

## *Supporting Information*

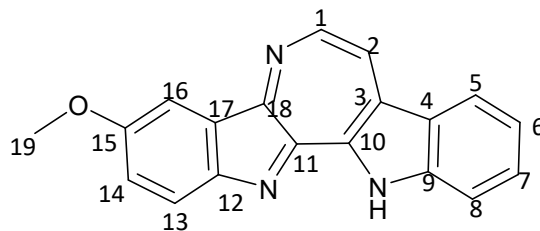
### **Direct, four-step synthetic pathway to iheyamine A and several analogues**

Wenfei Wei,<sup>†</sup> Dinglei Xiang,<sup>†</sup> and Sheng Liu\*

**Table S1** Comparison of Natural vs. Synthetic Iheyamine A (Free base, <sup>1</sup>H NMR only).

**Table S2** Comparison of Natural vs. Synthetic Iheyamine A (TFA salt, <sup>1</sup>H and <sup>13</sup>C NMR).

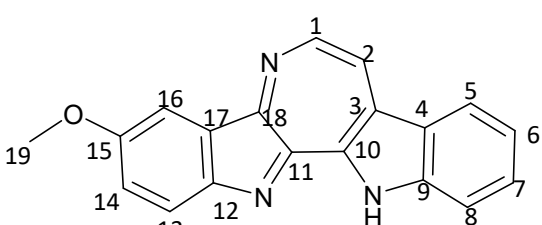
NMR and HRMS of compounds **6**, **6a-i**, **7**, **7a-i**, **8a**, Iheyamines A (**1**), **1a-i**.

**Table S1** Comparison of Natural vs. Synthetic Iheyamine A (Free base, <sup>1</sup>H NMR only).**Iheyamine A-Free Base****<sup>1</sup>H NMR**

Pos.	Lit <sup>1</sup> . (500 MHz, CDCl <sub>3</sub> )	Synthetic (600 MHz, CDCl <sub>3</sub> )
1	9.04, d (6.4)	9.05, d (6.5)
2	8.55, d (6.4)	8.56, d (6.5)
3	-	-
4	-	-
5	8.37, d (7.9)	8.39, d (7.8)
6	7.52, dd (7.9, 7.0)	7.53, t (7.4)
7	7.74, dd (7.9, 7.0)	7.72, t (7.6)
8	7.86, d (7.9)	7.81, d (7.8)
9	-	-
10	-	-
11	-	-
12	-	-
13	7.70, d (8.9)	7.64, d (8.7)
14	7.37, dd (8.9, 2.4)	7.35, dd (8.7, 2.4)
15	-	-
16	8.01, d (2.4)	8.03, d (2.4)
17	-	-
18	-	-
19	4.02, s	4.04, s

**Table S2** Comparison of Natural vs. Synthetic Iheyamine A (TFA salt,  $^1\text{H}$  and  $^{13}\text{C}$  NMR).

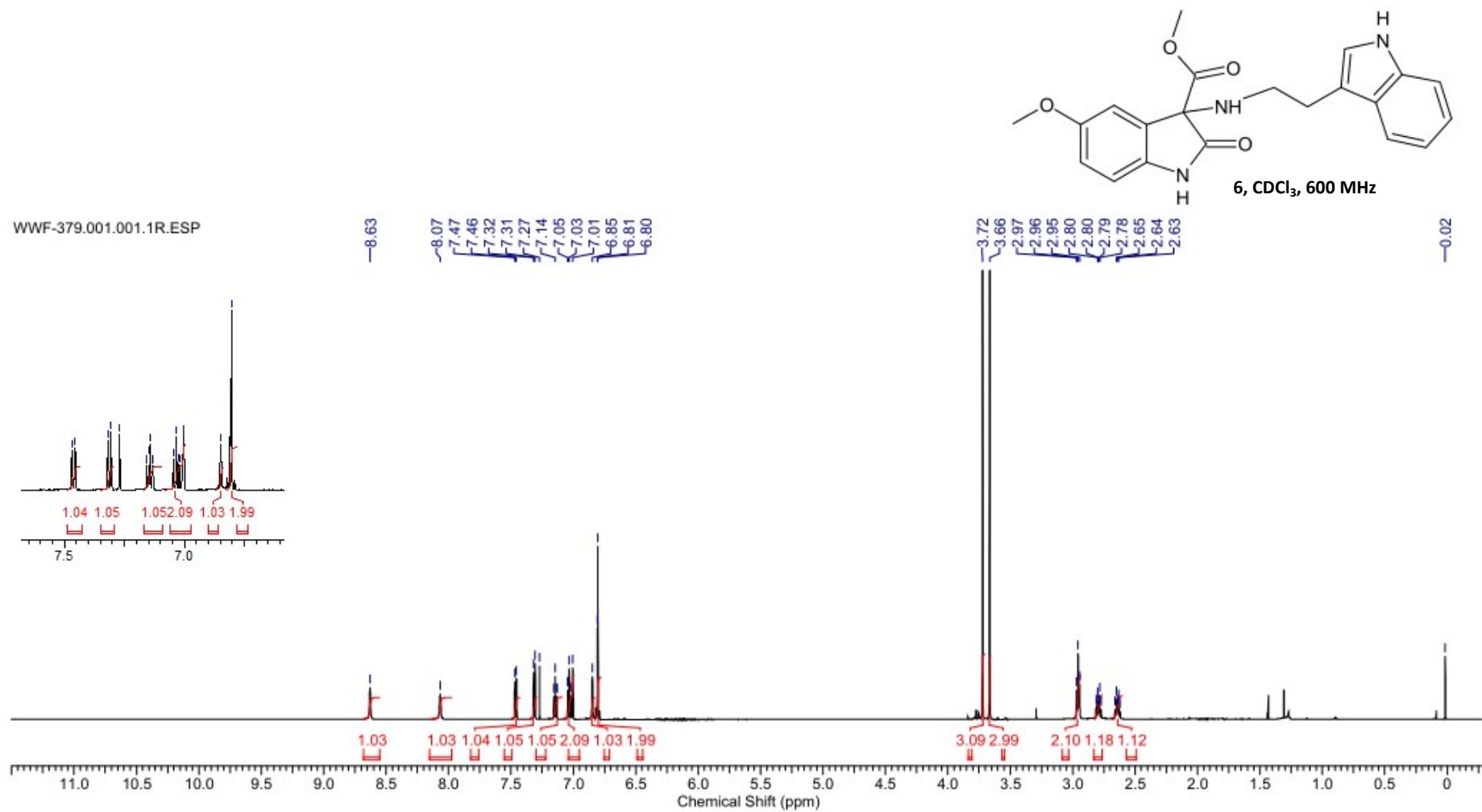
**Iheyamine A-TFA Salt**



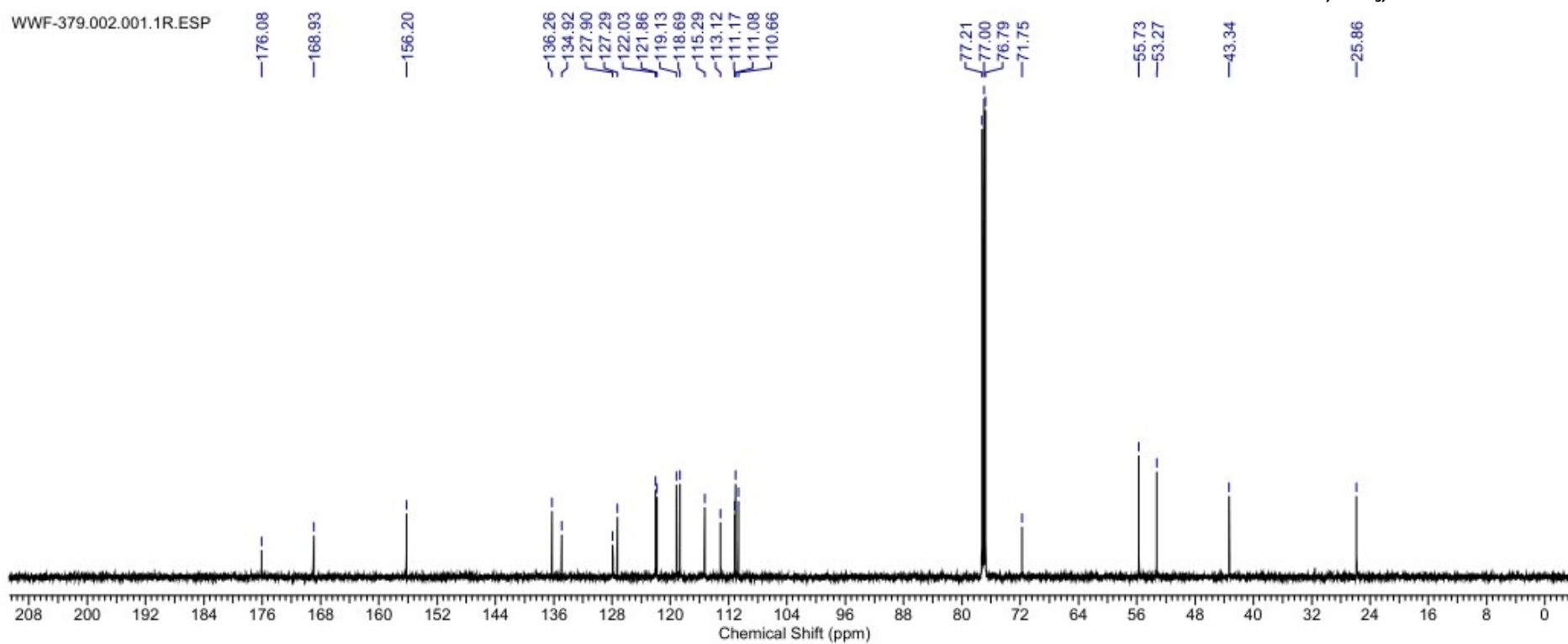
$^1\text{H}$ NMR		$^{13}\text{C}$ NMR			
Pos.	Lit. <sup>1</sup> (500 MHz, $\text{CDCl}_3$ )	Synthetic (500 MHz, $\text{CDCl}_3$ )	Lit. <sup>1</sup> (600 MHz, $\text{CDCl}_3$ )	Synthetic (600 MHz, $\text{CDCl}_3$ )	(150 MHz, $\text{CDCl}_3$ )
1	9.38, d (6.4)	9.36, d (6.5)	143.2, CH	143.2, CH	
2	8.85, d (6.4)	8.82, d (6.7)	124.5, CH	124.5, CH	
3	-	-	128.3, C	127.9, C	
4	-	-	123.8, C	123.8, C	
5	8.42, d (7.9)	8.39, d (8.0)	121.4, CH	121.4, CH	
6	7.61, dd (7.9, 7.0)	7.59, t (7.5)	124.4, CH	124.4, CH	
7	7.84, dd (7.9, 7.0)	7.89, d (2.4)	132.8, CH	132.8, CH	
8	8.05, d (7.9)	7.98, d (8.2)	115.1, CH	114.9, CH	
9	-	-	144.0, C	143.8, C	
10	-	-	138.1, C	138.0, C	
11	-	-	148.9, C	148.7, C	
12	-	-	138.2, C	138.0, C	
13	7.99, d (8.9)	7.94, d (8.7)	115.7, CH	115.6, CH	
14	7.52, dd (8.9, 2.4)	7.50, dd (8.7, 2.5)	124.1, CH	124.0, CH	
15	-	-	157.5, C	157.4, C	
16	7.96, d (2.4)	7.89, d (2.4)	102.8, CH	102.6, CH	
17	-	-	126.1, C	126.0, C	
18	-	-	135.7, C	135.5, C	
19	4.02, s	4.01, s	56.0, Me	55.9, Me	

1 T. Sasaki, I. I. Ohtani, J. Tanaka and T. Higa, *Tetrahedron Lett.*, 1999, **40**, 303.

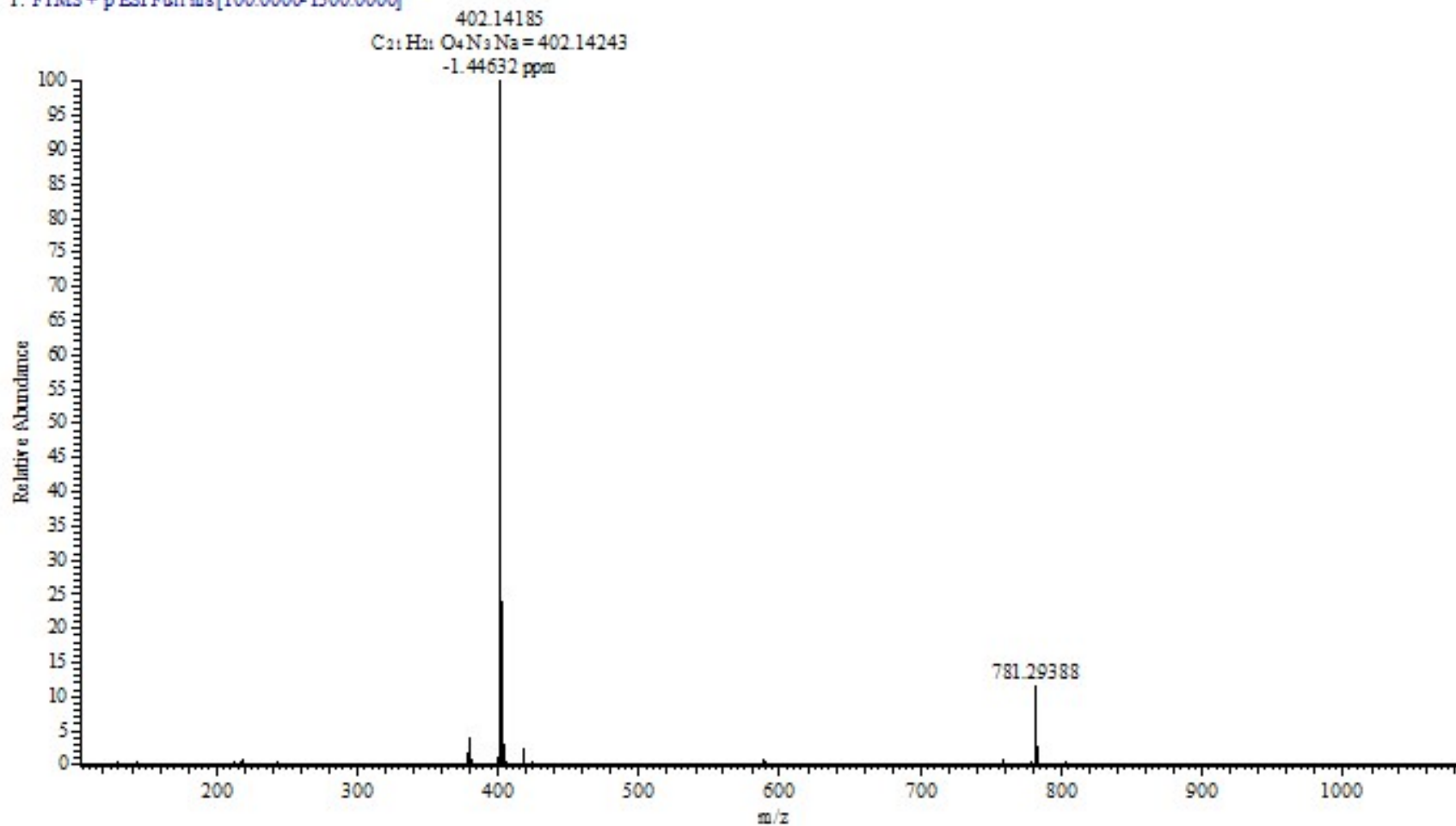




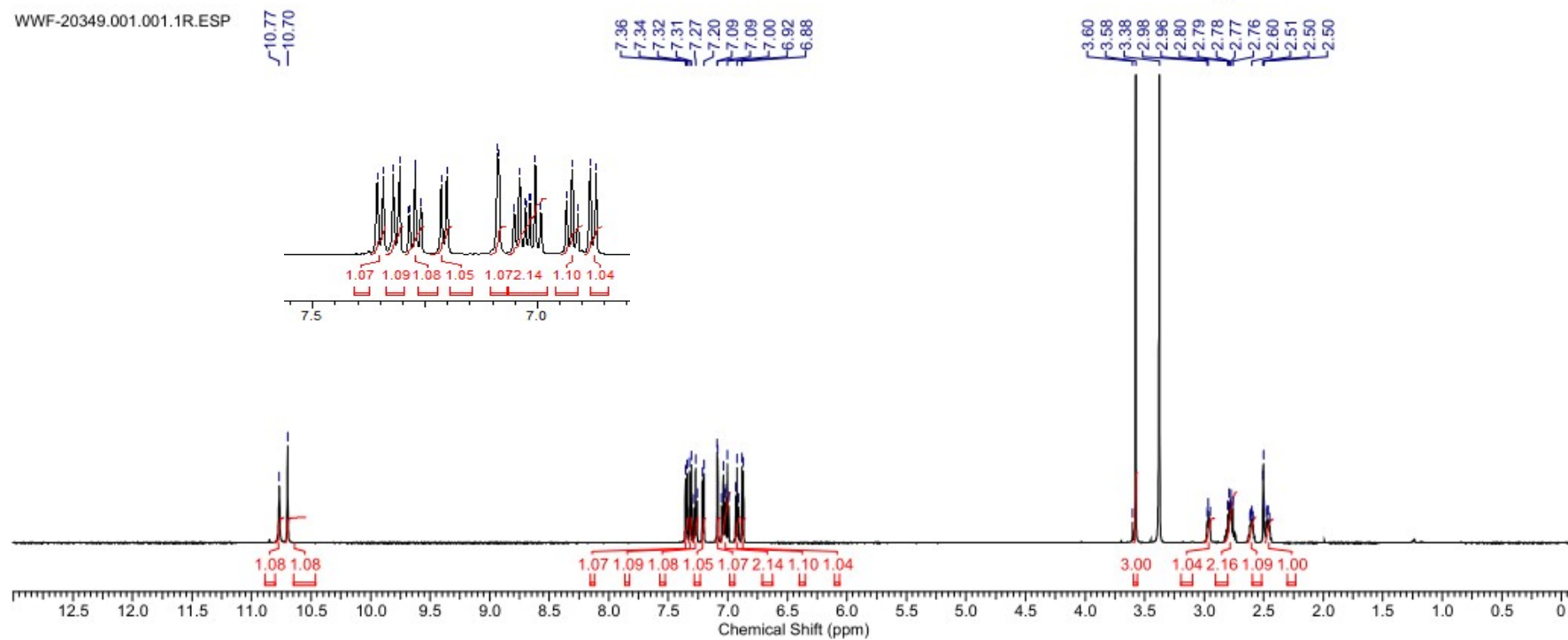
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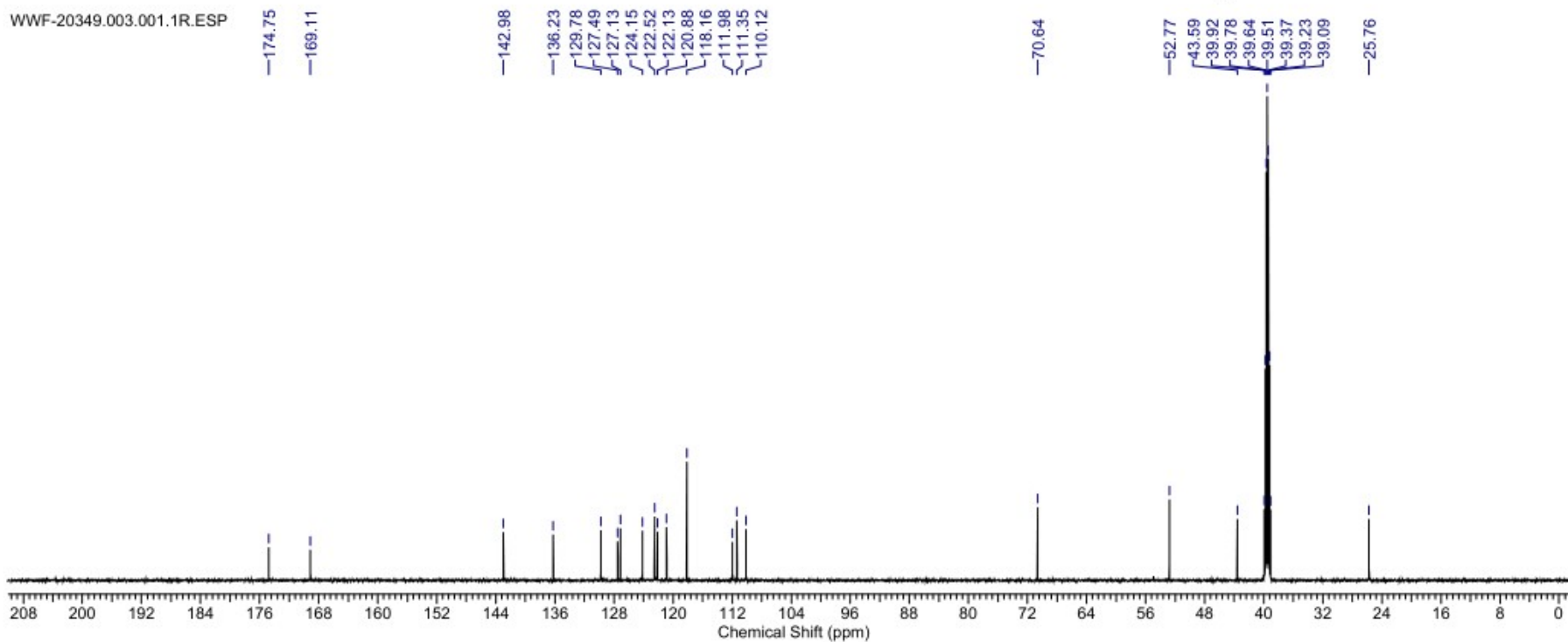


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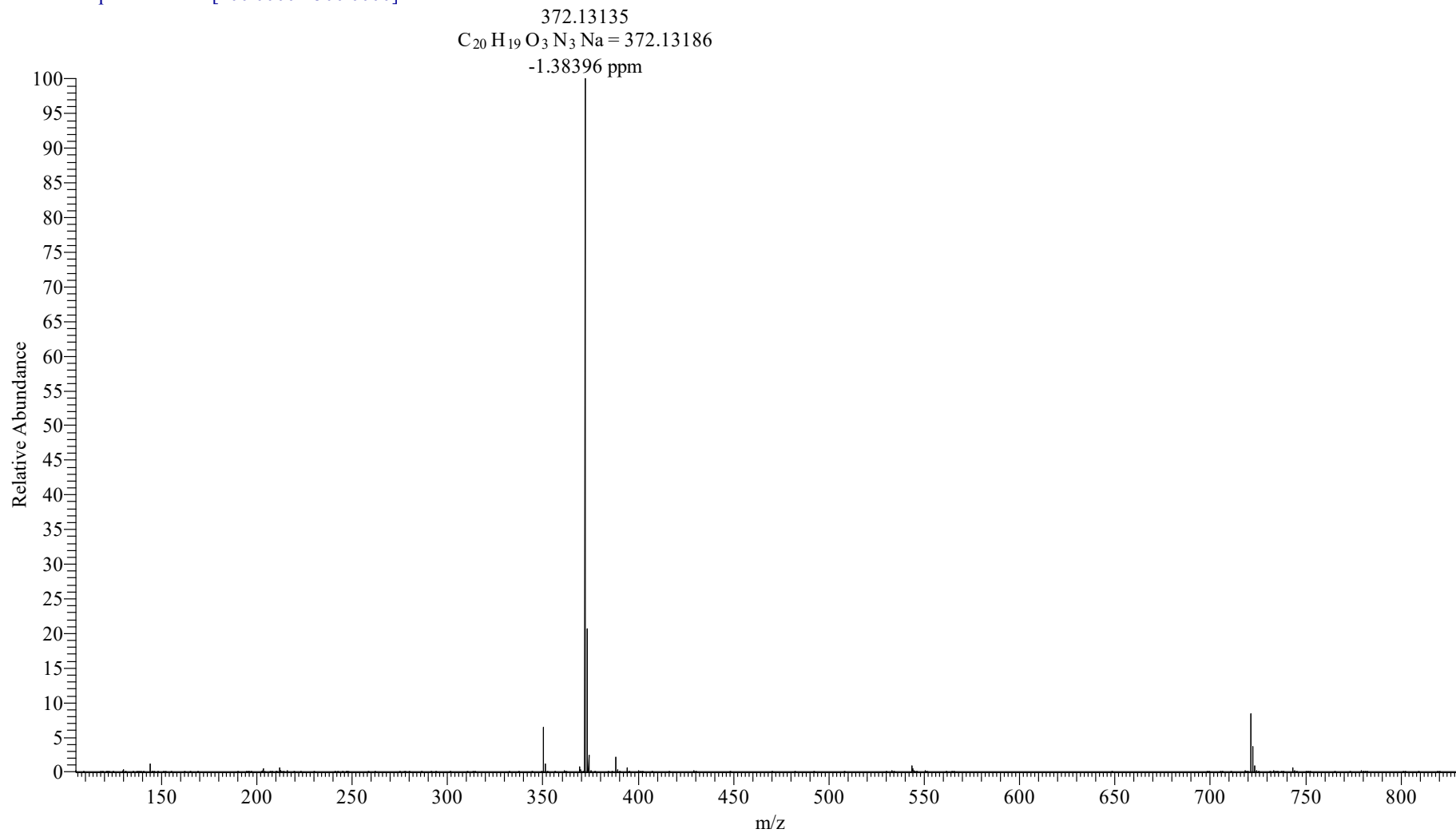


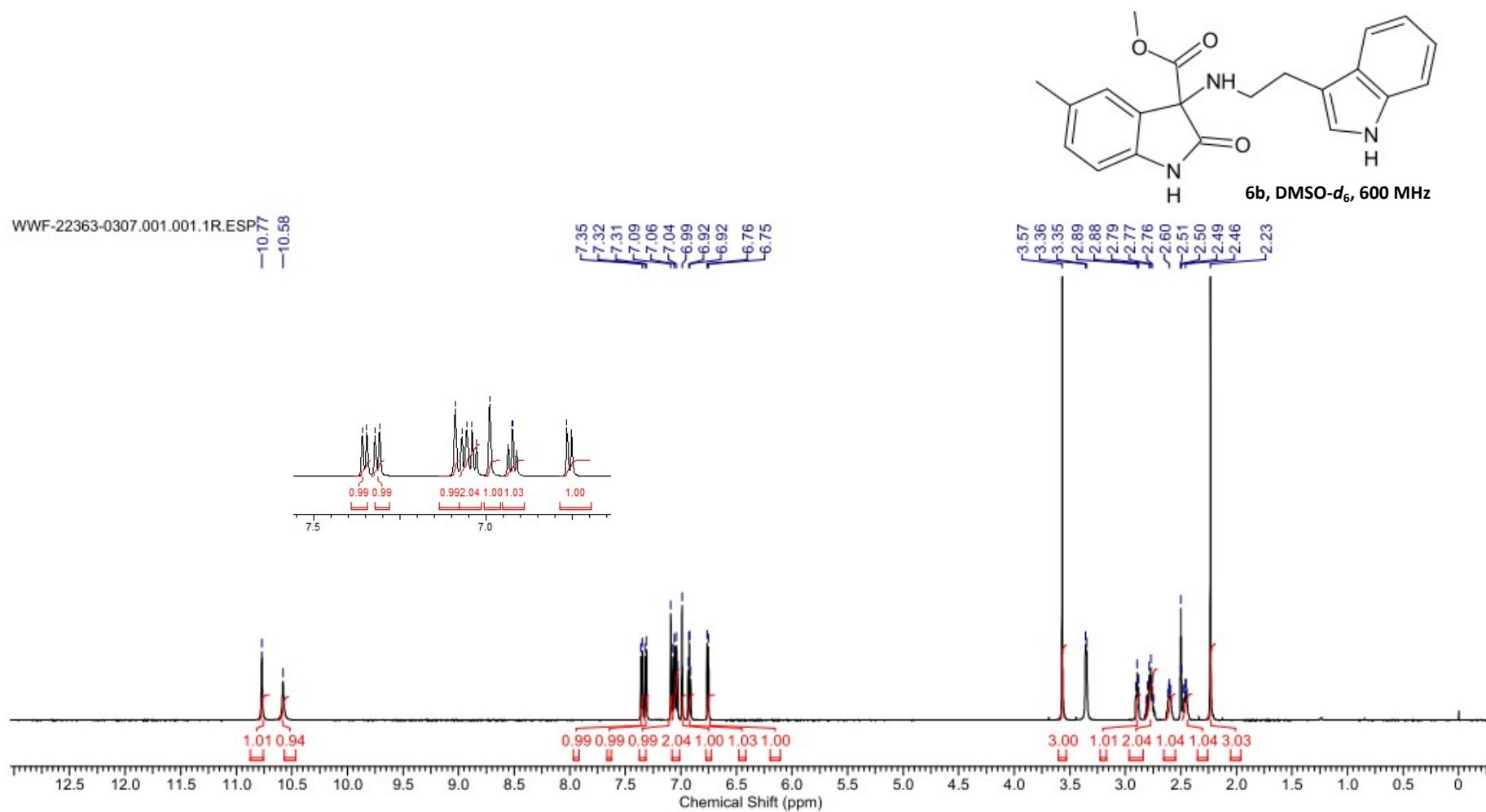


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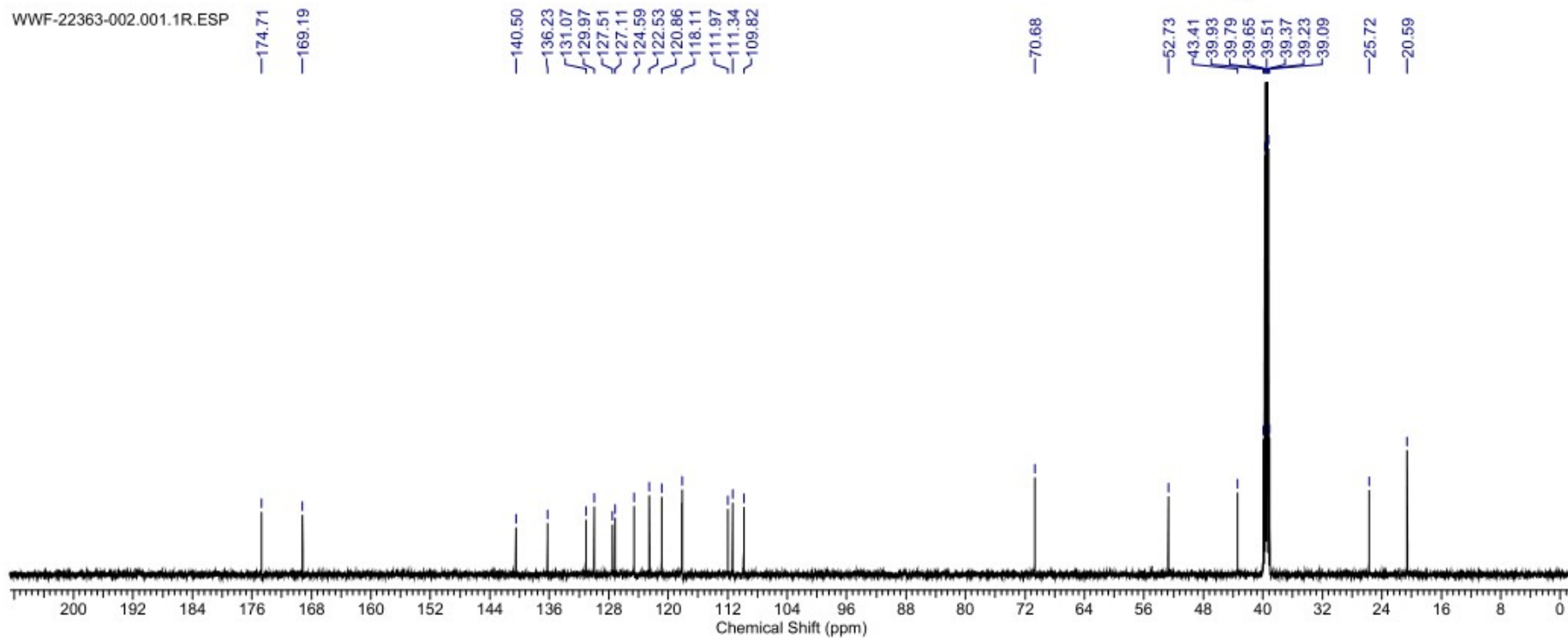


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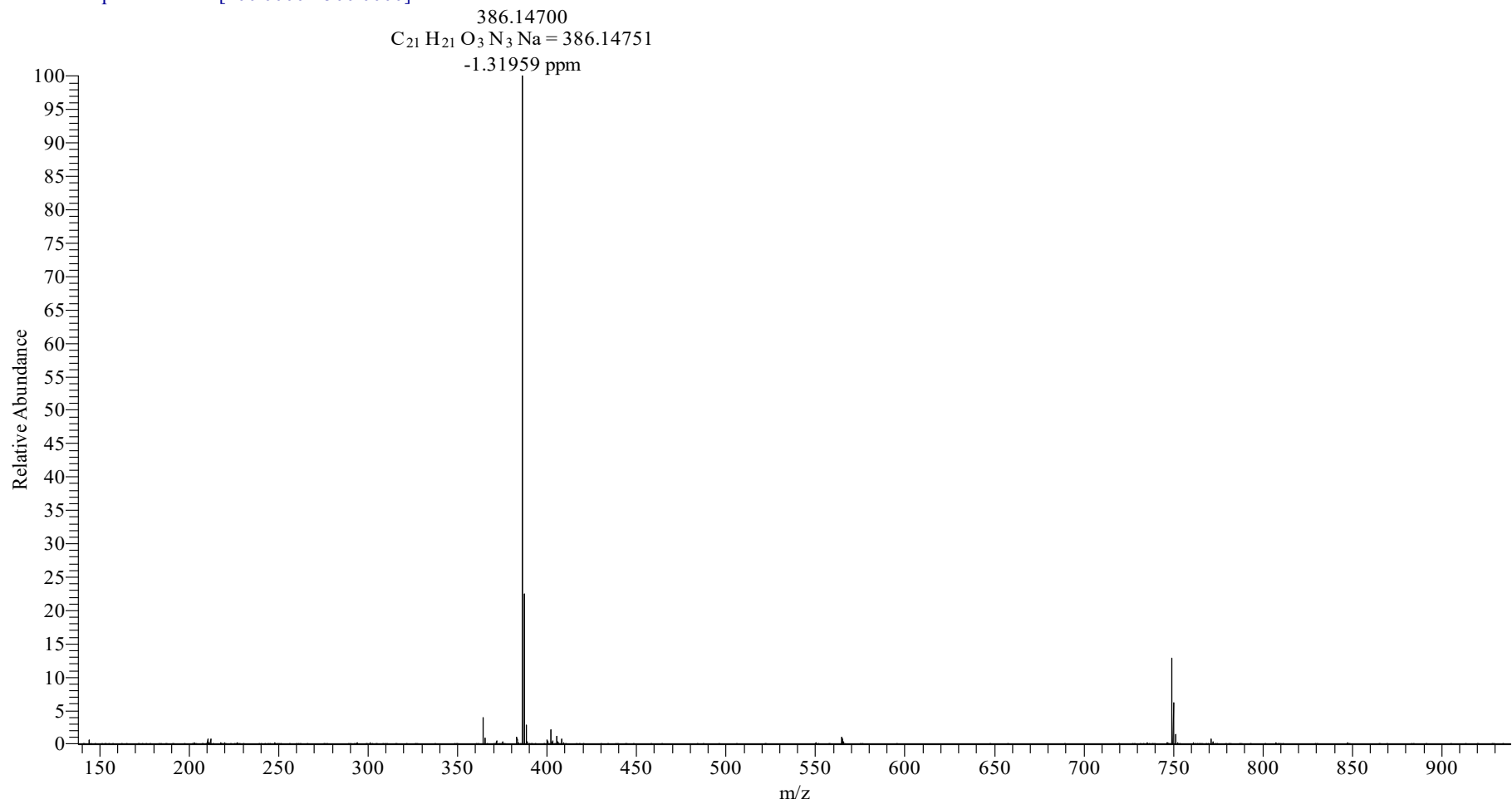


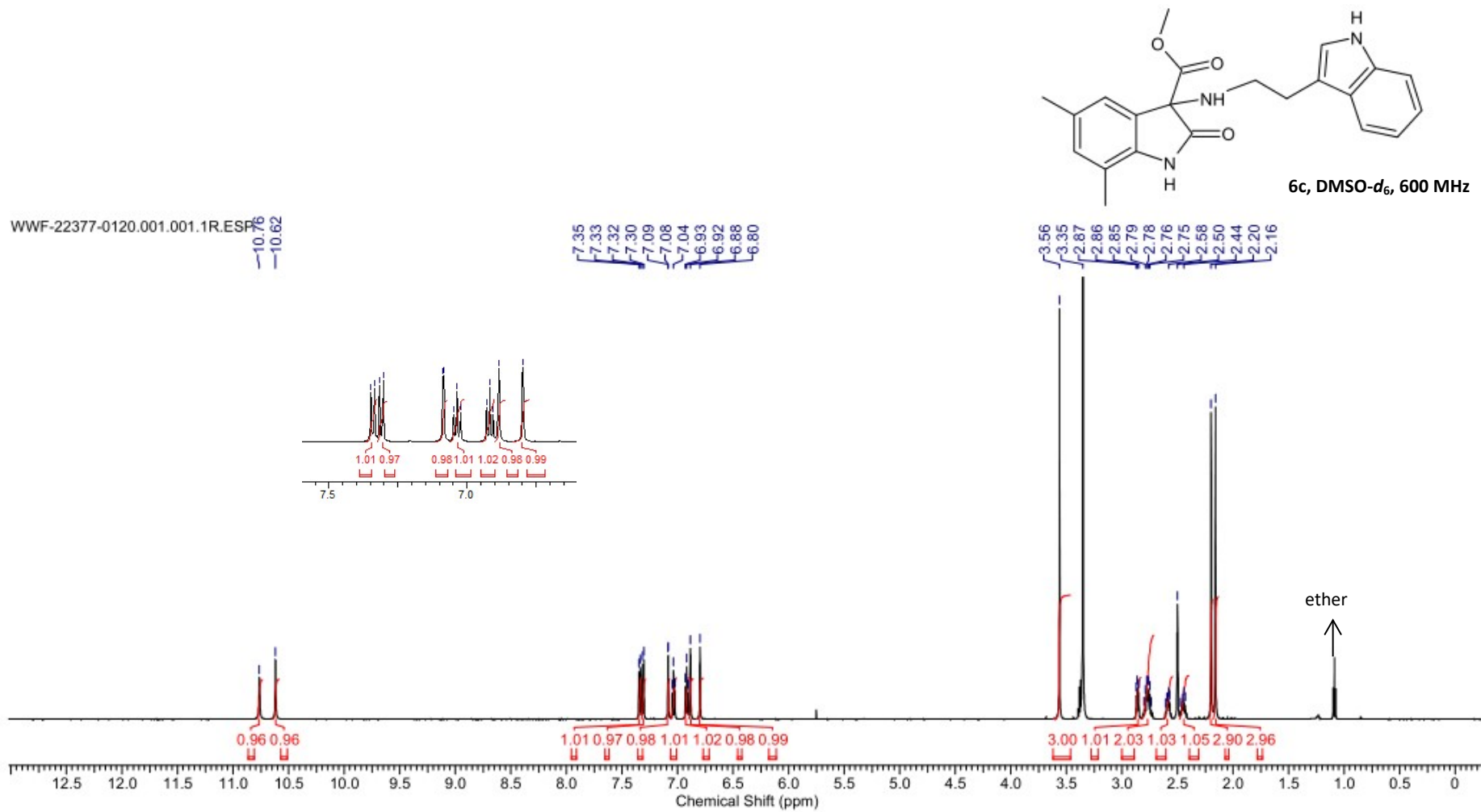


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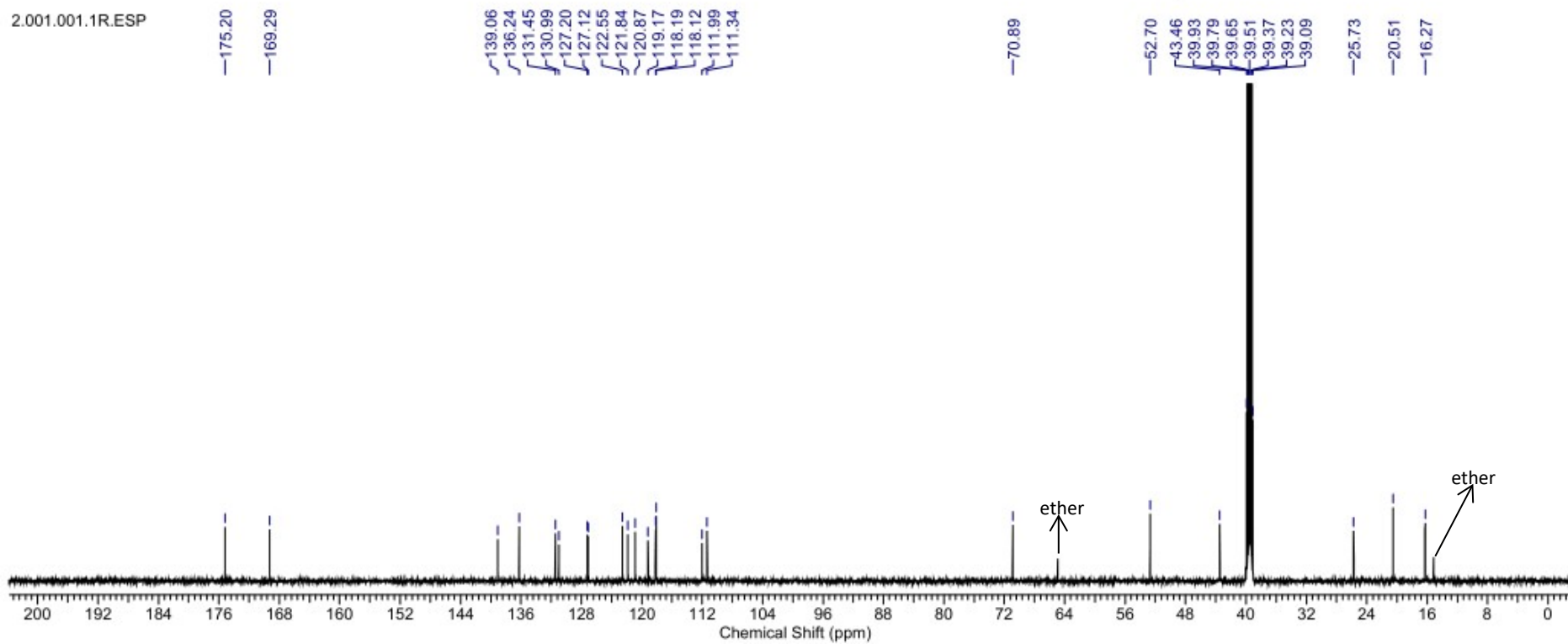


