Supporting Information

Copper-catalysed oxidative C–H/N–H cross-coupling between formamides and amides through chelation-assisted N–H activation

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I. General remarks

NMR spectra were obtained on a Bruker AMX-400. The $^1$H NMR (400 MHz) chemical shifts were measured relative to CDCl$_3$ as the internal reference (CDCl$_3$: $\delta$ = 7.26 ppm). The $^{13}$C NMR (100 MHz) chemical shifts were given using CDCl$_3$ as the internal standard (CDCl$_3$: $\delta$ = 77.16 ppm). High-resolution mass spectra (HR-MS) were obtained with a Waters-Q-TOF-Premier (ESI). Melting points were determined with XRC-1 and are uncorrected.

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. CuBr (99.0 %) was purchased from Shanghai Xin Bao Fine Chemical Engineering Reagent (China) CO., Ltd., TBHP (65 wt% in water) was purchased from Sinopharm Chemical Reagent (China) Co., Ltd., $N,N$-dimethylformamide was purchased from Chengdu Ke Long Chemical Engineering Reagent (China) CO., Ltd., $N,N$-diethylformamide was purchased from Chengdu Best-reagent (China) CO., Ltd., and 4-formylmorpholine was purchased from Accela ChemBio (China) Co. Ltd.. $N$-Substituted-2-picolinamides$^1$, $N$-(pyridin-2-yl)amides$^2$, $N$-phenyl-3-picolinamide$^1$, $N$-(pyridin-3-yl)benzamide$^2$, 1-formylpiperidine$^3$, and 1-formylpyrrolidine$^3$ were prepared according to the literature procedures.

II. Optimization of the oxidative C–H/N–H cross-coupling of $N,N$-dimethylformamide with $N$-phenyl-2-picolinamide

Table $S1$: Optimization of reaction conditions$^6$

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* Reaction conditions: *N*-phenyl-2-picolinamide (1a, 0.5 mmol, 1.0 equiv), *N,N*-dimethylformamide (2a, 1 mL), catalyst (5 mol%), oxidant (1.5 equiv).  
² Isolated yield.  
³ Not Detected.  
⁴ 3.0 equiv DMF.  
⁵ 1 mL.  
⁶ 1.0 equiv TEMPO (2,2,6,6-tetramethylpiperidine N-oxide).  
TBHP = tert-butyl hydroperoxide. DTBP = di-tert-butyl peroxide.  
TBPB = tert-butyl perbenzoate. DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone.

**III. General procedure for the oxidative C–H/N–H cross-coupling of formamides with amides**

TBHP (65 wt% in water, 1.5 equiv) was added to a mixture of amide (1 or 4, 0.5 mmol, 1.0 equiv), CuBr (5 mol%) and formamide (2, 1 mL) in a Schlenk tube under N₂ atmosphere. Then the reaction temperature was increased to 80 °C and the reaction mixture was stirred for 12 hours. After cooling to room temperature, the reaction mixture was extracted with ethyl acetate (20 mL), washed with water followed by...
brine, and dried over anhydrous Na$_2$SO$_4$. Removal of the solvent under vacuum afforded the crude product, which was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1 ~ 1/2, v/v) to afford the required product (3 or 5).

**IV. Procedure for the removal of the 2-pyridoyl group**

The mixture of 3a (0.4 mmol, 1.0 equiv) and NaOH (3.0 equiv) in MeOH (2 mL) was stirred at 50 °C for 12 hours. TLC (petroleum ether/ethyl acetate/dichloromethane = 1/2/1, v/v/v) indicated that 3a was disappeared and the product was generated. After cooling to room temperature, the reaction mixture was extracted with ethyl acetate (20 mL), washed with water followed by brine, and dried over anhydrous Na$_2$SO$_4$. Removal of the solvent under vacuum afforded the crude product, which was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) to afford the required product 6a.

