An efficient nickel/silver co-catalyzed remote C–H amination of 8-aminoquinolines with azodicarboxylates at room temperature

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Experimental Section

Instrumentation and chemicals

1H NMR, 13C NMR spectra were recorded on a Bruker DPX-400 spectrometer with CDCl3 as the solvent and TMS as an internal standard, operating at 400 MHz for 1H NMR and 100 MHz for 13C NMR. Melting points were
measured by SGW X-4A microscopic apparatus. The X-ray crystallography was measured on Bruker D8 VENTURE PHOTON instrument. HRMS-ESI were measured by Q Exactive LC/HRMS spectrometer. Dichloromethane, ethyl acetate and hexane were used for column chromatography without further purification. All solvents and chemicals were obtained from commercial sources and used as received unless otherwise noted. All the N-(8-quinolyl)amides (1) were synthesized through the coupling between corresponding aryl or alkyl acids and 8-aminoquinoline as our previous work.¹

**Experimental procedures**

**General procedure for the nickel/silver co-catalyzed C−H amination of 8-aminoquinoline.** A mixture of N-(8-quinoliny)amide (0.2 mmol), azodicarboxylate (0.4 mmol), AgNO₃ (3 mol%) and Ni(acac)₂ (3 mol%) were added into a vial containing a stirring bar and sealed with a Teflon-lined cap. Then acetone (2 mL) was introduced. The resulting mixture was stirred at 25 °C for 12 h. After the reaction was complete, the mixture was added into H₂O (25 mL) and extracted with ethyl acetate (10 mL) for three times. The combined organic layer was dried over anhydrous MgSO₄ and filtered. After removal of the solvent in vacuo, the residue was purified by column chromatography (ethyl acetate/hexane) to afford the pure product.

**Characterization Data**

**Diethyl 1-(8-acetamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3aa)**

White solid, mp 130–132 °C; ¹H NMR (400 MHz, CDCl₃): δ 9.83 (s, 1H), 8.81 (dd, J = 4.28 Hz, J = 1.60 Hz, 1H), 8.74 (d, J = 8.32 Hz, 1H), 8.58 (s, 1H), 7.63 (d, J = 8.36 Hz, 1H), 7.51 (dd, J = 8.56 Hz, J = 4.20 Hz, 1H), 7.45 (s, 1H), 4.23–4.17 (m, 4H), 2.35 (s, 3H), 1.29–1.23 (m, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 168.9, 148.4, 138.3, 134.9, 132.6, 131.9, 126.6, 125.4, 122.1, 115.8, 63.2, 62.3, 25.1, 14.4. HRMS-ESI(m/z): calcd for C₁₇H₂₀N₄O₅ (M+H⁺): 361.1512, found 361.1515.

**Diethyl 1-(8-propionamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ba)**

White solid, mp 152–153 °C; ¹H NMR (400 MHz, CDCl₃): δ 9.86 (s, 1H), 8.80 (dd, J = 4.32 Hz, J = 1.64 Hz, 1H), 8.75 (d, J = 8.32 Hz, 1H), 8.58 (s, 1H), 7.66–7.63 (m, 2H), 7.50 (dd, J = 8.52 Hz, J = 4.16Hz, 1H), 4.22–4.16 (m, 4H), 2.63–2.57 (m, 2H), 1.33 (t, J = 7.56 Hz, 3H), 1.26–1.05 (m, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 172.7, 156.5, 156.2, 148.3, 138.4, 134.9, 132.6, 131.8, 126.6, 125.4, 122.1, 115.7, 63.3, 62.3, 31.3, 14.4, 9.7. HRMS-ESI(m/z): calcd for C₁₈H₂₀N₄O₅ (M+H⁺): 375.1668, found 375.1670.
Diethyl 1-(8-butyramidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ca)
White solid, mp 149–151 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 9.85 (s, 1H), 8.81 (dd, \(J = 4.32\) Hz, \(J = 1.68\) Hz, 1H), 8.76 (d, \(J = 8.32\) Hz, 1H), 8.59–8.57 (m, 1H), 7.66–7.61 (m, 2H), 7.50 (dd, \(J = 8.48\) Hz, \(J = 4.16\)Hz, 1H), 4.23–4.16 (m, 4H), 2.54 (t, \(J = 7.64\) Hz, 2H), 1.88–1.81 (m, 2H), 1.34–1.22 (m, 6H), 1.05 (t, \(J = 7.40\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 172.0, 156.5, 156.1, 148.3, 134.9, 132.6, 131.8, 126.6, 125.4, 122.1, 115.7, 63.2, 62.3, 40.1, 19.1, 14.4, 13.8. HRMS-ESI(m/z): calcd for C\(_{19}\)H\(_{24}\)N\(_4\)O\(_5\)(M+H\(^+\)): 389.1825, found 389.1827.