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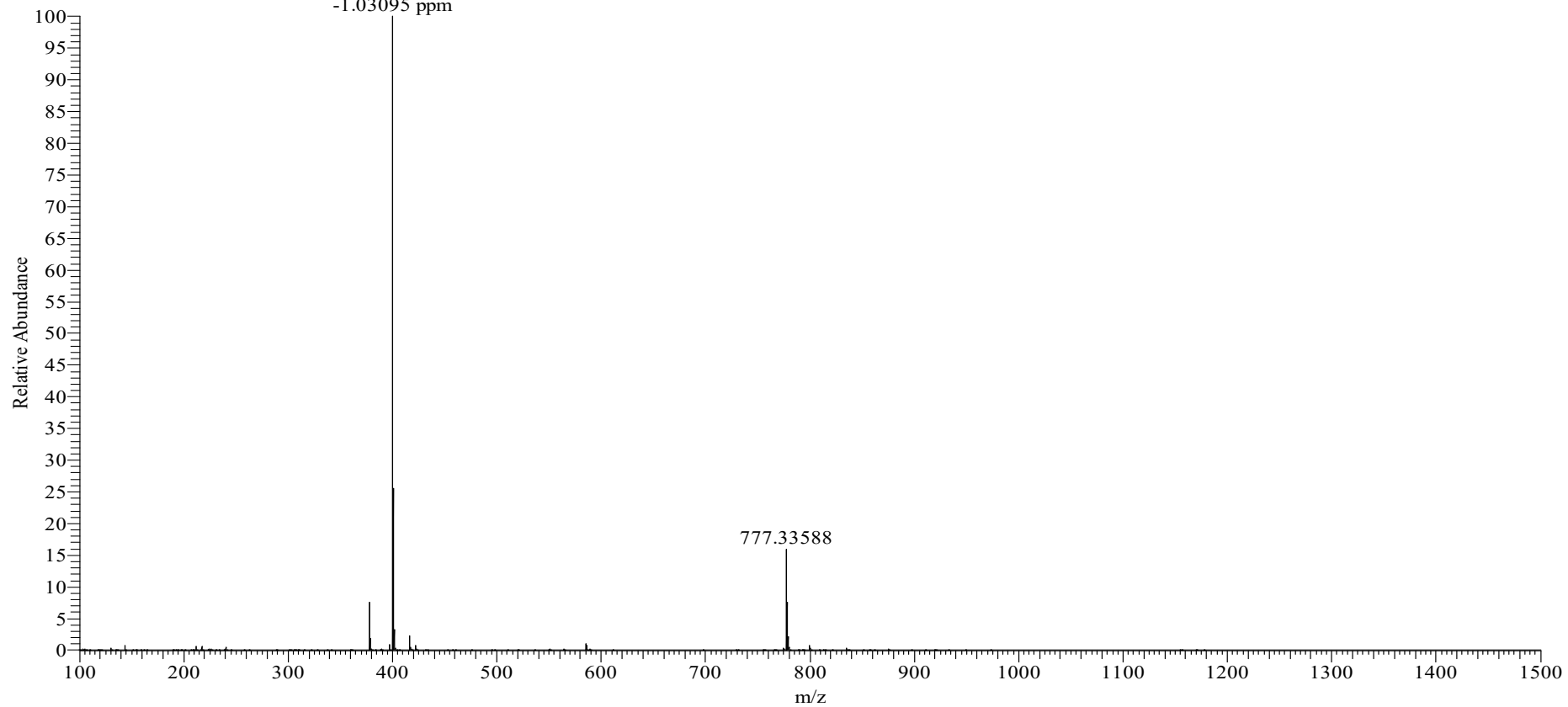
2.001.001.1R.ESP



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 $C_{22}H_{23}O_3N_3Na = 400.16316$   
-1.03095 ppm

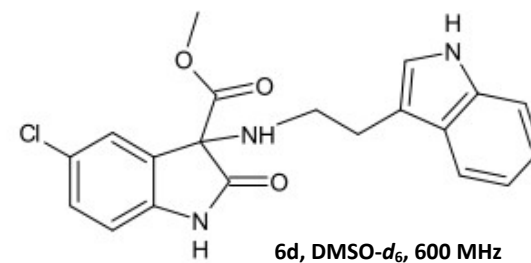




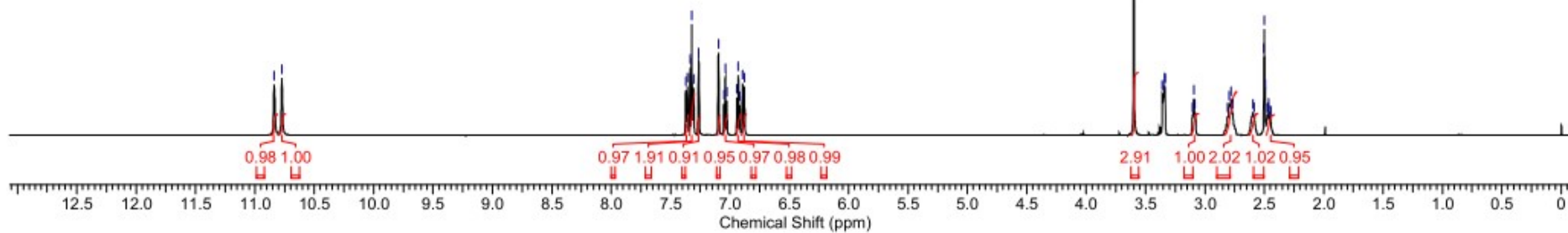
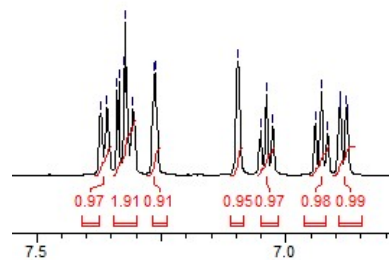
WWF-21383.001.001.1R.ESP

10.84  
10.77

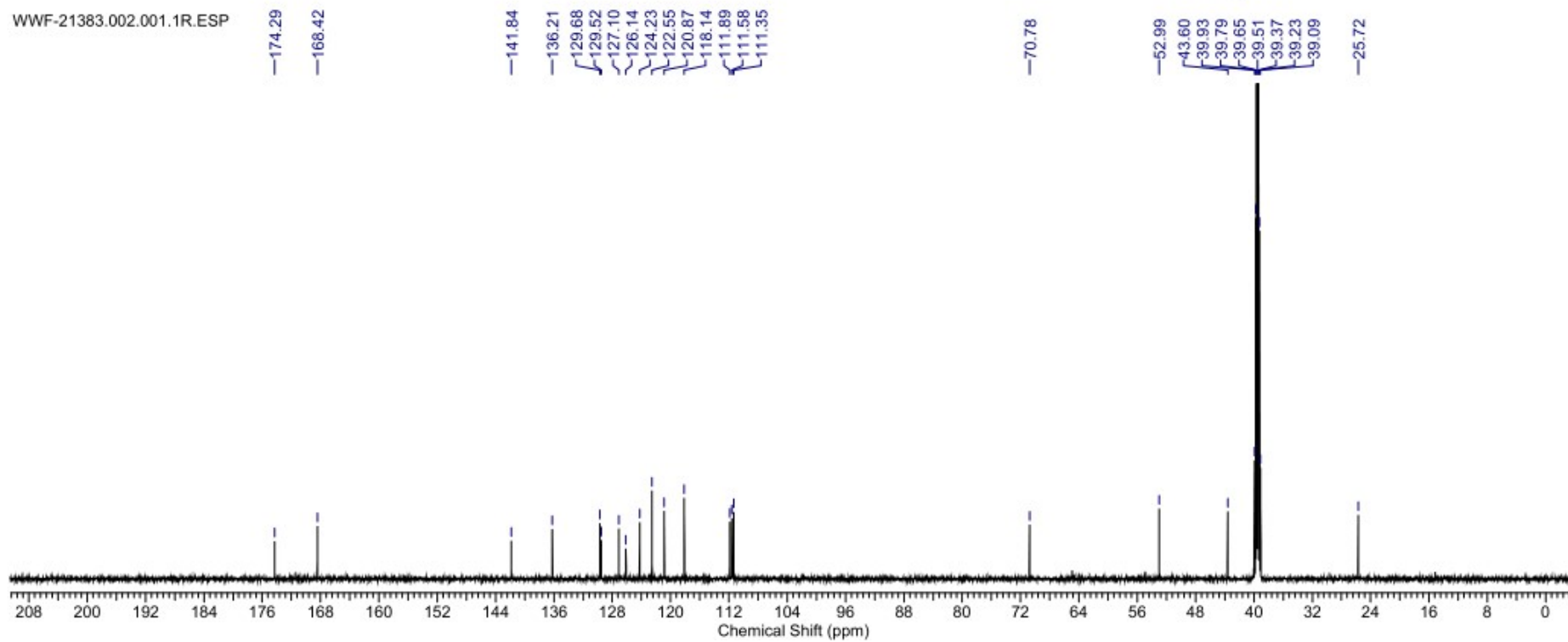
7.37  
7.36  
7.34  
7.32  
7.26  
7.26  
7.10  
7.04  
6.93  
6.89  
6.88



3.60  
3.36  
3.35  
3.34  
3.33  
3.09  
3.08  
2.80  
2.78  
2.60  
2.50  
2.50  
2.49  
2.46



WWF-21383.002.001.1R.ESP



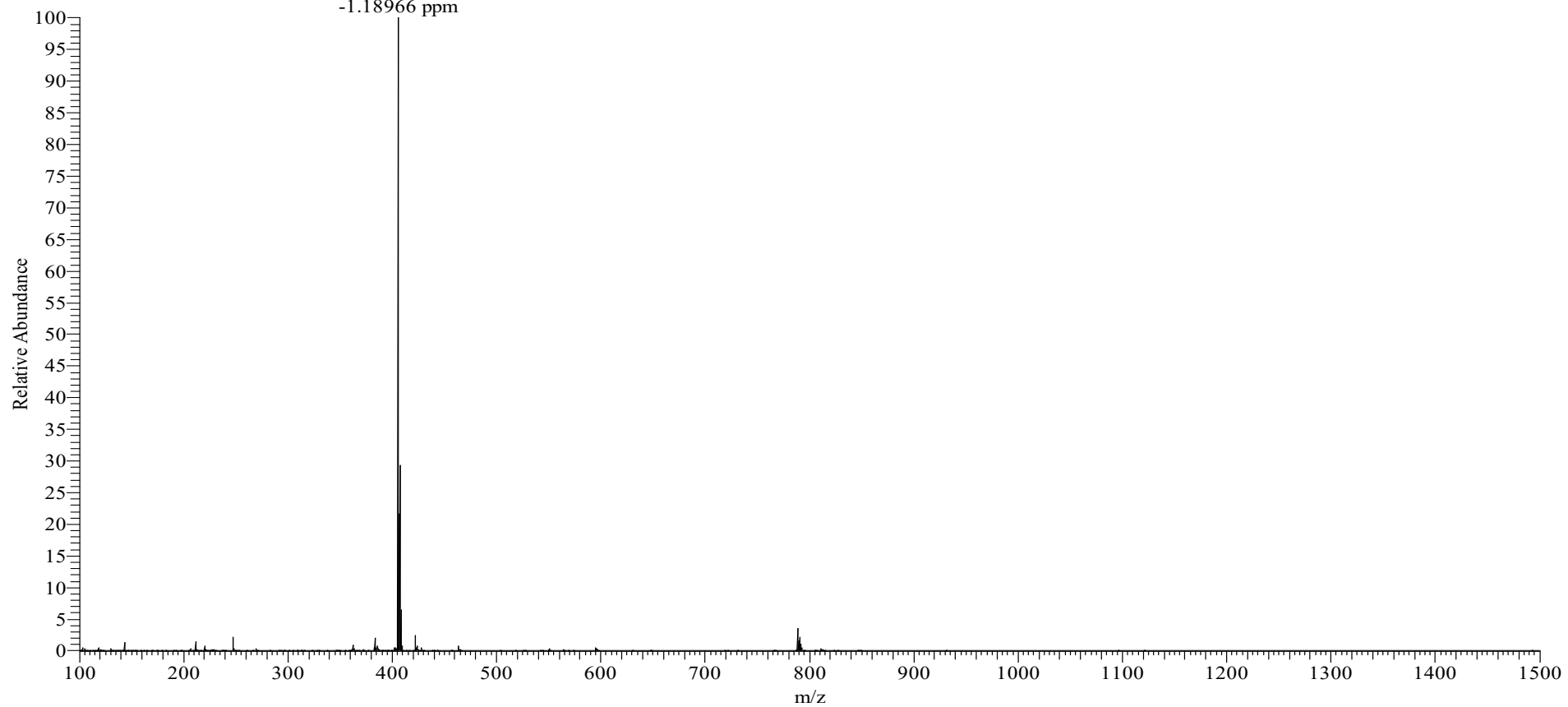
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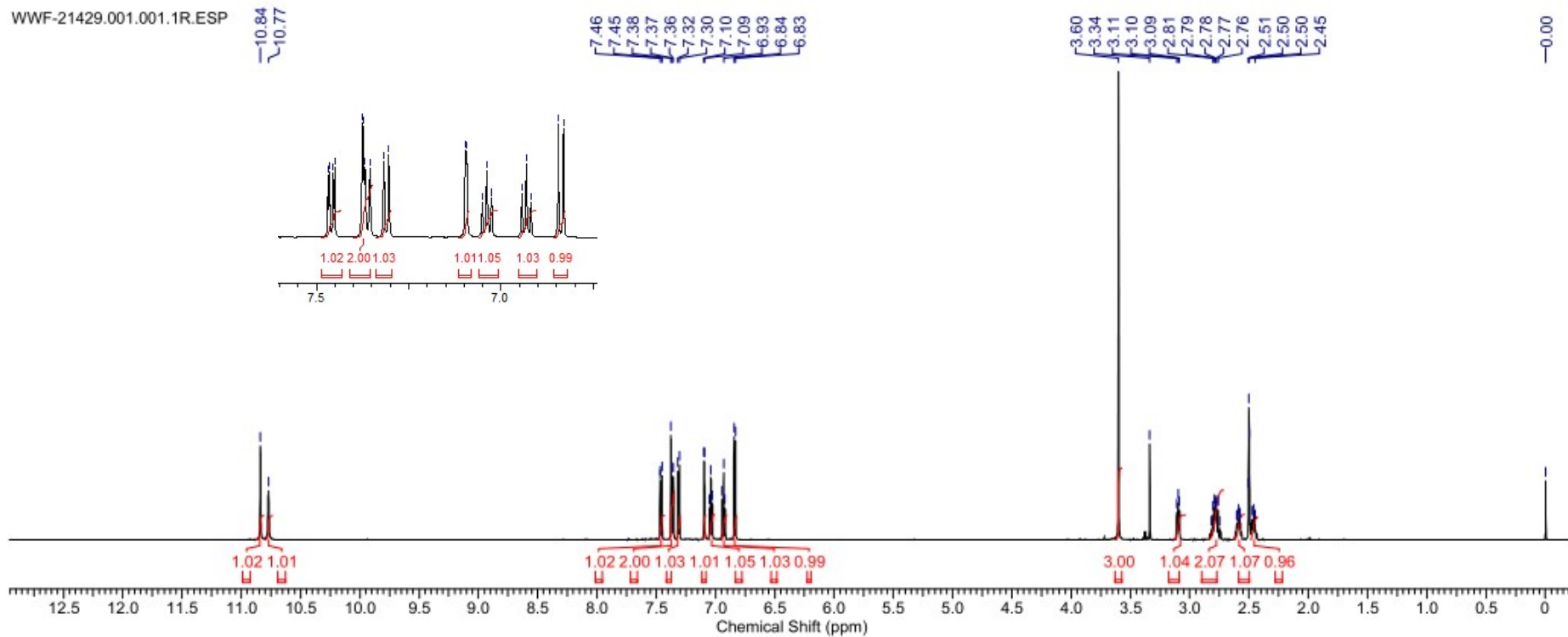
406.09241

$C_{20}H_{18}O_3N_3ClNa = 406.09289$

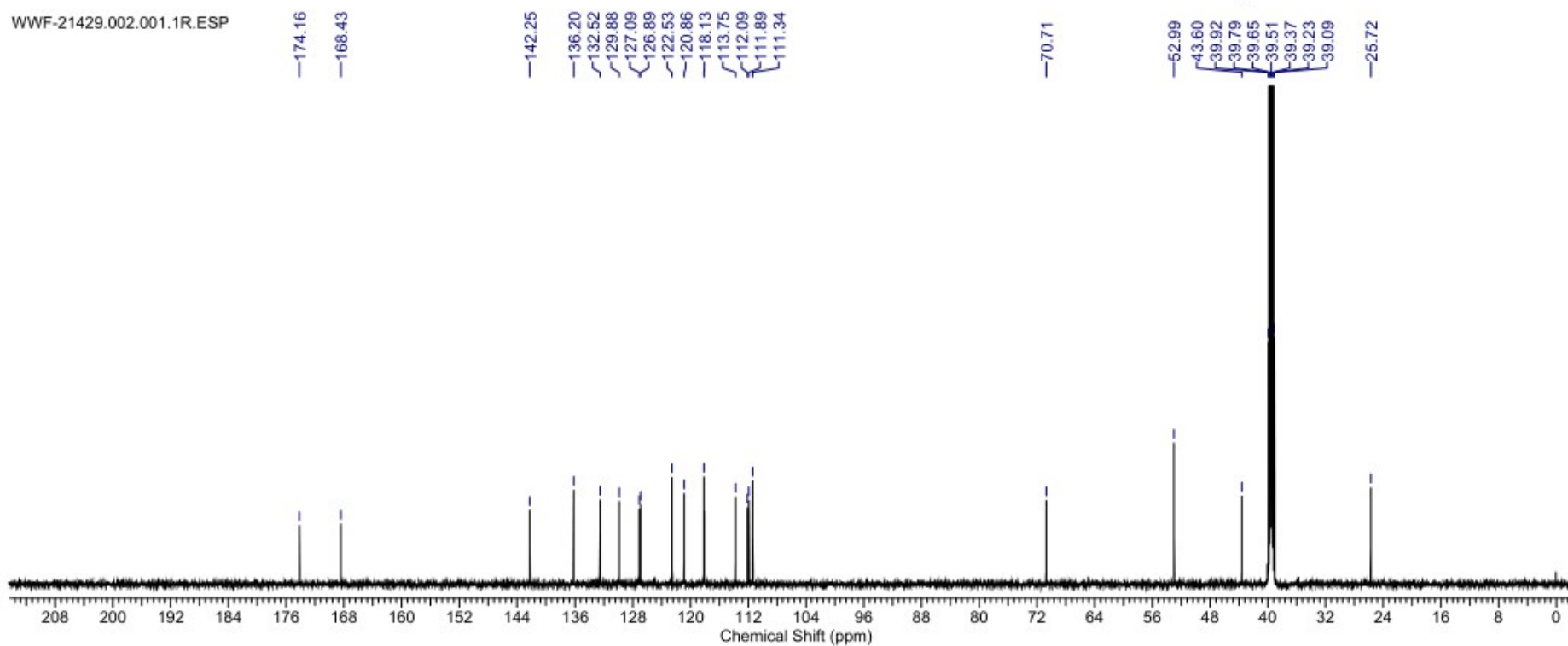
-1.18966 ppm



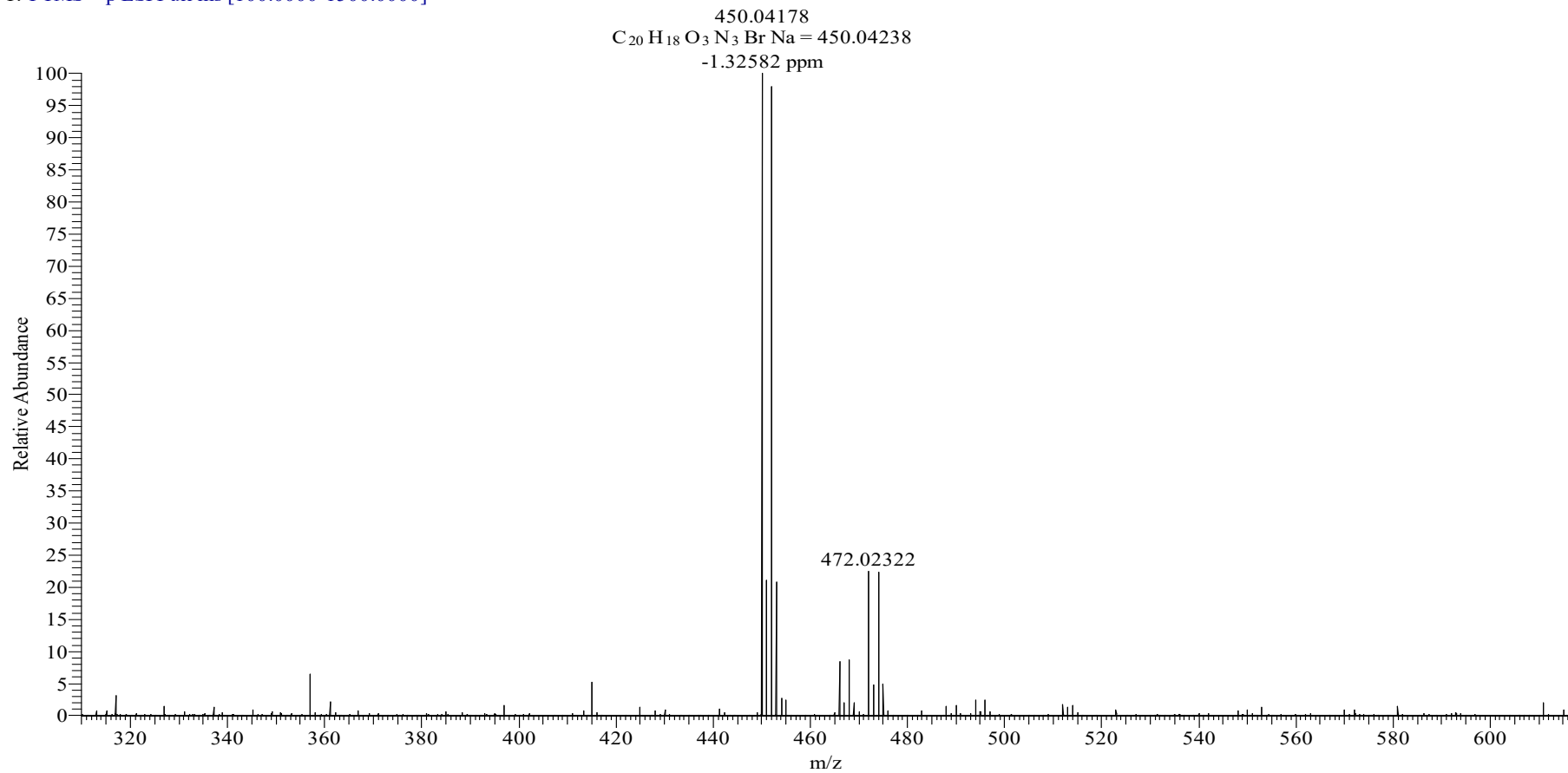
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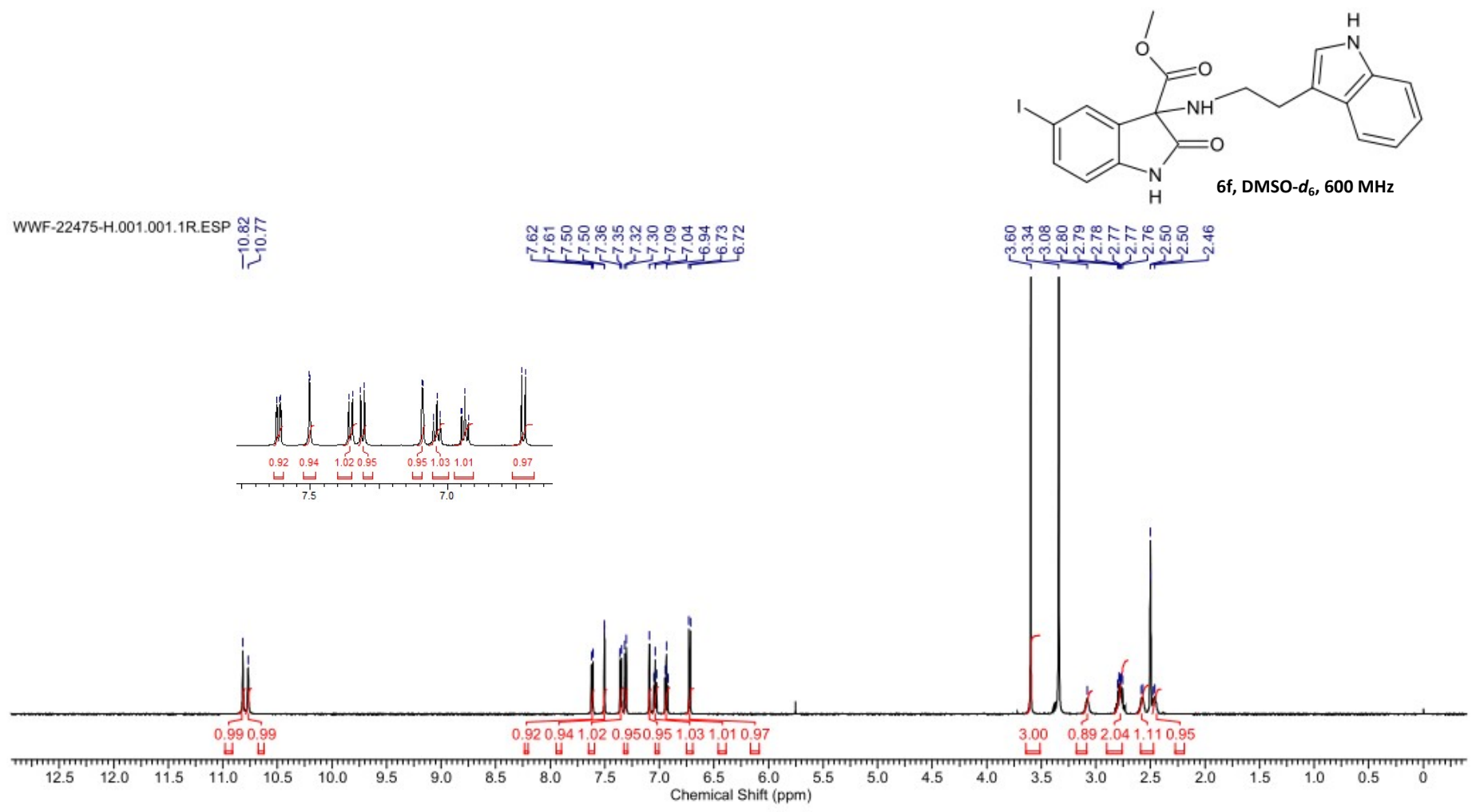


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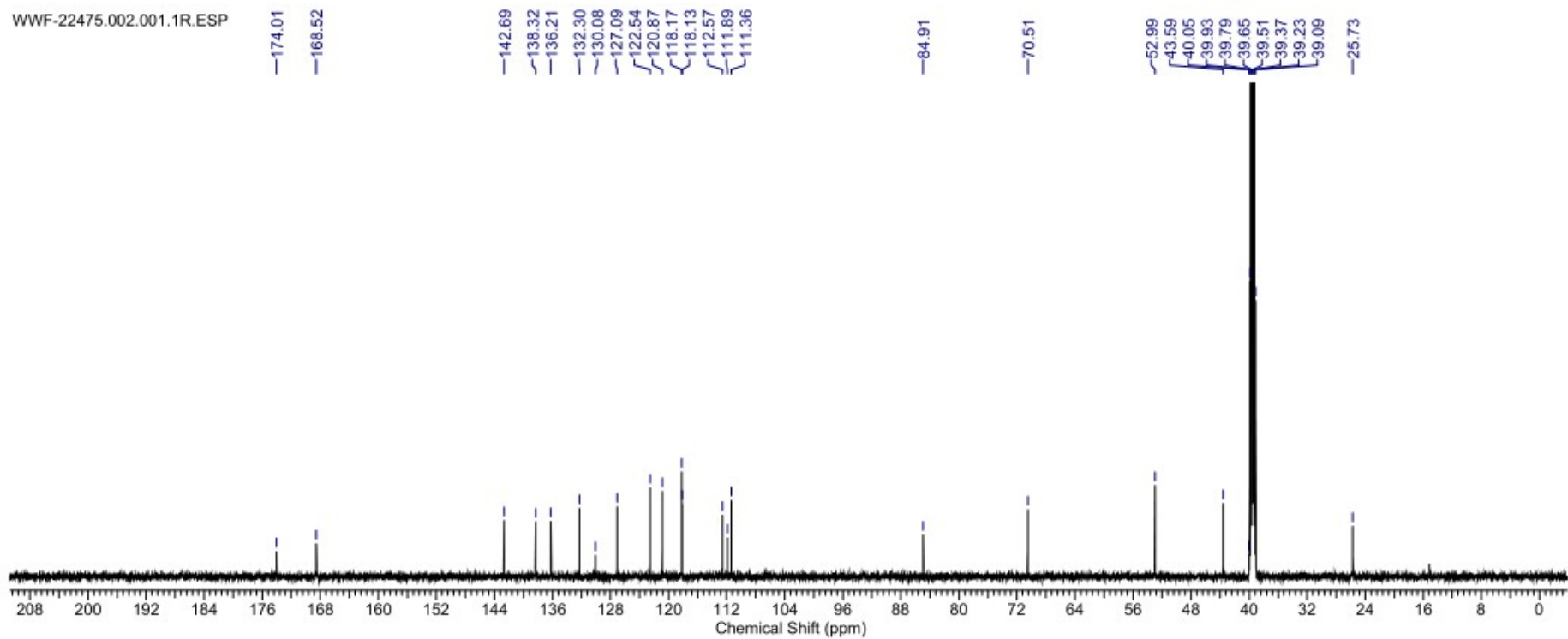


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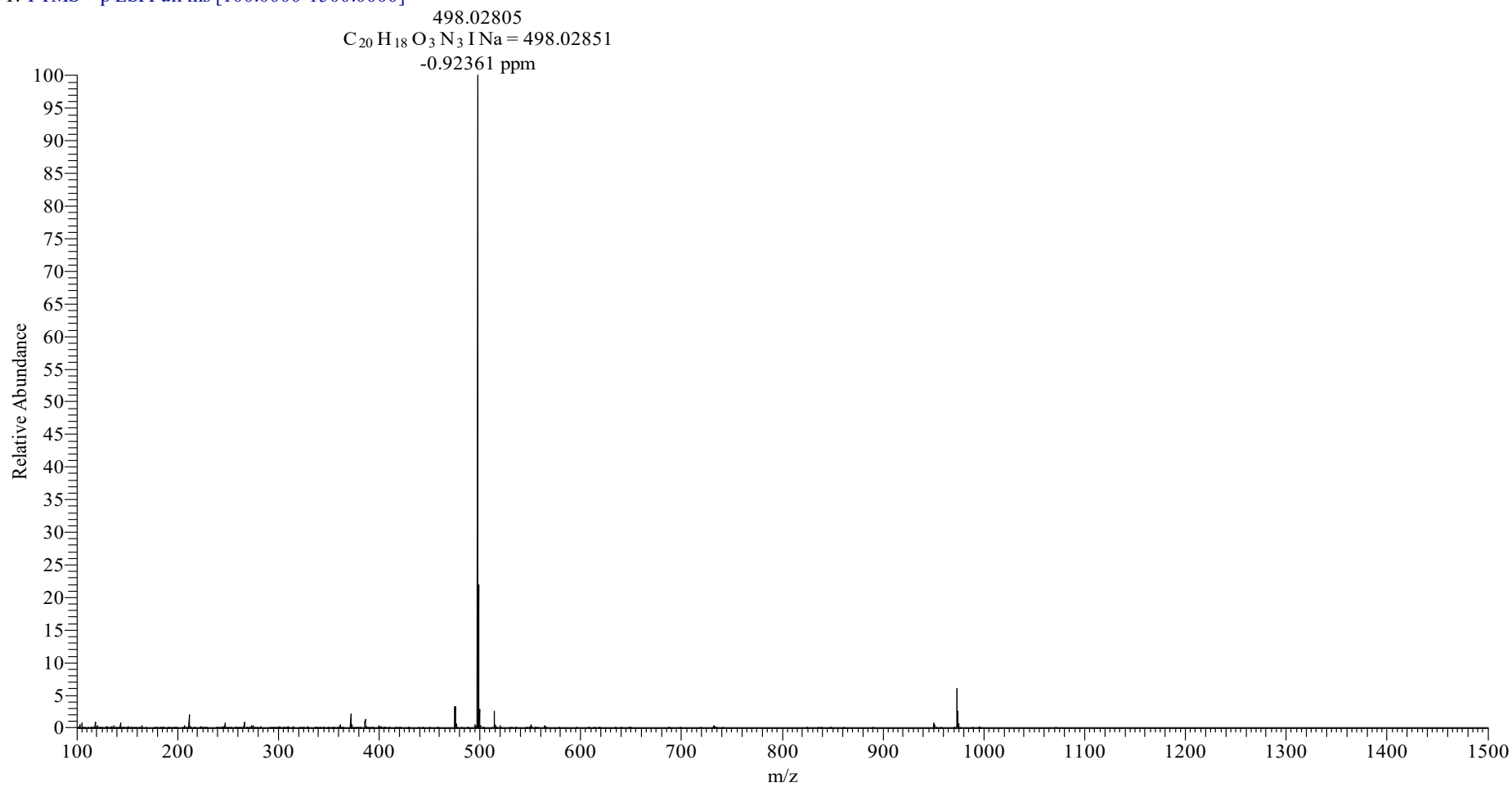


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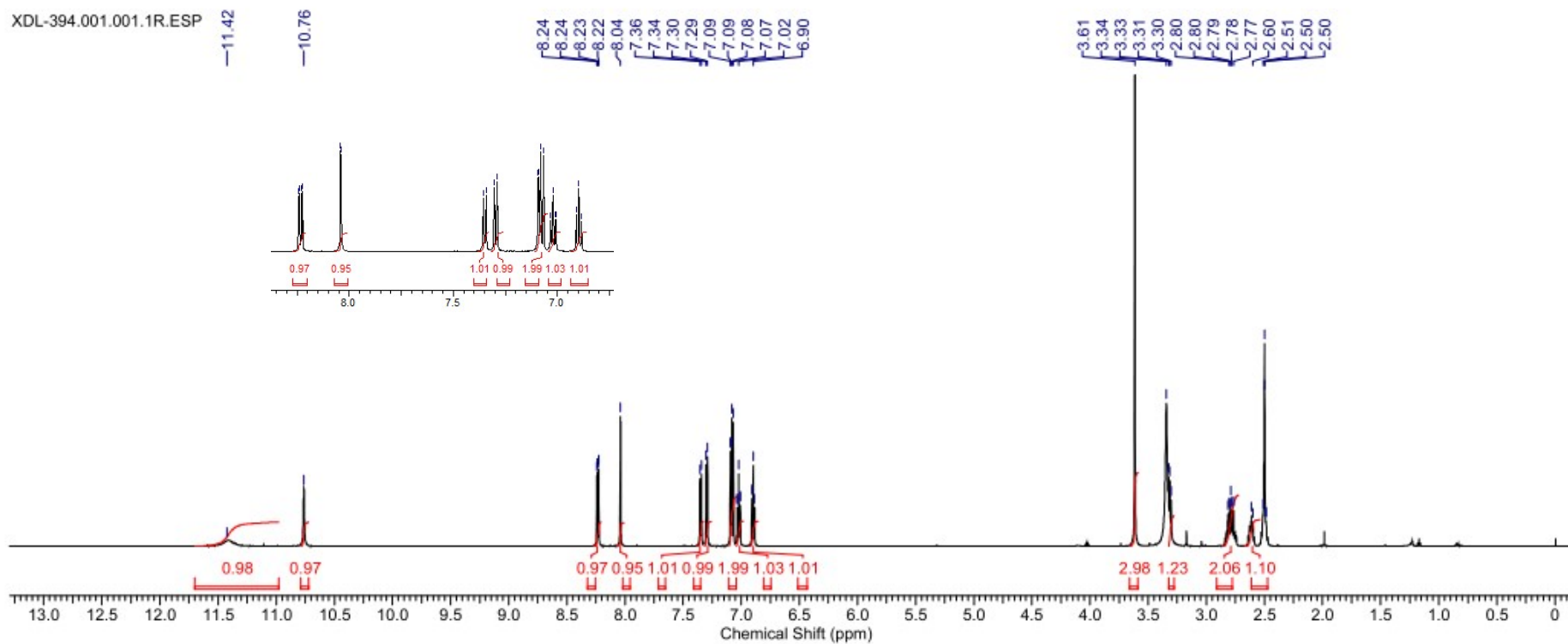




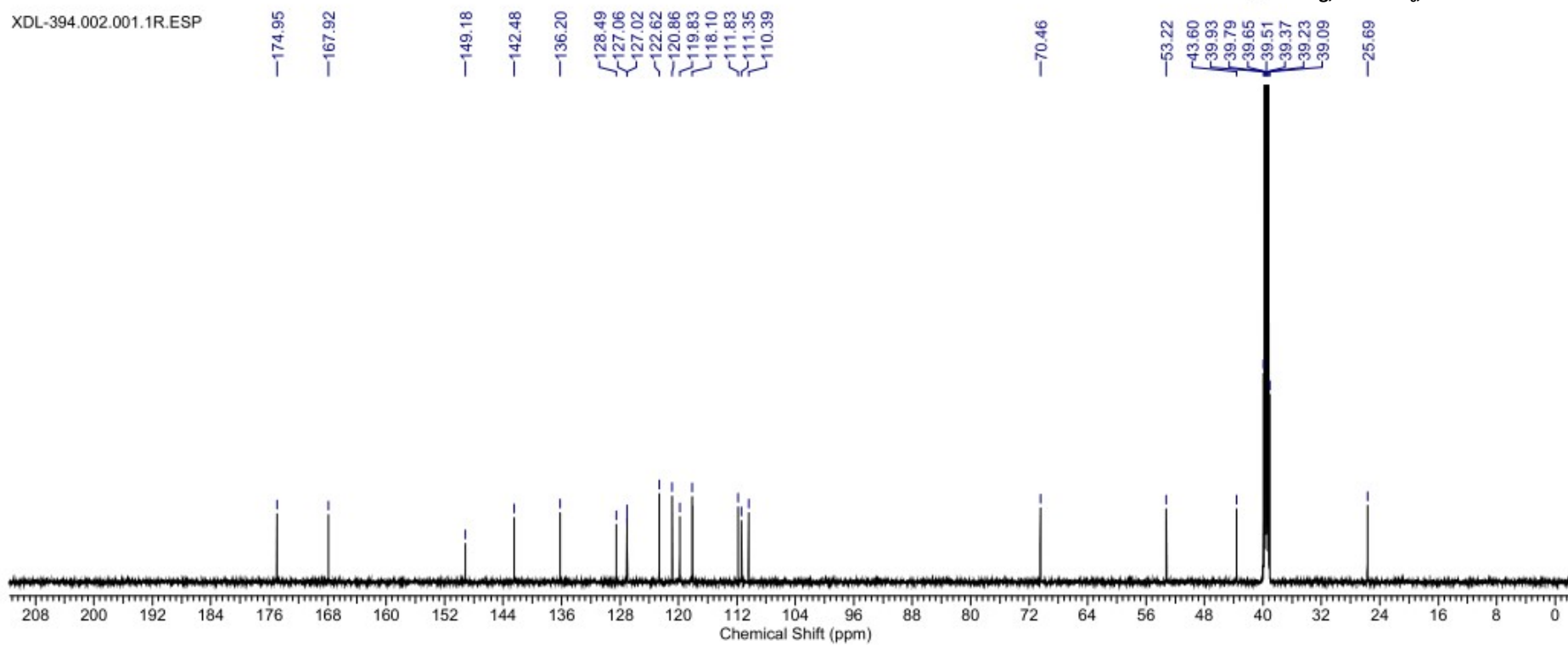
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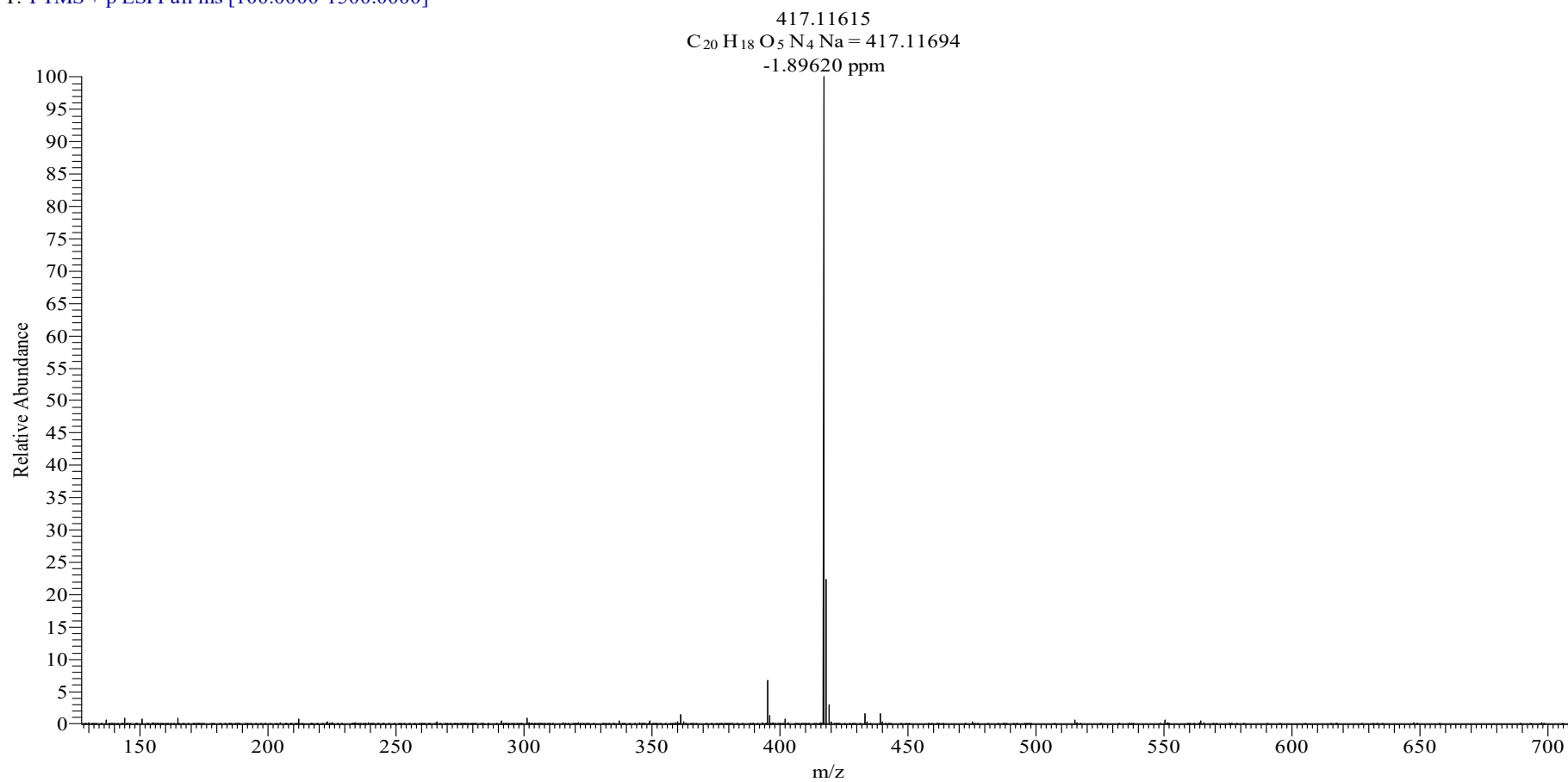
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XDL-394.002.001.1R.ESP



