Supporting Information

Copper–Catalyzed Transformation of Ketones to Amides via C(CO)–C(alkyl) Bond Cleavage Directed by Picolinamide
Haojie Ma, Xiaoqiang Zhou, Zhenzhen Zhan, Daidong Wei, Chong Shi, Xingxing Liu, Guosheng Huang*
State Key Laboratory of Applied Organic Chemistry, Key Laboratory of Nonferrous Metal Chemistry and Resources Utilization of Gansu Province, Department of Chemistry, Lanzhou University, Lanzhou, P. R. China.
E-mail: hgs@lzu.edu.cn

Experimental section S2
Analytical data for products S2
NMR spectra of all compounds S7
Experimental Section

General experimental details

$^1$H-NMR spectra were recorded at 400 MHz. Chemical shifts (in ppm) were referenced to DMSO ($\delta = 2.50$ ppm) in DMSO as an internal standard. $^{13}$C-NMR spectra were obtained at 100 MHz and were calibrated with DMSO ($\delta = 39.50$ ppm). The high resolution mass spectra (HRMS) were recorded on an FT-ICR mass spectrometer using electrospray ionization (ESI). Products were purified by flash chromatography on 200–300 mesh silica gels. Unless otherwise noted, commercially available reagents and solvents were used without further purification. All melting points were determined without correction.

Typical procedure for the preparation of N-(2-carbamoylphenyl)picolinamide (2a)

A test tube was charged with 1a (0.2 mmol), NaN$_3$ (0.6 mmol), Cu(OAc)$_2$ (20 mol %), AcOH (4 equiv) in DMSO (1 mL). The reaction tube was evacuated and back-filled with O$_2$ (3 times, balloon). Then the reaction mixture was stirred at 80 °C (oil bath temperature) under O$_2$ atmosphere. After cooling to room temperature, the solvent was extracted with ethyl acetate and washed with brine, dried with Na$_2$SO$_4$. After the solvent was evaporated in vacuo, the residues were purified by column chromatography, eluting with petroleum ether / ethyl acetate to afford pure 2a.

Analytical data for products

N-(2-carbamoylphenyl)picolinamide (2a).

White solid (41.0 mg, yield 85%), m.p. 219-221 °C. $^1$H NMR (400 MHz, DMSO) $\delta$ 13.08 (s, 1H), 8.73 (m, 2H), 8.30 – 8.20 (m, 1H), 8.17 (dd, $J = 7.8, 1.0$ Hz, 1H), 8.06 (m, 1H), 7.80 (dd, $J = 7.8, 1.4$ Hz, 1H), 7.67 (m, 2H), 7.59 – 7.53 (m, 1H), 7.19 (m, 1H). $^{13}$C NMR (100 MHz, DMSO) $\delta$ 170.3, 162.6, 149.8, 148.7, 138.5, 138.1, 131.9, 128.6, 127.0, 122.9, 122.3, 121.6, 120.3. HRMS calcd for C$_{13}$H$_{12}$N$_3$O$_2$ [M+H]$^+$ 242.0924, found 242.0927.

N-(2-carbamoylphenyl)-6-methylpicolinamide (2b).

White solid (41.8 mg, 82%), m.p. 239-241 °C. $^1$H NMR (400 MHz, DMSO) $\delta$ 13.23 (s, 1H), 8.77 (dd, $J = 8.3, 0.7$ Hz, 1H), 8.19 (d, $J = 22.4$ Hz, 1H), 7.94 (m, 2H), 7.82 (m, 1H), 7.77 (s, 1H), 7.58 – 7.52 (m, 1H), 7.51 (d, $J = 6.9$ Hz, 1H), 7.17 (m, 1H), 2.59 (s, 3H). $^{13}$C NMR (100 MHz, DMSO) $\delta$ 170.4, 162.8, 149.1, 148.0, 138.1, 131.9, 128.6, 127.0, 122.9, 122.3, 121.6, 120.3, 23.8. HRMS calcd for C$_{14}$H$_{14}$N$_3$O$_2$ [M+H]$^+$ 256.1081, found 256.1082.
**N-(2-carbamoylphenyl)-6-chloropicolinamide (2c).**

