

Supplementary Information

X-ray structure and molecular docking guided discovery of novel chitinase inhibitors with a scaffold of dipyridopyrimidine-3-carboxamide

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1 Additional Binding mode of 6k and 6p

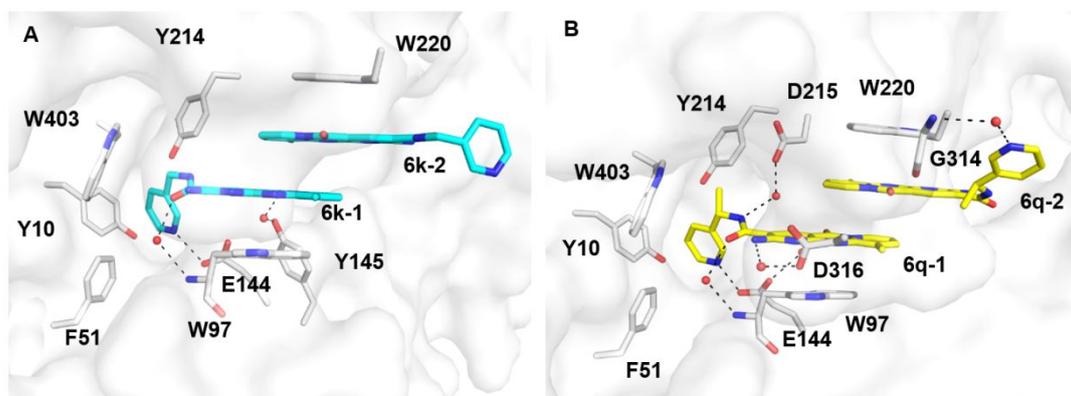


Figure S1 A. Two molecule binding mode of 6k; B. Two molecule binding mode of 6p.

The compound **6k-1** inserts deeply into the active site, whereas **6k-2** inserts shallowly and parts of **6k-2** stretch out of the binding cleft (**Figure S1A**). The pyridopyrimidine moieties of **6k-1** and **6k-2** are sandwiched by two tryptophan residues of Trp97 and Trp220 with strong π - π interactions. Interestingly, the distances between each of the two hydrophobic surfaces are the same and the bound two compounds occupy +1 and +2 subsites of the binding cleft. The 3-pyridine moiety of **6k-1** is embedded in the hydrophobic region of the binding cleft composed by Tyr10, Phe51, Tyr214 and Trp403. The 3-carboxamide oxygen atom and the 5-carbonyl group oxygen atom of **6k-1** form water-mediated hydrogen bonds with the side chain of Trp97 and Tyr145, respectively. In addition, the nitrogen atom in 3-pyridyl group formed hydrogen bond with key catalytic residue Glu144, which explained the decreased activity of changing the position of nitrogen atom.

In two molecules binding mode **6p** (**Figure S1B**), the pyridopyrimidine moieties of **6p-1** and **6p-2** are sandwiched by Trp97 and Trp220 with strong π - π interactions, which is similar to **6k**. The compounds **6p-1** inserts deeply into the active site, whereas **6p-2** inserts shallowly and parts of **6p-2** stretch out of the binding cleft. Three water mediated hydrogen bonds was found between **6p-1** and residues in activity: the 3-carboxamide nitrogen atom with Asp215, the 3-carboxamide oxygen atom with side chain of Trp97 and 2-amino nitrogen atom with Asp316. **6p-1** formed stronger hydrogen bond with

Glu144 than **6k-1**, as the hydrogen bond lengths were 2.5 Å and 2.7 Å respectively. Additionally, the nitrogen atom of 3-pyridine moiety in **6p-2** could form water-mediated hydrogen bond with the backbone of Gly314.

The existence of two molecule binding mode in both **6k** and **6p** suggests that the dipyridopyrimidine-3-carboxamide inhibitors insert into +1 and +2 subsites by two-molecule mode at high concentration, while the inhibitors insert by one-molecule mode at low concentration.

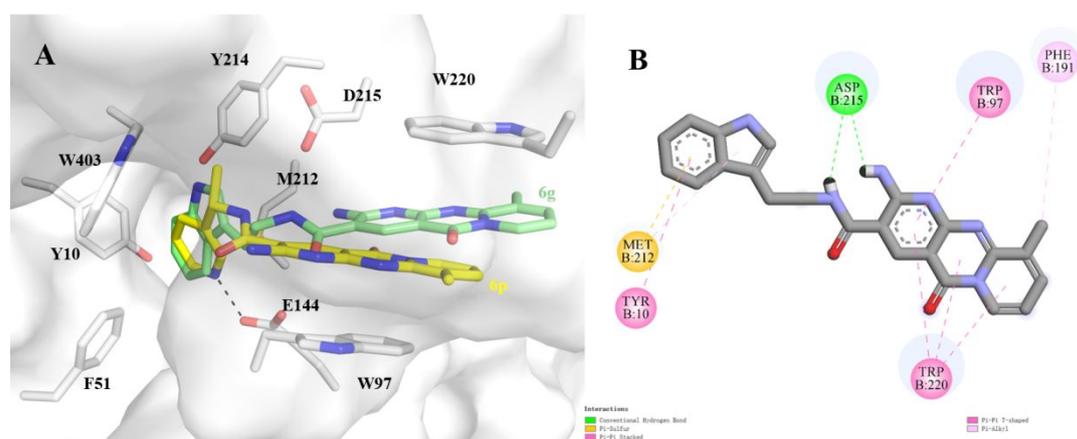


Figure S2 Docking results of **6g** with *SmChiB*: **A**. Superposition of docking result of **6g** with *SmChiB* and *SmChiB-6p*; **B**. 2D diagram of docking result of **6g** with *SmChiB*.

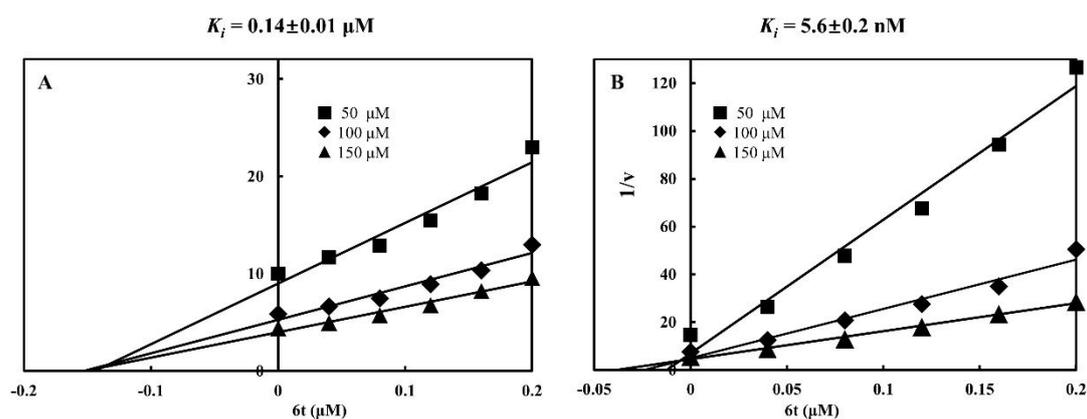


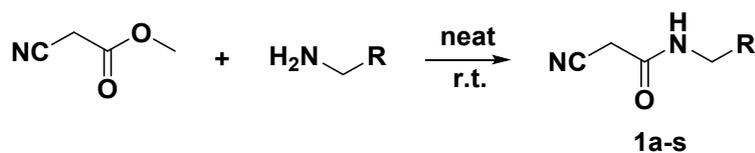
Figure S3 Dixon plots for inhibition chitinase *SmChiB* by **6t**(A) and chitinase *OfChi-h* by **6t**(B). The trend lines represent three substrate concentrations.

2 Materials and Methods

Unless otherwise noted, standard and analytical graded reagents and solvents were

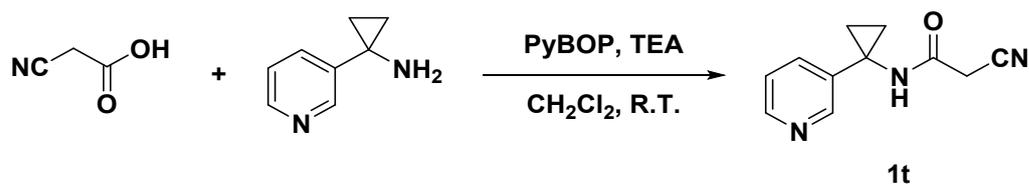
obtained from commercial sources and used without further purification. All reactions were under air atmosphere. ^1H NMR, ^{19}F NMR and ^{13}C NMR spectra were recorded on Bruker AM-400 (^1H at 400 MHz, ^{13}C at 100 MHz, ^{19}F at 376 MHz) spectrometer with $\text{DMSO-}d_6$ or CDCl_3 as solvent and TMS as internal standard. Chemical shifts are reported in δ (parts per million). High-resolution electron mass spectra (HRMS) was performed on Waters, Xevo G2 TOF spectrometer (MA, USA). Analytical thin-layer chromatography (TLC) was performed on precoated plates (silica gel 60 F254), and spots were visualized with ultraviolet (UV) light. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, coupling constant (Hz) and integration.

2.1 Synthetic Procedure of 1a-t



Scheme 1 General procedure of preparing 1a-s

The methyl cyanoacetate (1.0-1.2 equiv.) was added into amine (1.0 equiv.) and stirred at room temperature. After 0.5-12 h, precipitate will be filtered and washed with cold diethyl ether then dried on vacuum.



Scheme 2 Synthetic procedure of 1t

As for **1t**, it could not be synthesized by general procedure. The synthesis of **1t** is as follows: A solution cyanoacetic acid (170 mg, 2 mmol) and 1-Pyridin-3-yl-cyclopropylamine (270 mg, 2 mmol) in 10 mL CH_2Cl_2 is stirred at R.T. while the PyBOP(1.04 g, 2 mmol) is added, followed by the addition of triethylamine (410 mg, 4 mmol). The reaction is stirred at R.T. The reaction was completed after 5 hours, monitored by TLC. The mixture was quenched with water and the aqueous solution

was extracted with dichloromethane. The organic layer was washed with water, dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by silica gel column chromatography eluting with dichloromethane/methanol (15:1) to give **1t** as a white solid (289 mg, 72%).

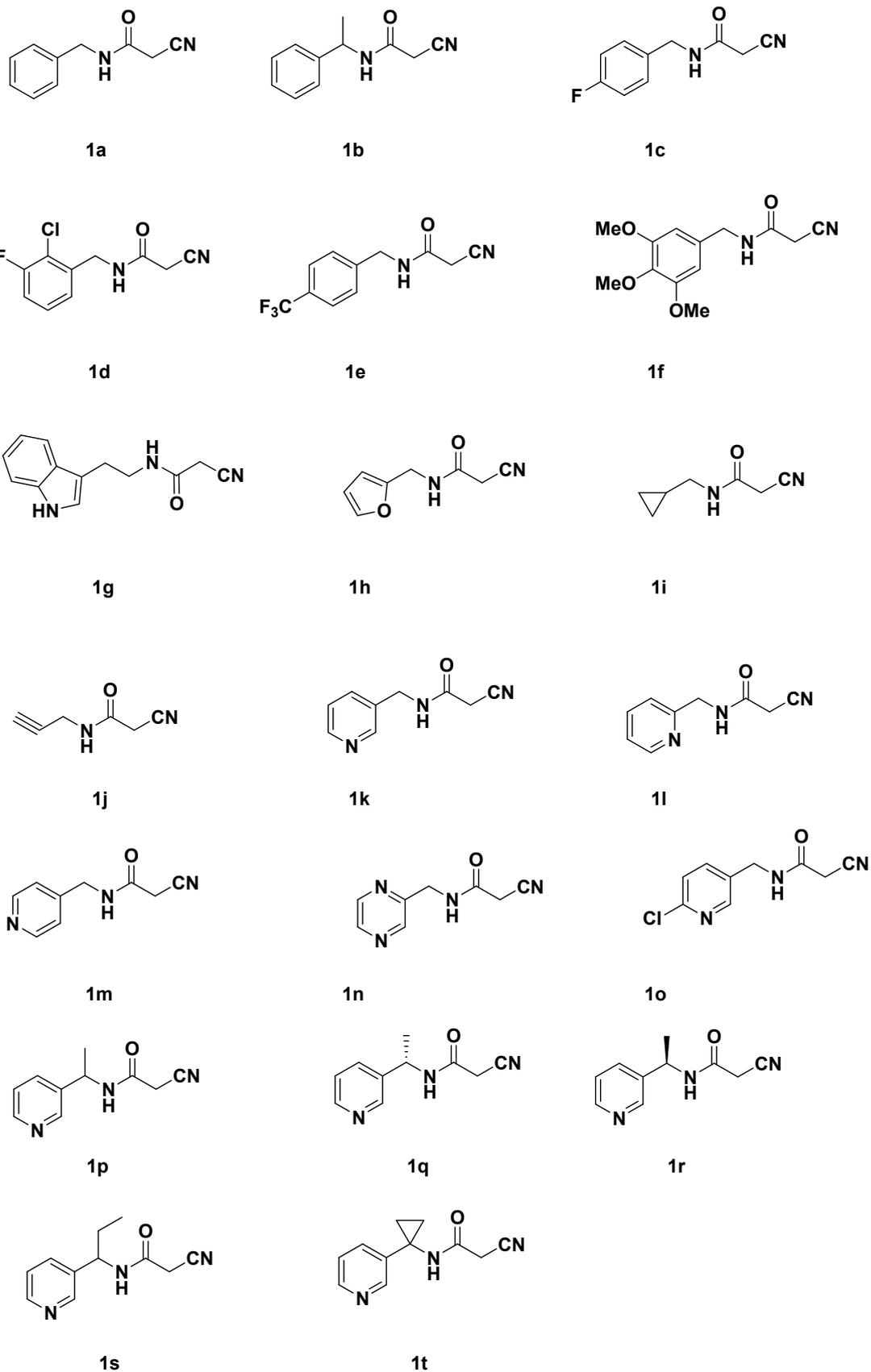
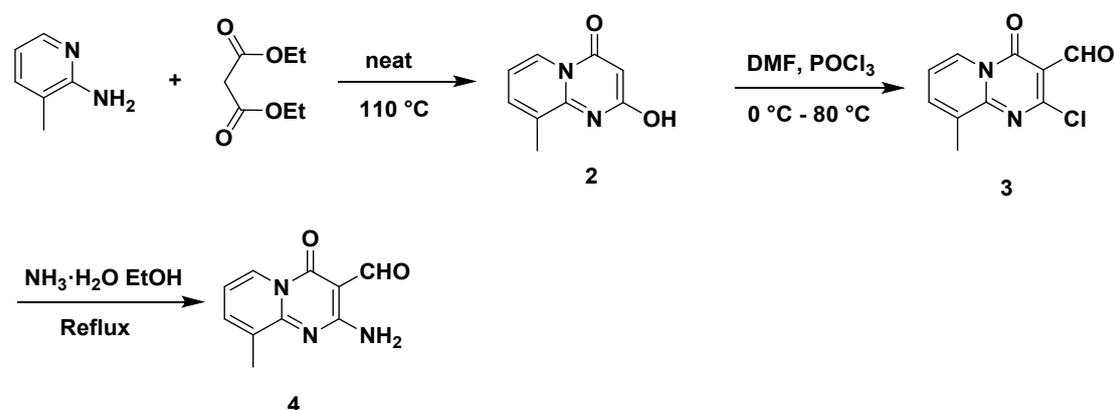


Figure S4 Structures of intermediates 1a-t

2.2 The synthesis of key intermediate 4



Scheme 3 The synthesis procedure of key intermediate 4

Step 1: 2-Hydroxy-9-methyl-4H-pyrido[1,2-a]pyrimidin-4-one 2

A mixture of 2-amino-3-picoline (100 mmol) and diethyl malonate (100 mmol) was stirred at 110 °C for 12 h. After cooling to room temperature, the dark residue was triturated with ethyl acetate (30 mL), and filtered. The solid was washed with ethyl acetate (20 mL) to give the titled compound. White solid, yield (16.2 g, 91%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 2.48 (s, 3H), 5.44 (s, 1H), 7.20 (t, *J* = 7.0 Hz, 1H), 7.87 (d, *J* = 6.8 Hz, 1H), 8.84 (d, *J* = 6.8 Hz, 1H), 11.52 (brs, 1H).

Step 2: 2-chloro-9-methyl-4-oxo-4H-pyrido[1,2-a]pyrimidine-3-carbaldehyde 3

To DMF (20 mL) was added POCl₃ (30 mmol) at 0 °C. After the mixture was stirred at 0 °C for 40 min, a solution of 2 (10 mmol) in DMF (20 mL) was added and stirred at 80 °C for 1 h. After cooling, the mixture was poured into ice water and stirred for 0.5h. The precipitate was filtered and washed thoroughly with cold water. The solid was recrystallized from ethanol to afford compound 3 in a yield of 78 %. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.24 (s, 1H), 9.04 (d, *J* = 6.9 Hz, 1H), 8.24 (d, *J* = 7.1 Hz, 1H), 7.58 (t, *J* = 7.0 Hz, 1H), 2.53 (s, 3H).

Step 3: 2-amino-9-methyl-4-oxo-4H-pyrido[1,2-a]pyrimidine-3-carbaldehyde 4

3 mL ammonium hydroxide solution (25%-28%) was added to a suspension of 2-chloro-9-methyl-4-oxo-4H-pyrido[1,2-a]pyrimidine-3-carbaldehyde 3 (2.223 g, 10 mmol) in 20 mL ethanol. The mixture was stirred at 70 °C for 2 h until the completion was detected by TLC. The reaction mixture was cooled to room temperature and removed the solvent by filtration to afford the crude product which was purified by silica gel column chromatography using AcOEt/PE (1:1) to give 4 (0.854 g, 42%) as white solid. ¹H NMR (400 MHz, Chloroform-*d*) δ 10.32 (s, 1H), 9.14 (s, 1H), 8.81 (dd,

$J = 7.2, 1.6$ Hz, 1H), 8.81 (d, $J = 7.2$ Hz, 1H), 7.60 (dt, $J = 6.9, 1.4$ Hz, 1H), 6.88 (t, $J = 7.0$ Hz, 1H), 5.83 (s, 1H), 2.44 (s, 3H).

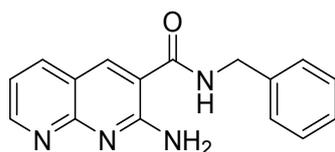
2.3 General Procedure of Preparing (5a-c,6a-t)

2-aminoaldehydes (1.0 equiv.), cyanoacetamide (1.0 equiv.) and NaOH (10 mol%) were mixed in 5 mL ethanol at 70 °C. The reaction was completed after 10-30 min, monitored by TLC. The formed precipitate was collected and washed by cold ethanol, then dried on vacuum.

The synthesis of **5a-c** and **6a-t** followed the procedure above, the yield were in the range of 58%-84%.

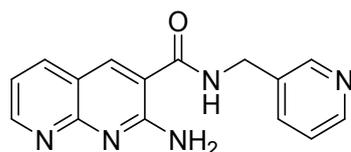
2.4 Characterizations of products

2-amino-N-benzyl-1,8-naphthyridine-3-carboxamide(5a)



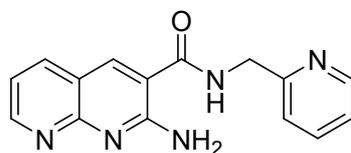
Yield: 84.7 %; White solid; M.p. 200.1-201.4 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 9.37 (s, 1H), 8.79 (d, $J = 4.8$ Hz, 1H), 8.53 (s, 1H), 8.14 (d, $J = 7.8$ Hz, 1H), 7.48 (s, 2H), 7.43 – 7.11 (m, 6H), 4.51 (s, 2H). ^{13}C NMR (100 MHz, DMSO- d_6) δ 166.79, 158.56, 156.77, 154.14, 139.03, 138.67, 137.55, 128.34, 127.36, 126.89, 117.96, 115.83, 115.60, 42.60. HRMS-ESI (m/z): calcd for $\text{C}_{16}\text{H}_{15}\text{N}_4\text{O}$ [$\text{M}+\text{H}^+$], 279.1246; found, 279.1245.

2-amino-N-(pyridin-3-ylmethyl)-1,8-naphthyridine-3-carboxamide(5b)



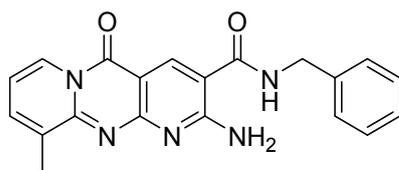
Yield: 81.4 %; White solid; M.p. 290.0 – 291.5 °C; ^1H NMR (400 MHz, DMSO- d_6) δ = 9.39 (s, 1H), 8.79 (dd, $J = 4.4, 2.0$ Hz, 1H), 8.61 (d, $J = 1.6$ Hz, 1H), 8.52 (s, 1H), 8.49 (dd, $J = 4.8, 1.6$ Hz, 1H), 8.14 (dd, $J = 8.0, 2.0$ Hz, 1H), 7.79 (dt, $J = 8.0, 2.0$ Hz, 1H), 7.43 (s, 2H), 7.39 (m, 1H), 7.23 (dd, $J = 8.0, 4.4$ Hz, 1H), 4.53 (d, $J = 5.8$ Hz, 2H). ^{13}C NMR (100 MHz, DMSO- d_6) δ = 166.92, 158.46, 156.78, 154.20, 148.89, 148.21, 138.76, 137.54, 135.25, 134.50, 123.50, 117.98, 115.80, 115.44, 40.38. HRMS-ESI (m/z): calcd for $\text{C}_{15}\text{H}_{14}\text{N}_5\text{O}$ [$\text{M}+\text{H}^+$], 280.1198; found, 280.1197.

2-amino-N-(pyridin-2-ylmethyl)-1,8-naphthyridine-3-carboxamide(5c)



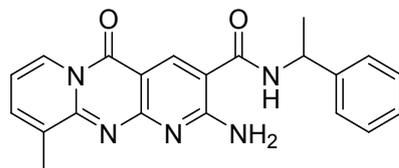
Yield: 75.1 %; White solid; M.p. 217.3 – 219.0 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.41 (s, 1H), 8.79 (dd, *J* = 4.4, 2.0 Hz, 1H), 8.56 (s, 1H), 8.54 (d, *J* = 4.4 Hz, 1H), 8.15 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.79 (td, *J* = 7.6, 2.0 Hz, 1H), 7.47 (s, 2H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.33 – 7.26 (m, 1H), 7.24 (dd, *J* = 8.0, 4.0 Hz, 1H), 4.60 (s, 2H). ¹³C NMR (100 MHz, DMSO) δ 166.94, 158.47, 158.14, 156.78, 154.13, 148.86, 138.68, 137.54, 136.79, 122.21, 121.12, 117.96, 115.83, 115.79, 44.53. HRMS-ESI (*m/z*): calcd for C₁₅H₁₄N₄O [M+H⁺], 280.1198; found, 280.1196.

2-amino-*N*-benzyl-10-methyl-5-oxo-5*H*-dipyrido[1,2-*a*:2',3'-*d*]pyrimidine-3-carboxamide(6a)



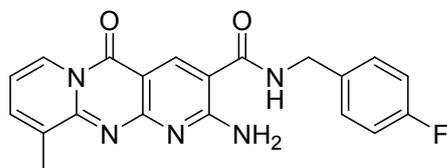
Yield: 83.2 %; White solid; M.p. 320.2 – 322.0 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.46 (t, *J* = 5.8 Hz, 1H), 8.87 (s, 1H), 8.68 (d, *J* = 7.0 Hz, 1H), 8.02 (s, 2H), 7.69 (d, *J* = 6.4 Hz, 1H), 7.36 (s, 2H), 7.35 (s, 2H), 7.27 (td, *J* = 8.0 Hz, *J* = 3.6 Hz, 1H), 6.99 (t, *J* = 6.8 Hz, 1H), 4.48 (d, *J* = 5.6 Hz, 2H), 2.45 (s, 3H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 166.33, 162.09, 158.20, 157.99, 150.44, 139.33, 137.42, 135.37, 133.16, 128.29, 127.34, 126.80, 125.13, 112.71, 110.88, 101.13, 42.54, 17.91. HRMS-ESI (*m/z*): calcd for C₂₀H₁₈N₅O₂ [M+H⁺], 360.1460; found, 360.1461.

2-amino-10-methyl-5-oxo-*N*-(1-phenylethyl)-5*H*-dipyrido[1,2-*a*:2',3'-*d*]pyrimidine-3-carboxamide(6b)



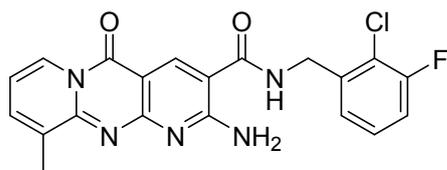
Yield: 79.4 %; White solid; M.p. 320.2 – 322.0 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.27 (d, *J* = 7.8 Hz, 1H), 8.93 (s, 1H), 8.70 (d, *J* = 7.2 Hz, 1H), 7.95 (s, 2H), 7.70 (dt, *J* = 6.8 Hz, *J* = 1.6 Hz, 1H), 7.46 – 7.39 (m, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.20 (m, 1H), 7.00 (t, *J* = 7.0 Hz, 1H), 5.16 (m, 1H), 2.45 (s, 3H), 1.51 (d, *J* = 7.0 Hz, 3H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 165.61, 162.08, 158.17, 158.00, 150.41, 144.67, 137.61, 135.34, 133.17, 128.26, 126.65, 126.04, 125.12, 112.73, 111.07, 101.07, 48.46, 22.01, 17.91. HRMS-ESI (*m/z*): calcd for C₂₁H₂₀N₅O₂ [M+H⁺], 374.1617; found, 374.1616.

2-amino-*N*-(4-fluorobenzyl)-10-methyl-5-oxo-5*H*-dipyrido[1,2-*a*:2',3'-*d*]pyrimidine-3-carboxamide(6c)



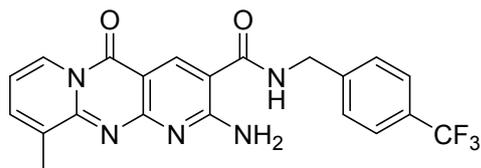
Yield: 76.5 %; White solid; M.p. 315.0 – 317.4 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.46 (t, *J* = 5.8 Hz, 1H), 8.86 (s, 1H), 8.68 (d, *J* = 7.2 Hz, 1H), 8.03 (s, 2H), 7.69 (d, *J* = 6.8 Hz, 1H), 7.46 – 7.36 (m, 2H), 7.24 – 7.12 (m, 2H), 7.00 (t, *J* = 7.0 Hz, 1H), 4.45 (d, *J* = 5.6 Hz, 2H), 2.45 (s, 3H). ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ -116.10. ¹³C NMR (100 MHz, DMSO) δ 166.34, 162.38, 161.04 (d, *J* = 214.3 Hz), 158.12 (d, *J* = 23.2 Hz), 150.46, 137.45, 135.54 (d, *J* = 2.9 Hz), 135.38, 133.17, 129.41, 129.33, 125.14, 115.02 (d, *J* = 21.1 Hz), 112.71, 110.82, 101.11, 41.88, 17.91. HRMS-ESI (m/z): calcd for C₂₀H₁₇FN₅O₂ [M+H⁺], 378.1366; found, 378.1367.

2-amino-*N*-(2-chloro-3-fluorobenzyl)-10-methyl-5-oxo-5*H*-dipyrido[1,2-*a*:2',3'-*d*]pyrimidine-3-carboxamide(6d)



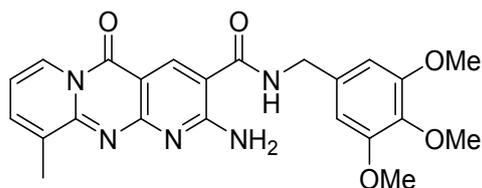
Yield: 71.3 %; White solid; M.p. 337.1 – 338.7 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.76 (t, *J* = 5.6 Hz, 1H), 8.56 (s, 1H), 8.45 (d, *J* = 7.2 Hz, 1H), 7.78 (s, 2H), 7.45 (d, *J* = 6.6 Hz, 1H), 6.75 (t, *J* = 7.0 Hz, 1H), 2.90 (t, *J* = 6.2 Hz, 2H), 2.20 (s, 3H). ¹³C NMR (100 MHz, DMSO) δ 166.60, 162.05, 158.60, 158.16 (d, *J* = 27.8 Hz), 157.38 (d, *J* = 244 Hz), 157.25, 150.53, 138.86, 137.75, 135.47, 133.19, 128.26 (d, *J* = 8.2 Hz), 125.17, 124.33 (d, *J* = 3.1 Hz), 118.67 (d, *J* = 17.5 Hz), 115.15 (d, *J* = 21.1 Hz), 112.77, 110.52, 101.16, 40.33 (d, *J* = 2.8 Hz), 17.91. ¹⁹F NMR (376 MHz, DMSO) δ -115.61. HRMS-ESI (m/z): calcd for C₂₀H₁₆Cl³⁵FN₅O₂ [M+H⁺], 412.0977; found, 412.0976, calcd for C₂₀H₁₆Cl³⁷FN₅O₂ [M+H⁺], 414.0947; found, 414.0946.

