

# Supplementary Information

## 1,3-Diarylpyrazolones as Potential Anti-Lung Cancer Agents: Synthesis and Antiproliferative Activity Evaluation

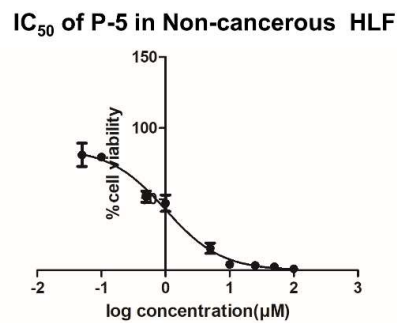
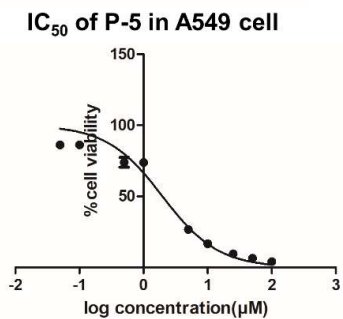
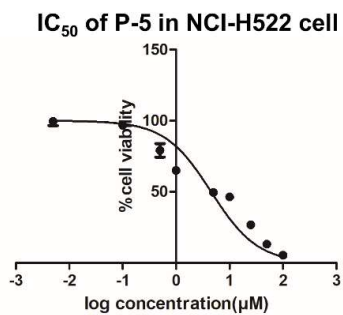
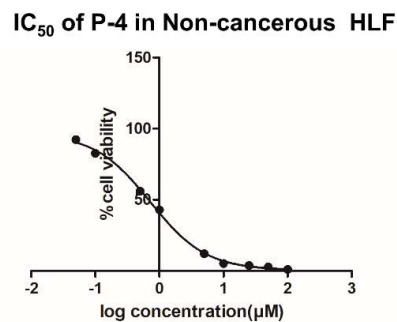
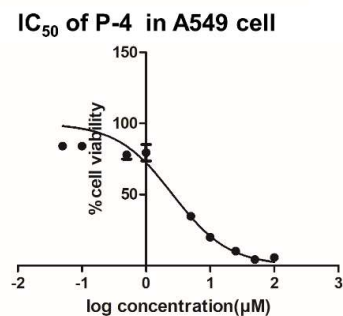
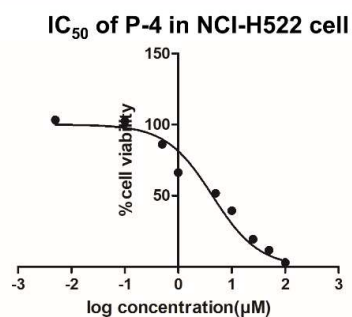
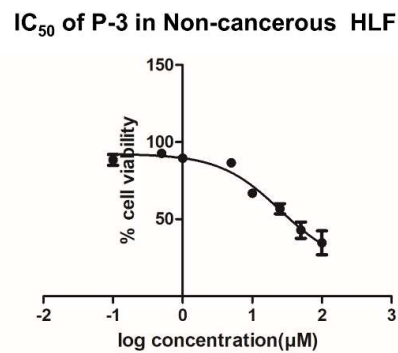
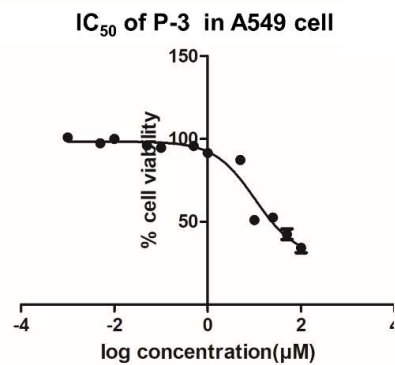
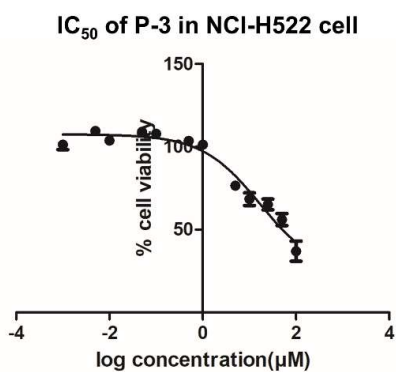
Achyut Dahal<sup>2</sup>, Mary Lo<sup>1</sup>, Sitanshu Singh<sup>2</sup>, Huu Vo<sup>1</sup>, Denzel ElHaze<sup>1</sup>, Seetharama D. Jois<sup>2</sup>, Siva Murru<sup>1,\*</sup>

<sup>1</sup>School of Sciences, College of Arts, Education & Sciences, University of Louisiana Monroe, Monroe, LA 71201. <sup>2</sup>School of Basic Pharmaceutical and Toxicological Sciences, College of Pharmacy, University of Louisiana Monroe, Monroe, LA, 71201. \*Address for Correspondence: Dr. Siva Murru

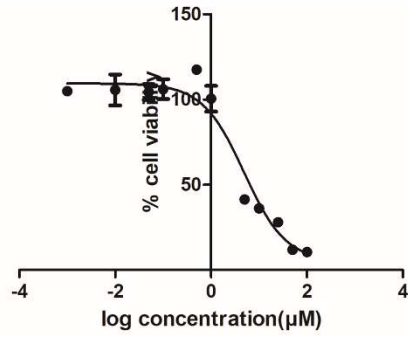
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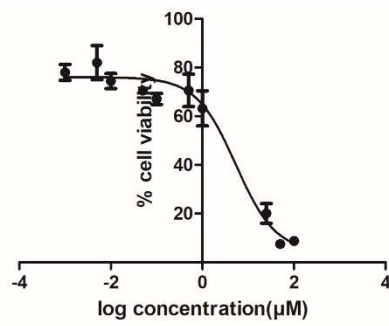
# 1. Antiproliferative activity dose-response curves against A549 and NCI-H522 cells after 72 h:



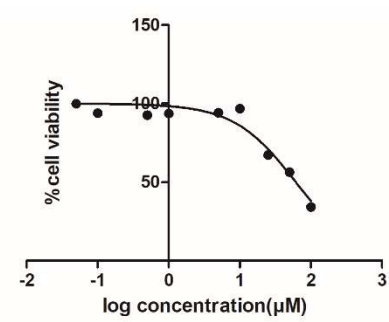
**IC<sub>50</sub> of P-7 in NCI-H522 cell**



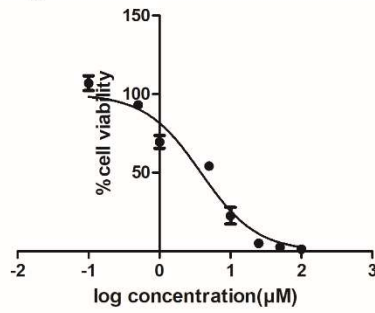
**IC<sub>50</sub> of P-7 in A549 cell**



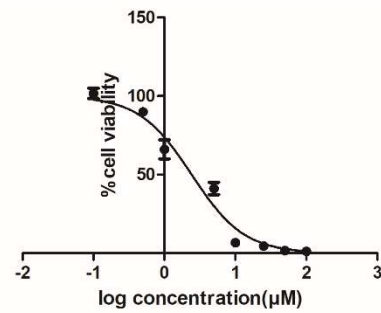
**IC<sub>50</sub> of P-7 in Non-cancerous HLF**



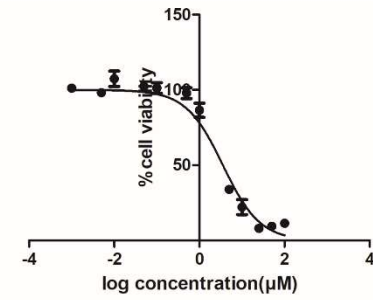
**IC<sub>50</sub> of P-13 in NCI-H522 cell**



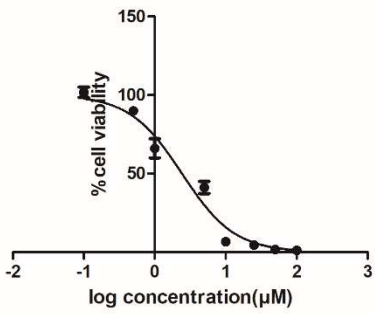
**IC<sub>50</sub> of P-13 in A549 cell**



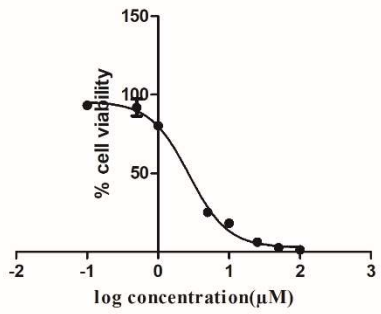
**IC<sub>50</sub> of P-13 in Non-cancerous HLF**



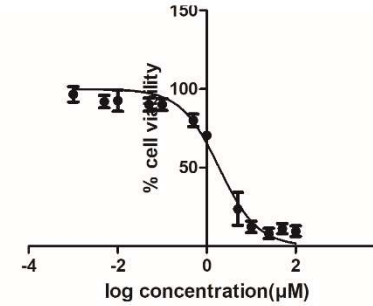
**IC<sub>50</sub> of P-14 in NCI-H522 cell**



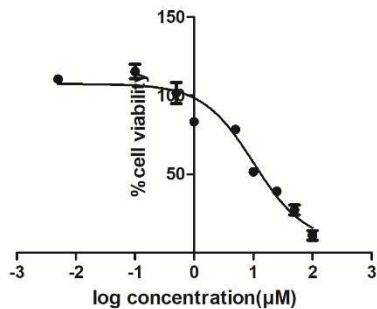
**IC<sub>50</sub> of P-14 in A549 cell**



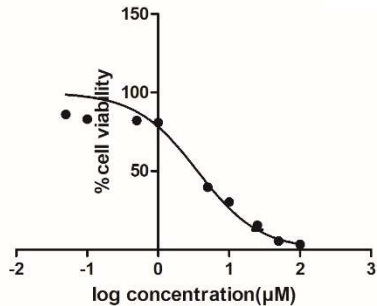
**IC<sub>50</sub> of P-14 in Non-cancerous HLF**



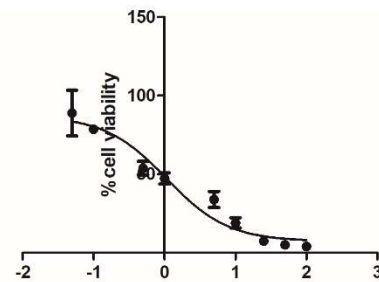
**IC<sub>50</sub> of P-15 in NCI-H522 cell**



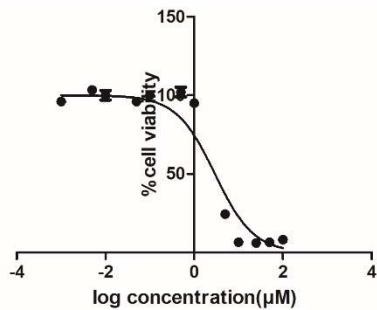
**IC<sub>50</sub> of P-15 in A549 cell**



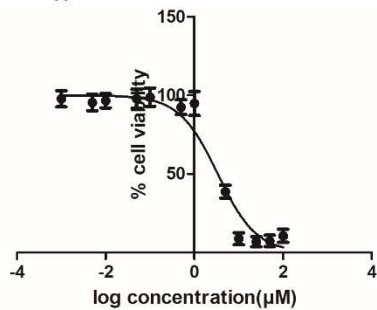
**IC<sub>50</sub> of P-15 in Non-cancerous HLF**



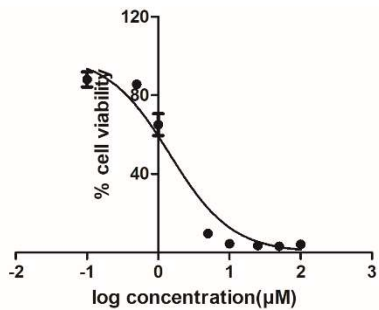
**IC<sub>50</sub> of P-16 in NCI-H522 cell**



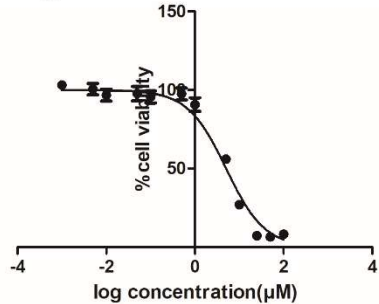
**IC<sub>50</sub> of P-16 in A549 cell**



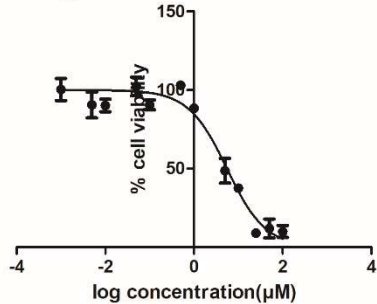
**IC<sub>50</sub> of P-16 in Non-cancerous HLF**



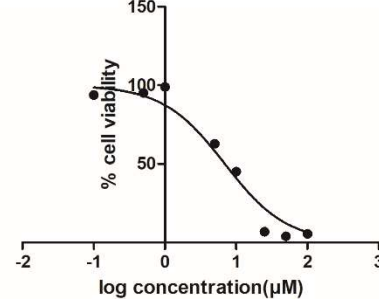
**IC<sub>50</sub> of P-17 in NCI-H522 cell**



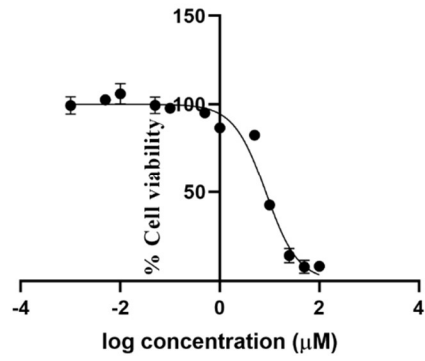
**IC<sub>50</sub> of P-17 in A549 cell**



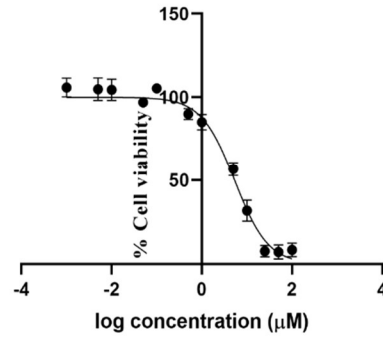
**IC<sub>50</sub> of P-17 in Non-cancerous HLF**



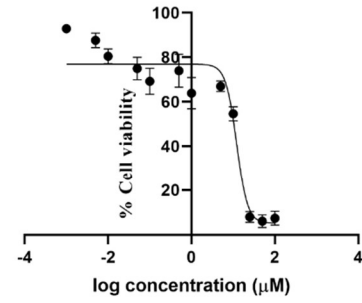
**Afatinib (IC<sub>50</sub>):**



**A549 Cells**

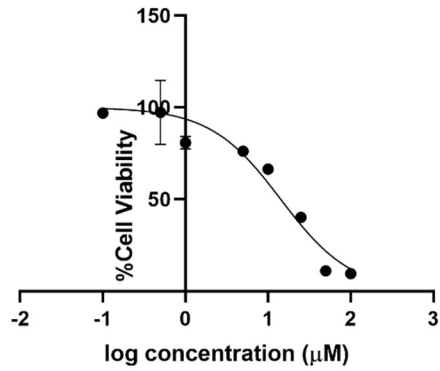


**NCI-5H22 Cells**

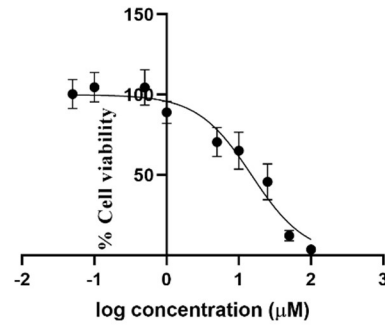


**Normal lung fibroblast cells**

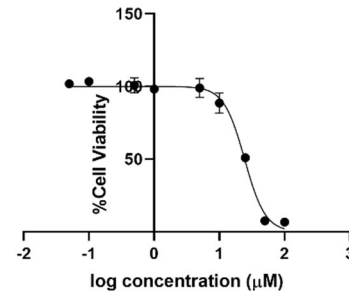
**Gefitinib (IC<sub>50</sub>):**



**A549 Cells**



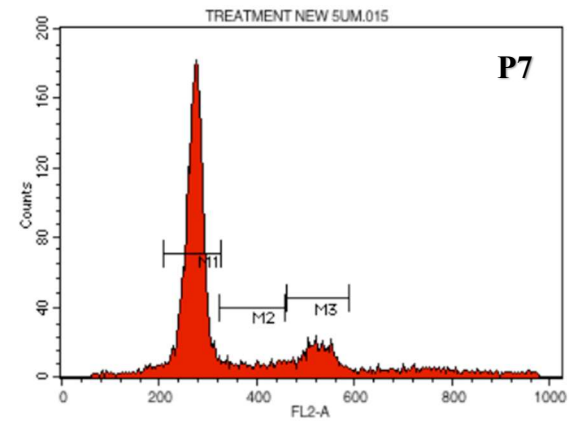
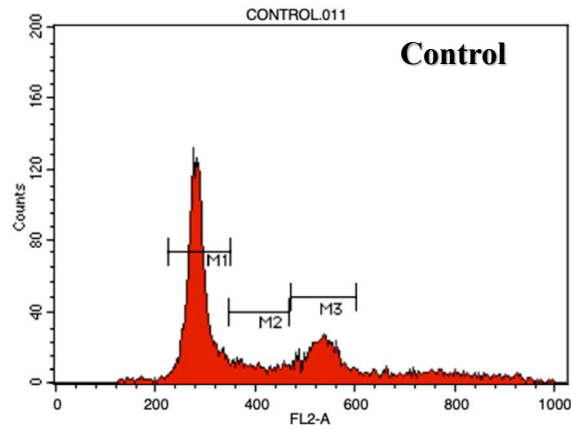
**NCI-5H22 Cells**



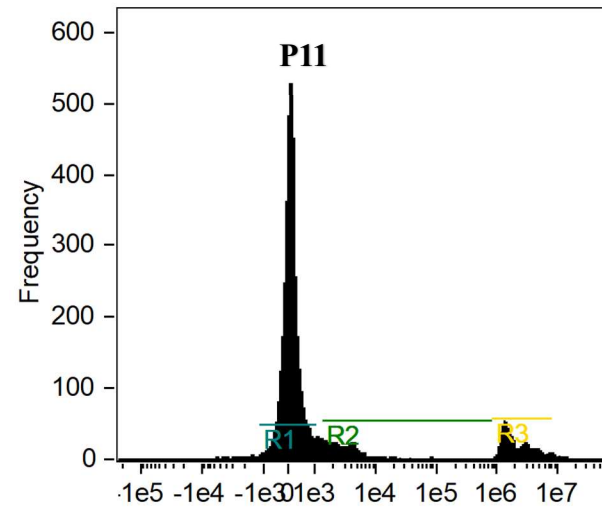
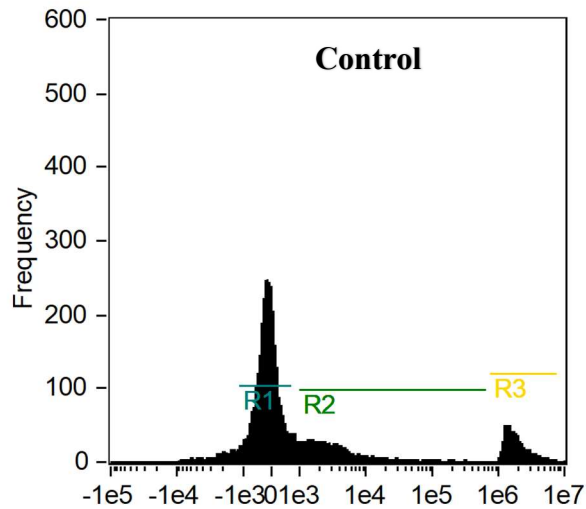
**Normal lung fibroblast cells**

## 2. Cell cycle analysis data

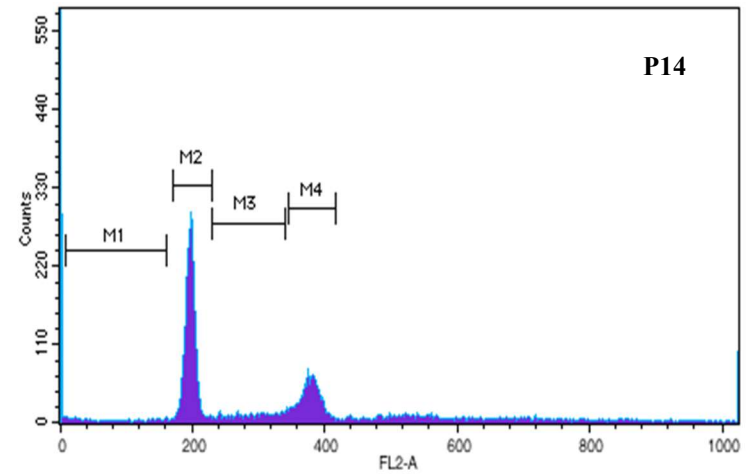
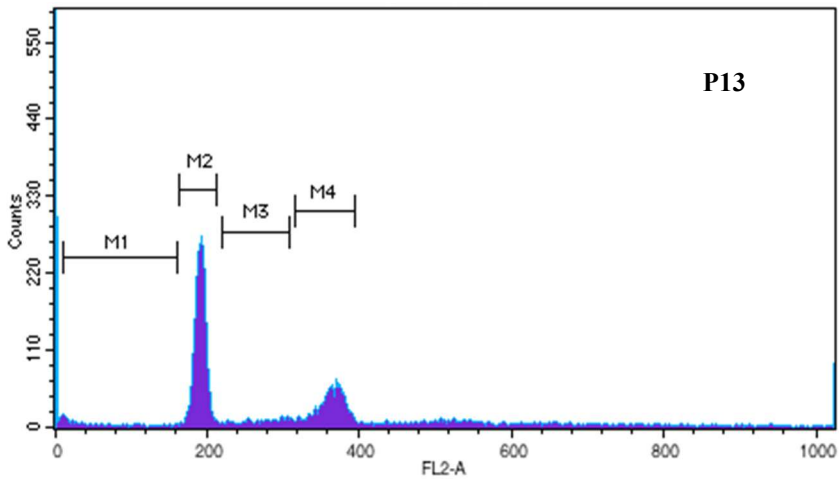
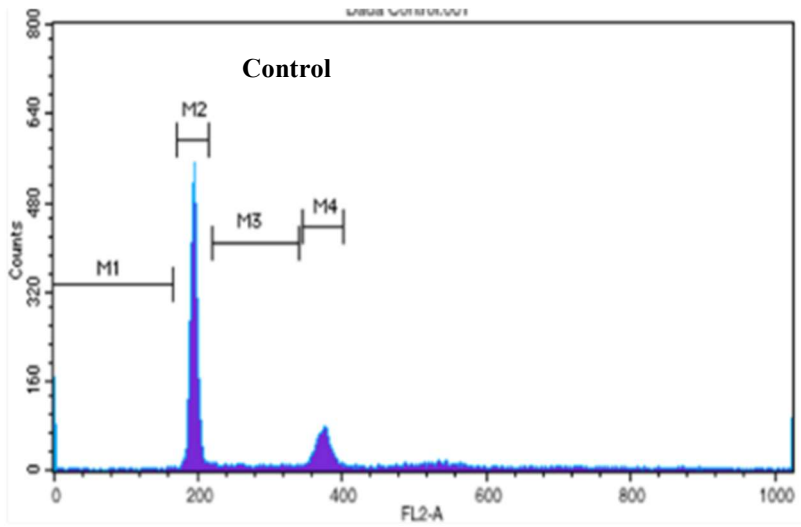
### a) Effects of pyrazolone P7 on the cell cycle progression of NCI-H522 cells:



### b) Effects of pyrazolone P11 on the cell cycle progression of NCI-H522 cells:

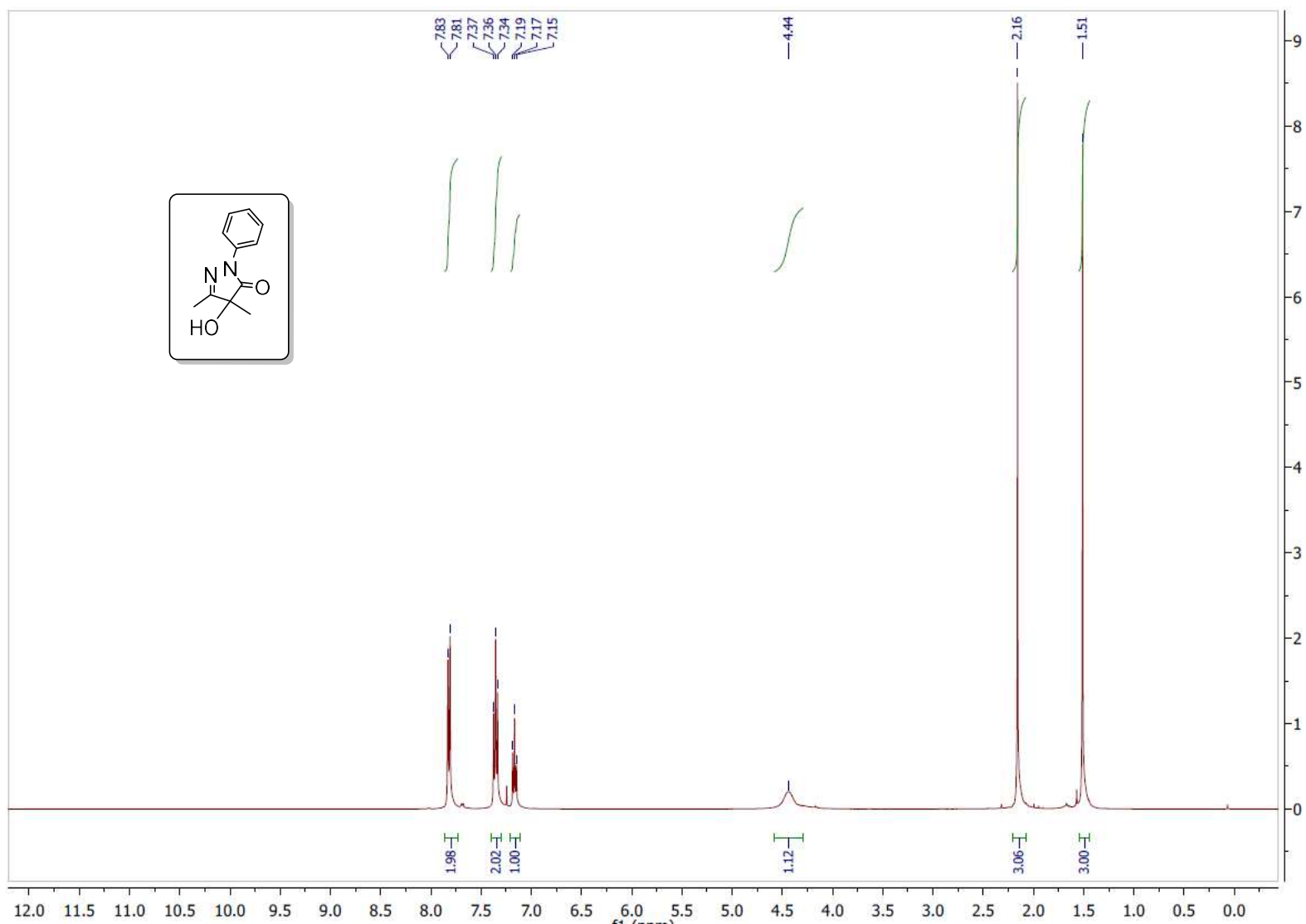


c) Effects of pyrazolones P13 and P14 on the cell cycle progression of NCI-H522 cells:



