

## Supporting Information

# Design, Synthesis and Bioactivity of Novel Low Bee-Toxicity Compounds Based on Flupyrimin

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**Table S1.** Crystal data and structure refinement for compound **2a**.

Name	Parameter
CCDC No.	2071276
Empirical formula	C <sub>17</sub> H <sub>14</sub> ClN <sub>3</sub> O <sub>2</sub> S
Formula weight	359.82
Temperature / K	108.0(3)
Crystal system	monoclinic
Space group	P2 <sub>1</sub> /n
a / Å, b / Å, c / Å	7.1231(2), 11.6414(3), 19.1788(6)
$\alpha$ / °, $\beta$ / °, $\gamma$ / °	90.00, 90.262(4), 90.00
Volume / Å <sup>3</sup>	1590.34(9)
Z	4
$\rho$ calc / mg mm <sup>-3</sup>	1.503
$\mu$ / mm <sup>-1</sup>	0.387
F(000)	744
Crystal size / mm <sup>3</sup>	0.34 × 0.27 × 0.23
2 $\Theta$ range for data collection	6.7 to 52°
Index ranges	-8 ≤ h ≤ 8, -14 ≤ k ≤ 9, -23 ≤ l ≤ 23
Reflections collected	7304
Independent reflections	3115[R(int) = 0.0269 (inf-0.9Å)]
Data/restraints/parameters	3115/0/217
Goodness-of-fit on F <sup>2</sup>	1.055
Final R indexes [I>2 $\sigma$ (I) i. e. Fo>4 $\sigma$ (Fo)]	R1 = 0.0378, wR2 = 0.0848
Final R indexes [all data]	R1 = 0.0456, wR2 = 0.0906
Largest diff. peak/hole / e Å <sup>-3</sup>	0.267/-0.458
Flack Parameters	N
Completeness	0.9971

**Table S2.** Bond lengths for compound **2a**.

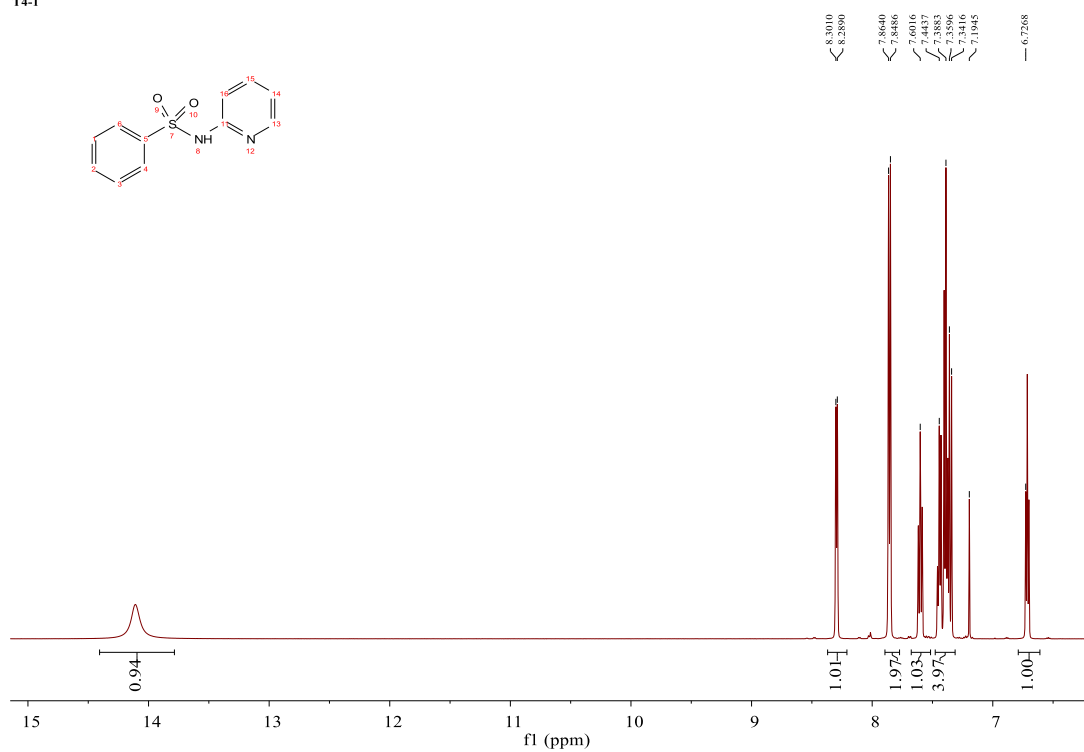
Chemical bond	Lengths [Å]	Chemical bond	Lengths [Å]
S1-O2	1.4454(14)	C2-C3	1.379(3)
S1-O1	1.4514(14)	C2-C1	1.387(3)

S1-N1	1.5957(17)	C7-C8	1.355(3)
S1-C12	1.767(2)	C13-C14	1.379(3)
Cl1-C1	1.754(2)	C13-C12	1.393(3)
N2-C7	1.362(3)	C17-C12	1.390(3)
N2-C11	1.374(2)	C17-C16	1.390(3)
N2-C6	1.481(2)	C3-C4	1.390(3)
N3-C1	1.314(3)	C6-C4	1.510(3)
N3-C5	1.349(3)	C4-C5	1.388(3)
N1-C11	1.335(3)	C9-C8	1.405(3)
C10-C11	1.426(3)	C14-C15	1.387(3)
C10-C9	1.361(3)	C15-C16	1.382(3)

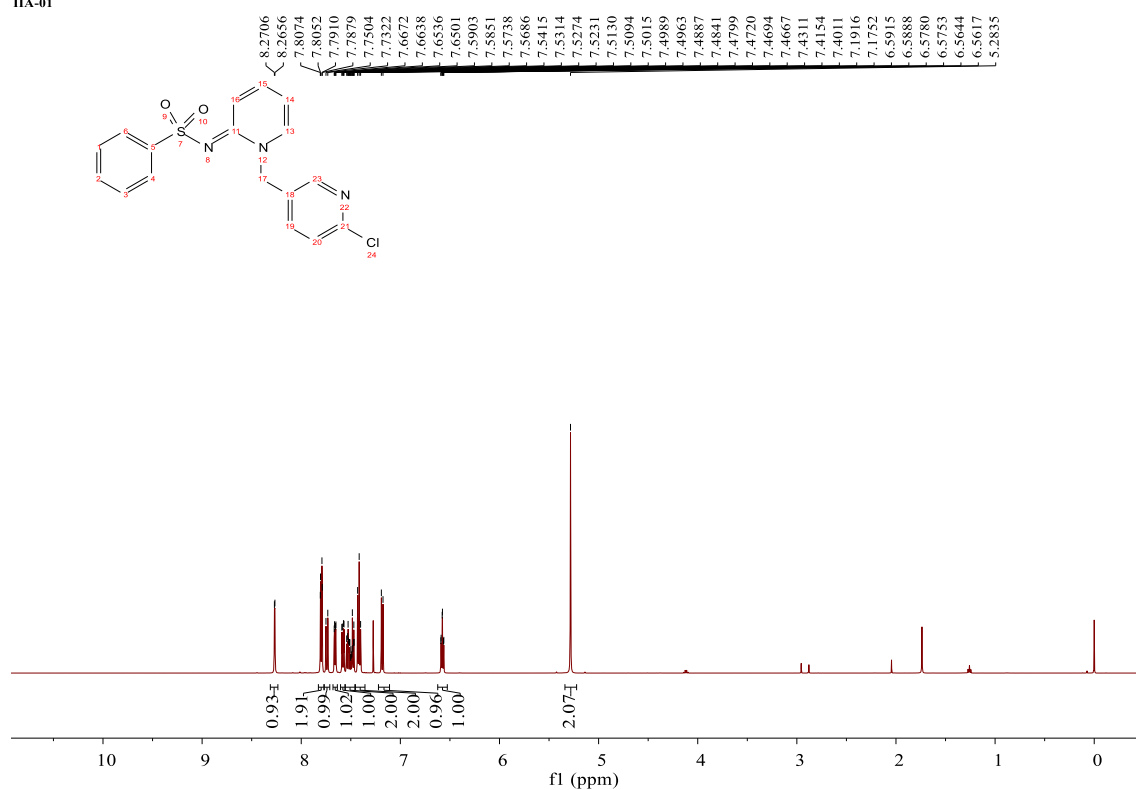
**Table S3.** Bond angles for compound **2a**.

Chemical bond	Angles [°]	Chemical bond	Angles [°]
O2-S1-O1	114.72(8)	C16-C17-C12	118.9(2)
O2-S1-N1	112.64(9)	C2-C3-C4	119.82(19)
O2-S1-C12	108.05(9)	N3-C1-Cl1	115.53(15)
O1-S1-N1	113.10(9)	N3-C1-C2	126.00(19)
O1-S1-C12	106.68(9)	C2-C1-Cl1	118.48(16)
N1-S1-C12	100.30(9)	N2-C6-C4	112.65(16)
C7-N2-C11	122.32(17)	C3-C4-C6	121.91(18)
C7-N2-C6	118.55(16)	C5-C4-C3	117.82(18)
C11-N2-C6	119.09(16)	C5-C4-C6	120.20(18)
C1-N3-C5	116.04(18)	C10-C9-C8	120.44(19)
C11-N1-S1	121.57(14)	C13-C14-C15	120.1(2)
C9-C10-C11	121.03(19)	N3-C5-C4	123.58(19)
C3-C2-C1	116.73(19)	C16-C15-C14	120.1(2)
C8-C7-N2	121.67(19)	C7-C8-C9	118.25(19)
N2-C11-C10	116.23(17)	C13-C12-S1	118.66(15)
N1-C11-N2	115.13(16)	C17-C12-S1	120.50(15)
N1-C11-C10	128.64(18)	C17-C12-C13	120.61(19)
C14-C13-C12	119.75(19)	C15-C16-C17	120.6(2)

T4-1

Figure S1. <sup>1</sup>H NMR of Intermediate 1.

IIA-01

Figure S2. <sup>1</sup>H NMR of compound 2a.

HA-01

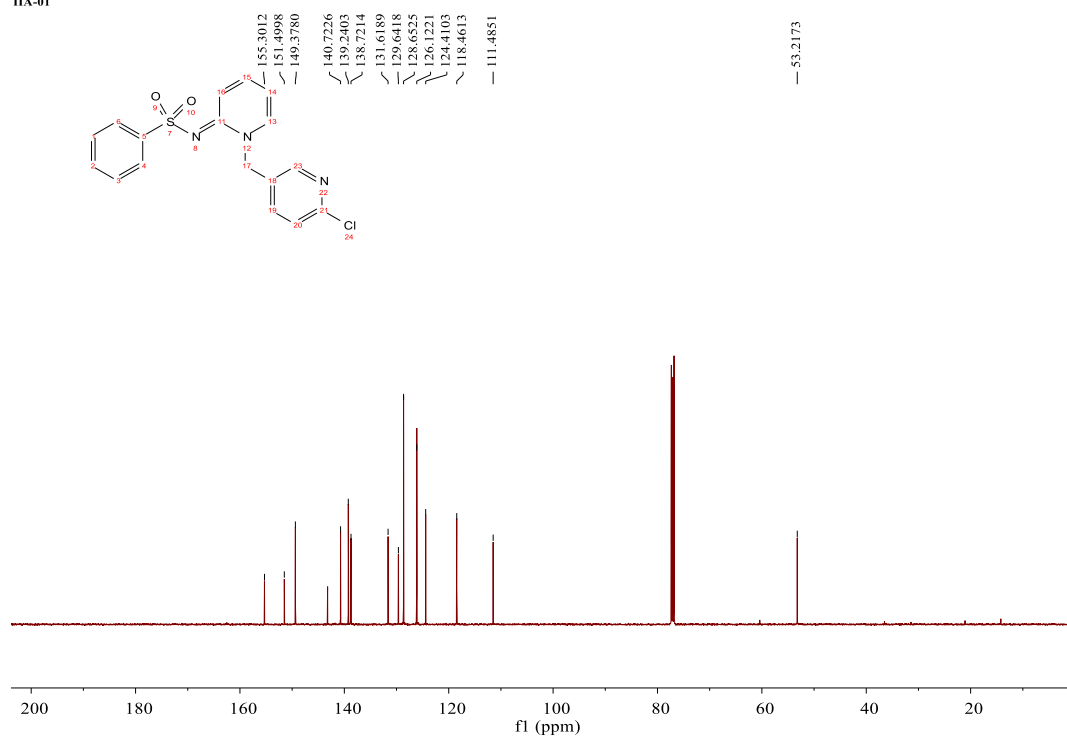


Figure S3. <sup>13</sup>C NMR of compound 2a.

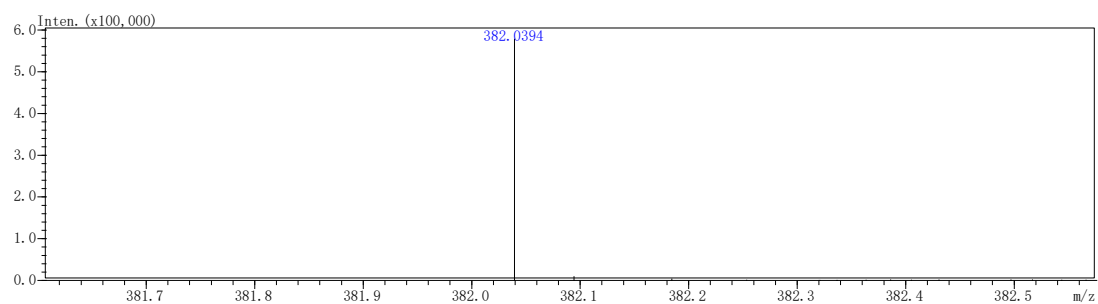


Figure S4. HRMS of compound 2a.

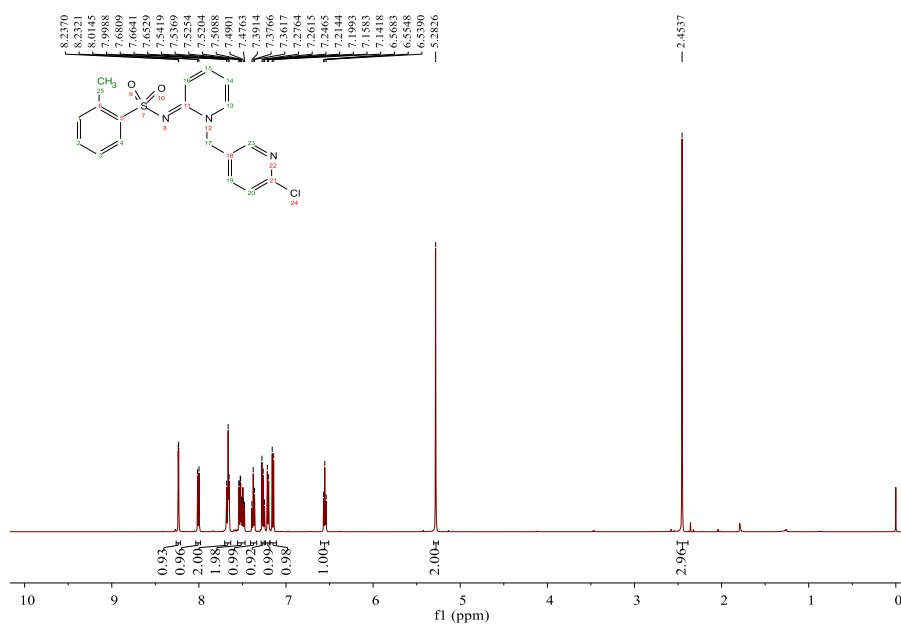


Figure S5. <sup>1</sup>H NMR of compound 2b.