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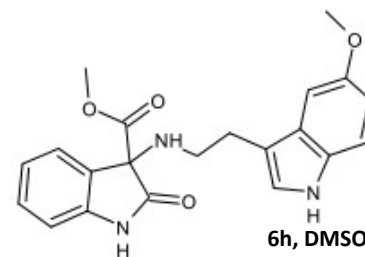


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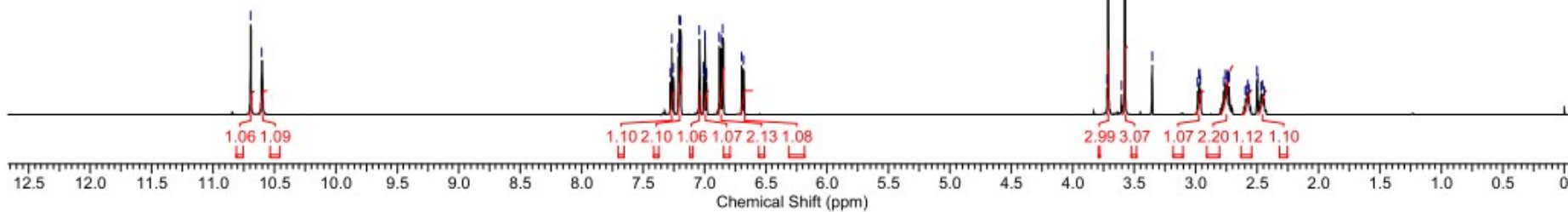
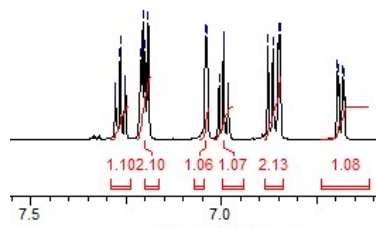
10.69  
10.60

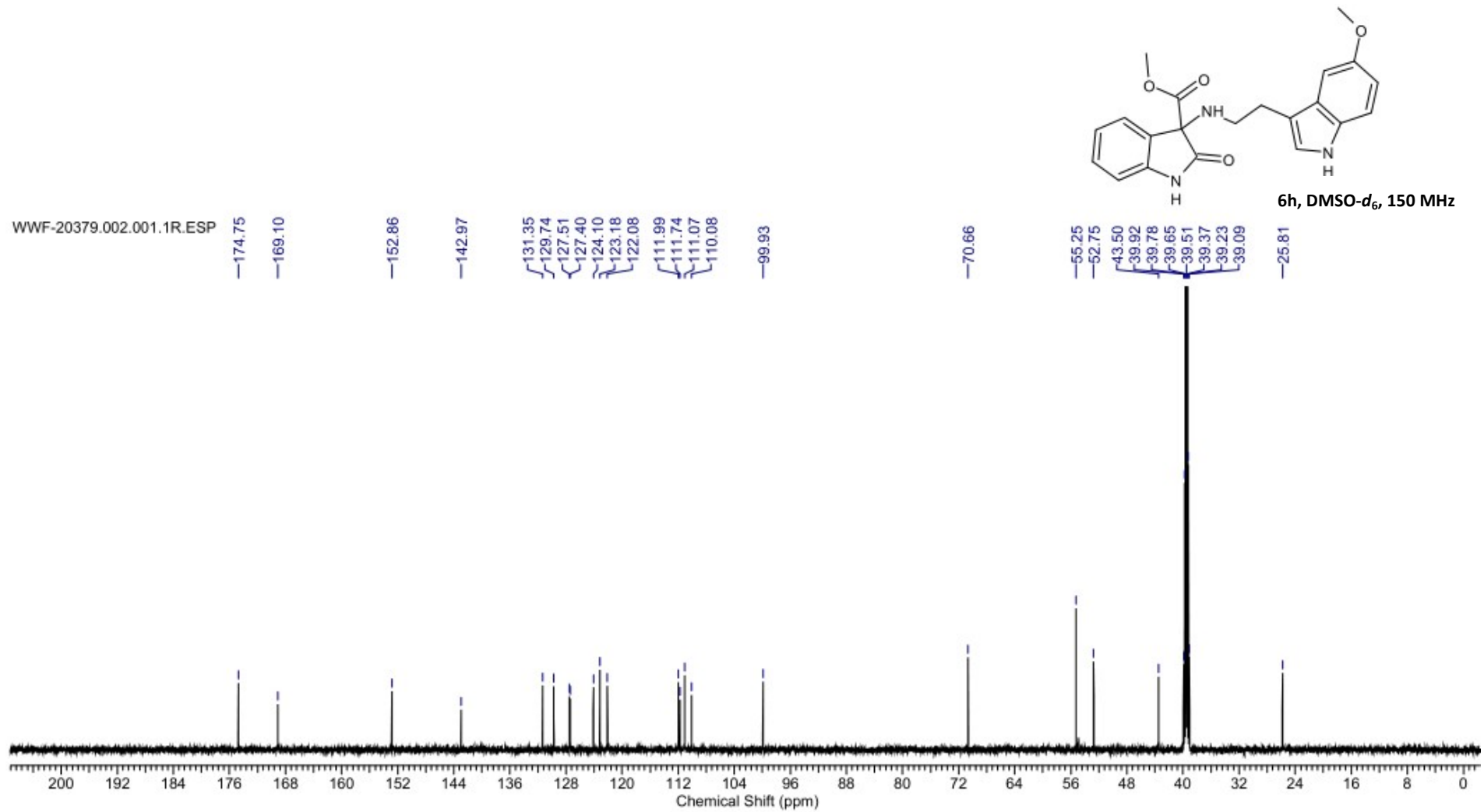
7.26  
7.21  
7.20  
7.19  
7.04  
6.99  
6.88  
6.86  
6.85  
6.70

3.72  
3.71  
3.60  
3.58  
3.35  
2.97  
2.96  
2.77  
2.76  
2.75  
2.74  
2.73  
2.50  
2.50

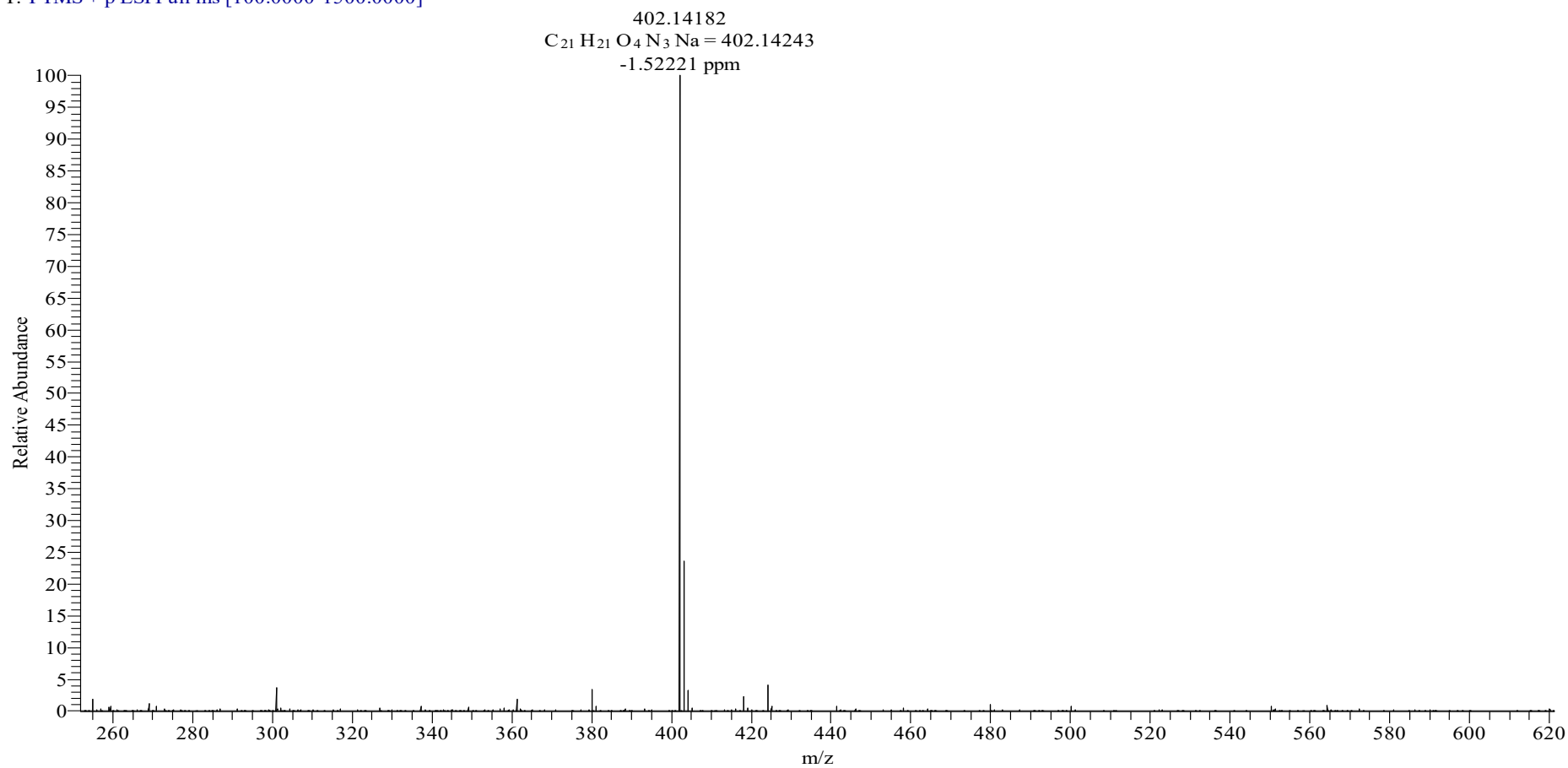


6h, DMSO-d<sub>6</sub>, 600 MHz





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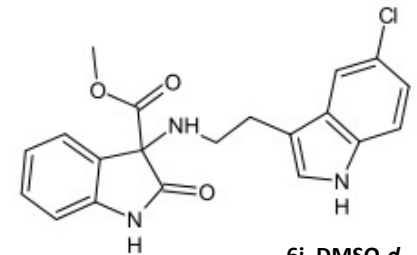


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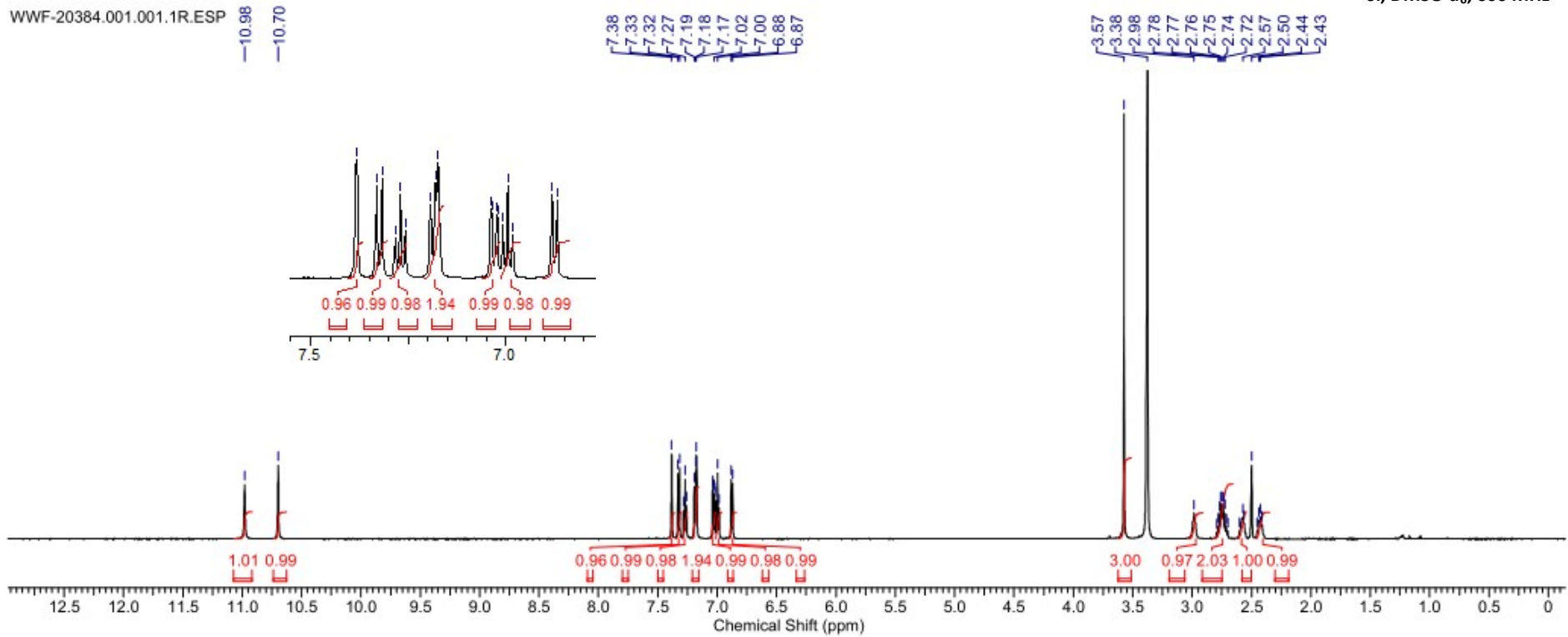
10.98  
10.70

7.38  
7.33  
7.32  
7.27  
7.19  
7.18  
7.17  
7.02  
7.00  
6.88  
6.87

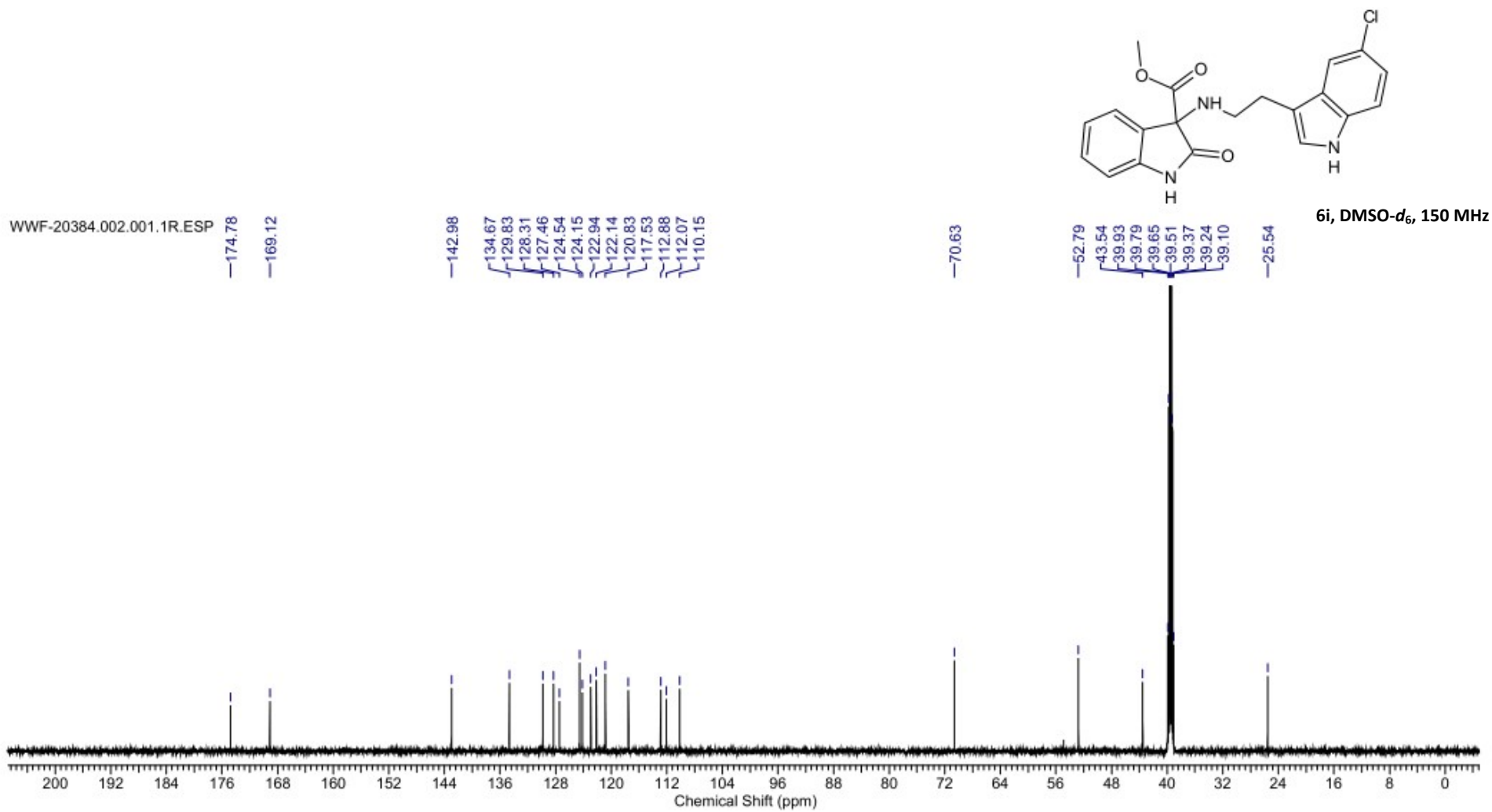
3.57  
3.38  
2.98  
2.78  
2.77  
2.76  
2.75  
2.74  
2.72  
2.57  
2.50  
2.44  
2.43



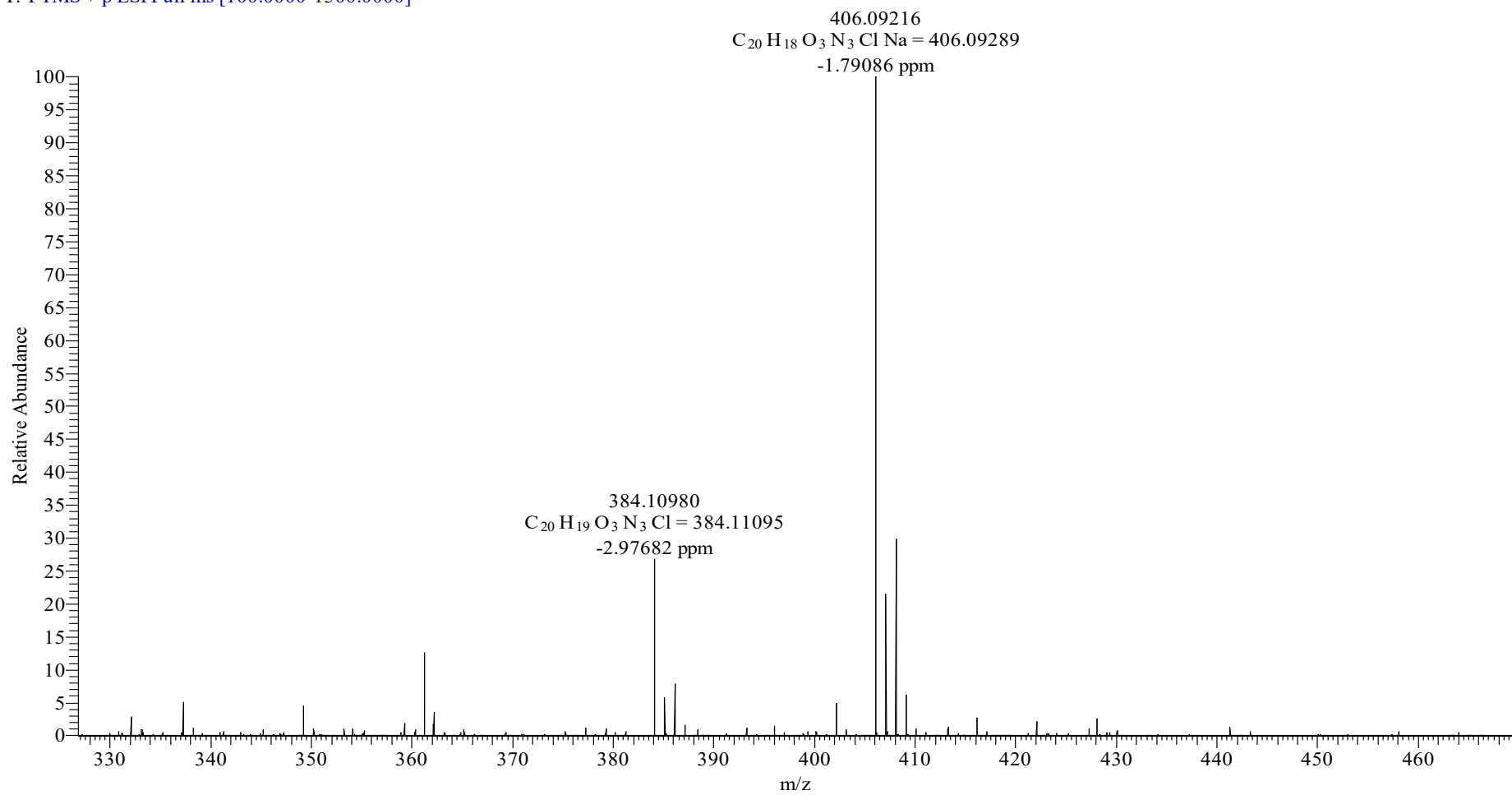
6i, DMSO-d<sub>6</sub>, 600 MHz

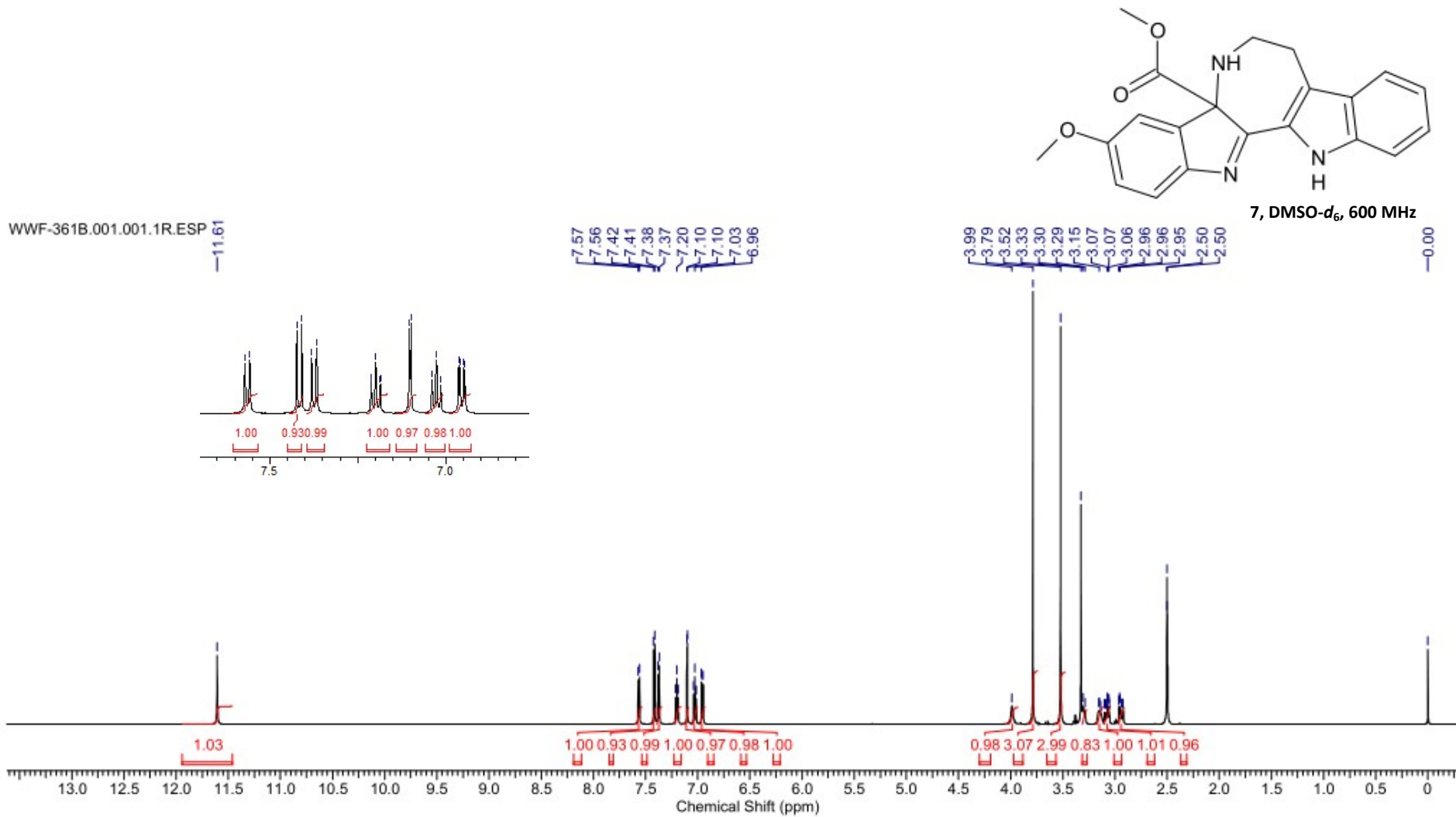




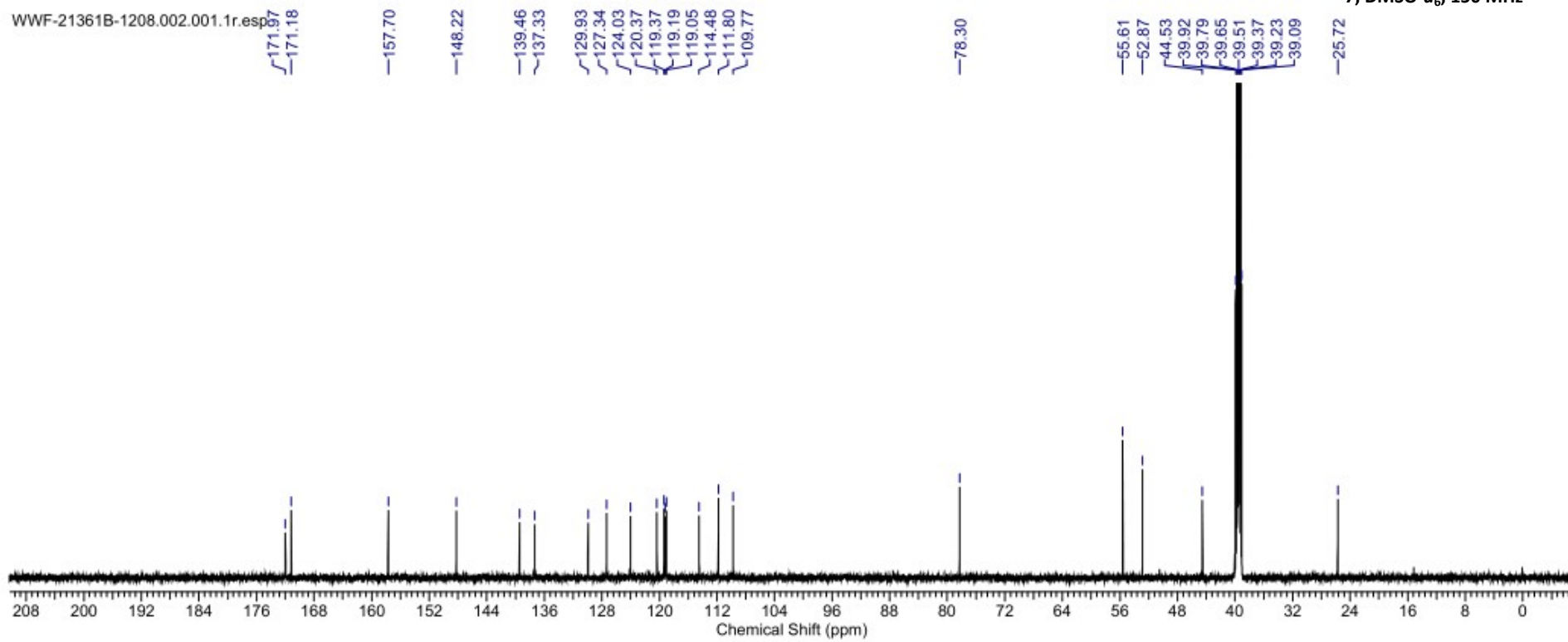


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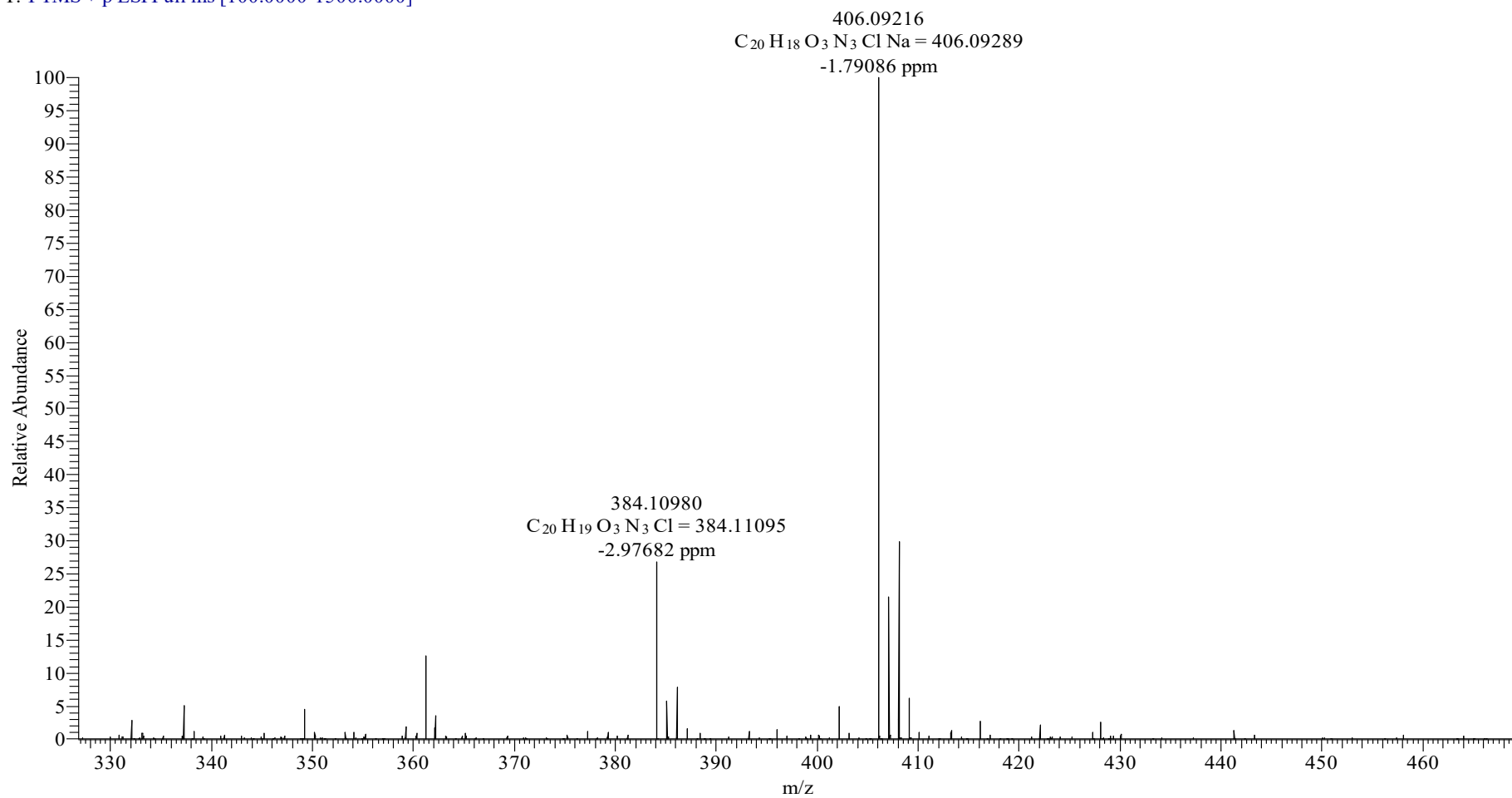


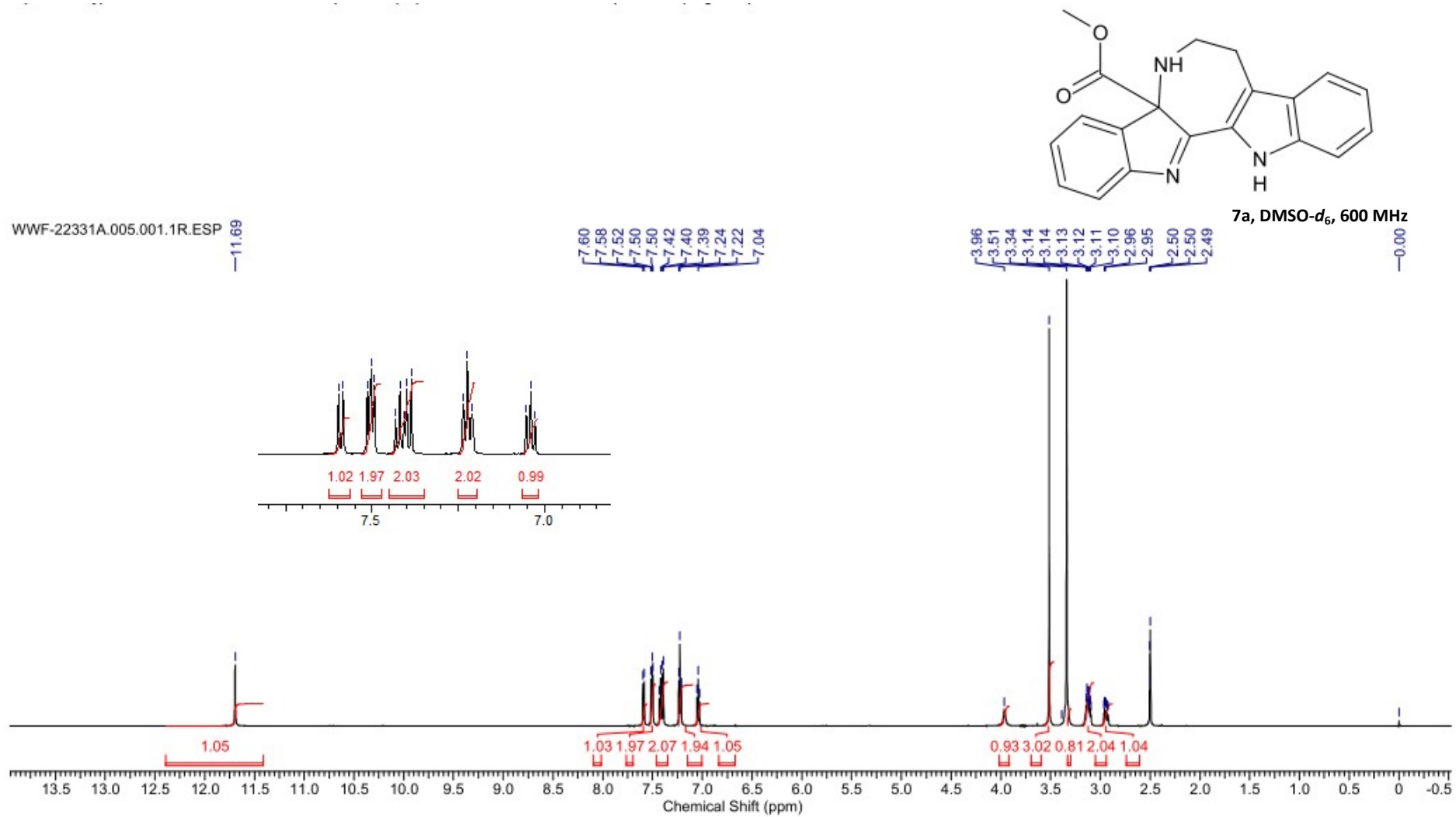


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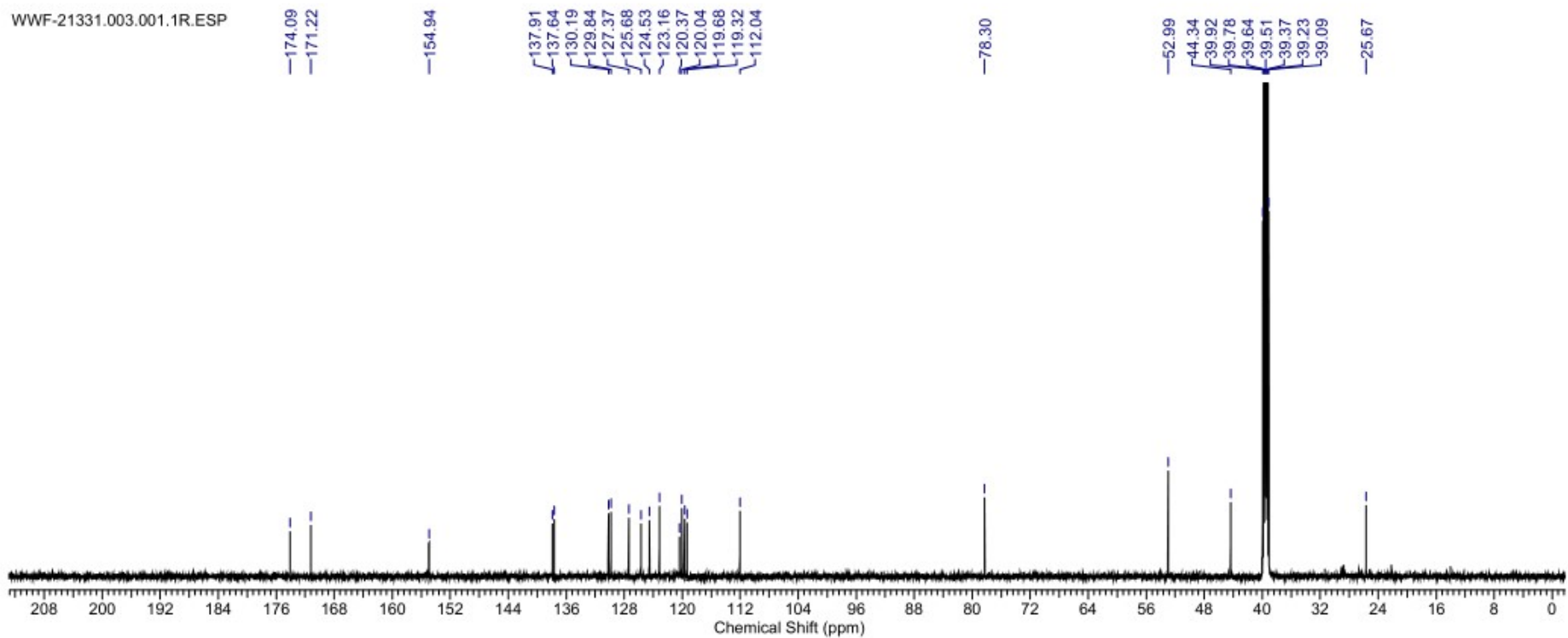


