Supporting Information

Efficient Copper-Catalyzed Cascade Synthesis of 4-Aminoquinazoline and 2,4-Diaminoquinazoline Derivatives

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**General experimental procedures**

All reactions were carried out under nitrogen atmosphere. Proton and carbon magnetic resonance spectra (¹H NMR and ¹³C NMR) were recorded using tetramethylsilane (TMS) in the solvent of DMSO-d₆ as the internal standard (¹H NMR: TMS at 0.00 ppm, DMSO at 2.50 ppm; ¹³C NMR: DMSO at 40.0 ppm).

**General procedure for synthesis of compounds 3a-m:** A 25 mL round bottom flask was charged with a magnetic stirrer and 3 mL of DMF, substituted 2-bromobenzonitrile (1) (1 mmol), amidine hydrochloride (2) (1.2 mmol), N,N'-dimethylethylenediamine (DMEDA) (0.2 mmol, 18 mg) and K₂CO₃ (2 mmol, 138 mg) (2 mmol (656 mg) of Cs₂CO₃ was used for acetamidine hydrochloride), after stirring of the mixture for 15 min under nitrogen atmosphere, and CuI (0.1 mmol, 19 mg) was added to the flask. The mixture was stirred at 80 °C for a time as shown in Table 2 (in text). The resulting mixture was cooled to room temperature and filtered. The solid was washed with DMF two times (2 × 3 mL), and the combined filtrate was concentrated by the rotary evaporator, and the residue was purified by column chromatography on silica gel using chloroform/methanol (40:1 to 5:1) as eluent to give the desired product.

![Structure of 3a](image1)

**2-Methyl-4-aminoquinazoline (3a).**¹ Eluent chloroform/methanol (40:1). Yield 111 mg (69%). White solid. ¹H NMR (DMSO-d₆, 300 MHz) δ 8.18 (d, 1H, J = 8.2 Hz), 7.73 (m, 3H), 7.59 (d, 1H, J = 8.2 Hz), 7.41 (t, 1H, J = 7.2 Hz), 2.43 (s, 3H). ¹³C NMR (DMSO-d₆, 75 MHz) δ 164.0, 162.3, 150.3, 133.2, 127.0, 125.0, 123.9, 113.0, 26.2. ESIMS [M+H]+ m/z 159.9.

![Structure of 3b](image2)

**2-Propyl-4-aminoquinazoline (3b).**¹ Eluent chloroform/methanol (40:1). Yield 149 mg (79%). White solid. ¹H NMR (DMSO-d₆, 300 MHz) δ 8.15 (d, 1H, J = 8.2 Hz), 7.65 (m,
4H), 7.39 (t, 1H, J = 7.2 Hz), 2.64 (t, 2H, J = 7.9 Hz), 1.76 (m, 2H), 0.92 (t, 3H, J = 7.2 Hz). $^{13}$C NMR (DMSO-$d_6$, 75 MHz) δ 166.8, 162.0, 150.3, 132.6, 127.1, 124.6, 123.5, 112.9, 41.5, 21.4, 14.1. ESIMS [M+H]$^+$ m/z 187.9.

2-Cyclopropyl-4-aminoquinazoline (3c). Eluent chloroform/methanol (40:1). Yield 134 mg (72%). White solid, mp 198-200 °C. $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 8.12 (d, 1H, J = 7.9 Hz), 7.58 (m, 4H), 7.34 (t, 1H, J = 7.4 Hz), 1.99 (m, 1H, J = 7.5 Hz), 1.05-0.87 (m, 4H). $^{13}$C NMR (DMSO-$d_6$, 75 MHz) δ 167.6, 162.3, 150.5, 133.2, 126.9, 124.5, 124.0, 113.4, 18.4, 9.4. HR-MS [M+H]$^+$ m/z Calcd for C$_{11}$H$_{11}$N$_3$: 186.1031. Found: 186.1037.

2-Phenyl-4-aminoquinazoline (3d). Eluent petroleum ether/ethyl acetate (3:1). Yield 187 mg (85%). White solid. $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 8.54-8.51 (m, 2H), 8.07 (d, 1H, J = 8.1 Hz), 7.89-7.80 (m, 4H), 7.53-7.50 (m, 4H). $^{13}$C NMR (DMSO-$d_6$, 75 MHz) δ 162.6, 160.2, 150.9, 139.1, 133.5, 130.4, 128.7, 128.4, 128.2, 125.6, 124.1, 113.8. ESIMS [M+H]$^+$ m/z 221.9.

2,6-Dimethyl-4-aminoquinazoline (3e). Eluent chloroform/methanol (40:1). Yield 128 mg (75%). White solid, mp 241-243 °C. $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 8.02-7.98 (m, 1H), 7.62-7.26 (m, 4H), 2.43 (s, 3H), 2.23 (s, 3H). $^{13}$C NMR (DMSO-$d_6$, 75 MHz) δ 162.9, 162.2, 149.2, 135.2, 134.6, 127.2, 123.2, 121.2, 26.5, 21.9. HR-MS [M+H]$^+$ m/z Calcd for C$_{10}$H$_{12}$N$_3$: 174.1031. Found: 174.1032.
6-Methyl-2-propyl-4-aminoquinazoline (3f). Eluent chloroform/methanol (40:1). Yield 158 mg (79%). White solid, mp 238-241 °C. $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 7.98 (m, 1H), 7.56-7.53 (m, 4H), 2.63 (t, 2H, $J$ = 7.4 Hz), 2.43 (s, 3H) 1.80-1.75 (m, 2H), 0.92 (t, 3H, $J$ = 7.4 Hz). $^{13}$C NMR (DMSO-$d_6$, 75 MHz) δ 166.2, 161.9, 148.8, 134.7, 134.2, 127.2, 122.9, 21.7, 21.6, 14.5. HR-MS [M+H]$^+$ m/z Calcd for C$_{12}$H$_{16}$N$_3$: 202.1344. Found: 202.1346.

