Supporting Information

Copper-Catalyzed Tandem N-Arylation/Condensation: Synthesis of Quinazolin-4(3H)-ones from 2-Halobenzonitrile and Amides

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General information
Unless otherwise noted, all chemcials were purchased from commercial suppliers and were used without further purification. All experiments were monitored by thin layer chromatography (TLC) and visualized under 254 nm UV light. Column chromatography was performed on Silicycle silica gel (200-300 mesh). Melting points were determined using XT4 micro-scope melting point apparatus. Infrared spectra was recorded on a Perkin Elmer FT-IR spectrophotometer with KBr pellets. 1H and 13C NMR spectra were recorded at a Varian mercury-plus 400 spectrometer in DMSO-d6 with TMS as the internal standard. ESI-MS was carried out on a Bruker APE XII FT-ICR using ESI ionization. HR-MS was recorded on a APEX IV FT-ICR Mass Spectrometer (Bruker, U.S.A.).

General experimental procedure for the synthesis of quinazolin-4(3H)-ones
A 25 ml vial equipped with a magnetic stirring bar was charged with 2-halobenzonitrile (1.0 mmol), amides (1.0 mmol), CuI (5 % mmol), NaOH (1.2 mmol), NMP (5.0 ml). The reaction proceeded under an air atmosphere and heated for 12 h at 120 °C. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature and diluted in ethyl acetate and washed with water. The aqueous phase was extracted twice with ethyl acetate. The organic layers were combined, dried over anhydrous Na2SO4, and the solvent was removed under reduced pressure and the crude product was purified by column chromatography or recrystallization using petroleum ether/EtOAc to provide the analytically pure product 3.
2-phenylquinazolin-4(3H)-one (3a)

White crystal; m.p. 240-242°C (Ref.¹ 234-236°C); IR (KBr, ν, cm⁻¹): 3194, 3167, 3061, 1668, 1602, 1481; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.57 (s, 1H), 8.20-8.16 (m, 3H), 7.85 (t, J = 15.2 Hz, 1H), 7.75 (d, J = 7.2 Hz, 6H), 7.62-7.52 (m, 4H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 162.25, 152.30, 148.75, 134.59, 132.71, 131.38, 128.60 (2C), 127.76 (2C), 127.50, 126.58, 125.84, 120.98; ESI-MS (m/z) = 222.9 ([M+H]+).

2-(p-tolyl)quinazolin-4(3H)-one (3b)

Light yellow crystal; m.p. 250-252°C (Ref.² 256-257°C); IR (KBr, ν, cm⁻¹): 3175, 3132, 3063, 1663, 1601, 1485; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.49 (s, 1H), 8.16-8.09 (m, 3H), 7.83 (t, J = 13.2 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.52 (t, J = 13.2 Hz, 1H), 7.36 (d, J = 7.6 Hz, 2H), 2.40 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 162.72, 152.67, 149.30, 135.02, 130.35, 129.64 (2C), 128.14 (2C), 127.88, 126.85, 126.30, 121.37, 21.45; ESI-MS (m/z) = 237.5 ([M+H]+).

2-(4-methoxyphenyl)quinazolin-4(3H)-one (3c)

White crystal; m.p. 258-259°C (Ref.² 250-251°C); IR (KBr, ν, cm⁻¹): 3176, 3133, 3066, 1677, 1601, 1483; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.42 (s, 1H), 8.19 (d, J = 8.4 Hz, 2H), 8.13 (d, J = 8.0 Hz, 1H), 7.82 (t, J = 15.2 Hz, 1H), 7.70 (d, J = 7.6 Hz, 1H), 7.48 (t, J = 15.2 Hz, 1H), 7.09 (d, J = 8.4 Hz, 2H), 3.85 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 162.77, 162.33, 152.32, 149.40, 135.00, 129.92 (2C), 127.75, 126.59, 125.26, 121.15, 114.46 (2C), 55.92; ESI-MS (m/z) = 253.1 ([M+H]+).

