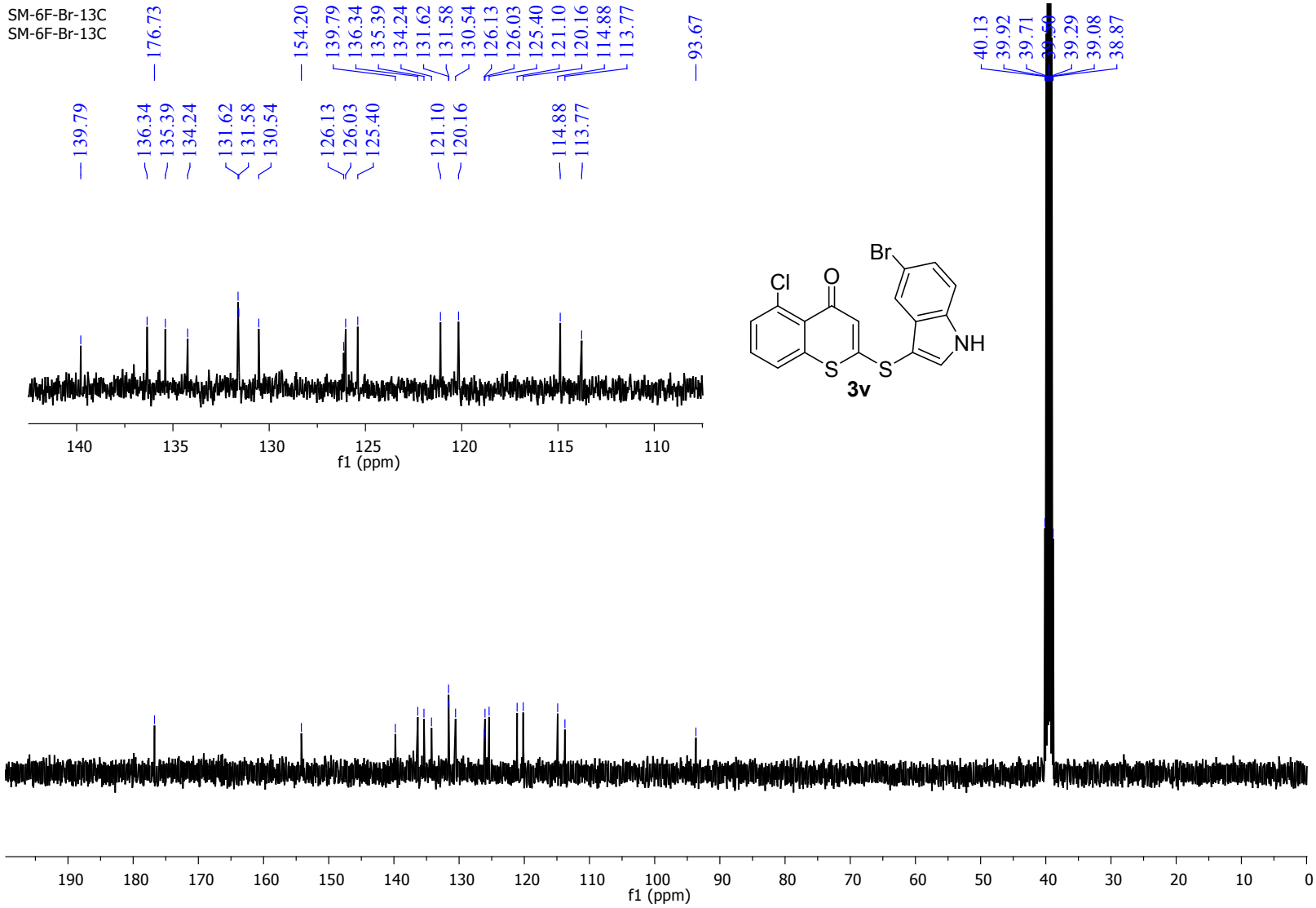
Sample Name	SM-6F-OME	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-6F-OME.d	**ACQ Method**		**Comment**		**Acquired Time**	8/6/2018 10:37:05 AM



^{1}H NMR spectra of compound: 3v

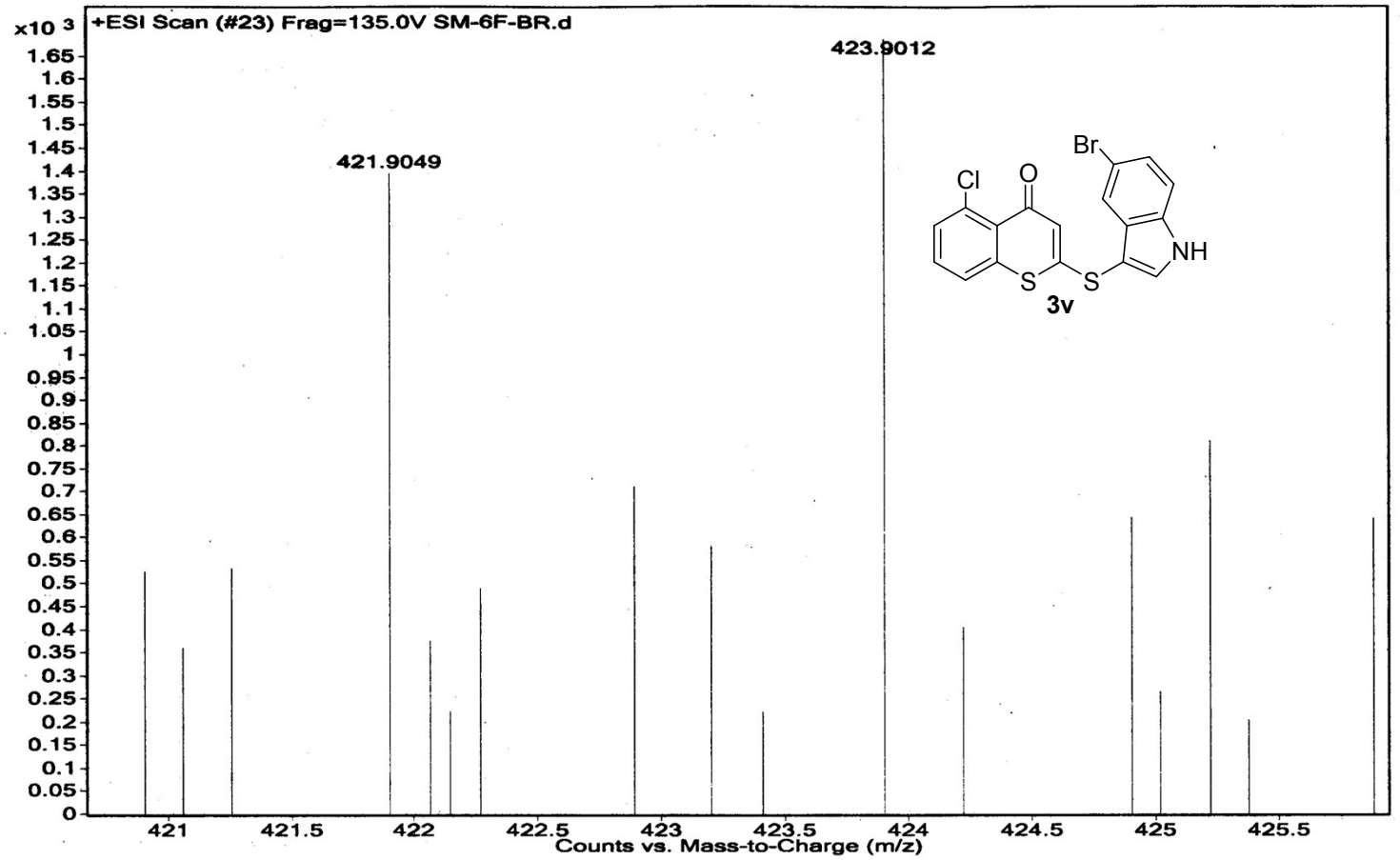


^{13}C NMR spectra of compound: 3v

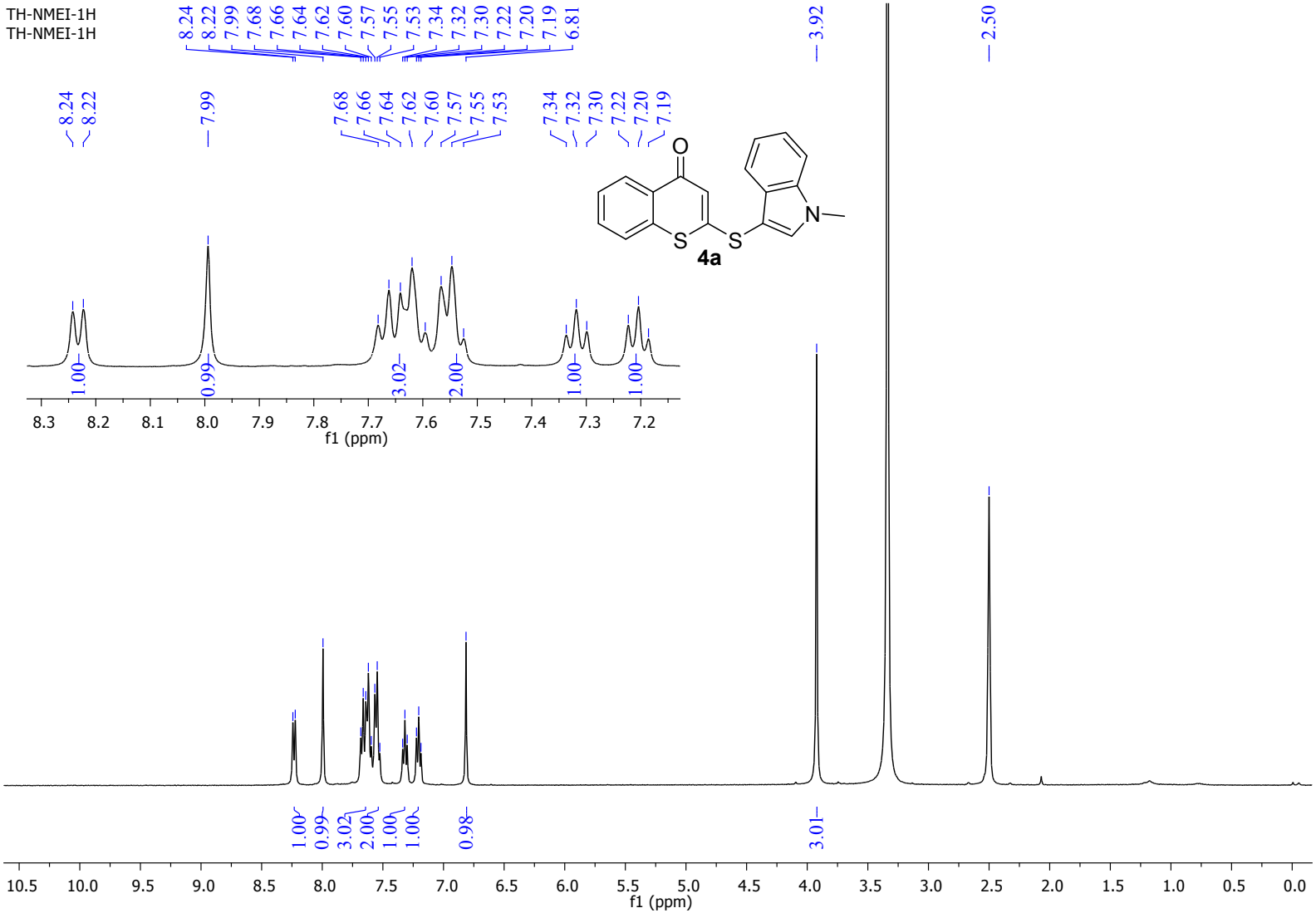


HRMS spectra of compound: 3v

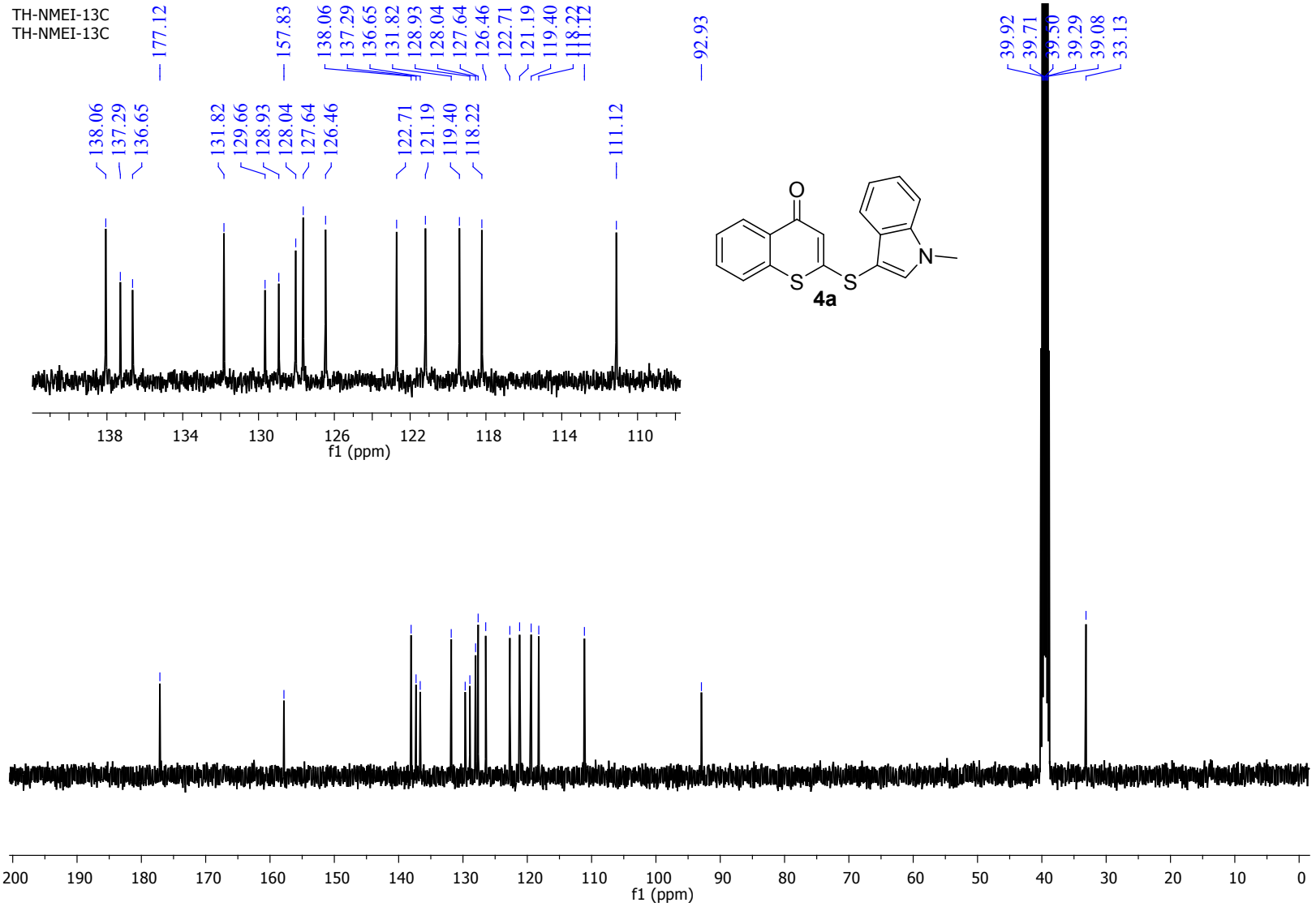
Sample Name	SM-6F-BR	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-6F-BR.d	**ACQ Method**		**Comment**		**Acquired Time**	8/17/2018 11:23:40 AM