**V. Procedure for the removal of the benzoyl group**

The mixture of 5a (0.4 mmol, 1.0 equiv) and NaOH (3.0 equiv) in MeOH (2 mL) was stirred at 50 °C for 12 hours. TLC (petroleum ether/ethyl acetate/dichloromethane = 1/3/1, v/v/v) indicated that 5a was disappeared and the product was generated. After cooling to room temperature, the reaction mixture was extracted with ethyl acetate (20 mL), washed with water followed by brine, and dried over anhydrous Na$_2$SO$_4$. Removal of the solvent under vacuum afforded the crude product, which was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/3, v/v) to afford the required product 7a.

**VI. Experimental data for the described substances**

![Chemical structure](image)

- N-(Dimethylcarbamoyl)-N-phenylpicolinamide (3a)
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 3a as a white solid (115 mg, 85% yield). M.p.: 97-99 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 2.99 (s, 6H), 7.29-7.33 (m, 1H), 7.36 (d, $J$ = 8.0 Hz, 2H), 7.40-7.46 (m, 3H), 7.84 (t, $J$ = 7.6 Hz, 1H), 8.01 (d, $J$ = 8.0 Hz, 1H), 8.57 (d, $J$ = 3.2 Hz, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 37.1, 38.5, 119.8, 124.5, 125.6, 126.2, 127.0, 129.2, 129.4, 137.1, 138.5, 148.3, 152.2, 157.9, 168.3 ppm. HRMS (ESI$^+$): calcd for C$_{15}$H$_{15}$N$_3$NaO$_2$ [M+Na]$^+$ 292.1062, found 292.1064.

![N-(Dimethylcarbamoyl)-N-(o-tolyl)picolinamide (3b)](image)

**N-(Dimethylcarbamoyl)-N-(o-tolyl)picolinamide (3b)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 3b as a white solid (120 mg, 85% yield). M.p.: 125-126 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 2.27 (s, 3H), 2.89 (s, 3H), 2.93 (s, 3H), 7.21-7.24 (m, 3H), 7.28-7.30 (m, 1H), 7.38 (t, $J$ = 6.2 Hz, 1H), 7.81 (t, $J$ = 7.8 Hz, 1H), 7.97 (d, $J$ = 7.6 Hz, 1H), 8.54 (d, $J$ = 4.4 Hz, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 18.4, 37.2, 37.7, 124.2, 125.7, 126.0, 126.9, 127.7, 131.3, 135.2, 136.9, 137.4, 148.3, 152.3, 158.3, 168.7 ppm. HRMS (ESI$^+$): calcd for C$_{16}$H$_{17}$N$_3$NaO$_2$ [M+Na]$^+$ 306.1218, found 306.1215.

![N-(Dimethylcarbamoyl)-N-(4-methoxyphenyl)picolinamide (3c)](image)

**N-(Dimethylcarbamoyl)-N-(4-methoxyphenyl)picolinamide (3c)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 3c as a white solid (114 mg, 76% yield). M.p.: 170-172 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 2.89 (s, 3H), 2.91 (s, 3H), 3.75 (s, 3H), 6.85-6.89 (m, 2H), 7.18-7.22 (m, 2H), 7.31 (dd, $J$ = 7.6 Hz, 4.8Hz, 1H), 7.73 (td, $J$ = 7.6 Hz, 1.6Hz, 1H), 7.90 (d, $J$ = 7.6 Hz, 1H), 8.46 (d, $J$ = 4.8 Hz, 1H) ppm. $^{13}$C NMR (100 MHz,

**N-(Dimethylcarbamoyl)-N-(2-fluorophenyl)picolinamide (3d)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 3d as a white solid (126 mg, 87% yield). M.p.: 139-141 °C. ¹H NMR (400 MHz, CDCl₃): δ = 2.97 (s, 6H), 7.16-7.21 (m, 2H), 7.30-7.36 (m, 2H), 7.39 (dd, J = 7.4 Hz, 5.0 Hz, 1H), 7.82 (t, J = 7.6 Hz, 1H), 8.02 (d, J = 7.6 Hz, 1H), 8.54 (d, J = 4.4Hz, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 37.1, 38.1, 116.6, 116.8, 124.6, 124.9, 125.0, 126.4, 127.3, 129.2, 129.3, 137.1, 148.4, 151.3, 155.9, 157.2, 158.5, 167.4 ppm. HRMS (ESI⁺): calcd for C₁₅H₁₄FN₃NaO₂ [M+Na⁺] 310.0968, found 310.0968.