2-amino-10-methyl-5-oxo-*N*-(4-(trifluoromethyl)benzyl)-5*H*-dipyrido[1,2-*a*:2',3'-*d*]pyrimidine-3-carboxamide(6e)



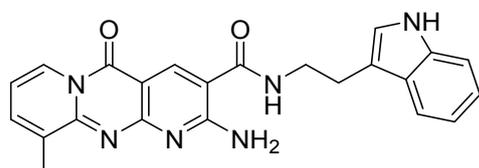
Yield: 78.2 %; White solid; M.p. 328.1 – 329.3 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.56 (t, *J* = 5.2 Hz, 1H), 8.90 (s, 1H), 8.69 (d, *J* = 7.2 Hz, 1H), 8.03 (s, 2H), 7.78-7.67 (m, 2H), 7.59 (s, 1H), 7.57 (s, 1H), 7.00 (t, *J* = 7.0 Hz, 1H), 4.56 (d, *J* = 5.2 Hz, 2H), 2.45 (s, 3H). ¹⁹F NMR (376 MHz, DMSO) δ -60.79. ¹³C NMR (100 MHz, DMSO) δ 166.50, 162.06, 158.26, 158.01, 150.50, 144.23, 137.57, 135.44, 133.17, 129.44 (q, *J* = 71.9 Hz), 127.97, 127.32, 125.22 (q, *J* = 2.7 Hz), 124.15 (q, *J* = 219.2 Hz), 112.75, 110.57, 101.16, 42.26, 17.91. HRMS-ESI (m/z): calcd for C₂₁H₁₇F₃N₅O₂ [M+H⁺], 428.1334; found, 428.1333.

2-amino-10-methyl-5-oxo-*N*-(3,4,5-trimethoxybenzyl)-5*H*-dipyrido[1,2-*a*:2',3'-*d*]pyrimidine-3-carboxamide(6f)



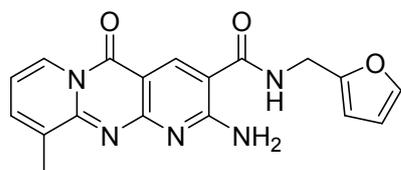
Yield: 74.1 %; White solid; M.p. 281.9 – 283.1 °C; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 9.38 (t, $J = 5.8$ Hz, 1H), 8.85 (s, 1H), 8.74 – 8.59 (m, 1H), 8.01 (s, 2H), 7.69 (d, $J = 6.4$ Hz, 1H), 7.00 (t, $J = 7.0$ Hz, 1H), 6.69 (s, 2H), 4.41 (d, $J = 5.2$ Hz, 2H), 3.77 (s, 6H), 3.64 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 166.33, 162.05, 158.19, 157.99, 152.76, 150.43, 137.42, 136.39, 135.36, 134.93, 133.16, 125.13, 112.72, 111.09, 104.84, 101.13, 59.94, 55.80, 42.85, 17.91. HRMS-ESI (m/z): calcd for $\text{C}_{23}\text{H}_{24}\text{N}_5\text{O}_5$ [$\text{M}+\text{H}^+$], 450.1777; found, 450.1776.

N-(2-(1H-indol-3-yl)ethyl)-2-amino-10-methyl-5-oxo-5H-dipyrido[1,2-a:2',3'-d]pyrimidine-3-carboxamide(6g)



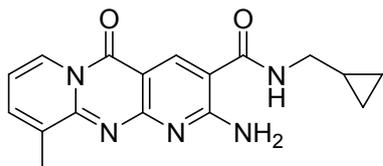
Yield: 58.1 %; Pale yellow solid; M.p. 301.3 – 301.8 °C; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 10.84 (s, 1H), 9.04 (t, $J = 5.6$ Hz, 1H), 8.79 (s, 1H), 8.73 – 8.64 (m, 2H), 8.04 (s, 2H), 7.69 (dt, $J = 6.8, 1.4$ Hz, 1H), 7.60 (d, $J = 7.8$ Hz, 1H), 7.35 (d, $J = 8.0$ Hz, 1H), 7.20 (d, $J = 2.2$ Hz, 1H), 7.00 (t, $J = 7.0$ Hz, 2H), 3.55 (q, $J = 7.4$ Hz, 2H), 2.98 (t, $J = 7.2$ Hz, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 166.28, 162.10, 158.13, 157.97, 150.37, 137.17, 136.21, 135.30, 133.15, 127.22, 125.15, 125.12, 122.60, 120.90, 118.22, 112.68, 111.79, 111.36, 111.33, 101.08, 40.05, 24.93, 17.92. HRMS-ESI (m/z): calcd for $\text{C}_{23}\text{H}_{21}\text{N}_6\text{O}_2$ [$\text{M}+\text{H}^+$], 413.1726; found, 413.1727.

2-amino-N-(furan-2-ylmethyl)-10-methyl-5-oxo-5H-dipyrido[1,2-a:2',3'-d]pyrimidine-3-carboxamide(6h)



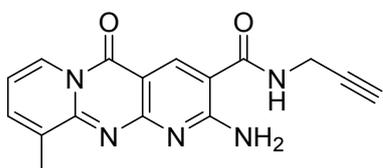
Yield: 69.3 %; White solid; M.p. 310.4 – 312.1 °C; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 9.39 (t, $J = 5.6$ Hz, 1H), 8.84 (s, 1H), 8.68 (d, $J = 7.2$ Hz, 1H), 8.01 (s, 2H), 7.70 (d, $J = 6.8$ Hz, 1H), 7.64 – 7.57 (m, 1H), 7.00 (t, $J = 7.0$ Hz, 1H), 6.42 (dd, $J = 3.2, 1.6$ Hz, 1H), 6.32 (d, $J = 3.2$ Hz, 1H), 4.46 (d, $J = 5.4$ Hz, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 166.26, 162.04, 158.21, 157.98, 152.04, 150.48, 142.09, 137.64, 135.40, 133.16, 125.14, 112.72, 110.66, 110.48, 107.07, 101.11, 35.87, 17.91. HRMS-ESI (m/z): calcd for $\text{C}_{18}\text{H}_{16}\text{N}_5\text{O}_3$ [$\text{M}+\text{H}^+$], 350.1253; found, 350.1252.

2-amino-N-(cyclopropylmethyl)-10-methyl-5-oxo-5H-dipyrido[1,2-a:2',3'-d]pyrimidine-3-carboxamide(6i)



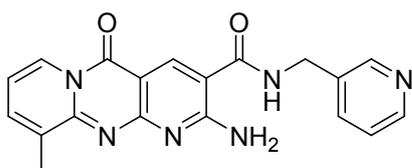
Yield: 65.2 %; White solid; M.p. 315.6 – 317.9 °C; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 9.00 (s, 1H), 8.80 (s, 1H), 8.69 (d, $J = 7.2$ Hz, 1H), 8.02 (s, 2H), 7.69 (d, $J = 4.8$ Hz, 1H), 7.00 (t, $J = 6.8$ Hz, 1H), 3.14 (t, $J = 6.4$ Hz, 2H), 2.45 (s, 3H), 1.06 (s, 1H), 0.46 (d, $J = 6.0$ Hz, 2H), 0.34 – 0.19 (m, 2H). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 166.26, 162.09, 158.11, 157.96, 150.34, 137.20, 135.26, 133.14, 125.08, 112.66, 111.26, 101.05, 43.53, 17.90, 10.80, 3.37. HRMS-ESI (m/z): calcd for $\text{C}_{17}\text{H}_{18}\text{N}_5\text{O}_2$ [$\text{M}+\text{H}^+$], 324.1460; found, 324.1461.

2-amino-10-methyl-5-oxo-N-(prop-2-yn-1-yl)-5H-dipyrido[1,2-a:2',3'-d]pyrimidine-3-carboxamide(6j)



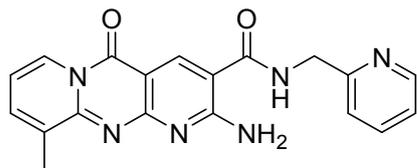
Yield: 72.2 %; White solid; M.p. 298.7 – 300.3 °C ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 9.34 (s, 1H), 8.82 (s, 1H), 8.69 (d, $J = 7.2$ Hz, 1H), 8.02 (s, 2H), 7.70 (dt, $J = 6.4, 1.6$ Hz, 1H), 7.00 (t, $J = 7.0$ Hz, 1H), 4.05 (d, $J = 2.4$ Hz, 2H), 3.16 (t, $J = 2.4$ Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 166.17, 162.00, 158.24, 157.97, 150.51, 137.71, 135.43, 133.16, 125.15, 112.72, 110.40, 101.12, 81.02, 72.94, 28.46, 17.91. HRMS-ESI (m/z): calcd for $\text{C}_{16}\text{H}_{14}\text{N}_5\text{O}_2$ [$\text{M}+\text{H}^+$], 308.1147; found, 308.1145.

2-amino-10-methyl-5-oxo-N-(pyridin-3-ylmethyl)-5H-dipyrido[1,2-a:2',3'-d]pyrimidine-3-carboxamide(6k)



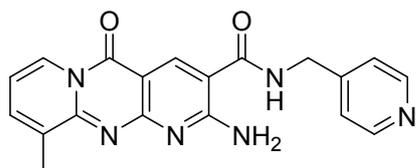
Yield: 78.6 %; Pale yellow solid; M.p. 287.0 - 290.1 °C ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ = 9.49 (t, $J = 5.8$ Hz, 1H), 8.86 (s, 1H), 8.68 (d, $J = 6.8$ Hz, 1H), 8.64 – 8.56 (d, $J = 1.6$ Hz 1H), 8.48 (dd, $J = 4.8, 1.6$ Hz, 1H), 8.00 (s, 2H), 7.77 (d, $J = 7.8$ Hz, 1H), 7.69 (d, $J = 6.8$ Hz, 1H), 7.39 (dd, $J = 7.6, 4.8$ Hz, 1H), 6.99 (t, $J = 7.0$ Hz, 1H), 4.50 (d, $J = 5.6$ Hz, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ = 166.46, 162.03, 158.23, 157.98, 150.47, 148.93, 148.13, 137.53, 135.41, 135.26, 134.76, 133.16, 125.13, 123.50, 112.73, 110.64, 101.14, 40.35, 17.90. HRMS-ESI (m/z): calcd for $\text{C}_{19}\text{H}_{17}\text{N}_6\text{O}_2$ [$\text{M}+\text{H}^+$], 361.1413; found, 361.1415.

2-amino-10-methyl-5-oxo-N-(pyridin-2-ylmethyl)-5H-dipyrido[1,2-a:2',3'-d]pyrimidine-3-carboxamide(6l)



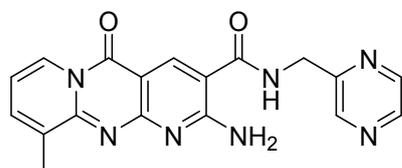
Yield: 71.6 %; Pale yellow solid; M.p. 285.3 – 286.7.1 °C ^1H NMR (400 MHz, DMSO- d_6) δ 9.51 (t, $J = 5.6$ Hz, 1H), 8.92 (s, 1H), 8.69 (d, $J = 7.2$ Hz, 1H), 8.54 (d, $J = 4.6$ Hz, 1H), 8.02 (s, 2H), 7.78 (t, $J = 7.6$ Hz, 1H), 7.69 (d, $J = 6.6$ Hz, 1H), 7.38 (d, $J = 7.8$ Hz, 1H), 7.33 – 7.25 (m, 1H), 7.00 (t, $J = 7.0$ Hz, 1H), 4.57 (d, $J = 5.6$ Hz, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, DMSO- d_6) δ 166.57, 162.07, 158.47, 158.25, 158.01, 150.48, 148.86, 137.57, 136.73, 135.40, 133.18, 125.16, 122.11, 121.01, 112.73, 110.93, 101.17, 44.54, 17.91. HRMS-ESI (m/z): calcd for $\text{C}_{19}\text{H}_{19}\text{N}_6\text{O}_3$ [$\text{M}+\text{H}_3\text{O}^+$], 379.1519; found, 379.1518.

2-amino-10-methyl-5-oxo-N-(pyridin-4-ylmethyl)-5H-dipyrido[1,2-a:2',3'-d]pyrimidine-3-carboxamide(6m)



Yield: 75.4 %; White solid; M.p. 298.3 – 299.6 °C ^1H NMR (400 MHz, DMSO- d_6) δ 9.52 (t, $J = 5.6$ Hz, 1H), 8.92 (s, 1H), 8.69 (d, $J = 7.0$ Hz, 1H), 8.53 (d, $J = 5.6$ Hz, 2H), 8.02 (s, 2H), 7.69 (d, $J = 6.6$ Hz, 1H), 7.35 (d, $J = 5.2$ Hz, 2H), 7.00 (t, $J = 7.0$ Hz, 1H), 4.50 (d, $J = 5.6$ Hz, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, DMSO- d_6) δ 166.64, 162.06, 158.28, 158.01, 150.52, 149.56, 148.28, 137.62, 135.44, 133.18, 125.16, 122.20, 112.74, 110.52, 101.18, 41.69, 17.90. HRMS-ESI (m/z): calcd for $\text{C}_{19}\text{H}_{19}\text{N}_6\text{O}_3$ [$\text{M}+\text{H}_3\text{O}^+$], 379.1519; found, 379.1520.

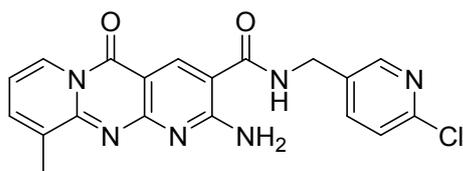
2-amino-10-methyl-5-oxo-N-(pyrazin-2-ylmethyl)-5H-dipyrido[1,2-a:2',3'-d]pyrimidine-3-carboxamide(6n)



Yield: 63.2 %; White solid; M.p. 298.3 – 299.6 °C ^1H NMR (400 MHz, DMSO- d_6) δ 9.57 (s, 1H), 8.91 (s, 1H), 8.69 (q, $J = 3.1$ Hz, 2H), 8.62 (t, $J = 2.0$ Hz, 1H), 8.56 (d, $J = 2.6$ Hz, 1H), 8.01 (s, 2H), 7.70 (d, $J = 6.7$ Hz, 1H), 7.00 (t, $J = 7.0$ Hz, 1H), 4.63 (s, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, DMSO- d_6) δ 166.66, 162.01, 158.25, 157.98, 154.03, 150.48, 143.95, 143.50, 143.19, 137.71, 135.40, 133.16, 125.14, 112.71, 110.57, 101.16, 42.68, 17.90. HRMS-ESI (m/z): calcd for $\text{C}_{18}\text{H}_{16}\text{N}_7\text{O}_2$ [$\text{M}+\text{H}^+$], 362.1365; found, 362.1366.

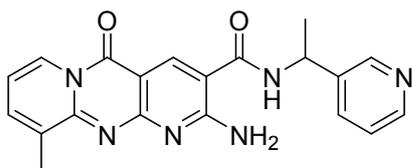
2-amino-N-((6-chloropyridin-3-yl)methyl)-10-methyl-5-oxo-5H-dipyrido[1,2-

***a:2',3'-d*]pyrimidine-3-carboxamide(6o)**



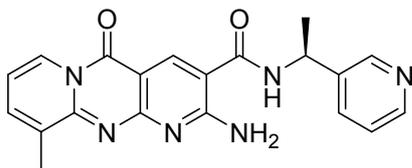
Yield: 61.8 %; White solid; M.p. 309.9 – 311.7 °C ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.48 (t, *J* = 5.8 Hz, 1H), 8.86 (s, 1H), 8.68 (m, 1H), 8.42 (d, *J* = 2.4 Hz, 1H), 8.02 (s, 3H), 7.84 (m, 1H), 7.70 (m, 1H), 7.51 (d, *J* = 8.2 Hz, 1H), 4.48 (d, *J* = 5.6 Hz, 2H), 2.45 (s, 3H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 166.52, 162.01, 158.26, 158.01, 150.51, 149.10, 148.75, 139.12, 137.61, 135.45, 134.44, 133.17, 125.18, 124.03, 112.75, 110.50, 101.15, 21.86, 17.90. HRMS-ESI (*m/z*): calcd for C₁₉H₁₆Cl³⁵N₆O₂ [M+H⁺], 395.1023; found, 395.1024; calcd for C₁₉H₁₆Cl³⁷N₆O₂ [M+H⁺], 397.0994; found, 397.1024.

2-amino-10-methyl-5-oxo-*N*-(1-(pyridin-3-yl)ethyl)-5*H*-dipyrido[1,2-*a:2',3'-d*]pyrimidine-3-carboxamide(6p)



Yield: 78.3 %; White solid; M.p. 312.2 – 313.5 °C ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.32 (d, *J* = 7.6 Hz, 1H), 8.93 (s, 1H), 8.69 (d, *J* = 7.2 Hz, 1H), 8.65 (d, *J* = 2.2 Hz, 1H), 8.47 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.96 (s, 2H), 7.84 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.68 (d, *J* = 6.8 Hz, 1H), 7.39 (dd, *J* = 8.0, 4.8 Hz, 1H), 7.00 (t, *J* = 7.0 Hz, 1H), 5.20 (p, *J* = 7.2 Hz, 1H), 2.44 (s, 3H), 1.55 (d, *J* = 7.2 Hz, 3H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 165.78, 162.03, 158.19, 157.98, 150.42, 147.99, 147.89, 139.84, 137.72, 135.36, 133.68, 133.17, 125.11, 123.48, 112.72, 110.79, 101.08, 46.63, 21.60, 17.90. HRMS-ESI (*m/z*): calcd for C₂₀H₁₉N₆O₂ [M+H⁺], 375.1569; found, 375.1568.

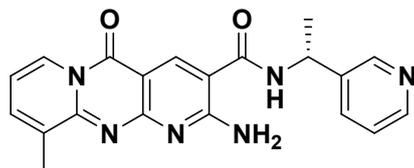
(*S*)-2-amino-10-methyl-5-oxo-*N*-(1-(pyridin-3-yl)ethyl)-5*H*-dipyrido[1,2-*a:2',3'-d*]pyrimidine-3-carboxamide(6q)



Yield: 68.1 %; White solid; M.p. 331.6 – 332.5 °C ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.31 (d, *J* = 7.5 Hz, 1H), 8.93 (s, 1H), 8.70 (d, *J* = 7.1 Hz, 1H), 8.64 (d, *J* = 1.8 Hz, 1H), 8.47 (dd, *J* = 4.7, 1.3 Hz, 1H), 7.94 (s, 2H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.69 (d, *J* = 6.6 Hz, 1H), 7.39 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.00 (t, *J* = 7.0 Hz, 1H), 5.20 (p, *J* = 7.2 Hz, 1H), 2.45 (s, 3H), 1.55 (d, *J* = 7.1 Hz, 3H). ¹³C NMR (101 MHz, DMSO) δ

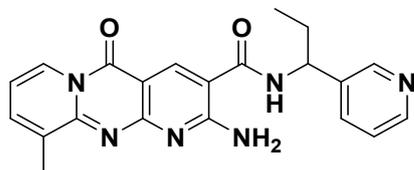
165.80, 162.05, 158.23, 158.02, 150.46, 148.01, 147.91, 139.85, 137.74, 135.39, 133.70, 133.19, 125.14, 123.49, 112.75, 110.82, 101.10, 46.64, 21.60, 17.90. HRMS-ESI (m/z): calcd for C₂₀H₁₉N₆O₂ [M+H⁺], 375.1569; found, 375.1570.

(R)-2-amino-10-methyl-5-oxo-N-(1-(pyridin-3-yl)ethyl)-5H-dipyrido[1,2-a:2',3'-d]pyrimidine-3-carboxamide(6r)



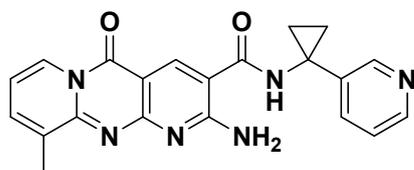
Yield: 72.3 %; White solid; M.p. 329.8 – 330.4 °C ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.31 (d, *J* = 7.6 Hz, 1H), 8.93 (s, 1H), 8.70 (d, *J* = 6.9 Hz, 1H), 8.64 (d, *J* = 2.3 Hz, 1H), 8.47 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.94 (s, 2H), 7.83 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.70 (dt, *J* = 6.8, 1.4 Hz, 1H), 7.39 (ddd, *J* = 7.9, 4.8, 0.9 Hz, 1H), 7.00 (t, *J* = 7.0 Hz, 1H), 5.20 (p, *J* = 7.0 Hz, 1H), 2.45 (s, 3H), 1.55 (d, *J* = 7.0 Hz, 3H). ¹³C NMR (100 MHz, DMSO) δ 165.80, 162.04, 158.22, 158.02, 150.46, 148.01, 147.90, 139.85, 137.74, 135.40, 133.70, 133.19, 125.14, 123.50, 112.76, 110.82, 101.10, 46.64, 21.60, 17.90. HRMS-ESI (m/z): calcd for C₂₀H₁₉N₆O₂ [M+H⁺], 375.1569; found, 375.1570.

2-amino-10-methyl-5-oxo-N-(1-(pyridin-3-yl)propyl)-5H-dipyrido[1,2-a:2',3'-d]pyrimidine-3-carboxamide(6s)



Yield: 75.7 %; White solid; M.p. 332.3 – 333.3 °C ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.26 (d, *J* = 8.0 Hz, 1H), 8.93 (s, 1H), 8.70 (d, *J* = 6.9 Hz, 0H), 8.63 (d, *J* = 1.9 Hz, 1H), 7.92 (s, 2H), 7.83 (dt, *J* = 7.9, 1.8 Hz, 2H), 7.69 (d, *J* = 6.7 Hz, 1H), 7.39 (dd, *J* = 7.8, 4.8 Hz, 1H), 4.95 (q, *J* = 8.3 Hz, 1H), 2.45 (s, 3H), 2.08 – 1.75 (m, 1H), 0.94 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 166.14, 162.04, 158.23, 158.03, 150.46, 148.38, 148.35, 138.93, 137.63, 135.40, 134.11, 133.20, 125.14, 123.52, 112.76, 110.88, 101.10, 52.84, 28.33, 17.89, 11.23. HRMS-ESI (m/z): calcd for C₂₁H₂₁N₆O₂ [M+H⁺], 389.1726; found, 389.1727.

2-amino-10-methyl-5-oxo-N-(1-(pyridin-3-yl)cyclopropyl)-5H-dipyrido[1,2-a:2',3'-d]pyrimidine-3-carboxamide(6t)



Yield: 79.2 %; White solid; M.p. 299.5 – 300.4 °C ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 9.65 (s, 1H), 8.93 (s, 1H), 8.70 (d, $J = 7.1$ Hz, 1H), 8.49 (d, $J = 2.1$ Hz, 1H), 8.39 (dd, $J = 4.7, 1.3$ Hz, 2H), 7.96 (s, 2H), 7.69 (d, $J = 6.7$ Hz, 1H), 7.64 (dt, $J = 8.0, 1.8$ Hz, 2H), 7.32 (dd, $J = 7.9, 4.7$ Hz, 1H), 7.00 (t, $J = 7.0$ Hz, 1H), 2.45 (s, 3H), 1.35 (s, 4H). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 167.32, 162.06, 158.27, 157.99, 150.50, 146.87, 146.68, 138.68, 137.85, 135.43, 133.19, 132.72, 125.14, 123.08, 112.74, 110.62, 101.12, 32.94, 17.90, 17.46. HRMS-ESI (m/z): calcd for $\text{C}_{21}\text{H}_{19}\text{N}_6\text{O}_2$ [$\text{M}+\text{H}^+$], 387.1569; found, 387.1570.

2.5 ^1H , ^{13}C , ^{19}F NMR and HRMS data

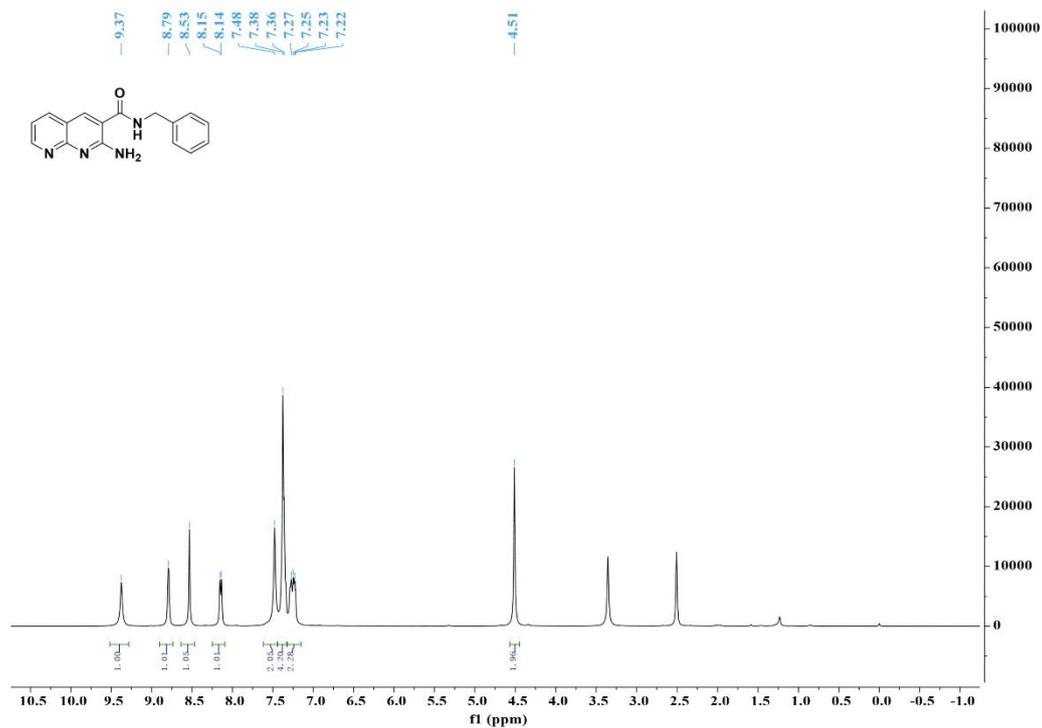


Figure S5 ^1H NMR (400 MHz, $\text{DMSO-}d_6$) spectrum of compound 5a

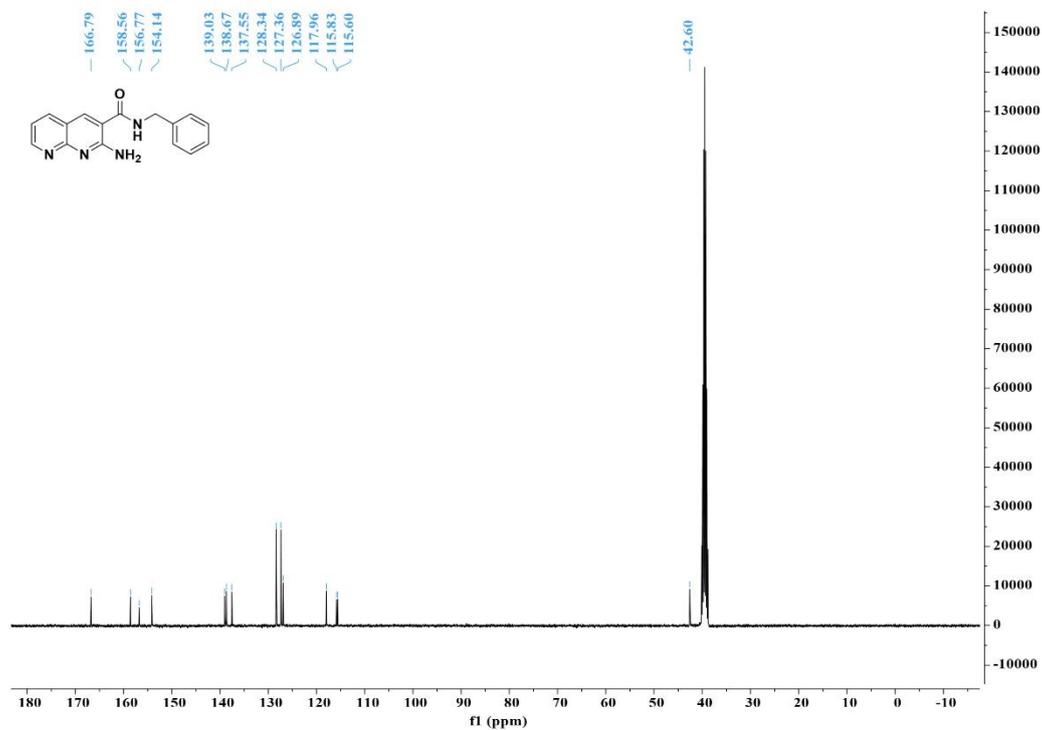


Figure S6 ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) spectrum of compound 5a

