Supporting Information

Novel Pyrimido[1,2-*a*]imidazole Derivatives as Potent Pks13-TE Inhibitors: Structure-Based Virtual Screening and Rational Design

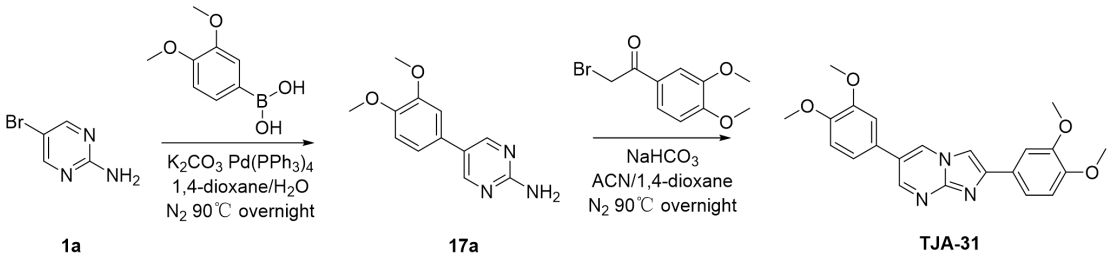
Xiangying Li[a,b#], Yuanyuan Liu[b,c#], Wen Shao[b#], Deling Jiang[a,b], Xupeng Huang[b*], Zihe Rao[f*], Wei Peng[a,b,c,d,e*], Yuying Fang[b*]

[a] School of Pharmaceutical Science, University of South China, Hengyang 421001, China
[b] Innovative Center for Pathogen Research, Guangzhou National Laboratory, Guangzhou, 510005, China
[c] School of Chemistry and Chemical Engineering, University of South China, Hengyang 421001, China
[d] Guangzhou Medical University, Guangzhou, 511436, China
[e] Department of Infectious Diseases, The Key Laboratory of Advanced Interdisciplinary Studies, The First Affiliated Hospital, Guangzhou Medical University, State Key Laboratory of Respiratory Disease, Guangzhou, 511436, China
[f] Laboratory of Structural Biology, School of Life Sciences and School of Medicine, Tsinghua University, Beijing, China.

* To whom correspondence should be addressed. huang_xupeng@gzlab.ac.cn (X. Huang), raozh@mail.tsinghua.edu.cn (Z. Rao), peng_wei@gzlab.ac.cn (W. Peng), fang_yuying@gzlab.ac.cn (Y. Fang).
[#] The authors contributed equally to this work.

Contents

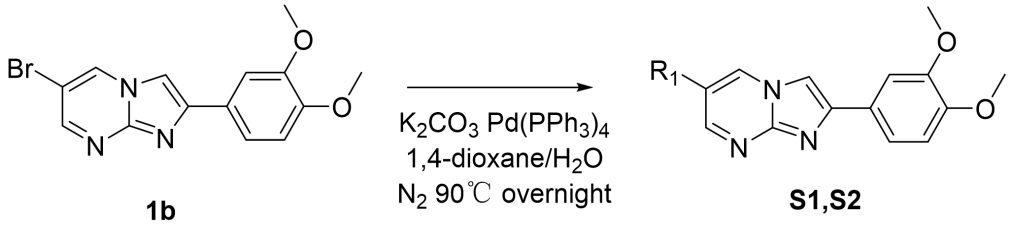
Supplementary Synthesis routes



Scheme S1. Synthesis of Compound **TJA-31**.

17a: A solution of 2-amino-5-bromopyrimidine (30 mg, 1.15 mmol) in 1,4-dioxane (15 mL) and water (3 mL) was treated with 3-thiopheneboronic acid (210 mg, 1.15 mmol), $Pd(PPh_3)_4$ (130 mg, 0.11 mmol) and K_2CO_3 (320 mg, 2.30 mmol). The mixture was stirred at 90 ℃ for 12 hours under N_2 atmosphere. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (DCM/MeOH) to afford **17a** (pale yellow solid, 200 mg, yield: 75%). ESI-MS m/z: 232.0 $[M+H]^+$.

TJA-31: A solution of **17a** (30 mg, 0.13 mmol) in ACN (2 mL) and MB (2 mL) was treated with 2-bromo-1-(3,4-dimethoxyphenyl)ethanone (67 mg, 0.26 mmol) and $NaHCO_3$ (33 mg, 0.39 mmol). The mixture was stirred at 90 ℃ for 12 hours under N_2 atmosphere. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (PE/EA) to afford TJA-31 (white solid, 20 mg, yield: 39.2%). ESI-MS m/z: 392.1 $[M+H]^+$. ^1H NMR (600 MHz, Chloroform-d) δ 8.72 (d, J = 2.5 Hz, 1H), 8.49 (d, J = 2.5 Hz, 1H), 7.79 (s, 1H), 7.72 (d, J = 2.0 Hz, 1H), 7.48 (dd, J = 8.3, 2.0 Hz, 1H), 7.11 (dd, J = 8.2, 2.2 Hz, 1H), 7.04 (d, J = 2.1 Hz, 1H), 6.99 (d, J = 8.3 Hz, 1H), 6.92 (d, J = 8.3 Hz, 1H), 4.00 (s, 3H), 3.97 (s, 3H), 3.94 (s, 3H), 3.92 (s, 3H).



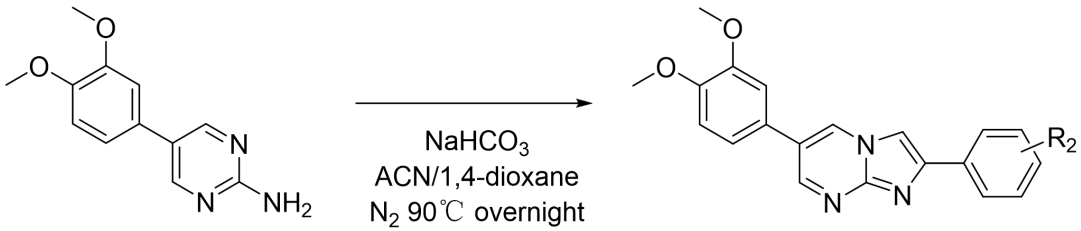
Scheme S2. Synthesis of Compound **S1, S2**.

2-(3,4-dimethoxyphenyl)-6-(1-methyl-1H-pyrazol-4-yl)imidazo[1,2-a]pyrimidine (S1)

A solution of **1b** (17 mg, 0.05 mmol) in 1,4-dioxane (3 mL) and water (0.6 mL) was treated with 1-methyl-1H-pyrazole-4-boronic acid (7 mg, 0.05 mmol), $Pd(PPh_3)_4$ (5 mg, 0.005 mmol and K_2CO_3 (14 mg, 0.1 mmol). The mixture was stirred at 90 ℃ for 12 hours under N_2 atmosphere. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by TLC (DCM/MeOH) to afford **S1** (white solid, 5 mg, yield: 29%). ESI-MS m/z: 336.0 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 9.11 (d, J = 2.5 Hz, 1H), 8.79 (d, J = 2.4 Hz, 1H), 8.27 (s, 1H), 8.26 (s, 1H), 7.98 (d, J = 0.8 Hz, 1H), 7.60 (d, J = 2.0 Hz, 1H), 7.57 (dd, J = 8.2, 2.0 Hz, 1H), 7.05 (d, J = 8.3 Hz, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 3.81 (s, 3H).

2-(3,4-dimethoxyphenyl)-6-(thiophen-3-yl)imidazo[1,2-a]pyrimidine (S2)

White solid, 5 mg, yield: 20%. ESI-MS m/z: 338.0 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 9.29 (d, J = 2.5 Hz, 1H), 8.96 (d, J = 2.5 Hz, 1H), 8.28 (s, 1H), 8.09 (dd, J = 2.9, 1.4 Hz, 1H), 7.76 (dd, J = 5.0, 2.9 Hz, 1H), 7.67 (dd, J = 5.0, 1.4 Hz, 1H), 7.61 (d, J = 2.0 Hz, 1H), 7.58 (dd, J = 8.2, 2.0 Hz, 1H), 7.06 (d, J = 8.3 Hz, 1H), 3.87 (s, 3H), 3.81 (s, 3H).



17a **S3,S4**

Scheme S3. Synthesis of Compound **S3, S4**.

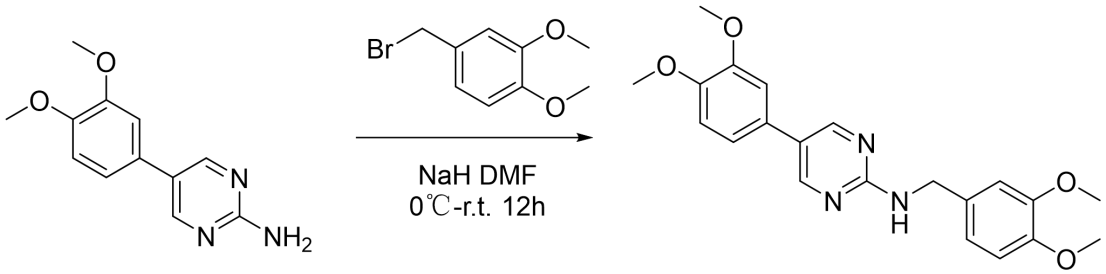
4-bromo-2-(6-(3,4-dimethoxyphenyl)imidazo[1,2-a]pyrimidin-2-yl)phenol (S3)

A solution of **17a** (30 mg, 0.13 mmol) in ACN (2 mL) and MB (2 mL) was treated with 2-bromo-1-(5-bromo-2-hydroxyphenyl)ethanone (76 mg, 0.26 mmol) and $NaHCO_3$ (33 mg, 0.39 mmol). The mixture was stirred at 90 ℃ for 12 hours under N_2 atmosphere. After the reaction reached completion, the mixture was concentrated

under reduced pressure. The crude residue was first purified by silica gel column chromatography using a gradient of PE and EA (from 20:1 to 5:1) to isolate the target fraction. The collected fraction, which contained the desired product **S3** along with minor impurities, was then subjected to recrystallization from a mixed solvent system of DCM and PE. This two-step purification procedure afforded **S3** (white solid, 12 mg, yield: 22%). ESI-MS m/z: 427.0 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 11.36 (s, 1H), 9.33 (d, J = 2.5 Hz, 1H), 8.97 (d, J = 2.5 Hz, 1H), 8.49 (s, 1H), 8.26 (d, J = 2.6 Hz, 1H), 7.39 (d, J = 2.2 Hz, 1H), 7.36 (dd, J = 8.6, 2.6 Hz, 1H), 7.34 (dd, J = 8.3, 2.2 Hz, 1H), 7.12 (d, J = 8.3 Hz, 1H), 6.95 (d, J = 8.6 Hz, 1H), 3.88 (s, 3H), 3.82 (s, 3H).

2-(5-bromo-2-methoxyphenyl)-6-(3,4-dimethoxyphenyl)imidazo[1,2-a]pyrimidine (S4)

White solid, 5 mg, yield: 11%. ESI-MS m/z: 441.0 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 9.30 (d, J = 2.6 Hz, 1H), 8.96 (d, J = 2.6 Hz, 1H), 8.42 (d, J = 2.7 Hz, 1H), 8.39 (s, 1H), 7.52 (dd, J = 8.8, 2.6 Hz, 1H), 7.37 (d, J = 2.2 Hz, 1H), 7.33 (dd, J = 8.2, 2.2 Hz, 1H), 7.17 (d, J = 8.8 Hz, 1H), 7.11 (d, J = 8.4 Hz, 1H), 4.01 (s, 3H), 3.88 (s, 3H), 3.82 (s, 3H).



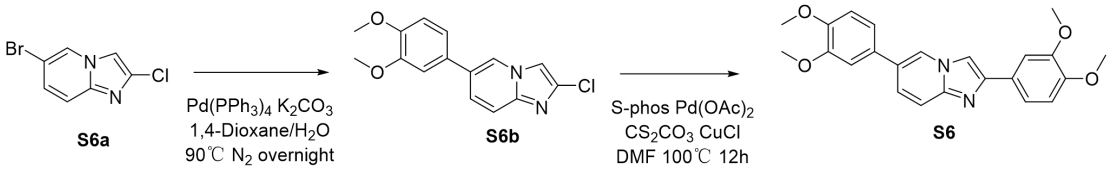
17a **S5**

Scheme S4. Synthesis of Compound **S5.**

N-(3,4-dimethoxybenzyl)-5-(3,4-dimethoxyphenyl)pyrimidin-2-amine (S5)

A solution of 4-(bromomethyl)-1,2-dimethoxybenzene (40 mg, 0.17 mmol) and NaH (7.8 mg, 0.24 mmol) in DMF (5 mL) was stirred at 0 ℃ for 15 minutes under N_2 atmosphere. **17a** (20 mg, 0.086 mmol) was added after these operations are completed and turn the reaction to room temperature stirred 12 hours. After completion of the

reaction, the mixture was quenched with water (10 mL) and extract with ethyl acetate. The combined organic layers were washed with saturated brine and dried over Na_2SO_4 filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (PE/EA) to afford **S5** (pale yellow solid, 14 mg, yield: 42%). ESI-MS m/z: 382.0 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 8.60 (s, 2H), 7.73 (t, J = 6.4 Hz, 1H), 7.20 – 7.16 (m, 1H), 7.12 (dd, J = 8.3, 2.1 Hz, 1H), 7.00 (d, J = 8.3 Hz, 1H), 6.97 (s, 1H), 6.86 (t, J = 9.6 Hz, 2H), 4.46 (d, J = 6.3 Hz, 2H), 3.79 (d, J = 31.2 Hz, 6H), 3.72 (d, J = 10.7 Hz, 6H).



Scheme S5. Synthesis of Compound **S6.**

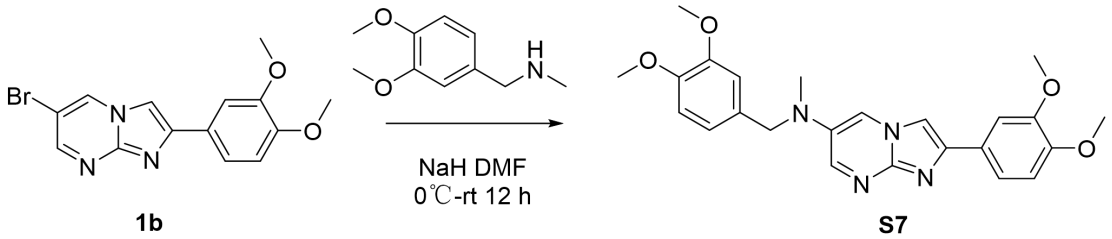
2-chloro-6-(3,4-dimethoxyphenyl)imidazo[1,2-a]pyridine (S6b)

A solution of 6-bromo-2-chloroimidazo[1,2-*a*]pyridine (100 mg, 0.43 mmol) in 1,4-dioxane (10 mL) and water (2 mL) was treated with 3,4-dimethoxyphenylboronic acid (94 mg, 0.52 mmol), $Pd(PPh_3)_4$ (50 mg, 0.043 mmol) and K_2CO_3 (120 mg, 0.86 mmol). The mixture was stirred at 90 ℃ for 12 hours under N_2 atmosphere. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (DCM/MeOH) to afford **S6b** (white solid, 80 mg, yield: 65%). ESI-MS m/z: 289.0 $[M+H]^+$.

2,6-bis(3,4-dimethoxyphenyl)imidazo[1,2-a]pyridine (S6)

A solution of **S6b** (50 mg, 0.17 mmol) in DMF (2 mL) was treated with 3,4-dimethoxyphenylboronic acid (63 mg, 0.35 mmol), CuCl (17 mg, 0.17 mmol), Cs_2CO_3 (226 mg, 0.69 mmol), $Pd(OAc)_2$ (2 mg, 0.0085 mmol), and 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (14 mg, 0.034 mmol). The mixture was stirred at 100 ℃ for 12 hours under N_2 atmosphere. Upon reaction completion, the reaction mixture was diluted with water (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic extracts were washed with saturated brine (20

mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to obtain the crude product. The crude material was then purified by preparative thin-layer chromatography using a solvent system of DCM:MeOH=20:1. The band corresponding to the target compound was carefully scraped off and extracted with a mixture of DCM:MeOH=10:1. After filtration and concentration, compound **S6** (yellow solid, 4 mg, yield: 6%). ESI-MS m/z: 391.0 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 8.80 (s, 1H), 8.32 (d, J = 5.4 Hz, 1H), 7.66 – 7.55 (m, 3H), 7.51 (t, J = 7.1 Hz, 1H), 7.33 – 7.20 (m, 1H), 7.08 (t, J = 6.6 Hz, 1H), 7.03 (d, J = 7.2 Hz, 1H), 3.87 (t, J = 6.9 Hz, 6H), 3.81 (d, J = 5.6 Hz, 6H).



Scheme S6. Synthesis of Compound **S7.**

N-(3,4-dimethoxybenzyl)-2-(3,4-dimethoxyphenyl)-N-methylimidazo[1,2-a]pyrimidin-6-amine (S7)

A solution of **1b** (30 mg, 0.09 mmol) and NaH (4.1 mg, 0.18 mmol) in DMF (5 mL) was stirred at 0 ℃ for 15 minutes under N_2 atmosphere. (3,4-dimethoxybenzylL)methylamine (32.6 mg, 0.18 mmol) was added after these operations are completed and turn the reaction to room temperature stirred 12 hours. After completion of the reaction, the mixture was quenched with water (10 mL) and extract with ethyl acetate. The combined organic layers were washed with saturated brine and dried over Na_2SO_4 filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (PE/EA) to afford **S7** (pale yellow solid, 3 mg, yield: 8%). ESI-MS m/z: 435.0 $[M+H]^+$. ^1H NMR (600 MHz, DMSO-d_6) δ 8.28 (s, 1H), 8.17 (s, 1H), 7.59 (s, 2H), 6.97 (d, J = 66.2 Hz, 2H), 6.80 (s, 2H), 6.40 (s, 1H), 4.57 (s, 2H), 3.76 (dd, J = 72.9, 31.9 Hz, 12H), 2.96 (s, 3H).

Supplementary Tables

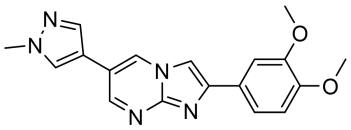
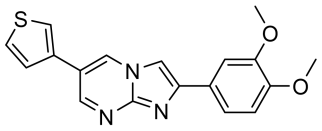
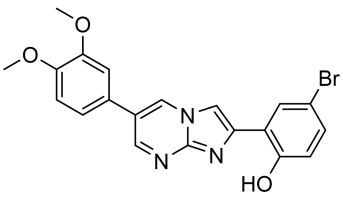
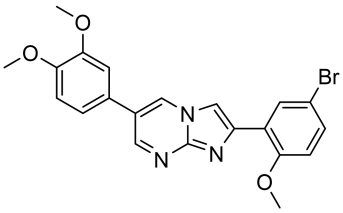
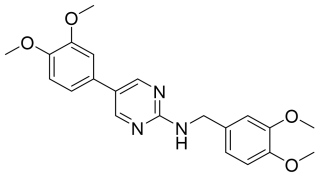
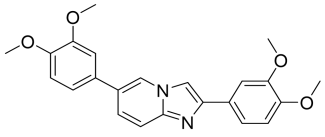
Table S1. Physicochemical Parameters and docking score of Compounds **1-43.**

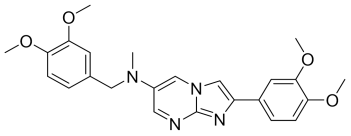
Compd	LogP[a]	Hammett[b]	Docking score[c]	MM GBSA	Compd	LogP	Hammett	Docking score	MM GBSA
TJA-31	3.28	-0.15	-10.8	-87.7	**23**	4.61	0.35	-10.6	-96.0
1	3.64	/	-9.8	-88.1	**24**	3.39	0.66	-11.1	-93.0
2	3.65	/	-9.8	-96.6	**25**	4.53	0.54	-11.4	-88.8
3	3.67	0.12	-9.8	-90.5	**26**	3.65	/	-10.2	-80.9
4	3.69	-0.27	-10.3	-92.5	**27**	3.67	0.12	-10.4	-81.8
5	4.07	-0.24	-10.4	-106.7	**28**	2.91	/	-9.9	-89.0
6	3.80	0.06	-10.4	-73.4	**29**	2.91	/	-9.0	-87.9
7	4.32	0.23	-10.2	-99.8	**30**	3.49	/	-9.7	-81.0
8	4.61	0.35	-9.7	-89.6	**31**	4.09	/	-9.6	-74.3
9	4.53	0.54	-10.8	-96.3	**32**	4.43	0.12	-10.1	-88.5
10	3.39	0.66	-10.5	-100.1	**33**	4.54	0.45	-10.6	-86.0
11	2.74	/	-11.0	-80.9	**34**	4.82	0.32	-10.4	-77.3
12	2.44	/	-9.8	-103.6	**35**	4.43	0.35	-9.7	-91.1
13	2.38	/	-11.3	-92.1	**36**	4.54	0.57	-10.7	-85.8
14	3.11	/	-10.9	-76.9	**37**	5.05	0.60	-10.7	-88.2
15	3.51	/	-11.8	-82.0	**38**	4.93	0.60	-10.8	-90.3
16	2.94	/	-11.6	-97.1	**39**	5.14	0.66	-10.4	-93.1
17	3.69	-0.27	-11.0	-102.2	**40**	4.54	/	-10.8	-97.8
18	4.09	-0.17	-10.8	-94.2	**41**	3.93	/	-11.0	-99.5
19	3.16	-0.37	-10.7	-86.3	**42**	3.50	/	-11.2	-97.0
20	3.80	0.06	-11.0	-91.0	**43**	2.65	/	-11.8	-98.3
21	4.32	0.23	-10.6	-87.1	**K6C**	/	/	-15.0	-120.3
22	4.45	0.23	-10.6	-90.4					

[a] LogP: values were calculated as miLogP using Molinspiration property calculation service (www.molinspiration.com). [b] Hammett substituent constants were taken from:

Hansch, C.; Leo, A.; Taft, R. W. A Survey of Hammett Substituent Constants and Resonance and Field Parameters. Chem. Rev. 1991, 91, 165–195.[c] Molecular docking was performed using Glide within the Schrödinger Maestro suite. The docking score represents the predicted binding affinity, where more negative values indicate stronger predicted binding.

Table S2. Physicochemical Parameters and Pks13 Inhibitory Activity of Compounds **S1-S7.**

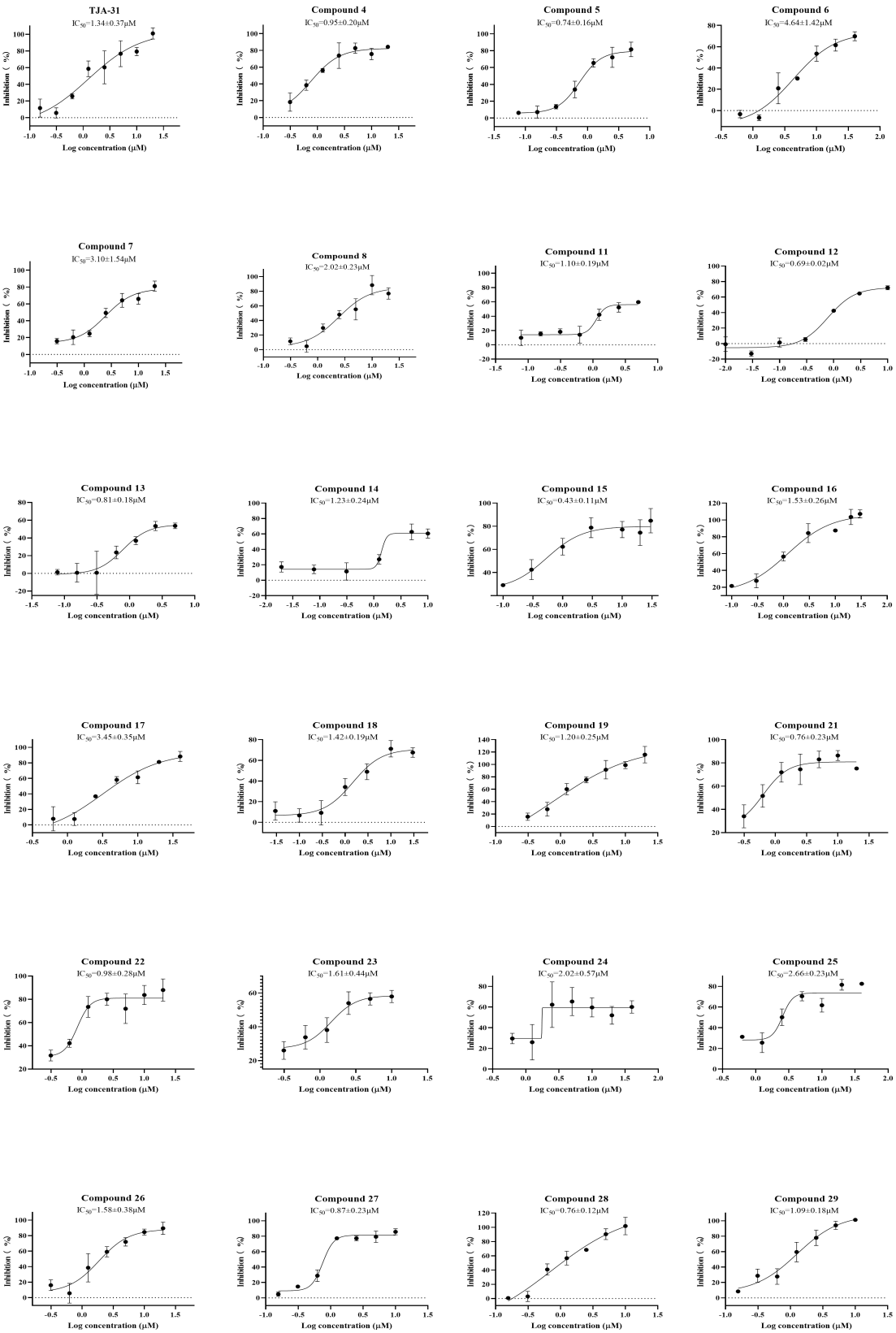
Compd	Structure	LogP[a]	Hammett[b]	Docking score[c]	MM GBSA	IC_{50} (μM)
S1		3.81	/	-9.8	-84.3	>10
S2		5.02	/	-9.6	-86.0	>10
S3		4.16	/	-9.6	-88.3	>10
S4		4.43	/	-9.7	-93.6	>10
S5		3.24	/	-9.3	-87.0	>10
S6		4.01	/	-9.7	-122.8	>10

S7		2.99	/	-11.4	-90.0	>10

[a] LogP: values were calculated as miLogP using Molinspiration property calculation service (www.molinspiration.com).

[b] Hammett substituent constants were taken from: Hansch, C.; Leo, A.; Taft, R. W. A Survey of Hammett Substituent Constants and Resonance and Field Parameters. Chem. Rev. 1991, 91, 165–195.[c] Molecular docking was performed using Glide within the Schrödinger Maestro suite. The docking score represents the predicted binding affinity, where more negative values indicate stronger predicted binding.