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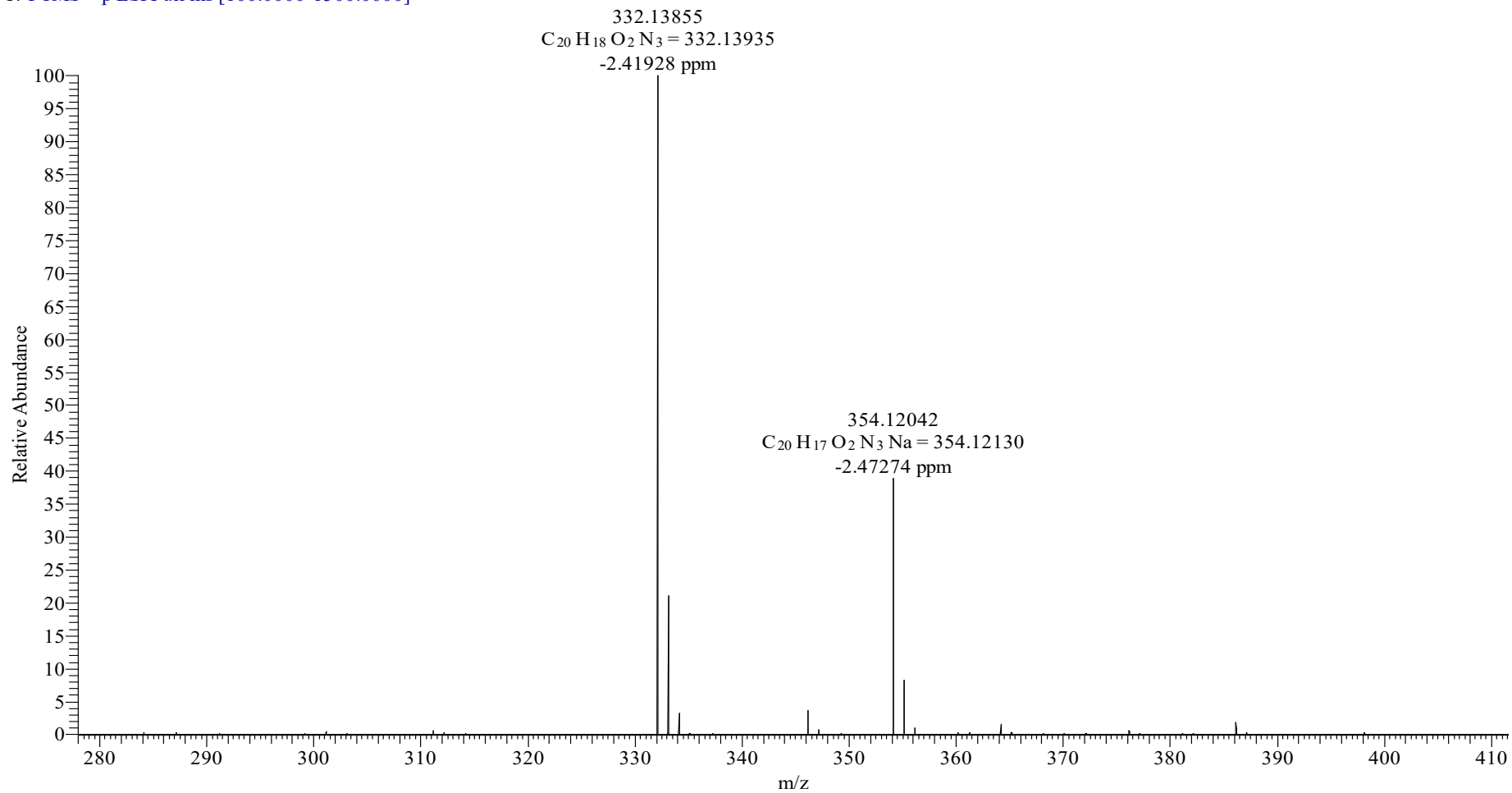




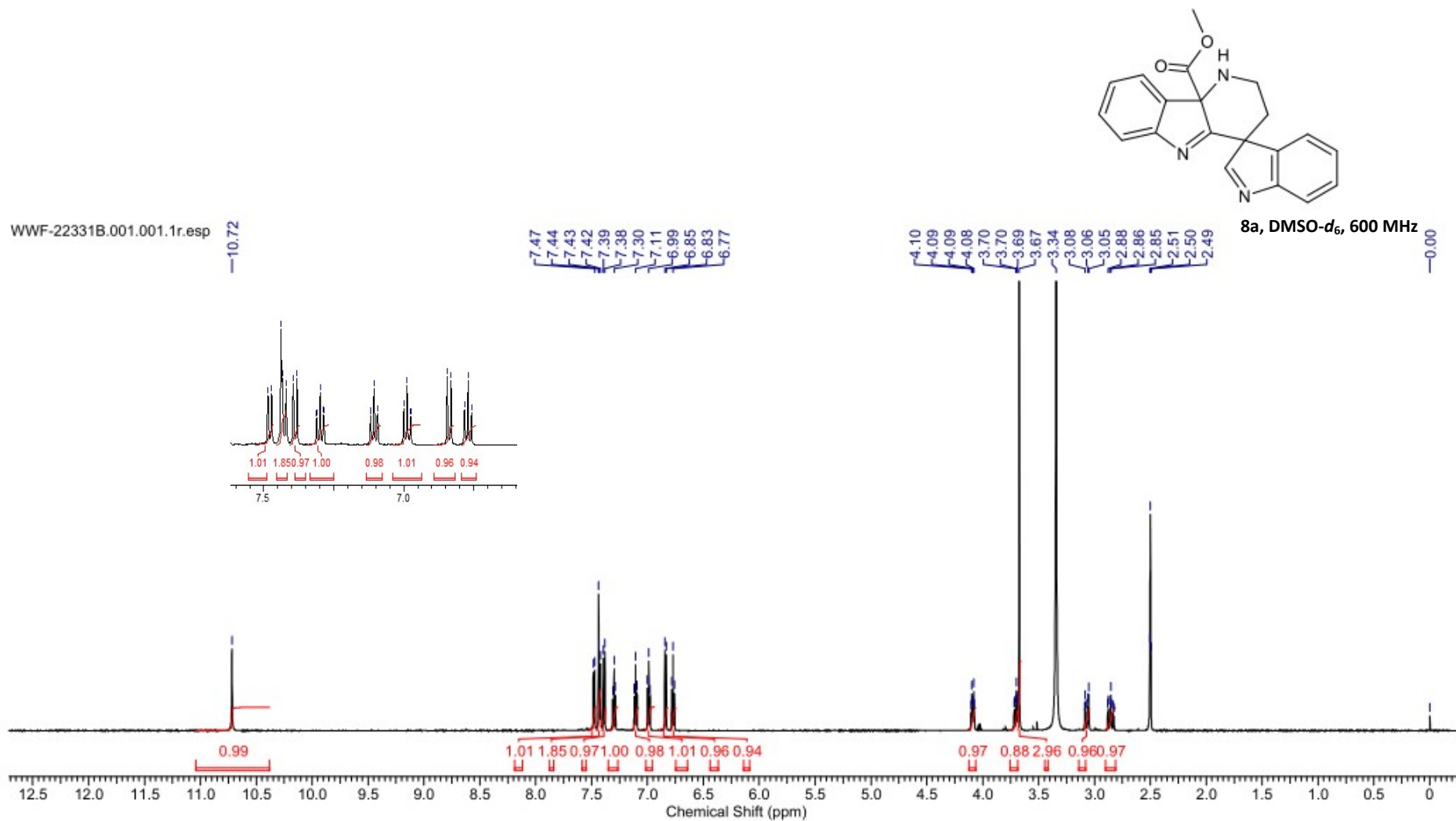
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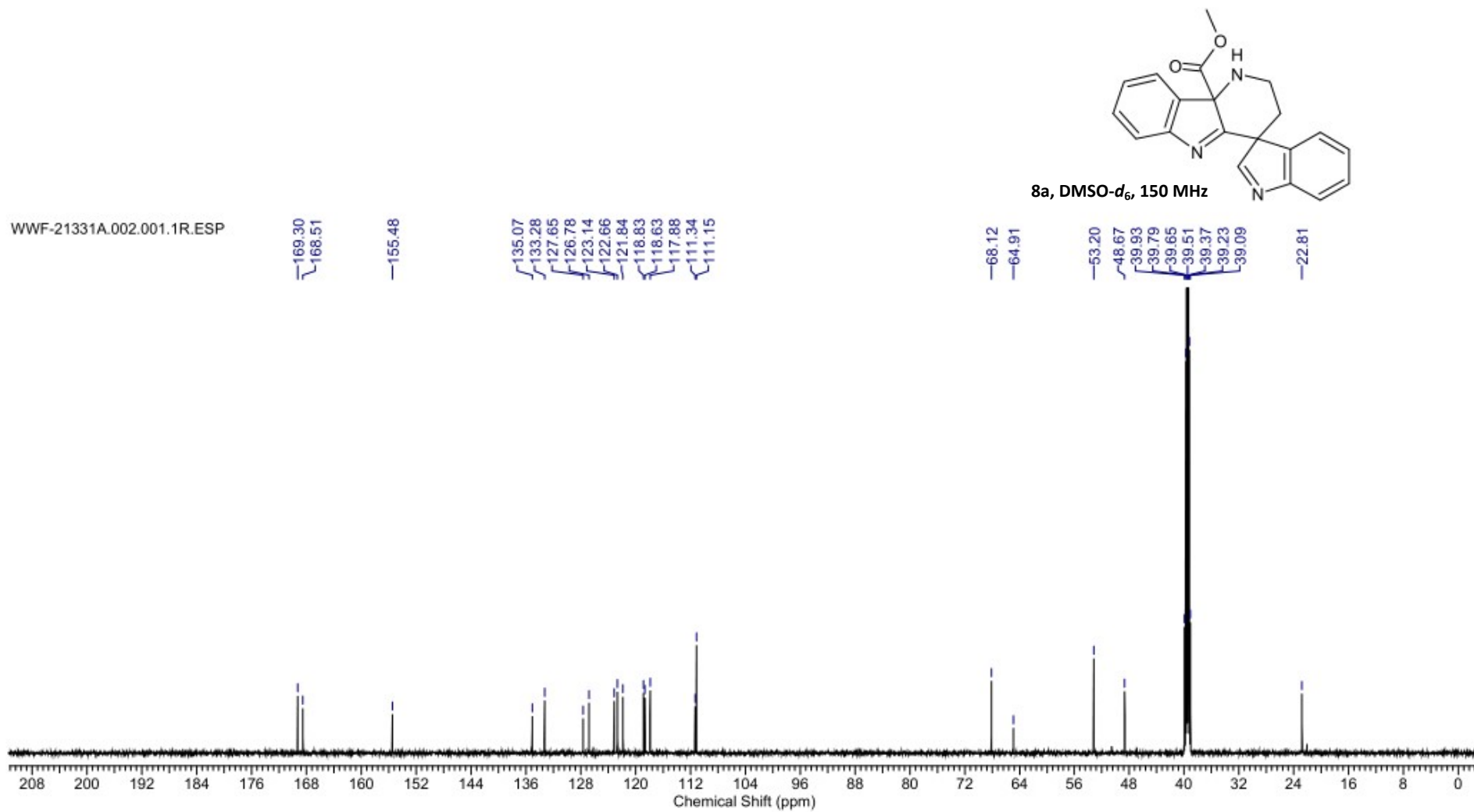


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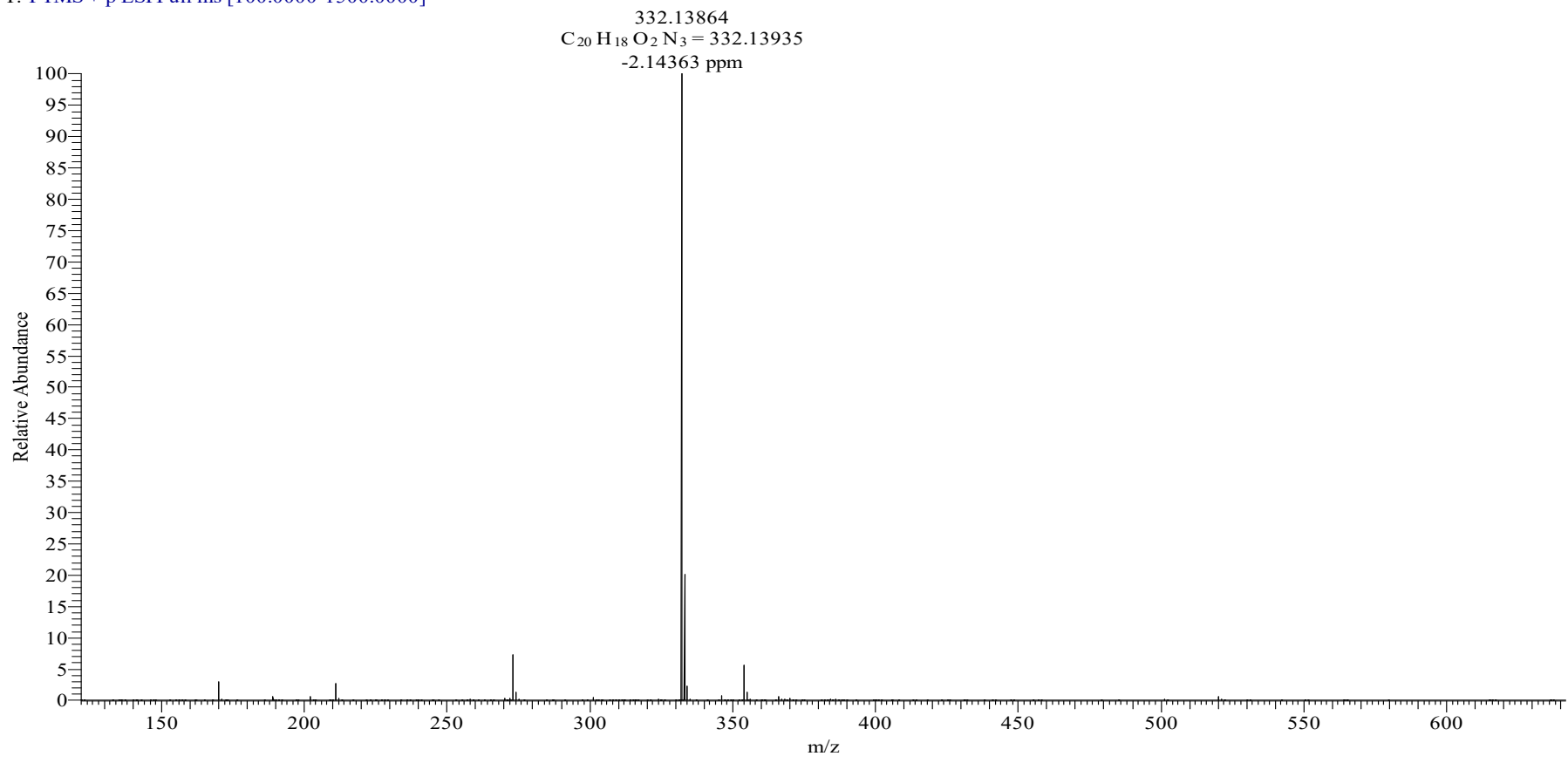


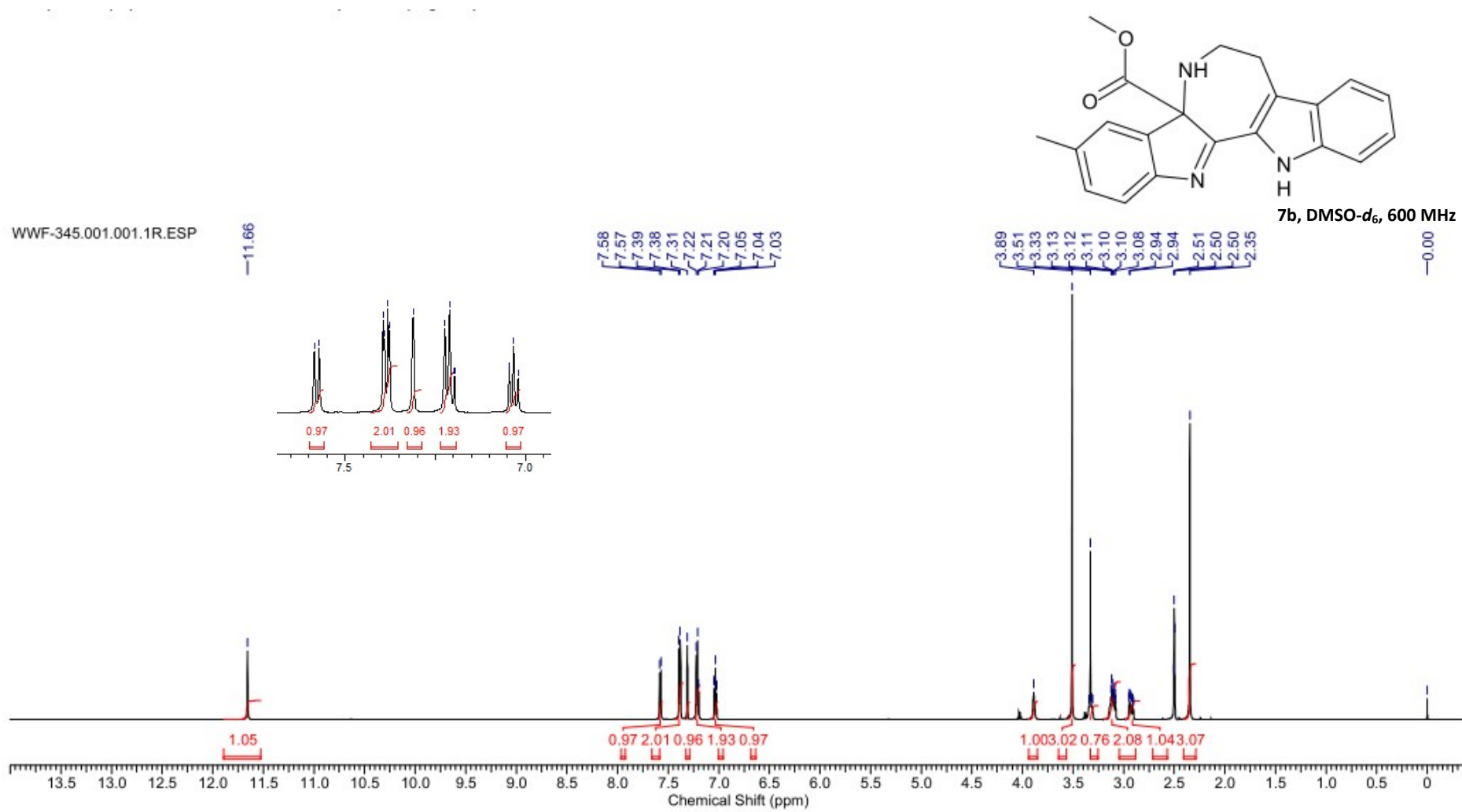






WWF-22331B #22 RT: 0.10 AV: 1 NL: 3.24E9  
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WWF-345.003.001.1R.ESP

173.14  
171.18

152.69

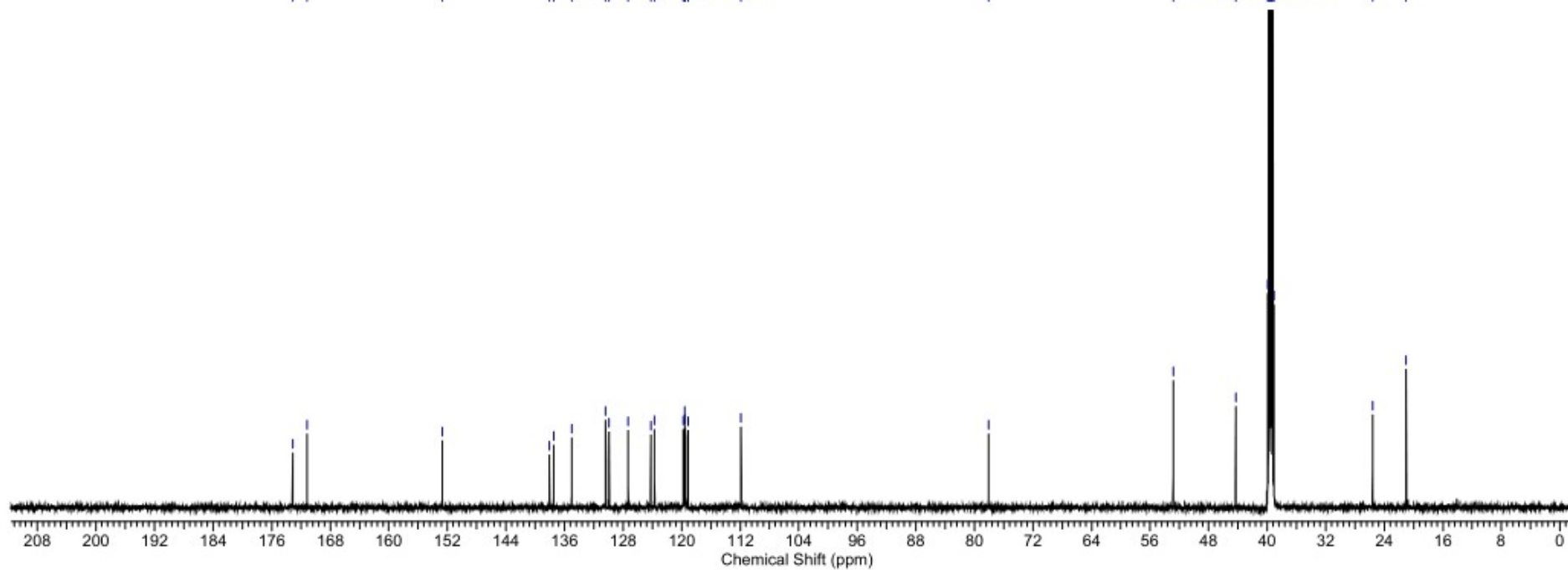
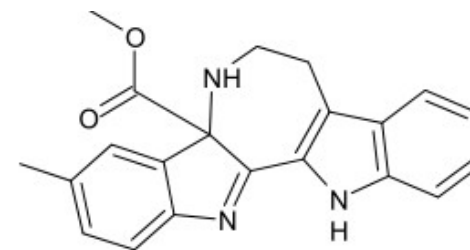
138.05  
137.47  
135.01  
130.37  
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124.21  
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119.77  
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119.48  
119.11  
111.88

78.06

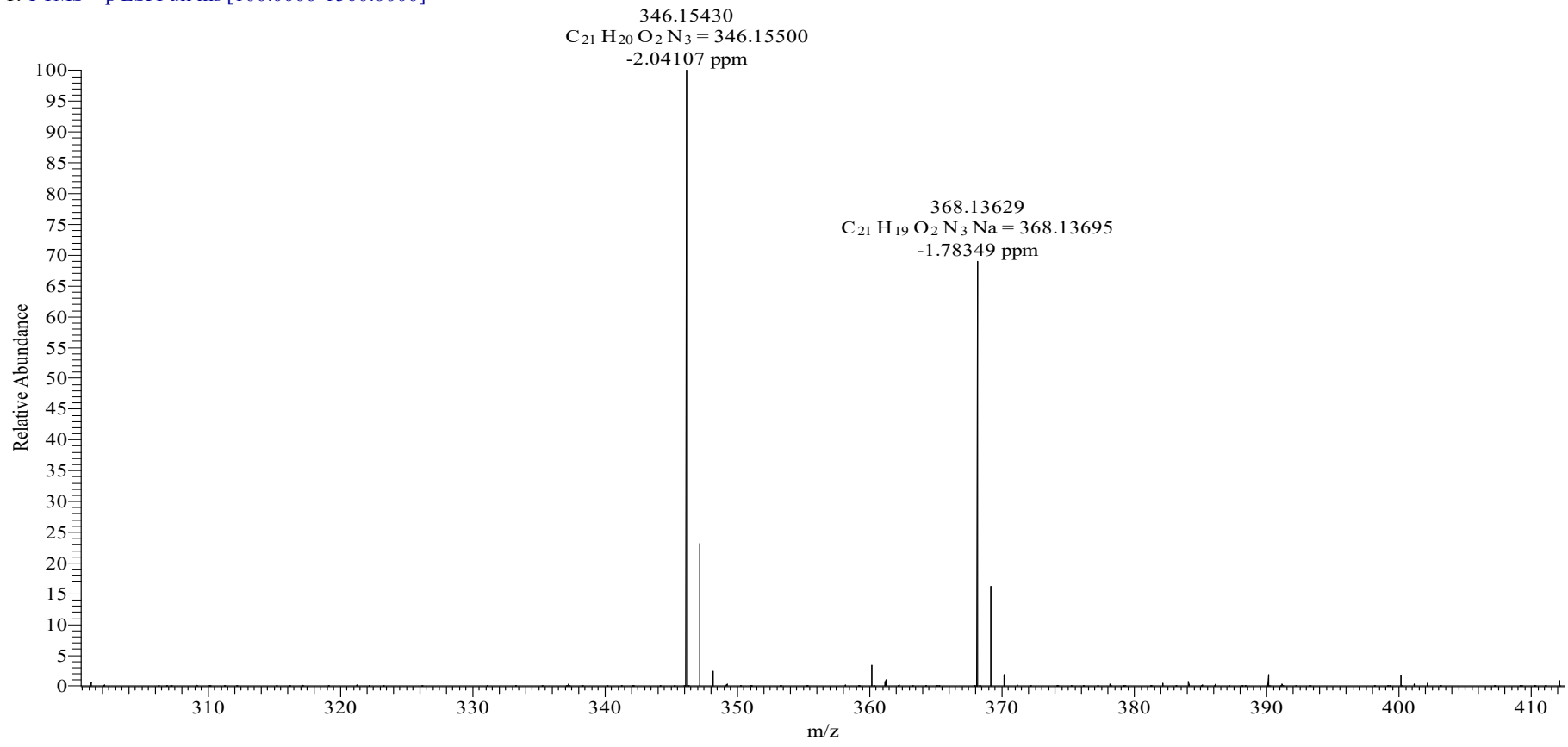
52.84  
44.30  
39.93  
39.79  
39.65  
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39.10

7b, DMSO-*d*<sub>6</sub>, 150 MHz

25.60  
21.01

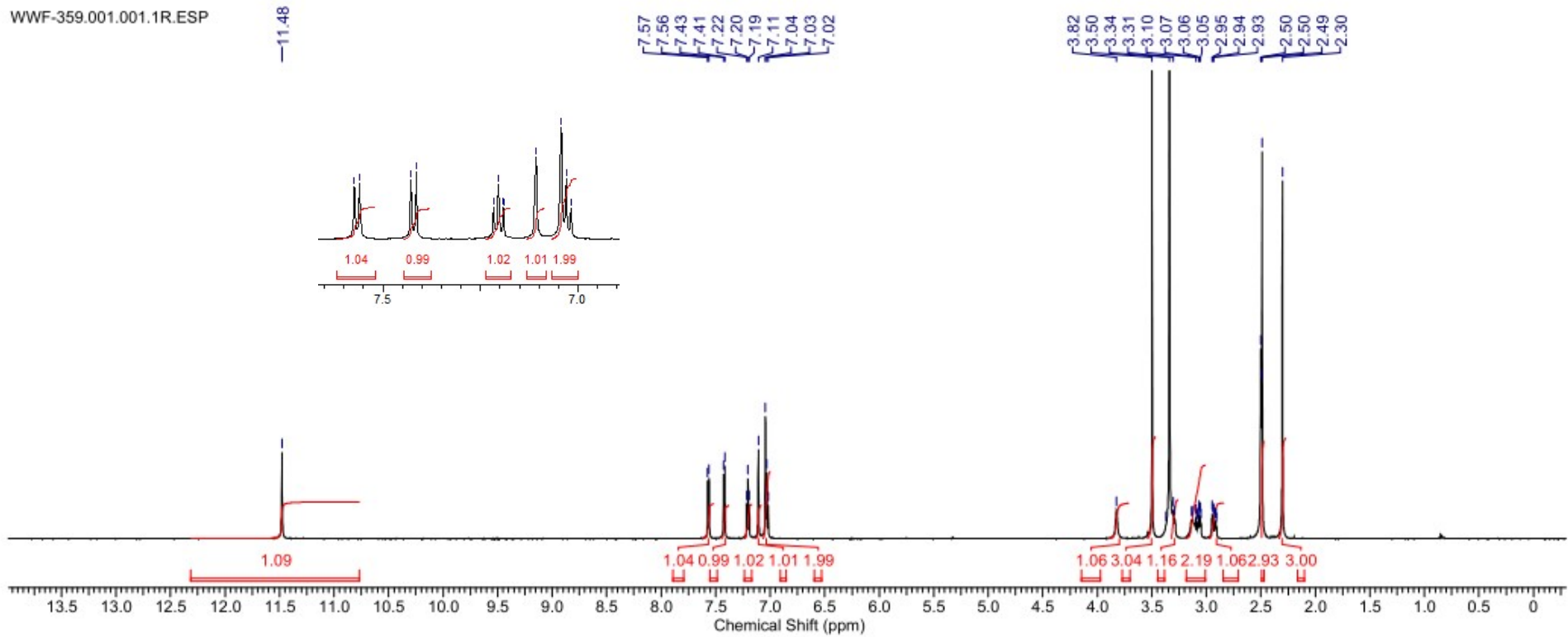


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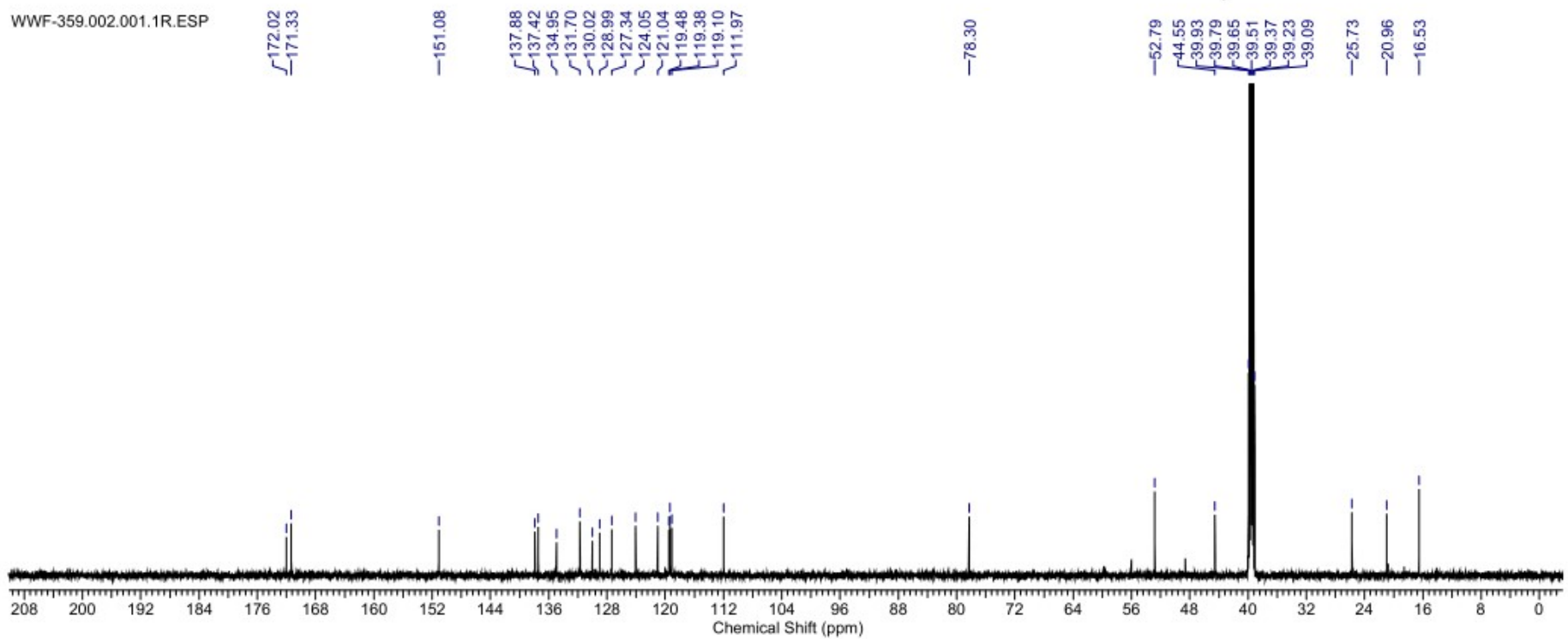


WWF-359.001.001.1R.ESP

—11.48

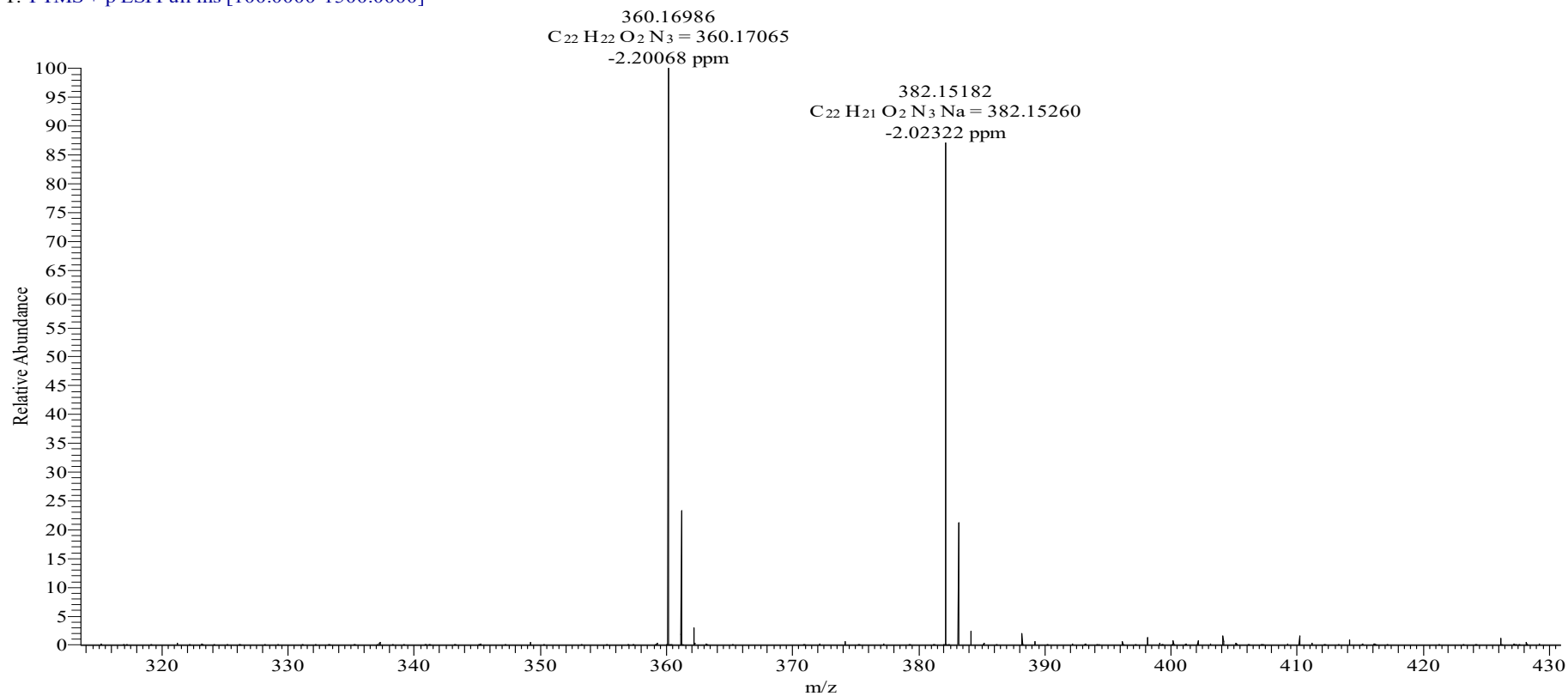


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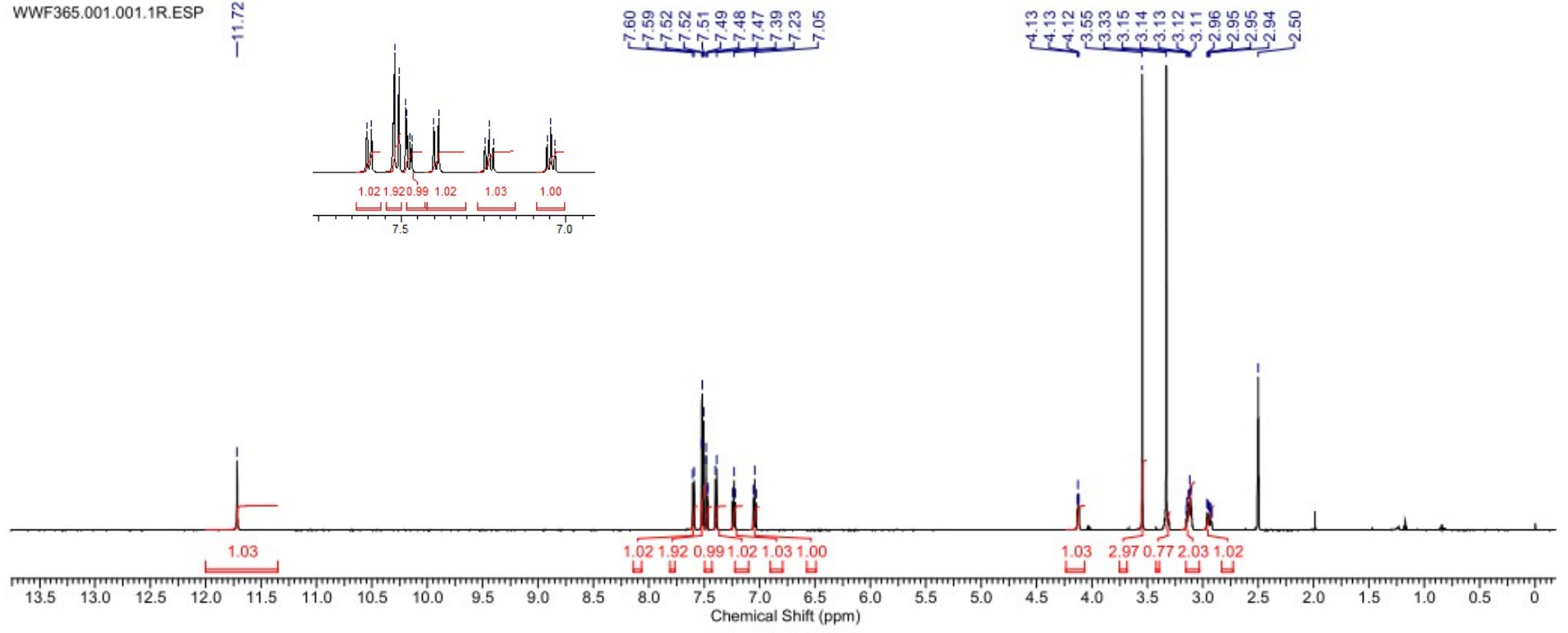
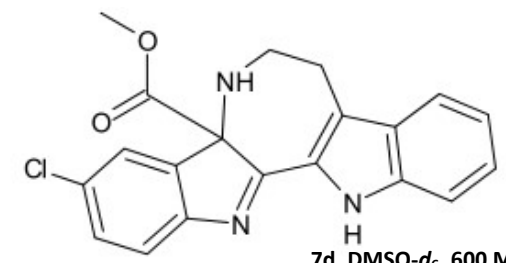


WWF-22359 #22 RT: 0.10 AV: 1 NL: 1.33E9  
T: FTMS + p ESI Full ms [100.0000-1500.0000]