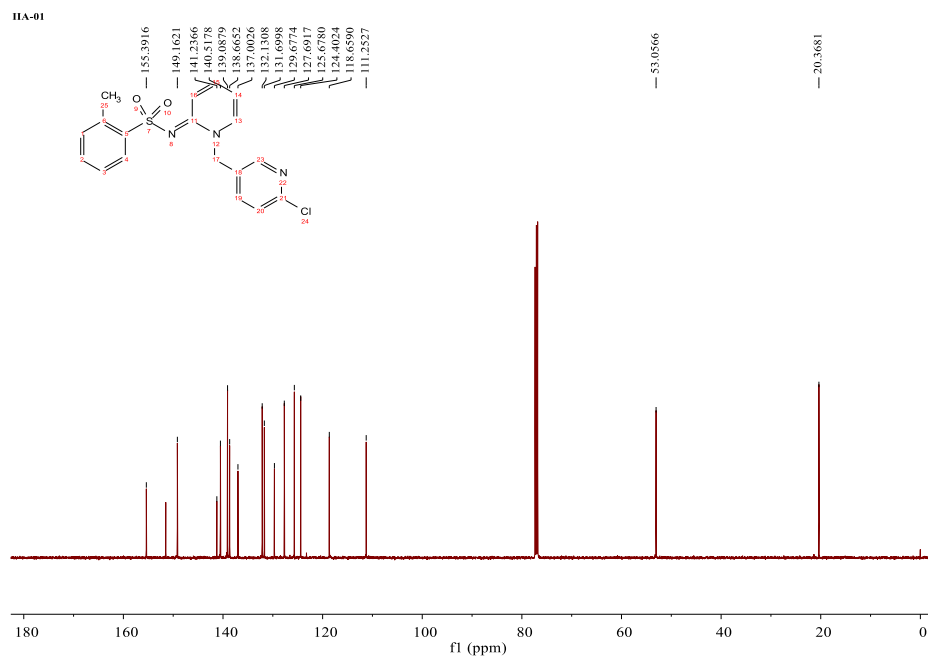


Figure S6.  $^{13}\text{C}$  NMR of compound 2b.

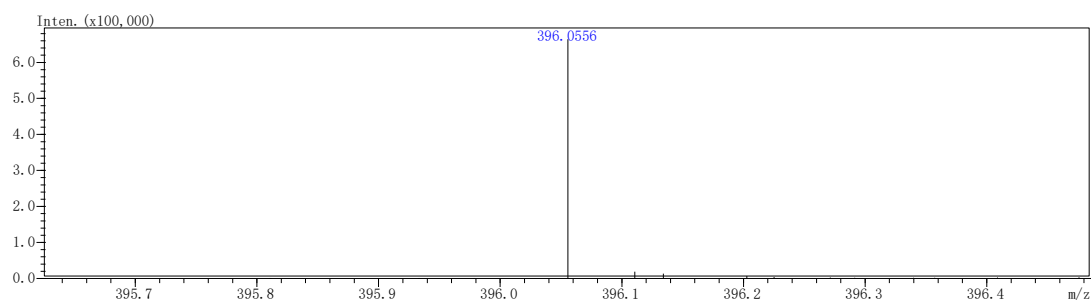


Figure S7. HRMS of compound 2b.

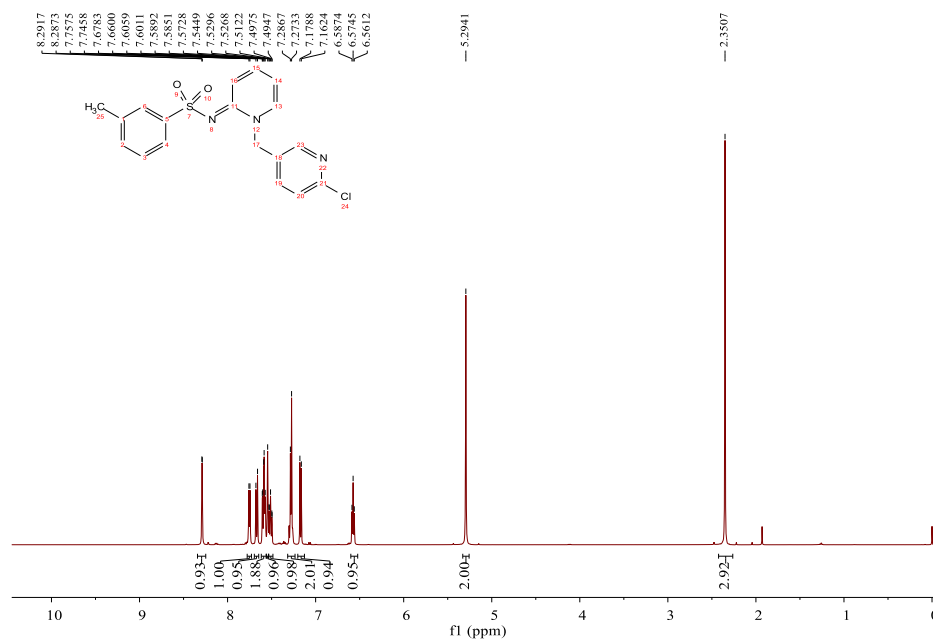


Figure S8.  $^1\text{H}$  NMR of compound 2c.

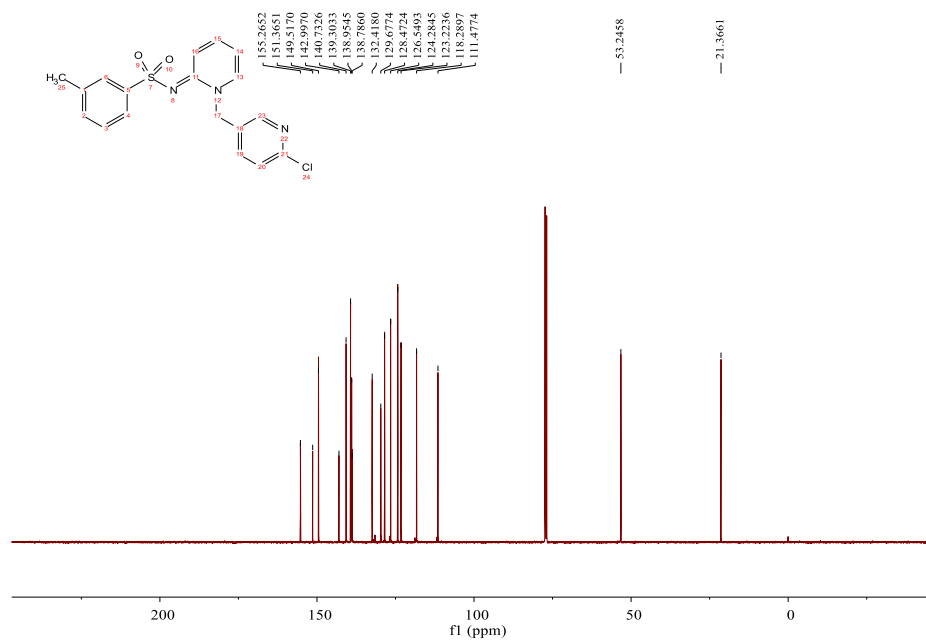


Figure S9.  $^{13}\text{C}$  NMR of compound 2c.

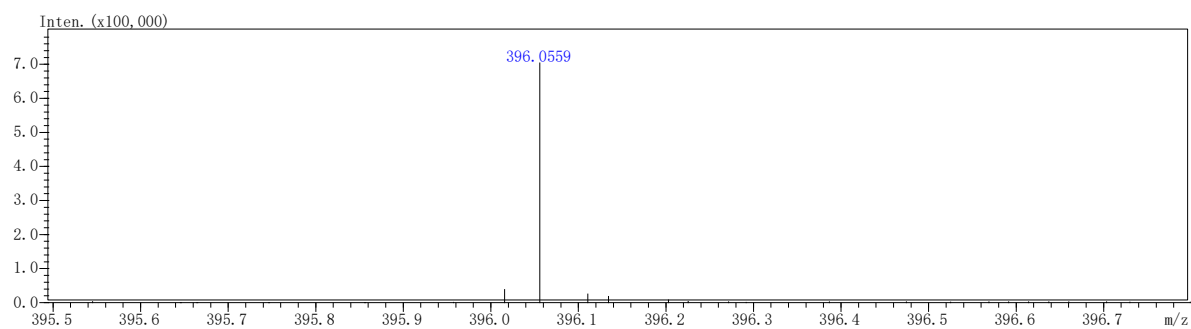


Figure S10. HRMS of compound 2c.

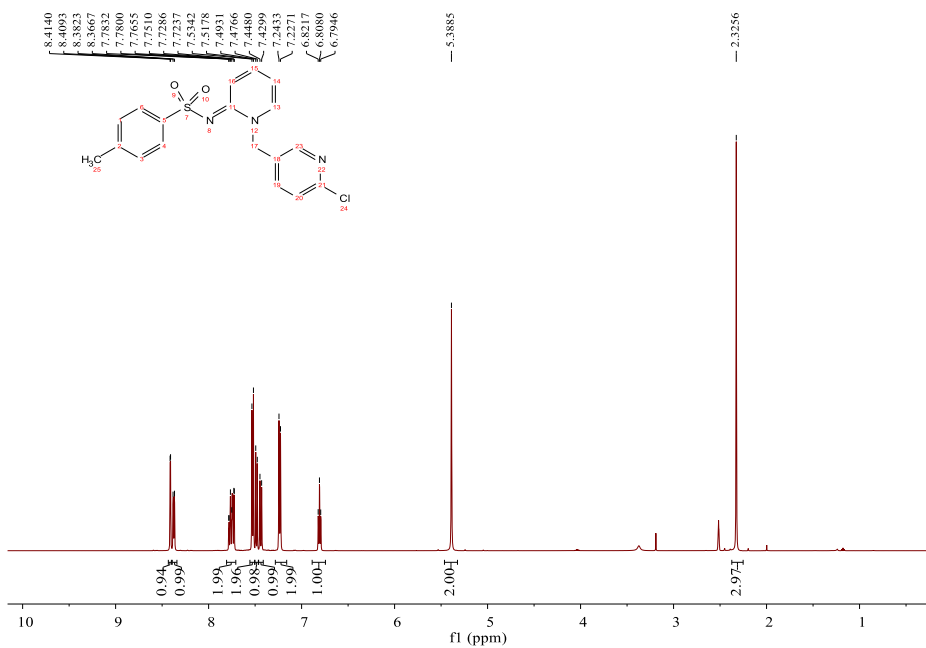


Figure S11.  $^1\text{H}$  NMR of compound 2d.

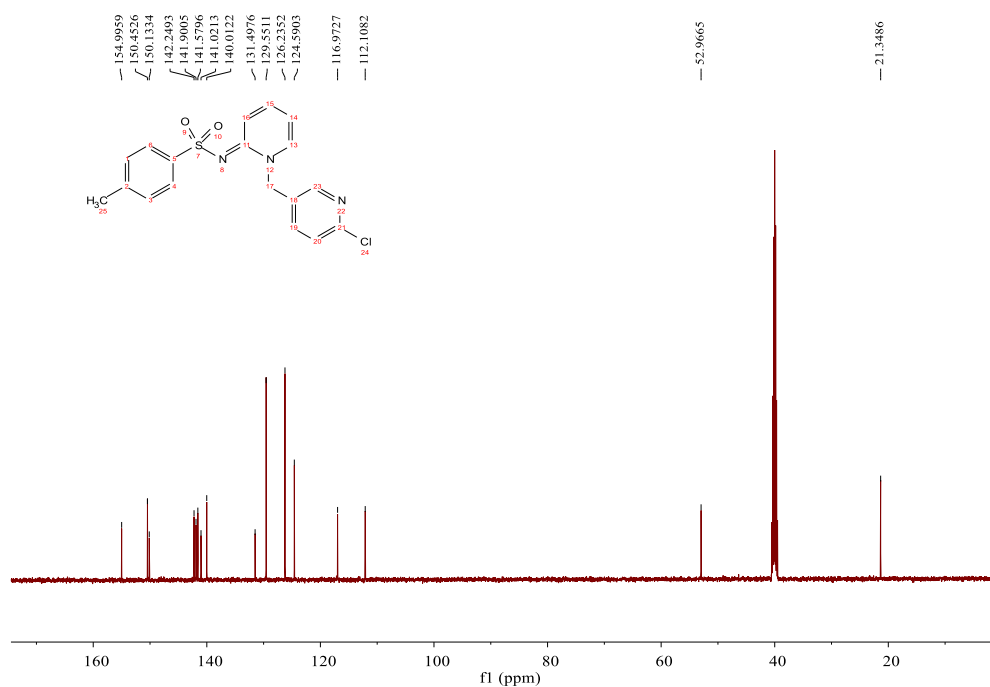


Figure S12. <sup>13</sup>C NMR of compound 2d.

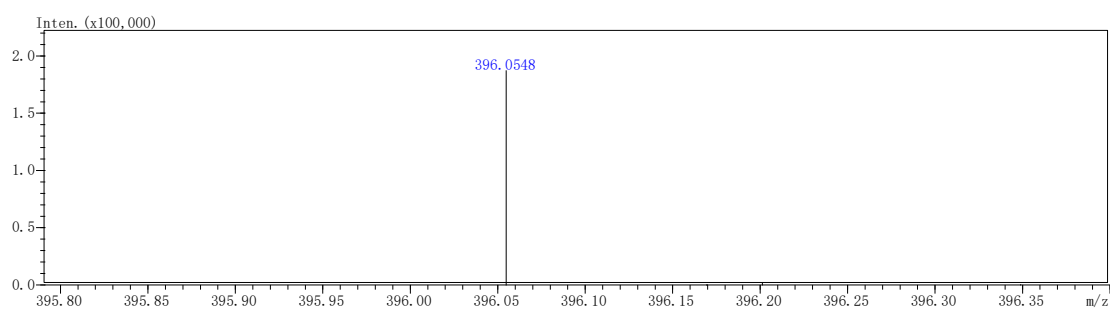


Figure S13. HRMS of compound 2d.

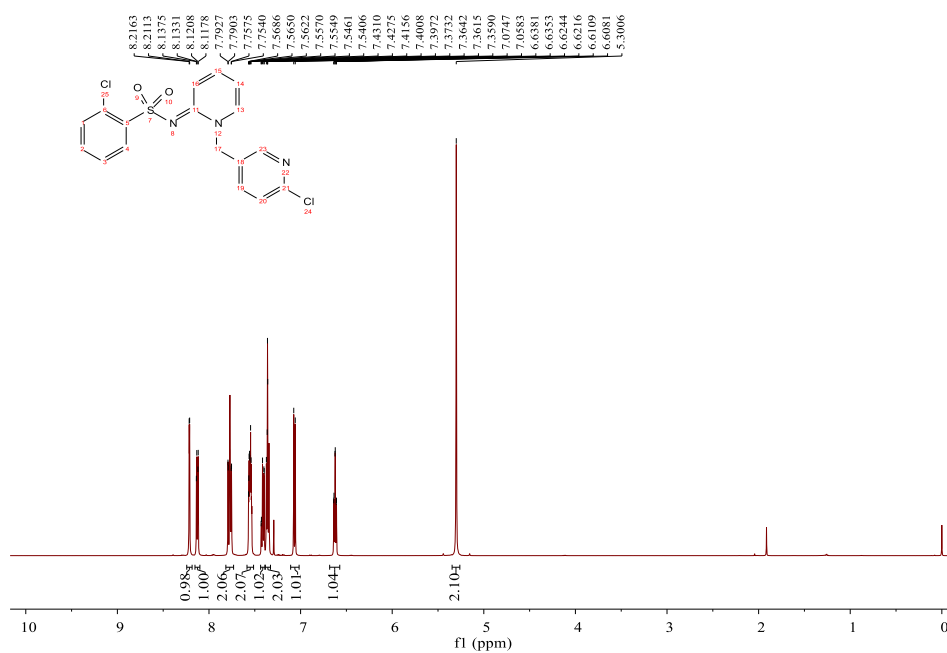


Figure S14. <sup>1</sup>H NMR of compound 2e.

