SUPPORTING INFORMATION

Palladium-Catalyzed C(sp²)-H Aminoimidoylation of Isocynano-Containing Arenes: Synthesis of Amino Substituted N-Heterocycles

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I. General Information

$^1$H NMR (400 MHz) and $^{13}$C NMR (125 MHz) were registered on 400 M and 500 M spectrometers. Chemical shifts were reported in units (ppm) by assigning TMS resonance in the $^1$H spectrum as 0.00 ppm, CDCl$_3$ resonance in the $^{13}$C spectrum as 77.0 ppm. All coupling constants ($J$ values) were reported in Hertz (Hz). NMR analysis was carried out at 298 K unless noted otherwise. IR spectra were recorded on a Bruker Tensor 27 spectrometer using a diamond comb. Melting points were performed on an X-6 spectrometer. HRMS was obtained on an ESI-LC-MS/MS spectrometer. Isocyanides and N-benzoyloxyamines were prepared according to the following literatures:


II. General Procedure

**General procedure A:** An oven-dried 25 mL Schlenk tube charged with Pd(OAc)$_2$ (0.01 mmol, 2.24 mg), PPh$_3$ (0.02 mmol, 5.24 mg), Cs$_2$CO$_3$ (0.10 mmol, 32.6 mg) and 2 (0.15 mmol) was refilled with Ar for 3 times. Then a solution of pivalic acid (0.06 mmol, 7.0 μL) in 0.5 mL of dioxane was added by syringe and the tube was placed in a 110 °C oil-bath. A solution of 1 (0.1 mmol) in 1.0 mL of dioxane was added dropwise within 1 h by a syringe pump to the reaction mixture. After reacting for another 1-2 h, the reaction was completed. The crude reaction mixture was extracted with EA (20 mL × 3) and washed with brine (20 mL). The organic phase was concentrated in vacuo and the residue was purified by silica gel flash column chromatography to afford the corresponding amino-substituted
phenanthridines 3.

**General procedure B:** An oven-dried 25 mL Schlenk tube charged with Pd(OAc)$_2$ (0.01 mmol, 2.24 mg), PPh$_3$ (0.02 mmol, 5.24 mg), CsOPiv (0.12 mmol, 28.08 mg) and 2 (0.15 mmol) was refilled with Ar for 3 times. Then 0.5 mL of dioxane was added by syringe and the tube was placed in a 100 °C oil-bath. A solution of 4 (0.10 mmol) in 1.0 mL of dioxane was added dropwise within 1 h by a syringe pump to the reaction mixture. After reacting for another 1-2 h, the reaction was completed. The crude reaction mixture was extracted with EA (20 mL × 3) and washed with brine (20 mL). The organic phase was concentrated in *vacuo* and the residue was purified by silica gel flash column chromatography to afford the corresponding amino-substituted isoquinolines 5.
III. Characterization Data

4-(2,4-dimethylphenanthridin-6-yl)morpholine (3a)

Prepared from 2-isocyno-3,5-dimethyl-1,1'-biphenyl (20.7 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.1 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 30) furnished the product 3a as a white solid (23 mg, 0.078 mmol, 78% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.55 (d, $J$ = 8.3 Hz, 1H), 8.19 (d, $J$ = 8.1 Hz, 1H), 8.09 (s, 1H), 7.74 (t, $J$ = 7.2 Hz, 1H), 7.59 (t, $J$ = 7.2 Hz, 1H), 7.36 (s, 1H), 4.01 (t, $J$ = 4.5 Hz, 4H), 3.51 (t, $J$ = 4.6 Hz, 4H), 2.74 (s, 3H), 2.54 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 157.9, 140.4, 136.3, 135.3, 134.0, 131.2, 129.8, 126.4, 126.2, 123.1, 122.3, 121.0, 119.4, 67.2, 51.9, 21.9, 18.2; IR (KBr): 3069, 2967, 2913, 2890, 2857, 1607, 1574, 1522, 1447, 1278, 772 cm$^{-1}$; HRMS: calcd for C$_{19}$H$_{20}$N$_2$O (M$^+$H$^+$) 293.1648; found 293.1645; mp: 118-120 °C.

