

Electronic Supporting Information

Synthesis of biologically active fused 1,4-oxathiin derivatives from 4-hydroxydithiocoumarins, arylacetylenes and dimethyl sulfoxide by Cu(I)-catalyzed C-H functionalization and cross-dehydrogenative C-S coupling reaction^{‡†}

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1. General Information and Methods

¹H and ¹³C NMR spectra were recorded on 600 MHz, 500 MHz and 400 MHz spectrometers, TMS as internal reference; chemical shifts (δ scale) are reported in parts per million (ppm). ¹H 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 (CCDC no. 2049895) 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. General Information and Methods for Biological Assay

Materials

Dulbecco's Modified Eagle's Medium (DMEM) from Sigma, Fetal Bovine Serum (FBS) from Gibco Thermo-Fisher Scientific, 3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyltetrazolium bromide (MTT) from Himedia, Tissue culture –Sterile PS 96wells plate from Tarsons, Human breast

cancer cell line (MCF-7)&Human cervical cancer cell line (HeLa) were procured from National Centre for Cell Science (NCCS), Pune, Dimethyl Sulfoxide (DMSO) from Emplura, Merck.

Methods

Cell Culture

Human breast cancer cell line (MCF-7)and human cervical cancer cell line (HeLa) were cultured and maintained in DMEM media, supplemented with 10% FBS, at 37 °C in aCO₂ incubator (HERA cell 150i; TheroFisher Scientific) supplied with 5% CO₂.

Cell Viability Assay

*In vitro*assessment of cytotoxicity was measured using MTT based cell-viability assay in two different cancer cell lines (MCF-7and HeLa), under 24hr observation with triplicate confirmations. MCF-7 and HeLa were seeded in 96-well plates at a uniform density of 5×10^3 cells per well and incubated for 24hr at 37 °C supplemented with 5% CO₂. Following the attachment, media containing increasing concentrations of the compounds were added to the seeded cells. 24 hours post-treatment, MTT solution was added to each well, and the plates were incubated in a CO₂incubator. MTT, a yellow tetrazolium dye, react with dehydrogenase enzymes in viable cells and isreducedto insoluble purple Formazan crystals, intensity of purple coloris directly proportional to the viable cells. Followed the Incubation, DMSO was added in each well to dissolve the insoluble purple Formazan product. The absorbance was measured at 570nm, with reference filter at 655nm in microplate reader (Bio-Rad).

Cell Viability (%) with relation to untreated cells (control) was calculated using the following formula,

$$\text{Cell Viability (\%)} = \frac{(\text{Abs } 570 - \text{Abs } 655)\text{Sample}}{(\text{Abs } 570 - \text{Abs } 655)\text{Control}} \times 100$$

3. Crystal Data and Structure Refinement for Compounds 3fa

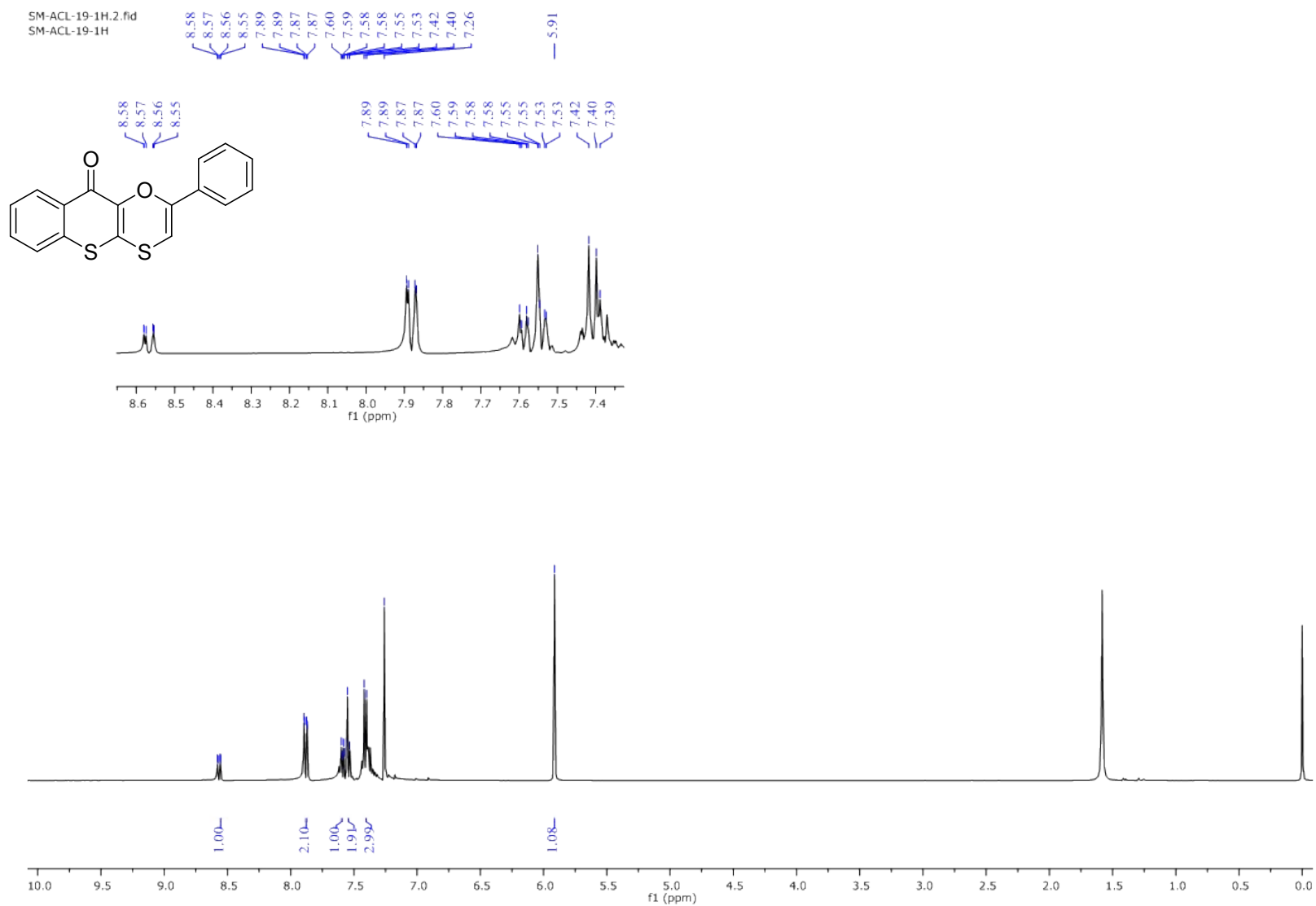
Table S1. Crystal data and structure refinement for compound 3fa.

Entry	Identification code	Compound 3fa
01	Empirical formula	C ₁₇ H ₉ FO ₂ S ₂
02	Formula weight	328.36
03	Temperature	296 K
04	Wavelength	0.71073
05	Radiation type	Mo K α
06	Radiation source	Fine-focus sealed tube
07	Crystal system	Monoclinic
08	Space group	P 2 ₁ / n
09	Cell length	a 14.147(2) b 5.4814(8) c 18.975(3)
10	Cell Angle	α 90 β 109.360(4)

		δ 90
11	Cell Volume	1388.2(4)
12	Density	1.571
13	Completeness to theta	23°/ 100%
14	Absorption correction	multi-scan
15	Refinement method	Full-matrix least-squares on F2
16	Index ranges	-16<= <i>h</i> <=16, -6<= <i>k</i> <=6, -22<= <i>l</i> <=22
17	Reflection number	8296
18	Theta range	2.38- 23.59
19	Cell formula units Z	1
20	CCDC no	2049895

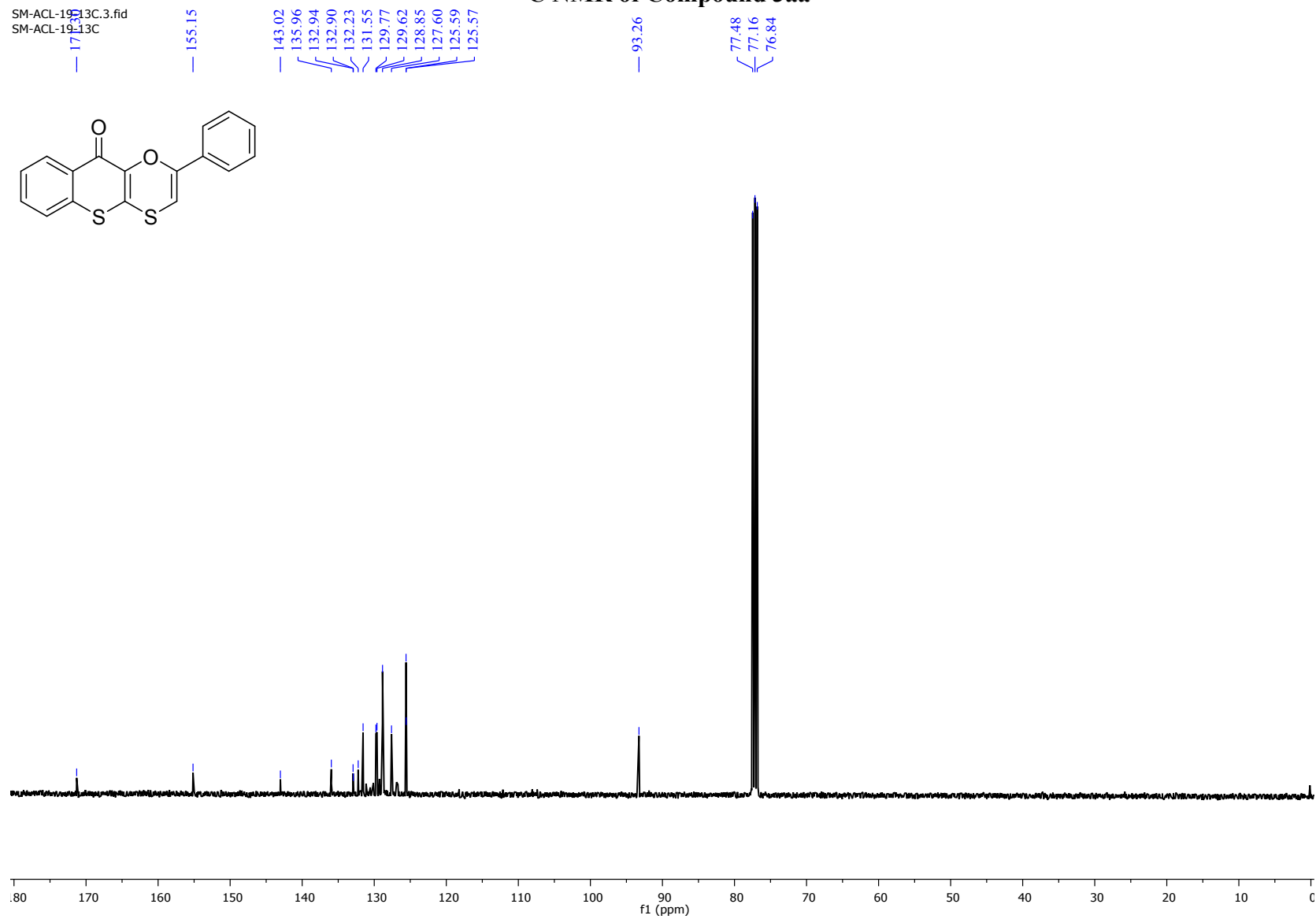
4. Copies of ^1H NMR, ^{13}C NMR and HRMS spectra of Compounds

^1H NMR of Compound 3aa



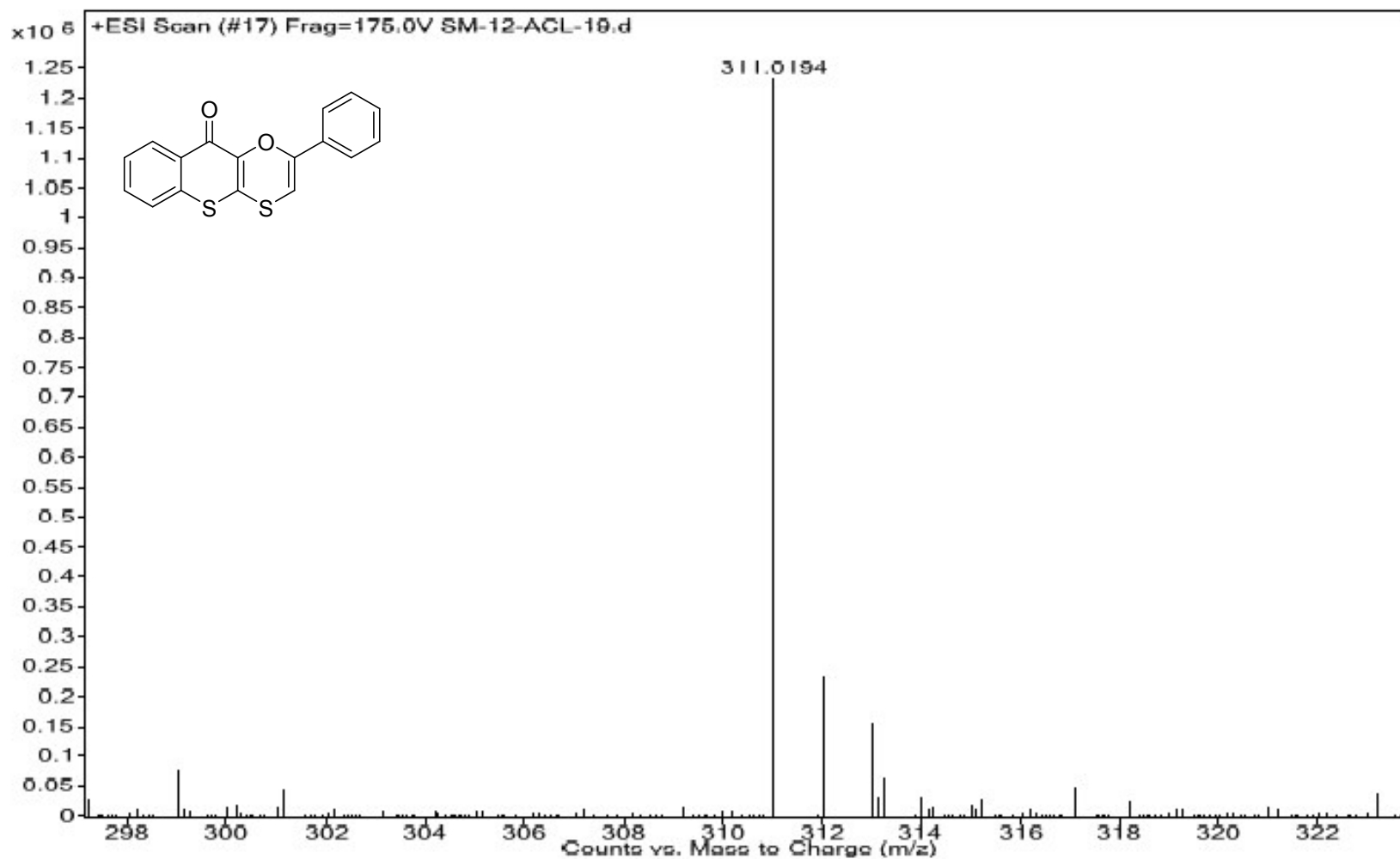
¹³C NMR of Compound 3aa

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SM-ACL-1913C



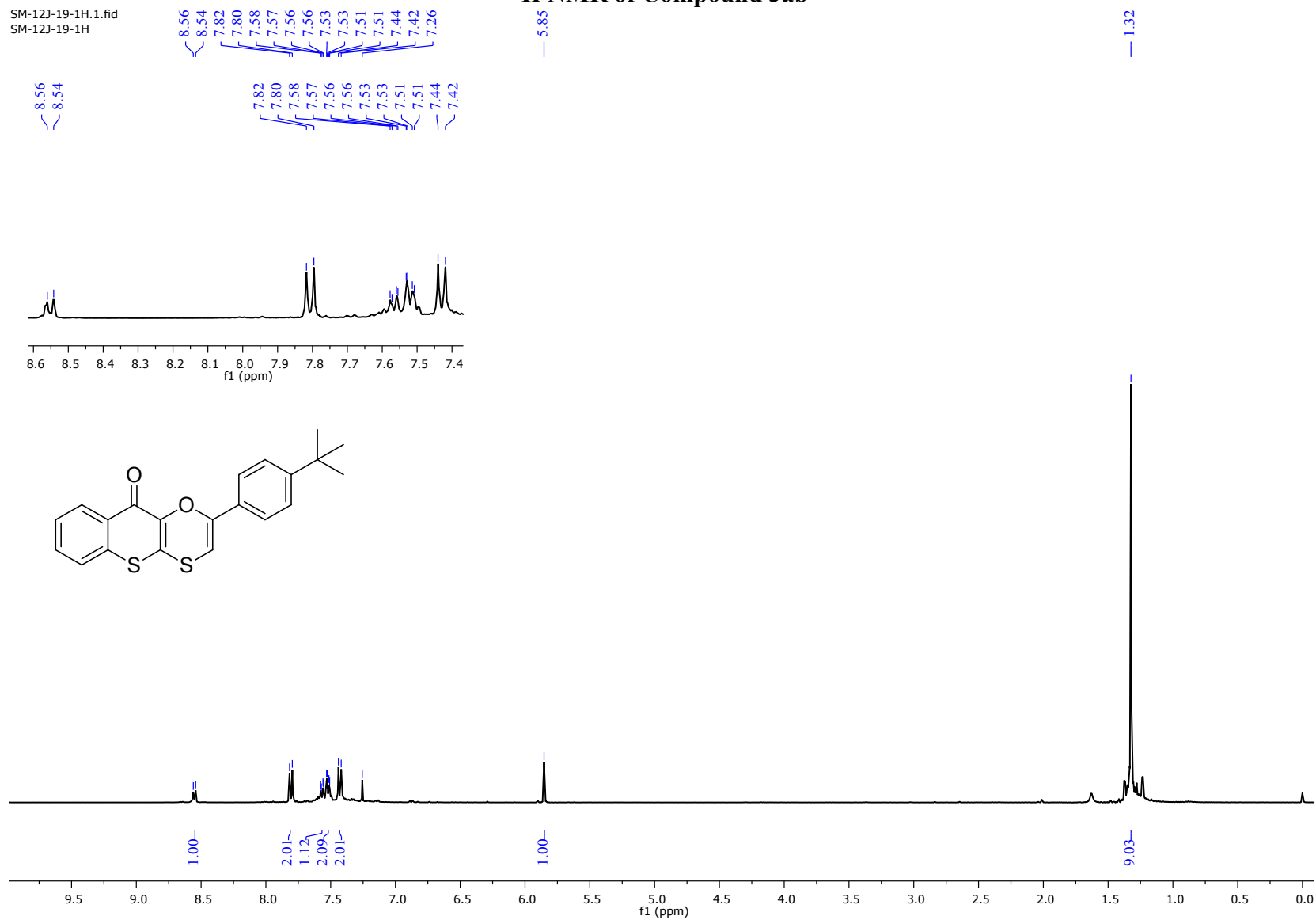
HRMS of Compound 3aa

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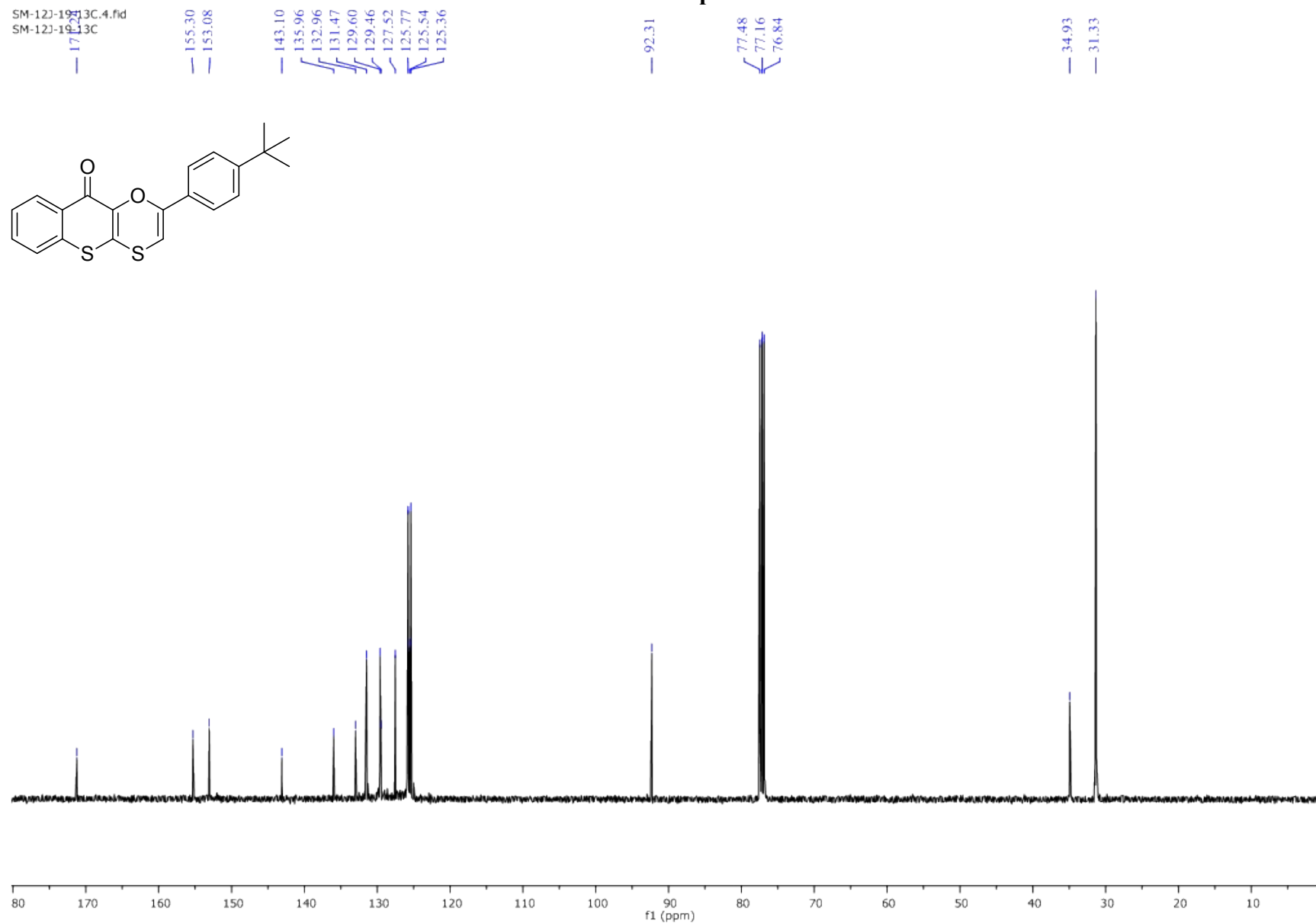
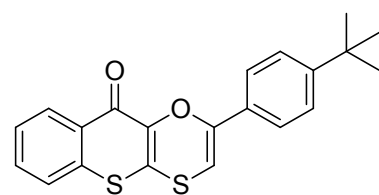
¹H NMR of Compound 3ab

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SM-12J-19-1H



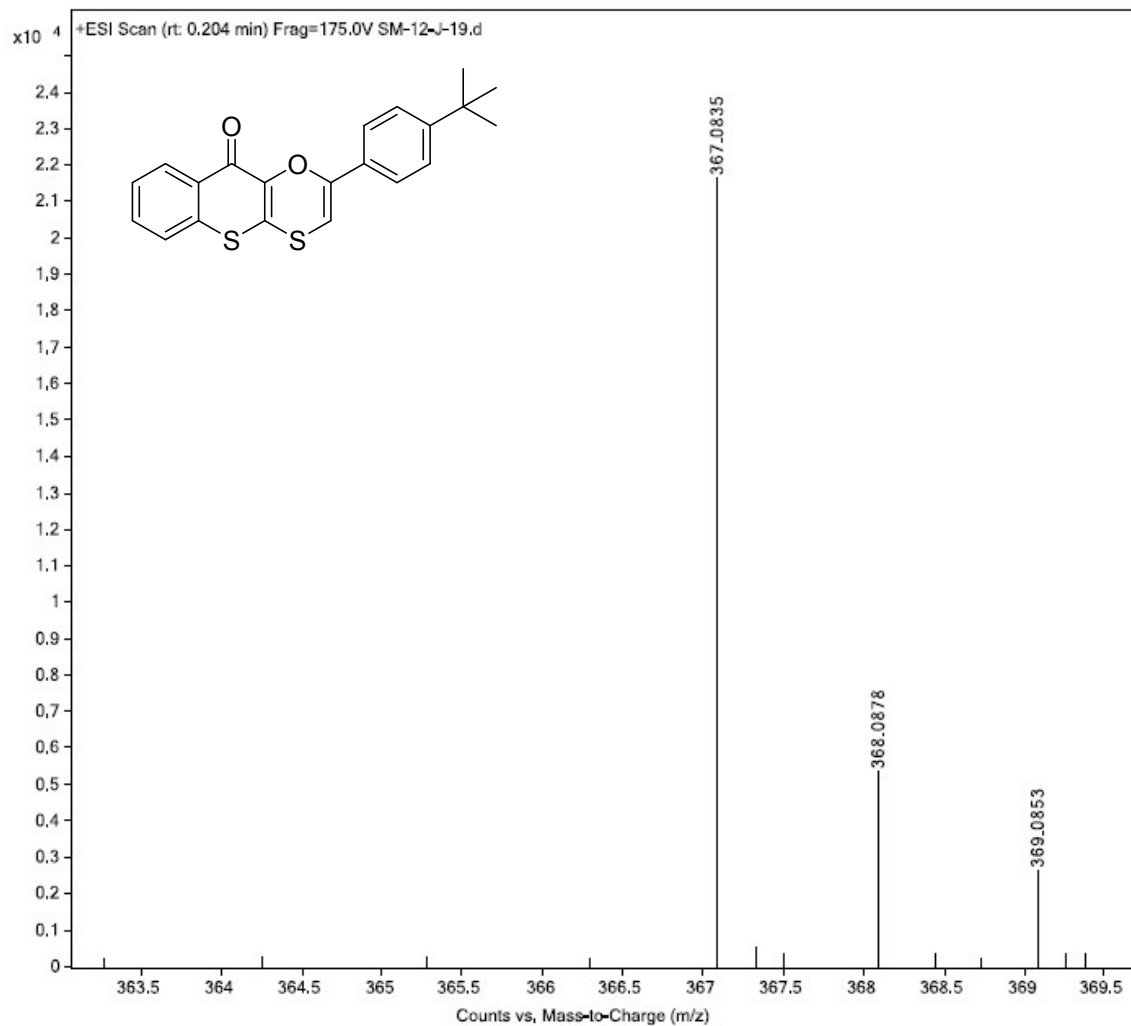
¹³C NMR of Compound 3ab

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SM-12J-1913C



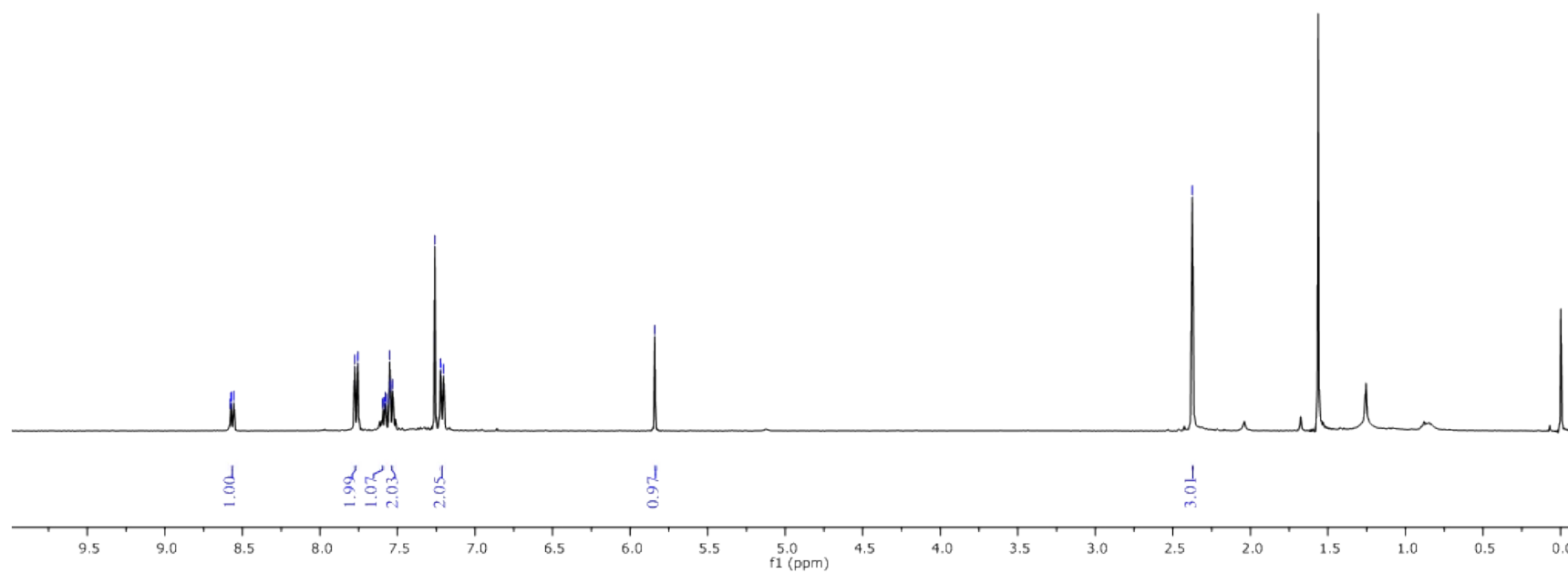
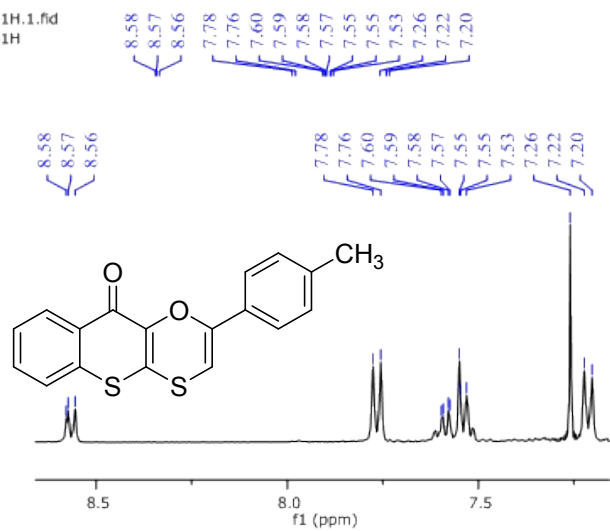
HRMS of Compound 3ab

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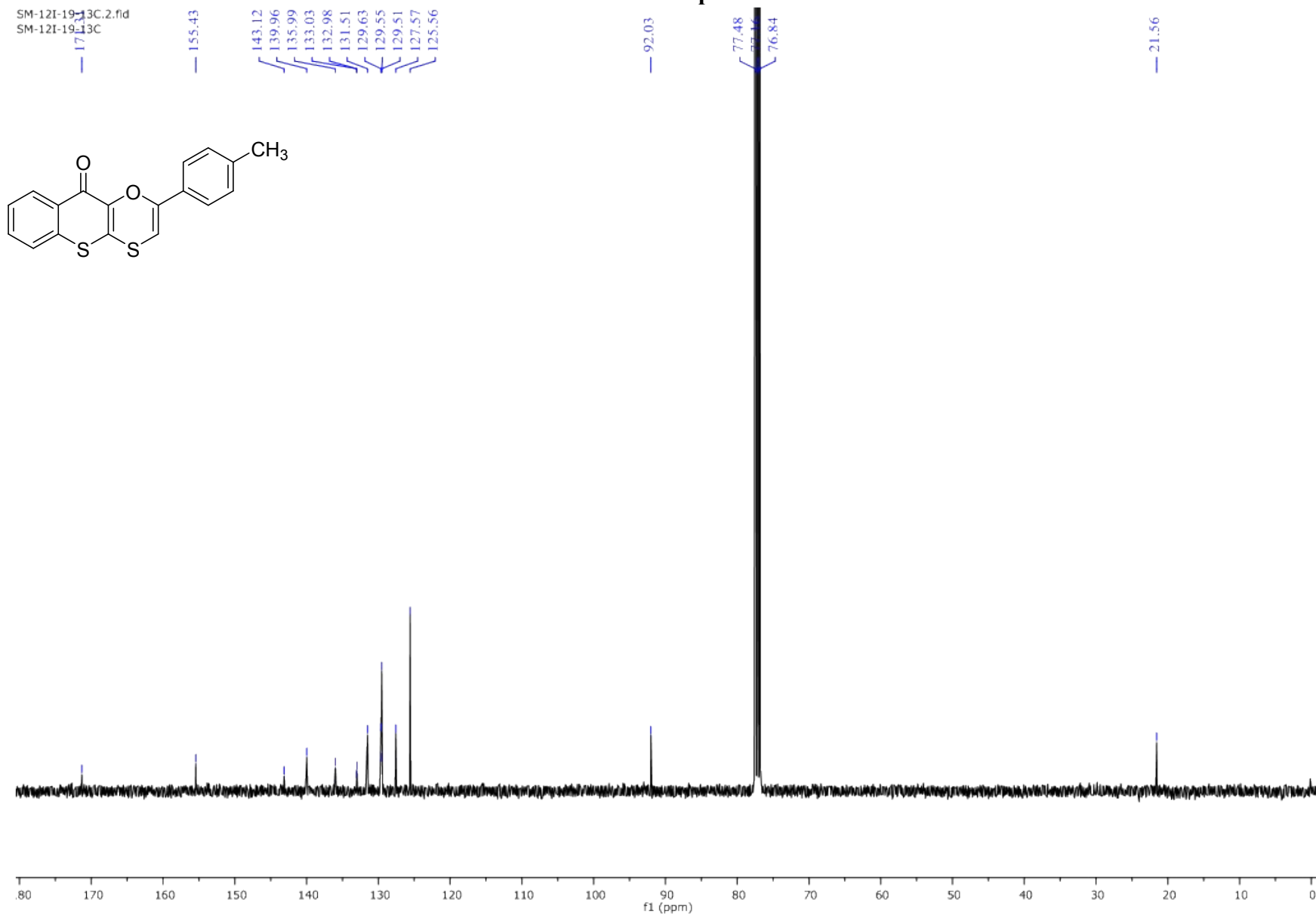


