**A metal-free C–C/C–O bond formation for the synthesis of 2-amino-5-oxo-4-aryl-*4H*,*5H*-pyrano[3,2-*c*]chromene-3-carboxamide catalyzed by polystyrene-supported *p*-toluenesulfonic acid (PS-PTSA)**

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**1. Experimental**

Chemicals were purchased from Aldrich and Alfa Aesar Chemical Companies and used without further purification. NMR spectra were recorded in parts per million (ppm) in DMSO-d6 on a Jeol JNM ECP 600 NMR instrument using TMS as internal standard. Standard abbreviations were used to denote signal multiplicities (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Mass spectra were recorded on a Jeol JMS-700 mass spectrometer. All melting points were determined using open capillaries on an Electrothermal-9100 (Japan) instrument and are uncorrected.

**2. General procedures for the synthesis of 2-amino-5-oxo-4-aryl-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide**



**Procedure:** Synthesis of 2-amino-4-(4-chlorophenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4a)**

A mixture of 4-hydroxycoumarin (**1**, 1 mmol), 4-chlorobenzaldehyde (**2a**, 1 mmol) and cyanoacetamide (**3**, 1 mmol) and PS-PTSA (10 mol %) was stirred at 80 °C in EtOH conditions. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was washed with ethanol. The residue dissolved in chloroform, and the insoluble PS-PTSA was separated by simple filtration and washed with chloroform. The solvent was evaporated under reduced pressure and the obtained crude was recrystallized from ethanol to afford the pure white product 4a in excellent yield (94%). The recovered catalyst was washed with ethyl acetate and acetone, dried and reused. Compounds 4b-4u were also synthesized by adopting this procedure.

**3.** **Spectral data of the compounds**

2-amino-4-(4-chlorophenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4a)**



Yield 94%; white solid; Mp: 264-266 oC; 1H NMR (600 MHz, DMSO-*d*6) δ 7.88 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.59 – 7.56 (m, 2H), 7.35 (dd, *J* = 8.3, 0.8 Hz, 2H), 7.32 – 7.29 (m, 2H), 7.27 – 7.25 (m, 2H), 7.17 – 7.15 (m, 2H), 6.30 (s, 1H), 13C NMR (151 MHz, DMSO-*d*6) δ 164.61, 164.33, 151.86, 136.44, 133.94, 131.13, 128.06, 126.21, 123.40, 123.04, 117.65, 115.30, 104.01, 35.46; HRMS (ESI, m/z): calcd for C19H13ClN2O4 (M+H+) 368.0564, found: 368.0566.

2-amino-4-(4-methoxyphenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4b)**



Yield 91%; white solid; Mp: 257-259 oC; 1H NMR (600 MHz, DMSO-*d*6) δ 7.90 (d, *J* = 7.2 Hz, 2H), 7.62 – 7.58 (m, 2H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.06 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 6.29 (s, 1H), 3.70 (s, 3H), 13C NMR (151 MHz, DMSO-*d*6) δ 165.20, 164.86, 157.35, 152.23, 131.95, 127.82, 123.88, 117.95, 116.02, 113.53, 104.42, 54.99, 35.28; HRMS (ESI, m/z): calcd for C20H16N2O5 (M+H+) 364.1059, found: 364.1059.

2-amino-5-oxo-4-(p-tolyl)-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4c)**



Yield 90%; white solid; Mp: 280-282 oC; 1H NMR (600 MHz, DMSO-*d*6) δ 7.89 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.61 – 7.58 (m, 2H), 7.36 (d, *J* = 7.9 Hz, 2H), 7.33 – 7.30 (m, 2H), 7.02 (s, 4H), 6.30 (s, 1H), 2.24 (s, 3H), 13C NMR (151 MHz, DMSO-*d*6) δ 164.61, 164.33, 151.86, 136.44, 133.94, 131.13, 128.06, 126.21, 123.40, 123.04, 117.65, 115.30, 104.01, 35.46, 19.85; HRMS (ESI, m/z): calcd for C20H16N2O4 (M+H+) 348.1110, found: 348.1112.

