Supporting Information

A concise and unexpected one-pot methodology for synthesis of pyrazinone-fused pyridones

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General Experimental

^{1}H and ^{13}C NMR were recorded on a Bruker 400 spectrometer. ^{1}H NMR data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constant (Hz), relative intensity. ^{13}C NMR data are reported as follows: chemical shift in ppm (δ). LC/MS analyses were performed on a Shimadzu-2020 LC-MS instrument using the following conditions: Shim-pack VP-ODS C18 column (reverse phase, 150 x 4.6 mm); a linear gradient from 10% water and 90% acetonitrile to 75% acetonitrile and 25% water over 6.0 min; flow rate of 0.5 mL/min; UV photodiode array detection from 200 to 400 nm. The products were purified by Biotage Isolera™ Spektra Systems and hexane/EtOAc solvent systems. All reagents and solvents were obtained from commercial sources and used without further purification. All microwave irradiation experiments were carried out in a Biotage® Initiator Classic microwave apparatus with continuous irradiation power from 0 to 400W with utilization of the standard absorbance level of 250W maximum power (external surface sensor for temperature monitoring). The reactions were carried out in 10 mL glass tubes, sealed with microwave cavity. The reaction was irradiated at a required ceiling temperature using maximum power for the stipulated time. Then it was cooled to 50 ℃ with gas jet cooling.

Experimental Sections

(a) General procedures for compound 7a-7o.

Aldehyde (0.3 mmol) and propargylamine (0.3 mmol) were stirred in TFE (2.0 mL) for 30 min, then phenylacetic acid (0.3 mmol) and aromatic isocyanide (0.3 mmol) were added to TFE solution. Subsequently, the four-component reaction was stirred for 5 h at room temperature. The reaction mixture was monitored by TLC. When the reaction was completed, the solvent was removed under nitrogen blowing. Then the crude residue was subjected to DIPA (2.0 equiv.) and DMF (2.0 mL) solution at 130 ^{o}C for 2 h. After the reaction was cooled to room temperature and the solvent was removed, the residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford the relative targeted product **7a-7o**.

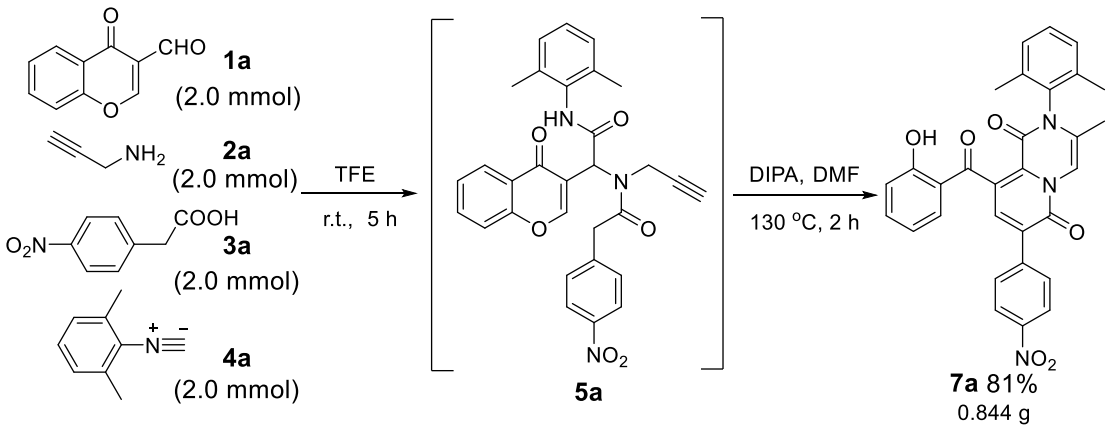
(b) General procedures for compound 7p-7t.

Aldehyde (0.3 mmol) and propargylamine (0.3 mmol) were stirred in TFE (2.0 mL) for 30 min, then phenylacetic acid (0.3 mmol) and aliphatic isocyanide (0.3 mmol) were added to TFE solution. Subsequently, the four-component reaction was stirred for 5 h at room temperature. The reaction mixture was monitored by TLC. When the reaction was completed, the solvent was removed under nitrogen blowing. Then the crude residue was subjected to DIPA (2.0 equiv.) and DMF (2.0 mL) solution at 130 ^{o}C for 2 h. After evaporated the solvent, the residue was directly subjected to the solution of 50% HCl/AcOH under microwave irradiation condition at 120 ^{o}C for 10 min. The crude compound was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford the relative targeted product **7p-7t**.

(c) General procedures for compound 11a-11h.

Aldehyde (0.3 mmol) and amine (0.3 mmol) were stirred in TFE (2.0 mL) for 30 min, then phenylacetic acid (0.3 mmol) and isocyanide (0.3 mmol) were added to TFE solution. Subsequently, the four-component reaction was stirred for 5 h at room temperature. The reaction mixture was monitored by TLC. When the reaction was completed, the solvent was removed under nitrogen blowing. Then the crude residue was subjected to DIPA (2.0 equiv.) and DMF (2.0 mL) at 130 ^{o}C for 2 h. After the reaction was cooled to room temperature, the residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford the relative targeted product **11a-11h**.

(d) Gram scale for compound 7a

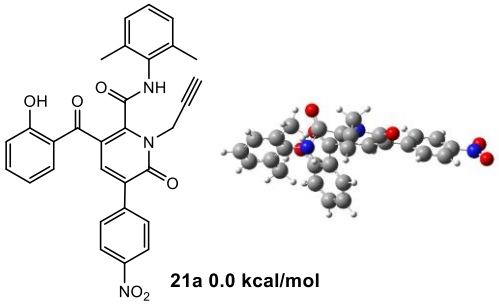


The mixture of Chromone-3-carboxaldehyde (2.0 mmol) and propargylamine (2.0 mmol) was stirred in TFE (10.0 mL) at room temperature for 30 min. Then 4-nitrophenylacetic acid (2.0 mmol) and 2,6-dimethylphenyl isocyanide (2.0 mmol) were added, respectively. When the addition was completed, the reaction was stirred under room temperature for 6 h. When the reaction was completed, the solvent was removed under reduced pressure. Then the crude residue was subjected to DIPA (2.0 equiv.) and DMF (10.0 mL) at 130 ^{o}C for 2 h. The compound **7a** was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) in yield of 81% (0.844 g).

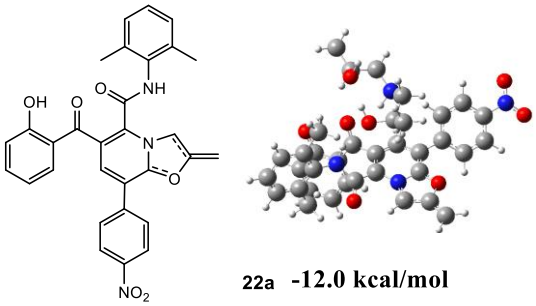
(e) General procedures for compounds 14 and 17.

3-Methylbutanal **12** or cyclohexanone **16** (0.3 mmol) and prop-2-yn-1-amine **2** (0.3 mmol) were stirred in MeOH (2.0 mL) for 30 min, then benzo[*d*][1,3]dioxole-5-carboxylic acid **13** (0.3 mmol) and 2,6-dimethylphenyl isocyanide **4a** (0.3 mmol) were added to MeOH solution. Subsequently, the four-component reaction was stirred overnight at room temperature. The reaction mixture was monitored by TLC. When the reaction was completed, the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford the relative targeted product **14** with 92% yield and product **17** with 89% yield.

(f) Density functional theory (DFT) calculations, unit: kcal/mol.



21a 0.0 kcal/mol



22a -12.0 kcal/mol

The mechanism was investigated via DFT using the B3LYP functional[1] with the 6-31G* basis sets[2] as implemented in Gaussian 09 package,[3] which was used in the geometric optimizations of intermediates (IMs) and transition states (TSs). To considerate the weak interaction, the D3 version of Grimme's dispersion with Becke-Johnson damping were employed during the optimization[4]. To check the IMs and TSs structures, vibrational frequency calculations at the same level of theory were performed. Intrinsic reaction coordinates (IRC)[5] were performed to confirm the transition states connecting with the corresponding reactant and product intermediates.

1. a) A. D. Becke, Phys. Rev. A, 1988, 38, 3098; b) B. Miehlich, A. Savin, H. Stoll, and H. Preuss, *Chem. Phys. Lett.* **1989**, *157*, 200.

2. R. Ditchfield, W. J. Hehre, J. A. Pople, *J. Chem. Phys.* **1971**, *54*, 724.

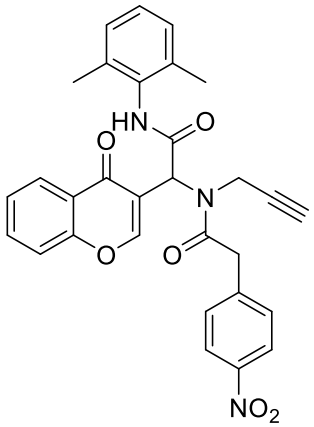
3. Gaussian 09, Revision E.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, et al, Gaussian, Inc., Wallingford CT, 2009.

4. S. Grimme, S. Ehrlich and L. Goerigk, *J. Comp. Chem.* **2011**, *32*, 1456.

5. a) K. Fukui, *Acc. Chem. Res.* **1981**, *14*, 363; b) H. P. Hratchian and H. B. Schlegel, in Theory and Applications of Computational Chemistry: The First 40 Years, Ed. C. E. Dykstra, G. Frenking, K. S. Kim, and G. Scuseria (Elsevier, Amsterdam, 2005) 195-249.

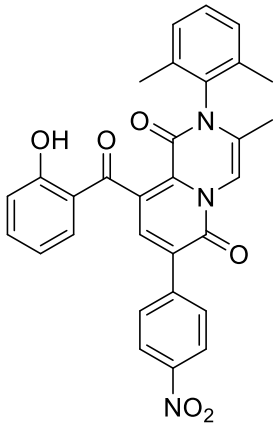
NMR Characterization Data and Figures of Products

N-(2,6-dimethylphenyl)-2-(2-(4-nitrophenyl)-N-(prop-2-yn-1-yl)acetamido)-2-(4-oxo-4H-chromen-3-yl)acetamide



5a white solid, 140 mg, 89% (EA/Hex = 30%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.09 (d, *J* = 12.1 Hz, 3H), 7.93 (s, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.11 – 7.06 (m, 1H), 7.03 (d, *J* = 7.1 Hz, 2H), 6.24 (s, 1H), 4.64 (d, *J* = 19.2 Hz, 1H), 4.32 (d, *J* = 19.0 Hz, 1H), 3.95 (q, *J* = 16.1 Hz, 2H), 2.20 (s, 1H), 2.18 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.50, 170.37, 166.85, 157.36, 155.89, 146.77, 141.71, 135.30, 133.89, 133.18, 130.18, 128.10, 127.44, 125.52, 125.32, 123.42, 118.61, 118.15, 78.97, 73.30, 53.70, 40.14, 36.55, 18.44, LC-MS (ESI) m/z calcd for $C_{30}H_{26}N_3O_6^+$ $(M+H)^+$ 524.18, found 524.18.

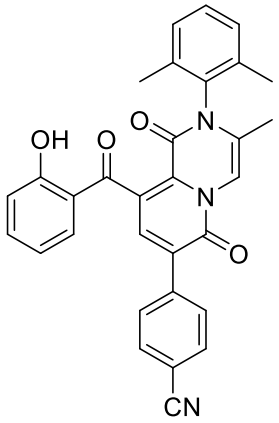
2-(2,6-dimethylphenyl)-9-(2-hydroxybenzoyl)-3-methyl-7-(4-nitrophenyl)-2H-pyrido[1,2-a]pyrazine-1,6-dione



7a yellow solid, 130 mg, 84% (EA/Hex = 30%, R_f = 0.35), ^{1}H NMR (400 MHz,

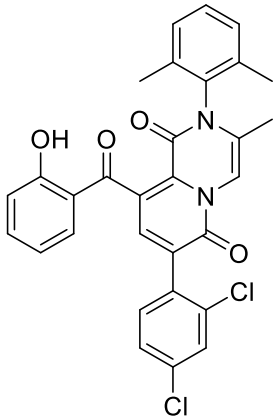
$CDCl_3$) δ 11.71 (s, 1H), 8.31 (d, *J* = 8.8 Hz, 2H), 8.01 (d, *J* = 8.6 Hz, 3H), 7.73 (s, 1H), 7.48 – 7.40 (m, 1H), 7.24 (dd, *J* = 4.5, 3.1 Hz, 1H), 7.17 (d, *J* = 7.3 Hz, 1H), 7.12 (d, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.78 (t, *J* = 7.6 Hz, 1H), 2.12 (s, 3H), 2.00 (s, 3H), 1.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.51, 162.49, 156.21, 155.24, 136.50, 135.66, 131.68, 129.84, 129.59, 129.14, 128.91, 128.47, 123.69, 119.45, 118.83, 118.69, 103.86, 29.70, 17.36. LC-MS (ESI) m/z calcd for $C_{30}H_{24}N_3O_6^+$ $(M+H)^+$ 522.17, found 522.17.

4-(2-(2,6-dimethylphenyl)-9-(2-hydroxybenzoyl)-3-methyl-1,6-dioxo-1,6-dihydro-2H-pyrido[1,2-a]pyrazin-7-yl)benzonitrile



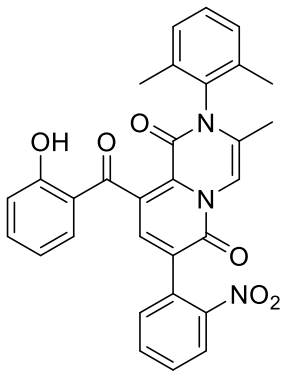
7b yellow solid, 117 mg, 78% (EA/Hex = 30%, R_f = 0.30), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.70 (s, 1H), 8.00 (s, 1H), 7.95 (d, *J* = 8.3 Hz, 2H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.68 (s, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.23 (d, *J* = 7.2 Hz, 2H), 7.14 (dd, *J* = 18.6, 7.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.77 (t, *J* = 7.5 Hz, 1H), 2.11 (s, 3H), 1.99 (s, 3H), 1.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.57, 162.52, 156.23, 155.27, 139.95, 136.45, 135.46, 132.24, 131.69, 129.82, 129.34, 128.34, 120.53, 119.50, 118.80, 118.69, 118.59, 112.41, 103.86, 29.71, 17.33. LC-MS (ESI) m/z calcd for $C_{31}H_{24}N_3O_4^+$ $(M+H)^+$ 502.18, found 502.18.

7-(2,4-dichlorophenyl)-2-(2,6-dimethylphenyl)-9-(2-hydroxybenzoyl)-3-methyl-2H-pyrido[1,2-a]pyrazine-1,6-dione



7c light yellow solid, 93 mg, 57% (EA/Hex = 30%, R_f = 0.40), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.70 (s, 1H), 7.94 (d, *J* = 6.0 Hz, 1H), 7.52 (dd, *J* = 9.3, 1.6 Hz, 2H), 7.39 (d, *J* = 6.6 Hz, 2H), 7.32 (d, *J* = 7.5 Hz, 1H), 7.23 – 7.19 (m, 2H), 7.12 (dd, *J* = 18.6, 6.5 Hz, 2H), 6.98 – 6.94 (m, 1H), 6.79 – 6.73 (m, 1H), 2.10 (s, 3H), 1.98 (s, 3H), 1.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.52, 162.31, 155.90, 155.25, 137.20, 136.34, 135.28, 134.93, 134.06, 132.90, 132.23, 131.68, 129.86, 129.70, 129.04, 127.24, 120.43, 118.77, 118.54, 116.90, 29.66, 17.35. LC-MS (ESI) m/z calcd for $C_{30}H_{23}Cl_2N_2O_4^+$ $(M+H)^+$ 545.10, found 545.10.

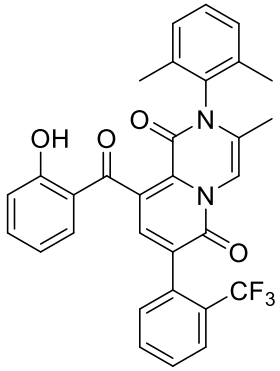
2-(2,6-dimethylphenyl)-9-(2-hydroxybenzoyl)-3-methyl-7-(2-nitrophenyl)-2H-pyrido [1,2-a]pyrazine-1,6-dione



7d yellow solid, 123 mg, 79% (EA/Hex = 30%, R_f = 0.35), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.71 (s, 1H), 8.09 (d, *J* = 8.1 Hz, 1H), 7.87 (s, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.62 – 7.59 (m, 1H), 7.58 (dd, *J* = 12.6, 4.5 Hz, 1H), 7.42 (dd, *J* = 15.0, 7.9 Hz, 2H), 7.26 (d, *J* = 9.1 Hz, 1H), 7.20 (d, *J* = 7.5 Hz, 1H), 7.11 (dd, *J* = 16.9, 7.3 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.78 (t, *J* = 7.6 Hz, 1H), 2.10 (s, 3H), 1.98 (s, 3H), 1.81 (s,

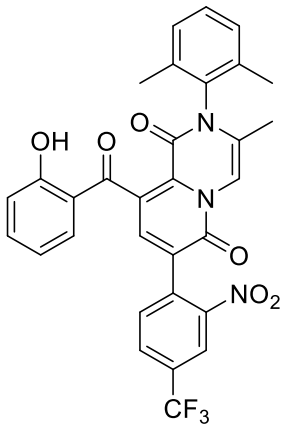
3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.60, 162.36, 155.96, 155.27, 149.15, 136.36, 134.43, 134.04, 133.38, 131.95, 131.76, 129.79, 129.68, 129.00, 128.89, 127.88, 124.65, 120.49, 119.36, 118.89, 118.48, 103.86, 29.68, 17.18. LC-MS (ESI) m/z calcd for $C_{30}H_{24}N_3O_6^+$ $(M+H)^+$ 522.17, found 522.17.

2-(2,6-dimethylphenyl)-9-(2-hydroxybenzoyl)-3-methyl-7-(2-(trifluoromethyl)phenyl)-2H-pyrido[1,2-a]pyrazine-1,6-dione



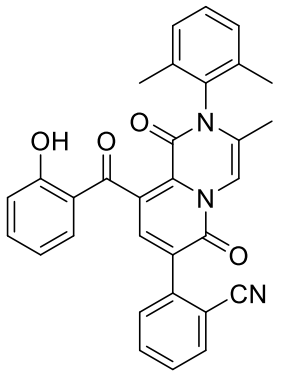
7e yellow solid, 108 mg, 66% (EA/Hex = 30%, R_f = 0.35), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.69 (s, 1H), 7.90 (s, 1H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.65 – 7.58 (m, 1H), 7.55 – 7.49 (m, 1H), 7.45 – 7.35 (m, 3H), 7.23 – 7.17 (m, 2H), 7.14 (d, *J* = 6.6 Hz, 1H), 7.10 (d, *J* = 7.0 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.80 – 6.74 (m, 1H), 2.12 (s, 3H), 1.99 (s, 3H), 1.83 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.00 (s), 175.75, 175.02, 174.13, 162.75, 156.96, 155.68, 154.56, 137.75, 136.84, 136.69, 135.42, 134.52, 134.47, 133.36, 132.15, 132.01, 131.62, 130.81, 130.02, 129.83, 129.35, 129.31, 129.25, 129.15, 128.59, 128.56, 128.10, 126.89, 126.29, 125.93, 120.83, 119.18, 119.02, 118.79, 118.49, 104.24, 30.08, 17.55. LC-MS (ESI) m/z calcd for $C_{31}H_{24}F_3N_2O_4^+$ $(M+H)^+$ 545.17, found 545.17.

2-(2,6-dimethylphenyl)-9-(2-hydroxybenzoyl)-3-methyl-7-(2-nitro-4-(trifluoromethyl)phenyl)-2H-pyrido[1,2-a]pyrazine-1,6-dione



7f yellow solid, 145 mg, 82% (EA/Hex = 30%, R_f = 0.35), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.67 (s, 1H), 8.35 (s, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.87 (s, 1H), 7.64 (d, *J* = 1.6 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.42 (dd, *J* = 8.4, 7.2 Hz, 1H), 7.25 (d, *J* = 2.8 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.14 (d, *J* = 7.4 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 8.5 Hz, 1H), 6.78 (t, *J* = 7.6 Hz, 1H), 2.10 (s, 3H), 1.99 (s, 3H), 1.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.22, 162.40, 155.64, 155.11, 136.49, 134.87, 133.92, 132.84, 131.65, 129.79, 129.05, 128.95, 128.47, 122.02, 120.42, 119.29, 118.93, 118.58, 103.77, 29.68, 17.21. LC-MS (ESI) m/z calcd for $C_{31}H_{23}F_3N_3O_6^+$ $(M+H)^+$ 590.15, found 590.15.

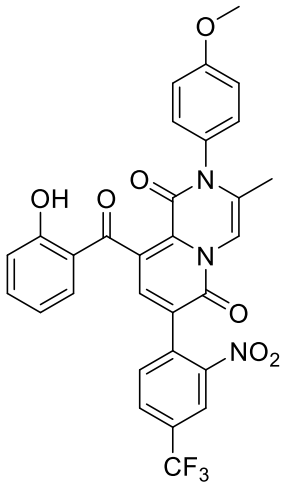
2-(2-(2,6-dimethylphenyl)-9-(2-hydroxybenzoyl)-3-methyl-1,6-dioxo-1,6-dihydro-2H-pyrido[1,2-a]pyrazin-7-yl)benzonitrile



7g yellow solid, 71% (EA/Hex = 30%, R_f = 0.35), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.70 (s, 1H), 8.00 (s, 1H), 7.95 (d, *J* = 8.3 Hz, 2H), 7.77 – 7.66 (m, 3H), 7.43 (dd, *J* = 11.5, 4.1 Hz, 1H), 7.23 (d, *J* = 7.2 Hz, 2H), 7.14 (dd, *J* = 18.6, 7.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.77 (t, *J* = 7.5 Hz, 1H), 2.11 (s, 3H), 1.99 (s, 3H), 1.88 (s, 3H). ^{13}C

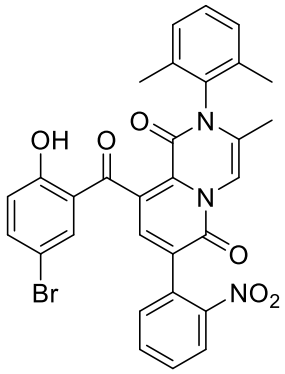
NMR (100 MHz, $CDCl_3$) δ 198.57, 162.52, 156.23, 155.27, 139.95, 136.45, 135.37, 134.94, 134.08, 132.24, 131.69, 129.82, 129.34, 128.71, 128.34, 120.53, 119.50, 118.80, 118.69, 112.41, 103.86, 29.71, 17.33. LC-MS (ESI) m/z calcd for $C_{31}H_{24}N_3O_4^+$ $(M+H)^+$ 502.18, found 502.18.

9-(2-hydroxybenzoyl)-2-(4-methoxyphenyl)-3-methyl-7-(2-nitro-4-(trifluoromethyl)phenyl)-2H-pyrido[1,2-a]pyrazine-1,6-dione



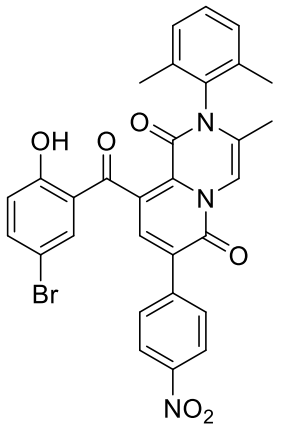
7h yellow solid, 133 mg, 75% (EA/Hex = 35%, R_f = 0.45), ^1H NMR (400 MHz, $CDCl_3$) δ 11.65 (s, 1H), 8.29 (d, *J* = 8.3 Hz, 1H), 7.99 (d, *J* = 8.3 Hz, 2H), 7.54 – 7.47 (m, 2H), 7.32 (s, 1H), 7.08 (d, *J* = 12.1 Hz, 2H), 6.98 (s, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 3.80 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.78, 161.21, 160.18, 159.52, 157.18, 156.16, 139.17, 135.08, 133.86, 129.58, 128.85, 123.64, 121.31, 120.61, 115.24, 114.34, 110.45, 103.51, 55.56, 18.34. LC-MS (ESI) m/z calcd for $C_{30}H_{22}F_3N_3O_7^+$ $(M+H)^+$ 592.13, found 592.13.

9-(5-bromo-2-hydroxybenzoyl)-2-(2,6-dimethylphenyl)-3-methyl-7-(2-nitrophenyl)-2H-pyrido[1,2-a]pyrazine-1,6-dione



7i yellow solid, 138 mg, 77% (EA/Hex = 30%, R_f = 0.35), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.71 (s, 1H), 8.09 (d, *J* = 8.1 Hz, 1H), 7.87 (s, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.61 – 7.59 (m, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.42 (dd, *J* = 15.0, 7.9 Hz, 2H), 7.20 (d, *J* = 7.5 Hz, 1H), 7.11 (dd, *J* = 16.9, 7.3 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.78 (t, *J* = 7.6 Hz, 1H), 2.10 (s, 3H), 1.98 (s, 3H), 1.81 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.60, 162.36, 155.96, 149.15, 136.36, 135.02, 134.43, 134.04, 133.38, 131.86, 130.90, 129.73, 128.95, 124.65, 120.49, 119.36, 118.89, 118.48, 103.86, 29.68, 17.77. LC-MS (ESI) m/z calcd for $C_{30}H_{23}BrN_3O_6^+$ $(M+H)^+$ 600.08, found 600.08.

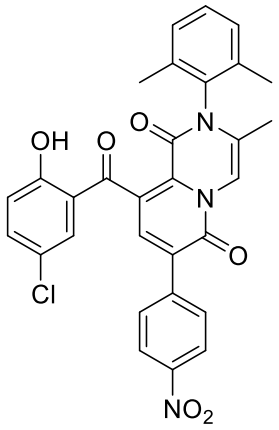
9-(5-bromo-2-hydroxybenzoyl)-2-(2,6-dimethylphenyl)-3-methyl-7-(4-nitrophenyl)-2 H-pyrido[1,2-a]pyrazine-1,6-dione



7j yellow solid, 145 mg, 80% (EA/Hex = 30%, R_f = 0.35), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.65 (s, 1H), 8.32 (dd, *J* = 9.2, 2.2 Hz, 2H), 8.07 – 8.01 (m, 3H), 7.72 (s, 1H), 7.49 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.31 (d, *J* = 2.4 Hz, 1H), 7.24 (s, 1H), 7.16 (t, *J* = 7.2 Hz, 2H), 6.90 (d, *J* = 8.9 Hz, 1H), 2.11 (s, 3H), 2.05 (s, 3H), 1.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.66, 161.23, 156.20, 155.29, 147.81, 141.66, 138.96,

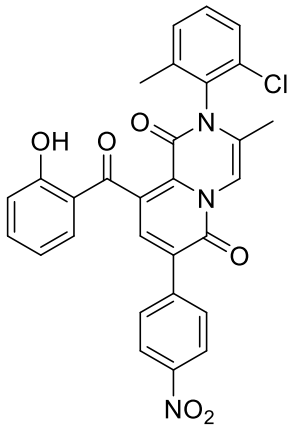
135.57, 135.12, 134.95, 133.91, 133.36, 131.63, 129.94, 129.61, 129.22, 129.11, 128.56, 123.70, 121.93, 120.80, 118.37, 110.39, 104.06, 29.52, 17.15. LC-MS (ESI) m/z calcd for $C_{30}H_{23}BrN_3O_6^+$ $(M+H)^+$ 600.08, found 600.08.

9-(5-chloro-2-hydroxybenzoyl)-2-(2,6-dimethylphenyl)-3-methyl-7-(4-nitrophenyl)-2H-pyrido[1,2-a]pyrazine-1,6-dione



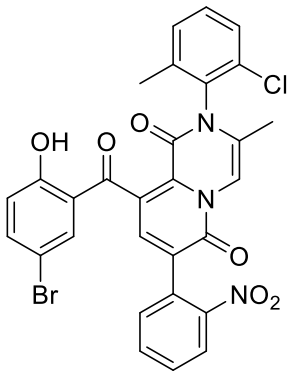
7k yellow solid, 129 mg, 77% (EA/Hex = 30%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.64 (s, 1H), 8.33 (d, *J* = 8.7 Hz, 2H), 8.07 – 7.99 (m, 3H), 7.72 (s, 1H), 7.37 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.24 (s, 1H), 7.17 (dd, *J* = 9.9, 5.4 Hz, 3H), 6.96 (d, *J* = 8.9 Hz, 1H), 2.11 (s, 3H), 2.04 (s, 3H), 1.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.72, 160.79, 156.19, 155.29, 147.78, 141.66, 136.23, 135.55, 135.11, 134.90, 133.89, 131.61, 130.35, 129.95, 129.61, 129.22, 129.13, 128.56, 123.72, 123.51, 121.22, 120.42, 118.41, 104.05, 17.53. LC-MS (ESI) m/z calcd for $C_{30}H_{23}ClN_3O_6^+$ $(M+H)^+$ 556.13, found 556.13.

2-(2-chloro-6-methylphenyl)-9-(2-hydroxybenzoyl)-3-methyl-7-(4-nitrophenyl)-2H-pyrido[1,2-a]pyrazine-1,6-dione



7l yellow solid, 110 mg, 67% (EA/Hex = 30%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.68 (s, 1H), 8.34 – 8.25 (m, 2H), 8.03 – 7.90 (m, 3H), 7.70 (d, *J* = 3.4 Hz, 1H), 7.45 – 7.40 (m, 1H), 7.34 – 7.29 (m, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 7.17 (d, *J* = 17.6 Hz, 1H), 7.01 – 6.92 (m, 1H), 6.77 (d, *J* = 6.8 Hz, 1H), 2.18 (s, 3H), 1.92 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.50, 162.41, 156.12, 147.69, 141.68, 136.61, 135.62, 132.46, 132.08, 130.78, 129.65, 129.55, 128.21, 128.06, 123.64, 119.05, 118.47, 103.80, 29.67, 17.14. LC-MS (ESI) m/z calcd for $C_{29}H_{21}ClN_3O_6^+$ $(M+H)^+$ 542.11, found 542.11.