**N-(2-Chlorophenyl)-N-(dimethylcarbamoyl)picolinamide (3e)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 3e as a white solid (121 mg, 80% yield). M.p.: 99-100 °C. ¹H NMR (400 MHz, CDCl₃): δ = 2.97 (s, 6H), 7.27-7.40 (m, 4H), 7.49 (d, J = 7.2 Hz, 1H), 7.80 (t, J = 7.6 Hz, 1H), 8.00 (d, J = 7.6 Hz, 1H), 8.54 (d, J = 2.8 Hz, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 37.2, 38.1, 120.4, 124.6, 126.3, 128.0, 128.9, 130.7, 131.9, 136.5, 137.0, 142.1, 148.5, 151.6, 168.1 ppm. HRMS (ESI⁺): calcd for C₁₅H₁₄ClN₃NaO₂ [M+Na⁺] 326.0672, found 326.0675.
**N-(3-Bromophenyl)-N-(dimethylcarbamoyl)picolinamide (3f)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 3f as a white solid (133 mg, 76% yield). M.p.: 107-109 °C. \(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 2.96\) (s, 6H), 7.24-7.28 (m, 2H), 7.38-7.42 (m, 2H), 7.50 (s, 1H), 7.81 (t, \(J = 7.6\) Hz, 1H), 7.98 (d, \(J = 7.6\) Hz, 1H), 8.52 (d, \(J = 4.4\) Hz, 1H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 37.1, 38.5, 122.7, 124.2, 124.6, 126.4, 128.6, 130.1, 130.6, 137.2, 139.8, 148.3, 151.7, 157.3, 168.0\) ppm. HRMS (ESI\(^+\)): calcd for C\(_{15}\)H\(_{14}\)BrN\(_3\)NaO\(_2\) [M+Na]\(^+\) 370.0167, found 370.0167.

**N-(Dimethylcarbamoyl)-N-(4-iodophenyl)picolinamide (3g)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 3g as a white solid (159 mg, 80% yield). M.p.: 130-132 °C. \(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 2.96\) (s, 6H), 7.09 (d, \(J = 8.4\) Hz, 2H), 7.40 (t, \(J = 6.2\) Hz, 1H), 7.73 (d, \(J = 8.4\) Hz, 2H), 7.82 (t, \(J = 7.6\) Hz, 1H), 7.99 (d, \(J = 8.0\) Hz, 1H), 8.53 (d, \(J = 4.4\) Hz, 1H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 37.1, 38.5, 121.7, 122.6, 124.6, 126.4, 127.4, 137.2, 138.1, 138.3, 138.5, 148.3, 151.8, 157.1, 168.0\) ppm. HRMS (ESI\(^+\)): calcd for C\(_{15}\)H\(_{14}\)IN\(_3\)NaO\(_2\) [M+Na]\(^+\) 418.0028, found 418.0030.

**N-Benzyl-N-(dimethylcarbamoyl)picolinamide (3h)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 3h as pale yellow oil (82 mg, 58% yield). Increasing the loading of
TBHP to 2.5 equiv, 3h was afforded in 81% yield (115 mg). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 2.47$ (s, 3H), 2.79 (s, 3H), 4.96 (s, 2H), 7.26-7.34 (m, 3H), 7.36-7.39 (m, 1H), 7.48 (d, $J = 6.8$ Hz, 2H), 7.80 (td, $J = 7.8$ Hz, 1.2 Hz, 1H), 7.99 (d, $J = 7.6$ Hz, 1H), 8.54 (d, $J = 4.8$ Hz, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 36.6, 37.9, 50.3, 124.3, 126.0, 127.8, 128.6, 129.1, 136.7, 137.0, 148.1, 151.7, 158.1, 166.9$ ppm. HRMS (ESI$^+$): calcd for C$_{16}$H$_{17}$N$_3$NaO$_2$ [M+Na]$^+$ 306.1218, found 306.1220.

