Multi-component Cascade Reaction of 3-Formylchromones: Highly Selective Synthesis of 4,5-Dihydro-[4,5'-bipyrimidin] -6(1*H*)-one Derivatives

Li Chen, Rong-Huang, Xing-Han Yun, Tian-Hui Hao and Sheng-Jiao Yan*

Key Laboratory of Medicinal Chemistry for Natural Resources, Ministry of Education; Yunnan Provincial Center for Research & Development of Natural Products; School of Chemical Science and Technology, Yunnan University, Kunming, 650091, P. R. China

Supporting Information

Table of Contents:

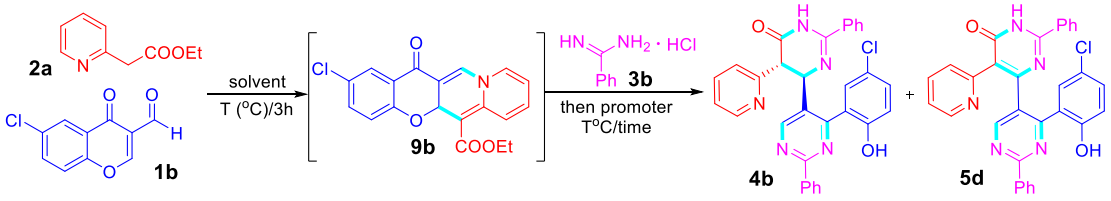
General Information

All compounds were fully characterised by spectroscopic data. The NMR spectra were recorded on a Bruker DRX600. Chemical shifts (δ) are expressed in ppm, J values are given in Hz, and deuterated DMSO-d_6 or $CDCl_3$ was used as solvent, the solvent residue in DMSO-d_6 (^{13}CNMR: 39.52 ppm, ^{1}H NMR, 2.50 ppm; the solvent residue in $CDCl_3$ (^{13}CNMR: 7.26 ppm, ^{1}H NMR, 77.16 ppm). IR spectra were recorded on a FT-IR Thermo Nicolet Avatar 360 using a KBr pellet. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF_{254}. The melting points were determined on a XT-4A melting point apparatus and are uncorrected. HRMs were performed on an Agilent LC/Msd TOF instrument.

The materials were purchased from Adamas-beta Corporation Limited. All chemicals and solvents were used as received without further purification unless otherwise stated. Two kinds of reagents which were used in the experiment were commercially available reagents.

Optimized Conditions for the Synthesis of 4b & 5d

Table S1 Optimized conditions for the synthesis of **4b** & **5d**[a]



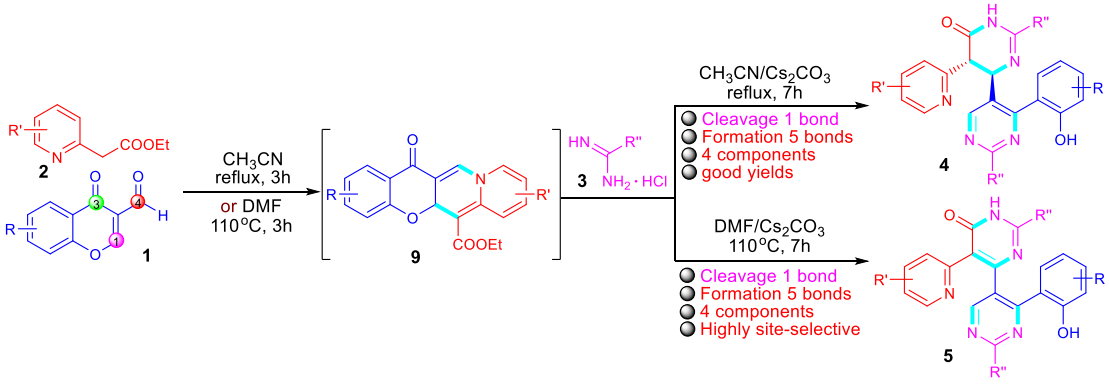
Entry	Solvent	Promoter	T (°C)	Time (h)	**4b**/**5d** (%)[b]
1	EtOH	Cs_2CO_3	reflux	9	–/–
2	MeCN	Cs_2CO_3	reflux	9	72/–
3	H_2O	Cs_2CO_3	reflux	9	–/–
4	1,4-dioxane	Cs_2CO_3	reflux	9	14/33
5	DMF	Cs_2CO_3	110	9	–/83
6	PC	Cs_2CO_3	110	9	–/–
7	PE (1000)	Cs_2CO_3	110	9	–/–
8	[OMIM]PF_6	Cs_2CO_3	110	9	–/–
9	MeCN	K_2CO_3	reflux	9	53/–
10	MeCN	Et_3N	reflux	9	–/–
11	MeCN	Cs_2CO_3[c]	reflux	9	58/–
12	MeCN	Cs_2CO_3[d]	reflux	9	70/–
13	MeCN	Cs_2CO_3	reflux	7	76/–
14	MeCN	Cs_2CO_3	reflux	11	71/trace
15	DMF	K_2CO_3	110	9	trace/32
16	DMF	DBU	110	9	20/64
17	DMF	Cs_2CO_3	100	9	15/75
18	DMF	Cs_2CO_3	120	9	–/81
19	DMF	Cs_2CO_3	110	7	–/83

[a] The reaction conditions: **1** (0.5 mmol), **2** (0.5 mmol), **3** (1.1 mmol), and promoter (2.0 equiv.) in 3.0 mL of solvent. [b] Isolated yield based on **1**. [c] Promoter (1.0 equiv.). [d] Promoter (2.5 equiv.).

The cascade reaction of 3-formylchromone **1b**, ethyl 2-(pyridine-2-yl)acetate **2a** and benzimidamide hydrochloride **3b** was used as the model reaction to determinate the optimal conditions including the solvent, promoter, temperature, and time. We first explored the effect of different solvents, such as ethanol, acetonitrile, water, 1,4-dioxane, DMF, PEG1000, 3-methyl-1-octylimidazolium hexafluorophosphate ([OMIM]PF_6), and propylene carbonate (PC) on the reaction yield. From the solvent screen, we discovered that acetonitrile was the optimal solvent for the synthesis of 4,5-dihydro-[4,5'-bipyrimidin]-6(1*H*)-one (DBPMO) **4b**, furnishing the product in 72% yield (Table S1, entry 2 vs. entry 1 and entries 3–8). Interestingly, DMF (in the presence of Cs_2CO_3) favored the formation of [4,5'-bipyrimidin]-6(1*H*)-one (BPMO) **5d** (Table S1, entry 5 vs. entries 1–4 and 6–8). Next, we screened different bases, including K_2CO_3, Et_3N, and Cs_2CO_3, that would promote the generation of target compound **4b** in high yield. From this base screen, we determined and that Cs_2CO_3 was the optimal base for promoting this reaction (Table S1, entry 2 vs. 9–10). After screening the amount of Cs_2CO_3, we found that 2.0 equiv. of Cs_2CO_3 was ideal for promoting this cascade reaction (Table S1, entry 2 vs. 11–12). Finally, the reaction time was assessed, and it was determined that 7 hours was most beneficial for enabling high-yielding reactions (Table S1, entry 2 vs. 13–14). Based on the above results, we determined that the optimal conditions for selective synthesis of compound **4b** entailed acetonitrile as the solvent, 2.0 equiv. of Cs_2CO_3 as the base promoter, and stirring at reflux for about 7 hours (Table S1, entry 13).

As previously mentioned, the use of DMF as the solvent in the presence of Cs_2CO_3 led to the selective formation of product **5d**. In an attempt to determine the optimal conditions to enable the selective synthesis of **5d**, different base promoters, including K_2CO_3 and DBU, were screened in this reaction. The results of the base screen showed that Cs_2CO_3 was the optimal base for promoting this reaction (Table S1, entry 5 vs. 15–16). We then screened the reaction temperature, the results of which demonstrated that 110 ℃ was the optimal temperature for this cascade reaction (Table S1, entry 5 vs. 17–18). Lastly, after a reaction duration screen, it was determined that a reaction time of 10 hours selectively afforded **5d** in excellent yield (83%). Therefore, the results of the reaction optimization indicated that DMF as the solvent, 2.0 equiv. of Cs_2CO_3 as the base promoter, a temperature of 110 ℃, and a duration of about 7 hours was best-suited for the selective synthesis of compound **5d** (Table S1, entry 19).

General Procedure for the Preparation of 4 and 5

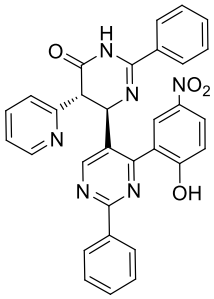


A round-bottom flask was charged with the chromone-3-carboxaldehyde **1** (0.5 mmol). Then, the flask was supplemented with MeCN (3 mL) and ethyl 2-(pyridin-2-yl)acetate **2** (0.5 mmol, and the mixture was stirred under reflux for approximately 3 hours while monitoring the reaction by TLC until the intermediate was completely consumed. Next, intermediate **3** (1.1 mmol) and Cs_2CO_3 (2.0 equiv.) were subsequently added to the above mixture, which was stirred under reflux for 7 hours until the substrates were completely consumed. After cooling the reaction to room temperature, the mixture was extracted with ethyl acetate (3 × 15 mL). The organic layer was washed with water and brine, and the combined organic phases were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the crude product. Finally, product **4** was purified from the crude mixture by flash column chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (2:1-1:1, v/v) as the eluent.

A round-bottom flask was charged with the chromone-3-carboxaldehyde **1** (0.5 mmol). Then, the flask was supplemented with DMF (3 mL) and ethyl 2-(pyridin-2-yl)acetate **2** (0.5 mmol, and the mixture was stirred at 110°C for approximately 3 hours while monitoring the reaction by TLC until the intermediate was completely consumed. Next, intermediate **3** (1.1 mmol) and Cs_2CO_3 (2.0 equiv.) were subsequently added to the above mixture, which was stirred at 110°C for 7 hours until the substrates were completely consumed. After cooling the reaction to room temperature, the mixture was extracted with ethyl acetate (3 × 15 mL). The organic layer was washed with water and brine, and the combined organic phases were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the crude product. Finally, product **5** was purified from the crude mixture by flash column chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (2:1-1:1, v/v) as the eluent.

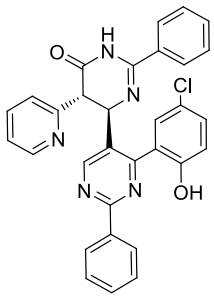
Spectroscopic Data of 4a-5v

4'-(2-Hydroxy-5-nitrophenyl)-2,2'-diphenyl-5-(pyridin-2-yl)-4,5-dihydro-[4,5'-bipyrimidin]-6(1*H*)-one (4a)



White solid (83%, 225 mg); Mp: 253.2-254.3 ℃; IR (KBr): 3766, 3409, 2273, 1613, 1589, 1473, 1134,1075, 757, 647, 540 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 4.26 (d, J = 12.7 Hz, 1H, CH), 5.35 (d, J = 12.8 Hz, 1H, CH), 6.65 (s, 1H, ArH), 6.72-6.89 (m, 2H, ArH), 7.17-7.19 (m, 1H, ArH), 7.43-7.55 (m, 8H, ArH), 7.96-8.01 (m, 2H, ArH), 8.18 (t, J = 4.0 Hz, 1H, ArH), 8.33-8.35 (m, 2H, ArH), 9.06 (s, 1H, ArH), 10.15 (s, 1H, ArOH), 11.18 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 53.4, 59.6, 110.6, 118.4, 122.4, 125.2, 127.8, 127.8, 127.8, 128.2, 128.2, 128.8, 128.8, 129.2, 129.2, 131.2, 131.5, 131.5, 133.2, 133.3, 133.7, 136.6, 137.4, 149.5, 152.6, 153.8, 156.2, 158.6, 162.3, 162.4, 170.9 ppm. HRMS (TOF ES^{+}): *m/z* calcd for $C_{31}H_{23}N_6O_4$ [$(M+H)^{+}$], 543.1775; found, 543.1762.

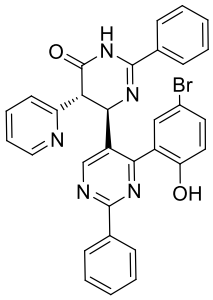
4'-(5-Chloro-2-hydroxyphenyl)-2,2'-diphenyl-5-(pyridin-2-yl)-4,5-dihydro-[4,5'-bipyrimidin]-6(1*H*)-one (4b)



White solid (76%, 202 mg); Mp: 225.4-226.6 ℃; IR (KBr): 3422, 2374, 1693, 1604, 1434, 1377, 1105, 702, 653, 616, 572 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): ^{1}H NMR (600 MHz, DMSO-d_6): δ = 4.24 (d, J = 12.5 Hz, 1H, CH), 5.36 (d, J = 12.7 Hz, 1H, CH), 6.53 (s, 1H, ArH), 6.87 (d, J = 7.6 Hz, 1H, ArH), 6.93 (d, J = 8.7 Hz, 1H, ArH), 7.15-7.17 (m, 1H, ArH), 7.31-7.32 (m, 1H, ArH), 7.47-7.56 (m, 7H, ArH), 7.97 (d, J = 7.6 Hz, 1H, ArH), 7.99 (s, 1H, ArH), 8.17 (d, J = 4.2 Hz, 1H, ArH), 8.33-8.34 (m, 2H, ArH), 9.05 (s, 1H, ArH), 10.12 (s, 1H, ArOH), 11.17 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 53.4, 59.6, 117.9, 122.4, 123.0, 123.2, 125.2, 127.2, 127.7, 128.1, 128.2, 128.8, 128.8, 129.2, 130.3, 130.5, 131.2, 131.5, 131.5, 133.2, 133.6, 136.6, 137.4, 149.4, 152.5, 153.4, 156.3, 158.6,

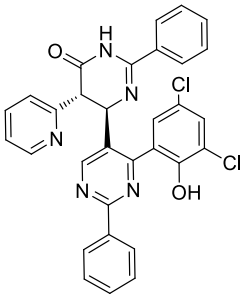
162.3, 162.4, 170.8 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{31}H_{23}ClN_5O_2$ $[(M+H)^+]$, 532.1535; found, 532.1539.

4'-(5-Bromo-2-hydroxyphenyl)-2,2'-diphenyl-5-(pyridin-2-yl)-4,5-dihydro-[4,5'-bipyrimidin]-6(1*H*)-one (4c)



White solid (78%, 225mg); Mp: 248.0-249.2 ℃; IR (KBr): 3774, 3416, 2350, 1709, 1606, 1432, 1106, 695, 619, 557, 513 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 4.26 (d, *J* = 12.7 Hz, 1H, CH), 5.35 (d, *J* = 12.7 Hz, 1H, CH), 6.66 (s, 1H, ArH), 6.88 (t, *J* = 8.6 Hz, 2H, ArH), 7.18 (t, *J* = 5.4 Hz, 1H, ArH), 7.43-7.44 (m, 1H, ArH), 7.49-7.56 (m, 7H, ArH), 7.97 (d, *J* = 7.5 Hz, 1H, ArH), 8.00 (s, 1H, ArH), 8.18 (d, *J* = 3.9 Hz, 1H, ArH), 8.34 (d, *J* = 4.3 Hz, 2H, ArH), 9.06 (s, 1H, ArH), 10.15 (s, 1H, ArOH) ppm, 11.18 (s, 1H, NH); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 53.4, 59.6, 110.6, 118.4, 122.4, 125.2, 127.8, 127.8, 127.8, 128.1, 128.2, 128.8, 128.8, 129.1, 129.1, 131.2, 131.5, 133.2, 133.2, 133.3, 133.6, 136.6, 137.4, 149.5, 152.5, 153.8, 156.2, 158.6, 162.3, 162.4, 170.9 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{31}H_{23}BrN_5O_2$ $[(M+H)^+]$, 576.1030; found, 576.1033.

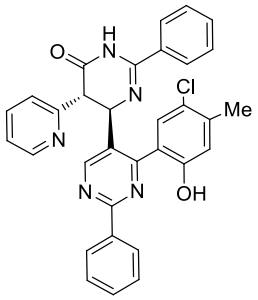
4'-(3,5-Dichloro-2-hydroxyphenyl)-2,2'-diphenyl-5-(pyridin-2-yl)-4,5-dihydro-[4,5'-bipyrimidin]-6(1*H*)-one (4d)



White solid (77%, 218 mg); Mp: 233.1-234.2 ℃; IR (KBr): 3786, 3413, 2251, 1703, 1656, 1412, 1007, 895, 766, 654, 606 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 4.32 (d, *J* = 13.1 Hz, 1H, CH), 5.33 (d, *J* = 12.8 Hz, 1H, CH), 6.60 (s, 1H, ArH), 6.99 (d, *J* = 7.6 Hz, 1H, ArH), 7.19 (t, *J* = 5.3 Hz, 1H, ArH), 7.50-7.52 (m, 5H, ArH), 7.55-7.59 (m, 2H, ArH), 7.61 (s, 1H, ArH), 7.97-8.01 (m, 2H, ArH), 8.23 (t, *J* = 4.5 Hz, 1H, ArH), 8.34 (d, *J* = 6.7 Hz, 2H, ArH), 9.09 (s, 1H, ArH), 11.22 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 53.0, 59.4, 122.6, 123.0, 123.8, 125.5, 127.8, 128.2, 128.3, 128.3, 128.8, 128.8, 128.8, 129.2, 129.2, 129.4, 130.1, 131.3, 131.5, 133.0, 133.6, 136.8, 137.2, 149.5, 149.5, 152.6, 156.1,

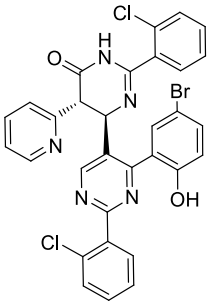
159.1, 161.7, 162.3, 170.8 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{31}H_{22}Cl_2N_5O_2$ [(M+H)$^+$], 566.1145; found, 566.1149.

4'-(5-Chloro-2-hydroxy-4-methylphenyl)-2,2'-diphenyl-5-(pyridin-2-yl)-4,5-dihydro-[4,5'-bipyrimidin]-6(1*H*)-one (4e)



White solid (70%, 191 mg); Mp: ＞300 ℃; IR (KBr): 3802, 3409, 1622, 1605, 1433, 1299, 1104, 882, 700, 611, 556, 530 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 2.32 (s, 3H, CH_3), 4.24 (d, *J* = 12.6 Hz, 1H, CH), 5.37 (d, *J* = 12.7 Hz, 1H, CH), 6.53 (s, 1H, ArH), 6.85 (d, *J* = 5.3 Hz, 2H, ArH), 7.14 (m, 1H, ArH),7.48-7.55 (m, 7H, ArH), 7.96 (d, *J* = 7.4 Hz, 2H, ArH), 8.14 (d, *J* = 4.4 Hz, 1H, ArH), 8.32-8.34 (m, 2H, ArH), 9.03 (s, 1H, ArH), 10.0 (s, 1H, ArOH), 11.17 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 20.1, 53.4, 59.5, 118.6, 119.1, 122.4, 123.4, 125.0, 125.2, 127.7, 127.7，128.1, 128.2, 128.8, 128.8,129.1，130.9, 131.2, 131.5, 133.3, 133.6, 136.6, 137.4, 137.7, 149.4, 152.5 153.2, 156.3, 158.5, 162.2, 162.4, 170.9 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{32}H_{25}ClN_5O_2$ [(M+H)$^+$], 546.1691; found, 546.1695.

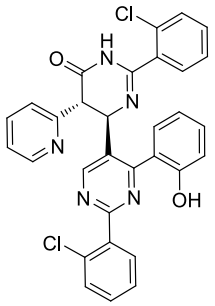
4'-(5-Bromo-2-hydroxyphenyl)-2,2'-bis(2-chlorophenyl)-5-(pyridin-2-yl)-4,5-dihydro-[4,5'-bipyrimidin]-6(1*H*)-one (4f)



White solid (69% 222 mg); Mp: 190.0-191.1 ℃; IR (KBr): 3760, 3433, 1720, 1665, 1595, 1486, 1435, 1272, 1104, 831, 750, 611, 553 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.10 (d, *J* = 13.3 Hz, 1H, CH), 5.92 (d, *J* = 13.3 Hz, 1H, CH), 6.90-6.99 (m, 2H, ArH), 7.12 (t, *J* = 5.0 Hz, 1H, ArH), 7.36-7.54 (m, 9H, ArH), 7.67-7.73 (m, 3H, ArH), 8.29 (d, *J* = 4.8 Hz, 1H, ArH), 9.09 (s, 1H, ArH), 9.99 (s, 1H, ArOH) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 53.0, 59.4, 111.7, 120.4, 122.8, 123.3, 125. 1, 127.0, 127.5, 129.9, 130.4, 130.5, 130.5, 130.9, 130.9, 131.7, 131.9, 132.1, 132.4, 132.5, 133.5, 134.7, 136.4, 136.8, 149.7, 153.3, 155.3,

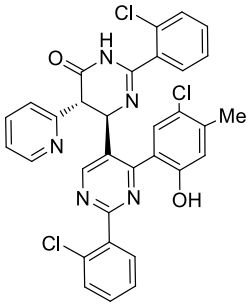
159.2, 162.4, 162.9, 168.8 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{31}H_{21}BrCl_2N_5O_2$ [$(M+H)^+$], 644.0250; found, 644.0257.

2,2'-Bis(2-chlorophenyl)-4'-(2-hydroxyphenyl)-5-(pyridin-2-yl)-4,5-dihydro-[4,5'-bipyrimidin]-6(1*H*)-one (4g)



White solid (63%, 178 mg); Mp: 198.0-199.2; IR (KBr): 3802, 3425, 1700, 1638, 1577, 1433, 1405, 1202, 1004, 750, 633, 543 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 4.19 (d, *J* = 10.9 Hz, 1H, CH), 5.45 (d, *J* = 10.9 Hz, 1H, CH), 6.77 (t, *J* = 9.1 Hz, 2H, ArH), 6.82 (t, *J* = 7.5 Hz, 1H, ArH), 6.94 (d, *J* = 8.1 Hz, 1H, ArH), 7.15-7.17 (m, 1H, ArH), 7.28-7.30 (m, 1H, ArH), 7.49-7.43 (m, 3H, ArH), 7.51-7.61 (m, 5H, ArH), 7.70-7.72 (m, 1H, ArH), 8.18 (t, *J* = 4.0Hz, 1H, ArH), 9.07 (s, 1H, ArH), 9.81 (s, 1H, ArOH), 11.15 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 53.2, 59.8, 116.3, 119.5, 122.6, 124.7, 127.6, 127.6, 127.7, 130.1, 130.2, 130.5, 130.6, 130.9, 131.1, 131.4, 131.8, 131.9, 132.0, 132.2, 134.6, 136.7, 137.9, 149.6, 152.7, 154.4, 156.3, 157.4, 163.3, 163.9, 169.8 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{31}H_{22}Cl_2N_5O_2$ [$(M+H)^+$], 566.1145; found, 566.1143.

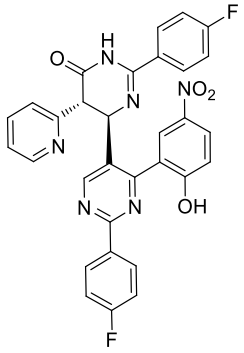
4'-(5-Chloro-2-hydroxy-4-methylphenyl)-2,2'-bis(2-chlorophenyl)-5-(pyridin-2-yl)-4,5-dihydro-[4,5'-bipyrimidin]-6(1*H*)-one (4h)



White solid (65%, 200 mg); Mp: 221.4-222.7 ℃; IR (KBr): 3759, 3409, 1701, 1655, 1600, 1471, 1436, 1222, 1107, 748, 599, 530 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 2.32 (s, 3H, CH_3), 4.22 (d, *J* = 12.5 Hz, 1H, CH), 5.43 (d, *J* = 12.7 Hz, 1H, CH), 6.46 (s, 1H, ArH), 6.86 (t, *J* = 7.8 Hz, 1H, ArH), 7.16-7.18 (m, 1H, ArH), 7.43-7.50 (m, 4H, ArH), 7.51-7.61 (m, 5H, ArH), 7.70 (d, *J* = 7.6 Hz, 1H, ArH), 8.12 (s, 1H, ArH), 9.11 (s, 1H, ArH), 10.00 (s, 1H, ArOH), 11.12 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 20.1, 53.7, 60.0, 118.5, 122.4,

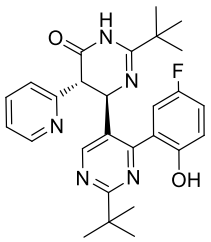
123.4, 124.4, 125.3, 127.6, 127.7, 130.1, 130.6, 131.0, 131.2, 131.8, 131.8, 131.9, 131.9, 132.1, 133.1, 134.6, 136.5, 137.8, 137.9, 149.4, 152.6 153.1, 156.1, 158.1, 161.9, 163.3, 170.0 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{32}H_{23}Cl_3N_5O_2$ $[(M+H)^+]$, 614.0912; found, 614.0913.

2,2'-Bis(4-fluorophenyl)-4'-(2-hydroxy-5-nitrophenyl)-5-(pyridin-2-yl)-4,5-dihydro-[4,5'-bipyrimidin]-6(1*H*)-one (4i)



White solid (73%, 211 mg); Mp: ＞300 ℃; IR (KBr): 3766, 3396, 2277, 1606, 1505, 1385, 1122, 1048, 755, 605, 550 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 4.29 (d, *J* = 13.3 Hz, 1H, CH), 5.32 (d, *J* = 13.3 Hz, 1H, CH), 6.93 (d, *J* = 7.6 Hz, 1H, ArH), 7.02-7.04 (m, 1H, ArH), 7.09 (d, *J* = 9.1 Hz, 1H, ArH), 7.31-7.40 (m, 5H, ArH), 7.50-7.52 (m, 1H, ArH), 8.02-8.06 (m, 3H, ArH), 8.17-8.22 (m, 1H, ArH), 8.37-8.39 (m, 2H, ArH), 9.13 (s, 1H, ArH), 11.25 (s, 1H, ArOH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 53.4, 59.5, 115.7, 115.8, 116.1, 116.2, 116.8, 122.4, 125.6, 126.0, 126.9, 127.4, 130.0，130.3, 130.5, 130.6, 133.5, 133.7，136.6, 139.0, 149.2, 151.7, 156.1, 159.3, 160.9, 161.4, 161.5, 163.6, 164.2 (d, J_1 = 246 Hz), 165.3, 170.9 ppm; ^{19}F NMR (564 MHz, DMSO-d_6): δ = -110.28, -109.60 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{31}H_{20}F_2N_6O_4$ $[(M+H)^+]$, 579.1587; found, 579.1587.

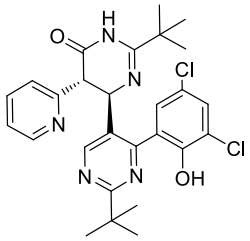
2,2'-Di-tert-butyl-4'-(5-fluoro-2-hydroxyphenyl)-5-(pyridin-2-yl)-4,5-dihydro-[4,5'-bipyrimidin]-6(1*H*)-one (4j)



White solid (74%, 176 mg); Mp: 138.5-139.5 ℃; IR (KBr): 3761, 3420, 2966, 1707, 1658, 1575, 1483, 1441, 1361, 1273, 1140, 867, 833, 769, 711, 607 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 1.32 (s, 9H, $C(CH_3)_3$), 1.38 (s, 9H, $C(CH_3)_3$), 3.82 (d, *J* = 12.8 Hz, 1H, CH), 5.61 (d, *J* = 12.4 Hz, 1H, CH), 6.77 (d, *J* = 7.4 Hz, 1H, ArH), 6.95-6.97 (m, 1H, ArH), 7.04-7.07 (m, 2H, ArH), 7.44-7.46 (m, 1H,

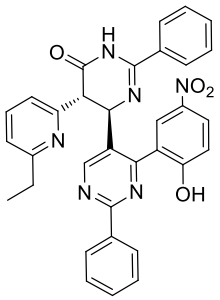
ArH), 7.55 (d, J = 9.1 Hz, 1H, ArH), 8.30 (s, 1H, ArH), 8.43 (s, 1H, ArOH), 8.81 (s, 1H, ArH), 10.90 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 27.5, 27.5, 27.5, 29.3, 29.3, 29.3, 37.1, 39.1, 52.6, 59.0, 117.4 (d, J_2 = 25.5 Hz), 118.6 (d, J_2 = 22.5 Hz), 119.3 (d, J_3 = 7.5 Hz), 121.3, 122.5, 124.5, 128.5, 136.4, 149.8, 153.3, 154.2, 154.0, 156.5, 159.6, 161.2 (d, J_1 = 228.0 Hz), 170.3, 174.5 ppm; ^{19}F NMR (564 MHz, $CDCl_3$): δ = -124.09 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{31}FN_5O_2$ [(M+H)$^+$], 476.2456; found, 476.2460.

2,2'-Di-tert-butyl-4'-(3,5-dichloro-2-hydroxyphenyl)-5-(pyridin-2-yl)-4,5-dihydro-[4,5'-bipyrimidin]-6(1*H*)-one (4k)



White solid (75%, 197 mg); Mp: ＞300 ℃; IR (KBr): 3766, 3398, 2974, 1710, 1652, 1591, 1441, 1364, 1142, 752, 646, 618, 572, 529 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.17-1.27 (m, 9H, $C(CH_3)_3$), 1.28-1.36 (m, 9H, $C(CH_3)_3$), 3.76 (d, J = 12.8 Hz, 1H, CH), 5.44 (d, J = 12.8 Hz, 1H, CH), 6.74 (d, J = 7.7 Hz, 1H, ArH), 6.98-7.00 (m, 1H, ArH), 7.36 (d, J = 2.5 Hz, 1H, ArH), 7.41 (d, J = 1.6 Hz, 1H, ArH), 7.59 (d, J = 2.3 Hz, 1H, ArH), 8.21 (d, J = 4.3 Hz, 1H, ArH), 8.75 (s, 1H, ArH), 11.67 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 27.6, 27.6, 27.6, 29.3, 29.3, 29.4, 37.1, 39.1, 52.6, 58.8, 122.6, 124.0, 124.0, 124.5, 128.7, 129.4, 129.4, 131.5, 131.5, 136.6, 149.7, 151.9 153.9, 159.4, 161.2, 169.9, 174.7 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{30}Cl_2N_5O_2$ [(M+H)$^+$], 526.1771; found, 526.1776.

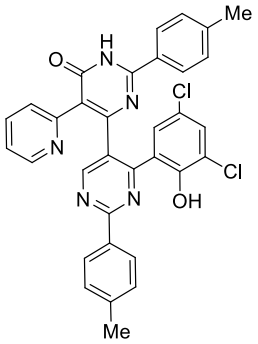
5-(6-Ethylpyridin-2-yl)-4'-(2-hydroxy-5-nitrophenyl)-2,2'-diphenyl-4,5-dihydro-[4,5'-bipyrimidin]-6(1*H*)-one (4l)



White solid (80%, 228 mg); Mp: 206.4-207.7 ℃; IR (KBr): 3760, 3415, 1606, 1425, 1345, 1107, 765, 703, 656, 612, 549, 519, 509 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 1.11 (t, J = 7.6 Hz, 3H, CH_3), 2.46 (m, 2H, CH_2), 4.26 (d, J = 13.3 Hz, 1H, CH), 5.35 (d, J = 13.4 Hz, 1H, CH), 6.84 (d, J = 7.9 Hz, 1H, ArH), 7.11 (d,

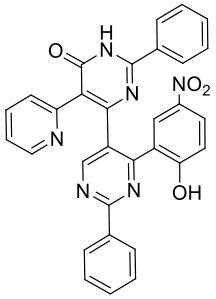
J = 9.1 Hz, 1H, ArH), 7.35 (d, *J* = 6.5 Hz, 1H, ArH), 7.45-7.57 (m, 7H, ArH), 7.92 (s, 1H, ArH), 7.97 (d, *J* = 7.6 Hz, 2H, ArH), 8.24 (d, *J* = 12.8 Hz, 1H, ArH), 8.34 (d, *J* = 5.6 Hz, 2H, ArH), 9.15 (s, 1H, ArH), 11.19 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 15.2, 25.2, 53.0, 59.5, 116.8, 125.0, 126.8, 127.4, 127.7, 128.1, 128.1, 128.8, 128.8, 129.2, 129.2, 131.3, 135.7, 137.2, 137.7, 139.8, 148.9, 153.4, 161.0, 162.4 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{33}H_{27}N_6O_4$ [(M+H)$^+$], 571.2088; found, 571.2091.

4'-(3,5-Dichloro-2-hydroxyphenyl)-5-(pyridin-2-yl)-2,2'-di-p-tolyl-[4,5'-bipyrimidin]-6(1*H*)-one (5a)



Yellow solid (81%, 240mg); Mp: 295.5-296.0 ℃; IR (KBr): 3739, 3411, 2430, 1644, 1535, 1439, 1357, 1121, 730, 665, 622, 548, 513 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 2.35-2.44 (m, 6H, CH_3), 7.06 (s, 1H, ArH), 7.23-7.28 (m, 1H, ArH), 7.33 (t, *J* = 8.9 Hz, 4H, ArH), 7.46 (d, *J* = 7.7 Hz, 1H, ArH), 7.54 (s, 1H, ArH), 7.74 (t, *J* = 7.7 Hz, 1H, ArH), 7.86-8.00 (m, 2H, ArH), 8.27-8.34 (m, 3H, ArH), 8.86 (s, 1H, ArH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 21.5, 21.5, 122.8, 123.0, 123.7, 126.9, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.9, 129.0, 129.7, 129.7, 129.7, 129.9, 129.9, 129.9, 130.3, 130.3, 131.1, 134.2, 136.7, 141.7, 142.8, 148.7, 150.2, 151.9, 158.8, 160.9, 162.9 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{33}H_{24}Cl_2N_5O_2$ [(M+H)$^+$], 592.1302; found, 592.1302.

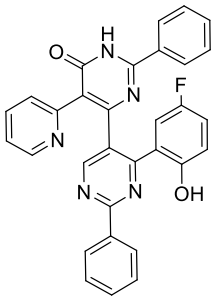
4'-(2-Hydroxy-5-nitrophenyl)-2,2'-diphenyl-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5b)



Yellow solid (86%, 233 mg); Mp: ＞300 ℃; IR (KBr): 3788, 3430, 2370, 1650, 1595, 1404, 1349, 1194, 1104, 829, 728, 690, 607, 536 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 6.93 (d, *J* = 9.0 Hz, 1H, ArHs), 7.08-7.11 (m, 2H, ArH), 7.42-7.44

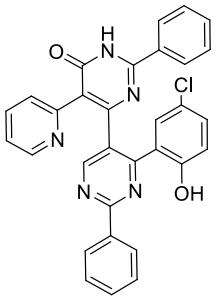
(m, 1H, ArH), 7.54-7.57 (m, 7H, ArH), 8.10-8.12 (m, 1H, ArH), 8.18-8.31 (m, 3H, ArH), 8.43-8.45 (m, 2H, ArH), 9.10 (s, 1H, ArH), 11.50 (s, 1H, ArOH), 13.20 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 29.9, 30.0, 30.1, 30.2, 30.4, 30.5, 30.7, 116.7, 122.5, 126.2, 126.3, 126.9, 127.0, 128.3, 128.3, 128.4, 129.1, 129.2, 129.2, 129.3, 131.6, 132.5, 135.6, 137.1, 140.4, 148.8, 152.1, 159.2, 159.8, 161.4, 163.1 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{31}H_{21}N_6O_4$ [(M+H)$^+$], 541.1619; found, 541.1619.

4'-(5-Fluoro-2-hydroxyphenyl)-2,2'-diphenyl-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one(5c)



Yellow solid (82% 211 mg); Mp: ＞300 ℃; IR (KBr): 3751, 3449, 2367, 1649, 1512, 1432, 1362, 1107, 881, 690, 603, 538 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 6.59-6.61 (m, 1H, ArH), 6.73-6.75 (m, 1H, ArH), 7.05 (d, *J* = 3.2 Hz, 1H, ArH), 7.17-7.19 (m, 2H, ArH), 7.52-7.61 (m, 7H, ArH), 8.11 (d, *J* = 7.6 Hz, 2H, ArH), 8.27 (d, *J* = 3.8 Hz, 1H, ArH), 8.41-8.43 (m, 2H, ArH), 8.94 (s, 1H, ArH), 9.79 (s, 1H, ArOH), 13.16 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 116.4, 116.5, 117.2, 117.2, 117.6, 117.7, 122.6, 126.4, 126.5, 126.5, 128.3, 128.3, 128.4, 128.4, 129.1, 129.1, 129.3, 129.3, 131.3, 131.5, 132.4, 136.1, 137.2, 148.8, 151.5, 152.4, 155.2, 156.8, 158.9, 161.2, 162.7 ppm. ^{19}F NMR (564 MHz, DMSO-d_6): δ = -125.95 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{31}H_{21}FN_5O_2$ [(M+H)$^+$], 514.1674; found, 514.0672.

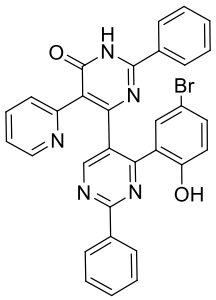
4'-(5-Chloro-2-hydroxyphenyl)-2,2'-diphenyl-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5d)



Yellow solid (83%, 220 mg); Mp: ＞300 ℃; IR (KBr): 3765, 3452, 2344, 1645, 1590, 1401, 1385, 1121, 708, 615, 569, 513 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6):

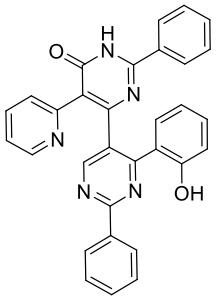
δ = 6.70 (d, *J* = 2.3 Hz, 1H, ArH), 6.76 (d, *J* = 8.7 Hz, 1H, ArH), 7.12 (d, *J* = 7.9 Hz, 1H, ArH), 7.17-7.19 (m, 1H, ArH), 7.22-7.23 (m, 1H, ArH), 7.53-7.58 (m, 6H, ArH), 7.61 (d, *J* = 7.3 Hz, 1H, ArH), 8.13 (d, *J* = 7.6 Hz, 2H, ArH), 8.26 (d, *J* = 4.3 Hz, 1H, ArH), 8.41-8.43 (m, 2H, ArH), 8.98 (s, 1H, ArH), 10.07 (s, 1H, ArOH), 13.14 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 117.8, 122.4, 123.5, 126.4, 127.3, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 129.1, 129.1, 129.1, 129.3, 129.3, 129.3, 129.3, 129.9, 130.7, 131.4, 131.6, 132.4, 136.1, 137.2, 148.7, 152.2, 154.0, 158.9, 160.9, 162.8 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{31}H_{21}ClN_5O_2$ [(M+H)$^+$], 530.1378; found, 530.1376.

4'-(5-Bromo-2-hydroxyphenyl)-2,2'-diphenyl-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5e)



Yellow solid (80%, 230 mg); Mp: ＞300 ℃; IR (KBr): 3454, 2366, 1642, 1586, 1400, 1387, 1116, 698, 610, 556 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 6.72 (d, *J* = 8.7 Hz, 1H, ArH), 6.84 (s, 1H, ArH), 7.13-7.20 (m, 2H, ArH), 7.33-7.37 (m, 1H, ArH), 7.45-7.68 (m, 7H, ArH), 8.15 (t, *J* = 7.6 Hz, 2H, ArH), 8.22-8.26 (m, 1H, ArH), 8.32-8.43 (m, 2H, ArH), 8.98 (s, 1H, ArH), 10.12 (s, 1H, ArOH), 13.13 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ =111.1, 118.3, 122.4, 126.4, 127.8, 128.3, 128.3, 128.4, 128.4, 128.4, 129.1, 129.1, 129.1, 129.3, 129.3, 129.3, 131.4, 131.4, 131.5, 131.5, 132.3, 132.7, 133.5, 136.2, 137.2, 148.7, 152.3, 154.4, 158.9, 160.9, 162.8 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{31}H_{21}BrN_5O_2$ [(M+H)$^+$], 574.0873; found, 574.0875.

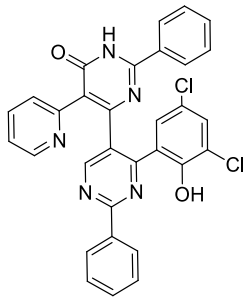
4'-(2-Hydroxyphenyl)-2,2'-diphenyl-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5f)



Yellow solid (80%, 198 mg); Mp: ＞300 ℃; IR (KBr): 3446, 2363, 1644, 1509, 1428, 1359, 1107, 898, 655, 572, 542 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ =

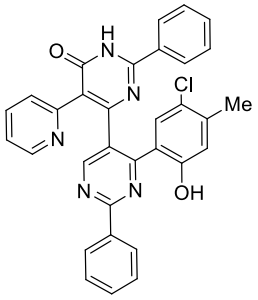
6.75-6.78 (m, 2H, ArH), 7.06 (d, J = 7.3 Hz, 1H, ArH), 7.16-7.23 (m, 3H, ArH), 7.49-7.61 (m, 7H, ArH), 8.01 (d, J = 7.6 Hz, 2H, ArH), 8.31 (t, J_1 = 8.3 Hz, J_2 = 4.2 Hz, 1H, ArH), 8.41 (t, J_1 = 5.3 Hz, J_2 = 2.5 Hz, 2H, ArH), 8.81 (s, 1H, ArH), 9.94 (s, 1H, ArOH), 13.12 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 116.3, 119.6, 122.7, 125.3, 126.5, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 129.0, 129.0, 129.0, 129.2, 129.2, 129.2, 131.0, 131.2, 131.5, 132.3, 136.3, 137.3, 148.7, 152.6, 155.4, 156.5, 158.7, 159.3, 162.5, 162.8 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{31}H_{22}N_5O_2$ [(M+H)$^+$], 496.1768; found, 496.1768.

4'-(3,5-Dichloro-2-hydroxyphenyl)-2,2'-diphenyl-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5g)



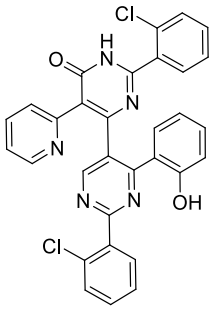
Yellow solid (83%, 234 mg); Mp: ＞300 ℃; IR (KBr): 3837, 3422, 2967, 1749, 1593, 1434, 1390, 1194, 1104, 819, 674, 602, 572 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 6.99 (d, J = 2.5 Hz, 1H, ArH), 7.23-7.25 (m, 1H, ArH), 7.42 (d, J = 8.0 Hz, 1H, ArH), 7.52-7.58 (m, 6H, ArH), 7.61 (t, J = 7.3 Hz, 1H, ArH), 7.71-7.74 (m, 1H, ArH), 8.06 (d, J = 7.5 Hz, 2H, ArH), 8.28 (d, J = 4.5 Hz, 1H, ArH), 8.39-8.41 (m, 2H, ArH), 8.84 (s, 1H, ArH), 10.54 (s, 1H, ArOH), 13.23 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ =122.8, 123.0, 123.8, 126.9, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.4, 128.9, 129.1, 129.1, 129.1, 129.3, 129.3, 129.3, 130.3, 131.4, 131.8, 132.6, 136.7, 136.9, 148.8, 150.1, 151.8, 158.4, 158.9, 160.8, 162.9 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{31}H_{20}ClN_5O_2$ [(M+H)$^+$], 564.0989; found, 564.0992.

4'-(5-Chloro-2-hydroxy-4-methylphenyl)-2,2'-diphenyl-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5h)



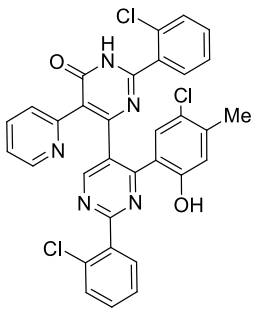
Yellow solid (82%, 223 mg); Mp: ＞300 ℃; IR (KBr): 3785, 3403, 2374, 1641, 1532, 1434, 1385, 1106, 695, 616, 555 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 2.26 (s, 3H, CH_3), 6.70 (s, 1H, ArH), 6.72 (s, 1H, ArH), 7.11 (d, J = 7.9 Hz, 1H, ArH), 7.15-7.17 (m, 1H, ArH), 7.52-7.62 (m, 7H, ArH), 8.12 (d, J = 7.4 Hz, 2H, ArH), 8.24 (d, J = 4.1 Hz, 1H, ArH), 8.40-8.42 (m, 2H, ArH), 8.95 (s, 1H, ArH), 9.97 (s, 1H, ArOH), 13.15 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 20.0, 118.4, 122.4, 124.0, 124.9, 126.5, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 129.1, 129.1, 129.1, 129.3, 129.3, 129.3, 130.3, 131.2, 131.5, 132.4, 136.0, 137.2, 138.5, 148.7, 152.3, 153.9, 158.9, 160.9, 162.8 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{32}H_{23}ClN_5O_2$ [$(M+H)^+$], 544.1535; found, 544.1538.

2,2'-Bis(2-chlorophenyl)-4'-(2-hydroxyphenyl)-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5i)



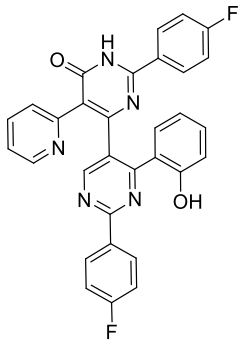
Yellow solid (77%, 217 mg); Mp: 240.7–241.8 ℃; IR (KBr): 3759, 3402, 2366, 2022, 1605, 1516, 1488, 1387, 1123, 764, 681, 616, 557, 535 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 6.0 (t, J = 7.4 Hz, 1H, ArH), 6.82 (d, J = 8.2 Hz, 1H, ArH), 6.99 (d, J = 7.4 Hz, 1H, ArH), 7.19 (t, J = 3.7 Hz, 2H, ArH), 7.23-7.26 (m, 1H, ArH), 7.48-7.63 (m, 8H, ArH), 7.77-7.79 (m, 1H, ArH), 8.27 (s, 1H, ArH), 8.56 (s, 1H, ArH), 10.04 (s, 1H, ArOH), 13.27 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 116.5, 119.7, 122.8, 124.2, 126.5, 127.6, 127.7, 127.7, 130.3, 130.7, 130.7, 130.7, 131.3, 131.4, 131.6, 131.6, 132.0, 132.0, 132.1, 132.2, 132.5, 133.4, 136.2, 137.6, 148.6, 152.1, 155.7, 158.3, 159.0, 161.9, 163.5 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{31}H_{20}Cl_2N_5O_2$ [$(M+H)^+$], 564.0989; found, 564.0991.

4'-(5-Chloro-2-hydroxy-4-methylphenyl)-2,2'-bis(2-chlorophenyl)-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5j)



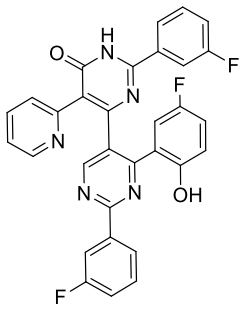
Yellow solid (80%, 244 mg); Mp: ＞300 ℃; IR (KBr): 3737, 3426, 1695, 1605, 1500, 1385, 1107, 764, 726, 692, 664, 602, 573 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 2.27 (s, 3H, CH_3), 6.68 (s, 1H, ArH), 6.77 (s, 1H, ArH), 7.11 (d, J = 7.9 Hz, 1H, ArH), 7.20 (s, 1H, ArH), 7.49-7.66 (m, 8H, ArH), 7.79 (d, J = 7.3 Hz, 1H, ArH), 8.22 (s, 1H, ArH), 8.96 (s, 1H, ArH), 10.11 (s, 1H, ArOH), 13.31 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 20.1, 118.6, 122.5, 123.8, 124.0, 126.5, 127.6, 127.8, 127.8, 130.4, 130.4, 130.6, 130.7, 130.7, 131.5, 131.6, 132.1, 132.1, 132.1, 132.1, 132.5, 133.4, 136.0, 137.6, 138.9, 148.6, 151.8, 154.1, 158.5, 158.7, 160.1, 163.7 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{32}H_{21}Cl_3N_5O_2$ $[(M+H)^+]$, 612.0755; found, 612.0753.

2,2'-Bis(4-fluorophenyl)-4'-(2-hydroxyphenyl)-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5k)



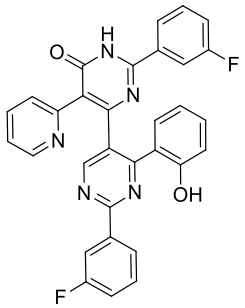
Yellow solid (82%, 218 mg); Mp: 304.3-305.5 ℃; IR (KBr): 3759, 3393, 1643, 1606, 1519, 1439, 1384, 1106, 852, 700, 617, 554 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 6.74-6.77 (m, 2H, ArH), 7.03 (d, J = 7.3 Hz, 1H, ArH), 7.16-7.22 (m, 3H, ArH), 7.33-7.37 (m, 4H, ArH), 7.57-7.60 (m, 1H, ArH), 8.07-8.09 (m, 2H, ArH), 8.31 (d, J = 4.1 Hz, 1H, ArH), 8.44-8.46 (m, 2H, ArH), 8.79 (s, 1H, ArH), 9.87 (s, 1H, ArOH), 13.13 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 116.0, 116.1, 116.1, 116.2, 116.3, 119.7, 122.7, 125.4, 126.5, 129.3, 130.7, 130.8, 130.9, 131.0, 131.0, 131.1, 131.2, 133.8, 136.3, 148.7, 152.6, 155.3, 158.7, 159.3, 161.7, 162.9, 163.1, 163.7, 163.9, 165.4, 165.6 ppm; ^{19}F NMR (564 MHz, DMSO-d_6): δ = -110.06, -108.21 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{31}H_{20}F_2N_5O_2$ $[(M+H)^+]$, 532.1580; found, 532.1576

4'-(5-Fluoro-2-hydroxyphenyl)-2,2'-bis(3-fluorophenyl)-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5l)



Yellow solid (79%, 217 mg); Mp: 222.6–223.2 ℃; IR (KBr): 3766, 3429, 1650, 1532, 1327, 1131, 711, 608, 559, 502 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 6.56-6.57 (m, 1H, ArH), 6.65-6.67 (m, 1H, ArH), 6.97-6.99 (m, 1H, ArH), 7.10-7.13 (m, 2H, ArH), 7.32-7.40 (m, 2H, ArH), 7.50-7.57 (m, 3H, ArH), 7.79 (d, J = 10.1 Hz, 2H, ArH), 8.30 (d, J = 3.8 Hz, 1H, ArH), 8.61 (d, J = 8.2 Hz, 2H, ArH), 8.88 (s, 1H, ArH), 9.69 (s, 1H, ArOH), 13.12 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 114.7 (d, J_2 = 24.0 Hz), 115.0, 115.1, 116.5 (d, J_2 = 22.5 Hz), 117.2, 117.2, 117.8 (d, J_2 = 24.0 Hz), 118.4 (d, J_2 = 21.0 Hz), 119.1, 119.2, 122.7, 124.4, 126.4 (d, J_2 = 22.5 Hz), 126.4, 131.2, 131.3 (d, J_2 = 22.5 Hz), 131.4, 131.6, 136.2, 139.7 (d, J_3 = 7.5 Hz), 148.8, 151.4, 152.2, 155.3, 156.8, 159.0, 161.4, 161.6, 161.8, 163.0 (d, J_1 = 241.5 Hz), 163.4 ppm; ^{19}F NMR (564 MHz, DMSO-d_6): δ = -125.83, -112.73, -112.34 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{31}H_{19}F_3N_5O_2$ $[(M+H)^+]$, 550.1485; found, 550.1487.

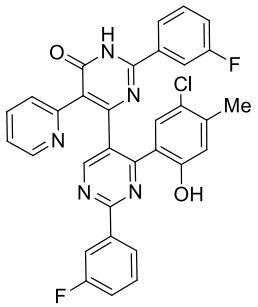
2,2'-Bis(3-fluorophenyl)-4'-(2-hydroxyphenyl)-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5m)



Yellow solid (75%, 199 mg); Mp: ＞300 ℃; IR (KBr): 3420, 3078, 1647, 1560, 1433, 1365, 1205, 1150, 1010, 896, 760, 615, 525 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 6.78 (t, J = 5.3 Hz, 2H, ArH), 7.07 (d, J = 7.0 Hz, 1H, ArH), 7.18-7.23 (m, 3H, ArH), 7.38-7.44 (m, 2H, ArH), 7.53-7.62 (m, 3H, ArH), 7.76 (d, J = 10.1 Hz, 1H, ArH), 7.89 (d, J = 7.8 Hz, 1H, ArH), 8.10 (d, J = 9.7 Hz, 1H, ArH), 8.25 (d, J = 7.9 Hz, 1H, ArH), 8.33 (d, J = 4.2 Hz, 1H, ArH), 8.82 (d, J = 13.5 Hz, 1H, ArH), 9.86 (s, 1H, ArOH), 13.16 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 114.6 (d, J_2 = 22.5 Hz), 115.1 (d, J_2 = 22.5 Hz), 116.2, 118.2, 118.4, 119.0, 119.1, 119.7, 122.8, 124.4, 124.5, 125.4, 126.5, 131.0, 131.1, 131.1, 131.1, 131.3, 131.4, 135.4, 136.4, 139.8, 139.9, 148.8, 152.5, 155.3, 158.7,

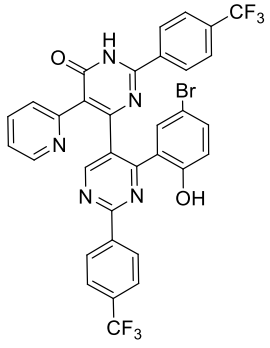
162.2, 162.2 (d, J_1 = 247.5 Hz), 162.5 (d, J_1 = 241.5 Hz), 163.8 ppm; ^{19}F NMR (564 MHz, DMSO-d_6): δ = -112.76, -112.43 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{31}H_{20}F_2N_5O_2$ [(M+H)$^+$], 532.1580; found, 532.1578.

4'-(5-Chloro-2-hydroxy-4-methylphenyl)-2,2'-bis(3-fluorophenyl)-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5n)



Yellow solid (79%, 229 mg); Mp: ＞300 ℃; IR (KBr): 3422, 2425, 1749, 1594, 1515, 1311, 1270, 1141, 1123, 1056, 856, 788, 619, 555 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 2.26 (s, 3H, CH_3), 6.69 (s, 1H, ArH), 6.74 (s, 1H, ArH), 7.11 (d, J = 7.9 Hz, 1H, ArH), 7.18-7.20 (m, 1H, ArH), 7.39-7.48 (m, 2H, ArH), 7.56-7.62 (m, 3H, ArH), 7.86 (d, J = 10.1 Hz, 1H, ArH), 8.00 (t, J = 7.7 Hz, 1H, ArH), 8.11 (d, J = 10.3 Hz, 1H, ArH), 8.26 (t, J = 5.2 Hz, 2H, ArH), 8.96 (s, 1H, ArH), 9.94 (s, 1H, ArOH), 13.21 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 20.0, 114.6 (d, J_2 = 24.0 Hz), 115.1 (d, J_2 = 24.0 Hz), 118.3, 118.4, 118.4, 119.1, 119.2, 122.5, 124.1, 124.4, 124.5, 124.9, 126.4, 130.3, 131.2, 131.3, 131.4, 131.4, 136.2, 138.6, 139.7, 139.8, 148.8, 152.1, 153.8, 159.0, 161.1, 161.7, 162.2, 162.6 (d, J_1 = 243.0 Hz), 163.8 ppm; ^{19}F NMR (564 MHz, DMSO-d_6): δ = -112.71, -112.32 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{32}H_{21}ClF_2N_5O_2$ [(M+H)$^+$], 580.1346; found, 580.1345.