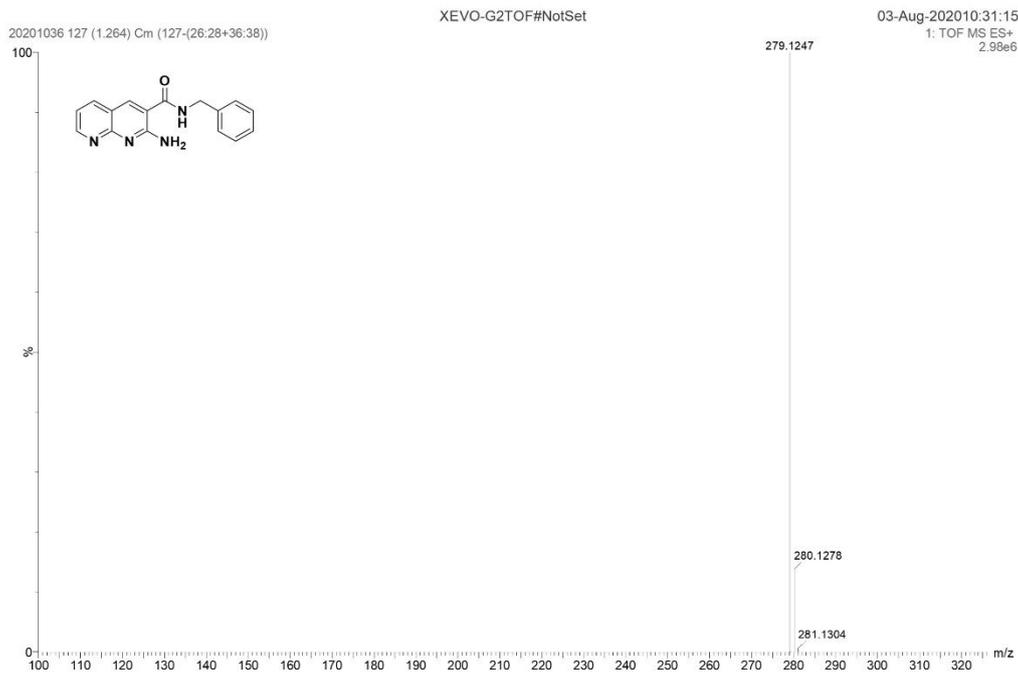


Figure S7 HRMS of compound 5a

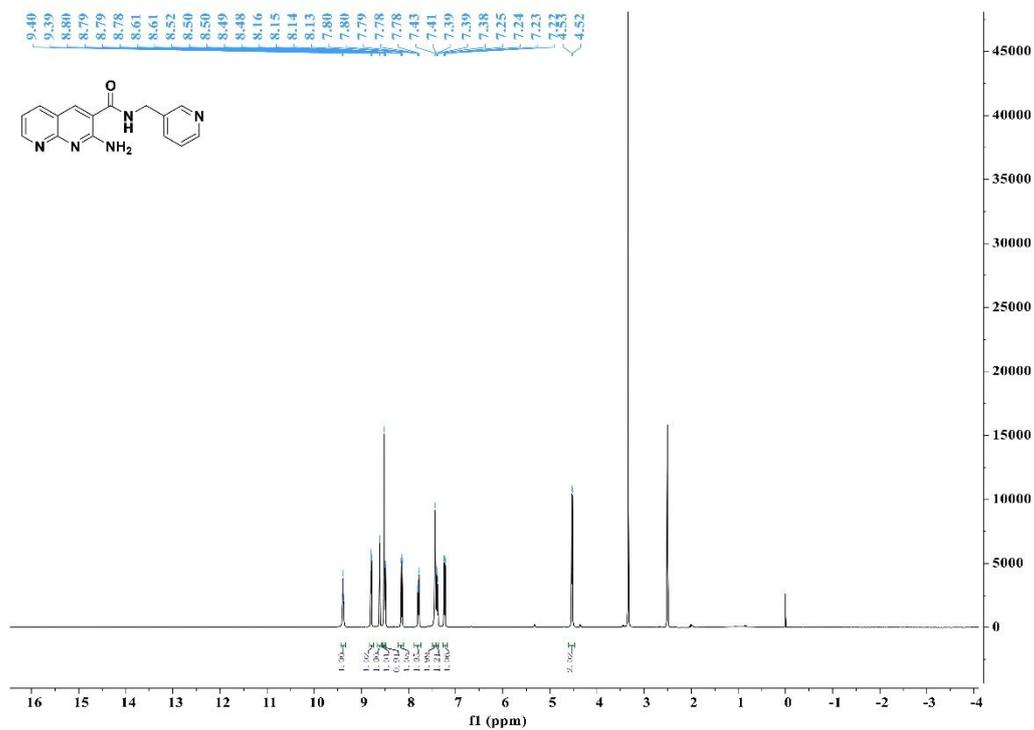


Figure S8 ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound 5b

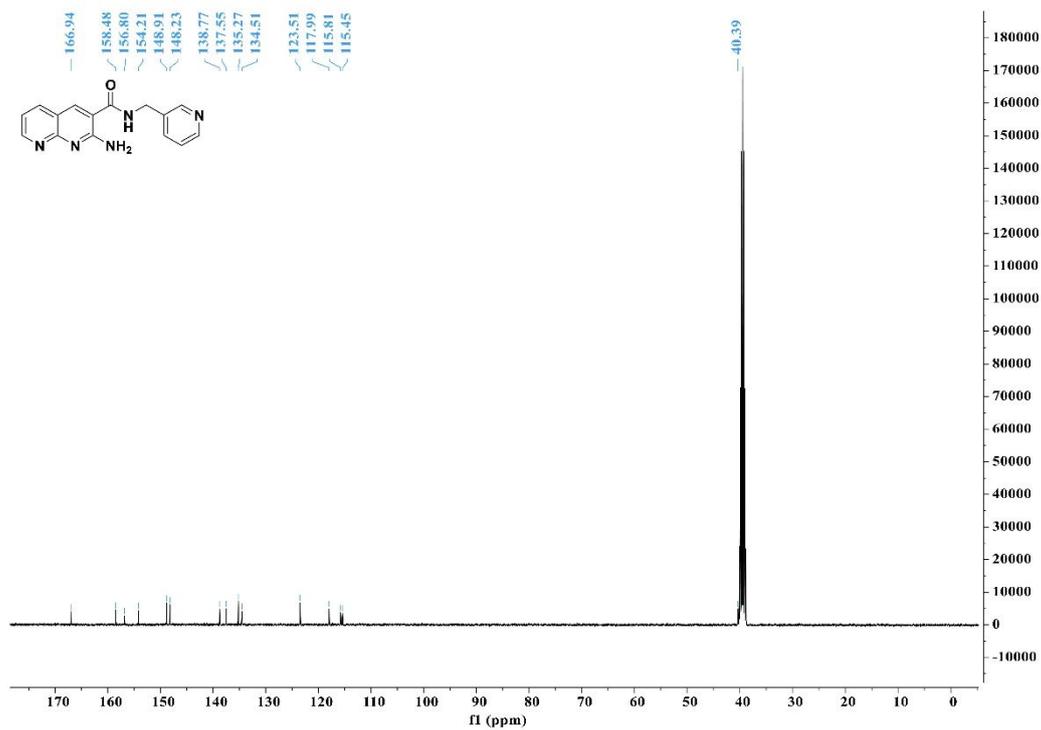


Figure S9 ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) spectrum of compound 5b

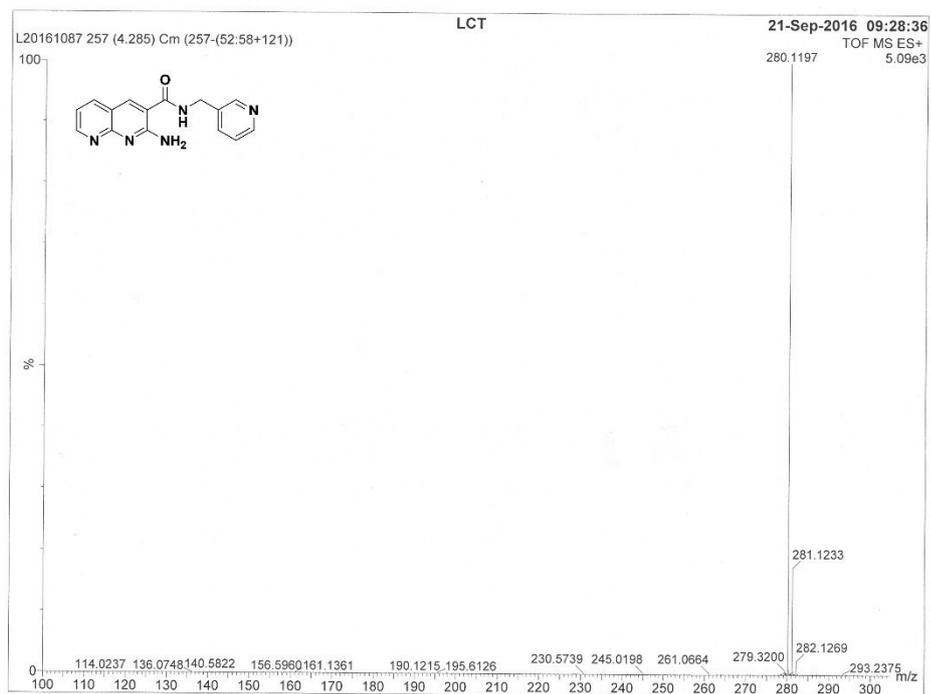


Figure S10 HRMS of compound 5b

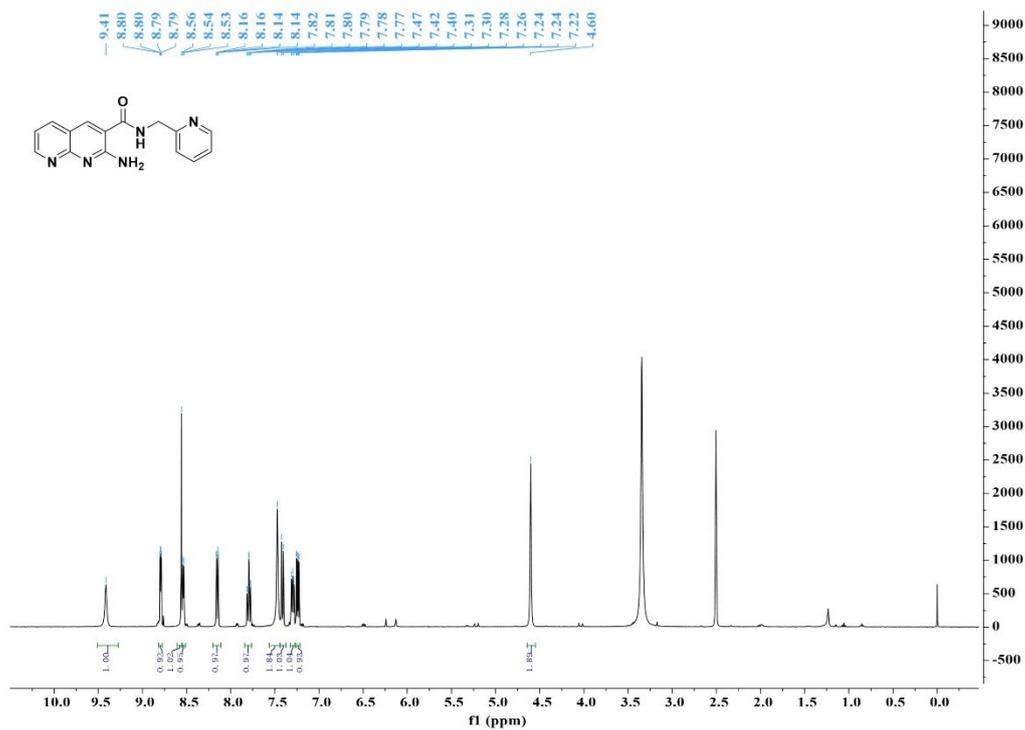


Figure S11 ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound 5c

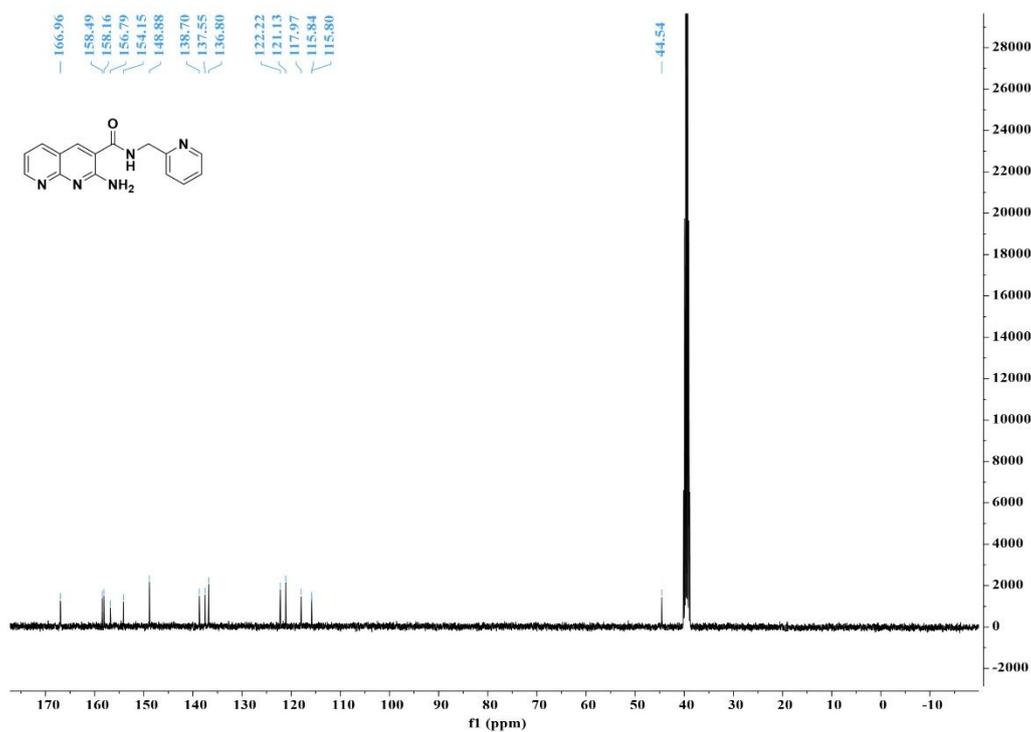


Figure S12 ¹³C NMR (100 MHz, DMSO-*d*₆) spectrum of compound 5c

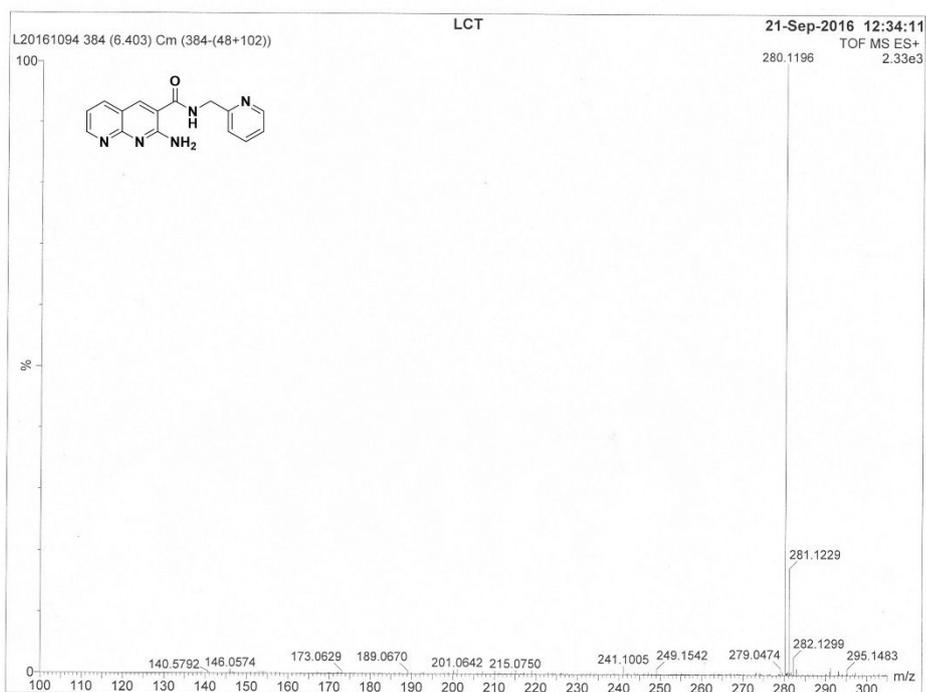


Figure S13 HRMS of compound 5c

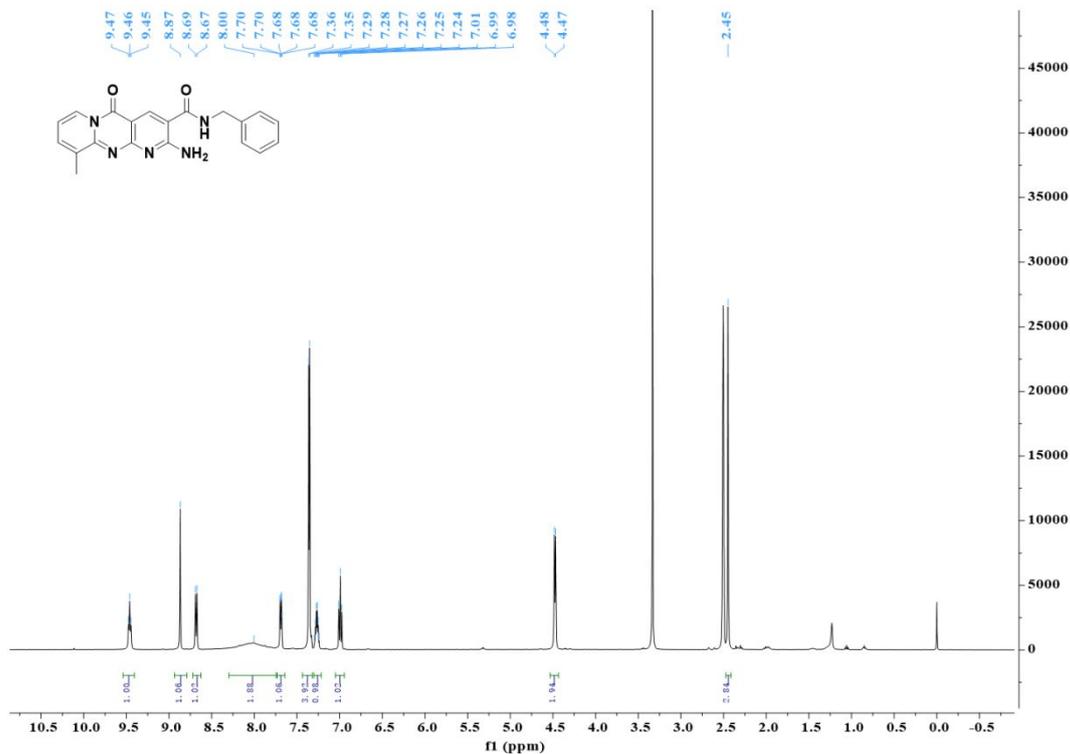


Figure S14 ^1H NMR (400 MHz, $\text{DMSO}-d_6$) spectrum of compound 6a

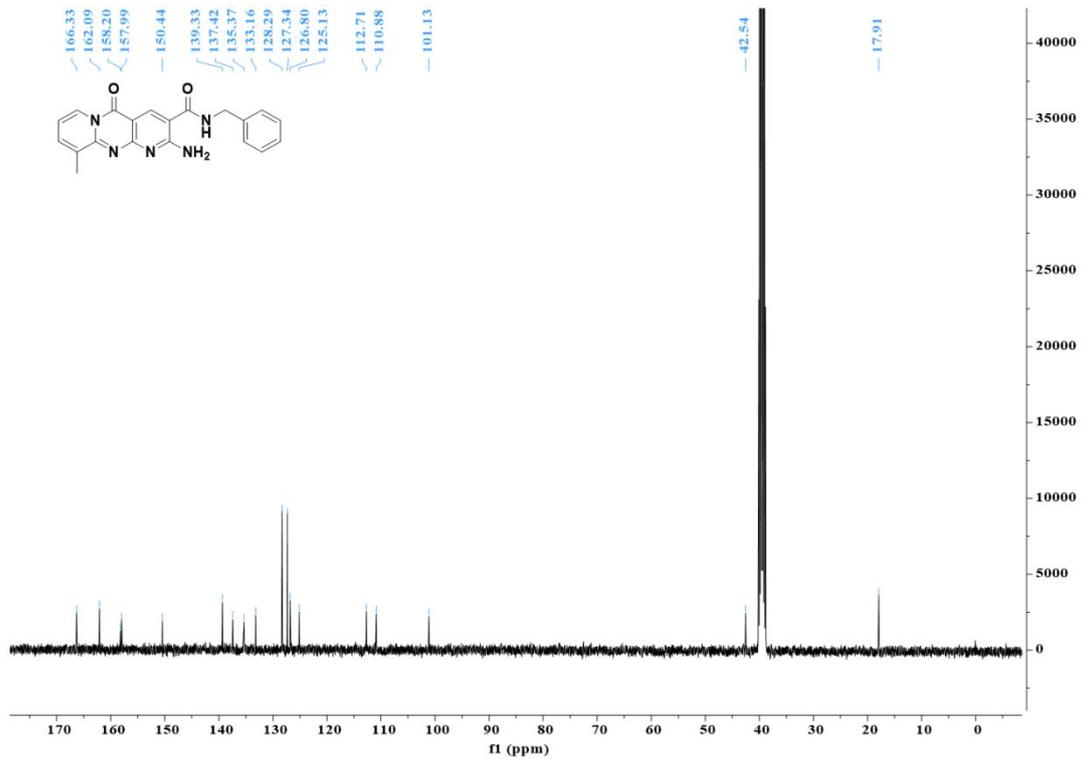


Figure S15 ¹³C NMR (100 MHz, DMSO-*d*₆) spectrum of compound 6a

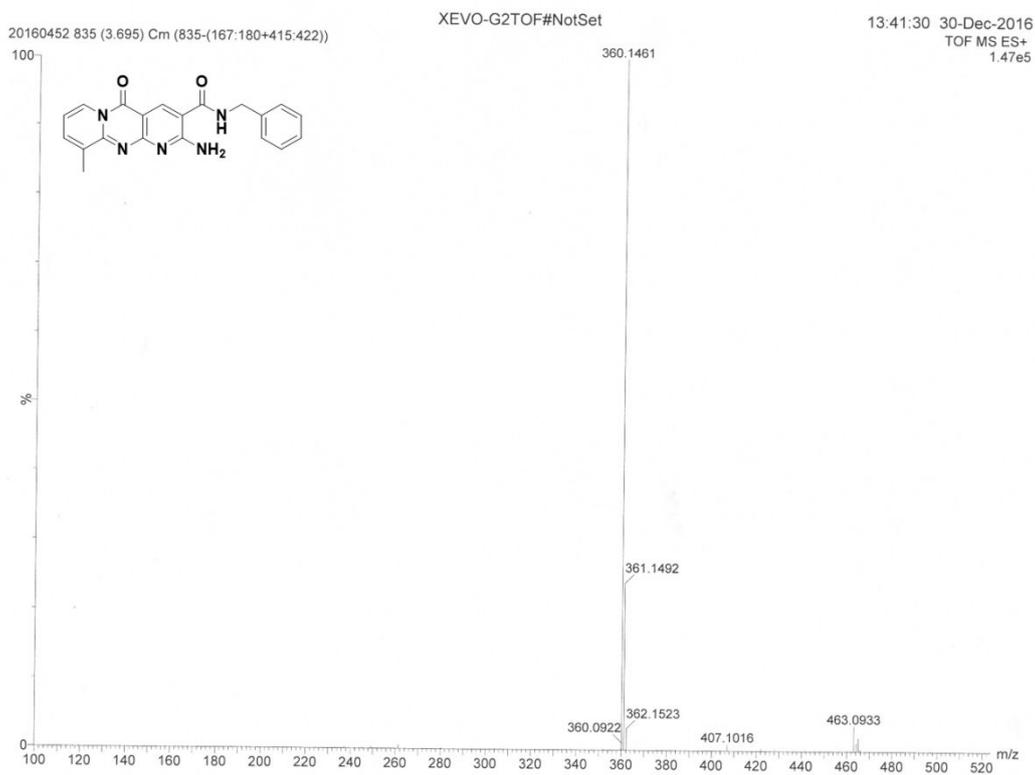


Figure S16 HRMS of compound 6a

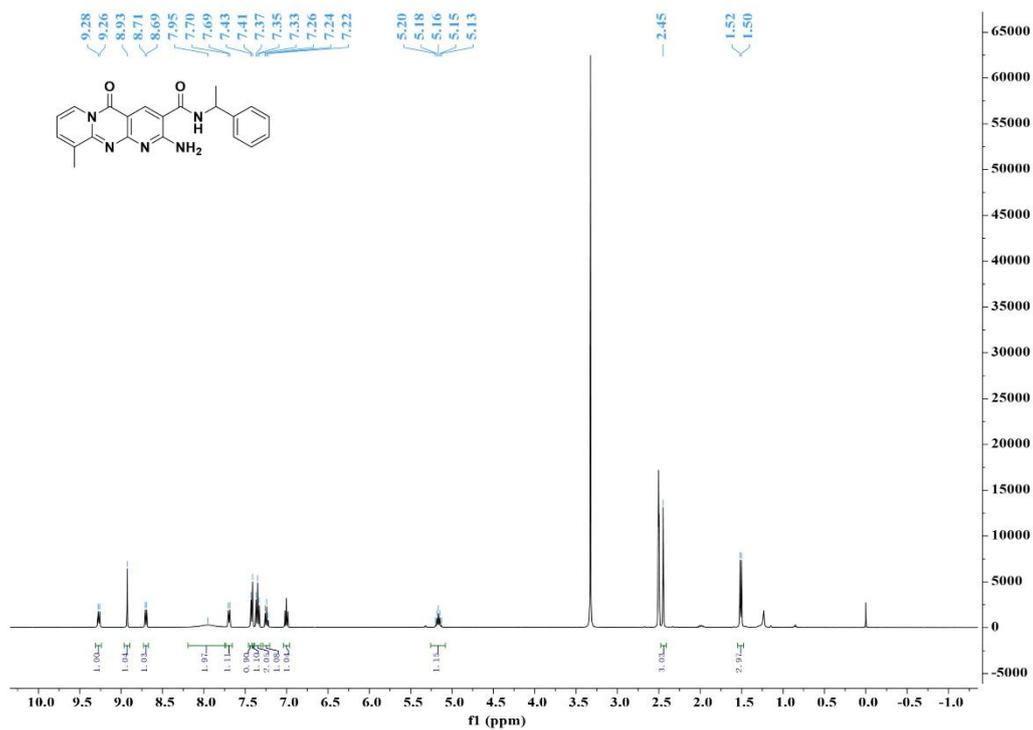


Figure S17 ^1H NMR (400 MHz, $\text{DMSO-}d_6$) spectrum of compound 6b

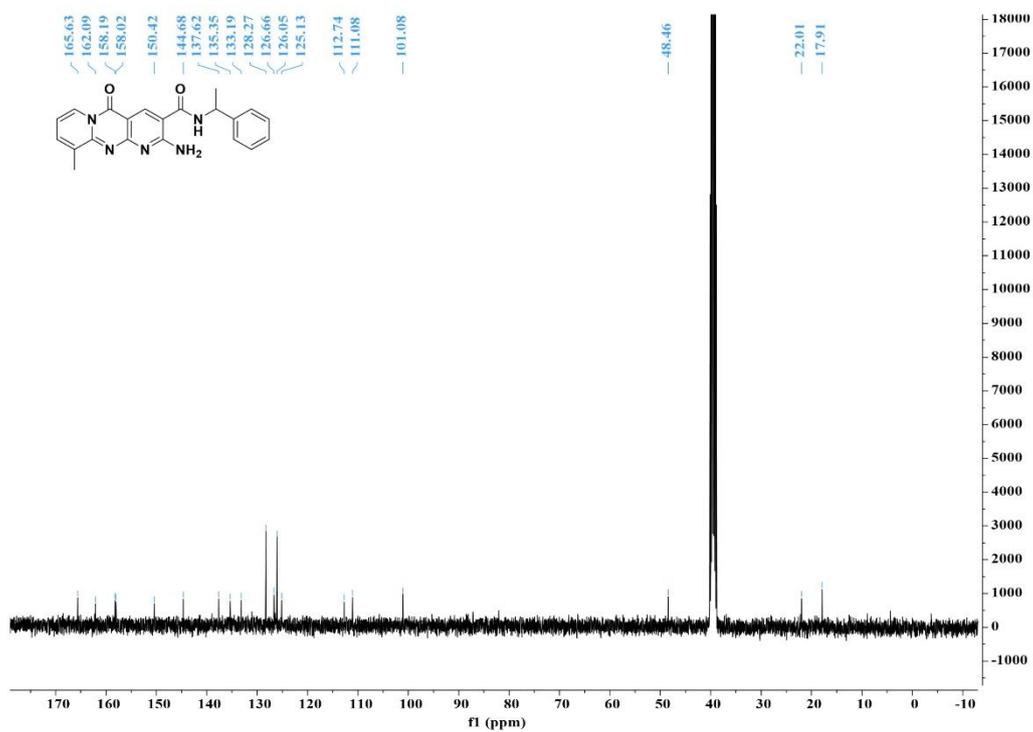


Figure S18 ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) spectrum of compound 6b