$N$-(Dimethylcarbamoyl)-$N$-propylpicolinamide (3i)

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 3i as pale yellow oil (70 mg, 59% yield). Increasing the loading of TBHP to 2.5 equiv, 3i was afforded in 78% yield (92 mg). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 0.96$ (t, $J = 7.4$ Hz, 3H), 1.70-1.79 (m, 2H), 2.85 (s, 6H), 3.65 (s, 2H), 7.33-7.37 (m, 1H), 7.78 (td, $J = 7.6$ Hz, 1.6Hz, 1H), 7.96 (d, $J = 8.0$ Hz, 1H), 8.50-8.51 (m, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 11.5, 21.6, 36.6, 38.2, 48.5, 124.2, 126.7, 137.0, 148.1, 151.9, 158.6, 167.1$ ppm. HRMS (ESI$^+$): calcd for C$_{12}$H$_{17}$N$_3$O$_2$ [M+Na]$^+$ 258.1218, found 258.1216.

$N$-(Diethylcarbamoyl)-$N$-phenylpicolinamide (3j)

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded 3j as a white solid (116 mg, 78% yield), M.p.: 74-77 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 0.61$ (t, $J = 6.8$ Hz, 3H), 1.09 (t, $J = 6.8$ Hz, 3H), 3.25 (s, 2H), 3.38 (s, 2H), 7.19-7.23 (m, 1H), 7.26-7.36 (m, 5H), 7.73 (t, $J = 7.8$ Hz, 1H), 7.89 (d, $J = 8.0$ Hz, 1H), 8.42 (d, $J = 4.4$ Hz, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 11.3, 12.1, 40.7, 42.9, 119.8, 124.4, 125.7, 126.1, 126.9, 128.8, 129.3, 137.0, 139.0, 147.8,$
152.5, 156.8, 168.7 ppm. HRMS (ESI⁺): calcd for C₁₇H₁₉N₃NaO₂ [M+Na]⁺ 320.1375, found 320.1374.

\[ \text{N-}(\text{Diethylcarbamoyl})\text{-N-propylpicolinamide (3k)} \]

Employing the general procedure except that the loading of TBHP was 2.5 equiv, and purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded 3k as a pale yellow oil (94 mg, 71% yield). ¹H NMR (400 MHz, CDCl₃): \( \delta = 0.96 \) (t, \( J = 7.4 \) Hz, 3H), 1.10 (t, \( J = 7.2 \) Hz, 6H), 1.71-1.80 (m, 2H), 3.30-3.36 (m, 6H), 7.33 (dd, \( J = 7.6 \) Hz, 4.8Hz, 1H), 7.76 (t, \( J = 7.8 \) Hz, 1H), 7.92 (d, \( J = 7.6 \) Hz, 1H), 8.46 (d, \( J = 4.4 \) Hz, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): \( \delta = 11.3 \), 11.6, 13.2, 21.4, 40.1, 42.7, 48.8, 124.1, 125.8, 136.9, 147.7, 151.9, 157.6, 167.4 ppm. HRMS (ESI⁺): calcd for C₁₄H₂₁N₃NaO₂ [M+Na]⁺ 286.1531, found 286.1532.

\[ \text{N-Phenyl-N-(piperidine-1-carbonyl)picolinamide (3l)} \]