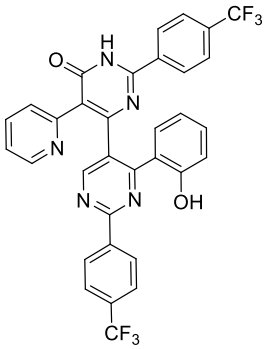
4'-(5-Bromo-2-hydroxyphenyl)-5-(pyridin-2-yl)-2,2'-bis(4-(trifluoromethyl)phenyl)-[4,5'-bipyrimidin]-6(1*H*)-one (5o)



Yellow solid (86%, 305 mg); Mp: 174.8–175.4 ℃; IR (KBr): 3751, 3434, 2939, 2343, 1651, 1600, 1385, 1327, 1129, 859, 675, 611, 516 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 6.70 (d, J = 8.7 Hz, 1H, ArH), 6.76 (d, J = 2.0 Hz, 1H, ArH), 7.09(d, J = 7.9 Hz, 1H, ArH), 7.19-7.21 (m, 1H, ArH), 7.34-7.36 (m, 1H,

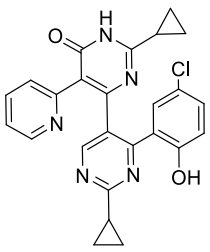
ArH), 7.57-7.60 (m, 1H, ArH), 7.92-7.94 (m, 4H, ArH), 8.25 (d, *J* = 4.4 Hz, 1H, ArH), 8.37 (d, *J* = 8.2 Hz, 2H, ArH), 8.62 (d, *J* = 8.2 Hz, 2H, ArH), 9.10 (s, 1H, ArH), 10.06 (s, 1H, ArOH), 13.38 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 111.1, 118.3, 121.9, 122.5, 123.5, 123.7, 125.3, 125.6, 126.0, 126.2, 126.2, 126.3, 126.3, 127.4, 127.5, 129.1, 129.1, 129.1, 129.3, 129.3, 131.2, 131.5, 132.1, 132.6, 133.7, 136.3, 140.9, 148.7, 151.9, 154.3, 159.1, 161.0, 161.6 ppm; ^{19}F NMR (564 MHz, DMSO-d_6): δ = -61.39, -61.39, -61.39, -61.28, -61.28, -61.28 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{33}H_{18}BrF_6N_5O_2$ [(M+H)$^+$], 710.0621; found, 710.0624.

4'-(2-Hydroxyphenyl)-5-(pyridin-2-yl)-2,2'-bis(4-(trifluoromethyl)phenyl)-[4,5'-bipyrimidin]-6(1*H*)-one (5p)



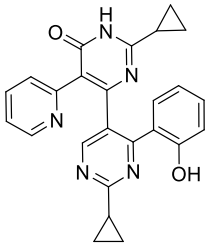
Yellow solid (84%, 265 mg); Mp: 209.3–210.9 ℃; IR (KBr): 3760, 3435, 2367, 1669, 1600, 1327, 1130, 751, 665, 598, 572 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 6.76 (t, *J* = 7.9 Hz, 2H, ArH), 7.00 (d, *J* = 7.4 Hz, 1H, ArH), 7.18-7.23 (m, 3H, ArH), 7.59 (t, *J* = 7.0 Hz, 1H, ArH), 7.88-7.91 (m, 4H, ArH), 8.23 (d, *J* = 8.0 Hz, 2H, ArH), 8.30 (d, *J* = 3.8 Hz, 1H, ArH), 8.61 (d, *J* = 8.2 Hz, 2H, ArH), 8.91 (s, 1H, ArH), 9.82 (s, 1H, ArOH), 13.31 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 116.2, 119.8, 122.8, 123.5, 123.7, 125.3, 125.3, 125.5, 125.9, 126.2, 126.2, 126.4, 129.0, 129.0, 129.0, 129.3, 129.3, 129.3, 131.0, 131.2, 131.4, 131.7, 131.8, 132.0, 136.4, 137.0, 141.0, 148.7, 152.3, 155.2, 158.8, 161.3, 163.0 ppm. ^{19}F NMR (564 MHz, DMSO-d_6): δ = -61.40, -61.40, -61.40, -61.28, -61.28, -61.28 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{33}H_{20}F_6N_5O_2$ [(M+H)$^+$], 632.1516; found, 632.1514.

4'-(5-Chloro-2-hydroxyphenyl)-2,2'-dicyclopropyl-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5q)



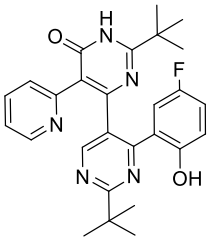
Yellow solid (86%, 197 mg); Mp: 216.3–217.9 ℃; IR (KBr): 3808, 3406, 2370, 1632, 1604, 1470, 1387, 1114, 714, 683, 614, 571, 523 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 0.82 (s, 2H, CH_2), 0.96-1.05 (m, 6H, CH_2), 1.91 (t, J = 4.0 Hz, 1H, CH), 2.17-2.20 (m, 1H, CH), 6.71 (s, 1H, ArH), 6.74 (d, J = 8.7 Hz, 1H, ArH), 7.13-7.21 (m, 3H, ArH), 7.57 (t, J = 7.5 Hz, 1H, ArH), 8.26 (d, J = 3.6 Hz, 1H, ArH), 8.38 (s, 1H, ArH), 10.07 (s, 1H, ArOH), 12.98 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 10.3, 10.3, 11.1, 11.1, 13.7, 18.3, 117.9, 121.4, 122.3, 123.0, 126.5, 127.0, 129.8, 130.1, 130.4, 136.1, 148.6, 152.7, 154.1, 158.0, 159.1, 160.6, 161.9, 163.5, 170.4 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{25}H_{21}ClN_5O_2$ [$(M+H)^+$], 458.1378; found, 458.1380.

2,2'-Dicyclopropyl-4'-(2-hydroxyphenyl)-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5r)



Yellow solid (85%, 180 mg); Mp: 240.7-241.7 ℃; IR (KBr): 3858, 3452, 2366, 1642, 1501, 1489, 1376, 1119, 625, 547 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 0.65 (s, 2H, CH_2), 0.86-0.88 (m, 2H, CH_2), 0.97-1.05 (m, 4H, CH_2), 1.83-1.87 (m, 1H, CH), 2.15-2.20 (m, 1H, CH), 6.73-6.77 (m, 2H, ArH), 7.06 (d, J = 7.4 Hz, 1H, ArH), 7.14-7.22 (m, 2H, ArH), 7.29 (d, J = 7.9 Hz, 1H, ArH), 7.62 (t, J = 7.5 Hz, 1H, ArH), 8.22 (s, 1H, ArH), 8.30 (d, J = 4.3 Hz, 1H, ArH), 10.12 (s, 1H, ArOH), 12.98 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 10.3, 10.3, 11.0, 11.0, 13.6, 18.2, 116.5, 119.3, 121.6, 122.6, 124.7, 126.6, 129.6, 130.9, 131.0, 136.3, 148.7, 153.0, 155.6, 157.8, 159.5, 162.0, 162.5, 163.5, 170.0 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{25}H_{22}N_5O_2$ [$(M+H)^+$], 424.1768; found, 424.1766.

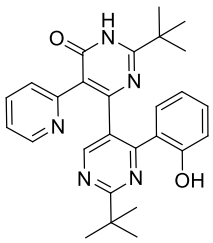
2,2'-Di-tert-butyl-4'-(5-fluoro-2-hydroxyphenyl)-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5s)



Yellow solid (85%, 201 mg); Mp: 274.3–275.4 ℃; IR (KBr): 3692, 3412, 2405, 1653, 1582, 1486, 1385, 1121, 873, 744, 680, 615, 567, 521 cm^{-1}; ^1H NMR (600

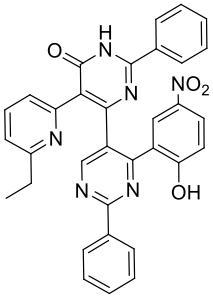
MHz, DMSO-d_6): δ = 1.16 (s, 9H, $C(CH_3)_3$), 1.35 (s, 9H, $C(CH_3)_3$), 6.78 (t, 1H, *J* = 4.7 Hz, ArH), 6.82-6.84 (m, 1H, ArH), 7.08 (s, 1H, ArH), 7.21 (d, *J* = 1.6 Hz, 1H, ArH), 7.31 (d, *J* = 7.9 Hz, 1H, ArH), 7.66 (d, *J* = 1.7 Hz, 1H, ArH), 8.33 (d, *J* = 4.4 Hz, 1H, ArH), 8.45 (s, 1H, ArH), 10.09 (s, 1H, ArOH), 12.45 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 28.0, 28.0, 28.0, 29.8, 29.8, 29.8, 37.6, 39.5, 116.7 (d, J_2 = 24.0 Hz), 117.4, 117.4, 117.6 (d, J_2 = 22.5 Hz), 122.8, 125.9, 126.6, 129.6, 136.3, 148.8, 152.1, 152.9, 154.9, 157.3 (d, J_1 = 241.5 Hz), 157.9, 160.9, 162.7, 167.1, 175.3 ppm. ^{19}F NMR (564 MHz, DMSO-d_6): δ = -126.34 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{29}FN_5O_2$ [$(M+H)^+$], 474.2300; found, 474.2296.

2,2'-Di-tert-butyl-4'-(2-hydroxyphenyl)-5-(pyridin-2-yl)-[4,5'-bipyrimidin]-6(1*H*)-one (5t)



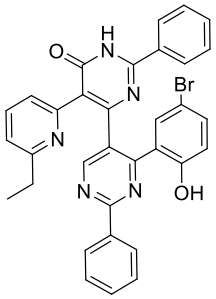
Yellow solid (84%, 191 mg); Mp: ＞300 ℃; IR (KBr): 3766, 3422, 2969, 2374, 1656, 1582, 1487, 1436, 1386, 1105, 1015, 754, 607, 560, 517 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 1.12 (s, 9H, $C(CH_3)_3$), 1.35 (s, 9H, $C(CH_3)_3$), 6.76-6.80 (m, 2H, ArH), 7.20-7.24 (m, 3H, ArH), 7.36 (d, *J* = 7.9 Hz, 1H, ArH), 7.65-7.67 (m, 1H, ArH), 7.66 (d, *J* = 1.7 Hz, 1H, ArH), 8.34 (d, *J* = 4.4 Hz, 1H, ArH), 8.37 (s, 1H, ArH), 10.47 (s, 1H, ArOH), 12.44 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 28.0, 28.0, 28.0, 29.8, 29.8, 29.8, 37.6, 39.4, 116.6, 119.2, 119.2, 122.8, 124.1, 126.6, 129.2, 131.2, 131.3, 136.3, 148.8, 153.0, 156.3, 157.9, 158.4, 162.3, 162.8, 167.1, 174.9 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{30}N_5O_2$ [$(M+H)^+$], 456.2394; found, 456.2393.

5-(6-Ethylpyridin-2-yl)-4'-(2-hydroxy-5-nitrophenyl)-2,2'-diphenyl-[4,5'-bipyrimidin]-6(1*H*)-one (5u)



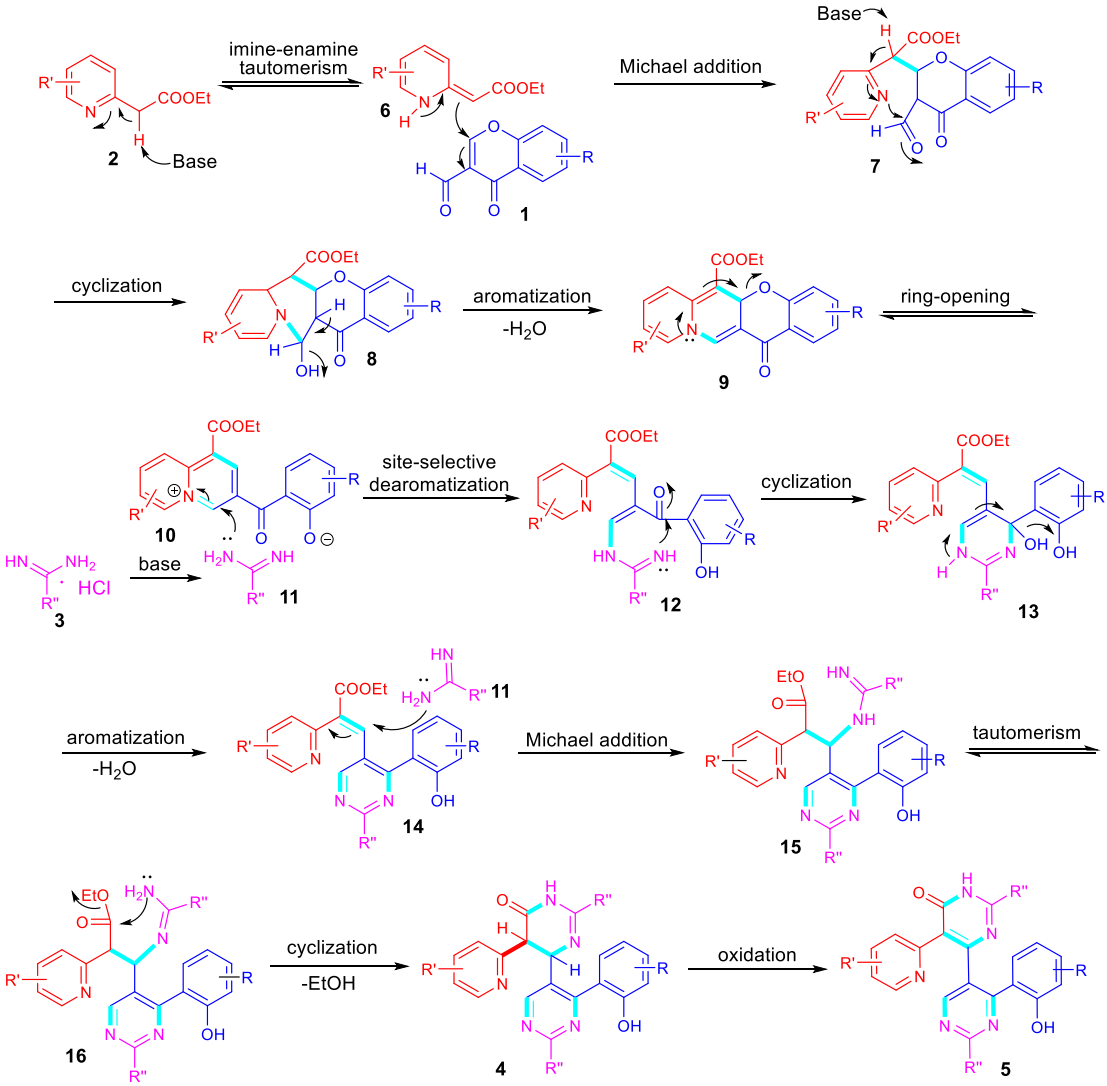
Yellow solid (83%, 236 mg); Mp: ＞300 ℃; IR (KBr): 3708, 3433, 2368, 1656, 1506, 1433, 1355, 1104, 823, 735, 695, 606, 544 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 2.74 (s, 2H, CH_2), 2.89 (s, 3H, CH_3), 6.71 (d, J = 8.7 Hz , 1H, ArH), 6.83 (d, J = 1.56 Hz, 1H, ArH), 7.12 (d, J = 7.9 Hz, 1H, ArH), 7.19 (s, 1H, ArH), 7.33-7.35 (m, 1H, ArH) , 7.54-7.62 (m, 5H, ArH), 7.96 (s, 1H, ArH), 8.13 (d, J = 7.5 Hz, 2H, ArH), 8.26 (d, J = 4.0 Hz , 1H, ArH), 8.42 (t, J = 4.5 Hz, 2H, ArH), 8.98 (s, 1H, ArH), 10.10 (s, 1H, ArOH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 31.3, 36.3, 111.0, 118.3, 122.4, 126.4, 127.8, 128.3, 128.3, 128.4, 128.4, 128.4, 129.1, 129.1, 129.1, 129.3, 129.3, 129.3, 131.4, 131.6, 132.4, 132.7, 133.5, 136.2, 137.0, 137.2, 148.7, 152.2, 154.4, 158.9, 160.9, 162.8, 162.9 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{33}H_{25}N_6O_4$ [$(M+H)^+$], 569.1932; found, 569.1929.

4'-(5-Bromo-2-hydroxyphenyl)-5-(6-ethylpyridin-2-yl)-2,2'-diphenyl-[4,5'-bipyrimidin]-6(1*H*)-one (5v)



Yellow solid (83%, 249 mg); Mp: ＞300 ℃; IR (KBr): 3749, 3451, 2343, 1651, 1533, 1402, 1367, 1105, 879, 688, 606, 544 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 1.16-1.22 (m, 3H, CH_3), 2.58-2.62 (m, 2H, CH_2), 6.70 (d, J = 8.7 Hz, 1H, ArH), 6.78 (d, J = 1.7 Hz, 1H, ArH), 7.03 (d, J = 8.1 Hz, 1H, ArH), 7.32-7.34 (m, 1H, ArH), 7.42-7.44 (m, 1H, ArH), 7.53-7.62 (m, 6H, ArH), 8.11 (s, 1H, ArH), 8.15 (d, J = 7.5 Hz, 2H, ArH), 8.41-8.42 (m, 2H, ArH), 9.01 (s, 1H, ArH), 10.06 (s, 1H, ArOH), 13.09 (s, 1H, NH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 15.4, 25.6, 111.0, 118.2, 125.9, 127.8, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.4, 129.1, 129.3, 131.5, 131.5, 131.5, 131.6, 131.6, 131.6, 132.3, 132.6, 133.4, 135.4, 137.2, 137.8, 148.1, 149.7, 154.4, 158.9, 160.8, 162.8 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{33}H_{25}BrN_5O_2$ [$(M+H)^+$], 602.1186; found, 602.1186.

The Proposed Mechanism of the Cascade Reaction



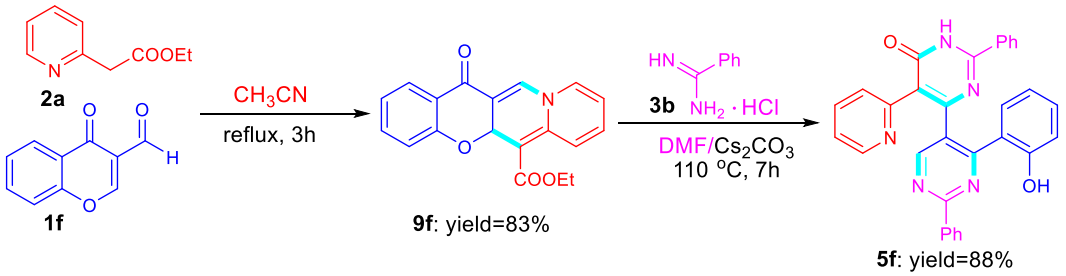
Scheme S1. The proposed mechanism of the cascade reaction.

The proposed mechanism of the multi-component cascade reaction is shown in Scheme S1 of the supporting information. First, the ethyl 2-(pyridine-2-yl)acetate derivatives **2** underwent base-catalyzed imine-enamine tautomerization to form the enamine ester intermediate **6**. Then, the *α*-carbon of intermediates **6** attacked the double bonds of 3-formylchromones **1** and formed the intermediates **7** through a Michael addition. The intermediate **7** produced intermediate **9** via an intramolecular condensation with the concomitant loss of one molecule of water. Intermediate **9** then underwent a reversible ring-opening tautomerization to generate intermediate **10**. Upon the deprotonation of the amidine hydrochloride **3** by the base promoter, intermediate **11** attacked the double bond of pyridinium salts through a site-selective dearomatization reaction to produce intermediate **12**. Next, intermediate **13** was formed through an intramolecular condensation-cyclization of intermediate **11**. The amine of intermediate **11** underwent Michael addition to the double bond of

intermediate **14** to form intermediate **15**, which then underwent reversible tautomerization and subsequent intramolecular condensation reaction to form the target compound **4**. Finally, compound **4** formed target compound **5** via an oxidation reaction facilitated by heat.

To verify the mechanism of this reaction, 3-formylchromone **1f**, 2-(pyridine-2 -yl)acetate **2a** and benzimidamide hydrochloride **3b** and DMF were charged in round-bottom flask, and then Cs_2CO_3 were added to the mixture. The mixture was stirred at 110 ^{0}C for approximately 35minutes. Subsequently, the reaction mixture was analyzed by high-performance liquid chromatography-high resolution mass spectrometry (HPLC-HRMS). The molecular ion peaks that appeared in the high-resolution mass spectrum were: HRMS (TOF ES$^+$): *m/z* calcd. for $C_{10}H_7O_3$ $[M+H]^+$, 175.0390; found, 175.0383, which is the HRMS spectrum of **1f** (SI, Figure S84); HRMS (TOF ES$^+$): *m/z* calcd. for $C_9H_{12}NO_2$ $[M+H]^+$, 166.0863; found, 166.0857, which is the HRMS spectra of **2a/6a** (SI, Figure S85); HRMS (TOF ES$^+$): *m/z* calcd. for $C_{19}H_{18}NO_5$ $[M+H]^+$, 340.1179; found, 340.1174, which is the HRMS spectra of intermediate **7f**/**8f** (SI, Figure S86); HRMS (TOF ES$^+$): *m/z* calcd. for $C_{19}H_{16}NO_4$ $[M+H]^+$, 322.1074; found, 322.1069. HRMS (TOF ES$^+$): *m/z* calcd. for $C_{19}H_{16}NO_4$ $[M+H]^+$, 322.1074; found, 322.1068. There are the HRMS spectra of intermediates **9f/10f** (SI, Figure S87−S88); HRMS (TOF ES$^+$): *m/z* calcd. for $C_{26}H_{24}N_3O_4$ $[M+H]^+$, 442.1761; found, 442.1755. HRMS (TOF ES$^+$): *m/z* calcd. for $C_{26}H_{24}N_3O_4$ $[M+H]^+$, 442.1761; found, 442.1750. There are the HRMS spectra of intermediates **12f/13f** (SI, Figure S89−S90); HRMS (TOF ES$^+$): *m/z* calcd. for $C_{26}H_{22}N_3O_3$ $[M+H]^+$, 424.1656; found, 424.1647, which is the HRMS spectrum of intermediate **14f** (SI, Figure S91). HRMS (TOF ES$^+$): *m/z* calcd. for $C_{33}H_{30}N_5O_3$ $[M+H]^+$, 544.2343; found, 544.2332. HRMS (TOF ES$^+$): *m/z* calcd. for $C_{33}H_{30}N_5O_3$ $[M+H]^+$, 544.2343; found, 544.2349, which are the HRMS spectrum of the target compound **15f/16f** (SI, Figure S92−93). HRMS (TOF ES$^+$): *m/z* calcd. for $C_{31}H_{24}N_5O_2$ $[M+H]^+$, 498.1925; found, 498.1932, which is the HRMS spectrum of **4** (SI, Figure S95); HRMS (TOF ES$^+$): *m/z* calcd. for $C_{31}H_{22}N_5O_2$ $[M+H]^+$, 496.1768; found, 496.1774, which is the HRMS spectrum of **5f** (SI, Figure S96); Based on the molecular ion peaks of intermediates **7f–16f**, the proposed mechanism of the cascade reaction is reasonable (Scheme S1).

Control Experiments

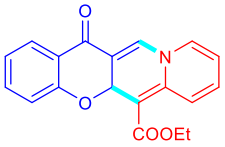


Scheme S2. Control experiments

First, 3-formylchromone **1f** (1.0 mmol) and 2-(pyridine-2-yl)acetate **2a** (1.0 mmol) were charged into a round-bottom flask. Then, acetonitrile (6 ml) was added to the mixture. The mixture was stirred at reflux for approximately 3 hours and monitored by TLC until the intermediate was completely consumed. The reaction mixture was cooled to room temperature and was extracted with ethyl acetate (3 × 15 mL). The organic layer was washed with water and brine, and the combined organic phases were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the crude product. Finally, product **9f** was purified from the crude mixture by flash column chromatography.

A round-bottom flask were charged with compound **9f** (0.5 mmol), benzimidamide hydrochlorides **3b** (0.5 mmol) and DMF (3 mL), and the mixture was stirred under reflux for approximately 10 hours while monitoring the reaction by TLC until the compound **9f** was completely consumed. After cooling the reaction to room temperature, the mixture was extracted with ethyl acetate (3 × 15 mL). The organic layer was washed with water and brine, and the combined organic phases were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the crude product. Finally, product **5f** was purified from the crude mixture by flash column chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (2:1, v/v) as the eluent.

Ethyl 13-oxo-5a,13-dihydrochromeno[2,3-*b*]quinolizine-6-carboxylate (9f)



Red solid (83%, 133 mg); Mp: 231.5-232.3 ℃; IR (KBr): 2928, 1674, 1641, 1593, 1526, 1489, 1384, 1338, 1222, 1192, 1043, 773 cm^{-1}; ^1H NMR (600 MHz,

DMSO-d_6): δ = 1.27 (t, J = 6.9 Hz, 3H, CH_3), 4.16-4.19 (m, 2H, CH_2), 7.10-7.13 (m, 2H, ArH), 7.19 (t, J = 6.3 Hz, 1H, ArH), 7.47 (s, 1H, ArH), 7.63 (t, J = 7.0 Hz, 1H, ArH), 7.80-7.83 (m, 2H, ArH), 7.91 (s, 1H, ArH), 8.34 (d, J = 5.9 Hz, 1H, ArH), 8.81 (d, J = 8.9 Hz, 1H, ArH) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 14.9, 59.6, 89.0, 90.8, 107.3, 116.3, 118.5, 122.0, 123.2, 124.2, 127.1, 133.0, 136.2, 139.3, 139.6, 148.0, 154.8, 165.3, 178.4 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{19}H_{16}NO_4$ [$(M+H)^+$], 322.1074; found, 322.1071.

X-ray Structure and Data of 4j and 5d.

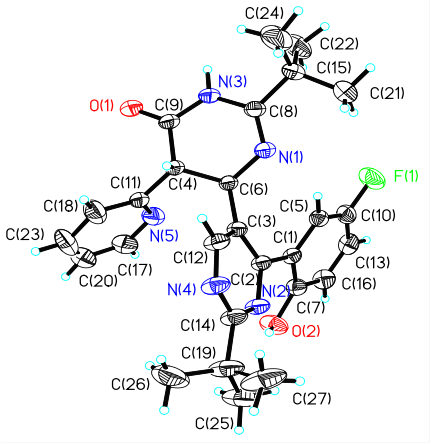


Figure S1. X-Ray crystal structure of **4j**

Table S2. Crystal data and structure refinement for **4j**

Identification code	1	
Empirical formula	$C_{27}H_{30}FN_5O_{2.5}$	
Formula weight	483.56	
Temperature	296.15 K	
Crystal system	triclinic	
Space group	P-1	
Unit cell dimensions	a = 11.2453(13) Å	α = 92.075(2) °.
	b = 11.7271(13) Å	β = 114.267(2) °.
	c = 12.9426(16) Å	γ = 104.496(2) °.
Volume	1487.7(3) $Å^3$	
Z	2	
Density (calculated)	1.079 g/cm^3	
Absorption coefficient	0.075 mm^{-1}	
F(000)	512	
Theta range for data collection	4.654 to 55.29 °.	
Index ranges	-14<=h<=14, -6<=k<=15, -16<=l<=16	
Reflections collected	9078	
Independent reflections	6522 [R(int) = 0.0207, R(sigma) = 0.0549]	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6522 / 90 / 372	
Goodness-of-fit on F^2	1.014	
Final R indexes [I>=2sigma(I)]	R_1 = 0.0884, wR_2 = 0.2421	
Final R indexes (all data)	R_1 = 0.1587, wR_2 = 0.3077	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.78 /-0.31e.$Å^{-3}$	

Table S3. Bond Lengths for **4j**

Atom	**Atom**	**Length/Å**	**Atom**	**Atom**	**Length/Å**
F1	C10	1.370(4)	C4	C11	1.508(4)
O1	C9	1.215(4)	C5	C10	1.367(4)
O2	C7	1.356(4)	C7	C16	1.390(4)
N1	C6	1.458(4)	C8	C15	1.524(5)
N1	C8	1.269(4)	C10	C13	1.371(5)
N2	C2	1.360(4)	C11	C18	1.384(5)
N2	C14	1.327(4)	C13	C16	1.365(5)
N3	C8	1.405(4)	C14	C19	1.515(5)
N3	C9	1.350(4)	C15	C21	1.531(6)
N4	C12	1.332(4)	C15	C22	1.538(6)
N4	C14	1.341(4)	C15	C24	1.505(6)
N5	C11	1.324(4)	C17	C20	1.326(6)
N5	C17	1.340(5)	C18	C23	1.403(7)
C1	C2	1.488(4)	C19	C25	1.533(15)
C1	C5	1.397(4)	C19	C26	1.497(12)
C1	C7	1.398(4)	C19	C27	1.617(13)
C2	C3	1.392(4)	C19	C25A	1.46(2)
C3	C6	1.514(4)	C19	C27A	1.333(14)
C3	C12	1.383(4)	C19	C26A	1.78(2)
C4	C6	1.538(4)	C20	C23	1.368(7)
C4	C9	1.516(4)			

Table S4. Bond Angles for **4j**

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C8	N1	C6	117.0(3)	C5	C10	C13	123.0(3)
C14	N2	C2	119.2(2)	N5	C11	C4	116.2(3)
C9	N3	C8	124.1(3)	N5	C11	C18	122.4(3)
C12	N4	C14	114.9(3)	C18	C11	C4	121.4(3)
C11	N5	C17	117.7(3)	N4	C12	C3	125.6(3)
C5	C1	C2	120.0(2)	C16	C13	C10	118.0(3)
C5	C1	C7	118.3(3)	N2	C14	N4	124.4(3)
C7	C1	C2	121.5(3)	N2	C14	C19	118.1(3)
N2	C2	C1	115.0(2)	N4	C14	C19	117.5(3)
N2	C2	C3	119.9(2)	C8	C15	C21	110.0(3)
C3	C2	C1	125.1(2)	C8	C15	C22	108.8(3)
C2	C3	C6	124.5(2)	C21	C15	C22	108.0(4)
C12	C3	C2	114.8(2)	C24	C15	C8	109.3(3)
C12	C3	C6	120.6(2)	C24	C15	C21	111.1(4)
C9	C4	C6	109.3(2)	C24	C15	C22	109.6(4)
C11	C4	C6	112.3(2)	C13	C16	C7	121.3(3)
C11	C4	C9	112.4(3)	C20	C17	N5	125.0(5)

C10	C5	C1	119.3(3)	C11	C18	C23	117.1(4)
N1	C6	C3	112.3(2)	C14	C19	C25	112.3(8)
N1	C6	C4	113.3(2)	C14	C19	C27	104.2(6)
C3	C6	C4	111.3(2)	C14	C19	C26A	101.3(7)
O2	C7	C1	122.5(3)	C25	C19	C27	111.8(8)
O2	C7	C16	117.5(3)	C26	C19	C14	108.5(5)
C16	C7	C1	120.0(3)	C26	C19	C25	110.6(9)
N1	C8	N3	122.9(3)	C26	C19	C27	109.2(8)
N1	C8	C15	121.3(3)	C25A	C19	C14	111.6(11)
N3	C8	C15	115.7(3)	C25A	C19	C26A	102.4(13)
O1	C9	N3	122.1(3)	C27A	C19	C14	118.7(7)
O1	C9	C4	123.0(3)	C27A	C19	C25A	119.7(14)
N3	C9	C4	114.8(3)	C27A	C19	C26A	98.3(12)
F1	C10	C13	118.7(3)	C17	C20	C23	117.8(4)
C5	C10	F1	118.3(3)	C20	C23	C18	120.0(4)

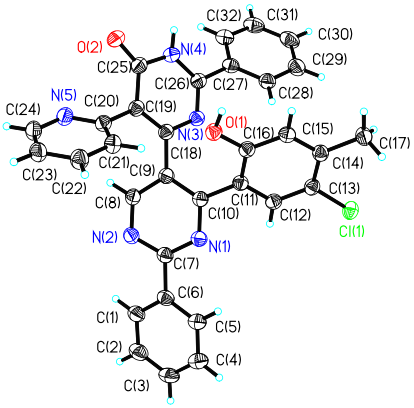


Figure S2. X-Ray crystal structure of **5d**

Table S5. Crystal data and structure refinement for **5d**

Identification code	1	
Empirical formula	$C_{31}H_{20}ClN_5O_2$	
Formula weight	529.97	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system, space group	Monoclinic, P 21/n	
Unit cell dimensions	a = 15.007(3) Å	α = 90.0 °.
	b = 15.204(3) Å	β = 113.696(4) °.
	c = 16.146(3) Å	γ = 90.0 °.
Volume	3373.3(12) $Å^3$	
Z	4	
Density (calculated)	1.044 Mg/m^3	
Absorption coefficient	0.143 mm^{-1}	
F(000)	1096	
Theta range for data collection	1.566 to 25.150 °.	
Crystal size	0.220 x 0.200 x 0.180 mm	
Limiting indices	-17<=h<=17, -18<=k<=14, -19<=l<=19	
Reflections collected / unique	15794 / 6022 [R(int) = 0.0618]	
Independent reflections	6522 [R(int) = 0.0207, R(sigma) = 0.0549]	
Completeness to theta = 25.242	98.6 %	
Absorption correction	Semi-empirical from equivalents	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6022 / 0 / 342	
Goodness-of-fit on F^2	1.013	
Final R indexes [I>=2sigma(I)]	R_1 = 0.0871, wR_2 = 0.2178	
Final R indexes (all data)	R_1 = 0.1644, wR_2 = 0.2813	
Extinction coefficient	0.0028(9)	
Largest diff. peak and hole	0.624 and -0.415 e.$Å^{-3}$	

Table S6. Bond Lengths [**Å**] for **5d**

Atom	**Atom**	**Length/Å**	**Atom**	**Atom**	**Length/Å**
C11	C12	1.3900	C2	C3	1.382(8)
C11	C16	1.3900	C3	C4	1.380(8)
C11	C10	1.476(6)	C4	C5	1.365(7)
C12	C13	1.3900	C5	C6	1.397(7)
C13	C14	1.3900	C6	C7	1.478(7)
C14	C15	1.3900	C7	C8	1.390(7)
C15	C16	1.3900	C8	C9	1.380(7)
Cl1	C4	1.733(6)	C8	C17	1.466(7)
N1	C7	1.350(4)	C17	C18	1.371(7)
N1	C10	1.337(6)	C18	C19	1.436(7)
N2	C9	1.329(6)	C18	C21	1.481(7)
N2	C10	1.330(6)	C20	C26	1.463(7)
N3	C20	1.306(6)	C21	C22	1.381(7)
N3	C17	1.381(6)	C22	C23	1.370(7)
N4	C20	1.356(6)	C23	C24	1.371(8)
N4	C19	1.377(6)	C24	C25	1.370(8)
N5	C21	1.327(6)	C26	C27	1.342(8)
N5	C25	1.353(6)	C26	C31	1.414(8)
O1	C1	1.380(6)	C27	C28	1.383(8)
O2	C19	1.247(6)	C28	C29	1.311(9)
C1	C2	1.383(7)	C29	C30	1.423(10)
C1	C6	1.381(7)	C30	C31	1.382(9)

Table S7. Bond Angles for **5d**

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C12	C11	C16	120.0	N2	C9	C8	123.8(5)
C12	C11	C10	119.5(3)	N2	C10	N1	117.4(4)
C16	C11	C10	120.5(3)	N1	C10	C11	117.3(4)
C11	C12	C13	120.0	C18	C17	N3	123.1(5)
C14	C13	C12	120.0	C18	C17	C8	125.4(4)
C13	C14	C15	120.0	N3	C17	C8	111.4(4)
C16	C15	C14	120.0	C17	C18	C19	117.6(5)
C15	C16	C11	120.0	C17	C18	C21	124.3(5)
C7	N1	C10	117.9(4)	C19	C18	C21	118.1(4)
C9	N2	C10	116.1(4)	O2	C19	N4	118.7(5)
C20	N3	C17	118.6(4)	O2	C19	C18	125.5(5)

C20	N4	C19	123.6(4)	N4	C19	C18	115.8(5)
C21	N5	C25	117.7(5)	N3	C20	N4	121.1(5)
O1	C1	C2	121.1(5)	N3	C20	C26	119.5(4)
O1	C1	C6	117.4(5)	N4	C20	C26	119.3(5)
C2	C1	C6	121.4(5)	N5	C21	C22	122.4(5)
C3	C2	C1	120.2(5)	N5	C21	C18	116.2(4)
C4	C3	C2	118.7(5)	C22	C21	C18	121.4(5)
C5	C4	C3	121.0(5)	C23	C22	C21	119.3(5)
C5	C4	Cl1	119.7(5)	C24	C23	C22	119.1(5)
C3	C4	Cl1	119.3(4)	C23	C24	C25	118.7(6)
C4	C5	C6	121.1(5)	N5	C25	C24	122.8(5)
C5	C6	C1	117.5(5)	C27	C26	C31	118.8(6)
C5	C6	C7	118.2(5)	C27	C26	C20	124.6(5)
C1	C6	C7	124.3(5)	C31	C26	C20	116.5(5)
N1	C7	C8	120.4(4)	C26	C27	C28	121.5(6)
N1	C7	C6	114.6(4)	C29	C28	C27	121.6(6)
C8	C7	C6	125.0(5)	C28	C29	C30	118.7(7)
C7	C8	C9	116.3(5)	C31	C30	C29	120.0(7)
C7	C8	C17	126.9(4)	C30	C31	C26	118.7(7)
C9	C8	C17	116.7(4)				