2-(4-fluorophenyl)quinazolin-4(3H)-one (3d)

Light yellow crystal; m.p. 262-265°C (Ref.¹ 284-287°C); IR (KBr, ν, cm⁻¹): 3174, 3132, 3049, 1681, 1611, 1484; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.59 (s, 1H), 8.27-8.23 (m, 2H), 8.15 (d, J = 8.0 Hz, 1H), 7.84 (t, J = 5.2 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 14.8 Hz, 1H), 7.40 (t, J = 16.8 Hz, 2H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 164.51 (d, J = 198.4 Hz), 162.67, 151.84, 149.12, 135.11, 130.85 (d, J = 7.1 Hz), 129.70 (d, J = 2.1 Hz), 127.93, 127.09, 126.32, 121.35, 116.10 (d, J = 17.4 Hz); ESI-MS (m/z) = 241.0 ([M+H]+).

2-(3-fluorophenyl)quinazolin-4(3H)-one (3e)

Light yellow crystal; m.p. 261-263°C (Ref.³ 267°C); IR (KBr, ν, cm⁻¹): 3192, 3161, 3055, 1682, 1608, 1480; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.62 (s, 1H), 8.17 (d, J = 7.6 Hz, 1H), 8.07-8.00 (m, 2H), 7.86 (t, J = 14.0 Hz, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.63-7.53 (m, 2H), 7.47-7.43 (m, 1H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 162.58, 162.55 (d, J = 193.9 Hz), 151.48, 148.92, 135.47 (d, J = 6.3 Hz), 135.17, 131.21 (d, J = 6.5 Hz), 128.07, 127.39, 126.34, 124.40 (d, J = 1.9 Hz), 121.59, 118.73 (d, J = 16.7 Hz), 115.00 (d, J = 18.9 Hz); ESI-MS (m/z) = 241.0 ([M+H]+).

2-methylquinazolin-4(3H)-one (3f)

White crystal; m.p. 236-237°C; IR (KBr, ν, cm⁻¹): 3170, 3120, 2869, 1681, 1615, 1468; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.20 (s, 1H), 8.06 (d, J = 8.0 Hz, 1H), 7.77-7.73 (m, 1H), 7.56 (d, J = 8.4 Hz, 1H), 7.44 (t, J = 14.8 Hz, 1H), 2.34 (s, 1H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 161.69, 154.25, 148.98, 134.27, 126.58, 125.85, 125.67, 120.61, 21.42; ESI-MS (m/z) = 161.0 ([M+H]+).

2-ethylquinazolin-4(3H)-one (3g)

White crystal; m.p. 230-232°C (Ref.⁵ 229-231°C); IR (KBr, ν, cm⁻¹): 3169, 3111, 2980, 1679, 1620, 1468; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.16 (s, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.79-7.75 (m, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.45 (t, J = 14.4 Hz, 1H), 2.65-2.59 (m, 2H), 1.24 (t, J = 14.8 Hz, 3H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 162.26, 158.77, 149.43, 134.69,

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127.27, 126.35, 126.14, 121.30, 28.30, 11.73; ESI-MS (m/z) = 175.0 ([M+H]+).

**2-propylquinazolin-4(3H)-one (3b)**

White crystal; m.p. 206-207°C (Ref.5 200-202°C); IR (KBr, ν, cm⁻¹): 3174, 3132, 3049, 1681, 1611, 1484; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.18 (s, 1H), 8.07 (d, J = 7.6 Hz, 1H), 7.76 (t, J = 14.8 Hz, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.45 (t, J = 15.2 Hz, 1H), 2.56 (t, J = 14.8 Hz, 2H), 1.74 (d, J = 15.2 Hz, 2H), 0.94-0.91 (m, 3H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 162.28, 157.76, 149.42, 134.71, 127.26, 126.36, 126.13, 121.26, 36.81, 20.66, 13.96; ESI-MS (m/z) = 189.4 ([M+H]+).

**2-isopropylquinazolin-4(3H)-one (3i)**

White crystal; m.p. 234-236°C (Ref.5 225-228°C); IR (KBr, ν, cm⁻¹): 3169, 3125, 2969, 1682, 1621, 1474; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.15 (s, 1H), 8.08 (d, J = 8.8 Hz, 1H), 7.77 (t, J = 14.8 Hz, 1H), 7.61 (d, J = 7.2 Hz, 1H), 7.46 (t, J = 15.6 Hz, 1H), 2.92-2.85 (m, 1H), 1.26 (d, J = 7.6 Hz, 6H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 162.41, 162.03, 149.35, 134.71, 127.4, 126.43, 126.13, 121.40, 20.83 (2C); ESI-MS (m/z) = 189.4 ([M+H]+).

