Supporting Information for

Synthesis, biological activity, and binding modes of novel guanidino-containing neonicotinoid derivatives

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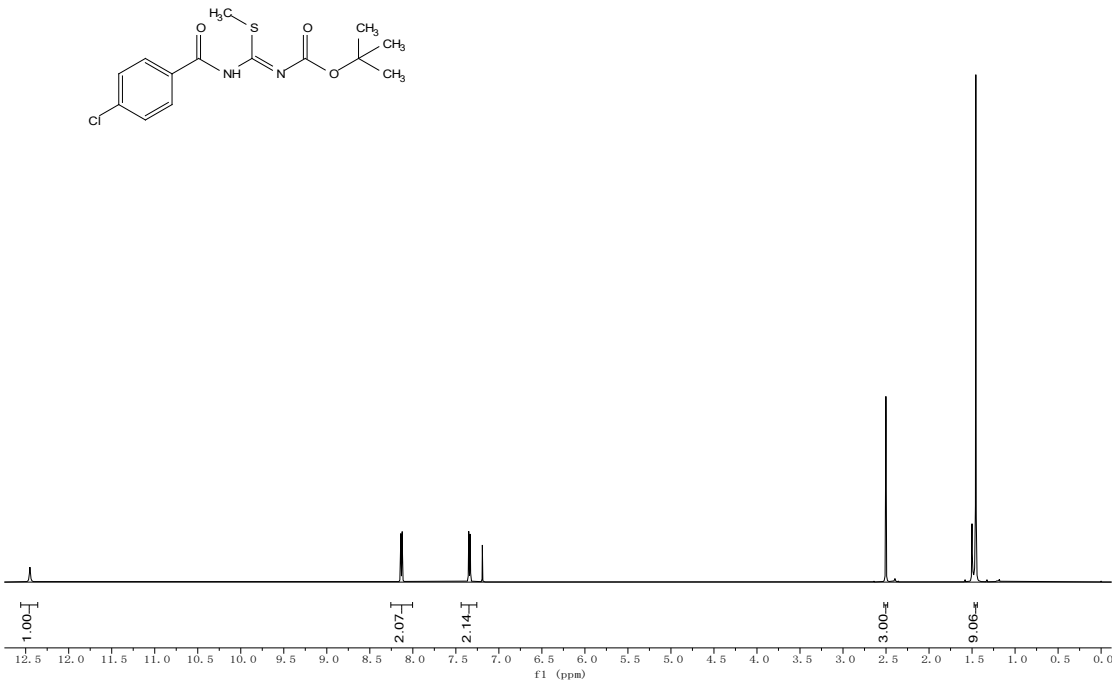

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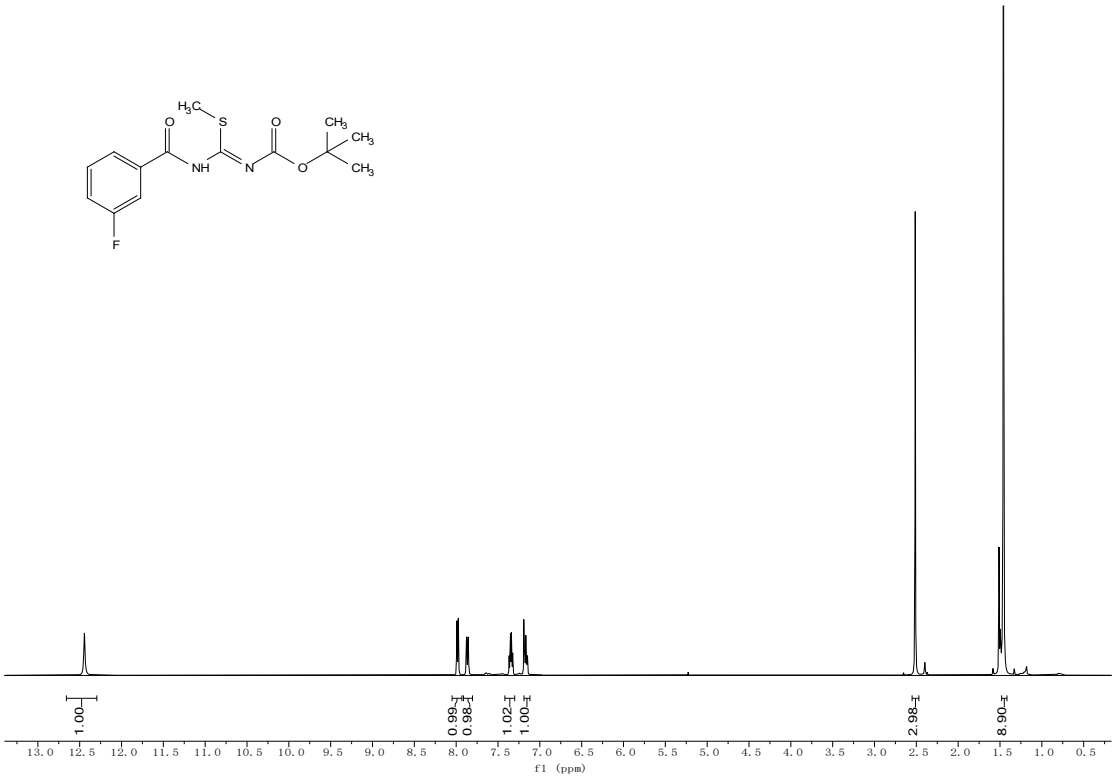

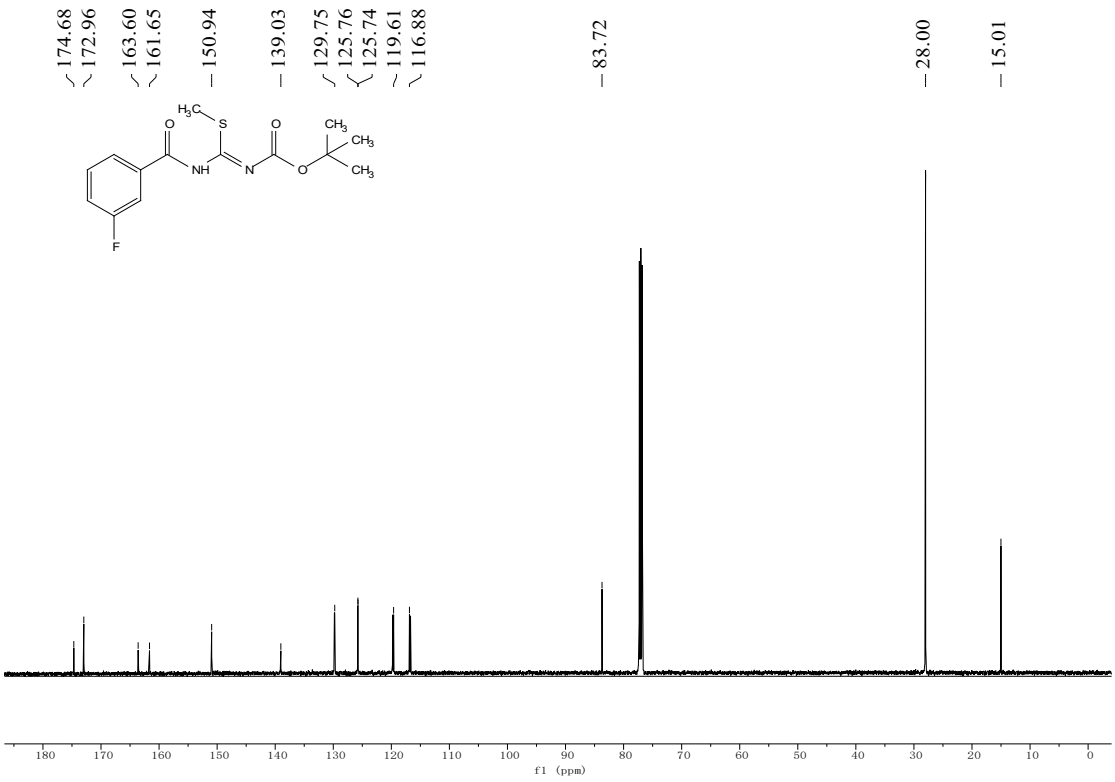

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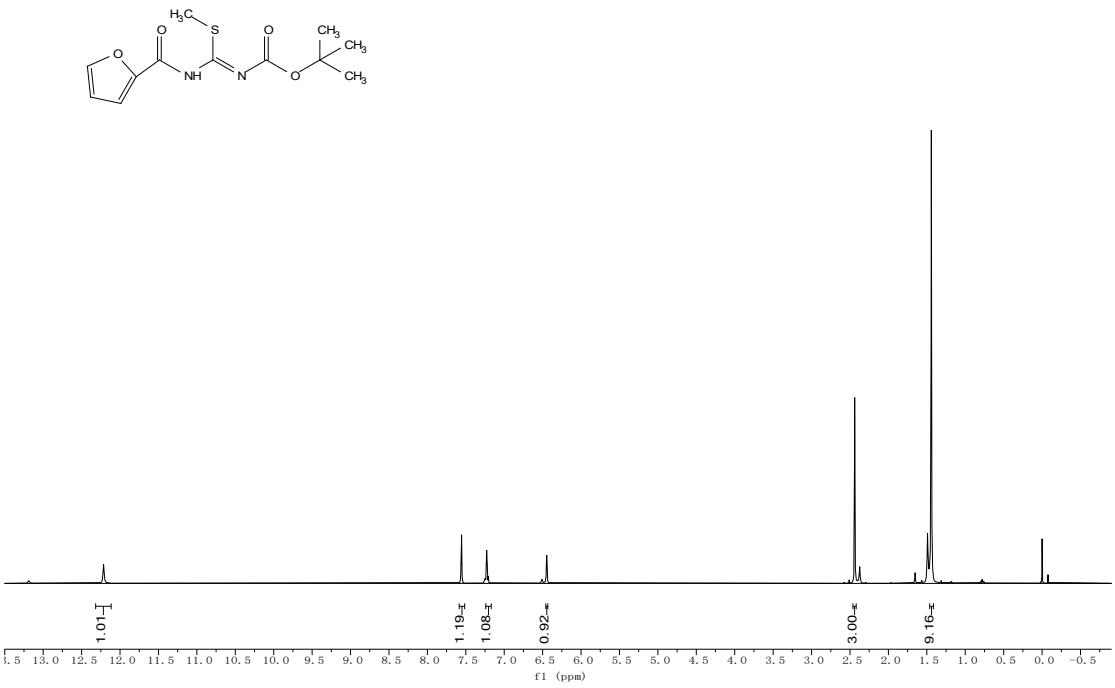


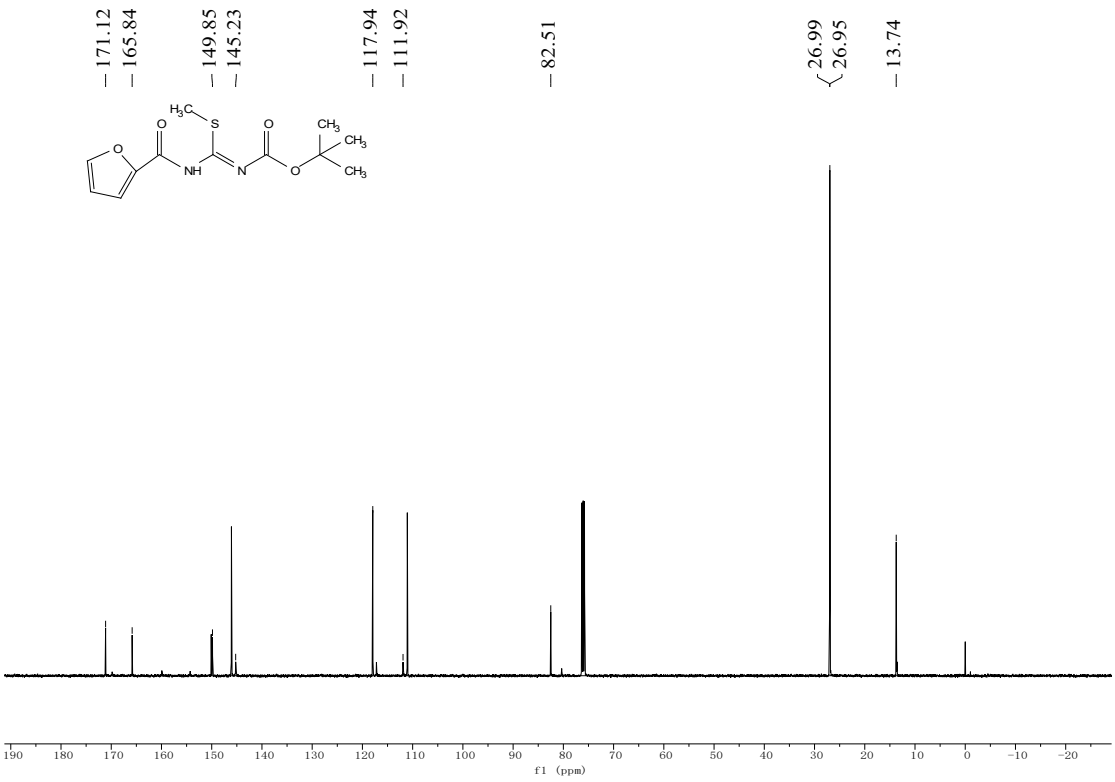
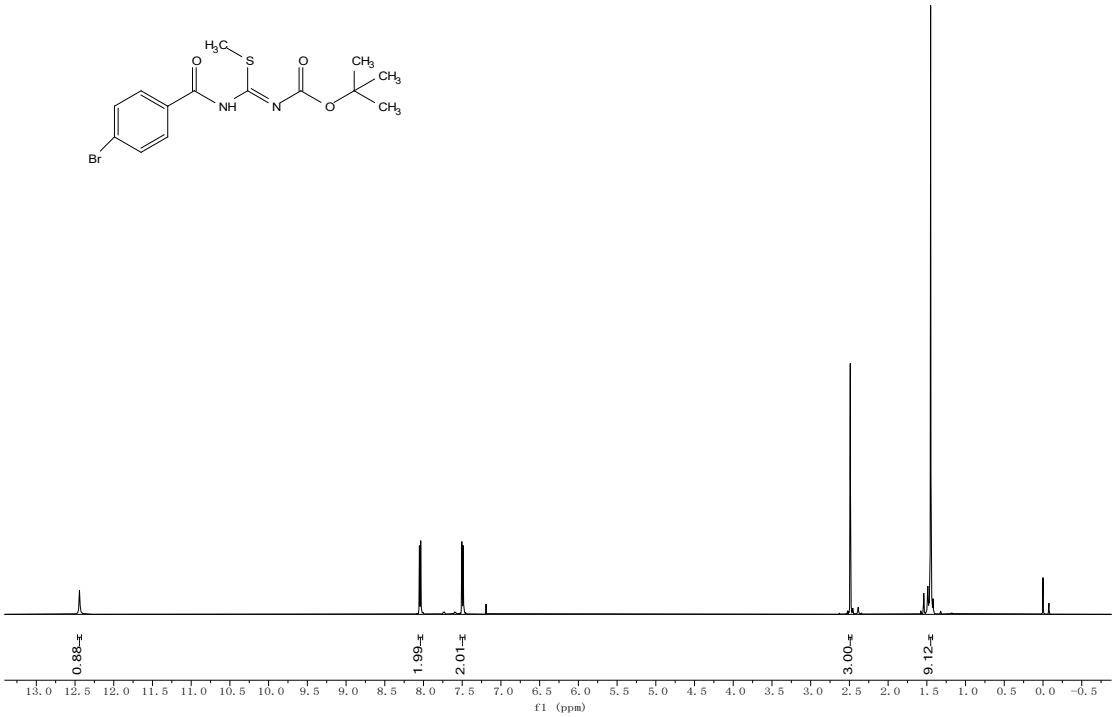


Fig S5. ^{1}H, ^{13}C spectra of **4g**



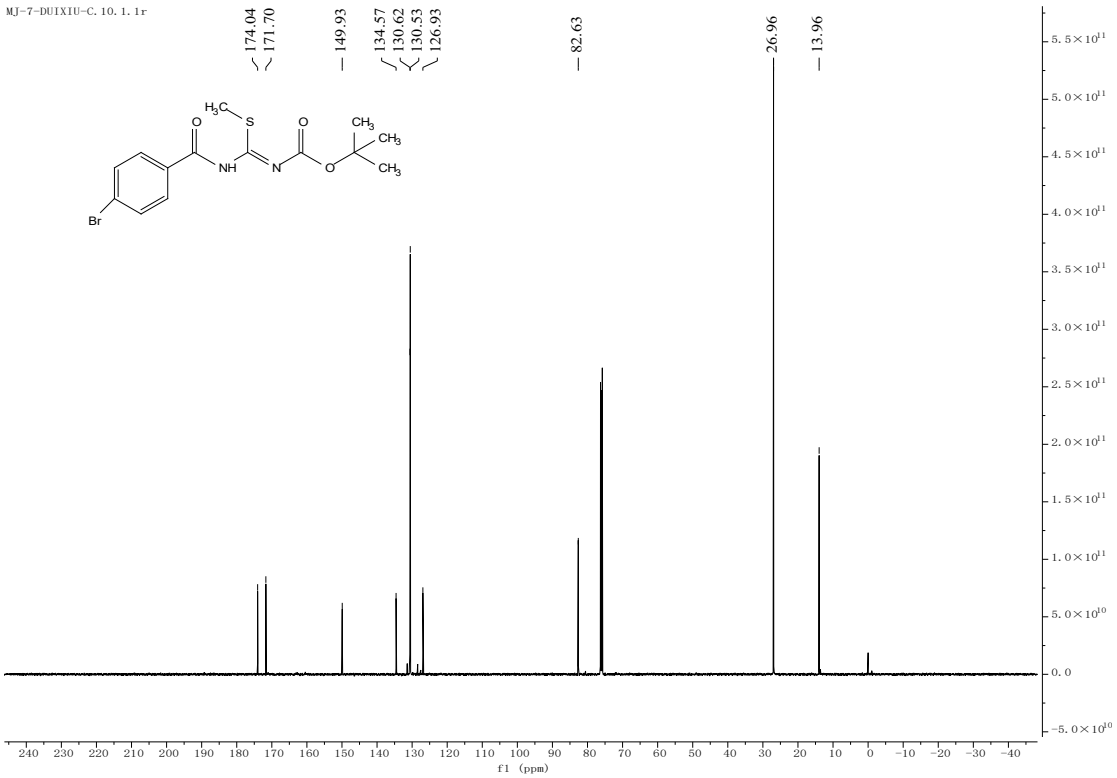
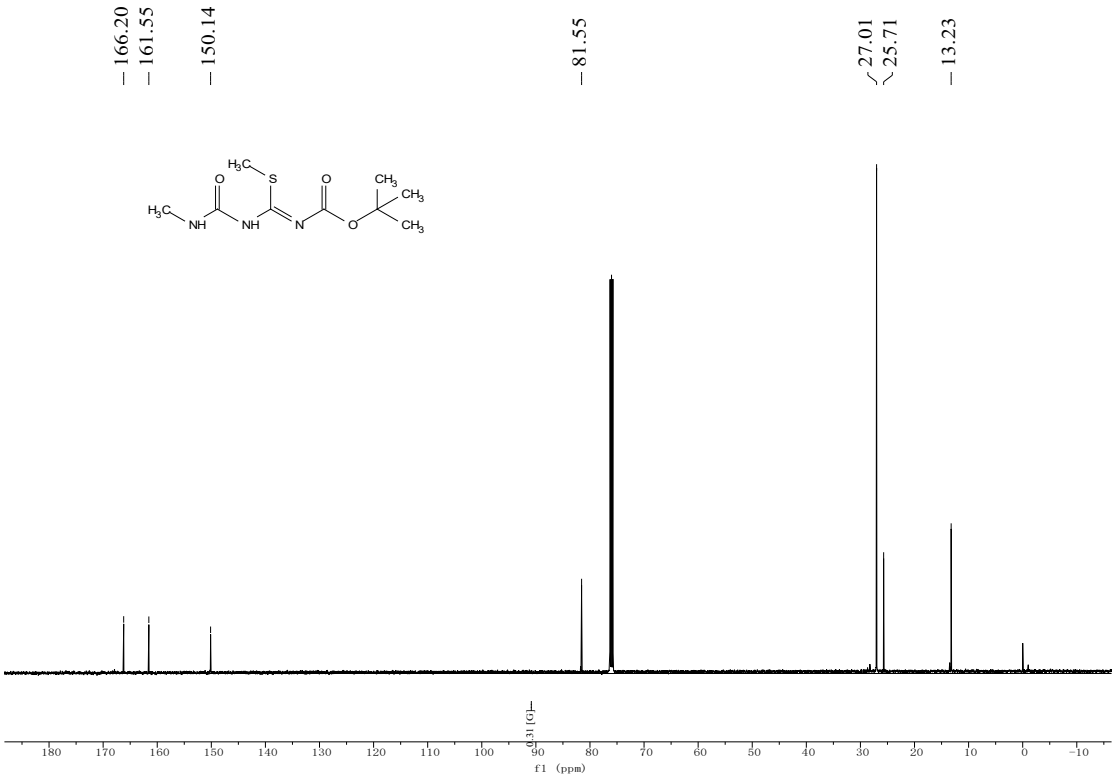


Fig S6. ^{1}H, ^{13}C spectra of **4h**



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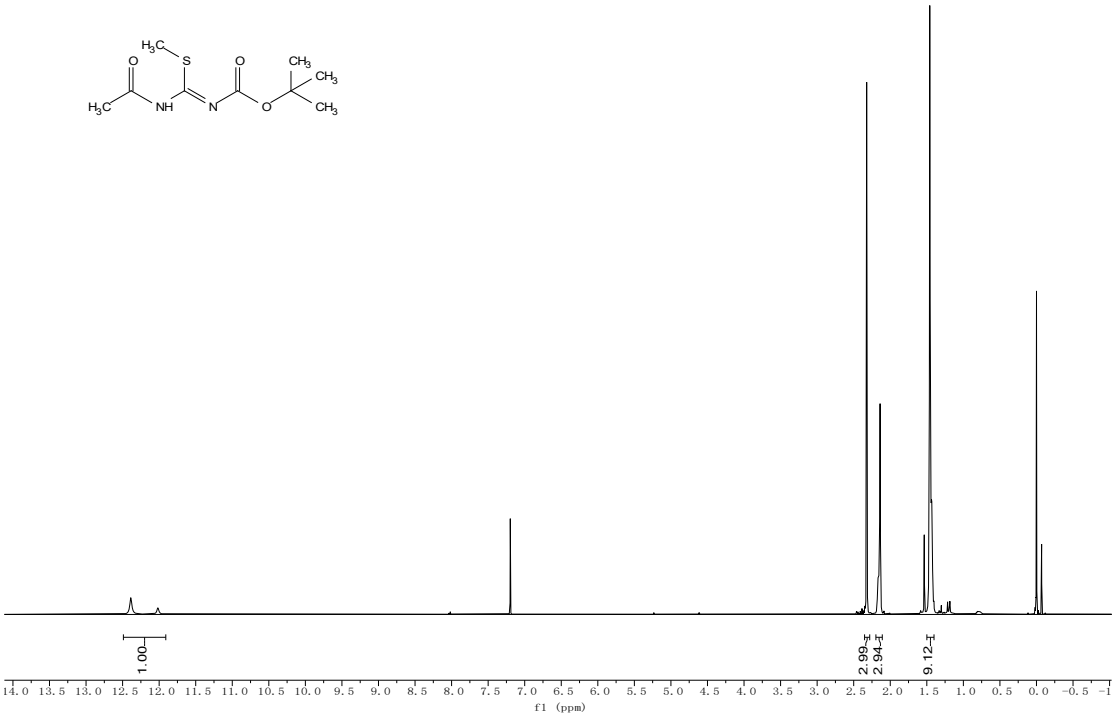

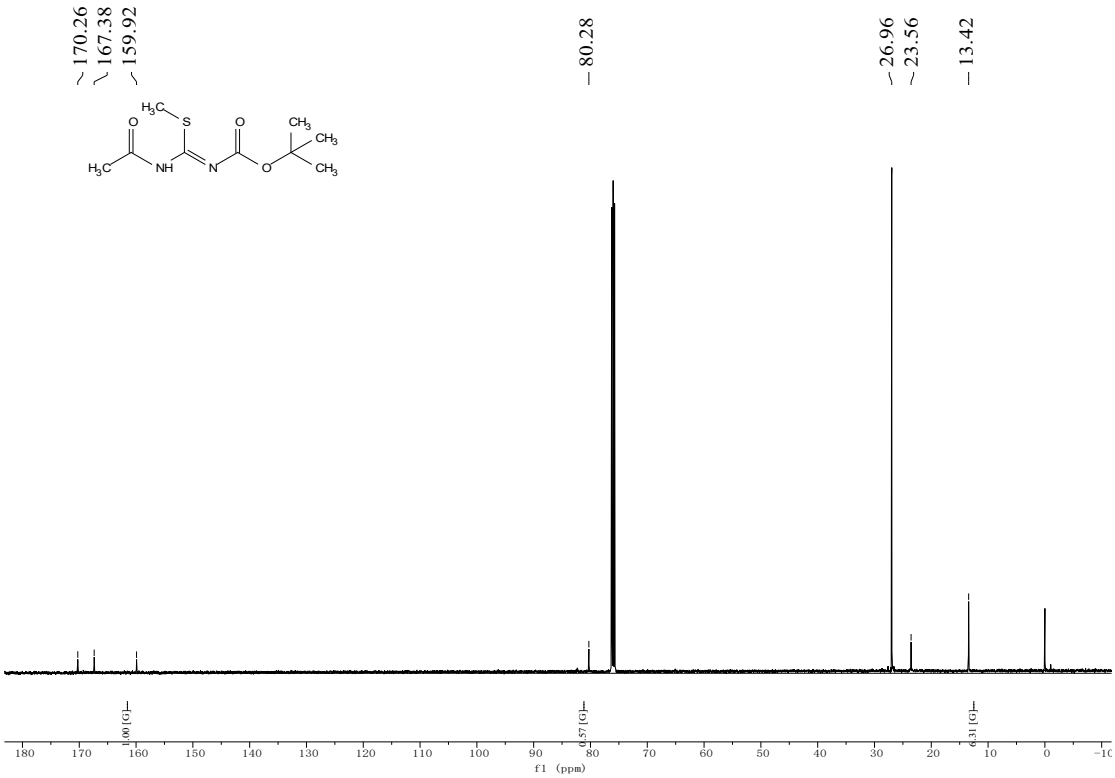

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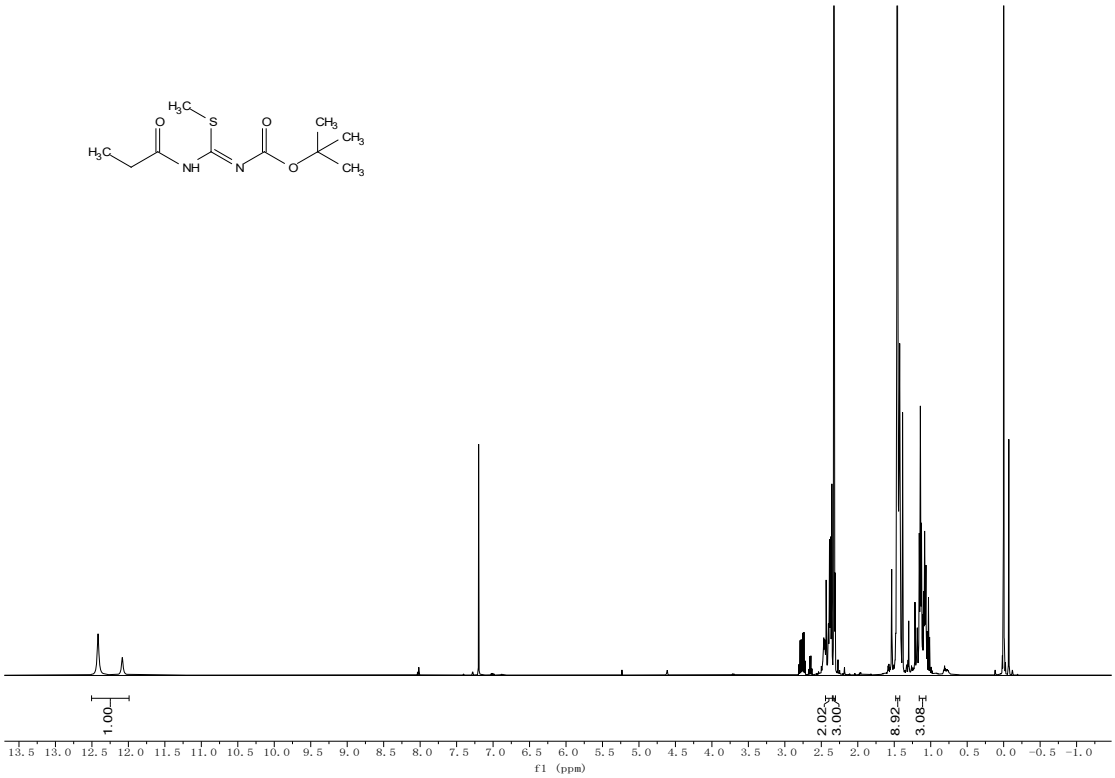