WWF365.001.001.1R.ESP

—11.72



DESKTOP.001.001.1R.ESP

—174.57  
—170.62

—153.71

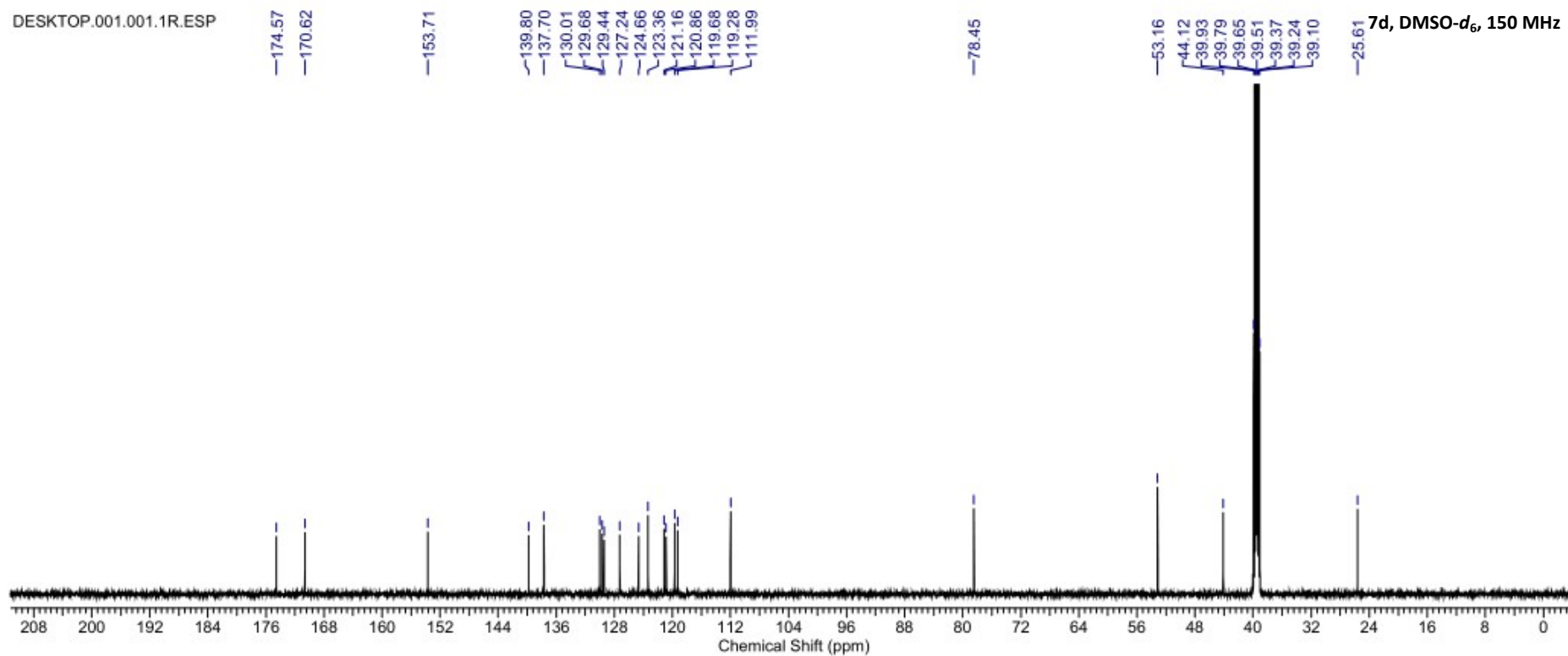
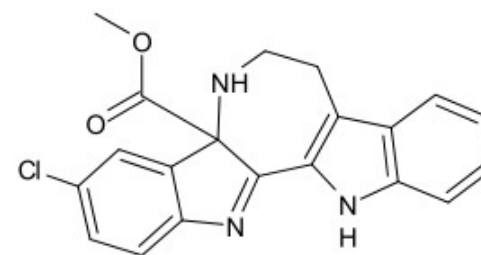
—139.80  
—137.70  
—130.01  
—129.68  
—129.44  
—127.24  
—124.66  
—123.36  
—121.16  
—120.86  
—119.68  
—119.28  
—111.99

—78.45

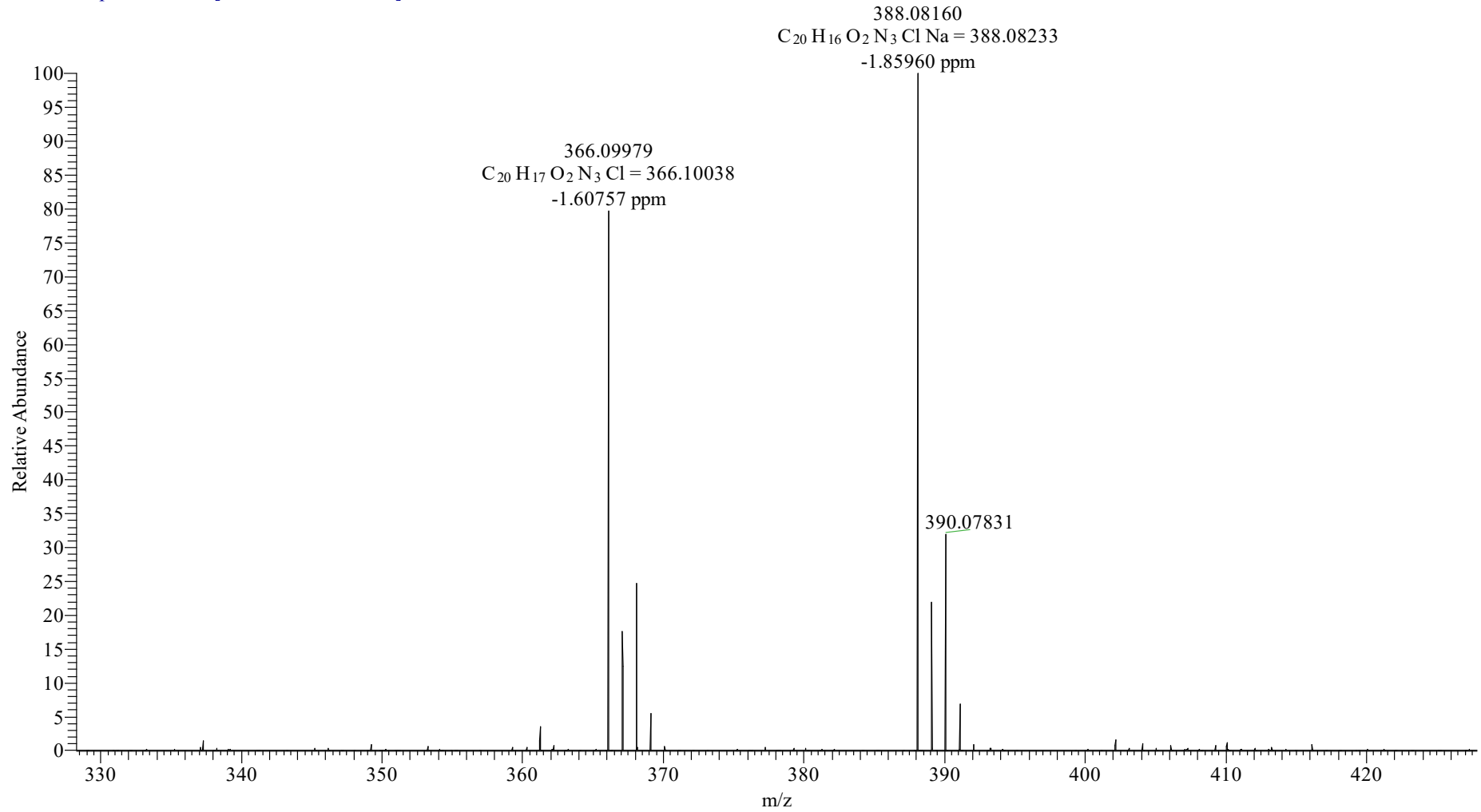
—53.16  
—44.12  
—39.93  
—39.79  
—39.65  
—39.51  
—39.37  
—39.24  
—39.10

—25.61

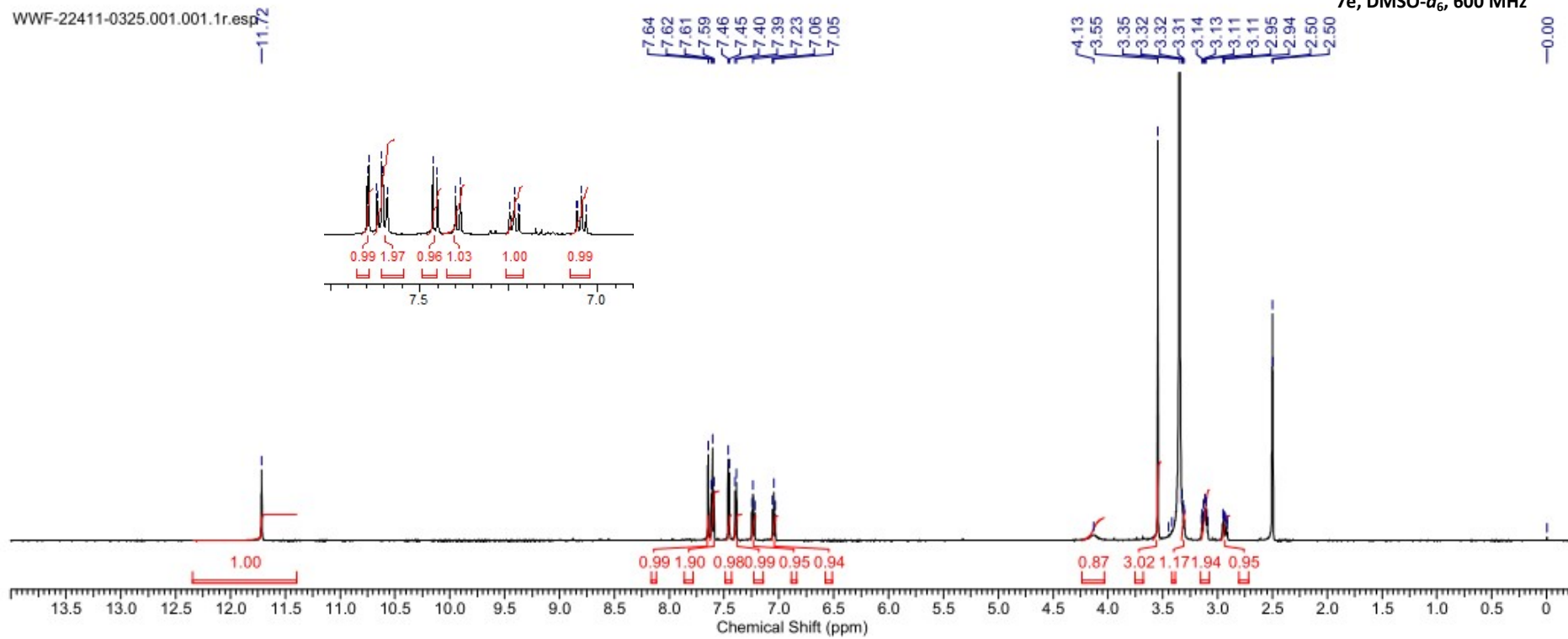
7d, DMSO-*d*<sub>6</sub>, 150 MHz



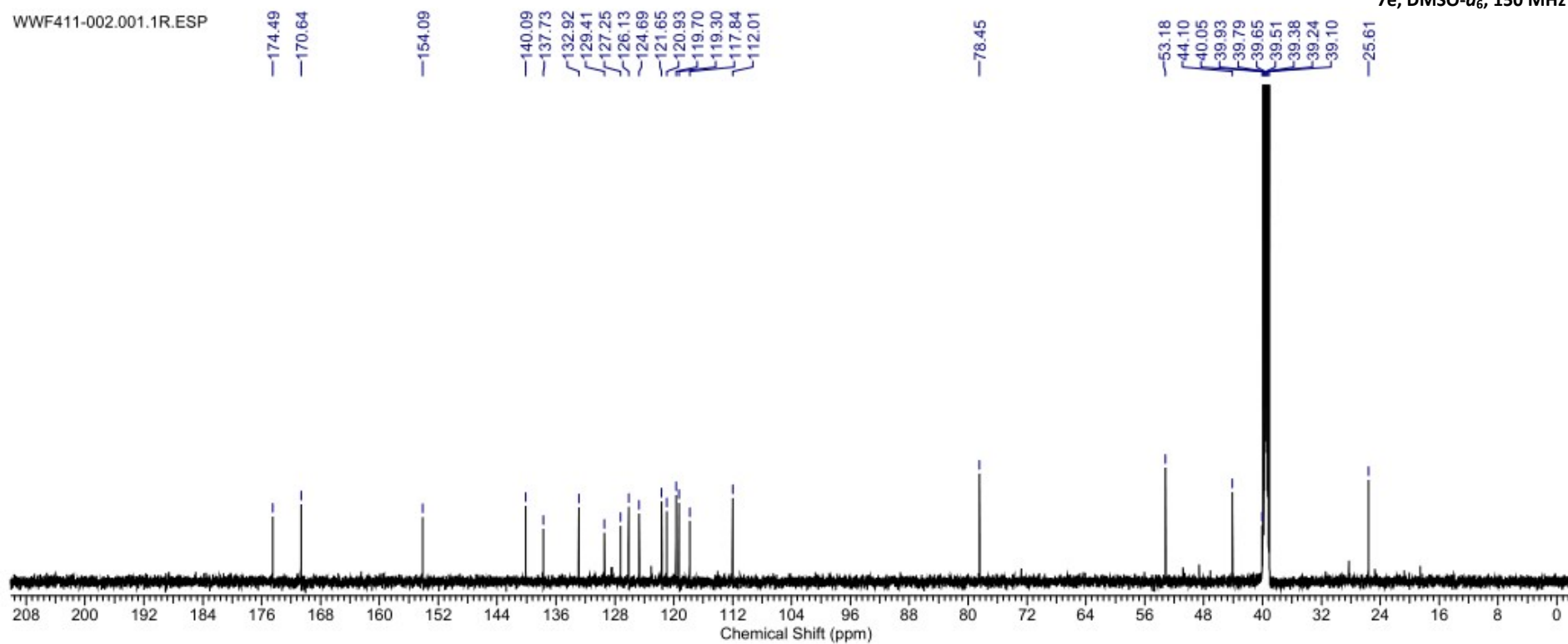
WWF-22365 #23 RT: 0.10 AV: 1 NL: 1.00E9  
T: FTMS + p ESI Full ms [100.0000-1500.0000]



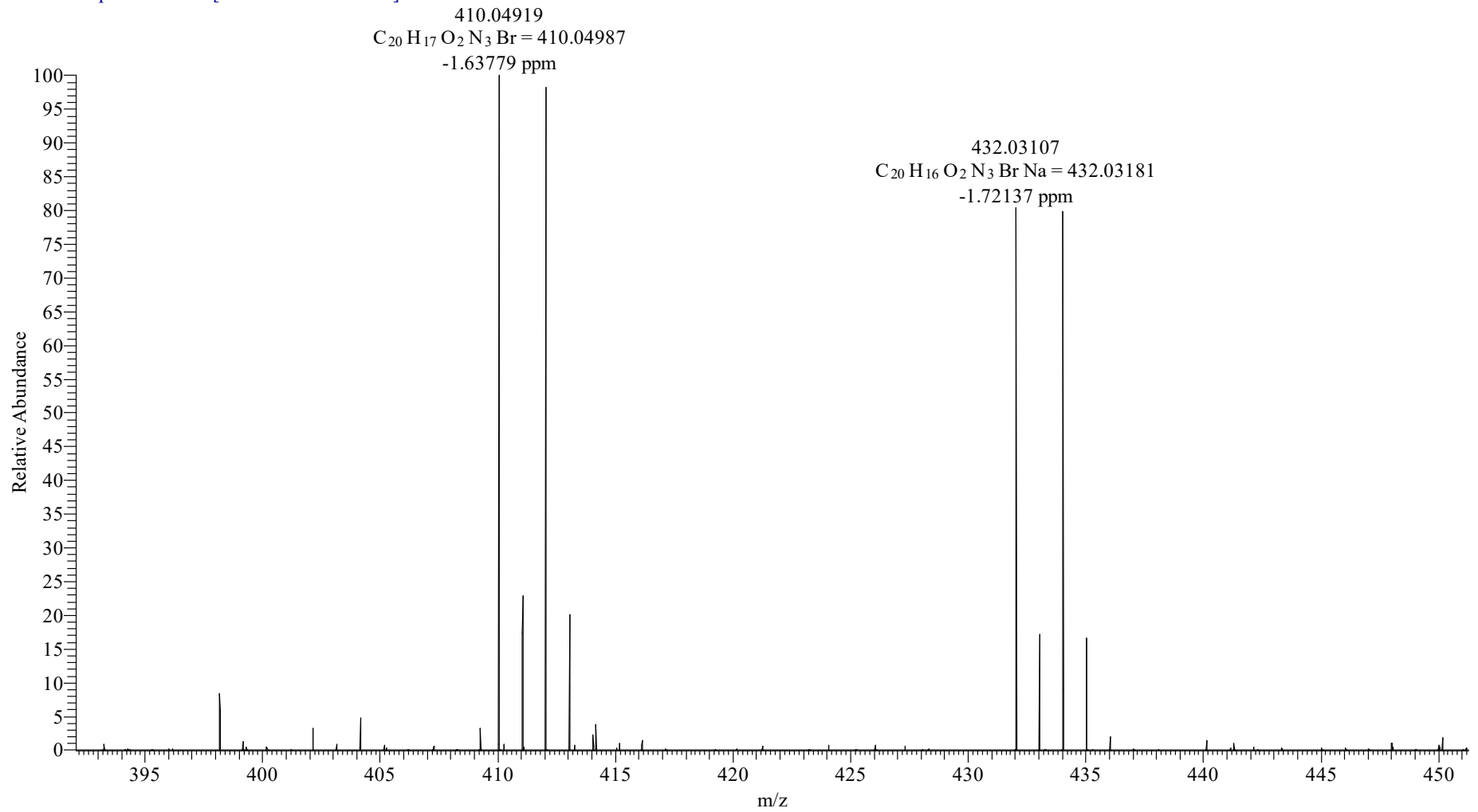
WWF-22411-0325.001.001.1r.esp2



WWF411-002.001.1R.ESP



WWF-22411-5 #22 RT: 0.10 AV: 1 NL: 2.97E8  
T: FTMS + p ESI Full ms [100.0000-1500.0000]



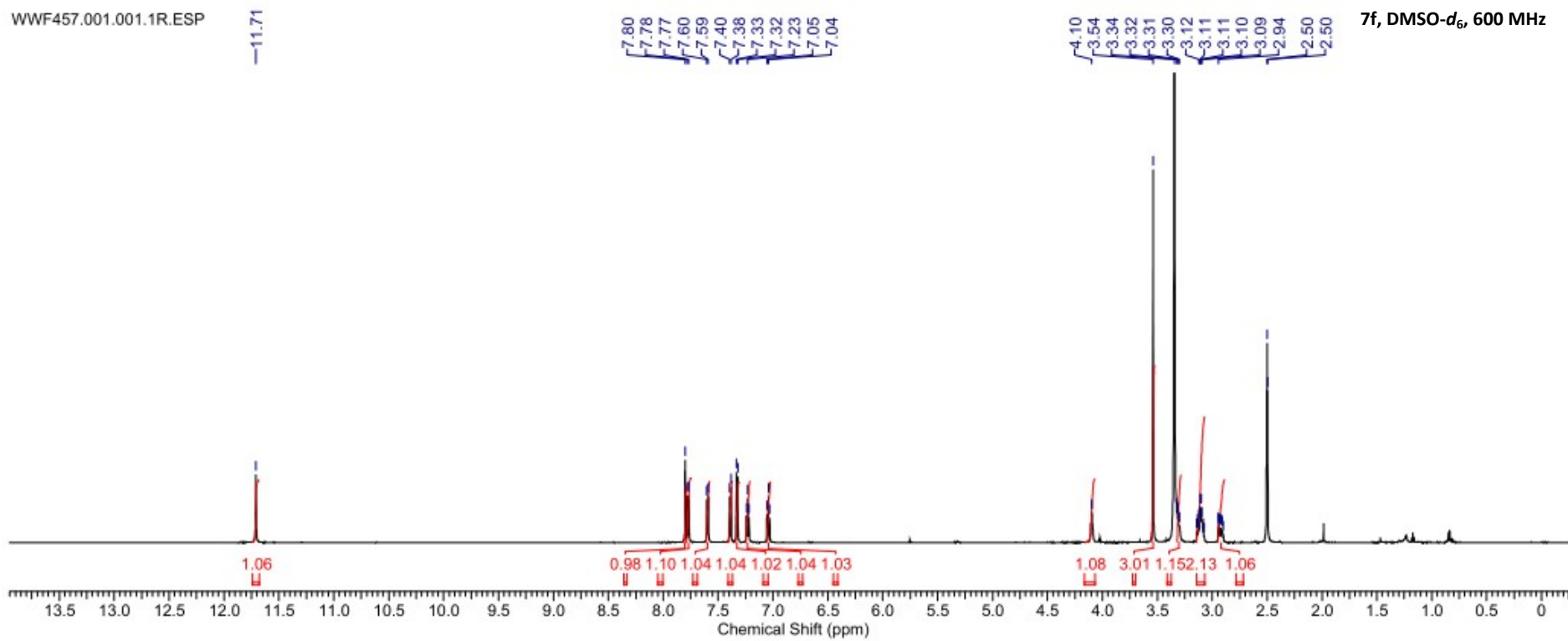
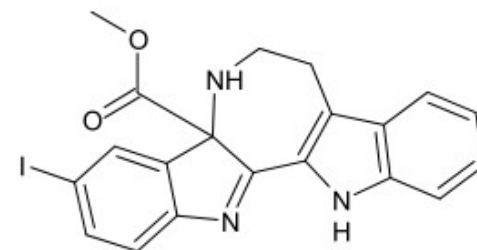
WWF457.001.001.1R.ESP

11.71

7.80  
7.78  
7.77  
7.60  
7.59  
7.40  
7.38  
7.33  
7.32  
7.23  
7.05  
7.04

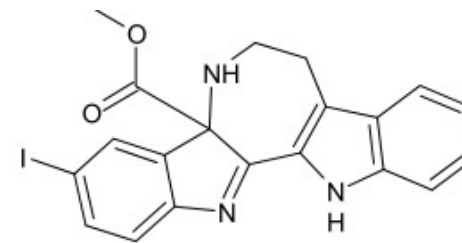
4.10  
3.54  
3.34  
3.32  
3.31  
3.30  
3.12  
3.11  
3.10  
3.09  
2.94  
2.50  
2.50

7f, DMSO-d<sub>6</sub>, 600 MHz

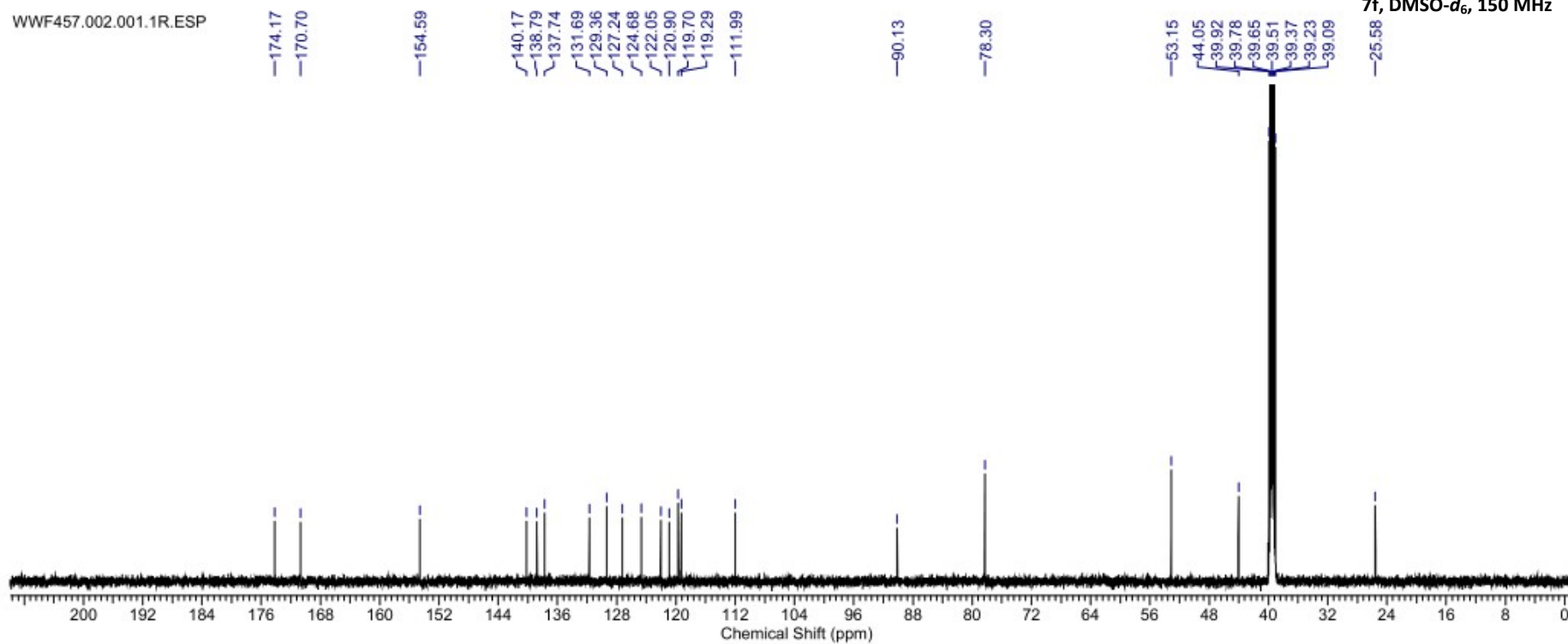




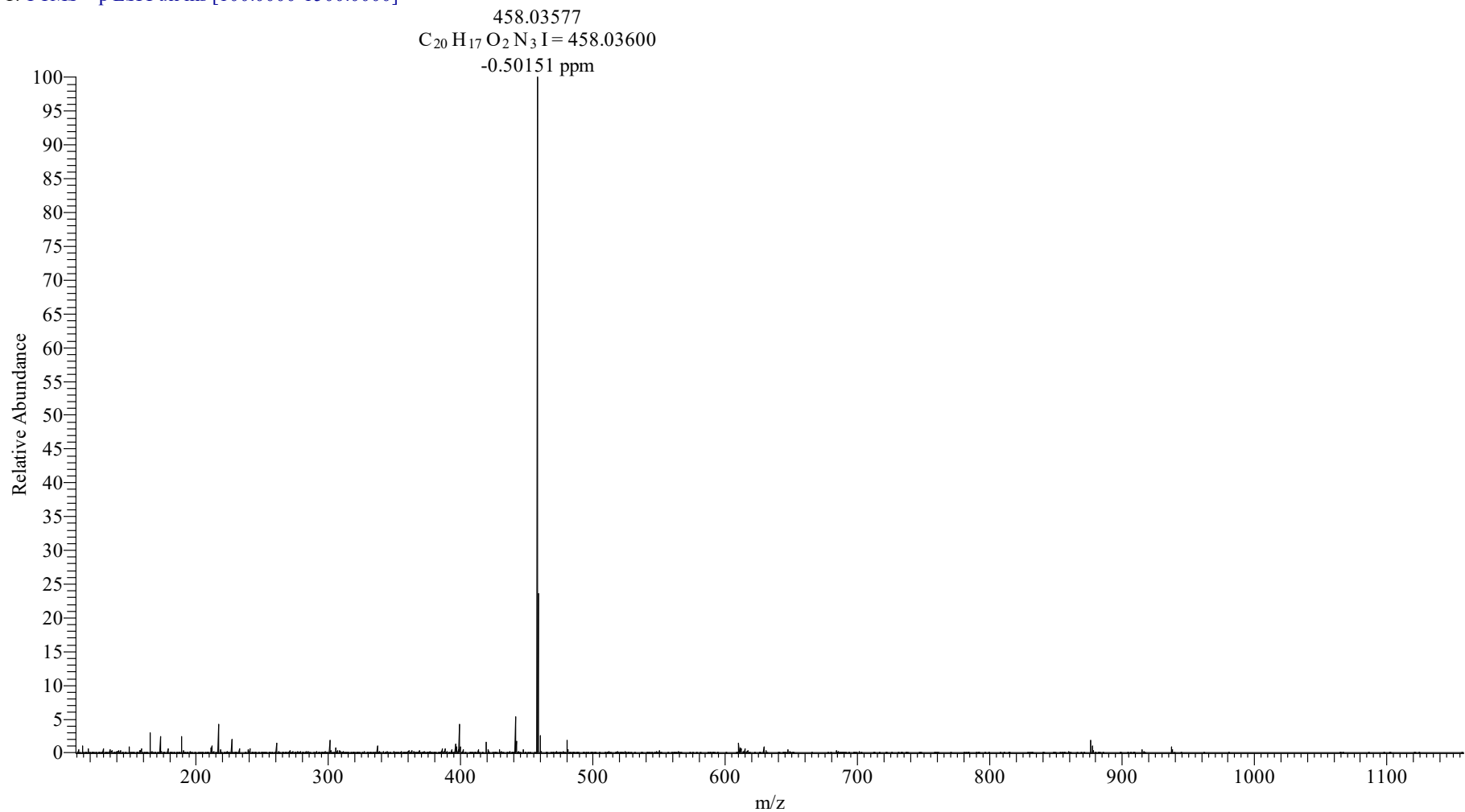
WWF457.002.001.1R.ESP



7f, DMSO-*d*<sub>6</sub>, 150 MHz



WWF-22457 #24 RT: 0.10 AV: 1 NL: 8.84E8  
T: FTMS + p ESI Full ms [100.0000-1500.0000]

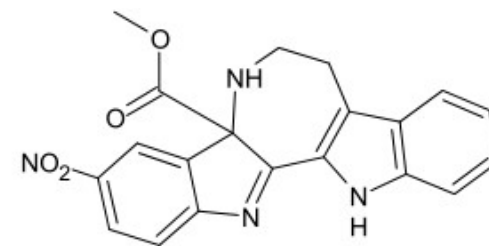


WWF376.001.001.1R.ESP

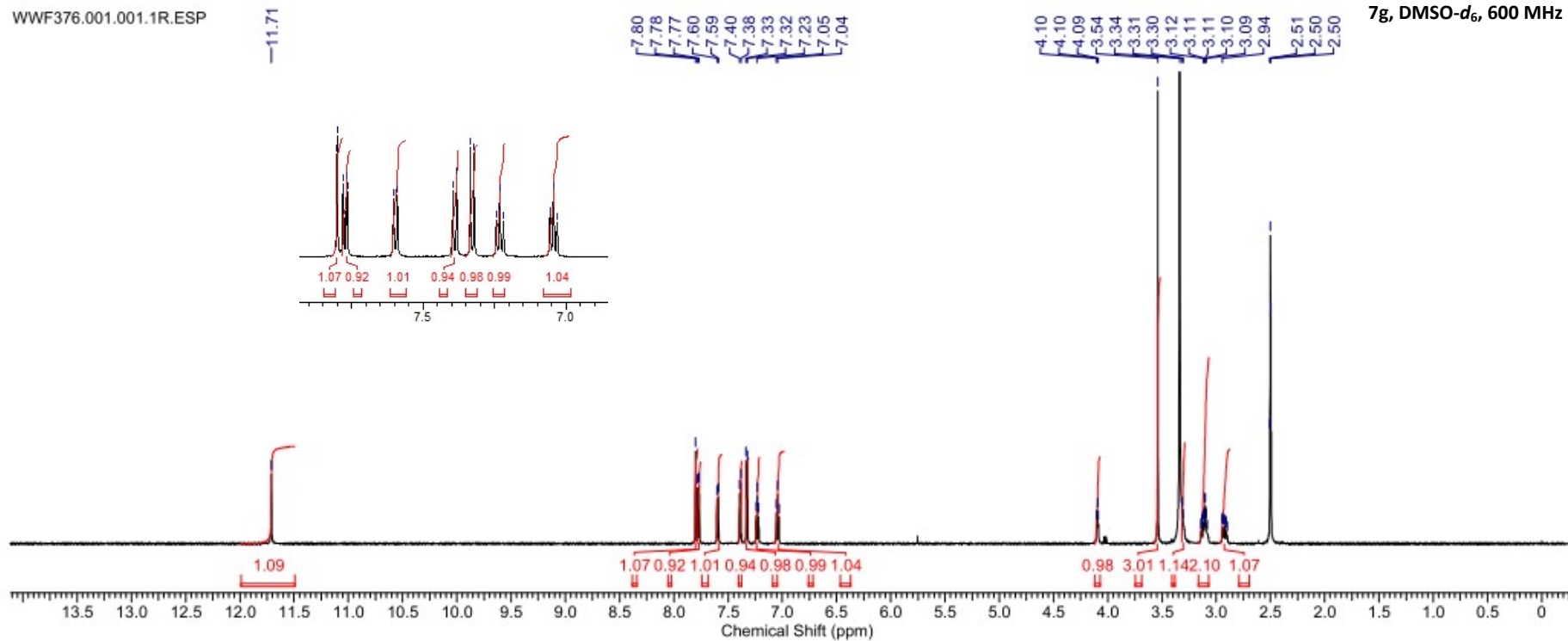
11.71

7.80  
7.78  
7.77  
7.60  
7.59  
7.40  
7.38  
7.33  
7.32  
7.23  
7.05  
7.04

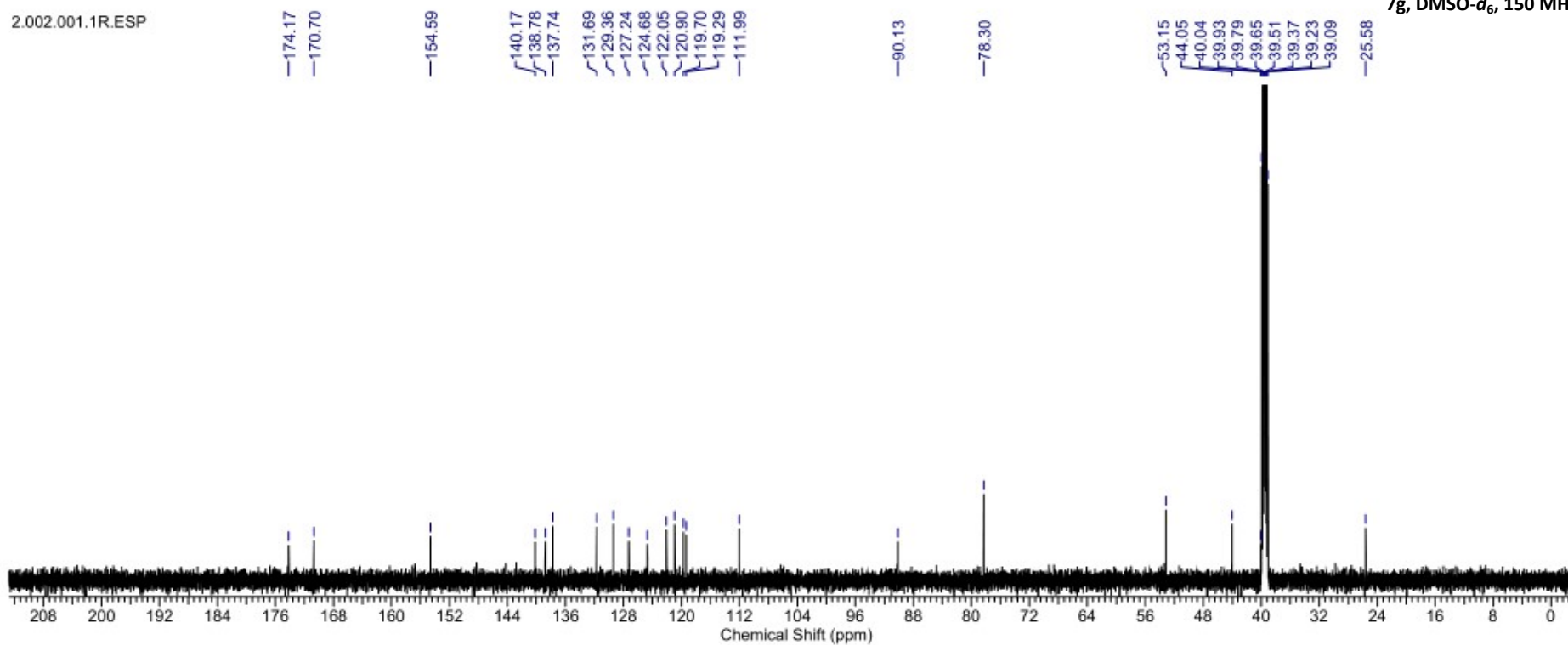
4.10  
4.10  
4.09  
3.94  
3.34  
3.31  
3.30  
3.12  
3.11  
3.10  
3.09  
2.94  
2.51  
2.50  
2.50



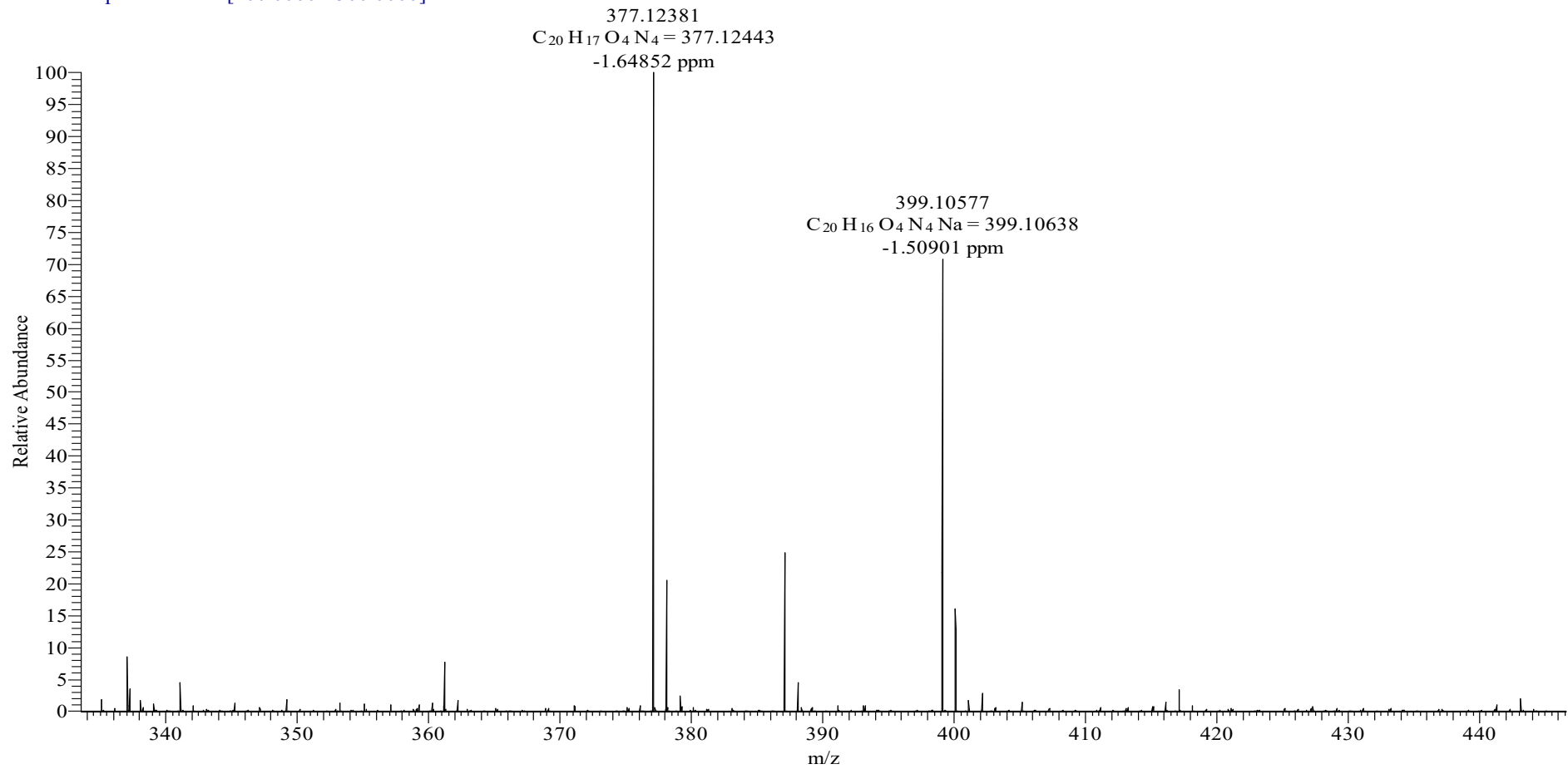
7g, DMSO-d<sub>6</sub>, 600 MHz



2.002.001.1R.ESP

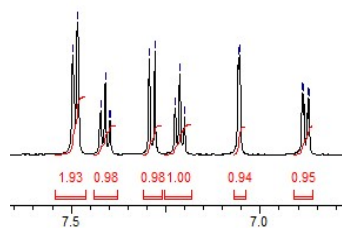


WWF-22376 #24 RT: 0.10 AV: 1 NL: 2.39E8  
T: FTMS + p ESI Full ms [100.0000-1500.0000]