¹H NMR of Compound 3ac

SM-12I-19-1H.1.fid
SM-12I-19-1H

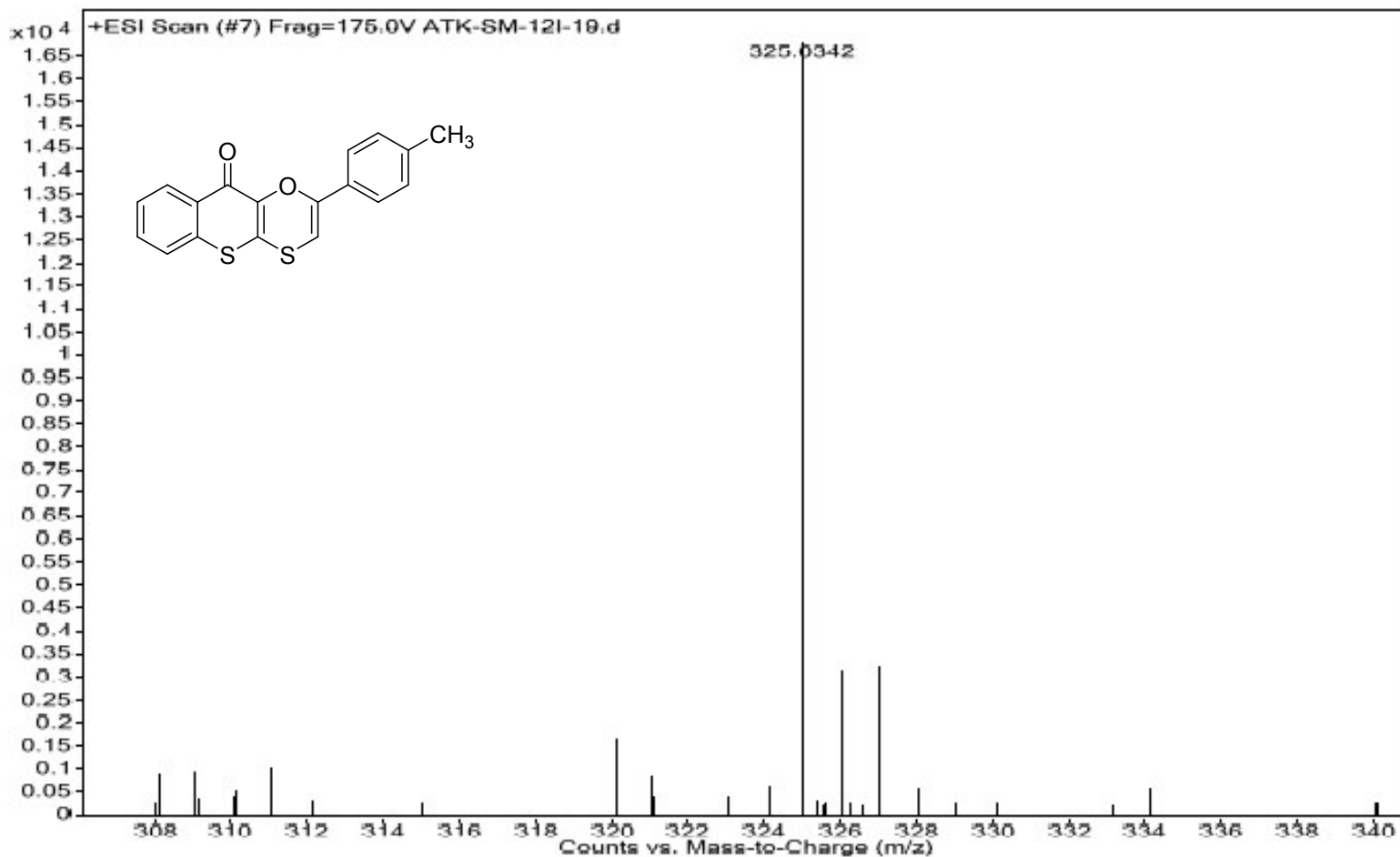


¹³C NMR of Compound 3ac



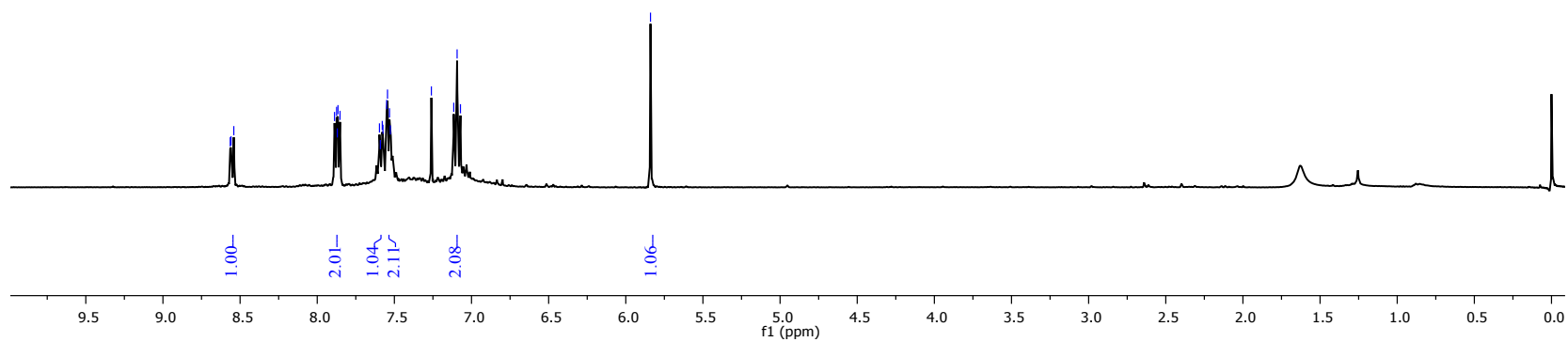
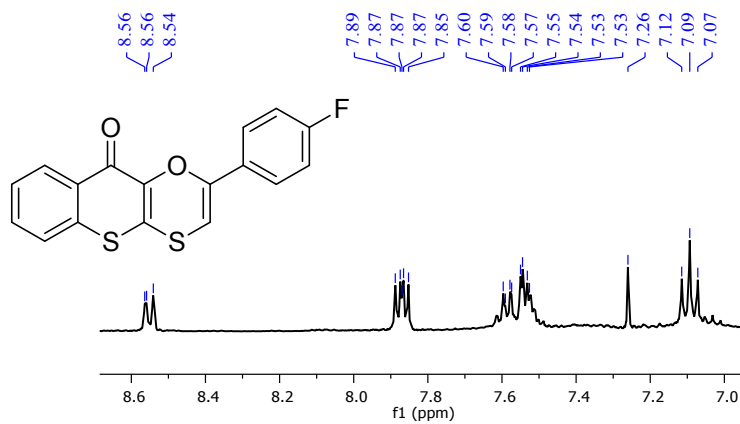
HRMS of Compound 3ac

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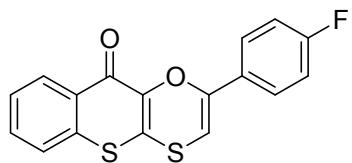
¹H NMR of Compound 3ad

SM-120-19-1H.1.fid
SM-120-19-1H

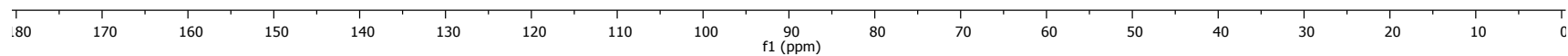


¹³C NMR of Compound 3ad

SM-120-19-13C.146d
SM-120-19-13C
— 177.39
— 164.96
— 162.44
— 154.33
142.87
135.95
133.14
132.88
131.60
129.57
128.49
128.45
127.70
127.64
127.61
125.58
116.02
115.80

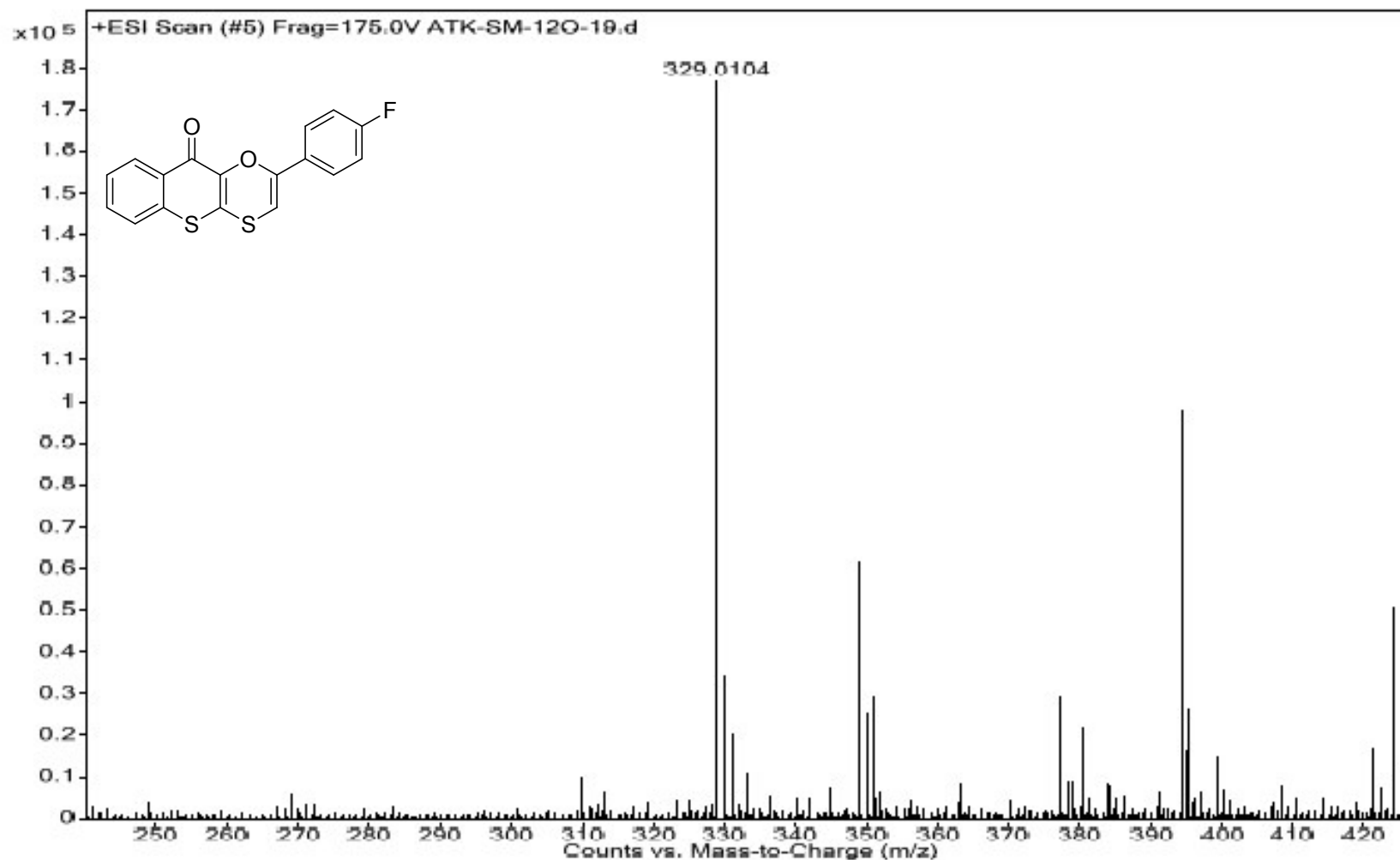


92.96
92.94
77.48
77.16
76.84



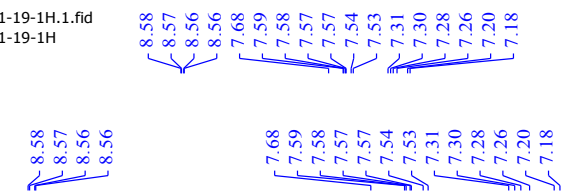
HRMS of Compound 3ad

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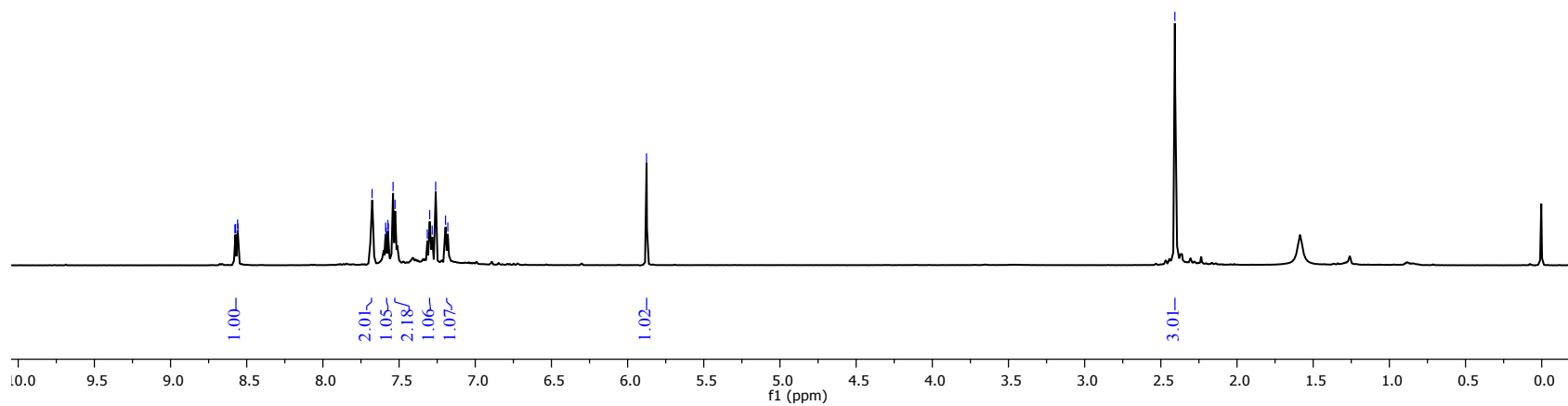
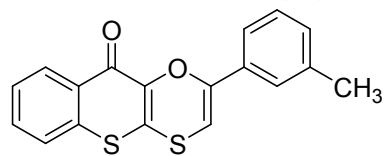
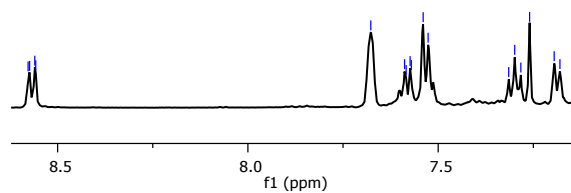
¹H NMR of Compound 3ae

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SM-12A1-19-1H

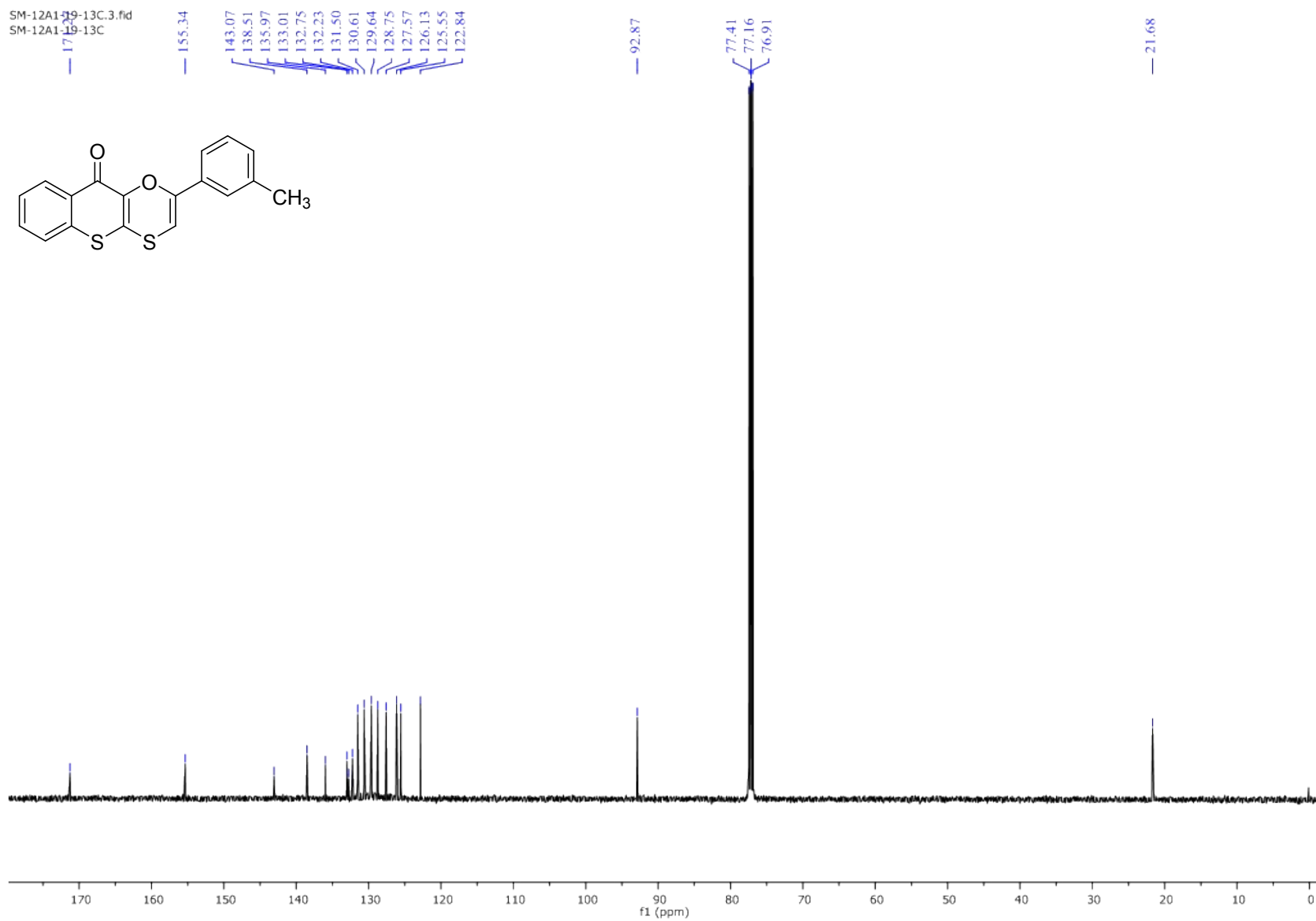


— 5.88

— 2.41

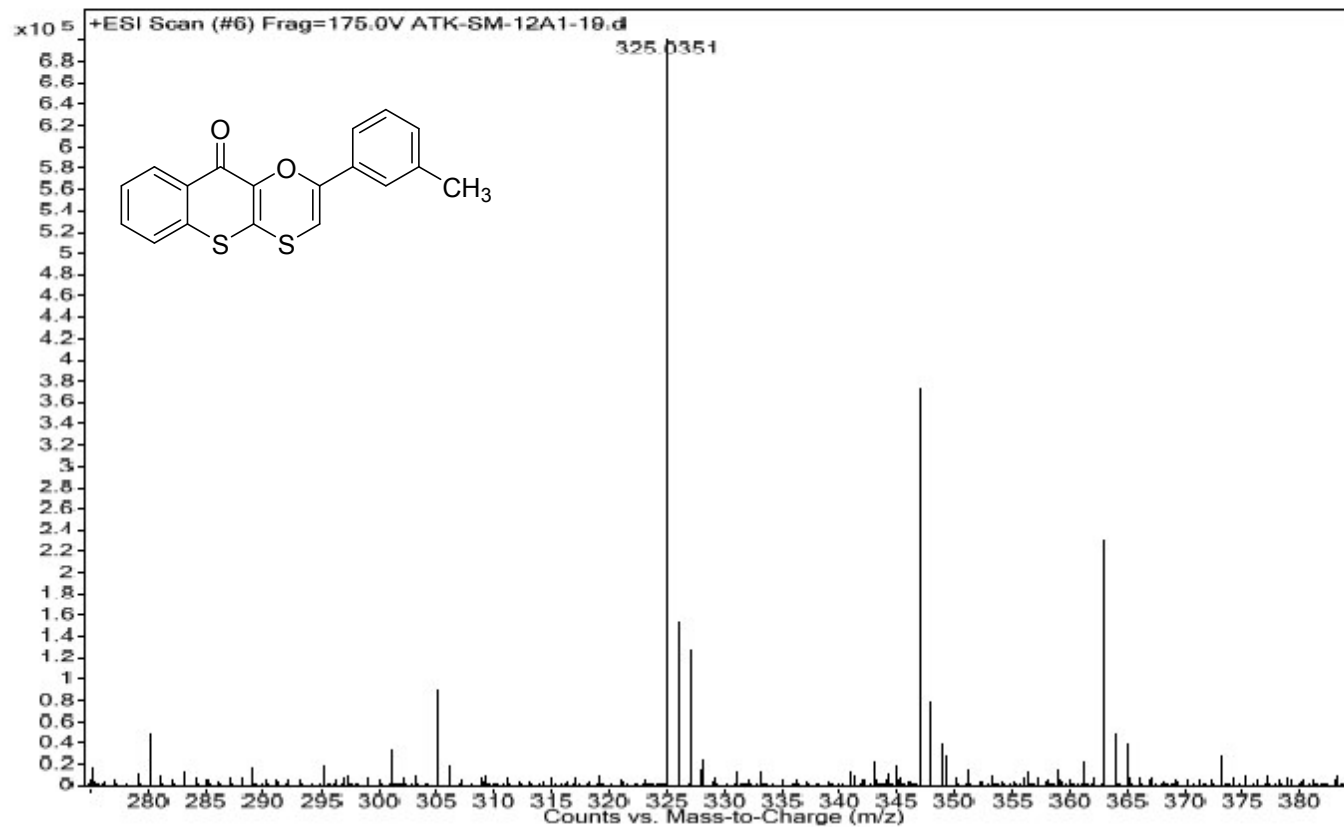


¹³C NMR of Compound 3ae

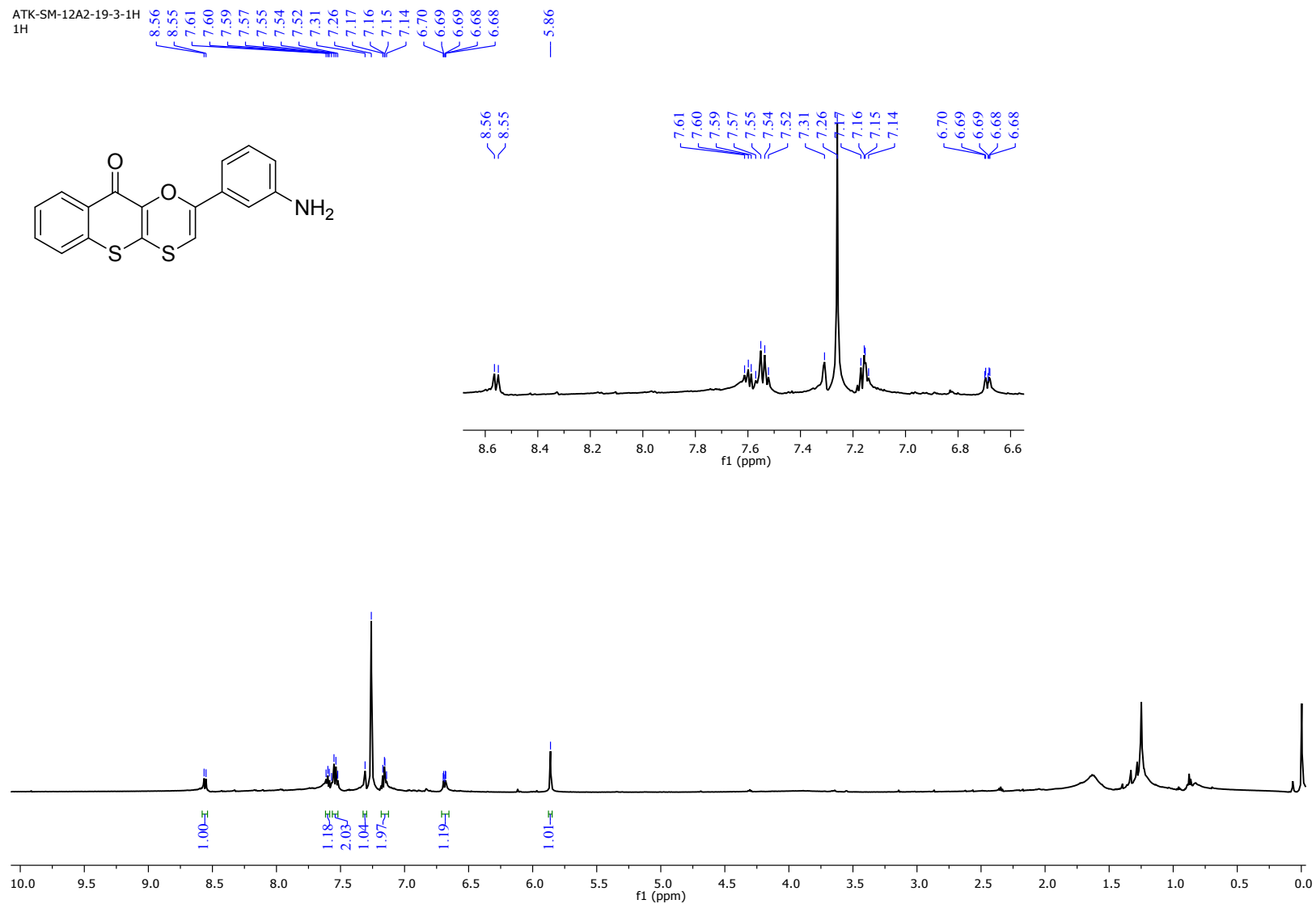


HRMS of Compound 3ae

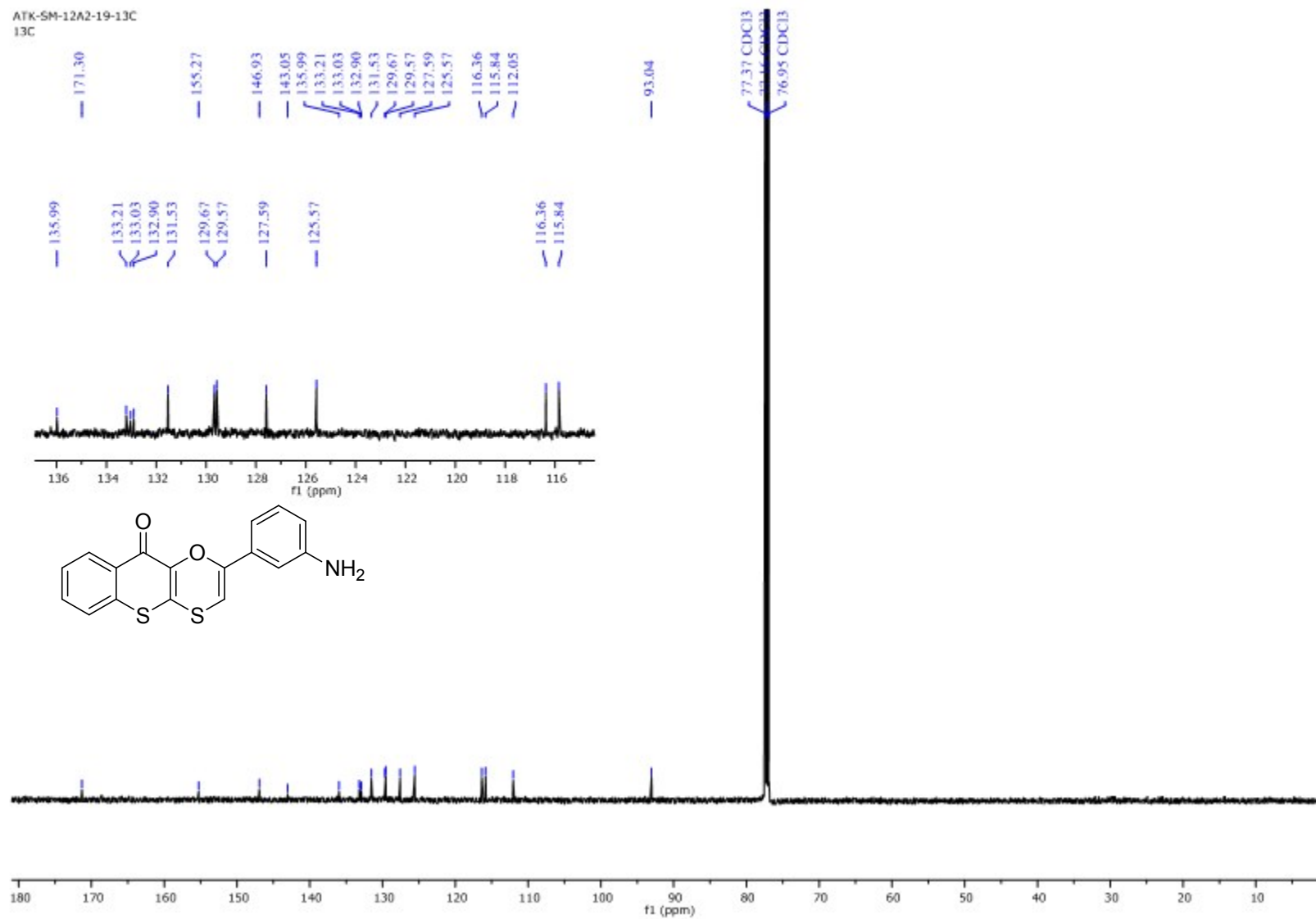
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¹H NMR of Compound 3af

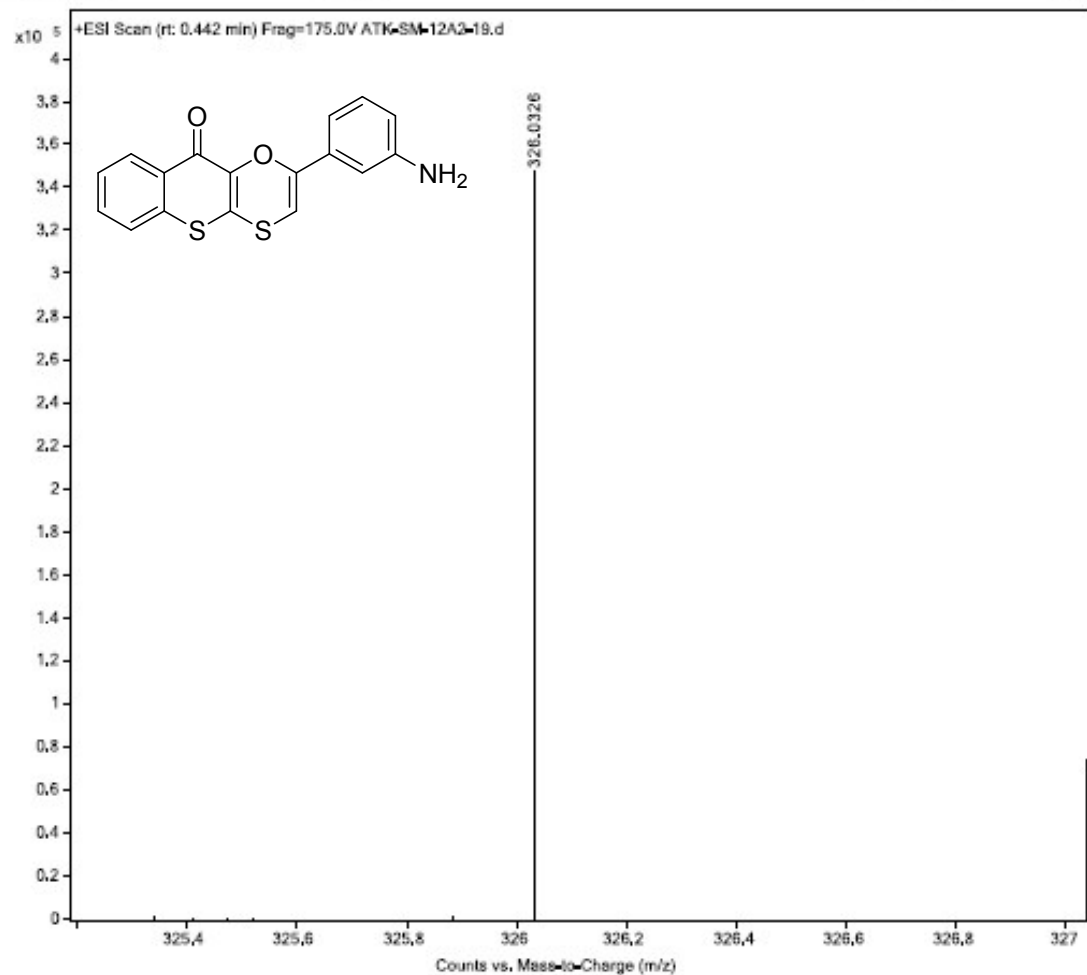


¹³C NMR of Compound 3af



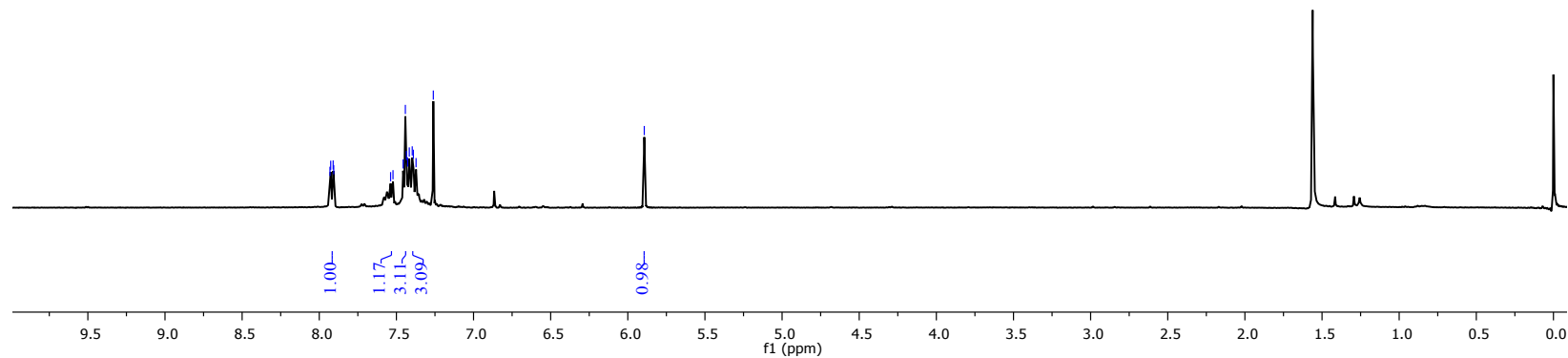
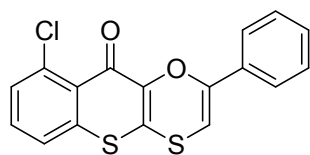
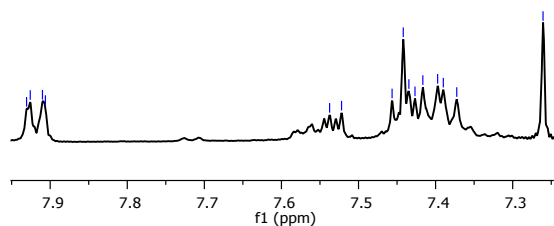
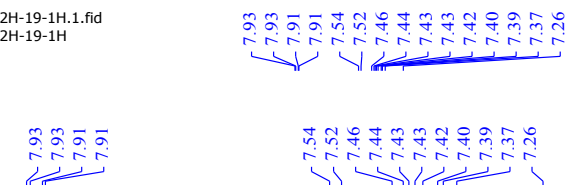
HRMS of Compound 3af

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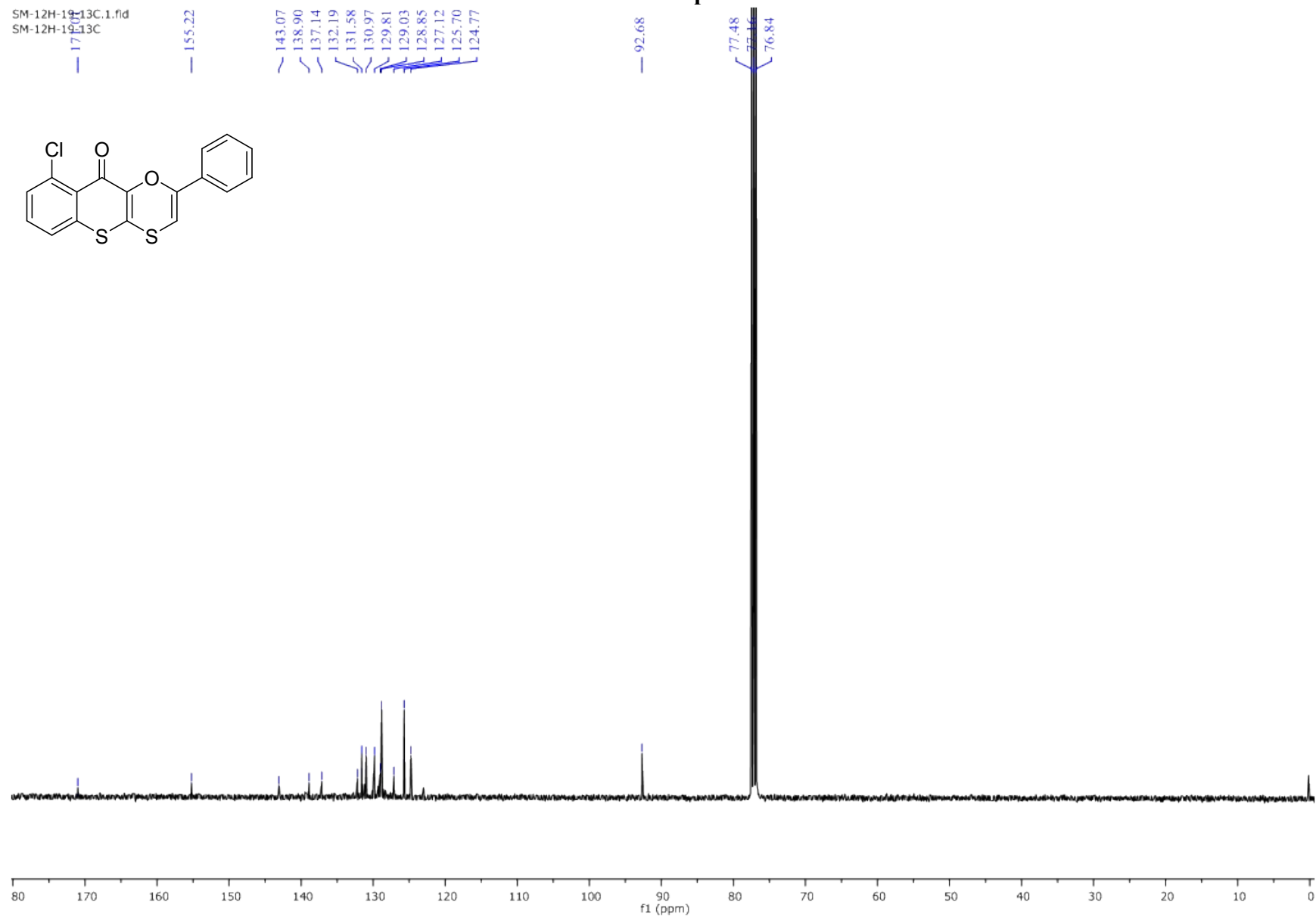
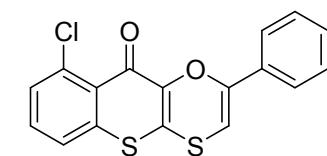
¹H NMR of Compound 3ba

