

Supplementary Material

Late-stage functionalization of 4-arylphthalazin-1(2H)-ones by a regioselective iridium-catalyzed C-H bond amidation reaction

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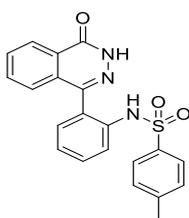
1. General Information

All reactions were carried out under air atmosphere in oven-dried glassware with magnetic stirring, unless otherwise specified. All other reagents and solvents were purchased from Energy Chemical or J&K Chemical Company and used without any further purification. TLC information was recorded on GF-254 (Qingdao Haiyang Chemical Co., Ltd. P. R. China) plates. Purification of reaction products was carried out by flash chromatography using Silica gel (200-300 mesh, Qingdao Haiyang Chemical Co. Ltd. P. R. China). All products were recorded using Bruker Avance-400 instruments, calibrated to TMS (^1H NMR spectra) and CDCl_3 (^{13}C NMR spectra) as the internal reference (0.00 ppm for ^1H NMR spectra and 100.00 ppm for ^{13}C NMR spectra). High-resolution mass spectra (HRMS) were recorded on a Bruker Apex IV FTMS mass spectrometer using ESI (electrospray ionization). Melting points were measured uncorrected. The substrates 4-aryl phthalazin-1(2H)-ones and 6-aryl pyridazin-3(2H)-one **1**^[1] were prepared according to well-known literature procedures.

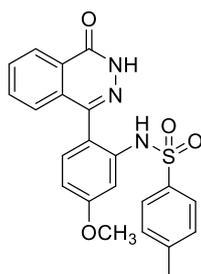
2. General Procedure for Ir(III)-Catalyzed C–H amidation of 4-arylphthalazin-1(2H)-ones and its anaglou

A mixture of 4-arylphthalazin-1(2H)-ones **1** (0.20 mmol), TsN_3 **2a** (momoamidation for 0.22 mmol; diamidation for 0.5 mmol), $[\text{Cp}^*\text{IrCl}_2]_2$ (0.008 mmol, 4 mol %), AgNTf_2 and DCE (1mL) were charged into a reaction tube. The reaction mixture was stirred at 100 °C for 12 h. After the mixture cooled to room temperature, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using petroleum ether/EtOAc to afford the desired products **3** or **4**.

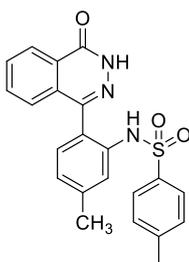
2. Characterization Data for products 3-4



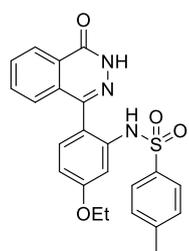
4-Methyl-N-[2-(4-oxo-3,4-dihydro-phthalazin-1-yl)-phenyl]-benzenesulfonamide (3a). White solid, mp 244-245 °C; ^1H NMR (400 MHz, $\text{DMSO-}d_6$): δ 12.71 (s, 1H), 9.55 (s, 1H), 8.22 (dd, $J = 8.0, 1.3$ Hz, 1H), 7.75 (t, $J = 7.6$ Hz, 1H), 7.65 (t, $J = 7.0$ Hz, 1H), 7.41 (d, $J = 8.3$ Hz, 2H), 7.35 (d, $J = 2.5$ Hz, 2H), 7.27 – 7.22 (m, 1H), 7.17 (ddd, $J = 7.9, 5.3, 3.1$ Hz, 1H), 7.11 (d, $J = 8.0$ Hz, 2H), 6.97 (d, $J = 8.0$ Hz, 1H), 2.21 (s, 3H); ^{13}C NMR (101 MHz, $\text{DMSO-}d_6$): δ 160.16, 144.37, 143.57, 137.49, 136.29, 133.46, 131.60, 130.23, 129.95, 128.57, 128.42, 126.95, 126.60, 126.01, 125.16, 122.97, 121.58, 118.38, 21.41; HRMS (ESI) m/z Calcd for $\text{C}_{21}\text{H}_{17}\text{N}_3\text{O}_3\text{S}$ $[\text{M}+\text{H}]^+$ 392.1063, found 392.1062.



N-[5-Methoxy-2-(4-oxo-3,4-dihydro-phthalazin-1-yl)-phenyl]-4-methyl-benzenesulfonamide (3b). White solid, mp 251-252 °C; ^1H NMR: (400 MHz, DMSO) δ 12.67 (s, 1H), 9.55 (s, 1H), 8.22 (d, $J = 7.9$ Hz, 1H), 7.73 (t, $J = 7.6$ Hz, 1H), 7.68 – 7.61 (m, 1H), 7.44 (d, $J = 8.1$ Hz, 2H), 7.13 (t, $J = 7.9$ Hz, 3H), 6.99 (d, $J = 8.0$ Hz, 1H), 6.91 (d, $J = 2.6$ Hz, 1H), 6.73 (dd, $J = 8.6, 2.5$ Hz, 1H), 3.67 (s, 3H), 2.19 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 160.32, 160.17, 144.21, 143.70, 137.48, 137.31, 133.36, 132.84, 131.49, 130.57, 129.99, 128.64, 127.06, 126.67, 125.99, 110.08, 108.11, 55.69, 21.40. HRMS (ESI) m/z Calcd for $\text{C}_{22}\text{H}_{19}\text{N}_3\text{O}_4\text{S}$ $[\text{M}+\text{H}]^+422.1169$, found 422.1167.

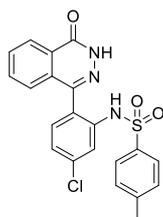


4-methyl-N-(5-methyl-2-(4-oxo-3,4-dihydrophthalazin-1-yl)phenyl)benzenesulfonamide (3c). White solid, mp 225-226 °C; ^1H NMR (400 MHz, DMSO) δ 14.25 (s, 1H), 13.02 (d, $J = 7.9$ Hz, 1H), 12.57 (t, $J = 7.6$ Hz, 1H), 12.45 (t, $J = 7.7$ Hz, 1H), 12.19 (d, $J = 8.0$ Hz, 2H), 12.01 (s, 1H), 11.92 (dd, $J = 16.4, 7.9$ Hz, 3H), 11.80 (dd, $J = 14.4, 7.9$ Hz, 2H), 7.07 (s, 3H), 7.01 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 164.83, 149.08, 148.25, 144.54, 142.18, 140.79, 138.14, 136.41, 136.30, 135.02, 134.64, 133.32, 131.66, 131.44, 130.74, 130.47, 128.55, 26.23, 26.18; HRMS (ESI) m/z Calcd for $\text{C}_{22}\text{H}_{19}\text{N}_3\text{O}_3\text{S}$ $[\text{M}+\text{H}]^+406.1220$, found 406.1220.

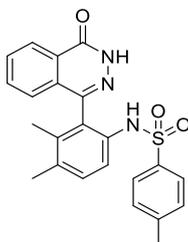


N-(5-ethoxy-2-(4-oxo-3,4-dihydrophthalazin-1-yl)phenyl)-4-methylbenzenesulfonamide (3d). White solid, mp 205-206 °C; ^1H NMR (400 MHz, DMSO) δ 12.74 (s, 1H),

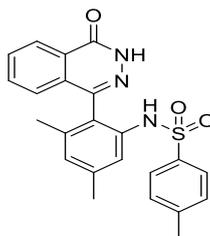
9.61 (s, 1H), 8.29 (d, $J = 7.9$ Hz, 1H), 7.82 (t, $J = 7.6$ Hz, 1H), 7.72 (t, $J = 7.6$ Hz, 1H), 7.52 (d, $J = 7.9$ Hz, 2H), 7.21 (d, $J = 8.2$ Hz, 3H), 7.07 (d, $J = 8.0$ Hz, 1H), 6.97 (d, $J = 2.5$ Hz, 1H), 6.79 (d, $J = 8.5$ Hz, 1H), 4.01 (q, $J = 6.9$ Hz, 2H), 2.28 (s, 3H), 1.33 (t, $J = 6.9$ Hz, 3H). ^{13}C NMR (100 MHz, DMSO) δ 160.16, 159.59, 144.22, 143.70, 137.48, 137.36, 133.38, 132.84, 131.52, 130.60, 130.02, 128.65, 127.03, 126.69, 126.00, 120.13, 110.75, 108.44, 63.78, 21.43, 14.97 ; HRMS (ESI) m/z Calcd for $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_4\text{S}$ $[\text{M}+\text{H}]^+436.1523$, found 436.1328.



