Palladium-catalyzed facile synthesis of furoquinolinones and furopyridinones

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**Supplementary Information**

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# 1 General Experimental

Reactions were monitored by thin layer chromatography (TLC), on glass plates coated with silica gel with fluorescent indicator (Huanghai, HSGF254). Flash chromatography was performed on silica gel (Huanghai, 300-400) using PE-EtOAc as eluent. 1H NMR and 13C NMR spectra were recorded on a Bruker (500, 400MHz) with chemical shift values in ppm relative to TMS (δH 0.00 and δC 0.0) or residual chloroform (δH 7.28 and δC 77.1) as standard. Mass spectra were recorded on HP-5989A instrument.

# 2 General procedure for the synthesis of furoquinolinones and furopyridinones

The mixture of 4-hydroxyquinolinones 1 (0.25 mmol), alkenes 2 (0.5 mmol) and Pd(TFA)2 (20 mol%, 16.4 mg) in xylenes (1 mL) was stirred at 80 oC under air for 10 hours, then cooled down to room temperature, diluted with 20 mL ethyl acetate and washed with 10 mL H2O. The aqueous layer was extracted twice with ethyl acetate (5 mL) and the combined organic phase was dried over Na2SO4. After evaporation of the solvents the residue was purified by flash column chromatography (silica gel, PE/EtOAc) to afford the desired products **3**. Physical and spectroscopic data follow.



Purified by flash chromatograph column (PE : EtOAc = 2 : 1). Yellow solid;[1] mp 199-201oC

**1H NMR (500 MHz, CDCl3)** δ 3.82 (s, 3H), 7.30 (s, 1H), 7.35 (q, *J* = 7.5 Hz, 2H), 7.45 - 7.48 (m, 3H), 7.56 (td, *J* = 1.5, 8.5 Hz, 1H), 7.85 (d, *J* = 7.5 Hz, 2H), 8.10 (dd, *J* = 1.0, 7.5 Hz, 1H)

**13C NMR (125 MHz, CDCl3)** 29.6, 103.0, 113.3, 115.3, 117.4, 121.3, 122.5, 124.7, 128.8, 129.1, 129.6, 129.9, 138.4, 154.7, 155.8, 159.6

**IR (KBr)** 2922, 2852, 2364, 1662, 1458, 1242, 1103, 750cm-1

**HRMS for** **C18H14NO2+(M++H)**: calcd. 276.1019, found 276.1024



Purified by flash chromatograph column (PE : EtOAc = 2 : 1). Yellow solid; mp 244-246oC

**1H NMR (500 MHz, CDCl3)** δ 2.32 (s, 3H), 3.72 (s, 3H), 7.14 (s, 1H), 7.18 (d, *J* = 7.0 Hz, 2H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 8.5 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 8.00 (d, *J* = 8.0 Hz, 1H)

**13C NMR (125 MHz, CDCl3)** 21.5, 29.6, 102.2, 113.3, 115.2, 117.4, 121.2, 122.5, 124.6, 127.2, 129.4, 129.7, 138.2, 138.8, 154.4, 156.0, 159.6

**IR (KBr)** 2922, 2852, 2362, 1665, 1458, 1082, 820, 742cm-1

**HRMS for** **C19H16NO2+(M++H)**: calcd. 290.1176, found 290.1180



Purified by flash chromatograph column (PE : EtOAc = 2 : 1). Yellow solid; mp 237-239oC

**1H NMR (500 MHz, CDCl3)** δ 2.61 (s, 3H), 2.83 (s, 3H), 7.20 (s, 1H), 7.30 – 7.36 (m, 4H), 7.48 (d, *J* = 8.5 Hz, 1H), 7.57 (td, *J* = 1.0, 8.5 Hz, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 8.09 (dd, *J* = 1.0, 7.5 Hz, 1H)

**13C NMR (125 MHz, CDCl3)** 22.2, 29.7, 106.6, 113.2, 115.3, 117.2, 121.4, 122.5, 126.4, 127.7, 128.8, 129.2, 129.6, 131.6, 135.6, 138.4, 154.3, 155.3, 159.7

**IR (KBr)** 2921, 2850, 2364, 1662, 1445, 1267, 1040, 750cm-1

**HRMS for** **C19H16NO2+(M++H)**: calcd. 290.1176, found 290.1180



Purified by flash chromatograph column (PE : EtOAc = 2 : 1). Yellow solid; mp 179-181oC

**1H NMR (500 MHz, CDCl3)** δ 3.80 (s, 3H), 3.87 (s, 3H), 6.99 (d, *J* = 9.0 Hz, 2H), 7.14 (s, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 8.5 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.77 (d, *J* = 9.0 Hz, 1H), 8.07 (d, *J* = 8.0 Hz, 1H)