Diethyl 1-(8-(3-phenylpropanamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3da)
yellow solid, mp 121–123 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 9.83 (s, 1H), 8.79–8.75 (m, 2H), 8.57 (s, 1H), 7.64 (d, \(J = 8.36\) Hz, 1H), 7.52–7.45 (m, 2H), 7.30–7.27 (m, 4H), 7.22–7.17 (m, 1H), 4.23–4.17 (m, 4H), 3.16–3.12 (m, 2H), 2.92–2.87 (m, 2H), 1.29–1.23 (m, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 170.9, 156.5, 156.2, 148.3, 138.3, 134.8, 132.5, 131.9, 128.6, 128.4, 126.6, 126.3, 125.4, 122.1, 115.8, 63.3, 62.3, 39.7, 31.4, 14.4. HRMS-ESI(m/z): calcd for C\(_{24}\)H\(_{26}\)N\(_4\)O\(_5\)(M+H\(^+\)): 451.1981, found 451.1983.

Diethyl 1-(8-isobutyramidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ea)
yellow solid, mp 158–160 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 9.94 (s, 1H), 8.81 (dd, \(J = 4.28\) Hz, \(J = 1.68\) Hz, 1H), 8.76 (d, \(J = 8.40\) Hz, 1H), 8.59 (s, 1H), 7.68–7.63 (m, 2H), 7.50 (dd, \(J = 8.48\) Hz, \(J = 4.16\) Hz, 1H), 4.23–4.15 (m, 4H), 2.82–2.73 (m, 1H), 1.38–1.18 (m, 12H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 175.9, 156.5, 156.1, 148.4, 138.5, 135.0, 132.6, 131.8, 126.7, 125.4, 122.1, 115.8, 63.2, 62.3, 37.1, 19.7, 14.4. HRMS-ESI(m/z): calcd for C\(_{19}\)H\(_{24}\)N\(_4\)O\(_5\)(M+H\(^+\)): 389.1825, found 389.1828.

Diethyl 1-(8-pivalamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3fa)
Light yellow solid, mp 108–110 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 10.31 (s, 1H), 8.82 (dd, \(J = 4.28\) Hz, \(J = 1.56\)Hz, 1H), 8.77 (d, \(J = 8.32\) Hz, 1H), 8.57 (s, 1H), 7.64 (d, \(J = 8.36\) Hz, 1H), 7.53–7.46 (m, 2H), 4.22–4.16 (m, 4H), 1.42 (s, 9H), 1.29–1.22 (m, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 177.4, 156.4, 155.3, 152.3, 148.4, 138.8, 135.1, 132.5, 131.8, 126.6, 125.4, 122.0, 115.5, 64.1, 63.2, 62.5, 62.3, 40.4, 27.7, 14.4, 14.1. HRMS-ESI(m/z): calcd for C\(_{20}\)H\(_{26}\)N\(_4\)O\(_5\)(M+H\(^+\)): 403.1981, found 403.1980.

Diethyl 1-(8-(cyclohexanecarboxamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3ga)
White solid, mp 170–172 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 9.93 (s, 1H), 8.83–8.81 (m, 1H), 8.77 (d, \(J = 8.36\) Hz, 1H), 8.58 (s, 1H), 7.63 (d, \(J = 8.32\) Hz, 1H), 7.51 (dd, \(J = 8.56\) Hz, \(J = 4.24\) Hz, 1H), 7.43 (s, 1H), 4.24–4.14 (m, 4H), -S3-
2.52–2.43 (m, 1H), 2.11–2.03 (m, 2H), 1.91–1.84 (m, 2H), 1.77–1.69 (m, 2H), 1.68–1.57 (m, 2H), 1.44–1.36 (m, 2H), 1.26–1.07 (m, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 175.0, 156.4, 148.3, 138.6, 135.1, 132.6, 131.7, 126.6, 125.4, 122.1, 115.7, 63.2, 62.3, 46.9, 29.7, 25.8, 25.7, 14.4. HRMS-ESI(m/z): calcd for C$_{22}$H$_{38}$N$_4$O$_5$ (M+H$^+$): 429.2138, found 429.2140.