^{1}H NMR spectra of compound 4a

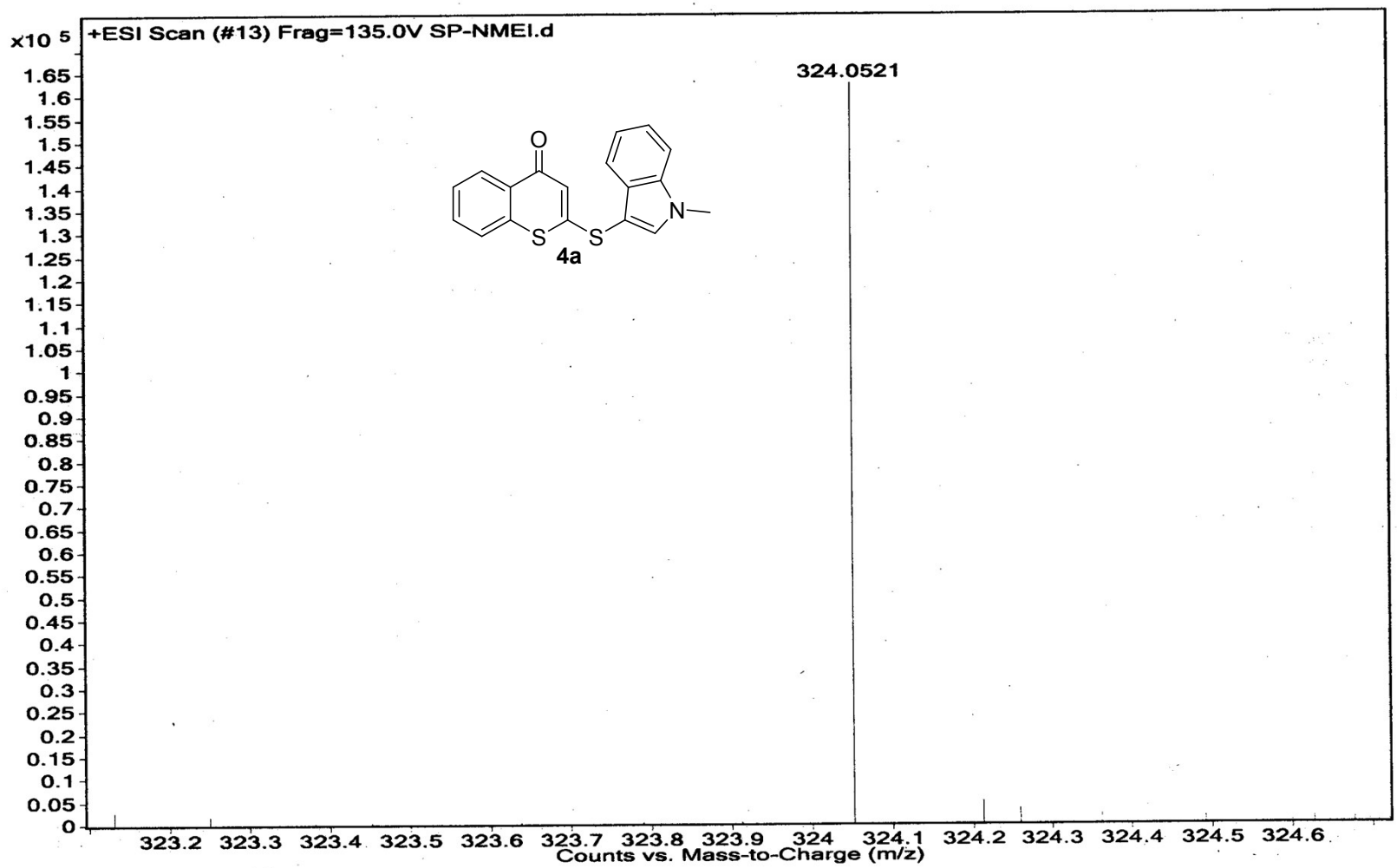


^{13}C NMR spectra of compound 4a

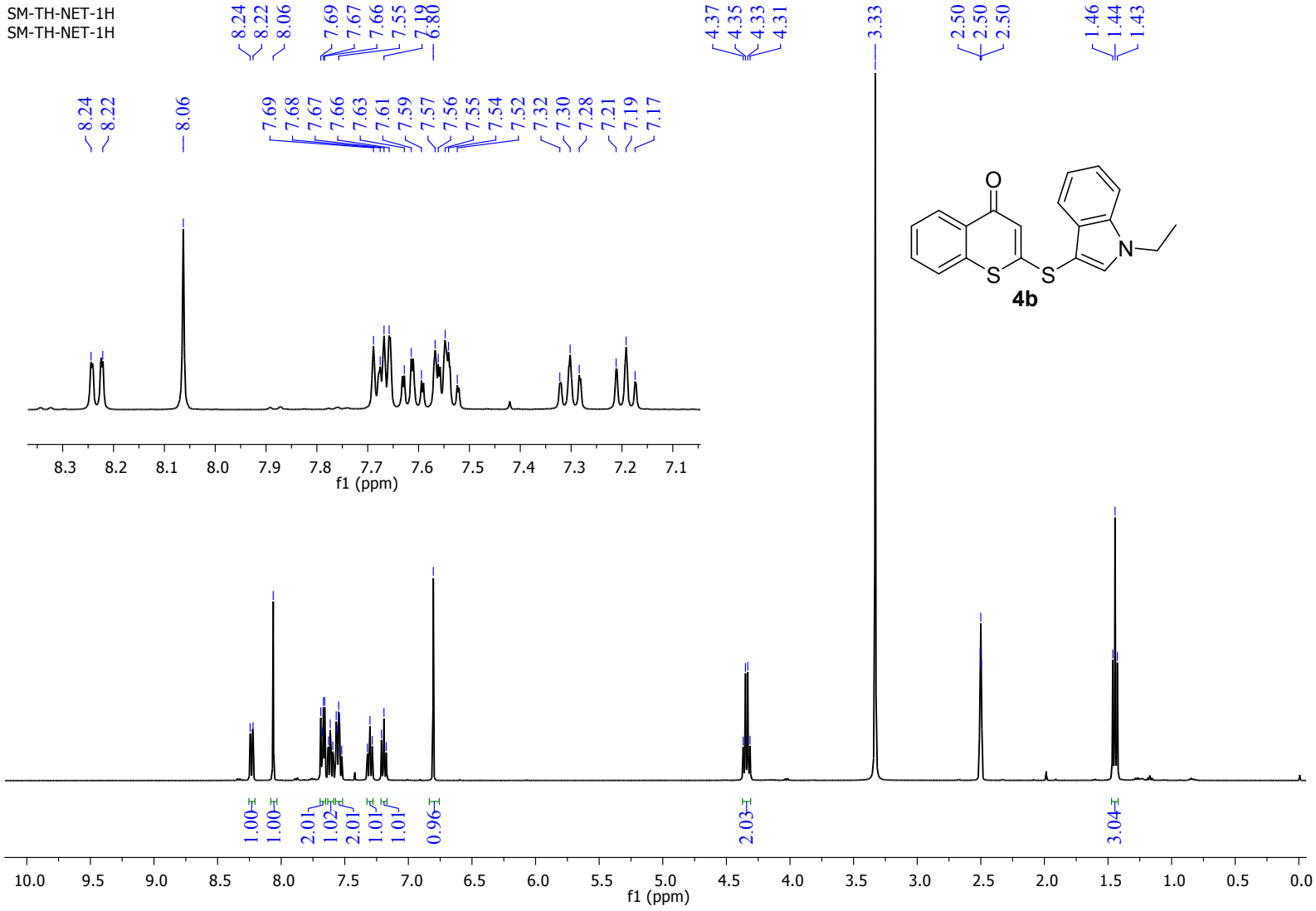


HRMS spectra of compound 4a

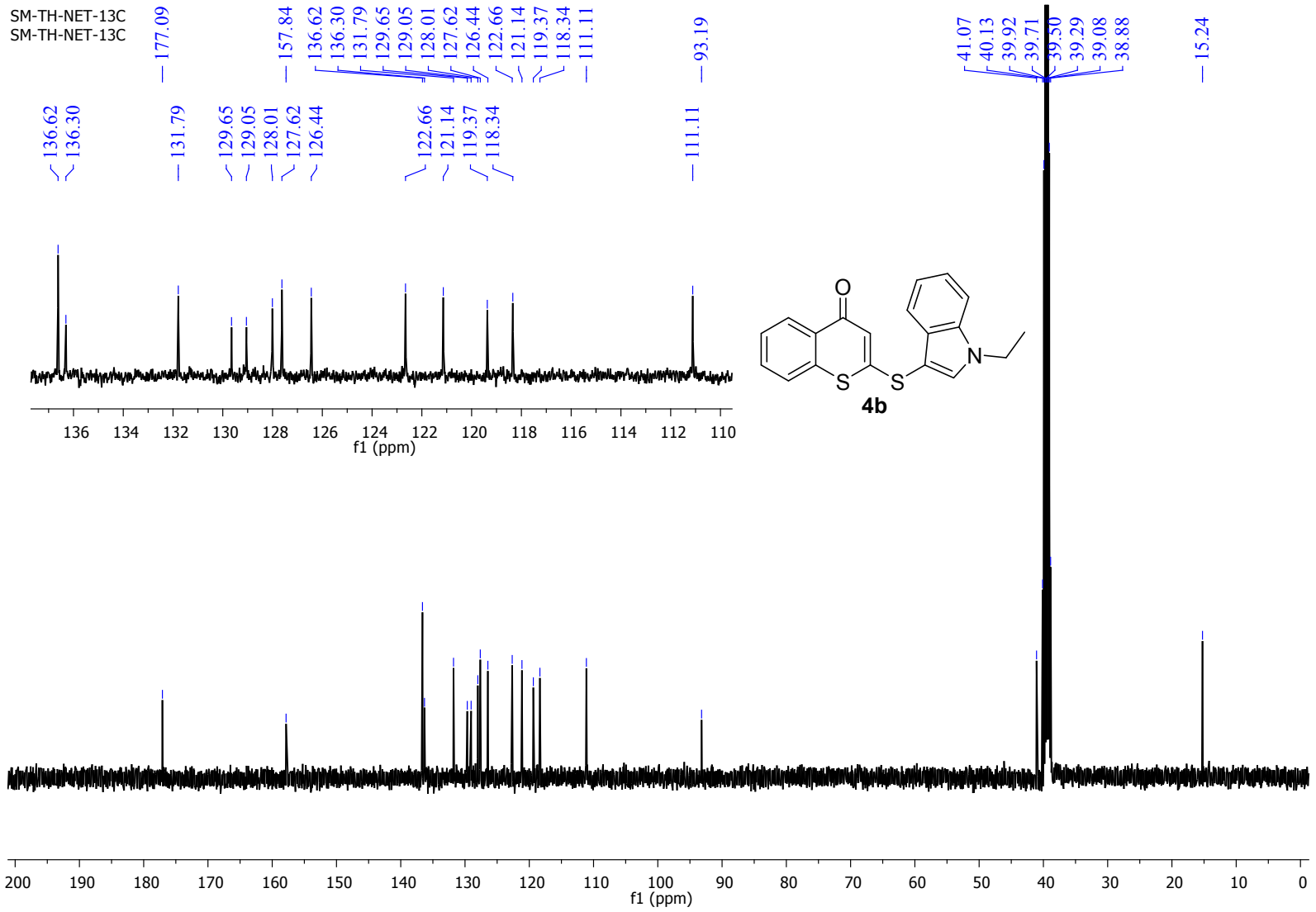
Sample Name	**Position**	**Instrument Name**	**User Name**
Inj Vol	**InjPosition**	**SampleType**	**IRM Calibration Status**
Data Filename	**ACQ Method**	**Comment**	**Acquired Time**



^{1}H NMR spectra of compound 4b

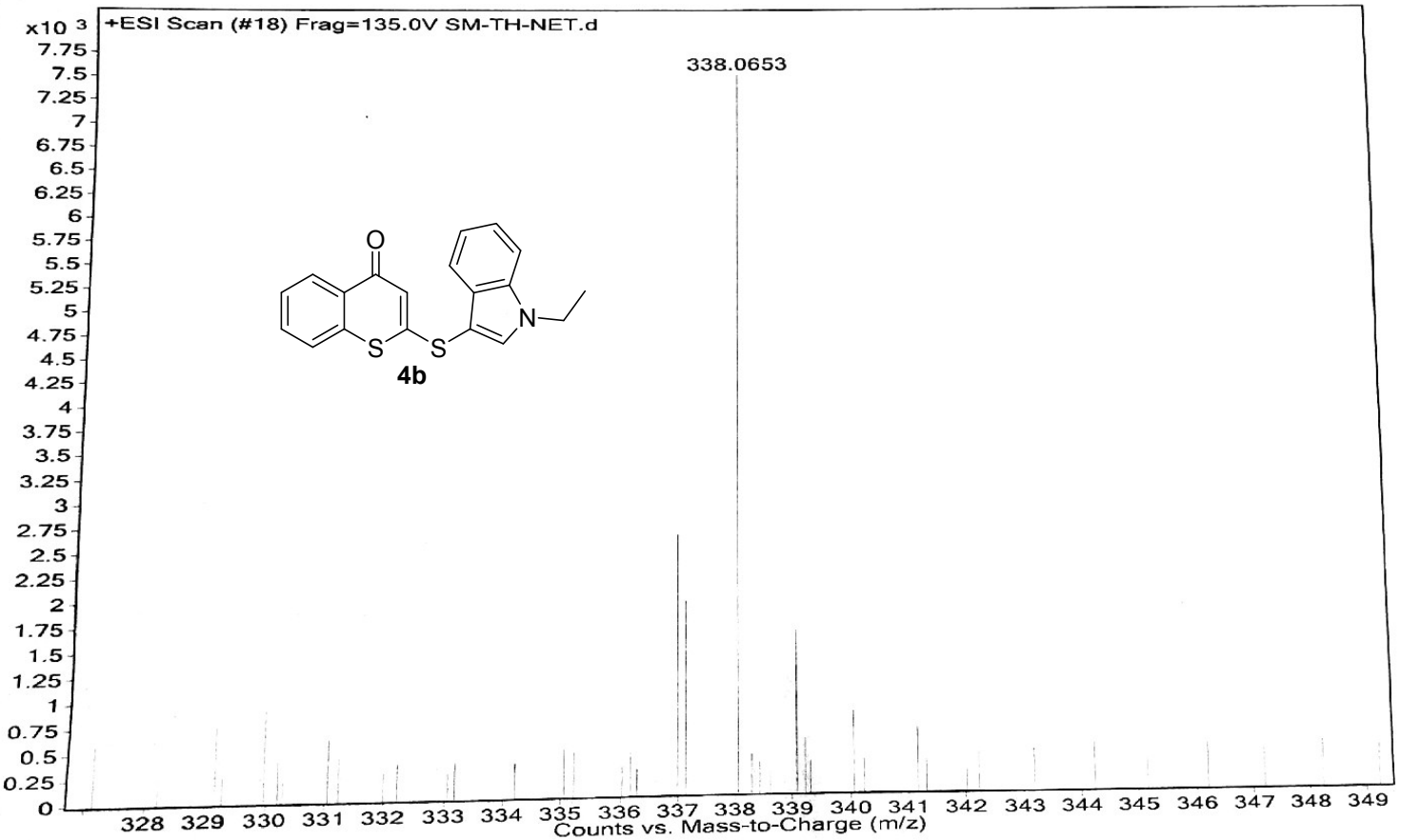


^{13}C NMR spectra of compound 4b

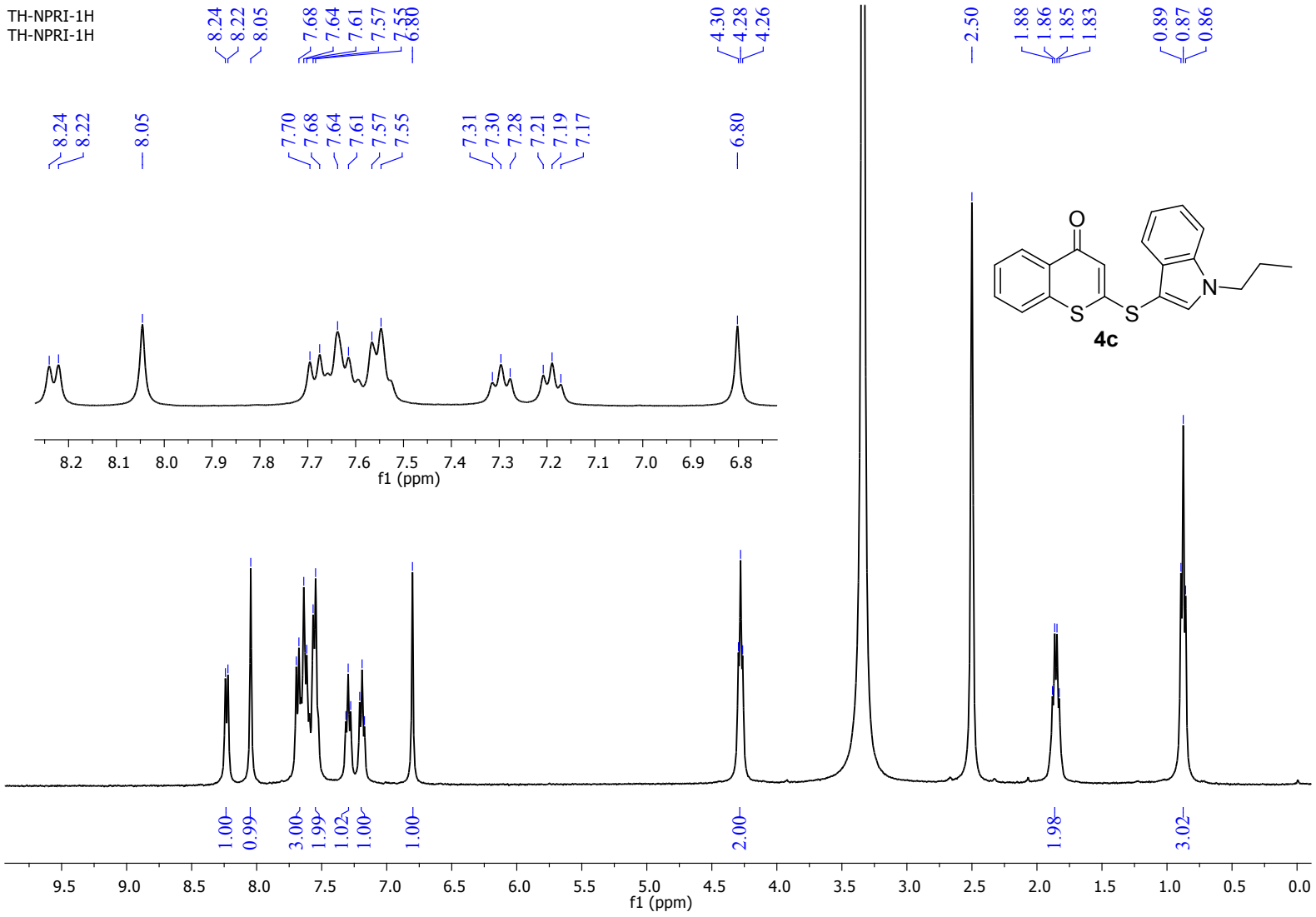


HRMS spectra of compound 4b

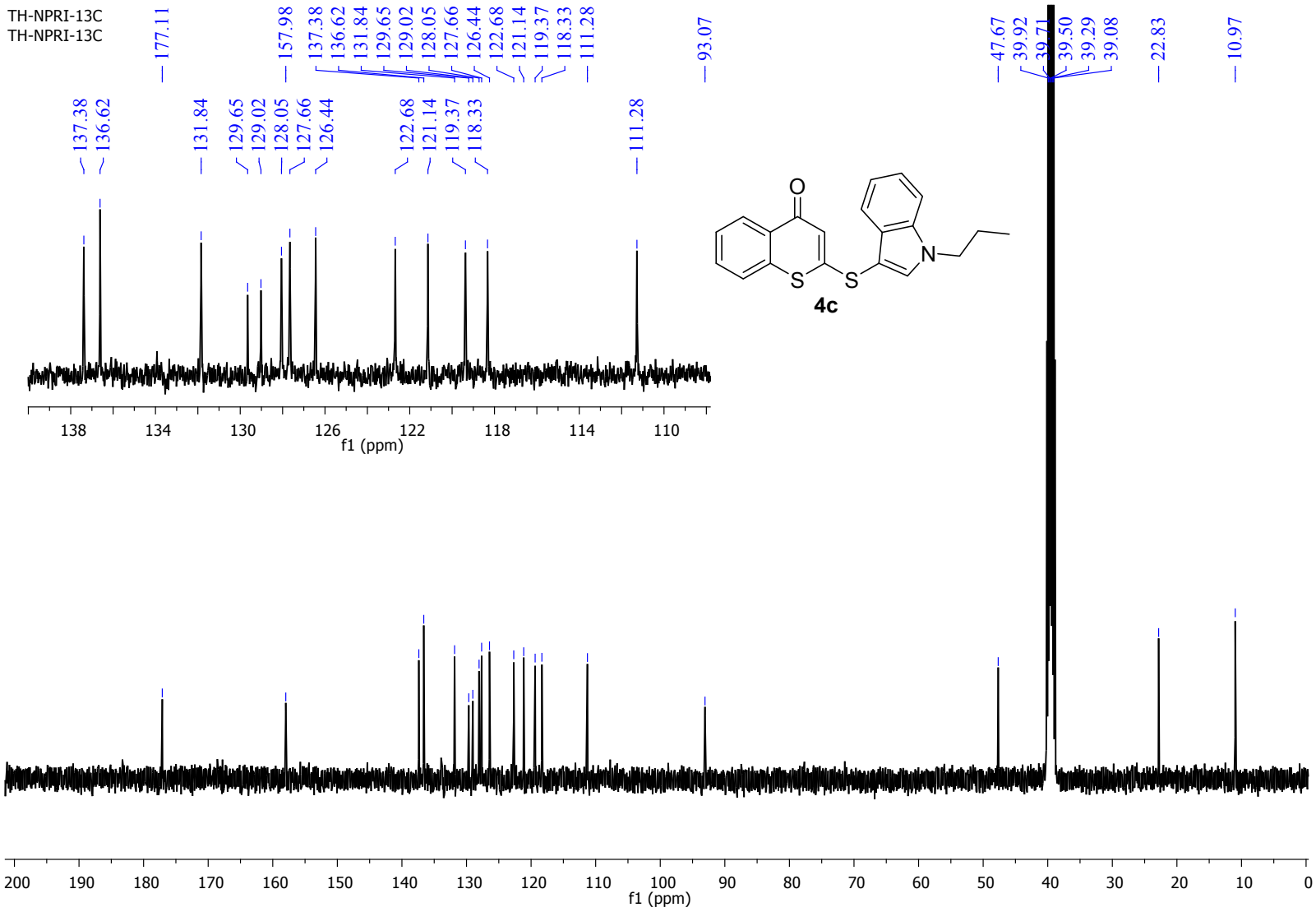
Sample Name	SM-TH-NET	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-TH-NET.d	**ACQ Method**		**Comment**		**Acquired Time**	8/17/2018 11:21:45 AM