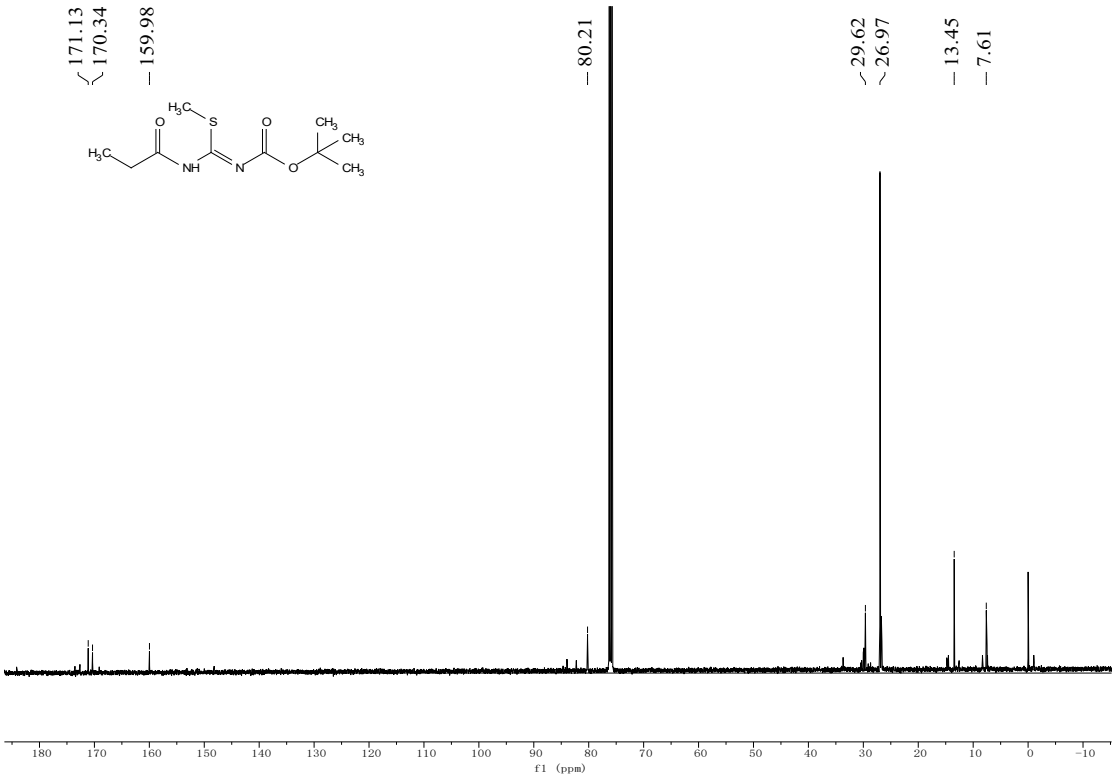

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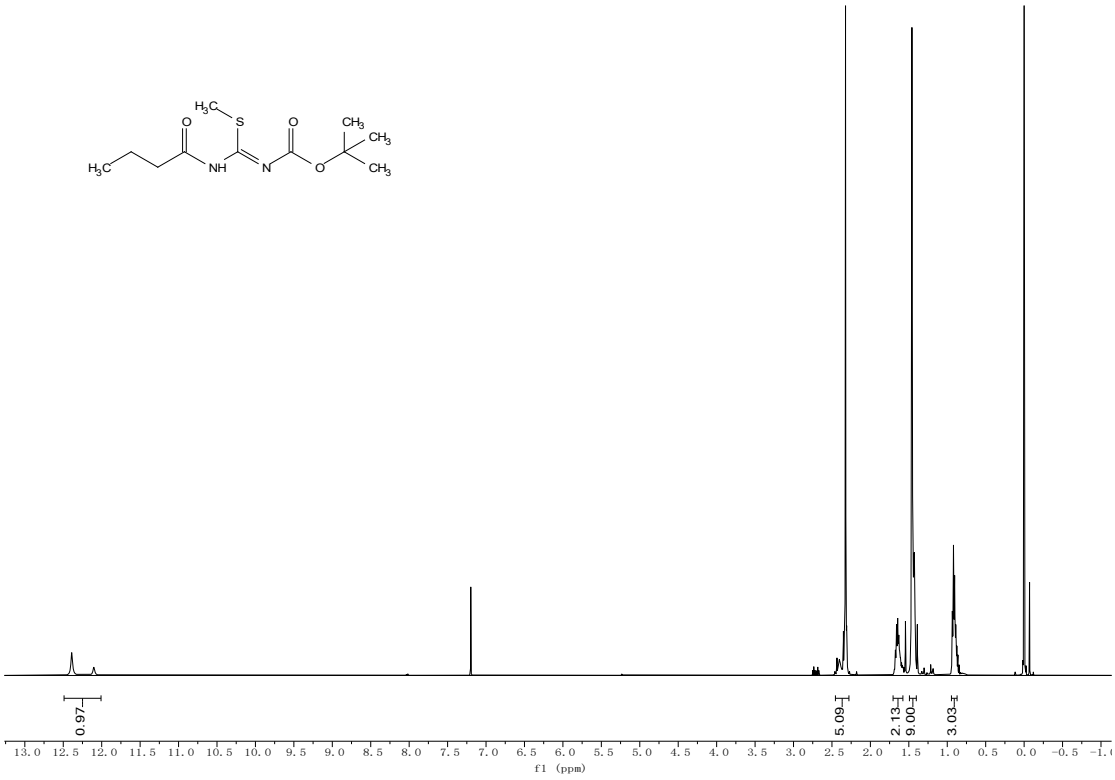

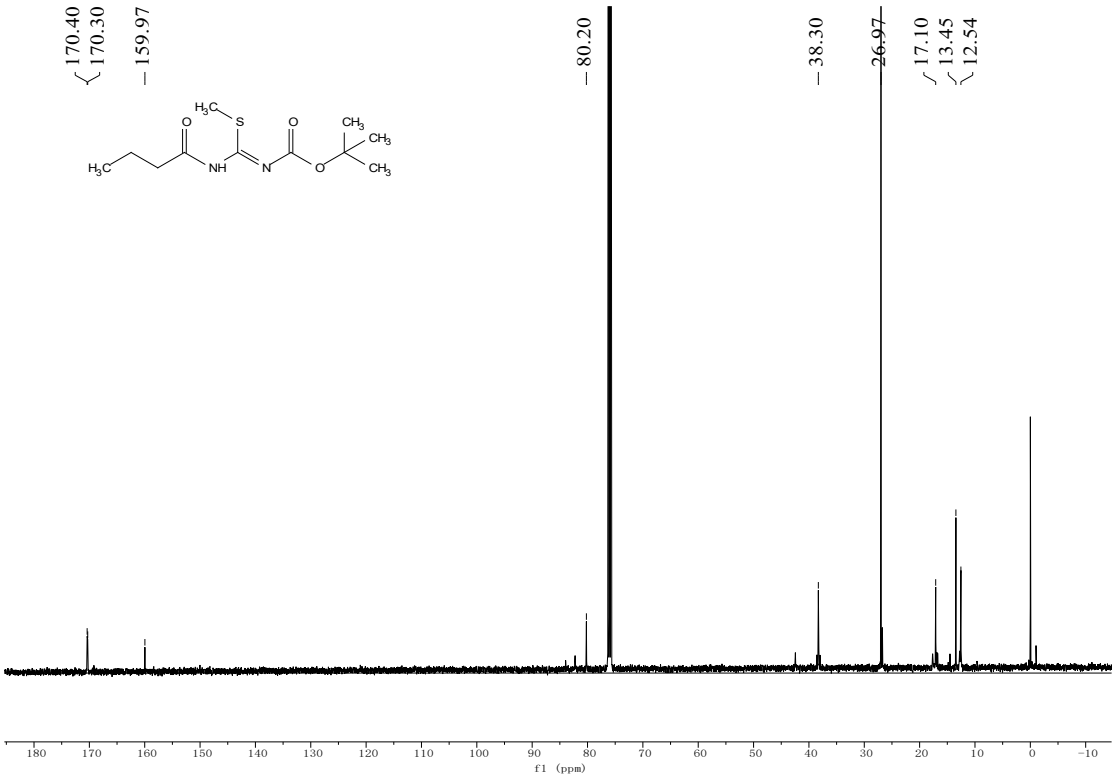

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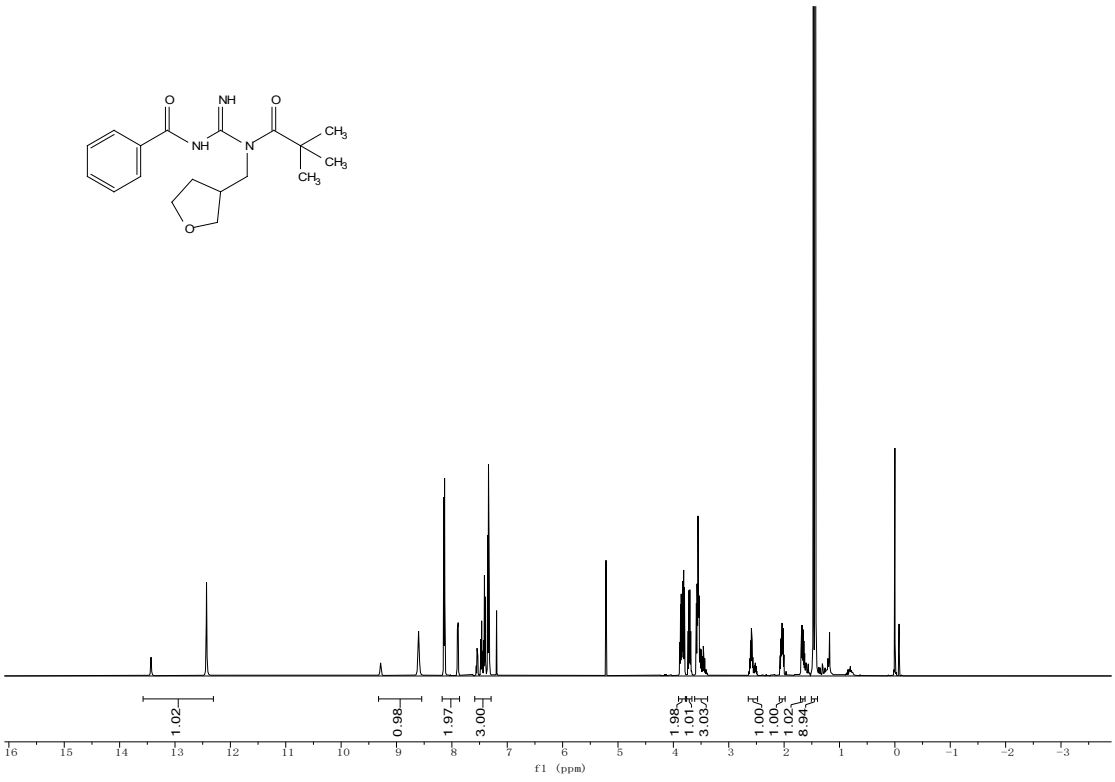

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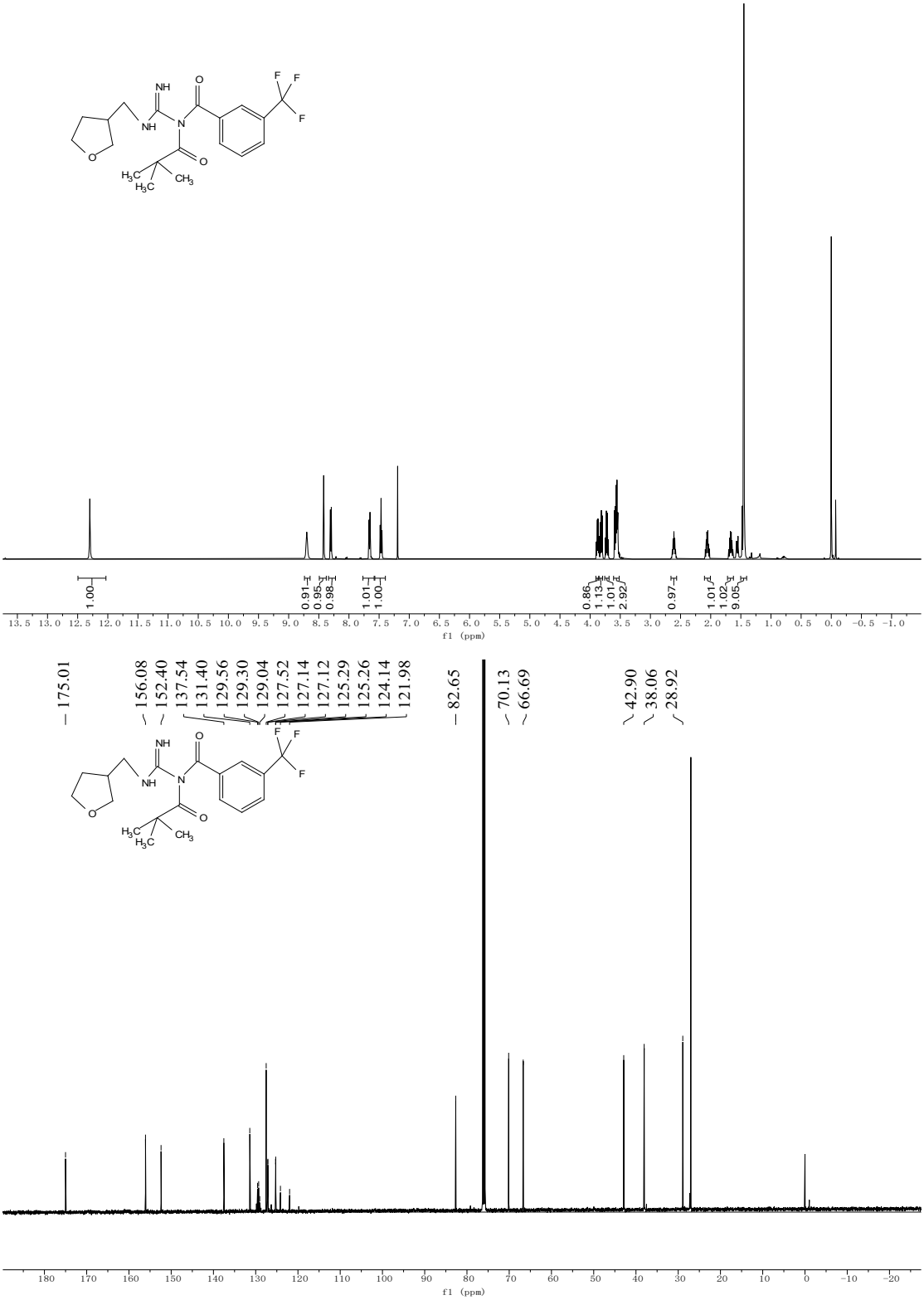

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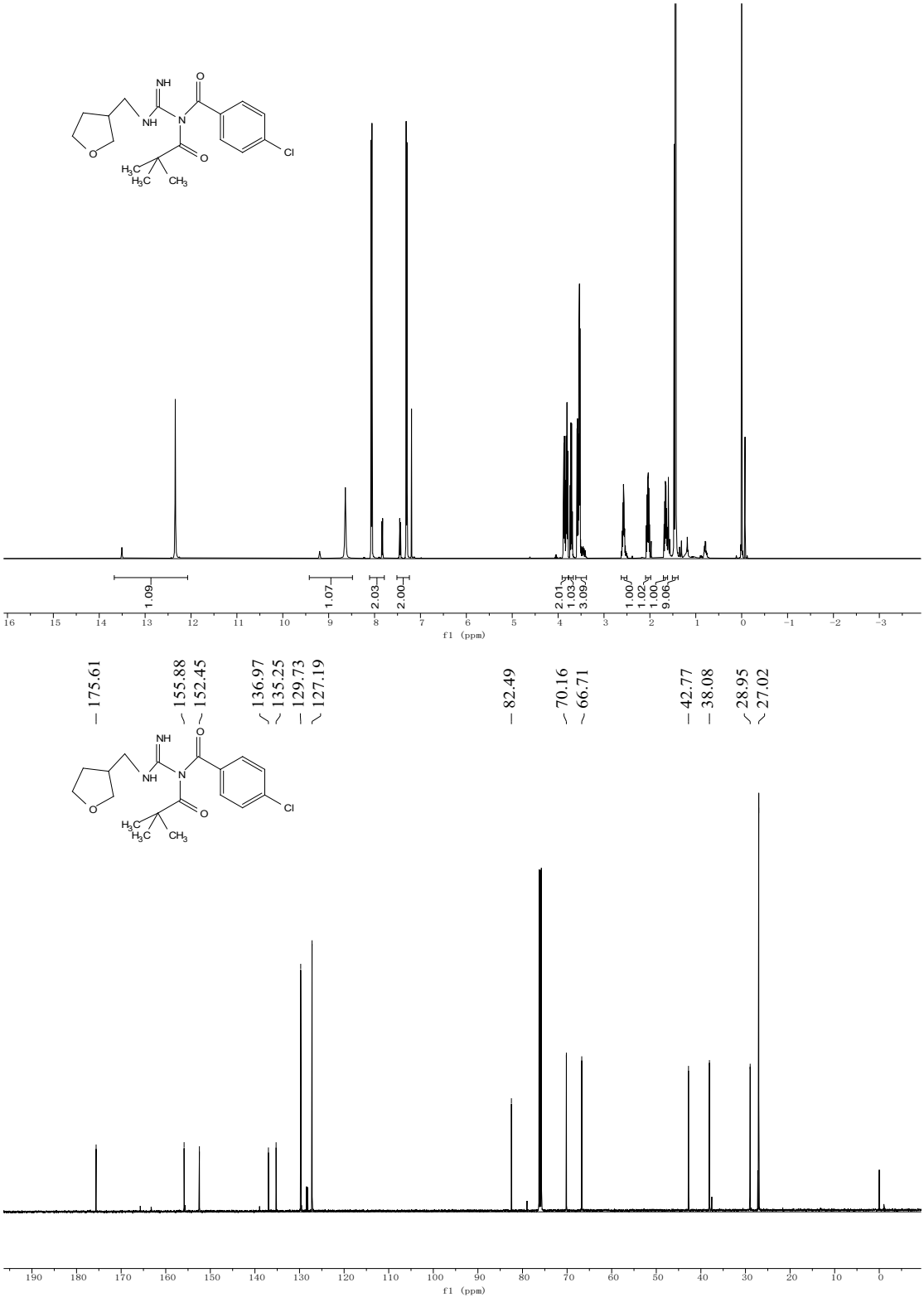

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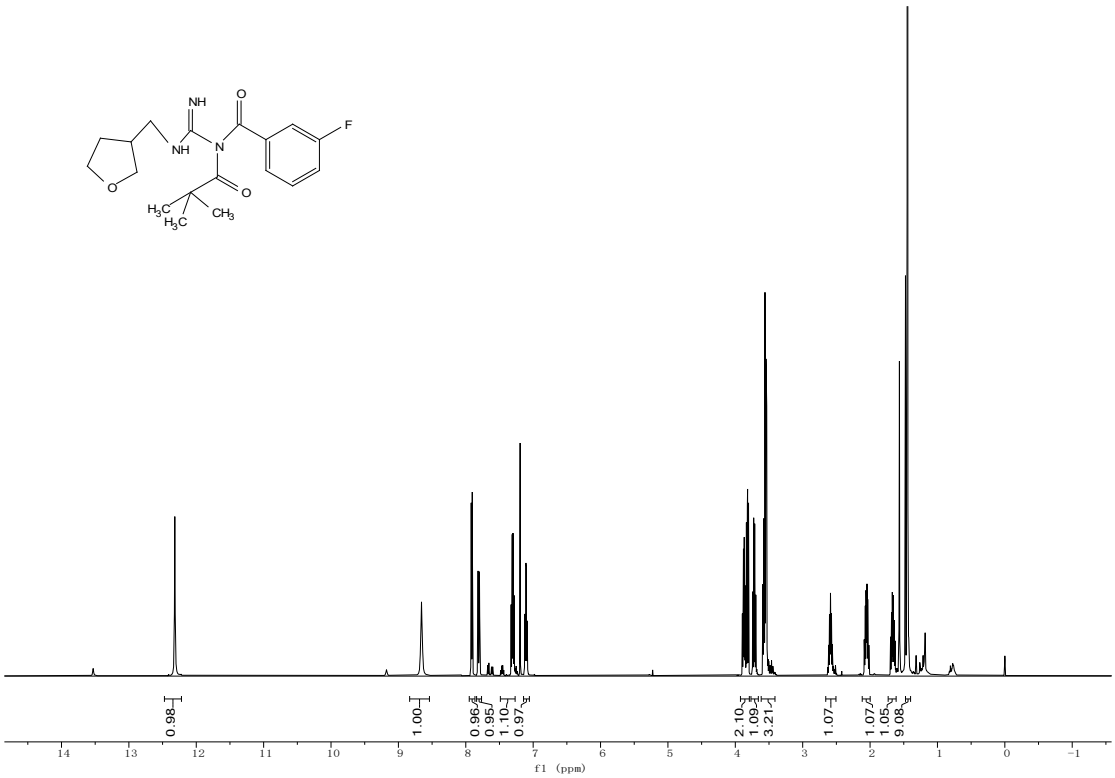

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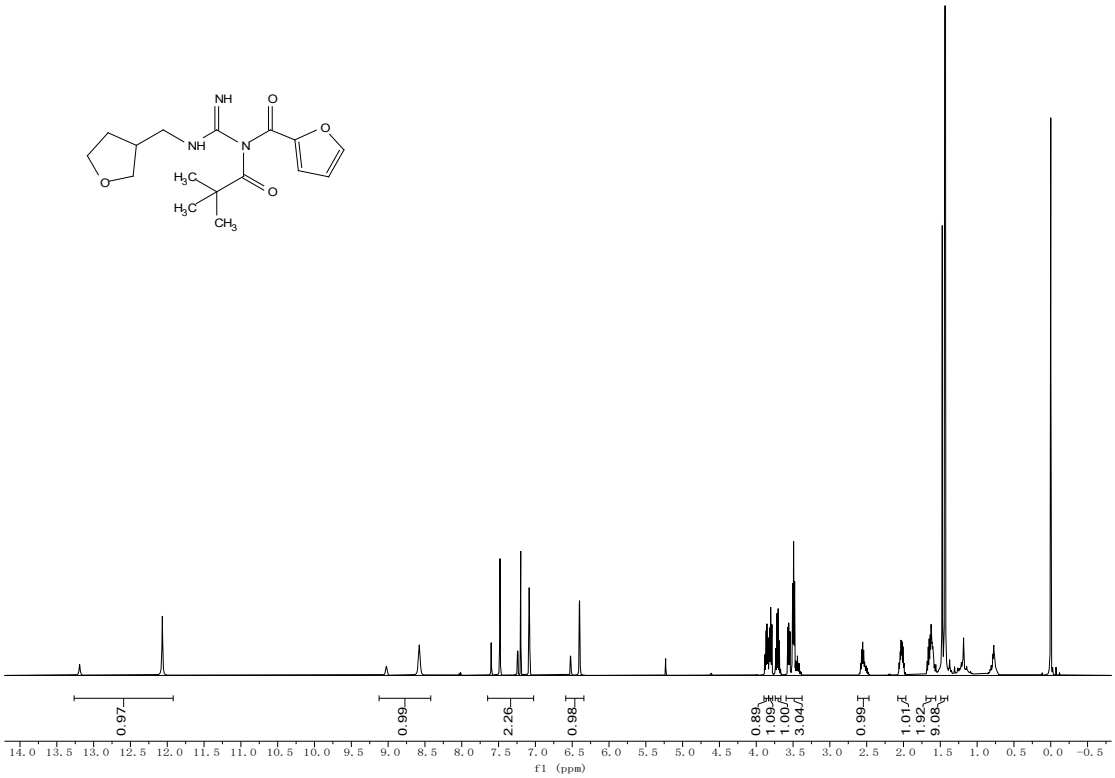

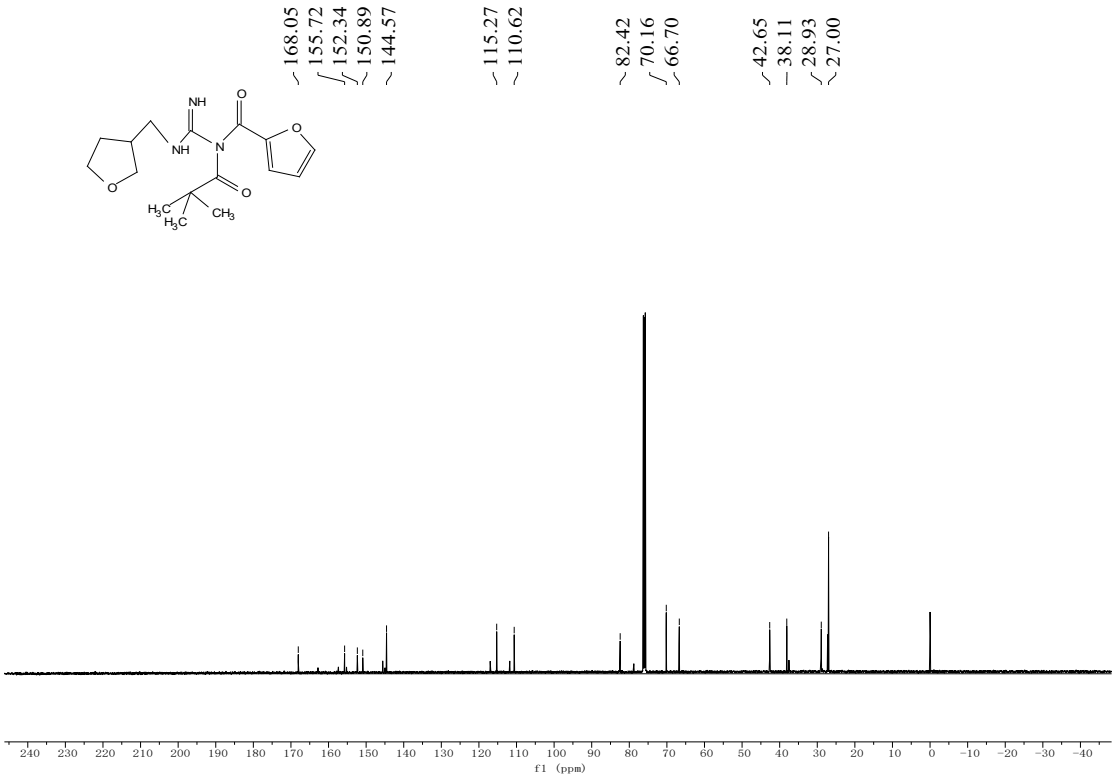

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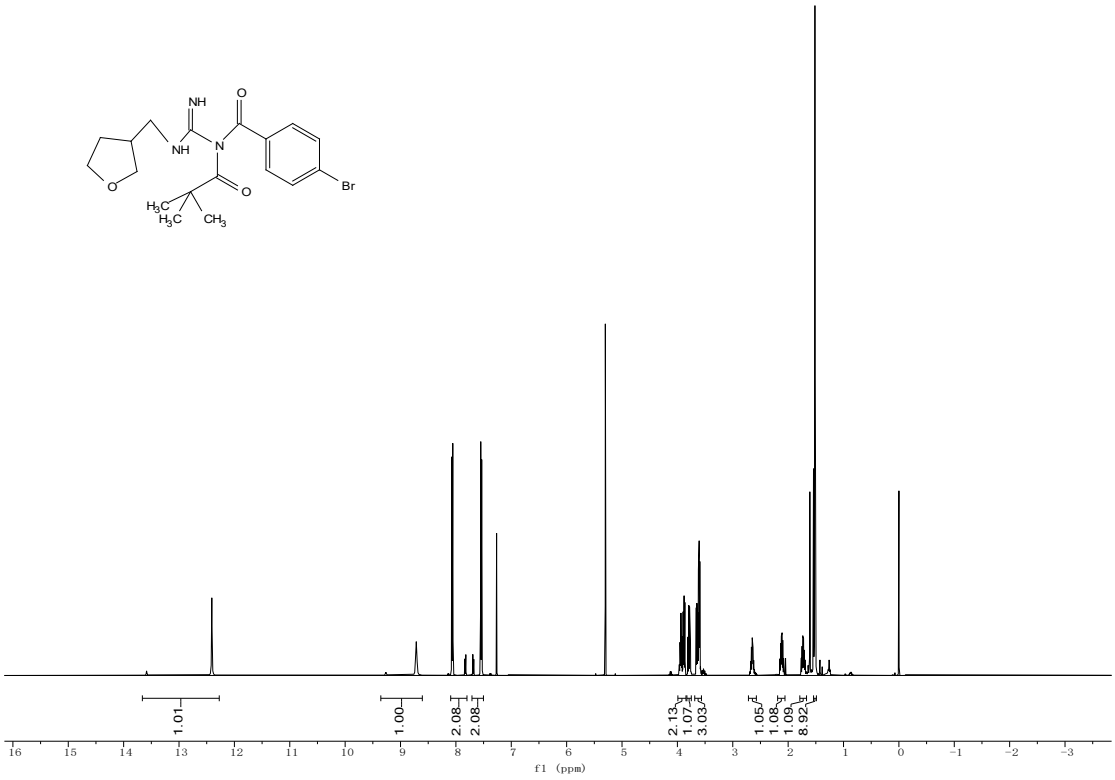

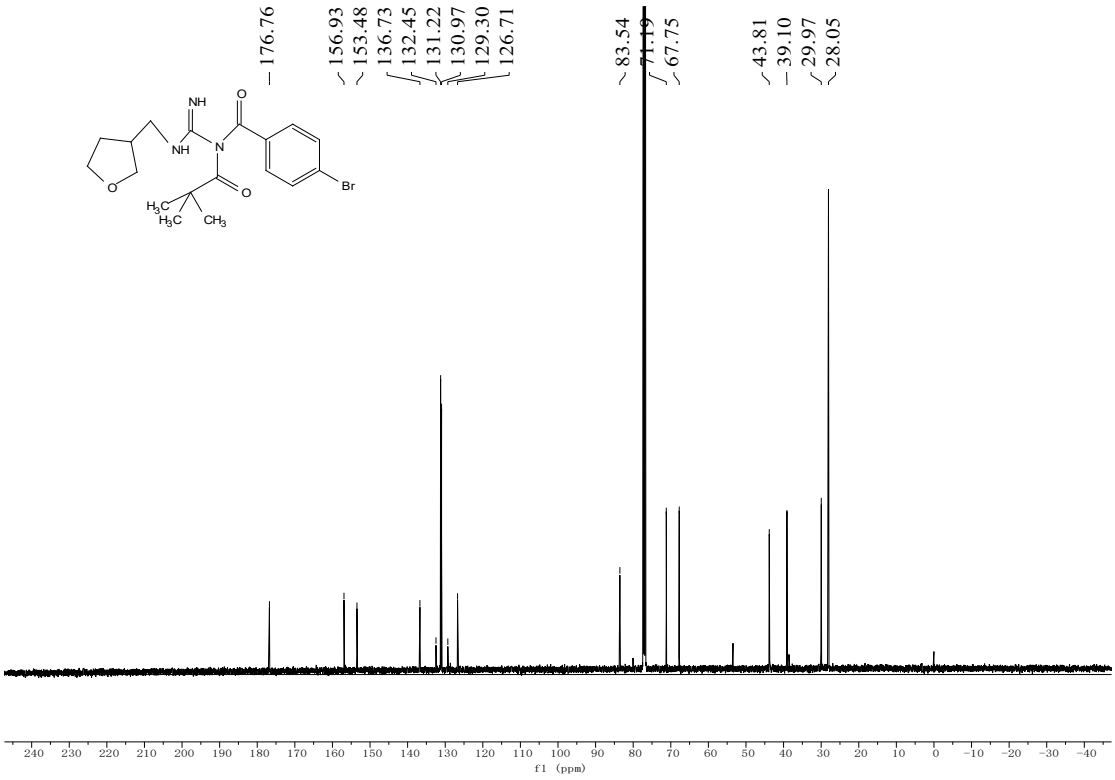

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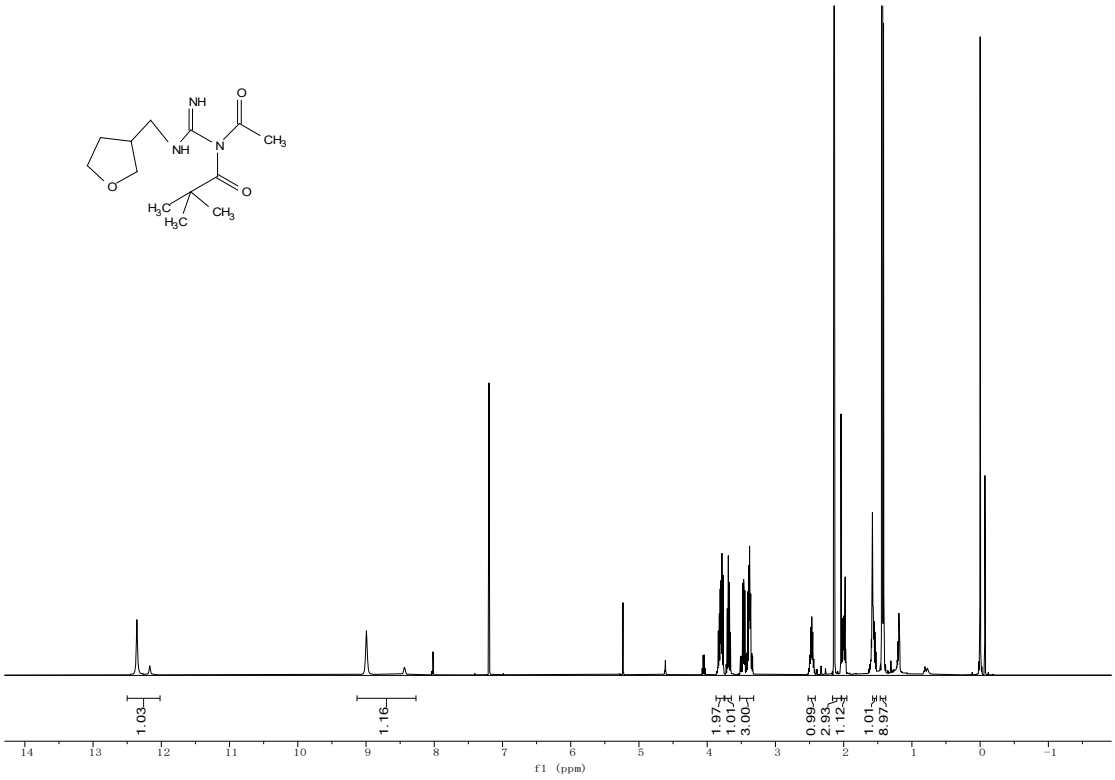