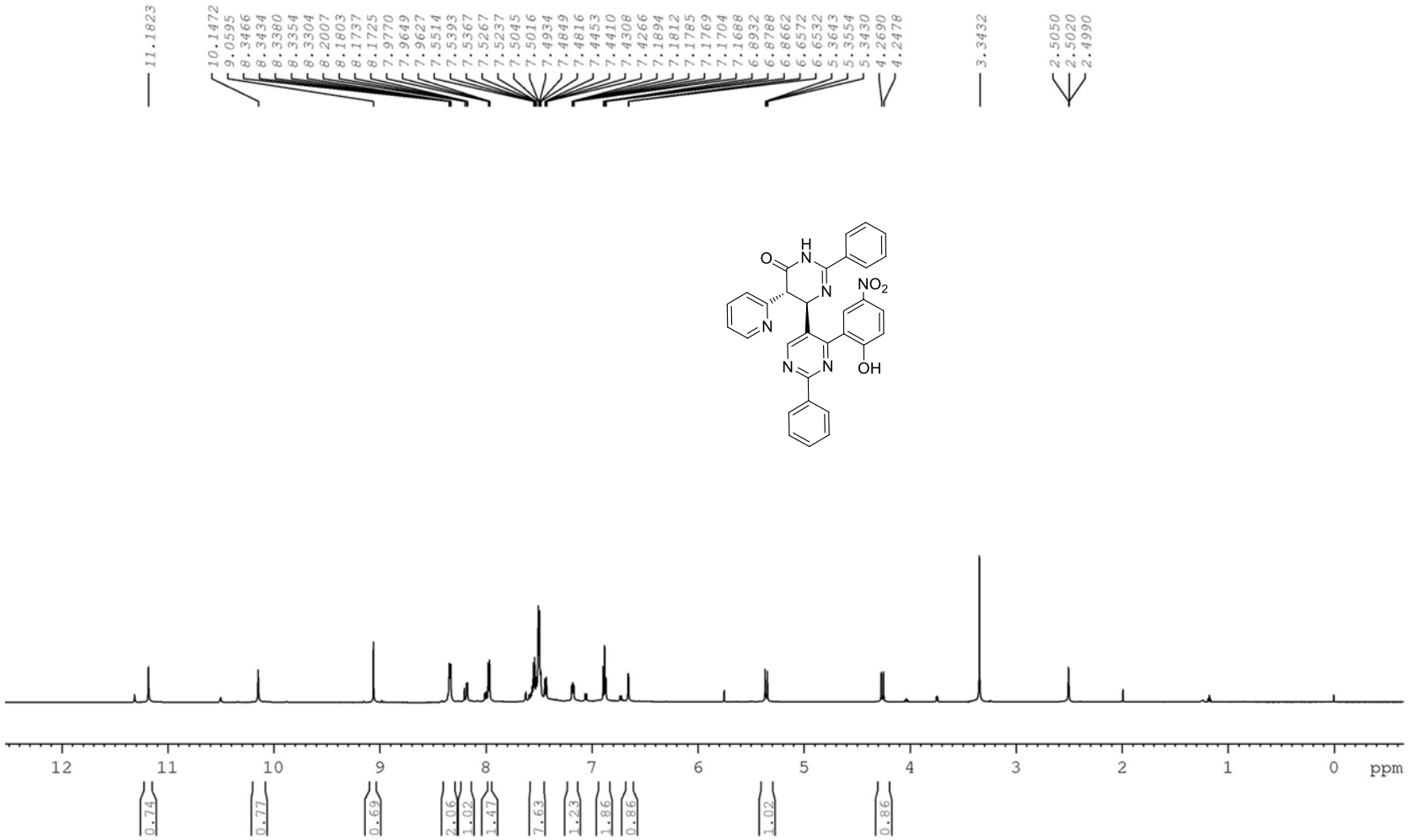


Figure S3. ^{1}H NMR (**600** MHz, DMSO-d_6) spectra of compound **4a**

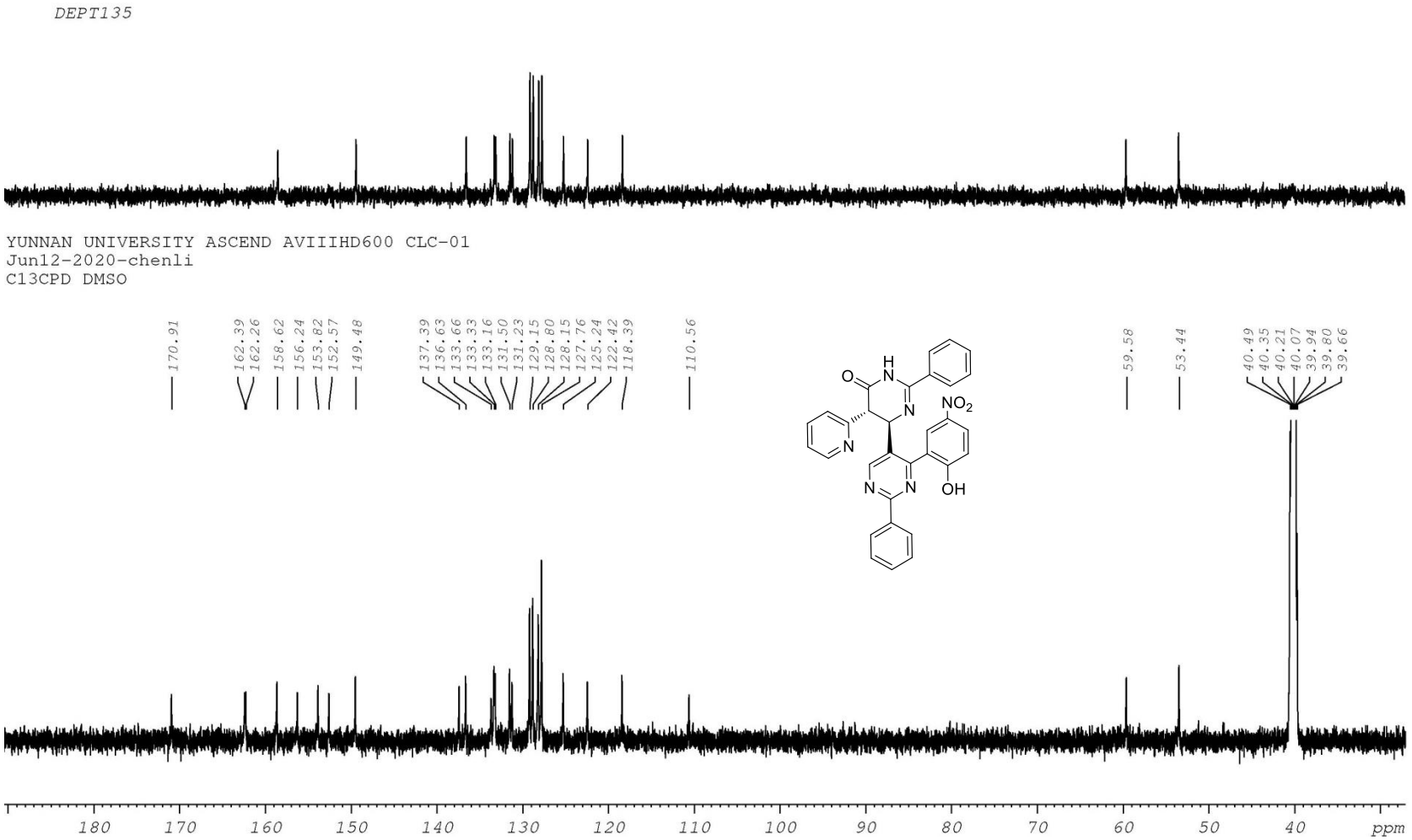


Figure S4. ^{13}C NMR (**150** MHz, DMSO-d_6) spectra of compound **4a**

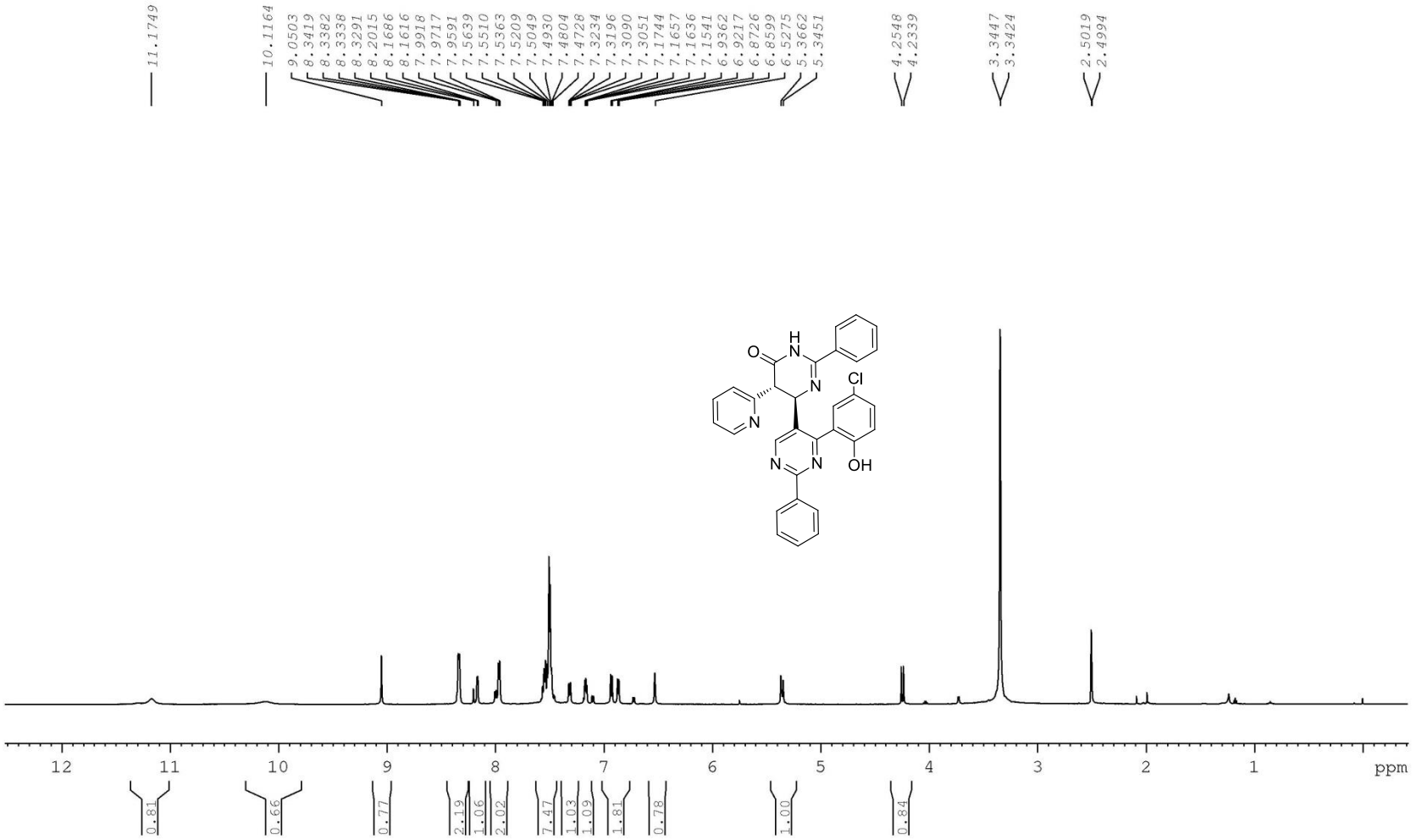


Figure S5. ^{1}H NMR (**600** MHz, DMSO-d_6) spectra of compound **4b**

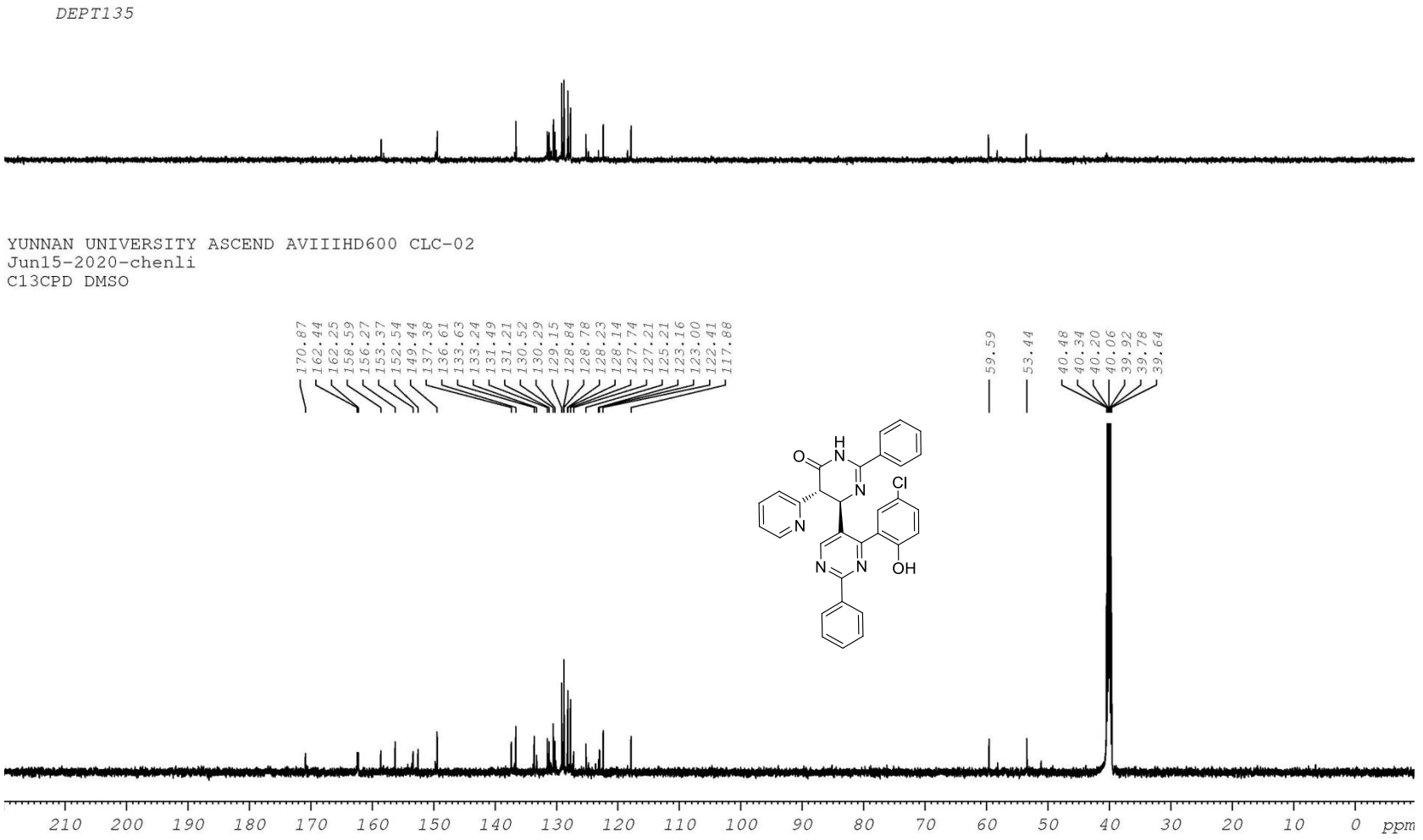


Figure S6. ^{13}C NMR (**150** MHz, DMSO-d_6) spectra of compound **4b**

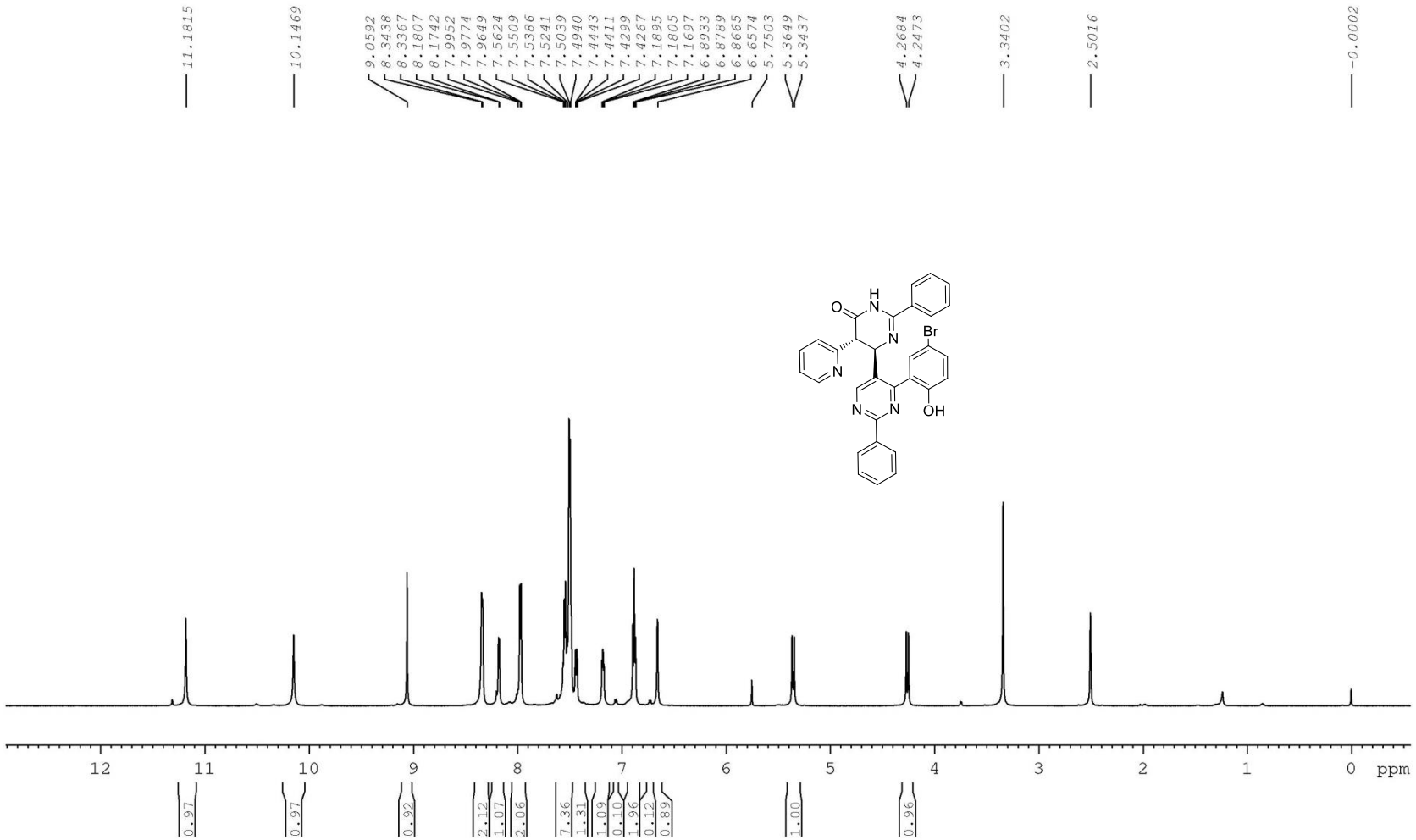


Figure S7. ^{1}H NMR (**600** MHz, DMSO-d_6) spectra of compound **4c**

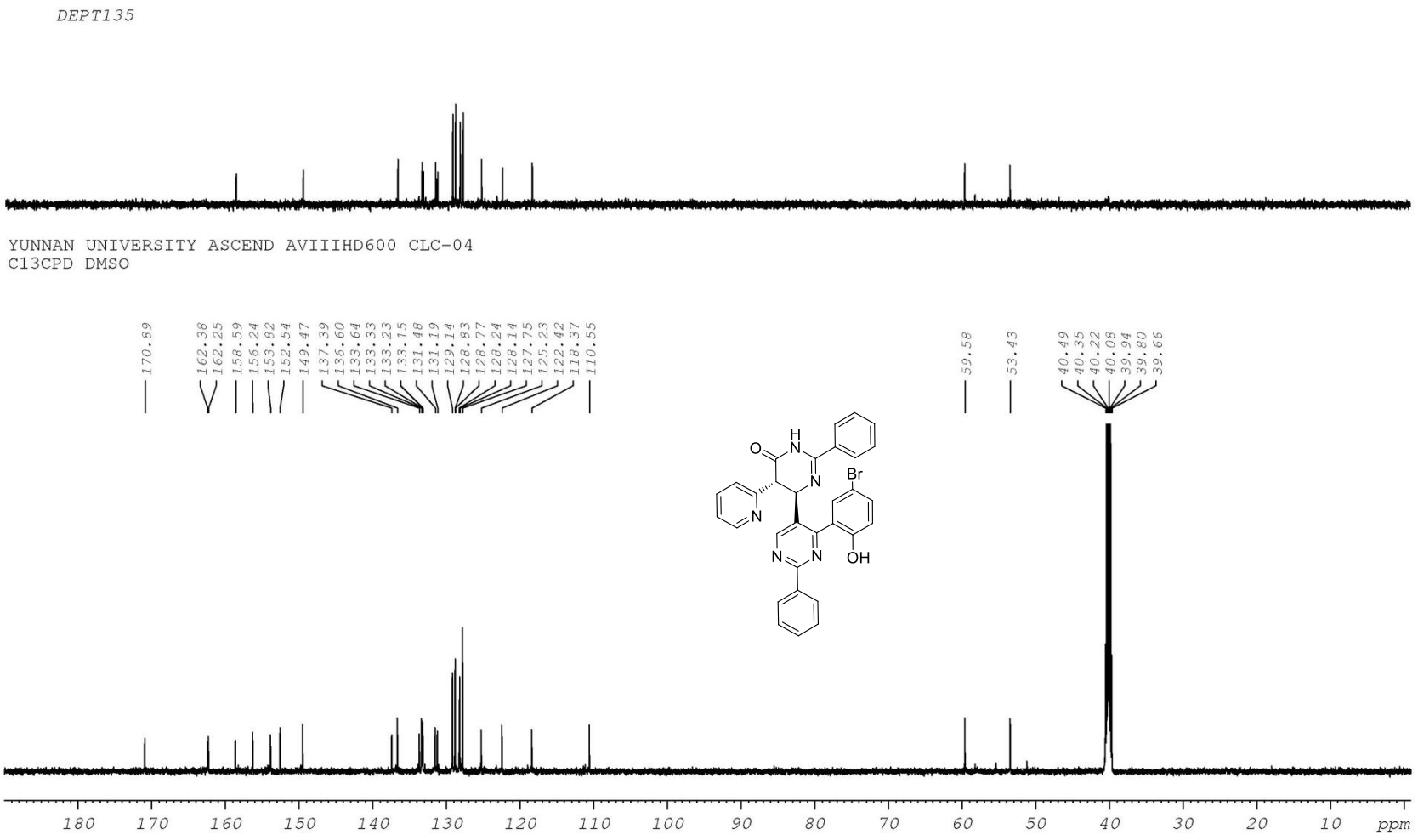


Figure S8. ^{13}C NMR (**150** MHz, DMSO-d_6) spectra of compound **4c**

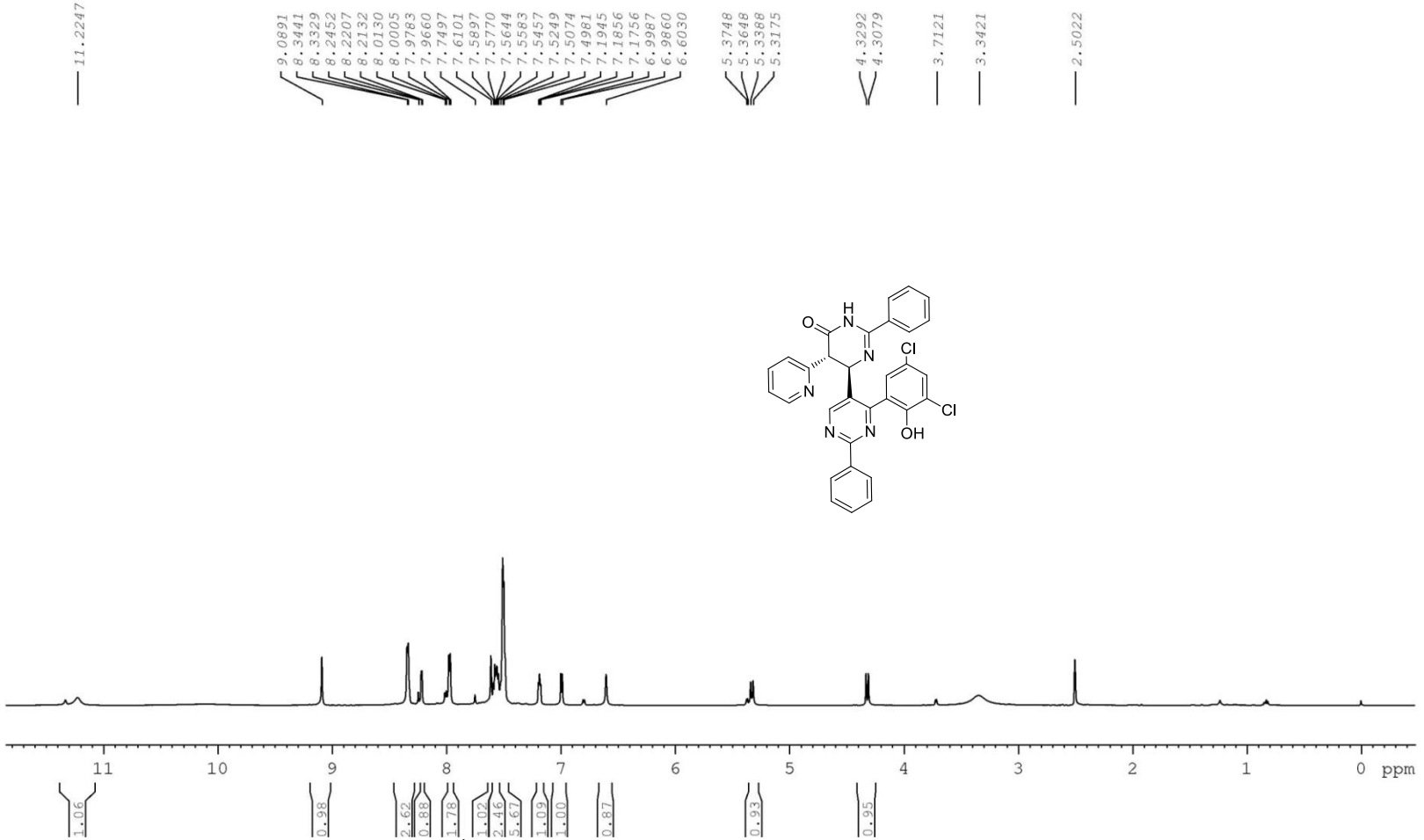


Figure S9. ^{1}H NMR (**600** MHz, DMSO-d_6) spectra of compound **4d**

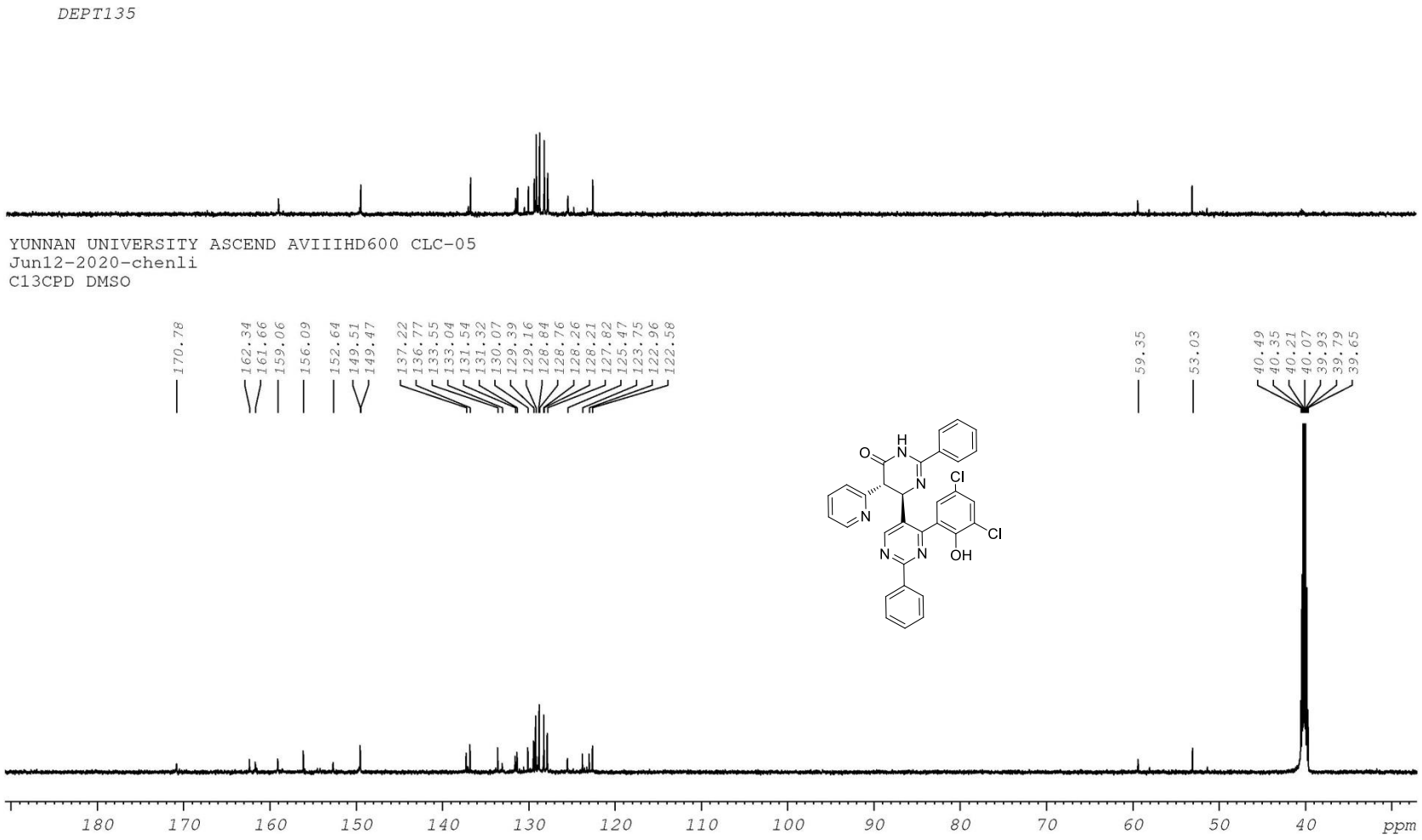


Figure S10. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **4d**

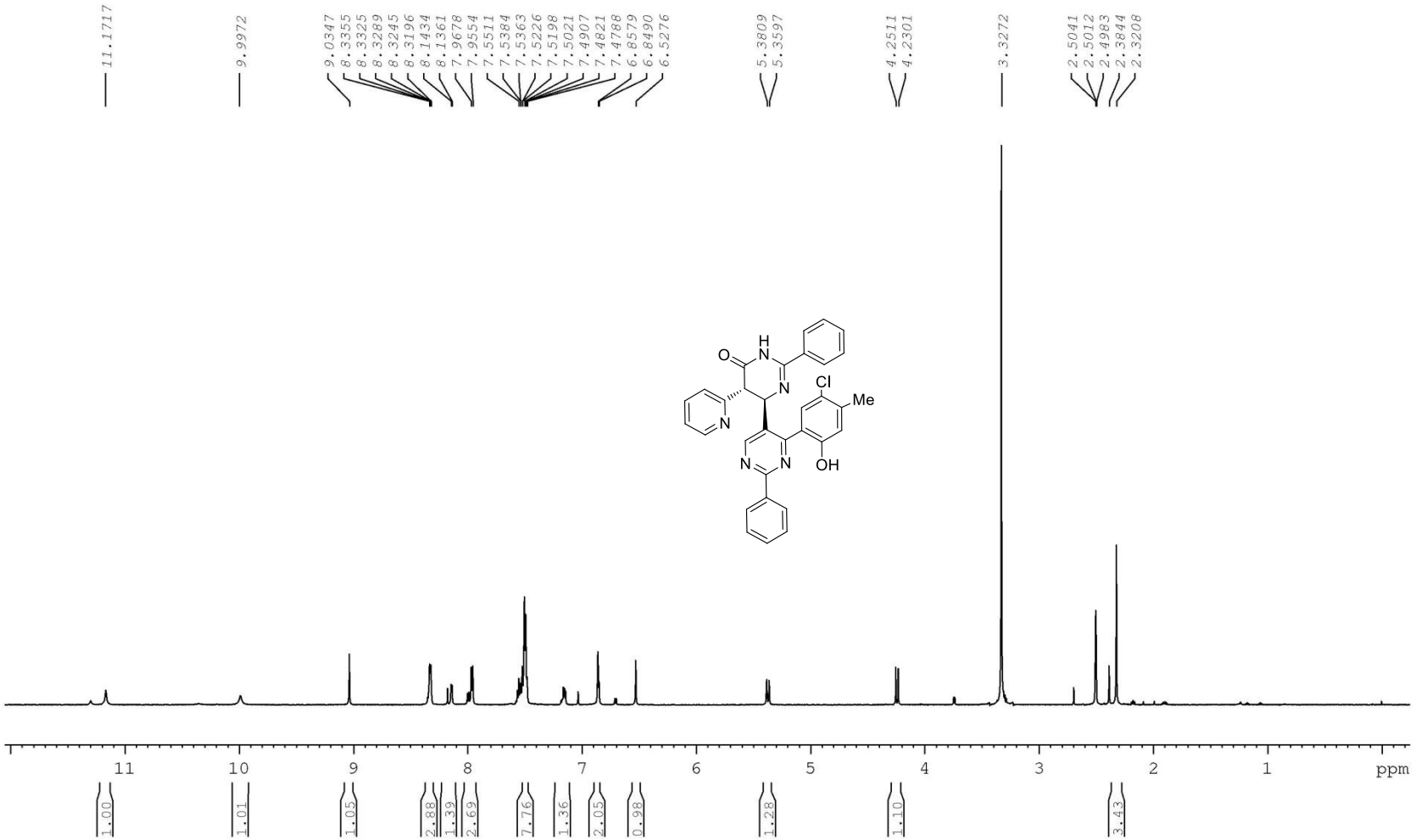


Figure S11. ^{1}H NMR (**600** MHz, DMSO-d_6) spectra of compound **4e**

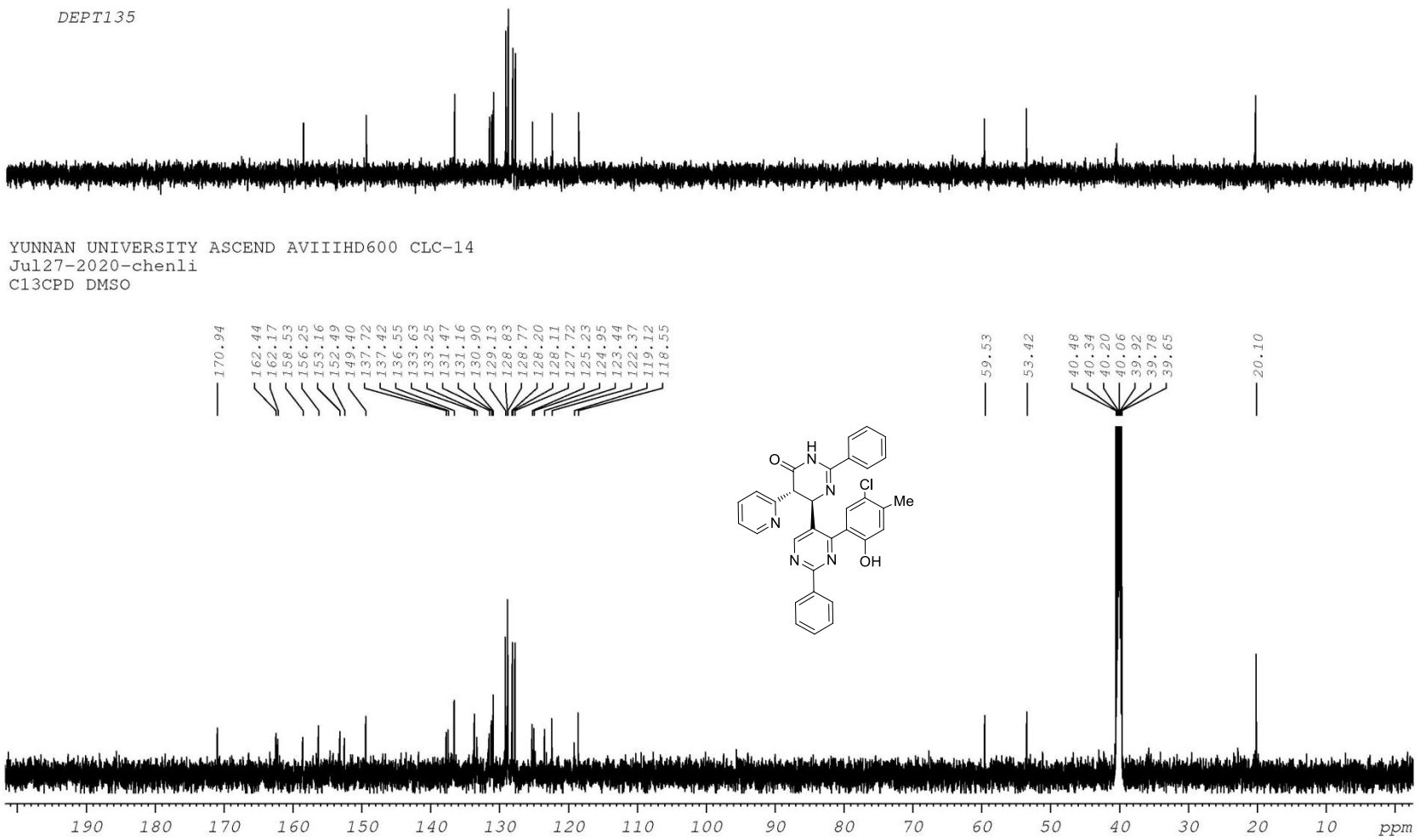


Figure S12. ^{13}C NMR (**150** MHz, DMSO-d_6) spectra of compound **4e**

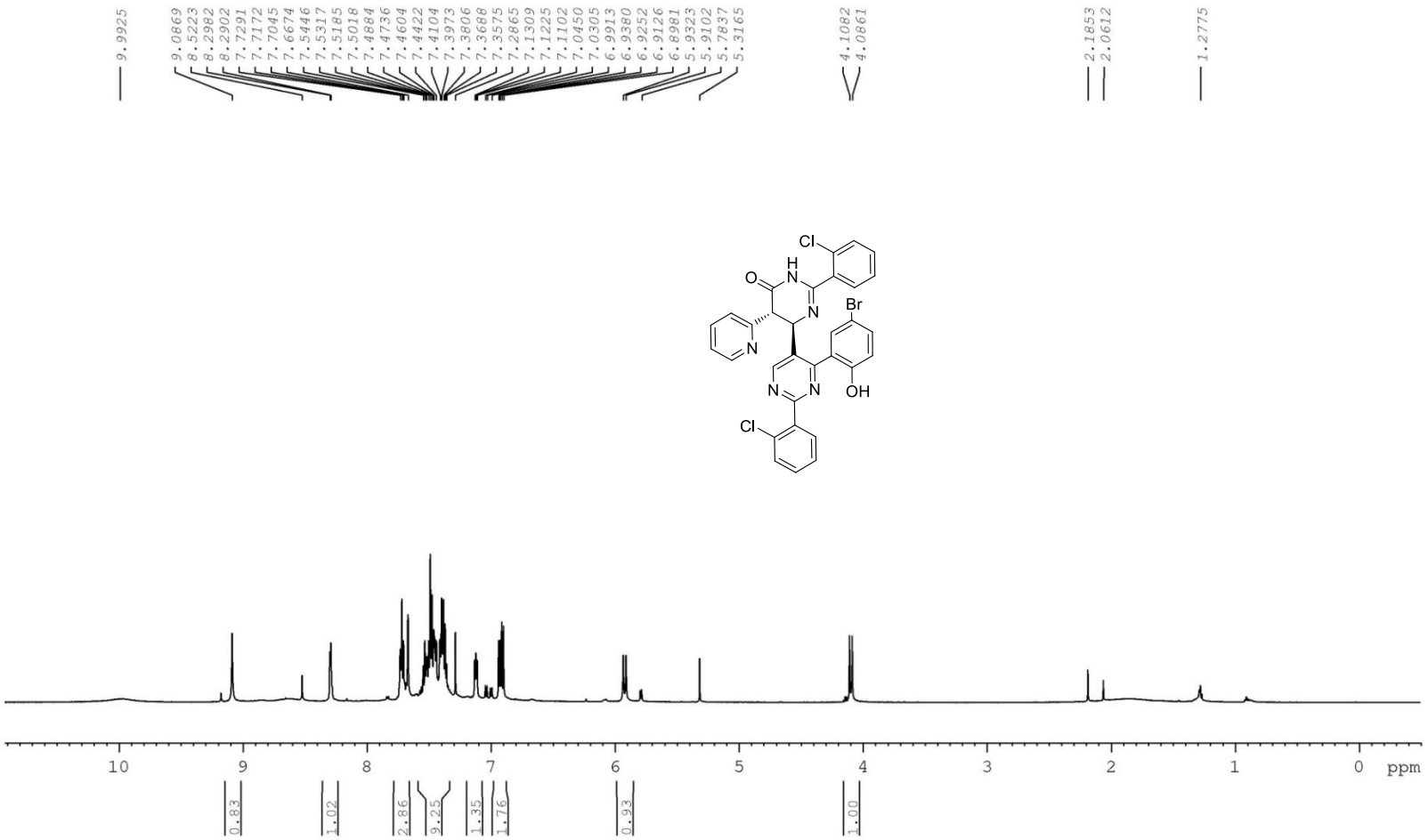


Figure S13. ^{1}H NMR (**600** MHz, $CDCl_3$) spectra of compound **4f**

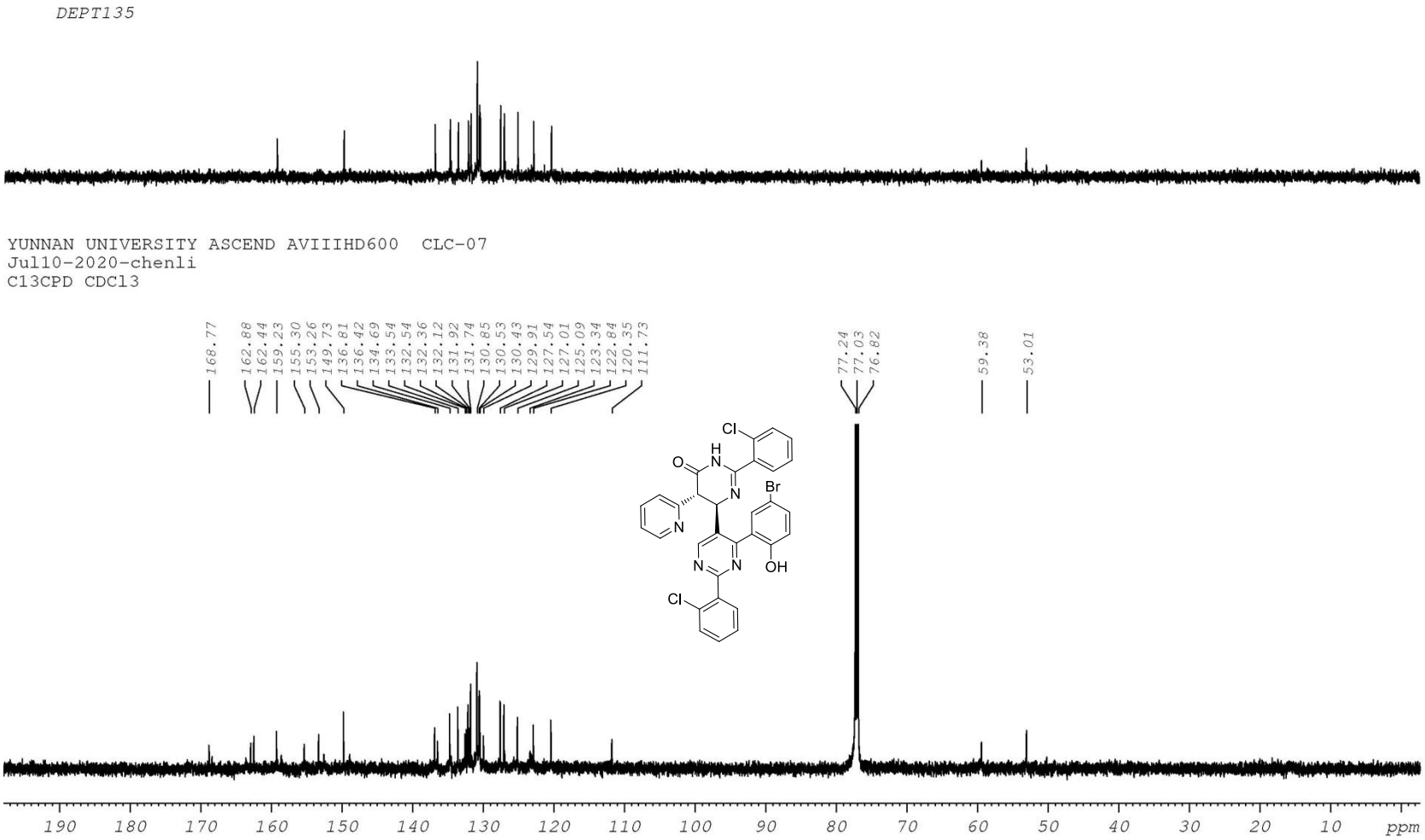


Figure S14. ^{13}C NMR (**150** MHz, $CDCl_3$) spectra of compound **4f**

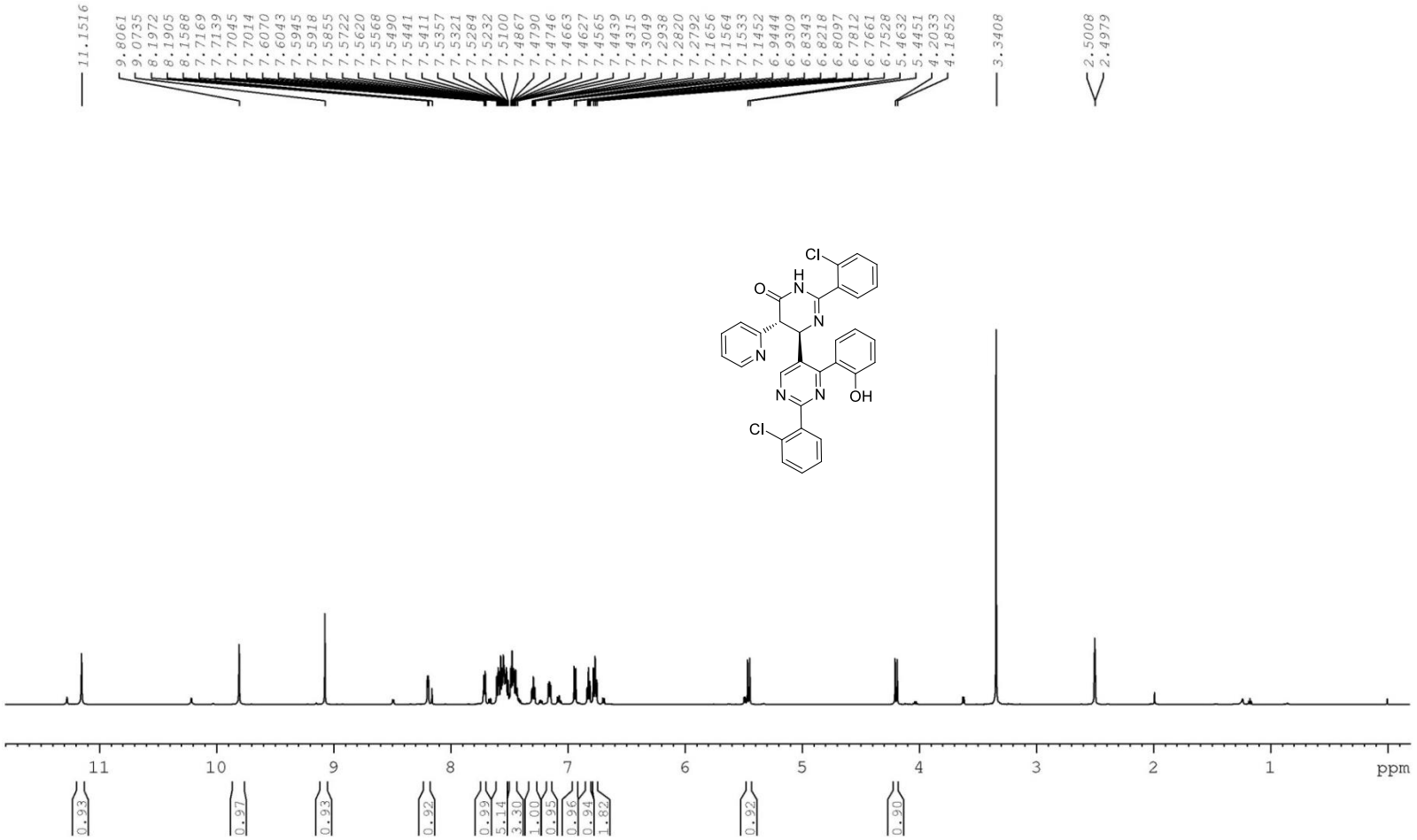


Figure S15. ^{1}H NMR (**600** MHz, DMSO-d_6) spectra of compound **4g**

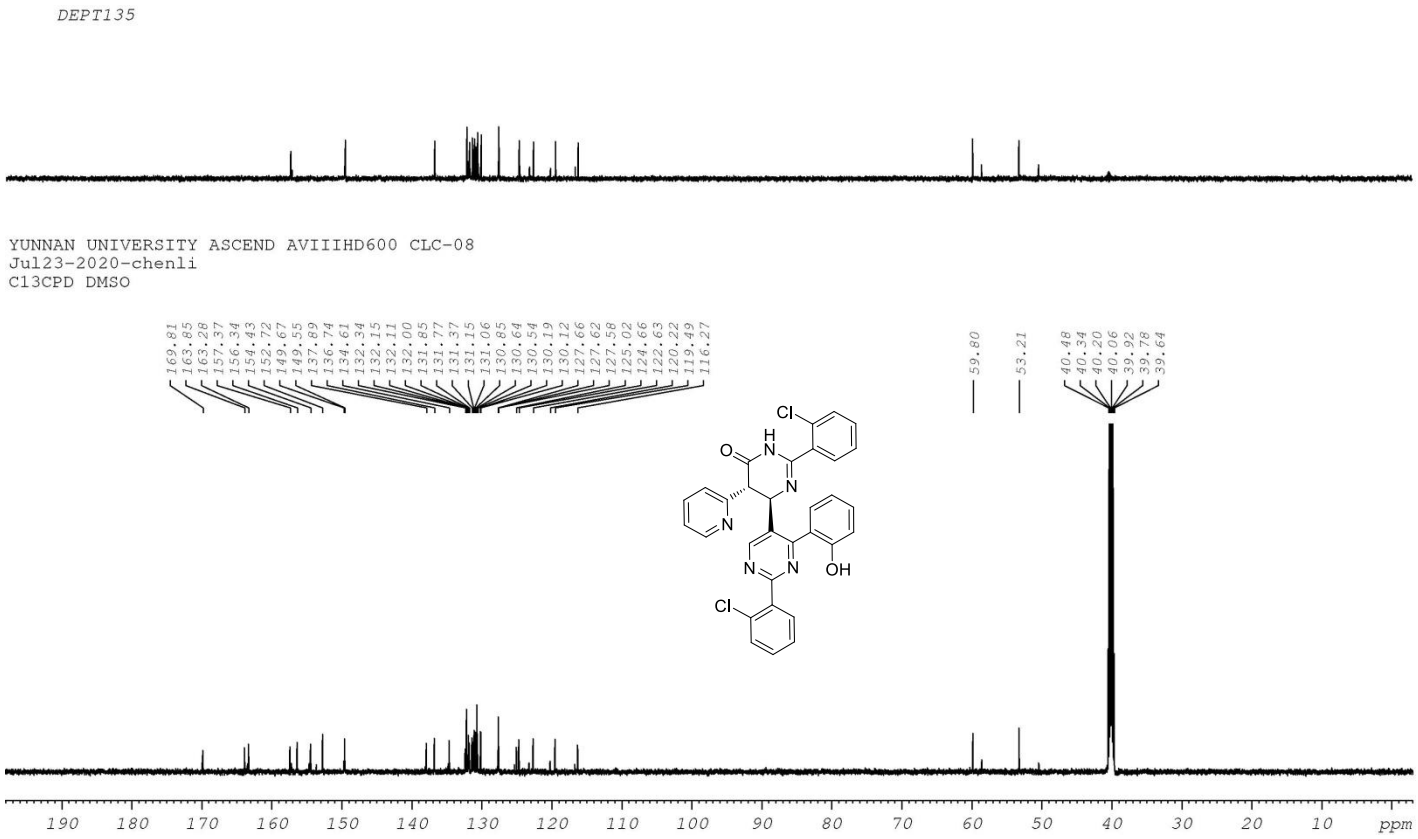


Figure S16. ^{13}C NMR (**150** MHz, DMSO-d_6) spectra of compound **4g**

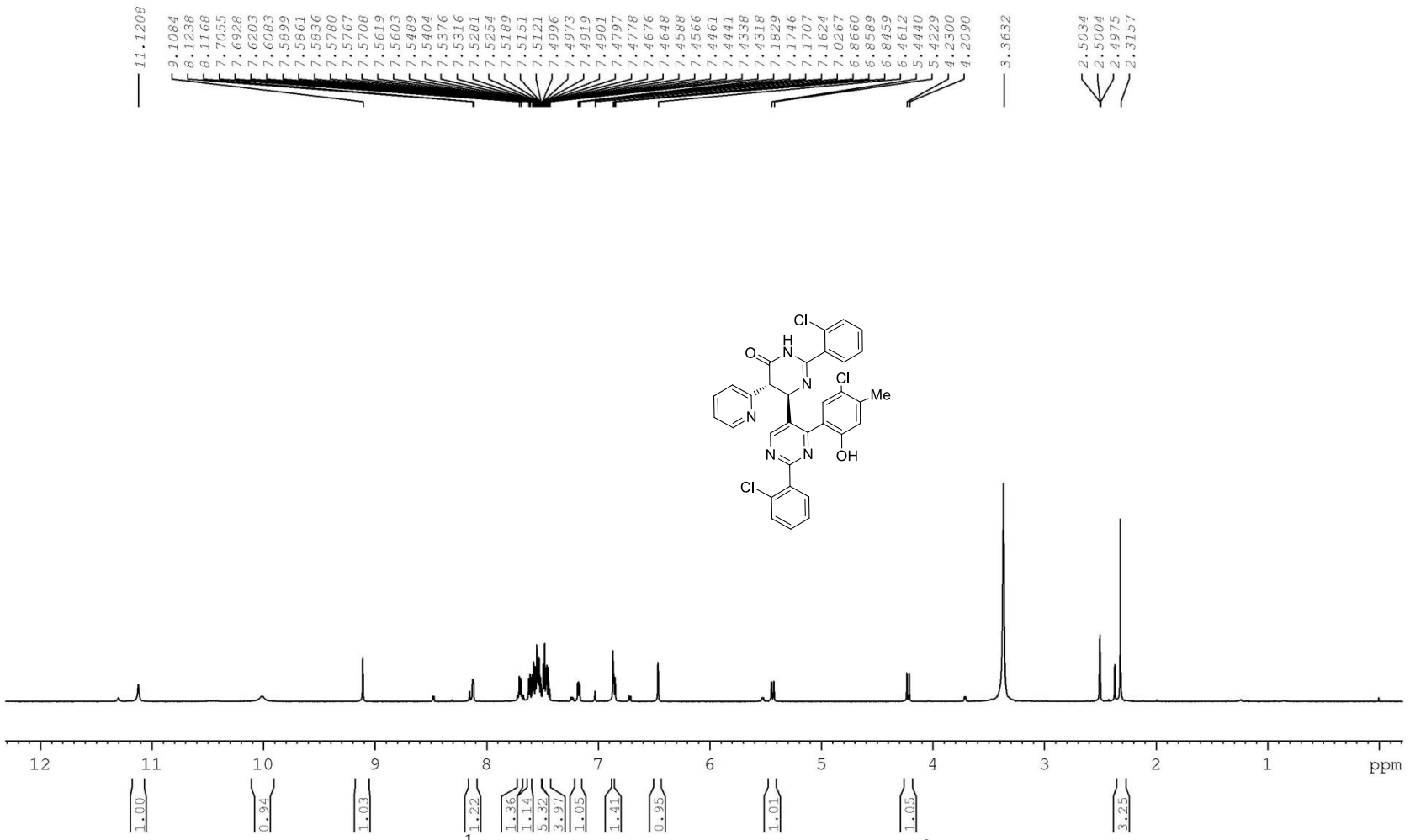


Figure S17. ^{1}H NMR (**600** MHz, DMSO-d_6) spectra of compound **4h**

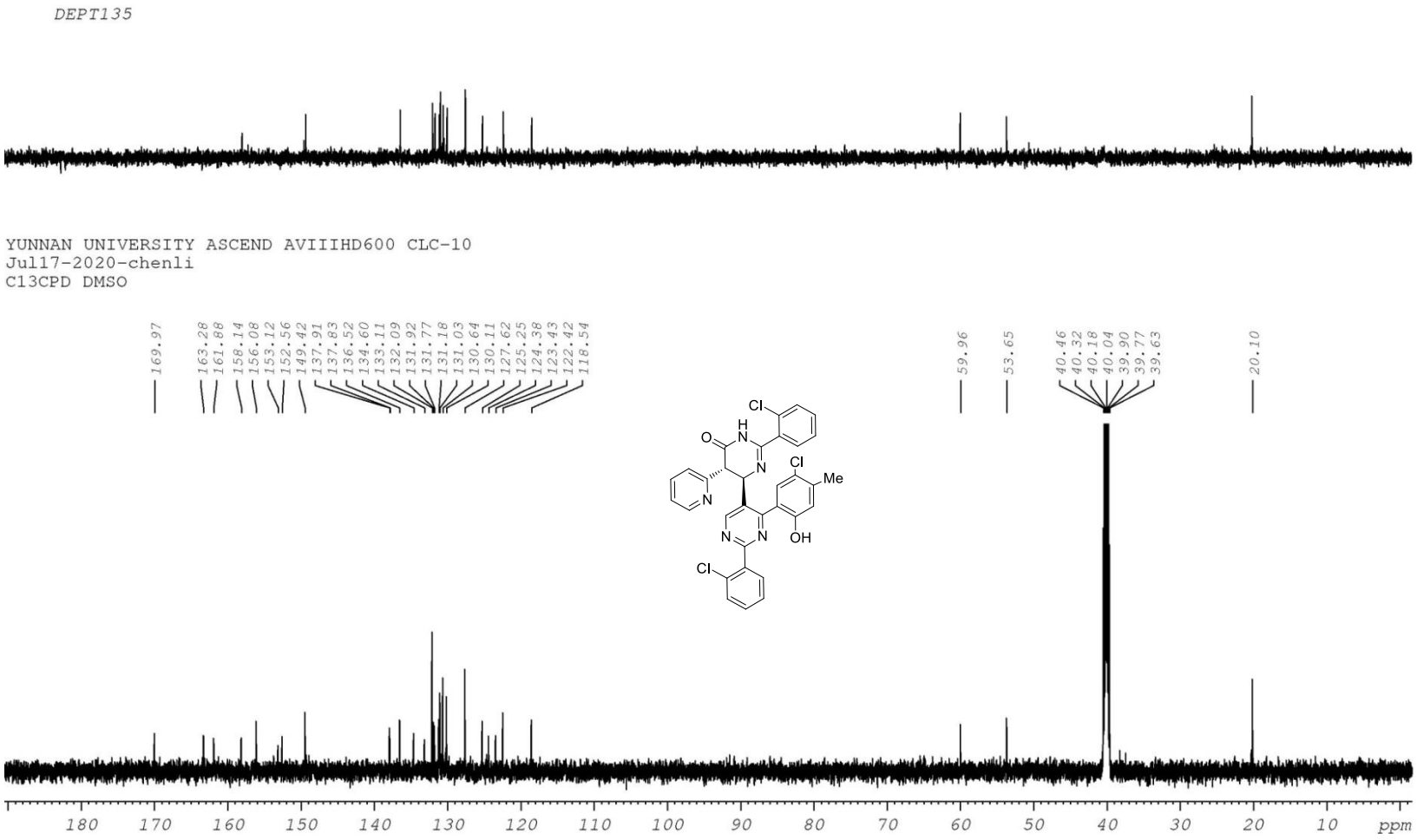


