Supplementary Data

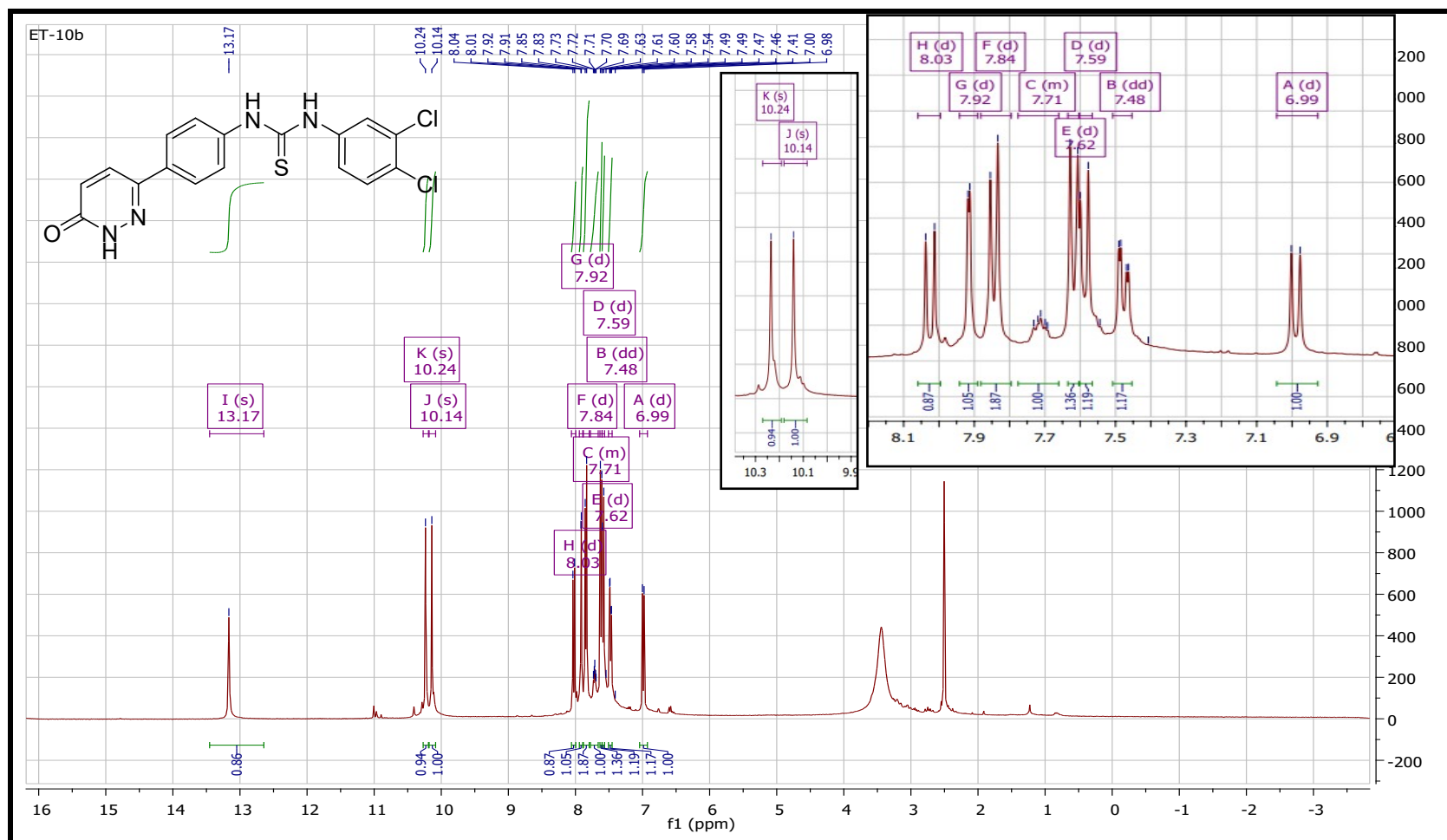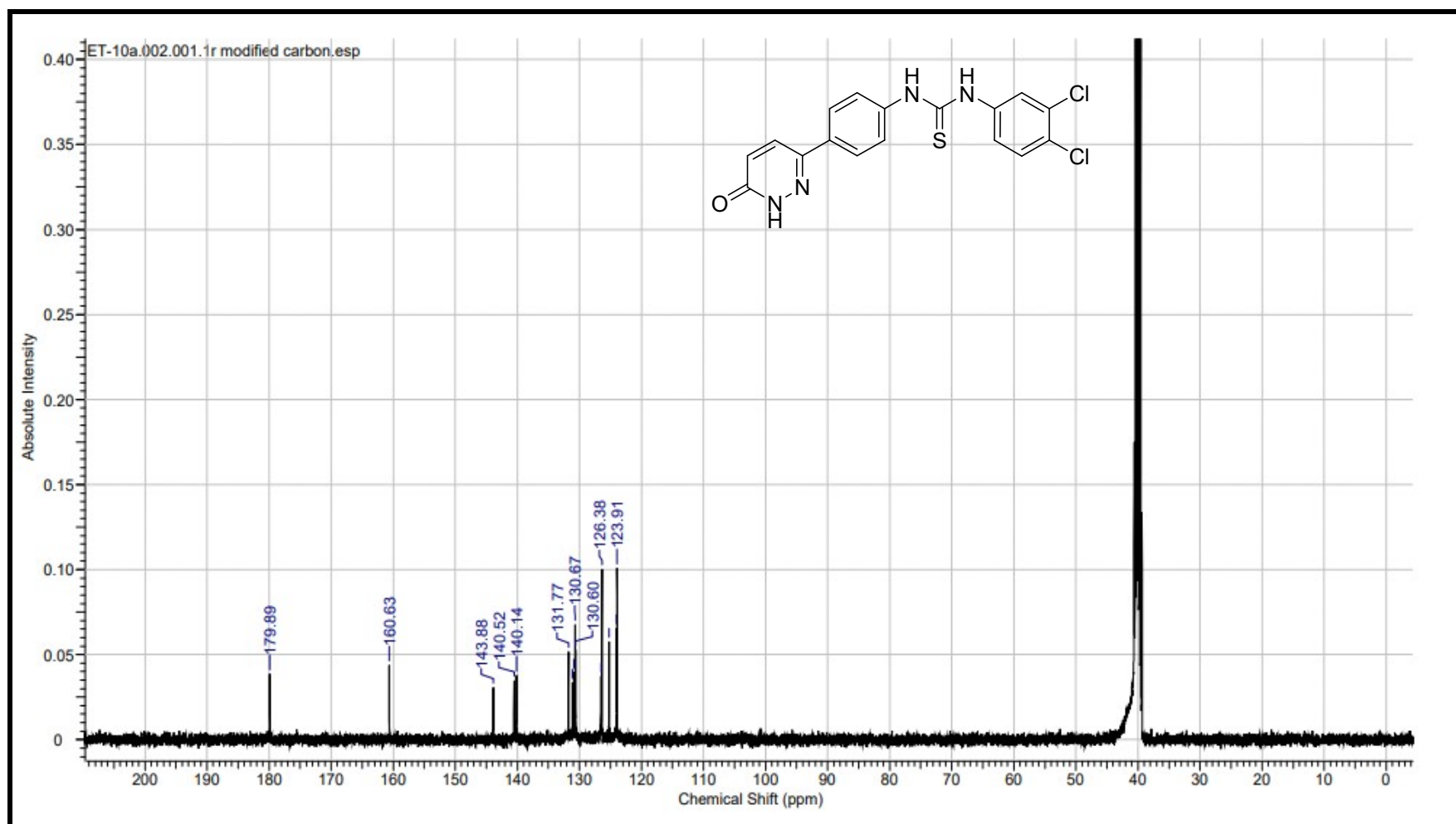# Table of Contents

1. Spectral data of Series I:

1.1. Compound 8a

Figure 1a. ¹H NMR spectrum (400 MHz) of compound 8a in DMSO-d₆.

Figure 1b. ^{13}C NMR spectrum (100 MHz) of compound 8a in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 20.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
572 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-30 H: 0-30 N: 0-5 O: 0-2 S: 0-1 35Cl: 0-2 37Cl: 0-1

ET-10b/AJ   SYNAPTG2-Si#NotSet   07-Mar-2023
67581   09:50:34
0653 304 (0.615) Cm (302:429-92:112)
1: TOF MS ES+

4.30e+006
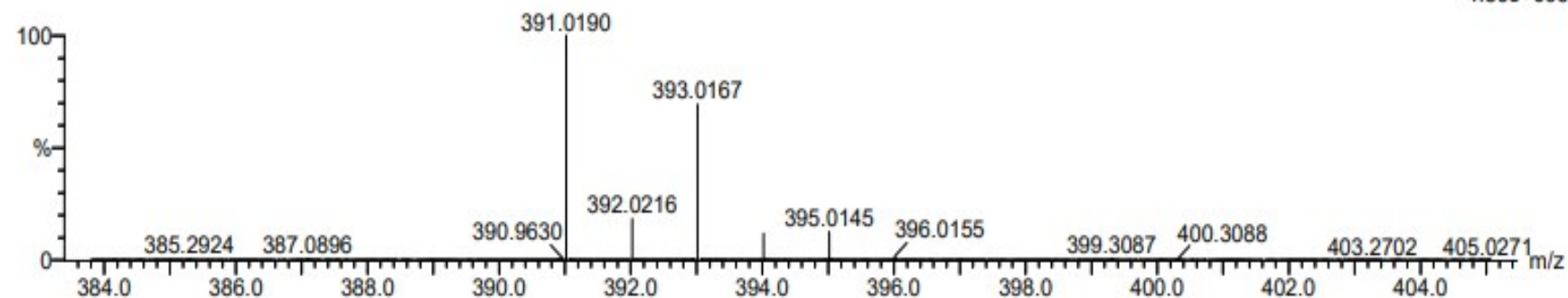
Minimum:			-1.5
Maximum:	5.0	3.0	20.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
391.0190	391.0187	0.3	0.8	12.5	3385.1	C17 H13 N4 O S 35Cl2

Figure 1c. HRMS of compound 8a.

3
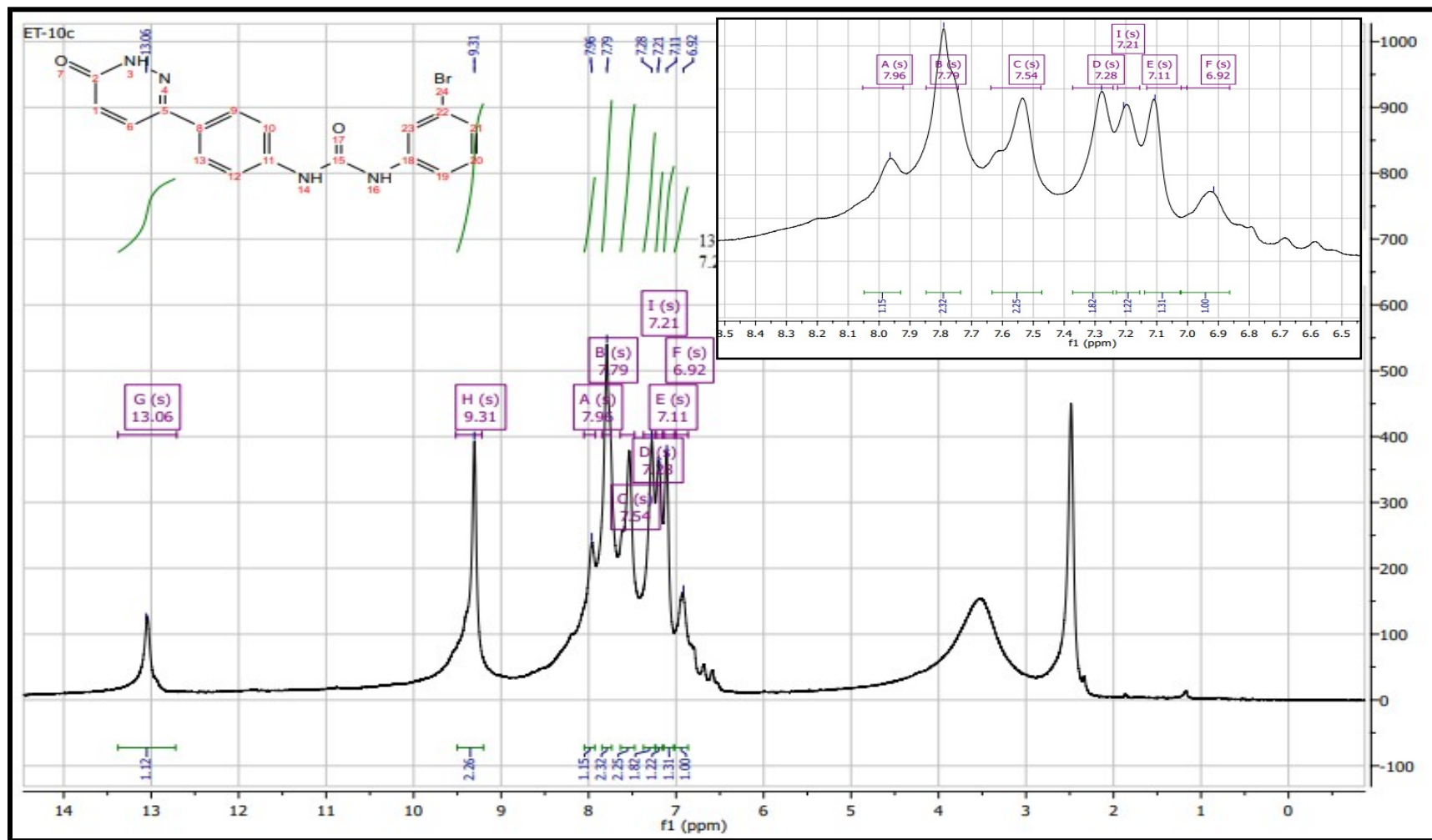
1.2. Compound 8b

Figure 2a. ¹H NMR spectrum (400 MHz) of compound 8b in DMSO-d₆.
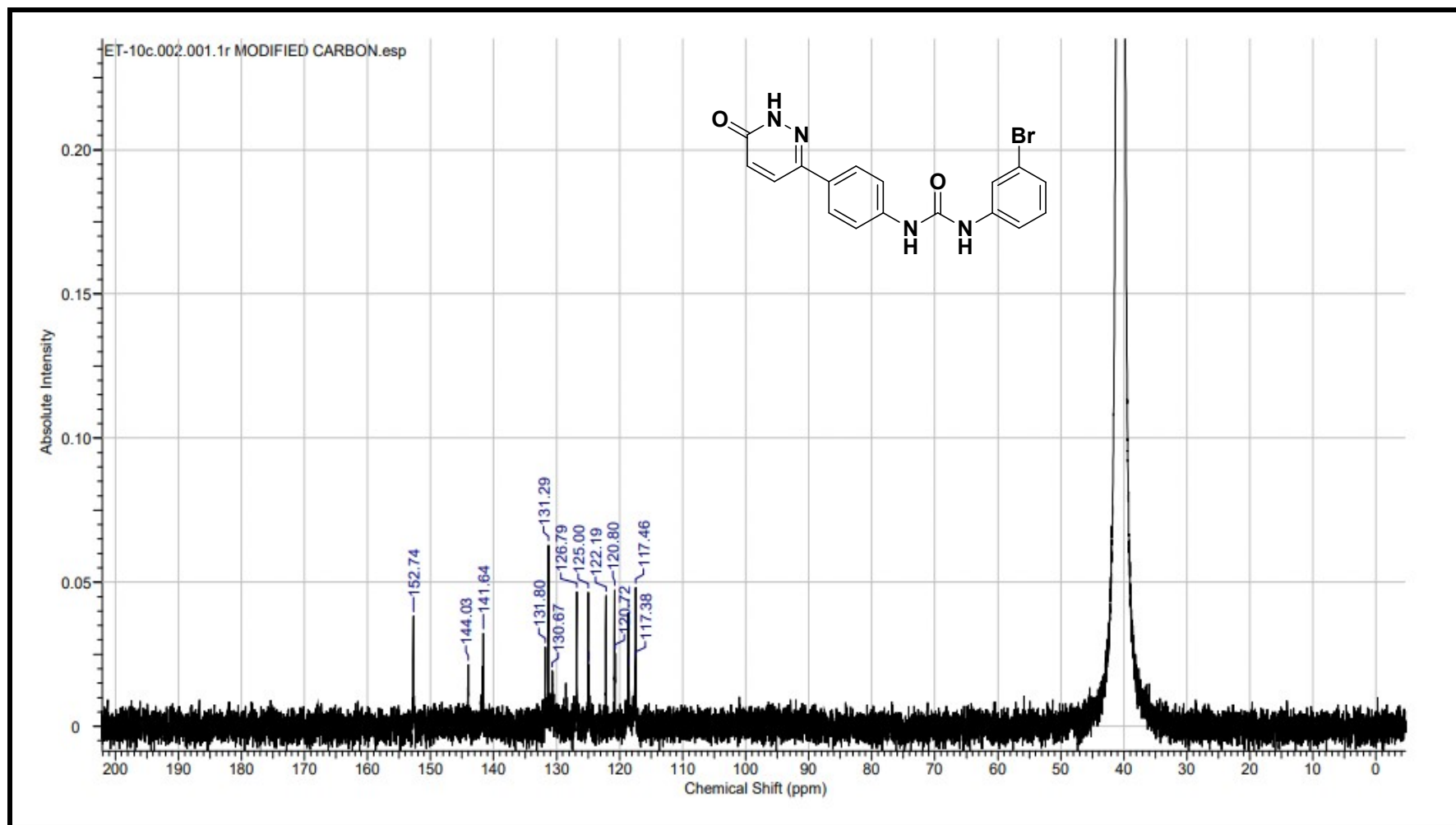
Figure 2b. ^{13}C NMR spectrum (100 MHz) of compound 8b in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 25.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
127 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-20 H: 0-20 N: 0-4 O: 0-4 79Br: 0-1 81Br: 0-1

ET-10c/AJ
67594
0672 689 (1.372) Cm (624:827)
1: TOF MS ES+

SYNAPTG2-Si#NotSet

07-Mar-2023
13:38:43

9.39e+006
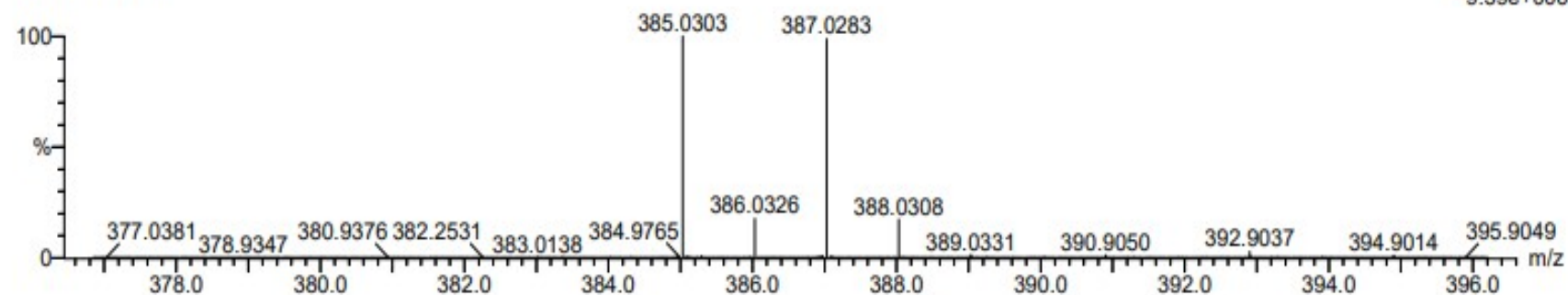
		Minimum:	-1.5			
	Maximum:	5.0	3.0	25.0		

| Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
385.0303	385.0300	0.3	0.8	12.5	3927.6	C17 H14 N4 O2 79Br

Figure 2c. HRMS of compound 8b.

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1.3. Compound 8c

Figure 3a. ^1H NMR spectrum (400 MHz) of compound 8c in DMSO-d$_6$.

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Figure 3b. ^{13}C NMR spectrum (100 MHz) of compound 8c in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 15.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
400 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-50   H: 0-50   N: 0-5   O: 0-3   S: 0-1   F: 0-1

ET-10d/AJ   SYNAPTG2-Si#NotSet   06-Mar-2023
67577   15:36:36
0648 726 (1.443) Cm (708:730)
1: TOF MS ES+

6.41e+005
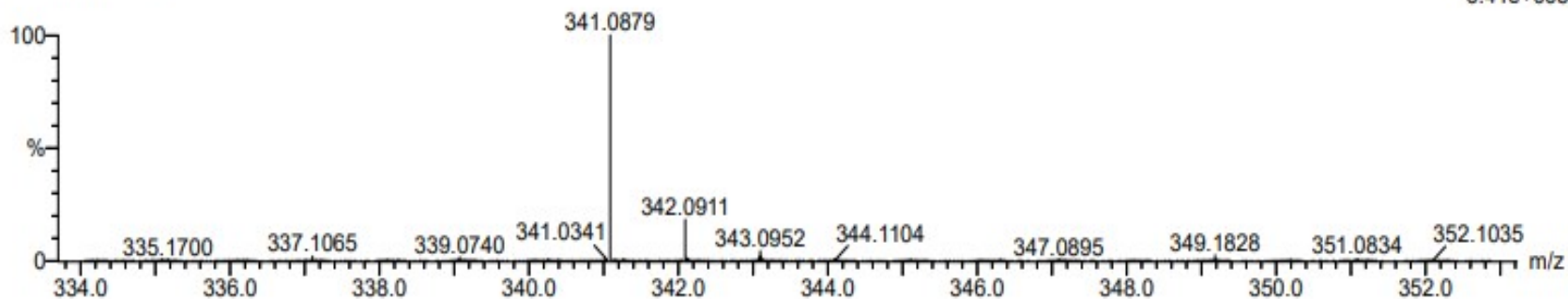
Minimum:			-1.5		
Maximum:	5.0	3.0	15.0		

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
341.0879	341.0872	0.7	2.1	12.5	1979.2	C17 H14 N4 O S F

Figure 3c. HRMS of compound 8c.

9
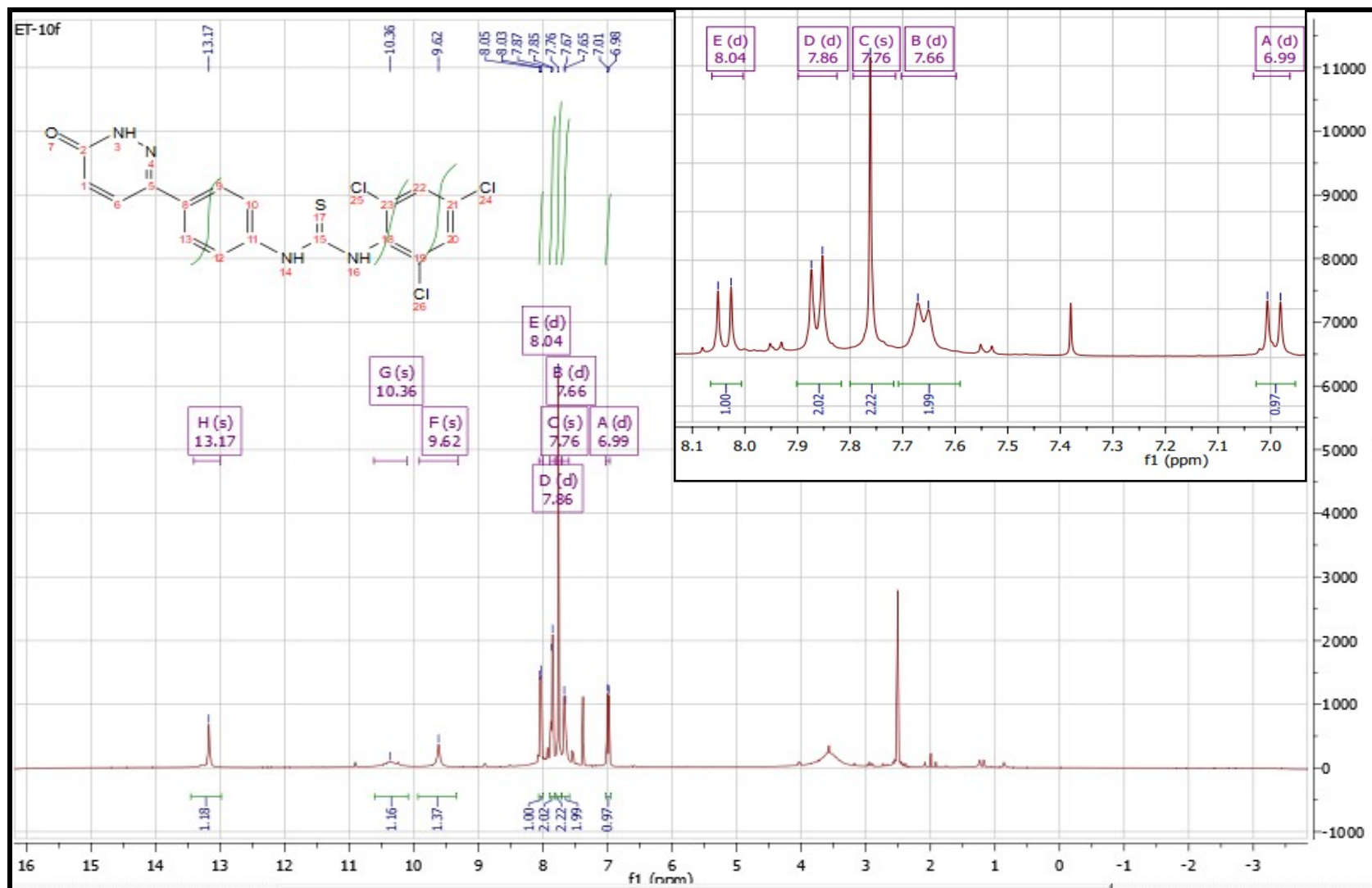
1.4. Compound 8d

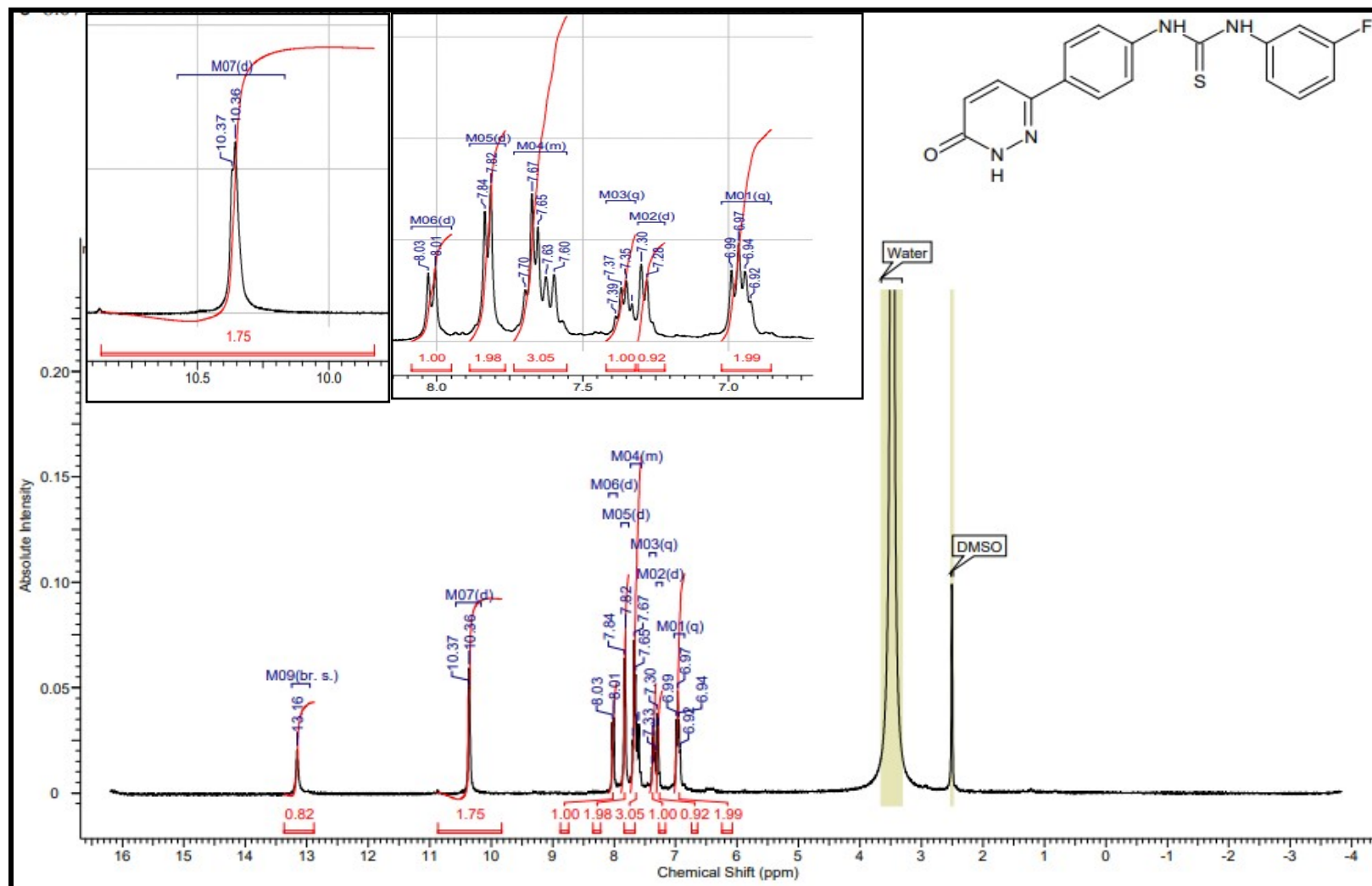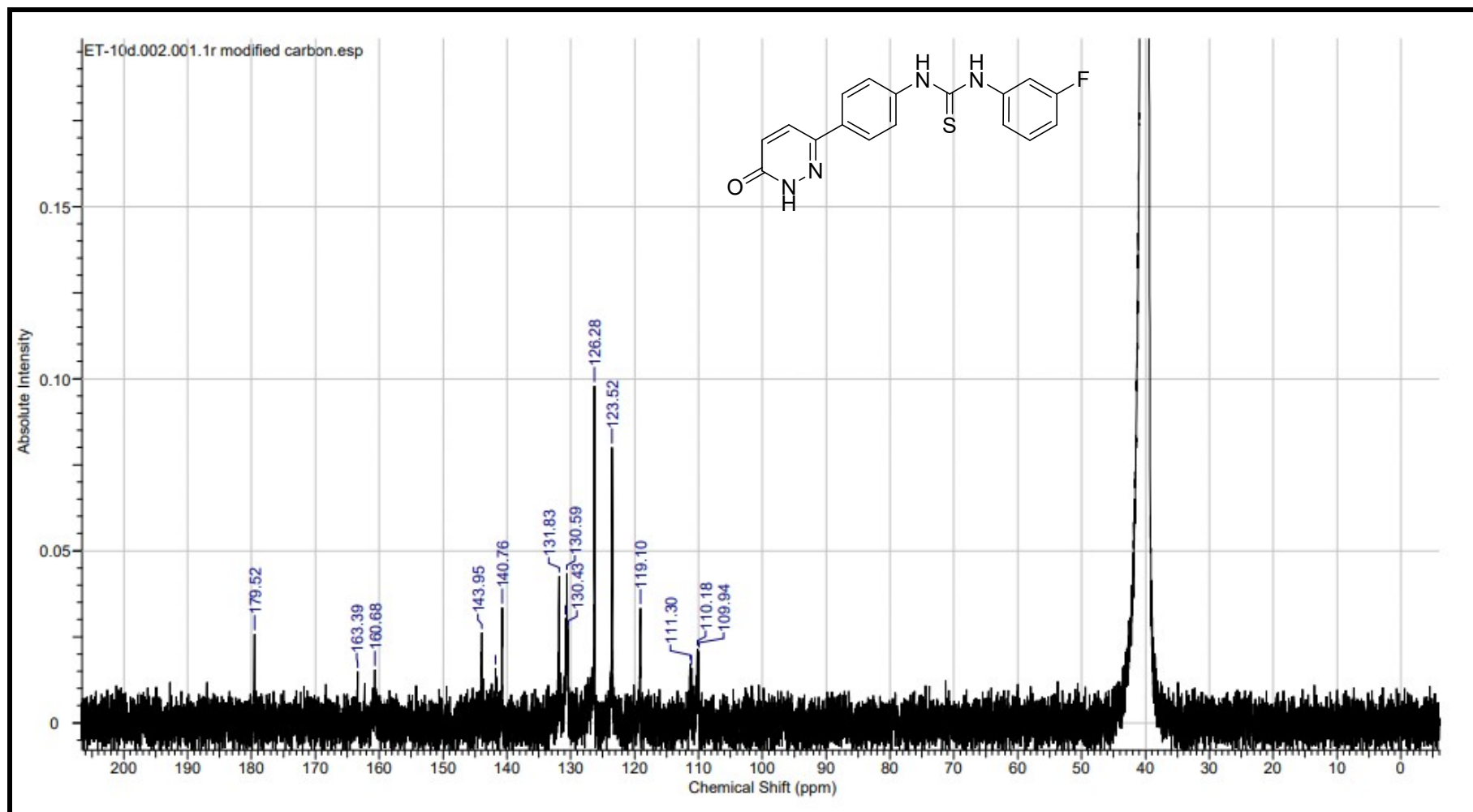**Figure 4a.** ^1H NMR spectrum (400 MHz) of compound 8d in DMSO-d_6.

Figure 4b. ^{13}C NMR spectrum (100 MHz) of compound 8d in DMSO-d$_6$.

Figure 4c. HRMS of compound 8d.

1.5. Compound 8e

Figure 5a. ¹H NMR spectrum (400 MHz) of compound 8e in DMSO-d₆.
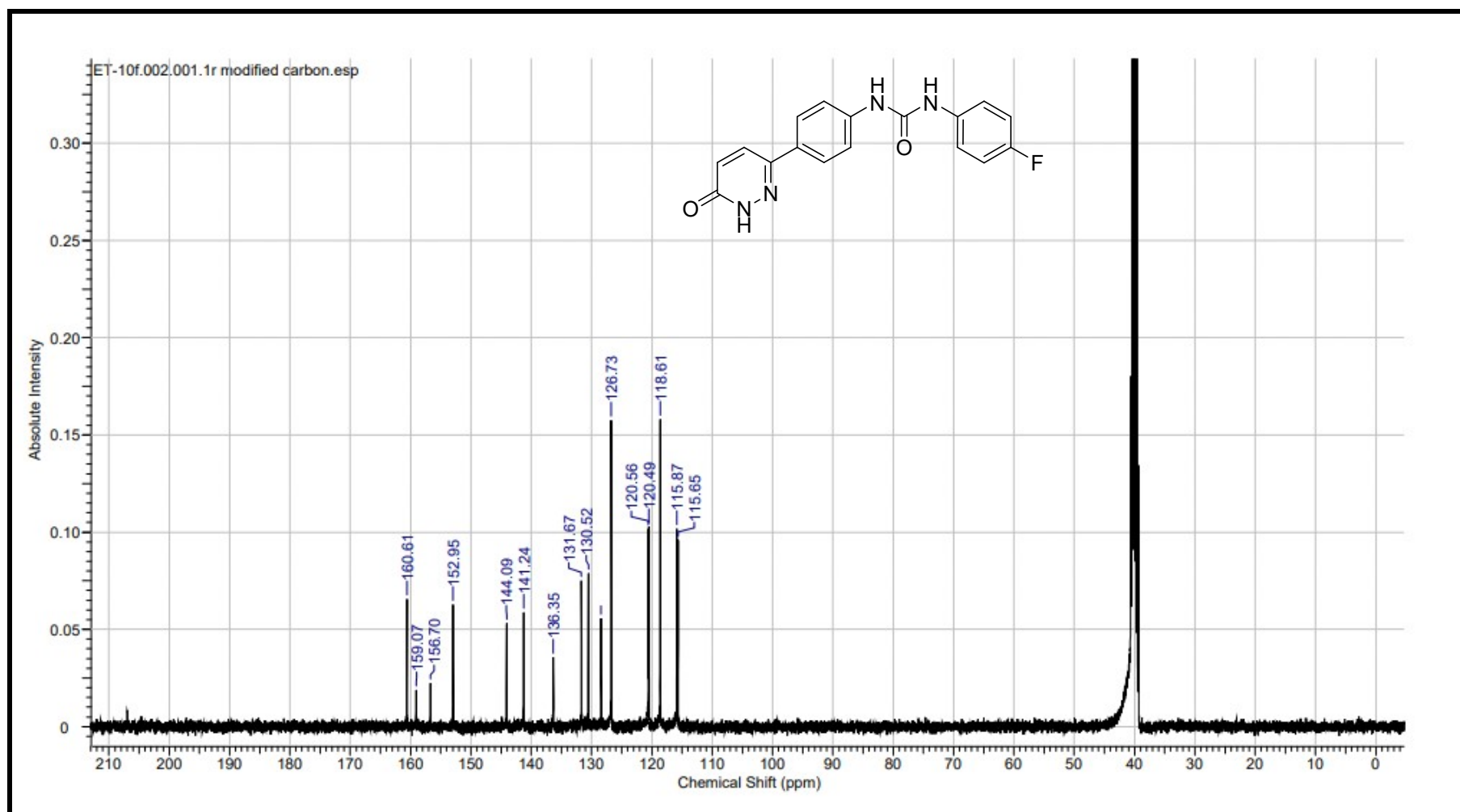
Figure 5b. ^{13}C NMR spectrum (100 MHz) of compound 8e in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 20.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
192 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-30   H: 0-30   N: 0-5   O: 0-5   F: 0-1

ET-10G/AJ   SYNAPTG2-Si#NotSet   07-Mar-2023
67590   13:24:09
0668 67 (0.149) Cm (67:84)
1: TOF MS ES+
5.02e+005
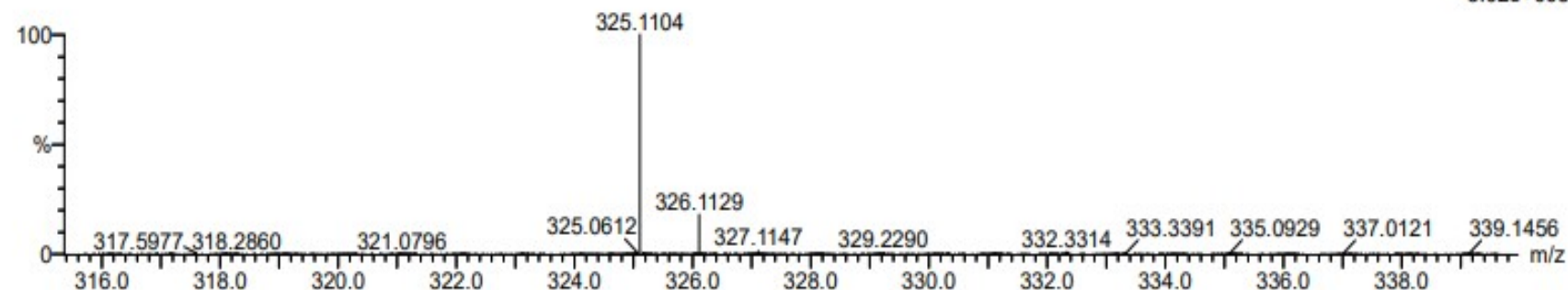
| Minimum: | | | -1.5 | | | |
| Maximum: | 5.0 | 3.0 | 20.0 | | | |

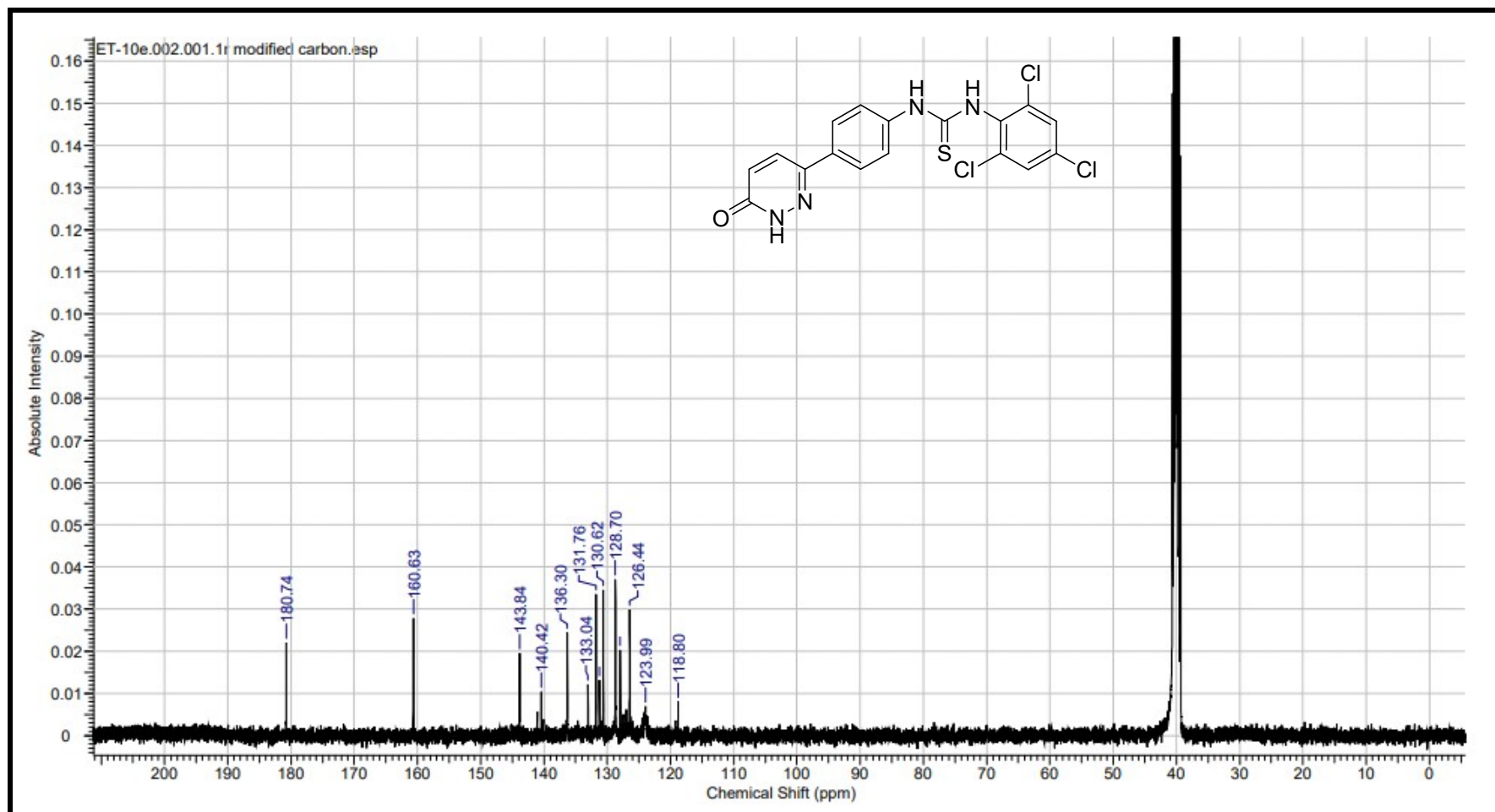| Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
325.1104	325.1101	0.3	0.9	12.5	1348.2	C17 H14 N4 O2 F

Figure 5c. HRMS of compound 8e.

1.6. Compound 8f

Figure 6a. ¹H NMR spectrum (400 MHz) of compound 8f in DMSO-d₆.

Figure 6b. ^{13}C NMR spectrum (100 MHz) of compound 8f in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 30.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
292 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-50   H: 0-50   N: 0-5   O: 0-2   35Cl: 0-1   37Cl: 0-1

ET-10k/AJ   SYNAPTG2-Si#NotSet   09-Mar-2023
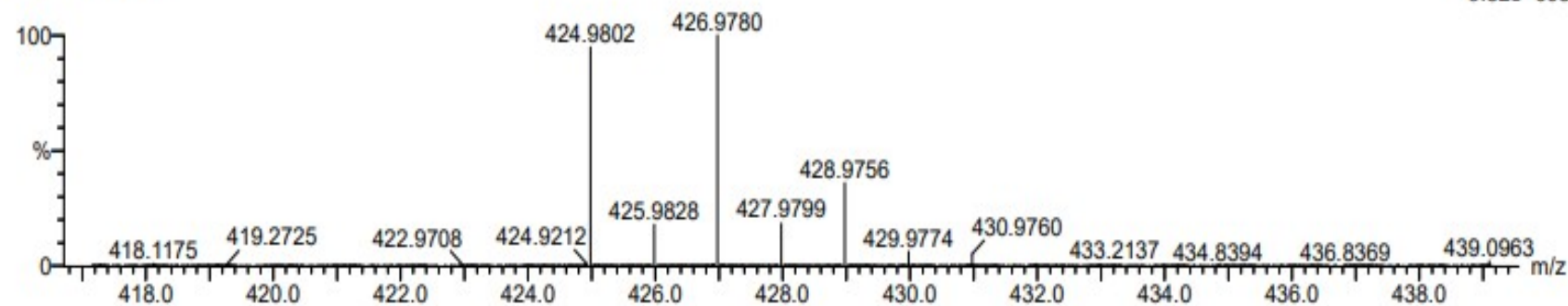67580   14:21:09
0652A 658 (1.308) Cm (653:667)
1: TOF MS ES+

6.46e+005
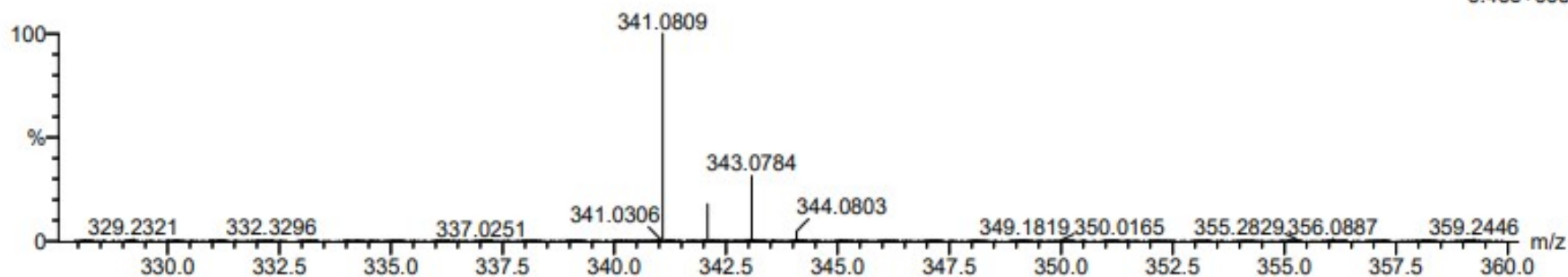
Minimum:			-1.5		
Maximum:		5.0	3.0	30.0	

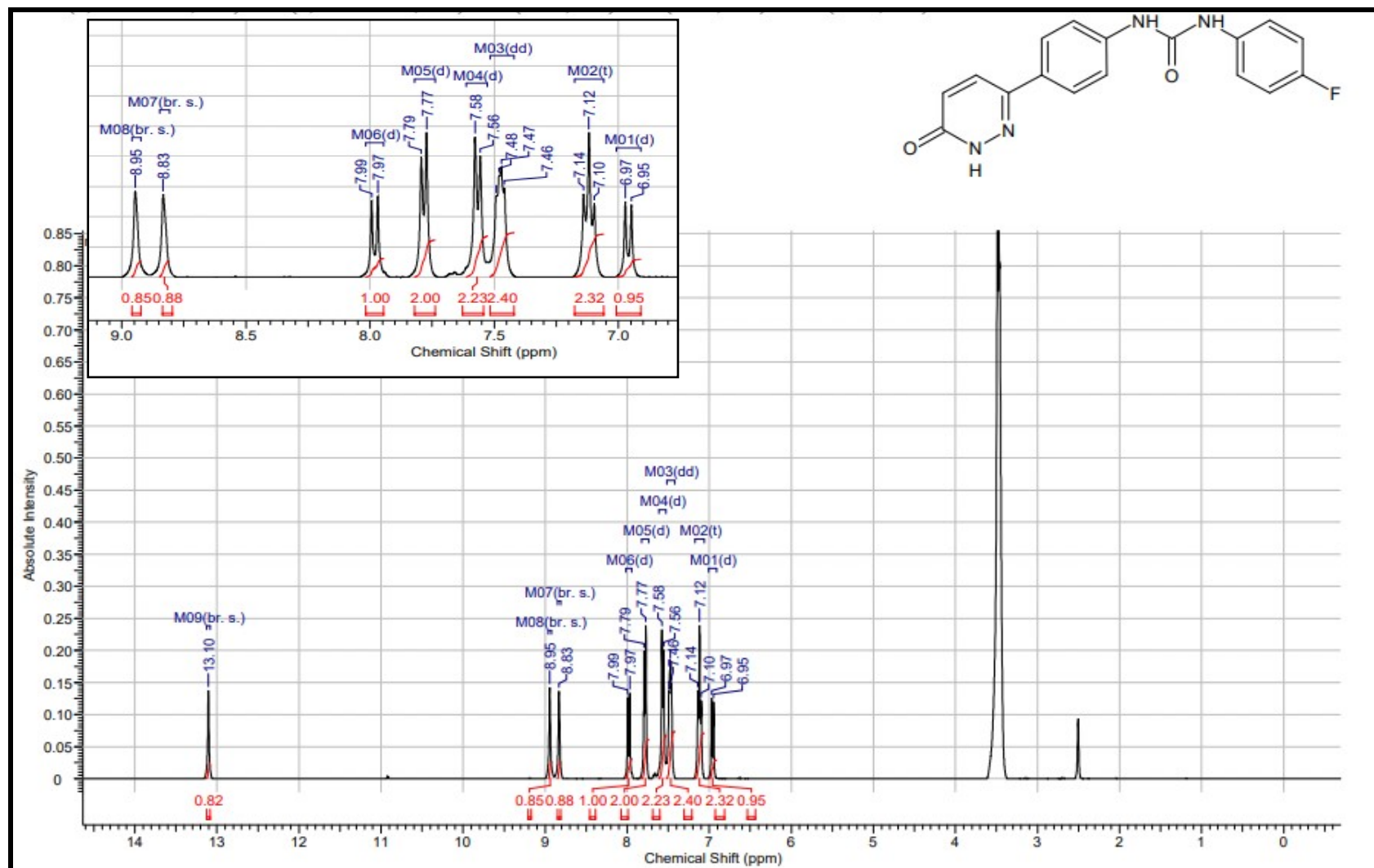| Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
341.0809	341.0805	0.4	1.2	12.5	1797.8	C17 H14 N4 O2 35Cl

Figure 6c. HRMS of compound 8f.