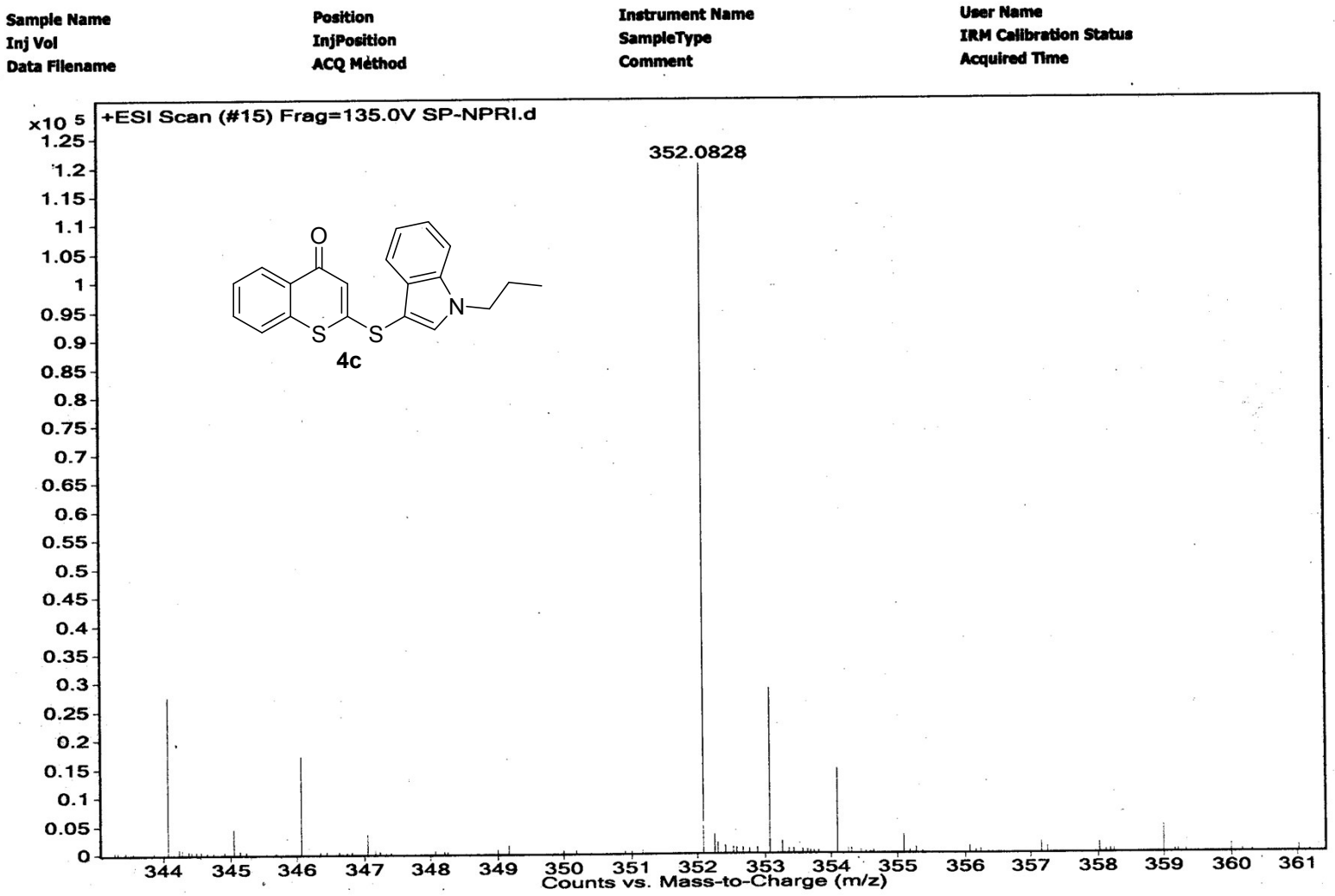
^{1}H NMR spectra of compound: 4c



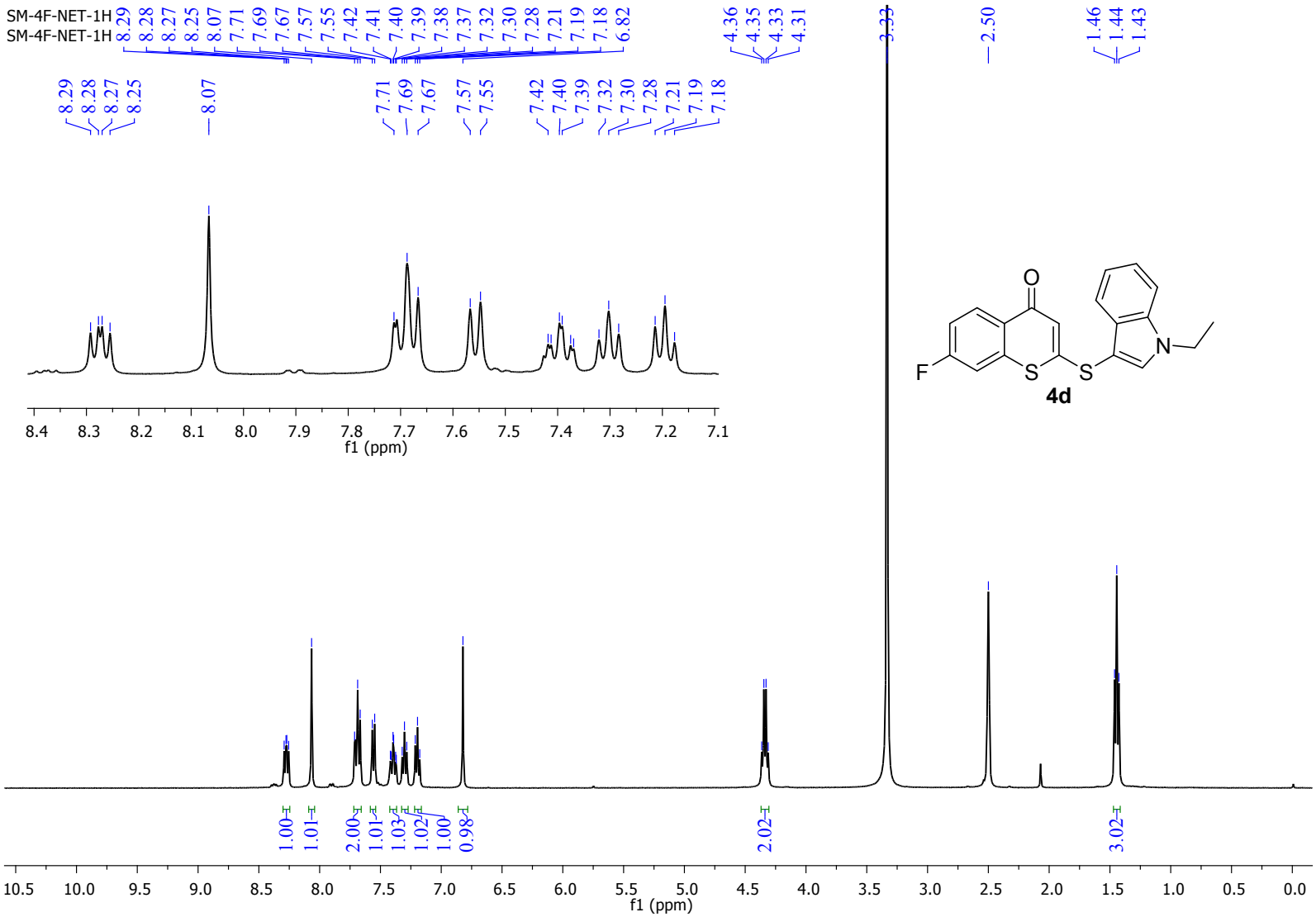
^{13}C NMR spectra of compound 4c



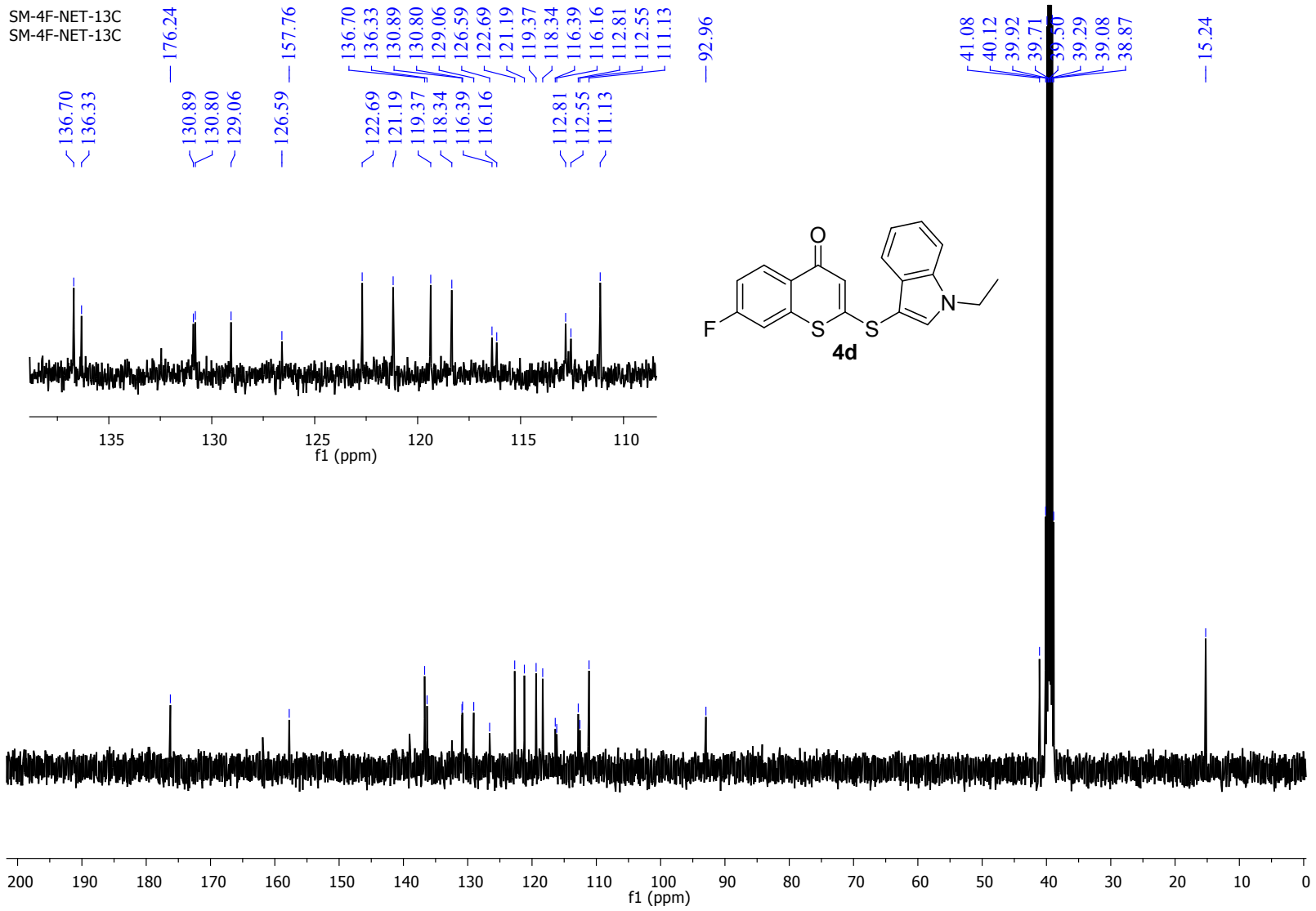
HRMS spectra of compound 4c



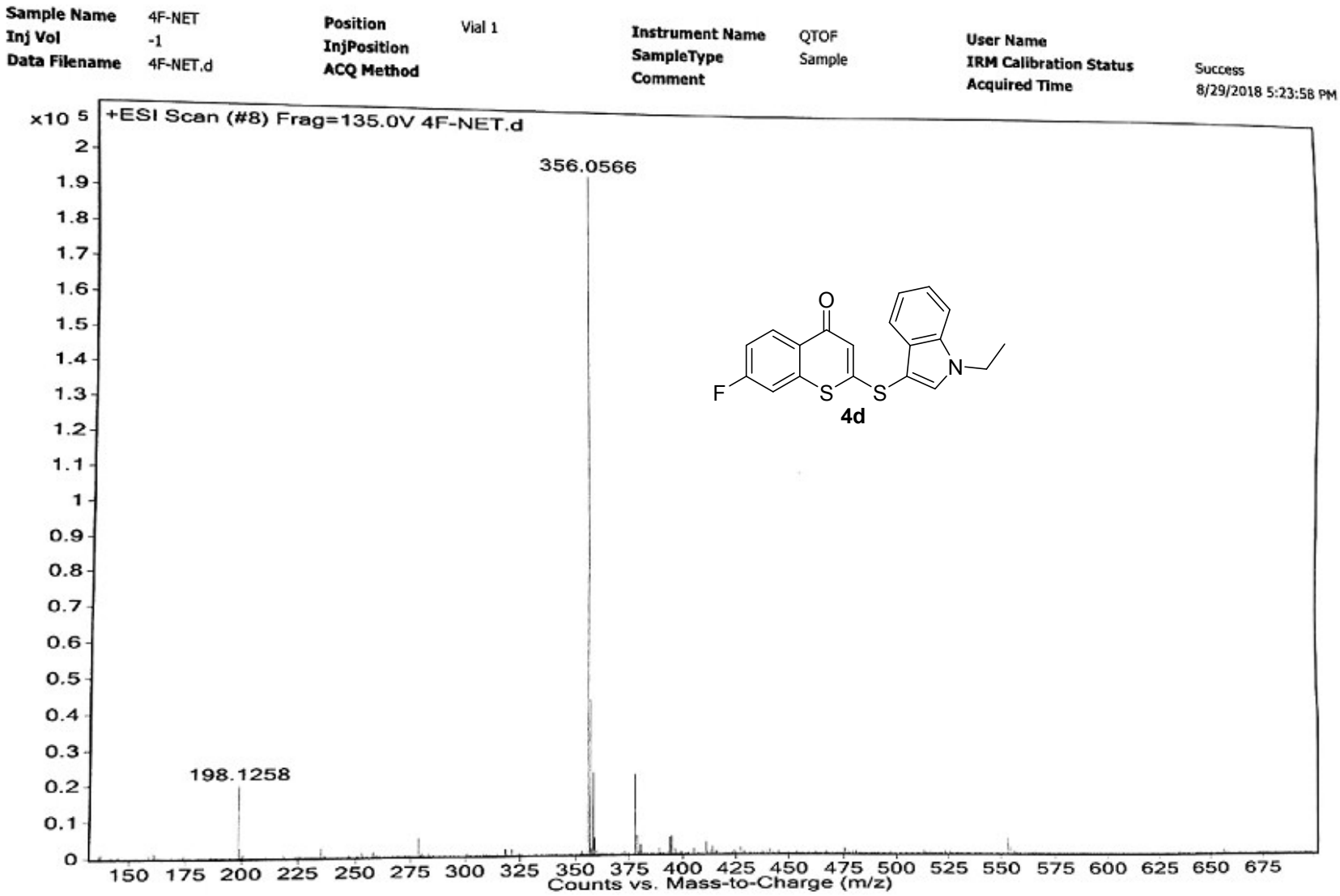
^{1}H NMR spectra of compound 4d



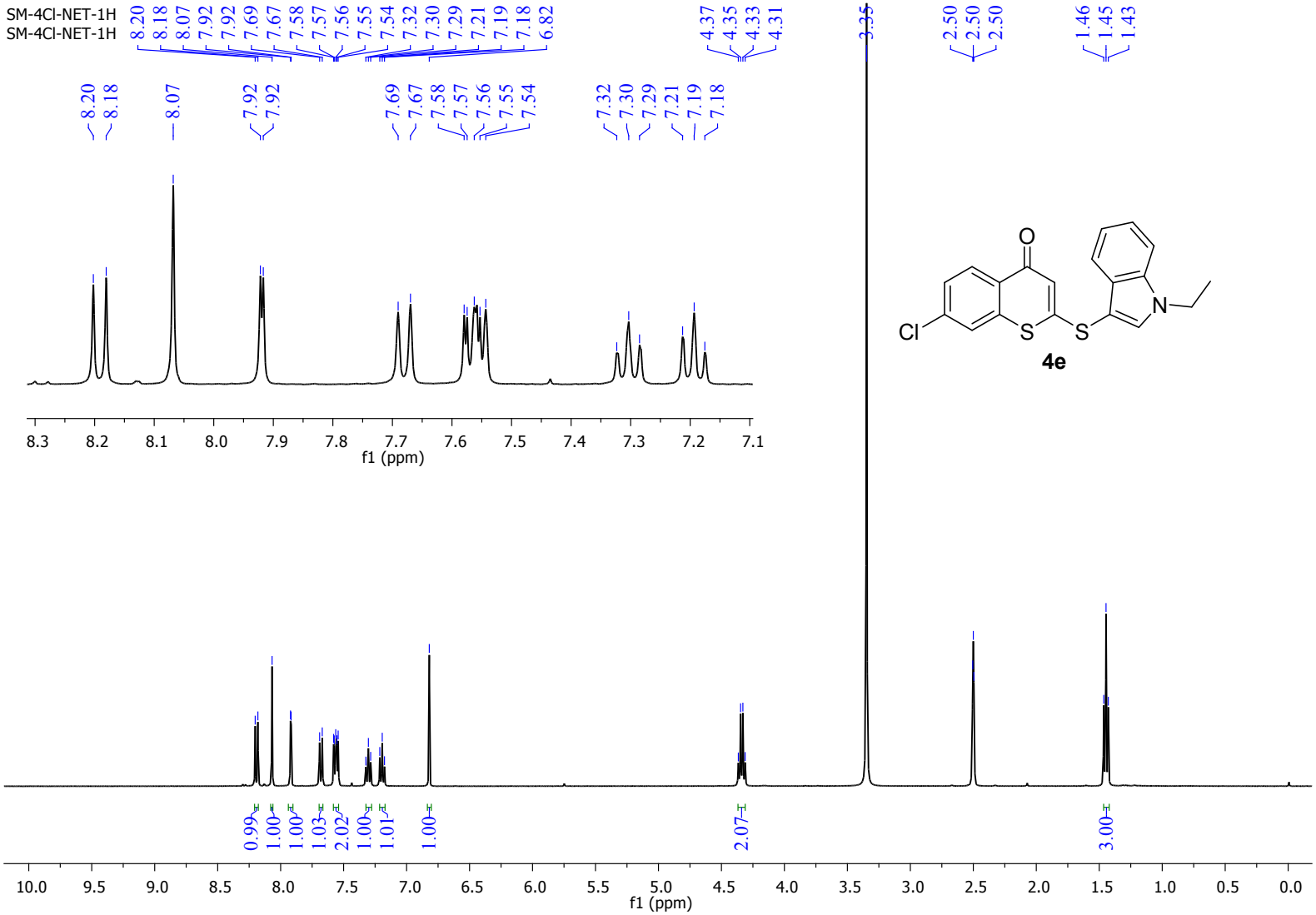
^{13}C NMR spectra of compound 4d



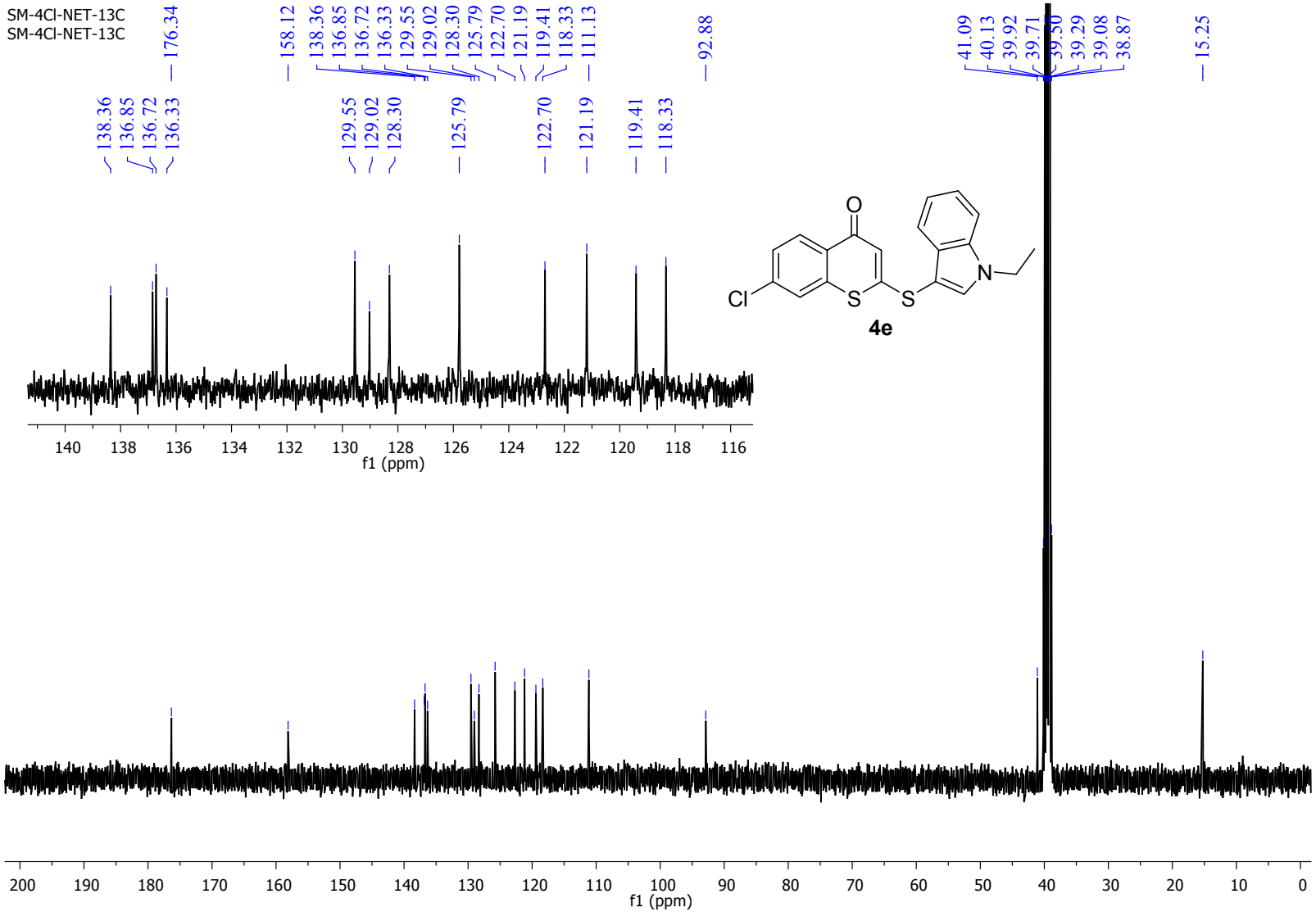