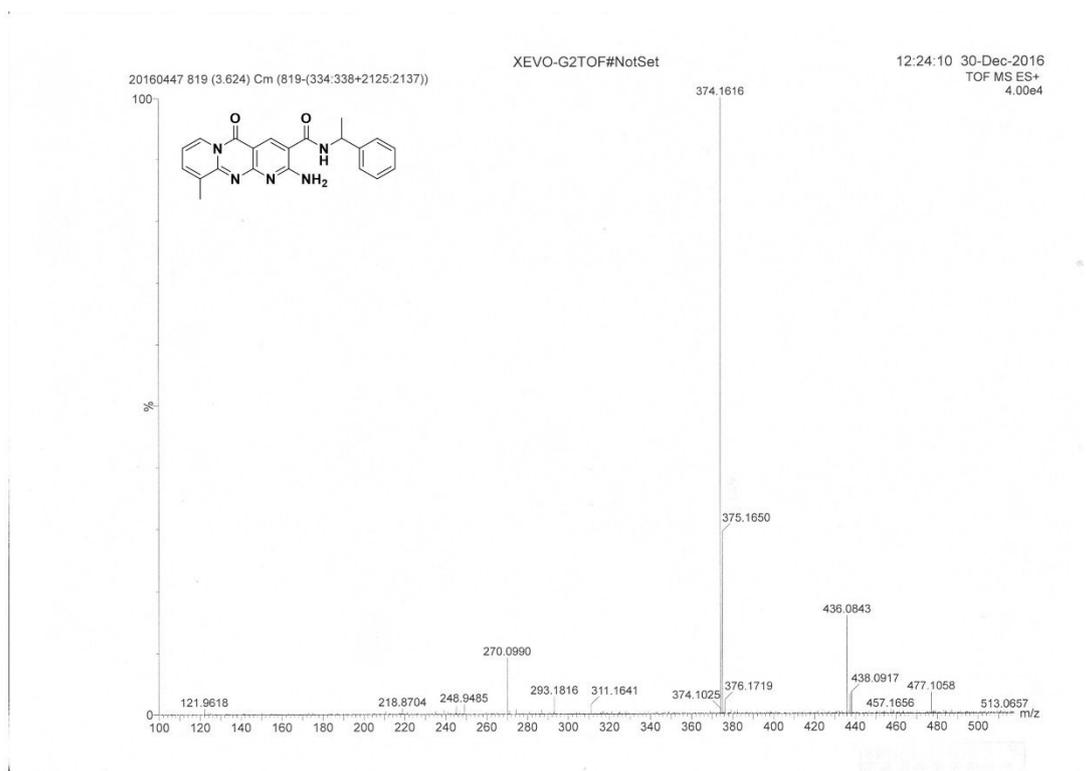


Figure S19 HRMS of compound 6b

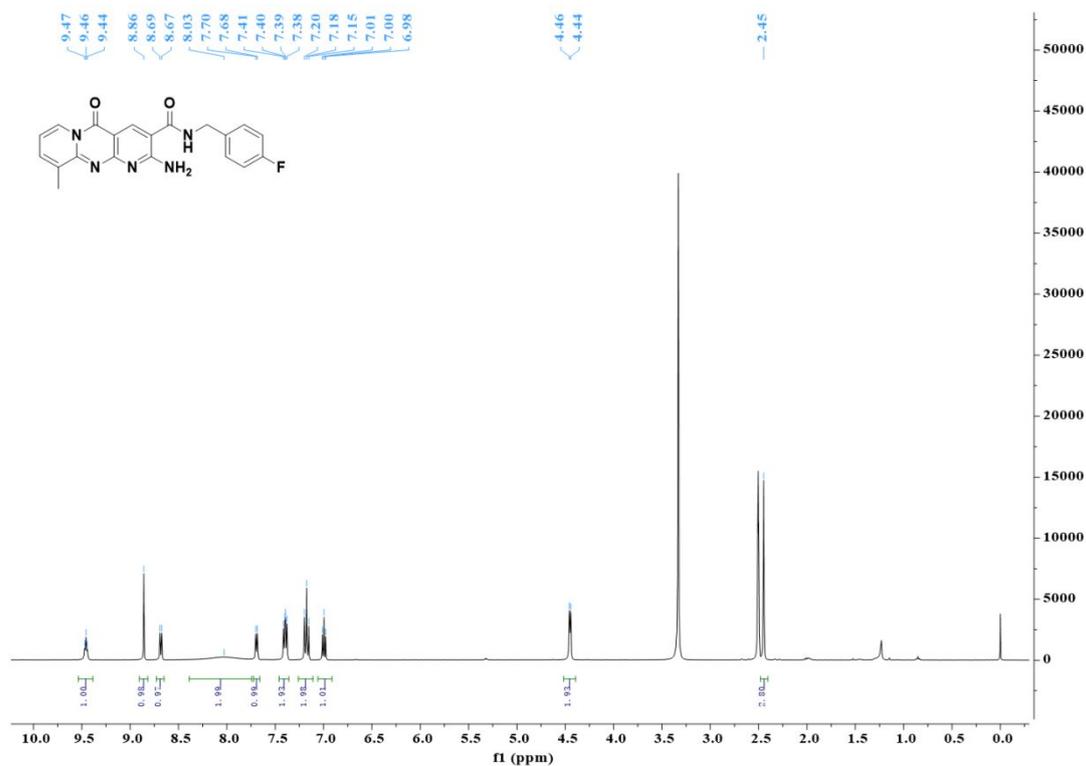


Figure S20 ^1H NMR (400 MHz, $\text{DMSO-}d_6$) spectrum of compound 6c

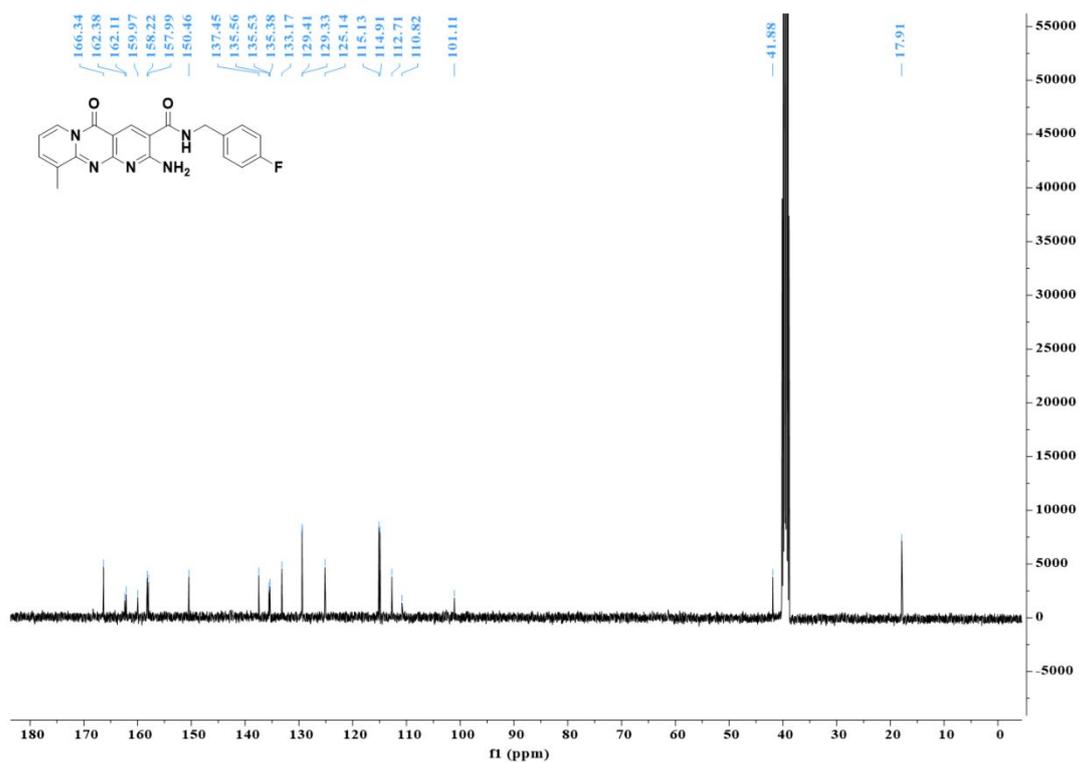


Figure S21 ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) spectrum of compound 6c