White solid (28.6 mg, 52%), m.p. 243-245 °C. **\(^{1}H\) NMR (400 MHz, DMSO) \(\delta\) 13.23 (s, 1H), 8.75 (dd, \(J = 8.3, 0.7\) Hz, 1H), 8.30 (d, \(J = 25.6\) Hz, 1H), 8.17 – 8.09 (m, 2H), 7.82 (m, 3H), 7.60 – 7.54 (m, 1H), 7.20 (m, 1H). **\(^{13}C\) NMR (100 MHz, DMSO) \(\delta\) 170.4, 161.2, 150.5, 149.2, 141.6, 138.6, 132.1, 128.6, 127.6, 123.1, 121.6, 120.9, 120.2. HRMS calcd for C\(_{13}\)H\(_{11}\)ClN\(_3\)O\(_2\) [M+H]\(^+\) 276.0535, found 276.0539.

**N-(2-carbamoylphenyl)quinoline-2-carboxamide (2d).**

White solid (44.2 mg, 76%), m.p. 266-268 °C. **\(^{1}H\) NMR (400 MHz, DMSO) \(\delta\) 13.52 (s, 1H), 8.82 (dd, \(J = 8.4, 0.9\) Hz, 1H), 8.66 – 8.60 (m, 1H), 8.34 – 8.22 (m, 2H), 8.15 – 8.08 (m, 2H), 7.94 – 7.85 (m, 2H), 7.75 (m, 1H), 7.62 – 7.56 (m, 1H), 7.24 – 7.17 (m, 1H). **\(^{13}C\) NMR (100 MHz, DMSO) \(\delta\) 170.5, 162.7, 149.9, 145.8, 138.8, 138.2, 132.1, 130.7, 129.2, 128.9, 128.7, 128.4, 128.1, 122.9, 121.2, 120.2, 118.6. HRMS calcd for C\(_{17}\)H\(_{14}\)N\(_3\)O\(_2\) [M+H]\(^+\) 292.1081, found 292.1080.

**N-(2-carbamoyl-6-methylphenyl)picolinamide (2e).**

White solid (27.0 mg, 53%), m.p. 171-173 °C. **\(^{1}H\) NMR (400 MHz, DMSO) \(\delta\) 11.01 (s, 1H), 8.74 (m, 1H), 8.13 (d, \(J = 7.8\) Hz, 1H), 8.05 (m, 1H), 7.91 (s, 1H), 7.67 (m, 1H), 7.42 (dd, \(J = 13.5, 8.1\) Hz, 3H), 7.26 (t, \(J = 7.6\) Hz, 1H), 2.24 (d, \(J = 9.1\) Hz, 3H). **\(^{13}C\) NMR (100 MHz, DMSO) \(\delta\) 169.7, 161.9, 149.4, 148.7, 138.0, 135.4, 133.9, 132.4, 132.0, 127.0, 125.7, 125.6, 122.2, 18.8. HRMS calcd for C\(_{14}\)H\(_{14}\)N\(_3\)O\(_2\) [M+H]\(^+\) 256.1081, found 256.1083.