4-(2,4,8-trimethylphenanthridin-6-yl)morpholine (3b)

Prepared from 2-isocyno-3,4',5-trimethyl-1,1'-biphenyl (22.1 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.1 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 16) furnished the product 3b as a light yellow solid (16 mg, 0.052 mmol, 52% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.44 (d, $J$ = 8.4 Hz, 1H), 8.06 (s, 1H), 7.96 (s, 1H), 7.56 (d, $J$ = 8.4 Hz, 1H), 7.33 (s, 1H), 4.02 (t, $J$ = 4.5 Hz, 4H), 3.50 (t, $J$ = 4.6 Hz, 4H), 2.73 (s, 3H), 2.58 (s, 3H), 2.54 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 157.7, 140.0, 136.3, 136.2, 133.9, 133.1, 131.5, 130.8, 125.6, 123.1, 122.4, 121.1, 119.2, 67.2, 51.9, 22.0, 21.9, 18.2; IR (KBr): 3010, 2954, 2919, 2890, 2867, 1605, 1573, 1528, 1451, 1282, 789 cm$^{-1}$; HRMS: calcd for C$_{20}$H$_{22}$N$_2$O (M$^+$H$^+$) 307.1805; found
4-(8-fluoro-2,4-dimethylphenanthridin-6-yl)morpholine (3c)

Prepared from 4'-fluoro-2,4'-isocyano-3,5-dimethyl-1,1'-biphenyl (22.5 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.1 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 8) furnished the product 3c as a light yellow solid (21 mg, 0.068 mmol, 68% yield). $^1$H NMR (400 MHz, CDCl$_3$): δ 8.55–8.51 (m, 1H), 8.02 (s, 1H), 7.81–7.78 (m, 1H), 7.51–7.45 (m, 1H), 7.35 (s, 1H), 4.01 (t, $J$ = 4.5 Hz, 4H), 3.46 (t, $J$ = 4.6 Hz, 4H), 2.72 (s, 3H), 2.53 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 162.2 (d, $J$ = 246.8 Hz), 157.3 (d, $J$ = 4.1 Hz), 140.0, 136.6, 134.6, 131.8 (d, $J$ = 1.8 Hz), 131.1, 125.7 (d, $J$ = 8.23 Hz), 122.5 (d, $J$ = 7.4 Hz), 121.9, 119.2, 119.0 (d, $J$ = 23.8 Hz), 110.9 (d, $J$ = 21.8 Hz), 67.1, 51.8, 21.9, 18.2; IR (KBr): 3071, 2981, 2916, 2895, 2859, 1617, 1576, 1529, 1450, 1282, 752 cm$^{-1}$; HRMS: calcd for C$_{19}$H$_{19}$F$_{2}$N$_{2}$O (M+H$^+$) 311.1554; found 311.1554; mp: 127-129 °C.

4-(2,4-dimethyl-8-(trifluoromethyl)phenanthridin-6-yl)morpholine (3d)

Prepared from 2-isocyano-3,5-dimethyl-4’-(trifluoromethyl)-1,1’-biphenyl (27.5 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.1 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 16) furnished the product 3d as a white solid (26 mg, 0.072 mmol, 72% yield). $^1$H NMR (400 MHz, CDCl$_3$): δ 8.63 (d, $J$ = 8.7 Hz, 1H), 8.45 (s, 1H), 8.07 (s, 1H), 7.91 (d, $J$ = 8.7 Hz, 1H), 7.42 (s, 1H), 4.02 (t, $J$ = 4.5 Hz, 4H), 3.49 (t, $J$ = 4.6 Hz, 4H), 2.73 (s, 3H), 2.55 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 157.7, 141.2, 137.5, 136.7, 134.7, 132.4, 128.4 (q, $J$ = 32.7 Hz), 125.7 (q, $J$ = 3.53 Hz),
125.4 (q, $J = 272.3$ Hz), 124.2, 123.8 (q, $J = 4.2$ Hz), 121.4, 120.4, 119.7, 66.9, 51.9, 21.9, 18.1; IR (KBr): 3015, 2973, 2920, 2867, 2848, 1625, 1577, 1456, 1435, 1274, 797 cm$^{-1}$; HRMS: calcd for C$_{20}$H$_{19}$F$_{3}$N$_{2}$O (M+H$^+$) 361.1522; found 361.1521; mp: 127-129 °C.

4-(2,4,10-trimethylphenanthridin-6-yl)morpholine (3e)

Prepared from 2-isocyno-2',3,5-trimethyl-1,1'-biphenyl (22.1 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.1 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 16) furnished the product 3e as a white solid (24 mg, 0.076 mmol, 76% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.35 (s, 1H), 8.18 (d, $J = 7.9$ Hz, 1H), 7.58 (d, $J = 7.0$ Hz, 1H), 7.49 (t, $J = 7.6$ Hz, 1H), 7.38 (s, 1H), 4.01 (t, $J = 4.5$ Hz, 4H), 3.46 (t, $J = 4.6$ Hz, 4H), 3.09 (s, 3H), 2.76 (s, 3H), 2.55 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 158.6, 141.3, 136.2, 135.9, 134.8, 134.2, 132.9, 130.5, 126.0, 124.8, 124.3, 123.8, 122.4, 67.2, 51.9, 27.1, 22.3, 18.8; IR (KBr): 3018, 2952, 2918, 2884, 2850, 1614, 1583, 1528, 1448, 1279, 750 cm$^{-1}$; HRMS: calcd for C$_{20}$H$_{22}$N$_{2}$O (M+H$^+$) 307.1805; found 307.1804; mp: 125-127 °C.