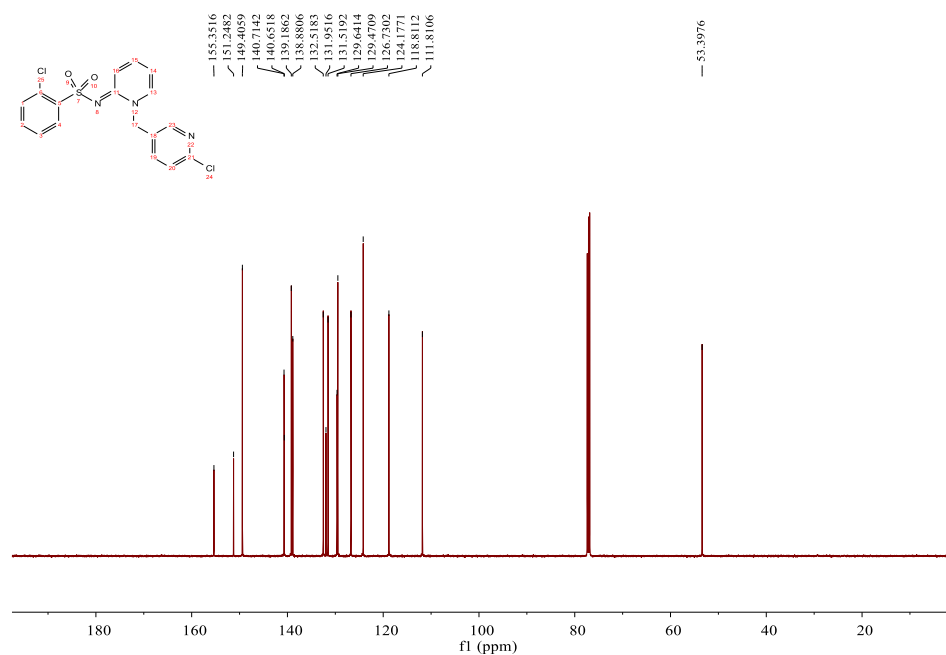


Figure S15.  $^{13}\text{C}$  NMR of compound 2e.

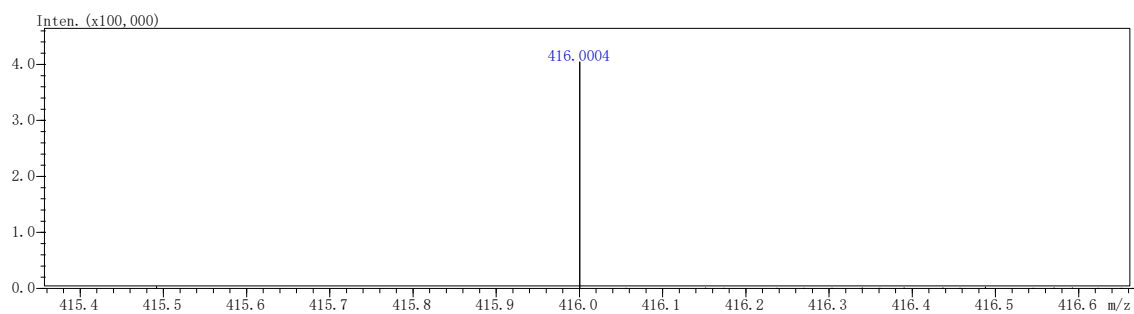


Figure S16. HRMS of compound 2e.

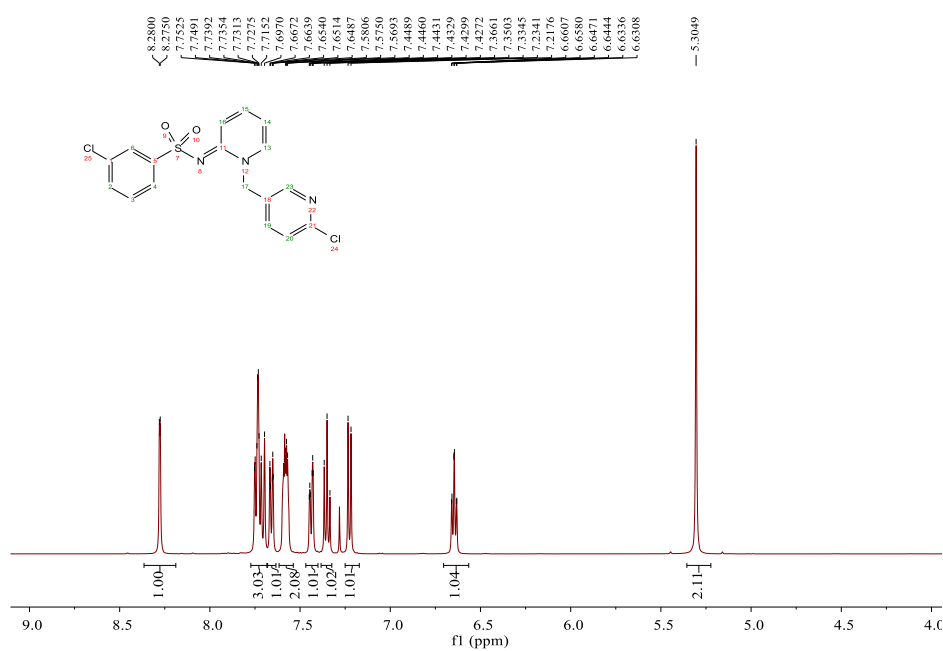


Figure S17.  $^1\text{H}$  NMR of compound 2f.



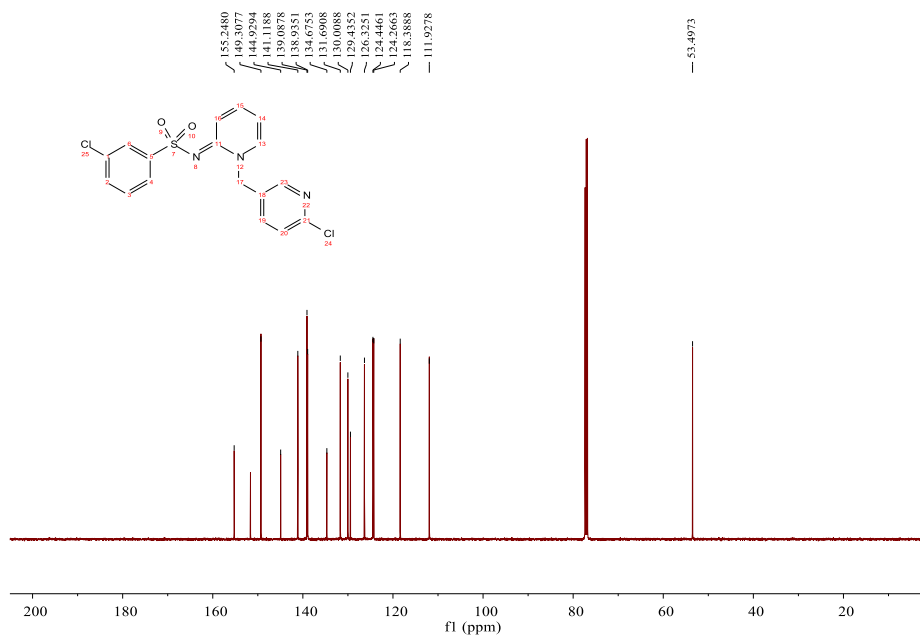


Figure S18. <sup>13</sup>C NMR of compound 2f.

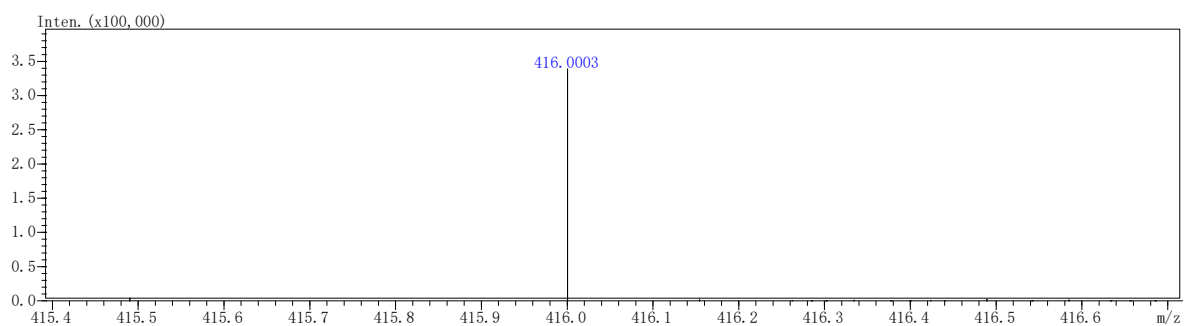


Figure S19. HRMS of compound 2f.

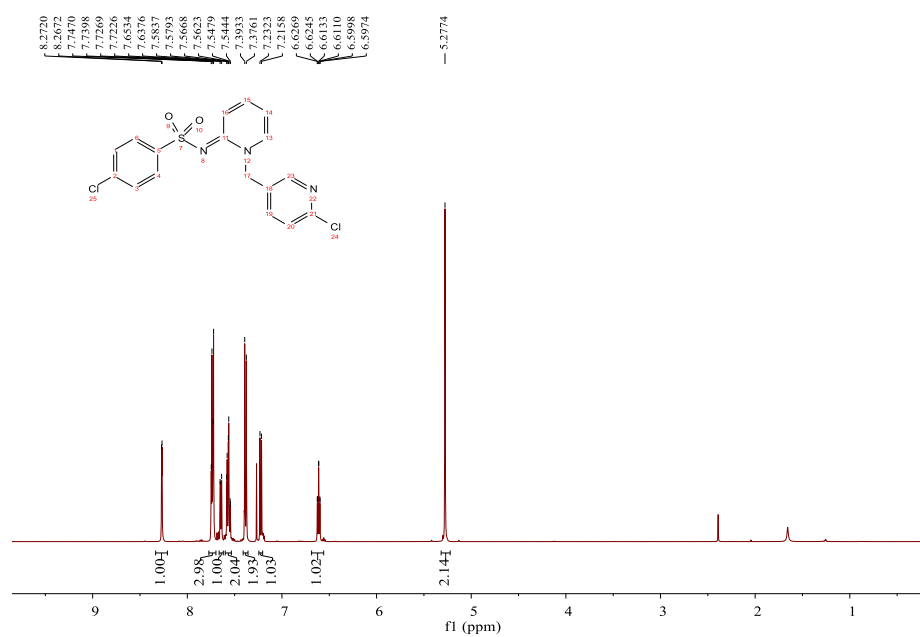


Figure S20. <sup>1</sup>H NMR of compound 2g.

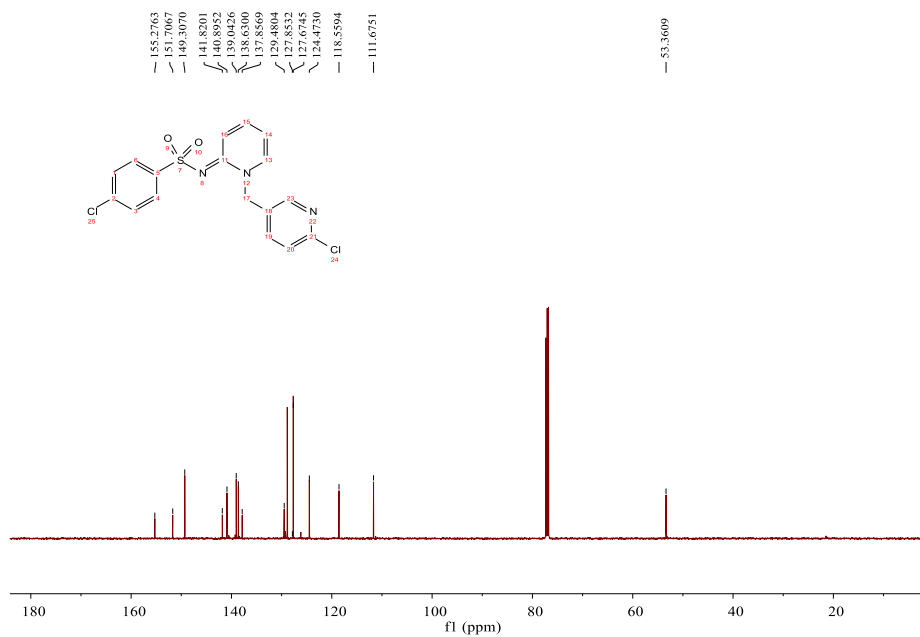


Figure S21. <sup>13</sup>C NMR of compound 2g.

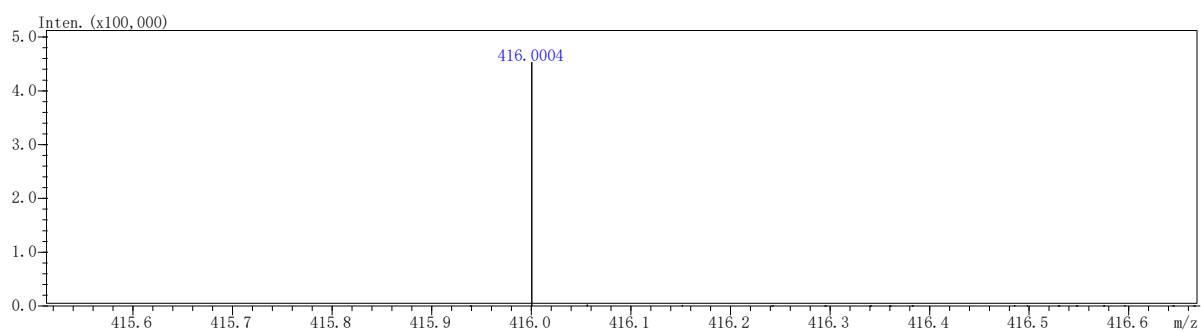


Figure S22. HRMS of compound 2g.

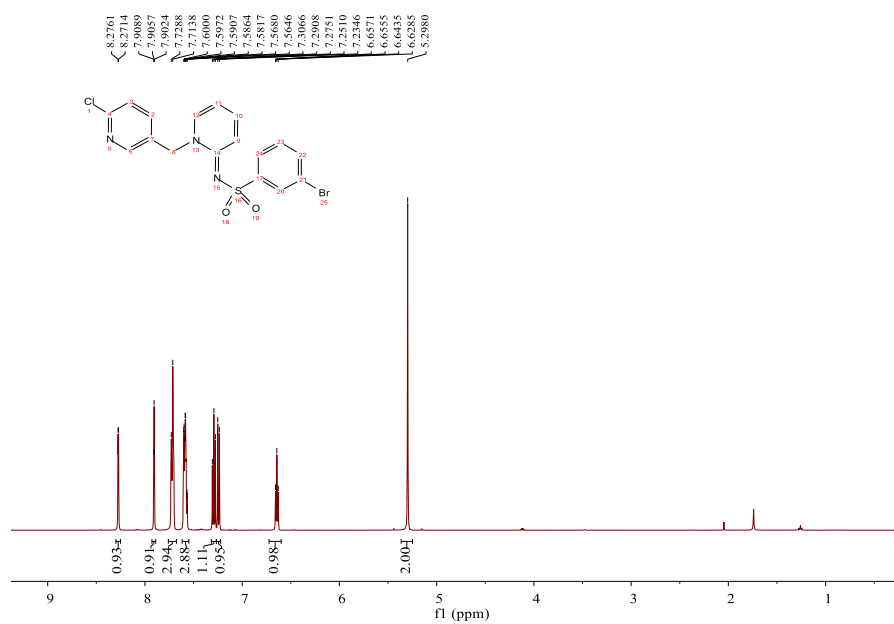


Figure S23. <sup>1</sup>H NMR of compound 2h.