2-amino-4-(3-fluorophenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4d)**



Yield 92%; white solid; Mp: 240-242 oC; 1H NMR (600 MHz, DMSO-*d*6) δ 7.92 (dd, *J* = 7.8, 0.7 Hz, 2H), 7.61 – 7.57 (m, 2H), 7.36 – 7.30 (m, 4H), 7.26 (dd, *J* = 14.4, 7.5 Hz, 1H), 7.01 (d, *J* = 7.9 Hz, 1H), 6.96 (t, *J* = 8.9 Hz, 2H), 6.38 (s, 1H), 13C NMR (151 MHz, DMSO-*d*6) δ 164.69, 163.23, 161.63, 152.31, 131.90, 129.79, 124.05, 124.04, 123.03, 122.87, 115.96, 113.65, 113.49, 103.77, 36.03; HRMS (ESI, m/z): calcd for C19H13FN2O4 (M+H+) 352.0859, found: 352.0861.

2-amino-4-(4-fluorophenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4e)**



Yield 94%; white solid; Mp: 224-226 oC; 1H NMR (600 MHz, DMSO-*d*6) δ 7.92 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.60 (t, *J* = 7.8 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.19 (dd, *J* = 9.1, 3.3 Hz, 2H), 7.04 (dd, *J* = 8.5, 3.0 Hz, 2H), 6.34 (s, 1H), 13C NMR (151 MHz, DMSO-*d*6) δ 165.26, 164.76, 161.33, 159.73, 152.24, 135.92, 131.97, 128.60, 123.92, 123.78, 117.87, 115.99, 114.75, 114.61, 104.19, 35.50; HRMS (ESI, m/z): calcd for C19H13FN2O4 (M+H+) 352.0859, found: 352.0862.

2-amino-4-(4-nitrophenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4f)**



Yield 90%; white solid; Mp: 242-244 oC; 1H NMR (600 MHz, DMSO-*d*6) δ 8.09 – 8.07 (m, 2H), 7.89 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.57 (ddd, *J* = 8.6, 7.4, 1.6 Hz, 2H), 7.44 (dd, *J* = 8.9, 0.8 Hz, 2H), 7.33 (dd, *J* = 8.2, 0.6 Hz, 2H), 7.31 – 7.28 (m, 2H), 6.43 (s, 1H), 13C NMR (151 MHz, DMSO-*d*6) δ 167.02, 164.93, 152.96, 150.73, 146.06, 132.25, 128.58, 124.58, 123.86, 123.71, 123.47, 119.13, 116.38, 103.80, 37.25; HRMS (ESI, m/z): calcd for C19H13N3O6 (M+H+) 379.0804, found: 379.0806.

2-amino-4-(3-nitrophenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4g)**



Yield 87%; white solid; Mp: 216-218 °C; 1H NMR (600 MHz, DMSO-*d*6) δ 8.03 – 8.01 (m, 1H), 7.93 (s, 1H), 7.88 (dd, *J* = 7.9, 1.0 Hz, 2H), 7.64 – 7.62 (m, 1H), 7.59 – 7.56 (m, 2H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.31 – 7.27 (m, 2H), 6.39 (s, 1H), 13C NMR (151 MHz, DMSO-*d*6) δ 166.64, 164.36, 152.45, 147.84, 144.17, 133.95, 131.69, 129.47, 124.07, 123.46, 121.22, 120.62, 118.72, 115.85, 103.13, 36.32; HRMS (ESI, m/z): calcd for C19H13N3O6 (M+H+) 379.0804, found: 379.0804.

2-amino-4-(3-bromophenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamid **(4h)**



Yield 90%; white solid; Mp: 232-234 °C; 1H NMR (600 MHz, DMSO-*d*6) δ 7.89 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.59 – 7.56 (m, 2H), 7.33 (ddd, *J* = 5.0, 2.8, 0.7 Hz, 3H), 7.32 – 7.29 (m, 2H), 7.27 (d, *J* = 1.3 Hz, 1H), 7.20 – 7.15 (m, 2H), 6.32 (s, 1H), 13C NMR (151 MHz, DMSO-*d*6) δ 165.92, 164.56, 152.32, 143.86, 131.79, 130.17, 129.32, 128.40, 126.04, 123.99, 123.60, 121.53, 118.30, 115.91, 36.02; HRMS (ESI, m/z): calcd for C19H13BrN2O4 (M+H+) 412.0059, found: 412.0061.