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded 3l as a white solid (81 mg, 52% yield), M.p.: 96-99 °C. ¹H NMR (400 MHz, CDCl₃): \( \delta = 1.39 \) (s, 2H), 1.56 (s, 4H), 3.46 (s, 4H), 7.26-7.30 (m, 1H), 7.33 (d, \( J = 8.0 \) Hz, 2H), 7.38-7.43 (m, 3H), 7.81 (t, \( J = 7.8 \) Hz, 1H), 7.97 (d, \( J = 7.6 \) Hz, 1H), 8.54 (d, \( J = 4.8 \) Hz, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): \( \delta = 24.3 \), 25.1, 45.1, 48.0, 119.8, 124.4, 125.6, 126.2, 126.9, 128.8, 129.3, 137.0, 139.0, 148.0, 152.3, 156.3, 168.7 ppm. HRMS (ESI⁺): calcd for C₁₈H₁₉N₃NaO₂ [M+Na]⁺ 332.1375, found 332.1379.
Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded 3m as a white solid (101 mg, 58 % yield), M.p.: 120-123 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 3.51-3.77\) (m, 8H), 7.30-7.35 (m, 3H), 7.43-7.44 (m, 1H), 7.50 (d, \(J = 7.2\) Hz, 1H), 7.84 (t, \(J = 7.6\) Hz, 1H), 8.03 (d, \(J = 7.6\) Hz, 1H), 8.57 (s, 1H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 44.4, 66.2, 121.0, 124.7, 126.6, 128.1, 129.1, 130.8, 131.5, 136.5, 137.2, 143.5, 148.1, 151.2, 168.2\) ppm. HRMS (ESI\(^{+}\)):
calc'd for C\(_{17}\)H\(_{16}\)ClN\(_3\)NaO\(_3\) [M+Na]\(^+\) 368.0778, found 368.0775.

N-(2-Chlorophenyl)-N-picolinoylmorpholine-4-carboxamide (3n)

Employing the general procedure except that the loading of TBHP was 2.5 equiv, and purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded 3n as a white solid (99 mg, 64 % yield), M.p.: 82-83 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 1.48\) (s, 2H), 1.63 (s, 2H), 2.80 (s, 2H), 3.33 (s, 2H), 4.98 (s, 2H), 7.26-7.33 (m, 3H), 7.38 (dd, \(J = 7.4\) Hz, 5.0 Hz, 1H), 7.49 (d, \(J = 7.2\)Hz, 2H), 7.80 (td, \(J = 7.6\) Hz, 1.6 Hz, 1H), 7.98 (d, \(J = 7.6\) Hz, 1H), 8.54 (d, \(J = 4.8\) Hz, 1H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 24.4, 25.4, 46.5, 47.5, 49.8, 124.1, 125.9, 127.7, 128.5, 129.0, 136.8, 136.9, 147.9, 151.8, 155.8, 166.4\) ppm. HRMS (ESI\(^{+}\)):
calc'd for C\(_{19}\)H\(_{19}\)N\(_3\)NaO\(_2\) [M+Na]\(^+\) 332.1375, found 332.1371.
N-(Dimethylcarbamoyl)-N-(pyridin-2-yl)benzamide (5a)

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 5a as a white solid (108 mg, 80% yield). M.p.: 121-122 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 2.96$ (s, 6H), 7.15 (dd, $J = 7.2$ Hz, 5.2Hz, 1H), 7.38 (t, $J = 7.6$ Hz, 3H), 7.48 (t, $J = 7.0$ Hz, 1H), 7.67-7.71 (m, 3H), 8.44 (d, $J = 4.4$ Hz, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 36.8$, 37.7, 121.0, 121.7, 128.45, 128.54, 132.1, 134.9, 138.2, 148.8, 152.8, 156.3, 169.5 ppm. HRMS (ESI$^+$): calcd for C$_{15}$H$_{15}$N$_3$NaO$_2$ [M+Na]$^+$ 292.1062, found 292.1061.

N-(Dimethylcarbamoyl)-2-fluoro-N-(pyridin-2-yl)benzamide (5b)

Employing the general procedure except that the reaction was carried out at room temperature, purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 5b as pale yellow oil (58 mg, 40% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.00$ (s, 6H), 6.99 (t, $J = 9.2$ Hz, 1H), 7.14-7.21 (m, 2H), 7.38-7.43 (m, 2H), 7.62-7.71 (m, 2H), 8.40 (d, $J = 4.4$ Hz, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 36.9$, 37.9, 115.7, 115.9, 119.9, 121.7, 123.7, 123.9, 124.4, 124.5, 130.31, 130.34, 132.75, 132.84, 137.9, 148.8, 152.0, 155.2, 157.7, 160.1, 165.5 ppm. HRMS (ESI$^+$): calcd for C$_{15}$H$_{14}$FN$_3$NaO$_2$ [M+Na]$^+$ 310.0968, found 310.0969.

