

Discovery of novel BCAT2 inhibitors: design, synthesis, in vitro evaluation, and molecular modeling studies

Dong Xu^{①abc}, Wenxiu Weng^{②de}, Huining Cao^{abc}, Chao Zhang^{bc}, Yudi Zhang^{de}, Yan Li^{de}, Junhai Xiao^{bc}, Hua Xie^{*de}, Jialin Guo^{*bc}, Guoliang Chen^{*a}

^a Key Laboratory of Structure-Based Drug Design & Discovery of Ministry of Education, School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang 110016, China

^b National Engineering Research Center for the Emergency Prevention and Control Drugs, Beijing 100039, China

^c Academy of Military Medical Sciences, Beijing, 100850, China

^d Zhongshan Institute for Drug Discovery, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Zhongshan 528400, China

^e Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China

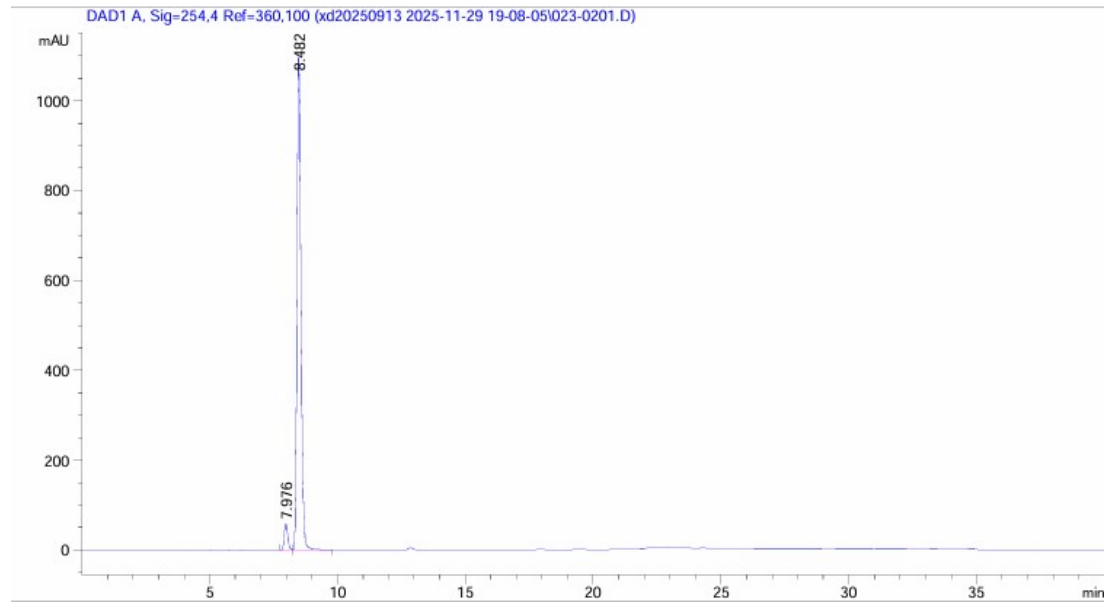
E-mail: spucgl@163.com (Chen Guoliang), shandongguojialin@163.com (Guo Jialin), hxie@simm.ac.cn (Hua Xie)

1. HPLC Characterization of purity

Purity of compound **C10** and **C11** was measured by HPLC was carried out on the Agilent 1260 HPLC system with an Agilent ZORBAX Eclipse XDBC18 column (5 μ m, 4.6 \times 100 mm).

Method: The gradient profile was as follows: 10-90% acetonitrile (0-30 min), returned to 10% (31 min), and held for 9 min for column equilibration (total run time: 40 min).

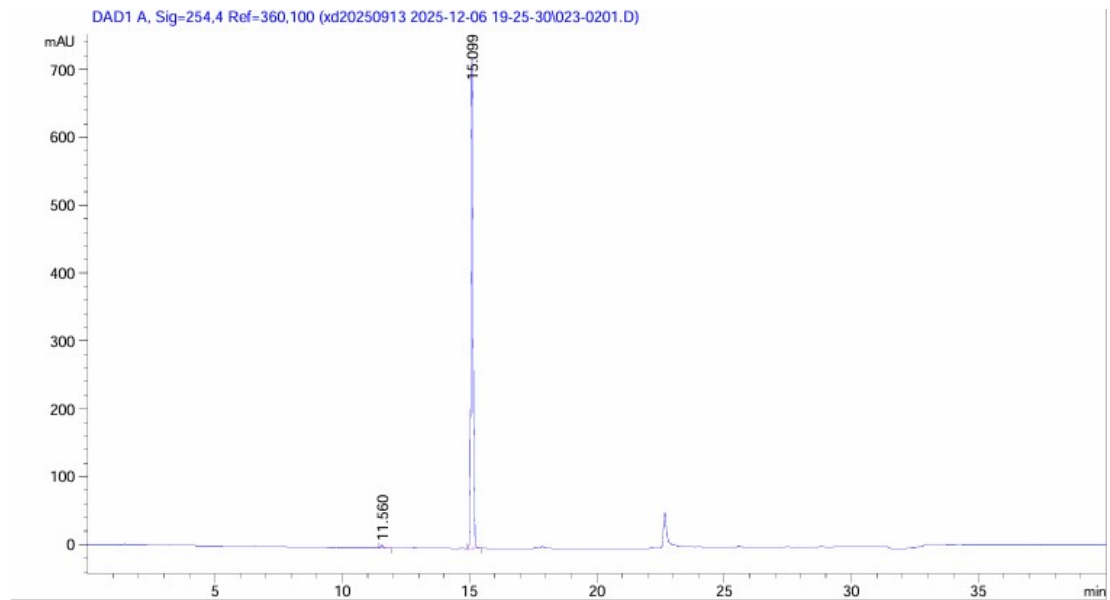
Purity: **C10**, 95.4761%; **C11**, 99.4221%.



信号 1: DAD1 A, Sig=254,4 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	7.976	BV	0.1449	551.56104	59.07063	4.5239
2	8.482	VB	0.1639	1.16406e4	1096.04370	95.4761

Figure 1. HPLC Characterization of purity for C10



信号 1: DAD1 A, Sig=254,4 Ref=360,100

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 [mAU*s]	峰高 [mAU]	峰面积 %
1	11.560	BB	0.0842	24.30776	4.41556	0.5779
2	15.099	BB	0.0894	4181.91357	723.90521	99.4221
总量:				4206.22133	728.32077	

Figure 2. HPLC Characterization of purity for C11

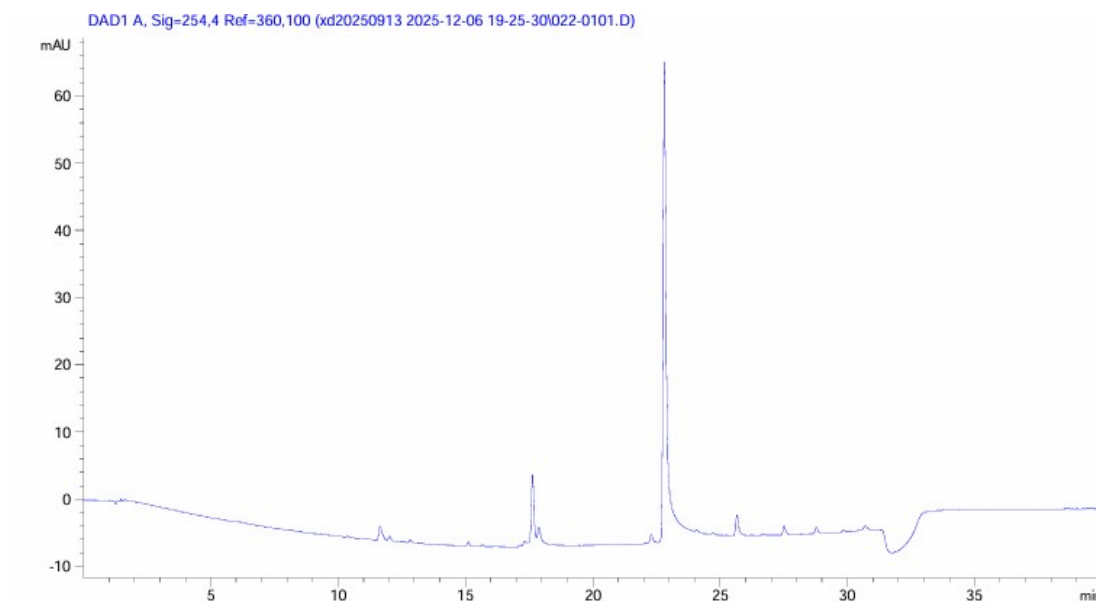


Figure 3. HPLC characterization of C11 solvent purity

2. Compound Data Characterization

N²-phenyl-1H-indole-2,5-dicarboxamide (A1). White solid, m.p. 275-277°C. Yield: 68.5%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 12.11 (s, 1H), 10.44 (s, 1H), 8.30 (s, 1H), 7.95 (s, 1H), 7.86 (d, *J* = 7.5 Hz, 1H), 7.80 (d, *J* = 10.3 Hz, 1H), 7.59 (s, 1H), 7.48 (d, *J* = 8.8 Hz, 1H), 7.37 (t, *J* = 7.9 Hz, 2H), 7.19 (s, 1H), 7.11 (t, *J* = 7.4 Hz, 1H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 169.13, 159.88, 139.42, 138.70, 133.29, 129.14, 126.86, 126.75, 124.08, 123.97, 122.54, 120.69, 112.25, 105.76. HRMS (ESI) calculated for C₁₆H₁₂N₃O₂ [M - H]⁻: 278.0935, found: 278.0935.

N²-cyclohexyl-1H-indole-2,5-dicarboxamide (A2). White solid, m.p. 306-308°C. Yield: 71.0%. ¹H NMR (600 MHz, DMSO) δ 11.75 (s, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 8.21 (s, 1H), 7.88 (s, 1H), 7.73 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.42 (d, *J* = 8.6 Hz, 1H), 7.26 (s, 1H), 7.15 (s, 1H), 3.79 (s, 1H), 1.85 (s, 2H), 1.75 (s, 2H), 1.62 (d, *J* = 11.2 Hz, 1H), 1.33 (dt, *J* = 9.7, 5.1 Hz, 4H), 1.20-1.06 (m, 1H). ¹³C NMR (151 MHz, DMSO) δ 169.19, 160.31, 138.27, 133.70, 126.95,

126.48, 123.34, 122.21, 112.10, 103.90, 48.49, 33.01, 25.73, 25.41. HRMS (ESI) calculated for $C_{16}H_{18}N_3O_2 [M - H]^-$: 284.1405, found: 284.1405.

N²-(pyridin-3-yl)-1H-indole-2,5-dicarboxamide (A3). White solid, m.p. 334-336°C. Yield: 73.2%. ¹H NMR (600 MHz, DMSO) δ 12.06 (s, 1H), 10.50 (s, 1H), 8.98 (d, $J = 2.6$ Hz, 1H), 8.33 (dd, $J = 4.7, 1.5$ Hz, 1H), 8.31 (d, $J = 1.7$ Hz, 1H), 8.22 (ddd, $J = 8.3, 2.6, 1.5$ Hz, 1H), 7.93 (s, 1H), 7.81 (dd, $J = 8.7, 1.7$ Hz, 1H), 7.56 (s, 1H), 7.48 (d, $J = 8.6$ Hz, 1H), 7.42 (dd, $J = 8.3, 4.7$ Hz, 1H), 7.21 (s, 1H). ¹³C NMR (151 MHz, DMSO- d_6) δ 169.05, 160.31, 145.03, 142.25, 138.82, 136.04, 132.67, 127.63, 126.90, 126.84, 124.18, 124.12, 122.64, 112.34, 105.81, 40.52. HRMS (ESI) calculated for $C_{15}H_{11}N_4O_2 [M - H]^-$: 279.0887, found: 279.0887.

N²-(pyridin-2-yl)-1H-indole-2,5-dicarboxamide (A4). White solid, m.p. 314-316°C. Yield: 74.5%. ¹H NMR (600 MHz, DMSO- d_6) δ 11.98 (s, 1H), 10.86 (s, 1H), 8.37 (dd, $J = 4.8, 2.0, 0.9$ Hz, 1H), 8.24 (d, $J = 0.8$ Hz, 1H), 8.20 (d, $J = 8.4$ Hz, 1H), 7.88 (s, 1H), 7.82 (dd, $J = 8.4, 7.3, 2.0$ Hz, 1H), 7.76 (dd, $J = 8.6, 1.7$ Hz, 1H), 7.71 (d, $J = 0.9$ Hz, 1H), 7.44 (d, $J = 8.5$ Hz, 1H), 7.14 (dd, $J = 7.4, 4.8, 1.0$ Hz, 2H). ¹³C NMR (151 MHz, DMSO- d_6) δ 169.03, 160.30, 152.44, 148.45, 138.90, 138.70, 132.52, 126.87, 126.81, 124.29, 122.67, 120.23, 115.07, 112.33, 106.66. HRMS (ESI) calculated for $C_{15}H_{11}N_4O_2 [M - H]^-$: 279.0887, found: 279.0888.

N²-propyl-1H-indole-2,5-dicarboxamide (A5). White solid, m.p. 257-259°C. Yield: 80.6%. ¹H NMR (600 MHz, DMSO- d_6) δ 11.85-11.83 (m, 1H), 8.62 (t, $J = 5.7$ Hz, 1H), 8.23 (d, $J = 1.7$ Hz, 1H), 7.90 (s, 1H), 7.74 (dd, $J = 8.6, 1.7$ Hz, 1H), 7.42 (d, $J = 8.6$ Hz, 1H), 7.31-7.21 (m, 1H), 7.15 (s, 1H), 3.31-3.18 (m, 2H), 1.56 (h, $J = 7.4$ Hz, 2H), 0.91 (t, $J = 7.4$ Hz, 3H). ¹³C NMR (151 MHz, DMSO- d_6) δ 169.20, 161.19, 138.28, 133.71, 126.93, 126.49, 123.38, 122.21, 112.10, 103.89, 41.07, 22.96, 11.95. HRMS (ESI) calculated for $C_{13}H_{14}N_3O_2 [M - H]^-$: 244.1902, found: 244.1092.

N²-butyl-1H-indole-2,5-dicarboxamide (A6). White solid, m.p. 229-231°C. Yield: 82.8%. ¹H NMR (600 MHz, DMSO- d_6) δ 11.77 (s, 1H), 8.50 (t, $J = 5.7$ Hz, 1H), 8.22 (s, 1H), 7.88 (s, 1H), 7.74 (dd, $J = 8.6, 1.7$ Hz, 1H), 7.42 (d, $J = 8.6$ Hz, 1H), 7.21 (d, $J = 1.1$ Hz, 1H), 7.15 (s, 1H), 3.33-3.26 (m, 2H), 1.56-1.49 (m, 2H), 1.39-1.31 (m, 2H), 0.91 (t, $J = 7.4$ Hz, 3H). ¹³C NMR (151 MHz, DMSO- d_6) δ 169.18, 161.18, 138.27, 133.66, 126.96, 126.51, 123.37, 122.19, 112.12, 103.65, 38.94, 31.81, 20.12, 14.19. HRMS (ESI) calculated for $C_{14}H_{16}N_3O_2 [M - H]^-$: 258.1248, found: 258.1248.

N²-(1,3,4-thiadiazol-2-yl)-1H-indole-2,5-dicarboxamide (A7). White solid, m.p. 371-374°C. Yield: 46.3%. ¹H NMR (600 MHz, DMSO- d_6) δ 13.18 (s, 1H), 12.20 (s, 1H), 9.23 (s, 1H), 8.32 (d, $J = 1.6$ Hz, 1H), 7.97 (s, 1H), 7.87-7.79 (m, 2H), 7.52 (d, $J = 8.7$ Hz, 1H), 7.21 (s, 1H). ¹³C NMR (151 MHz, DMSO- d_6) δ 168.90, 139.29, 127.15, 126.72, 124.97, 122.98, 112.50, 108.11. HRMS (ESI) calculated for $C_{12}H_8N_5O_2S [M - H]^-$: 286.0404, found: 286.0404.

N²-(thiophen-3-yl)-1H-indole-2,5-dicarboxamide (A8). White solid, m.p. 298-300°C. Yield:

69.3%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 11.99 (d, *J* = 2.2 Hz, 1H), 10.76 (s, 1H), 8.29 (d, *J* = 1.7 Hz, 1H), 7.92 (s, 1H), 7.79 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.74 (dd, *J* = 3.3, 1.2 Hz, 1H), 7.52 (dd, *J* = 5.1, 3.3 Hz, 1H), 7.47 (d, *J* = 8.6 Hz, 2H), 7.35 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.20 (s, 1H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 169.16, 159.09, 138.72, 137.03, 132.94, 126.94, 126.77, 125.23, 123.90, 122.52, 122.37, 112.28, 109.95, 104.92. HRMS (ESI) calculated for C₁₄H₁₀N₃O₂S [M - H]⁻: 284.0499, found: 284.0499.

N²-(tetrahydro-2H-pyran-4-yl)-1H-indole-2,5-dicarboxamide (**A9**). White solid, m.p. 318-320°C. Yield: 54.6%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 11.79 (s, 1H), 8.39 (d, *J* = 7.7 Hz, 1H), 8.23 (s, 1H), 7.88 (s, 1H), 7.77-7.68 (m, 1H), 7.43 (d, *J* = 8.6 Hz, 1H), 7.27 (s, 1H), 7.16 (s, 1H), 4.04 (td, *J* = 11.8, 8.3, 4.2 Hz, 1H), 3.97-3.80 (m, 2H), 3.48-3.36 (m, 2H), 1.79 (dd, *J* = 13.3, 4.3 Hz, 2H), 1.60 (, *J* = 12.0, 4.4 Hz, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 169.16, 160.53, 138.32, 133.49, 126.92, 126.54, 123.44, 122.26, 112.13, 104.05, 66.64, 45.93, 33.02. HRMS (ESI) calculated for C₁₅H₁₆N₃O₃ [M + H]⁺: 288.1343, found: 288.1343.

N²-benzyl-1H-indole-2,5-dicarboxamide (**A10**). White solid, m.p. 303-305°C. Yield: 80.6%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 11.87-11.81 (m, 1H), 9.11 (t, *J* = 6.1 Hz, 1H), 8.28-8.21 (m, 1H), 7.88 (s, 1H), 7.75 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.44 (d, *J* = 8.5 Hz, 1H), 7.37-7.31 (m, 4H), 7.29 (dd, *J* = 2.1, 0.9 Hz, 1H), 7.25 (tt, *J* = 5.8, 2.9 Hz, 1H), 7.16 (s, 1H), 4.53 (d, *J* = 6.1 Hz, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 169.16, 160.53, 138.32, 133.49, 126.92, 126.54, 123.44, 122.26, 112.13, 104.05, 66.64, 45.93, 33.02. HRMS (ESI) calculated for C₁₇H₁₆N₃O₂ [M + H]⁺: 294.1237, found: 294.1237.

N²-(2-(methylsulfonamido)phenyl)-1H-indole-2,5-dicarboxamide (**A11**). White solid, m.p. 279-281°C. Yield: 49.5%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.94 (s, 1H), 9.43 (s, 1H), 8.28 (dt, *J* = 2.1, 1.1 Hz, 1H), 7.72 (t, *J* = 1.1 Hz, 2H), 7.68 (s, 2H), 7.57 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.48 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.28 (d, *J* = 2.1 Hz, 1H), 7.20-7.09 (m, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 169.06, 160.16, 138.79, 132.81, 132.63, 130.33, 127.11, 126.93, 126.80, 126.56, 126.48, 125.86, 124.17, 122.50, 112.37, 105.22, 40.86. HRMS (ESI) calculated for C₁₇H₁₅N₄O₄S [M - H]⁻: 371.0819, found: 371.0819.

N²-(2-(2-amino-2-oxoethyl)phenyl)-1H-indole-2,5-dicarboxamide (**A12**). White solid, m.p. 280-282°C. Yield: 64.1%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 12.05 (d, *J* = 2.2 Hz, 1H), 11.46 (s, 1H), 8.29-8.25 (m, 1H), 8.02 (d, *J* = 2.6 Hz, 1H), 7.98-7.93 (m, 1H), 7.88 (s, 1H), 7.78 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.48 (dt, *J* = 8.7, 0.8 Hz, 1H), 7.42 (d, *J* = 2.5 Hz, 1H), 7.38 (dd, *J* = 2.1, 0.9 Hz, 1H), 7.32 (td, *J* = 7.0, 1.6 Hz, 2H), 7.21-7.11 (m, 2H), 3.59 (s, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 174.93, 169.08, 159.57, 138.74, 137.59, 133.52, 131.12, 128.57, 127.83, 126.91, 126.87, 125.00, 123.97, 123.77, 122.29, 112.36, 104.38, 40.90. HRMS (ESI) calculated for C₁₈H₁₅N₄O₃ [M - H]⁻: 335.1150, found: 335.1150.

N²-(3-(2-amino-2-oxoethyl)phenyl)-1H-indole-2,5-dicarboxamide (**A13**). White solid, m.p.

268-270°C. Yield: 70.3%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 11.95 (d, *J* = 2.2 Hz, 1H), 10.27 (s, 1H), 8.29 (d, *J* = 1.7 Hz, 1H), 7.92 (s, 1H), 7.79 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.74 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.68 (d, *J* = 1.9 Hz, 1H), 7.55 (d, *J* = 2.2 Hz, 1H), 7.53-7.45 (m, 2H), 7.30 (t, *J* = 7.8 Hz, 1H), 7.20 (s, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 6.93 (s, 1H), 3.40 (s, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 172.62, 169.13, 159.86, 139.16, 138.69, 137.49, 133.25, 128.94, 126.92, 126.76, 123.95, 122.52, 121.35, 118.82, 112.28, 105.31, 42.79. HRMS (ESI) calculated for C₁₈H₁₅N₄O₃ [M - H]⁻: 335.1150, found: 335.1150.

2-(2-(5-carbamoyl-1H-indole-2-carboxamido)phenyl)acetic acid (**A14**). White solid, m.p. 295-297°C. Yield: 67.9%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 12.39 (s, 1H), 11.97 (d, *J* = 2.3 Hz, 1H), 10.09 (s, 1H), 7.90 (s, 1H), 7.78 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.51 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.46 (d, *J* = 8.6 Hz, 1H), 7.41 (d, *J* = 2.1 Hz, 1H), 7.38-7.31 (m, 2H), 7.23 (td, *J* = 7.5, 1.3 Hz, 1H), 7.18 (s, 1H), 3.71 (s, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 173.19, 169.09, 159.99, 138.62, 136.60, 133.07, 131.55, 131.11, 127.78, 126.89, 126.76, 126.72, 126.31, 123.88, 122.37, 112.27, 104.97, 38.04. HRMS (ESI) calculated for C₁₈H₁₆N₃O₄ [M + H]⁺: 338.1135, found: 338.1133.

2-(3-(5-carbamoyl-1H-indole-2-carboxamido)phenyl)acetic acid (**A15**). White solid, m.p. 289-291°C. Yield: 73.0%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 12.39 (s, 1H), 11.96 (d, *J* = 2.2 Hz, 1H), 10.28 (s, 1H), 8.30 (d, *J* = 1.6 Hz, 1H), 7.92 (s, 1H), 7.78 (dd, *J* = 16.2, 8.8, 1.9 Hz, 2H), 7.69 (t, *J* = 1.9 Hz, 1H), 7.55 (d, *J* = 2.2 Hz, 1H), 7.48 (d, *J* = 8.6 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.20 (s, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 3.59 (s, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 173.11, 169.11, 159.89, 139.29, 138.71, 136.01, 133.20, 129.10, 126.91, 126.77, 125.26, 123.97, 122.53, 121.48, 119.06, 112.29, 105.34, 41.39. HRMS (ESI) calculated for C₁₈H₁₆N₃O₄ [M + H]⁺: 338.1135, found: 338.1132.

N²-(2-(hydroxymethyl)phenyl)-1H-indole-2,5-dicarboxamide (**A16**). Brown solid, m.p. 234-236°C. Yield: 50.9%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 12.04 (d, *J* = 2.2 Hz, 1H), 10.22 (s, 1H), 8.29 (d, *J* = 1.7 Hz, 1H), 7.91 (s, 1H), 7.79 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.74 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.50-7.43 (m, 2H), 7.36-7.30 (m, 2H), 7.24-7.17 (m, 2H), 5.64 (t, *J* = 5.3 Hz, 1H), 4.65 (d, *J* = 5.2 Hz, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 169.10, 159.76, 138.74, 135.99, 135.10, 133.17, 127.99, 127.79, 126.89, 125.45, 124.32, 123.97, 122.41, 112.34, 104.47, 61.33. HRMS (ESI) calculated for C₁₇H₁₆N₃O₃ [M + H]⁺: 310.1186, found: 310.1186.

N²-(3-(hydroxymethyl)phenyl)-1H-indole-2,5-dicarboxamide (**A17**). Brown solid, m.p. 272-275°C. Yield: 55.4%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 11.96 (s, 1H), 10.27 (s, 1H), 8.30 (s, 1H), 7.92 (s, 1H), 7.82-7.76 (m, 2H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.56 (s, 1H), 7.48 (d, *J* = 8.6 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.20 (s, 1H), 7.06 (d, *J* = 7.6 Hz, 1H), 5.25 (t, *J* = 5.7 Hz, 1H), 4.53 (d, *J* = 5.6 Hz, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 169.10, 159.86, 143.68, 139.20, 138.69, 133.27, 128.86, 126.92, 126.76, 123.94, 122.51, 122.17, 119.02, 118.76, 118.71, 112.28, 105.29, 63.36, 40.89, 40.51. HRMS (ESI) calculated for C₁₇H₁₆N₃O₃ [M + H]⁺:

310.1186, found: 310.1187.

N²-(2-(2-hydroxyethyl)phenyl)-1H-indole-2,5-dicarboxamide (**A18**). Brown solid, m.p. 254-256°C. Yield: 61.8%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 12.02 (d, *J* = 2.2 Hz, 1H), 10.40 (s, 1H), 8.27 (d, *J* = 1.6 Hz, 1H), 7.91 (s, 1H), 7.79 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.48 (d, *J* = 8.6 Hz, 1H), 7.38-7.25 (m, 3H), 7.24-7.13 (m, 2H), 5.47 (t, *J* = 4.3 Hz, 1H), 3.72 (q, *J* = 6.0 Hz, 2H), 2.84 (t, *J* = 6.3 Hz, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 169.11, 159.91, 138.66, 136.72, 134.80, 133.35, 130.95, 127.07, 126.91, 126.84, 125.95, 125.70, 123.89, 122.32, 62.65, 35.50. HRMS (ESI) calculated for C₁₈H₁₆N₃O₃ [M - H]⁻: 322.1197, found: 322.1197.

N²-(3-(2-hydroxyethyl)phenyl)-1H-indole-2,5-dicarboxamide (**A19**). Brown solid, m.p. 261-263°C. Yield: 65.9%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 11.95 (s, 1H), 10.21 (s, 1H), 8.29 (d, *J* = 1.7 Hz, 1H), 7.92 (s, 1H), 7.79 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.70 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.62 (t, *J* = 1.9 Hz, 1H), 7.54 (s, 1H), 7.48 (d, *J* = 8.6 Hz, 1H), 7.28 (t, *J* = 7.8 Hz, 1H), 7.20 (s, 1H), 6.98 (dt, *J* = 7.6, 1.4 Hz, 1H), 4.69 (t, *J* = 5.2 Hz, 1H), 3.64 (td, *J* = 7.1, 5.1 Hz, 2H), 2.74 (t, *J* = 7.1 Hz, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 169.10, 159.84, 140.55, 139.16, 138.68, 133.29, 128.95, 126.92, 126.77, 124.80, 123.93, 122.50, 121.17, 118.39, 112.27, 105.24, 62.62. HRMS (ESI) calculated for C₁₈H₁₆N₃O₃ [M - H]⁻: 322.1197, found: 322.1197.

N-(2-(2-amino-2-oxoethyl)phenyl)terephthalamide (**B1**). White solid, m.p. 272-274°C. Yield: 59.6%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 11.34 (s, 1H), 8.13 (s, 1H), 8.08 (d, *J* = 8.2 Hz, 2H), 8.03-7.99 (m, 2H), 7.96 (d, *J* = 2.6 Hz, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.55 (s, 1H), 7.38-7.33 (m, 1H), 7.30 (dd, *J* = 7.2, 4.2, 2.6 Hz, 2H), 7.15 (td, *J* = 7.5, 1.3 Hz, 1H), 3.58 (s, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 174.85, 167.64, 164.51, 137.69, 137.48, 137.35, 131.02, 129.20, 128.18, 127.77, 127.71, 125.30, 124.38. HRMS (ESI) calculated for C₁₆H₁₆N₃O₃ [M + H]⁺: 298.1186, found: 298.1177.

N-(3-(2-amino-2-oxoethyl)phenyl)terephthalamide (**B2**). White solid, m.p. 301-313°C. Yield: 63.5%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 10.32 (s, 1H), 8.12 (s, 1H), 8.06-7.97 (m, 4H), 7.70 (t, *J* = 1.9 Hz, 1H), 7.65 (dd, *J* = 8.2, 2.2, 1.1 Hz, 1H), 7.53 (s, 1H), 7.48 (s, 1H), 7.28 (t, *J* = 7.8 Hz, 1H), 7.02 (dt, *J* = 7.7, 1.3 Hz, 1H), 6.94-6.87 (m, 1H), 3.38 (s, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 172.56, 167.66, 165.31, 139.32, 137.69, 137.43, 137.26, 128.83, 128.06, 127.94, 125.23, 121.59, 119.00, 42.79. HRMS (ESI) calculated for C₁₆H₁₆N₃O₃ [M + H]⁺: 298.1186, found: 298.1186.

N-(2-(2-hydroxyethyl)phenyl)terephthalamide (**B3**). Brown solid, m.p. 274-276°C. Yield: 71.6%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 10.35 (s, 1H), 8.13 (s, 1H), 8.01 (s, 4H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.55 (s, 1H), 7.31 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.26 (td, *J* = 7.6, 1.6 Hz, 1H), 7.18 (td, *J* = 7.4, 1.4 Hz, 1H), 5.35 (t, *J* = 4.4 Hz, 1H), 3.68 (td, *J* = 6.4, 4.4 Hz, 2H), 2.81 (t, *J* = 6.4 Hz, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 167.62, 164.97, 137.37, 136.99, 134.99, 130.84, 128.13, 127.77,

126.97, 126.11, 126.02, 62.57, 35.43. HRMS (ESI) calculated for $C_{16}H_{17}N_2O_3$ $[M + H]^+$: 283.1088, found: 283.1088.

N-(3-(2-hydroxyethyl)phenyl)terephthalamide (**B4**). Brown solid, m.p. 263-265°C. Yield: 68.1%. 1H NMR (600 MHz, DMSO- d_6) δ 10.28 (s, 1H), 8.13 (s, 1H), 8.00 (d, $J = 2.4$ Hz, 4H), 7.62 (d, $J = 8.4$ Hz, 2H), 7.53 (s, 1H), 7.26 (t, $J = 7.7$ Hz, 1H), 6.97 (d, $J = 7.6, 1.5$ Hz, 1H), 4.71-4.68 (m, 1H), 3.62 (td, $J = 7.1, 5.2$ Hz, 2H), 2.72 (t, $J = 7.1$ Hz, 2H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 128.87, 128.00 (d, $J = 14.2$ Hz), 125.00, 121.41, 118.61, 62.62, 40.45. HRMS (ESI) calculated for $C_{16}H_{15}N_2O_3$ $[M - H]^-$: 283.1088, found: 283.1088.

N-(2-(methylsulfonamido)phenyl)terephthalamide (**B5**). White solid, m.p. 215-217°C. Yield: 73.8%. 1H NMR (600 MHz, DMSO- d_6) δ 9.90 (s, 1H), 9.17 (s, 1H), 8.14 (s, 1H), 8.03 (s, 4H), 7.73 (dd, $J = 7.8, 1.8$ Hz, 1H), 7.55 (s, 1H), 7.46 (dd, $J = 7.7, 1.8$ Hz, 1H), 7.33-7.26 (m, 2H), 2.98 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 167.61, 165.47, 137.59, 137.01, 132.70, 130.82, 128.11, 128.02, 126.87, 126.68, 126.35, 126.21. HRMS (ESI) calculated for $C_{15}H_{14}N_3O_4$ $[M - H]^-$: 332.0711, found: 332.0711.

N-(1,3,4-thiadiazol-2-yl)terephthalamide (**B6**). White solid, m.p. 300-302°C. Yield: 64.1%. 1H NMR (600 MHz, DMSO- d_6) δ 13.18 (s, 1H), 9.25 (s, 1H), 8.18 (d, $J = 8.2$ Hz, 3H), 8.03 (d, $J = 8.4$ Hz, 2H), 7.58 (s, 1H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 167.46, 149.63, 138.46, 128.85, 128.14. HRMS (ESI) calculated for $C_{10}H_7N_4O_2S$ $[M - H]^-$: 247.0295, found: 247.0296.

N¹-methyl-N⁴-(1,3,4-thiadiazol-2-yl)terephthalamide (**B7**). White solid, m.p. 305-307°C. Yield: 55.3%. 1H NMR (600 MHz, DMSO- d_6) δ 13.18 (s, 1H), 9.25 (s, 1H), 8.63 (d, $J = 4.7$ Hz, 1H), 8.18 (d, $J = 8.3$ Hz, 2H), 7.98 (d, $J = 8.4$ Hz, 2H), 2.81 (d, $J = 4.5$ Hz, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 166.19, 149.60, 138.64, 128.93, 127.74, 26.81. HRMS (ESI) calculated for $C_{11}H_9N_4O_2S$ $[M - H]^-$: 261.0452, found: 261.0452.

N¹-methyl-N⁴-(2-(methylsulfonamido)phenyl)terephthalamide (**B8**). White solid, m.p. 229-231°C. Yield: 72.1%. 1H NMR (600 MHz, DMSO- d_6) δ 10.23 (s, 1H), 9.51 (s, 1H), 8.70 (d, $J = 4.6$ Hz, 1H), 8.12 (d, $J = 8.4$ Hz, 2H), 8.00 (d, $J = 8.4$ Hz, 2H), 7.71 (dd, $J = 7.9, 1.7$ Hz, 1H), 7.44 (dd, $J = 7.8, 1.7$ Hz, 1H), 7.32-7.26 (m, 2H), 2.92 (s, 3H), 2.81 (d, $J = 4.5$ Hz, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 166.30, 165.43, 137.75, 136.68, 132.84, 130.95, 128.22, 127.69, 126.76, 126.74, 126.68, 126.56, 60.23, 26.78. HRMS (ESI) calculated for $C_{16}H_{16}N_3O_4S$ $[M - H]^-$: 346.0867, found: 346.0867.

2-(2-(4-(methylcarbamoyl)benzamido)phenyl)acetic acid (**B9**). White solid, m.p. 239-241°C. Yield: 68.5%. 1H NMR (600 MHz, DMSO- d_6) δ 12.37 (s, 1H), 10.10 (s, 1H), 8.59 (d, $J = 4.7$ Hz, 1H), 8.01 (d, $J = 8.0$ Hz, 2H), 7.96 (d, $J = 8.3$ Hz, 2H), 7.45 (d, $J = 7.9$ Hz, 1H), 7.36-7.28 (m, 2H), 7.25-7.21 (m, 1H), 3.67 (s, 2H), 2.82 (d, $J = 4.5$ Hz, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 173.17, 166.37, 165.23, 137.50, 137.14, 136.95, 131.50, 131.35, 128.09, 127.71, 127.57, 126.89, 126.42, 38.10, 26.79. HRMS (ESI) calculated for $C_{17}H_{17}N_2O_4$ $[M + H]^+$: 313.1183,

found: 313.1183.

2-((1-(2,4-difluorobenzoyl)piperidin-4-yl)amino)-N¹-phenylterephthalamide (**C1**). Yellow solid, m.p. 165-167°C. Yield: 76.4%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 10.21 (s, 1H), 8.06 (s, 1H), 7.78 (d, *J* = 8.1 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 2H), 7.54 (dd, *J* = 19.8, 7.8 Hz, 2H), 7.46 (s, 1H), 7.38-7.32 (m, 3H), 7.28 (s, 1H), 7.21-7.07 (m, 3H), 4.33 (d, *J* = 13.1 Hz, 1H), 3.87-3.79 (m, 1H), 3.41 (d, *J* = 13.7 Hz, 1H), 3.25 (t, *J* = 12.3 Hz, 1H), 3.20-3.12 (m, 1H), 2.13-2.05 (m, 1H), 1.95 (d, *J* = 12.6 Hz, 1H), 1.44-1.32 (m, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 168.15, 168.08, 163.07 (d, *J* = 243 Hz), 163.59, 158.49 (d, *J* = 256.5 Hz), 148.37, 139.30, 138.40, 130.75, 130.72, 130.74 (q, *J* = 6 Hz), 129.82, 129.00, 124.26, 121.42 (d, *J* = 18 Hz) 121.38, 117.96, 113.93, 112.68 (d, *J* = 21.75 Hz), 111.01, 104.85 (t, *J* = 10.5 Hz) 55.38, 48.29, 31.85. HRMS (ESI) calculated for C₂₆H₂₅F₂N₄O₃ [M + H]⁺: 479.1889, found: 479.1889.

2-((1-(2,4-difluorobenzoyl)piperidin-4-yl)amino)-N¹-(pyridin-2-yl)terephthalamide (**C2**). Yellow solid, m.p. 174-176°C. Yield: 81.2%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 10.83 (s, 1H), 8.41-8.38 (m, 1H), 8.05 (d, *J* = 8.3 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.86-7.82 (m, 1H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.39-7.35 (m, 1H), 7.34 (d, *J* = 1.6 Hz, 1H), 7.20-7.15 (m, 2H), 6.99 (d, *J* = 8.0, 1.5 Hz, 1H), 4.37 (d, *J* = 13.4 Hz, 1H), 3.85-3.78 (m, 1H), 3.40 (d, *J* = 13.5 Hz, 1H), 3.23 (t, *J* = 12.4 Hz, 1H), 3.10 (t, *J* = 12.1 Hz, 1H), 2.07 (d, *J* = 12.6 Hz, 1H), 1.91 (s, 1H), 1.36 (q, *J* = 12.9 Hz, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 168.67, 168.03, 163.59, 163.08 (d, *J* = 248.4 Hz), 158.49 (d, *J* = 256.5 Hz), 152.42, 148.68, 148.44, 138.77, 138.42, 130.74 (q, *J* = 6 Hz), 130.42, 121.43 (d, *J* = 18.7 Hz), 120.29, 116.93, 115.75, 113.95, 112.69 (d, *J* = 22.6 Hz), 111.14, 104.85 (t, *J* = 27 Hz), 48.36, 45.74, 31.83. HRMS (ESI) calculated for C₂₅H₂₄F₂N₅O₃ [M + H]⁺: 480.1842, found: 480.1842.

N¹-(2-(2-amino-2-oxoethyl)phenyl)-2-((1-(2,4-difluorobenzoyl)piperidin-4-yl)amino)terephthalamide (**C3**). Yellow solid, m.p. 239-241°C. Yield: 68.6%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 11.12 (s, 1H), 8.03 (s, 1H), 7.99 (d, *J* = 7.9 Hz, 1H), 7.92 (d, *J* = 2.6 Hz, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 7.4 Hz, 1H), 7.53 (q, *J* = 7.6 Hz, 1H), 7.48 (s, 1H), 7.36 (td, *J* = 9.7, 2.5 Hz, 1H), 7.32 (d, *J* = 2.5 Hz, 1H), 7.30-7.27 (m, 3H), 7.21-7.12 (m, 2H), 7.09 (dd, *J* = 8.2, 1.6 Hz, 1H), 4.32 (d, *J* = 13.1 Hz, 1H), 3.84 (d, *J* = 8.6 Hz, 1H), 3.54 (s, 2H), 3.41 (d, *J* = 14.0 Hz, 1H), 3.26 (t, *J* = 11.9 Hz, 1H), 3.23-3.15 (m, 1H), 2.10 (d, *J* = 10.6 Hz, 1H), 2.00-1.88 (m, 1H), 1.39 (d, *J* = 12.0 Hz, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 174.77, 168.08, 167.73, 163.07 (d, *J* = 243 Hz), 163.60, 158.49 (d, *J* = 256.5 Hz), 148.95, 138.61, 137.54, 130.93, 130.74 (q, *J* = 6 Hz), 129.54, 129.08, 127.56, 125.27, 124.90, 121.42 (d, *J* = 18 Hz) 116.97, 113.95, 112.68 (d, *J* = 21.75 Hz), 111.30, 104.85 (t, *J* = 27 Hz), 48.22, 45.71, 32.55, 31.85. HRMS (ESI) calculated for C₂₈H₂₈F₂N₅O₄ [M + H]⁺: 536.2104, found: 536.2104.

N¹-(3-(2-amino-2-oxoethyl)phenyl)-2-((1-(2,4-difluorobenzoyl)piperidin-4-yl)amino)terephthalamide (**C4**). Yellow solid, m.p. 201-203°C. Yield: 69.1%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 10.17 (s, 1H), 8.03 (s, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.63 (s, 1H), 7.54 (t, *J*

= 10.8 Hz, 3H), 7.47 (d, $J = 16.0$ Hz, 2H), 7.36 (td, $J = 9.7, 2.4$ Hz, 1H), 7.28-7.24 (m, 2H), 7.17 (td, $J = 8.5, 2.4$ Hz, 1H), 7.12 (d, $J = 8.1$ Hz, 1H), 7.01 (d, $J = 7.5$ Hz, 1H), 6.89 (s, 1H), 4.34 (d, $J = 13.1$ Hz, 1H), 3.82 (d, $J = 10.1$ Hz, 1H), 3.37 (s, 2H), 3.25 (t, $J = 12.1$ Hz, 1H), 3.18-3.11 (m, 1H), 2.09 (d, $J = 12.6$ Hz, 1H), 1.99 (s, 1H), 1.94 (s, 1H), 1.44-1.32 (m, 2H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 172.59, 168.10 (d, $J = 2.8$ Hz), 163.59, 163.07 (d, $J = 248.5$ Hz), 158.48 (d, $J = 247.8$ Hz), 148.37, 139.15, 138.38, 137.34, 130.74 (q, $J = 6.1$ Hz), 129.84, 128.71, 125.18, 122.04, 121.42 (d, $J = 2.8$ Hz), 119.48, 117.94, 113.89, 112.68 (d, $J = 21.75$ Hz), 110.98, 104.84 (t, $J = 27$ Hz), 56.49, 48.32, 42.77, 19.03. HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{28}\text{F}_2\text{N}_5\text{O}_4$ $[\text{M} + \text{H}]^+$: 536.2104, found: 536.2105.

N^1 -benzyl-2-((1-(2,4-difluorobenzoyl)piperidin-4-yl)amino)terephthalamide (**C5**). Yellow solid, m.p. 274-176°C. Yield: 81.6%. ^1H NMR (600 MHz, DMSO- d_6) δ 9.03 (t, $J = 6.0$ Hz, 1H), 8.05-7.97 (m, 2H), 7.71 (d, $J = 8.2$ Hz, 1H), 7.56-7.50 (m, 1H), 7.43 (s, 1H), 7.36 (td, $J = 9.9, 2.7$ Hz, 1H), 7.33 (d, $J = 6.3$ Hz, 4H), 7.27-7.22 (m, 2H), 7.18 (td, $J = 8.5, 2.4$ Hz, 1H), 7.06 (d, $J = 8.0$ Hz, 1H), 4.44 (d, $J = 5.9$ Hz, 2H), 4.29 (d, $J = 13.0$ Hz, 1H), 3.82-3.74 (m, 1H), 3.39 (d, $J = 14.1$ Hz, 1H), 3.27-3.15 (m, 2H), 2.13-2.03 (m, 1H), 1.97-1.86 (m, 1H), 1.39-1.29 (m, 2H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 169.12, 168.13, 163.58, 163.08 (d, $J = 248.5$ Hz), 158.49 (d, $J = 247.8$ Hz), 148.52, 140.06, 130.71 (q, $J = 6$ Hz), 129.04, 128.75, 127.62, 127.20, 121.43 (d, $J = 18.5$ Hz), 117.04, 113.79, 112.68 (d, $J = 21.75$ Hz), 111.06, 104.85 (t, $J = 25.9$ Hz), 48.18, 45.70, 42.78, 31.87. HRMS (ESI) calculated for $\text{C}_{27}\text{H}_{27}\text{F}_2\text{N}_4\text{O}_3$ $[\text{M} + \text{H}]^+$: 493.2046, found: 493.2046.

2-((1-(2,4-difluorobenzoyl)piperidin-4-yl)amino)- N^1 -(2-(methylsulfonamido)phenyl)terephthalamide (**C6**). Yellow solid, m.p. 214-216°C. Yield: 46.8%. ^1H NMR (600 MHz, DMSO- d_6) δ 9.75 (s, 1H), 9.18 (s, 1H), 8.09 (s, 1H), 7.85 (d, $J = 8.2$ Hz, 1H), 7.78-7.68 (m, 2H), 7.57 (d, $J = 7.7$ Hz, 1H), 7.53 (s, 1H), 7.49 (dd, $J = 7.8, 1.8$ Hz, 1H), 7.41 (td, $J = 9.7, 2.5$ Hz, 1H), 7.38-7.31 (m, 3H), 7.23 (td, $J = 8.5, 2.5$ Hz, 1H), 7.19 (dd, $J = 8.2, 1.6$ Hz, 1H), 4.35 (d, $J = 13.1$ Hz, 1H), 3.88 (s, 1H), 3.46 (s, 1H), 3.30 (t, $J = 12.1$ Hz, 1H), 3.23 (t, $J = 12.0$ Hz, 1H), 2.13 (d, $J = 12.6$ Hz, 1H), 1.98 (s, 1H), 1.48-1.36 (m, 2H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 168.24, 168.00, 163.58, 163.07 (d, $J = 248.5$ Hz), 158.19 (d, $J = 256.5$ Hz), 148.67, 138.76, 132.78, 130.93, 130.74 (q, $J = 6$ Hz), 129.50, 126.84, 126.68, 126.58, 126.28, 121.42 (d, $J = 18.4$ Hz), 116.97, 113.96, 112.68 (d, $J = 24.0$ Hz), 111.29, 104.85 (t, $J = 27$ Hz), 48.26, 45.70, 32.50, 31.80. HRMS (ESI) calculated for $\text{C}_{27}\text{H}_{26}\text{F}_2\text{N}_5\text{O}_5$ $[\text{M} - \text{H}]^-$: 570.1628, found: 570.1632.