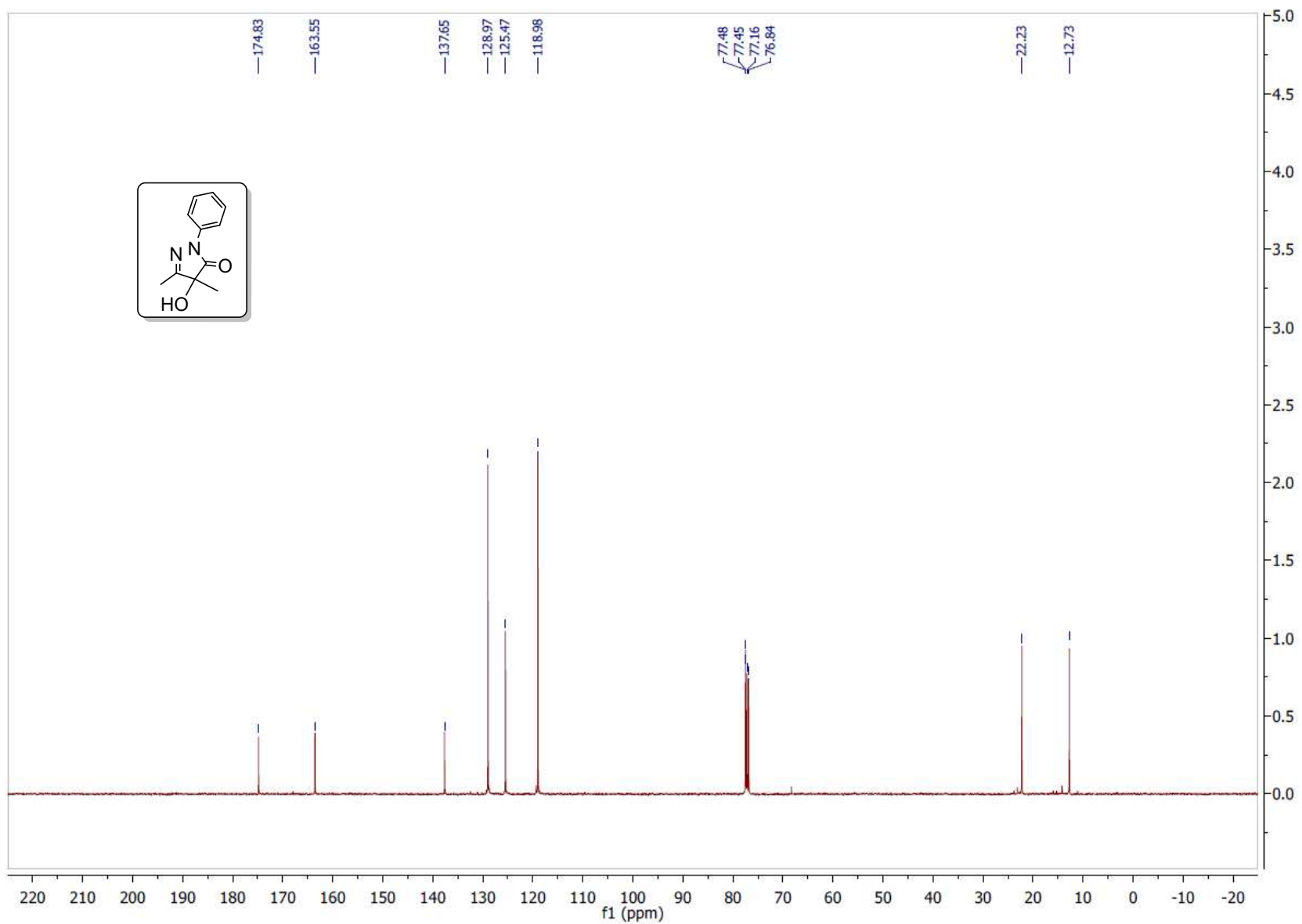
#### 4. NMR and HRMS (ESI-MS) Spectra of the Products

##### 4-hydroxy-4,5-dimethyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P1): $^1\text{H-NMR}$ ( $\text{CDCl}_3$ )

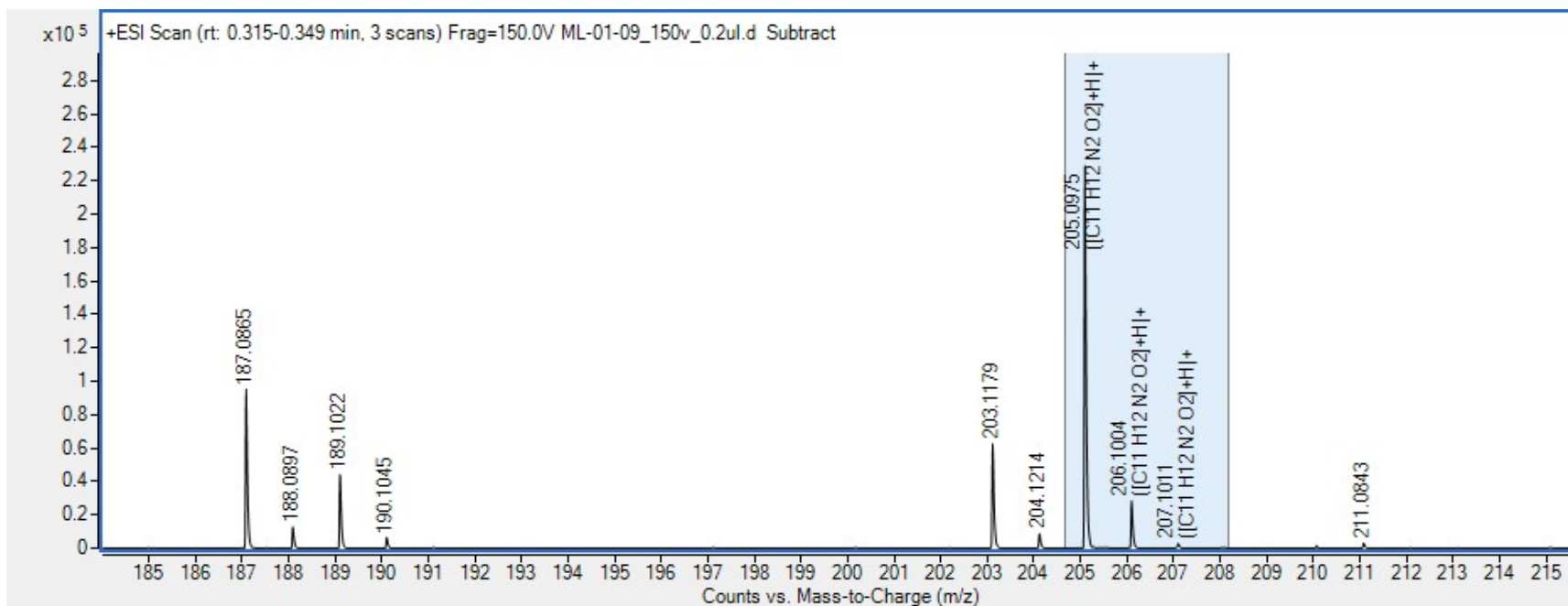




4-hydroxy-4,5-dimethyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P1):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )

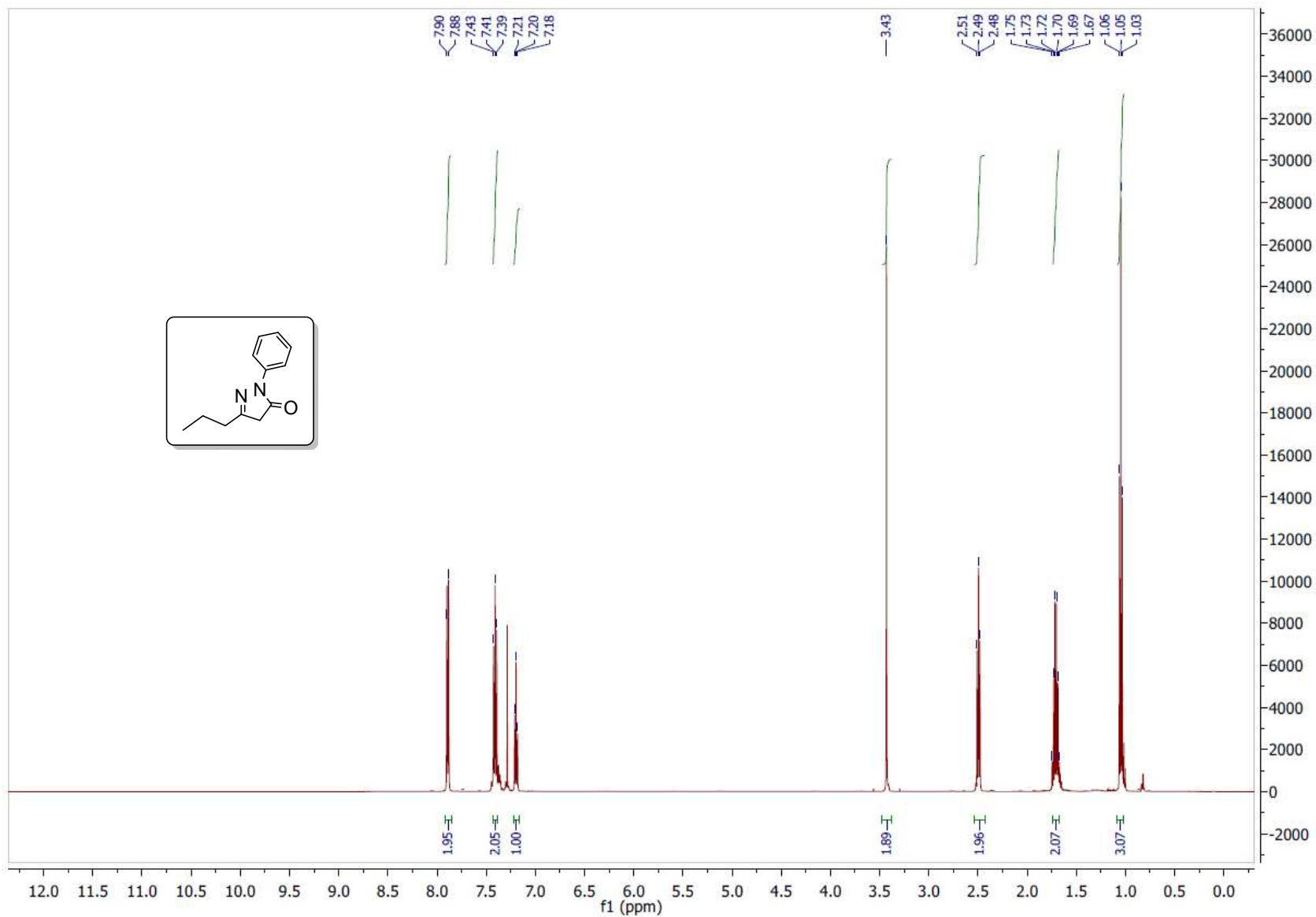


4-hydroxy-4,5-dimethyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P1): ESI-MS

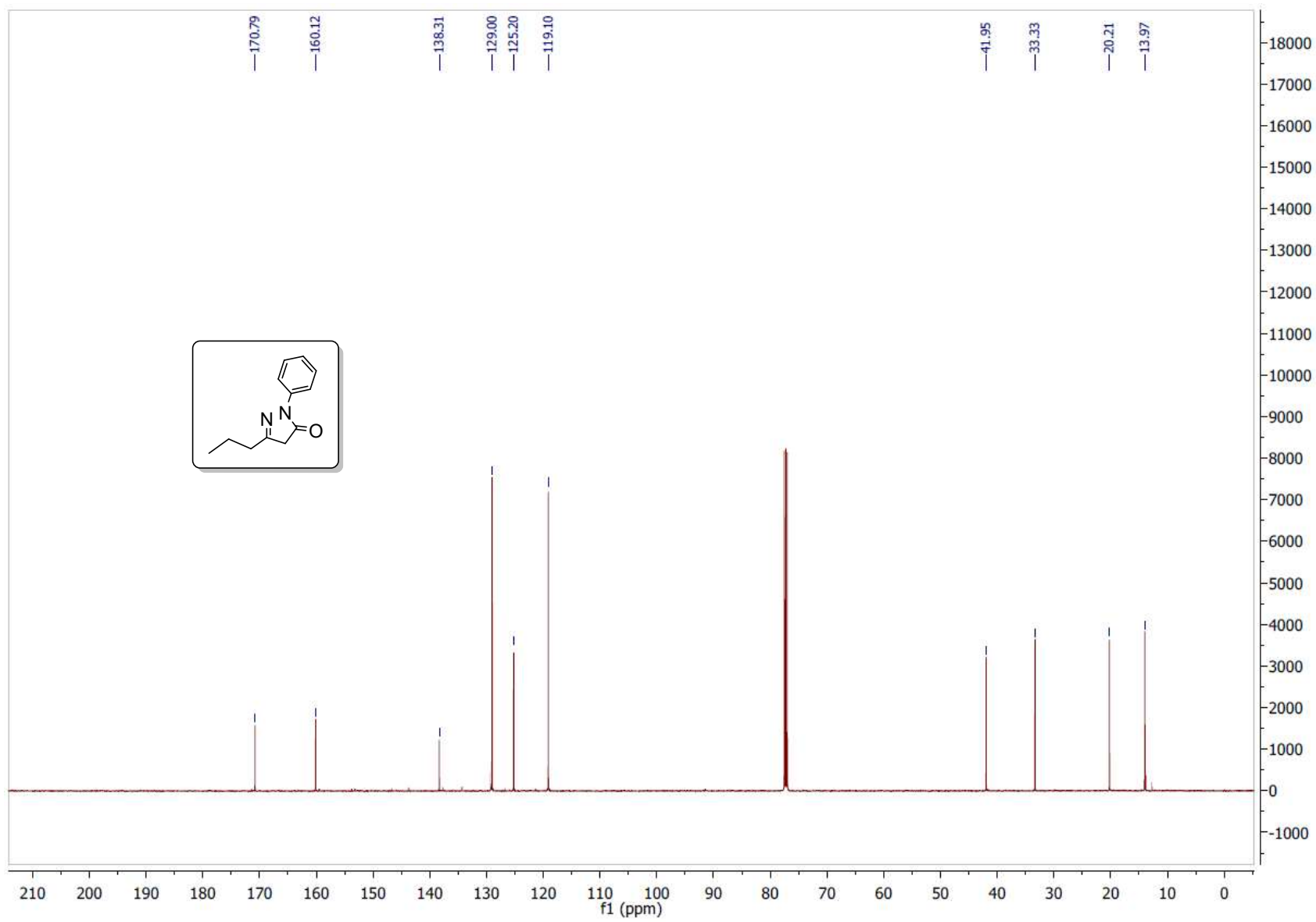


Formula	Species	m/z	Score	Diff (abs. ppm)	Mass
C11 H12 N2 O2	(M+H) <sup>+</sup>	205.0975	99.42	1.62	204.0902

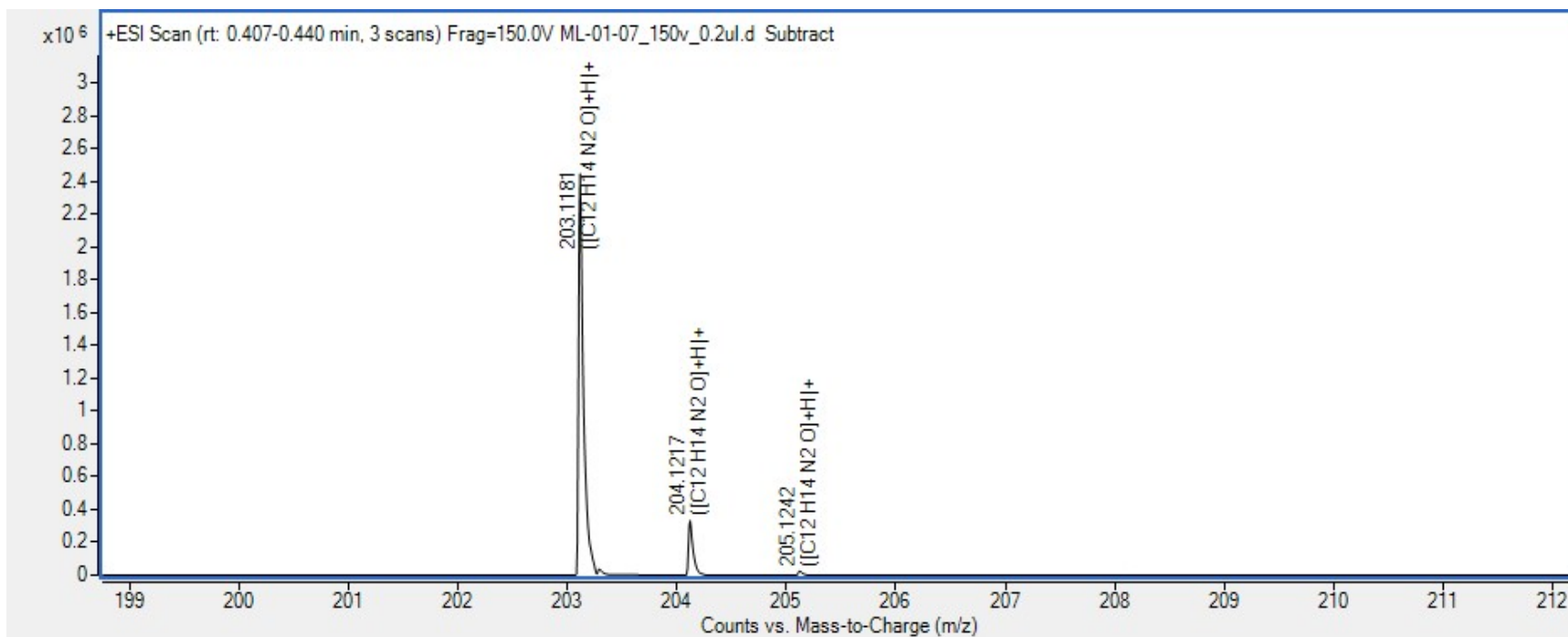
2-phenyl-5-propyl-2,4-dihydro-3H-pyrazol-3-one (P2):  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )



2-phenyl-5-propyl-2,4-dihydro-3H-pyrazol-3-one (P2):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )

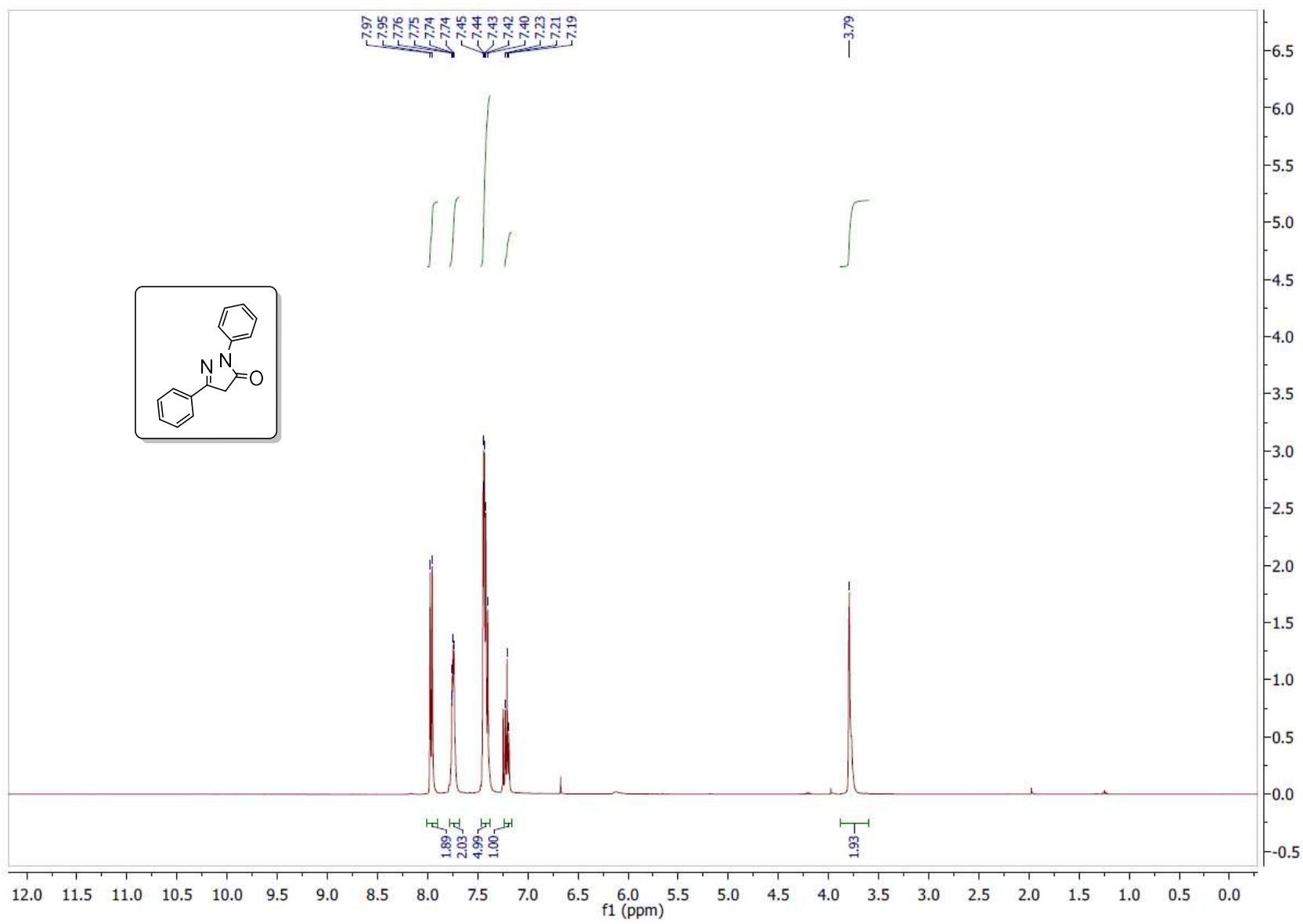


## 2-phenyl-5-propyl-2,4-dihydro-3H-pyrazol-3-one (P2): ESI-MS

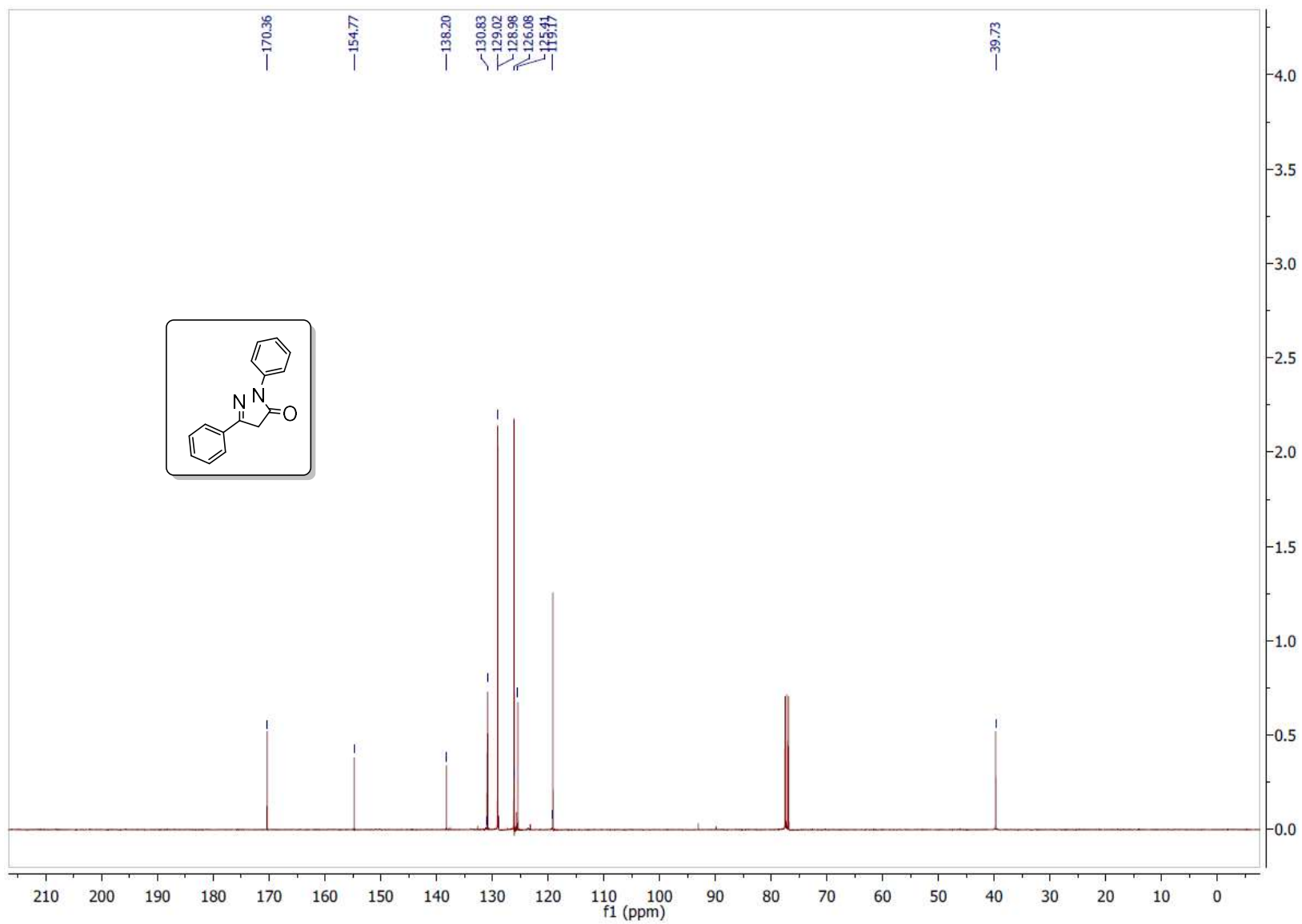


Formula,	Species,	m/z,	Score,	Diff (abs. ppm),	Mass
C12 H14 N2 O,	(M+H)+,	203.1181,	98.94,	1.5,	202.1109