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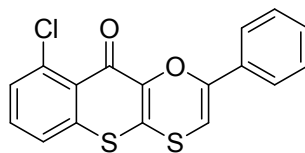
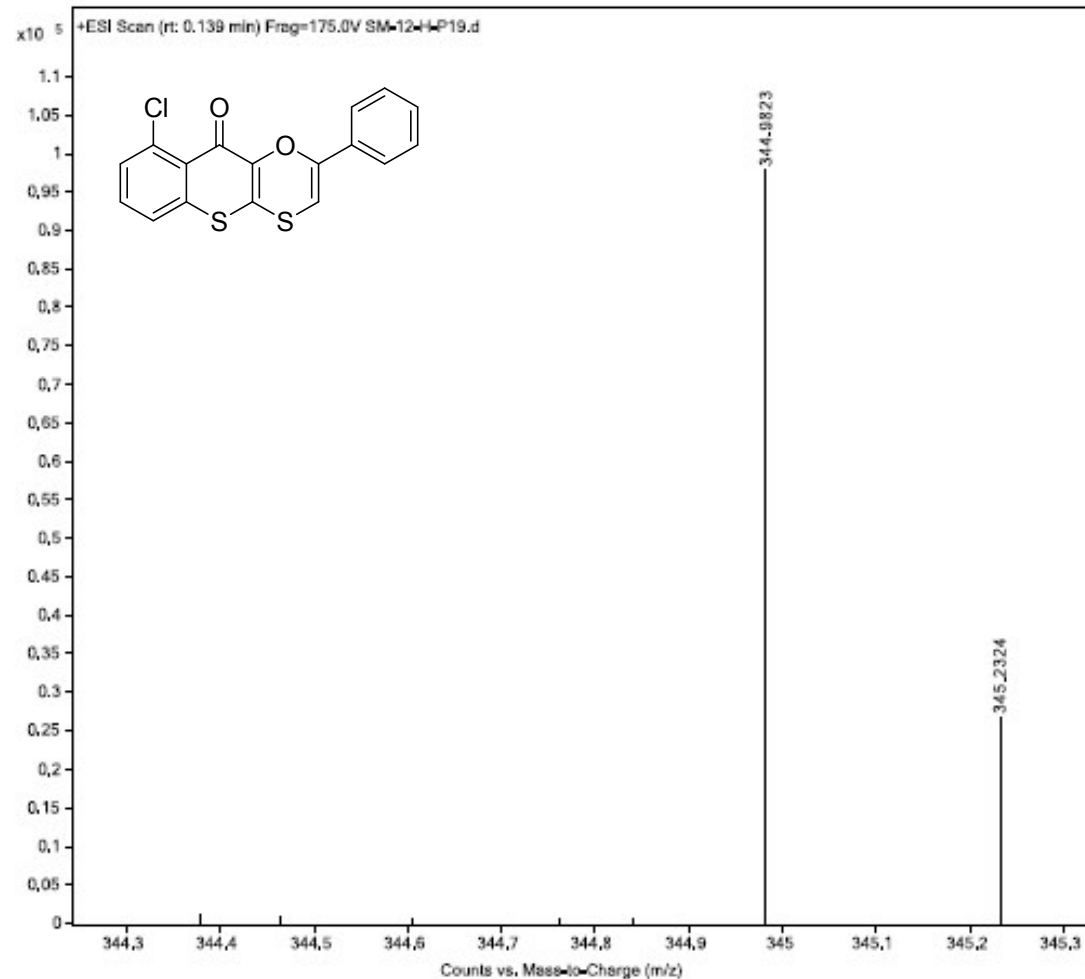
¹³C NMR of Compound 3ba

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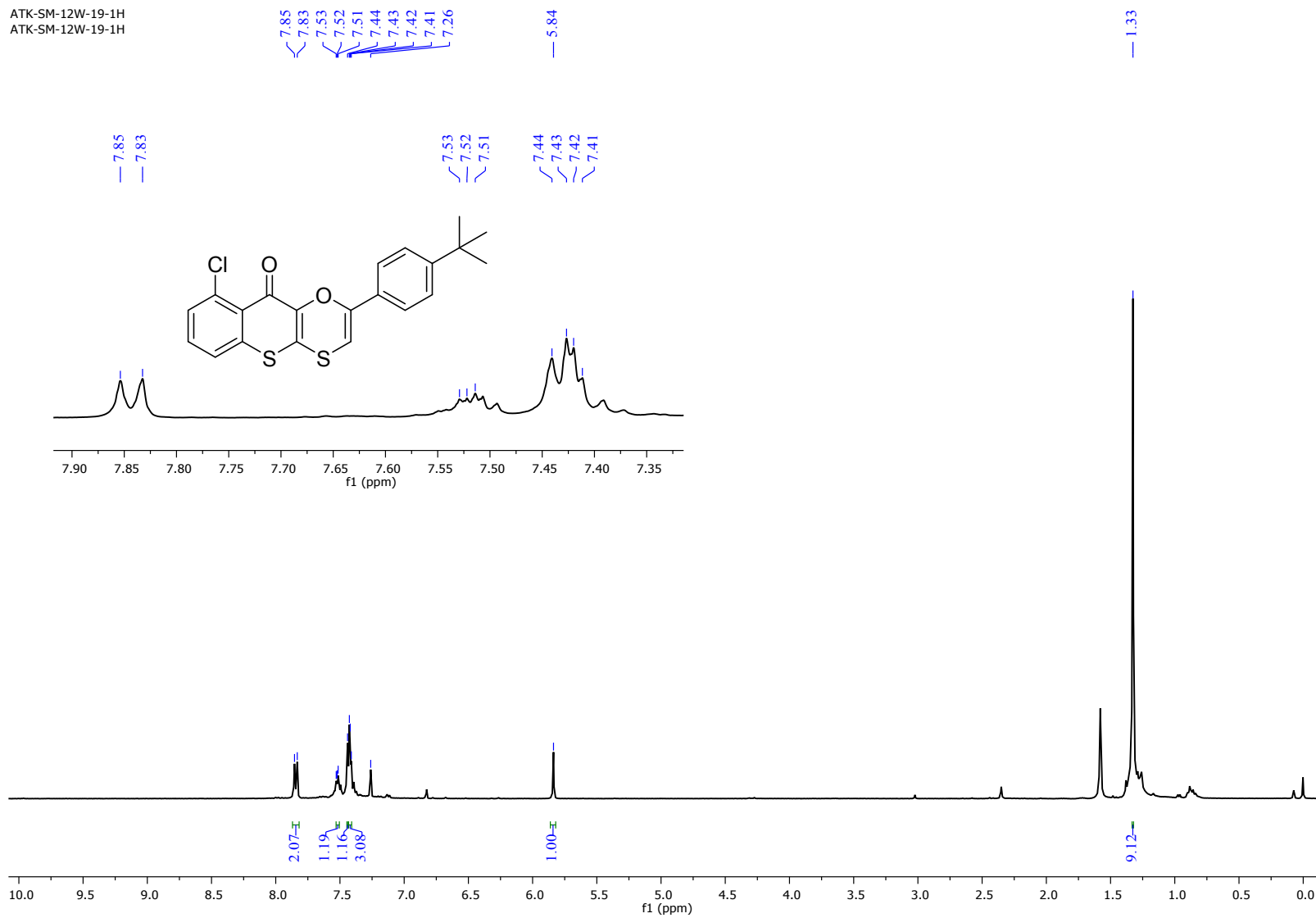
HRMS of Compound 3ba

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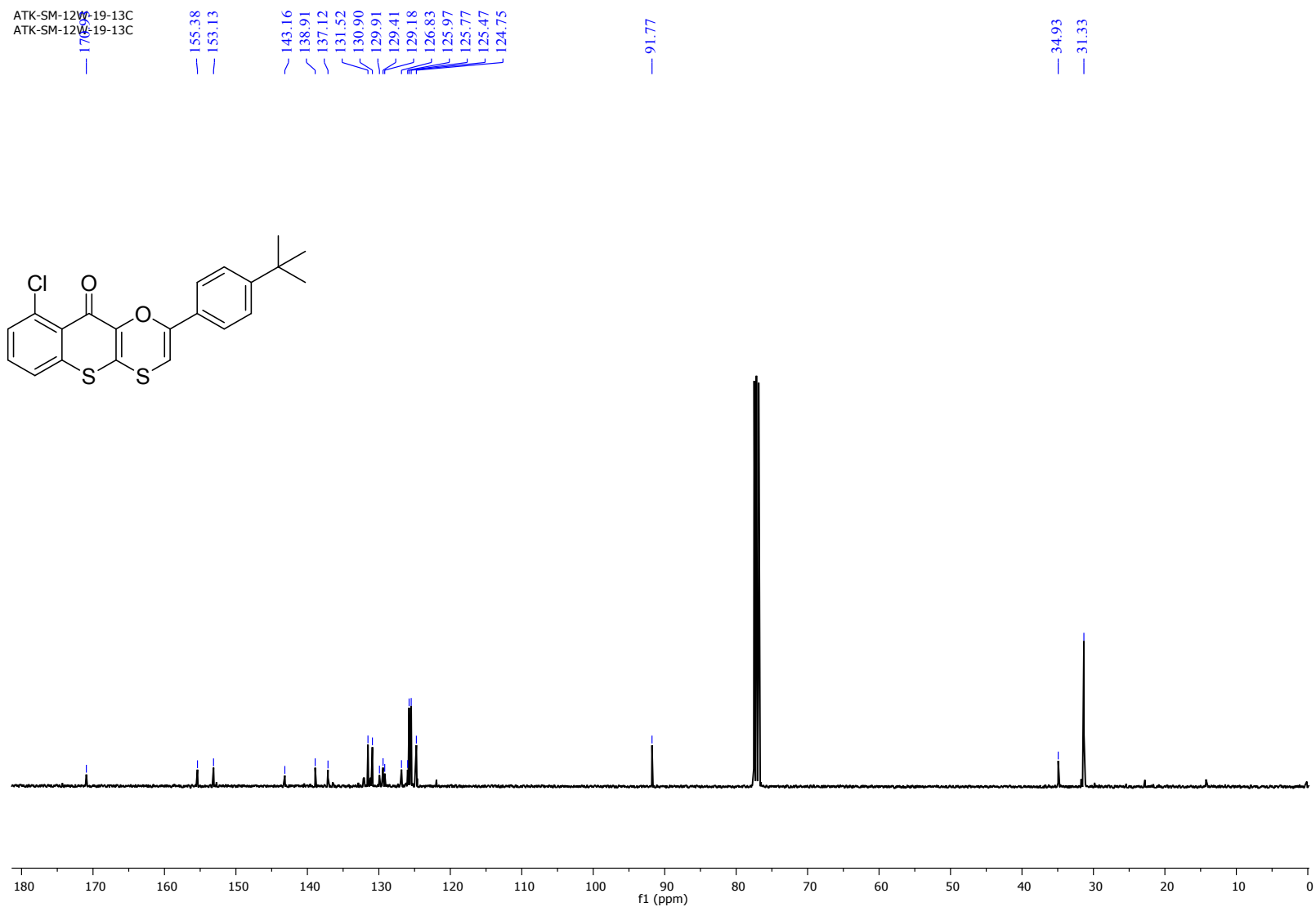


¹H NMR of Compound 3bb

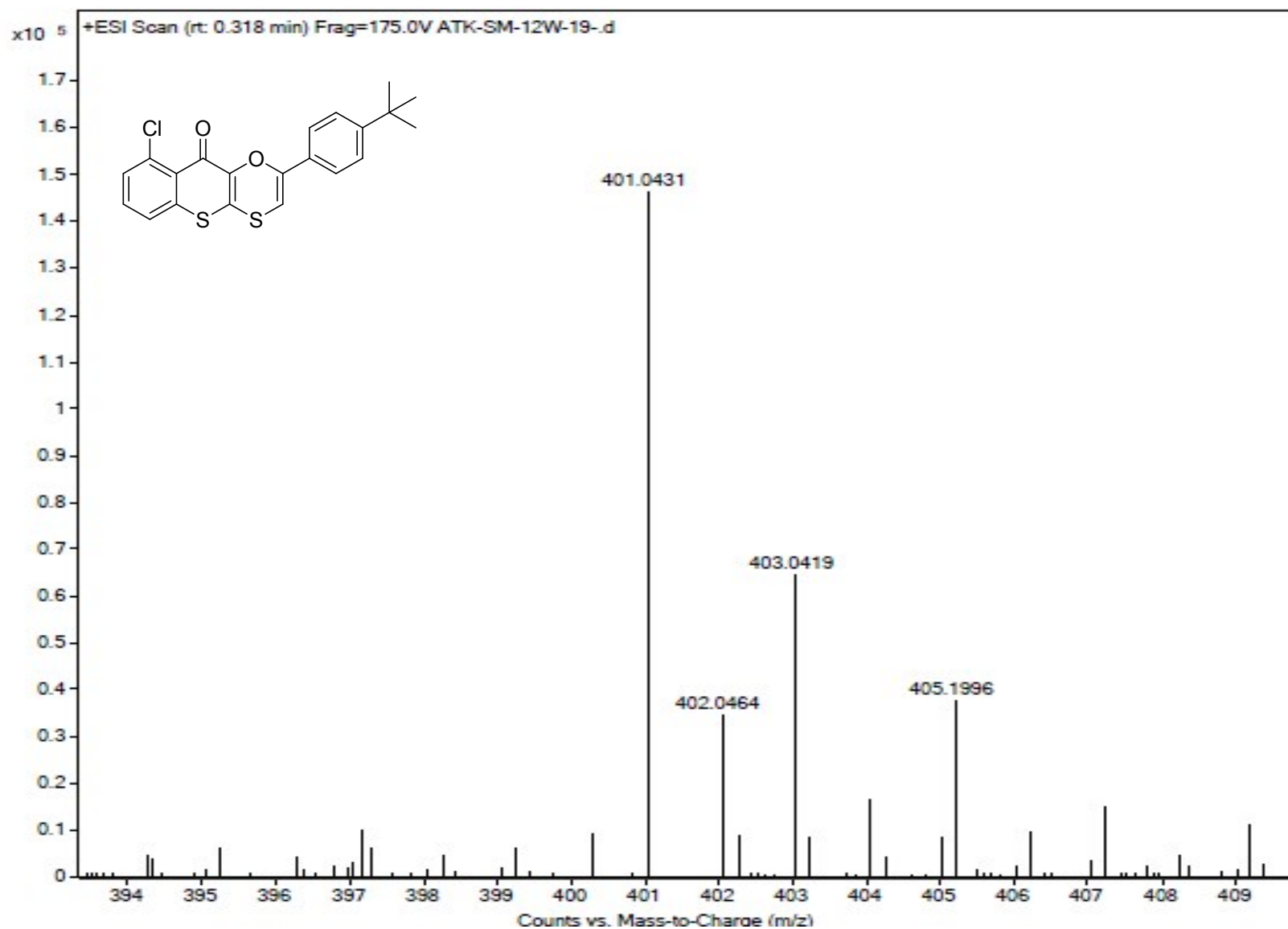
ATK-SM-12W-19-1H
ATK-SM-12W-19-1H



¹³C NMR of Compound 3bb

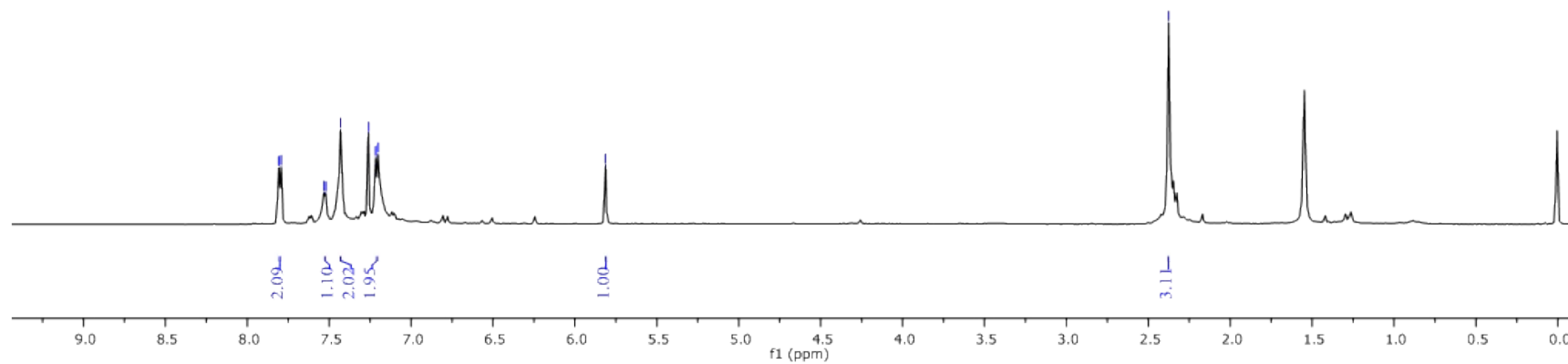
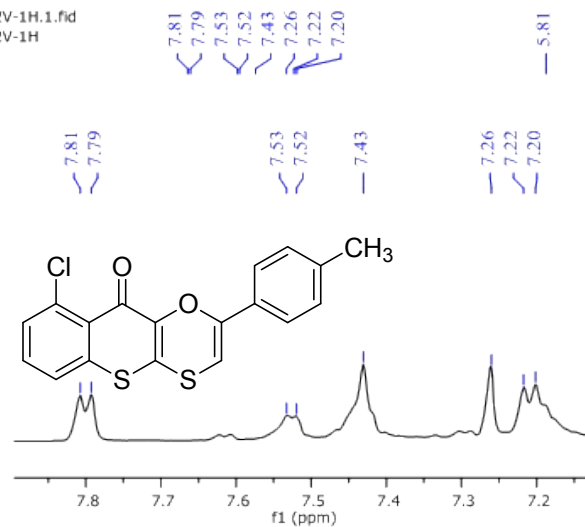


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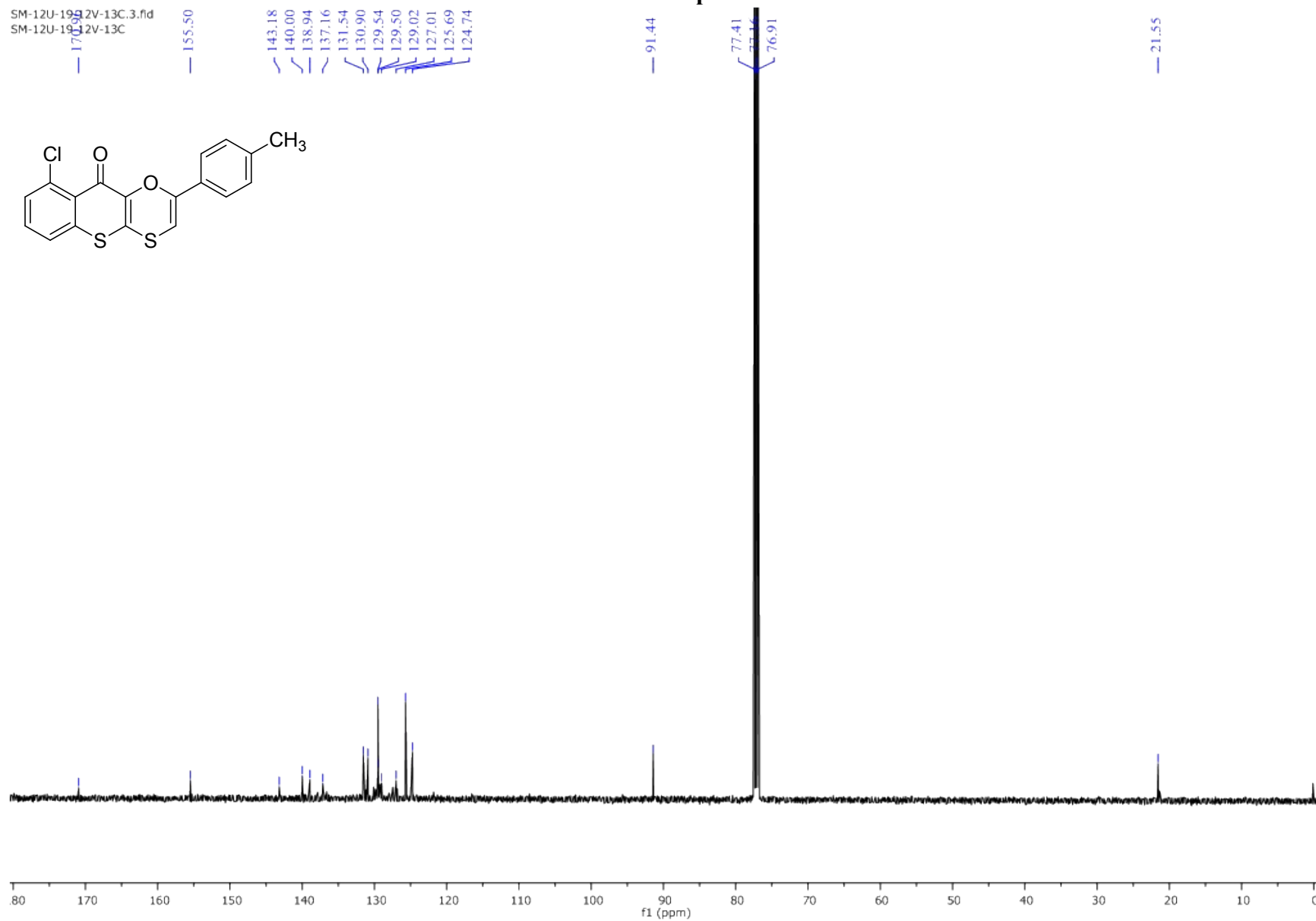


¹H NMR of Compound 3bc

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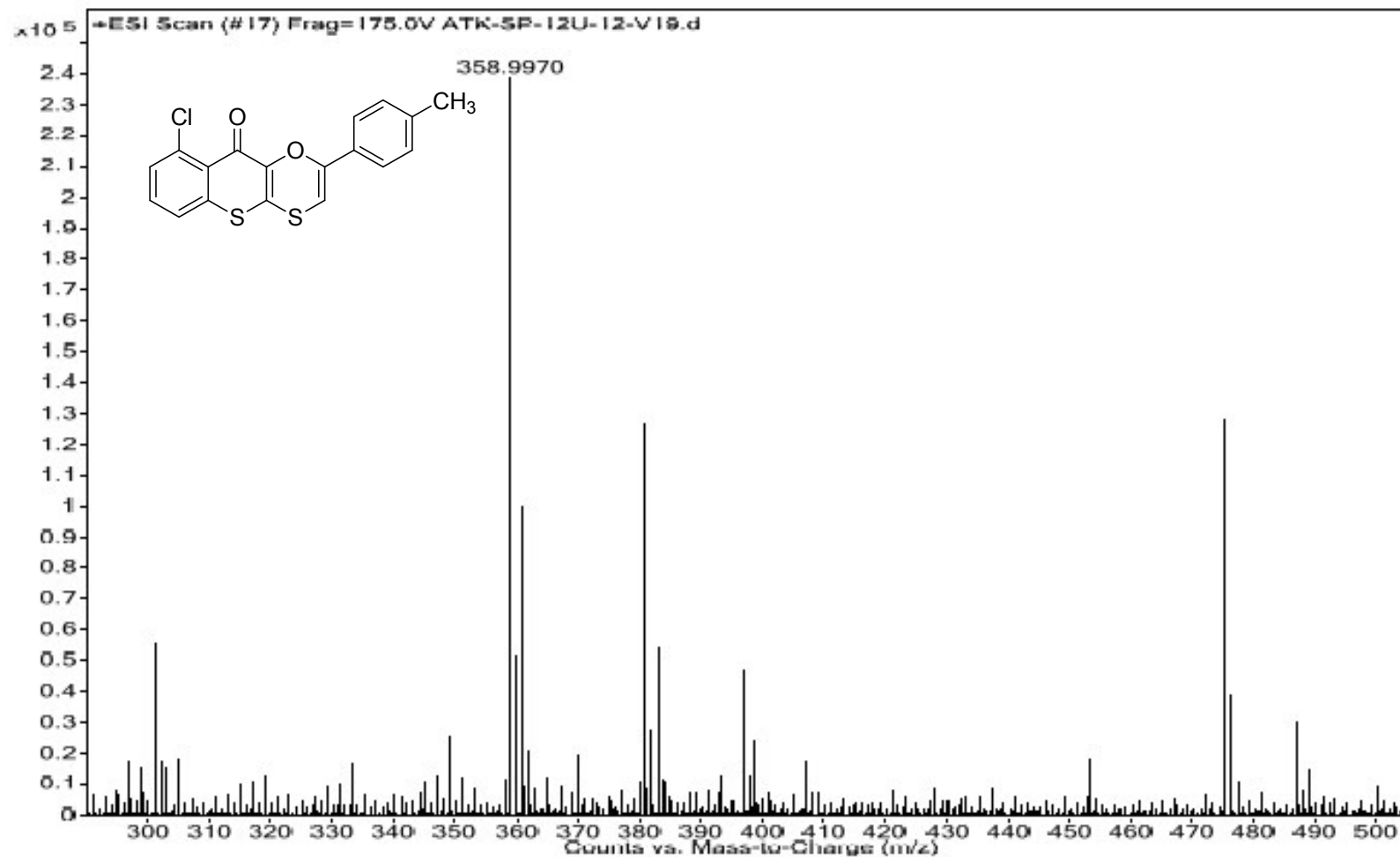


¹³C NMR of Compound 3bc



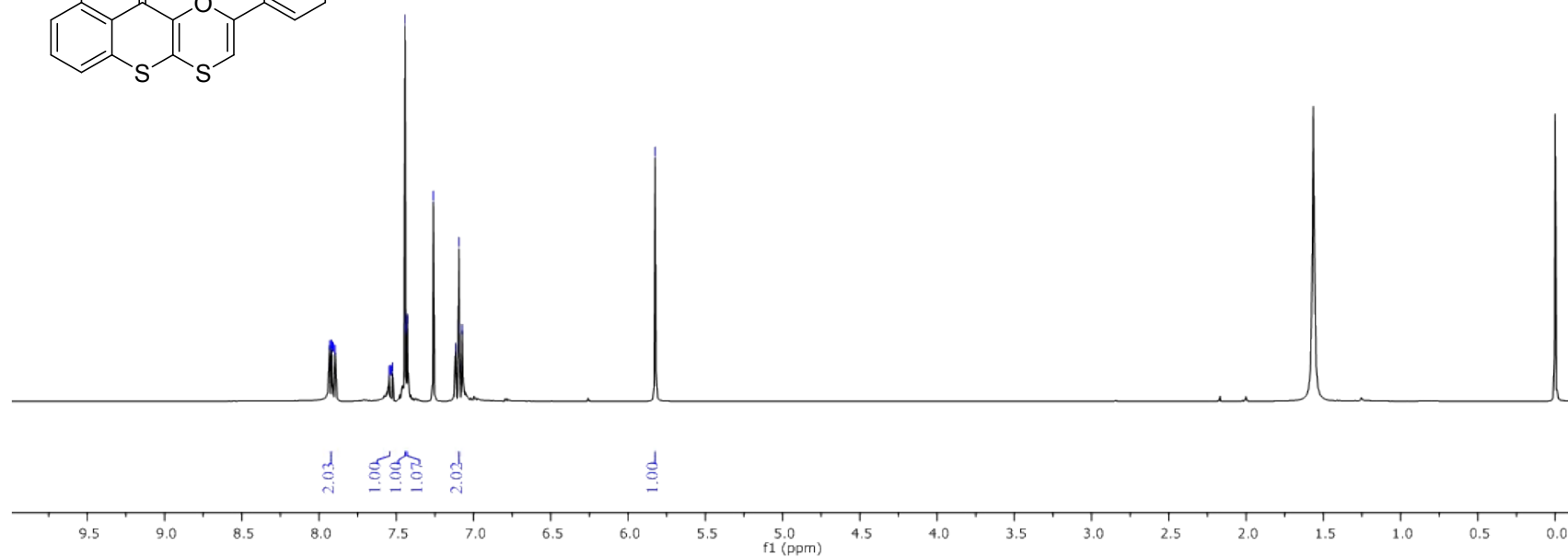
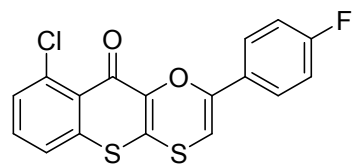
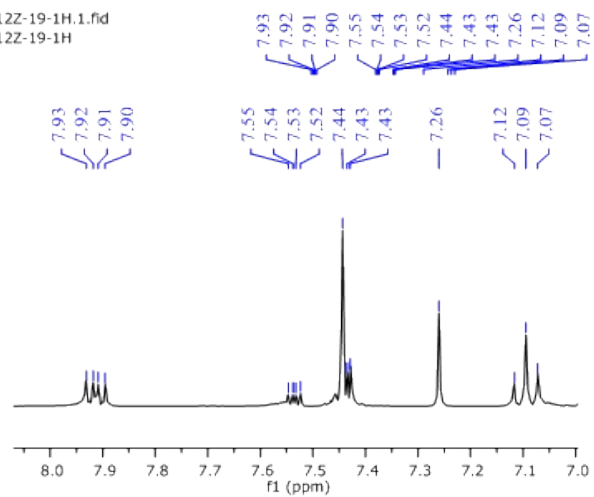
HRMS of Compound 3bc

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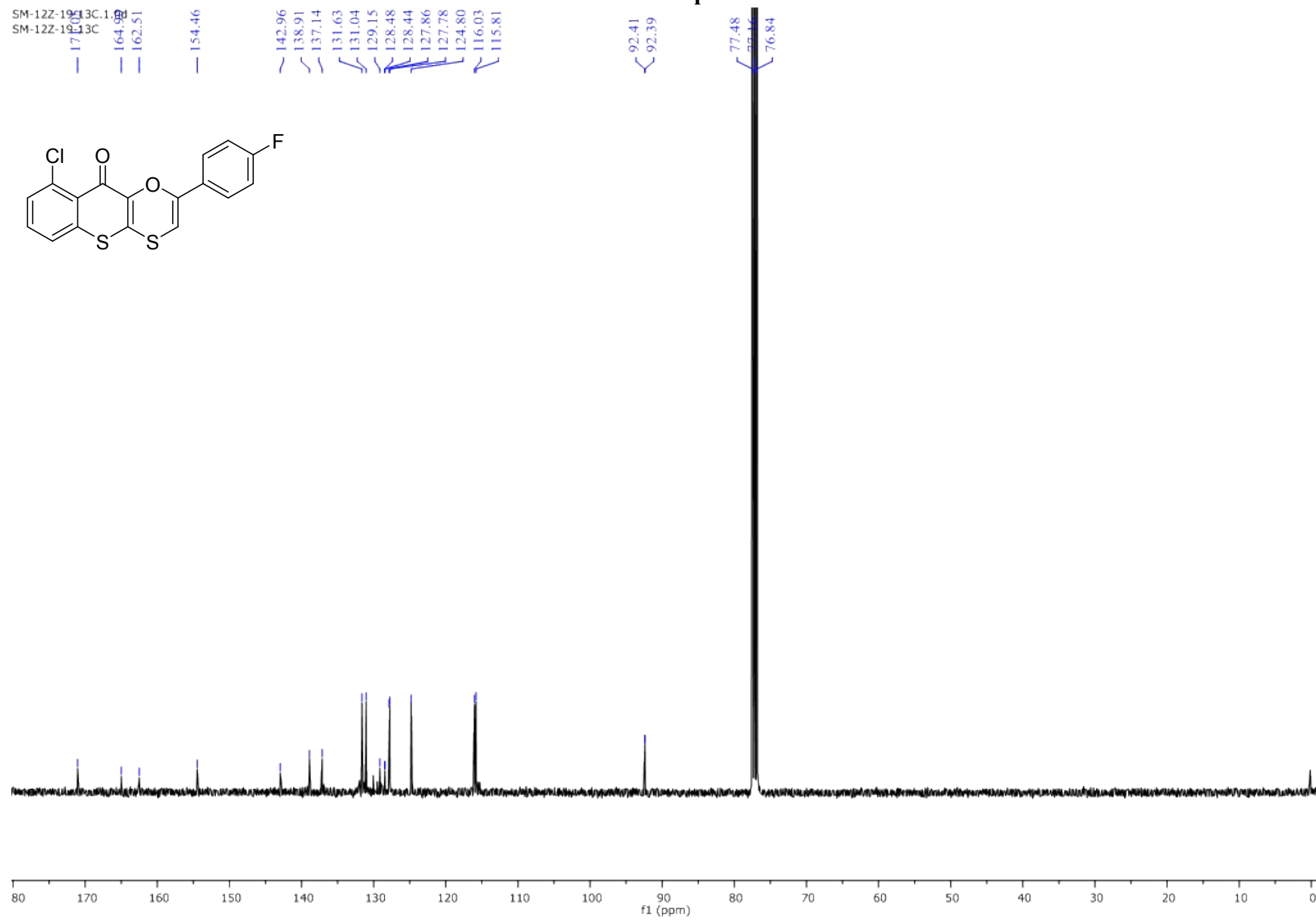