Diethyl 1-(8-(cyclopropanecarboxamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3ha)
Yellow solid, mp 212–214 °C; $^1$H NMR (400 MHz, CDCl$_3$): δ 10.06 (s, 1H), 8.85–8.82 (m, 1H), 8.72 (d, $J$ = 8.32 Hz, 1H), 8.57 (s, 1H), 7.61 (d, $J$ = 8.32 Hz, 1H), 7.55–7.51 (m, 1H), 7.21 (s, 1H), 4.25–4.17 (m, 4H), 1.85–1.77 (m, 1H), 1.29–1.23 (m, 6H), 1.17–1.15 (m, 2H), 0.95–0.90 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 172.4, 148.3, 138.3, 135.2, 132.5, 131.6, 126.6, 125.4, 122.1, 115.7, 63.2, 62.4, 16.3, 14.4, 8.3. HRMS-ESI(m/z): calcd for C$_{19}$H$_{22}$N$_4$O$_5$ (M+H$^+$): 387.1668, found 387.1665.

Diethyl 1-(8-methacrylamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ia)
Yellow solid, mp 154–155 °C; $^1$H NMR (400 MHz, CDCl$_3$): δ 10.41 (s, 1H), 8.84–8.79 (m, 2H), 8.59 (s, 1H), 7.66 (d, $J$ = 8.36 Hz, 1H), 7.54–7.50 (m, 2H), 6.05 (s, 1H), 5.57 (d, $J$ = 1.8 Hz, 1H), 4.24–4.16 (m, 4H), 2.18 (s, 1H), 1.28–1.23 (m, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 166.5, 156.5, 148.5, 140.6, 138.8, 134.9, 132.6, 132.1, 126.6, 125.5, 122.1, 120.9, 115.8, 63.2, 62.3, 18.7, 14.4. HRMS-ESI(m/z): calcd for C$_{19}$H$_{22}$N$_4$O$_5$ (M+H$^+$): 387.1668, found 387.1670.

Diethyl 1-(8-benzamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ja)
Yellow solid, mp 142–144 °C; $^1$H NMR (400 MHz, CDCl$_3$): δ 10.79 (s, 1H), 8.92 (d, $J$ = 8.32 Hz, 1H), 8.92 (d, $J$ = 8.36 Hz, 1H), 8.63–8.60 (m, 1H), 8.10–8.06 (m, 2H), 7.73–7.63 (m, 2H), 7.61–7.51 (m, 4H), 4.22–4.18 (m, 4H), 1.28–1.08 (m, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 165.6, 156.5, 156.0, 148.5, 140.6, 138.8, 134.9, 132.6, 132.1, 126.6, 125.5, 122.1, 115.9, 63.2, 62.3, 18.7, 14.4. HRMS-ESI(m/z): calcd for C$_{22}$H$_{38}$N$_4$O$_5$ (M+H$^+$): 423.1668, found 423.1670.