Supplementary Figures



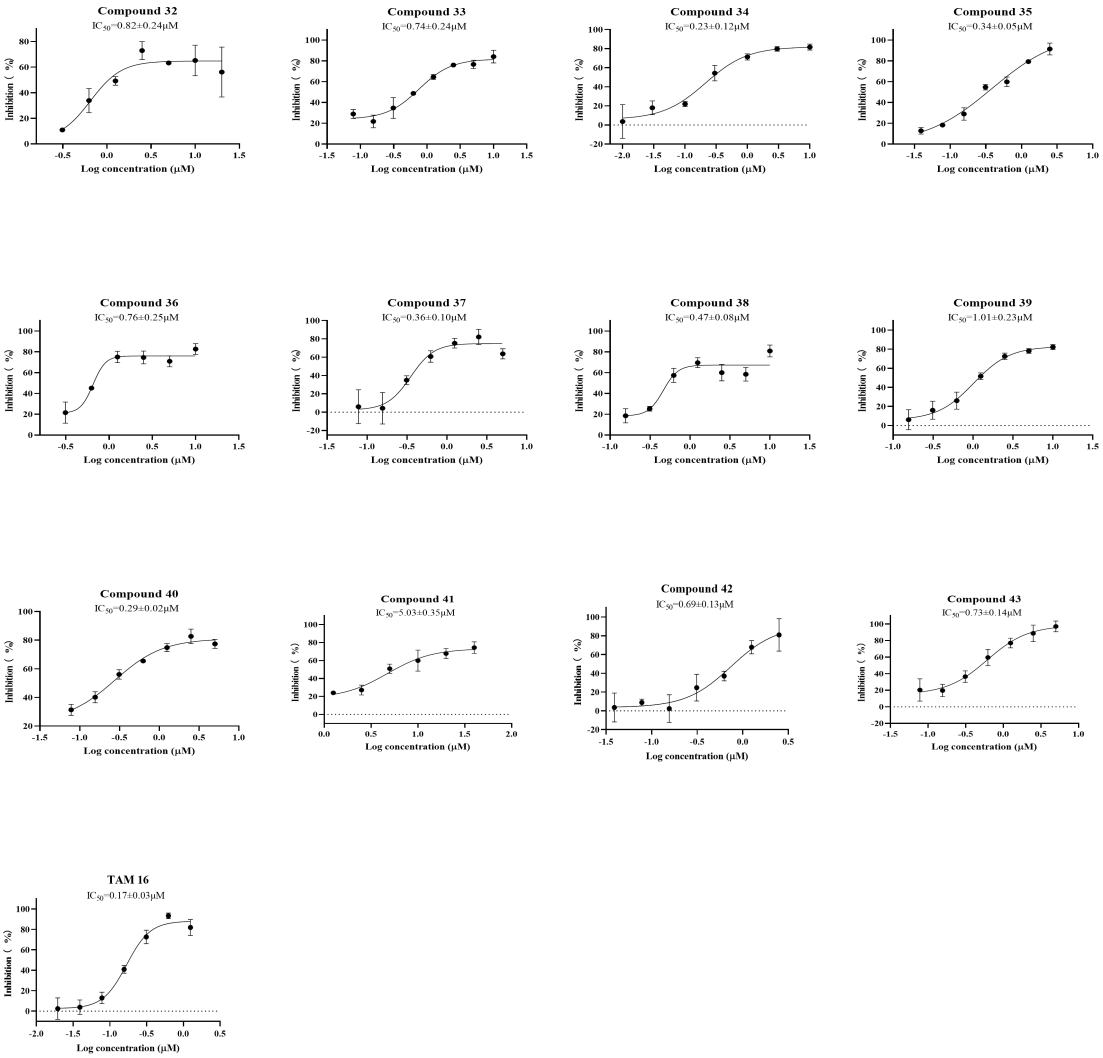


Figure S1. Dose-response curves of final compounds inhibiting the Pks 13-TE in an enzyme assay. The enzyme inhibition ratio (%) is plotted against the log inhibitor concentration (log μM). Each data point represents the mean of three independent technical replicates; error bars represent the standard deviation (±SD). The half-maximal inhibitory concentration (IC_{50}) values were determined by fitting the data to a four-parameter logistic (4PL) nonlinear regression model using GraphPad Prism 8 software, specifically using the analysis option: [Inhibitor] vs. response -- Variable slope (four parameters).

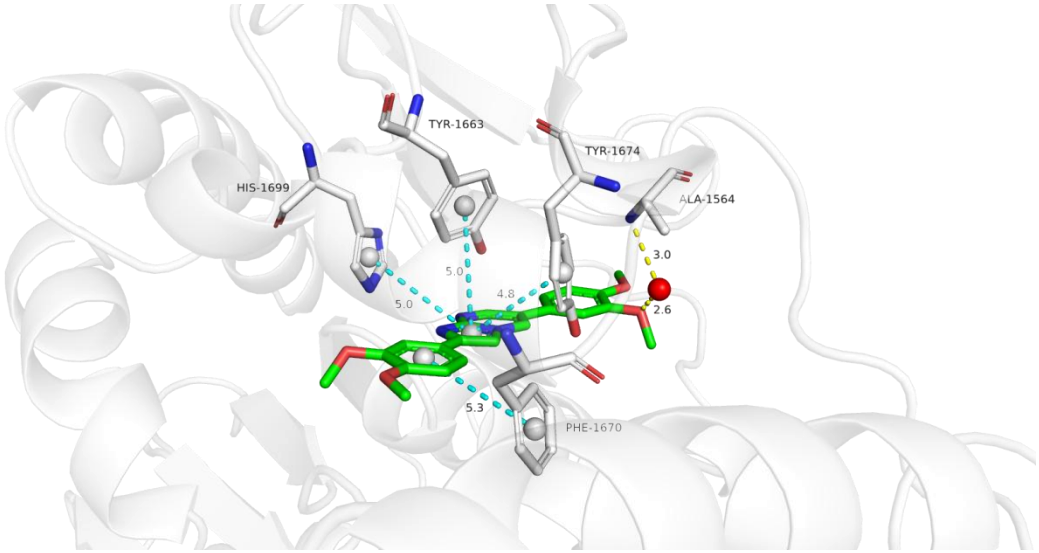


Figure S2. Proposed binding mode of compound **TJA-31** (colored green). The key residues located in the binding site of Pks13-TE (PDB ID: 8TR4) were shown. The cyan dotted line represents π–π stacking interaction, the brown dotted line represents halogen bond interaction, the yellow dotted line represents hydrogen bond interaction, , and the red spheres correspond to water molecules.

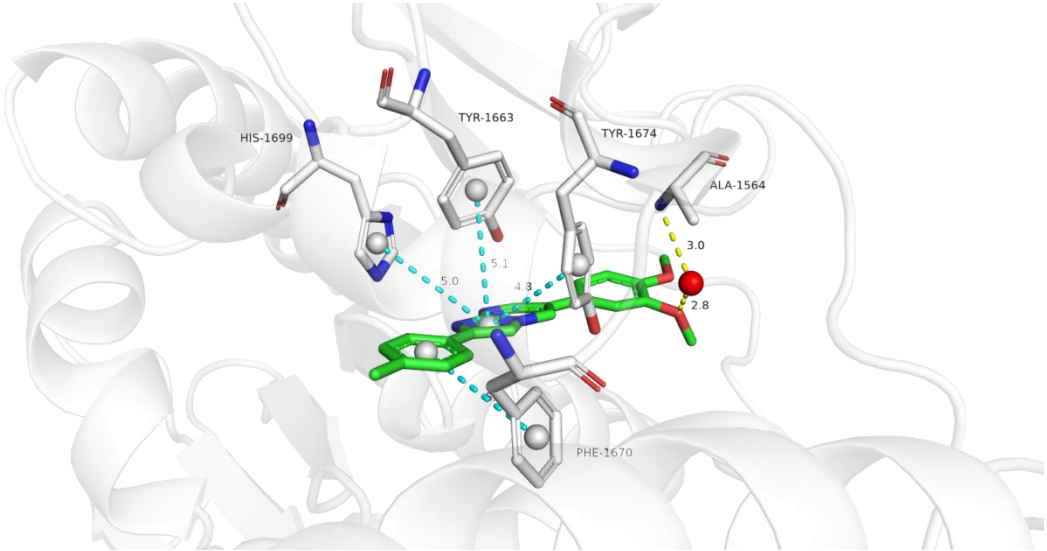


Figure S3. Proposed binding mode of compound **18** (colored green). The key residues located in the binding site of Pks13-TE (PDB ID: 8TR4) were shown. The cyan dotted line represents π–π stacking interaction, the brown dotted line represents

halogen bond interaction, the yellow dotted line represents hydrogen bond interaction, , and the red spheres correspond to water molecules.

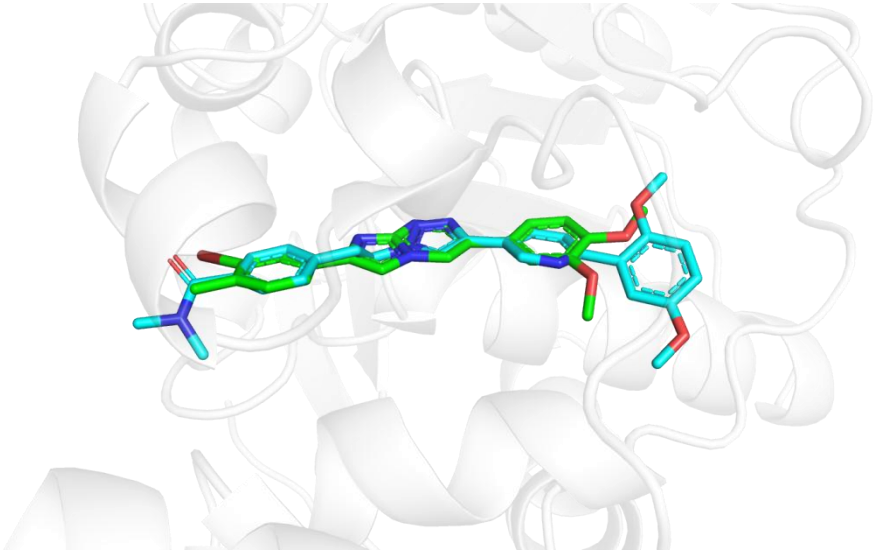
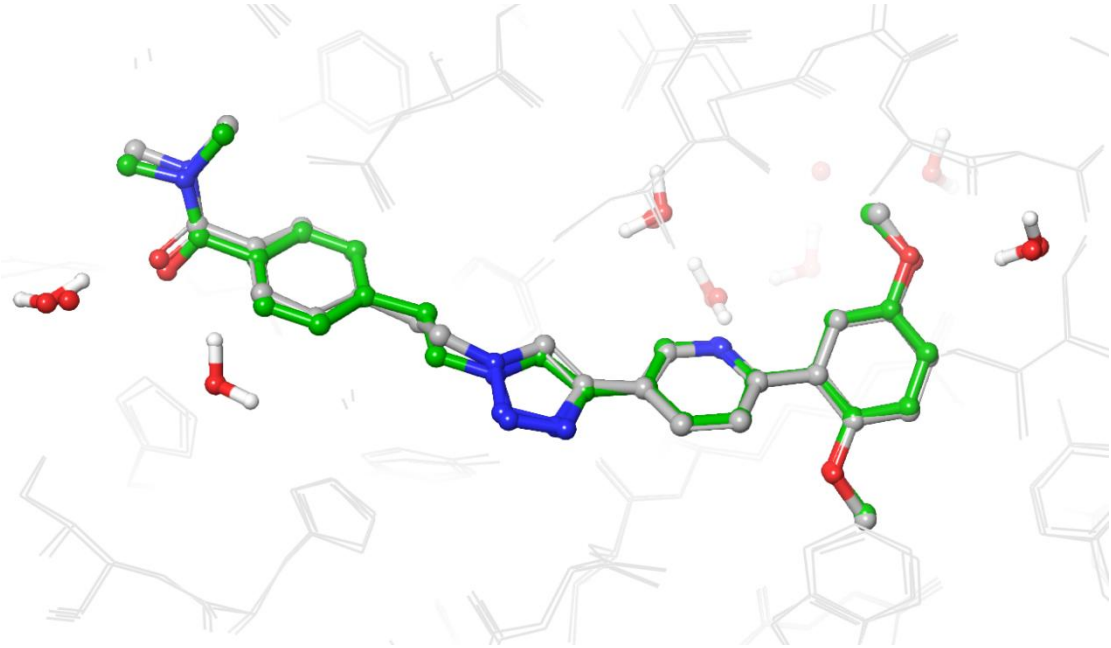


Figure S4. Overlay of the Docking Models for Compound **34** (colored green) and **K6C** (colored cyan) Bound to 8TR4.

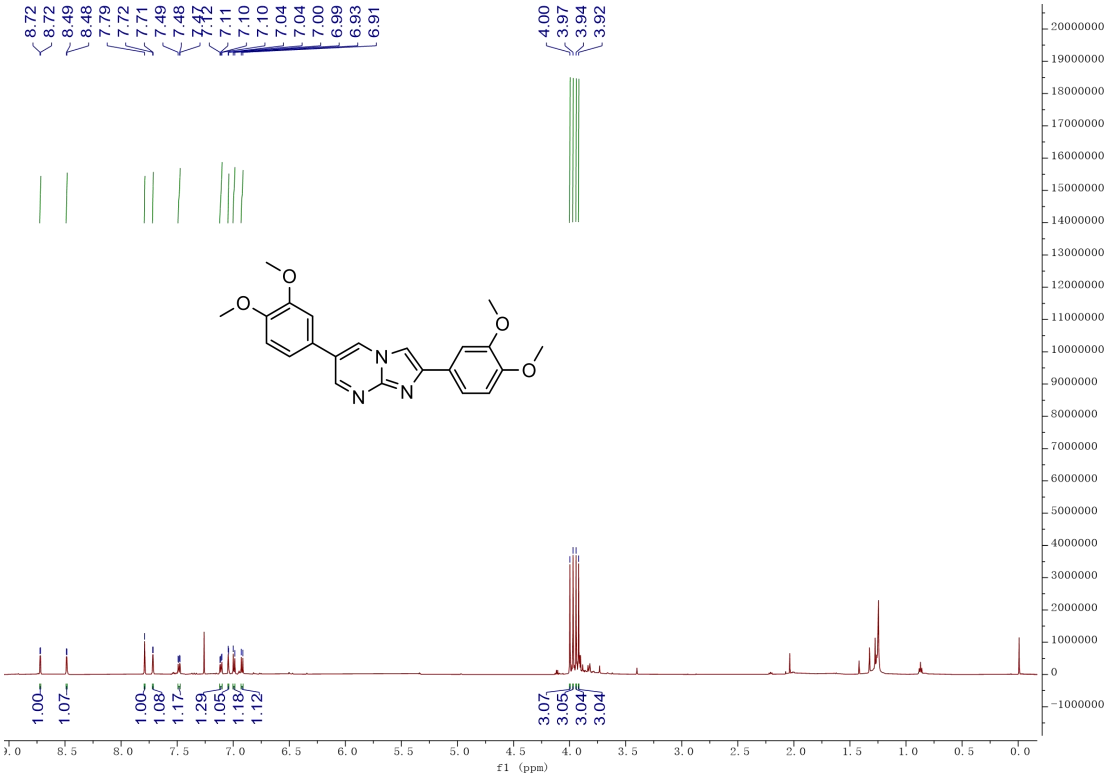


RMS:0.18 (method: C-alpha Atoms); RMS:0.22 (method: Protein backbone)

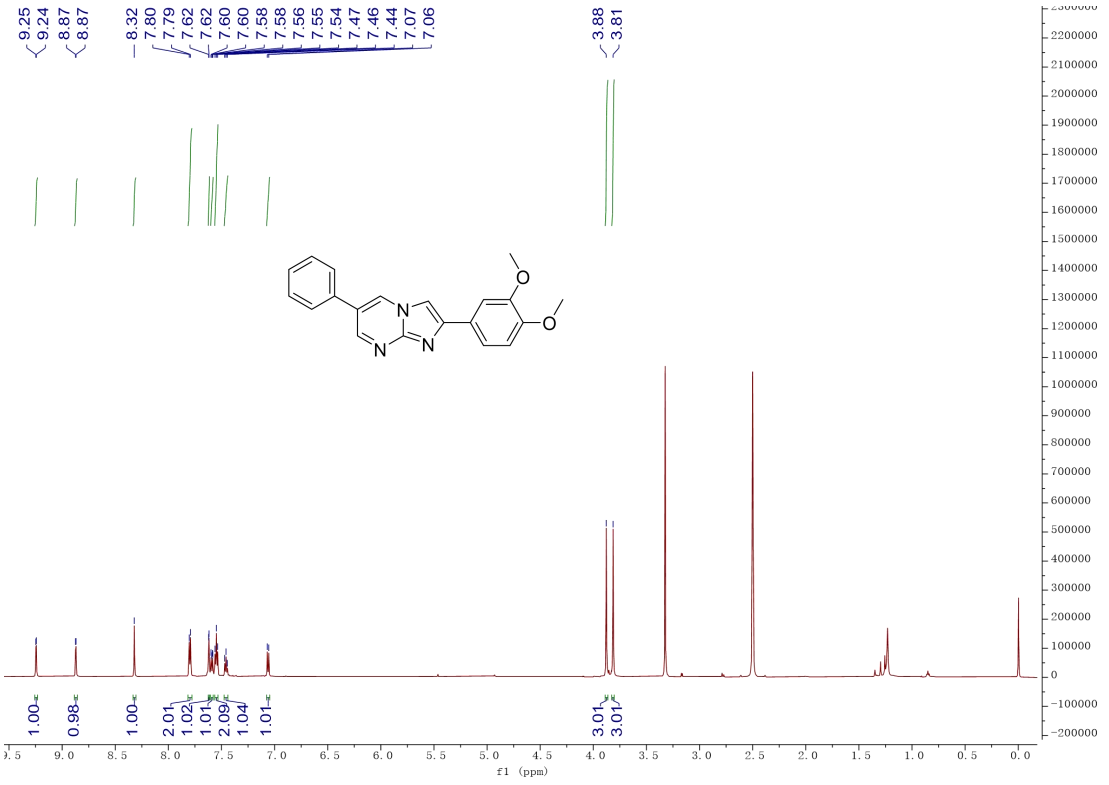
Figure S5. Overlay of the Docking Models for Compound **K6C** (colored gray and green) Bound to 8TR4.

Spectral data: ^{1}H NMR spectrum for compounds TJA-31, 1-43 and S1-S7.

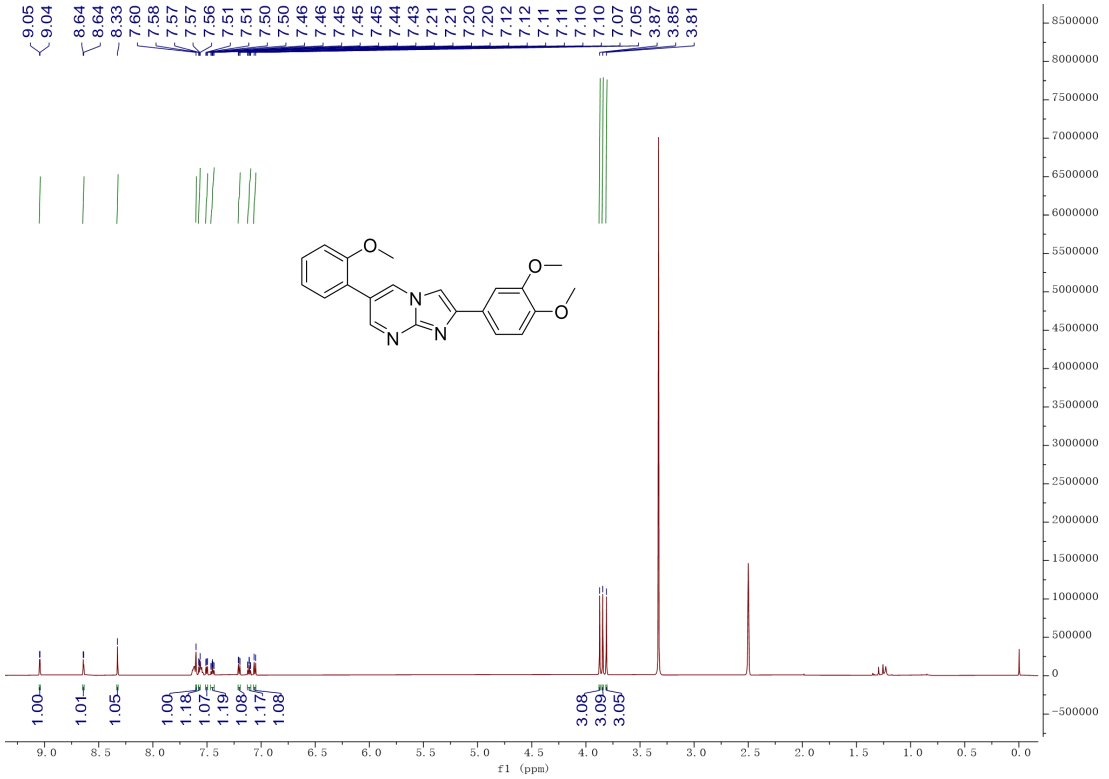
^{1}H NMR spectrum of compound **TJA-31**