HRMS Spectra of compound 4d



^{1}H NMR spectra of compound 4e

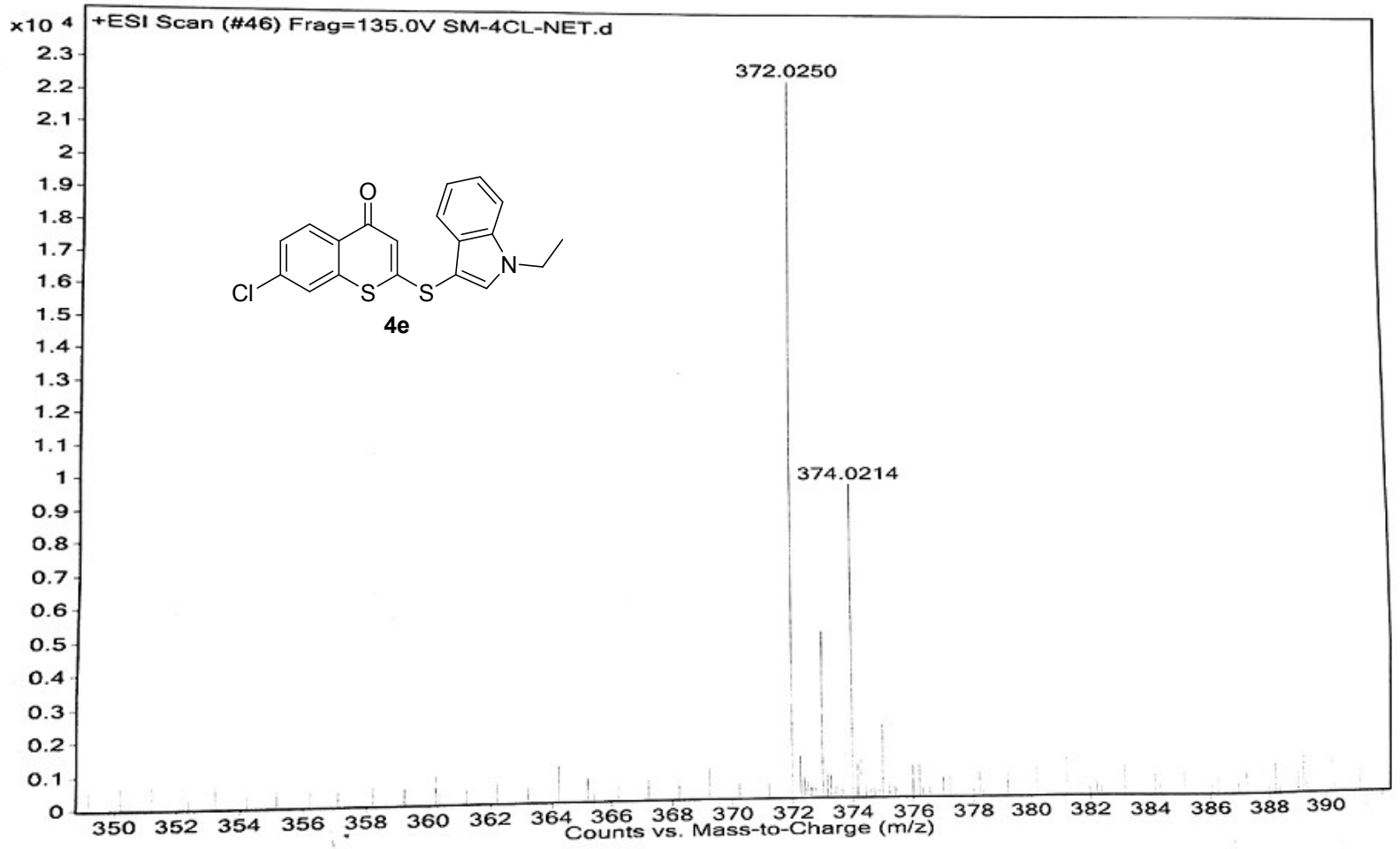


^{13}C NMR spectra of compound 4e

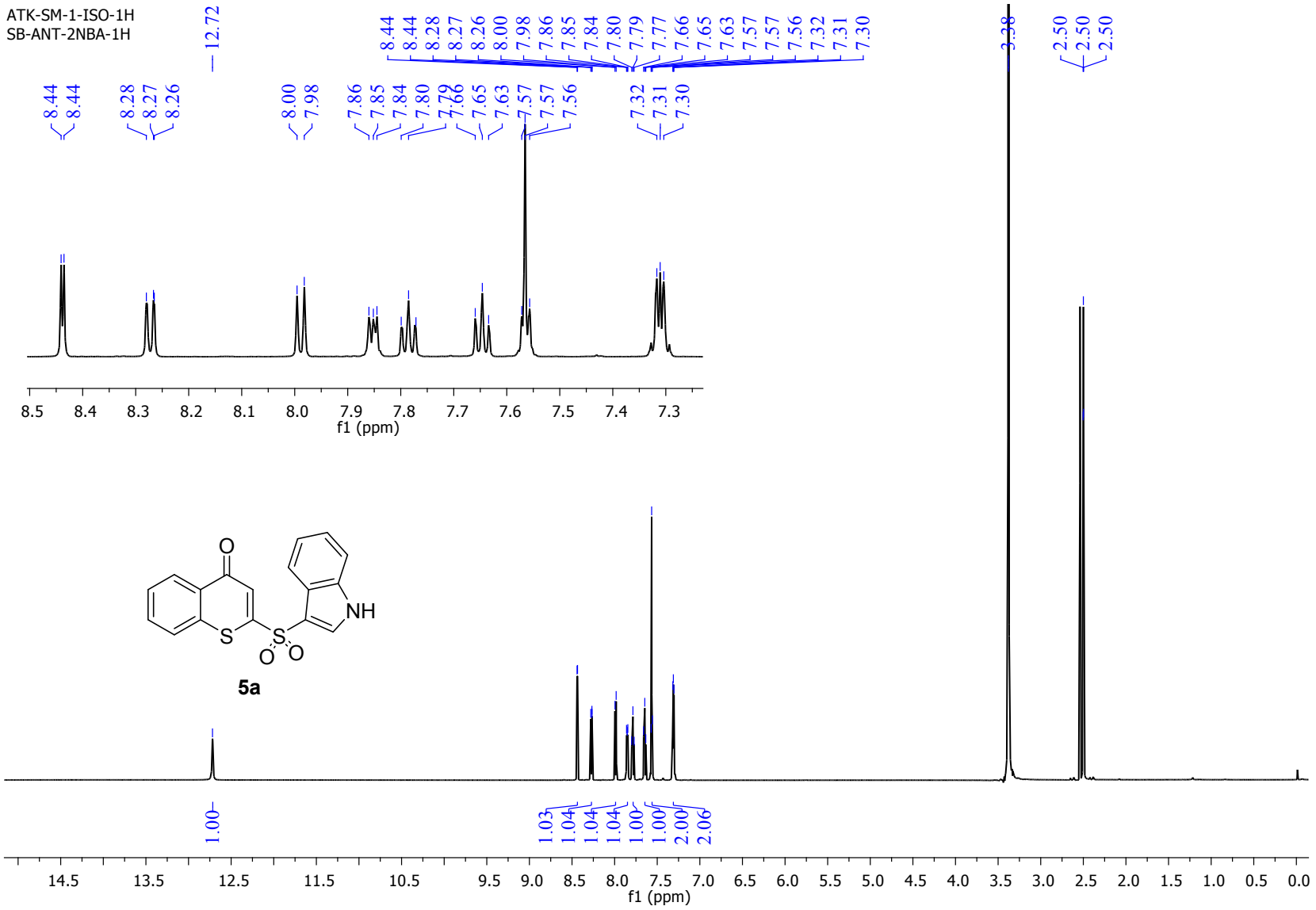


HRMS Spectra of compound 4e

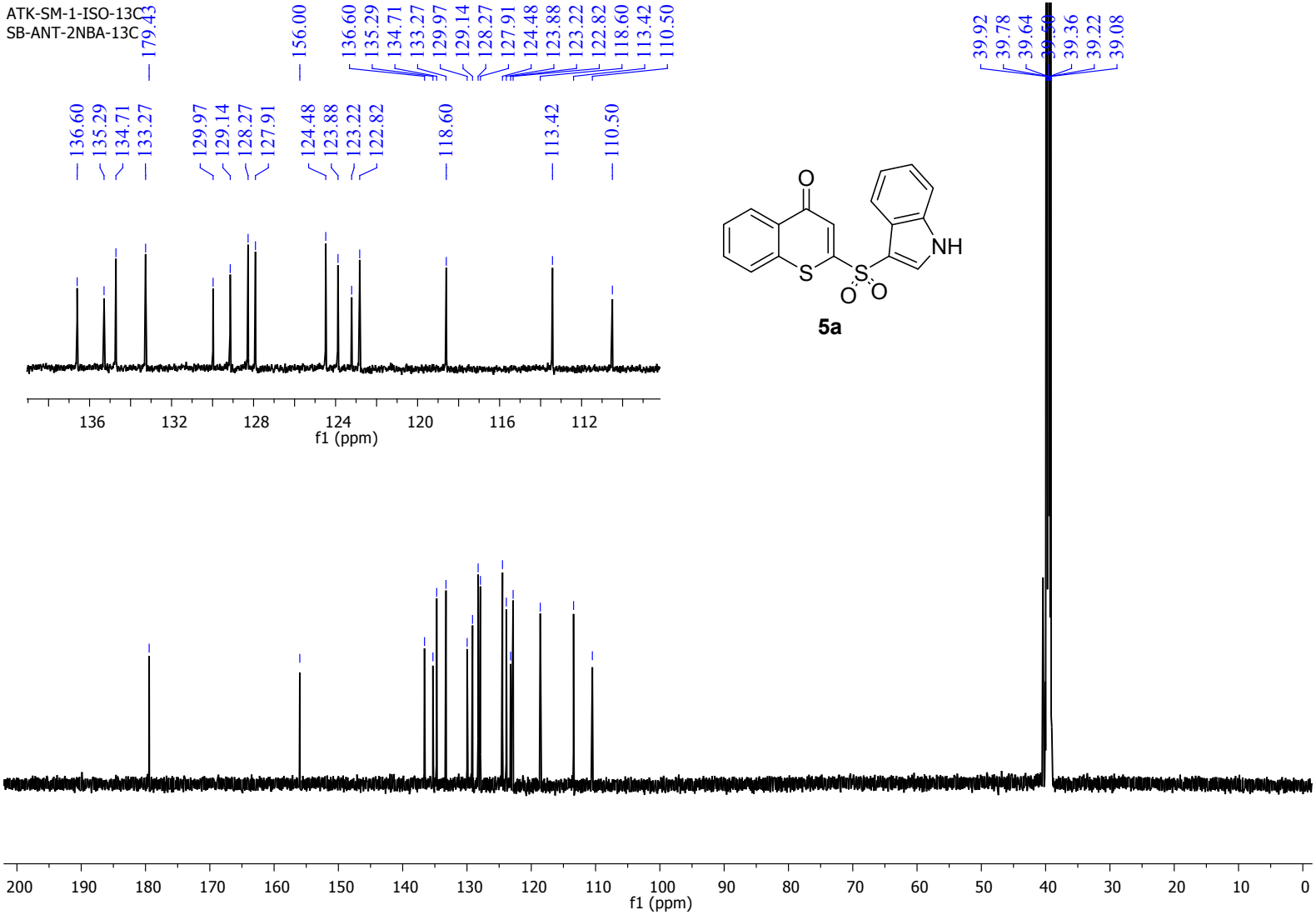
Sample Name	SM-4CL-NET	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-4CL-NET.d	**ACQ Method**		**Comment**		**Acquired Time**	8/17/2018 11:18:02 AM