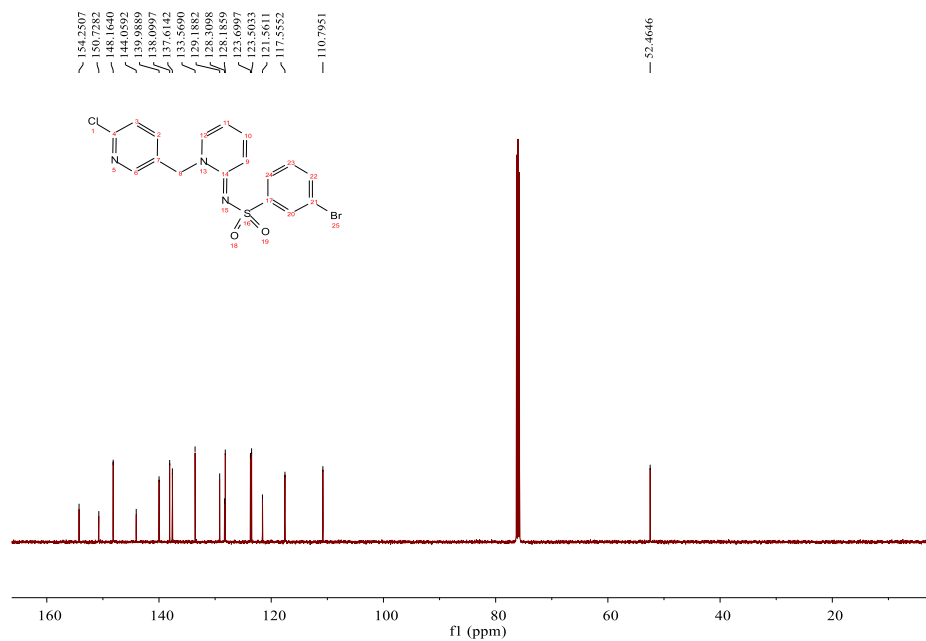


Figure S24. <sup>13</sup>C NMR of compound 2h.

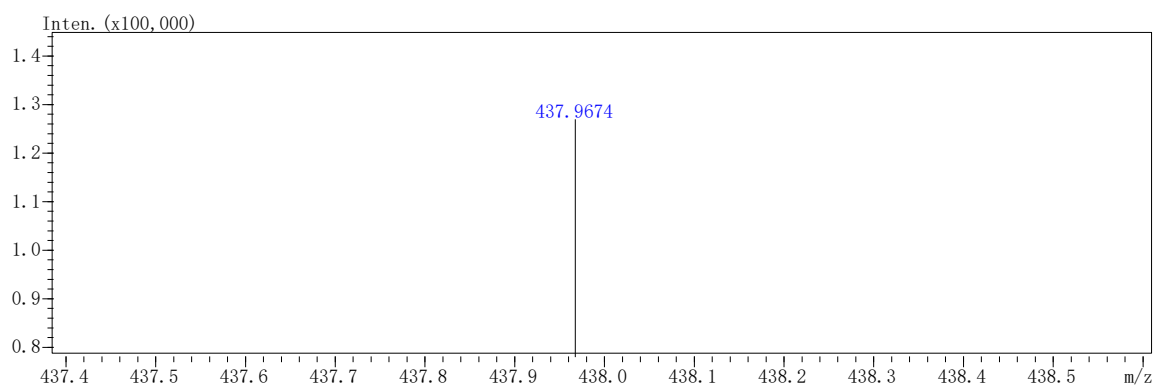


Figure S25. HRMS of compound 2h.

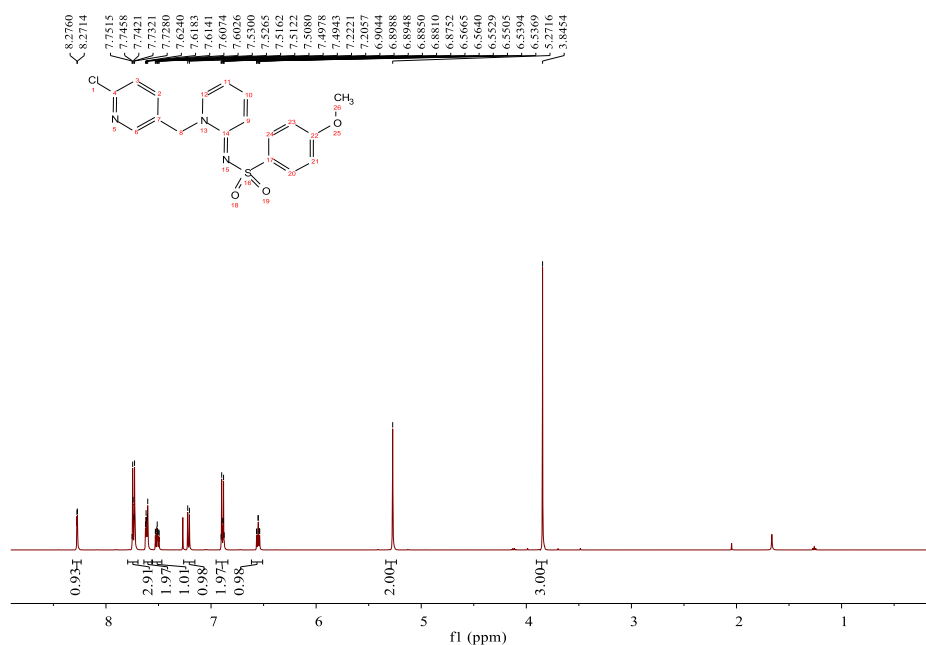


Figure S26. <sup>1</sup>H NMR of compound 2i.

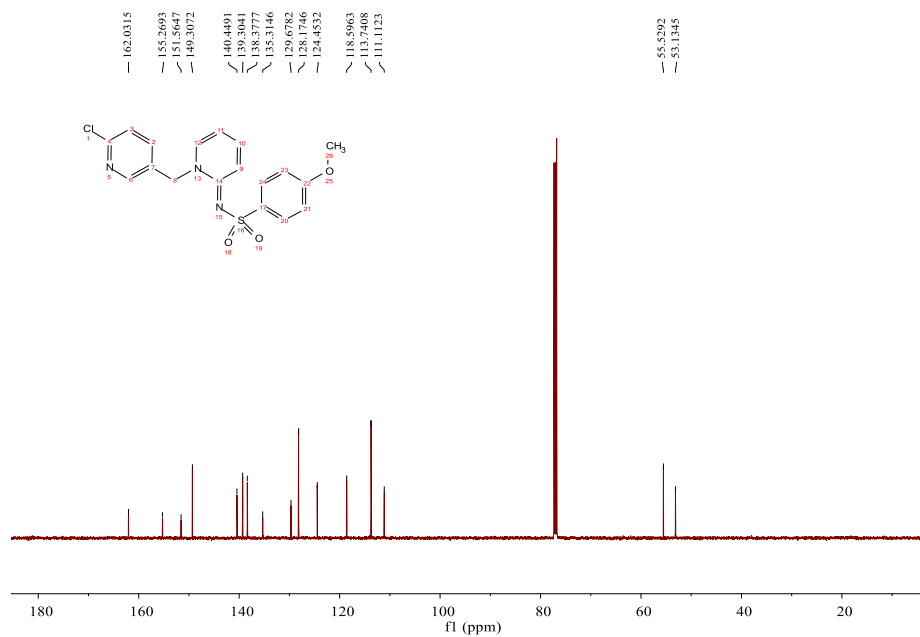


Figure S27. <sup>13</sup>C NMR of compound 2i.

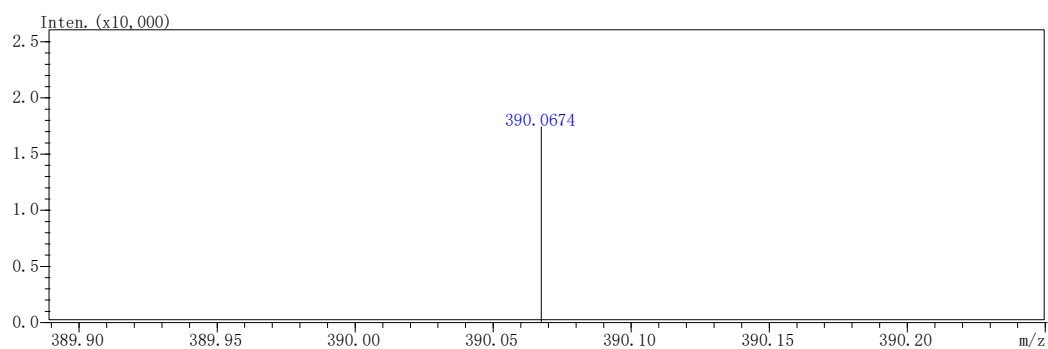


Figure S28. HRMS of compound 2i.

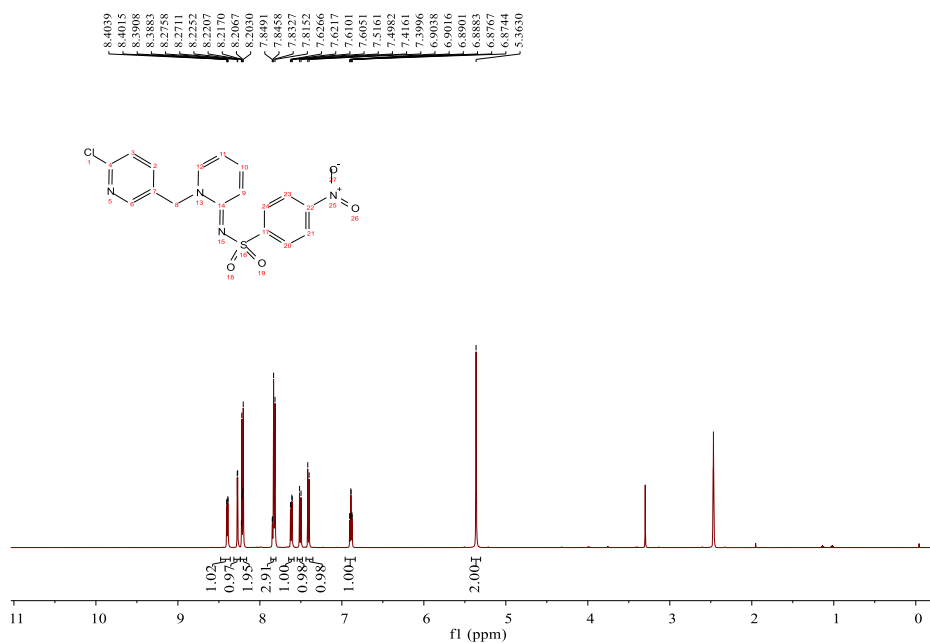


Figure S29. <sup>1</sup>H NMR of compound 2j.

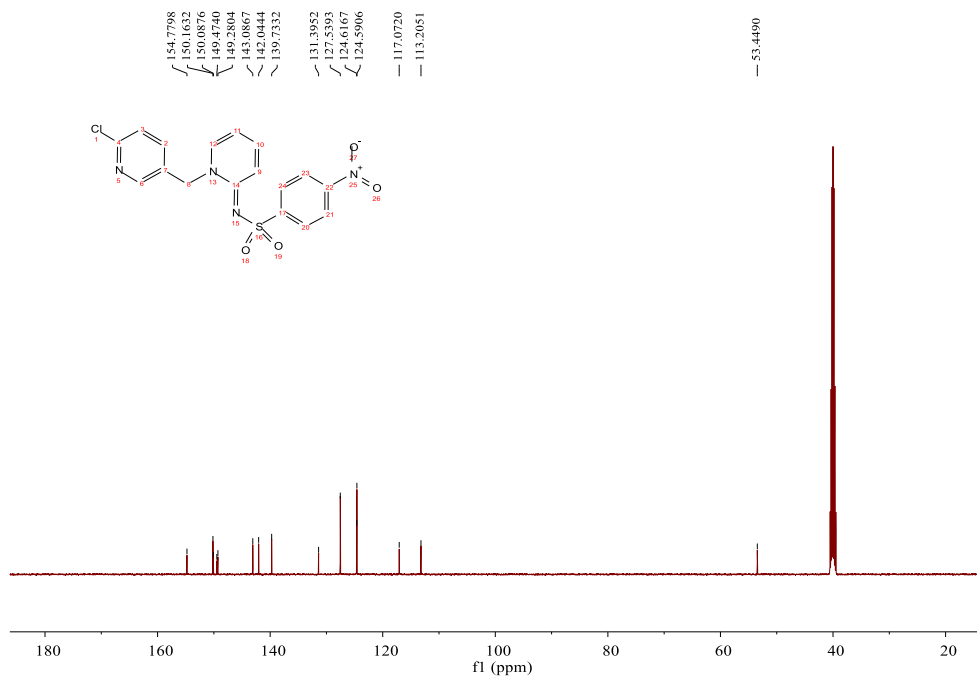


Figure S30.  $^{13}\text{C}$  NMR of compound 2j.

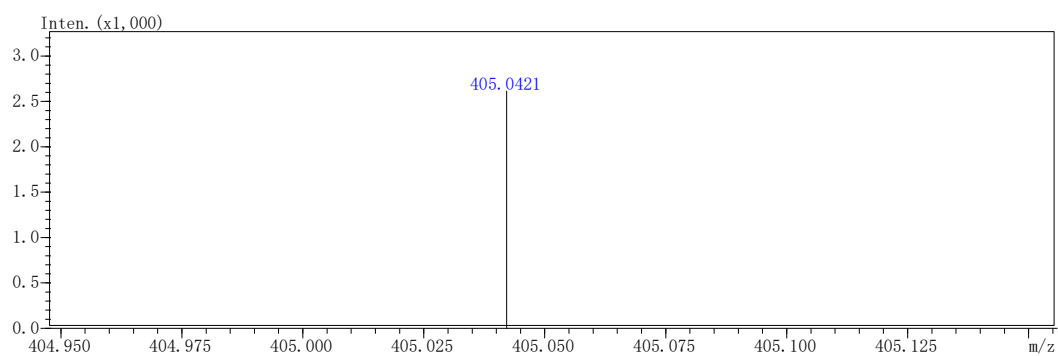


Figure S31. HRMS of compound 2j.

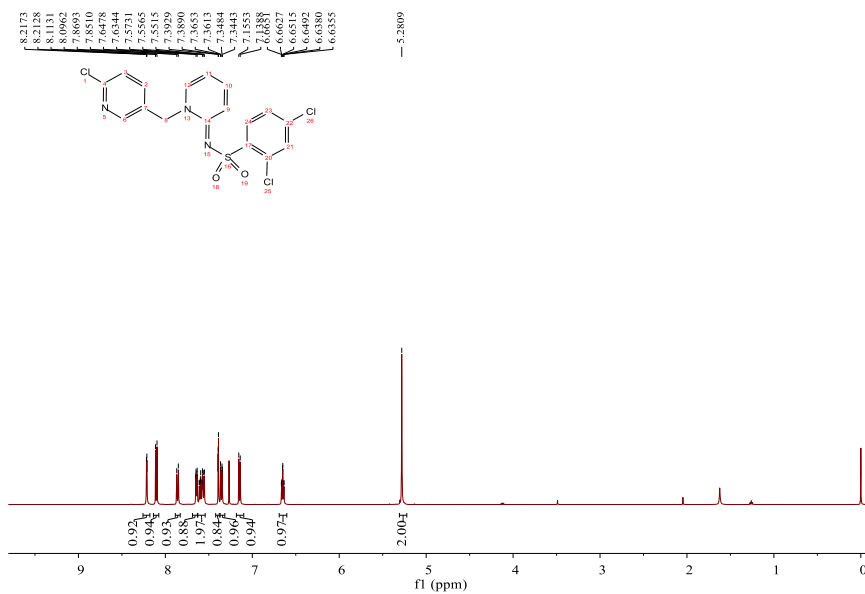


Figure S32.  $^1\text{H}$  NMR of compound 2k.