**13C NMR (125 MHz, CDCl3)** 29.6, 55.5, 101.3, 113.3, 114.5, 115.2, 117.5, 121.1, 122.5, 122.8, 126.2, 129.3, 138.1, 154.2, 155.9, 159.6, 160.2

**IR (KBr)** 2922, 2852, 2362, 1647, 1255, 829, 735cm-1

**HRMS for** **C19H16NO3+(M++H)**: calcd. 306.1125, found 306.1126



Purified by flash chromatograph column (PE : EtOAc = 2 : 1). Yellow solid; mp 198-200oC

**1H NMR (500 MHz, CDCl3)** δ 3.82 (s, 3H), 7.29 (s, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 8.5 Hz, 2H), 7.48 (d, *J* = 8.5 Hz, 1H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.5 Hz, 2H), 8.10 (d, *J* = 7.5 Hz, 1H)

**13C NMR (125 MHz, CDCl3)** 29.6, 103.6, 113.1, 115.3, 117.4, 121.3, 122.6, 125.8, 128.3, 129.3, 129.8, 134.6, 138.4, 154.6, 154.8, 159.4

**IR (KBr)** 2922, 2850, 2362, 1653, 1570, 1458, 1088, 827, 746cm-1

**HRMS for** **C18H13ClNO2+(M++H)**: calcd. 310.0629, found 310.0637



Purified by flash chromatograph column (PE : EtOAc = 2 : 1). Yellow solid; mp 166-168oC

**1H NMR (500 MHz, CDCl3)** δ 3.80 (s, 3H), 7.28 (s, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 1H), 7.58 (d, *J* = 8.5 Hz, 3H), 7.69 (d, *J* = 8.5 Hz, 2H), 8.08 (dd, *J* = 1.5, 8.0 Hz, 1H)

**13C NMR (125 MHz, CDCl3)** 29.6, 103.6, 113.1, 115.3, 117.4, 121.3, 122.6, 122.7, 126.0, 128.8, 129.8, 132.3, 138.4, 154.6, 154.8, 159.4

**IR (KBr)** 2920, 2848, 2362, 1662, 1550, 1387, 1070, 825, 748cm-1

**HRMS for** **C18H13BrNO2+(M++H)**: calcd. 354.0124, found 354.0126



Purified by flash chromatograph column (PE : EtOAc = 2 : 1). Yellow solid; mp204-205oC

**1H NMR (500 MHz, CDCl3)** δ 3.79 (s, 3H), 7.14 (t, *J* = 8.5 Hz, 2H), 7.20 (s, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 8.5 Hz, 1H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.78 – 7.81 (m, 2H), 8.05 (d, *J* = 7.5 Hz, 1H)

**13C NMR (125 MHz, CDCl3)** 29.6, 102.7, 113.1, 115.3, 116.1 (d, *J*C-F= 21.7 Hz), 117.4, 121.2, 122.5, 126.4, 126.5, 129.6, 138.3, 154.6, 154.8, 159.4, 163.0 (d, *J*C-F= 247.4 Hz)

**19F NMR (470 MHz, CDCl3)** δ -112.0

**IR (KBr)** 2922, 2850, 2362, 1662, 1496, 1221, 1105, 833, 741cm-1

**HRMS for** **C18H13FNO2+(M++H)**: calcd. 294.0925, found 294.0931



Purified by flash chromatograph column (PE : EtOAc = 2 : 1). Yellow solid; mp 196-198oC

**1H NMR (400 MHz, CDCl3)** δ 3.81 (s, 3H), 7.05 (td, *J* = 2.4, 8.4 Hz, 1H), 7.31 (s, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.41 - 7.48 (m, 2H), 7.52 – 7.61 (m, 3H), 8.09 (dd, *J* = 1.2, 7.6 Hz, 1H)

**13C NMR (100 MHz, CDCl3)** 29.7, 104.1, 111.5 (d, *J*C-F= 23.6 Hz), 113.1, 115.3, 115.5 (d, *J*C-F= 21.5 Hz), 117.3, 120.3 (d, *J*C-F= 3.6 Hz), 121.4, 122.6, 129.9, 130.7 (d, *J*C-F= 7.8 Hz), 131.8 (d, *J*C-F= 8.4 Hz), 138.5, 154.4, 154.9, 159.4, 163.3 (d, *J*C-F= 245 Hz)

**19F NMR (376 MHz, CDCl3)** δ -112.2

**IR (KBr)** 2922, 2852, 1676, 1437, 1244, 1103, 746cm-1

**HRMS for** **C18H13FNO2+(M++H)**: calcd. 294.0925, found 294.0931



Purified by flash chromatograph column (PE : EtOAc = 1 : 1). Yellow solid; mp 206-207oC