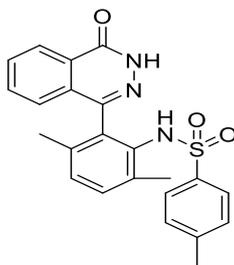
N-[5-Chloro-2-(4-oxo-3,4-dihydrophthalazin-1-yl)-phenyl]-4-methylbenzenesulfonamide (3e). White solid, mp 219-220°C; ^1H NMR (400 MHz, DMSO): δ 12.74 (d, $J = 2.3$ Hz, 1H), 9.85 (s, 1H), 8.22 (d, $J = 7.9$ Hz, 1H), 7.73 (t, $J = 7.6$ Hz, 1H), 7.61 (t, $J = 7.7$ Hz, 1H), 7.49 – 7.40 (m, 3H), 7.25 (d, $J = 8.2$ Hz, 1H), 7.19 (dd, $J = 8.2, 2.0$ Hz, 1H), 7.16 – 7.10 (m, 2H), 6.93 (d, $J = 8.0$ Hz, 1H), 2.20 (d, $J = 1.8$ Hz, 3H). ^{13}C NMR (100 MHz, DMSO) δ 160.26, 144.01, 143.29, 137.97, 137.08, 134.47, 133.54, 133.50, 131.67, 130.22, 130.13, 128.67, 127.02, 126.57, 126.25, 126.09, 124.72, 121.53, 21.44; HRMS (ESI) m/z Calcd for $\text{C}_{21}\text{H}_{16}\text{ClN}_3\text{O}_3\text{S}$ $[\text{M}+\text{H}]^+426.0674$, found 426.0682.



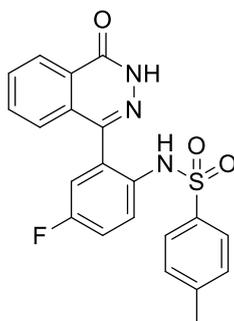
N-(3,4-dimethyl-2-(4-oxo-3,4-dihydrophthalazin-1-yl)phenyl)-4-methylbenzenesulfonamide (3f). White solid, mp 226-227 °C; ^1H NMR: (400 MHz, DMSO): δ 12.62 (s, 1H), 9.30 (s, 1H), 8.19 (dd, $J = 8.0, 1.3$ Hz, 1H), 7.77 – 7.70 (m, 1H), 7.62 (td, $J = 7.7, 1.4$ Hz, 1H), 7.32 (d, $J = 8.1$ Hz, 2H), 7.12 (s, 1H), 7.04 – 6.95 (m, 4H), 2.15 (d, $J = 4.4$ Hz, 6H), 2.11 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 160.01, 144.41, 143.30, 138.38, 137.51, 133.81, 133.54, 133.35, 132.44, 131.48, 130.18, 129.79, 128.47, 126.87, 126.84, 126.61, 125.93, 125.35, 21.42, 19.92, 19.05; HRMS (ESI) m/z Calcd for $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_3\text{S}_2$ $[\text{M}+\text{H}]^+419.1574$, found 419.1567.



N-(3,5-dimethyl-2-(4-oxo-3,4-dihydrophthalazin-1-yl)phenyl)-4-methylbenzenesulfonamide (3g). White solid, mp 206-207 °C; ^1H NMR (400 MHz, DMSO): δ 13.14 (s, 1H), 12.74 (s, 1H), 7.76 (d, $J = 8.4$ Hz, 2H), 7.68 – 7.61 (m, 2H), 7.29 (d, $J = 8.0$ Hz, 2H), 7.07 (s, 1H), 7.03 (s, 2H), 6.69 (d, $J = 7.6$ Hz, 1H), 2.25 (s, 3H), 2.23 (s, 3H), 1.88 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 162.69, 148.51, 144.74, 140.07, 138.97, 136.67, 136.11, 135.59, 131.72, 131.48, 131.34, 130.53, 130.06, 127.52, 126.93, 120.76, 118.16, 114.11, 21.41, 21.25, 19.54. ; HRMS (ESI) m/z Calcd for $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_3\text{S}_2$ $[\text{M}+\text{H}]^+419.1574$, found 419.1567.

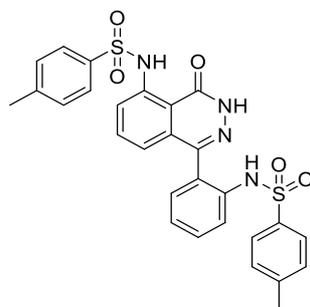


N-(3,6-dimethyl-2-(4-oxo-3,4-dihydrophthalazin-1-yl)phenyl)-4-methylbenzenesulfonamide (3h). White solid, mp 211-212 °C; ^1H NMR (400 MHz, DMSO): δ 13.15 (s, 1H), 12.73 (s, 1H), 7.75 (d, $J = 8.1$ Hz, 2H), 7.69 – 7.60 (m, 2H), 7.27 (d, $J = 8.1$ Hz, 2H), 7.12 (s, 2H), 6.95 (s, 1H), 6.70 – 6.64 (m, 1H), 2.21 (s, 3H), 2.18 (s, 3H), 1.85 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 162.69, 148.55, 144.71, 140.10, 136.14, 135.60, 135.41, 134.39, 133.67, 131.32, 130.62, 130.55, 130.51, 130.23, 127.51, 120.75, 118.24, 114.14, 21.39, 20.82, 19.10. ; HRMS (ESI) m/z Calcd for $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_3\text{S}_2$ $[\text{M}+\text{H}]^+419.1574$, found 419.1586.

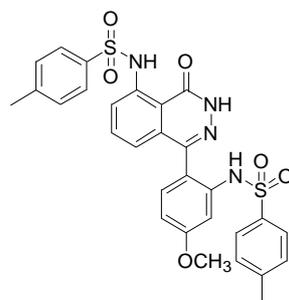


N-(4-fluoro-2-(4-oxo-3,4-dihydrophthalazin-1-yl)phenyl)-4-methylbenzenesulfonamide (3i). White solid, mp 237-238 °C; ^1H NMR (400 MHz, DMSO): δ 12.68 (s, 1H),

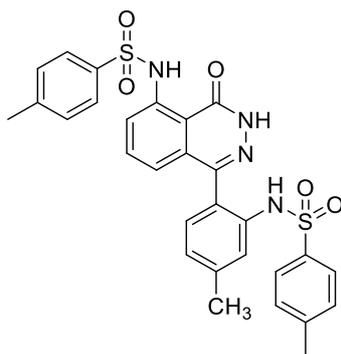
9.74 (s, 1H), 8.23-8.16 (m, 1H), 7.79 (dtt, $J = 10.1, 7.3, 3.7$ Hz, 2H), 7.51 – 7.41 (m, 2H), 7.27-7.21 (m, 2H), 7.20-7.16 (m, 2H), 6.97 (d, $J = 7.9$ Hz, 2H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 159.72, 142.78, 138.38, 136.82, 133.45, 131.59, 129.60, 129.42, 127.96, 127.55, 127.02, 126.01, 125.83, 121.56, 118.36, 117.38, 117.17, 21.44. HRMS (ESI) m/z Calcd for $\text{C}_{21}\text{H}_{16}\text{FN}_3\text{O}_3\text{S}$ $[\text{M}+\text{H}]^+$ 409.0896, found 409.0897.



4-methyl-N-[2-(5-Benzenesulfonylamino-4-oxo-3,4-dihydro-phthalazin-1-yl)-phenyl]-4-methyl-benzenesulfonamide (4a). White solid, mp 171-172 °C; ^1H NMR (400 MHz, DMSO) δ 13.10 (s, 1H), 12.78 (s, 1H), 9.51 (s, 1H), 7.79 (d, $J = 8.3$ Hz, 2H), 7.64 (d, $J = 8.2$ Hz, 1H), 7.49 (t, $J = 8.1$ Hz, 1H), 7.40 – 7.29 (m, 6H), 7.17 – 7.08 (m, 2H), 7.05 (d, $J = 8.0$ Hz, 2H), 6.45 (dd, $J = 8.0, 0.9$ Hz, 1H), 2.26 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 170.77, 163.10, 160.50, 145.70, 144.78, 143.77, 139.72, 137.57, 136.27, 134.94, 132.74, 132.04, 130.57, 129.98, 127.56, 127.08, 120.43, 119.48, 117.47, 114.44, 109.86, 107.48, 55.70, 21.40, 21.18; HRMS (ESI) m/z Calcd for $\text{C}_{21}\text{H}_{17}\text{N}_3\text{O}_3\text{S}$ $[\text{M}+\text{H}]^+$ 561.1261, found 561.1249.