2-amino-4-(4-bromophenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4i)**



Yield 94%; white solid; Mp: 278-280 °C; 1H NMR (600 MHz, DMSO-*d*6) δ 7.89 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.58 (ddd, *J* = 8.6, 7.3, 1.6 Hz, 2H), 7.40 – 7.38 (m, 2H), 7.35 (d, *J* = 7.7 Hz, 2H), 7.32 – 7.29 (m, 2H), 7.11 (dd, *J* = 8.6, 1.0 Hz, 2H), 6.29 (s, 1H), 13C NMR (151 MHz, DMSO-*d*6) δ 165.79, 164.62, 152.30, 140.13, 131.80, 130.80, 129.13, 123.96, 123.61, 118.44, 118.34, 115.90, 35.78; HRMS (ESI, m/z): calcd for C19H13BrN2O4 (M+H+) 412.0059, found: 412.0059.

2-amino-4-(4-ethoxyphenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4j)**



Yield 89%; white solid; Mp: 244-246 °C; 1H NMR (600 MHz, DMSO-*d*6) δ 7.90 (dd, *J* = 7.9, 1.4 Hz, 2H), 7.61 – 7.58 (m, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.34 – 7.31 (m, 2H), 7.04 (d, *J* = 8.1 Hz, 2H), 6.79 – 6.76 (m, 2H), 6.29 (s, 1H), 3.96 (q, *J* = 7.0 Hz, 2H), 1.29 (t, *J* = 7.0 Hz, 3H), 13C NMR (151 MHz, DMSO-*d*6) δ 165.16, 164.79, 156.58, 152.18, 131.84, 127.74, 123.87, 123.71, 117.95, 115.92, 113.97, 104.35, 62.84, 35.24, 14.71; HRMS (ESI, m/z): calcd for C21H18N2O5 (M+H+) 378.1216, found: 378.1218.

2-amino-4-(3-methoxyphenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4k)**



Yield 90%; white solid; Mp: 264-266 °C; 1H NMR (600 MHz, DMSO-*d*6) δ 7.91 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.60 (ddd, *J* = 8.6, 7.3, 1.6 Hz, 2H), 7.37 (d, *J* = 7.8 Hz, 2H), 7.34 – 7.31 (m, 2H), 7.15 (t, *J* = 8.0 Hz, 1H), 6.74 (dd, *J* = 8.0, 2.7 Hz, 2H), 6.68 (d, *J* = 2.3 Hz, 1H), 6.34 (s, 1H), 3.64 (s, 3H), 13C NMR (151 MHz, DMSO-*d*6) δ 165.37, 164.84, 159.28, 152.25, 141.73, 131.98, 129.15, 123.96, 123.79, 119.22, 117.94, 116.03, 113.30, 110.23, 104.13, 54.90, 35.98; HRMS (ESI, m/z): calcd for C20H16N2O5 (M+H+) 364.1059, found: 364.1061.

2-amino-5-oxo-4-(3,4,5-trimethoxyphenyl)-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4l)**



Yield 88%; white solid; Mp: 275-277 °C; 1H NMR (600 MHz, DMSO-*d*6) δ 7.93 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.61 – 7.58 (m, 2H), 7.37 (d, *J* = 7.8 Hz, 2H), 7.35 – 7.32 (m, 2H), 6.47 (d, *J* = 0.7 Hz, 2H), 6.31 (s, 1H), 3.64 (s, 3H), 3.59 (s, 6H), 13C NMR (151 MHz, DMSO-*d*6) δ 165.14, 164.79, 152.67, 152.24, 135.92, 135.72, 131.99, 123.90, 118.60, 117.84, 116.08, 104.63, 104.38, 60.03, 55.96, 36.30; HRMS (ESI, m/z): calcd for C22H20N2O7 (M+H+) 424.1271, found: 424.1271.