Figure S18. ^{13}C NMR (**150** MHz, DMSO-d_6) spectra of compound **4h**

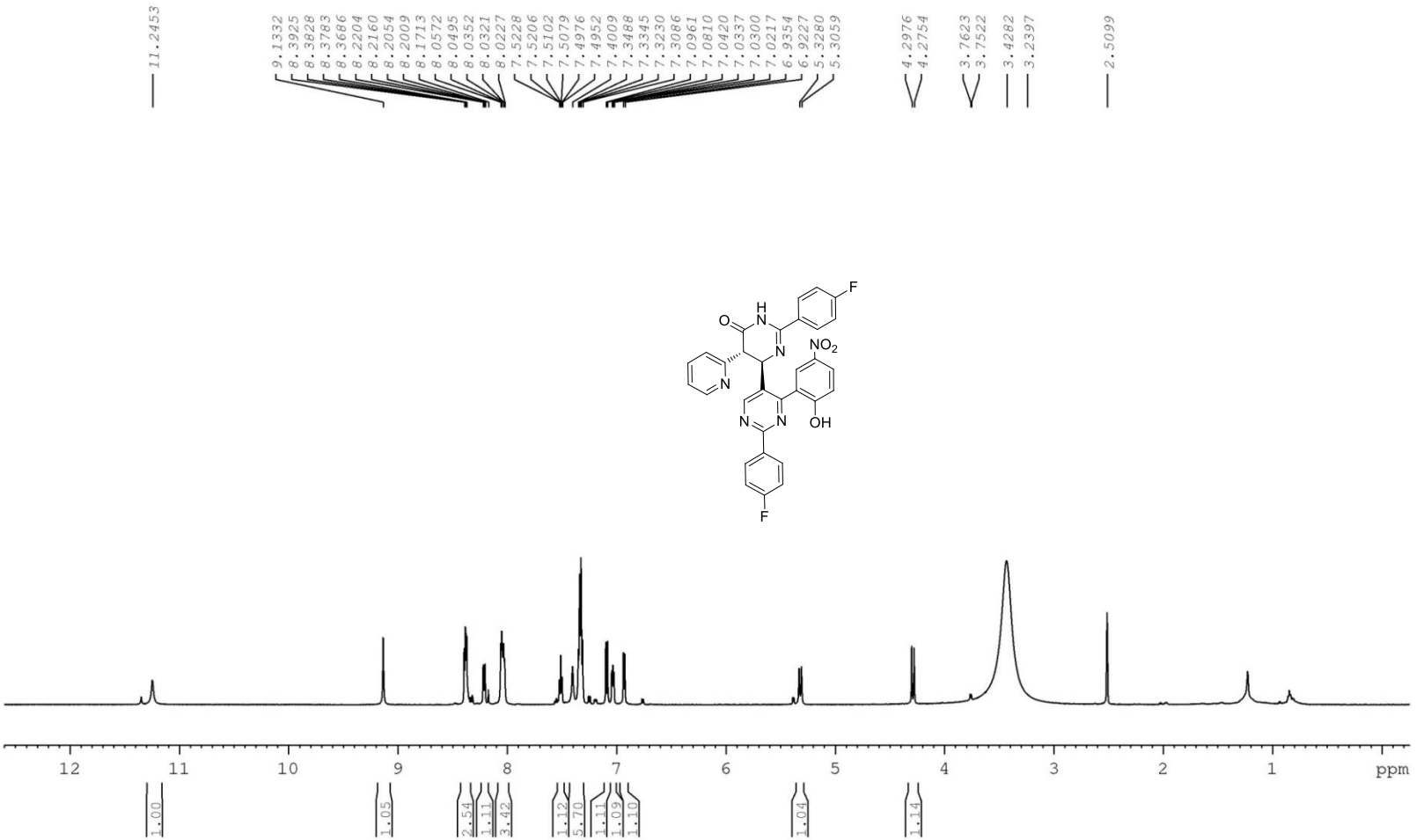


Figure S19. ^{1}H NMR (**600** MHz, DMSO-d_6) spectra of compound **4i**

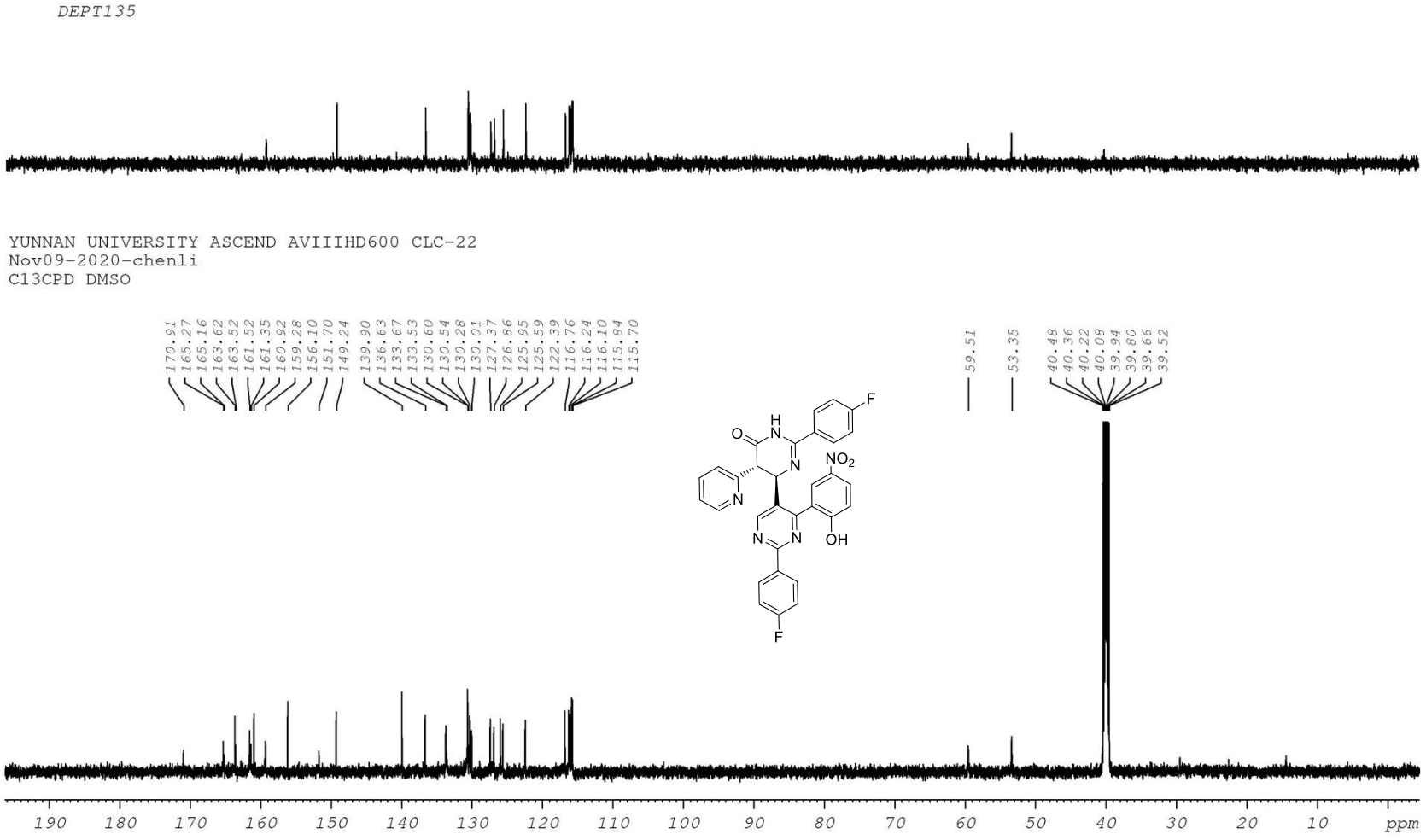


Figure S20. ^{13}C NMR (**150** MHz, DMSO-d_6) spectra of compound **4i**

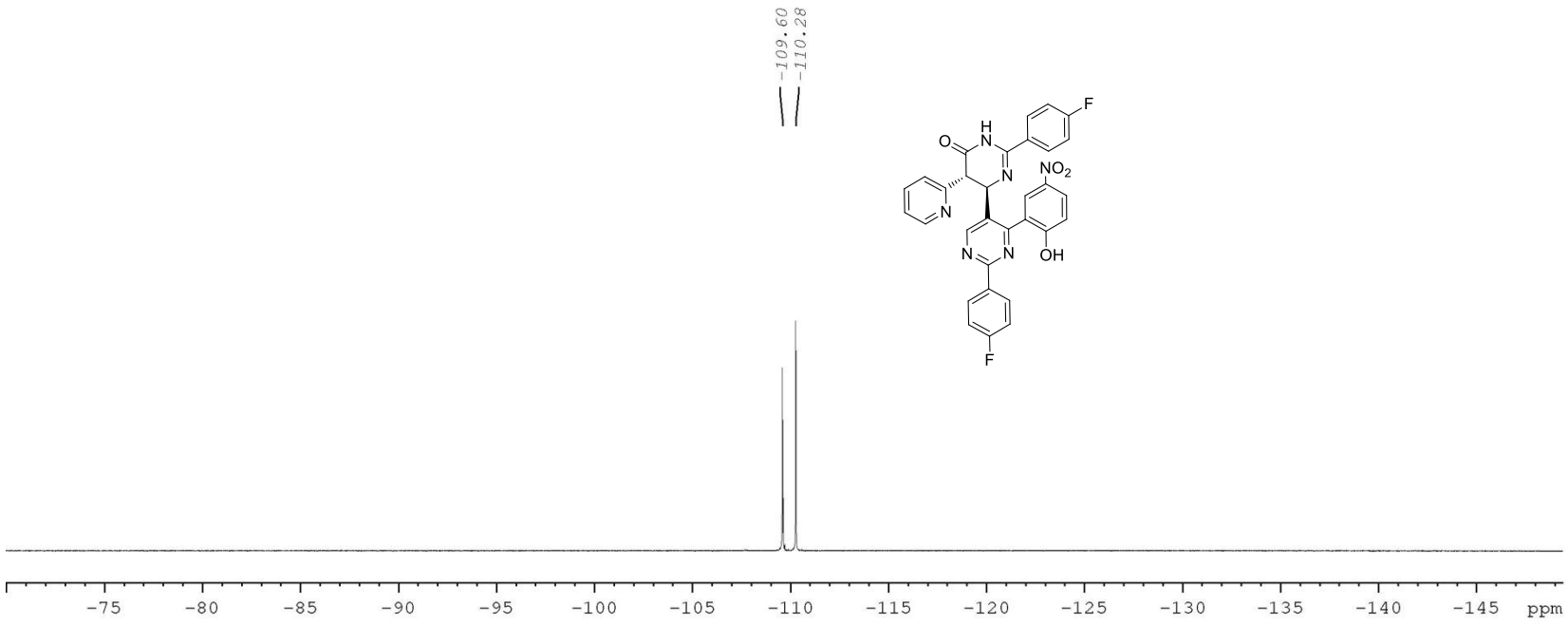


Figure S21. ^{19}F NMR (564 MHz, DMSO-d_6) spectra of compound **4i**

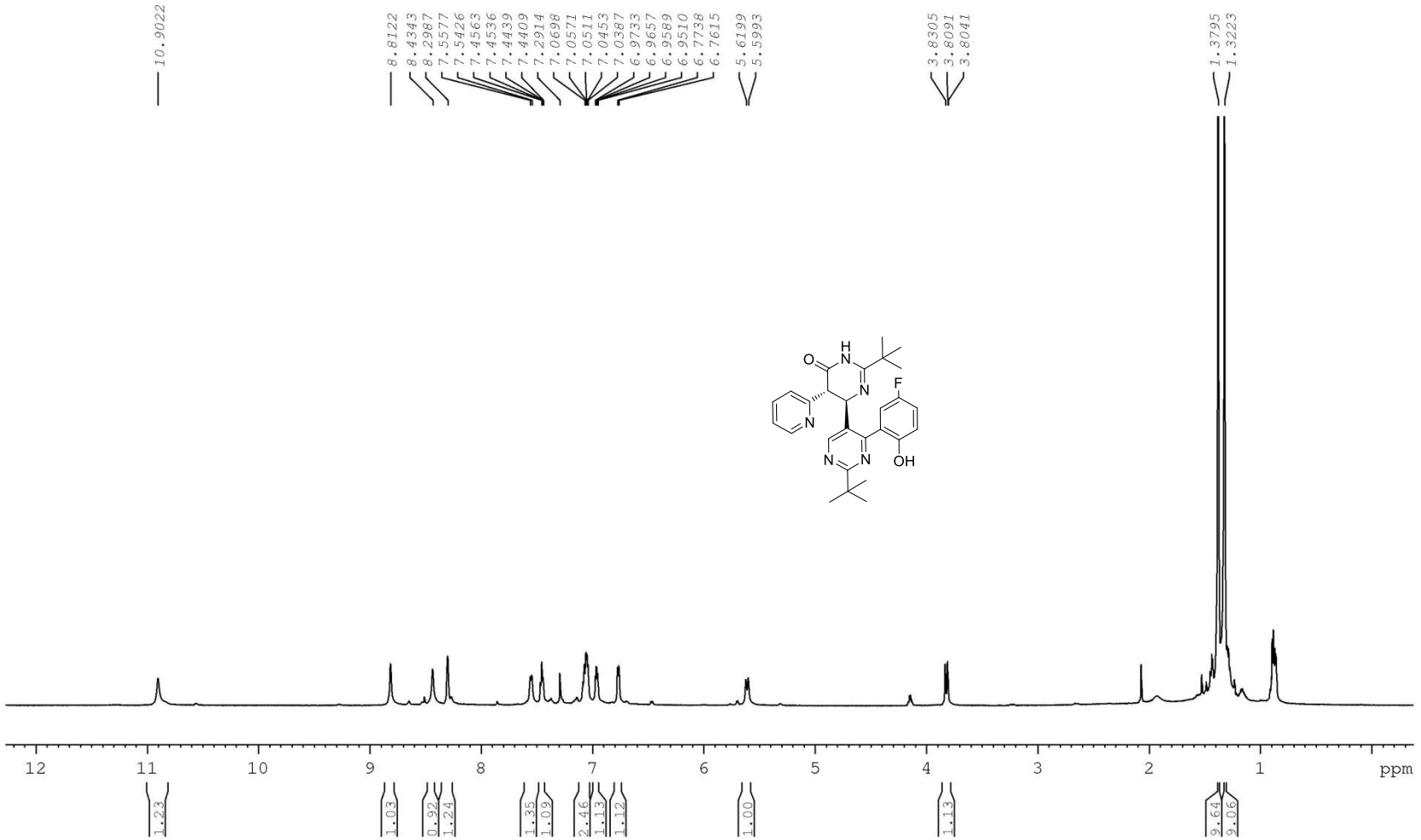


Figure S22. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4j**

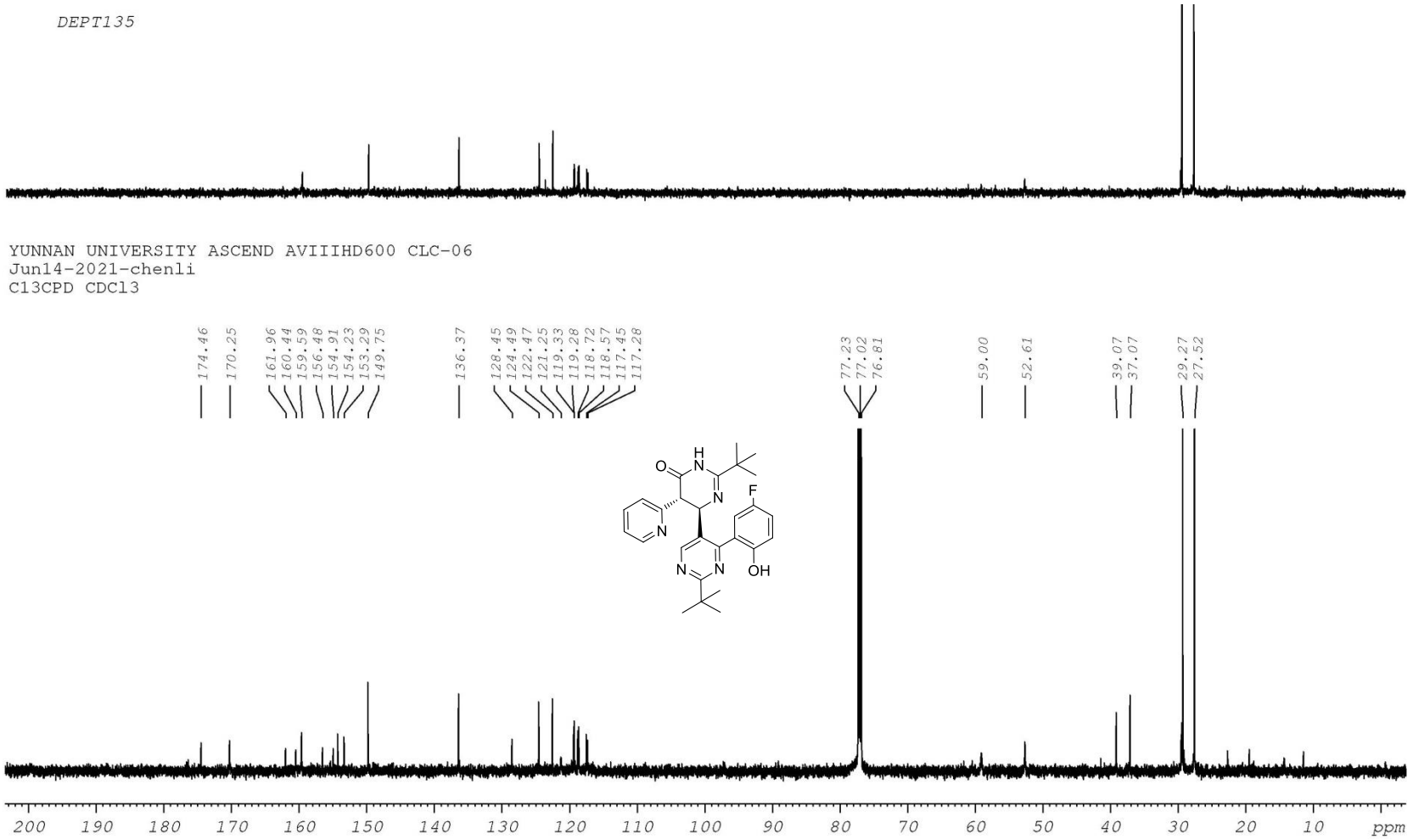


Figure S23. ^{13}C NMR (**150** MHz, $CDCl_3$) spectra of compound **4j**

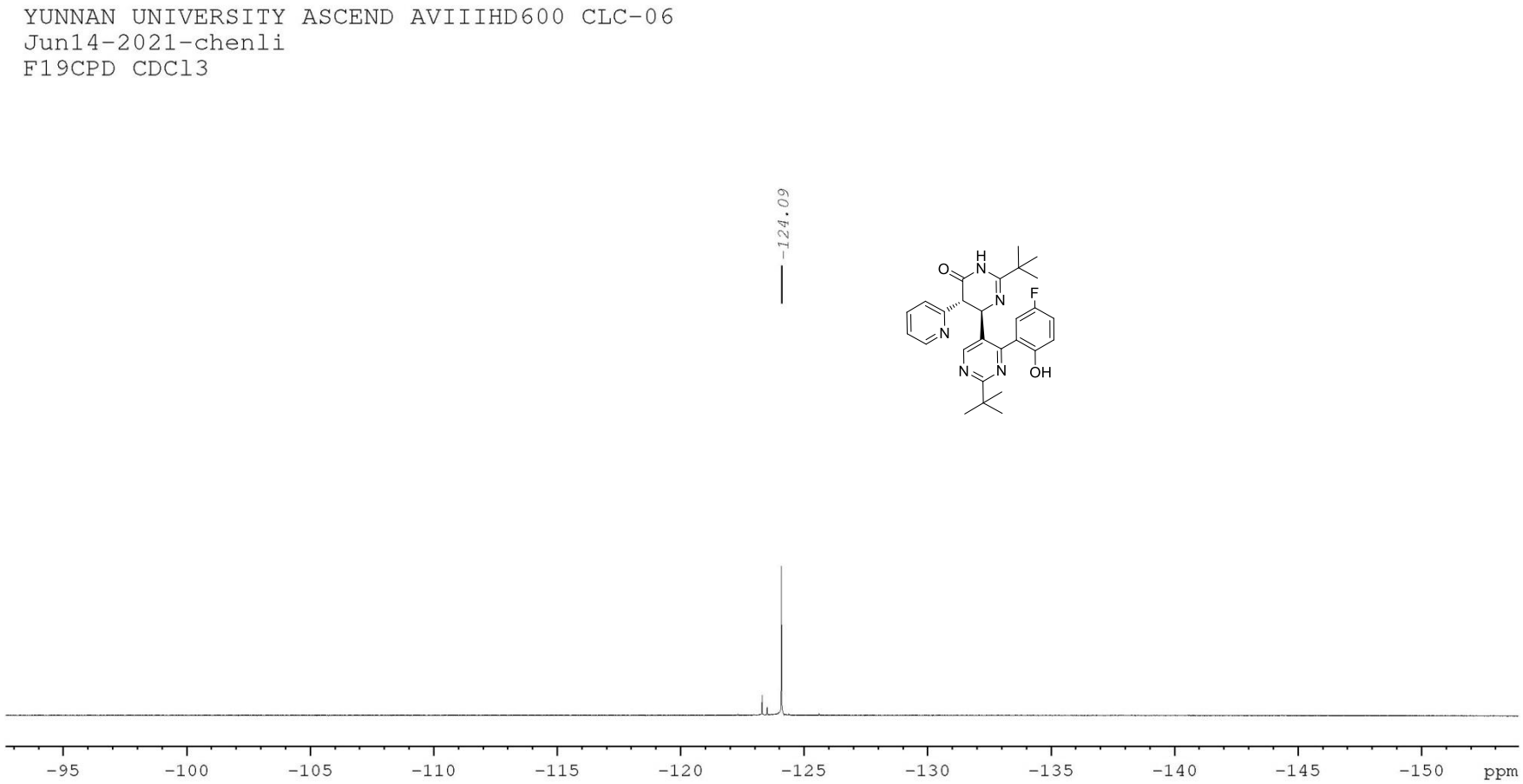


Figure S24. ^{19}F NMR (**564** MHz, $CDCl_3$) spectra of compound **4j**

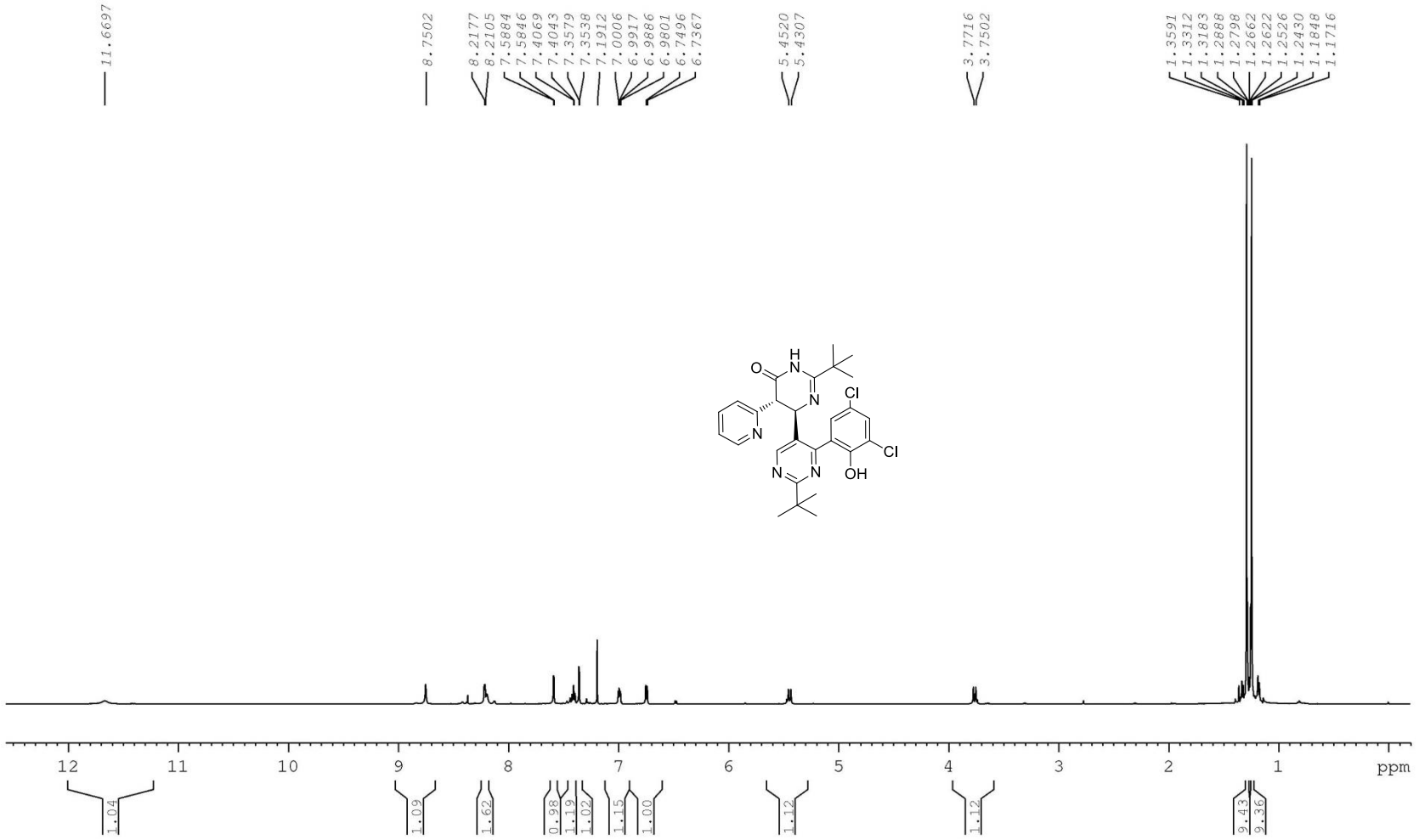


Figure S25. ^{1}H NMR (**600** MHz, $CDCl_3$) spectra of compound **4k**

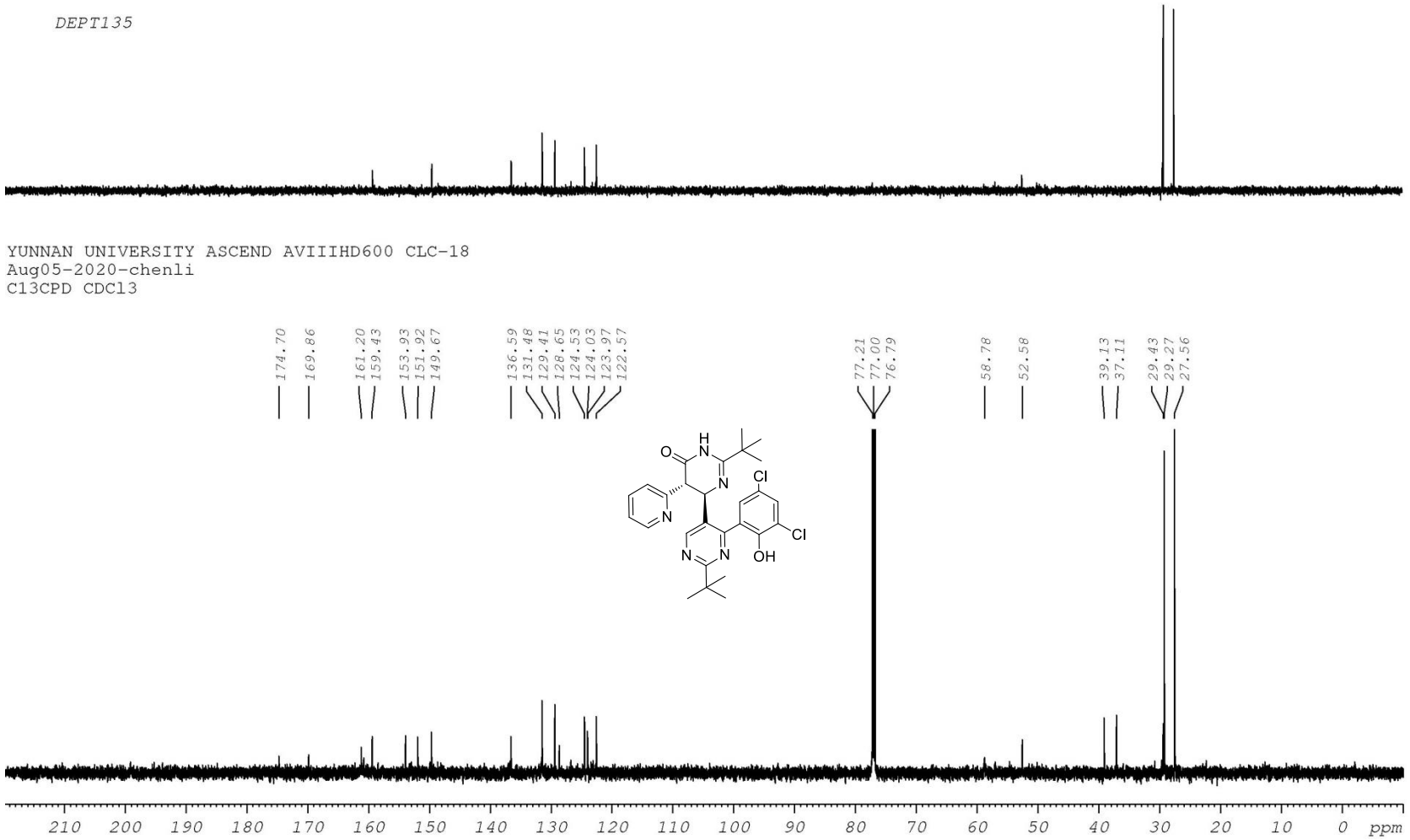


Figure S26. ^{13}C NMR (**150** MHz, $CDCl_3$) spectra of compound **4k**

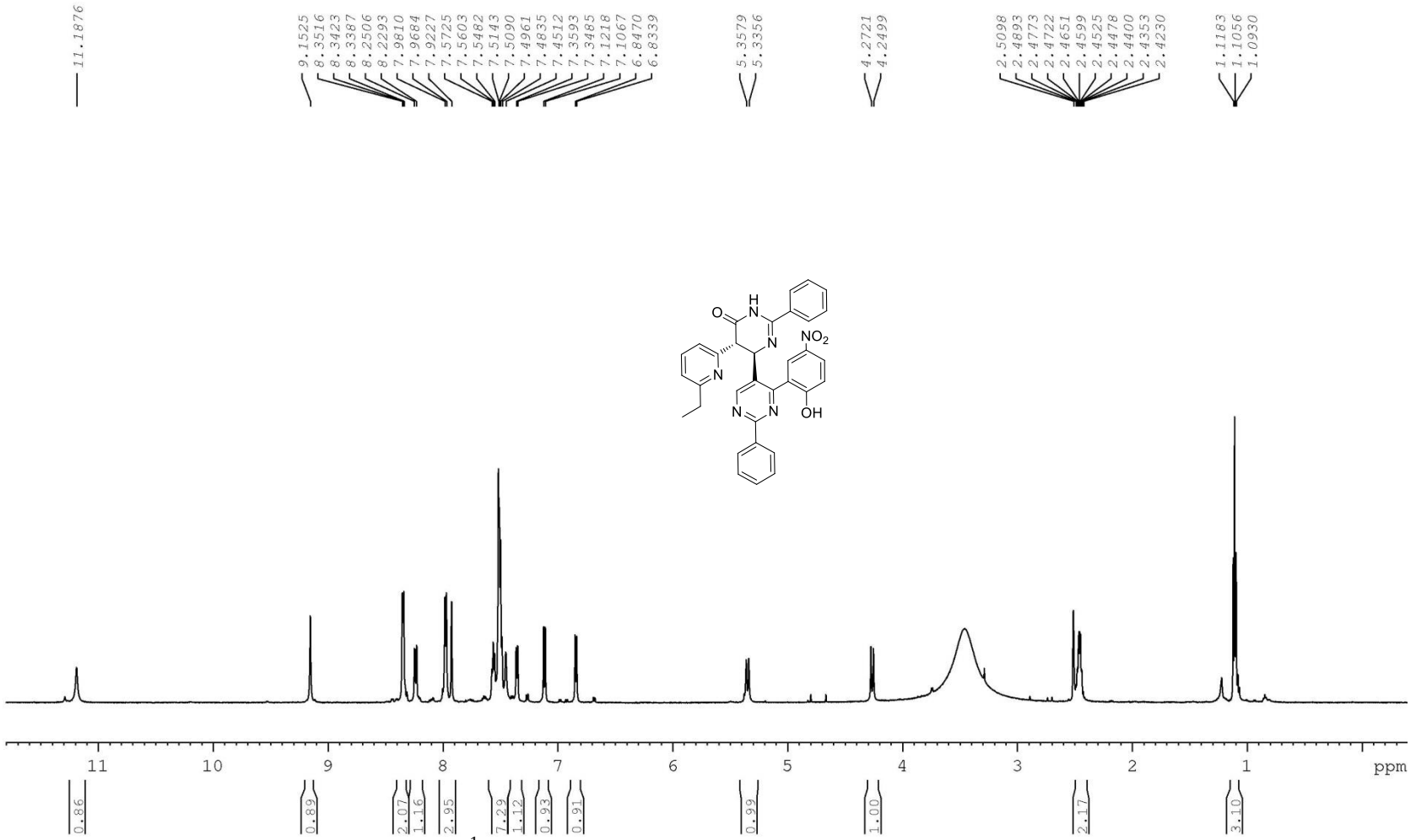


Figure S27. ^{1}H NMR (**600** MHz, DMSO-d_6) spectra of compound **4l**

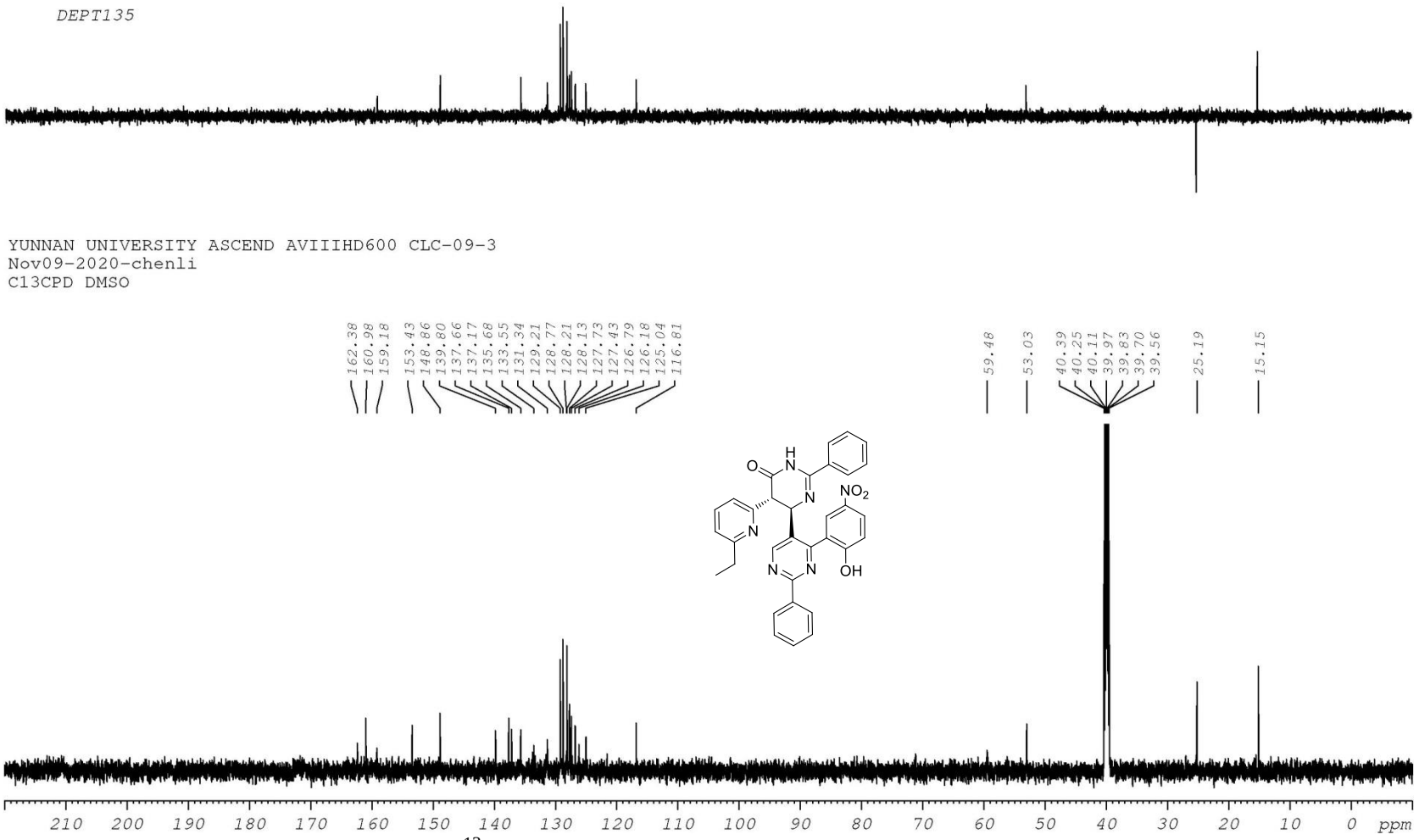


Figure S28. ^{13}C NMR (**150** MHz, DMSO-d_6) spectra of compound **4l**

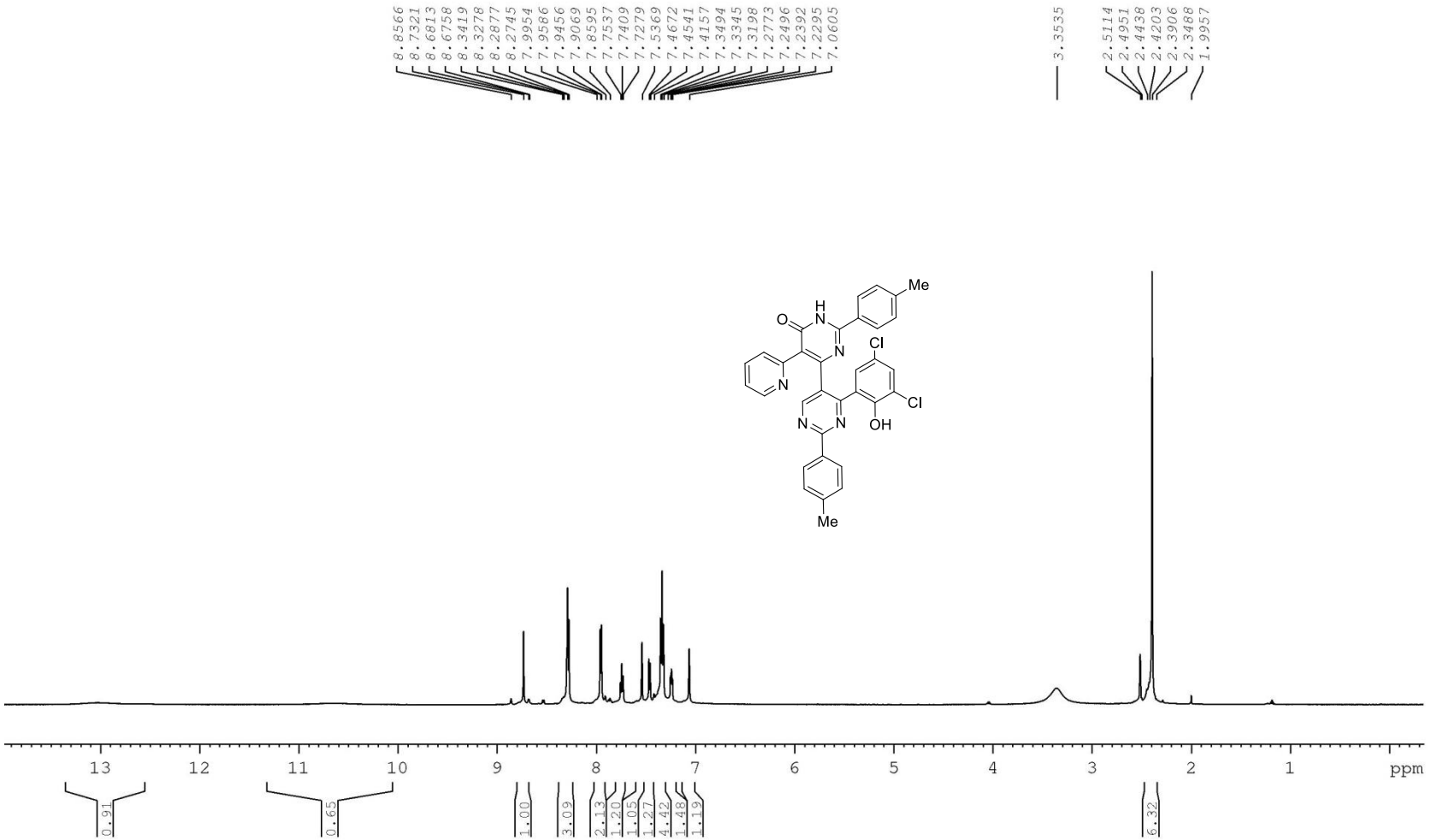


Figure S29. ^{1}H NMR (**600** MHz, DMSO-d_6) spectra of compound **5a**

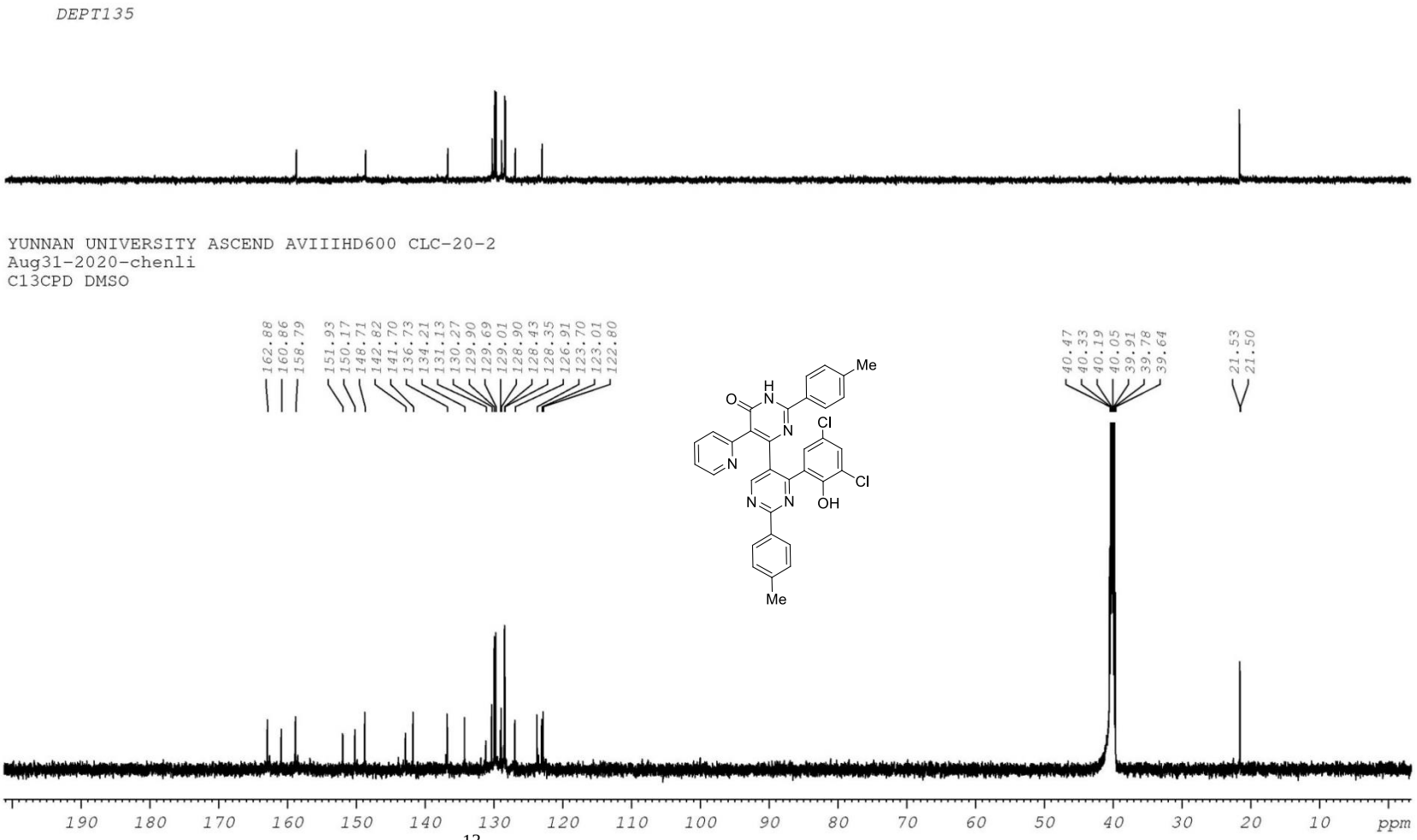


Figure S30. ^{13}C NMR (**150** MHz, DMSO-d_6) spectra of compound **5a**

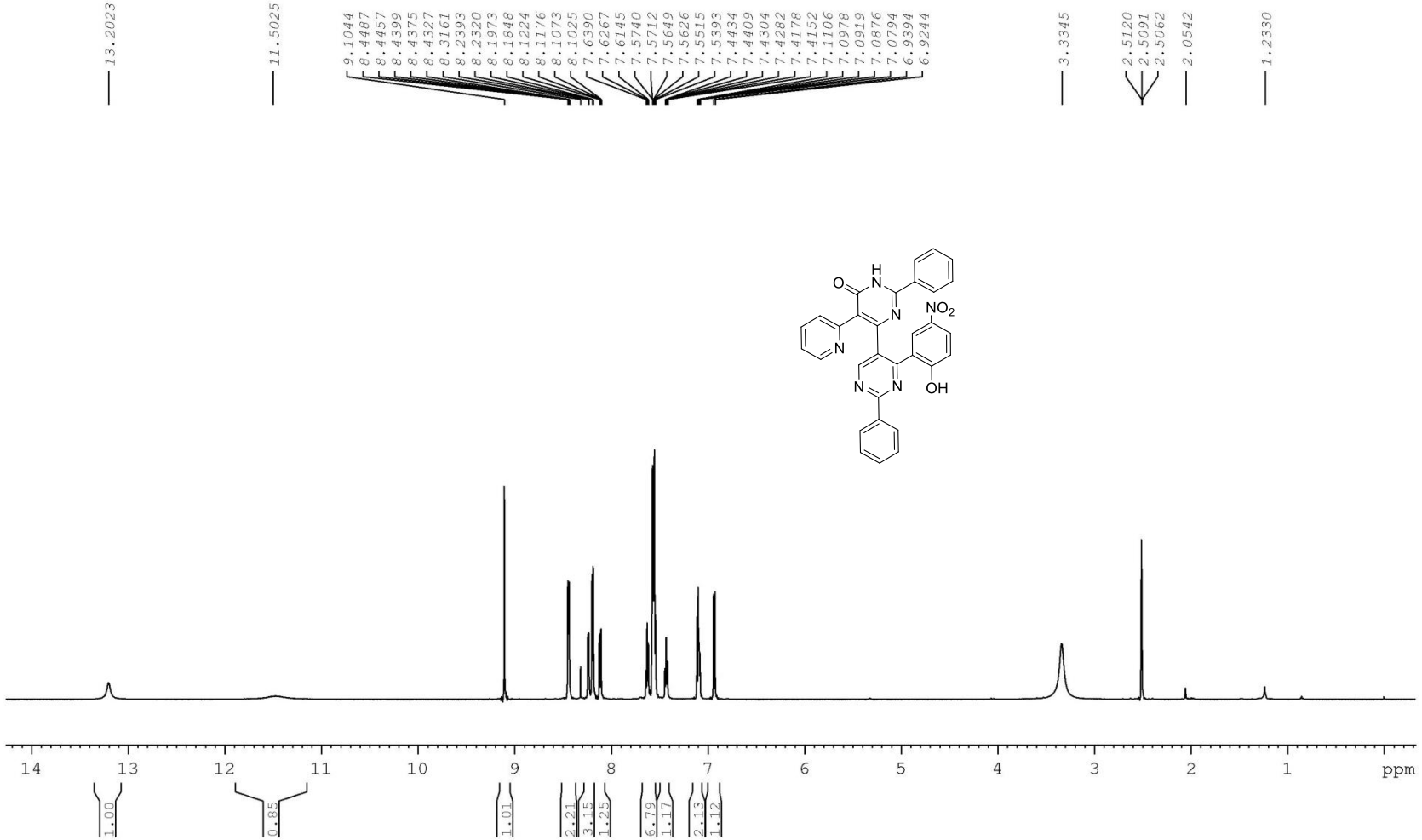


Figure S31. ^{1}H NMR (**600** MHz, DMSO-d_6) spectra of compound **5b**

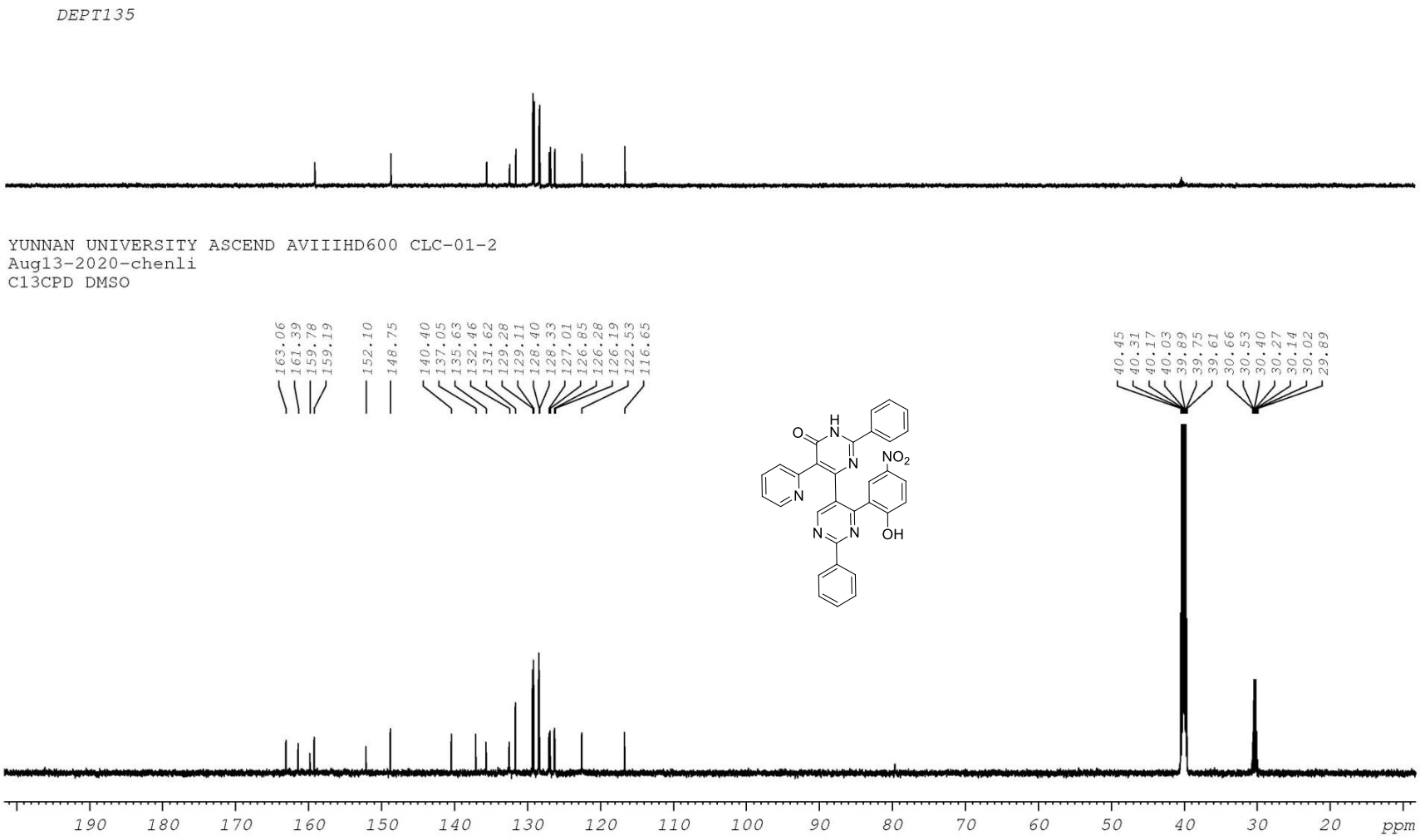


Figure S32. ^{13}C NMR (**150** MHz, DMSO-d_6) spectra of compound **5b**

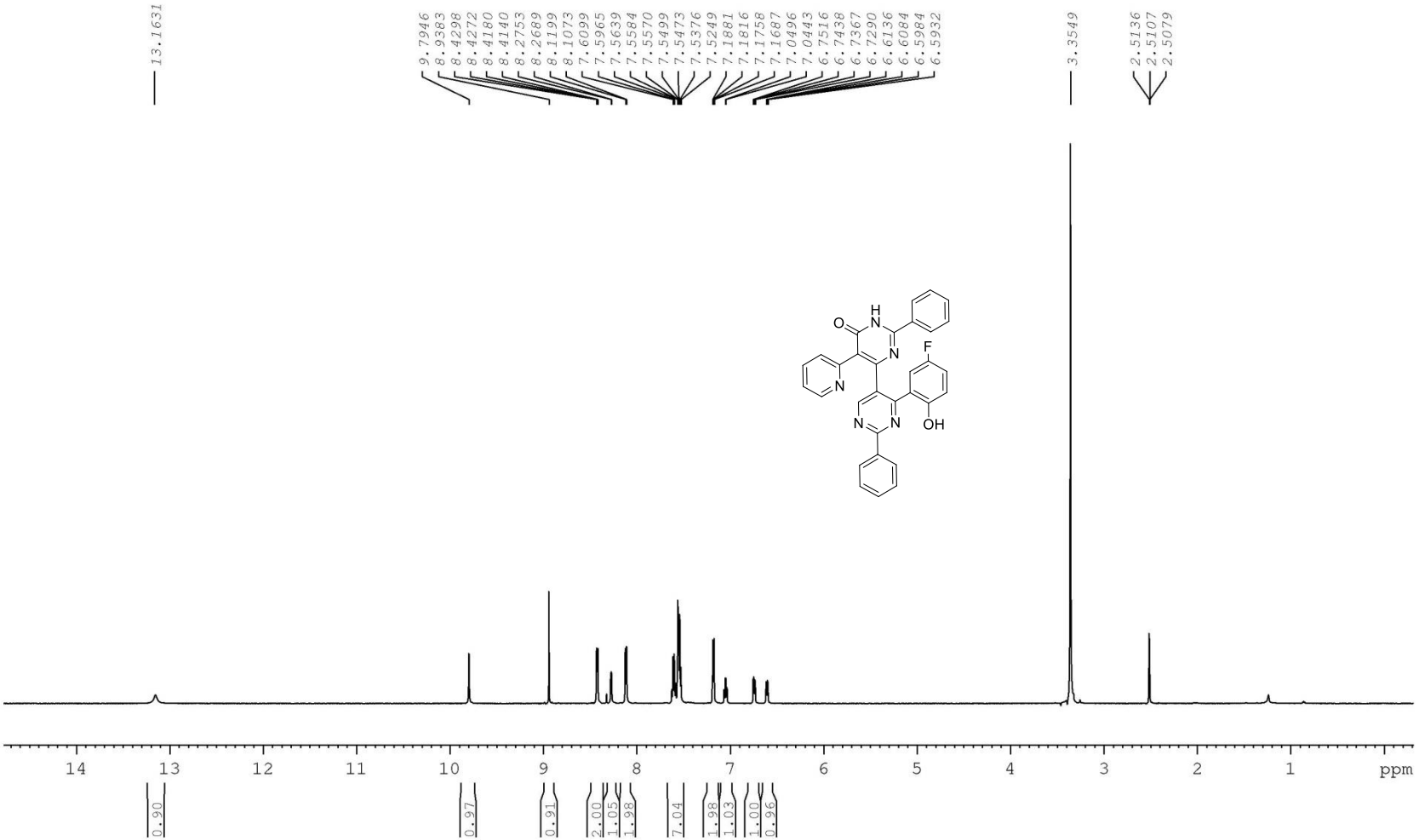


Figure S33. ^{1}H NMR (**600** MHz, DMSO-d_6) spectra of compound **5c**