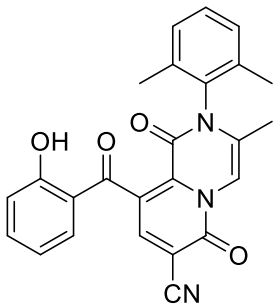
9-(5-bromo-2-hydroxybenzoyl)-2-(2-chloro-6-methylphenyl)-3-methyl-7-(2-nitrophenyl)-2H-pyrido[1,2-a]pyrazine-1,6-dione



7m yellow solid, 130 mg, 70% (EA/Hex = 30%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.67 (s, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.88 (s, 1H), 7.68 (d, *J* = 7.3 Hz, 1H), 7.60 (s, 2H), 7.48 (d, *J* = 9.5 Hz, 3H), 7.34 (d, *J* = 16.6 Hz, 2H), 7.28 (s, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 2.11 (s, 3H), 1.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.46, 160.91, 134.35, 133.76, 133.38, 132.43, 131.96, 130.76, 130.44, 129.93, 129.60,

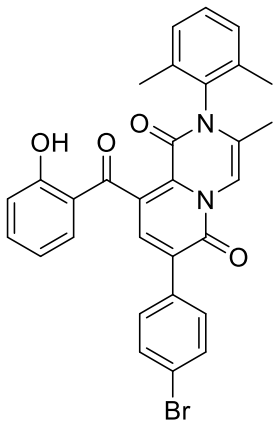
128.10, 124.71, 120.67, 120.44, 118.43, 29.88, 16.67. LC-MS (ESI) m/z calcd for $C_{29}H_{20}BrClN_3O_6^+$ $(M+H)^+$ 620.02, found 620.02.

2-(2,6-dimethylphenyl)-9-(2-hydroxybenzoyl)-3-methyl-1,6-dioxo-1,6-dihydro-2H-pyrido[1,2-a]pyrazine-7-carbonitrile



7n yellow solid, 105 mg, 82% (EA/Hex = 30%, R_f = 0.20), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.49 (s, 1H), 7.94 (s, 1H), 7.83 (s, 1H), 7.46 – 7.38 (m, 1H), 7.27 – 7.18 (m, 2H), 7.17 – 7.10 (m, 2H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.76 (t, *J* = 7.3 Hz, 1H), 2.06 (s, 3H), 1.93 (s, 3H), 1.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.52, 162.42, 155.18, 142.47, 136.80, 134.80, 134.51, 133.57, 131.42, 130.58, 130.07, 129.23, 129.11, 120.07, 118.99, 118.71, 118.38, 114.55, 103.93, 103.54, 29.67, 17.34. LC-MS (ESI) m/z calcd for $C_{25}H_{20}N_3O_4^+$ $(M+H)^+$ 426.14, found 426.14.

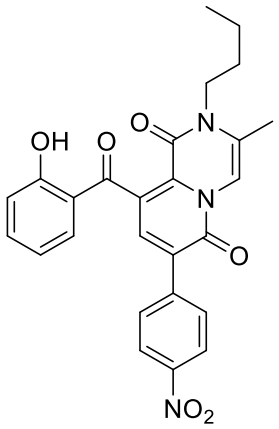
7-(4-bromophenyl)-2-(2,6-dimethylphenyl)-9-(2-hydroxybenzoyl)-3-methyl-2H-pyrido[1,2-a]pyrazine-1,6-dione



7o yellow solid, 55 mg, 33% (EA/Hex = 30%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.72 (s, 1H), 7.98 (s, 1H), 7.73 – 7.66 (m, 2H), 7.61 (d, *J* = 2.5 Hz, 1H), 7.57 (d, *J*

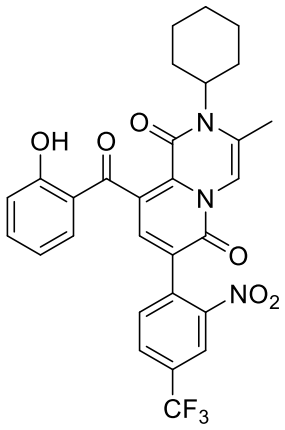
= 6.3 Hz, 2H), 7.41 (s, 1H), 7.20 (d, *J* = 7.7 Hz, 1H), 7.12 (d, *J* = 18.4 Hz, 2H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.75 (d, *J* = 7.7 Hz, 1H), 2.09 (s, 3H), 1.97 (s, 3H), 1.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.88, 162.51, 156.49, 155.08, 136.31, 134.92, 134.45, 131.73, 131.65, 130.22, 129.67, 129.02, 128.88, 127.77, 123.27, 118.73, 118.54, 103.86, 29.53, 17.29. LC-MS (ESI) m/z calcd for $C_{30}H_{23}BrN_2O_4^+$ $(M+H)^+$ 555.09, found 555.09.

2-butyl-9-(2-hydroxybenzoyl)-3-methyl-7-(4-nitrophenyl)-2H-pyrido[1,2-a]pyrazine-1,6-dione



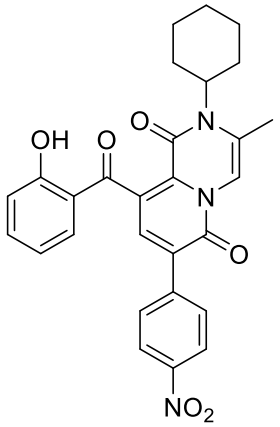
7p yellow solid, 75 mg (for three steps), 64% (EA/Hex = 30%, R_f = 0.40), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.79 (s, 1H), 8.30 – 8.22 (m, 2H), 8.00 – 7.93 (m, 2H), 7.84 (s, 1H), 7.66 (s, 1H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.78 (t, *J* = 7.6 Hz, 1H), 3.93 – 3.75 (m, 2H), 2.38 (s, 3H), 1.62 – 1.57 (m, 2H), 1.34 (d, *J* = 7.4 Hz, 2H), 0.90 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.00, 162.41, 156.05, 147.52, 141.85, 136.51, 135.46, 132.02, 129.48, 128.30, 127.61, 123.58, 120.44, 118.98, 118.68, 118.56, 103.68, 44.18, 29.67, 20.04, 17.34, 13.61. LC-MS (ESI) m/z calcd for $C_{26}H_{24}N_3O_6^+$ $(M+H)^+$ 474.17, found 474.17.

2-cyclohexyl-9-(2-hydroxybenzoyl)-3-methyl-7-(2-nitro-4-(trifluoromethyl)phenyl)-2H-pyrido[1,2-a]pyrazine-1,6-dione



7q yellow solid, 63 mg, 37% (EA/Hex = 30%, R_f = 0.40), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.81 (d, *J* = 2.6 Hz, 1H), 8.31 (s, 1H), 7.90 (s, 1H), 7.64 (s, 1H), 7.56 (d, *J* = 4.7 Hz, 2H), 7.45 (s, 1H), 7.22 (s, 1H), 7.04 (s, 1H), 6.80 (s, 1H), 3.90 (d, *J* = 6.8 Hz, 1H), 2.33 (s, 3H), 1.82 (s, 3H), 1.57 (s, 3H), 0.83 (d, *J* = 8.6 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.89, 162.31, 156.17, 155.36, 149.14, 136.35, 134.90, 134.13, 132.84, 132.03, 131.78, 129.70, 128.77, 127.51, 121.97, 120.51, 119.04, 118.33, 11820, 103.65, 60.30, 29.53, 26.16, 24.41, 18.34. LC-MS (ESI) m/z calcd for $C_{29}H_{25}F_3N_3O_6^+$ $(M+H)^+$ 568.17, found 568.17.

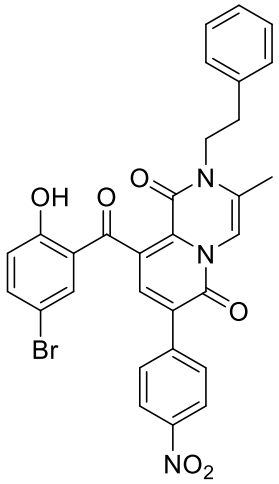
2-cyclohexyl-9-(2-hydroxybenzoyl)-3-methyl-7-(4-nitrophenyl)-2H-pyrido[1,2-a]pyrazine-1,6-dione



7r yellow solid, 41 mg, 28% (EA/Hex = 30%, R_f = 0.40), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.82 (s, 1H), 8.25 (d, *J* = 7.5 Hz, 2H), 7.95 (d, *J* = 8.1 Hz, 2H), 7.76 (s, 1H), 7.63 (s, 1H), 7.46 (s, 1H), 7.19 (d, *J* = 7.5 Hz, 1H), 7.06 (d, *J* = 8.2 Hz, 1H), 6.77 (s, 1H), 3.98 – 3.84 (m, 1H), 2.37 (s, 3H), 1.86 – 1.75 (m, 3H), 1.61 (d, *J* = 3.8 Hz, 3H), 0.87 –

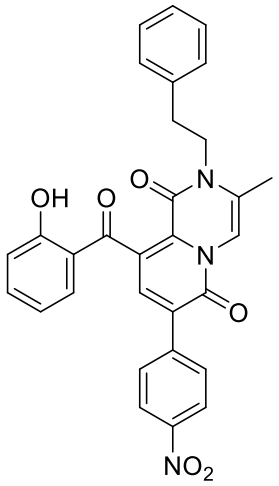
0.80 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.19, 162.22, 156.16, 155.39, 142.04, 136.33, 135.60, 131.83, 129.60, 129.42, 128.62, 127.34, 123.62, 120.57, 118.83 118.41, 60.29, 28.94, 26.11, 25.22, 11.44. LC-MS (ESI) m/z calcd for $C_{28}H_{26}N_3O_6^+$ $(M+H)^+$ 500.18, found 500.18.

9-(5-bromo-2-hydroxybenzoyl)-3-methyl-7-(4-nitrophenyl)-2-phenethyl-2H-pyrido[1,2-a]pyrazine-1,6-dione



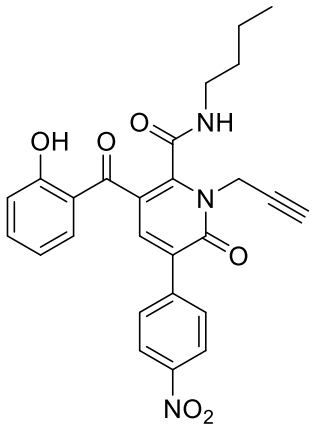
7s yellow solid, 66 mg, 36% (EA/Hex = 30%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.78 (s, 1H), 8.31 (d, *J* = 8.7 Hz, 2H), 8.01 (d, *J* = 8.7 Hz, 2H), 7.81 (s, 1H), 7.68 (s, 1H), 7.57 (d, *J* = 8.9 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 4H), 7.14 (d, *J* = 7.1 Hz, 2H), 7.02 (d, *J* = 8.9 Hz, 1H), 4.16 – 4.04 (m, 2H), 2.93 (dd, *J* = 15.2, 7.9 Hz, 2H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.29, 161.56, 156.14, 150.01, 147.93, 141.72, 139.20, 137.22, 135.26, 133.63, 131.05, 129.59, 128.93, 128.80, 128.59, 127.28, 123.71, 120.74, 110.64, 103.76, 46.09. 34.43, 17.49. LC-MS (ESI) m/z calcd for $C_{30}H_{23}BrN_3O_6^+$ $(M+H)^+$ 600.08, found 600.08.

9-(2-hydroxybenzoyl)-3-methyl-7-(4-nitrophenyl)-2-phenethyl-2H-pyrido[1,2-a]pyrazine-1,6-dione



7t yellow solid, 62 mg, 40% (EA/Hex = 30%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.85 (s, 1H), 8.30 (d, *J* = 8.0 Hz, 2H), 8.00 (d, *J* = 7.6 Hz, 2H), 7.80 (s, 1H), 7.70 (s, 1H), 7.51 (s, 1H), 7.29 (s, 2H), 7.26 – 7.20 (m, 2H), 7.17 – 7.08 (m, 3H), 6.83 (s, 1H), 4.15 – 4.01 (m, 2H), 2.92 (d, *J* = 6.7 Hz, 2H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.00, 162.52, 156.16, 155.97, 147.63, 141.86, 137.32, 136.64, 135.52, 132.03, 131.05, 129.56, 128.89, 128.81, 128.43, 127.92, 127.16, 123.66, 120.54, 119.09, 118.82, 118.66, 103.58, 46.08, 34.19, 17.38. LC-MS (ESI) m/z calcd for $C_{30}H_{24}N_3O_6^+$ $(M+H)^+$ 522.17, found 522.17.

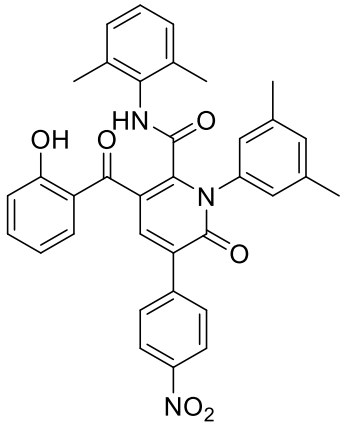
N-butyl-3-(2-hydroxybenzoyl)-5-(4-nitrophenyl)-6-oxo-1-(prop-2-yn-1-yl)-1,6-dihydropyridine-2-carboxamide



8p yellow solid, 118 mg, 83% (EA/Hex = 30%, R_f = 0.30), ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.51 (s, 1H), 8.22 – 8.15 (m, 2H), 7.96 – 7.88 (m, 2H), 7.81 (d, *J* = 6.6 Hz, 1H), 7.57 (s, 1H), 7.19 – 7.11 (m, 1H), 7.07 (s, 1H), 6.89 – 6.82 (m, 1H), 6.63 (dd,

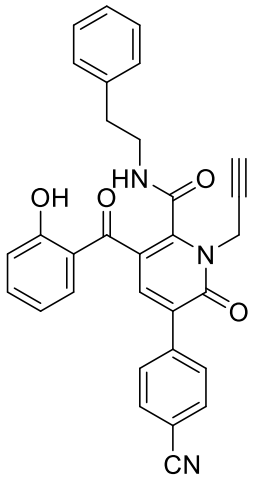
J = 8.1, 1.0 Hz, 1H), 5.44 (dd, *J* = 16.2, 2.3 Hz, 1H), 5.30 (dd, *J* = 16.2, 2.3 Hz, 1H), 3.22 (s, 1H), 2.86 – 2.74 (m, 1H), 1.45 – 1.36 (m, 1H), 1.33 – 1.24 (m, 1H), 1.15 (dq, *J* = 14.7, 7.3 Hz, 2H), 0.73 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-*d6*) δ 161.96, 159.99, 154.56, 147.11, 142.97, 136.33, 132.92, 130.44, 130.20, 130.13, 129.22, 129.09, 123.59, 122.94, 119.33, 116.34, 86.72, 79.41, 74.54, 31.91, 30.17, 20.17, 14.01. LC-MS (ESI) m/z calcd for $C_{26}H_{24}N_3O_6^+$ $(M+H)^+$ 474.17, found 474.17.

N-(2,6-dimethylphenyl)-1-(3,5-dimethylphenyl)-3-(2-hydroxybenzoyl)-5-(4-nitrophenyl)-6-oxo-1,6-dihydropyridine-2-carboxamide



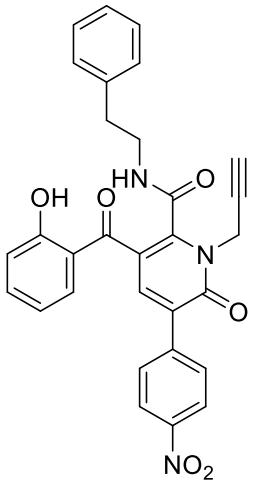
11a yellow solid, 140 mg, 79% (EA/Hex = 30%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.61 (s, 1H), 8.22 (d, *J* = 8.9 Hz, 2H), 7.93 (d, *J* = 9.0 Hz, 2H), 7.71 (s, 1H), 7.65 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.09 (s, 3H), 7.05 – 7.00 (m, 2H), 6.93 (dd, *J* = 7.3, 4.3 Hz, 3H), 2.34 (s, 6H), 1.80 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.99, 163.49, 160.46, 158.10, 147.57, 141.35, 139.84, 137.91, 137.31, 136.94, 135.03, 132.95, 131.86, 131.71, 129.49, 129.13, 128.43, 127.86, 126.13, 123.43, 119.59, 118.97, 118.82, 117.06, 29.68, 21.21, 17.95. LC-MS (ESI) m/z calcd for $C_{35}H_{30}N_3O_6^+$ $(M+H)^+$ 588.21, found 588.21.

5-(4-cyanophenyl)-3-(2-hydroxybenzoyl)-6-oxo-N-phenethyl-1-(prop-2-yn-1-yl)-1,6-dihydropyridine-2-carboxamide



11b yellow solid, 122 mg, 81% (EA/Hex = 30%, R_f = 0.25), ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.59 (s, 1H), 7.88 (dd, *J* = 20.5, 6.7 Hz, 5H), 7.61 (s, 1H), 7.31 – 7.12 (m, 5H), 7.03 (d, *J* = 6.7 Hz, 2H), 6.94 (t, *J* = 7.1 Hz, 1H), 6.68 (d, *J* = 7.7 Hz, 1H), 5.47 (d, *J* = 16.3 Hz, 1H), 5.34 (d, *J* = 16.3 Hz, 1H), 3.49 – 3.35 (m, 2H), 3.26 (s, 1H), 3.12 – 3.00 (m, 1H), 2.84 (d, *J* = 11.5 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d6*) δ 161.95, 160.06, 154.68, 141.05, 139.42, 135.98, 132.72, 132.42, 130.94, 130.63, 129.83, 129.35, 129.29, 128.98, 128.76, 126.73, 122.92, 119.48, 119.20, 116.48, 110.97, 86.82, 79.47, 74.60, 41.58, 34.23, 31.99. LC-MS (ESI) m/z calcd for $C_{31}H_{24}N_3O_4^+$ $(M+H)^+$ 502.18, found 502.18.

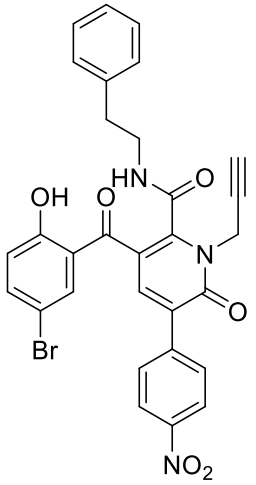
3-(2-hydroxybenzoyl)-5-(4-nitrophenyl)-6-oxo-N-phenethyl-1-(prop-2-yn-1-yl)-1,6-dihydropyridine-2-carboxamide



11c yellow solid, 120 mg, 77% (EA/Hex = 30%, R_f = 0.25), ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.61 (s, 1H), 8.23 (d, *J* = 8.5 Hz, 2H), 7.95 (dd, *J* = 19.4, 7.8 Hz, 3H),

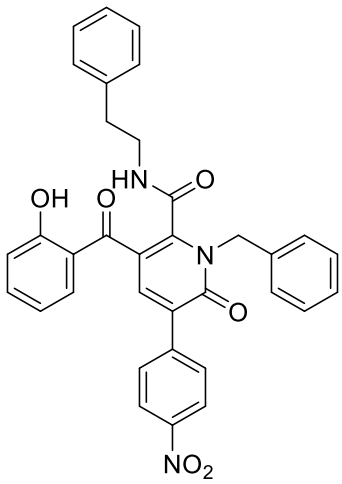
7.66 (s, 1H), 7.32 – 7.13 (m, 5H), 7.04 (d, *J* = 6.6 Hz, 2H), 6.95 (t, *J* = 7.0 Hz, 1H), 6.69 (d, *J* = 7.6 Hz, 1H), 5.49 (d, *J* = 16.3 Hz, 1H), 5.36 (d, *J* = 16.2 Hz, 1H), 3.44 (td, *J* = 12.8, 4.8 Hz, 2H), 3.27 (s, 1H), 3.07 (t, *J* = 9.8 Hz, 1H), 2.86 (t, *J* = 11.7 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d6*) δ 161.91, 160.05, 154.69, 147.21, 143.00, 139.41, 136.27, 133.02, 130.66, 130.48, 130.22, 129.35, 129.29, 128.98, 128.76, 126.74, 123.65, 122.89, 119.49, 116.50, 86.82, 79.45, 74.64, 41.58, 34.21, 32.04. LC-MS (ESI) m/z calcd for $C_{30}H_{24}N_3O_6^+$ $(M+H)^+$ 522.17, found 522.17.

3-(5-bromo-2-hydroxybenzoyl)-5-(4-nitrophenyl)-6-oxo-N-phenethyl-1-(prop-2-yn-1-yl)-1,6-dihydropyridine-2-carboxamide



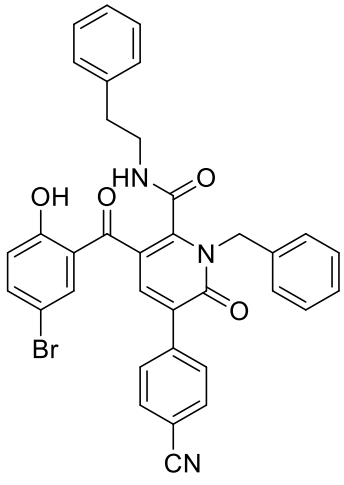
11d yellow solid, 150 mg, 84% (EA/Hex = 30%, R_f = 0.25), ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.99 (s, 1H), 8.23 (d, *J* = 8.9 Hz, 2H), 8.01 (dd, *J* = 10.4, 5.6 Hz, 3H), 7.77 (s, 1H), 7.44 – 7.35 (m, 2H), 7.27 (t, *J* = 7.4 Hz, 2H), 7.19 (t, *J* = 7.3 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 2H), 6.65 (d, *J* = 8.6 Hz, 1H), 5.39 (dt, *J* = 17.9, 9.1 Hz, 2H), 3.50 – 3.40 (m, 1H), 3.27 (s, 1H), 3.13 – 3.01 (m, 1H), 2.91 – 2.80 (m, 1H), 2.64 – 2.53 (m, 1H). ^{13}C NMR (100 MHz, DMSO-*d6*) δ 161.92, 160.03, 154.05, 147.23, 142.90, 139.32, 136.36, 133.25, 133.06, 131.83, 130.59, 130.31, 129.00, 128.79, 128.49, 126.78, 125.51, 123.59, 118.73, 110.61, 86.22, 79.39, 74.67, 41.50, 34.23, 32.05. LC-MS (ESI) m/z calcd for $C_{30}H_{23}BrN_3O_6^+$ $(M+H)^+$ 600.08, found 600.08.

1-benzyl-3-(2-hydroxybenzoyl)-5-(4-nitrophenyl)-6-oxo-N-phenethyl-1,6-dihydropyridine-2-carboxamide



11e yellow solid, 140 mg, 81% (EA/Hex = 30%, R_f = 0.25), ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.61 (s, 1H), 8.19 (d, *J* = 8.9 Hz, 2H), 7.94 (t, *J* = 7.0 Hz, 3H), 7.66 (s, 1H), 7.48 – 7.33 (m, 4H), 7.32 – 7.11 (m, 6H), 7.03 (d, *J* = 7.1 Hz, 2H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 5.93 (d, *J* = 13.5 Hz, 1H), 5.77 (d, *J* = 13.9 Hz, 1H), 3.52 – 3.38 (m, 1H), 3.15 – 3.03 (m, 1H), 2.92 – 2.80 (m, 1H), 2.55 (dd, *J* = 12.6, 5.5 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d6*) δ 162.30, 160.64, 154.67, 147.10, 143.23, 139.45, 137.63, 137.24, 132.77, 130.64, 130.35, 130.17, 129.39, 129.15, 128.94, 128.87, 128.80, 128.28, 127.69, 126.69, 123.59, 123.13, 119.52, 116.53, 86.60, 45.39, 41.58, 34.21, 31.42, 22.53, 14.43. LC-MS (ESI) m/z calcd for $C_{34}H_{28}N_3O_6^+$ $(M+H)^+$ 574.20, found 574.20.

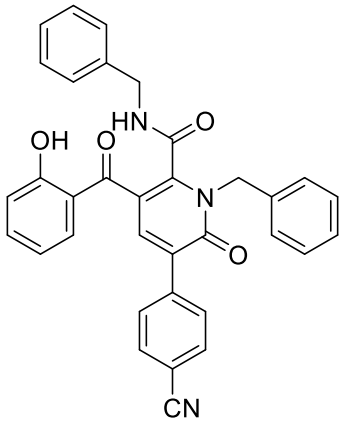
1-benzyl-3-(5-bromo-2-hydroxybenzoyl)-5-(4-cyanophenyl)-6-oxo-N-phenethyl-1,6-dihydropyridine-2-carboxamide



11f yellow solid, 148 mg, 78% (EA/Hex = 30%, R_f = 0.25), ^{1}H NMR (400 MHz,

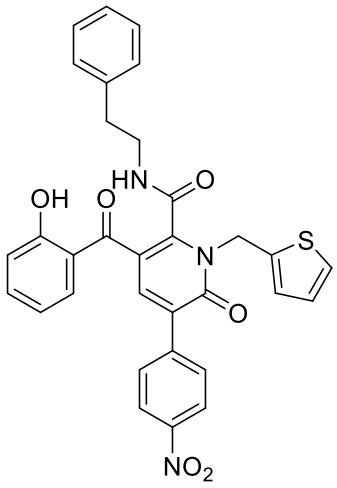
DMSO-*d6*) δ 9.98 (s, 1H), 8.05 (s, 1H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.71 (s, 1H), 7.45 – 7.32 (m, 6H), 7.27 (dd, *J* = 15.1, 7.4 Hz, 3H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 2H), 6.69 (d, *J* = 8.6 Hz, 1H), 5.90 (d, *J* = 13.5 Hz, 1H), 5.76 (d, *J* = 13.5 Hz, 1H), 3.53 – 3.42 (m, 1H), 3.15 – 3.04 (m, 1H), 2.91 – 2.79 (m, 1H), 2.60 (td, *J* = 12.3, 5.7 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d6*) δ 162.37, 160.65, 154.04, 141.17, 139.38, 137.60, 137.01, 133.20, 132.49, 132.30, 131.88, 130.96, 129.87, 128.95, 128.86, 128.83, 128.37, 128.29, 127.70, 126.73, 125.78, 119.23, 118.76, 110.84, 110.66, 86.04, 45.35, 41.49, 34.27. LC-MS (ESI) m/z calcd for $C_{305}H_{27}BrN_3O_4^+$ $(M+H)^+$ 632.12, found 632.12.

N,1-dibenzyl-5-(4-cyanophenyl)-3-(2-hydroxybenzoyl)-6-oxo-1,6-dihydropyridine-2-carboxamide



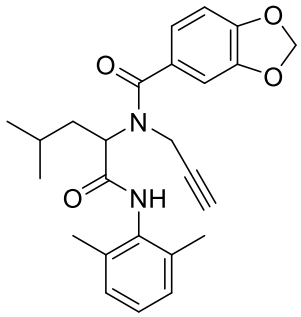
11g yellow solid, 114 mg, 70% (EA/Hex = 30%, R_f = 0.25), ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.56 (s, 1H), 7.95 – 7.74 (m, 5H), 7.59 (s, 1H), 7.42 – 7.32 (m, 4H), 7.27 (t, *J* = 7.0 Hz, 1H), 7.24 – 7.10 (m, 7H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 5.91 (d, *J* = 13.7 Hz, 1H), 5.81 – 5.65 (m, 1H), 4.42 (d, *J* = 15.6 Hz, 1H), 4.06 (d, *J* = 15.6 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d6*) δ 162.87, 160.64, 154.55, 141.24, 137.97, 137.65, 136.88, 132.54, 132.36, 130.96, 130.49, 129.79, 129.45, 129.17, 128.84, 128.28. 128.23, 128.20, 127.66, 127.07, 123.02, 119.38, 119.21, 116.48, 110.82, 86.82, 45.42, 43.58. LC-MS (ESI) m/z calcd for $C_{34}H_{26}N_3O_4^+$ $(M+H)^+$ 540.19, found 540.19.

3-(2-hydroxybenzoyl)-5-(4-nitrophenyl)-6-oxo-N-phenethyl-1-(thiophen-2-ylmethyl)-1,6-dihydropyridine-2-carboxamide



11h yellow solid, 120 mg, 70% (EA/Hex = 30%, R_f = 0.20), ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.57 (s, 1H), 8.23 (d, *J* = 8.9 Hz, 2H), 7.95 (dd, *J* = 15.6, 8.3 Hz, 3H), 7.63 (s, 1H), 7.46 (dd, *J* = 5.1, 1.0 Hz, 1H), 7.33 – 7.15 (m, 6H), 7.06 (d, *J* = 7.3 Hz, 2H), 7.01 (dd, *J* = 5.0, 3.6 Hz, 1H), 6.94 (t, *J* = 7.5 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.06 (d, *J* = 12.7 Hz, 1H), 5.91 (d, *J* = 13.0 Hz, 1H), 3.55 – 3.43 (m, 1H), 3.16 – 3.03 (m, 1H), 2.87 (td, *J* = 12.2, 5.0 Hz, 1H), 2.58 (td, *J* = 12.0, 5.6 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d6*) δ 162.19, 160.40, 154.68, 147.16, 143.16, 139.47, 138.91, 136.58, 132.82, 130.63, 130.30, 130.17, 129.37, 129.26, 129.07, 128.95, 128.83, 127.26, 126.99, 126.70, 123.65, 123.00, 119.48, 116.50, 86.78, 41.58, 34.23, 31.42. LC-MS (ESI) m/z calcd for $C_{32}H_{26}N_3O_6S^+$ $(M+H)^+$ 580.15, found 580.15.