4-(2,4-dimethyl-9-(trifluoromethyl)phenanthridin-6-yl)morpholine (3f)

Prepared from 2-isocyno-3,5-dimethyl-3'-trifluoromethyl)-1,1'-biphenyl (27.5 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.1 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 16) furnished the product 3f as a light yellow solid (16 mg, 0.045 mmol, 45% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.80 (s, 1H), 8.29 (d, $J = 8.6$ Hz, 1H), 8.08 (s, 1H), 7.79 (d, $J = 8.6$ Hz, 1H), 7.41 (s, 1H), 4.02 (t, $J = 4.5$ Hz, 4H), 3.46 (t, $J = 4.6$ Hz, 4H), 3.09 (s, 3H), 2.76 (s, 3H), 2.55 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 158.6, 141.3, 136.2, 135.9, 134.8, 134.2, 132.9, 130.5, 126.0, 124.8, 124.3, 123.8, 122.4, 67.2, 51.9, 27.1, 22.3, 18.8; IR (KBr): 3018, 2952, 2918, 2884, 2850, 1614, 1583, 1528, 1448, 1279, 750 cm$^{-1}$; HRMS: calcd for C$_{20}$H$_{22}$N$_{2}$O (M+H$^+$) 307.1805; found 307.1804; mp: 125-127 °C.
3.49 (t, \( J = 4.7 \) Hz, 4H), 2.73 (s, 3H), 2.56 (s, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \( \delta \) 157.2, 140.7, 136.5, 134.9, 134.7, 132.0, 131.5 (q, \( J = 32.3 \) Hz), 127.2, 125.2 (q, \( J = 273.0 \) Hz), 122.5, 122.2 (q, \( J = 3.6 \) Hz), 121.6, 120.5 (q, \( J = 3.8 \) Hz), 119.3, 66.9, 51.7, 21.8, 17.9; IR (KBr): 3050, 2960, 2916, 2893, 2857, 1727, 1585, 1517, 1453, 1278, 798 cm\(^{-1}\); HRMS: calcd for C\(_{20}\)H\(_{19}\)F\(_3\)N\(_2\)O (M+H\(^+\)) 361.1522; found 361.1526; mp: 168-170 °C.

4-(4-methylphenanthridin-6-yl)morpholine (3g)

Prepared from 2-isocyno-3-methyl-1, 1'-biphenyl (19.3 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.1 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 16) furnished the product 3g as a light yellow solid (16 mg, 0.058 mmol, 58% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.57 (d, \( J = 8.3 \) Hz, 1H), 8.30 (d, \( J = 8.1 \) Hz, 1H), 8.20 (d, \( J = 8.0 \) Hz, 1H), 7.76 (t, \( J = 8.2 \) Hz, 1H), 7.61 (t, \( J = 8.0 \) Hz, 1H), 7.52 (d, \( J = 7.1 \) Hz, 1H), 7.40 (t, \( J = 7.5 \) Hz, 1H), 4.02 (t, \( J = 4.5 \) Hz, 4H), 3.54 (t, \( J = 4.7 \) Hz, 4H), 2.78 (s, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \( \delta \) 158.5, 142.2, 136.6, 135.5, 130.0, 129.5, 126.6, 126.3, 124.5, 123.2, 122.4, 120.9, 119.7, 67.1, 51.8, 18.3; IR (KBr): 3021, 2958, 2917, 2884, 2852, 1610, 1576, 1522, 1458, 1273, 786 cm\(^{-1}\); HRMS: calcd for C\(_{18}\)H\(_{18}\)N\(_2\)O (M+H\(^+\)) 279.1492; found 279.1493; mp: 109-110 °C.

Methyl 6-morpholinophenanthridine-4-carboxylate (3h)