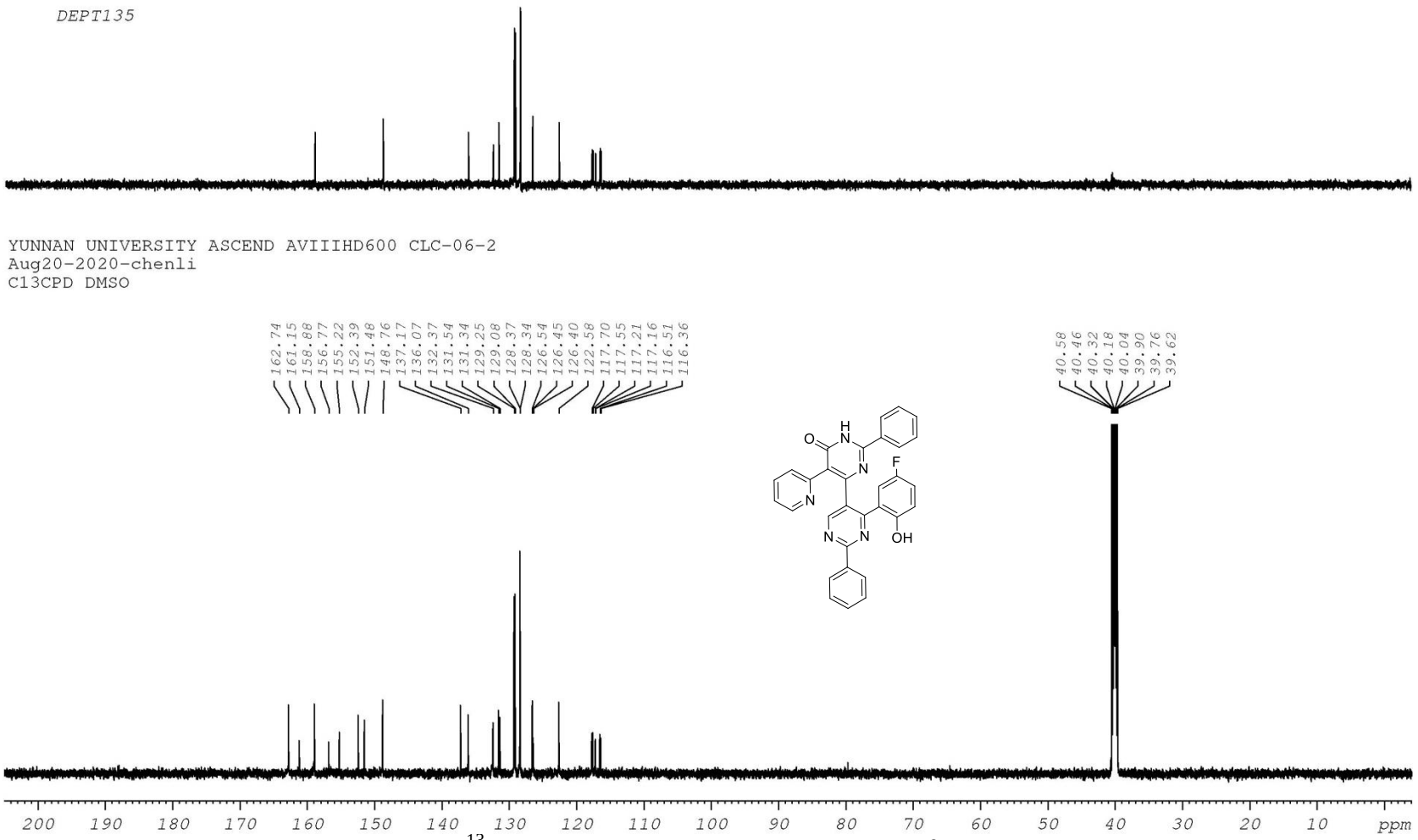


Figure S34. ^{13}C NMR (**150** MHz, DMSO-d_6) spectra of compound **5c**

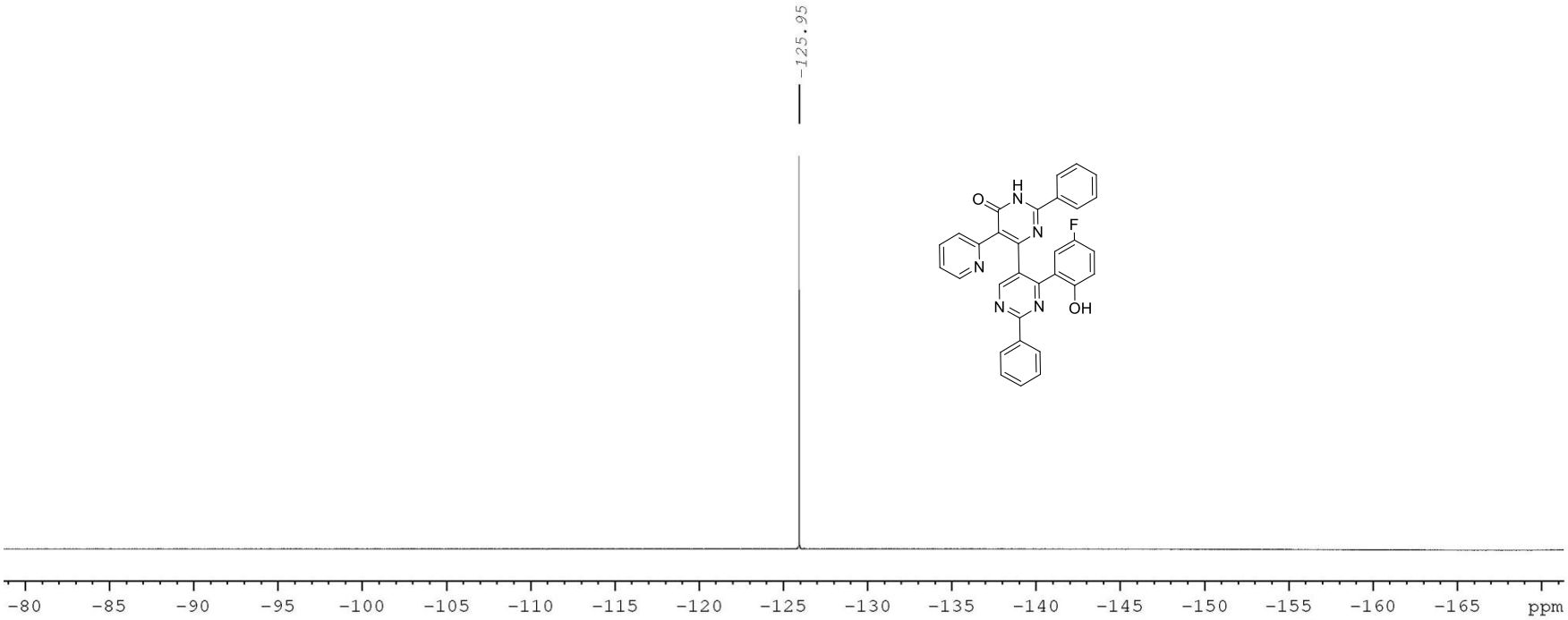


Figure S35. ^{19}F NMR (**564** MHz, DMSO-d_6) spectra of compound **5c**

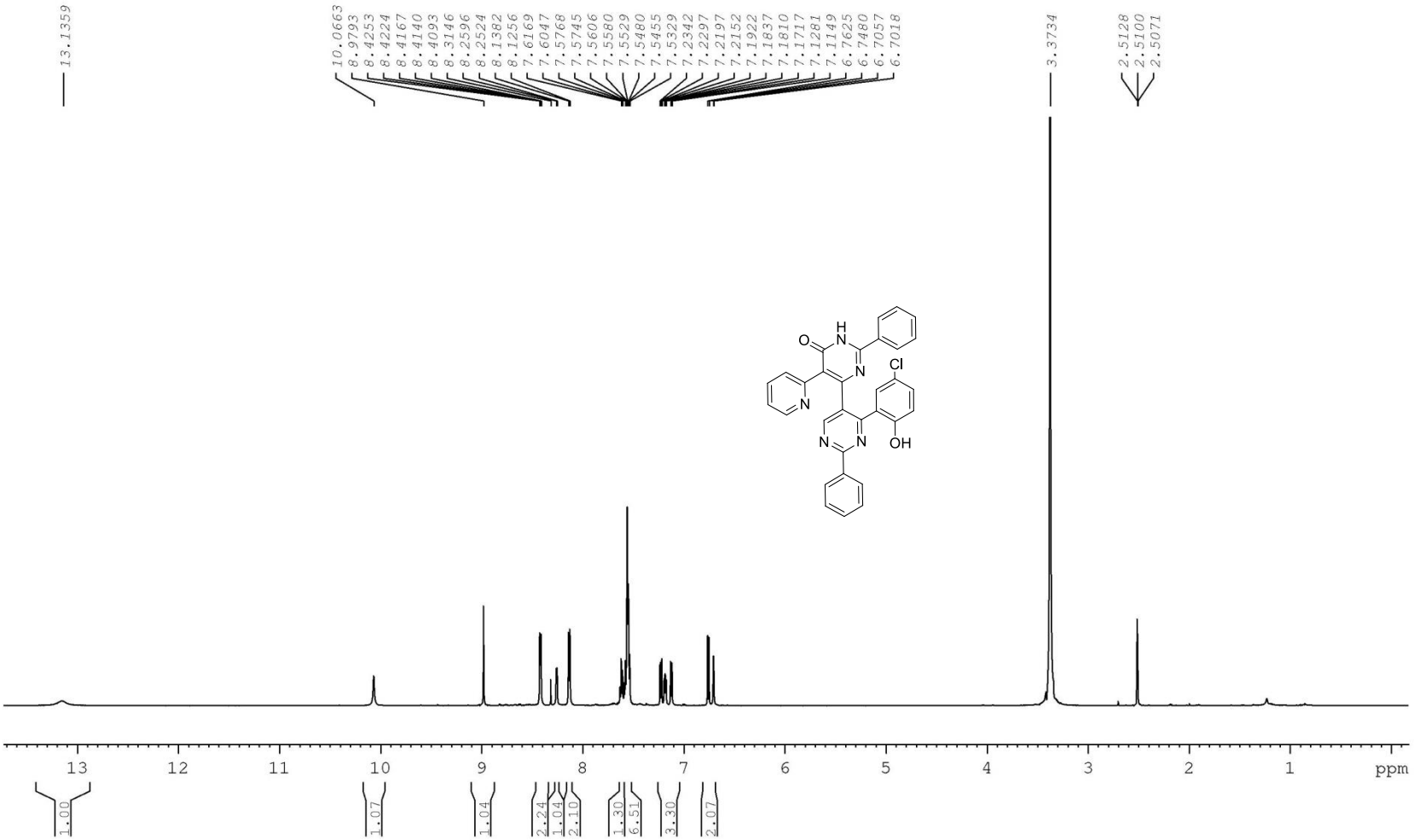


Figure S36. ^{1}H NMR (**600** MHz, DMSO-d_6) spectra of compound **5d**

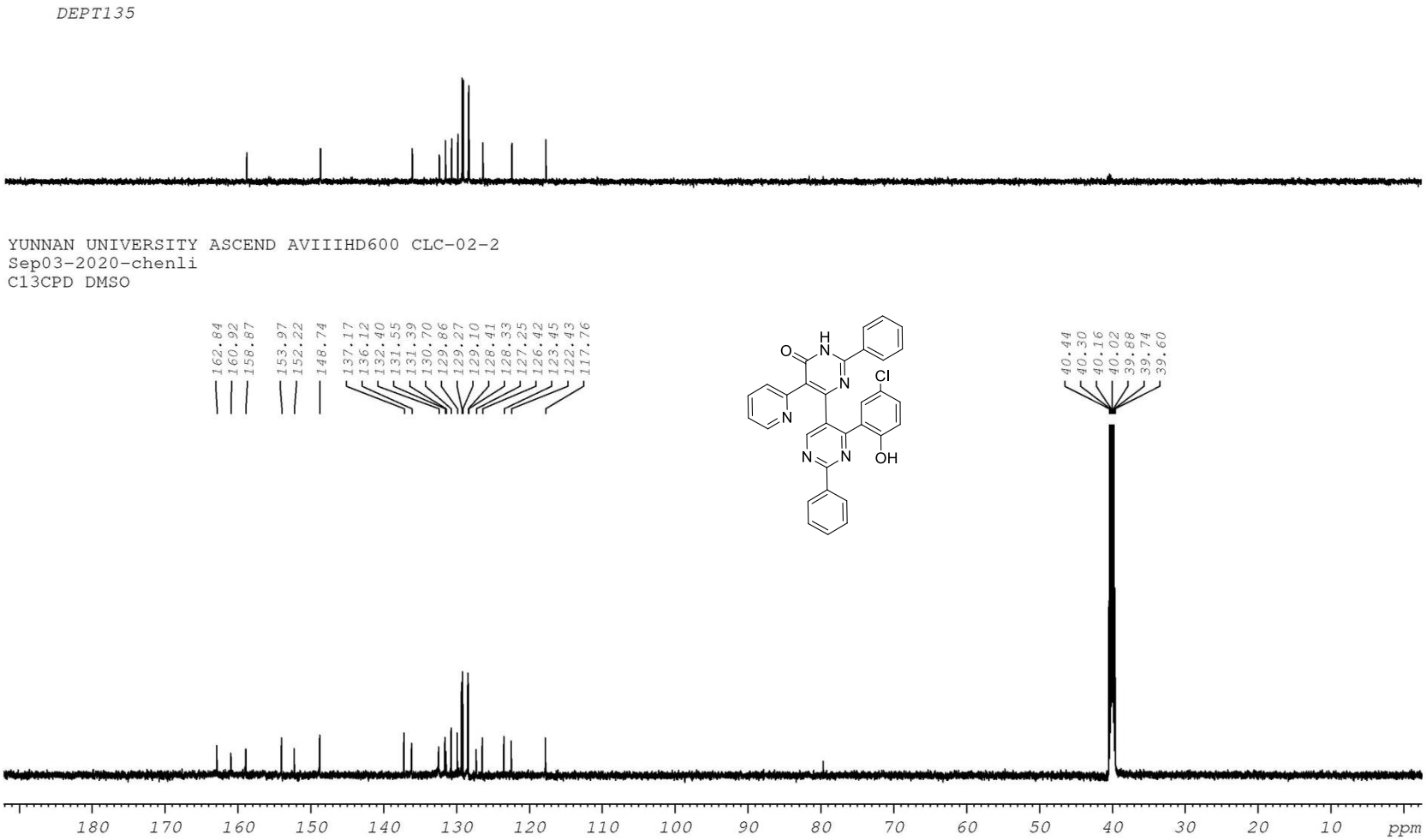


Figure S37. ^{13}C NMR (**150** MHz, DMSO-d_6) spectra of compound **5d**

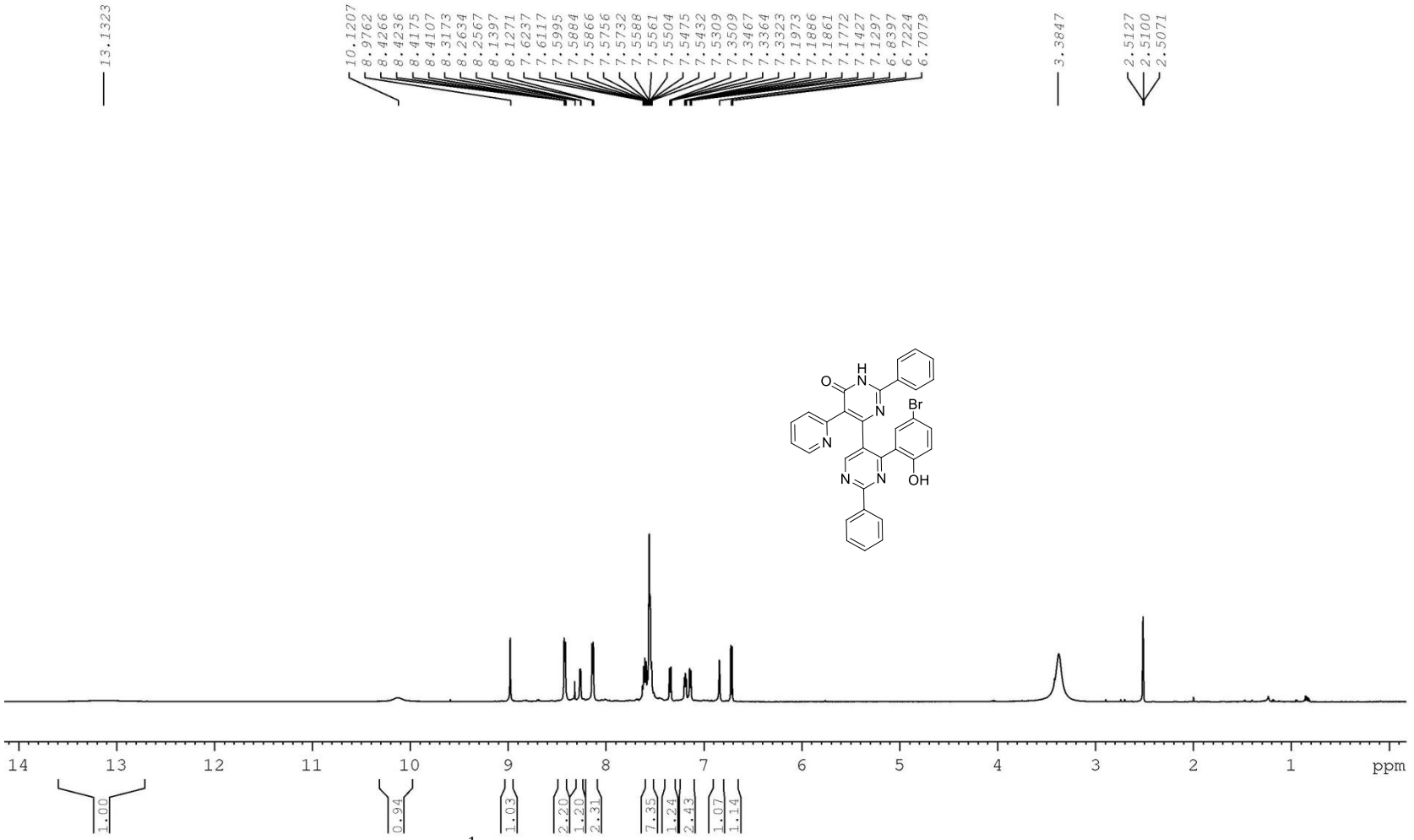


Figure S38. ^{1}H NMR (**600** MHz, DMSO-d_6) spectra of compound **5e**

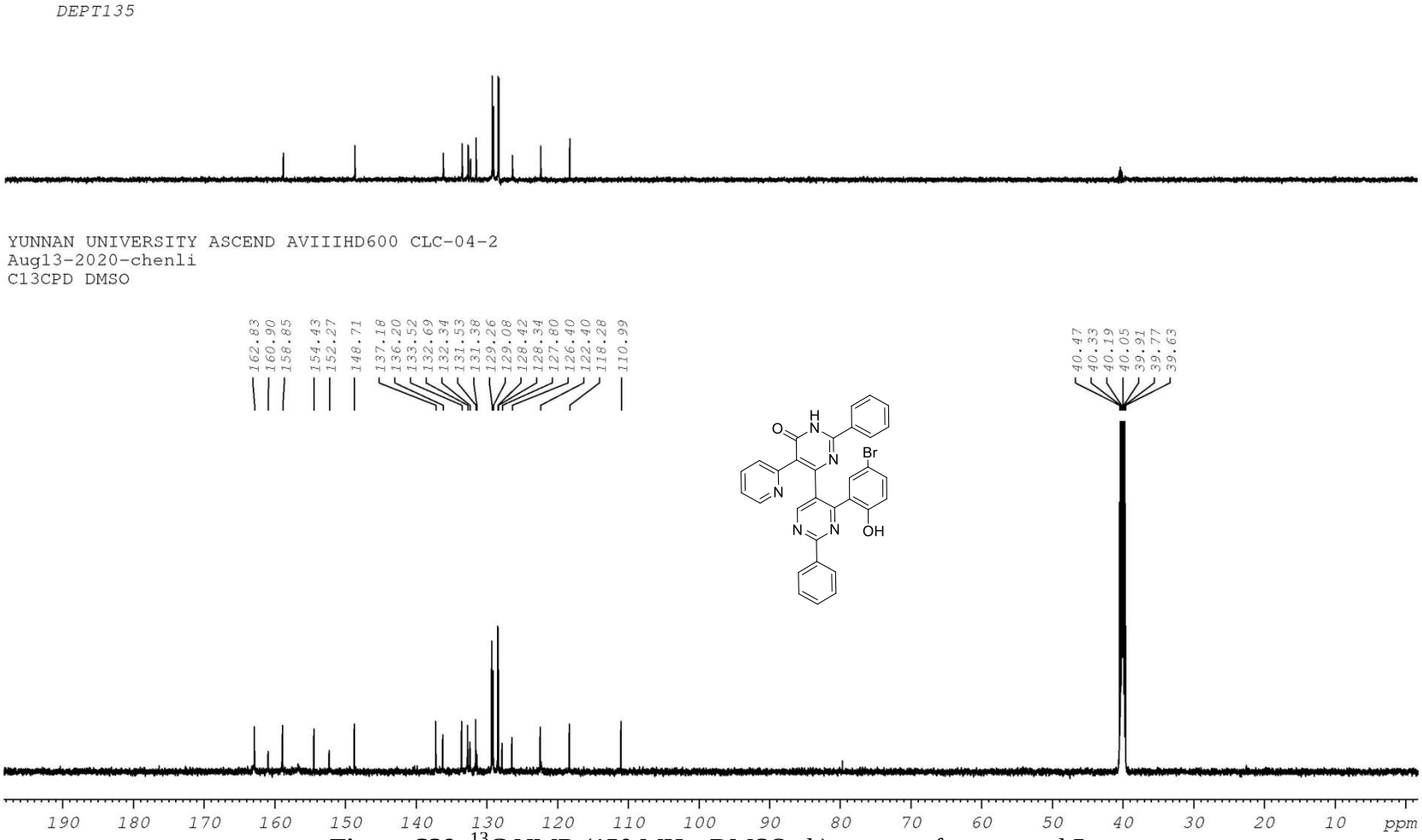


Figure S39. ^{13}C NMR (**150** MHz, DMSO-d_6) spectra of compound **5e**

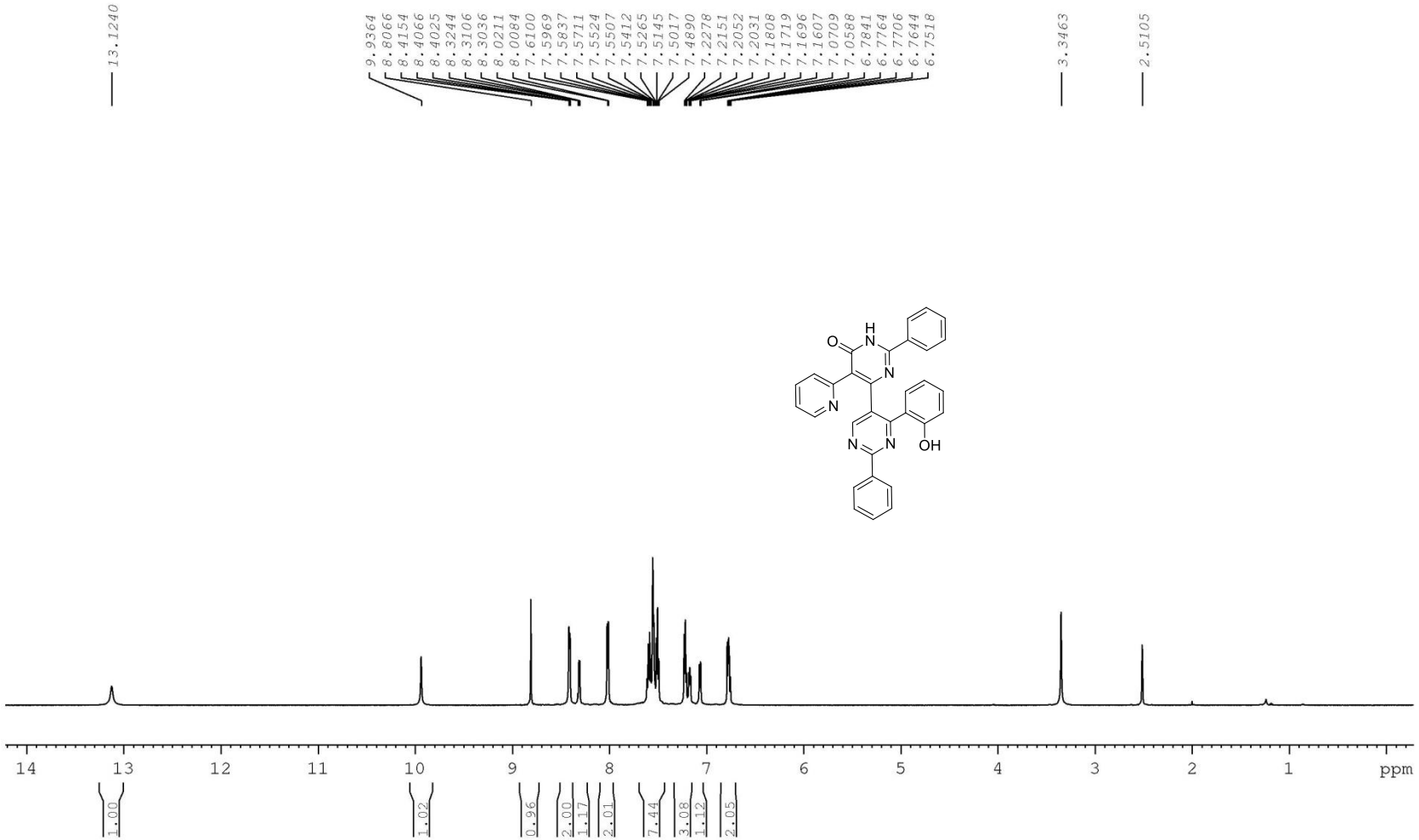


Figure S40. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5f**

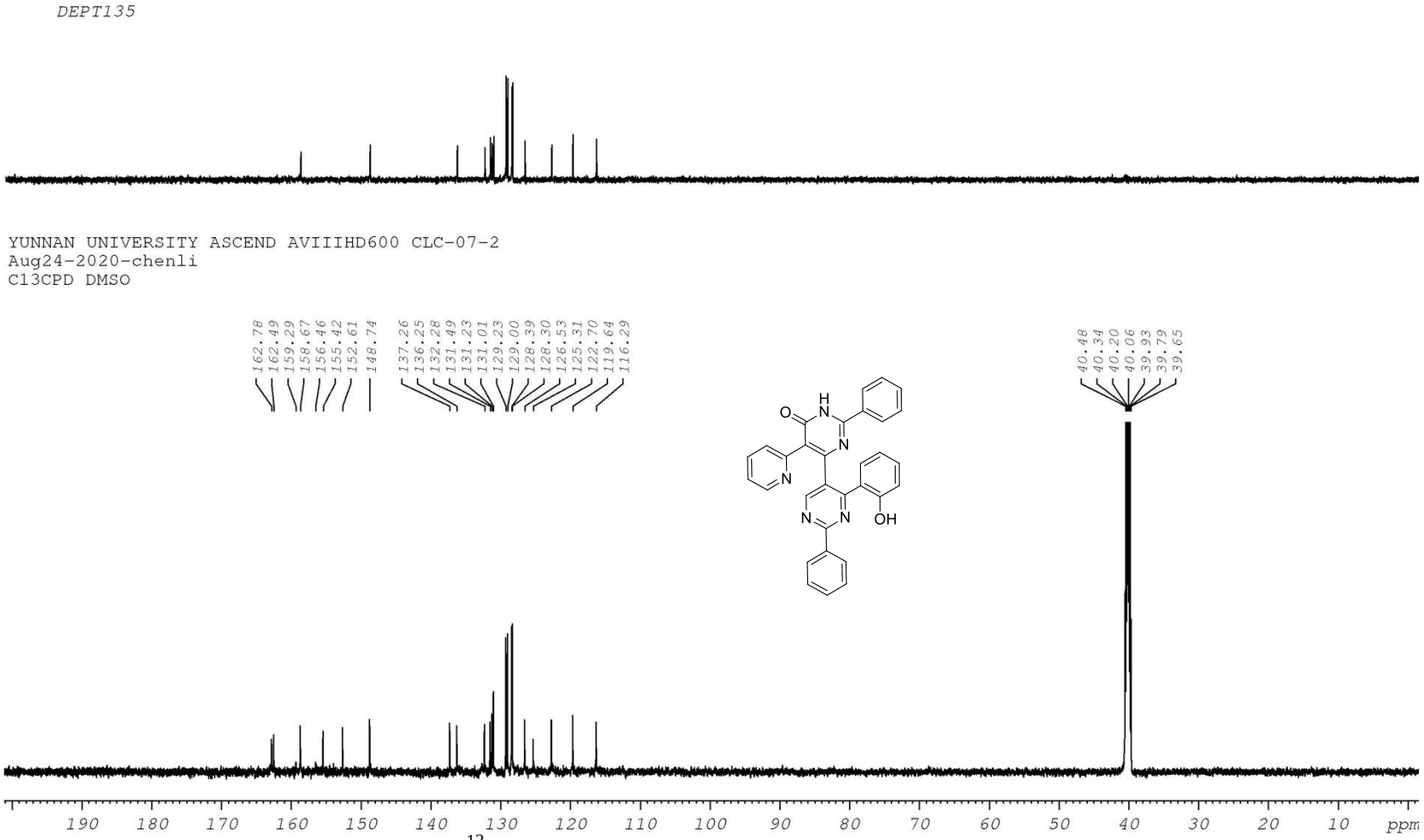


Figure S41. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5f**

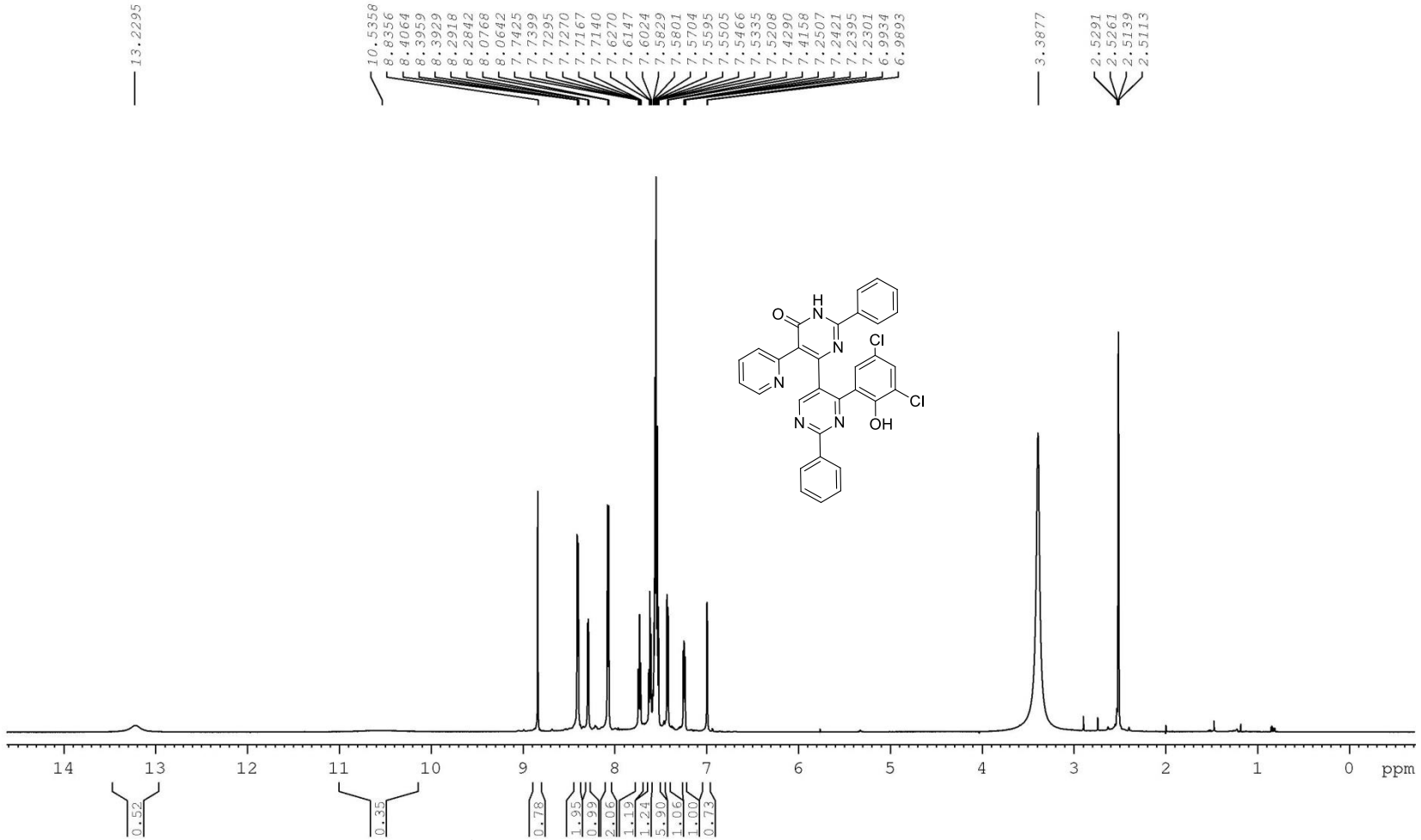


Figure S42. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5g**

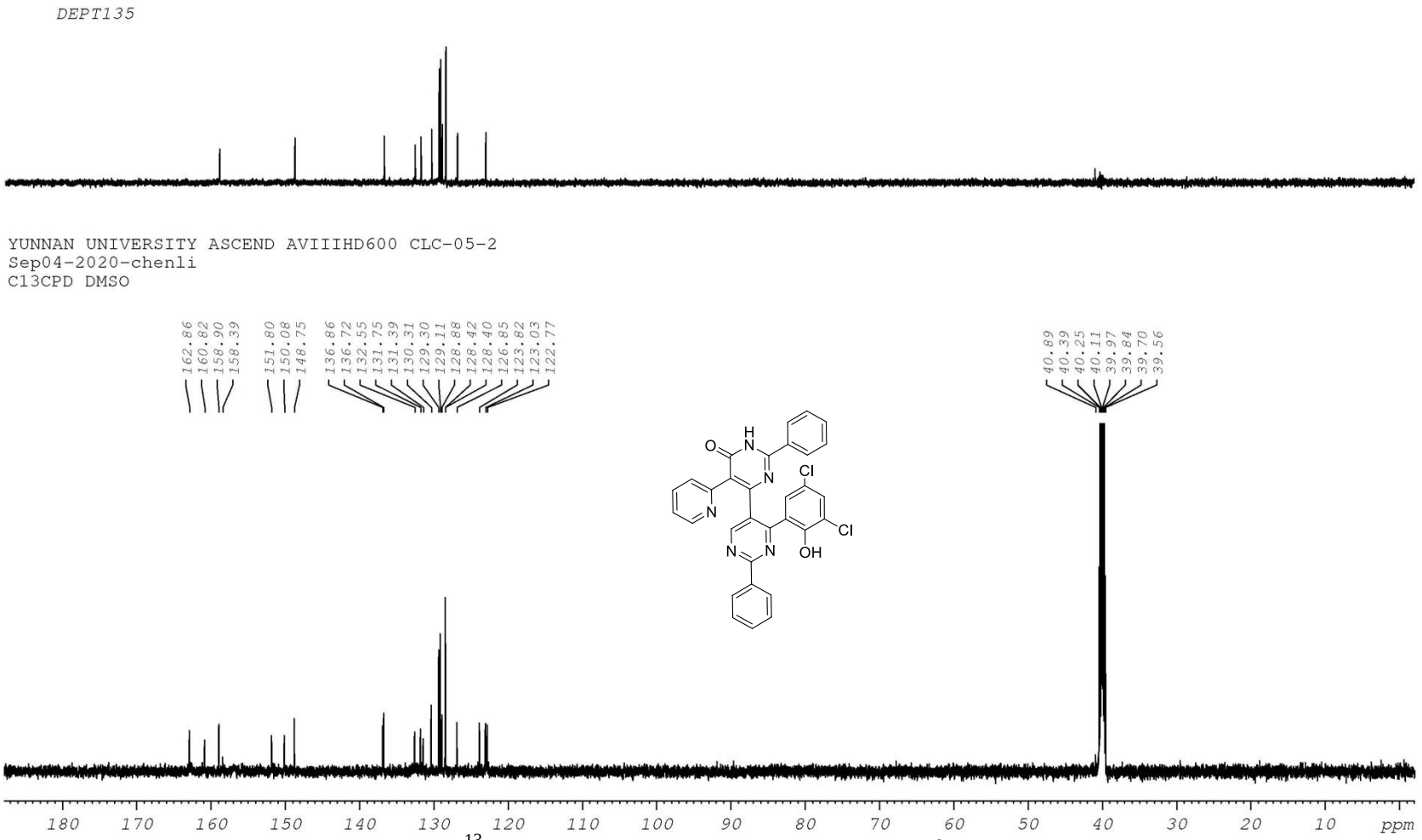


Figure S43. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5g**

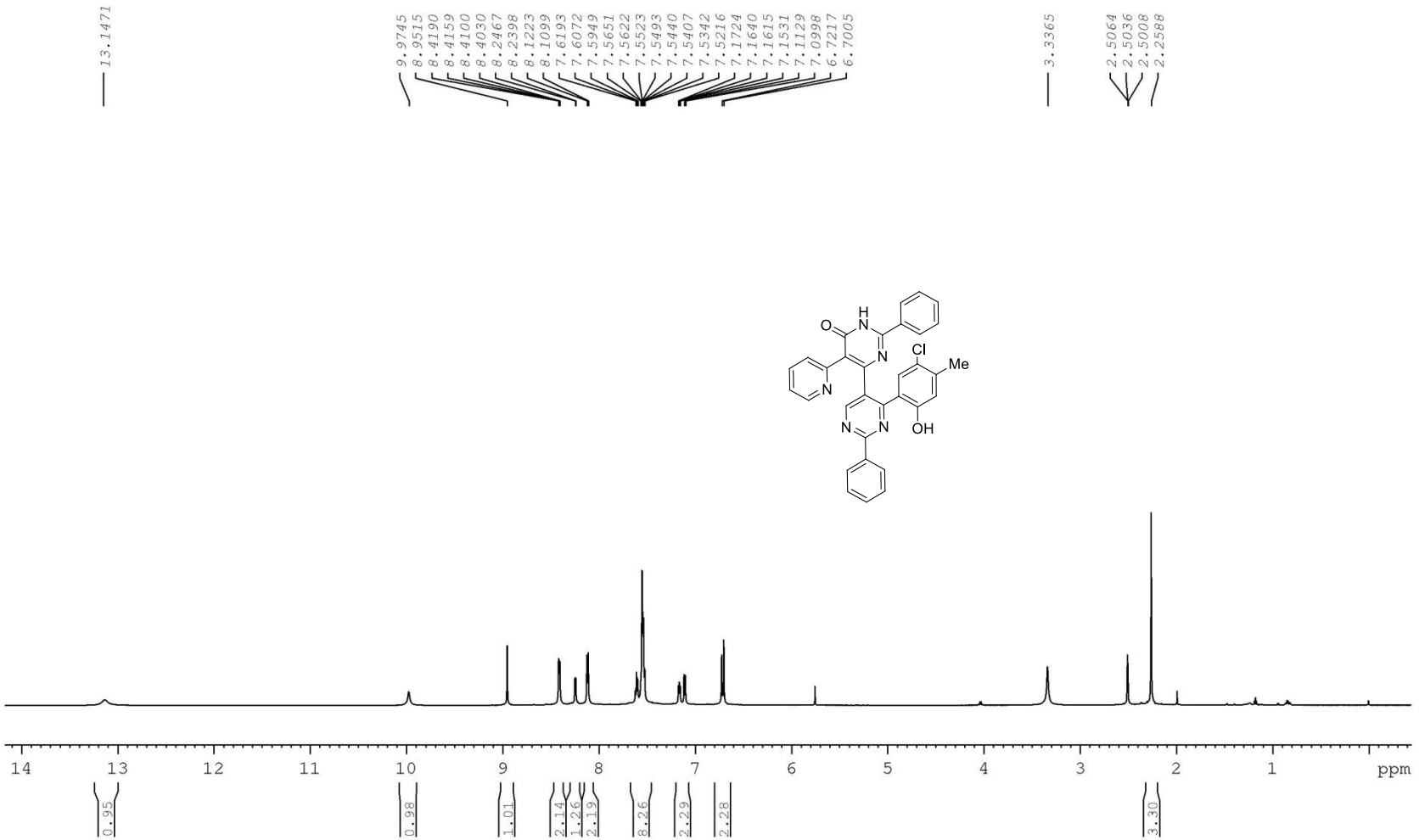


Figure S44. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5h**

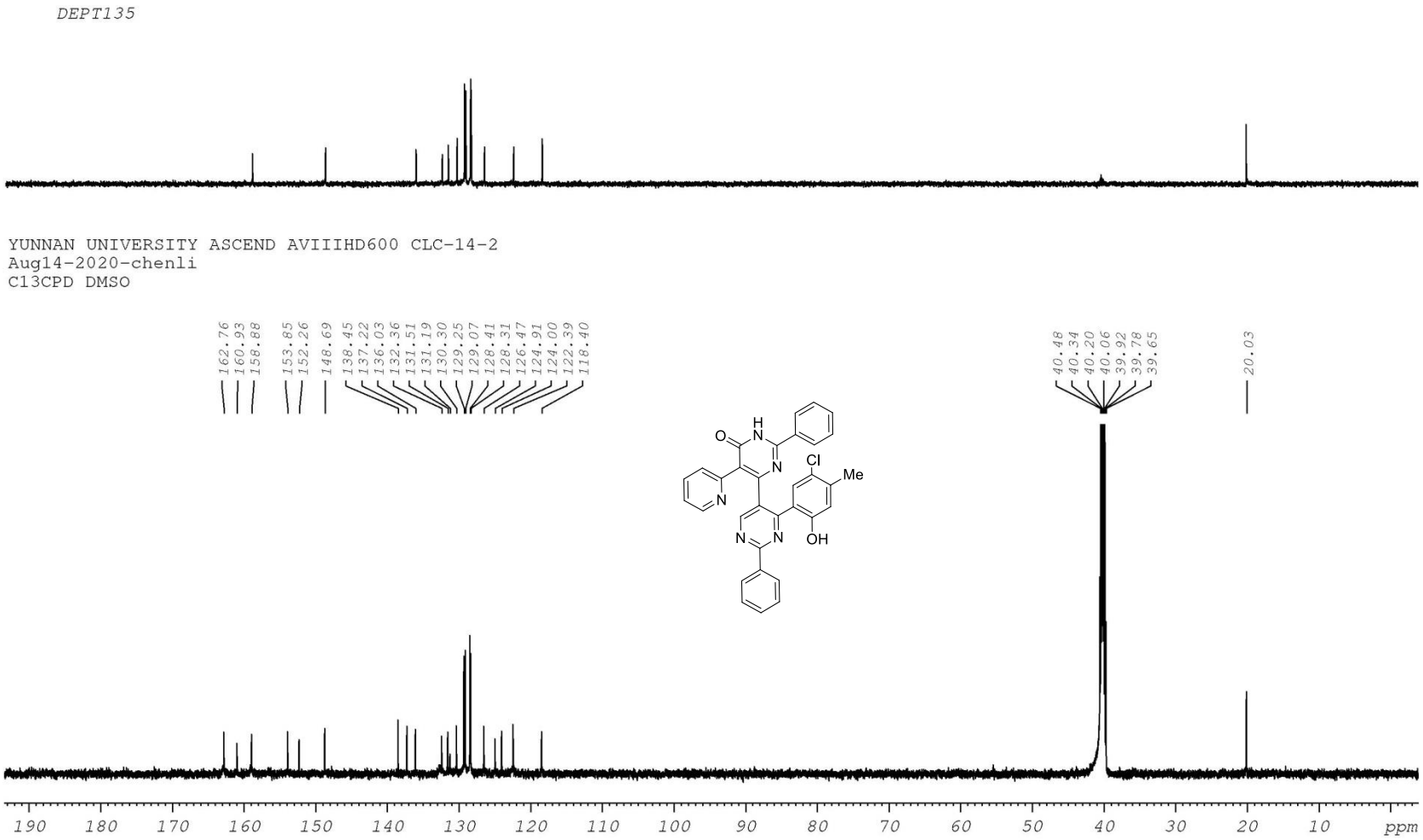


Figure S45. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5h**

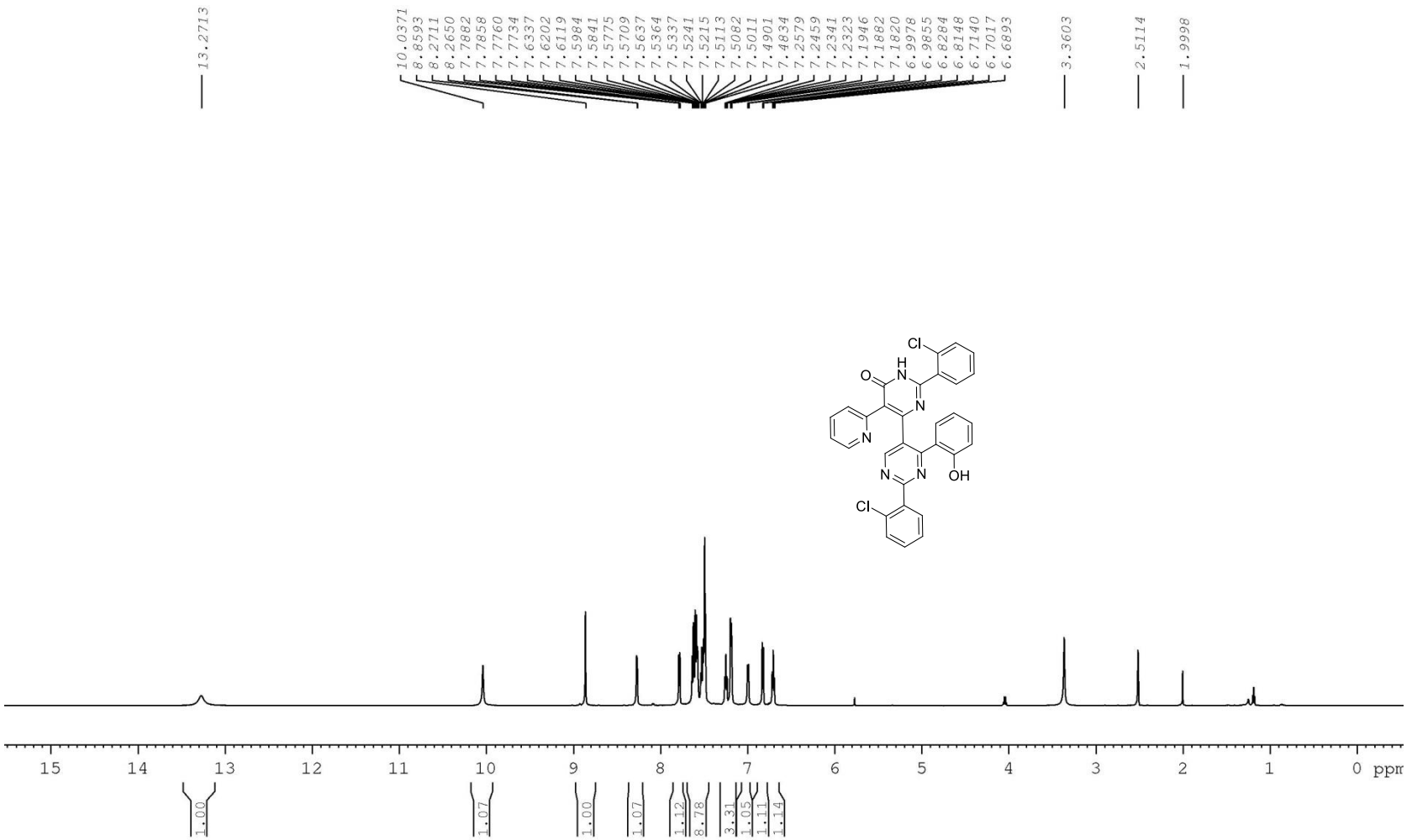


Figure S46. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5i**

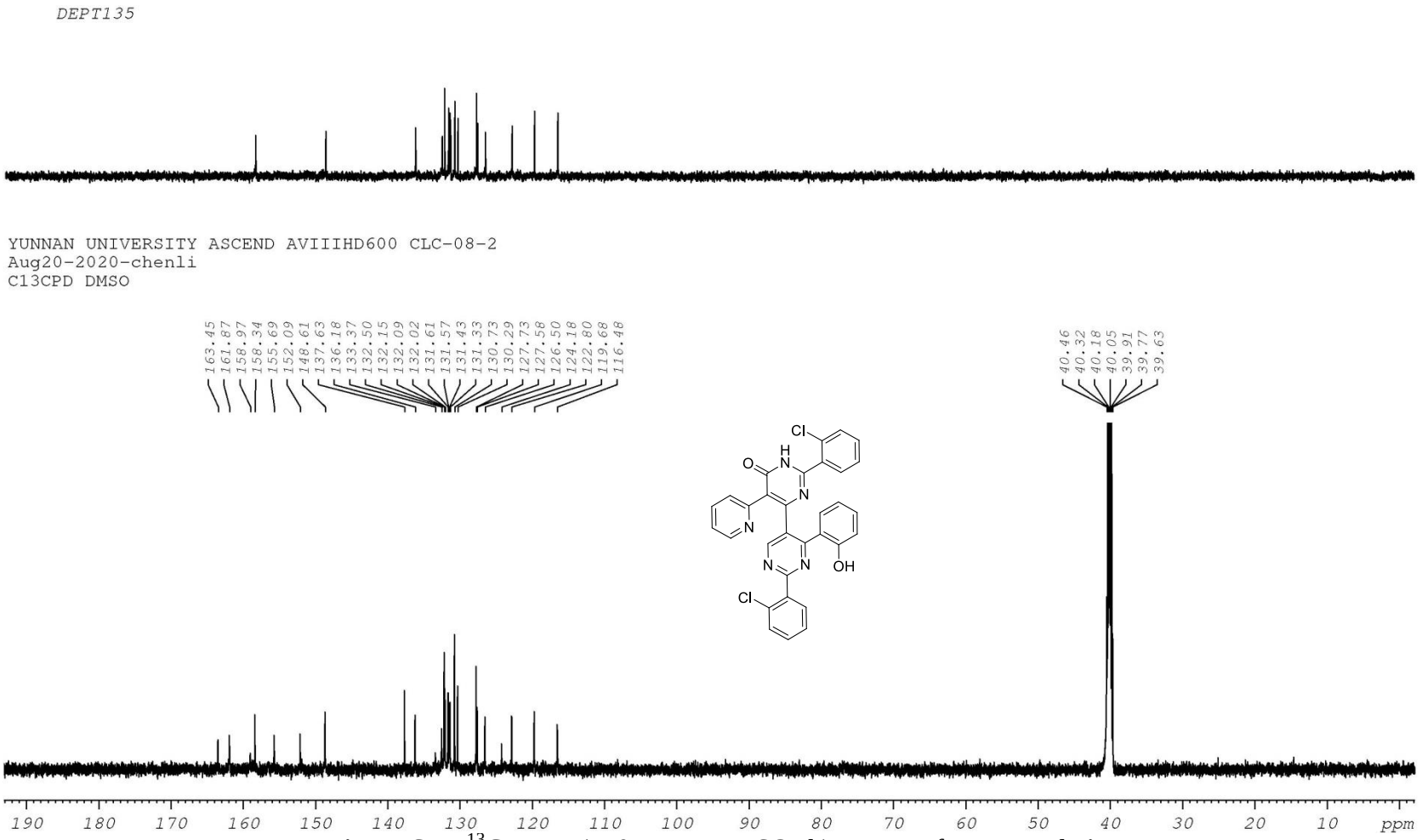


Figure S47. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5i**

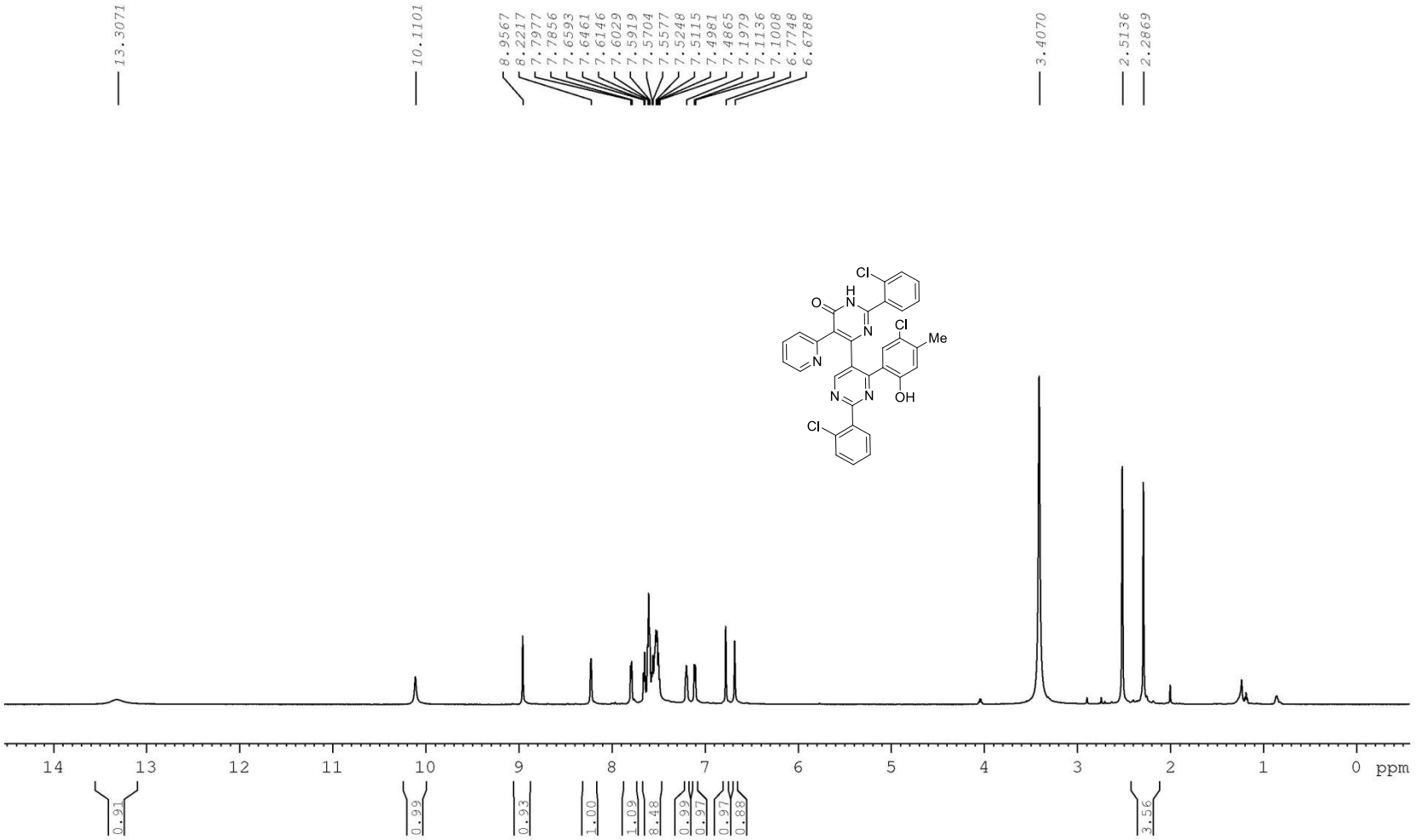


Figure S48. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5j**

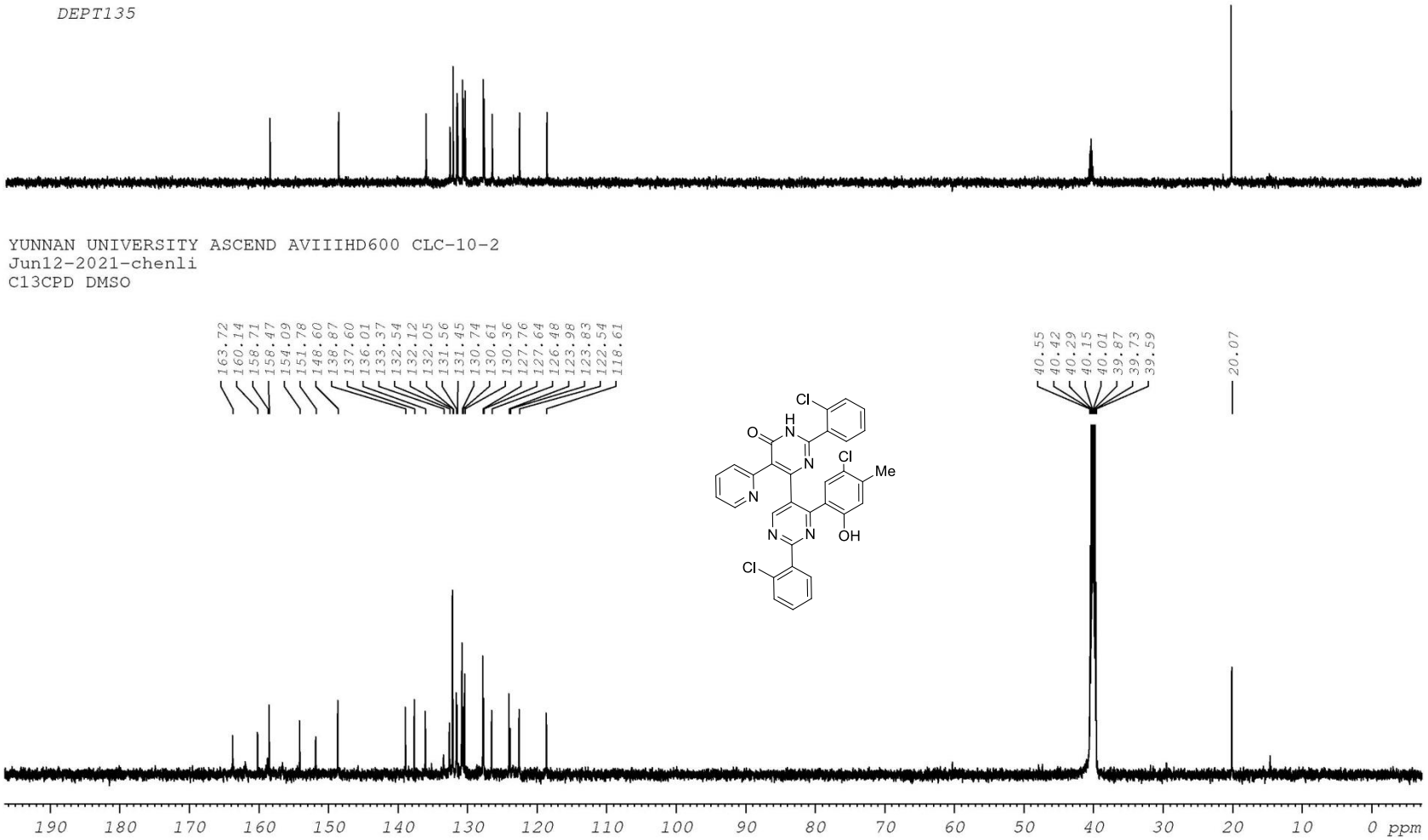


Figure S49. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5j**