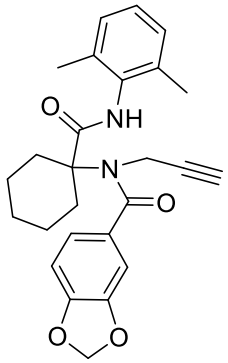
N-(1-((2,6-dimethylphenyl)amino)-4-methyl-1-oxopentan-2-yl)-N-(prop-2-yn-1-yl)benzo[d][1,3]dioxole-5-carboxamide



14 white solid, 116 mg, 92% (EA/Hex = 20%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$)

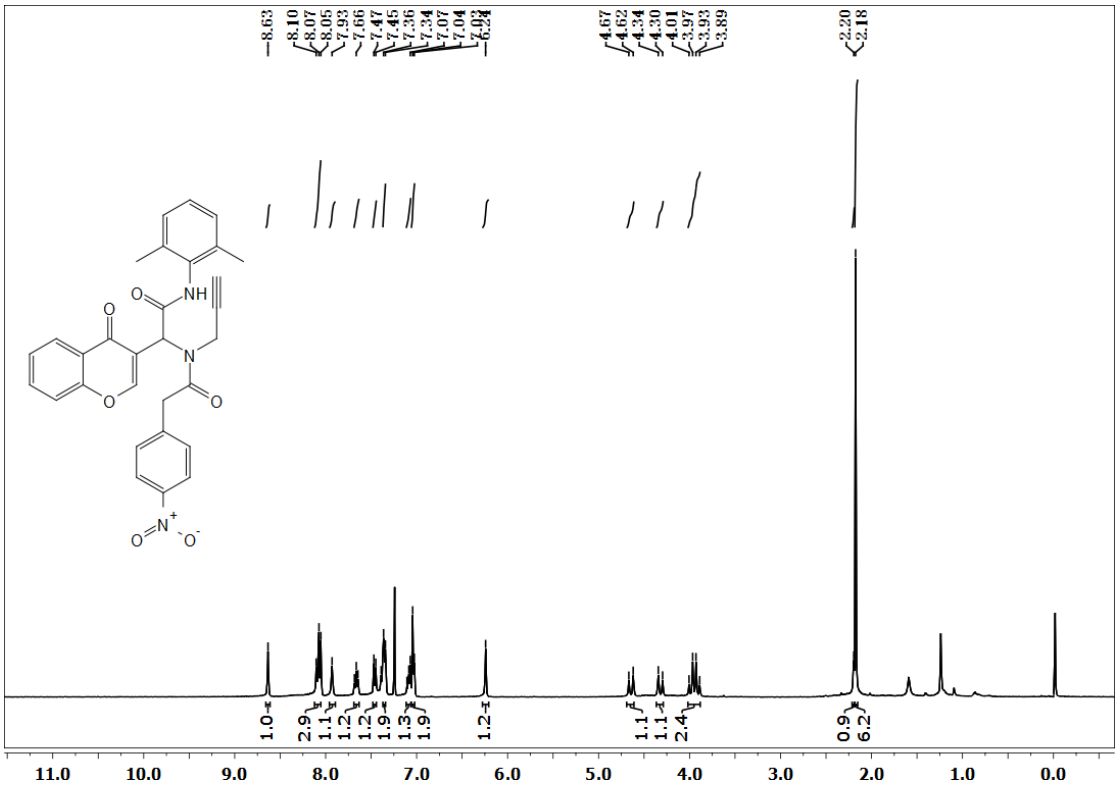
δ 8.35 (s, 1H), 7.22 (dd, *J* = 15.9, 4.1 Hz, 1H), 7.11 (s, 1H), 7.09 – 6.98 (m, 3H), 6.88 – 6.75 (m, 1H), 6.00 (s, 2H), 5.12 (s, 1H), 4.24 (d, *J* = 17.0 Hz, 1H), 4.06 (s, 1H), 2.36 (s, 1H), 2.18 (d, *J* = 4.2 Hz, 6H), 2.10 – 1.96 (m, 2H), 1.81 (s, 1H), 1.03 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.05, 168.99, 149.80, 147.66, 134.99, 133.72, 128.31, 128.10, 127.09, 122.30, 108.20, 108.07, 107.83, 101.72, 101.62, 80.28, 73.17, 57.37, 37.70, 37.31, 25.09, 22.49, 18.50. LC-MS (ESI) m/z calcd for $C_{25}H_{29}N_2O_4^+$ $(M+H)^+$ 421.21, found 421.21.

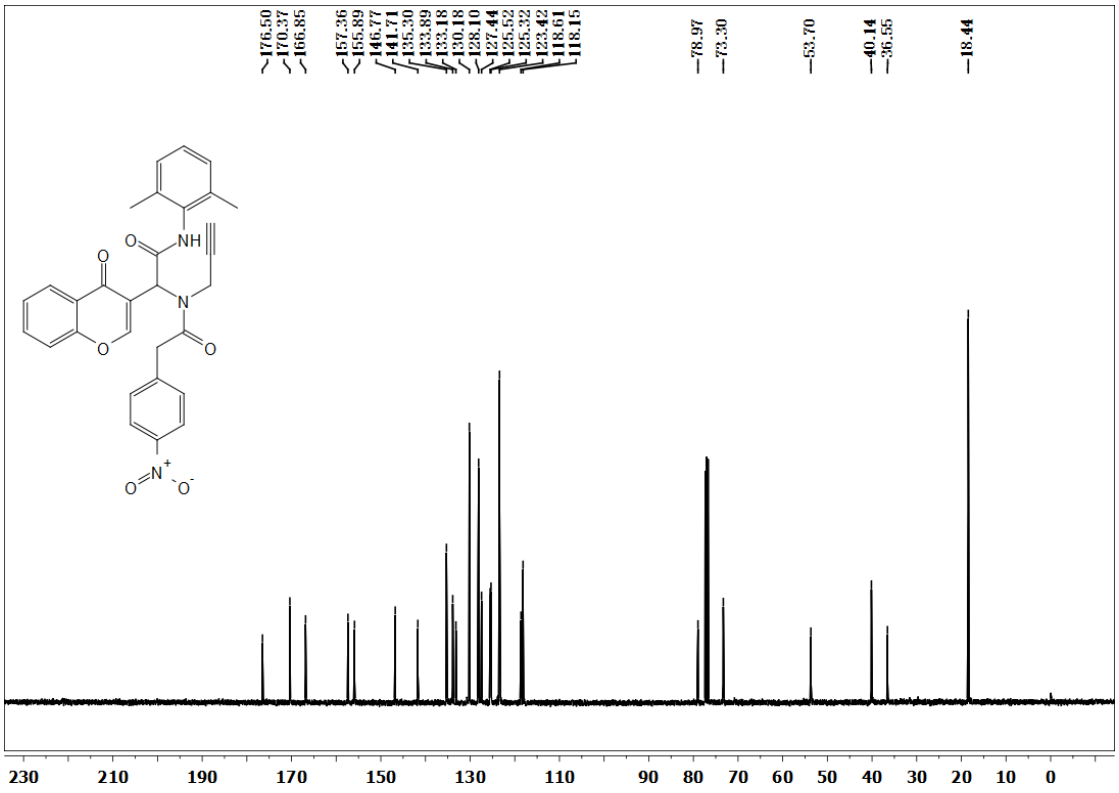
N-(1-((2,6-dimethylphenyl)carbamoyl)cyclohexyl)-N-(prop-2-yn-1-yl)benzo[d][1,3]dioxole-5-carboxamide



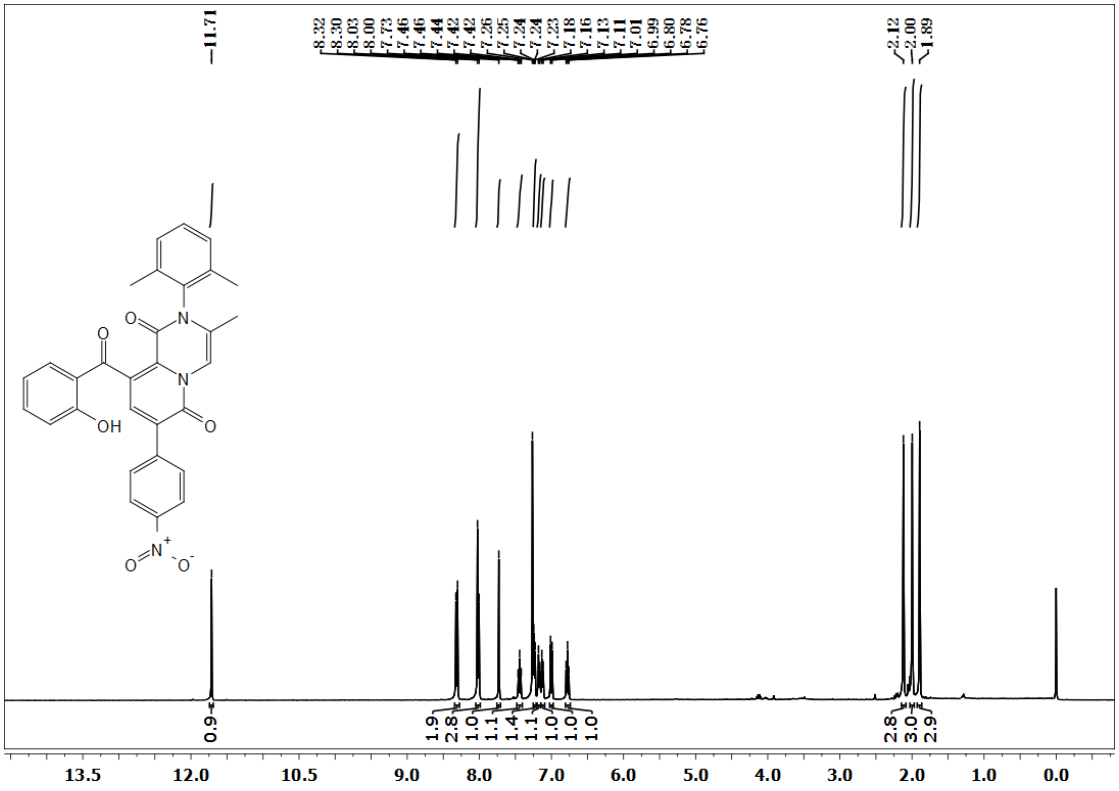
16 white solid, 115 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 7.25 – 7.20 (m, 1H), 7.12 (s, 1H), 7.04 (s, 3H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.00 (s, 2H), 4.13 (d, *J* = 1.7 Hz, 2H), 2.51 (s, 2H), 2.40 – 2.29 (m, 3H), 2.23 (s, 6H), 1.75 (s, 3H), 1.71 – 1.46 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.91, 171.85, 150.11, 147.78, 135.12, 134.38, 130.08, 128.14, 126.70, 123.00, 108.55, 108.27, 101.69, 80.37, 73.86, 67.16, 38.62, 32.86, 25.59, 22.80 (s), 18.91 (s). LC-MS (ESI) m/z calcd for $C_{26}H_{29}N_2O_4^+$ $(M+H)^+$ 432.20, found 432.20.

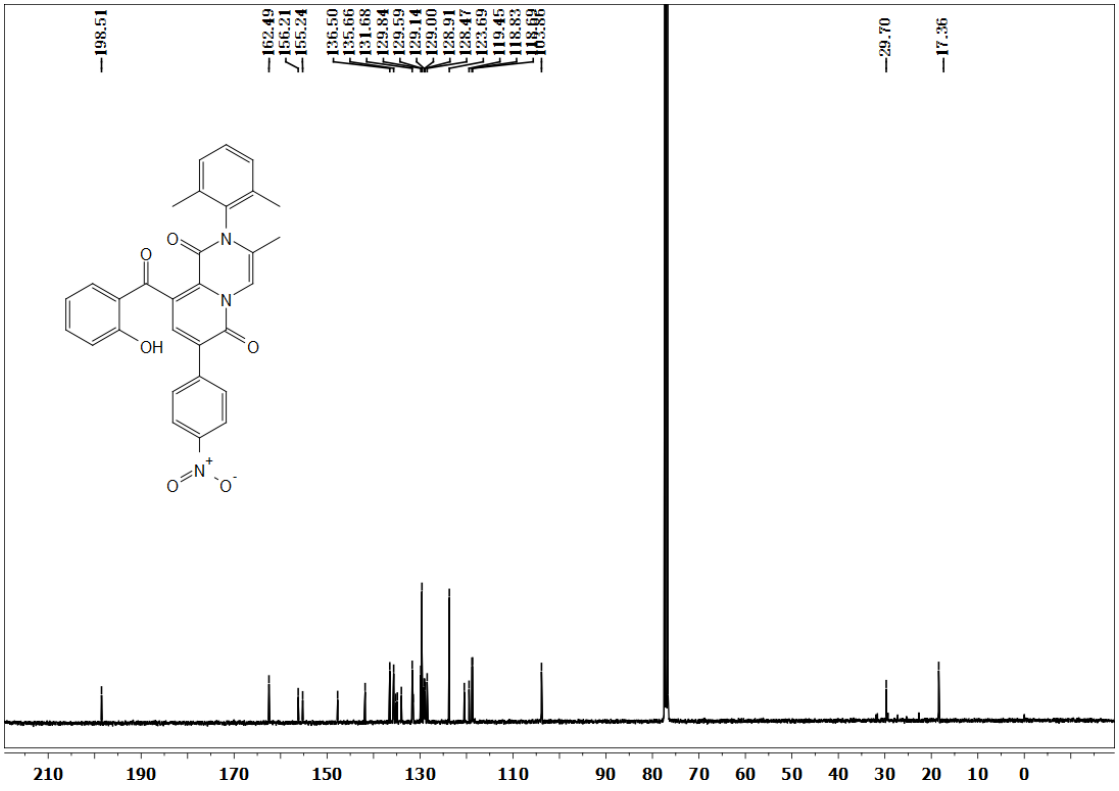
^{1}H NMR and ^{13}C NMR spectrum of **5a**



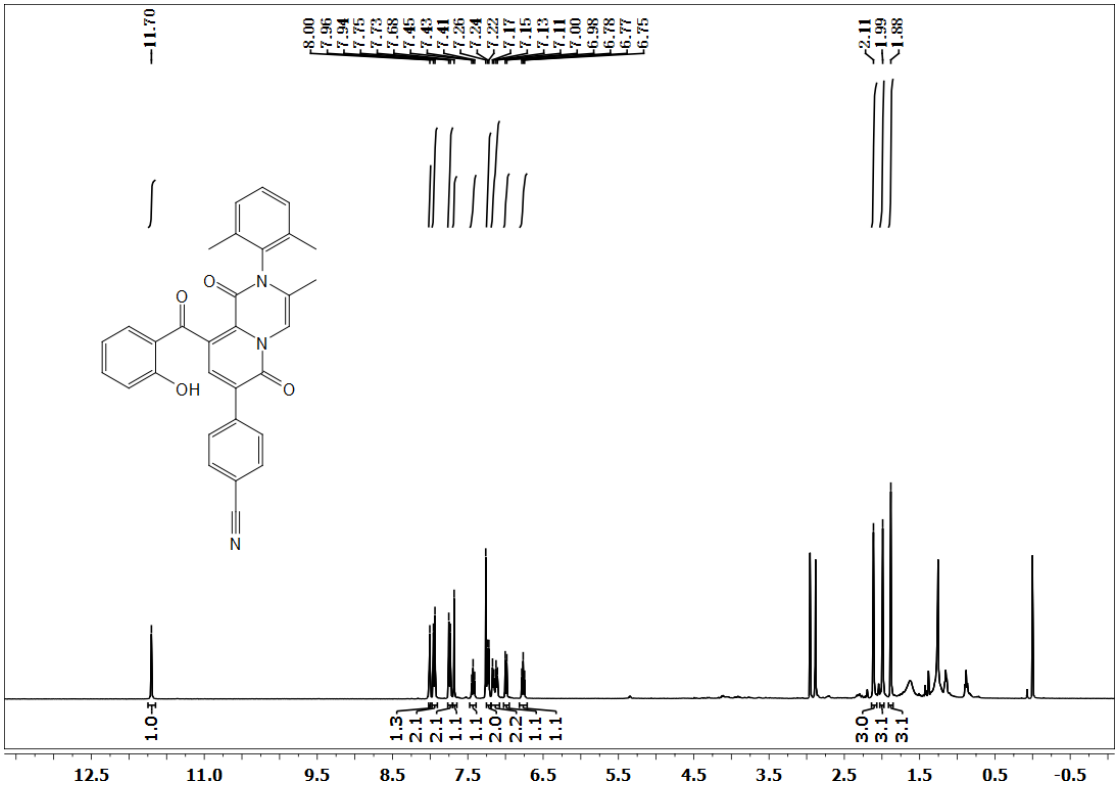


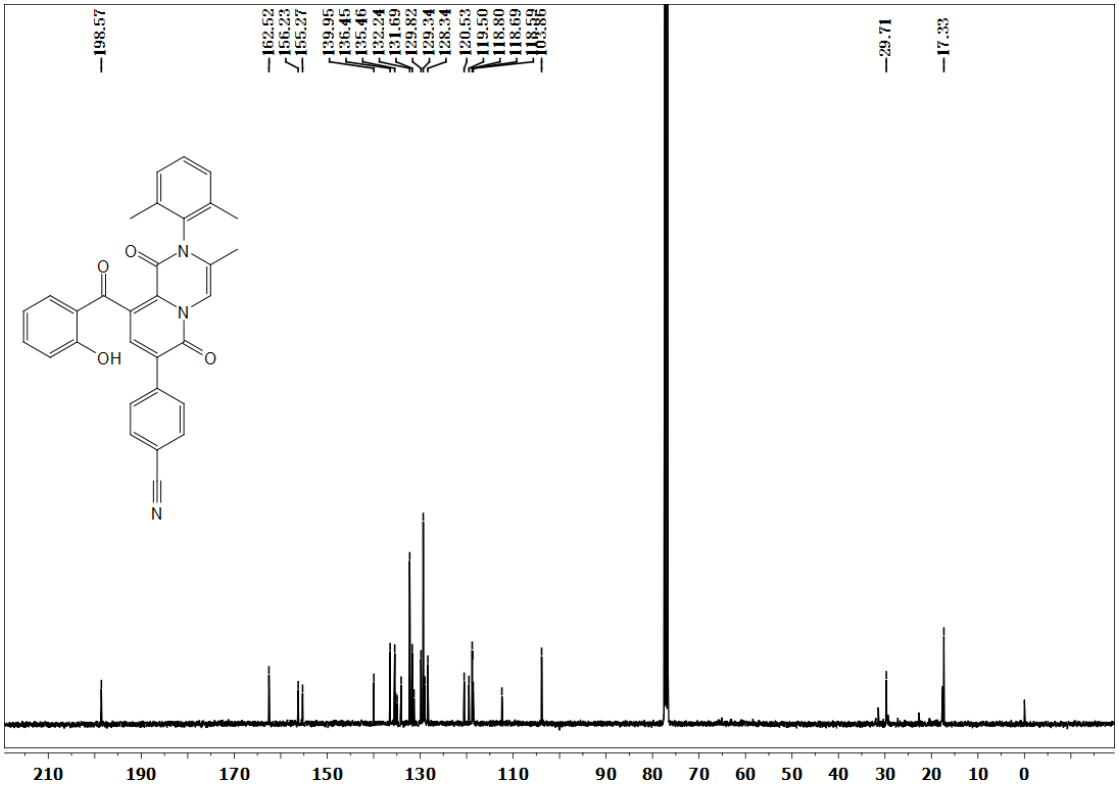
^{1}H NMR and ^{13}C NMR spectrum of **7a**



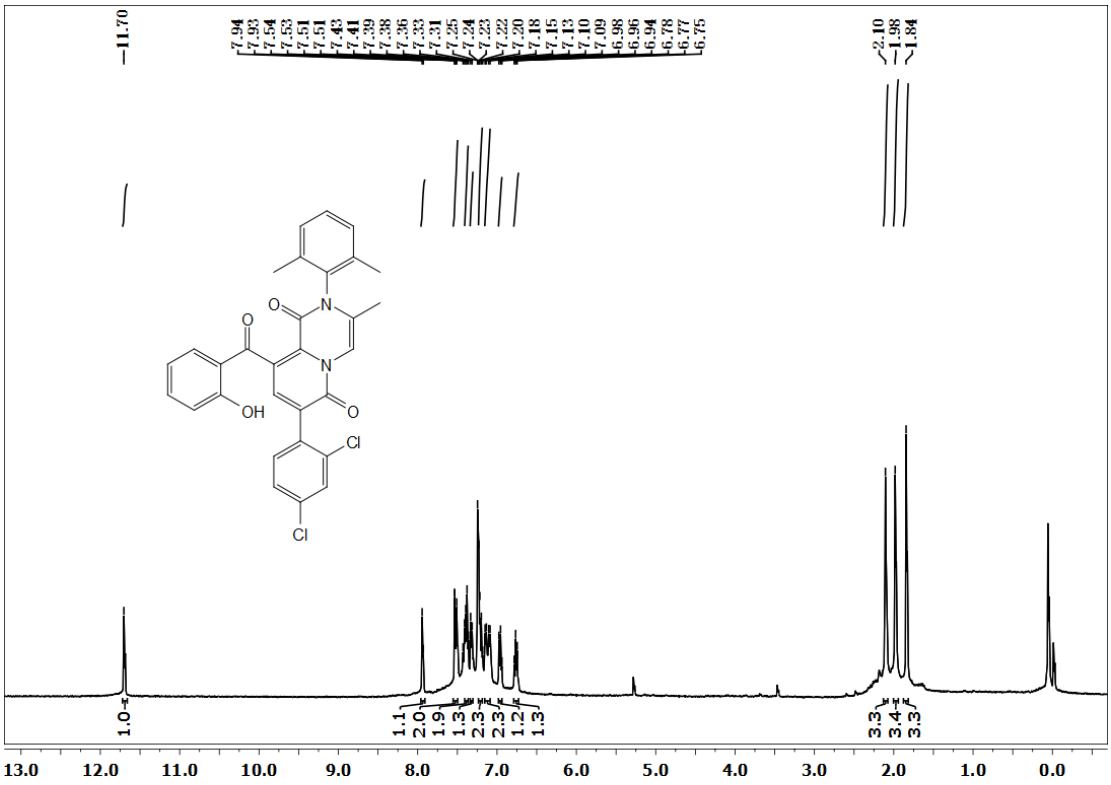


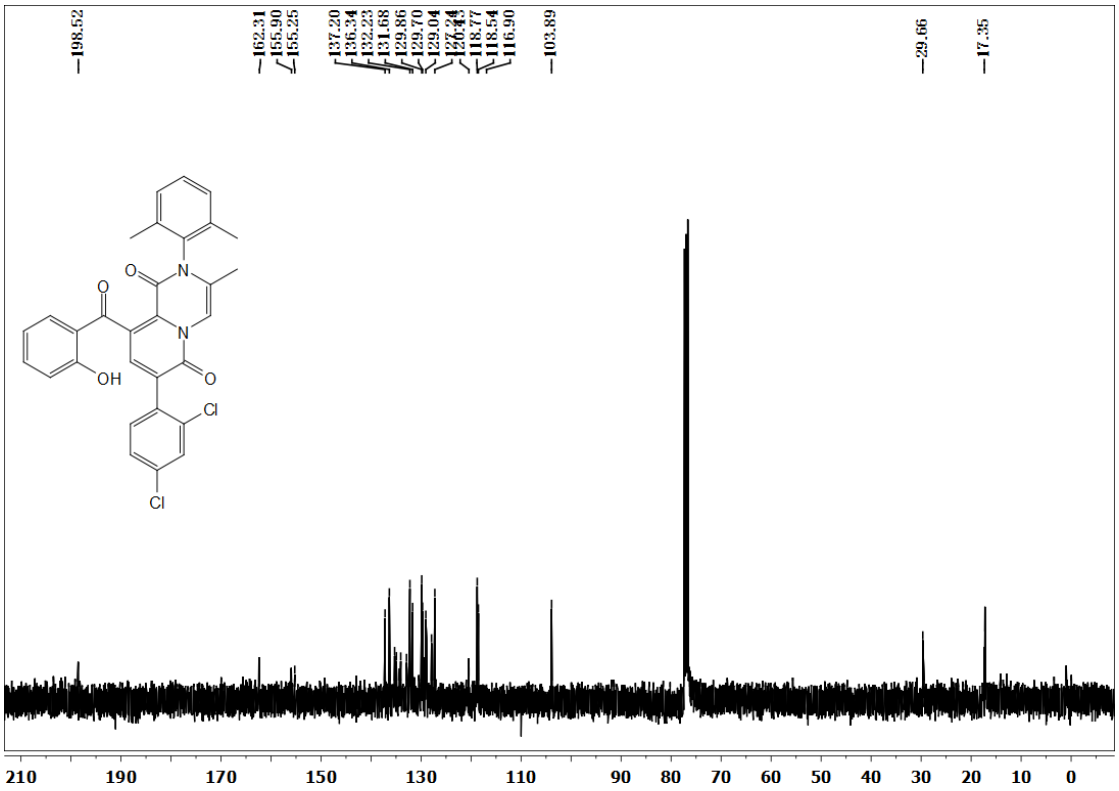
^{1}H NMR and ^{13}C NMR spectrum of **7b**



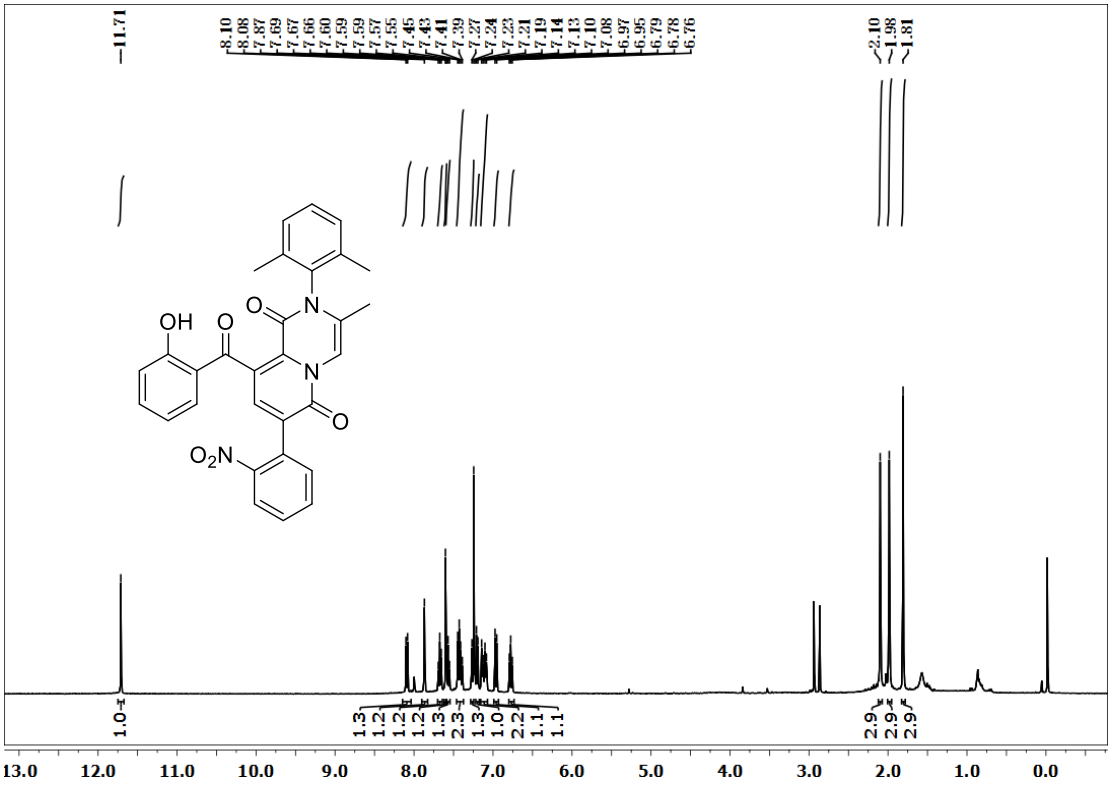


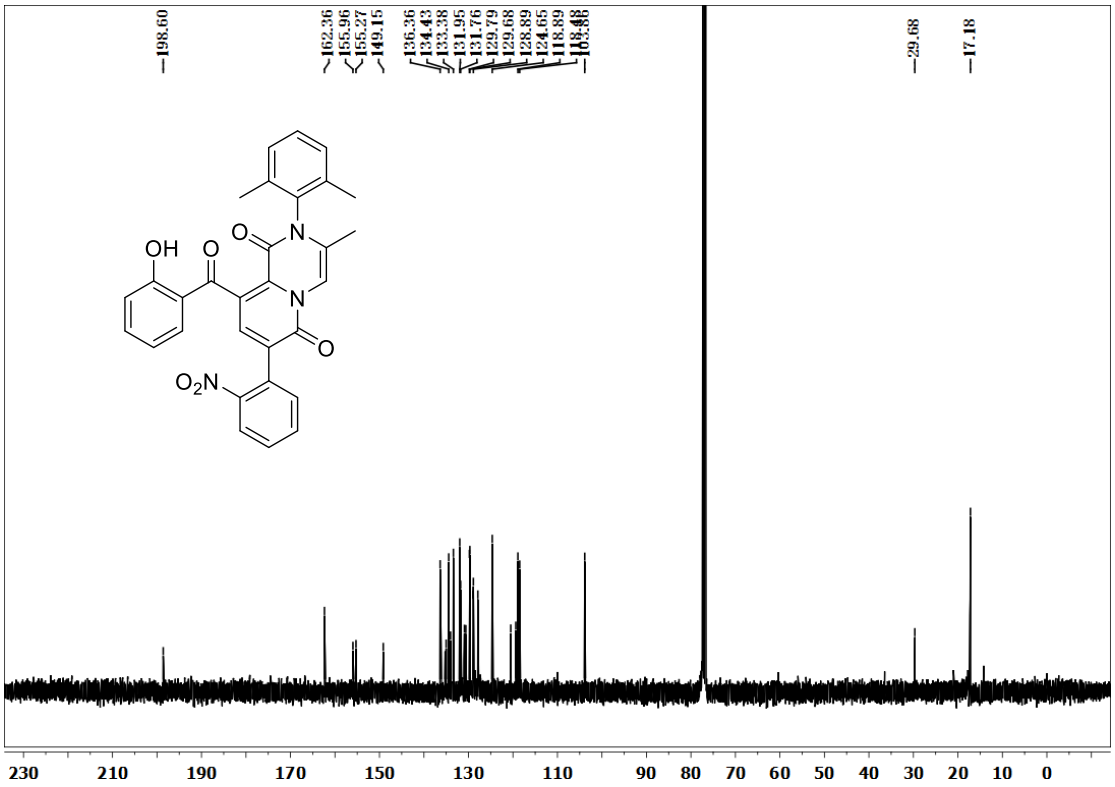
^{1}H NMR and ^{13}C NMR spectrum of **7c**