¹H NMR of Compound 3bd

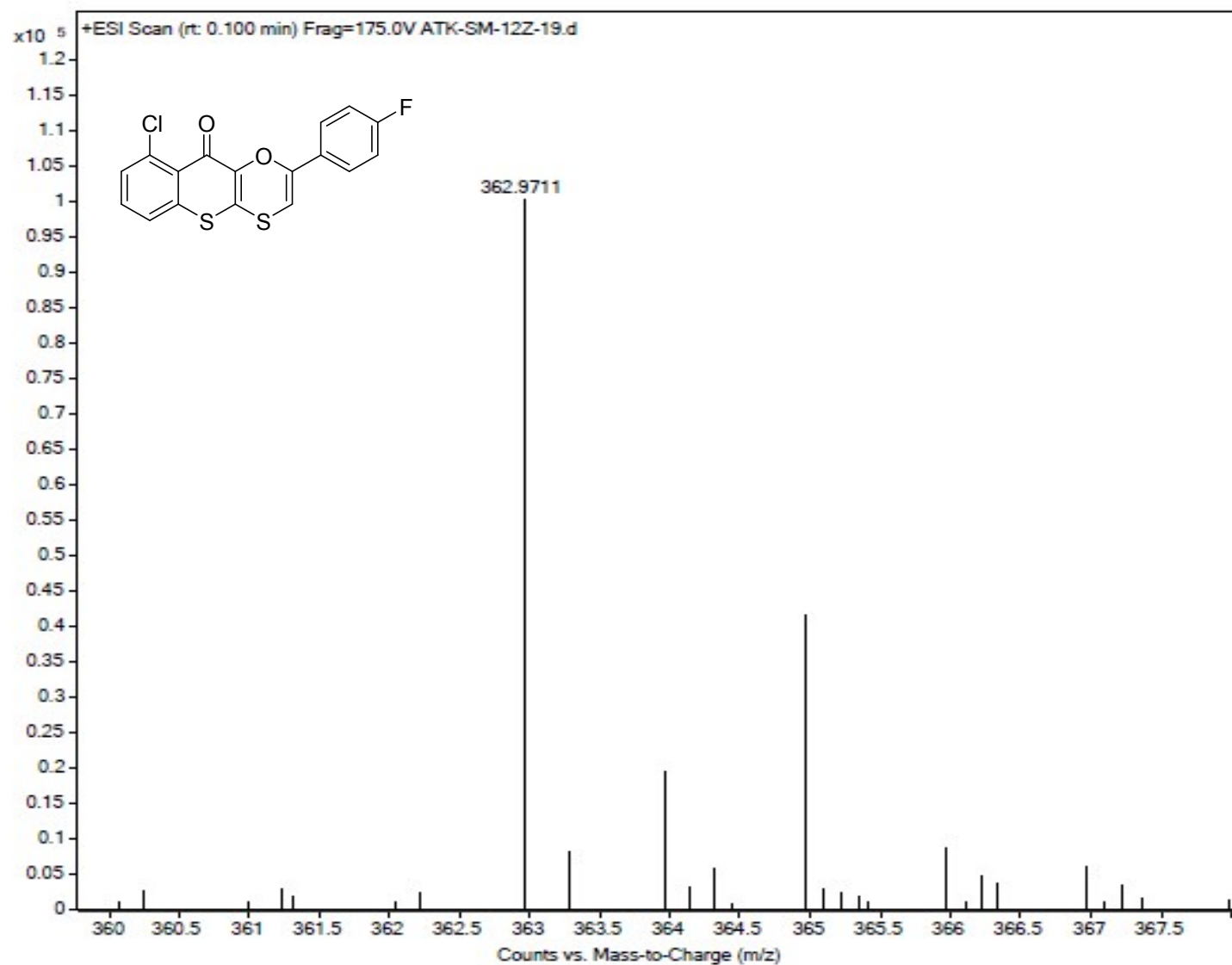
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¹³C NMR of Compound 3bd

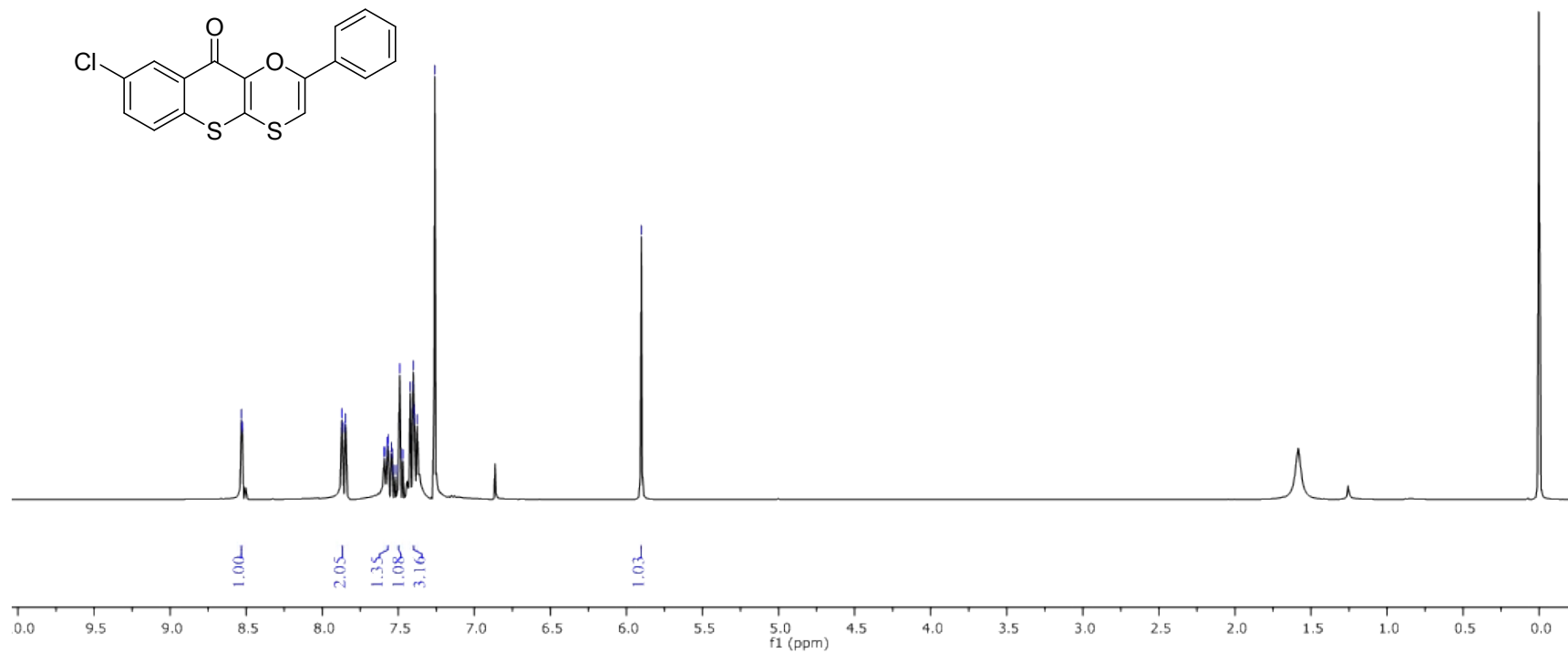
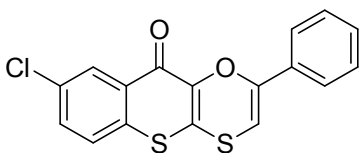
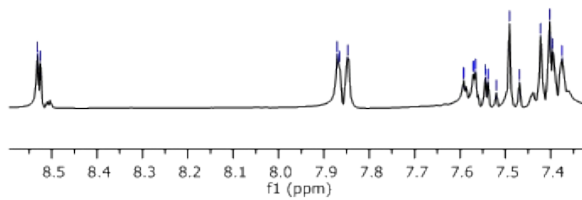


HRMS of Compound 3bd



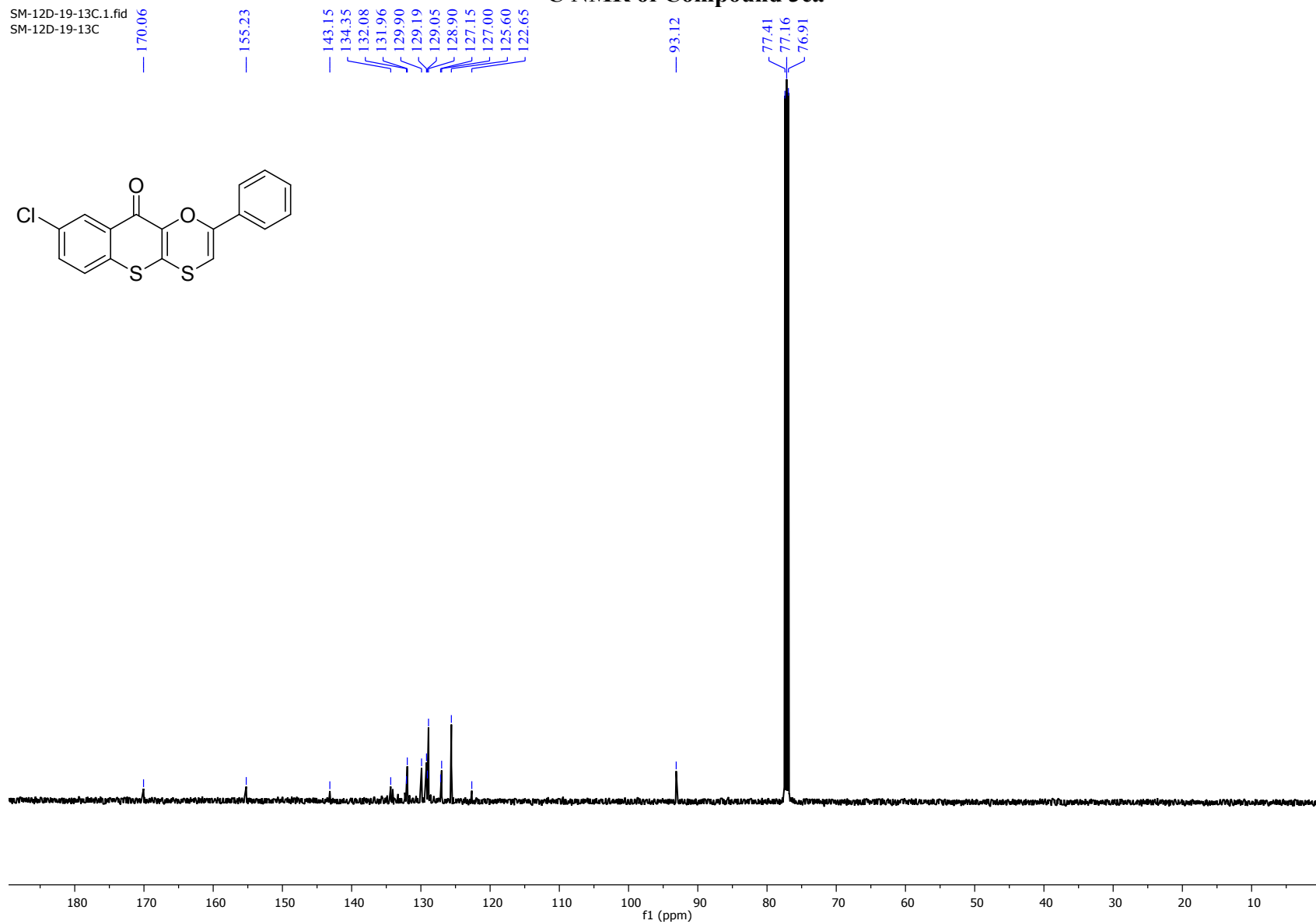
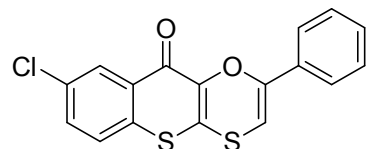
¹H NMR of Compound 3ca

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SM-12D-19-1H



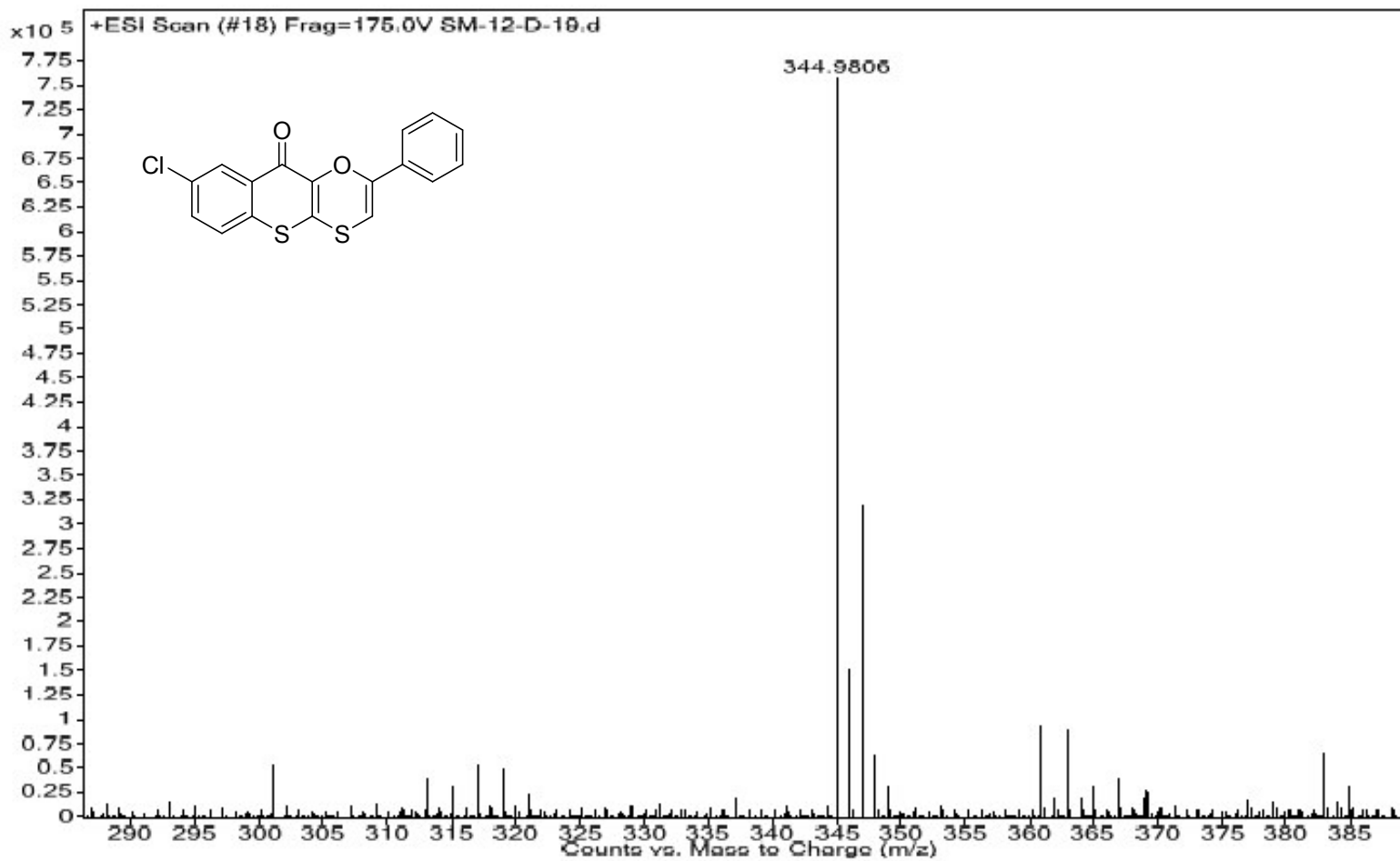
¹³C NMR of Compound 3ca

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SM-12D-19-13C



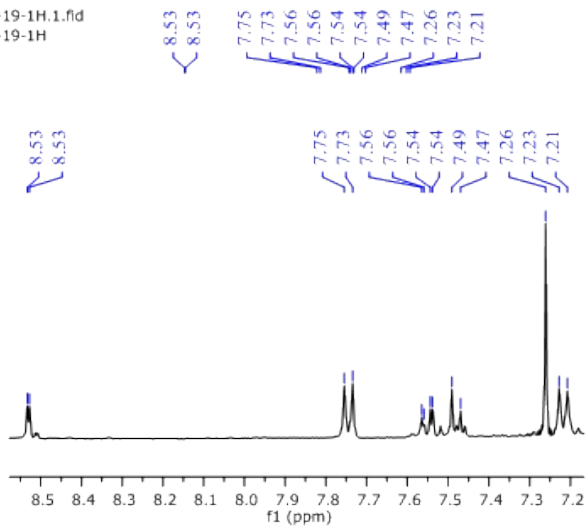
HRMS of Compound 3ca

Sample Name	SAMPLE	Position	P1-B3	Instrument Name	Instrument 1	User Name	
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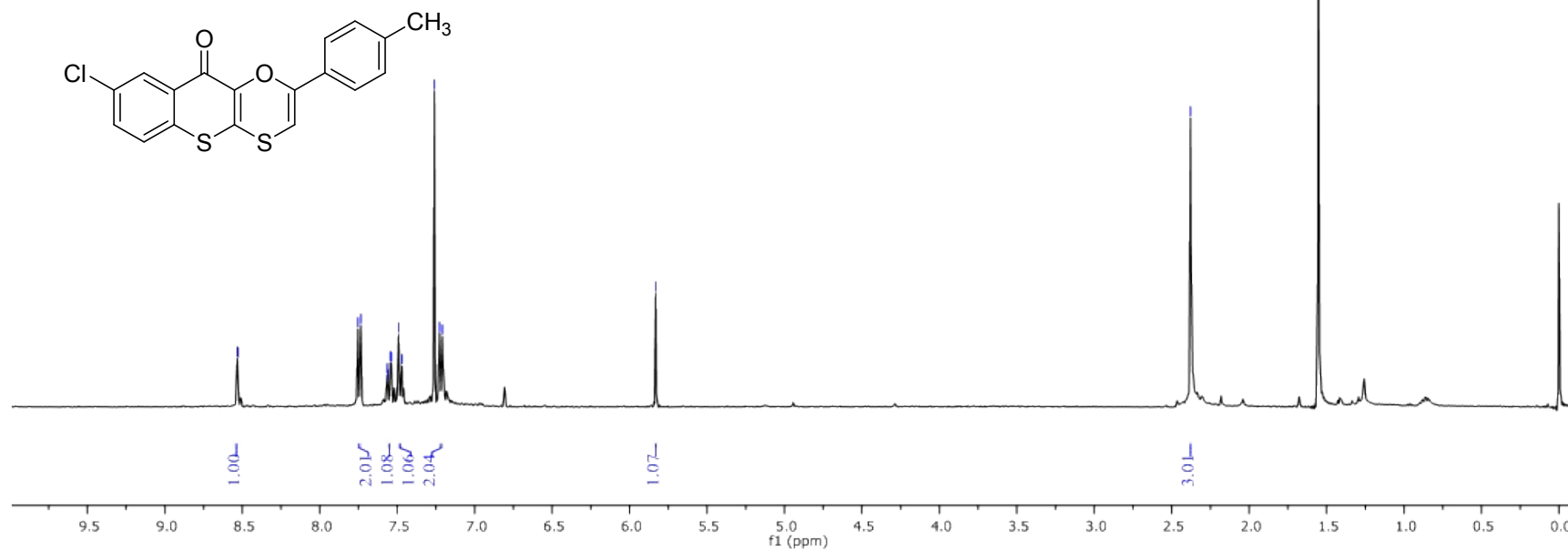
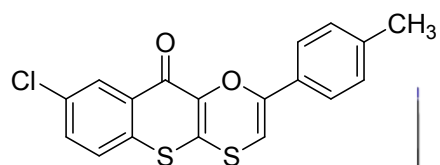
¹H NMR of Compound 3cc

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SM-12U-19-1H

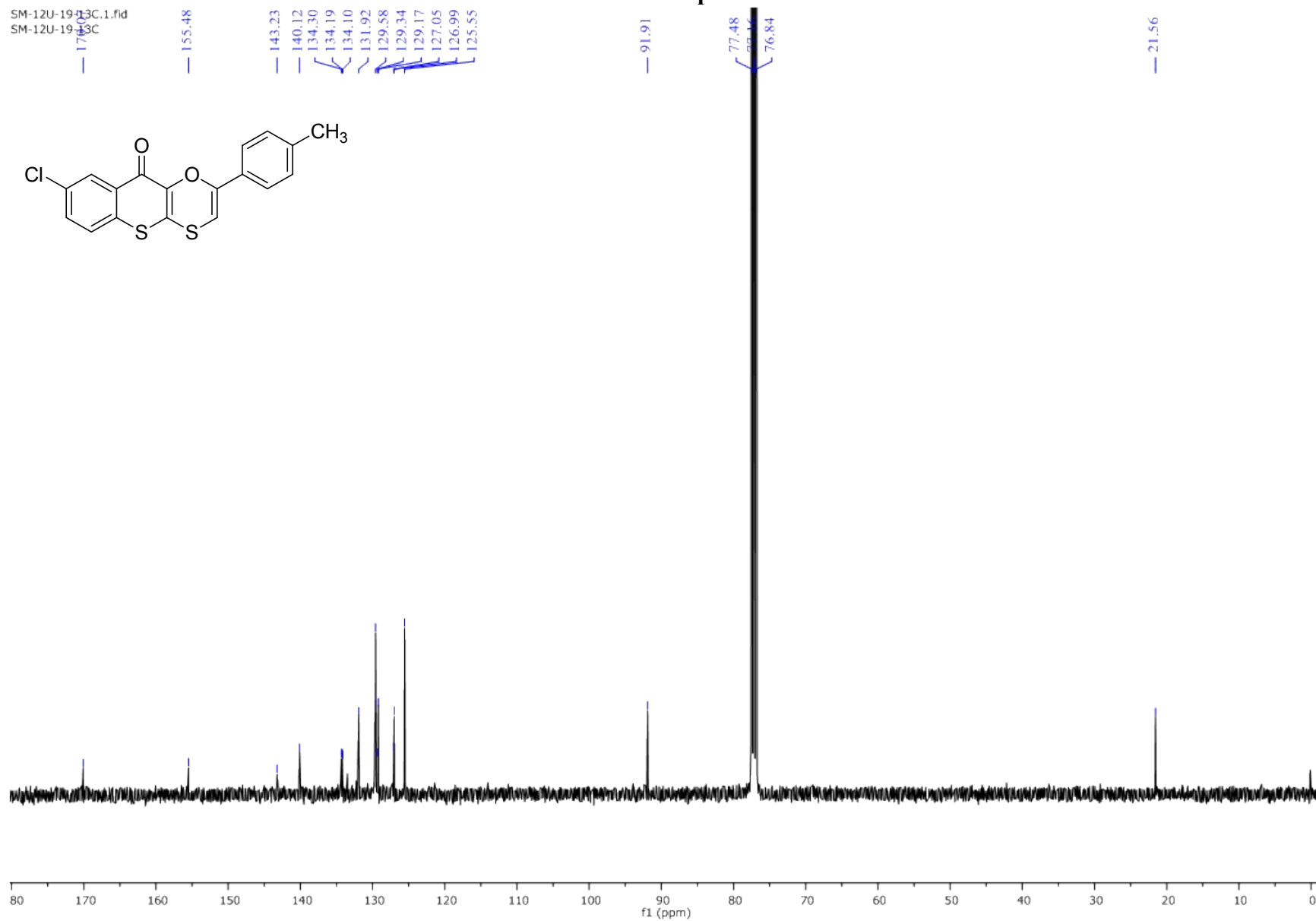


5.83

2.38

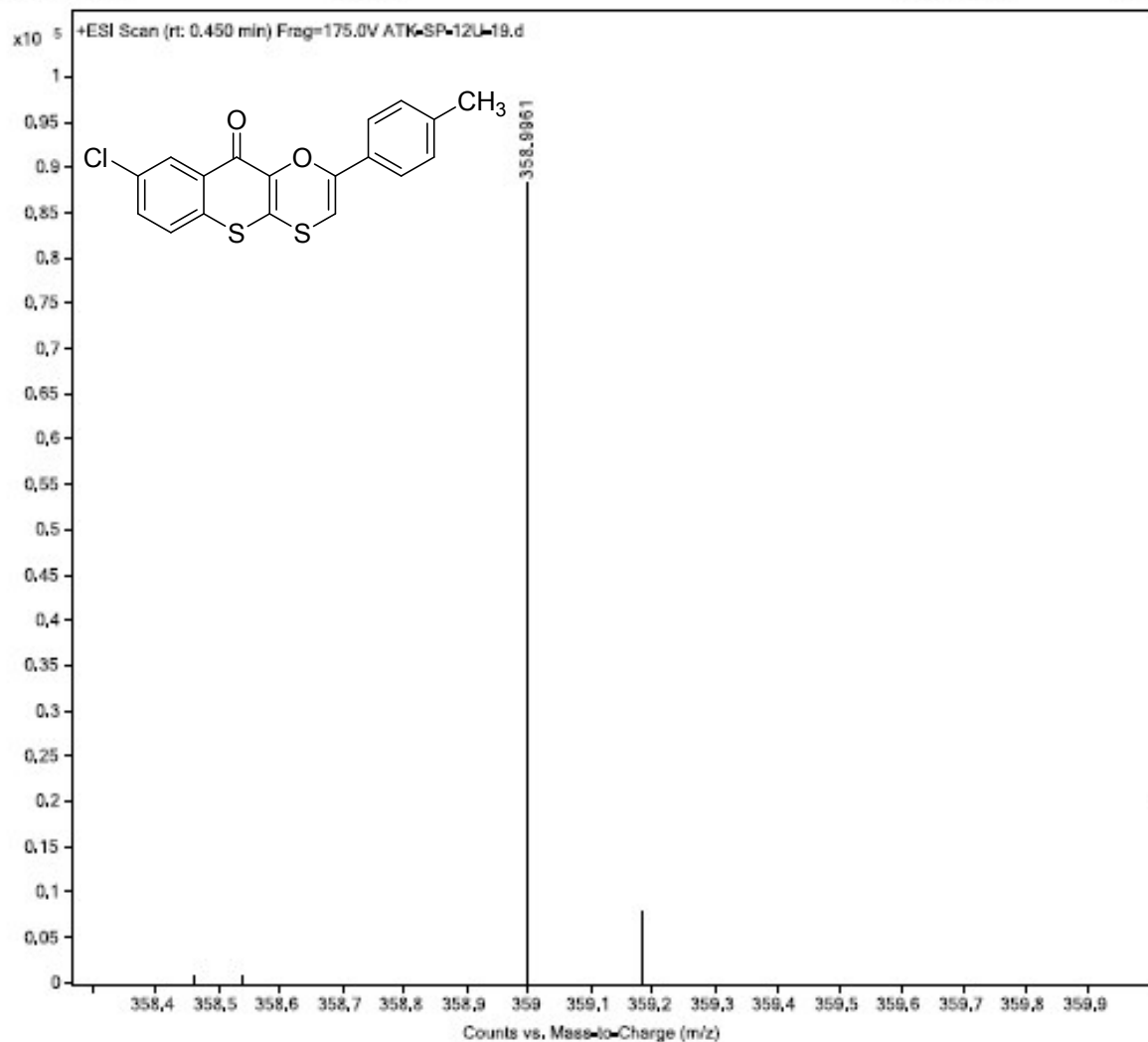


¹³C NMR of Compound 3cc



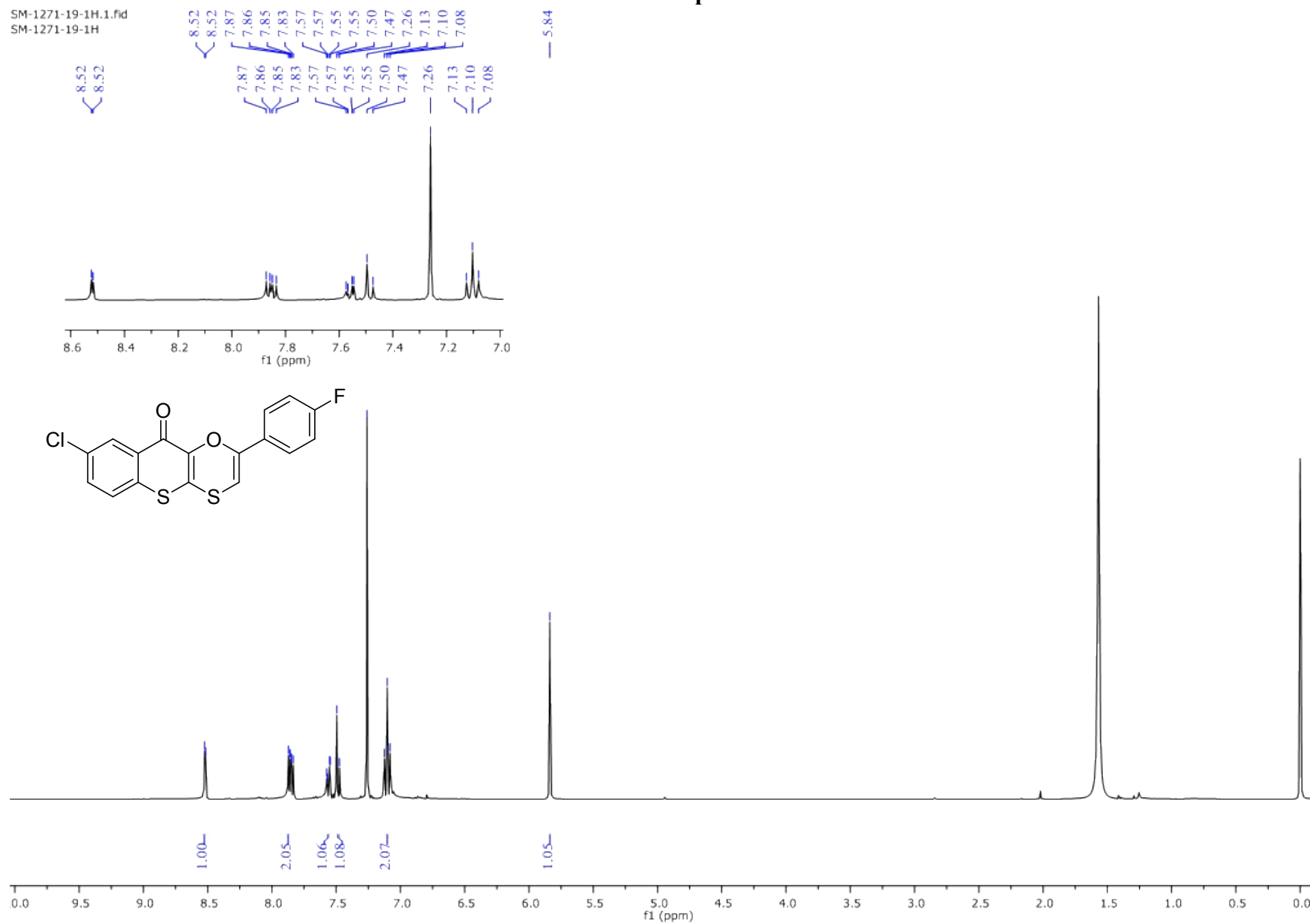
HRMS of Compound 3cc

Sample Name	ATK-SP-12U-19	Position	P1-B1	Instrument Name	Instrument 1
User Name		Inj Vol	Unknown / Injection Program	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	ATK-SP-12U-19.d
ACQ Method	ESI ALS 100=1000,m	Comment		Acquired Time	2020-11-20 10:29:42 (UTC+05:30)