N-[2-(5-Benzenesulfonylamino-4-oxo-3,4-dihydro-phthalazin-1-yl)-5-methoxy-phenyl]-4-methyl-benzenesulfonamide (4b). White solid, mp 192-193 °C; ^1H NMR (400 MHz, DMSO): δ 13.07 (s, 1H), 12.82 (s, 1H), 9.50 (s, 1H), 7.83 – 7.75 (m, 2H), 7.65 (d, $J = 8.2$ Hz, 1H), 7.49 (t, $J = 8.1$ Hz, 1H), 7.40 (d, $J = 8.1$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 7.06 (dd, $J = 12.7, 8.4$ Hz, 3H), 6.92 (d, $J = 2.4$ Hz, 1H), 6.67 (dt, $J = 8.6, 1.9$ Hz, 1H), 6.48 (d, $J = 8.0$ Hz, 1H), 3.65 (s, 3H), 2.24 (s, 3H), 2.19 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 170.77, 163.10, 160.50, 145.70, 144.78, 143.77, 139.72, 137.57, 136.27, 134.94, 132.74, 132.04, 130.57, 129.98, 127.56, 127.08, 120.43, 119.48, 117.47, 114.44, 109.86, 107.48, 55.70, 21.40, 21.18. HRMS (ESI) m/z Calcd for $\text{C}_{29}\text{H}_{26}\text{N}_4\text{O}_6\text{S}_2$ $[\text{M}+\text{H}]^+$ 591.1367, found 591.1359.

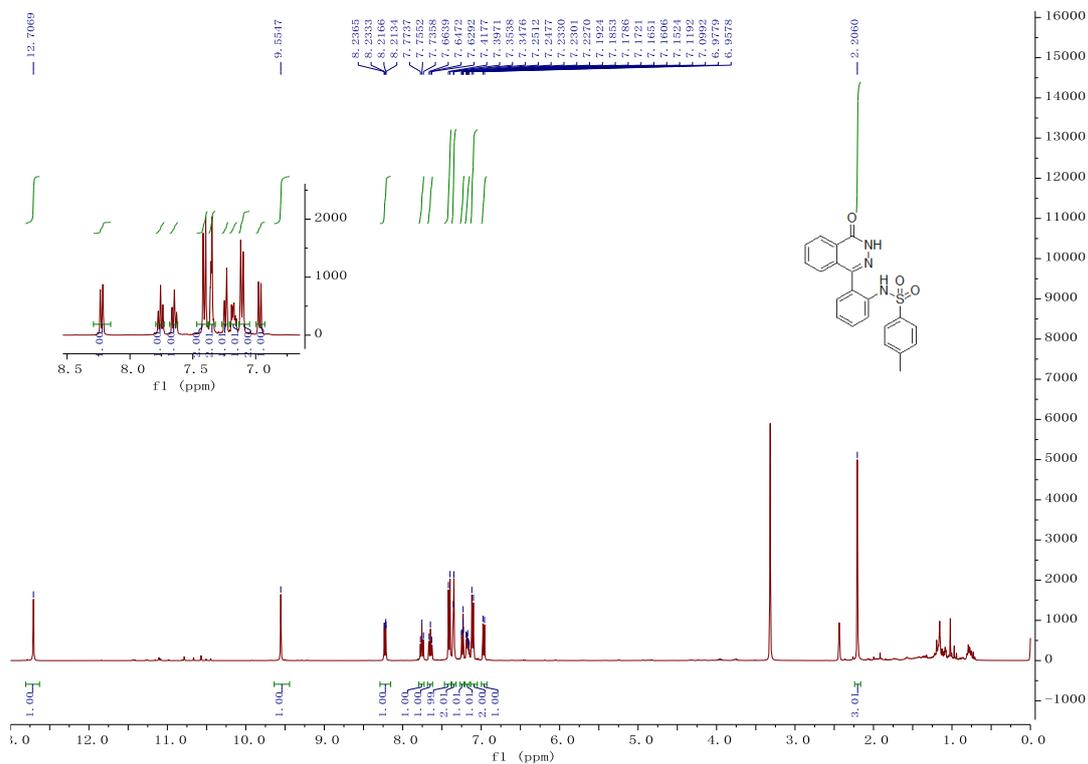
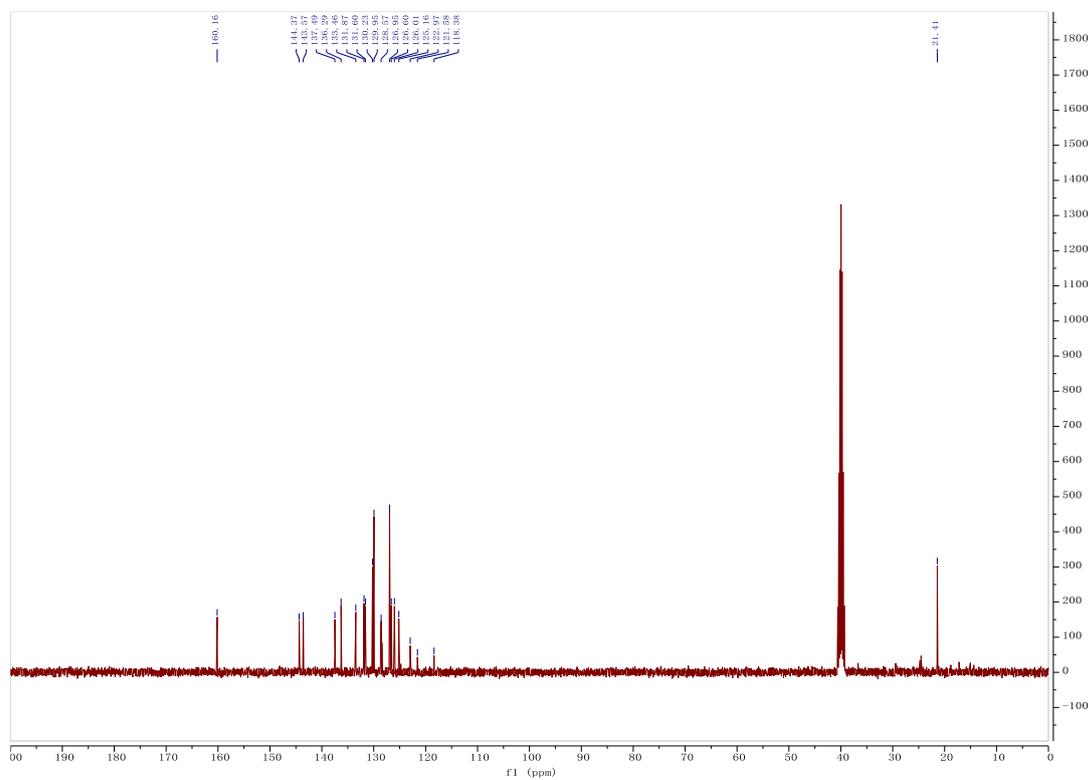


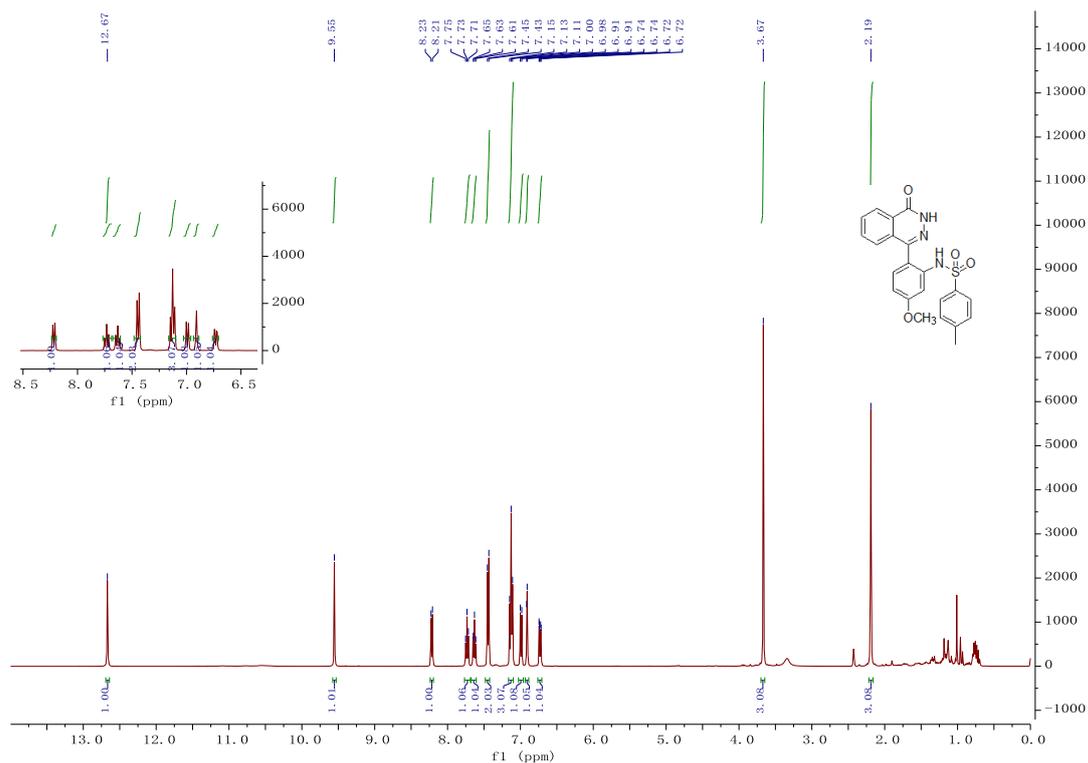
N-[2-(5-Benzenesulfonylamino-4-oxo-3,4-dihydro-phthalazin-1-yl)-5-methyl-phenyl]-4-methyl-benzenesulfonamide (4c). White solid, mp 257-258 °C; ^1H NMR (400 MHz, DMSO): δ 13.06 (s, 1H), 12.78 (s, 1H), 9.40 (s, 1H), 7.81-7.77 (m, 2H), 7.63 (dd, J = 7.6, 1.6 Hz, 1H), 7.48 (t, J = 8.2 Hz, 1H), 7.34 (dd, J = 8.3, 3.3 Hz, 4H), 7.21 (d, J = 1.7 Hz, 1H), 7.05 – 6.99 (m, 3H), 6.94 (dd, J = 8.0, 1.6 Hz, 1H), 6.45 (dd, J = 8.1, 0.9 Hz, 1H), 2.26 (s, 3H), 2.22 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, DMSO₆) δ 1663.99, 145.82, 144.79, 143.55, 140.07, 139.68, 137.42, 136.24, 136.10, 134.95, 131.70, 130.59, 129.84, 127.56, 126.92, 126.09, 125.75, 123.17, 120.44, 117.48, 114.34, 21.49, 21.42, 21.38. HRMS (ESI) m/z Calcd for C₂₉H₂₆N₄O₅S₂ [M+H]⁺575.1417, found 575.1421.