Prepared from methyl 2-isocyno-[1,1'-biphenyl]-3-carboxylate (23.7 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.1 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 4) furnished the product 3h as a white solid (21 mg, 0.066 mmol, 66% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.53 (t, \( J = 8.2 \) Hz, 1H), 8.15 (d, \( J = 8.1 \) Hz, 1H), 8.00 (d, \( J = 8.0 \) Hz, 1H), 7.80 (t, \( J = 8.0 \) Hz, 1H), 7.60 (t, \( J = 8.0 \) Hz, 1H), 7.50 (d, \( J = 7.5 \) Hz, 1H), 4.00 (t, \( J = 4.5 \) Hz, 4H), 3.50 (t, \( J = 4.7 \) Hz, 4H), 2.78 (s, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \( \delta \) 158.5, 142.2, 136.6, 135.5, 130.0, 129.5, 126.6, 126.3, 124.5, 123.2, 122.4, 120.9, 119.7, 67.1, 51.8, 18.3; IR (KBr): 3021, 2958, 2917, 2884, 2852, 1610, 1576, 1522, 1458, 1273, 786 cm\(^{-1}\); HRMS: calcd for C\(_{18}\)H\(_{18}\)N\(_2\)O (M+H\(^+\)) 279.1492; found 279.1493; mp: 109-110 °C.
Hz, 1H), 7.86 (d, J = 7.3 Hz, 1H), 7.78 (t, J = 7.3 Hz, 1H), 7.63 (t, J = 7.3 Hz, 1H), 7.48 (t, J = 7.8 Hz, 1H), 4.03 (s, 3H), 3.98 (t, J = 4.5 Hz, 4H), 3.57 (t, J = 4.7 Hz, 4H); 13C NMR (125 MHz, CDCl₃): δ 169.7, 159.6, 141.3, 134.8, 130.5, 128.8, 127.2, 126.5, 124.7, 123.8, 123.1, 122.9, 120.9, 67.0, 52.4, 51.5; IR (KBr): 3067, 2998, 2954, 2919, 2829, 1610, 1573, 1523, 1453, 1276, 768 cm⁻¹; HRMS: calcd for C₁₉H₁₈N₂O₃ (M+H⁺) 323.1390; found 323.1391; mp: 110-112 °C.

![Methyl 2-chloro-6-morpholinophenanthridine-4-carboxylate (3i)](image)

Methyl 2-chloro-6-morpholinophenanthridine-4-carboxylate (3i)

Prepared from methyl 5-chloro-2-isocyano-[1,1'-biphenyl]-3-carboxylate (27.2 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.1 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 16) furnished the product 3i as a white solid (24 mg, 0.067 mmol, 67% yield). ¹H NMR (400 MHz, CDCl₃): δ 8.45-8.43 (m, 2H), 8.14 (d, J = 8.0 Hz, 1H), 7.81 (s, 1H), 7.78 (d, J = 8.3 Hz, 1H), 7.66 (t, J = 7.2 Hz, 1H), 4.02 (s, 3H), 3.96 (t, J = 4.5 Hz, 4H), 3.57 (t, J = 4.7 Hz, 4H); 13C NMR (125 MHz, CDCl₃): δ 168.2, 159.7, 139.9, 133.9, 132.4, 130.8, 129.4, 129.0, 127.9, 126.6, 124.2, 123.1, 121.0, 66.9, 52.6, 51.5; IR (KBr): 3076, 2970, 2948, 2890, 2846, 1613, 1583, 1524, 1448, 1260, 758 cm⁻¹; HRMS: calcd for C₁₉H₁₇ClN₂O₃ (M+H⁺) 357.1000; found 357.1002; mp: 131-133 °C.

![4-(2,4-dichlorophenanthridin-6-yl)morpholine (3j)](image)

4-(2,4-dichlorophenanthridin-6-yl)morpholine (3j)

Prepared from 3,5-dichloro-2-isocyano-1,1'-biphenyl (24.8 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.1 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 16) furnished the product 3j as a light yellow solid (22 mg, 0.066 mmol, 66% yield). ¹H NMR (400 MHz, CDCl₃): δ 8.45 (d, J = 8.2 Hz, 1H), 8.28 (d, J = 2.2 Hz,
1H), 8.17 (d, J = 7.9 Hz, 1H), 7.80 (t, J = 8.2 Hz, 1H), 7.71 (d, J = 2.2 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 4.00 (t, J = 4.5 Hz, 4H), 3.62 (t, J = 4.5 Hz, 4H); 13C NMR (125 MHz, CDCl3): δ 159.9, 138.9, 134.2, 133.8, 130.9, 129.6, 129.3, 127.9, 126.7, 124.7, 123.4, 121.3, 120.5, 66.9, 51.7; IR (KBr): 3082, 2970, 2916, 2863, 2848, 1611, 1583, 1517, 1444, 1272 cm⁻¹; HRMS: calcd for C17H14Cl2N2O (M+H⁺) 333.0556; found 333.0557; mp: 204-206 °C.