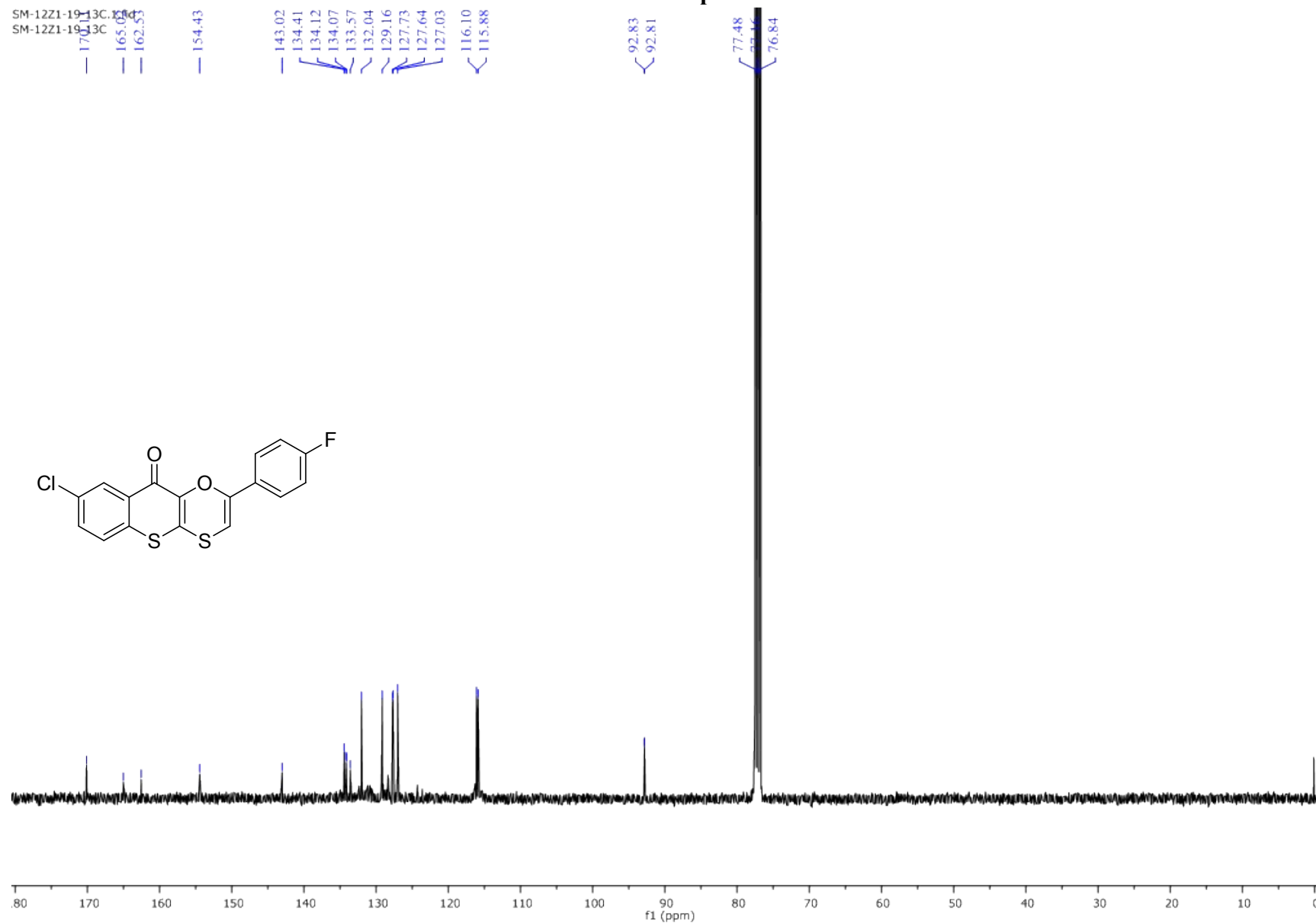


¹H NMR of Compound 3cd

SM-1271-19-1H.1.fid
SM-1271-19-1H

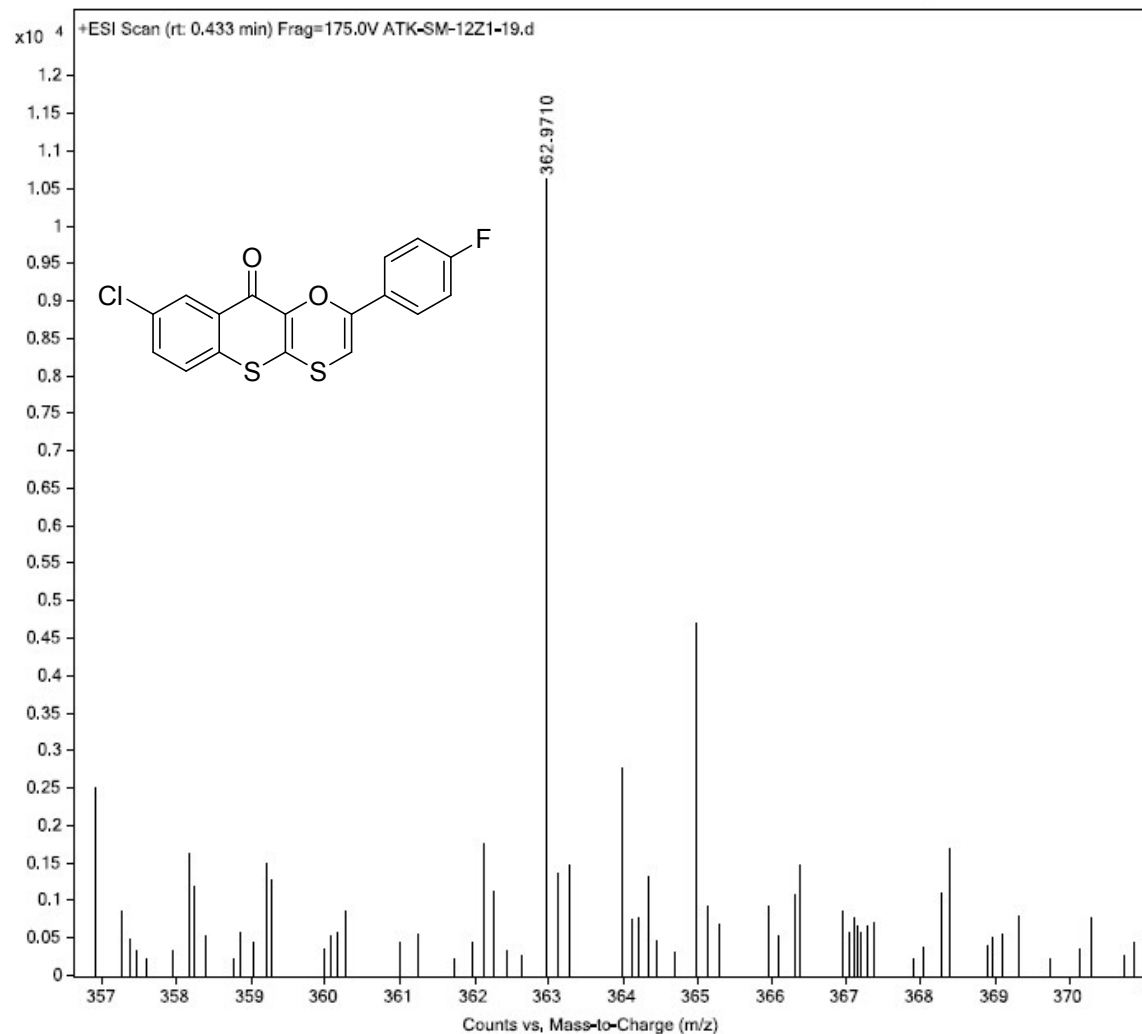


¹³C NMR of Compound 3cd



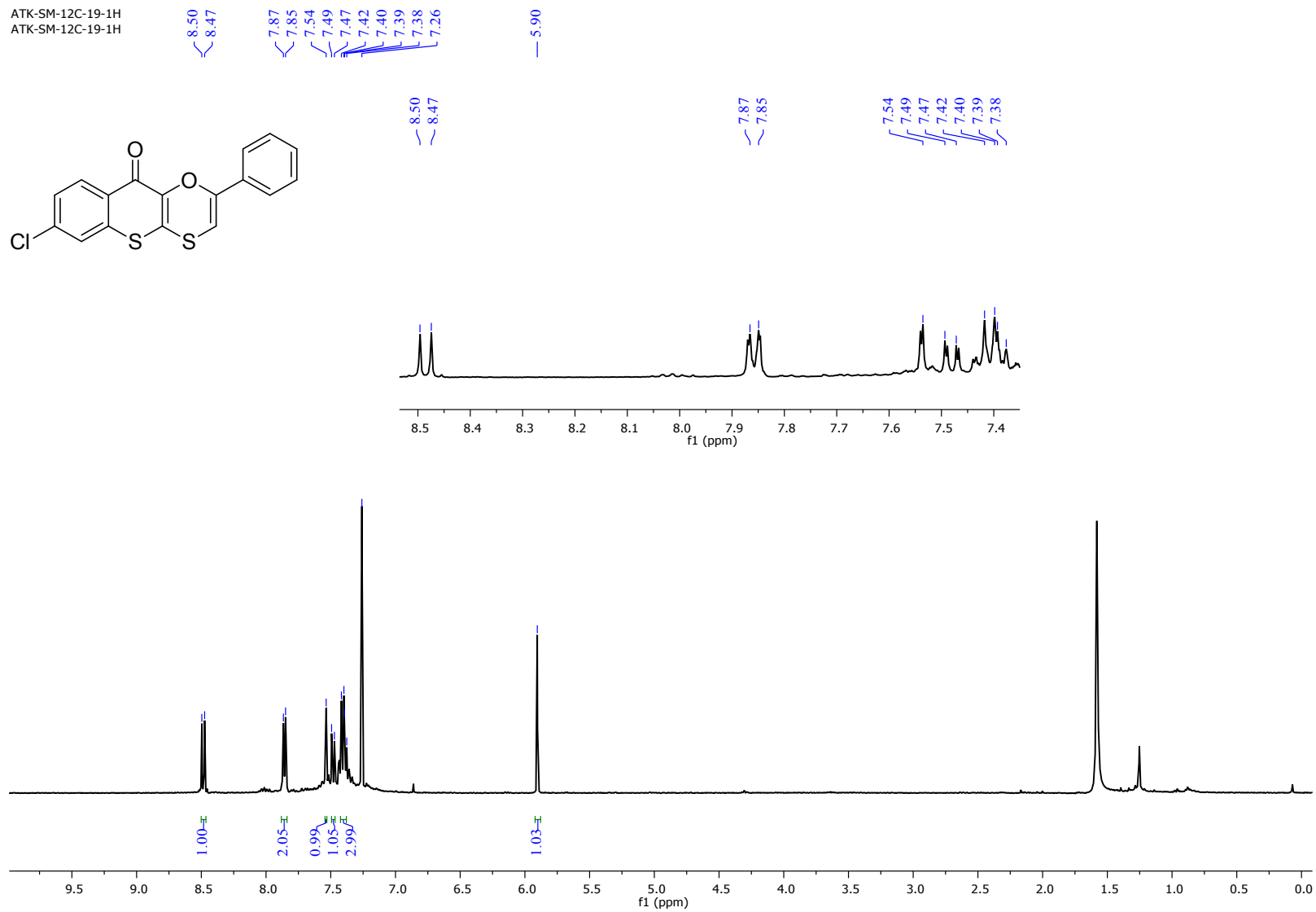
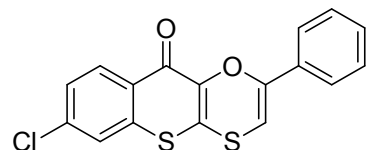
HRMS of Compound 3cd

Sample Name	ATK-SM-12Z1-19	Position	P1-A4	Instrument Name	Instrument 1
User Name		Inj Vol	20	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	ATK-SM-12Z1-19.d
ACQ Method	ESI ALS 100-1000,m	Comment		Acquired Time	02-12-2020 11:45:55 (UTC+05:30)



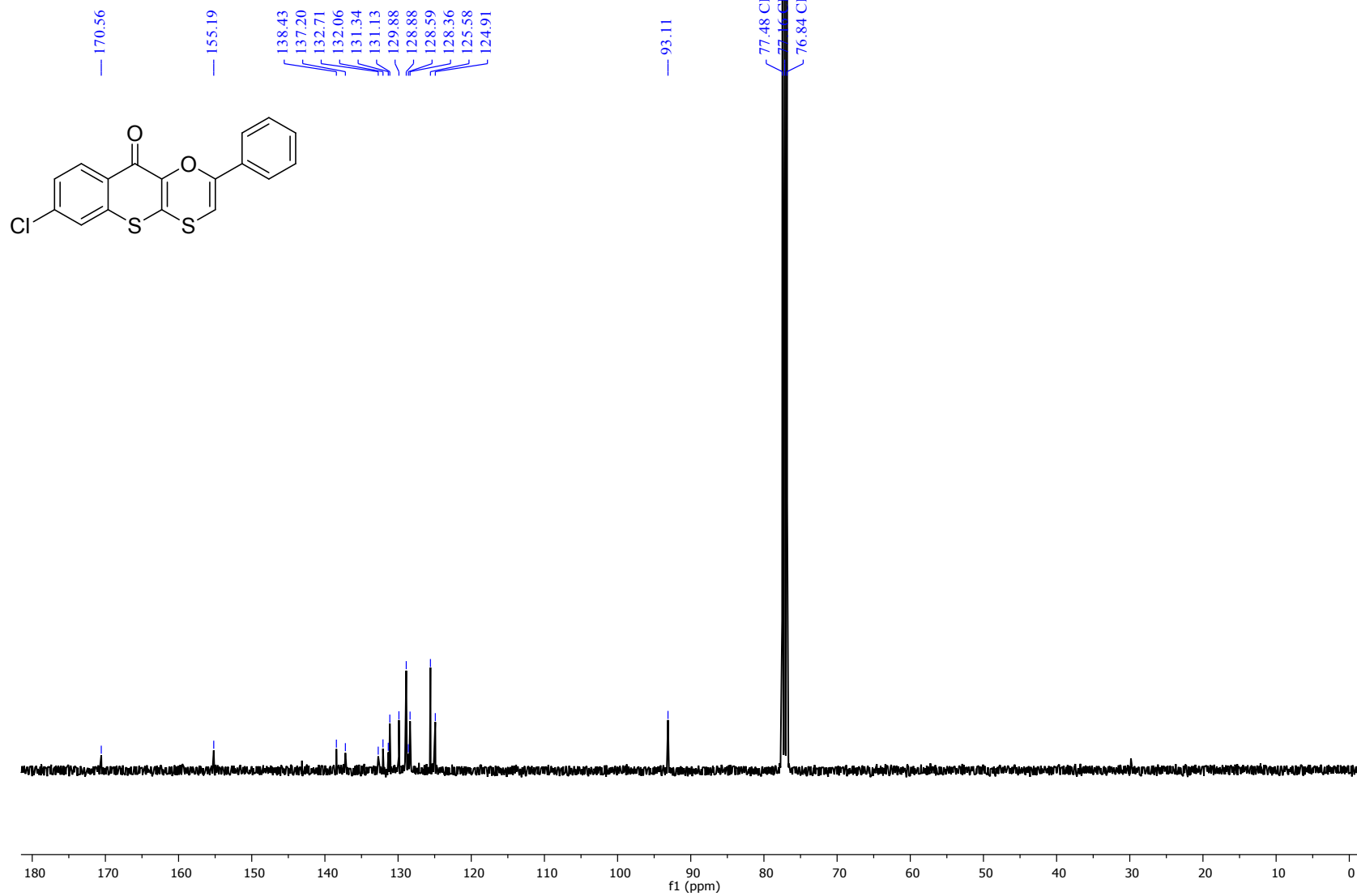
¹H NMR of Compound 3da

ATK-SM-12C-19-1H
ATK-SM-12C-19-1H



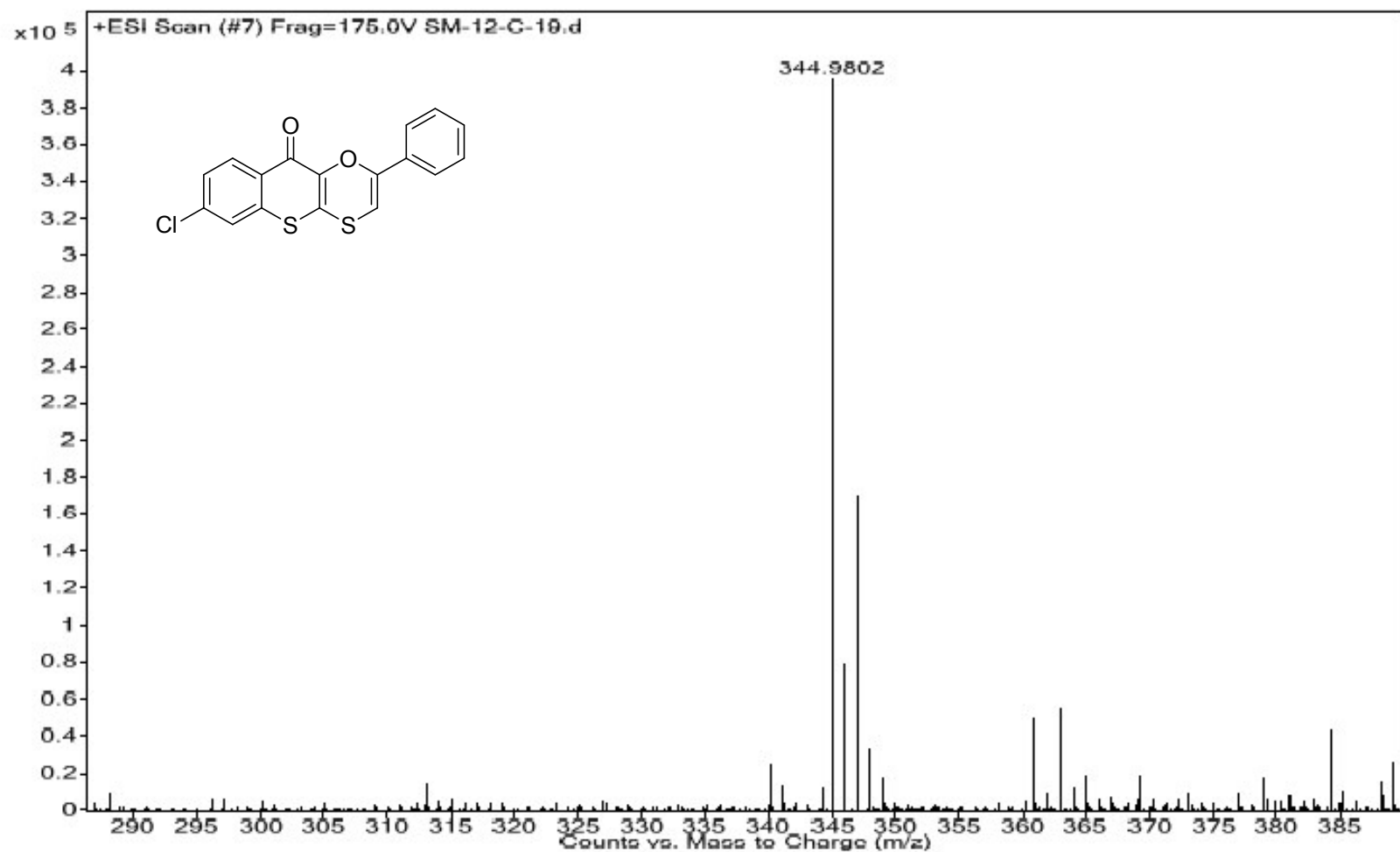
¹³C NMR of Compound 3da

ATK-SM-12C-19-13C
ATK-SM-12C-19-13C



HRMS of Compound 3da

Sample Name	SAMPLE	Position	P1-B2	Instrument Name	Instrument 1	User Name	
Inj Vol	20	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	SM-12-C-19.d	ACQ Method	ESI ALS 100-1000.m	Comment		Acquired Time	10/28/2019 4:57:24 PM



¹H NMR of Compound 3db

ATK-SM-12M2-19-1H
ATK-SM-12M2-19-1H

8.49
8.47
7.80
7.78
7.54
7.53
7.49
7.48
7.46
7.46
7.44
7.42
7.26

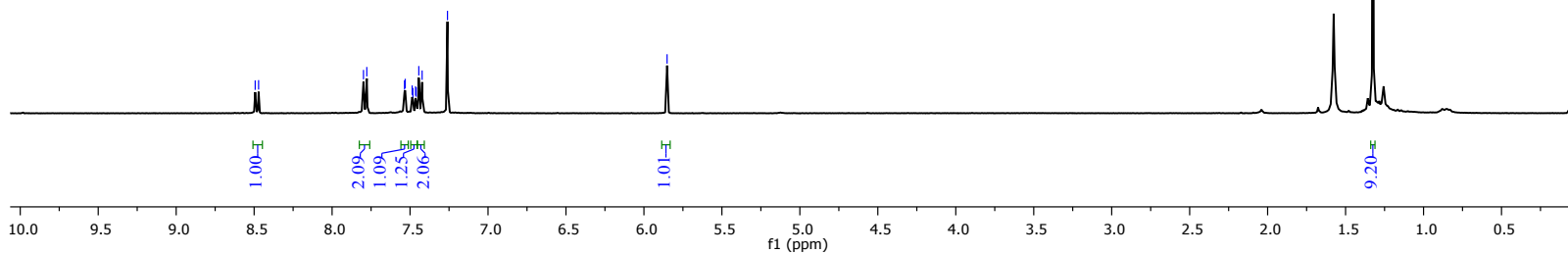
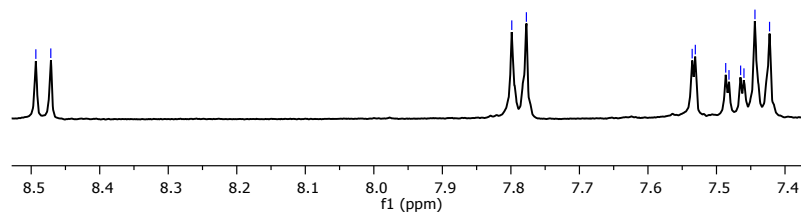
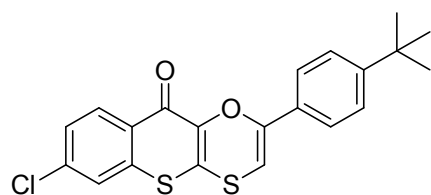
5.85

1.32

8.49
8.47

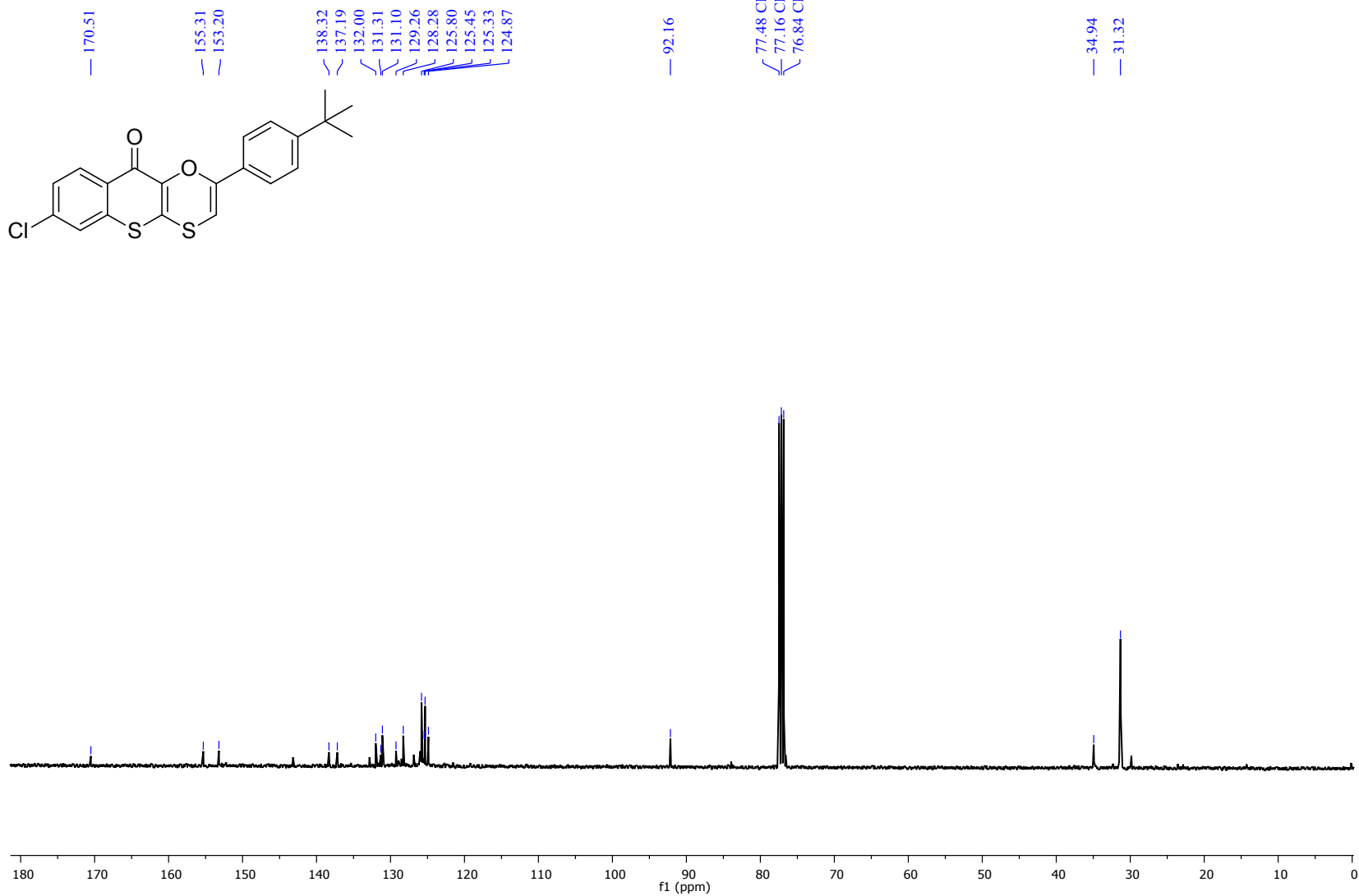
7.80
7.78

7.54
7.53
7.49
7.48
7.46
7.46
7.44
7.42



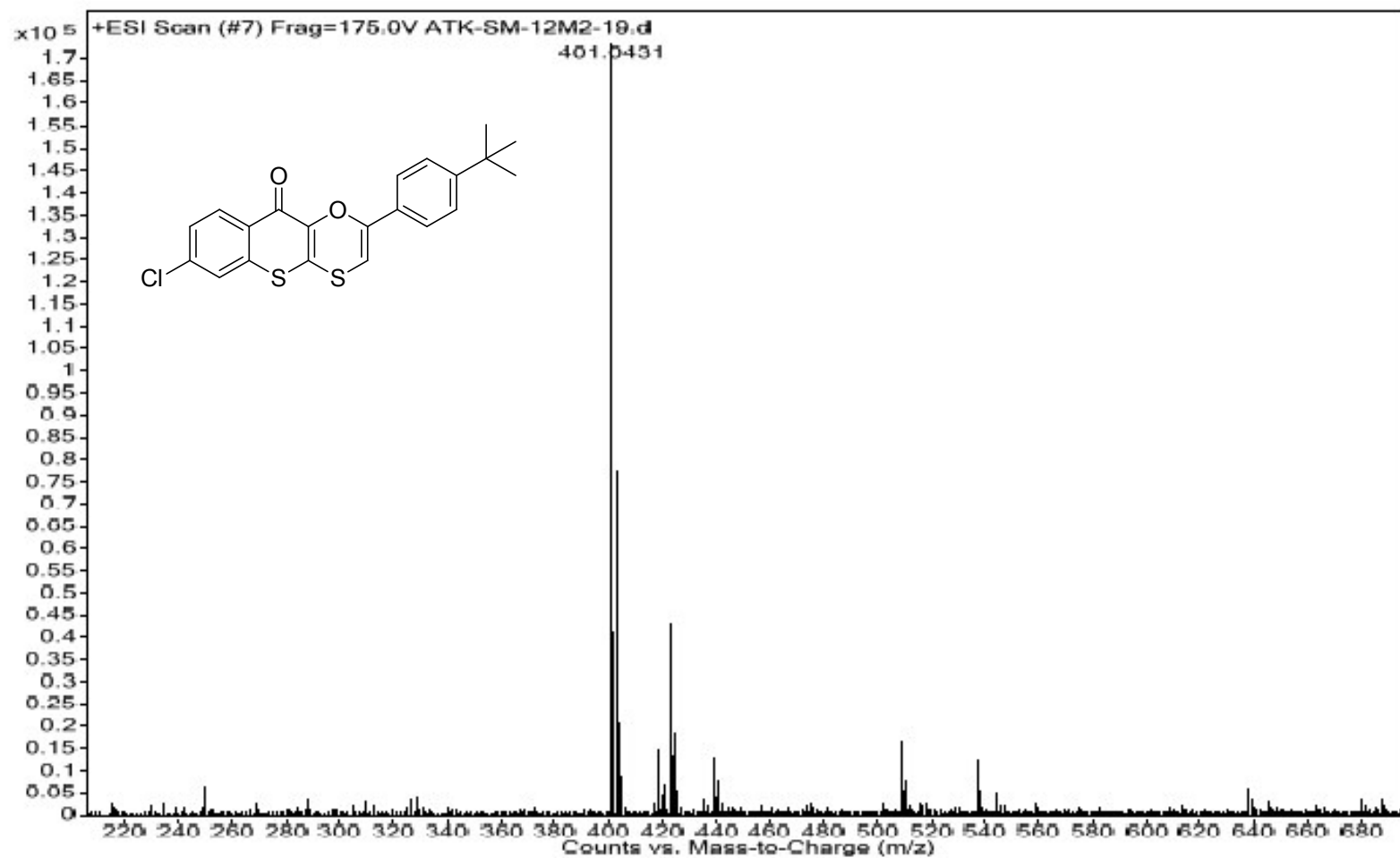
¹³C NMR of Compound 3db

ATK-SM-12M2-19-13C
ATK-SM-12M2-19-13C



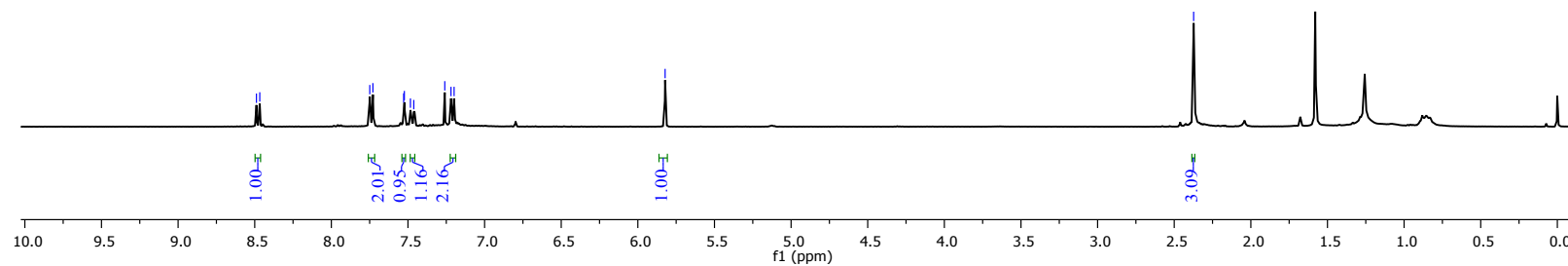
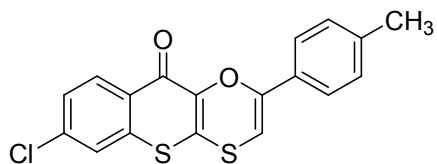
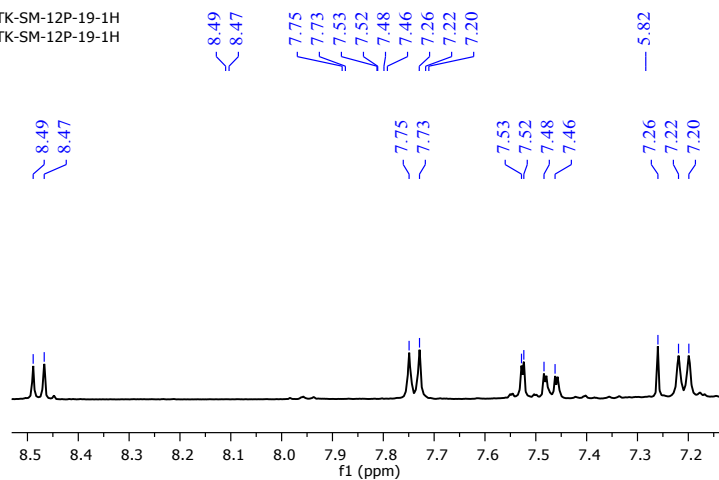
HRMS of Compound 3db

Sample Name	ATK-SM-12M2-19	Position	P1-A6	Instrument Name	Instrument 1	User Name	
Inj Vol	20	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	ATK-SM-12M2-19.d	ACQ Method	ESI ALS 100-1000.m	Comment		Acquired Time	11/26/2020 11:14:32 AM

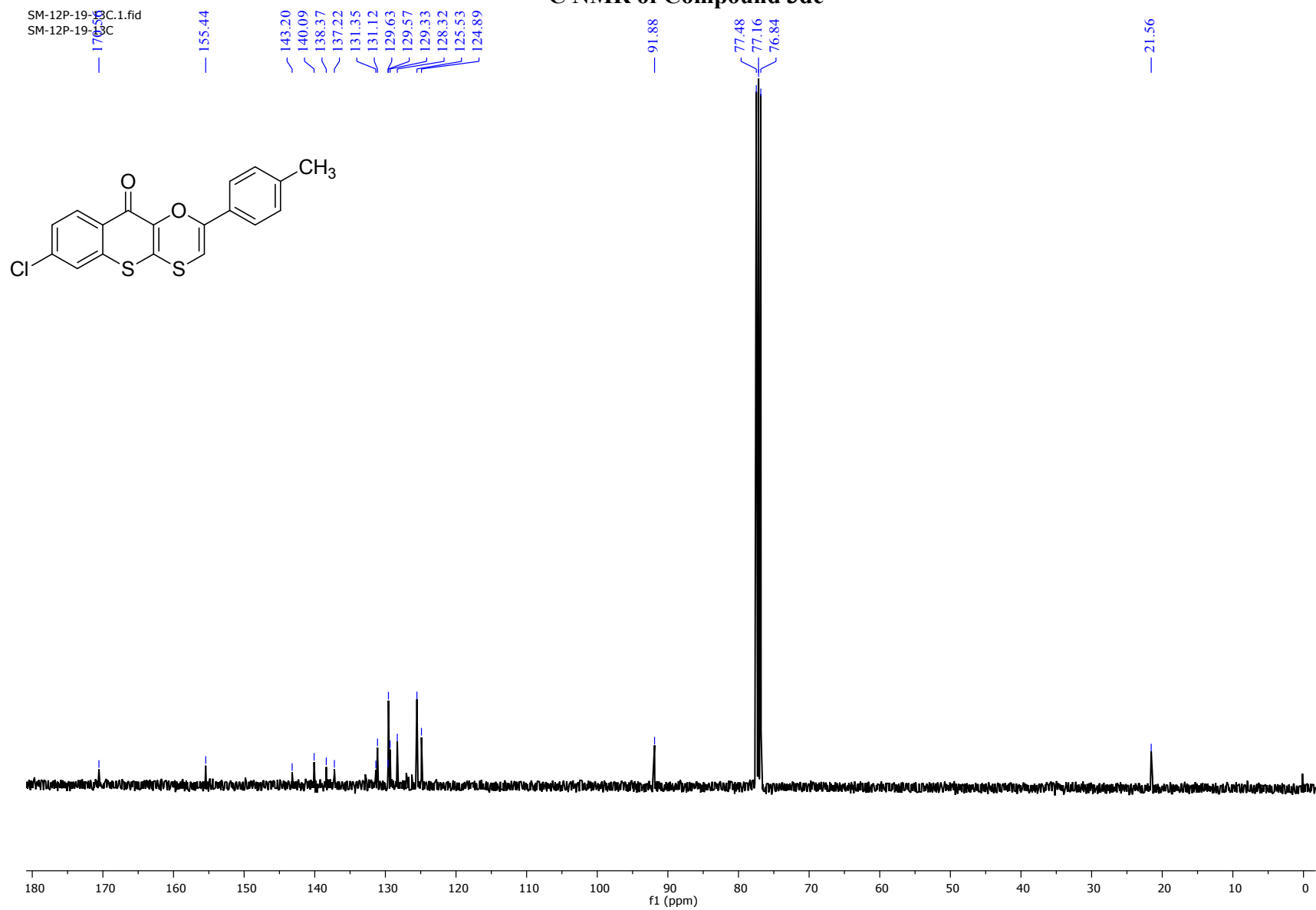


¹H NMR of Compound 3dc

ATK-SM-12P-19-1H
ATK-SM-12P-19-1H

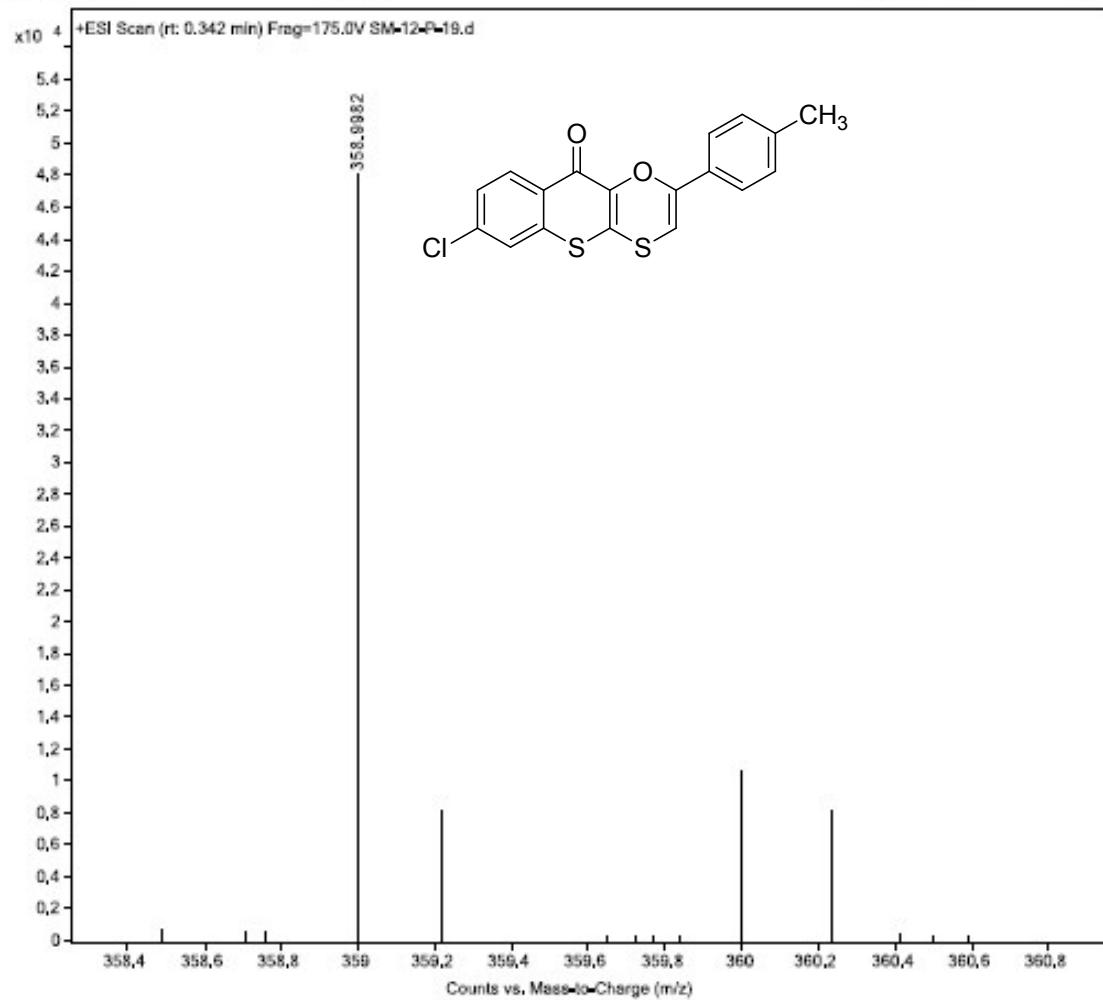


¹³C NMR of Compound 3dc



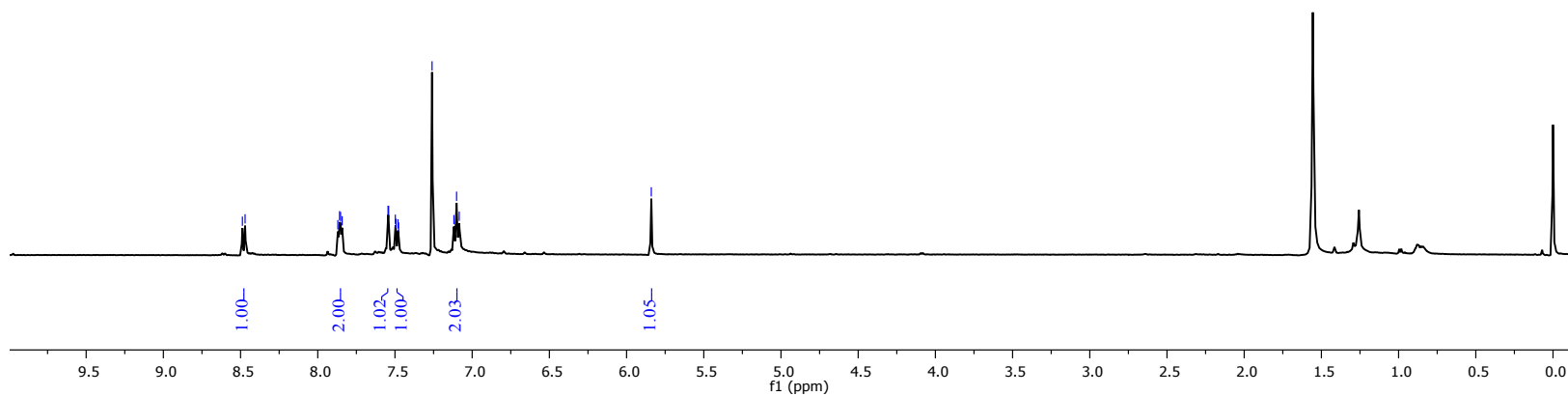
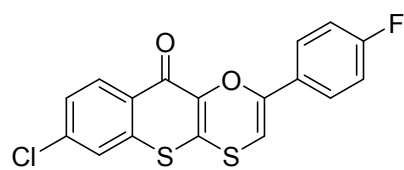
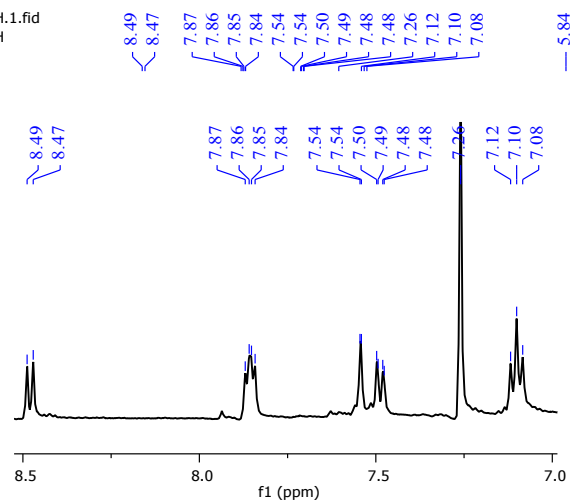
HRMS of Compound 3dc