4. References

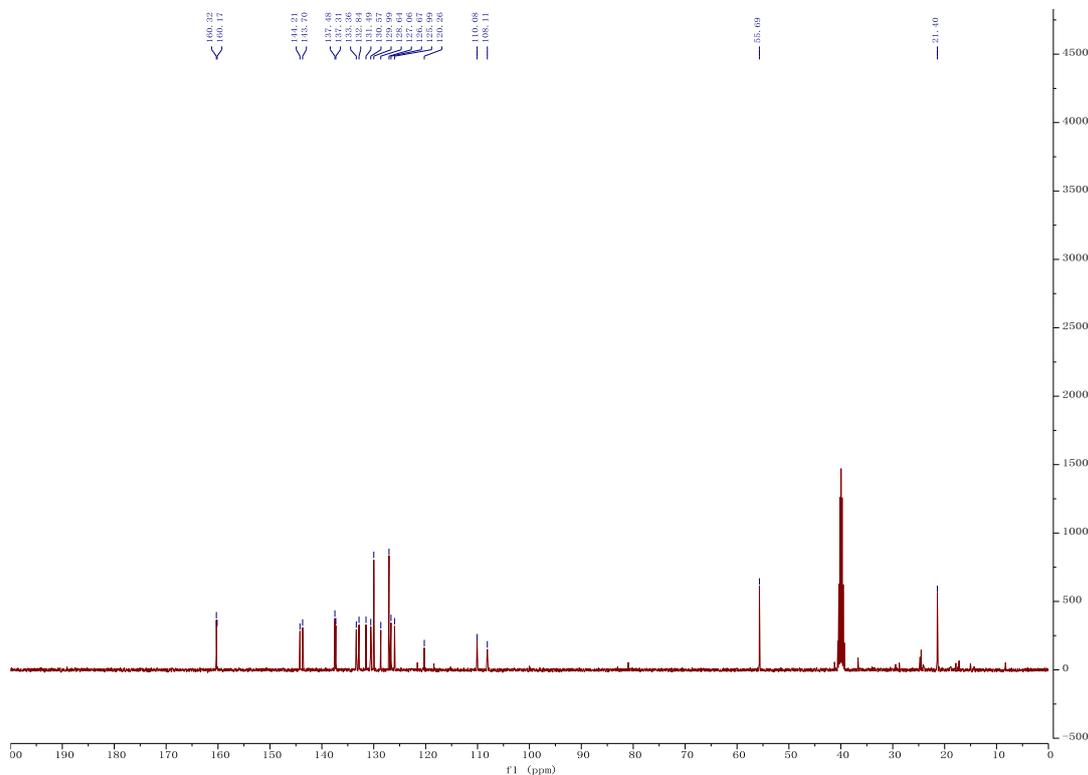
[1] Du, X.; Hou, H.; Zhao, Y.; Sheng, S.; Chen, J. *Eur. J. Org. Chem.*, **2020**, 1100-1107.

5. NMR Spectra

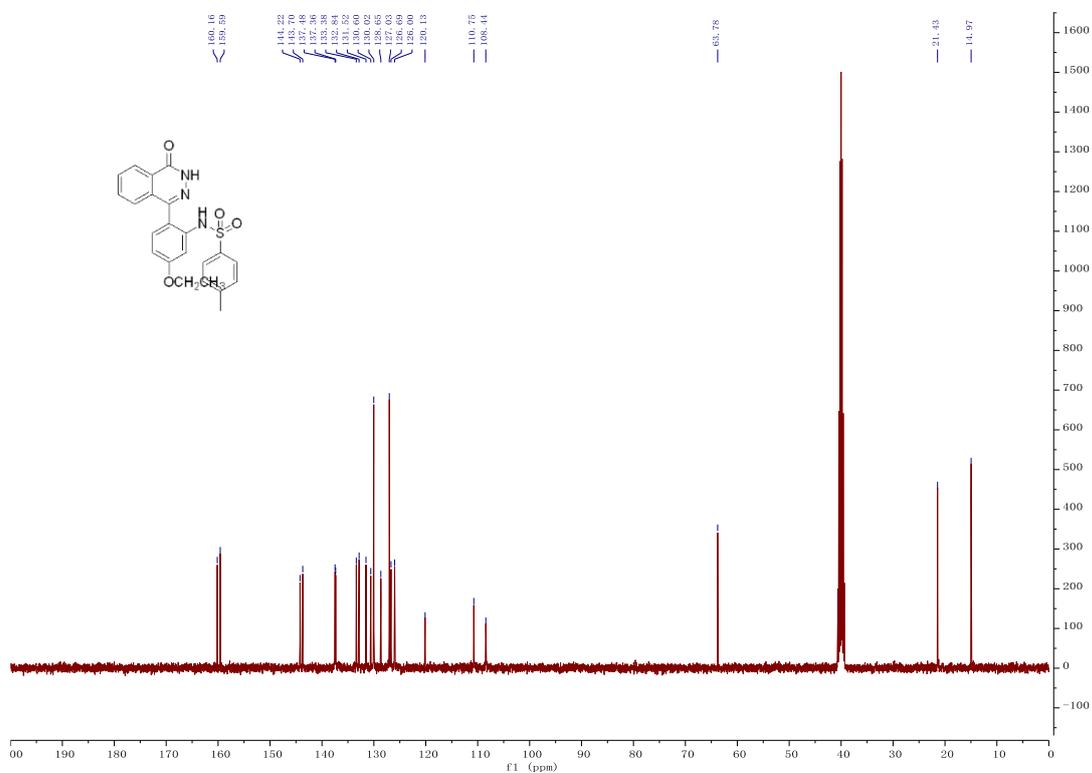
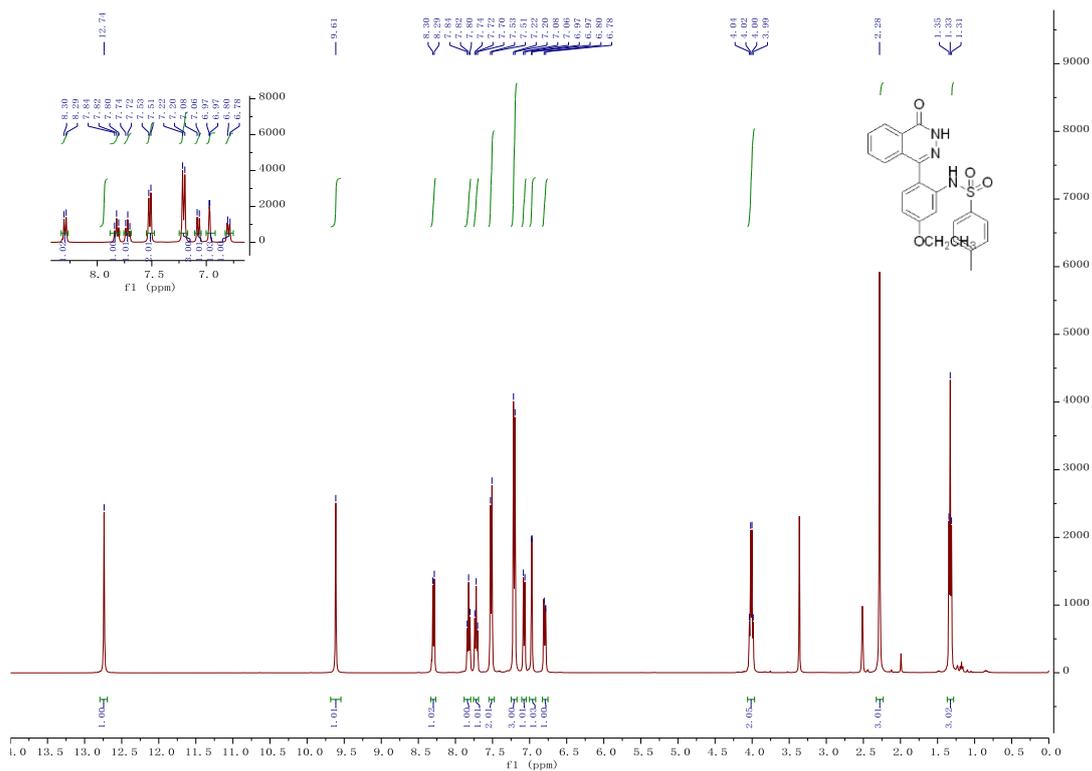
**¹H NMR spectrum of 3a (400 MHz, DMSO)****¹³C NMR spectrum of 3a (100 MHz, DMSO)**