^{1}H NMR spectra of compound 5a

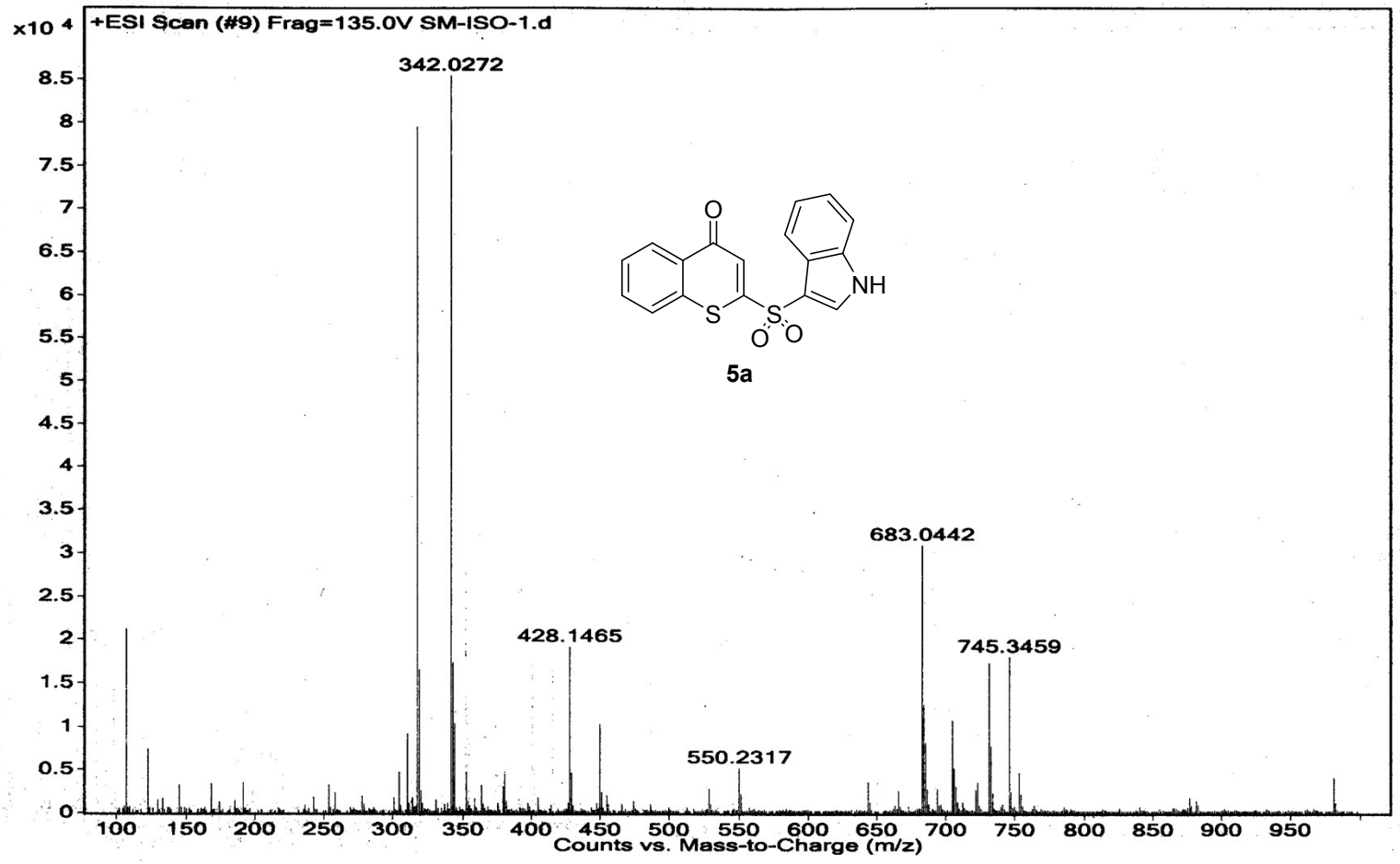


^{13}C NMR spectra of compound 5a



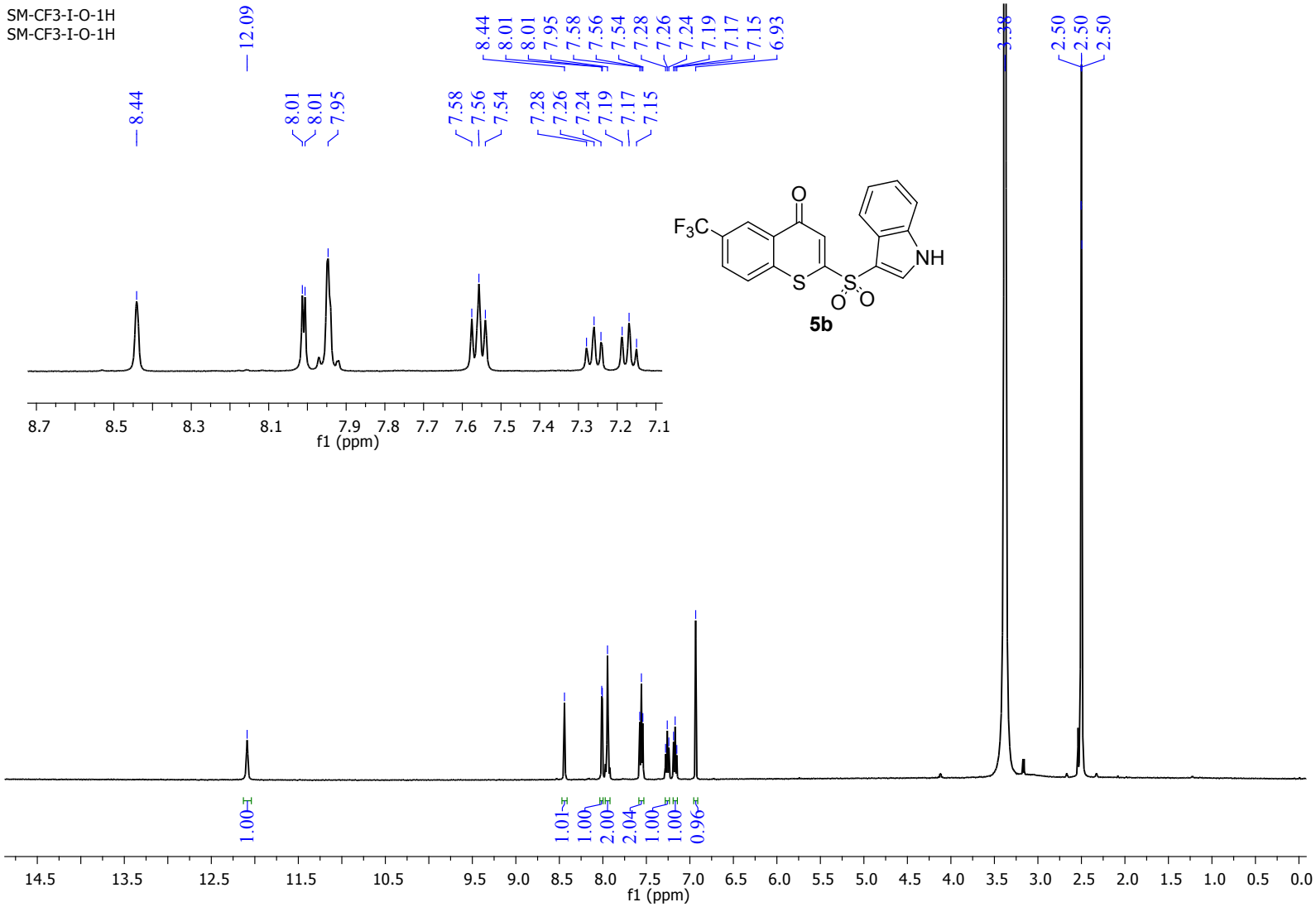
HRMS spectra of compound 5a

Sample Name	SM-ISO-1	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-ISO-1.d	**ACQ Method**		**Comment**		**Acquired Time**	7/30/2018 9:33:57 AM

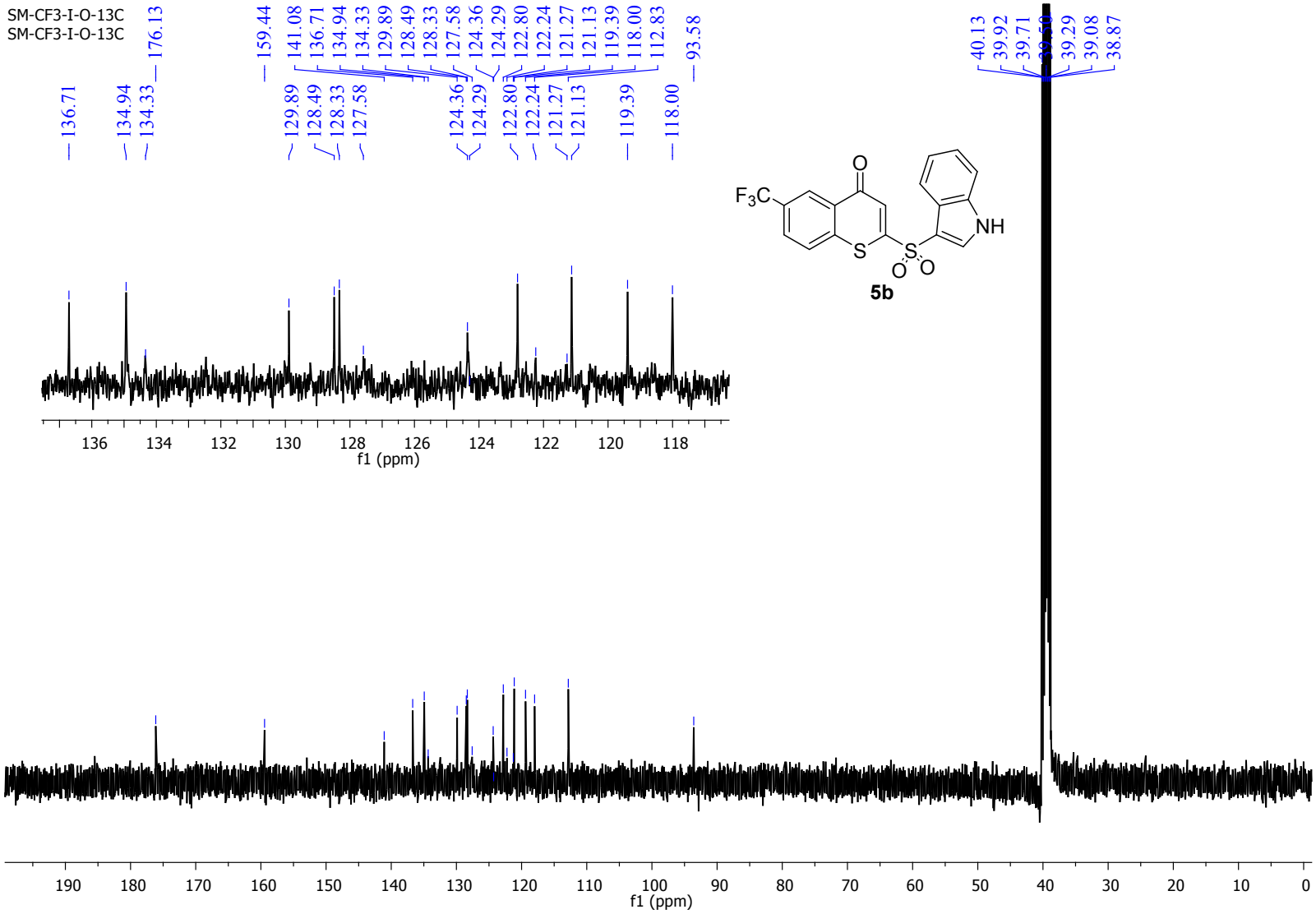


5a

^{1}H NMR spectra of compound 5b

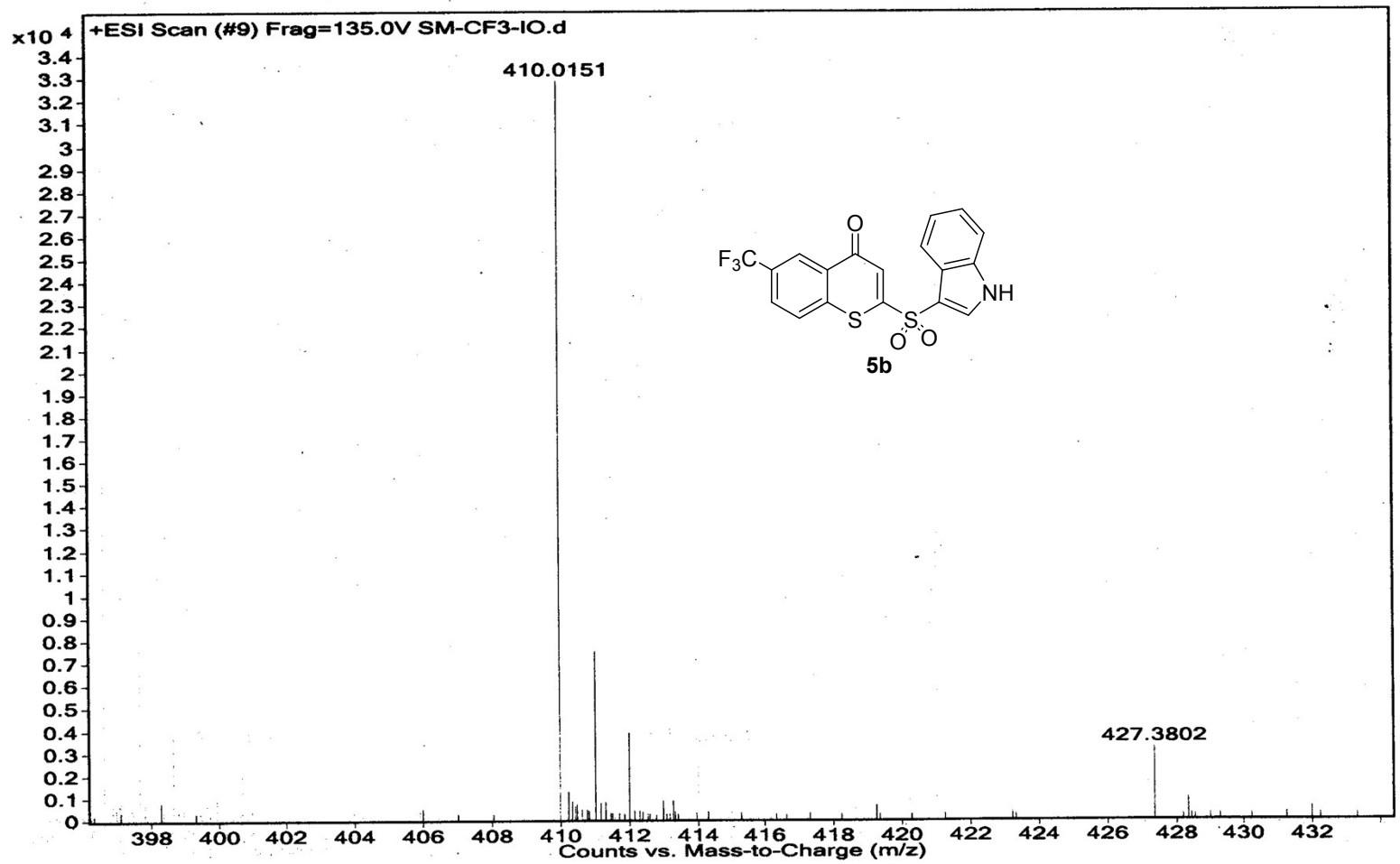


^{13}C NMR spectra of compound 5b

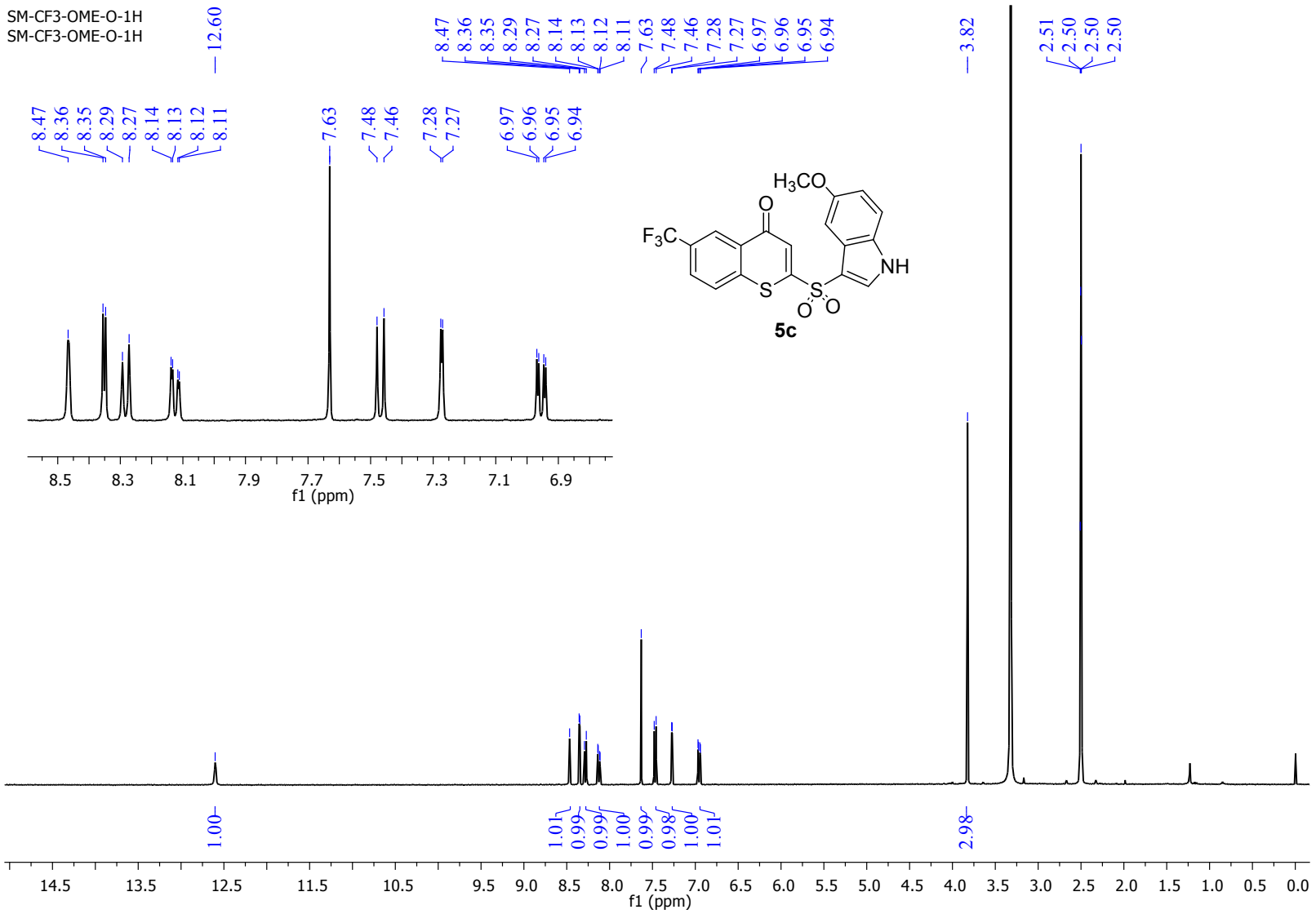


HRMS spectra of compound 5b

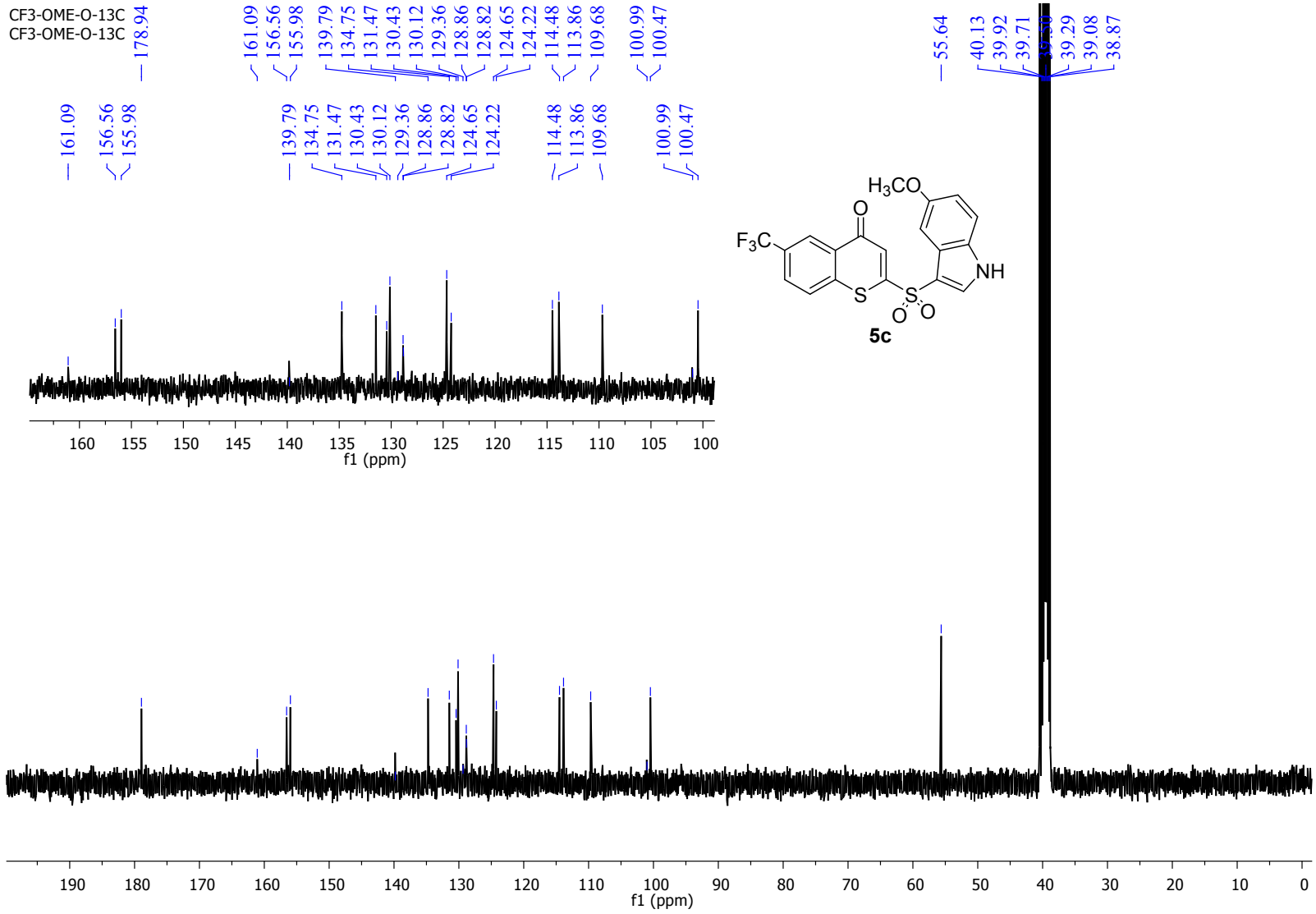
Sample Name	SM-CF3-IO	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-CF3-IO.d	**ACQ Method**		**Comment**		**Acquired Time**	7/30/2018 9:45:32 AM