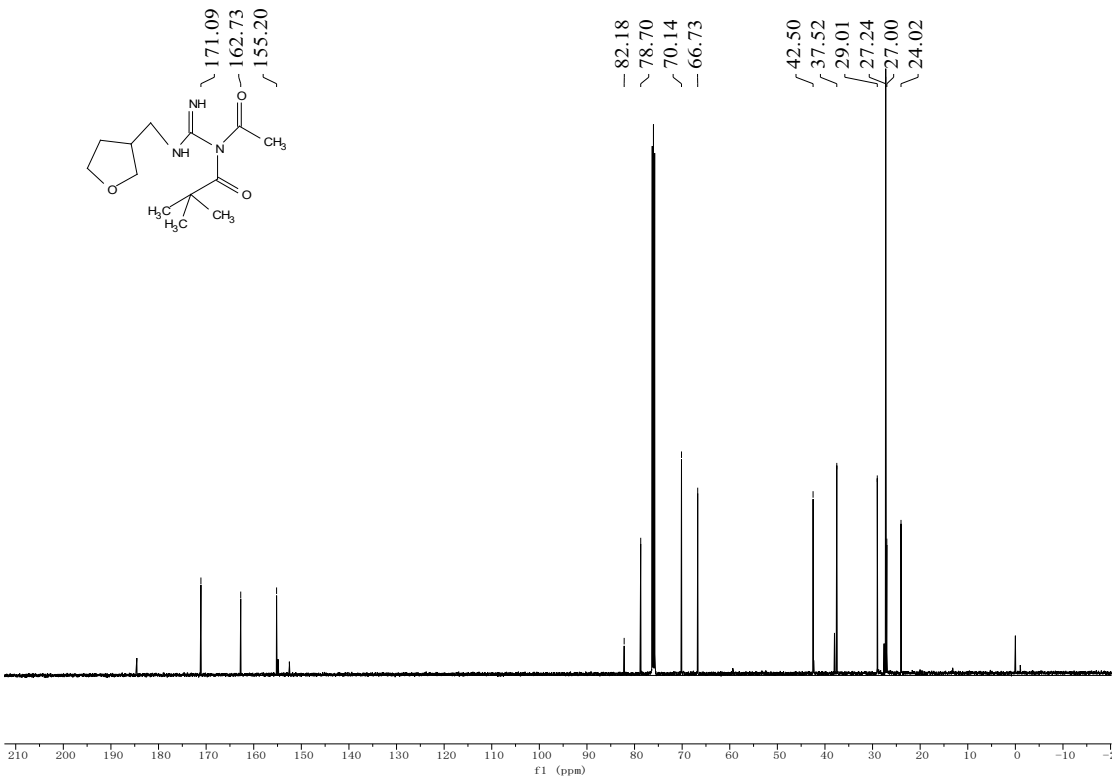

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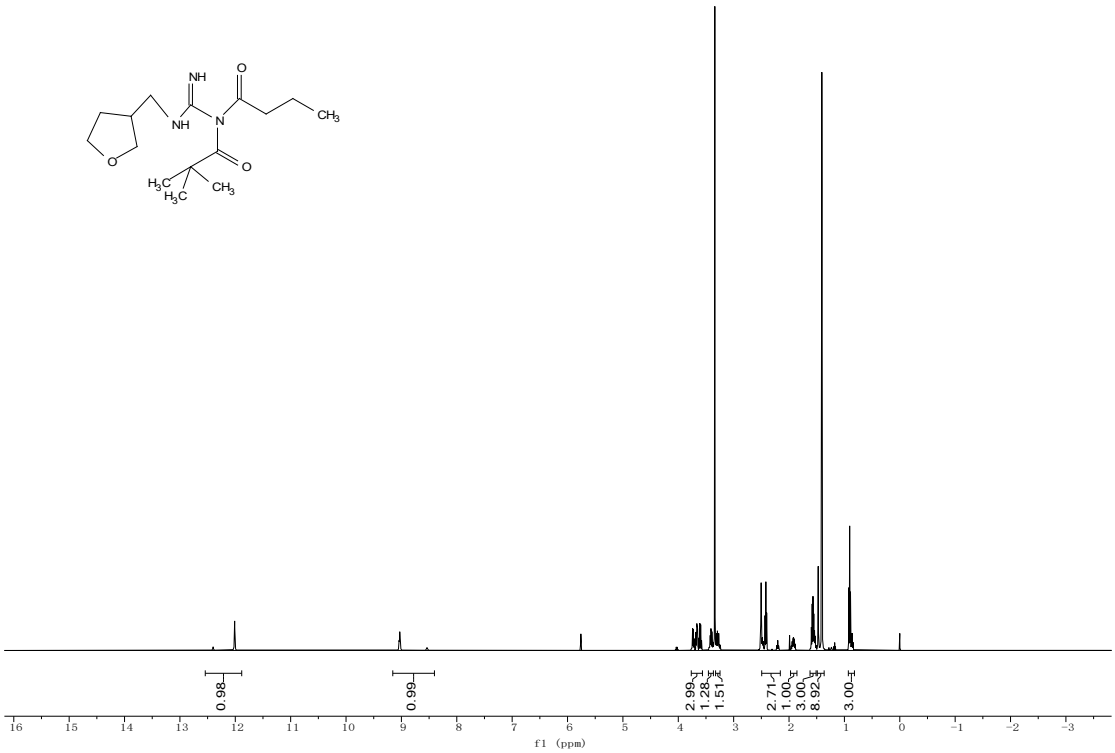

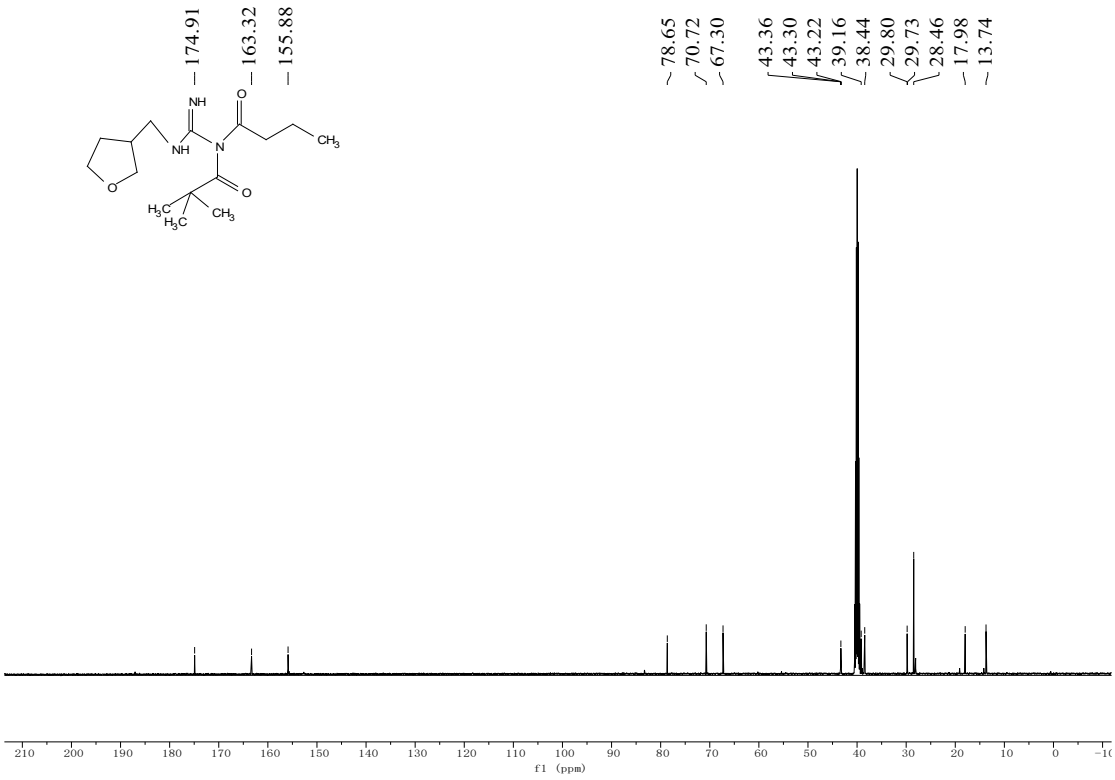

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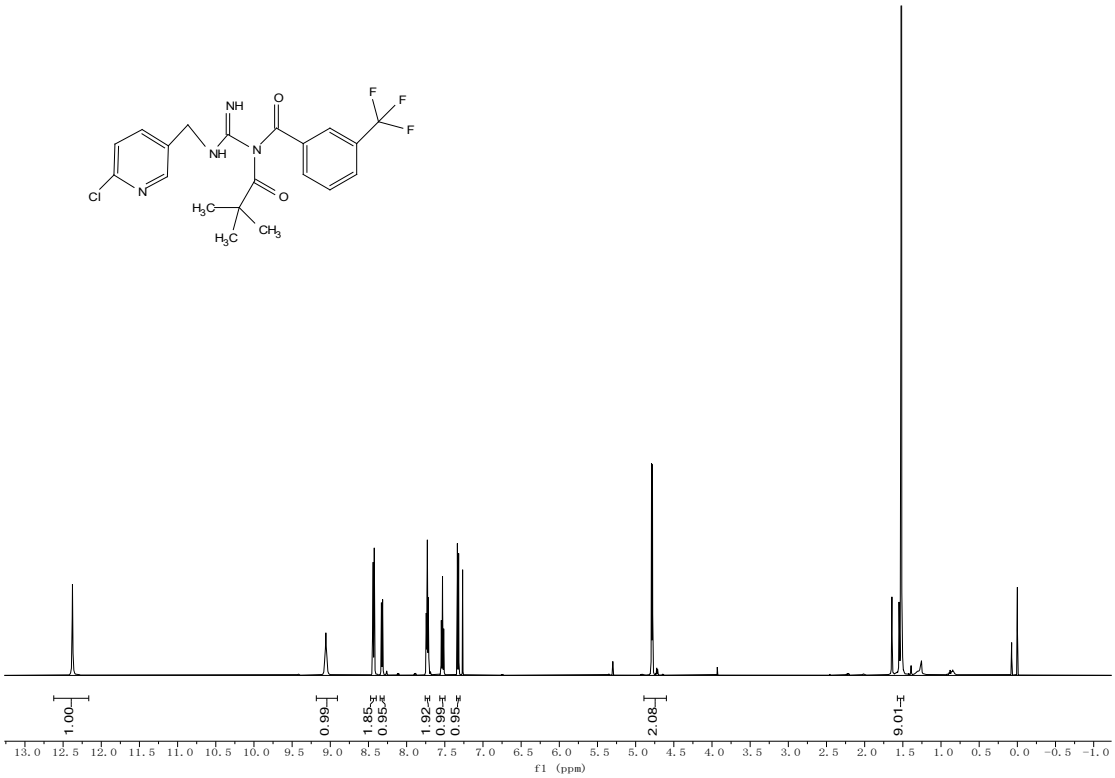

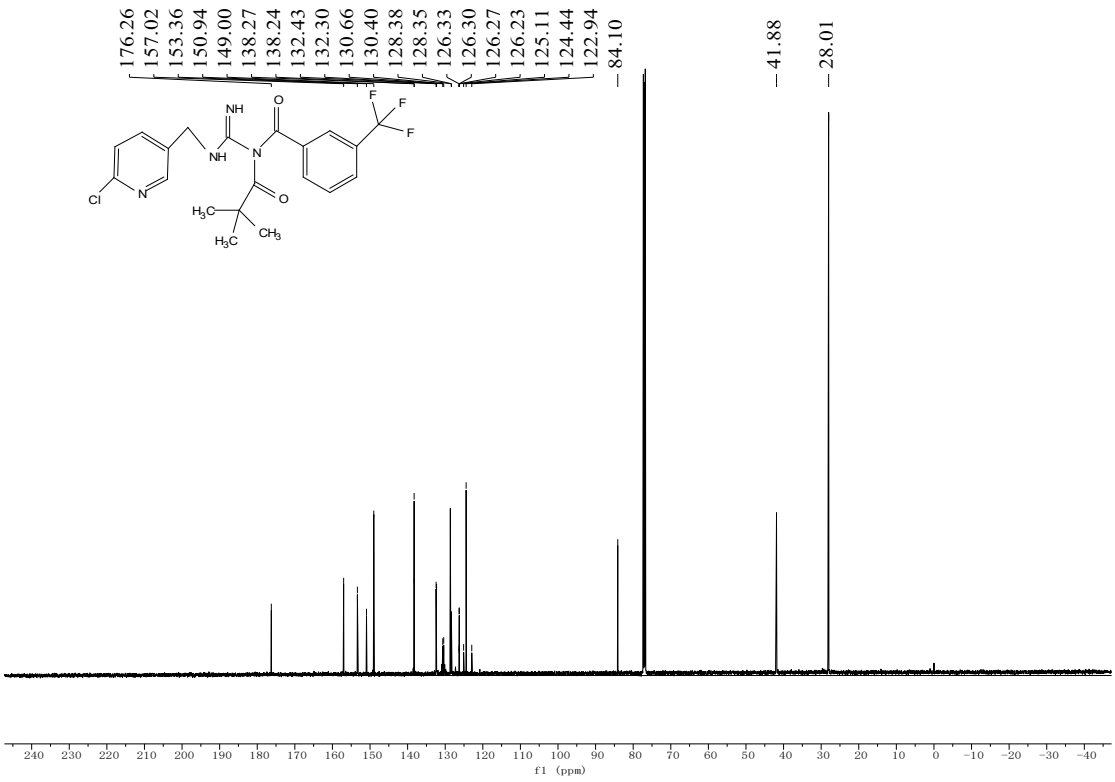

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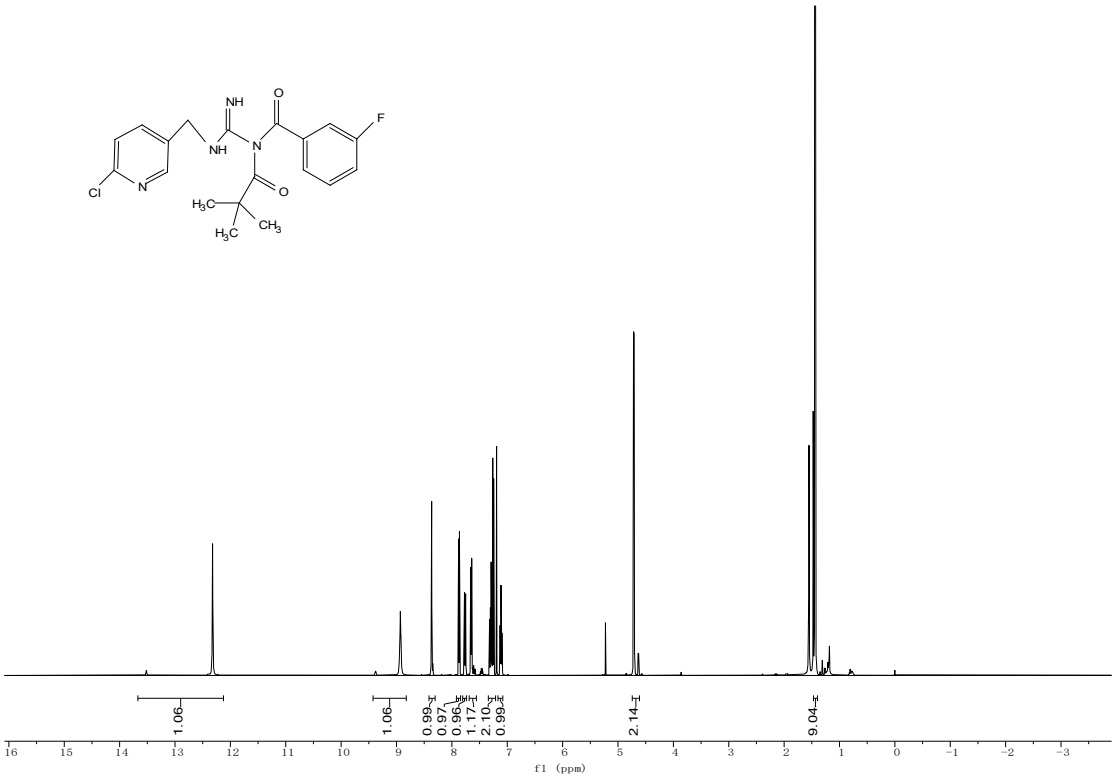

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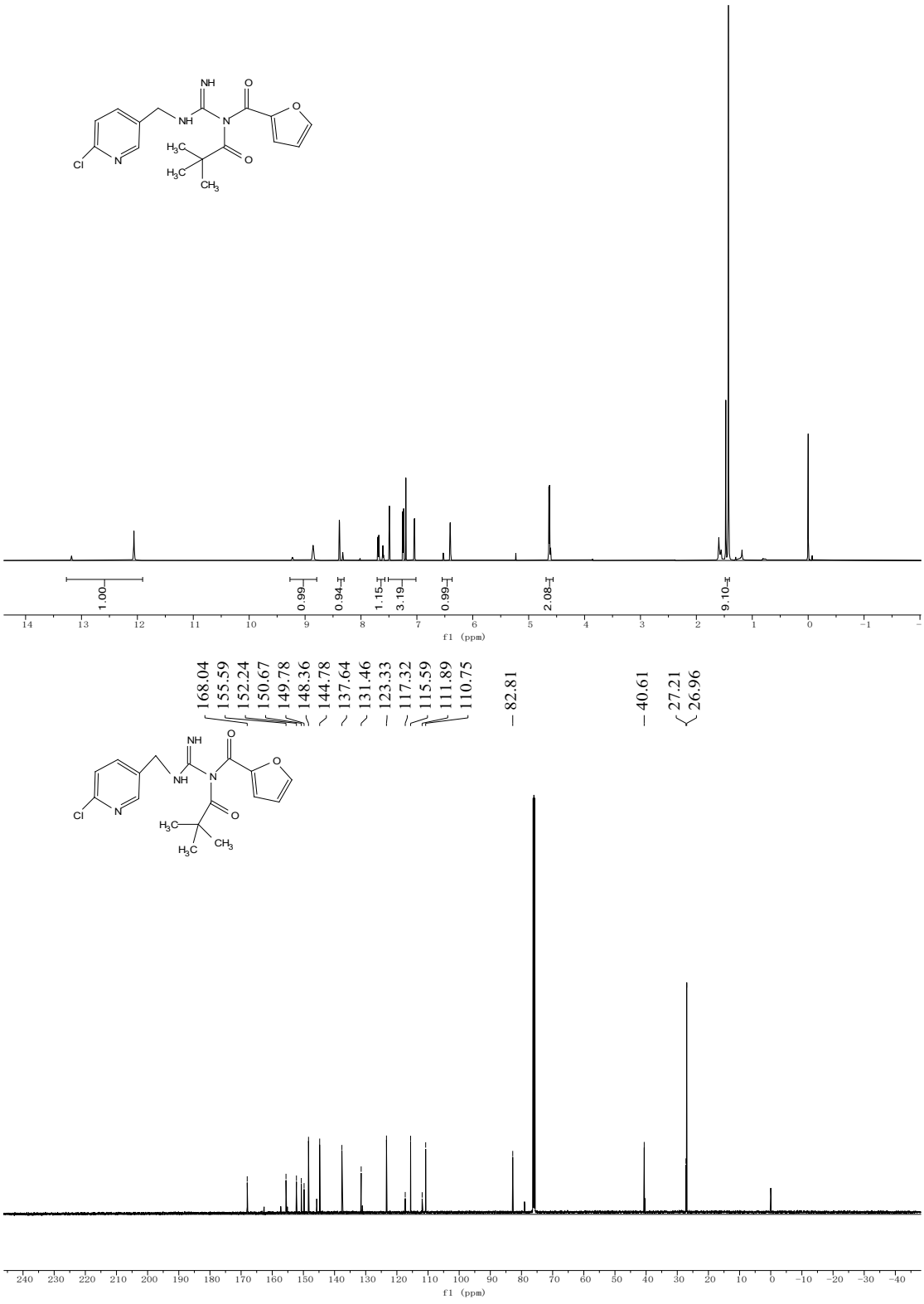
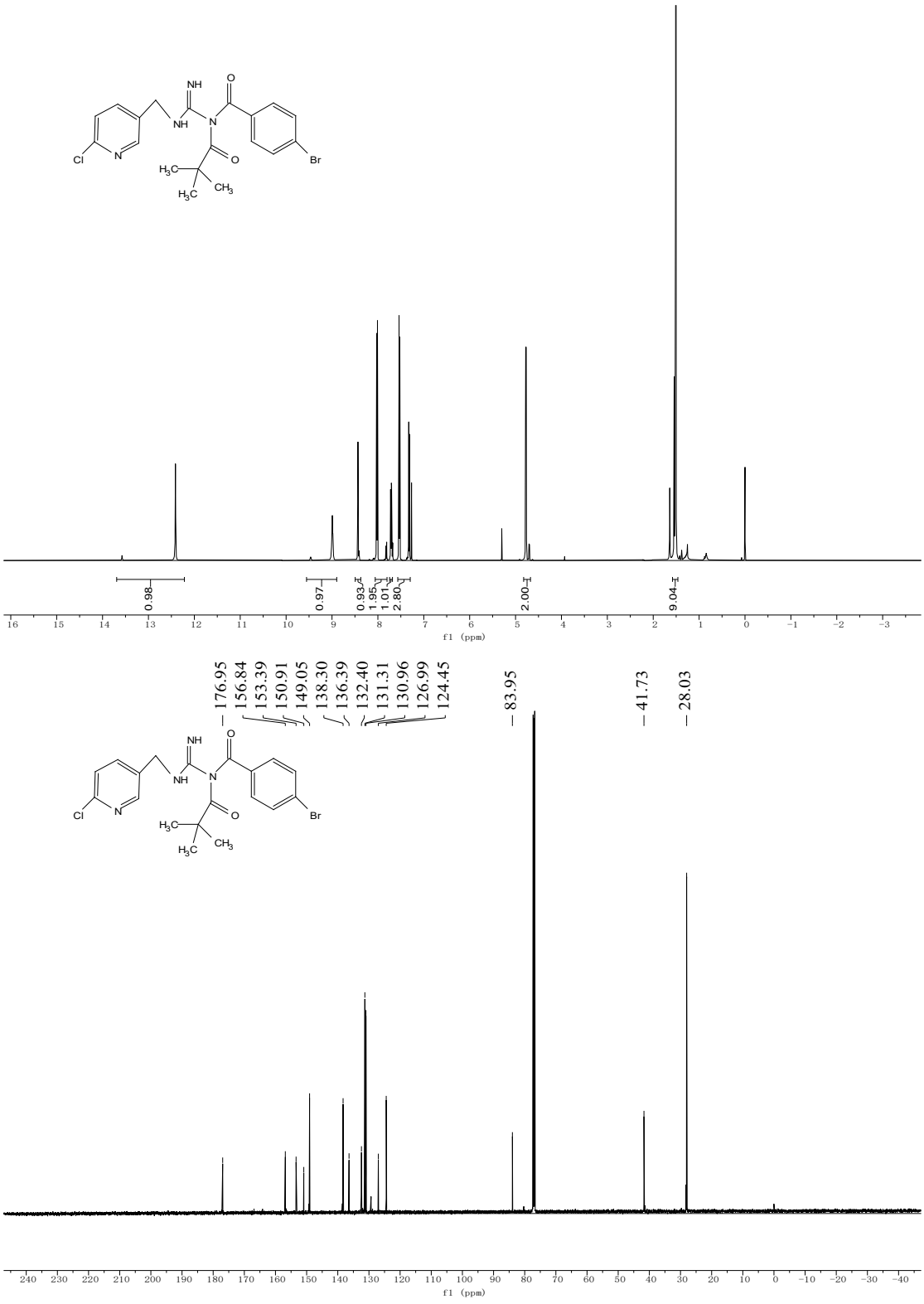


Fig S22. ^{1}H, ^{13}C spectra of **6n**



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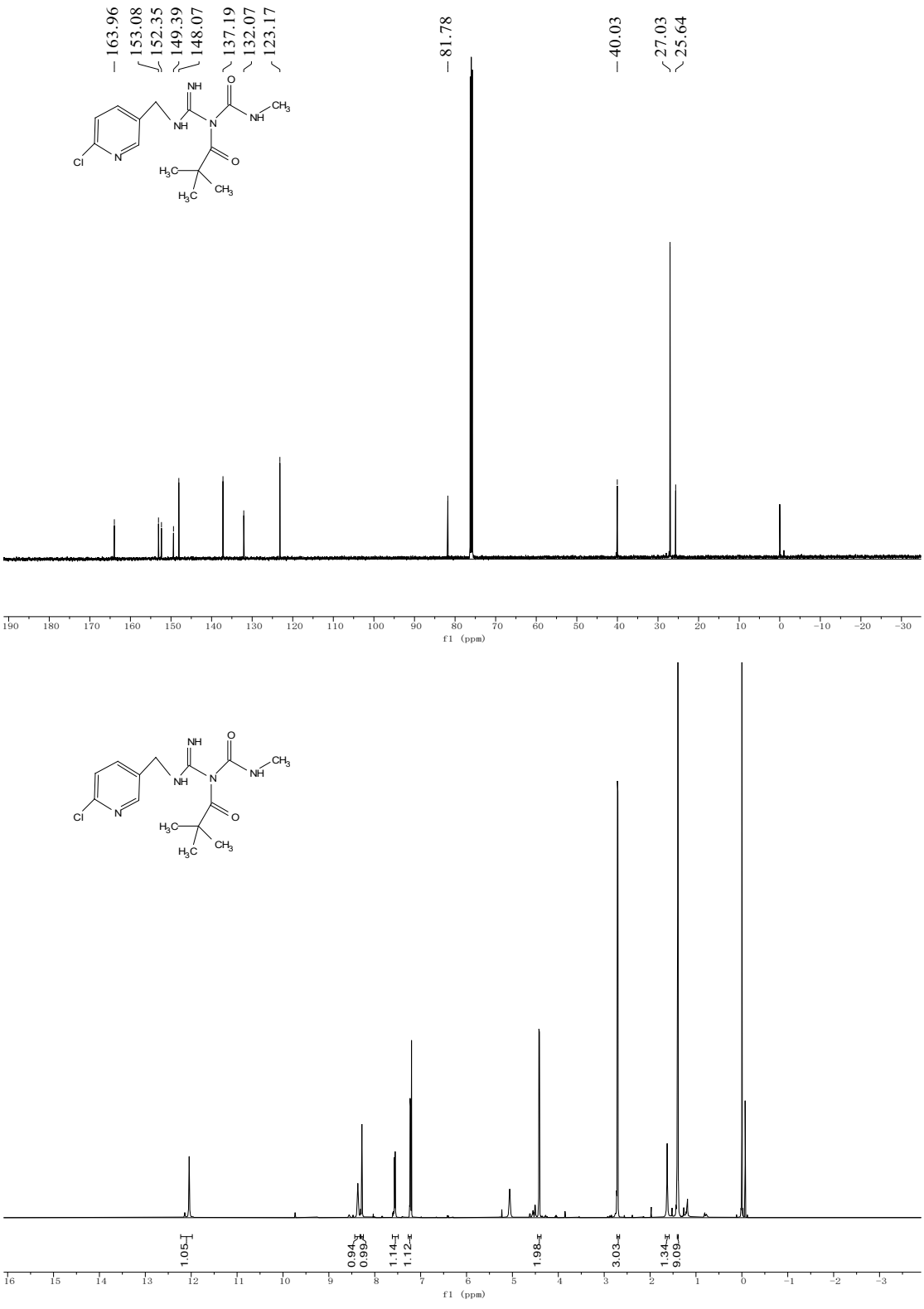

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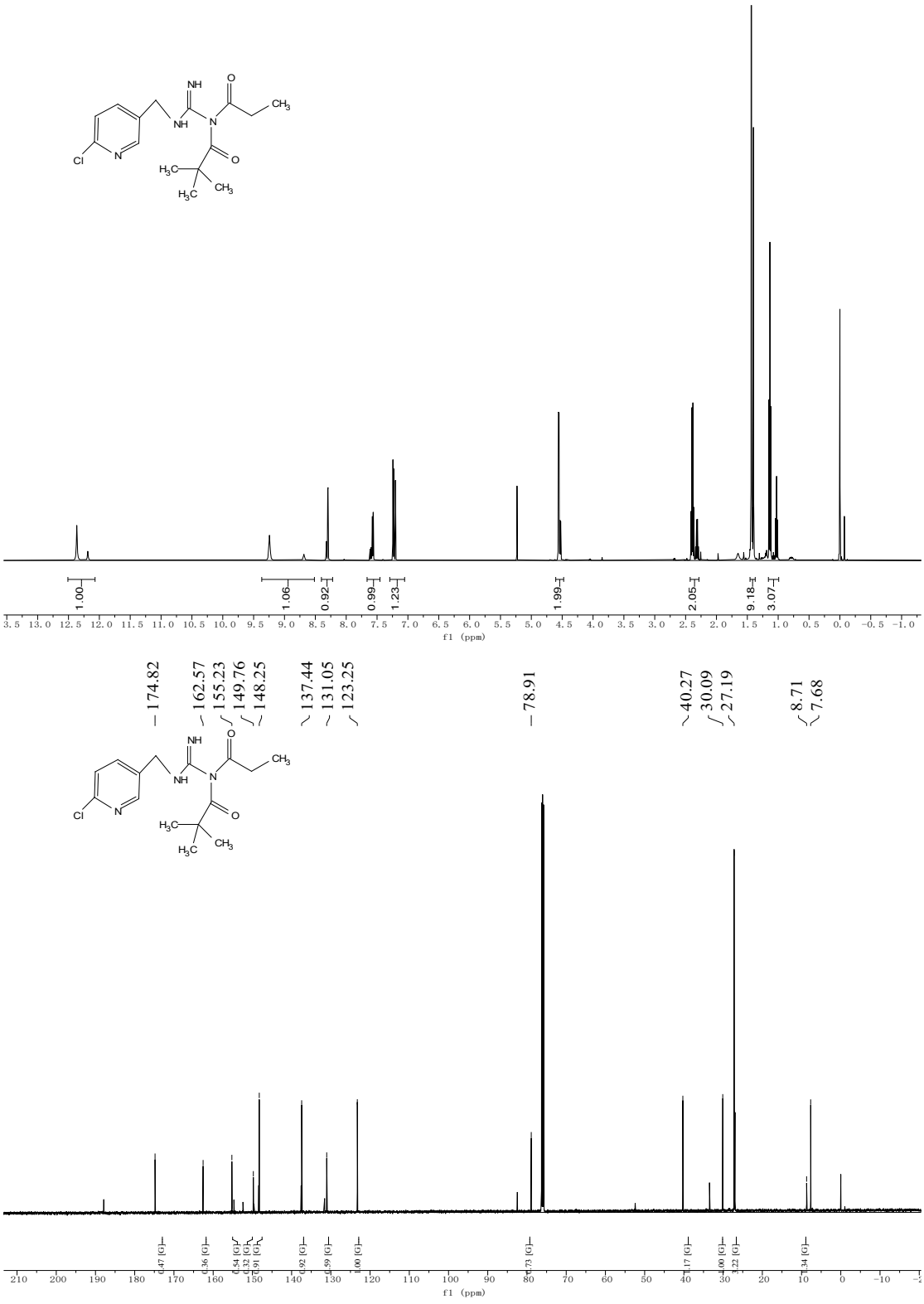