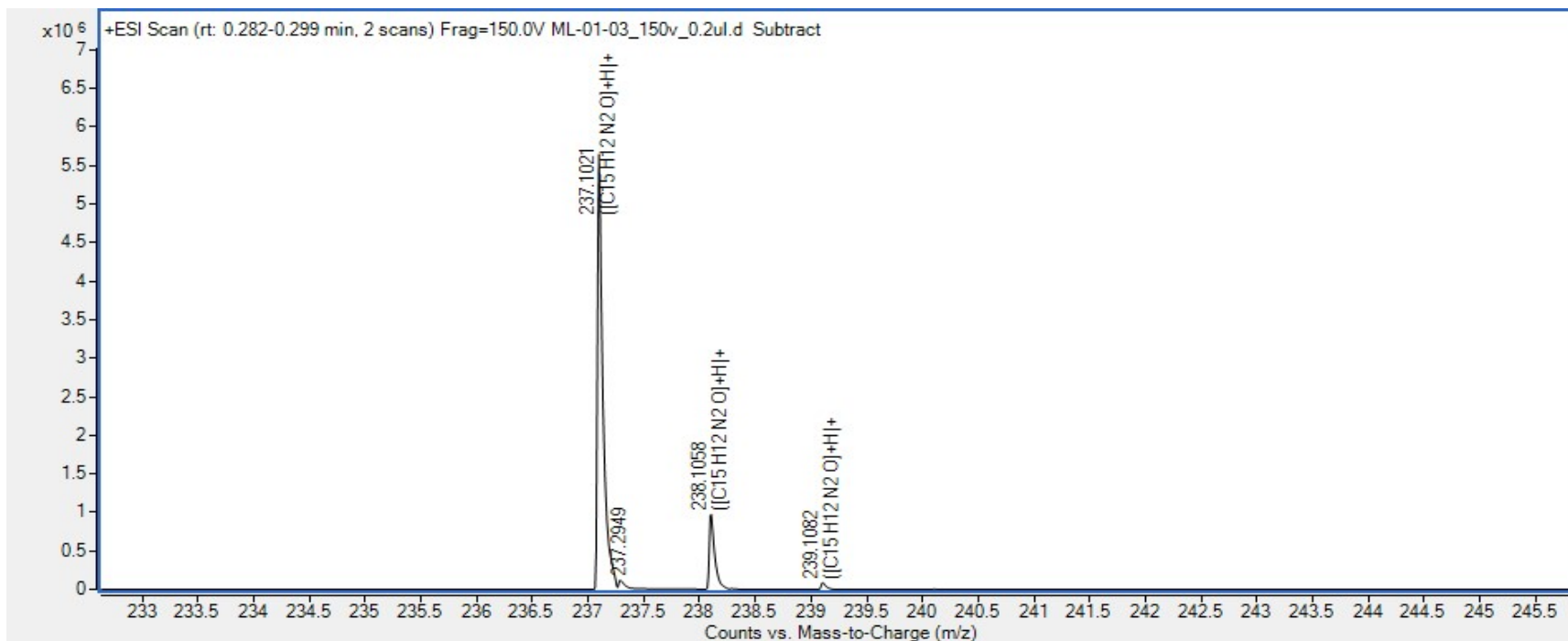
2,5-diphenyl-2,4-dihydro-3H-pyrazol-3-one (P3):  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )



2,5-diphenyl-2,4-dihydro-3H-pyrazol-3-one (P3):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )



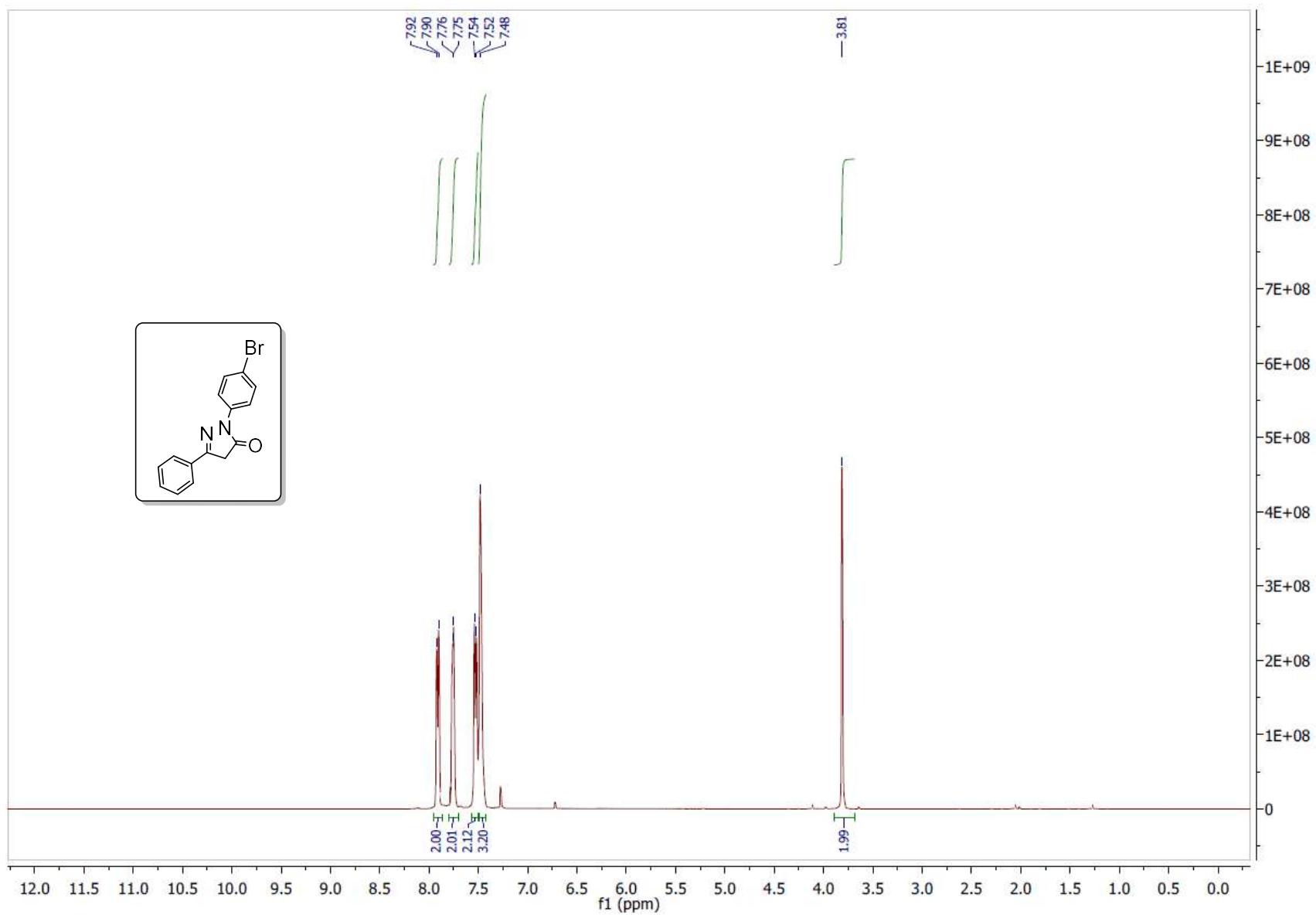
### 2,5-diphenyl-2,4-dihydro-3H-pyrazol-3-one (P3): ESI-MS



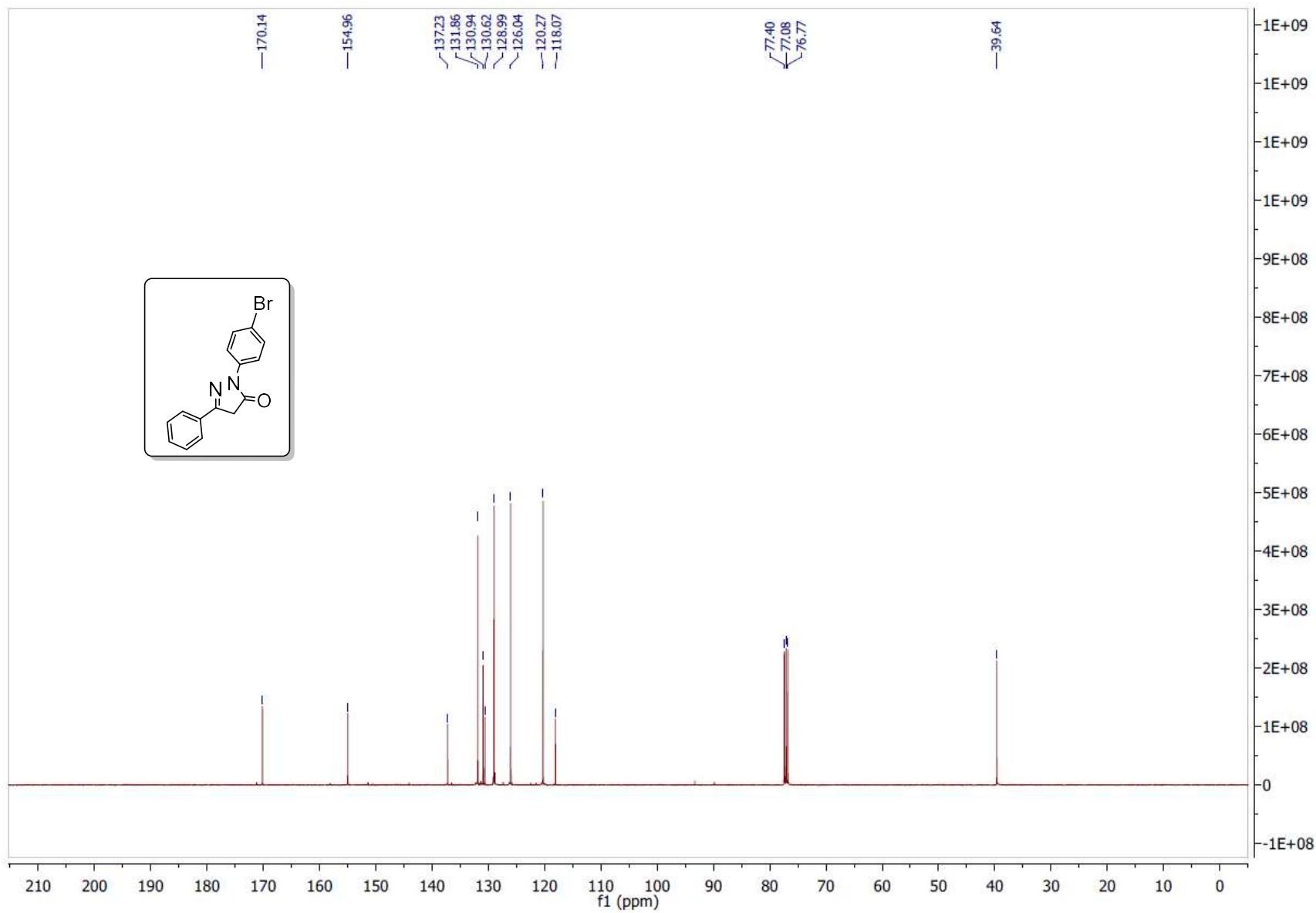
Formula	Species	m/z	Score	Diff (abs. ppm)	Mass
C15 H12 N2 O	(M+H) <sup>+</sup>	237.1021	99.46	0.16	236.0949



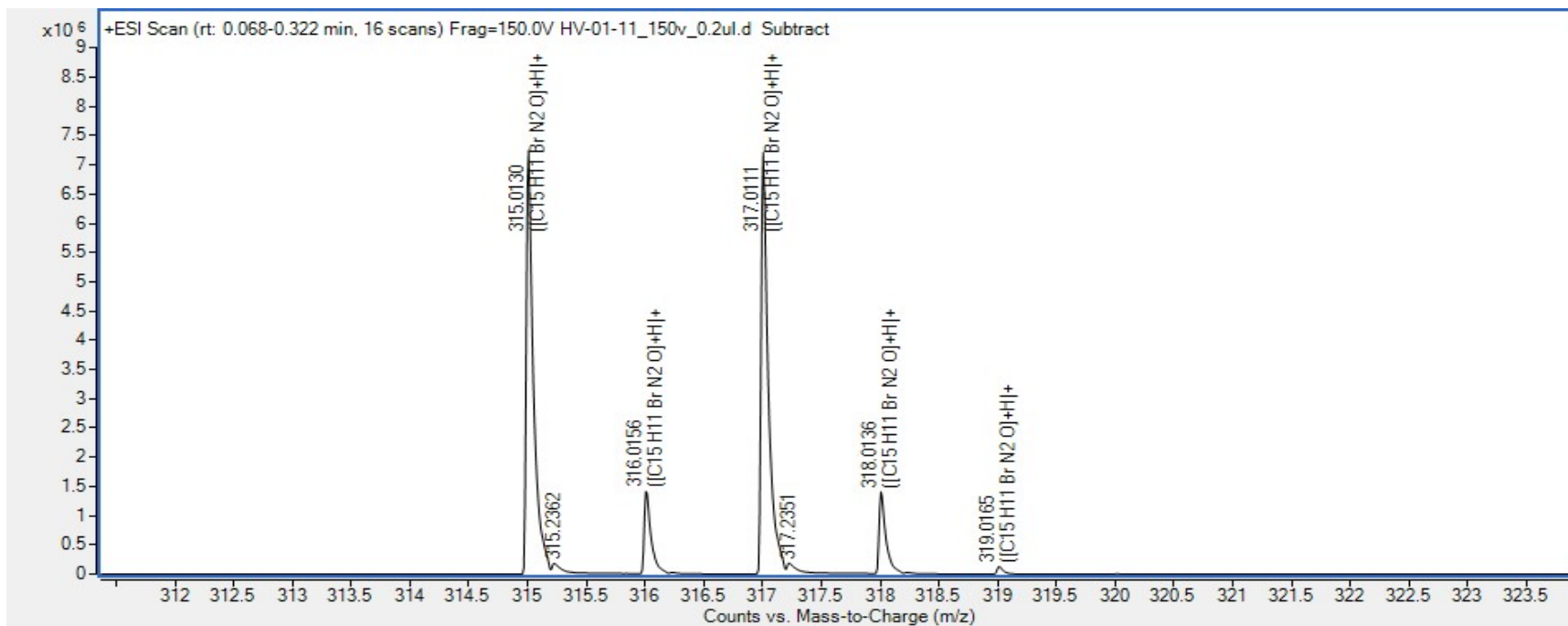
2-(4-bromophenyl)-5-phenyl-2,4-dihydro-3H-pyrazol-3-one (P4):  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )



2-(4-bromophenyl)-5-phenyl-2,4-dihydro-3H-pyrazol-3-one (P4):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )

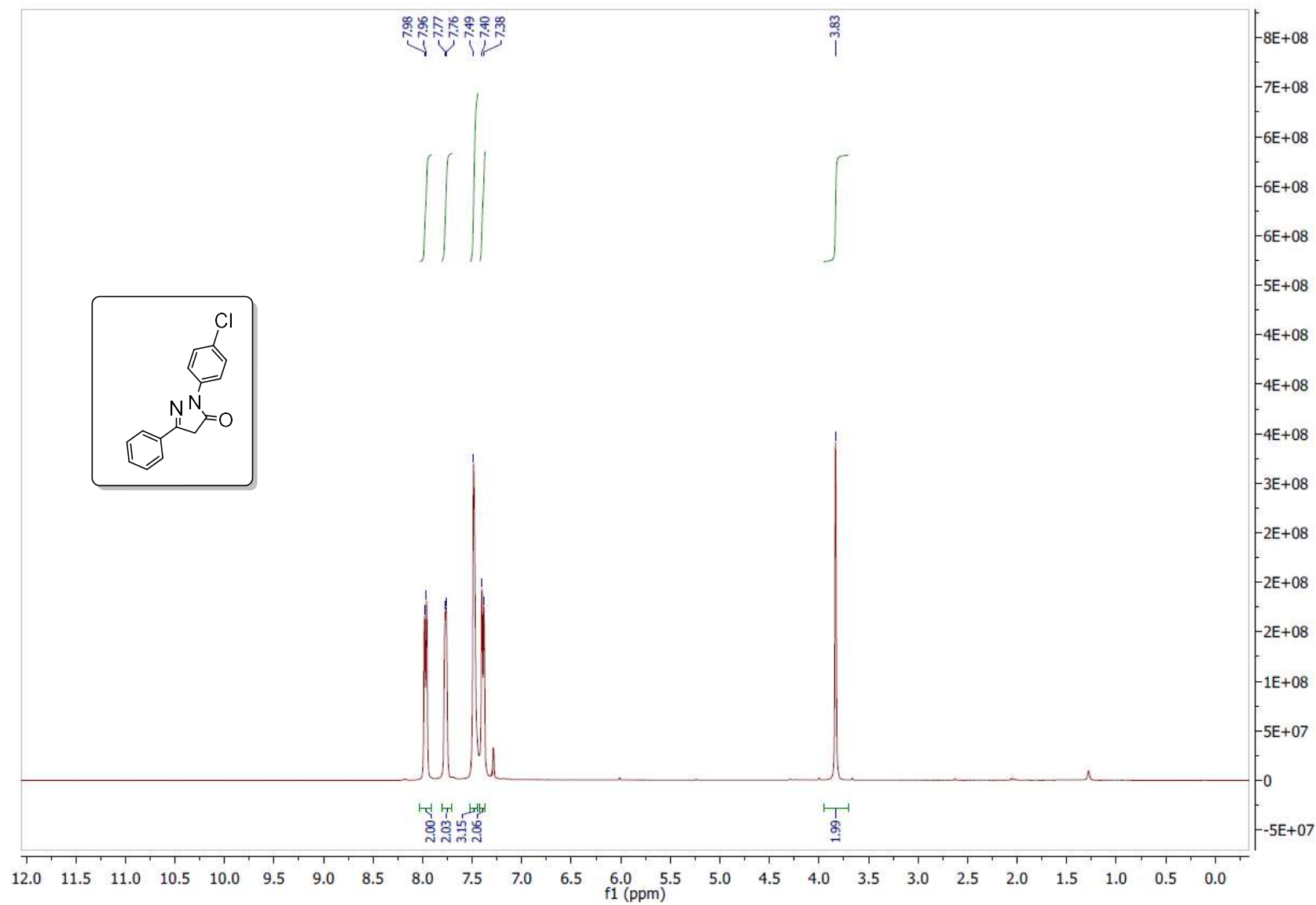


**2-(4-bromophenyl)-5-phenyl-2,4-dihydro-3H-pyrazol-3-one (P4): ESI-MS**

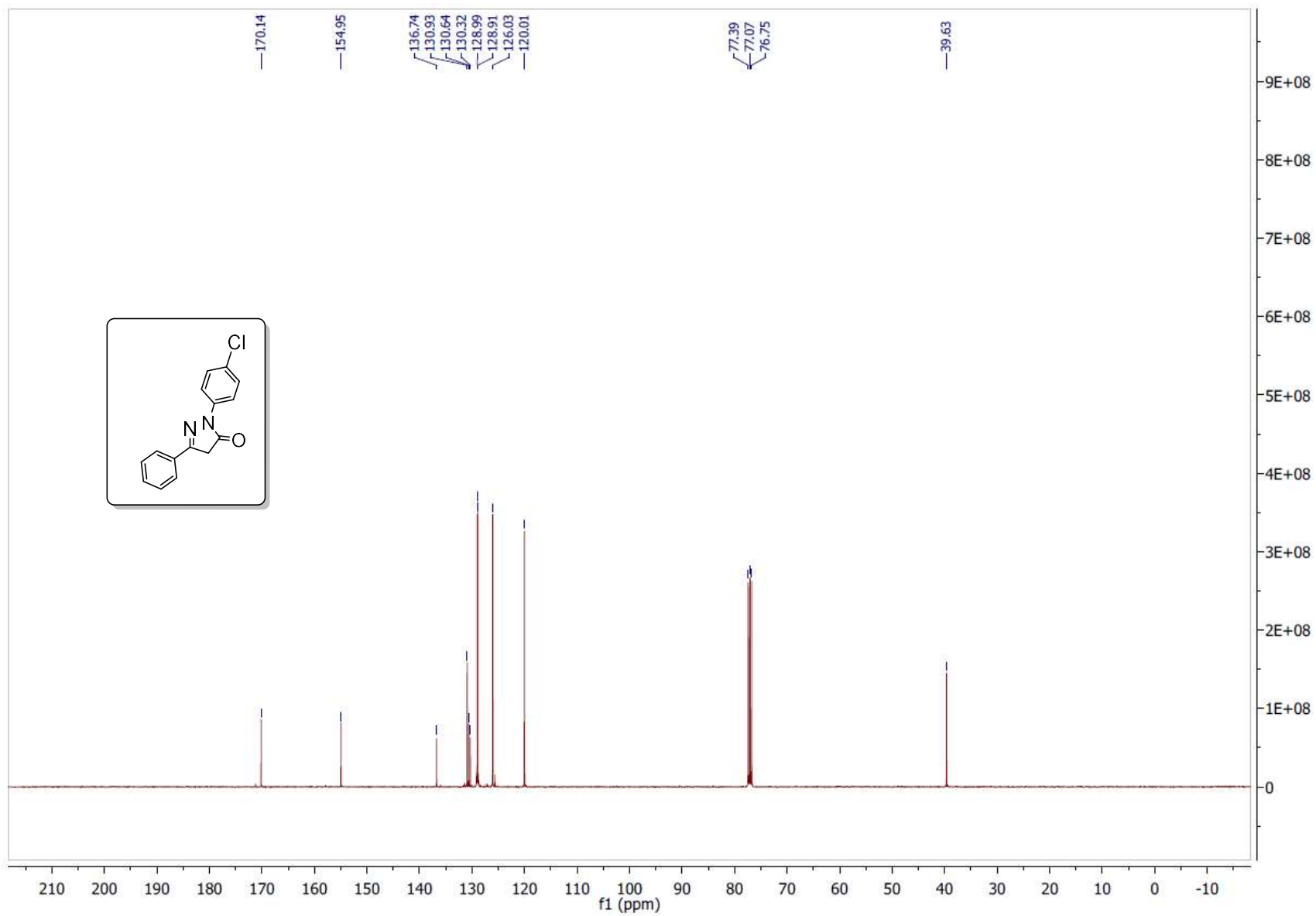


Formula,	Species,	m/z,	Score,	Diff (abs. ppm),	Mass
C15 H11 Br N2 O,	(M+H)+,	315.0130,	98.13,	0.43,	314.0056

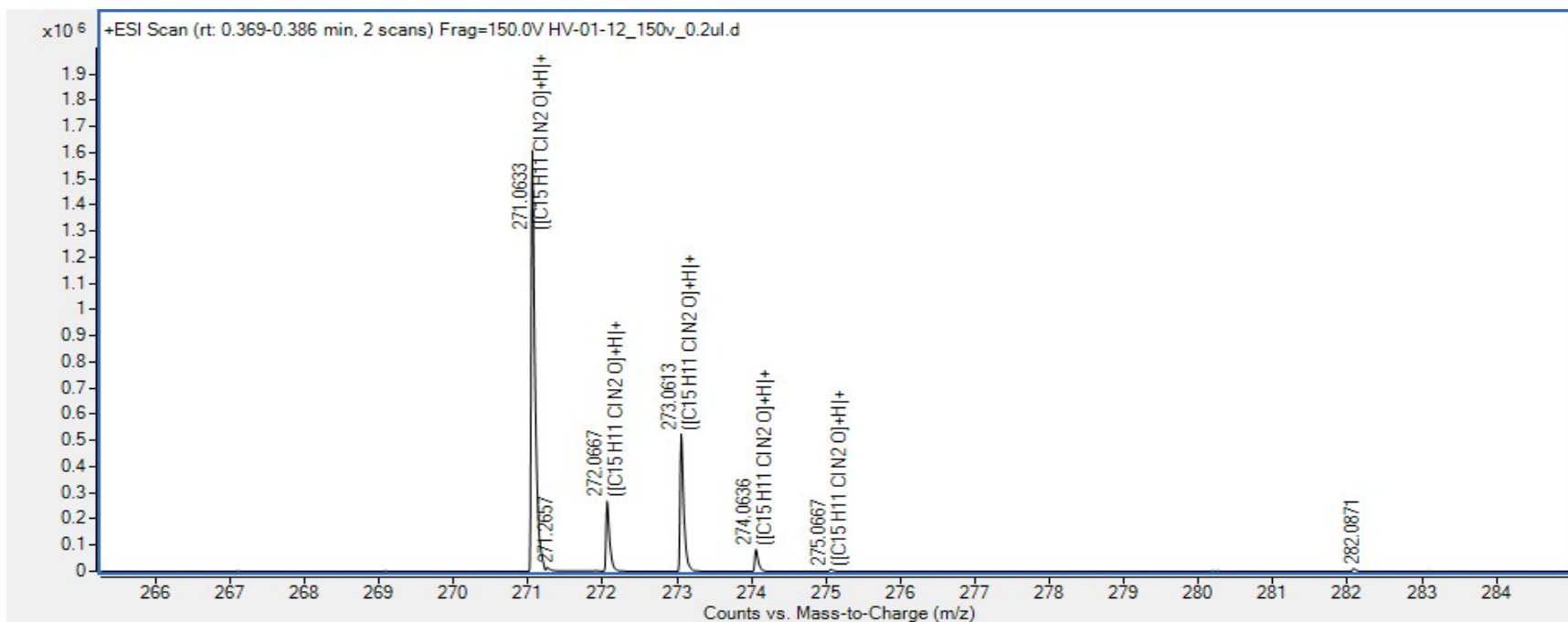
2-(4-chlorophenyl)-5-phenyl-2,4-dihydro-3H-pyrazol-3-one (P5):  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )



2-(4-chlorophenyl)-5-phenyl-2,4-dihydro-3H-pyrazol-3-one (P5):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )

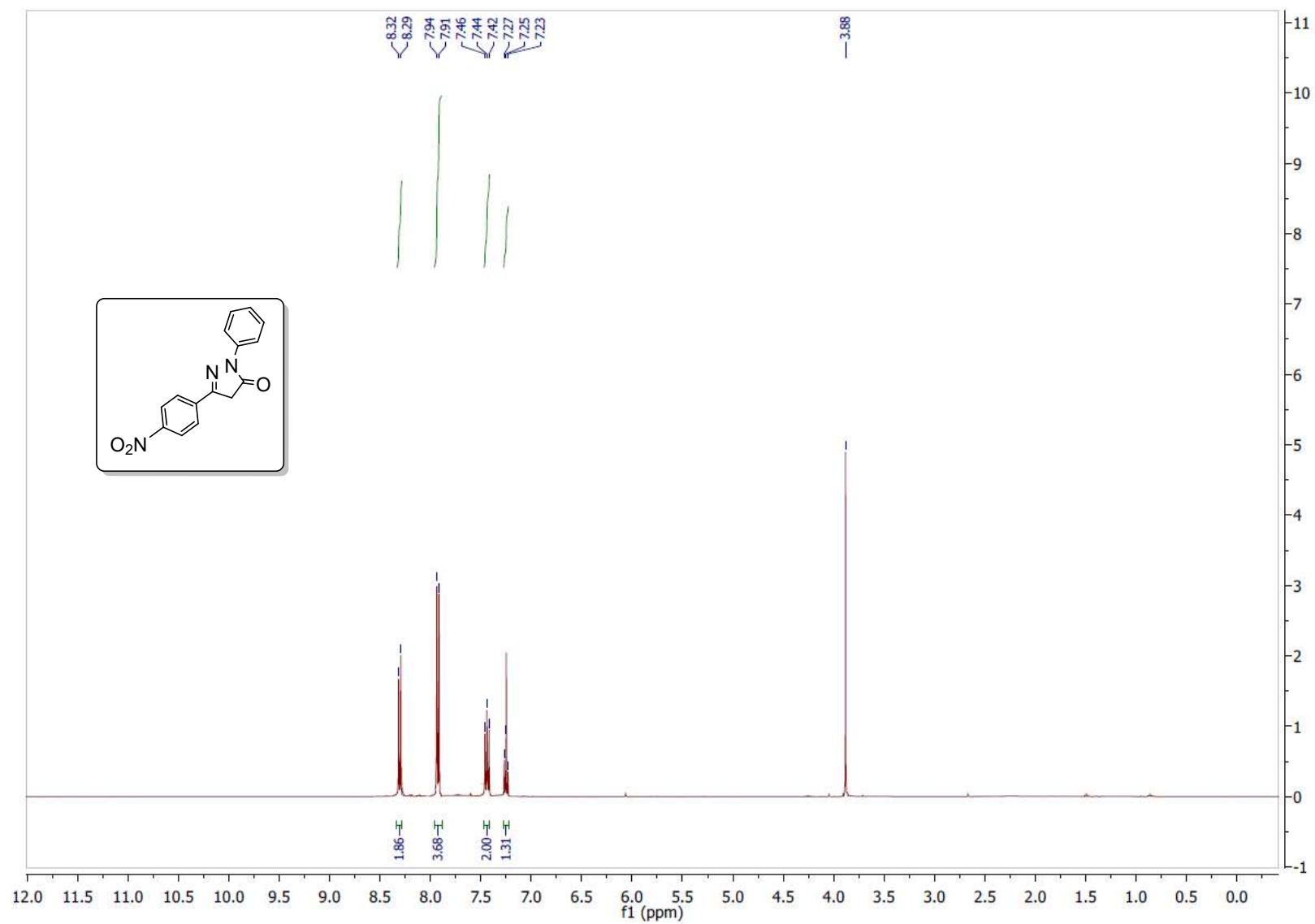


## 2-(4-chlorophenyl)-5-phenyl-2,4-dihydro-3H-pyrazol-3-one (P5): ESI-MS

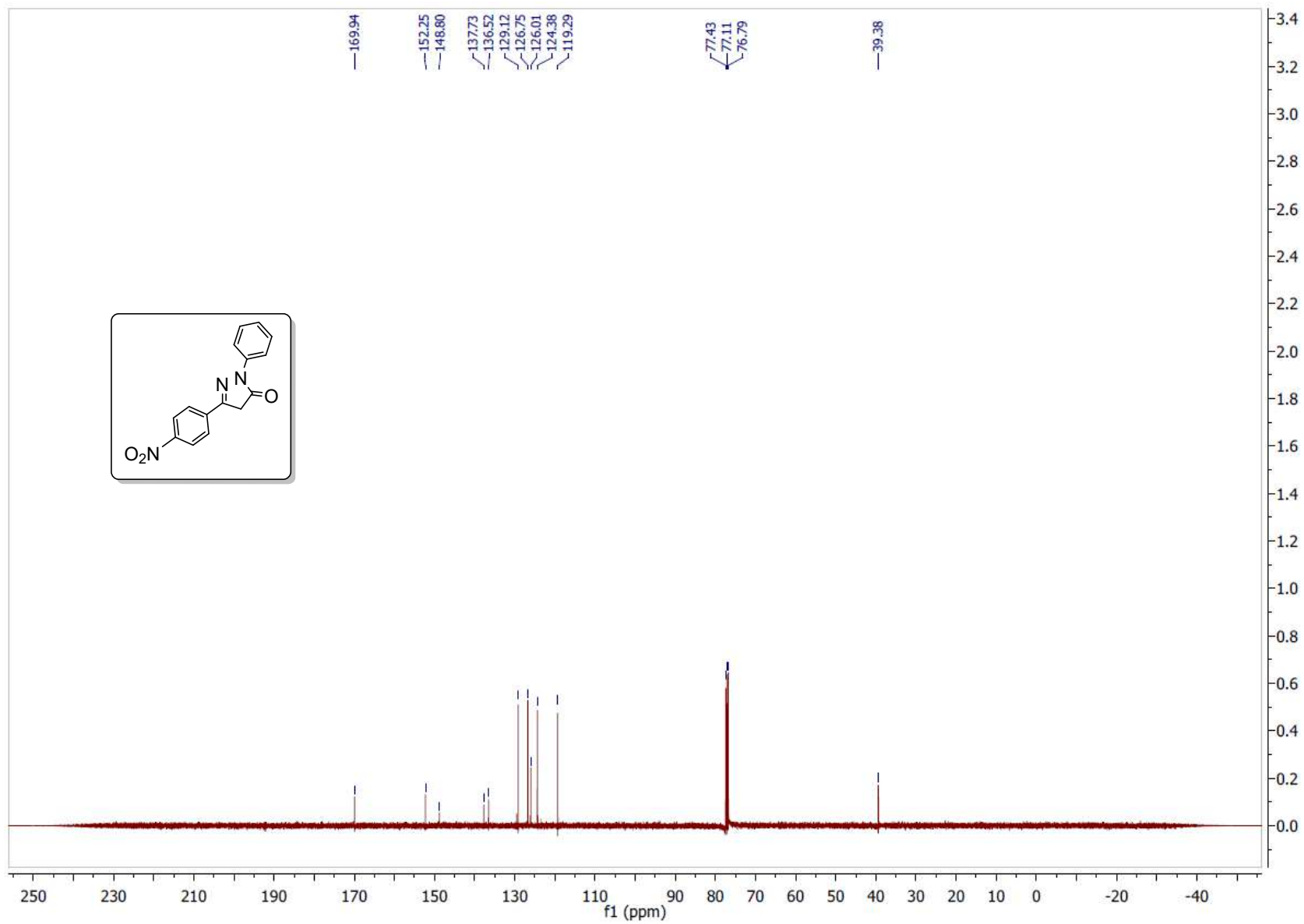


Formula,	Species,	m/z,	Score,	Diff (abs. ppm),	Mass
C15 H11 Cl N2 O,	(M+H)+,	271.0633,	99.5,	0.76,	270.0562

5-(4-nitrophenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P6):  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )

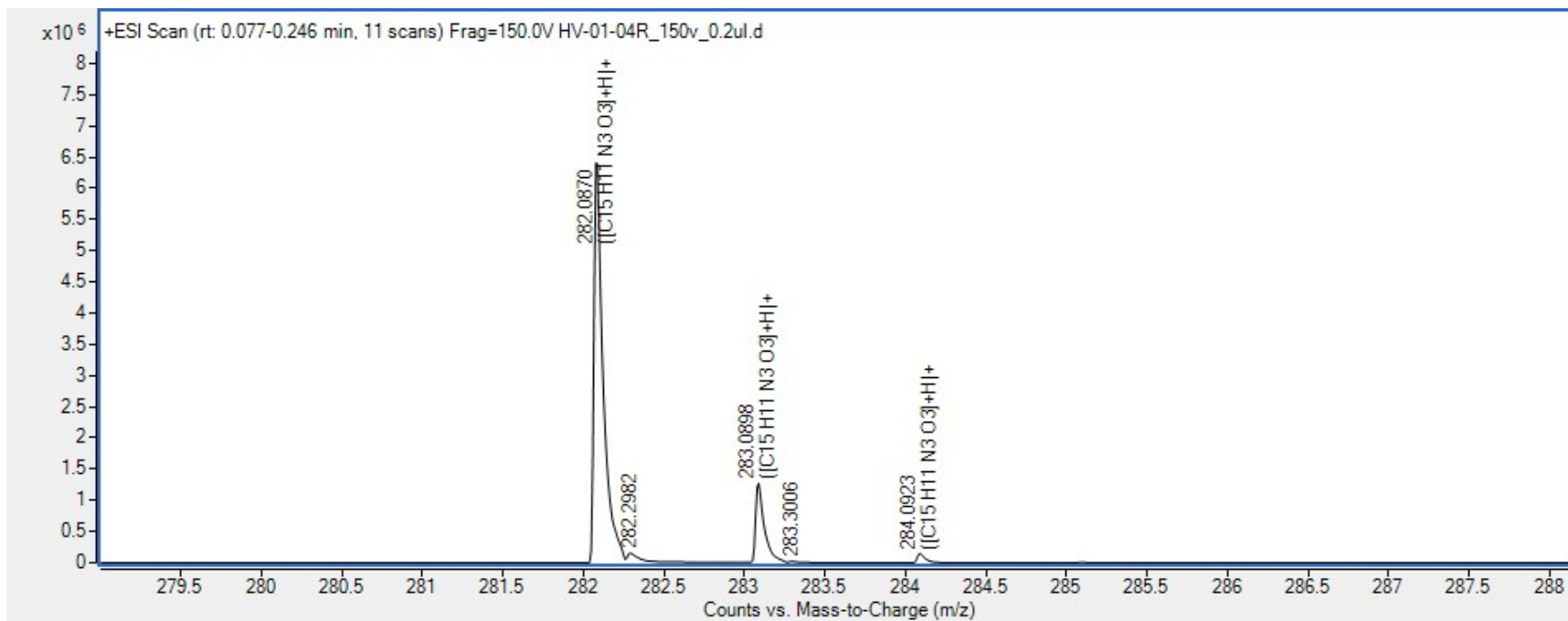


5-(4-nitrophenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P6):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )



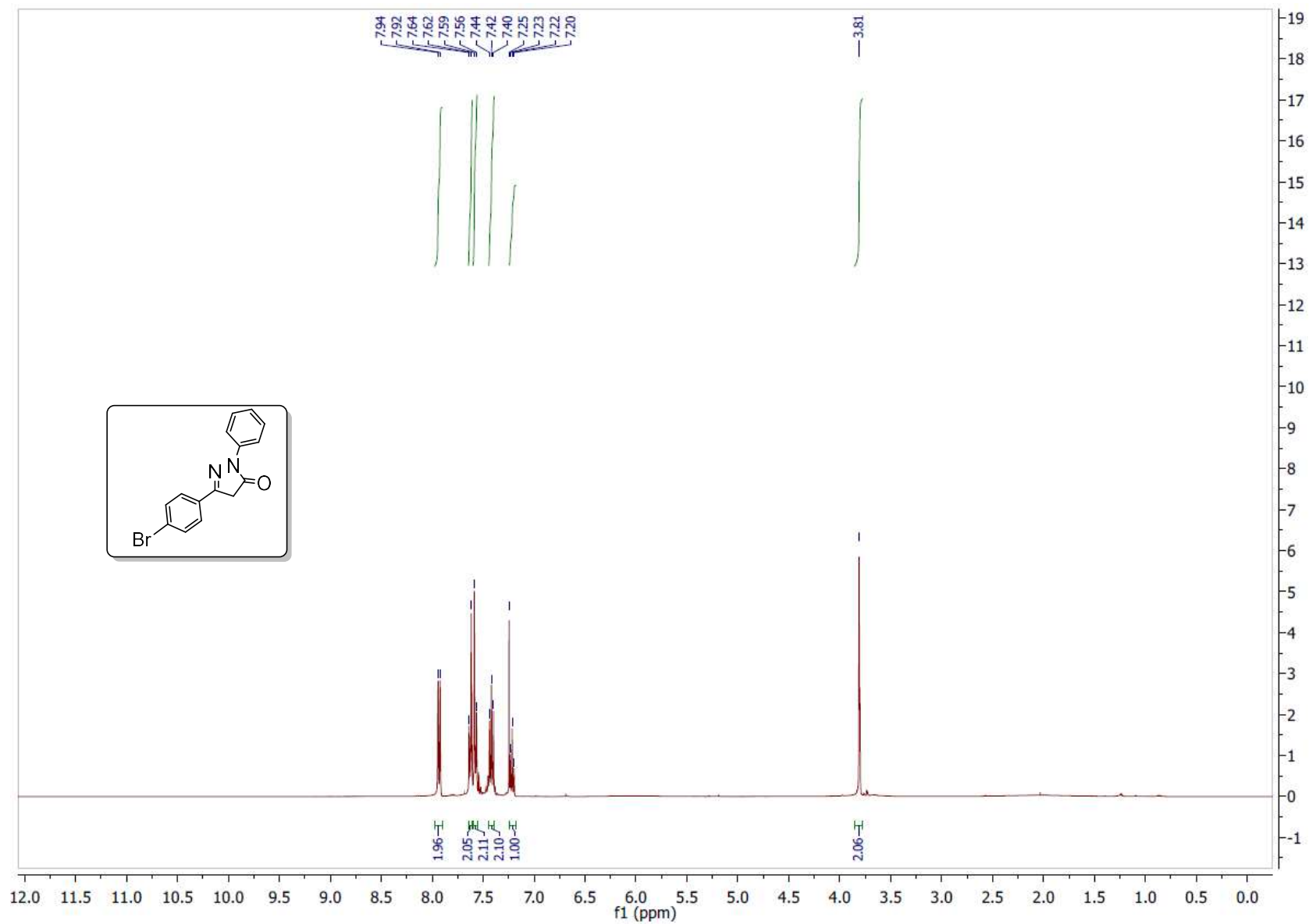


### 5-(4-nitrophenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P6): ESI-MS

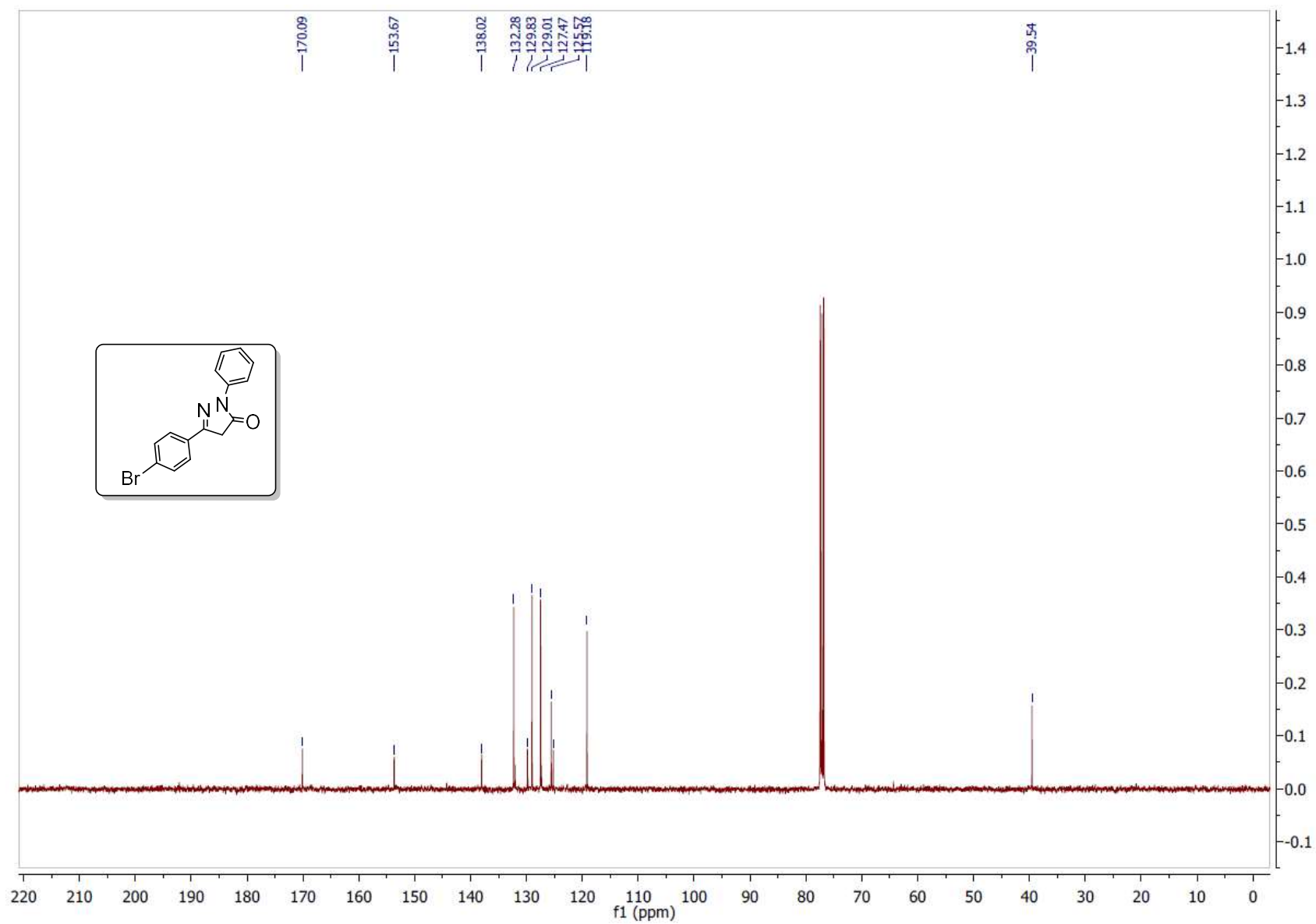


Formula,	Species,	m/z,	Score,	Diff (abs. ppm),	Mass
C15 H11 N3 O3,	(M+H)+,	282.0870,	98.66,	1.35,	281.0797

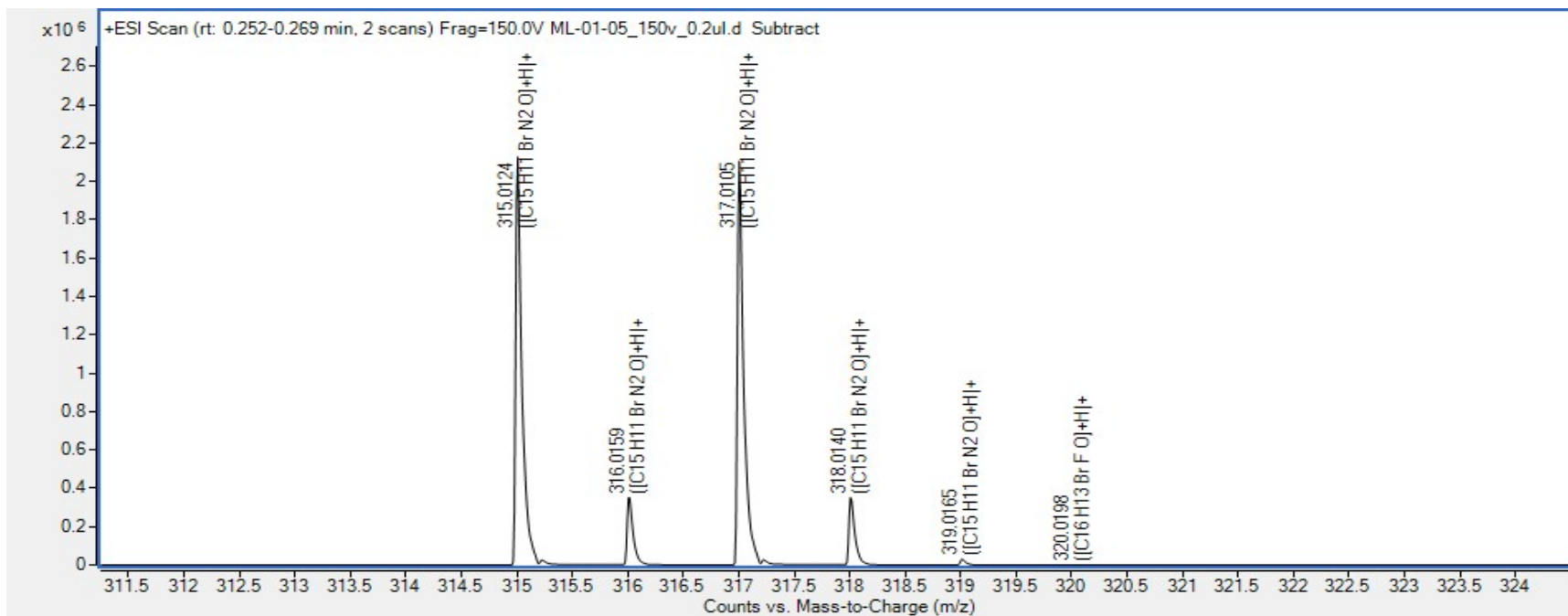
5-(4-bromophenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P7):  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )



5-(4-bromophenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P7):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )

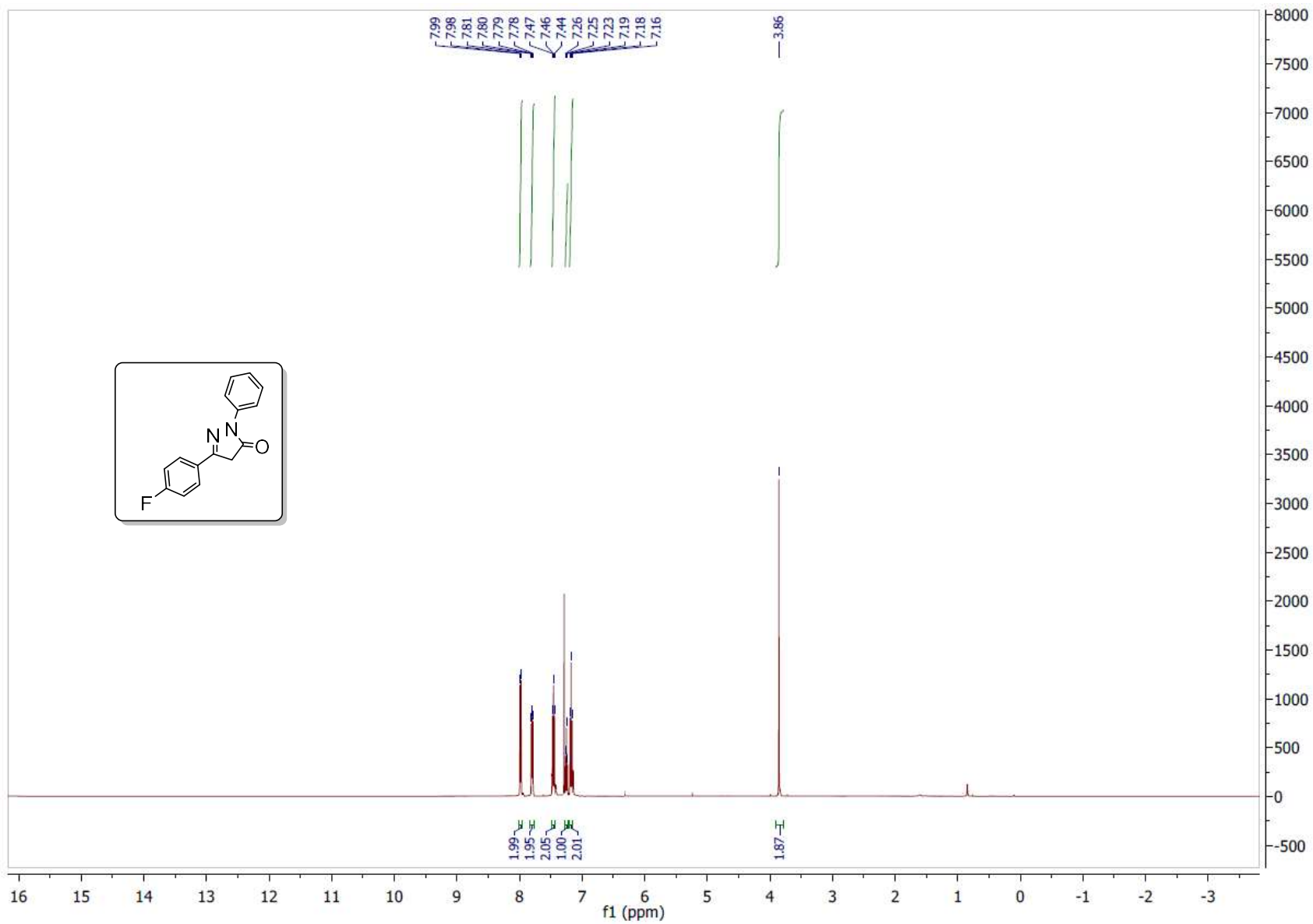


5-(4-bromophenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P7): ESI-MS

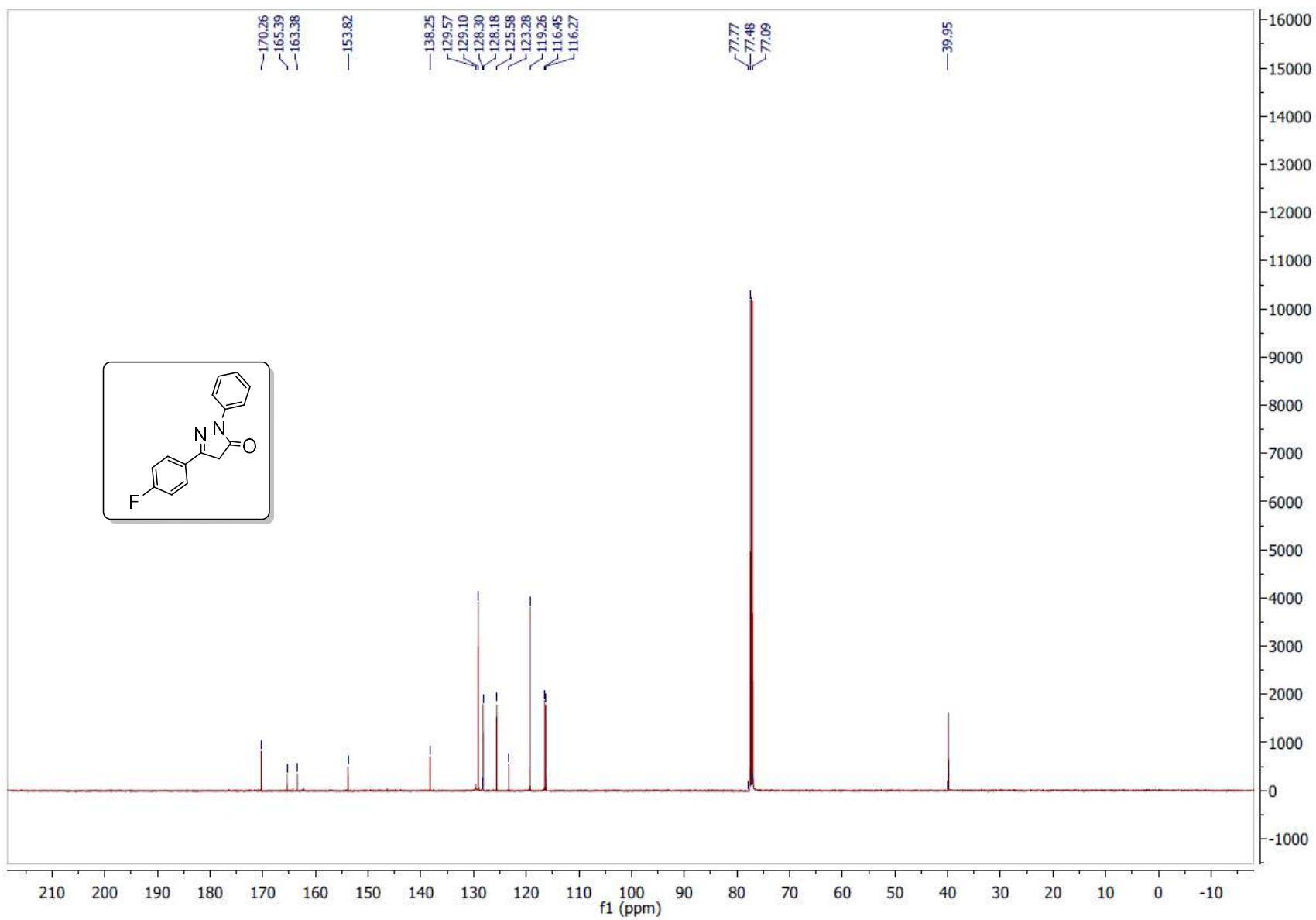


Formula,	Species,	m/z,	Score,	Diff (abs. ppm),	Mass
C <sub>15</sub> H <sub>11</sub> Br N <sub>2</sub> O,	(M+H) <sup>+</sup> ,	315.0124,	99.41,	0.92,	314.0052