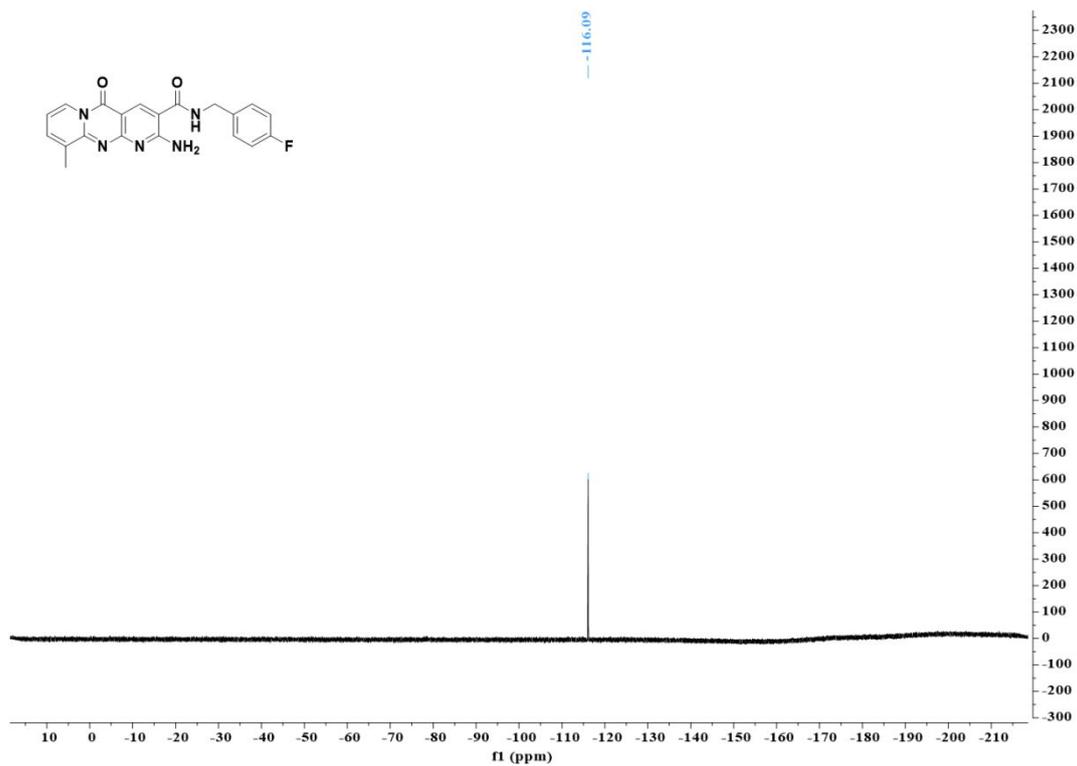


Figure S22 ^{19}F NMR (376 MHz, $\text{DMSO-}d_6$) spectrum of compound 6c

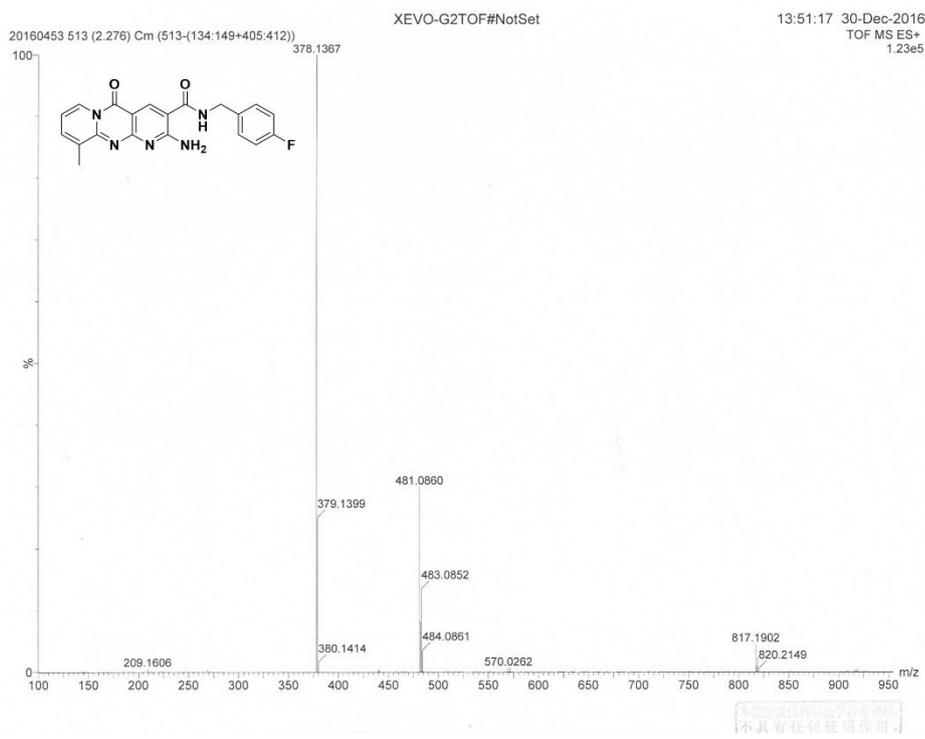


Figure S23 HRMS of compound 6c

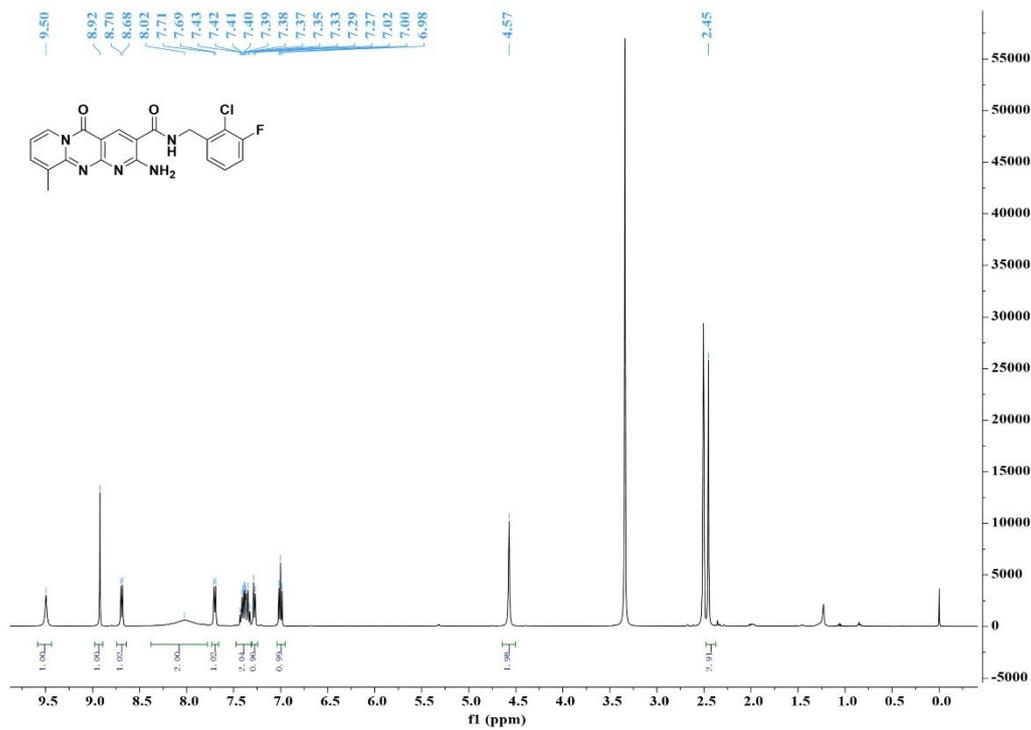


Figure S24 ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound 6d

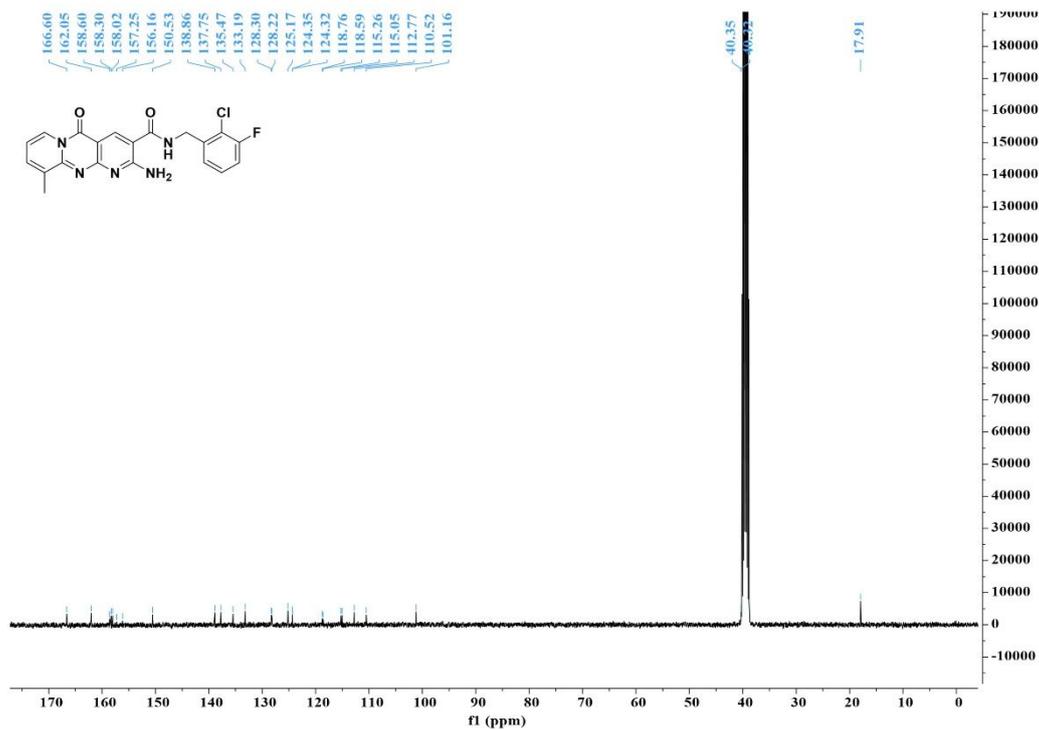


Figure S 25 ¹³C NMR (100 MHz, DMSO-*d*₆) spectrum of compound 6d

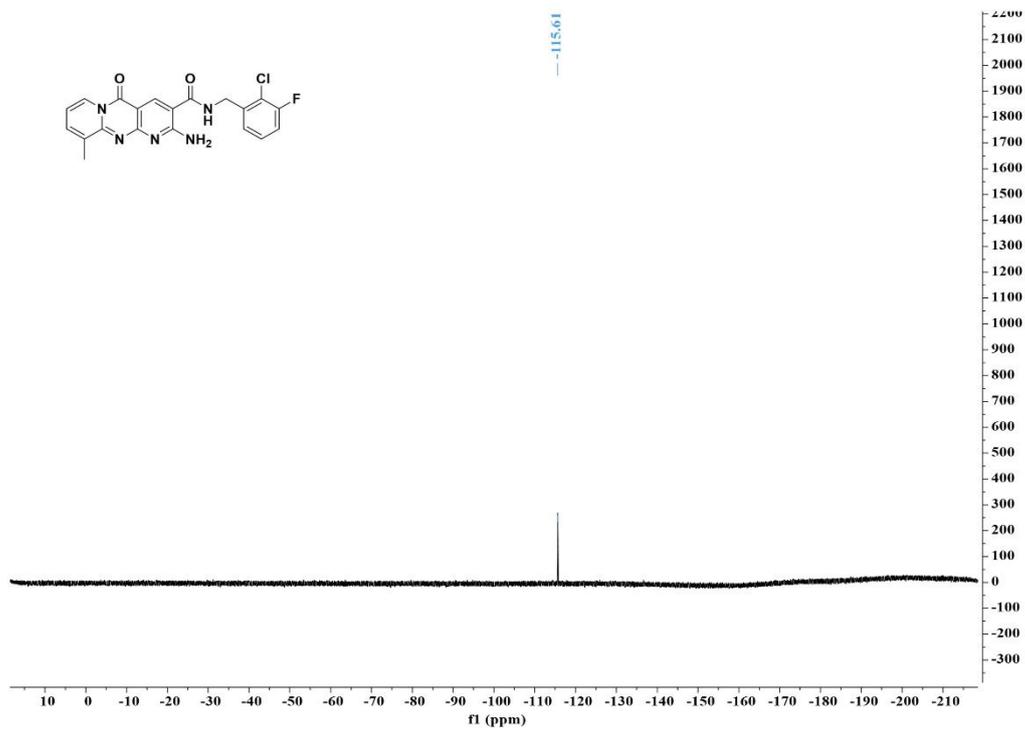


Figure S26 ¹⁹F NMR (376 MHz, DMSO-*d*₆) spectrum of compound 6d

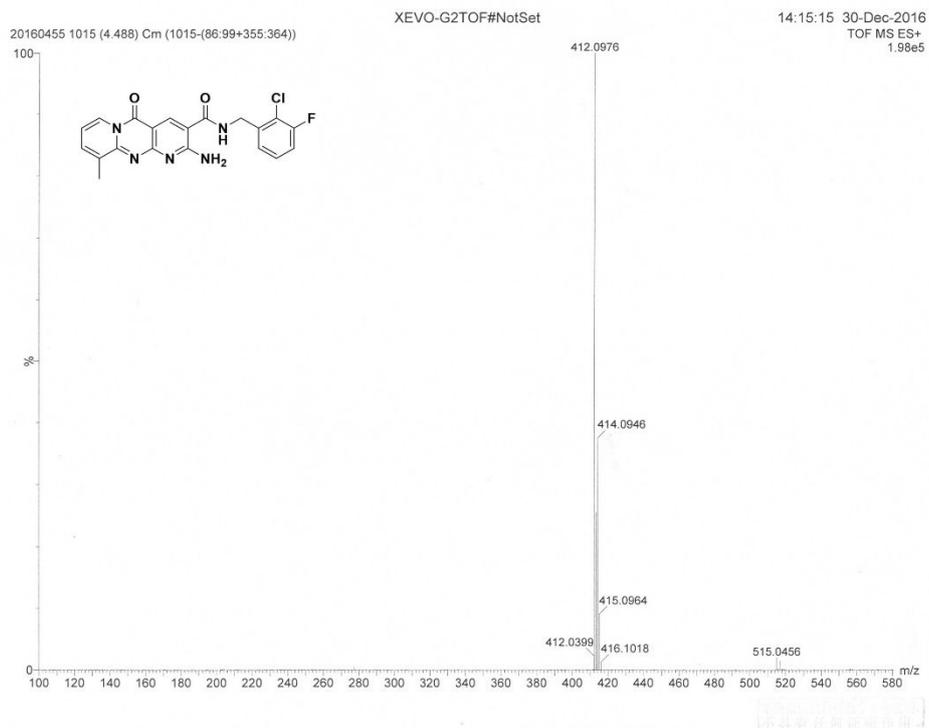


Figure S27 HRMS of compound 6d

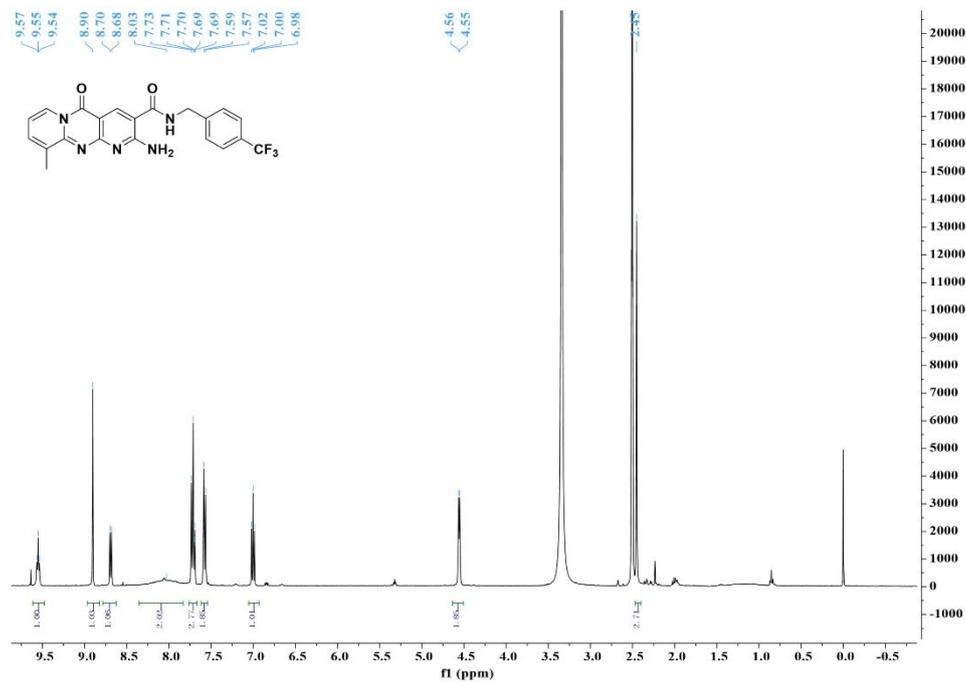


Figure S28 ^1H NMR (400 MHz, $\text{DMSO-}d_6$) spectrum of compound 6e

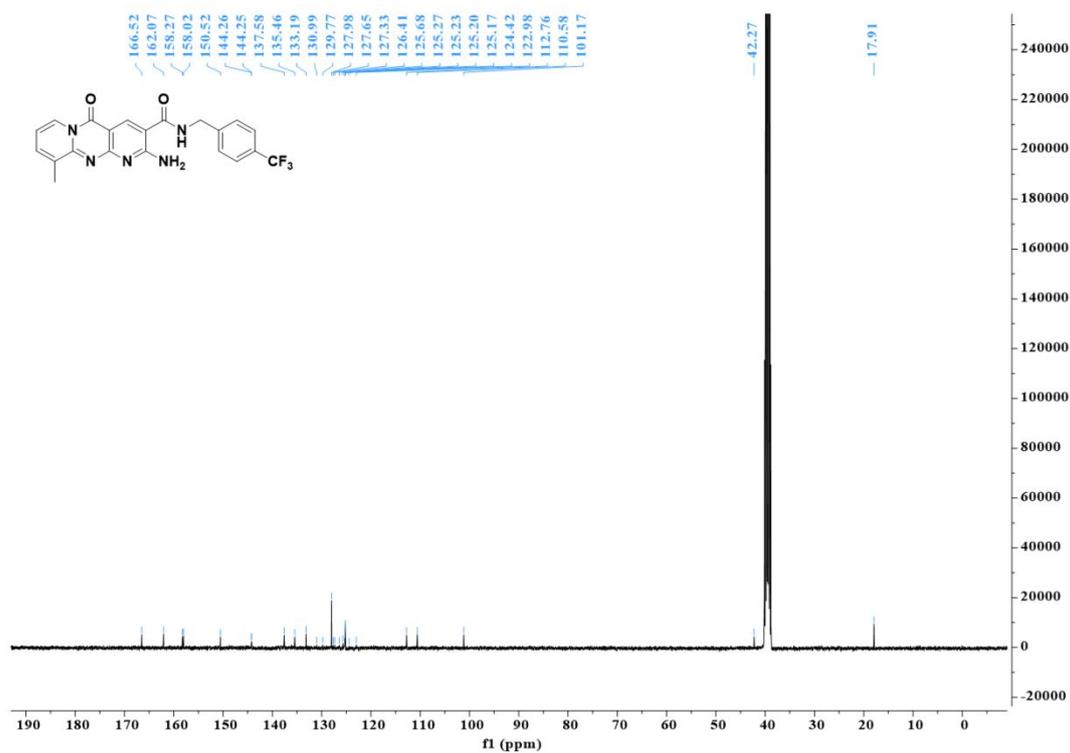


Figure S29 ¹³C NMR (100 MHz, DMSO-*d*₆) spectrum of compound 6e

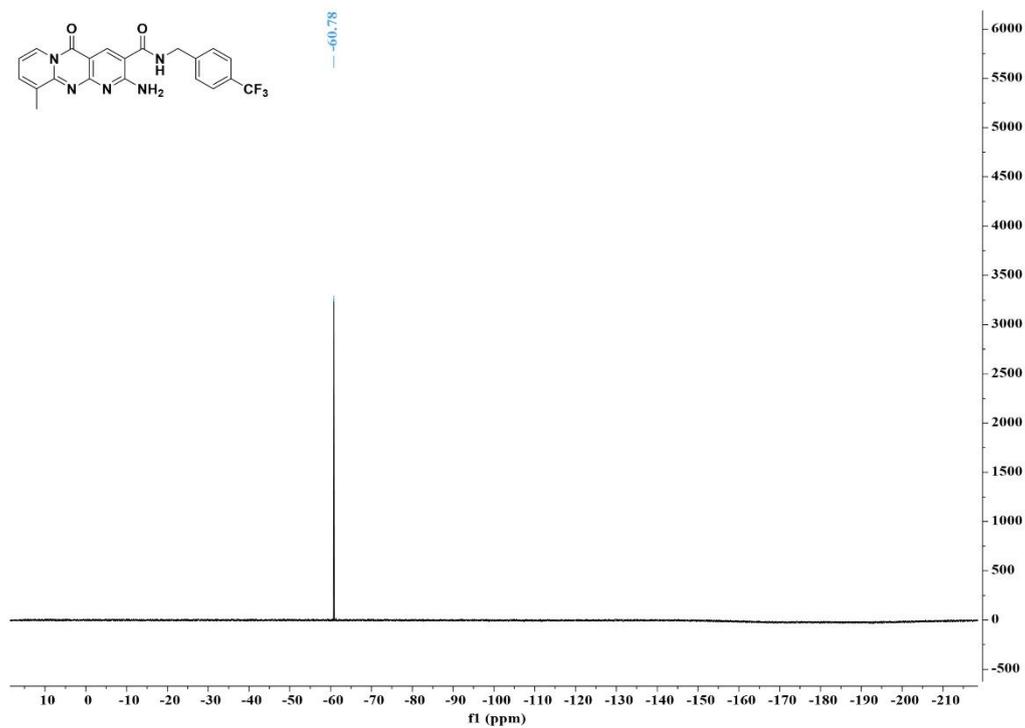


Figure S30 ¹⁹F NMR (376 MHz, DMSO-*d*₆) spectrum of compound 6e

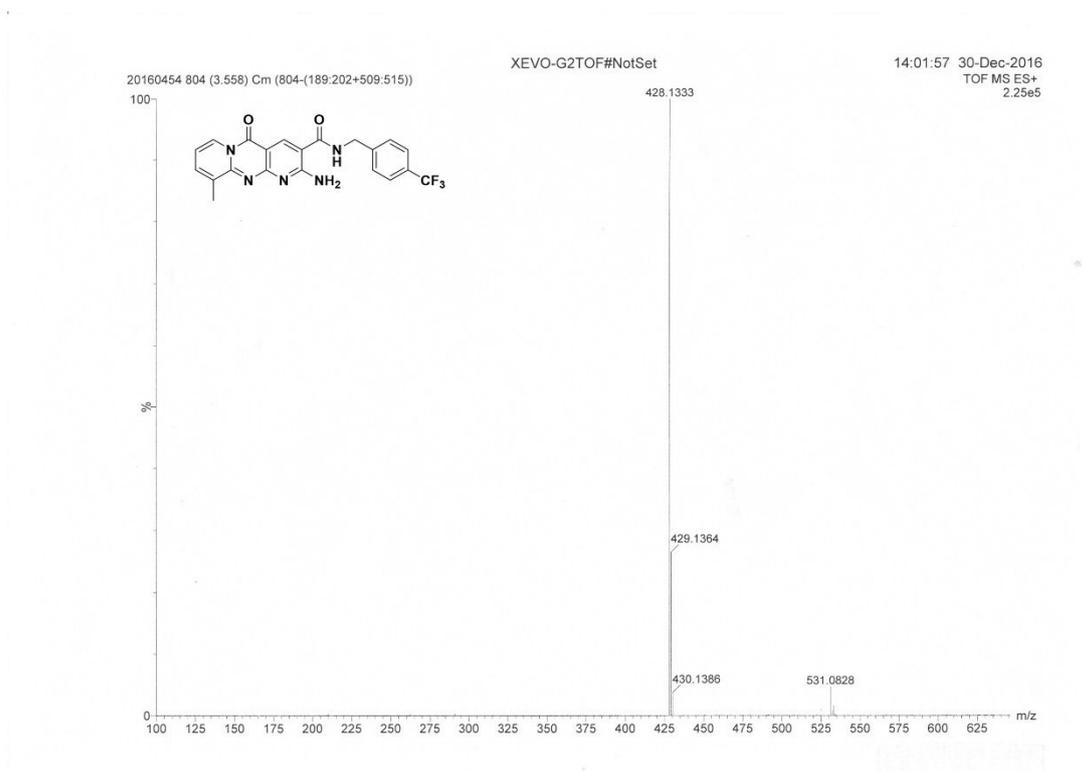


Figure S31 HRMS of compound 6e

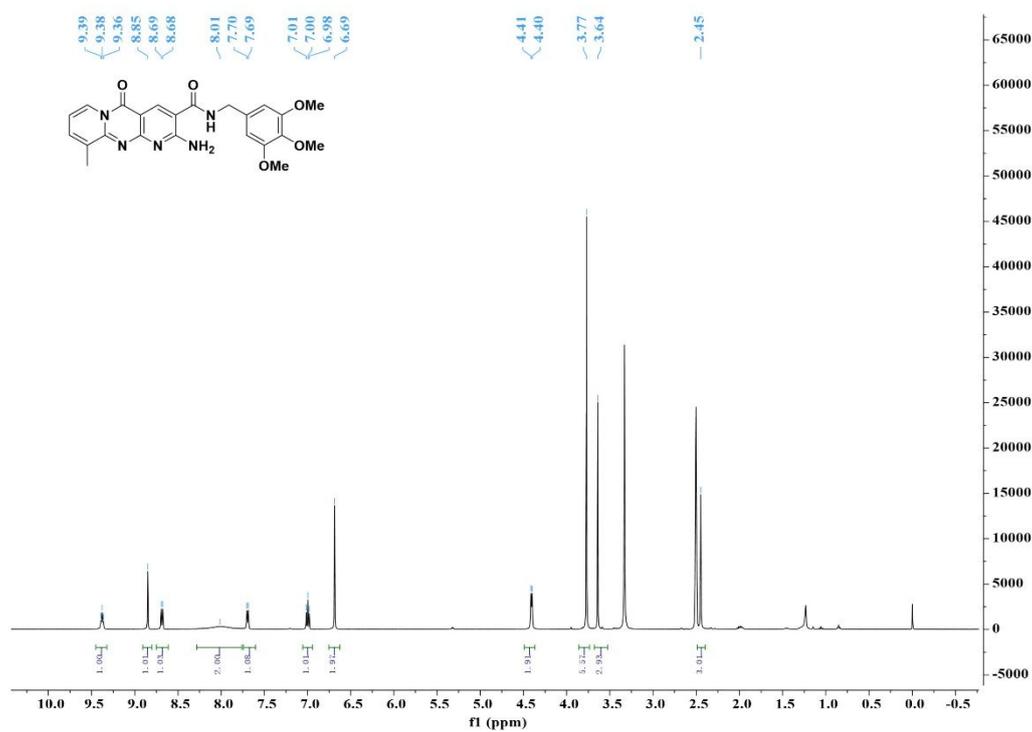


Figure S32 ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound 6f

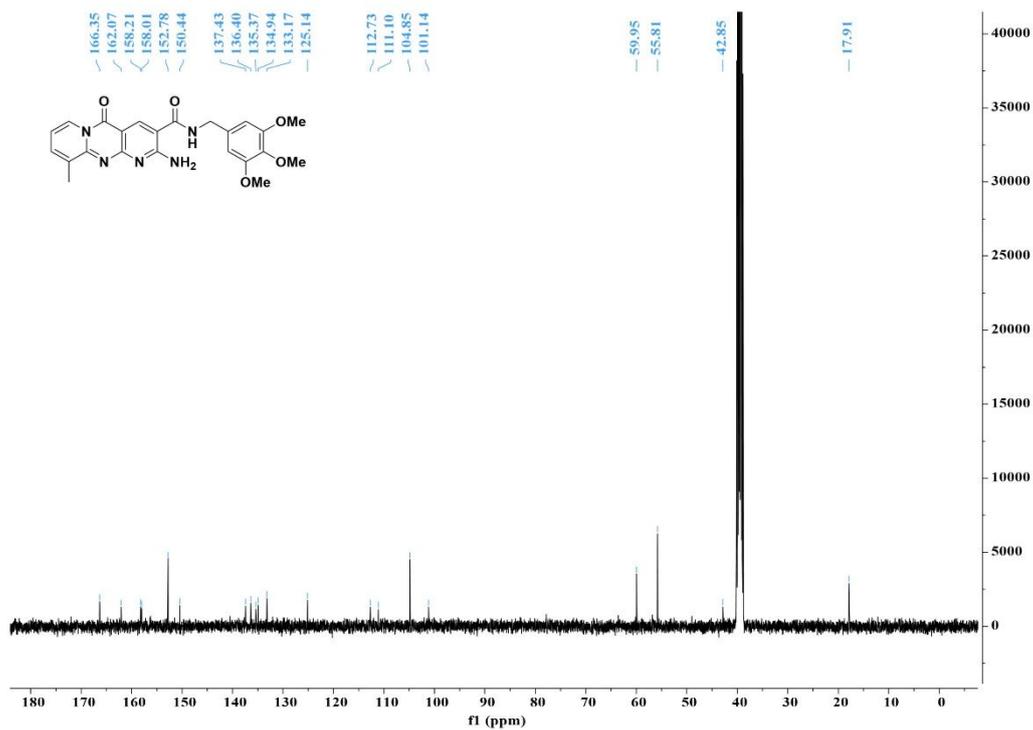


Figure S33 ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) spectrum of compound 6f

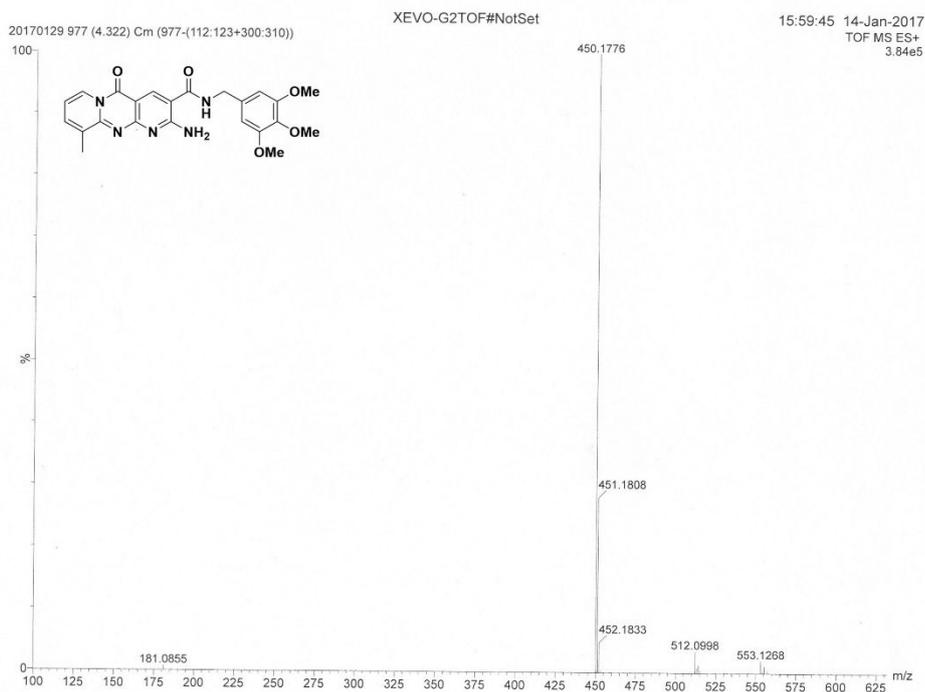


Figure S34 HRMS of compound 6f

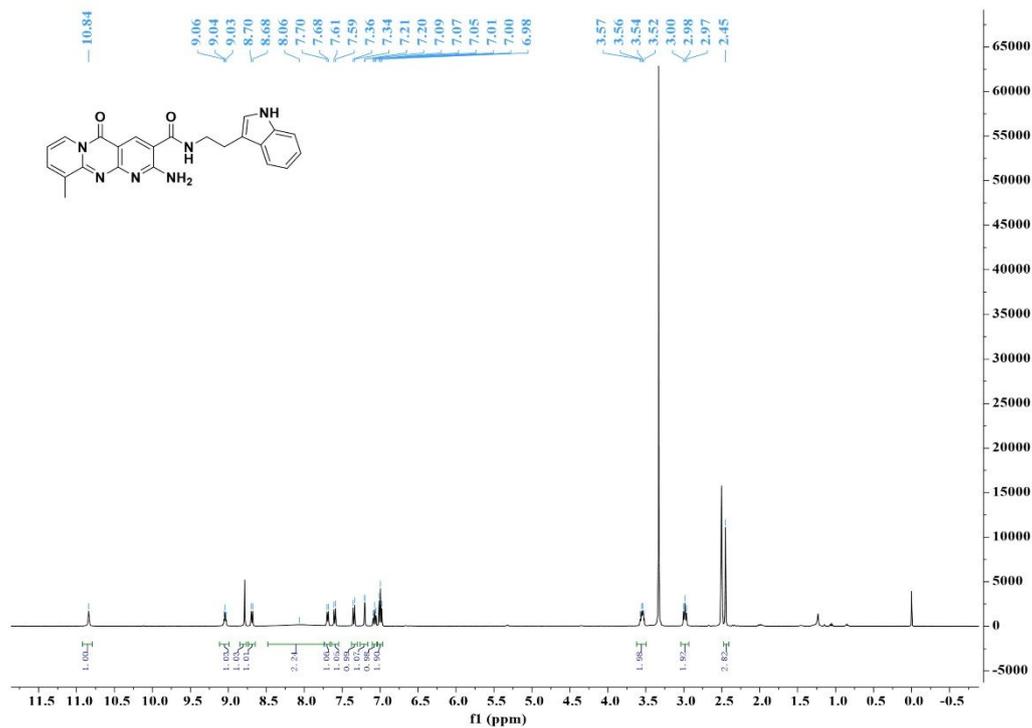


Figure S 35 ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound 6g

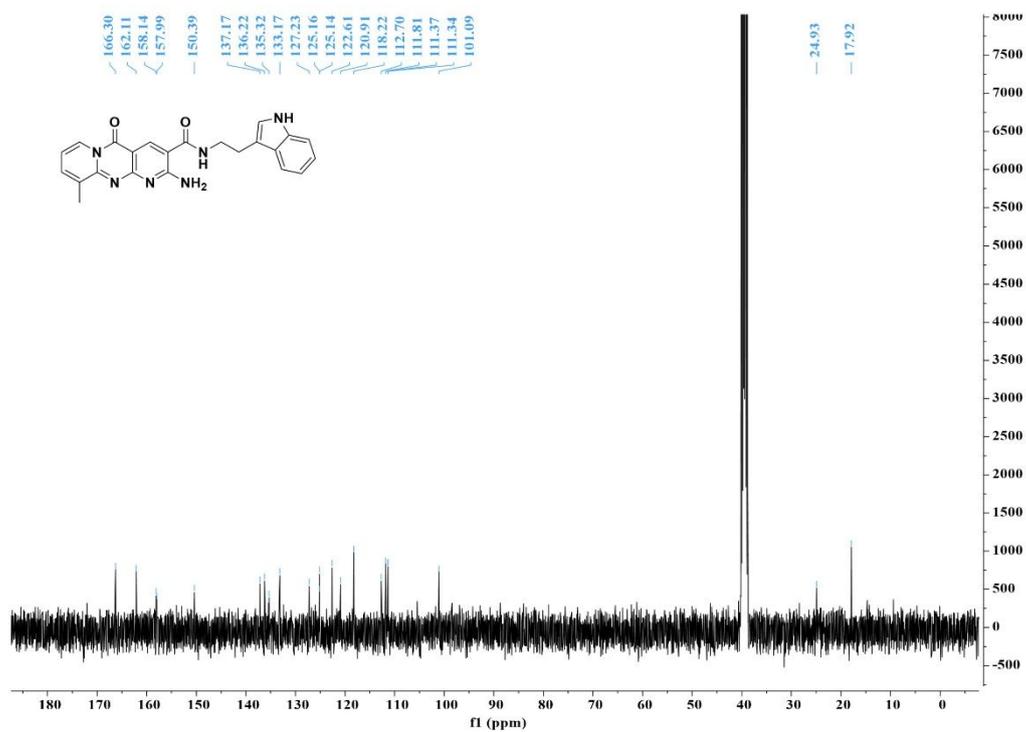


Figure S36 ¹³C NMR (100 MHz, DMSO-*d*₆) spectrum of compound 6g

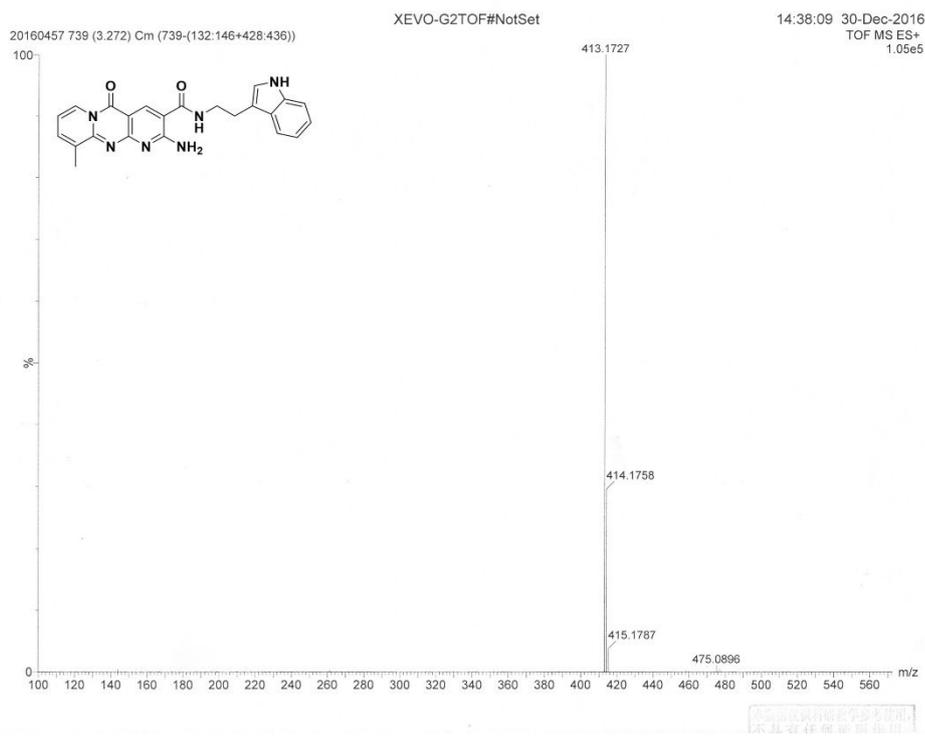


Figure S37 HRMS of compound 6g

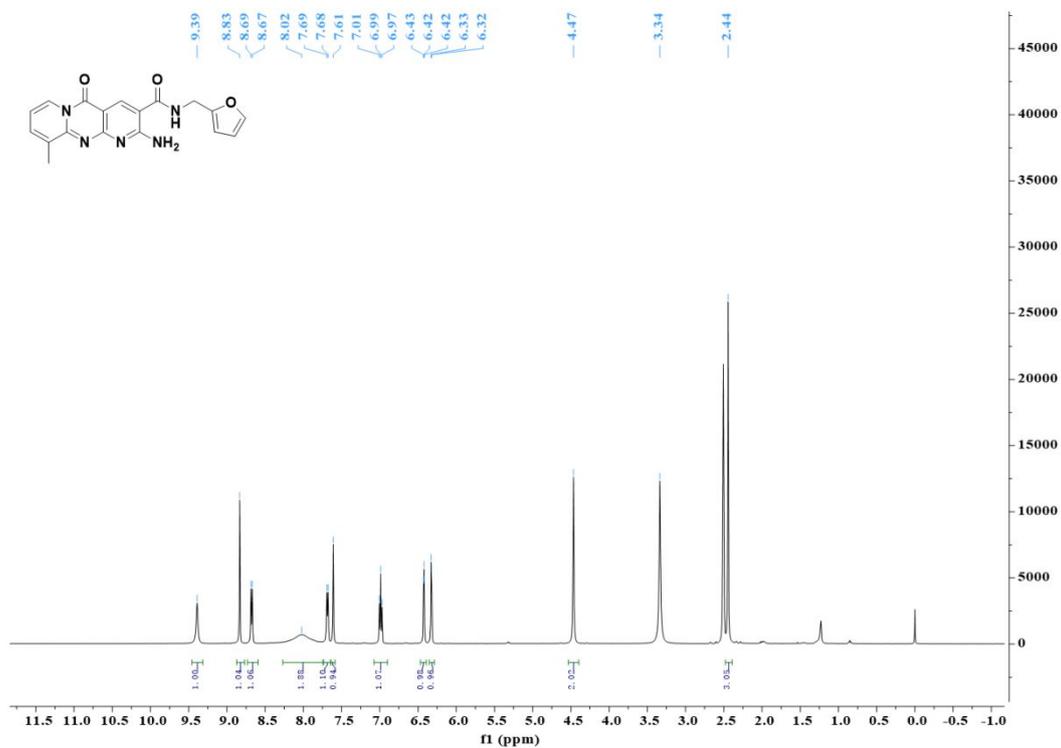


Figure S38 ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound 6h

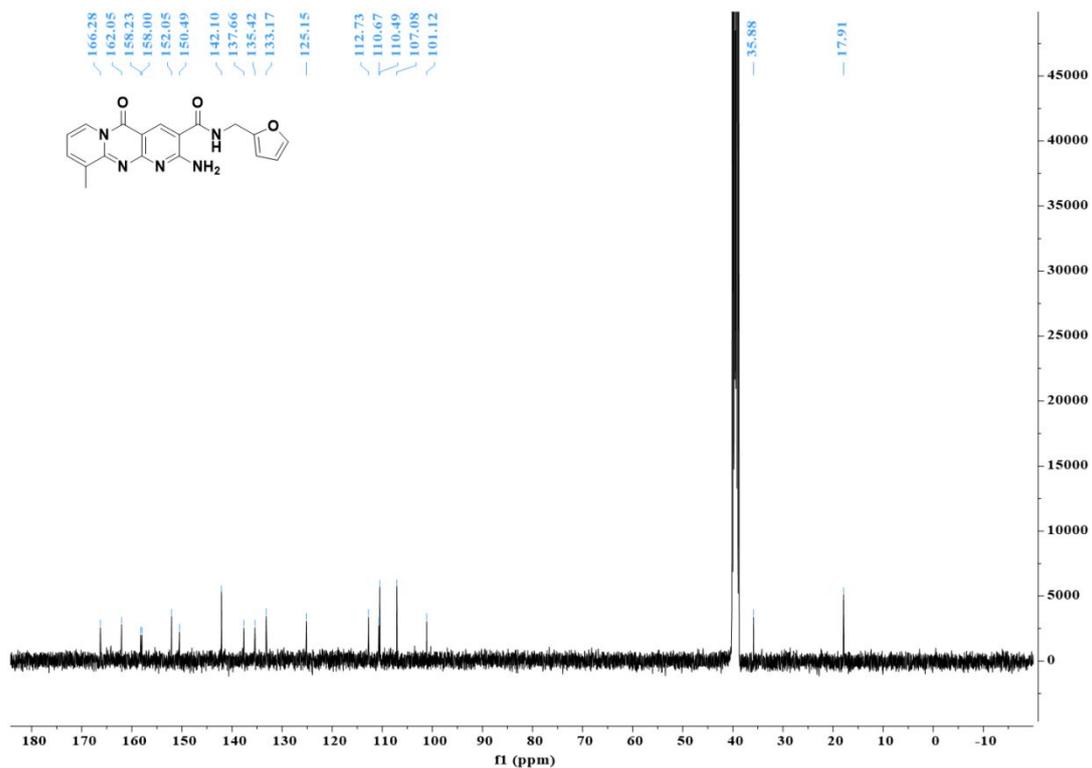


Figure S39 ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) spectrum of compound 6h