2-(2-(4-carbamoyl-2-((1-(2,4-difluorobenzoyl)piperidin-4-yl)amino)benzamido)phenyl)acetic acid (**C7**). Yellow solid, m.p. 244-246°C. Yield: 39.5%. ^1H NMR (600 MHz, DMSO- d_6) δ 12.35 (s, 1H), 9.95 (s, 1H), 8.01 (s, 1H), 7.77 (d, $J = 8.2$ Hz, 1H), 7.72 (s, 1H), 7.52 (q, $J = 7.7$ Hz, 1H), 7.45 (s, 1H), 7.39-7.28 (m, 4H), 7.26 (d, $J = 1.7$ Hz, 1H), 7.17 (td, $J = 8.5, 2.5$ Hz, 1H), 7.09 (dd, $J = 8.1, 1.6$ Hz, 1H), 4.30 (d, $J = 13.1$ Hz, 1H), 3.81 (s, 1H), 3.62 (s, 2H), 3.40

(s, 1H), 3.24 (t, $J = 12.0$ Hz, 1H), 3.21 – 3.14 (m, 1H), 2.07 (d, $J = 12.7$ Hz, 1H), 1.92 (s, 1H), 1.42-1.31 (m, 2H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 168.26, 167.82, 163.61, 163.07 (d, $J = 248.6$ Hz), 158.48 (d, $J = 248.1$ Hz), 148.94, 138.28, 137.75, 131.29, 130.84, 130.74 (q, $J = 6$ Hz), 129.57, 126.58, 124.74, 124.67, 121.40 (d, $J = 18.9$ Hz), 117.42, 113.97, 112.69 (d, $J = 21.2$ Hz), 111.07, 104.84 (t, $J = 25.9$ Hz), 55.37, 48.18, 45.71, 31.87. HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{25}\text{F}_2\text{N}_4\text{O}_5$ $[\text{M} - \text{H}]^-$: 535.1798, found: 535.1798.

N^1 -butyl-2-((1-(2,4-difluorobenzoyl)piperidin-4-yl)amino)terephthalamide (**C8**). Yellow solid, m.p. 174-176°C. Yield: 75.6%. ^1H NMR (600 MHz, DMSO- d_6) δ 8.40 (t, $J = 5.7$ Hz, 1H), 7.97 (d, $J = 9.8$ Hz, 2H), 7.59 (d, $J = 8.2$ Hz, 1H), 7.55-7.50 (m, 1H), 7.40 (s, 1H), 7.38-7.33 (m, 1H), 7.21-7.15 (m, 2H), 7.04 (dd, $J = 8.1, 1.6$ Hz, 1H), 4.29 (d, $J = 13.1$ Hz, 1H), 3.80-3.72 (m, 1H), 3.42-3.37 (m, 1H), 3.27-3.14 (m, 4H), 2.06 (d, $J = 8.9$ Hz, 1H), 1.92 (d, $J = 12.2$ Hz, 1H), 1.52-1.46 (m, 2H), 1.38-1.29 (m, 4H), 0.90 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 169.01, 168.19, 163.59, 163.08 (d, $J = 248.5$ Hz), 158.49 (d, $J = 247.7$ Hz), 148.31, 137.90, 130.71 (q, $J = 9.9$ Hz), 128.94, 121.43 (d, $J = 18.4$ Hz), 117.67, 113.75, 112.69 (d, $J = 21.5$ Hz), 110.93, 104.84 (t, $J = 25.9$ Hz), 48.15, 45.70, 32.58, 31.87, 31.58, 20.15, 14.18. HRMS (ESI) calculated for $\text{C}_{24}\text{H}_{29}\text{F}_2\text{N}_4\text{O}_3$ $[\text{M} + \text{H}]^+$: 459.2202, found: 459.2202.

2-((1-(2,4-difluorobenzoyl)piperidin-4-yl)amino)- N^1 -(1,3,4-thiadiazol-2-yl)terephthalamide (**C9**). Yellow solid, m.p. 284-286°C. Yield: 40.8%. ^1H NMR (600 MHz, DMSO- d_6) δ 12.85 (s, 1H), 9.23 (s, 1H), 8.20 (s, 1H), 8.02 (s, 1H), 7.69 (s, 1H), 7.55 (s, 1H), 7.49 (s, 1H), 7.39-7.34 (m, 2H), 7.18 (td, $J = 8.5, 2.5$ Hz, 1H), 7.10 (dd, $J = 8.1, 1.6$ Hz, 1H), 4.38 (d, $J = 13.1$ Hz, 1H), 3.93 (s, 1H), 3.42 (d, $J = 13.8$ Hz, 1H), 3.28 (t, $J = 12.4$ Hz, 1H), 3.14 (t, $J = 12.1$ Hz, 1H), 2.11 (d, $J = 12.7$ Hz, 1H), 1.96 (s, 1H), 1.42 (s, 2H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 174.77, 168.08, 167.73, 163.07 (d, $J = 243$ Hz), 163.60, 158.49 (d, $J = 256.5$ Hz), 148.95, 138.61, 137.54, 130.93, 130.74 (q, $J = 6$ Hz), 129.54, 129.08, 127.56, 125.27, 124.90, 121.42 (d, $J = 18$ Hz), 116.97, 113.95, 112.68 (d, $J = 21.75$ Hz), 111.30, 104.85 (t, $J = 10.5$ Hz), 48.22, 45.71, 32.55, 31.85. HRMS (ESI) calculated for $\text{C}_{22}\text{H}_{21}\text{F}_2\text{N}_6\text{O}_3\text{S}$ $[\text{M} + \text{H}]^+$: 485.1213, found: 485.1211.

2-((1-(4-chloro-2,6-difluorobenzoyl)piperidin-4-yl)amino)- N^1 -(2-(methylsulfonamido)phenyl)terephthalamide (**C10**). White solid, m.p. 244-246°C. Yield: 69.4%. ^1H NMR (600 MHz, DMSO- d_6) δ 9.70 (s, 1H), 9.13 (s, 1H), 8.03 (s, 1H), 7.80 (d, $J = 8.2$ Hz, 1H), 7.71-7.65 (m, 2H), 7.54-7.50 (m, 2H), 7.48 (s, 1H), 7.43 (dd, $J = 7.6, 1.8$ Hz, 1H), 7.31-7.23 (m, 3H), 7.14 (dd, $J = 8.2, 1.5$ Hz, 1H), 4.31 (d, $J = 13.4$ Hz, 1H), 3.84 (d, $J = 9.8$ Hz, 1H), 3.45 (d, $J = 13.9$ Hz, 1H), 3.28 (dd, $J = 13.8, 3.0$ Hz, 1H), 3.21 (td, $J = 10.7, 5.5$ Hz, 1H), 2.97 (s, 3H), 2.09 (d, $J = 10.3$ Hz, 1H), 1.96 (d, $J = 12.9$ Hz, 1H), 1.37-1.27 (m, 2H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 168.23, 168.13, 159.30 (q, $J = 10.5$ Hz), 157.65 (q, $J = 10.5$ Hz), 148.61, 138.69, 135.67 (t, $J = 13.3$ Hz), 132.82, 130.88, 129.51, 126.95, 126.67 (d, $J = 5.3$ Hz), 126.36, 117.07, 114.06, 113.77 (d, $J = 24.21$ Hz), 113.39, 111.30, 48.12, 45.49, 32.75, 31.88.

HRMS (ESI) calculated for $C_{27}H_{25}ClF_2N_5O_5S$ $[M - H]^-$: 604.1238, found: 604.1231.

2-((1-(4-bromo-2-fluorobenzoyl)piperidin-4-yl)amino)-N¹-(2-(methylsulfonamido)phenyl)terephthalamide (**C11**). Yellow solid, m.p. 169-171°C. Yield: 56.4%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 9.69 (s, 1H), 9.12 (s, 1H), 8.03 (s, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.70-7.65 (m, 3H), 7.52-7.47 (m, 2H), 7.43 (dd, *J* = 7.6, 1.9 Hz, 2H), 7.31-7.23 (m, 3H), 7.13 (dd, *J* = 8.1, 1.5 Hz, 1H), 4.29 (d, *J* = 13.1 Hz, 1H), 3.82 (d, *J* = 10.7 Hz, 1H), 3.38 (d, *J* = 13.9 Hz, 1H), 3.24 (t, *J* = 12.3 Hz, 1H), 3.17 (t, *J* = 12.1 Hz, 1H), 2.96 (s, 3H), 2.07 (d, *J* = 12.7 Hz, 1H), 1.92 (s, 1H), 1.35 (d, *J* = 21.5 Hz, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 168.19 (d, *J* = 3.4 Hz), 163.53, 158.82, 157.16, 148.63, 138.67, 132.82, 130.94, 130.71 (d, *J* = 4.5 Hz), 129.47, 128.65, 126.84, 126.56 (d, *J* = 13.6 Hz), 126.27, 124.10 (d, *J* = 18.3 Hz), 123.31 (d, *J* = 9.4 Hz), 119.73 (d, *J* = 24.9 Hz), 117.04, 114.00, 111.30, 48.23, 45.69, 32.46, 31.76. HRMS (ESI) calculated for $C_{27}H_{26}BrFN_5O_5S$ $[M - H]^-$: 630.0828, found: 630.0829.

2-((1-(4-chloro-2-fluorobenzoyl)piperidin-4-yl)amino)-N¹-(2-(methylsulfonamido)phenyl)terephthalamide (**C12**). Yellow solid, m.p. 159-161°C. Yield: 64.3%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 10.10 (s, 1H), 9.58 (s, 1H), 8.15 (s, 1H), 7.95 (d, *J* = 8.2 Hz, 1H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.66 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.55 (dd, *J* = 9.4, 2.0 Hz, 1H), 7.48 (d, *J* = 15.7 Hz, 2H), 7.42 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.38 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.33 (d, *J* = 1.7 Hz, 1H), 7.30-7.23 (m, 2H), 7.14 (dd, *J* = 8.1, 1.6 Hz, 1H), 4.29 (dd, *J* = 12.7, 6.1 Hz, 1H), 3.90-3.84 (m, 1H), 3.26 (t, *J* = 12.1 Hz, 1H), 3.23-3.15 (m, 1H), 2.91 (s, 3H), 2.13-2.05 (m, 1H), 1.93 (t, *J* = 7.9 Hz, 1H), 1.42-1.29 (m, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 168.33, 168.01, 163.38, 158.91, 157.26, 148.74, 138.67, 135.19 (d, *J* = 10.2 Hz), 132.94, 131.19, 130.51 (d, *J* = 4.9 Hz), 129.77, 126.88 (d, *J* = 13.7 Hz), 126.51 (d, *J* = 26.4 Hz), 125.75, 123.91, 123.79, 116.99 (d, *J* = 25.4 Hz), 116.78, 113.99, 111.29, 48.17, 45.69, 32.54, 31.84. HRMS (ESI) calculated for $C_{27}H_{26}ClFN_5O_5S$ $[M - H]^-$: 586.1333, found: 586.1327.

2-((1-(5-bromothiophene-2-carbonyl)piperidin-4-yl)amino)-N¹-(2-(methylsulfonamido)phenyl)terephthalamide (**C13**). Yellow solid, m.p. 166-168°C. Yield: 65.4%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 9.70 (s, 1H), 9.12 (s, 1H), 8.05 (s, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.71-7.64 (m, 2H), 7.48 (s, 1H), 7.43 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.30 (s, 1H), 7.29-7.22 (m, 4H), 7.14 (dd, *J* = 8.2, 1.6 Hz, 1H), 4.10 (d, *J* = 13.3 Hz, 2H), 3.84 (d, *J* = 8.9 Hz, 1H), 3.30 (s, 2H), 2.96 (s, 3H), 2.04 (dd, *J* = 13.3, 4.0 Hz, 2H), 1.43 (d, *J* = 11.1 Hz, 2H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 168.21, 168.01, 161.36, 148.67, 139.92, 138.74, 132.78, 130.98, 130.32, 129.49, 126.75, 126.59, 126.55, 126.23, 117.01, 115.77, 113.95, 111.33, 48.27, 40.90, 32.15. HRMS (ESI) calculated for $C_{25}H_{25}BrN_5O_5S_2$ $[M - H]^-$: 620.0465, found: 620.0451.

2-((1-(2,4-difluorobenzyl)piperidin-4-yl)amino)-N¹-(2-(methylsulfonamido)phenyl)terephthalamide (**C14**). Yellow solid, m.p. 241-243°C. Yield: 57.6%. ¹H NMR (600 MHz, DMSO-*d*₆) δ 9.70 (s, 1H), 9.17 (s, 1H), 8.04 (s, 1H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.72-7.63 (m, 2H), 7.47-7.41 (m, 3H), 7.30-7.24 (m, 2H), 7.22 (d, *J* = 1.6 Hz, 1H),

7.21-7.16 (m, 1H), 7.10 (dd, $J = 8.2, 1.6$ Hz, 1H), 7.06 (td, $J = 8.5, 2.6$ Hz, 1H), 3.53 (s, 2H), 3.51 (s, 1H), 2.95 (s, 3H), 2.74-2.67 (m, 2H), 2.25 (d, $J = 10.9$ Hz, 2H), 1.97-1.91 (m, 2H), 1.45-1.37 (m, 2H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 168.23, 168.14, 162.51 (d, $J = 57$ Hz), 160.73 (d, $J = 104.9, 12.4$ Hz), 148.89, 138.64, 133.27 (q, $J = 6$ Hz), 132.82, 131.07, 129.44, 126.72, 126.50 (d, $J = 6.8$ Hz), 126.24, 121.29 (d, $J = 18$ Hz), 116.66, 113.66, 111.67 (d, $J = 21.2$ Hz), 111.24, 104.02 (t, $J = 26.1$ Hz), 56.52, 54.54, 51.43, 31.99, 18.98. HRMS (ESI) calculated for $\text{C}_{27}\text{H}_{28}\text{F}_2\text{N}_5\text{O}_4\text{S} [\text{M} - \text{H}]^-$: 556.1836, found: 556.1836.

2-((1-(4-chloro-2,6-difluorobenzyl)piperidin-4-yl)amino)-N1-(2-(methylsulfonamido)phenyl)terephthalamide (**C15**). Yellow solid, m.p. 229-231°C. Yield: 58.4%. ^1H NMR (600 MHz, DMSO- d_6) δ 9.67 (s, 1H), 9.15 (s, 1H), 8.02 (s, 1H), 7.76 (d, $J = 8.2$ Hz, 1H), 7.68-7.59 (m, 2H), 7.47-7.39 (m, 2H), 7.36 (d, $J = 7.1$ Hz, 2H), 7.29-7.22 (m, 2H), 7.20 (d, $J = 1.6$ Hz, 1H), 7.10 (dd, $J = 8.1, 1.6$ Hz, 1H), 3.59 (s, 2H), 3.46 (s, 1H), 2.95 (s, 3H), 2.72 (d, $J = 11.2$ Hz, 2H), 2.24 (t, $J = 10.8$ Hz, 2H), 1.92 (dd, $J = 13.3, 3.8$ Hz, 2H), 1.37 (d, $J = 10.5$ Hz, 2H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 168.21, 168.03, 162.61 (d, $J = 10.3$ Hz), 160.96 (d, $J = 10.2$ Hz), 148.87, 138.65, 133.75 (t, $J = 13.3$ Hz), 132.77, 131.08, 129.40, 126.68, 126.48 (d, $J = 4.8$ Hz), 126.15, 116.65, 113.67, 112.99 (d, $J = 30.3$ Hz), 112.68, 111.19, 51.17, 48.57, 40.87, 32.02. HRMS (ESI) calculated for $\text{C}_{27}\text{H}_{29}\text{ClF}_2\text{N}_5\text{O}_4\text{S} [\text{M} + \text{H}]^+$: 592.1591, found: 592.1592.

2-((1-(4-bromo-2-fluorobenzyl)piperidin-4-yl)amino)-N1-(2-(methylsulfonamido)phenyl)terephthalamide (**C16**). Yellow solid, m.p. 220-222°C. Yield: 45.3%. ^1H NMR (600 MHz, DMSO- d_6) δ 9.76 (s, 1H), 9.18 (d, $J = 103.4$ Hz, 1H), 8.04 (s, 1H), 7.80 (d, $J = 8.3$ Hz, 1H), 7.72-7.64 (m, 2H), 7.50-7.48 (m, 1H), 7.45-7.41 (m, 2H), 7.40-7.37 (m, 2H), 7.29-7.23 (m, 2H), 7.22 (d, $J = 1.7$ Hz, 1H), 7.11 (dd, $J = 8.2, 1.6$ Hz, 1H), 3.52 (s, 2H), 3.50 (s, 1H), 2.94 (s, 3H), 2.71 (d, $J = 11.3$ Hz, 2H), 2.24 (t, $J = 10.7$ Hz, 2H), 1.94 (dd, $J = 13.2, 3.8$ Hz, 2H), 1.45-1.36 (m, 2H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 168.24, 168.03, 161.96, 160.31, 148.92, 138.67, 133.60 (d, $J = 5.3$ Hz), 132.79, 131.25, 129.49, 127.82 (d, $J = 3.5$ Hz), 126.47 (d, $J = 11.2$ Hz), 126.21, 124.83 (d, $J = 14.8$ Hz), 120.73 (d, $J = 9.8$ Hz), 118.98 (d, $J = 25.8$ Hz), 116.63, 113.65, 111.24, 56.50, 54.58, 51.56, 32.09, 19.03. HRMS (ESI) calculated for $\text{C}_{27}\text{H}_{28}\text{BrFN}_5\text{O}_4\text{S} [\text{M} - \text{H}]^-$: 618.1014, found: 618.1010.

2-((1-(4-chloro-2-fluorobenzyl)piperidin-4-yl)amino)-N1-(2-(methylsulfonamido)phenyl)terephthalamide (**C17**). Yellow solid, m.p. 168-170°C. Yield: 40.6%. ^1H NMR (600 MHz, DMSO- d_6) δ 9.87 (s, 1H), 8.04 (s, 1H), 7.80 (dd, $J = 7.9, 1.6$ Hz, 1H), 7.72 (d, $J = 8.2$ Hz, 2H), 7.48-7.40 (m, 2H), 7.38 (dd, $J = 9.8, 2.1$ Hz, 1H), 7.34 (dd, $J = 8.0, 1.5$ Hz, 1H), 7.26 (dd, $J = 8.2, 2.1$ Hz, 1H), 7.21 (d, $J = 1.7$ Hz, 1H), 7.12-7.08 (m, 2H), 7.06-6.99 (m, 1H), 3.54 (s, 2H), 3.51 (s, 1H), 2.83 (s, 3H), 2.76-2.66 (m, 2H), 2.24 (t, $J = 10.7$ Hz, 2H), 1.95 (dd, $J = 13.1, 3.7$ Hz, 2H), 1.47-1.36 (m, 2H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 168.13, 167.68, 161.91, 160.27, 148.83, 138.51, 134.15, 133.26 (d, $J = 5.4$ Hz), 132.80 (d, J

= 10.5 Hz), 132.03, 129.04, 125.59, 124.91 (d, $J = 3.3$ Hz), 124.43 (d, $J = 15.0$ Hz), 123.85, 123.46 (d, $J = 31.4$ Hz), 117.15, 116.21 (d, $J = 26.0$ Hz), 113.77, 111.28, 54.54, 51.55, 32.09, 21.95, 19.01. HRMS (ESI) calculated for $C_{27}H_{28}ClFN_5O_4S$ $[M - H]^-$: 572.1540, found: 572.1531.