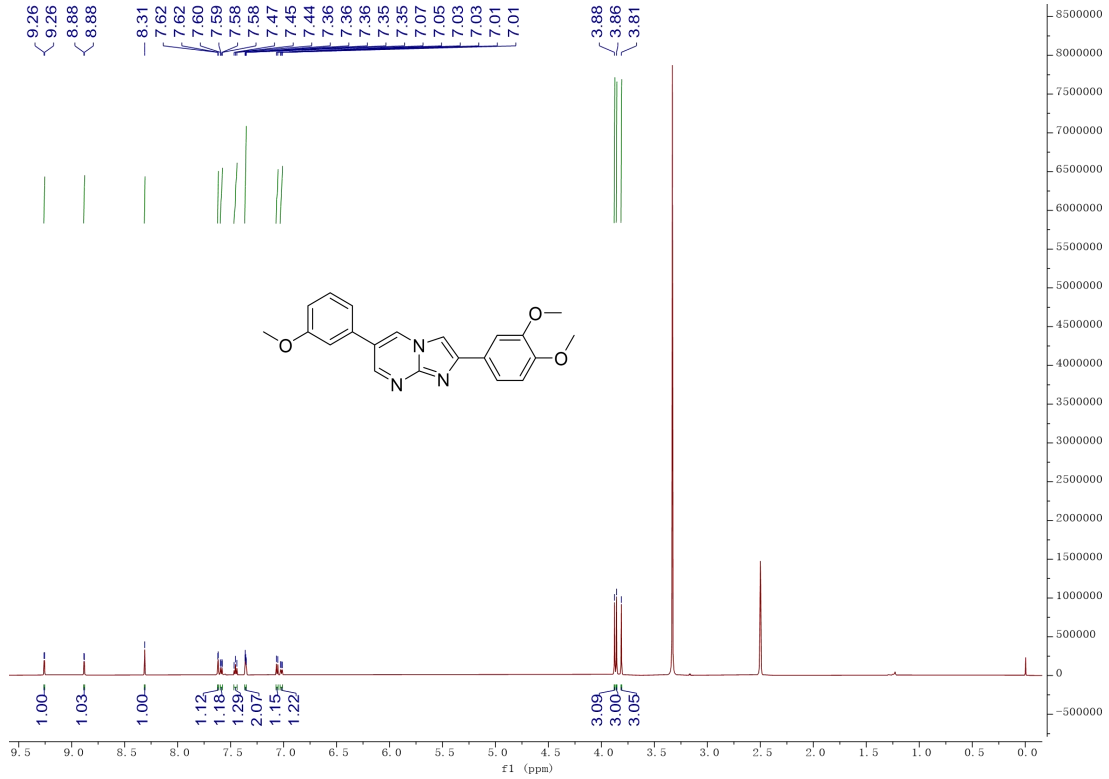
^{1}H NMR spectrum of compound **1**



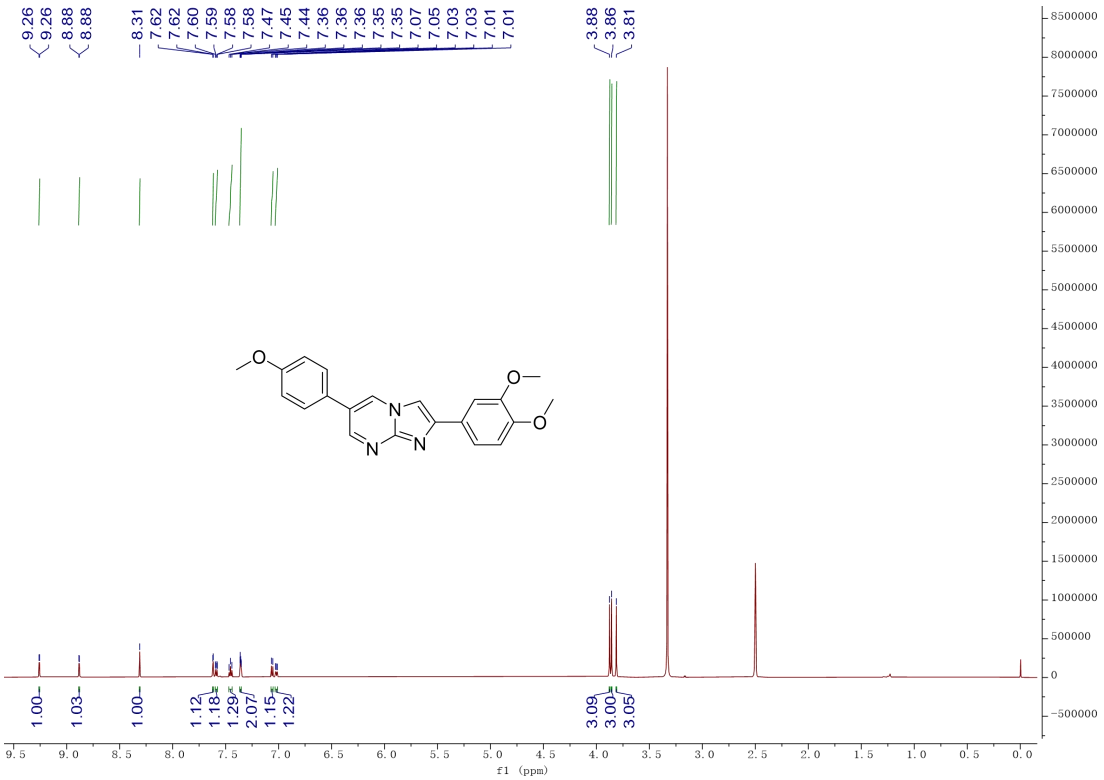
^{1}H NMR spectrum of compound **2**



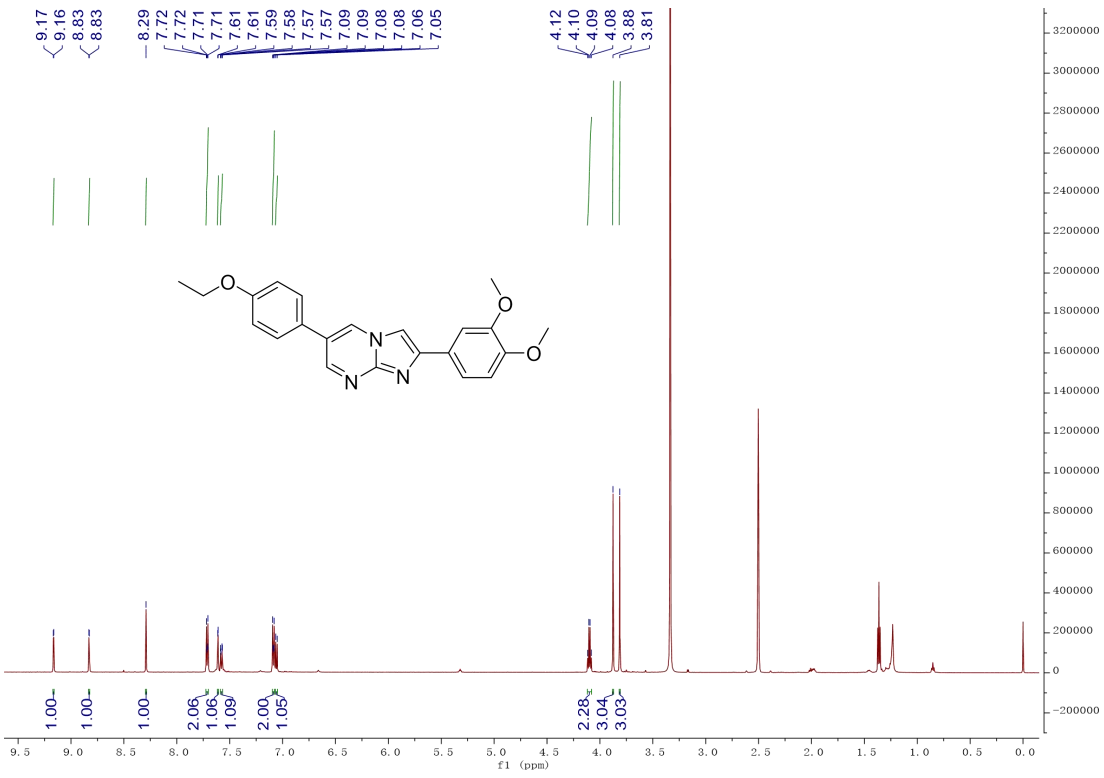
^{1}H NMR spectrum of compound **3**



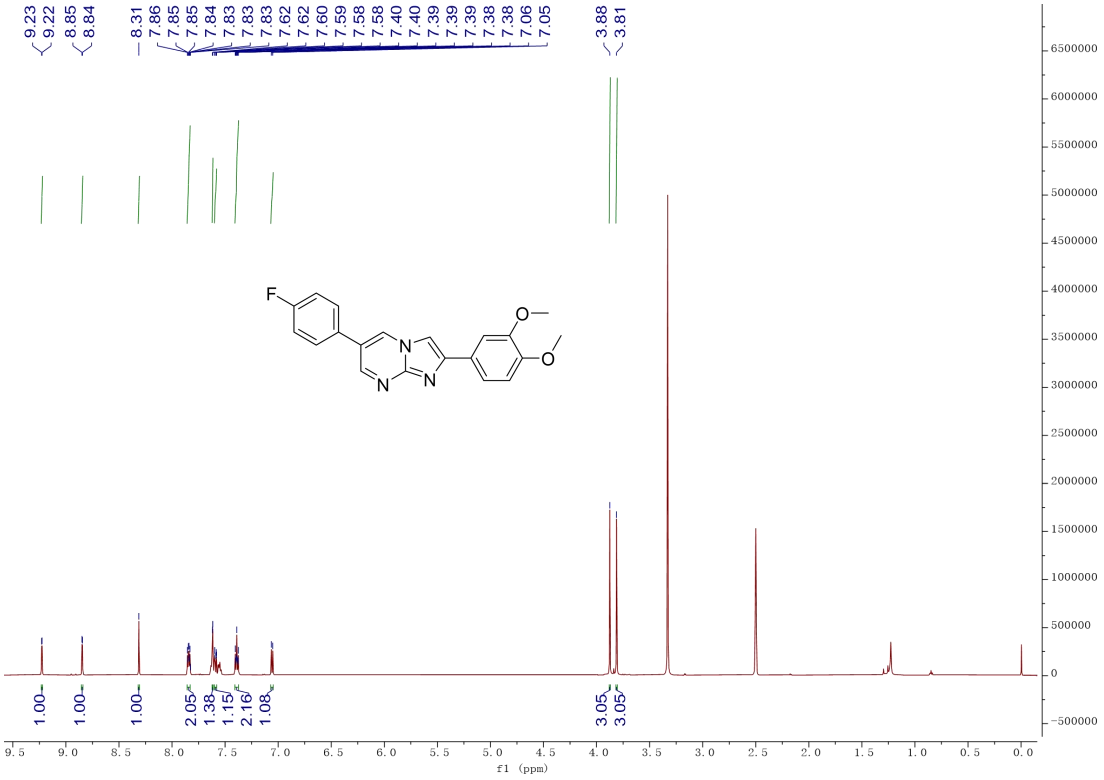
^{1}H NMR spectrum of compound **4**



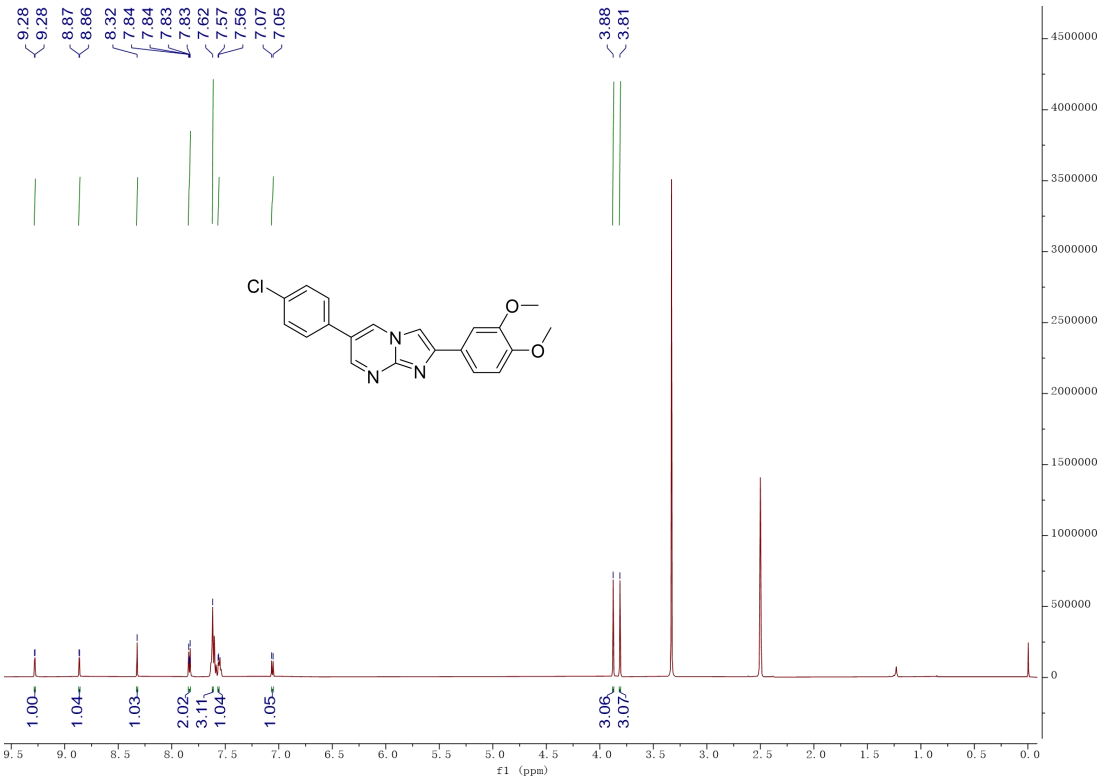
^{1}H NMR spectrum of compound **5**



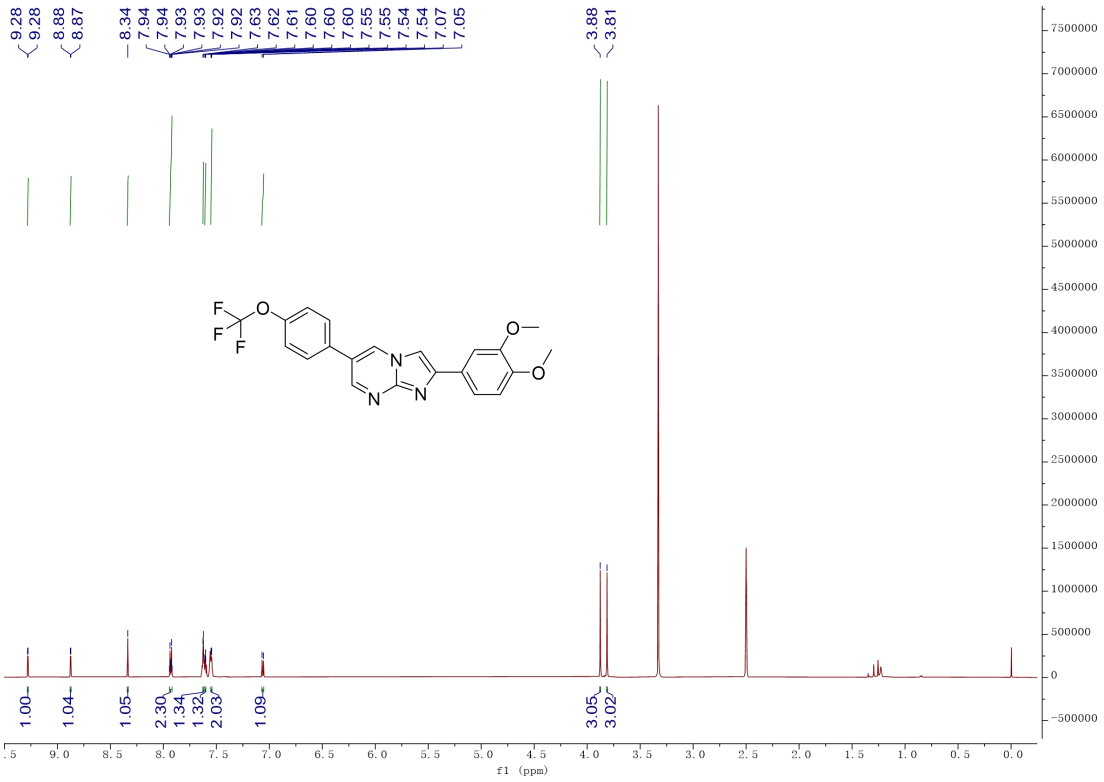
^{1}H NMR spectrum of compound **6**



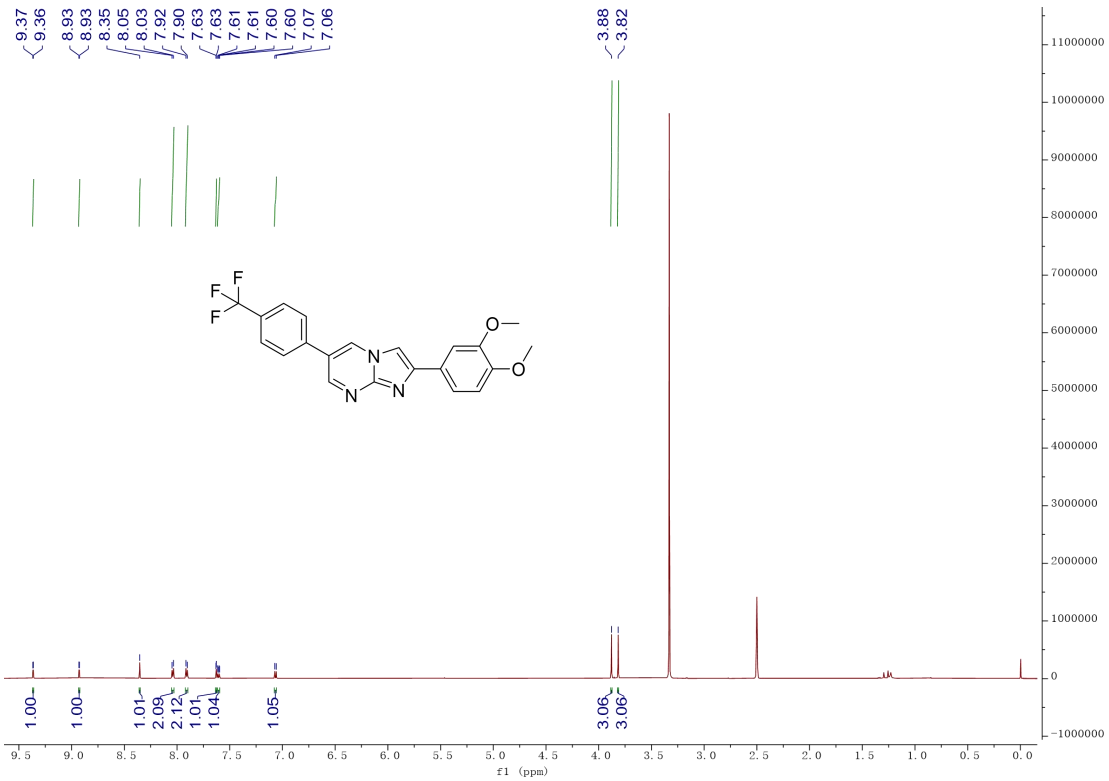
^{1}H NMR spectrum of compound **7**



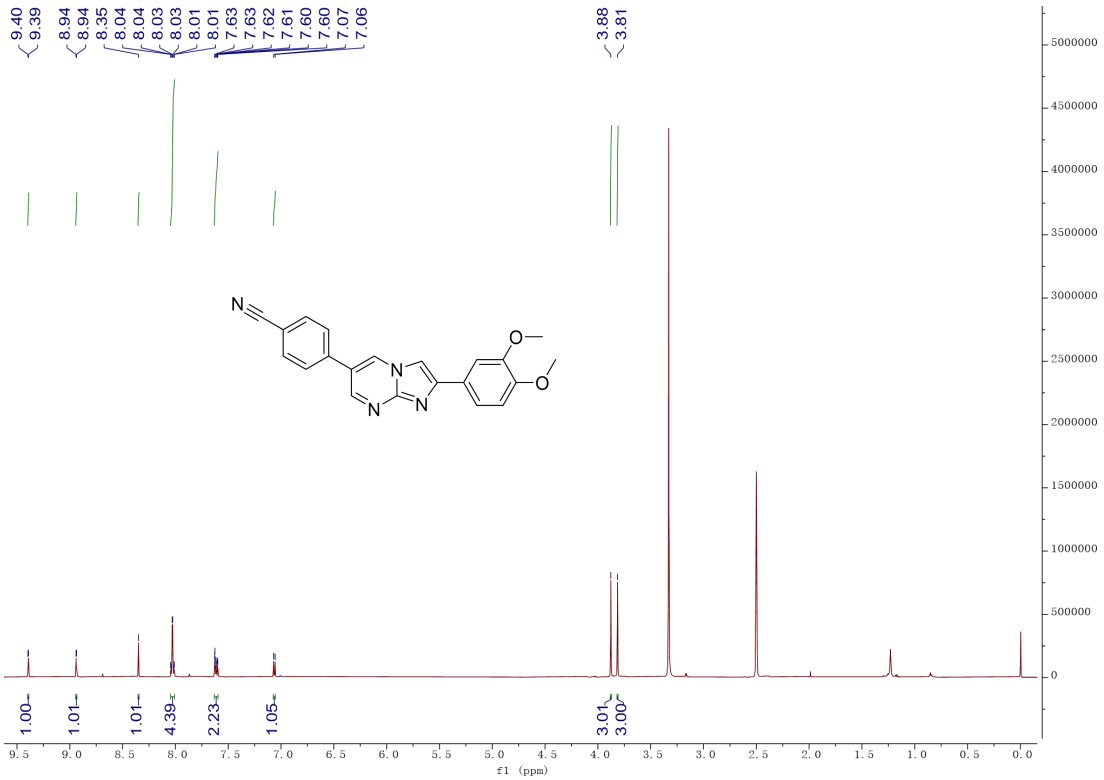
^{1}H NMR spectrum of compound **8**



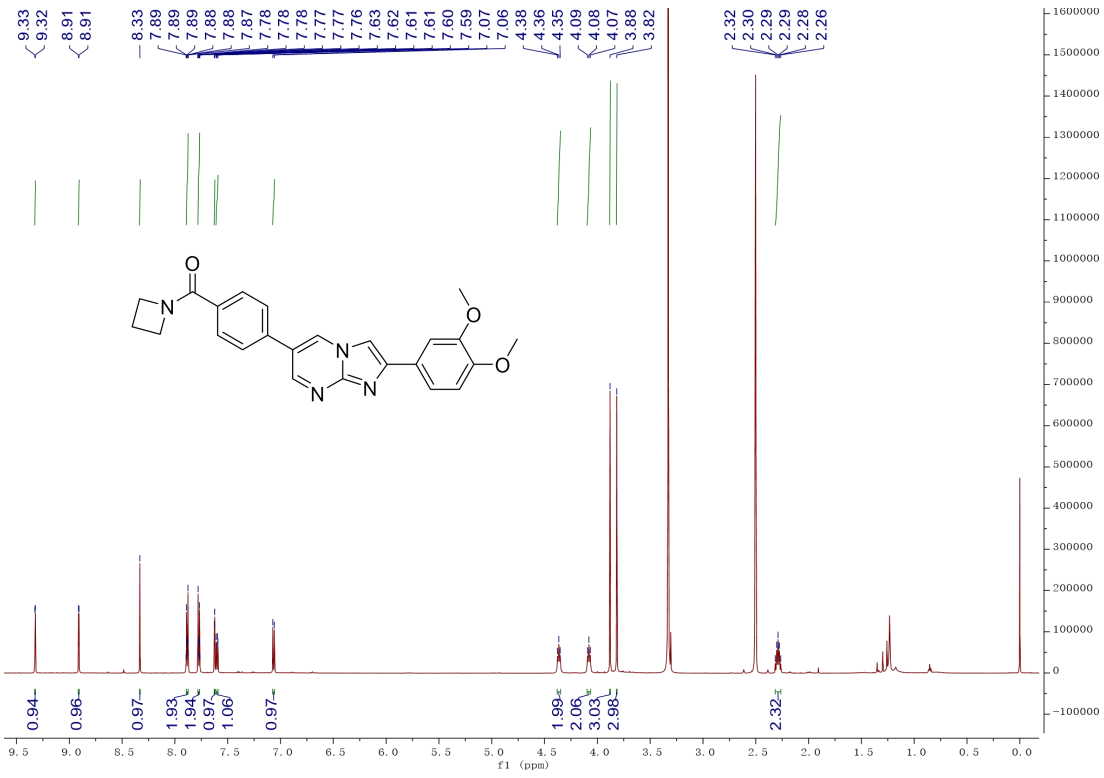
^{1}H NMR spectrum of compound **9**



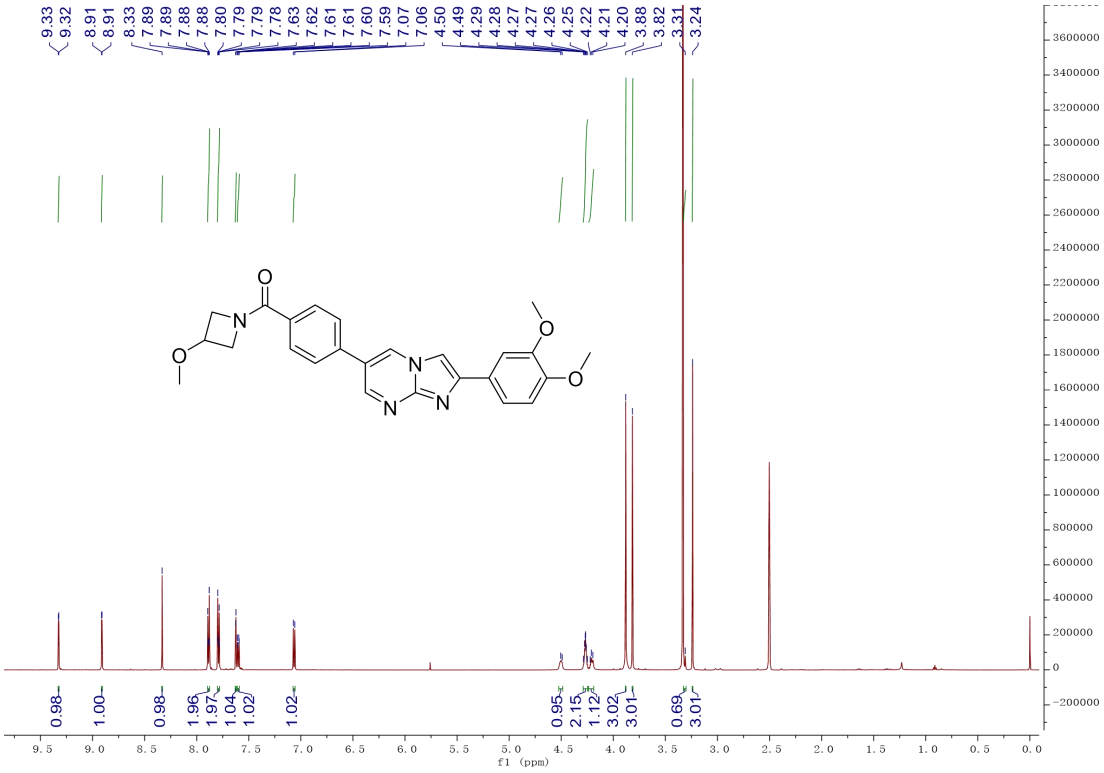
[1]H NMR spectrum of compound **10**



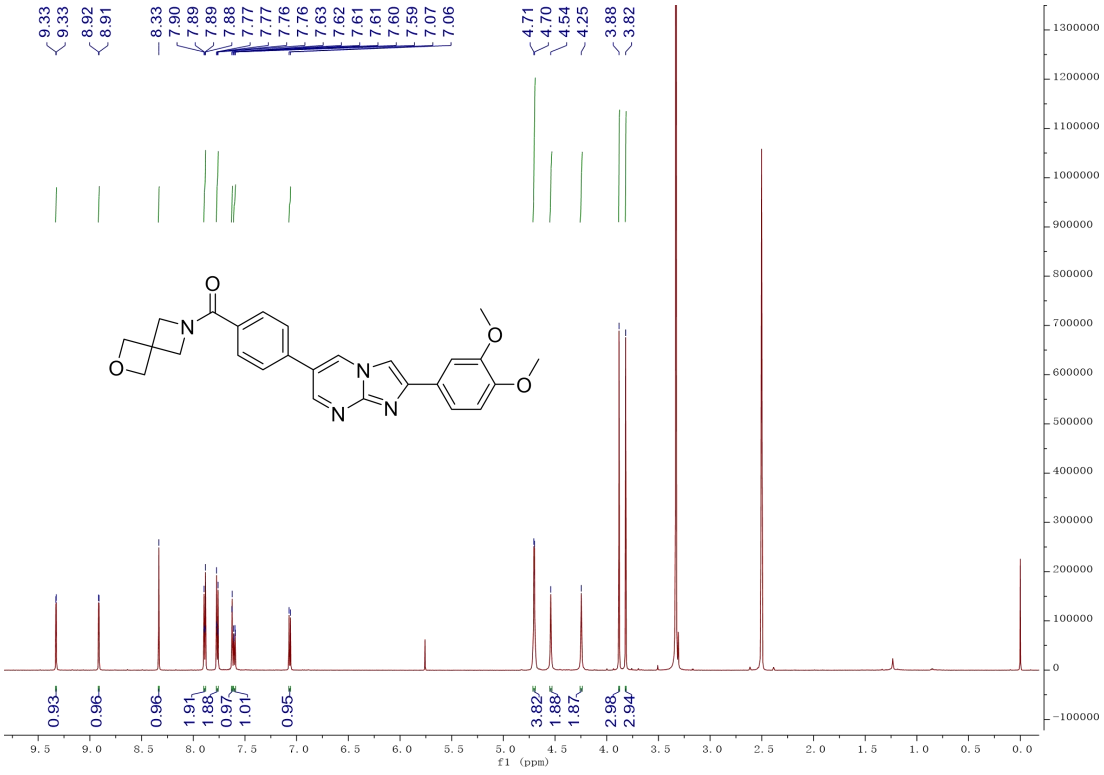
[1]H NMR spectrum of compound **11**



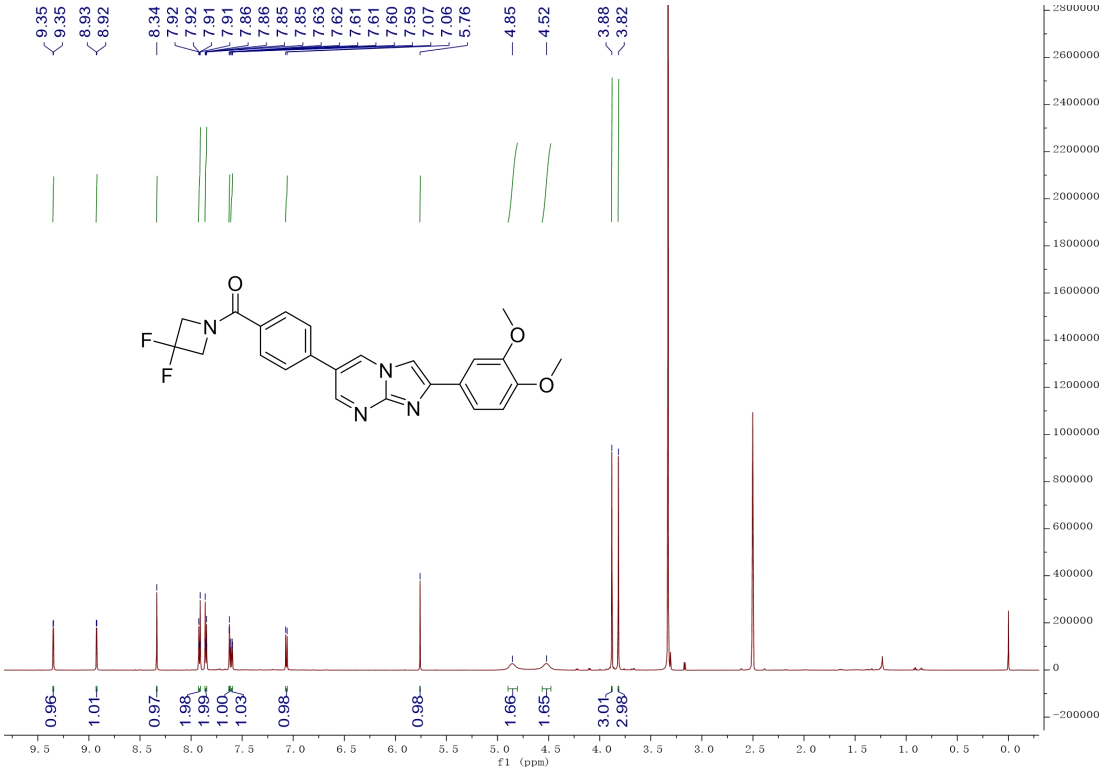