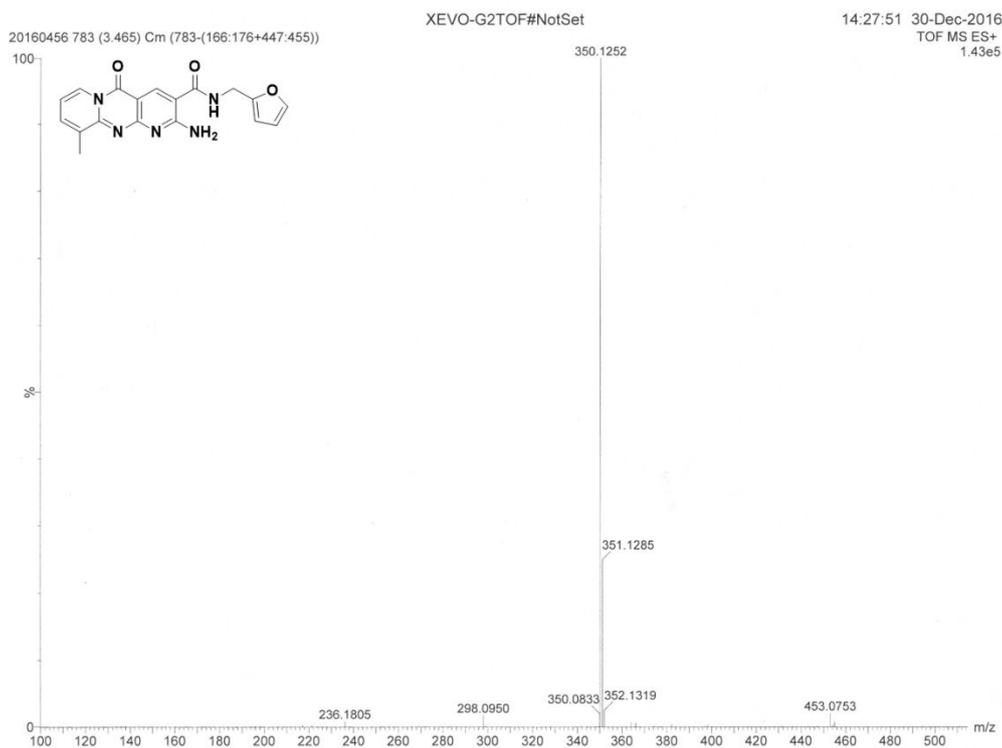


Figure S40 HRMS of compound 6h

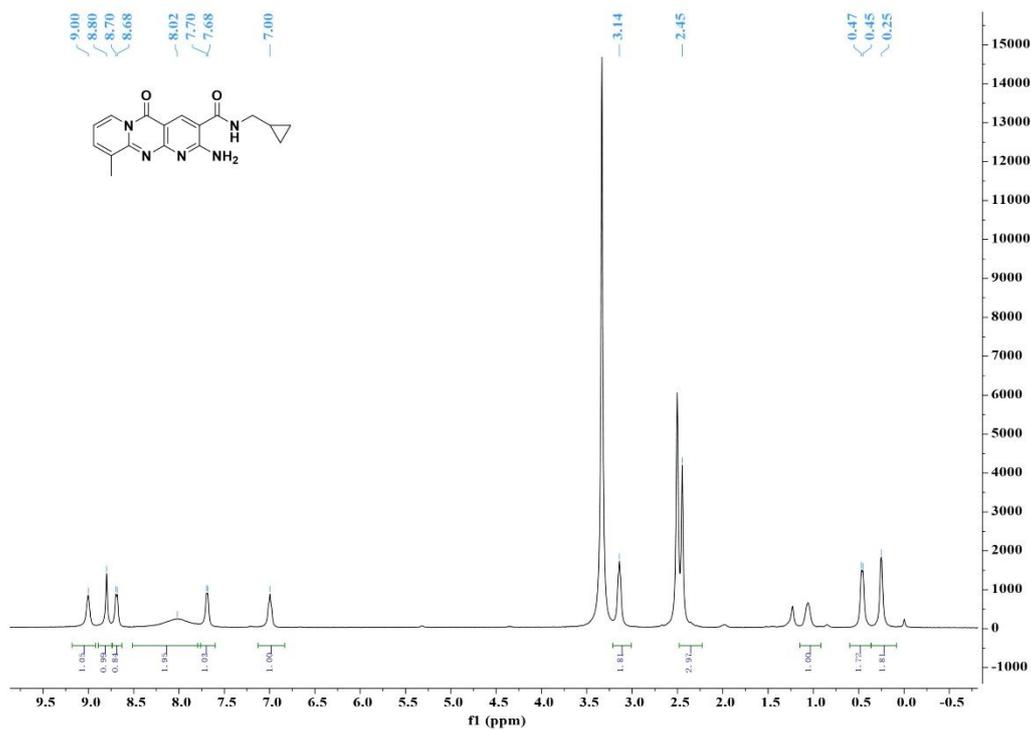


Figure S41 ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound 6i

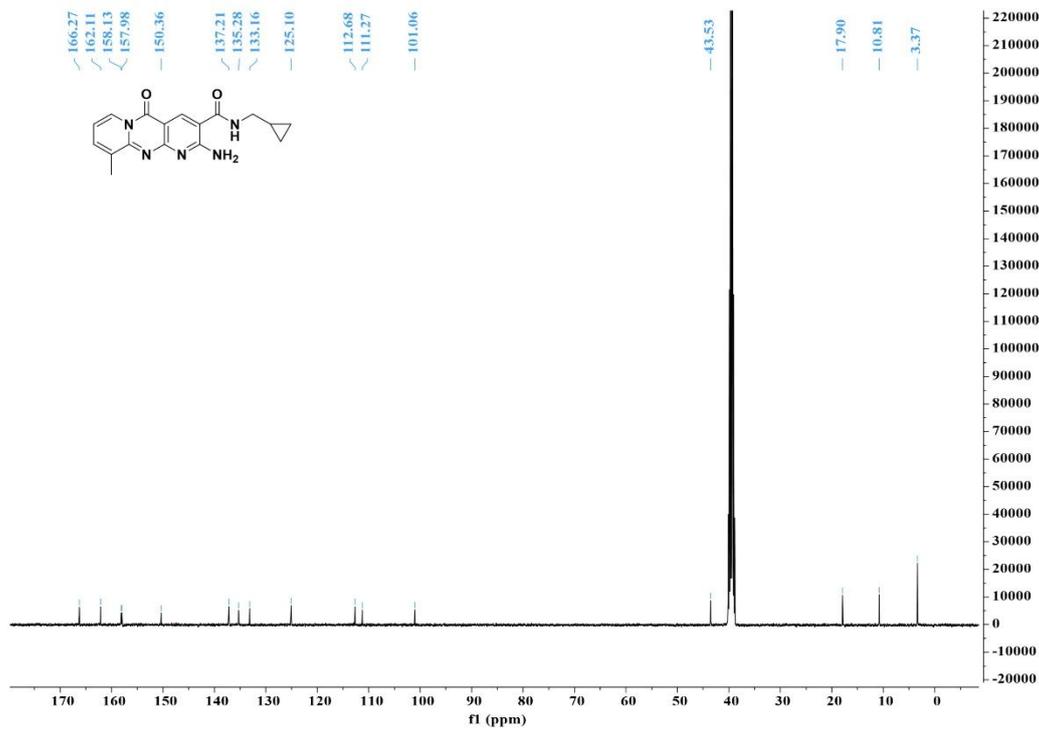


Figure S42 ¹³C NMR (100 MHz, DMSO-*d*₆) spectrum of compound 6i

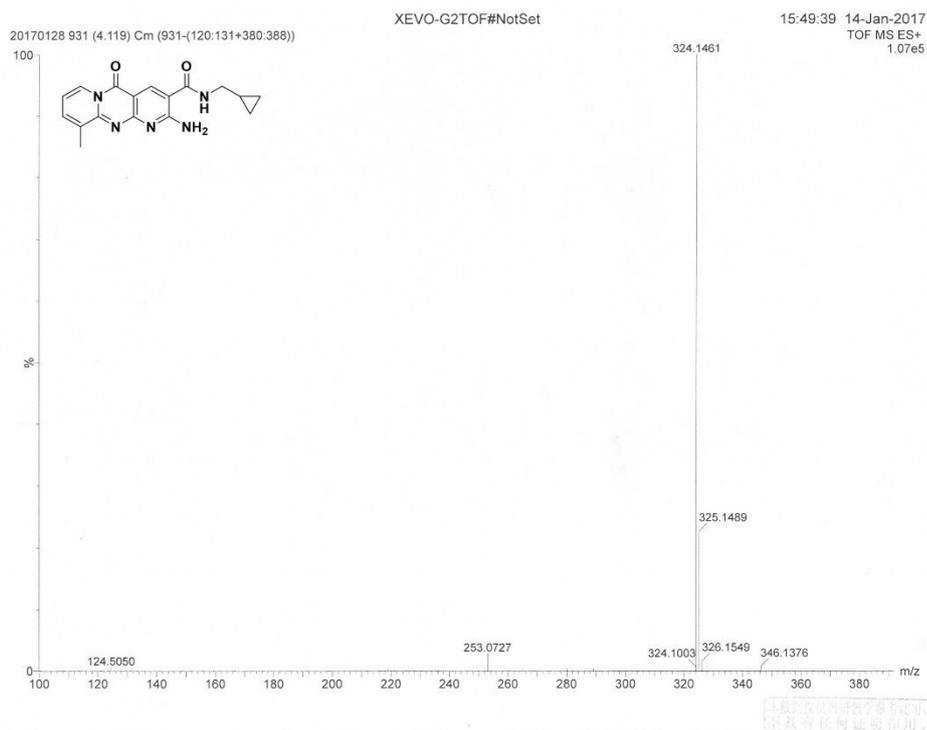


Figure S43 HRMS of compound 6i

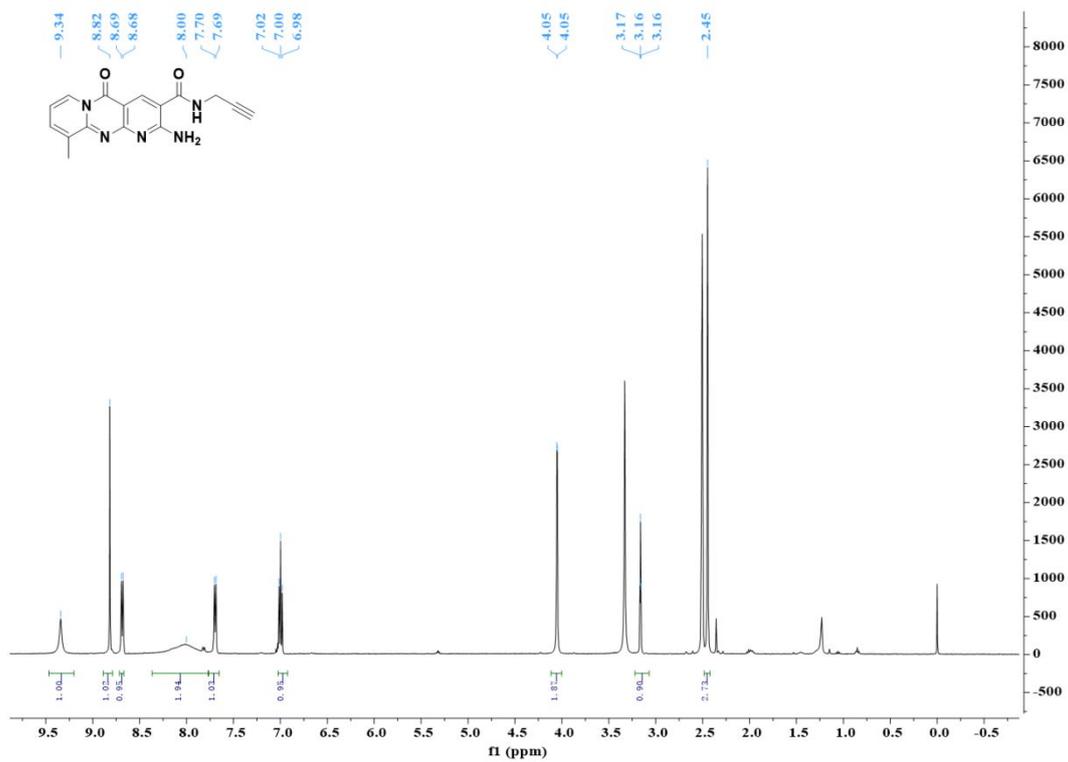


Figure S44 ^1H NMR (400 MHz, $\text{DMSO}-d_6$) spectrum of compound 6j

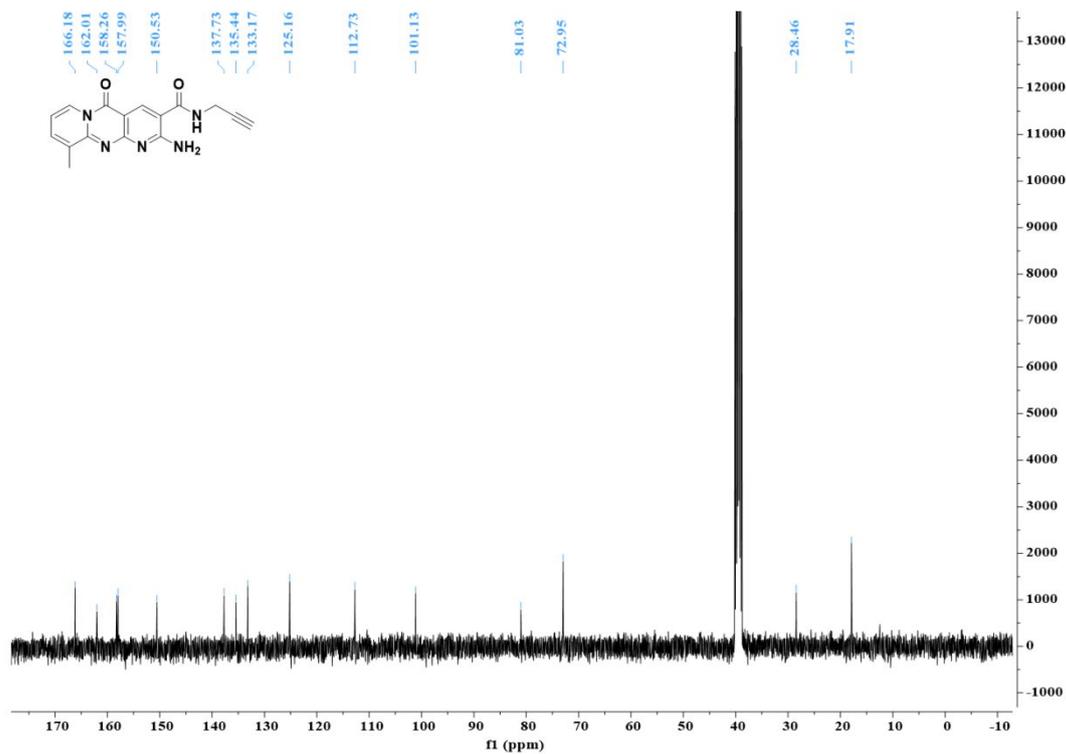


Figure S45 ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) spectrum of compound 6j

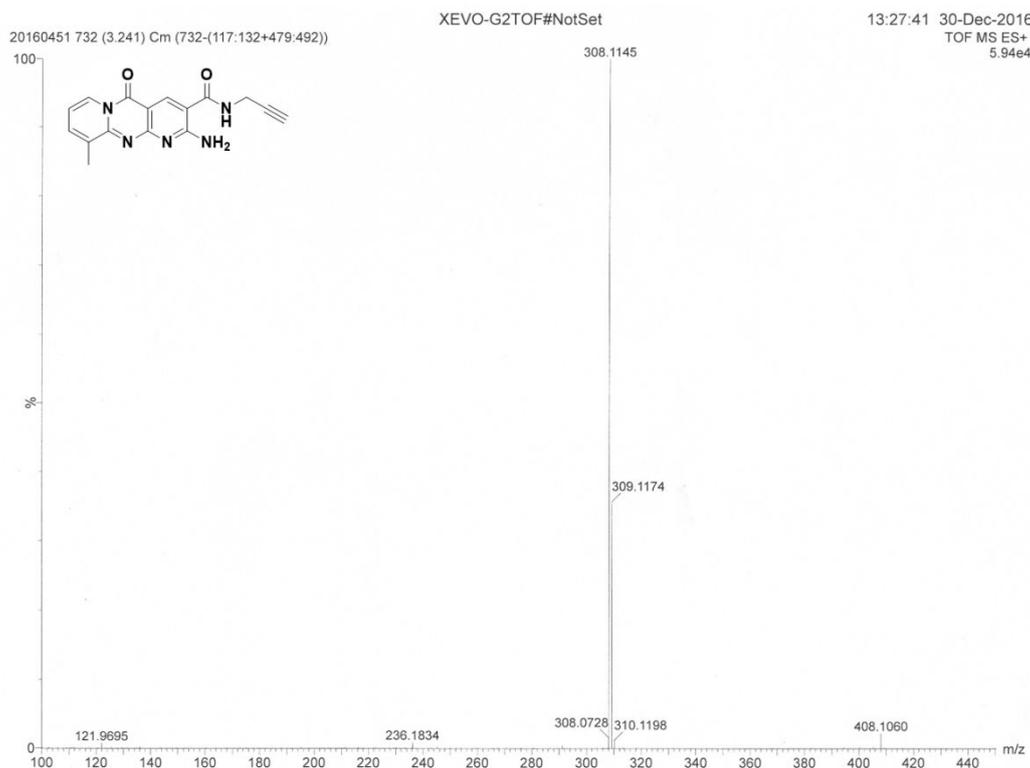


Figure S46 HRMS of compound 6j

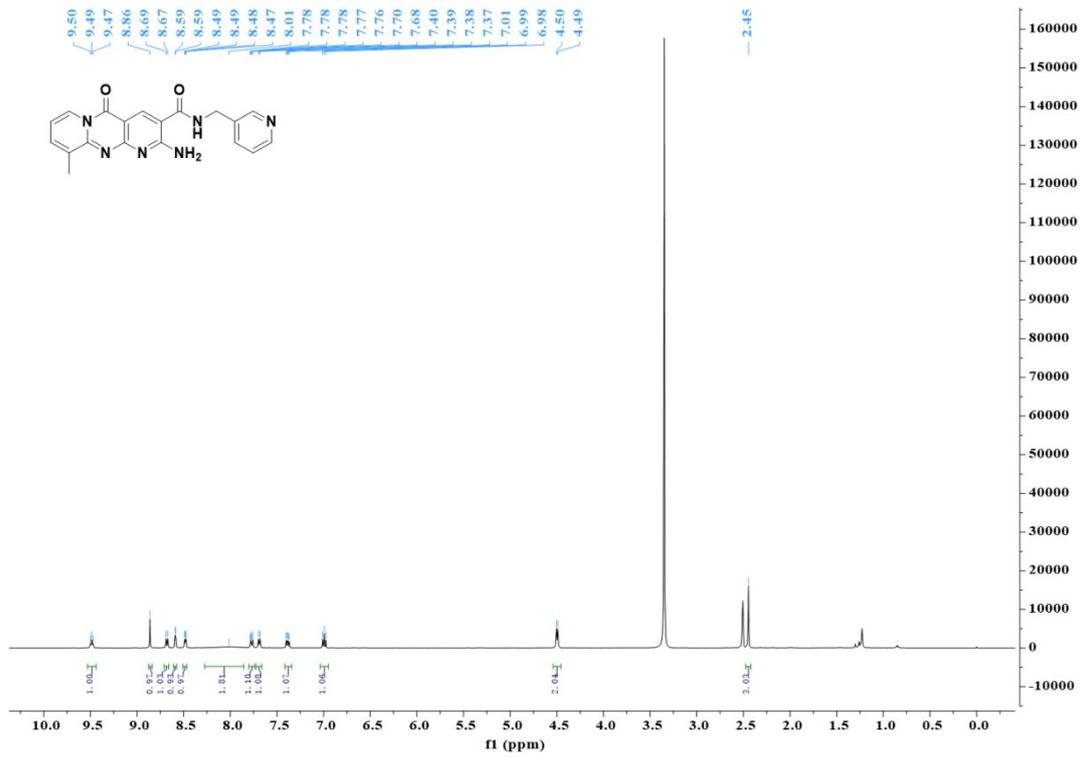


Figure S47 $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) spectrum of compound 6k

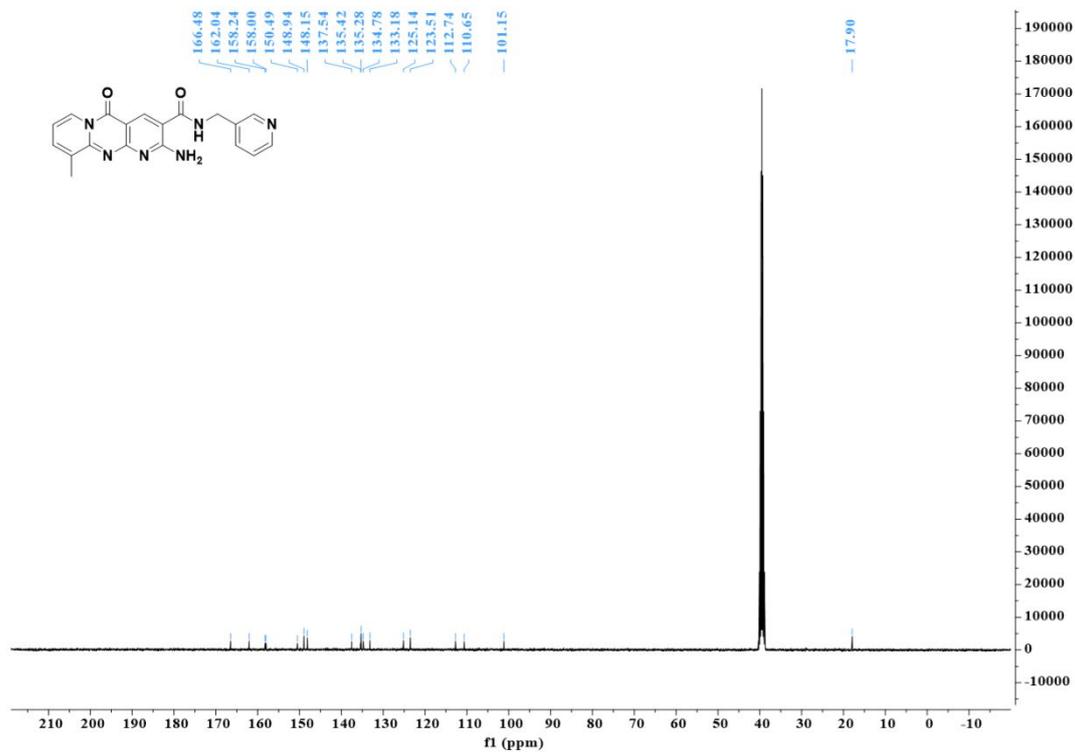


Figure S48 $^{13}\text{C NMR}$ (100 MHz, $\text{DMSO-}d_6$) spectrum of compound 6k

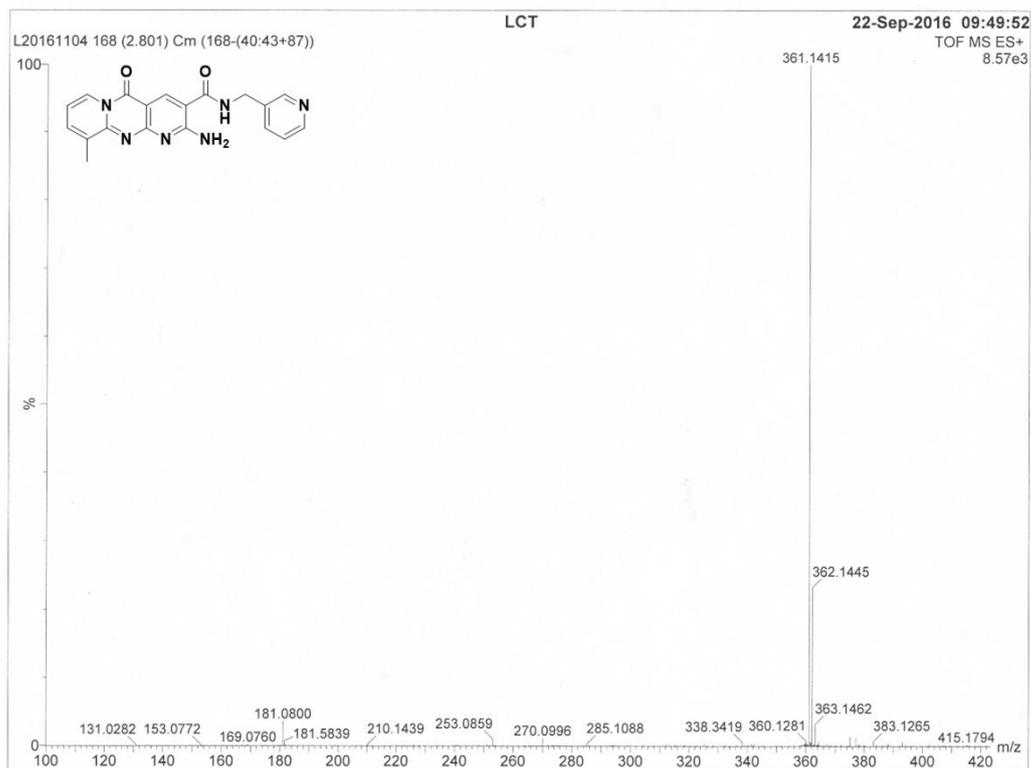


Figure S49 HRMS of compound 6k

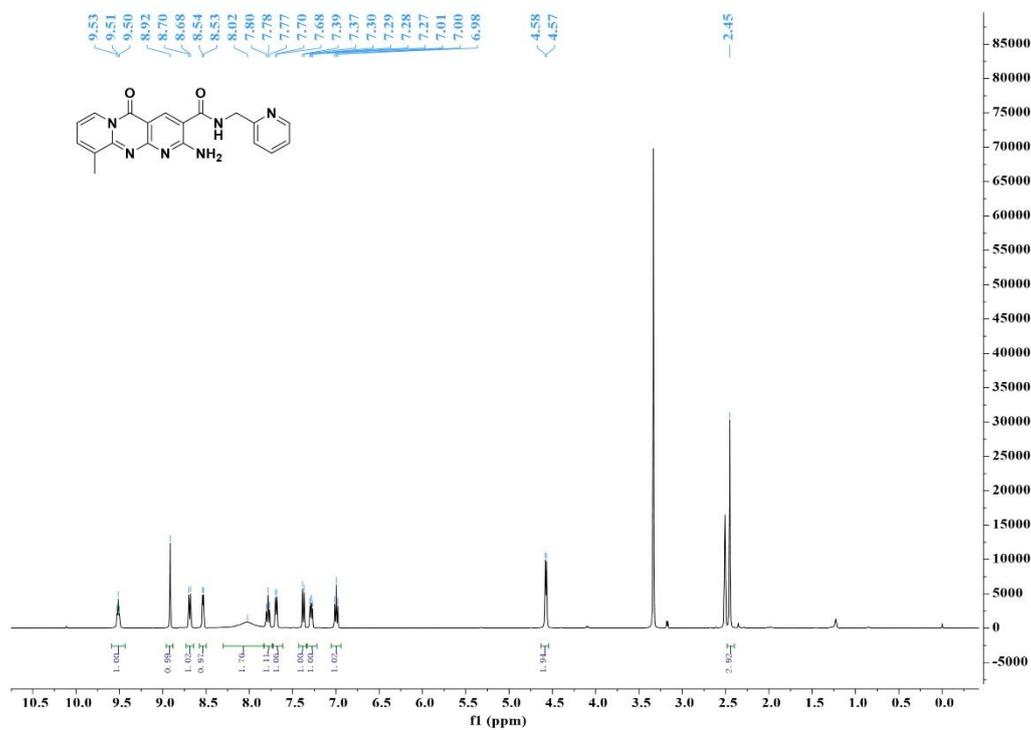


Figure S50 ^1H NMR (400 MHz, $\text{DMSO-}d_6$) spectrum of compound 6l

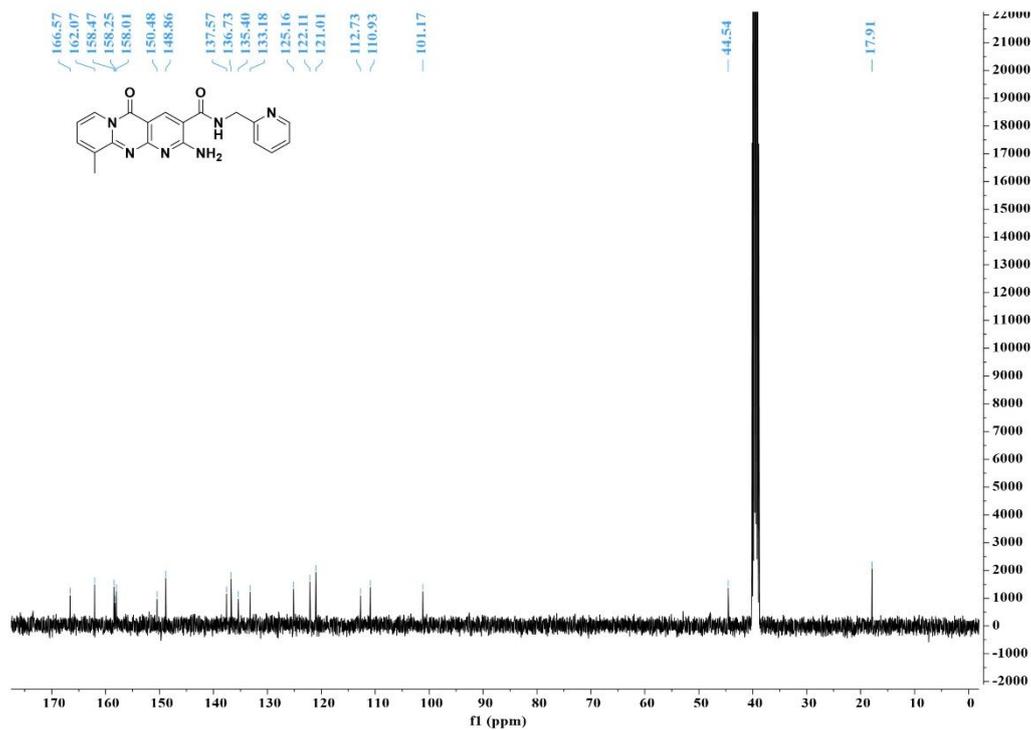


Figure S51 ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) spectrum of compound 6l

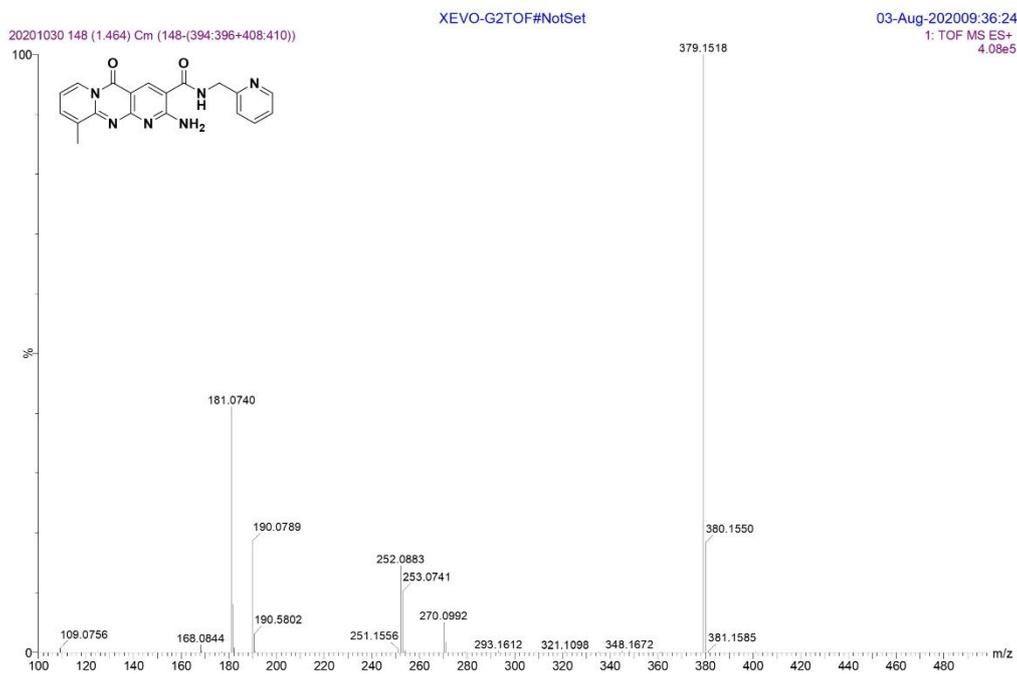


Figure S52 HRMS of compound 6l

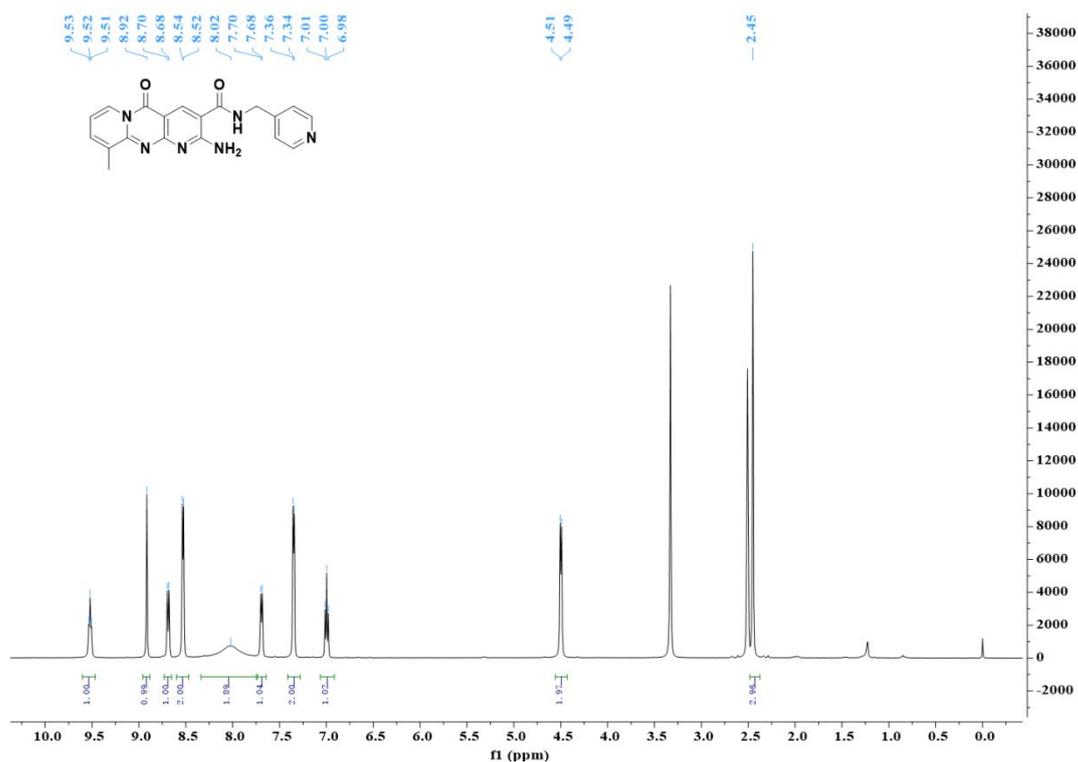


Figure S53 $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) spectrum of compound 6m