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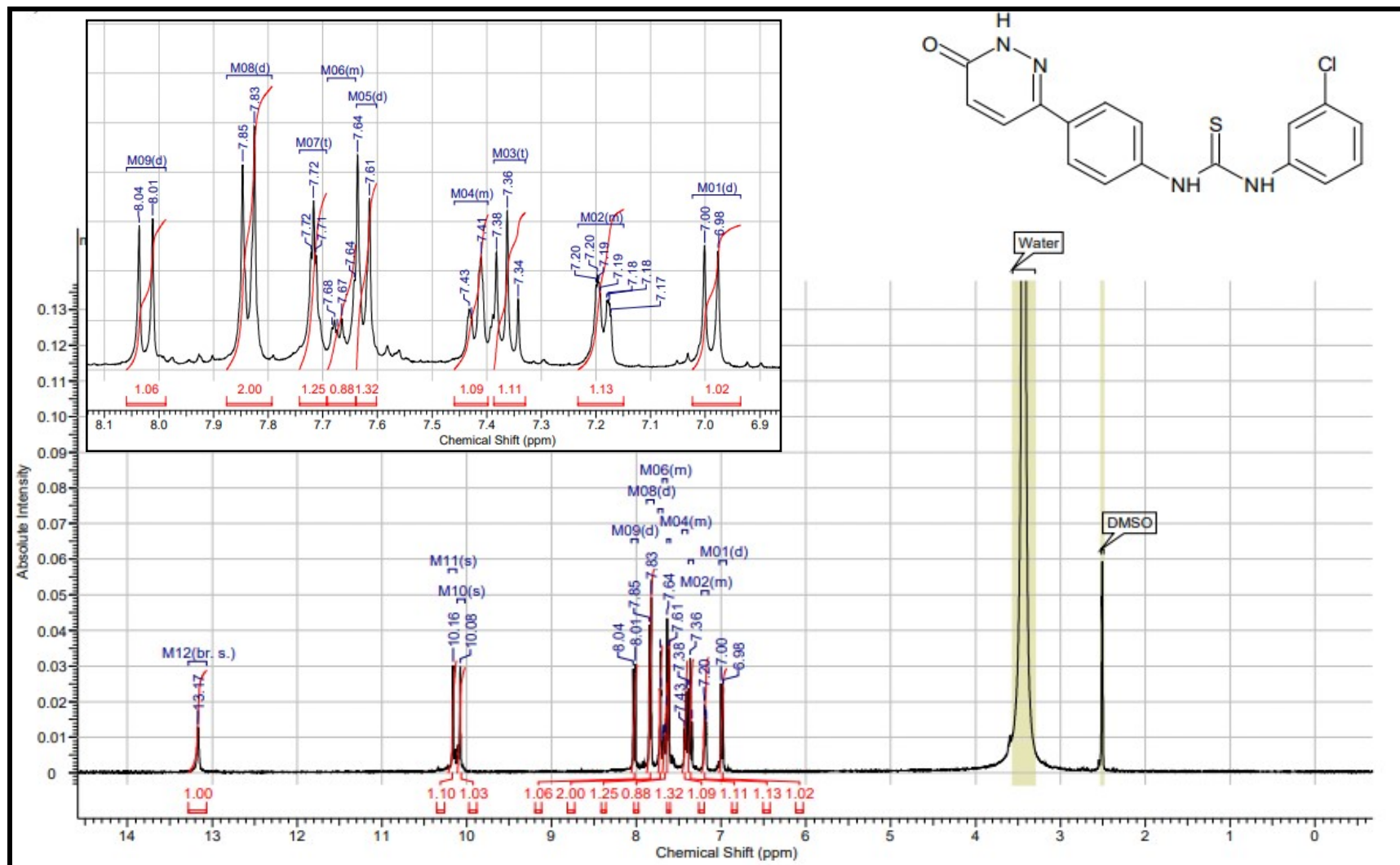
1.7. Compound 8g

Figure 7a. ¹H NMR spectrum (400 MHz) of compound 8g in DMSO-d₆.

Figure 7b. ^{13}C NMR spectrum (100 MHz) of compound 8g in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 20.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Odd and Even Electron Ions
146 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-30   H: 0-20   N: 0-4   O: 0-1   S: 0-1   35Cl: 0-1   37Cl: 0-1

ET-10I/AJ
67585
0663 517 (1.034) Cm (469:548-98:132)
1: TOF MS ES+

SYNAPTG2-Si#NotSet

07-Mar-2023
12:25:31

2.64e+006
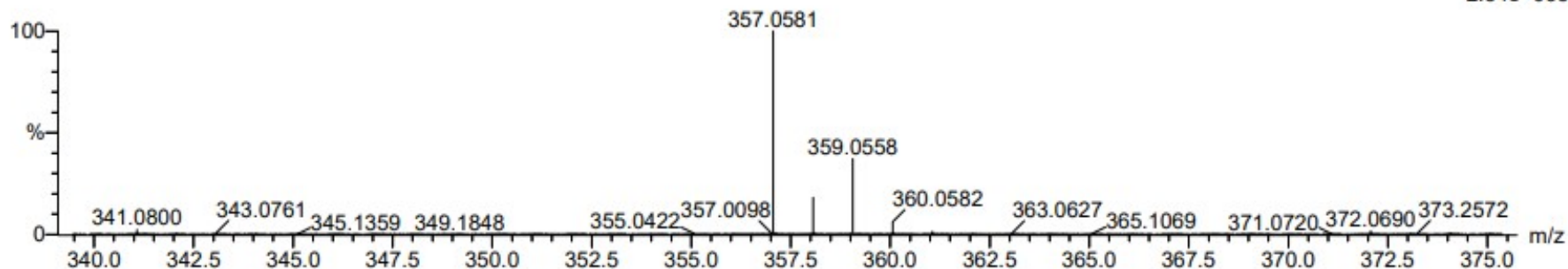
| Minimum: | | | | -1.5 | | | |
| Maximum: | | 5.0 | 3.0 | 20.0 | | | |

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula	
357.0581	357.0577	0.4	1.1	12.5	2715.5	C17 H14 N4 O S 35Cl	

Figure 7c. HRMS of compound 8g.

1.8. Compound 8h
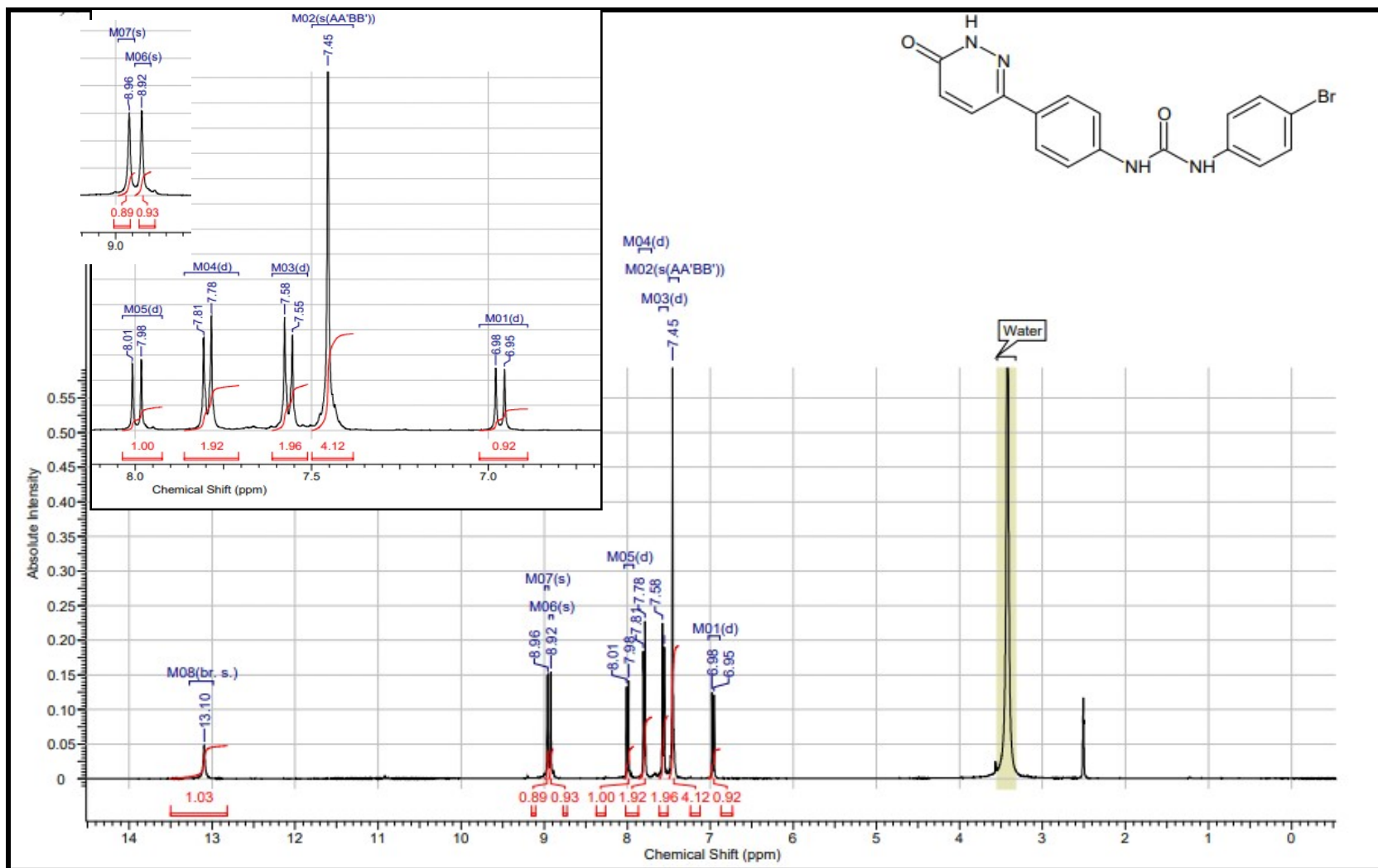
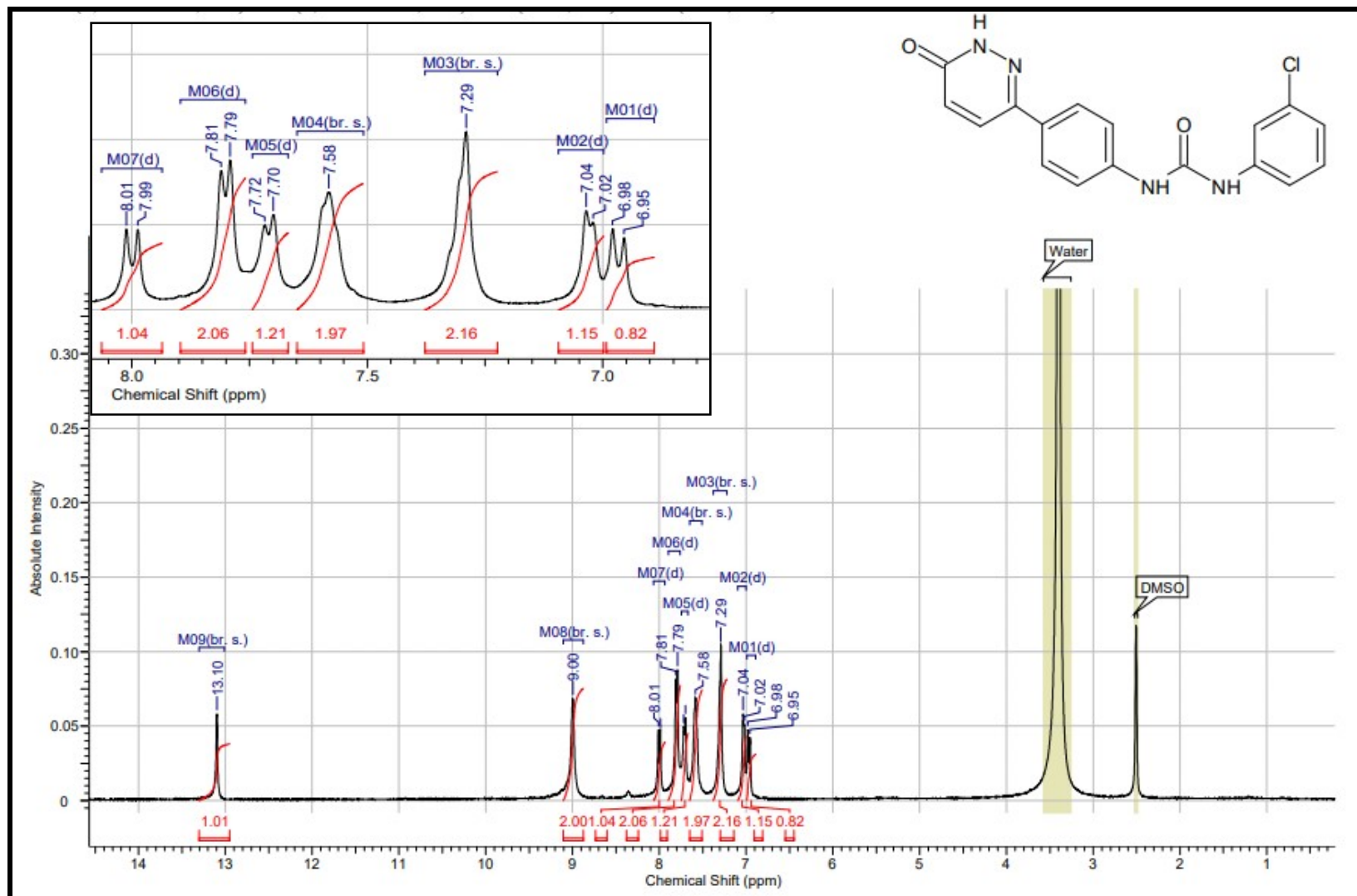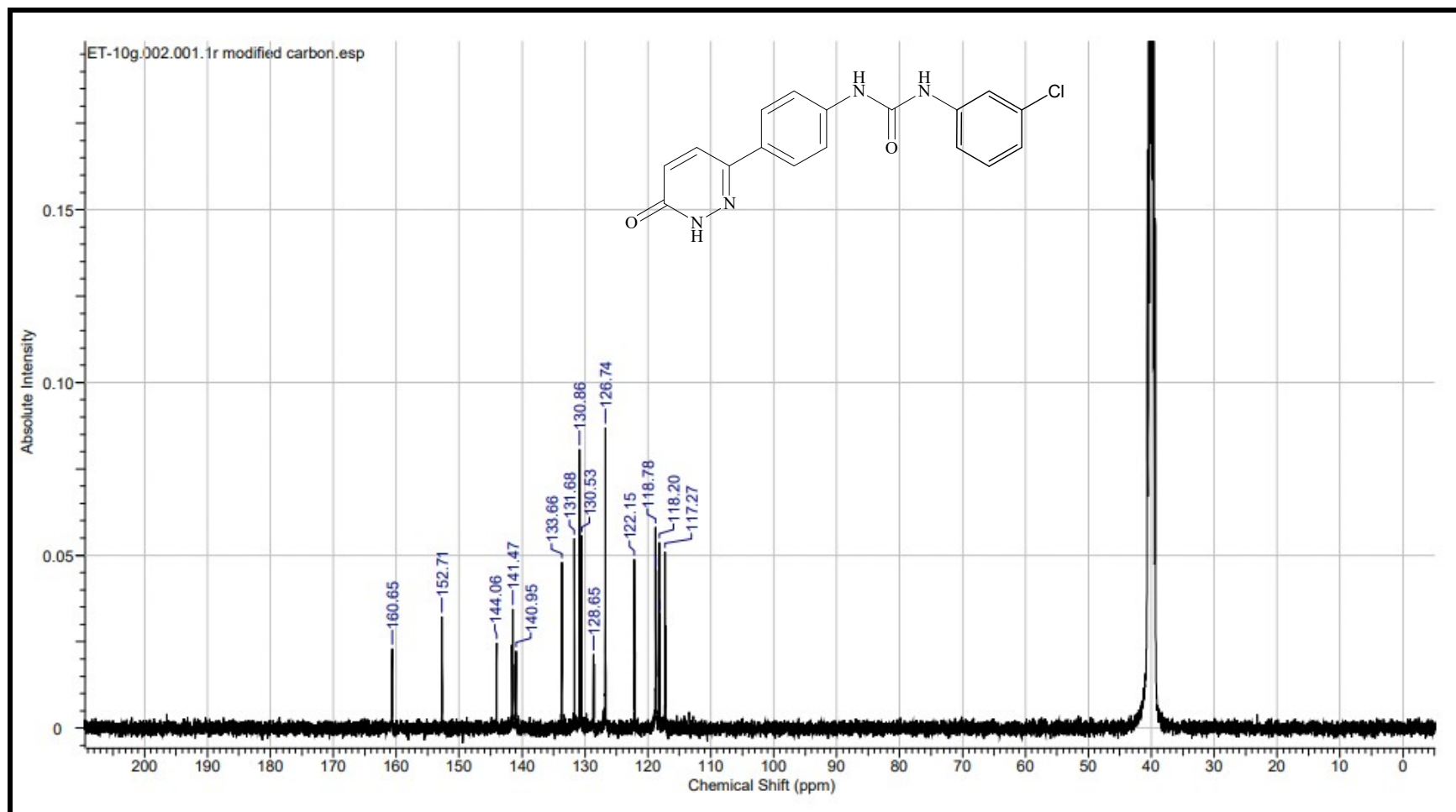**Figure 8a.** ^1H NMR spectrum (400 MHz) of compound 8h in DMSO-d_6.
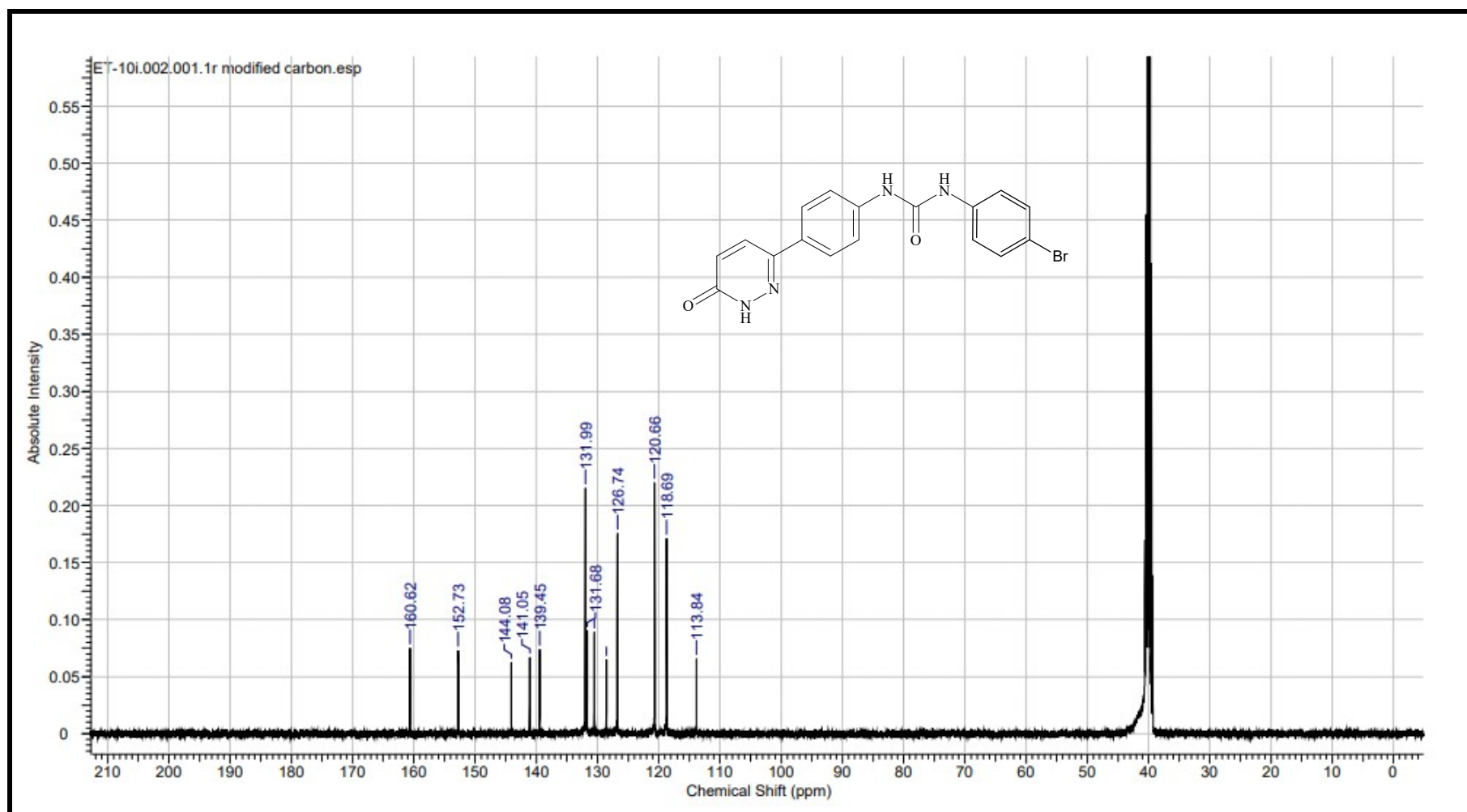
Figure 8b. ^{13}C NMR spectrum (100 MHz) of compound 8h in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 15.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
176 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-50   H: 0-20   N: 0-5   O: 0-3   79Br: 0-1   81Br: 0-1

ET-10m/AJ   SYNAPTG2-Si#NotSet   06-Mar-2023
67578   15:40:18
0649 670 (1.331)
1: TOF MS ES+
                                                                                            4.52e+006
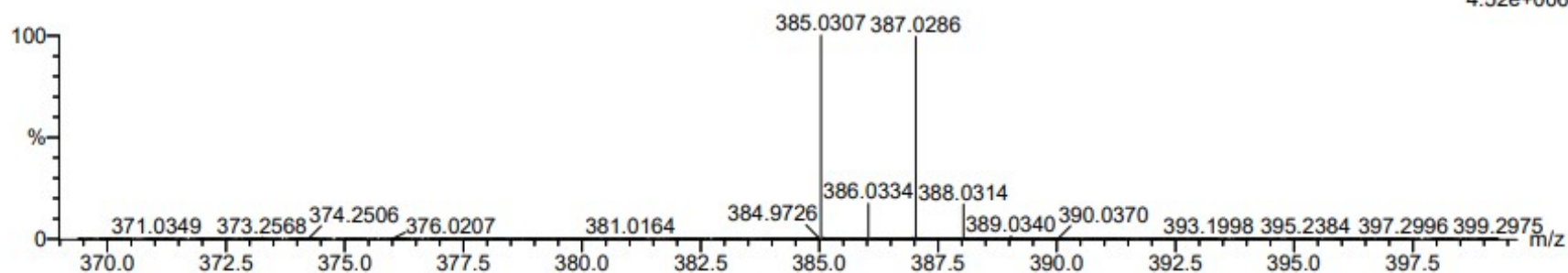
Minimum:			-1.5		
Maximum:	5.0	3.0	15.0		

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
385.0307	385.0300	0.7	1.8	12.5	3291.8	C17 H14 N4 O2 79Br

Figure 8c. HRMS of compound 8h.

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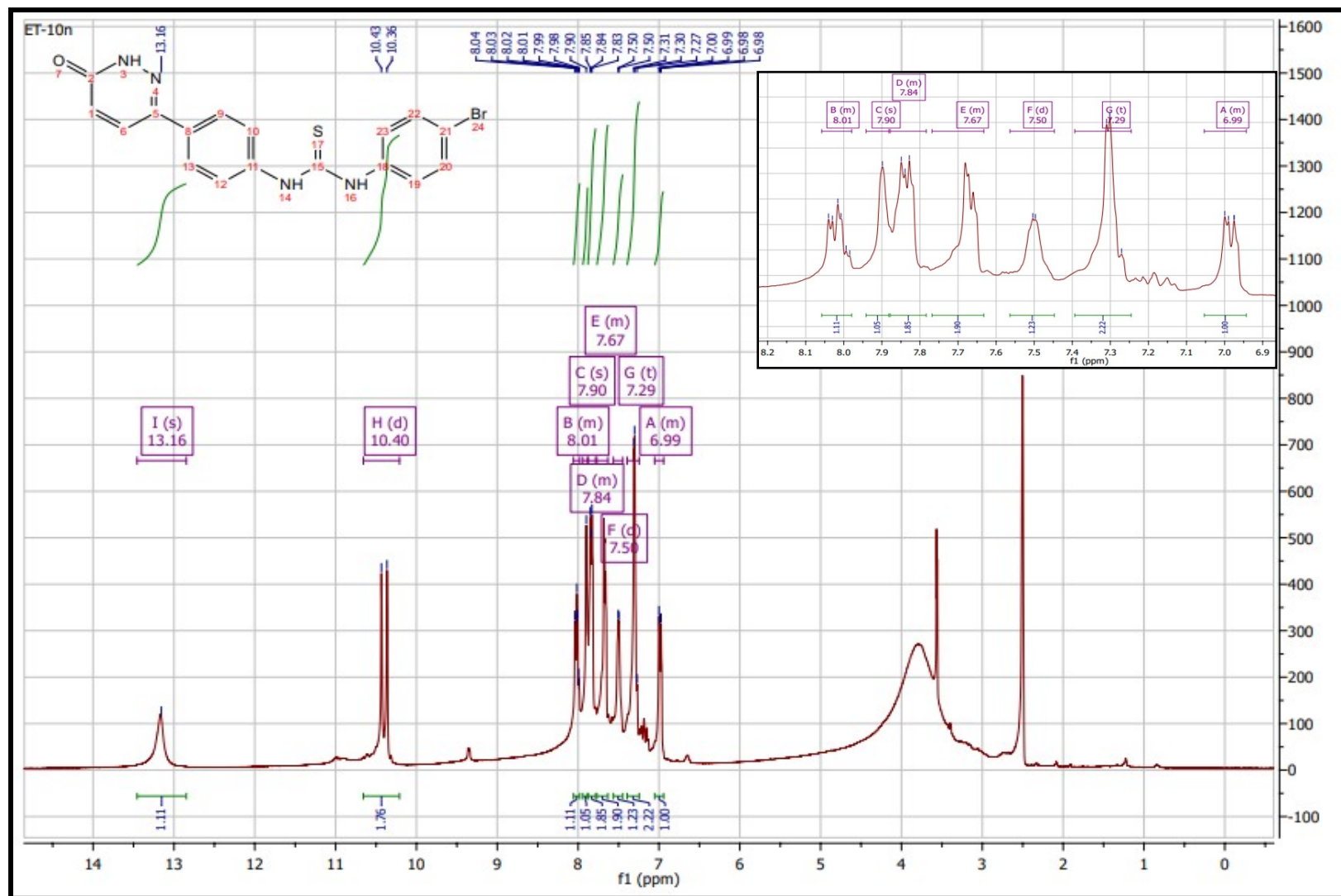
1.9. Compound 8i

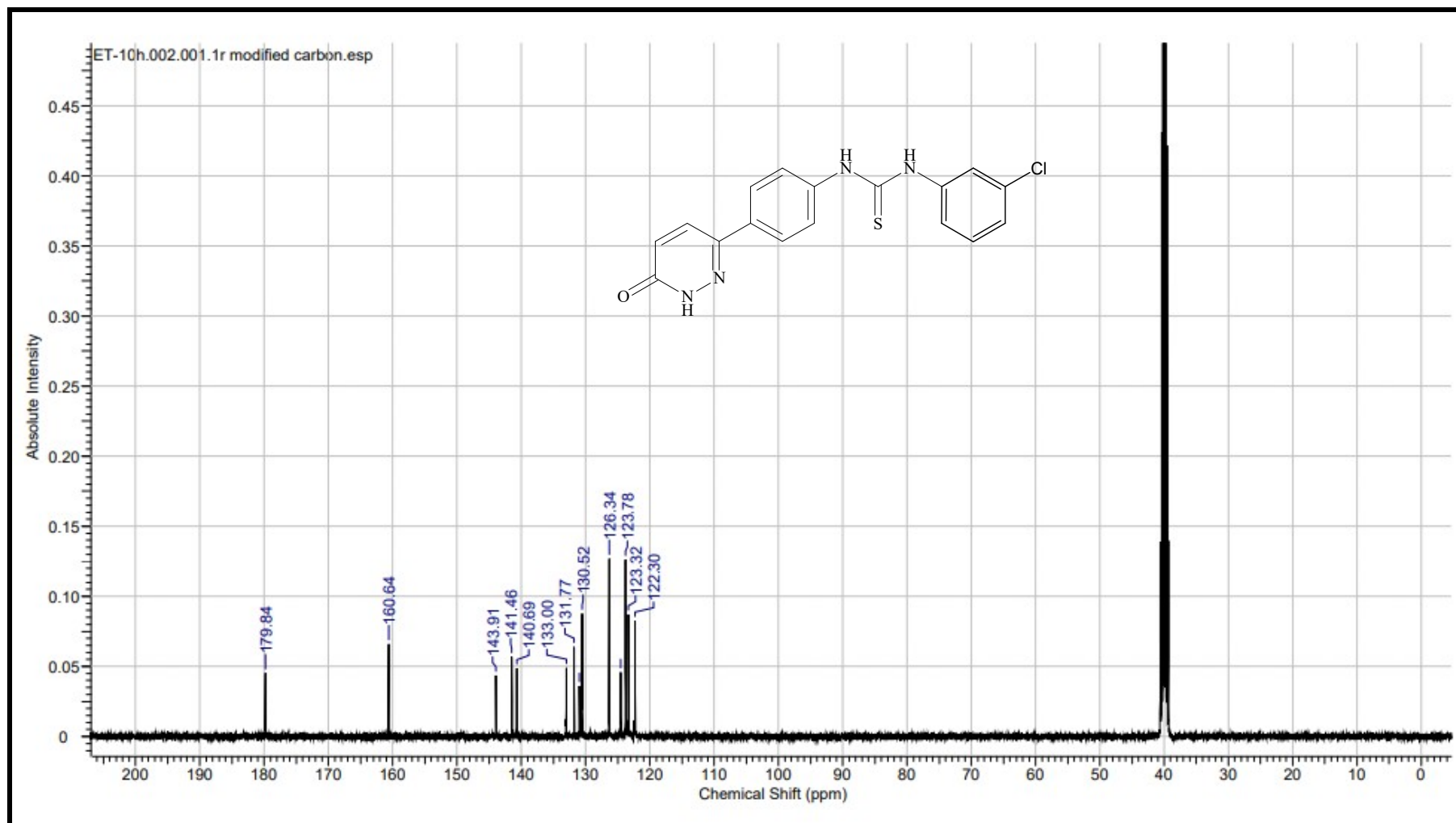**Figure 9a.** ^1H NMR spectrum (400 MHz) of compound 8i in DMSO-d_6.
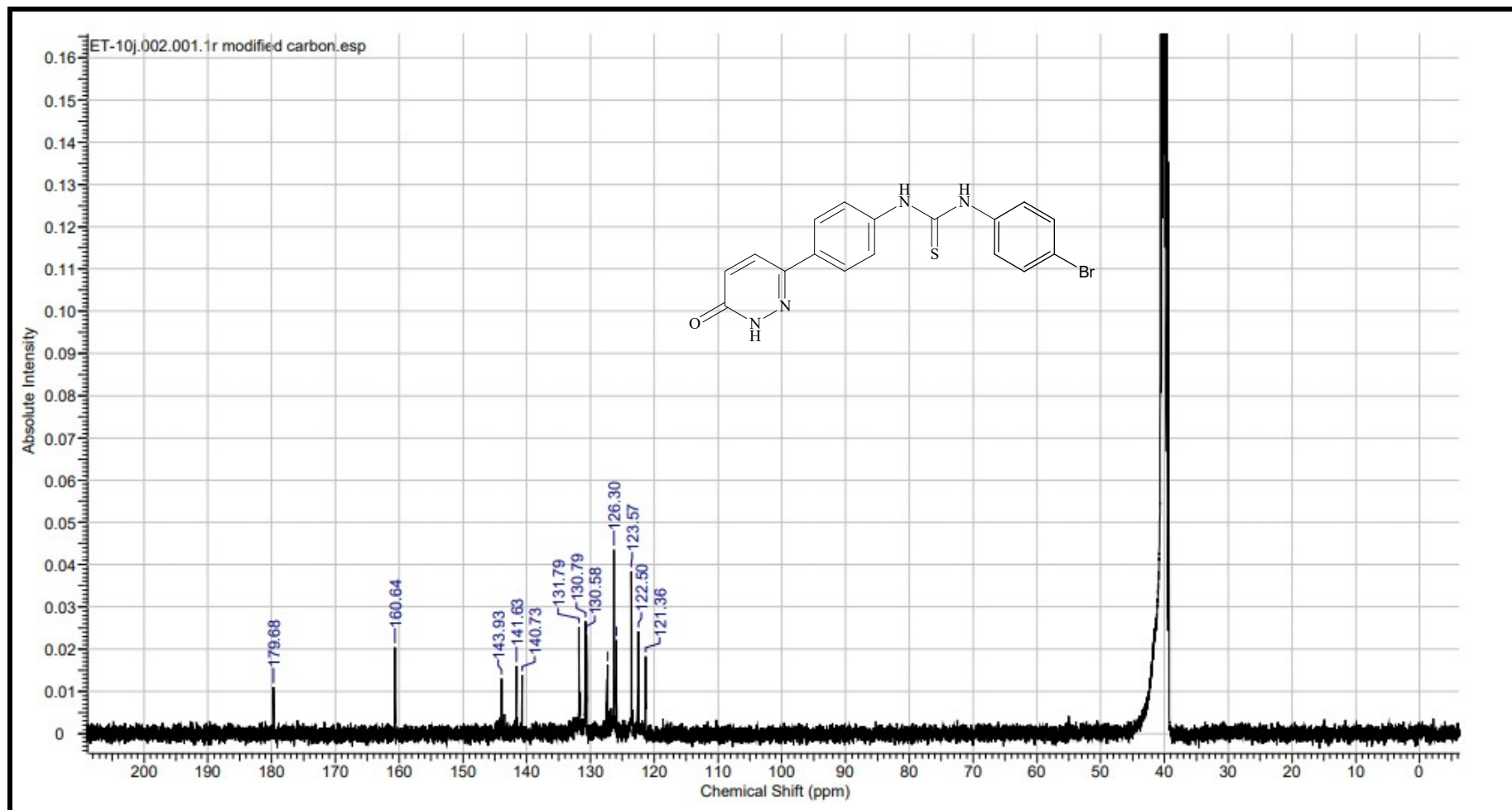
Figure 9b. ^{13}C NMR spectrum (100 MHz) of compound 8i in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 25.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
539 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-30   H: 0-30   N: 0-5   O: 0-2   S: 0-1   79Br: 0-2   81Br: 0-1

ET-10n/AJ   SYNAPTG2-Si#NotSet   14-Mar-2023
67591   15:23:46
0669A 521 (1.045) Cm (411:820)
1: TOF MS ES+

4.31e+007
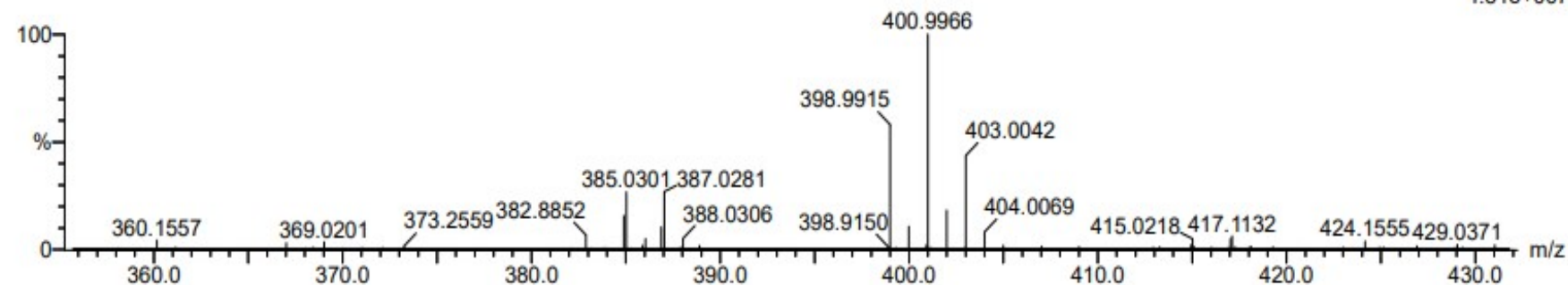
```
Minimum:                        -1.5
Maximum:           5.0    3.0    25.0

Mass      Calc. Mass   mDa    PPM    DBE    i-FIT    Formula
385.0301   385.0300    0.1    0.3    12.5   4631.4   C17 H14 N4 O2 79Br
```

Figure 9c. HRMS of compound 8i.

27
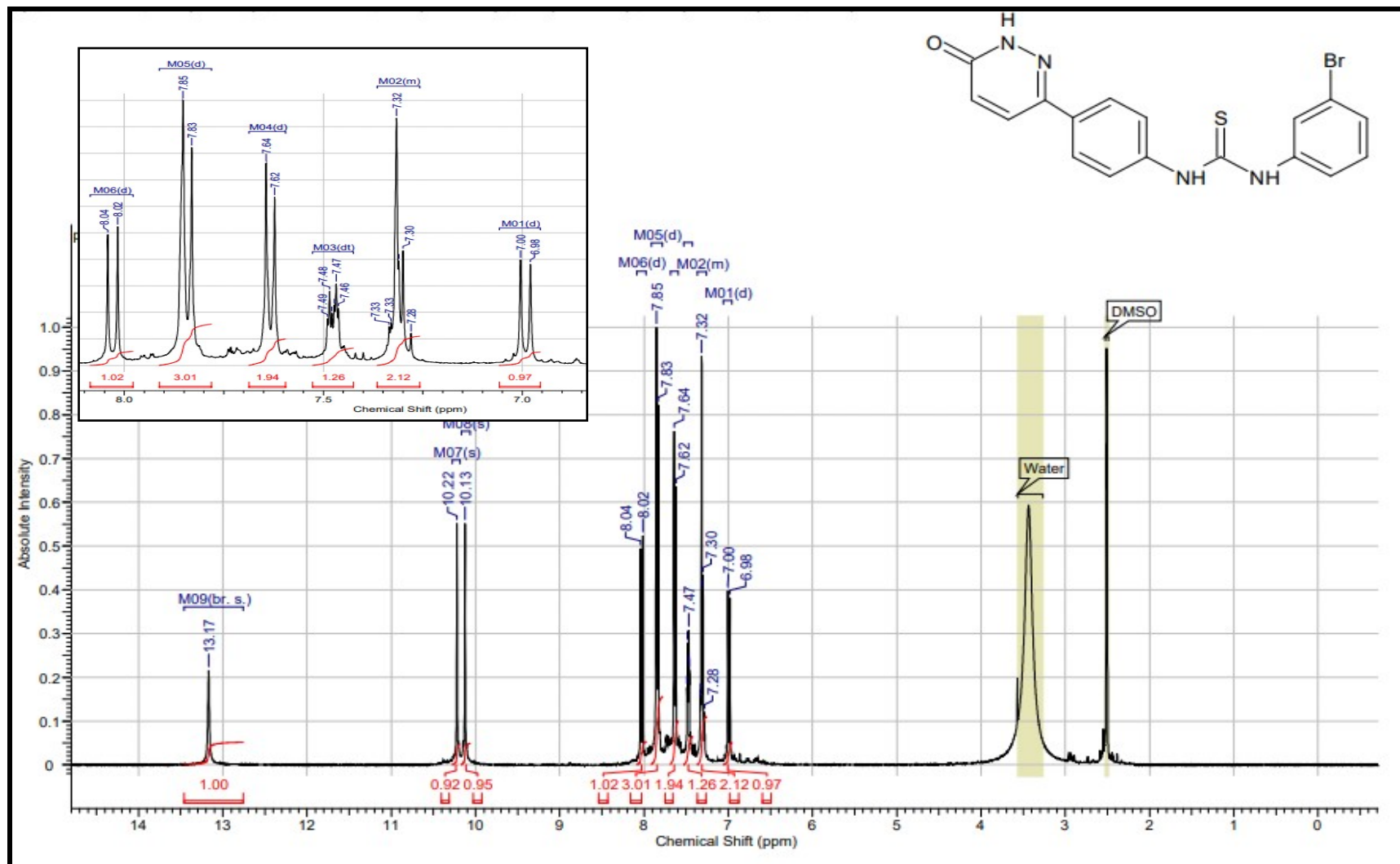
1.10.   Compound 8j

Figure 10a. ¹H NMR spectrum (400 MHz) of compound 8j in DMSO-d₆.
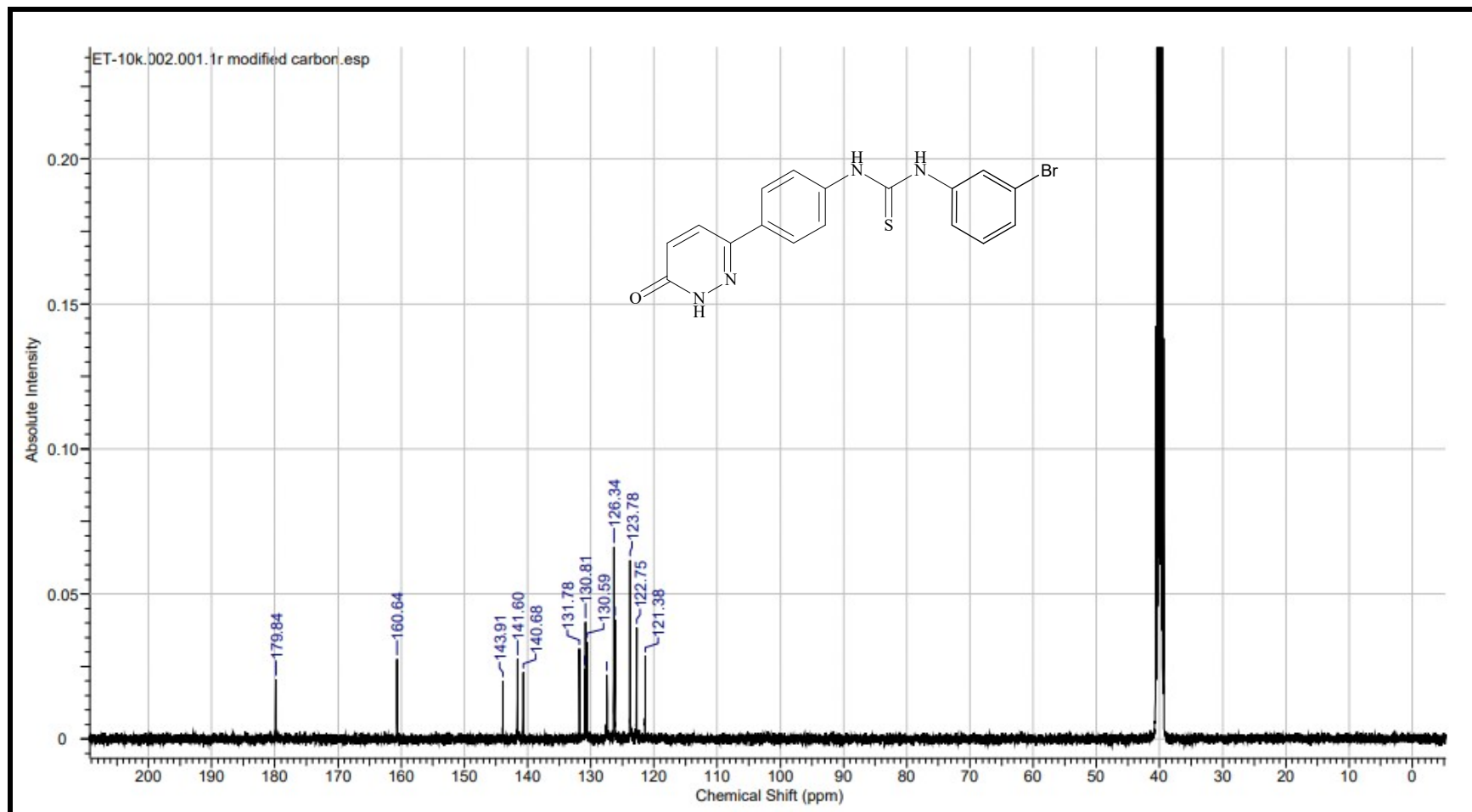
Figure 10b. ^{13}C NMR spectrum (100 MHz) of compound 8j in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 20.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
304 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-30   H: 0-24   N: 0-5   O: 0-2   S: 0-1   79Br: 0-1   81Br: 0-1

ET-10O/AJ   SYNAPTG2-Si#NotSet   07-Mar-2023
67592   13:31:27
0670 517 (1.035) Cm (517:591)
1: TOF MS ES+
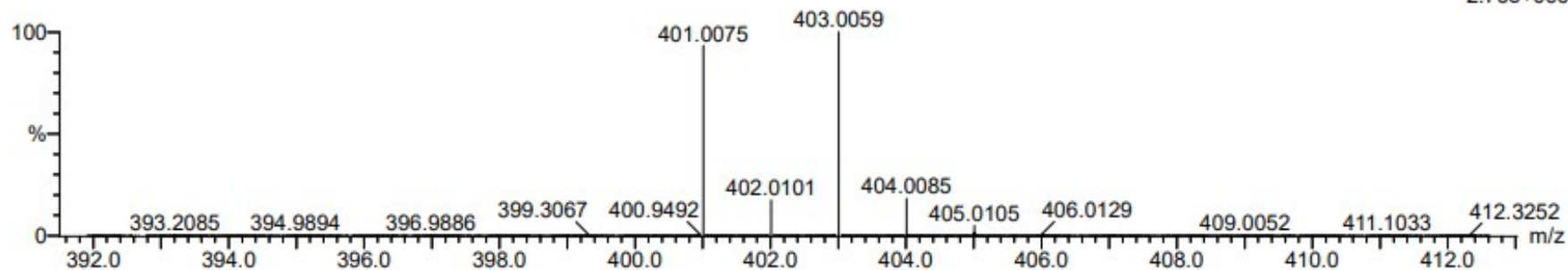
Minimum: -1.5
Maximum: 5.0   3.0   20.0

Mass   Calc. Mass   mDa   PPM   DBE   i-FIT   Formula
401.0075   401.0072   0.3   0.7   12.5   3033.7   C17 H14 N4 O S 79Br

Figure 10c. HRMS of compound 8j.