**1H NMR (500 MHz, CDCl3)** δ 3.80 (s, 3H), 7.35 – 7.39 (m, 2H), 7.45 (d, *J* = 8.5 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 8.0 Hz, 1H), 7.84 – 7.93 (m, 4H), 8.16 (d, *J* = 7.5 Hz, 1H), 8.32 (s, 1H)

**13C NMR (125 MHz, CDCl3)** 29.6, 103.6, 113.2, 115.3, 117.5, 121.4, 122.5, 122.5, 123.4, 126.7, 126.9, 127.1, 128.0, 128.5, 128.9, 129.6, 133.4, 133.5, 138.4, 154.8, 155.8, 159.5

**IR (KBr)** 2922, 2850, 2362, 1653, 1558, 1105, 818, 746cm-1

**HRMS for** **C22H16NO2+(M++H)**: calcd. 326.1176, found 326.1179



Purified by flash chromatograph column (PE : EtOAc = 1 : 1). Yellow solid; mp 252-254 oC

**1H NMR (400 MHz, CDCl3)** δ 3.74 (m,3H), 7.28 – 7.37 (m, 4H), 7.42 – 7.47 (m, 4H), 7.52 – 7.59 (m, 5H), 8.14 (dd, *J* = 1.2, 8.0 Hz, 1H)

**13C NMR (100 MHz, CDCl3)** 29.3, 113.0, 115.1, 115.8, 121.3, 121.5, 122.4, 126.7, 128.1, 128.4, 128.5, 128.6, 129.7, 130.2, 130.6, 131.7, 138.5, 150.6, 154.2, 159.4

**IR (KBr)** 2906, 2362, 1668, 1508, 1238, 1103, 777, 721cm-1

**HRMS for** **C24H18NO2+(M++H)**: calcd. 352.1332, found 352.1332



Purified by flash chromatograph column (PE : EtOAc = 2 : 1). Yellow solid; mp 171-172oC

**1H NMR (400 MHz, CDCl3)** δ 2.51 (s, 3H), 3.80 (s, 3H), 7.29 (s, 1H), 7.35 – 7.38 (m, 3H), 7.47 (t, *J* = 7.2 Hz, 2H), 7.86 (d, *J* = 7.2 Hz, 2H), 7.91 (s, 1H)

**13C NMR (100 MHz, CDCl3)** 20.9, 29.6, 103.1, 113.2, 115.2, 117.4, 121.1, 124.7, 128.7, 129.1, 130.0, 130.8, 132.3, 136.5, 154.6, 155.6, 159.5

**IR (KBr)** 2920, 2850, 2362, 1649, 1458, 1046, 789cm-1

**HRMS for** **C19H16NO2+(M++H)**: calcd. 290.1176, found 290.1180



Purified by flash chromatograph column (PE : EtOAc = 2 : 1). Yellow solid; mp 151-153oC

**1H NMR (400 MHz, CDCl3)** δ 3.80 (s, 3H), 3.97 (s, 3H), 7.17 (dd, *J* = 3.2, 9.2 Hz, 1H), 7.31 (s, 1H), 7.40 (t, *J* = 8.8 Hz, 2H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.52 (d, *J* = 2.8 Hz, 1H), 7.87 (d, *J* = 7.2 Hz, 2H)

**13C NMR (100 MHz, CDCl3)** 29.5, 56.0, 103.1, 103.3, 113.8, 116.8, 117.9, 118.3, 124.7, 128.8, 129.1, 129.9, 133.0, 154.3, 155.2, 155.8, 159.1

**IR (KBr)** 2922, 2850, 2362, 1653, 1448, 1217, 138, 769cm-1

**HRMS for** **C19H16NO3+(M++H)**: calcd. 306.1125, found 306.1126



Purified by flash chromatograph column (PE : EtOAc = 2 : 1). Yellow solid; mp 208-209oC

**1H NMR (500 MHz, CDCl3)** δ 3.79 (s, 3H), 7.29 (s, 1H), 7.34 (d, *J* = 9.0 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.63 (dd, *J* = 2.5, 9.0 Hz, 1H), 7.86 (d, *J* = 7.0 Hz, 2H), 8.22 (d, *J* = 2.5 Hz, 1H)

**13C NMR (125 MHz, CDCl3)** 29.5, 103.1, 114.7, 115.7, 117.0, 118.3, 123.7, 124.8, 129.1, 129.1, 129.6, 132.2, 137.2, 153.2, 156.5, 159.2