^{1}H NMR spectrum of compound **12**



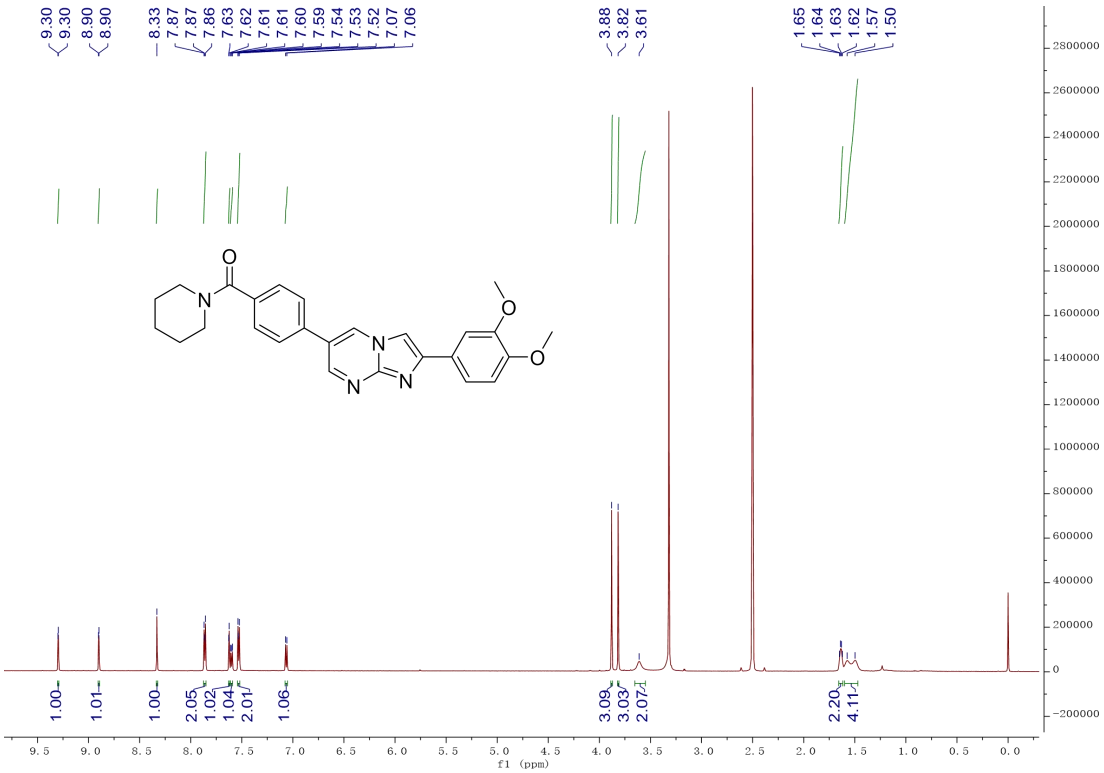
^{1}H NMR spectrum of compound **13**



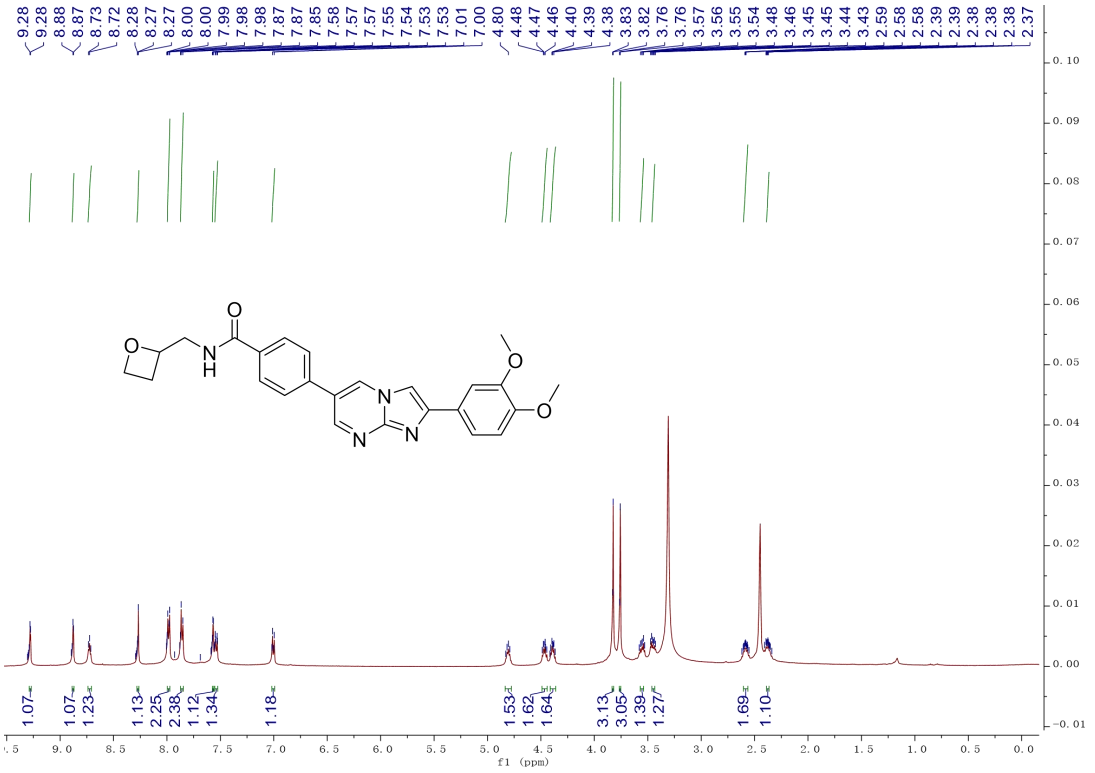
^{1}H NMR spectrum of compound **14**



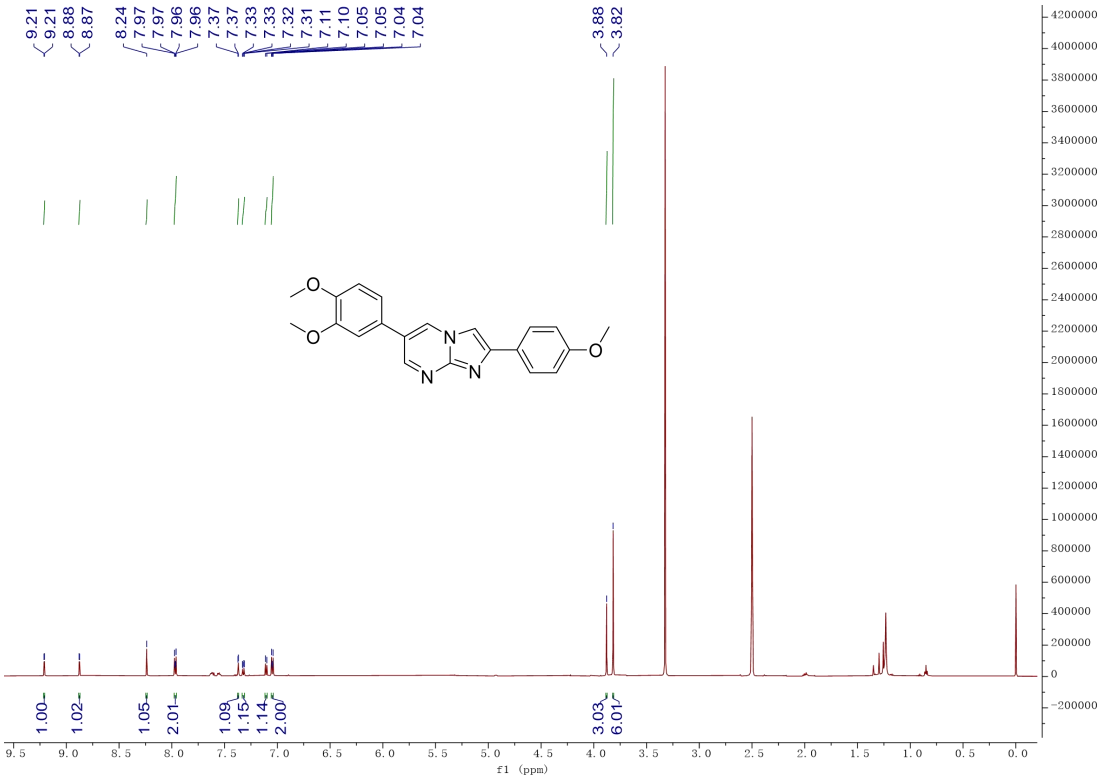
^{1}H NMR spectrum of compound **15**



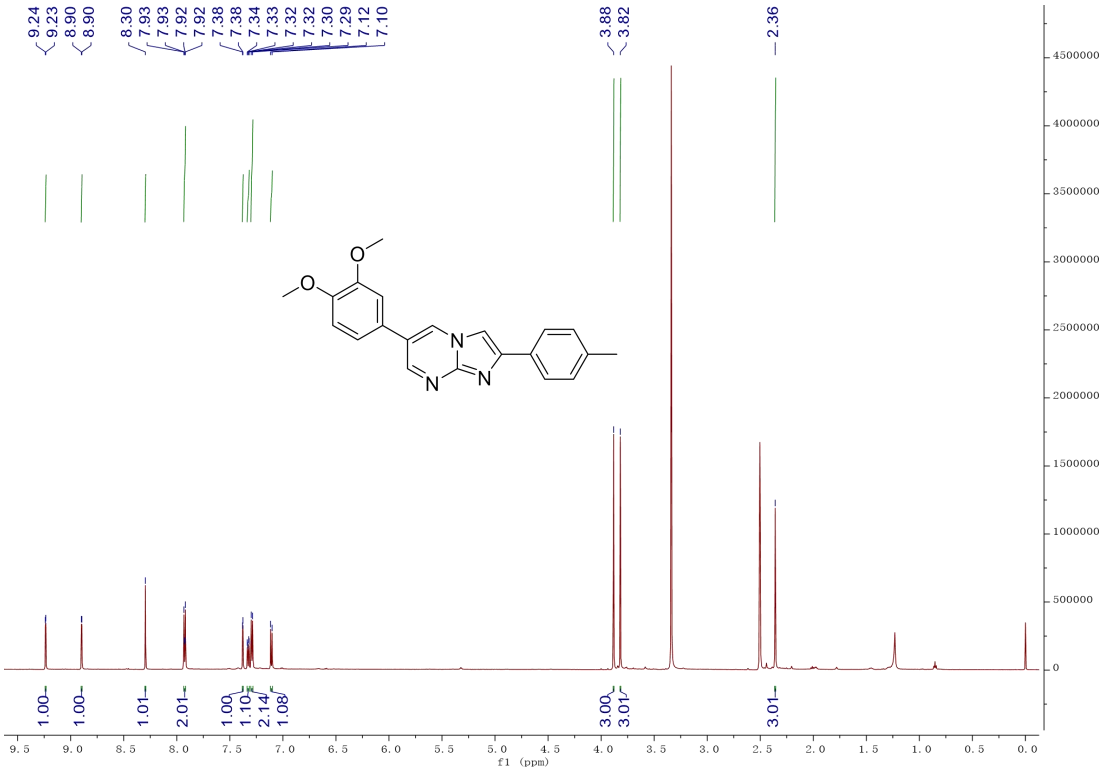
^{1}H NMR spectrum of compound **16**



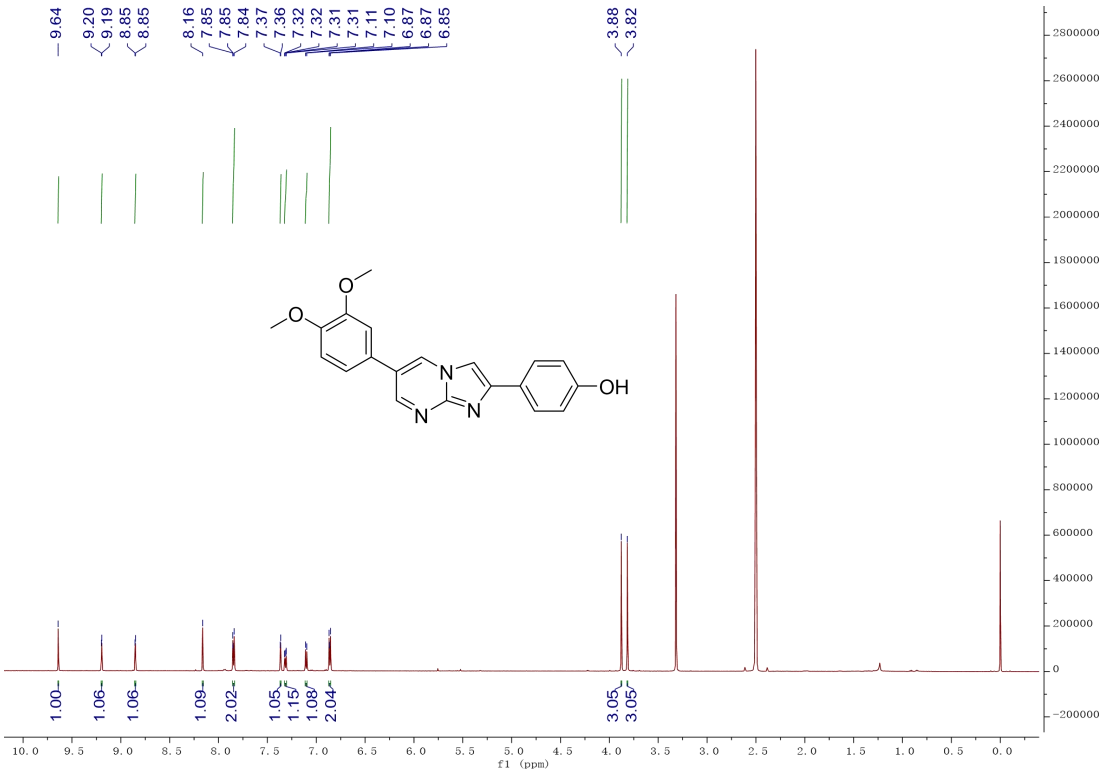
^{1}H NMR spectrum of compound **17**



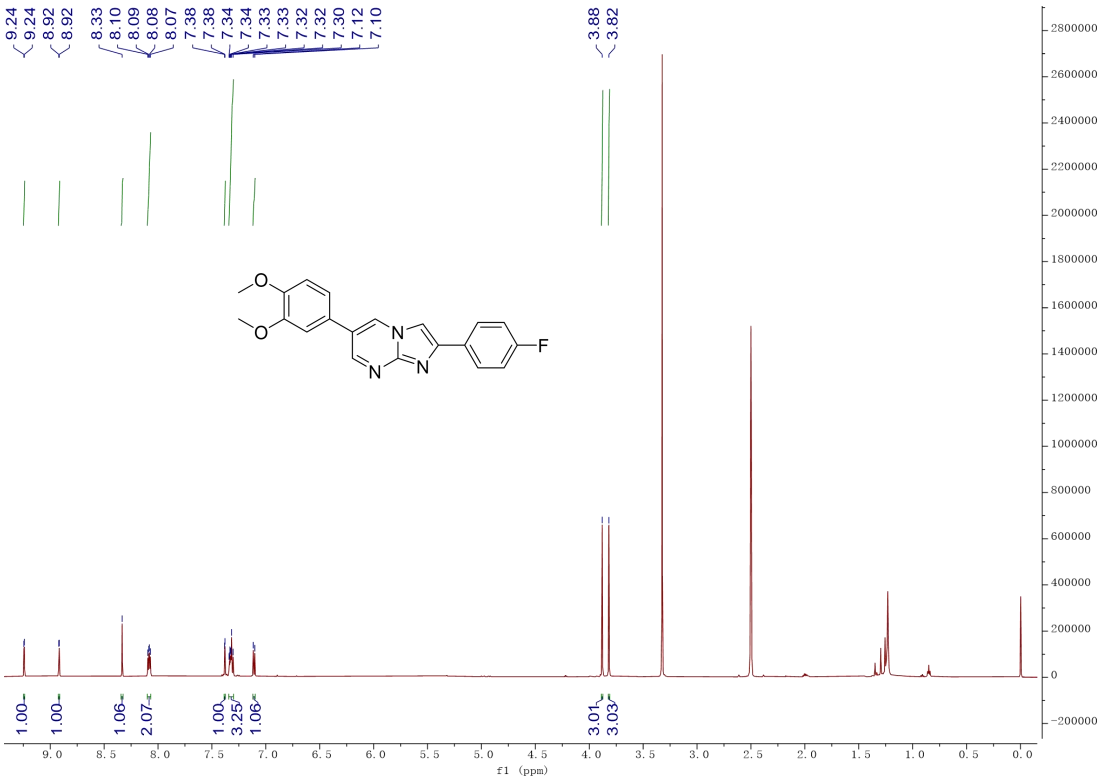
^{1}H NMR spectrum of compound **18**



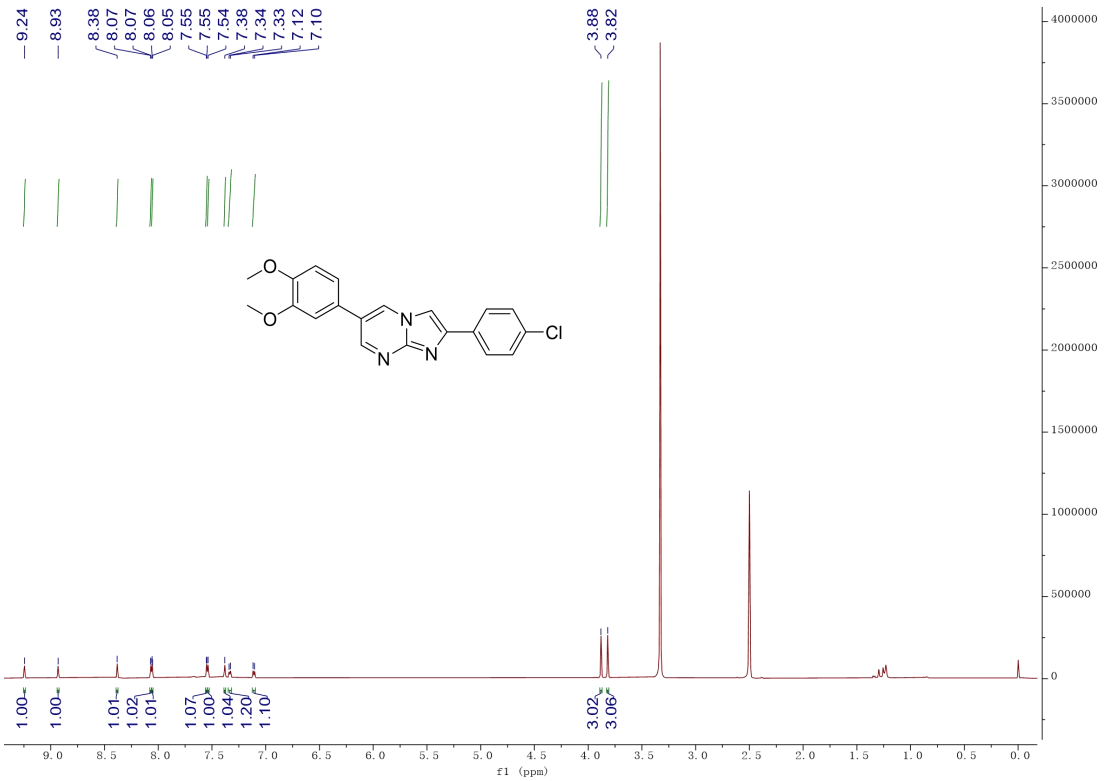
^{1}H NMR spectrum of compound **19**



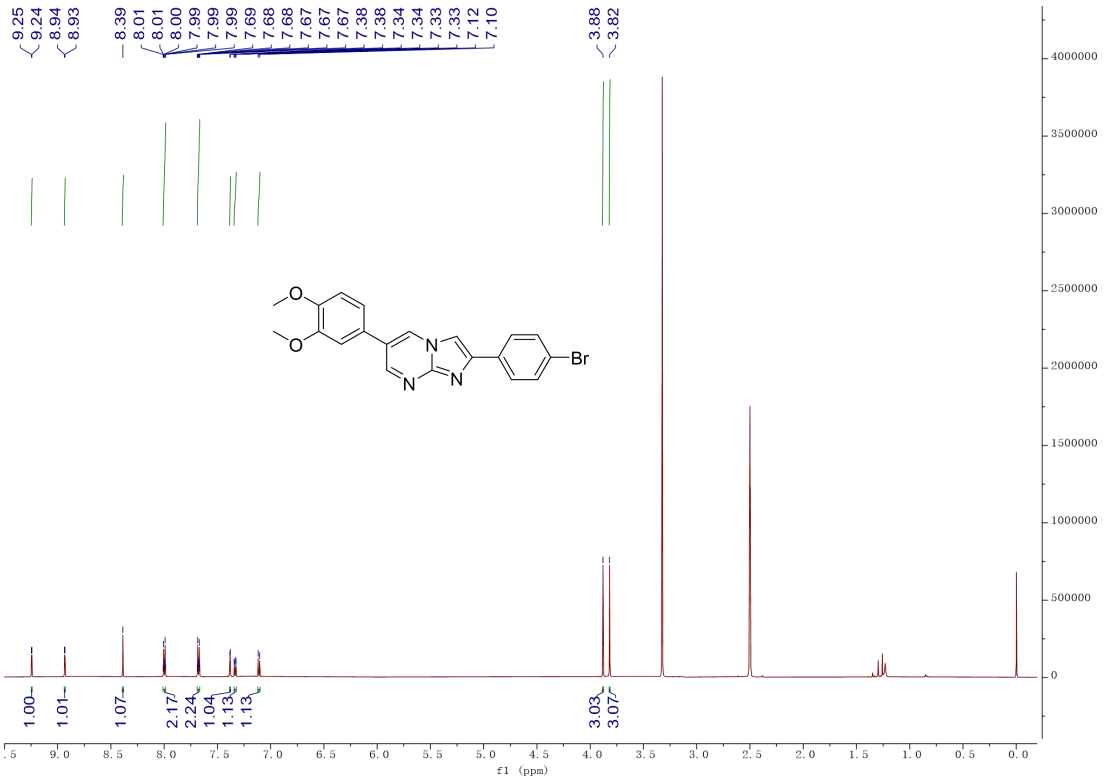
^{1}H NMR spectrum of compound **20**



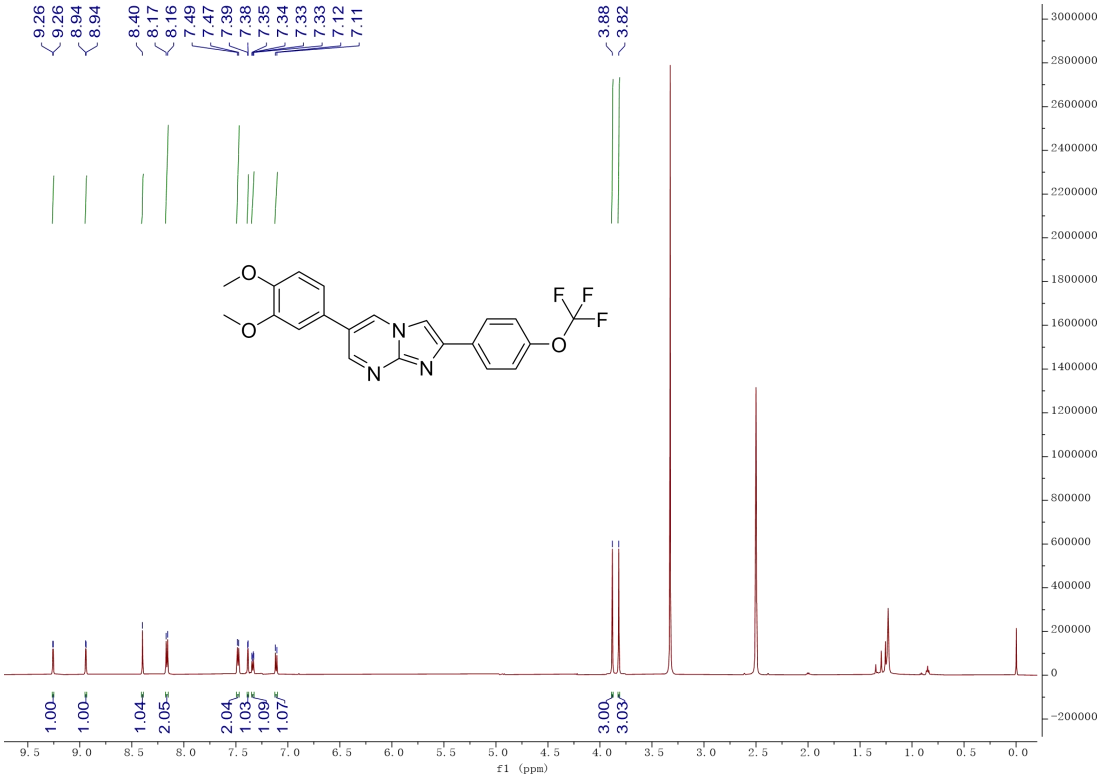
^{1}H NMR spectrum of compound **21**



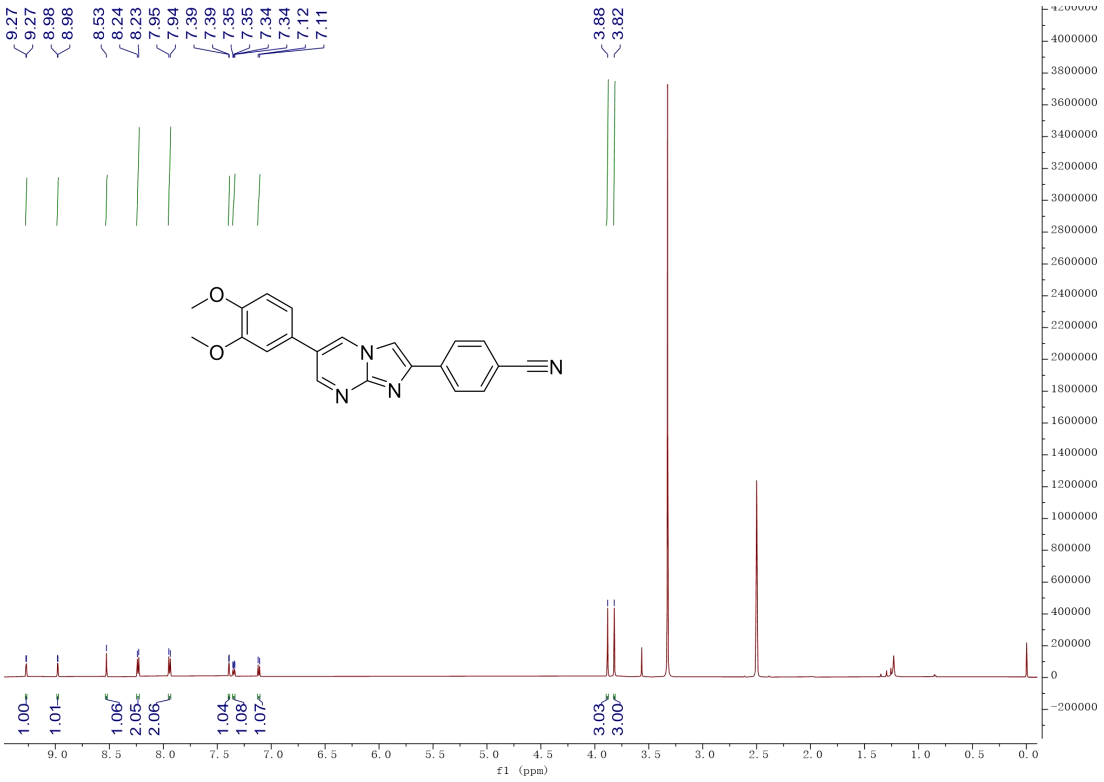
^{1}H NMR spectrum of compound **22**



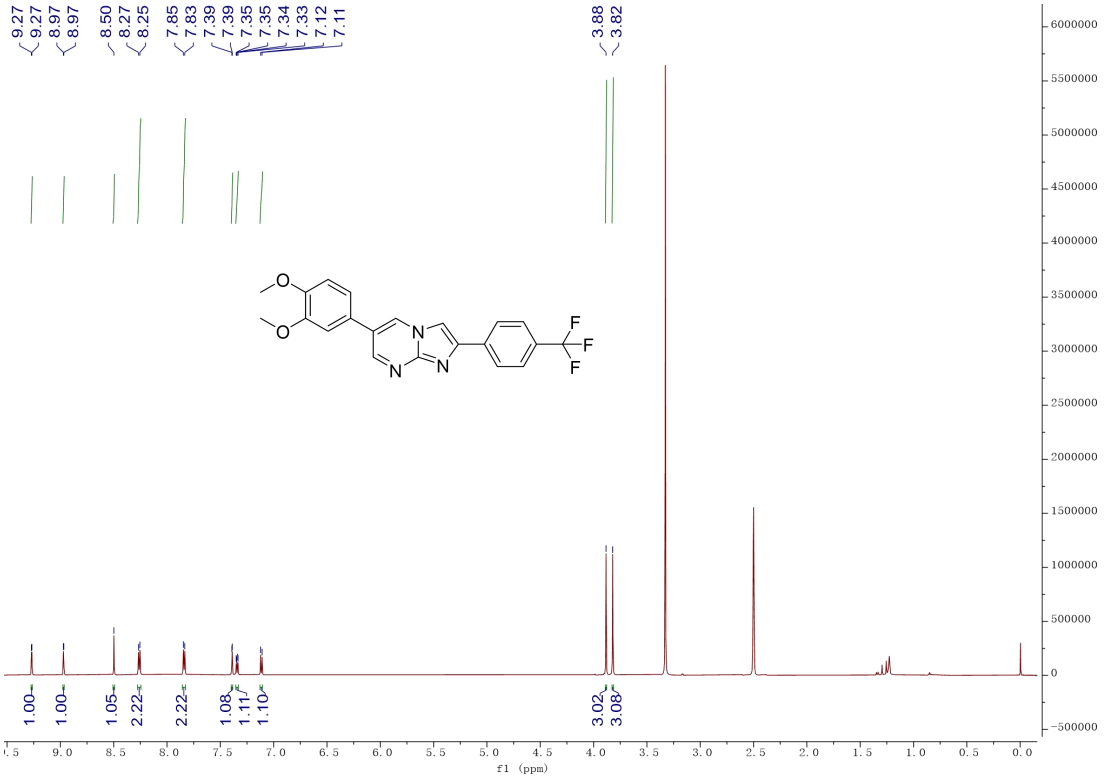
^{1}H NMR spectrum of compound **23**