2. Spectral data of series II

2.1. Compound 9a

Figure 11a. ^1H NMR spectrum (400 MHz) of compound 9a in DMSO-d_6.
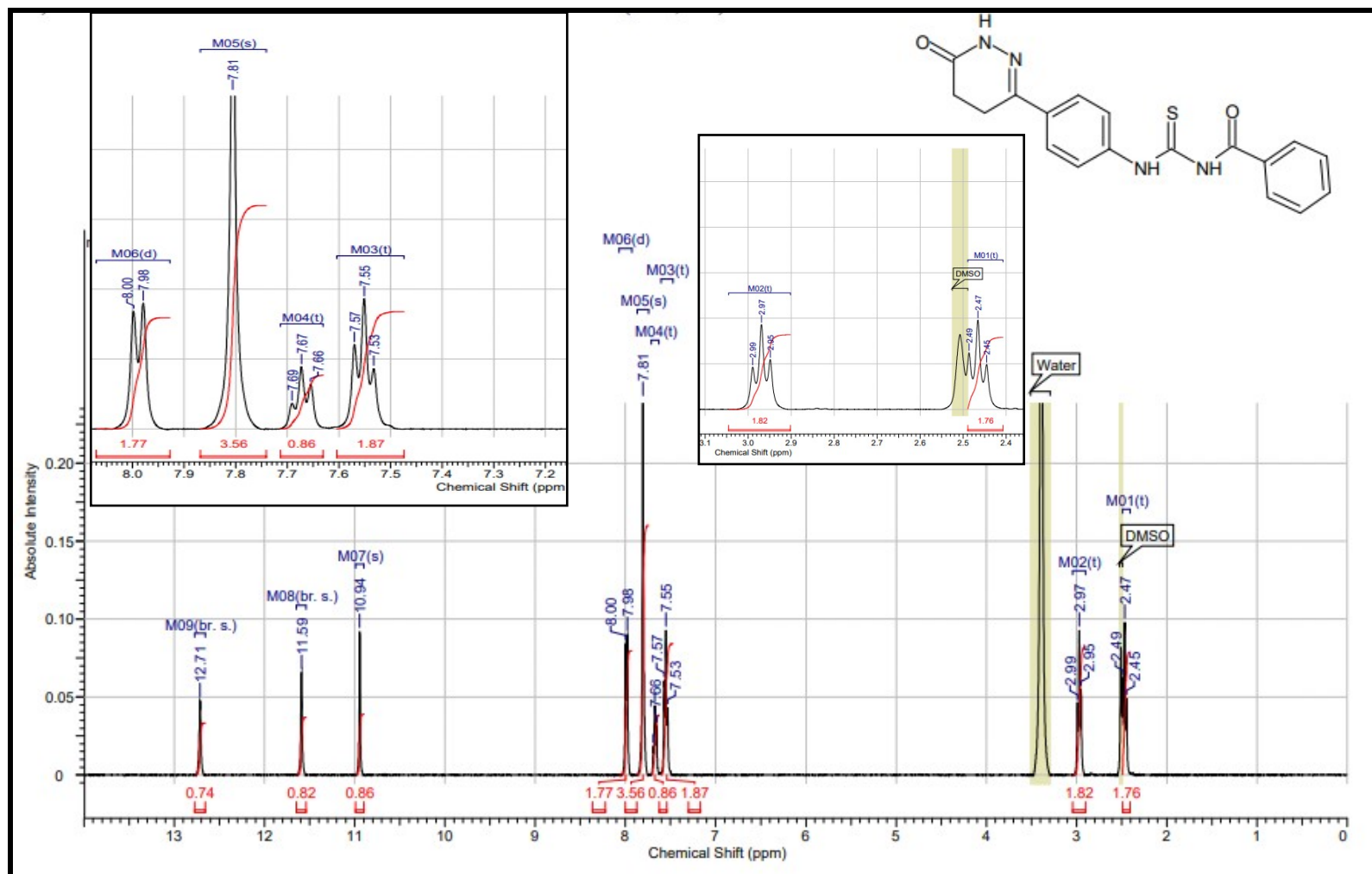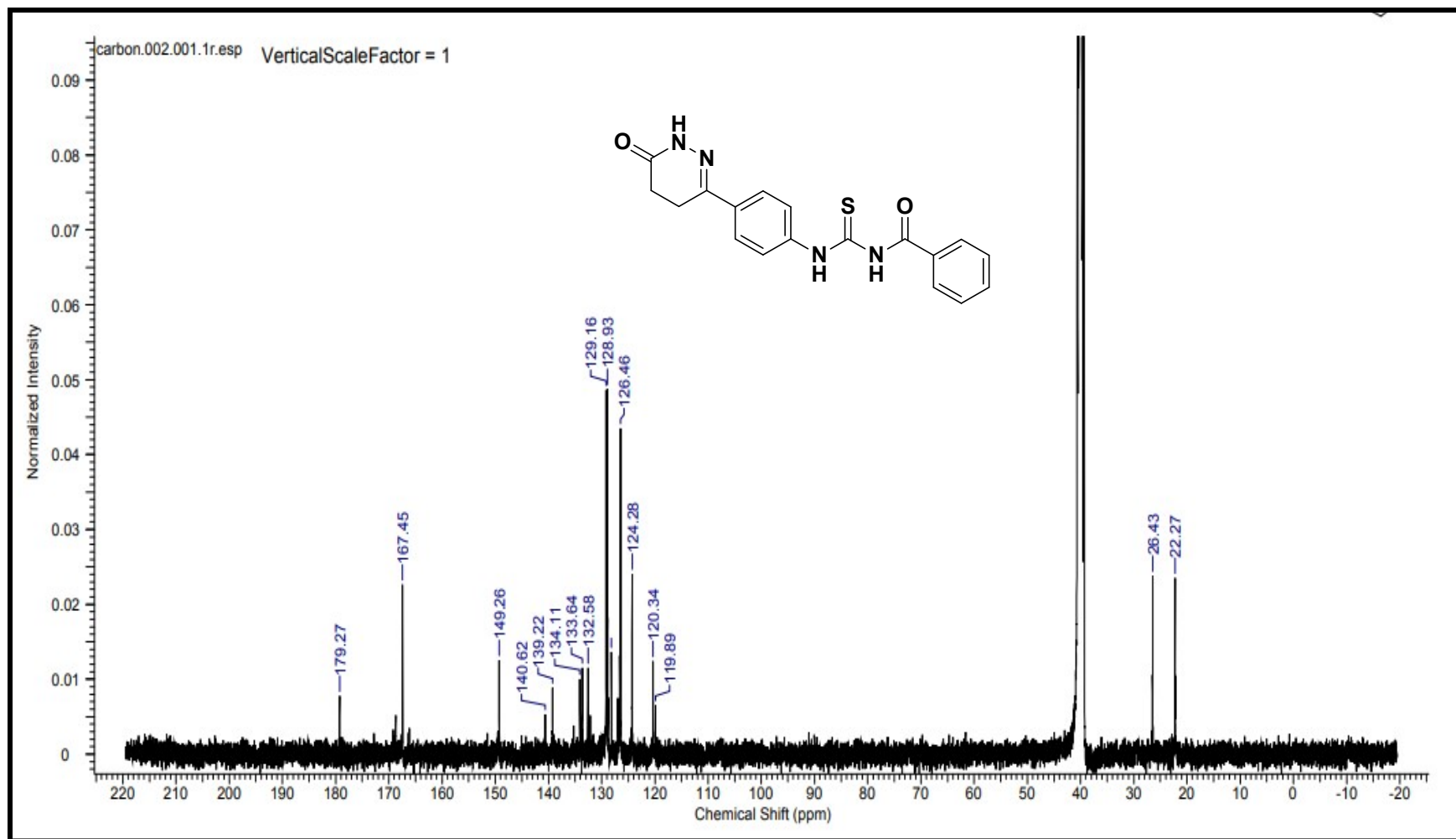
Figure 11b. ^{13}C NMR spectrum (100 MHz) of compound 9a in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 13.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
110 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-30   H: 0-20   N: 0-5   O: 0-4   S: 0-1

ET-4a/AJ   SYNAPTG2-Si#NotSet   27-Feb-2023
67563   11:59:58
0566 129 (0.272) Cm (80:482)
1: TOF MS ES+
4.09e+005
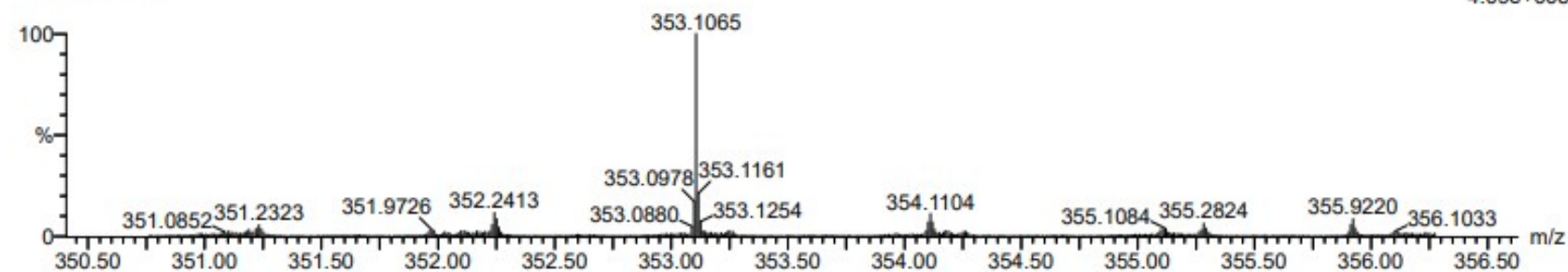
Minimum:			-1.5		
Maximum:	5.0	3.0	13.0		

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
353.1065	353.1072	-0.7	-2.0	12.5	3879.9	C18 H17 N4 O2 S

Figure 11c. HRMS of compound 9a.

2.2. Compound 9b

Figure 12a. ^{1}H NMR spectrum (400 MHz) of compound 9b in DMSO-d$_6$.

Figure 12b. ^{13}C NMR spectrum (100 MHz) of compound **9b** in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 13.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
436 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-30   H: 0-20   N: 0-5   O: 0-4   S: 0-1   35Cl: 0-1   37Cl: 0-1

ET-4b/AJ   SYNAPTG2-Si#NotSet   27-Feb-2023
67562   12:03:38
0567 81 (0.176) Cm (80:93)
1: TOF MS ES+

5.17e+004
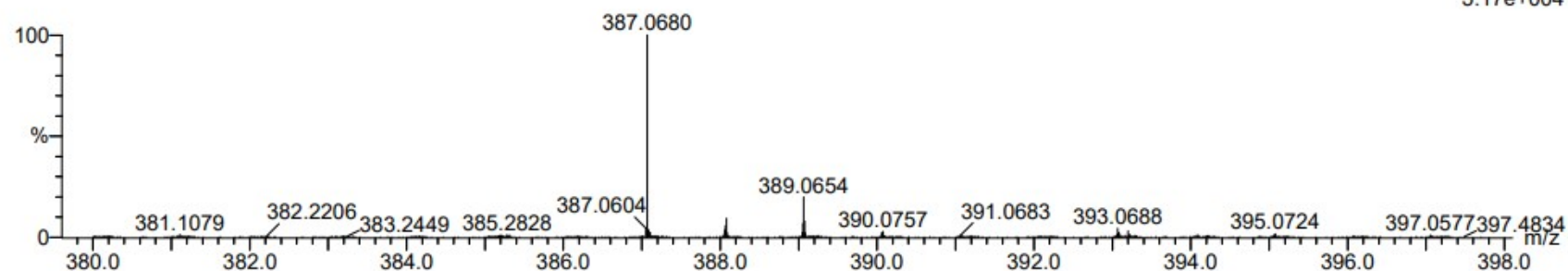
| Minimum: | | | -1.5 | | | |
| Maximum: | 5.0 | 3.0 | 13.0 | | | |

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
387.0680	387.0682	-0.2	-0.5	12.5	1063.8	C18 H16 N4 O2 S 35Cl

Figure 12c. HRMS of compound 9b.

2.3. Compound 9c
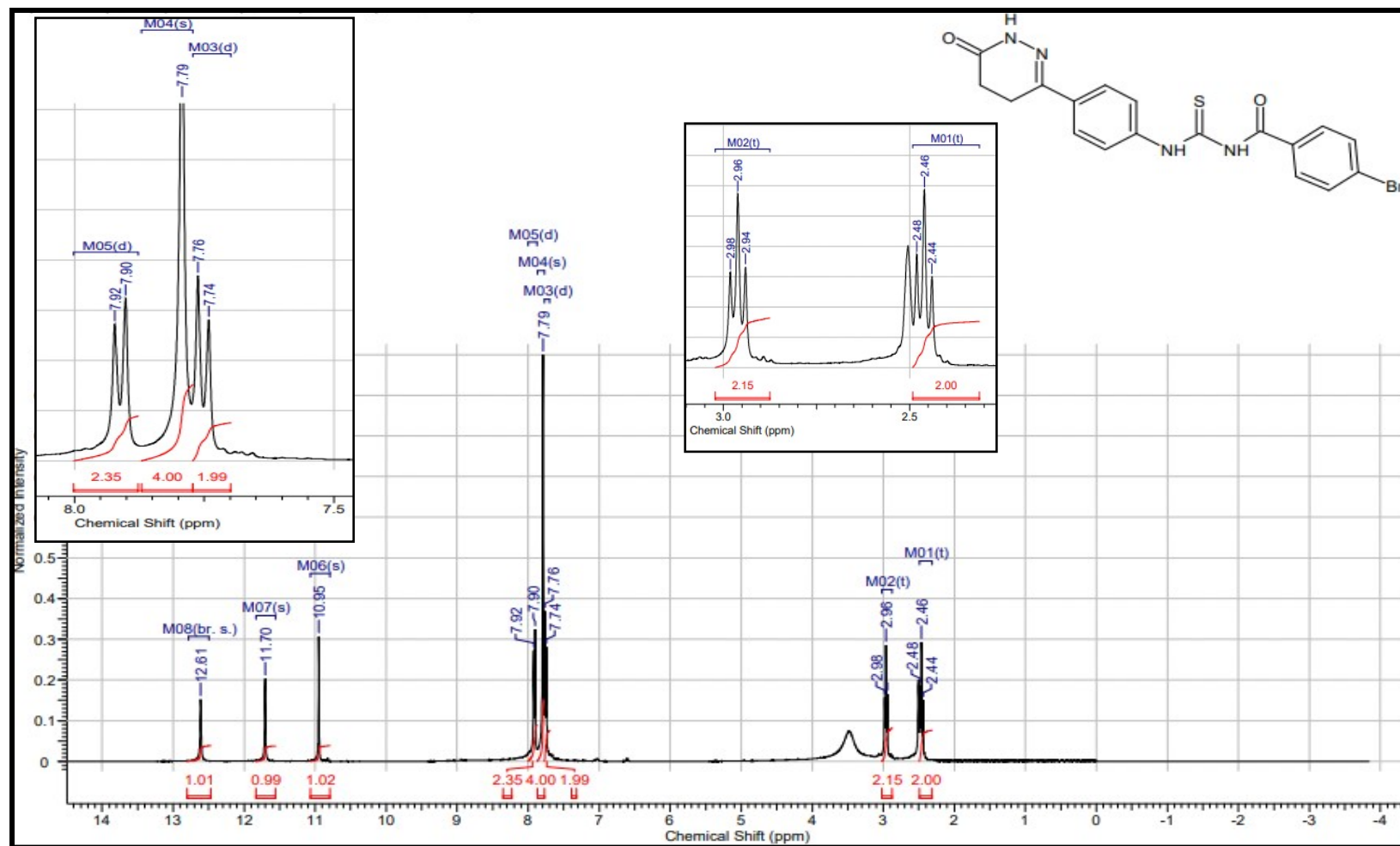
Figure 13a. ¹H NMR spectrum (400 MHz) of compound 9c in DMSO-d₆.
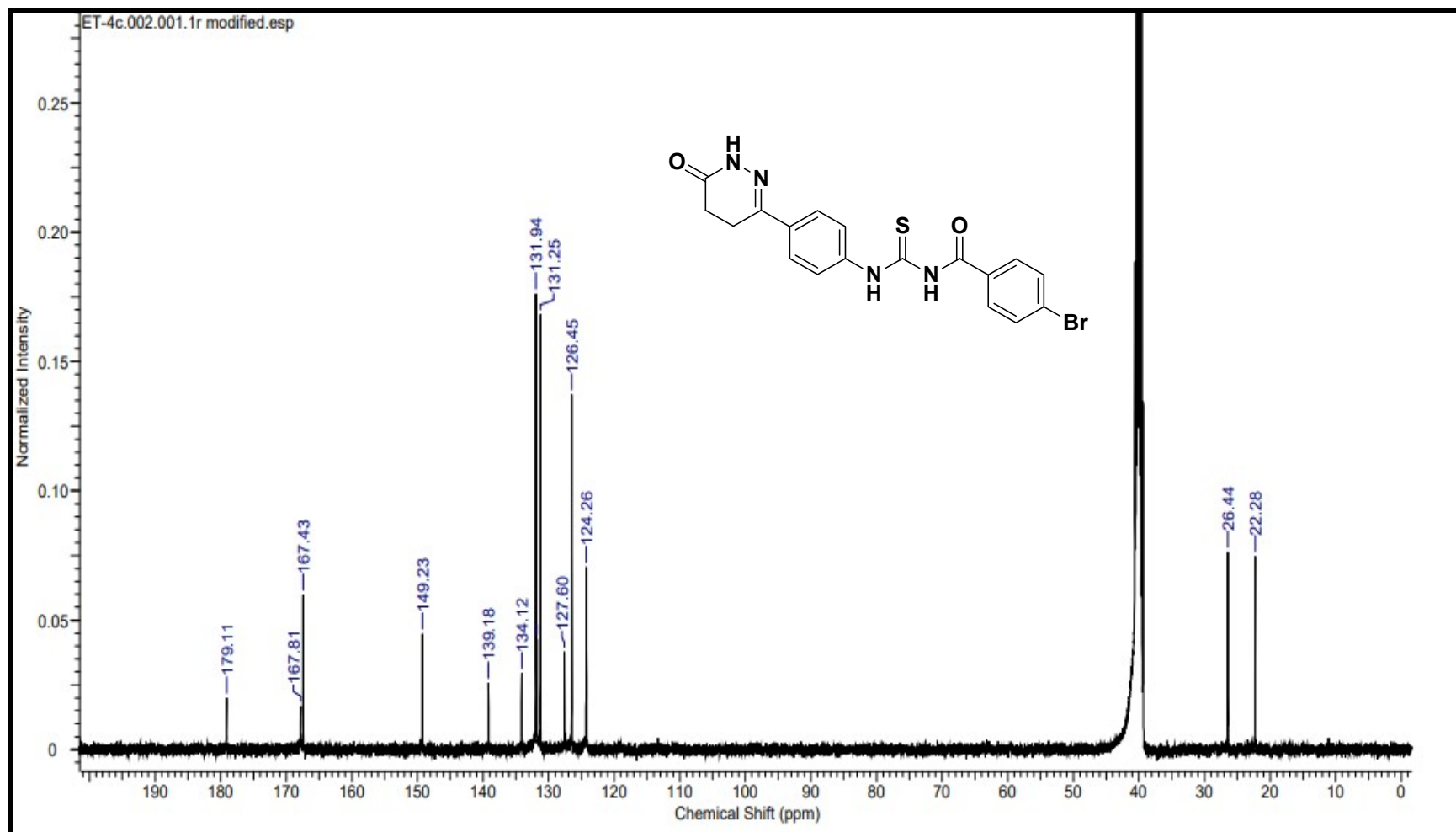
Figure 13b. ^{13}C NMR spectrum (100 MHz) of compound **9c** in DMSO-d$_6$.

Figure 13c. HRMS of compound 9c.

2.4. Compound 9d

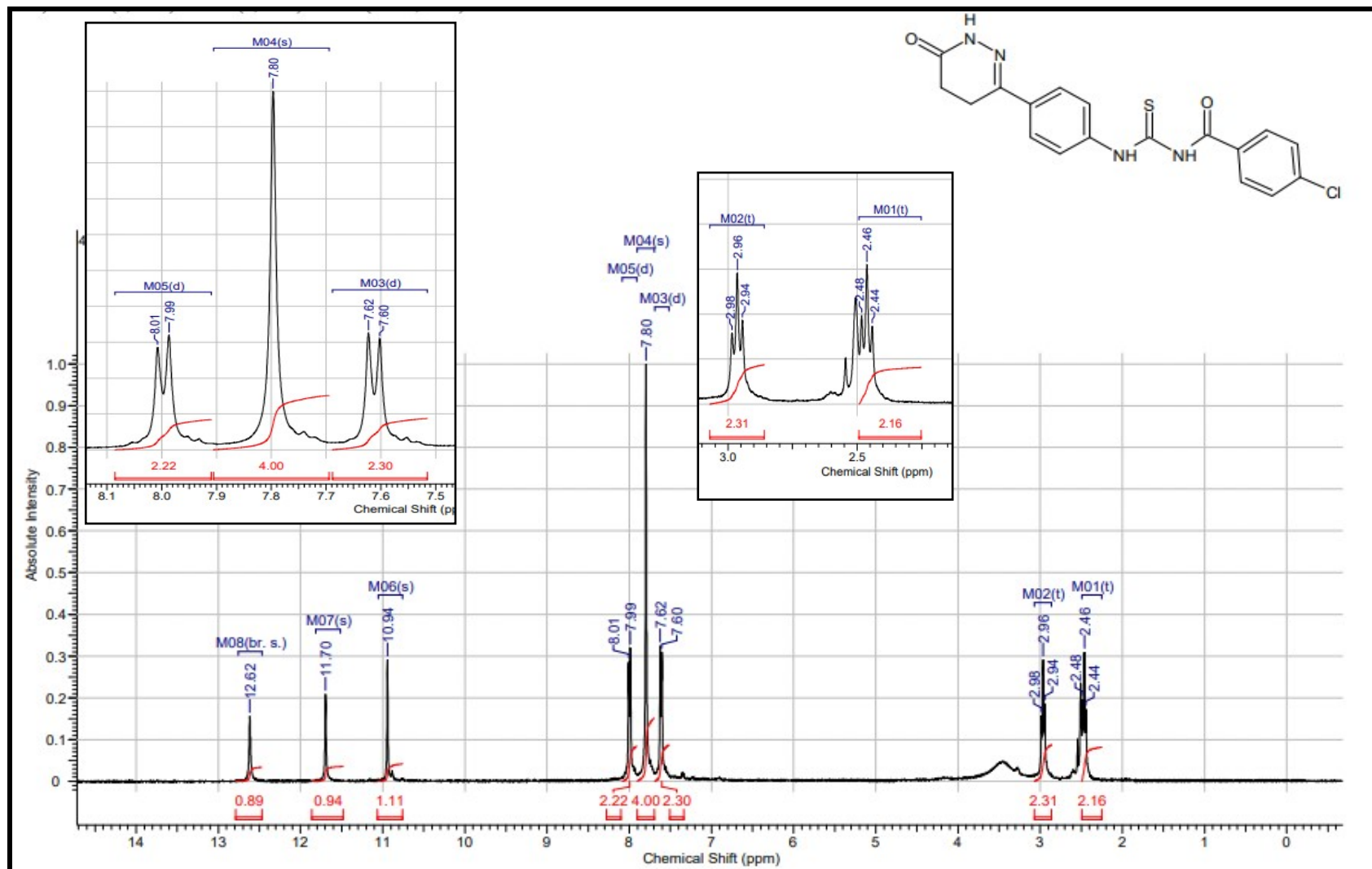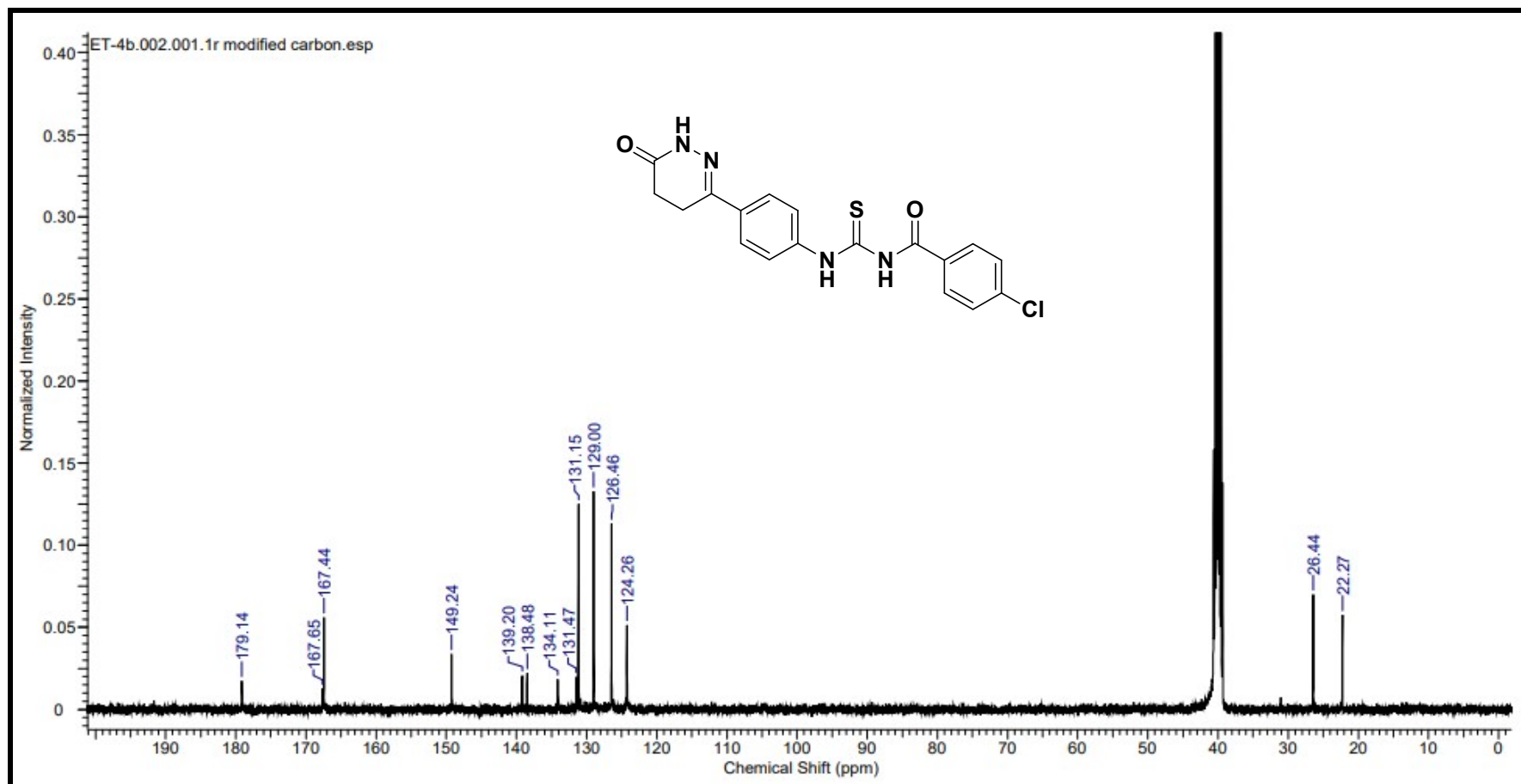**Figure 14a.** ^1H NMR spectrum (400 MHz) of compound 9d in DMSO-d_6.
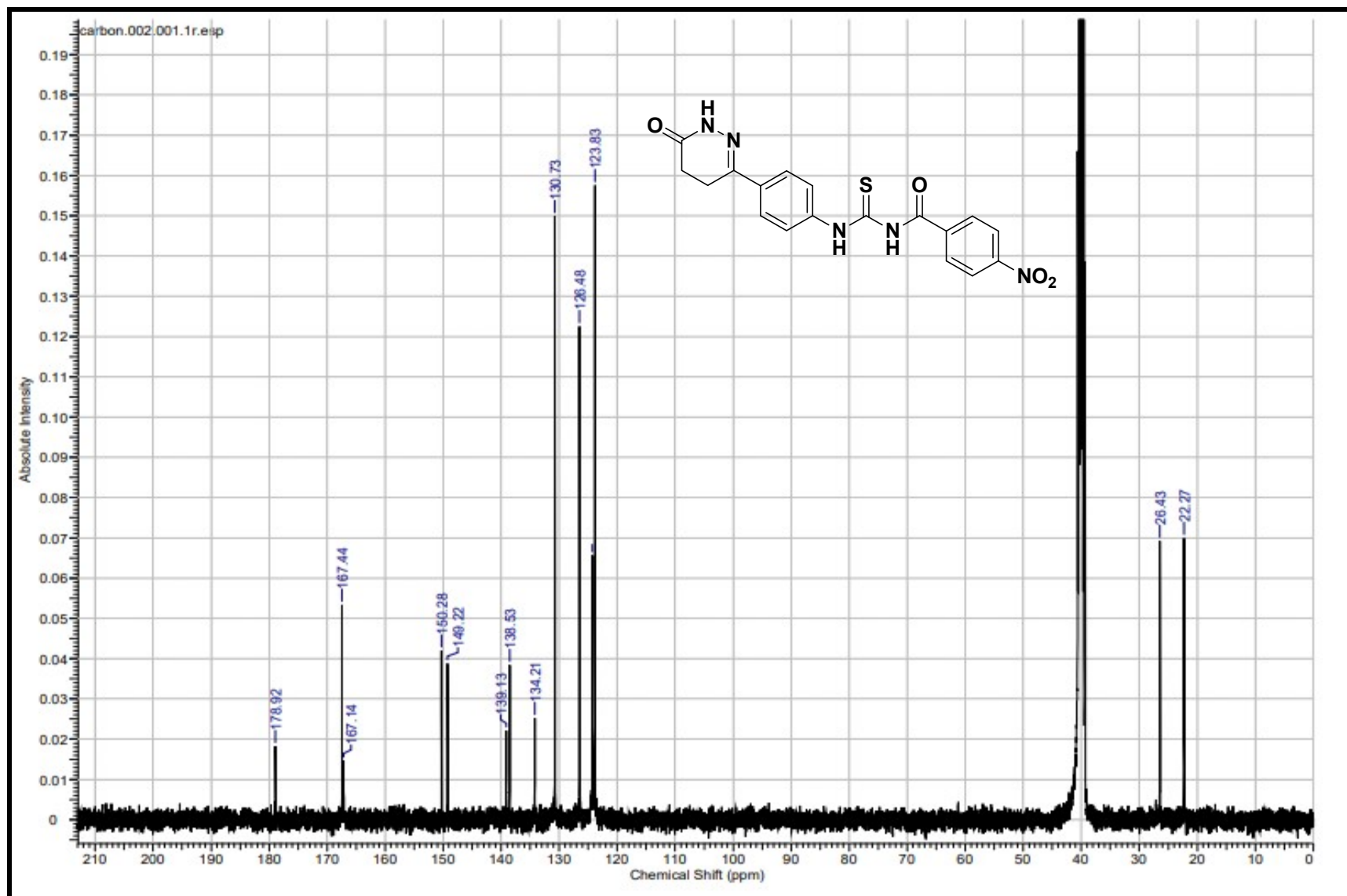
Figure 14b. ^{13}C NMR spectrum (100 MHz) of compound 9d in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 14.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
105 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-30   H: 0-20   N: 0-5   O: 0-4   S: 0-1
ET-4d/AJ   SYNAPTG2-Si#NotSet   27-Feb-2023
67560   12:10:55
0569 185 (0.383) Cm (184:197)
1: TOF MS ES+
                                                                                                           7.04e+004
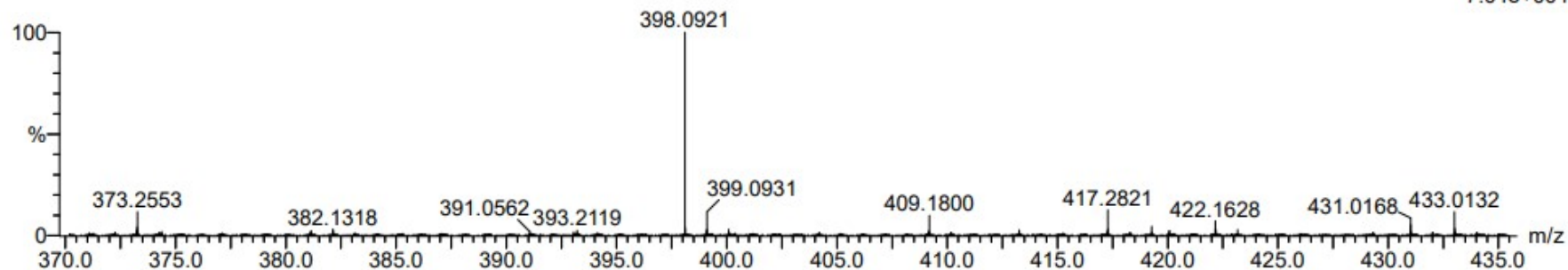
Minimum:			-1.5		
Maximum:		5.0	3.0	14.0	

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
398.0921	398.0923	-0.2	-0.5	13.5	1163.4	C18 H16 N5 O4 S

Figure 14c. HRMS of compound 9d.

3. Spectral data of series III:

3.1. Compound 10a

Figure 15a. ^{1}H NMR spectrum (400 MHz) of compound 10a in DMSO-d$_6$.
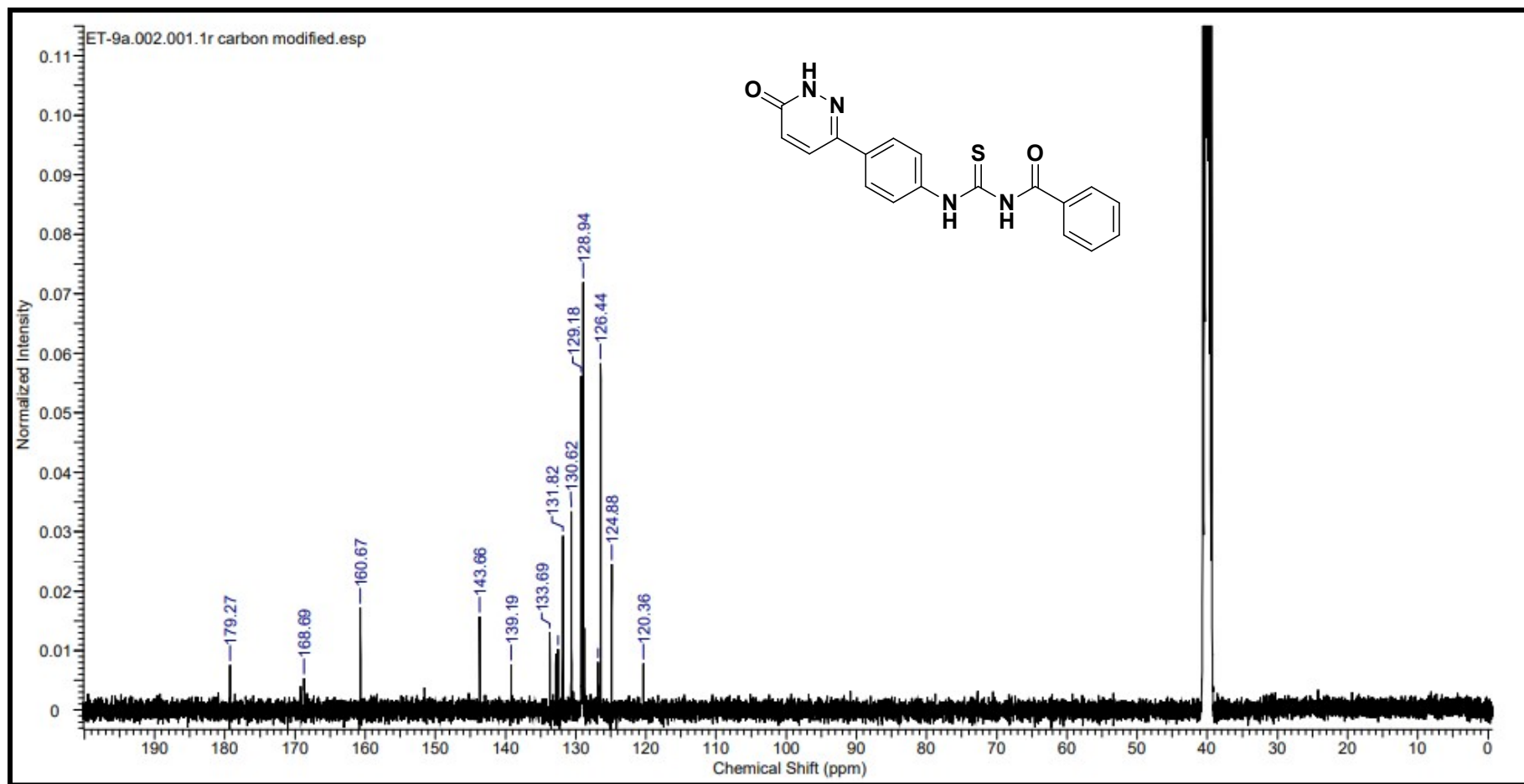
Figure 15b. ^{13}C NMR spectrum (100 MHz) of compound 10a in DMSO-d$_6$.

Figure 15c. HRMS of compound 10a.

3.2. Compound 10b

Figure 16a. ¹H NMR spectrum (400 MHz) of compound 10b in DMSO-d₆.

Figure 16b. ^{13}C NMR spectrum (100 MHz) of compound 10b in DMSO-d_6.

Figure 16c. HRMS of compound 10b.

3.3. Compound 10c

Figure 17a. ¹H NMR spectrum (400 MHz) of compound 10c in DMSO-d₆.

Figure 17b. ^{13}C NMR spectrum (100 MHz) of compound 10c in DMSO-d_6.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 20.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
637 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-40 H: 0-60 N: 0-5 O: 0-2 S: 0-1 79Br: 0-1 81Br: 0-1

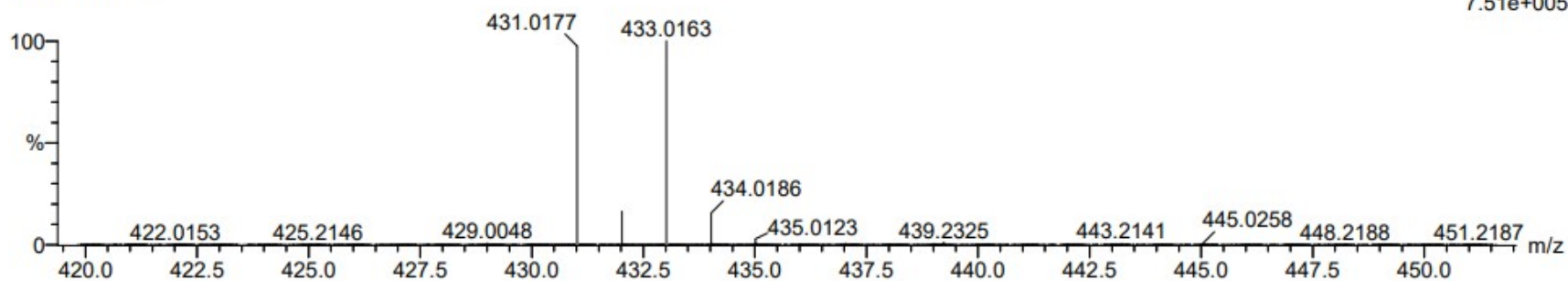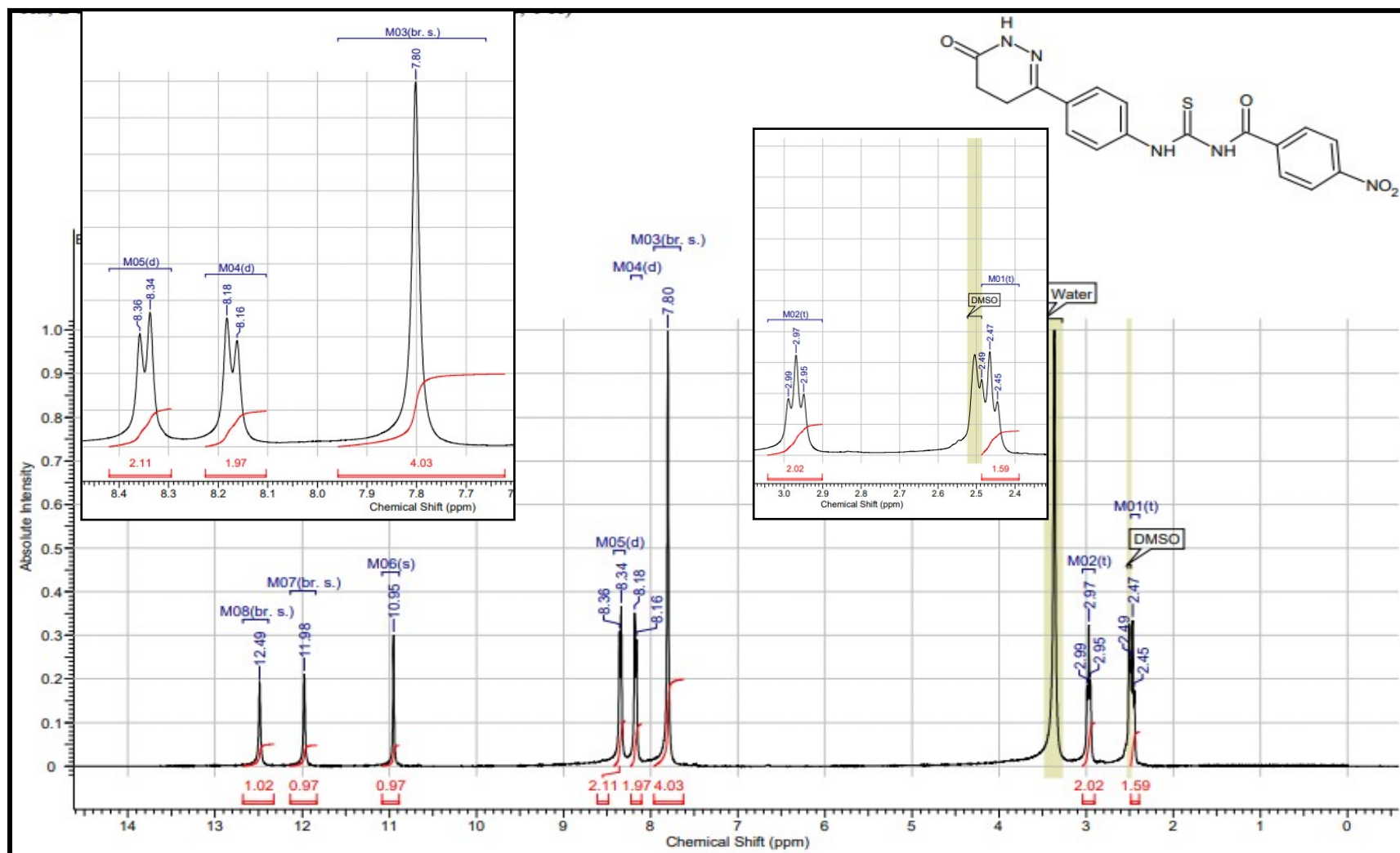ET-9c-HRESI/AJ   SYNAPTG2-Si#NotSet   21-Feb-2023
67548   14:58:49
0503 924 (1.829) Cm (912:928)
1: TOF MS ES+

                                                                                                       1.31e+005
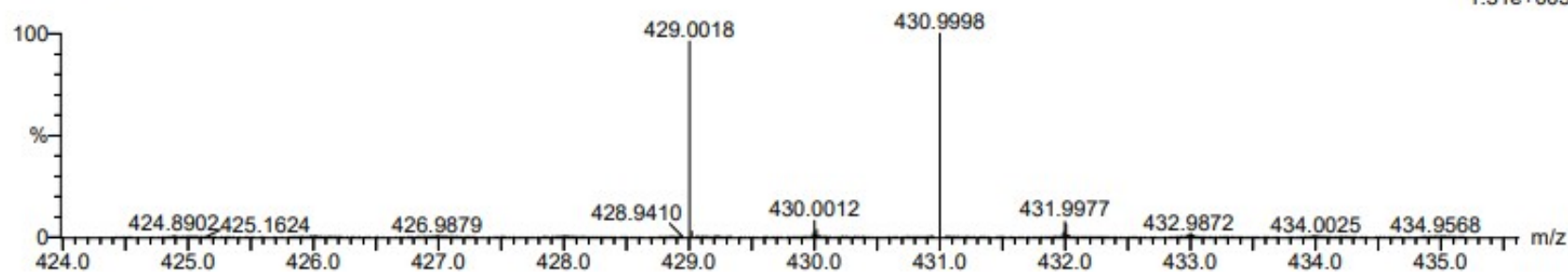
Minimum:			-1.5		
Maximum:		5.0	3.0	20.0	

| Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
429.0018	429.0021	-0.3	-0.7	13.5	1459.3	C18 H14 N4 O2 S 79Br

Figure 17c. HRMS of compound 10c.

3.4. Compound 10d
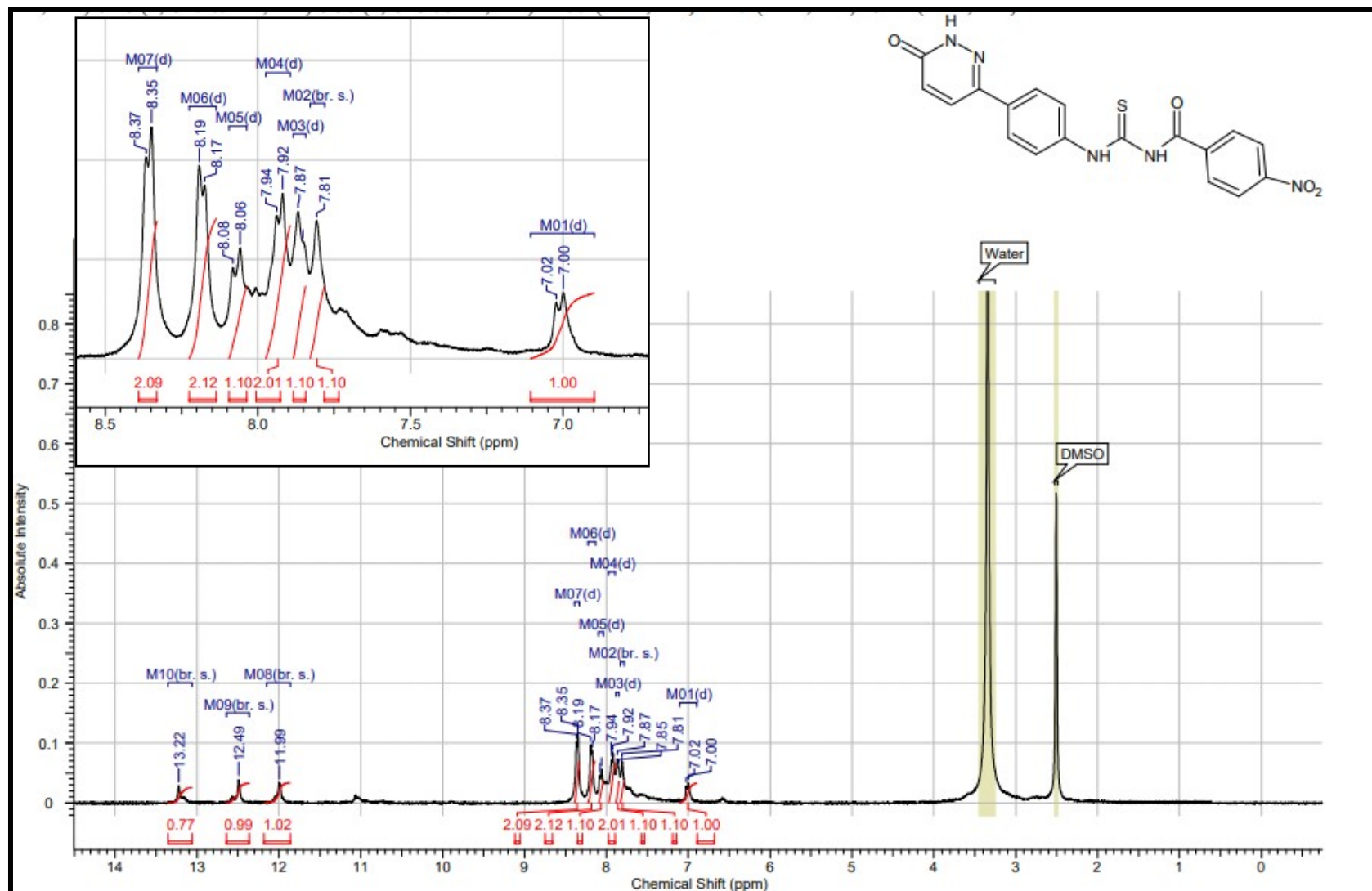
Figure 18a. ^{1}H NMR spectrum (400 MHz) of compound 10d in DMSO-d$_6$.