Sample Name	SM-12-P-19	Position	P1-C3	Instrument Name	Instrument 1
User Name		Inj Vol	20	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	SM-12-P-19.d
ACQ Method	ESI ALS 100-1000,m	Comment		Acquired Time	28-10-2020 13:02:06 (UTC+05:30)



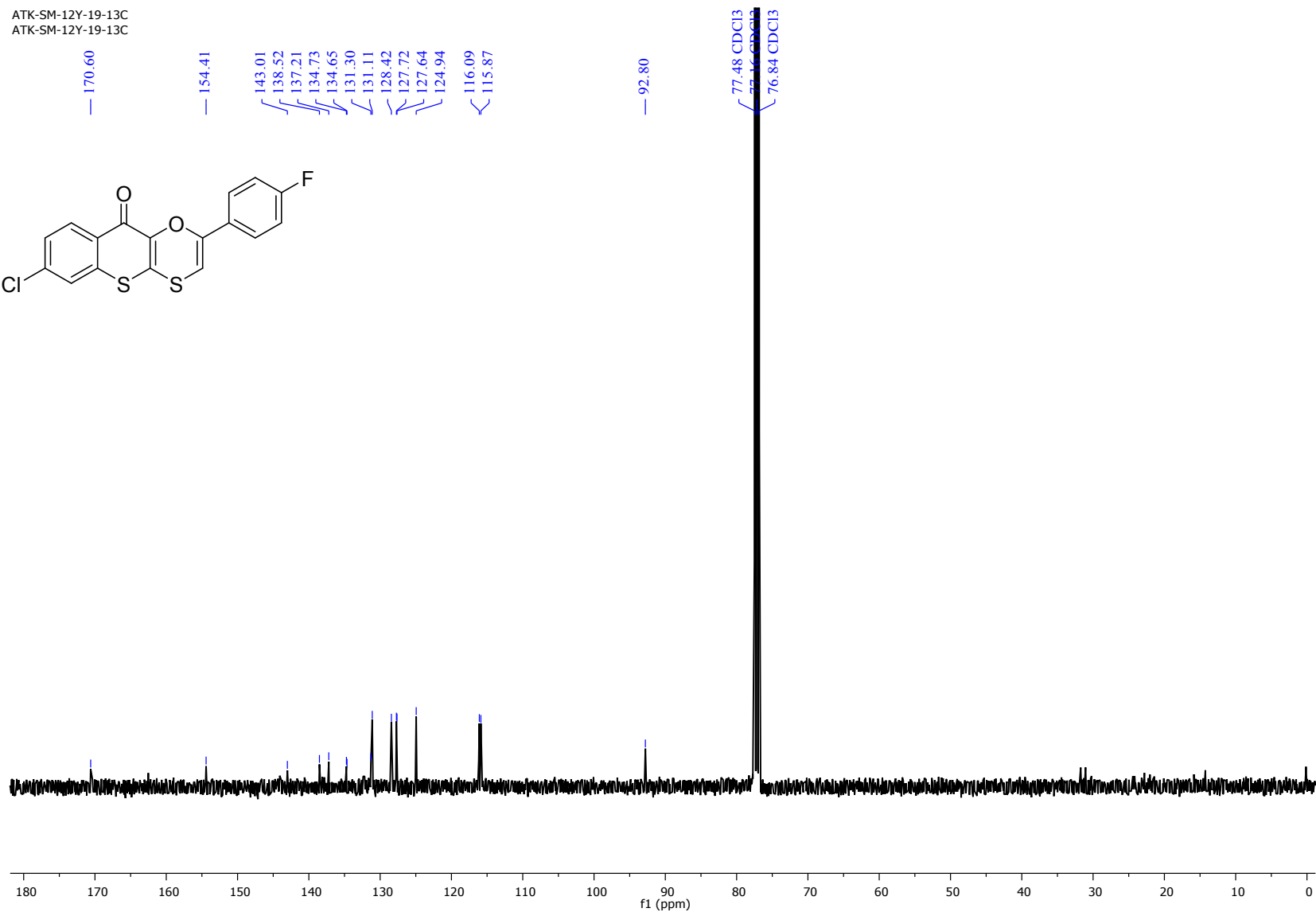
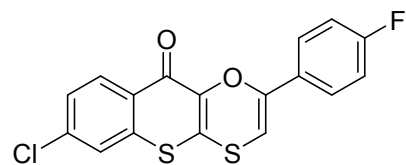
SM-12Y-19-1H.1.fid
SM-12Y-19-1H

¹H NMR of Compound 3dd

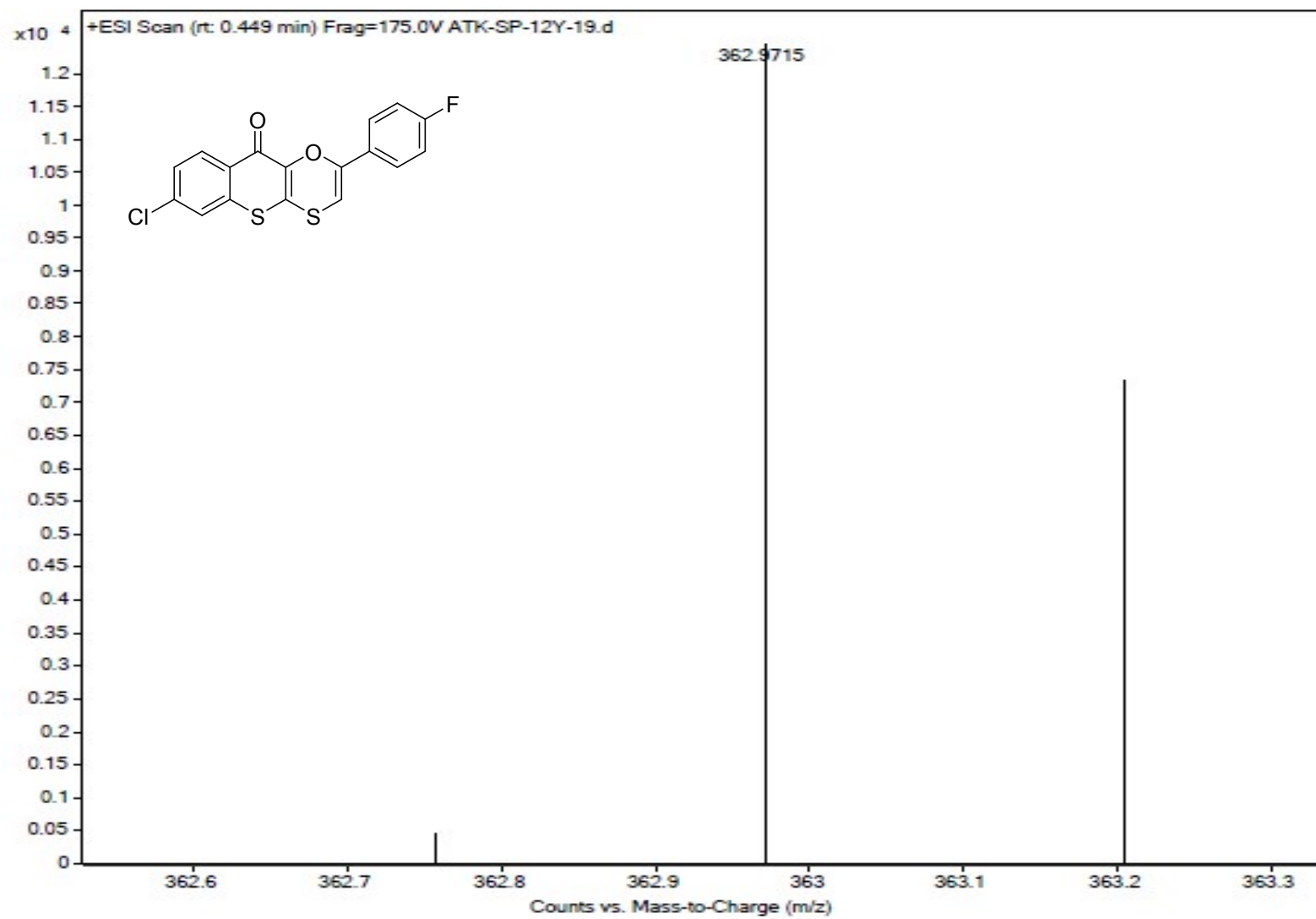


¹³C NMR of Compound 3dd

ATK-SM-12Y-19-13C
ATK-SM-12Y-19-13C

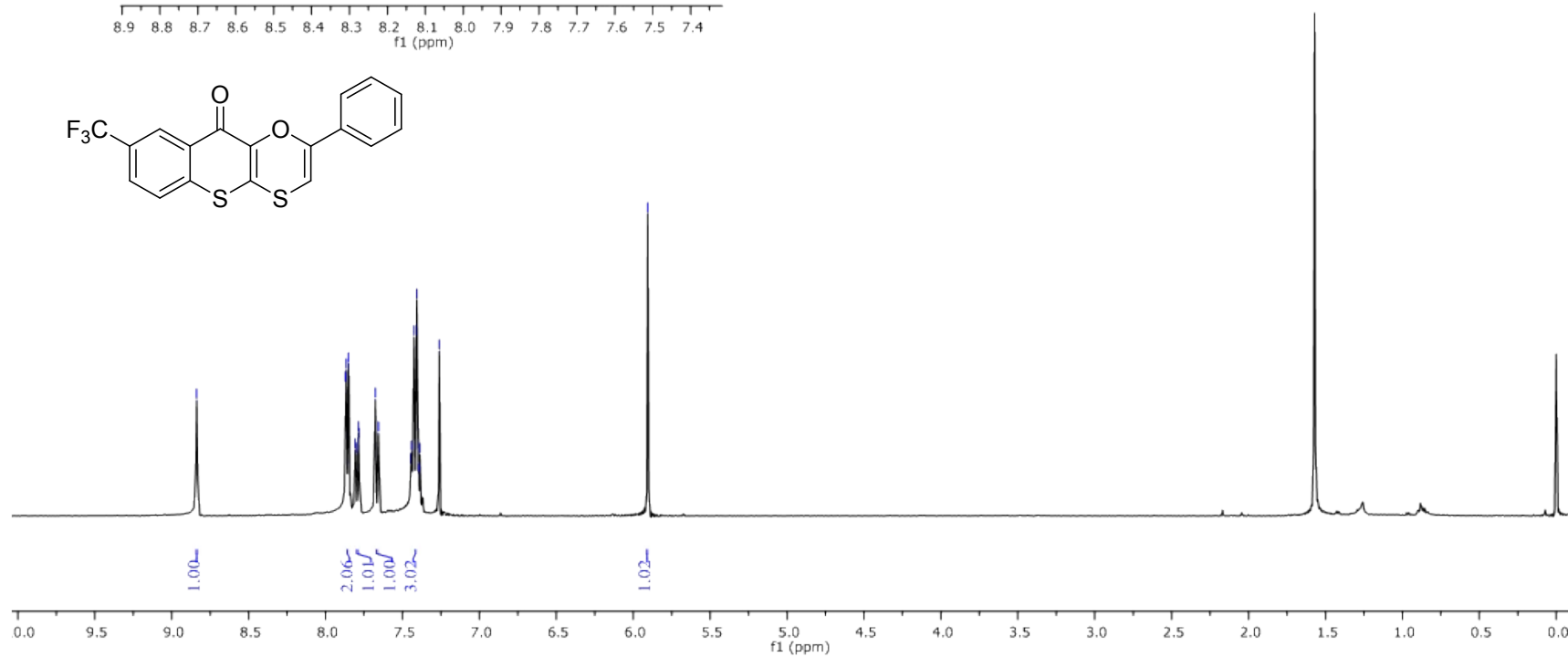
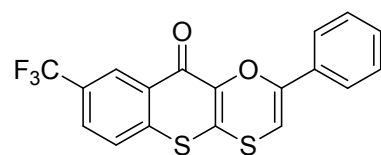
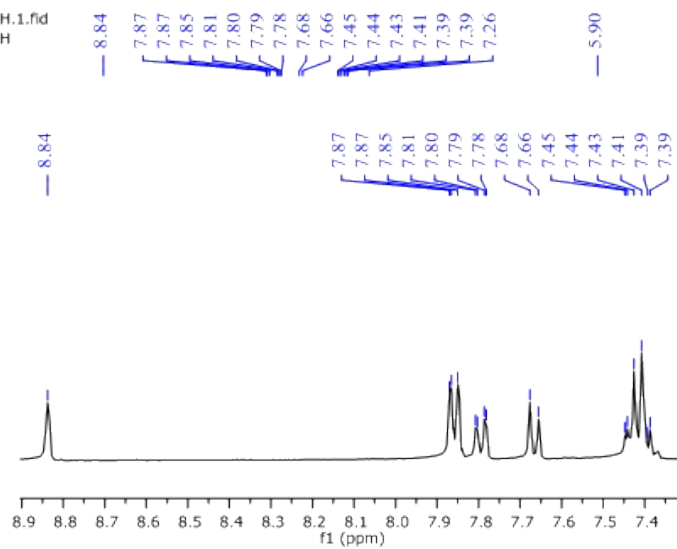


HRMS of Compound 3dd

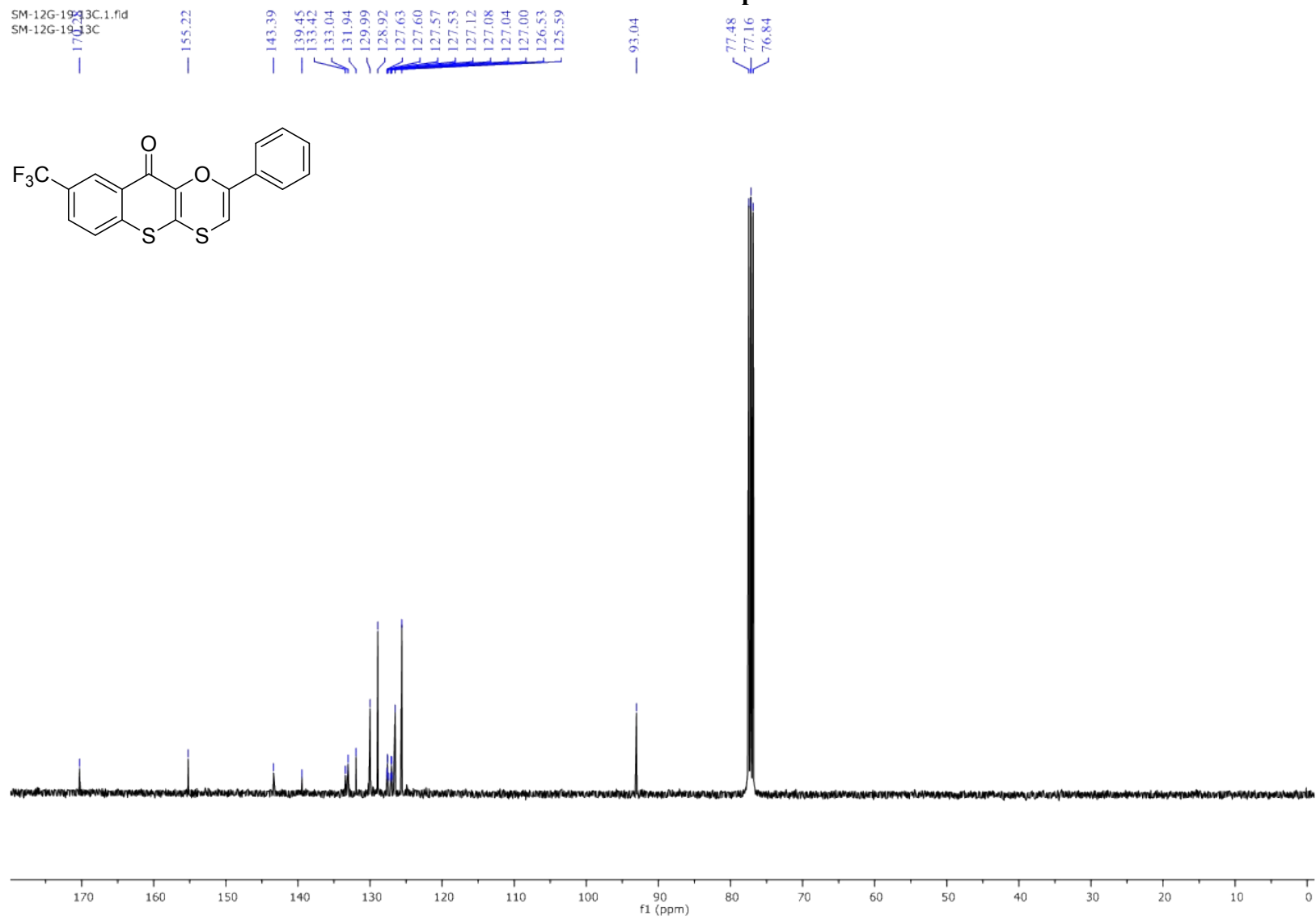


¹H NMR of Compound 3ea

SM-12G-19-1H.1.fid
SM-12G-19-1H

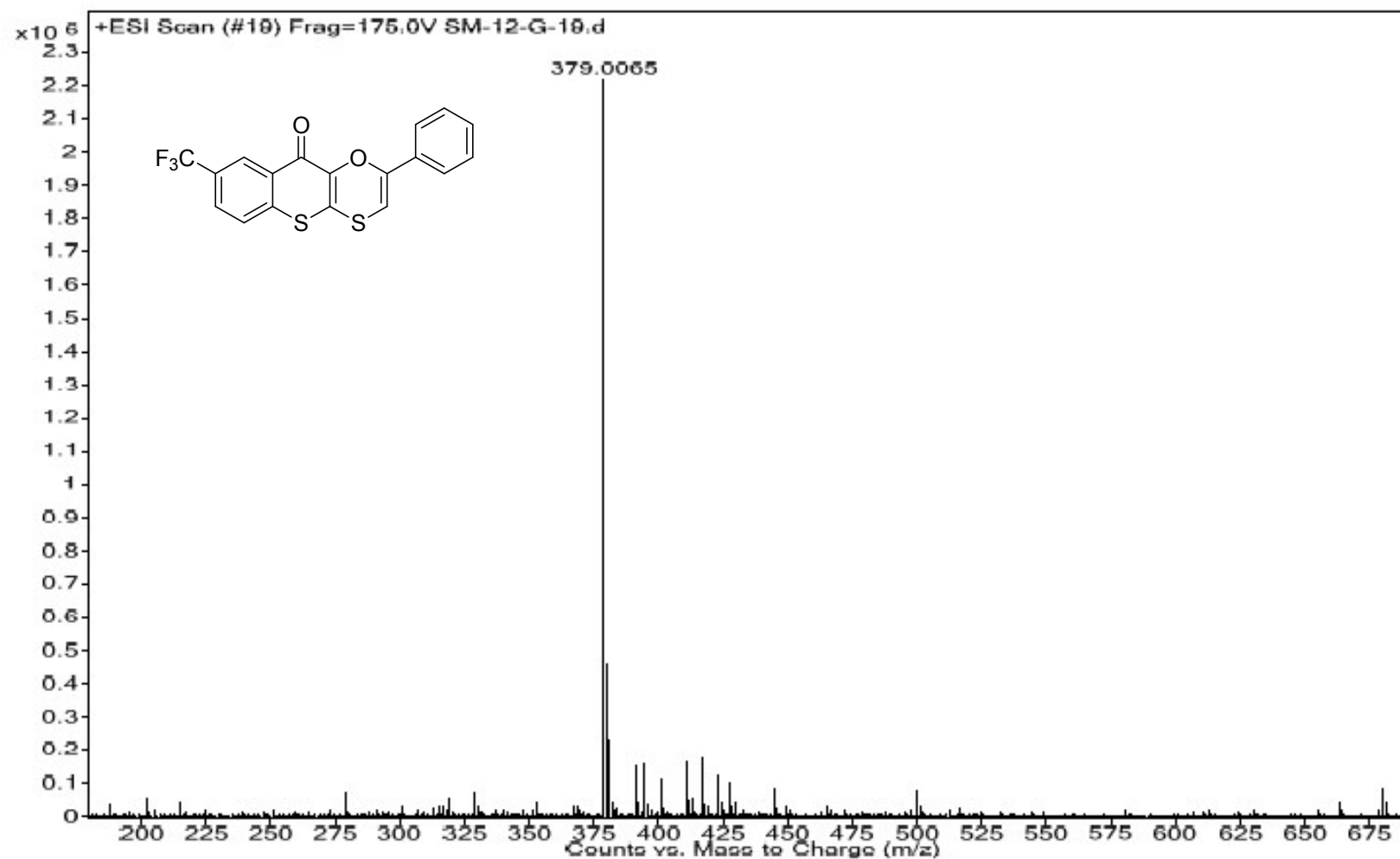


¹³C NMR of Compound 3ea



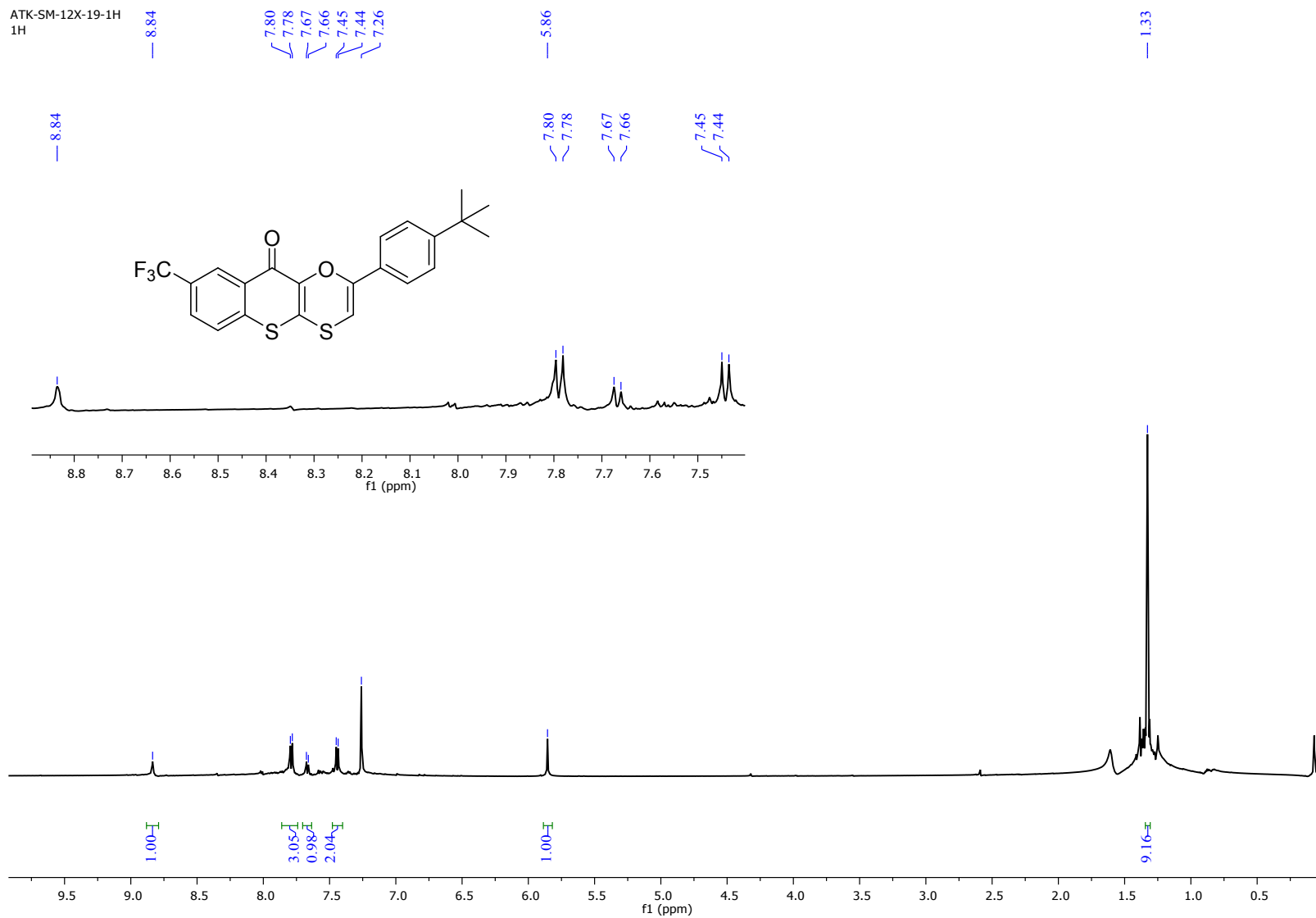
HRMS of Compound 3ea

Sample Name	SAMPLE	Position	P1-B5	Instrument Name	Instrument 1	User Name	
Inj Vol	20	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	SM-12-G-19.d	ACQ Method	ESI ALS 100-1000.m	Comment		Acquired Time	10/28/2019 5:02:55 PM