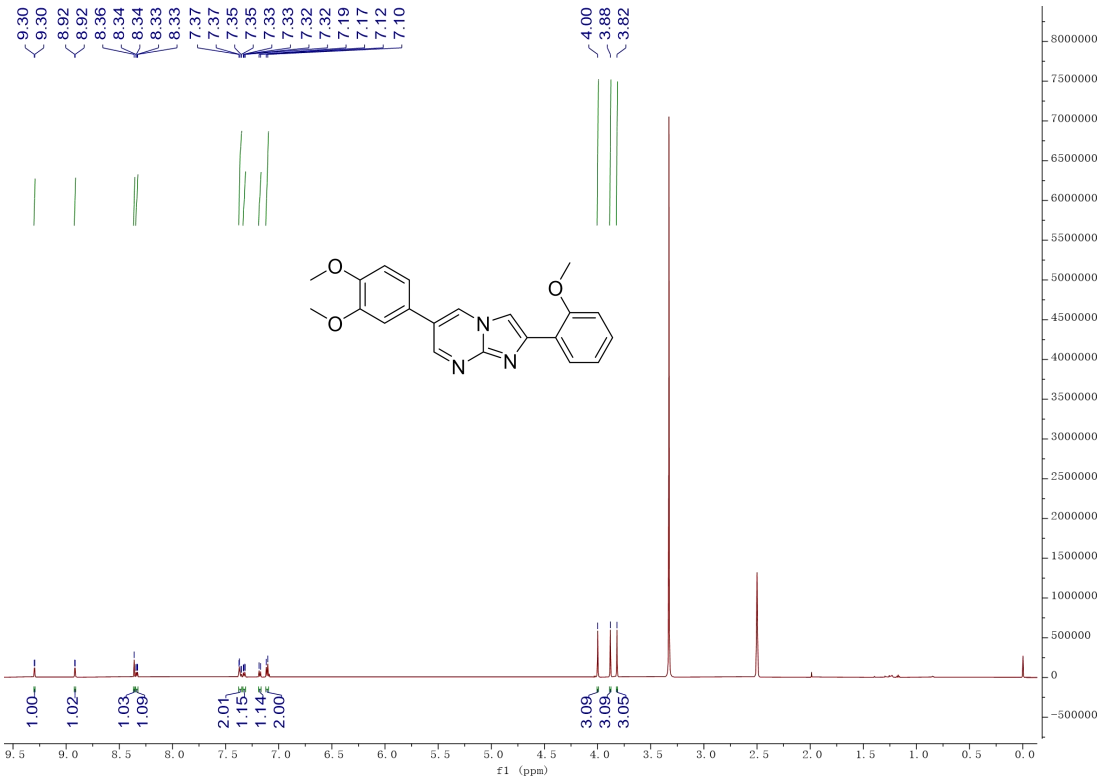
^{1}H NMR spectrum of compound **24**



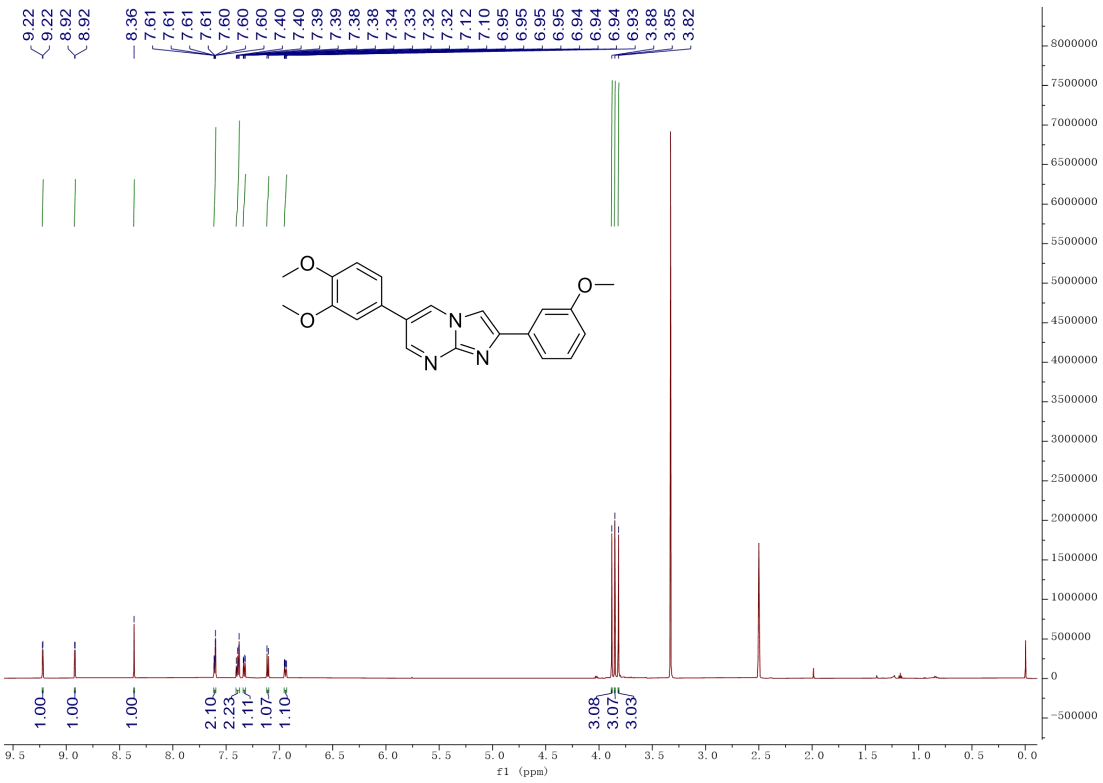
^{1}H NMR spectrum of compound **25**



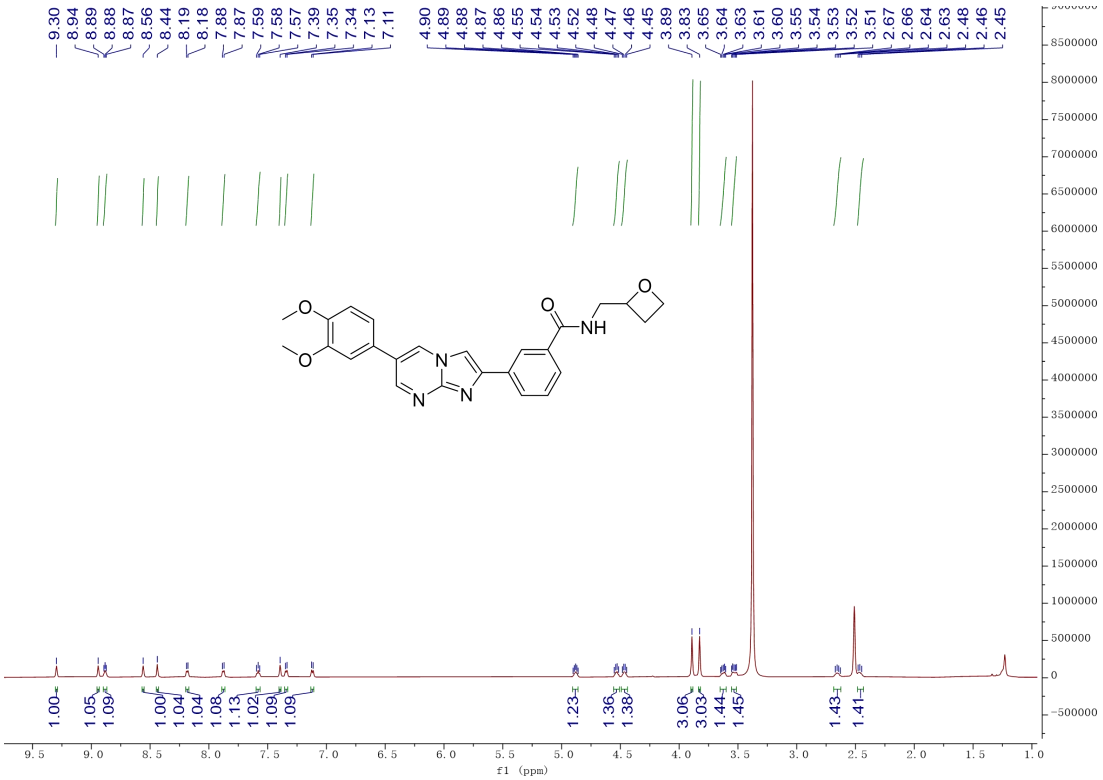
^{1}H NMR spectrum of compound **26**



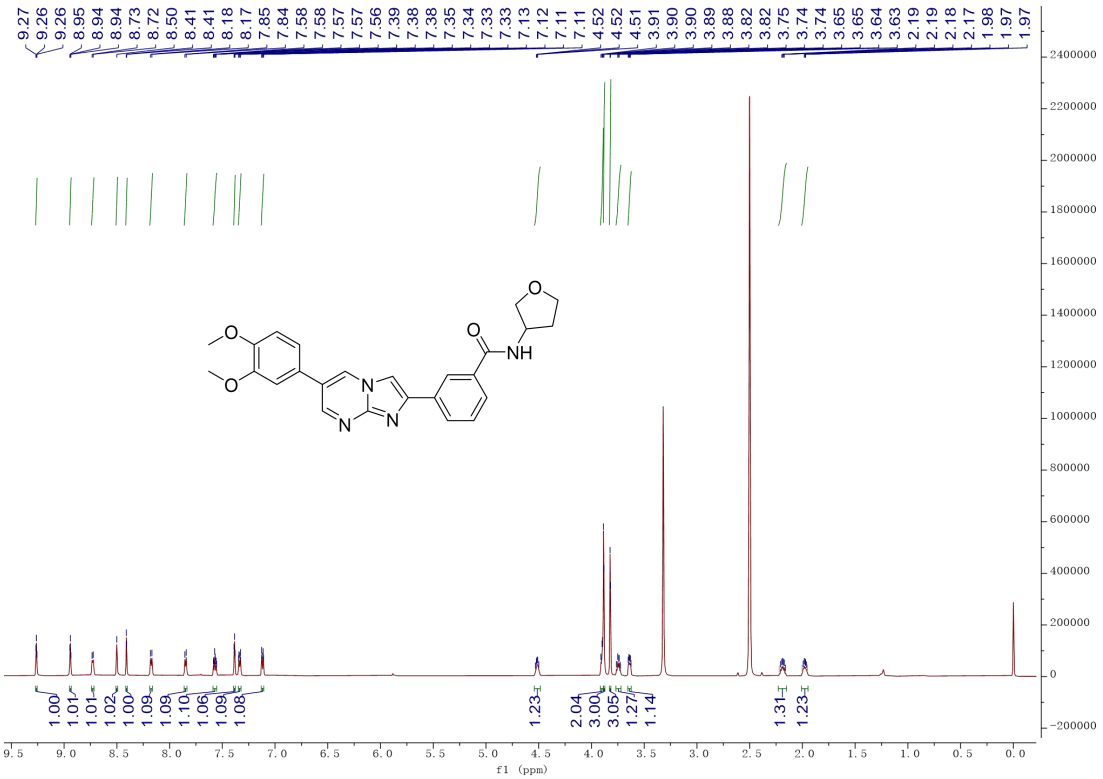
^{1}H NMR spectrum of compound **27**



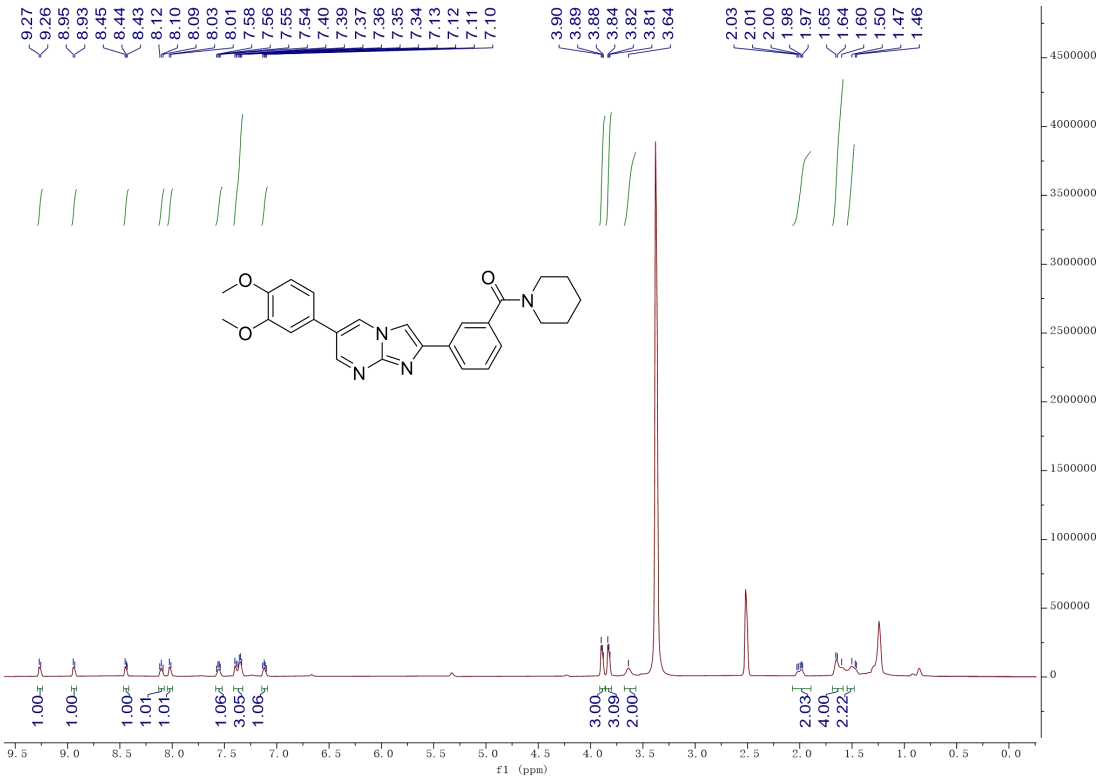
^{1}H NMR spectrum of compound **28**



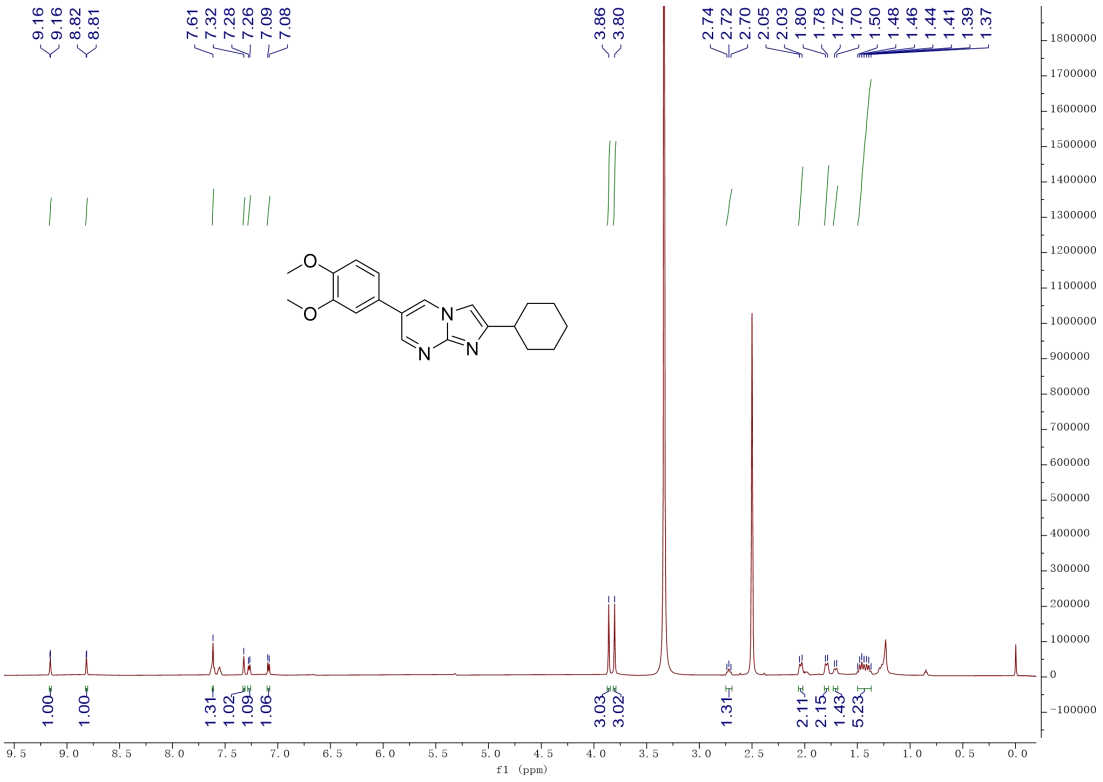
^{1}H NMR spectrum of compound **29**



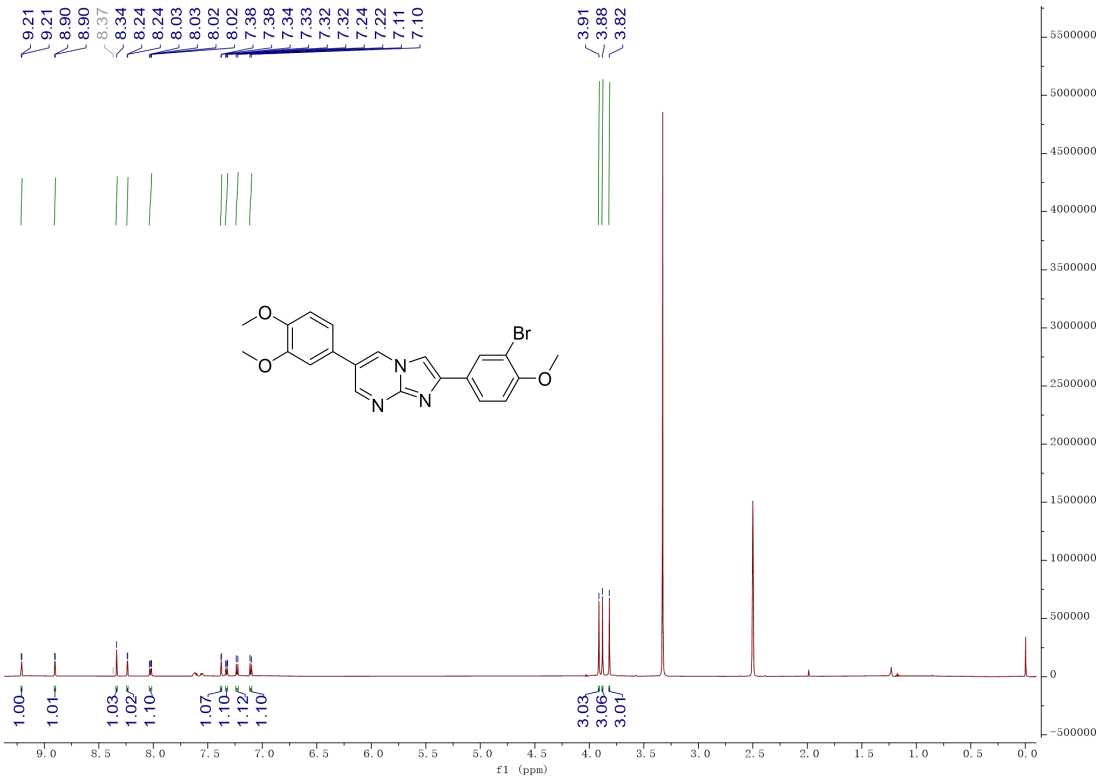
^{1}H NMR spectrum of compound **30**



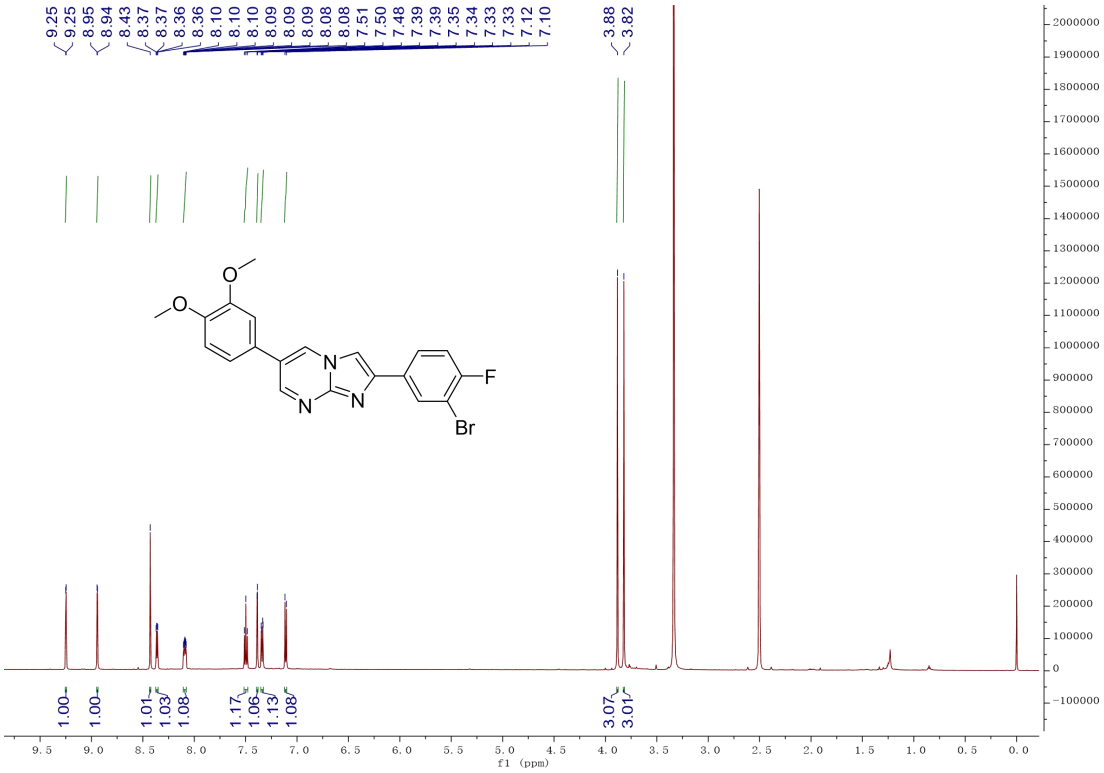
^{1}H NMR spectrum of compound **31**



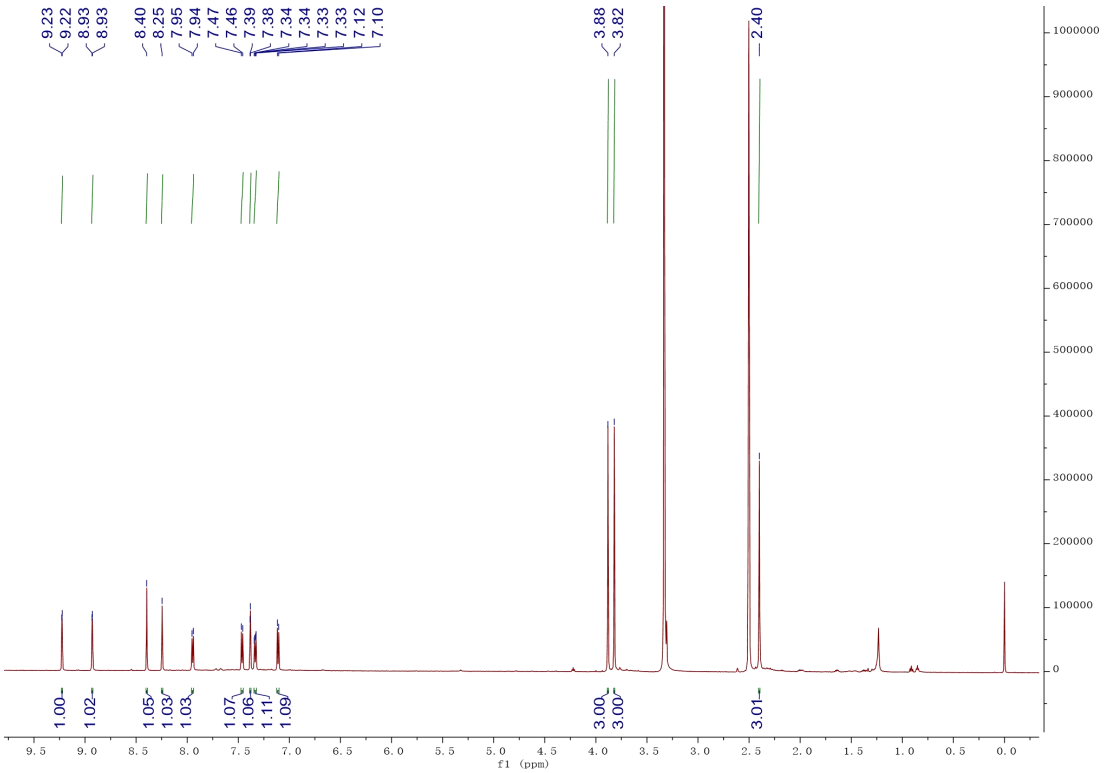
^{1}H NMR spectrum of compound **32**



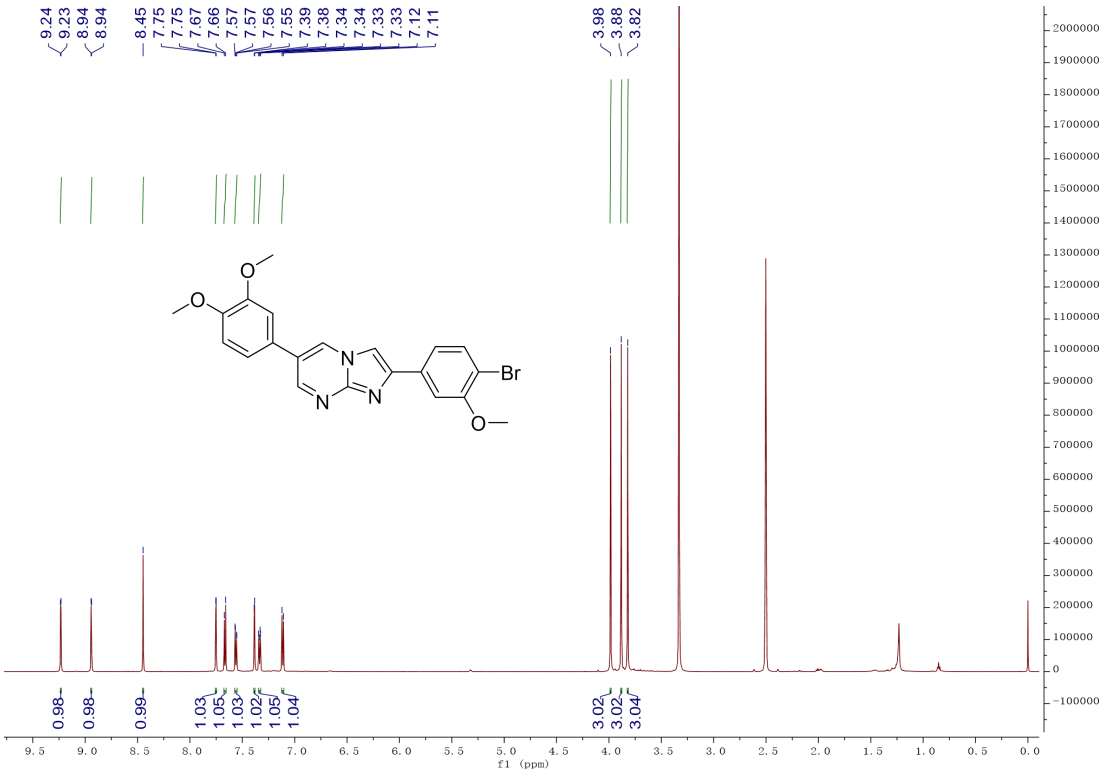
^{1}H NMR spectrum of compound **33**



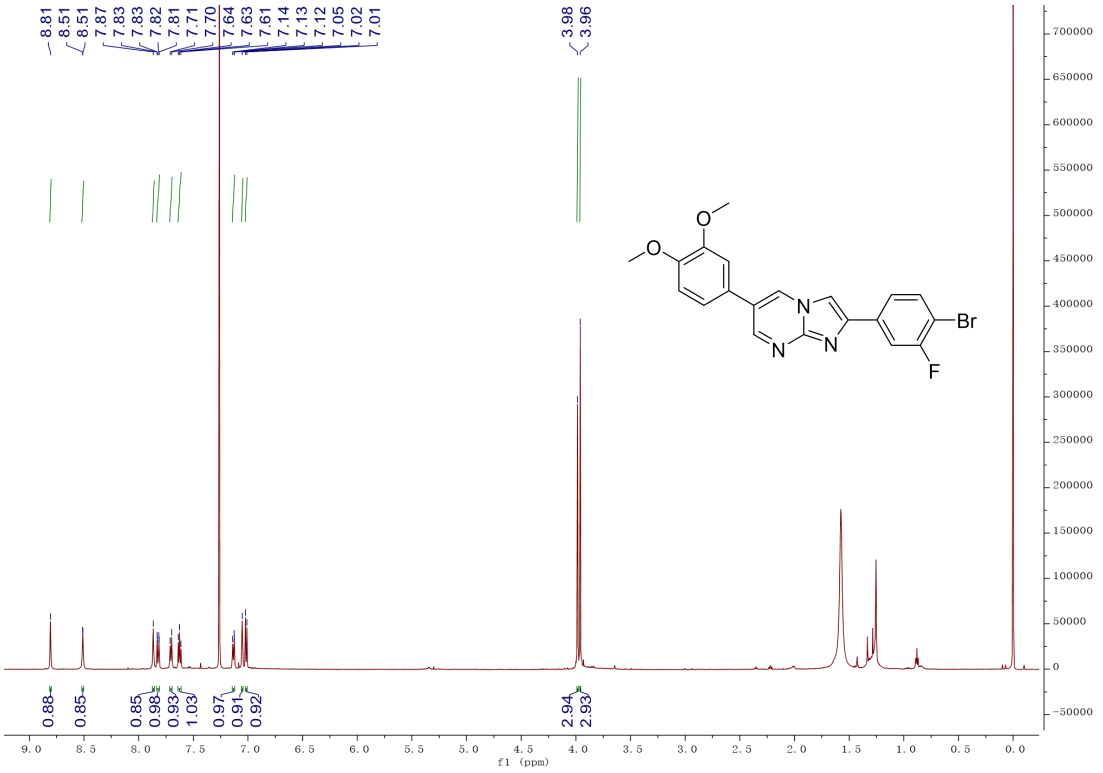
^{1}H NMR spectrum of compound **34**