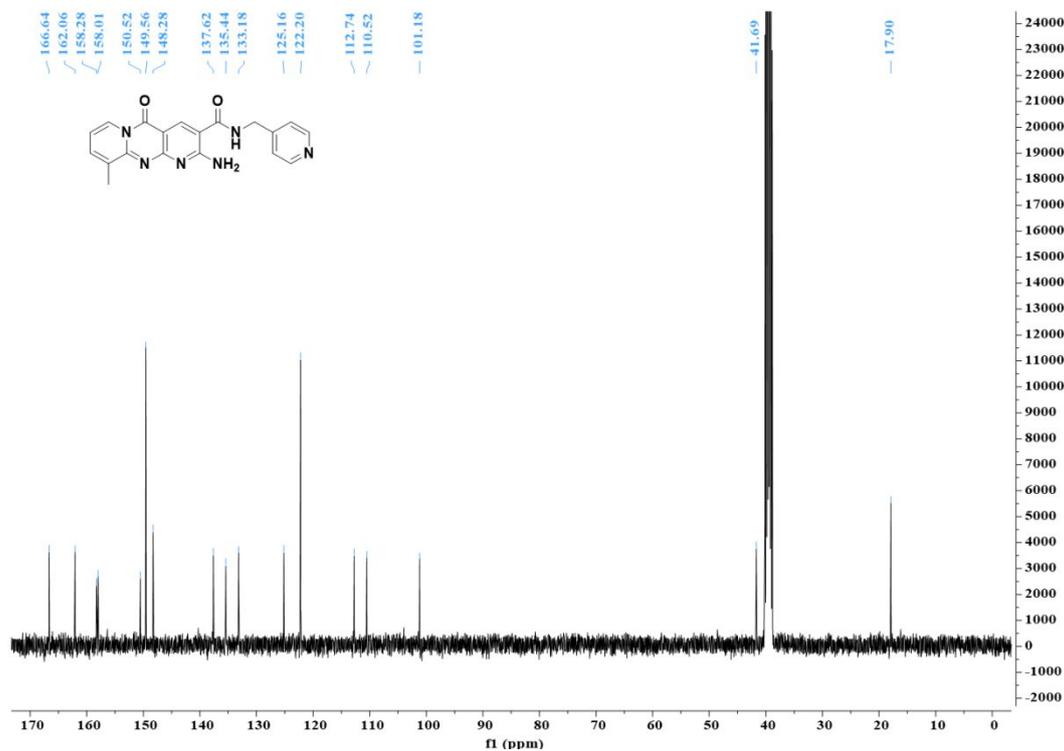


Figure S54 $^{13}\text{C NMR}$ (100 MHz, $\text{DMSO-}d_6$) spectrum of compound 6m

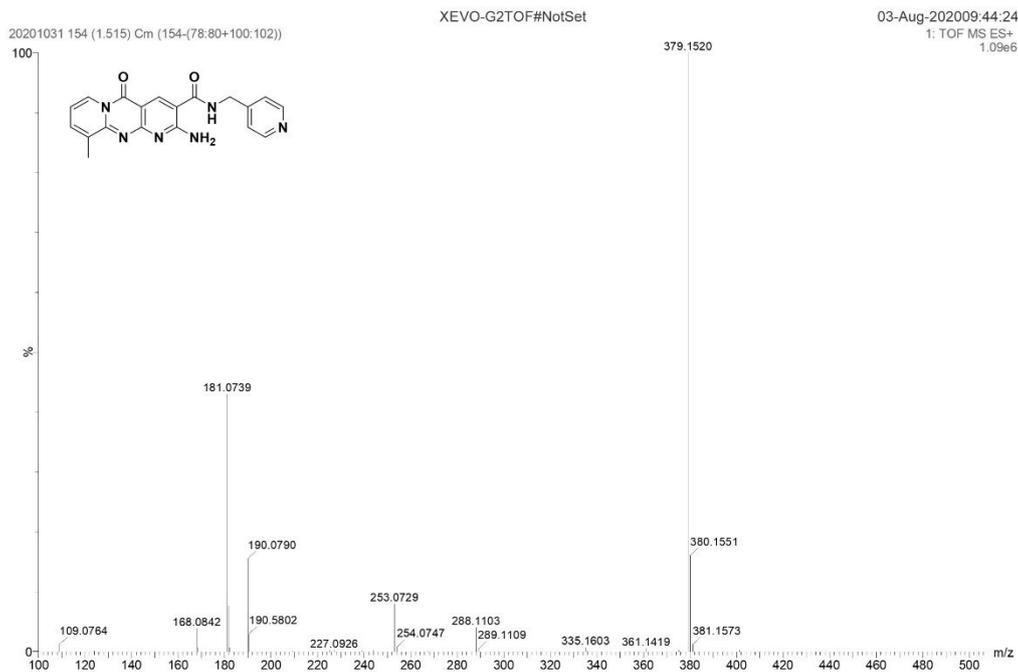


Figure S55 HRMS of compound 6m

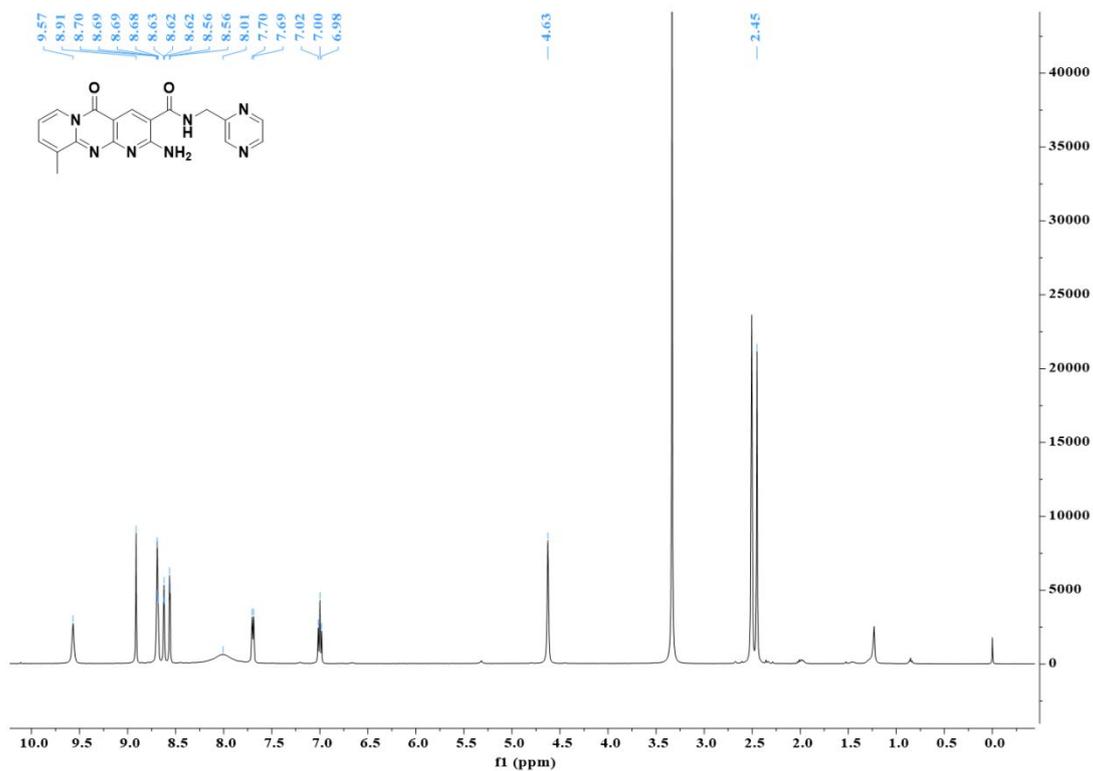


Figure S56 ^1H NMR (400 MHz, $\text{DMSO-}d_6$) spectrum of compound 6m

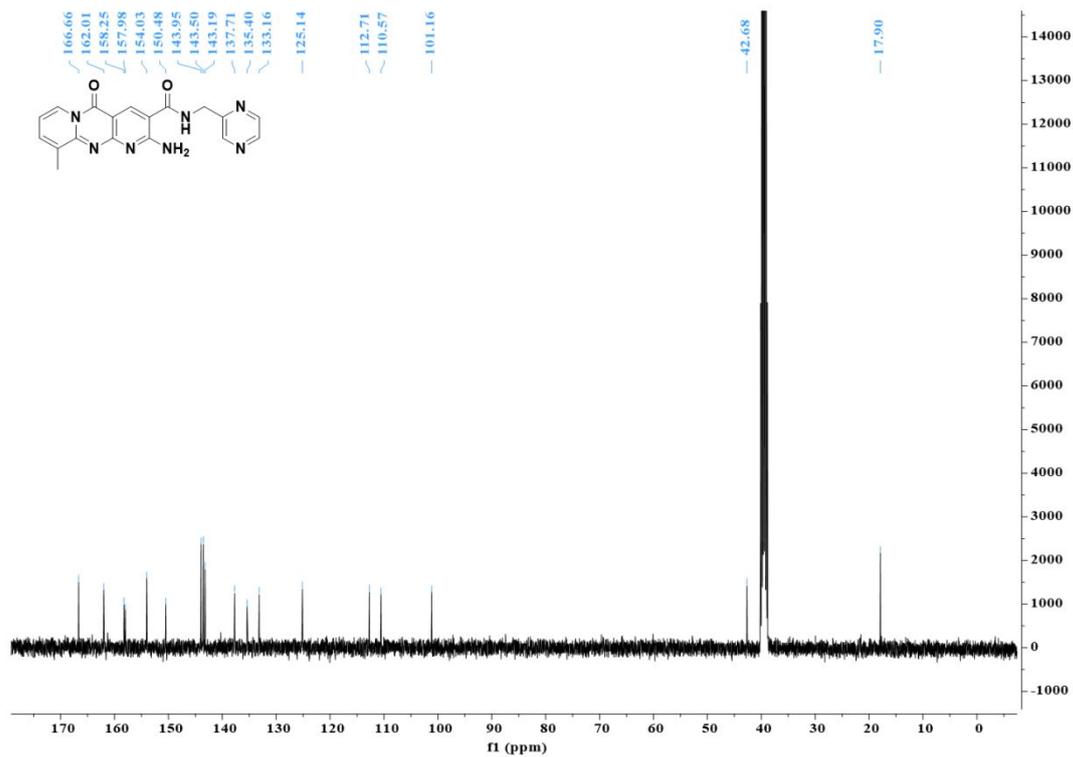


Figure S57 ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) spectrum of compound 6n

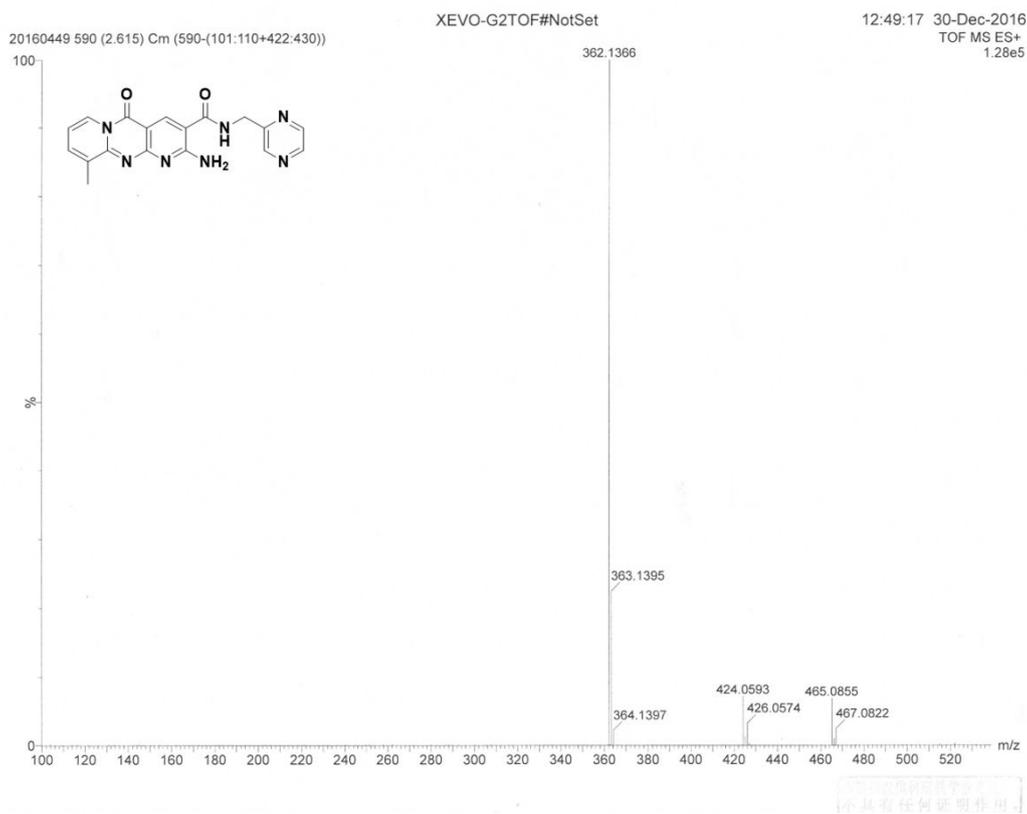


Figure S58 HRMS of compound 6n

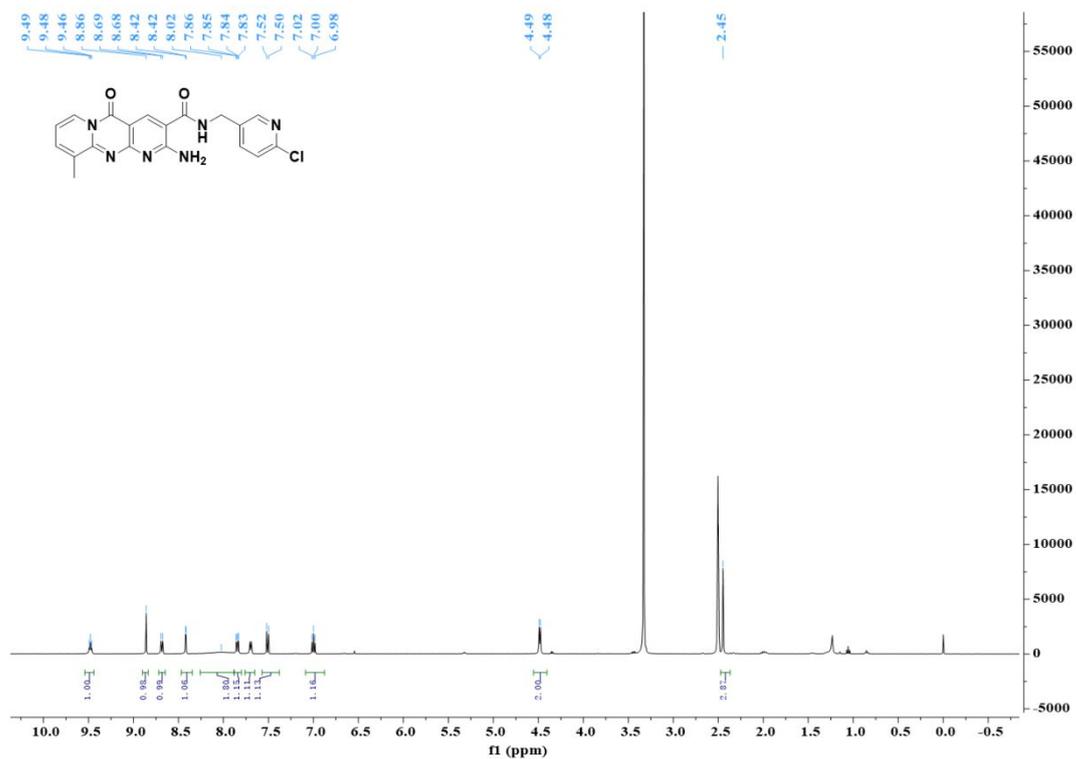


Figure S59 ^1H NMR (400 MHz, $\text{DMSO-}d_6$) spectrum of compound 60

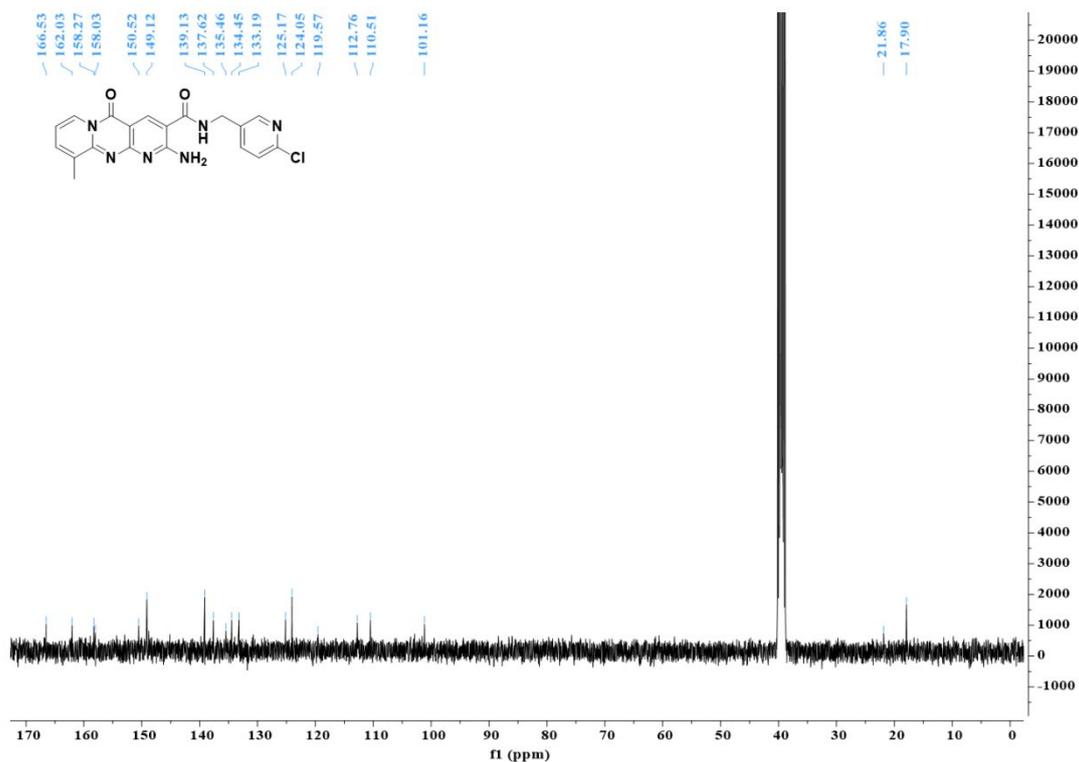


Figure S60 ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) spectrum of compound 60