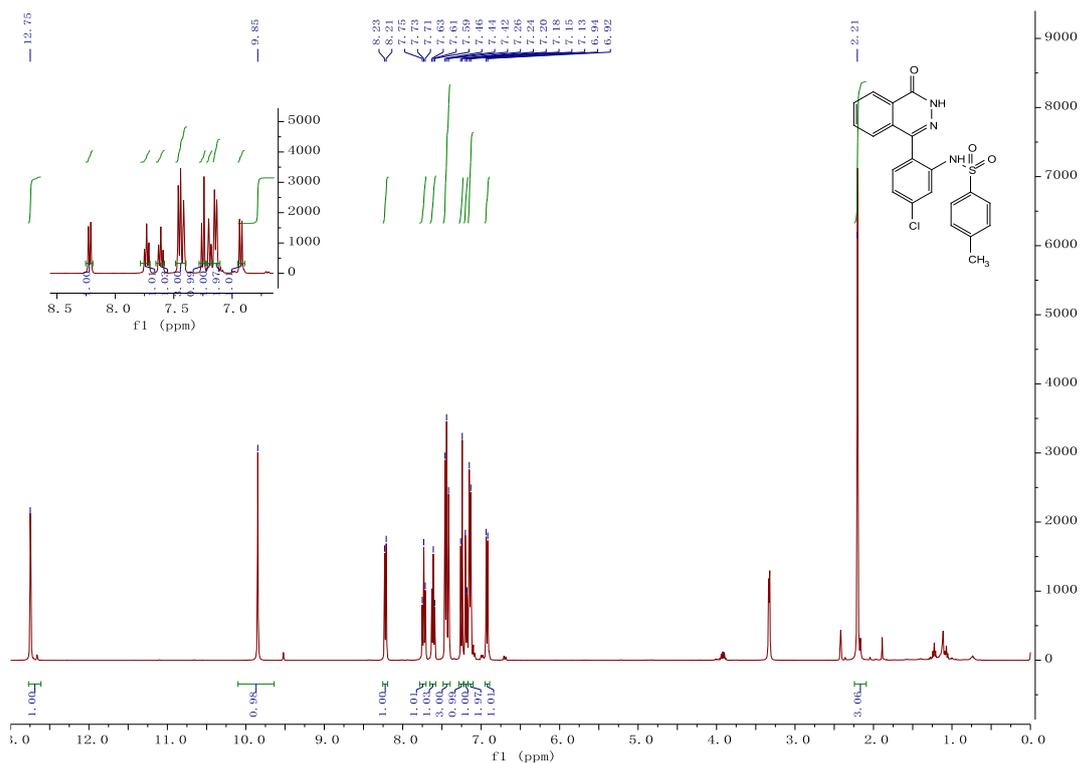


¹H NMR spectrum of 3b (400 MHz, DMSO)

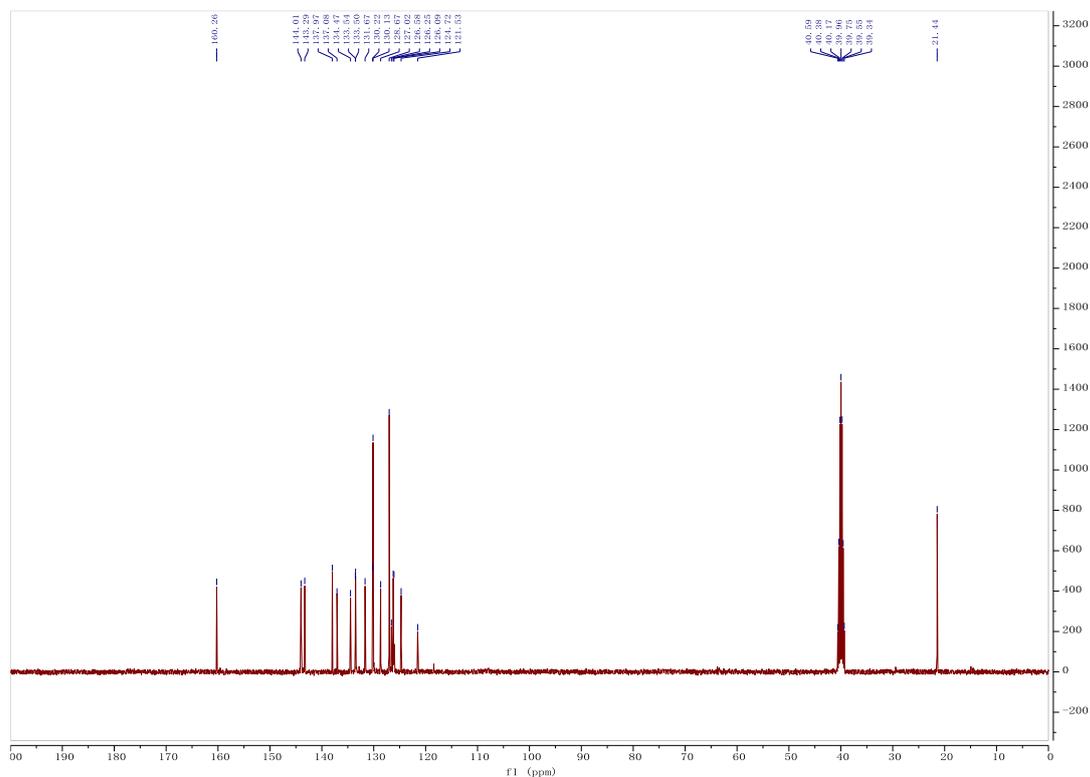


¹³C NMR spectrum of 3b (100 MHz, DMSO)