Diethyl 1-(8-(2-methylbenzamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3ka)
White solid, mp 59–62 °C; $^1$H NMR (400 MHz, CDCl$_3$): δ 10.26 (s, 1H), 8.93 (d, $J$ = 8.36 Hz, 1H), 8.87–8.85 (m, 1H), 8.63–8.60 (m, 1H), 7.61–8.06 (m, 2H), 7.73–7.63 (m, 2H), 7.61–7.51 (m, 4H), 4.22–4.18 (m, 4H), 1.28–1.08 (m, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 165.6, 156.5, 156.0, 148.5, 138.8, 135.0, 134.9, 132.6, 132.0, 128.9, 127.3, 126.7, 125.5, 122.2, 115.9, 63.2, 62.3, 14.4. HRMS-ESI(m/z): calcd for C$_{22}$H$_{38}$N$_4$O$_5$ (M+H$^+$): 423.1668, found 423.1670.
Diethyl 1-(8-(4-methylbenzamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3la)
Yellow solid, mp 139–141 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.76 (s, 1H), 8.91 (d, J = 8.36 Hz, 1H), 8.88–8.85 (m, 1H), 8.61 (s, 1H), 7.99–7.96 (m, 2H), 7.70 (d, J = 8.36 Hz, 1H), 7.56–7.51 (m, 2H), 7.34 (d, J = 8.00 Hz, 2H), 4.26–4.17 (m, 4H), 2.45 (s, 3H), 1.27–1.08 (m, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 165.6, 156.4, 148.5, 142.6, 138.8, 135.1, 132.6, 132.1, 129.5, 127.4, 126.7, 125.5, 122.2, 115.8, 63.2, 62.3, 21.6, 14.4, 14.2. HRMS-ESI(m/z): calcd for C₂₃H₂₄N₄O₅ (M+H⁺): 437.1825, found 437.1824.

Diethyl 1-(8-(4-methoxybenzamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3ma)
White solid, mp 204–205 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.72 (s, 1H), 8.90 (d, J = 8.32 Hz, 1H), 8.60 (s, 1H), 8.08–8.03 (m, 2H), 7.69 (d, J = 8.40 Hz, 1H), 7.56–7.52 (m, 1H), 7.41 (s, 1H), 7.06–7.02 (m, 2H), 4.24–4.17 (m, 4H), 3.90 (s, 3H), 1.27–1.09 (m, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 165.1, 162.7, 148.4, 138.8, 135.2, 132.6, 131.9, 129.2, 127.2, 126.7, 125.5, 122.2, 115.7, 114.1, 63.2, 62.4, 55.5, 14.4. HRMS-ESI(m/z): calcd for C₂₃H₂₄N₄O₆ (M+H⁺): 453.1774, found 453.1775.

Diethyl 1-(8-(4-fluorobenzamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3na)
White solid, mp 127–129 °C; ¹H NMR (500 MHz, CDCl₃): δ 10.74 (s, 1H), 8.90–8.85 (m, 2H), 8.61 (s, 1H), 8.12–8.06 (m, 2H), 7.70 (d, J = 8.32 Hz, 1H), 7.57–7.53 (m, 1H), 7.46–7.43 (m, 1H), 7.25–7.19 (m, 2H), 4.25–4.17 (m, 4H), 1.28–1.08 (m, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 166.4, 164.4, 163.9, 148.6, 138.8, 134.9, 132.7, 132.2, 131.1 (d, J = 3.11 Hz), 129.8, 129.7, 126.6, 125.5, 122.3, 116.0 (d, J = 21.87 Hz), 115.9, 63.3, 62.4, 14.4. HRMS-ESI(m/z): calcd for C₂₂H₂₁FN₄O₅ (M⁺H⁺): 441.1578, found 441.1578.

Diethyl 1-(8-(4-chlorobenzamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3oa)
White solid, mp 142–144 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.75 (s, 1H), 8.90–8.85 (m, 2H), 8.61 (s, 1H), 8.03–7.99 (m, 2H), 7.70 (d, J = 8.40Hz, 1H), 7.57–7.50 (m, 4H), 4.26–4.17 (m, 4H), 1.27–1.08 (m, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 164.4, 156.5, 148.6, 138.8, 134.7, 133.3, 132.7, 129.1, 128.8, 126.6, 125.5, 122.3, 116.0, 63.3, 62.4, 14.4. HRMS-ESI(m/z): calcd for C₂₂H₂₁ClN₄O₅ (M⁺H⁺): 457.1279, found 457.1280.