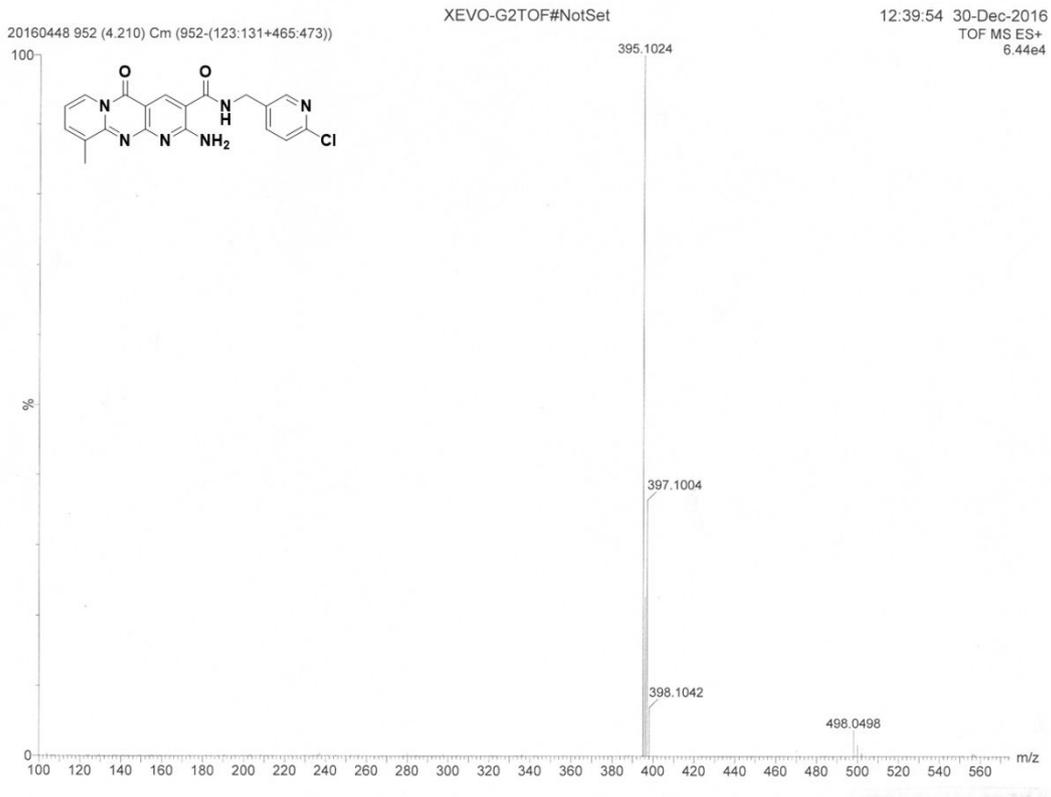


Figure S61 HRMS of compound 6o

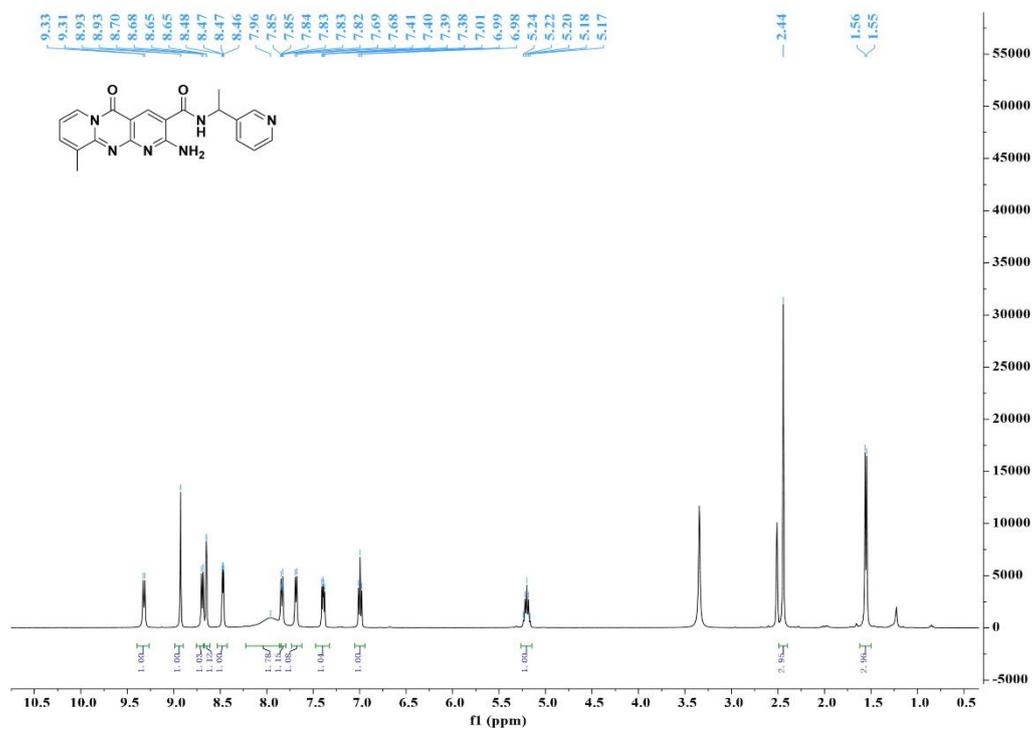


Figure S62 ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound 6p

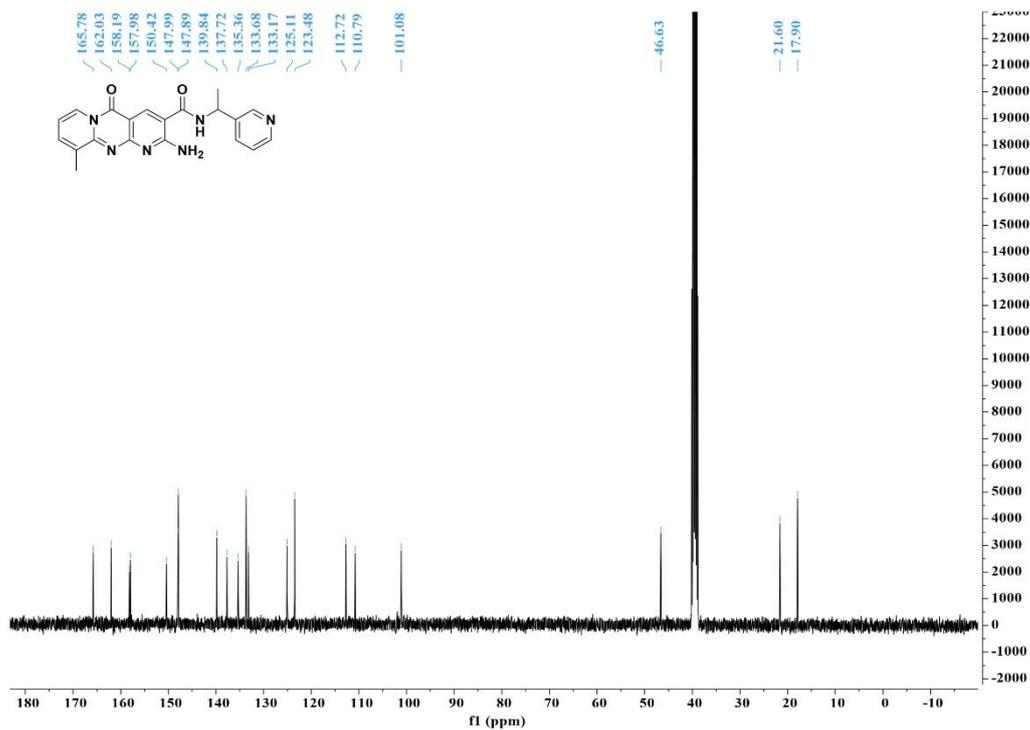


Figure S63 ¹³C NMR (100 MHz, DMSO-*d*₆) spectrum of compound 6p

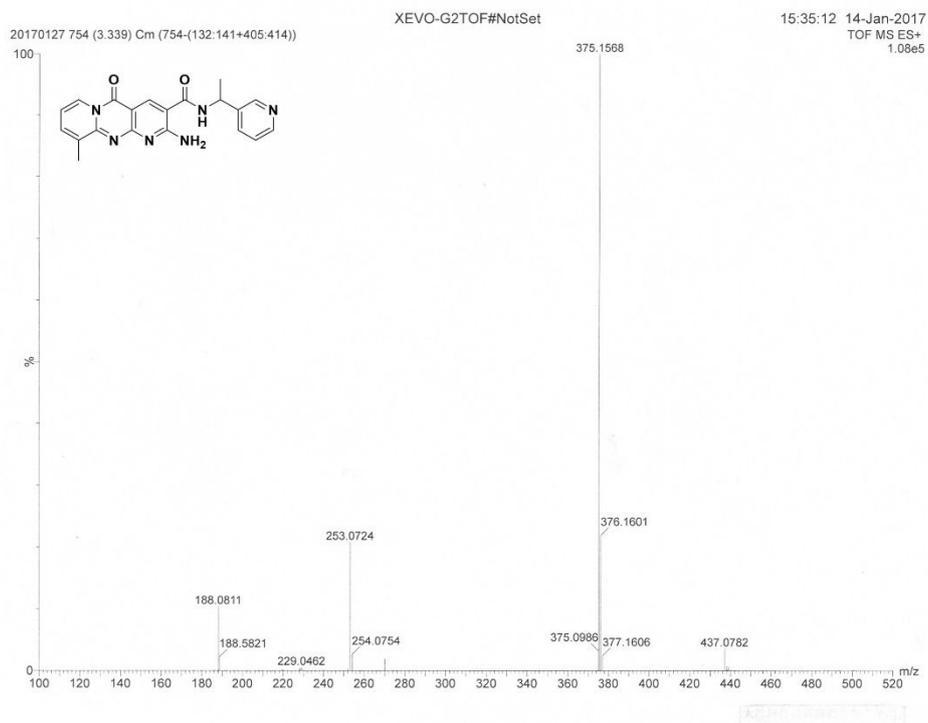


Figure S64 HRMS of compound 6p

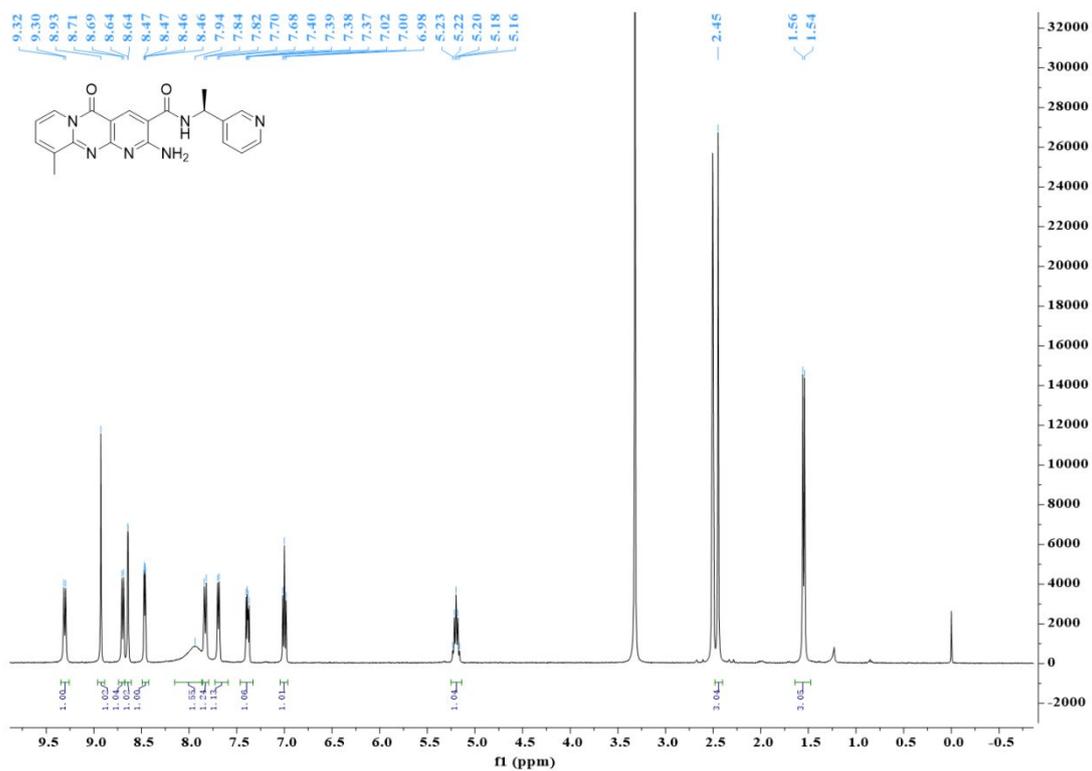


Figure S65 ^1H NMR (400 MHz, $\text{DMSO-}d_6$) spectrum of compound **6q**

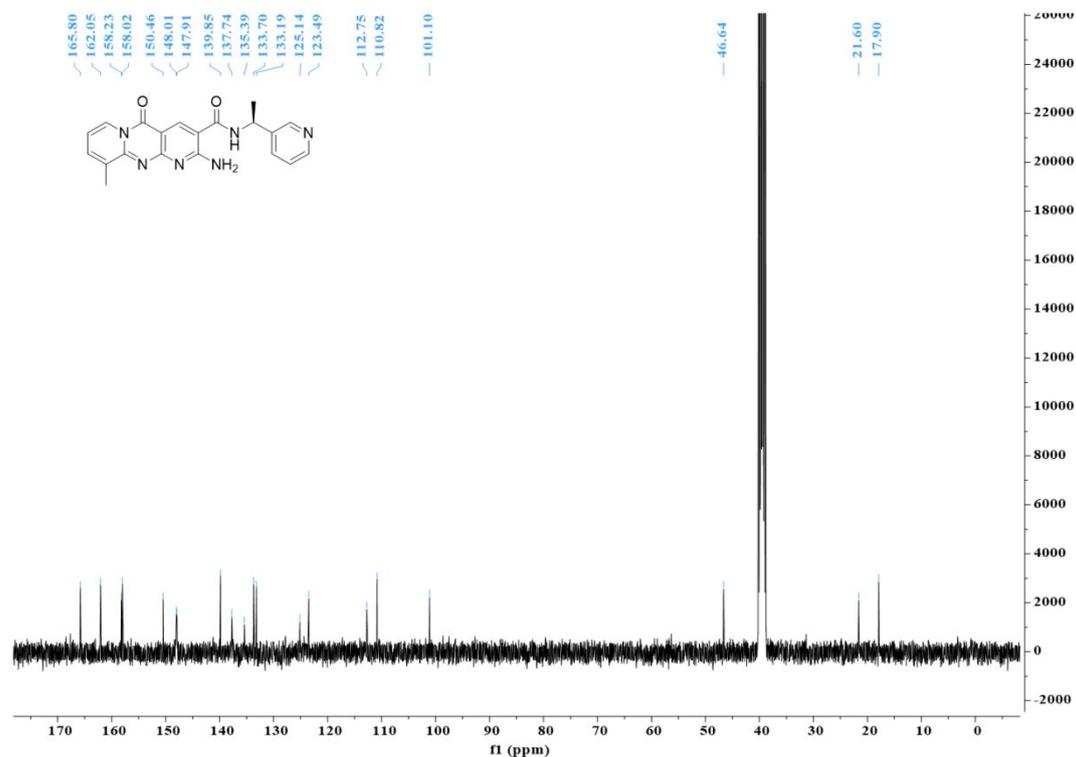


Figure S66 ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) spectrum of compound **6q**

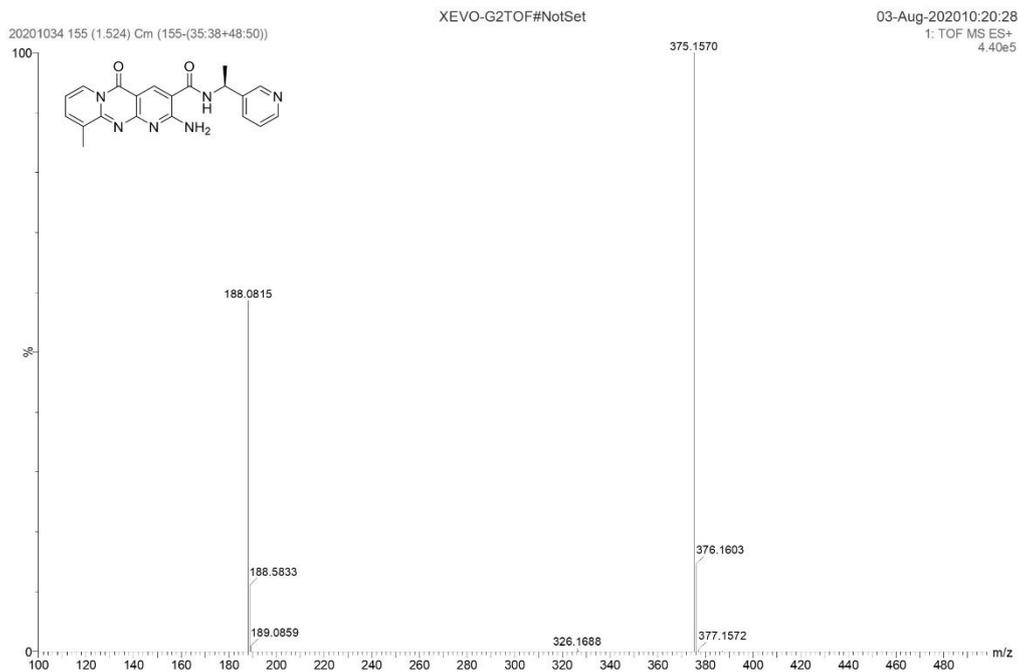


Figure S67 HRMS of compound 6q

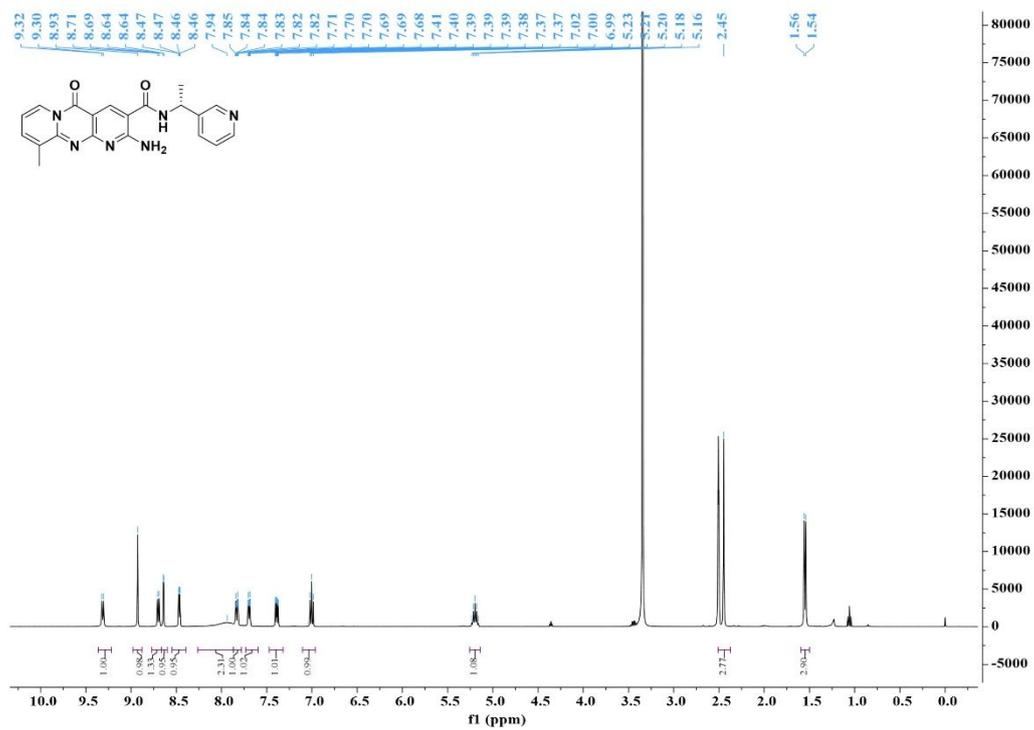


Figure S68 ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound 6r

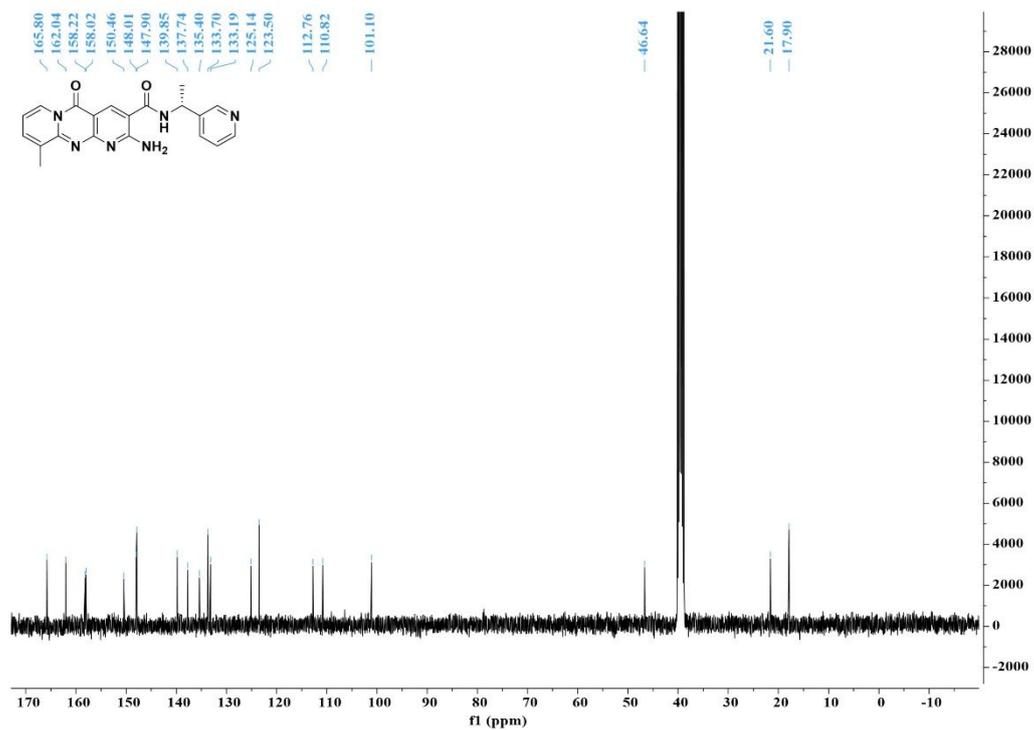


Figure S69 ¹³C NMR (100 MHz, DMSO-*d*₆) spectrum of compound 6r

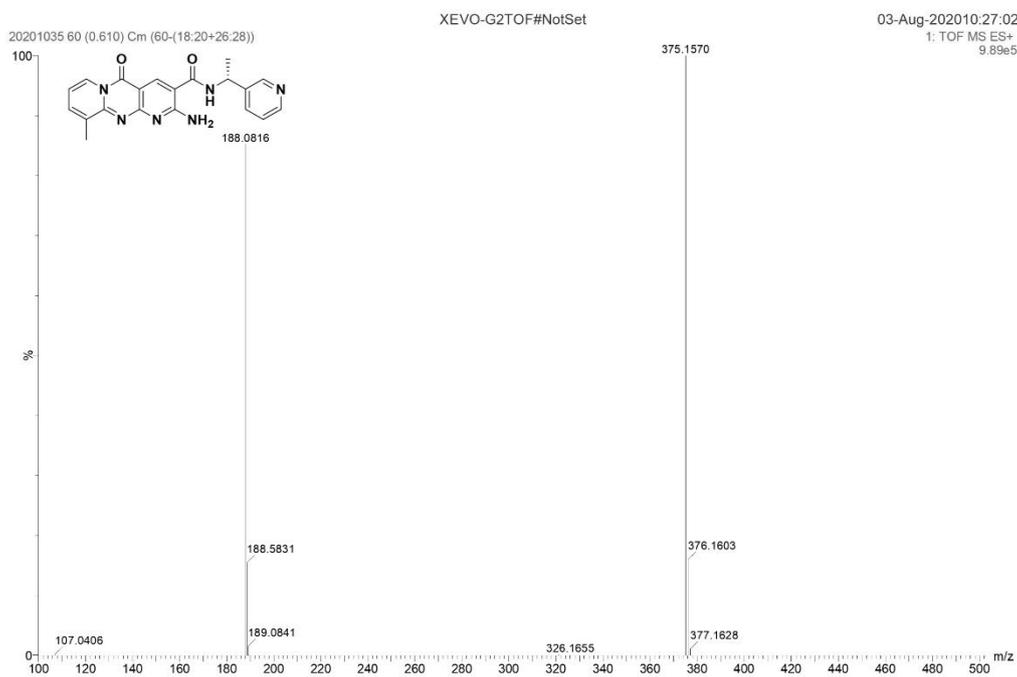


Figure S70 HRMS of compound 6r

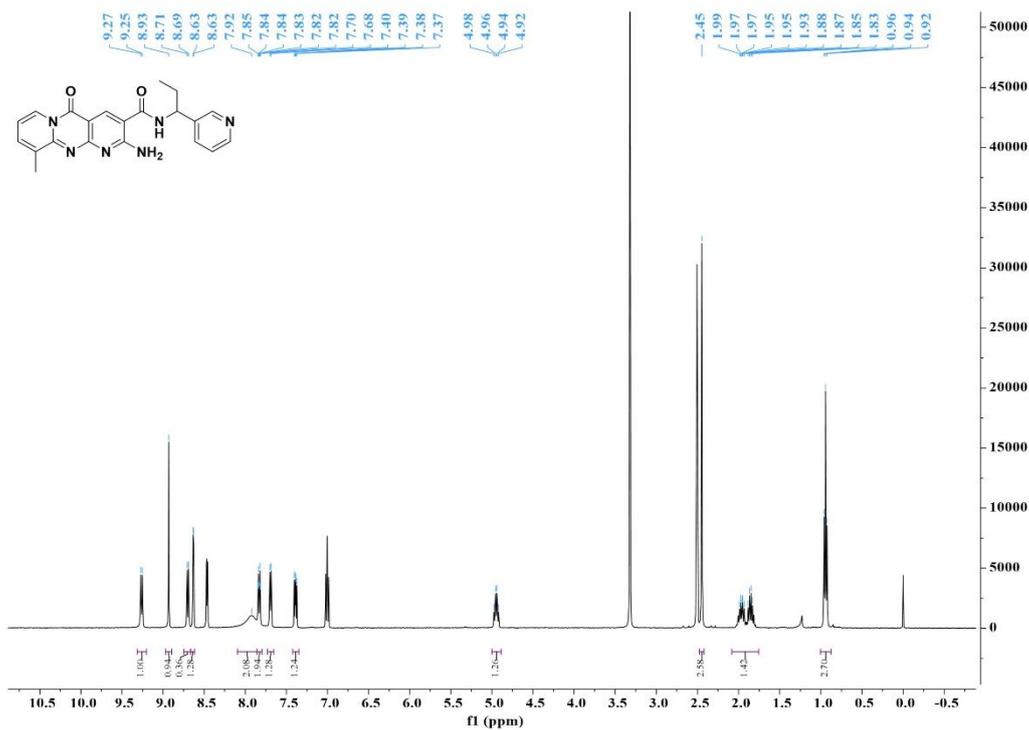


Figure S71 ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound 6s

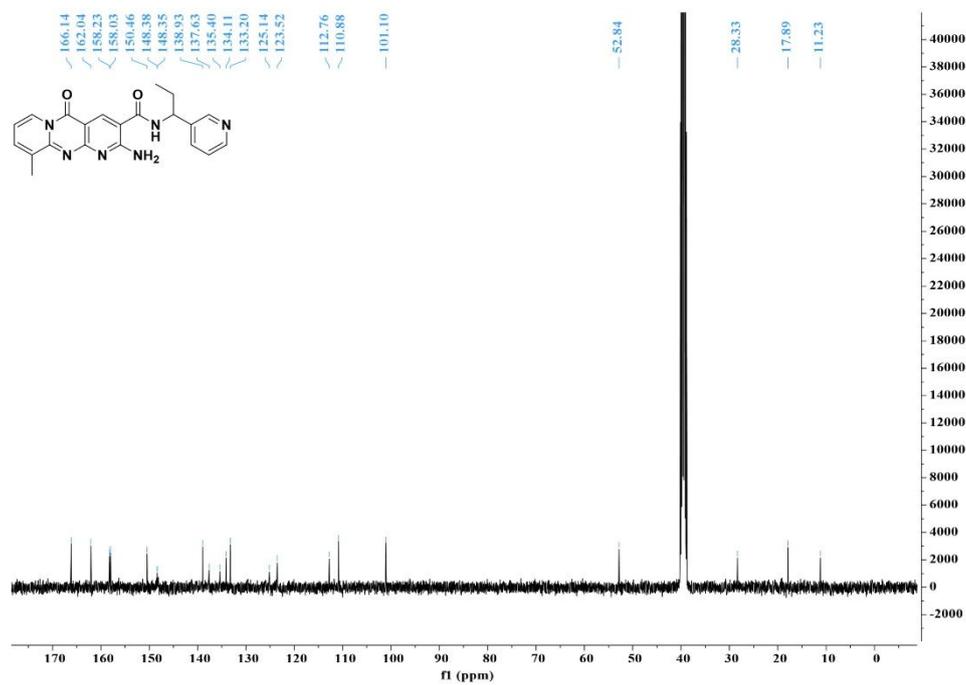


Figure S72 ¹³C NMR (100 MHz, DMSO-*d*₆) spectrum of compound 6s

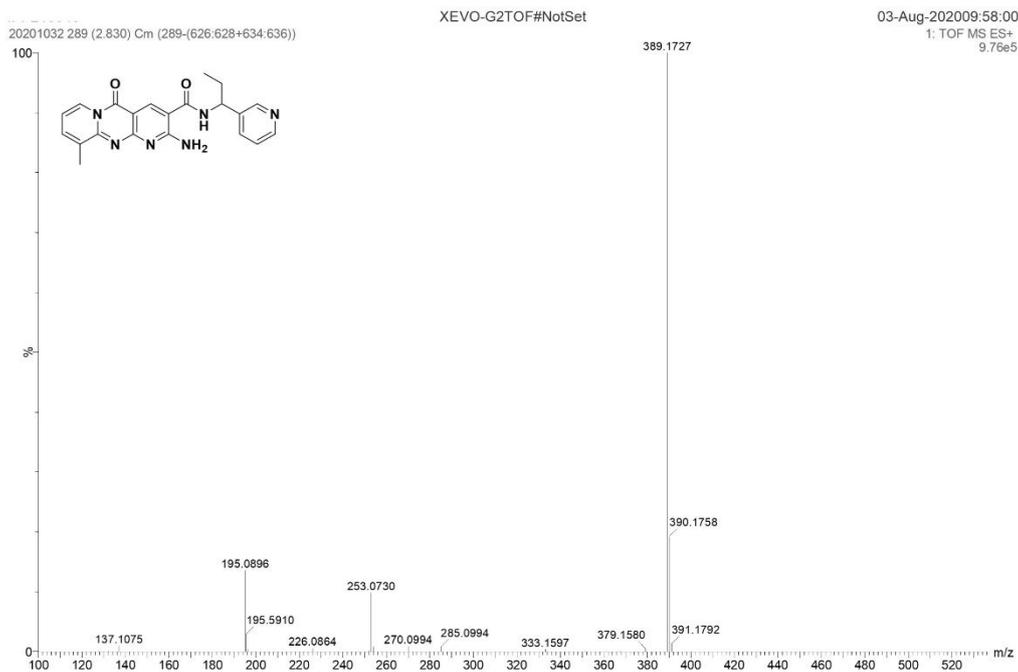


Figure S73 HRMS of compound 6s

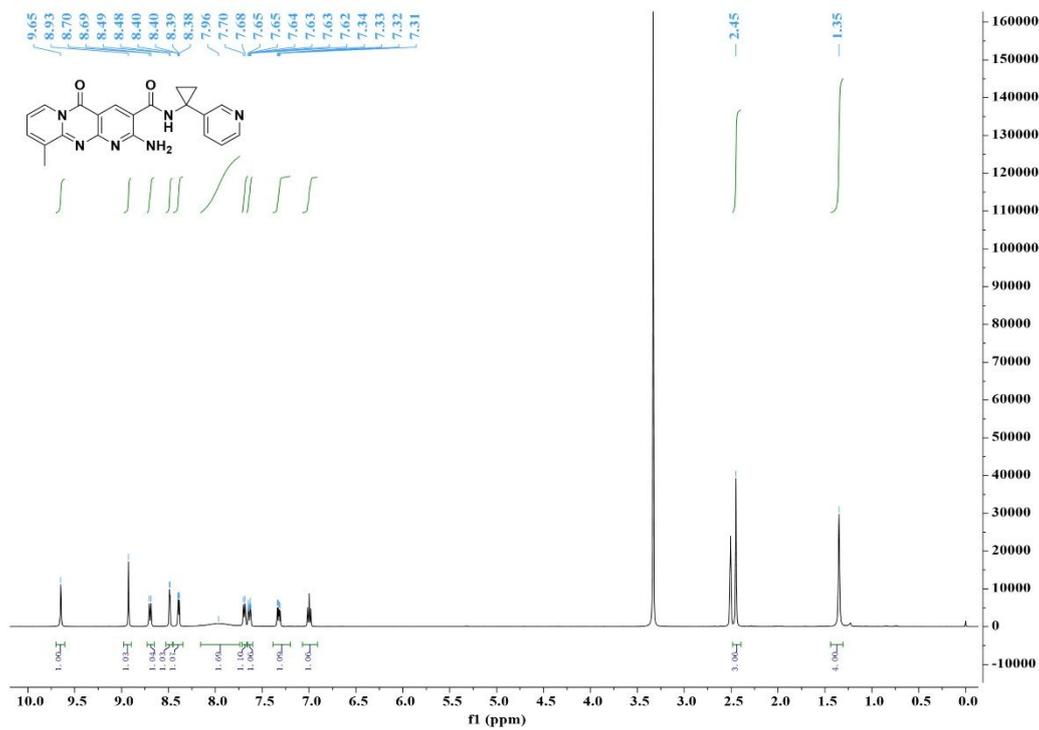


Figure S74 ¹H NMR (400 MHz, DMSO-*d*₆) spectrum of compound 6t

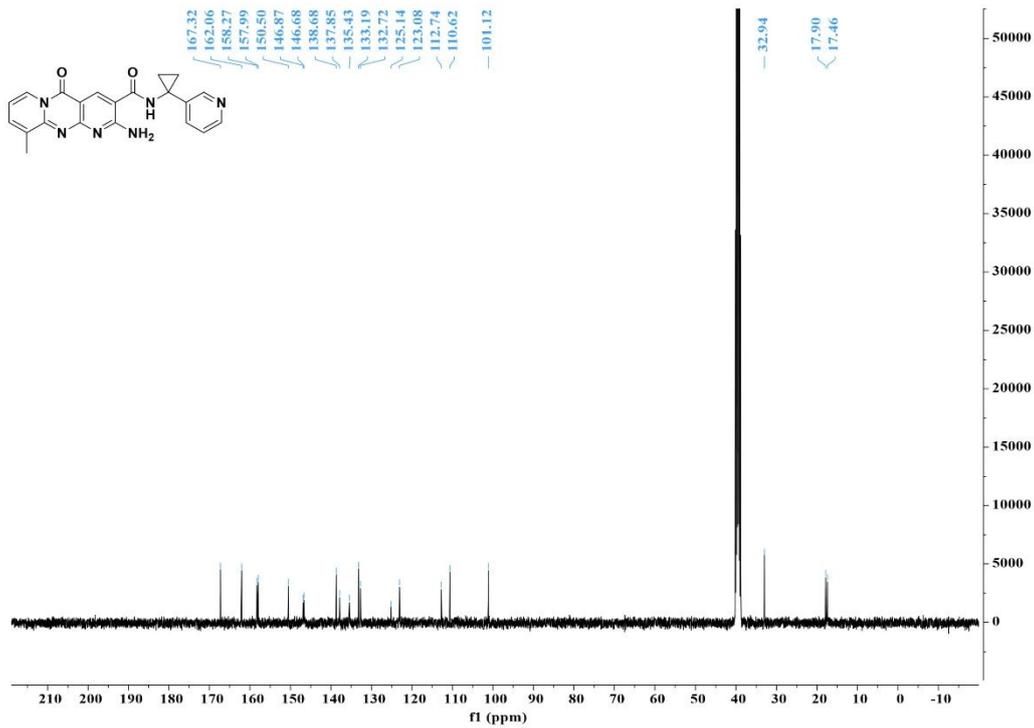


Figure S75 ¹³C NMR (100 MHz, DMSO-*d*₆) spectrum of compound 6t

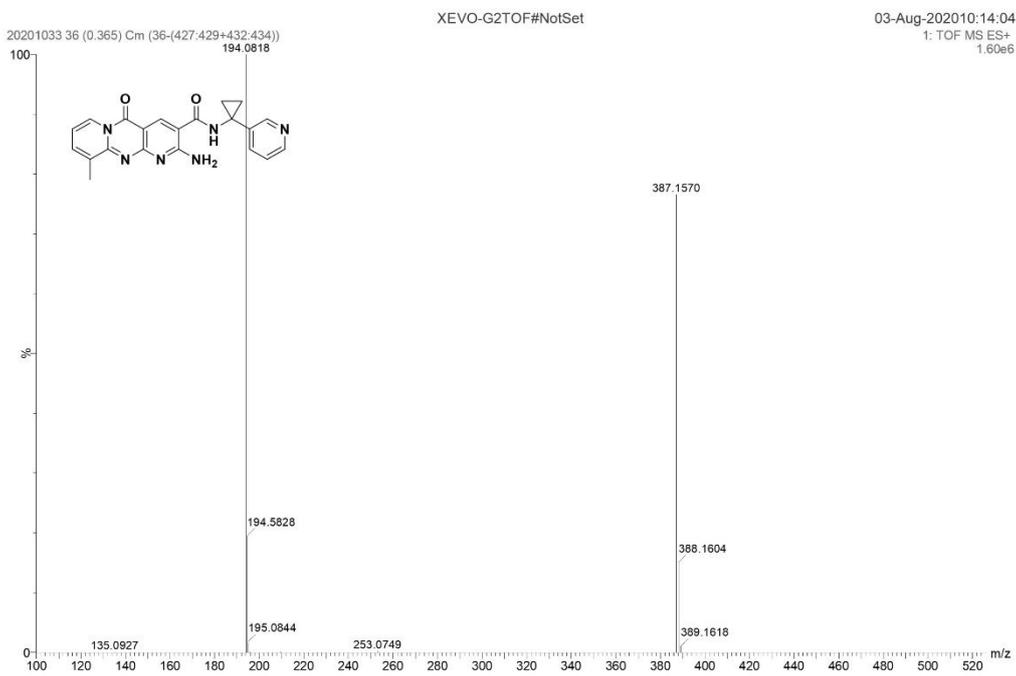


Figure S76 HRMS of compound 6t