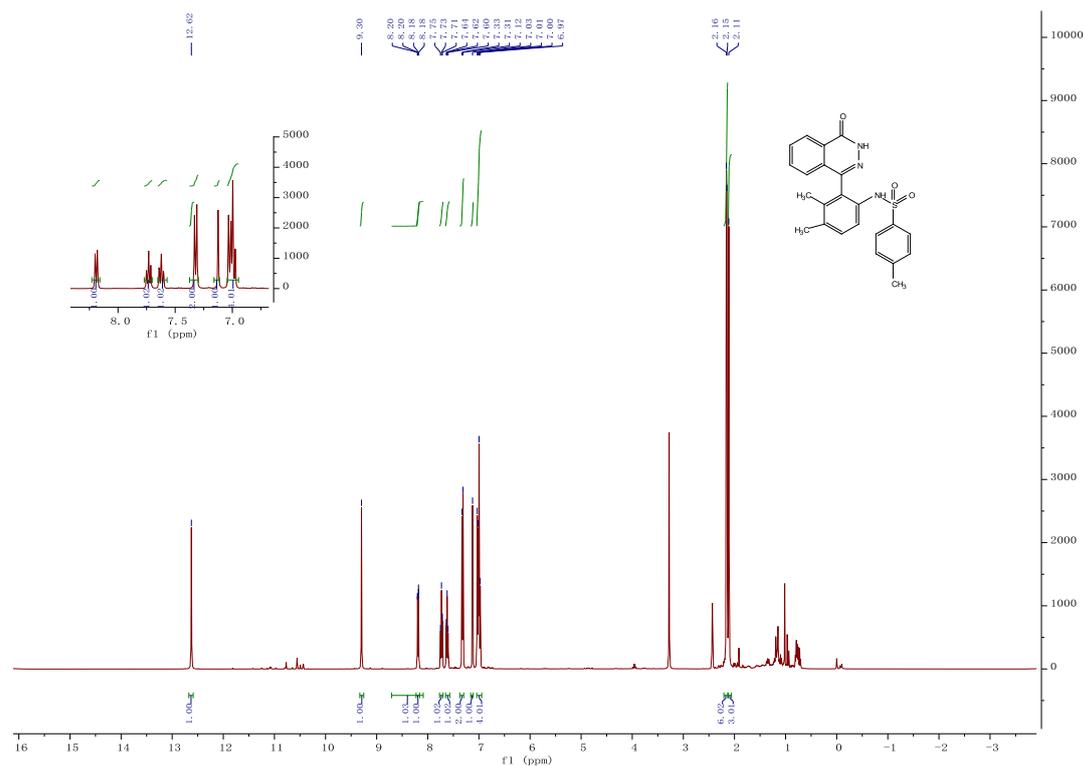




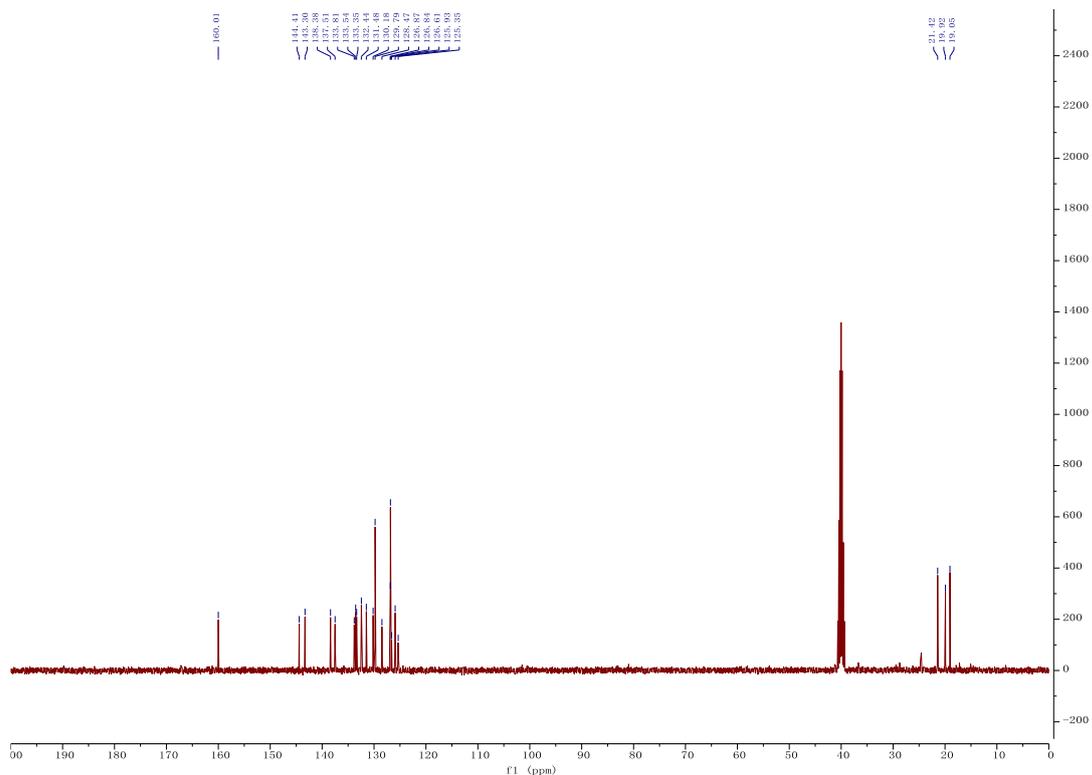
¹H NMR spectrum of 3e (400 MHz, DMSO)

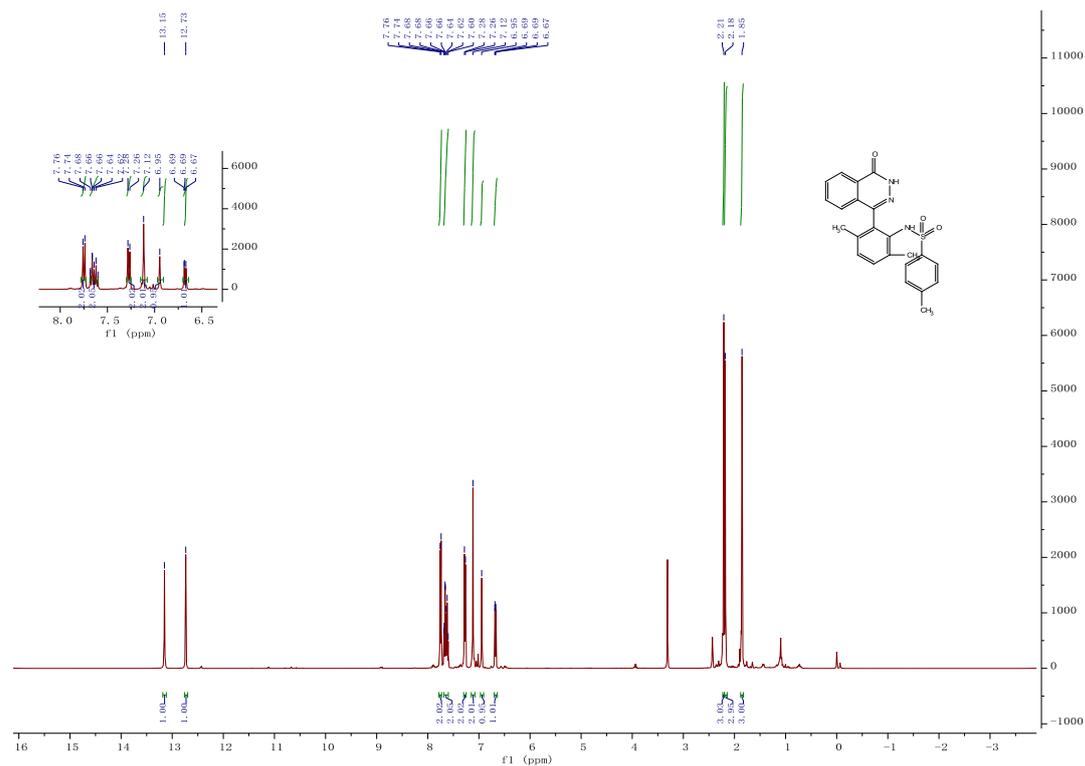


¹³C NMR spectrum of 3e (100 MHz, DMSO)