2-Cyclopropyl-6-methyl-4-aminoquinazoline (3g). Eluent chloroform/methanol (40:1). Yield 110 mg (55%). White solid, mp 230-232 °C. $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 7.93-7.89 (m, 1H), 7.52-7.45 (m, 4H), 2.38 (s, 3H), 1.98-1.95 (m, 1H), 0.97-0.85 (m, 4H). $^{13}$C NMR (DMSO-$d_6$, 75 MHz) δ 167.2, 161.8, 149.3, 134.8, 133.7, 126.8, 123.0, 21.6, 18.4, 9.2. HR-MS [M+H]$^+$ m/z Calcd for C$_{12}$H$_{14}$N$_3$: 200.1188. Found: 200.1192.

6-Methyl-2-phenyl-4-aminoquinazoline (3h). Eluent petroleum ether/ethyl acetate (3:1). Yield 156 mg (67%). White solid. $^1$H NMR (DMSO-$d_6$, 300 MHz) δ 8.46-8.43 (m, 2H), 8.05 (m, 1H), 7.71-7.60 (m, 4H), 7.47 (m, 3H), 2.48 (s, 3H). $^{13}$C NMR (DMSO-$d_6$, 75 MHz) δ 162.2, 160.0, 149.6, 139.2, 135.1, 130.2, 128.6, 128.2, 128.0, 123.1, 113.6, 21.7. ESIMS [M+H]$^+$ m/z 236.1.

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2-Methyl-7-nitroquinazolin-4-amine (3i). Eluent chloroform/methanol (40:1). Yield 128 mg (63%). Yellow solid, mp 217-220 °C. 1H NMR (DMSO-\(d_6\), 300 MHz) \(\delta\) 8.42 (d, 1H, \(J = 8.1\) Hz), 8.31 (m, 1H), 8.15-8.12 (m, 3H), 2.47 (s, 3H). 13C NMR (DMSO-\(d_6\), 75 MHz) \(\delta\) 167.2, 162.1, 150.8, 150.6, 126.5, 122.4, 118.3, 116.5, 26.4. ESIMS [M+H]^+ m/z 205.0.

7-Nitro-2-propyl-4-aminoquinazoline (3j). Eluent chloroform/methanol (40:1). Yield 176 mg (76%). Yellow solid, mp 208-211 °C. 1H NMR (DMSO-\(d_6\), 300 MHz) \(\delta\) 8.42 (d, 1H, \(J = 8.7\) Hz), 8.32 (m, 1H), 8.15-8.09 (m, 3H), 2.71 (t, 2H, \(J = 7.2\) Hz), 1.82-1.77 (m, 2H), 0.94-0.88 (t, 3H, \(J = 7.9\) Hz). 13C NMR (DMSO-\(d_6\), 75 MHz) \(\delta\) 169.9, 162.5, 151.0, 150.8, 126.7, 123.0, 118.6, 117.2, 41.1, 21.9, 14.7. HR-MS [M+H]^+ m/z Calcd for C_{11}H_{13}N_{4}O_{2}: 233.1039. Found: 233.1044.

6-Methyl-2,4-diaminoquinazoline (3k).\(^{4}\) Eluent chloroform/methanol (10:1). Yield 98 mg (57%). White solid. 1H NMR (DMSO-\(d_6\), 300 MHz) \(\delta\) 8.56 (s, 2H), 8.03 (s, 1H), 7.58 (d, 1H, \(J = 8.2\) Hz), 7.43 (s, 2H), 7.32 (d, 1H, \(J = 8.2\) Hz), 2.38 (s, 3H). 13C NMR (DMSO-\(d_6\), 75 MHz) \(\delta\) 163.3, 155.9, 140.6, 136.6, 133.4, 124.5, 118.4, 21.2. ESIMS [M+H]^+ m/z 175.0.

2,4-Diaminoquinazoline (3l).\(^{5}\) Eluent chloroform/methanol (5:1). Yield 105 mg (66%). White solid. 1H NMR (DMSO-\(d_6\), 300 MHz) \(\delta\) 8.33-8.10 (m, 3H), 7.66 (t, 1H, \(J = 7.5\) Hz), 7.35 (d, 1H, \(J = 8.2\) Hz), 7.23 (t, 1H, \(J = 7.4\) Hz), 7.03 (s, 2H). 13C NMR (DMSO-\(d_6\), 75 MHz) \(\delta\) 163.2, 159.1, 148.3, 133.9, 124.5, 122.1, 121.9, 110.5. ESIMS [M+H]^+ m/z
7-Nitro-2,4-diaminoquinazoline (3m). Eluent chloroform/methanol (5:1). Yield 172 mg (85%). Yellow solid, mp 221-223 °C. $^1$H NMR (DMSO-$d_6$, 300 MHz) $\delta$ 8.21 (d, 1H, $J = 8.1$ Hz), 7.90-7.72 (m, 4H), 6.51 (s, 2H). $^{13}$C NMR (DMSO-$d_6$, 75 MHz) $\delta$ 163.8, 162.0, 153.8, 150.8, 126.3, 119.2, 115.2, 113.3. HR-MS [M+H]$^+$ m/z Calcd for C$_8$H$_8$N$_5$O$_2$: 206.0678. Found: 206.0668.

References
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