2,4-dimethyl-6-morpholinobenzofuro[3,2-c]quinoline (3k)

Prepared from 2-(2-isocyno-3,5-dimethylphenyl)benzofuran (24.7 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.1 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 16) furnished the product 3k as a light yellow solid (21 mg, 0.061 mmol, 61% yield). 1H NMR (400 MHz, CDCl3): δ 7.93 (s, 1H), 7.84 (d, J = 7.6 Hz, 1H), 7.72 (d, J = 7.9 Hz, 1H), 7.51-7.43 (m, 2H), 7.39 (s, 1H), 4.05 (t, J = 4.5 Hz, 4H), 3.64 (t, J = 4.5 Hz, 4H), 2.75 (s, 3H), 2.54 (s, 3H); 13C NMR (125 MHz, CDCl3): δ 159.7, 155.8, 154.9, 143.7, 136.0, 133.9, 132.1, 126.2, 123.9, 123.0, 122.2, 117.7, 114.9, 111.9, 108.5, 67.1, 49.9, 21.7, 18.4; IR (KBr): 3030, 2950, 2916, 2857, 2819, 1634, 1594, 1507, 1435, 1275, 752 cm⁻¹; HRMS: calcd for C21H20N2O2 (M+H⁺) 333.1598; found 333.1596; mp: 107-109 °C.

2,4-dimethyl-6-(piperidin-1-yl)phenanthidine (3l)

Prepared from 2-isocyno-3,5-dimethyl-1,1'-biphenyl (20.7 mg, 0.10 mmol, 1.0 equiv) and piperidin-1-yl benzoate (30.8 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 60) furnished the product 3l as a light yellow solid (24 mg, 0.081 mmol, 81%
yield. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.53 (d, $J = 8.2$ Hz, 1H), 8.19 (d, $J = 8.0$ Hz, 1H), 8.08 (s, 1H), 7.72 (t, $J = 7.2$ Hz, 1H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.35 (s, 1H), 3.46 (t, $J = 5.1$ Hz, 4H), 2.75 (s, 3H), 2.54 (s, 3H), 1.91-1.85 (m, 4H), 1.76-1.71 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 159.2, 140.7, 136.1, 135.2, 133.4, 131.0, 129.6, 126.7, 126.2, 122.9, 122.1, 121.6, 119.4, 52.7, 26.3, 25.2, 21.9, 18.1; IR (KBr): 3068, 2967, 2928, 2854, 1646, 1610, 1584, 1520, 1464, 1264, 774 cm$^{-1}$; HRMS: calcd for C$_{20}$H$_{22}$N$_2$(M+H$^+$) 291.1856; found 291.1852; mp: 97-99 °C.

2,4-dimethyl-6-(4-methylpiperidin-1-yl)phenanthridine (3m)

Prepared from 2-isocyano-3, 5-dimethyl-1',1'-biphenyl (20.7 mg, 0.10 mmol, 1.0 equiv) and 4-methylpiperidin-1-yl benzoate (32.9 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 60) furnished the product 3m as a light yellow solid (21 mg, 0.070 mmol, 70% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.53 (d, $J = 8.2$ Hz, 1H), 8.18 (d, $J = 8.2$ Hz, 1H), 8.08 (s, 1H), 7.72 (t, $J = 7.7$ Hz, 1H), 7.58 (t, $J = 7.7$ Hz, 1H), 7.35 (s, 1H), 3.94 (d, $J = 13.2$ Hz, 1H), 3.01 (t, $J = 12.6$ Hz, 4H), 2.75 (s, 3H), 2.54 (s, 3H), 1.90-1.80 (m, 2H), 1.74-1.52 (m, 3H), 1.09 (d, $J = 6.1$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 158.9, 140.7, 136.1, 135.1, 133.4, 131.0, 129.6, 126.7, 126.2, 122.9, 122.1, 121.6, 119.4, 51.9, 34.7, 31.6, 22.3, 21.9, 18.2; IR (KBr): 3069, 2955, 2922, 2861, 2826, 1609, 1574, 1520, 1453, 1281, 773 cm$^{-1}$; HRMS: calcd for C$_{21}$H$_{24}$N$_2$(M+H$^+$) 305.2012; found 305.2011; mp: 96-98 °C.

Ethyl 1-(2,4-dimethylphenanthridin-6-yl)piperidine-4-carboxylate (3n)

Prepared from 2-isocyano-3, 5-dimethyl-1',1'-biphenyl (20.7 mg, 0.10 mmol, 1.0 equiv) and ethyl 1-(benzoyloxy)piperidine-4-carboxylate (41.6 mg, 0.15 mmol, 1.5
equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 16) furnished the product 3n as a light yellow oil (18 mg, 0.050 mmol, 50% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.53 (d, $J = 8.2$ Hz, 1H), 8.17 (d, $J = 8.2$ Hz, 1H), 8.07 (s, 1H), 7.72 (t, $J = 7.7$ Hz, 1H), 7.58 (t, $J = 7.7$ Hz, 1H), 7.34 (s, 1H), 4.21 (q, $J = 7.1$ Hz, 2H), 3.95-3.90 (m, 2H), 3.10-3.03 (m, 2H), 2.73 (s, 3H), 2.63-2.57 (m, 1H), 2.53 (s, 3H), 2.14-2.08 (m, 4H), 1.32 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 175.4, 158.6, 140.5, 136.2, 135.1, 133.7, 131.1, 129.7, 126.4, 126.3, 122.9, 122.2, 121.4, 119.4, 60.5, 51.1, 41.9, 28.6, 21.9, 18.1, 14.4; IR (KBr): 3071, 2955, 2923, 2854, 2820, 1610, 1576, 1521, 1446, 1289, 776 cm$^{-1}$; HRMS: calcd for C$_{23}$H$_{26}$N$_2$O$_2$ (M+H$^+$) 363.2067; found 363.2070.