**7-methyl-2-phenylquinazolin-4(3H)-one (3j)**

Light yellow solid; m.p. 240-241°C (Ref.6 240-241°C); IR (KBr, ν, cm⁻¹): 3129, 3055, 3035, 1670, 1605, 1457; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.45 (s, 1H), 8.17 (d, J = 7.2 Hz, 2H), 8.03 (d, J = 7.6 Hz, 1H), 7.57 (d, J = 10.0 Hz, 4H), 7.35 (d, J = 8.8 Hz, 1H), 2.38 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 120.63, 156.5, 145.32, 145.53, 133.24, 131.80, 129.64, 129.06, 128.48, 128.17, 128.08, 127.62, 126.17, 119.06, 21.83; ESI-MS (m/z) = 237.1 ([M+H]+).

**7-methyl-2-propylquinazolin-4(3H)-one (3k)**

White crystal; m.p. 226-228°C (Ref.7 232-234°C); IR (KBr, ν, cm⁻¹): 3171, 3129, 3043, 1675, 1615, 1461; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.07 (s, 1H), 7.96 (d, J = 7.6 Hz, 1H), 7.41 (s, 1H), 7.28 (d, J = 7.2 Hz, 1H), 2.56 (t, J = 14.4 Hz, 2H), 2.43 (s, 3H) 1.76-1.69 (m, 2H), 0.93 (t, J = 14.4 Hz, 3H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 162.17, 157.75, 145.12, 127.76, 125.99, 118.86, 36.77, 21.79, 20.63, 13.94; ESI-MS (m/z) = 203.1 ([M+H]+).

**6-methoxy-2-phenylquinazolin-4(3H)-one (3l)**

Yellow solid; m.p. 246-248°C (Ref.2 247-248°C); IR (KBr, ν, cm⁻¹): 3161, 3055, 3028, 1672, 1492; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.51 (s, 1H), 8.16 (d, J = 6.8 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 7.59-7.52 (m, 4H), 7.46-7.43 (m, 1H), 3.86 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 162.50, 158.22, 150.55, 143.68, 133.27, 131.50, 130.17, 129.70, 129.04, 127.96, 124.57, 106.35, 56.12; ESI-MS (m/z) = 253.1 ([M+H]+).

**2-ethyl-6-methoxyquinazolin-4(3H)-one (3m)**

Light yellow solid; m.p. 241-243°C; IR (KBr, ν, cm⁻¹): 3162, 3014, 1669, 1624, 1488; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.11 (s, 1H), 7.54 (d, J = 9.6 Hz, 1H), 7.46 (d, J = 2.4 Hz, 1H), 7.37 (t, J = 9.2 Hz, 1H), 3.85 (s, 3H), 2.61-2.56 (m, 2H), 1.23 (t, J = 14.8 Hz, 3H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 162.09, 157.64, 156.36, 143.90, 128.91, 124.08, 122.00, 106.24, 55.99, 28.10, 11.75; HRESI ESI ([M+H]+) m/z calcd for C₁₁H₁₃N₂O₂: 205.09715, found 205.09710.

**6-fluoro-2-phenylquinazolin-4(3H)-one (3n)**

Yellow solid; m.p. 279-281°C (Ref.8 > 280°C); IR (KBr, ν, cm⁻¹): 3163, 3104, 3036, 1662, 1605, 1485; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.67 (s, 1H), 8.17 (d, J = 6.4 Hz, 2H), 7.81 (t, J = 13.2 Hz, 2H), 7.75-7.70 (m, 1H), 7.61-7.53 (m, 3H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 162.13 (d, J = 2.6 Hz), 160.46 (d, J = 195.2 Hz), 152.32, 146.10, 133.02, 131.89, 130.80 (d, J = 6.6 Hz), 129.08, 128.21, 123.55 (d, J = 19.0 Hz), 122.68 (d, J = 6.6 Hz), 110.98 (d, J = 18.6 Hz); ESI-MS (m/z) = 241.0
6-fluoro-2-propylquinazolin-4(3H)-one (3o)