**N-(2-carbamoyl-5-methylphenyl)picolinamide (2f).**

White solid (38.8 mg, 76%), m.p. 246-248 °C. **\(^{1}H\) NMR (400 MHz, DMSO) \(\delta\) 13.20 (s, 1H), 8.74 – 8.68 (m, 1H), 8.62 (d, \(J = 0.5\) Hz, 1H), 8.17 (d, \(J = 7.8\) Hz, 2H), 8.06 (m, 1H), 7.72 (d, \(J = 8.0\) Hz, 1H), 7.65 (m, 1H), 7.56 (s, 1H), 7.00 (dd, \(J = 8.0, 0.9\) Hz, 1H), 2.37 (s, 3H). **\(^{13}C\) NMR (100 MHz, DMSO) \(\delta\) 170.3, 162.6, 149.9, 148.6, 142.0, 138.8, 138.0, 128.6, 126.9, 123.5, 122.3, 120.7, 118.5, 21.4. HRMS calcd for C\(_{14}\)H\(_{14}\)N\(_3\)O\(_2\) [M+H]\(^+\) 256.1081, found 256.1079.
N-(2-carbamoyl-4-methylphenyl)picolinamide (2g).
White solid (42.3 mg, 83%), m.p. 245-247 °C. $^1$H NMR (400 MHz, DMSO) δ 12.96 (s, 1H), 8.71 (d, $J = 4.2$ Hz, 1H), 8.63 (d, $J = 8.4$ Hz, 1H), 8.22 – 8.13 (m, 2H), 8.05 (m, 1H), 7.68 – 7.60 (m, 3H), 7.38 (dd, $J = 8.5$, 1.4 Hz, 1H), 2.32 (s, 3H). $^{13}$C NMR (100 MHz, DMSO) δ 170.3, 162.4, 149.9, 148.6, 138.0, 136.1, 132.3, 132.0, 128.9, 126.9, 122.2, 121.5, 120.3, 20.4. HRMS calcd for C$_{14}$H$_{14}$N$_{3}$O$_{2}$ [M+H]$^+$ 256.1081, found 256.1084.

N-(2-carbamoyl-4-methoxyphenyl)picolinamide (2h).
White solid (41.7 mg, 77%), m.p. 246-248 °C. $^1$H NMR (400 MHz, DMSO) δ 12.80 (s, 1H), 8.71 (d, $J = 4.1$ Hz, 1H), 8.67 – 8.62 (m, 1H), 8.25 (s, 1H), 8.16 (d, $J = 7.8$ Hz, 1H), 8.05 (m, 1H), 7.70 – 7.61 (m, 2H), 7.35 (d, $J = 2.9$ Hz, 1H), 7.16 (dd, $J = 9.1$, 2.9 Hz, 1H), 3.81 (s, 3H). $^{13}$C NMR (100 MHz, DMSO) δ 169.9, 162.1, 154.5, 150.0, 148.6, 138.0, 131.7, 126.8, 122.9, 122.2, 121.9, 117.3, 113.6, 55.5. HRMS calcd for C$_{14}$H$_{14}$N$_{3}$O$_{3}$ [M+H]$^+$ 272.1030, found 272.1032.

N-(6-carbamoyl-2,3-dimethylphenyl)picolinamide (2i).
White solid (29.6 mg, 55%), m.p. 206-208 °C. $^1$H NMR (400 MHz, DMSO) δ 11.11 (s, 1H), 8.76 – 8.71 (m, 1H), 8.12 (d, $J = 7.8$ Hz, 1H), 8.04 (m, 1H), 7.85 (s, 1H), 7.66 (m, 1H), 7.40 – 7.32 (m, 2H), 7.16 (d, $J = 7.8$ Hz, 1H), 2.32 (s, 3H), 2.08 (s, 3H). $^{13}$C NMR (100 MHz, DMSO) δ 169.8, 162.1, 149.5, 148.7, 139.8, 138.0, 134.0, 133.9, 129.3, 126.9, 125.1, 122.2, 20.3, 15.4. HRMS calcd for C$_{15}$H$_{16}$N$_{3}$O$_{2}$ [M+H]$^+$ 270.1237, found 270.1238.