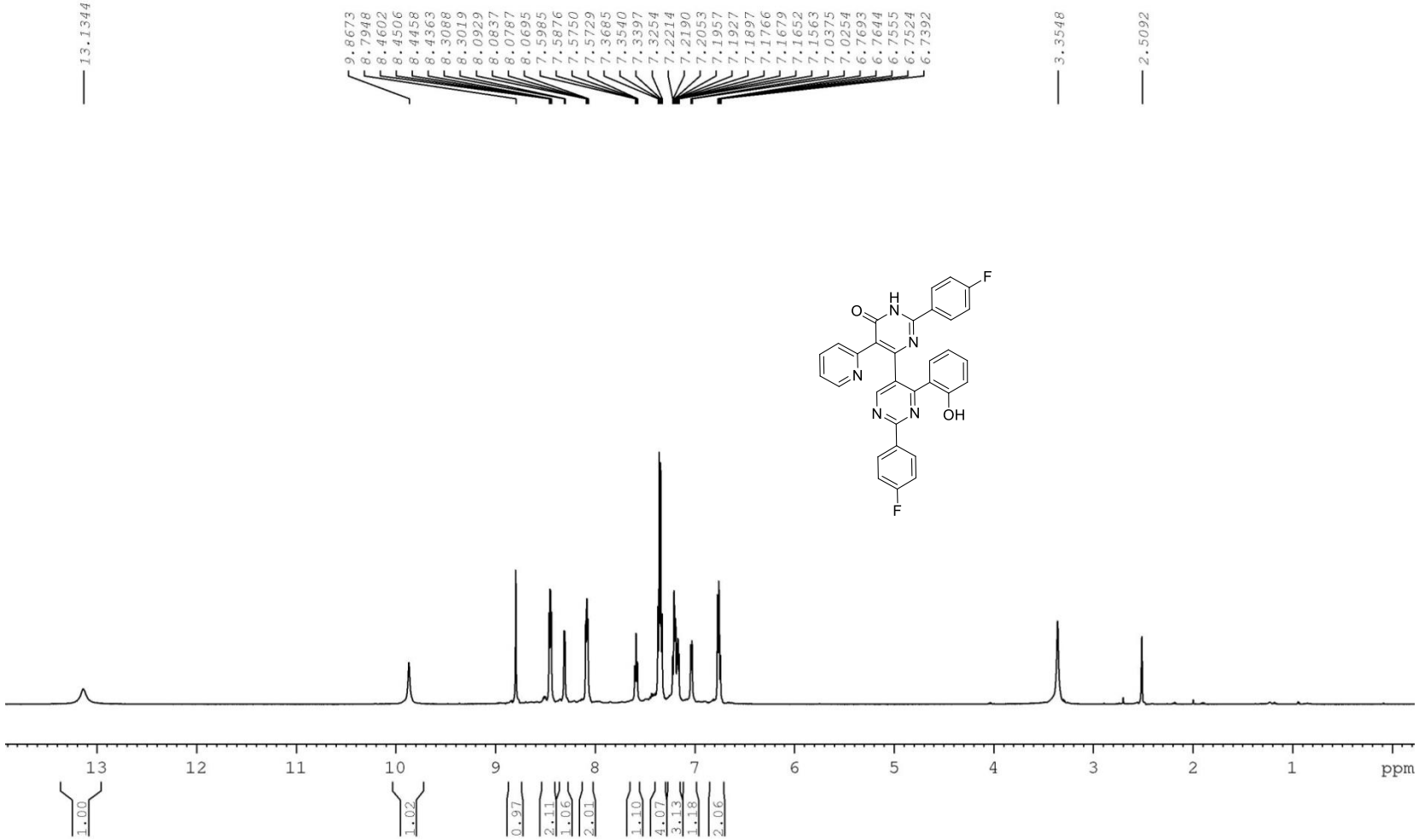


Figure S50. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5k**

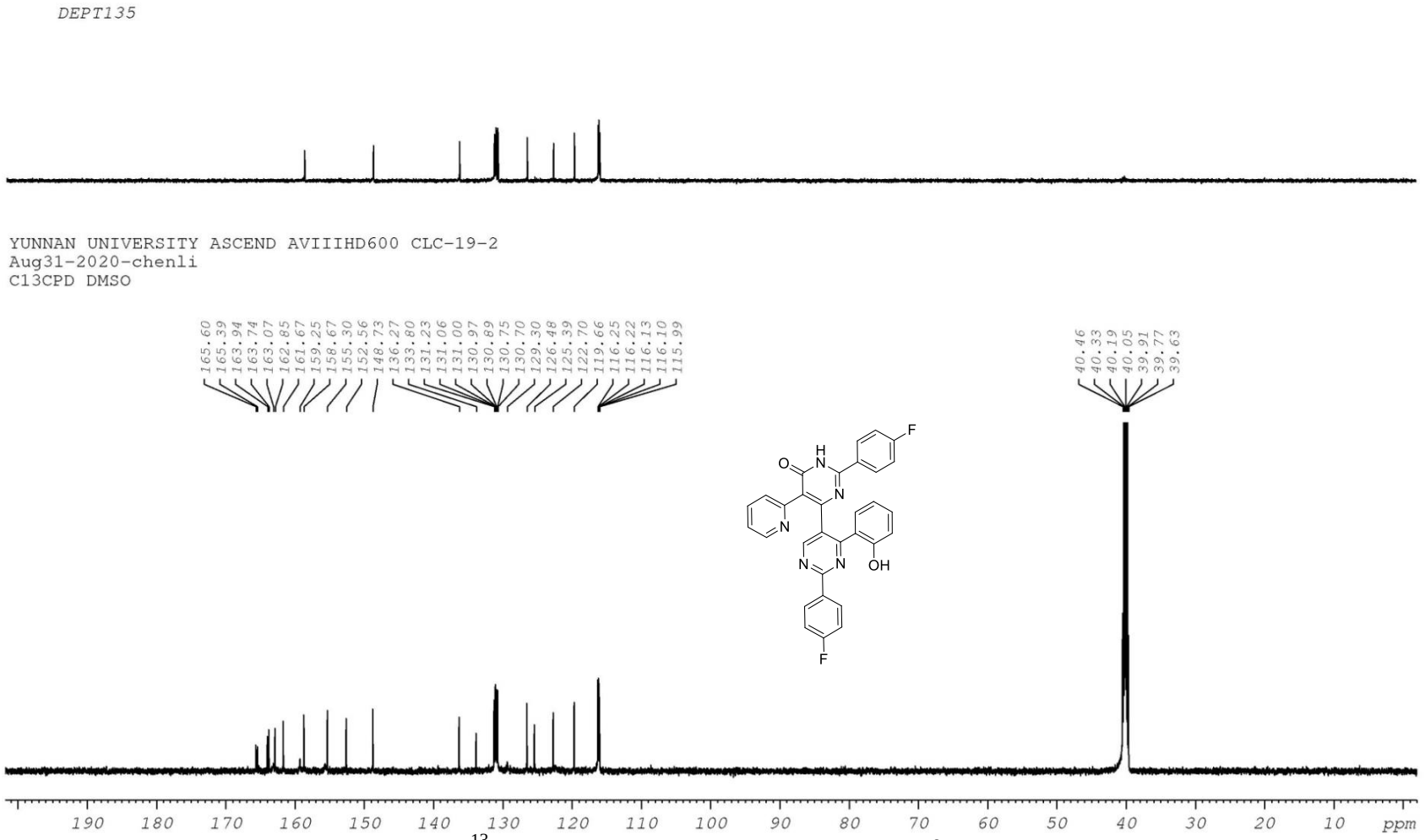


Figure S51. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5k**

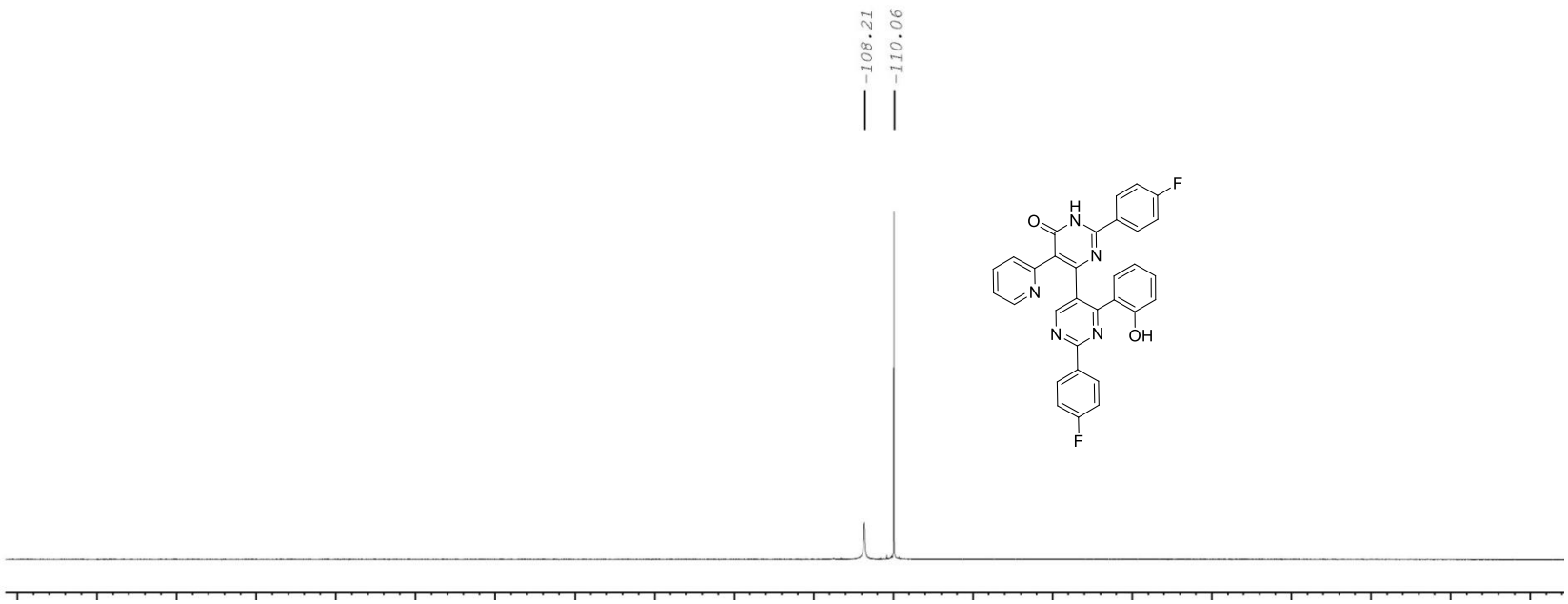


Figure S52. ^{19}F NMR (564 MHz, DMSO-d_6) spectra of compound **5k**

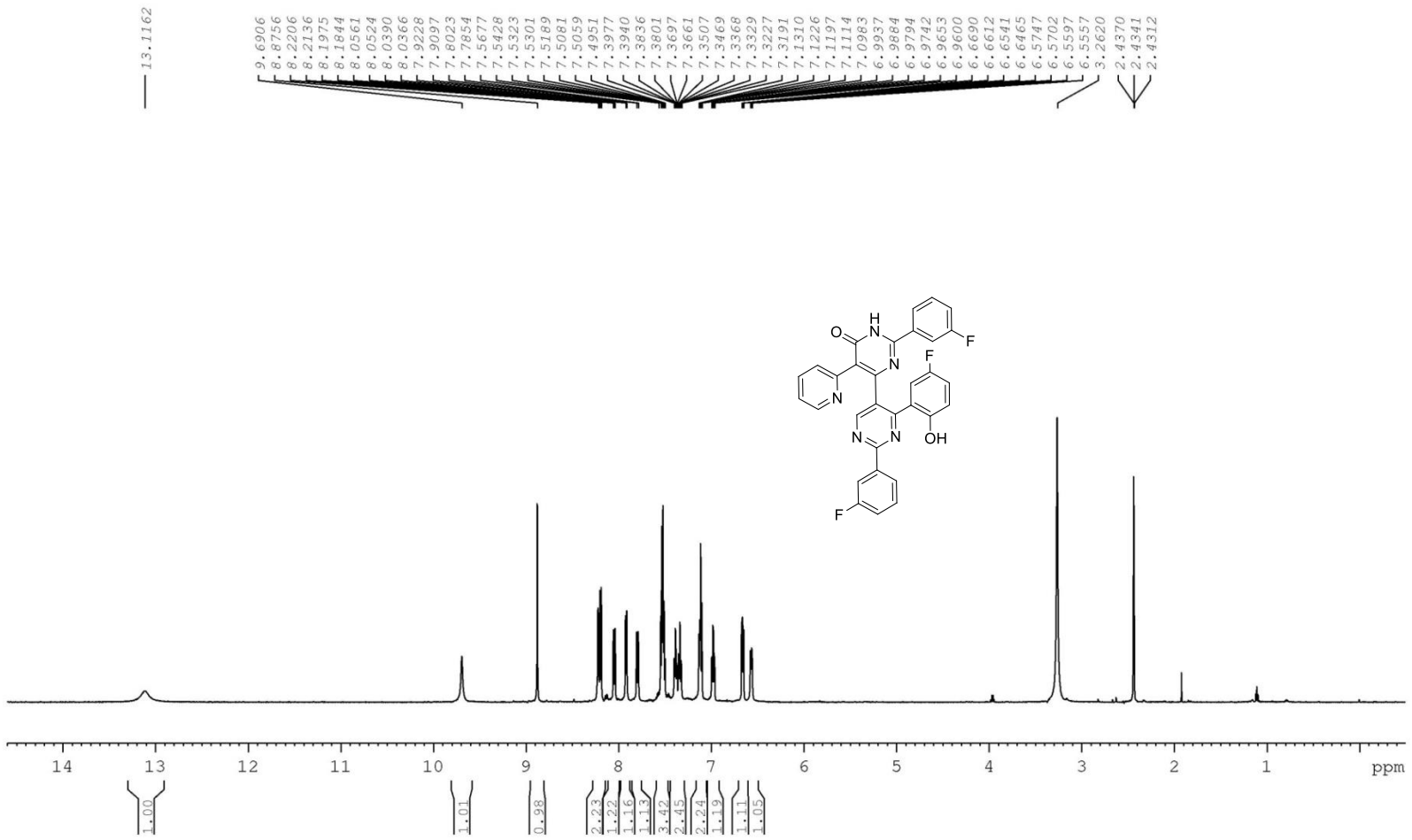


Figure S53. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5l**

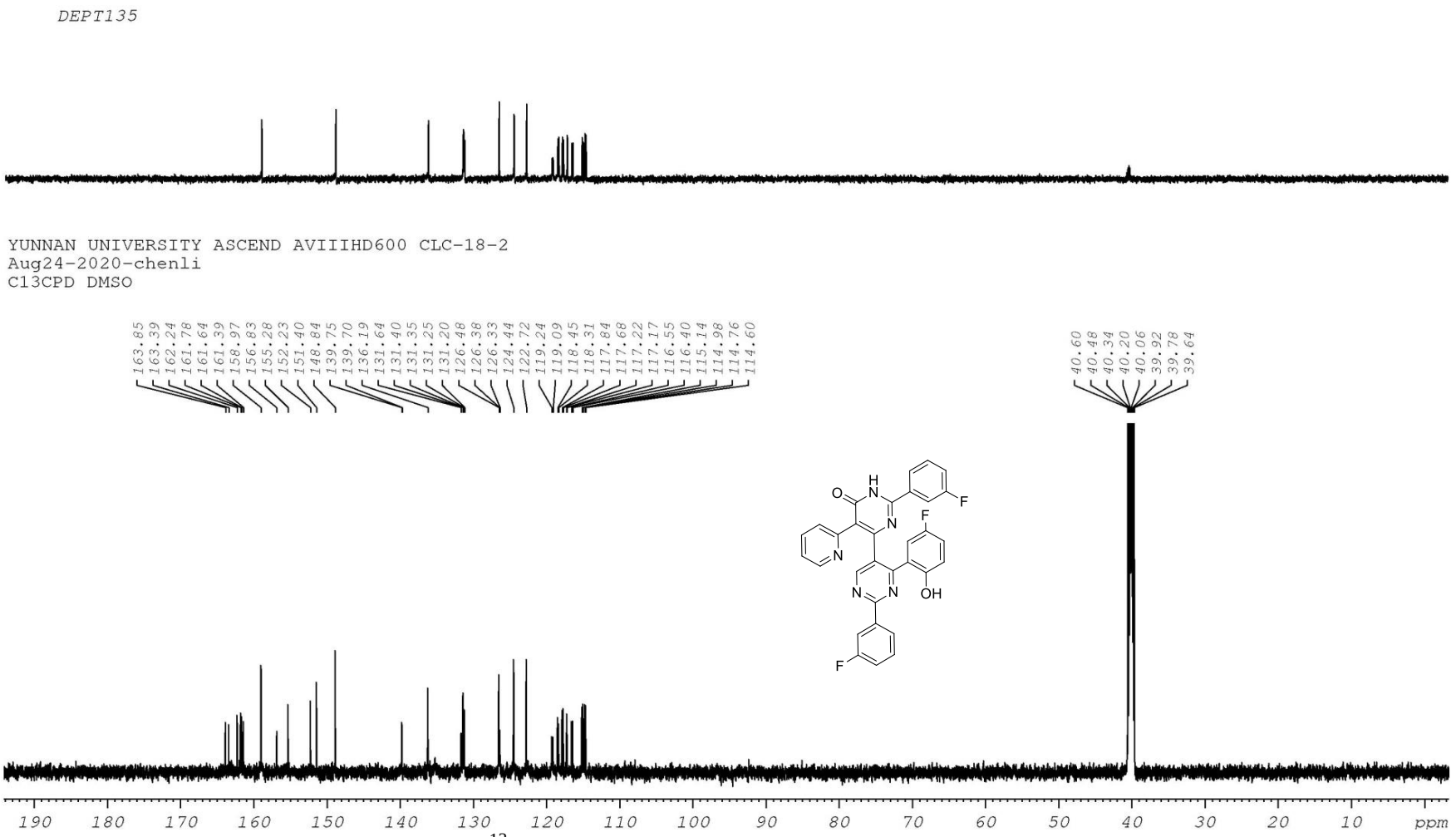


Figure S54. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5l**

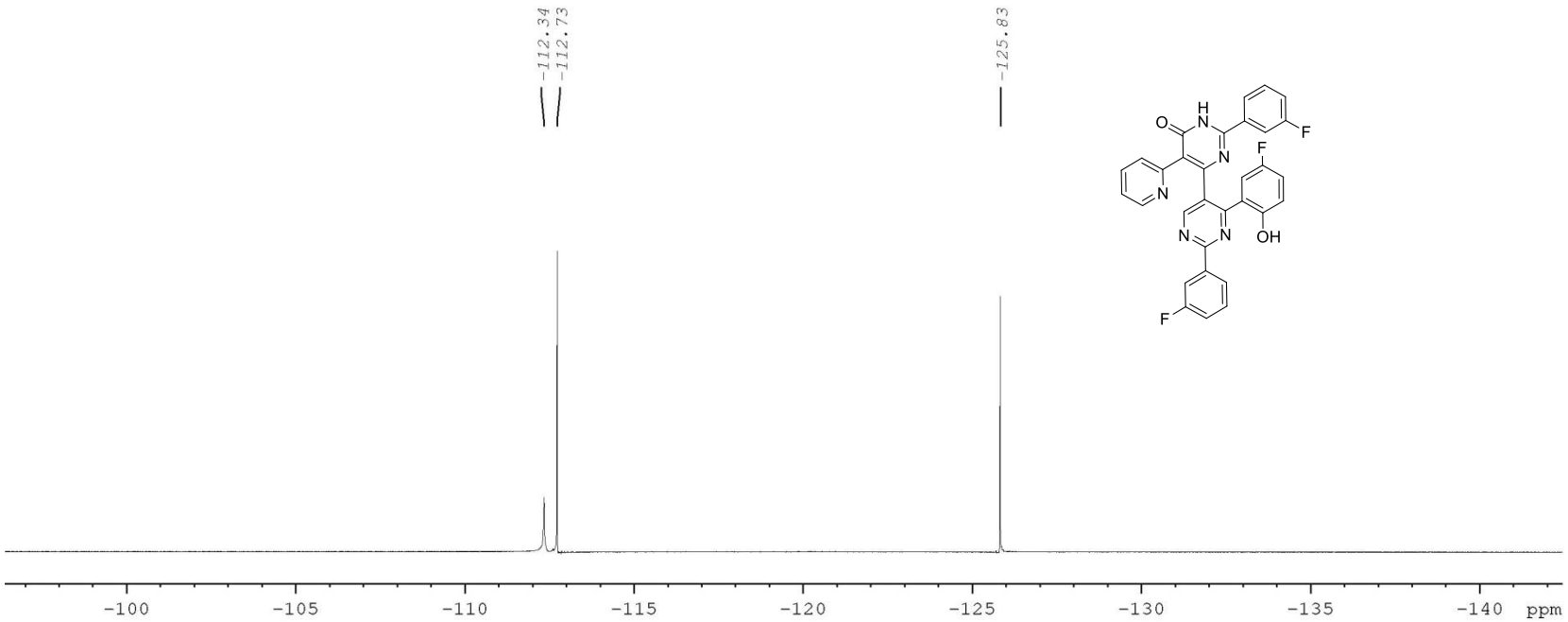


Figure S55. ^{19}F NMR (564 MHz, DMSO-d_6) spectra of compound **5l**

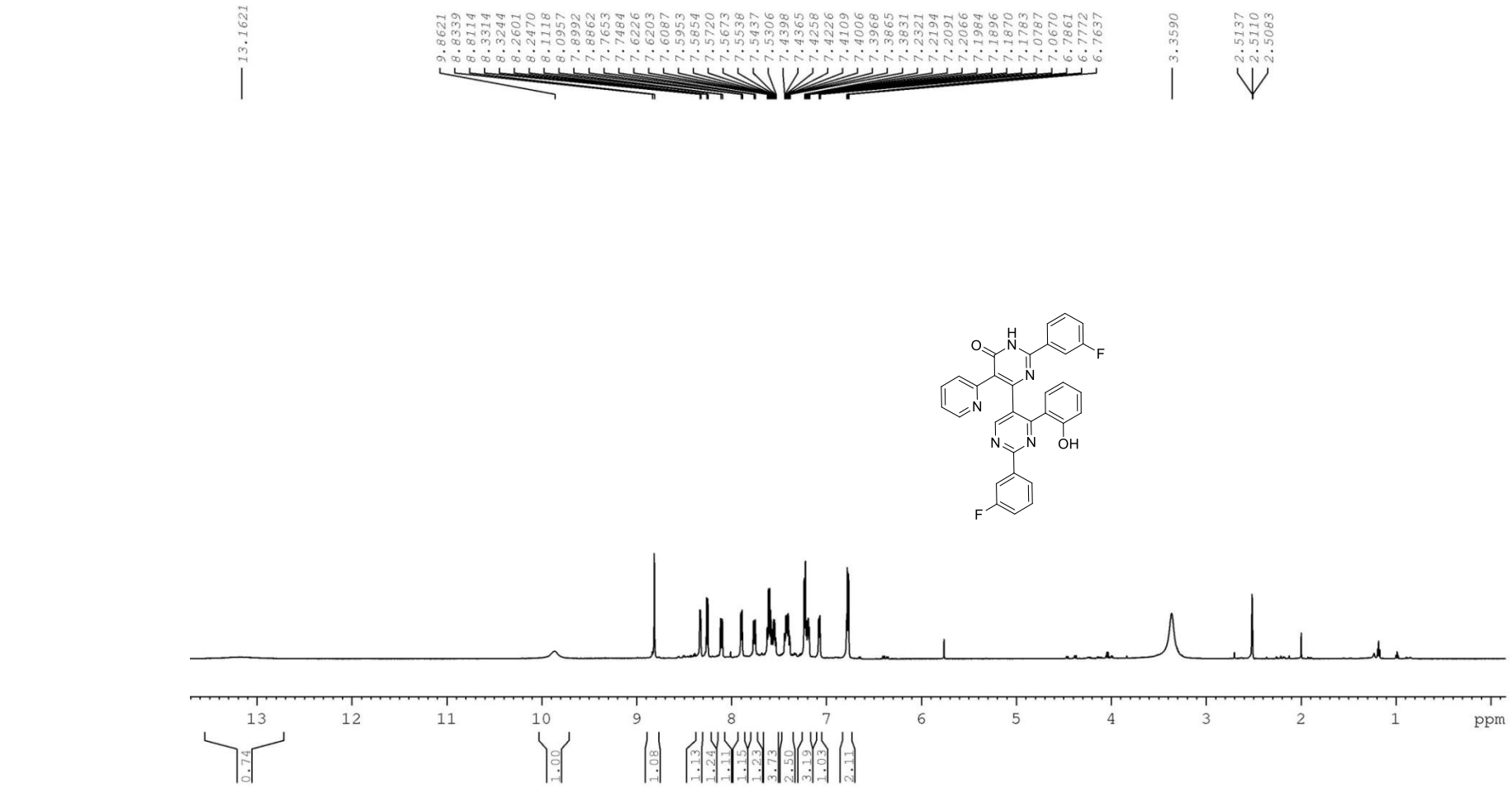


Figure S56. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5m**

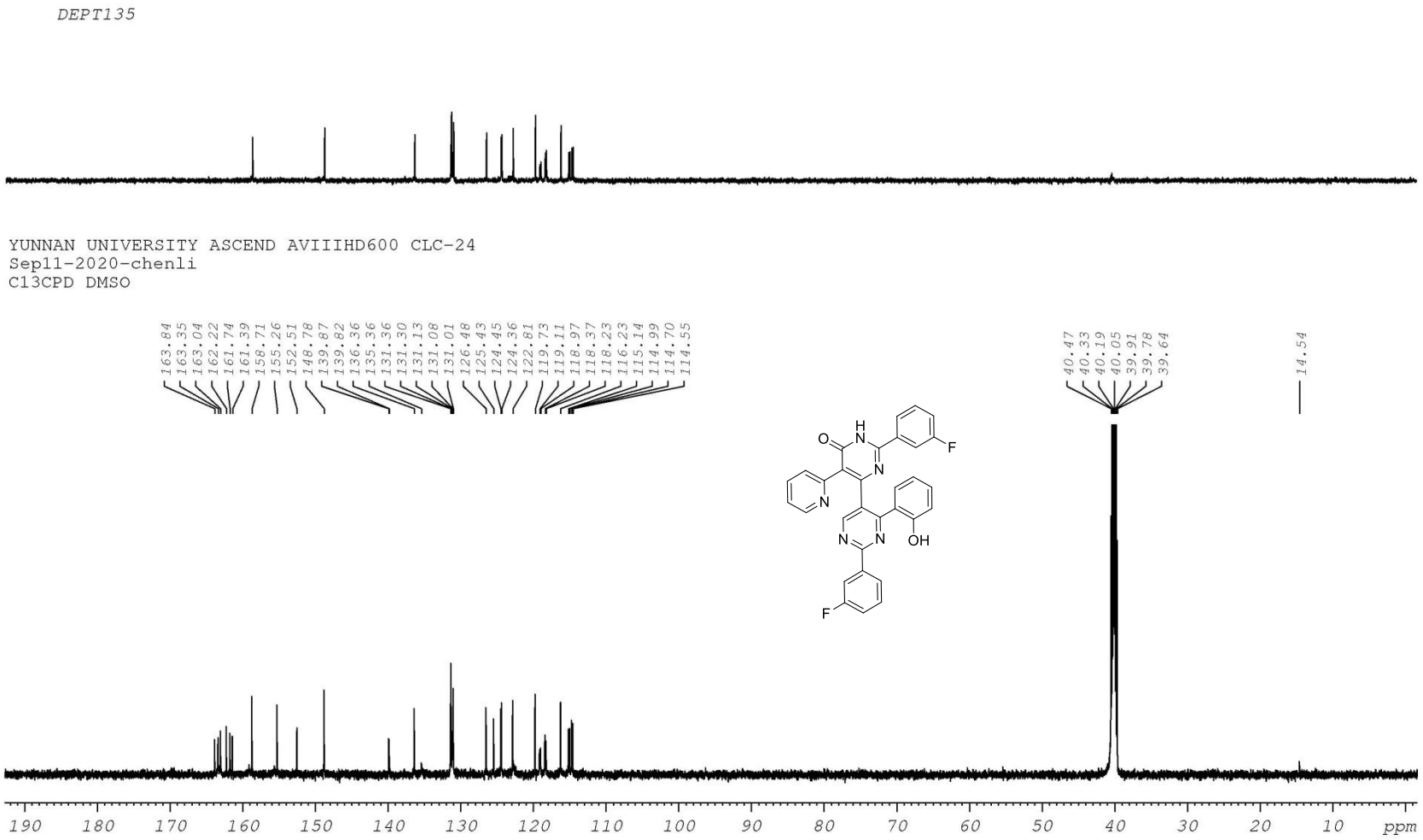


Figure S57. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5m**

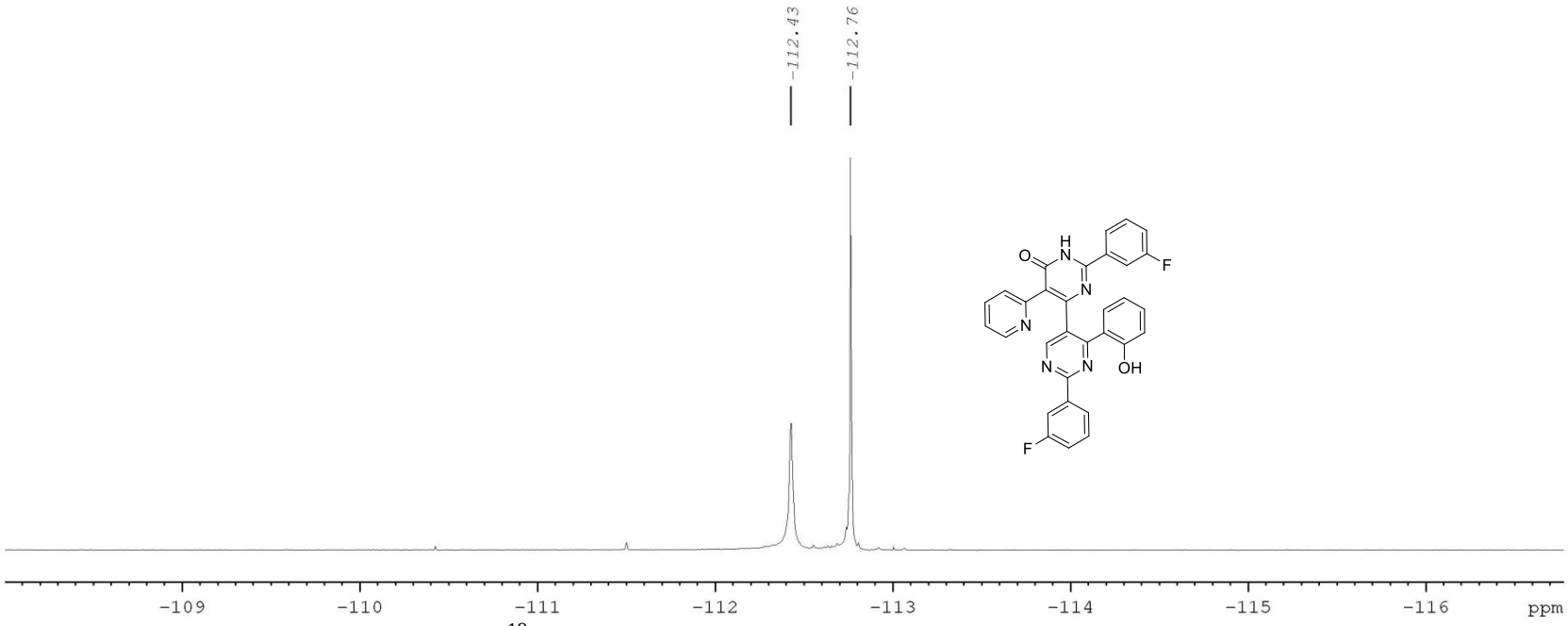


Figure S58. ^{19}F NMR (564 MHz, DMSO-d_6) spectra of compound **5m**

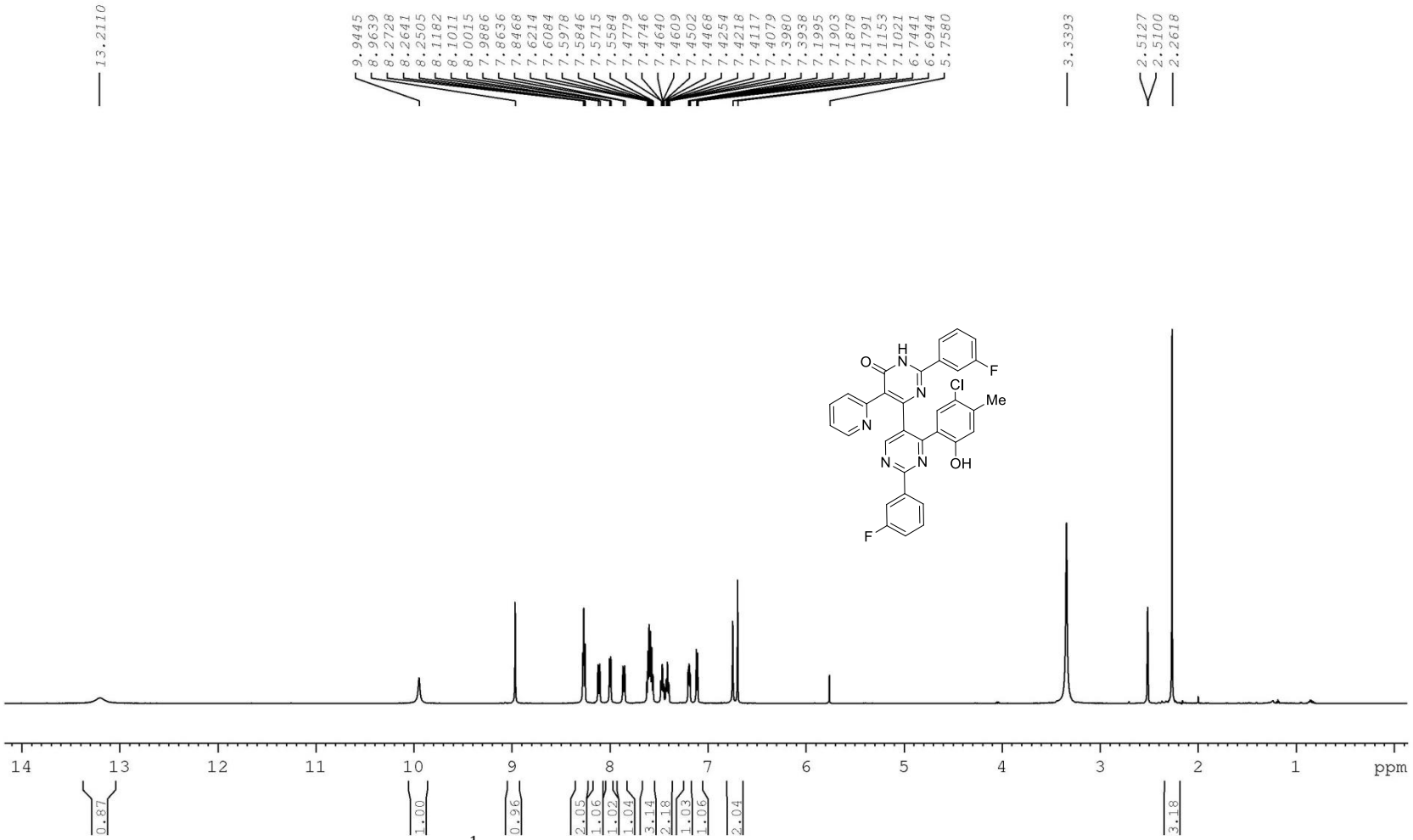


Figure S59. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5n**

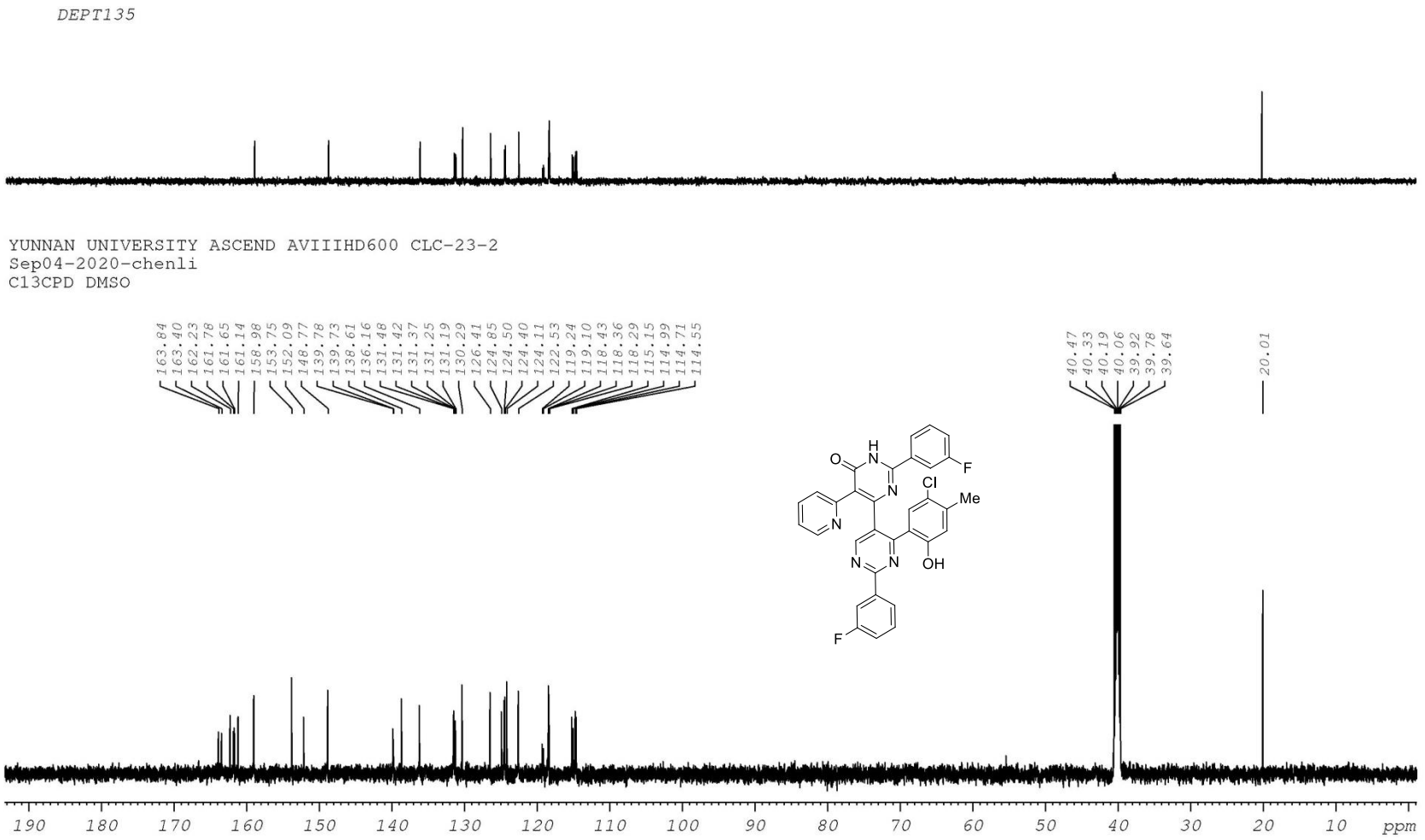


Figure S60. ^{13}C NMR (**150** MHz, DMSO-d_6) spectra of compound **5n**

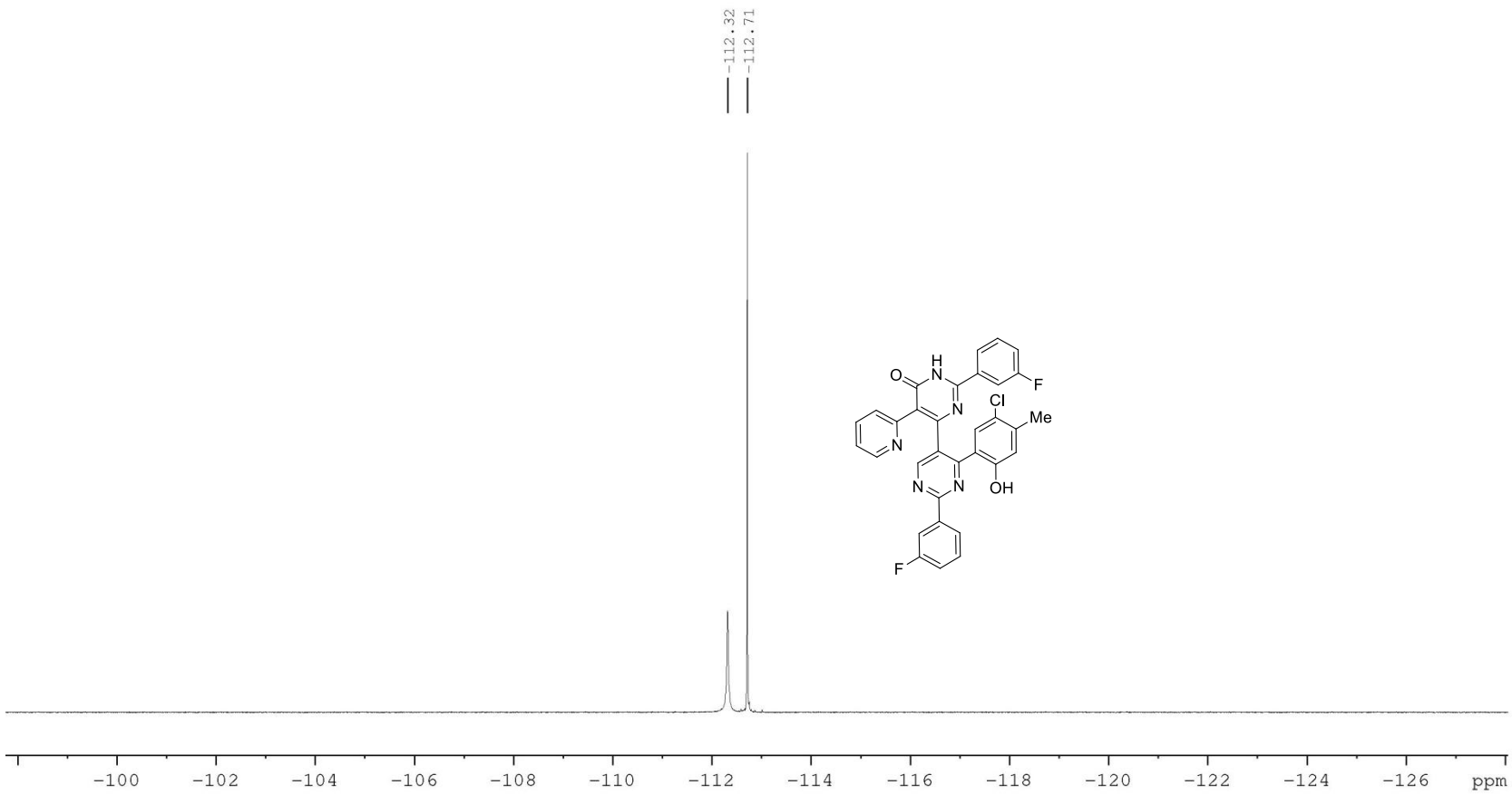


Figure S61. ^{19}F NMR (564 MHz, DMSO-d_6) spectra of compound **5n**

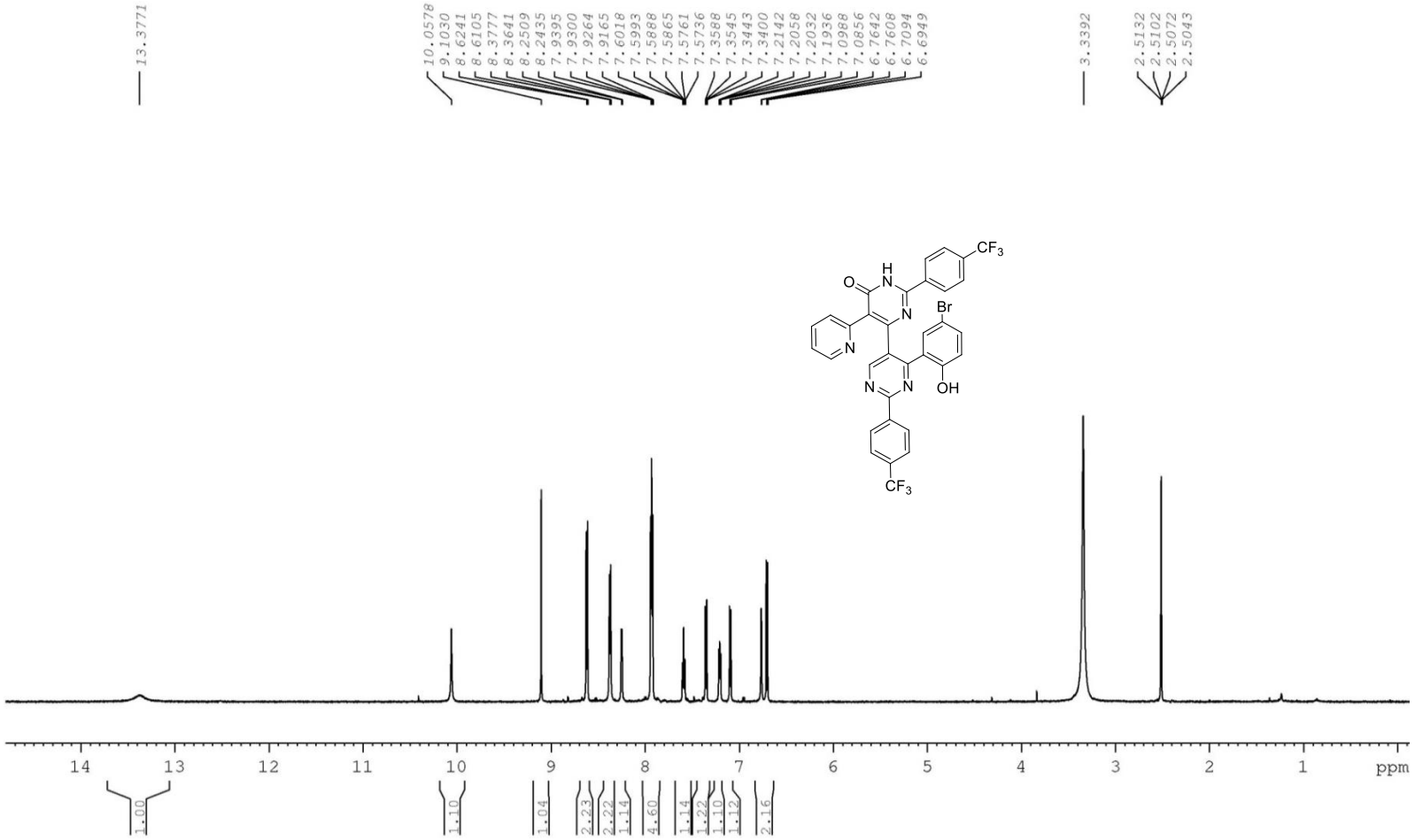


Figure S62. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5o**

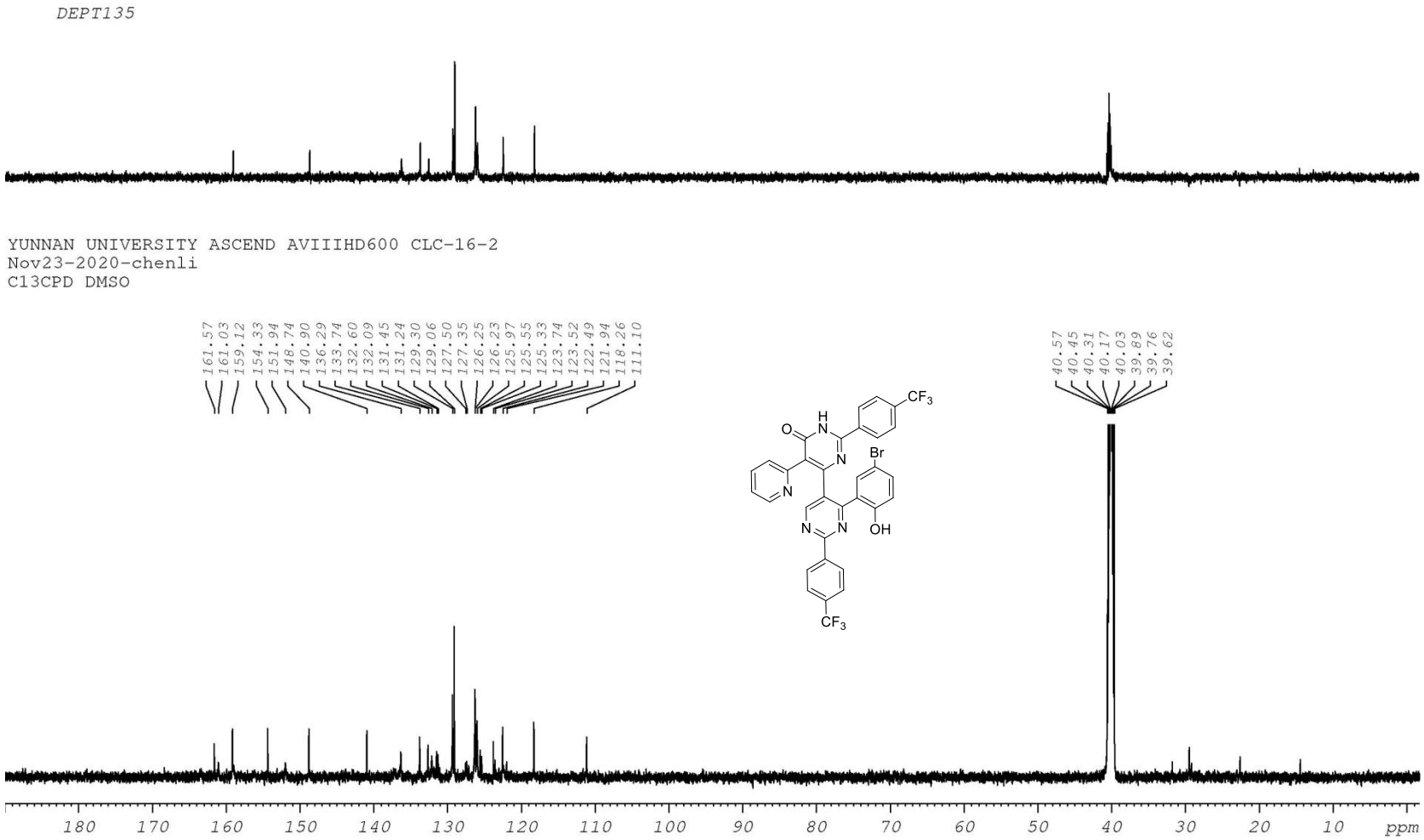


Figure S63. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5o**

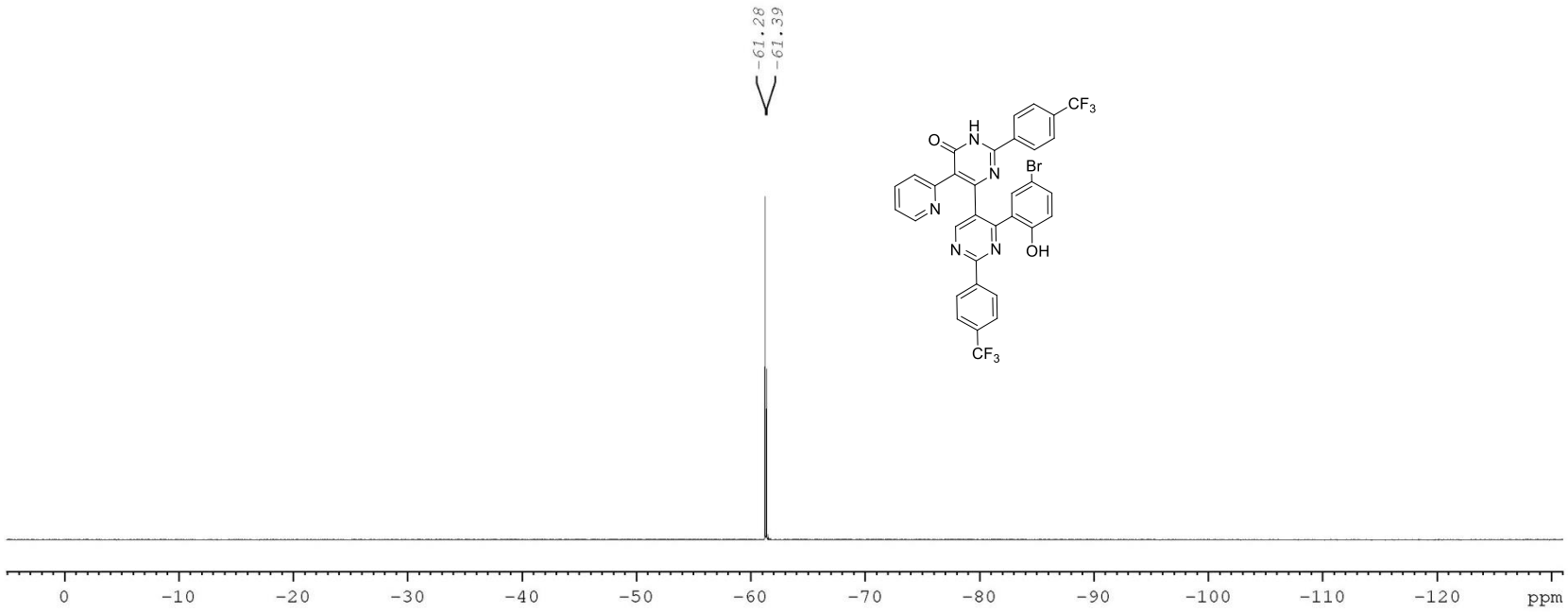


Figure S64. ^{19}F NMR (564 MHz, DMSO-d_6) spectra of compound **5o**

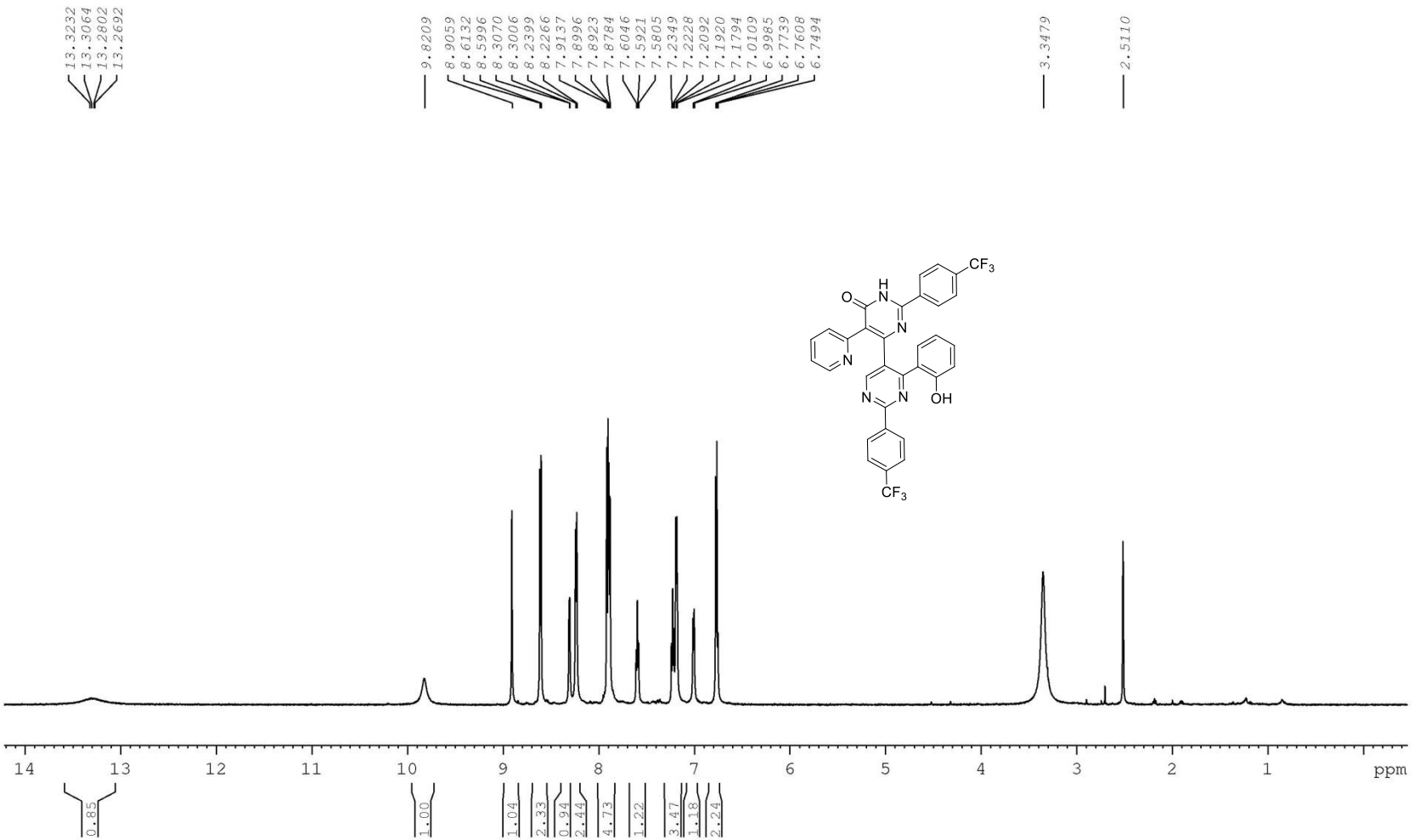


Figure S65. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5p**