4-Chloro-N-(dimethylcarbamoyl)-N-(pyridin-2-yl)benzamide (5c)

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 5c as a white solid (95 mg, 63% yield). M.p.: 132-133 °C. $^1$H NMR
(400 MHz, CDCl₃): δ = 2.97 (s, 6H), 7.18 (dd, J = 7.2 Hz, 5.2 Hz, 1H), 7.34-7.38 (m, 3H), 7.64 (d, J = 8.4 Hz, 2H), 7.73 (td, J = 7.8 Hz, 1.6 Hz, 1H), 8.45 (s, 1H) ppm. 

¹³C NMR (100 MHz, CDCl₃): δ = 36.3, 37.6, 120.8, 121.8, 128.8, 129.8, 133.1, 138.2, 138.5, 148.6, 152.3, 155.9, 168.4 ppm. HRMS (ESI⁺): calcd for C₁₅H₁₄ClN₃NaO₂ [M+Na⁺] 326.0672, found 326.0668.

![4-Bromo-N-(dimethylcarbamoyl)-N-(pyridin-2-yl)benzamide (5d)](image)

4-Bromo-N-(dimethylcarbamoyl)-N-(pyridin-2-yl)benzamide (5d)

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 5d as a white solid (123 mg, 71% yield). M.p.: 141-143 °C. 

¹H NMR (400 MHz, CDCl₃): δ = 2.97 (s, 6H), 7.18 (t, J = 6.0 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.50-7.57 (m, 4H), 7.73 (t, J = 7.8 Hz, 1H), 8.44 (d, J = 4.8 Hz, 1H) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 36.8, 37.7, 120.9, 122.0, 126.9, 130.0, 131.9, 133.7, 138.6, 148.7, 152.4, 156.0, 168.6 ppm. HRMS (ESI⁺): calcd for C₁₅H₁₄BrN₃NaO₂ [M+Na⁺] 370.0167, found 370.0169.

![N-(Dimethylcarbamoyl)-2-iodo-N-(pyridin-2-yl)benzamide (5e)](image)

N-(Dimethylcarbamoyl)-2-iodo-N-(pyridin-2-yl)benzamide (5e)

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 5e as a white solid (150 mg, 76% yield). M.p.: 136-138 °C. 

¹H NMR (400 MHz, CDCl₃): δ = 2.99 (s, 6H), 7.05 (t, J = 7.6 Hz, 1H), 7.14 (t, J = 5.6 Hz, 1H), 7.28 (t, J = 7.2Hz, 1H), 7.40 (d, J = 6.0 Hz, 1H), 7.58 (s, 1H), 7.70 (t, J = 7.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 8.39 (s, 1H) ppm. 

¹³C NMR (100 MHz, CDCl₃): δ = 37.0, 38.5, 93.4, 120.4, 121.9, 127.6, 128.7, 131.3, 138.4, 140.1, 148.6, 151.6, 154.7, 168.6 ppm. HRMS (ESI⁺): calcd for C₁₅H₁₄IN₃NaO₂ [M+Na⁺] 418.0028, found 418.0029.
**(5f)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **5f** as a white solid (97 mg, 69%). M.p.: 97-99°C. ¹H NMR (400 MHz, CDCl₃): δ = 2.34 (s, 3H), 2.96 (s, 6H), 7.13 (dd, J = 7.2 Hz, 4.8 Hz, 1H), 7.21-7.28 (m, 2H), 7.33 (d, J = 8.4 Hz, 1H), 7.44 (d, J = 7.6 Hz, 1H), 7.53 (s, 1H), 7.67 (td, J = 7.8 Hz, 2.0 Hz, 1H), 8.42-8.44 (m, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 21.2, 37.3, 120.8, 121.5, 125.3, 128.2, 129.0, 132.7, 134.7, 137.9, 138.3, 148.8, 152.9, 156.2, 169.6 ppm. HRMS (ESI⁺): calcd for C₁₆H₁₇N₃NaO₂ [M+Na]⁺ 306.1218, found 306.1222.