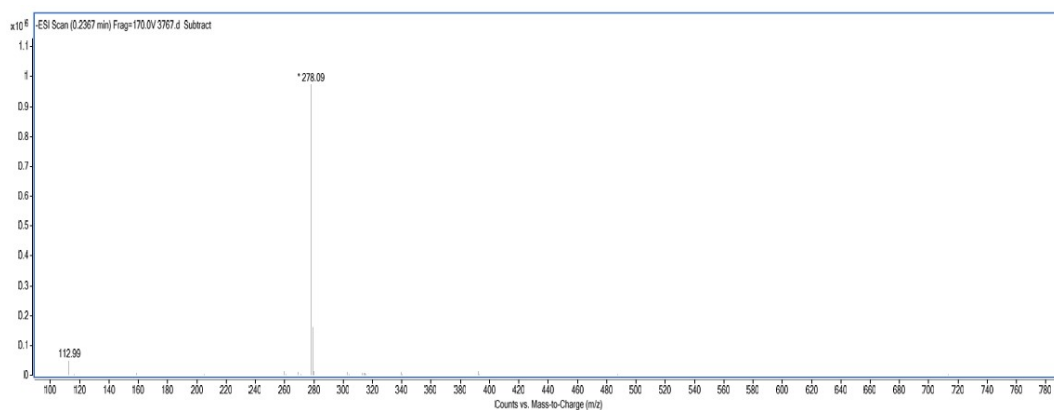


Figure 4. HRMS spectrum of compound A1

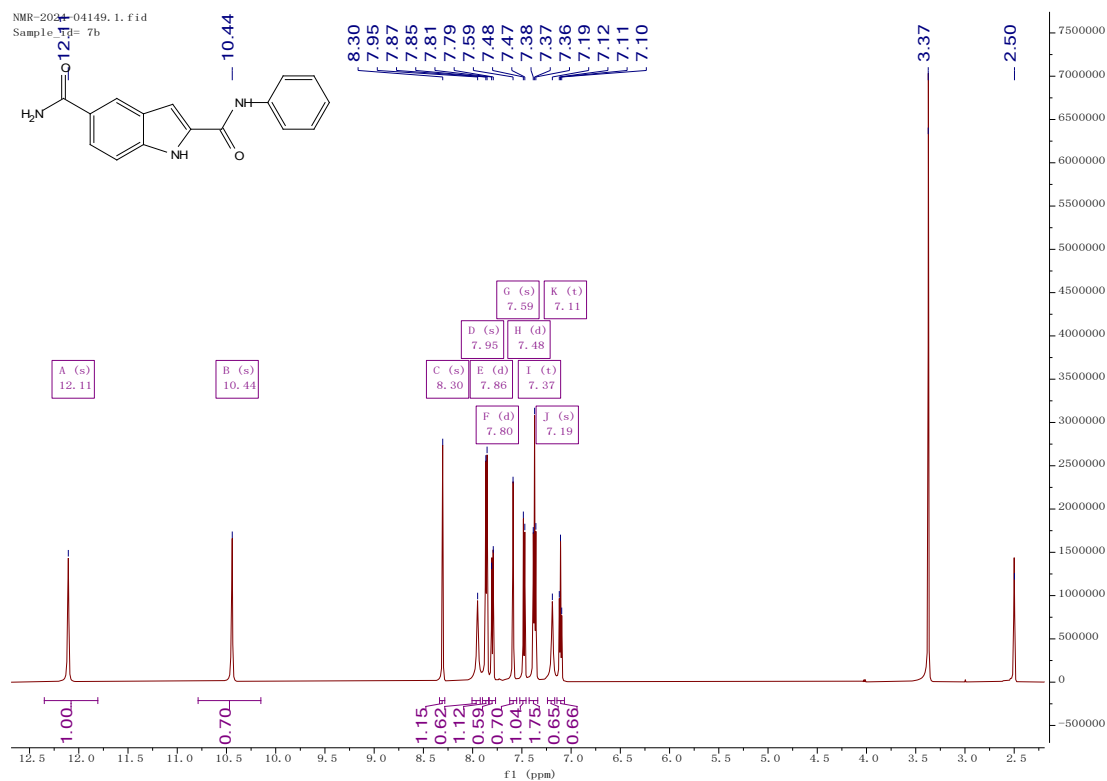


Figure 5. 1H NMR spectrum of compound A1

NMR-2025-02196.1.fid
Sample_id= zd-1a

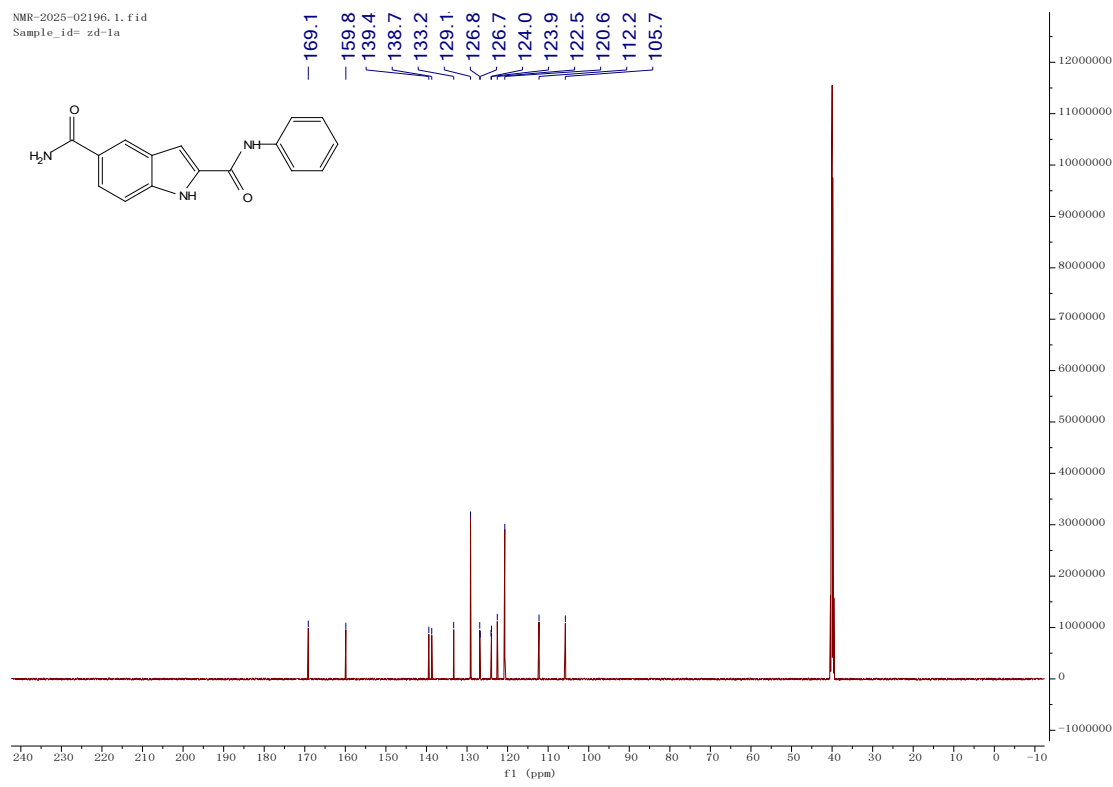


Figure 6. ^{13}C NMR spectrum of compound A1

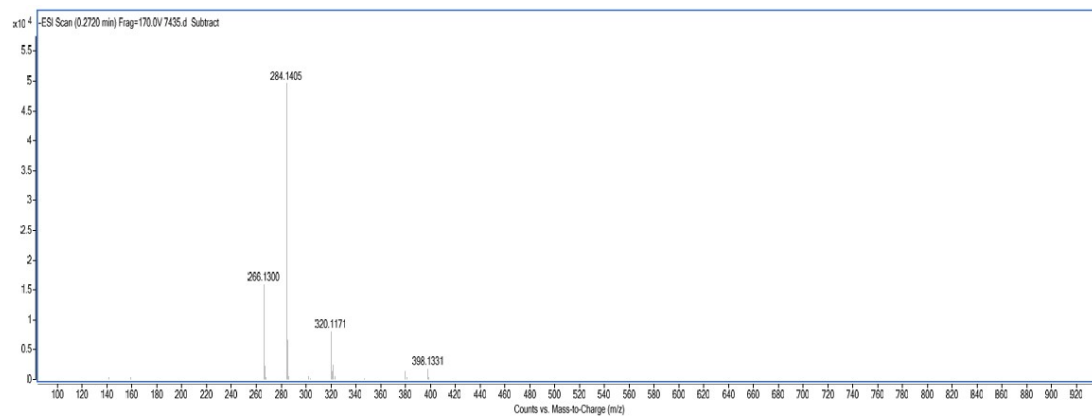


Figure 7. HRMS spectrum of compound A2

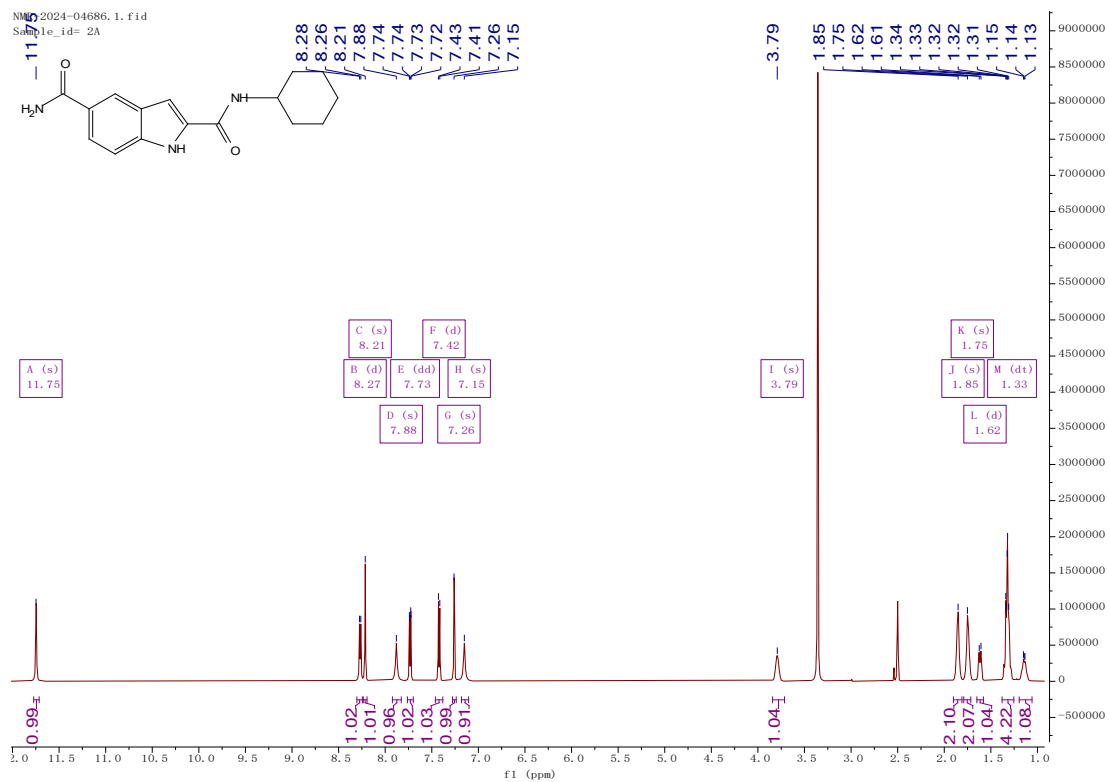


Figure 8. ^1H NMR spectrum of compound A2

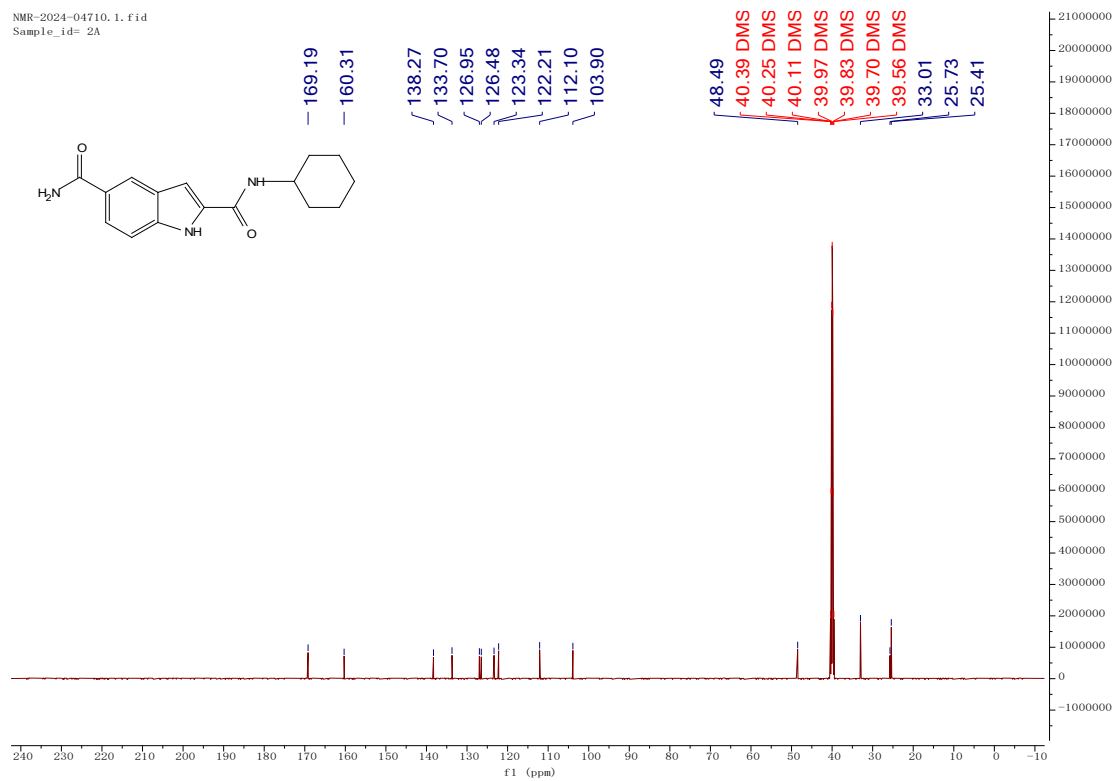


Figure 9. ^{13}C NMR spectrum of compound A2

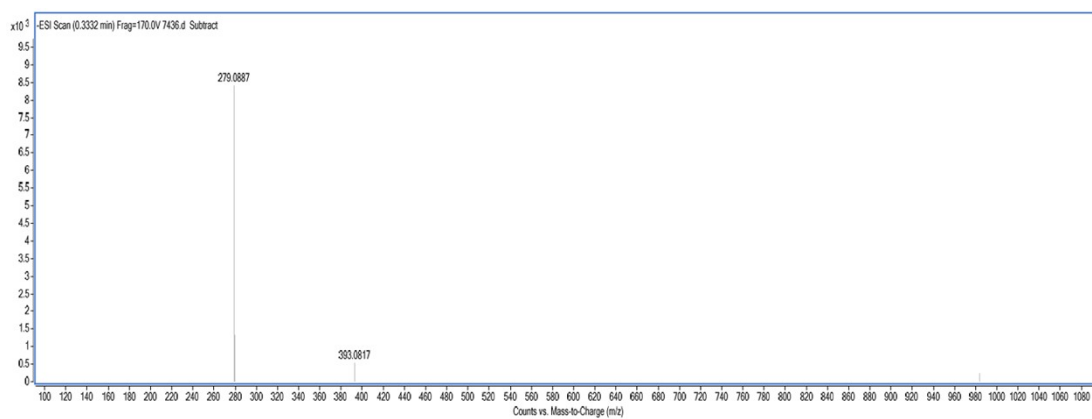


Figure 10. HRMS spectrum of compound A3

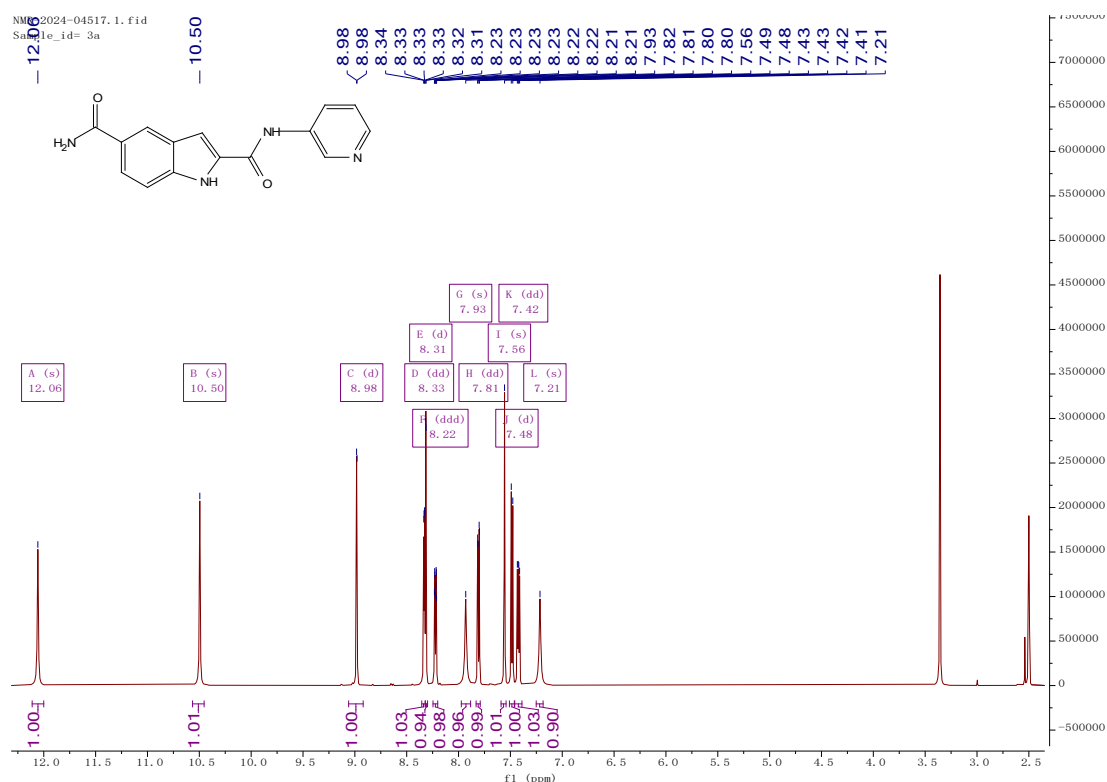


Figure 11. ¹H NMR spectrum of compound A3

NMR-2024-04534.1.fid
Sample_id= 3A

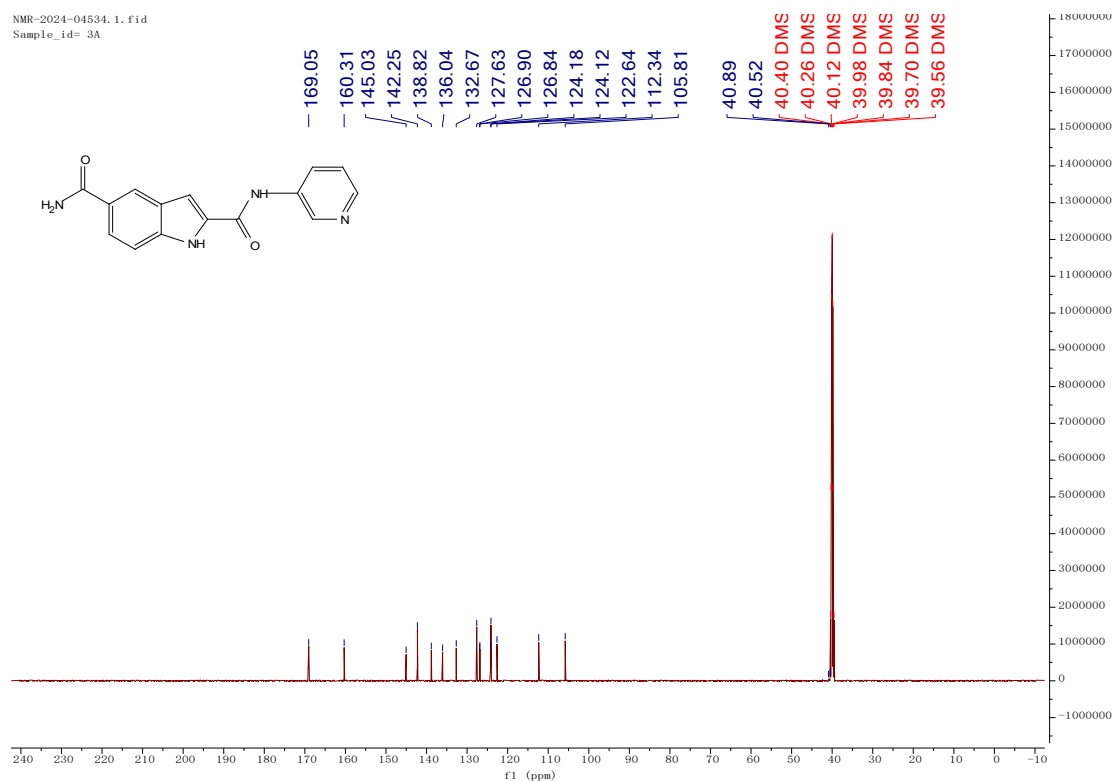


Figure 12. ^{13}C NMR spectrum of compound A3

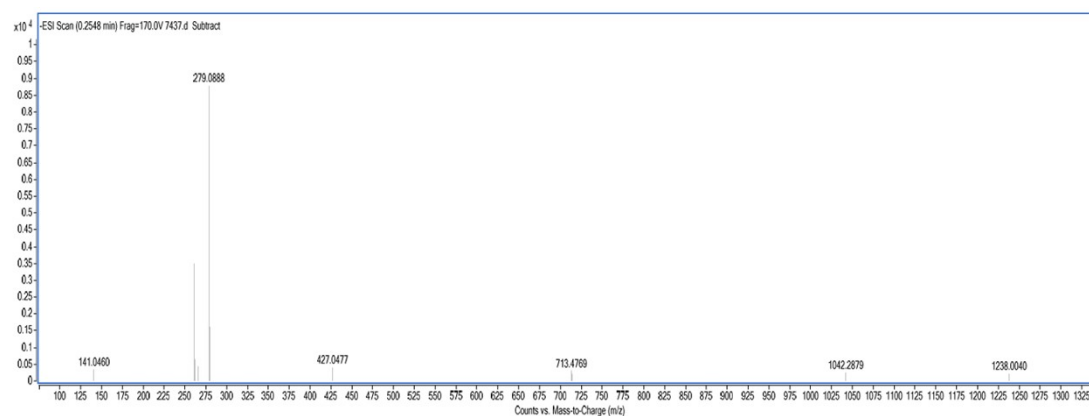


Figure 13. HRMS spectrum of compound A4

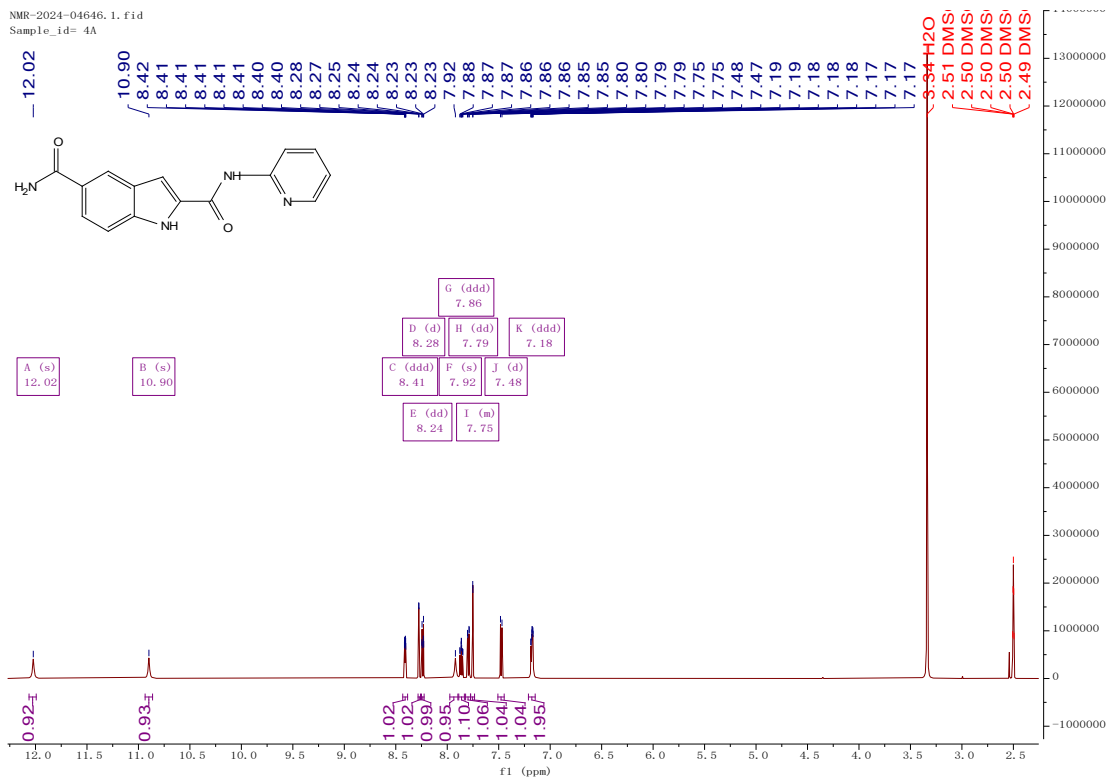


Figure 14. ¹H NMR spectrum of compound A4

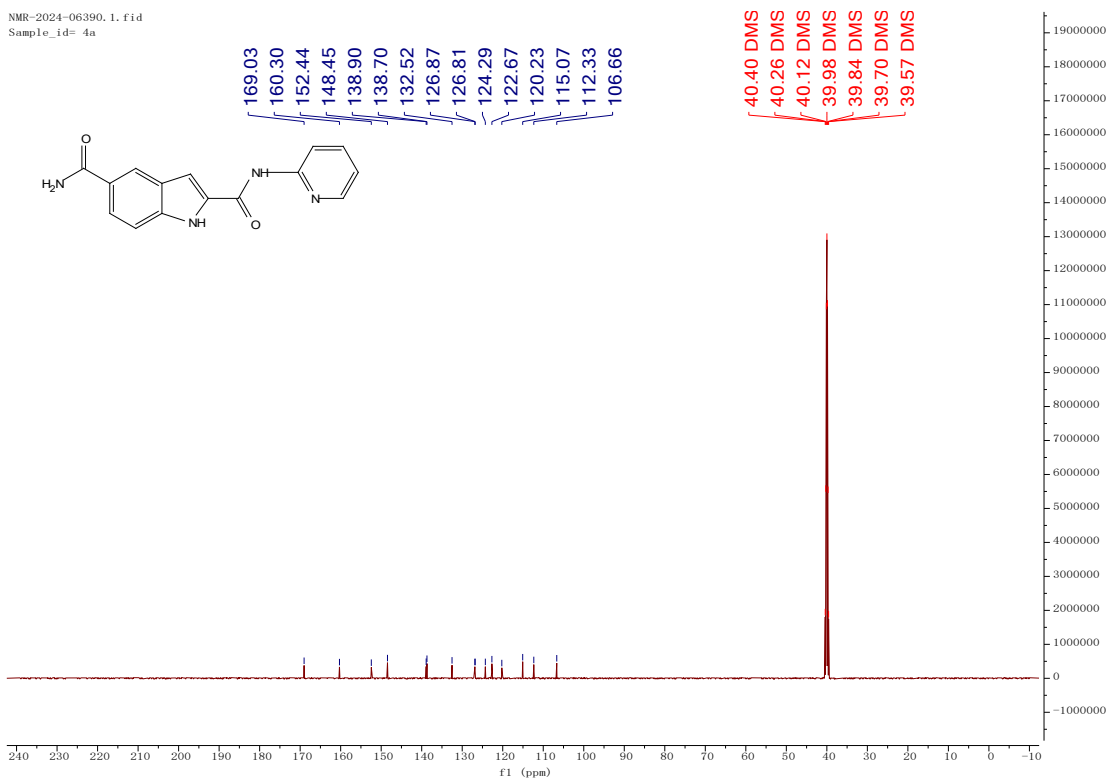


Figure 15. ¹³C NMR spectrum of compound A4

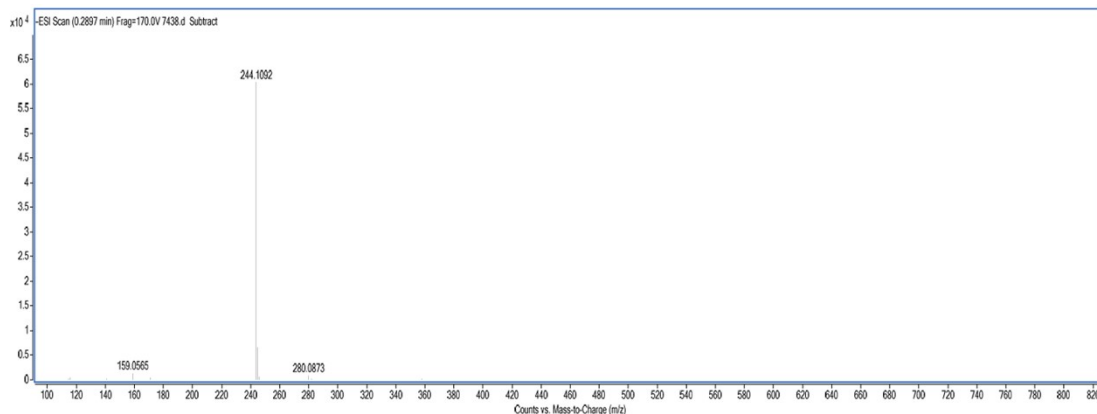


Figure 16. HRMS spectrum of compound A5

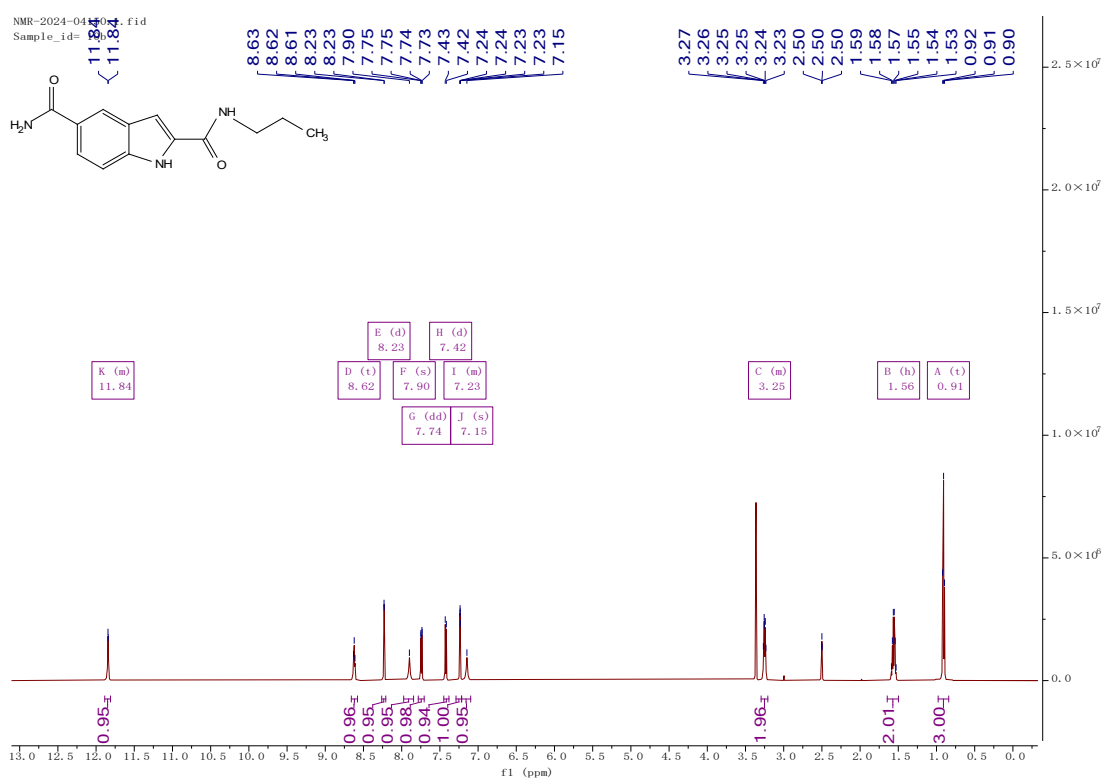


Figure 17. ¹H NMR spectrum of compound A5

NMR-2024-04179_1.fid
Sample_id= 10b

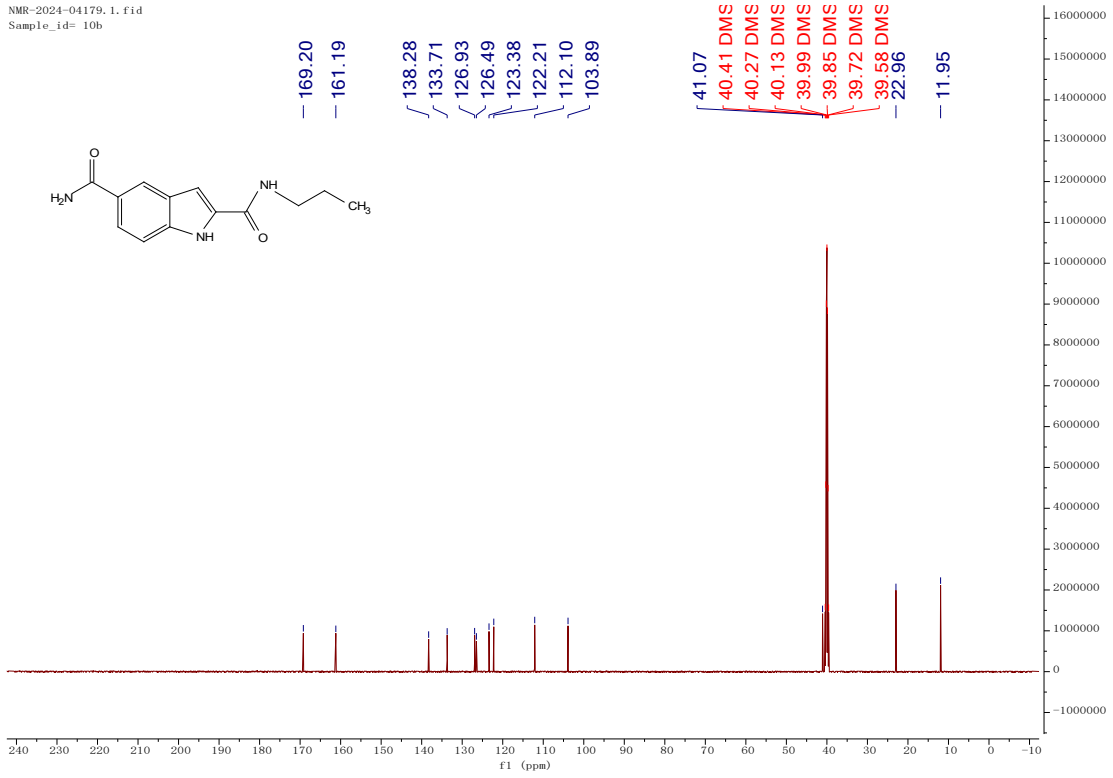


Figure 18. ^{13}C NMR spectrum of compound A5

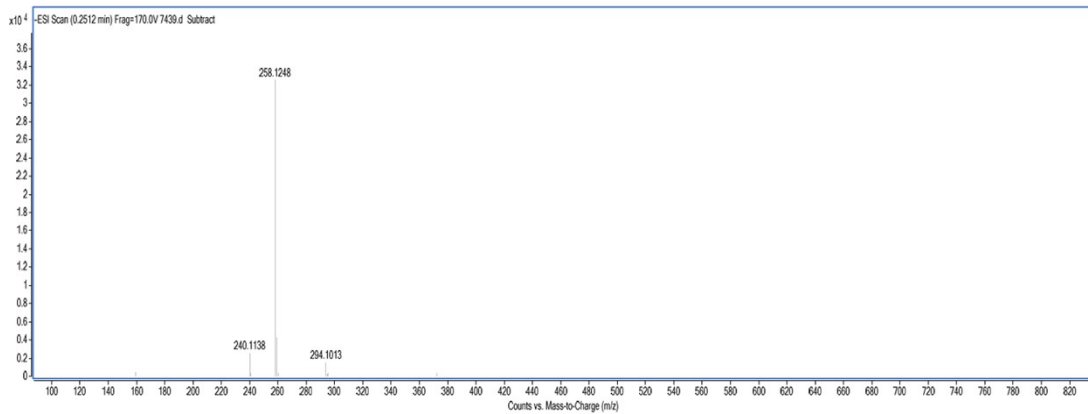


Figure 19. HRMS spectrum of compound A6

NMR-2024-04564.1.fid
Sample_id= 6A

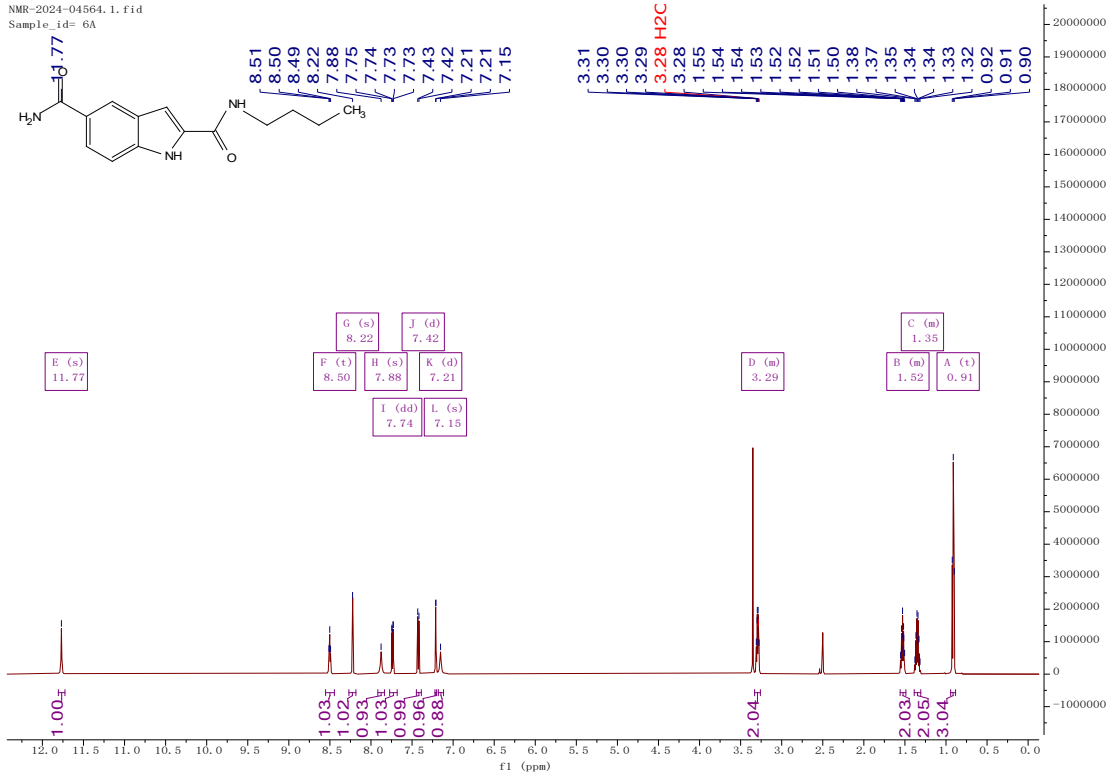


Figure 20. ¹H NMR spectrum of compound A6

NMR-2024-04629.1.fid
Sample_id= 6A

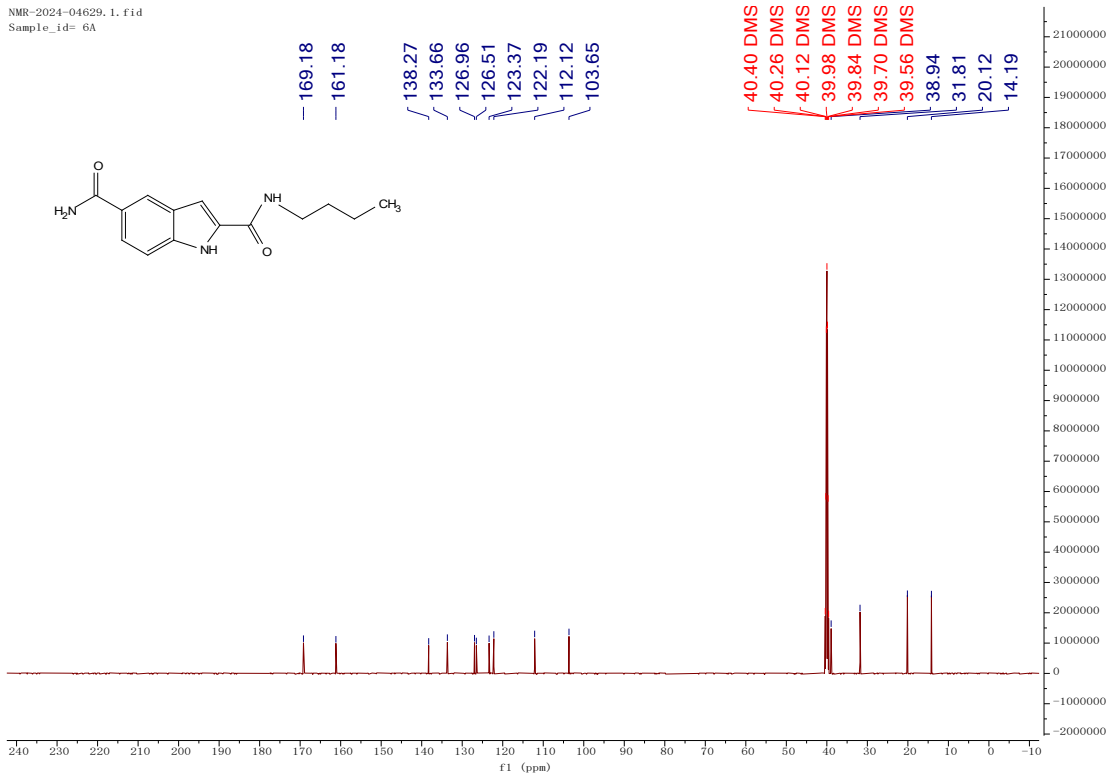


Figure 21. ¹³C NMR spectrum of compound A6

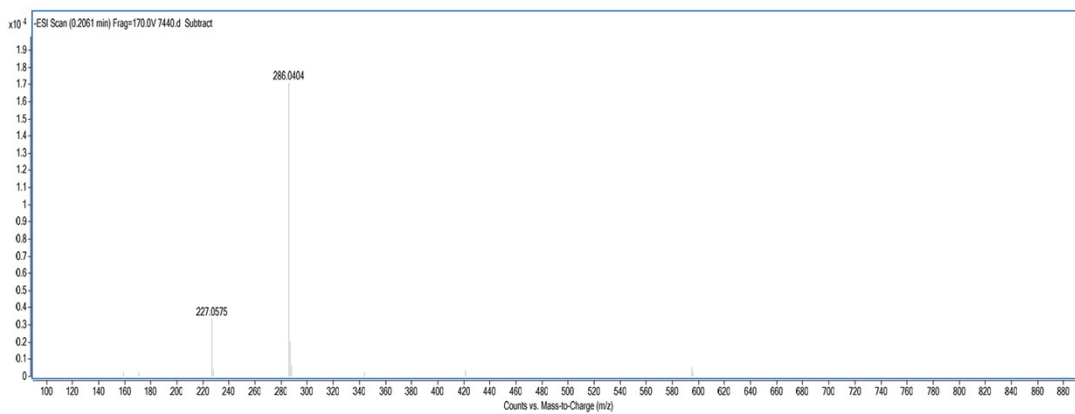


Figure 22. HRMS spectrum of compound A7

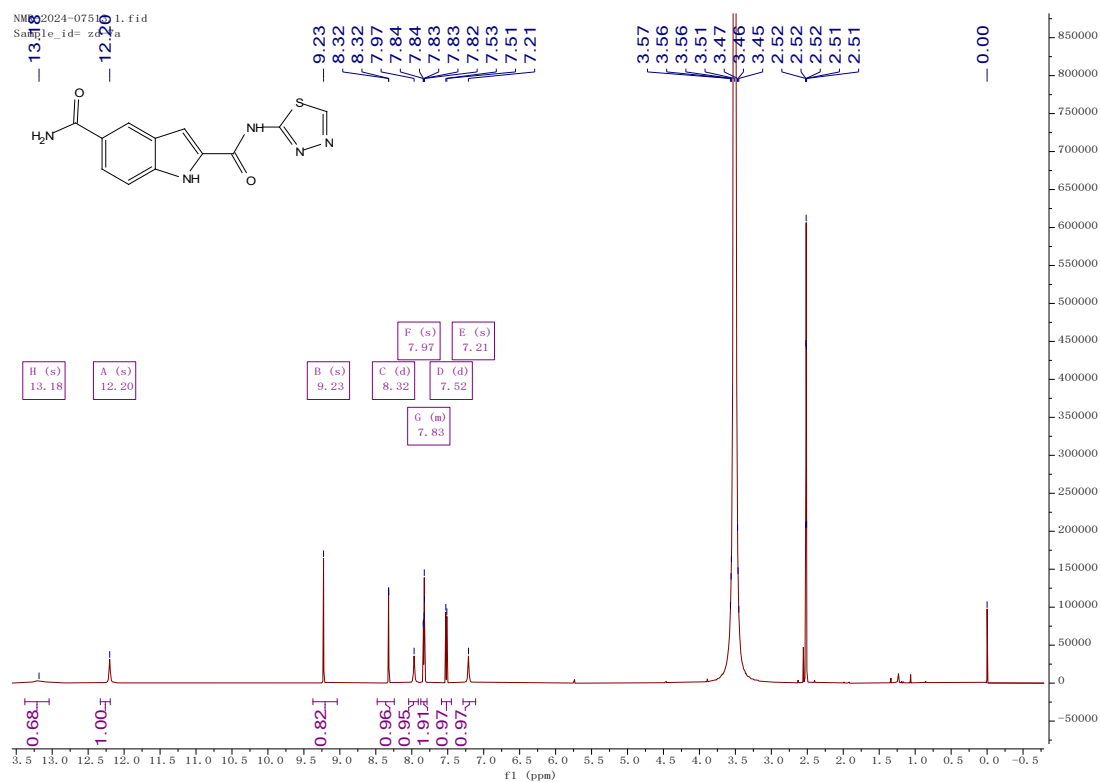


Figure 23. ¹H NMR spectrum of compound A7

NMR-2025-02870_1.fid
Sample_id= ZD-7a

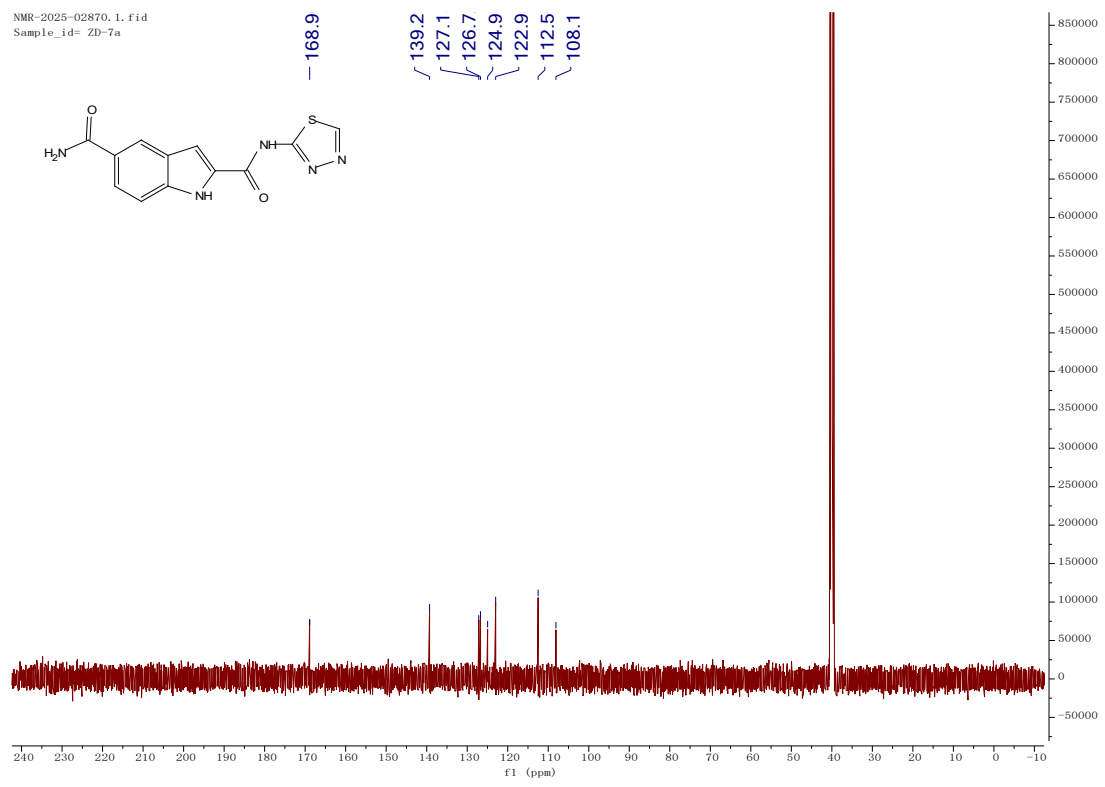


Figure 24. ¹³C NMR spectrum of compound A7

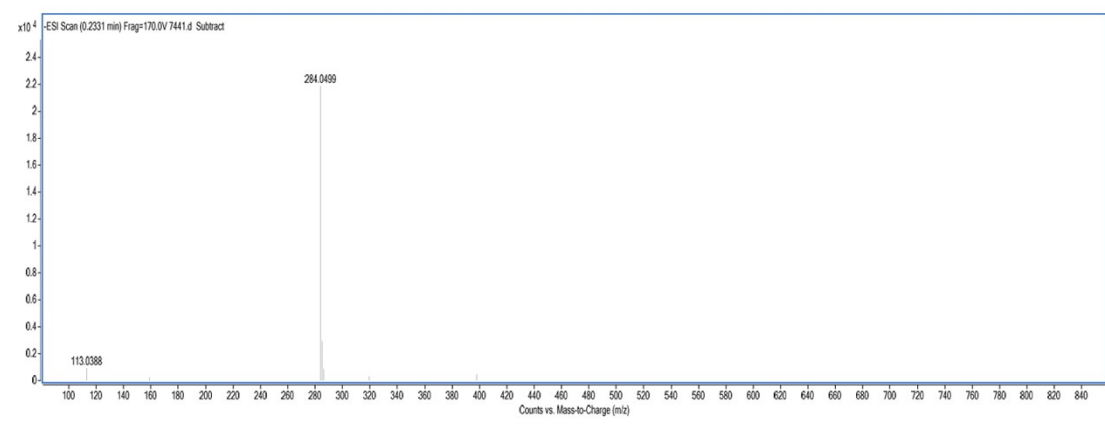