^{1}H NMR spectra of compound 5c

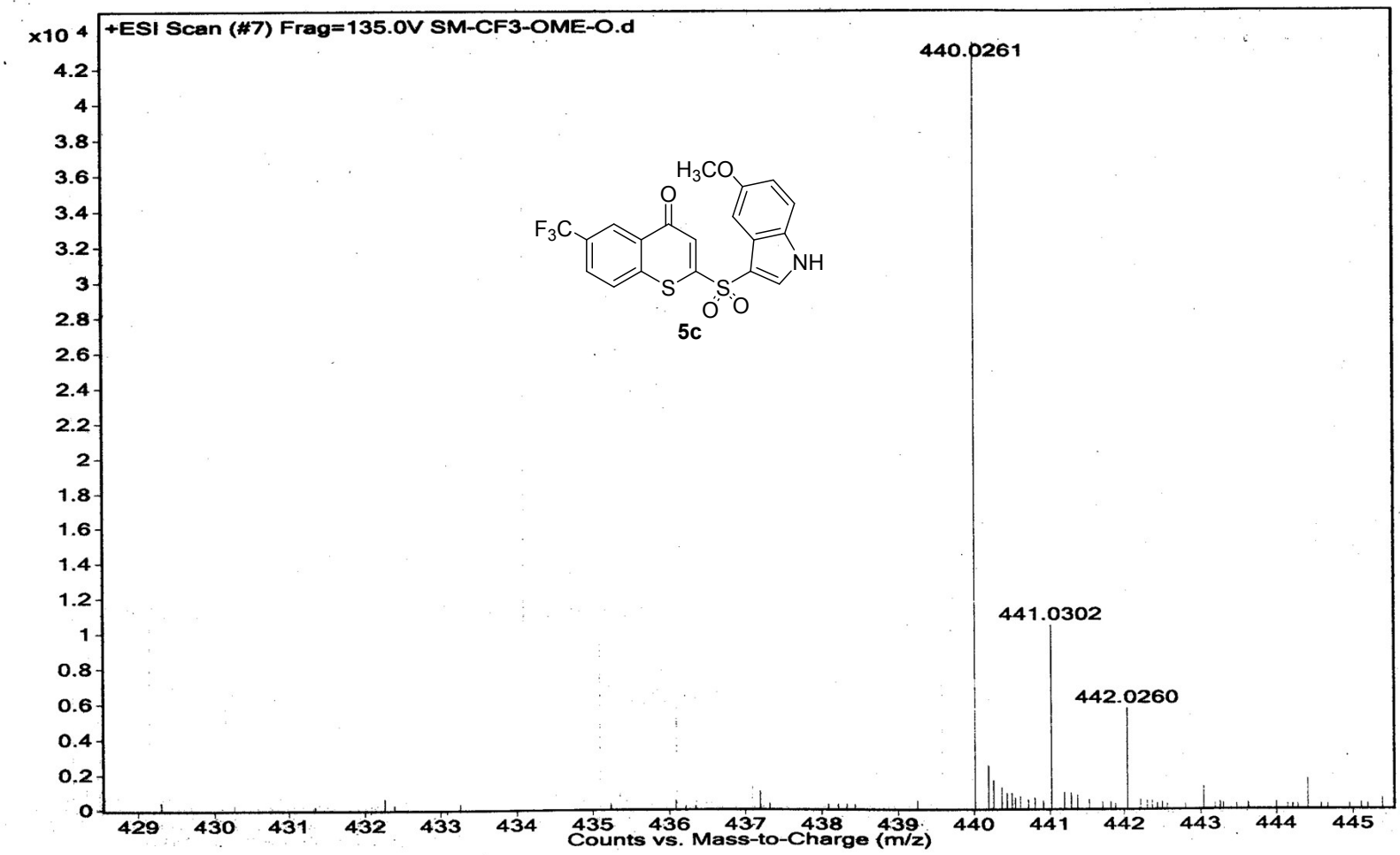


^{13}C NMR spectra of compound: 5c

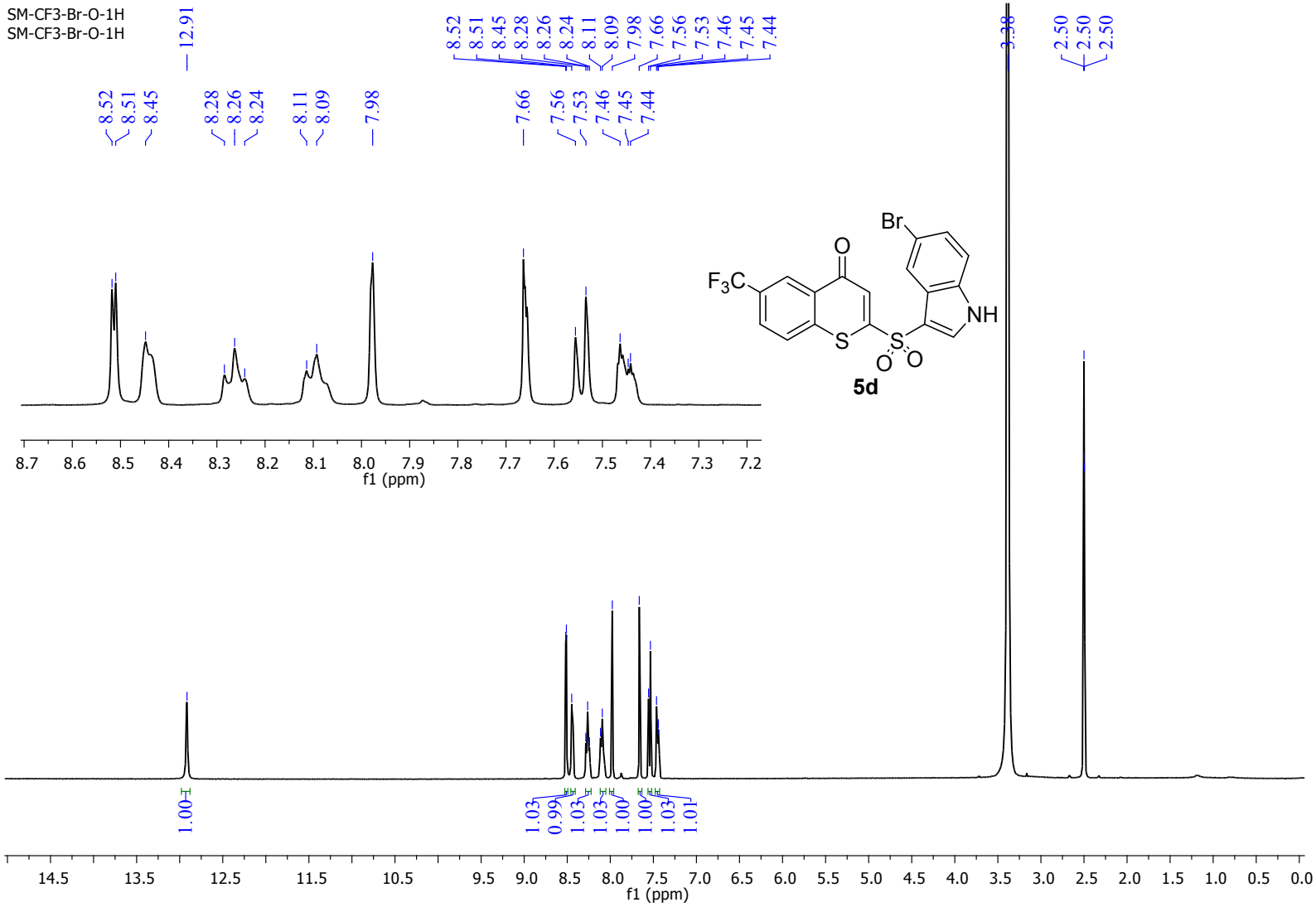


HRMS spectra of compound: 5c

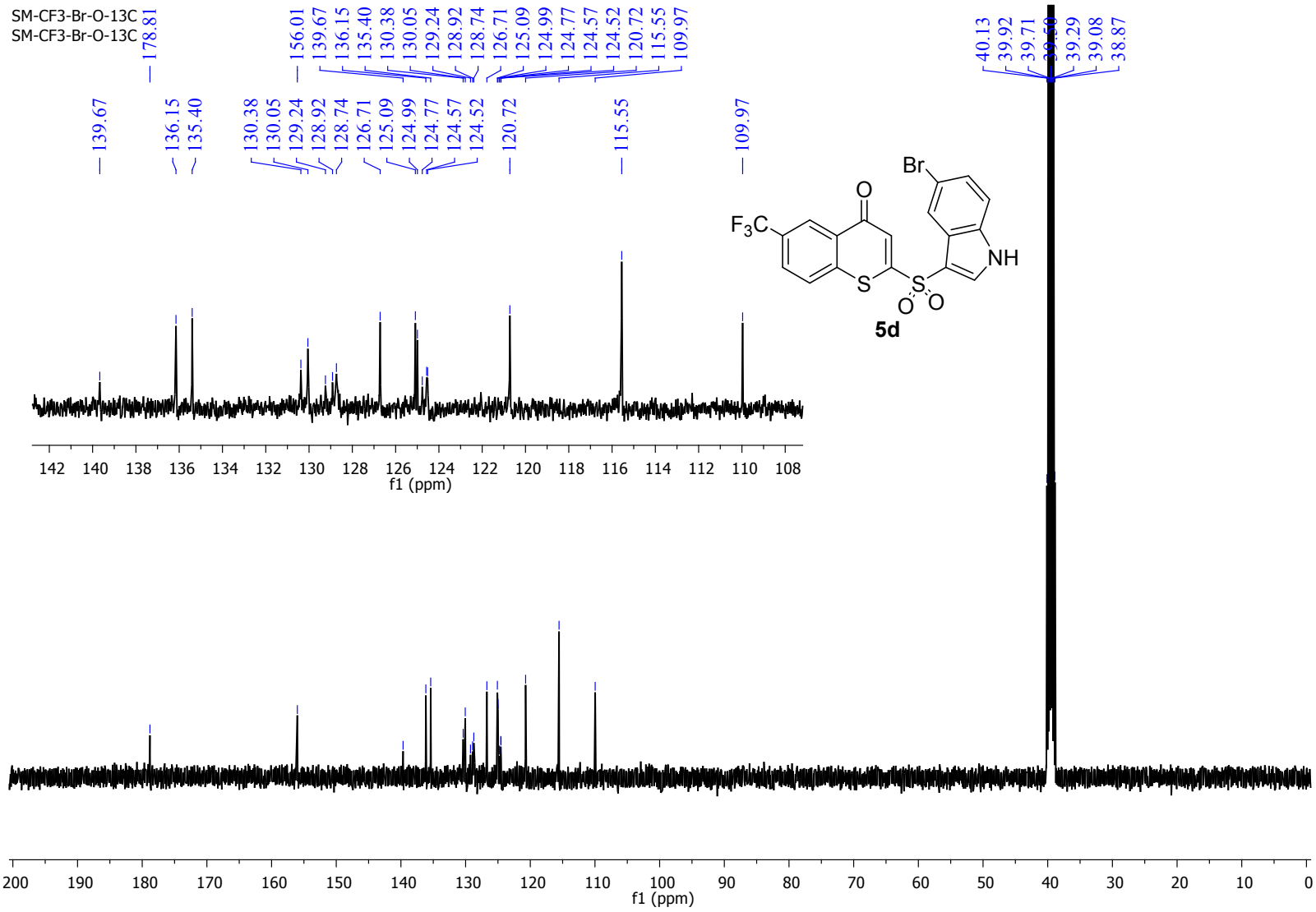
Sample Name	SM-CF3-OME-O	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-CF3-OME-O.d	**ACQ Method**		**Comment**		**Acquired Time**	7/30/2018 9:48:45 AM