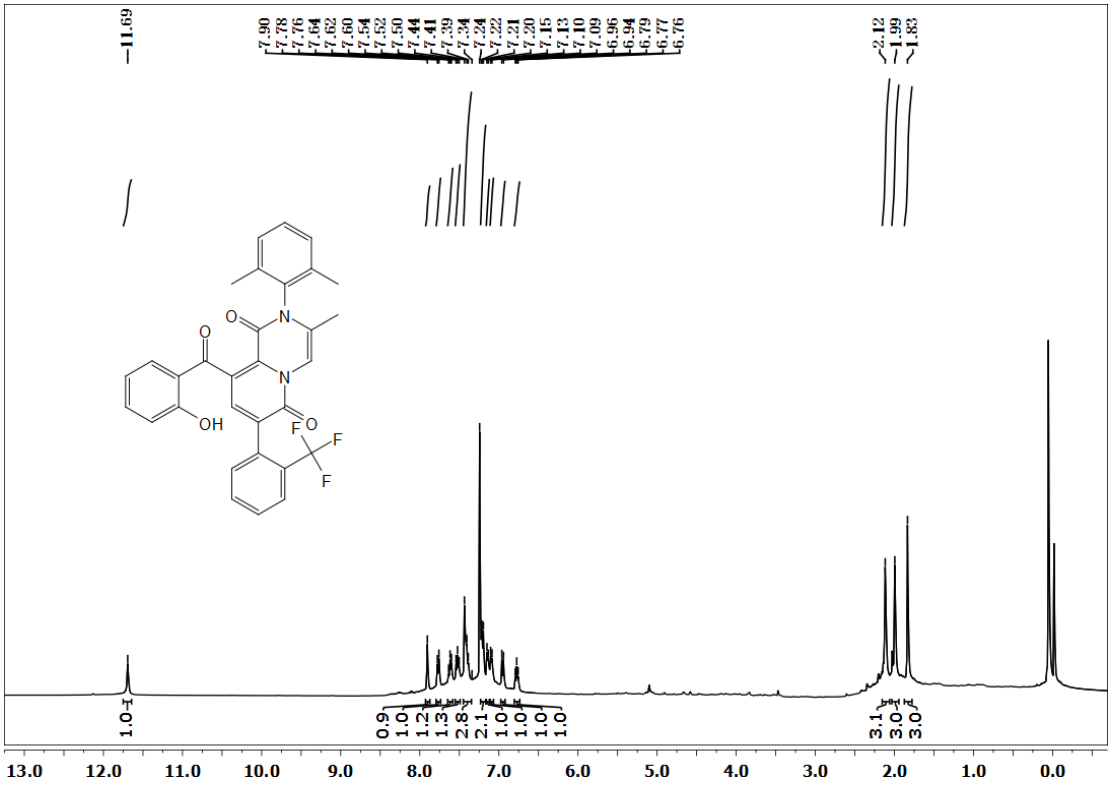


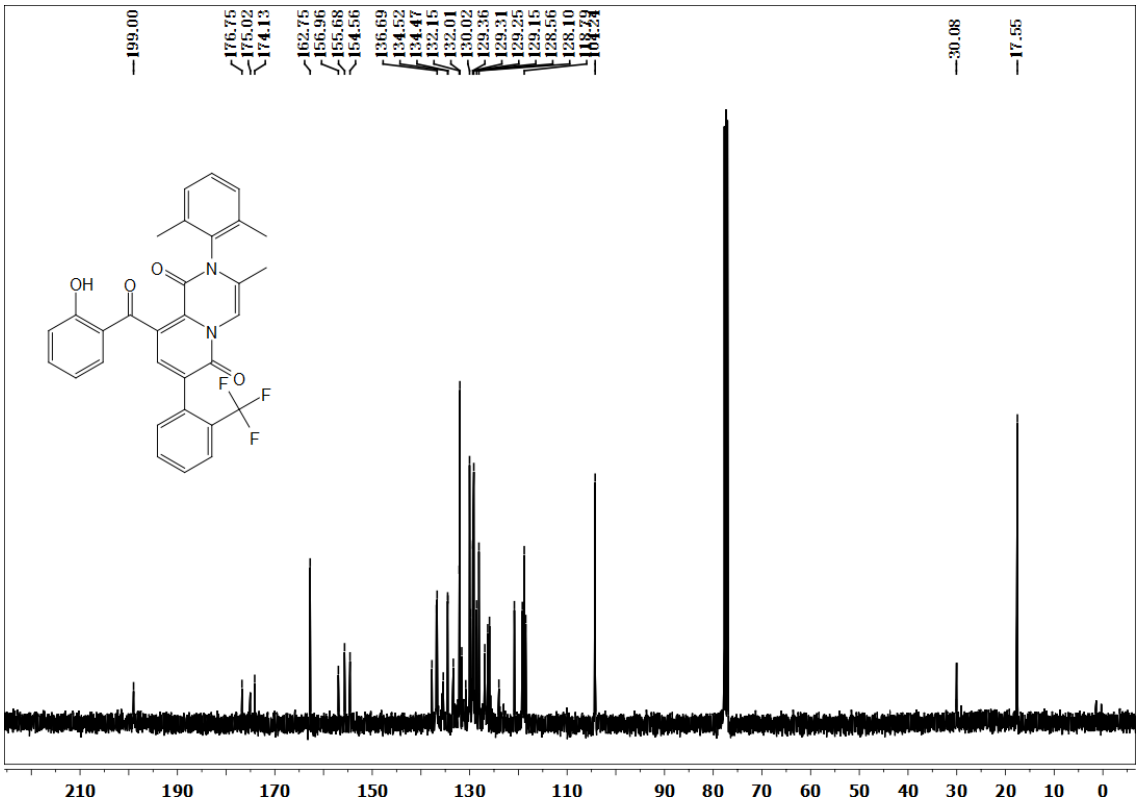
^{1}H NMR and ^{13}C NMR spectrum of **7d**



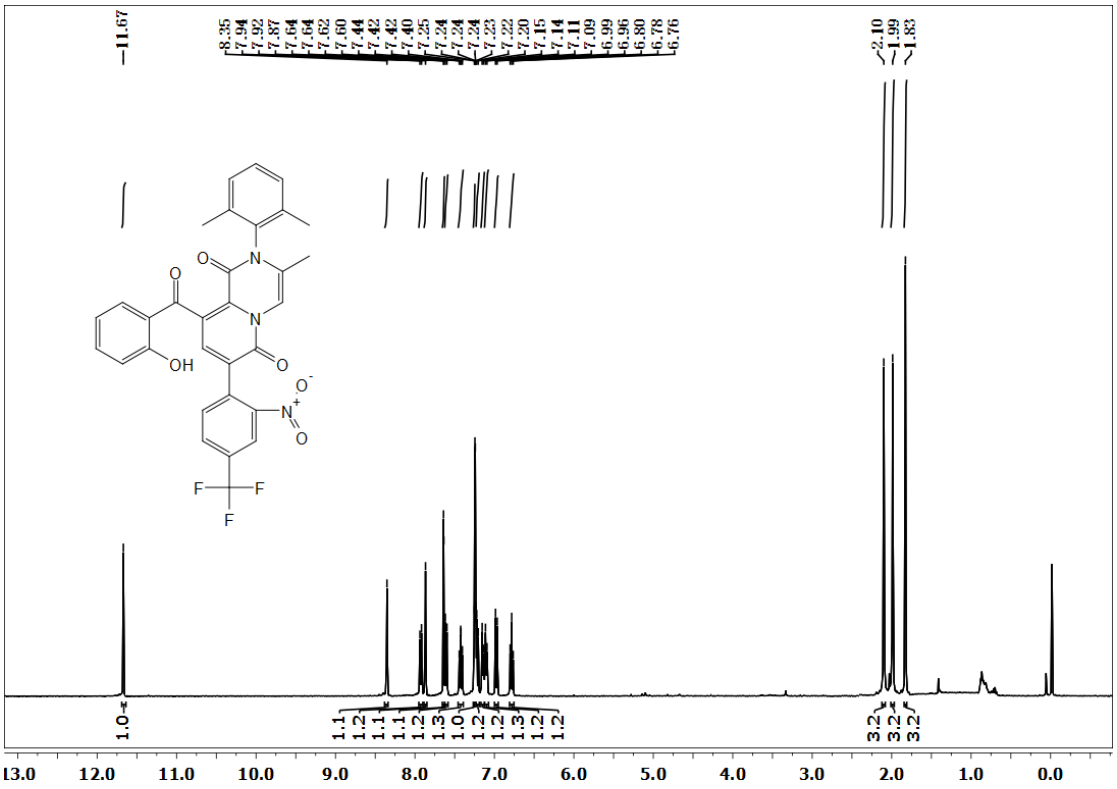


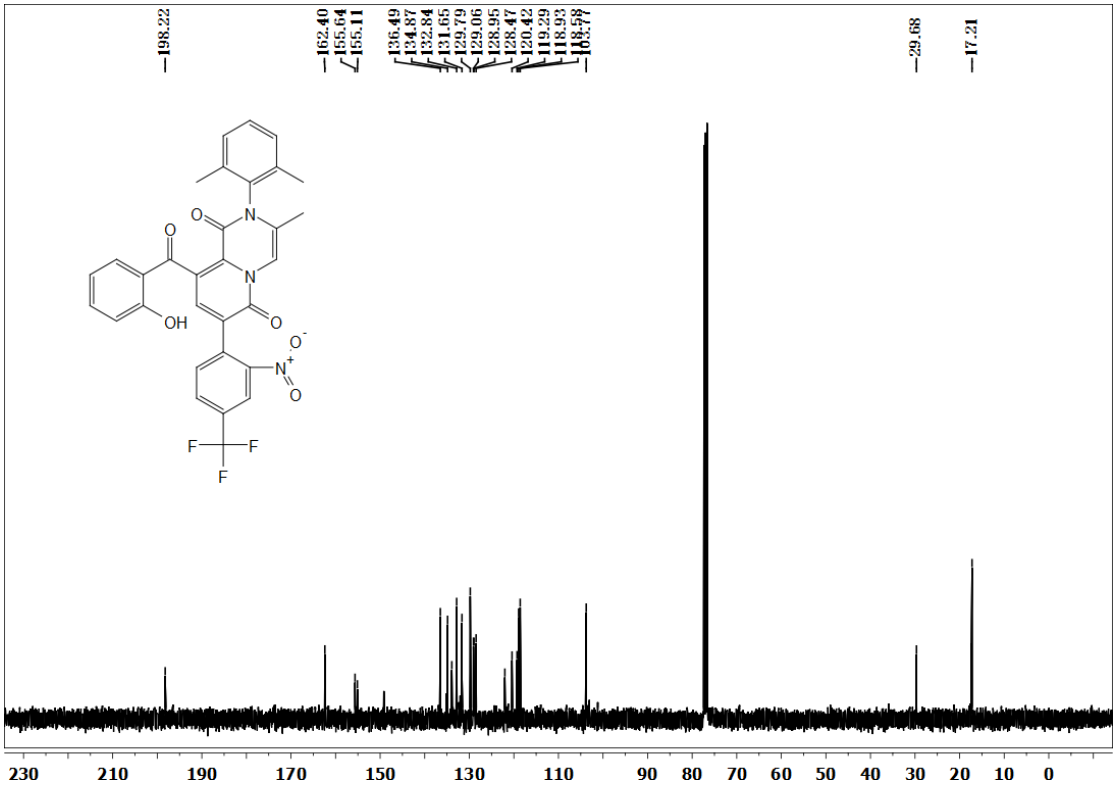
^{1}H NMR and ^{13}C NMR spectrum of **7e**



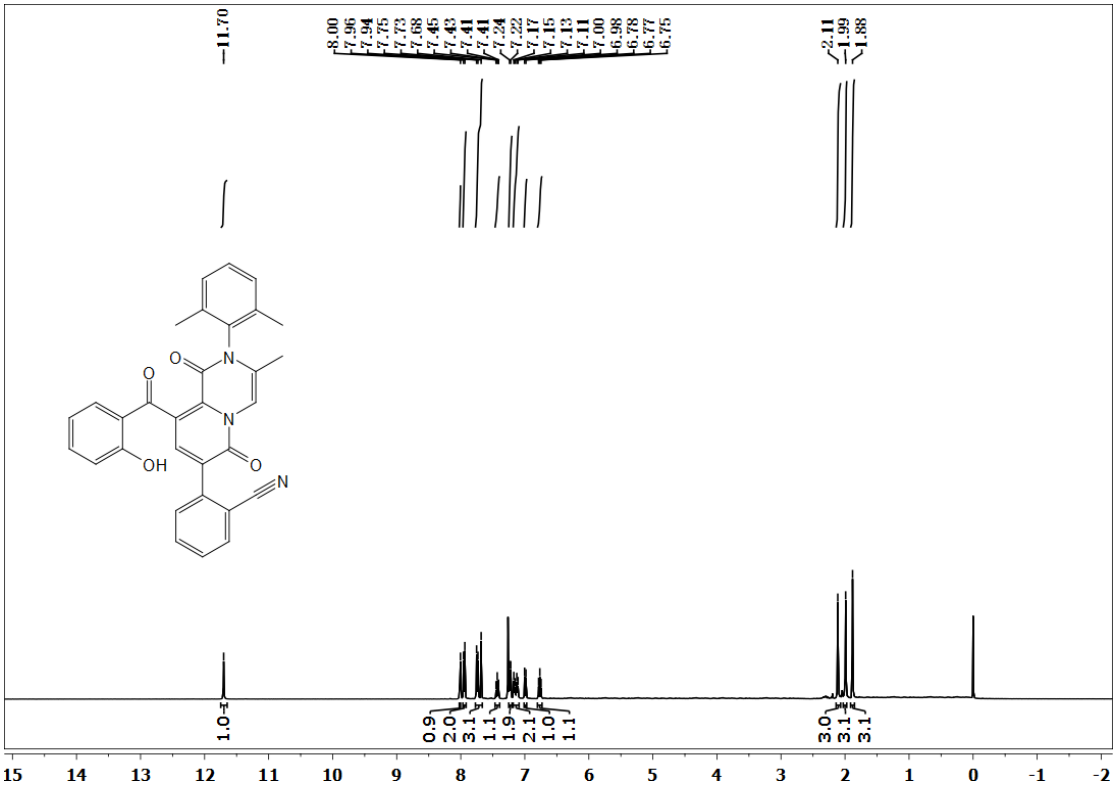


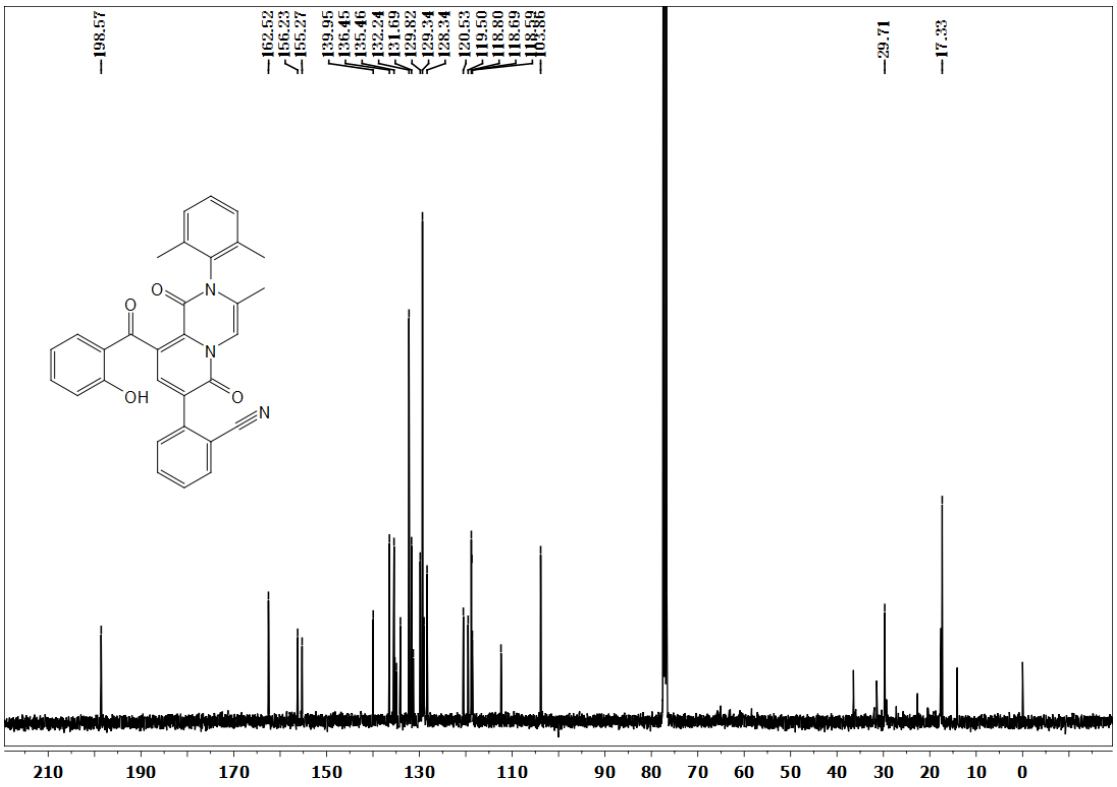
^{1}H NMR and ^{13}C NMR spectrum of **7f**



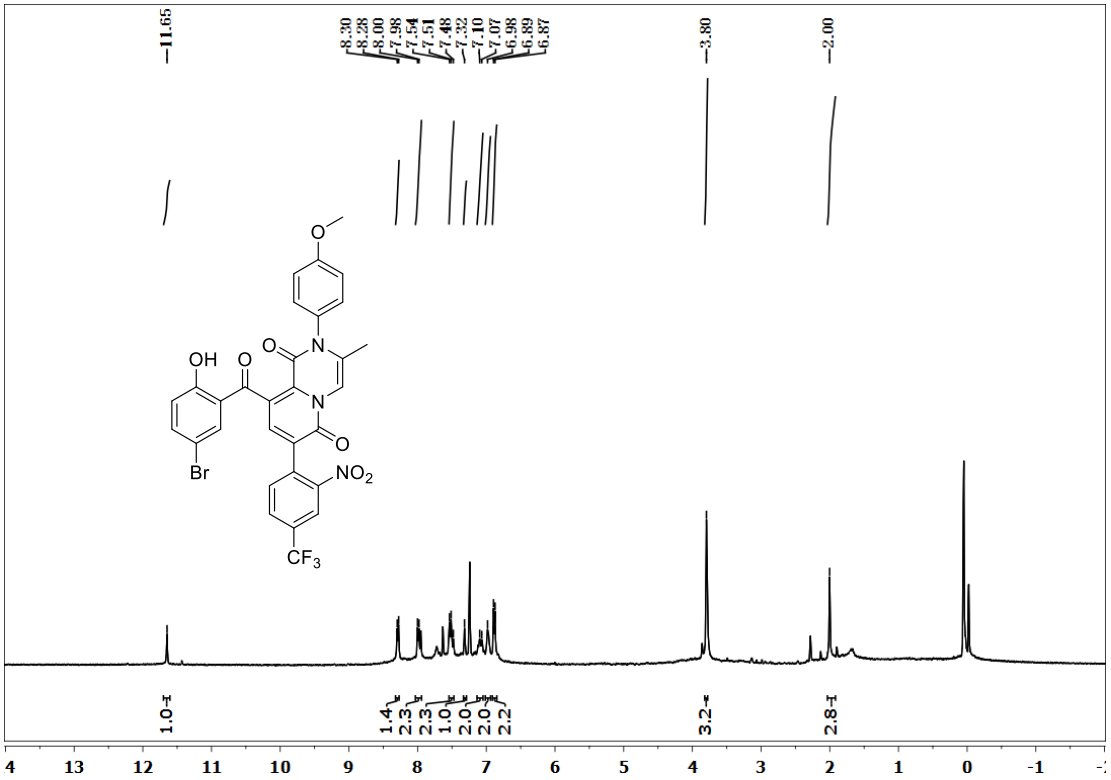


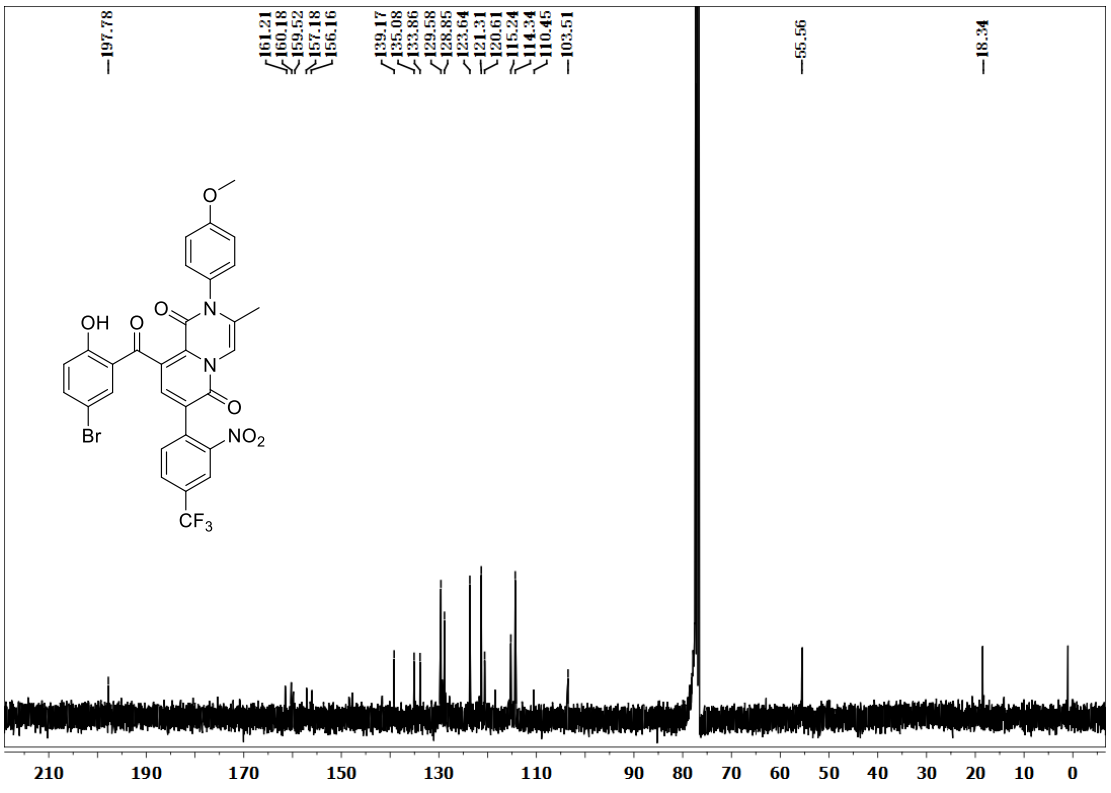
^{1}H NMR and ^{13}C NMR spectrum of **7g**



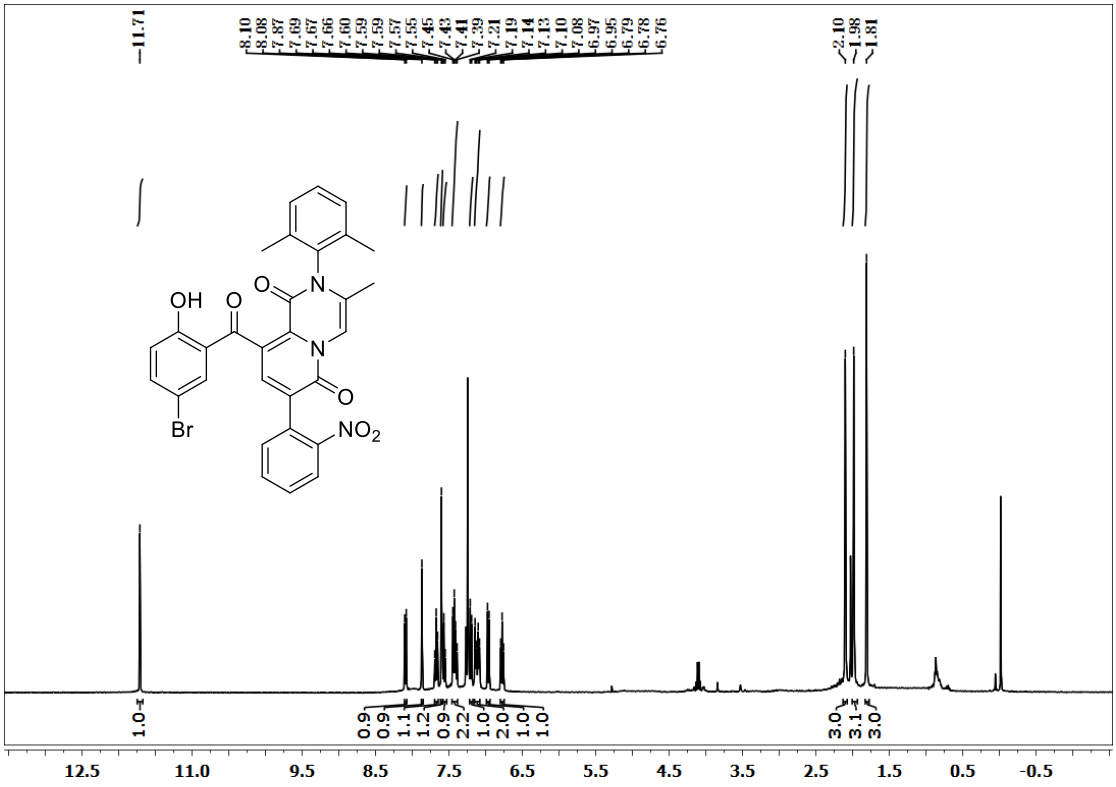


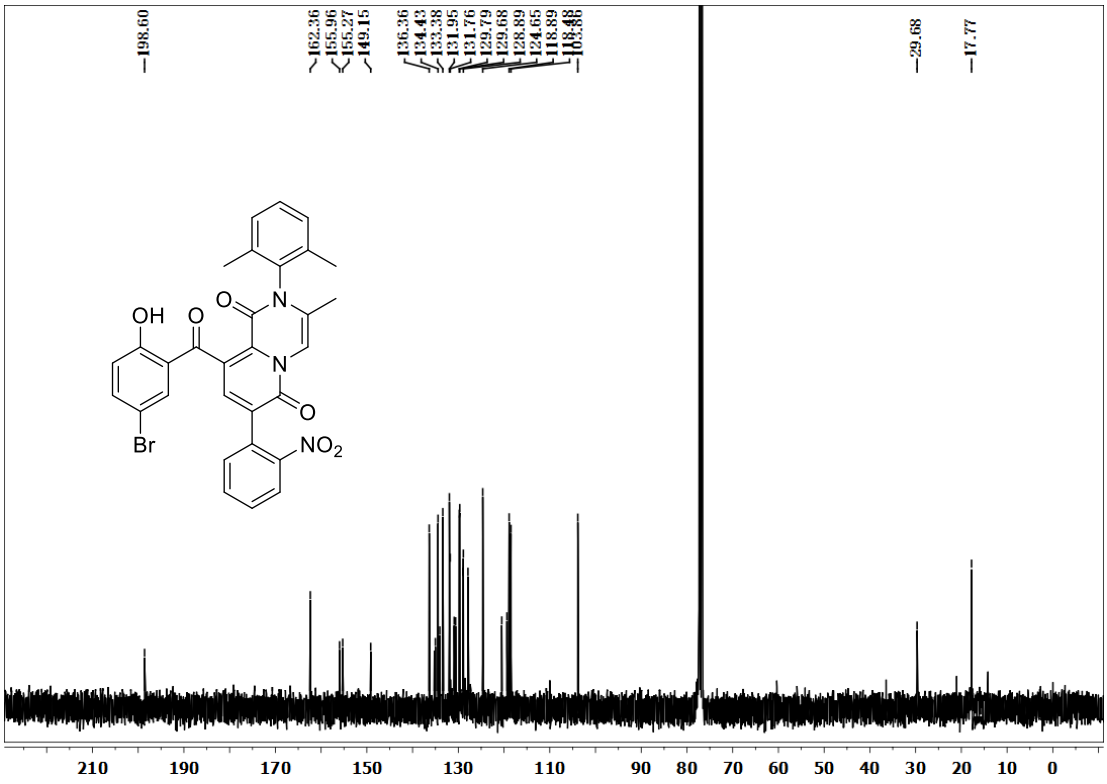
^{1}H NMR and ^{13}C NMR spectrum of **7h**