![Chemical Structure](image)

6-(4-methoxypiperidin-1-yl)-2,4-dimethylphenanthridine (3o)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (20.7 mg, 0.10 mmol, 1.0 equiv) and 4-methoxypiperidin-1-yl benzoate (35.3 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 16) furnished the product 3o as a white solid (18 mg, 0.057 mmol, 57% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.53 (d, $J = 8.2$ Hz, 1H), 8.17 (d, $J = 8.1$ Hz, 1H), 8.07 (s, 1H), 7.72 (t, $J = 7.1$ Hz, 1H), 7.58 (t, $J = 7.1$ Hz, 1H), 7.34 (s, 1H), 3.86-3.80 (m, 2H), 3.49-3.47 (m, 1H), 3.44 (s, 3H), 3.22-3.15 (m, 2H), 2.73 (s, 3H), 2.53 (s, 3H), 2.19-2.15 (m, 2H), 1.94-1.84 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 158.5, 140.5, 136.2, 135.1, 133.6, 131.1, 129.7, 126.5, 126.4, 122.9, 122.2, 121.4, 119.4, 55.8, 49.2, 31.3, 21.9, 18.2; IR (KBr): 3019, 2955, 2923, 2854, 1719, 1599, 1576, 1504, 1455, 1272, 768 cm$^{-1}$; HRMS: calcd for C$_{21}$H$_{24}$N$_2$O (M+H$^+$) 321.1961; found 321.1966; mp: 108-110 °C.
8-(2,4-dimethylphenanthridin-6-yl)-1,4-dioxa-8-azaspiro[4.5]decane (3p)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (20.7 mg, 0.10 mmol, 1.0 equiv) and 1,4-dioxa-8-azaspiro[4.5]decan-8-yl benzoate (39.5 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 16) furnished the product 3p as a light yellow solid (22 mg, 0.064 mmol, 64% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.54 (d, $J = 8.3$ Hz, 1H), 8.18 (d, $J = 8.2$ Hz, 1H), 8.07 (s, 1H), 7.73 (t, $J = 7.6$ Hz, 1H), 7.59 (t, $J = 7.6$ Hz, 1H), 7.34 (s, 1H), 4.04 (s, 4H), 3.63 (t, $J = 5.4$ Hz, 4H), 2.73 (s, 3H), 2.54 (s, 3H), 2.03 (t, $J = 5.7$ Hz, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 158.1, 140.5, 136.2, 135.2, 133.6, 131.1, 129.7, 126.4, 126.3, 122.9, 122.1, 121.3, 119.3, 107.9, 64.5, 49.4, 35.2, 21.9, 18.2; IR (KBr): 3071, 2979, 2918, 2856, 2838, 1611, 1582, 1545, 1277, 758 cm$^{-1}$; HRMS: calcd for C$_{22}$H$_{24}$N$_2$O$_2$ (M+H$^+$) 349.1911; found 349.1910; mp: 125-127 °C.

tert-butyl 4-(2,4-dimethylphenanthridin-6-yl)piperazine-1-carboxylate (3q)

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (20.7 mg, 0.10 mmol, 1.0 equiv) and tert-butyl 4-(benzoyloxy)piperazine-1-carboxylate (45.9 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 16) furnished the product 3q as a light yellow solid (27 mg, 0.070 mmol, 70% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.55 (d, $J = 8.2$ Hz, 1H), 8.19 (d, $J = 8.1$ Hz, 1H), 8.08 (s, 1H), 7.74 (t, $J = 7.7$ Hz, 1H), 7.59 (t, $J = 7.7$ Hz, 1H), 7.35 (s, 1H), 3.74 (t, $J = 5.1$ Hz, 4H), 3.46 (t, $J = 4.8$ Hz, 4H), 2.73 (s, 3H), 2.54 (s, 3H), 1.52 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 157.9, 155.1, 140.3, 136.3, 135.2, 134.1, 131.2, 129.9, 126.5, 126.2, 123.1, 122.3, 121.1, 119.4, 79.9, 51.2, 43.3, 28.6.
21.9, 18.2; IR (KBr): 3067, 2961, 2925, 2893, 2845, 1608, 1573, 1520, 1452, 1274, 773 cm\(^{-1}\); HRMS: calcd for C\(_{24}\)H\(_{29}\)N\(_3\)O\(_2\) (M+H\(^+\)) 392.2333; found 392.2332. mp: 139-141 °C.