^{1}H NMR spectra of compound: 5d

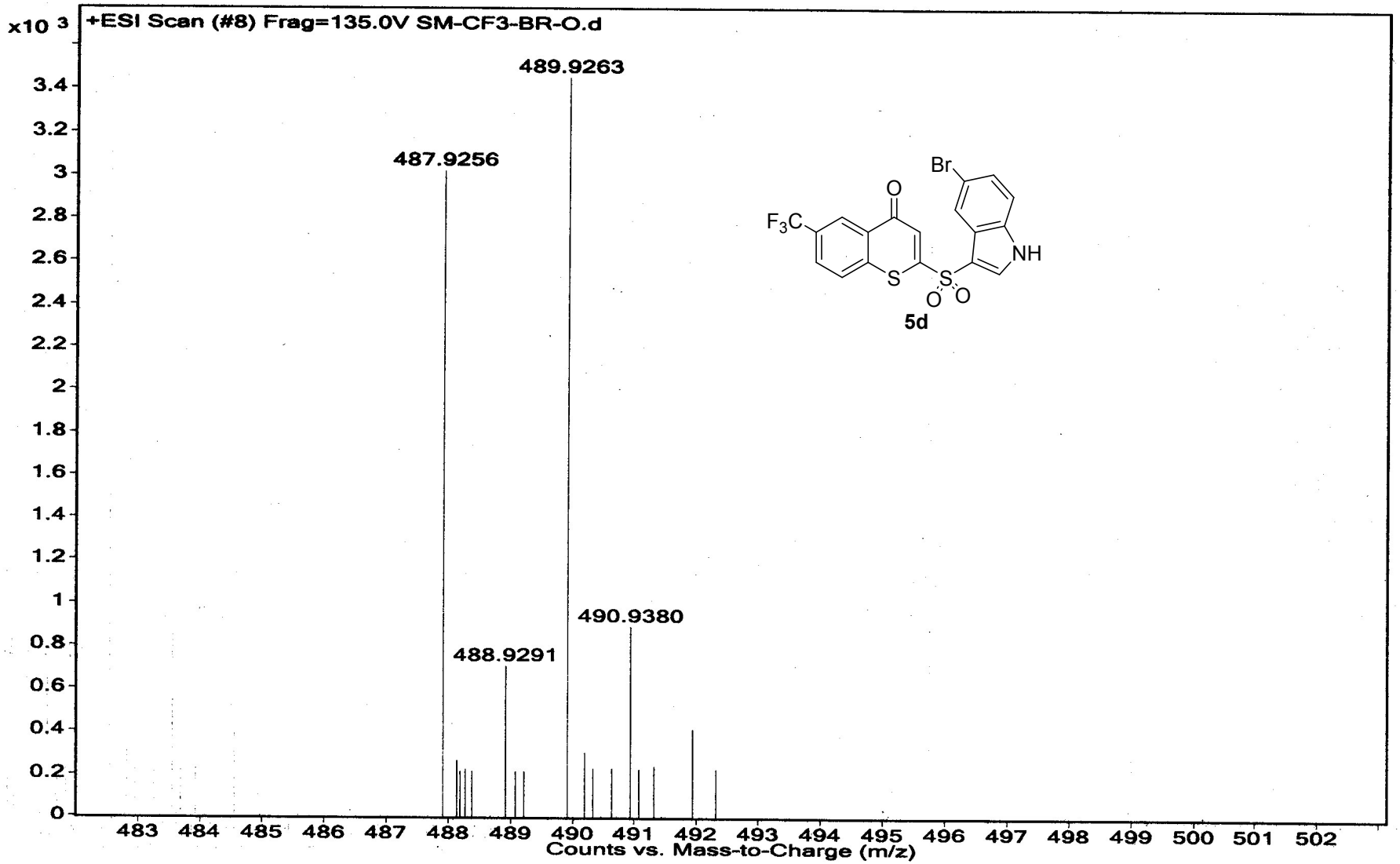


^{13}C NMR spectra of compound: 5d

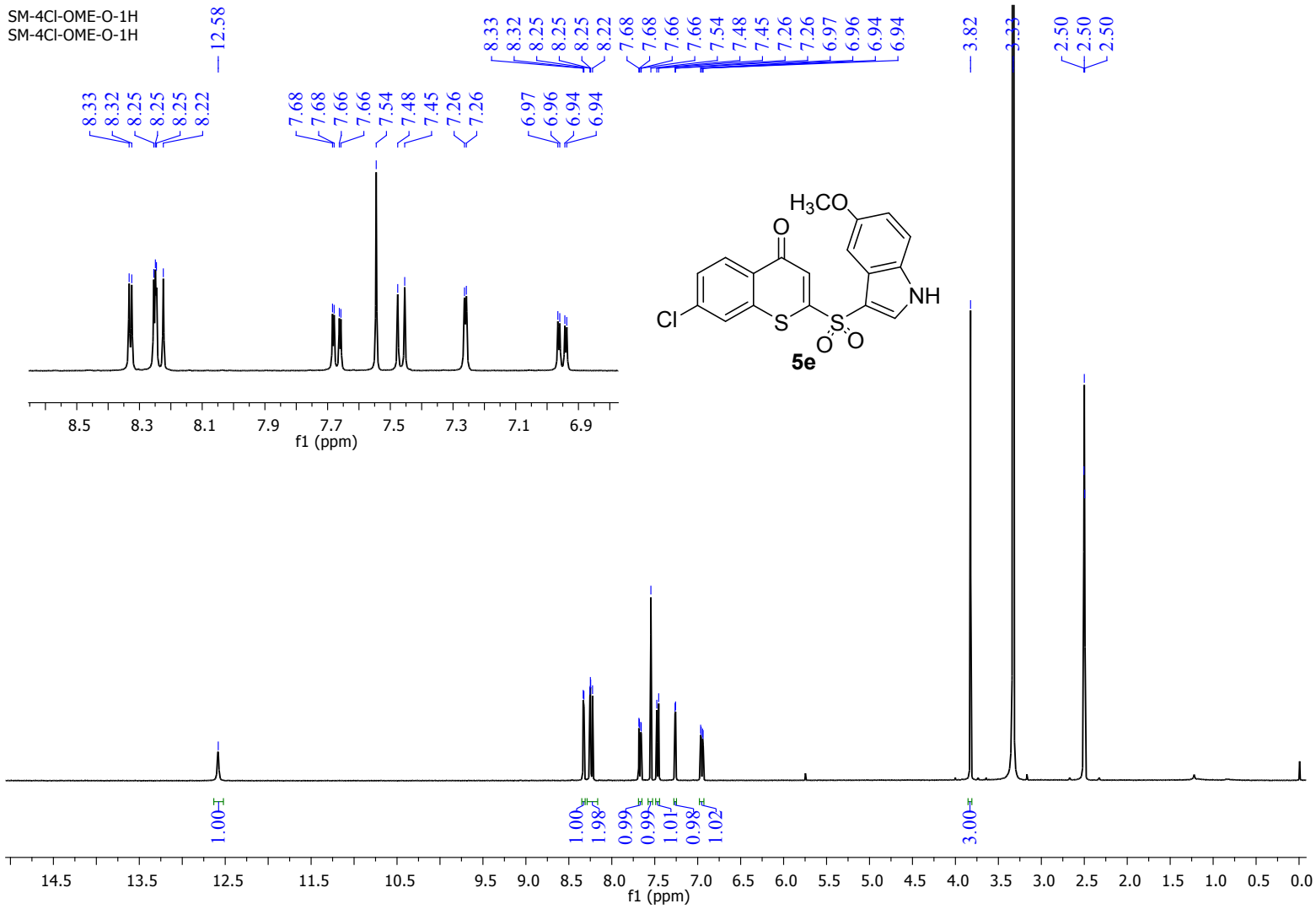


HRMS spectra of compound: 5d

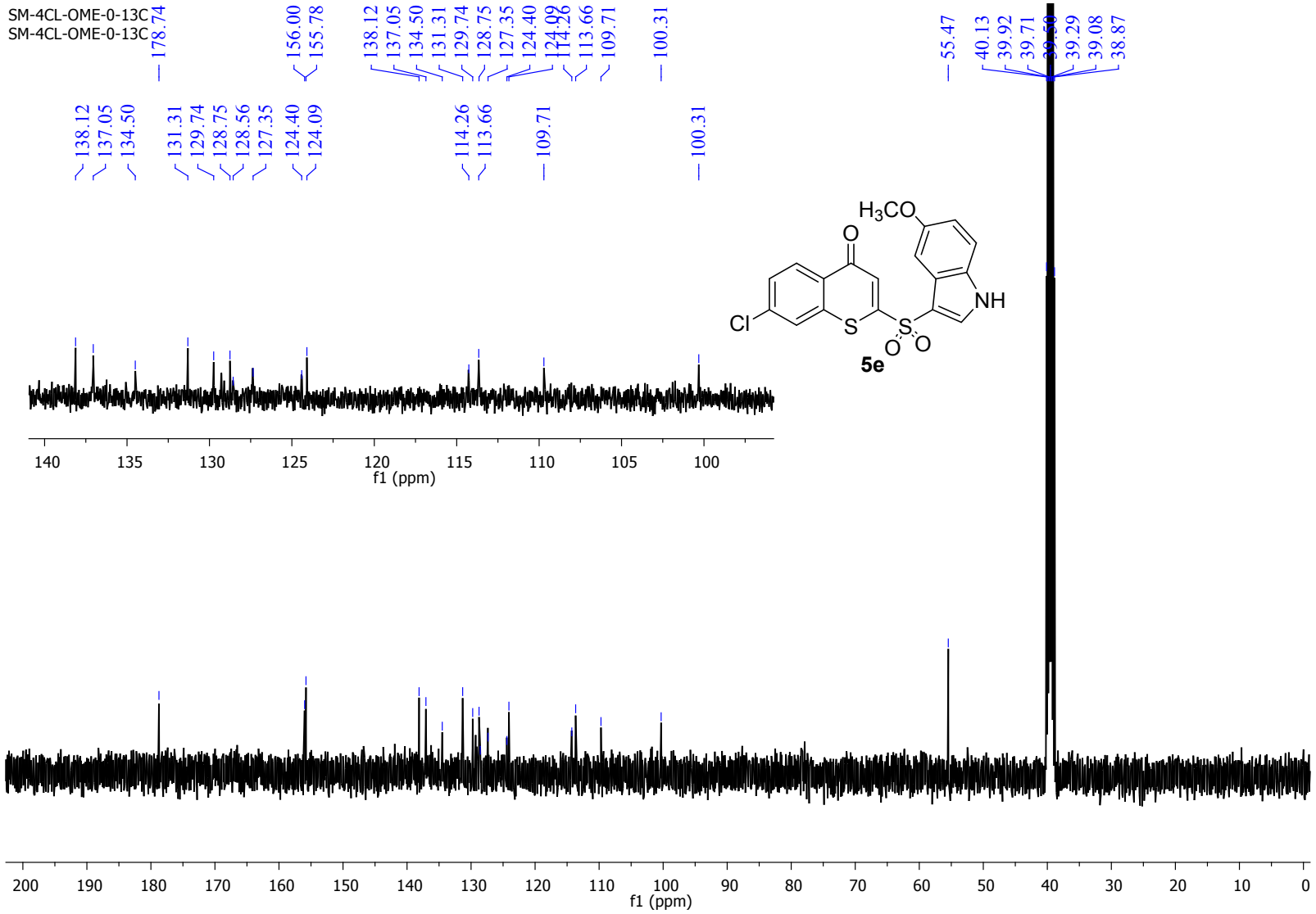
Sample Name	SM-CF3-BR-O	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-CF3-BR-O.d	**ACQ Method**		**Comment**		**Acquired Time**	7/30/2018 9:53:13 AM



^{1}H NMR spectra of compound 5e

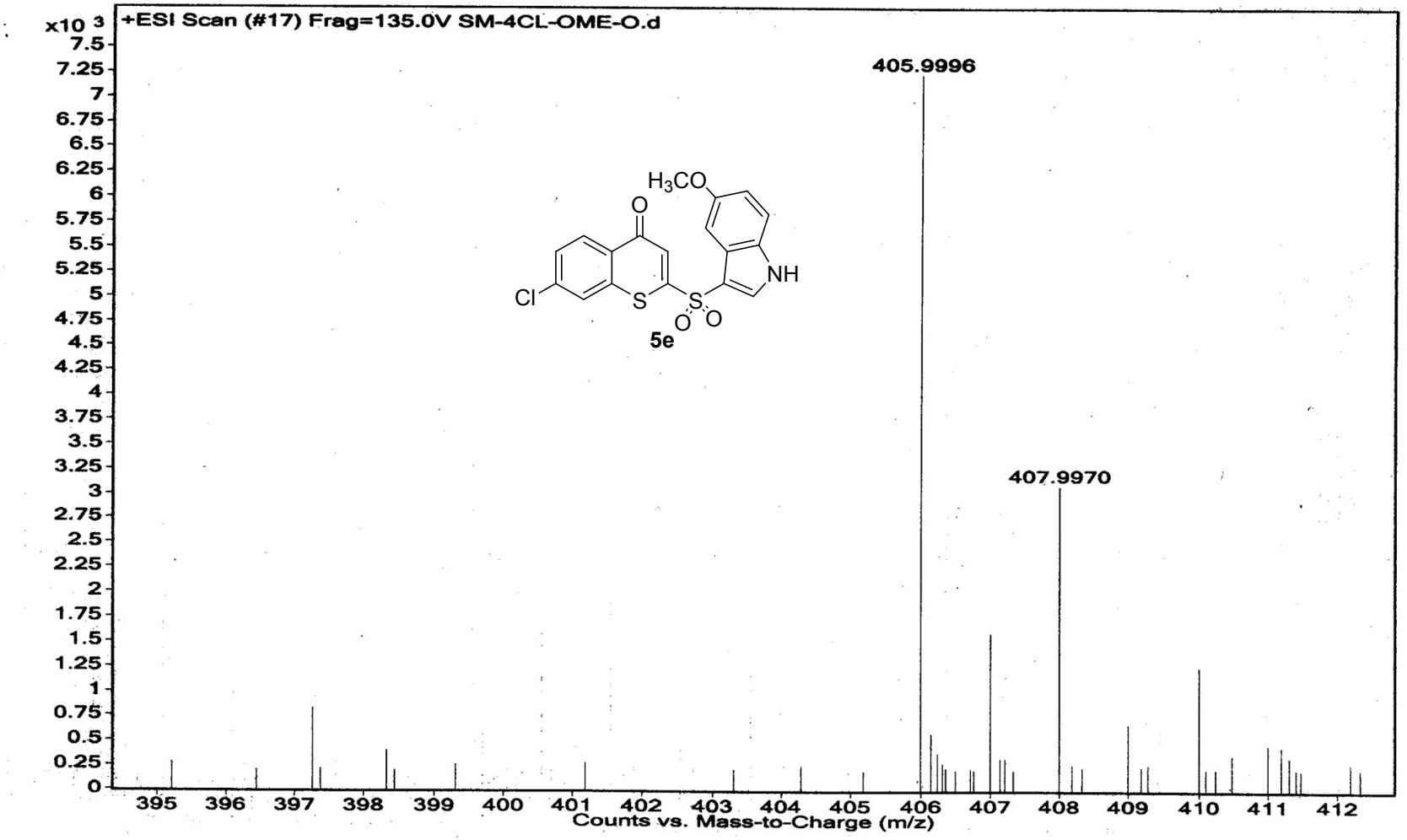


^{13}C NMR spectra of compound 5e

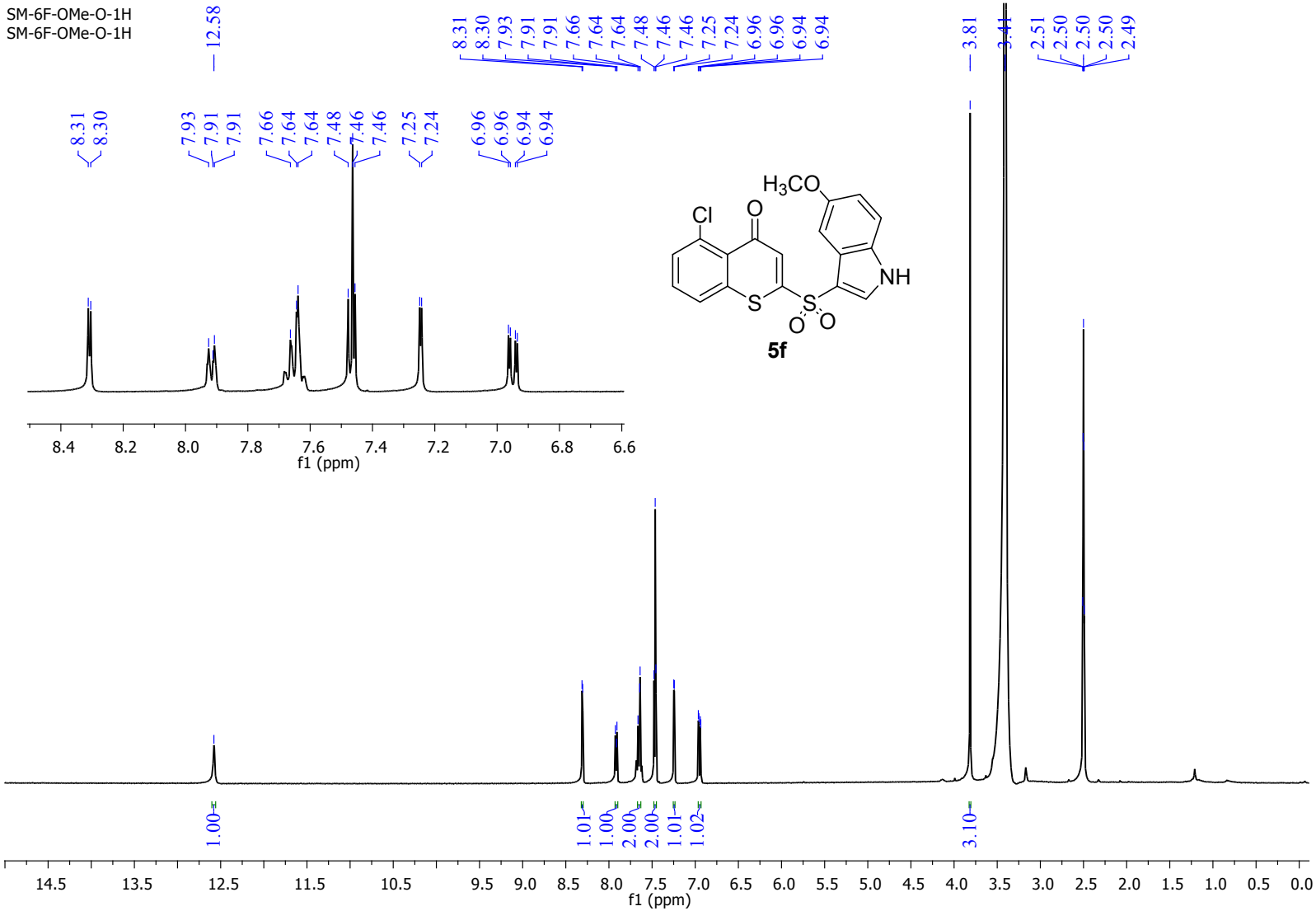


HRMS spectra of compound: 5e

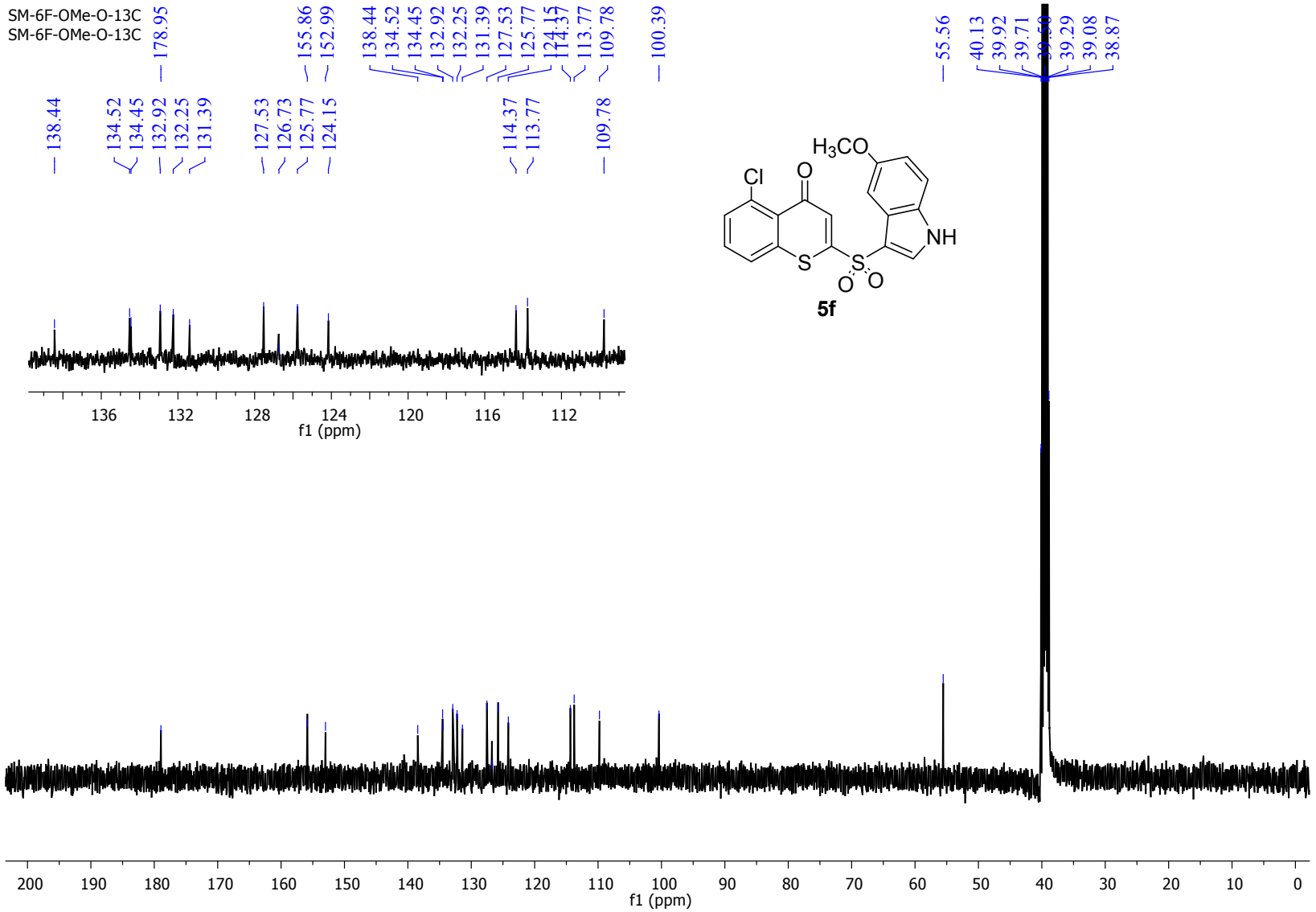
Sample Name	SM-4CL-OME-O	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-4CL-OME-O.d	**ACQ Method**		**Comment**		**Acquired Time**	7/30/2018 9:56:09 AM