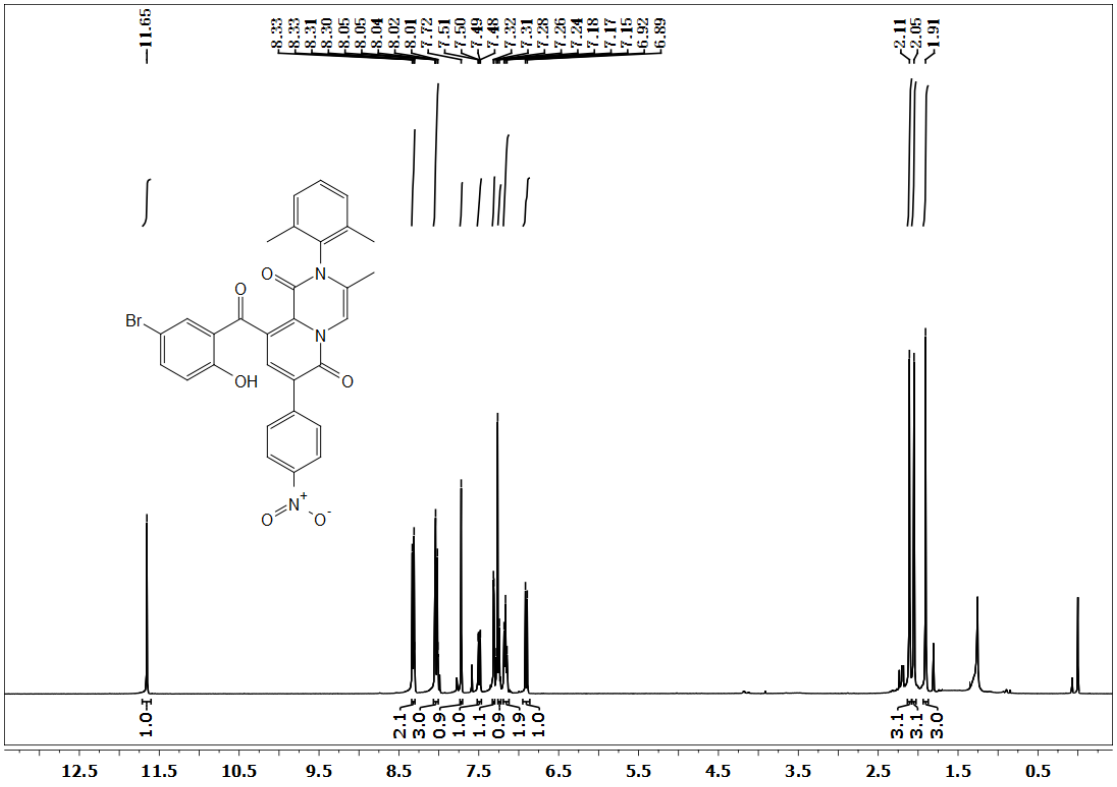


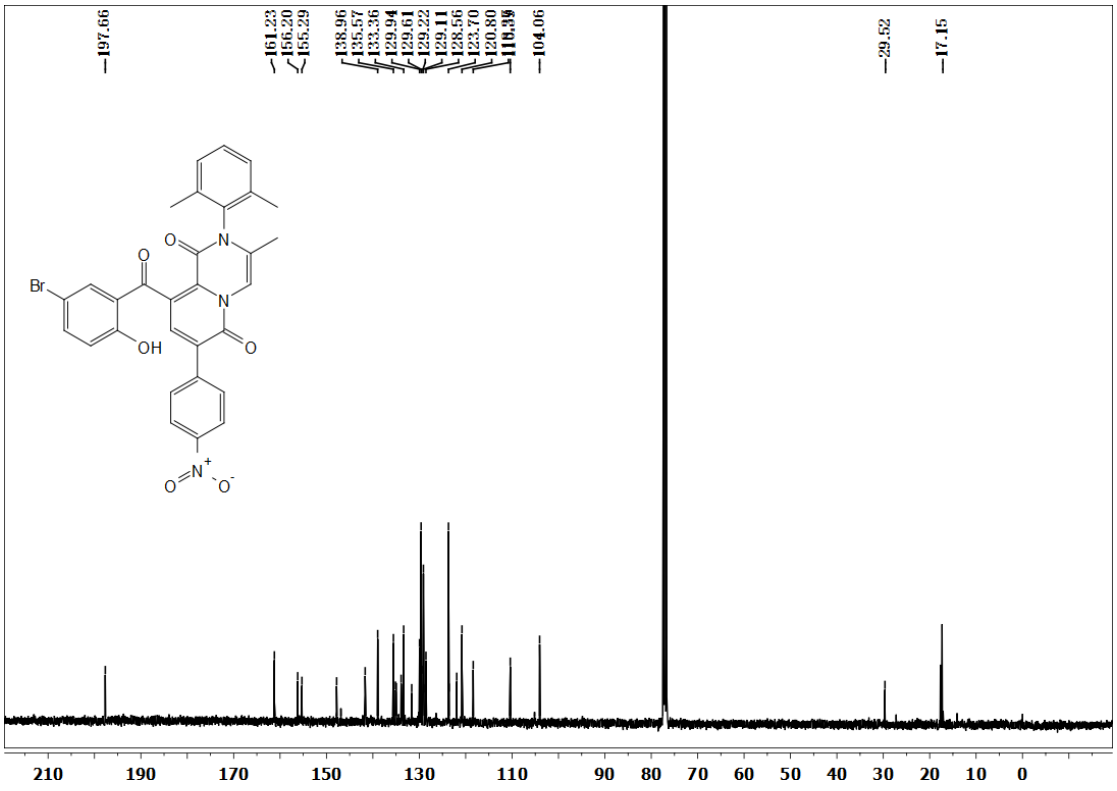
^{1}H NMR and ^{13}C NMR spectrum of **7i**



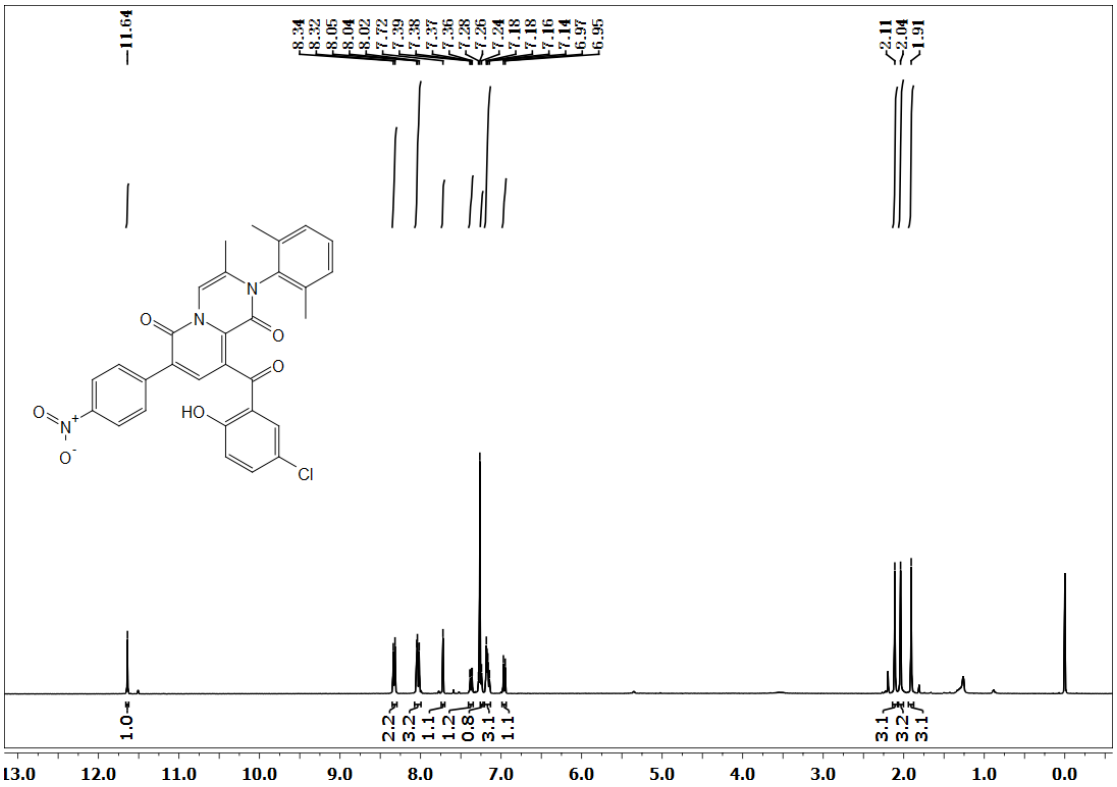


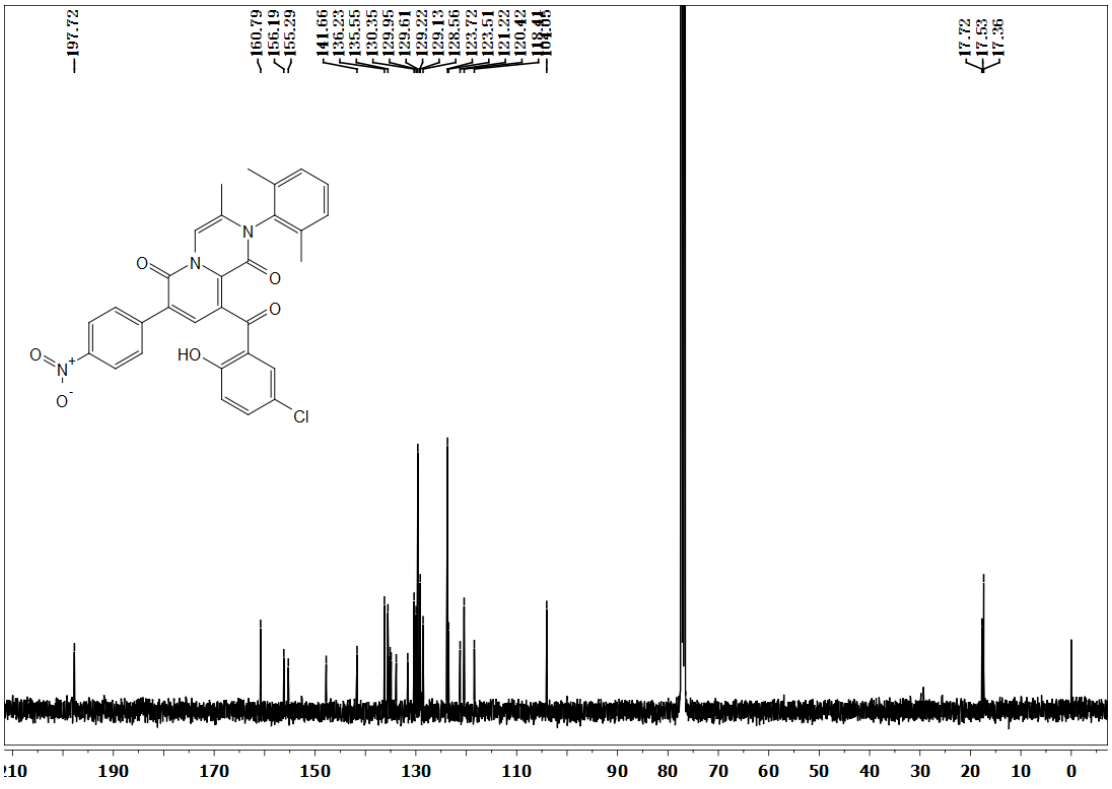
^{1}H NMR and ^{13}C NMR spectrum of **7j**



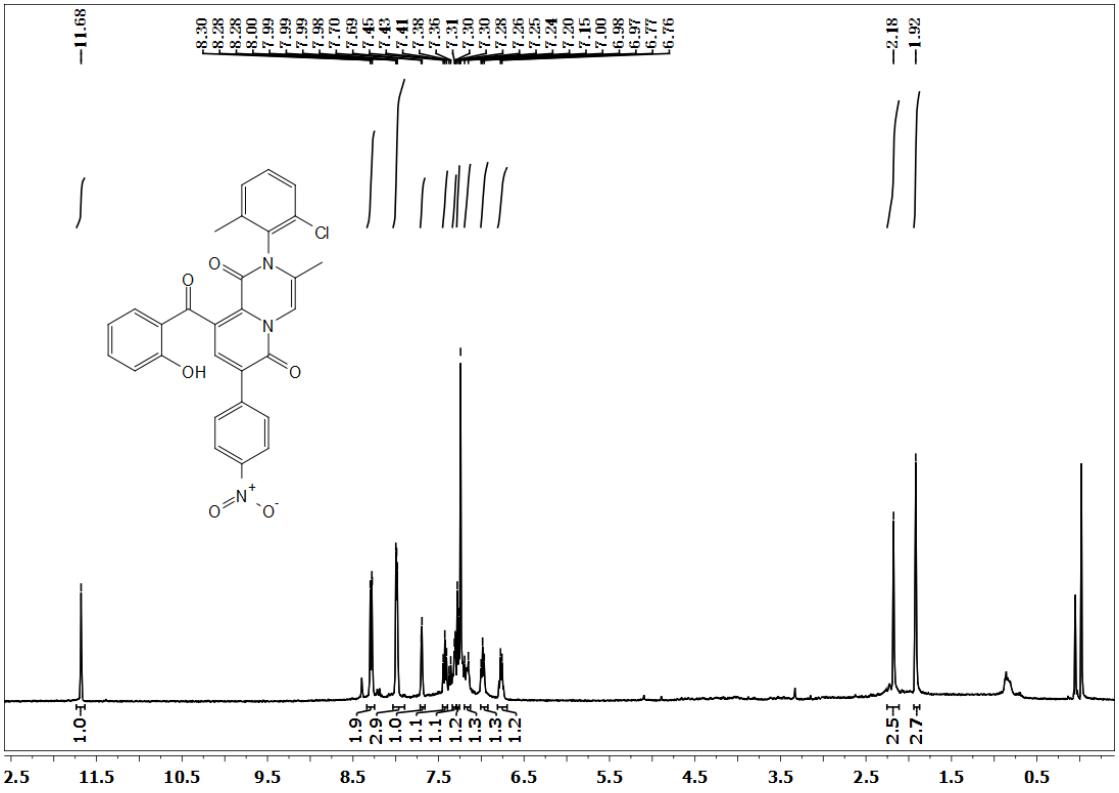


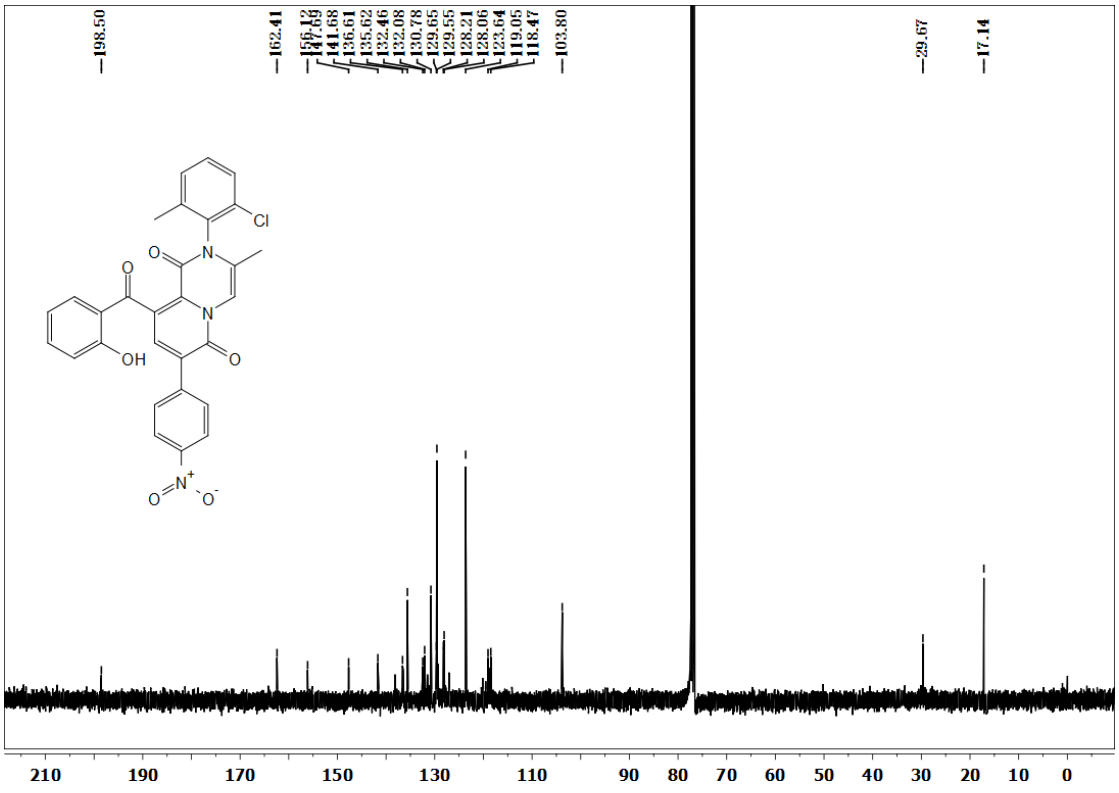
^{1}H NMR and ^{13}C NMR spectrum of **7k**



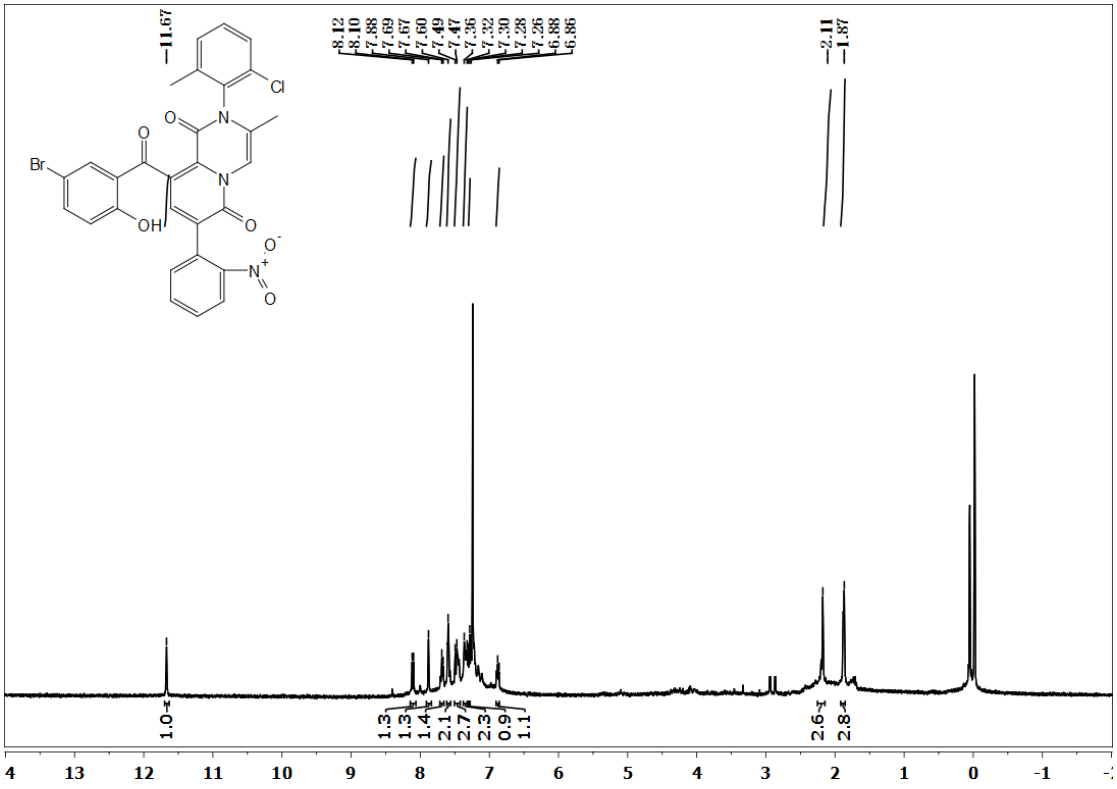


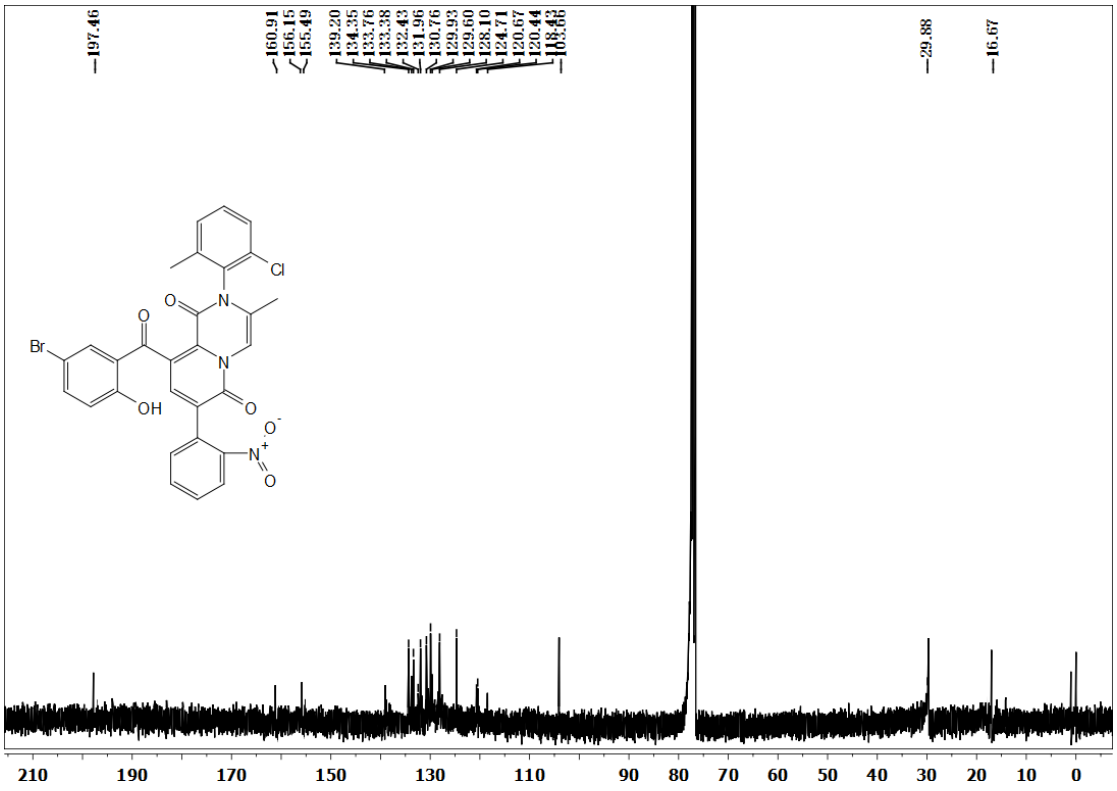
^{1}H NMR and ^{13}C NMR spectrum of **7l**



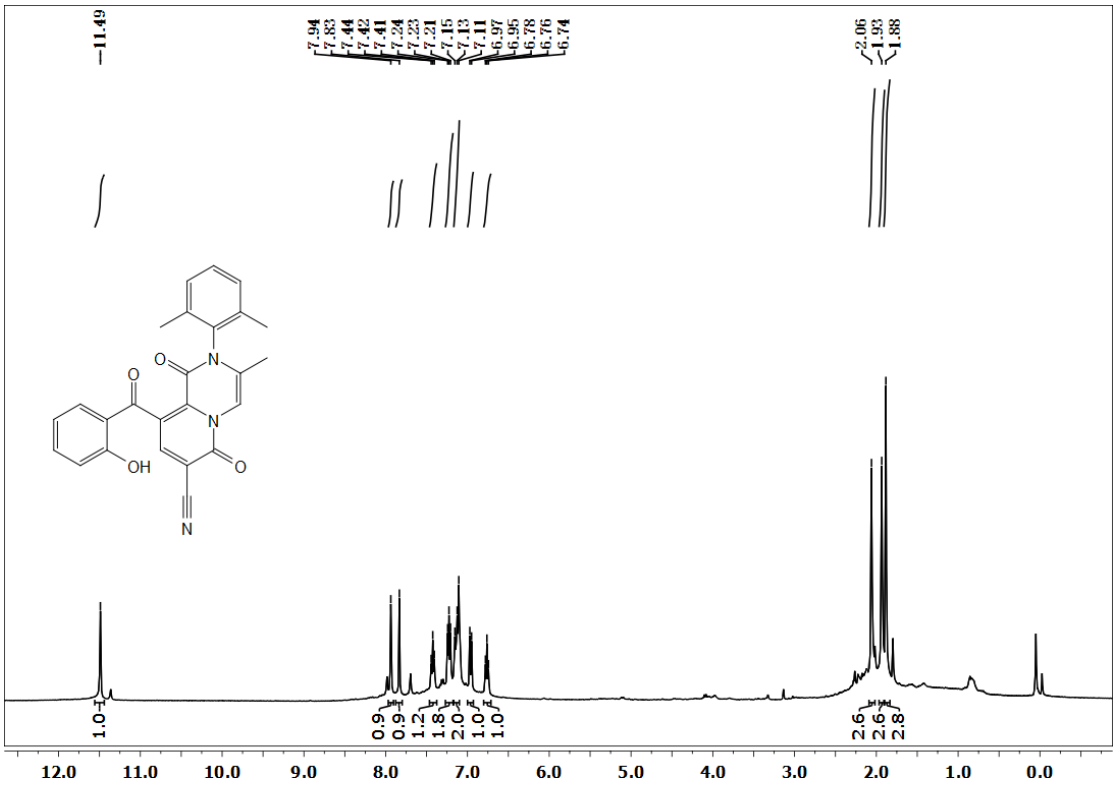


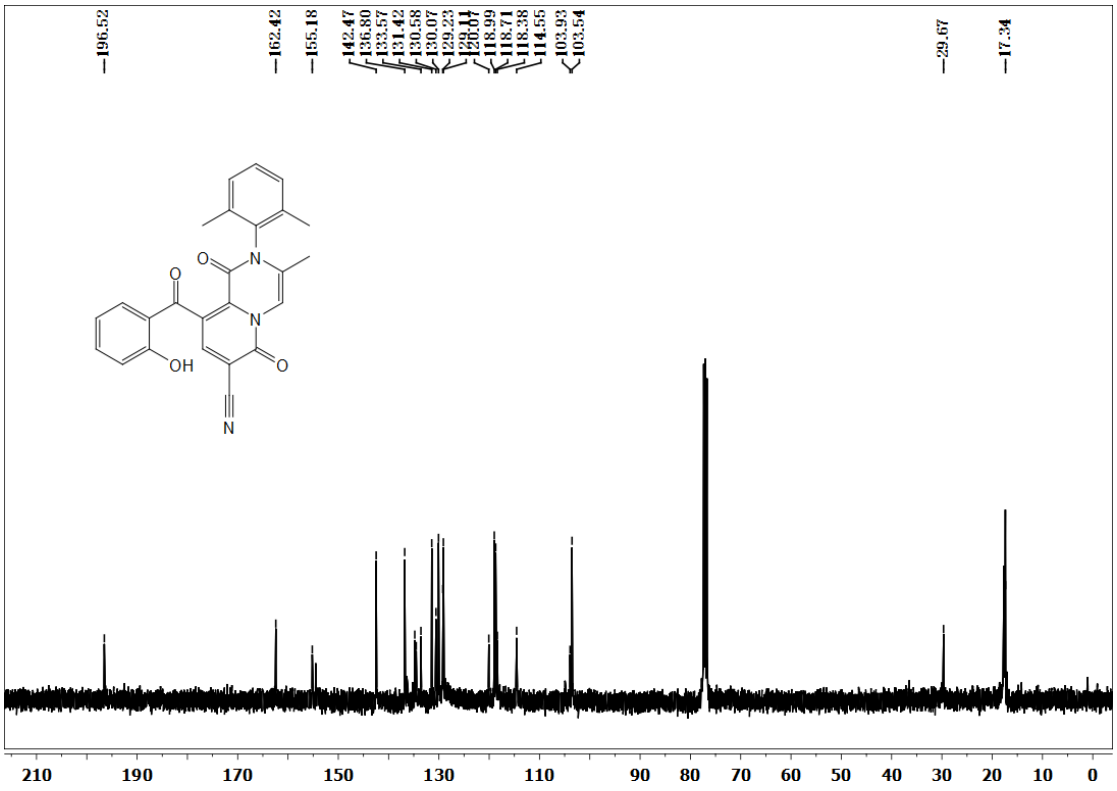
^{1}H NMR and ^{13}C NMR spectrum of **7m**