Figure 18b. ^{13}C NMR spectrum (100 MHz) of compound 10d in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 15.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
252 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
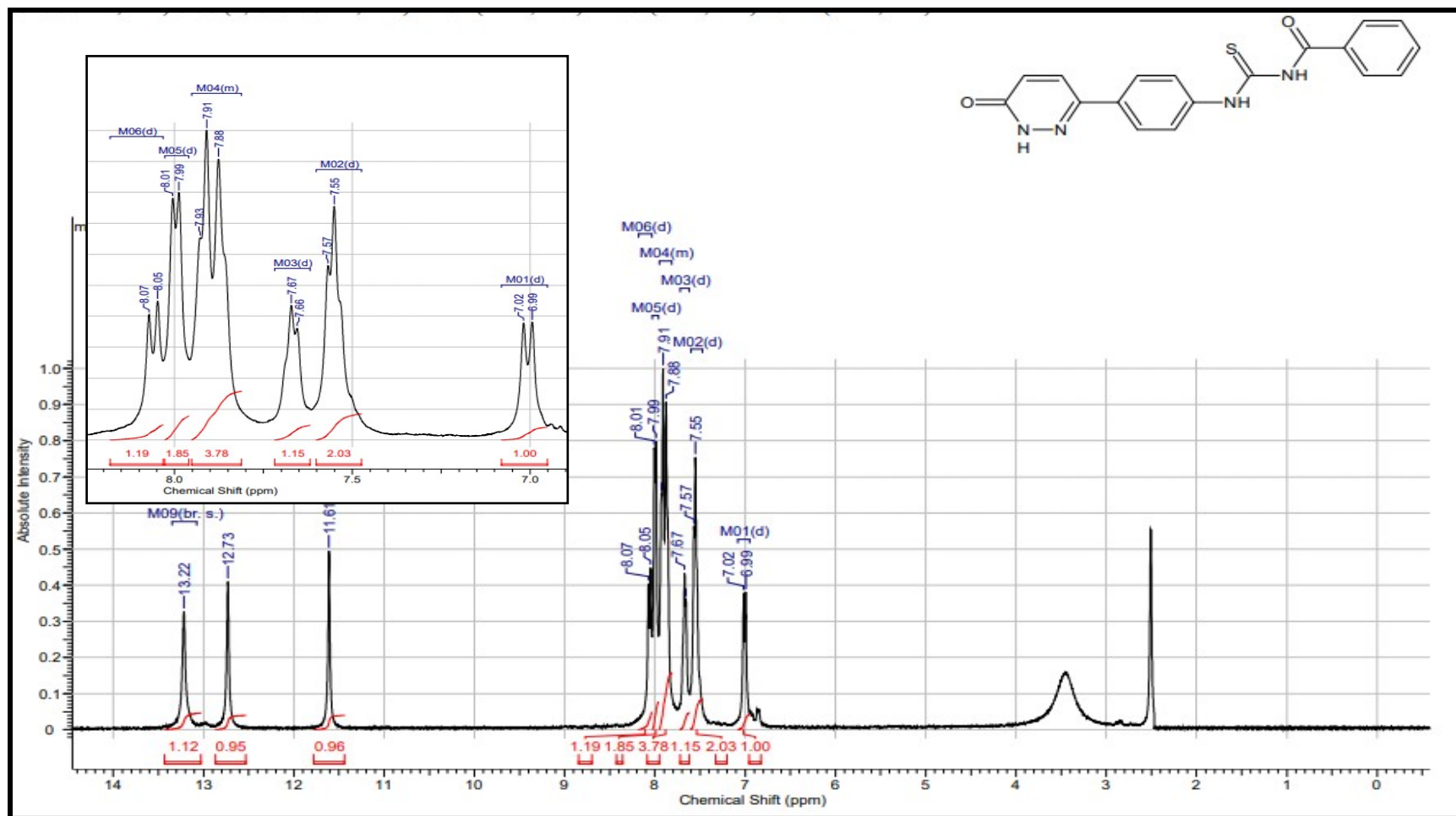Elements Used:
C: 0-40   H: 0-40   N: 0-5   O: 0-5   S: 0-1

ET-9d-HRESI/AJ   SYNAPTG2-Si#NotSet   22-Feb-2023
67549   13:02:32
0499 173 (0.360) Cm (165:285-87:110)
1: TOF MS ES+

2.38e+005
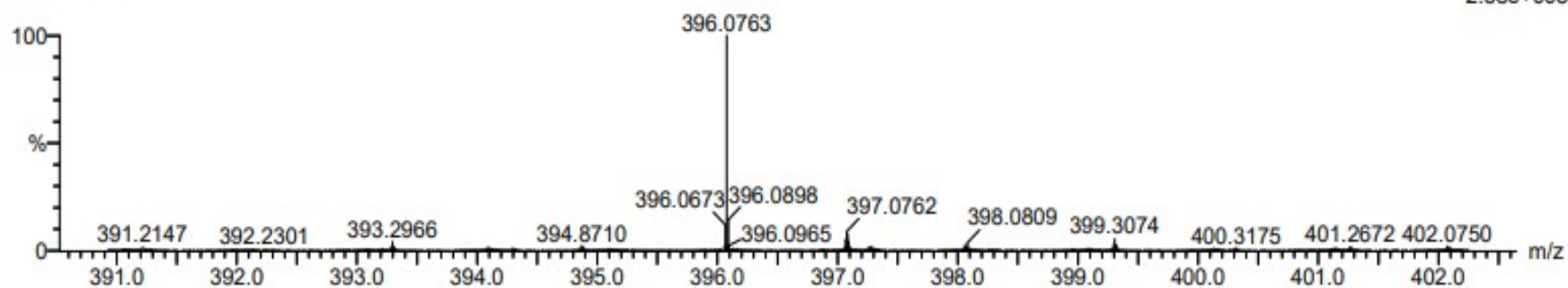
Minimum:			-1.5			
Maximum:	5.0	3.0	15.0			

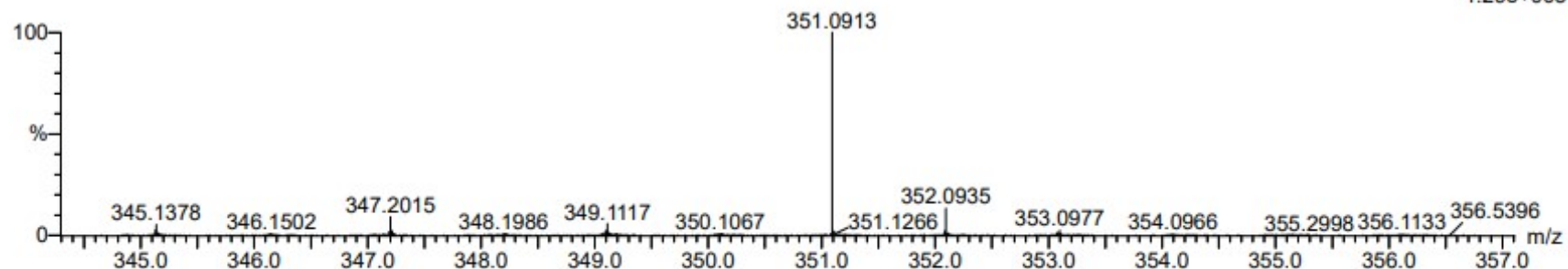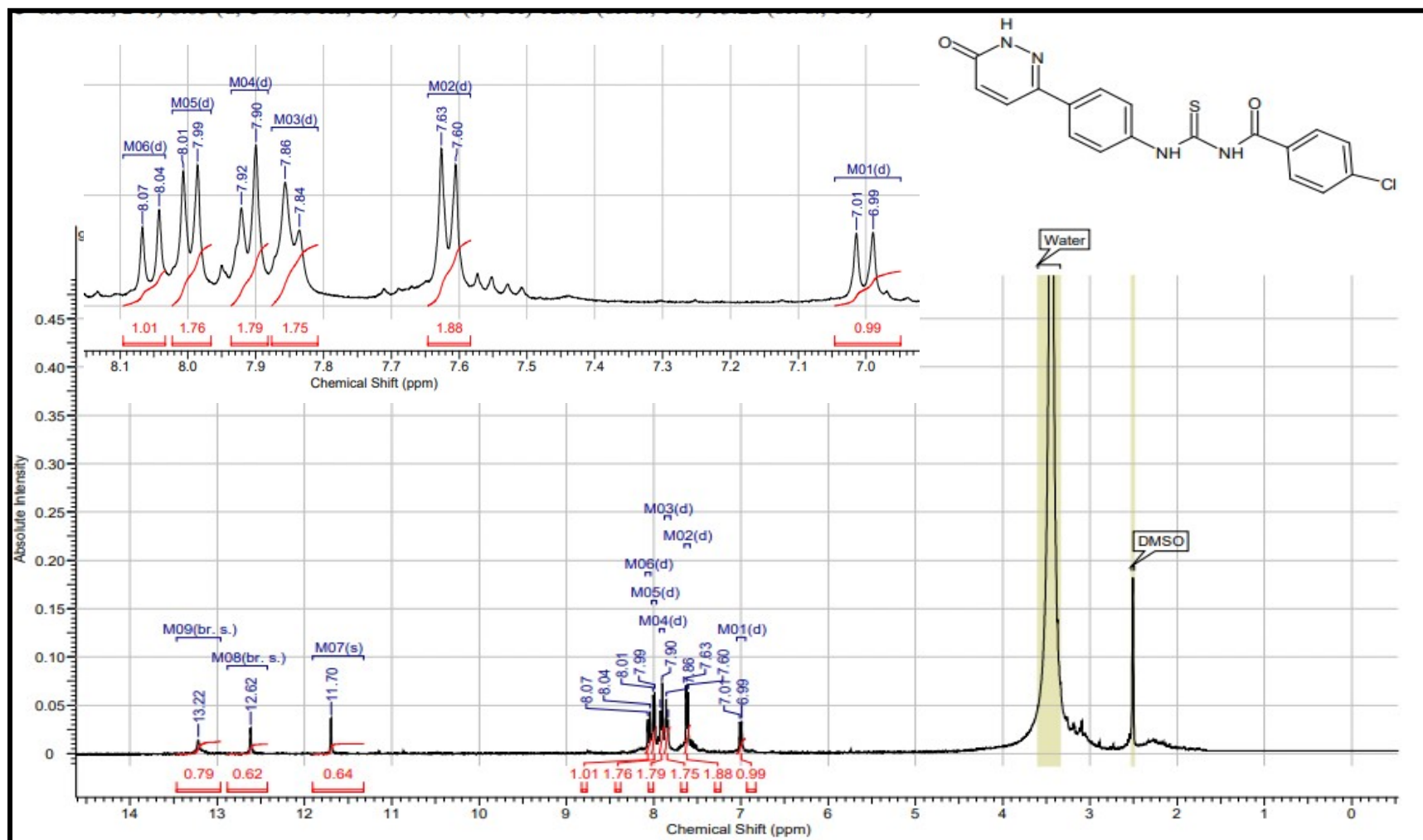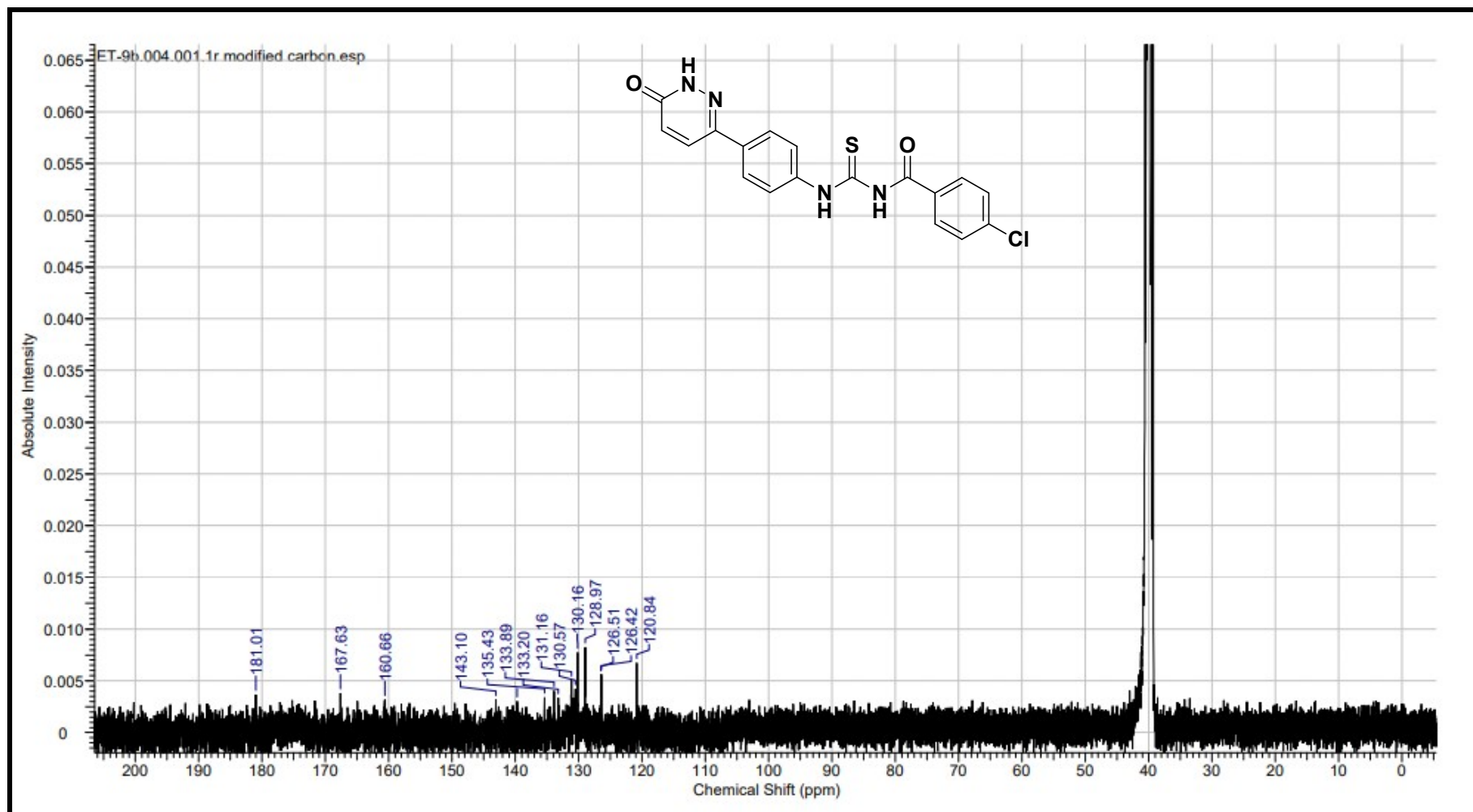| Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
396.0763	396.0766	-0.3	-0.8	14.5	2718.3	C18 H14 N5 O4 S

Figure 18c. HRMS of compound 10d.

3.5. Compound 10e
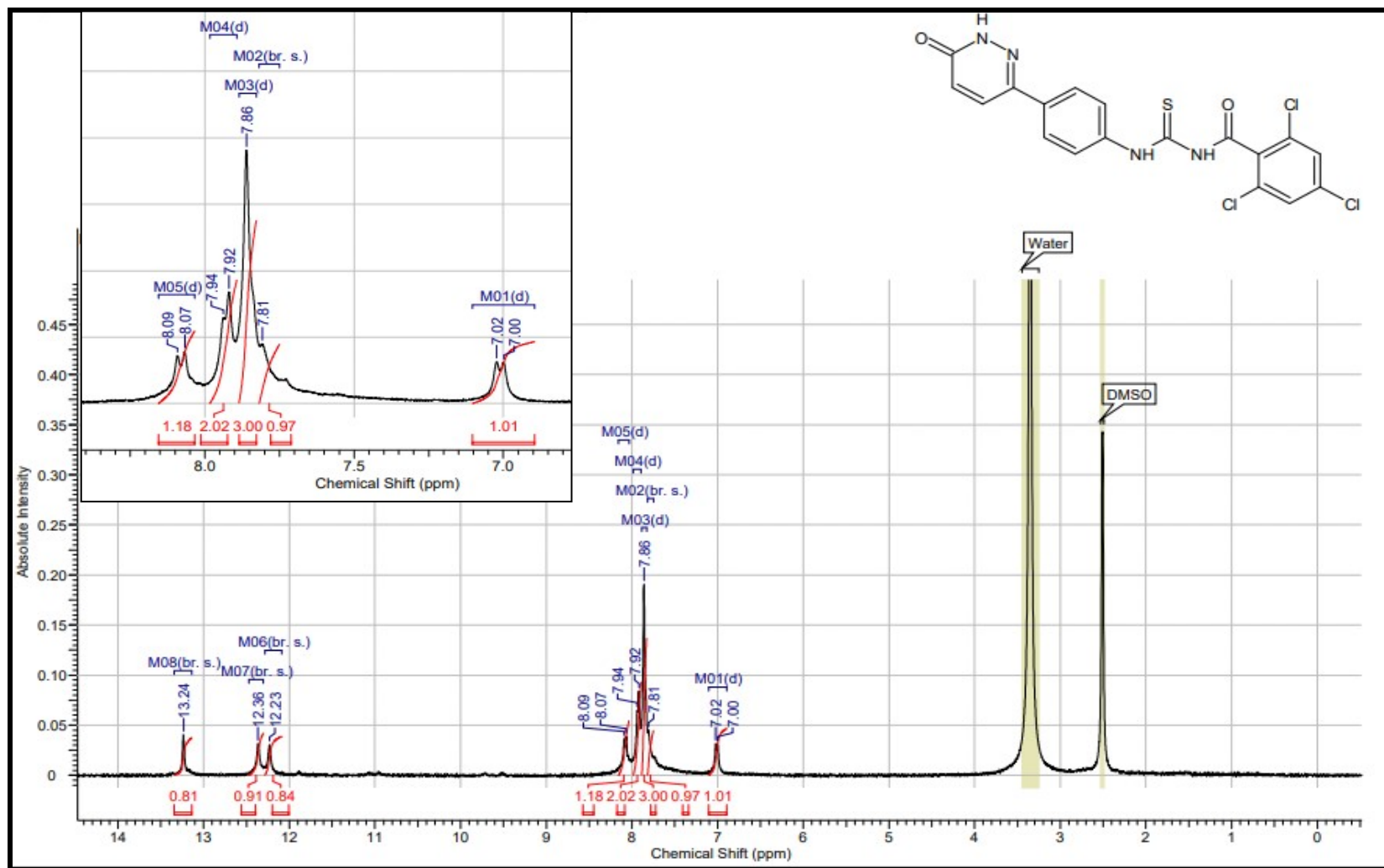
Figure 19a. ^{1}H NMR spectrum (400 MHz) of compound 10e in DMSO-d$_6$.

Figure 19b. ^{13}C NMR spectrum (100 MHz) of compound 10e in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 14.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
659 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-30   H: 0-16   N: 0-4   O: 0-2   S: 0-1   35Cl: 0-3   37Cl: 0-3

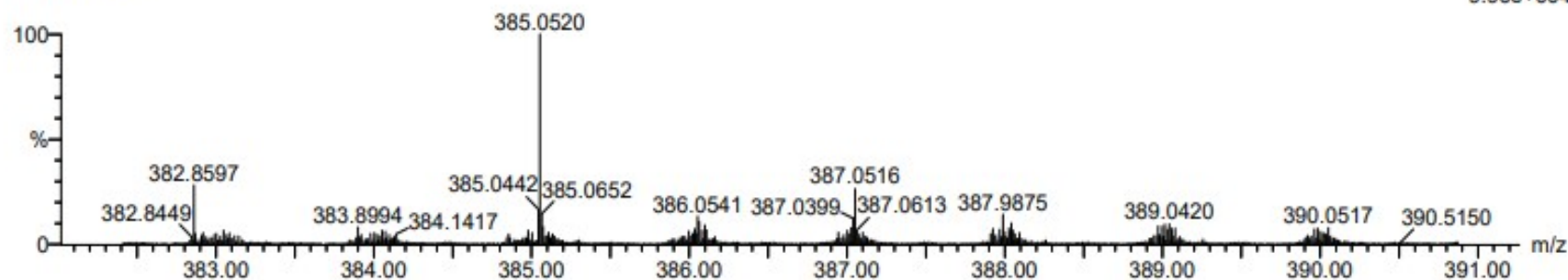ET-9e-HRESI/AJ   SYNAPTG2-Si#NotSet   21-Feb-2023
67550   15:57:37
0500C 389 (0.781) Cm (372:428)
1: TOF MS ES+

5.54e+005
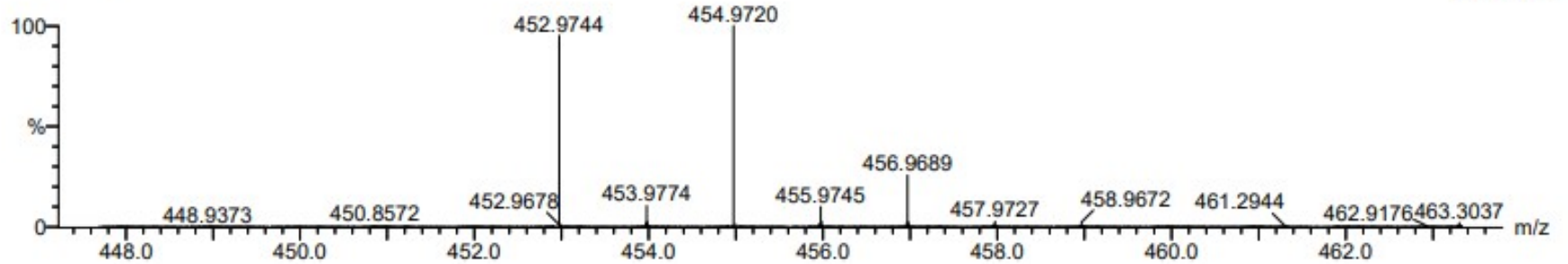
Minimum:			-1.5			
Maximum:		5.0	3.0	14.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
452.9744	452.9747	-0.3	-0.7	13.5	2845.0	C18 H12 N4 O2 S 35Cl3

Figure 19c. HRMS of compound 10e.

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3.6. Compound 10f

Figure 20a. ¹H NMR spectrum (400 MHz) of compound 10f in DMSO-d$_6$.

Figure 20b. ^{13}C NMR spectrum (100 MHz) of compound 10f in DMSO-d$_6$.
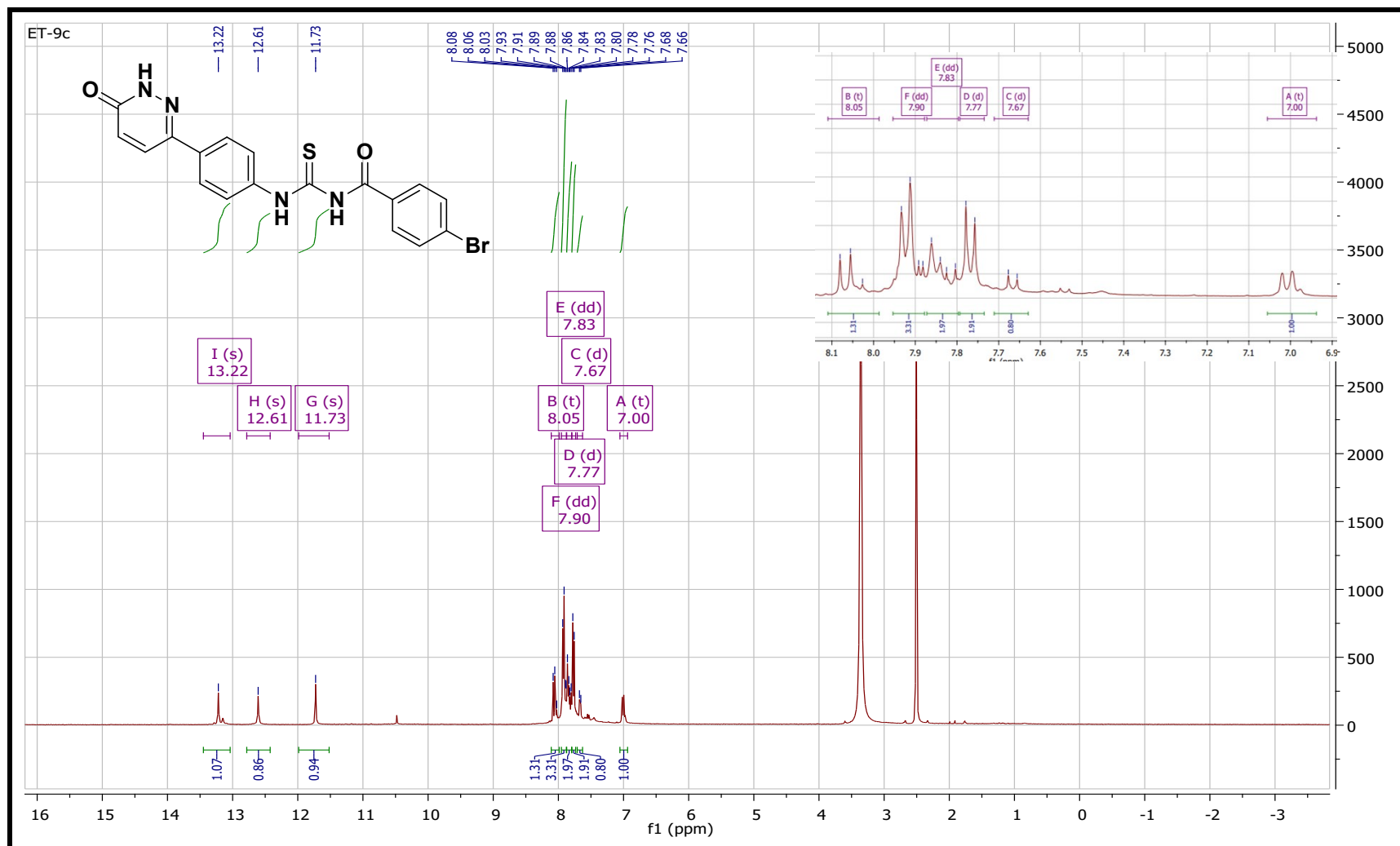
Figure 20c. HRMS of compound 10f.

3.7. Compound 10g

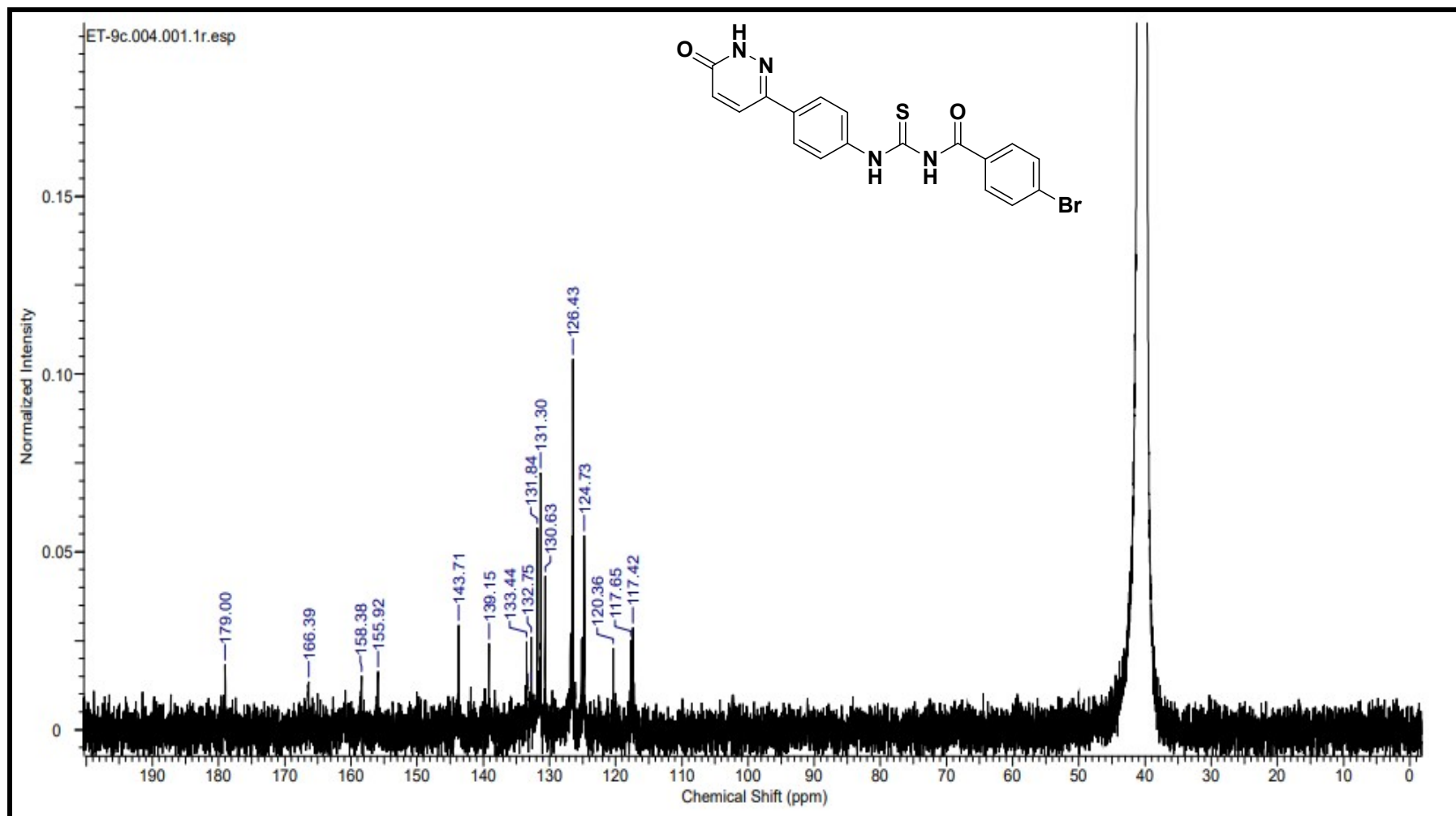**Figure 21a. ¹H NMR spectrum (400 MHz) of compound 10g in DMSO-d₆.**

Figure 21b. ^{13}C NMR spectrum (100 MHz) of compound 10g in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 15.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
384 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-30 H: 0-30 N: 0-5 O: 0-5 F: 0-1 S: 0-1

ET-9g-HRESI/AJ   SYNAPTG2-Si#NotSet   21-Feb-2023
67552   15:35:47
0506 1429 (2.852) Cm (1426:1446)
1: TOF MS ES+
2.93e+005
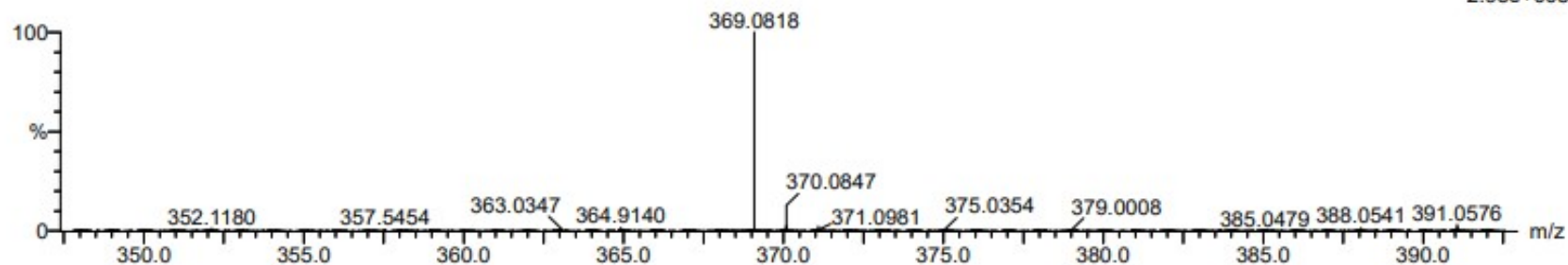
Minimum:			-1.5			
Maximum:	5.0	3.0	15.0			

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
369.0818	369.0821	-0.3	-0.8	13.5	1405.0	C18 H14 N4 O2 F S

Figure 21c. HRMS of compound 10g.

3.8. Compound 10h

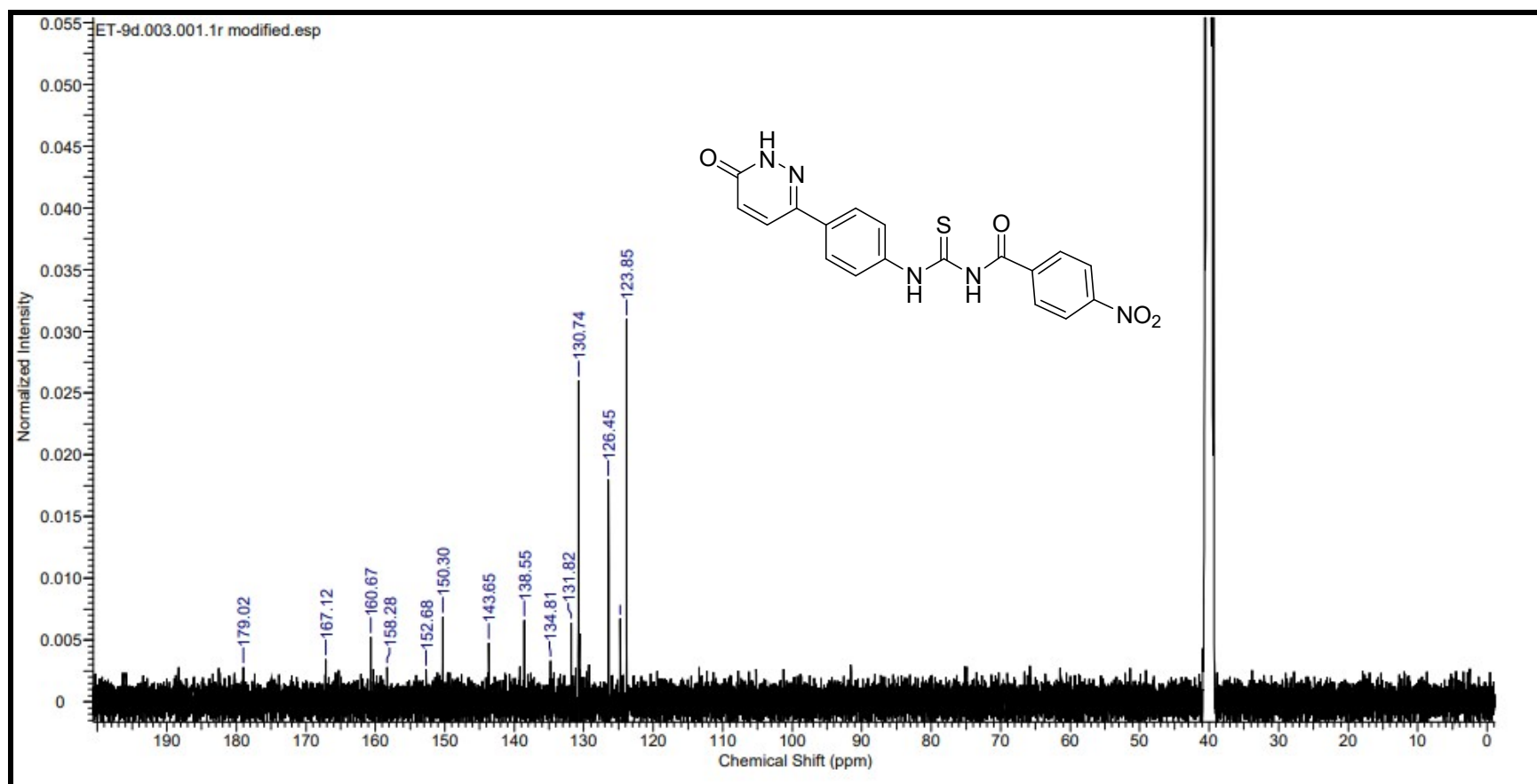

Figure 22a. ¹H NMR spectrum (400 MHz) of compound 10h in DMSO-d₆.

Figure 22b. ^{13}C NMR spectrum (100 MHz) of compound 10h in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 14.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
503 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-30   H: 0-20   N: 0-5   O: 0-5   S: 0-1   79Br: 0-1   81Br: 0-1

ET-9h-HRESI/AJ   SYNAPTG2-Si#NotSet   21-Feb-2023
67553   15:50:12
0508A 220 (0.450) Cm (213:230)
1: TOF MS ES+
   4.05e+004
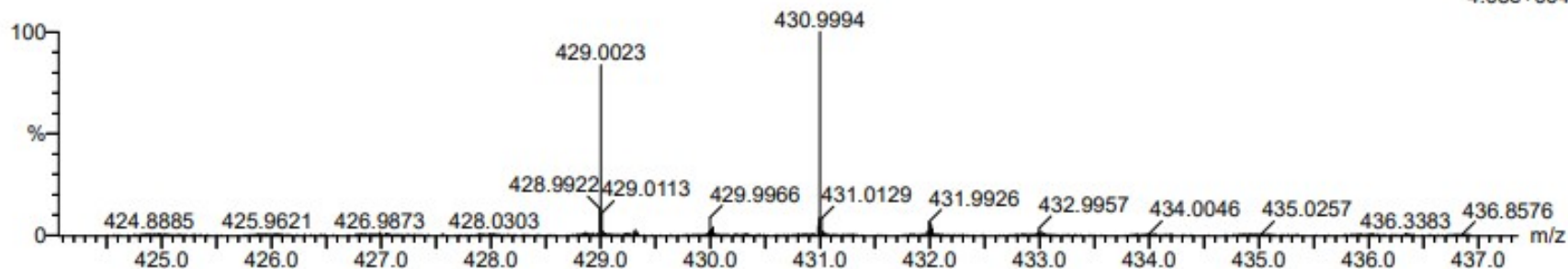
Minimum: -1.5
Maximum: 5.0   3.0   14.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
429.0023	429.0021	0.2	0.5	13.5	1469.3	C18 H14 N4 O2 S 79Br

Figure 22c. HRMS of compound 10h.
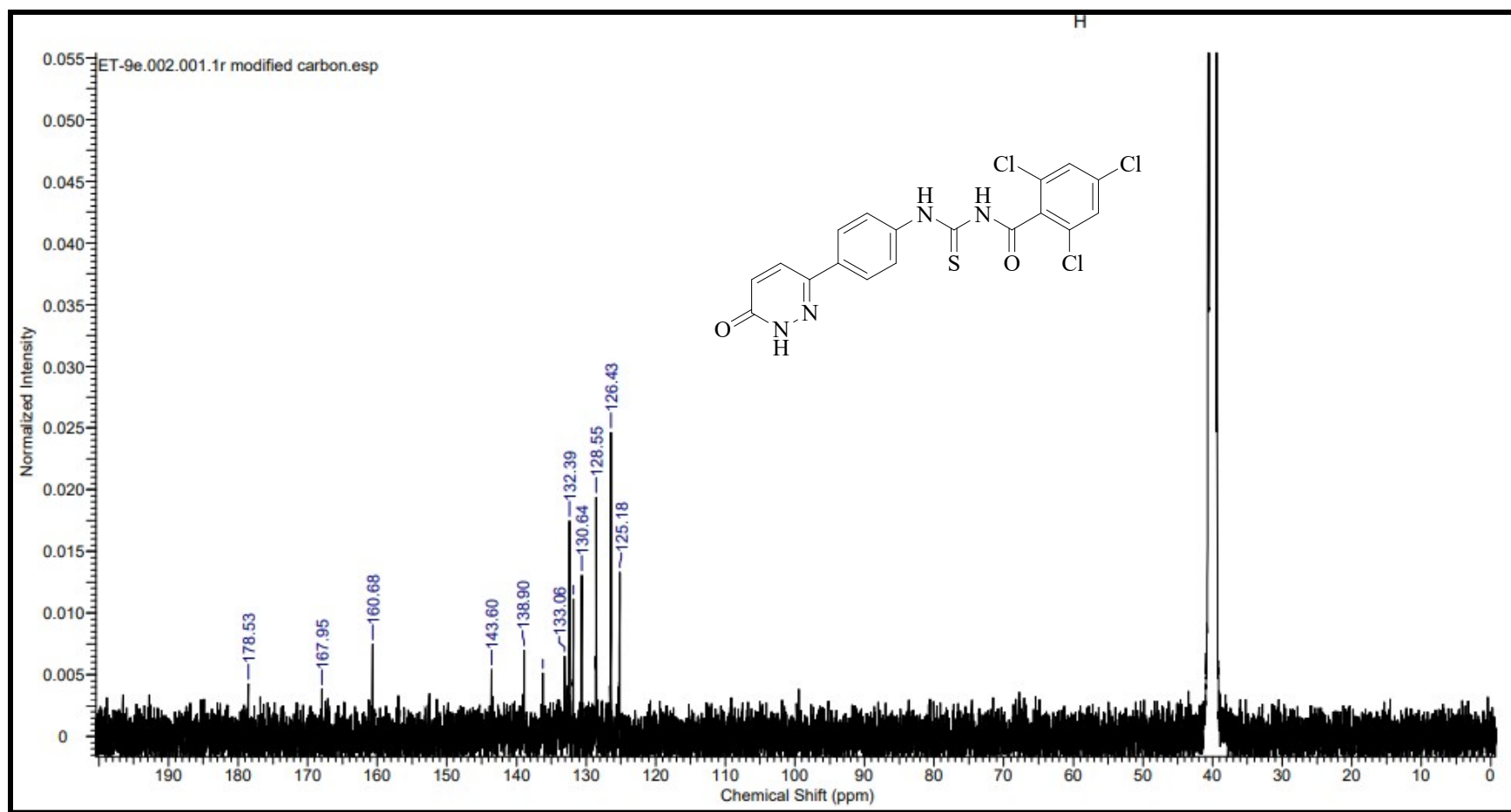
3.9. Compound 10i
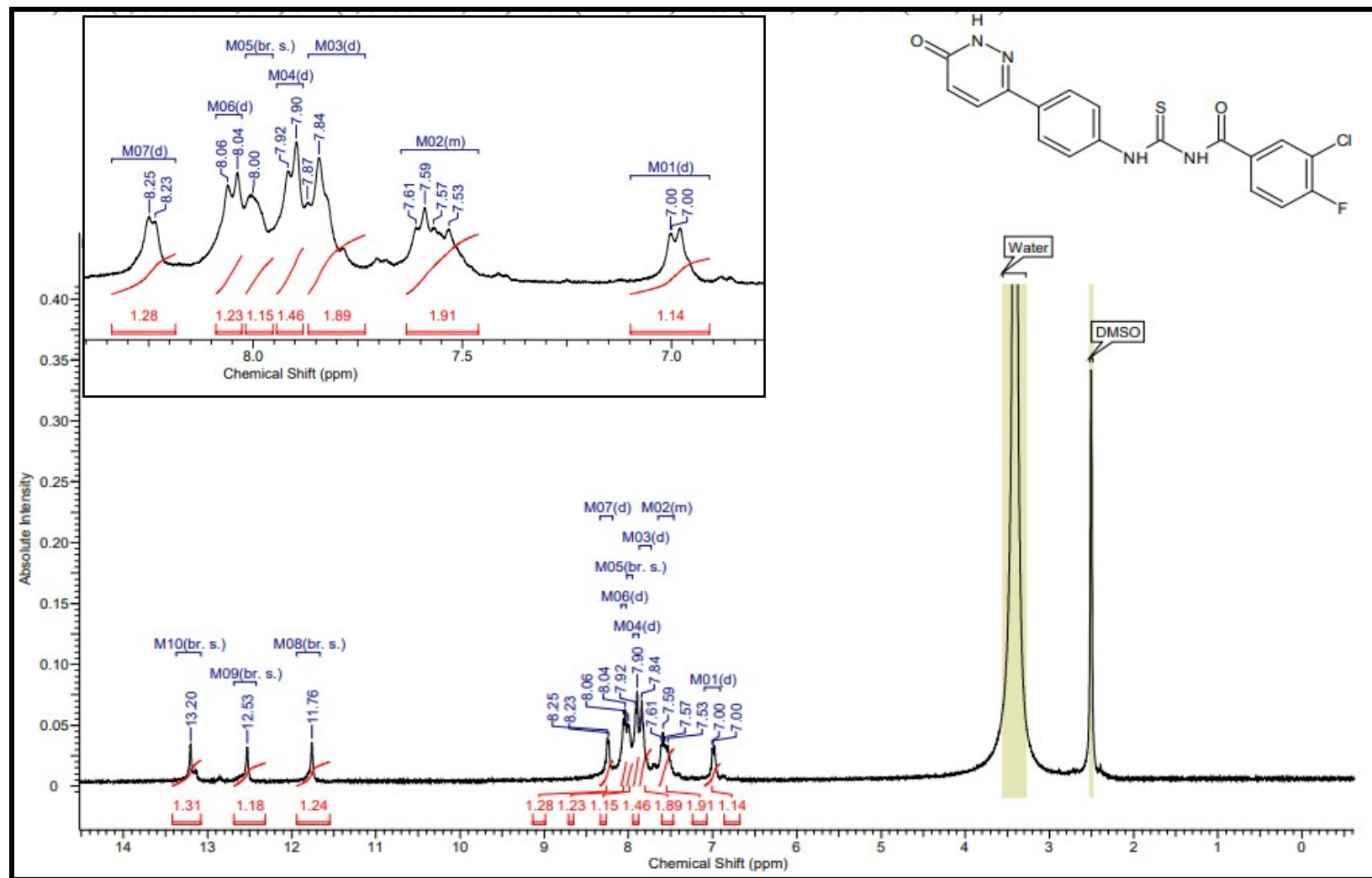
Figure 23a. ¹H NMR spectrum (400 MHz) of compound 10i in DMSO-d₆.
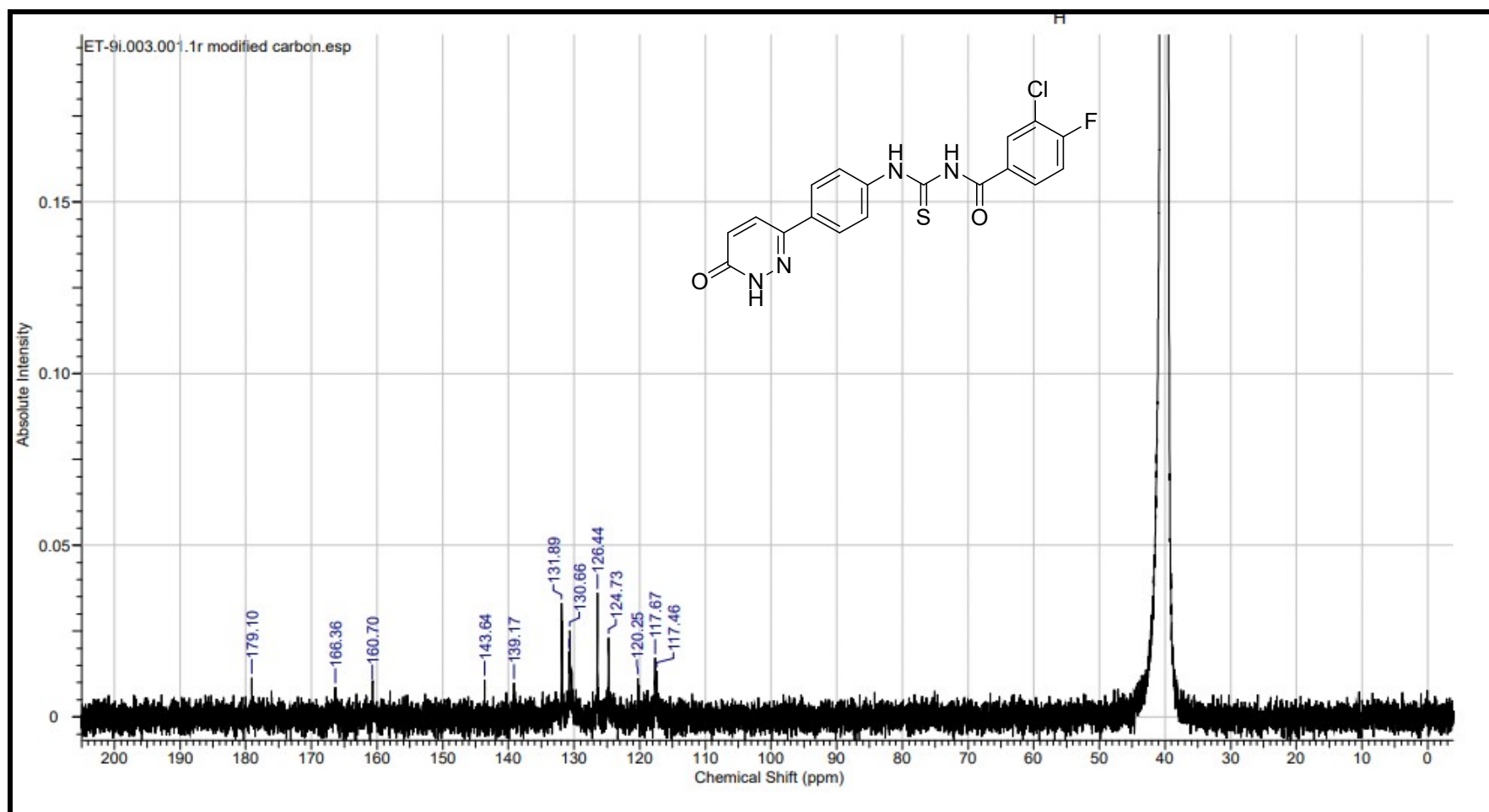
Figure 23b. ^{13}C NMR spectrum (100 MHz) of compound 10i in DMSO-d_6.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 14.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
516 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-30   H: 0-20   N: 0-5   O: 0-2   S: 0-1   F: 0-1   35Cl: 0-1   37Cl: 0-1

ET-9i-HRESI/AJ   SYNAPTG2-Si#NotSet   22-Feb-2023
67554   11:17:04
0511 689 (1.372) Cm (664:696)
1: TOF MS ES+
                                                                                                9.04e+005
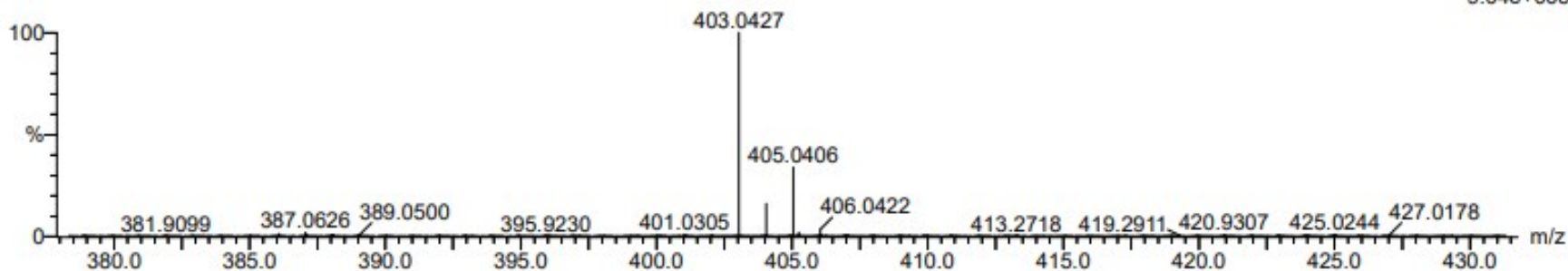
Minimum:			-1.5			
Maximum:		5.0	3.0	14.0		

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
403.0427	403.0432	-0.5	-1.2	13.5	2251.1	C18 H13 N4 O2 S F 35Cl

Figure 23c. HRMS of compound 10i.