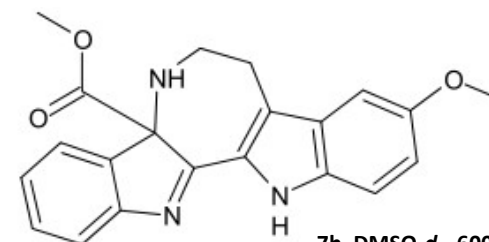


WWF-20361.001.001.1R.ESP

11.55

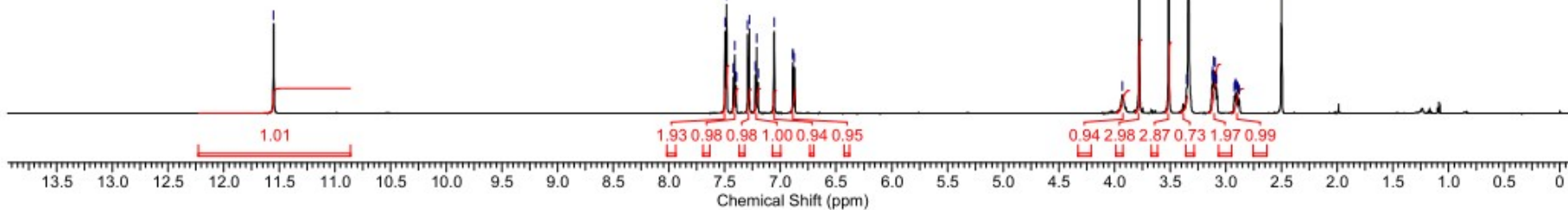


7.50  
7.48  
7.41  
7.29  
7.28  
7.23  
7.21  
7.05  
6.89  
6.89  
6.87

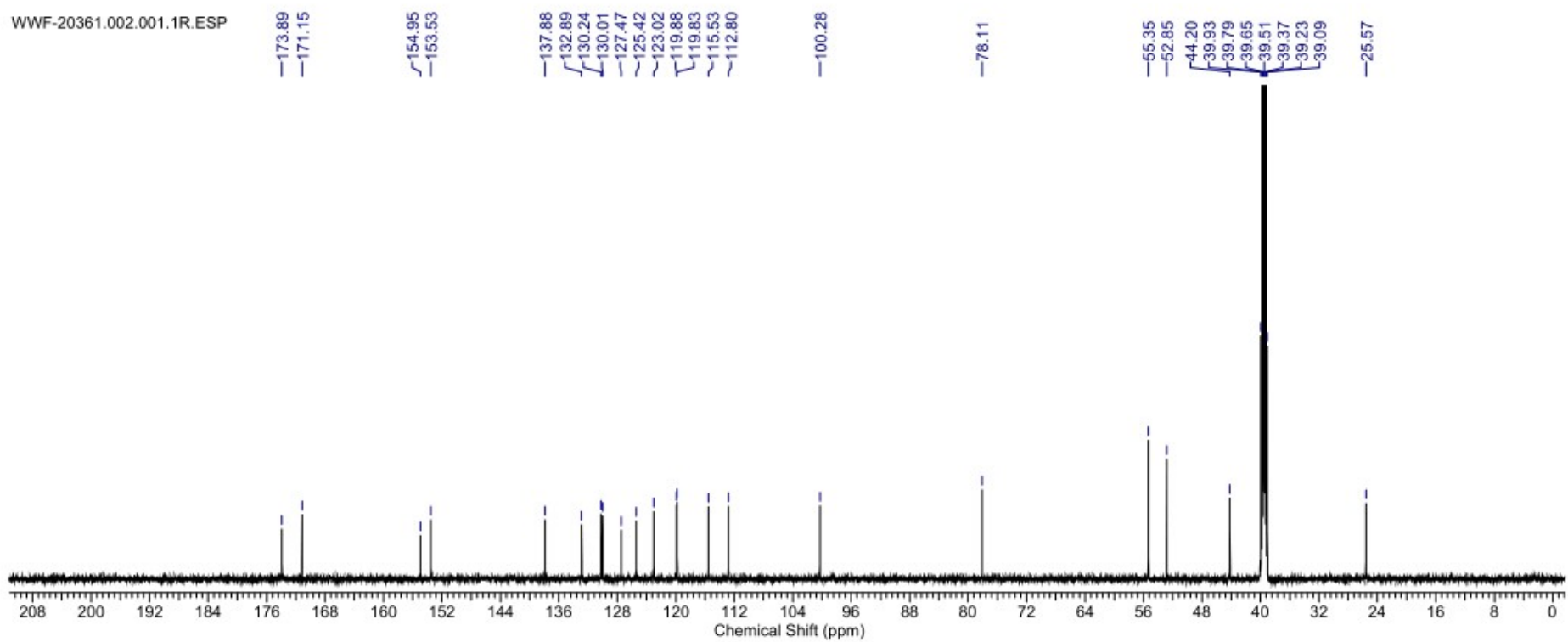


7h, DMSO-d<sub>6</sub>, 600 MHz

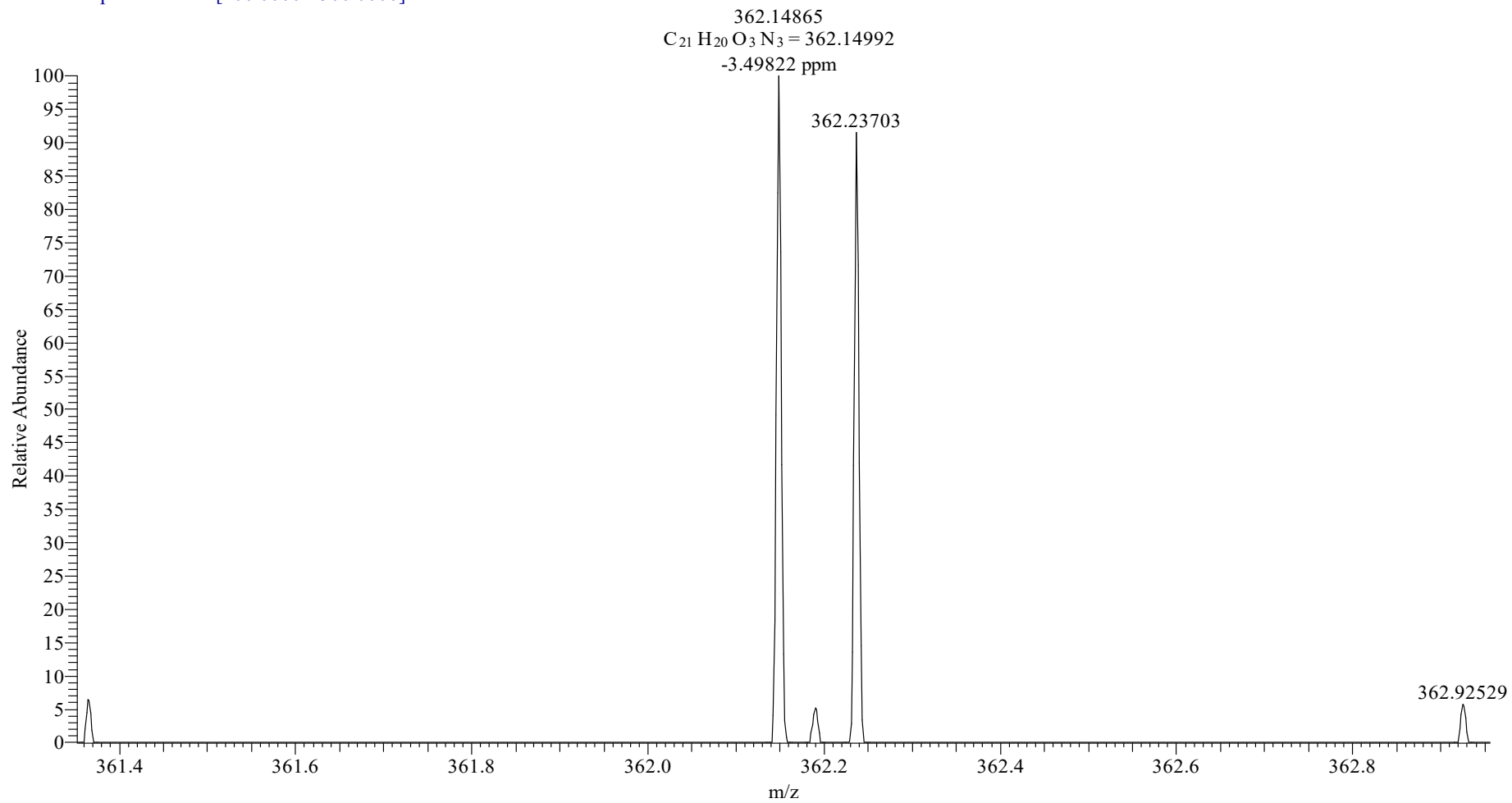
3.93  
3.78  
3.51  
3.33  
3.12  
3.12  
3.11  
3.10  
3.09  
3.09  
3.08  
2.92  
2.91  
2.50



WWF-20361.002.001.1R.ESP

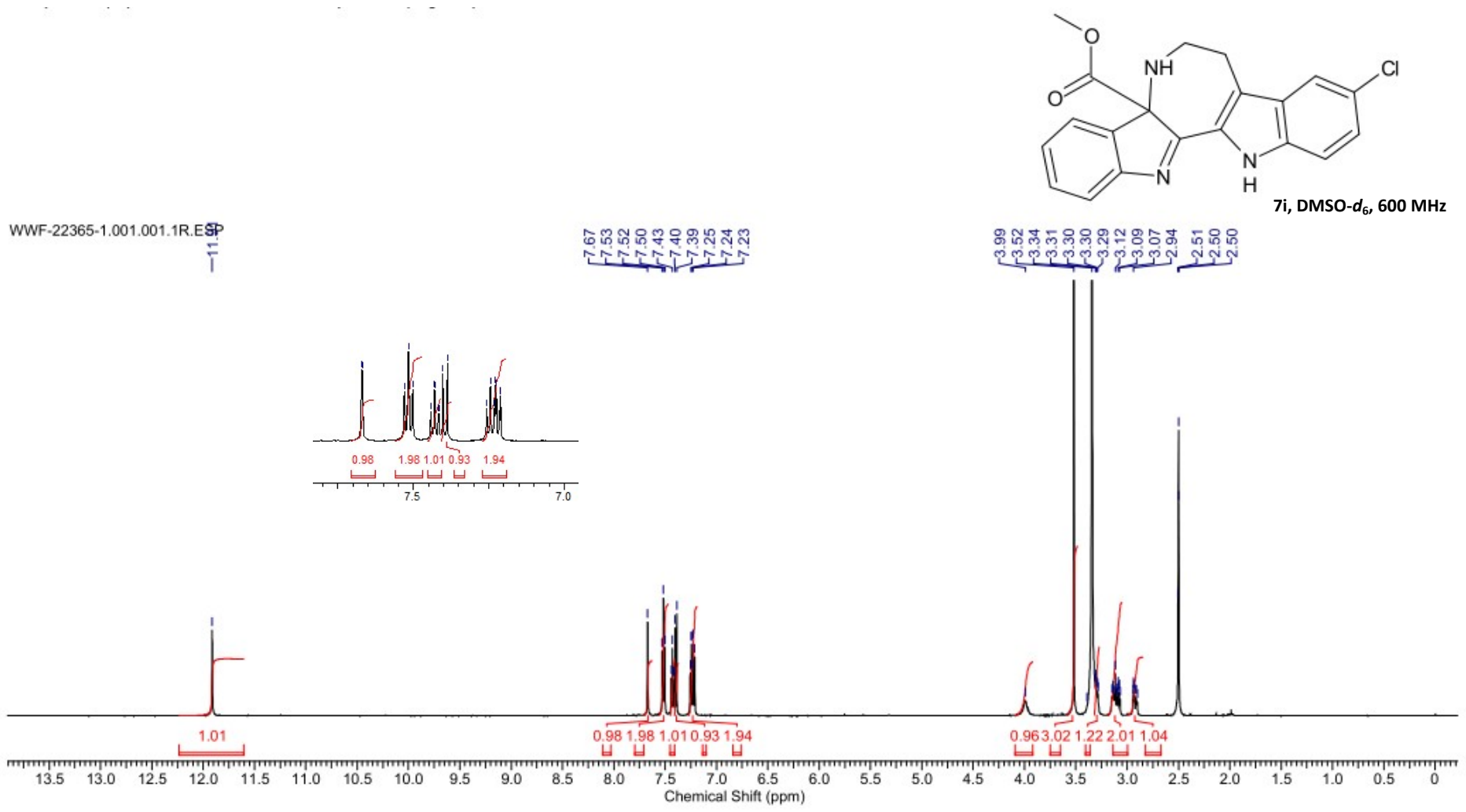


XDL-21361 #28 RT: 0.12 AV: 1 NL: 2.16E6  
T: FTMS + p ESI Full ms [100.0000-1500.0000]





WWF-22365-1.001.001.1R.ESF



2.001.001.1R.ESP

—173.95  
—170.95

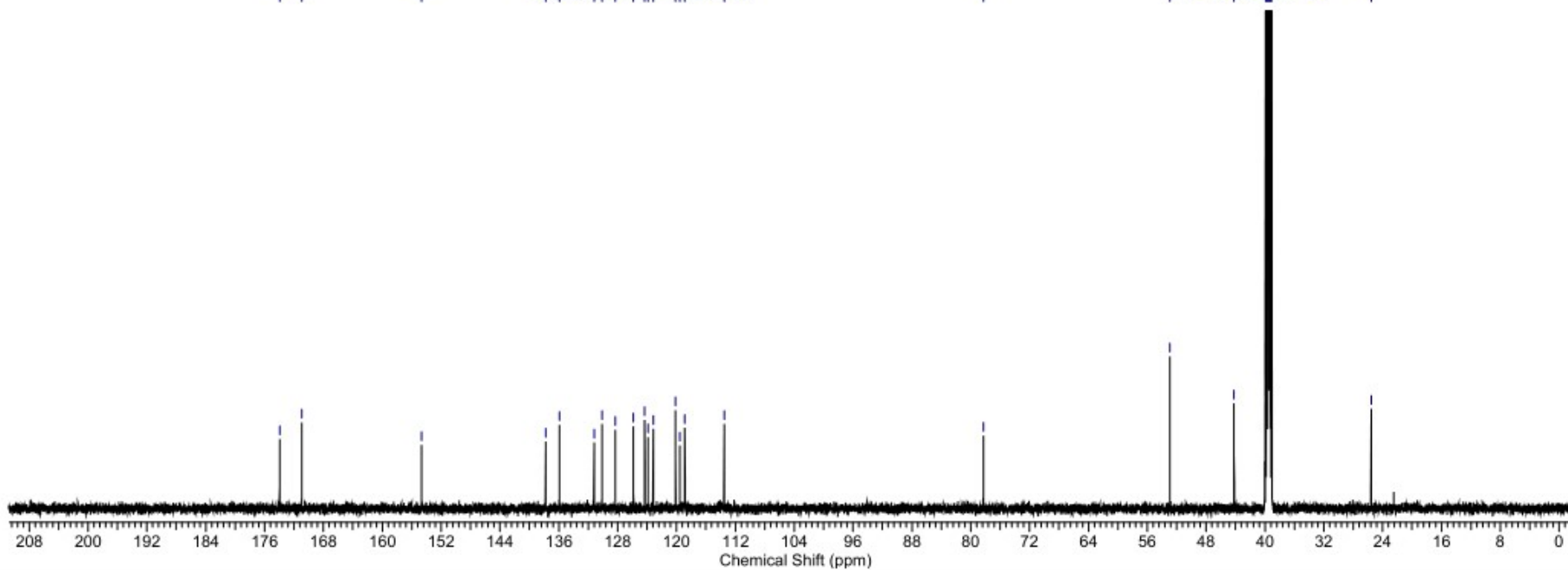
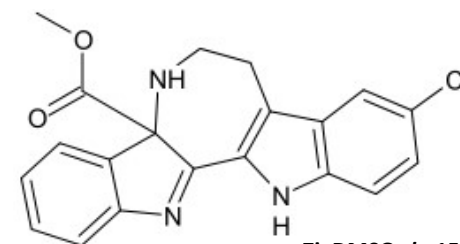
—154.67

—137.79  
—135.89  
—131.21  
—130.13  
—128.32  
—125.85  
—124.31  
—123.86  
—123.17  
—120.13  
—119.56  
—118.86  
—113.51

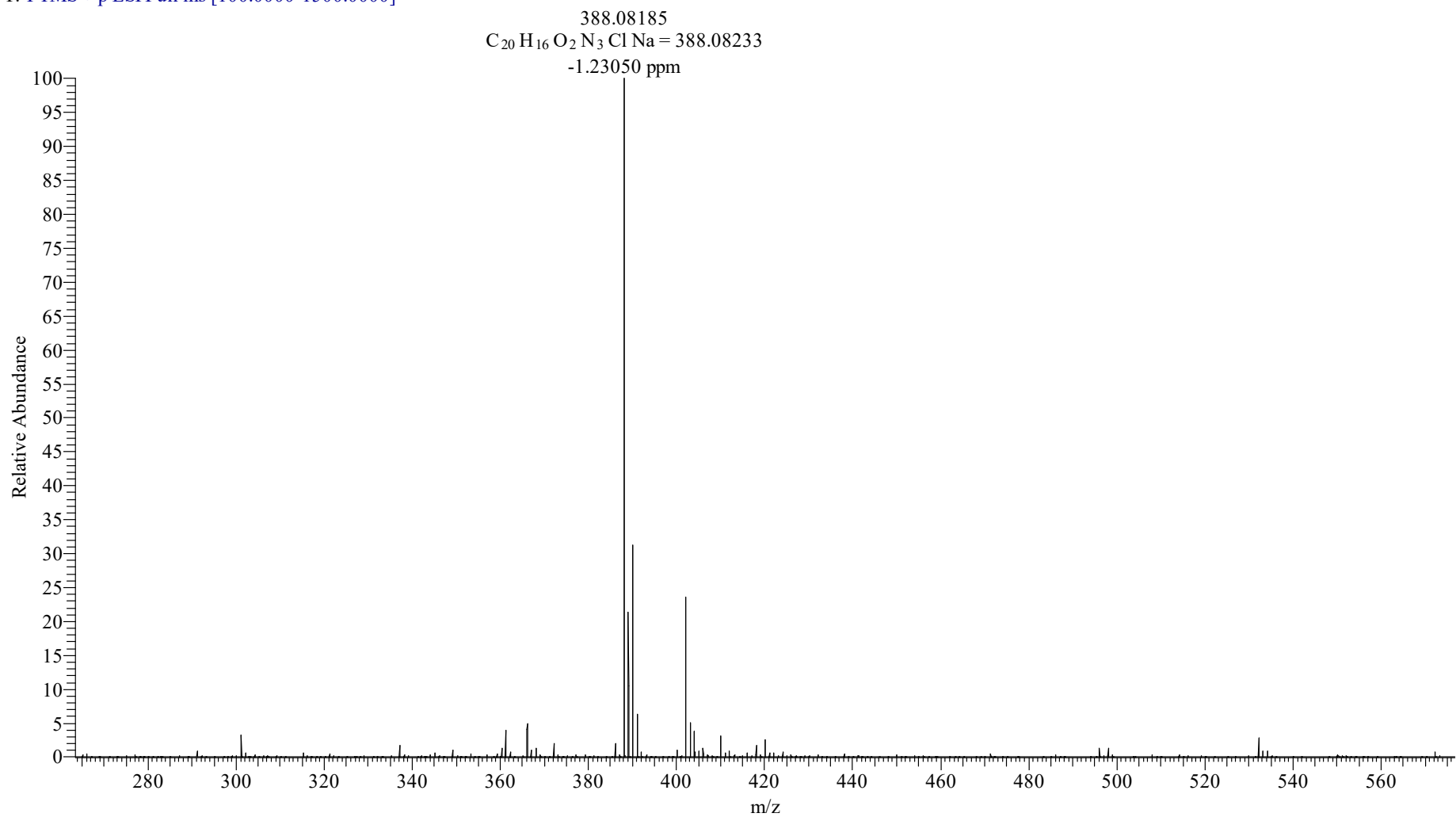
—78.28

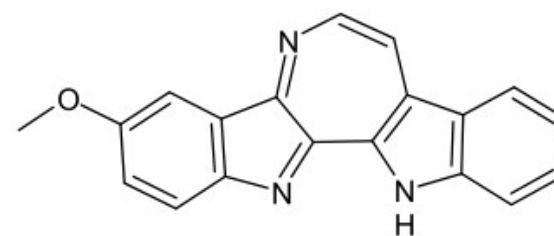
—52.93  
—44.20  
—39.92  
—39.78  
—39.65  
—39.51  
—39.37  
—39.23  
—39.09

7i, DMSO-*d*<sub>6</sub>, 150 MHz

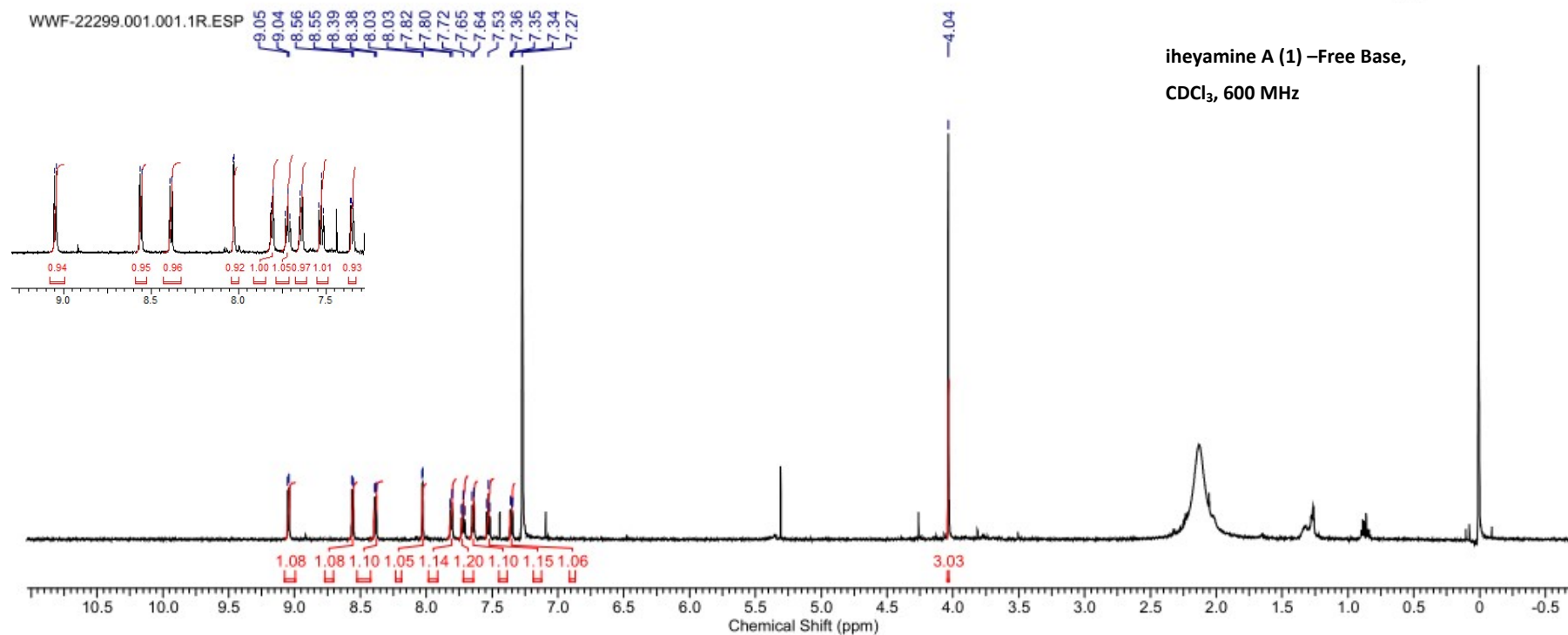


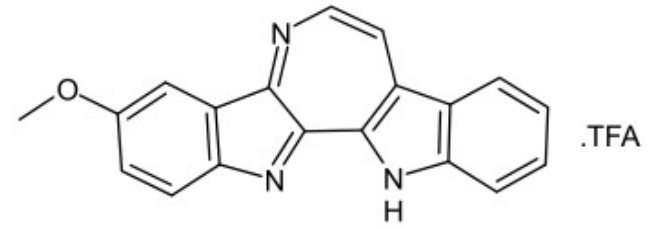
WWF-22365 #30 RT: 0.13 AV: 1 NL: 5.65E8  
T: FTMS + p ESI Full ms [100.0000-1500.0000]



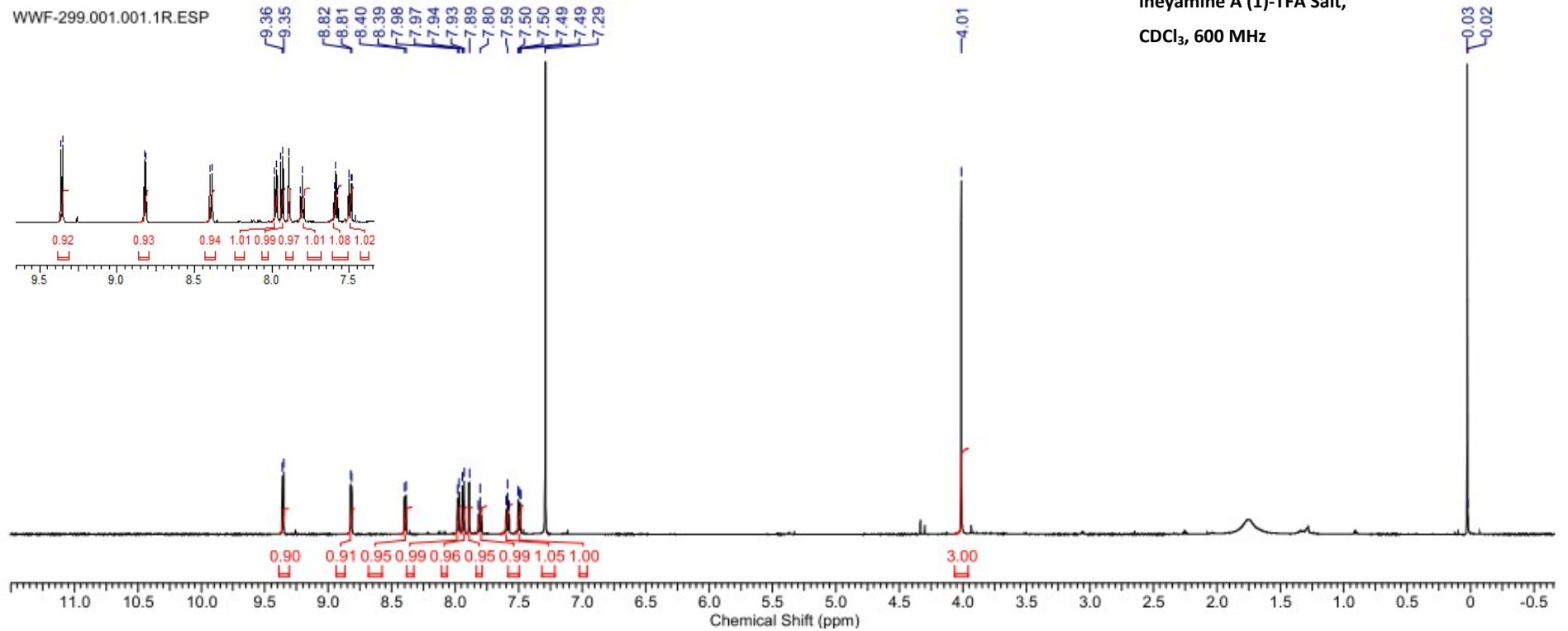


iheyamine A (1) -Free Base,  
CDCl<sub>3</sub>, 600 MHz

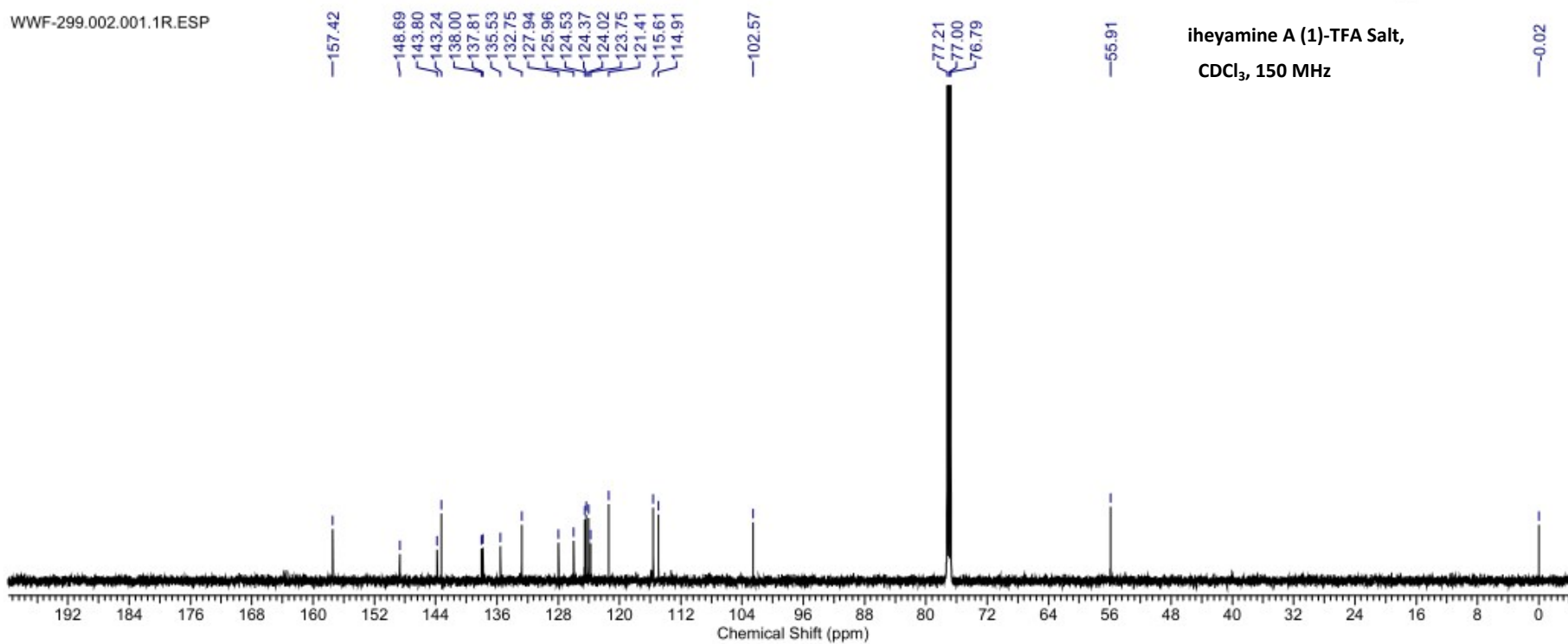




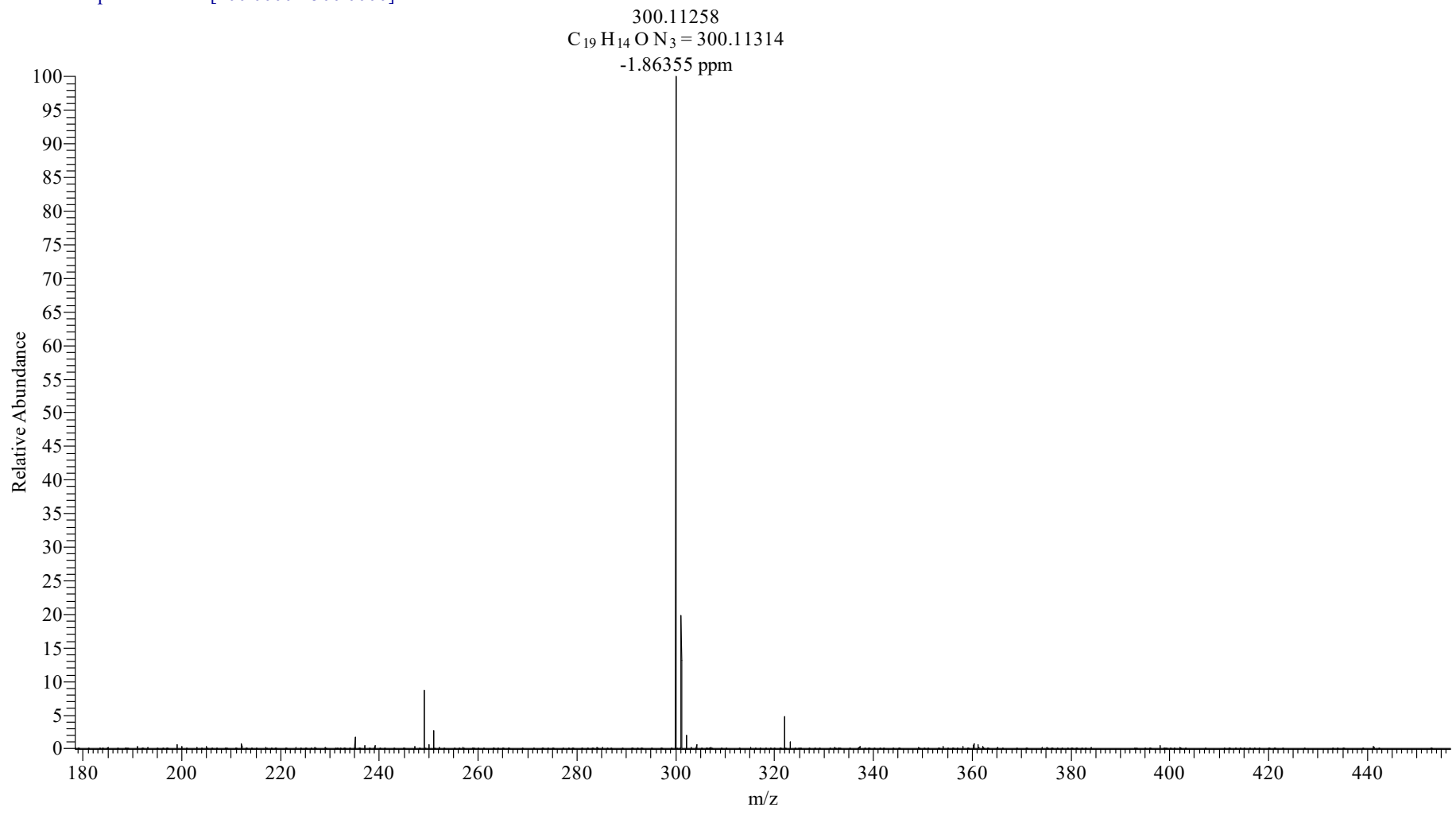
iheyamine A (1)-TFA Salt,  
CDCl<sub>3</sub>, 600 MHz

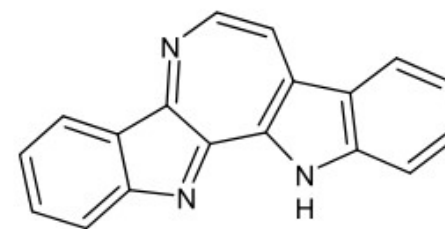


WWF-299.002.001.1R.ESP



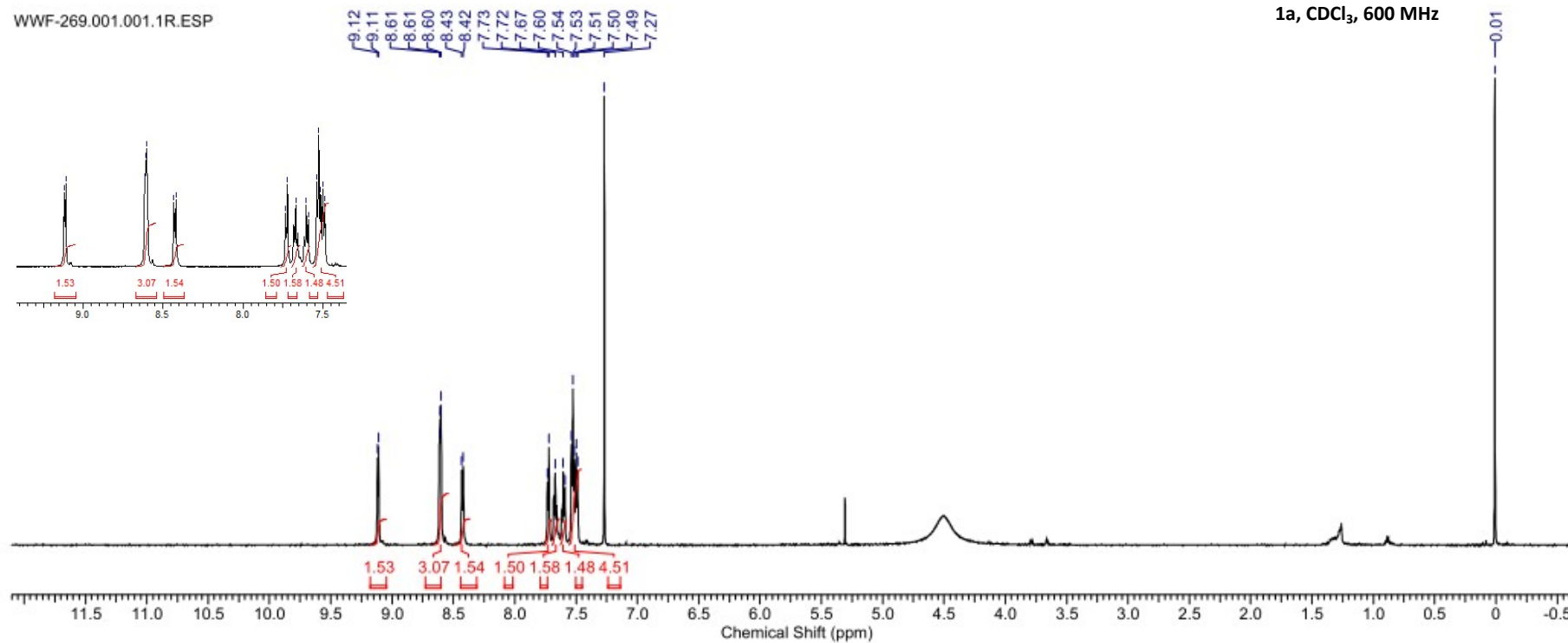
WWF-22299 #27 RT: 0.12 AV: 1 NL: 1.00E9  
T: FTMS + p ESI Full ms [100.0000-1500.0000]





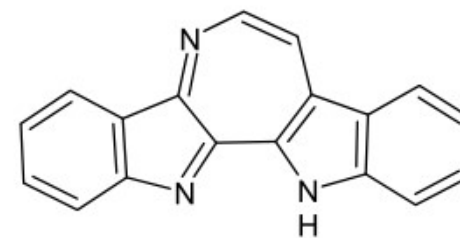
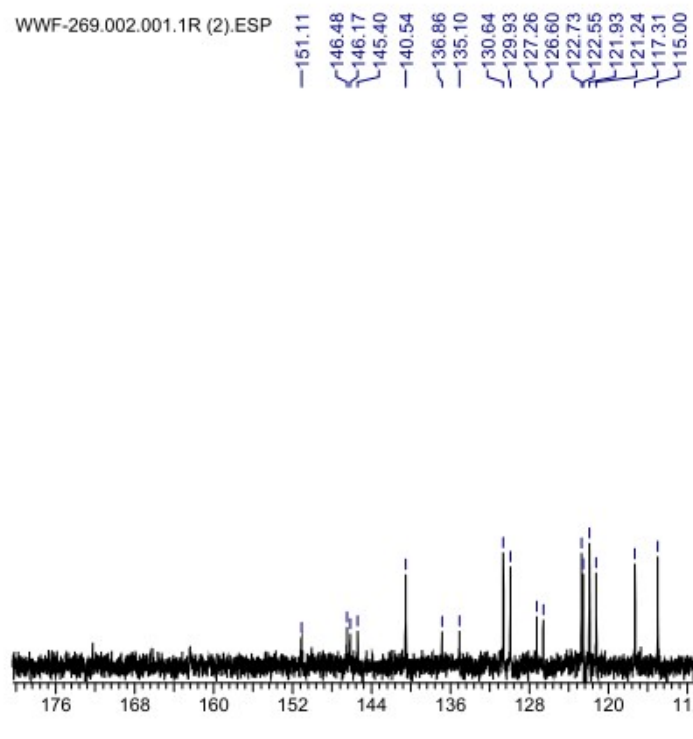
1a, CDCl<sub>3</sub>, 600 MHz

WWF-269.001.001.1R.ESP





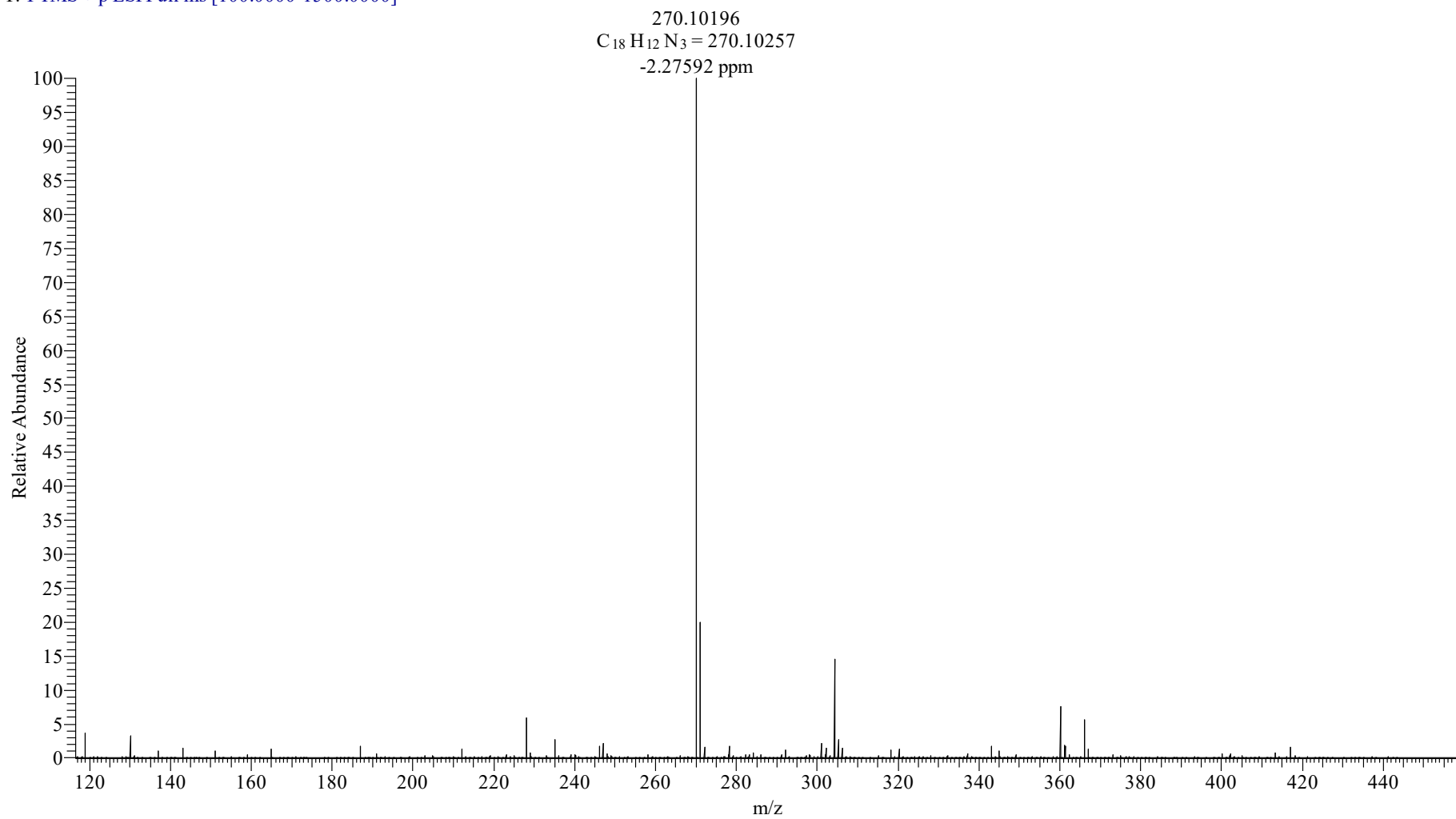
WWF-269.002.001.1R (2).ESP

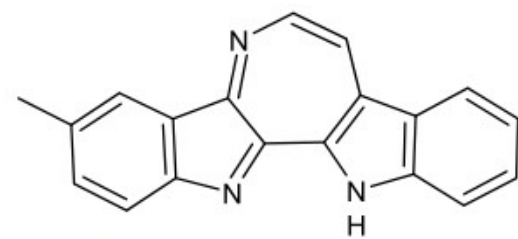


1a, CDCl<sub>3</sub>, 150 MHz

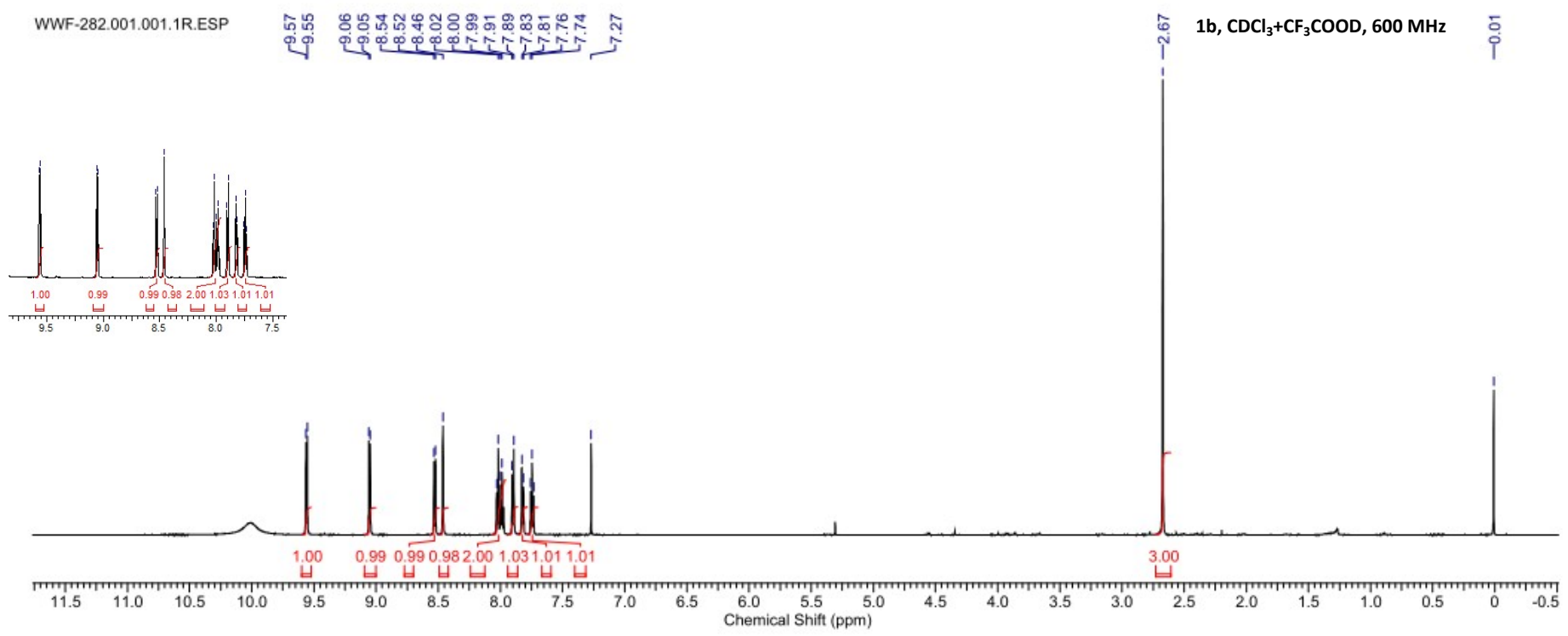
-0.02

WWF-21269 #23 RT: 0.10 AV: 1 NL: 8.46E8  
T: FTMS + p ESI Full ms [100.0000-1500.0000]