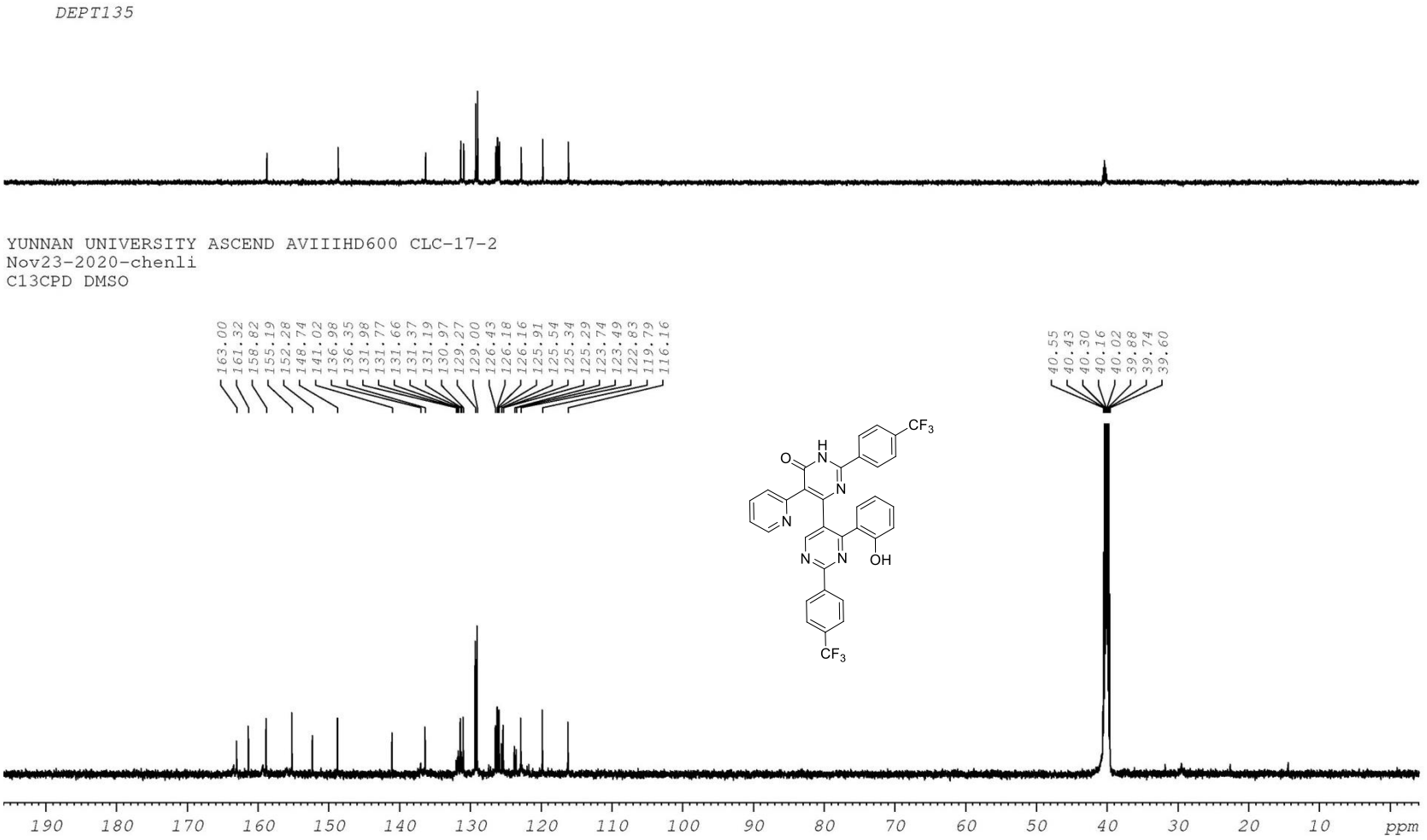


Figure S66. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5p**

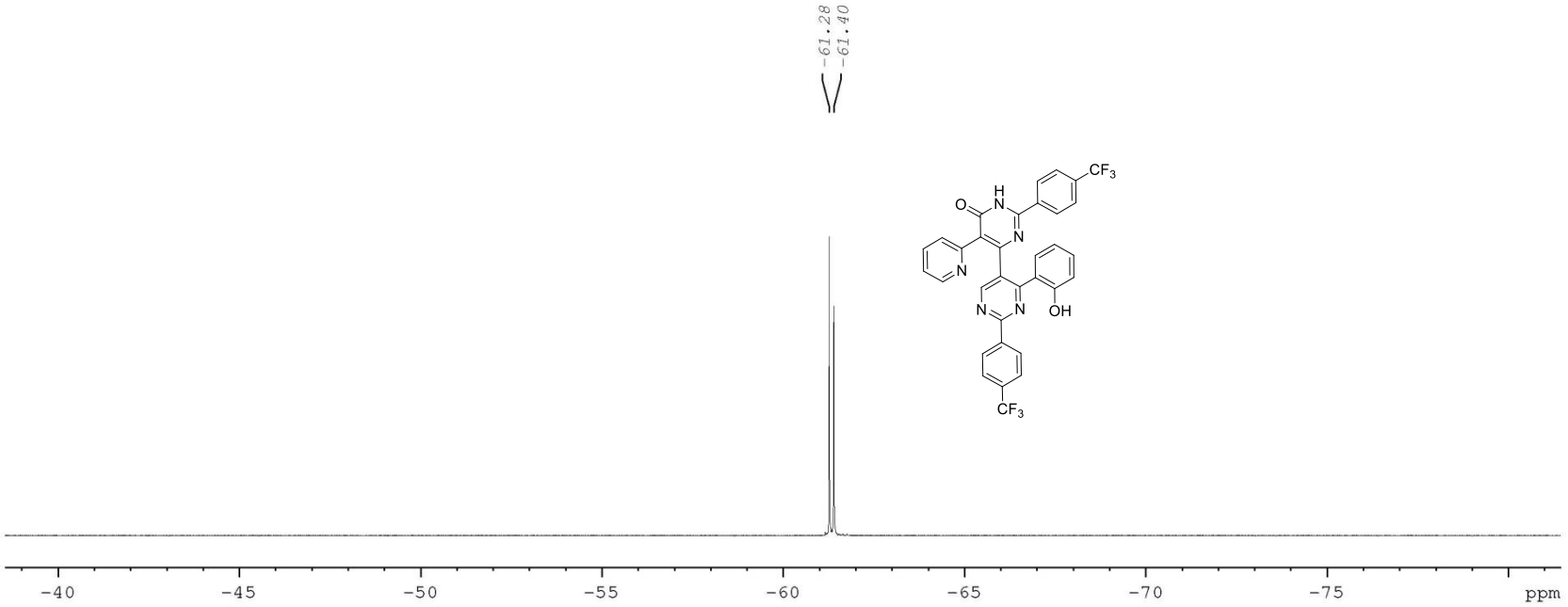


Figure S67. ^{19}F NMR (564 MHz, DMSO-d_6) spectra of compound **5p**

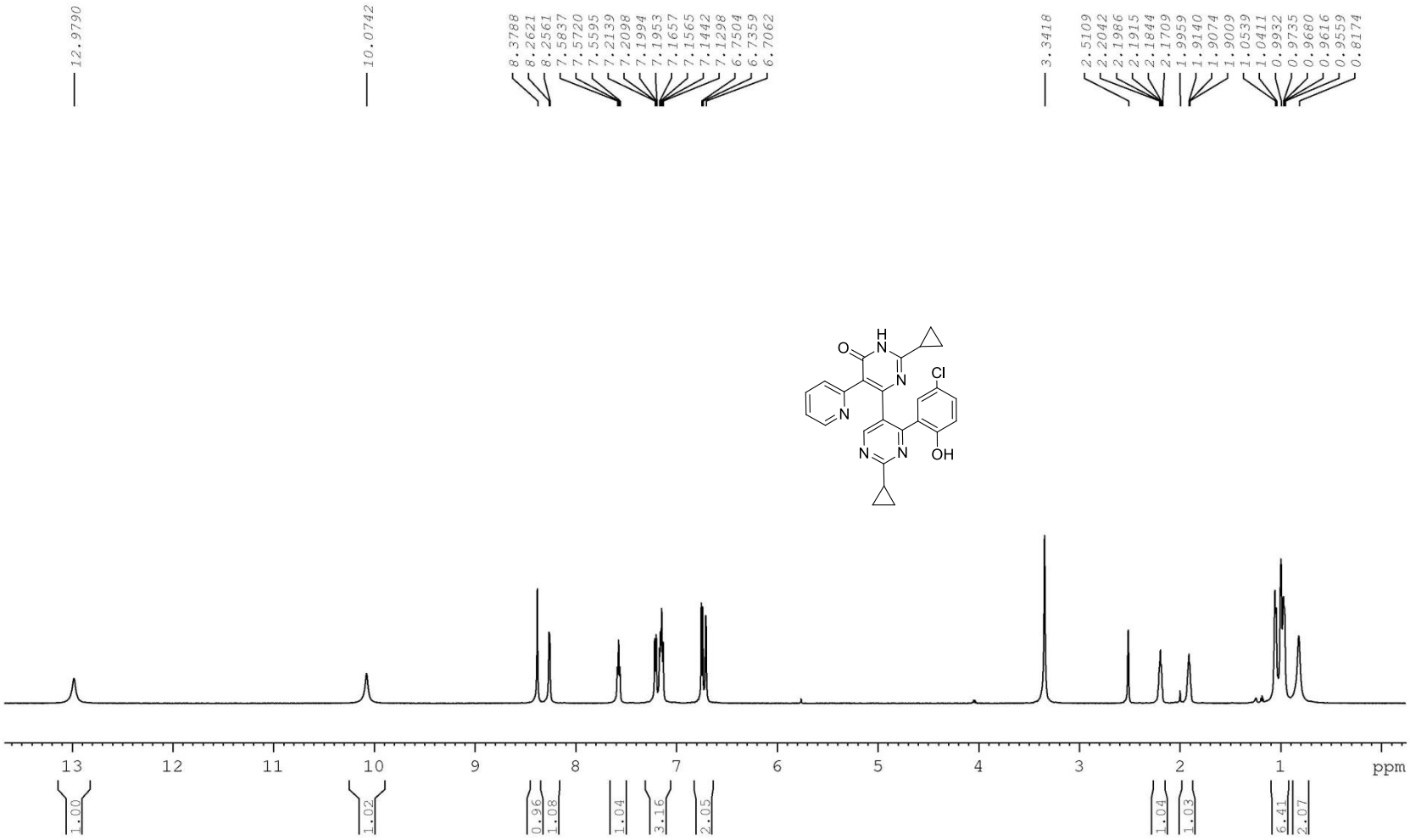


Figure S68. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5q**

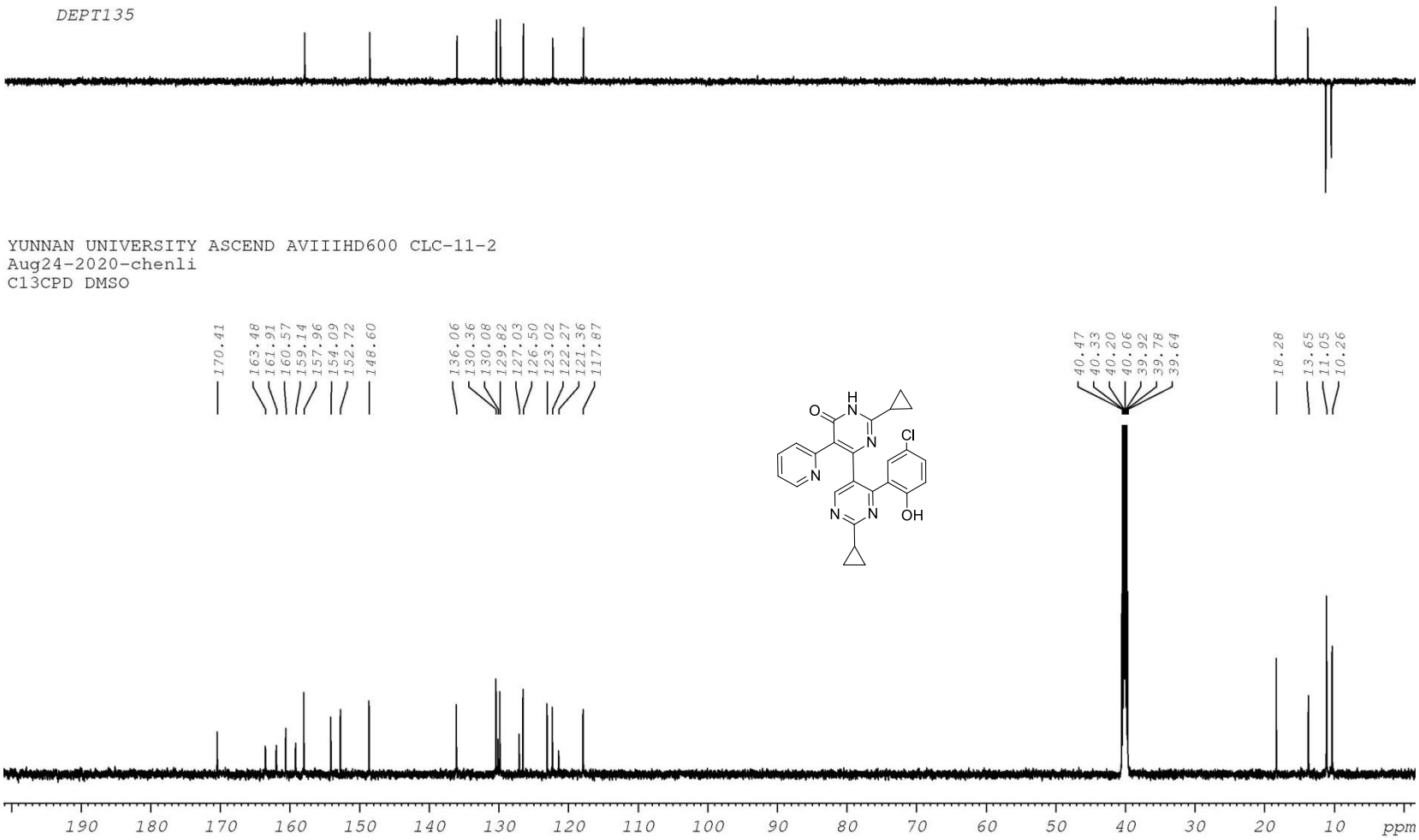


Figure S69. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5q**

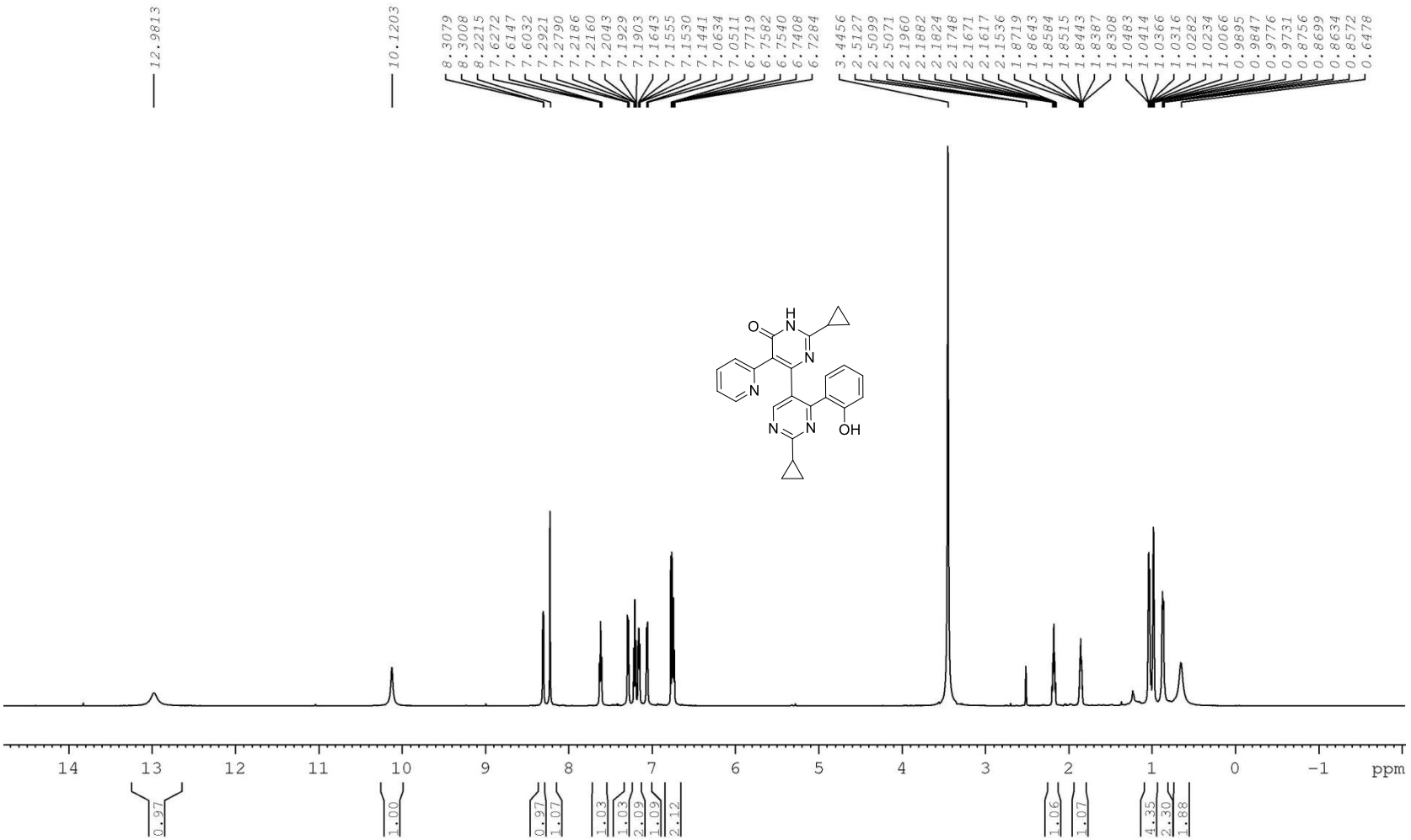


Figure S70. ^{1}H NMR (564 MHz, DMSO-d_6) spectra of compound **5r**

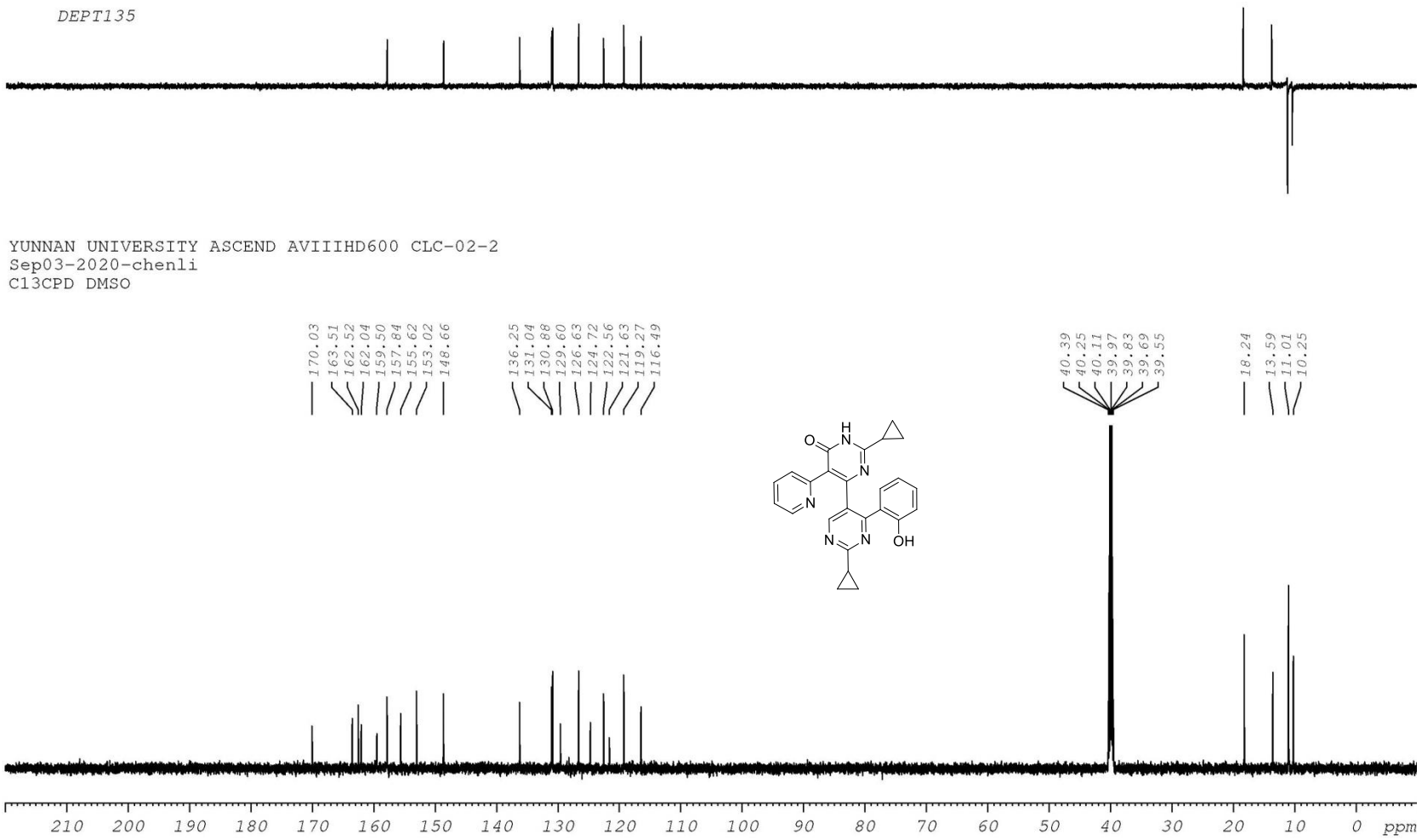


Figure S71. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5r**

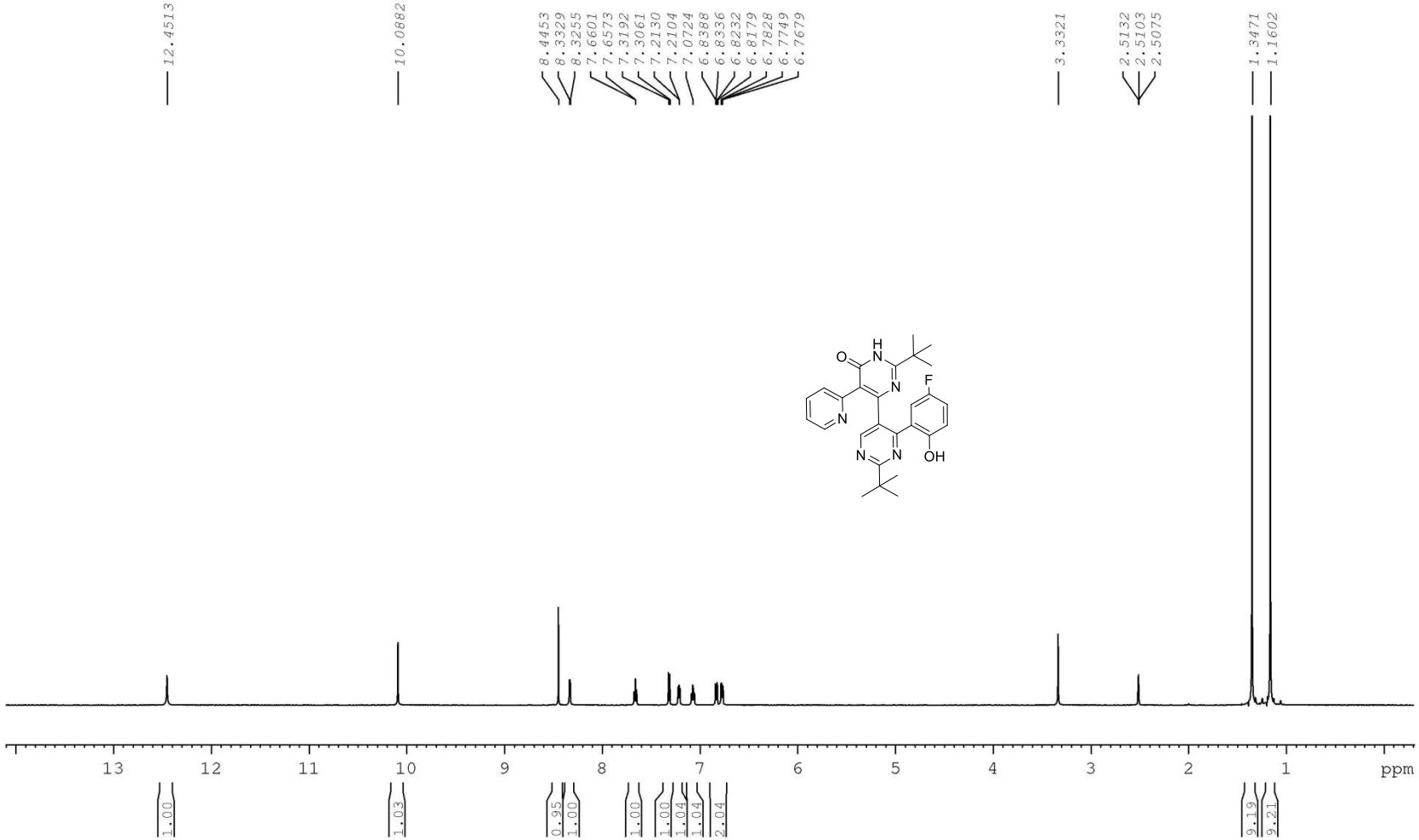


Figure S72. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5s**

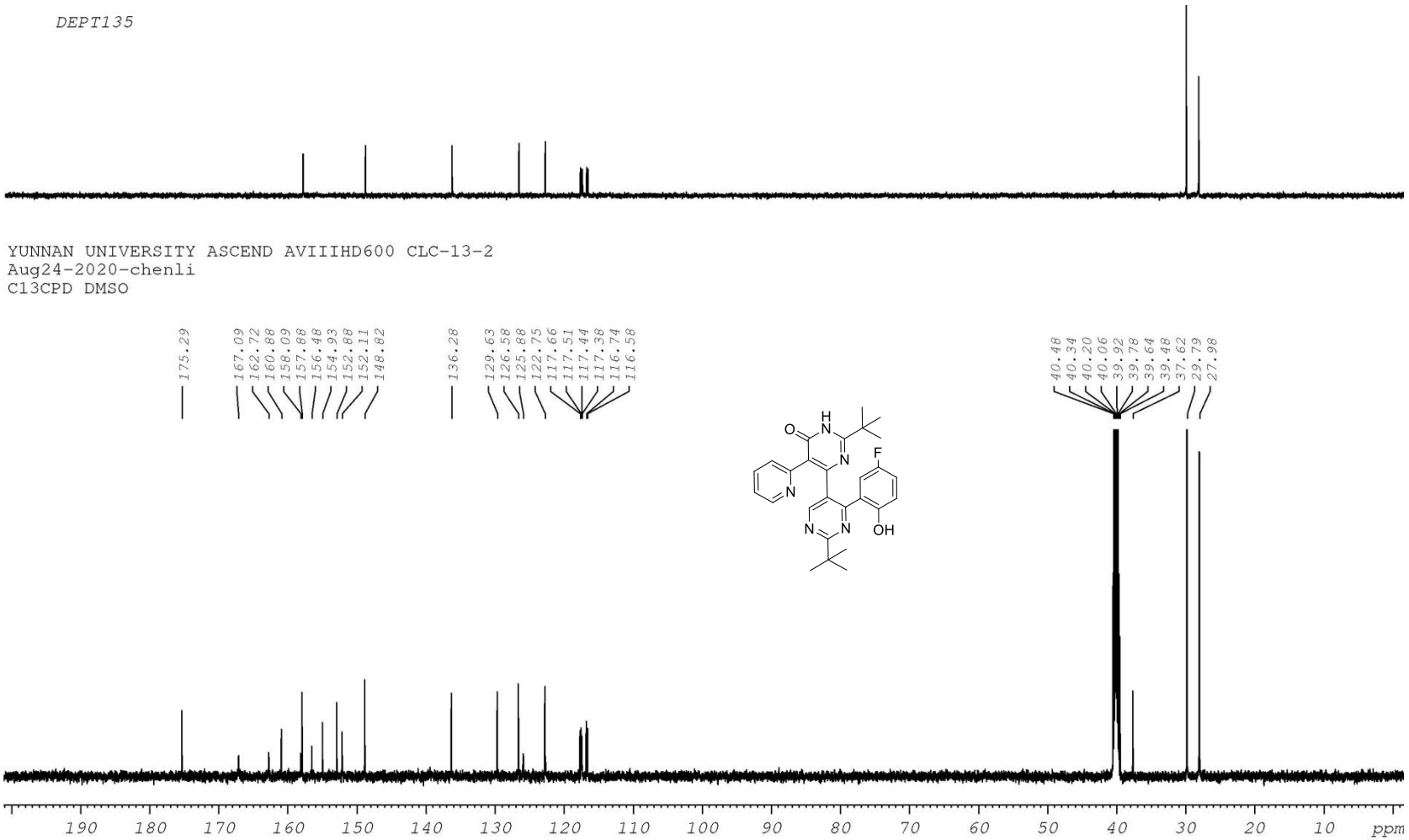


Figure S73. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5s**

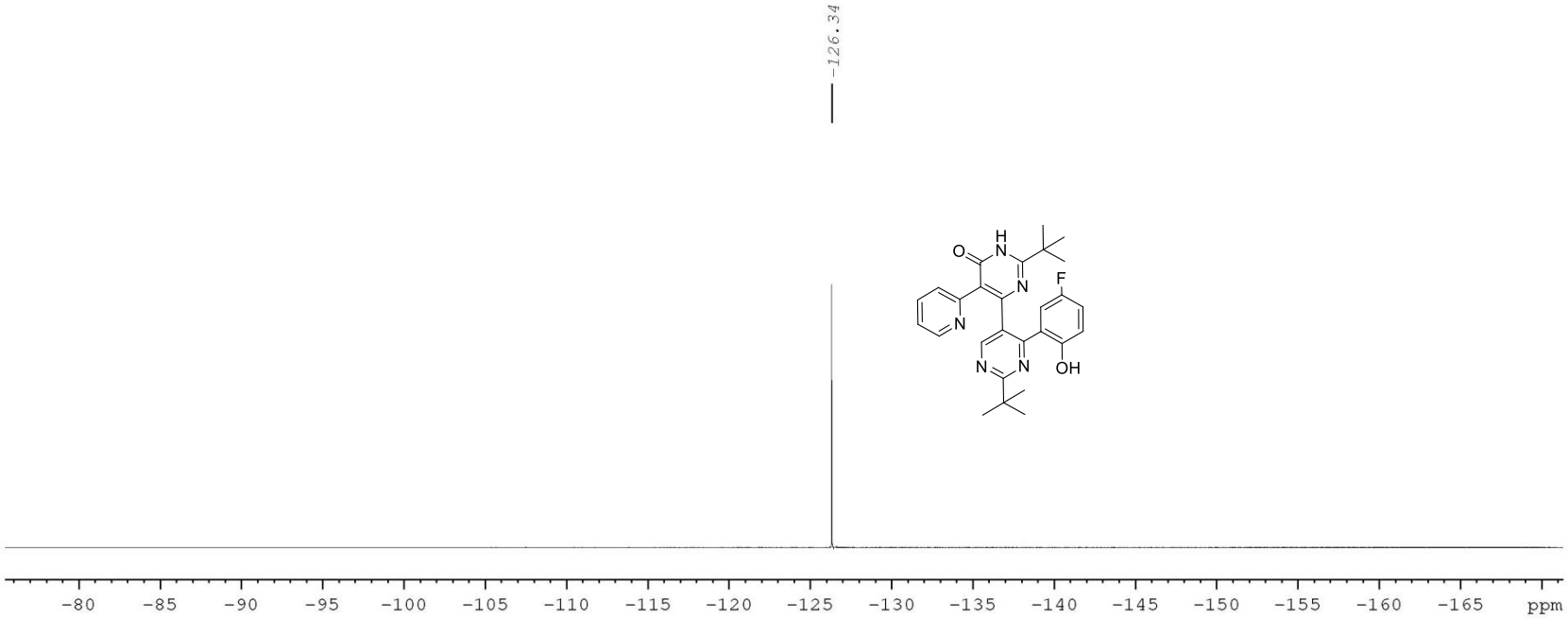


Figure S74. ^{19}F NMR (564 MHz, DMSO-d_6) spectra of compound **5s**

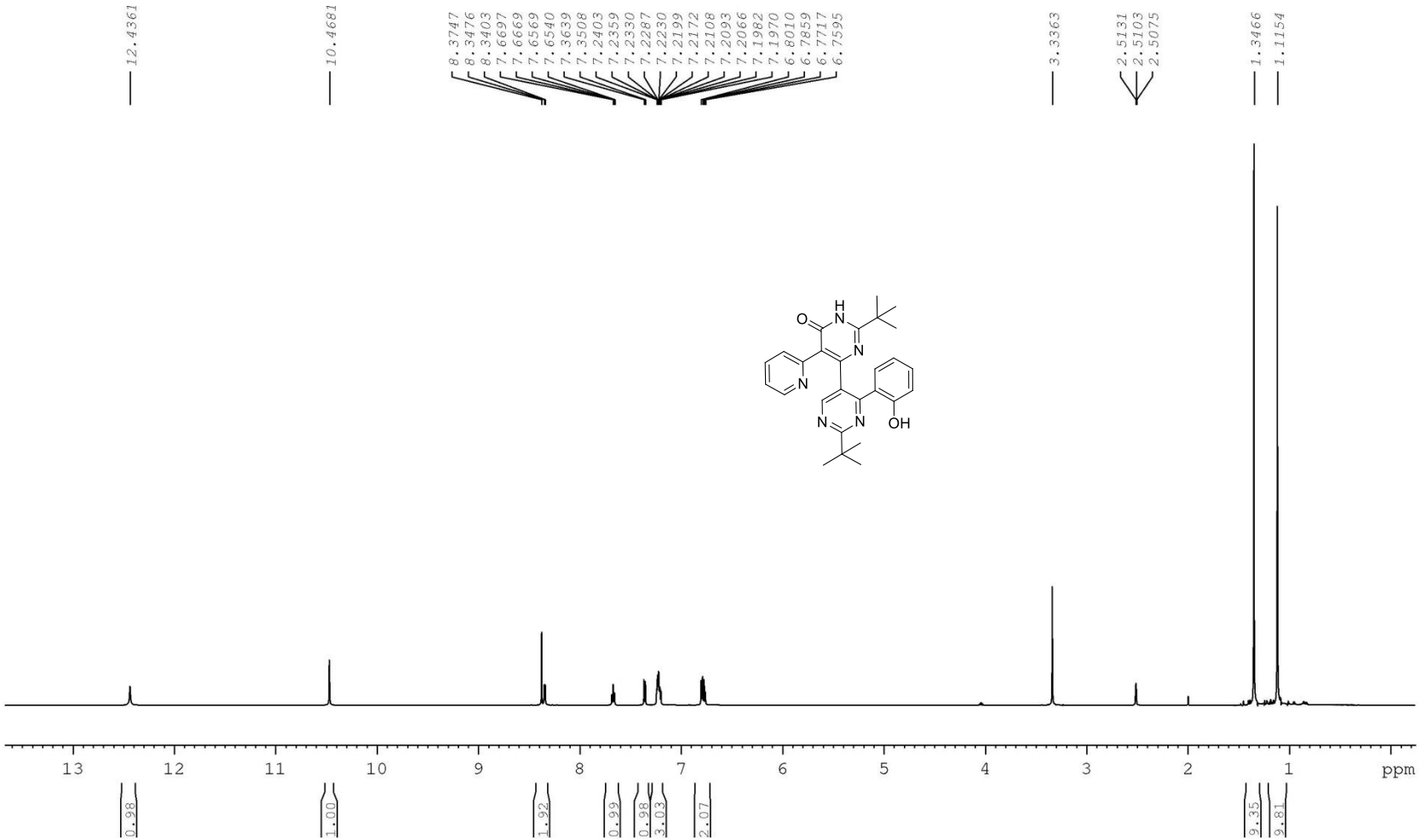


Figure S75. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5t**

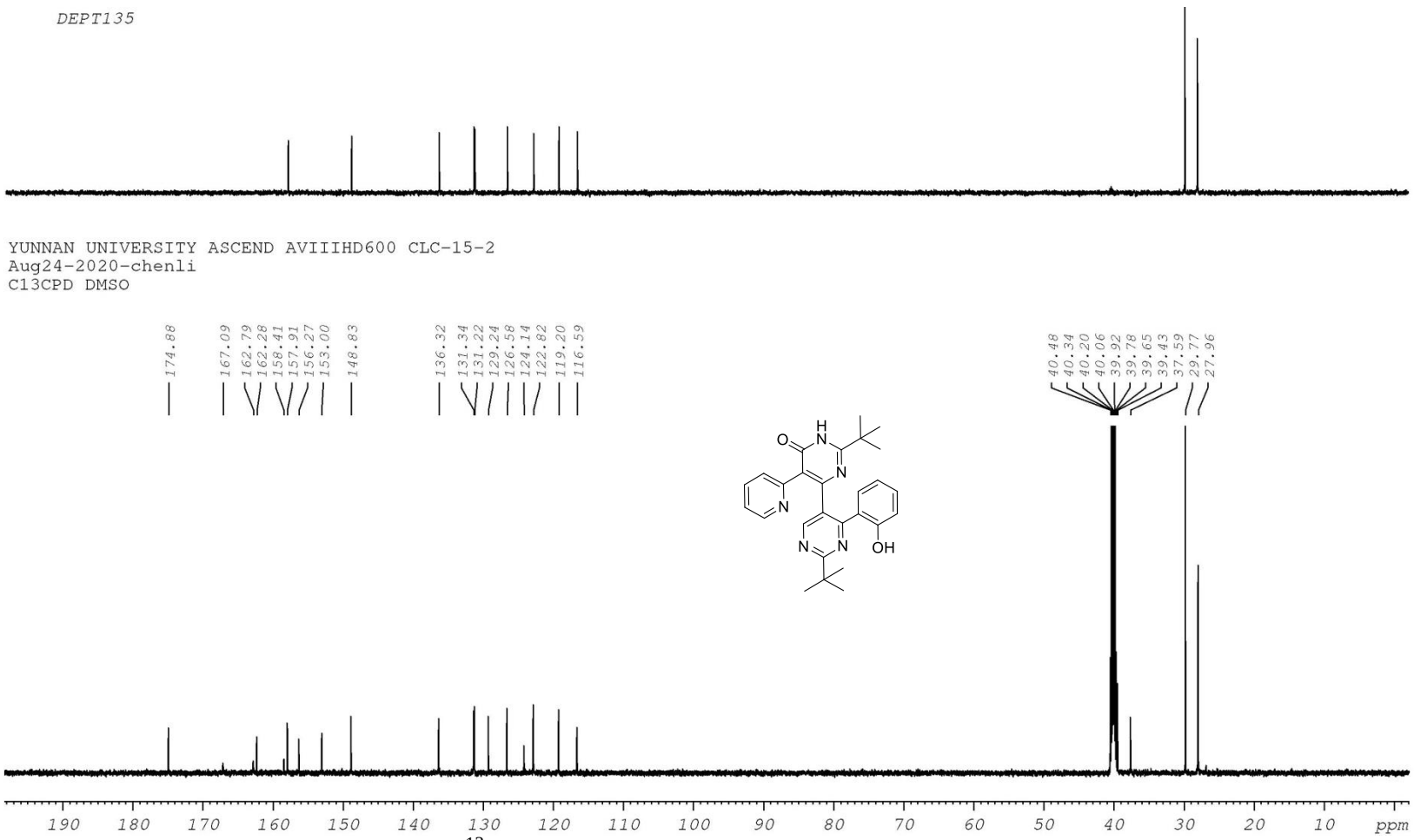


Figure S76. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5t**

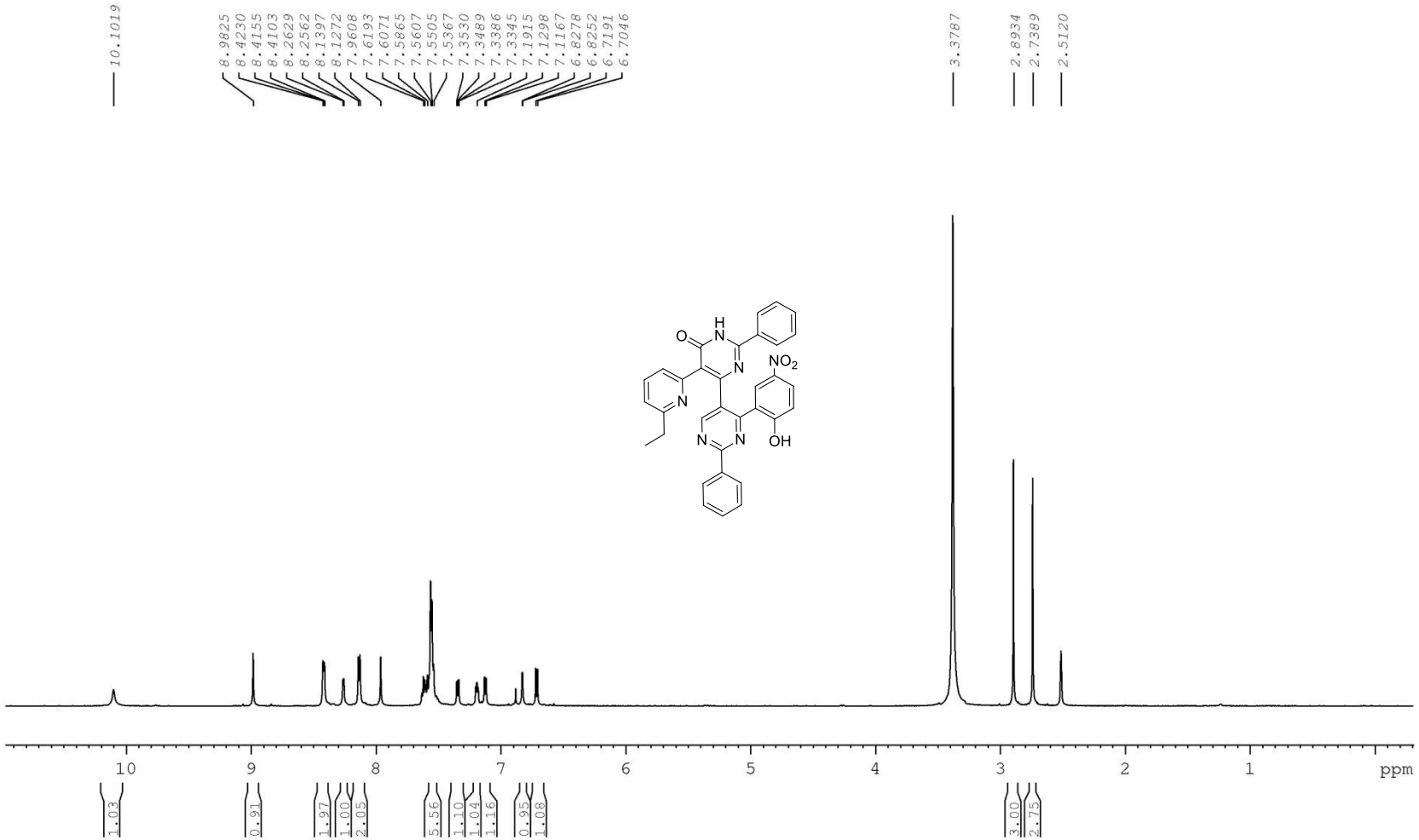


Figure S77. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5u**

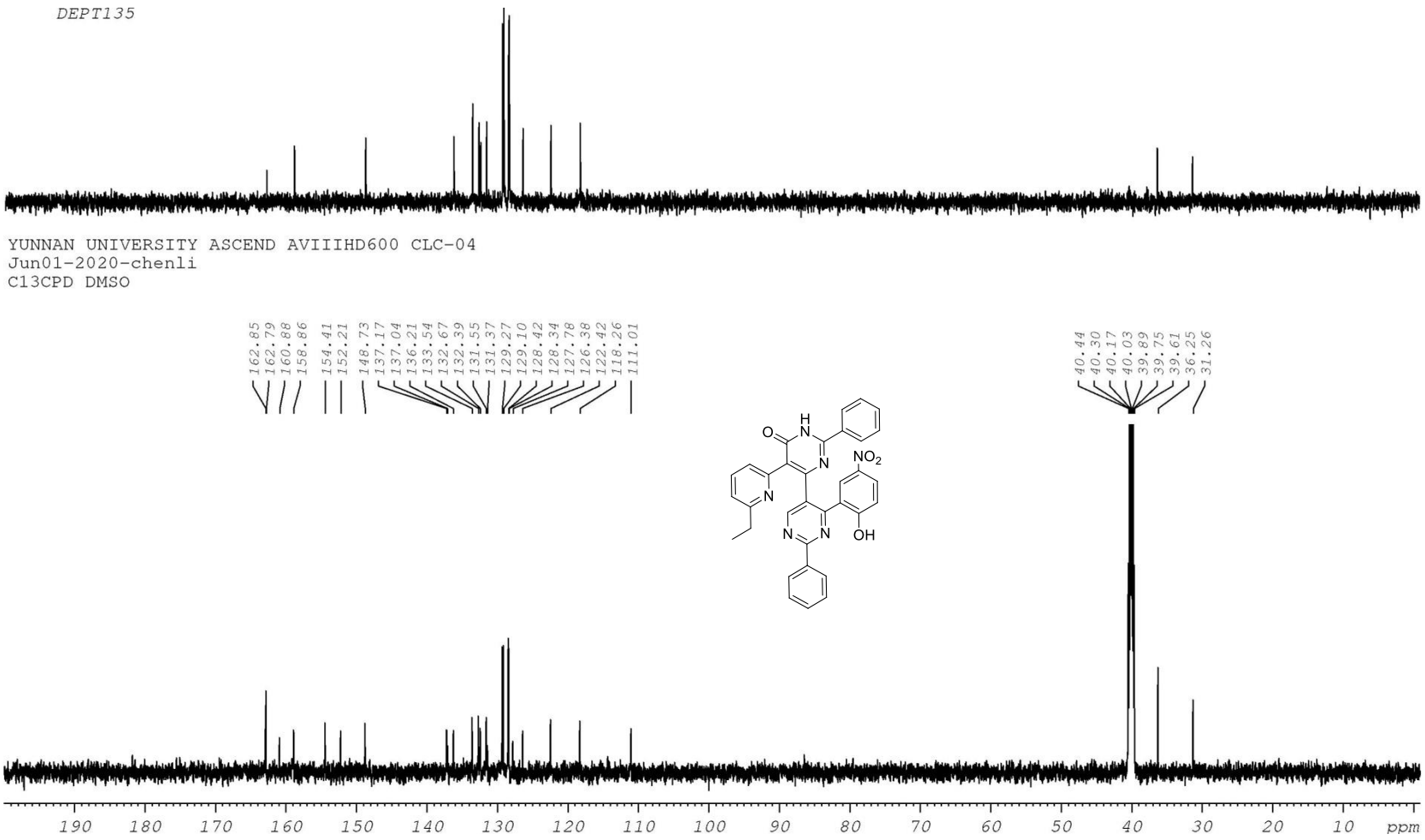


Figure S78. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5u**

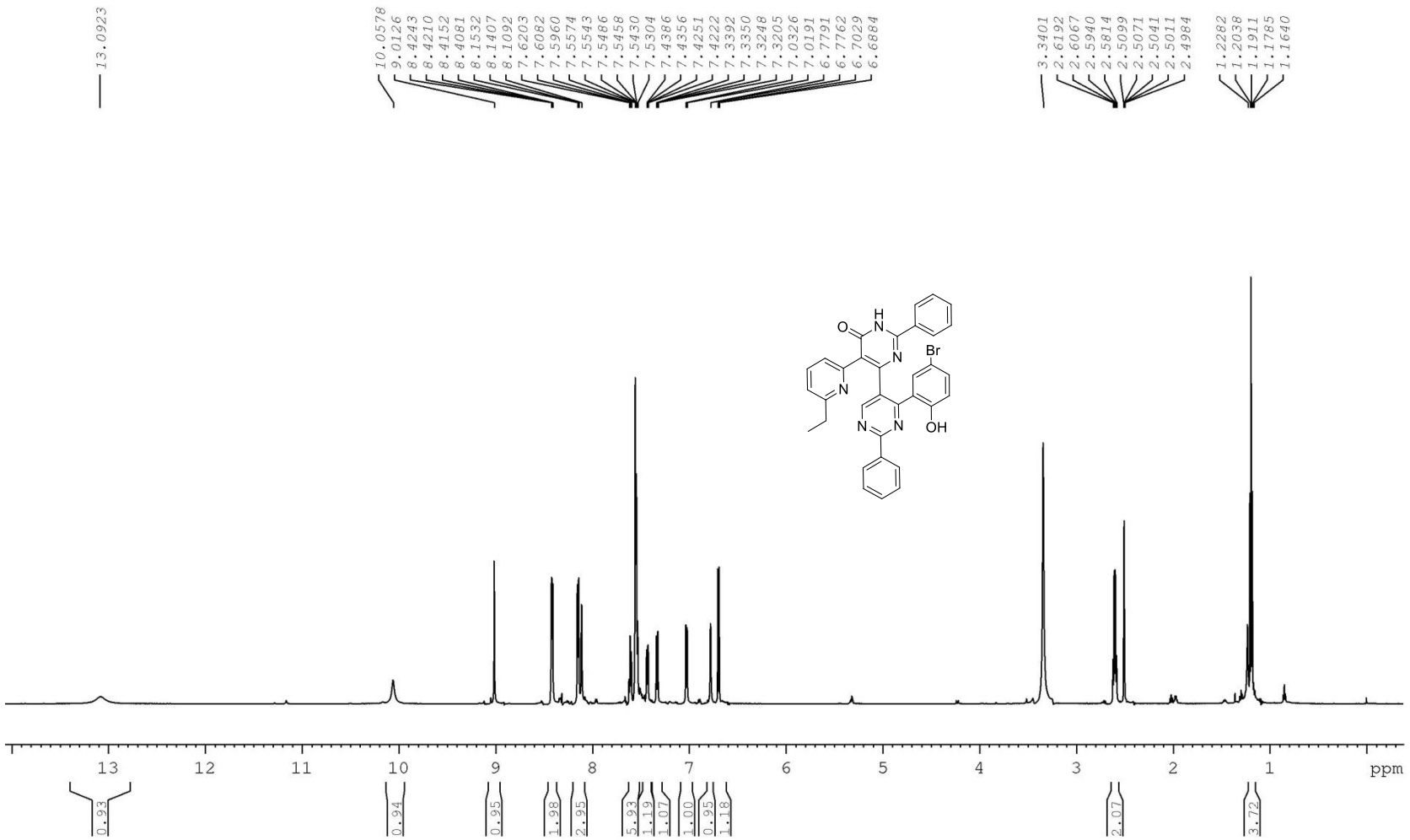


Figure S79. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5v**

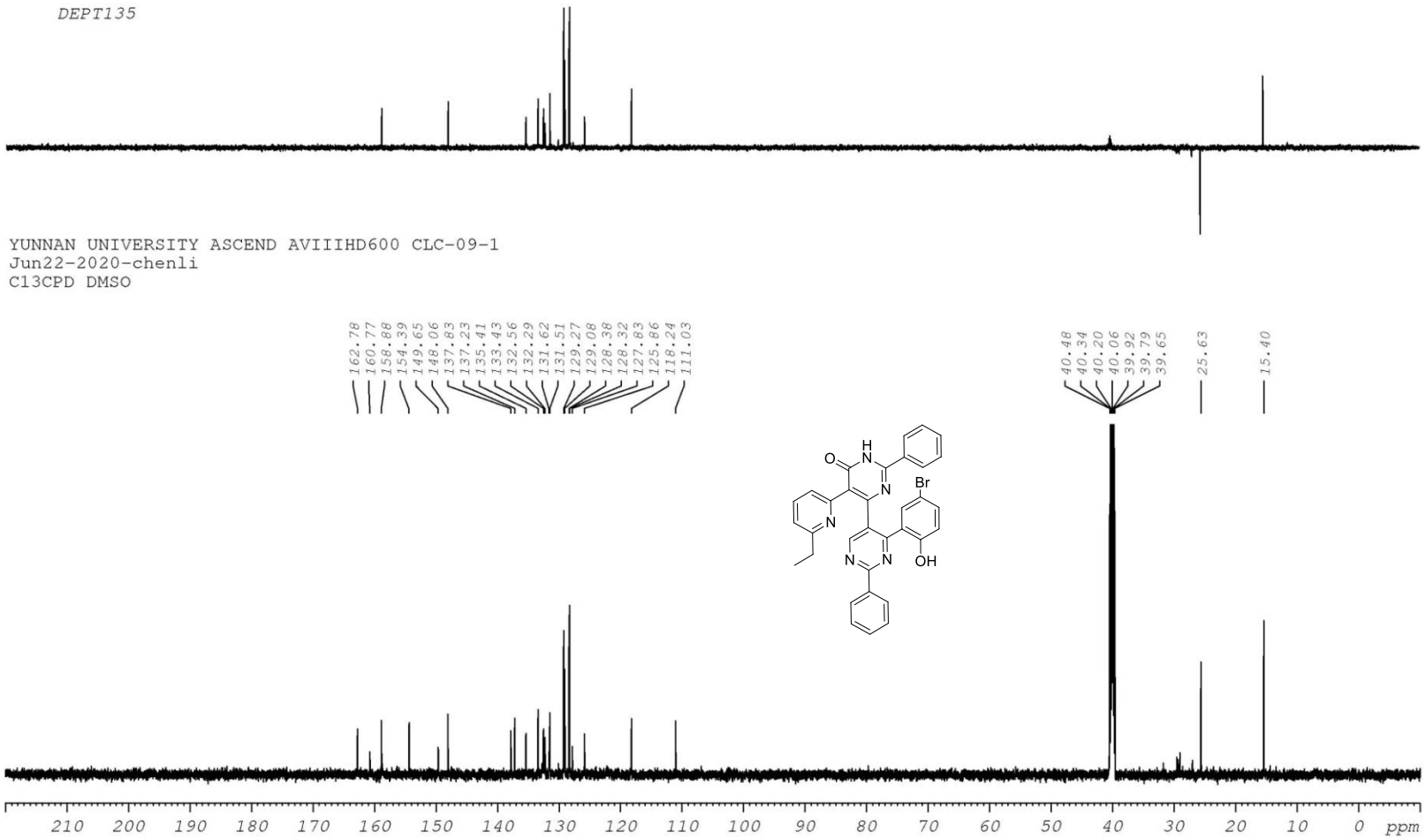


Figure S80. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5v**

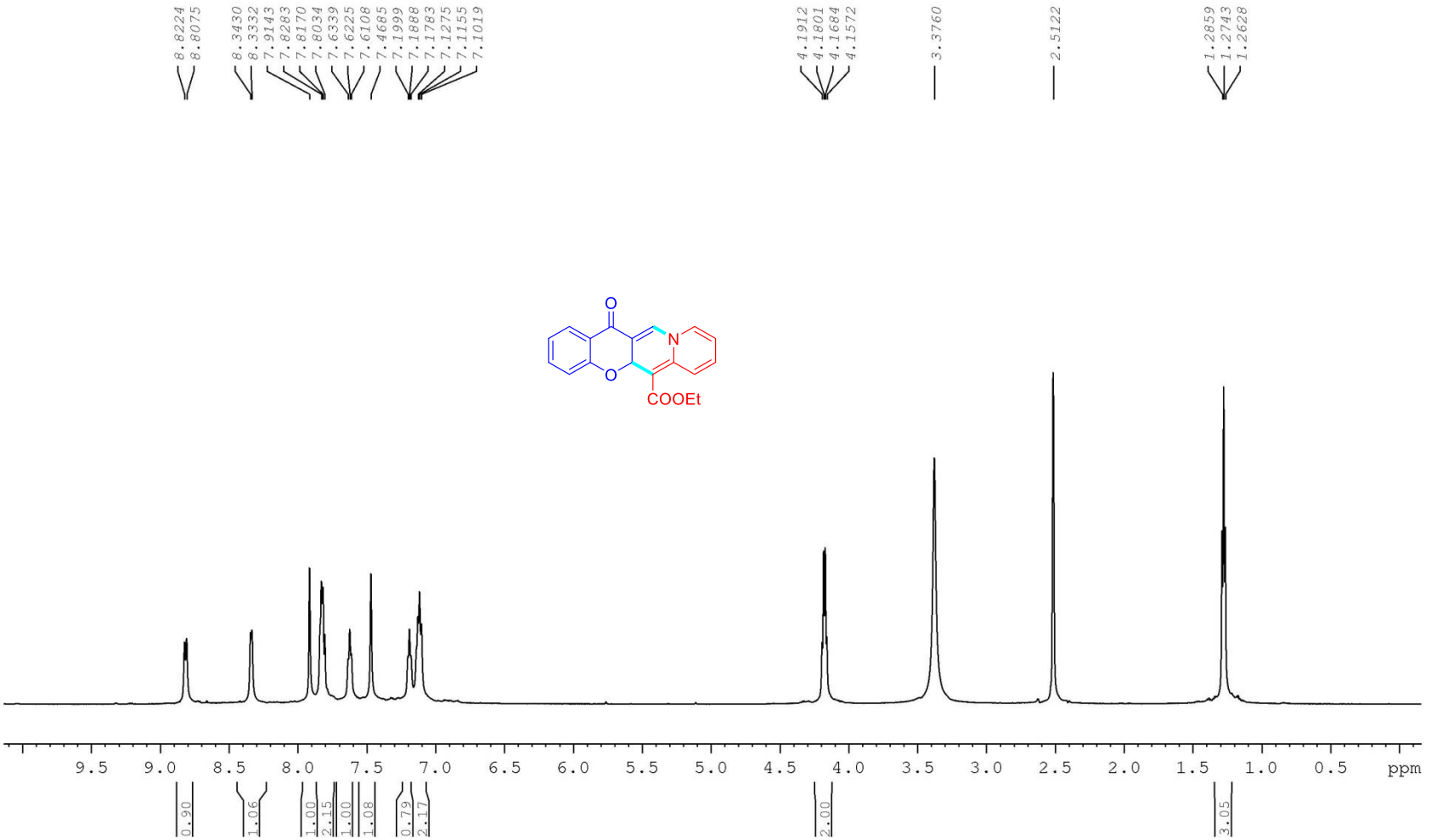


Figure S81. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of intermediate **9f**