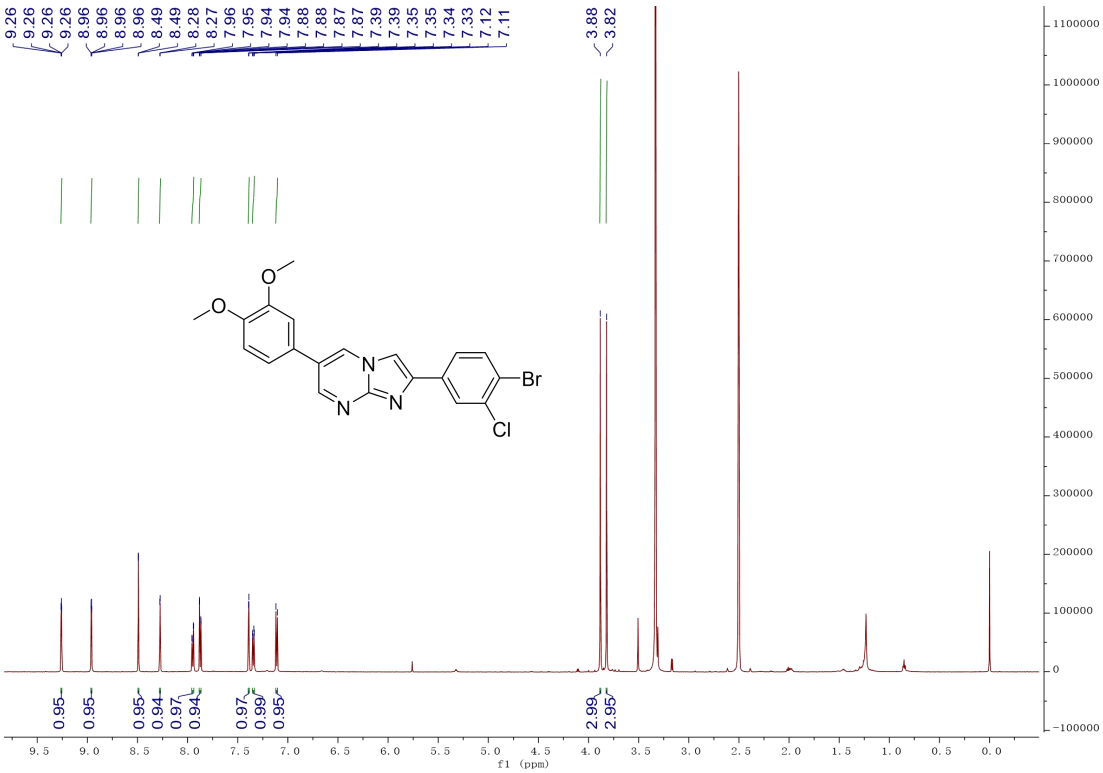
^{1}H NMR spectrum of compound **35**



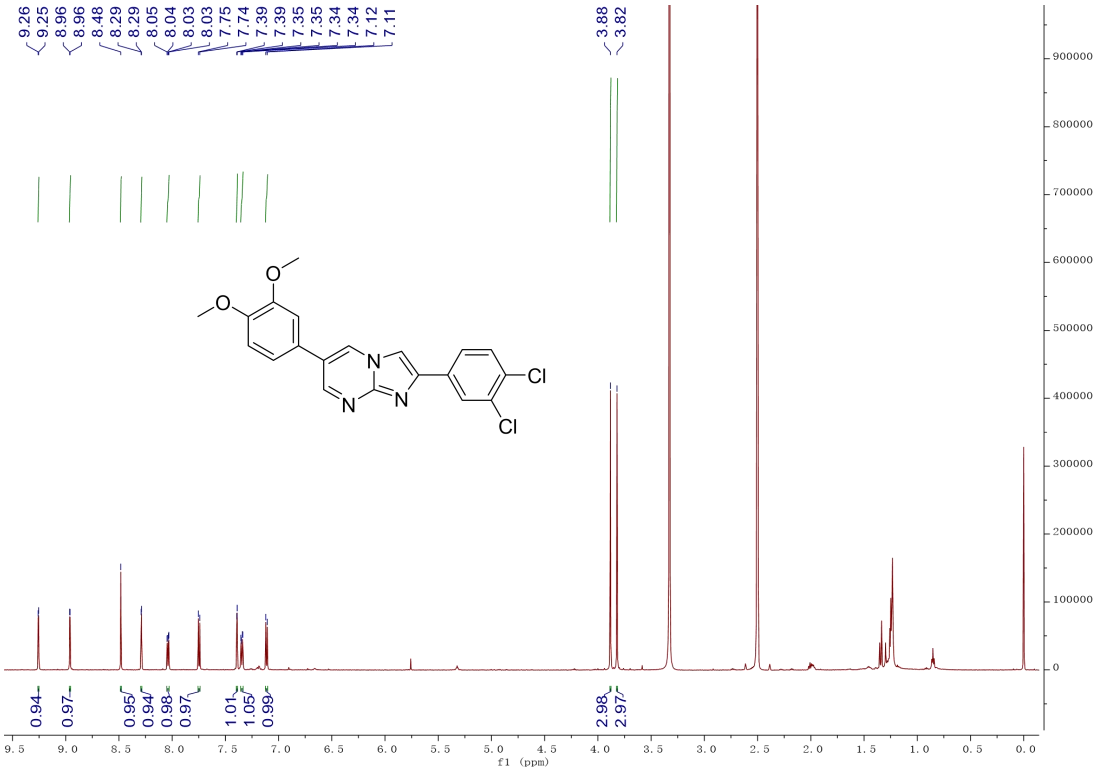
^{1}H NMR spectrum of compound **36**



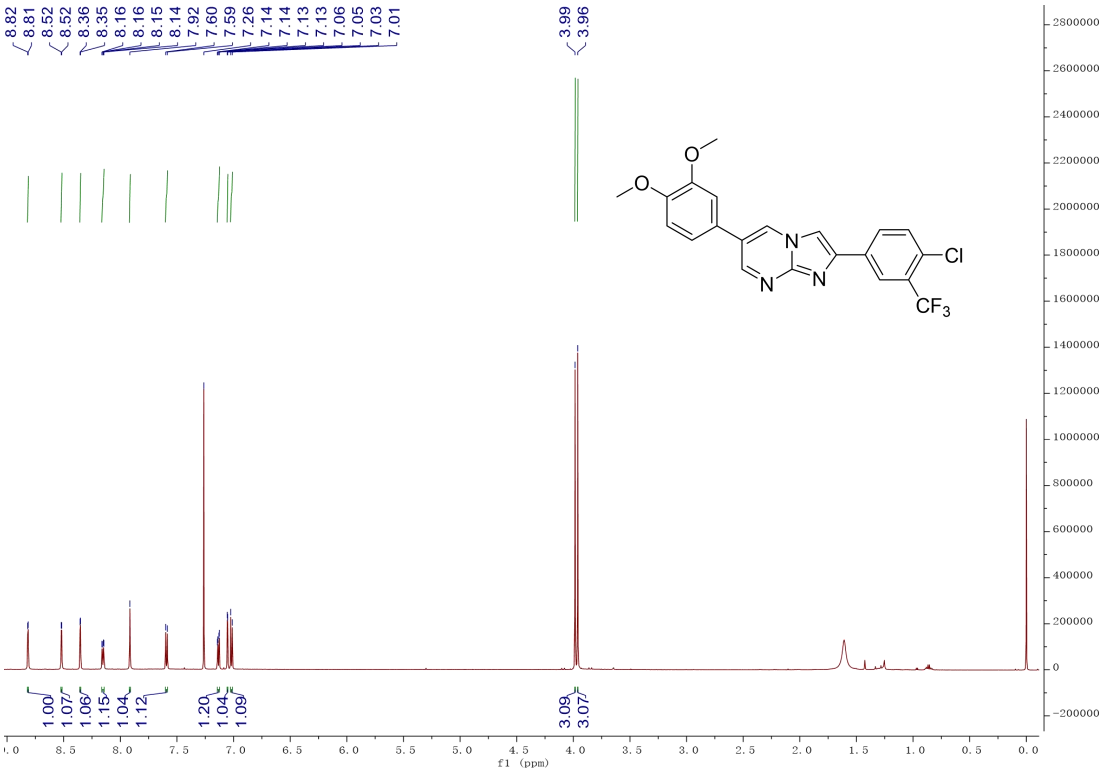
^{1}H NMR spectrum of compound **37**



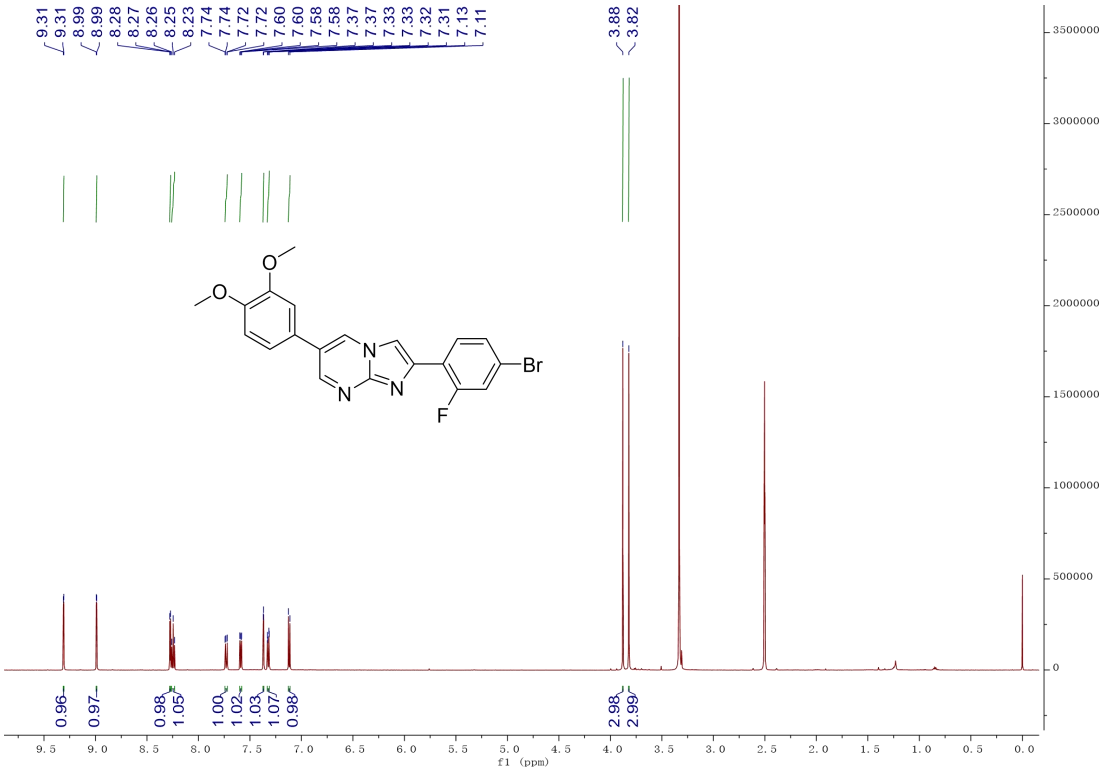
^{1}H NMR spectrum of compound **38**



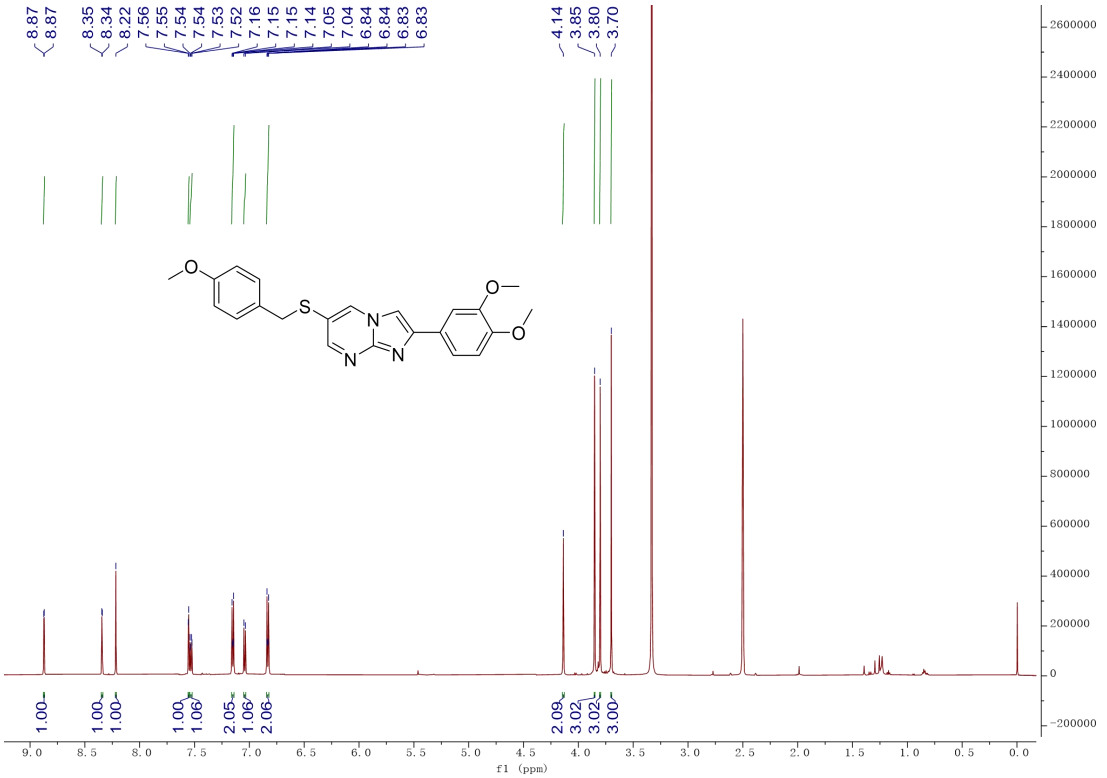
^{1}H NMR spectrum of compound **39**



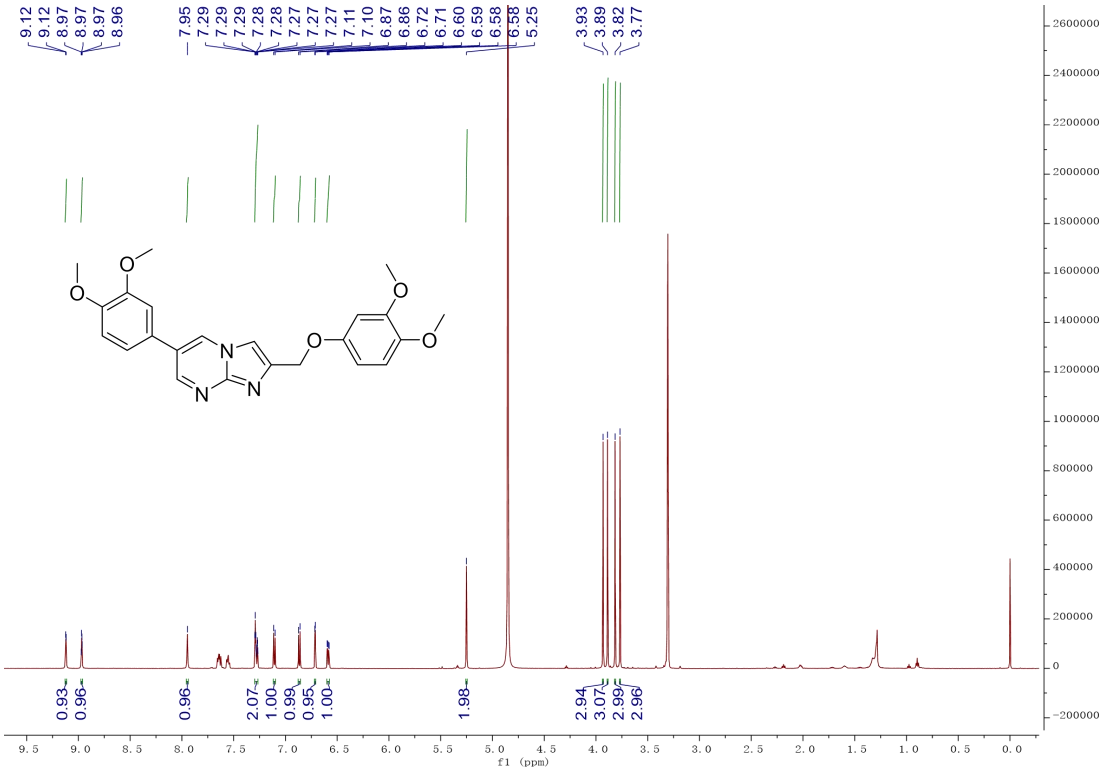
^{1}H NMR spectrum of compound **40**



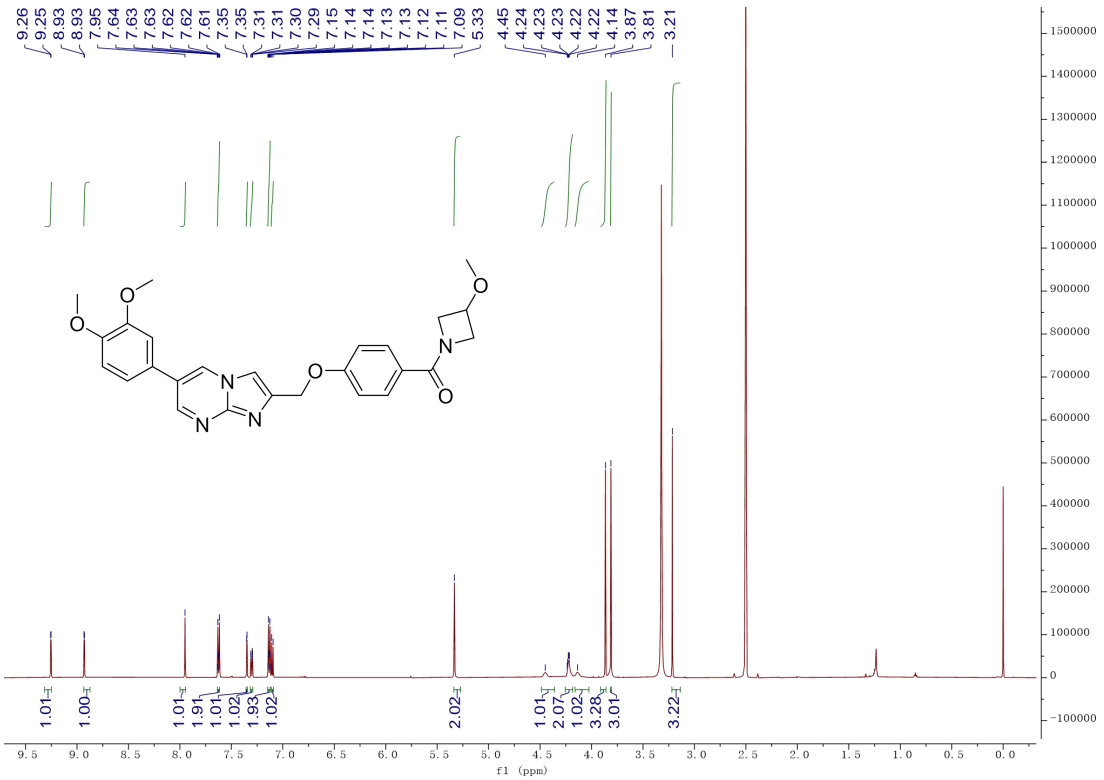
^{1}H NMR spectrum of compound **41**



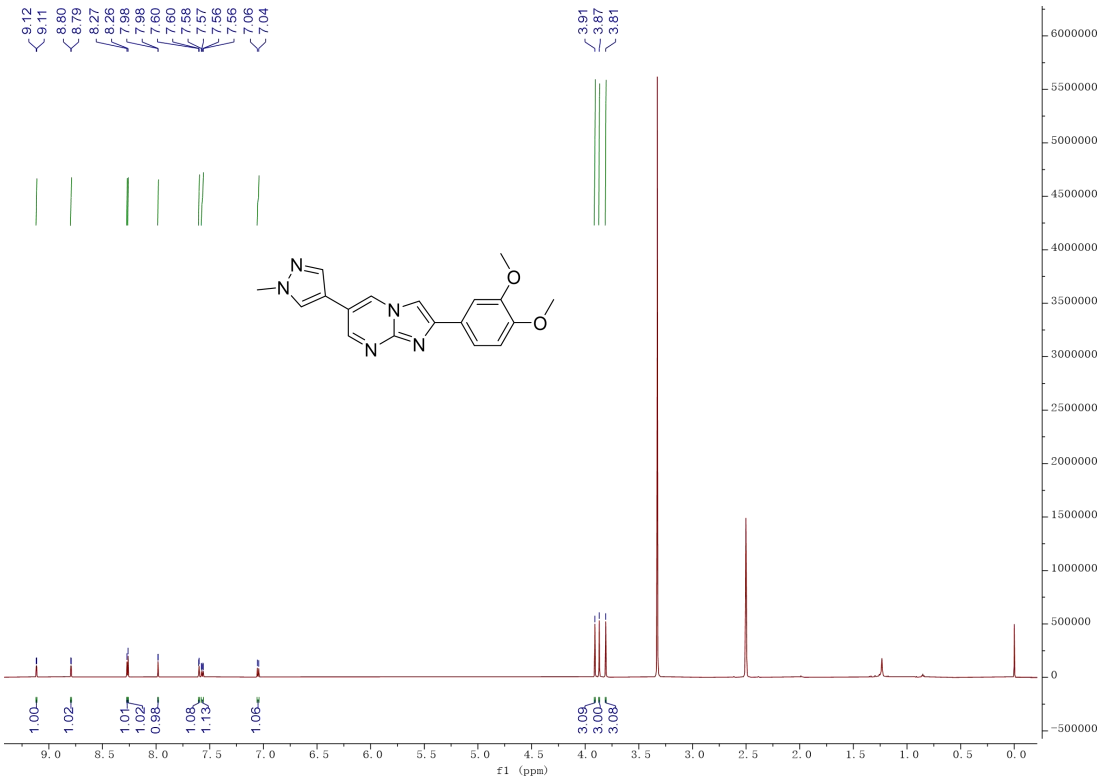
^{1}H NMR spectrum of compound **42**



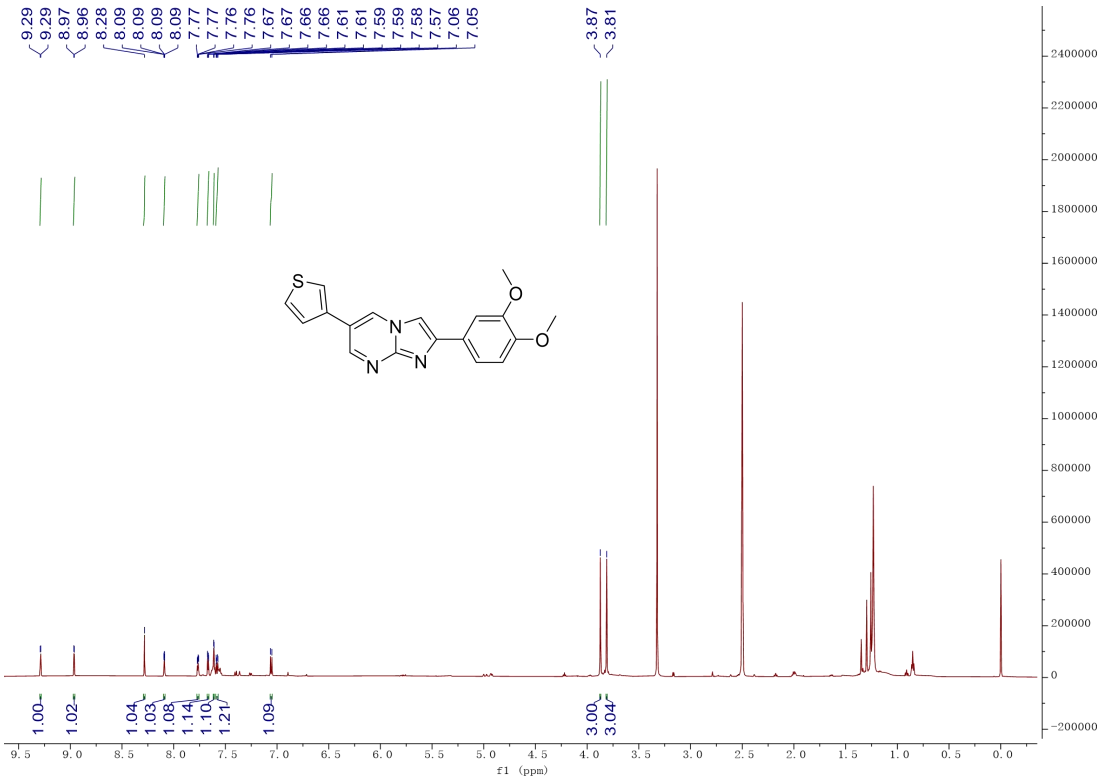
^{1}H NMR spectrum of compound **43**



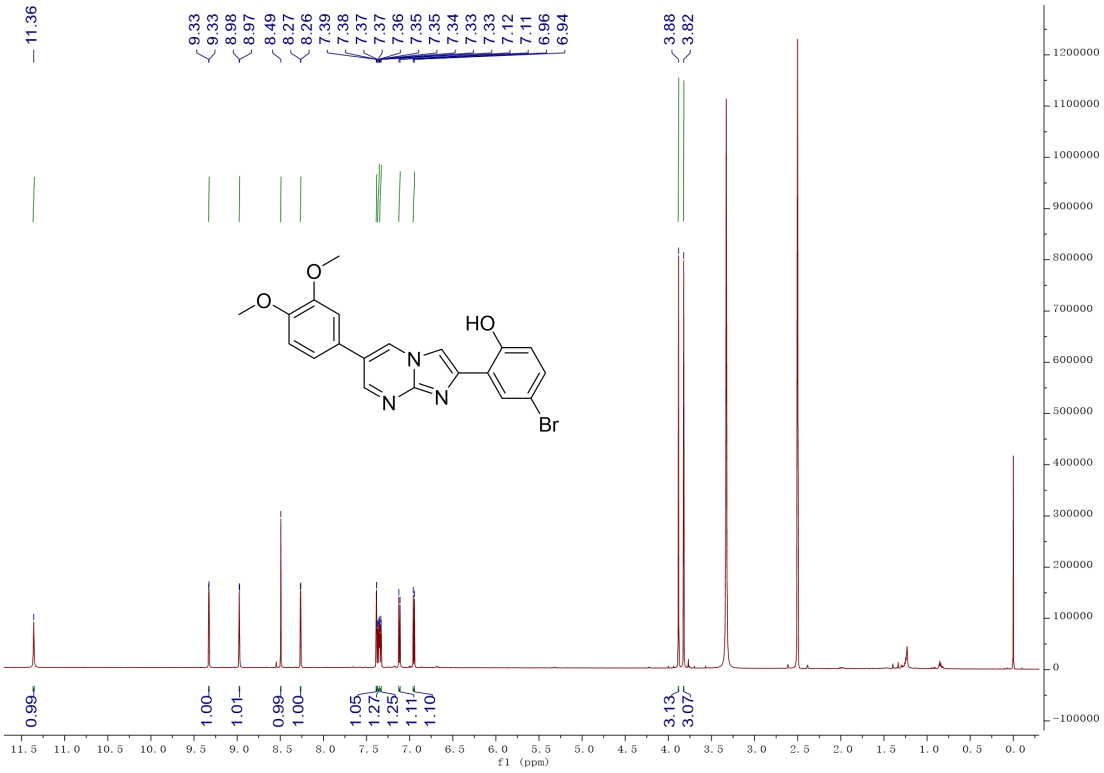
^{1}H NMR spectrum of compound **S1**



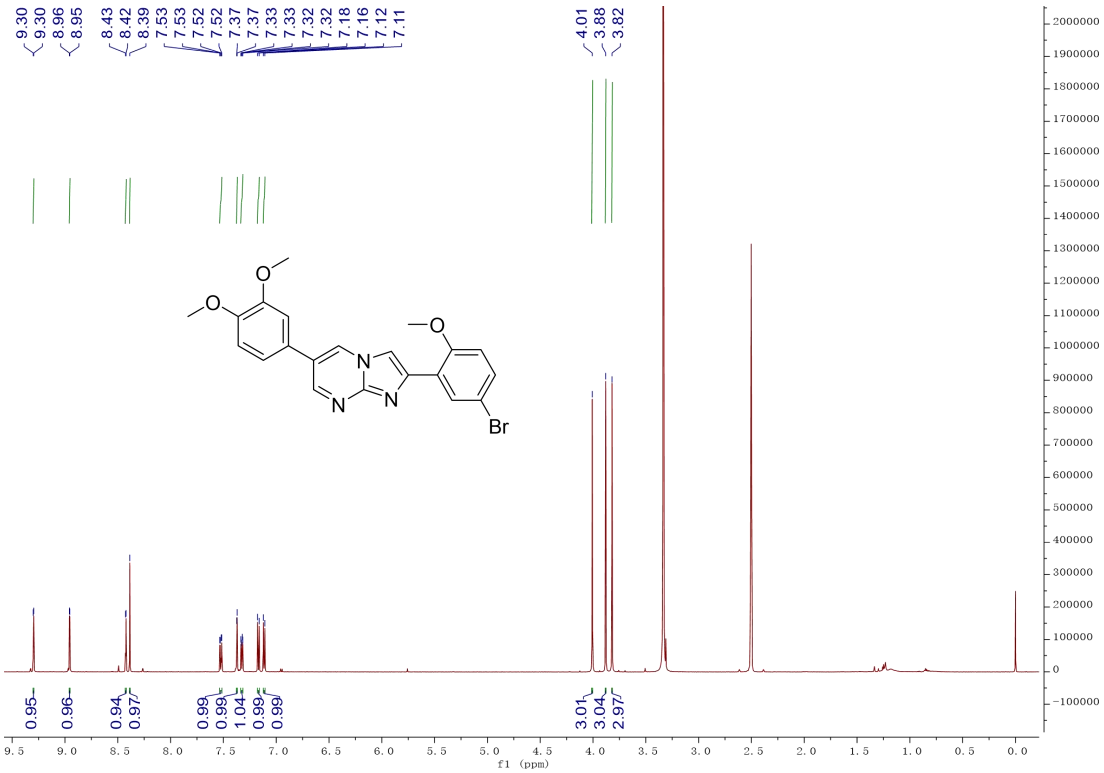
^{1}H NMR spectrum of compound **S2**



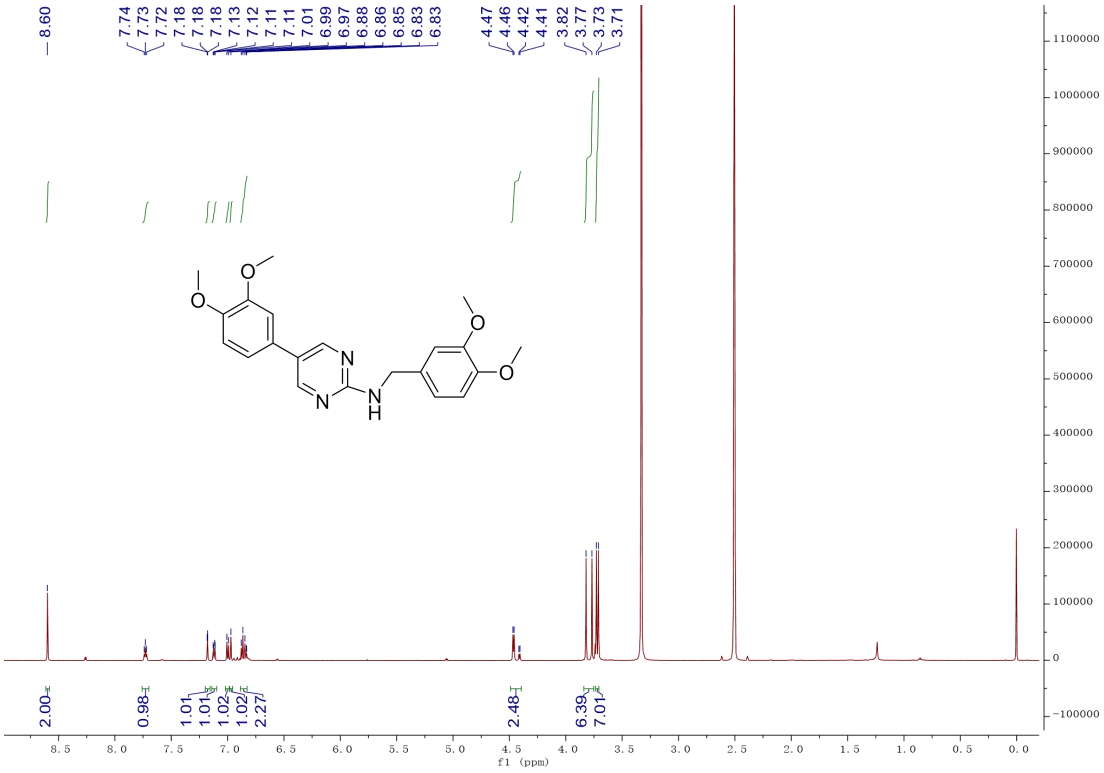