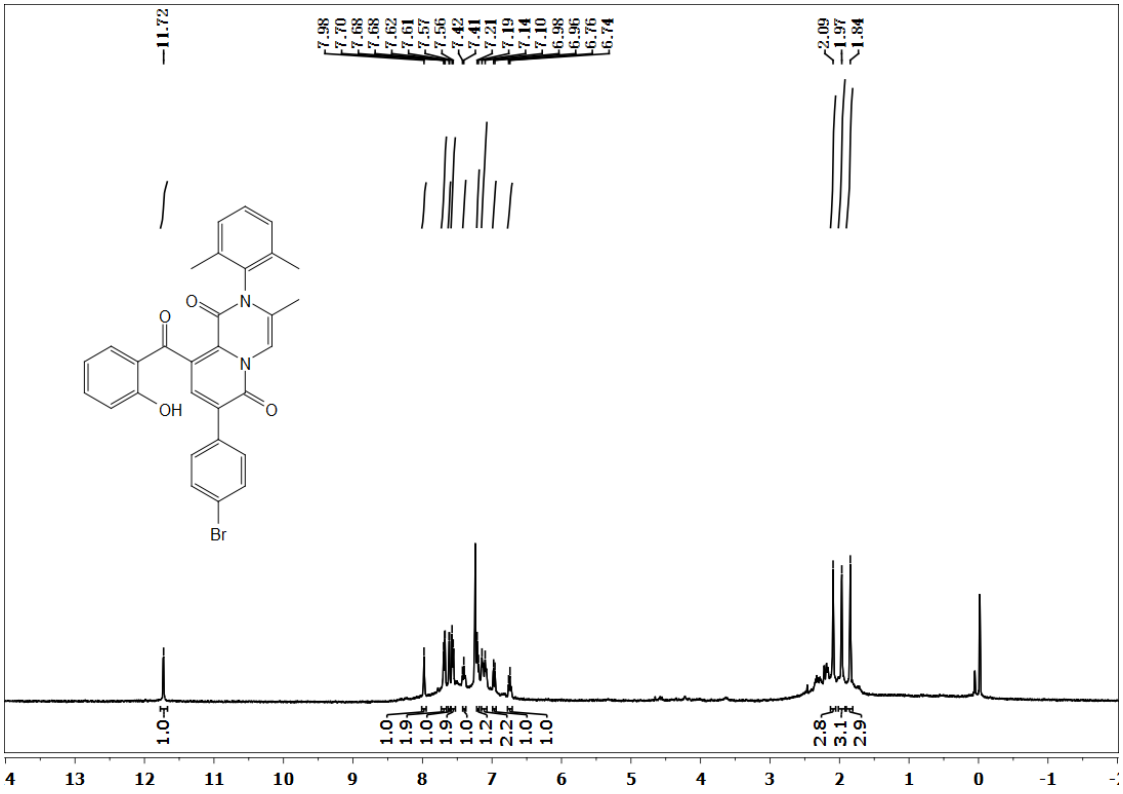


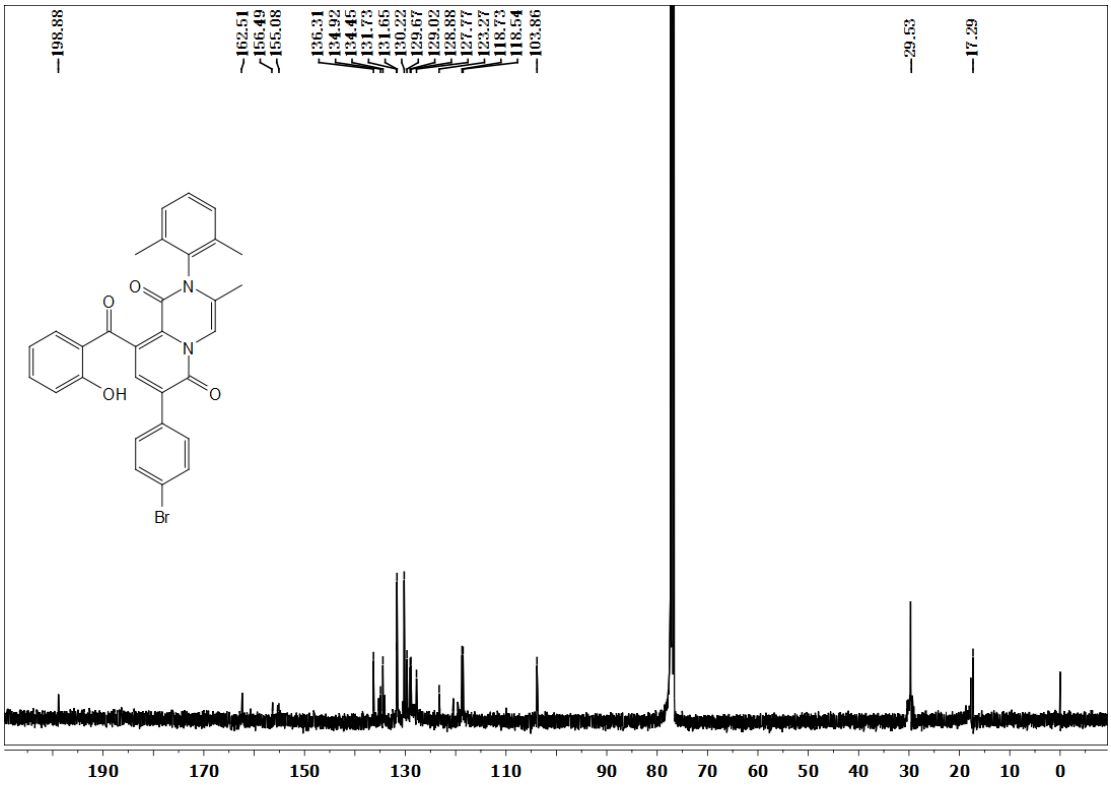
^{1}H NMR and ^{13}C NMR spectrum of **7n**



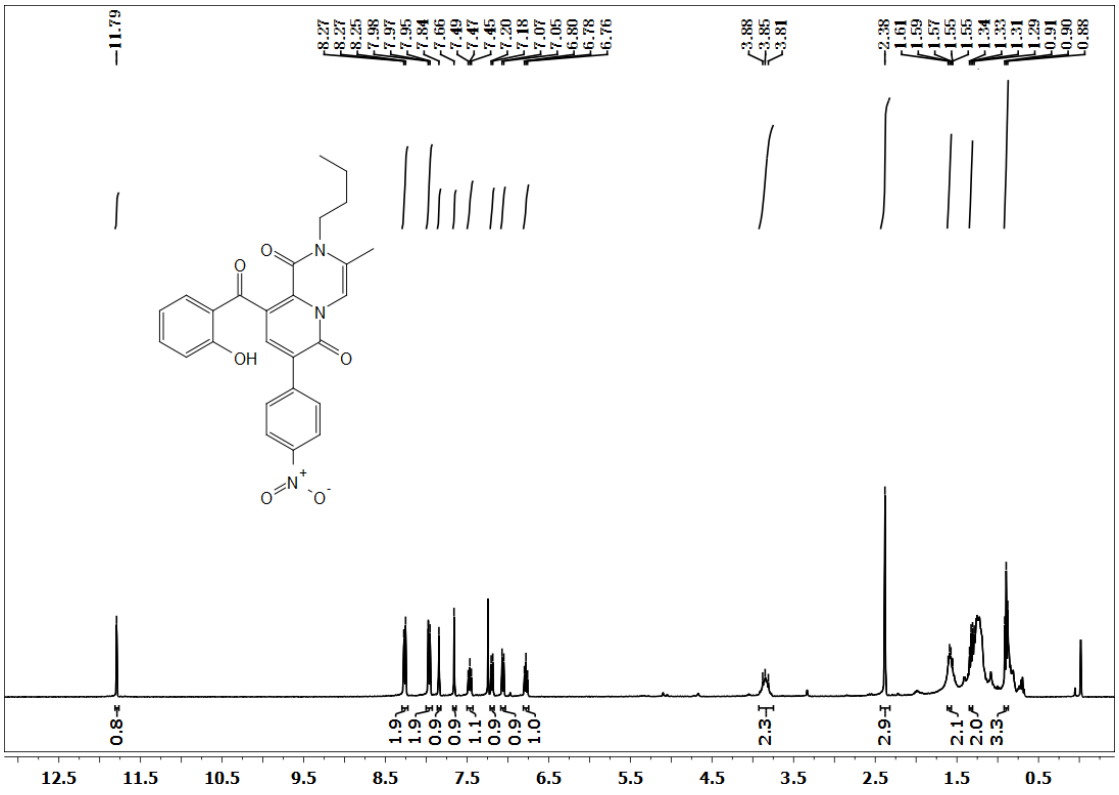


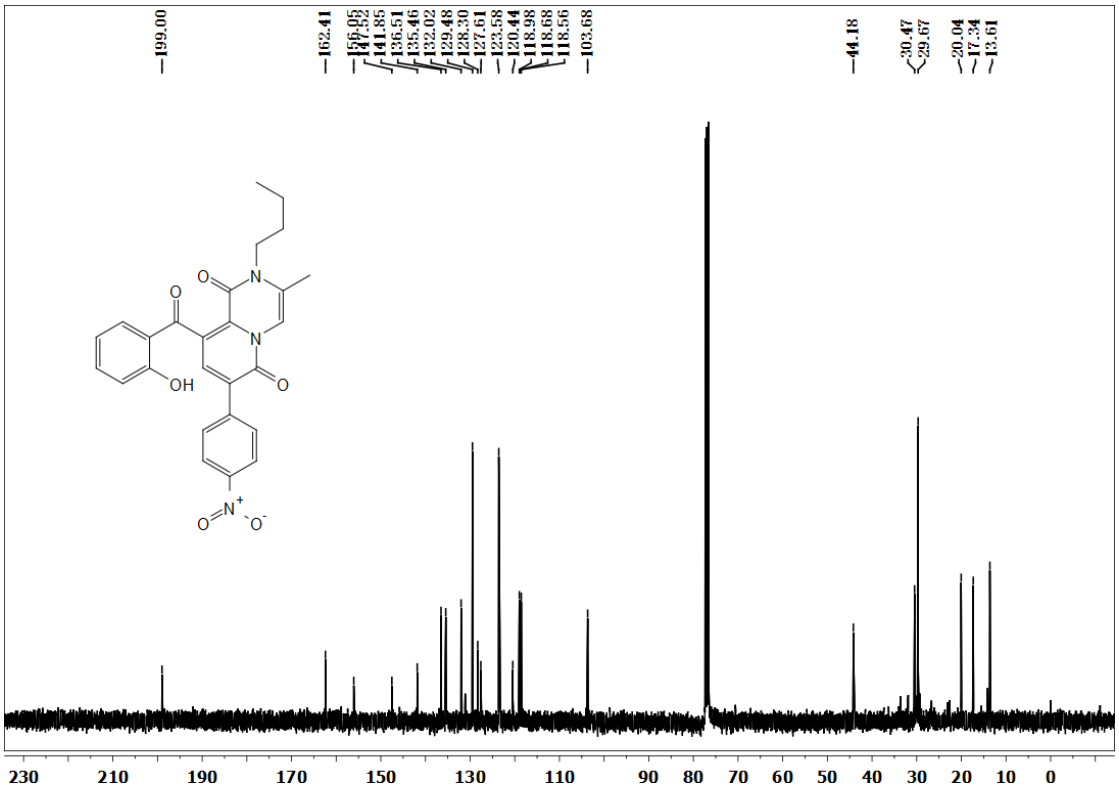
^{1}H NMR and ^{13}C NMR spectrum of **7o**



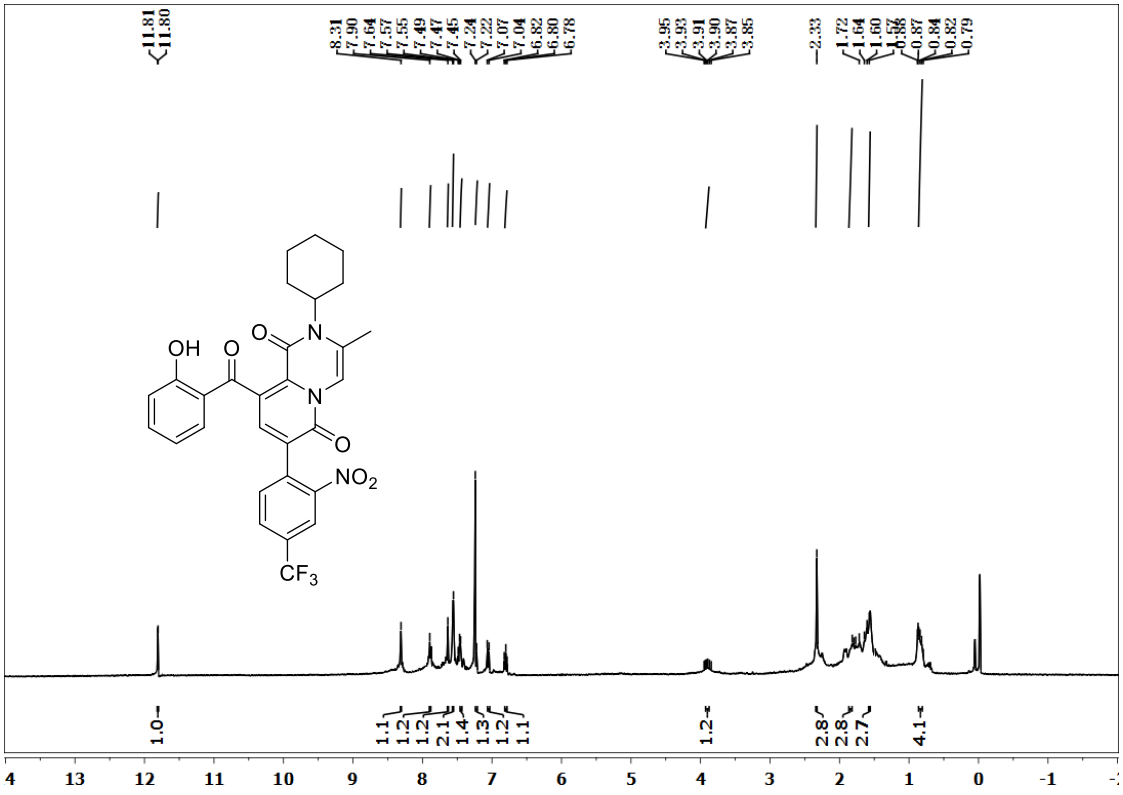


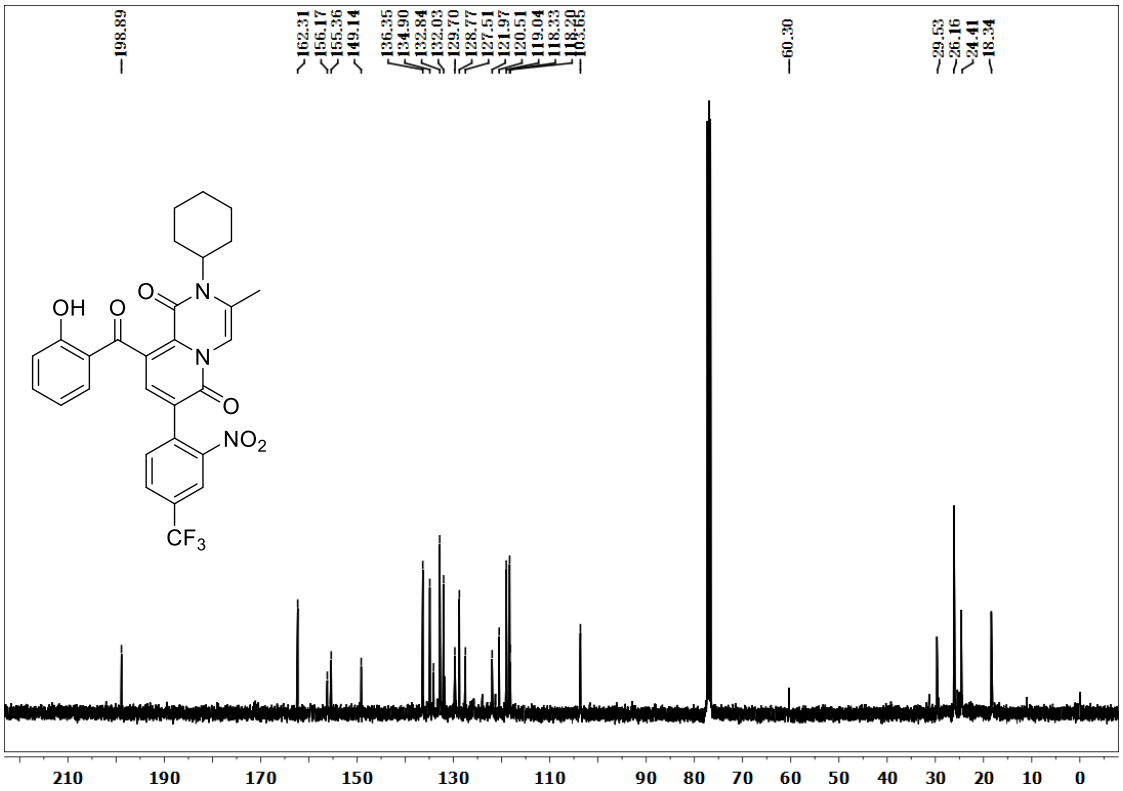
^{1}H NMR and ^{13}C NMR spectrum of **7p**



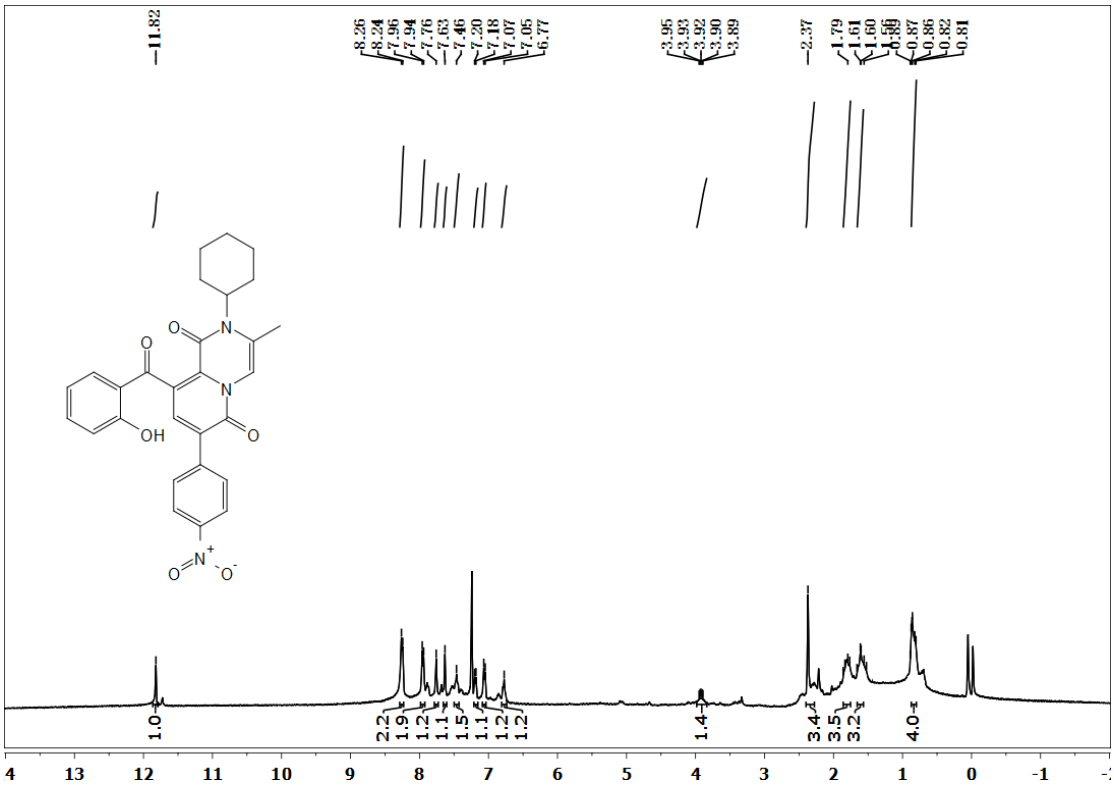


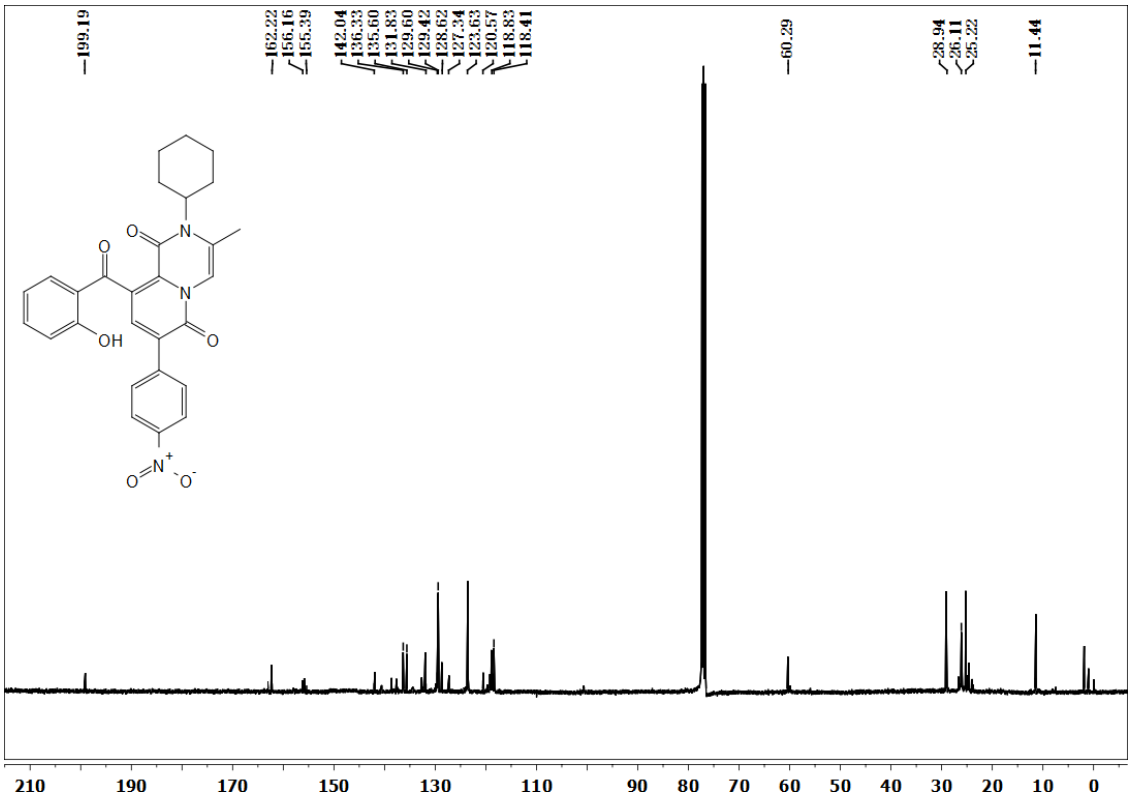
^{1}H NMR and ^{13}C NMR spectrum of **7q**



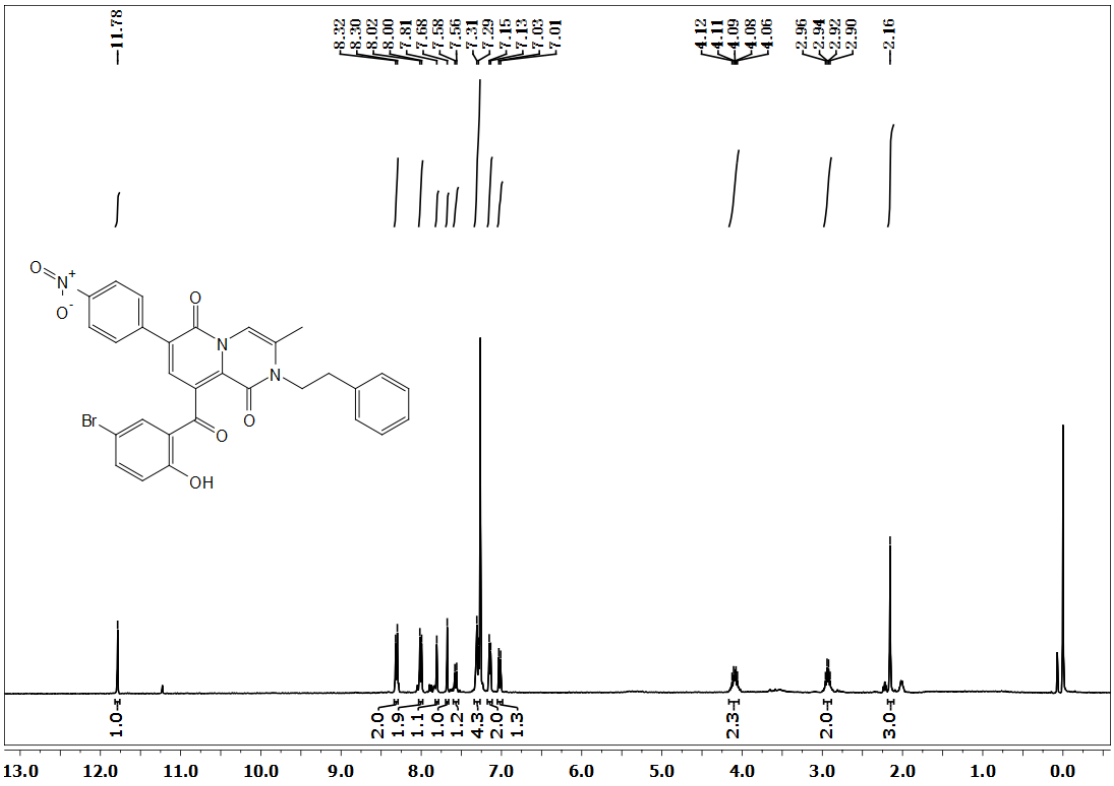


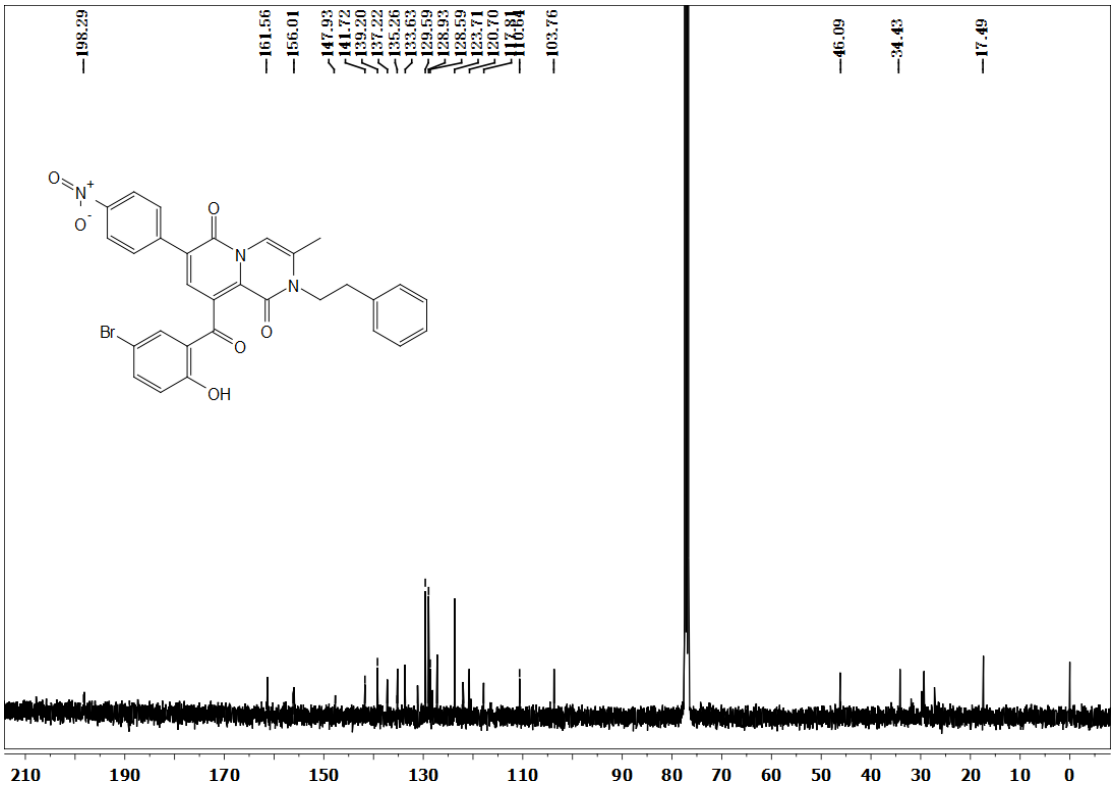
^{1}H NMR and ^{13}C NMR spectrum of **7r**



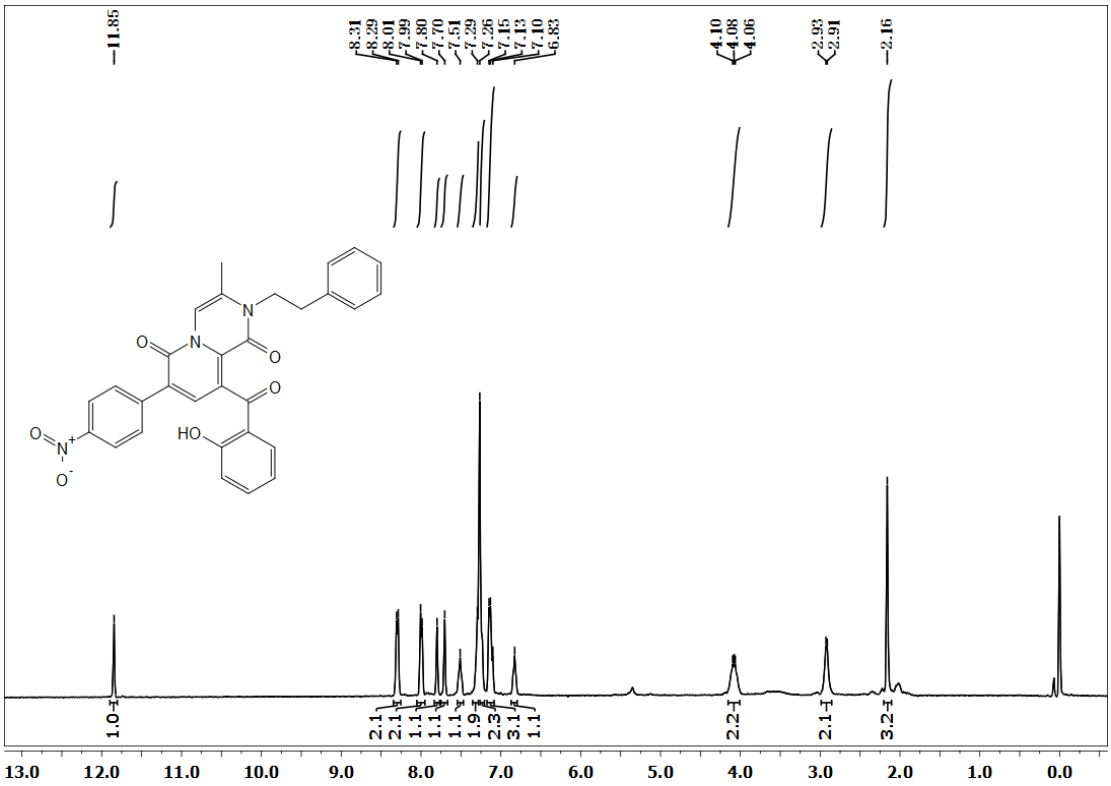


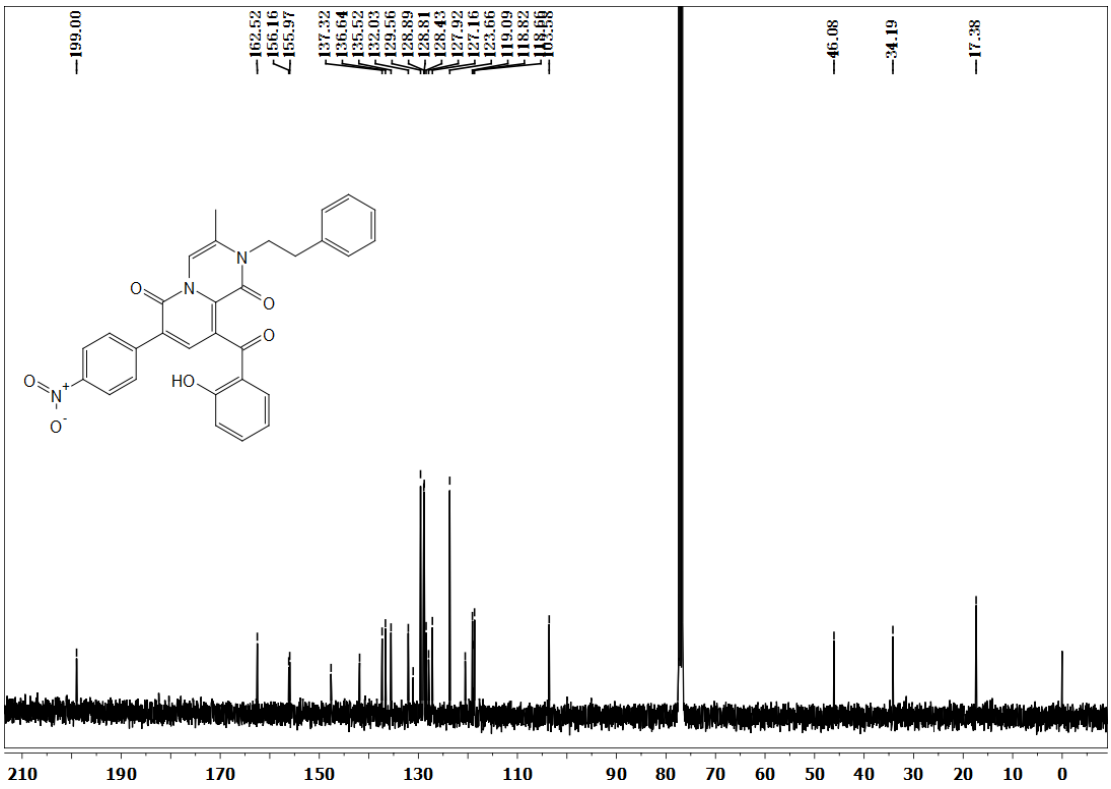
^{1}H NMR and ^{13}C NMR spectrum of **7s**