Figure 25. HRMS spectrum of compound A8

NMR-2024-04709.1.fid
Sample_id= 8A

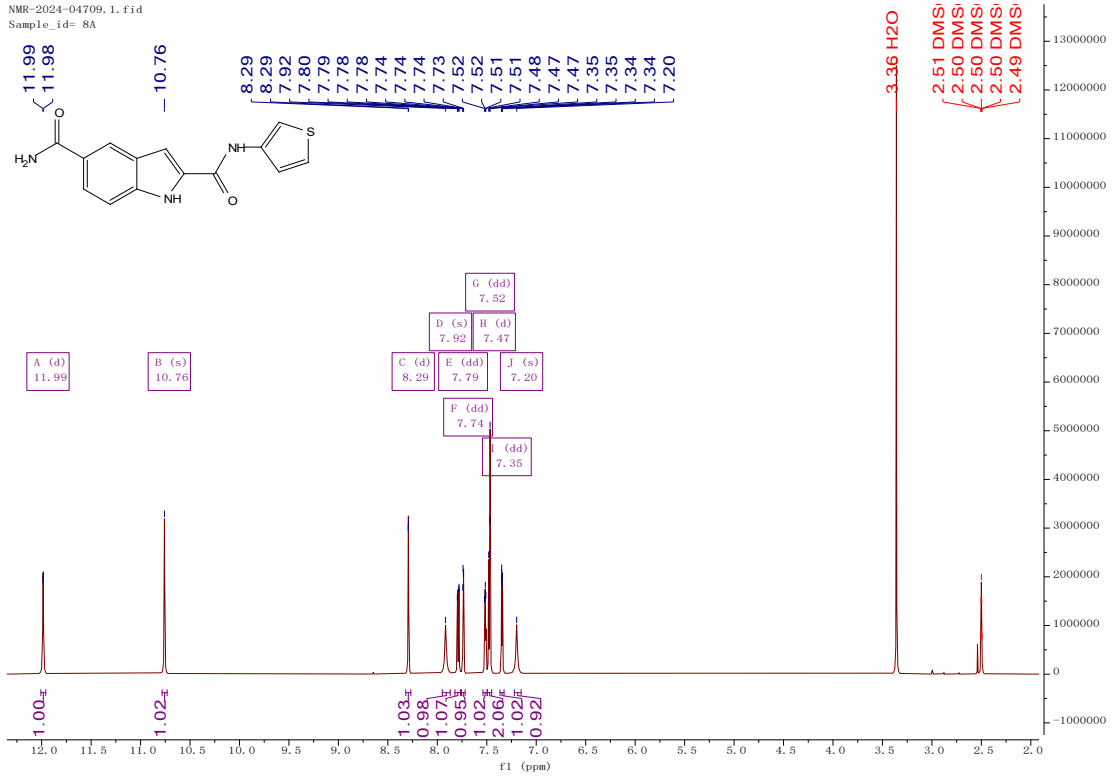


Figure 26. ¹H NMR spectrum of compound A8

NMR-2025-02497.1.fid
Sample_id= zd-8a

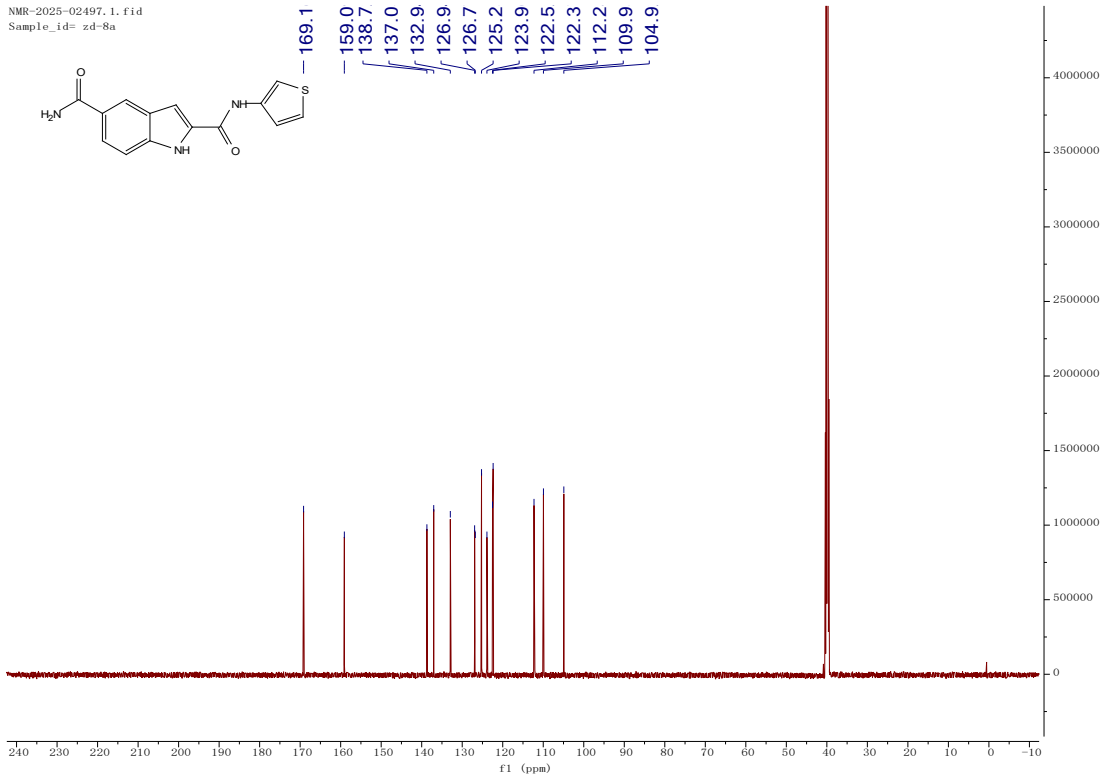


Figure 27. ¹³C NMR spectrum of compound A8

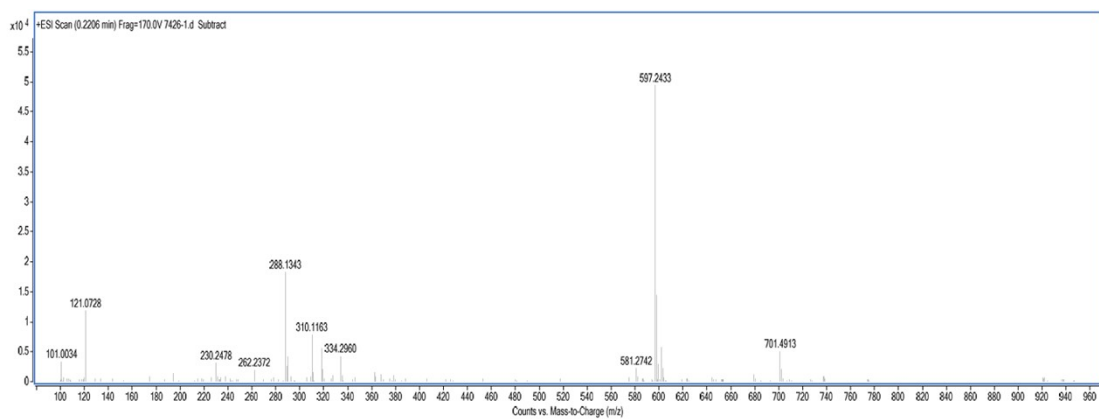


Figure 28. HRMS spectrum of compound A9

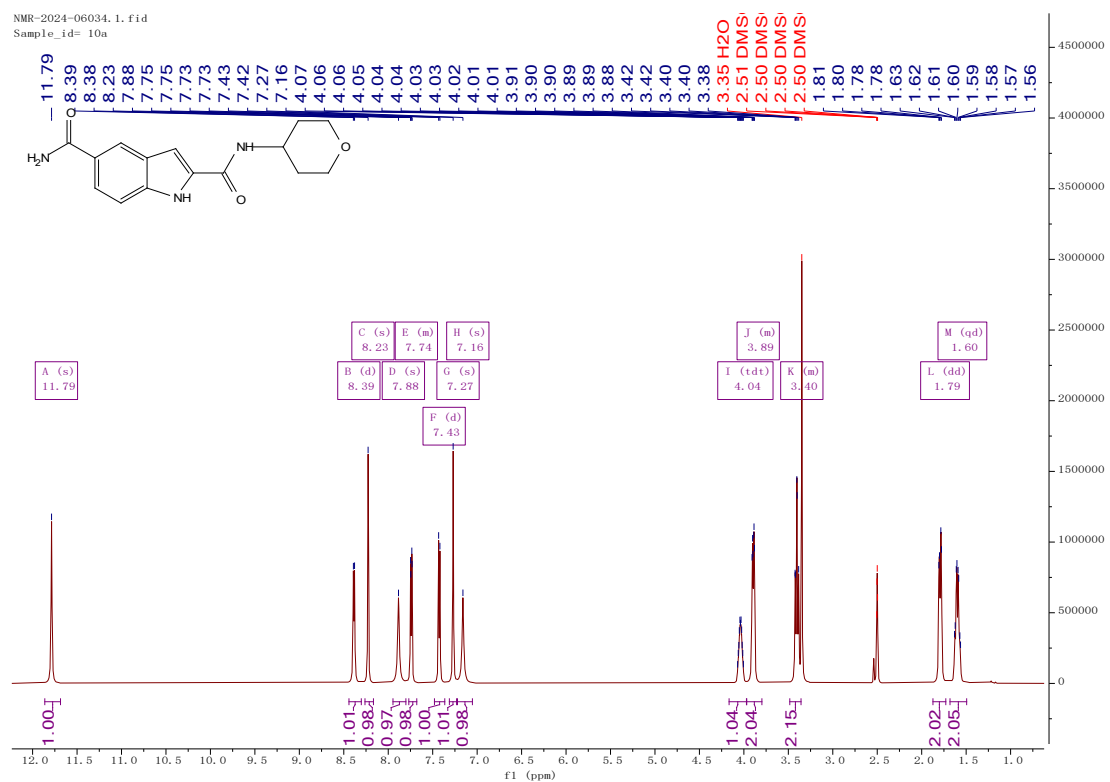


Figure 29. ¹H NMR spectrum of compound A9

NMR-2024-06076_1.fid
Sample_id= 10A

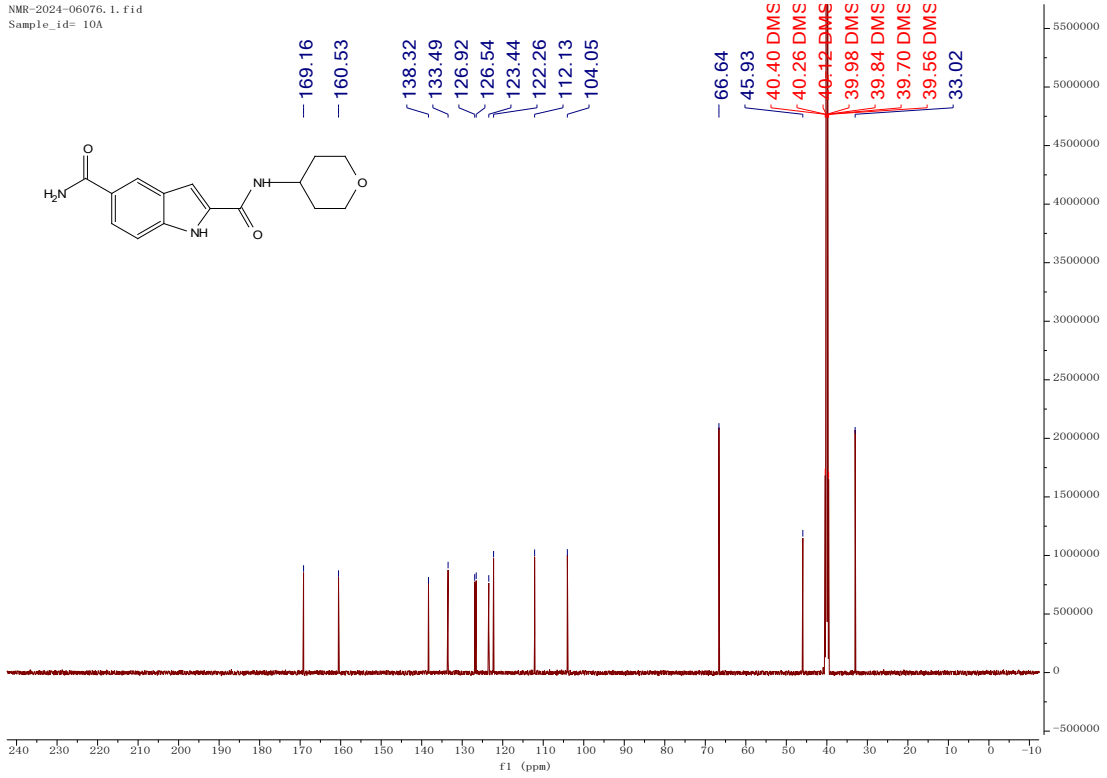


Figure 30. ^{13}C NMR spectrum of compound A9

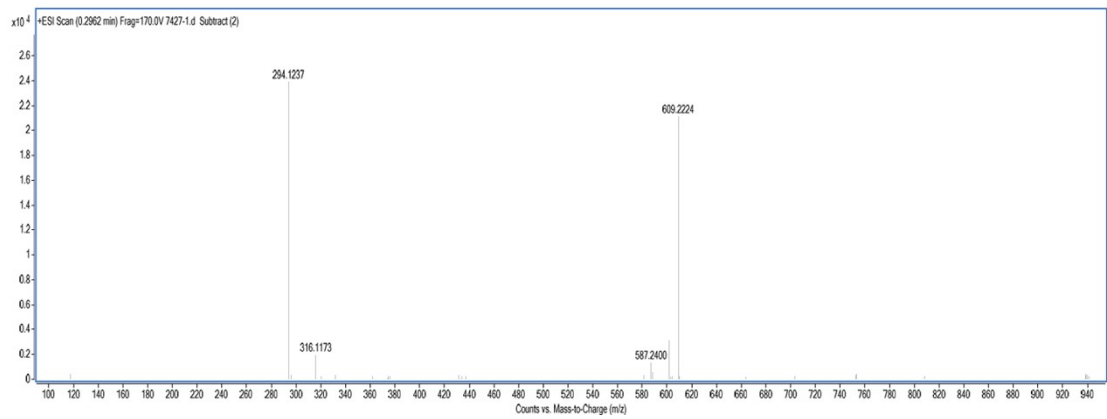


Figure 31. HRMS spectrum of compound A10

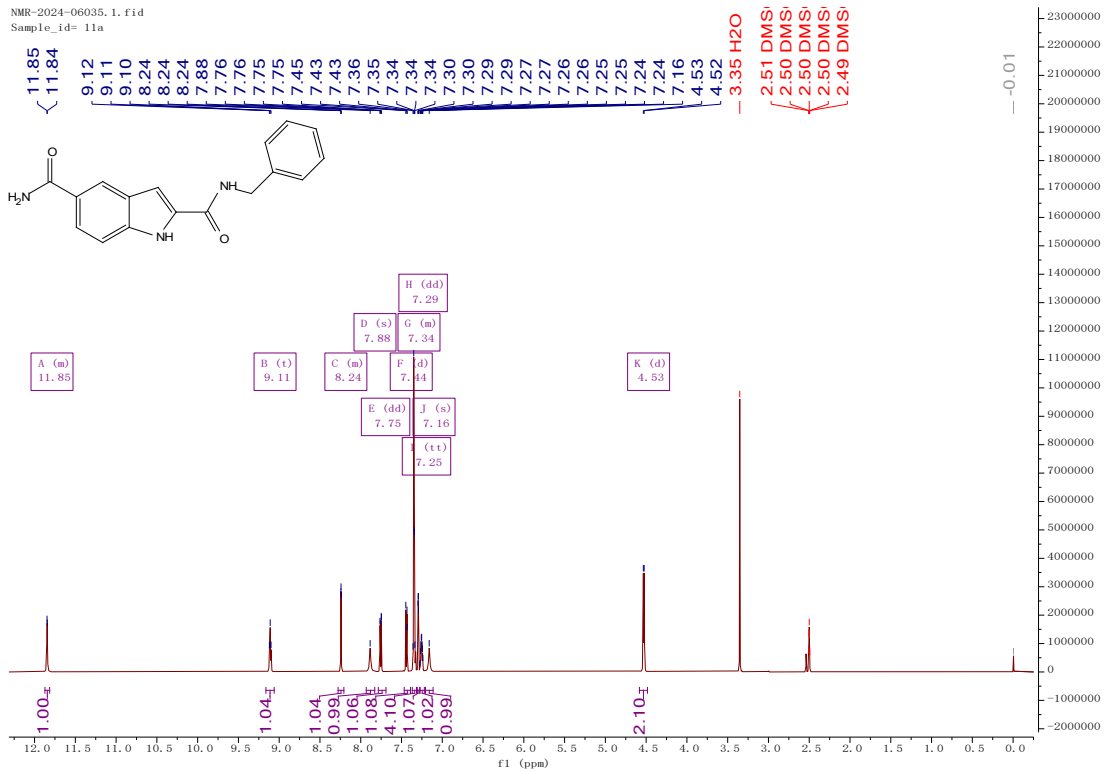


Figure 32. ¹H NMR spectrum of compound A10

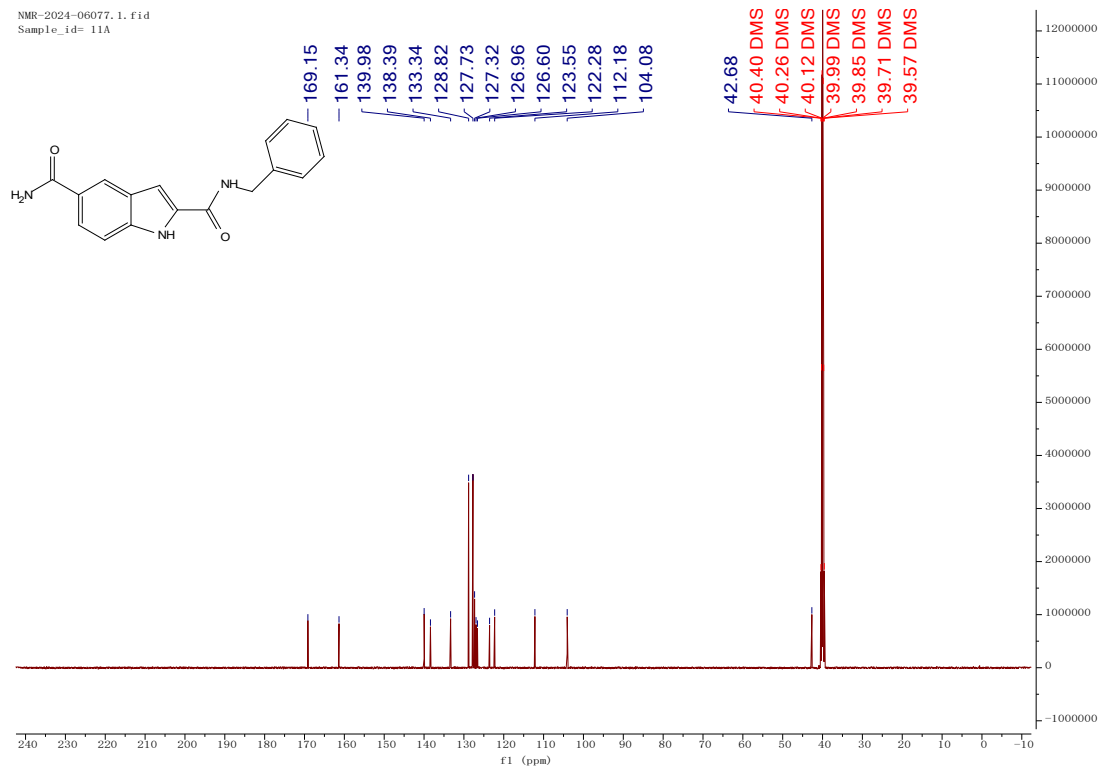


Figure 33. ¹³C NMR spectrum of compound A10

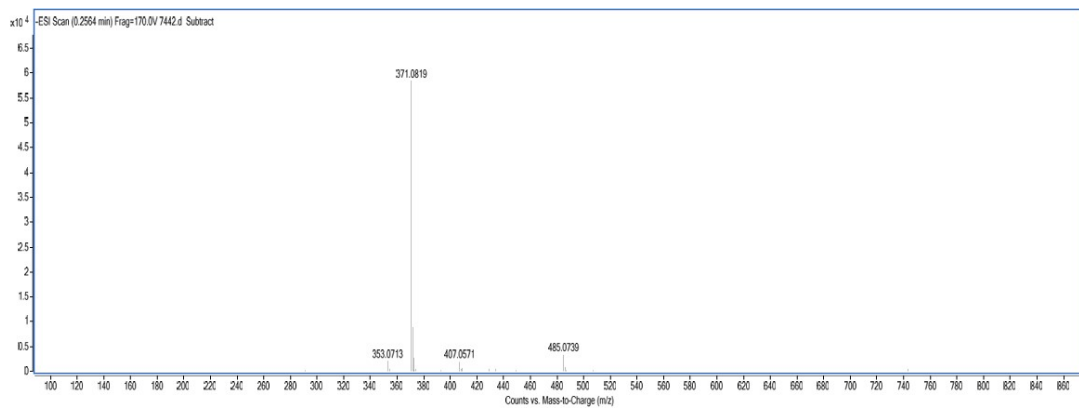


Figure 34. HRMS spectrum of compound A11

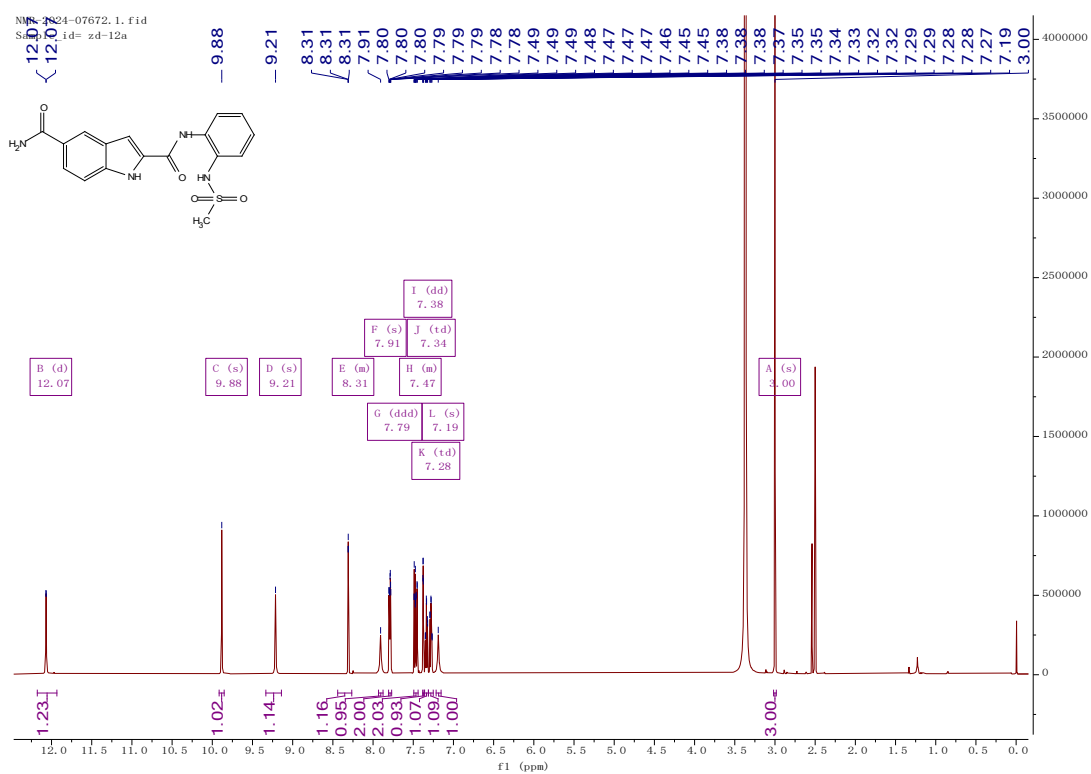


Figure 35. ¹H NMR spectrum of compound A11

NMR-2024-07694_1.fid
Sample_id= xd-12a

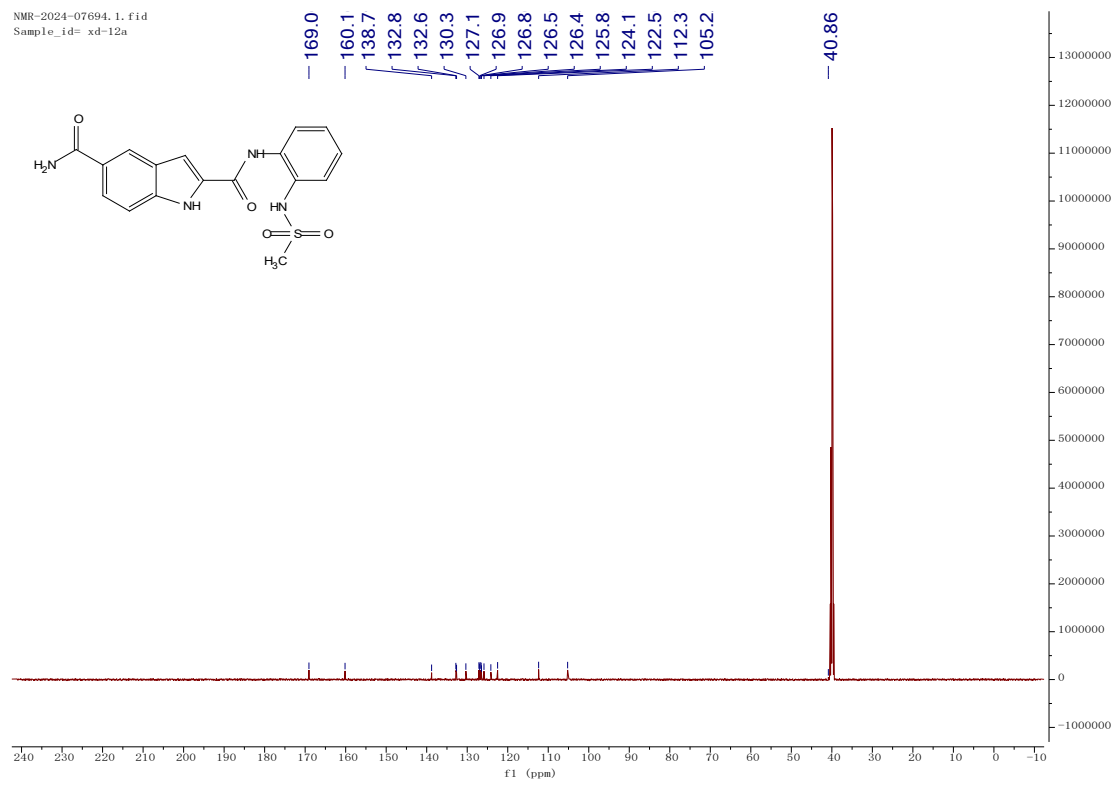


Figure 36. ¹³C NMR spectrum of compound A11

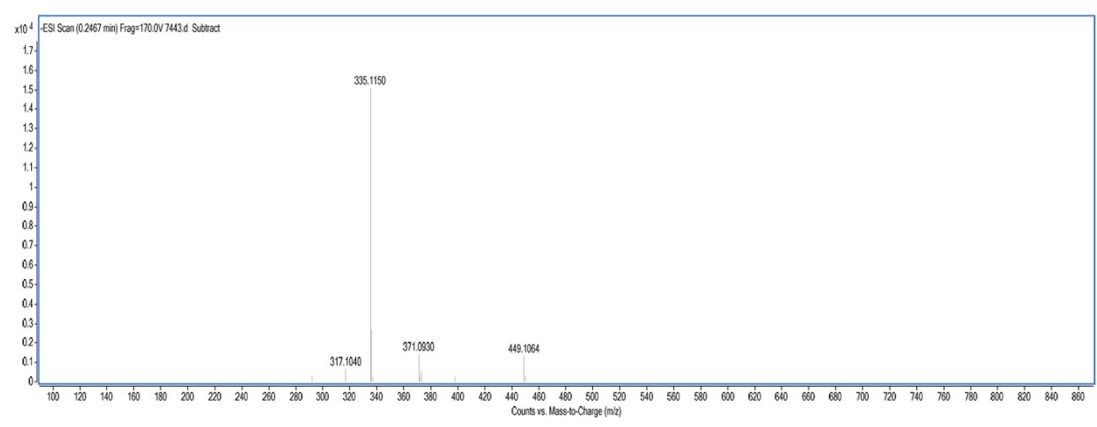


Figure 37. HRMS spectrum of compound A12

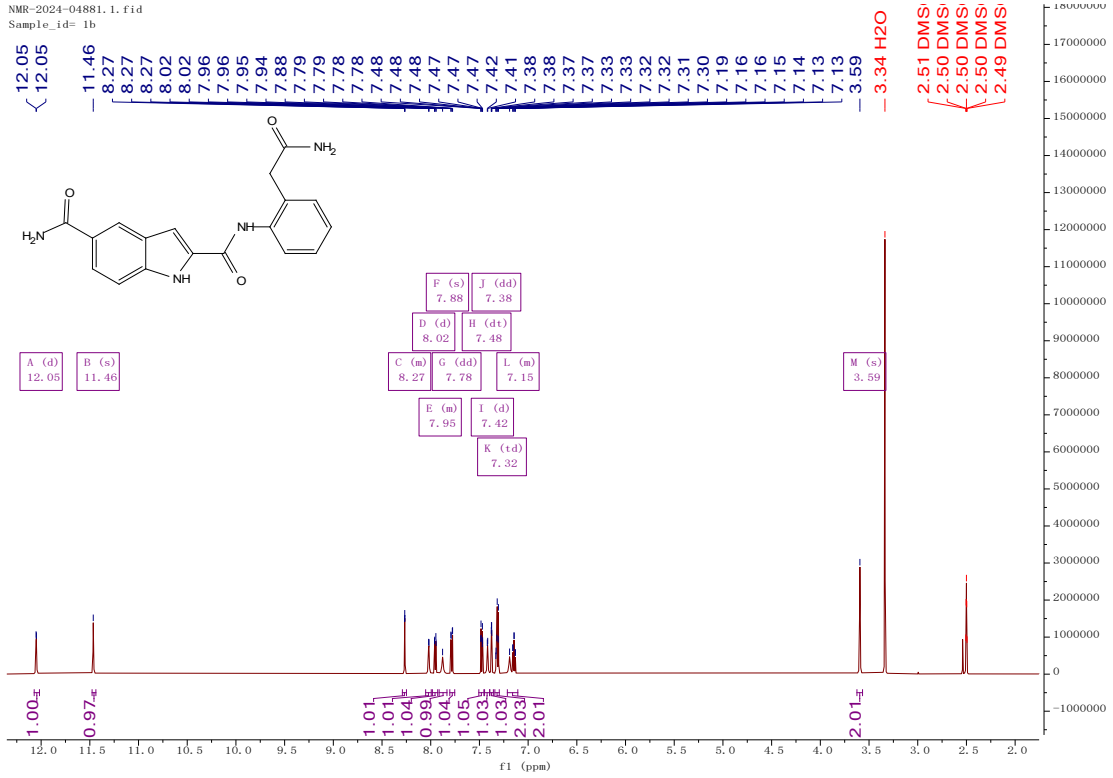


Figure 38. ¹H NMR spectrum of compound A12

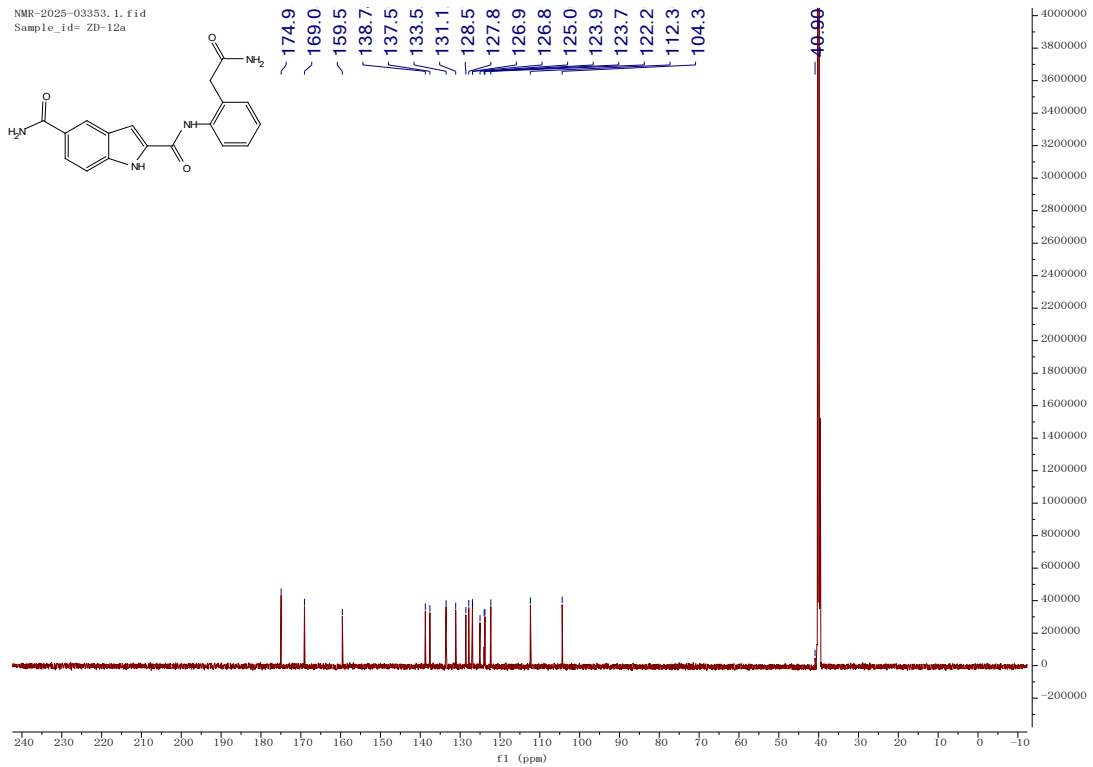


Figure 39. ¹³C NMR spectrum of compound A12

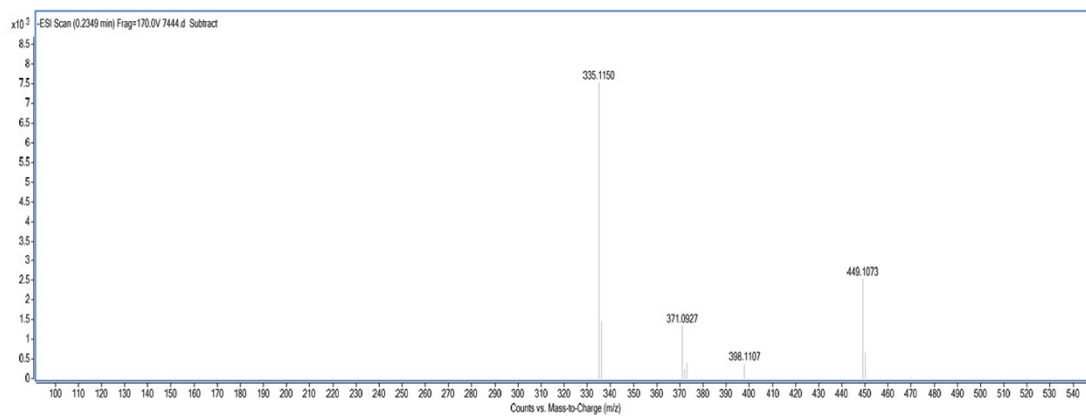


Figure 40. HRMS spectrum of compound A13

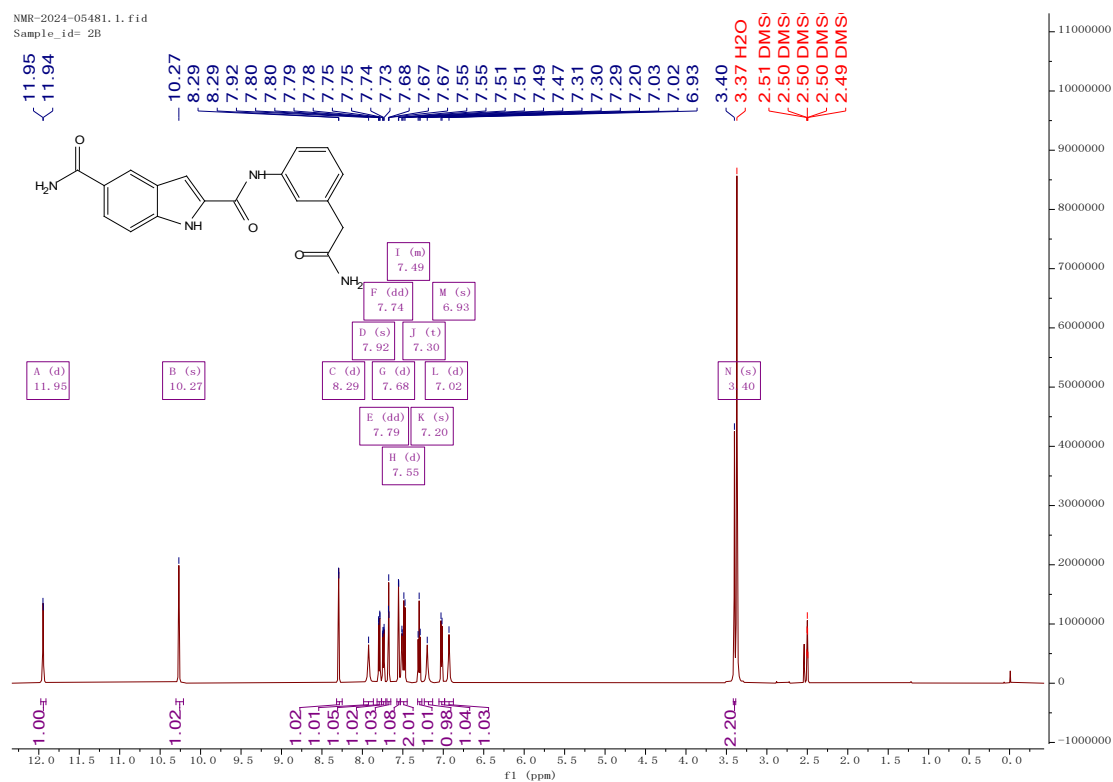


Figure 41. ¹H NMR spectrum of compound A13

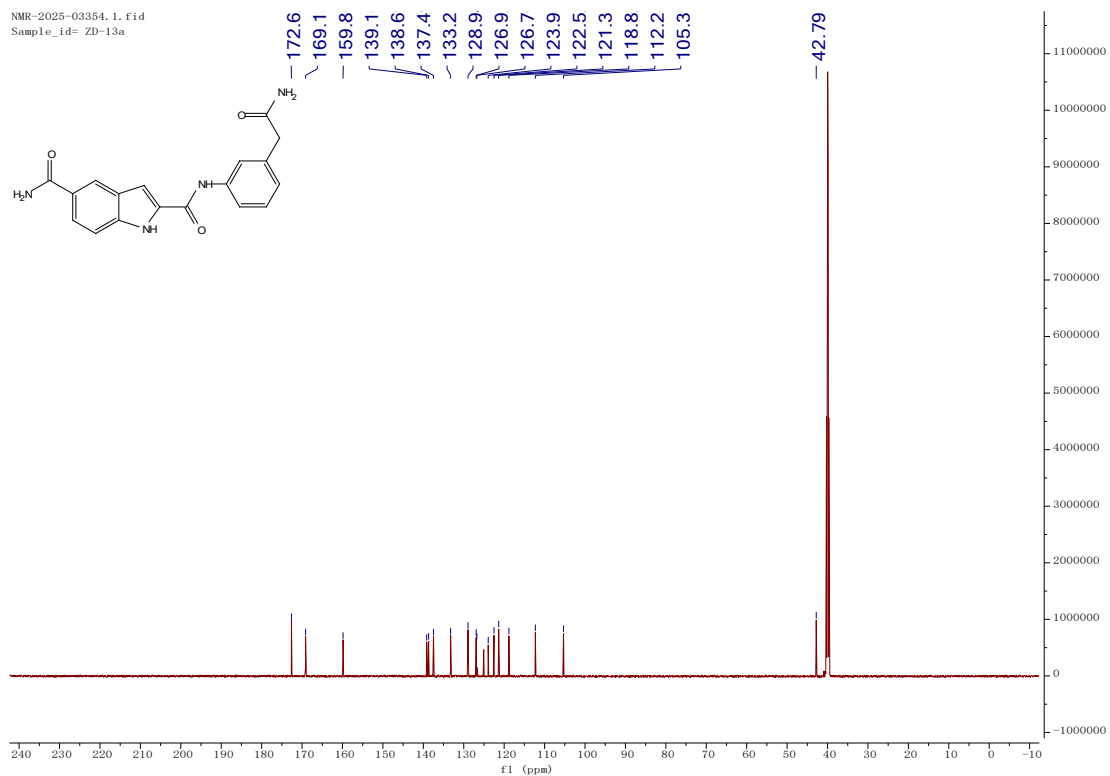


Figure 42. ^{13}C NMR spectrum of compound A13

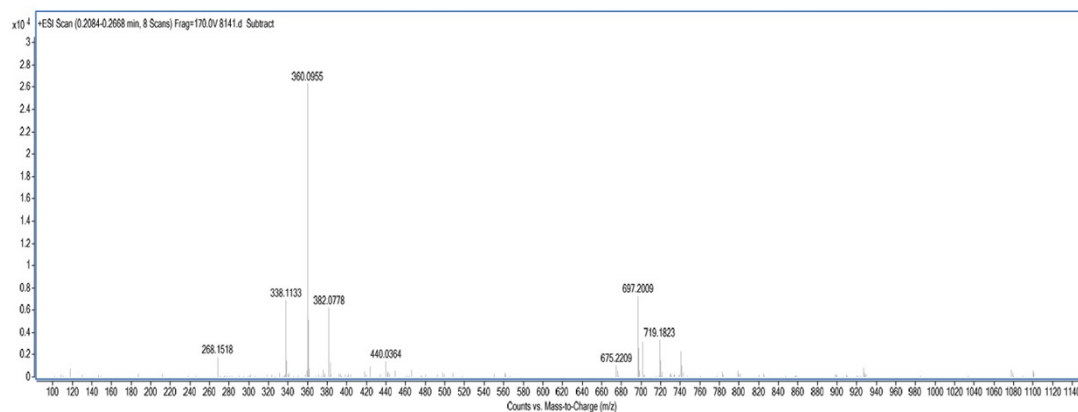


Figure 43. HRMS spectrum of compound A14

NMR-2024-05086. 1. fid
Sample_id= 1c

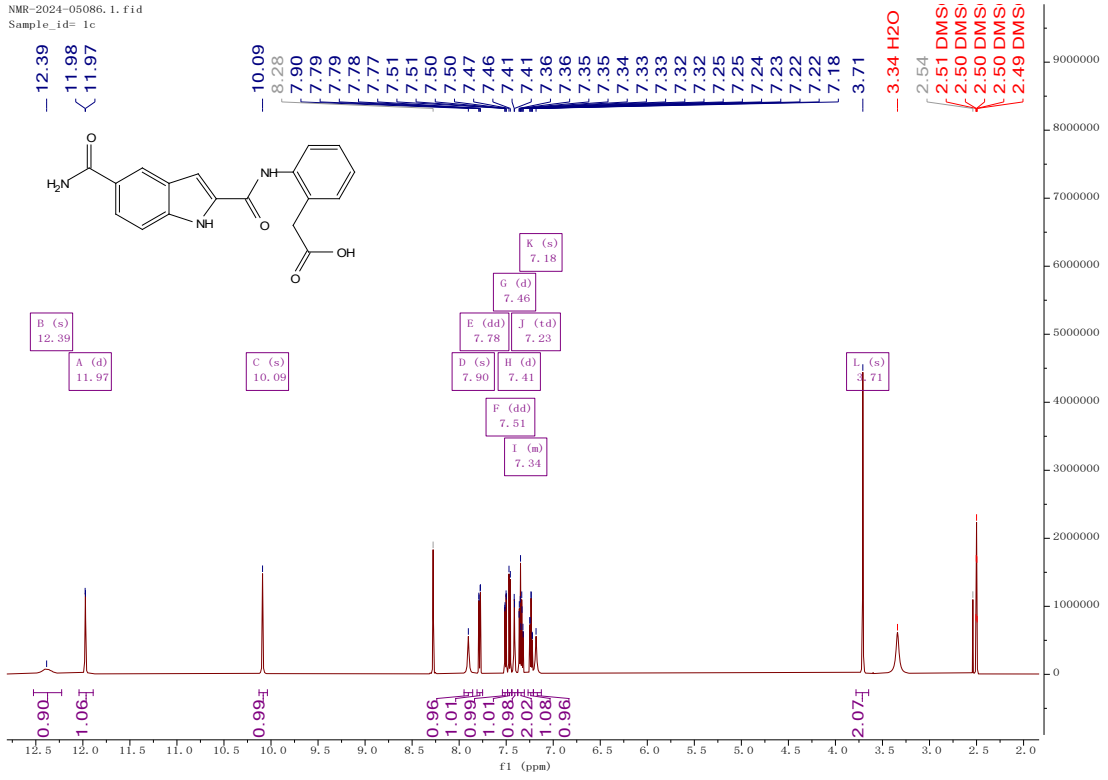


Figure 44. ¹H NMR spectrum of compound A14

NMR-2024-05692. 1. fid
Sample_id= 1C

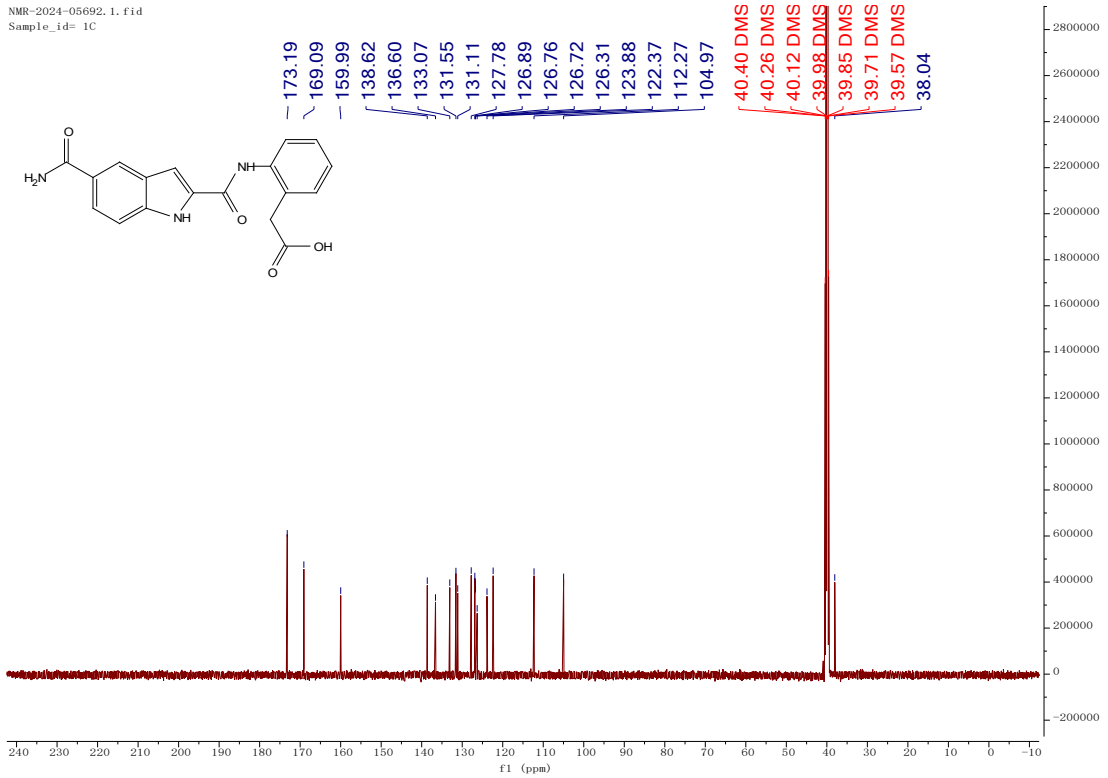


Figure 45. ¹³C NMR spectrum of compound A14

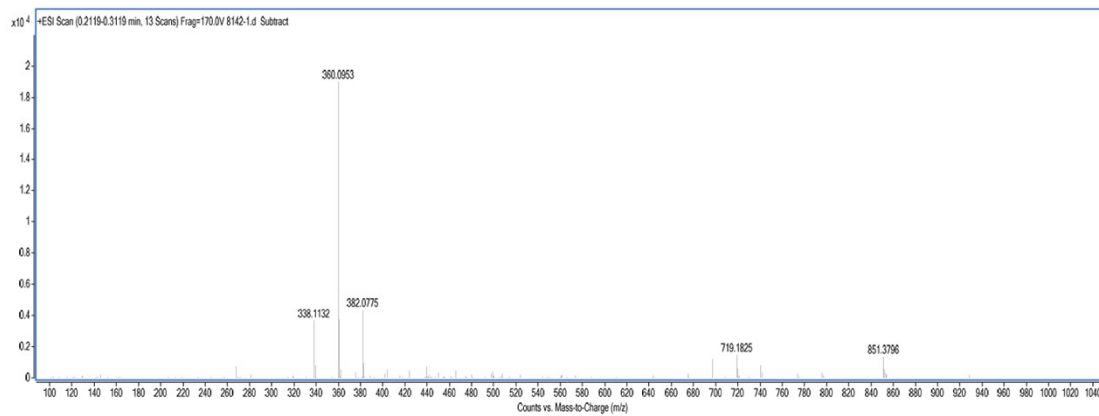