^{1}H NMR spectrum of compound **S3**



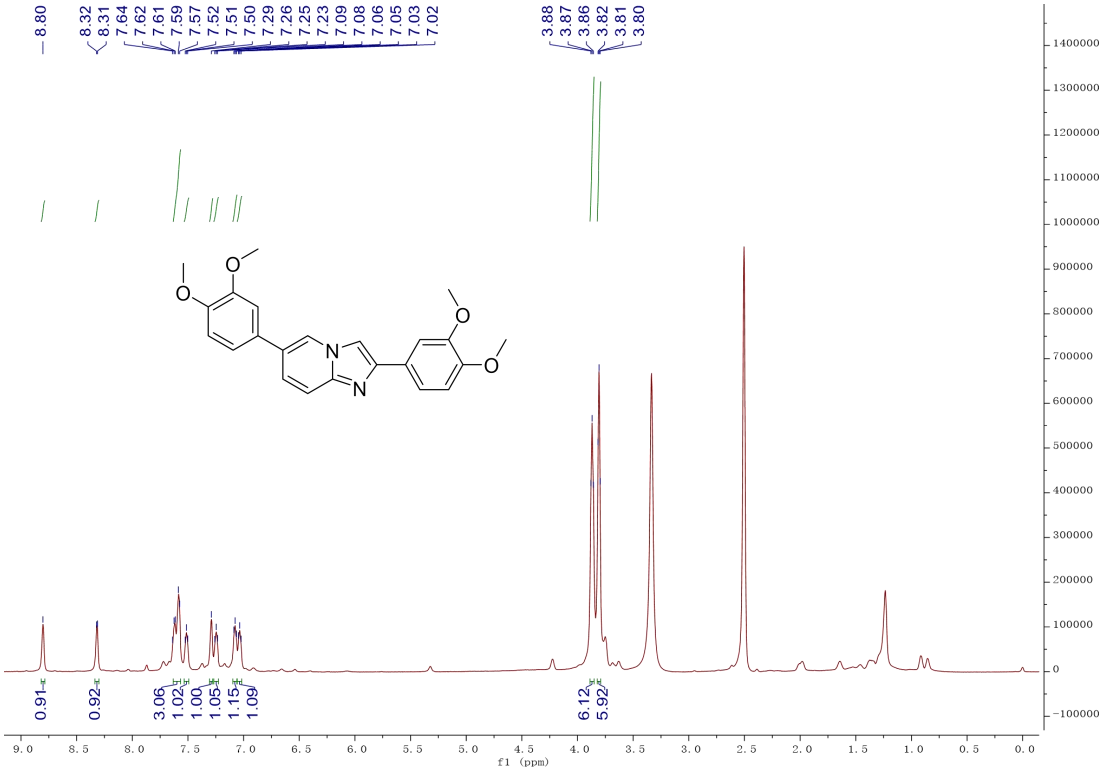
^{1}H NMR spectrum of compound **S4**



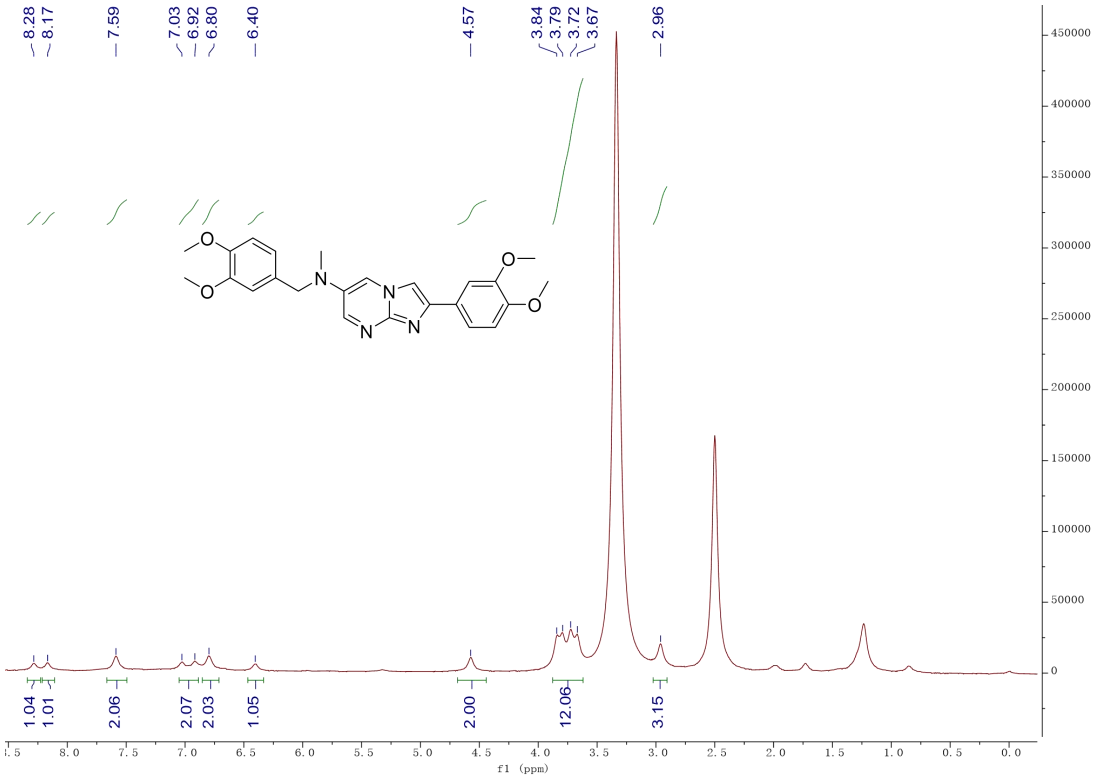
^{1}H NMR spectrum of compound **S5**



^{1}H NMR spectrum of compound **S6**

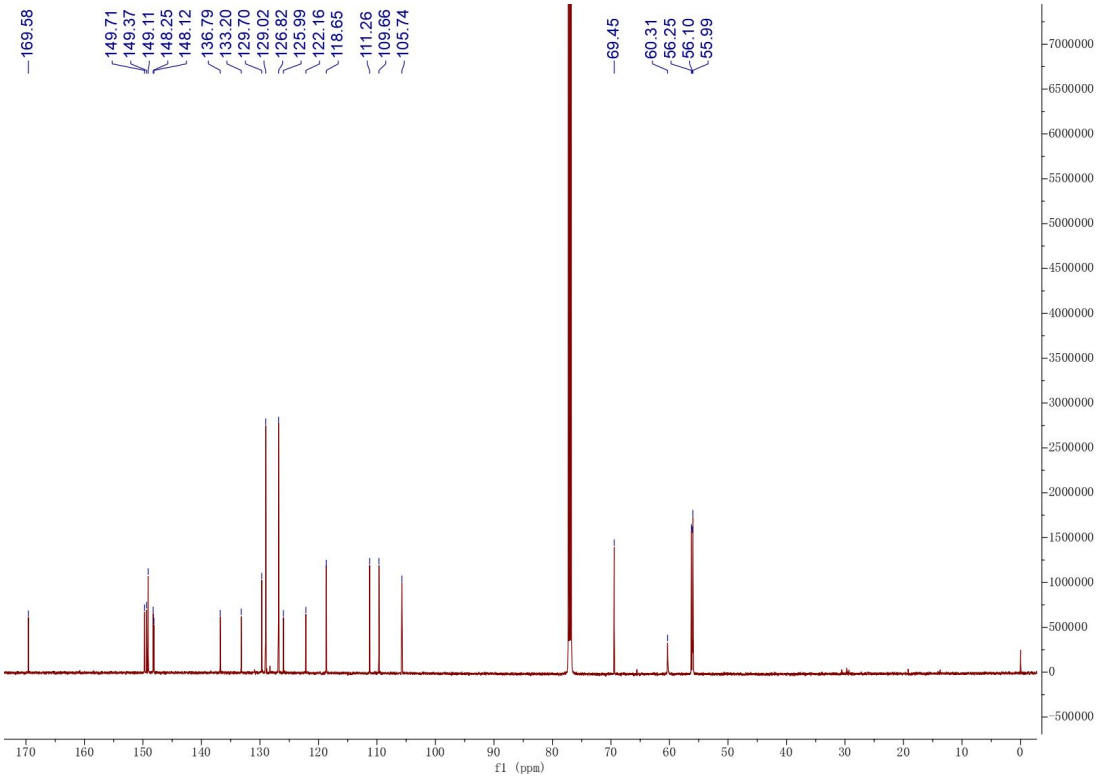


^{1}H NMR spectrum of compound **S7**

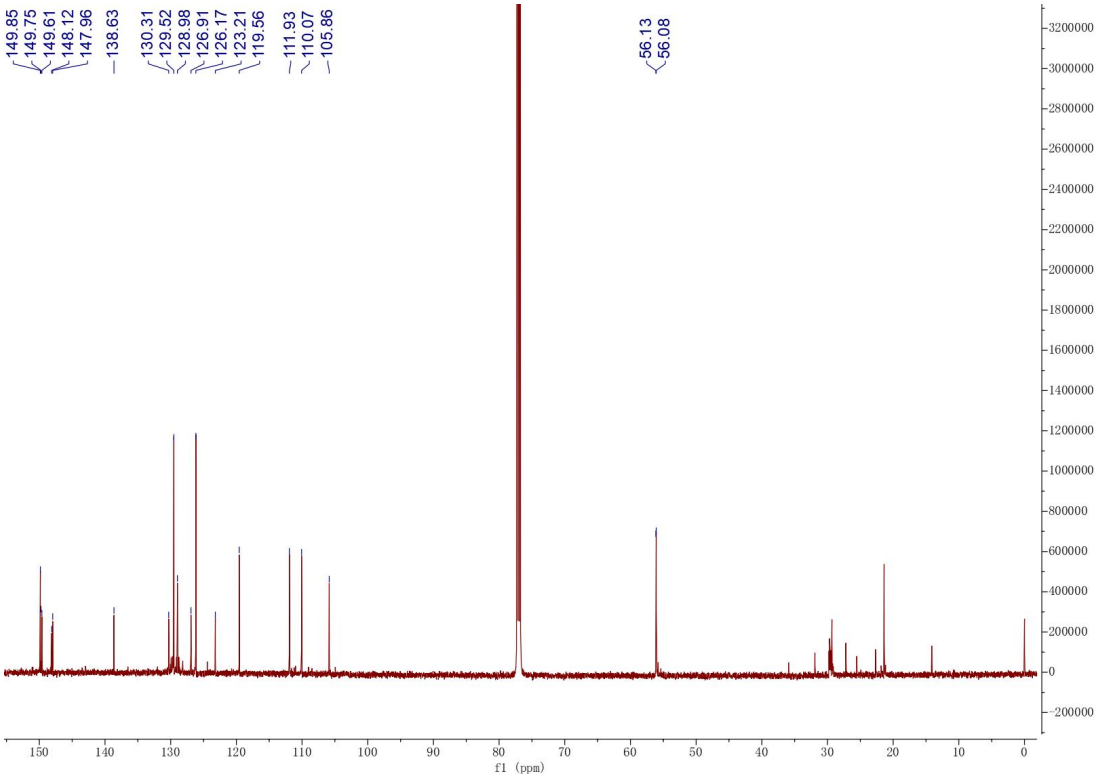


Spectral data: ^{13}C NMR, HR-ESI-MS and HPLC spectrum for compounds 12, 18, 33, 34, 35, 36, 37, 40, 43.

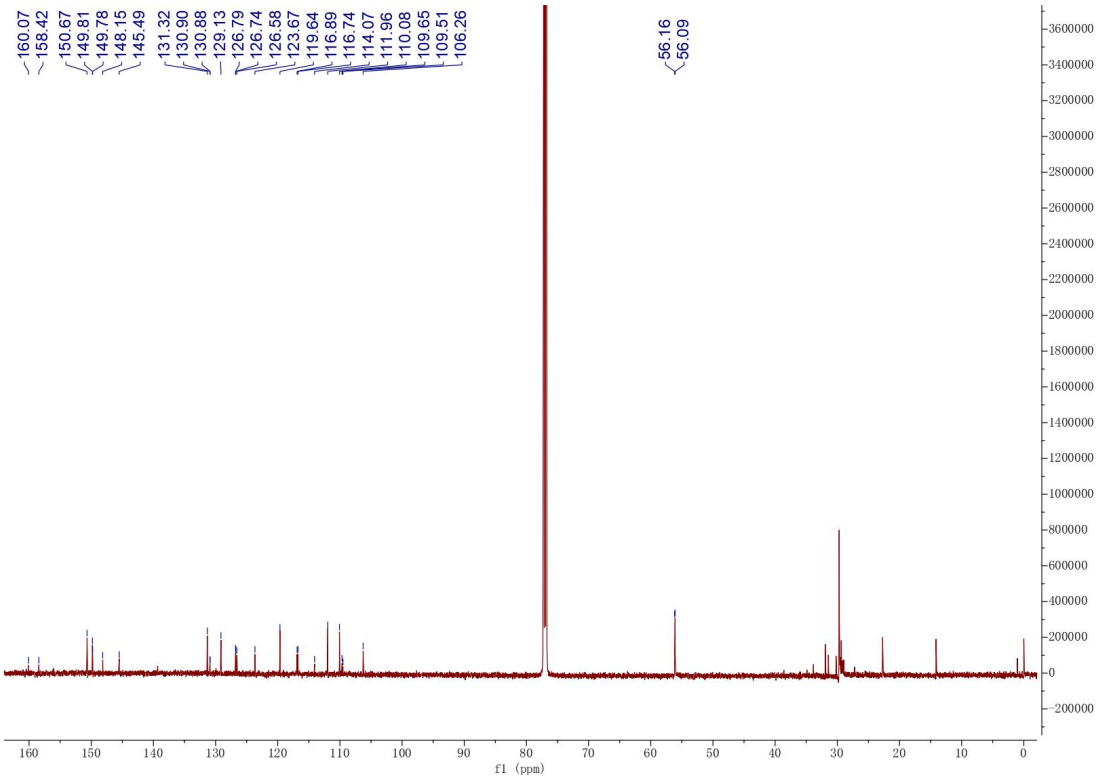
^{13}C NMR spectrum of compound **12**



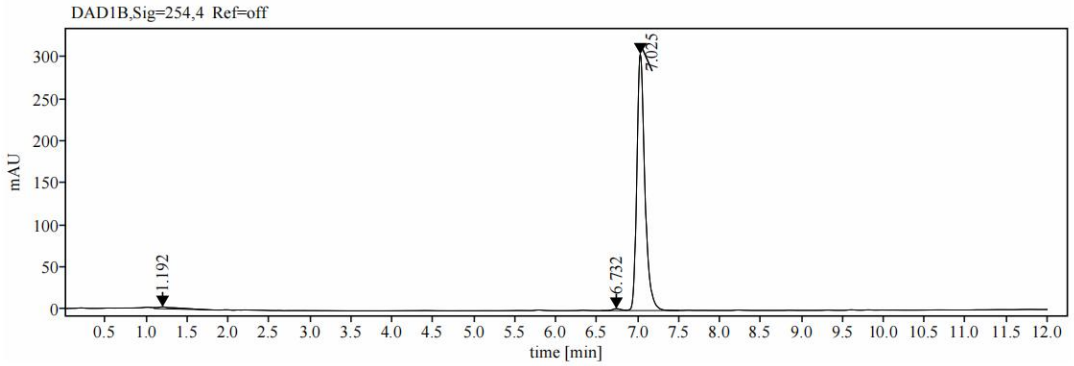
^{13}C NMR spectrum of compound **18**



^{13}C NMR spectrum of compound **33**

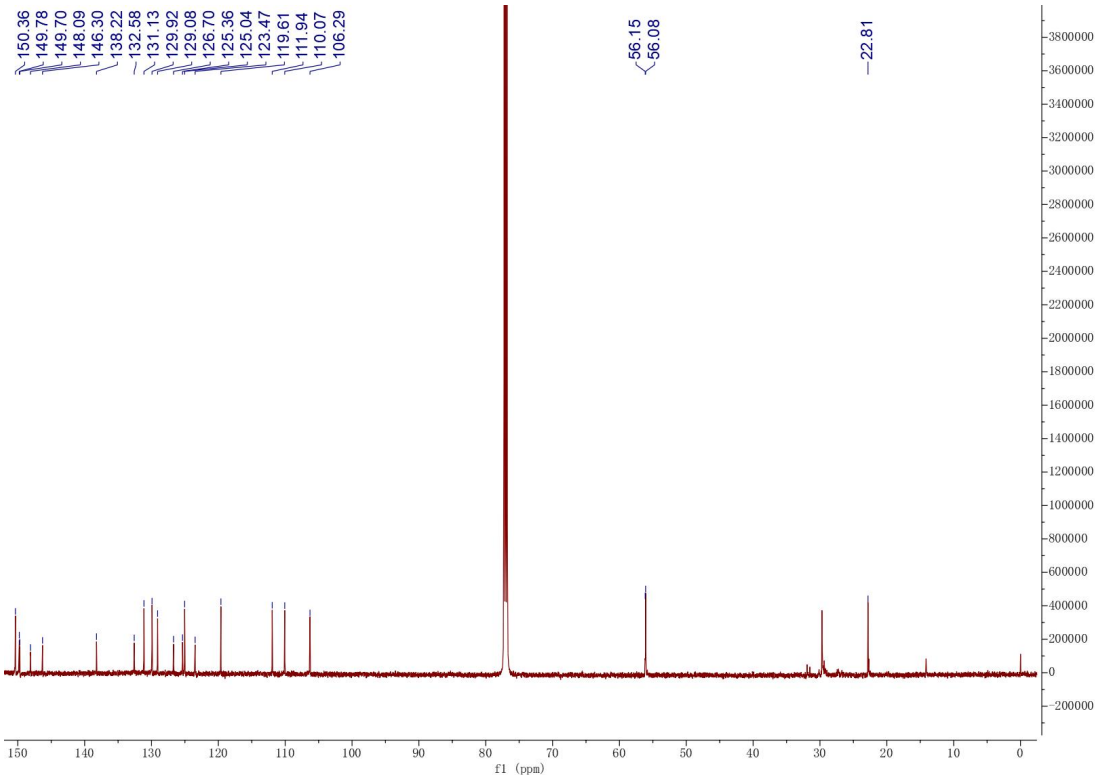


HPLC spectrum of compound **33**

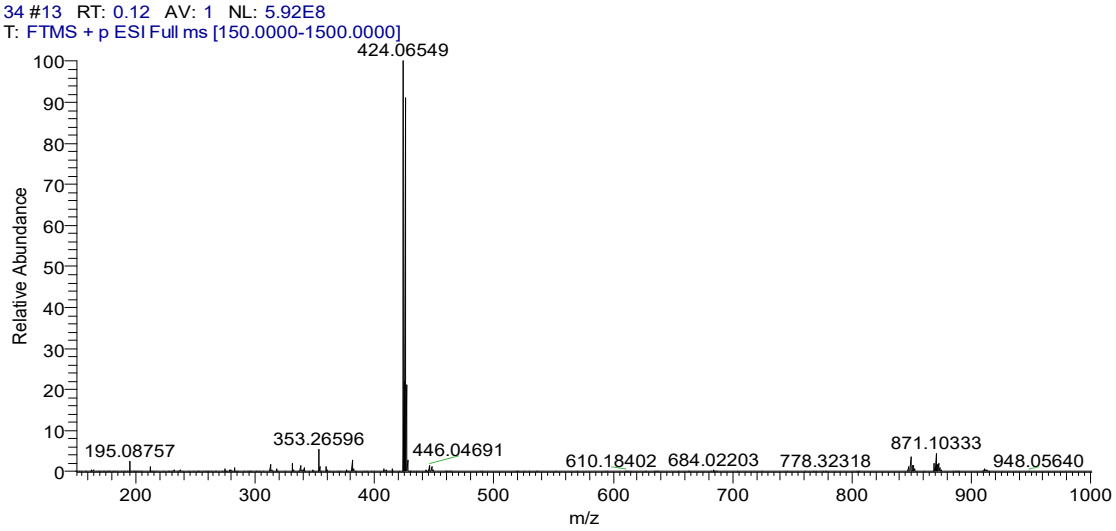


Peak#	Ret. Time	Area	Height	Area %
	1.19	44.05	2.34	2.06
	6.73	16.76	2.38	0.79
	7.02	2072.38	304.98	97.15
	Total	2133.19		