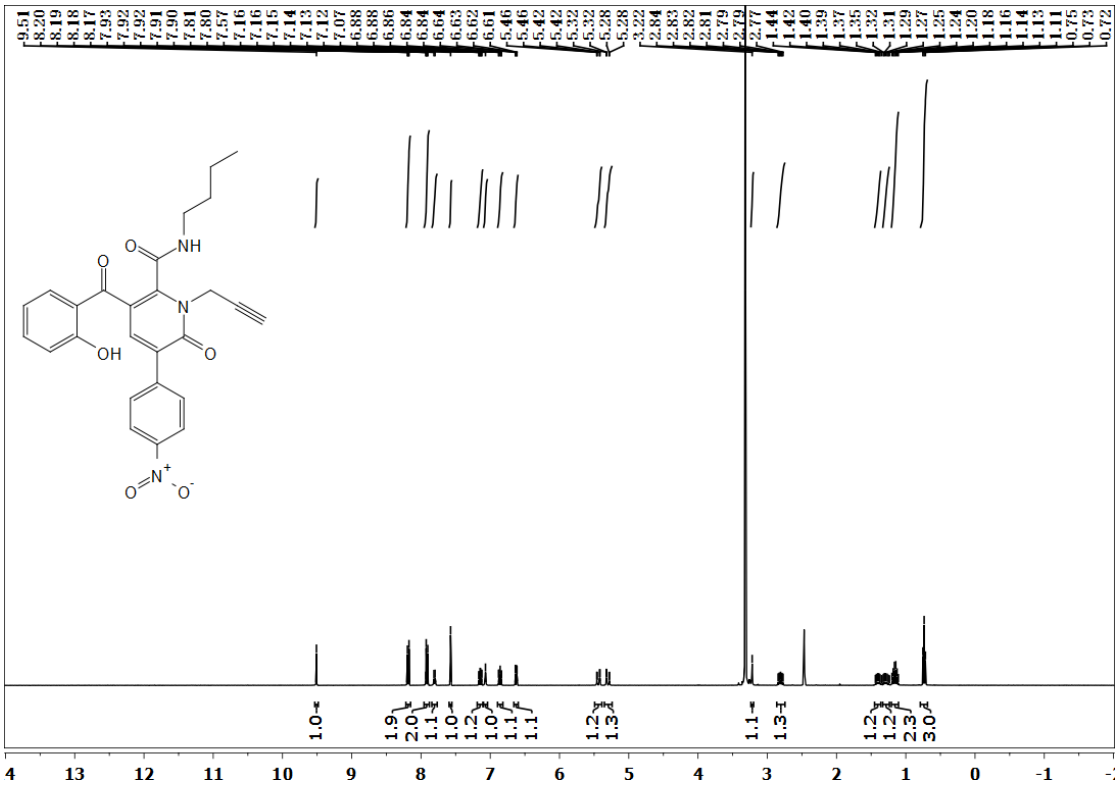


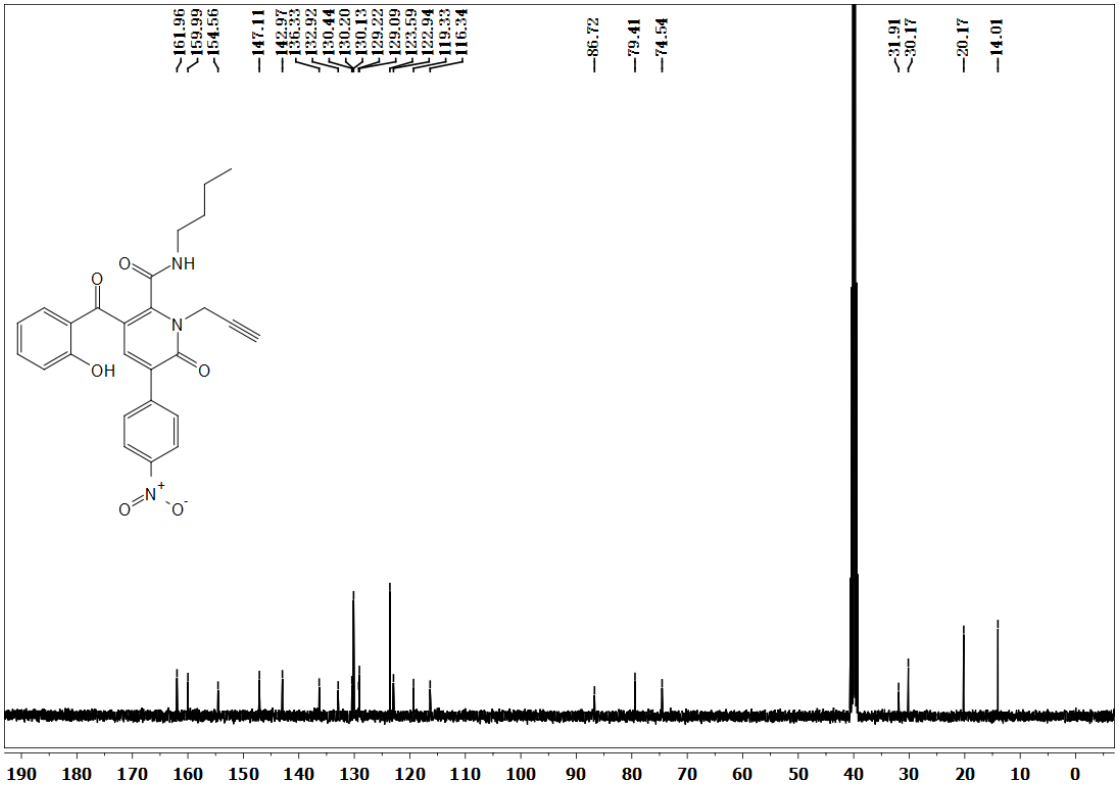
^{1}H NMR and ^{13}C NMR spectrum of **7t**



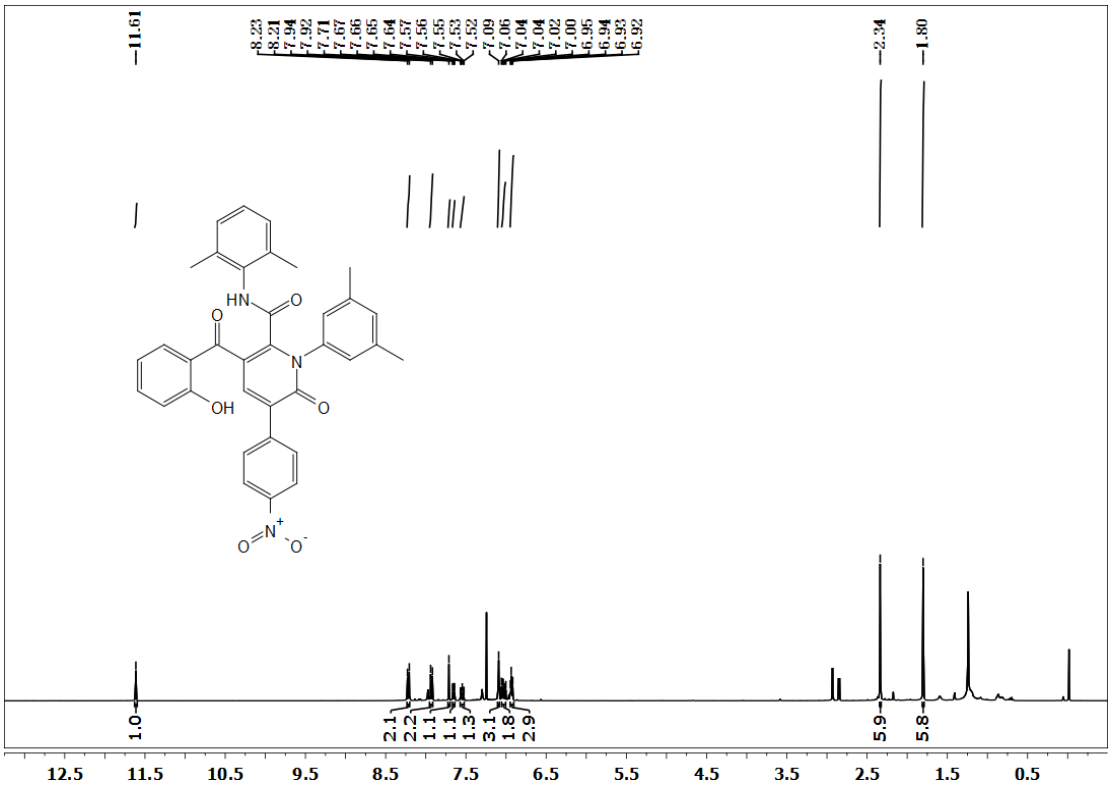


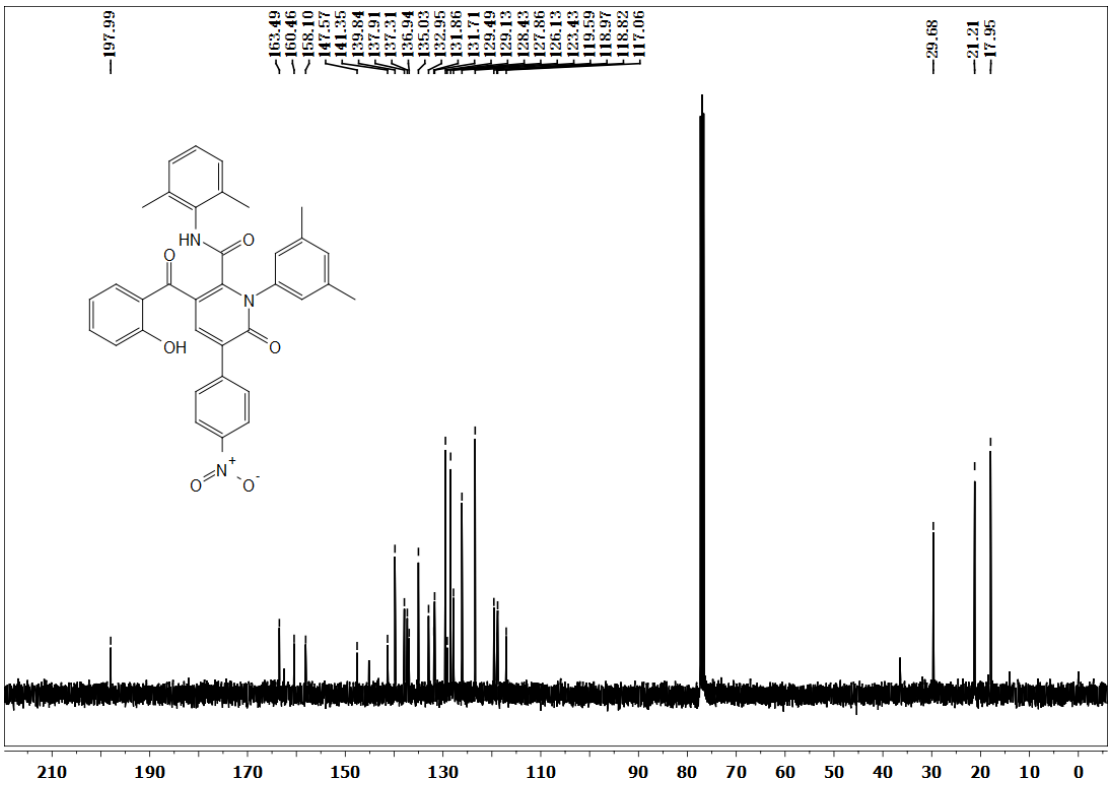
^{1}H NMR and ^{13}C NMR spectrum of **8p**



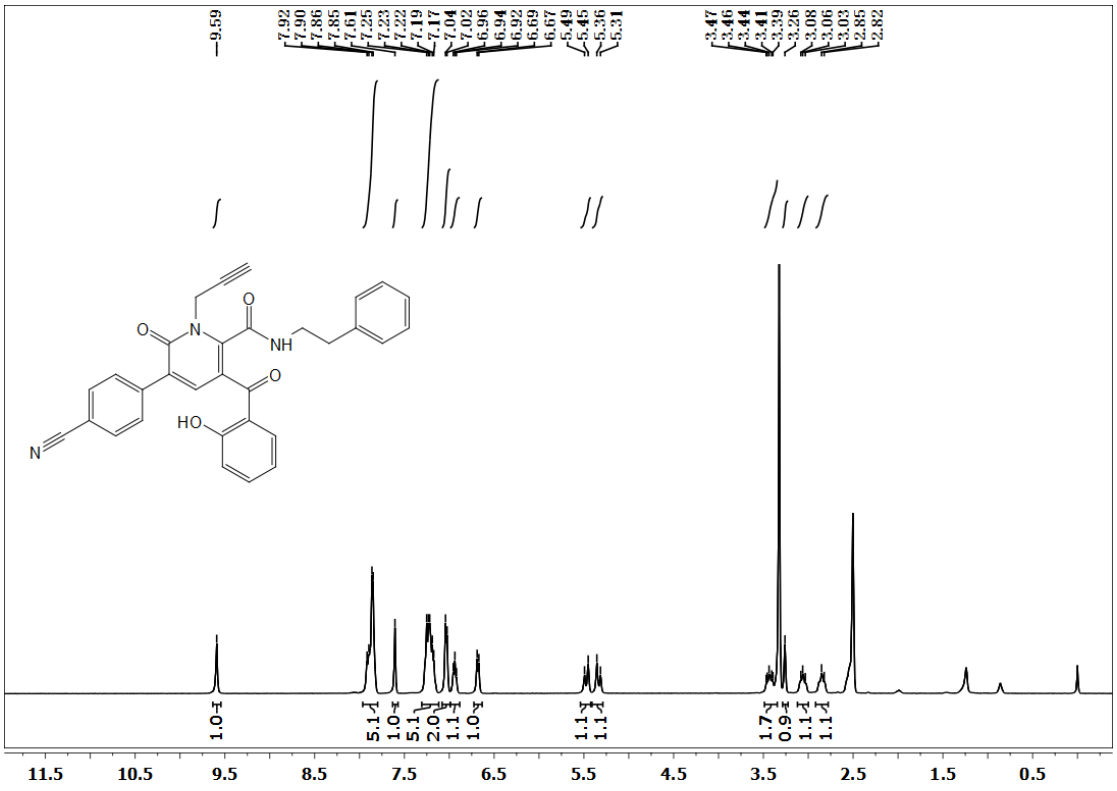


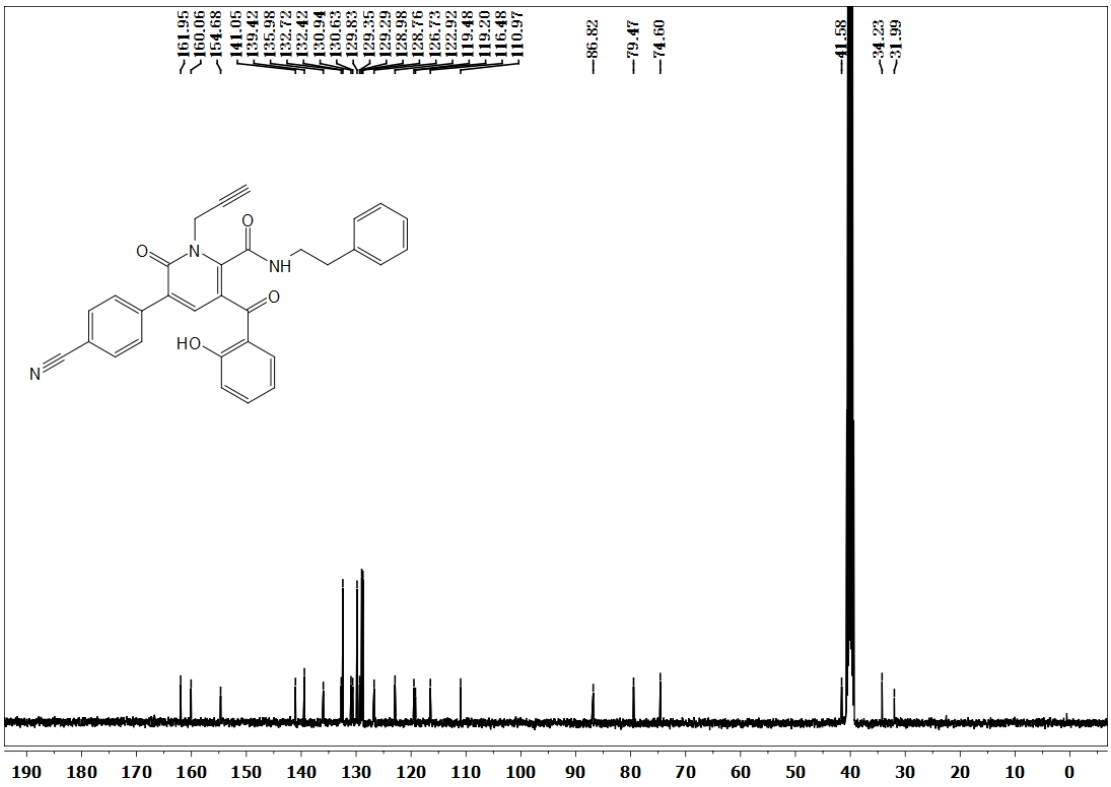
^{1}H NMR and ^{13}C NMR spectrum of **11a**



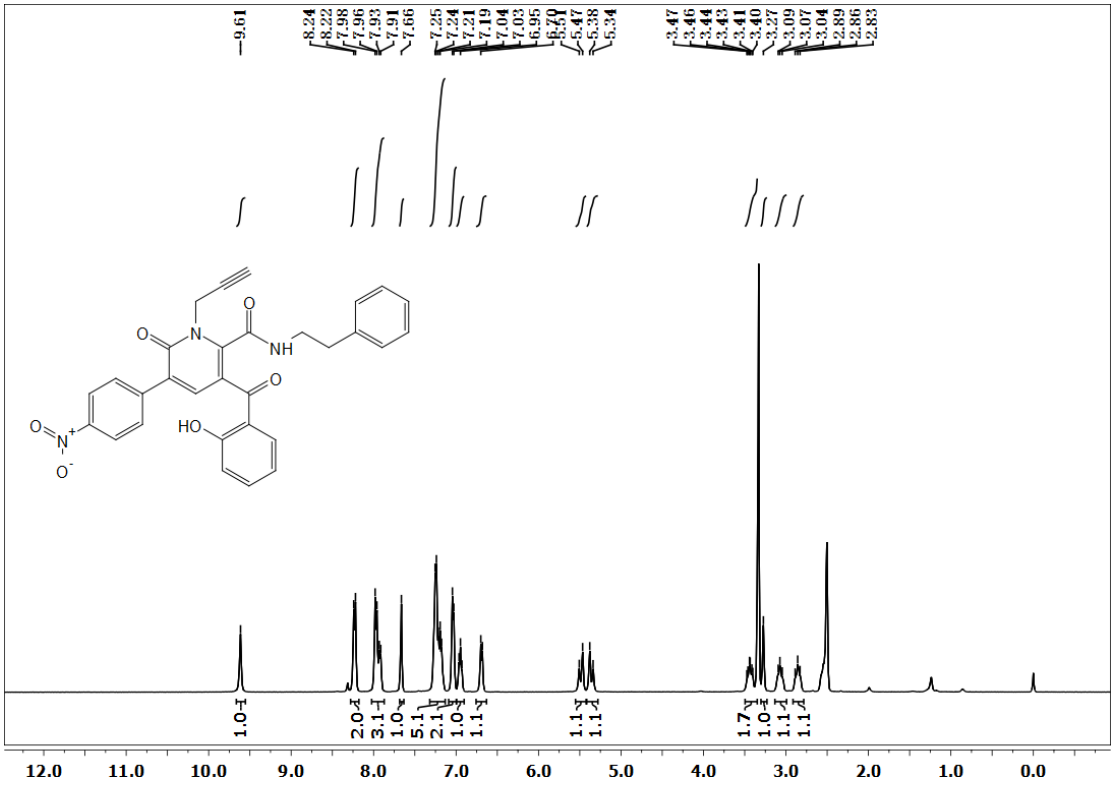


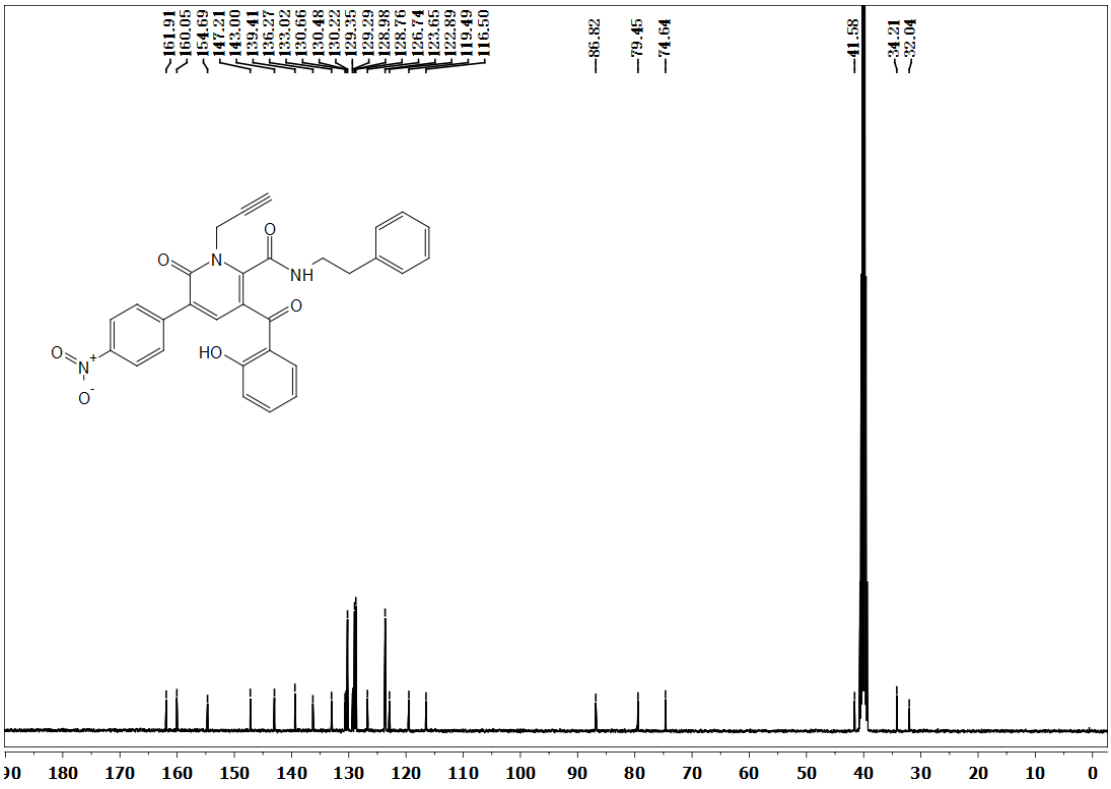
^{1}H NMR and ^{13}C NMR spectrum of **11b**



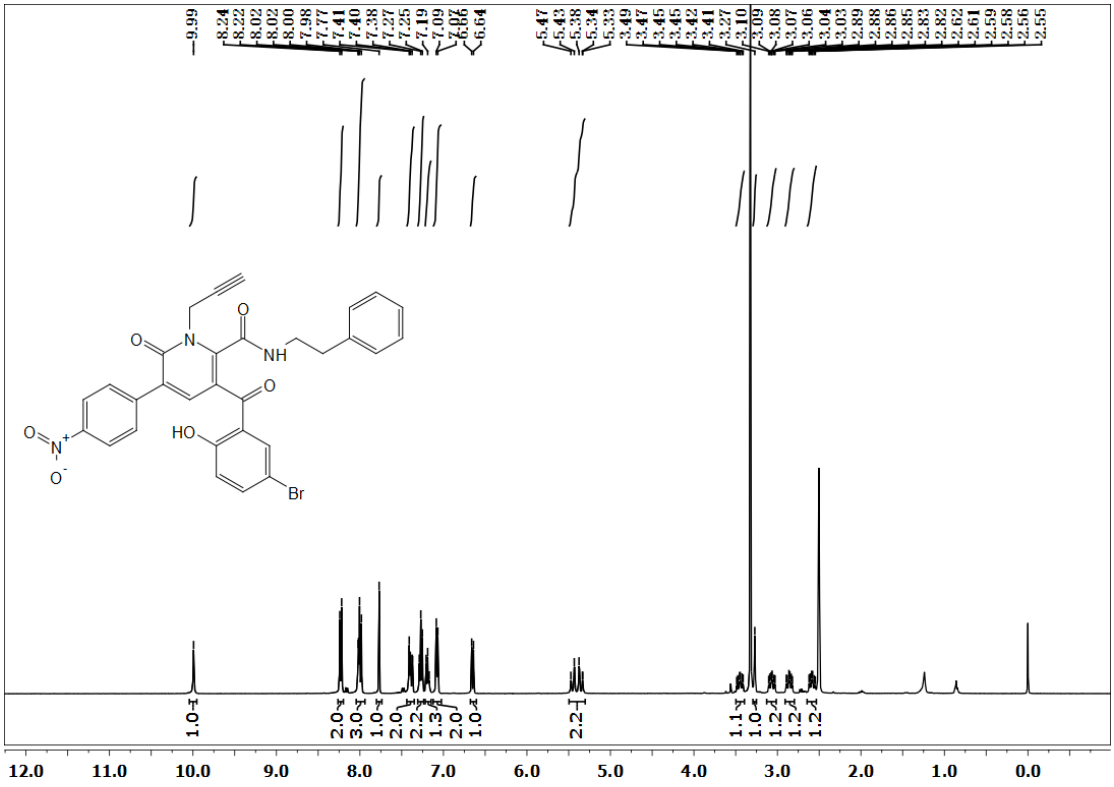


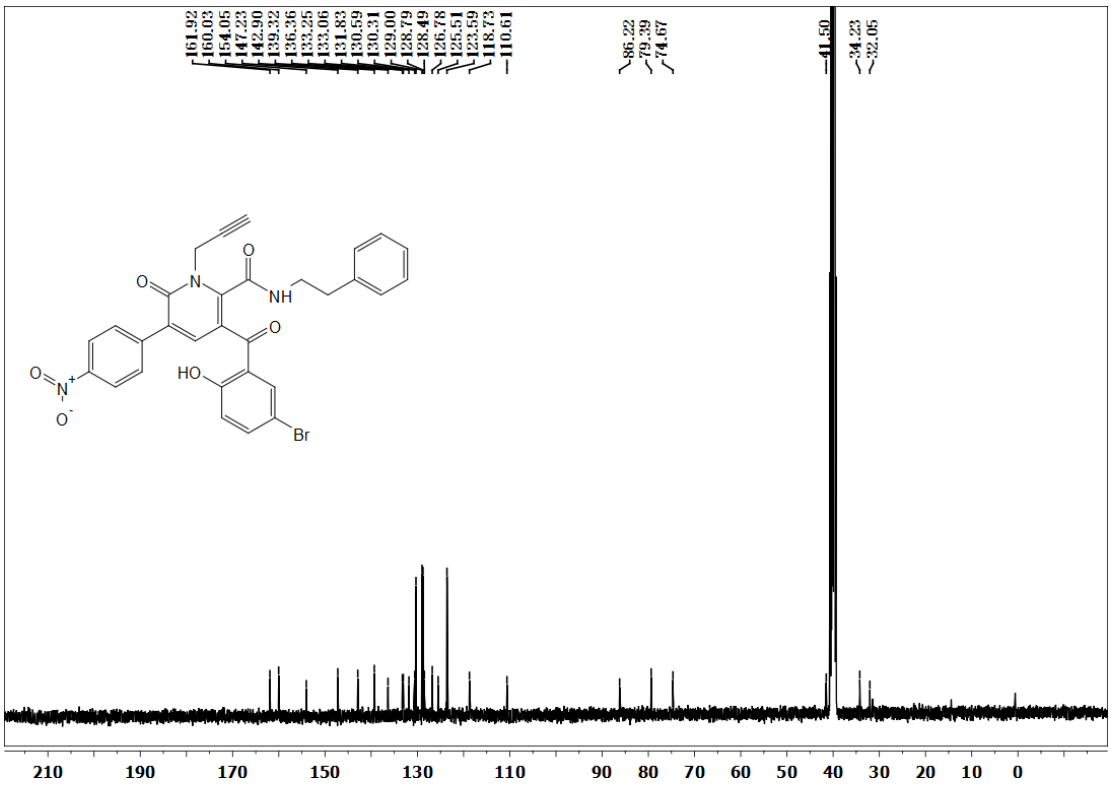
^{1}H NMR and ^{13}C NMR spectrum of **11c**