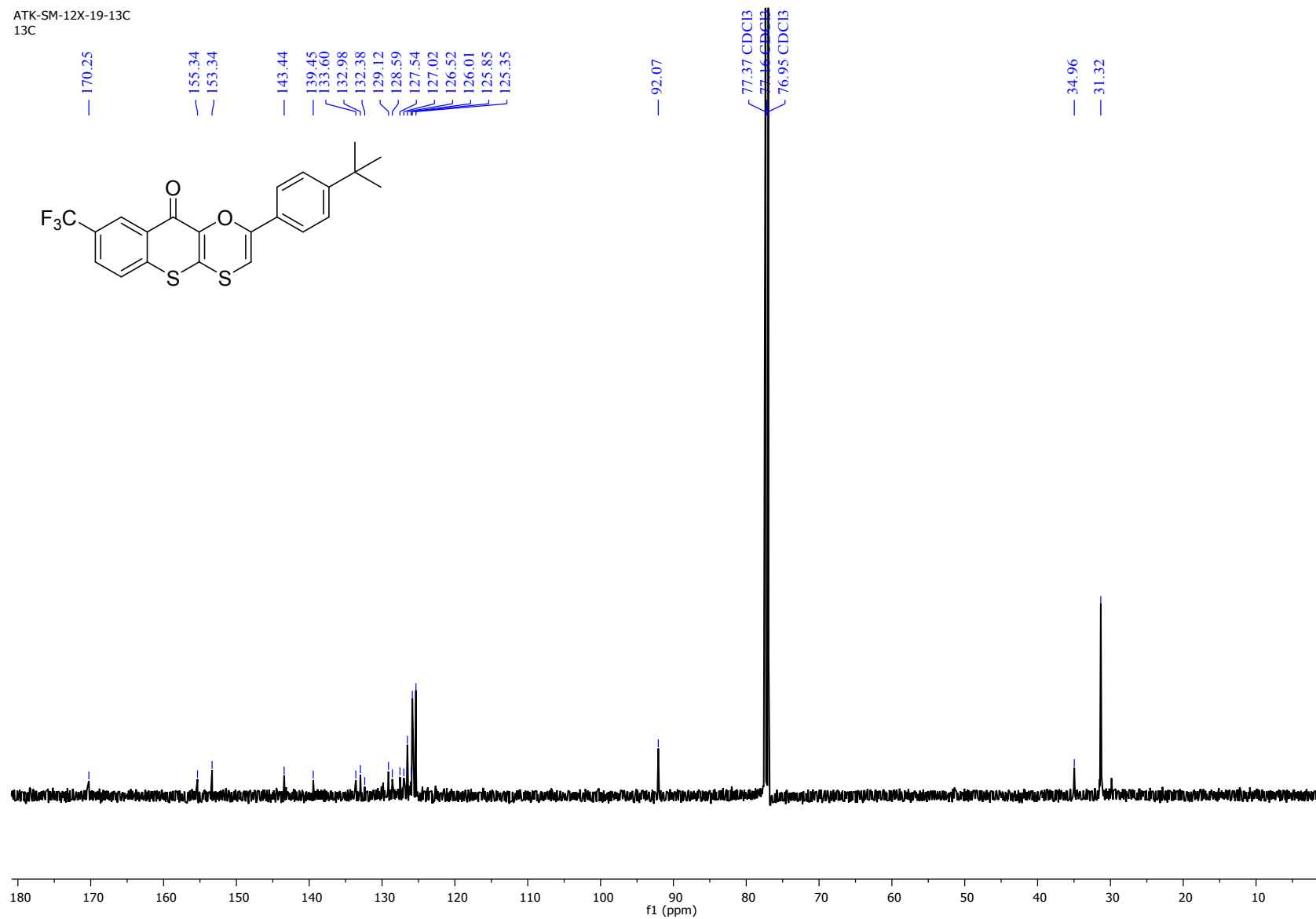
¹H NMR of Compound 3eb

ATK-SM-12X-19-1H
1H

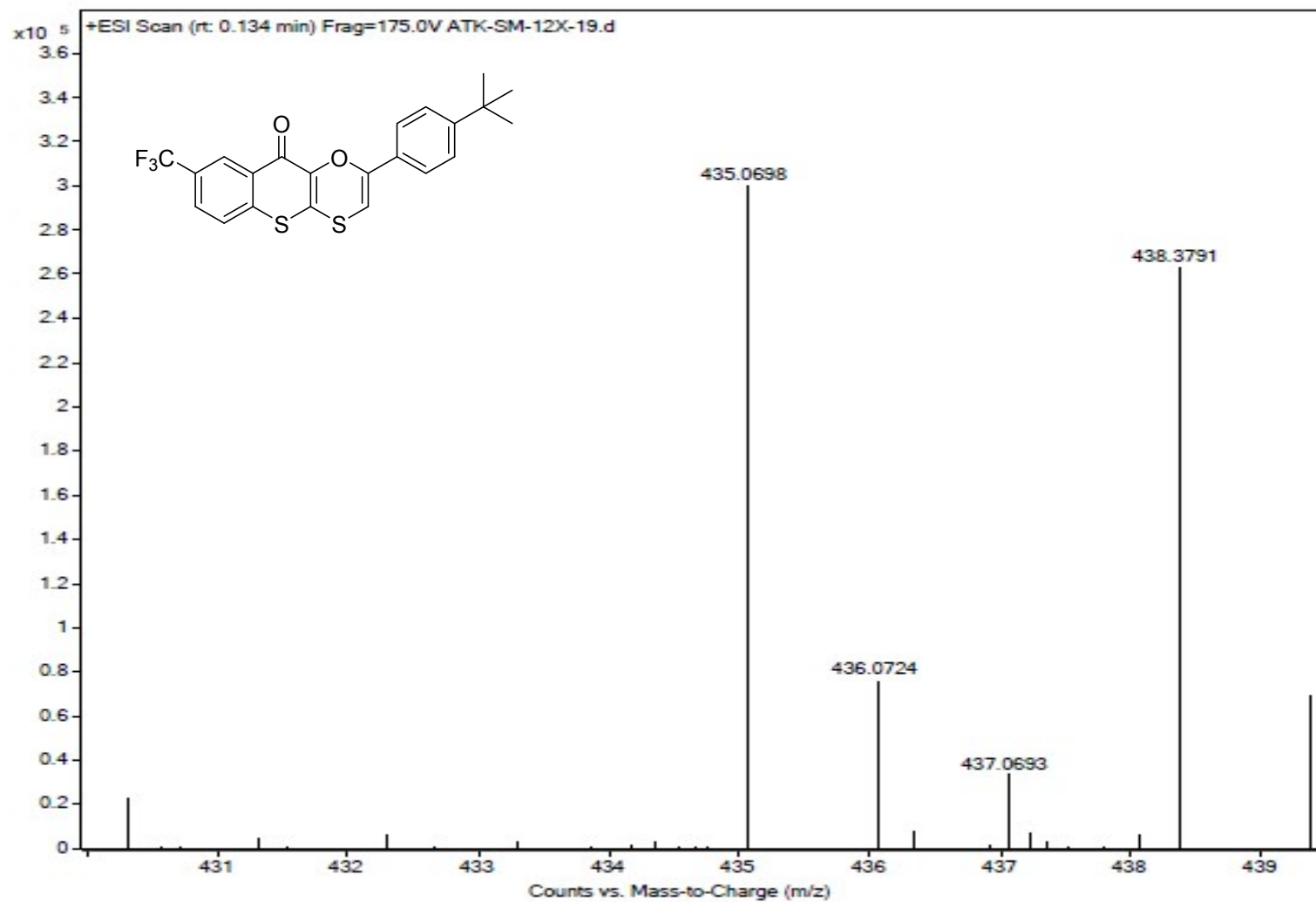


¹³C NMR of Compound 3eb

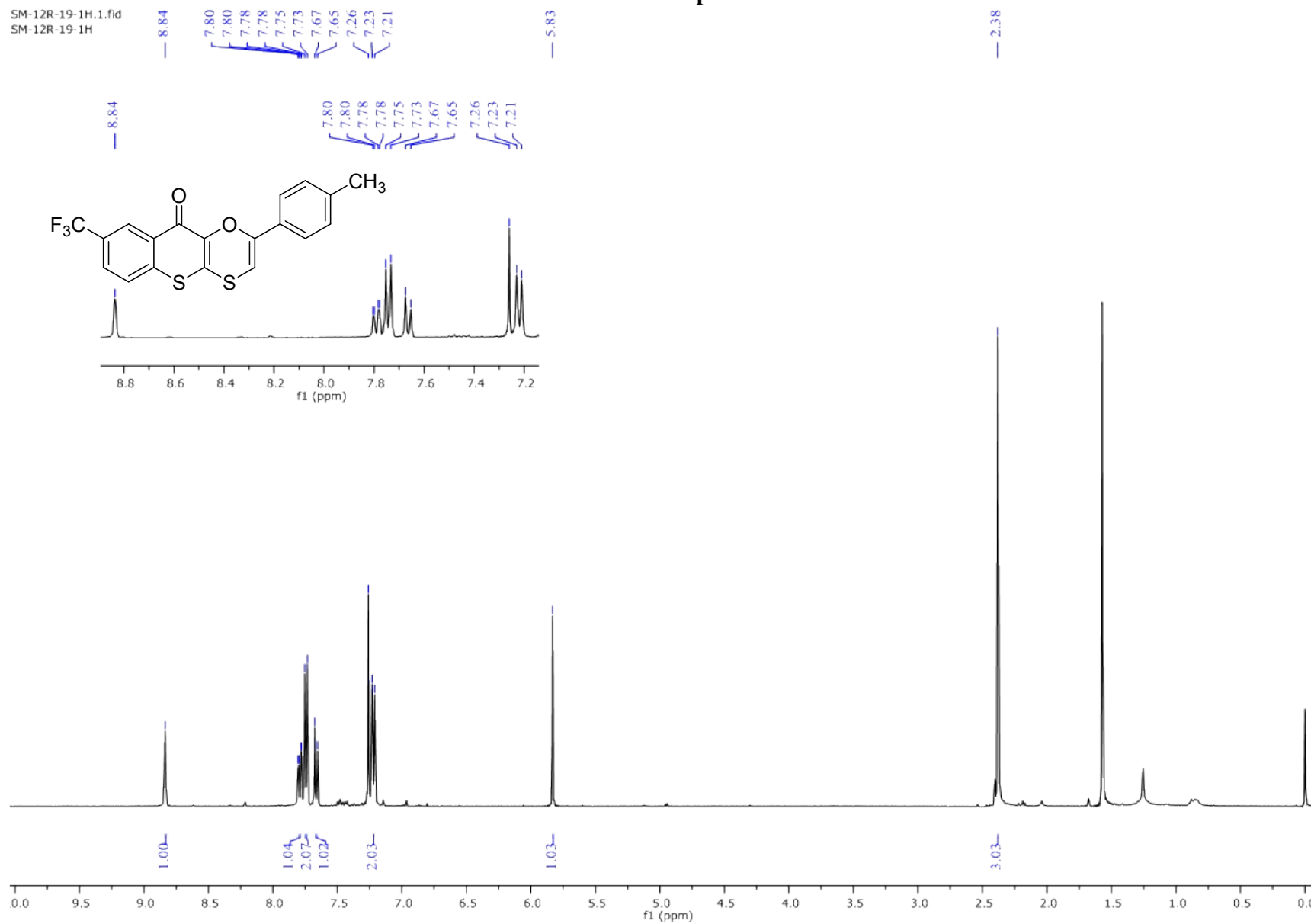
ATK-SM-12X-19-13C
13C



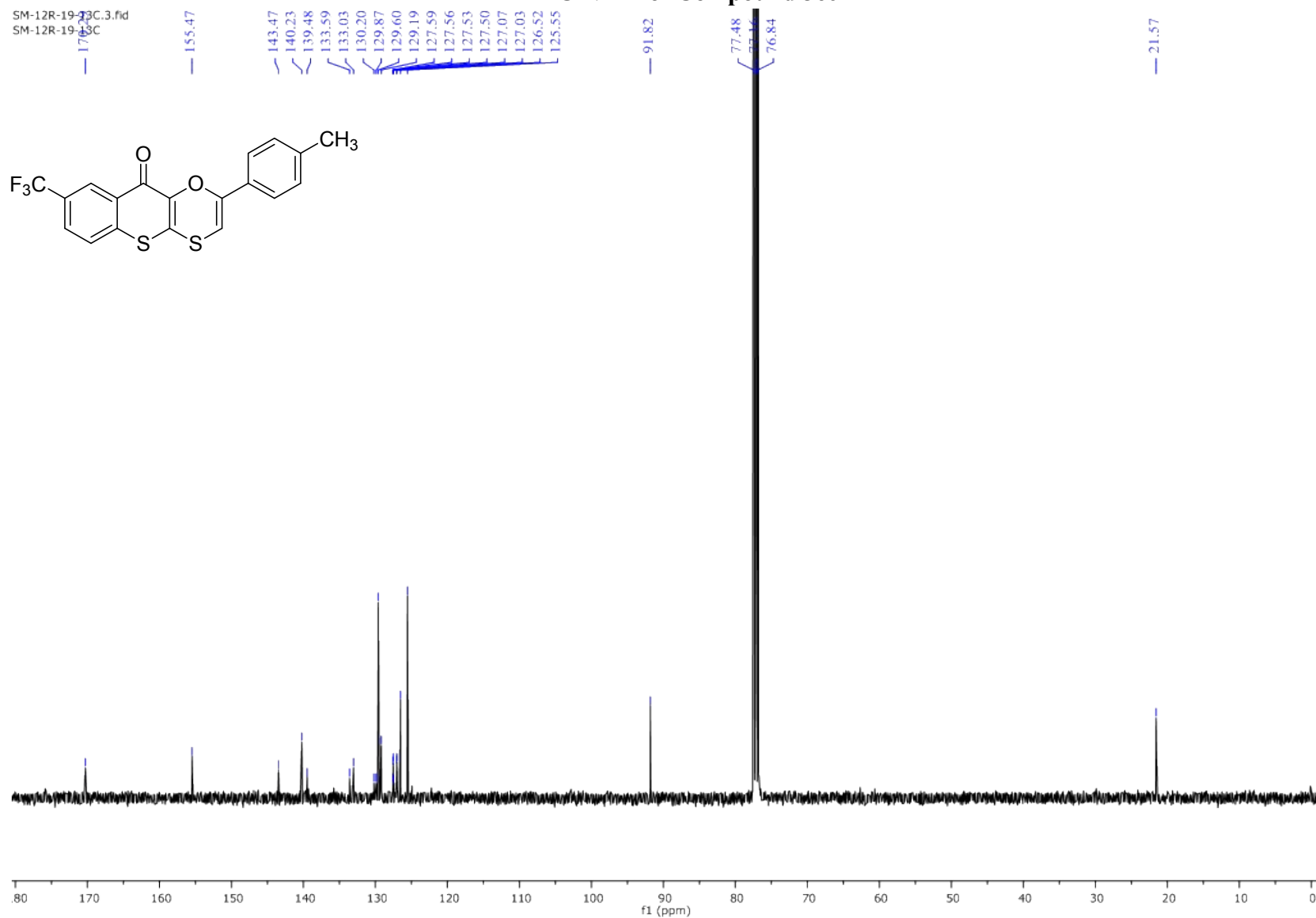
HRMS of Compound 3eb



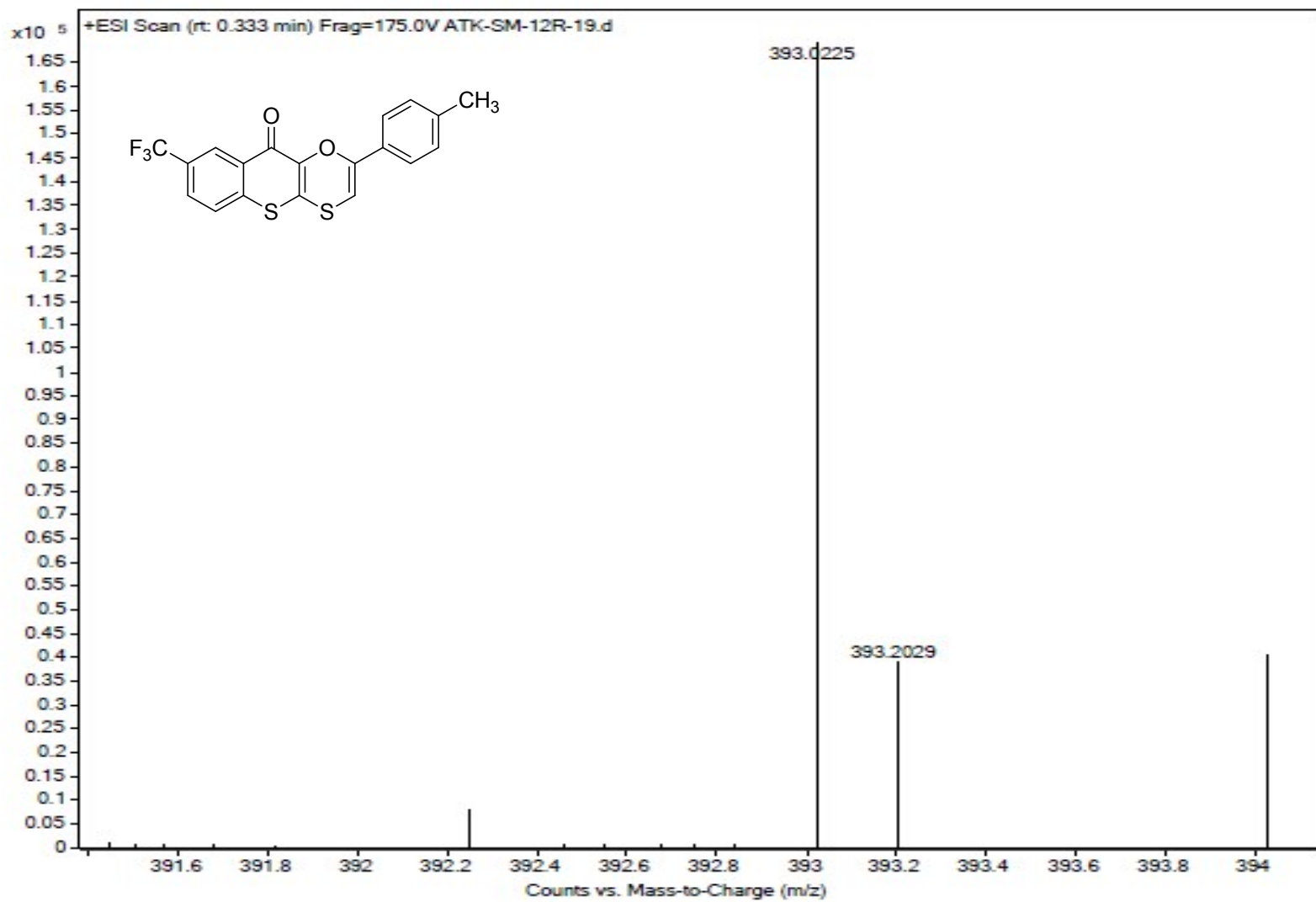
¹H NMR of Compound 3ec



¹³C NMR of Compound 3ec

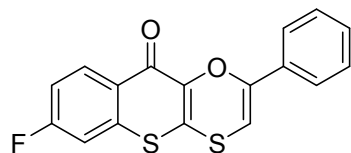


HRMS of Compound 3ec



¹H NMR of Compound 3fa

ATK-SM-12E-19-1H
ATK-SM-12E-19-1H

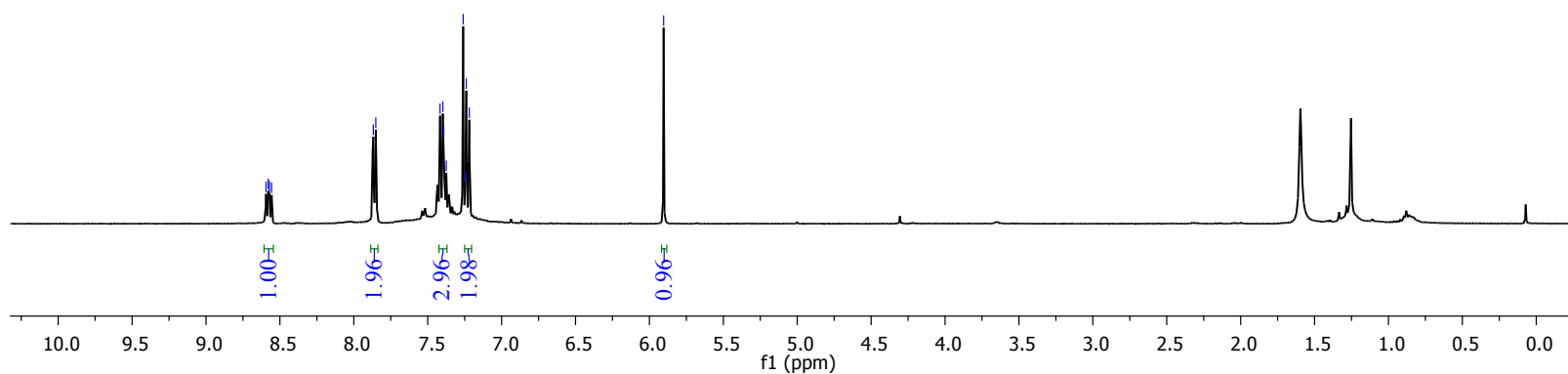
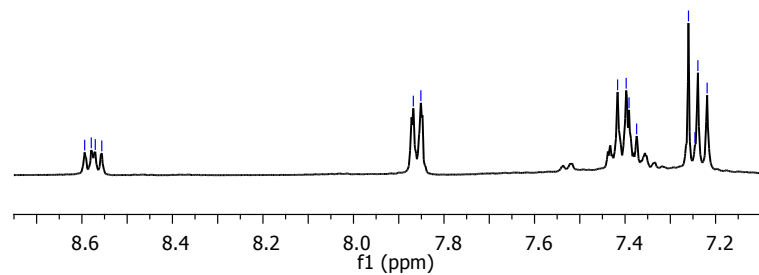


8.59
8.58
8.57
8.56
7.87
7.85
7.42
7.40
7.39
7.37
7.26
7.25
7.24
7.22
5.90

8.59
8.58
8.57
8.56

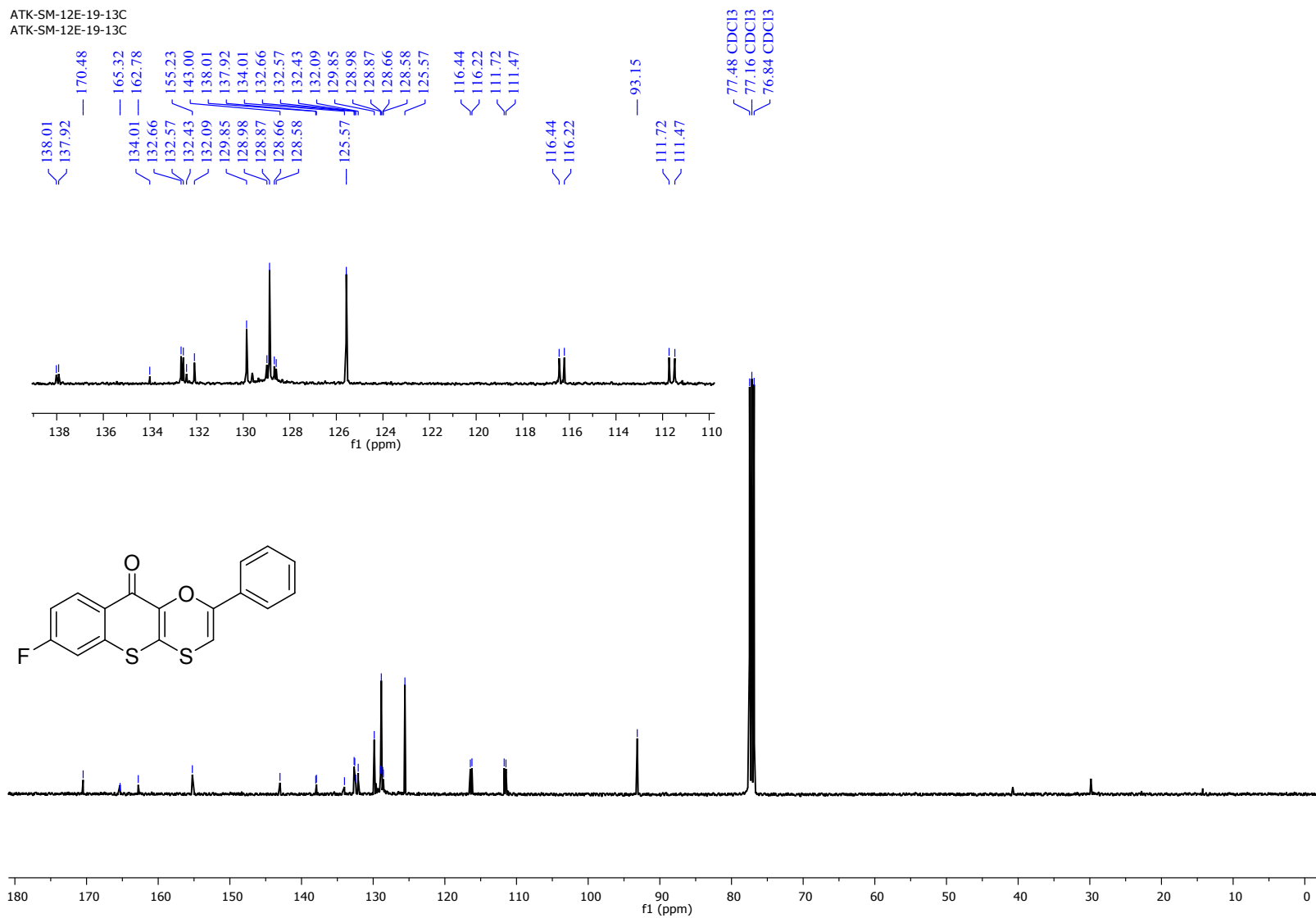
7.87
7.85

7.42
7.40
7.39
7.37
7.26
7.25
7.24
7.22



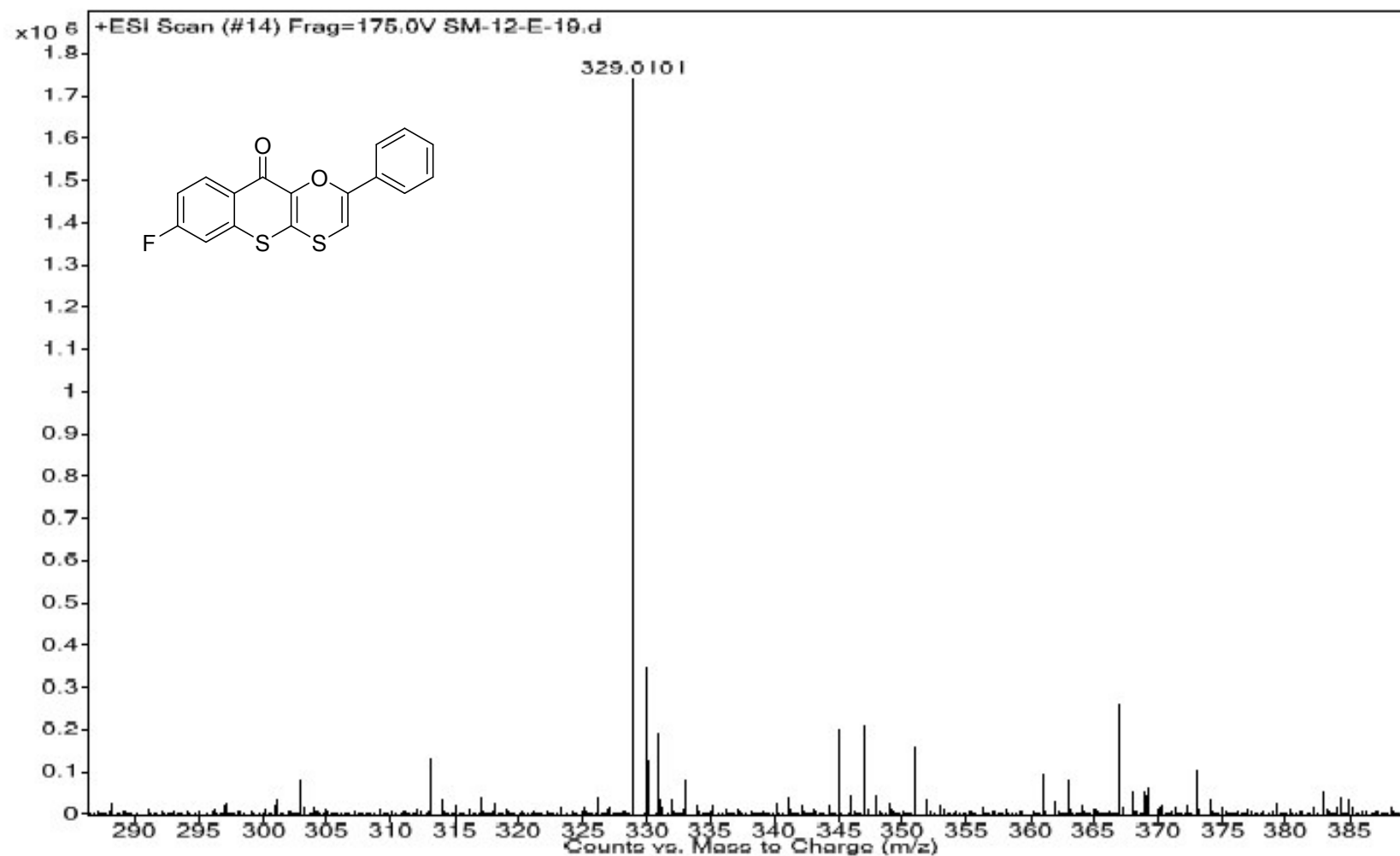
¹³H NMR of Compound 3fa

ATK-SM-12E-19-13C
ATK-SM-12E-19-13C



HRMS of Compound 3fa

Sample Name	SAMPLE	Position	P1-B4	Instrument Name	Instrument 1	User Name	
Inj Vol	20	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	SM-12-E-19.d	ACQ Method	ESI ALS 100-1000.m	Comment		Acquired Time	10/28/2019 5:01:03 PM



¹H NMR of Compound 3fc

ATK-SM-12T-19-1H
ATK-SM-12T-19-1H

8.59
8.57
8.56
8.55

7.75
7.73
7.26
7.23
7.22
7.21
7.20
7.17

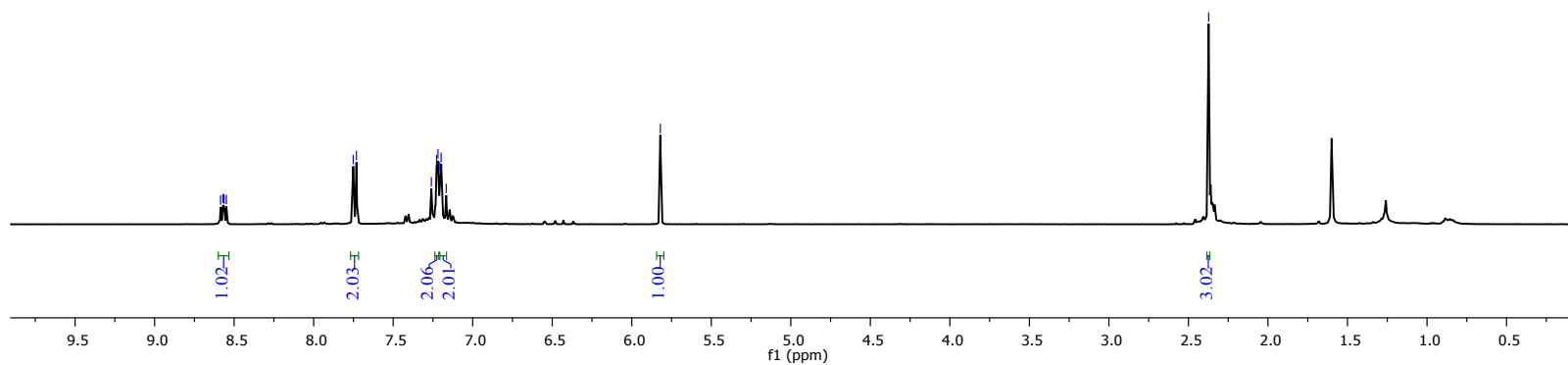
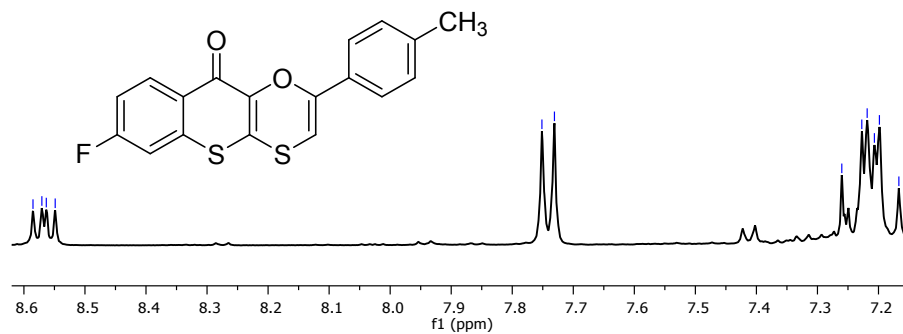
5.82

2.37

8.59
8.57
8.56
8.55

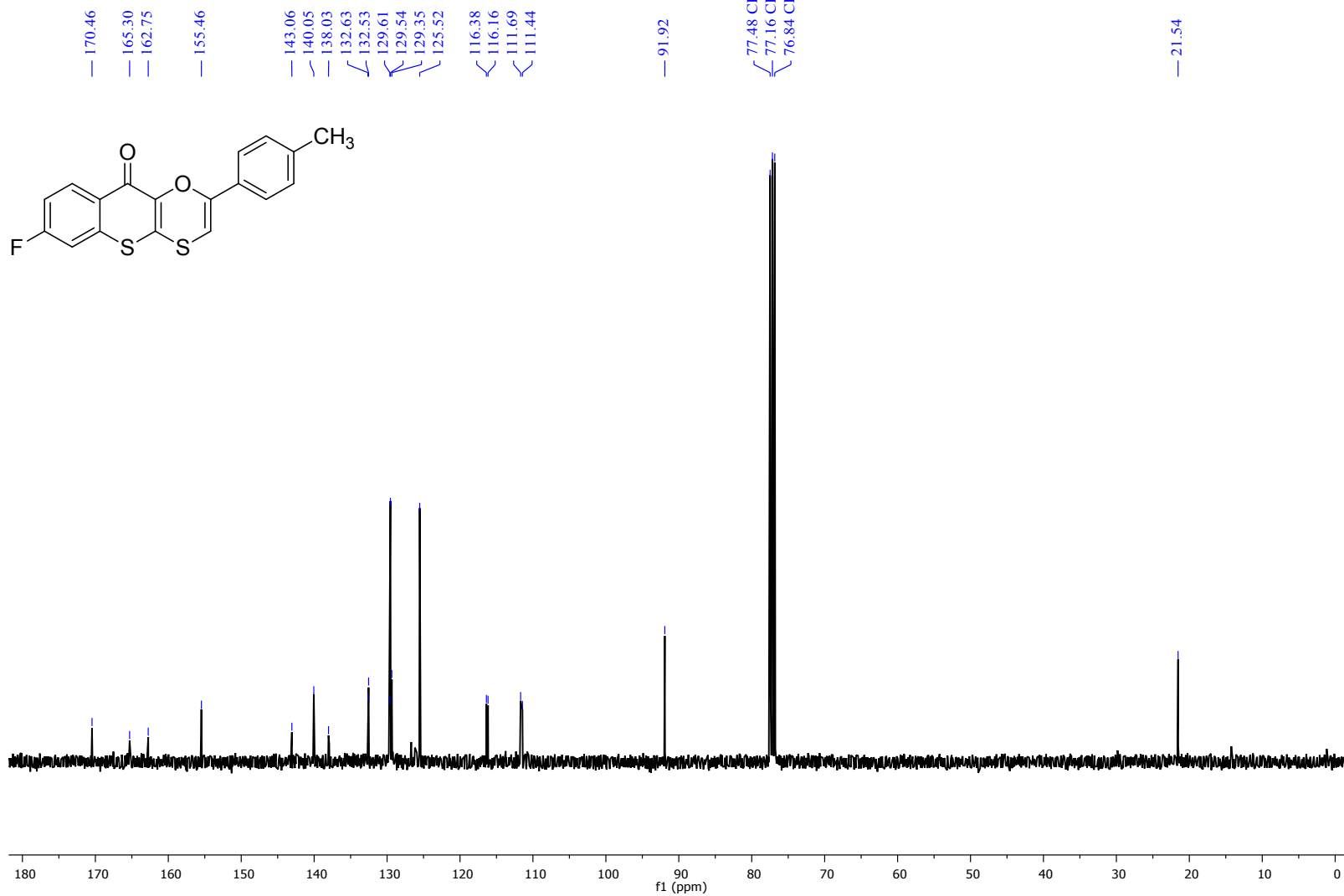
7.75
7.73

7.26
7.23
7.22
7.21
7.20
7.17



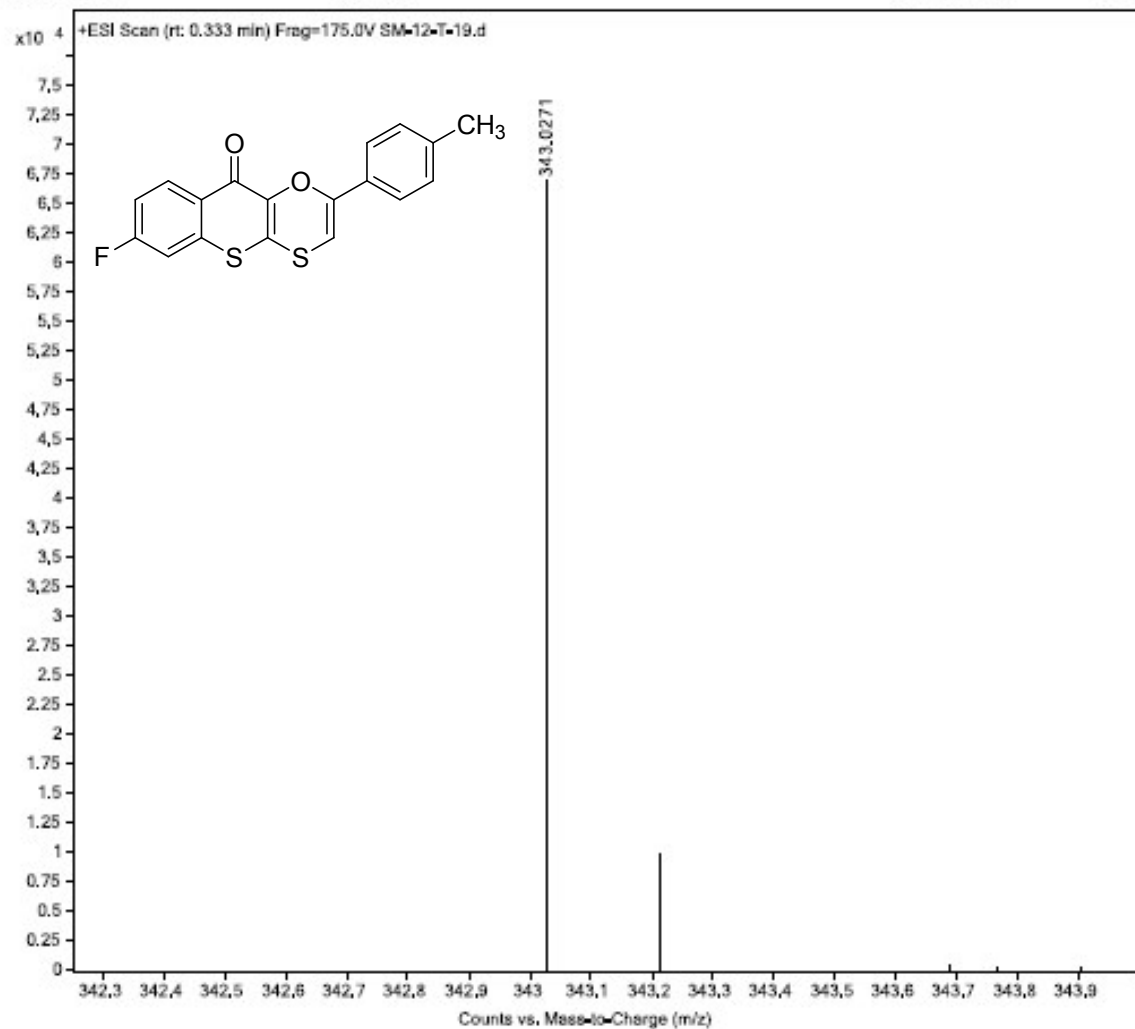
¹³C NMR of Compound 3fc

ATK-SM-12T-19-13C
ATK-SM-12T-19-13C

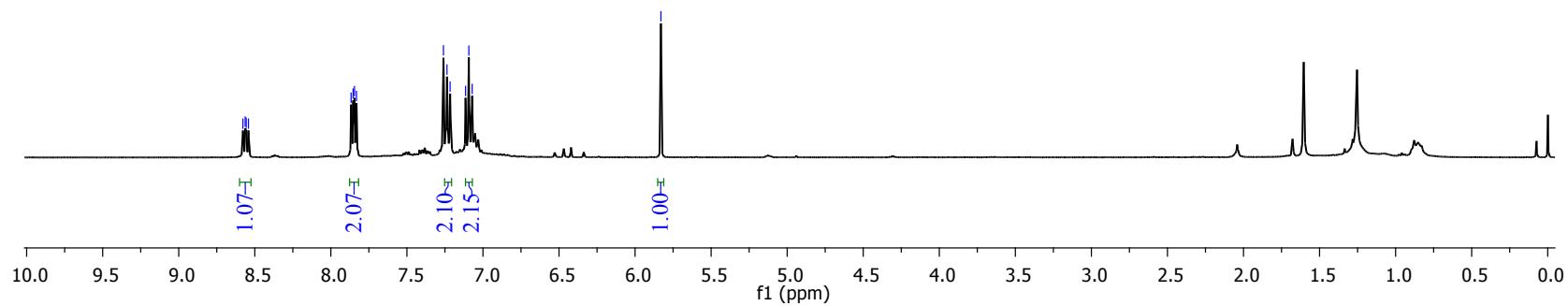
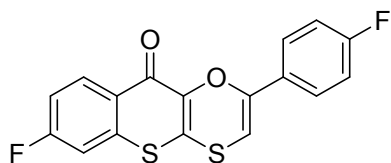
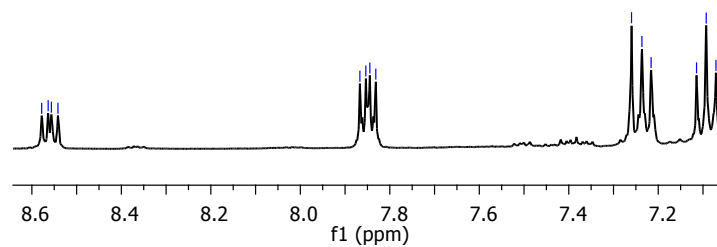
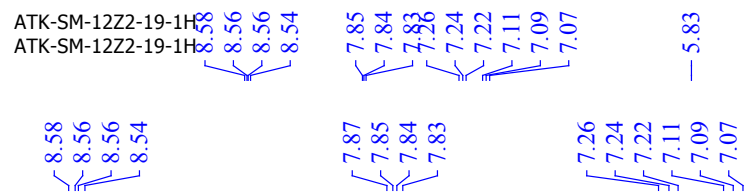


HRMS of Compound 3fc

Sample Name	SM-12-T-19	Position	P1-C5	Instrument Name	Instrument 1
User Name		Inj Vol	20	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	SM-12-T-19.d
ACQ Method	ESI ALS 100-1000.m	Comment		Acquired Time	28-10-2020 13:07:56 (UTC+05:30)

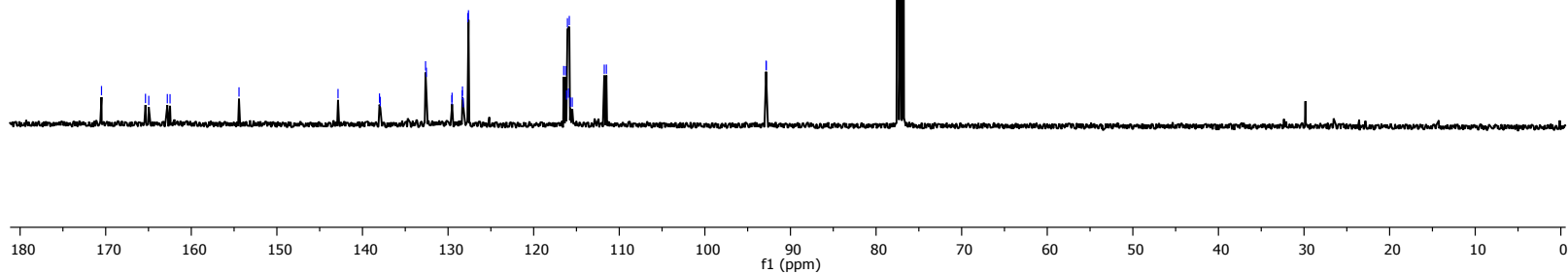
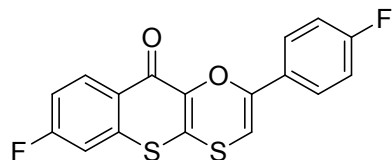
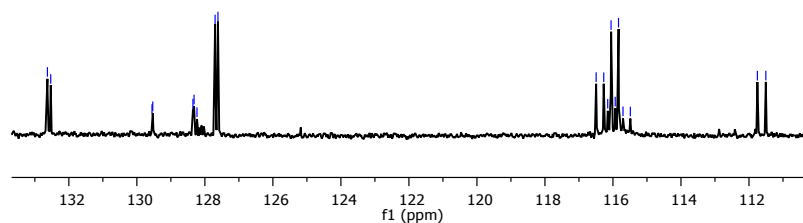
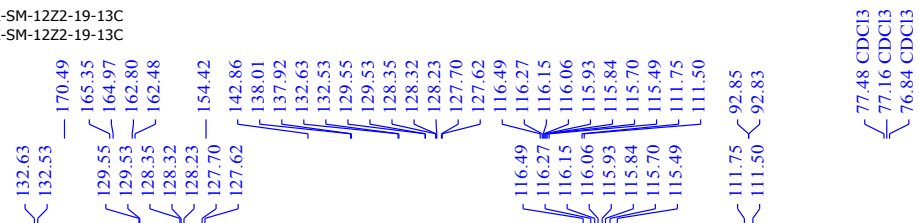