**(5g)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded **5g** as a white solid (89 mg, 63%). M.p.: 144-147°C. ¹H NMR (400 MHz, CDCl₃): δ = 2.27 (s, 3H), 2.99 (s, 6H), 7.17 (dd, J = 7.4 Hz, 5.0 Hz, 1H), 7.34 (t, J = 7.2 Hz, 2H), 7.45 (t, J = 7.2 Hz, 1H), 7.57 (d, J = 6.8 Hz, 1H), 7.71 (d, J = 7.2 Hz, 2H), 8.33 (d, J = 3.6 Hz, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 17.6, 36.9, 38.1, 123.3, 128.4, 128.5, 132.1, 134.6, 140.7, 146.4, 151.8, 156.3, 167.3, 169.4 ppm. HRMS (ESI⁺): calcd for C₁₆H₁₇N₃NaO₂ [M+Na]⁺ 306.1218, found 306.1224.
**N-(Diethylcarbamoyl)-N-(pyridin-2-yl)benzamide (5i)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded 5i as pale yellow oil (111 mg, 75%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 0.97 (t, $J$ = 7.2 Hz, 6H), 3.37 (s, 2H), 3.38 (s, 2H), 7.12 (dd, $J$ = 7.4 Hz, 5.0 Hz, 1H), 7.36 (t, $J$ = 7.6 Hz, 2H), 7.40-7.47 (m, 2H), 7.67 (d, $J$ = 7.2 Hz, 3H), 8.41 (d, $J$ = 4.4 Hz, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 11.4, 13.0, 40.9, 42.9, 120.3, 121.5, 128.3, 128.4, 131.7, 135.1, 138.0, 148.8, 152.9, 155.3, 170.0 ppm. HRMS (ESI$^+$): calcd for C$_{17}$H$_{19}$N$_3$NaO$_2$ [M+Na]$^+$ 320.1375, found 320.1373.

![Chemical structure of 5i](image)

**4-Bromo-N-(diethylcarbamoyl)-N-(pyridin-2-yl)benzamide (5j)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded 5j as pale yellow oil (120 mg, 64%). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 1.00 (s, 6H), 3.38 (s, 2H), 3.39 (s, 2H), 7.17 (dd, $J$ = 7.2 Hz, 5.2 Hz, 1H), 7.40 (d, $J$ = 8.0 Hz, 1H), 7.49-7.55 (m, 4H), 7.73 (t, $J$ = 7.8 Hz, 1H), 8.42 (d, $J$ = 4.8 Hz, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 11.5, 13.0, 40.9, 42.5, 120.3, 121.8, 126.5, 130.0, 131.7, 134.0, 138.2, 149.0, 152.7, 155.1, 169.1 ppm. HRMS (ESI$^+$): calcd for C$_{17}$H$_{18}$BrN$_3$NaO$_2$ [M+Na]$^+$ 398.0480, found 398.0477.

![Chemical structure of 5j](image)

**N-Benzoyl-N-(pyridin-2-yl)pyrrolidine-1-carboxamide (5k)**

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/2, v/v) afforded 5k as a white solid (74 mg, 50 %). M.p.: 120-123 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 1.82 (s, 4H), 3.40 (s, 2H), 3.46 (s, 2H), 7.13-7.14 (m, 1H), 7.35-7.38 (m, 3H), 7.46 (t, $J$ = 7.4 Hz, 1H), 7.68-7.72 (m, 3H), 8.43 (s, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 24.6, 25.6, 47.0, 47.5, 120.8, 121.5, 128.4, 128.5, 131.9, 155.3 ppm.
135.1, 138.0, 148.9, 152.8, 154.2, 169.4 ppm. HRMS (ESI\(^+\)): calcd for C\(_{17}\)H\(_{17}\)N\(_3\)NaO\(_2\) [M+Na]\(^+\) 318.1218, found 318.1220.