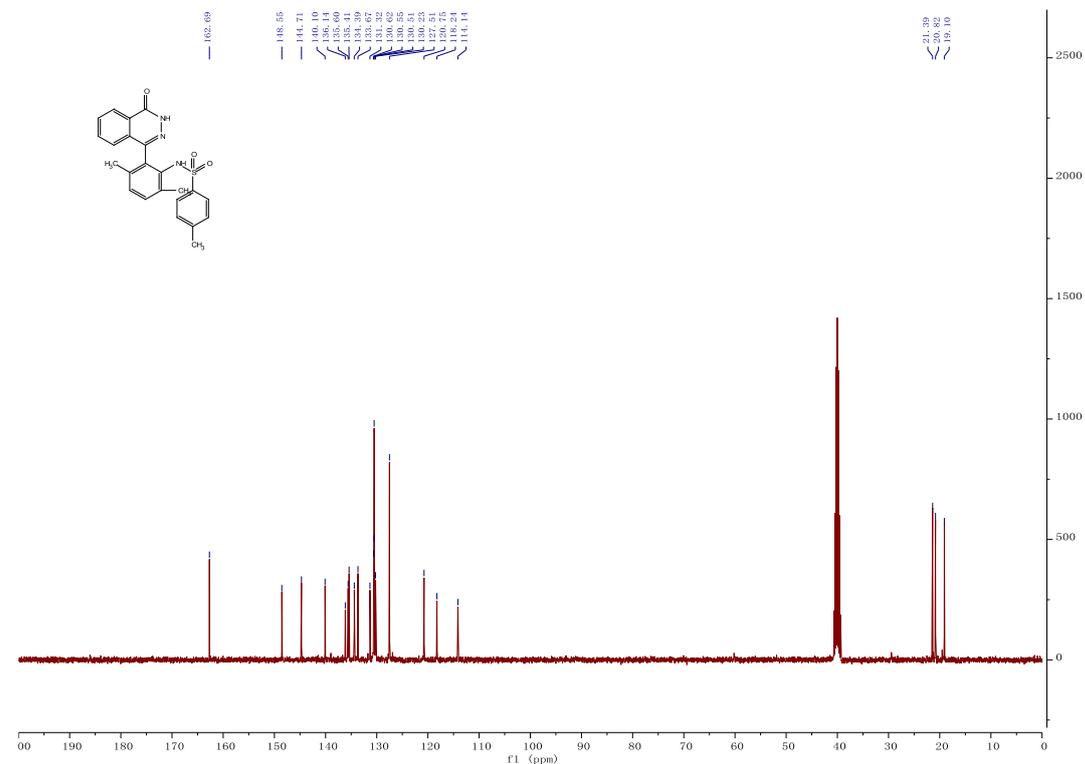


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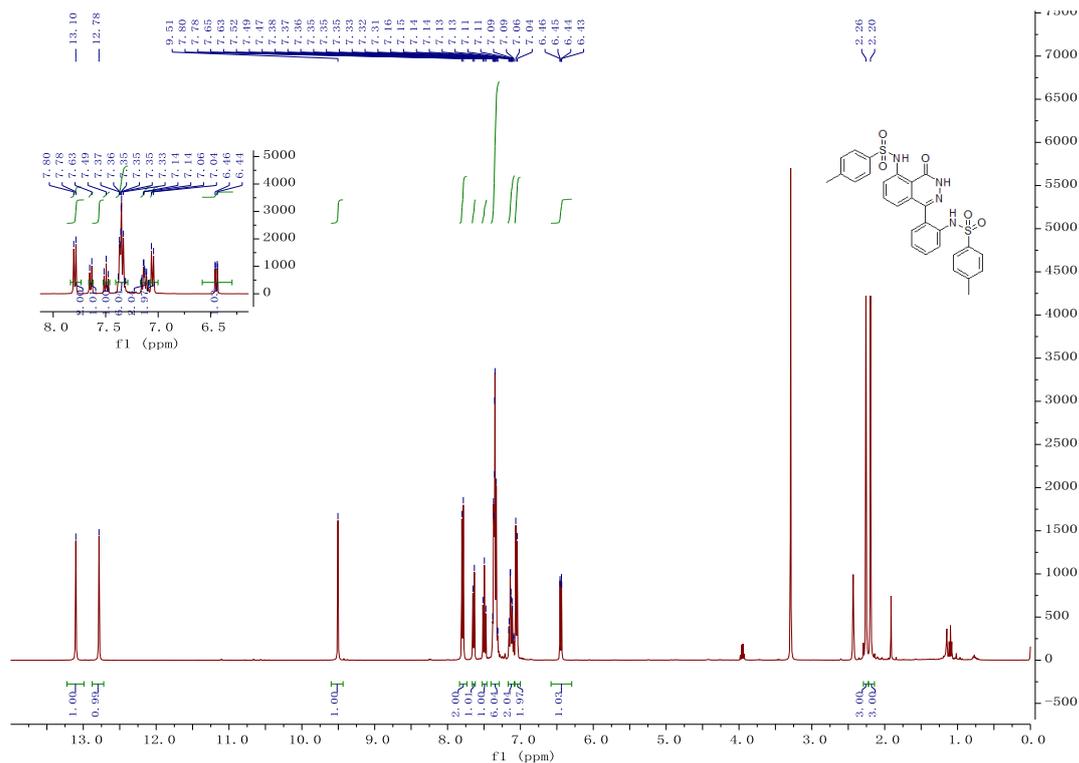
¹³C NMR spectrum of 3f (100 MHz, DMSO)



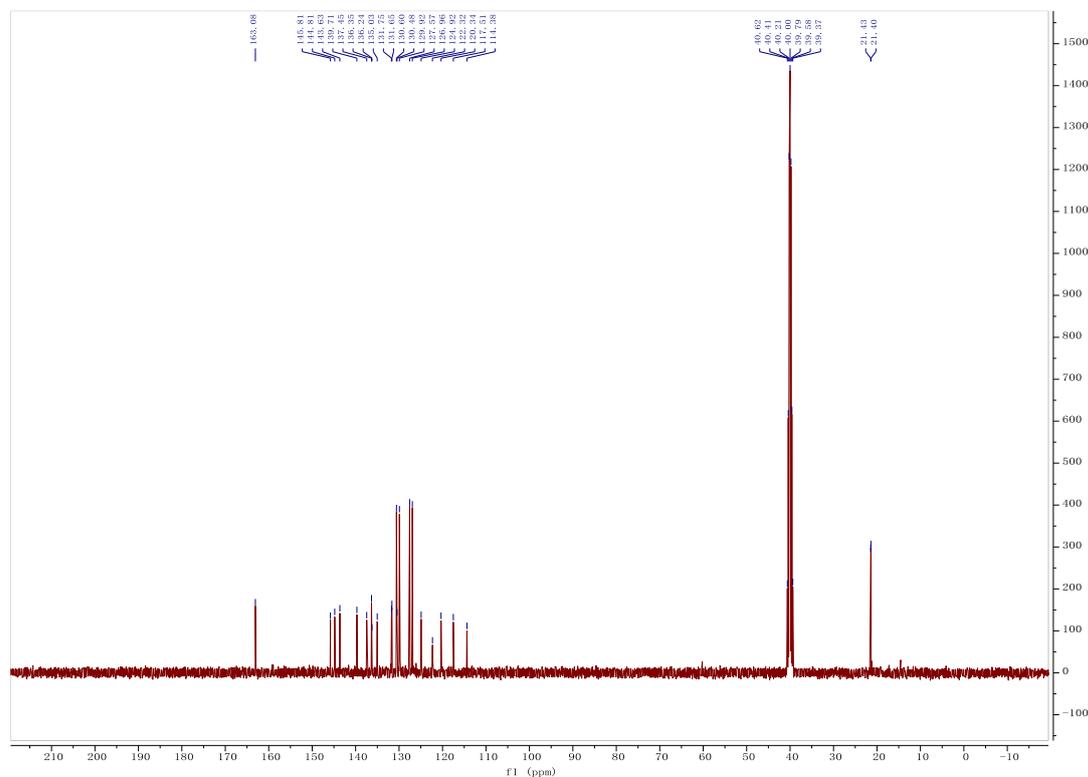
¹H NMR spectrum of 3h (400 MHz, DMSO)



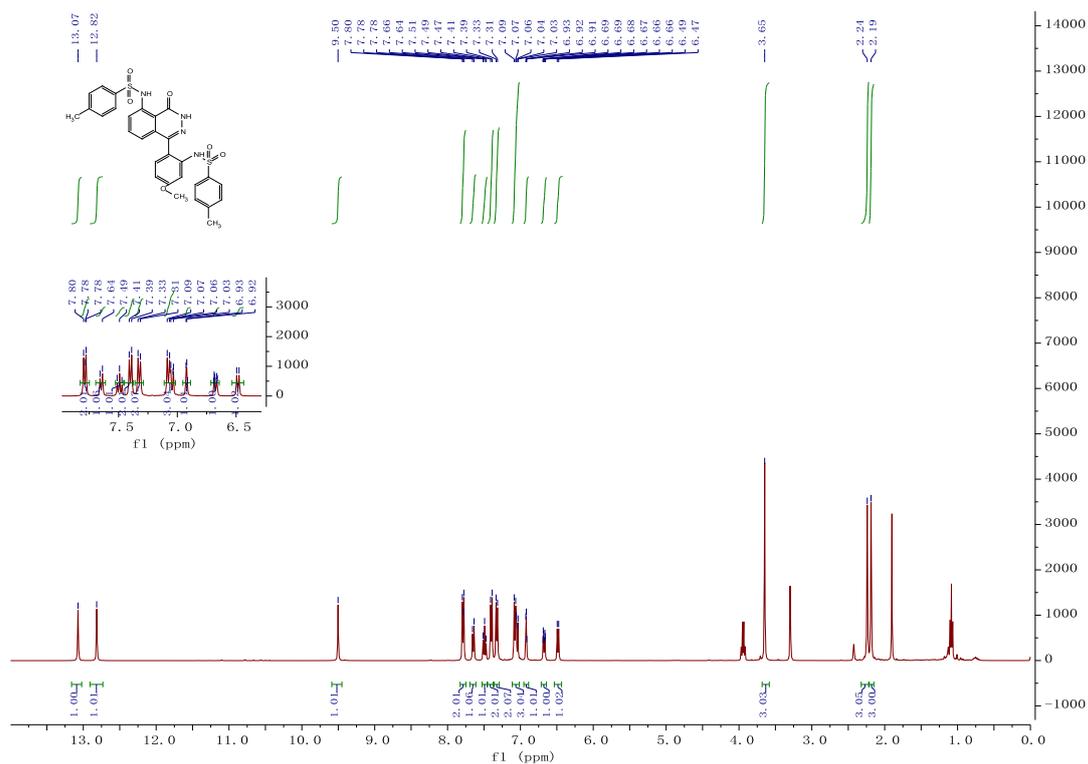
¹³C NMR spectrum of 3h (100 MHz, DMSO)