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3.10. Compound 10j

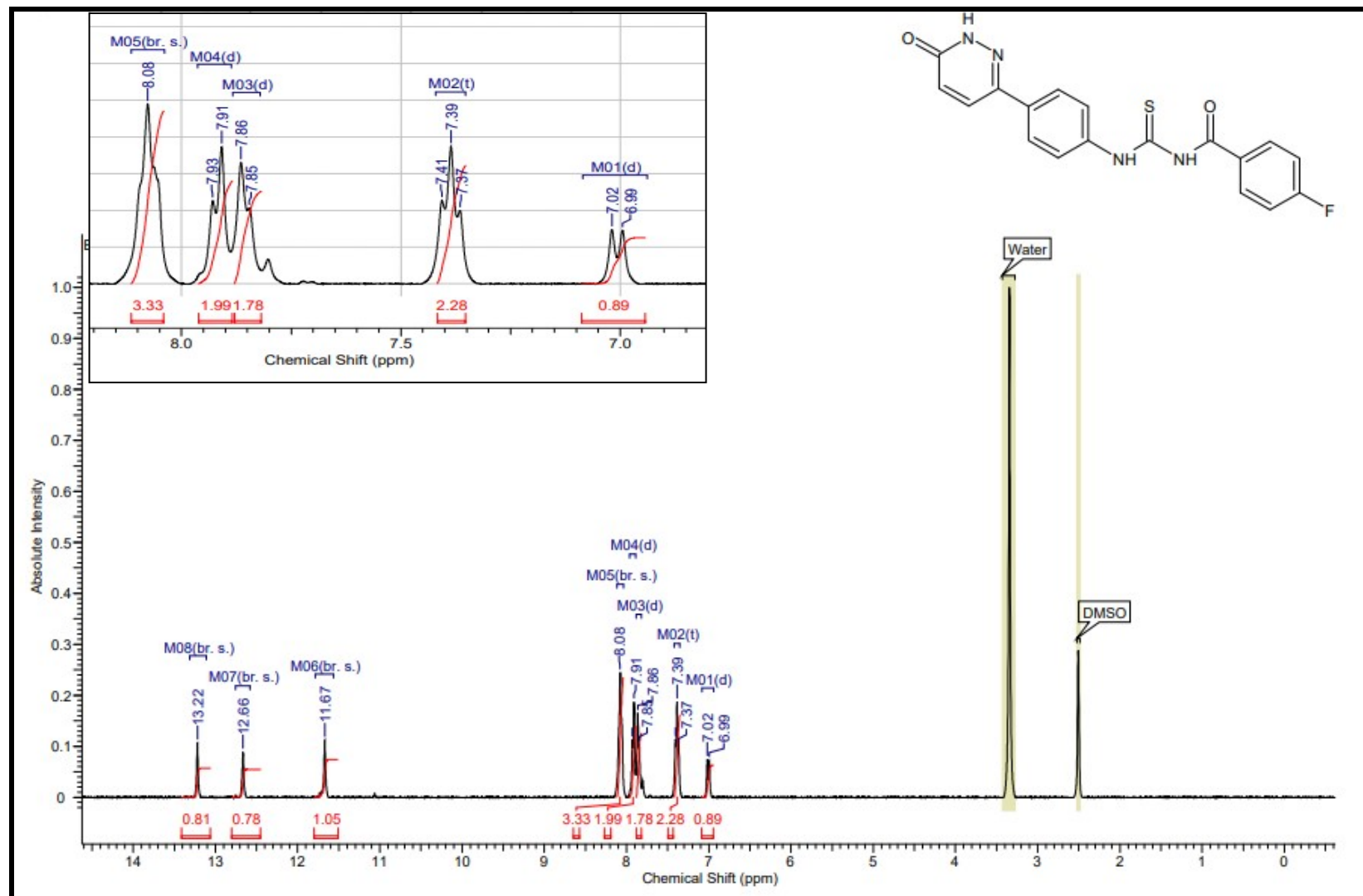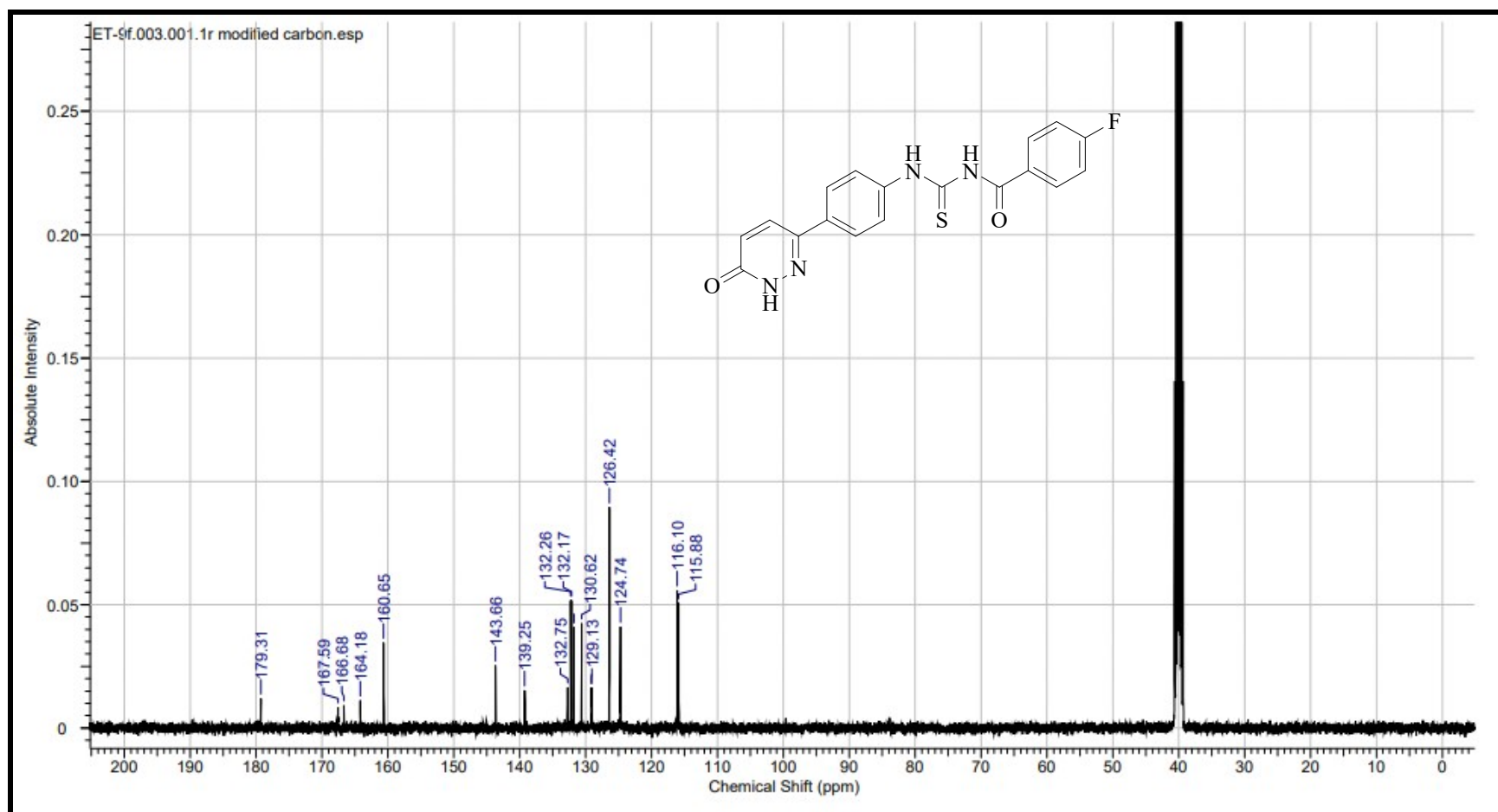**Figure 24a.** ¹H NMR spectrum (400 MHz) of compound 10j in DMSO-d₆.

Figure 24b. ^{13}C NMR spectrum (100 MHz) of compound 10j in DMSO-d_6.

Figure 24c. HRMS of compound 10j.

3.11. Compound 10k
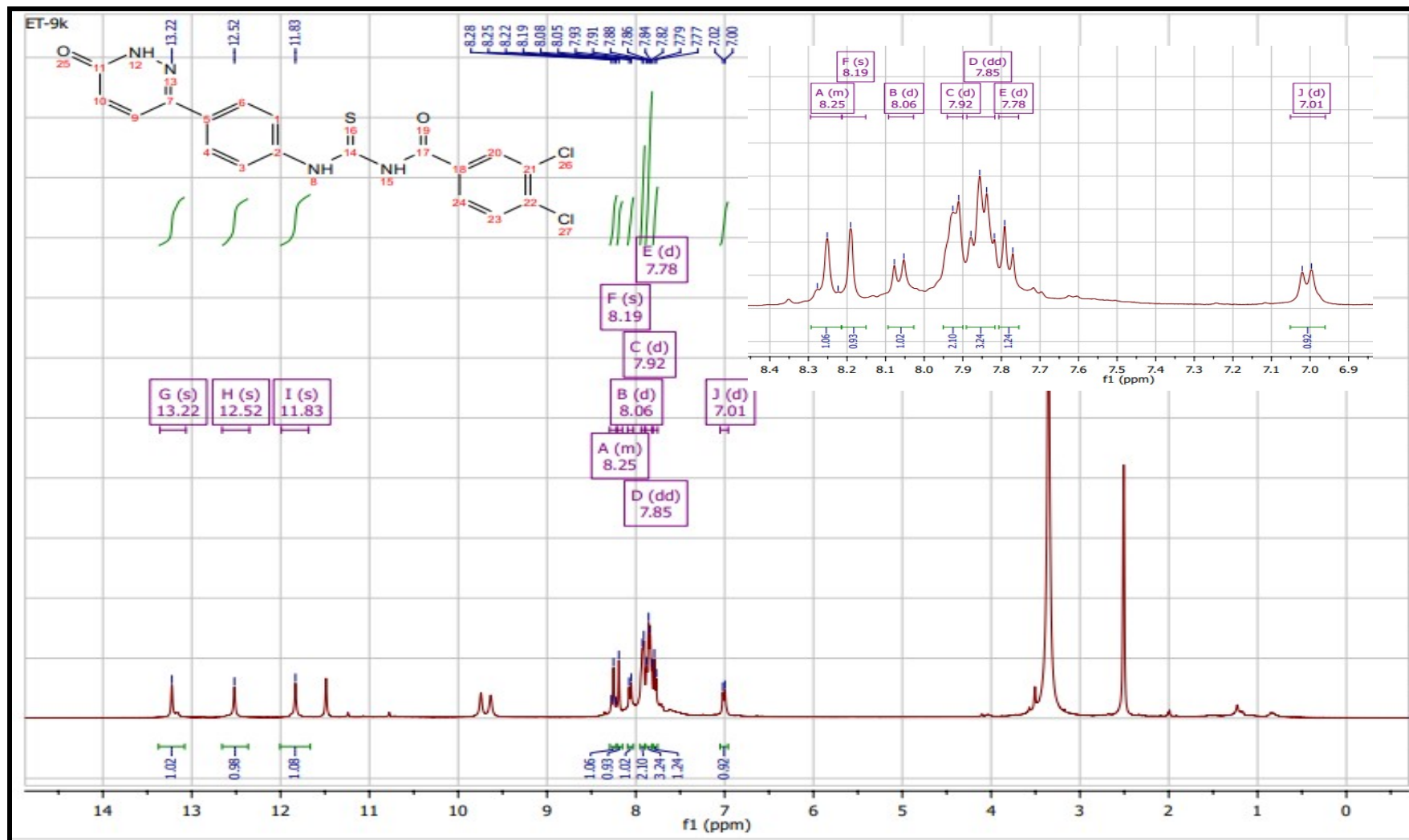
Figure 25a. ^{1}H NMR spectrum (400 MHz) of compound 10k in DMSO-d$_6$.
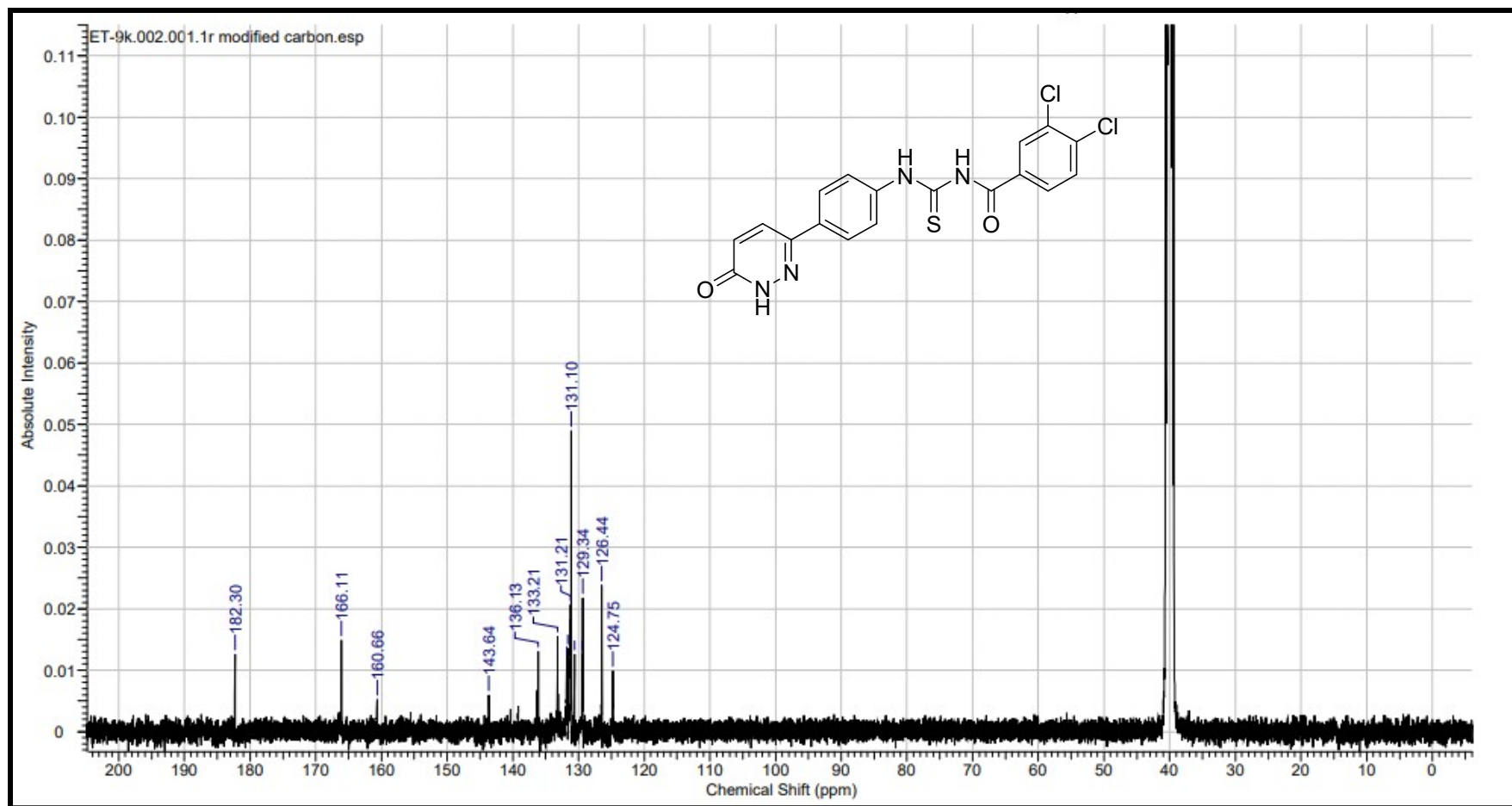
Figure 25b. ^{13}C NMR spectrum (100 MHz) of compound 10k in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 14.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
195 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
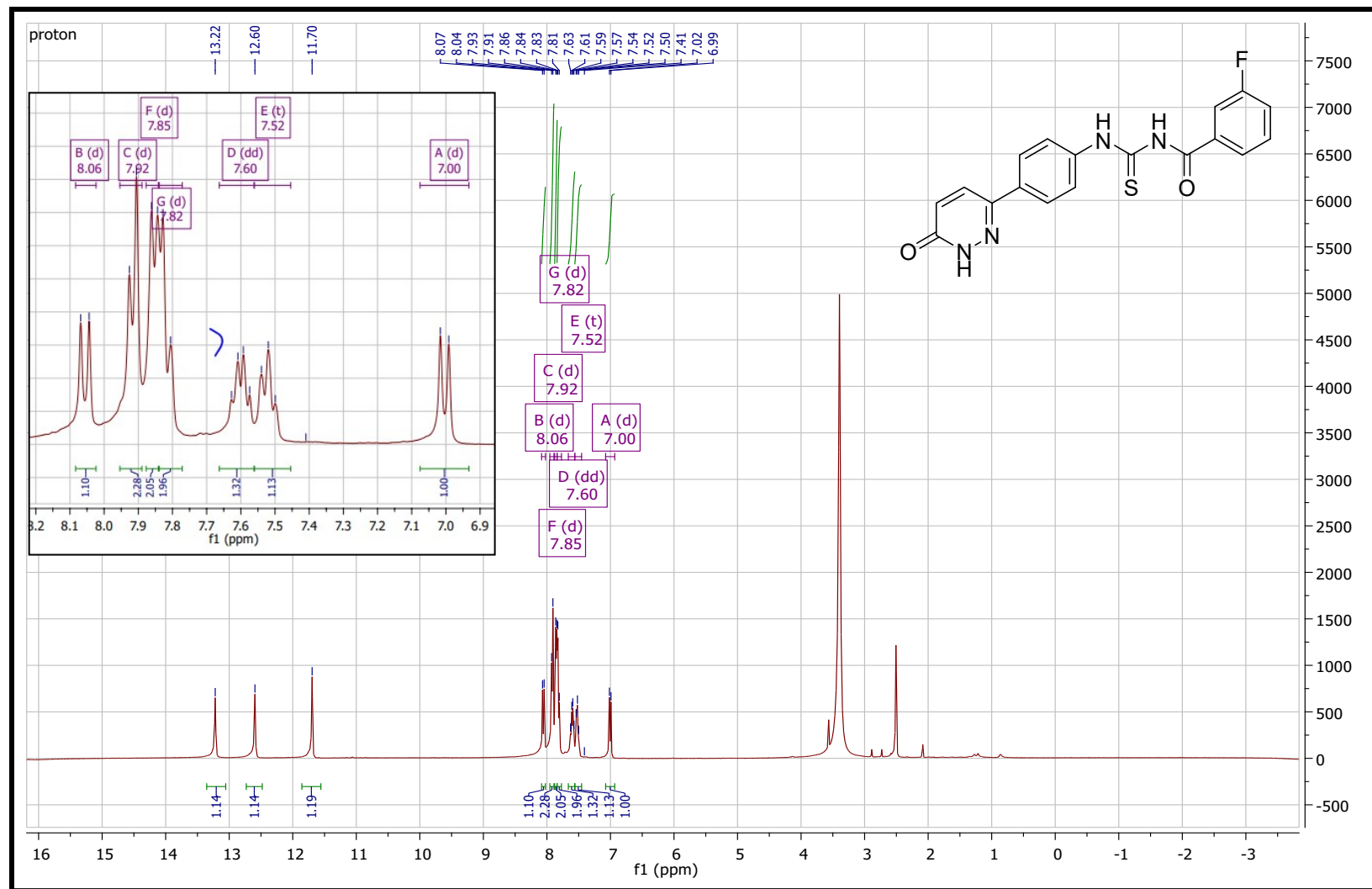C: 0-30   H: 0-20   N: 3-5   O: 0-2   S: 0-1   35Cl: 0-2   37Cl: 0-1

ET-9K/AJ
67556
0562A 1291 (2.552) Cm (1242:1346)
1: TOF MS ES+

SYNAPTG2-Si#NotSet

27-Feb-2023
11:14:44

4.44e+006
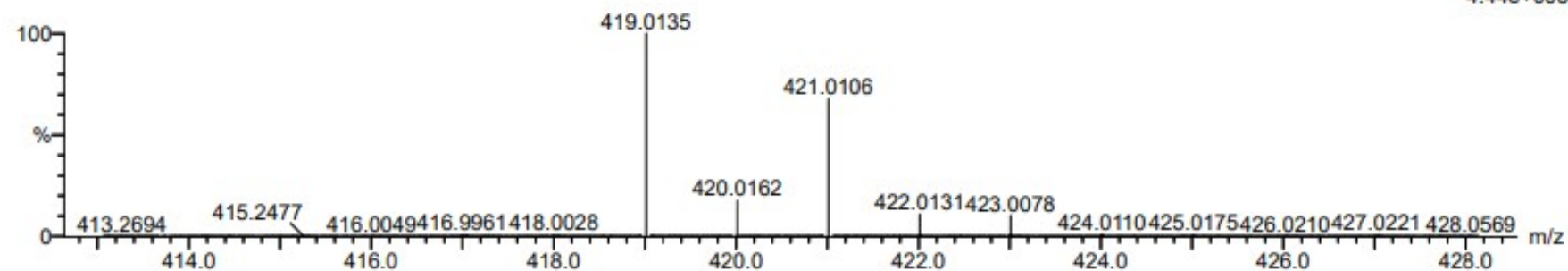
Minimum:			-1.5			
Maximum:	5.0	3.0	14.0			

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
419.0135	419.0136	-0.1	-0.2	13.5	3260.7	C18 H13 N4 O2 S 35Cl2

Figure 25c. HRMS of compound 10k.

75
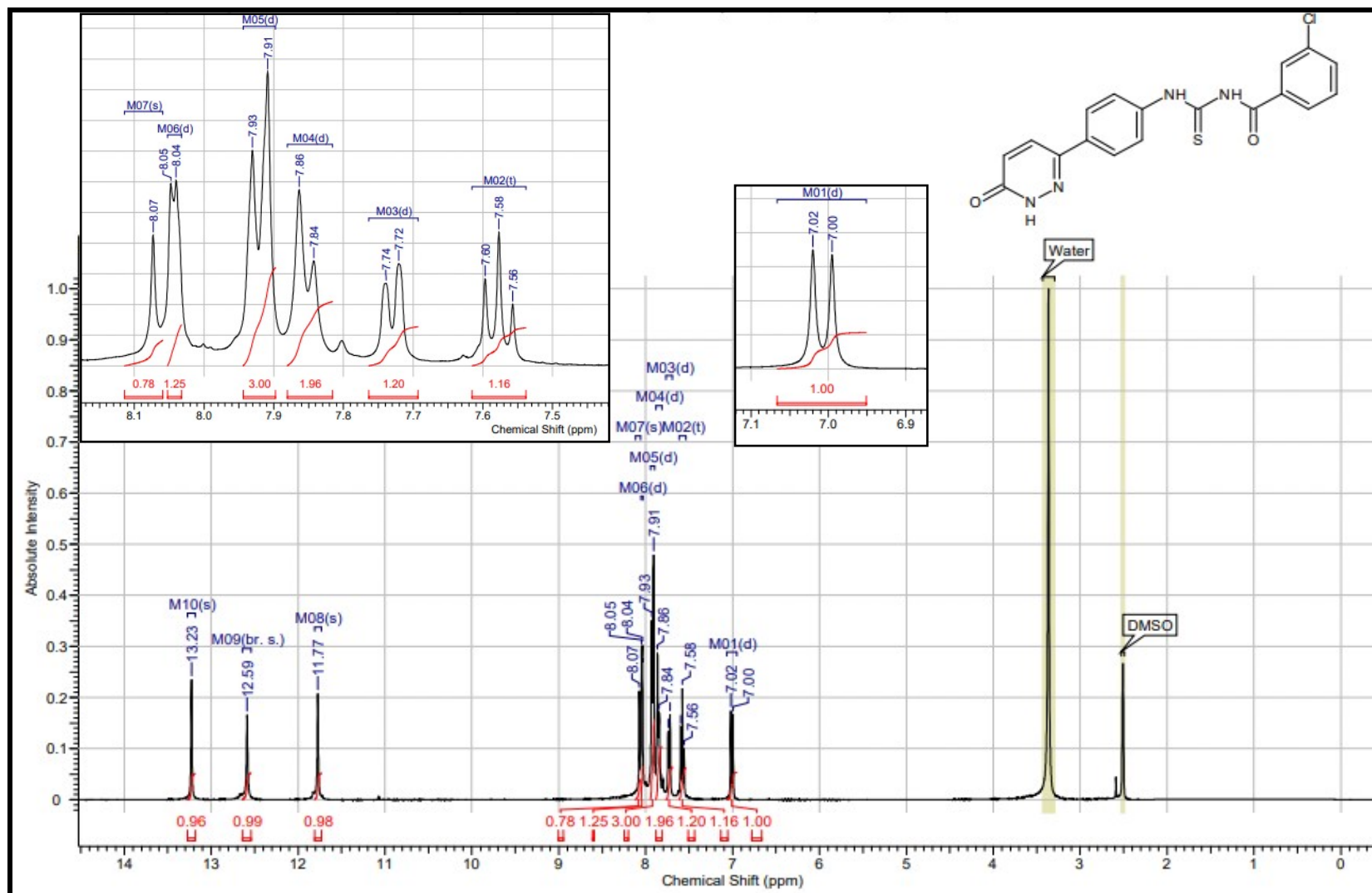
3.12.   Compound 10l
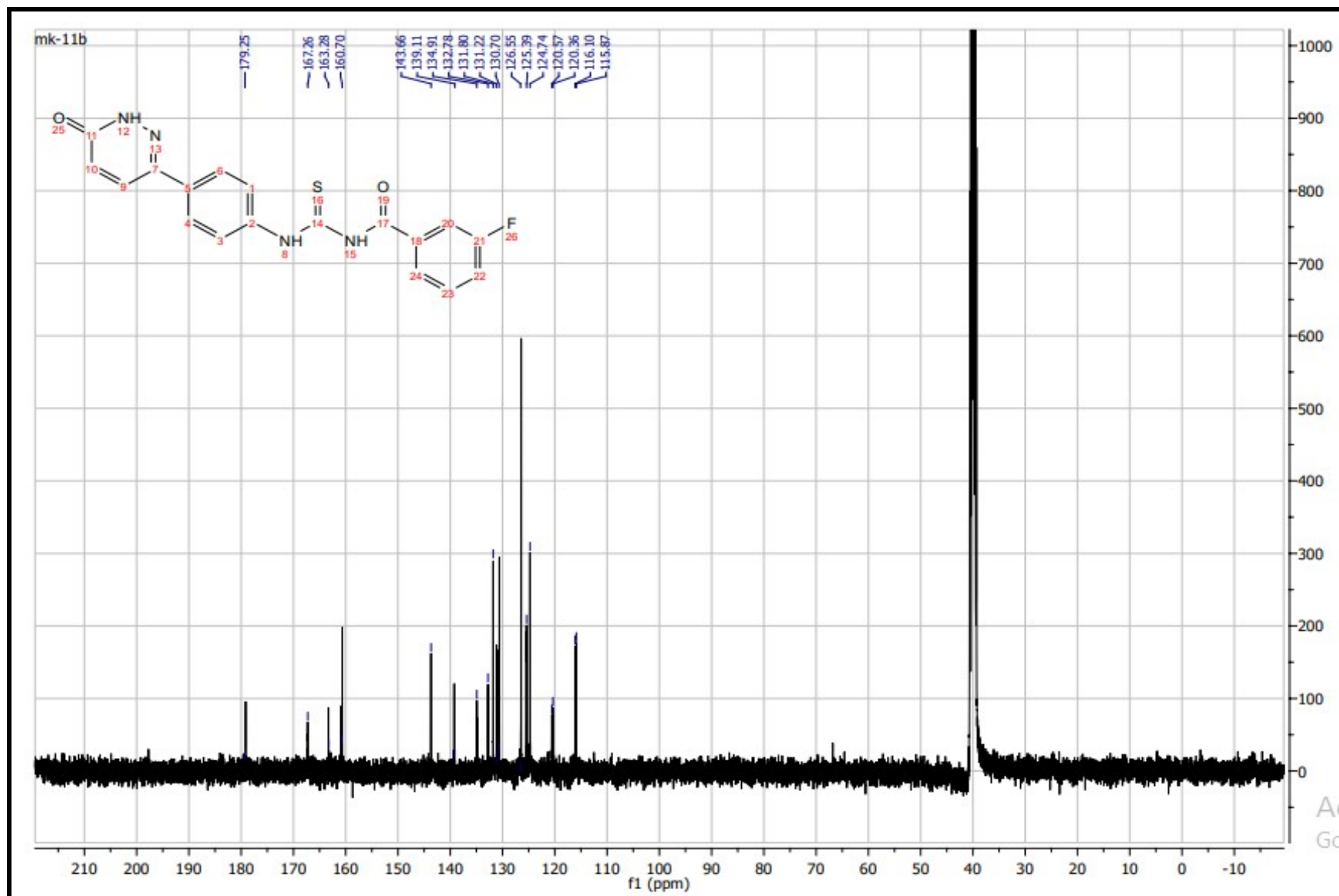

Figure 26a. ¹H NMR spectrum (400 MHz) of compound 10l in DMSO-d₆.
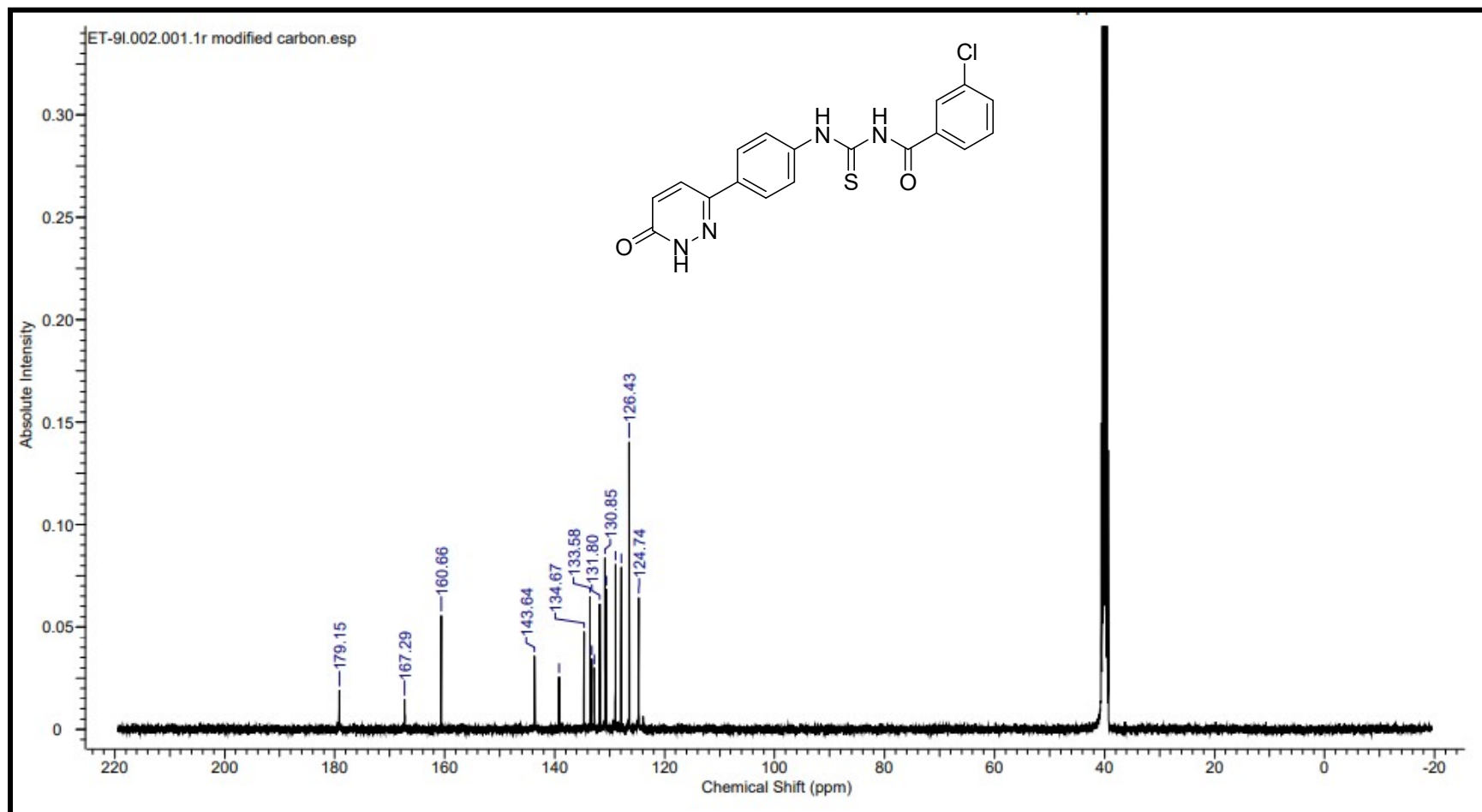
Figure 26b. ^{13}C NMR spectrum (100 MHz) of compound 10l in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 14.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
298 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-30   H: 0-20   N: 3-5   O: 0-2   S: 0-1   35Cl: 0-2   37Cl: 0-2

ET-9M/AJ
67558
0564A 1378 (2.723) Cm (1351:1378)
1: TOF MS ES+

SYNAPTG2-Si#NotSet

27-Feb-2023
15:23:41

2.56e+005
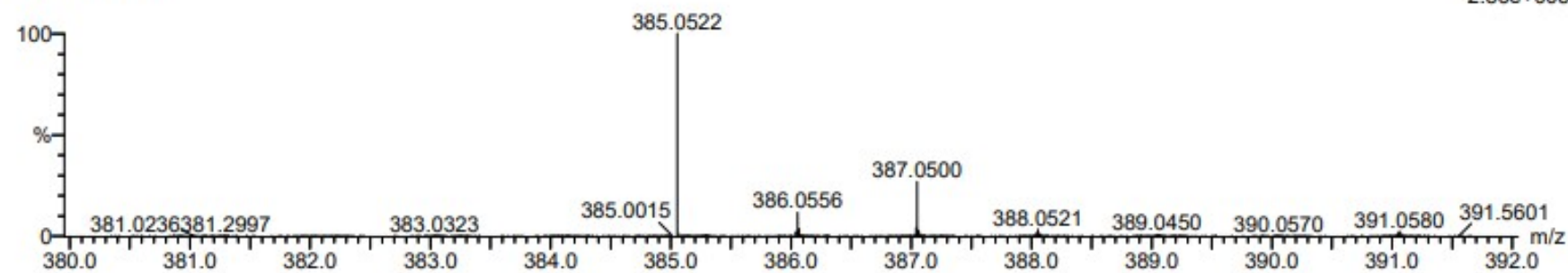
Minimum:				-1.5		
Maximum:		5.0	3.0	14.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
385.0522	385.0526	-0.4	-1.0	13.5	1466.3	C18 H14 N4 O2 S 35Cl

Figure 26c. HRMS of compound 10l.

4. Spectral data of series IV

4.1. Compound 11a
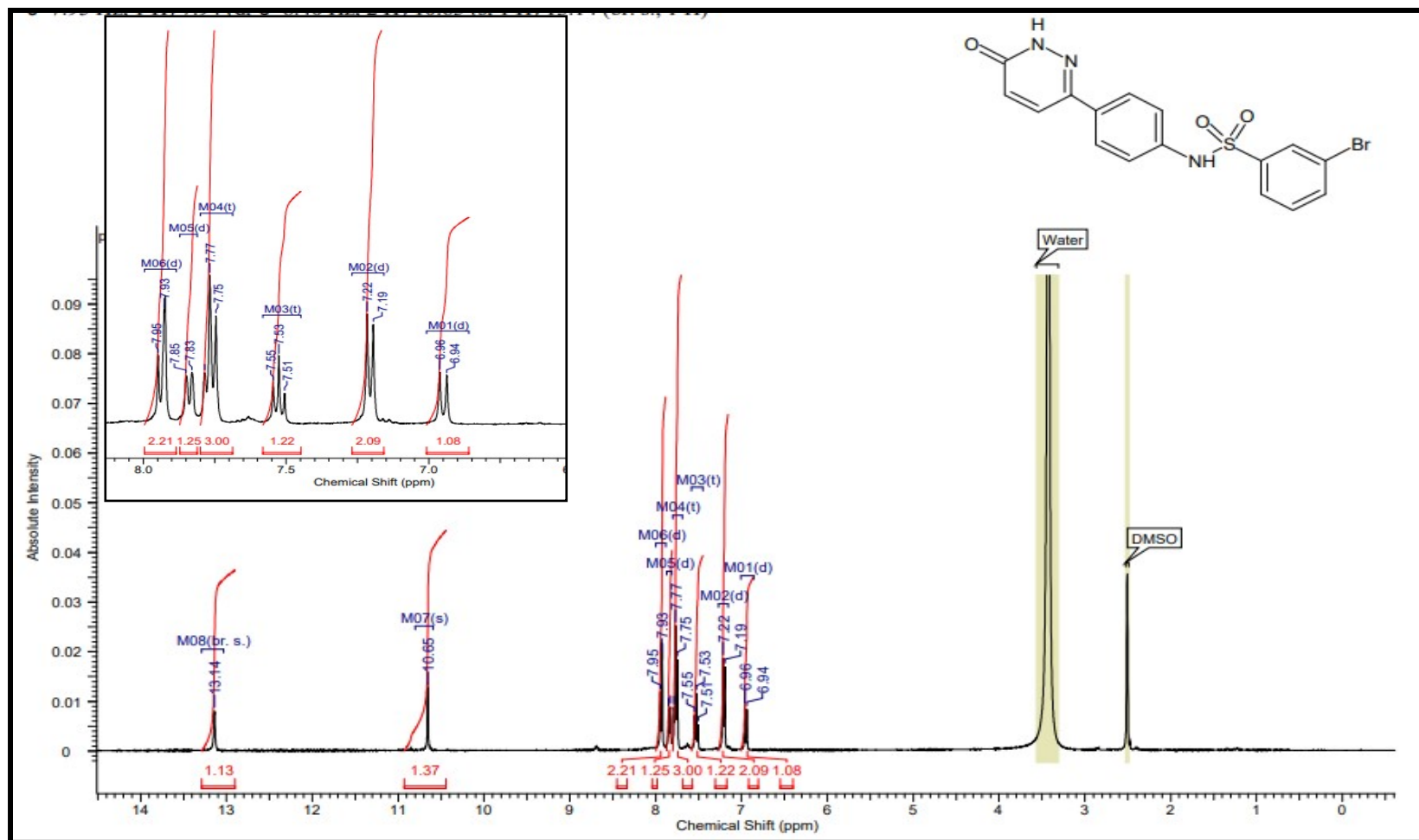
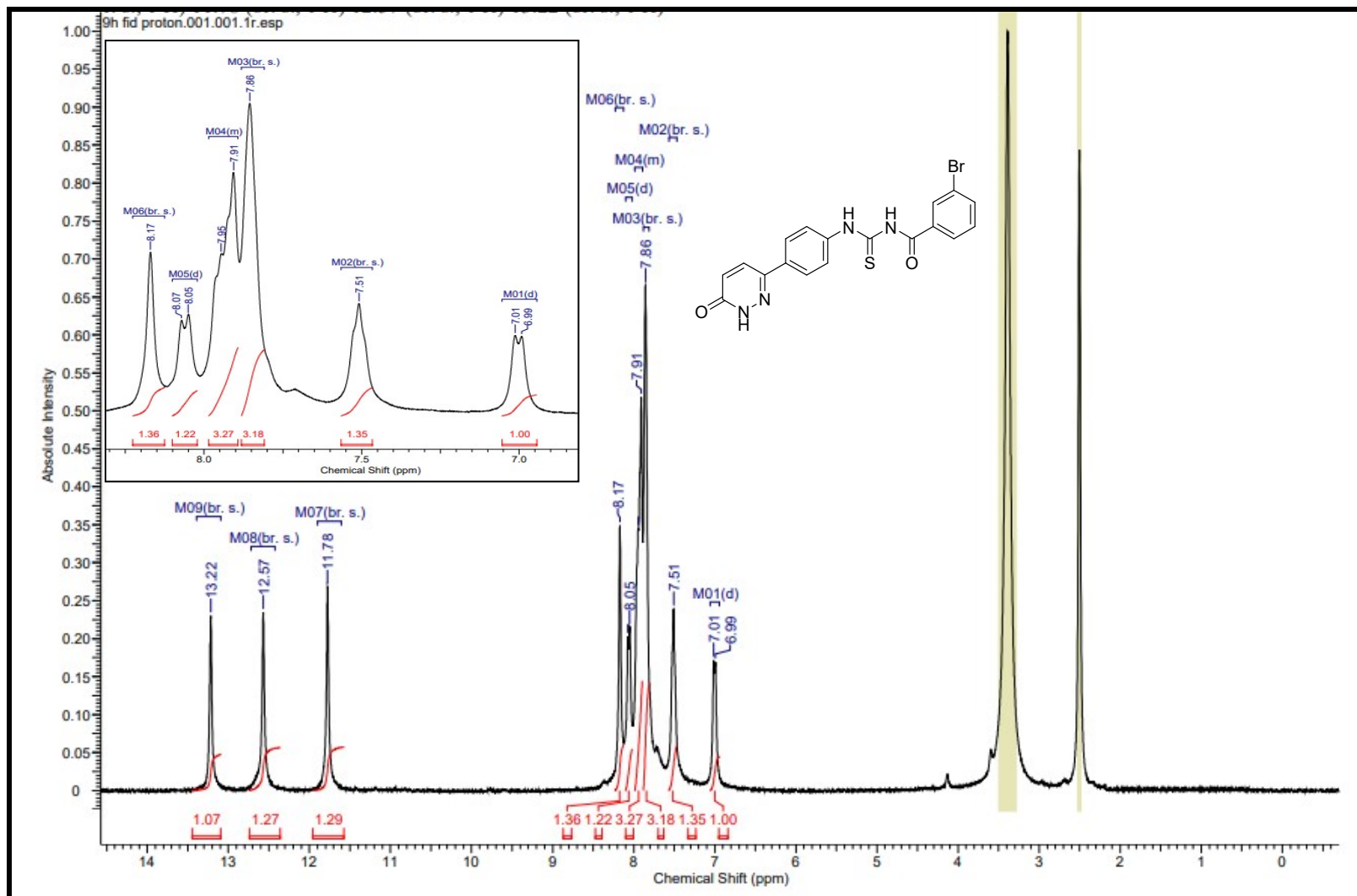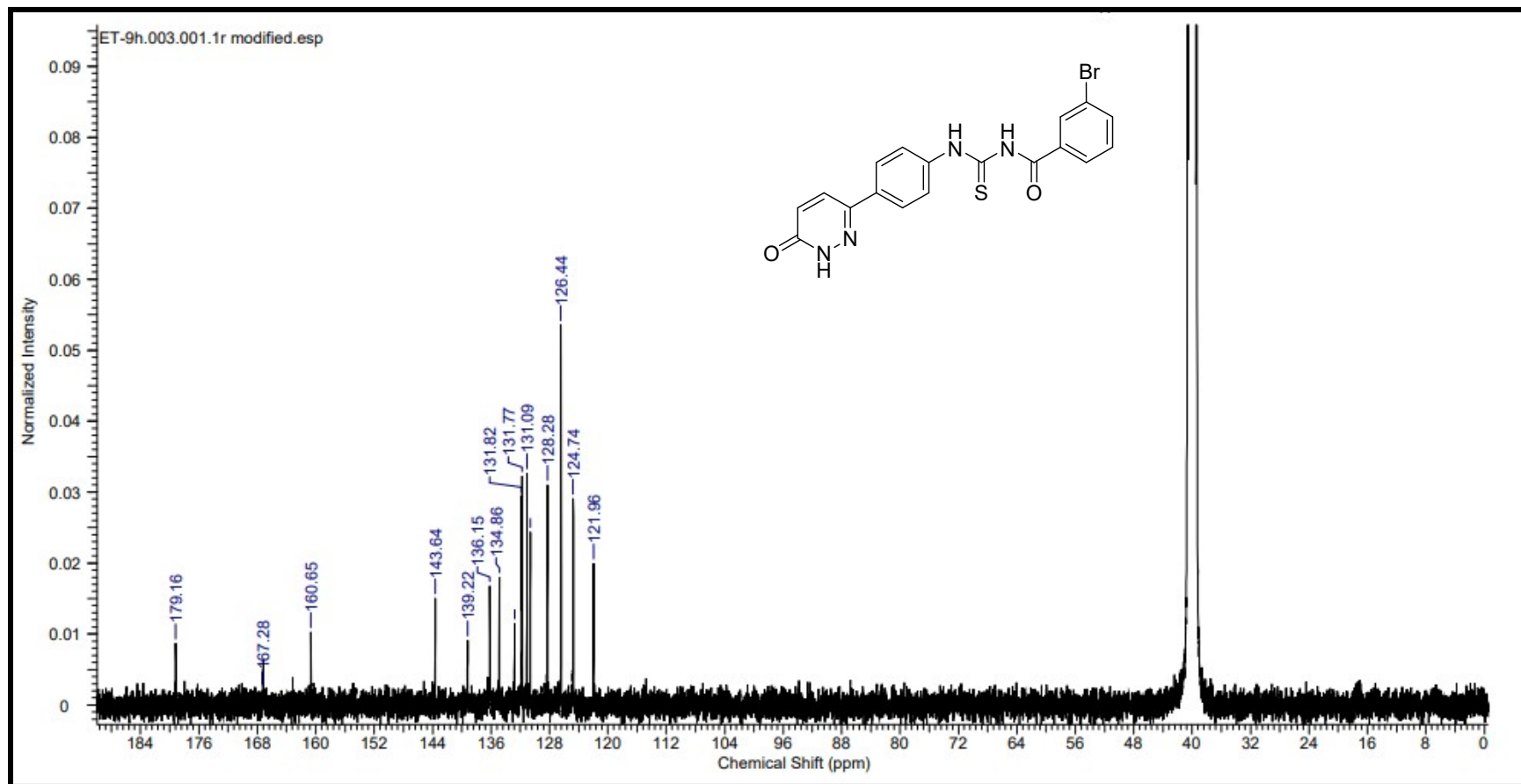**Figure 27a.** ^{1}H NMR spectrum (400 MHz) of compound 11a in DMSO-d$_6$.
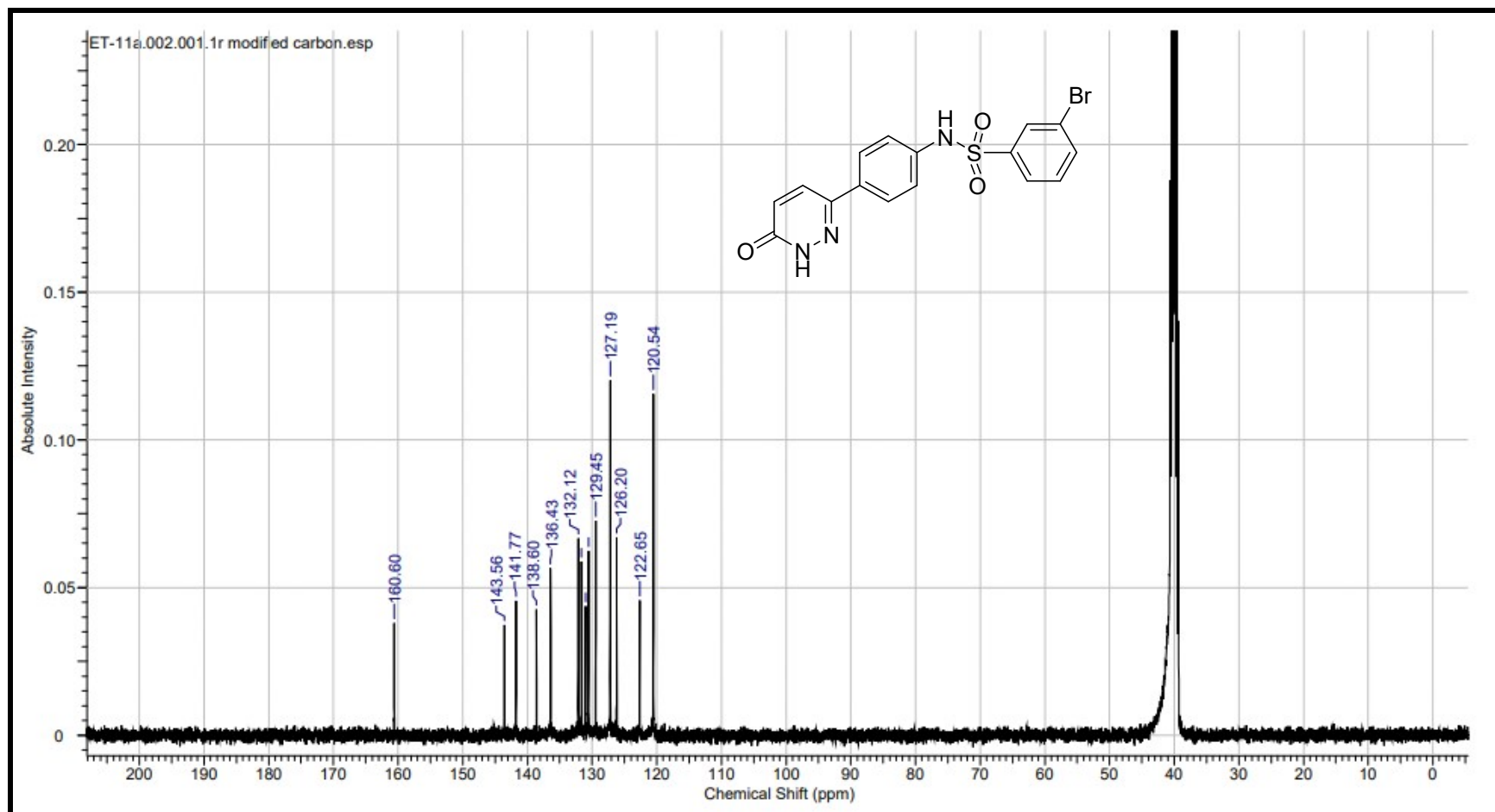
Figure 27b. ^{13}C NMR spectrum (100 MHz) of compound 11b in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 12.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
519 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-30 H: 0-20 N: 0-5 O: 0-5 S: 0-1 79Br: 0-1 81Br: 0-1

ET-11b/AJ   SYNAPTG2-Si#NotSet   07-Mar-2023
67583   09:57:51
0655 747 (1.483) Cm (745:760)
1: TOF MS ES+
                                                                                        1.39e+006
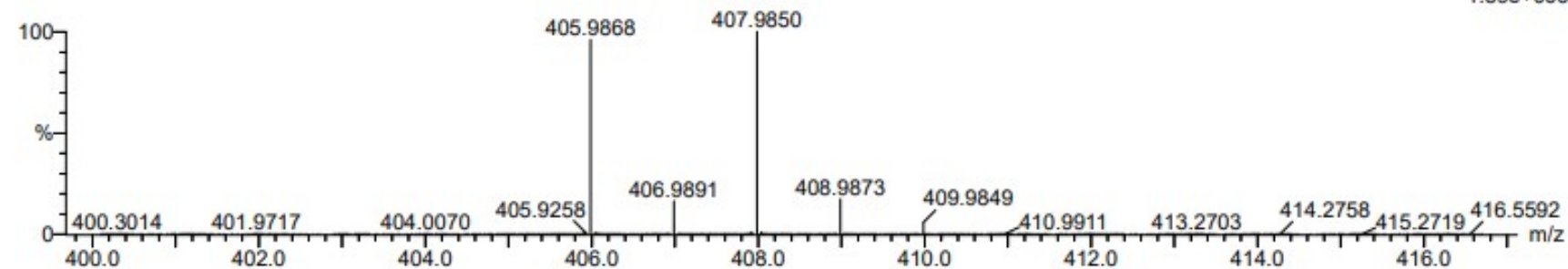
Minimum:			-1.5		
Maximum:	5.0	3.0	12.0		

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
405.9868	405.9861	0.7	1.7	11.5	2189.7	C16 H13 N3 O3 S 79Br

**Figure 27c. HRMS of compound 11a.**

4.2. Compound 11b
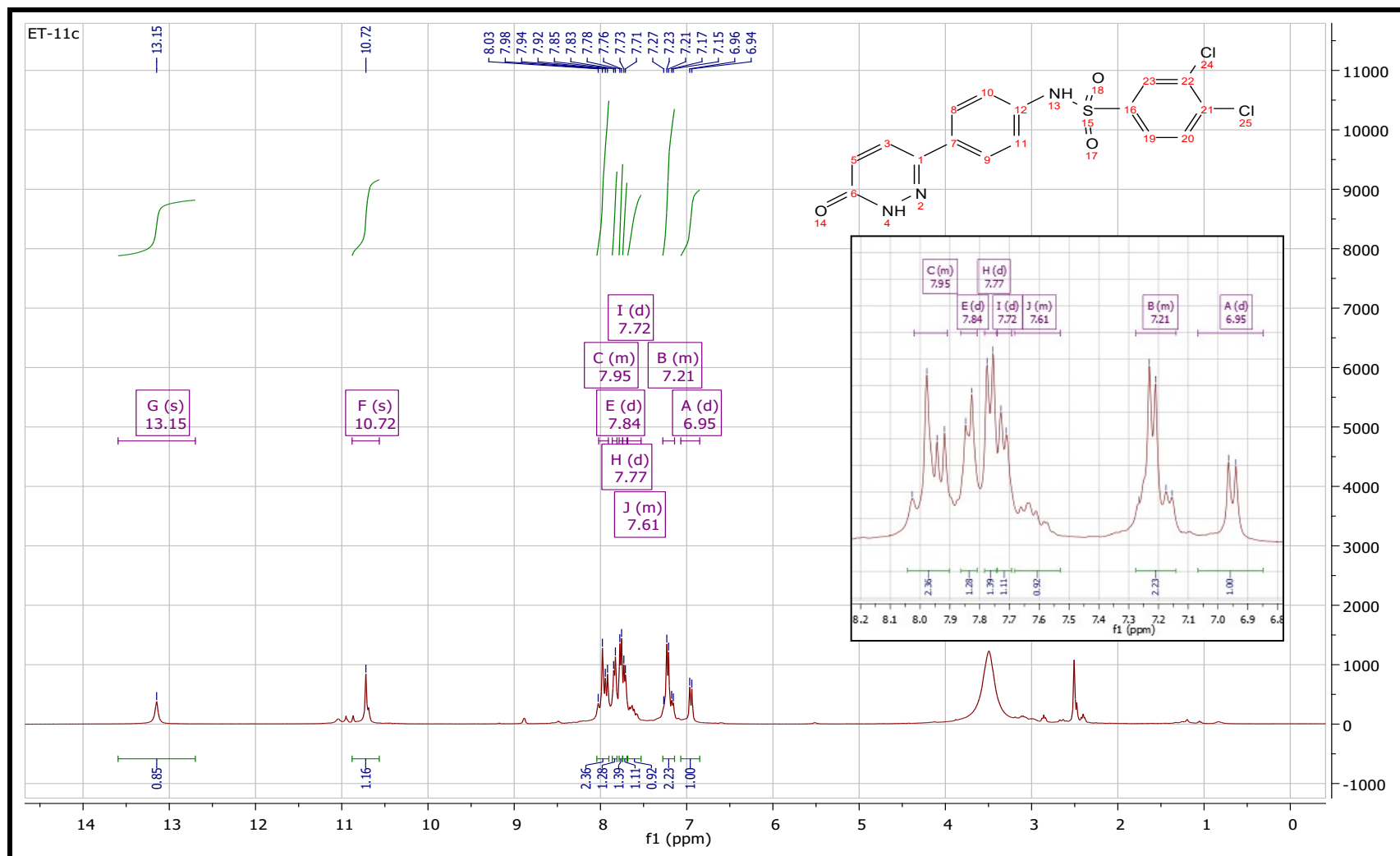
Figure 28a. ^{1}H NMR spectrum (400 MHz) of compound 11b in DMSO-d$_6$.