Figure 46. HRMS spectrum of compound A15

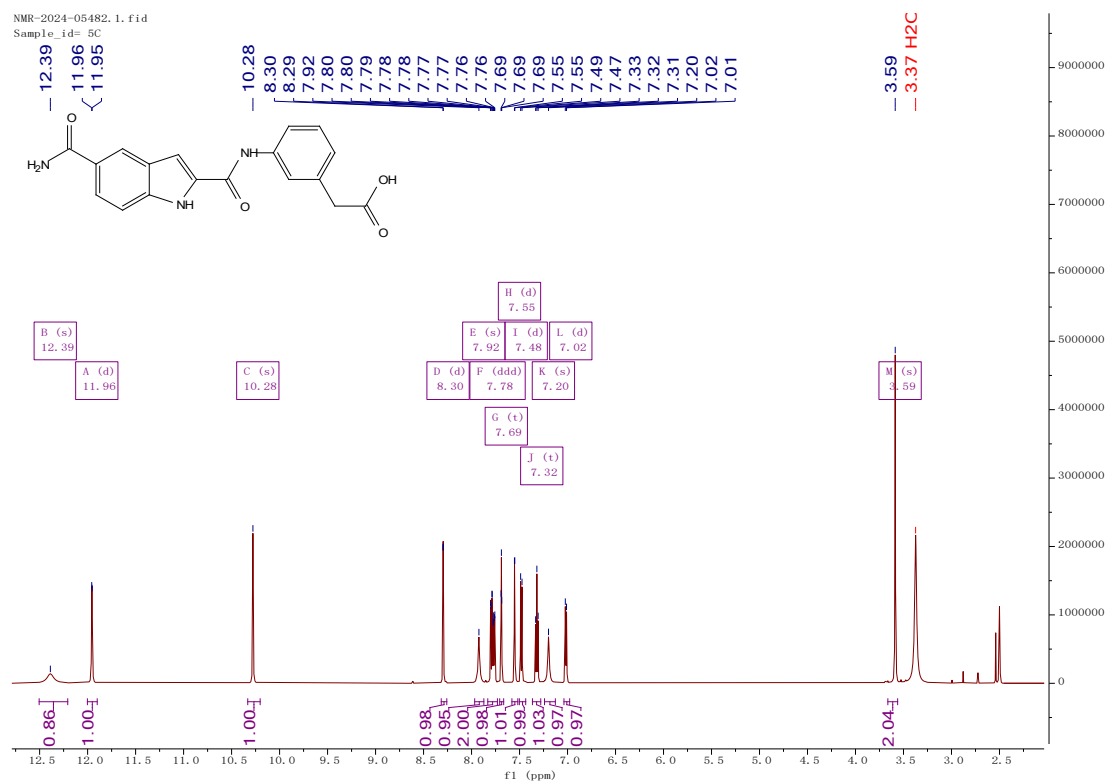


Figure 47. ¹H NMR spectrum of compound A15

NMR-2024-05833.1.fid
Sample_id= 5c

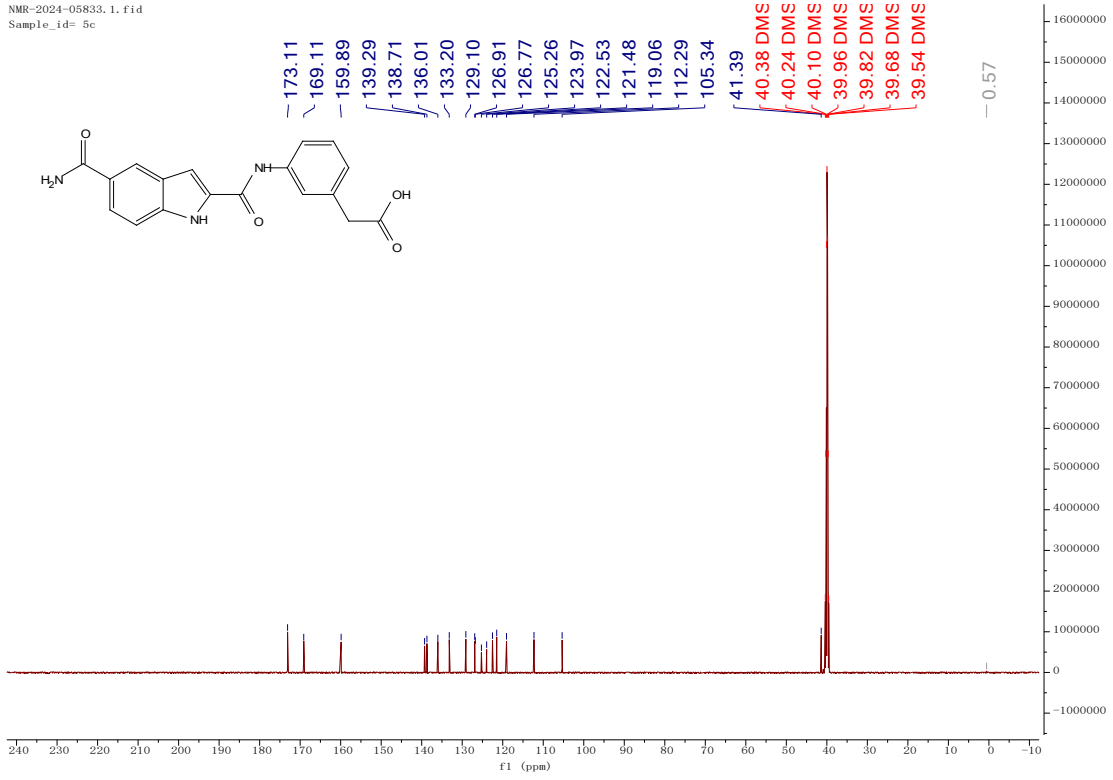


Figure 48. ¹³C NMR spectrum of compound A15

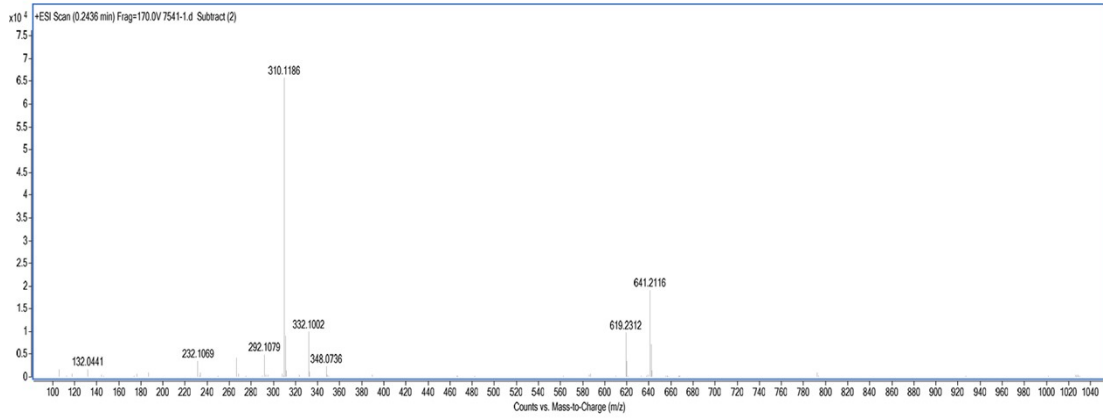


Figure 49. HRMS spectrum of compound A16

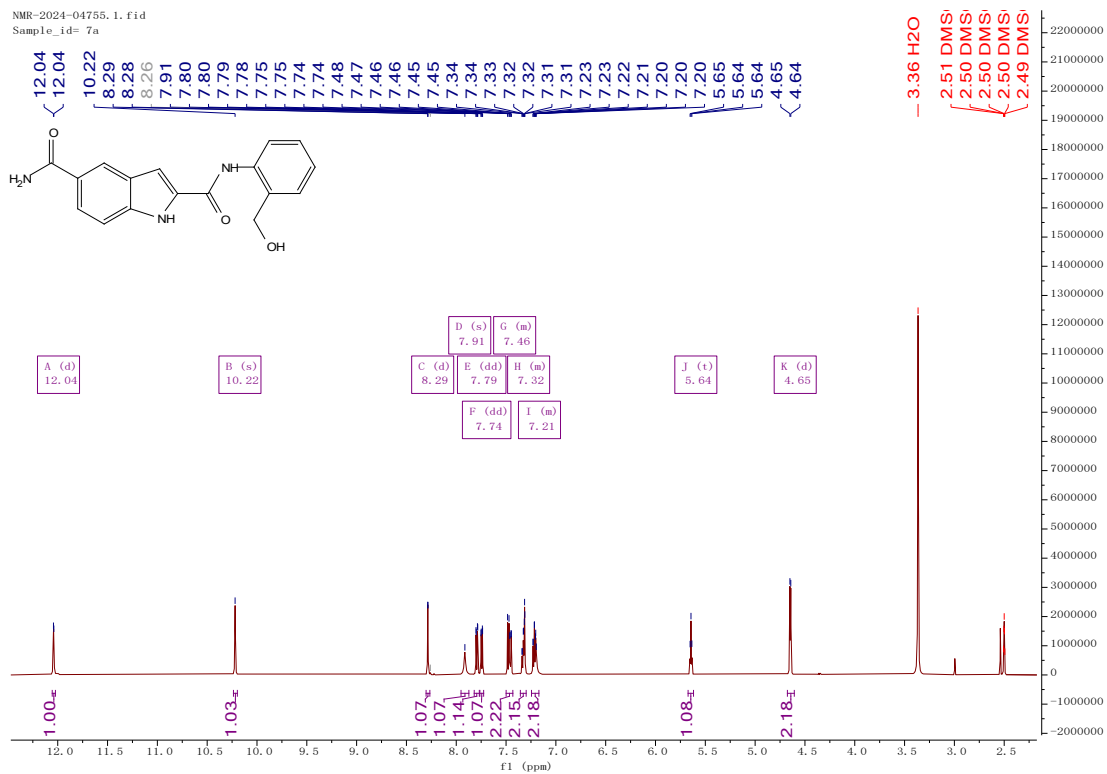


Figure 50. ^1H NMR spectrum of compound A16

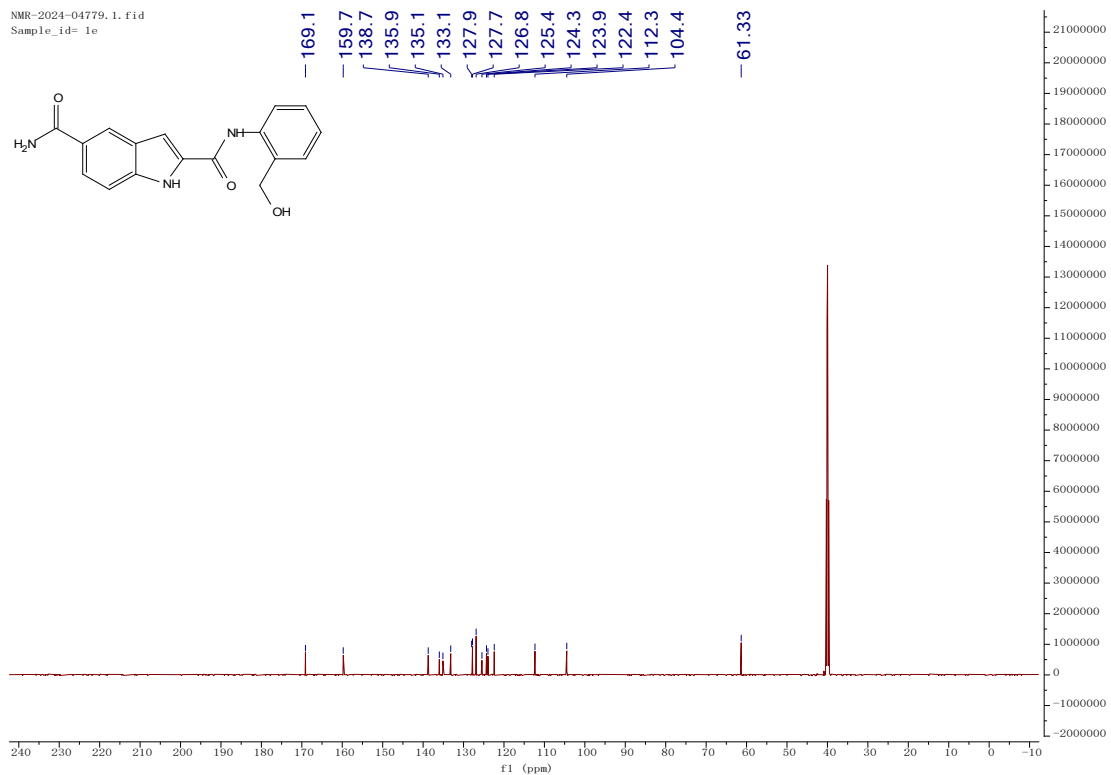


Figure 51. ^{13}C NMR spectrum of compound A16

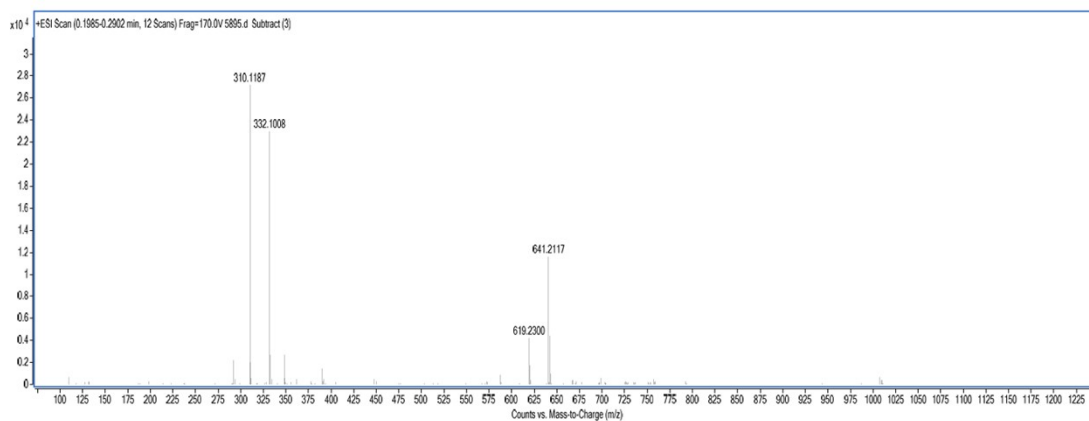


Figure 52. HRMS spectrum of compound A17

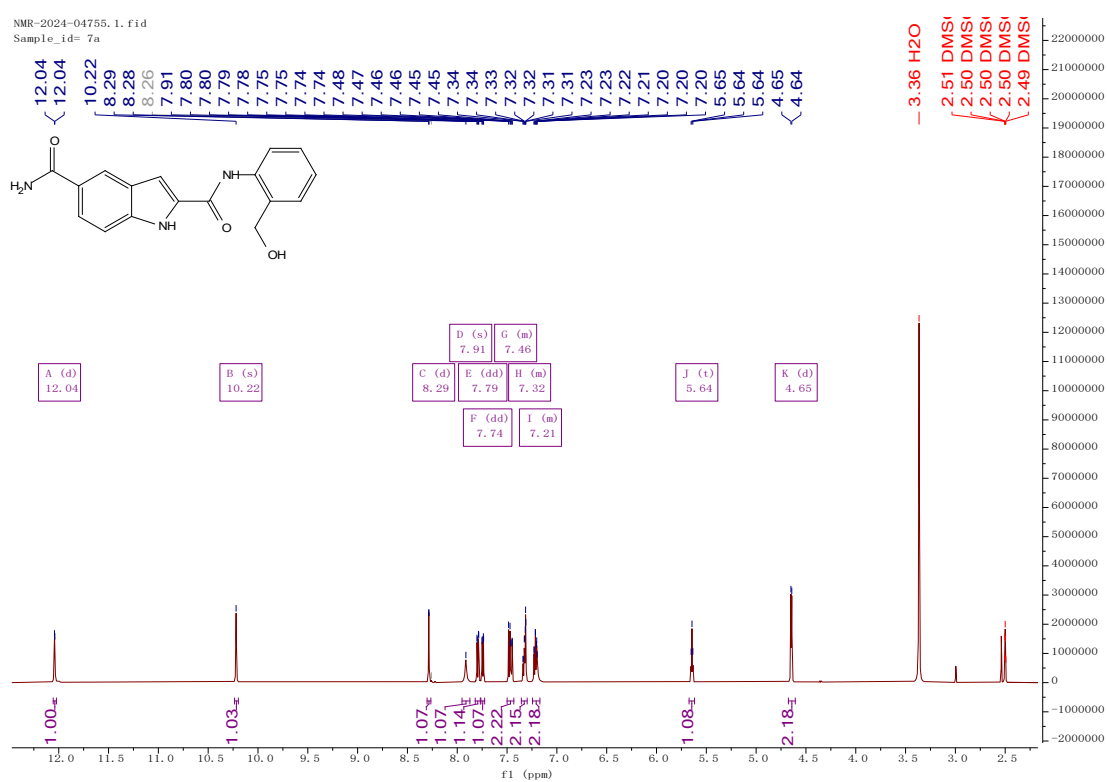


Figure 53. ¹H NMR spectrum of compound A17

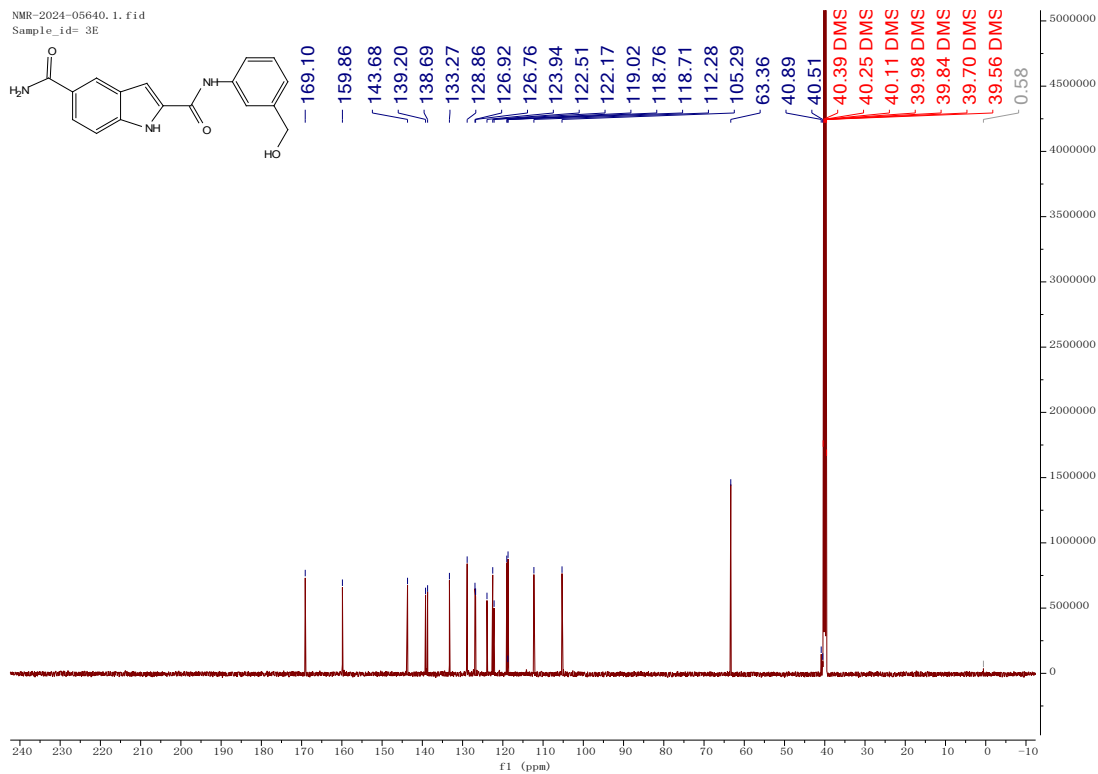


Figure 54. ^{13}C NMR spectrum of compound A17

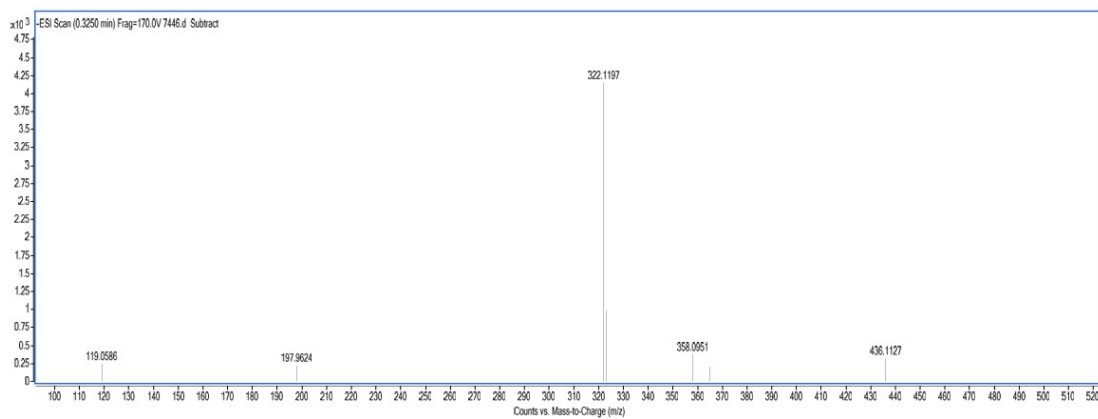


Figure 55. HRMS spectrum of compound A18

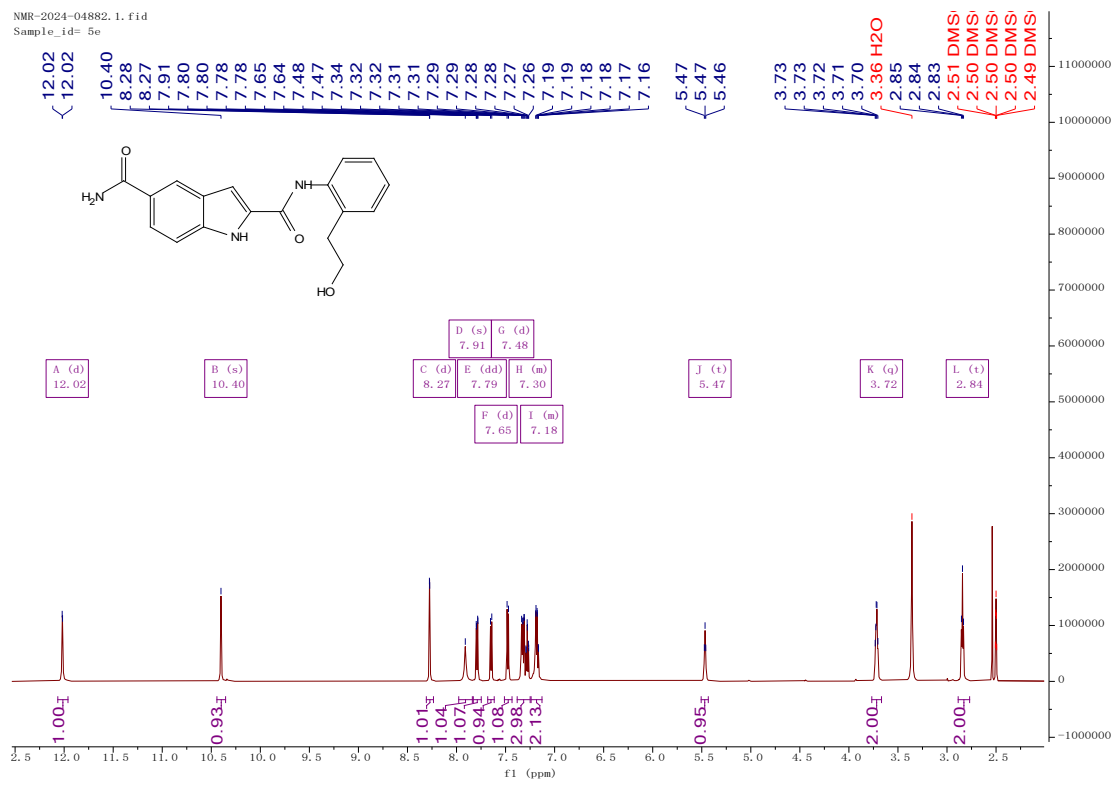


Figure 56. ¹H NMR spectrum of compound A18

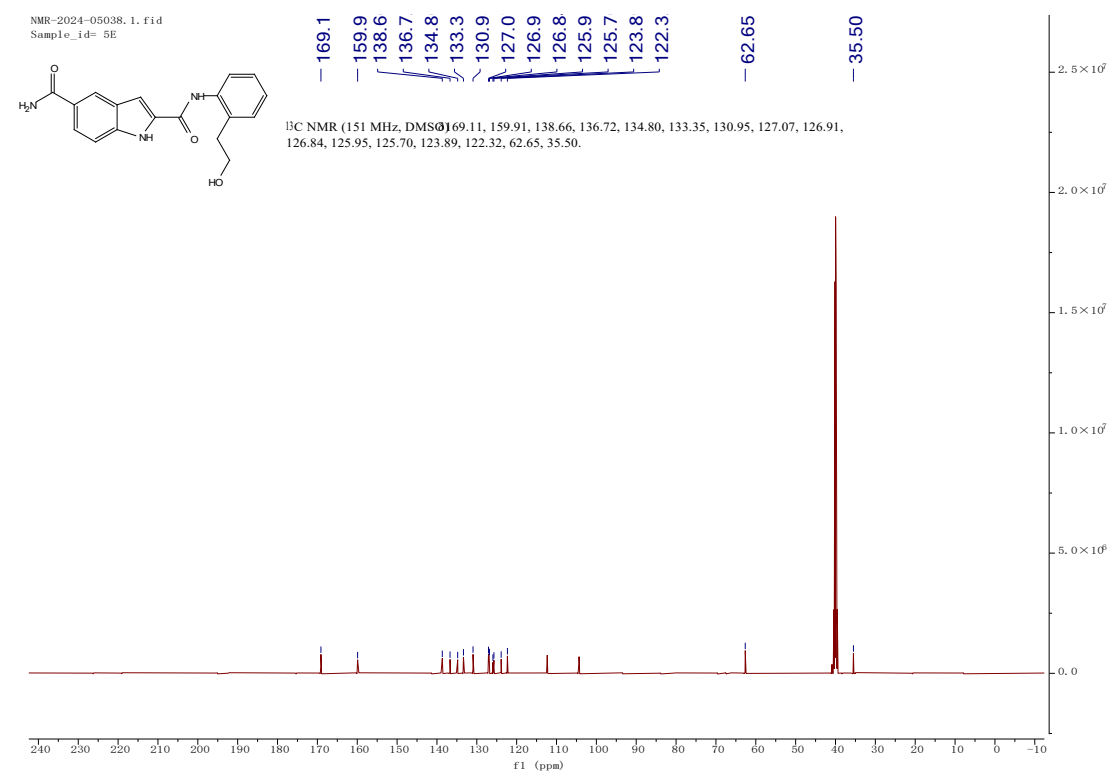


Figure 57. ¹³C NMR spectrum of compound A18

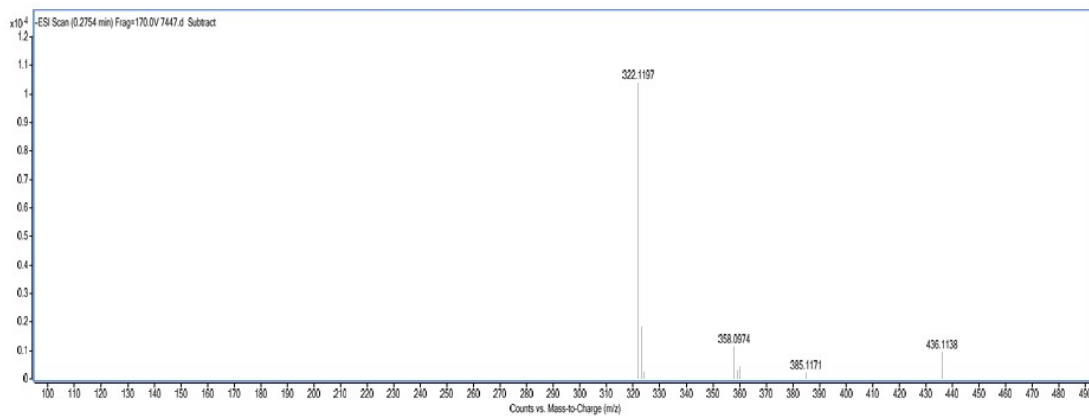


Figure 58. HRMS spectrum of compound A19

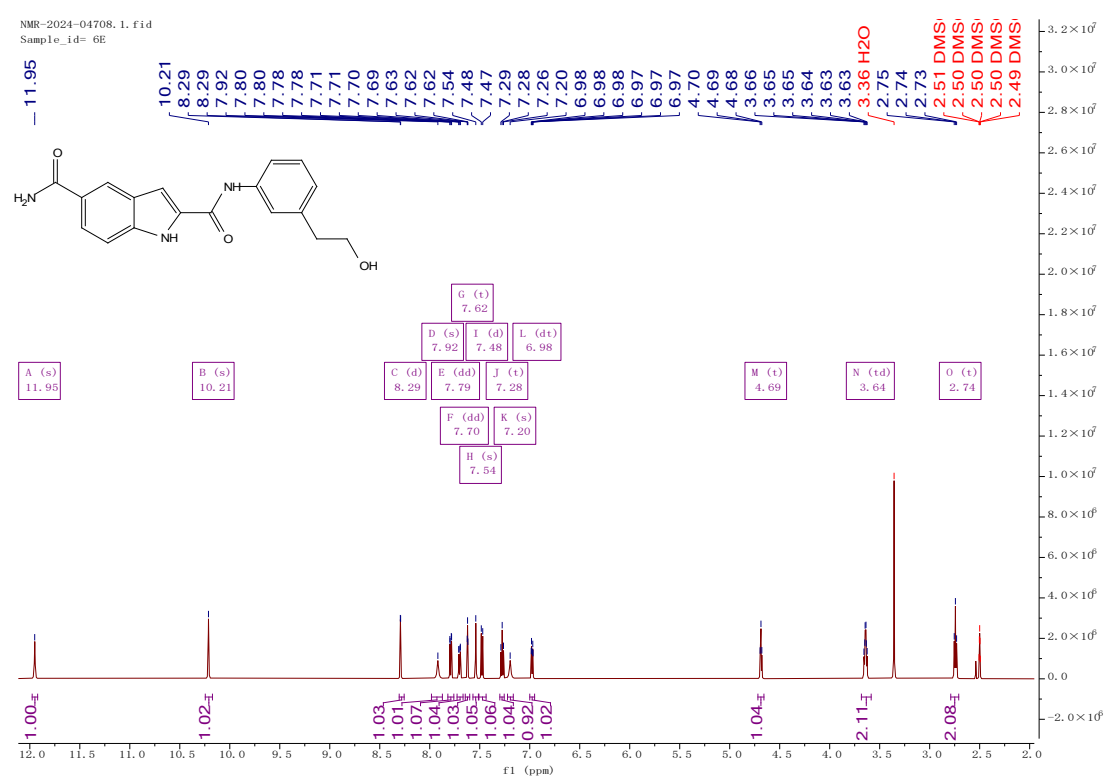


Figure 59. ¹H NMR spectrum of compound A19

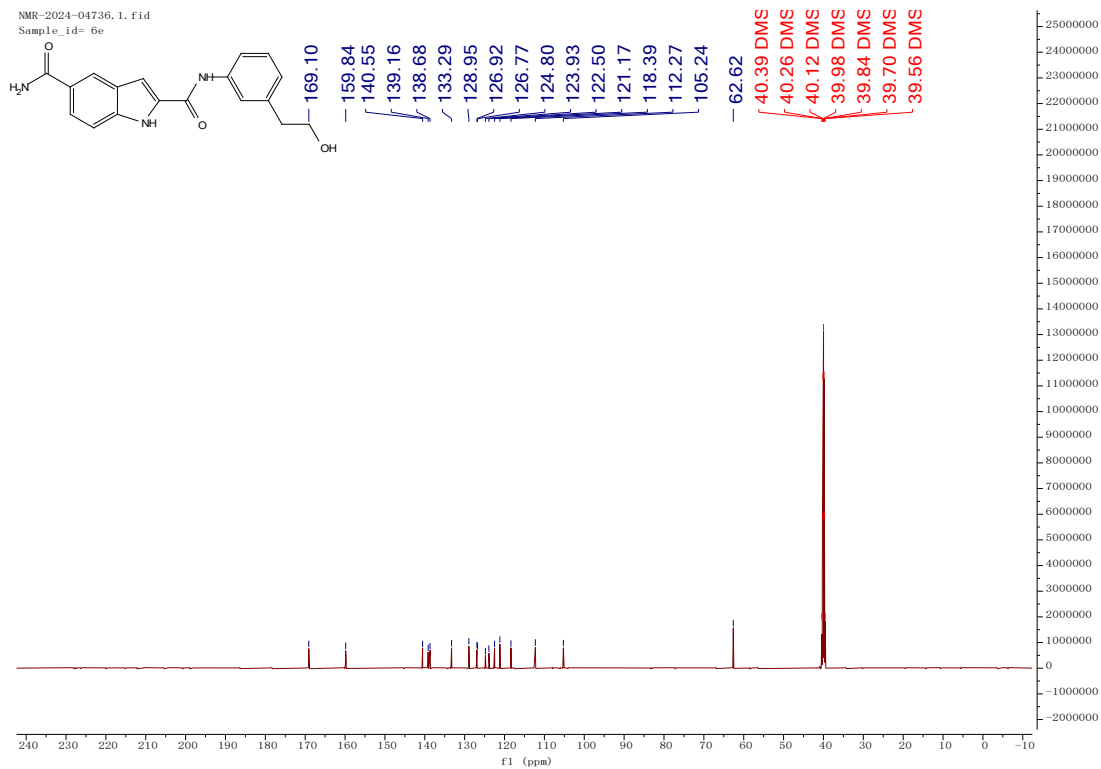


Figure 60. ^{13}C NMR spectrum of compound A19

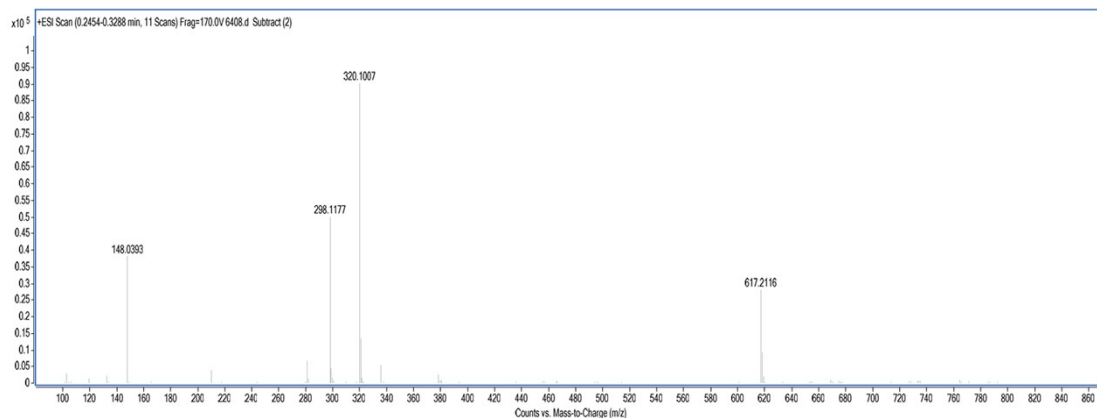


Figure 61. HRMS spectrum of compound B1

NMR-2024-06387.1.fid
Sample_id= 1b

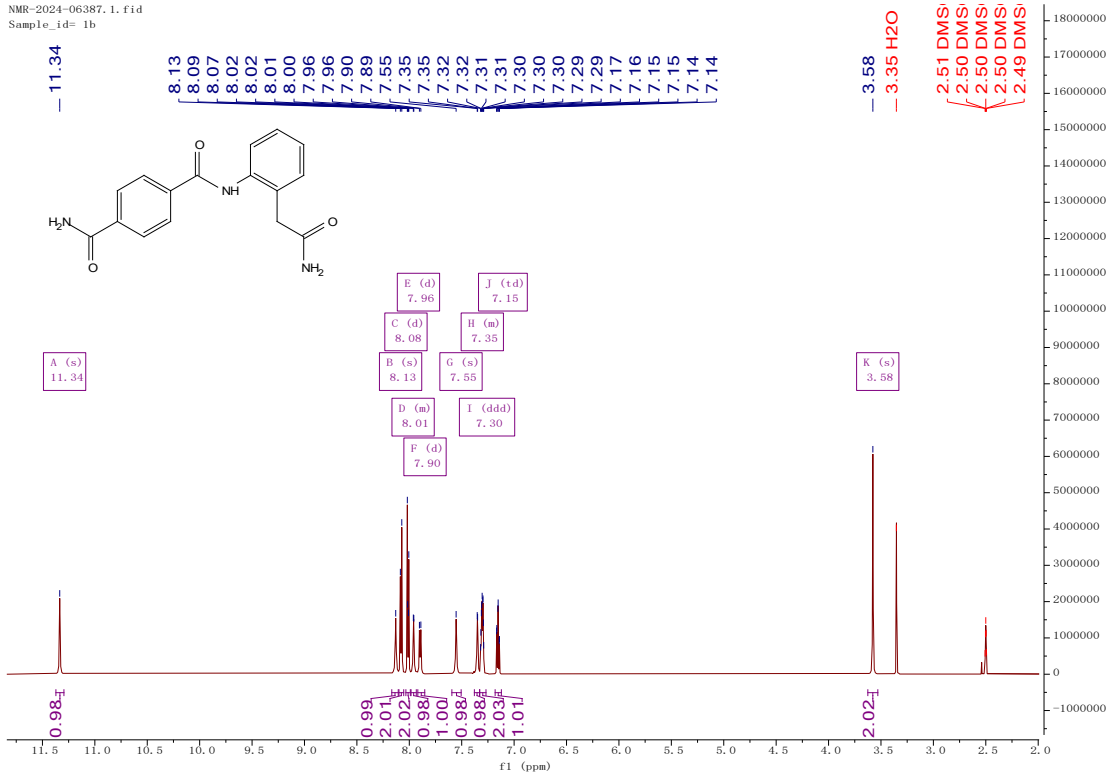


Figure 62. ¹H NMR spectrum of compound B1

NMR-2024-06454.1.fid
Sample_id= 1b

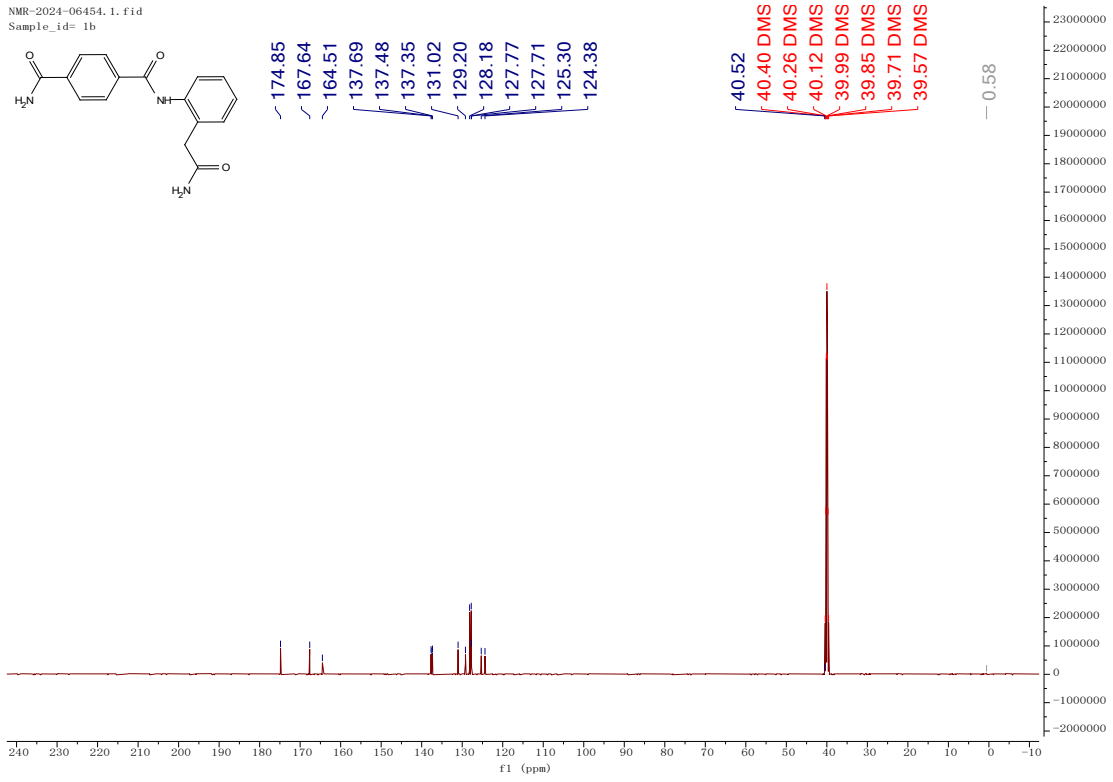


Figure 63. ¹³C NMR spectrum of compound B1

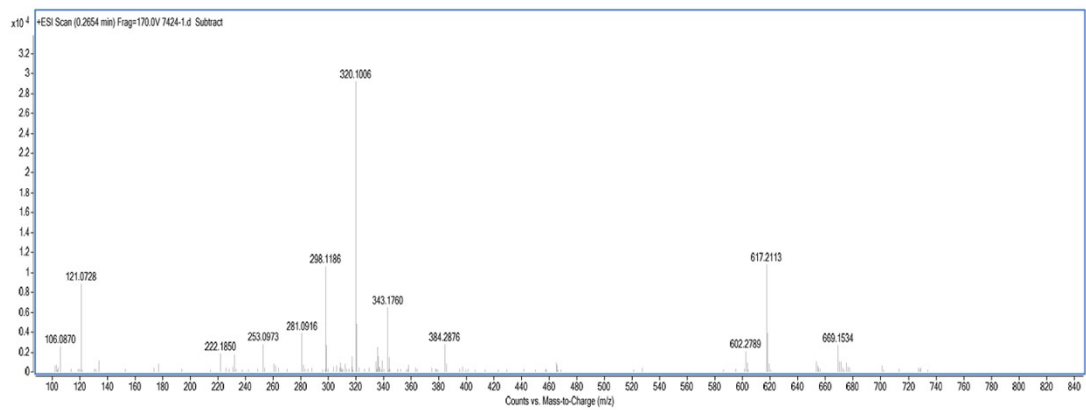


Figure 64. HRMS spectrum of compound B2

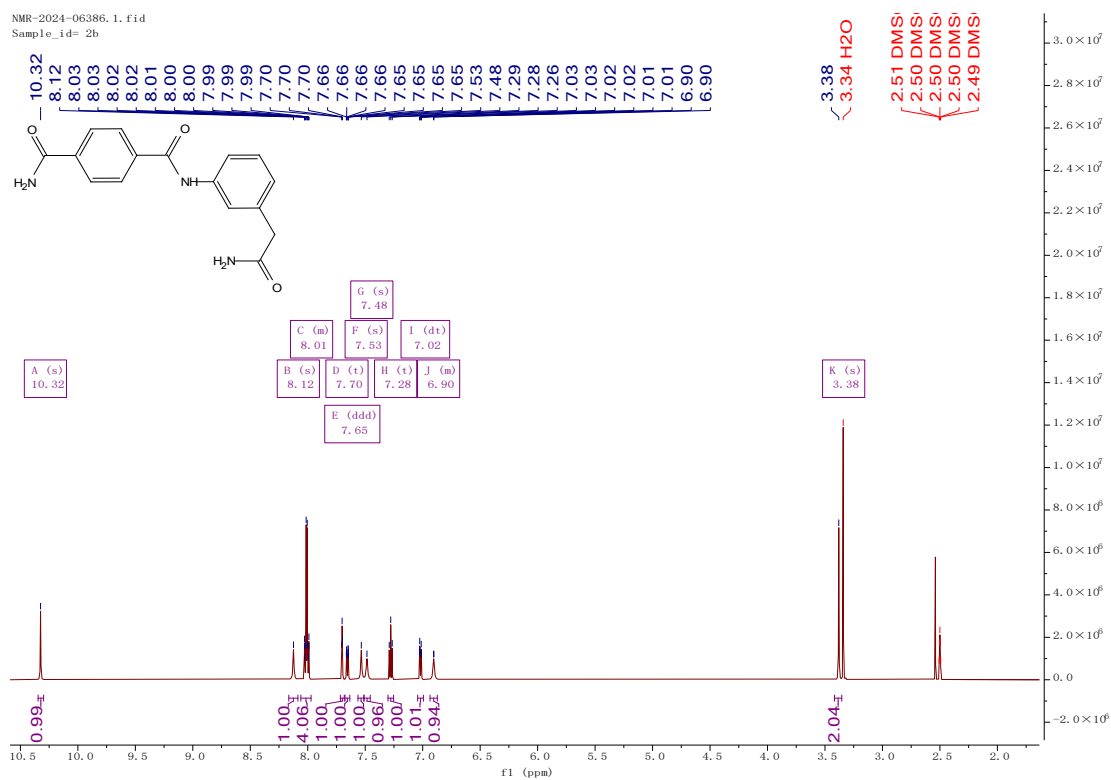


Figure 65. ¹H NMR spectrum of compound B2

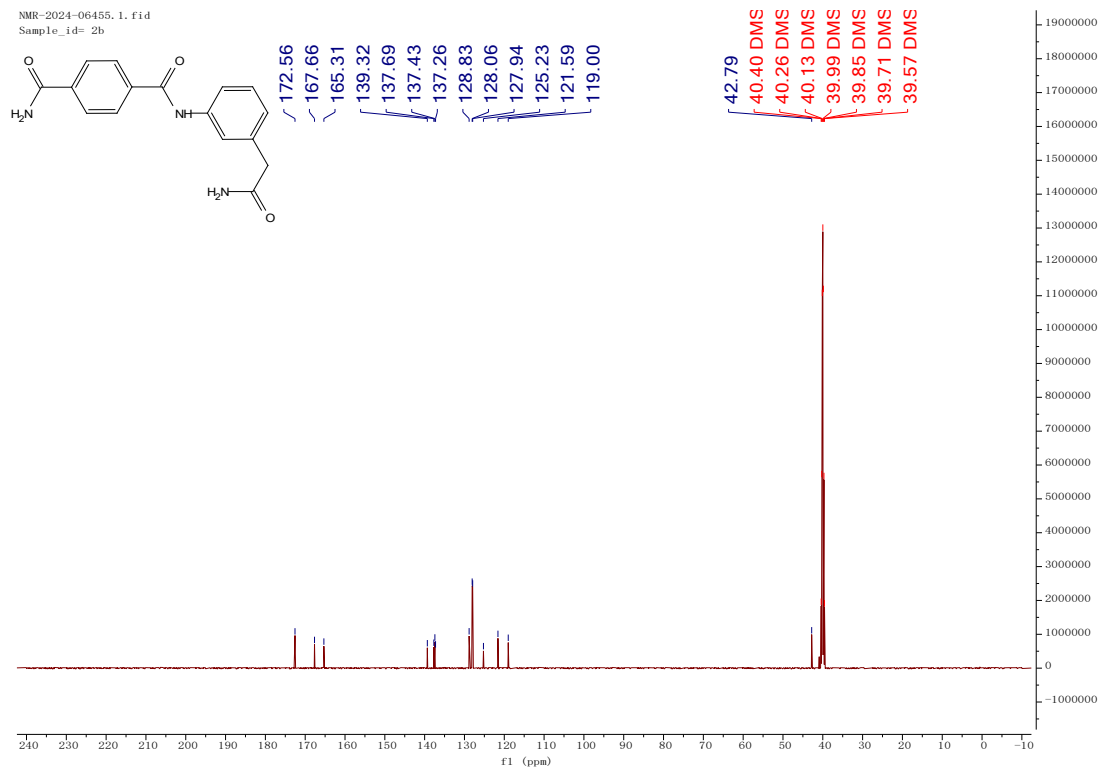


Figure 66. ^{13}C NMR spectrum of compound **B2**

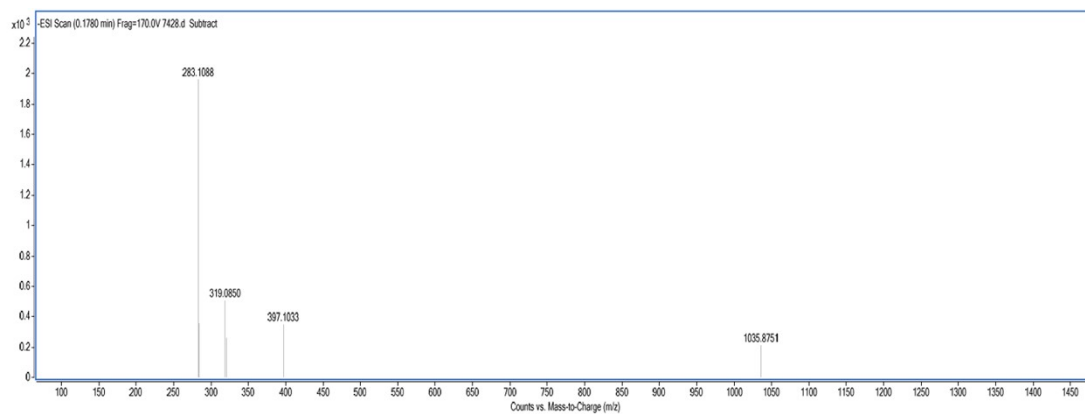


Figure 67. HRMS spectrum of compound **B3**

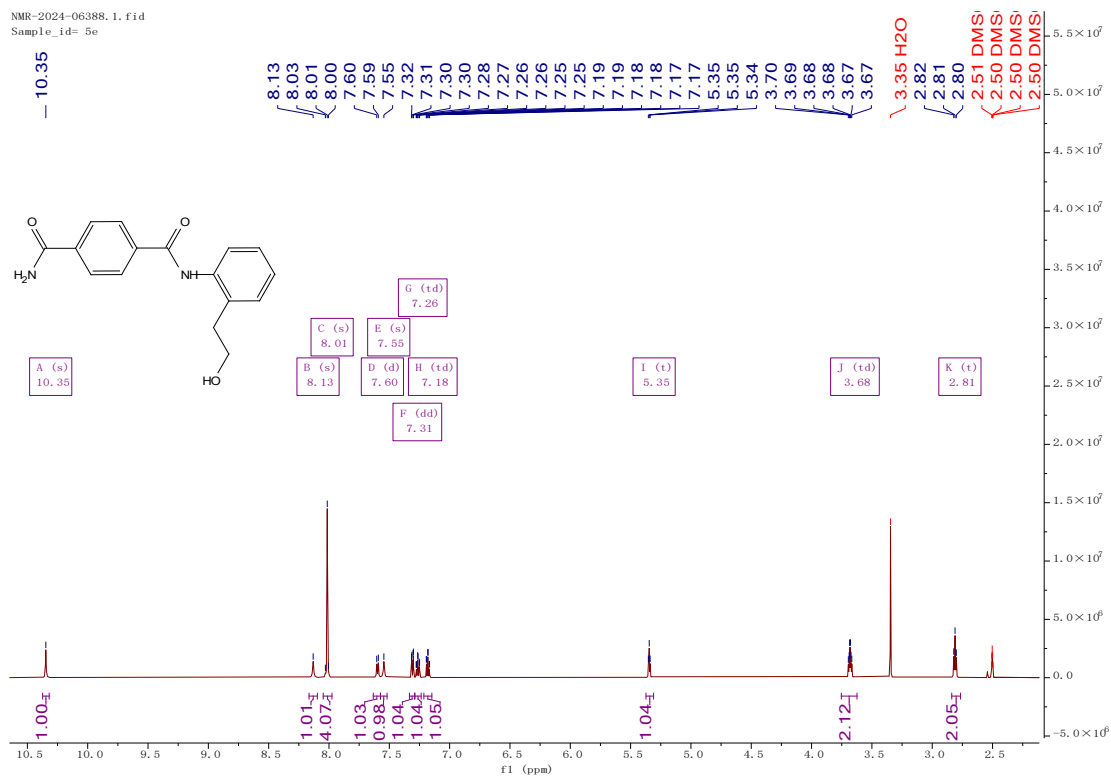


Figure 68. ^1H NMR spectrum of compound B3