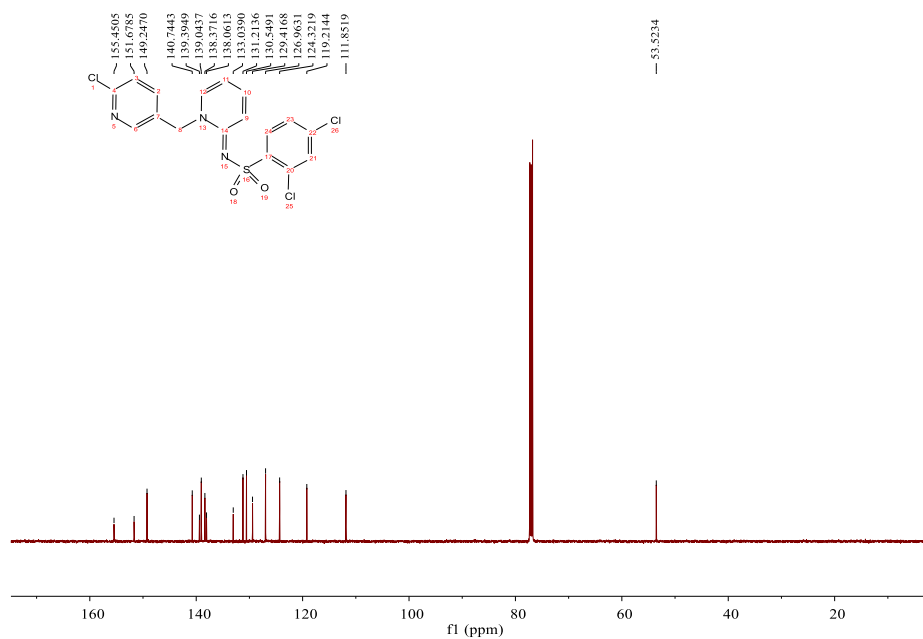


Figure S33.  $^{13}\text{C}$  NMR of compound 2k.

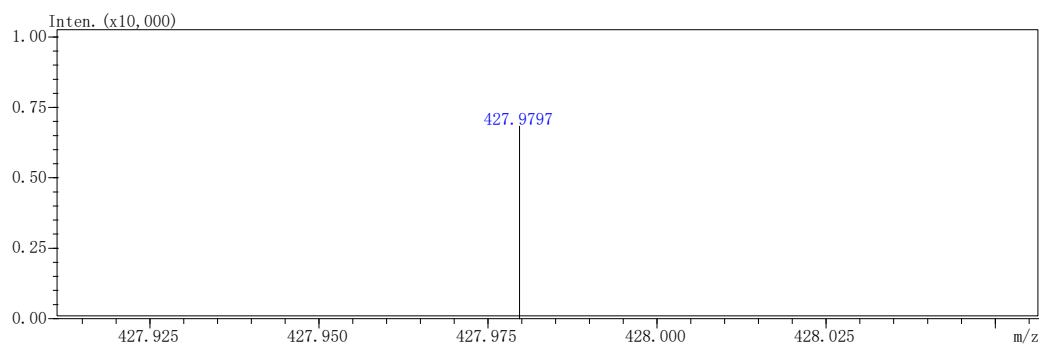


Figure S34. HRMS of compound 2k.

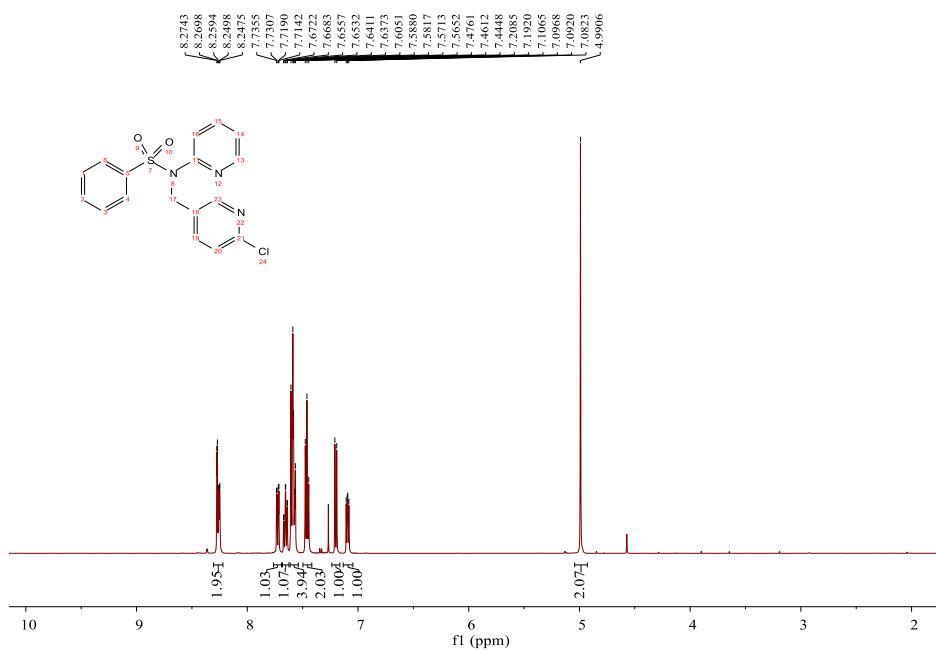


Figure S35.  $^1\text{H}$  NMR of compound 3a.

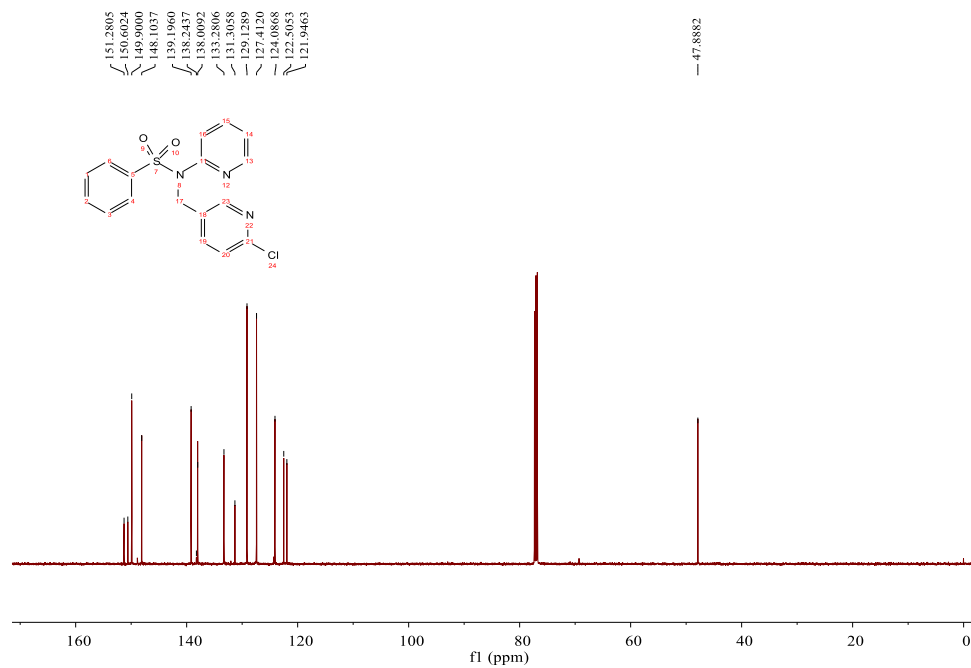


Figure S36. <sup>13</sup>C NMR of compound 3a.

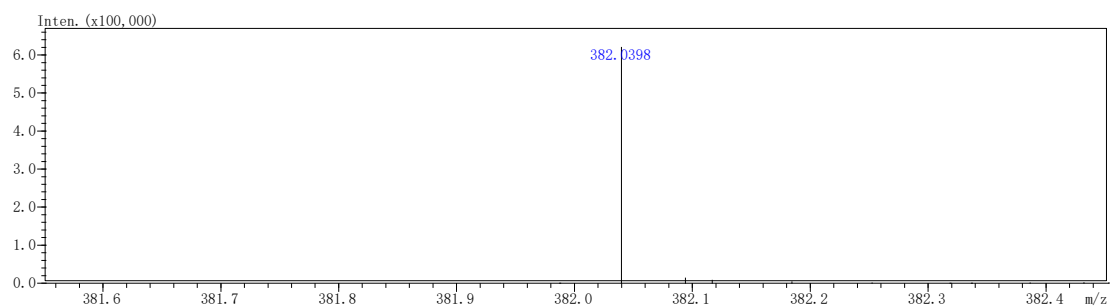


Figure S37. HRMS of compound 3a.

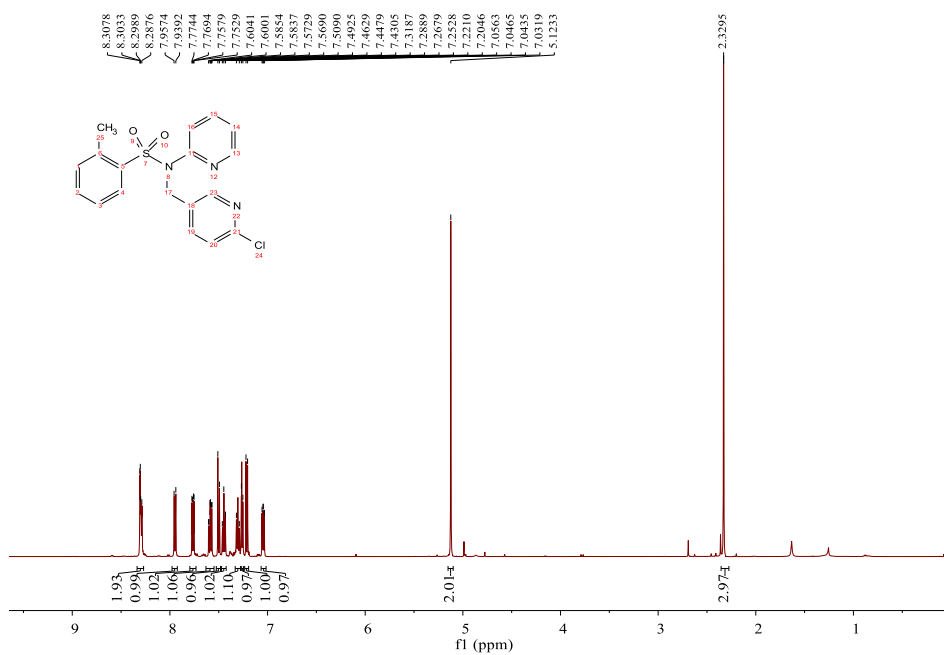


Figure S38. <sup>1</sup>H NMR of compound 3b.

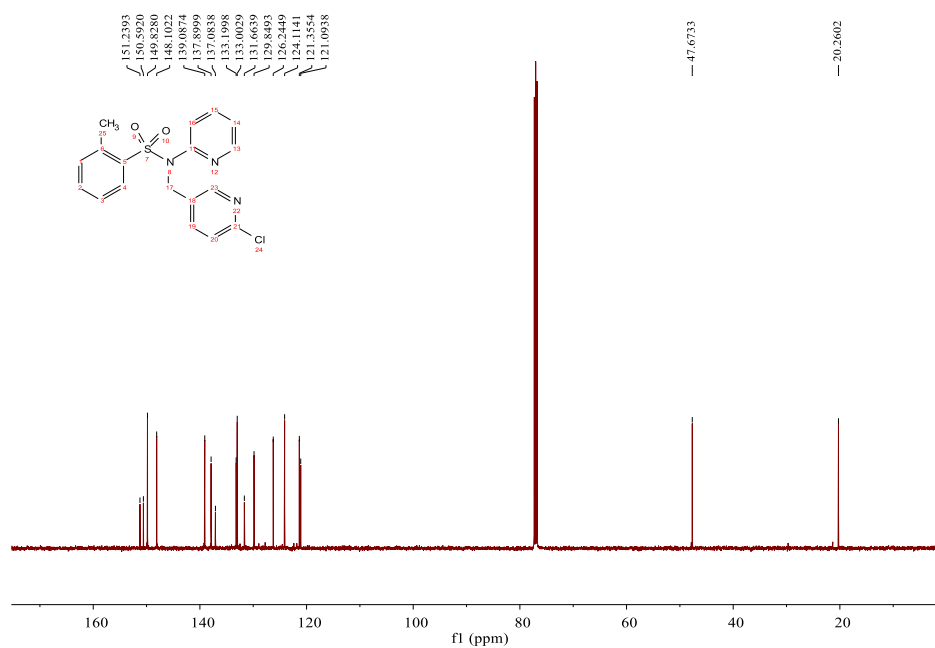


Figure S39. <sup>13</sup>C NMR of compound 3b.

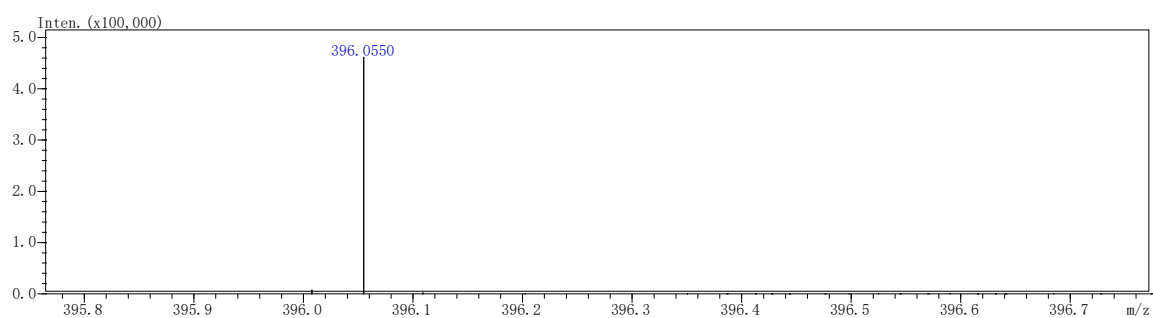


Figure S40. HRMS of compound 3b.

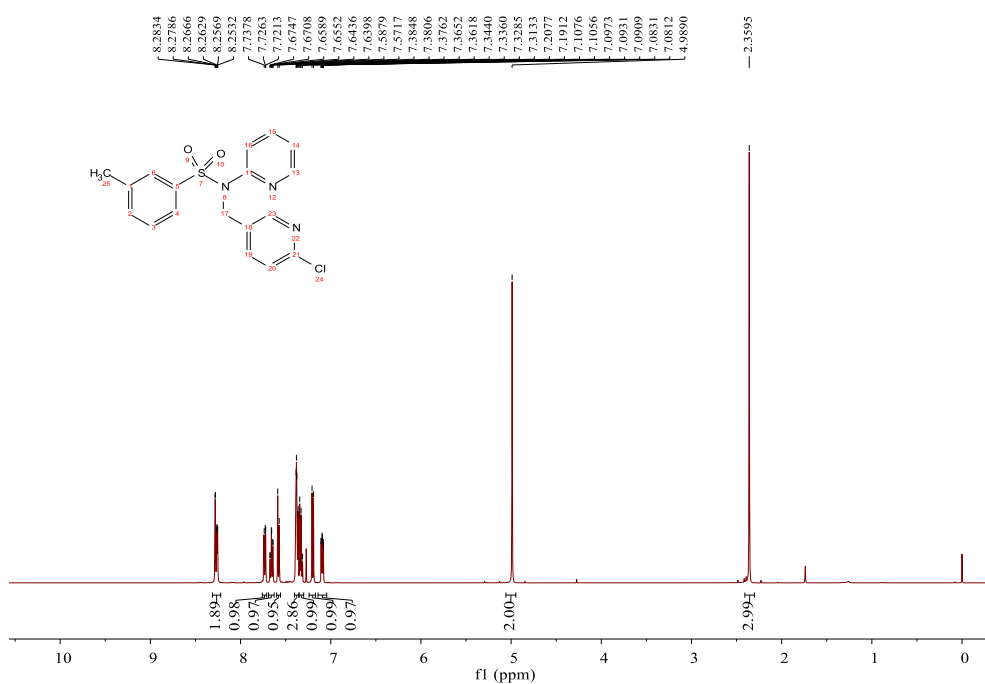


Figure S41. <sup>1</sup>H NMR of compound 3c.