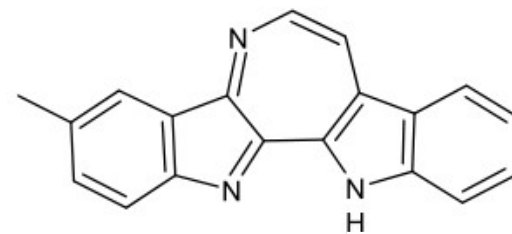
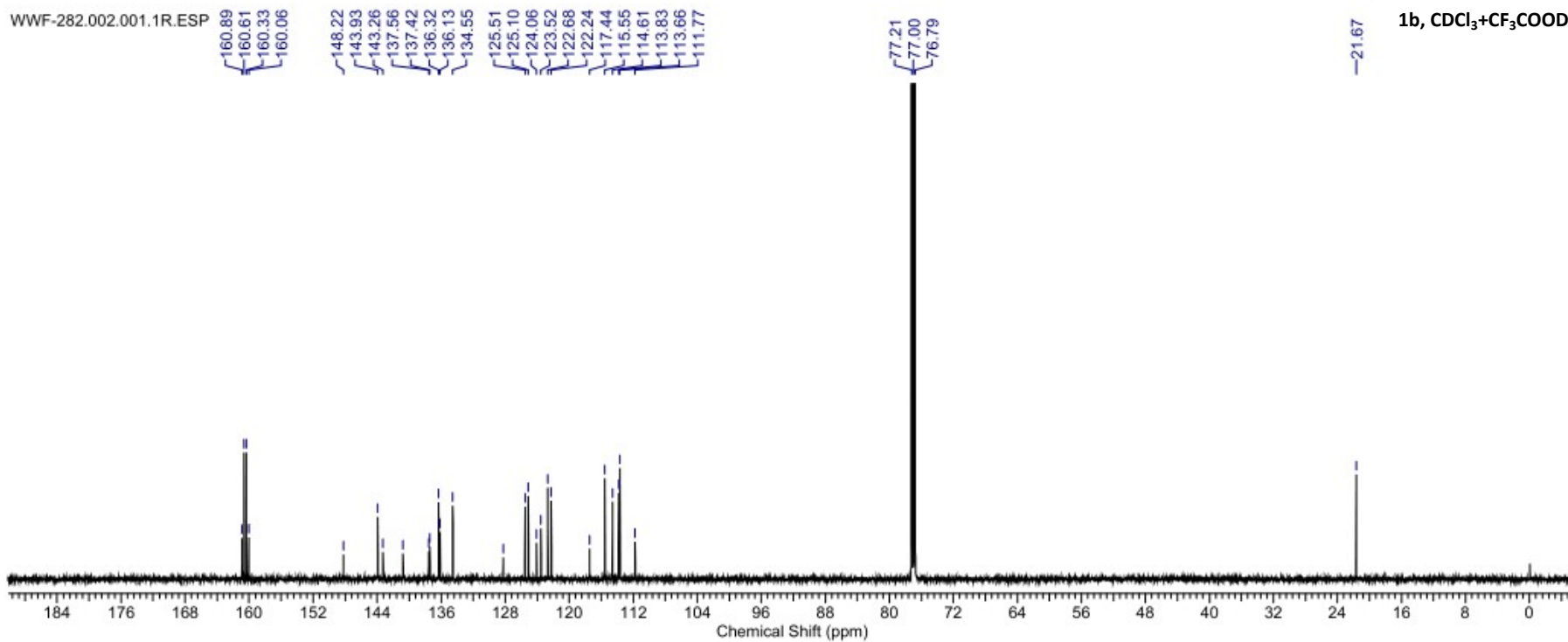




1b, CDCl<sub>3</sub>+CF<sub>3</sub>COOD, 600 MHz

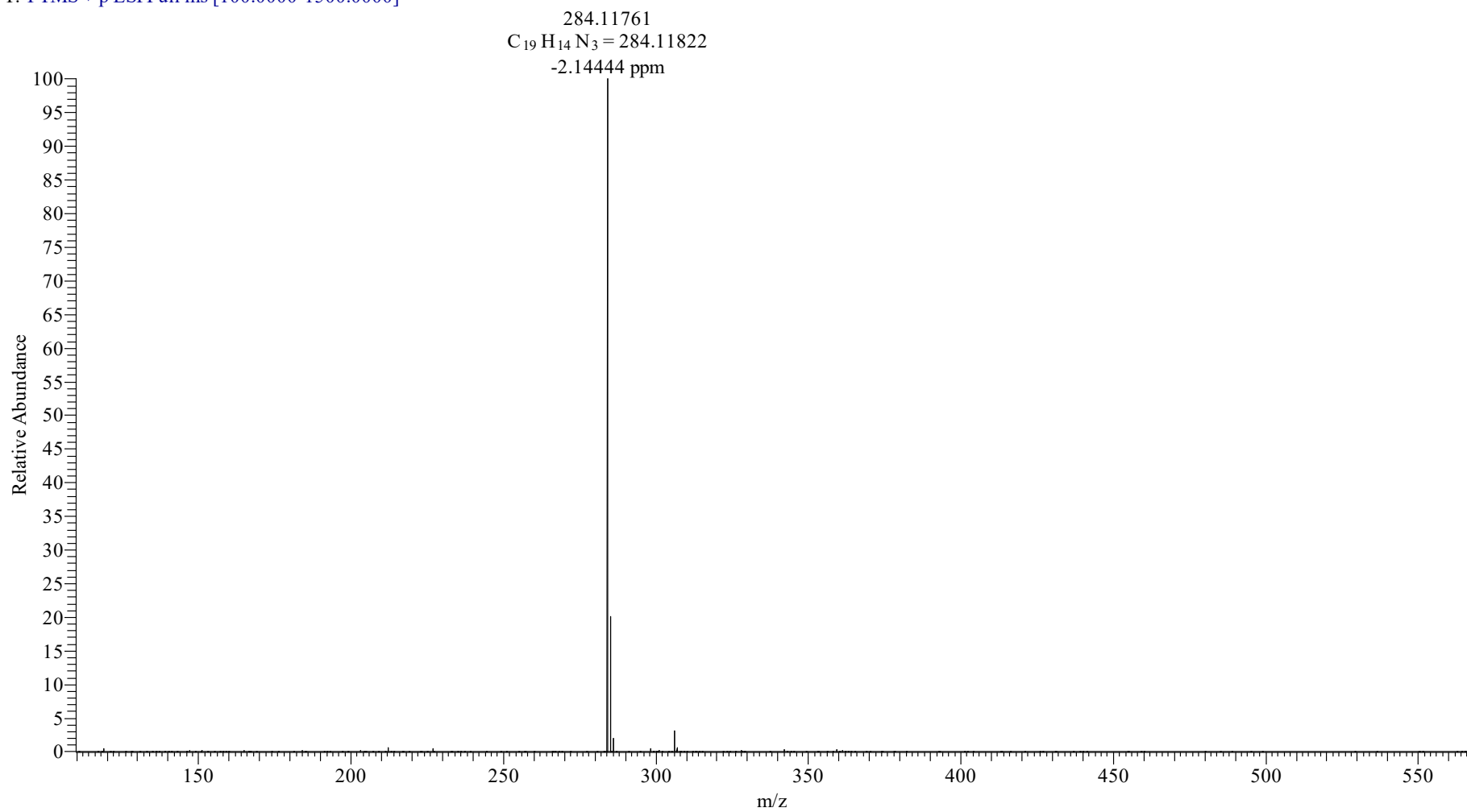


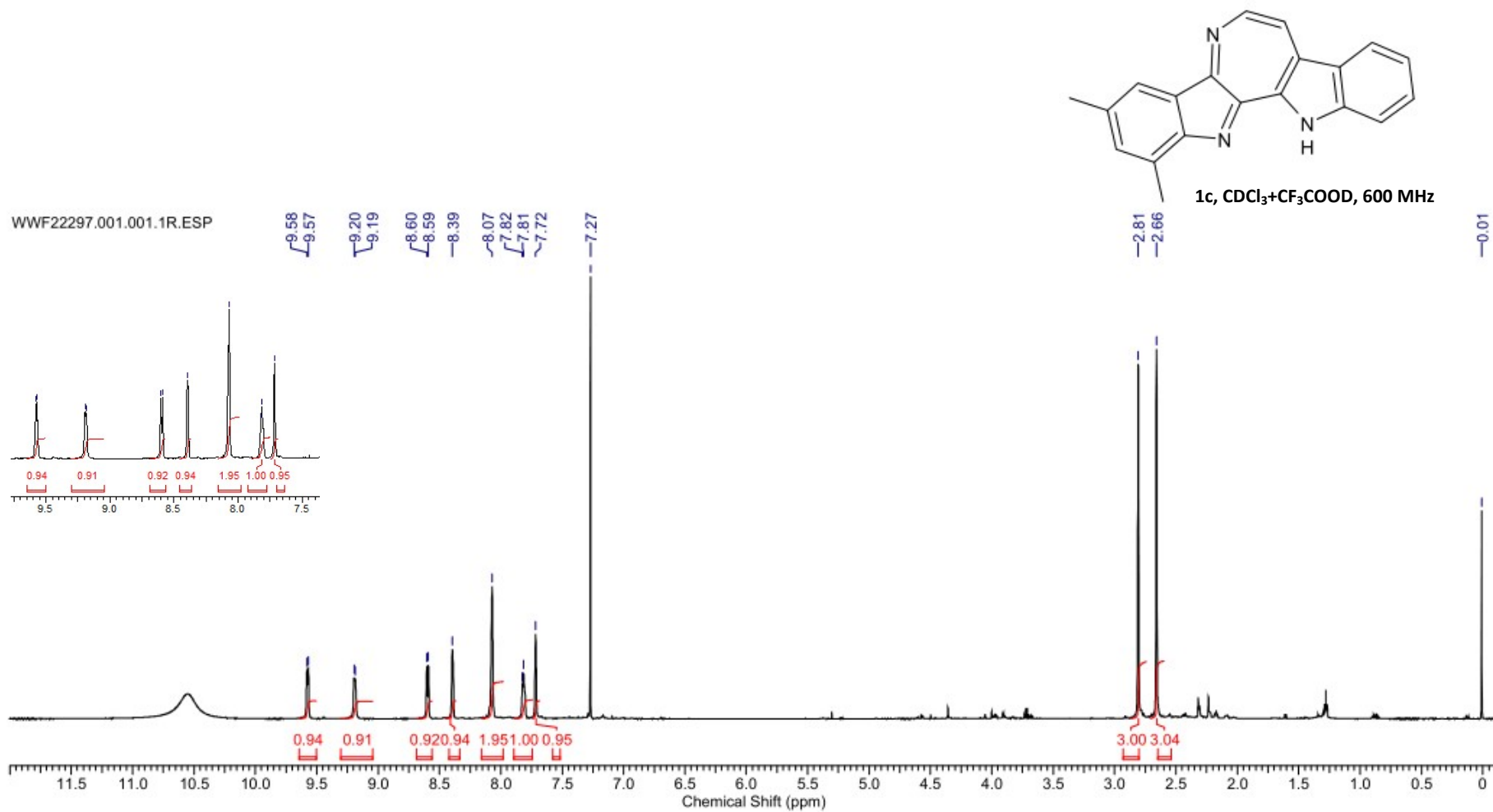
WWF-282.002.001.1R.ESP



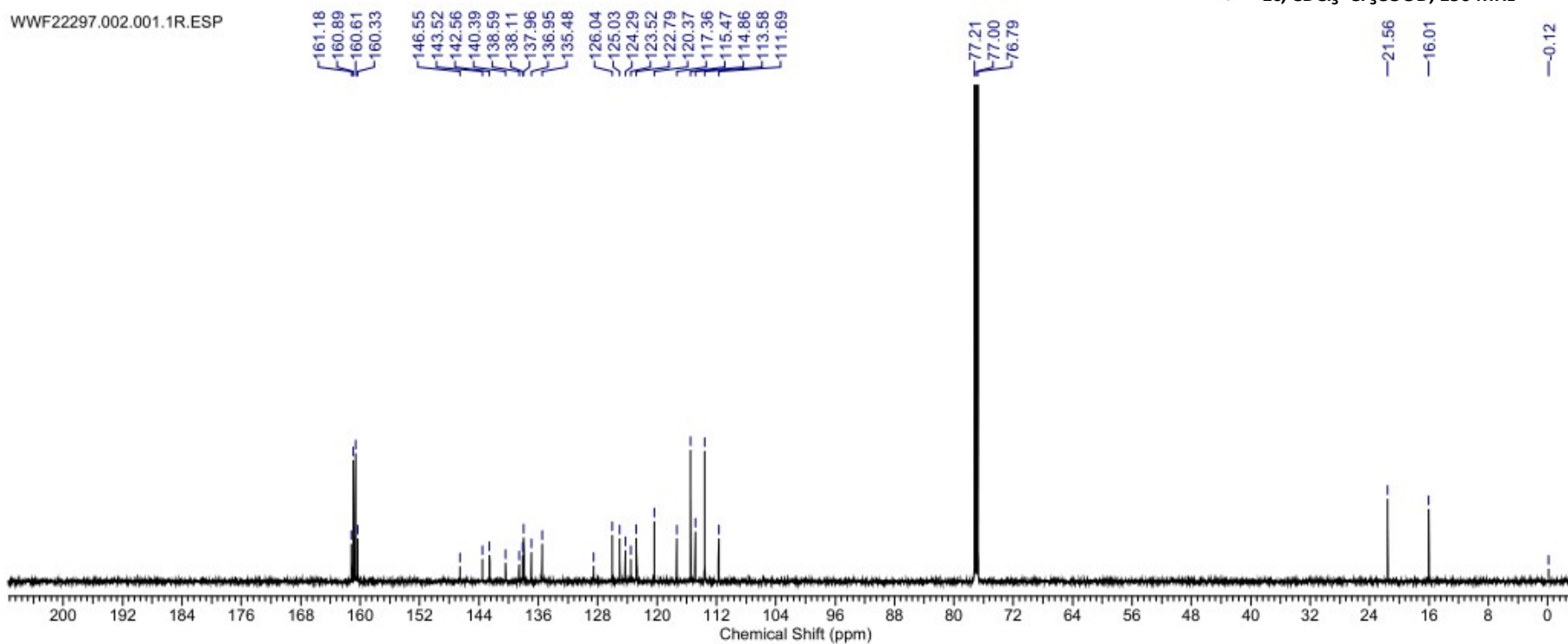
1b, CDCl<sub>3</sub>+CF<sub>3</sub>COOD, 150 MHz

WWF-22283 #27 RT: 0.12 AV: 1 NL: 3.10E9  
T: FTMS + p ESI Full ms [100.0000-1500.0000]

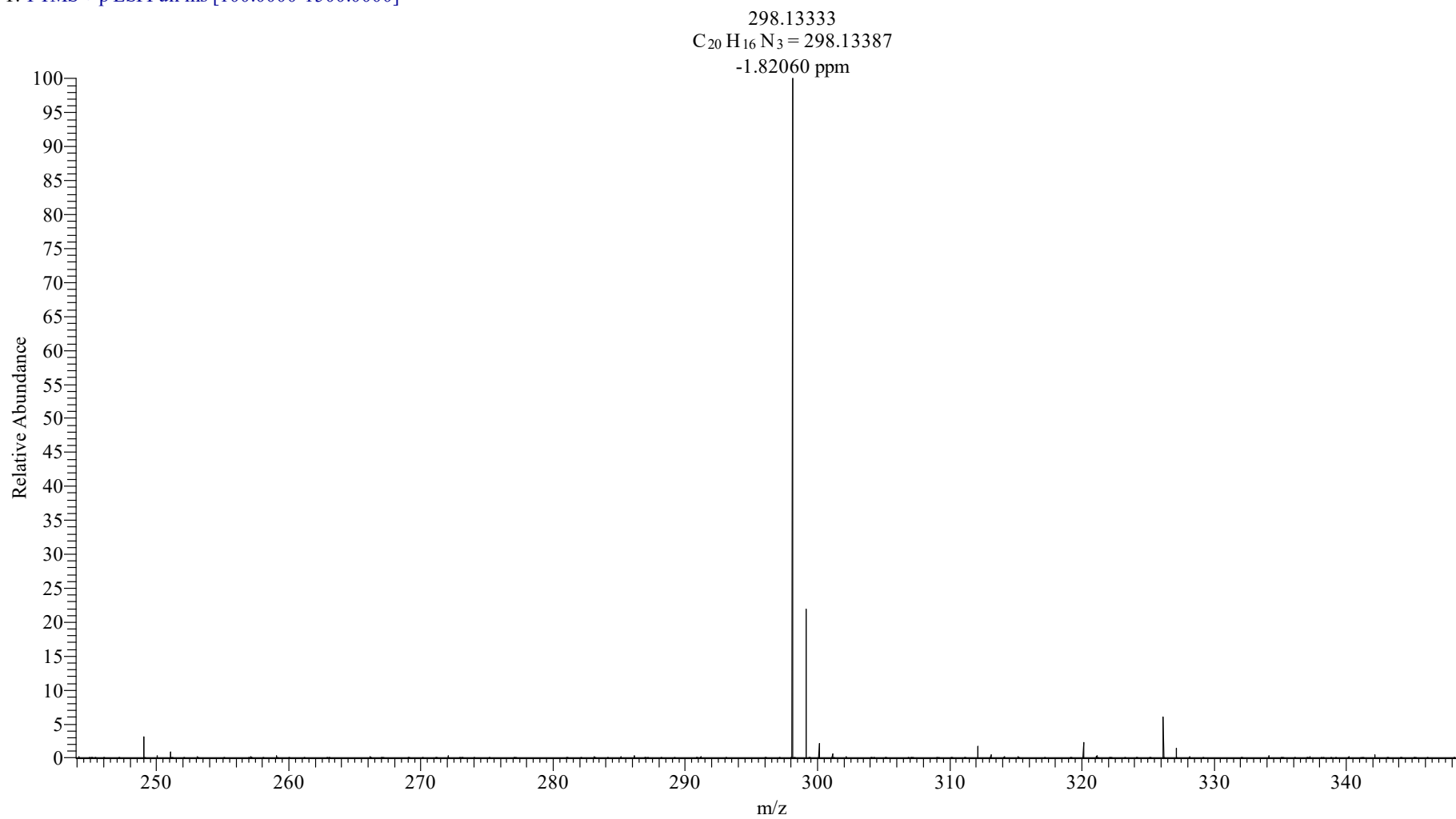




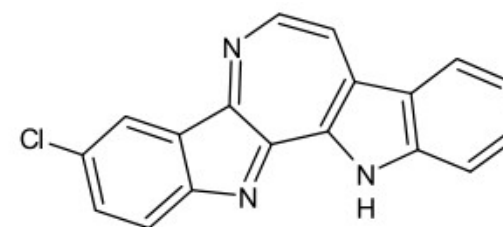
WWF22297.002.001.1R.ESP



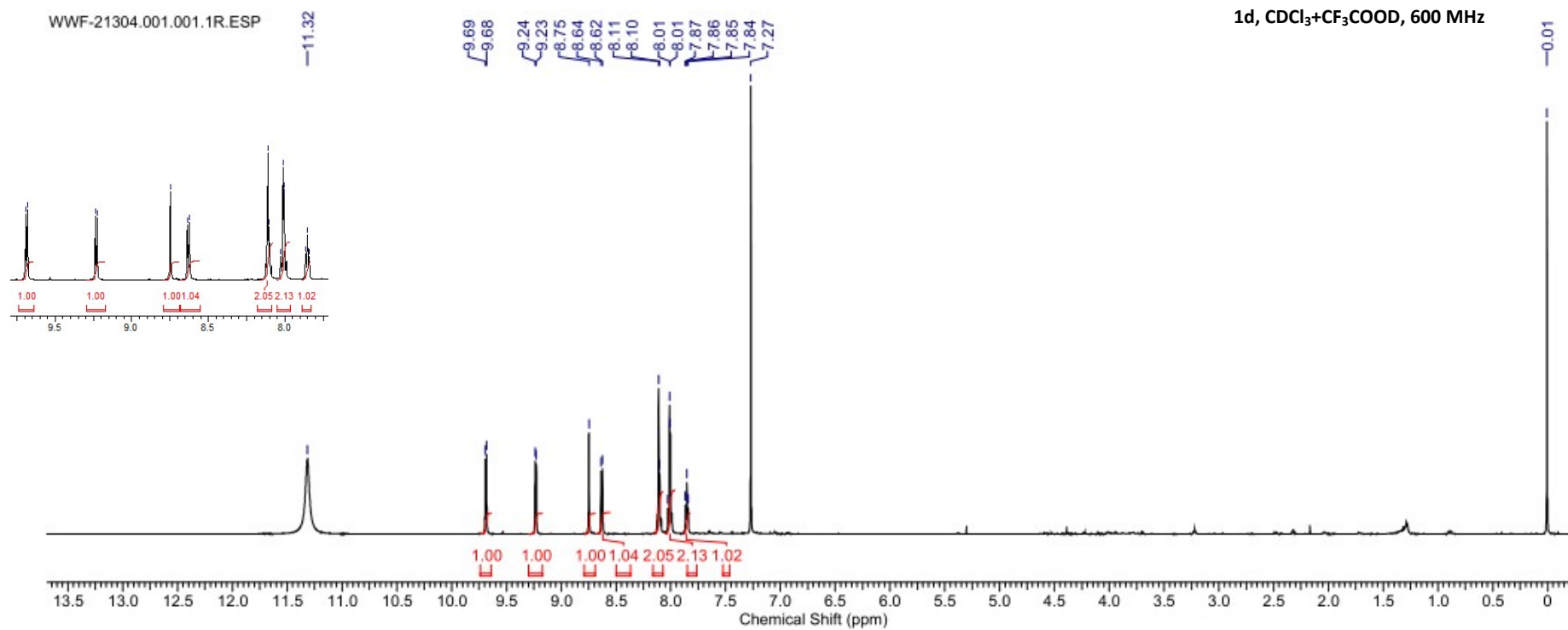
WWF-22297 #23 RT: 0.10 AV: 1 NL: 1.97E9  
T: FTMS + p ESI Full ms [100.0000-1500.0000]



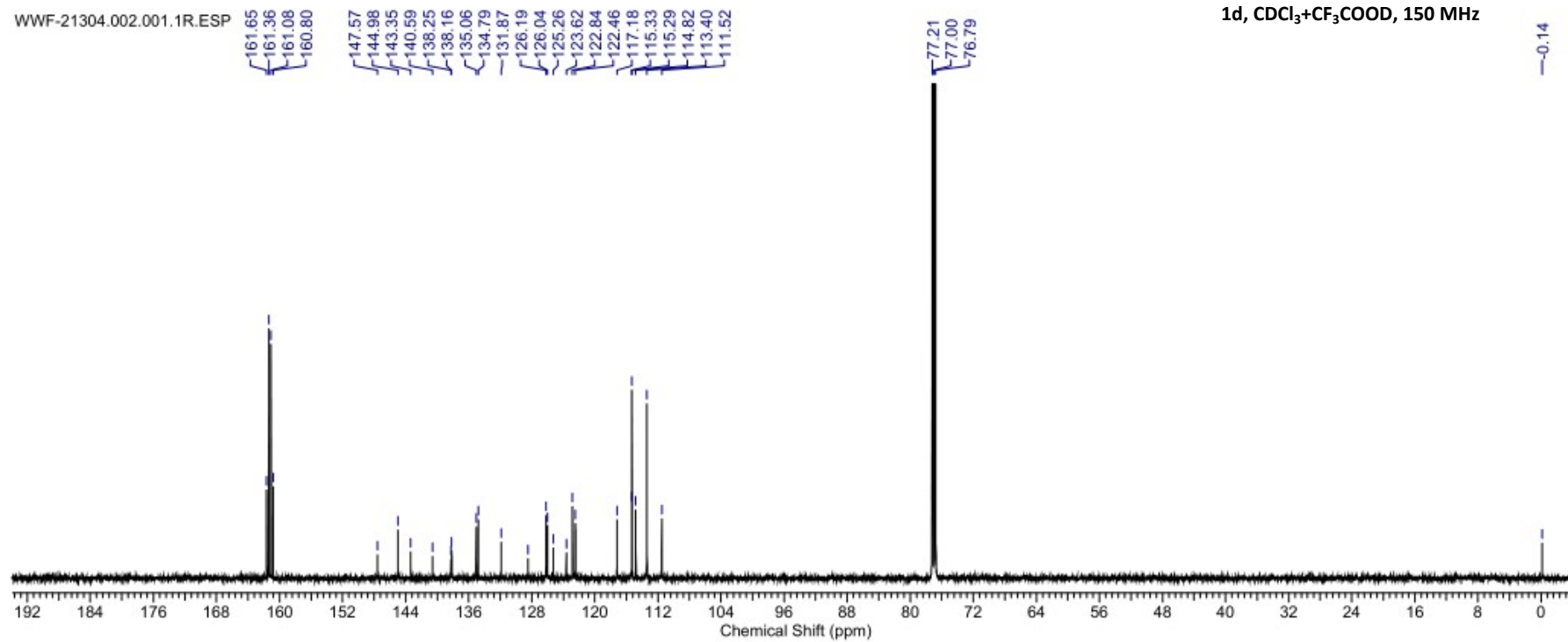




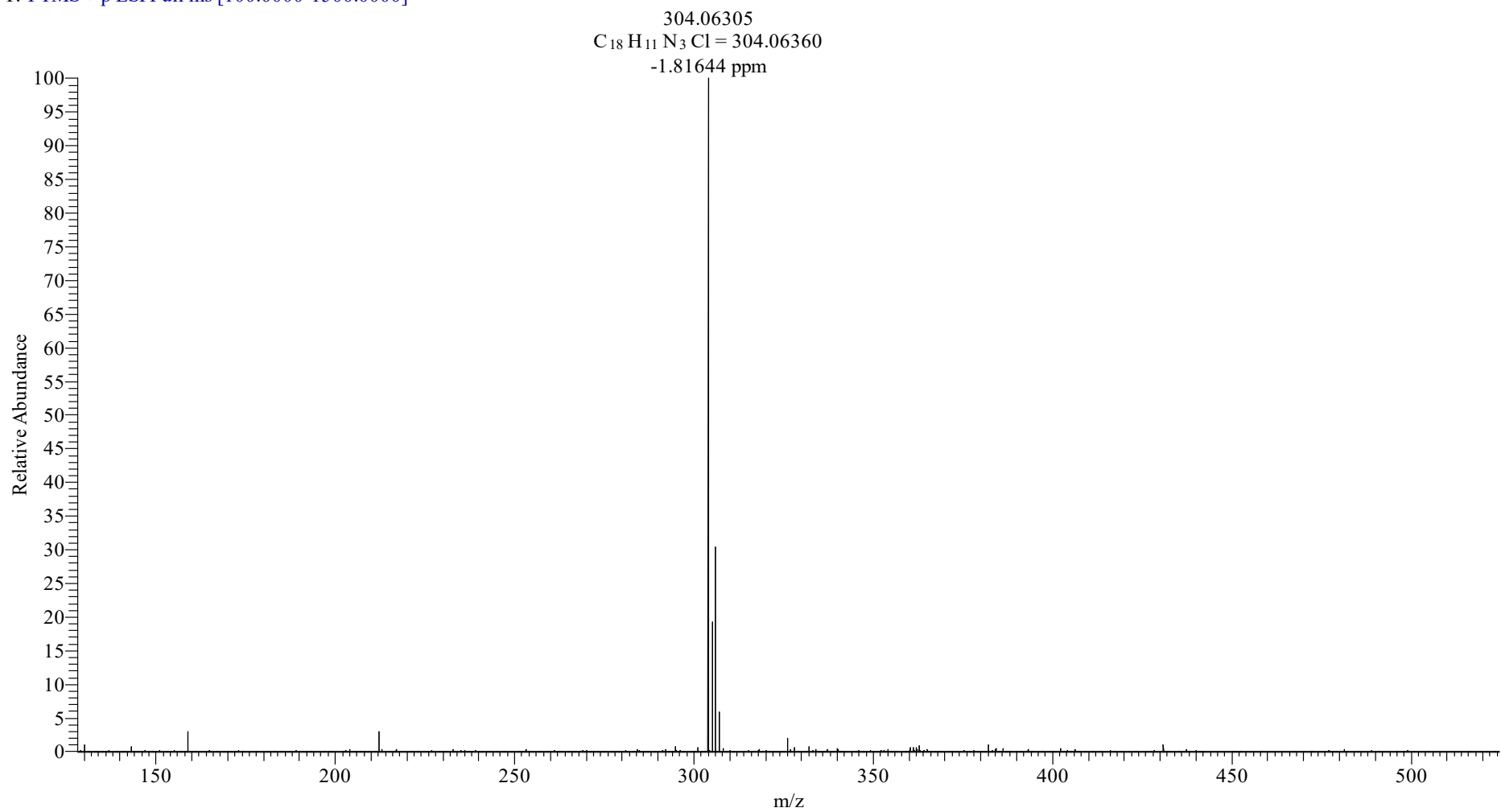
1d, CDCl<sub>3</sub>+CF<sub>3</sub>COOD, 600 MHz

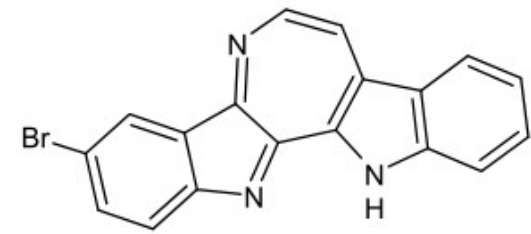


WWF-21304.002.001.1R.ESP

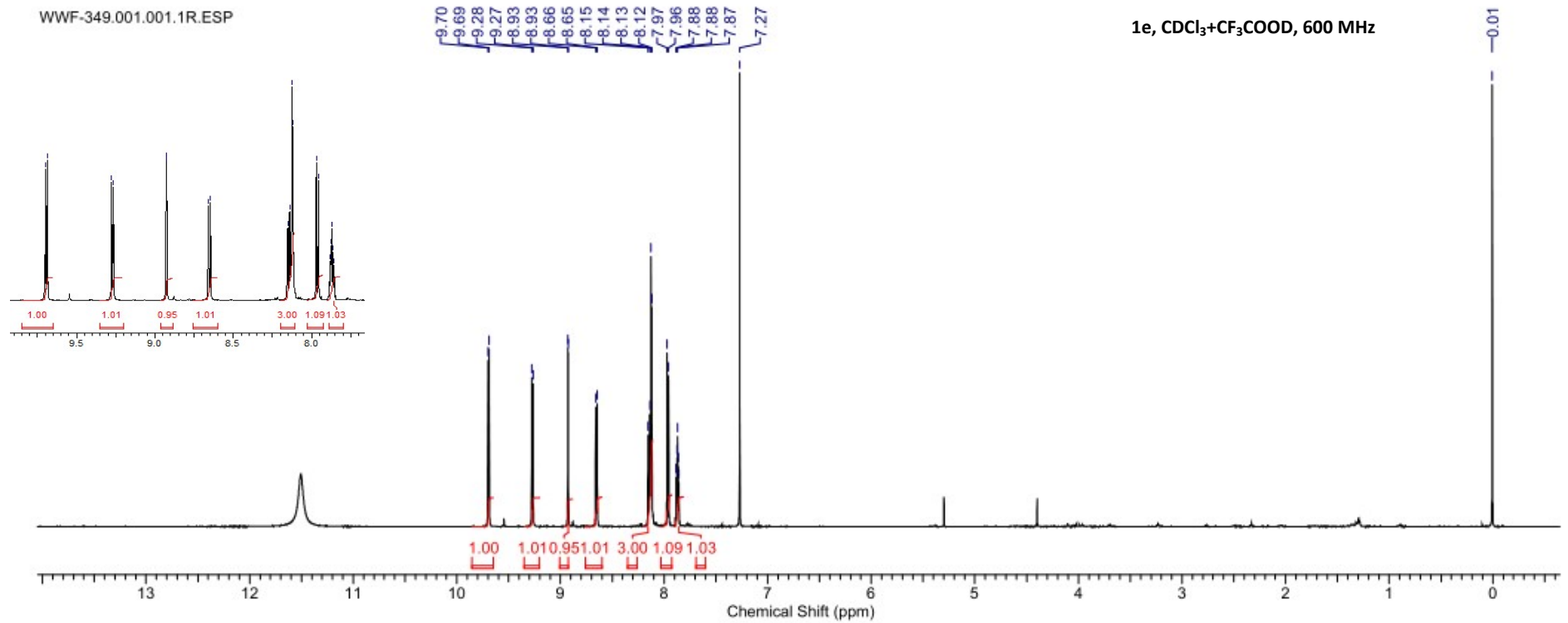


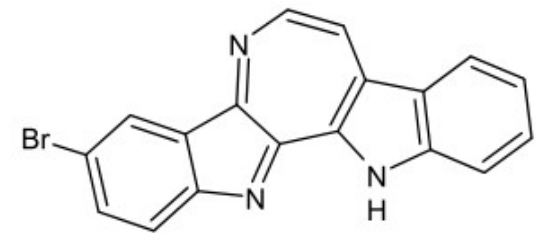
WWF-21304 #24 RT: 0.10 AV: 1 NL: 1.69E9  
T: FTMS + p ESI Full ms [100.0000-1500.0000]





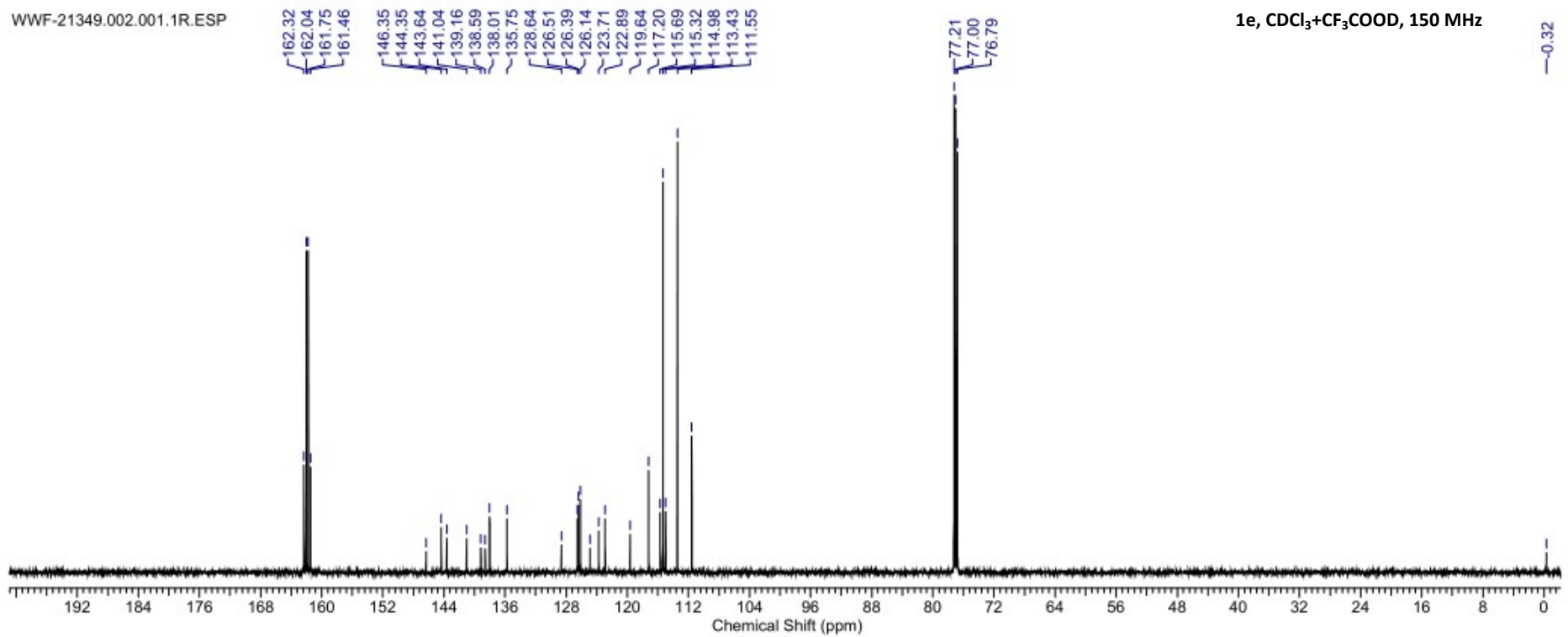
1e, CDCl<sub>3</sub>+CF<sub>3</sub>COOD, 600 MHz