\[
\text{6-(4-benzylpiperidin-1-yl)-2,4-dimethylphenanthridine (3r)}
\]

Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (20.7 mg, 0.10 mmol, 1.0 equiv) and 4-benzylpiperidin-1-yl benzoate (44.3 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 16) furnished the product 3r as a light yellow solid (26 mg, 0.068 mmol, 68% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 8.53 (d, \(J = 8.2\) Hz, 1H), 8.18 (d, \(J = 8.0\) Hz, 1H), 8.08 (s, 1H), 7.72 (t, \(J = 7.2\) Hz, 1H), 7.58 (t, \(J = 7.2\) Hz, 1H), 7.35-7.31 (m, 3H), 7.25-7.23 (m, 3H), 3.95 (d, \(J = 12.9\) Hz, 2H), 2.97 (t, \(J = 12.1\) Hz, 2H), 2.73 (s, 3H), 2.69 (d, \(J = 6.6\) Hz, 2H), 2.54 (s, 3H), 1.87-1.84 (m, 3H), 1.71-1.60 (m, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): δ 158.9, 140.9, 140.6, 136.1, 135.1, 133.5, 131.0, 129.6, 129.3, 128.4, 126.6, 126.2, 125.9, 122.9, 122.1, 121.5, 119.4, 51.9, 43.6, 38.8, 32.6, 21.9, 18.1; IR (KBr): 3070, 2981, 2914, 2849, 2822, 1608, 1573, 1520, 1444, 1284, 774 cm\(^{-1}\); HRMS: calcd for C\(_{27}\)H\(_{28}\)N\(_2\) (M+H\(^+\)) 381.2325; found 381.2327; mp: 101-103 °C.

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\text{N,N-diethyl-2,4-dimethylphenanthridin-6-amine (3s)}
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Prepared from 2-isocyano-3,5-dimethyl-1,1'-biphenyl (20.7 mg, 0.10 mmol, 1.0 equiv) and O-benzoyl-N,N-diethylhydroxylamine (28.9 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 60) furnished the product 3s as a light yellow oil (13 mg, 0.047 mmol, 47% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 8.54 (d, \(J = 8.2\) Hz, 1H), 8.21 (d, \(J = 8.2\) Hz, 1H), 8.19 (d, \(J = 8.2\) Hz, 1H), 8.15 (d, \(J = 8.2\) Hz, 1H), 8.08 (s, 1H), 7.72 (t, \(J = 7.2\) Hz, 1H), 7.58 (t, \(J = 7.2\) Hz, 1H), 7.35-7.31 (m, 3H), 7.25-7.23 (m, 3H), 3.95 (d, \(J = 12.9\) Hz, 2H), 2.97 (t, \(J = 12.1\) Hz, 2H), 2.73 (s, 3H), 2.69 (d, \(J = 6.6\) Hz, 2H), 2.54 (s, 3H), 1.87-1.84 (m, 3H), 1.71-1.60 (m, 2H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): δ 158.9, 140.9, 140.6, 136.1, 135.1, 133.5, 131.0, 129.6, 129.3, 128.4, 126.6, 126.2, 125.9, 122.9, 122.1, 121.5, 119.4, 51.9, 43.6, 38.8, 32.6, 21.9, 18.1; IR (KBr): 3070, 2981, 2914, 2849, 2822, 1608, 1573, 1520, 1444, 1284, 774 cm\(^{-1}\); HRMS: calcd for C\(_{27}\)H\(_{28}\)N\(_2\) (M+H\(^+\)) 381.2325; found 381.2327; mp: 101-103 °C.
= 8.2 Hz, 1H), 8.08 (s, 1H), 7.72 (t, J = 8.2 Hz, 1H), 7.57 (t, J = 7.1 Hz, 1H), 7.35 (s, 1H), 3.53 (q, J = 7.0 Hz, 4H), 2.74 (s, 3H), 2.54 (s, 3H), 1.29 (t, J = 7.0 Hz, 6H); $^{13}$CNMR (125 MHz, CDCl$_3$): δ 157.6, 140.6, 136.0, 135.2, 133.2, 130.9, 129.5, 126.5, 126.1, 122.9, 122.5, 121.8, 119.3, 46.1, 21.9, 18.2, 13.2; IR (KBr): 3072, 2965, 2921, 2852, 1728, 1611, 1574, 1520, 1455, 1288, 773 cm$^{-1}$; HRMS: calcd for C$_{19}$H$_{22}$N$_2$ (M+H$^+$) 279.1856; found 279.1852.