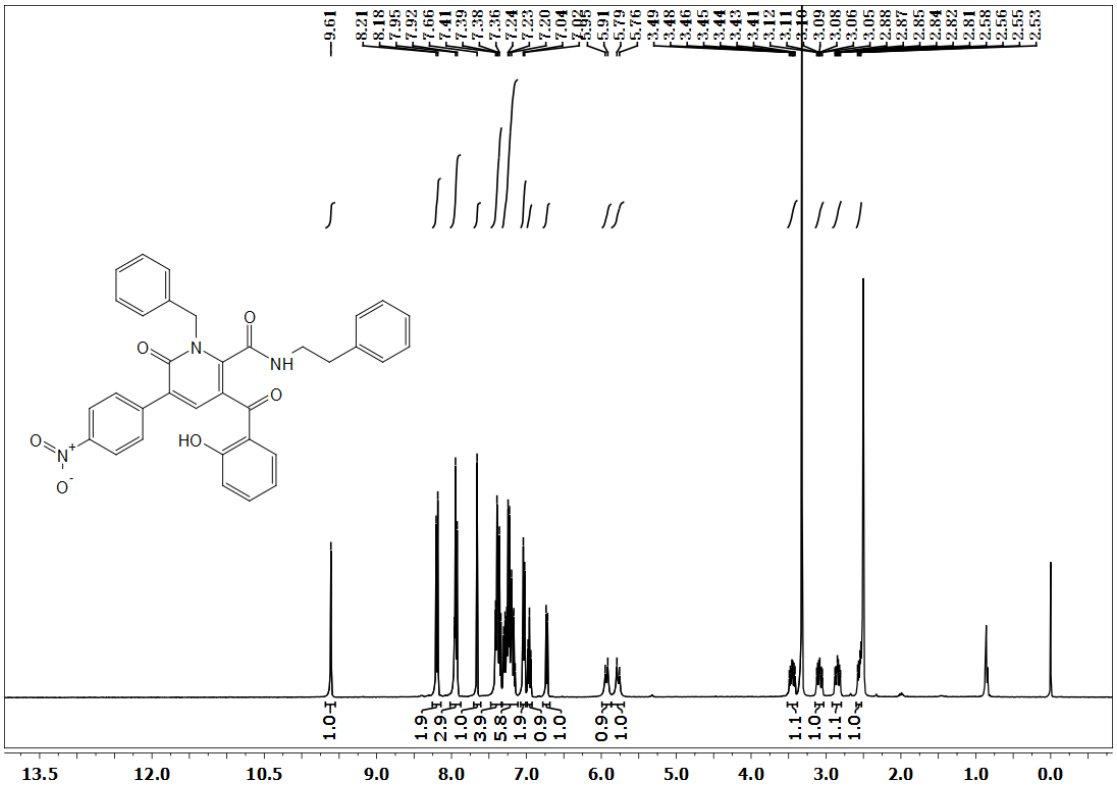


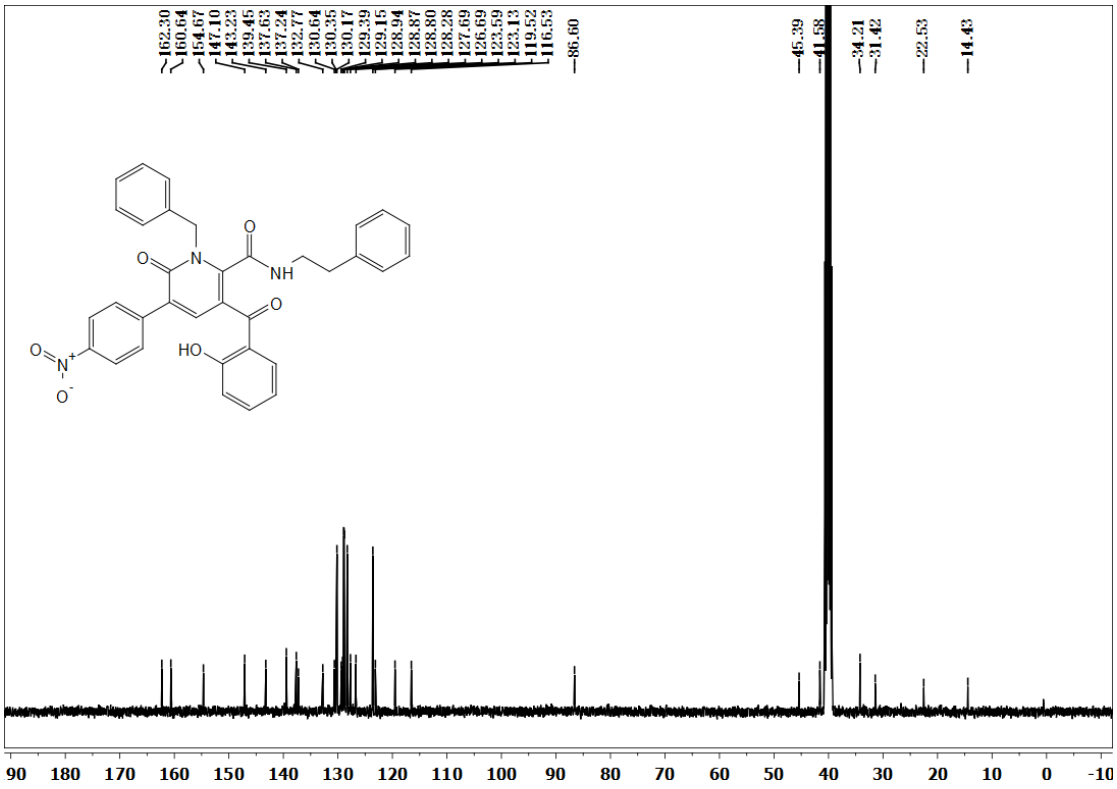
^{1}H NMR and ^{13}C NMR spectrum of **11d**



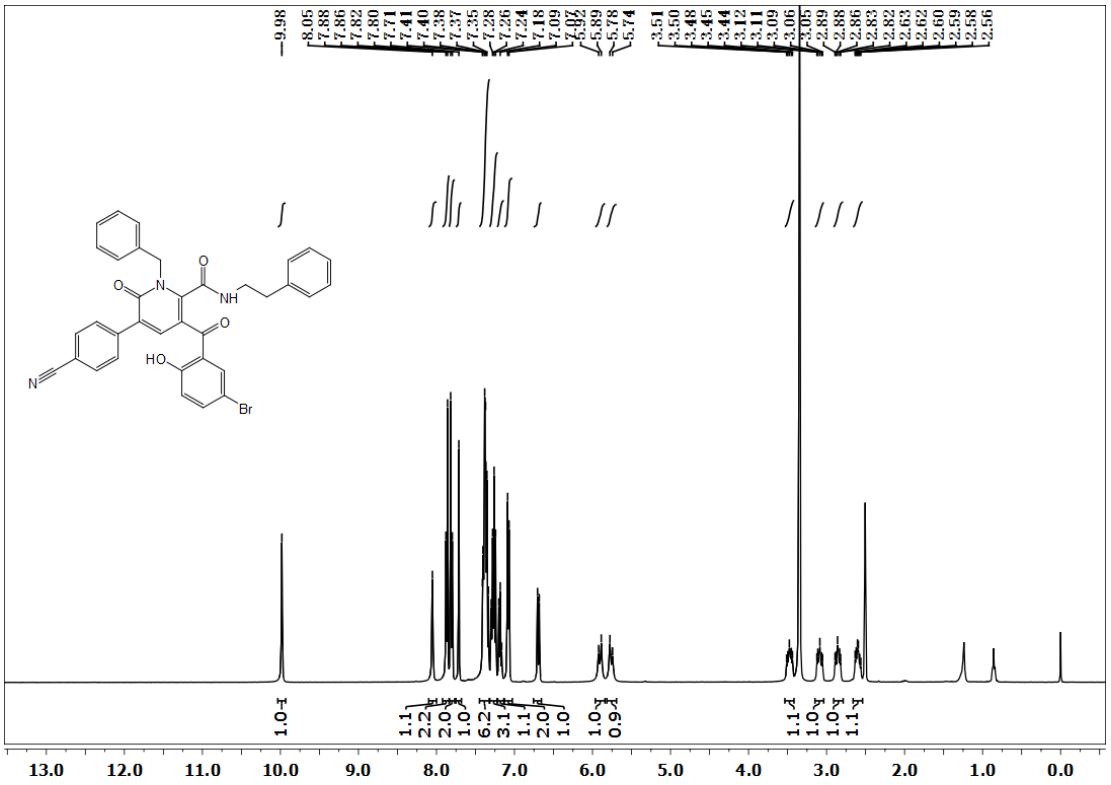


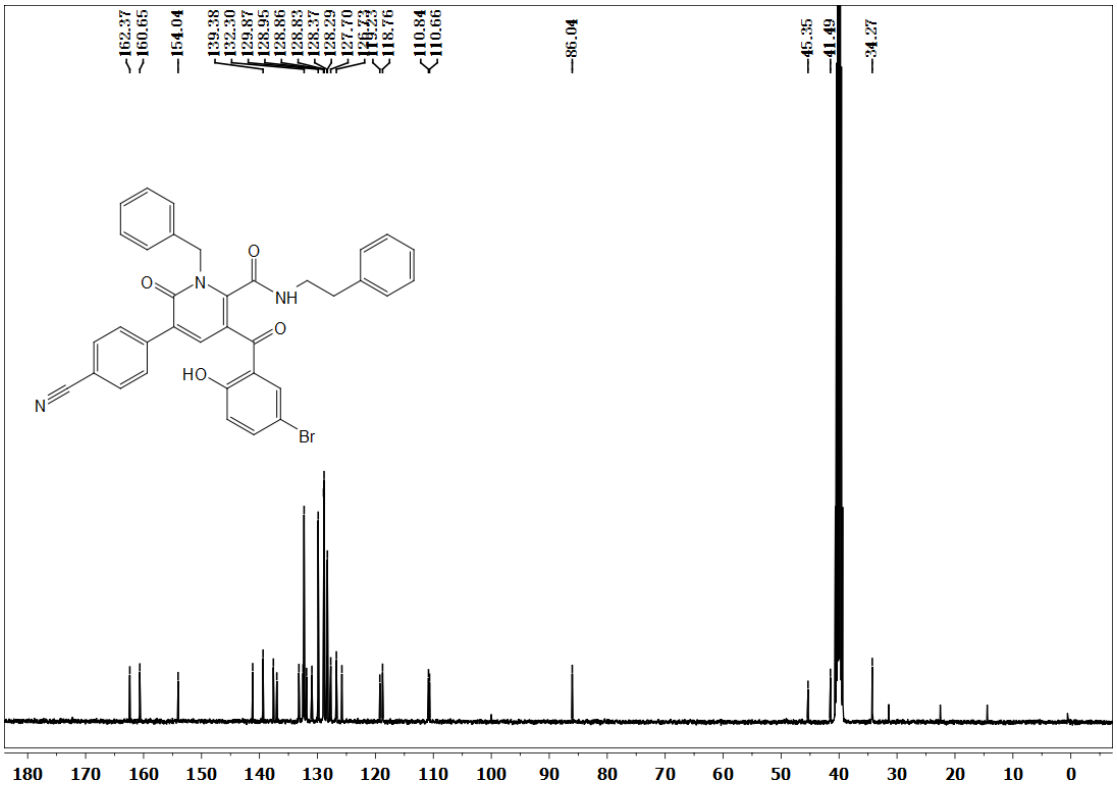
^{1}H NMR and ^{13}C NMR spectrum of **11e**



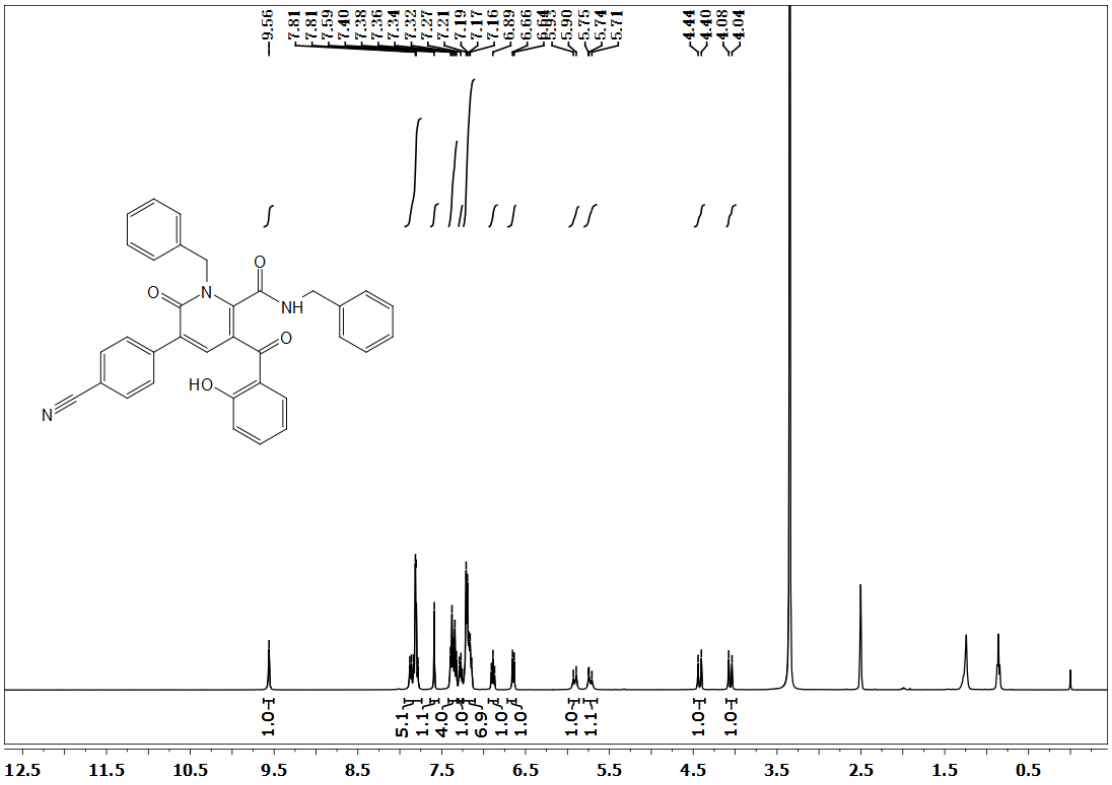


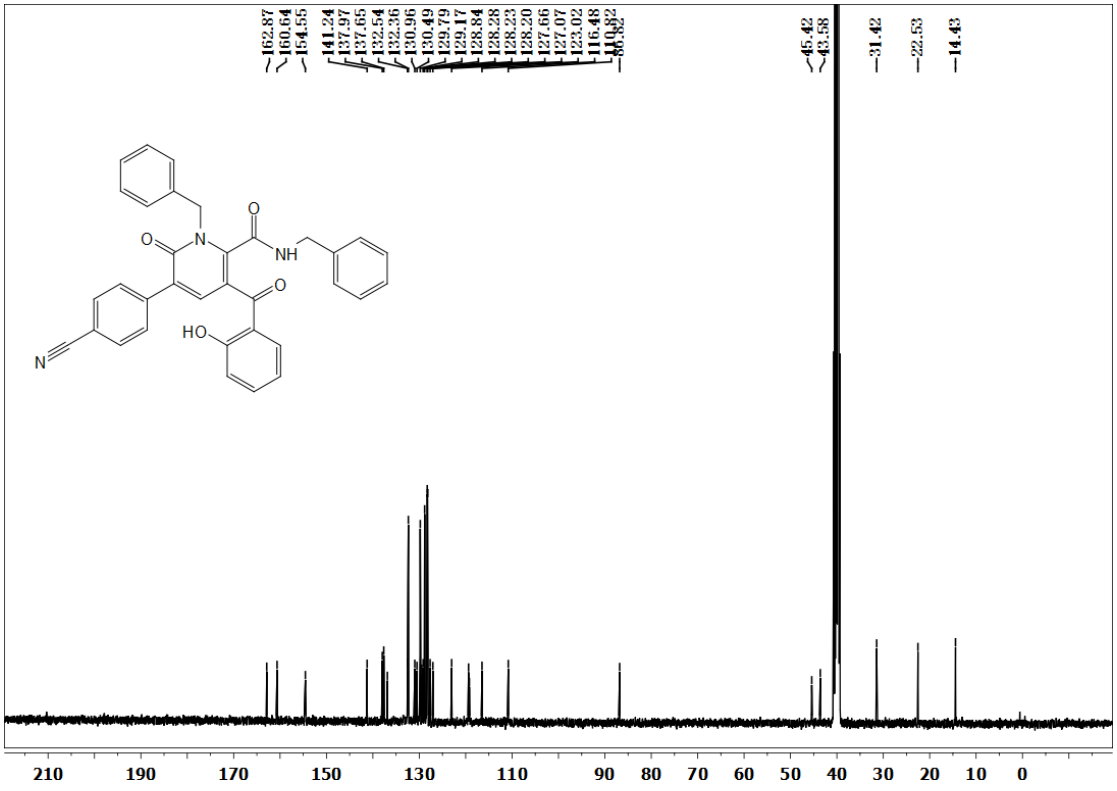
^{1}H NMR and ^{13}C NMR spectrum of **11f**



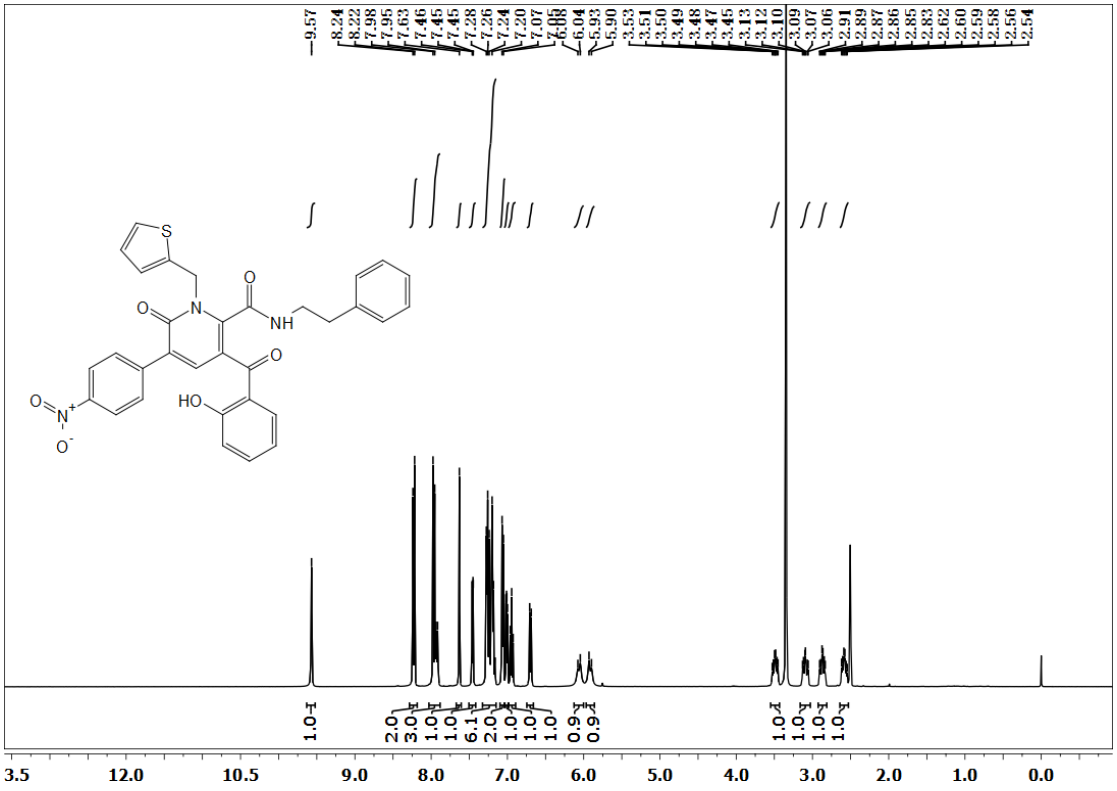


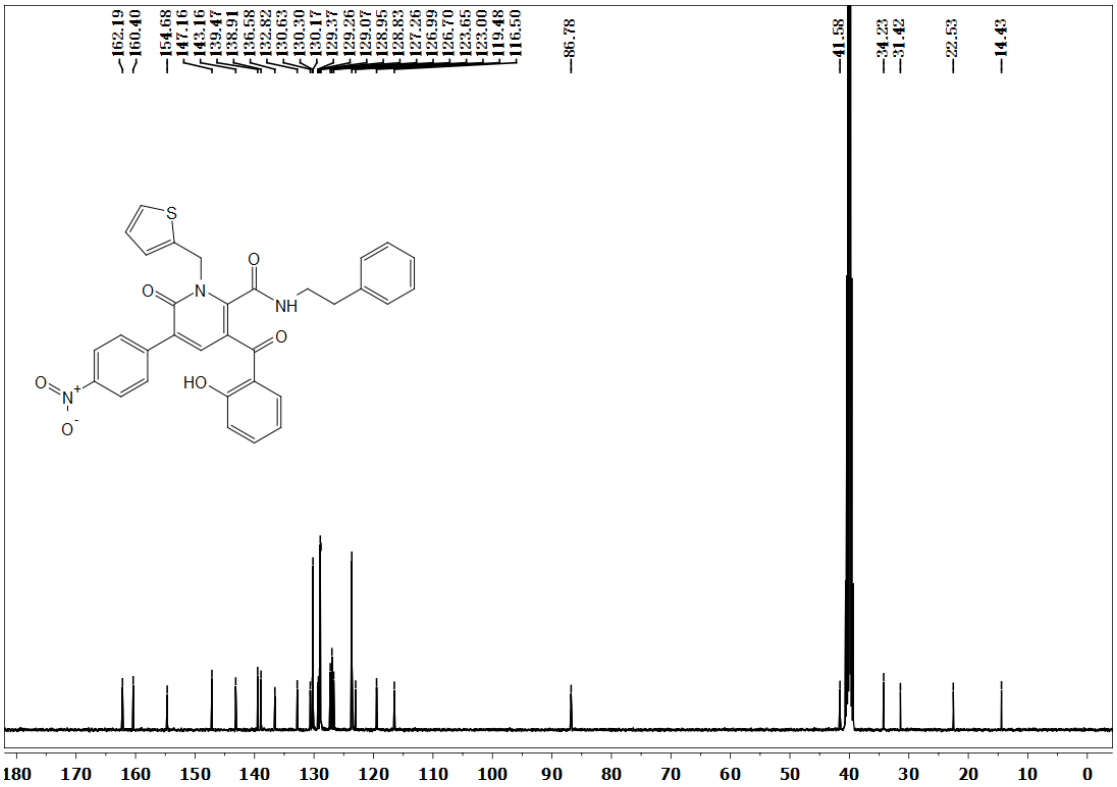
^{1}H NMR and ^{13}C NMR spectrum of **11g**



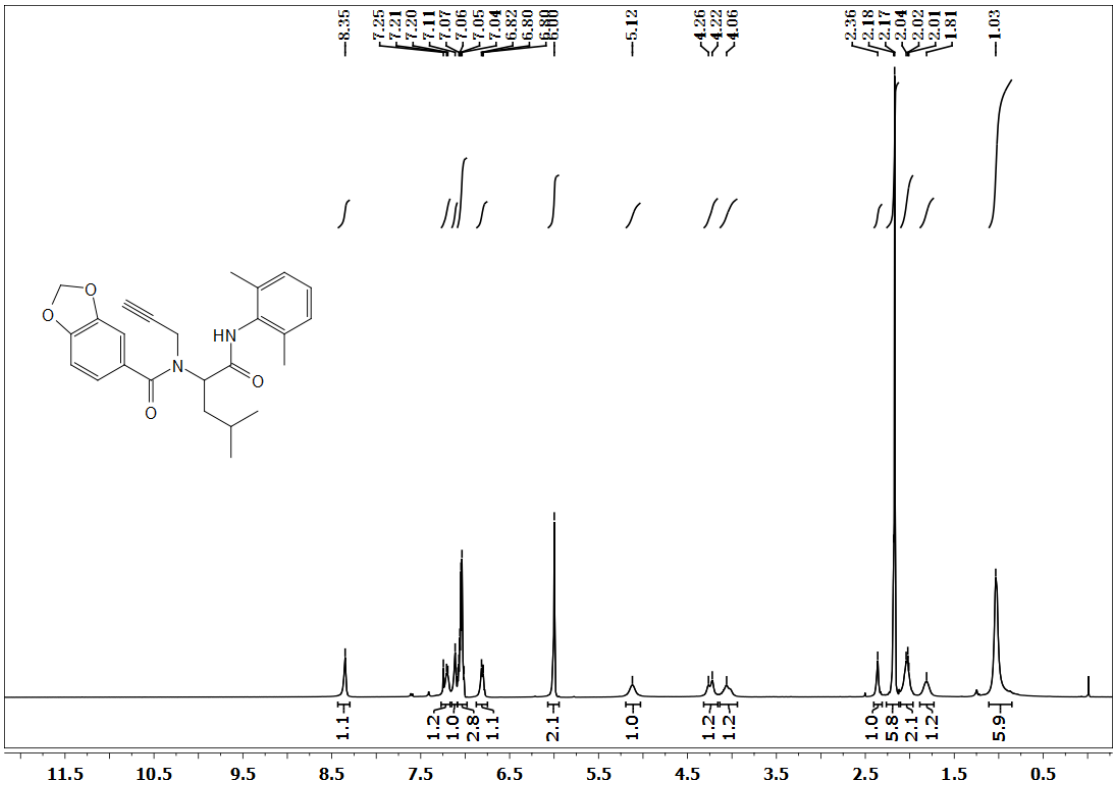


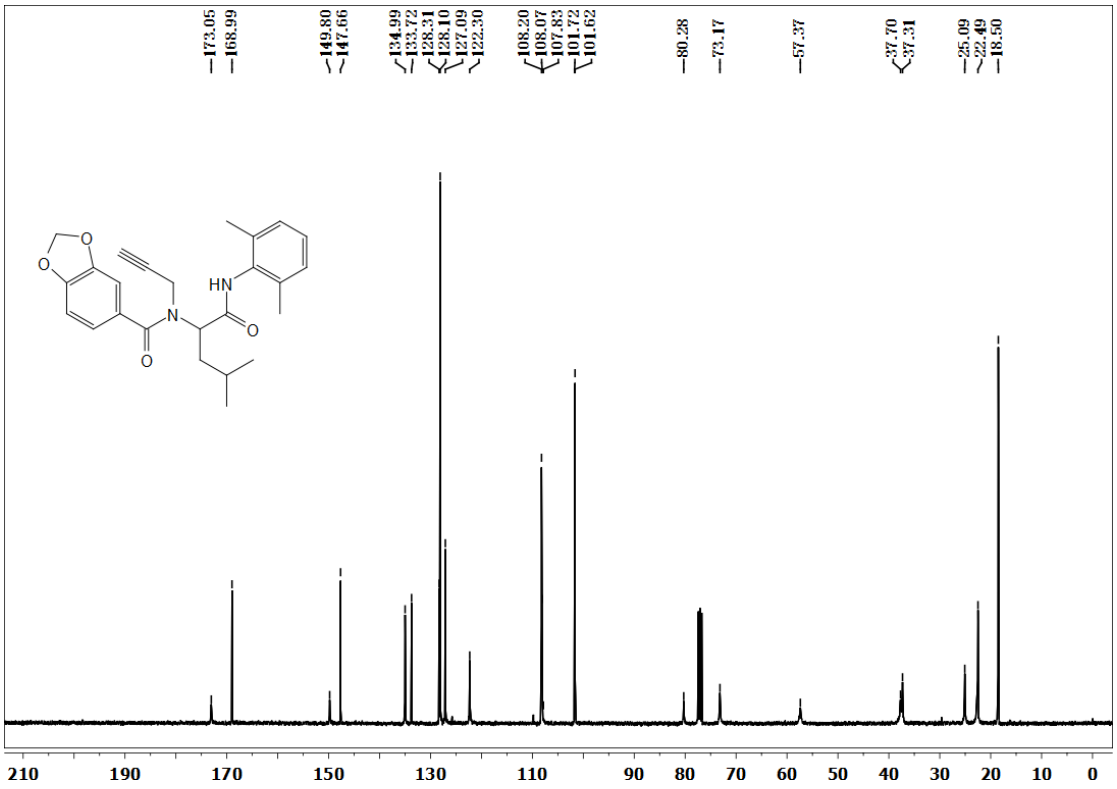
^{1}H NMR and ^{13}C NMR spectrum of **11h**





^{1}H NMR and ^{13}C NMR spectrum of **14**





^{1}H NMR and ^{13}C NMR spectrum of **17**