N-(2-carbamoyl-4-ethylphenyl)picolinamide (2j).
White solid (44.7 mg, 83%), m.p. 243-245 °C. $^1$H NMR (400 MHz, DMSO) δ 12.98 (s, 1H), 8.76 – 8.67 (m, 1H), 8.65 (d, $J = 8.5$ Hz, 1H), 8.27 – 8.10 (m, 2H), 8.05 (m, 1H), 7.69 – 7.54 (m, 3H), 7.39 (m, 1H), 2.62 (m, 2H), 1.22 (t, $J = 7.6$ Hz, 3H). $^{13}$C NMR (100 MHz, DMSO) δ 170.4, 162.4, 149.9, 148.6, 138.3, 138.0, 136.3, 131.1, 127.8, 126.9, 122.2, 121.6, 120.4, 27.6, 15.4. HRMS calcd for C$_{15}$H$_{16}$N$_{3}$O$_{2}$ [M+H]$^+$ 270.1237, found 270.1240.
N-(2-carbamoyl-5-fluorophenyl)picolinamide (2k).
White solid (44 mg, 85%), m.p. 210-212°C. ¹H NMR (400 MHz, DMSO) δ 13.40 (s, 1H), 8.72 (m, 1H), 8.61 (dd, J = 12.3, 2.7 Hz, 1H), 8.26 (s, 1H), 8.20 – 8.14 (m, 1H), 8.06 (m, 1H), 7.91 (dd, J = 8.8, 6.5 Hz, 1H), 7.75 – 7.60 (m, 2H), 7.09 – 6.99 (m, 1H). ¹³C NMR (100 MHz, DMSO) δ 169.5, 163.6 (d, J = 245 Hz), 163.1, 149.4, 148.7, 140.9 (d, J = 12 Hz), 138.1, 131.0 (d, J = 10 Hz), 127.2, 122.5, 117.5 (d, J = 2 Hz), 109.6 (d, J = 22 Hz), 107.9 (d, J = 28 Hz). HRMS calcd for C₁₃H₁₁FN₃O₂ [M+H]⁺ 260.0830, found 260.0832.

N-(2-carbamoyl-4-fluorophenyl)picolinamide (2l).
White solid (47.7 mg, 92%), m.p. 276-278°C. ¹H NMR (400 MHz, DMSO) δ 12.96 (s, 1H), 8.76 (dd, J = 9.2, 5.4 Hz, 1H), 8.72 (m, 1H), 8.30 (s, 1H), 8.20 – 8.14 (m, 1H), 8.06 (m, 1H), 7.80 (s, 1H), 7.69 – 7.63 (m, 2H), 7.48 – 7.41 (m, 1H). ¹³C NMR (100 MHz, DMSO) δ 169.0 (d, J = 1 Hz), 162.5, 157.0 (d, J = 240 Hz), 149.6, 148.7, 138.1, 135.0 (d, J = 2 Hz), 127.0, 123.1 (d, J = 6 Hz), 122.3, 122.2, 118.6 (d, J = 21 Hz), 115.2 (d, J = 24 Hz). HRMS calcd for C₁₃H₁₁FN₃O₂ [M+H]⁺ 260.0830, found 260.0834.

N-(2-carbamoyl-5-chlorophenyl)picolinamide (2m).
White solid (41.8 mg, 76%), m.p. 270-272°C. ¹H NMR (400 MHz, DMSO) δ 13.27 (s, 1H), 8.86 (d, J = 2.2 Hz, 1H), 8.73 (dd, J = 4.7, 0.6 Hz, 1H), 8.31 (s, 1H), 8.18 (d, J = 7.8 Hz, 1H), 8.07 (m, 1H), 7.84 (d, J = 8.5 Hz, 1H), 7.80 – 7.71 (m, 1H), 7.67 (m, 1H), 7.28 (dd, J = 8.5, 2.2 Hz, 1H). ¹³C NMR (100 MHz, DMSO) δ 169.4, 162.9, 149.3, 148.7, 139.9, 138.1, 136.4, 130.3, 127.2, 122.6, 122.5, 119.8, 119.6. HRMS calcd for C₁₃H₁₁ClN₃O₂ [M+H]⁺ 276.0535, found 276.0533.