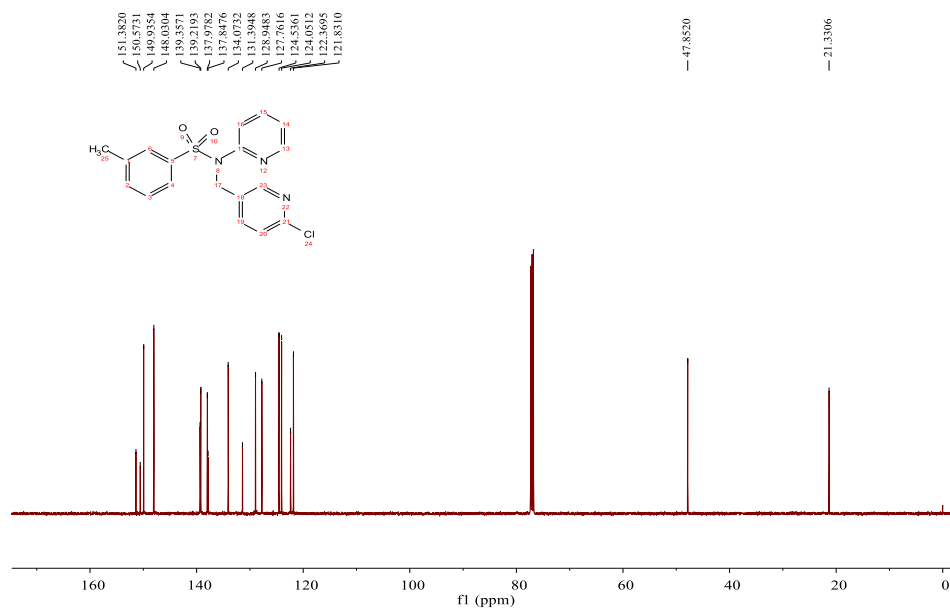


Figure S42. <sup>13</sup>C NMR of compound 3c.

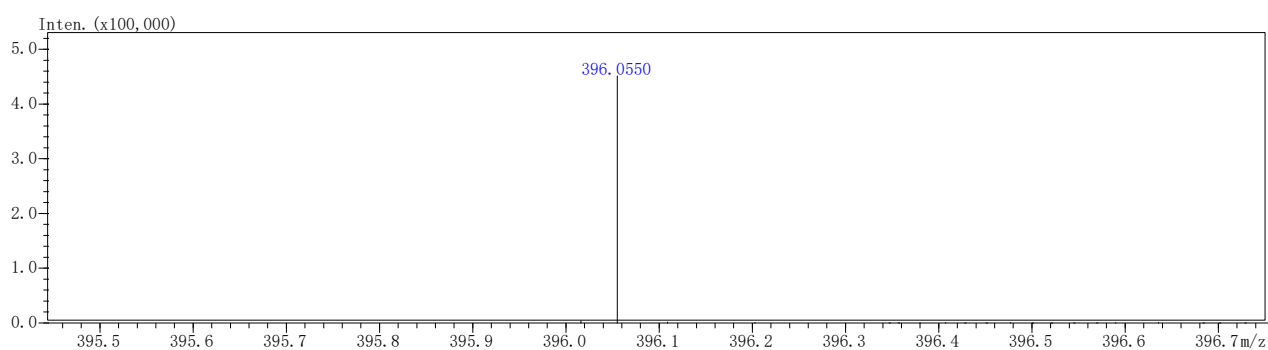


Figure S43. HRMS of compound 3c.

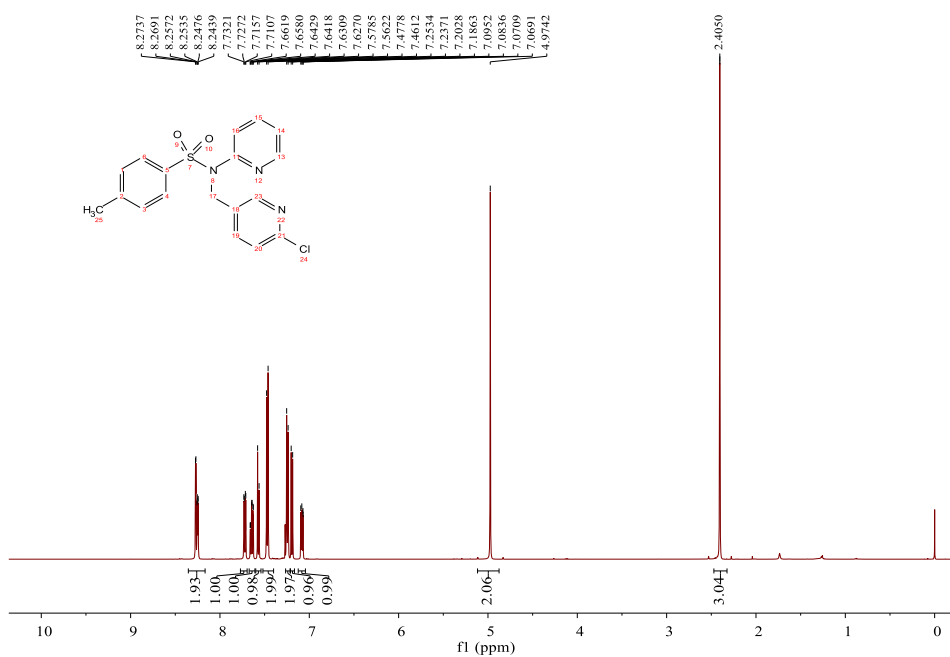


Figure S44. <sup>1</sup>H NMR of compound 3d.

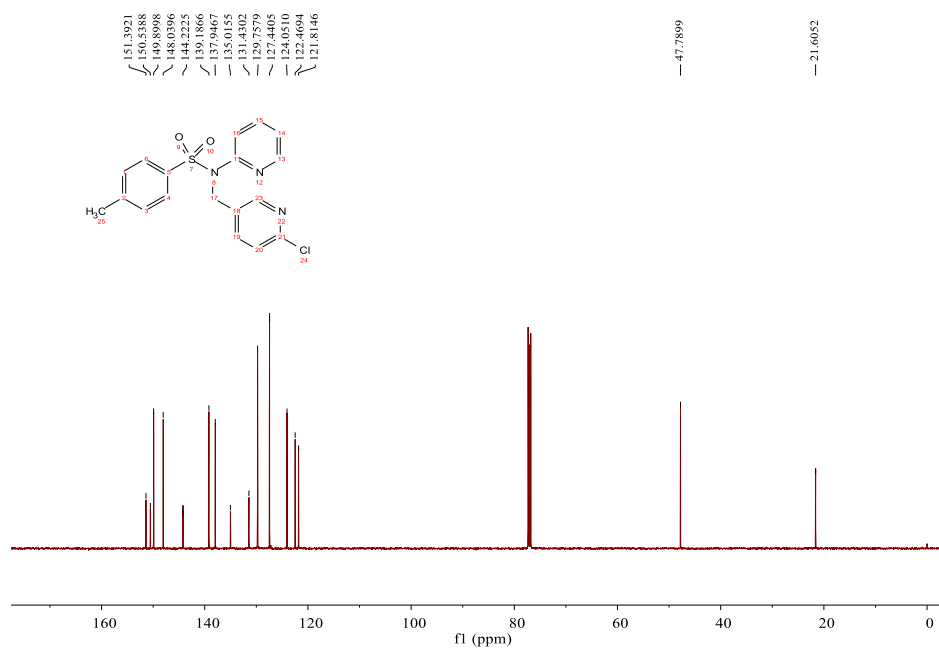


Figure S45. <sup>13</sup>C NMR of compound 3d.

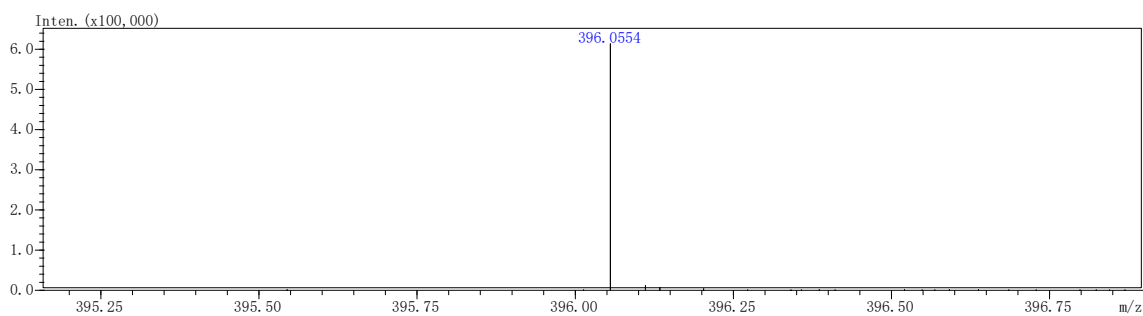


Figure S46. HRMS of compound 3d.

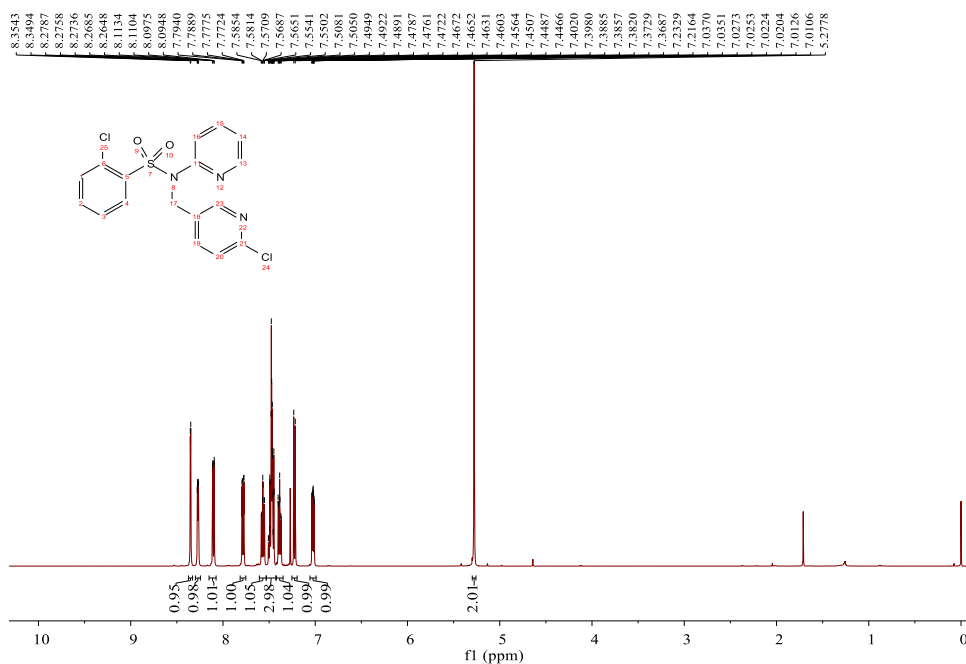


Figure S47. <sup>1</sup>H NMR of compound 3e.

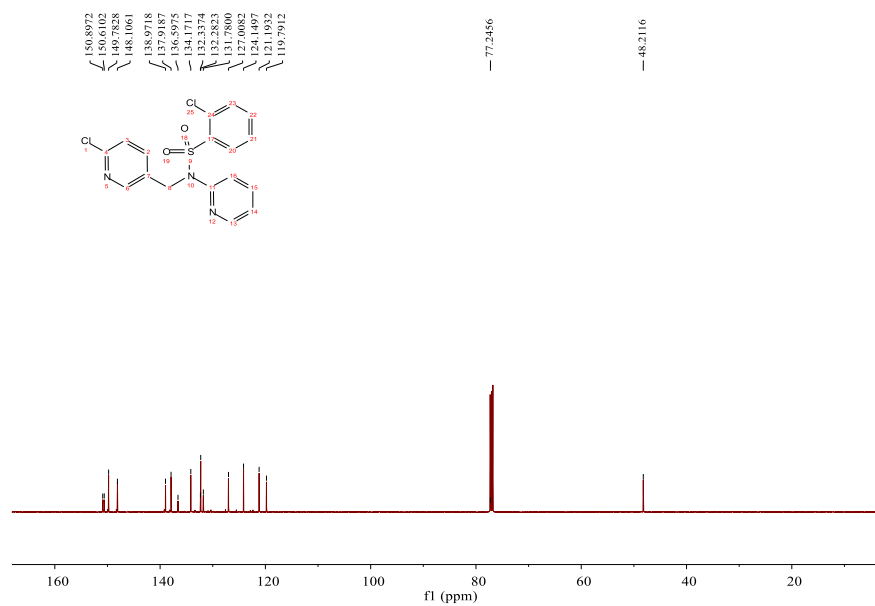


Figure S48. <sup>13</sup>C NMR of compound 3e.

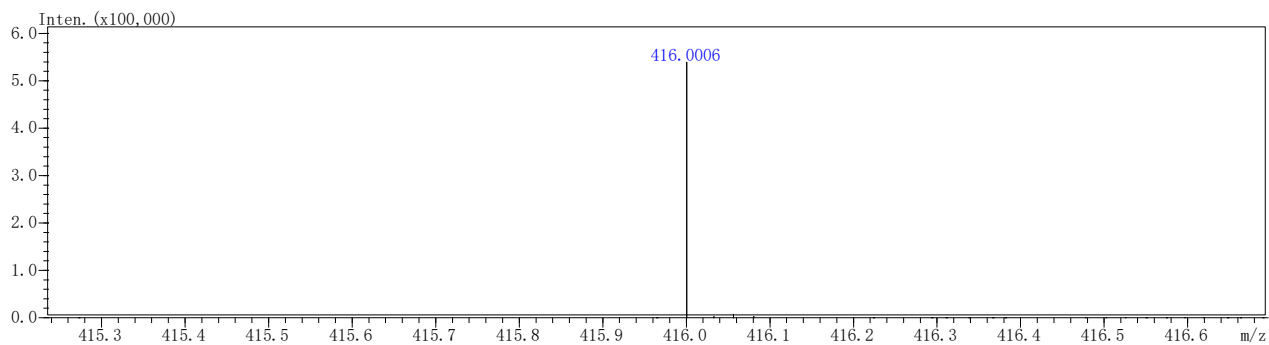


Figure S49. HRMS of compound 3e.