**IR (KBr)** 2922, 2852, 2362, 1662, 1443, 1261, 1099, 1020, 804cm-1

**HRMS for** **C18H13BrNO2+(M++H)**: calcd. 354.0124, found 354.0126



Purified by flash chromatograph column (PE : EtOAc = 2 : 1). Yellow solid; mp 173-175oC

**1H NMR (400 MHz, CDCl3)** δ 1.39 (t, *J* = 7.2 Hz, 3H), 2.50 (s, 3H), 4.44 (q, *J* = 7.2 Hz, 2H), 7.29 (s, 1H), 7.34 - 7.38 (m, 3H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.86 (d, *J* = 7.6 Hz, 2H), 7.91 (s, 1H)

**13C NMR (100 MHz, CDCl3)** 13.2, 20.9, 37.3, 103.1, 113.4, 115.1, 117.4, 121.3, 124.7, 128.7, 129.1, 130.0, 130.8, 132.0, 135.4, 154.6, 155.6, 159.0

**IR (KBr)** 2920, 2850, 2362, 1653, 1473, 1082, 750cm-1

**HRMS for** **C20H18NO2+(M++H)**: calcd. 304.1332, found 304.1336



Purified by flash chromatograph column (PE : EtOAc = 3 : 1). Yellow solid; mp 176-178oC

**1H NMR (400 MHz, CDCl3)** δ 2.45 (s, 3H), 3.60 (s, 3H), 6.45 (s, 1H), 7.17 (s, 1H), 7.31 (t, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.73 - 7.76 (m, 2H)

**13C NMR (100 MHz, CDCl3)** 21.9, 31.0, 95.9, 102.0, 115.6, 124.4, 128.3, 129.0, 130.1, 142.6, 154.1, 159.0, 160.4

**IR (KBr)** 2922, 2850, 2362, 1662, 1581, 1315, 1103, 764, 681cm-1

**HRMS for** **C15H14NO2+(M++H)**: calcd. 240.1019, found 240.1023



Purified by flash chromatograph column (PE : EtOAc = 3 : 1). Yellow solid; mp 227-228oC

**1H NMR (500 MHz, CDCl3)** δ 2.37 (s, 3H), 2.43 (s, 3H), 3.59 (s, 3H), 6.43 (s, 1H), 7.10 (s, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.63 (d, *J* = 8.0 Hz, 2H)

**13C NMR (125 MHz, CDCl3)** 21.4, 21.8, 31.0, 95.9, 101.2, 115.6, 124.4, 127.4, 129.6, 138.3, 142.3, 154.4, 158.8, 160.4

**IR (KBr)** 2918, 2850, 2360, 1666, 1581, 1318, 1104, 818, 777cm-1

**HRMS for** **C16H16NO2+(M++H)**: calcd. 254.1176, found 254.1180



Purified by flash chromatograph column (PE : EtOAc = 3 : 1). Yellow solid; mp 187-188oC

**1H NMR (500 MHz, CDCl3)** δ 2.43 (s, 3H), 3.58 (s, 3H), 6.41 (s, 1H), 7.08 – 7.11 (m, 3H), 7.67 – 7.70 (m, 2H)

**13C NMR (125 MHz, CDCl3)** 21.8, 31.0, 95.8, 101.6, 115.5, 116.0 (d, *J*C-F= 21.9 Hz), 126.2, 126.2, 126.4, 126.4, 142.7, 153.1, 158.9, 160.3, 161.9, 162.7 (d, *J*C-F= 247.4 Hz)

**19F NMR (470 MHz, CDCl3)** δ -112.7

**IR (KBr)** 3109, 2920, 2362, 1655, 1583, 1502, 1221, 1161, 1103, 839cm-1

**HRMS for** **C15H13FNO2+(M++H)**: calcd. 258.0925, found 258.0932

**Reference**

[1] Dey, A.; Hajra, A. *Org. Biomol. Chem*., **2017**, *15*, 8084

# 3 General procedure for antiproliferative activity assays

Exponentially growing cells were seeded into 96-well plates at a concentration of 5 ×103 cells per well. After 24 h incubation at 37 oC, the culture medium was removed and replaced with fresh medium containing the candidate compounds in different concentrations. The cells were incubated for another 72 h. Afterward, 20 μL of MTT solution (5 mg/mL) was added to all wells and incubated for 4 h at 37 oC. Discarded the suspension and added 150 μL of dimethyl sulfoxide (DMSO) to each well and shook the plates to dissolve the dark blue crystals (formazan); the absorbance was measured using a microplate reader at a wavelength of 562 nm. Each concentration was analyzed in triplicate and the experiment was repeated three times. The average 50% inhibitory concentration (IC50) was determined from the dose-response curves according to the inhibition ratio for each concentration.

# 3 Copies of 1H and 13C NMR Spectra















































































































