\[ \text{N-Benzyol-N-(pyridin-2-yl)morpholine-4-carboxamide (5l)} \]

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/2, v/v) afforded 5l as a white solid (99 mg, 64%). M.p.: 126-128 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 3.49\) (s, 4H), 3.57-3.58 (m, 4H), 7.18 (t, \(J = 6.2\) Hz, 1H), 7.37-7.42 (m, 3H), 7.50 (t, \(J = 7.4\) Hz, 1H), 7.69-7.74 (m, 3H), 8.44 (d, \(J = 4.4\) Hz, 1H) ppm.
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 45.9, 66.2, 120.7, 121.8, 128.4, 128.6, 132.2, 134.7, 138.1, 149.0, 152.8, 155.2, 169.5\) ppm. HRMS (ESI\(^+\)): calcd for C\(_{17}\)H\(_{17}\)N\(_3\)NaO\(_3\) [M+Na]\(^+\) 334.1168, found 334.1167.

\[ \text{N-(3-Methylbenzoyl)-N-(pyridin-2-yl)piperidine-1-carboxamide (5m)} \]

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1, v/v) afforded 5m as pale yellow oil (116 mg, 72%). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 1.45\) (s, 4H), 1.51 (s, 2H), 2.35 (s, 3H), 3.42 (s, 4H), 7.12 (t, \(J = 6.0\) Hz, 1H), 7.22-7.29 (m, 2H), 7.41 (d, \(J = 8.4\) Hz, 1H), 7.47 (d, \(J = 7.2\) Hz, 1H), 7.54 (s, 1H), 7.69 (t, \(J = 7.8\) Hz, 1H), 8.42 (d, \(J = 4.0\) Hz, 1H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 21.4, 24.1, 25.3, 46.6, 120.5, 121.5, 125.4, 128.2, 129.0, 132.7, 135.0, 138.0, 138.3, 148.9, 153.0, 155.0, 170.0\) ppm. HRMS (ESI\(^+\)): calcd for C\(_{19}\)H\(_{21}\)N\(_3\)NaO\(_2\) [M+Na]\(^+\) 346.1531, found 346.1528.
1,1-Dimethyl-3-phenylurea (6a)\(^4\)

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1, v/v) afforded 6a as a white solid (63 mg, 96 %). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 3.00\) (s, 6H), 6.34 (s, 1H), 7.00 (t, \(J = 7.2\) Hz, 1H), 7.26 (t, \(J = 7.2\) Hz, 2H), 7.36 (d, \(J = 8.0\) Hz, 2H) ppm. \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 36.5, 120.0, 123.0, 128.9, 139.3, 155.9\) ppm. HRMS (ESI\(^+\)): calcd for C\(_9\)H\(_{12}\)N\(_2\)O [M+Na]\(^+\) 187.0847, found 187.0850.

1,1-Dimethyl-3-(pyridin-2-yl)urea (7a)\(^5\)

Purification by column chromatography on silica gel (petroleum ether/ethyl acetate = 1/3, v/v) afforded 7a as pale yellow oil (45 mg, 68 %). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 3.03\) (s, 6H), 6.91 (dd, \(J = 6.2\) Hz, 5.8 Hz, 1H), 7.23 (s, 1H), 7.62 (t, \(J = 7.8\) Hz, 1H), 8.04 (d, \(J = 8.4\) Hz, 1H), 8.17 (d, \(J = 4.4\) Hz, 1H) ppm. \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 36.5, 113.2, 118.4, 138.2, 147.5, 152.9, 155.0\) ppm. HRMS (ESI\(^+\)): calcd for C\(_8\)H\(_{11}\)N\(_3\)NaO [M+Na]\(^+\) 188.0800, found 188.0802.

VII. References

VIII. Copies of $^1$H and $^{13}$C NMR spectra