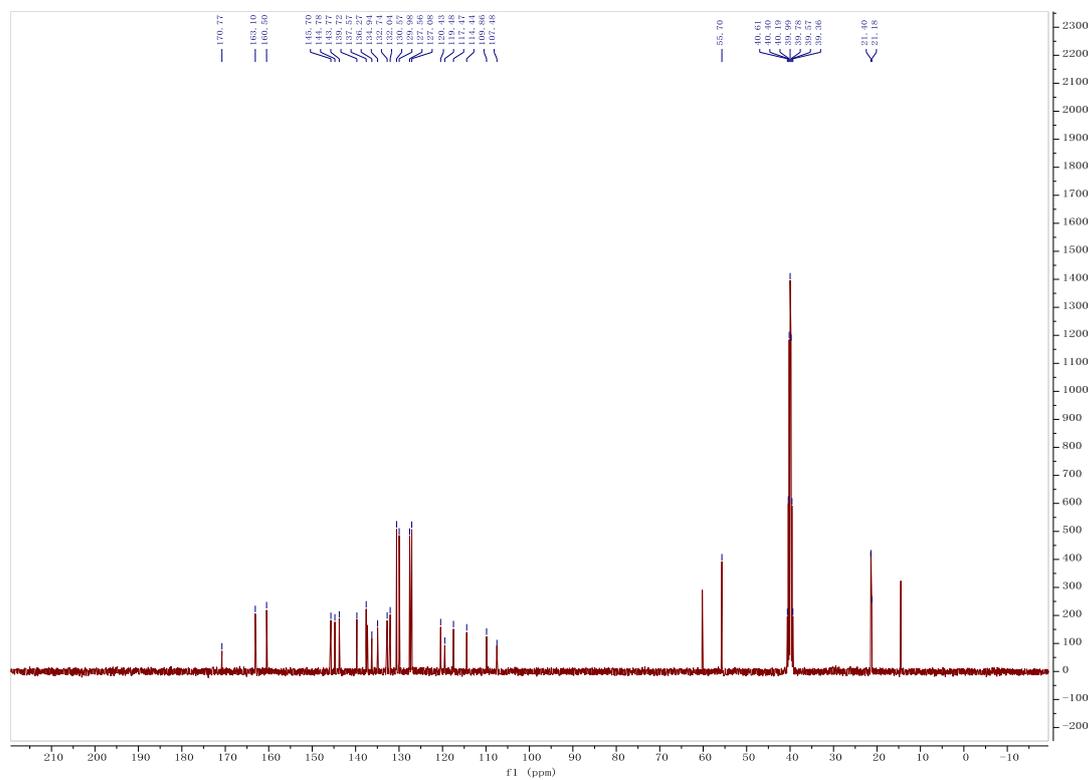
¹H NMR spectrum of 4a (400 MHz, DMSO)



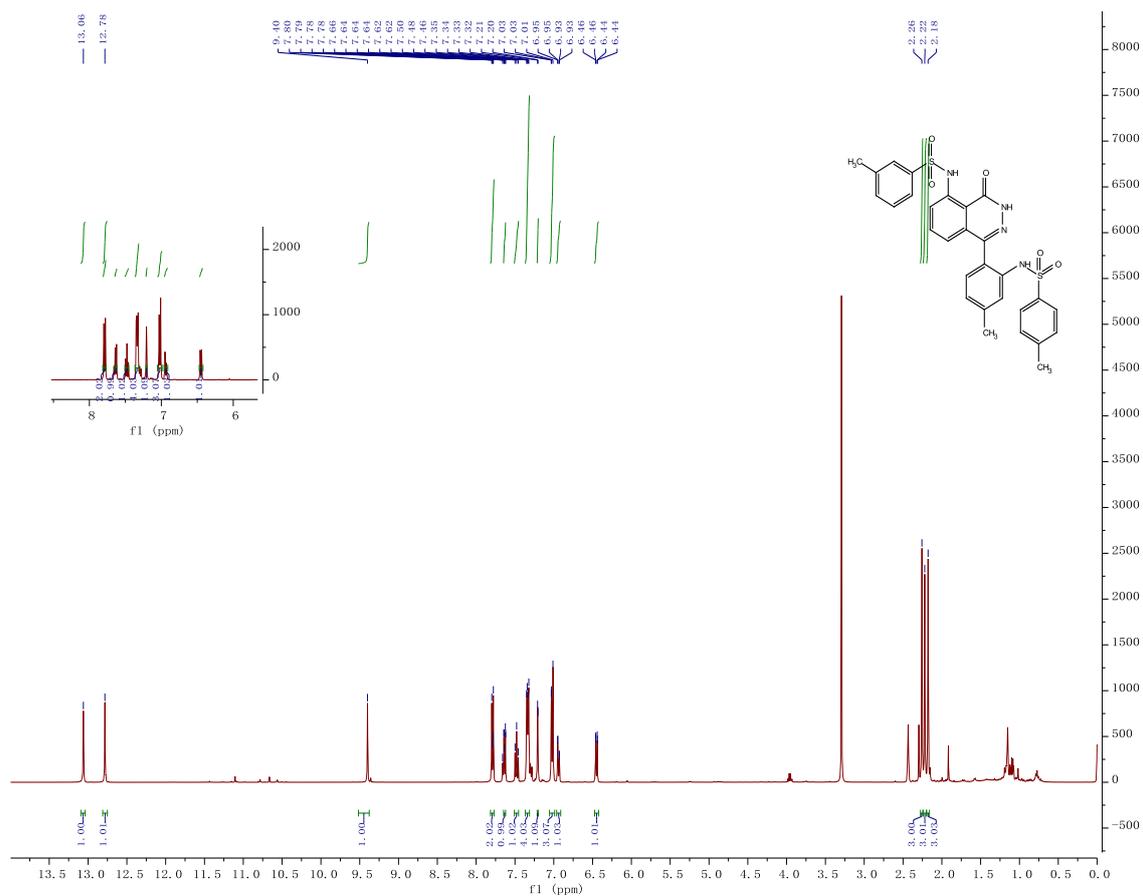
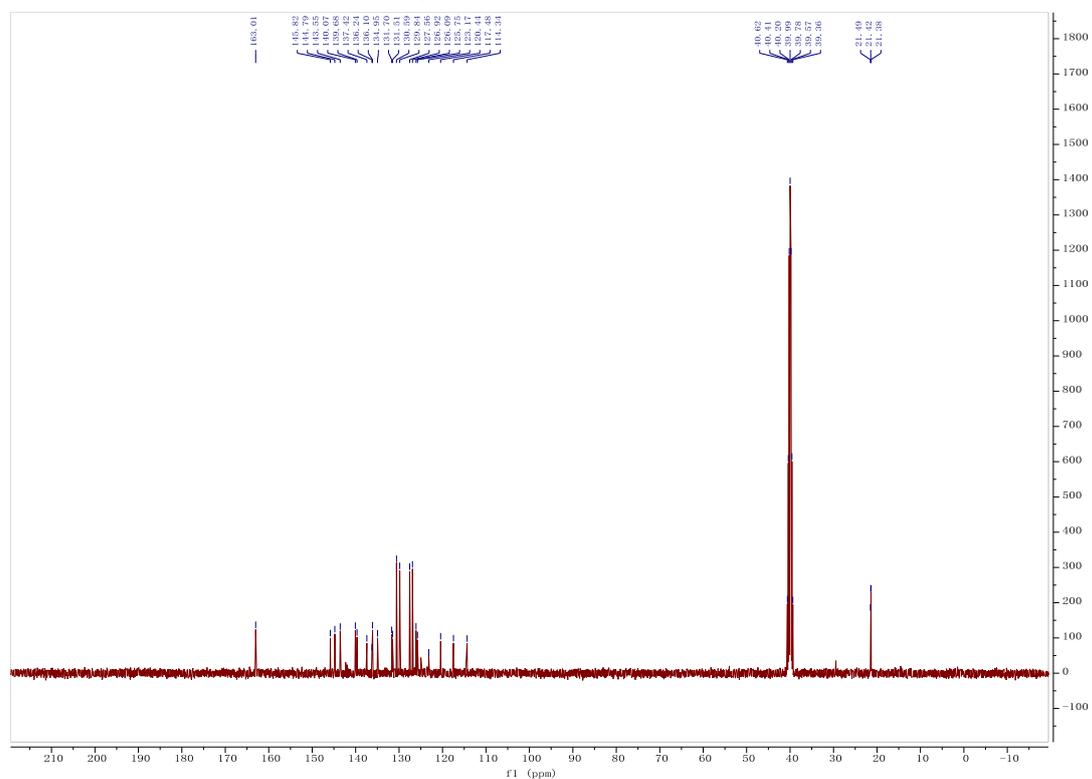
¹³C NMR spectrum of 4a (100 MHz, DMSO)



¹H NMR spectrum of 4b (400 MHz, DMSO)



¹³C NMR spectrum of 4b (100 MHz, DMSO)

**¹H NMR spectrum of 4c (400 MHz, DMSO)****¹³C NMR spectrum of 4c (400 MHz, DMSO)**