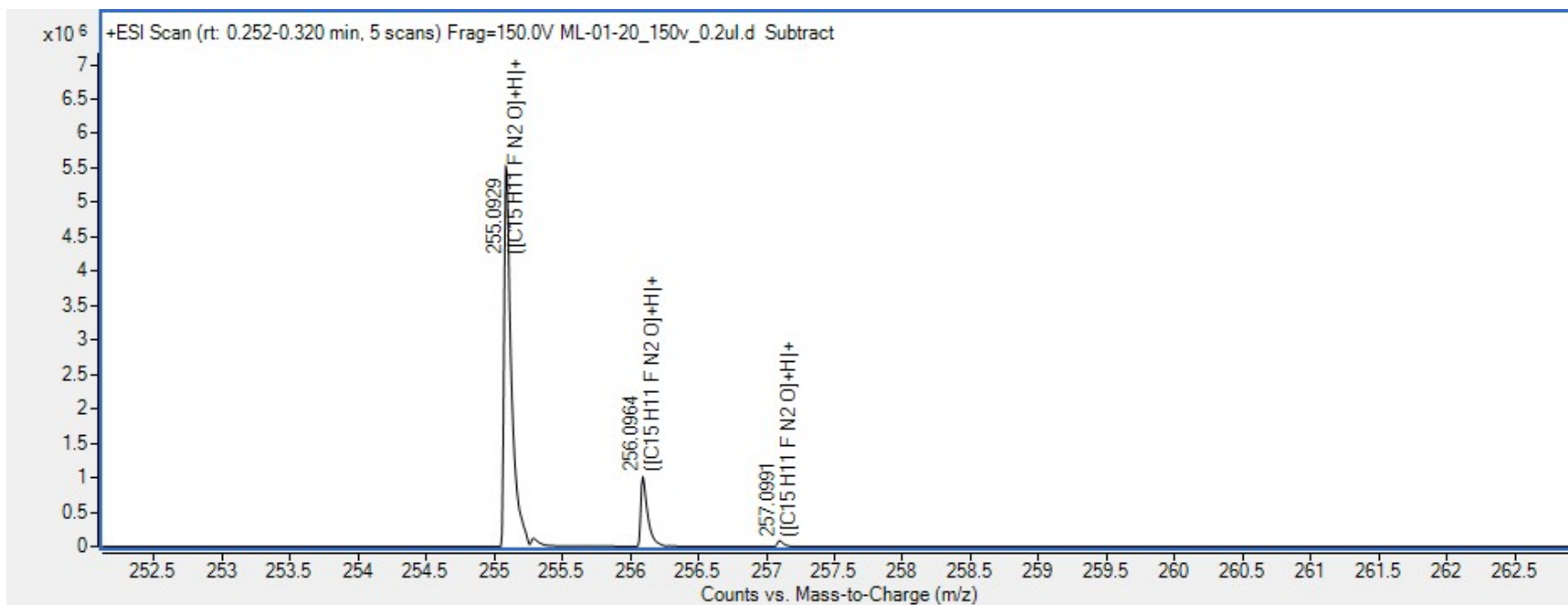
5-(4-fluorophenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P8):  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )



5-(4-fluorophenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P8):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )

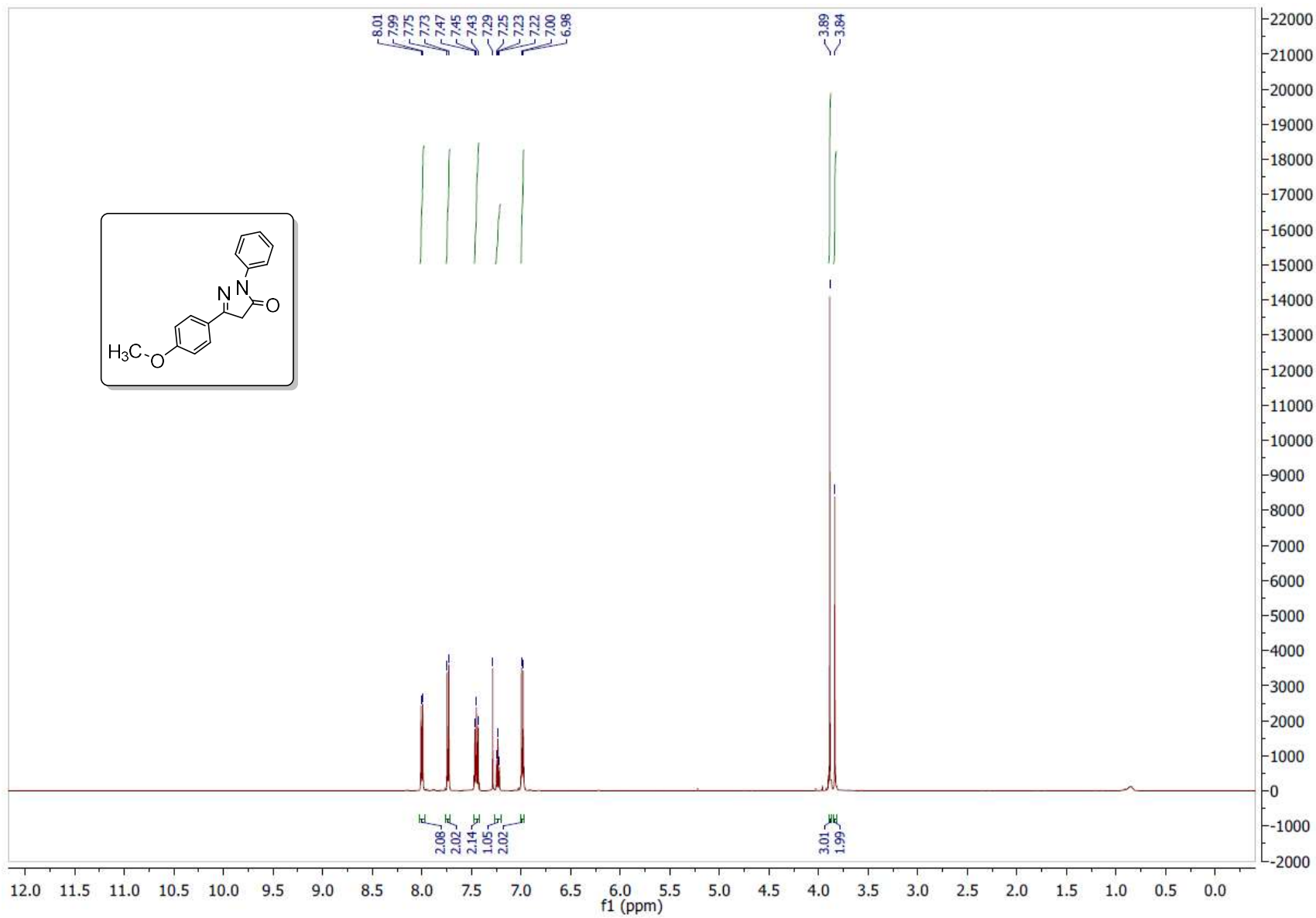


### 5-(4-fluorophenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P8): ESI-MS



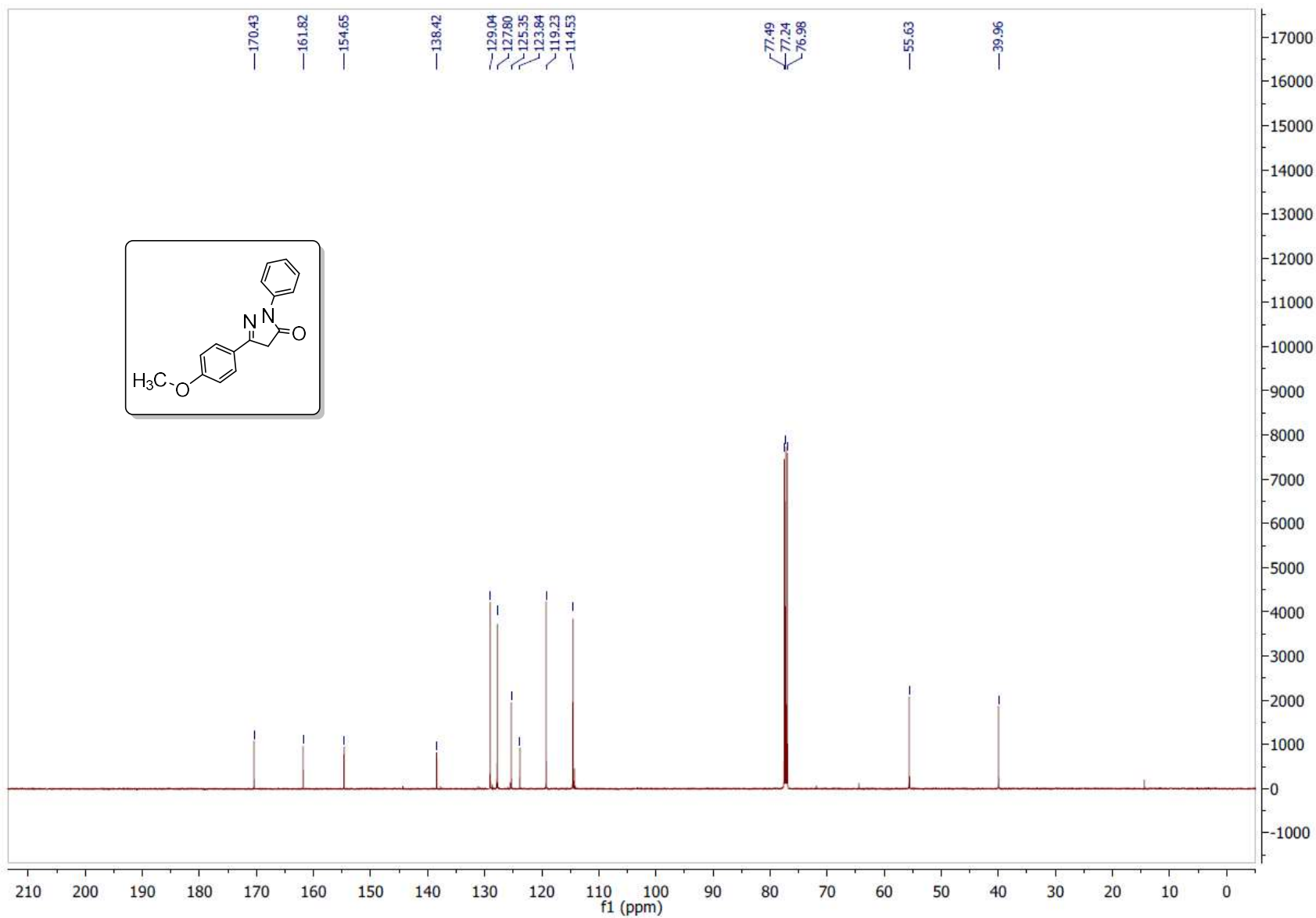
Formula,	Species,	m/z,	Score,	Diff (abs. ppm),	Mass
C15 H11 F N2 O,	(M+H)+,	255.0929,	99.45,	0.75,	254.0857

5-(4-methoxyphenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P9): <sup>1</sup>H-NMR (CDCl<sub>3</sub>)

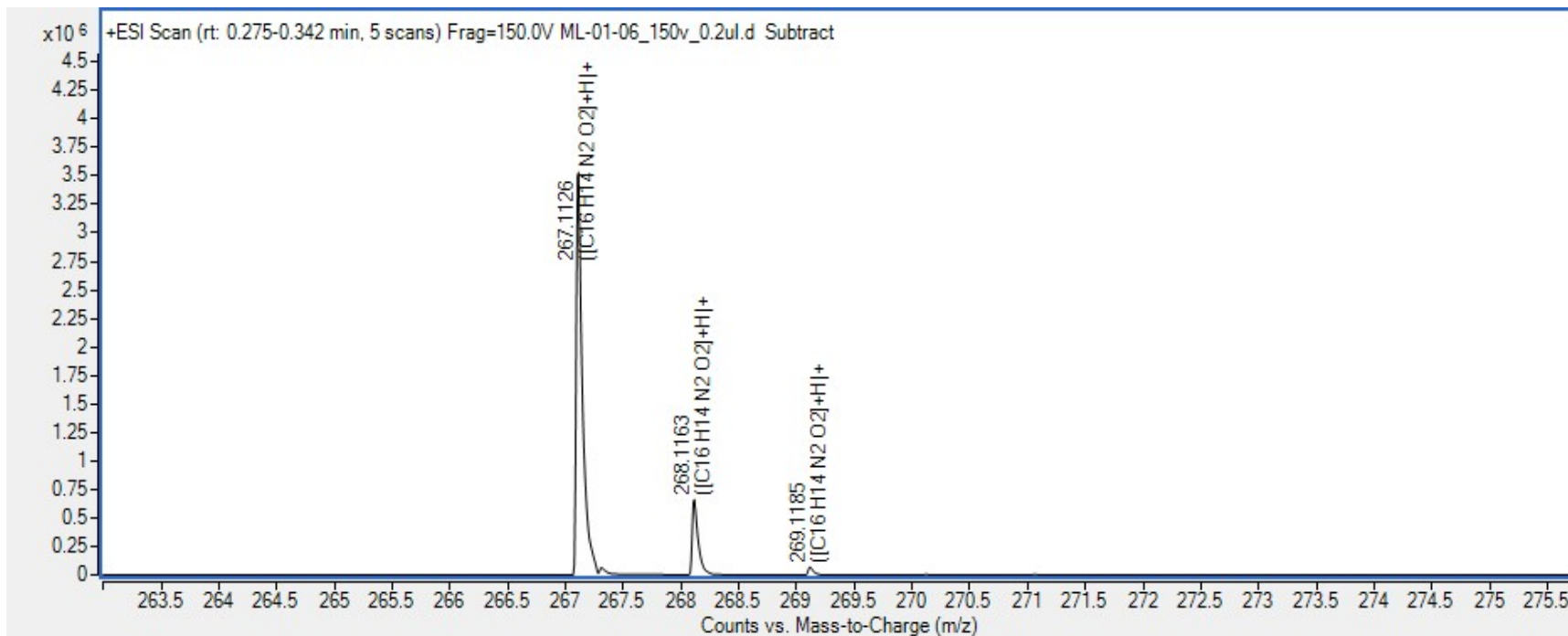




5-(4-methoxyphenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P9):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )

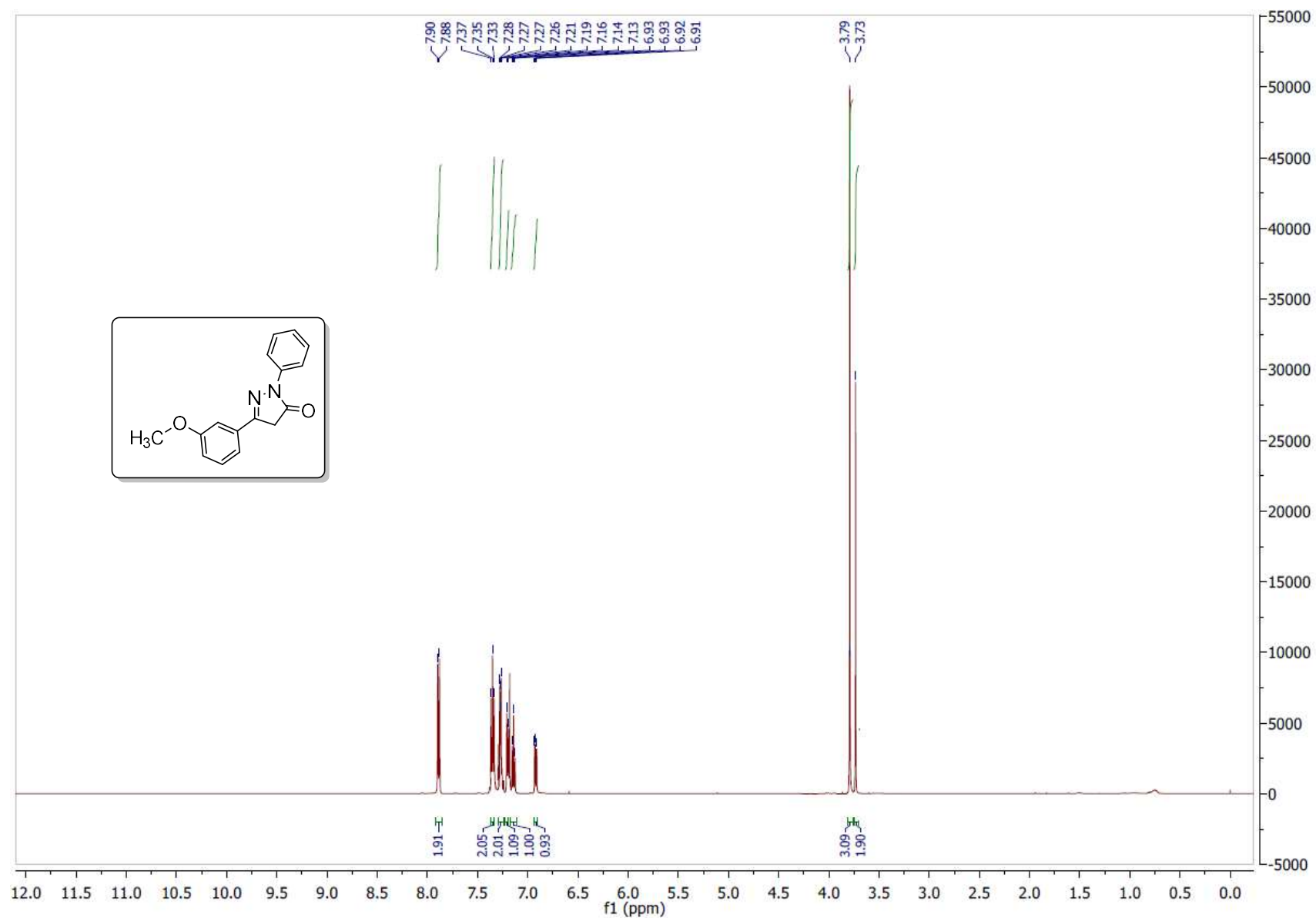


### 5-(4-methoxyphenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P9): ESI-MS

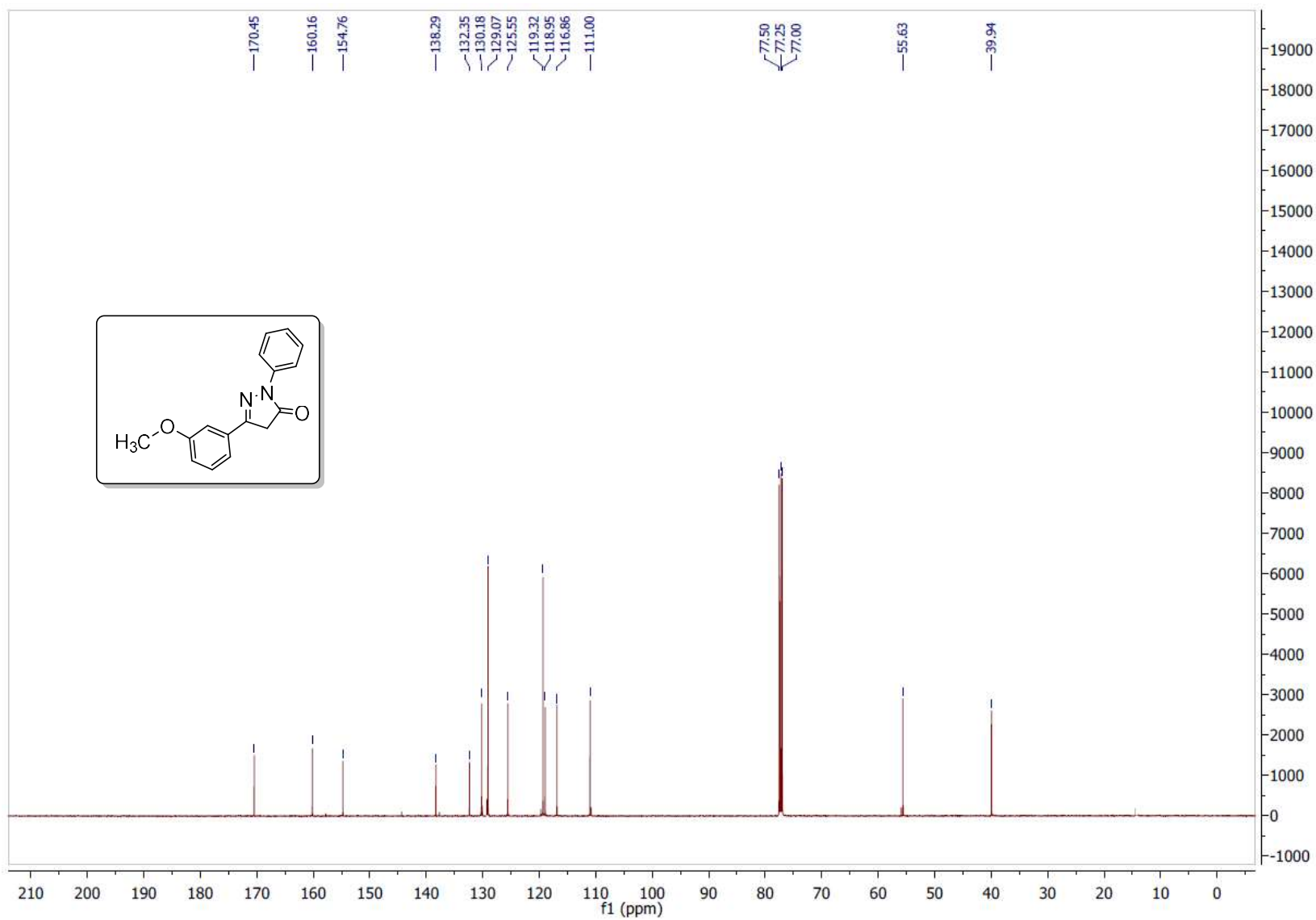


Formula	Species	m/z	Score	Diff (abs. ppm)	Mass
C16 H14 N2 O2	(M+H)+	267.1126	99.44	0.39	266.1054

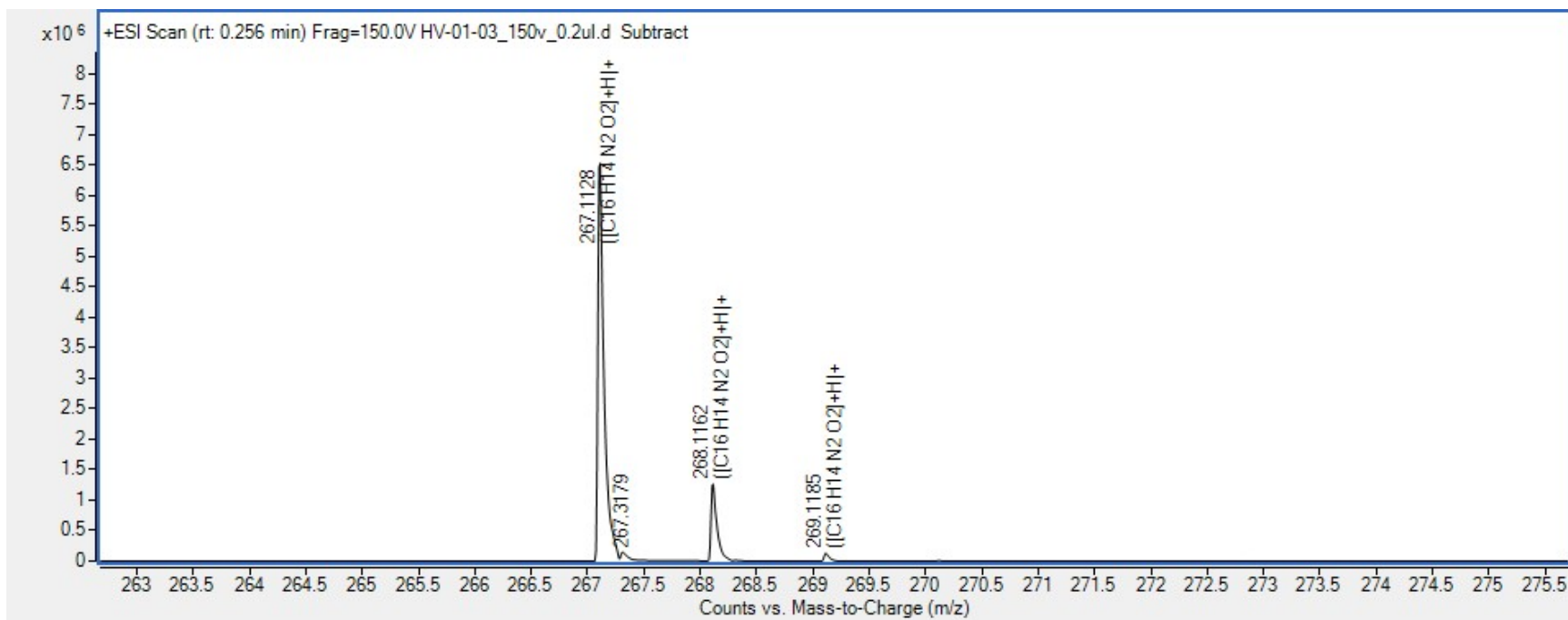
5-(3-methoxyphenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P10): <sup>1</sup>H-NMR (CDCl<sub>3</sub>)



5-(3-methoxyphenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P10):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )

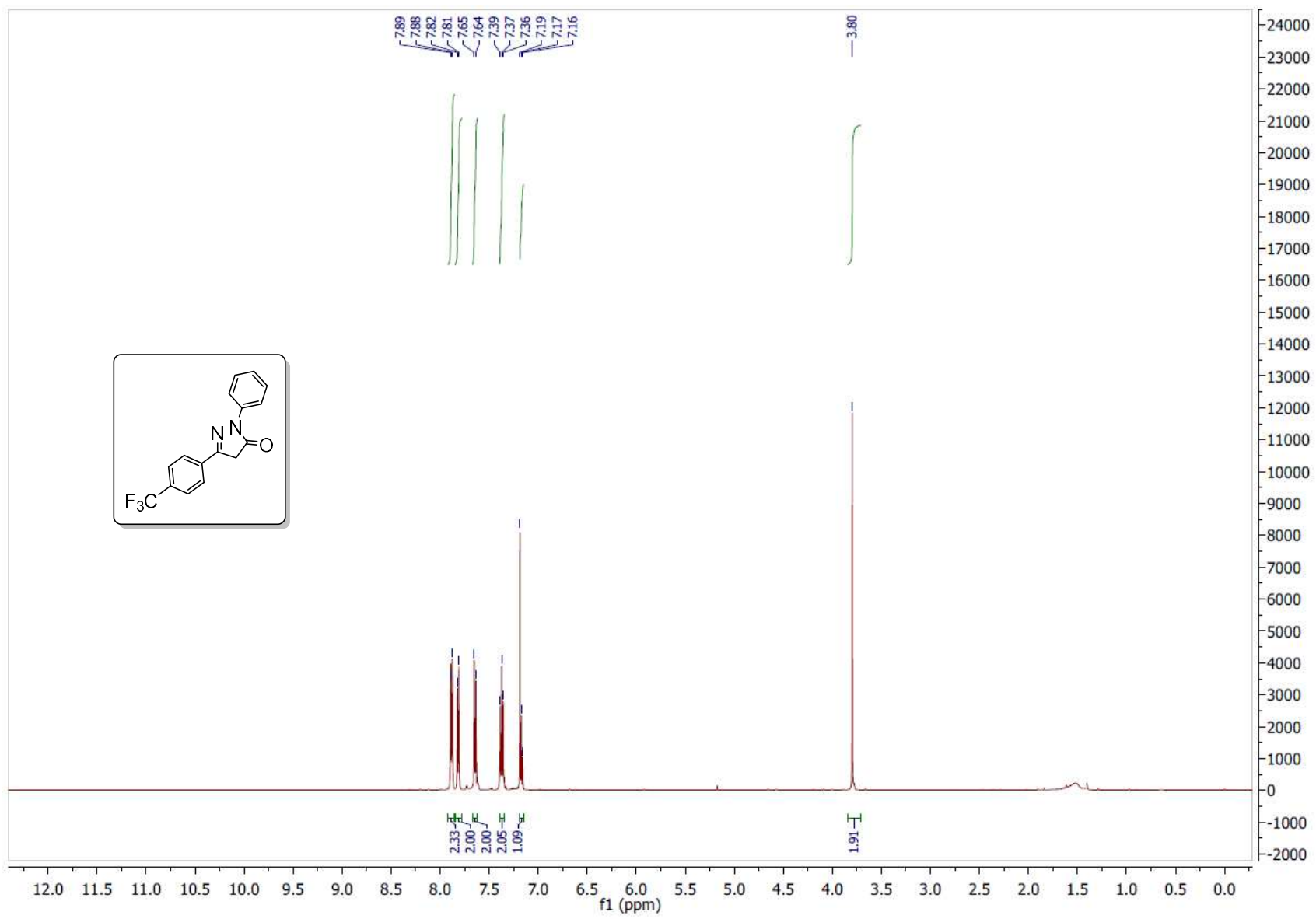


### 5-(3-methoxyphenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (P10): ESI-MS

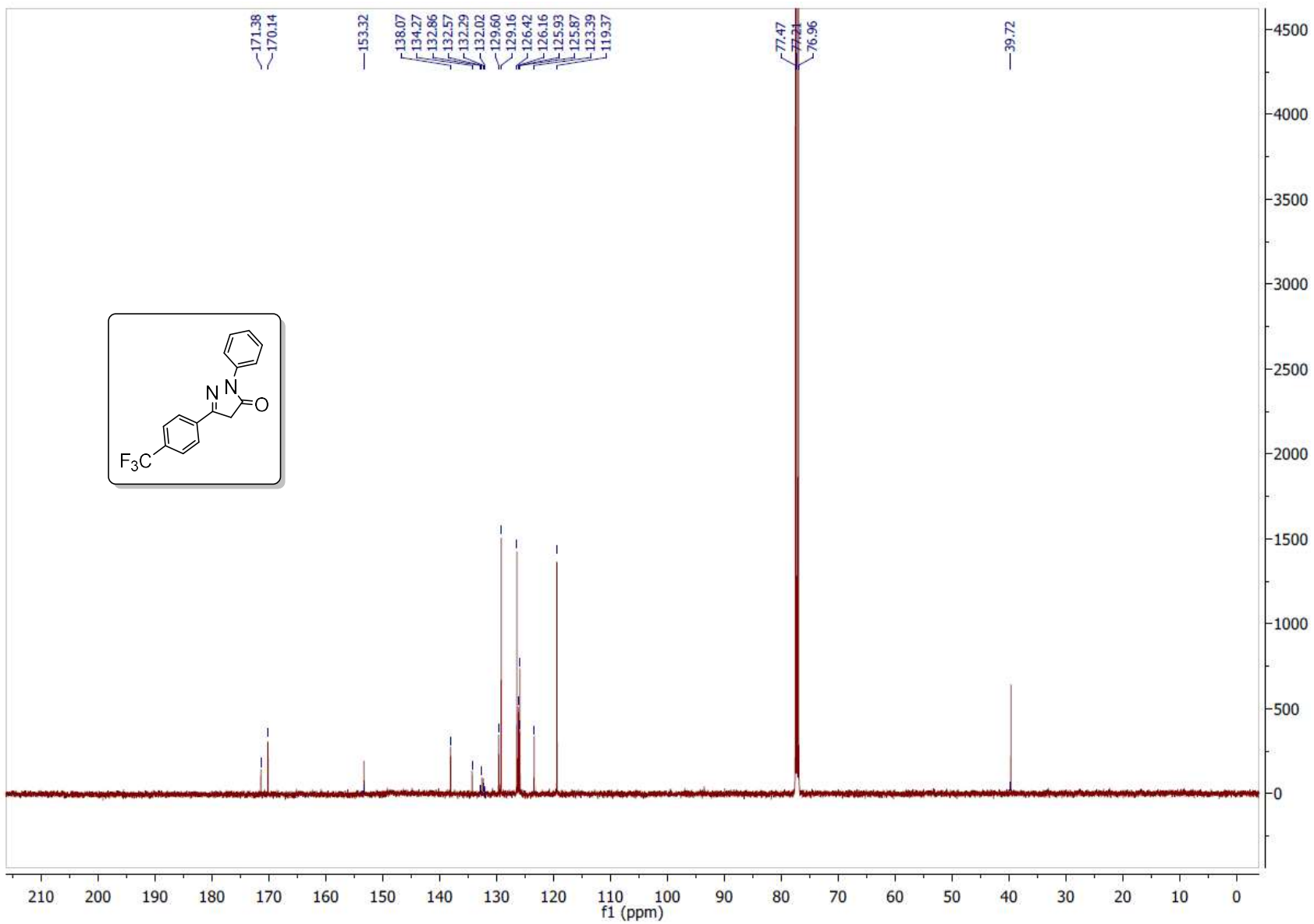


Formula,	Species,	m/z,	Score,	Diff (abs. ppm),	Mass
C16 H14 N2 O2,	(M+H)+,	267.1128,	99.59,	0.16,	266.1056

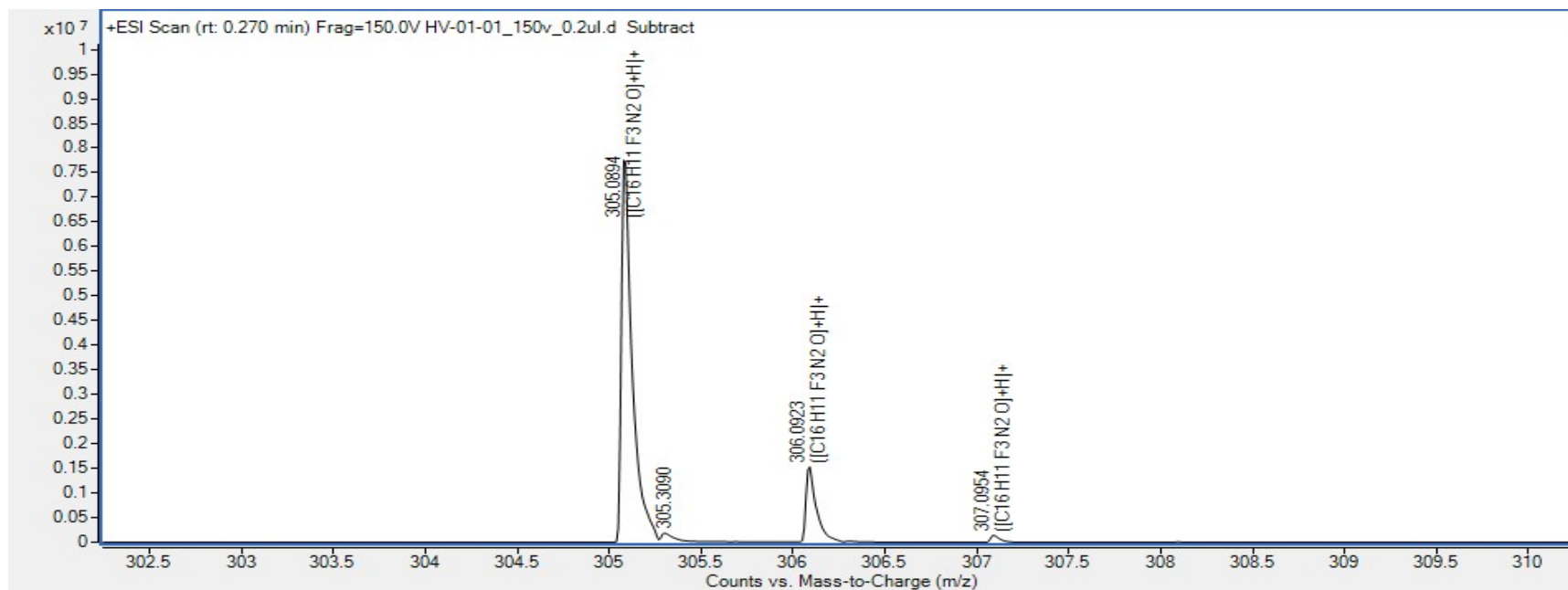
2-phenyl-5-(4-(trifluoromethyl)phenyl)-2,4-dihydro-3H-pyrazol-3-one (P11):  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )



2-phenyl-5-(4-(trifluoromethyl)phenyl)-2,4-dihydro-3H-pyrazol-3-one (P11):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )



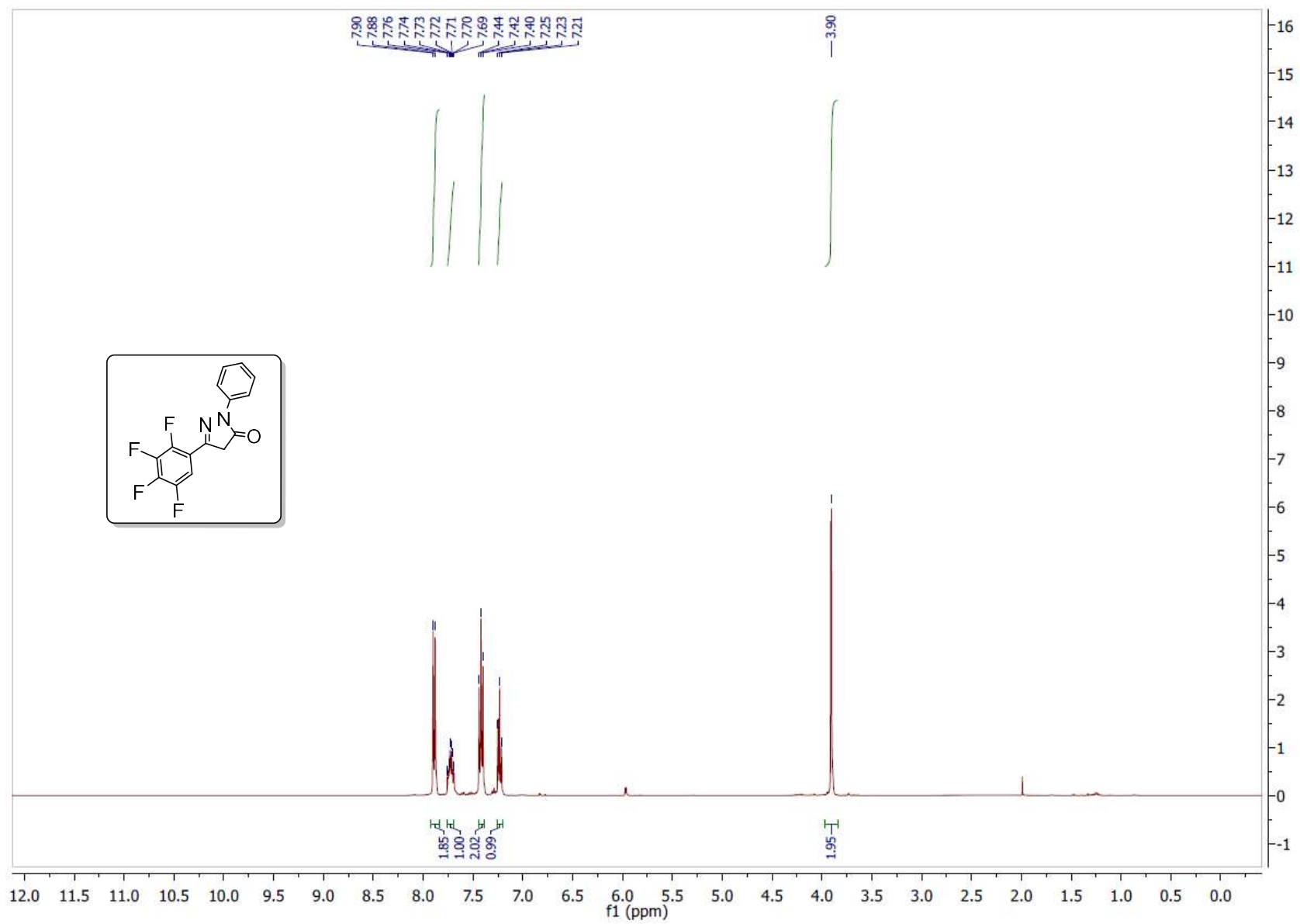
## 2-phenyl-5-(4-(trifluoromethyl)phenyl)-2,4-dihydro-3H-pyrazol-3-one (P11): ESI-MS



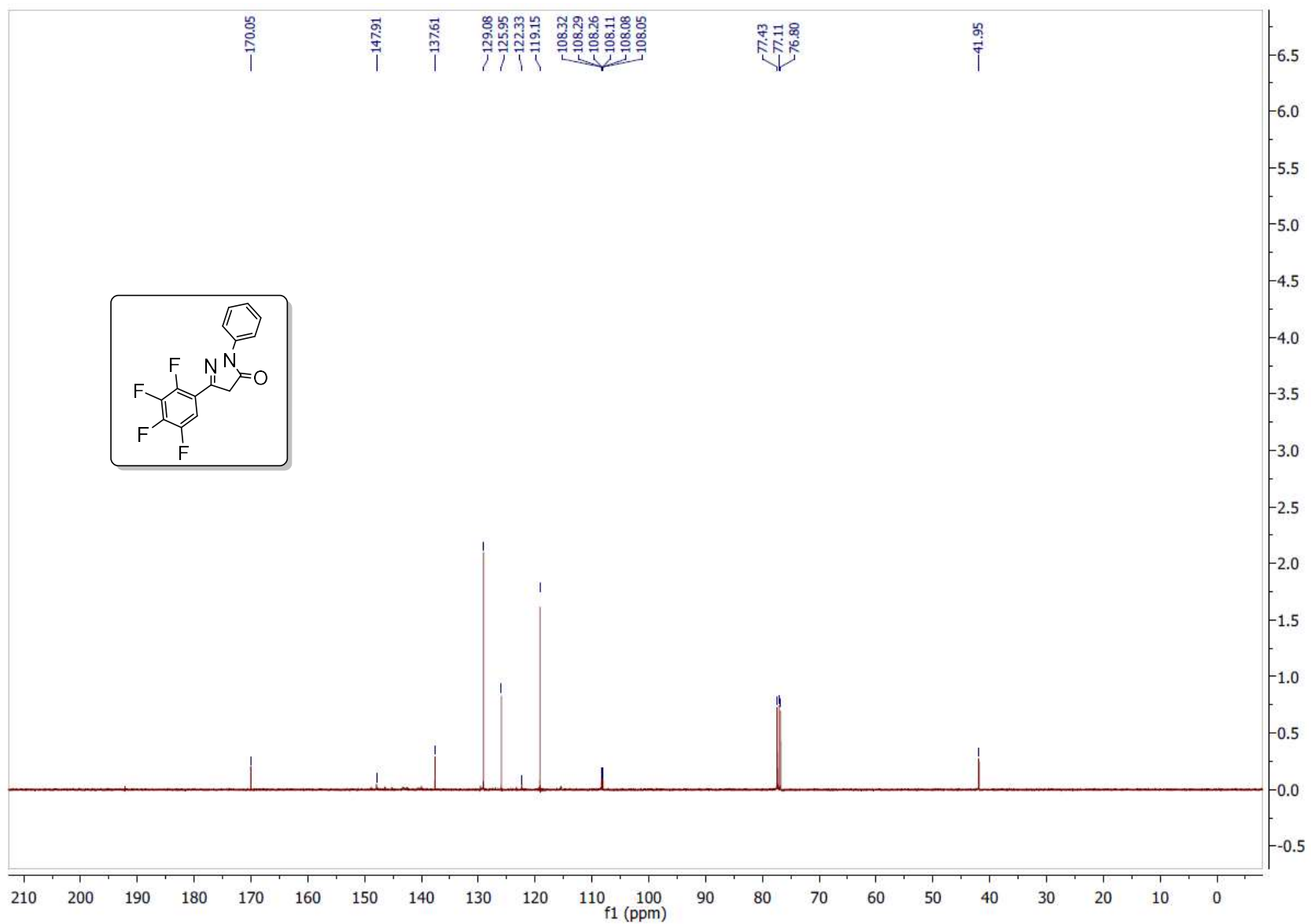
Formula,	Species,	m/z,	Score,	Diff (abs. ppm),	Mass
C16 H11 F3 N2 O,	(M+H)+,	305.0894,	99.34,	0.98,	304.0821



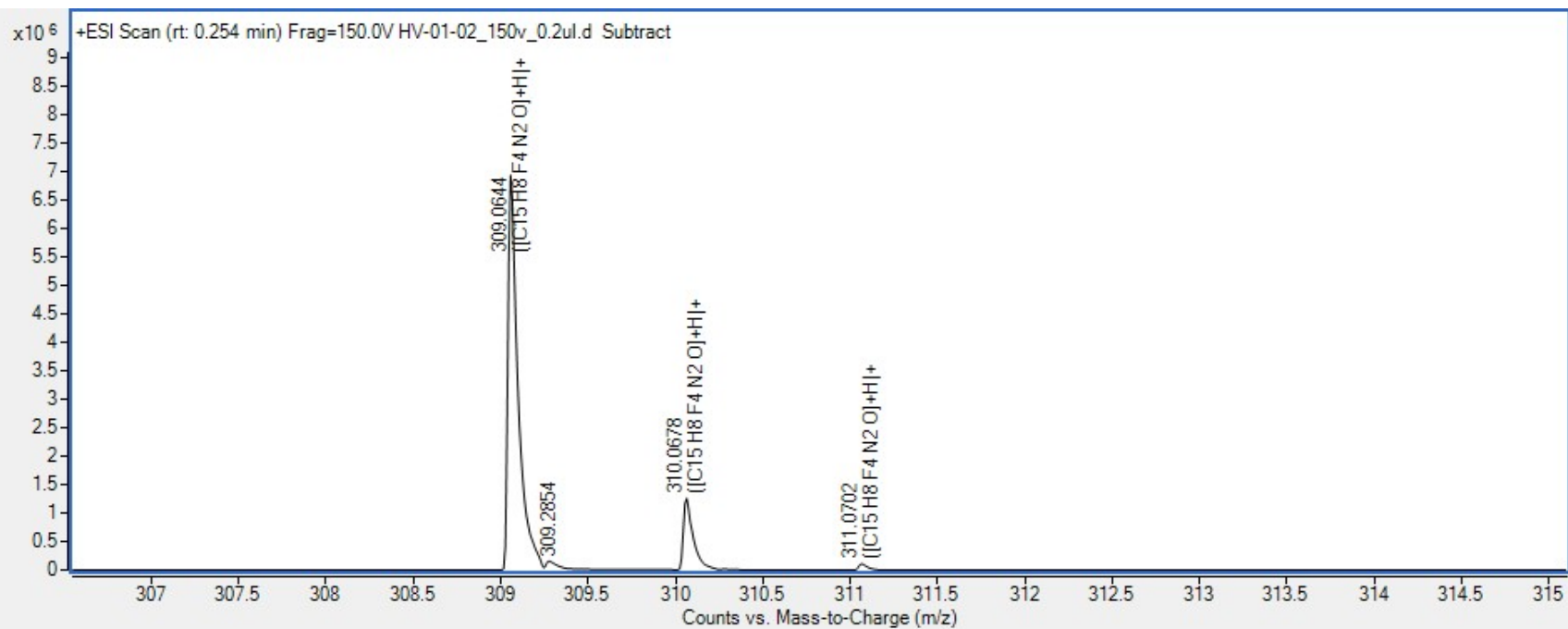
2-phenyl-5-(2,3,4,5-tetrafluorophenyl)-2,4-dihydro-3H-pyrazol-3-one (P12):  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )



2-phenyl-5-(2,3,4,5-tetrafluorophenyl)-2,4-dihydro-3H-pyrazol-3-one (P12):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )

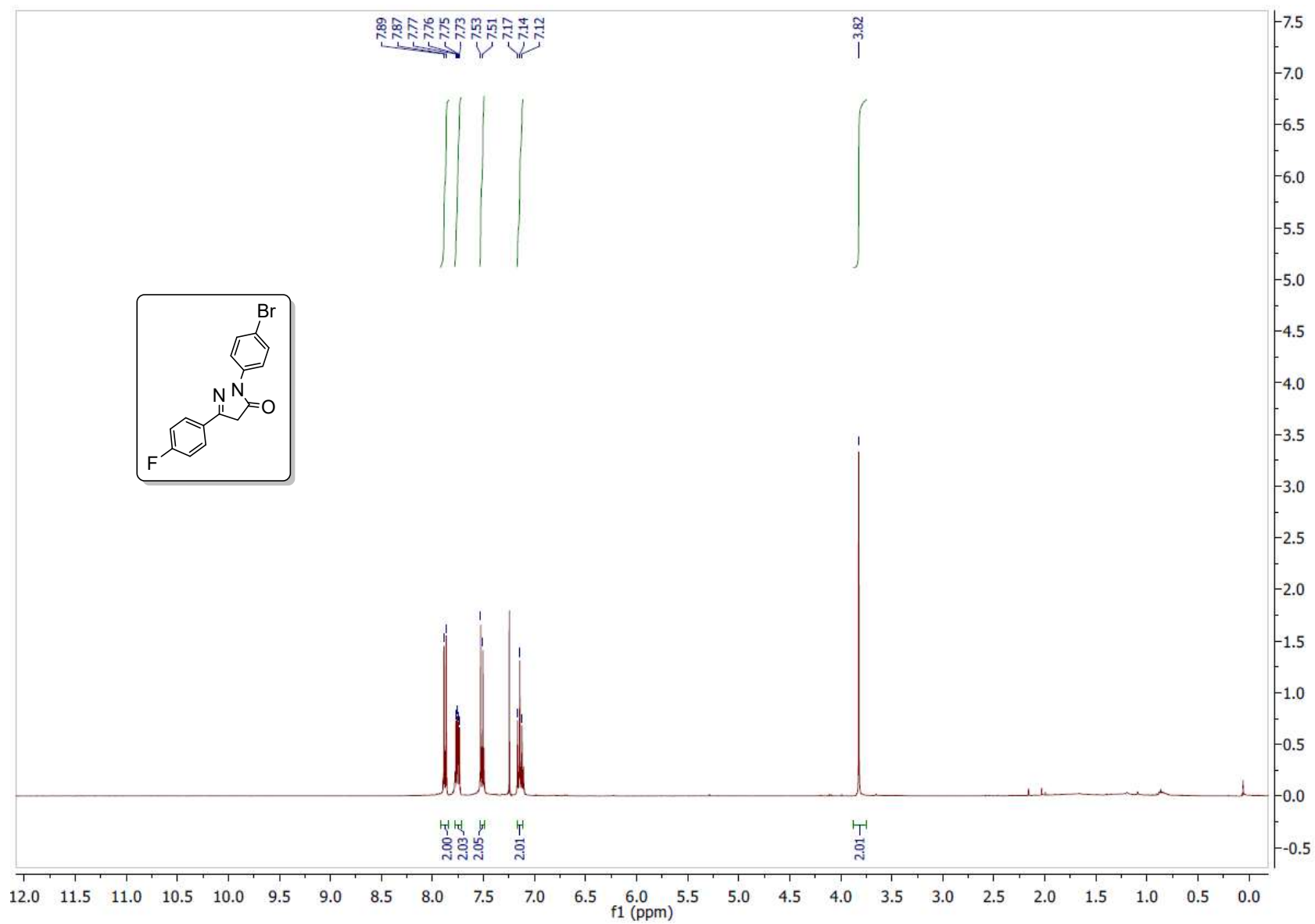


## 2-phenyl-5-(2,3,4,5-tetrafluorophenyl)-2,4-dihydro-3H-pyrazol-3-one (P12): ESI-MS

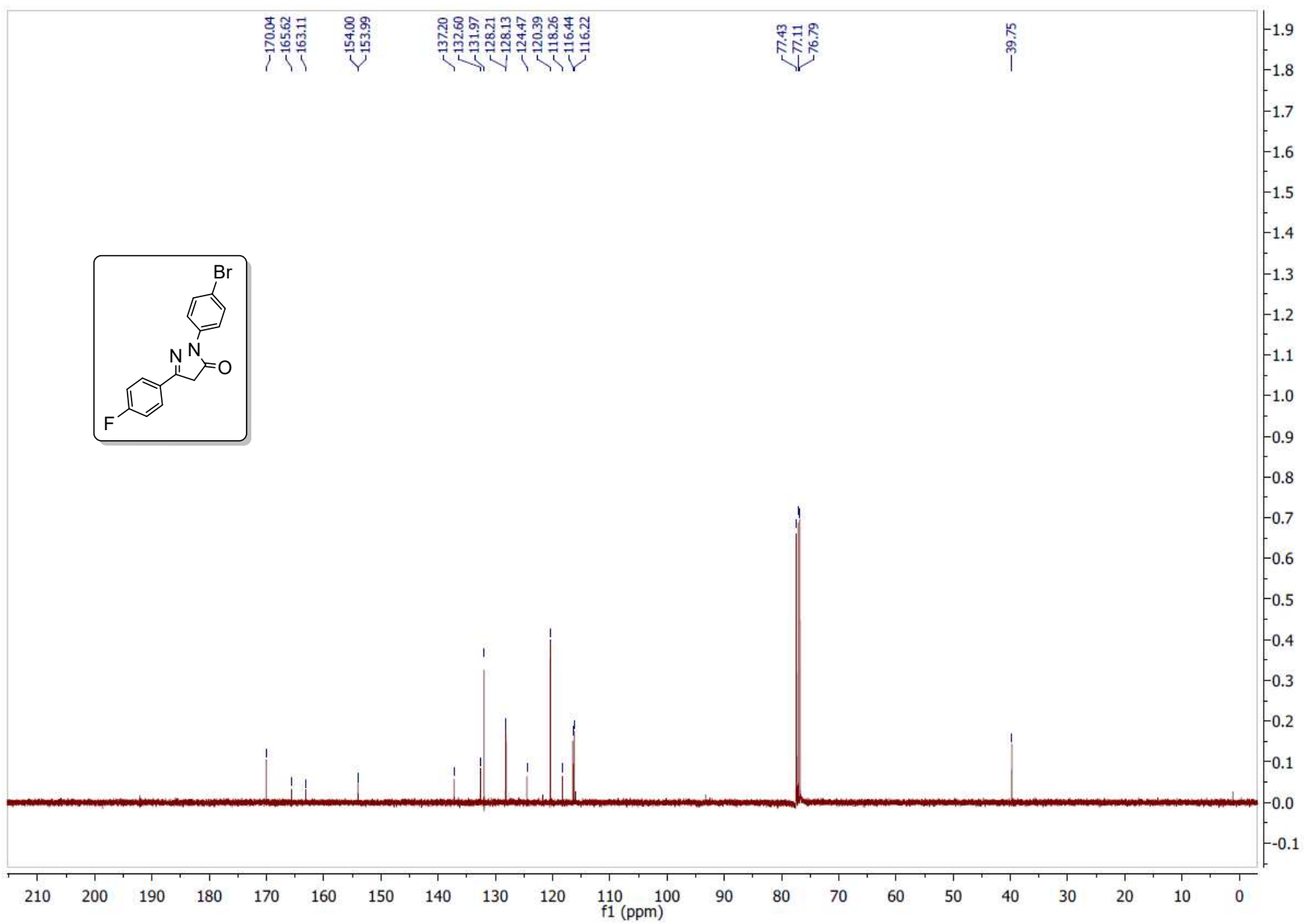


Formula,	Species,	m/z,	Score,	Diff (abs. ppm),	Mass
C15 H8 F4 N2 O,	(M+H) <sup>+</sup> ,	309.0644,	99.61,	0.28,	308.0572