Diethyl 1-(8-(4-bromobenzamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3pa)
White solid, mp 139–141 °C; ¹H NMR (400 MHz, CDCl₃): δ 10.75 (s, 1H), 8.90–8.85 (m, 2H), 8.61 (s, 1H), 7.96–
7.92 (m, 2H), 7.71–7.66 (m, 3H), 7.55 (dd, \( J = 7.76 \) Hz, \( J = 4.20 \) Hz, 1H), 7.39 (s, 1H), 4.25–4.19 (m, 4H), 1.29–1.09 (m, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta 164.5, 156.4, 148.6, 138.8, 134.8, 133.8, 132.7, 132.4, 132.1, 128.9, 126.8, 126.6, 125.5, 122.3, 116.0, 63.3, 62.4, 14.4. \) HRMS-ESI (m/z): calcd for C\(_{22}\)H\(_{21}\)BrN\(_4\)O\(_5\) (M+H\(^+\)): 501.0774, found 501.0775.

Diethyl 1-(8-(4-(trifluoromethyl)benzamido)quinolin-5-yl)hydrazine-1,2-dicarboxylate (3qa)

White solid, mp 158–160 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta 10.82 \) (s, 1H), 8.91–8.86 (m, 2H), 8.62 (s, 1H), 8.18 (d, \( J = 8.04 \) Hz, 2H), 7.82 (d, \( J = 8.32 \) Hz, 1H), 7.58–7.51 (m, 2H), 4.26–4.17 (m, 4H), 1.29–1.09 (m, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta 164.1, 156.4, 155.9, 148.7, 138.8, 138.2, 134.5, 133.7 \) (q, \( J = 32.57 \) Hz), 132.6, 127.8, 126.6, 126.0 (q, \( J = 3.64 \) Hz), 125.5, 125.0, 122.3, 116.1, 63.3, 62.4, 14.4. HRMS-ESI (m/z): calcd for C\(_{23}\)H\(_{21}\)F\(_3\)N\(_4\)O\(_5\) (M+H\(^+\)): 491.1542, found 491.1541.

Diethyl 1-(2-methyl-8-propionamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ra)

Yellow solid, mp 165–166 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta 9.93 \) (s, 1H), 8.73 (d, \( J = 8.28 \) Hz, 1H), 8.45 (s, 1H), 7.55 (d, \( J = 8.32 \) Hz, 1H), 7.44 (s, 1H), 7.38 (d, \( J = 8.60 \) Hz, 1H), 4.24–4.17 (m, 4H), 2.74 (s, 3H), 2.61 (dd, \( J = 15.12 \) Hz, \( J = 7.52 \) Hz, 2H), 1.37–1.23 (m, 9H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta 172.5, 157.5, 156.4, 137.8, 134.3, 132.6, 131.8, 125.5, 123.5, 123.0, 115.7, 63.1, 62.3, 31.2, 14.4, 9.7. \) HRMS-ESI (m/z): calcd for C\(_{19}\)H\(_{24}\)N\(_4\)O\(_5\) (M+H\(^+\)): 389.1825, found 389.1828.

Diethyl 1-(4-chloro-8-propionamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3sa)

Yellow solid, mp 92–95 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta 9.91–9.88 \) (m, 1H), 8.86–8.82 (m, 2H), 8.66–8.61 (m, 1H), 8.08–8.05 (m, 1H), 7.58–7.54 (m, 1H), 7.01–6.92 (m, 1H), 4.23–4.15 (m, 4H), 2.62–2.54 (m, 2H), 1.32–1.31 (m, 3H), 1.28–1.23 (m, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta 172.6, 156.3, 155.7, 155.5, 152.3, 147.1, 140.4, 140.2, 139.4, 139.2, 136.1, 135.9, 132.6, 132.1, 129.2, 124.8, 122.8, 122.5, 116.8, 64.1, 63.1, 62.5, 62.2, 31.3, 14.5, 14.4, 9.6. \) HRMS-ESI (m/z): calcd for C\(_{18}\)H\(_{21}\)ClN\(_4\)O\(_5\) (M+H\(^+\)): 409.1279, found 409.1277.

