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 CDCl3 (13C NMR spectra) as the internal reference (0.00 ppm for 1H NMR spectra and 100.00 ppm for 13C 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 anaglous

A mixture of 4-arylphthalazin-1(2H)-ones 1 (0.20 mmol), TsN3 2a (momoamidation for 0.22 mmol; diamidation for 0.5 mmol), [Cp*IrCl2]2 (0.008 mmol, 4 mol %), AgNTf2 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 ºC; 1H NMR (400 MHz, DMSO-d6): 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); 13C NMR (101 MHz, DMSO-d6): 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 C23H17N3O3S [M+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; $^1$H 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, 143.70, 137.48, 137.31, 133.6, 132.84, 131.49, 130.57, 129.99, 128.64, 127.06, 126.67, 126.5, 110.08, 108.11, 55.69, 21.40. HRMS (ESI) m/z Calcd for C$_{22}$H$_{19}$N$_3$O$_4$S [M+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; $^1$H 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, 136.3, 135.02, 133.5, 131.66, 131.44, 130.74, 130.47, 128.55, 26.23, 26.18; HRMS (ESI) m/z Calcd for C$_{22}$H$_{19}$N$_3$O$_3$S [M+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; $^1$H 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) $\delta$ 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 C$_{23}$H$_{21}$N$_3$O$_4$S [M+H]$^+$ 436.1523, found 436.1328.

$^\text{N-[5-Chloro-2-(4-oxo-3,4-dihydro-phthalazin-1-yl)-phenyl]-4-methyl-benzenesulfonamide (3e).}$ White solid, mp 219-220°C; $^1$H NMR (400 MHz, DMSO): $\delta$ 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) $\delta$ 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 C$_{23}$H$_{16}$ClN$_3$O$_3$S [M+H]$^+$ 426.0674, found 426.0682.

$^\text{N-[3,4-dimethyl-2-(4-oxo-3,4-dihydrophthalazin-1-yl)phenyl]-4-methylbenzenesulfonamide (3f).}$ White solid, mp 226-227 °C; $^1$H NMR (400 MHz, DMSO): $\delta$ 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) $\delta$ 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 C$_{23}$H$_{21}$N$_3$O$_5$S [M+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; $^1$H NMR (400 MHz, DMSO): $\delta$ 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) $\delta$ 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 C$_{23}$H$_{21}$N$_3$O$_3$S$_2$ [M+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; $^1$H NMR (400 MHz, DMSO): $\delta$ 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) $\delta$ 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 C$_{23}$H$_{21}$N$_3$O$_3$S$_2$ [M+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; $^1$H NMR (400 MHz, DMSO): $\delta$ 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 C\(_{21}\)H\(_{16}\)FN\(_{3}\)O\(_3\)S [M+H]^+ 409.0896, found 409.0897.

4-methyl-N-[2-(5-Benzencesulfonlamino-4-oxo-3,4-dihydro-phthalazin-1-yl)-phenyl]-4-methyl-benzenesulfonamide (4a). White solid, mp 171-172 °C; \(^1\)H 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 C\(_{21}\)H\(_{17}\)N\(_3\)O\(_3\)S [M+H]^+ 561.1261, found 561.1249.

N-[2-(5-Benzencesulfonlamino-4-oxo-3,4-dihydro-phthalazin-1-yl)-5-methoxy-phenyl]-4-methyl-benzenesulfonamide (4b). White solid, mp 192-193 °C; \(^1\)H 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) δ170.77,163.10, 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 C\(_{29}\)H\(_{26}\)N\(_4\)O\(_6\)S\(_2\) [M+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). ¹³C NMR (100 MHz, DMSO) δ 1663.99, 145.82, 144.79, 143.55, 140.07, 139.68, 137.42, 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
5. NMR Spectra

$^1$H NMR spectrum of $3a$ (400 MHz, DMSO)

$^{13}$C NMR spectrum of $3a$ (100 MHz, DMSO)
$^1$H NMR spectrum of 3b (400 MHz, DMSO)

$^{13}$C NMR spectrum of 3b (100 MHz, DMSO)
**1H NMR spectrum of 3d (400 MHz, DMSO)**

**13C NMR spectrum of 3d (100 MHz, DMSO)**
$^{1}$H NMR spectrum of 3e (400 MHz, DMSO)

$^{13}$C NMR spectrum of 3e (100 MHz, DMSO)
**H NMR spectrum of 3f (400 MHz, DMSO)**

**$^{13}$C NMR spectrum of 3f (100 MHz, DMSO)**
H NMR spectrum of 3g (400 MHz, DMSO)

$^3$C NMR spectrum of 3g (100 MHz, DMSO)
H NMR spectrum of 3h (400 MHz, DMSO)

$^{13}$C NMR spectrum of 3h (100 MHz, DMSO)
**1H NMR spectrum of 3i (400 MHz, DMSO)**

**13C NMR spectrum of 3i (100 MHz, DMSO)**
$^1$H NMR spectrum of 4a (400 MHz, DMSO)

$^{13}$C NMR spectrum of 4a (100 MHz, DMSO)
$^1$H NMR spectrum of 4b (400 MHz, DMSO)

$^{13}$C NMR spectrum of 4b (100 MHz, DMSO)
H NMR spectrum of 4c (400 MHz, DMSO)

$^{13}$H NMR spectrum of 4c (400 MHz, DMSO)