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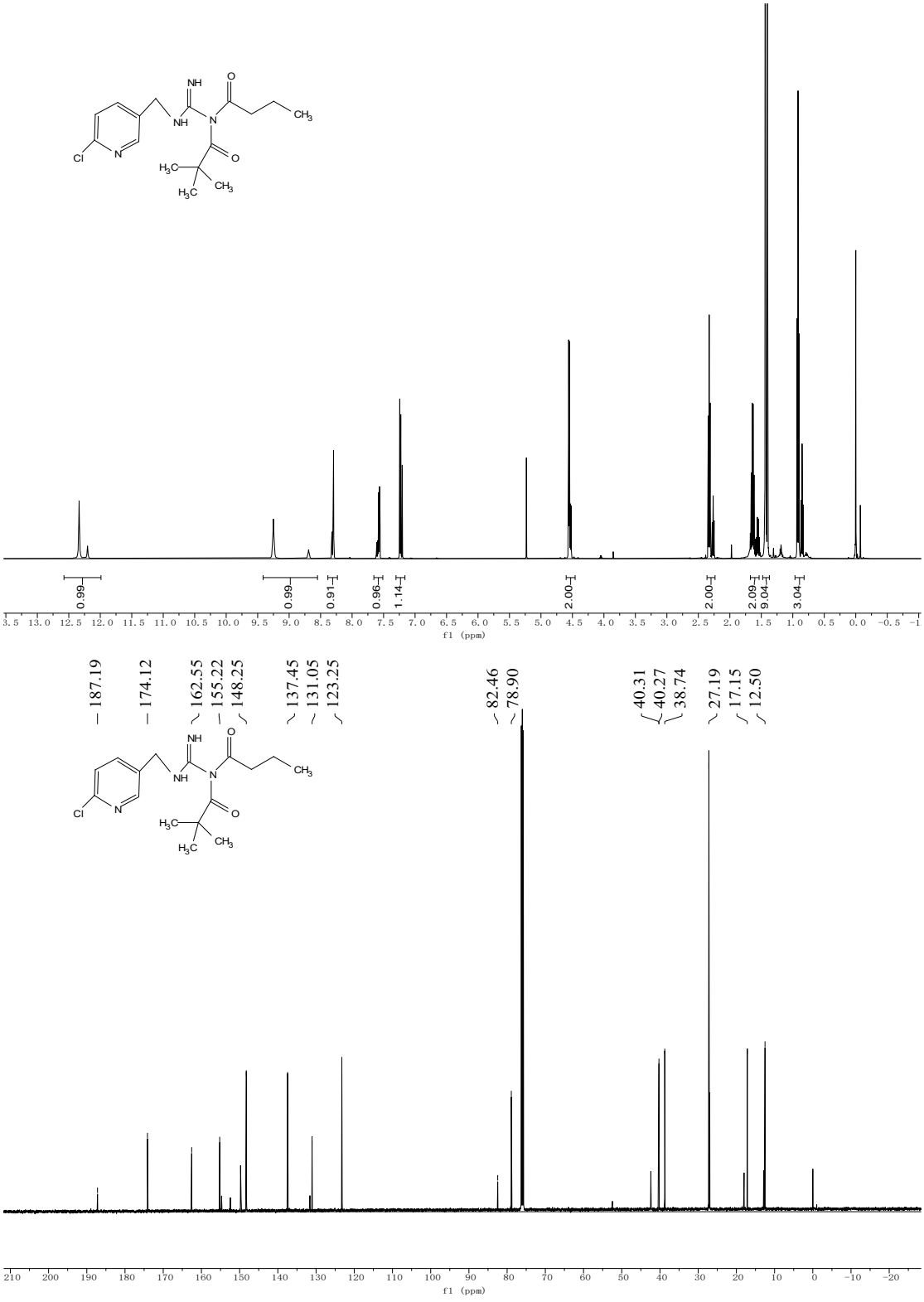

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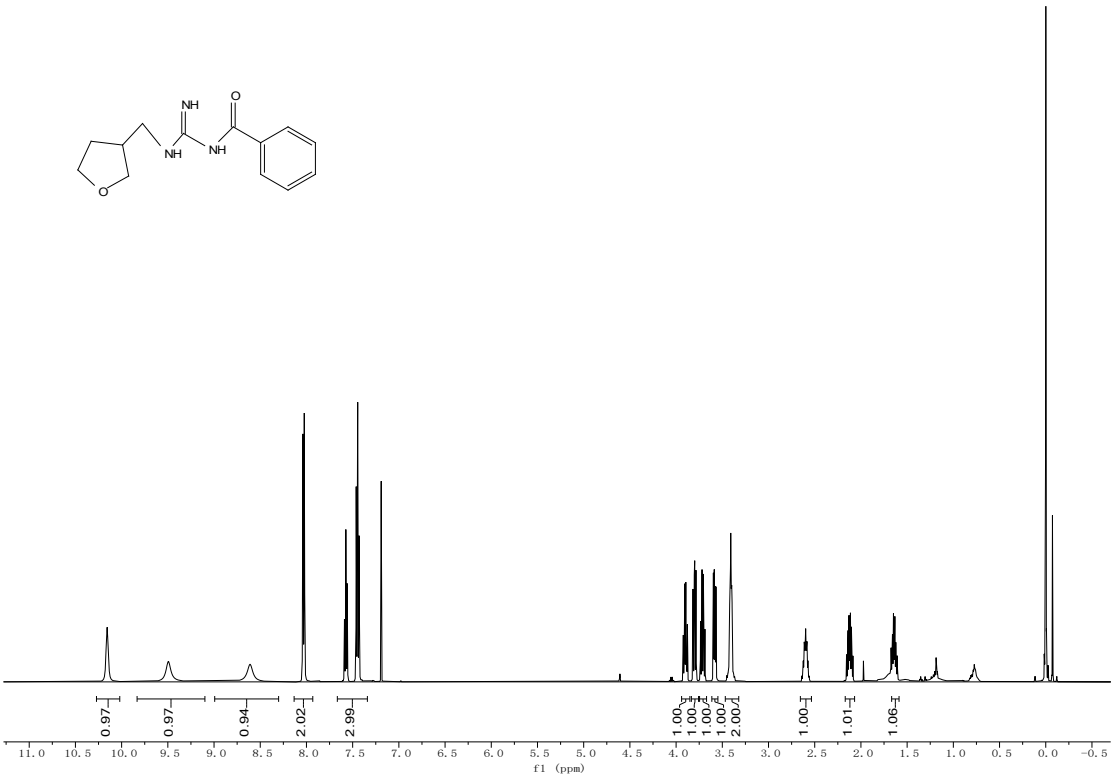
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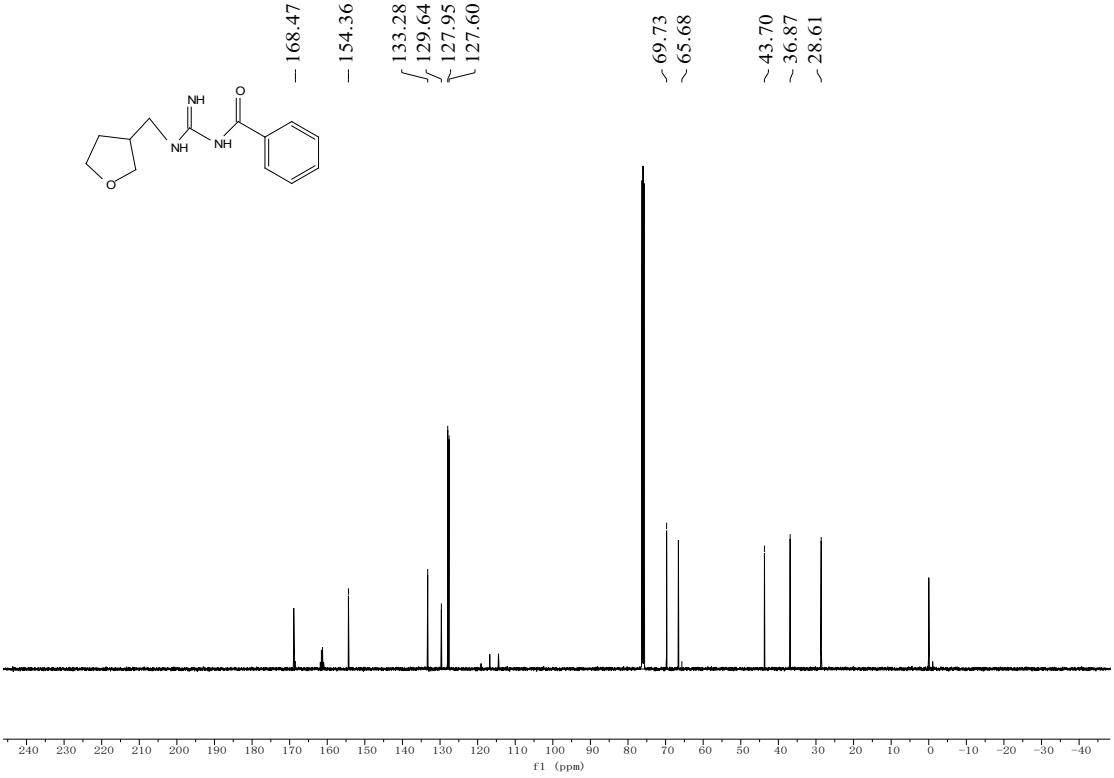
O
NH
NH
O
0.97
0.97
0.94
2.02
2.99
1.00
1.00
1.00
1.00
2.00
1.00
1.01
1.06
f1 (ppm)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154.36
133.28
129.64
127.95
127.60
69.73
65.68
43.70
36.87
28.61
NH
O
NH
NH
O
f1 (ppm)

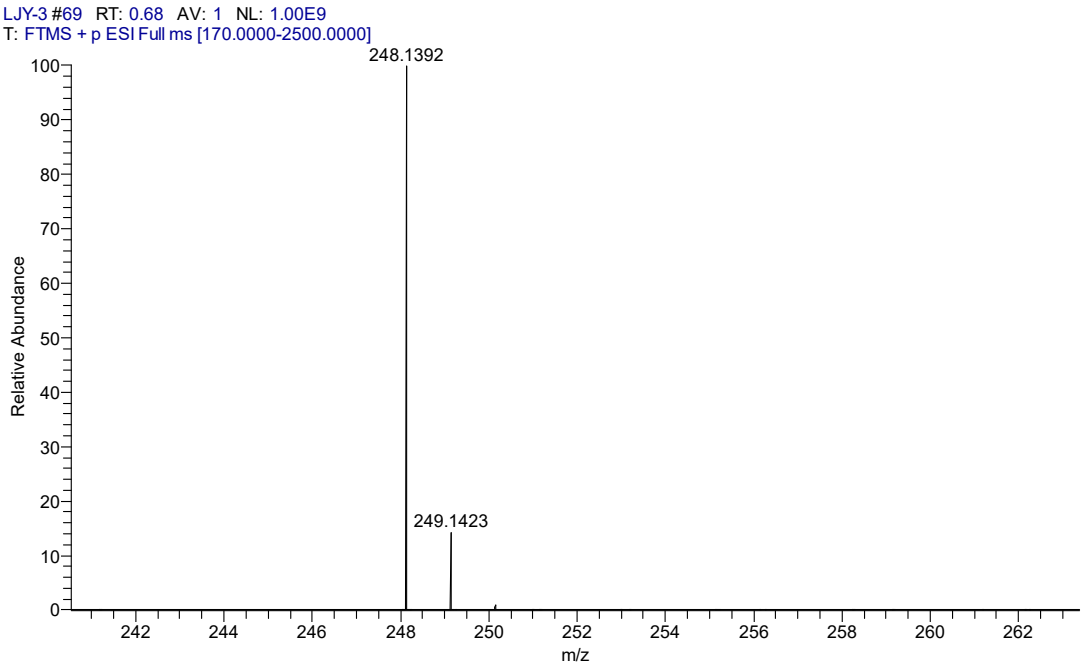
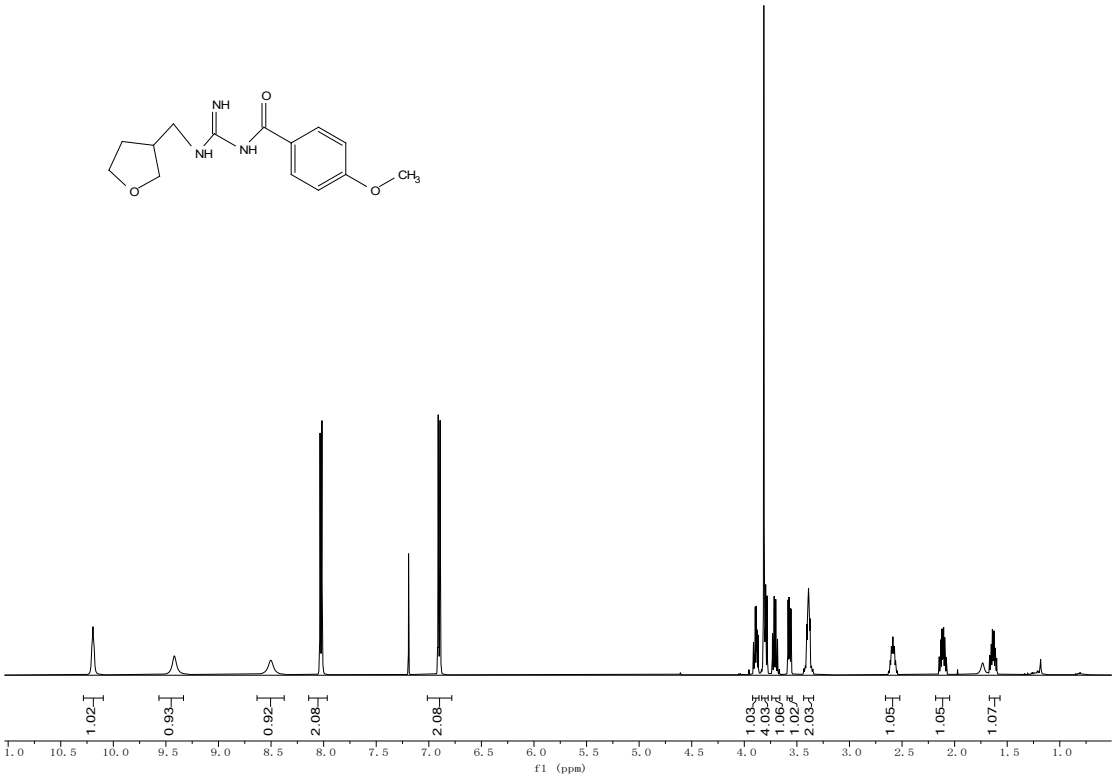
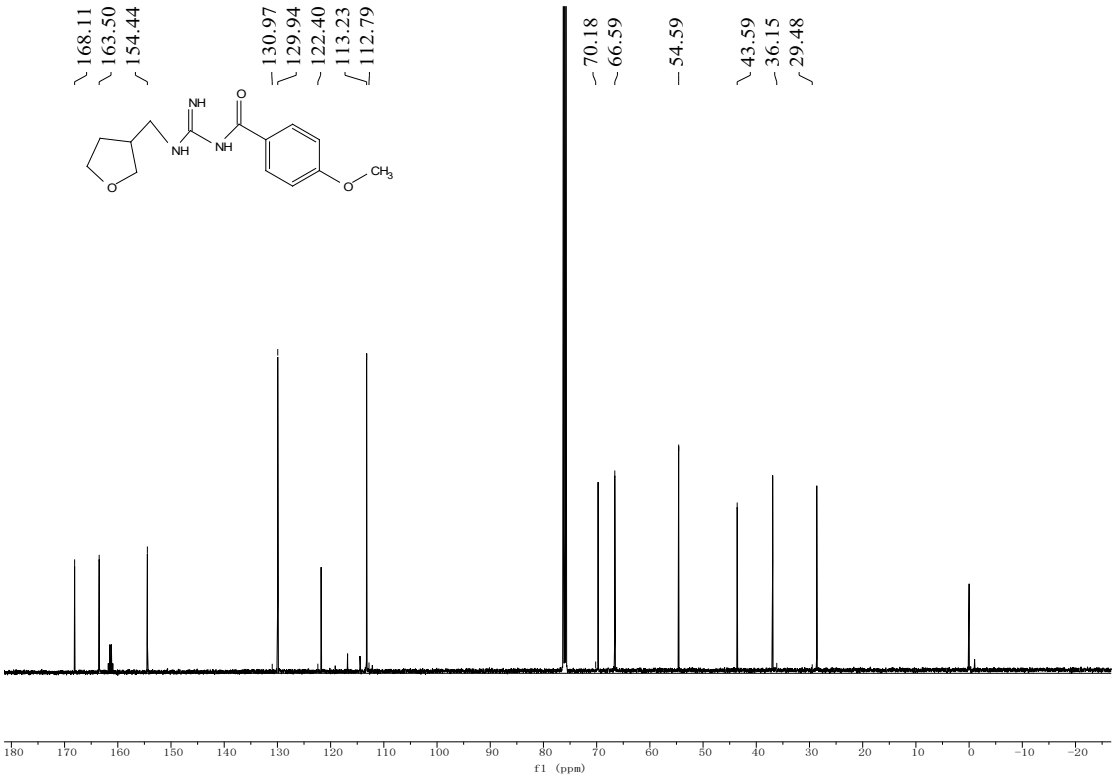


Fig S27. ^{1}H, ^{13}C spectra of **7a**





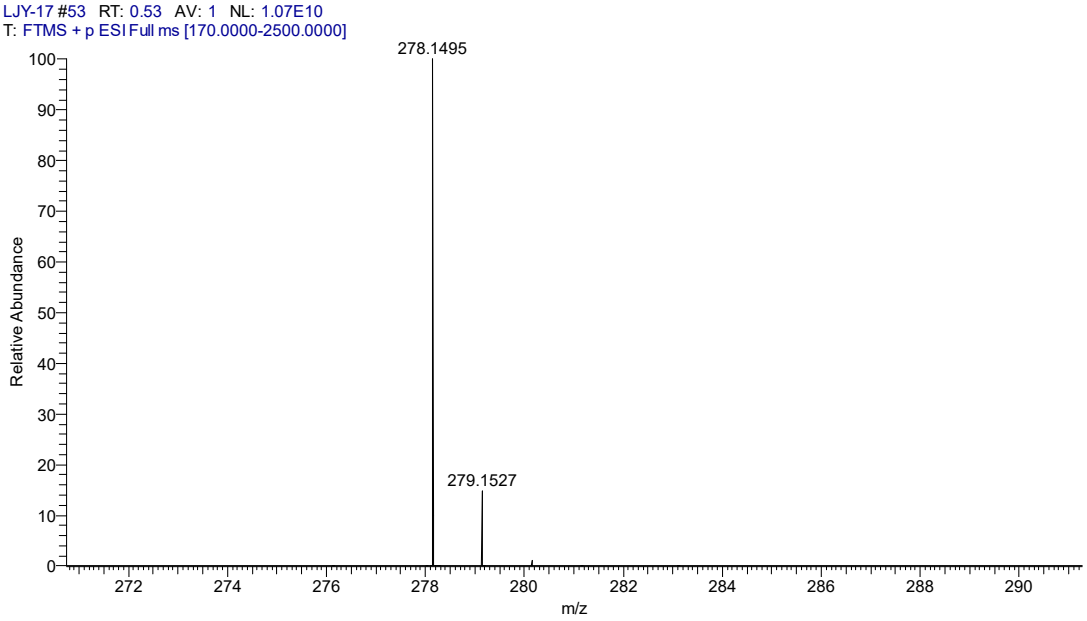
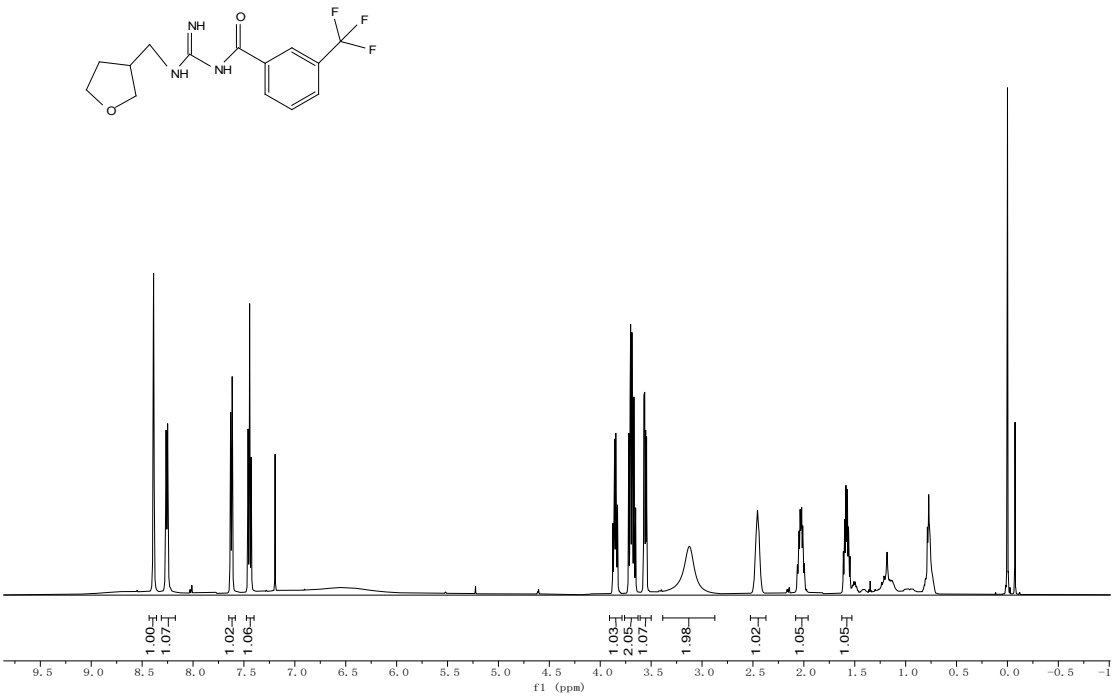
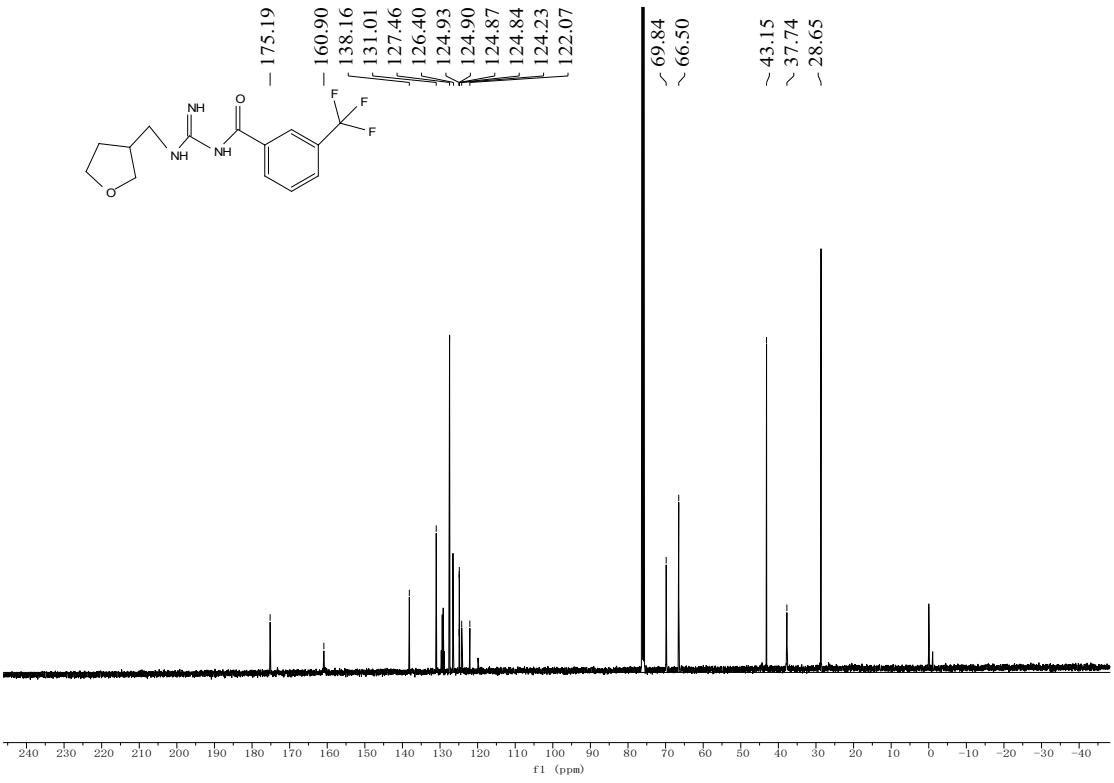


Fig S28. ^{1}H, ^{13}C spectra of **7b**


NH
O
NH
NH
F
F
F
O
1.00
1.07
1.02
1.06
1.03
2.05
1.07
1.98
1.02
1.05
1.05
f1 (ppm)


175.19
160.90
138.16
131.01
127.46
126.40
124.93
124.90
124.87
124.84
124.23
122.07
69.84
66.50
43.15
37.74
28.65
NH
O
NH
NH
F
F
F
O
f1 (ppm)

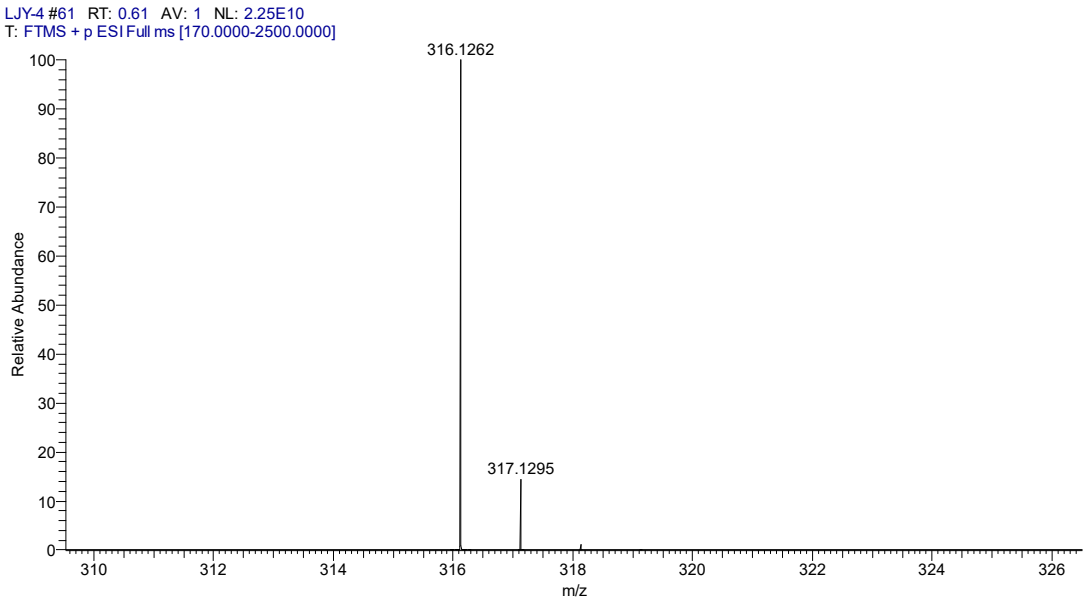
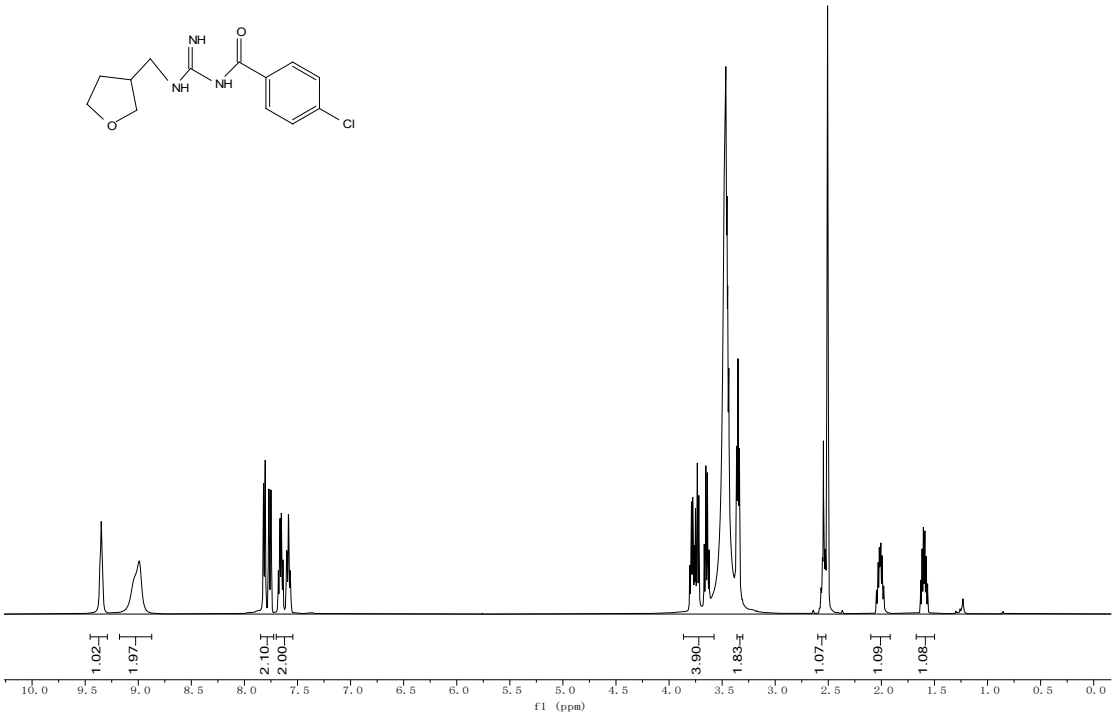
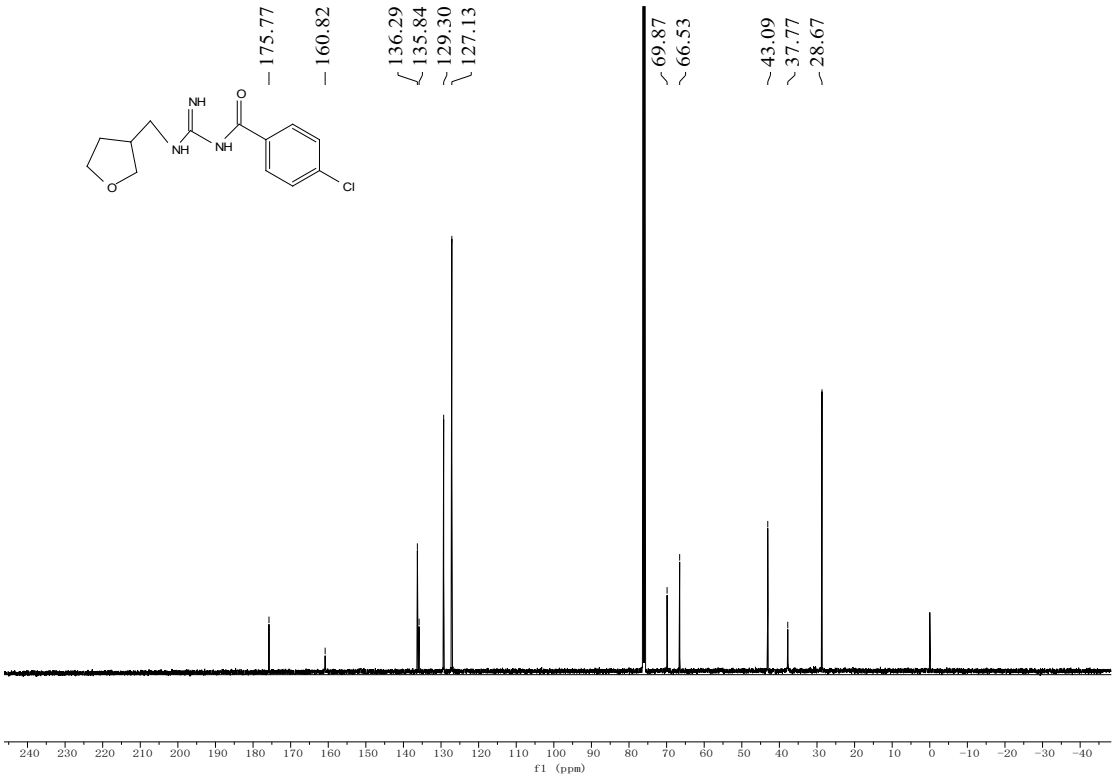