^{1}H NMR spectra of compound: 5f

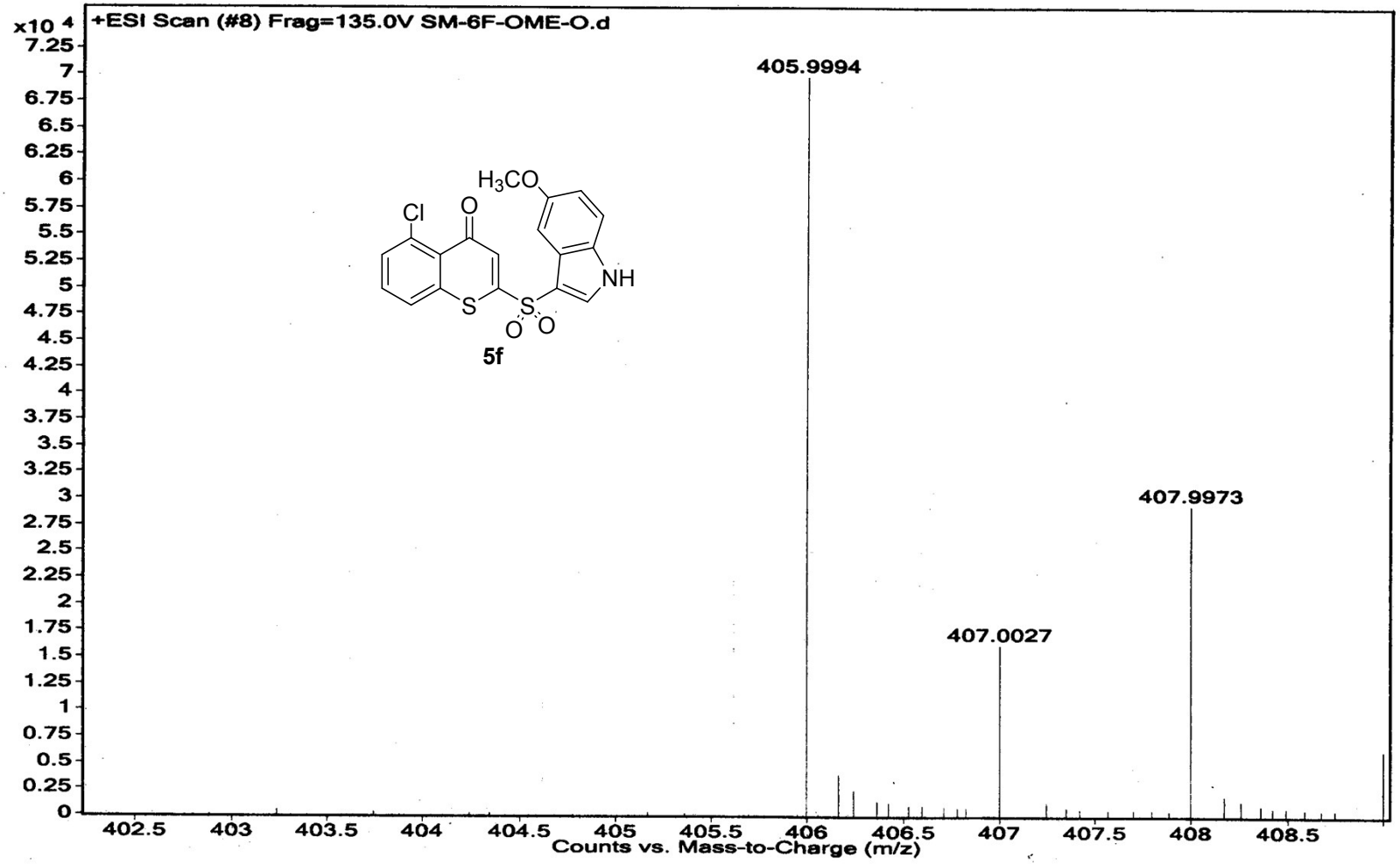


^{13}C NMR spectra of compound: 5f

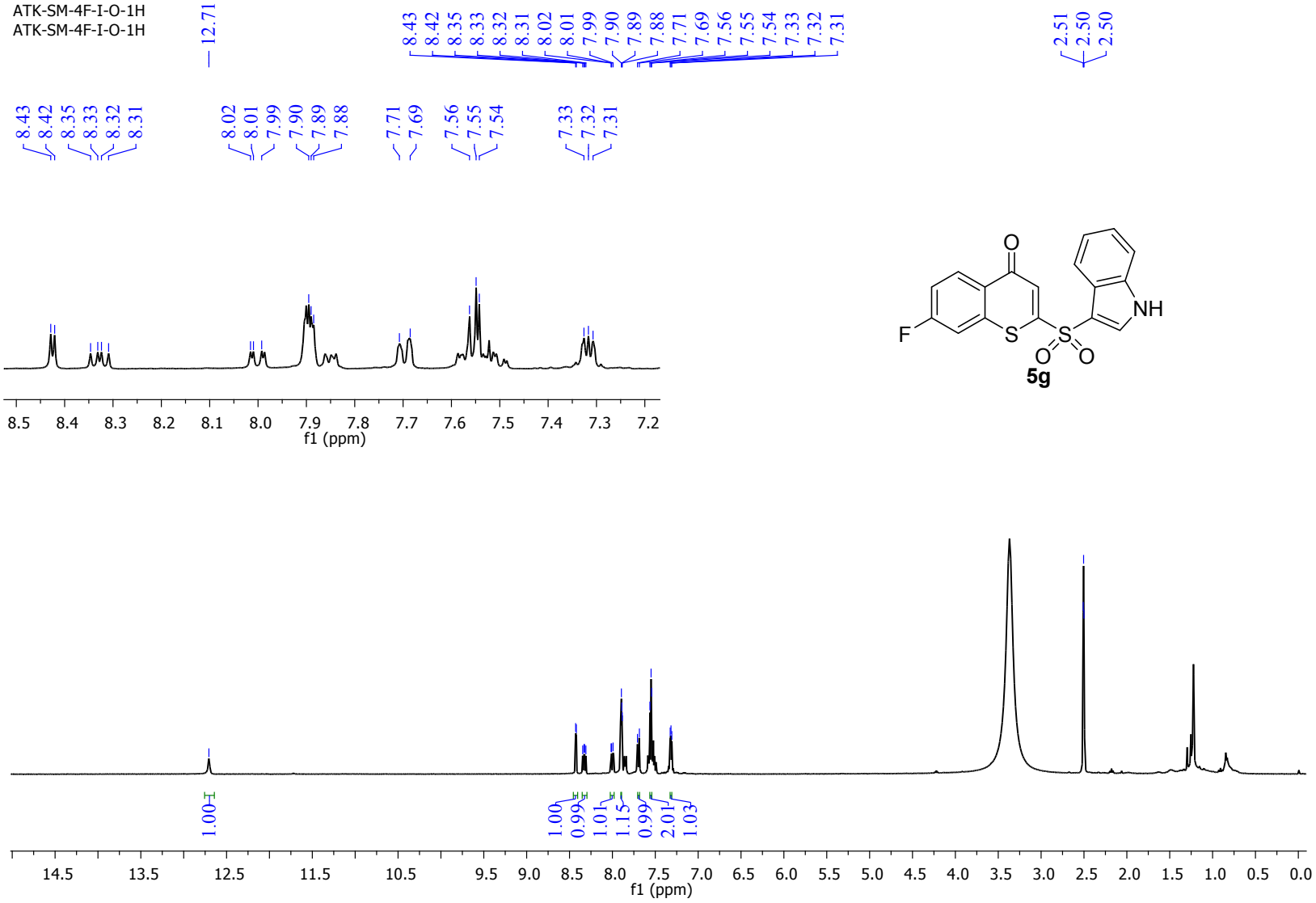


HRMS spectra of compound: 5f

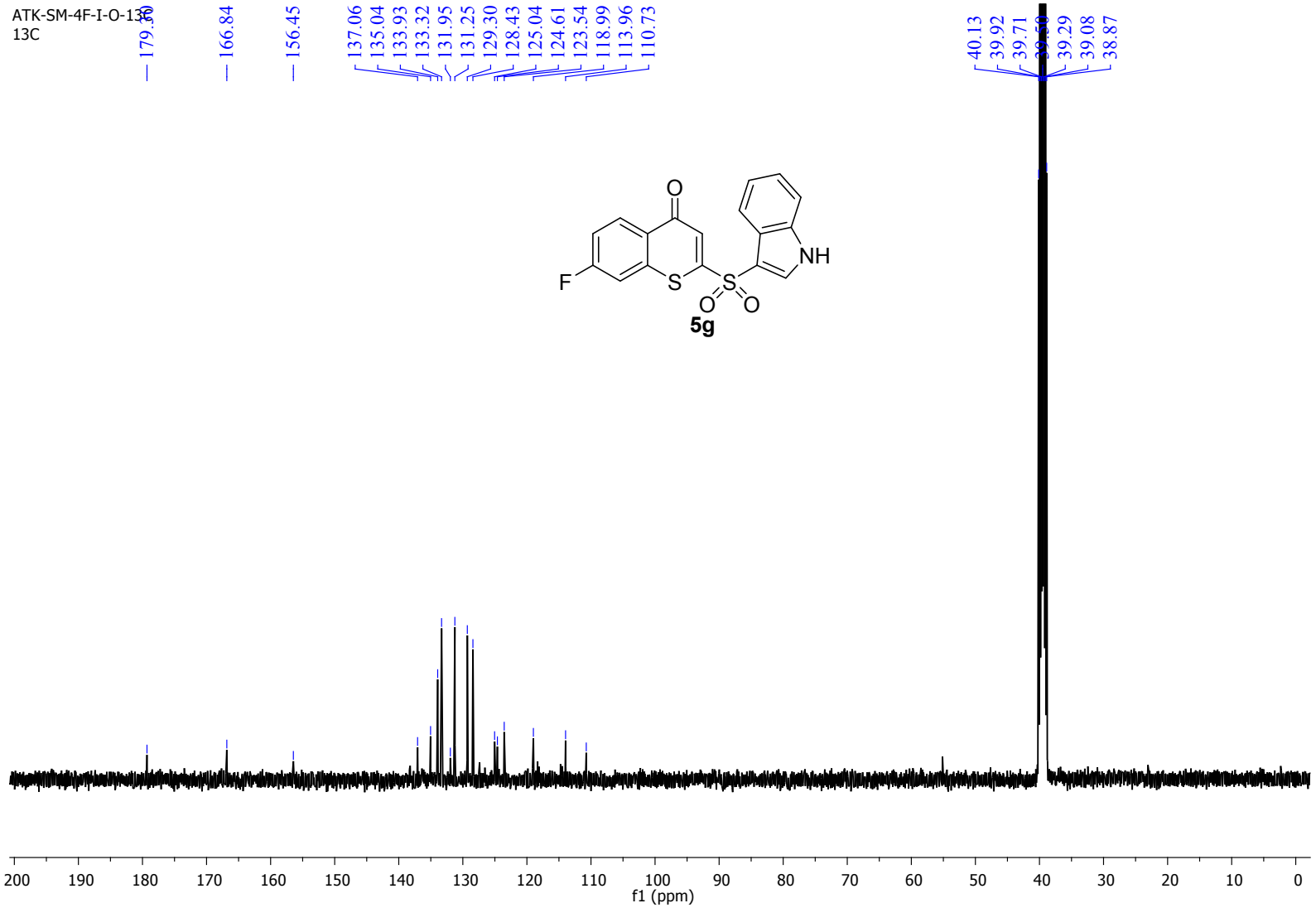
Sample Name	SM-6F-OME-O	**Position**	Vial 1	**Instrument Name**	QTOF	**User Name**	
Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	SM-6F-OME-O.d	**ACQ Method**		**Comment**		**Acquired Time**	7/30/2018 9:58:19 AM



^{1}H NMR spectra of compound: 5g

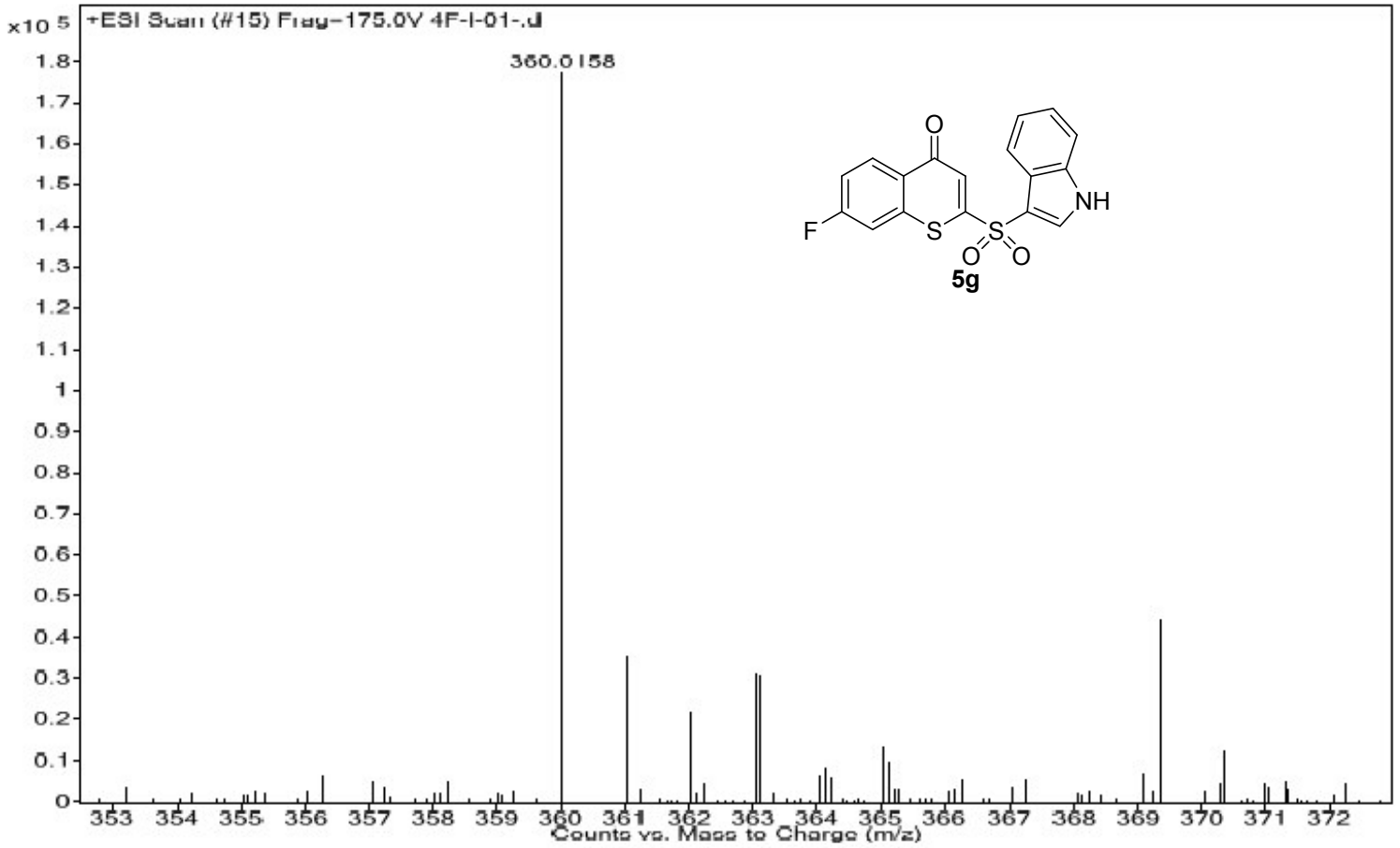


^{13}C NMR spectra of compound: 5g

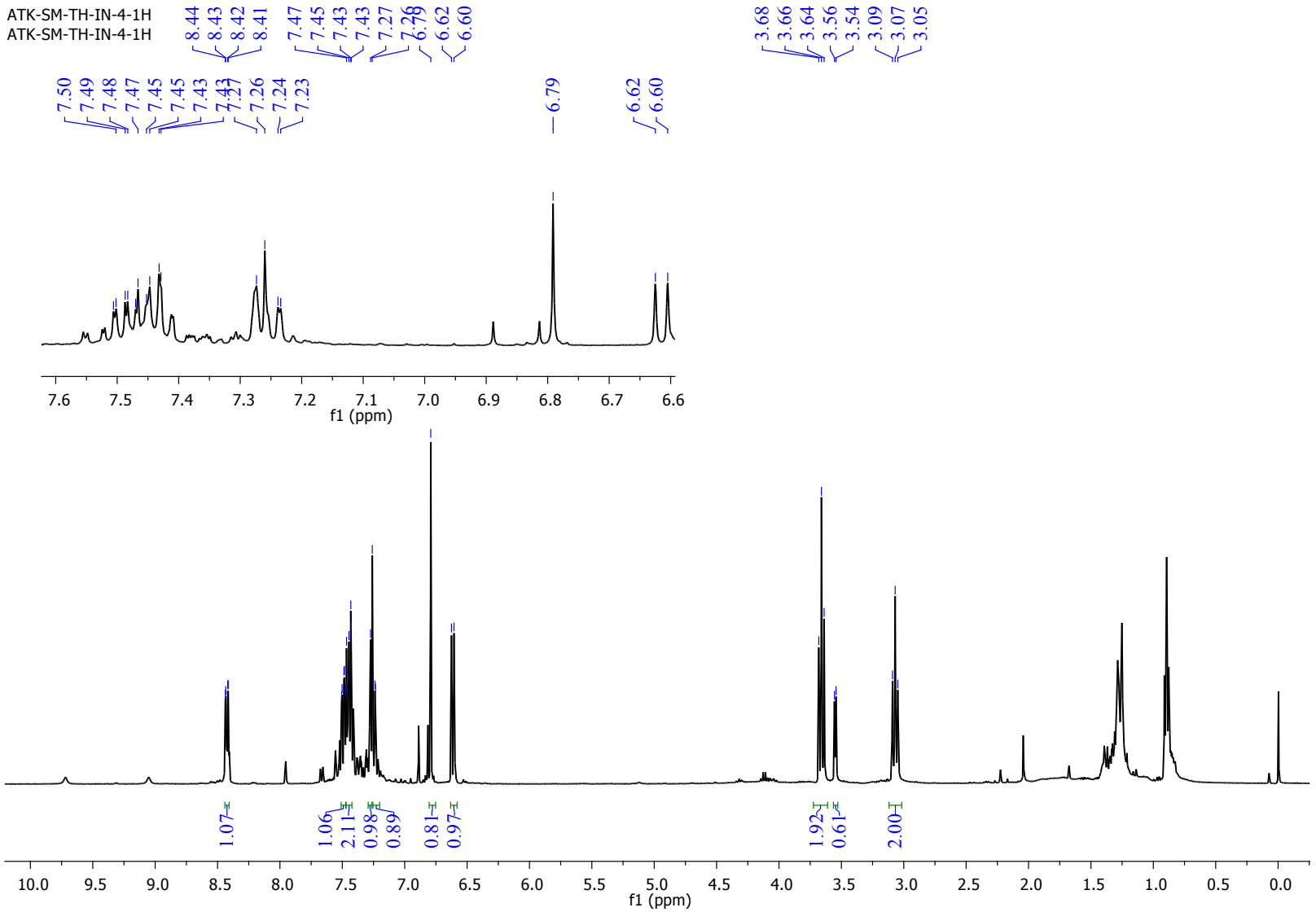


HRMS spectra of compound: 5g

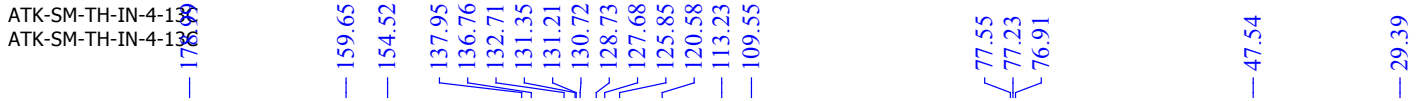
Sample Name	SAMPLE	**Position**	P2-D6	**Instrument Name**	Instrument 1	**User Name**	
Inj Vol	20	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	Success
Data Filename	4F-I-01-.d	**ACQ Method**	ESI ALS 100-1000.m	**Comment**		**Acquired Time**	6/27/2019 5:56:36 PM

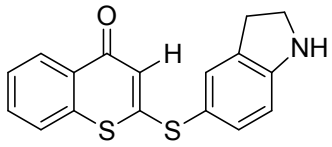


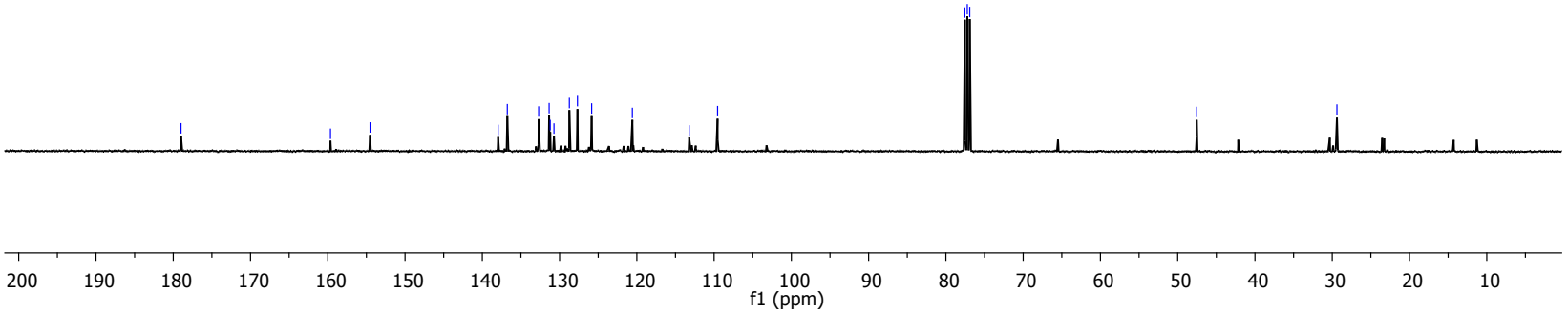
^{1}H NMR spectra of compound: 7



^{13}C NMR spectra of compound: 7







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