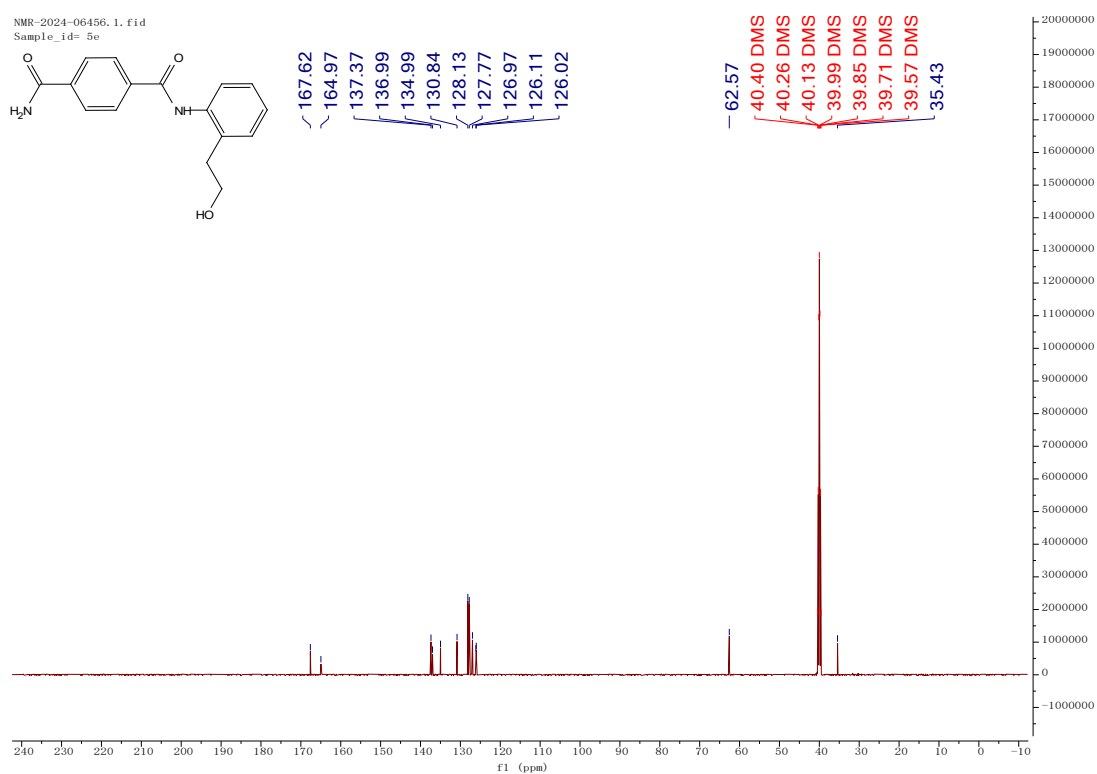


Figure 69. ^{13}C NMR spectrum of compound B3

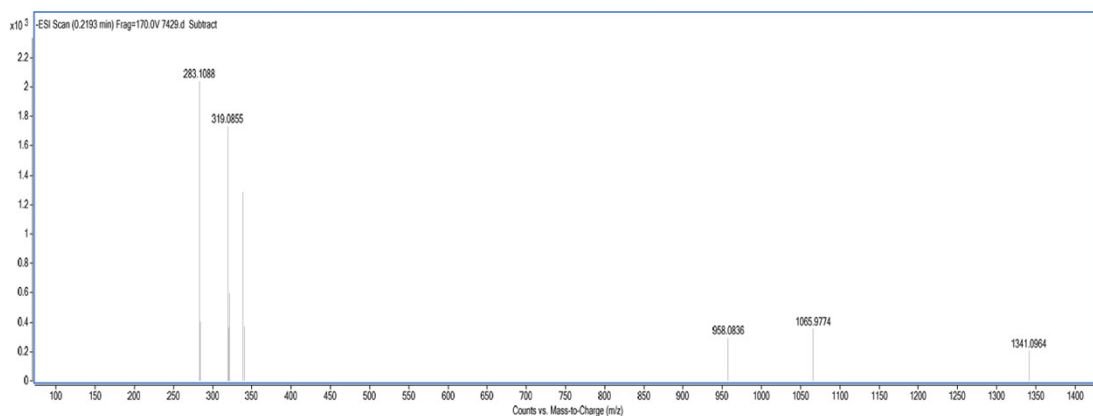


Figure 70. HRMS spectrum of compound B4

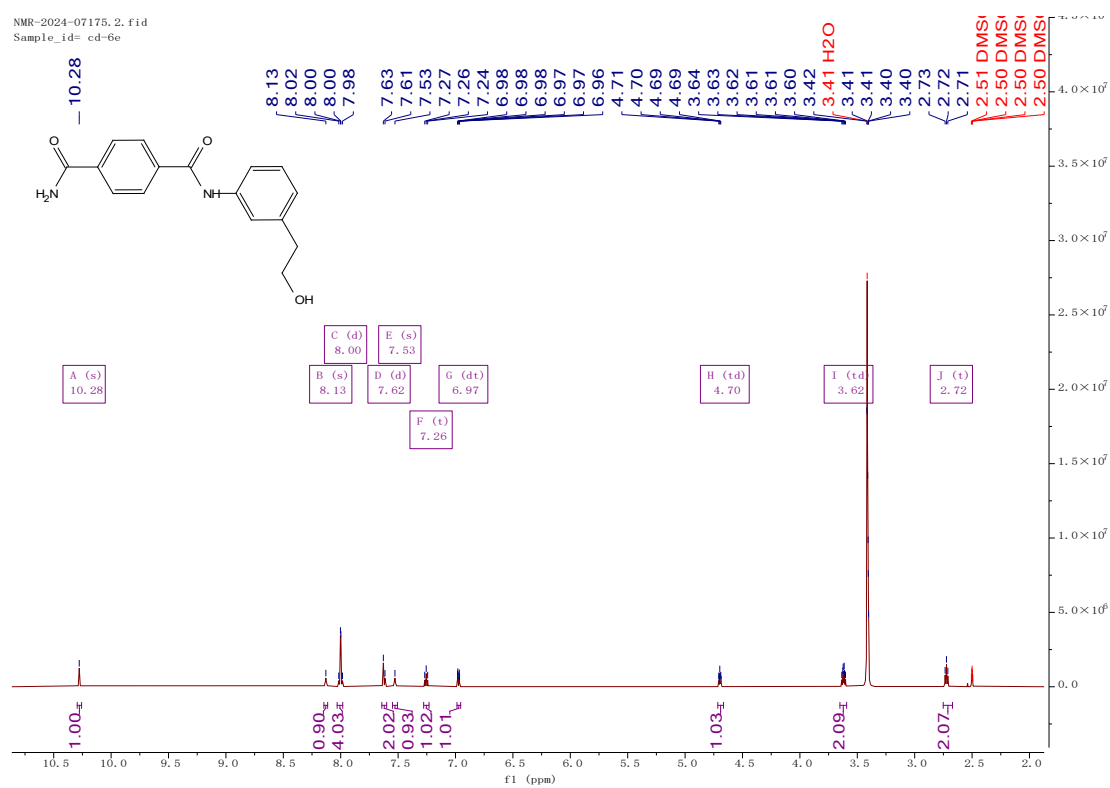


Figure 71. ¹H NMR spectrum of compound B4

NMR-2024-07220.1.fid
Sample_id= cd-6e

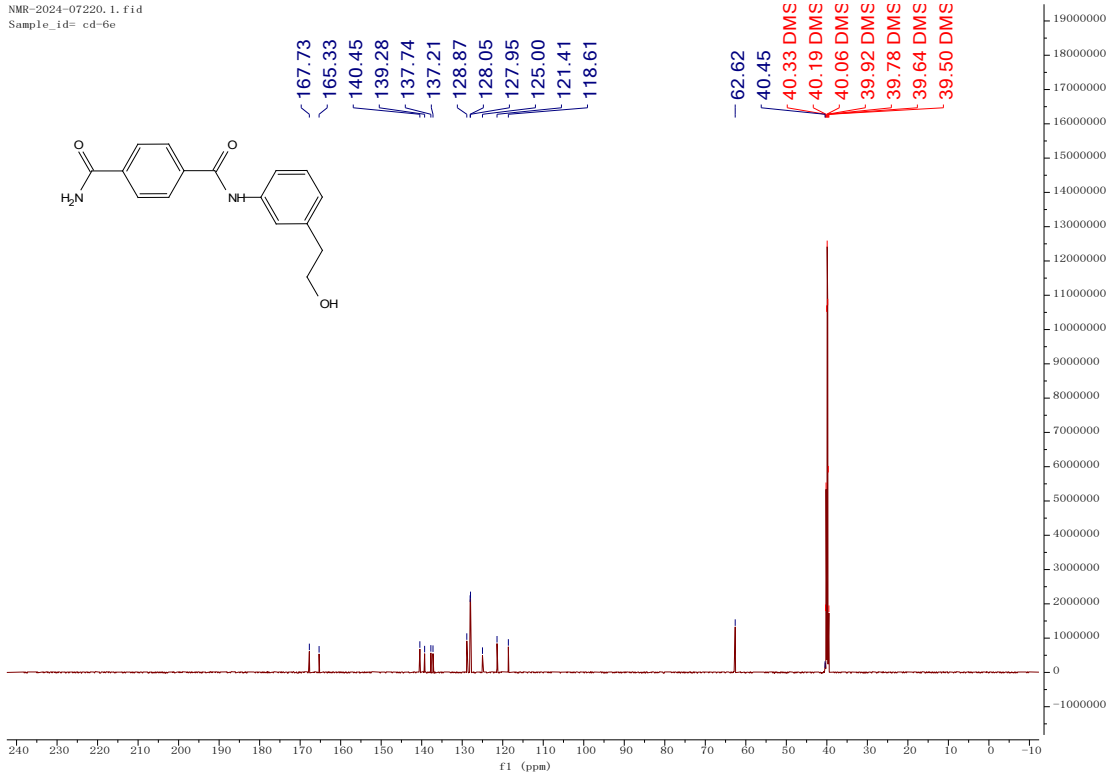


Figure 72. ¹³C NMR spectrum of compound B4

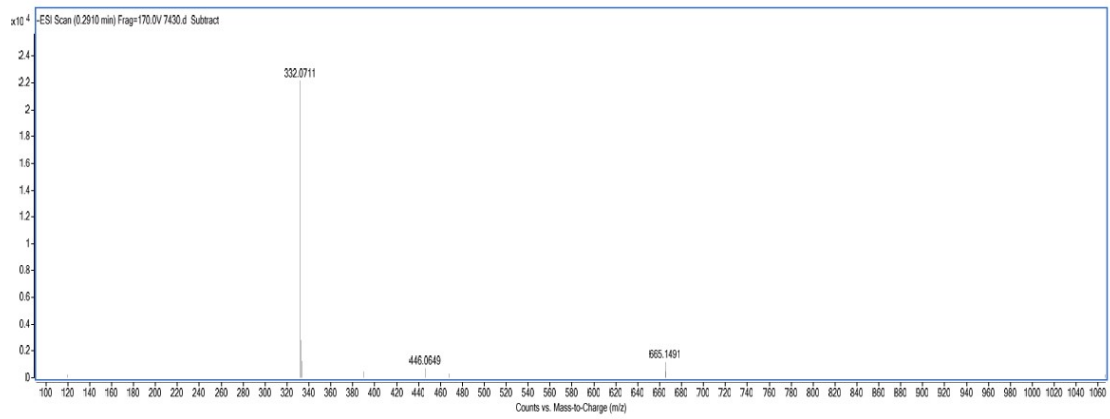


Figure 73. HRMS spectrum of compound B5

NMR-2024-07270.1.fid
Sample_id= cd-5a



Figure 74. ^1H NMR spectrum of compound B5

NMR-2024-07402.1.fid
Sample_id= cd-5a

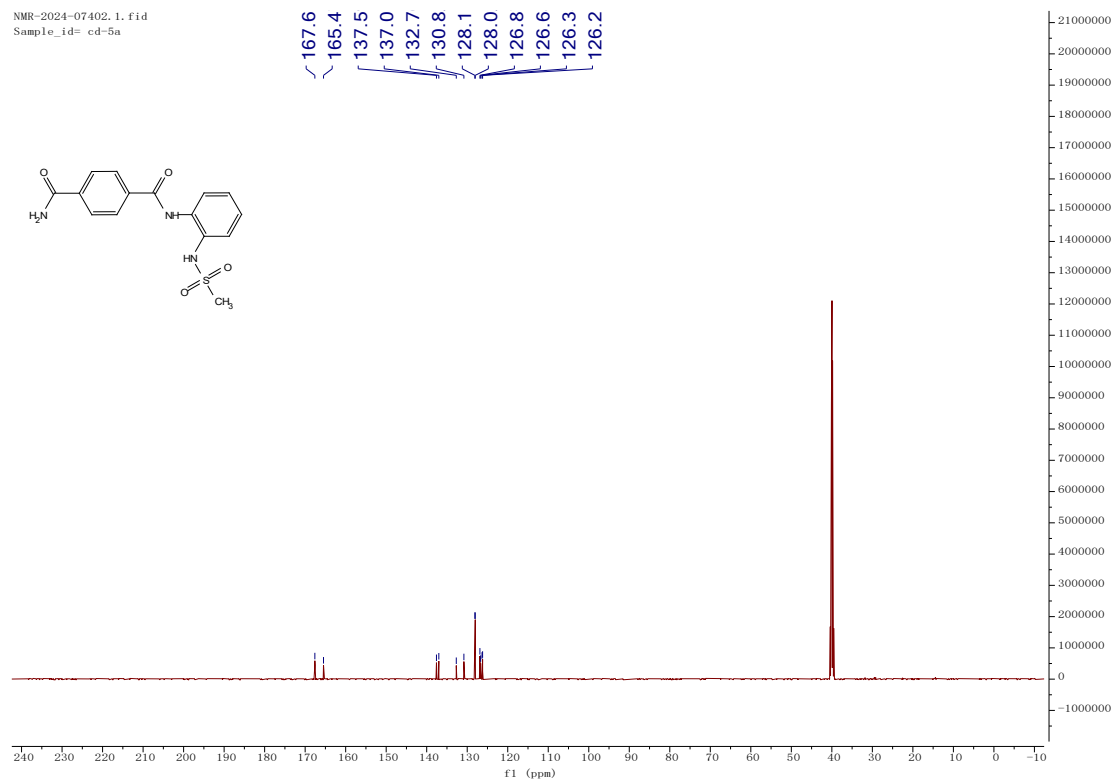


Figure 75. ^{13}C NMR spectrum of compound B5

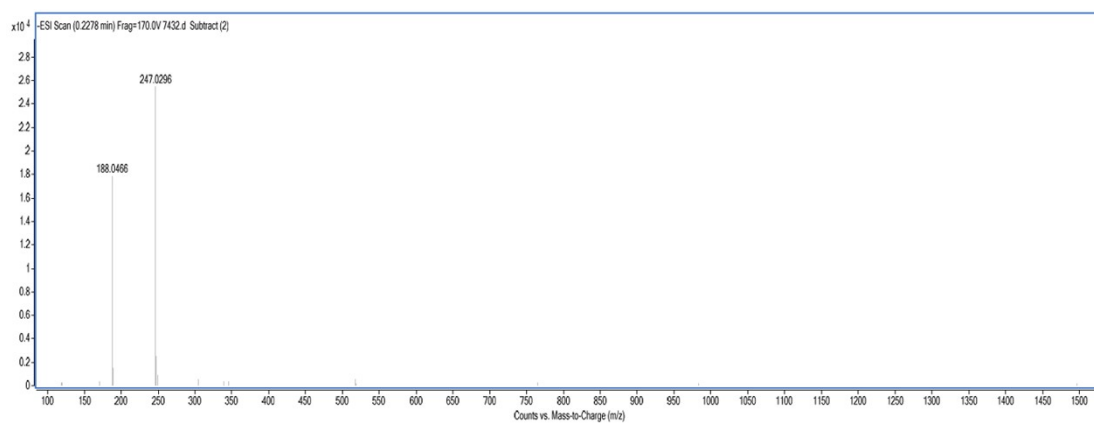


Figure 76. HRMS spectrum of compound **B6**

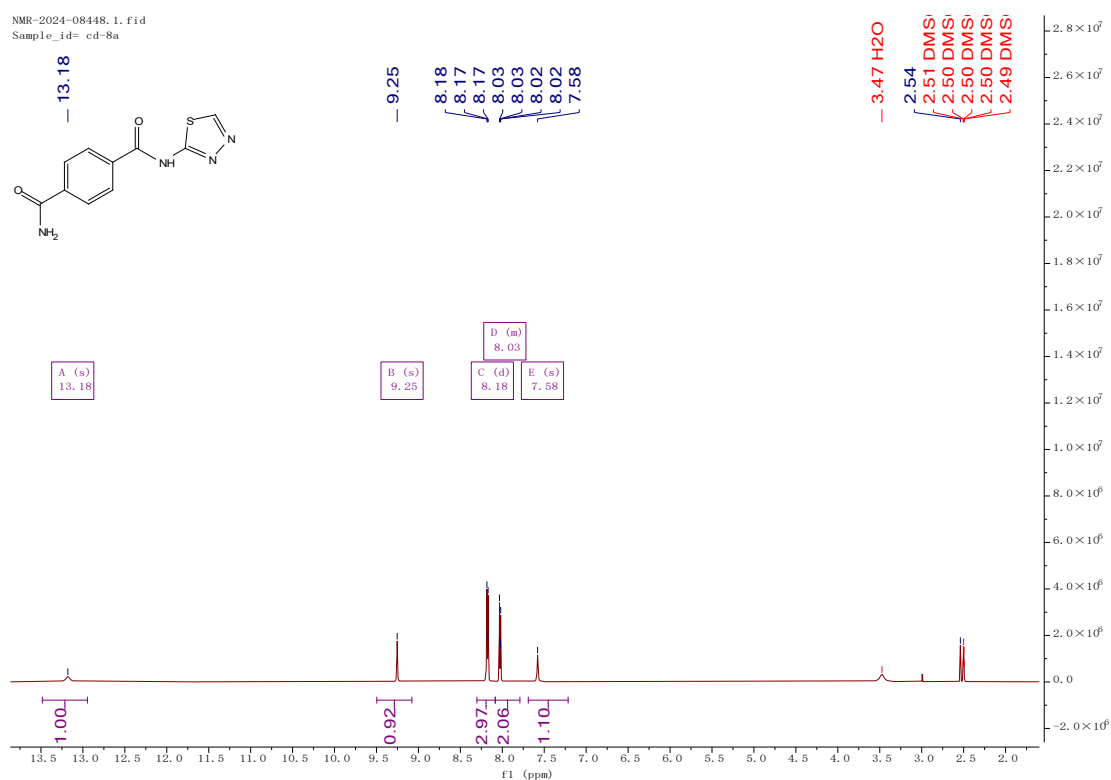


Figure 77. ¹H NMR spectrum of compound **B6**



Figure 78. ^{13}C NMR spectrum of compound **B6**

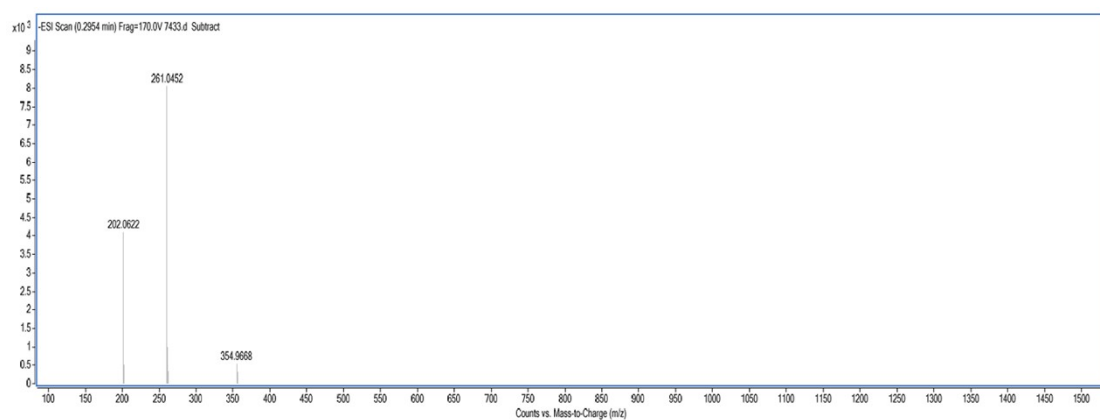


Figure 79. HRMS spectrum of compound **B7**

NMR-2024-08241.1.fid
Sample_id= cd-9a

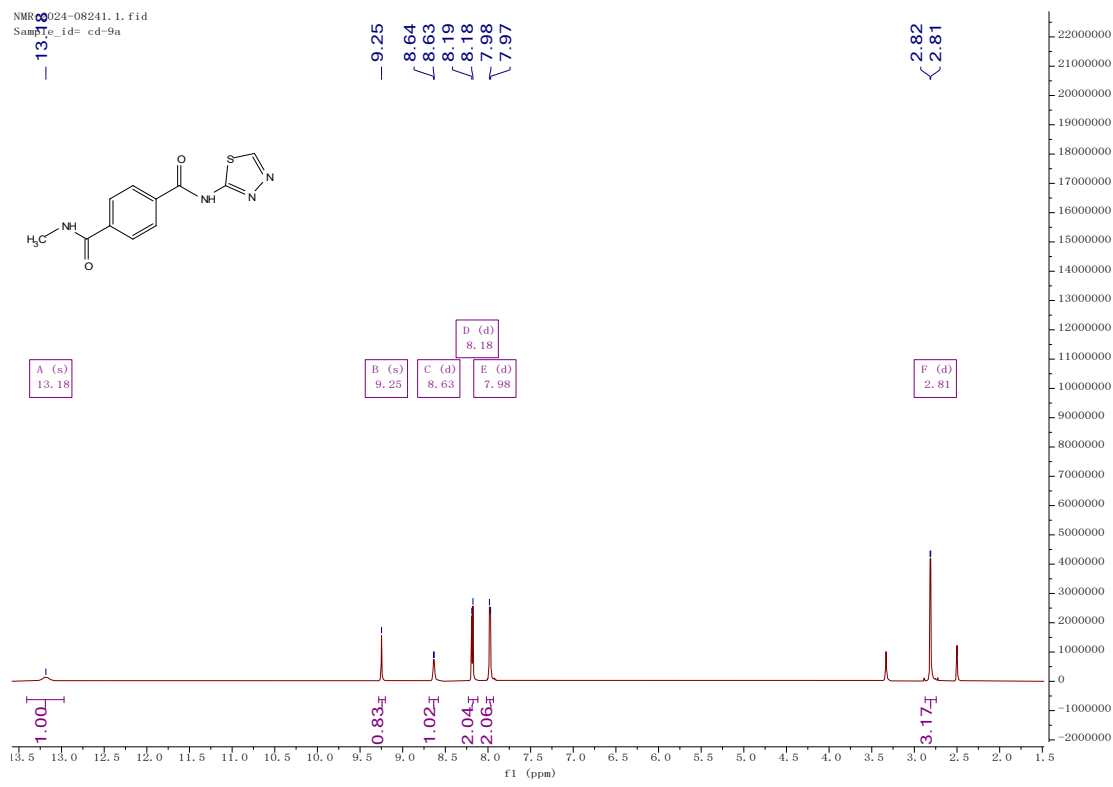


Figure 80. ¹H NMR spectrum of compound B7

NMR-2024-08317.1.fid
Sample_id= cd-9a

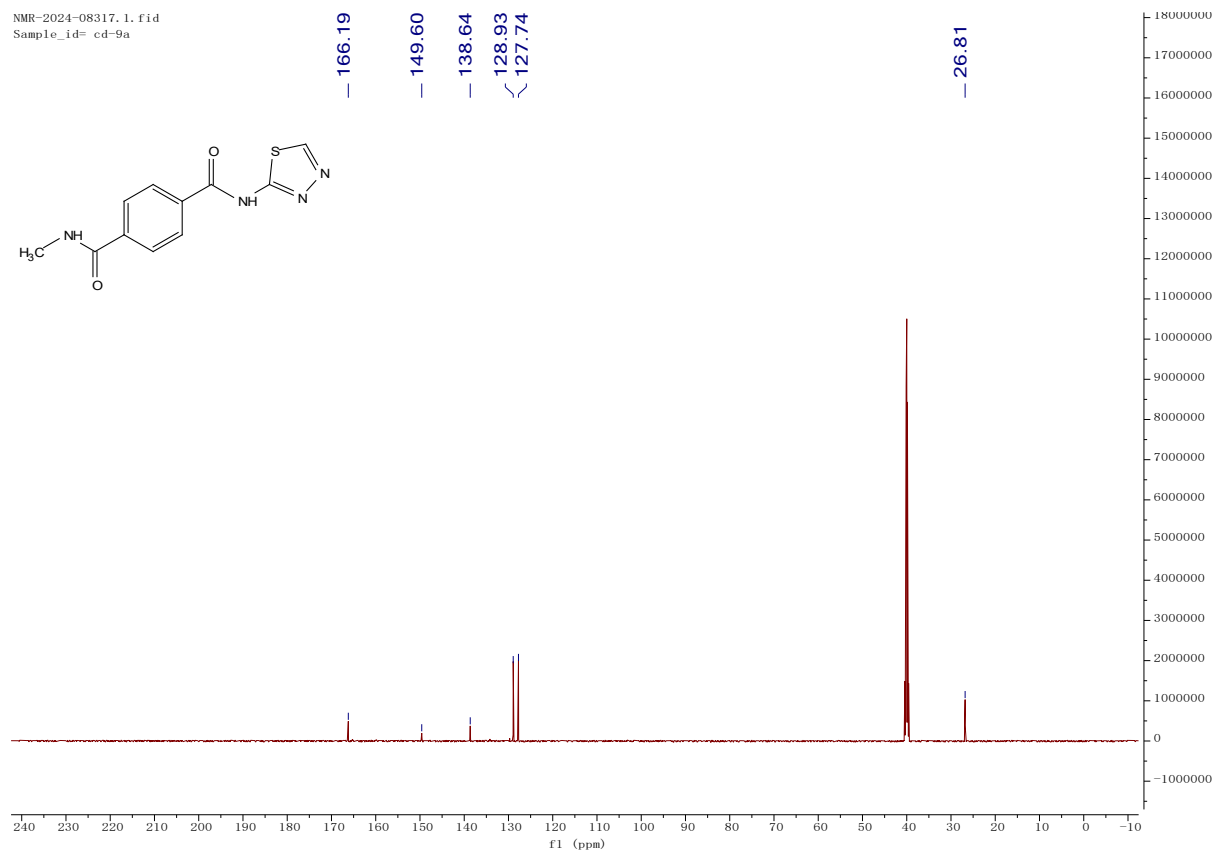


Figure 81. ^{13}C NMR spectrum of compound **B7**

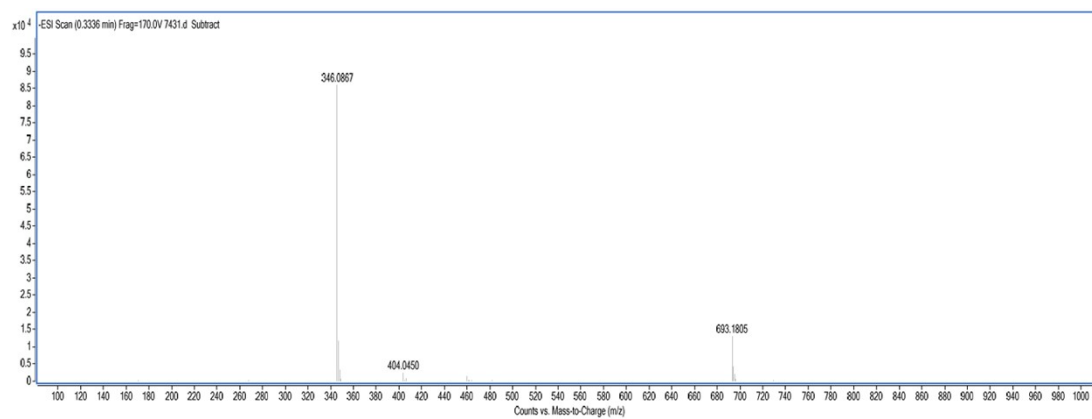


Figure 82. HRMS spectrum of compound **B8**

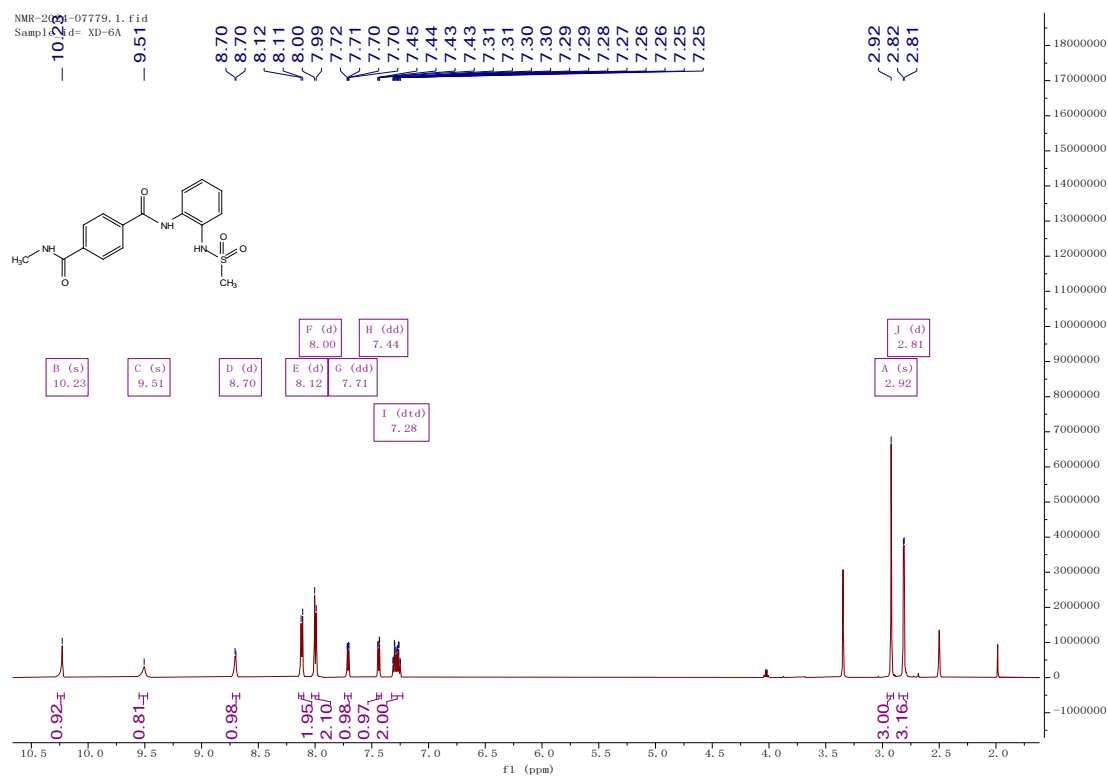


Figure 83. ^1H NMR spectrum of compound **B8**

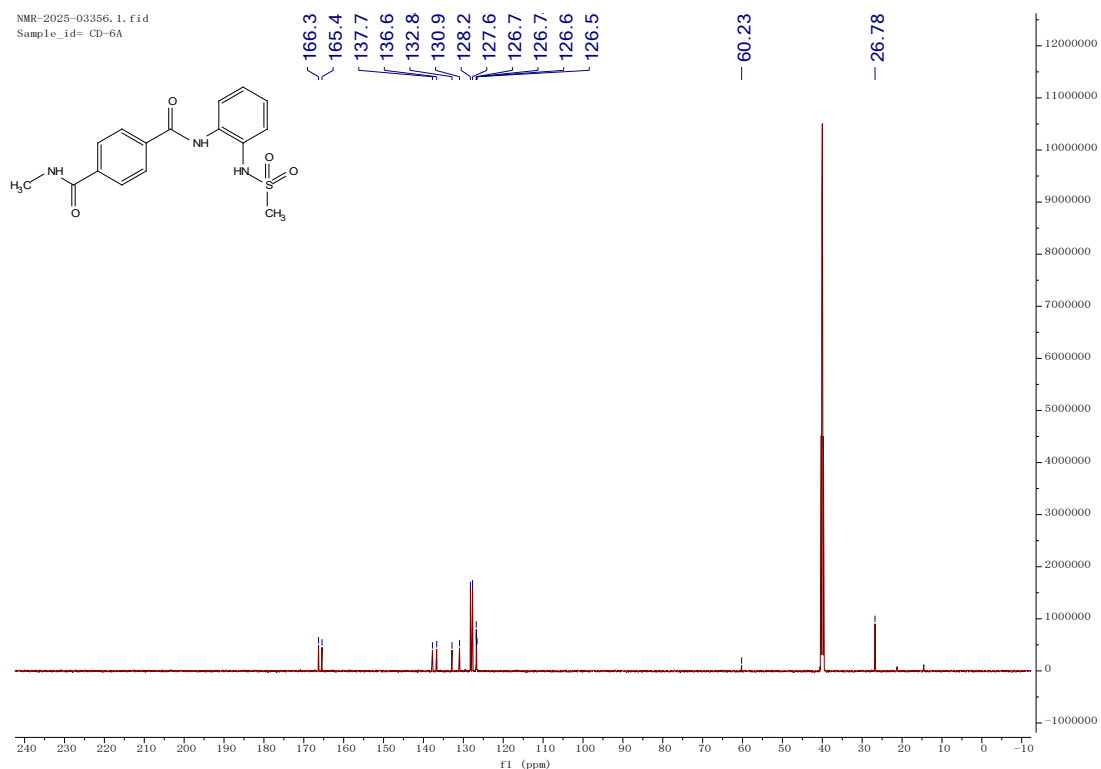


Figure 84. ^{13}C NMR spectrum of compound **B8**

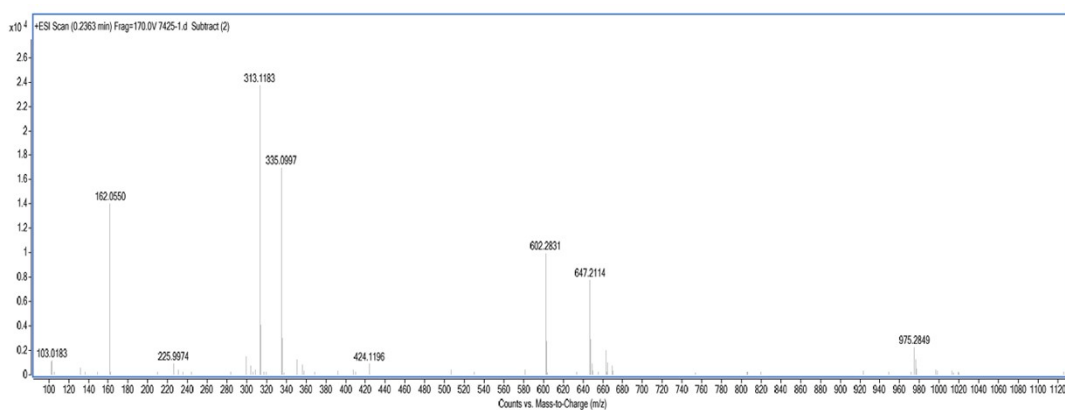


Figure 85. HRMS spectrum of compound **B9**

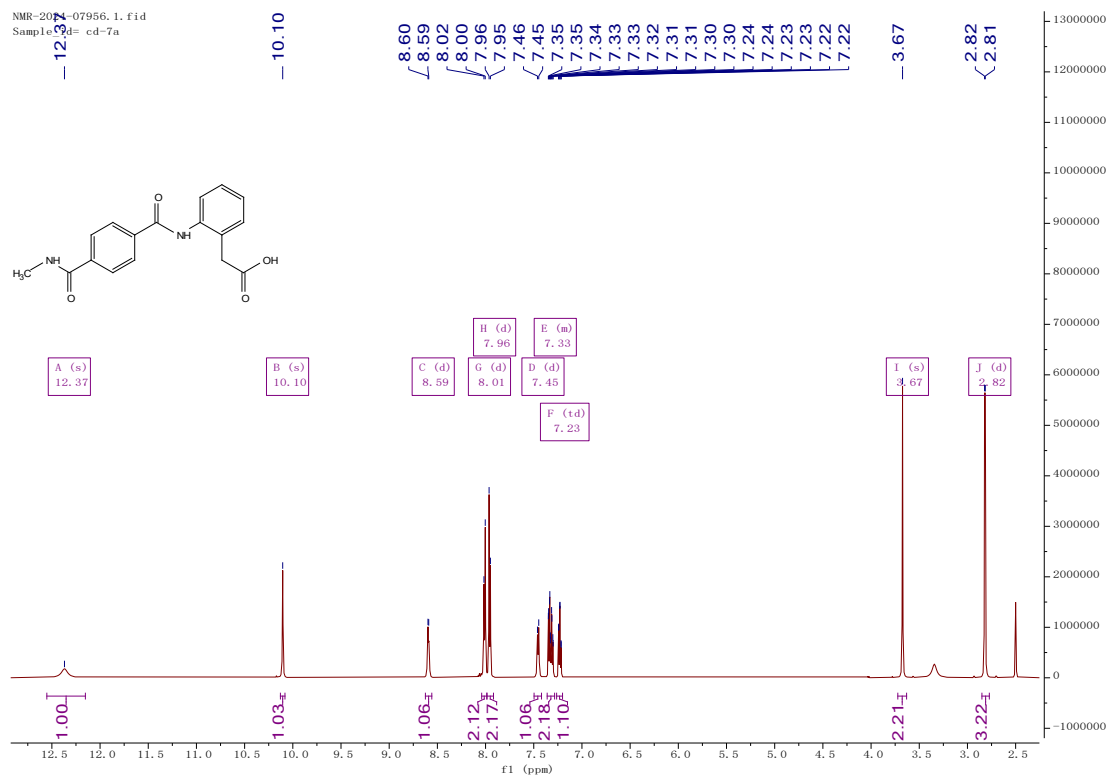


Figure 86. ¹H NMR spectrum of compound B9

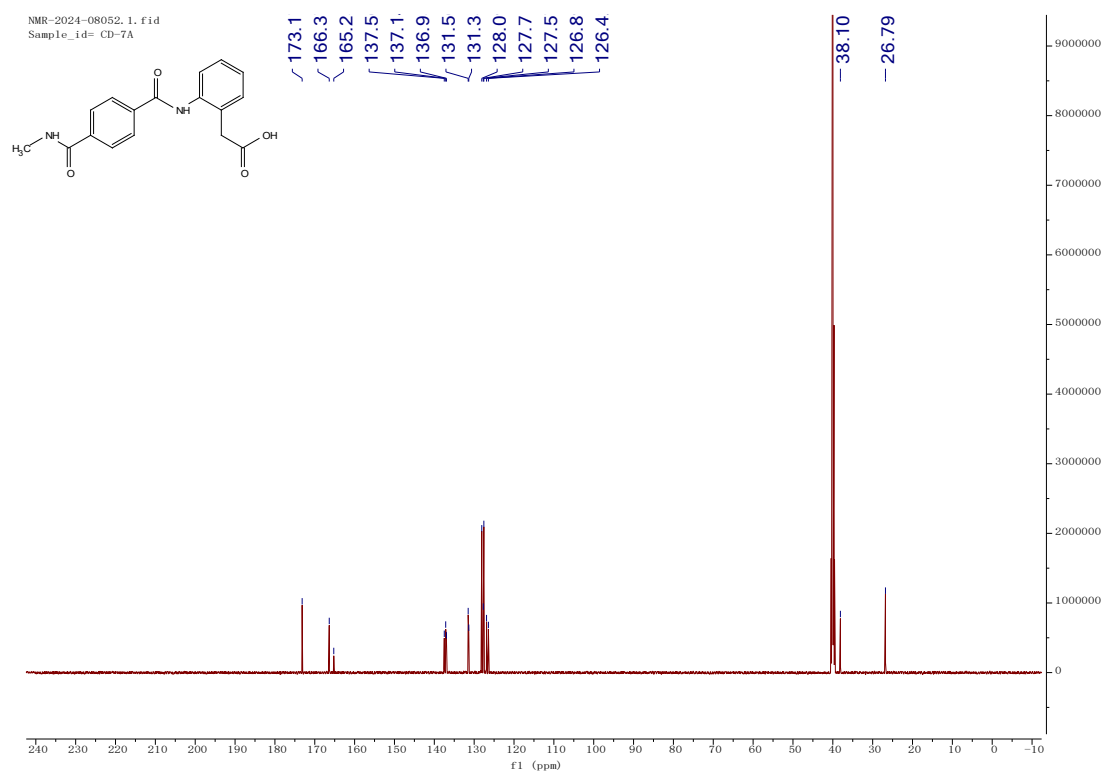


Figure 87. ¹³C NMR spectrum of compound B9

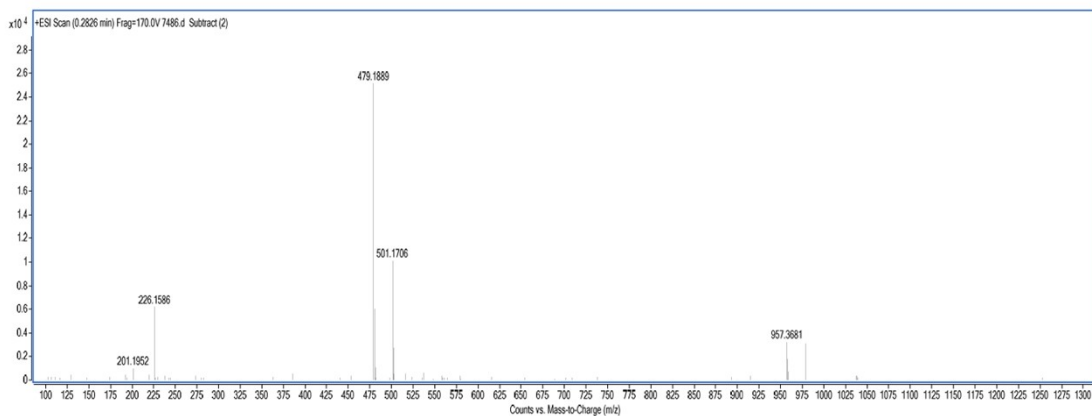


Figure 88. HRMS spectrum of compound C1

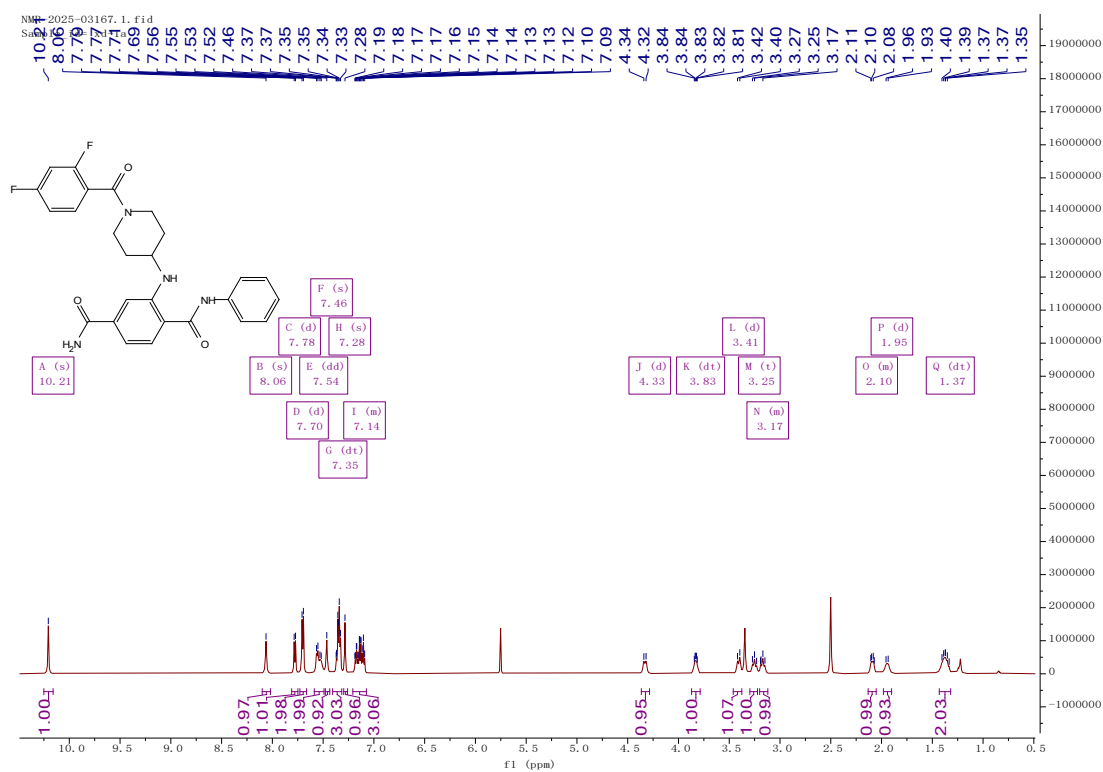


Figure 89. ¹H NMR spectrum of compound C1

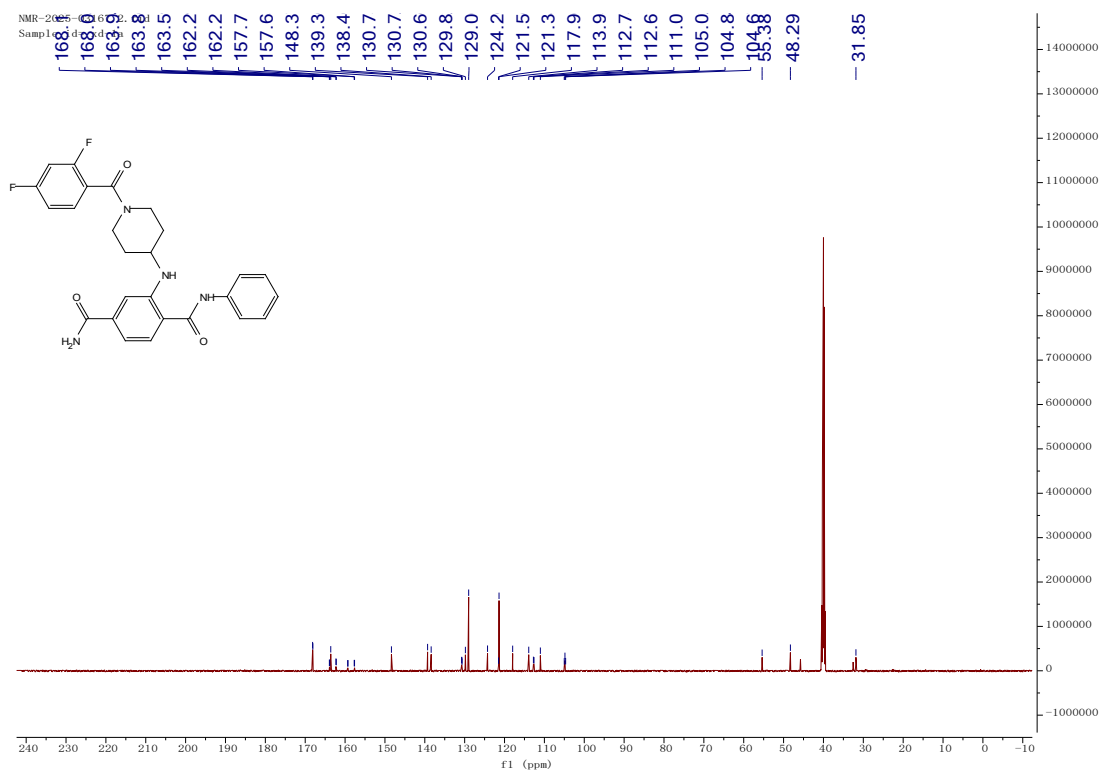


Figure 90. ¹³C NMR spectrum of compound C1

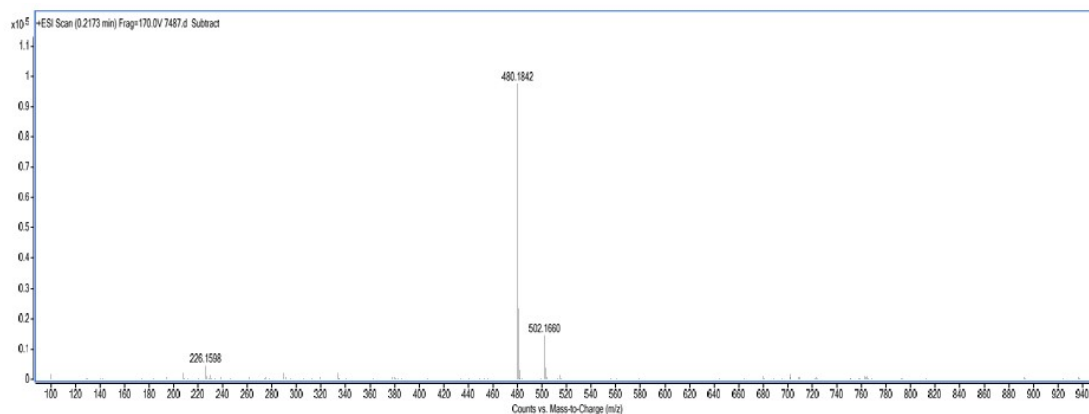