Fig S29. ^{1}H, ^{13}C spectra of **7c**





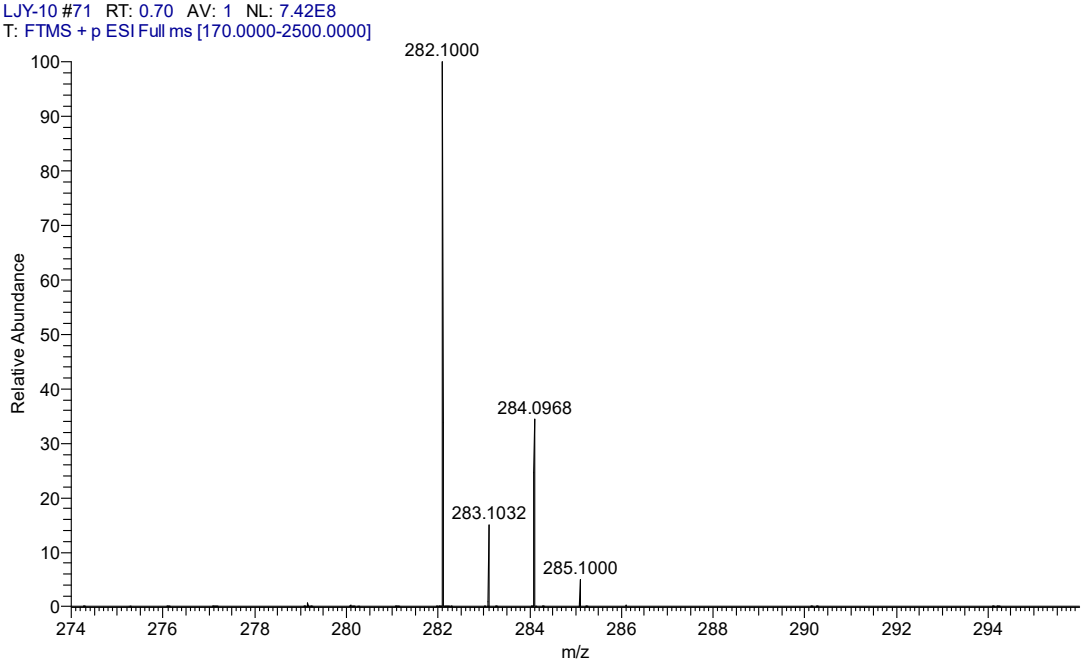
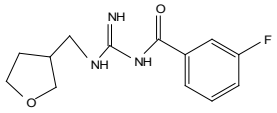
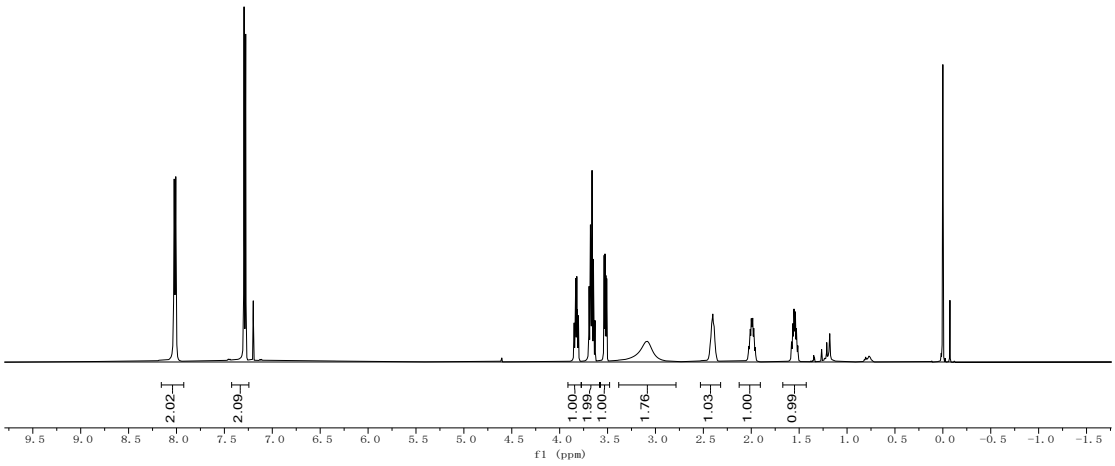
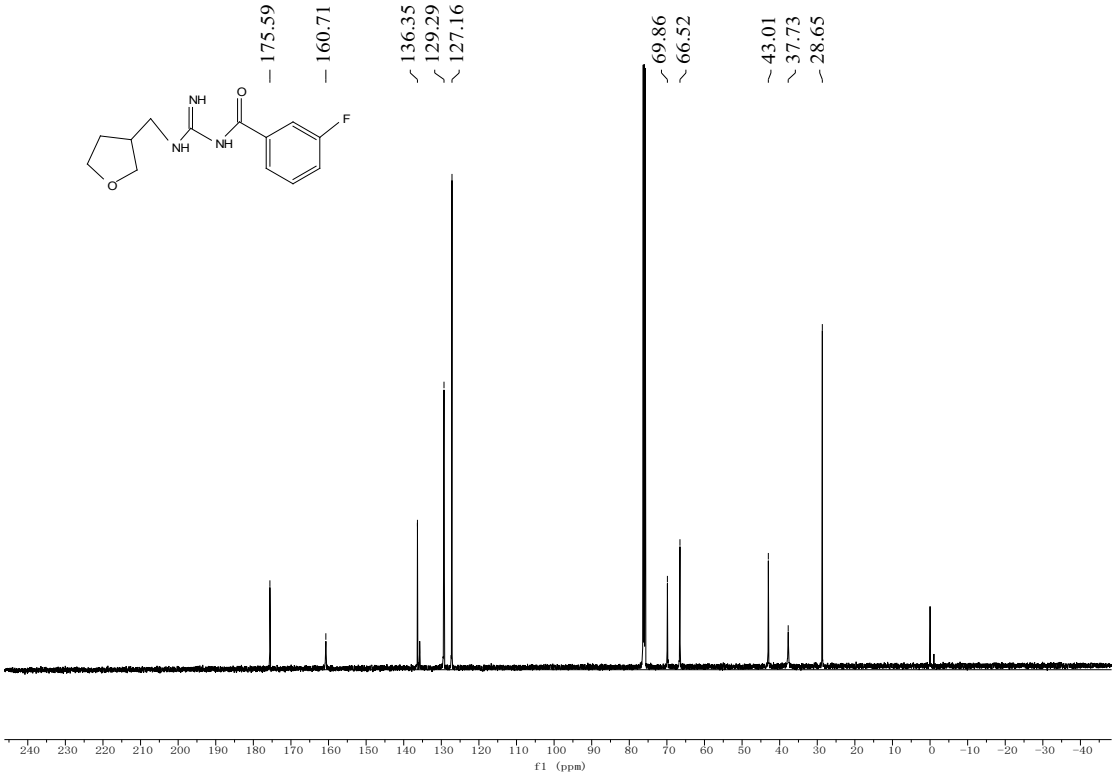


Fig S30. ^{1}H, ^{13}C spectra of **7d**


NH
O
F
NH
NH
O


2.02
2.09
1.00
1.99
1.00
1.76
1.03
1.00
0.99
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)


175.59
160.71
136.35
129.29
127.16
69.86
66.52
43.01
37.73
28.65
NH
O
F
NH
NH
O
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

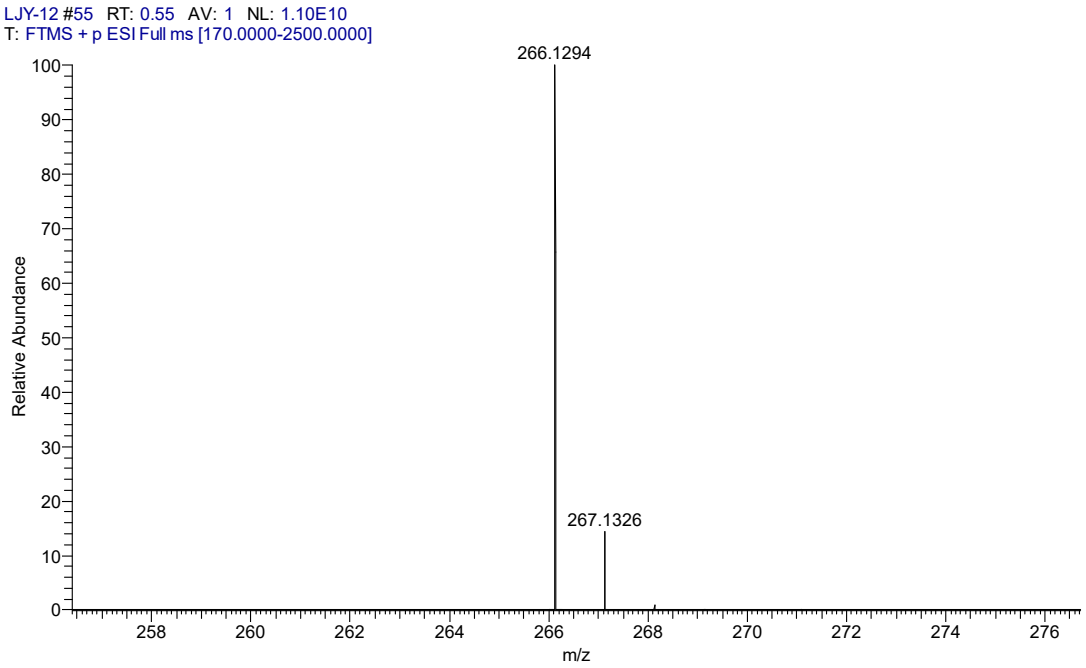
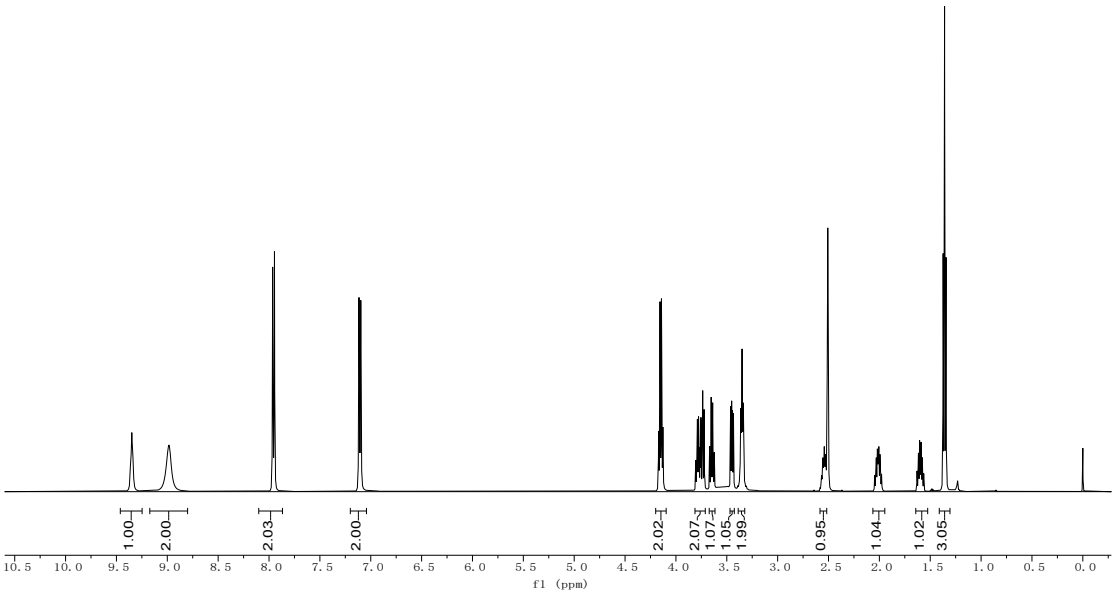
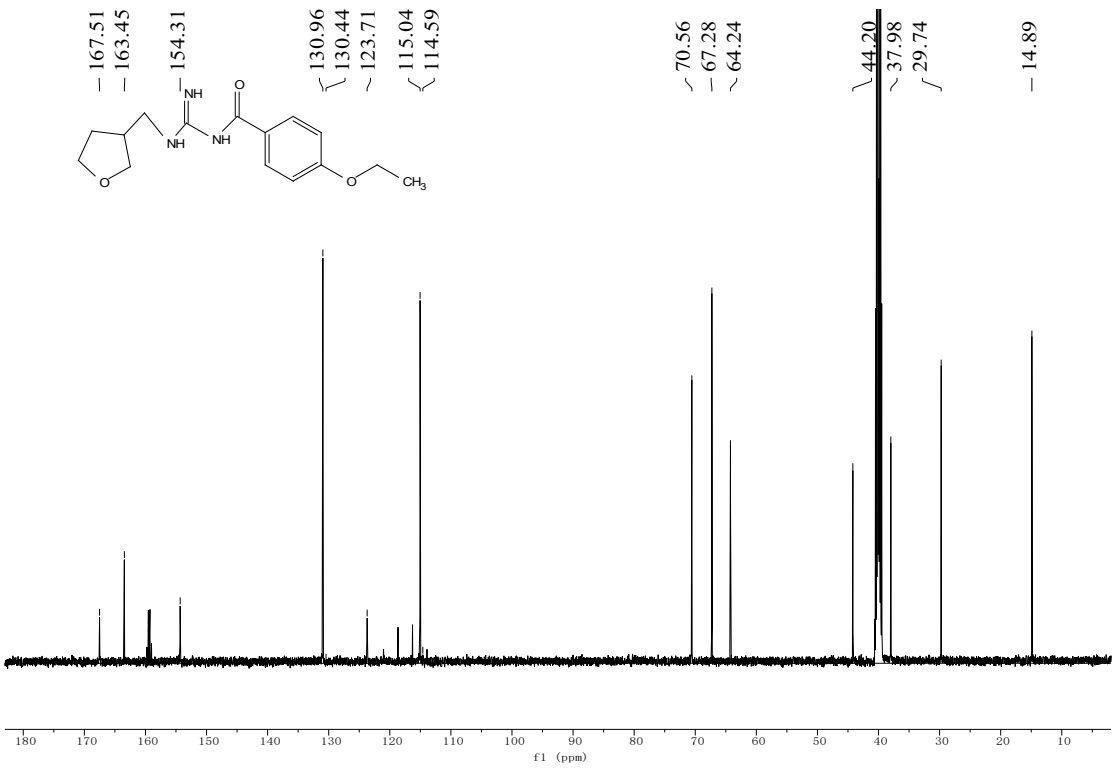


Fig S31. ^{1}H, ^{13}C spectra of **7e**





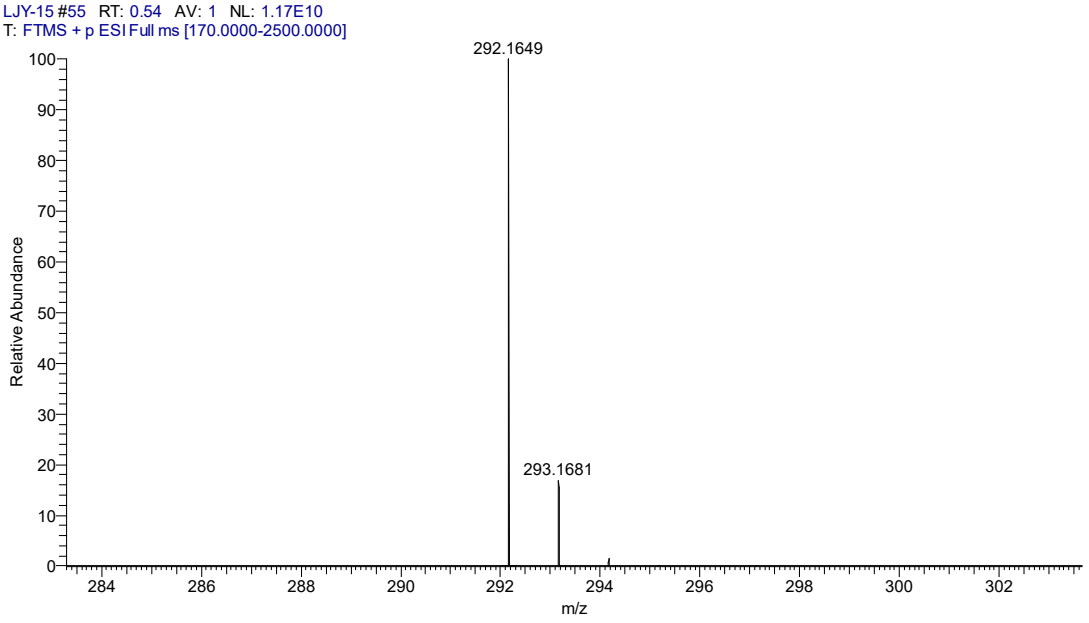
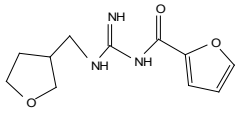
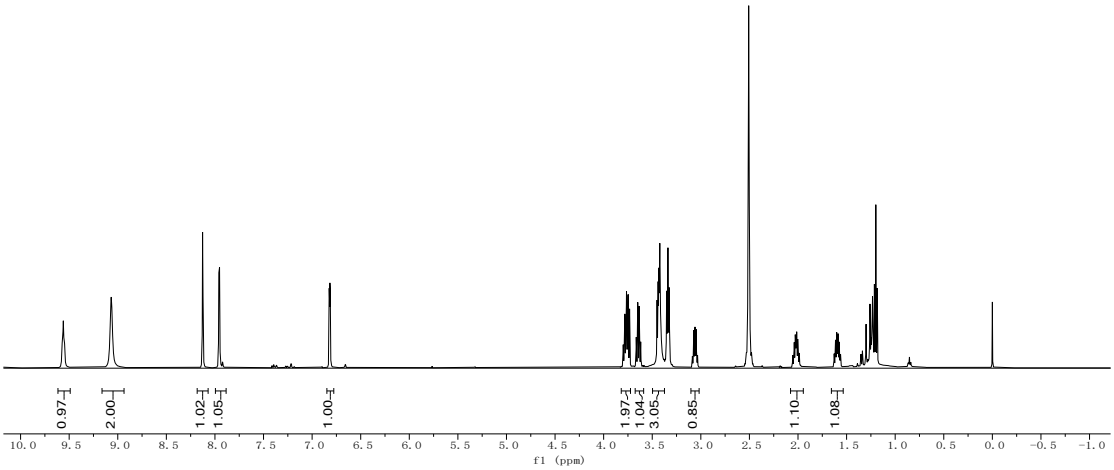
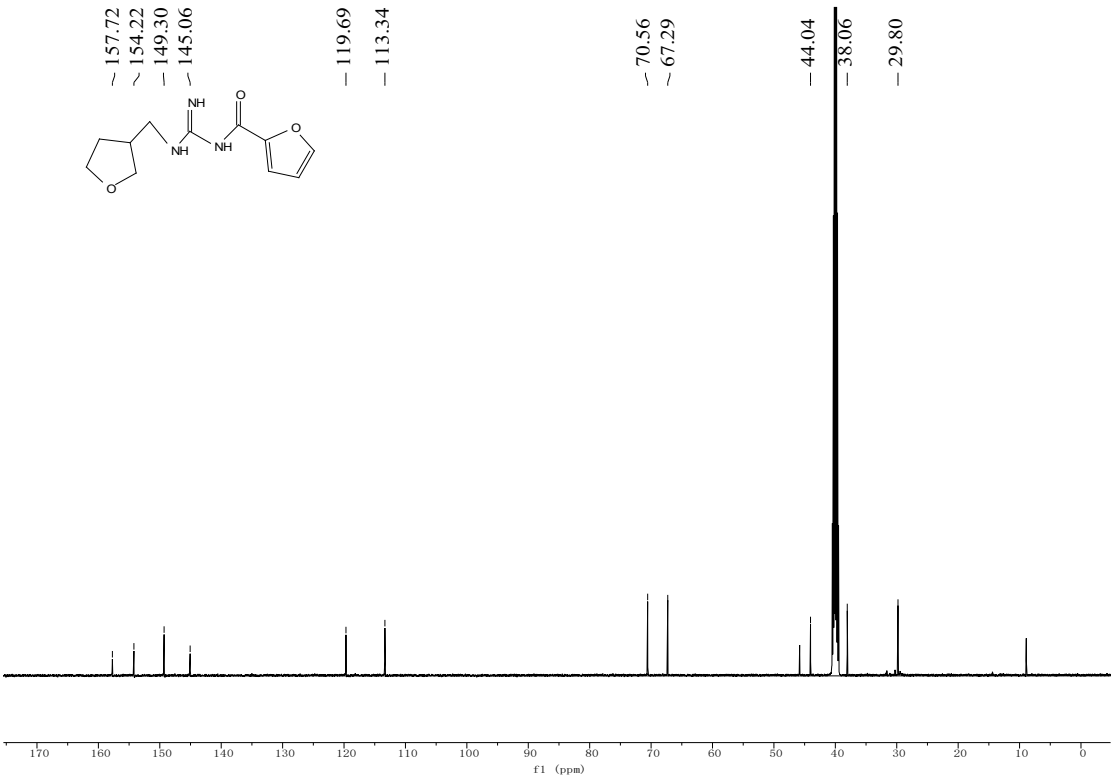


Fig S32. ^{1}H, ^{13}C spectra of **7f**


NH
O
NH
NH
O
O


0.97
2.00
1.02
1.05
1.00
1.97
1.04
3.05
0.85
1.10
1.08
f1 (ppm)


157.72
154.22
149.30
145.06
119.69
113.34
70.56
67.29
44.04
38.06
29.80
f1 (ppm)

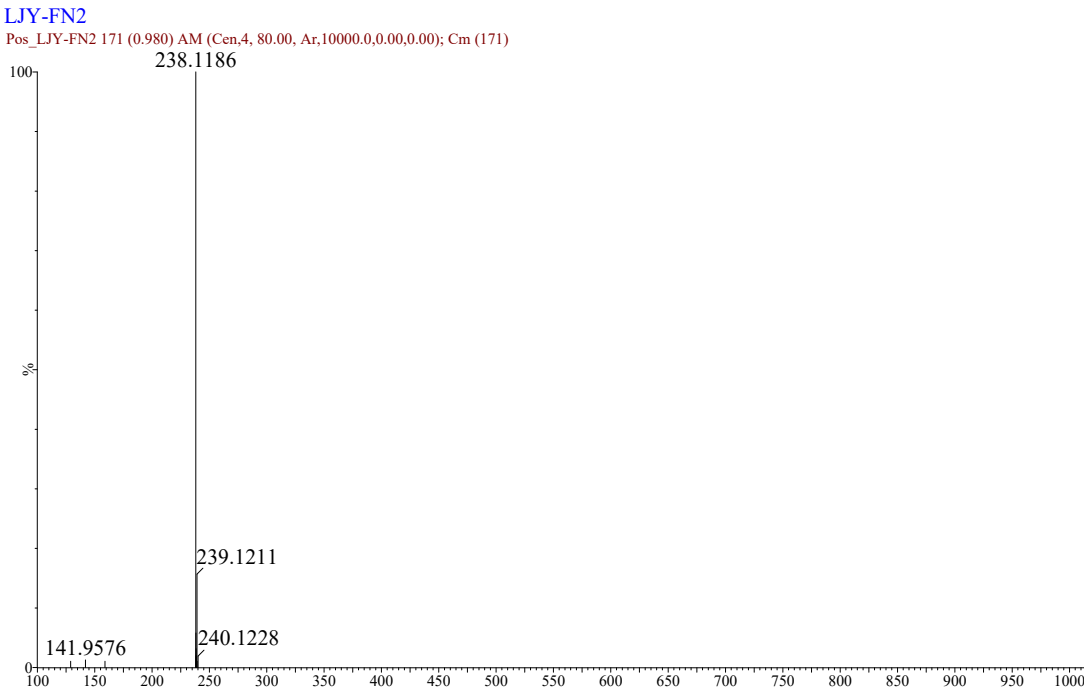
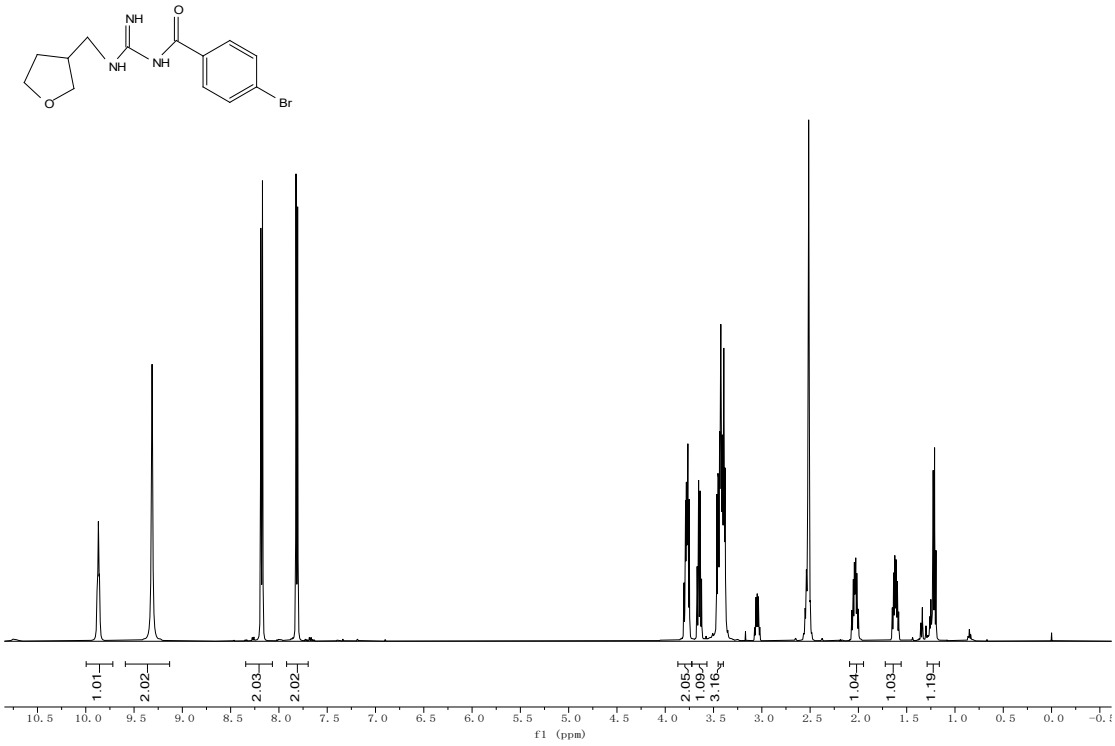
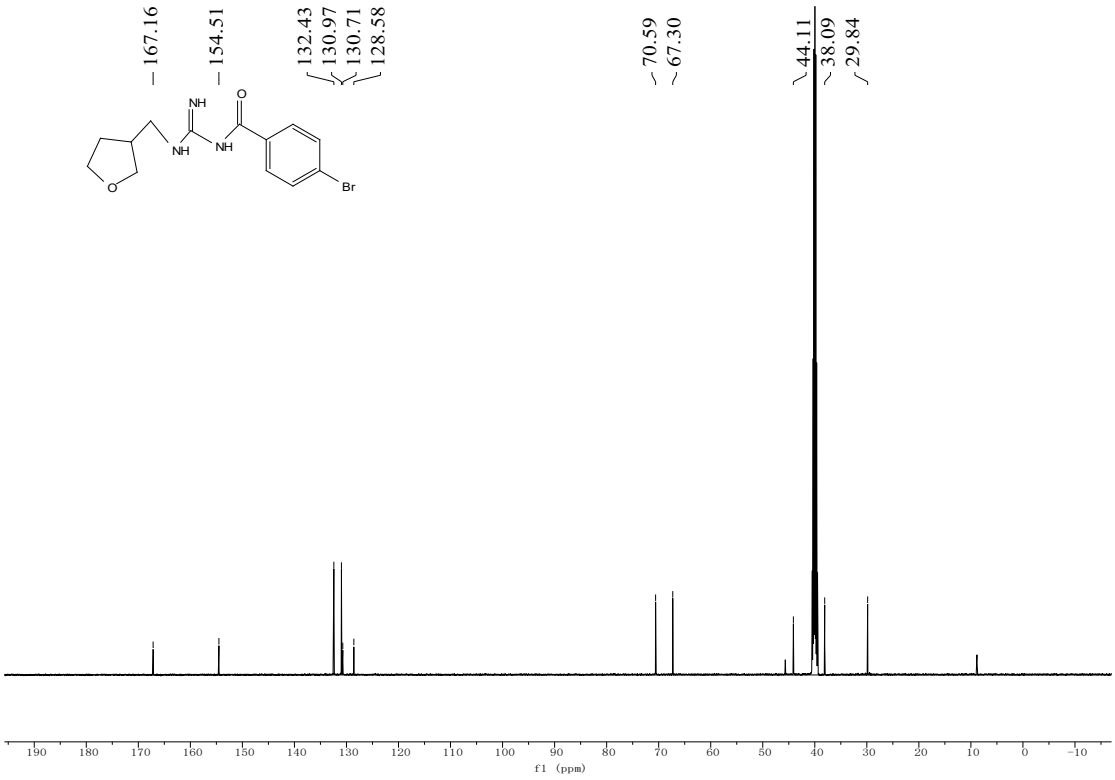