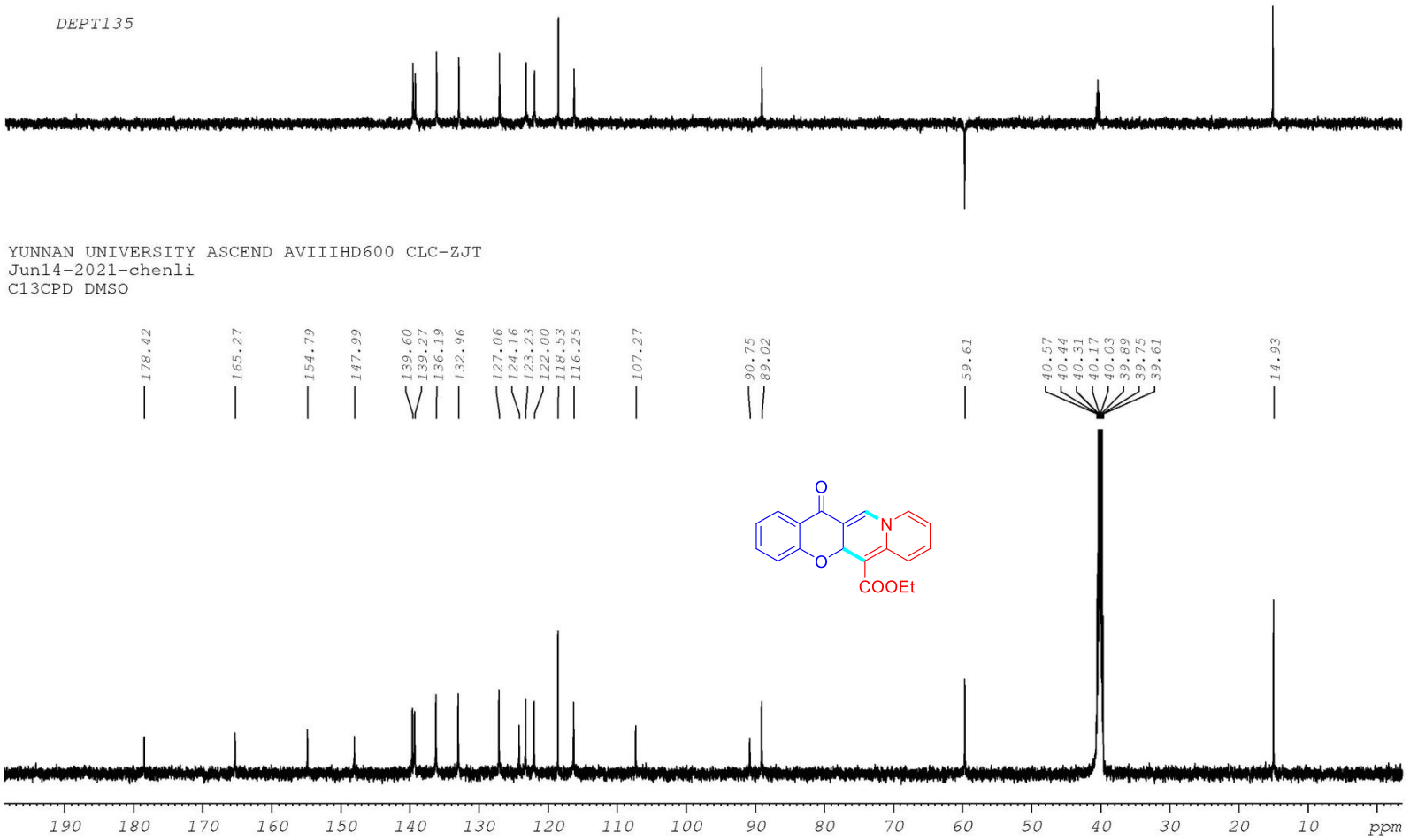


Figure S82. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of intermediate **9f**

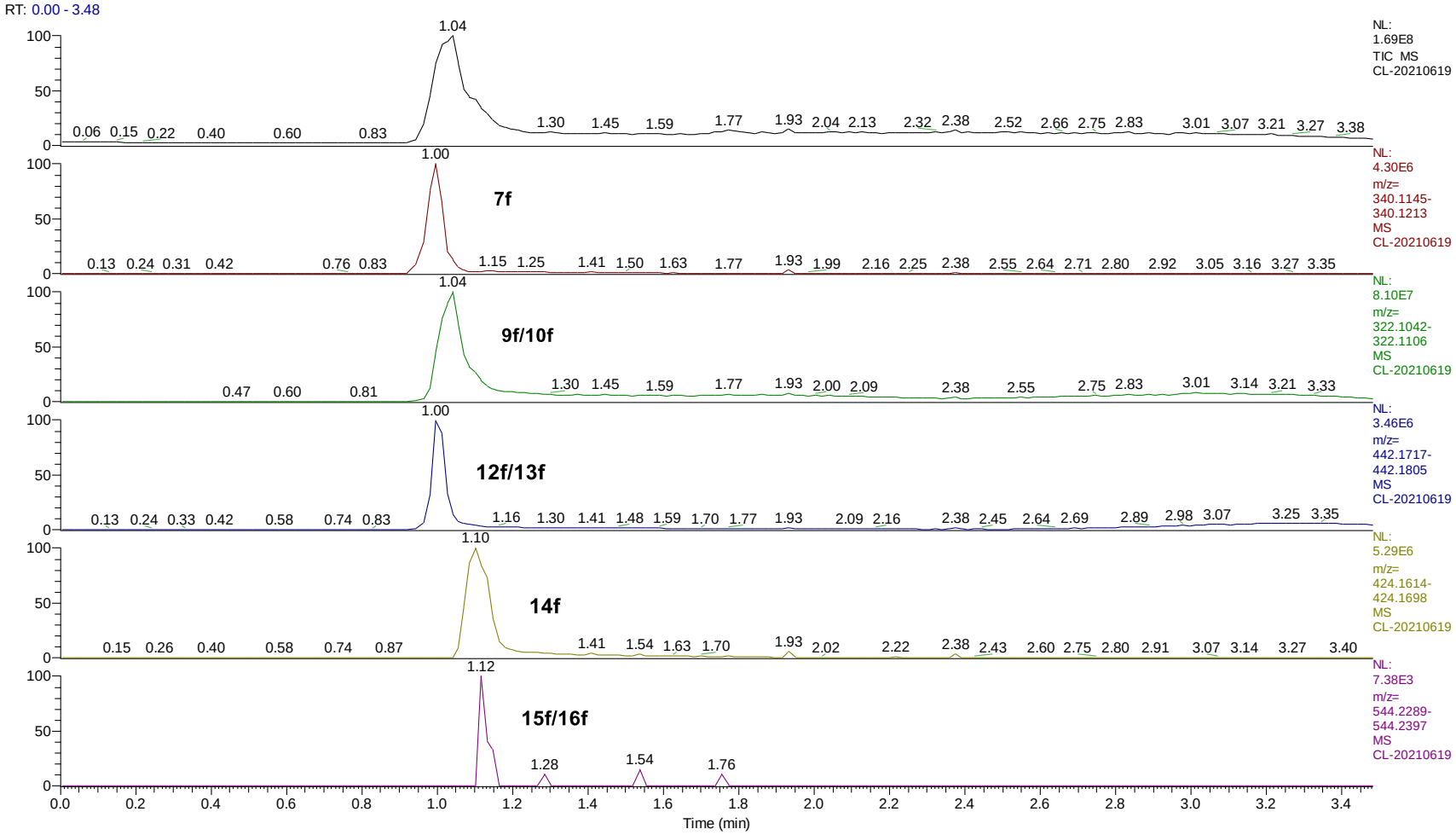


Figure S83. HPLC of the reaction mixture

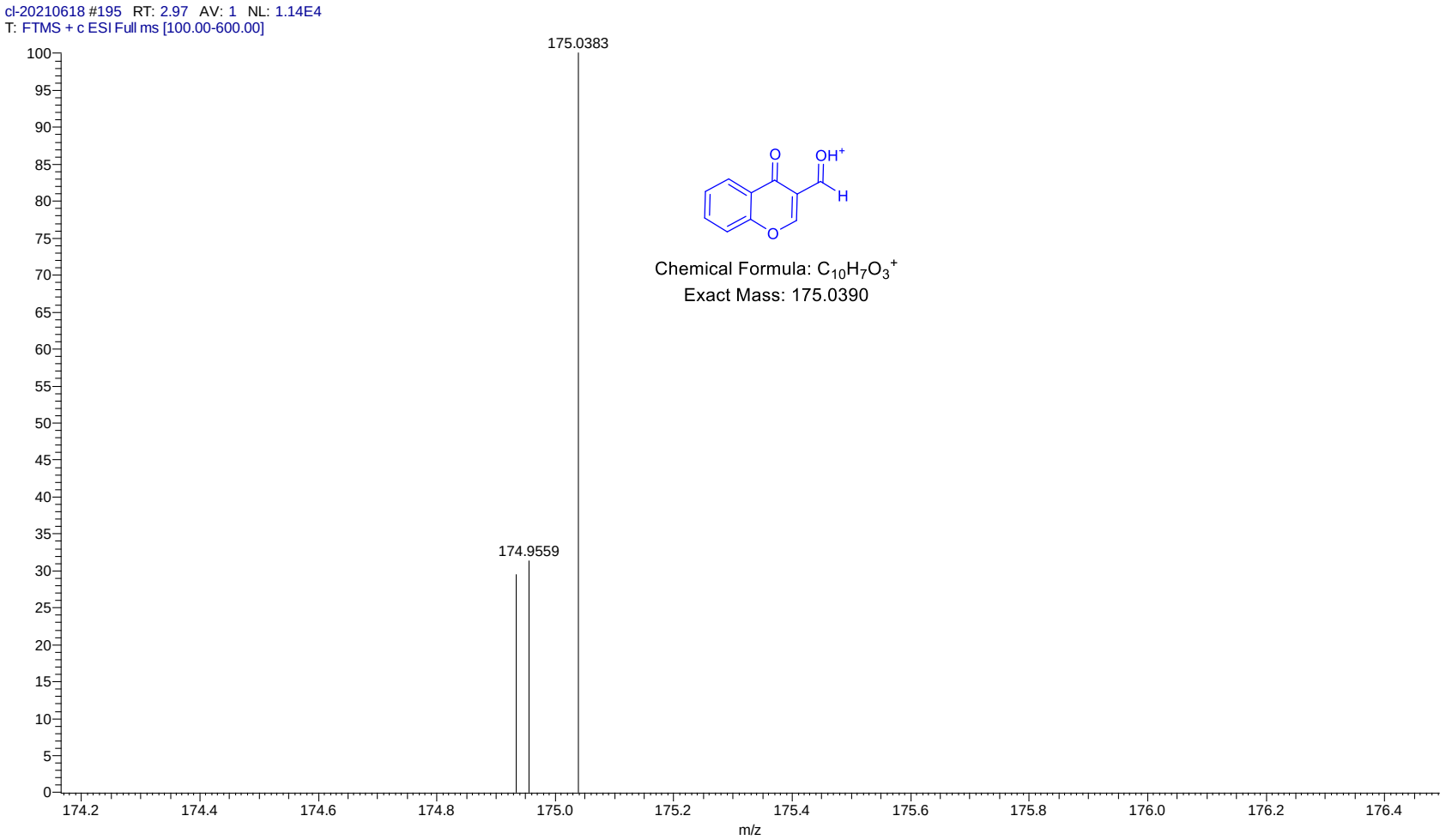


Figure S84. HRMS of intermediate **1f**

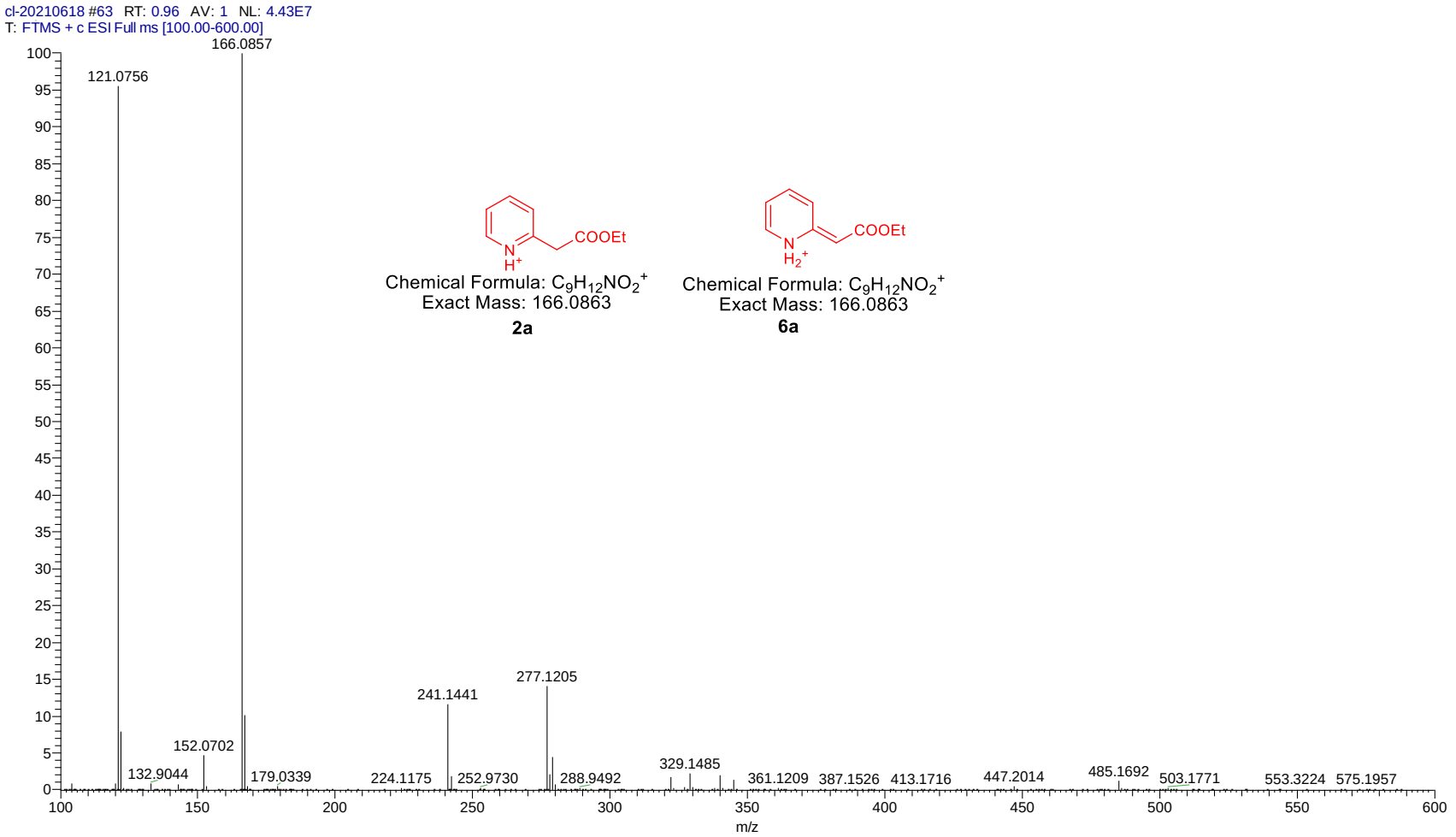


Figure S85. HRMS of intermediate **2a/6a**

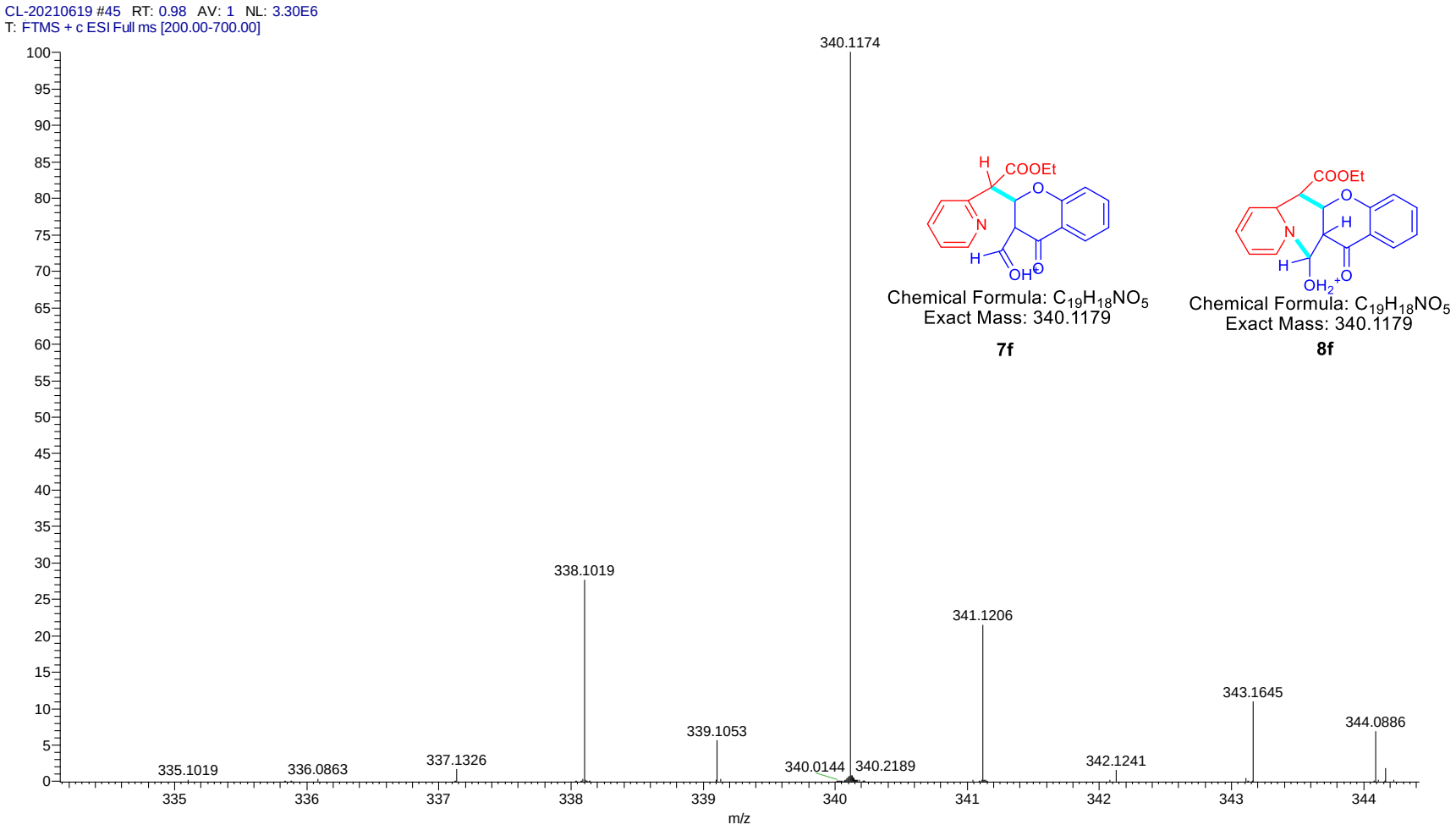


Figure S86. HRMS of intermediate **7f/8f**

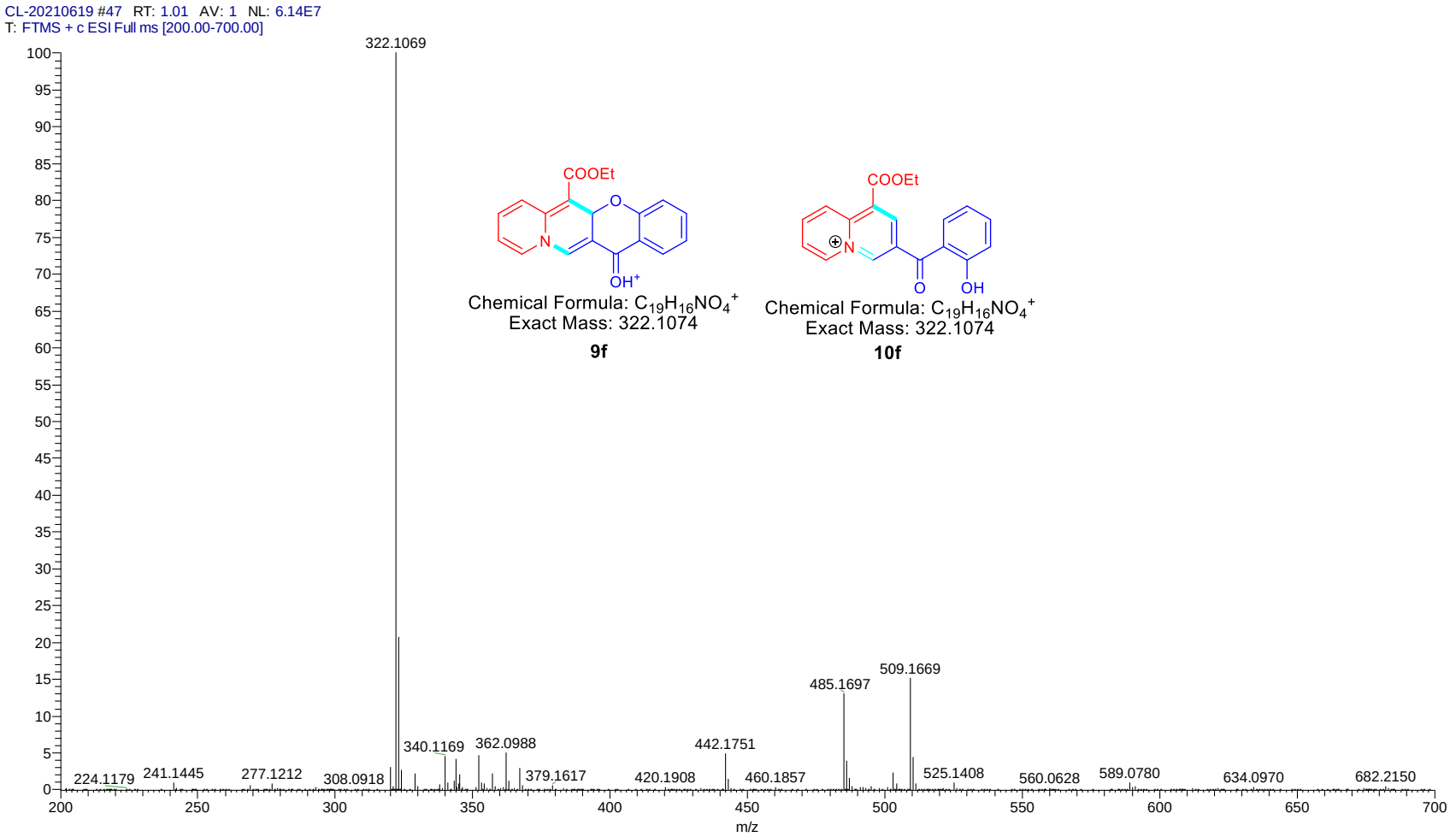


Figure S87. HRMS of intermediate **9f/10f**

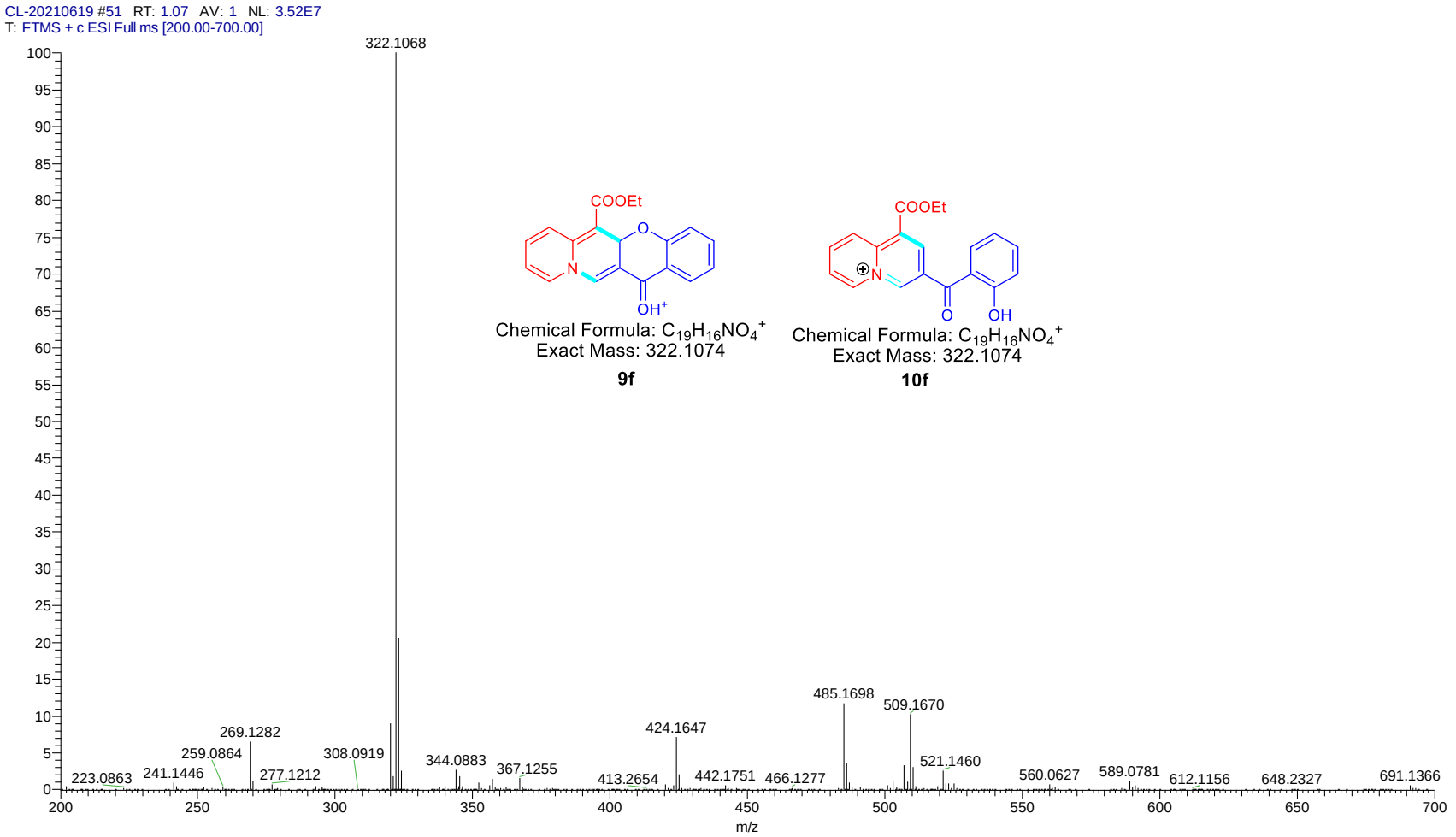


Figure S88. HRMS of intermediate **9f/10f**

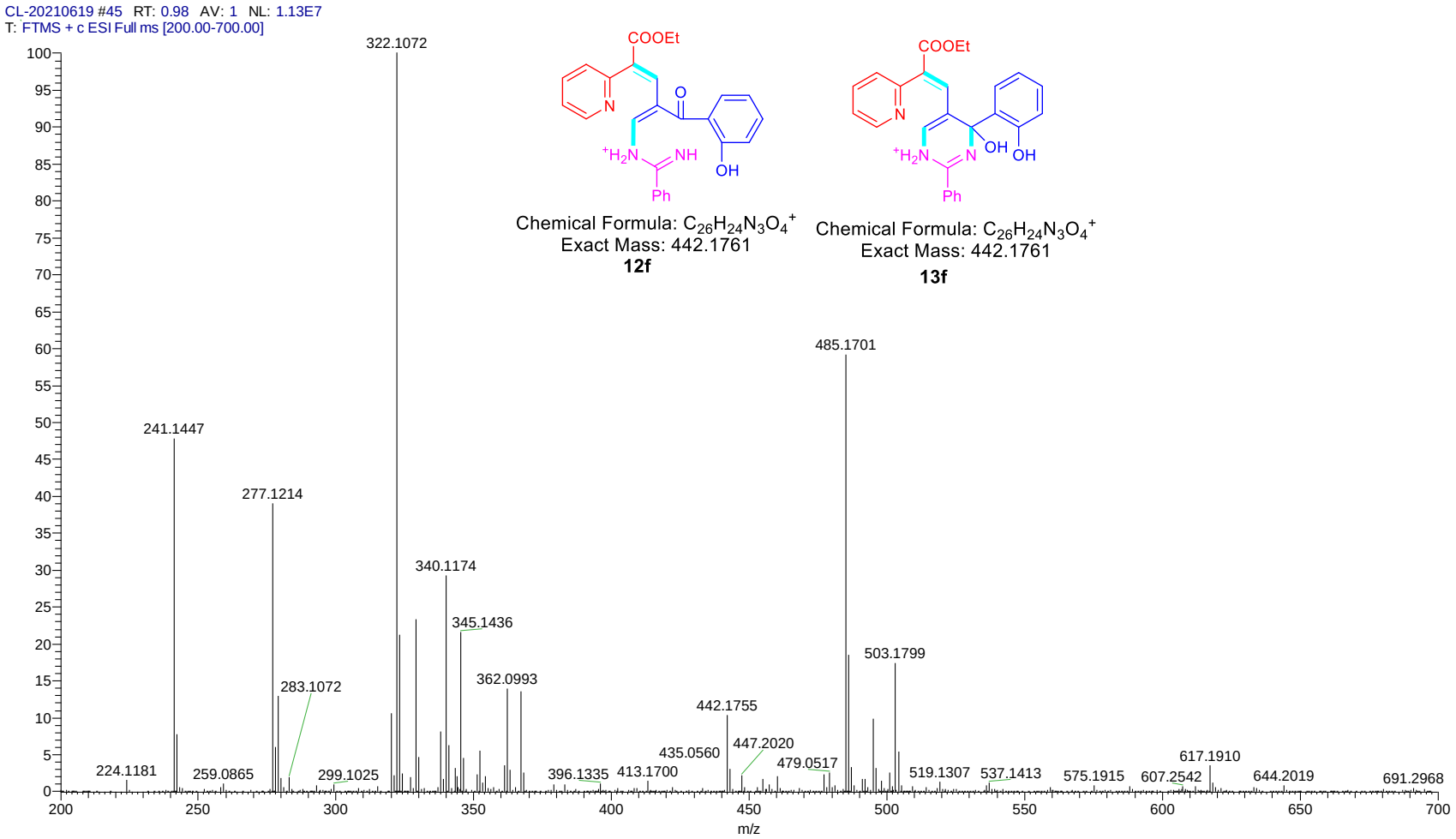


Figure S89. HRMS of intermediate **12f/13f**

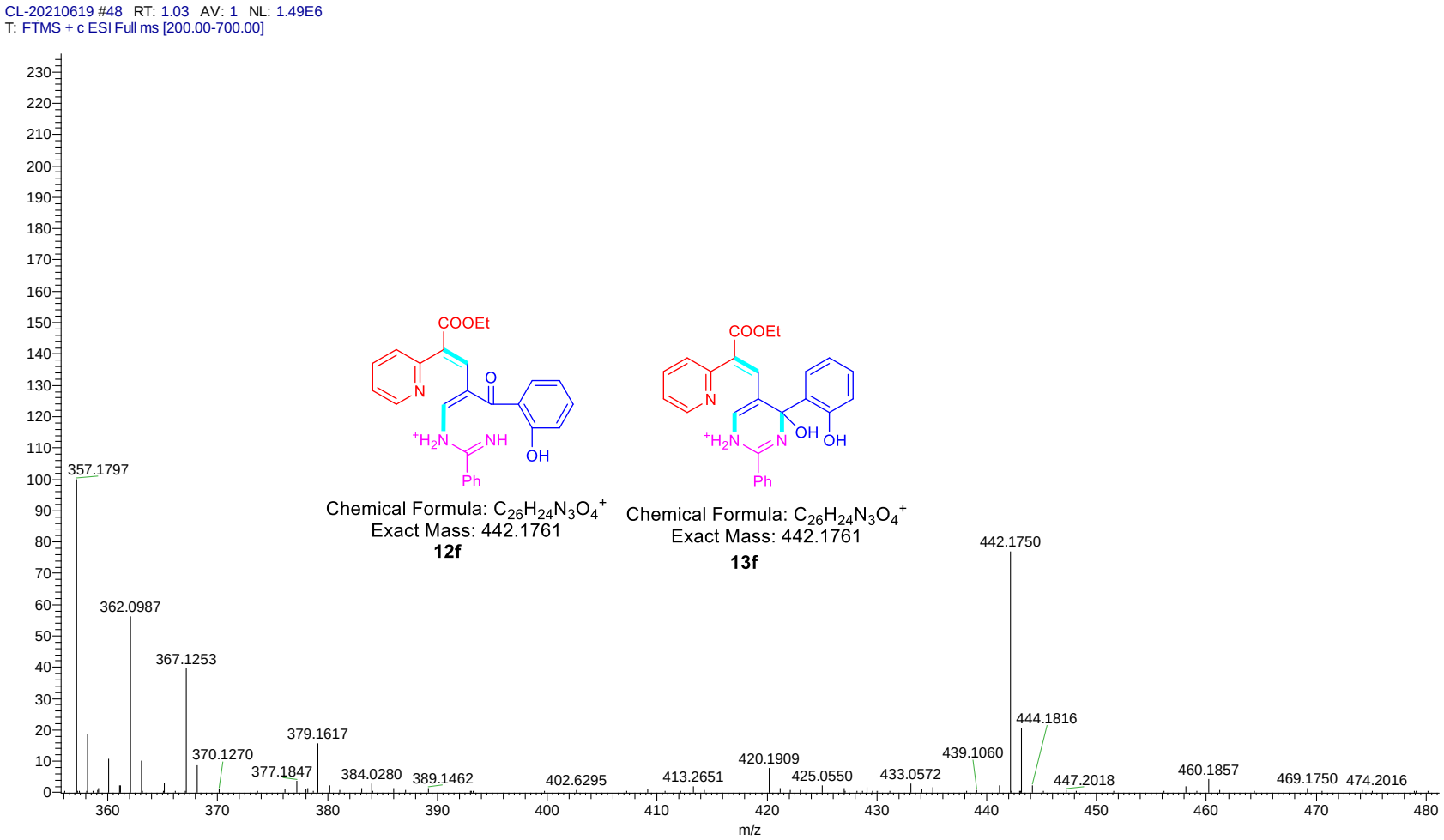


Figure S90. HRMS of intermediate **12f/13f**

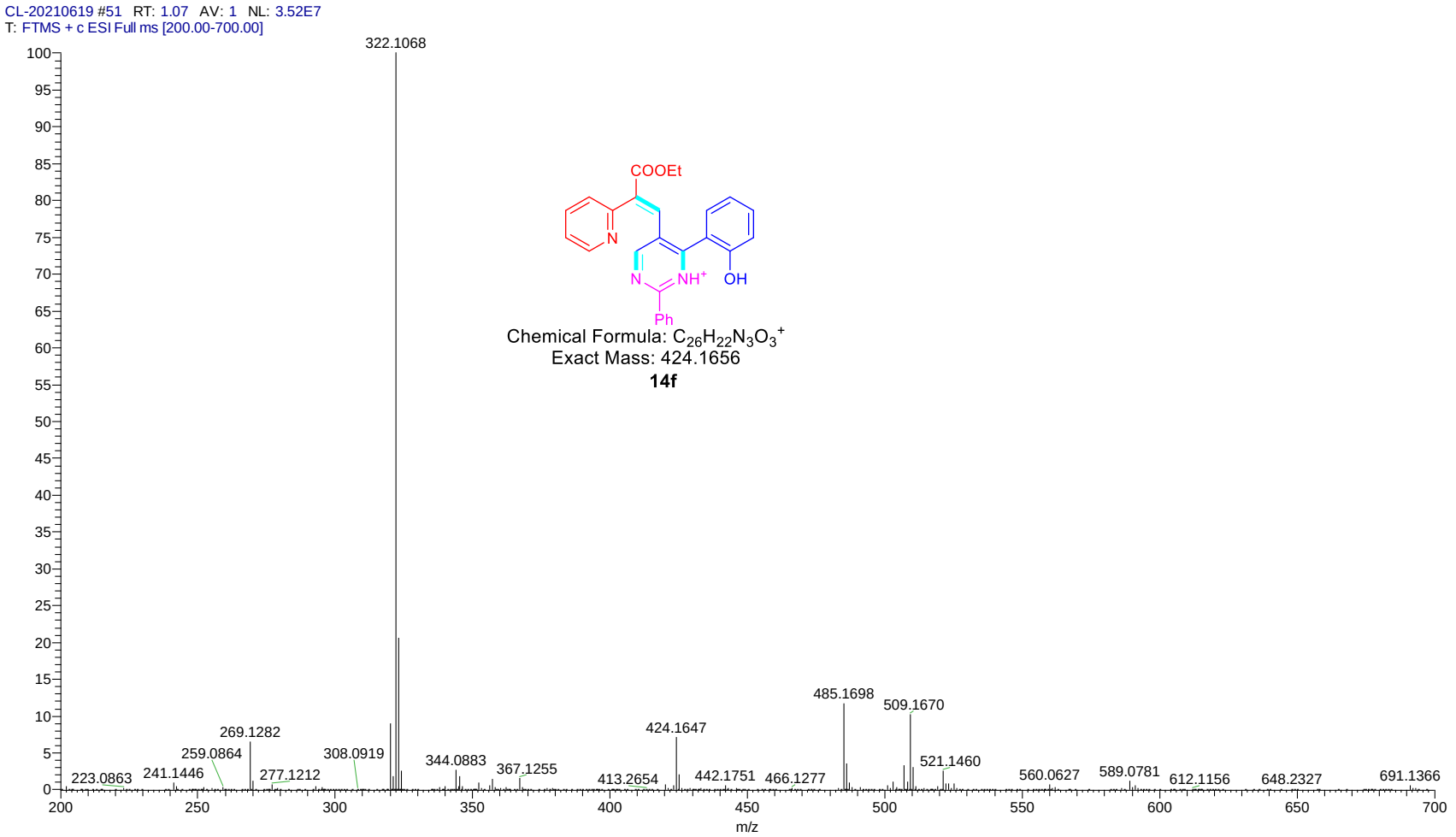


Figure S91. HRMS of intermediate **14f**

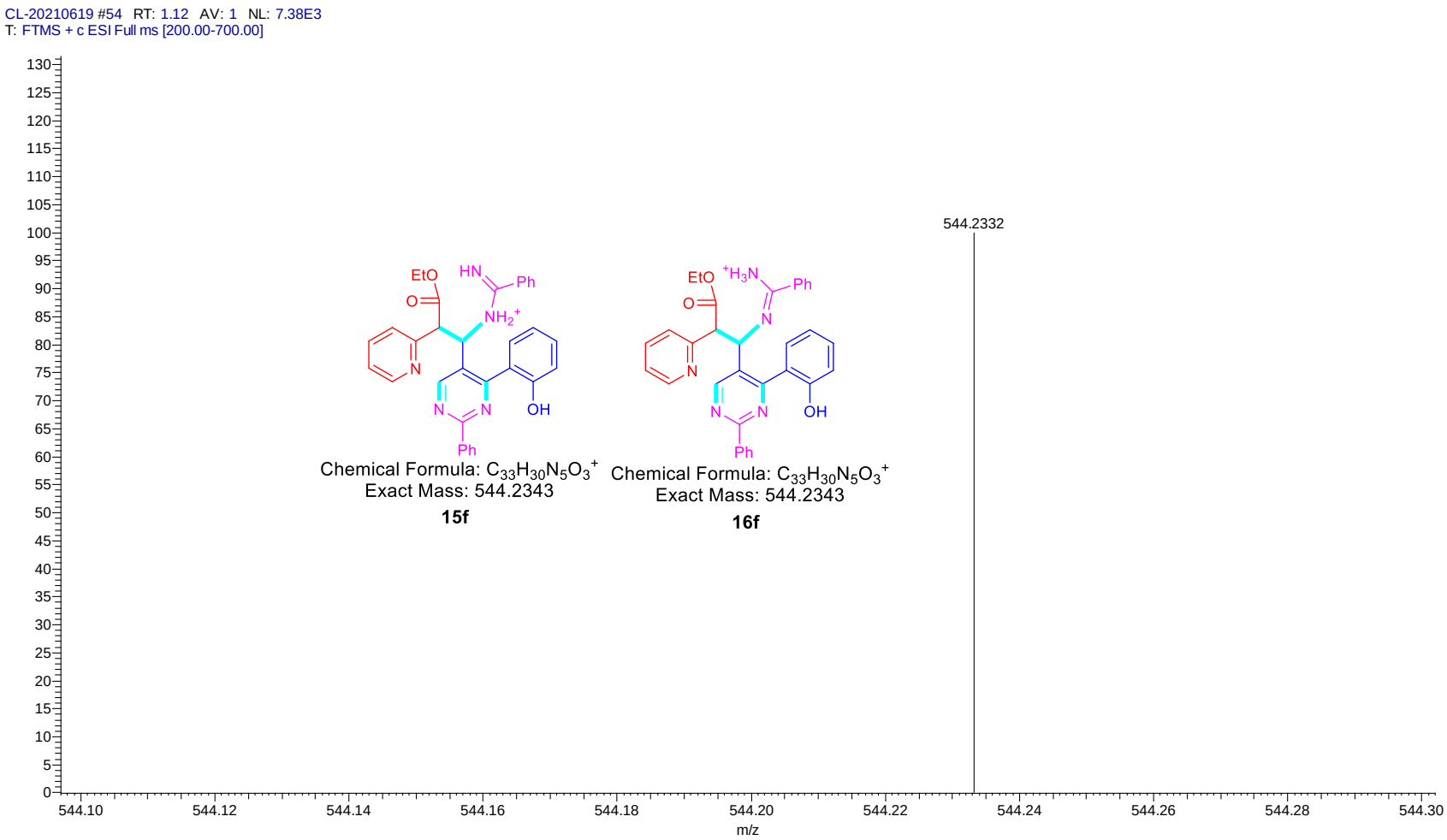


Figure S92. HRMS of intermediate **15f/16f**

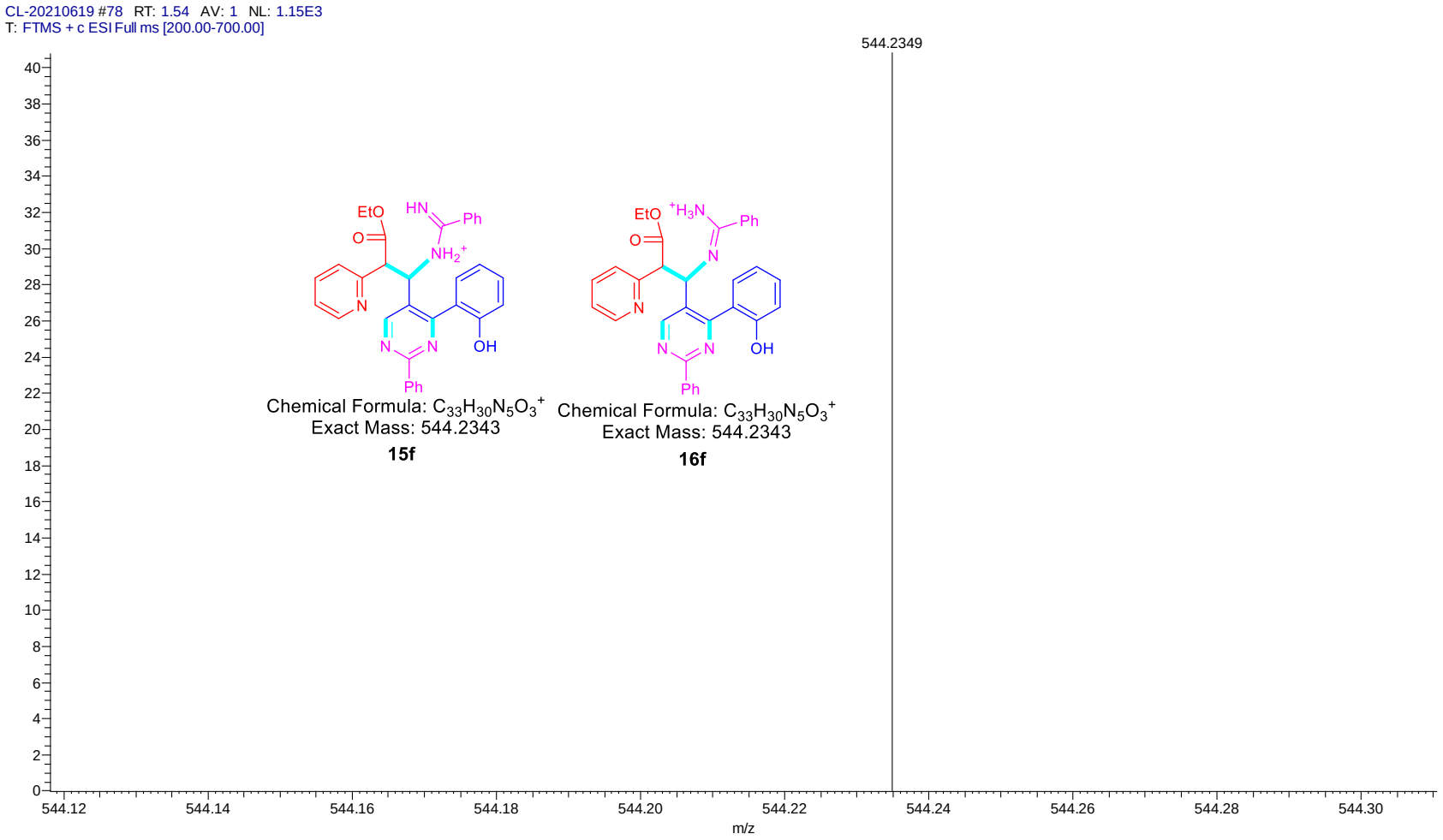


Figure S93. HRMS of intermediate **15f/16f**

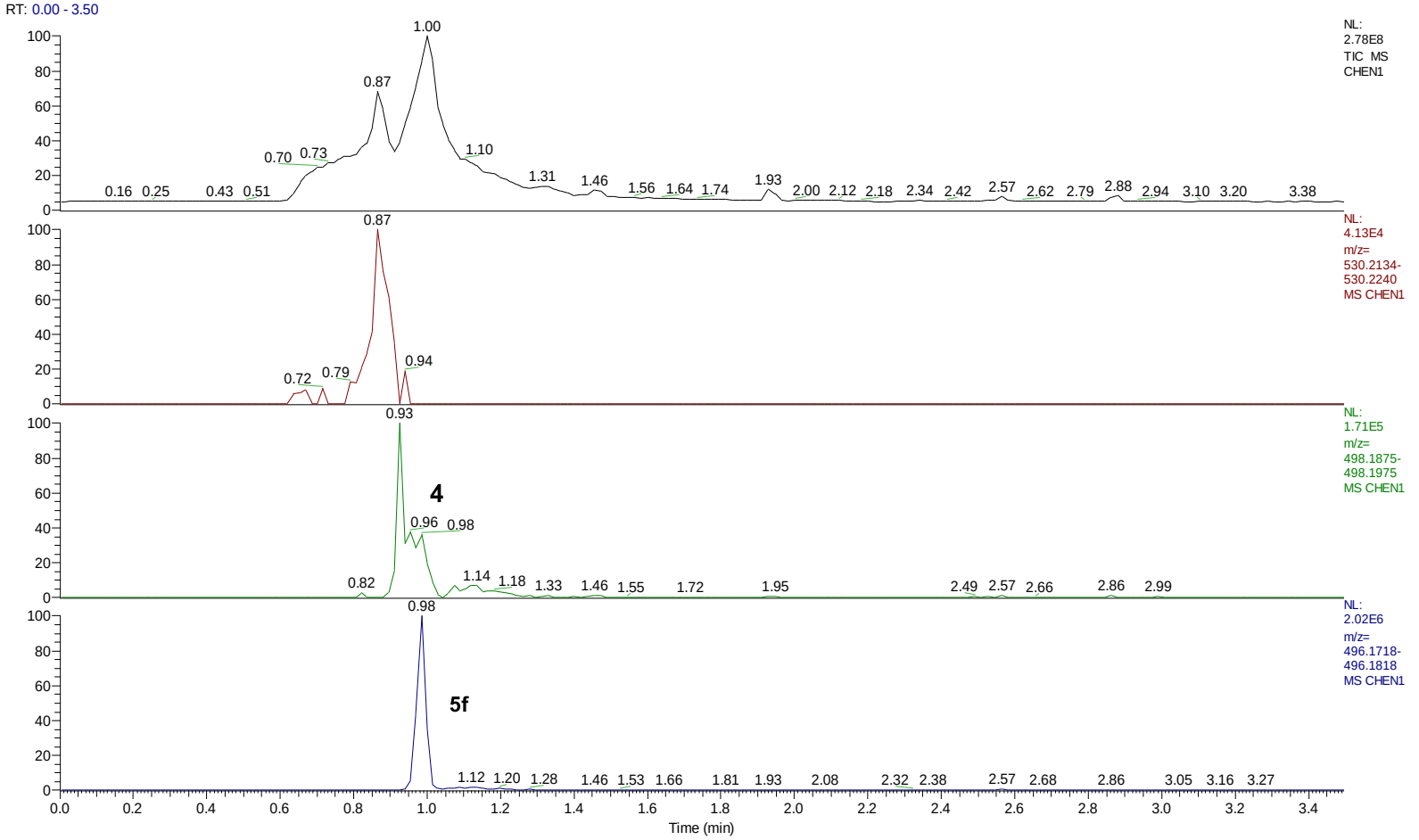


Figure S94. HPLC of the reaction mixture

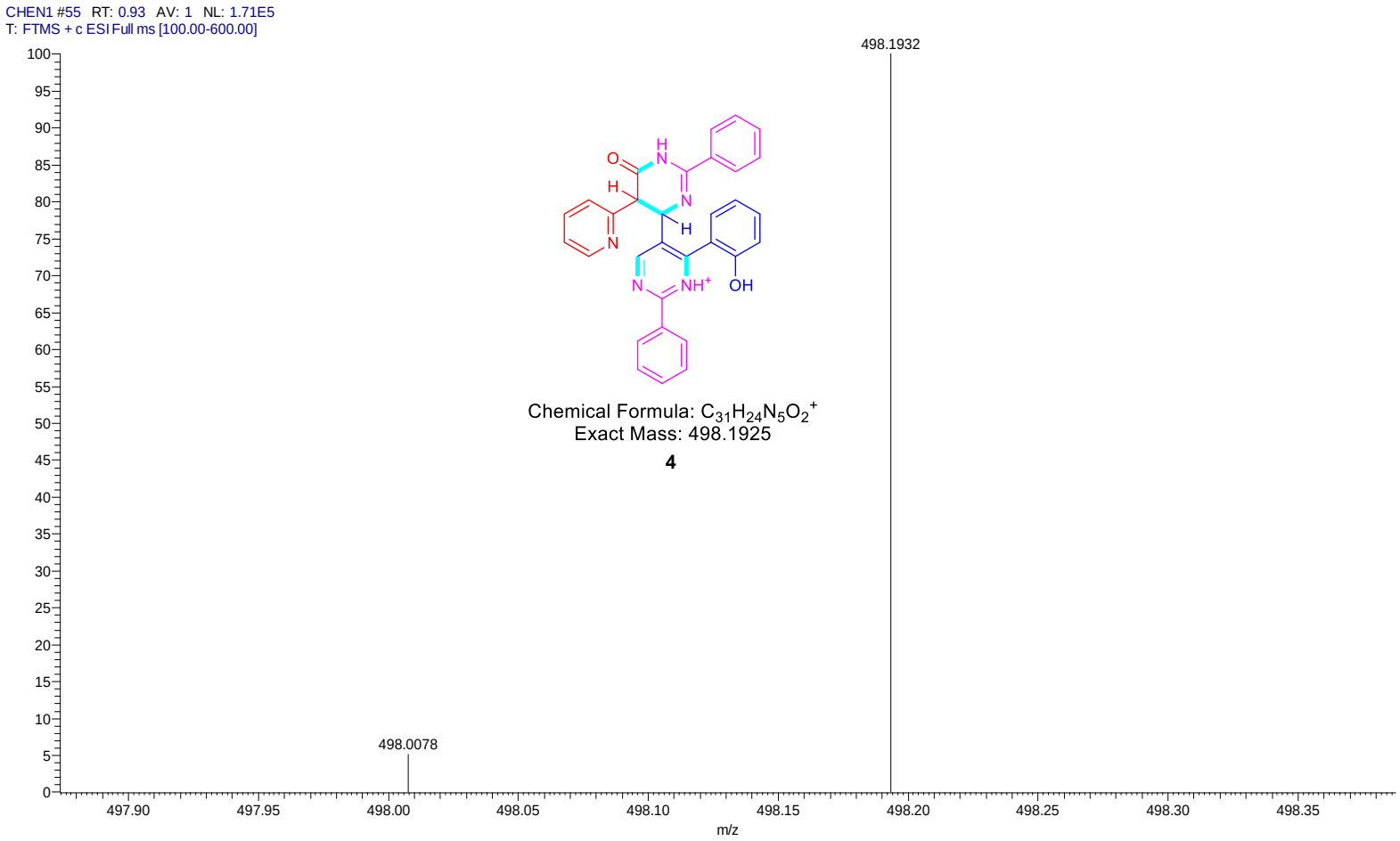


Figure S95. HRMS of intermediate **4**

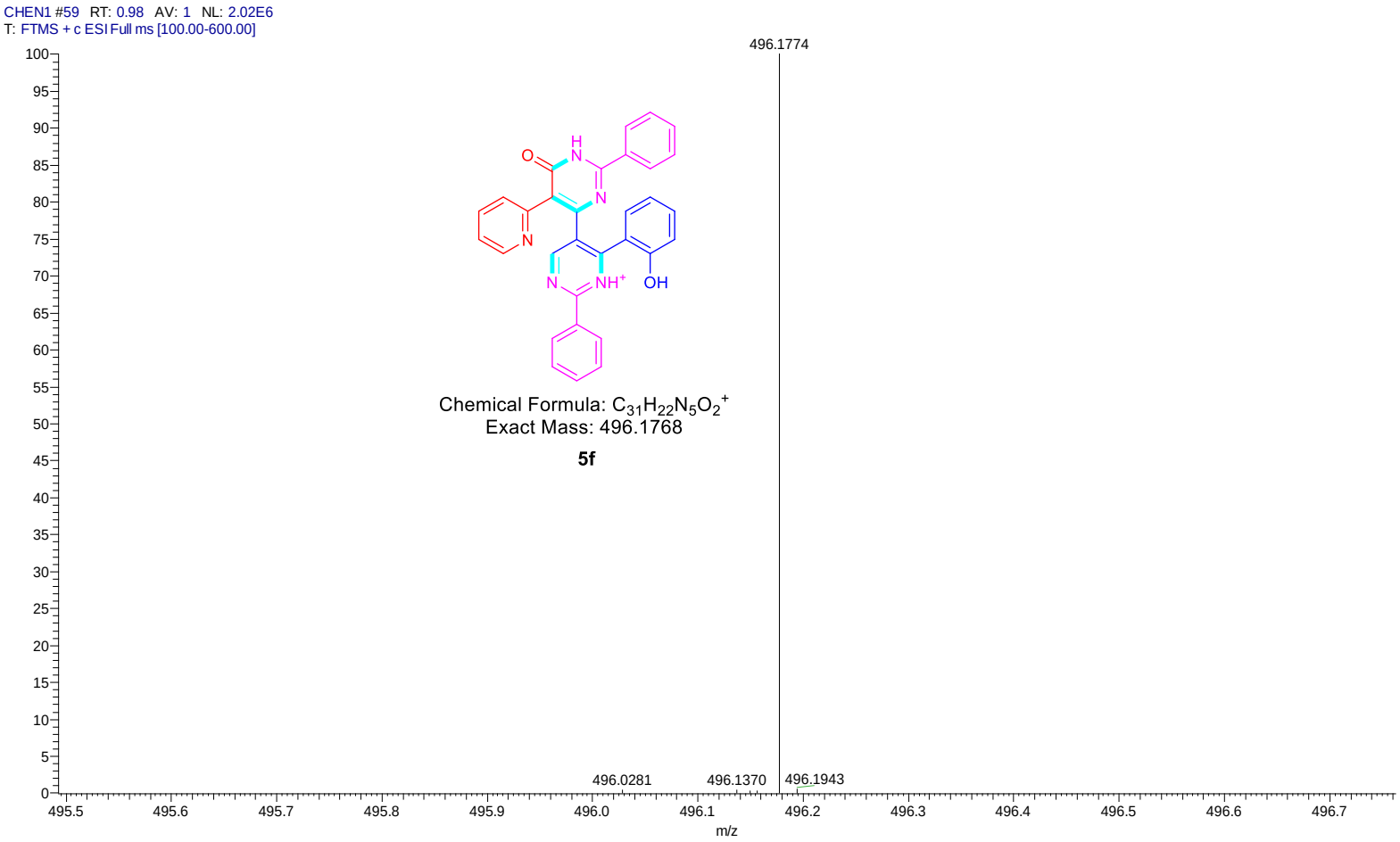


Figure S96. HRMS of intermediate **5f**