Figure 91. HRMS spectrum of compound C2

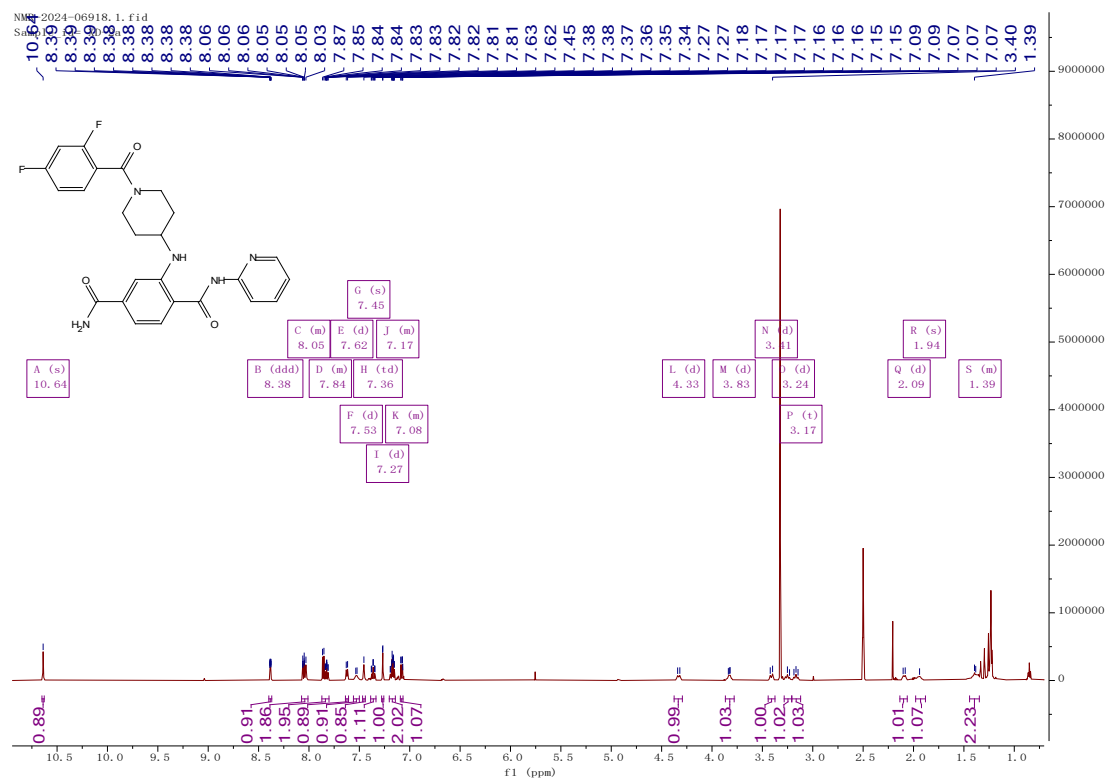


Figure 92. ¹H NMR spectrum of compound C2

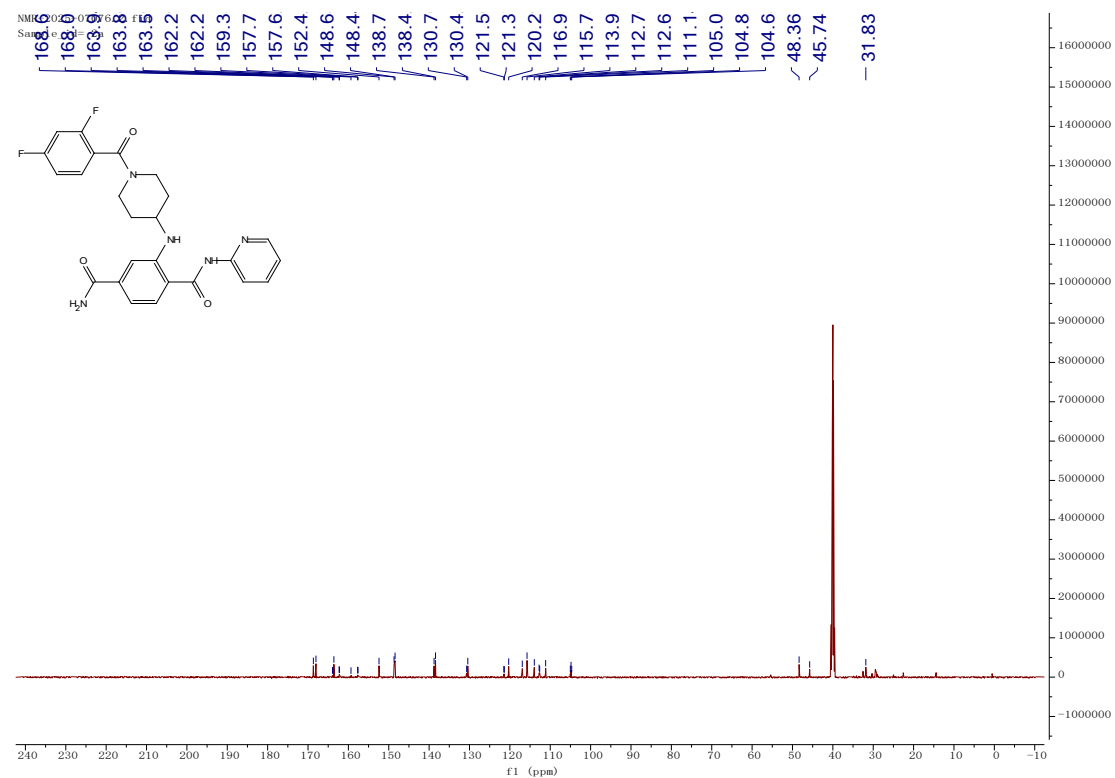


Figure 93. ¹³C NMR spectrum of compound C2

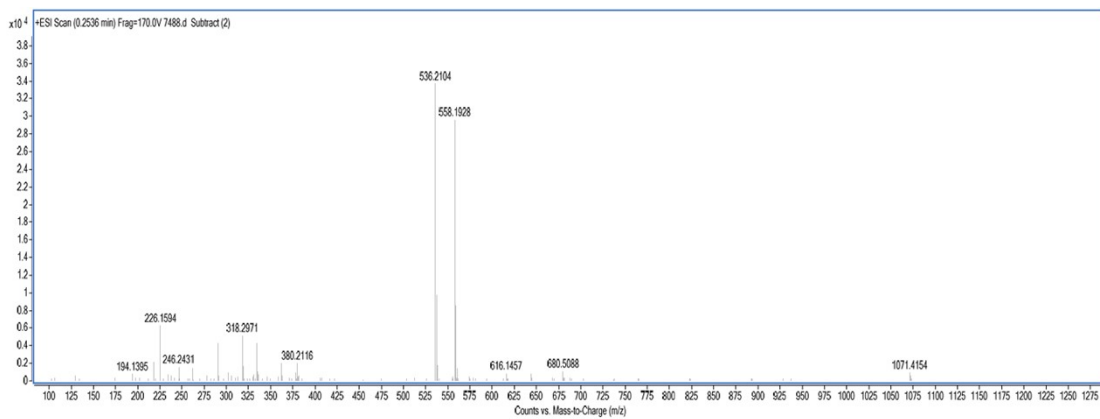


Figure 94. HRMS spectrum of compound C3

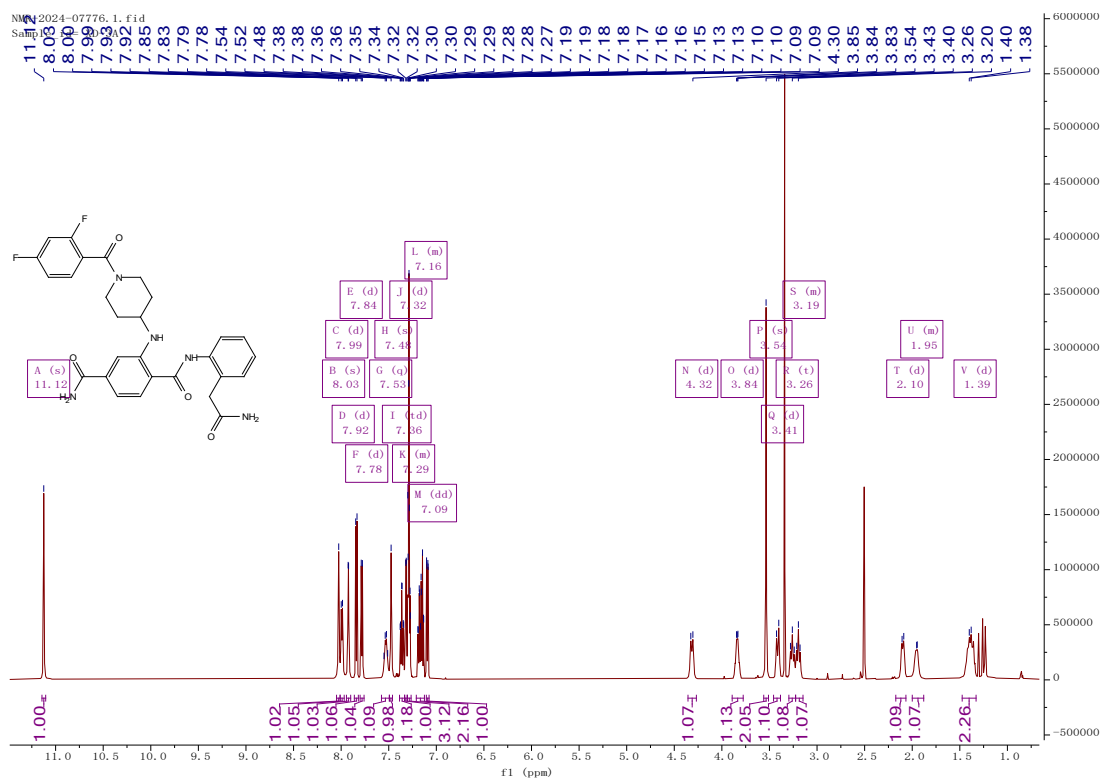


Figure 95. ¹H NMR spectrum of compound C3

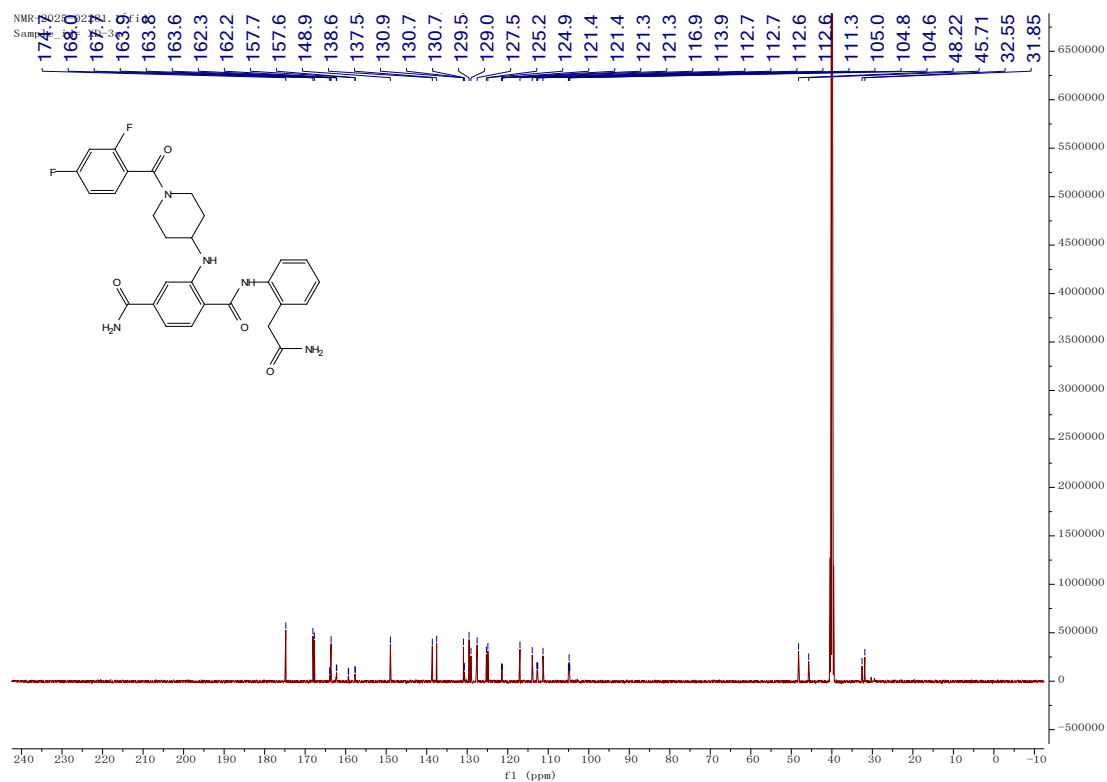


Figure 96. ^{13}C NMR spectrum of compound C3

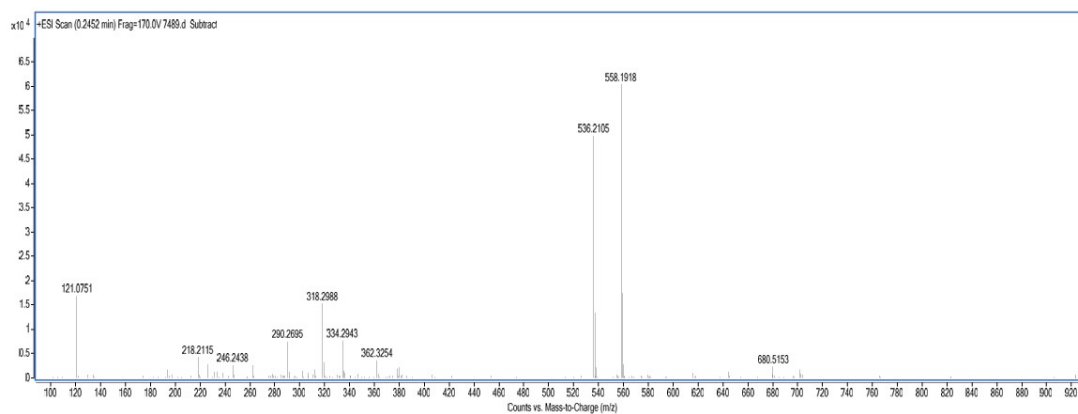


Figure 97. HRMS spectrum of compound C4



Figure 98. ¹H NMR spectrum of compound C4

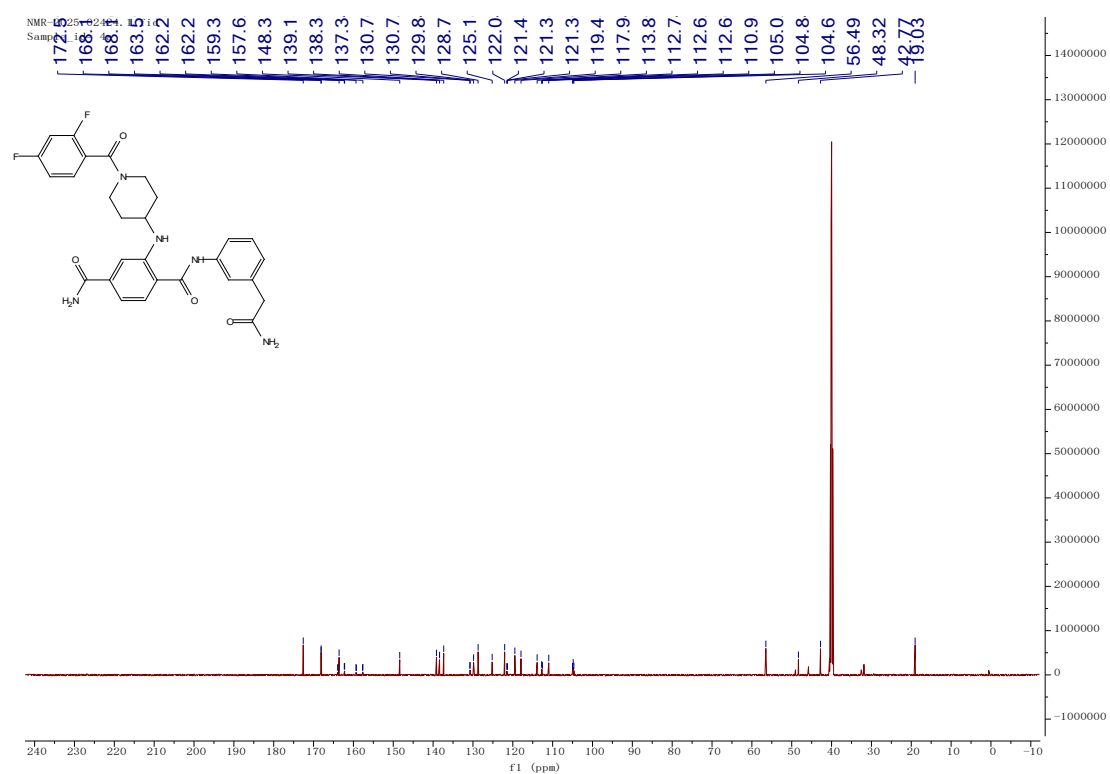


Figure 99. ¹³C NMR spectrum of compound C4

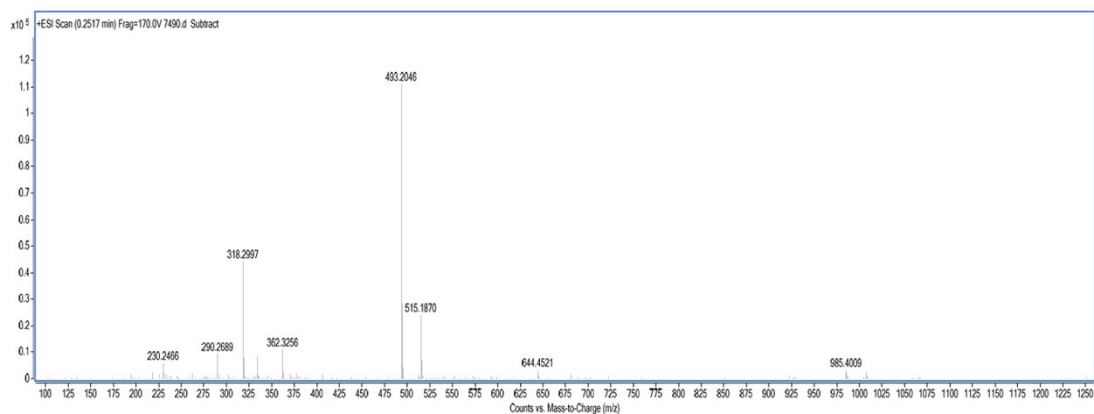


Figure 100. HRMS spectrum of compound C5

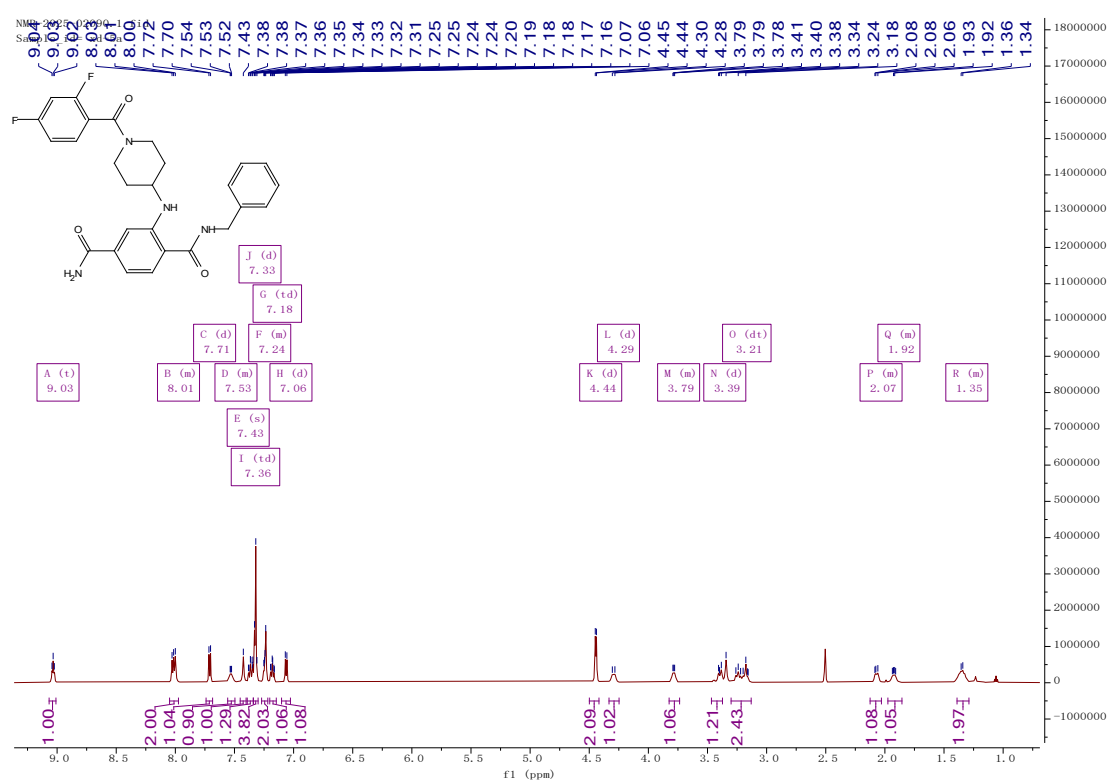


Figure 101. ¹H NMR spectrum of compound C5

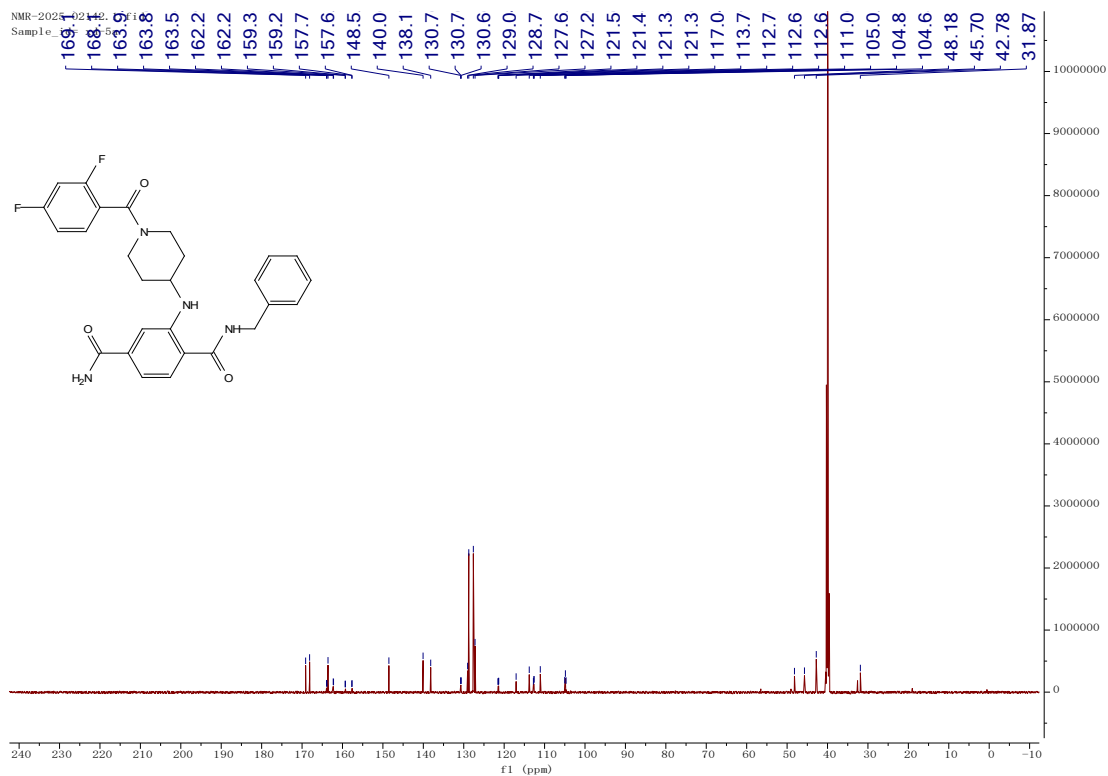


Figure 102. ^{13}C NMR spectrum of compound C5

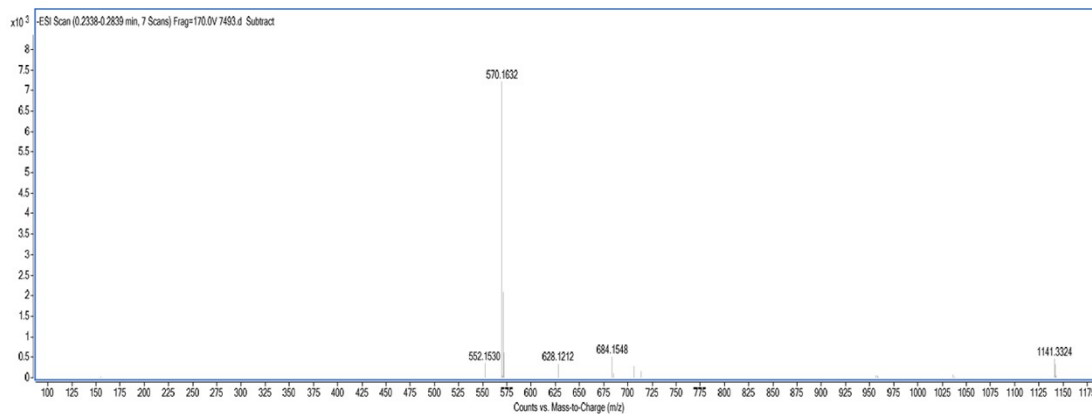


Figure 103. HRMS spectrum of compound C6

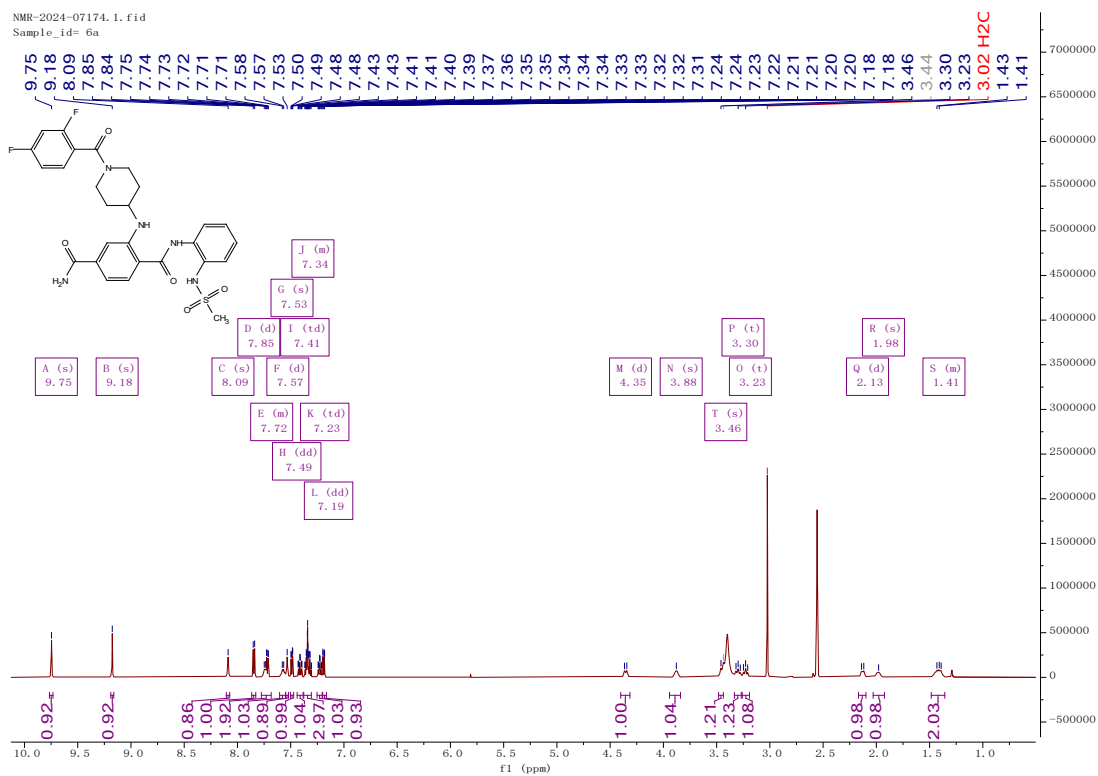


Figure 104. ^1H NMR spectrum of compound C6

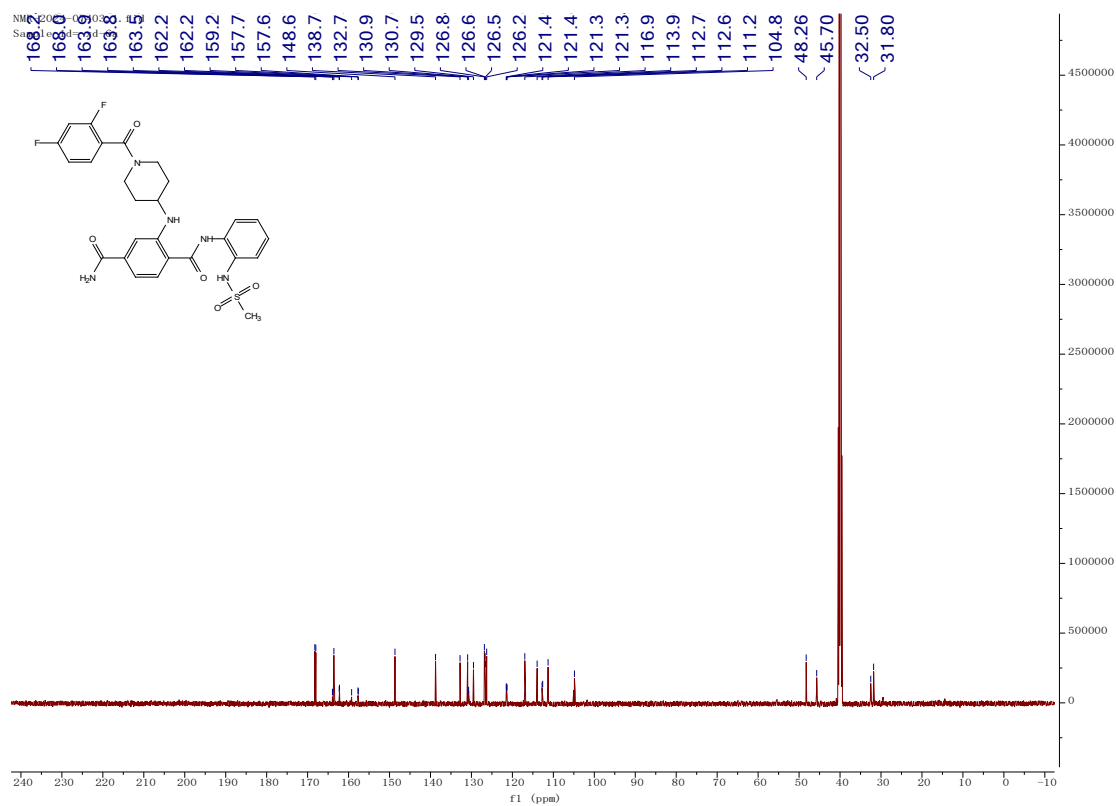


Figure 105. ^{13}C NMR spectrum of compound C6

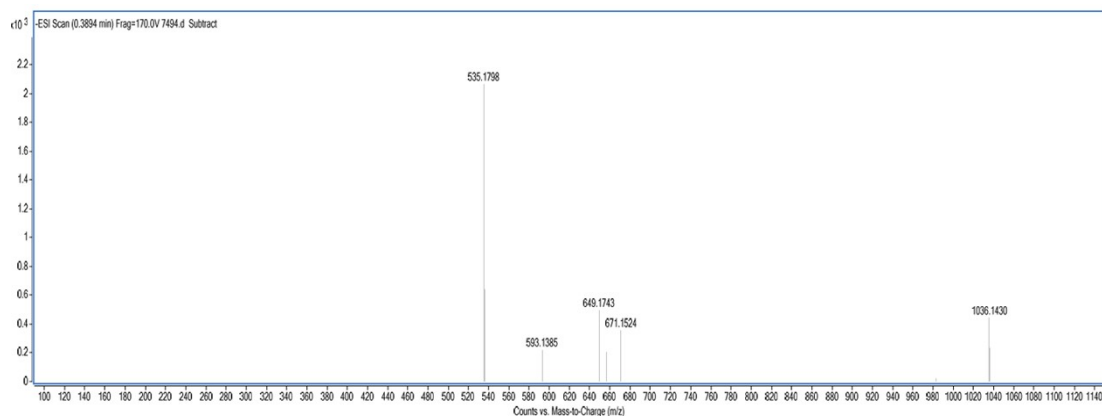


Figure 106. HRMS spectrum of compound C7

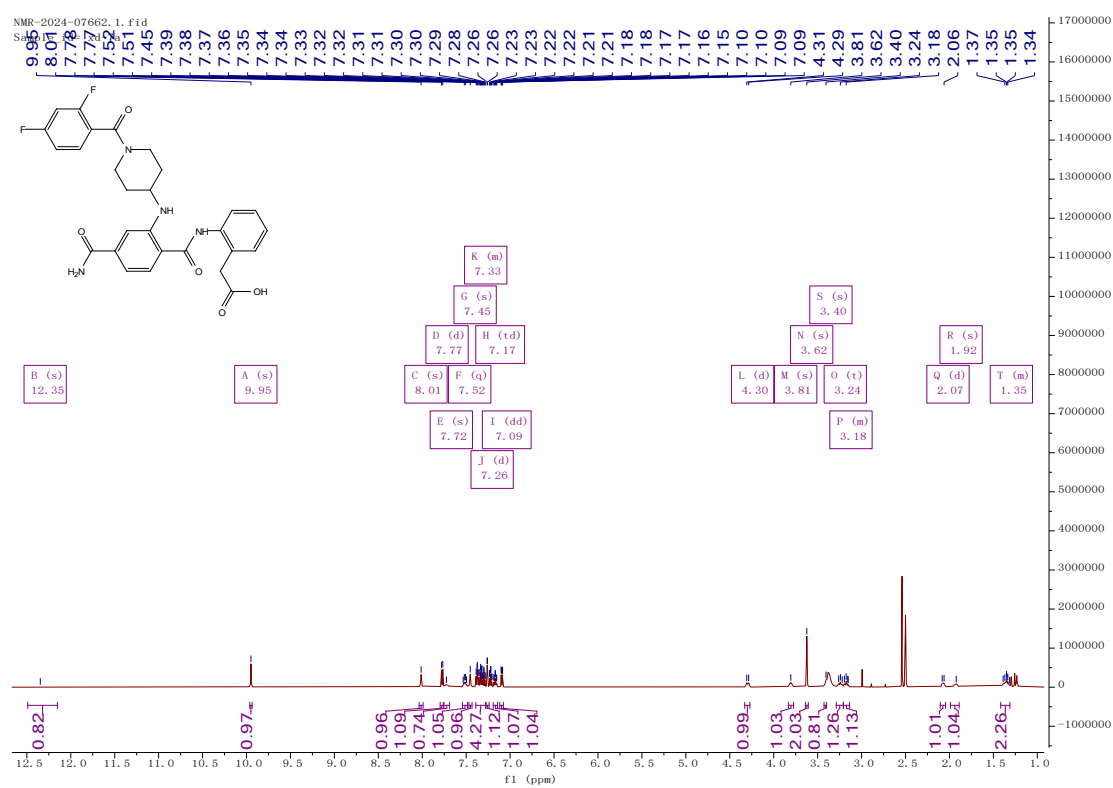


Figure 107. ¹H NMR spectrum of compound C7

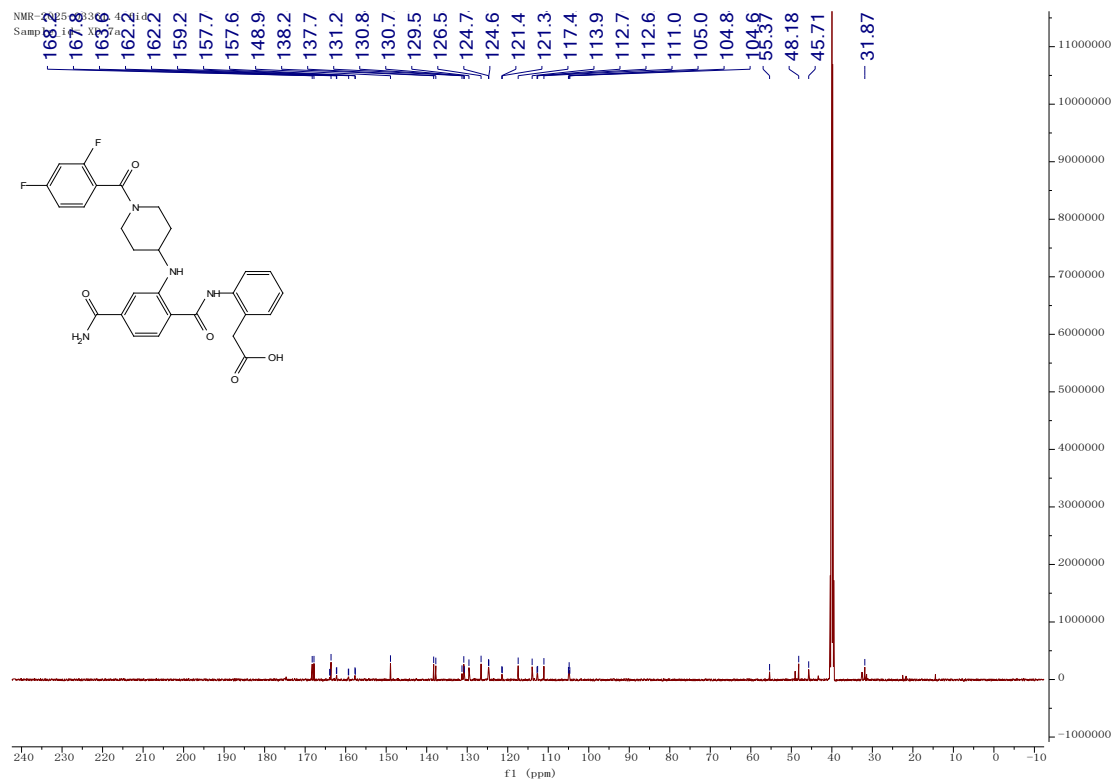


Figure 108. ^{13}C NMR spectrum of compound C7

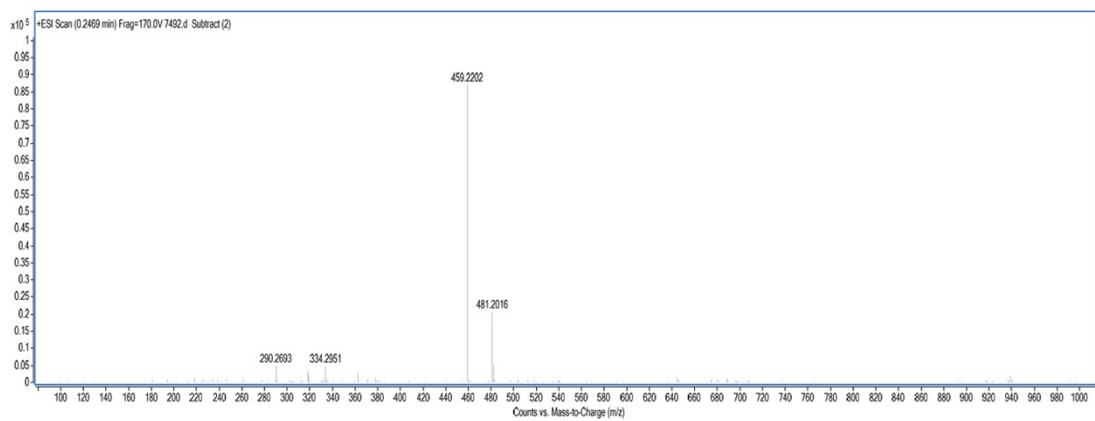


Figure 109. HRMS spectrum of compound C8

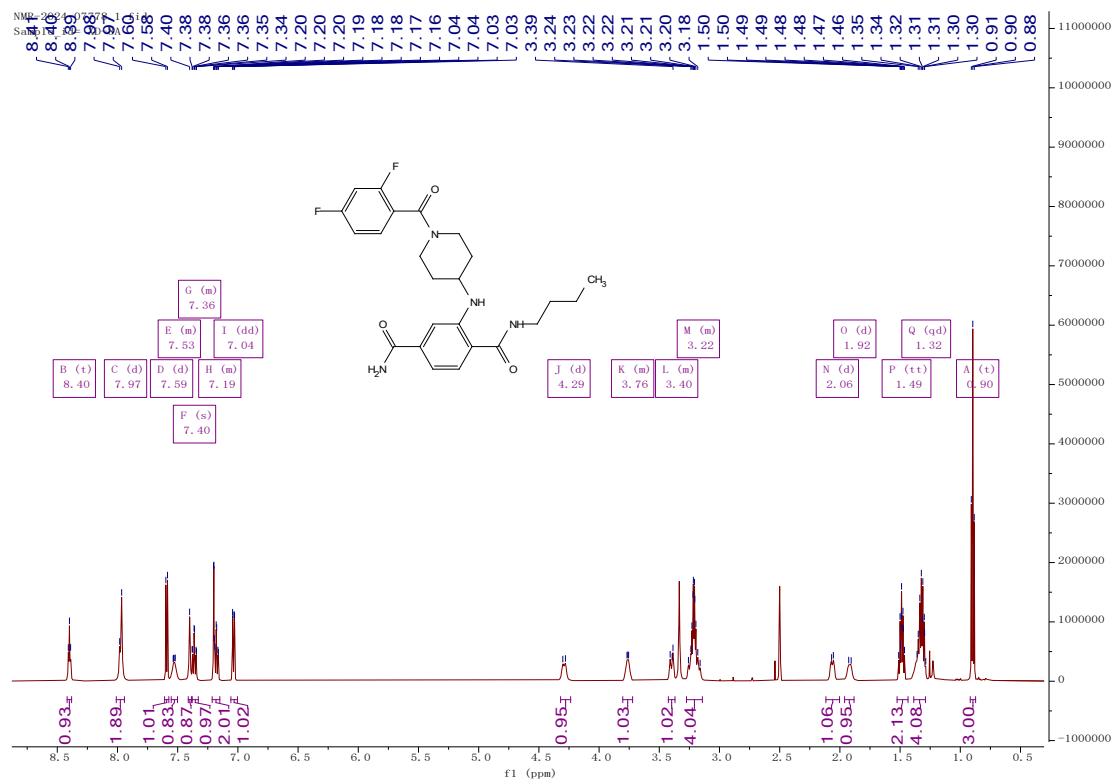


Figure 110. ¹H NMR spectrum of compound C8

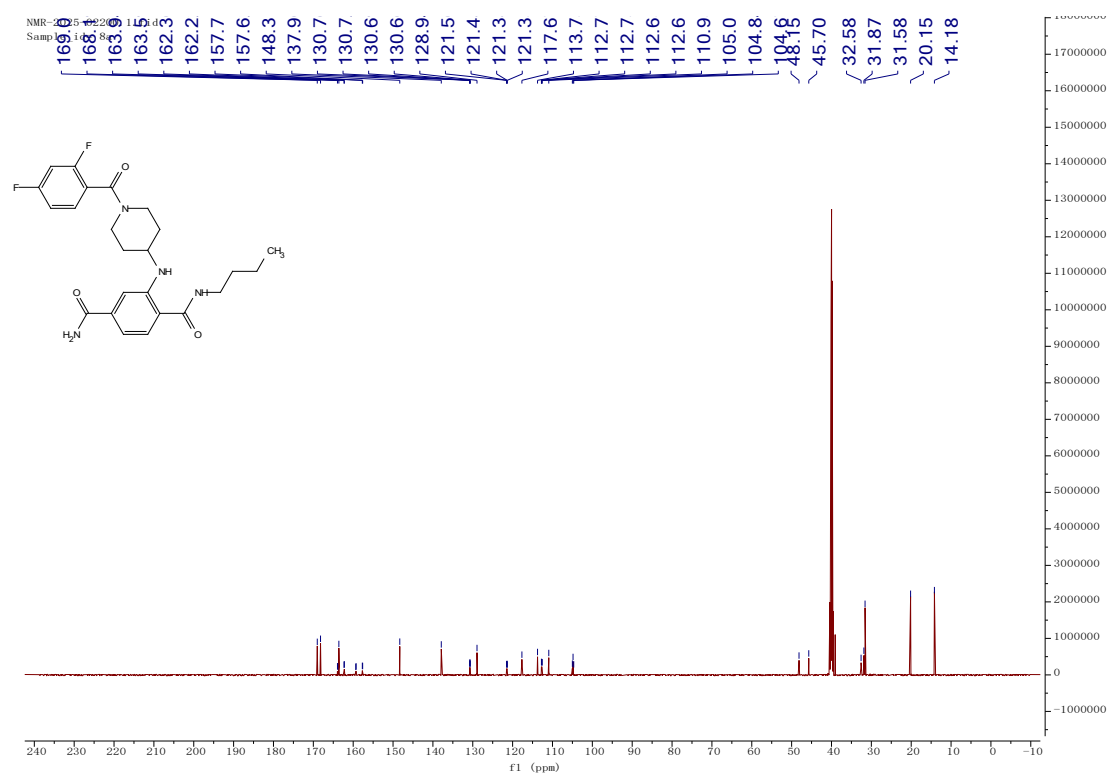


Figure 111. ¹³C NMR spectrum of compound C8

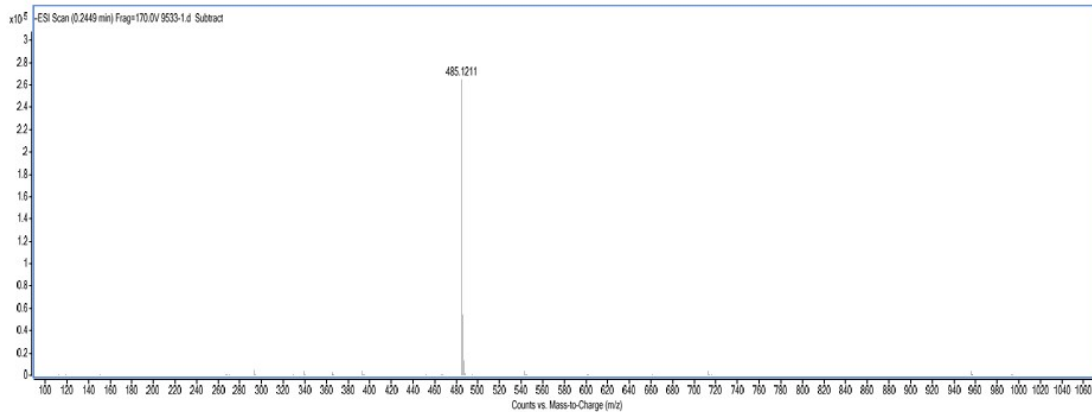


Figure 112. HRMS spectrum of compound C9

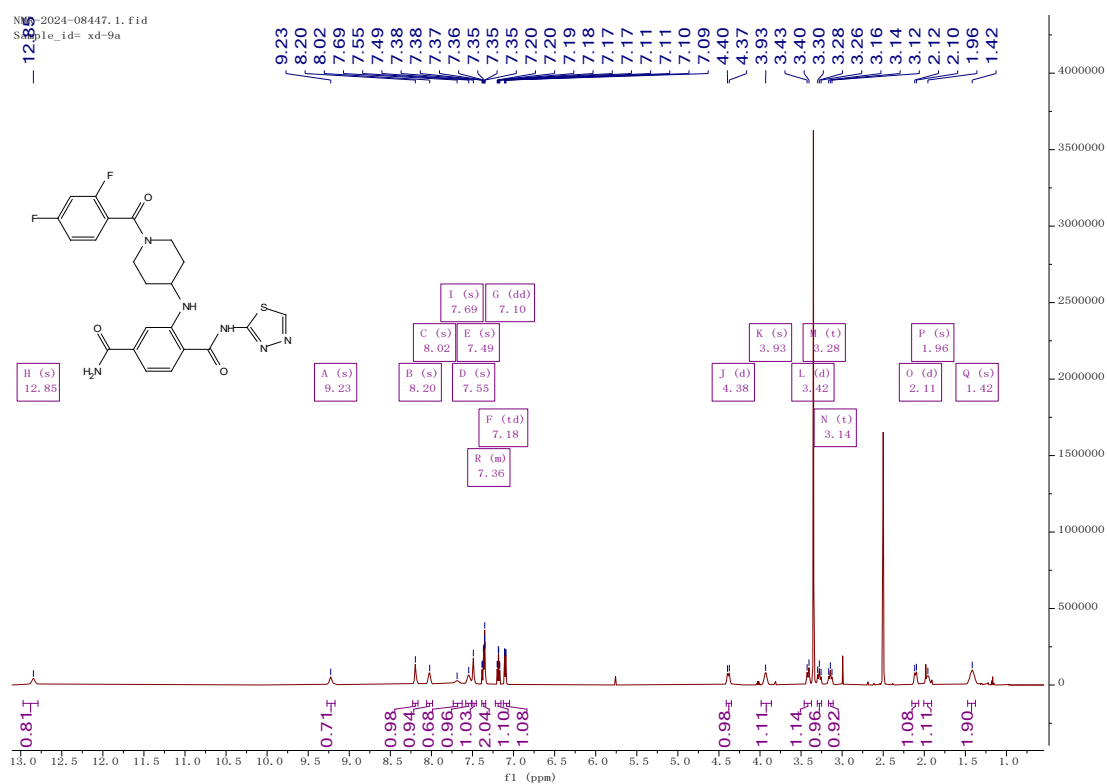


Figure 113. ¹H NMR spectrum of compound C9

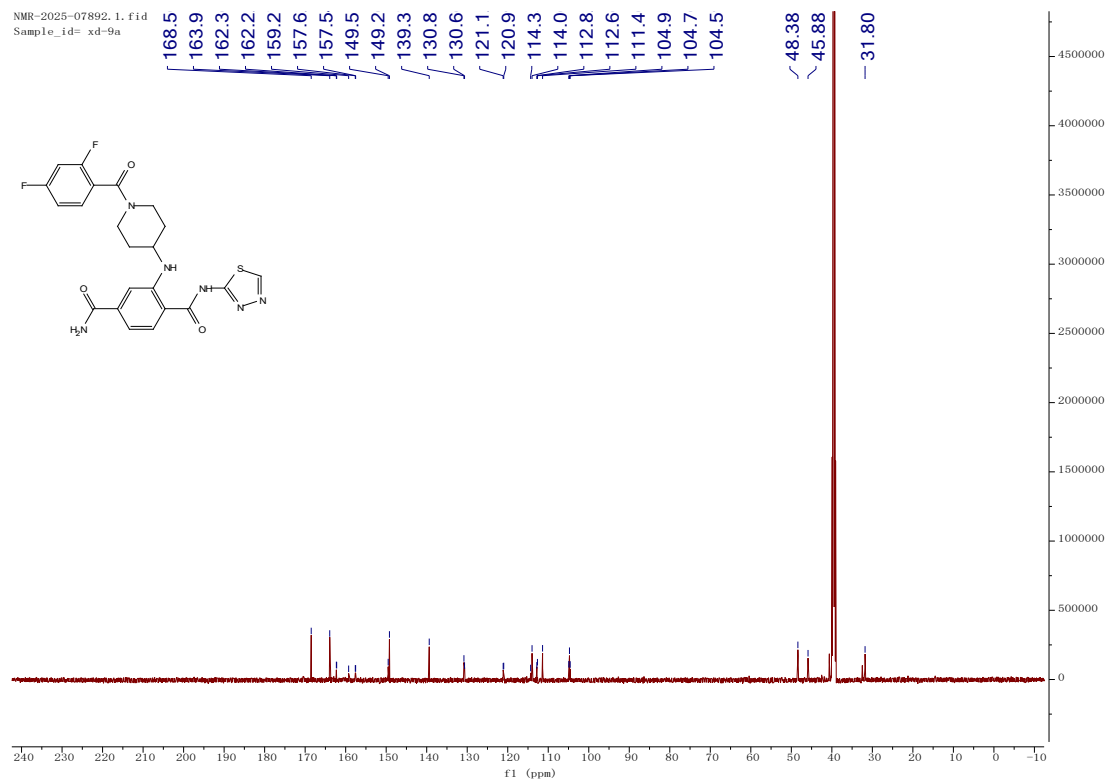


Figure 114. ^{13}C NMR spectrum of compound C9

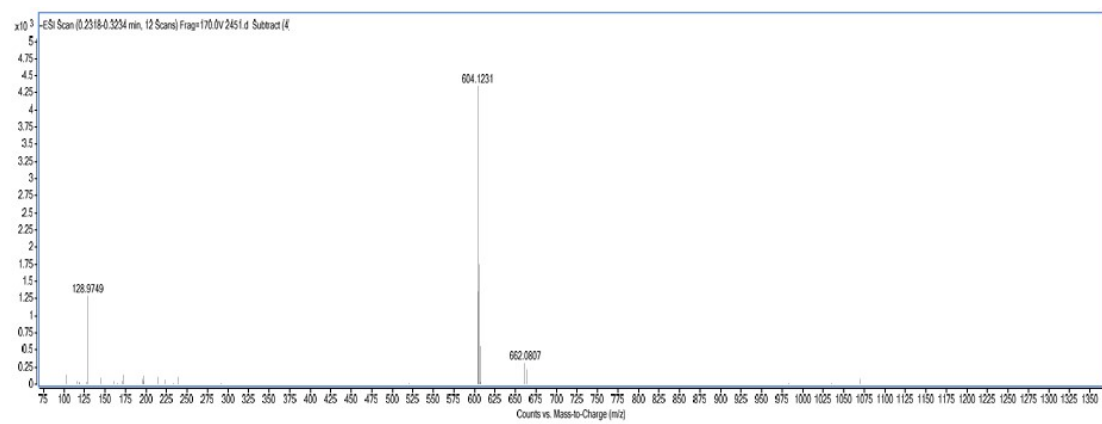