Fig S33. ^{1}H, ^{13}C spectra of **7g**





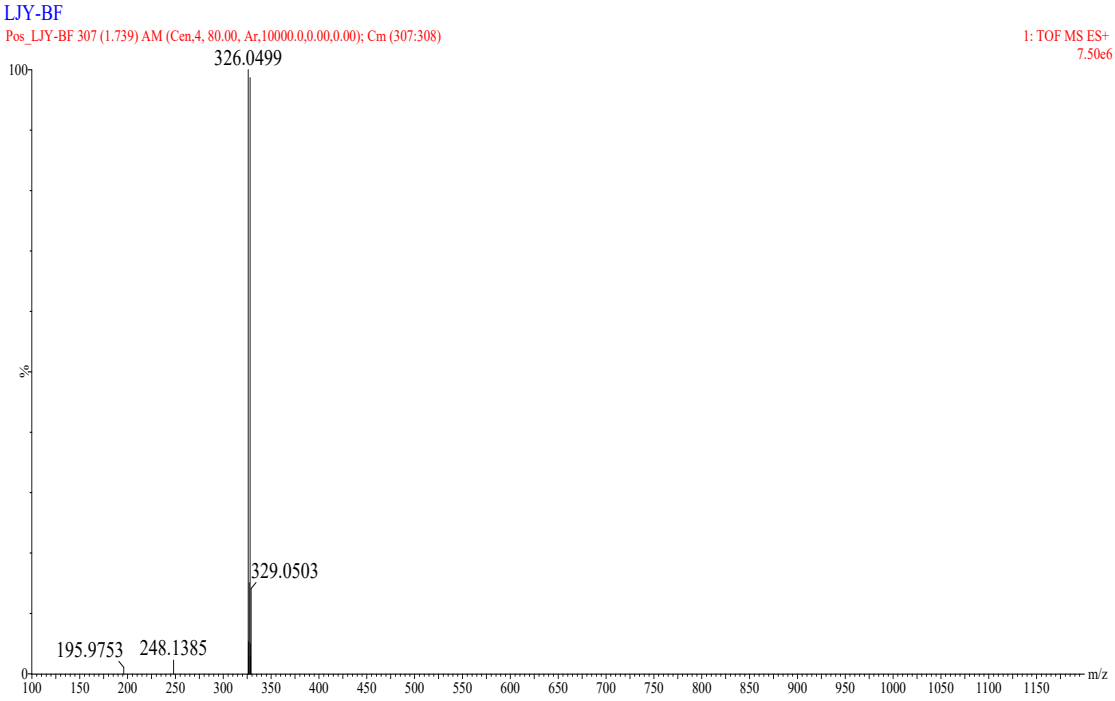
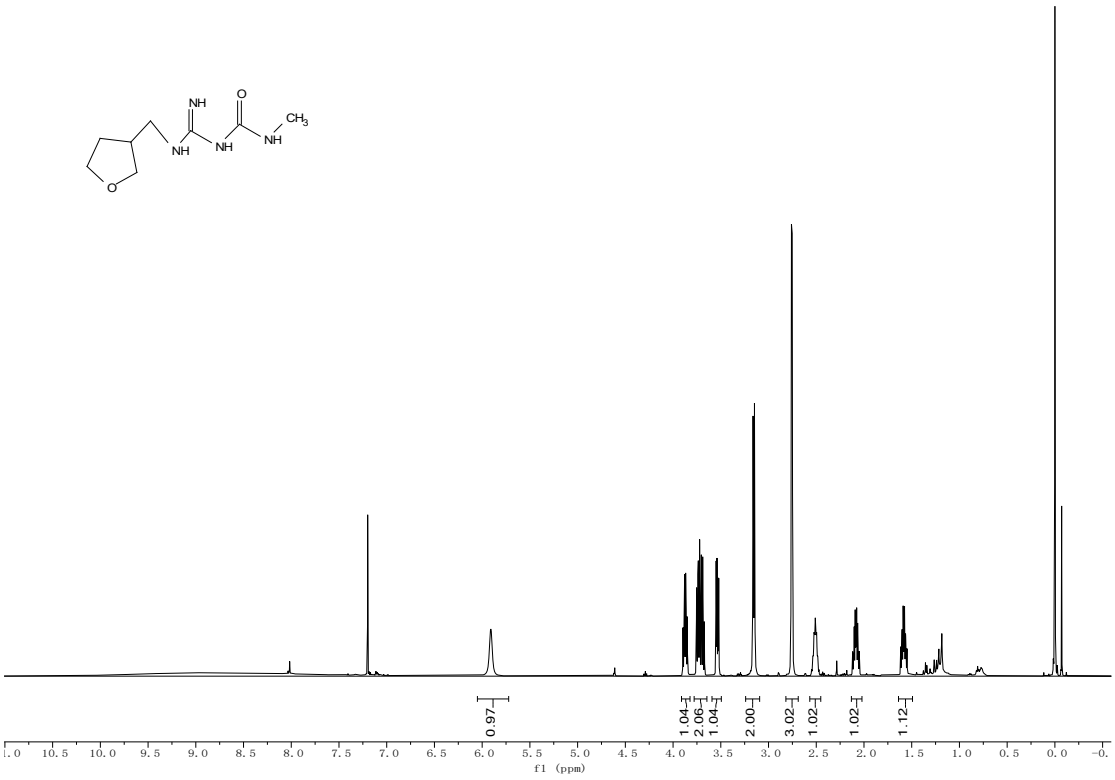
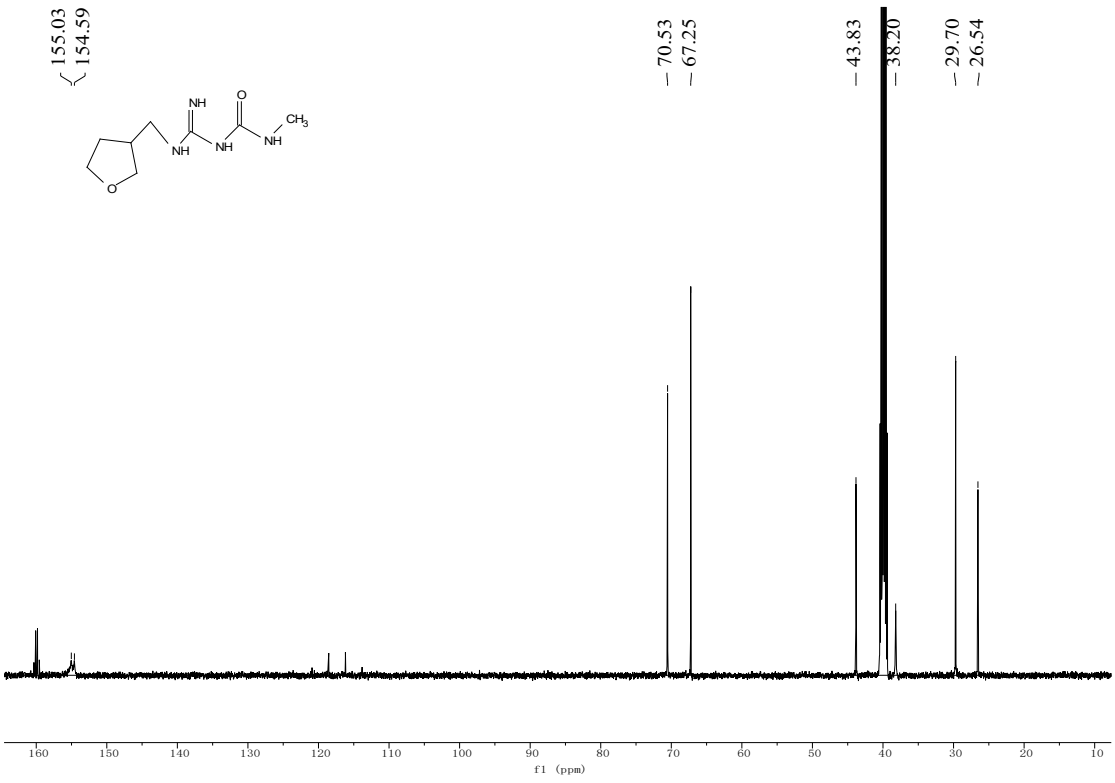


Fig S34. ^{1}H, ^{13}C spectra of **7h**


NH
O
CH3
NH
NH
NH
O
0.97
1.04
2.06
1.04
2.00
3.02
1.02
1.02
1.12
f1 (ppm)


155.03
154.59
70.53
67.25
43.83
38.20
29.70
26.54
NH
O
CH3
NH
NH
NH
O
f1 (ppm)

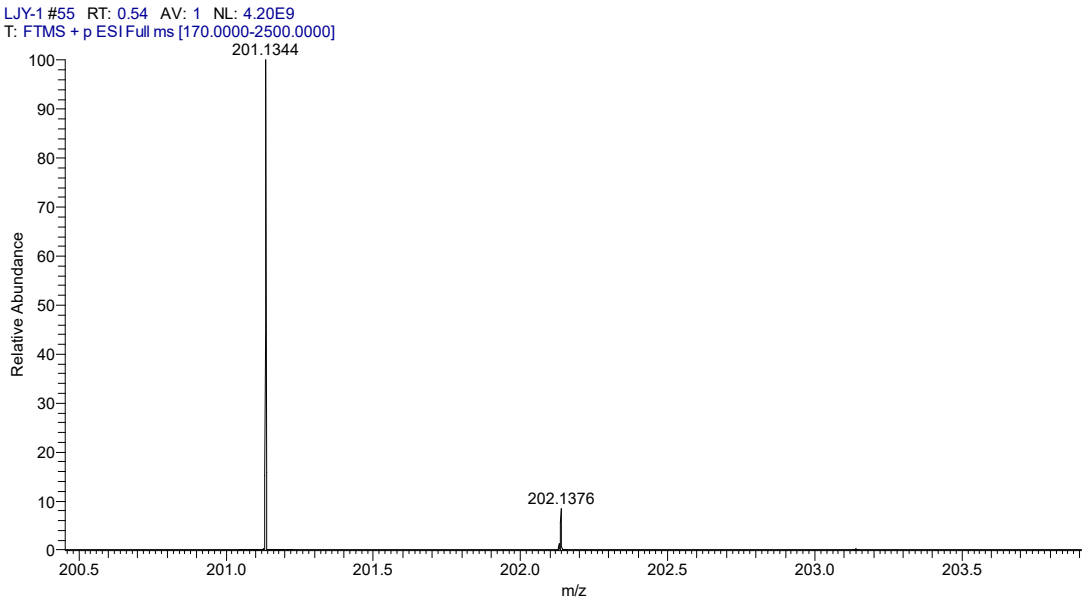
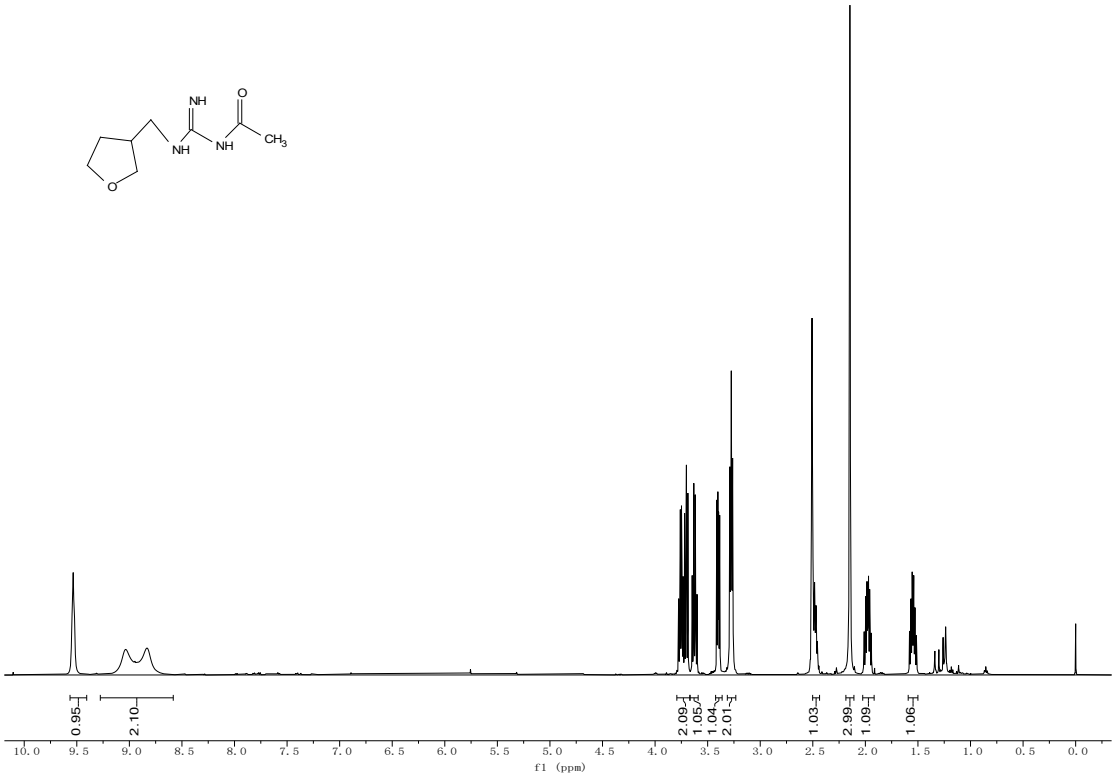
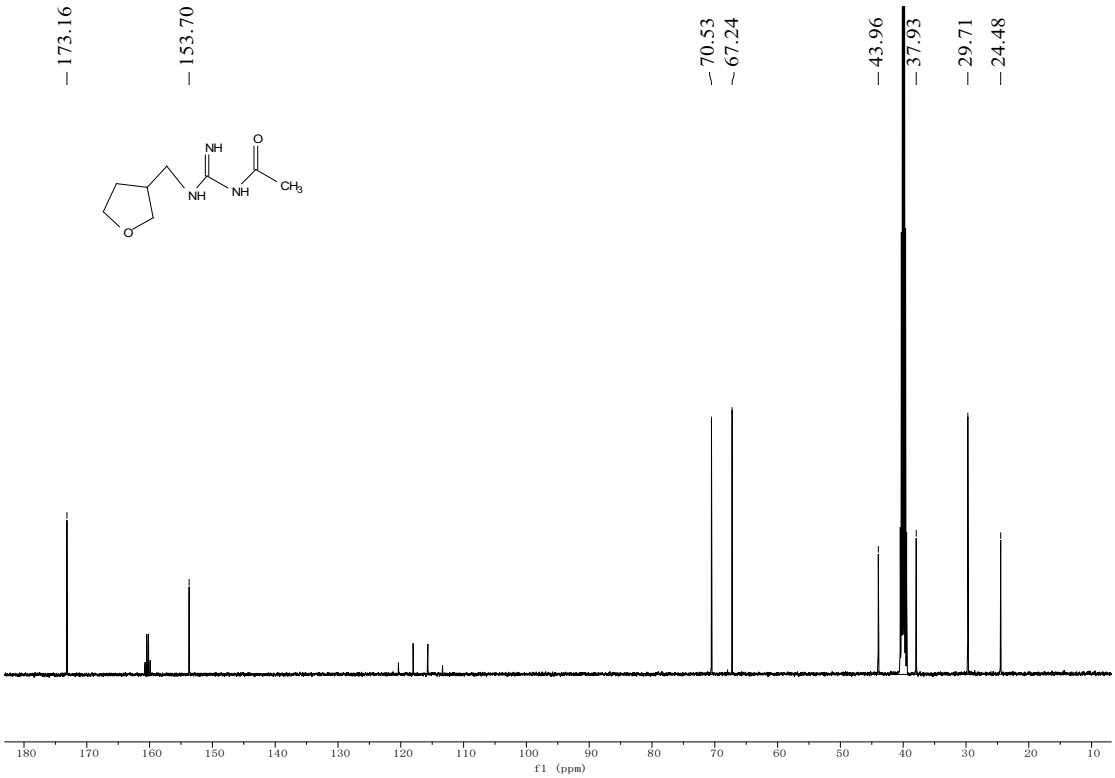


Fig S35. ^{1}H, ^{13}C spectra of **7i**





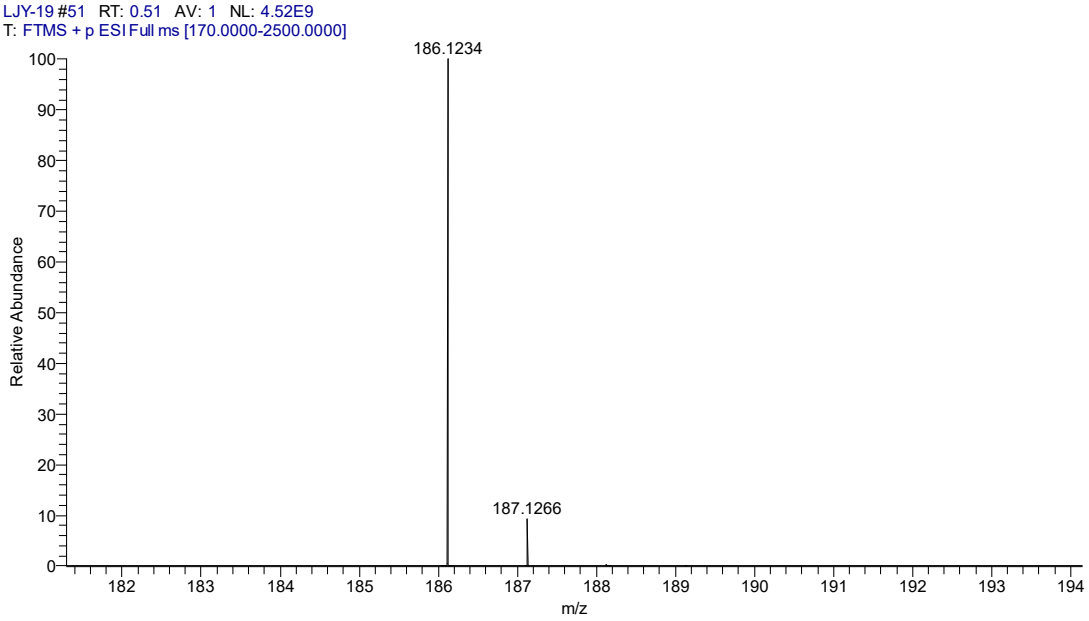
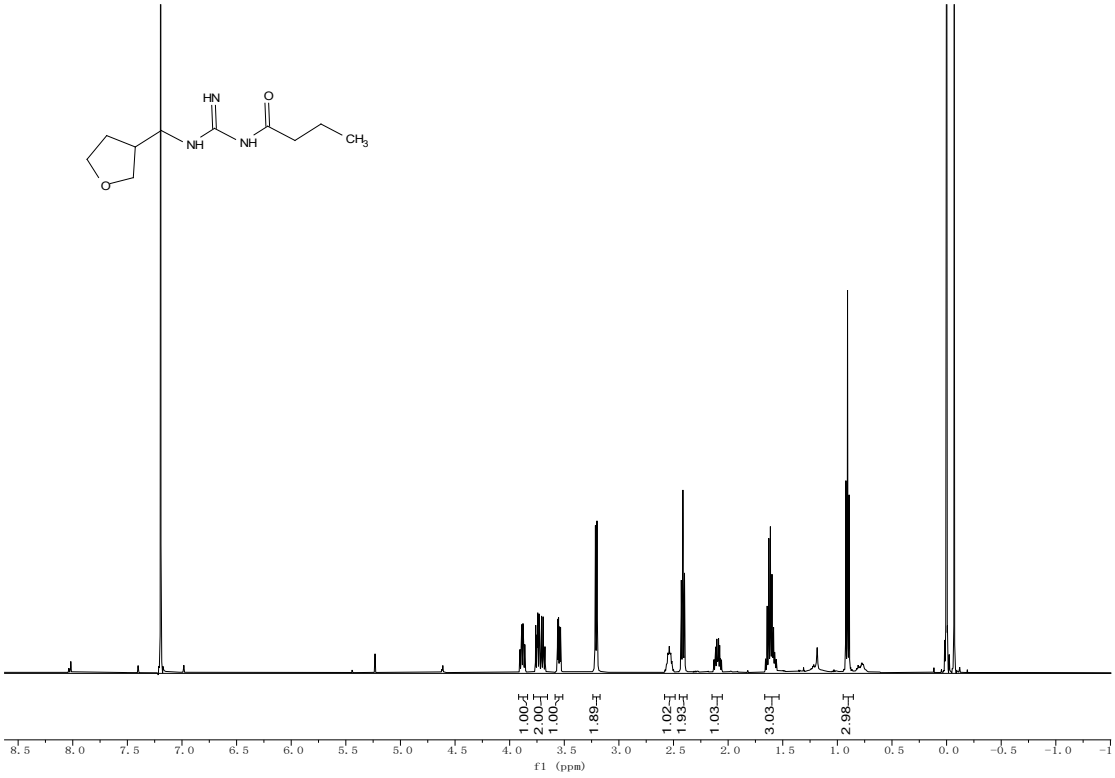
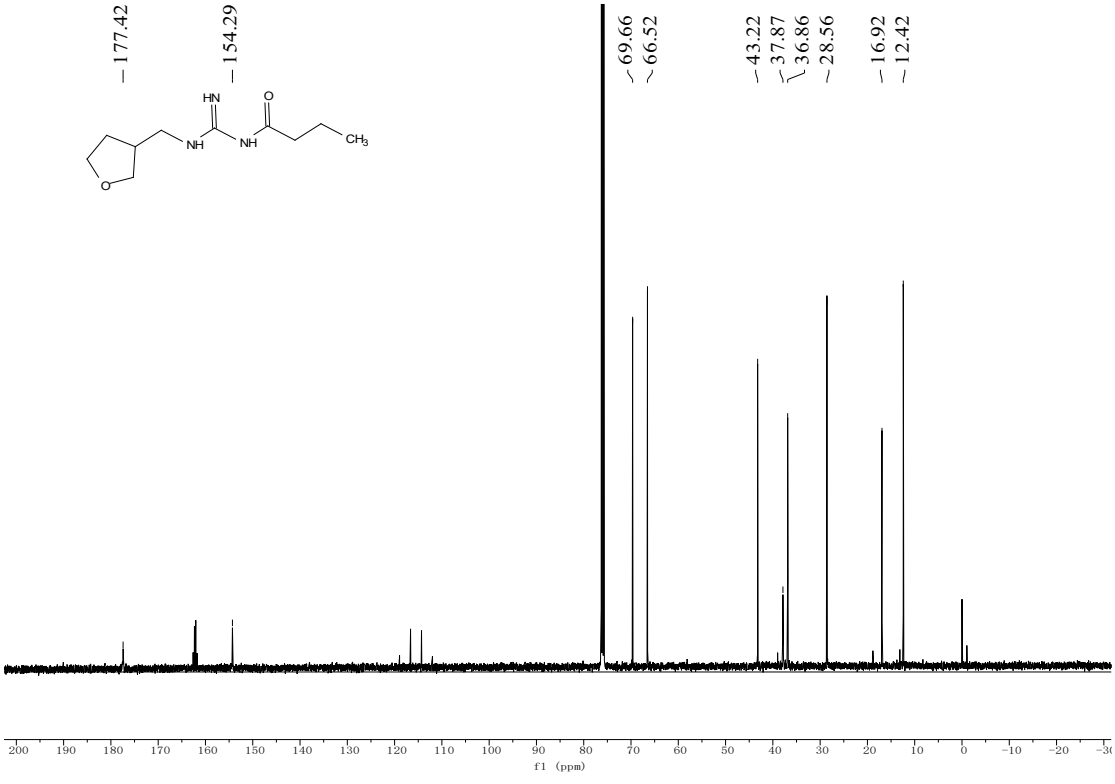


Fig S36. ^{1}H, ^{13}C spectra of **7j**


HN
O
NH
NH
CH3
O
1.00
2.00
1.00
1.89
1.02
1.93
1.03
3.03
2.98
f1 (ppm)


177.42
154.29
69.66
66.52
43.22
37.87
36.86
28.56
16.92
12.42
HN
O
NH
NH
CH3
O
f1 (ppm)

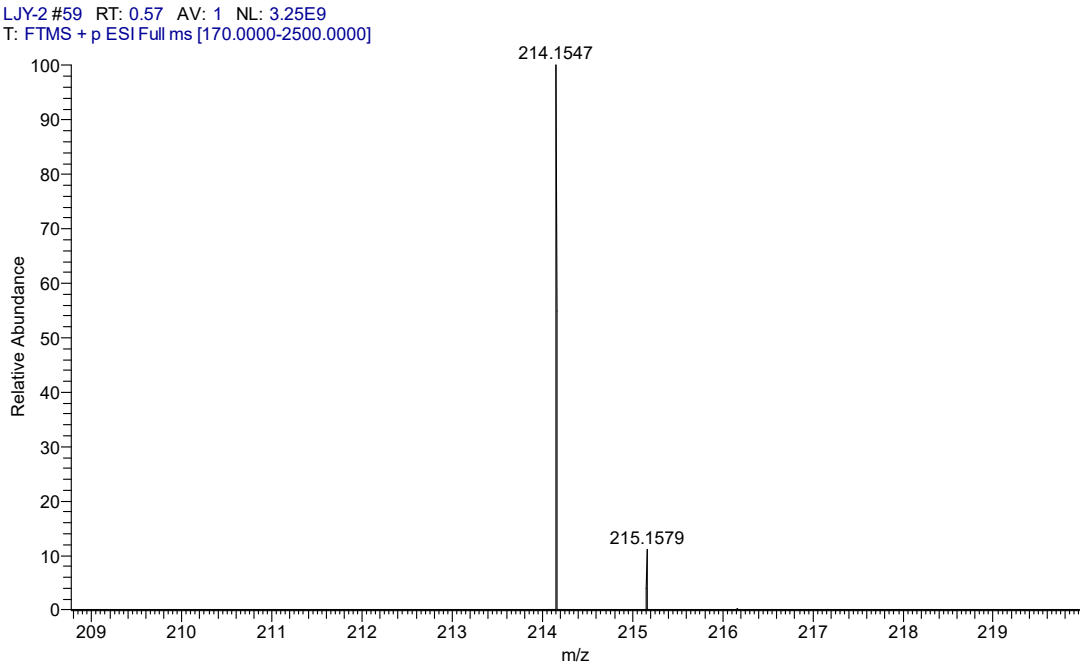
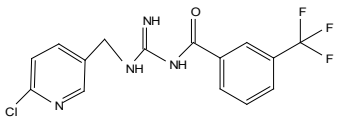
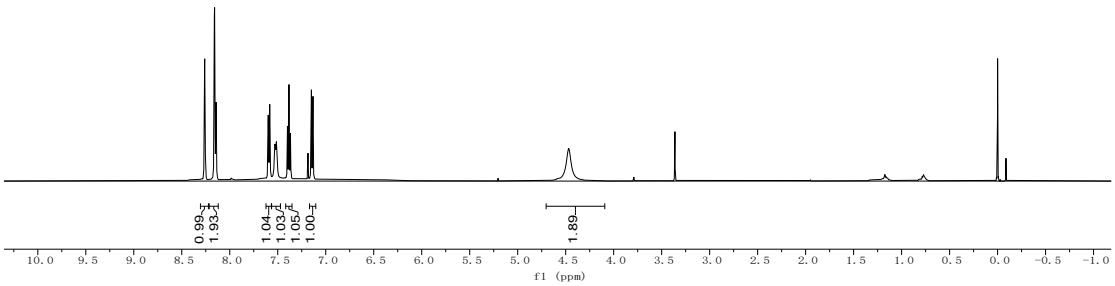
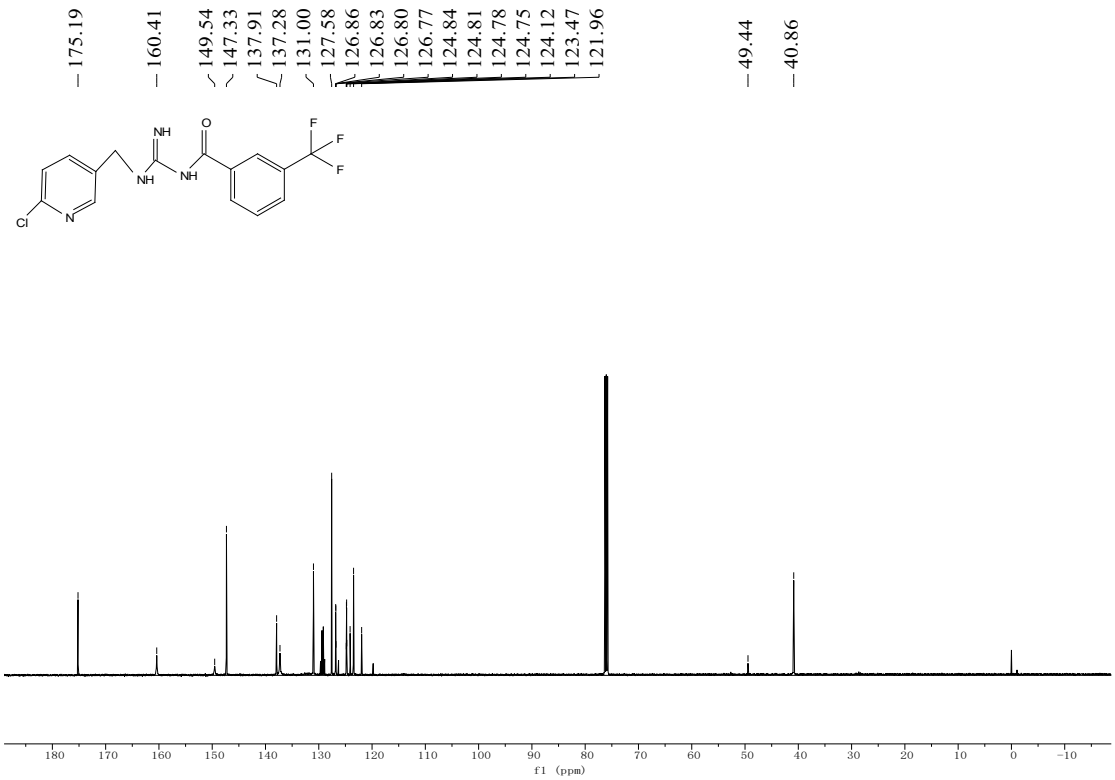