White crystal; m.p. 240-242°C; IR (KBr, v, cm⁻¹): 3184, 3108, 3035, 1670, 1605, 1457; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.29 (s, 1H), 7.73 (t, J = 10.4 Hz, 1H), 7.65 (t, J = 9.6 Hz, 2H), 2.57 (t, J = 15.6 Hz, 2H), 1.76-1.70 (m, 2H), 0.92 (t, J = 14.8 Hz, 3H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 161.65 (d, J = 2.6 Hz), 160.03 (d, J = 194.3 Hz), 157.20 (d, J = 1.2 Hz), 146.26, 130.09 (d, J = 6.6 Hz), 123.06 (d, J = 19.0 Hz), 122.40 (d, J = 6.6 Hz), 110.66 (d, J = 18.4 Hz), 36.70, 20.58, 13.90; ESI-MS (m/z) = 207.0 ([M+H⁺]).

2-phenyl-6-(trifluoromethyl)quinazolin-4(3H)-one (3p)

White solid; m.p. > 300°C; IR (KBr, v, cm⁻¹): 3167, 3108, 3052, 3028, 1671, 1626, 1602, 1317; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.88 (s, 1H), 8.39 (s, 1H), 8.21 (d, J = 7.2 Hz, 2H), 8.14 (t, J = 8.4 Hz, 1H), 7.92 (d, J = 8.4 Hz, 1H), 7.63-7.56 (m, 3H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 162.14, 155.16, 151.75, 132.75, 132.42, 130.98, 129.44, 129.15, 128.55, 126.88 (q, J = 26.0 Hz), 124.35 (q, J = 216.4 Hz), 123.78 (q, J = 3.1 Hz), 121.53; HR-ESI-MS (m/z) calcd for C₁₅H₁₀F₃N₂O 291.07397, found 291.07378.

2-ethyl-6-(trifluoromethyl)quinazolin-4(3H)-one (3q)

White solid; m.p. 260-261°C; IR (KBr, v, cm⁻¹): 3172, 3111, 3047, 3019, 1689, 1614, 1319; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.50 (s, 1H), 8.31 (s, 1H), 8.06-8.04 (m, 1H), 7.77 (d, J = 8.4 Hz, 1H), 2.69-2.63 (m, 2H), 1.25 (t, J = 15.6 Hz, 3H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 161.57, 161.55, 151.91, 130.63, 128.74, 126.39 (q, J = 25.9 Hz), 123.55 (q, J = 3.4 Hz), 123.34 (q, J = 216.1 Hz), 121.32, 28.44, 11.50; HR-ESI-MS (m/z) calcd for C₁₁H₁₀F₃N₂O 243.07397, found 243.07412.

2-phenyl-7-(trifluoromethyl)quinazolin-4(3H)-one (3r)

Light yellow solid; m.p. 194-196°C; IR (KBr, v, cm⁻¹): 3206, 3160, 3095, 1670, 1607, 1492; ¹H NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.84 (s, 1H), 8.33 (t, J = 24.8 Hz, 1H), 8.20 (d, J = 7.6 Hz, 2H), 8.04 (s, 1H), 7.80 (d, J = 8.4 Hz, 1H), 123.06 (d, J = 15.6 Hz, 3H); ¹³C NMR (100 MHz, DMSO-d₆) (δ, ppm): 161.57, 161.55, 151.91, 130.63, 128.74, 126.39 (q, J = 25.9 Hz), 123.55 (q, J = 3.4 Hz), 123.34 (q, J = 216.1 Hz), 121.32, 28.44, 11.50; HR-ESI-MS (m/z) calcd for C₁₅H₁₀F₃N₂O 291.1 ([M+H⁺]).

References

The $^1$H-NMR and $^{13}$C-NMR Spectra of products
ADVANCE III BRUKER A&T Center HNU
Sample: CHX-14022 Solvent: DMSO
Spectrum: beijing-lijiangong 0522-4 13C

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