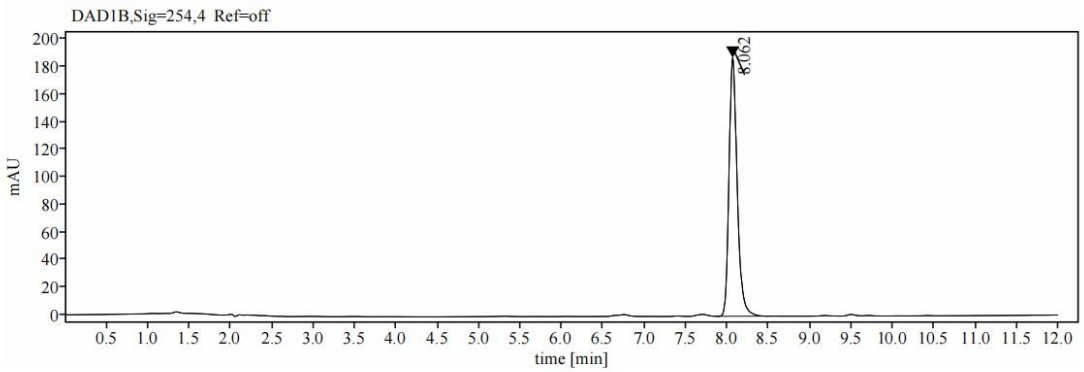
^{13}C NMR spectrum of compound **34**



HR-ESI-MS spectrum of compound **34**

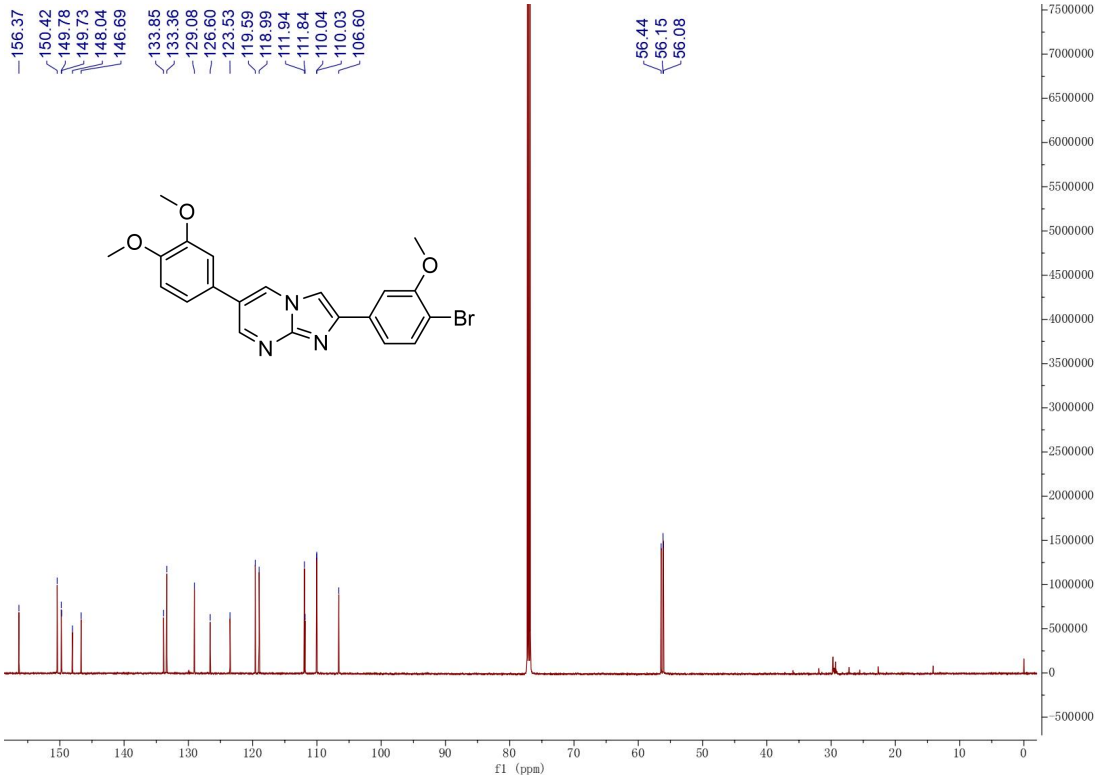


HPLC spectrum of compound **34**

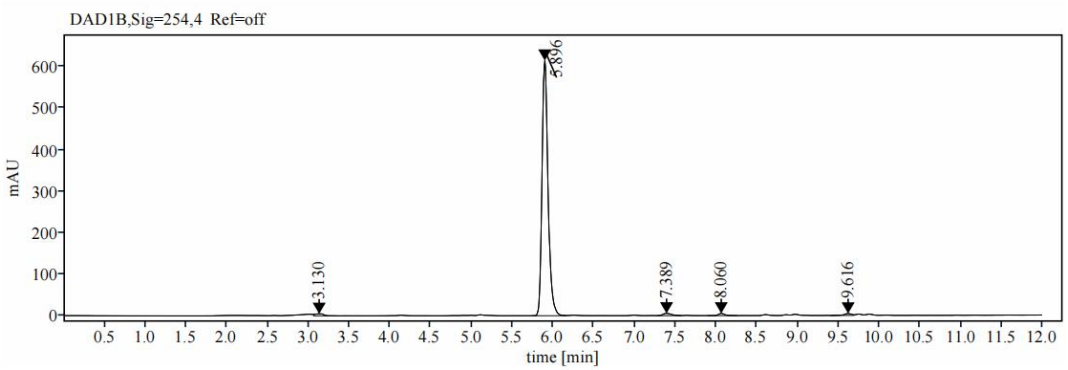


Peak#	Ret. Time	Area	Height	Area %
	8.06	1294.72	187.71	100.00
	Total	1294.72		

^{13}C NMR spectrum of compound **35**

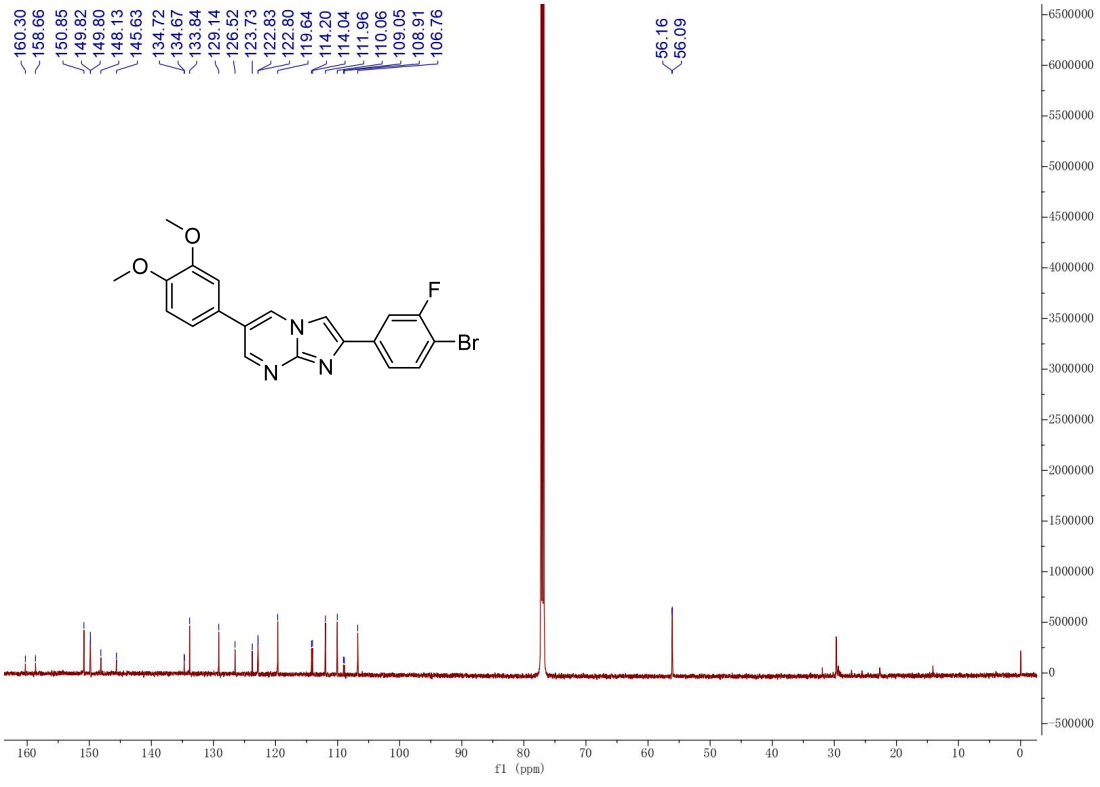


HPLC spectrum of compound **35**

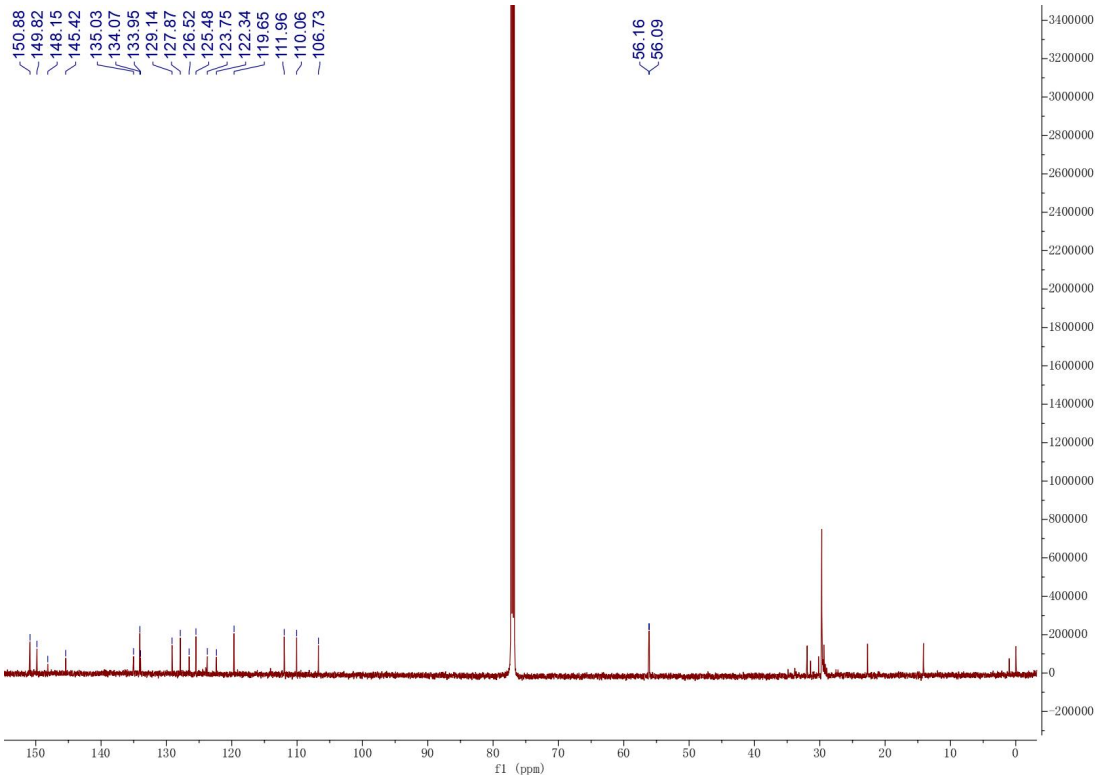


Peak#	Ret. Time	Area	Height	Area %
	3.13	35.47	4.83	1.07
	5.90	3173.72	616.23	95.97
	7.39	40.77	5.53	1.23
	8.06	28.18	5.39	0.85
	9.62	28.95	4.69	0.88
	Total	3307.10		

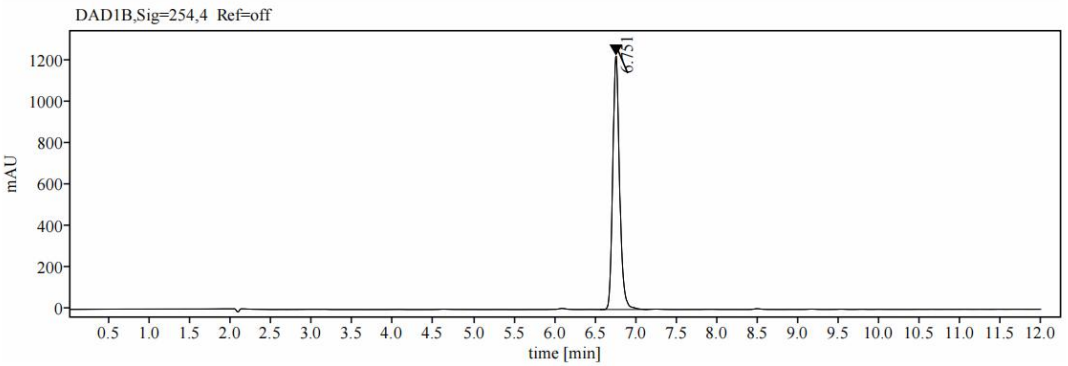
^{13}C NMR spectrum of compound **36**



^{13}C NMR spectrum of compound **37**

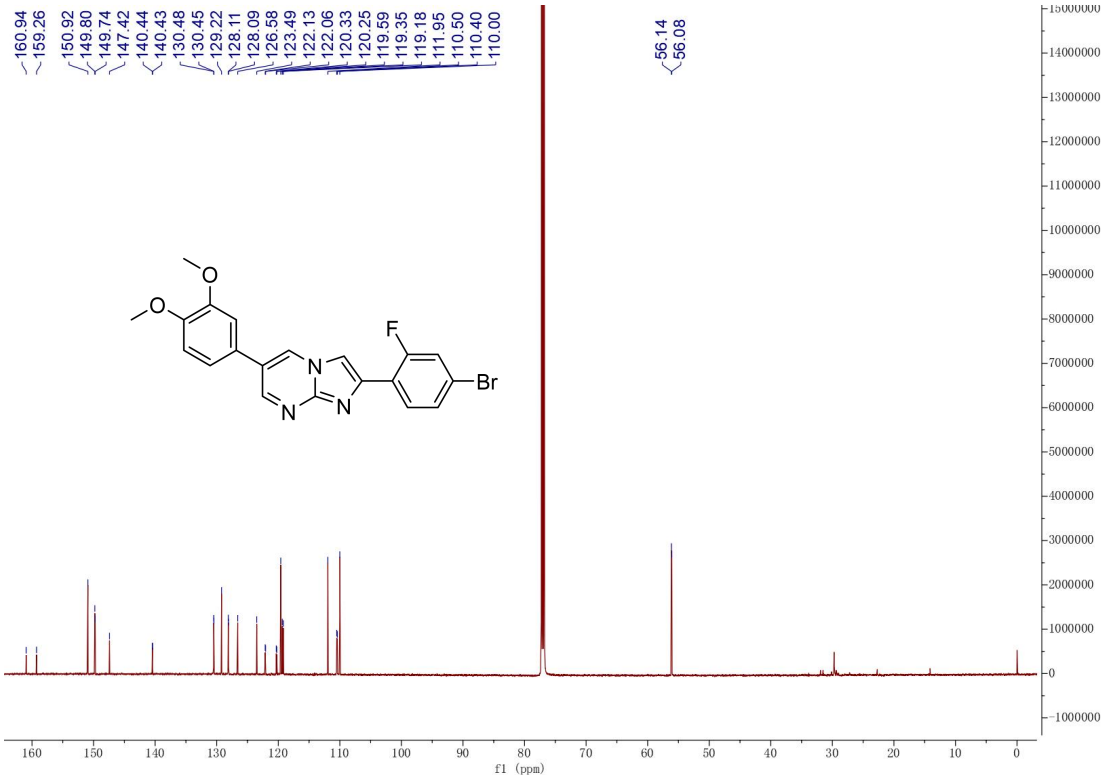


HPLC spectrum of compound **37**

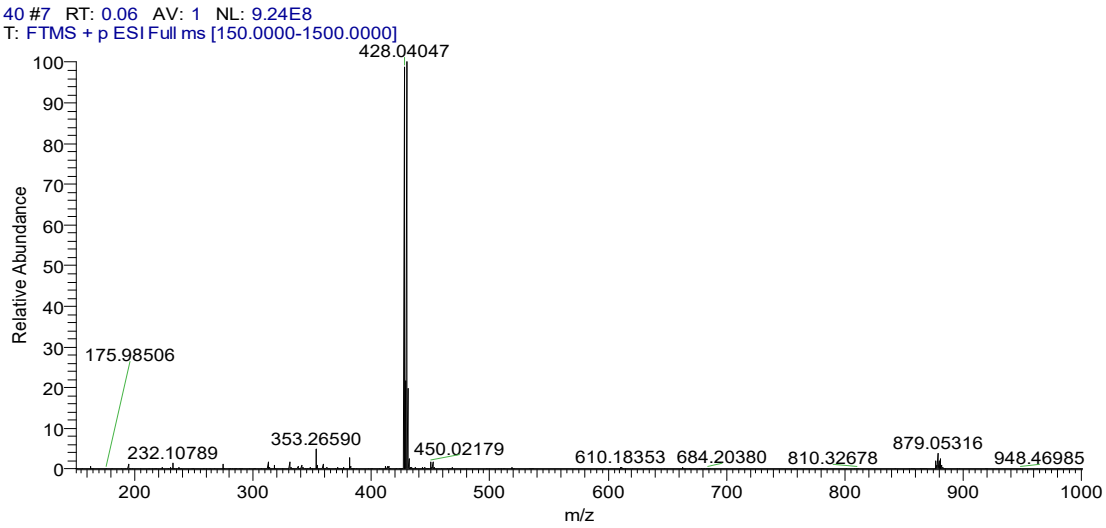


Peak#	Ret. Time	Area	Height	Area %
	6.75	7209.28	1224.51	100.00
	Total	7209.28		

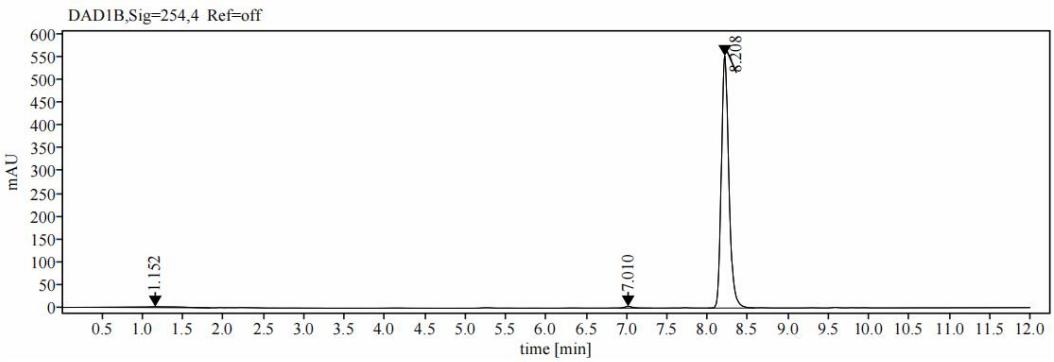
^{13}C NMR spectrum of compound **40**



HR-ESI-MS spectrum of compound **40**

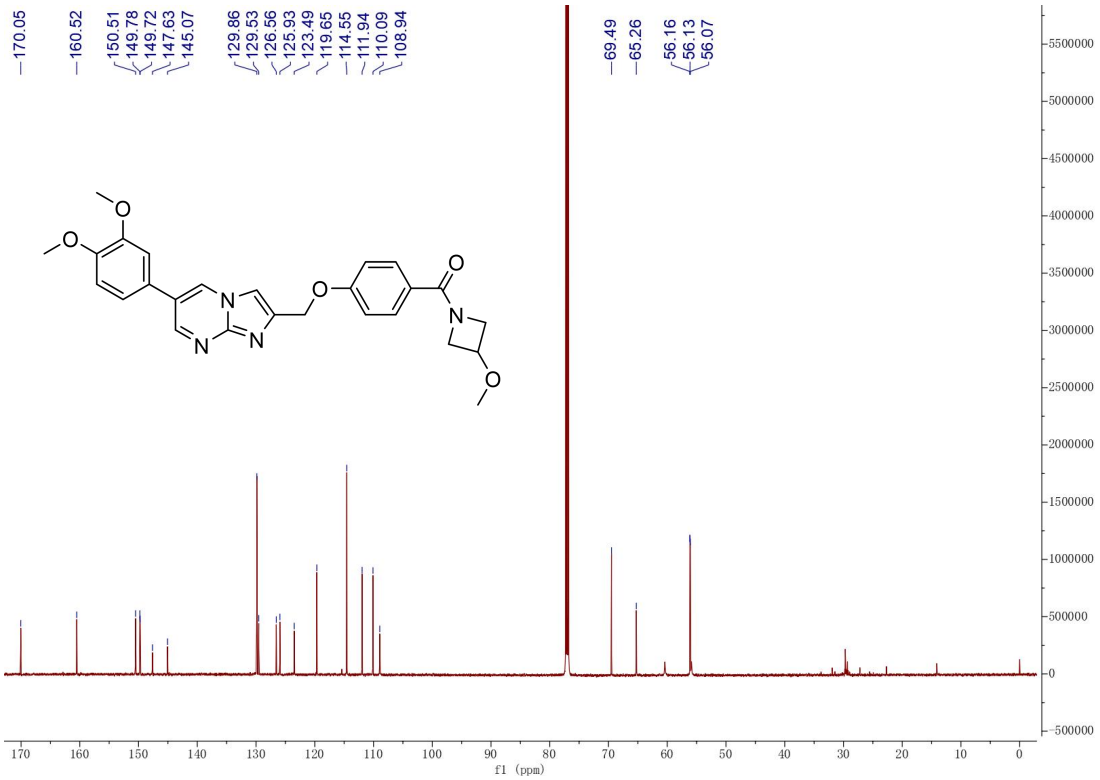


HPLC spectrum of compound **40**

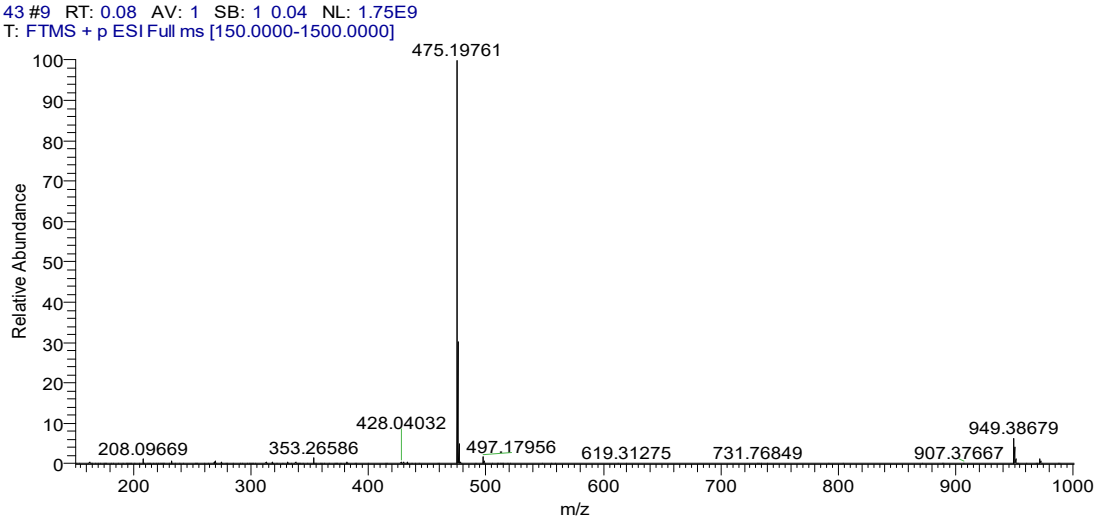


Peak#	Ret. Time	Area	Height	Area %
	1.15	84.11	2.02	2.26
	7.01	25.96	3.60	0.70
	8.21	3613.90	554.33	97.04
	Total	3723.98		

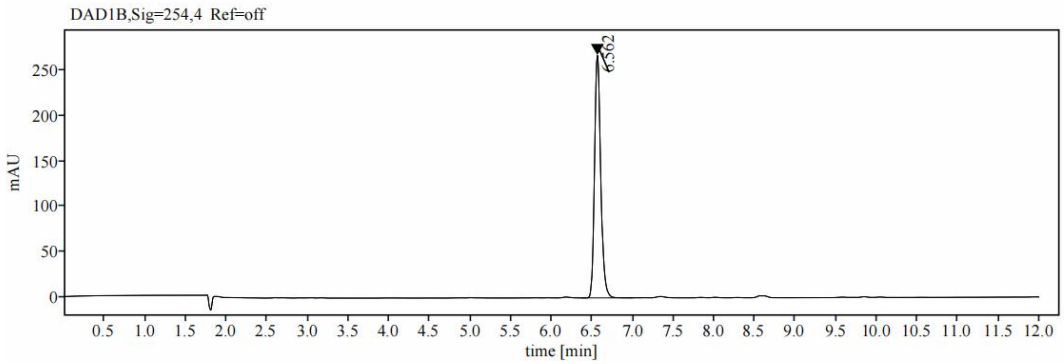
^{13}C NMR spectrum of compound **43**



HR-ESI-MS spectrum of compound **43**



HPLC spectrum of compound **43**



Peak#	Ret. Time	Area	Height	Area %
	6.56	1426.94	268.84	100.00
	Total	1426.94		