Fig S37. ^{1}H, ^{13}C spectra of **7k**







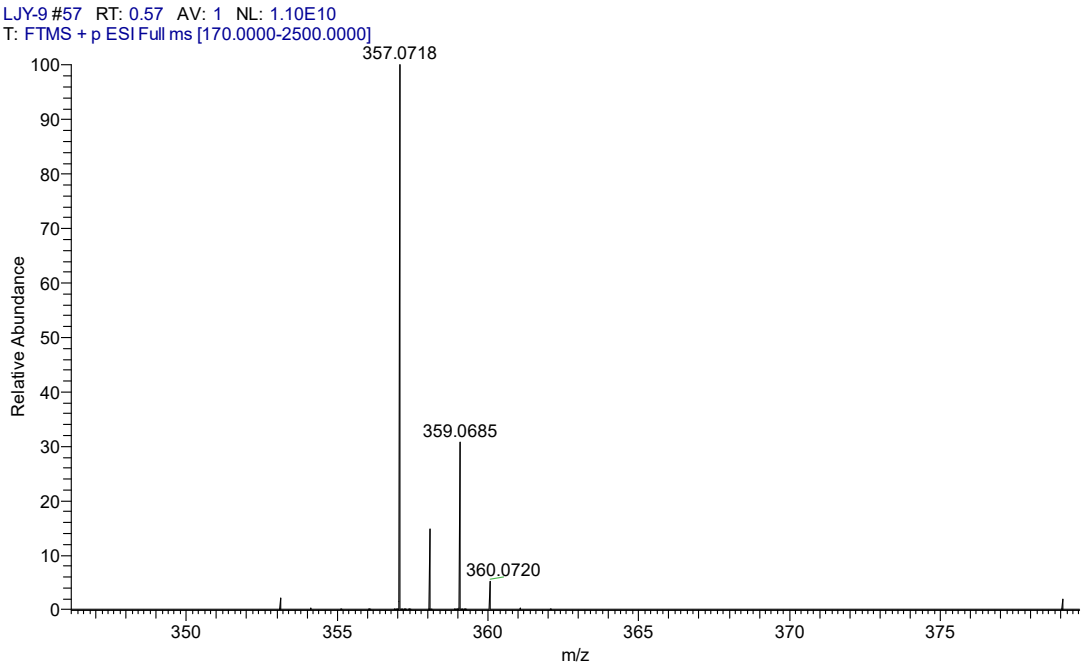
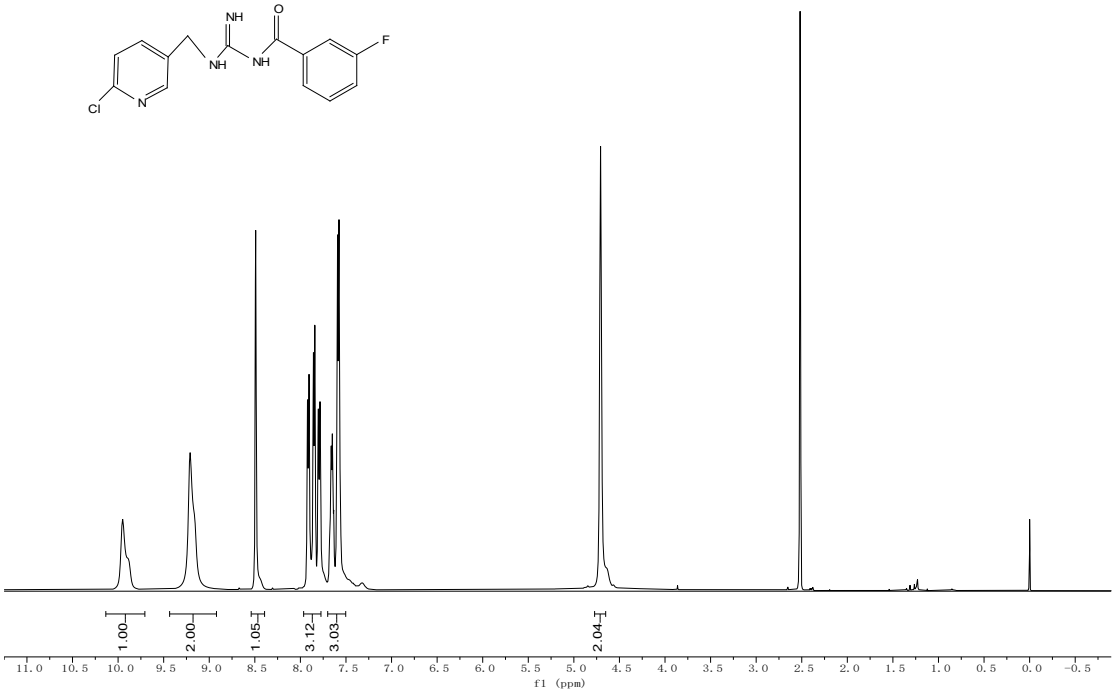
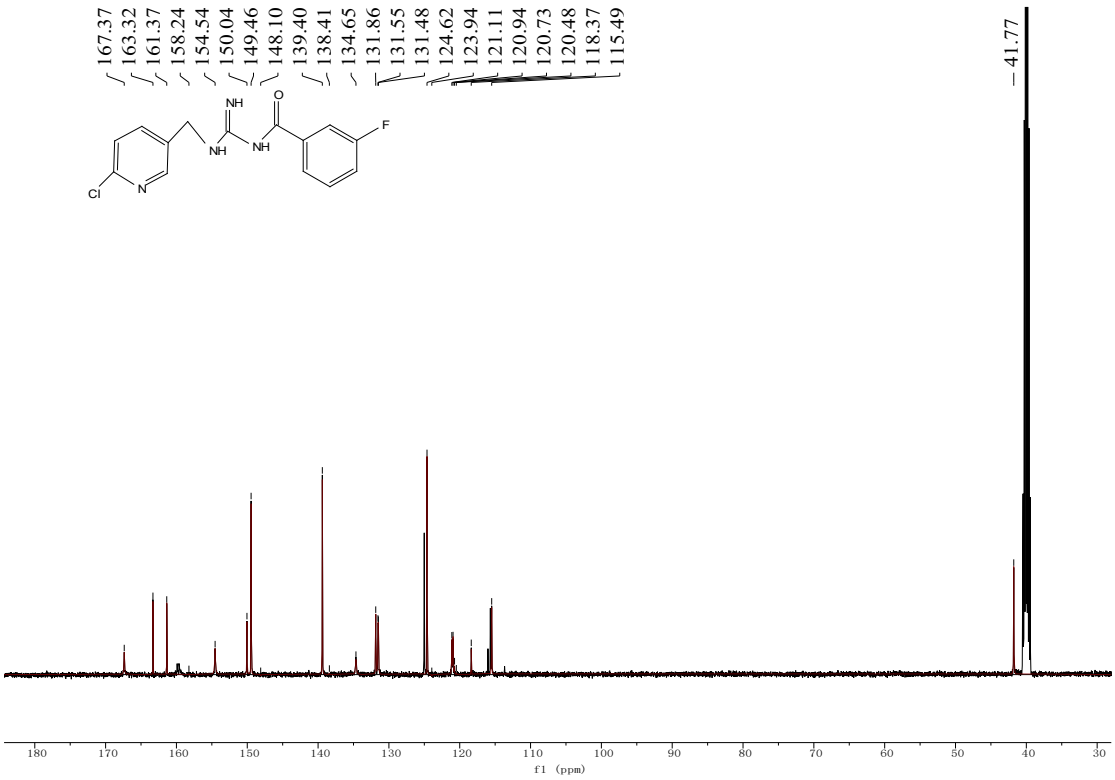


Fig S38. ^{1}H, ^{13}C spectra of **7l**


NH
O
NH
NH
NH
F
Cl
N
1.00
2.00
1.05
3.12
3.03
2.04
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


167.37
163.32
161.37
158.24
154.54
150.04
149.46
148.10
139.40
138.41
134.65
131.86
131.55
131.48
124.62
123.94
121.11
120.94
120.73
120.48
118.37
115.49
41.77
NH
O
NH
NH
NH
F
Cl
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30
f1 (ppm)

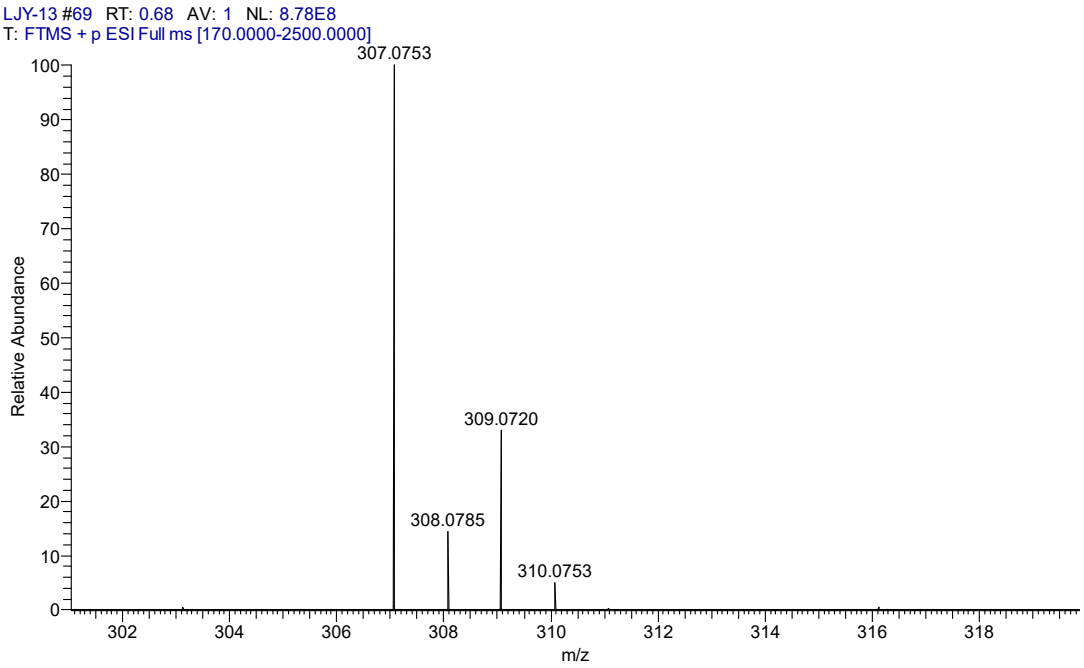
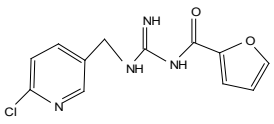
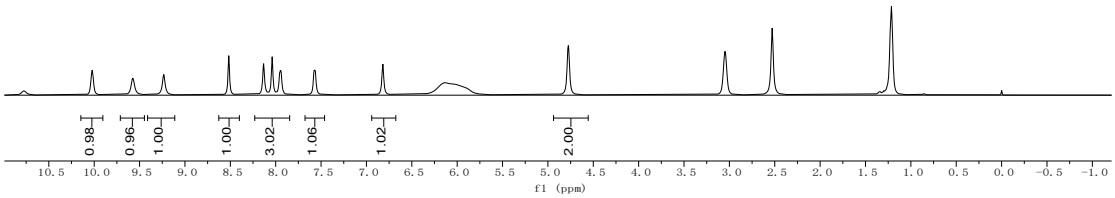
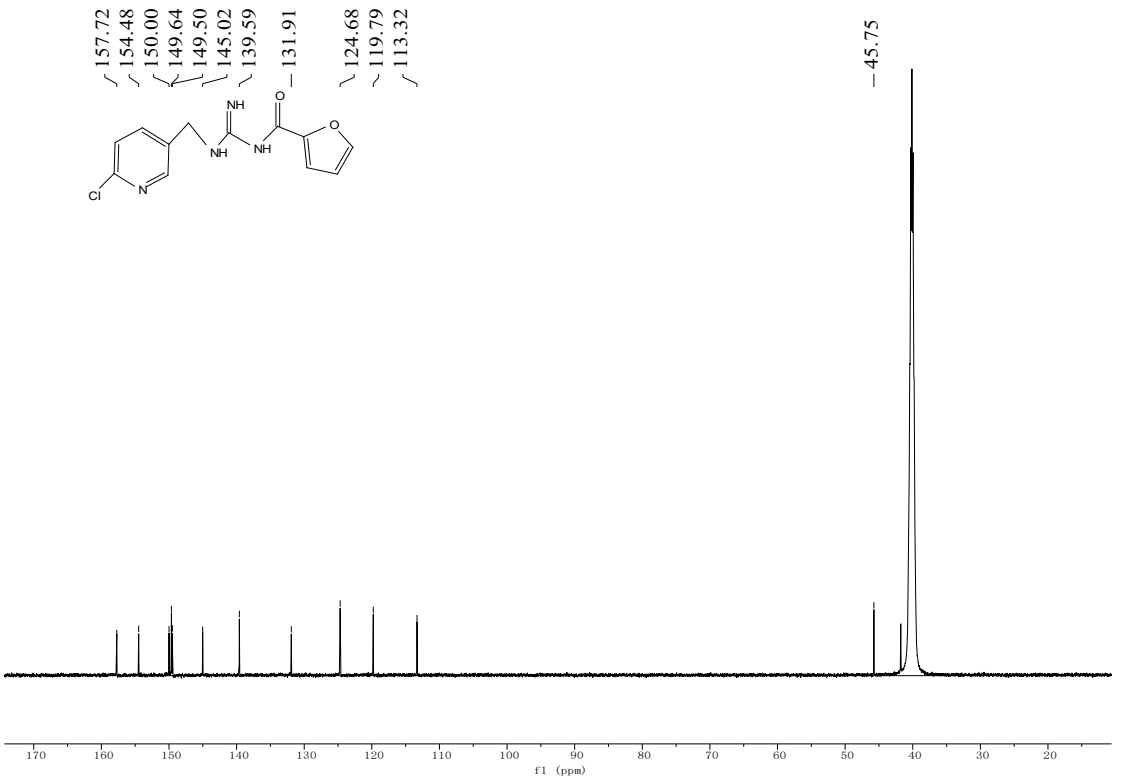


Fig S39. ^{1}H, ^{13}C spectra of **7m**







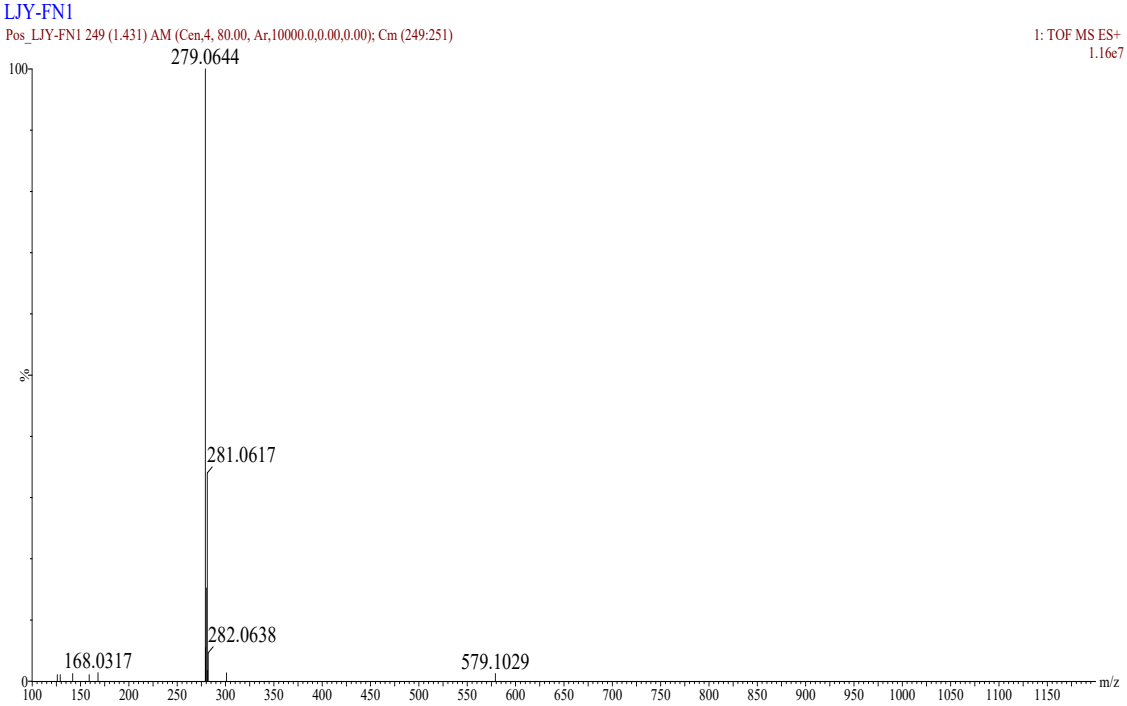
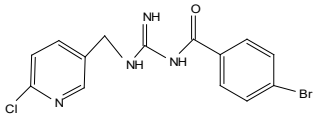
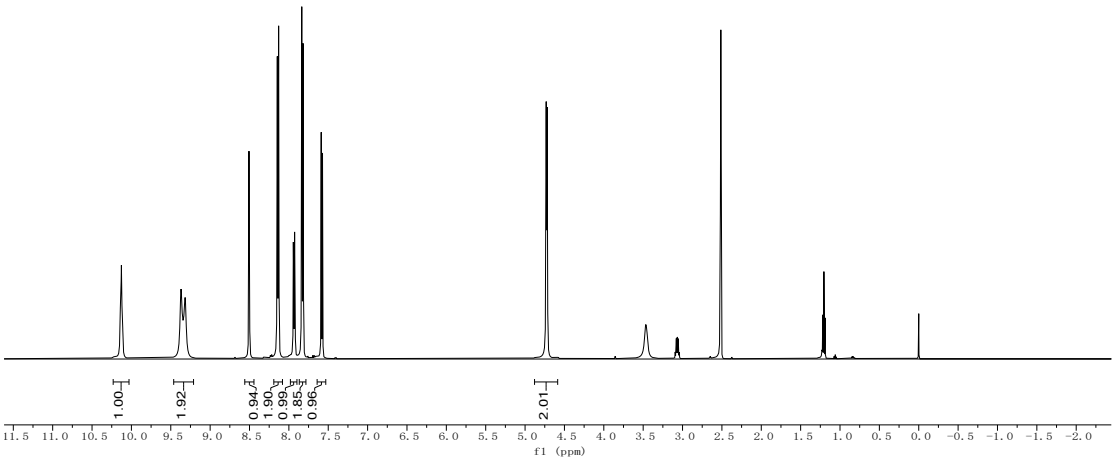
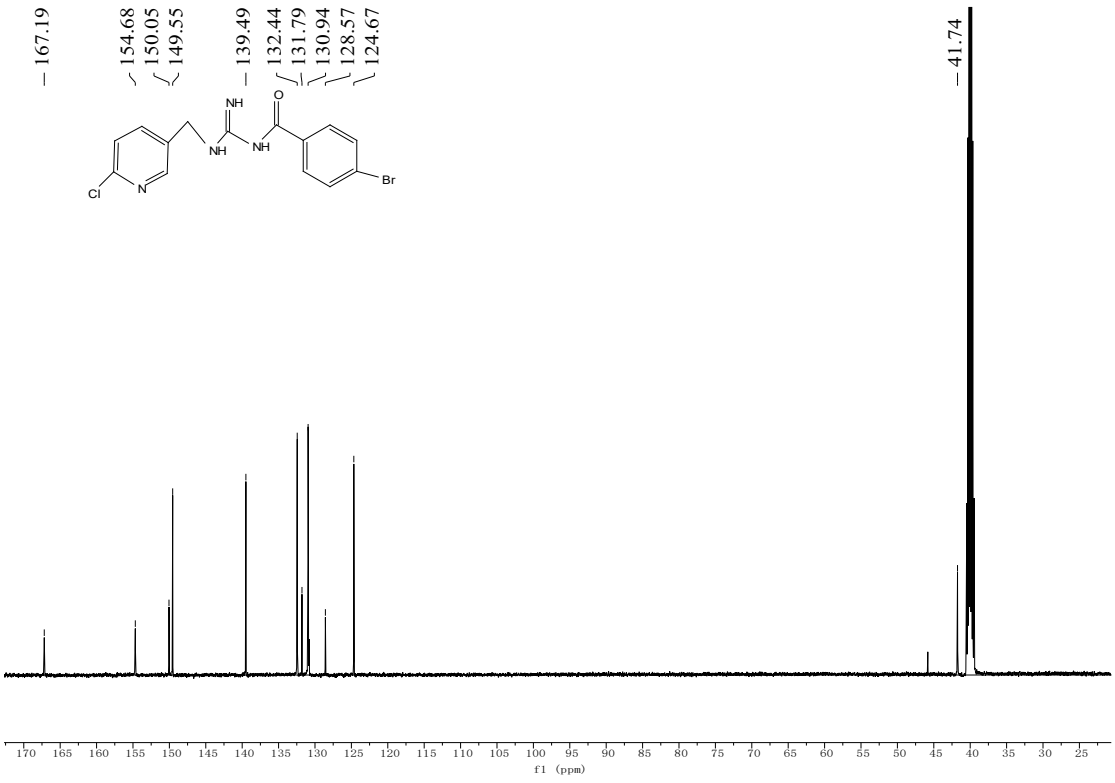


Fig S40. ^{1}H, ^{13}C spectra of **7n**


NH
O
NH
NH
NH
Cl
N
Br


1.00
1.92
0.94
1.90
0.99
1.85
0.96
2.01
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)


167.19
154.68
150.05
149.55
139.49
132.44
131.79
130.94
128.57
124.67
41.74
170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25
f1 (ppm)

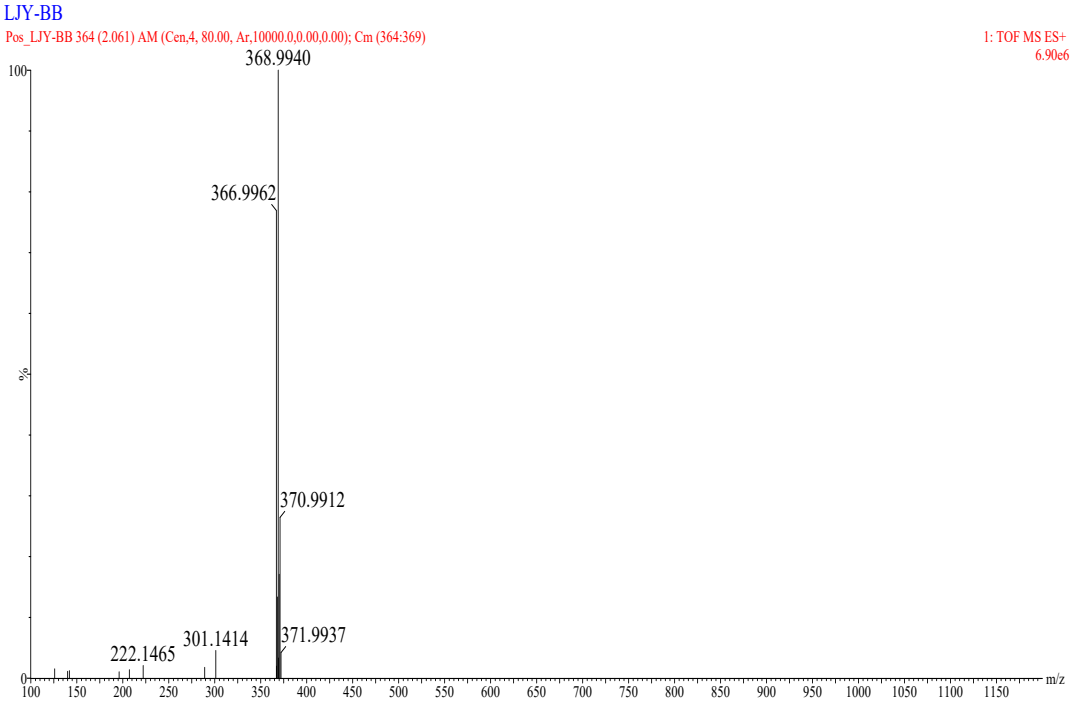
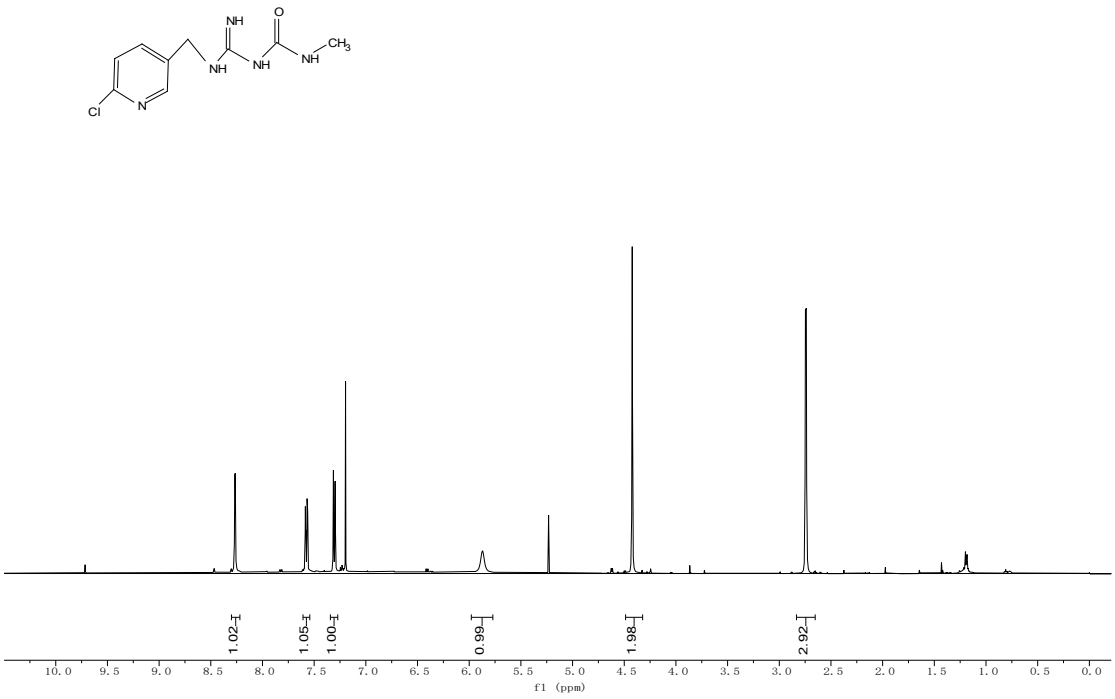
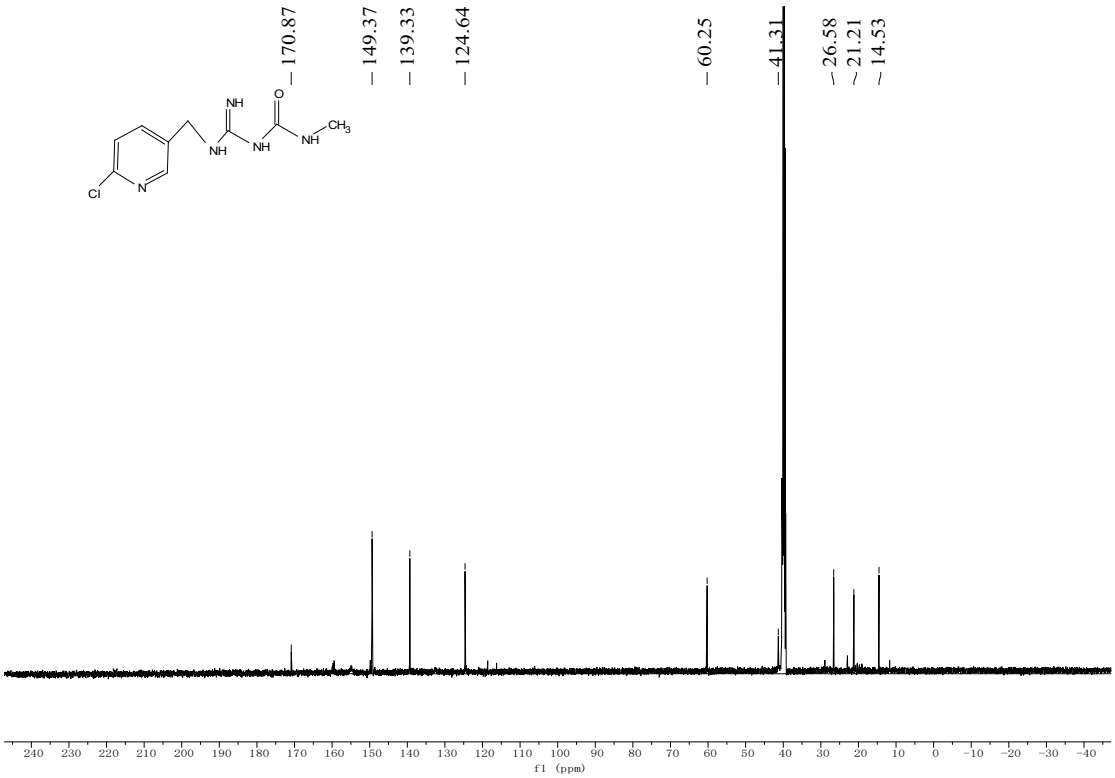


Fig S41. ^{1}H, ^{13}C spectra of **7o**





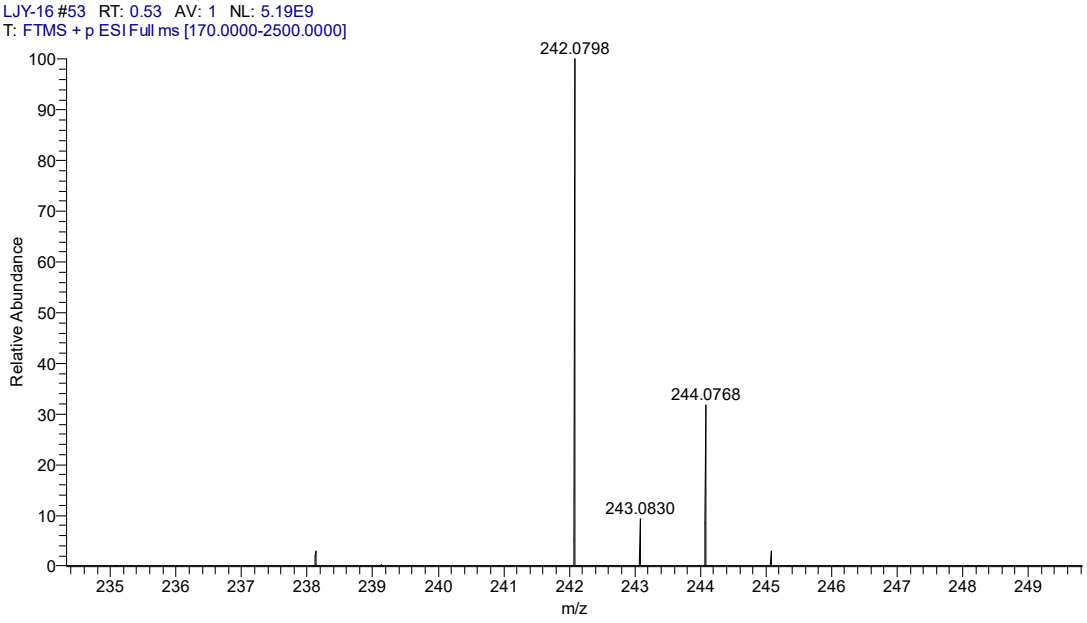
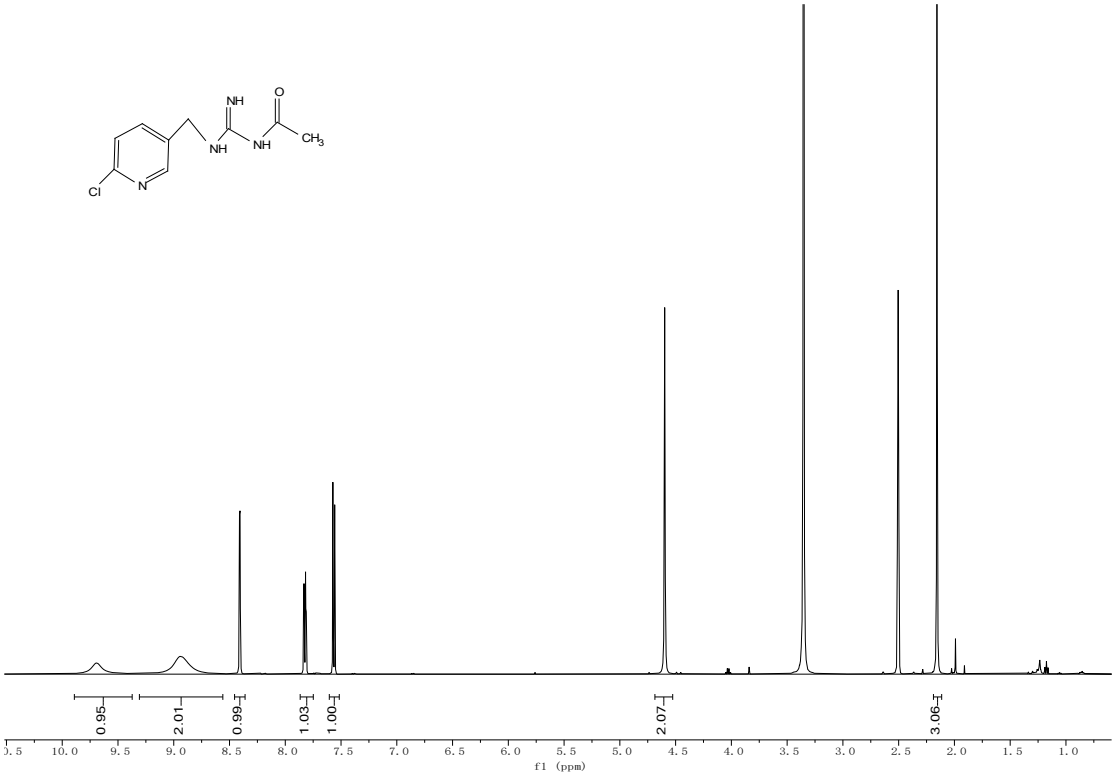
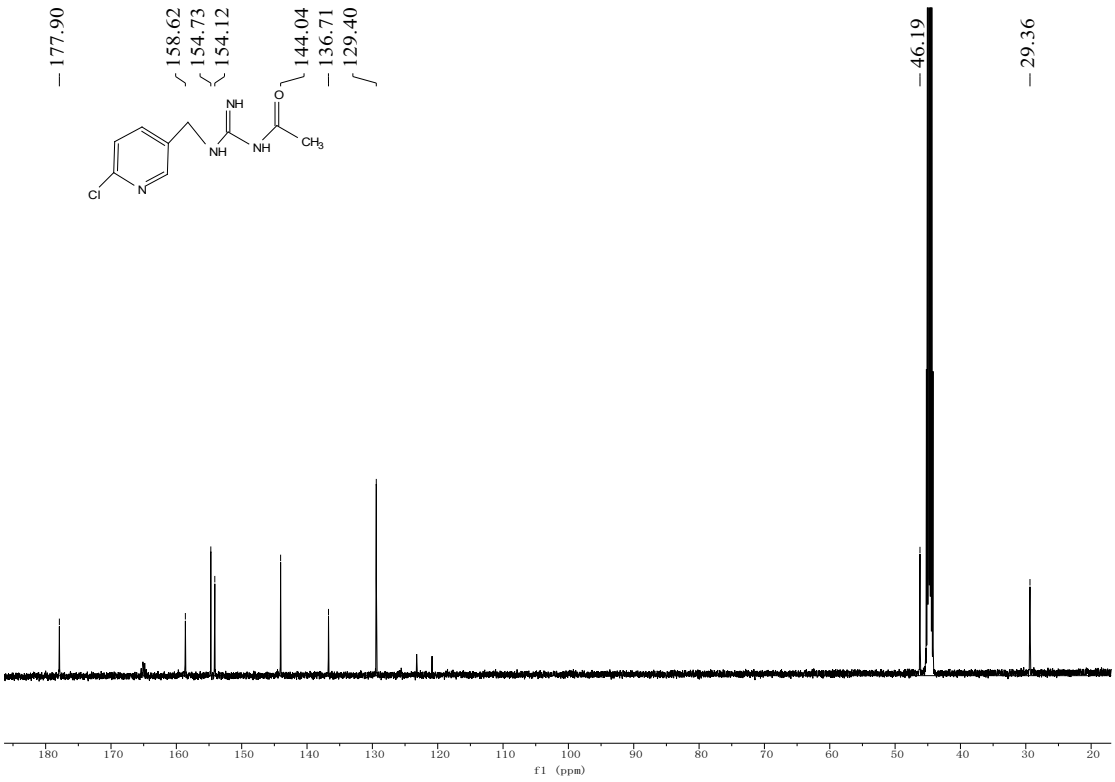