N-(2-carbamoyl-4-chlorophenyl)picolinamide (2n).
White solid (44.0 mg, 80%), m.p. 273-275°C. ¹H NMR (400 MHz, DMSO) δ 13.04 (s, 1H), 8.77 (d, J = 9.0 Hz, 1H), 8.74 – 8.69 (m, 1H), 8.35 (s, 1H), 8.17 (d, J = 7.8 Hz, 1H), 8.05 (m, 1H), 7.87 (d, J = 2.5 Hz, 1H), 7.79 (d, J = 8.7 Hz, 1H), 7.68 – 7.60 (m, 2H). ¹³C NMR (100 MHz, DMSO) δ 168.9, 162.7, 149.5, 148.7, 138.1, 137.4, 131.6, 128.2, 127.1, 126.7, 123.1, 122.4, 122.0. HRMS calcd for C₁₃H₁₁ClN₃O₂ [M+H]⁺ 276.0535, found 276.0532.
N-(5-bromo-2-carbamoylphenyl)picolinamide (2o).
White solid (35.7 mg, 56%), m.p. 274-276 °C. 1H NMR (400 MHz, DMSO) δ 13.23 (s, 1H), 9.01 (d, J = 2.0 Hz, 1H), 8.73 (m, 1H), 8.32 (s, 1H), 8.17 (d, J = 7.8 Hz, 1H), 8.07 (m, 1H), 7.77 (d, J = 8.4 Hz, 2H), 7.68 (m, 1H), 7.41 (dd, J = 8.4, 2.0 Hz, 1H). 13C NMR (100 MHz, DMSO) δ 169.5, 162.9, 149.3, 148.7, 139.9, 138.2, 130.4, 127.2, 125.6, 125.2, 122.6, 122.5, 120.2. HRMS calcd for C13H11BrN3O2 [M+H]+ 320.0029, found 320.0027.

N-(4-bromo-2-carbamoylphenyl)picolinamide (2p).
White solid (41.5 mg, 65%), m.p. 269-271 °C. 1H NMR (400 MHz, DMSO) δ 13.04 (s, 1H), 8.76 – 8.67 (m, 2H), 8.36 (s, 1H), 8.17 (d, J = 7.8 Hz, 1H), 8.06 (m, 1H), 7.99 (d, J = 2.3 Hz, 1H), 7.80 (s, 1H), 7.75 (dd, J = 8.9, 2.2 Hz, 1H), 7.66 (dd, J = 6.7, 4.9 Hz, 1H). 13C NMR (100 MHz, DMSO) δ 168.8, 162.7, 149.5, 148.7, 138.1, 137.8, 134.5, 131.0, 127.1, 123.4, 122.4, 122.2, 114.6. HRMS calcd for C13H11BrN3O2 [M+H]+ 320.0029, found 320.0025.

N-(2-carbamoyl-5-iodophenyl)picolinamide (2q).
White solid (36.7 mg, 50%), m.p. 259-261 °C. 1H NMR (400 MHz, DMSO) δ 13.15 (s, 1H), 9.19 (s, 1H), 8.72 (dd, J = 4.7, 0.6 Hz, 1H), 8.29 (s, 1H), 8.17 (d, J = 7.8 Hz, 1H), 8.07 (m, 1H), 7.78 – 7.70 (m, 1H), 7.69 – 7.65 (m, 1H), 7.58 (d, J = 0.8 Hz, 2H). 13C NMR (100 MHz, DMSO) δ 169.7, 162.8, 149.4, 148.7, 139.5, 138.2, 131.5, 130.2, 128.5, 127.2, 122.4, 120.6, 99.2. HRMS calcd for C13H11IN3O2 [M+H]+ 367.9891, found 367.9894.

N-(2-carbamoyl-5-chloro-4-methylphenyl)picolinamide (2r).
White solid (40.5 mg, 70%), m.p. 271-273 °C. 1H NMR (400 MHz, DMSO) δ 13.13 (s, 1H), 9.19 (s, 1H), 8.72 (dd, J = 4.7, 0.6 Hz, 1H), 8.29 (s, 1H), 8.17 (d, J = 7.8 Hz, 1H), 8.07 (m, 1H), 7.78 – 7.70 (m, 1H), 7.69 – 7.65 (m, 1H), 7.58 (d, J = 0.8 Hz, 2H). 13C NMR (100 MHz, DMSO) δ 169.7, 162.8, 149.4, 148.7, 139.5, 138.2, 131.5, 130.2, 128.5, 127.2, 122.4, 120.6, 99.2. HRMS calcd for C13H11ClN3O2 [M+H]+ 290.0691, found 290.0692.
NMR spectra of all compounds