2-amino-5-oxo-4-phenyl-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4m)**



Yield 94%; white solid; Mp: 239-241 °C; 1H NMR (600 MHz, DMSO-*d*6) δ 7.92 (dd, *J* = 7.9, 1.4 Hz, 2H), 7.62 – 7.59 (m, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.25 – 7.22 (m, 2H), 7.18 – 7.14 (m, 3H), 6.39 (s, 1H), 13C NMR (151 MHz, DMSO-*d*6) δ 165.19, 164.93, 152.24, 139.75, 132.06, 128.17, 126.76, 125.70, 123.92, 117.82, 116.07, 104.22, 35.99; HRMS (ESI, m/z): calcd for C19H14N2O4 (M+H+) 334.0954, found: 334.0956.

2-amino-4-(5-chloro-2-hydroxyphenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4n)**



Yield 87%; white solid; Mp: <300 °C; 1H NMR (600 MHz, DMSO-*d*6) δ 12.38 (s, 1H), 8.06 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.69 – 7.66 (m, 1H), 7.61 – 7.58 (m, 1H), 7.47 – 7.45 (m, 1H), 7.45 – 7.39 (m, 2H), 7.38 – 7.37 (m, 2H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.17 (d, *J* = 2.2 Hz, 1H), 5.72 (s, 1H), 13C NMR (151 MHz, DMSO-*d*6) δ 160.22, 152.28, 151.96, 132.61, 132.31, 128.73, 128.33, 127.92, 124.56, 123.99, 122.59, 118.23, 116.49, 116.28, 116.10, 113.57, 28.74; HRMS (ESI, m/z): calcd for C19H13ClN2O5 (M+H+) 384.0513, found: 384.0515.

2-amino-4-(3-chlorophenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4o)**



Yield 92%; white solid; Mp: 237-239 °C; 1H NMR (600 MHz, DMSO-*d*6) δ 7.90 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.60 – 7.57 (m, 2H), 7.36 – 7.34 (m, 2H), 7.32 – 7.29 (m, 2H), 7.25 (t, *J* = 7.8 Hz, 1H), 7.21 – 7.19 (m, 1H), 7.15 – 7.11 (m, 2H), 6.33 (s, 1H), 13C NMR (151 MHz, DMSO-*d*6) δ 165.96, 164.58, 152.34, 143.60, 132.81, 131.79, 129.83, 126.48, 125.69, 125.57, 123.99, 123.59, 118.33, 115.90, 103.55, 36.04; HRMS (ESI, m/z): calcd for C19H13ClN2O4 (M+H+) 368.0564, found: 368.0566.

2-amino-5-oxo-4-(o-tolyl)-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4p)**



Yield 89%; white solid; Mp: 222-224 °C;1H NMR (600 MHz, DMSO-*d*6) δ 7.89 (d, *J* = 7.2 Hz, 2H), 7.59 – 7.55 (m, 2H), 7.32 (dd, *J* = 17.2, 7.5 Hz, 4H), 7.24 (s, 1H), 7.07 (s, 3H), 6.13 (s, 1H), 2.09 (s, 3H), 13C NMR (151 MHz, DMSO-*d*6) δ 164.92, 163.92, 152.15, 139.22, 135.88, 131.63, 130.29, 127.83, 125.82, 125.27, 123.77, 123.59, 117.91, 115.88, 104.13, 35.68, 19.49; HRMS (ESI, m/z): calcd for C20H16N2O4 (M+H+) 348.1110, found: 348.1112.

2-amino-4-(5-bromo-2-hydroxy-3-methoxyphenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4q)**



Yield 86%; white solid; Mp: 280-282 °C; 1H NMR (600 MHz, DMSO-*d*6) δ 12.19 (s, 1H), 8.07 – 7.94 (m, 2H), 7.71 – 7.68 (m, 1H), 7.62 – 7.59 (m, 1H), 7.51 – 7.48 (m, 1H), 7.45 (d, *J* = 8.2 Hz, 1H), 7.35 (dd, *J* = 18.9, 6.6 Hz, 2H), 7.22 (d, *J* = 2.2 Hz, 1H), 6.86 (d, *J* = 1.9 Hz, 1H), 5.68 (s, 1H), 3.96 (s, 3H), 13C NMR (151 MHz, DMSO-*d*6) δ 160.20, 152.25, 151.91, 148.29, 132.58, 132.35, 124.69, 124.02, 122.30, 121.77, 116.55, 116.31, 116.07, 114.35, 113.68, 56.61, 28.56; HRMS (ESI, m/z): calcd for C20H16BrN2O6 (M+H+) 458.0113, found: 458.0115.