Fig S42. ^{1}H, ^{13}C spectra of **7p**


NH
O
NH
NH
CH3
Cl
N
0.95
2.01
0.99
1.03
1.00
2.07
3.06
f1 (ppm)


177.90
158.62
154.73
154.12
144.04
136.71
129.40
46.19
29.36
NH
O
NH
NH
CH3
Cl
N
f1 (ppm)

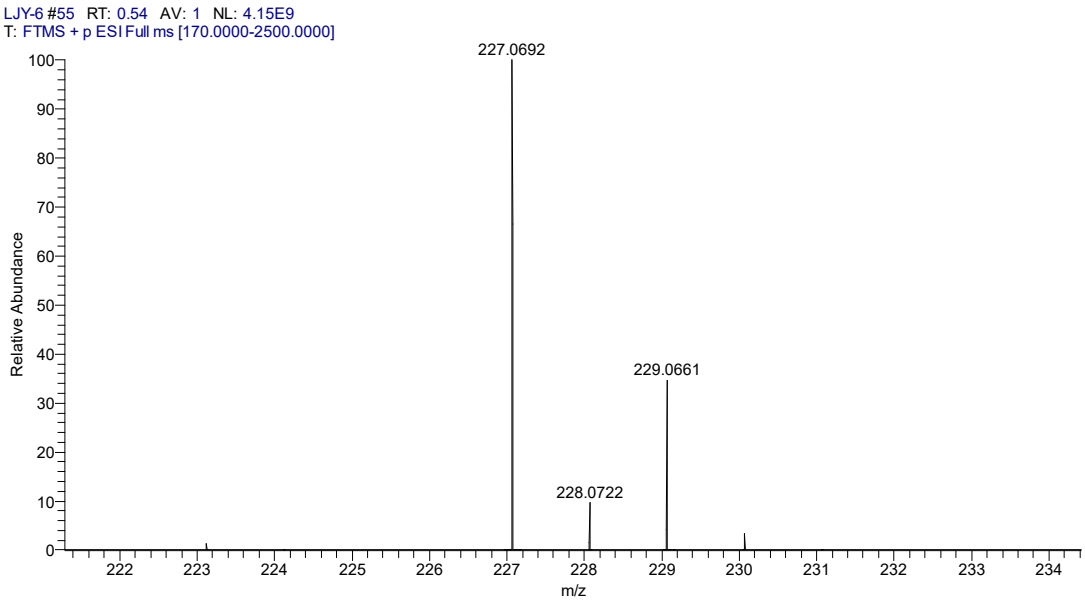
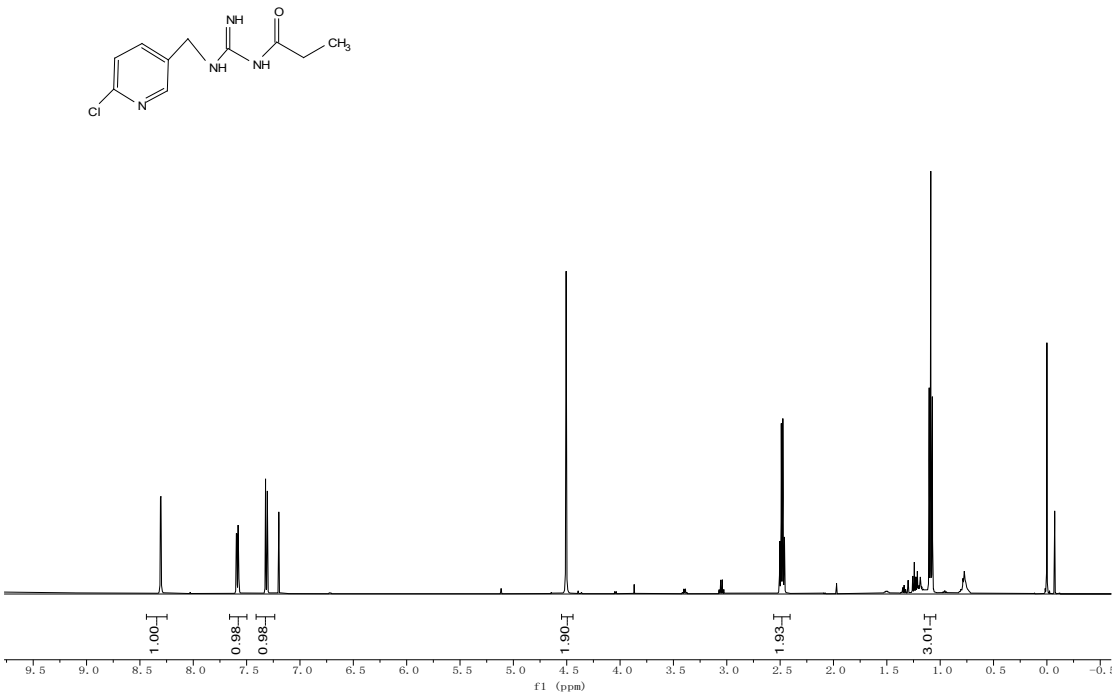
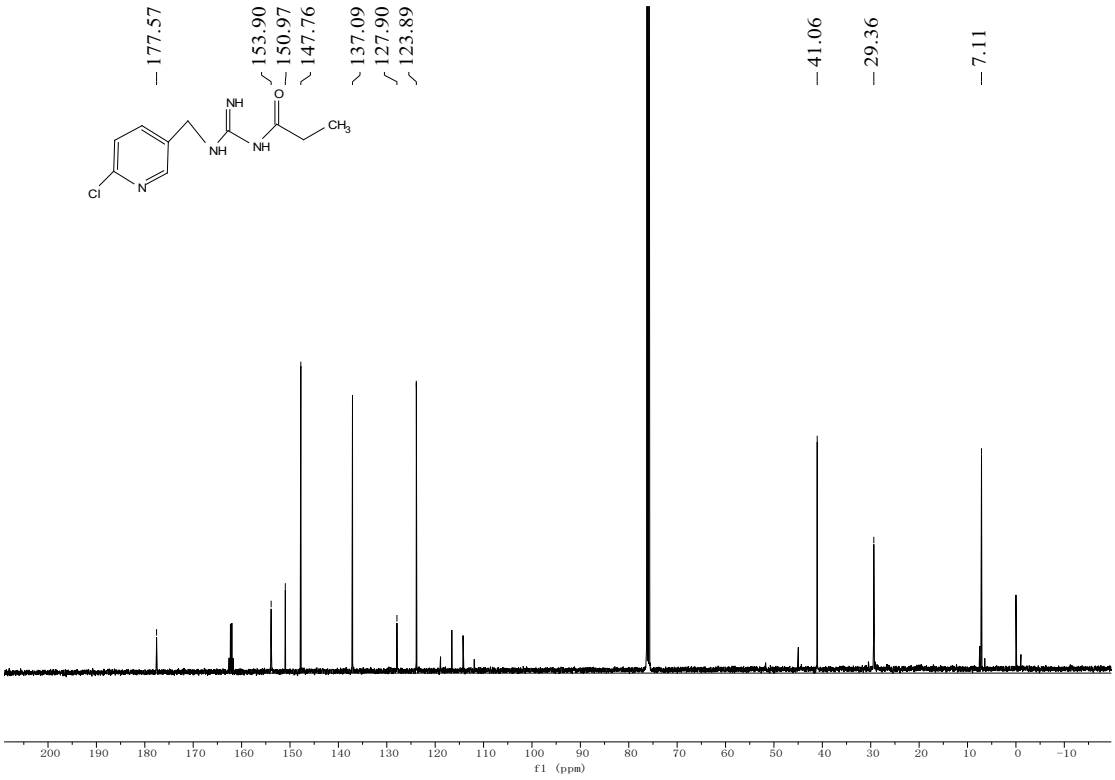


Fig S43. ^{1}H, ^{13}C spectra of **7q**





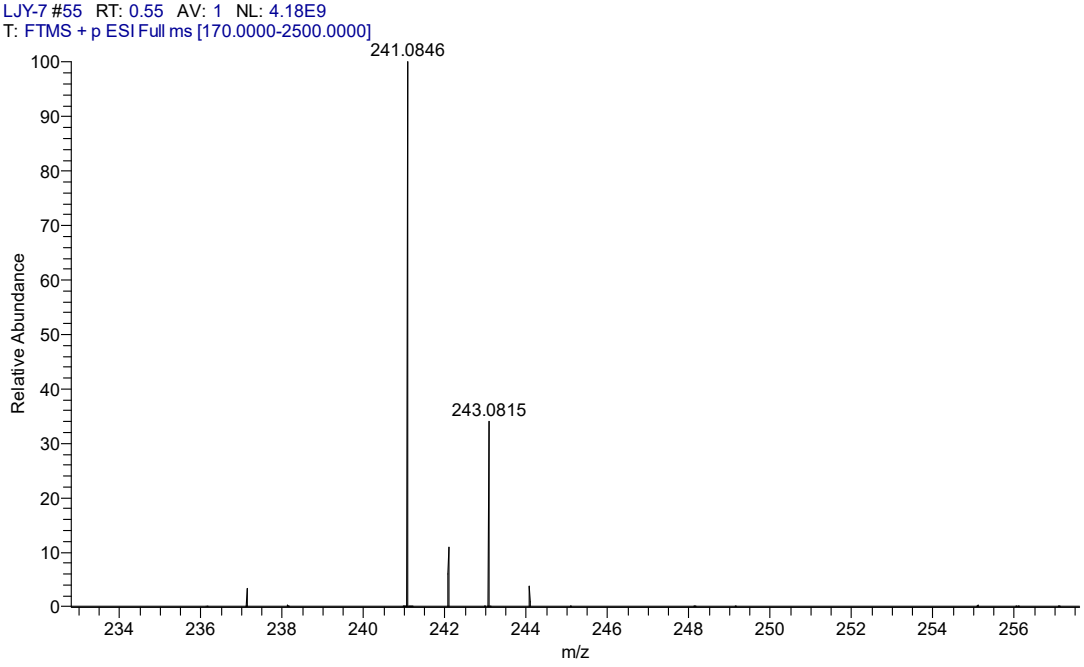
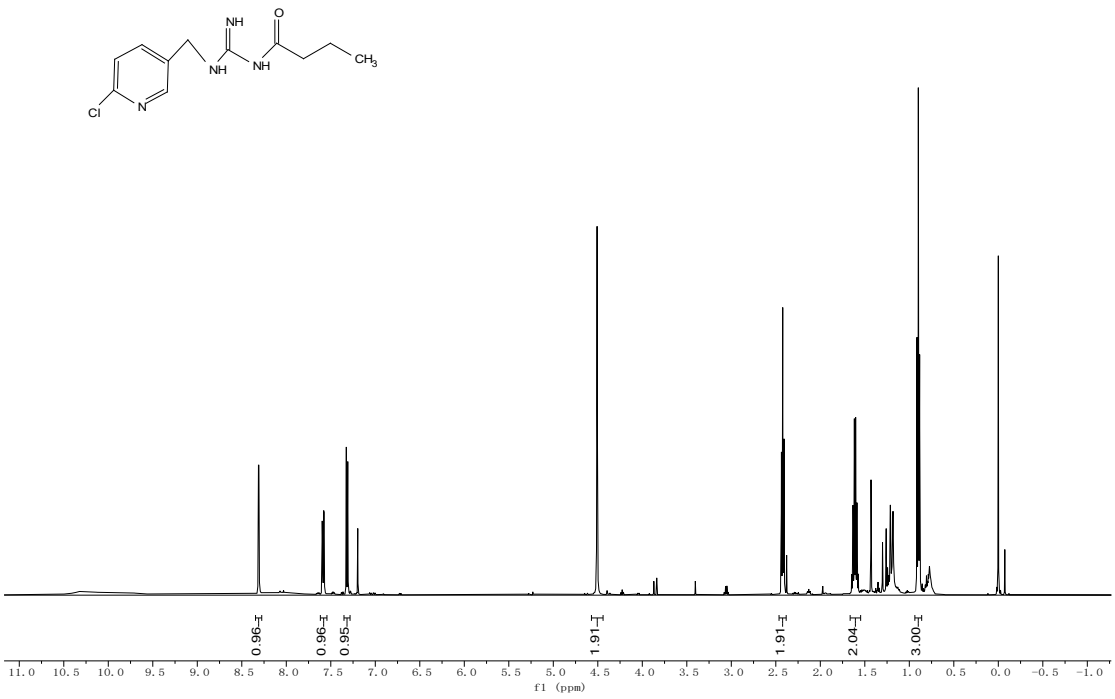
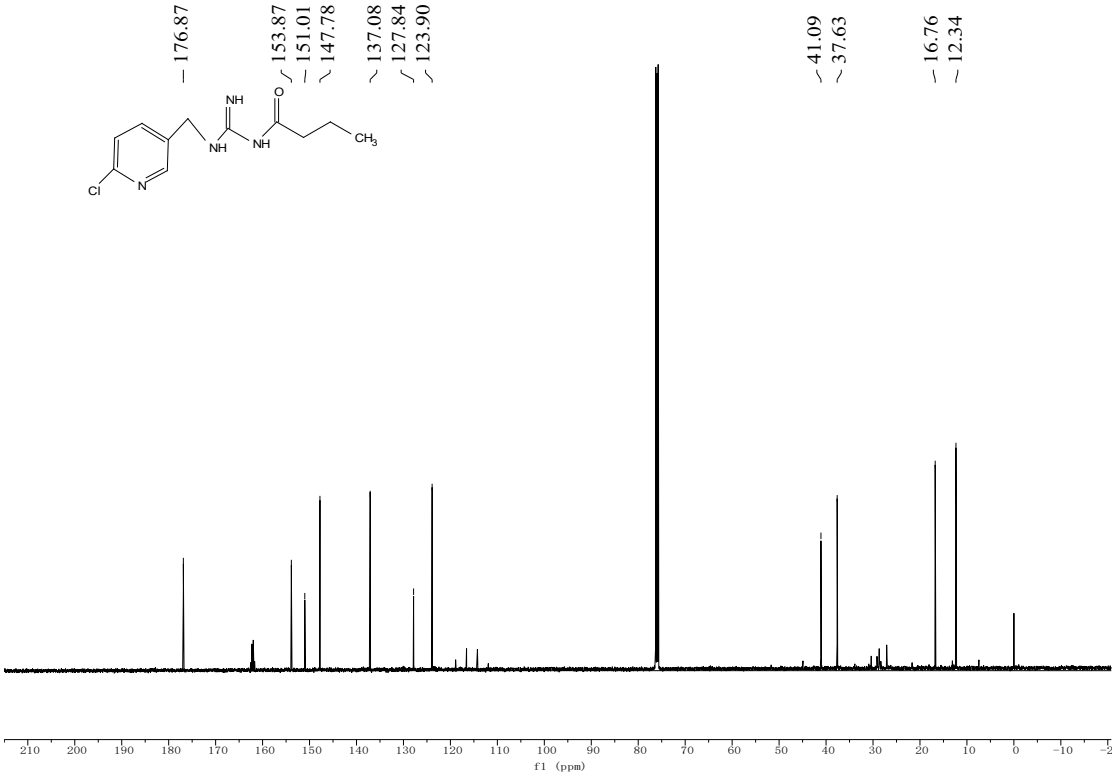


Fig S44. ^{1}H, ^{13}C spectra of **7r**


NH
O
NH
NH
NH
CH3
Cl
N
0.96
0.96
0.95
1.91
1.91
2.04
3.00
f1 (ppm)


176.87
153.87
151.01
147.78
137.08
127.84
123.90
41.09
37.63
16.76
12.34
NH
O
NH
NH
NH
CH3
Cl
N
f1 (ppm)

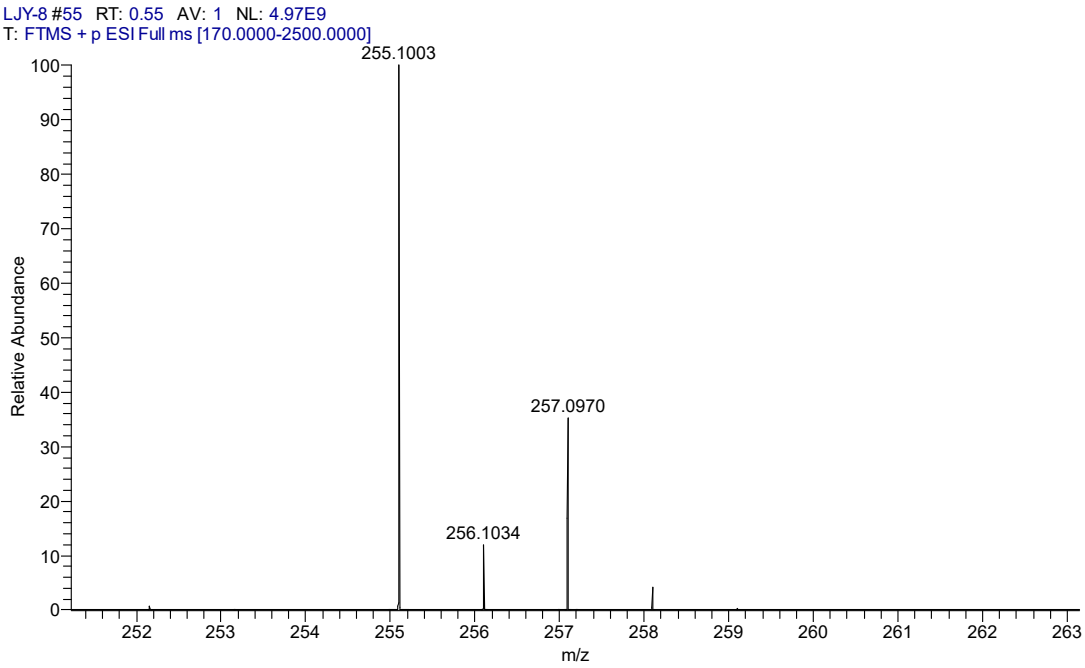


Fig S45. ^{1}H, ^{13}C spectra of **7s**

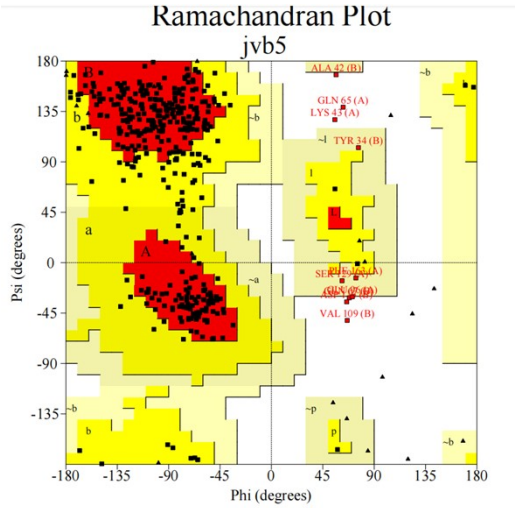


Fig S46. The Ramachandran Plot to modelled proteins.

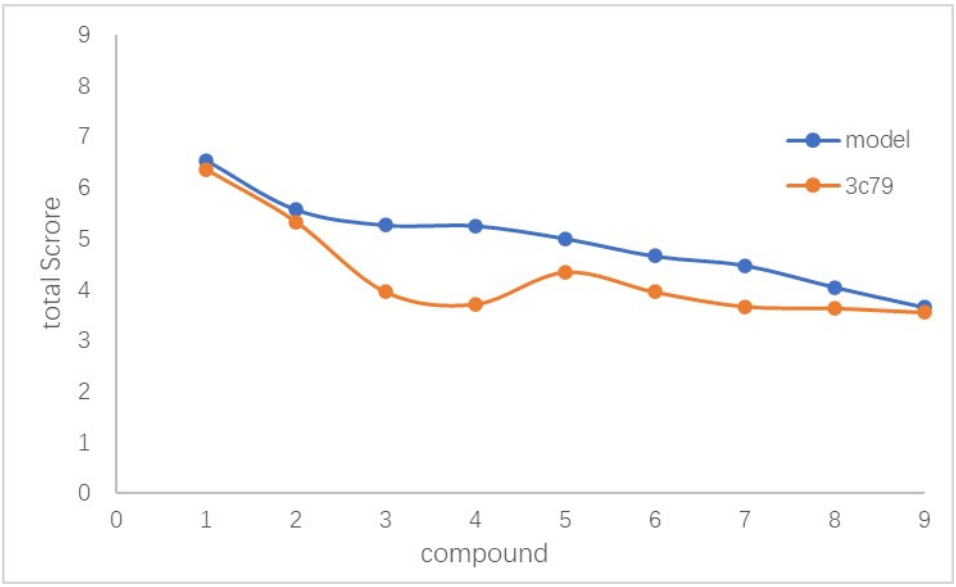


Fig S47. Scoring evaluation of commercial neonicotinoid insecticides with modeled proteins and 3C79(Compound name is consistent with **Table S1**)

Fig S48. Symptoms of *P. xylostella* larvae after 72 h treatment with DMSO and compounds **7a**, **7i** at 30 mg/L.

a b

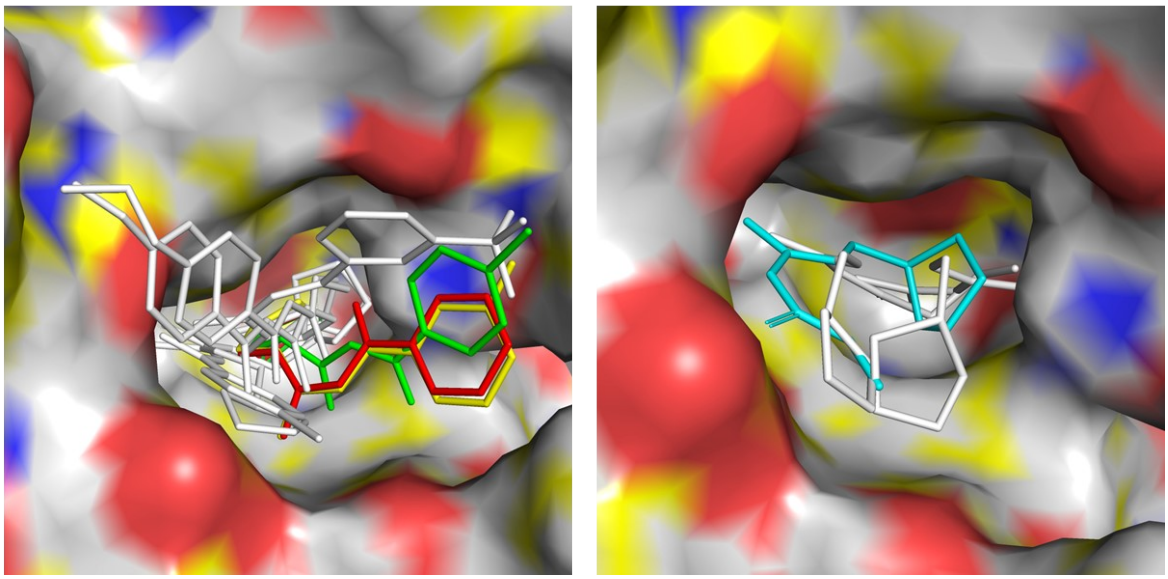


Fig S49. Stacked docking configurations of compounds 7**a-k**. (a) Stacked docking configuration of compounds **a-h**, where **7a** is in red, **7d** is in green and **7e** is in yellow. (a) Stacked docking configuration of compounds 7**i-k**, where **7i** is in blue.

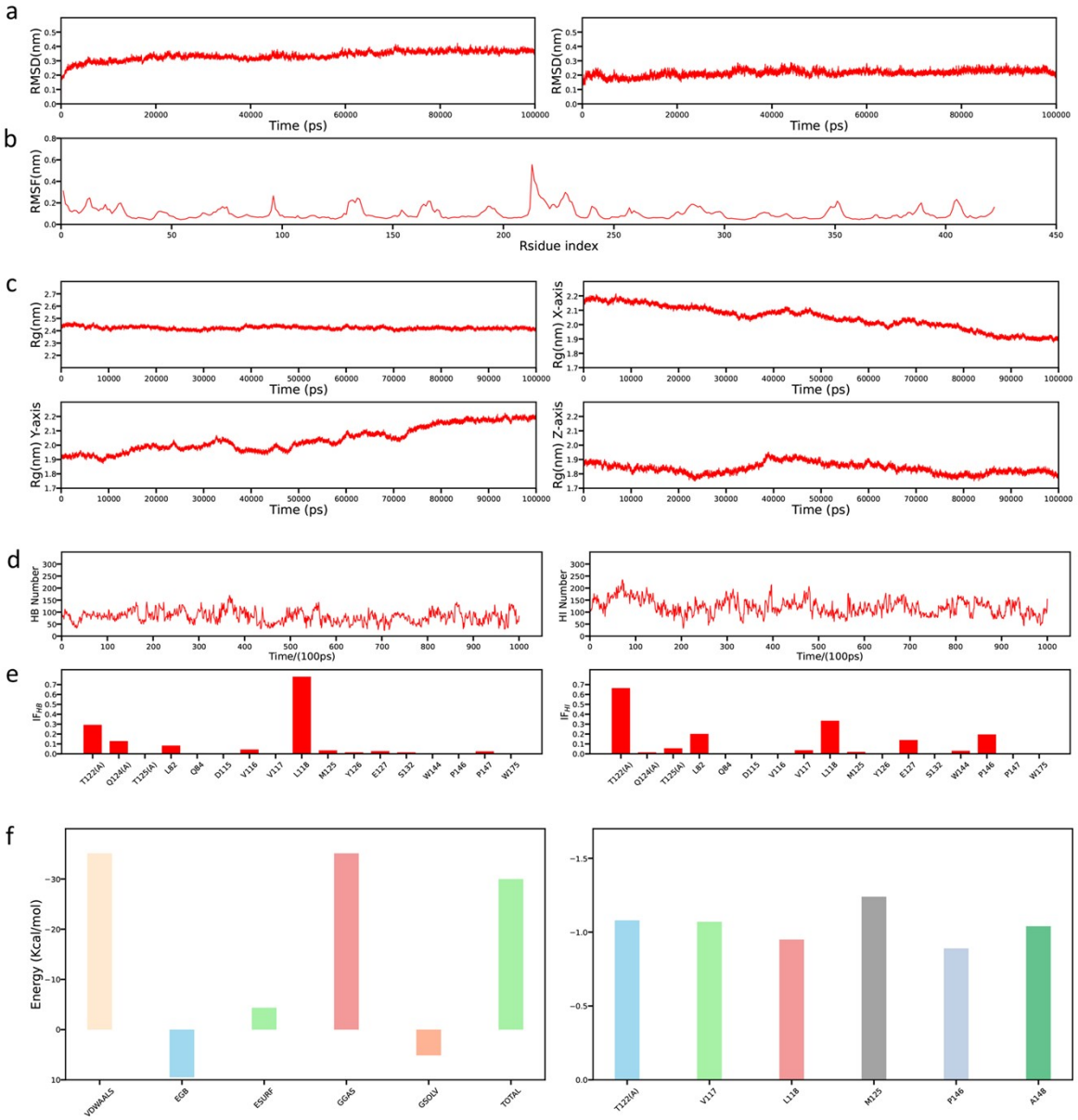


Fig S50. MD simulation analysis of compound 7e. (a) RMSD of the **7e** bound protein complexes over 100 ns MD simulations where the Y-axis represents RMSD value the X-axis represents the Time (PS). (b) RMSF changes of the proteins during 100 ns MD simulations. the Y-axis represents the RMSF value the X-axis represents the Residue index. (c) The four plots show the changes in overall protein Rg, X-axis Rg, Y-axis Rg, and Z-axis Rg during the 100 ns MD simulation. (d) Hydrogen Bond and Hydrophobic Interactions Formed by **7e** During 100 ns MD Simulation. (e) the H-bond (HB) and hydrophobic (HI) interaction fractions (IF) of the Inhibitors with protein during the last 50 ns MD Simulation. (f)Analysis of the Binding Free Energy Components and Residue Energy Decomposition for the **7e** Complexes with the Protein.

Table S1. Scoring evaluation of commercial neonicotinoid insecticides with modeled proteins and 3C79

NO	compound	model	3c79
1	Guadipyr	6.5352	6.3547
2	Nitenpyram	5.5692	5.3343
3	Dinotefuran	5.2625	3.9597
4	Thiamcthoxam	5.2486	3.7184
5	Cycloxaprid	4.9989	4.3421
6	Imidaclothiz	4.6569	3.9542
7	Acetamprid	4.4749	3.6701
8	Clothianiain	4.0503	3.6370
9	Sulfoxaflor	3.6582	3.5545