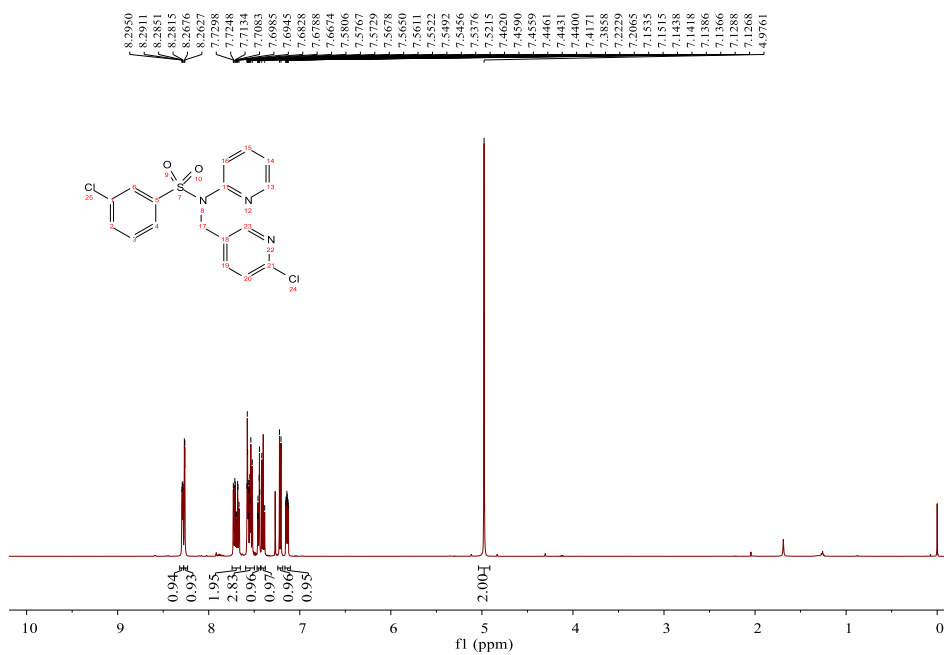


Figure S50. <sup>1</sup>H NMR of compound 3f.

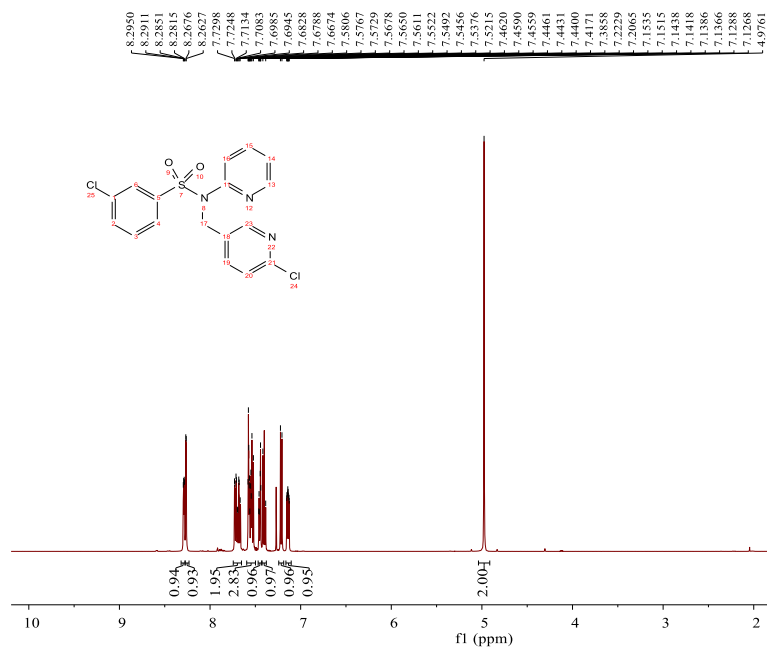


Figure S51. <sup>13</sup>C NMR of compound 3f.

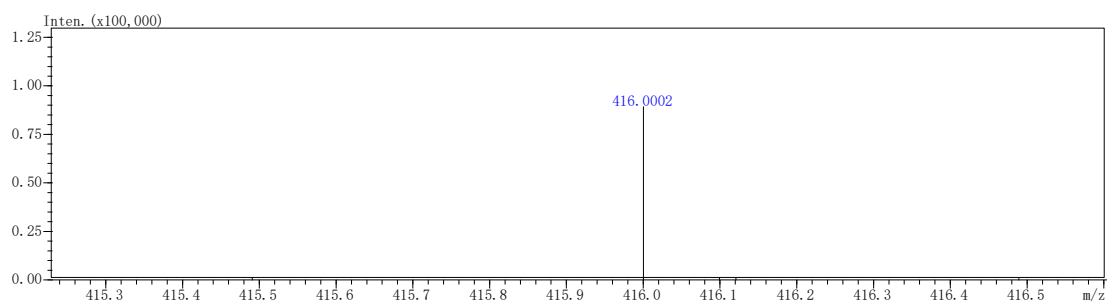


Figure S52. HRMS of compound 3f.

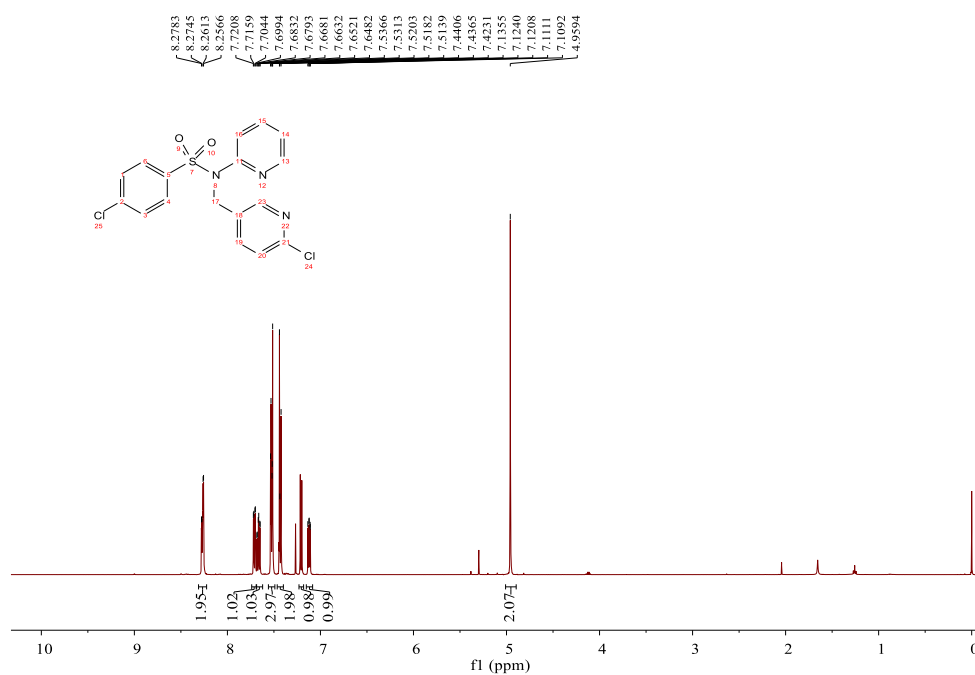


Figure S53. <sup>1</sup>H NMR of compound 3g.

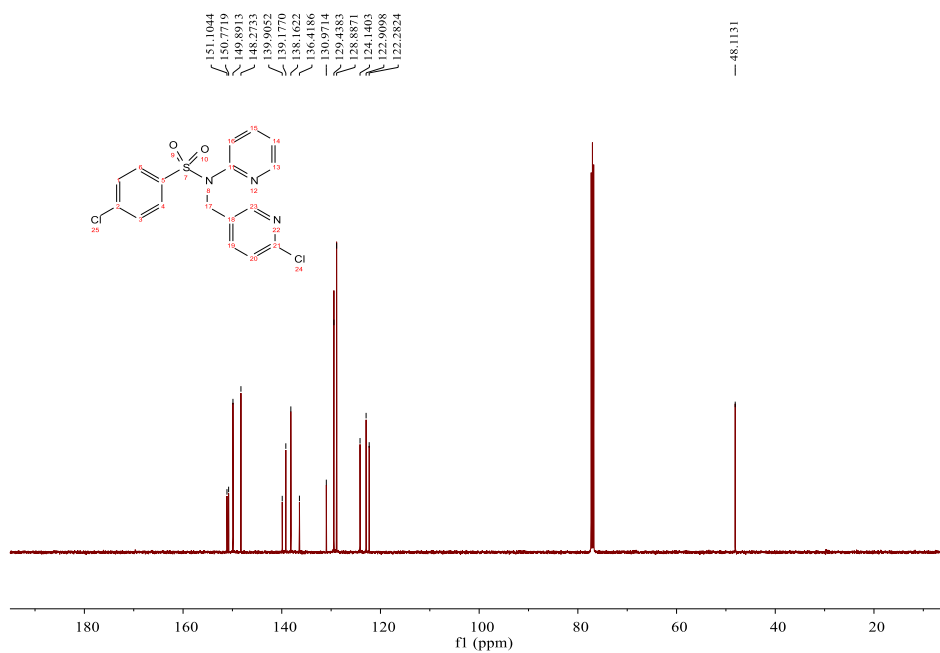


Figure S54. <sup>13</sup>C NMR of compound 3g.

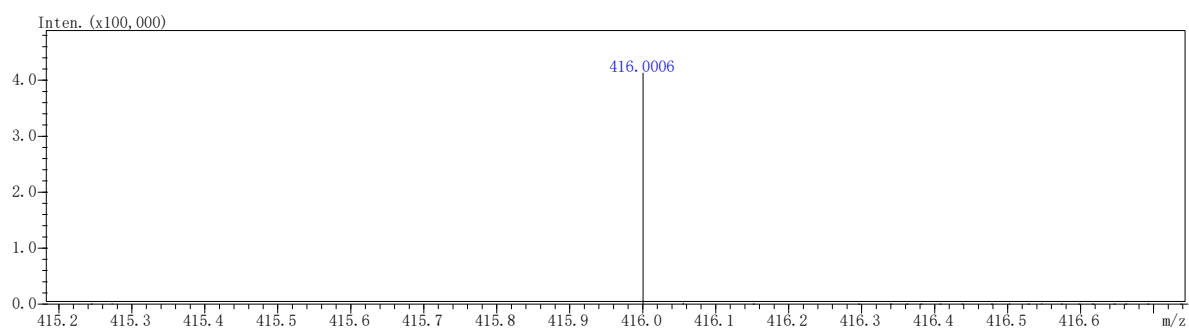


Figure S55. HRMS of compound 3g.

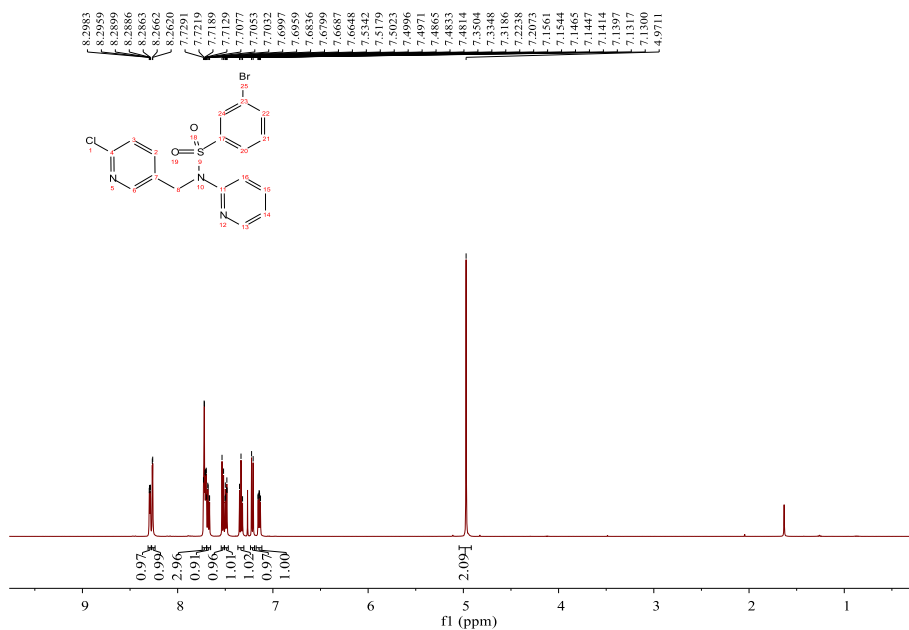


Figure S56. <sup>1</sup>H NMR of compound 3h.

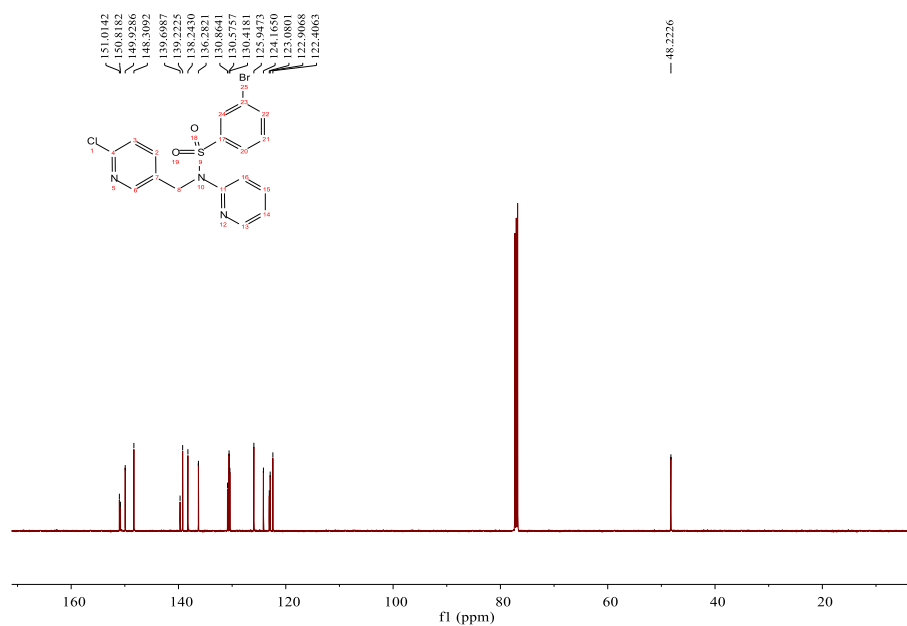


Figure S57. <sup>13</sup>C NMR of compound 3h.

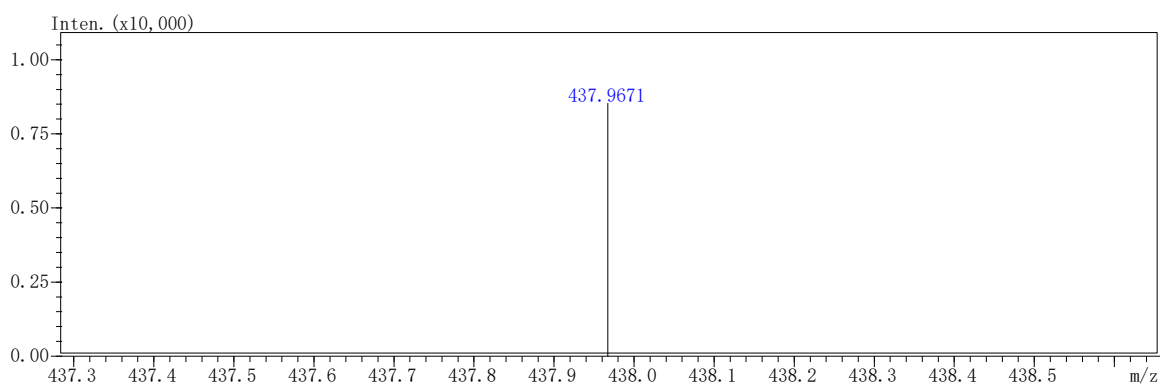


Figure S58. HRMS of compound 3h.