Diethyl 1-(6-methoxy-8-propionamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ta)

White solid, mp 145–147 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta 9.92 \) (s, 1H), 8.86–8.77 (m, 2H), 8.64–8.62 (m, 1H), 7.49–7.45 (m, 1H), 7.35 (s, 1H), 4.24–4.07 (m, 4H), 4.00 (s, 3H), 2.63–2.57 (m, 2H), 1.33–1.28 (m, 3H), 1.25–1.01 (m, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta 172.9, 156.9, 156.3, 153.5, 153.1, 146.2, 136.5, 133.4, 132.6, 126.8, 122.8, 117.2, 103.3, 63.0, 62.2, 62.0, 56.4, 31.2, 14.4, 9.5. \) HRMS-ESI (m/z): calcd for C\(_{19}\)H\(_{24}\)N\(_4\)O\(_6\) (M+H\(^+\)): 405.1774, found
Diisopropyl 1-(8-acetamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ab)

Yellow solid, mp 189–190 °C; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 9.83 (s, 1H), 8.81–8.79 (m, 1H), 8.73 (d, $J = 8.36$ Hz, 1H), 8.57 (s, 1H), 7.61 (d, $J = 8.40$ Hz, 1H), 7.52–7.48 (m, 1H), 7.29 (s, 1H), 5.02–4.96 (m, 2H), 2.35 (s, 3H), 1.26–1.04 (m, 12H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.9, 156.1, 148.3, 138.3, 134.8, 132.7, 132.1, 126.5, 125.4, 122.0, 115.8, 71.1, 70.2, 25.1, 22.0, 21.8. HRMS-ESI(m/z): calcd for C$_{19}$H$_{24}$N$_4$O$_5$ (M+H$^+$): 389.1825, found 389.1827.

Di-tert-butyl 1-(8-acetamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ac)

Yellow solid, mp 104–106 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.81 (s, 1H), 8.79 (dd, $J = 4.24$ Hz, $J = 1.64$ Hz, 1H), 8.73 (d, $J = 8.32$ Hz, 1H), 8.56–8.54 (m, 1H), 7.51 (dd, $J = 8.48$ Hz, $J = 4.20$ Hz, 1H), 7.03 (s, 1H), $\delta$ 2.34 (s, 3H), 1.52–1.26 (m, 18H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.8, 154.5, 148.2, 138.2, 134.5, 132.8, 126.1, 125.4, 121.8, 115.8, 82.4, 29.7, 28.2, 28.1, 25.1. HRMS-ESI(m/z): calcd for C$_{21}$H$_{28}$N$_4$O$_5$ (M+H$^+$): 417.2138, found 417.2137.

Dibenzyl 1-(8-acetamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ad)

White solid, mp 68–70 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.82 (s, 1H), 8.78 (d, $J = 4.16$ Hz, 1H), 8.72 (d, $J = 8.40$ Hz, 1H), 8.51 (s, 1H), 7.63–7.43 (m, 3H), 7.31–7.05 (m, 10H), 5.15 (s, 4H), 2.33 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 169.0, 156.2, 155.8, 148.3, 138.3, 135.4, 135.1, 132.5, 131.7, 128.6, 128.5, 128.4, 128.3, 128.2, 127.9, 126.6, 125.3, 122.1, 115.7, 68.6, 68.0, 25.1. HRMS-ESI(m/z): calcd for C$_{27}$H$_{24}$N$_4$O$_5$ (M+H$^+$): 485.1825, found 485.1825.

Bis(4-chlorobenzyl) 1-(8-acetamidoquinolin-5-yl)hydrazine-1,2-dicarboxylate (3ae)

White solid, mp 160–162 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.82 (s, 1H), 8.81–8.78 (m, 1H), 8.72 (d, $J = 8.32$ Hz, 1H), 8.47 (s, 1H), 7.62–7.44 (m, 3H), 7.29–7.26 (m, 2H), 7.22–6.97 (m, 6H), 5.10 (s, 4H), 2.34 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 169.0, 156.0, 148.4, 138.3, 137.5, 135.2, 134.4, 133.9, 132.3, 131.4, 129.6, 129.4, 128.8, 128.7, 126.7, 125.3, 122.2, 115.7, 67.8, 67.2, 25.1. HRMS-ESI(m/z): calcd for C$_{27}$H$_{22}$Cl$_2$N$_4$O$_5$ (M+H$^+$): 553.1046, found 553.1047.

[1] Y. Wang, Y. Wang, K. Jiang, Q. Zhang and D. Li, *Org. Biomol. Chem.* 2016, 14, 10180.
Copies of $^1$H and $^{13}$C NMR spectra