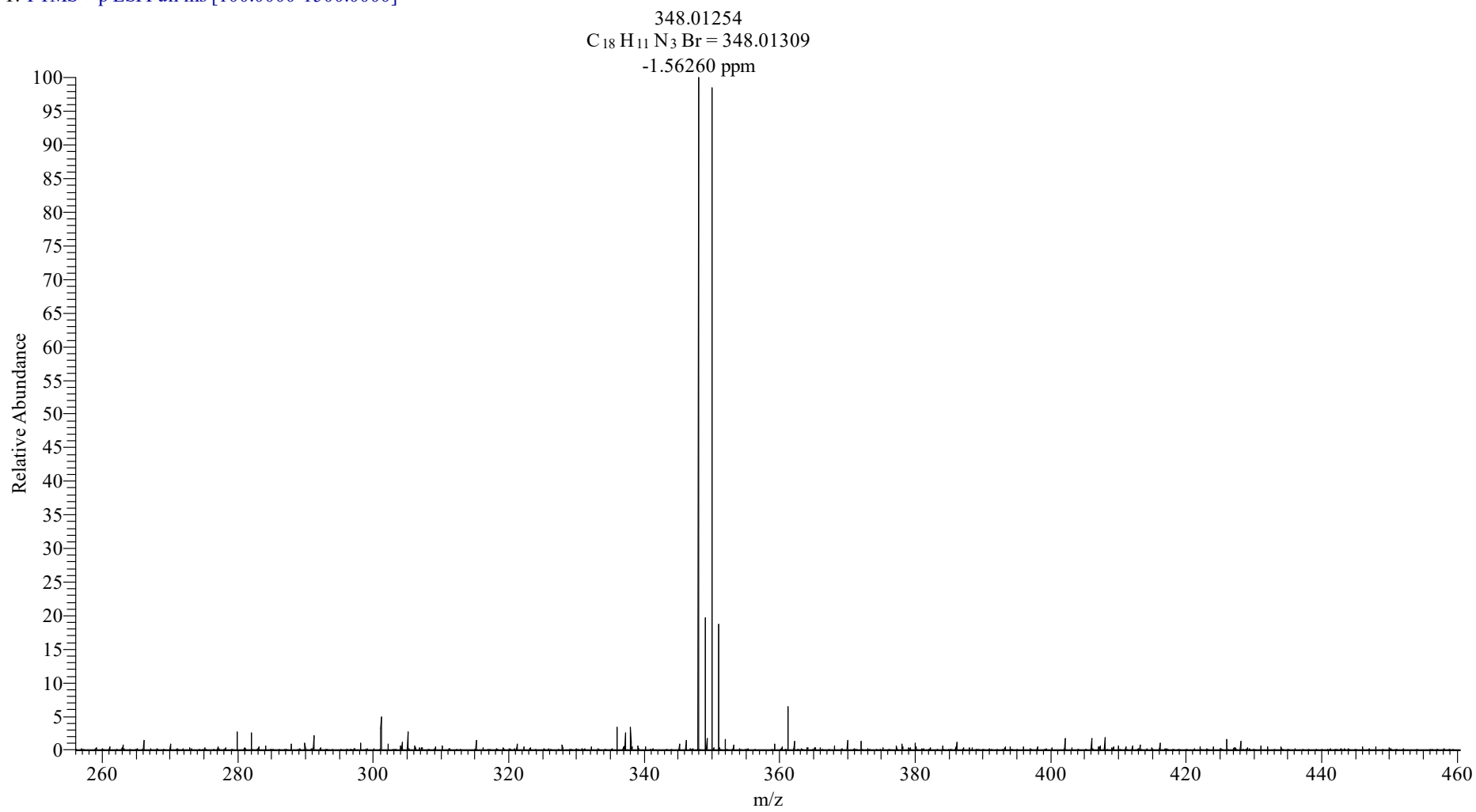


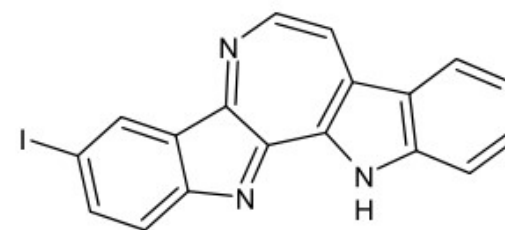
1e, CDCl<sub>3</sub>+CF<sub>3</sub>COOD, 150 MHz

—0.32

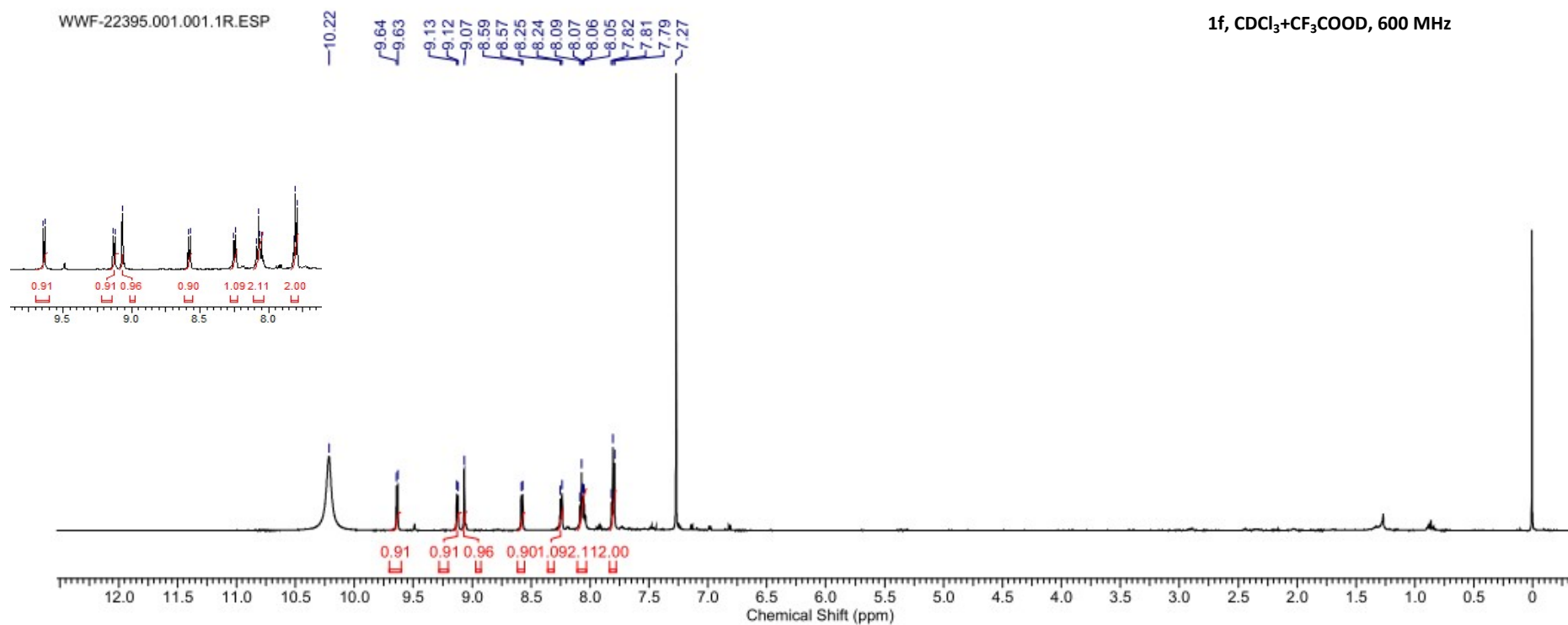


WWF-21349-5 #24 RT: 0.10 AV: 1 NL: 3.98E8  
T: FTMS + p ESI Full ms [100.0000-1500.0000]

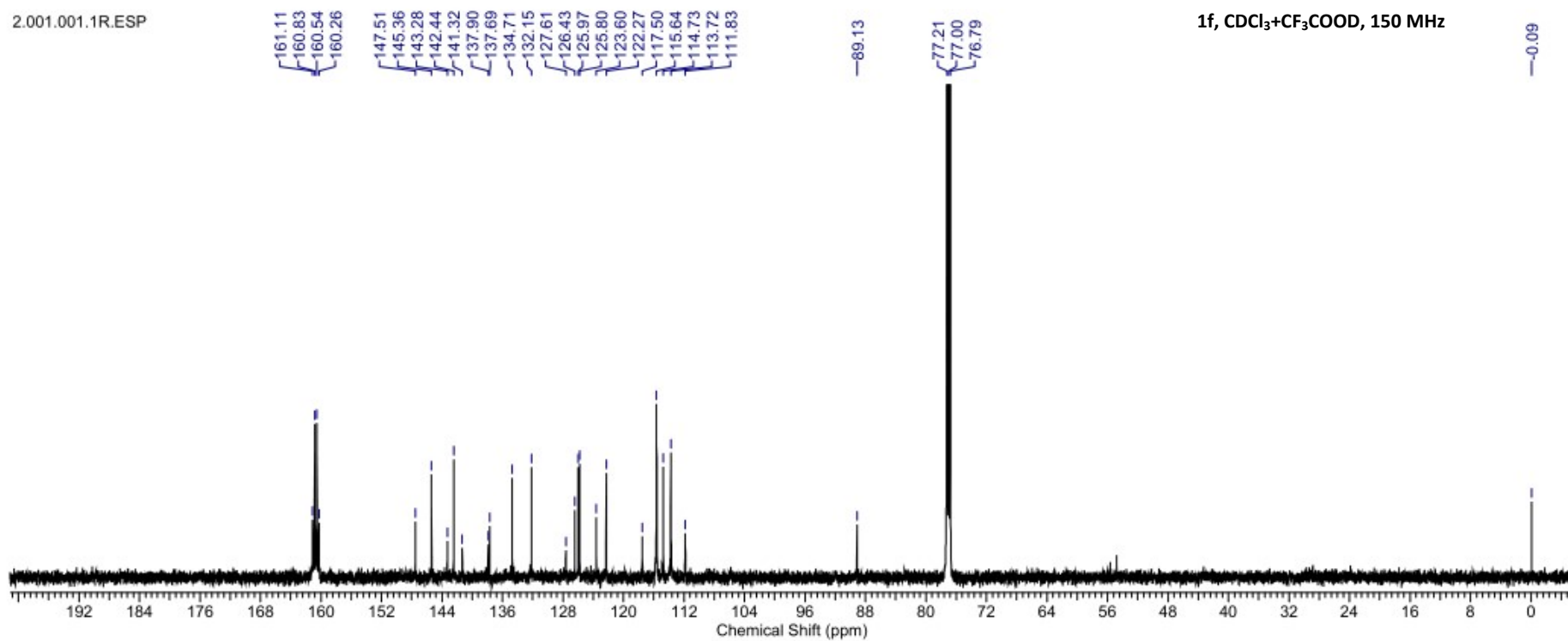




1f, CDCl<sub>3</sub>+CF<sub>3</sub>COOD, 600 MHz

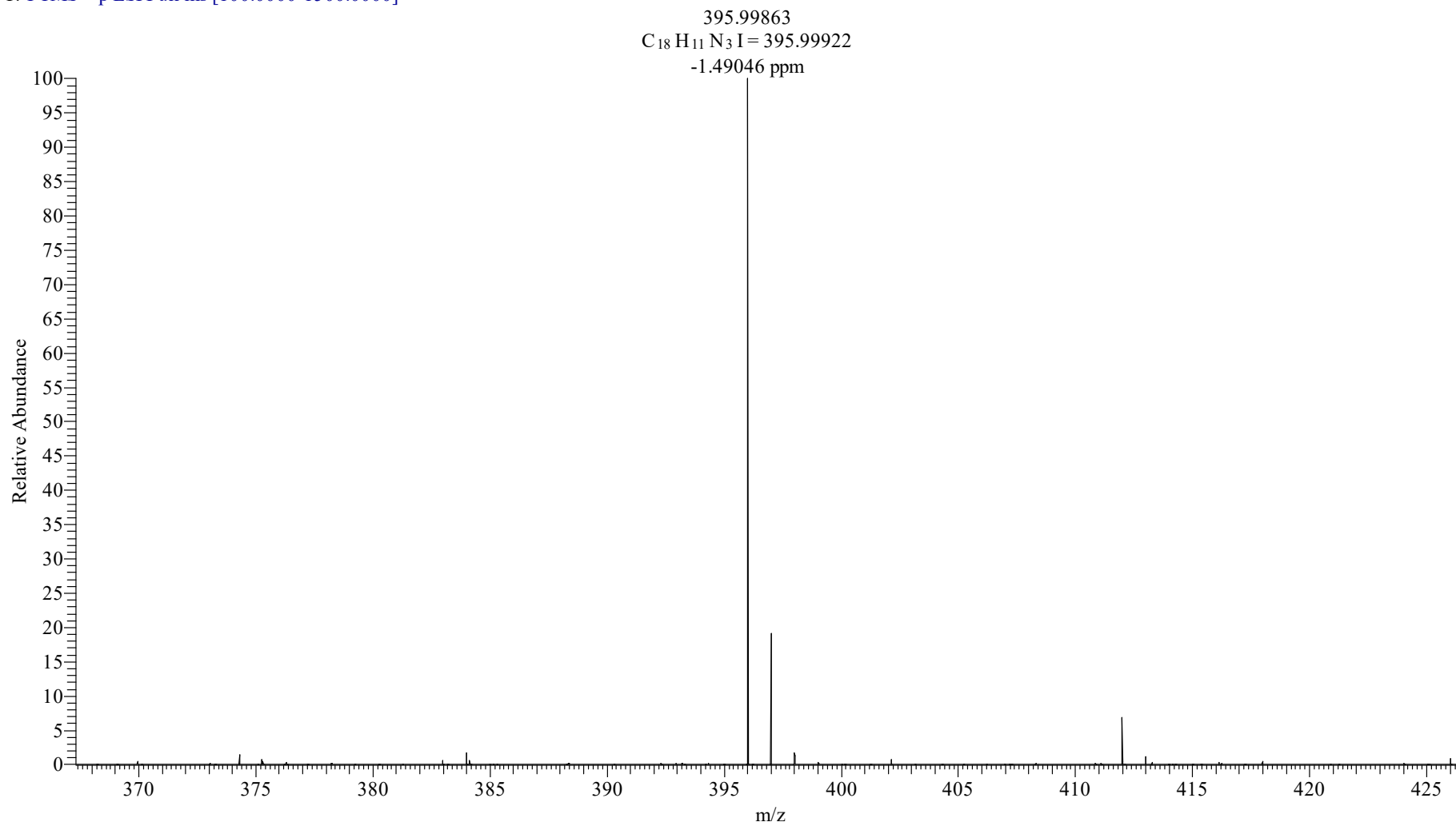


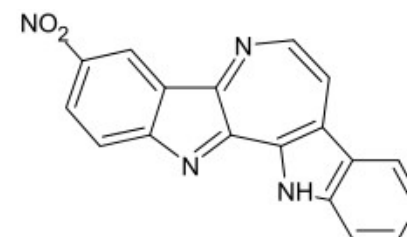
2.001.001.1R.ESP



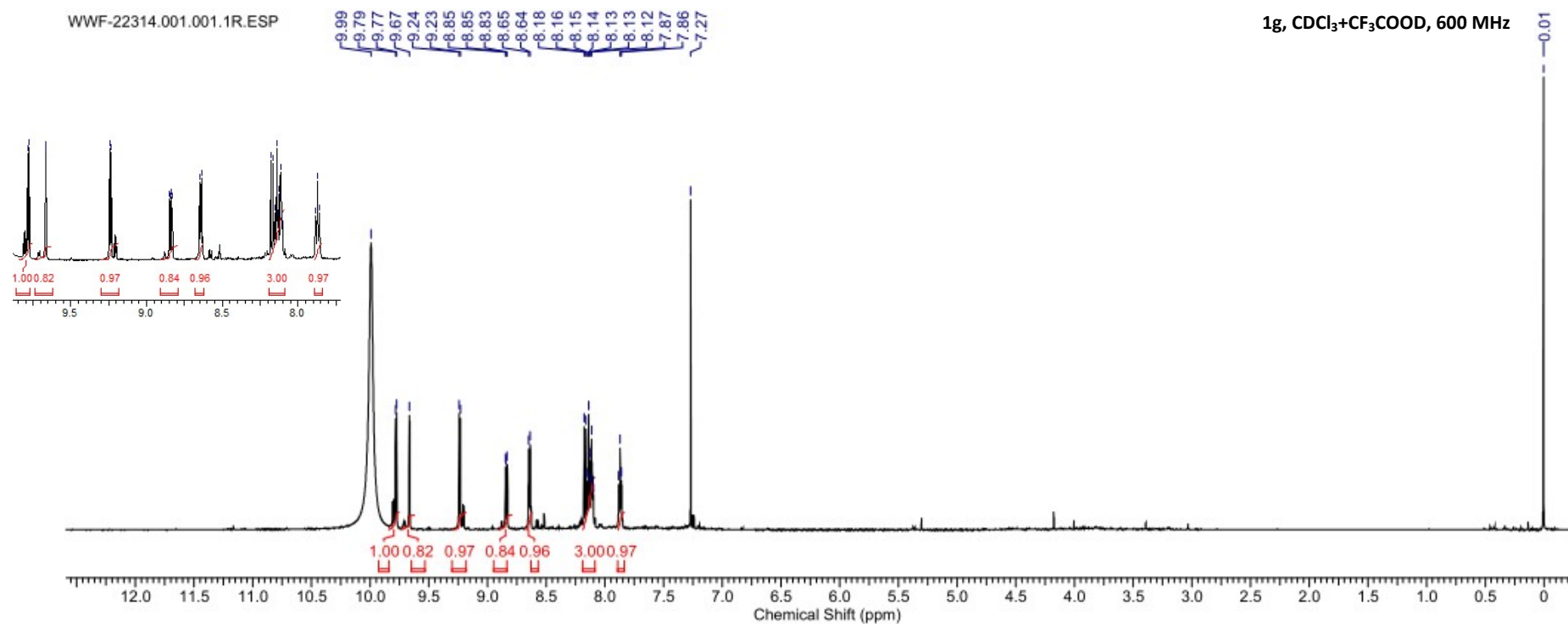


WWF-22395 #22 RT: 0.10 AV: 1 NL: 6.32E8  
T: FTMS + p ESI Full ms [100.0000-1500.0000]

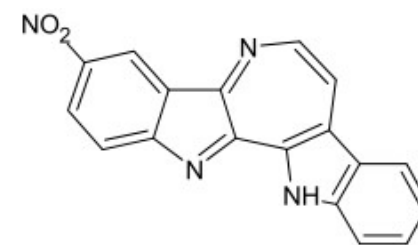
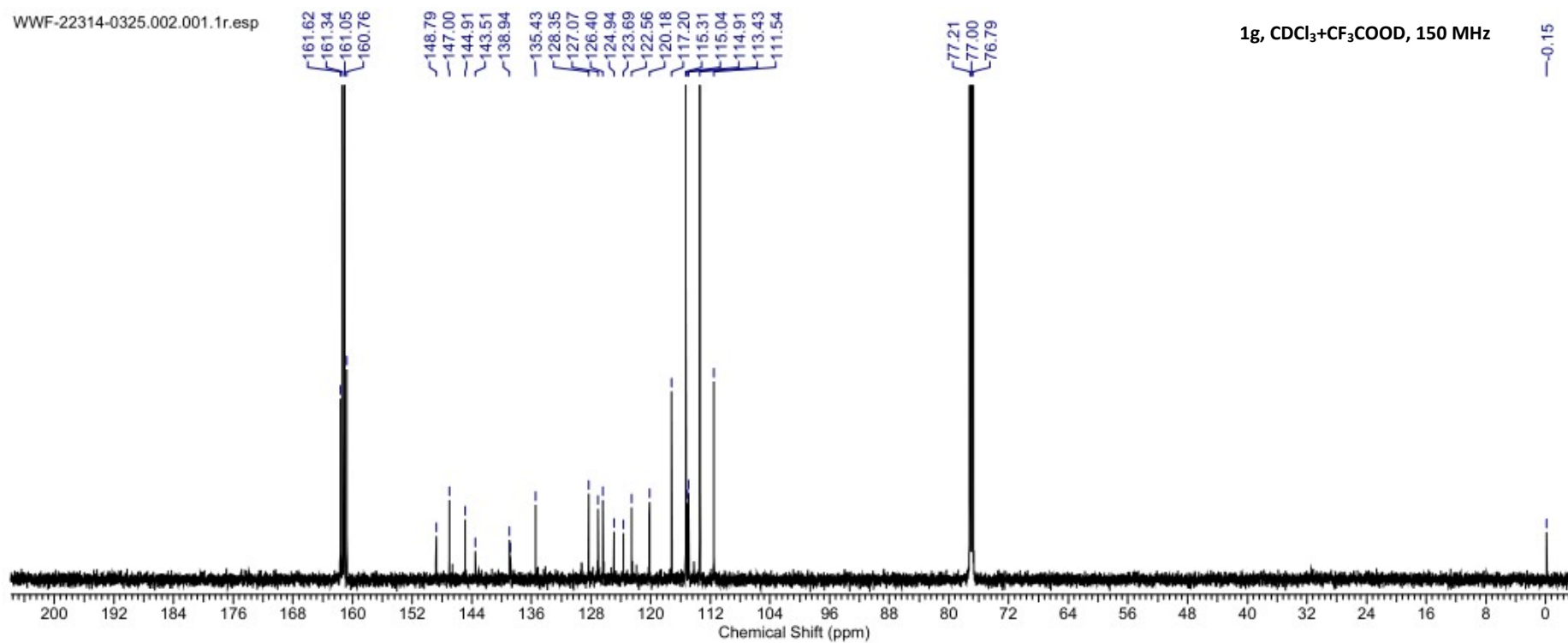




1g, CDCl<sub>3</sub>+CF<sub>3</sub>COOD, 600 MHz



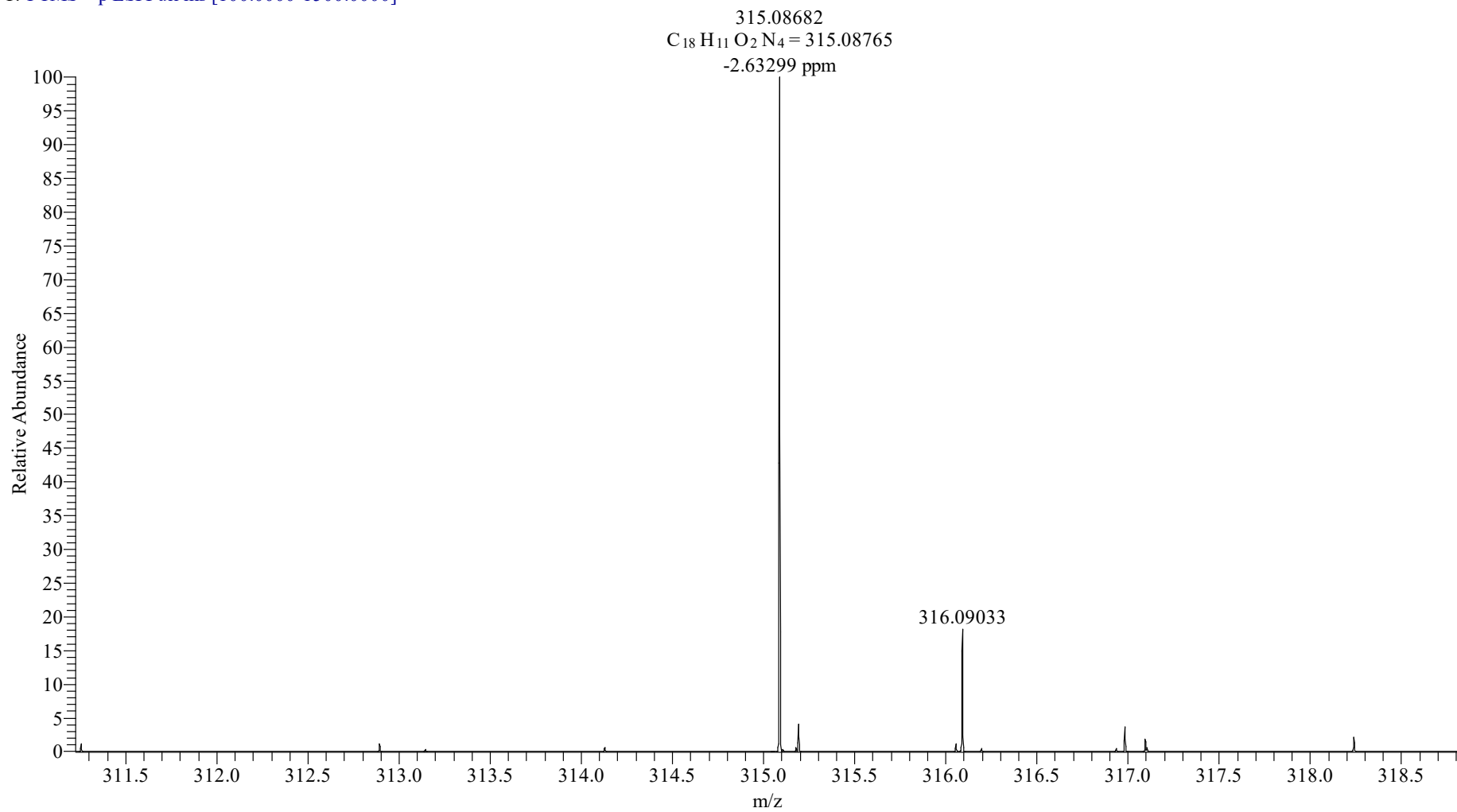
WWF-22314-0325.002.001.1r.esp



1g, CDCl<sub>3</sub>+CF<sub>3</sub>COOD, 150 MHz

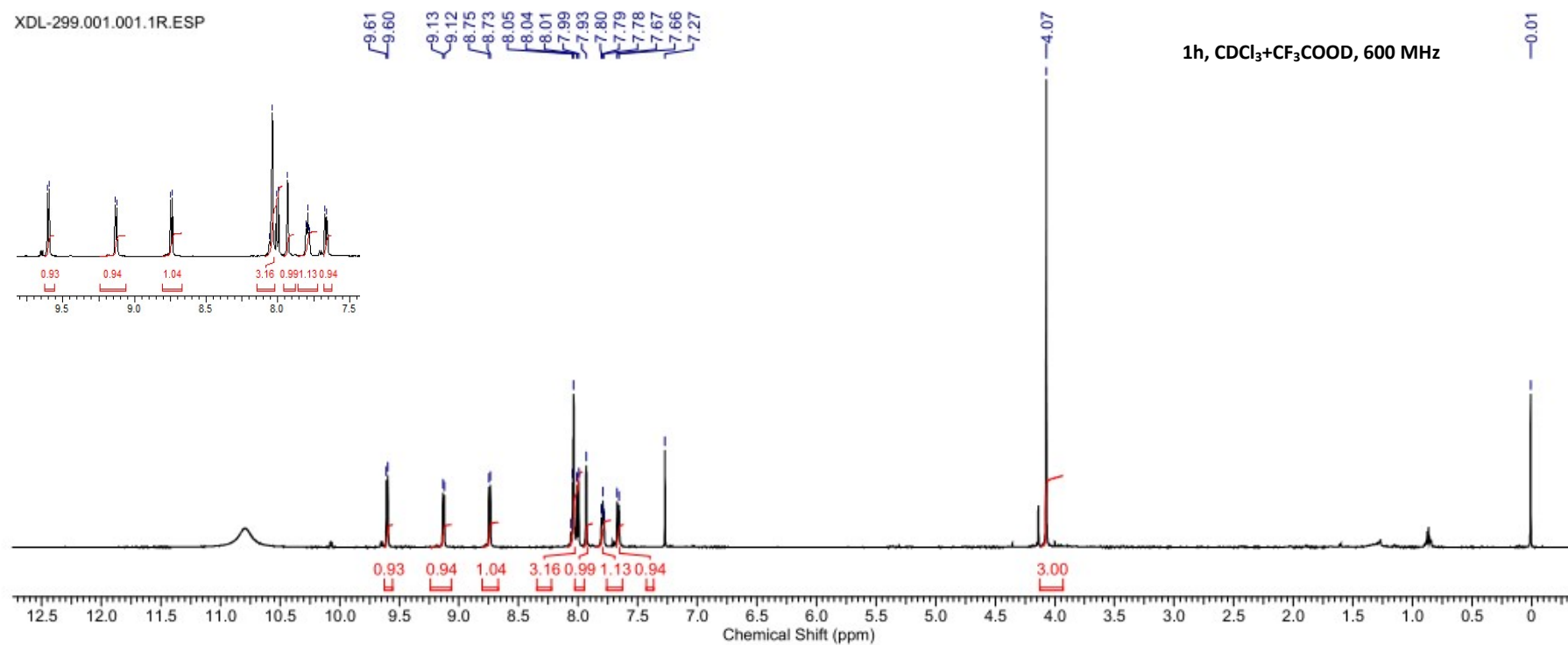
-0.15

WWF-22314 #31 RT: 0.14 AV: 1 NL: 3.17E7  
T: FTMS + p ESI Full ms [100.0000-1500.0000]

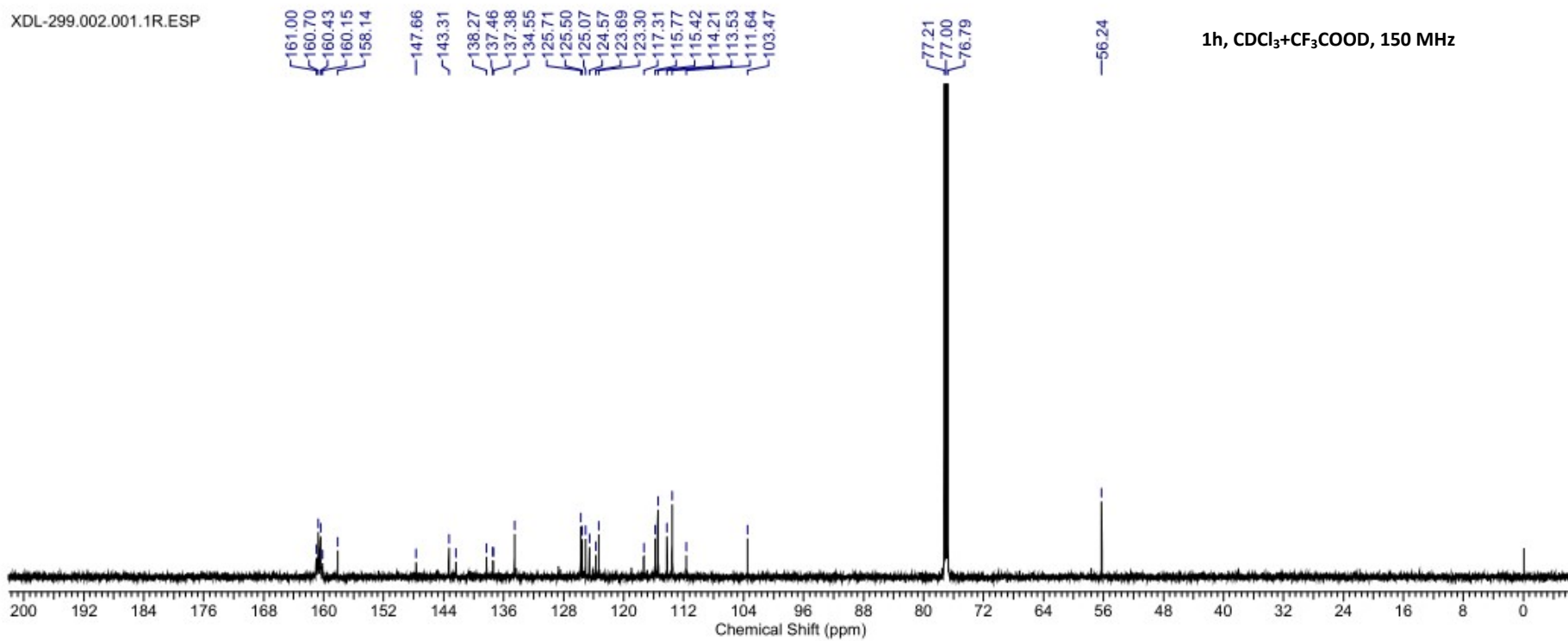


315.08682  
 $C_{18}H_{11}O_2N_4 = 315.08765$   
-2.63299 ppm

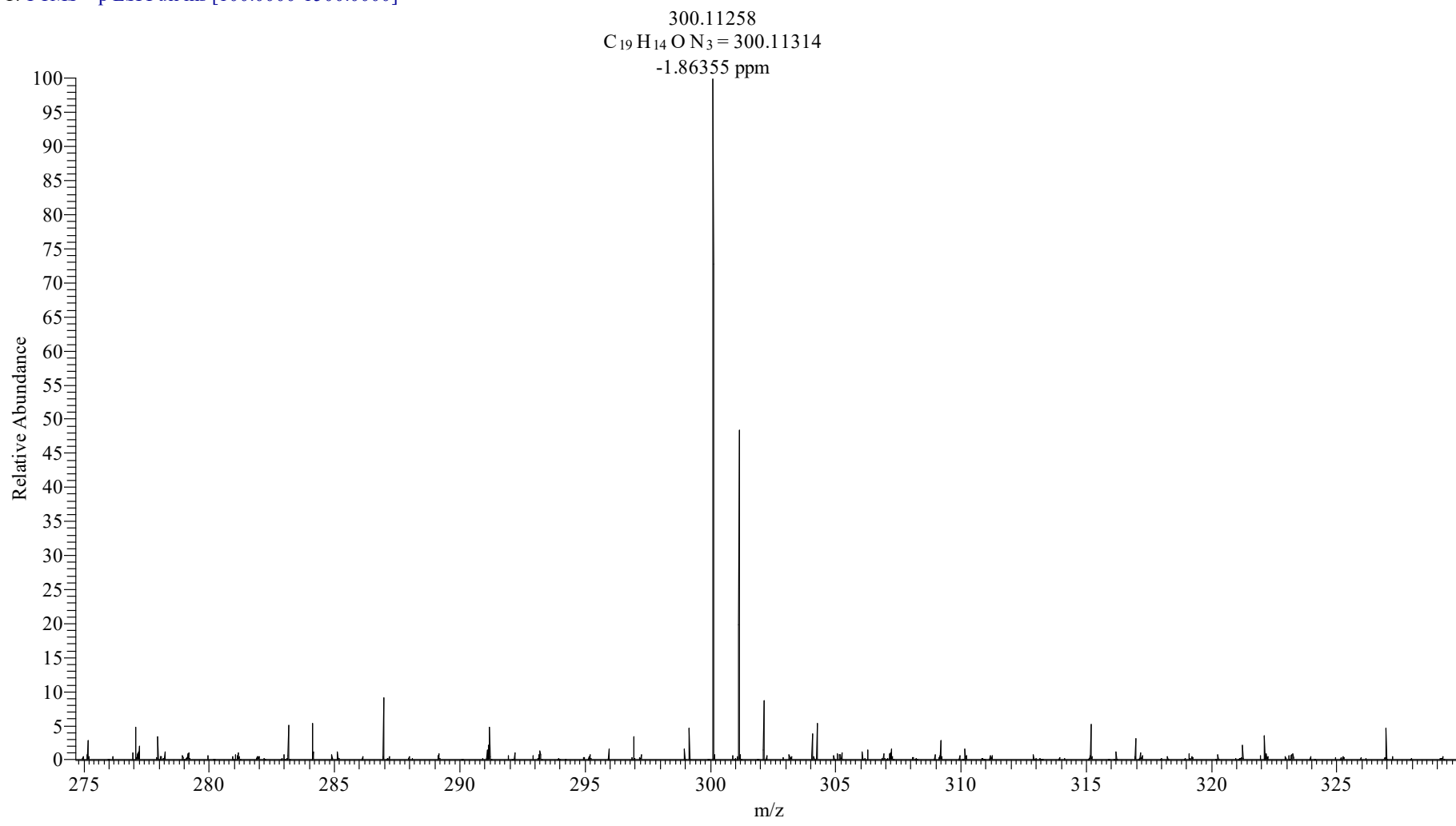
XDL-299.001.001.1R.ESP



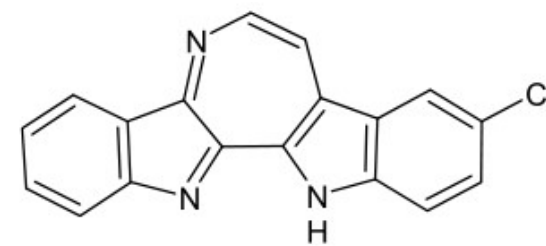
XDL-299.002.001.1R.ESP



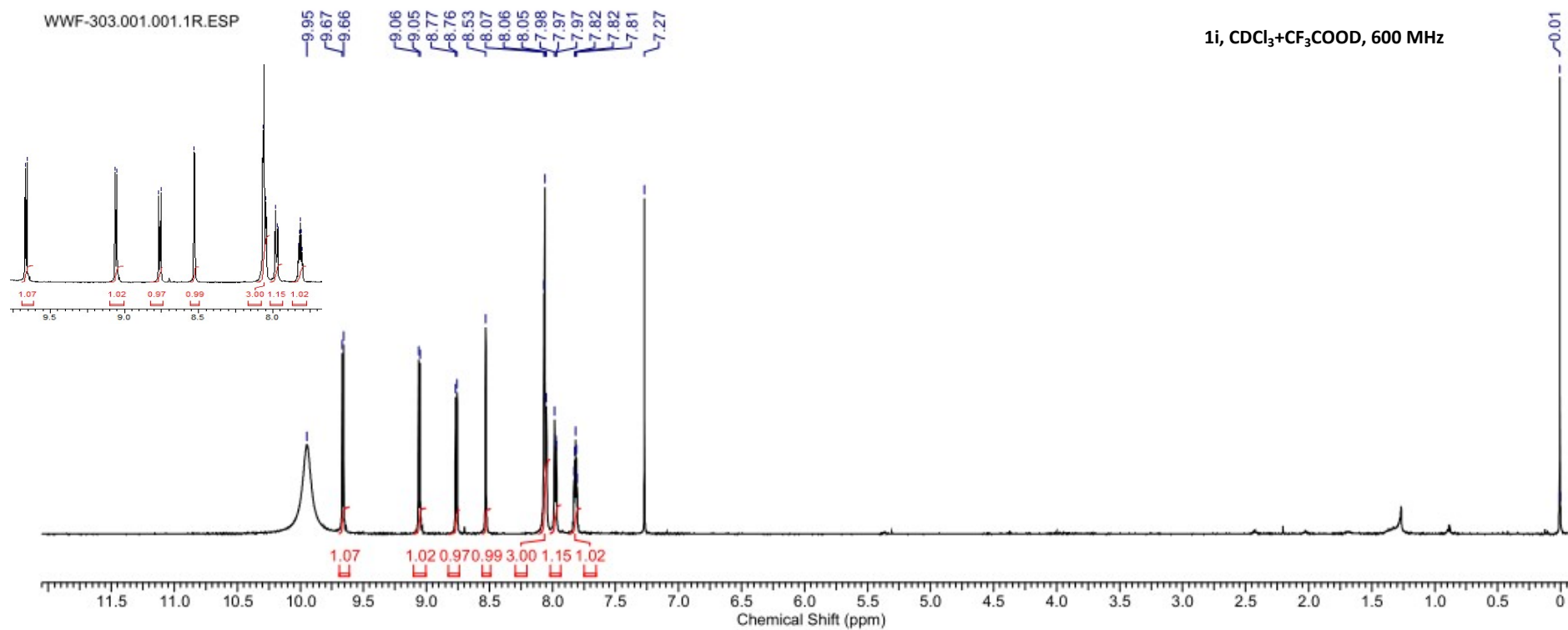
XDL-21299 #31 RT: 0.14 AV: 1 NL: 2.89E7  
T: FTMS + p ESI Full ms [100.0000-1500.0000]



300.11258  
 $C_{19}H_{14}O_3 = 300.11314$   
-1.86355 ppm

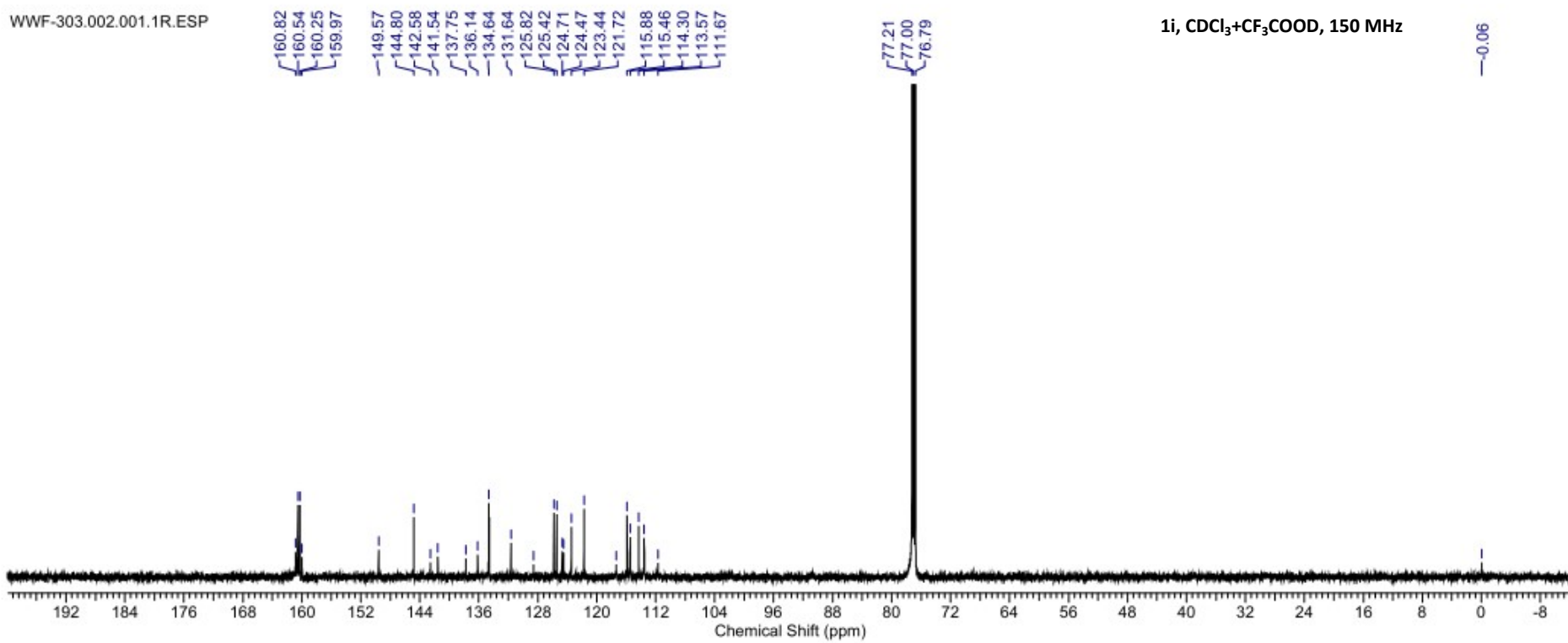


1i, CDCl<sub>3</sub>+CF<sub>3</sub>COOD, 600 MHz





WWF-303.002.001.1R.ESP



WWF-21304-1 #24 RT: 0.10 AV: 1 NL: 2.23E9  
T: FTMS + p ESI Full ms [100.0000-1500.0000]