Figure 28b. ^{13}C NMR spectrum (100 MHz) of compound 11b in DMSO-d$_6$.

Figure 28c. HRMS of compound 11b.

4.3. Compound 11c
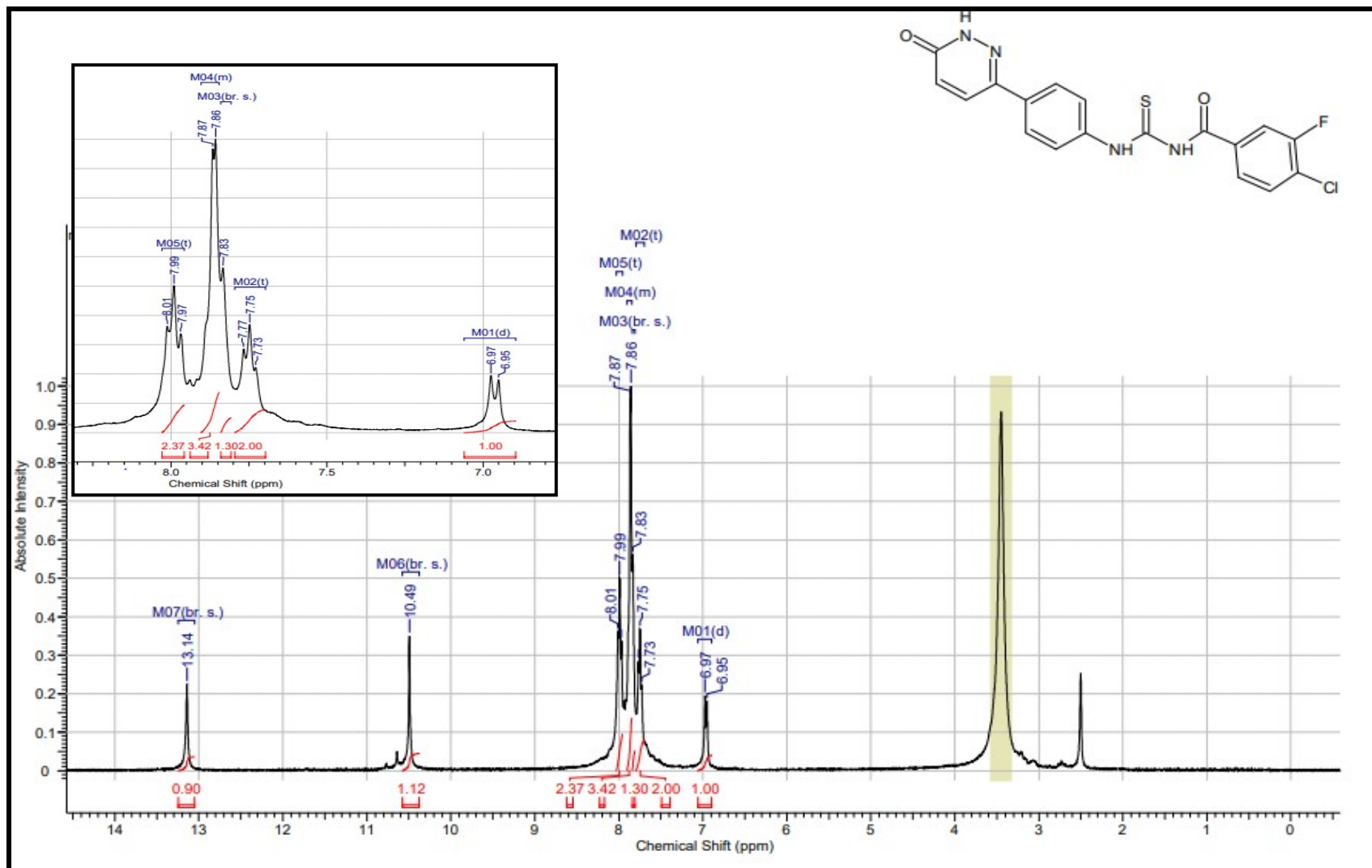

Figure 29a. ¹H NMR spectrum (400 MHz) of compound 11c in DMSO-d₆.
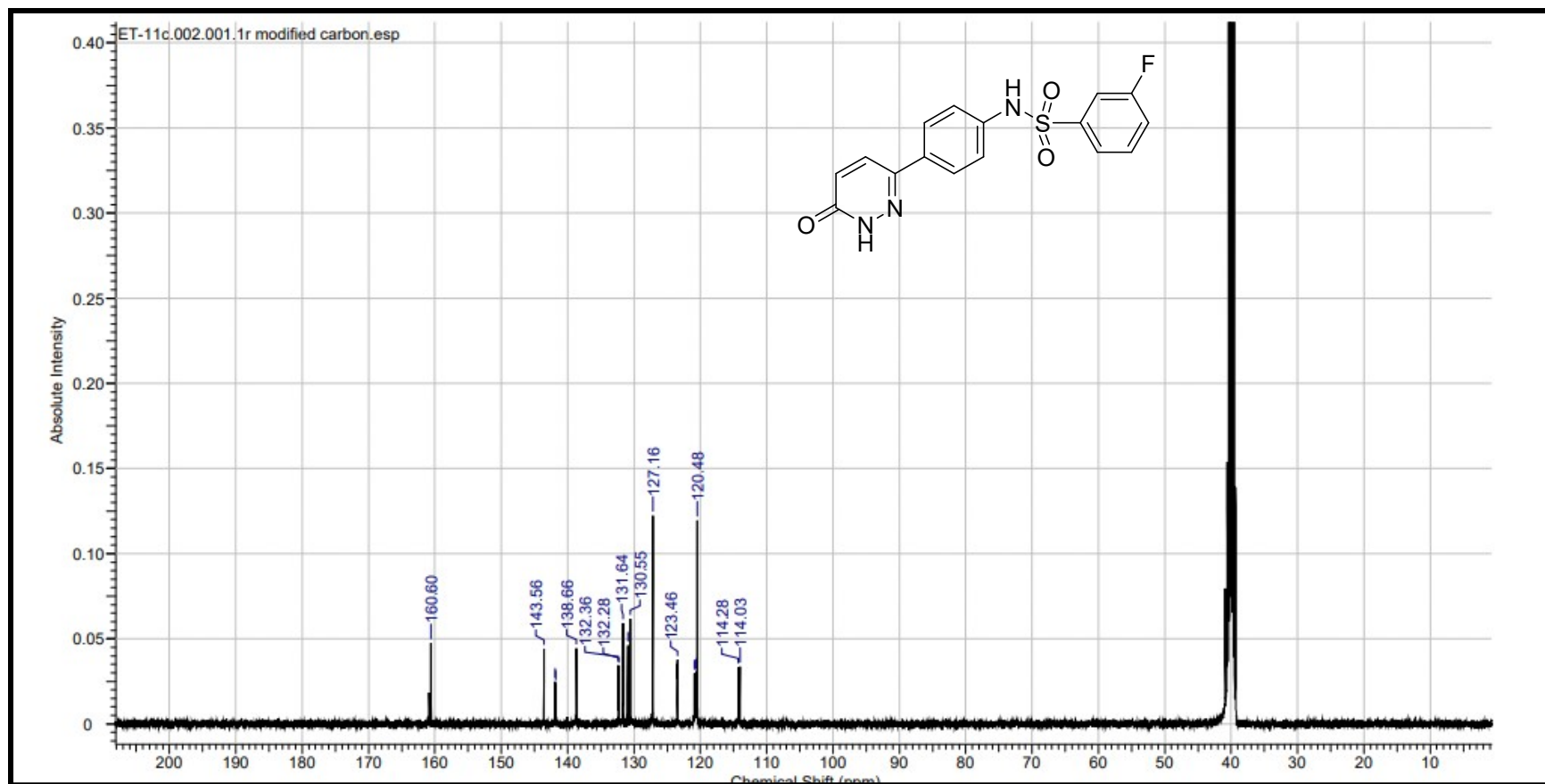
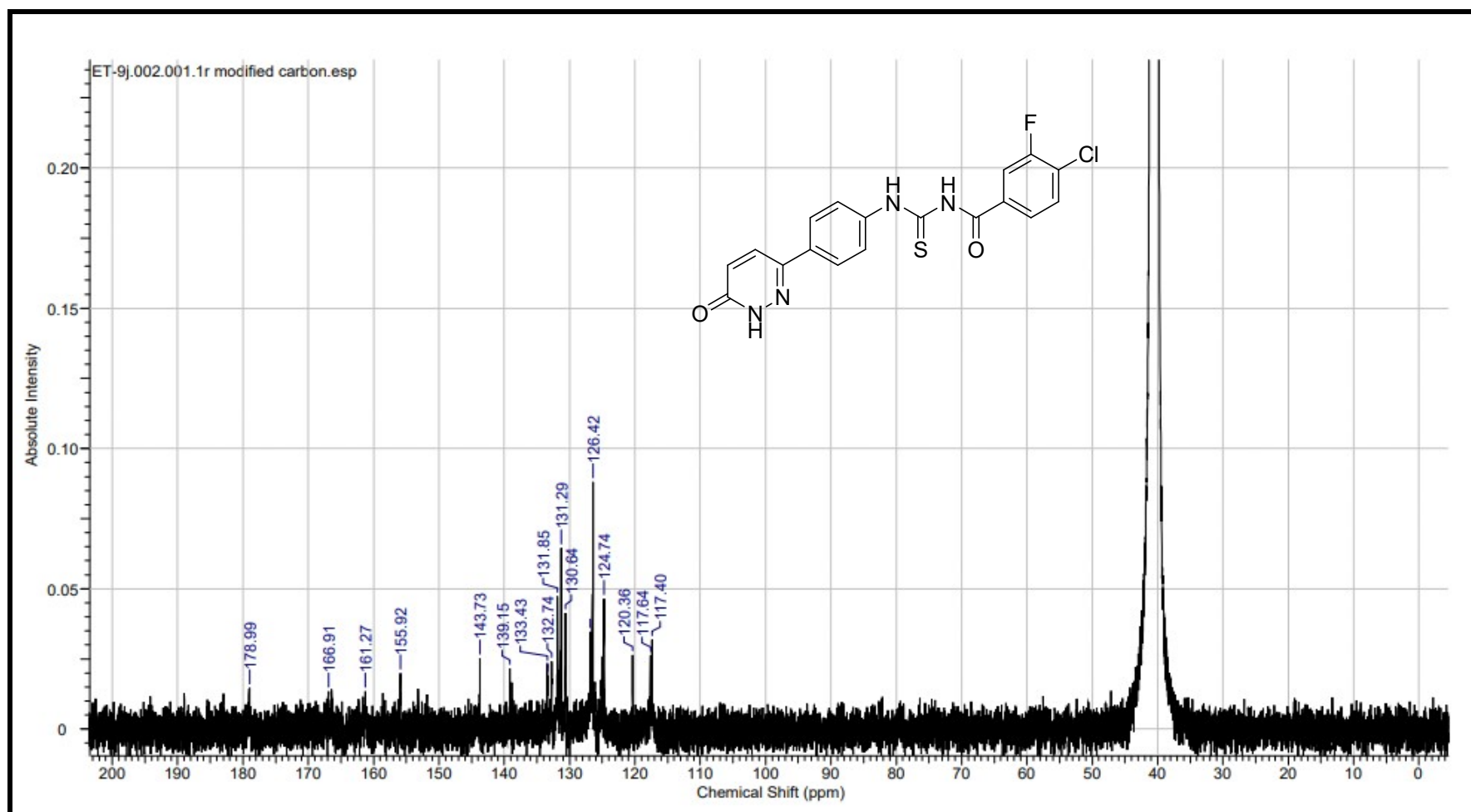**Figure 29b.** ^{13}C NMR spectrum (100 MHz) of compound 11c in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 15.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
581 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-60   H: 0-50   N: 0-5   O: 0-5   F: 0-1   S: 0-1

ET-11d/AJ   SYNAPTG2-Si#NotSet   07-Mar-2023
67596   13:45:59
0674 886 (1.757) Cm (868:889)
1: TOF MS ES+
                                                                                                       4.92e+005
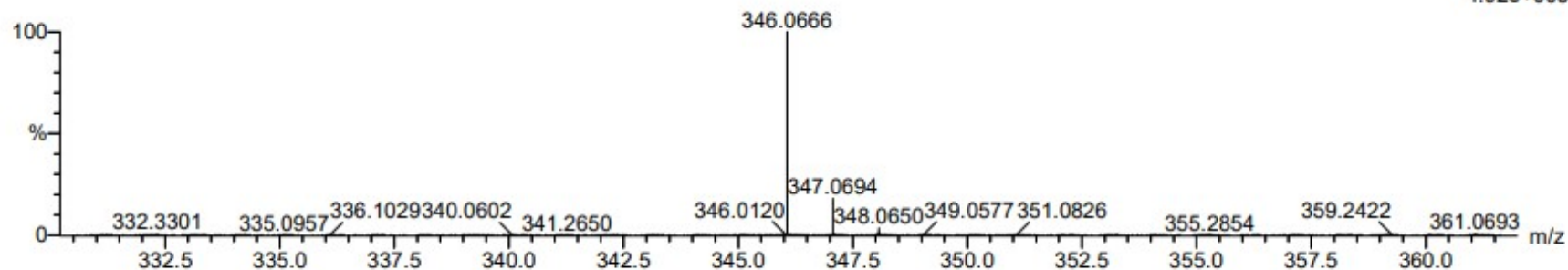
Minimum:				-1.5		
Maximum:		5.0	3.0	15.0		

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
346.0666	346.0662	0.4	1.2	11.5	1450.3	C16 H13 N3 O3 F S

Figure 29c. HRMS of compound 11c.

87
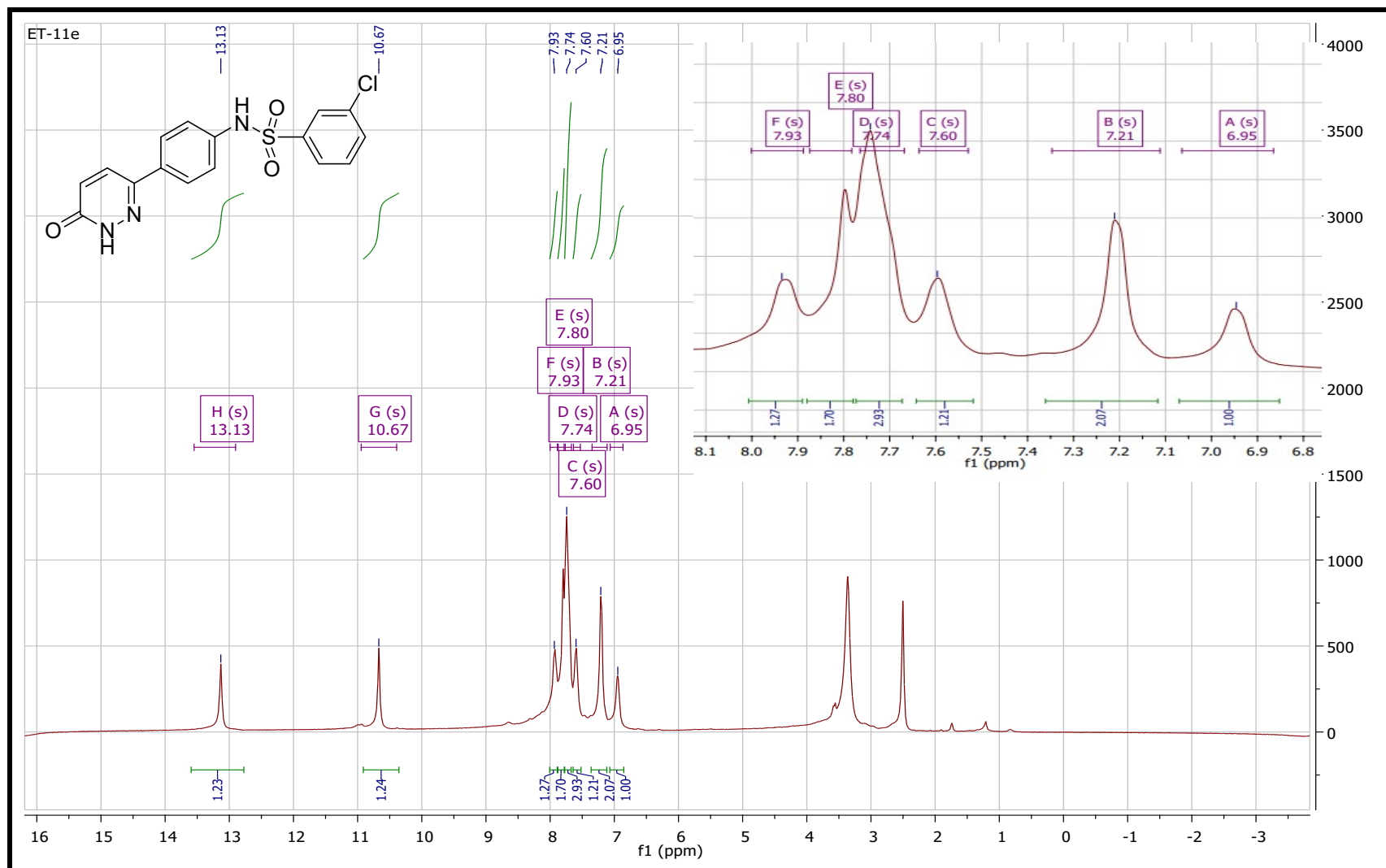
4.4. Compound 11d

Figure 30a. ^{1}H NMR spectrum (400 MHz) of compound 11d in DMSO-d$_6$.
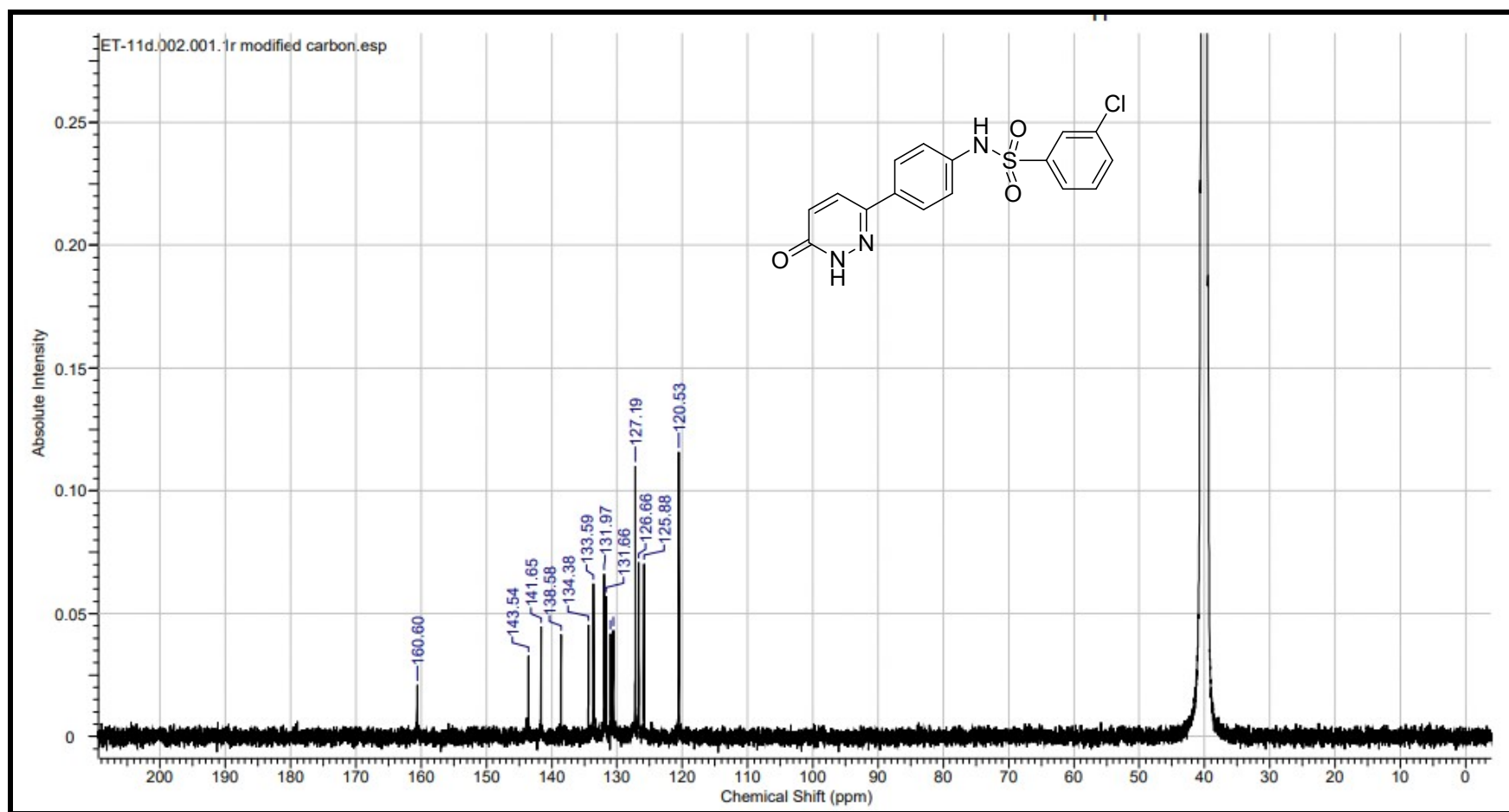
Figure 30b. ^{13}C NMR spectrum (100 MHz) of compound 11d in DMSO-d$_6$.

Single Mass Analysis
Tolerance = 3.0 PPM / DBE: min = -1.5, max = 20.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
789 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-60   H: 0-60   N: 0-5   O: 0-3   S: 0-1   35Cl: 0-1   37Cl: 0-1

ET-11e/AJ   SYNAPTG2-Si#NotSet   07-Mar-2023
67586   12:29:34
0664 1033 (2.046) Cm (1026:1038)
1: TOF MS ES+
                                                                                          2.76e+005
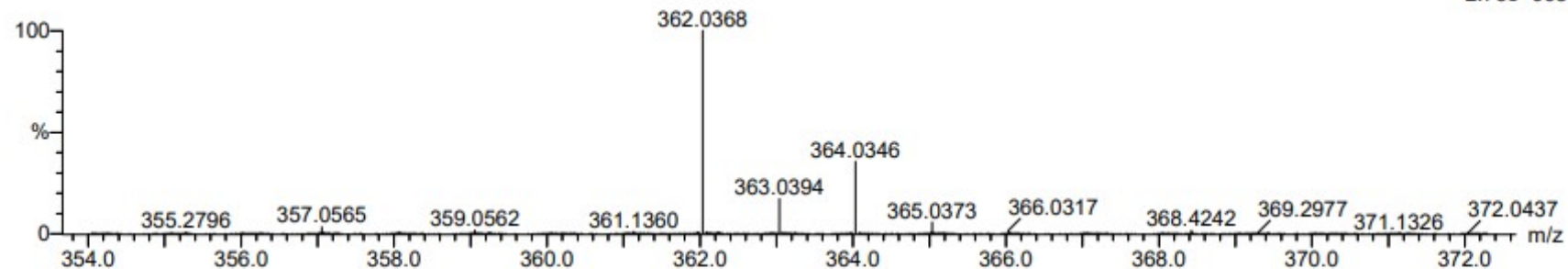
Minimum:				-1.5	
Maximum:		5.0	3.0	20.0	

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
362.0368	362.0366	0.2	0.6	11.5	1459.2	C16 H13 N3 O3 S 35Cl

Figure 30c. HRMS of compound 11d.

4.5. Compound 11e
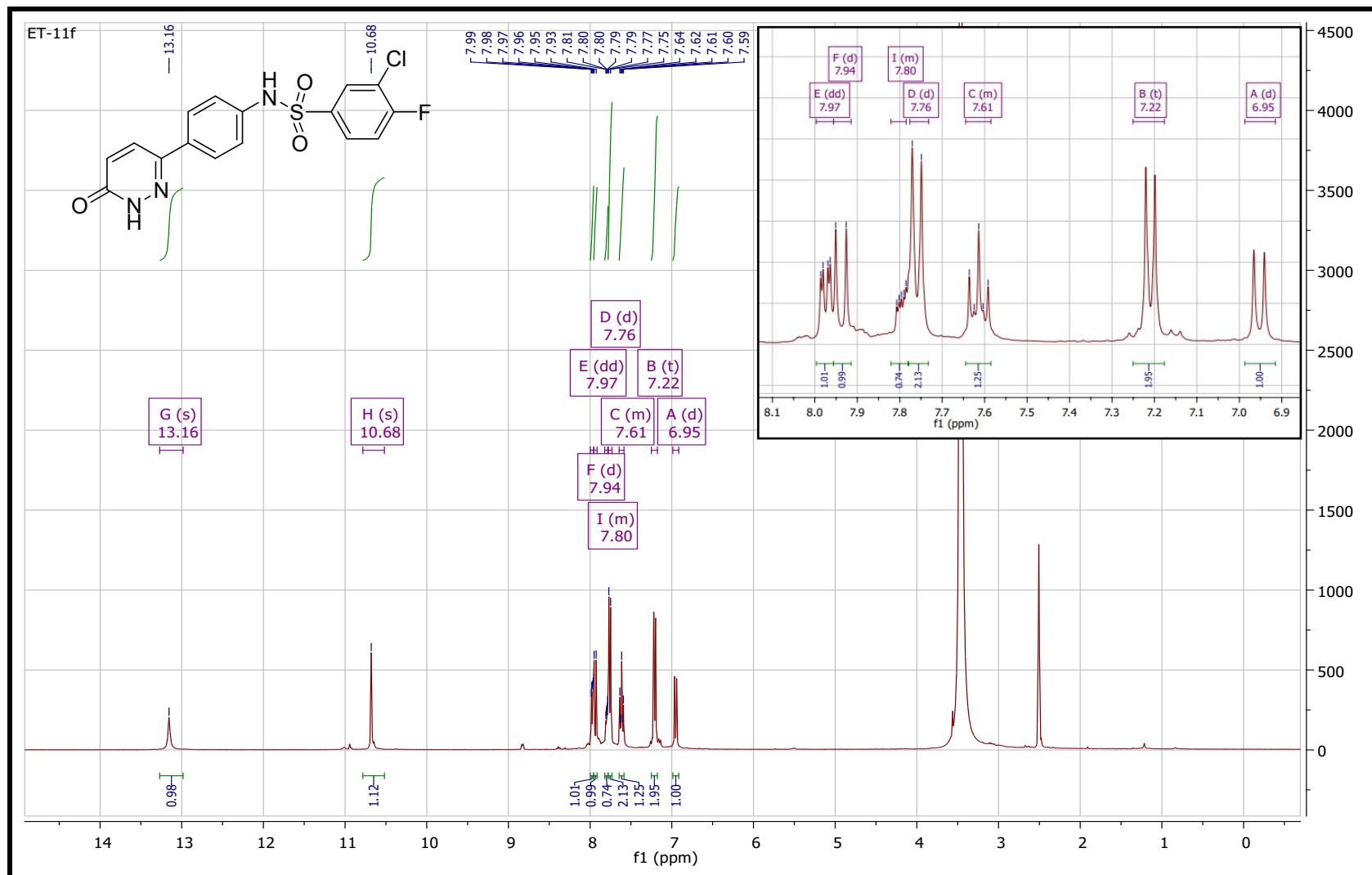
Figure 31a. ¹H NMR spectrum (400 MHz) of compound 11e in DMSO-d₆.
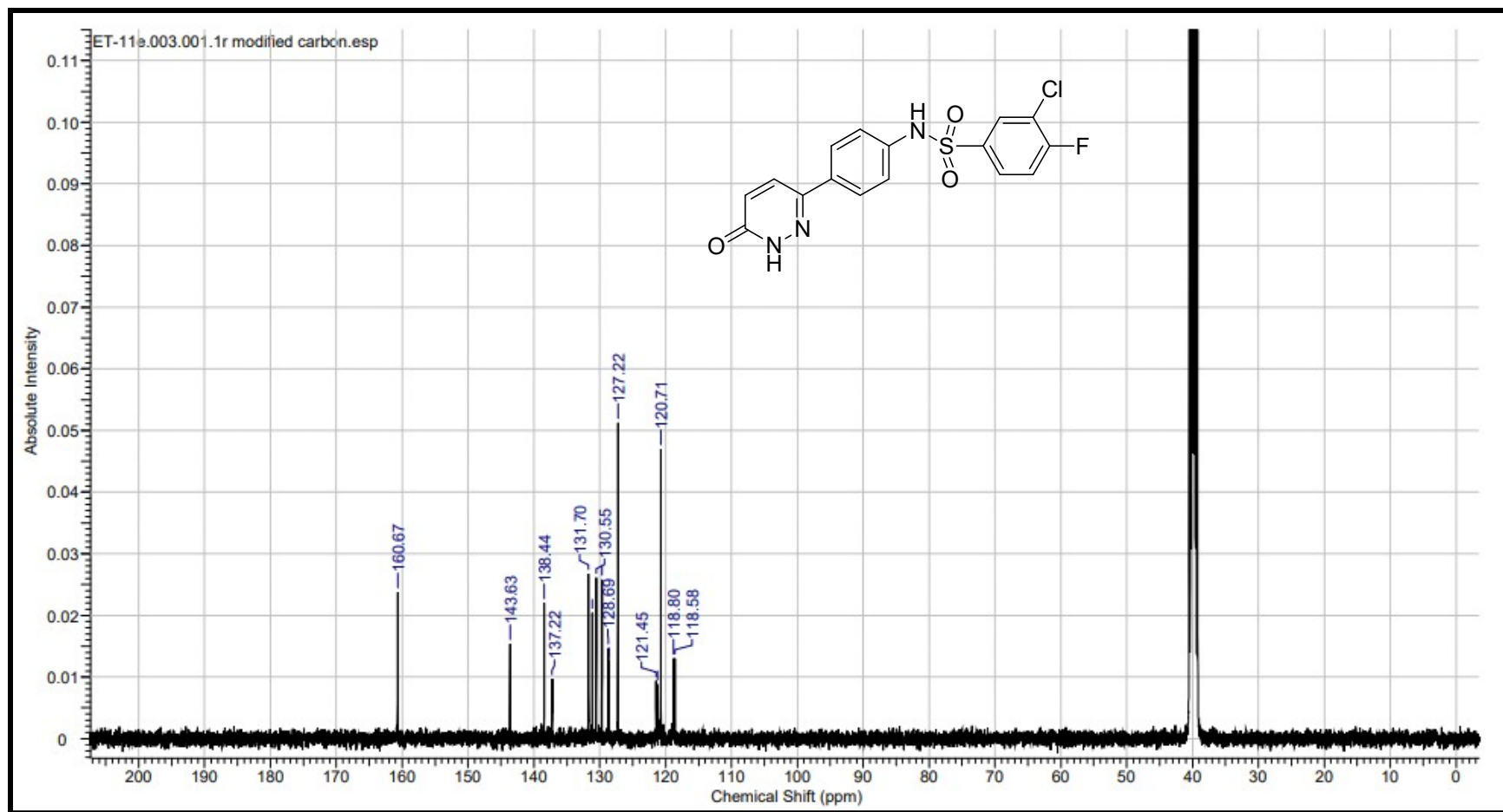
Figure 31b. ^{13}C NMR spectrum (100 MHz) of compound 11e in DMSO-d$_6$.

Figure 31c. HRMS of compound 11e.

4.6. Compound 11f

Figure 32a. ^{1}H NMR spectrum (400 MHz) of compound 11f in DMSO-d$_6$.

Figure 32b. ¹³C NMR spectrum (100 MHz) of compound 11f in DMSO-d₆.

Figure 32b. ^{13}C NMR spectrum (100 MHz) of compound 11f in DMSO-d_6.

Figure 32c. HRMS of compound 11f.

5. Spectral data of series V - VII

5.1. Compound 17a
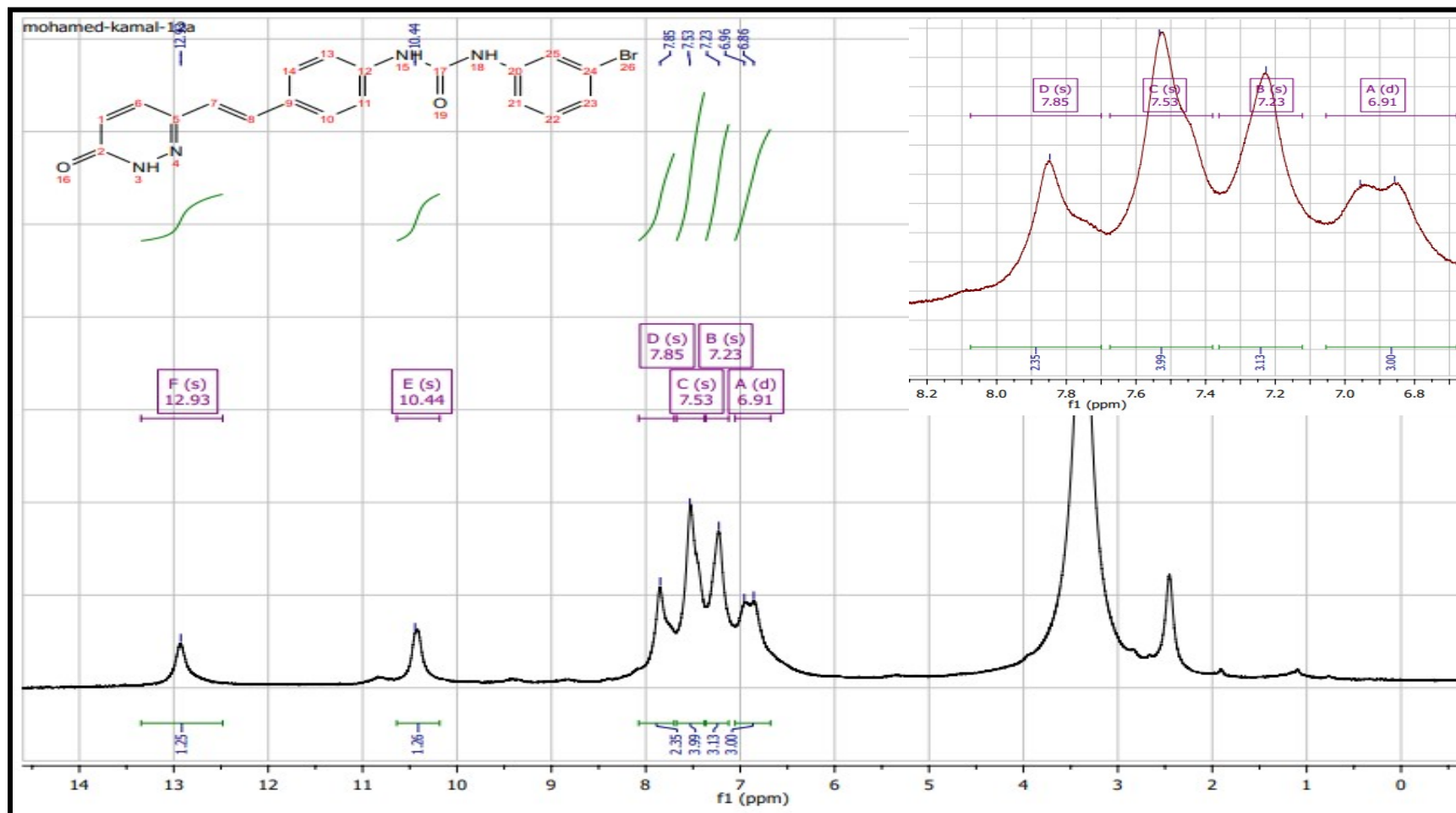
Figure 33. ^{1}H NMR spectrum (400 MHz) of compound 17a in DMSO-d$_6$.

5.2. Compound 17b

mohamed-kamal-18b--

^{1}H NMR (400 MHz, DMSO) δ 13.01 (s, 1H), 10.92 – 10.29 (m, 1H), 8.05 – 7.80 (m, 2H), 7.64 (d, J = 6.1 Hz, 1H), 7.57 (d, J = 7.4 Hz, 1H), 7.54 – 7.41 (m, 2H), 7.37 (d, J = 15.0 Hz, 1H), 7.29 (d, J = 18.5 Hz, 1H), 7.19 (d, J = 7.7 Hz, 1H), 7.09 – 6.96 (m, 1H), 6.91 (d, J = 7.9 Hz, 1H).
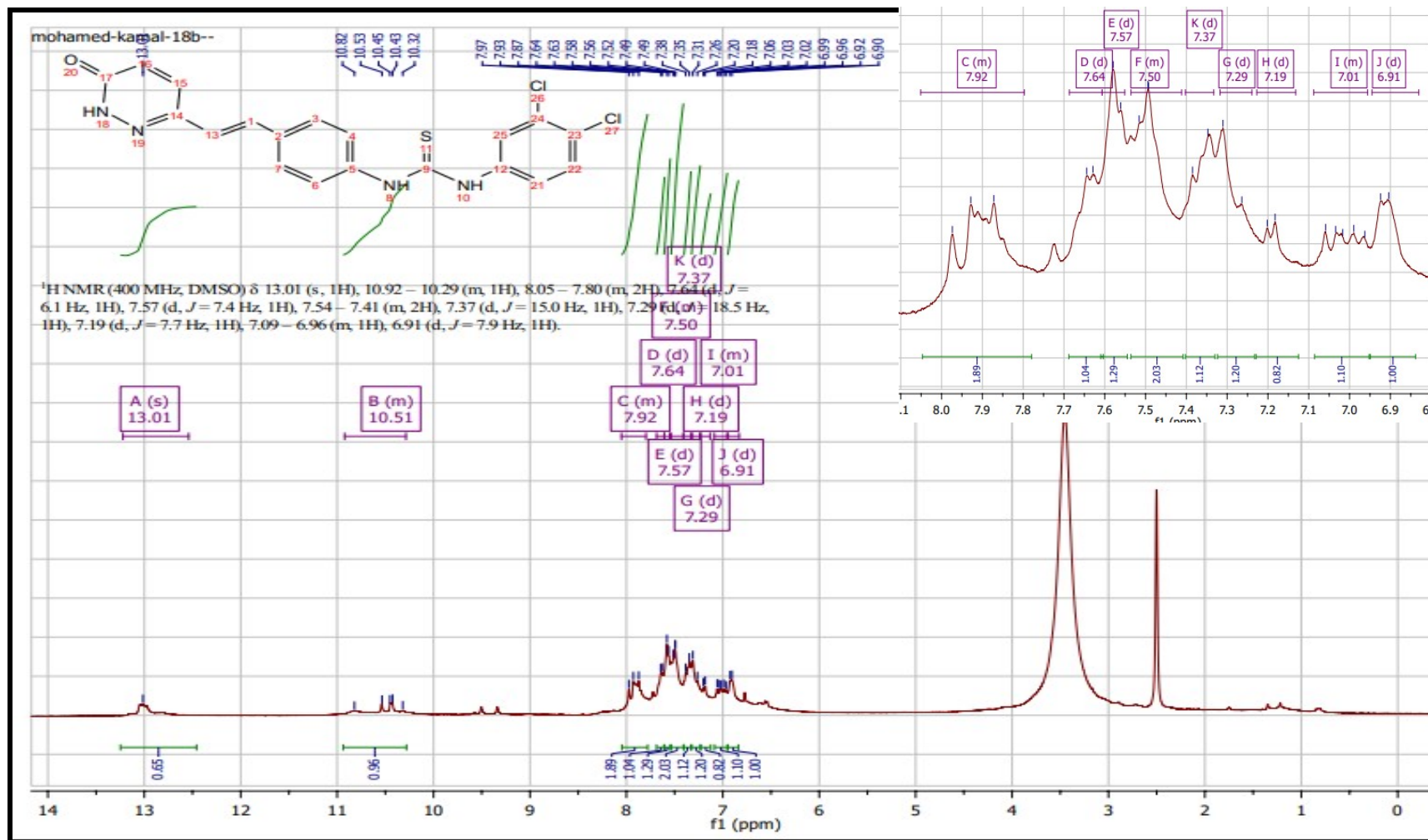
Figure 34. ^{1}H NMR spectrum (400 MHz) of compound 17b in DMSO-d$_6$.

5.3. Compound 18a
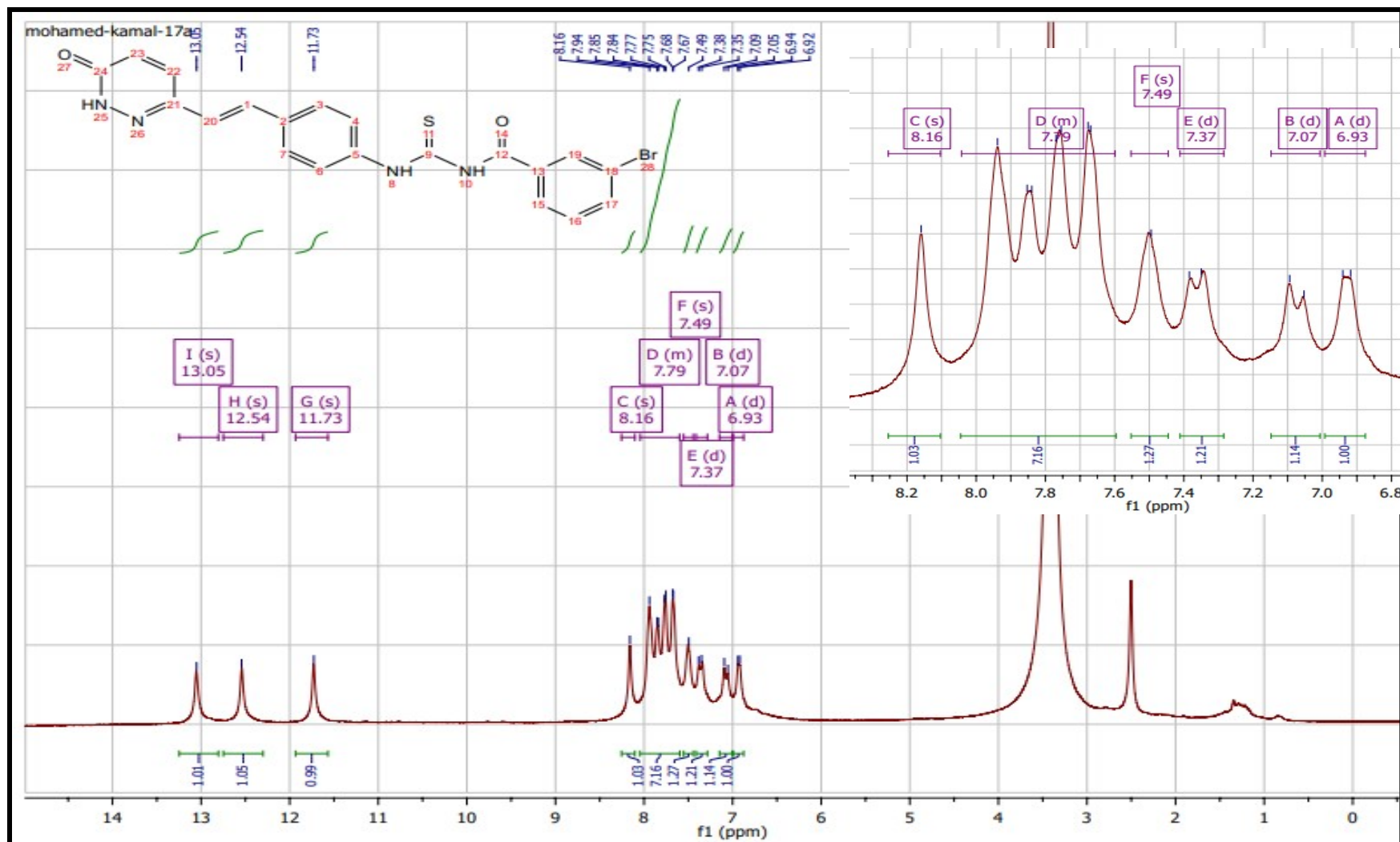
Figure 35. ^{1}H NMR spectrum (400 MHz) of compound 18a in DMSO-d$_6$.