¹H NMR of Compound 3fd



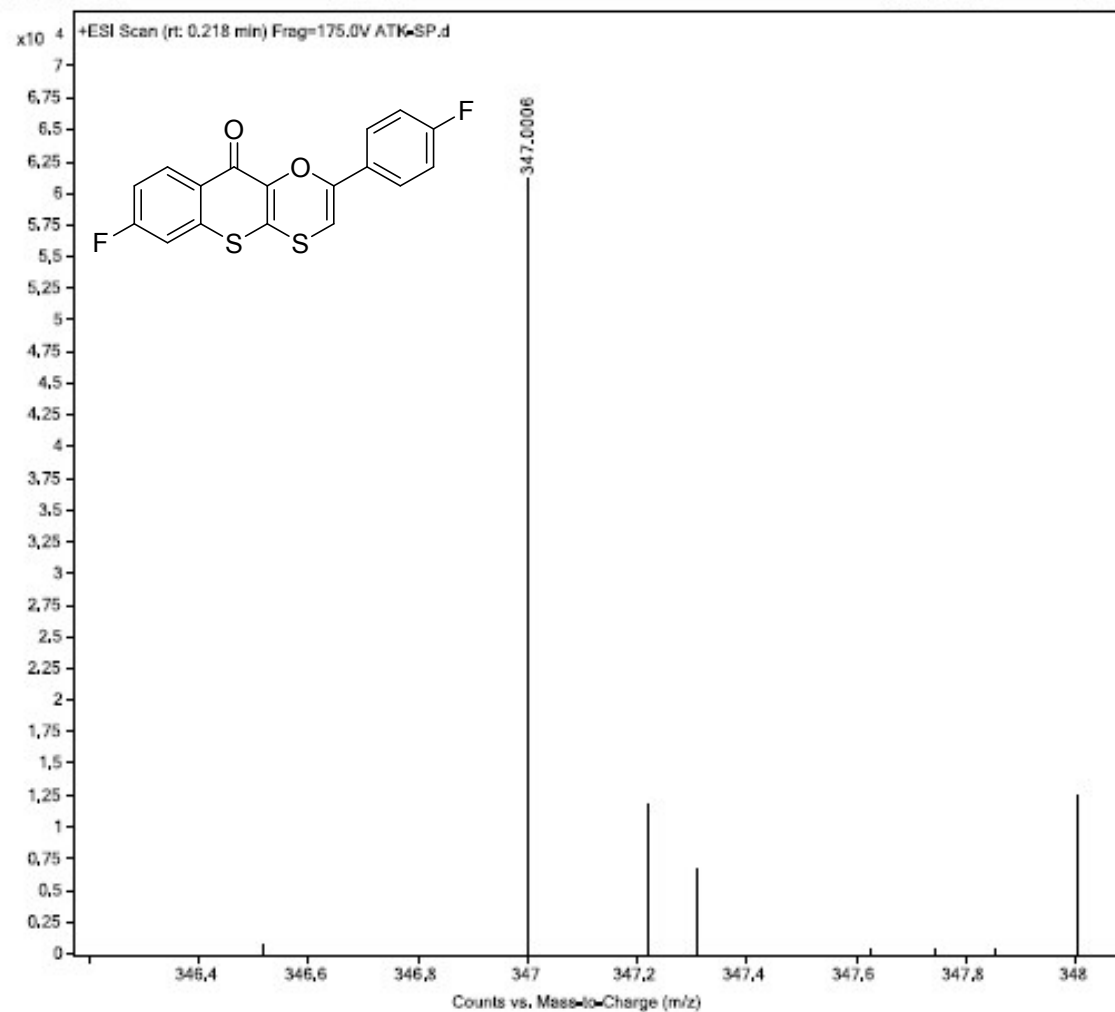
¹³C NMR of Compound 3fd

ATK-SM-12Z2-19-13C
ATK-SM-12Z2-19-13C

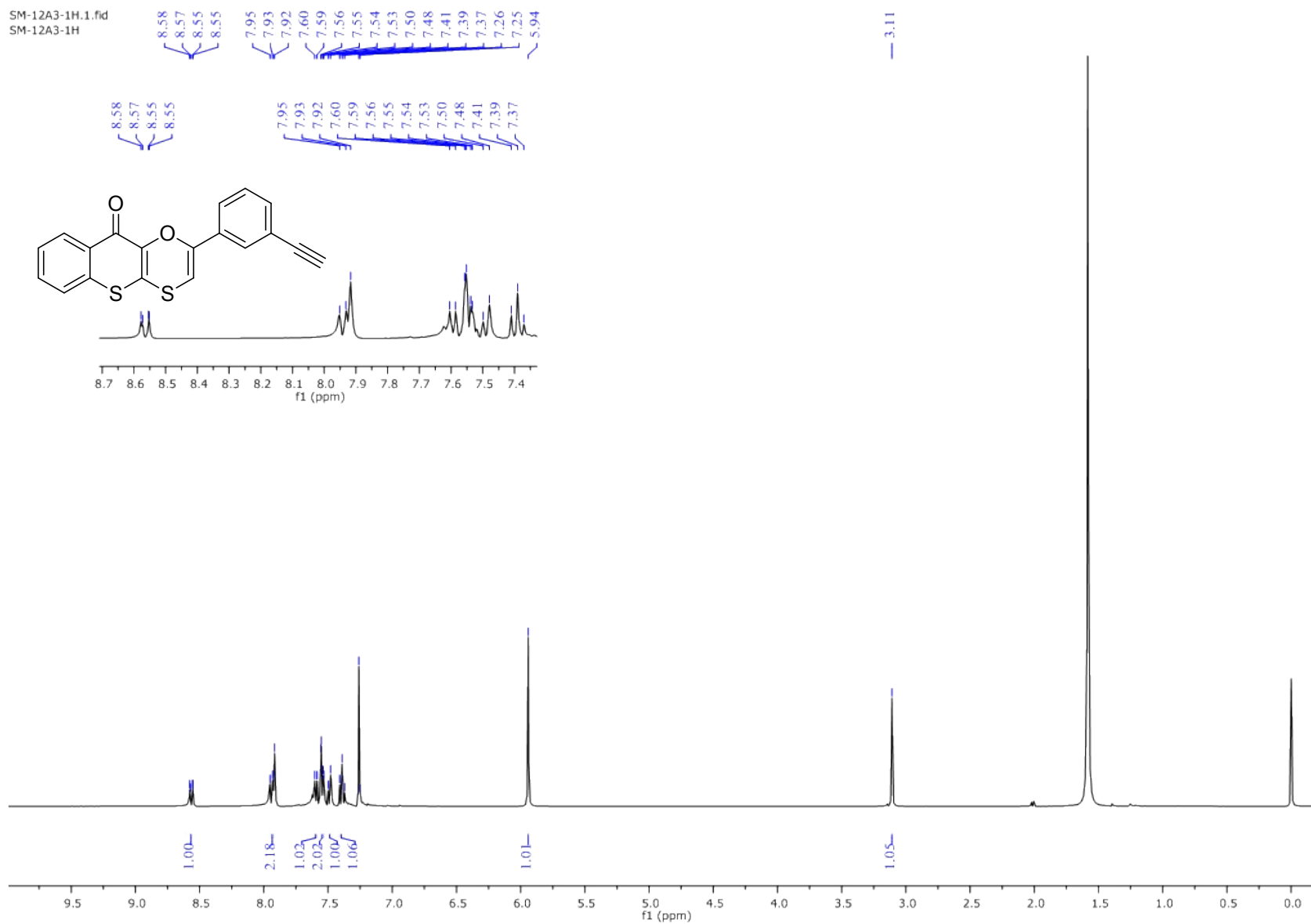


HRMS of Compound 3fd

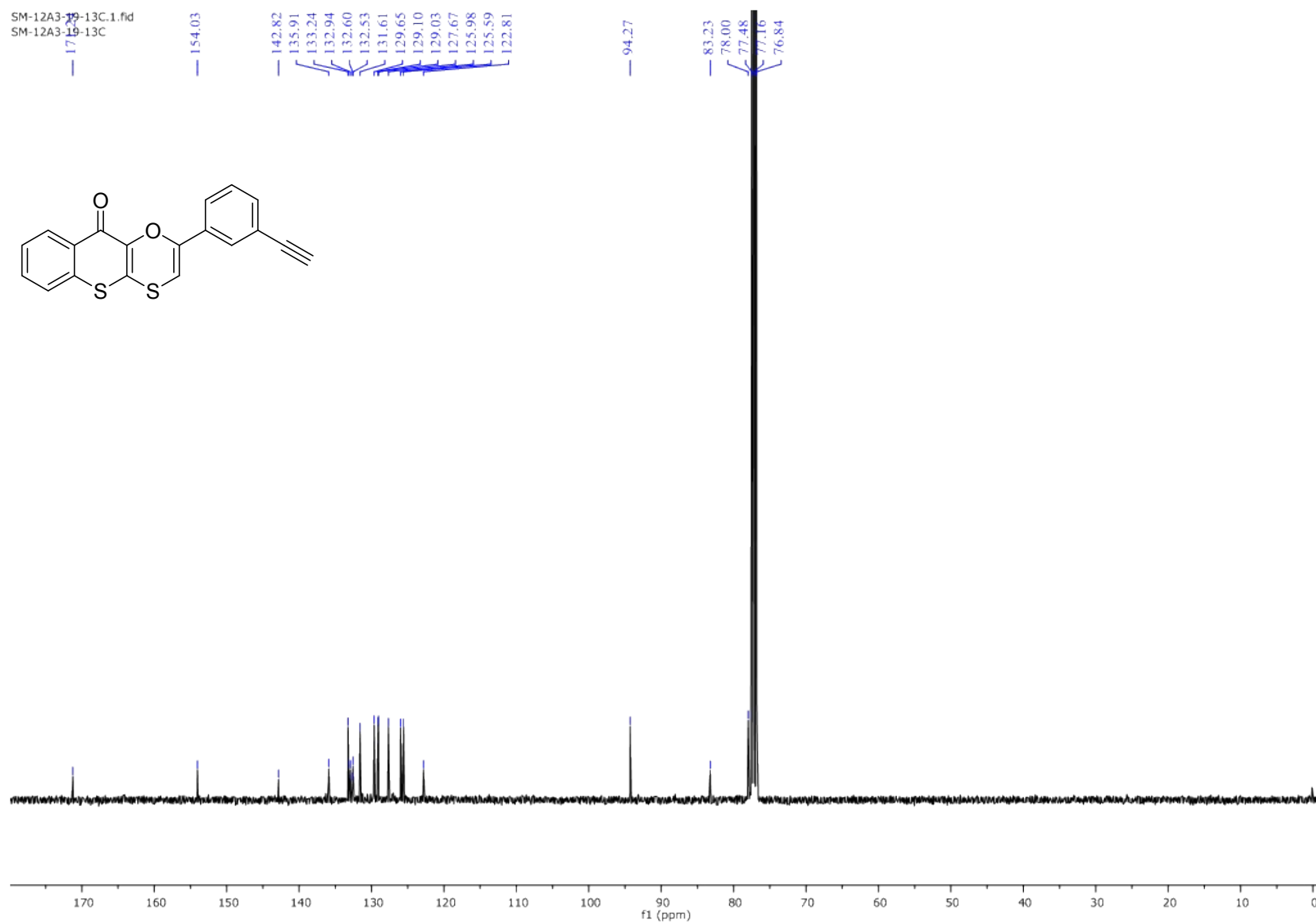
Sample Name	ATK-SP	Position	P1-88	Instrument Name	Instrument 1
User Name		Inj Vol	20	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	ATK-SP.d
ACQ Method	ESI ALS 100-1000.m	Comment		Acquired Time	01-12-2020 12:41:46 (UTC+05:30)



¹H NMR of Compound 3ag

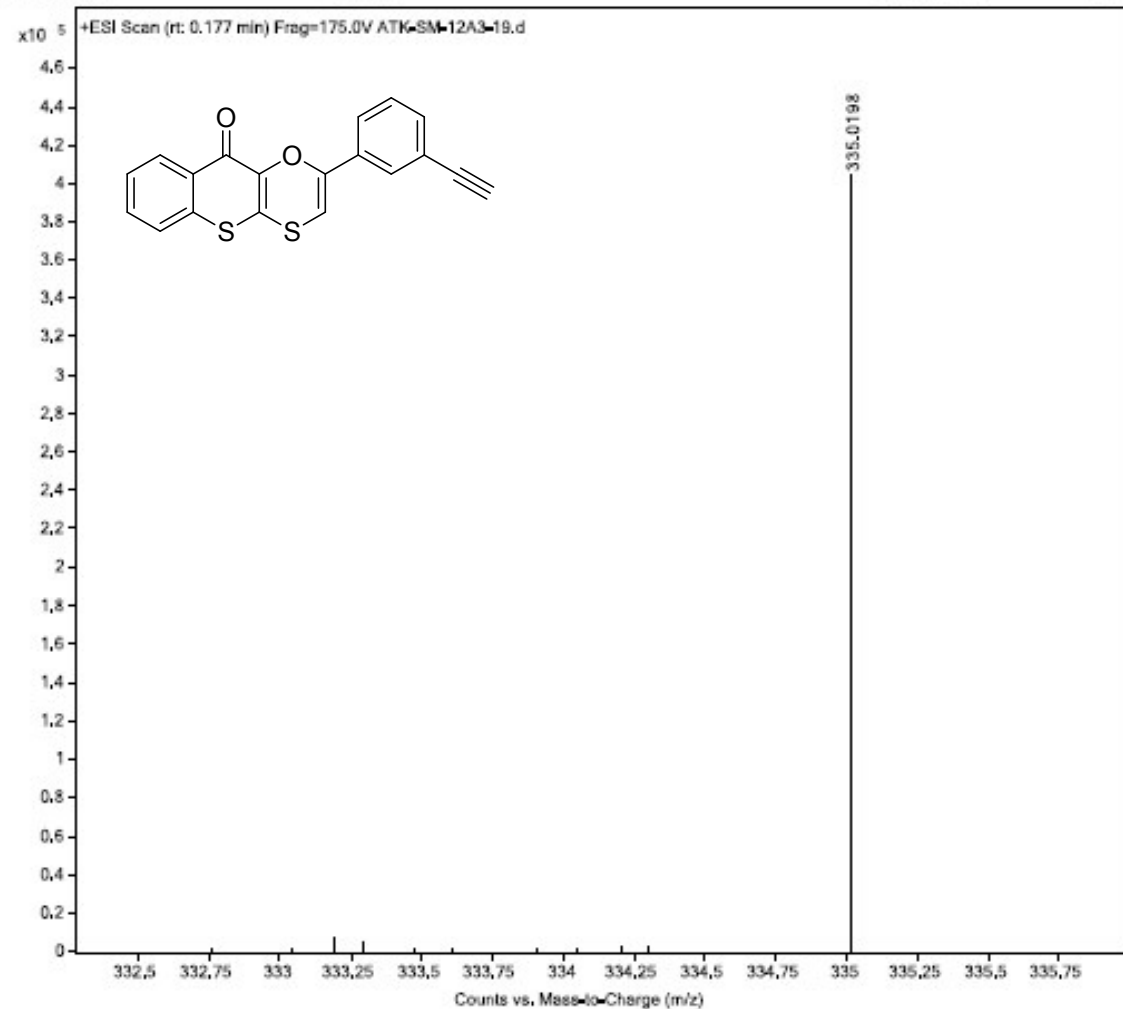


¹³C NMR of Compound 3ag



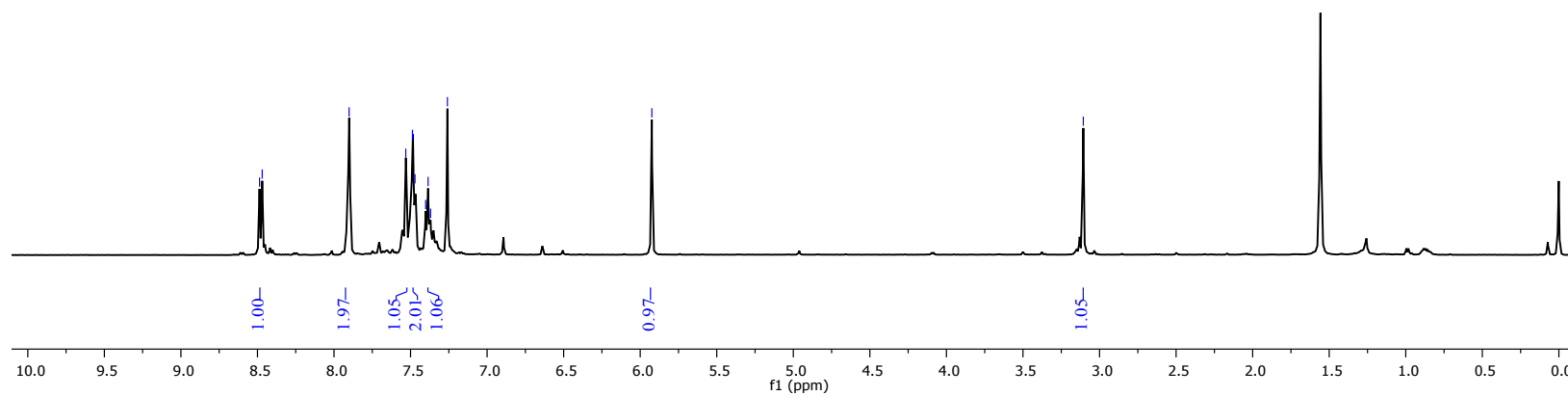
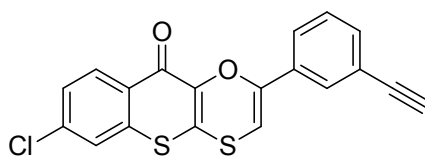
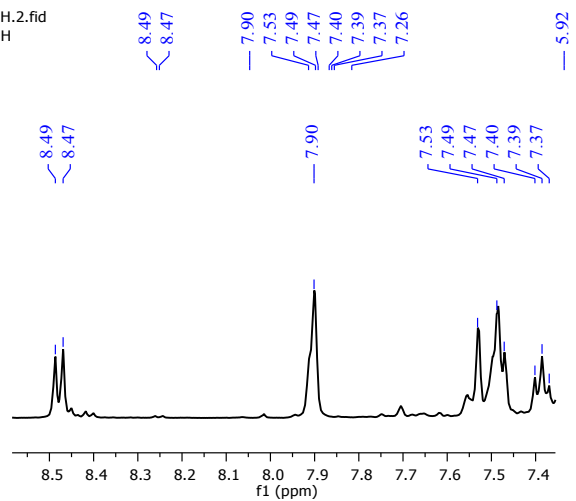
HRMS of compound 3ag

Sample Name	ATK-SM-12A3-19	Position	P1-A1	Instrument Name	Instrument 1
User Name		Inj Vol	Unknown / Injection Program	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	ATK-SM-12A3-19.d
ACQ Method	ESI ALS 200-800,m	Comment		Acquired Time	23-11-2020 16:14:27 (UTC+05:30)

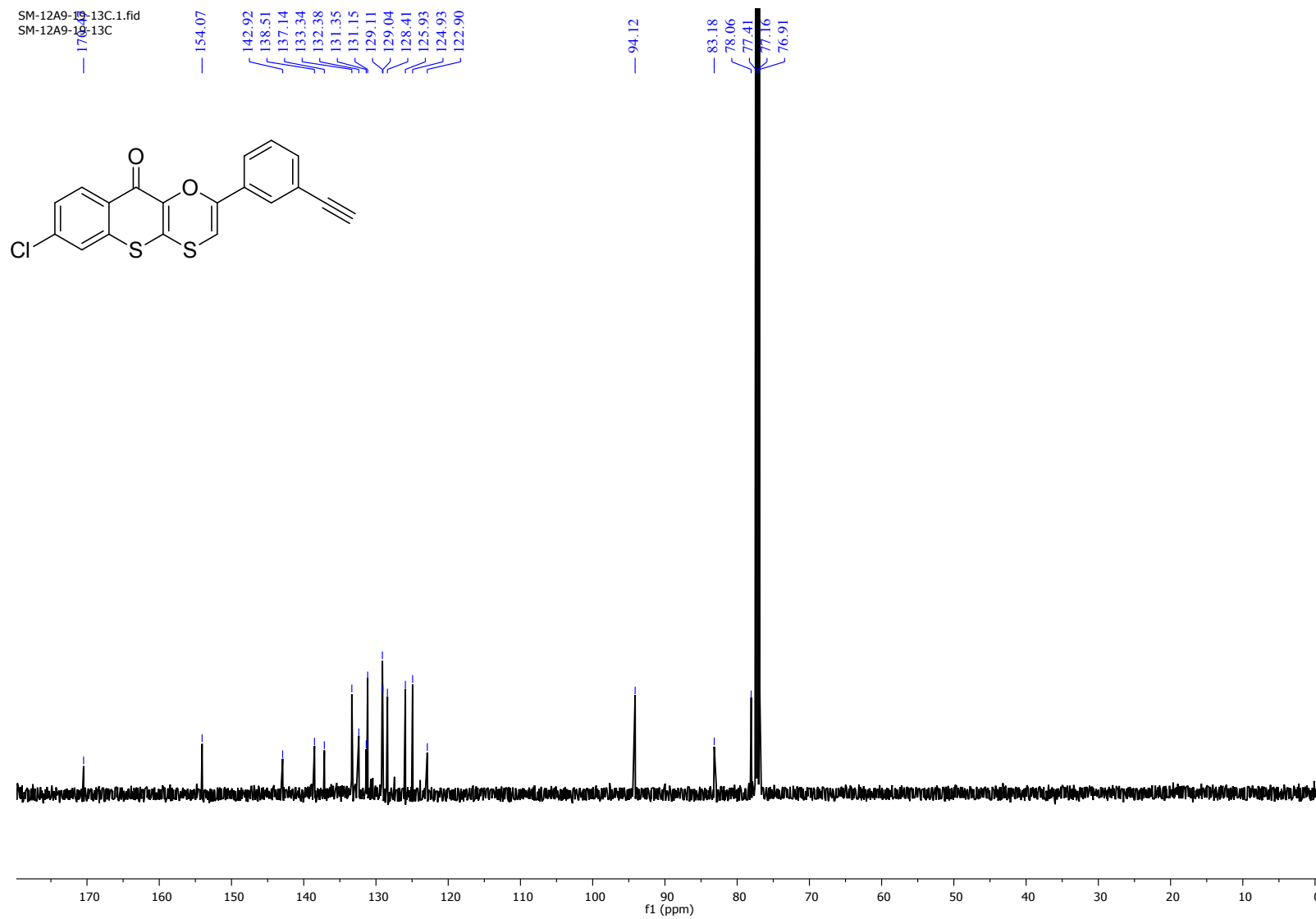


¹H NMR of Compound 3dg

SM-12A9-19-1H.2.fid
SM-12A9-19-1H

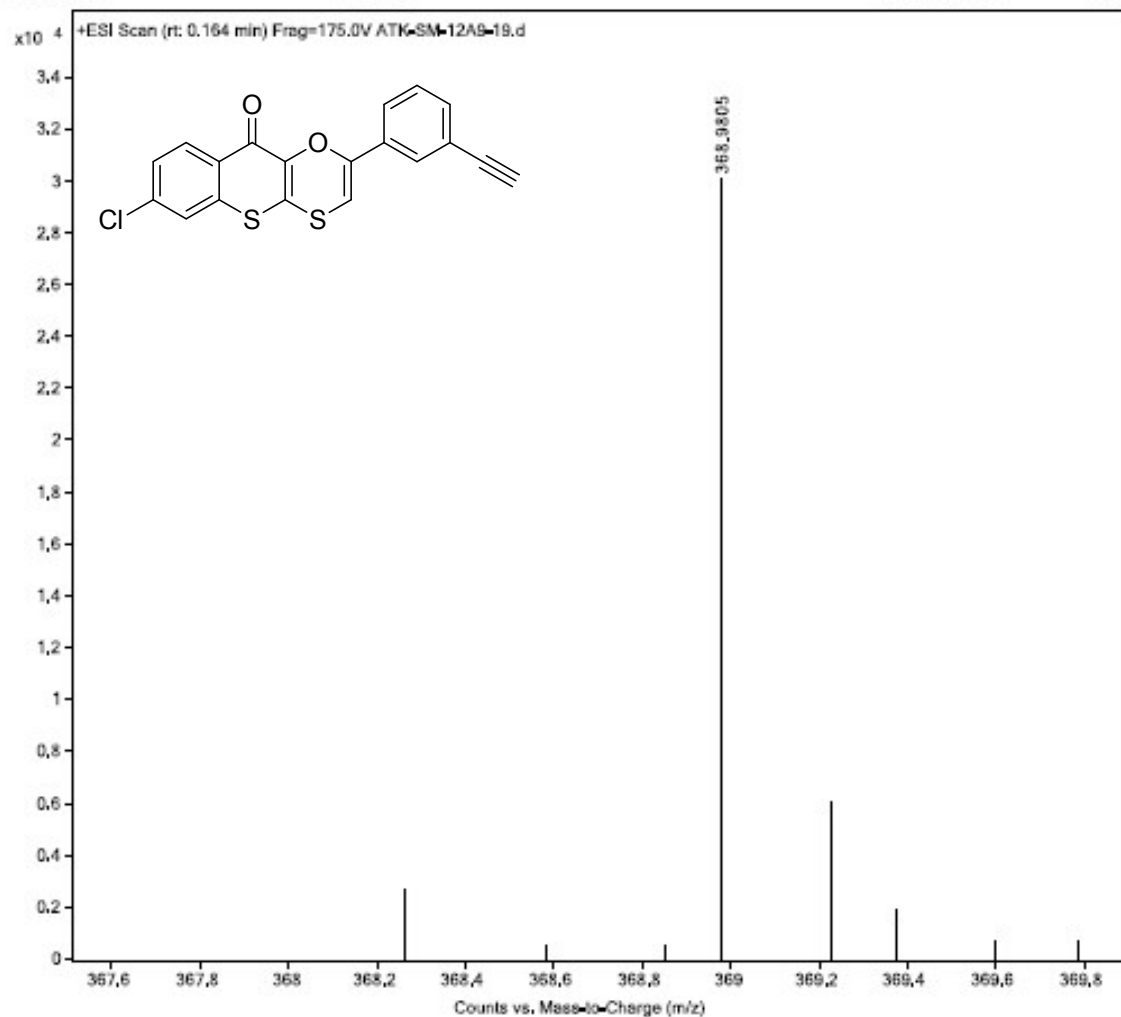


¹³C NMR of Compound 3dg



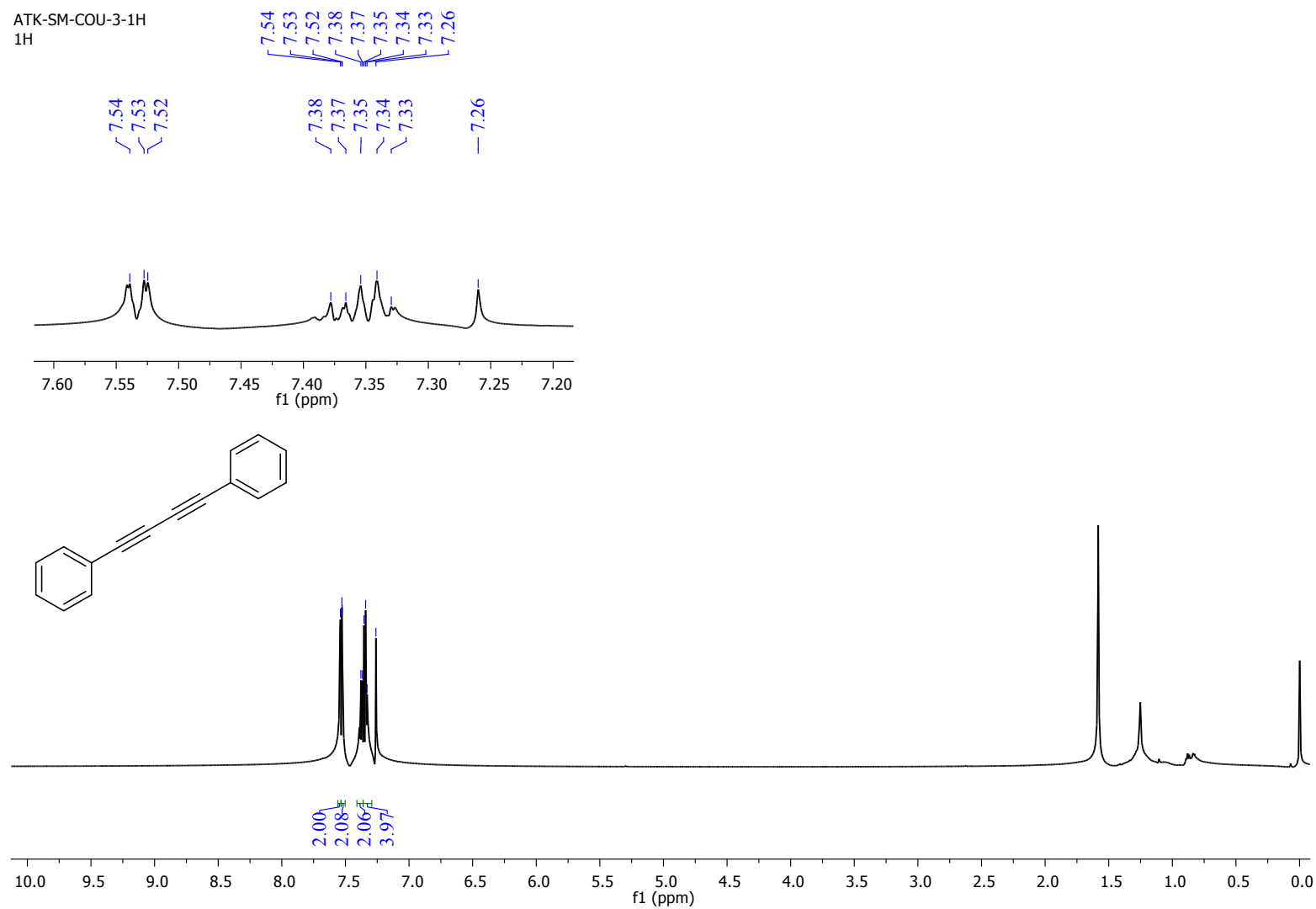
HRMS of Compound 3dg

Sample Name	ATK-SM-12A9-19	Position	P1-A1	Instrument Name	Instrument 1
User Name		Inj Vol	Unknown / Injection Program	InjPosition	
Sample Type	Sample	IRM Calibration Status	Success	Data Filename	ATK-SM-12A9-19.d
ACQ Method	ESI ALS 200-600,m	Comment		Acquired Time	23-11-2020 16:20:24 (UTC+05:30)



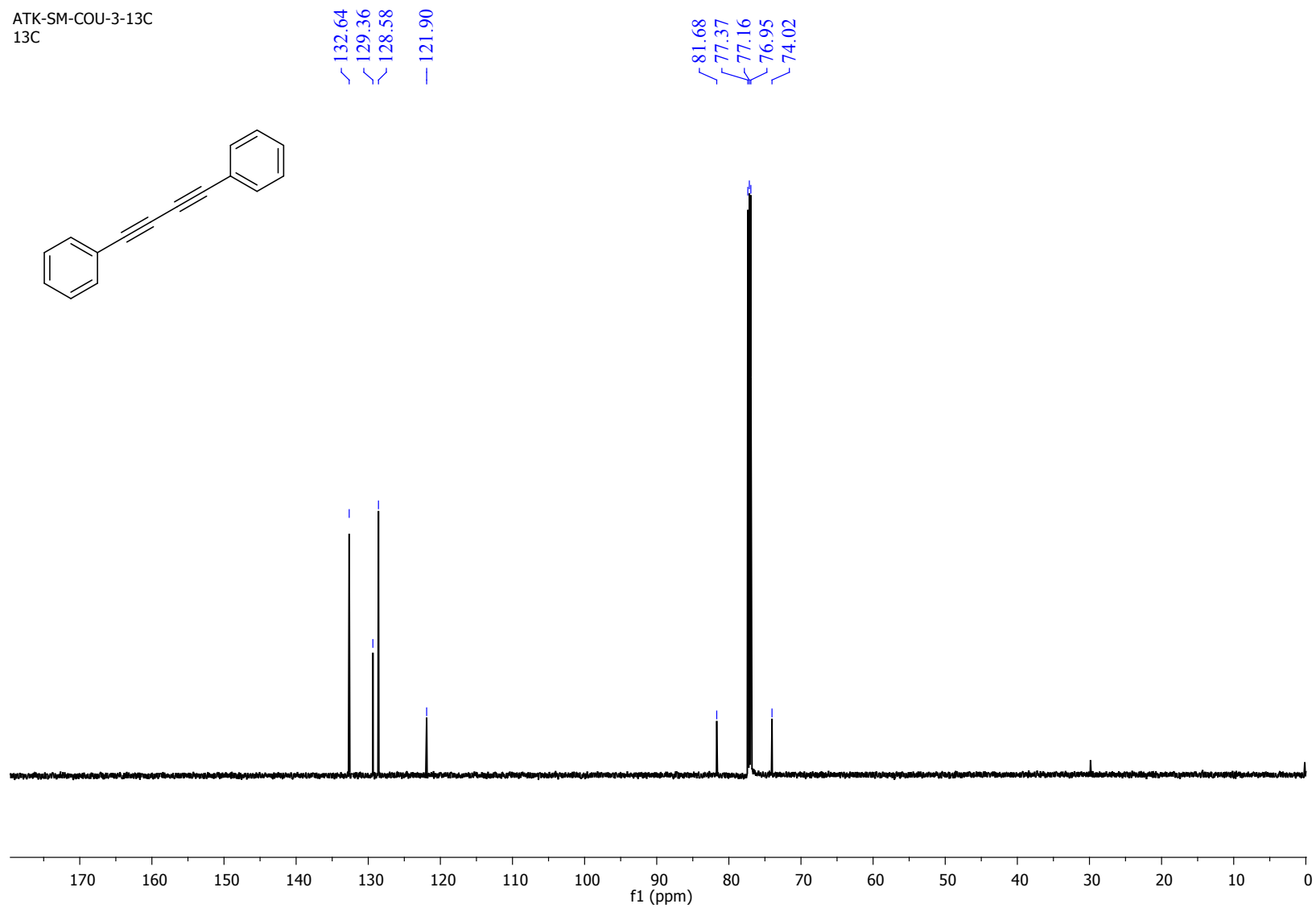
¹H NMR of Compound 4

ATK-SM-COU-3-1H
1H



¹³C NMR of Compound 4

ATK-SM-COU-3-13C
13C



HRMS of Compound intermediate N

Sample Name
Inj Vol
Data Filename

Position
InjPosition
ACQ Method

Instrument Name
SampleType
Comment

User Name
IRM Calibration Status
Acquired Time