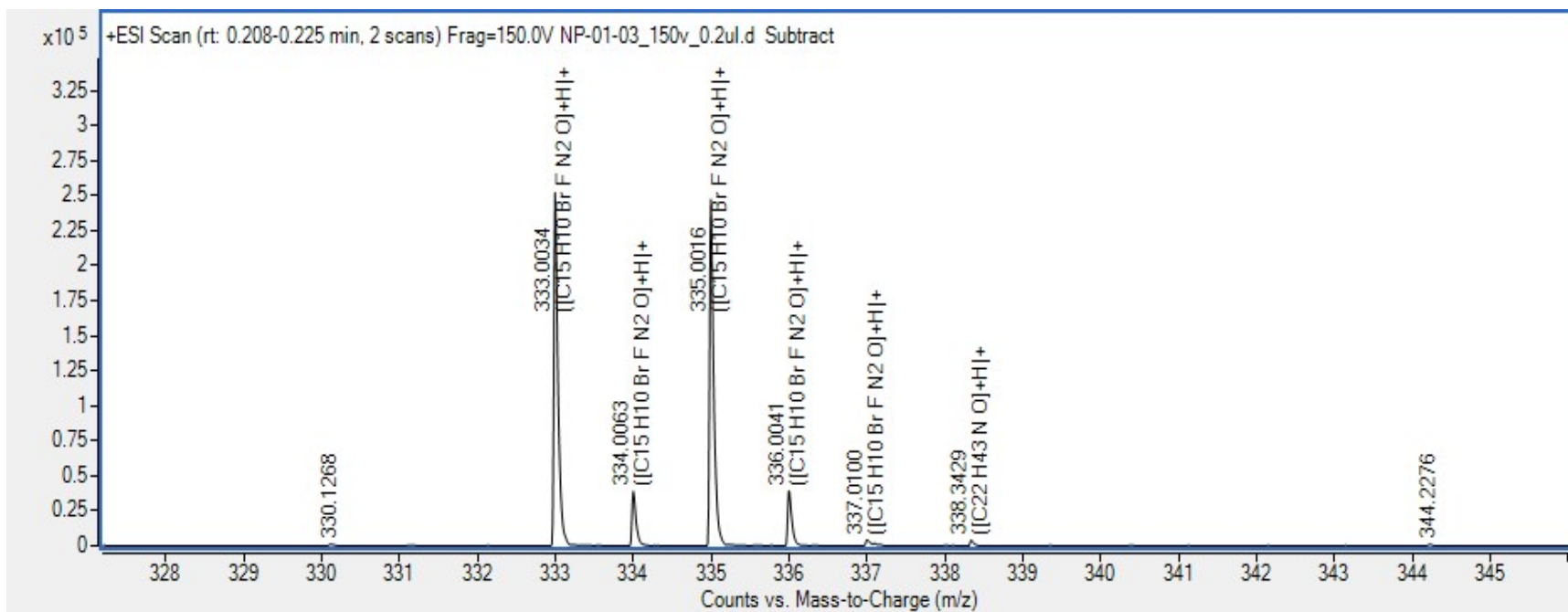
2-(4-bromophenyl)-5-(4-fluorophenyl)-2,4-dihydro-3H-pyrazol-3-one (P13): <sup>1</sup>H-NMR (CDCl<sub>3</sub>)



2-(4-bromophenyl)-5-(4-fluorophenyl)-2,4-dihydro-3H-pyrazol-3-one (P13):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )

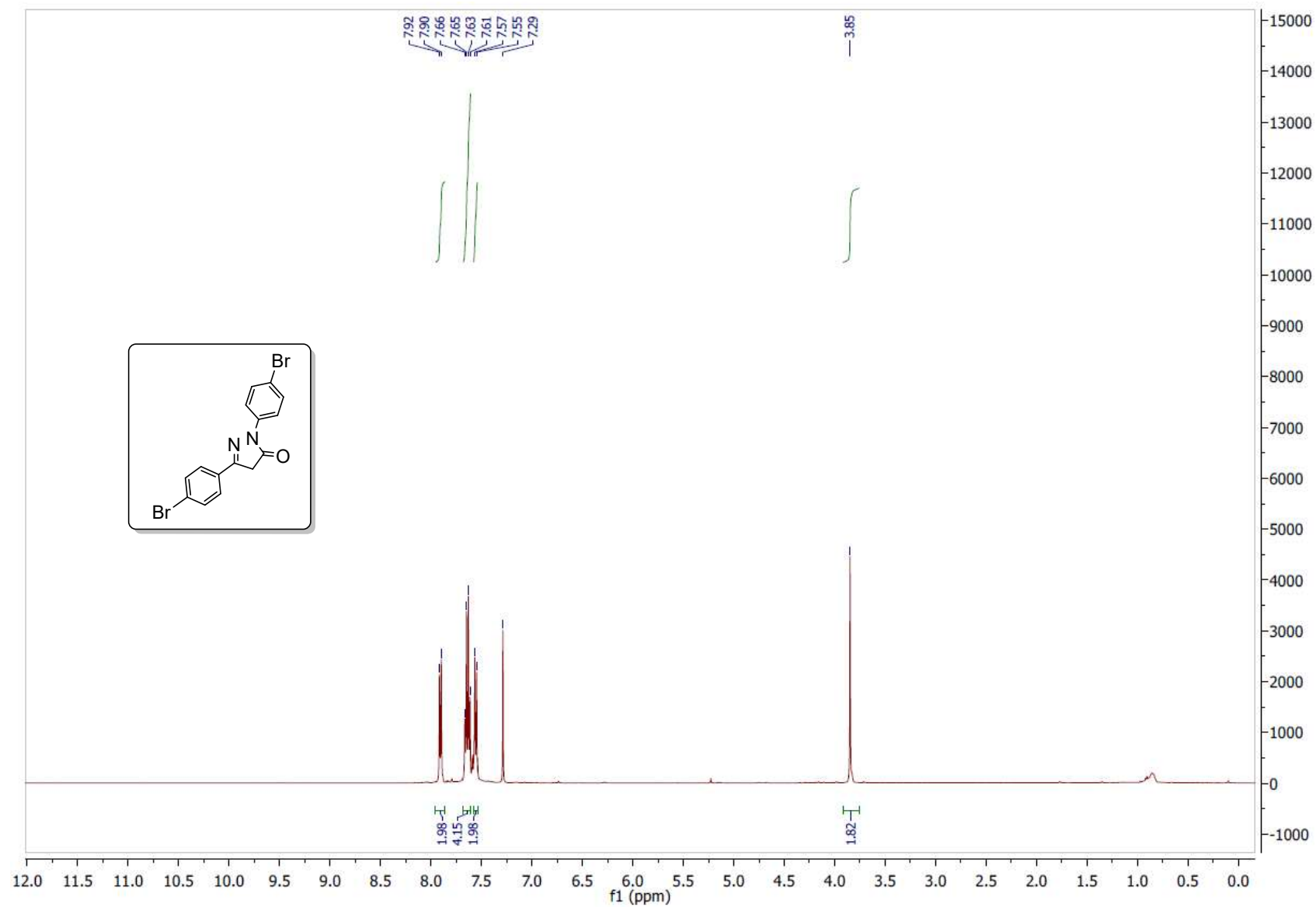


**2-(4-bromophenyl)-5-(4-fluorophenyl)-2,4-dihydro-3H-pyrazol-3-one (P13): ESI-MS**

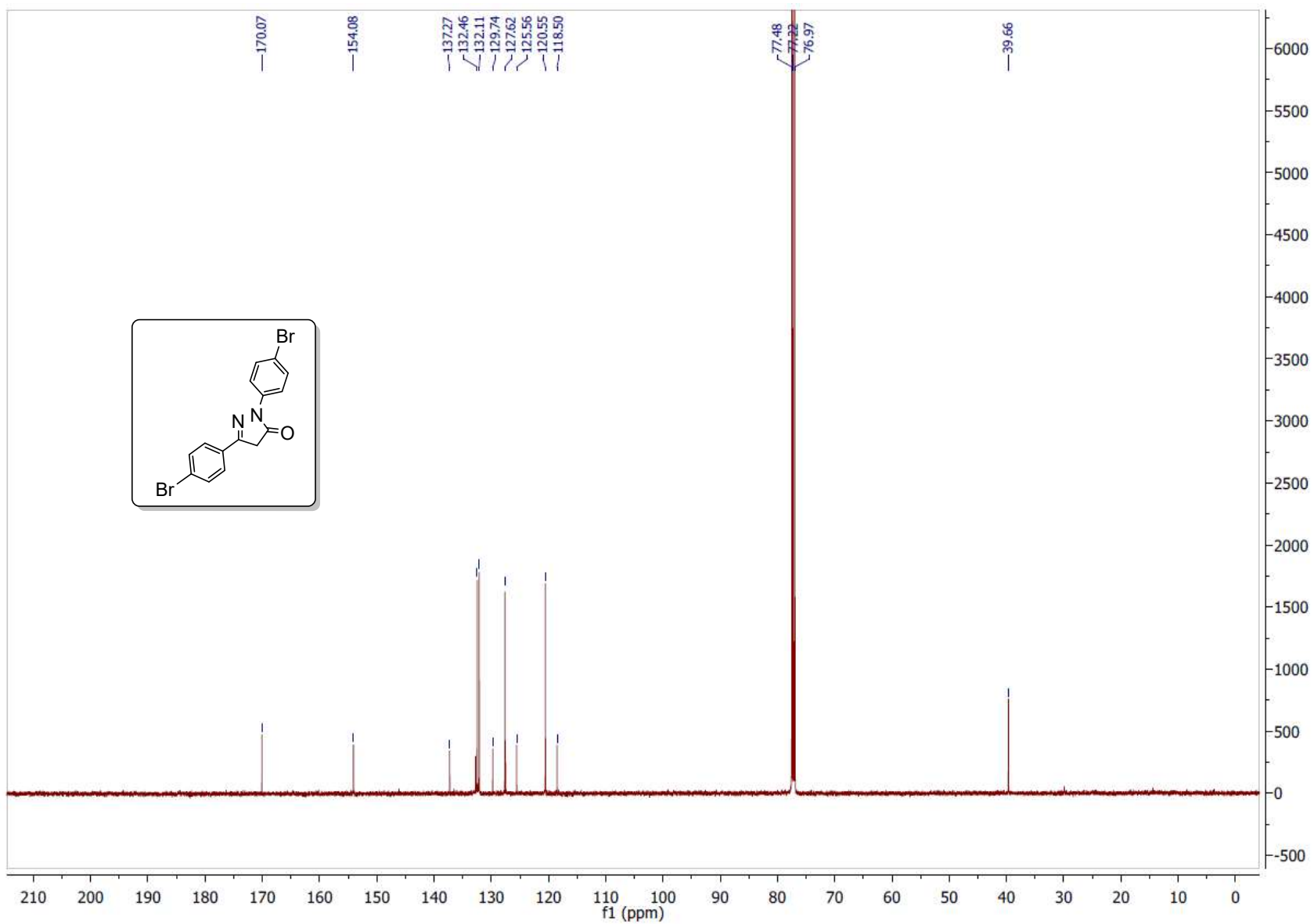


Formula,	Species,	m/z,	Score,	Diff (abs. ppm),	Mass
C15 H10 Br F N2 O,	(M+H)+,	333.0034,	99.67,	0.28,	331.9961

2,5-bis(4-bromophenyl)-2,4-dihydro-3H-pyrazol-3-one (P14):  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )

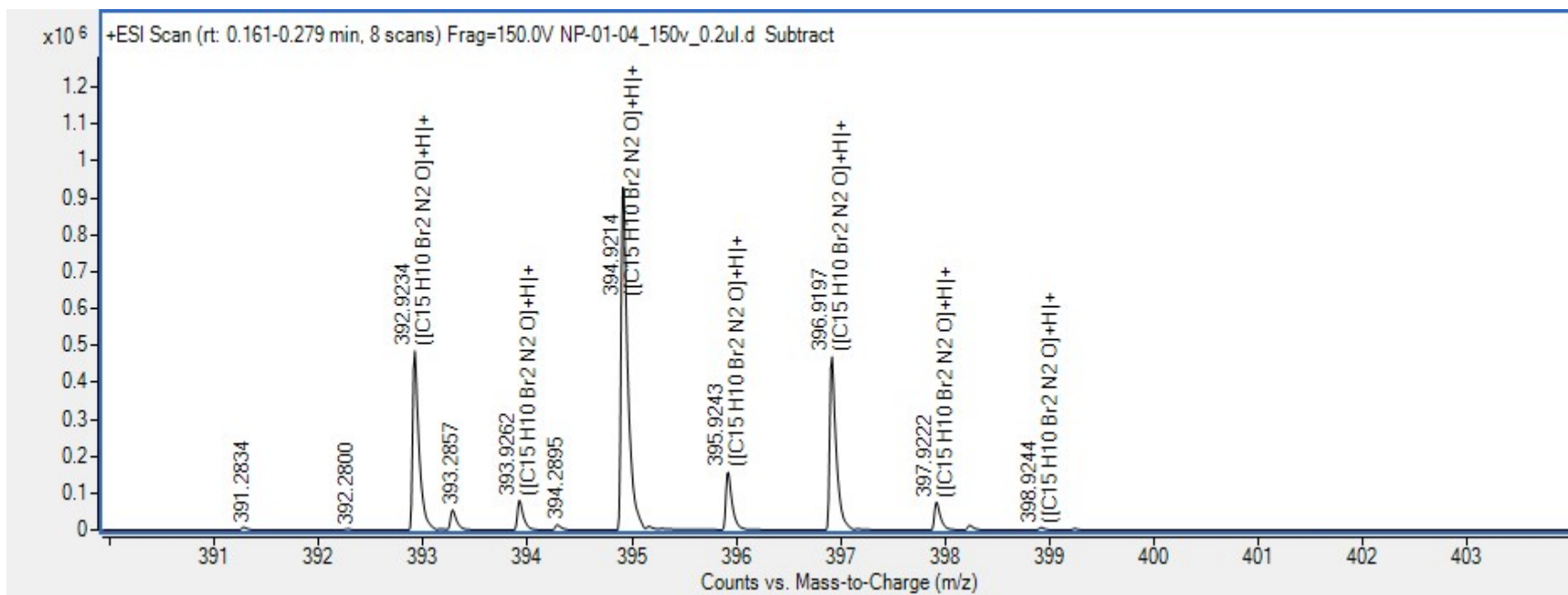


2,5-bis(4-bromophenyl)-2,4-dihydro-3H-pyrazol-3-one (P14):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )



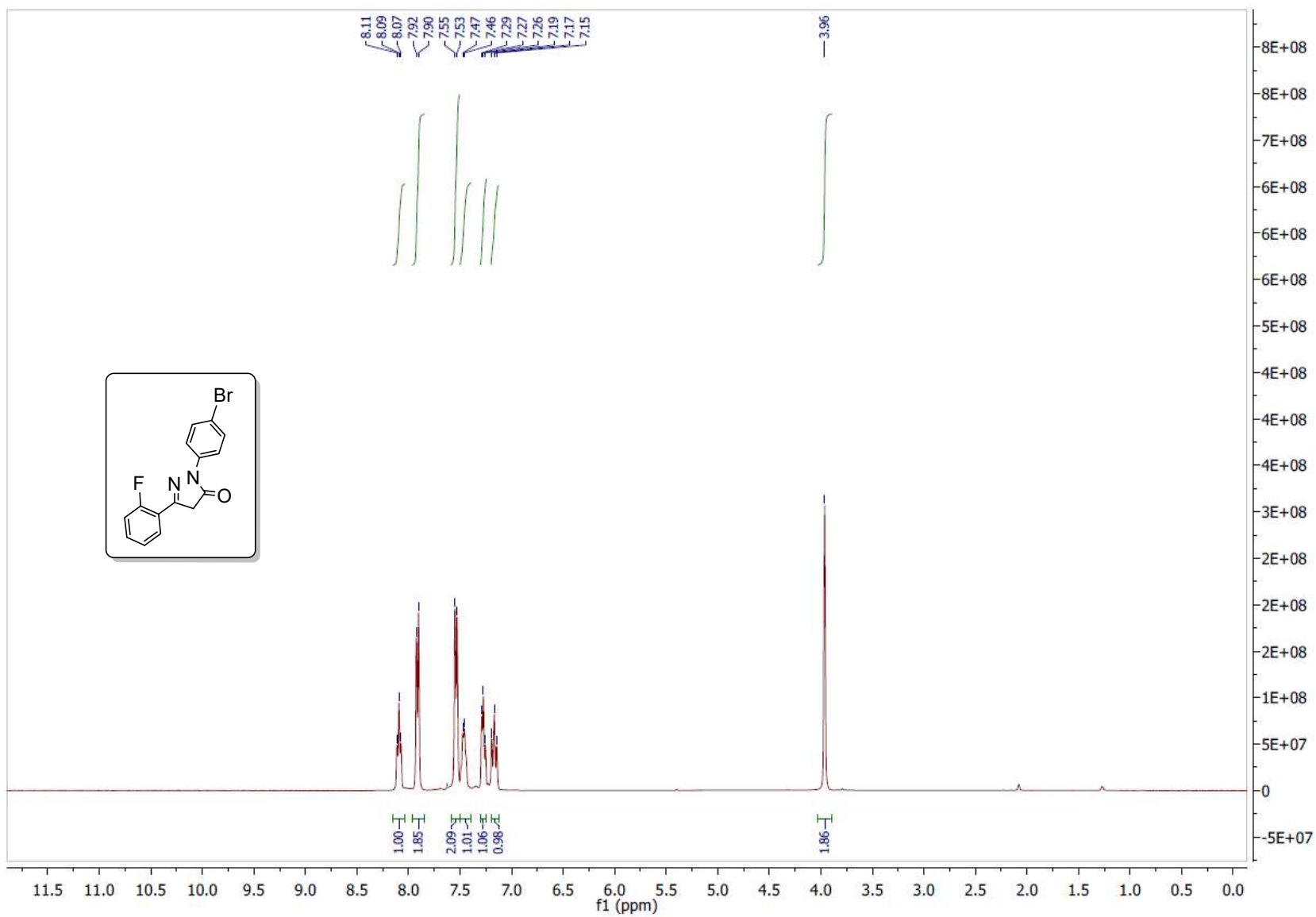


**2,5-bis(4-bromophenyl)-2,4-dihydro-3H-pyrazol-3-one (P14): ESI-MS**

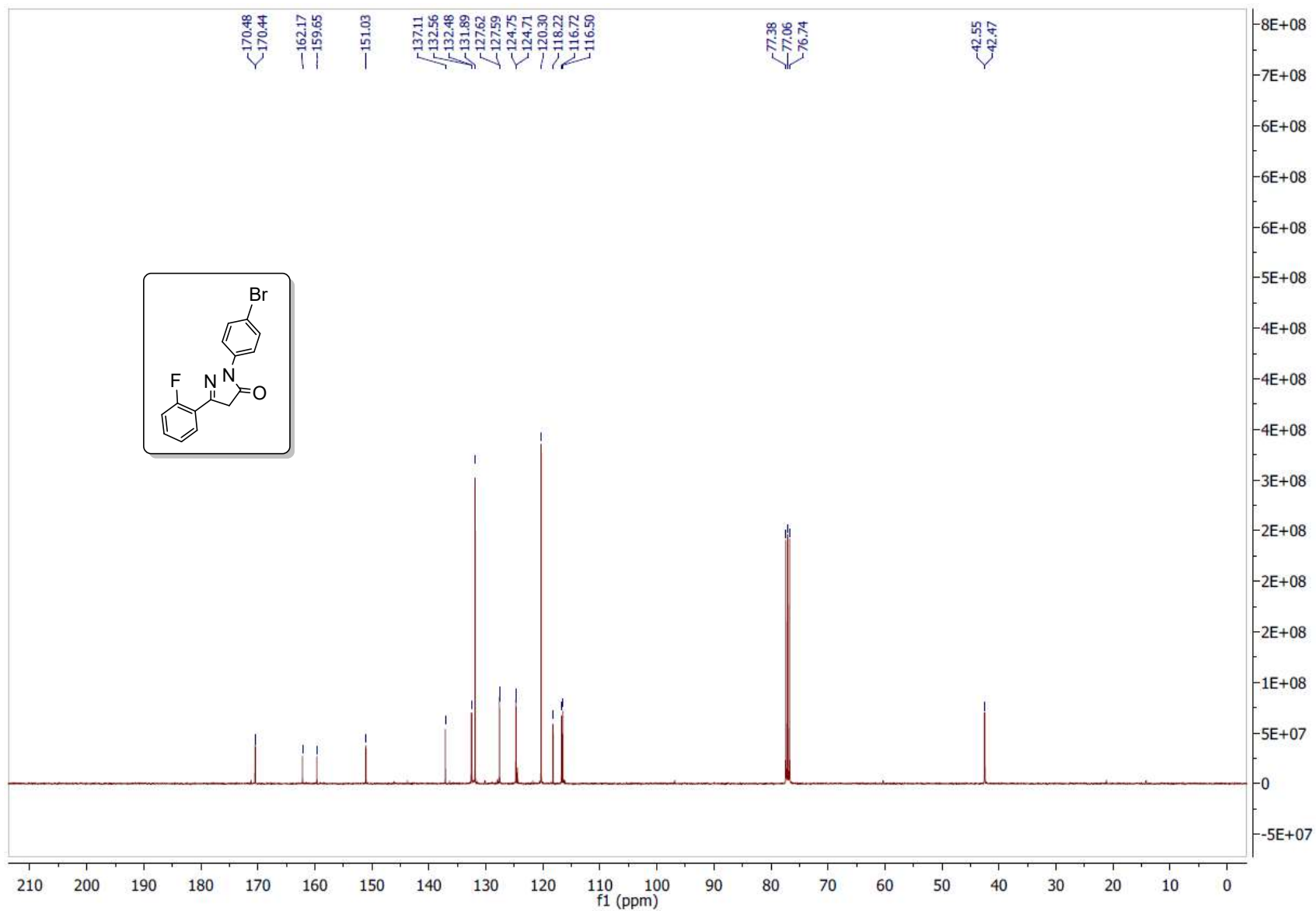


Formula,	Species,	m/z,	Score,	Diff (abs. ppm),	Mass
C <sub>15</sub> H <sub>10</sub> Br <sub>2</sub> N <sub>2</sub> O,	(M+H) <sup>+</sup> ,	392.9234,	99.77,	0.28,	391.9161

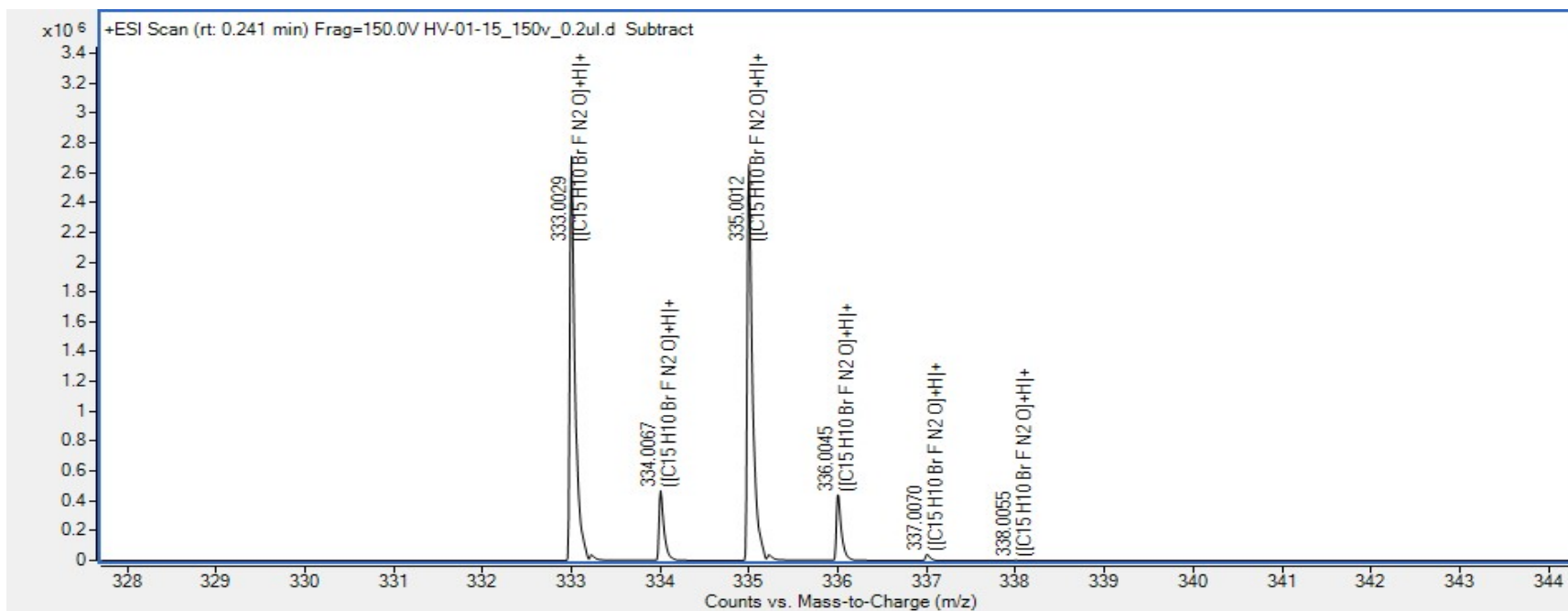
2-(4-bromophenyl)-5-(2-fluorophenyl)-2,4-dihydro-3H-pyrazol-3-one (P15):  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )



2-(4-bromophenyl)-5-(2-fluorophenyl)-2,4-dihydro-3H-pyrazol-3-one (P15):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )

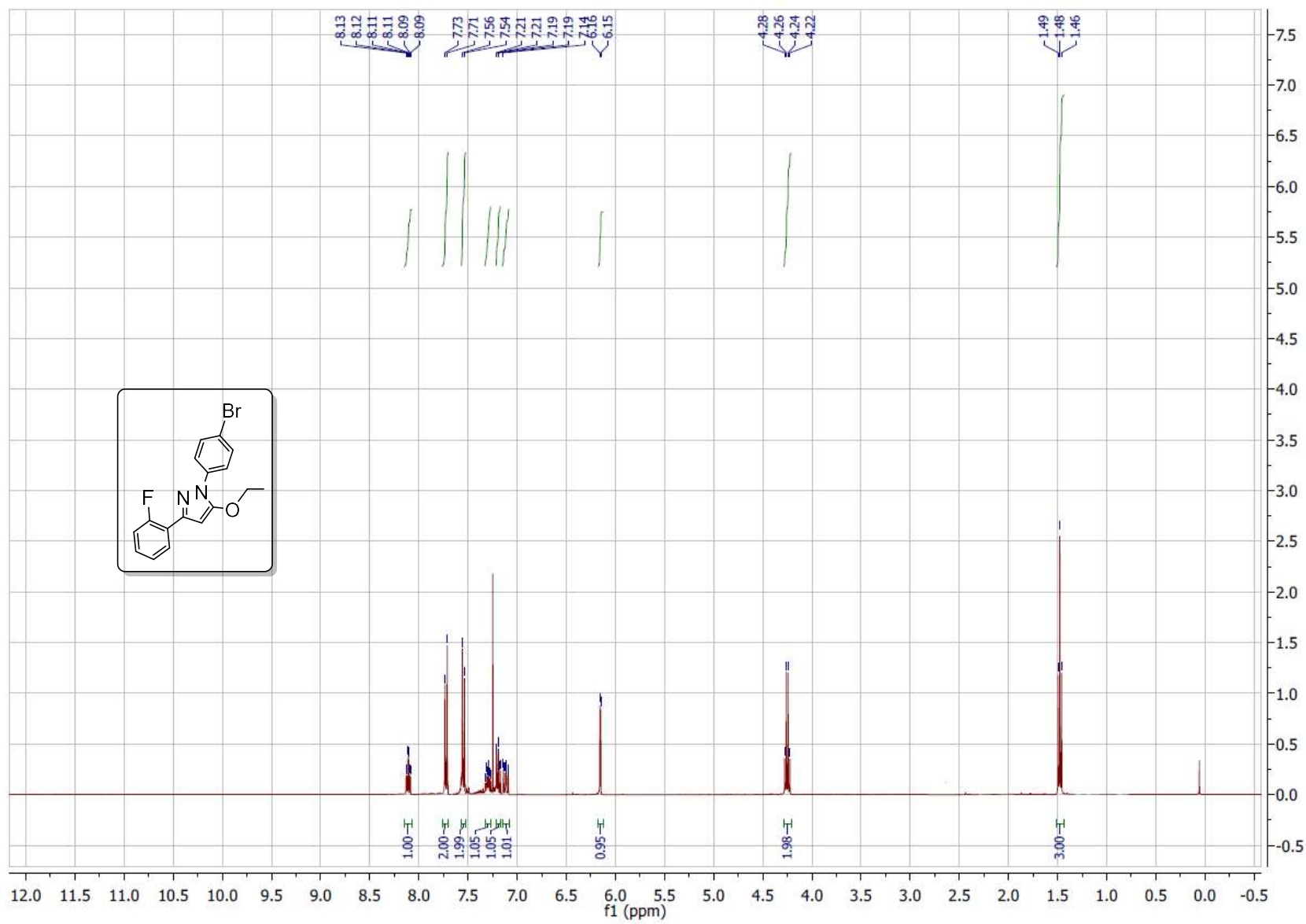


**2-(4-bromophenyl)-5-(2-fluorophenyl)-2,4-dihydro-3H-pyrazol-3-one (P15):**

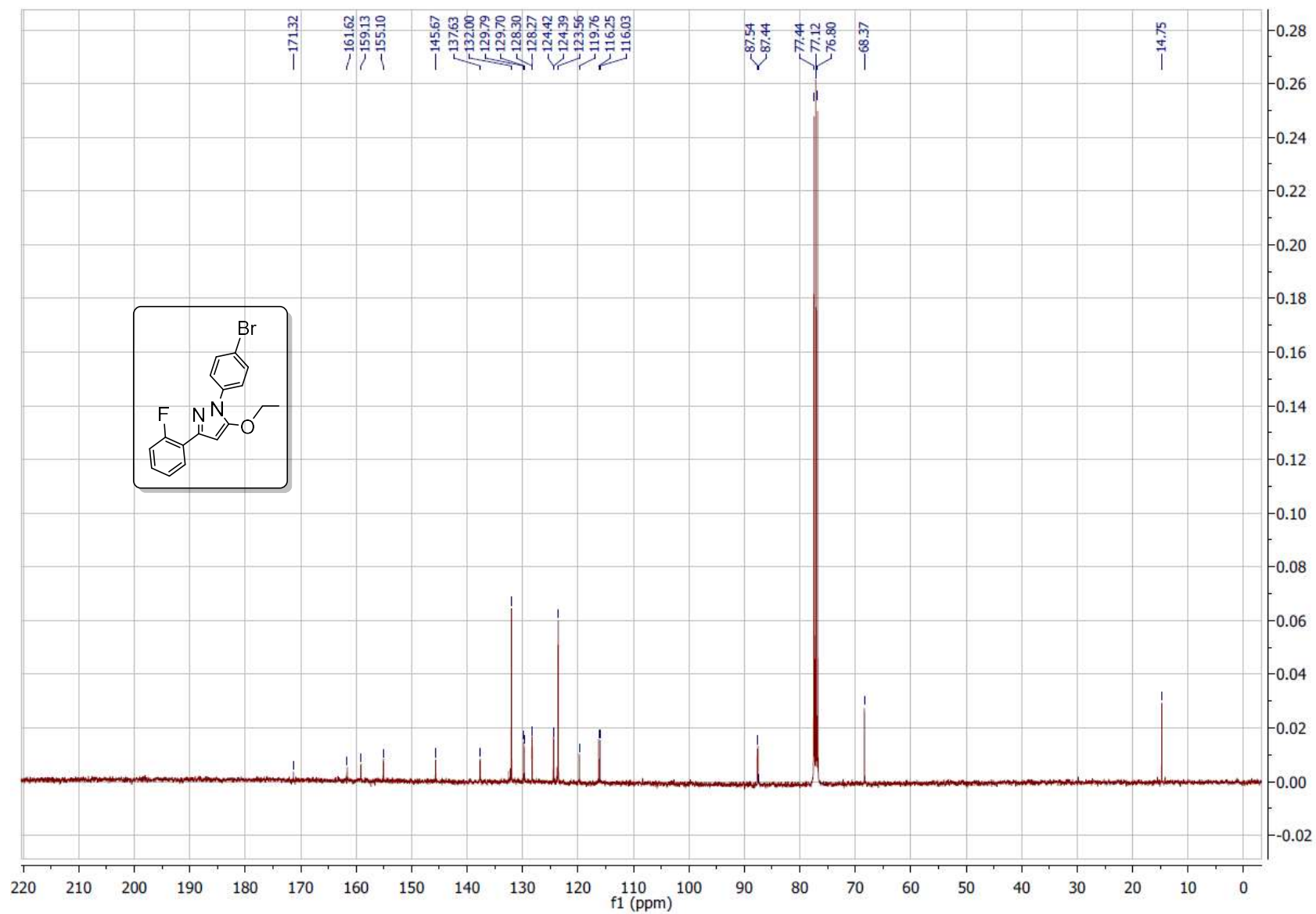


Formula,	Species,	m/z,	Score,	Diff (abs. ppm),	Mass
C15 H10 Br F N2 O,	(M+H) <sup>+</sup> ,	333.0029,	99.19,	0.73,	331.9958

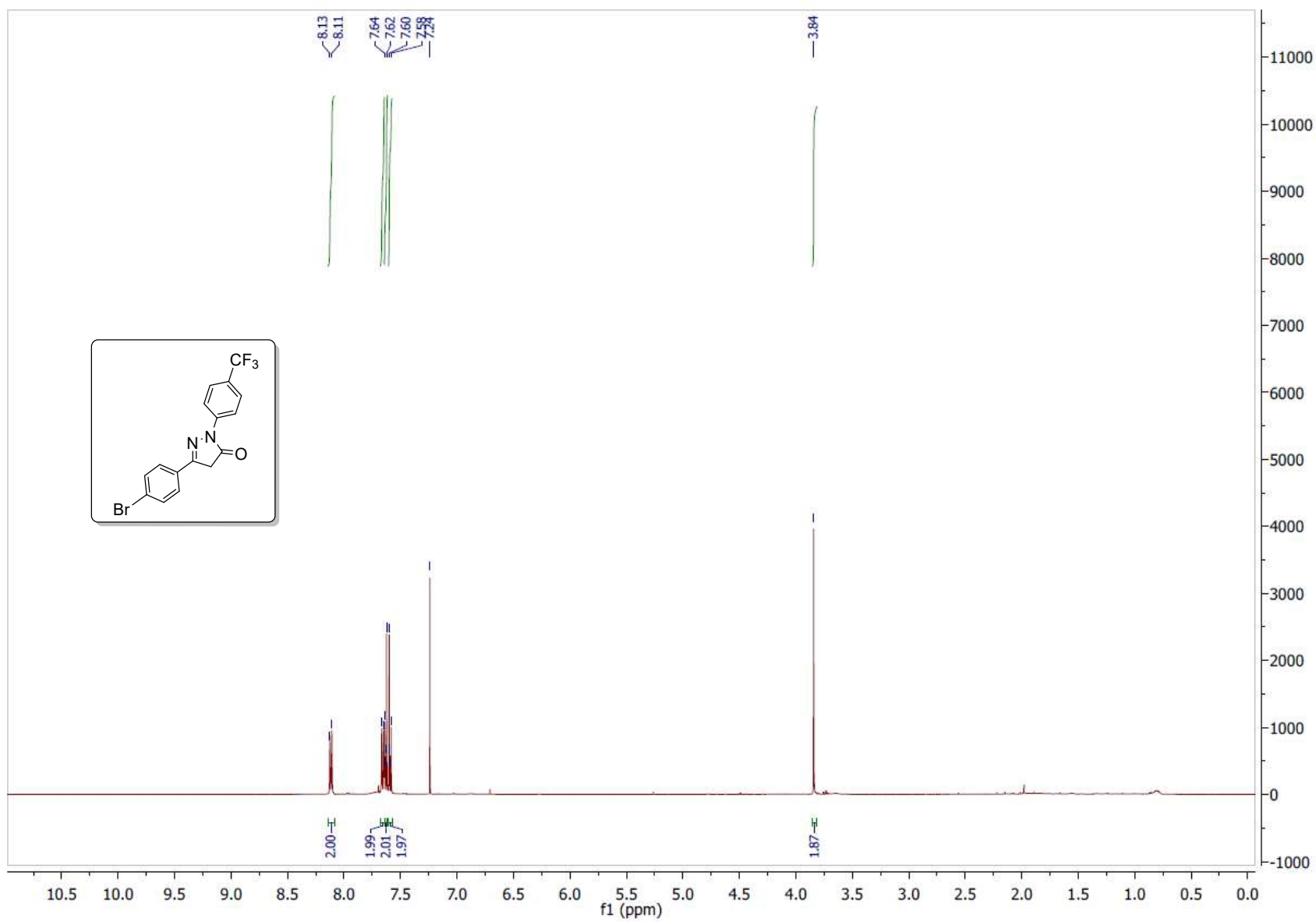
1-(4-bromophenyl)-5-ethoxy-3-(2-fluorophenyl)-1H-pyrazole (P15'):  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )



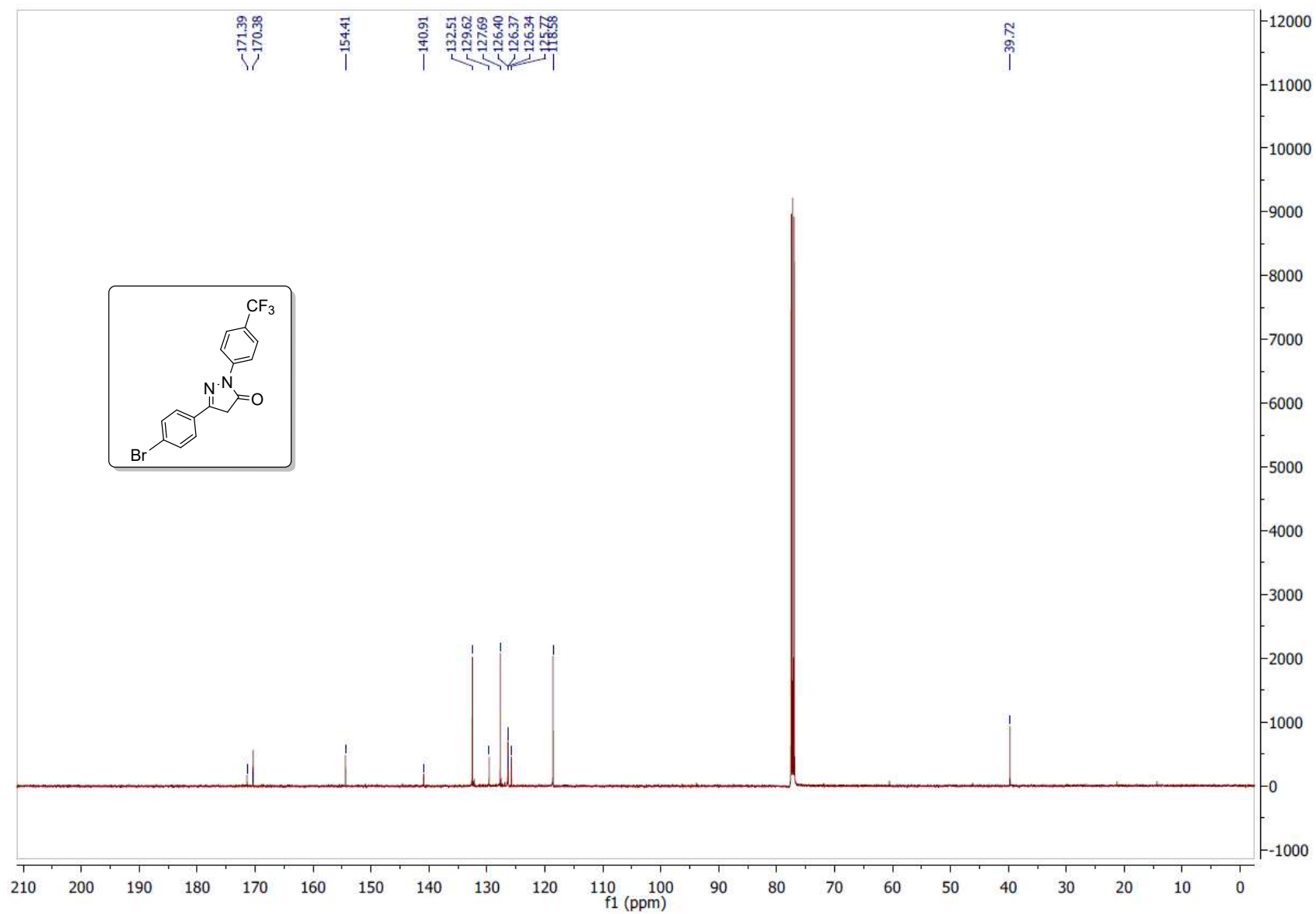
1-(4-bromophenyl)-5-ethoxy-3-(2-fluorophenyl)-1H-pyrazole (P15'):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )



5-(4-bromophenyl)-2-(4-(trifluoromethyl)phenyl)-2,4-dihydro-3H-pyrazol-3-one (P16):  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )

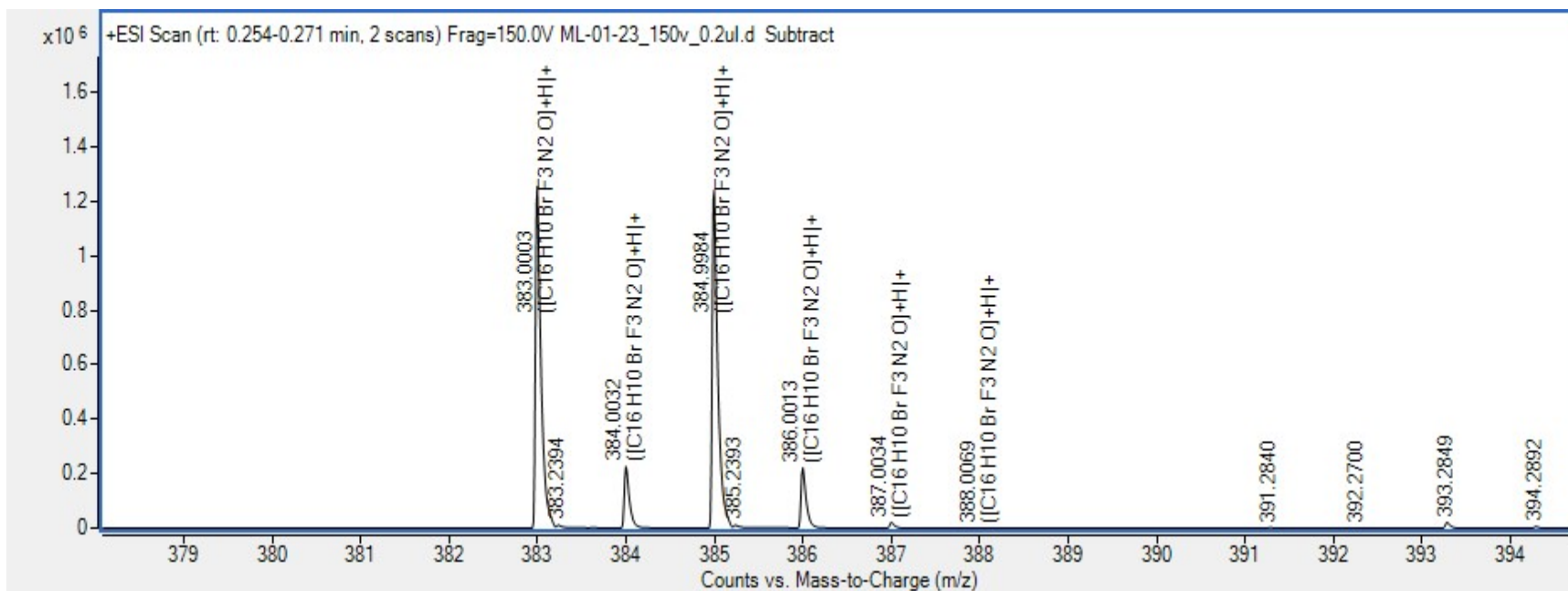


5-(4-bromophenyl)-2-(4-(trifluoromethyl)phenyl)-2,4-dihydro-3H-pyrazol-3-one (P16):  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )



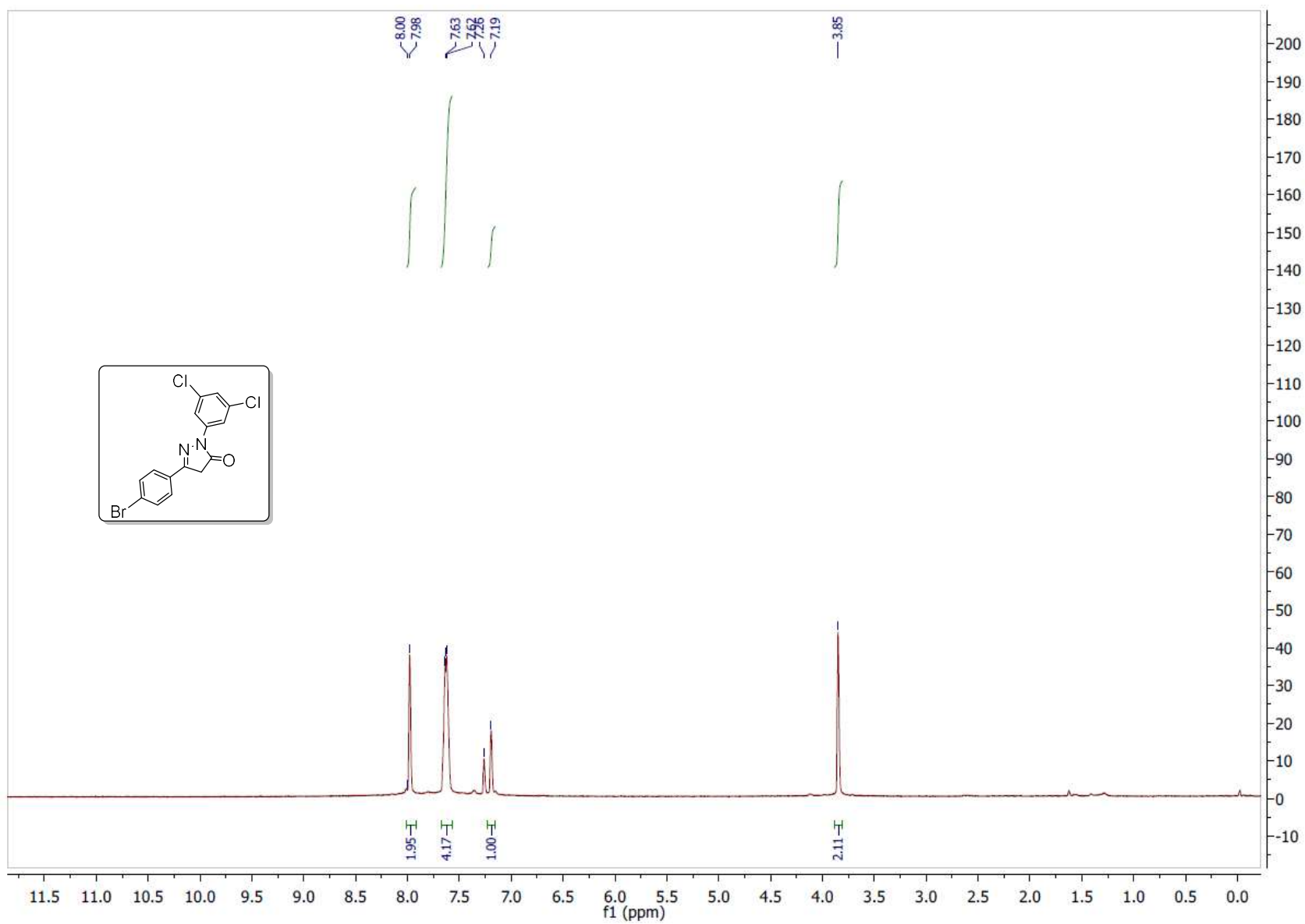


**5-(4-bromophenyl)-2-(4-(trifluoromethyl)phenyl)-2,4-dihydro-3H-pyrazol-3-one (P16): ESI-MS**

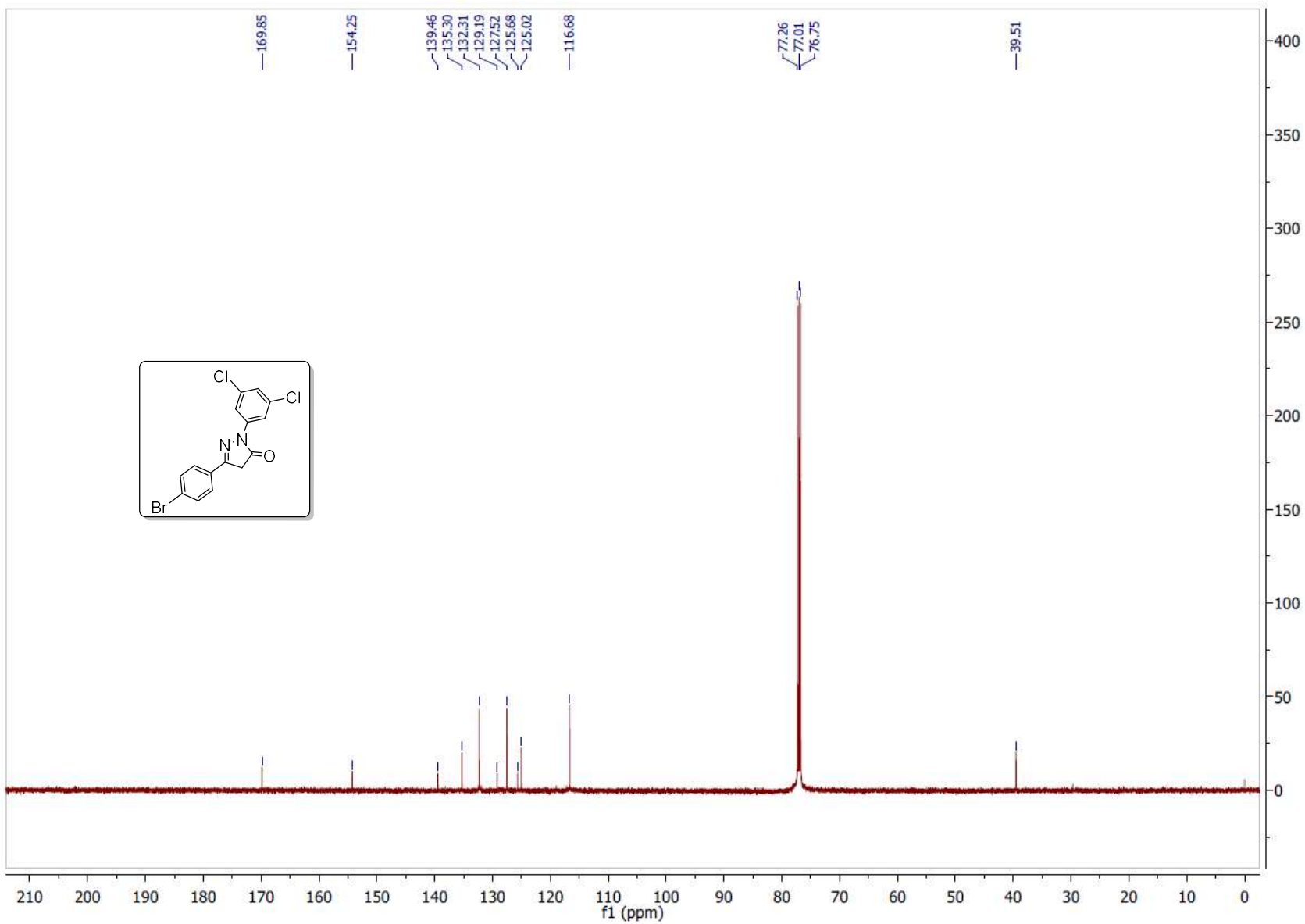


Formula,	Species,	m/z,	Score,	Diff (abs. ppm),	Mass
C16 H10 Br F3 N2 O,	(M+H) <sup>+</sup> ,	383.0003,	99.86,	0.41,	381.993

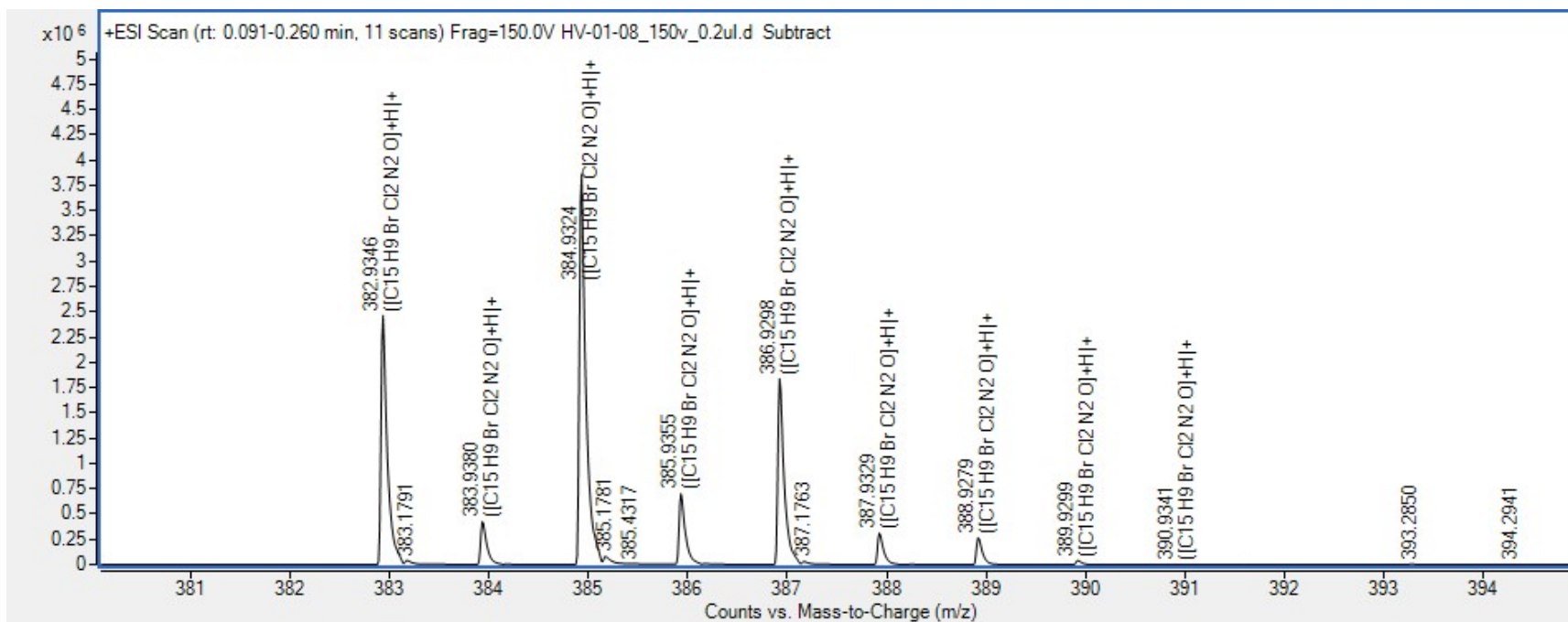
5-(4-bromophenyl)-2-(3,5-dichlorophenyl)-2,4-dihydro-3H-pyrazol-3-one (P17):  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )



5-(4-bromophenyl)-2-(3,5-dichlorophenyl)-2,4-dihydro-3H-pyrazol-3-one (P17): <sup>13</sup>C-NMR (CDCl<sub>3</sub>)



**5-(4-bromophenyl)-2-(3,5-dichlorophenyl)-2,4-dihydro-3H-pyrazol-3-one (P17): ESI-MS**



Formula,	Species,	m/z,	Score,	Diff (abs. ppm),	Mass
C15 H9 Br Cl2 N2 O,	(M+H)+,	382.9346,	99.67,	0.37,	381.9274