5.4. Compound 18b

^{1}H NMR (400 MHz, DMSO) δ 12.85 (s, 1H), 8.24 (d, J = 8.5 Hz, 1H), 8.01 – 7.81 (m, 2H), 7.64 – 7.47 (m, 1H), 7.36 – 7.24 (m, 2H), 7.16 (d, J = 16.5 Hz, 1H), 6.86 (d, J = 9.7 Hz, 1H), 6.71 (d, J = 16.5 Hz, 1H), 6.57 (d, J = 8.2 Hz, 2H).
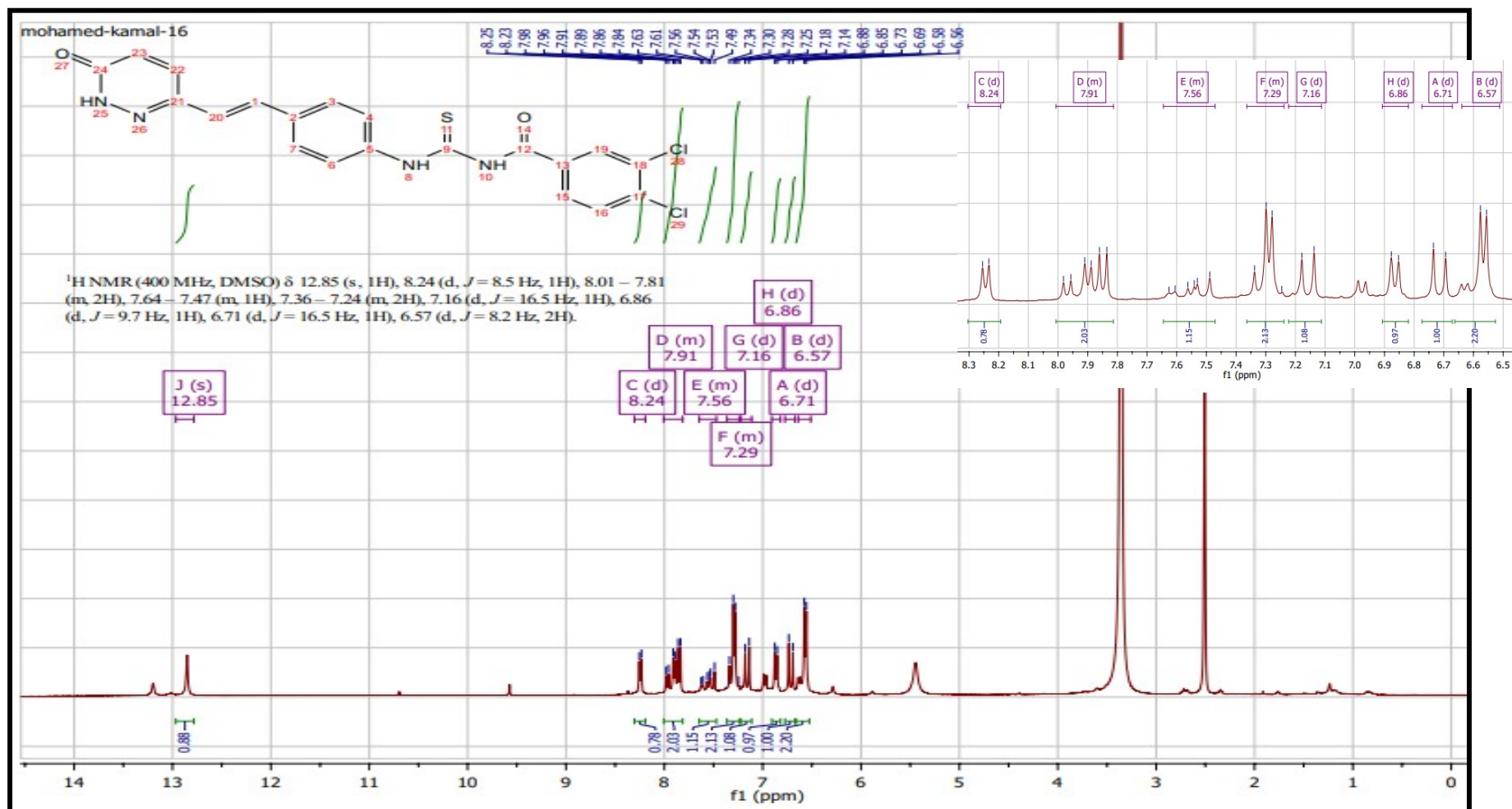
Figure 36. ^{1}H NMR spectrum (400 MHz) of compound 18b in DMSO-d$_6$.

5.5. Compound 19a
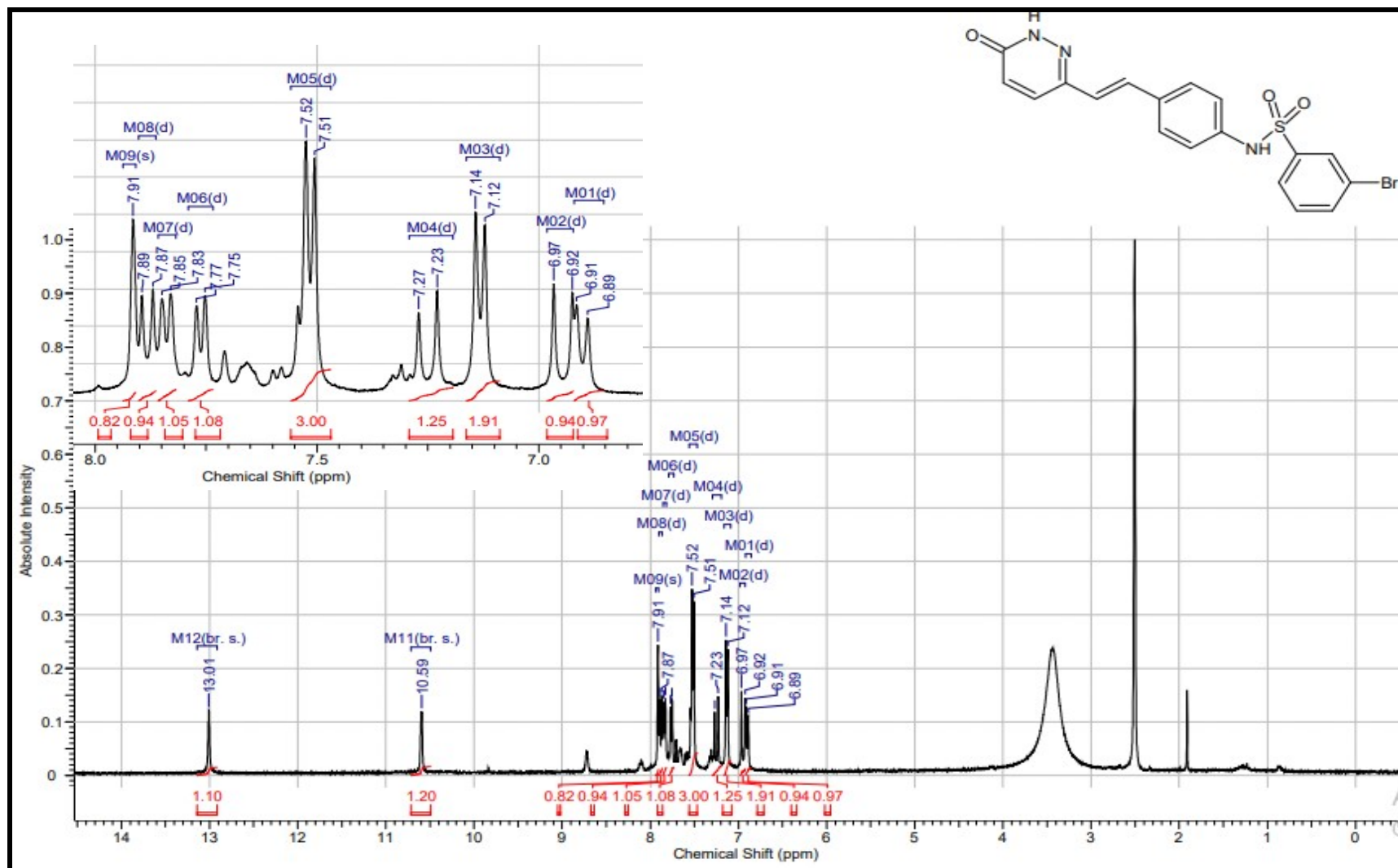
Figure 37. ^{1}H NMR spectrum (400 MHz) of compound 19a in DMSO-d$_6$.

5.6. Compound 19b

¹H NMR (400 MHz, DMSO) δ 13.02 (s, 1H), 10.63 (s, 1H), 7.95 (s, 1H), 7.86 (dd, J = 14.5, 9.2 Hz, 2H), 7.70 (d, J = 8.5 Hz, 1H), 7.52 (d, J = 8.3 Hz, 2H), 7.24 (d, J = 16.6 Hz, 1H), 7.13 (d, J = 8.2 Hz, 2H), 7.03 − 6.85 (m, 2H).
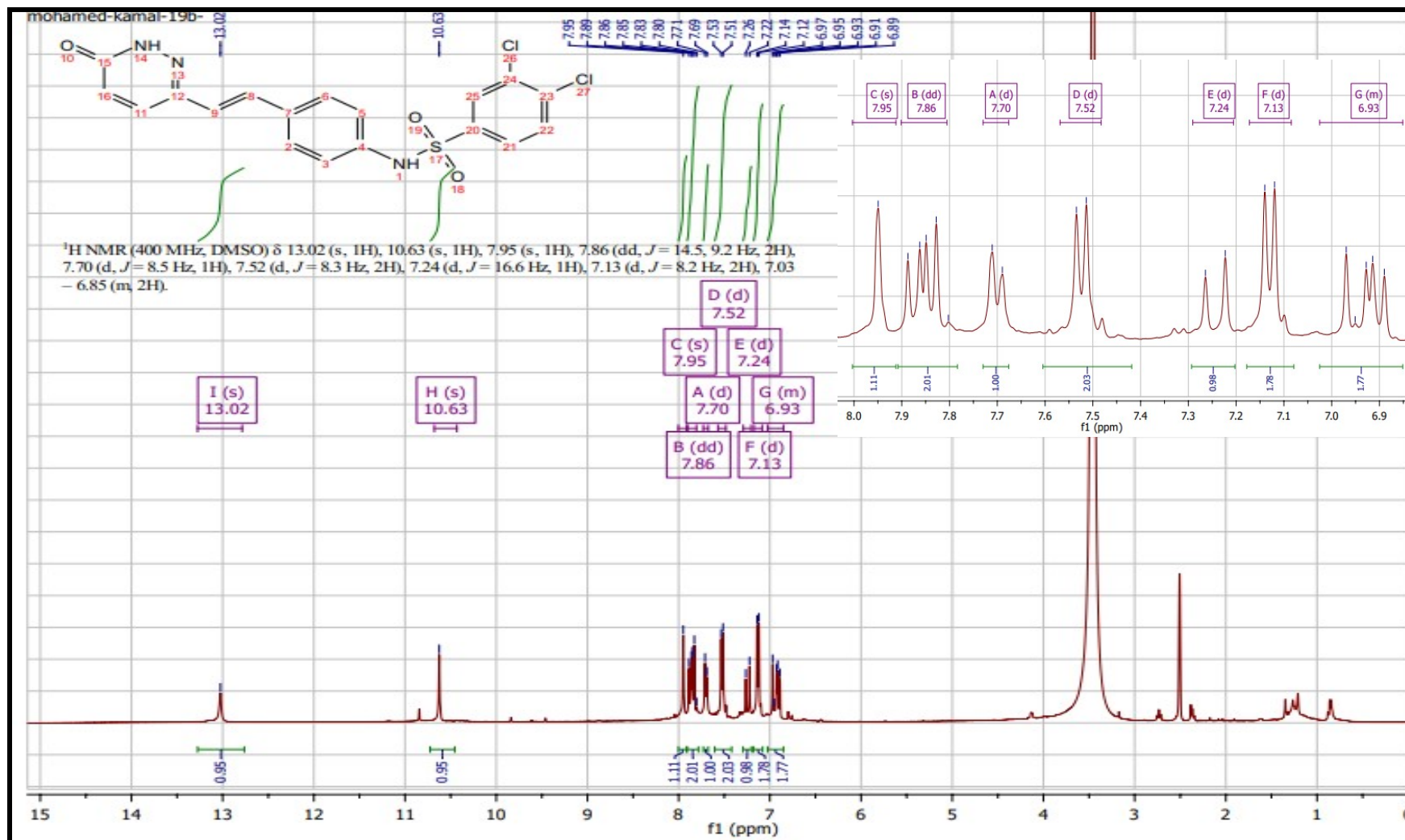
Figure 38. ¹H NMR spectrum (400 MHz) of compound 19b in DMSO-d₆.

6. Elemental analysis of some final compounds

Elemental Data	
Old code number	**New code number**
4B	10a
5B	10b
6B	10c
7B	10d
8B	10e
9B	Not included in the manuscript
10B	10f
11B	10g
12B	10h
14B	8a
15B	8b
16B	Not included in the manuscript
17B	10j
18B	8c
19B	Not included in the manuscript
20B	8d
21B	8e

Requester Data:

Name: **Dr.Mohamed Kamal Sayed Elnagar**
Authority: Faculty of Pharmacy, Saddat University

Sample Data:

Ten samples had been submitted for elemental analysis.

Analysis Report:

Sample Code	C%	H%	N%	S%
4B	61.94	4.21	16.25	9.23
5B	56.40	3.63	14.80	8.45
6B	50.59	3.23	13.29	7.60
7B	54.90	3.47	18.00	8.23
8B	47.92	2.60	12.59	7.21
9B	67.75	3.21	17.70	0
10B	58.90	3.43	15.49	8.67
11B	58.87	3.67	15.43	8.76
14B	52.40	3.23	14.59	8.34
15B	53.27	3.62	14.75	0

INVESTIGATOR   **DIRECTOR**

Figure 39a. Report 1 of elemental analysis.

Al-Azhar University
The Regional Center for Mycology and Biotechnology

Requester Data:

Name: Dr.Mohamed Kamal Sayed Elnagar
Authority: Faculty of Pharmacy, Saddat University

Sample Data:

Seven samples had been submitted for elemental analysis.

Analysis Report:

Sample Code	C%	H%	N%	S%
12B	50.57	3.22	13.29	7.55
16B	47.58	3.17	10.58	8.02
17B	53.51	3.24	14.15	8.03
18B	60.17	3.98	16.72	9.60
19B	57.45	3.81	15.89	9.07
20B	48.12	2.83	13.40	7.79
21B	62.82	4.15	17.51	0

INVESTIGATOR   DIRECTOR
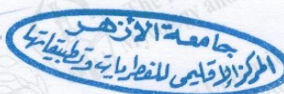
Figure 39b. Report 2 of elemental analysis.

7. X-ray powder diffraction (XRD) study:

Table 1: Crystal structure and lattice parameters of the basic chemical compounds 2, 6 and derivative compounds of 8j, 10h and 11a.

Compound	2	6	8j	10h	11a
Crystal class	Monoclinic	Triclinic	Monoclinic	Monoclinic	Orthorhombic
a(Å)	8.875(4)	7.612(4)	10.960 (2)	10.826(2)	7.360 (2)
b(Å)	9.498(1)	11.520(2)	9.697 (6)	9.769(6)	7.469 (3)
c(Å)	11.655(8)	11.898(4)	13.5885 (8)	18.349 (4)	33.061 (7)
$\alpha(^o)$	90	112.85(2)	90	90	90
$\beta(^o)$	110.97(4)	102.06(2)	98.644 (9)	98.644	90
$\gamma(^o)$	90	96.57(2)	90	90	90
Volume of Unit cell ($Å^3$)	917.39	920.34	1428.3	1918.53	1817.5
Density, (g cm^{-3})	$P2_1/a$	1.4	1.57	$P2_1$	1.36
Space group	1.40	P1	P2,	1.57	Phca
Crystal size (mm)	0.4 × 0.5 × 0.65	0.4 × 0.5 × 0.65		0.75 × 0.5 × 0.3	0.4 × 0.15 x 0.8

8. Biological results

8.1. Antimicrobial screening
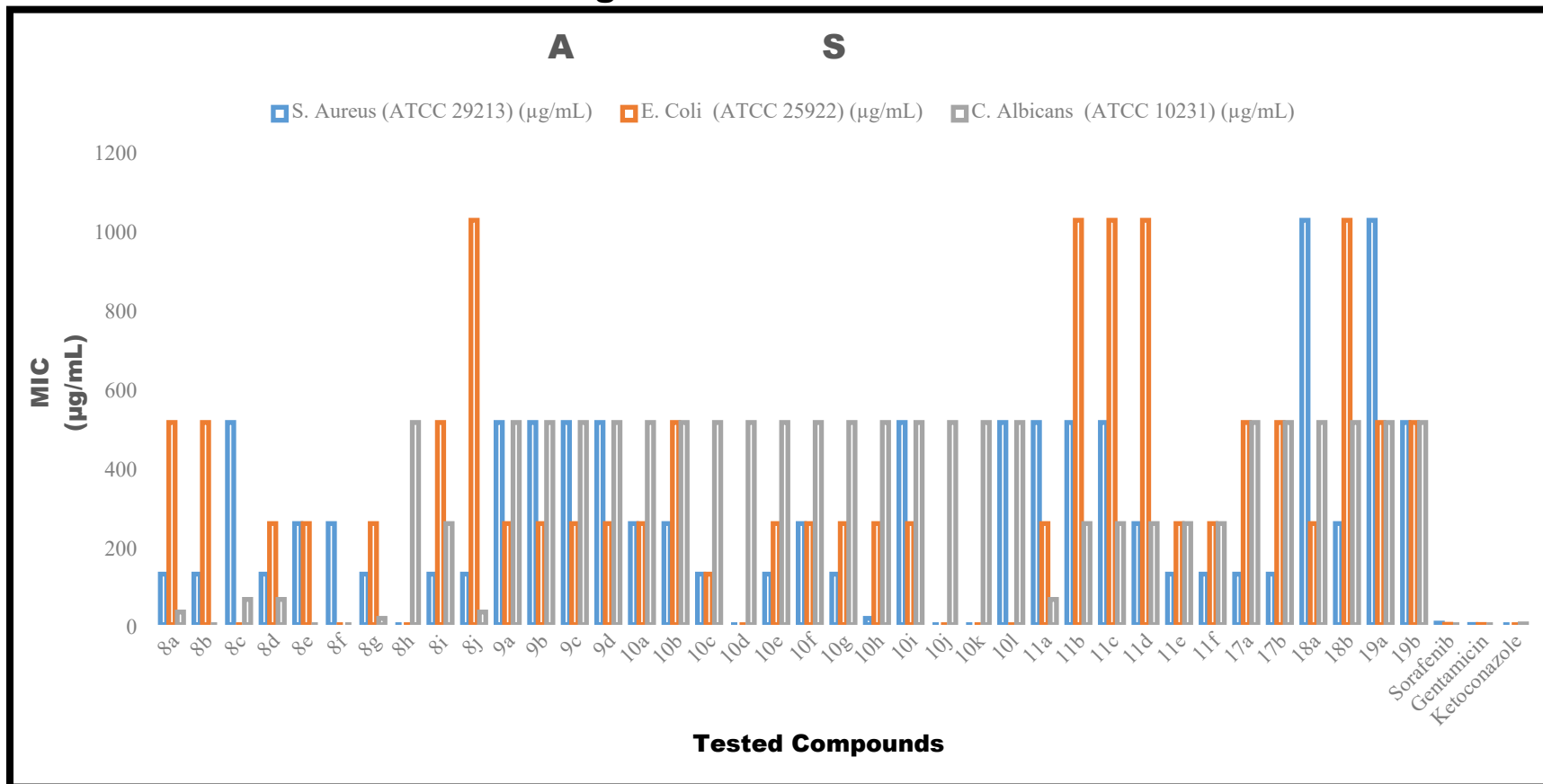
Figure 40. Antimicrobial screening of the tested compounds against *S. aureus*, *E. Coli* and *C. albicans* strains.

8.2. Antiproliferative results
8.2.1. Anti-VEGFR-2 screening

Thermo Fisher Scientific's SelectScreen™ Profiling Service: Single Point Results												

SelectScreen Scientist: Meera Kumar **Date:** 19-Sep-2023 **SSBK-Z'-LYTE (Madison, WI USA)**

Quality Assurance Review: Kat Smith **Date:** 19-Sep-2023 **Legend**

% Phosphorylation	Pass		< 40% Inhibition
Z' Determination	Pass		40% - 80% Inhibition
			≥ 80% Inhibition

Project #	Compound Name	1X Test Compound Concentration (nM)	[ATP] Tested (µM)	Kinase Tested	% Inhibition Point 1	% Inhibition Point 2	% Inhibition mean	Difference Between Data Points |Point 1 - Point 2|	Development Reaction Interference	Test Compound Interference Coumarin	Test Compound Interference Fluorescein	Z'
SSBK12643_65852	Sorafenib	10000	10	KDR (VEGFR2)	100	103	102	3	Pass	Pass	Pass	0.75
SSBK12643_65852	8a	10000	10	KDR (VEGFR2)	38	31	34	7	Pass	Pass	Pass	0.75
SSBK12643_65852	8e	10000	10	KDR (VEGFR2)	8	8	8	1	Pass	Pass	Pass	0.75
SSBK12643_65852	11c	10000	10	KDR (VEGFR2)	14	14	14	1	Pass	Pass	Pass	0.75
SSBK12643_65852	11f	10000	10	KDR (VEGFR2)	11	17	14	6	Pass	Pass	Pass	0.75
SSBK12643_65852	9b	10000	10	KDR (VEGFR2)	9	4	7	5	Pass	Pass	Pass	0.75
SSBK12643_65852	9c	10000	10	KDR (VEGFR2)	2	7	5	5	Pass	Pass	Pass	0.75
SSBK12643_65852	10j	10000	10	KDR (VEGFR2)	29	28	28	1	Pass	Pass	Pass	0.75
SSBK12643_65852	10l	10000	10	KDR (VEGFR2)	4	5	5	1	Pass	Pass	Pass	0.75
SSBK12643_65852	17a	10000	10	KDR (VEGFR2)	62	58	60	4	Pass	Pass	Pass	0.75
SSBK12643_65852	17b	10000	10	KDR (VEGFR2)	35	40	38	5	Pass	Pass	Pass	0.75

8.2.2. *In vitro* single dose assay of the active synthesized compound
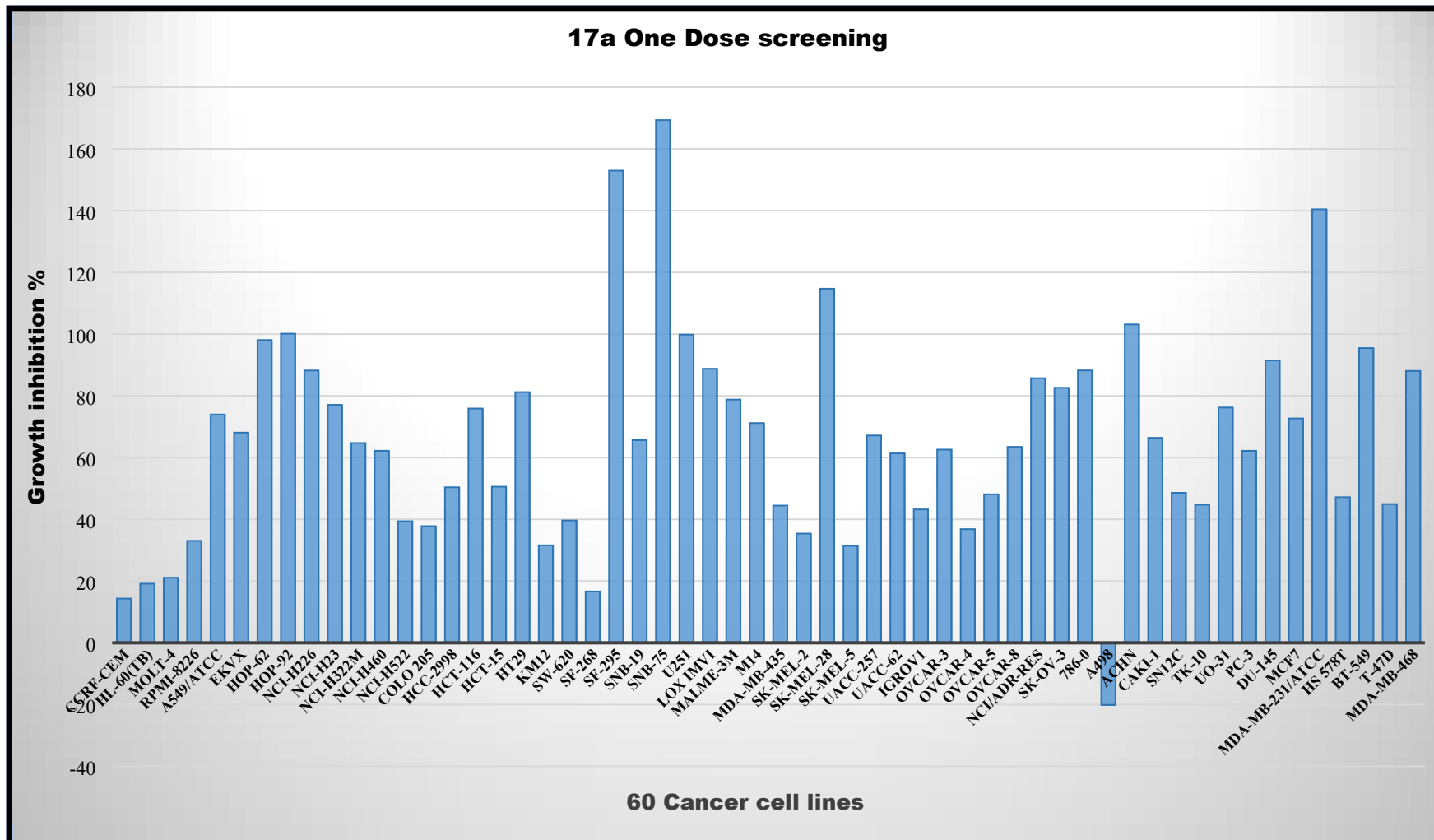
Figure 41. Growth inhibition % exerted by compound 17a at 10 µM concentration over NCI 60 cell line panel.
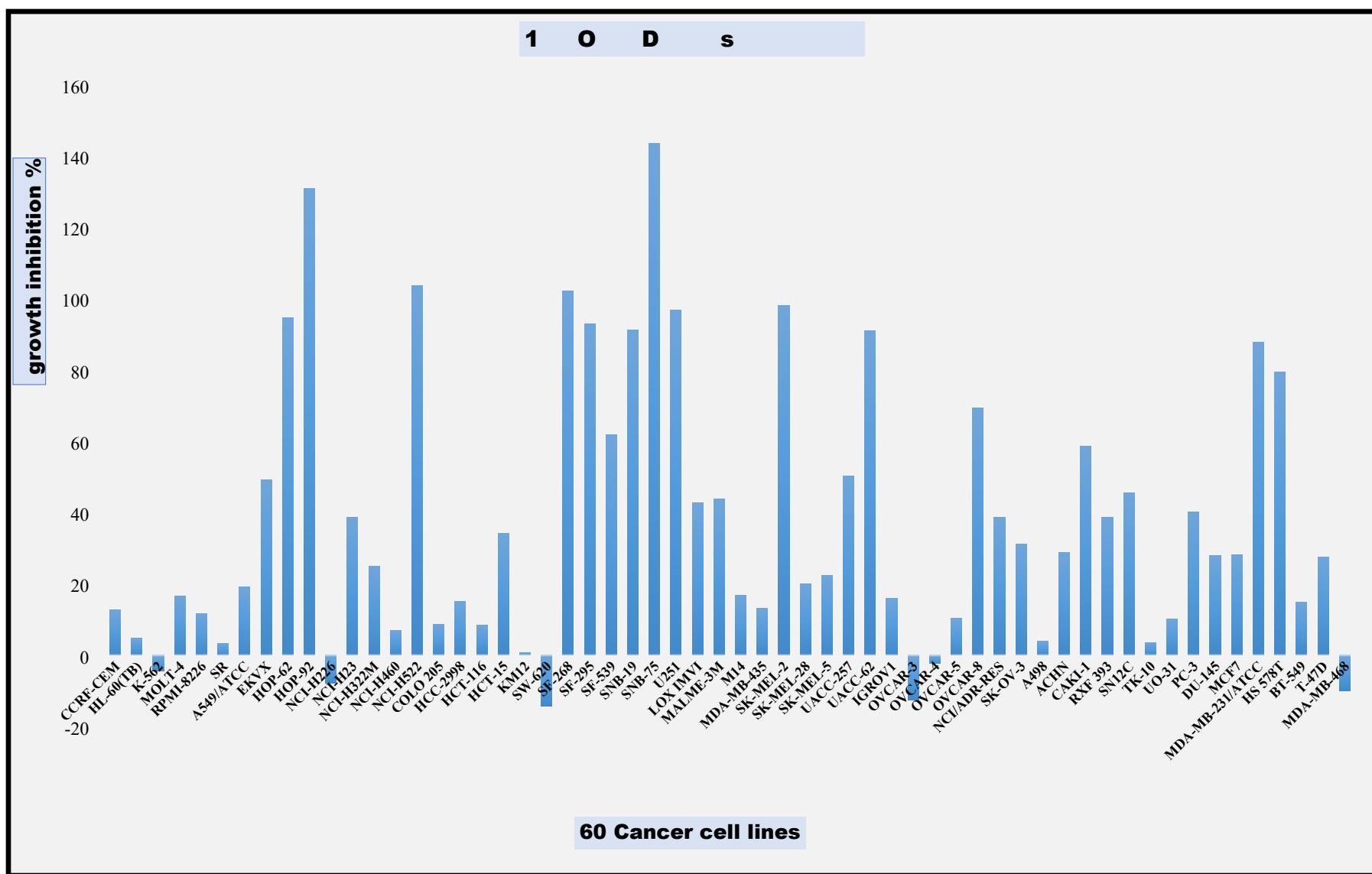
Figure 42. Growth inhibition % exerted by compound 10l at 10 μM concentration over NCI 60 cell line panel.
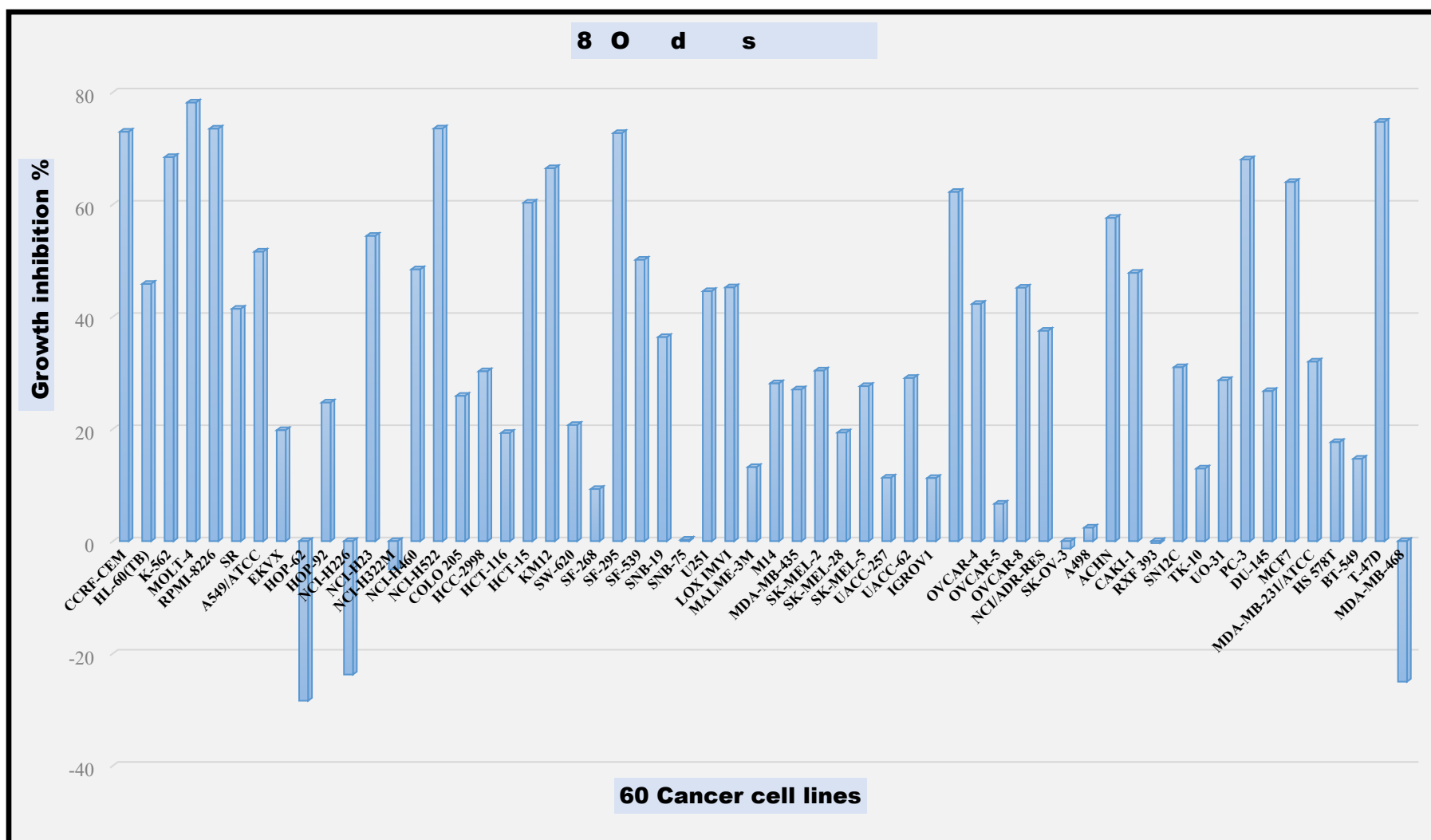
Figure 43. Growth inhibition % exerted by compound 8f at 10 μM concentration over NCI 60 cell line panel.

Table 2. Percentage of growth inhibition of NCI 60 cancer cell lines displayed by the final compounds (8a-j and 9a-d).

Panel/cell line	Percentage of Growth inhibition (GI %) in one-dose assay													
Compound No.	8a	8b	8c	8d	8e	8f	8g	8h	8i	8j	9a	9b	9c	9d
Leukemia														
CCRF-CEM	46.06	26.56	10.39	11.96	1.94	72.94	20.9	9.51	12.22	9.46	6.15	23.06	NI c	NI c
HL-60 (TB)	21.84	12.8	NI c	7.37	NI c	45.83	NI c	5.35	2.24	10.71	9.15	12.21	2.14	0.18
K-562	67.99	52.27	10.98	22.98	3.25	68.43	25.99	4.4	26.46	21.46	7.65	34.89	NI c	NI c
MOLT-4	58.82	41.1	7.9	13.46	5.06	78.14	27.57	15.53	15.88	18.51	0.77	25.58	2.17	NI c
RPMI-8226	59.24	53.35	12.51	36.32	5.46	73.49	25.09	11.48	13.85	25	19.53	9.03	NI c	5.50
SR	34.3	36.62	10.71	36.6	12.35	41.4	14.09	13.39	23.45	25.45	10.46	63.34	8.79	8.53
Non-small cell lung cancer														
A549/ATCC	41.72	36.51	NI c	21.45	7.29	51.57	10.47	8.211	15.68	11.22	1.18	NI c	3.96	6.35
EKVX	12.81	13.45	NI c	11.98	0.57	19.77	9.17	NI c	7.7	NI c	5.49	NI c	NI c	NI c
HOP-62	NI c	NI c	NI c	2.6	NI c	NI c	2.95	NI c	NI c	NI c	NI c	NI c	NI c	NI c
HOP-92	16.6	NI c	NI c	27.05	10.32	24.69	9.45	2.73	5.2	NI c	7.20	NI c	1.73	5.72
NCI-H226	31.13	NI c	16.27	0.86	NI c	NI c	NI c	NI c	NI c	NI c	24.85	NI c	NI c	9.06
NCI-H23	13.63	23.86	NI c	9.85	NI c	54.39	5.49	7.64	4.64	NI c	6.61	0.62	NI c	3.16
NCI-H322M	15.86	NI c	NI c	NI c	NI c	NI c	1.11	NI c	NI c	NI c	NI c	NI c	NI c	NI c
NCI-H460	15.76	26.8	5.73	21.45	7.29	51.57	10.47	8.211	15.68	11.22	NI c	NI c	NI c	NI c
NCI-H522	50.48	55.06	3.45	11.98	0.57	19.77	9.17	NI c	7.7	NI c	8.70	NI c	4.92	20.42
Colon cancer														
COLO 205	2.39	NI c	NI c	4.19	NI c	25.88	NI c	NI c	NI c	NI c	NI c	4.14	0.73	NI c
HCC-2998	26.84	2.18	NI c	NI c	NI c	30.26	NI c	NI c	NI c	NI c	NI c	NI c	NI c	NI c
HCT-116	20.9	8.45	NI c	6.33	NI c	19.27	NI c	NI c	14.62	0.64	NI c	NI c	NI c	NI c
HCT-15	24.5	28.64	3.78	11.42	9.79	60.3	1.58	4.85	10.36	1.43	3.52	5.12	NI c	NI c
KM12	41.09	55.15	NI c	12.29	11.56	66.44	6.77	28.23	36.68	4.61	NI c	NI c	NI c	NI c
SW-620	4.24	NI c	5.73	6.84	NI c	20.69	NI c	NI c	NI c	NI c	0.81	0.08	NI c	NI c
CNS cancer														
SF-268	15.31	1.16	17.15	11.45	-4.95	9.29	6.6	NI c	0.71	0.27	4.32	0.64	NI c	38.25
SF-295	33.32	38.7	6.2	6.81	16.98	72.7	3.87	NI c	3.32	1.14	13.94	13.14	NI c	NI c
SF-539	19.68	34.23	4.44	10.14	6.67	50.14	9	4.6	14.25	6.65	NI c	0.95	NI c	2.15

Compound No.	8a	8b	8c	8d	8e	8f	8g	8h	8i	8j	9a	9b	9c	9d
CNS cancer														
SNB-19	26.94	21.22	8.17	9.64	5.27	36.35	11.75	2.37	9.61	7.34	9.52	13.52	3.61	24.16
SNB-75	27.8	23.68	5.51	21.68	20.49	0.25	12.44	17.72	36.26	12.96	11.08	NI c	0.24	28.85
U251	31.65	25.12	NI c	12.98	5.66	44.54	4.88	0.95	9.93	2.91	0.06	8.47	NI c	18.44
Melanoma														
LOX IMVI	NI c	17.74	0.6	16.28	2.76	45.26	1.13	1.82	5.17	3.43	6.93	8.07	5.75	11.94
MALME-3M	22.26	7.47	NI c	NI c	NI c	13.18	0.29	NI c	NI c	NI c	1.62	NI c	NI c	1.68
M14	21.03	2.42	12.79	NI c	NI c	28.11	1.64	NI c	1.55	NI c	NI c	34.75	NI c	2.44
MDA-MB-435	9.58	12.29	NI c	4.92	2.94	27.03	9.63	4.72	1.77	1.3	3.75	NI c	NI c	0.26
SK-MEL-2	7.38	NI c	NI c	NI c	NI c	30.39	NI c	NI c	4.46	NI c	NI c	NI c	NI c	NI c
SK-MEL-28	43.36	9.41	NI c	4.06	NI c	19.35	NI c	NI c	NI c	NI c	NI c	3.33	NI c	NI c
SK-MEL-5	12.96	2.46	7.06	32.27	3.49	27.62	21.99	NI c	6.96	8.78	16.55	5.61	7.68	5.39
UACC-257	38.85	8.02	NI c	16.28	2.76	45.26	1.13	1.82	5.17	3.43	3.01	NI c	NI c	NI c
UACC-62	NI c	26.45	7.56	NI c	NI c	13.18	0.29	NI c	NI c	NI c	16.27	12.68	9.56	8.3
Ovarian cancer														
IGROV1	5.62	NI c	NI c	NI c	NI c	11.24	NI c	NI c	NI c	NI c	NI c	NI c	NI c	NI c
OVCAR-3	21.51	23.92	0.24	6.01	2.76	42.26	5.64	1.17	NI c	1.47	NI c	NI c	NI c	NI c
OVCAR-4	24.31	18.62	NI c	8.49	2.76	42.26	10.76	1.17	9.65	1.47	1.59	0.79	NI c	NI c
OVCAR-5	3.09	7.69	NI c	7.9	NI c	45.16	NI c	NI c	NI c	NI c	NI c	16.95	NI c	NI c
OVCAR-8	20.28	16.27	NI c	8.02	NI c	45.16	3.05	NI c	NI c	NI c	1.52	NI c	NI c	20.56
NCI/ADR-RES	5.62	7.66	NI c	0.54	NI c	NI c	NI c	NI c	NI c	NI c	7.44	NI c	NI c	1.64
SK-OV-3	NI c	10.5	NI c	NI c	NI c	NI c	NI c	NI c	3.35	NI c	NI c	NI c	NI c	NI c
Renal cancer														
786-0	NT a	NT a	7.65	NT a	NT a	NT a	NT a	NT a	NT a	NT a	NT a	5.76	NT a	NT a
A498	7.89	NI c	7.23	NI c	NI c	2.4	6.37	NI c	NI c	6.37	NI c	NI c	NI c	NI c
ACHN	50.83	42.46	1.04	20.8	NI c	57.59	7.7	0.41	9.78	6.18	5.5	NI c	NI c	NI c
CAKI-1	35.25	24.3	14.89	15.1	2.88	47.8	16.43	6.63	11.61	10.13	8.88	18.15	5.07	15.83
RXF 393	29.24	NI c	13.33	14.33	5.03	NI c	20.06	NI c	NI c	5.76	34.66	NI c	11.52	14.69
SN12C	17.28	4.36	13.32	15.79	11.29	30.98	9	3.56	4.97	1.5	12.55	1.95	NI c	5.98
TK-10	25.85	NI c	NI c	NI c	NI c	12.93	1.69	NI c	NI c	8.07	NI c	NI c	NI c	NI c
UO-31	NT a	NT a	7.65	15.91	4.27	28.68	20.29	4.6	16.22	21.01	12.75	NI c	6.198	10.01

Compound No.	8a	8b	8c	8d	8e	8f	8g	8h	8i	8j	9a	9b	9c	9d
Prostate cancer														
PC-3	43.56	31.33	0.15	5.39	2.32	68.01	15.02	3.55	10.86	2.34	5.89	9.42	1.59	6.73
DU-145	19.4	6.11	8.21	6.62	NI [c]	26.74	1.39	NI [c]	NI [c]	NI [c]	NI [c]	7.7	NI [c]	NI [c]
Breast cancer														
MCF7	53.57	33.89	20.9	33.49	16.25	63.99	13.3	26.24	25.44	20.17	12.41	NI [c]	1.884	13.46
MDA-MB-231/ATCC	19.91	5.24	2.21	14.42	NI [c]	31.99	4.62	NI [c]	2.38	NI [c]	3.42	52.19	NI [c]	6.38
HS 578T	2.11	15.62	2.19	6.35	0.52	17.64	0.8	8.3	12.45	NI [c]	5.75	14.62	NI [c]	11.51
BT-549	5.16	NI [c]	23.57	15.11	NI [c]	14.67	NI [c]	NI [c]	NI [c]	9.22	1.25	NI [c]	NI [c]	NI [c]
T-47D	58.91	59.22	13.3	35.67	15.92	74.71	53.92	15.72	40.99	40.26	8.75	NI [c]	NI [c]	2.11
MDA-MB-468	NI [c]	NI [c]	20.9	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	16.22	6.89	NI [c]	NI [c]

a: **NT**: indicates that this compound was not tested.
b: These compounds were selected for **five dose assays**.
C: NI: No inhibition effect

Table 3. Percentage of growth inhibition of NCI 60 cancer cell lines displayed by the final compounds (10a-l)

Panel/cell line	Percentage of Growth inhibition (GI %) in one-dose assay											
Compound No.	10a	10b	10c	10d	10e	10f	10g	10h	10i	10j	10k	10l [b]
Leukemia												
CCRF-CEM	4.72	NI [c]	14.51	3.72	2.40	13.47	NI [c]	NI [c]	43.39	18.78	20.49	12.75
HL-60 (TB)	NI [c]	5.88	15.25	9.81	NI [c]	12.39	11.83	11.05	36.8	21.15	21.02	4.71
K-562	6.91	10.95	49.52	8.12	NI [c]	17.56	0.85	NI [c]	23.81	71.89	43.23	NI [c]
MOLT-4	15.62	1.58	9.53	13.22	NI [c]	6.04	2.79	NI [c]	19.68	26.73	38.35	16.56
RPMI-8226	33.28	8.14	23.51	14.65	2.12	13.54	6.68	3.8	39.35	14.24	48.2	11.64
SR	3.11	0.59	52.03	21.51	4.52	37.74	11.40	NI [c]	35.17	74.55	31.41	3.25
Non-small cell lung cancer												
A549/ATCC	3.76	3.87	17.41	6.95	2.65	7.18	0.26	14.9	12.69	5.84	28.1	19.25
EKVX	9.03	12.57	NI [c]	5.01	12.8	18.38	NI [c]	9.25	3.73	3.72	20.43	49.29
HOP-62	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	5.15	NI [c]	11.5	NI [c]	10.28	12.03	94.61
HOP-92	21.87	NI [c]	6.09	0.45	3.47	27.33	NI [c]	25.81	NI [c]	12.61	11.46	130.9
NCI-H226	7.87	7.68	NI [c]	17.02	NI [c]	NI [c]	NI [c]	NI [c]	5.1	10.24	17.56	NI [c]
NCI-H23	2.73	NI [c]	6.1	1.81	7.92	19.33	NI [c]	3.97	7.14	15.24	49.11	38.64
NCI-H322M	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	15.11	25.06
NCI-H460	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	19.57	NI [c]	14.9	12.69	5.84	28.1	19.25
NCI-H522	24.96	16.35	18.17	15.37	8.03	27.1	4.77	9.25	3.73	3.72	20.43	49.29
Colon cancer												
COLO 205	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	4.1	NI [c]	NI [c]	NI [c]	NI [c]	0.59	8.59
HCC-2998	NI [c]	NI [c]	NI [c]	1.52	NI [c]	0.14	NI [c]	NI [c]	NI [c]	20.41	NI [c]	15.01
HCT-116	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	5.19	NI [c]	NI [c]	NI [c]	14.64	3.49	8.42
HCT-15	8.97	NI [c]	1.53	NI [c]	0.12	11.75	NI [c]	NI [c]	19.53	54.48	45.91	34.17
KM12	NI [c]	NI [c]	9.29	3.29	NI [c]	0.56	NI [c]	NI [c]	1.84	29.81	9.1	0.83
SW-620	NI [c]	NI [c]	12.98	NI [c]	NI [c]	2.92	NI [c]	NI [c]	2.43	34.03	NI [c]	NI [c]
CNS cancer												
SF-268	NI [c]	NI [c]	2.0	4.34	NI [c]	3.71	NI [c]	19.66	NI [c]	10.58	4.41	102.2
SF-295	19.35	NI [c]	7.31	NI [c]	6.52	37.22	NI [c]	NI [c]	5.8	17.07	51.42	93.03
SF-539	5.14	8.66	7.59	6.51	5.18	17.86	6.57	38.33	8.83	16.39	24.46	61.85
SNB-19	11.82	4.04	13.70	5.33	14.6	13.46	2.22	34.98	10.19	25.74	22.06	91.19
SNB-75	22.59	20.92	7.67	24.55	13.27	14.76	12.83	15.58	9.6	27.37	12.55	143.6

Compound No.	10a	10b	10c	10d	10e	10f	10g	10h	10i	10j	10k	10l [b]
U251	NI[c]	3.47	5.20	6.05	NI[c]	12.73	NI[c]	29.41	5.9	10.2	22.79	96.91
Melanoma												
LOX IMVI	15.48	21.23	15.28	12.61	4.02	15.63	4.62	15.54	29.62	27.24	31.04	42.87
MALME-3M	NI[c]	4.41	13.28	1.43	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	43.82
M14	11.34	NI[c]	10.07	NI[c]	NI[c]	16.81	0.56	NI[c]	NI[c]	40.25	2.87	16.83
MDA-MB-435	9.07	NI[c]	51.48	1.35	NI[c]	12.28	NI[c]	11.8	11.38	88.03	14.16	13.25
SK-MEL-2	0.62	NI[c]	NI[c]	5.02	NI[c]	3.76	NI[c]	NI[c]	NI[c]	13.1	5.08	98.03
SK-MEL-28	NI[c]	NI[c]	NI[c]	NI[c]	7.43	0.4	NI[c]	1.01	NI[c]	21.85	14.11	20
SK-MEL-5	16.25	22.57	15.34	6.52	27.9	17.63	5.43	28.41	8.27	25.93	49.08	22.47
UACC-257	NI[c]	11.77	9.06	0.71	NI[c]	2.41	0.85	12.67	7.51	0.12	3.68	50.24
UACC-62	20.63	18.69	28.42	17.27	7.95	15.89	7.19	15.72	16.5	36.49	39.16	91.02
Ovarian cancer												
IGROV1	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	5.38	NI[c]	15.94
OVCAR-3	2.76	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	22.03	7.53	NI[c]
OVCAR-4	7.71	1.49	6.86	NI[c]	3.47	11.07	NI[c]	45.23	0.8	NI[c]	13.19	NI[c]
OVCAR-5	2.64	NI[c]	NI[c]	NI[c]	1	9.93	NI[c]	NI[c]	2.82	8.82	19.61	10.38
OVCAR-8	3.17	0.43	5.38	NI[c]	NI[c]	6.61	NI[c]	31.91	0.97	2.95	19.06	69.34
NCI/ADR-RES	1.06	4.16	14.06	NI[c]	NI[c]	NI[c]	NI[c]	33.2	3.88	22.2	45.67	38.65
SK-OV-3	NI[c]	NI[c]	NI[c]	11.1	NI[c]	NI[c]	5.98	NI[c]	6.88	2.46	0.2	31.22
Renal cancer												
786-0	NT[a]	NT[a]	NT[a]	NT[a]	NT[a]	NT[a]	NT[a]	NT[a]	NT[a]	87.42	NT[a]	NT[a]
A498	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	0.69	NI[c]	NI[c]	NI[c]	12.94	NI[c]	3.86
ACHN	13.55	5.95	NI[c]	5.17	6.19	5.35	NI[c]	10.77	2.08	14.44	15.51	28.91
CAKI-1	15.23	5.83	18.72	15.7	11.38	15.54	8.81	18.38	11.26	18.21	12.59	58.56
RXF 393	20.6	NI[c]	11.3	NI[c]	13.13	30.93	NI[c]	18.31	3.14	32.42	15.89	38.74
SN12C	7.86	0.21	8.72	3.89	8.49	22.73	NI[c]	14.1	0.25	10.74	28.99	45.47
TK-10	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	3.60
UO-31	21.43	32.44	13.77	34.5	11.65	21.92	12.15	9.79	13.42	17.14	28.86	10.25
Prostate cancer												
PC-3	15.15	19.99	11.33	4.07	0.48	9.97	NI[c]	11.75	2.84	8.97	36.85	40.25
DU-145	NI[c]	NI[c]	NI[c]	NI[c]	NI[c]	1.12	NI[c]	NI[c]	NI[c]	2.95	1.92	28.06
Breast cancer												
MCF7	26.04	18.25	18.13	16.8	12.67	9.62	10.52	5.48	8.68	48.98	33.36	28.13
MDA-MB-231/ATCC	11.39	8.16	2.64	NI[c]	10.34	14.64	NI[c]	16.02	NI[c]	23.7	15.14	87.74
HS 578T	4.84	14.3	10.93	5.3	NI[c]	NI[c]	NI[c]	17.94	NI[c]	14.75	10.57	79.37

Compound No.	10a	10b	10c	10d	10e	10f	10g	10h	10i	10j	10k	10l [b]
BT-549	1.38	NI [c]	NI [c]	NI [c]	4.07	13.67	NI [c]	NI [c]	NI [c]	22.74	4.89	14.89
T-47D	28.42	27.71	12.85	14.9	NI [c]	24.08	11.69	18.57	8.81	42.3	30.92	27.54
MDA-MB-468	NI [c]	NI [c]	NI [c]	NI [c]	8.84	0.94	NI [c]	NI [c]	15.12	48.98	NI [c]	NI [c]

a*:* **NT**: indicates that this compound was not tested.
b: These compounds were selected for **five dose assays**.
C: NI: No inhibition effect

Table 4. Percentage of growth inhibition of NCI 60 cancer cell lines displayed by the final compounds (11a-f, 17a-b, 18a-b and 19a-b).