2-amino-5-oxo-4-(pyridin-2-yl)-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4r)**



Yield 90%; white solid; Mp: 268-270 °C; 1H NMR (600 MHz, DMSO-*d*6) δ 8.63 (d, *J* = 5.7 Hz, 1H), 8.48 – 8.44 (m, 1H), 7.92 – 7.86 (m, 2H), 7.82 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.59 – 7.55 (m, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.27 (t, *J* = 7.5 Hz, 2H), 6.54 (s, 1H), 13C NMR (151 MHz, DMSO-*d*6) δ 168.49, 163.83, 157.52, 152.79, 146.34, 141.73, 131.78, 125.82, 124.33, 123.24, 119.34, 115.78, 100.39, 36.57; HRMS (ESI, m/z): calcd for C18H13N3O4 (M+H+) 335.0906, found: 335.0908.

2-amino-5-oxo-4-(pyridin-4-yl)-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4s)**



Yield 92%; white solid; Mp: 280-282 °C; 1H NMR (600 MHz, DMSO-*d*6) δ 8.80 (d, *J* = 6.0 Hz, 2H), 8.66 (d, *J* = 6.5 Hz, 2H), 8.20 (s, 1H), 7.81 (d, *J* = 1.6 Hz, 1H), 7.56 – 7.53 (m, 2H), 7.31 (d, *J* = 7.8 Hz, 2H), 7.27 – 7.24 (m, 2H), 6.46 (s, 1H), 13C NMR (151 MHz, DMSO-*d*6) δ 168.12, 164.06, 161.87, 152.69, 150.46, 148.14, 141.12, 139.36, 131.58, 125.14, 124.21, 123.10, 119.38, 115.59, 111.64, 101.44, 37.74; HRMS (ESI, m/z): calcd for C18H13N3O4 (M+H+) 335.0906, found: 335.0906.

2-amino-4-(4-(dimethylamino)phenyl)-5-oxo-*4H,5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4t)**



Yield 88%; white solid; Mp: 224-226 °C; 1H NMR (600 MHz, DMSO-*d*6) δ 7.82 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.53 – 7.50 (m, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.28 (s, 1H), 7.27 (s, 2H), 7.25 (d, *J* = 1.7 Hz, 1H), 7.25 – 7.21 (m, 2H), 6.30 (s, 1H), 3.14 (s, 6H), 13C NMR (151 MHz, DMSO-*d*6) δ 167.53, 164.43, 152.50, 131.13, 128.18, 124.08, 123.00, 119.61, 115.56, 103.04, 45.54, 35.94; HRMS (ESI, m/z): calcd for C21H19N3O4 (M+H+) 377.1376, found: 377.1378.

2-amino-4-(2-bromo-6-chlorophenyl)-5-oxo-*4H*,*5H*-pyrano[3,2-*c*]chromene-3-carboxamide **(4u)**



Yield 90%; white solid; Mp: <300 °C; 1H NMR (600 MHz, DMSO-*d*6) δ 8.09 (dd, *J* = 7.9, 1.4 Hz, 1H), 8.04 (s, 1H), 7.71 – 7.67 (m, 1H), 7.61 – 7.57 (m, 1H), 7.47 (dd, *J* = 11.3, 3.9 Hz, 1H), 7.44 (d, *J* = 8.2 Hz, 1H), 7.39 – 7.35 (m, 3H), 7.29 (d, *J* = 8.2 Hz, 1H), 7.25 (p, *J* = 4.3 Hz, 1H), 5.69 (s, 1H), 13C NMR (151 MHz, DMSO-*d*6) δ 160.81, 160.12, 152.31, 151.96, 151.19, 132.81, 132.67, 132.24, 129.15, 125.87, 124.56, 123.94, 122.68, 116.52, 116.51, 115.55, 115.31, 113.43, 28.09; HRMS (ESI, m/z): calcd for C19H12BrClN2O4 (M+H+) 445.9669, found: 445.9671.

**4. 1H NMR and 13C NMR spectra of the compounds**



















































