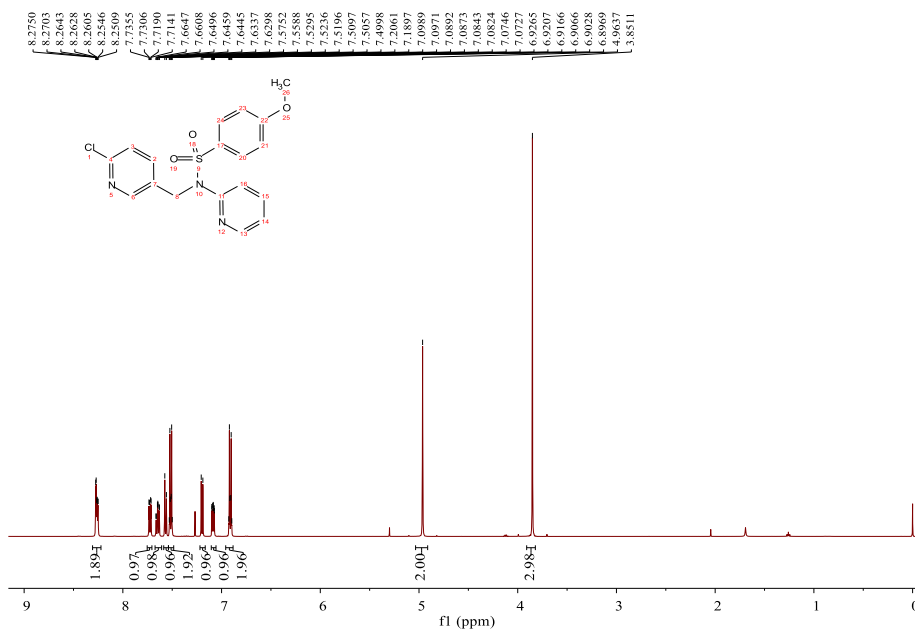


Figure S59. <sup>1</sup>H NMR of compound 3i.

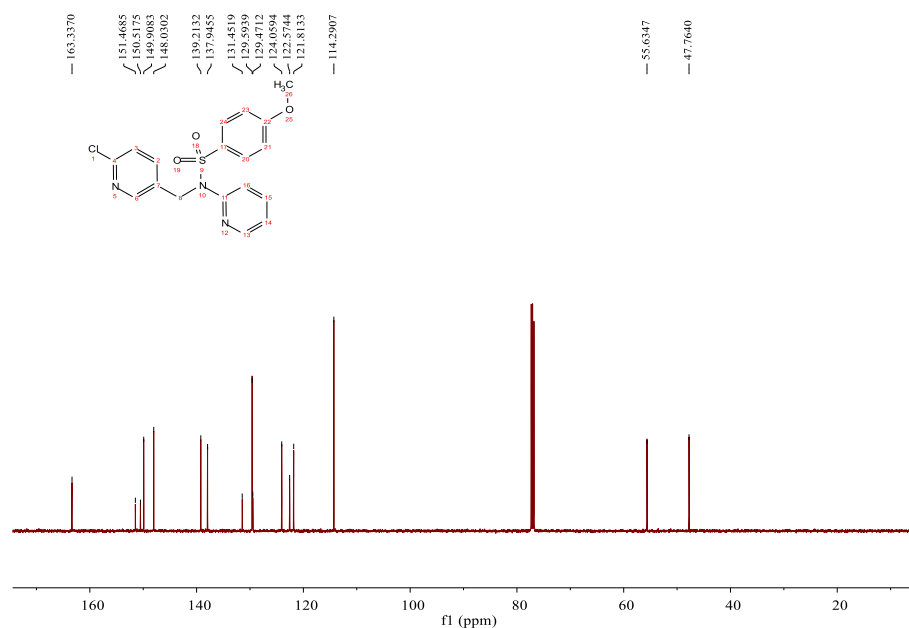


Figure S60.  $^{13}\text{C}$  NMR of compound 3i.

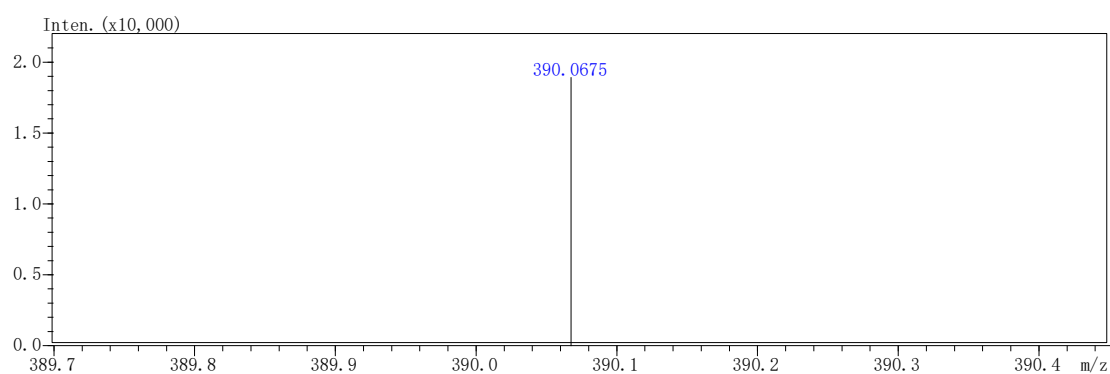


Figure S61. HRMS of compound 3i.

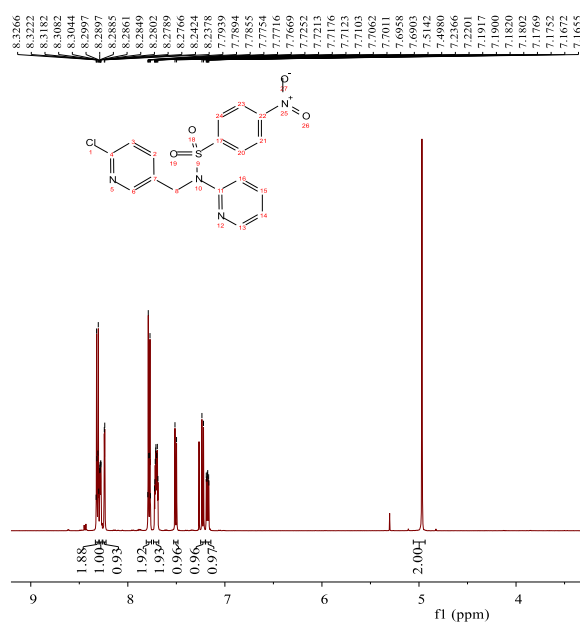


Figure S62.  $^1\text{H}$  NMR of compound 3j.

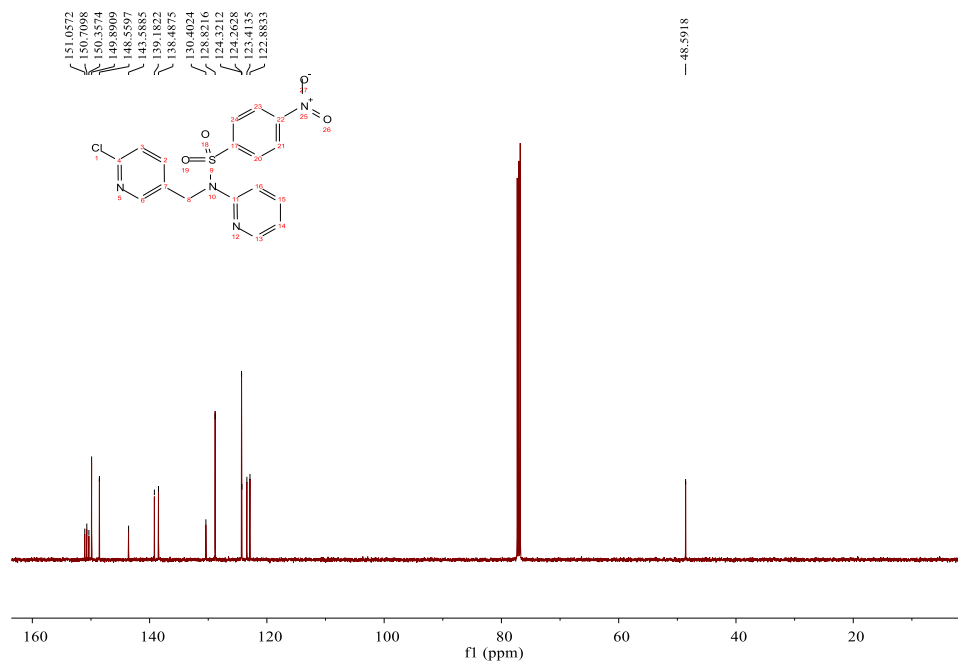


Figure S63.  $^{13}\text{C}$  NMR of compound 3j.

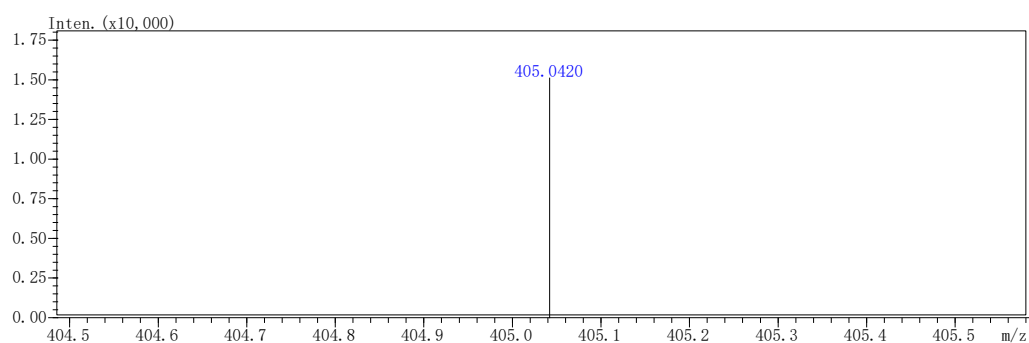


Figure S64. HRMS of compound 3j.

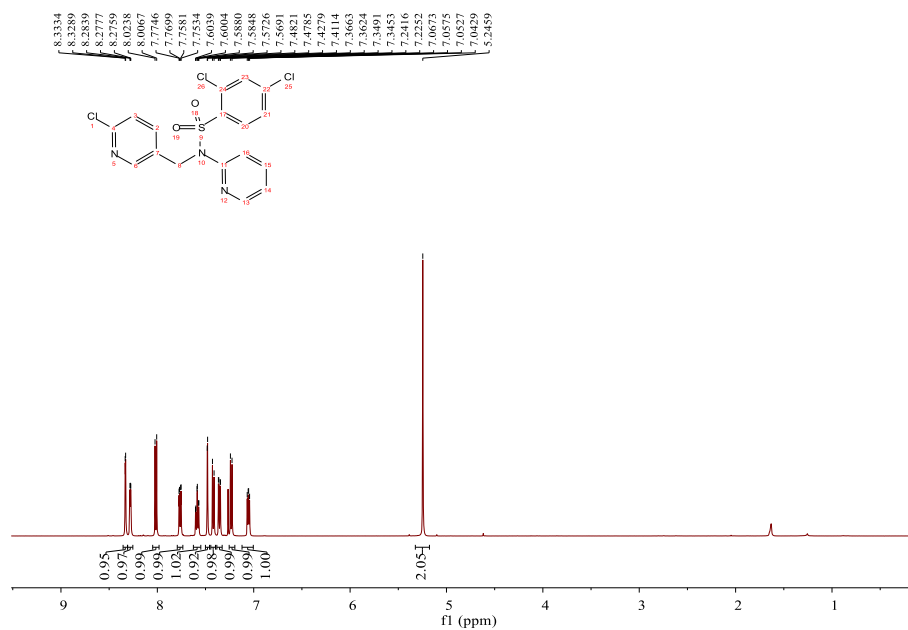
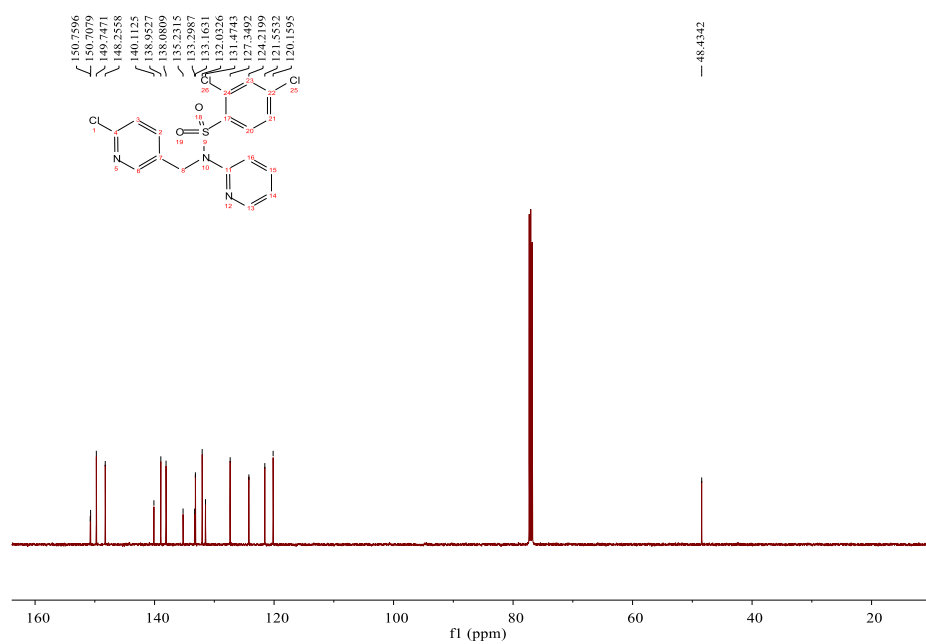
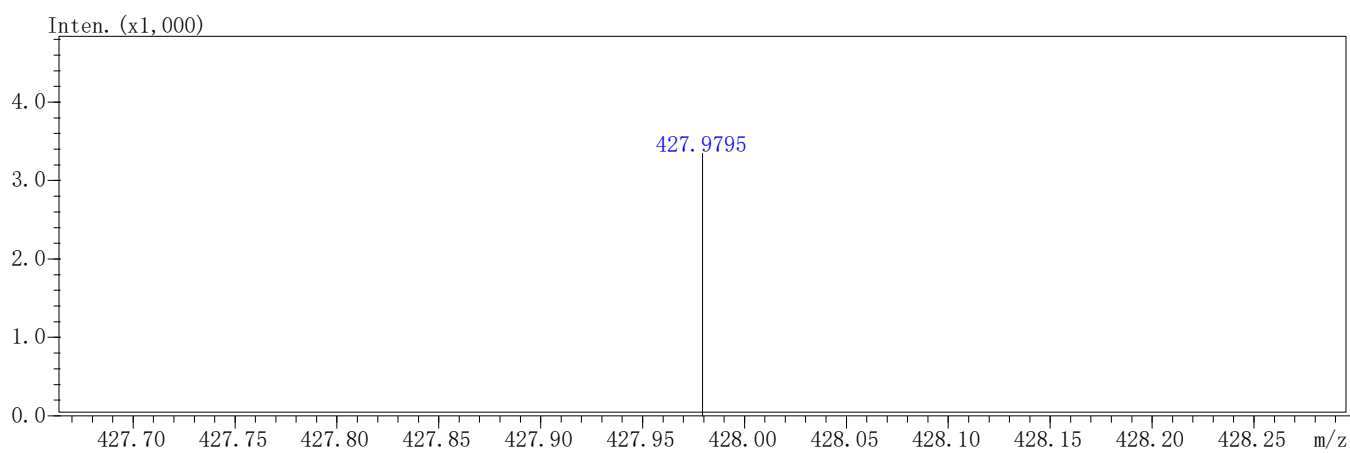


Figure S65.  $^1\text{H}$  NMR of compound 3k.





**Figure S66.**  $^{13}\text{C}$  NMR of compound **3k**.



**Figure S67.** HRMS of compound **3k**.