Figure 115. HRMS spectrum of compound C10

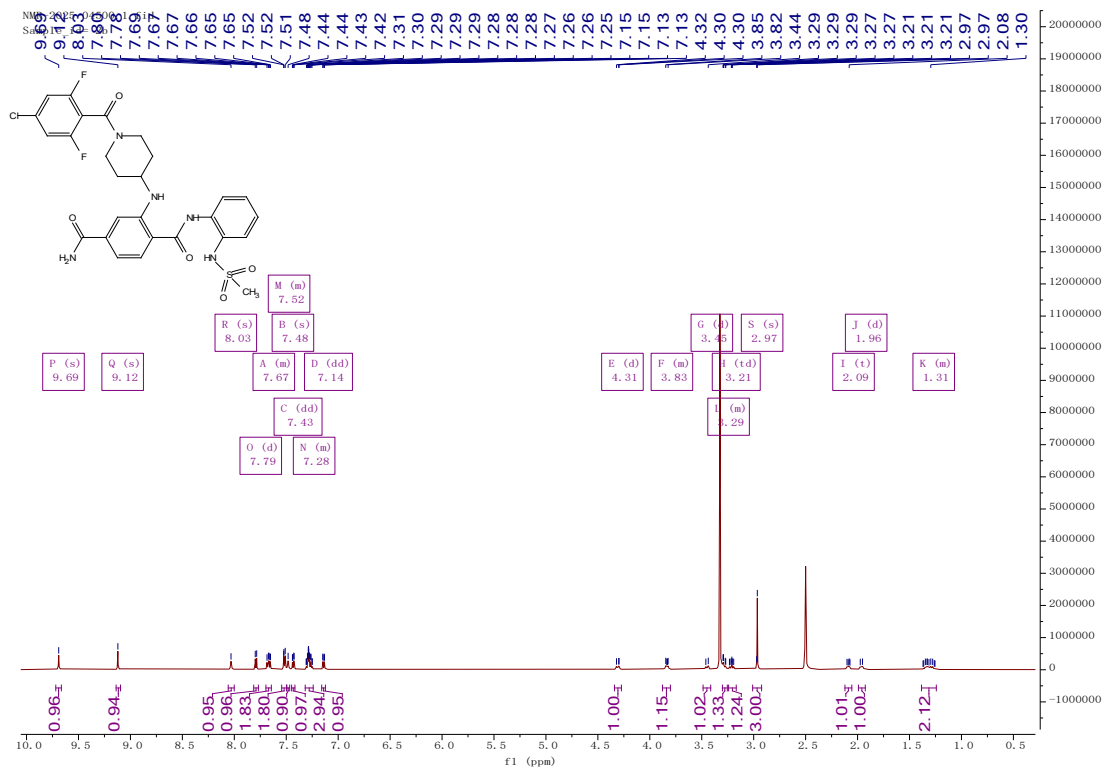


Figure 116. ¹H NMR spectrum of compound C10

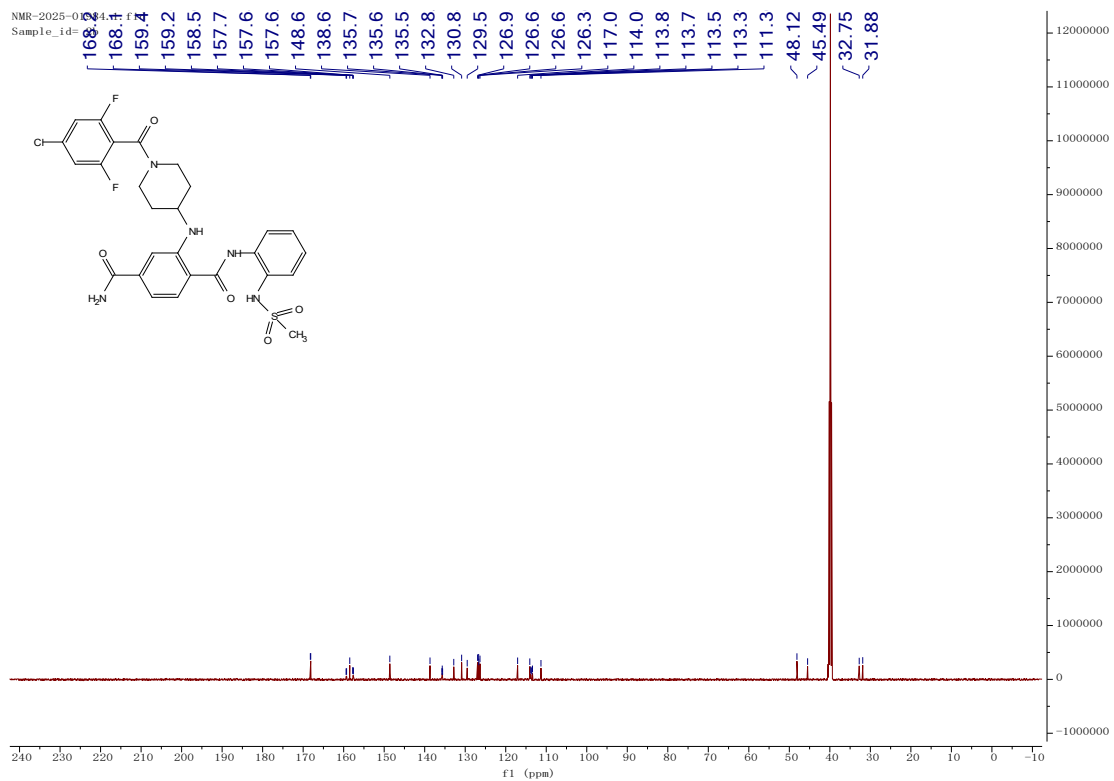


Figure 117. ¹³C NMR spectrum of compound C10

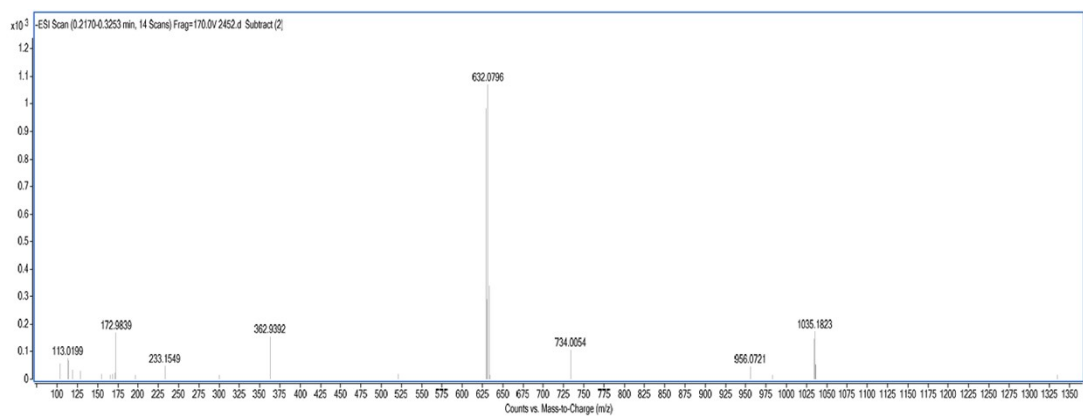


Figure 118. HRMS spectrum of compound C11

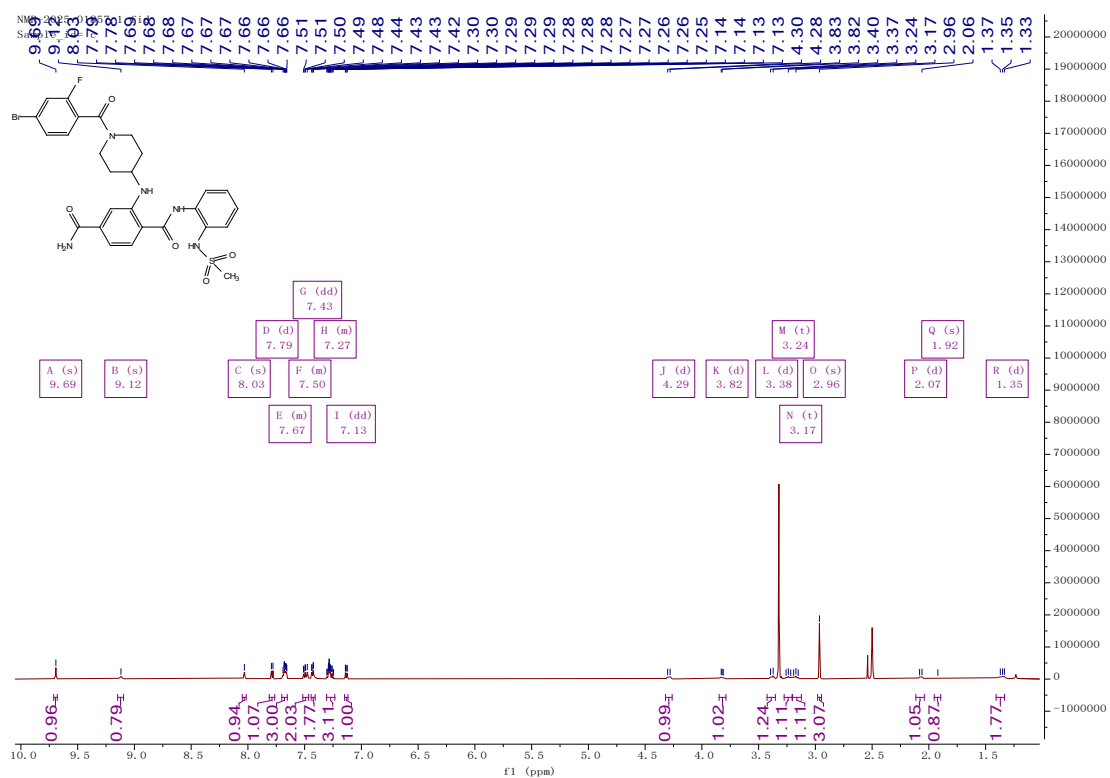


Figure 119. ¹H NMR spectrum of compound C11

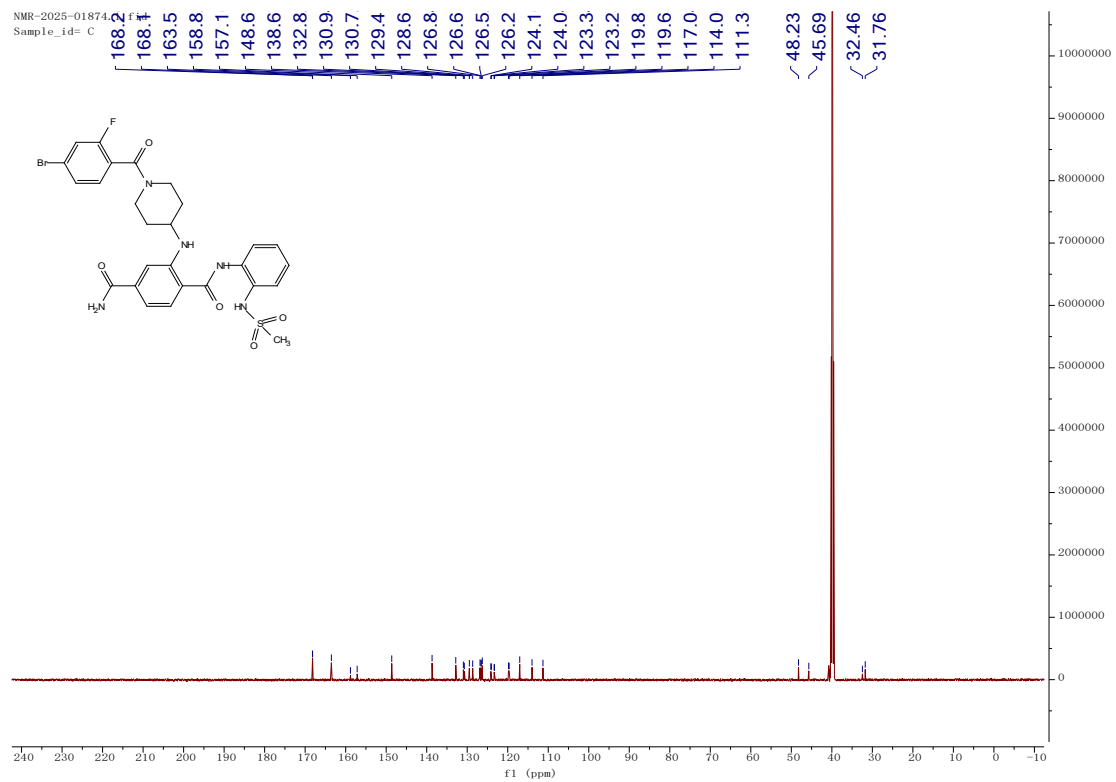


Figure 120. ^{13}C NMR spectrum of compound C11

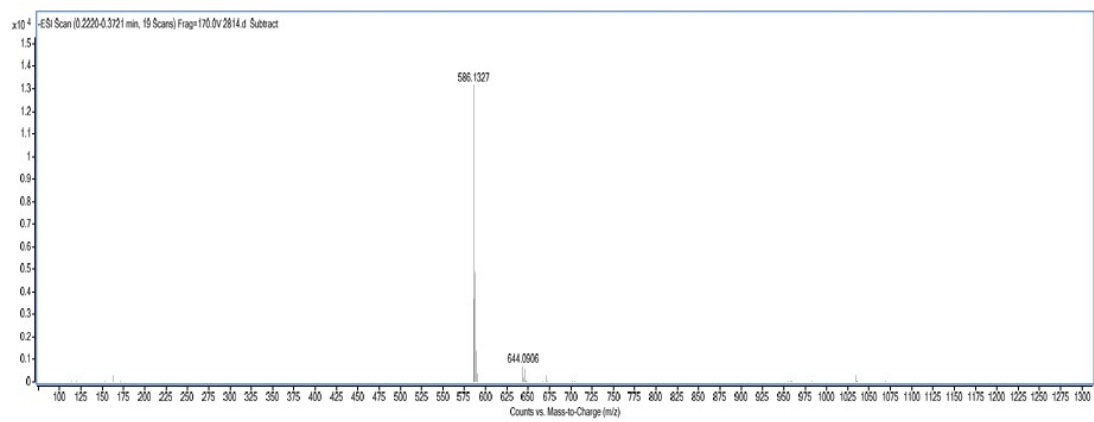


Figure 121. HRMS spectrum of compound C12

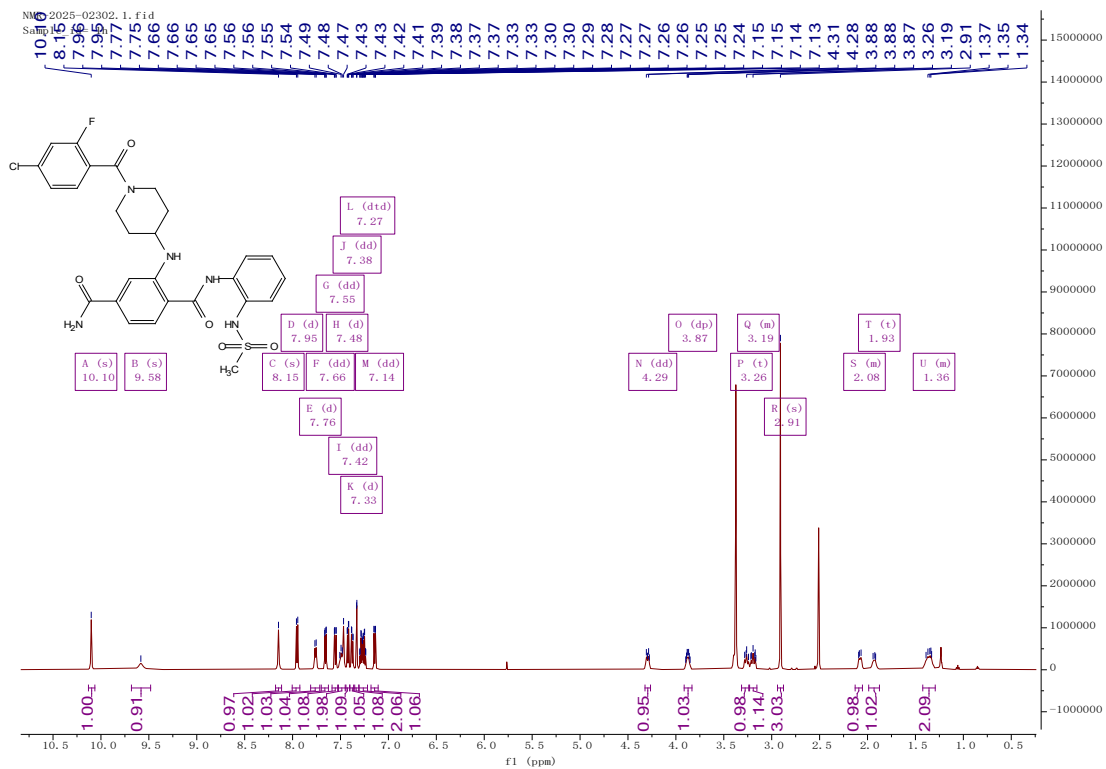


Figure 122. ¹H NMR spectrum of compound C12

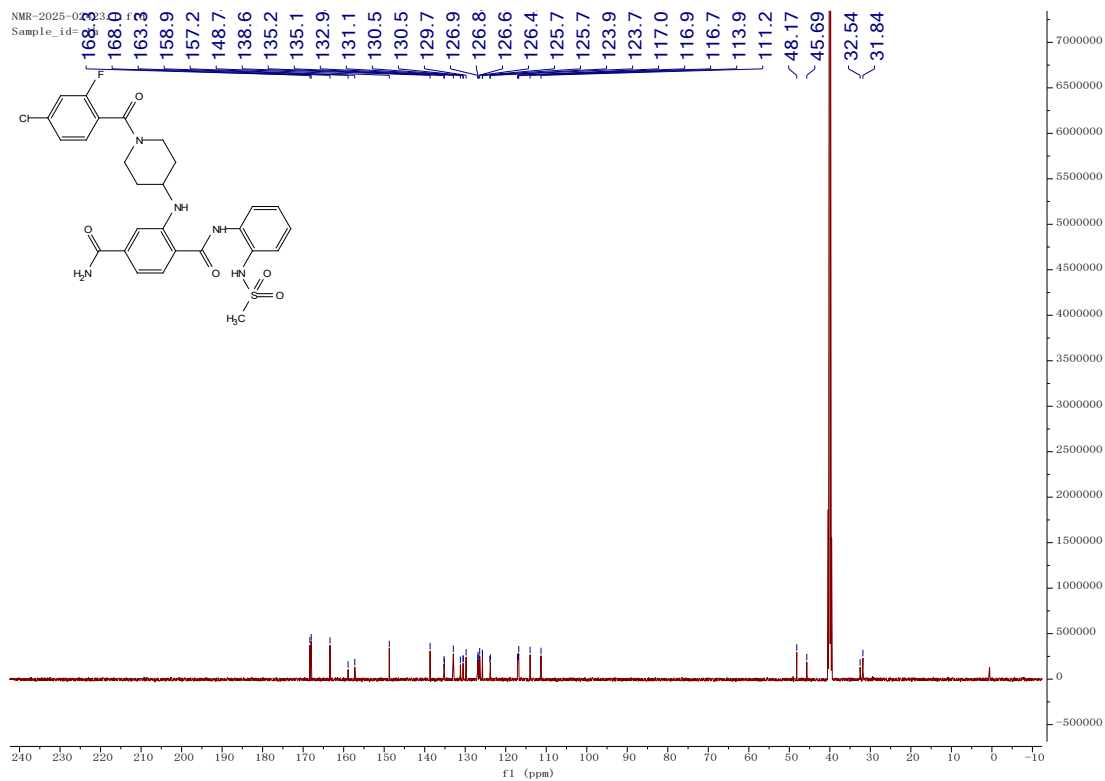


Figure 123. ¹³C NMR spectrum of compound C12

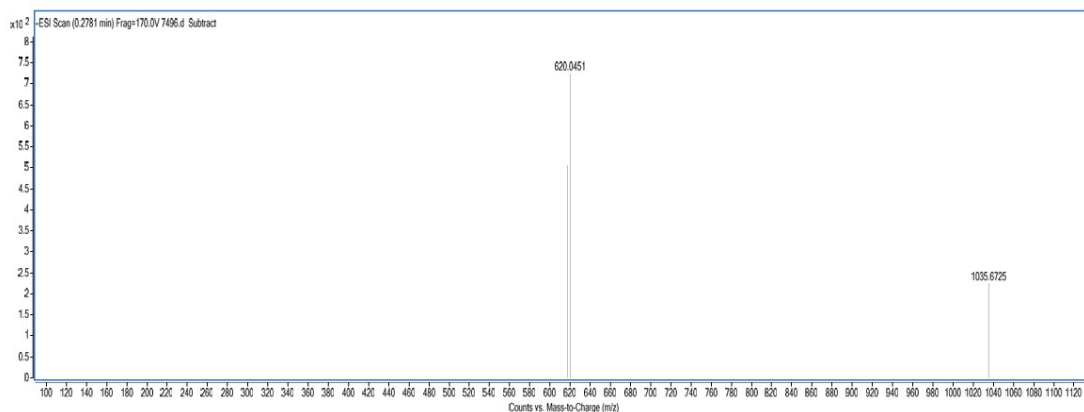


Figure 124. HRMS spectrum of compound C13

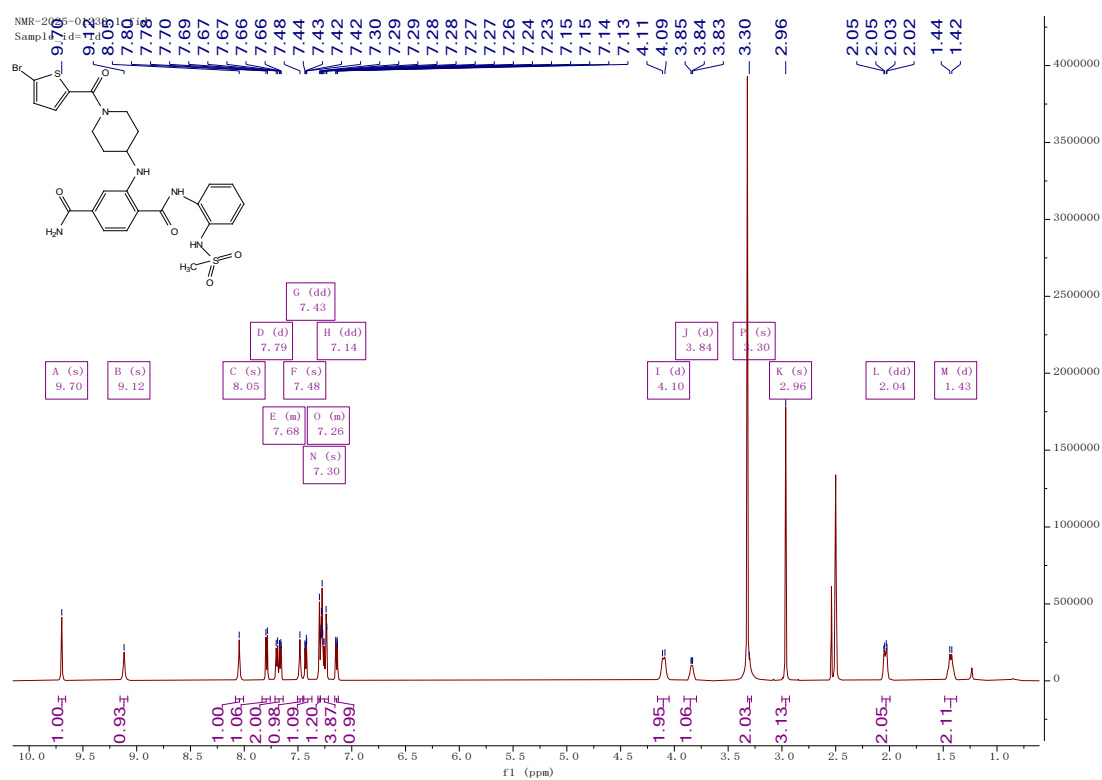


Figure 125. ¹H NMR spectrum of compound C13

NMR-2025-02197.1.fid
Sample_id= d

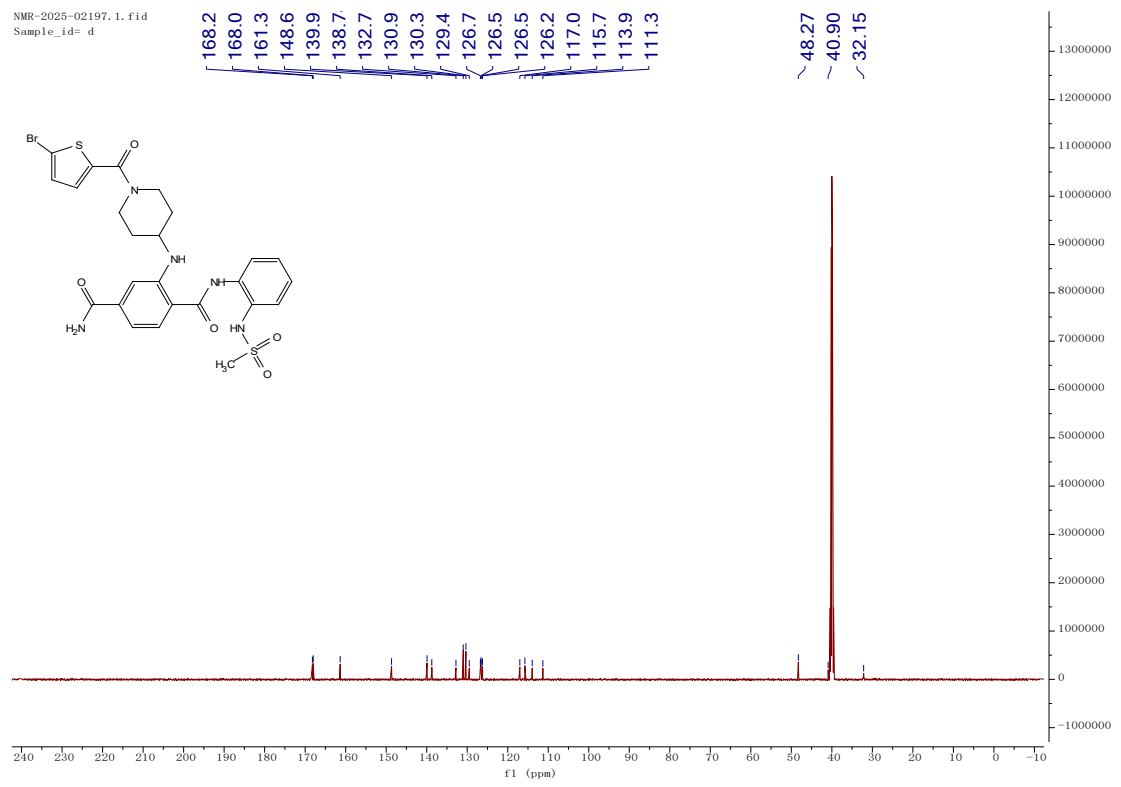


Figure 126. ¹³C NMR spectrum of compound C13

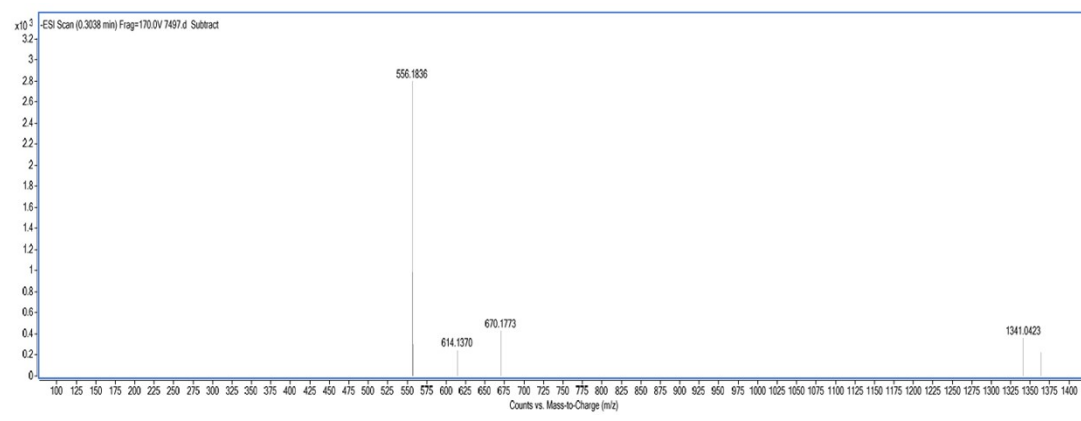


Figure 127. HRMS spectrum of compound C14

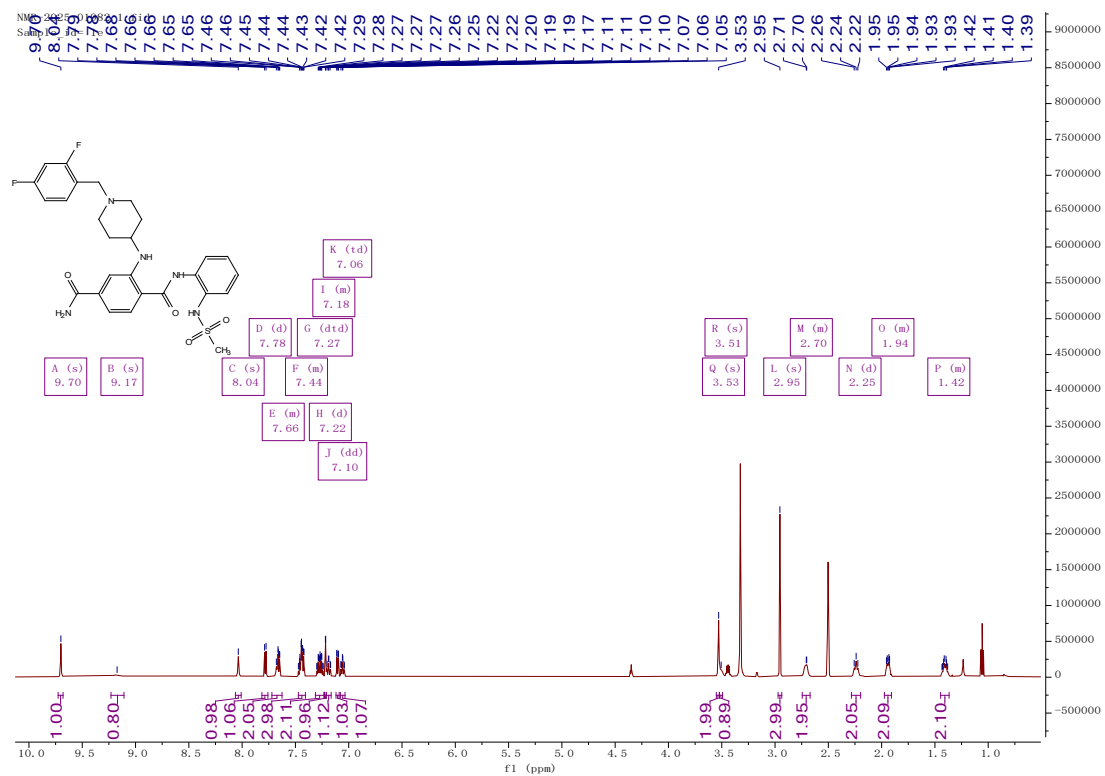


Figure 128. ^1H NMR spectrum of compound C14

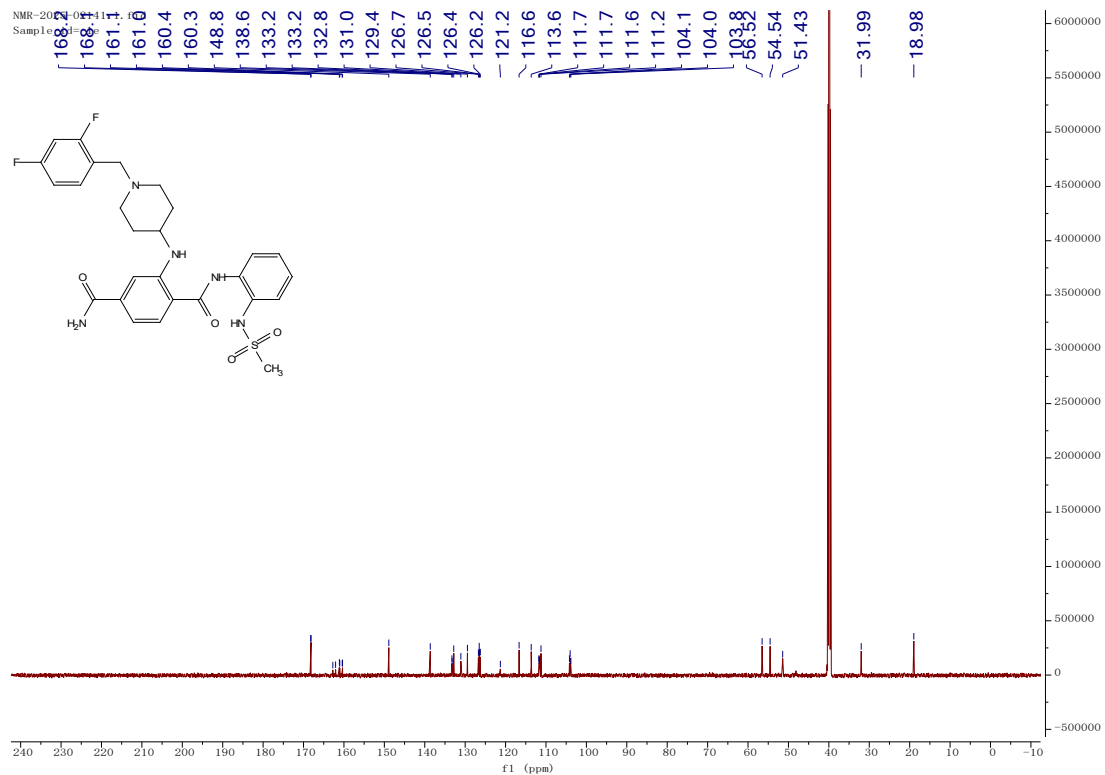


Figure 129. ^{13}C NMR spectrum of compound C14

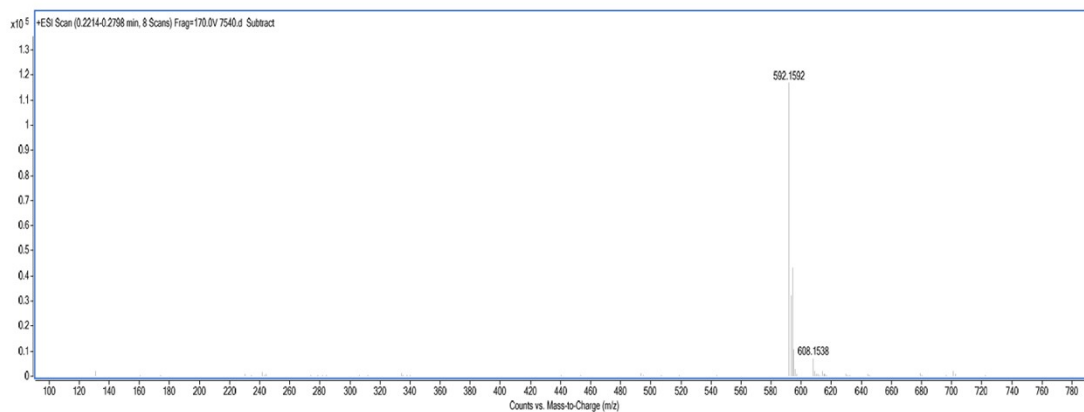


Figure 130. HRMS spectrum of compound C15

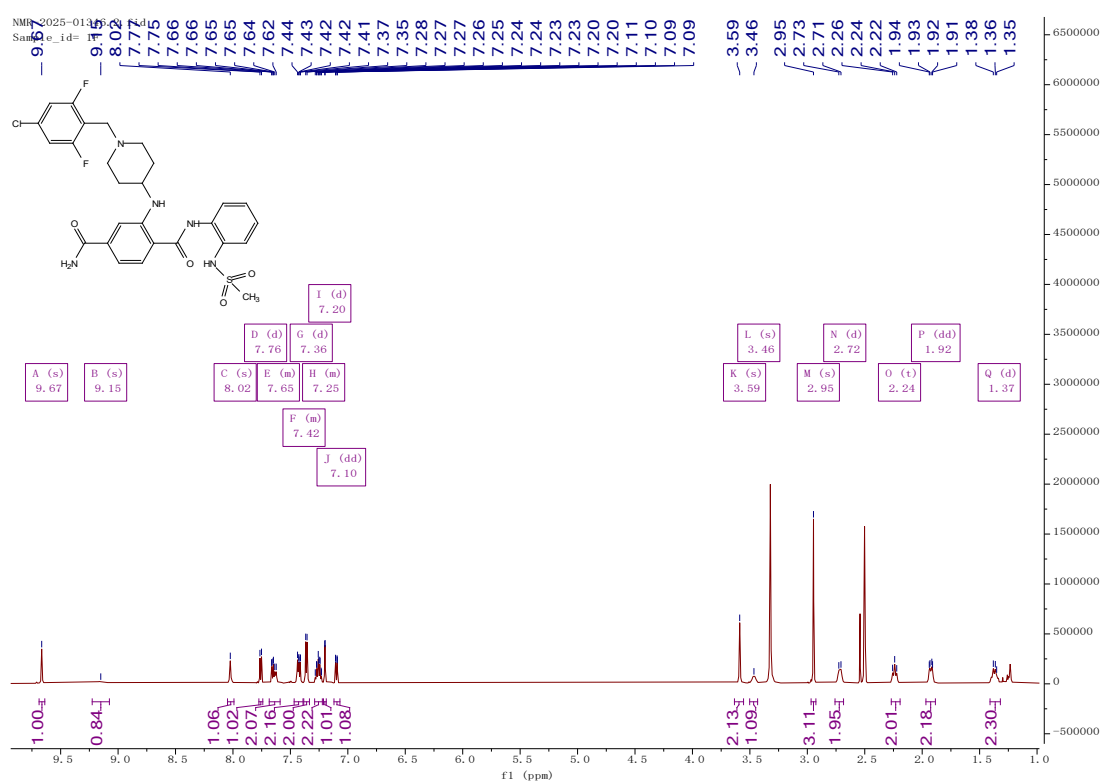


Figure 131. ^1H NMR spectrum of compound C15

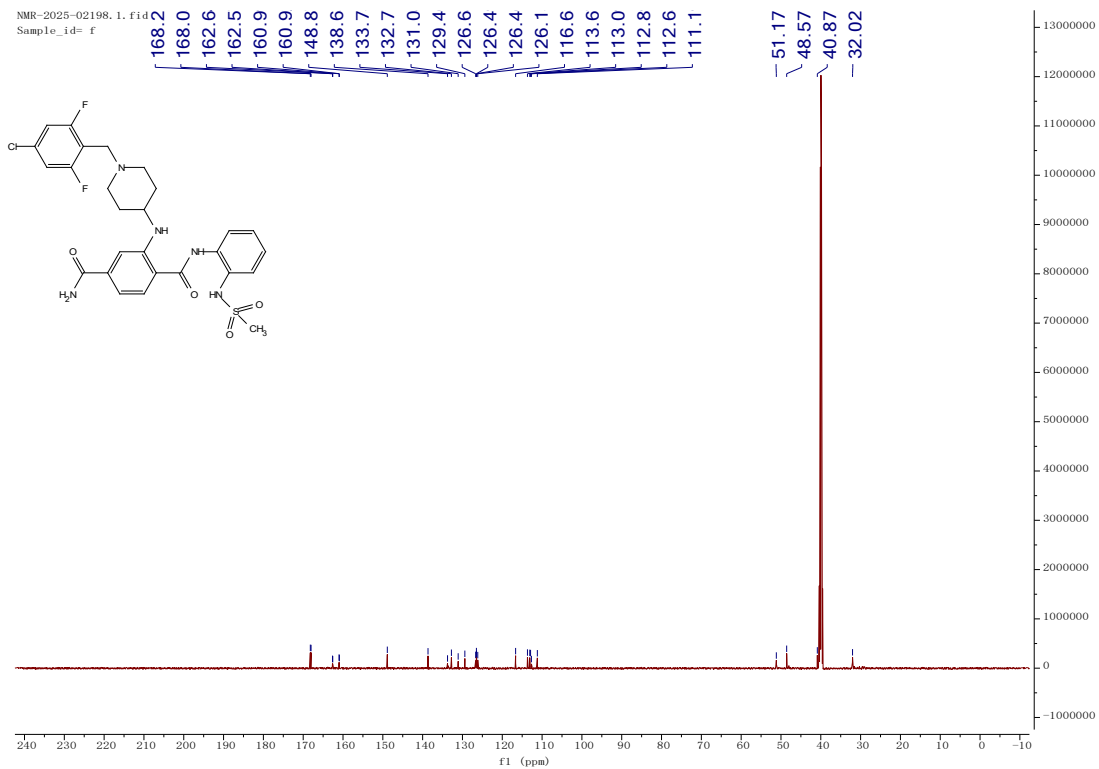


Figure 132. ^{13}C NMR spectrum of compound C15

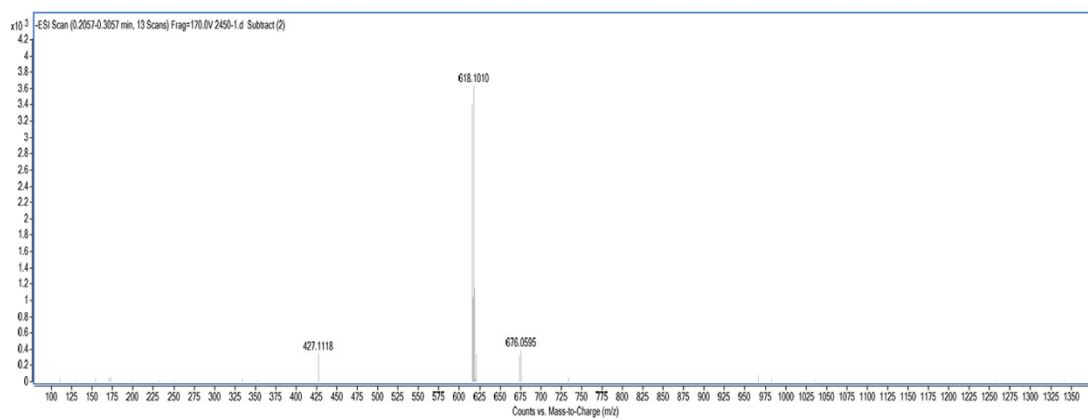


Figure 133. HRMS spectrum of compound C16



Figure 134. ¹H NMR spectrum of compound C16

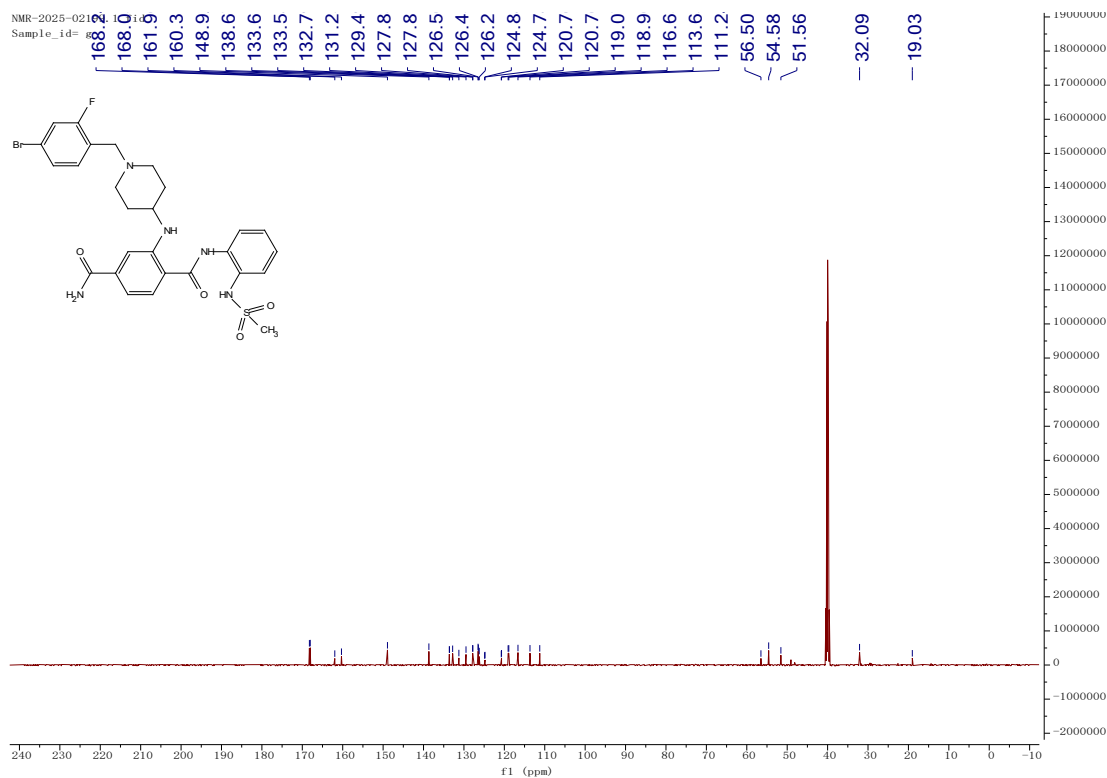


Figure 135. ¹³C NMR spectrum of compound C16

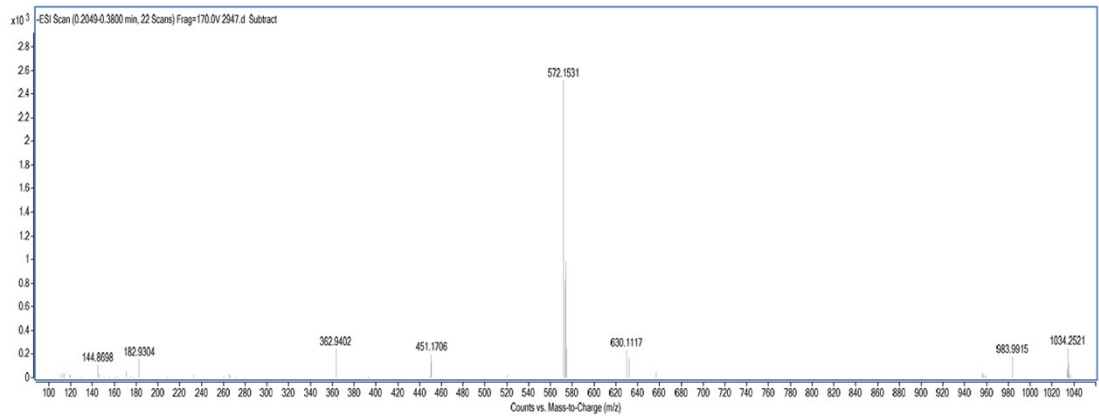


Figure 136. HRMS spectrum of compound C17

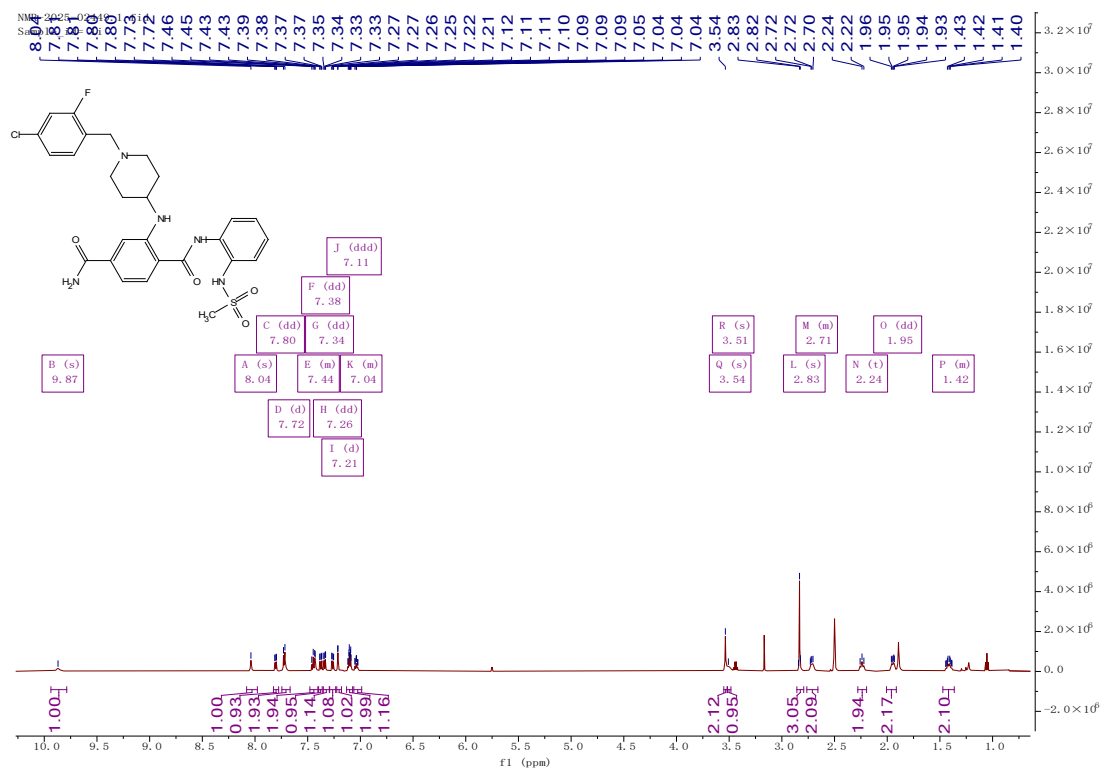


Figure 137. ¹H NMR spectrum of compound C17

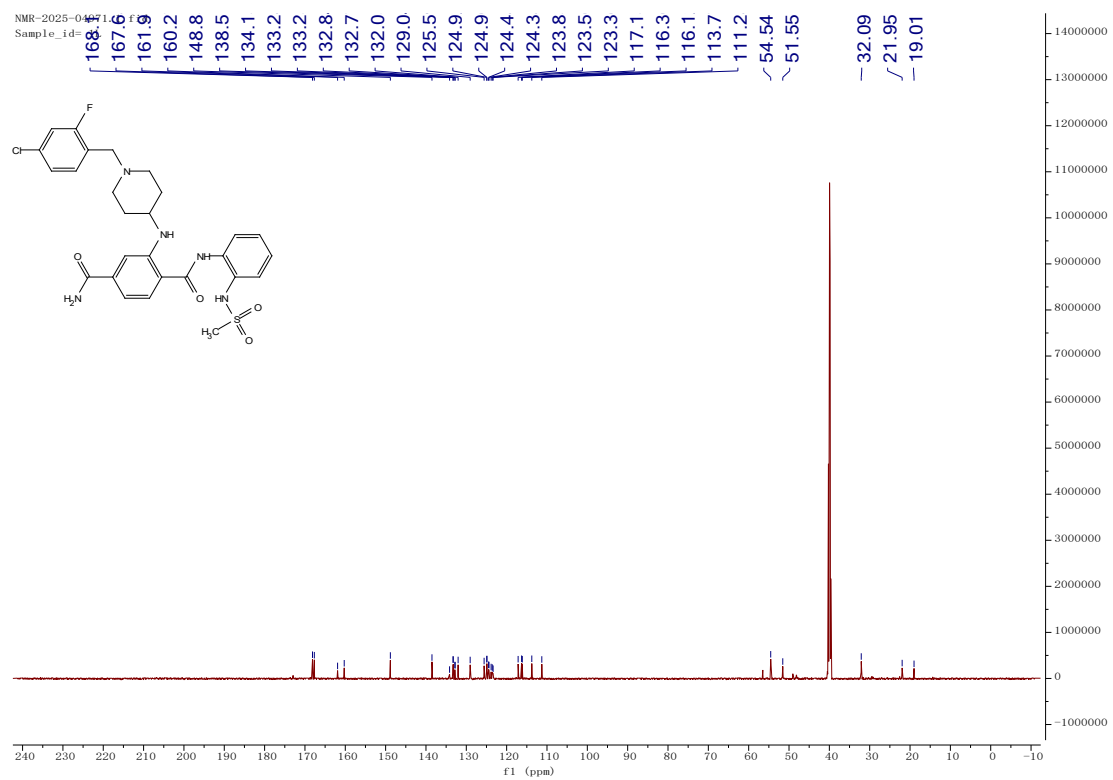


Figure 138. ^{13}C NMR spectrum of compound C17