Panel/cell line	Percentage of Growth inhibition (GI %) in one-dose assay											
Compound No.	11a	11b	11c	11d	11e	11f	17a[b]	17b	18a	18b	19a	19b
Leukemia												
CCRF-CEM	10.16	12.55	3.14	6.07	8.18	6.84	14.32	6.22	16.05	13.80	25.88	28.39
HL-60 (TB)	NI [c]	8.87	NI [c]	NI [c]	3.25	NI [c]	19.16	20.74	4.13	NI [c]	6.52	1.39
K-562	12.16	9.23	NI [c]	12.3	16.64	15.22	NT [a]	NT [a]	NT [a]	NT [a]	NT [a]	NT [a]
MOLT-4	7.01	34.65	NI [c]	7.12	11.79	6.91	21.08	8.21	23.34	9.25	8.54	15.61
RPMI-8226	27.72	28.6	8.19	21.41	23.27	15.48	33.03	6.22	19.77	16.34	22.64	30.27
SR	25.18	24.81	7.46	29.47	25.6	12.69	NT [a]	NT [a]	NT [a]	NT [a]	NT [a]	NT [a]
Non-small cell lung cancer												
A549/ATCC	8.52	11.66	3.72	13.11	7.2	5.68	<u>73.95</u>	NI [c]	7.69	NI [c]	NI [c]	0.89
EKVX	10.46	3.11	11	11.14	9.49	NI [c]	68.08	13.22	NI [c]	10.29	13.13	21.82
HOP-62	8.83	3.36	NI [c]	NI [c]	NI [c]	NI [c]	<u>98.09</u>	NI [c]	NI [c]	NI [c]	6.97	17.26
HOP-92	8.63	12.93	7.39	13.16	25.22	10.03	<u>100.14</u>	NI [c]	NI [c]	NI [c]	43.16	44.69
NCI-H226	NI [c]	16.32	17.57	NI [c]	NI [c]	18.44	<u>88.22</u>	NI [c]	NI [c]	2.46	16.26	18.58
NCI-H23	9.6	12.64	0.78	9.83	16.25	0.25	<u>77.09</u>	7.29	2.68	4.53	8.85	11.84
NCI-H322M	NI [c]	5.26	7.9	NI [c]	NI [c]	NI [c]	64.72	NI [c]	0.54	NI [c]	NI [c]	NI [c]
NCI-H460	NI [c]	1.11	NI [c]	NI [c]	NI [c]	0.7	62.21	NI [c]	3.42	NI [c]	NI [c]	0.66
NCI-H522	8.52	11.66	3.72	13.11	7.2	5.68	39.38	8.89	6.50	3.079	10.74	20.22
Colon Cancer												
COLO 205	NI [c]	1.92	6.39	NI [c]	NI [c]	2.30	37.79	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]
HCC-2998	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	50.38	NI [c]	NI [c]	NI [c]	NI [c]	7.56
HCT-116	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	2.59	<u>75.90</u>	5.63	11.08	7.16	7.98	9.37
HCT-15	5.74	1.89	NI [c]	2.17	NI [c]	4.40	50.57	7.03	10.45	2.16	4.92	11.86
HT29	NT [a]	NT [a]	NT [a]	NT [a]	NT [a]	NT [a]	<u>81.21</u>	NI [c]	NI [c]	NI [c]	7.35	NI [c]
KM12	NI [c]	NI [c]	1.31	NI [c]	NI [c]	NI [c]	31.57	NI [c]	9.65	6.51	NI [c]	2.45
SW-620	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	2.71	39.63	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]
CNS cancer												
SF-268	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	16.64	NI [c]	NI [c]	NI [c]	NI [c]	9.15
SF-295	5.04	1.95	NI [c]	5.91	10.50	6.6	152.92	NI [c]	13.85	1.08	14.25	30.14
SF-539	11.30	19.67	3.44	16.53	2.43	5.29	NT [a]	NT [a]	NT [a]	NT [a]	NT [a]	NT [a]

Compound No.	11a	11b	11c	11d	11e	11f	17a[b]	17b	18a	18b	19a	19b
SNB-19	9.08	7.90	8.66	9.31	10.82	14.91	65.65	NI [c]	1.14	4.25	5.43	11.81
SNB-75	18.07	18.81	23.17	14.35	14.35	16.94	169.29	NI [c]	NI [c]	84.53	10.55	25.38
U251	6.59	3.20	8.68	3.56	5.95	10.43	99.82	NI [c]	NI [c]	NI [c]	NI [c]	0.03
Melanoma												
LOX IMVI	8.69	12.73	8.12	10.89	11.04	2.19	88.79	NI [c]	12.30	5.55	11.04	13.49
MALME-3M	NI [c]	1.28	NI [c]	NI [c]	NI [c]	NI [c]	78.80	NI [c]	10.73	12.26	26.11	22.35
M14	8.02	2	6.6	NI [c]	NI [c]	0.95	71.18	NI [c]	0.50	2.28	3.83	4.75
MDA-MB-435	1.36	8.06	6.2	0.81	5.65	NI [c]	44.45	2.14	0.98	NI [c]	NI [c]	1.19
SK-MEL-2	NI [c]	3.9	NI [c]	NI [c]	NI [c]	2.24	35.38	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]
SK-MEL-28	NI [c]	NI [c]	1.82	NI [c]	NI [c]	NI [c]	114.70	NI [c]	NI [c]	NI [c]	NI [c]	3.82
SK-MEL-5	NI [c]	21.9	20.44	19.8	12.54	11.08	31.39	2.69	4.49	8.09	14.56	20.27
UACC-257	NI [c]	6	1.42	NI [c]	2.91	0.96	67.16	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]
UACC-62	18.9	24.94	14.44	27.84	29.57	19.38	61.36	5.86	13.68	4.15	31.18	44.05
Ovarian Cancer												
IGROV1	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	43.21	4.98	7.67	6.81	15.10	17.78
OVCAR-3	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	62.59	NI [c]	NI [c]	NI [c]	5.64	5.47
OVCAR-4	2.55	8.27	NI [c]	1.74	NI [c]	NI [c]	36.82	NI [c]	NI [c]	NI [c]	20.18	9.84
OVCAR-5	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]	48.10	NI [c]	NI [c]	NI [c]	9.81	12.82
OVCAR-8	3.85	6.47	0.82	1.32	3.43	5.33	63.48	NI [c]	NI [c]	NI [c]	1.14	7.74
NCI/ADR-RES	NI [c]	1.68	NI [c]	4.39	1.36	6.02	85.72	0.83	2.91	3.92	8.26	11.79
SK-OV-3	NI [c]	NI [c]	NI [c]	NI [c]	2.12	NI [c]	82.62	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]
Renal Cancer												
786-0	NT [a]	NT [a]	NT [a]	NT [a]	NT [a]	NT [a]	88.25	5.35	17.17	14.01	21.34	18.63
A498	NI [c]	2.07	NI [c]	2.51	NI [c]	4.12	NI [c]	NI [c]	1.03	9.20	4.87	9.72
ACHN	0.8	0.16	6.41	0.38	NI [c]	7.91	103.14	NI [c]	11.40	2.46	11.27	8.44
CAKI-1	9.78	15.42	12.61	15.37	16.84	4.43	66.40	11.32	24.64	9.55	40.57	38.22
RXF 393	0.15	0.76	7.67	29.53	34.88	24.31	NT [a]	NT [a]	NT [a]	NT [a]	NT [a]	NT [a]
SN12C	NI [c]	NI [c]	1.79	10.04	16.4	14.77	48.59	NI [c]	NI [c]	NI [c]	0.32	16.34
TK-10	7.59	1.85	NI [c]	NI [c]	7.16	4.98	44.74	NI [c]	NI [c]	NI [c]	9.62	6.55
UO-31	16.7	18.31	10.68	14.89	20.41	NI [c]	76.22	1.00	7.96	3.08	29.89	33.87
Prostate Cancer												
PC-3	9.4	16.82	8.51	4.84	13.56	16.72	62.20	NI [c]	NI [c]	NI [c]	16.70	23.02
DU-145	NI [c]	0.73	NI [c]	NI [c]	NI [c]	5.48	91.48	NI [c]	NI [c]	NI [c]	NI [c]	NI [c]

Compound No.	11a	11b	11c	11d	11e	11f	17a[b]	17b	18a	18b	19a	19b
Breast Cancer												
MCF7	20.68	20.86	10.13	9.02	13.6	14.85	<u>72.68</u>	14.89	27.12	24.04	20.64	25.87
MDA-MB-231/ATCC	10.33	10.74	6.56	NI [c]	3.55	7.78	140.43	NI [c]	NI [c]	7.22	18.59	27.50
HS 578T	9.19	10.87	12.28	13.67	6.47	14.44	47.16	10.30	11.98	10.41	33.05	29.69
BT-549	NI [c]	6.06	NI [c]	NI [c]	3.17	3.72	<u>95.48</u>	28.49	18.88	18.60	24.67	20.76
T-47D	15.15	12.93	2.97	1.5	8.75	4.35	44.94	18.97	24.75	17.61	26.15	26.87
MDA-MB-468	NI [c]	23.76	NI [c]	NI [c]	NI [c]	14.85	<u>88.08</u>	NI [c]	NI [c]	NI [c]	20.09	21.60

a*: **NT**: indicates that this compound was not tested.
b: These compounds were selected for five dose assays.
C: NI: No inhibition effect

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Table 5. *In vitro* tumor 50% Growth Inhibition (GI$_{50}$, μM), of compounds (Xl & XVIIa)

Panel cell line	GI$_{50}$ (μM) of the selected compounds	
	XVIIa	**Xl**
Leukemia		
CCRF-CEM	100	100
HL-60 (TB)	83.17	100
K-562	100	100
MOLT-4	100	100
RPMI-8226	5.49	100
SR	NT[a]	100
Non small cell lung cancer		
A549/ATCC	NT	65.10
EKVX	**3.54**	25.20
HOP-62	**1.82**	10.0
HOP-92	**2.51**	**3.18**
NCI-H226	6.45	22.60
NCI-H23	**3.54**	14.70
NCI-H322M	100	23.70
NCI-H460	34.67	21.30
NCI-H522	100	**4.55**
Colon cancer		
COLO 205	100	100
HCC-2998	100	18.90
HCT-116	27.54	23.20
HCT-15	100	26.80
HT29	24.0	100
KM12	27.50	100
SW-620	100	100
CNS cancer		
SF-268	**2.82**	**6.91**
SF-295	**2.69**	**7.23**
SF-539	NT[a]	11.10
SNB-19	**2.75**	10.60
SNB-75	**3.98**	**3.92**
U251	NT[a]	**6.94**
Melanoma		
LOX IMVI	100	37.30
MALME-3M	NT[a]	93.60
M14	**2.57**	59.40
MDA-MB-435	5.89	100
SK-MEL-2	**1.86**	11.30
SK-MEL-28	**2.0**	100
SK-MEL-5	NT[a]	100
UACC-257	**3.24**	**5.59**
UACC-62	**2.34**	**4.07**

Table 5. (continued)

| Panel/cell line	GI$_{50}$ (µM) of XVIIa	GI$_{50}$ (µM) of Xl
Ovarian cancer		
IGROV1	4.27	26.80
OVCAR-3	5.62	100
OVCAR-4	NT[a]	100
OVCAR-5	NT[a]	26.10
OVCAR-8	**3.47**	6.24
NCI/ADR-RES	NT[a]	19.80
SK-OV-3	NT[a]	15.30
Renal cancer		
786-0	NT[a]	14.0
A498	**2.09**	19.30
ACHN	3.24	17.90
CAKI-1	**2.57**	100
RXF 393	**1.66**	6.60
SN12C	**3.02**	18.90
TK-10	**2.82**	24.60
UO-31	NT[a]	86.10
Prostate cancer		
PC-3	**3.63**	53.80
DU-145	5.62	17.90
Breast cancer		
MCF7	**2.44**	100
MDA-MB-231/ATCC	NT[a]	6.83
HS 578T	**4.47**	5.80
BT-549	19.50	9.25
T-47D	NT[a]	28.50
MDA-MB-468	**1.66**	16.40

9. Molecular docking studies

Table 6. The docking poses and amino acids involved in the binding interactions of the tested compounds with VEGFR-2 enzyme.

Compound code	C- docker interaction energy	Common Binding Interactions	
Sorafenib	-52.93	**H- donor**	**Urea NH**----------------------GLU885 **Urea C=O**---------------------ASP046 **Pyridine amide NH**---------CYS919
		Arene-H	**Pyridine ring**--------------LEU1035, PHE1047, LEU840, VAL848, ALA866 **Phenyl ring**------ILE888, LEU889, ILE892, VAL898, LEU1019 & VAL916
8a 8b 8c 8d 8e 8f 8g 8h 8i 8j	-25.41 -39.83 -26.32 -13.23 -36.14 -38.31 -28.09 -39.66 -26.90 -29.46	**H- donor**	**2Urea NH**-----------------------GLU885 **Urea C=S**------------------------ASP1046 **Pyridazine C=O**----------------CYS919, **Pyridazine NH**------------------GLU917
		Arene-H	**Pyridazine ring**-----------------ALA866, VAL848 & LEU1035 **Phenyl ring**-----------ILE888, VAL916, LEU1019, LEU889 & LEU889
9a 9b 9c 9d	-25.56 -25.93 -27.22 -23.29	**H- donor**	**2Thiourea NH**--------------------GLU885 **2Thiourea NH**------------------ASP1046 **Pyridazine C=O**-----------------CYS919 **Pyridazine NH** ------------------GLU917
		Arene-H	**Phenyl ring**-----------------------ILE888, VAL848, ILE892, VAL916 & LYS868
10a 10b 10c 10d 10e 10f 10g 10h 10i 10j 10k 10l	-27.28 -27.99 -29.36 -25.23 -20.83 -28.42 -27.16 -31.24 -28.71 -27.69 -27.98 -30.05	**H- donor**	**Urea NH**--------------------------GLU885 **2Thiourea NH**------------------ASP1046 **Pyridazine C=O**-----------------CYS919
		Arene-H	**Pyridazine ring**-----------------ALA866, VAL848, LEU1035 **Phenyl ring**----------------------ILE888, VAL848, LEU1035, LEU889, ALA866 & VAL916

Table 6 (Continued)

Compound code	C- docker interaction energy	Common Binding Interactions		
11a **11b** **11c** **11d** **11e** **11f**	-24.15 -20.24 -25.39 -25.81 -21.62 -20.36	**H- donor**	**Sulfonamide NH**-----------------GLU885 **Sulfonamide S=O**--------------ASP1046 **Pyridazine C=O**-----------------CYS919, **Pyridazine NH**-------------------GLU917	
		Arene-H	**Pyridazine ring**----------------ALA866, VAL848 & LEU1035 **Phenyl ring**----------------------VAL916**,** VAL848 & LEU889.	
17a **17b**	-32.65 -30.73	**H- donor**	**2Urea NH**-----------------------GLU885 **Thiourea C=S**------------------ASP1046	
		Arene-H	**Pyridazine ring**-----------------ALA866, LEU1035 & PHE918 **Phenyl ring**-----------------------ILE892**,** VAL848, LEU1019, CYS1045,VAL916, HIS1026, LEU889 & LEU889.	
18a **18b**	-34.98 -32. 54	**H- donor**	**Benzoyl Thiourea C=O** --------CYS919	
		Arene-H	**Pyridazine ring**----------------- LEU889 **Phenyl ring**----------------------LEU840, VAL848, CYS1045, VAL916, HIS1026, LEU889 & VAL899.	
19a **19b**	-28.04 -24.98	**H- donor**	**Sulfonamide NH**-----------------GLU885 **Sulfonamide S=O**--------------ASP1046	
		Arene-H	**Pyridazine ring**---------------- ALA866, LEU1035 & PHE918 **Phenyl ring**-------------------- VAL848, LEU1035, LEU1019, LEU889, ILE892, VAL916& LEU889 & ALA866.	
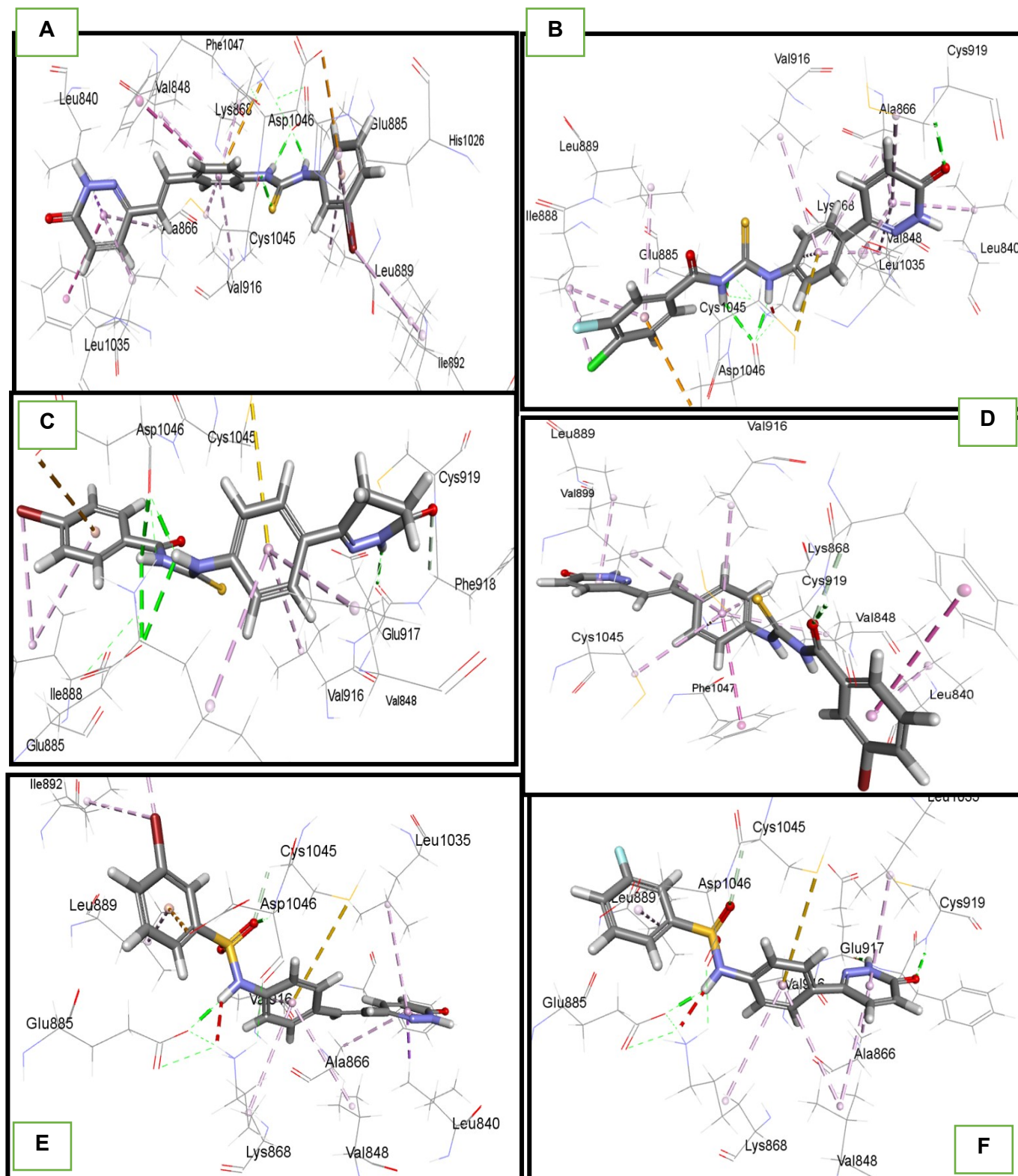
Figure 44. Docking poses (2D & 3D) and amino acids involved in the binding interactions of: [**A**] a representative compound of phenylthiourea in series **I (8a)**, [**B**] series **III (9j)**, [**C**] series **II (9c)**, [**D**] series **VI (18a)**, series **IV (11c)** and series **VII (19a)** into the active site.

10. Cell Cycle apoptosis

Table 7. Primer's sequence used for *qRT-PCR* of lung cancer cell lines

| Gene	Primer sequence	GenBank (accession no)
Bcl-2	F: CCT CGC TGC ACA AAT ACT CC R: TGG AGA GAA TGT TGG CGT CT	M14745.1
P53	F: TGG CCA TCT ACA AGC AGT CA R: GGT ACA GTC AGA GCC AAC CT	X60020.1
BAX	F: CTG TAT GTG GGA CTG GTG GT R: GGA AAT GAG GGG TGG AAG GA	XM_054373112.1
GAPDH	F: CAC ATC GCT CAG ACA CCA TG R: TGA CGG TGC CAT GGA ATT TG	AK026525.1

BCL-2: B-cell lymphoma-2 gene; *BAX*: Bcl-2-associated X protein encoding gene; *p53:* tumor suppressor gene.
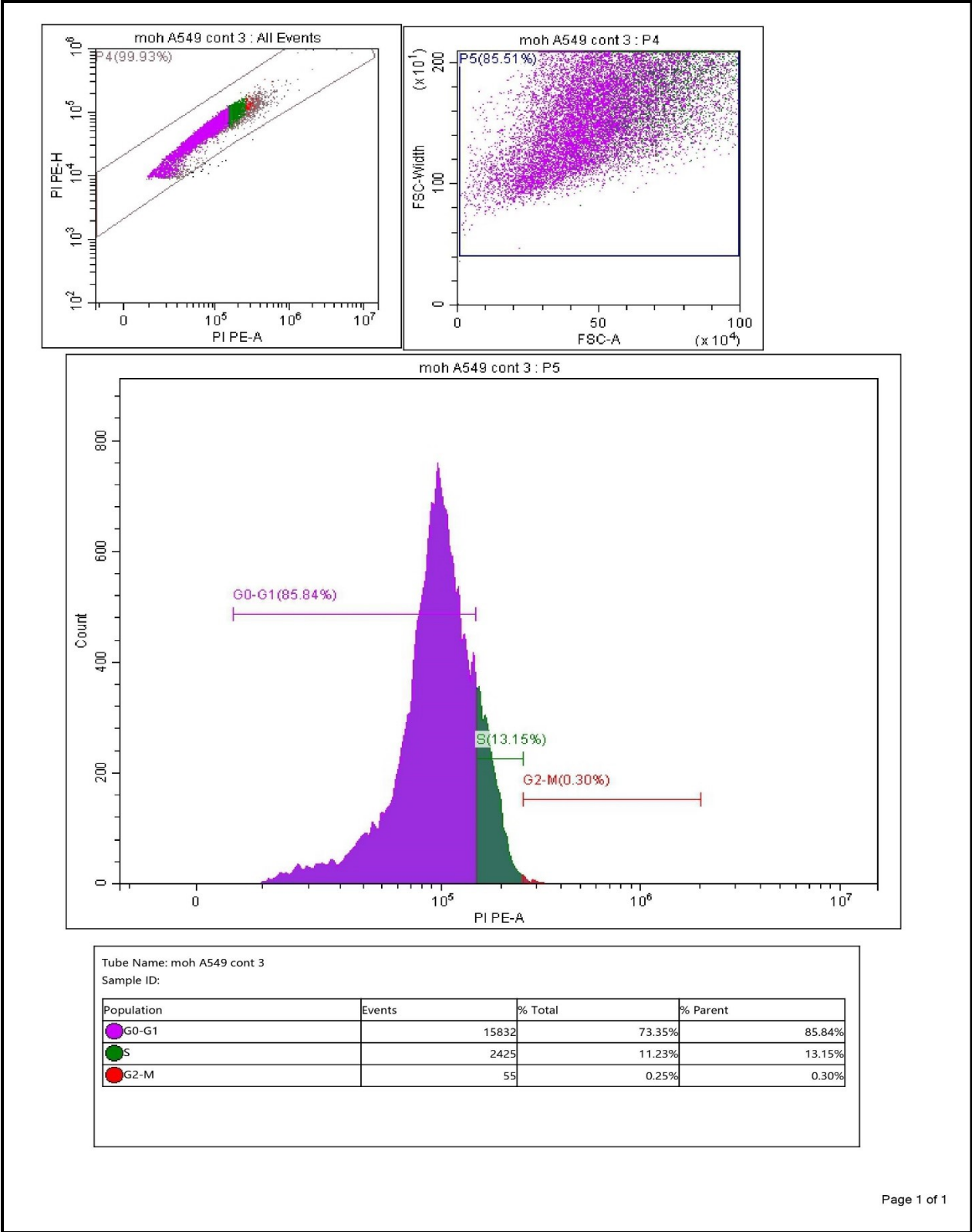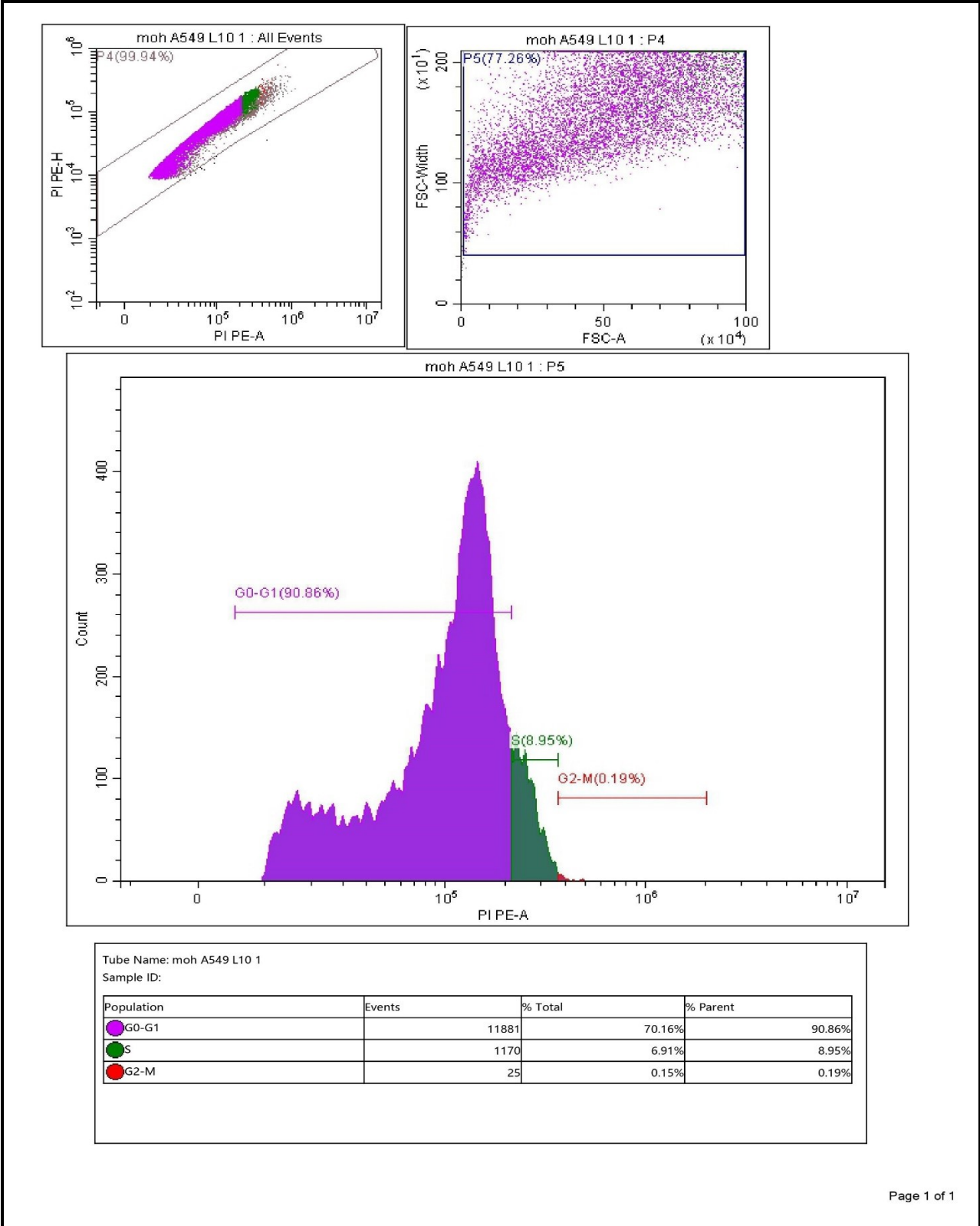
11. Cell Cycle analysis
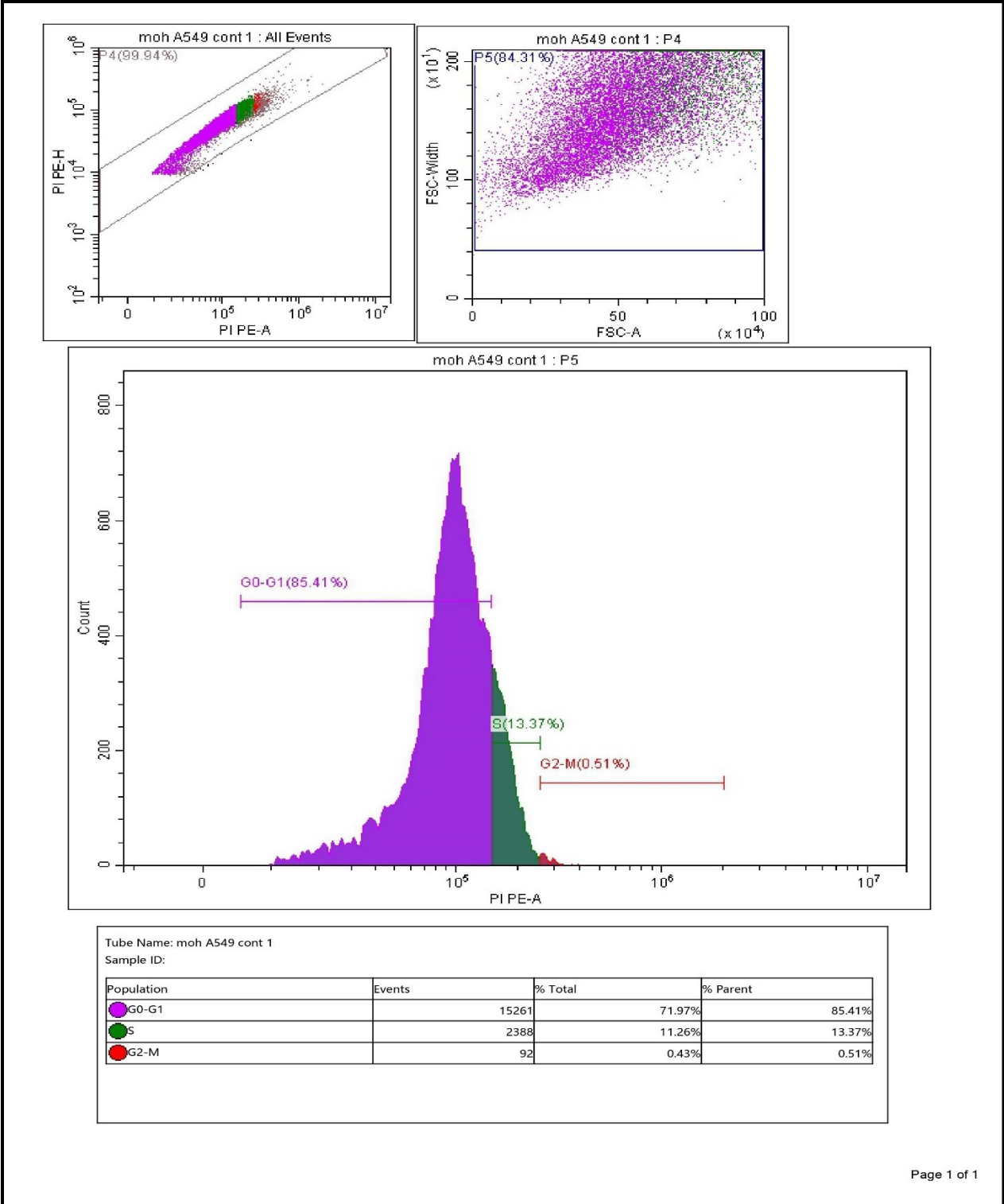
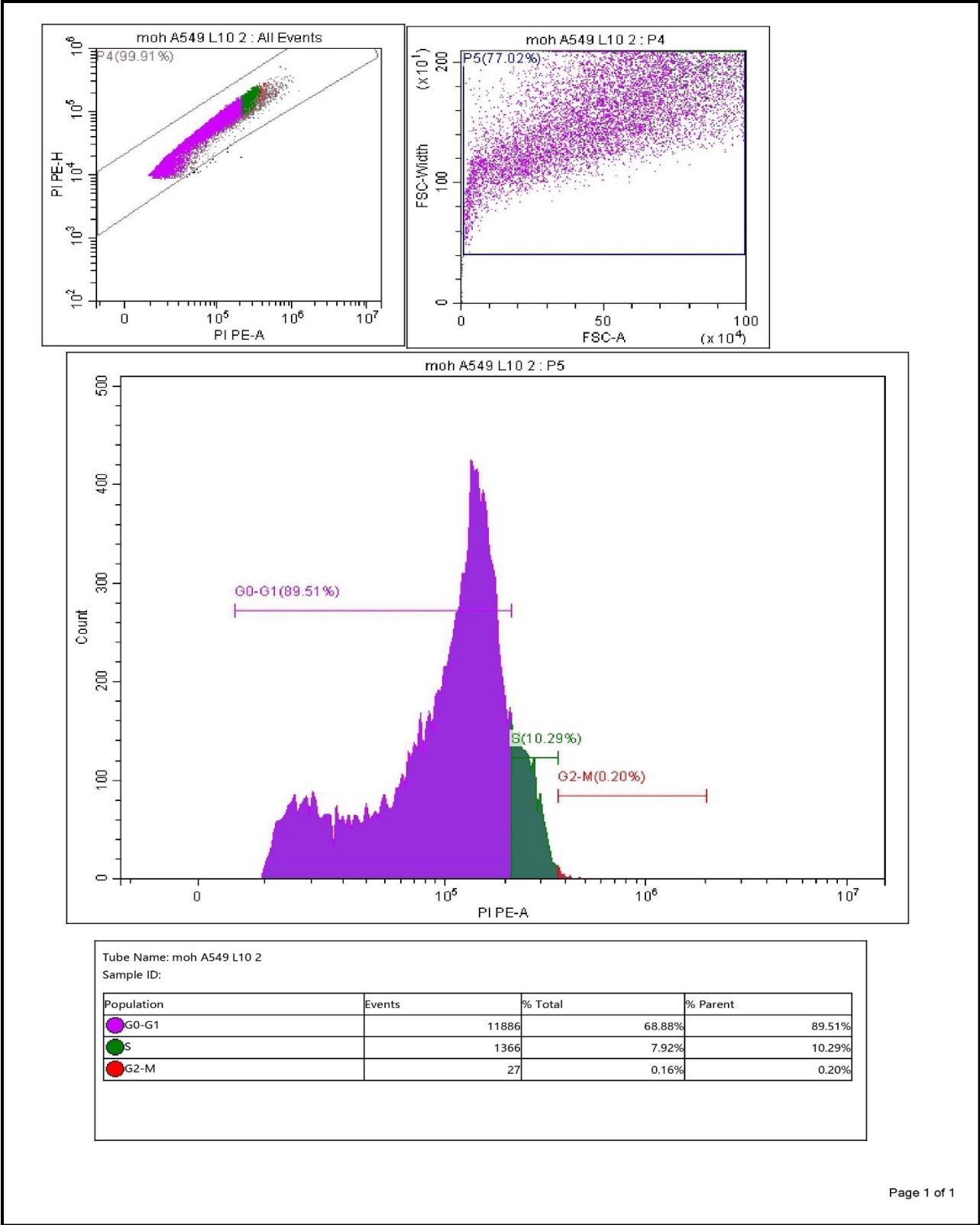**Figure 45a. Histograms of the cell cycle and the cell distribution in A549/ATCC cell line (control 1).**
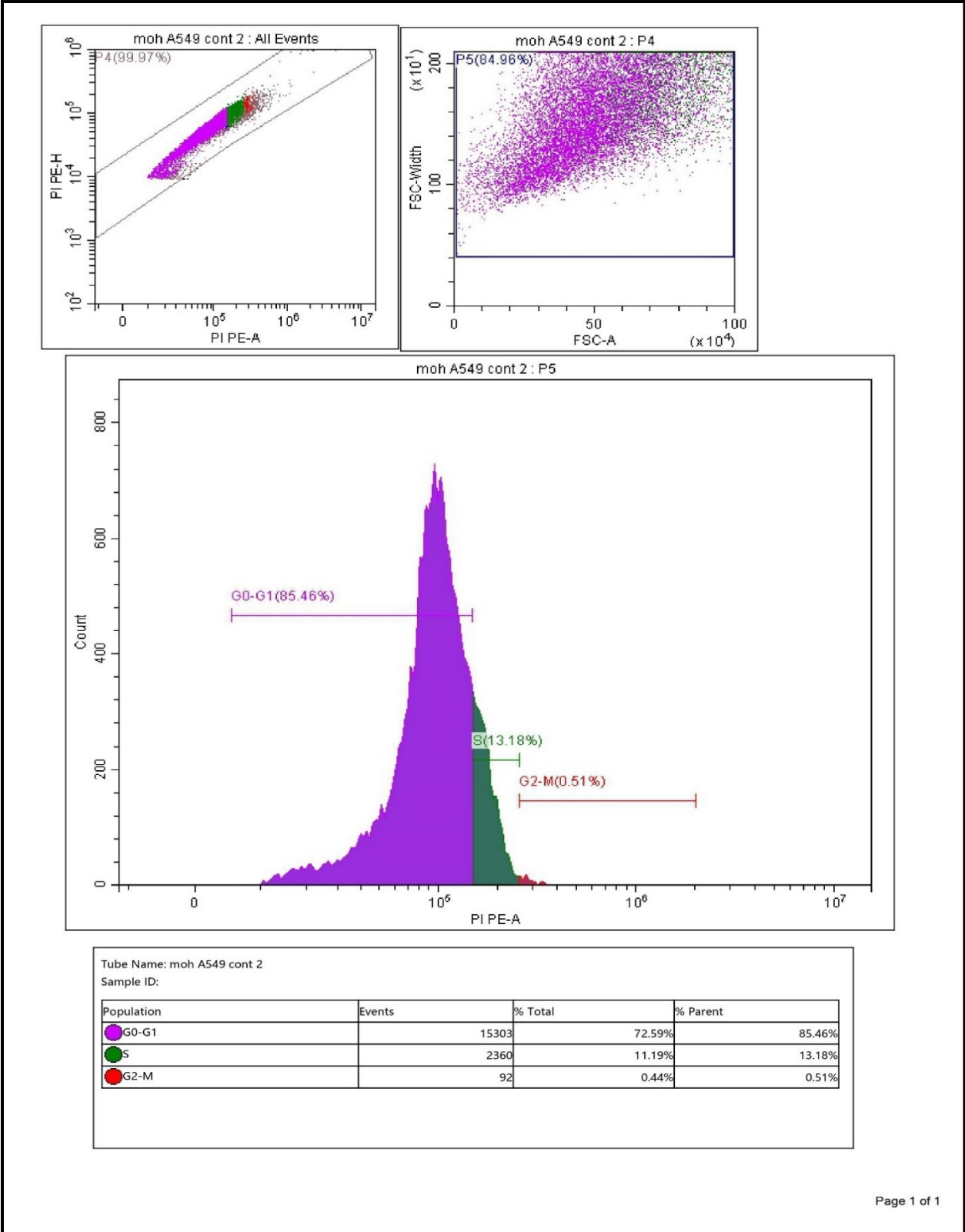
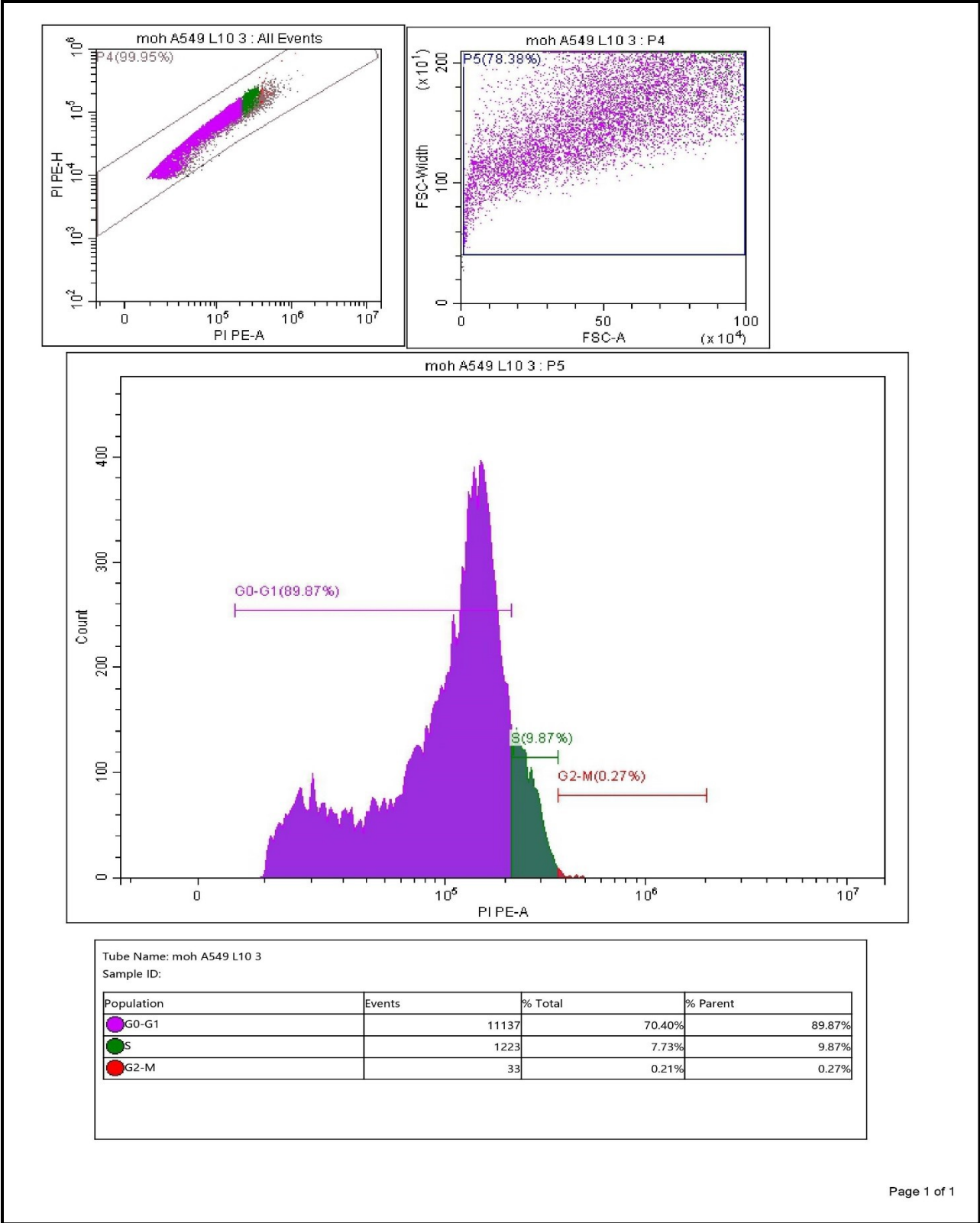**Figure 45b. Histograms of the cell cycle and the cell distribution in A549/ATCC cell line (control 2).**

Figure 45c. Histograms of the cell cycle and the cell distribution in A549/ATCC cell line (control 3).

Figure 45d. Histograms of the cell cycle and the cell distribution or compound 10I in A549/ATCC cell line (treatment 1).

Figure 45e. Histograms of the cell cycle and the cell distribution or compound 10l in A549/ATCC cell line (treatment 2).

Figure 45f. Histograms of the cell cycle and the cell distribution or compound 10l in A549/ATCC cell line (treatment 3).