Ethyl 1-morpholino-4-phenylisoquinoline-3-carboxylate (5a)

Prepared from ethyl 2-isocyano-3,3-diphenylacrylate (27.7 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.1 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 8) furnished the product 5a as a light yellow solid (22 mg, 0.061 mmol, 61% yield). $^1$H NMR (400 MHz, CDCl$_3$): δ 8.17-8.14 (m, 1H), 7.58-7.57 (m, 3H), 7.46-7.42 (m, 3H), 7.34-7.31 (m, 2H), 4.07 (q, J = 7.1 Hz, 2H), 3.99 (t, J = 4.2 Hz, 4H), 3.53 (t, J = 4.2 Hz, 4H), 0.93 (t, J = 7.1 Hz, 3H); $^{13}$CNMR (125 MHz, CDCl$_3$): δ 167.9, 160.4, 140.7, 137.9, 136.7, 130.4, 130.2, 128.3, 128.1, 127.8, 127.3, 127.1, 125.5, 121.9, 67.2, 61.1, 51.9, 13.7; IR (KBr): 3010, 2953, 2924, 2854, 1719, 1599, 1576, 1504, 1455, 1272, 768 cm$^{-1}$; HRMS: calcd for C$_{22}$H$_{22}$N$_2$O$_3$ (M+H$^+$) 363.1703; found 363.1700; mp: 189-191 °C.
Ethyl 7-methyl-1-morpholino-4-(p-tolyl)isoquinoline-3-carboxylate (5b)

Prepared from ethyl 2-isocyano-3,3-di-p-tolylacrylate (30.5 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.1 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 8) furnished the product 5b as a light yellow solid (21 mg, 0.054 mmol, 54% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.83 (s, 1H), 7.42 (d, \(J = 8.6\) Hz, 1H), 7.30 (d, \(J = 8.6\) Hz, 1H), 7.18 (d, \(J = 8.0\) Hz, 2H), 7.11 (d, \(J = 8.0\) Hz, 2H), 4.01 (q, \(J = 7.2\) Hz, 2H), 3.91 (t, \(J = 4.5\) Hz, 4H), 3.41 (t, \(J = 4.7\) Hz, 4H), 2.46 (s, 3H), 2.35 (s, 3H), 0.89 (t, \(J = 7.2\) Hz, 3H); \(^13\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 168.1, 159.7, 139.9, 137.4, 137.3, 136.2, 133.8, 132.2, 130.1, 128.9, 128.5, 127.1, 124.4, 67.2, 61.1, 51.9, 22.1, 21.4, 13.8; IR (KBr): 3025, 2977, 2921, 2882, 2850, 1646, 1573, 1518, 1441, 1276, 739 cm\(^{-1}\); HRMS: calcd for C\(_{24}\)H\(_{26}\)N\(_2\)O\(_3\) (M+H\(^+\)) 391.2016; found 391.2019; mp: 105-107 °C.

![Chemical structure](image)

Ethyl 7-methoxy-4-(4-methoxyphenyl)-1-morpholinoisoquinoline-3-carboxylate (5c)

Prepared from ethyl 3,3-bis(4-chlorophenyl)-2-isocyanoacrylate (33.7 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.05 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 8) furnished the product 5c as a light yellow solid (26 mg, 0.062 mmol, 62% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.53 (d, \(J = 9.2\) Hz, 1H), 7.45 (s, 1H), 7.22 (d, \(J = 8.5\) Hz, 2H), 6.98 (d, \(J = 8.7\) Hz, 2H), 4.10 (q, \(J = 7.1\) Hz, 2H), 3.99 (t, \(J = 4.4\) Hz, 4H), 3.95 (s, 3H), 3.87 (s, 3H), 3.48 (t, \(J = 4.6\) Hz, 4H), 1.00 (t, \(J = 7.1\) Hz, 3H); \(^13\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 168.2, 159.4, 159.1, 158.8, 139.0, 133.2, 131.3, 128.9, 128.6, 123.6, 121.9, 113.8, 104.4, 67.2, 61.0, 55.6, 55.5, 51.6, 13.9; IR (KBr): 3030, 2982, 2966, 2920, 2846, 1646, 1582, 1517, 1444, 1272, 835 cm\(^{-1}\); HRMS: calcd for C\(_{24}\)H\(_{26}\)N\(_2\)O\(_5\) (M+H\(^+\)) 423.1914; found 423.1912; mp: 133-135 °C.
Ethyl 7-chloro-4-(4-chlorophenyl)-1-morpholinoisoquinoline-3-carboxylate (5d)

Prepared from ethyl 3,3-bis(4-chlorophenyl)-2-isocyanoacrylate (34.6 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.1 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 8) furnished the product 5d as a light yellow solid (16 mg, 0.037 mmol, 37% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.10 (s, 1H), 7.52 (d, $J$ = 9.0 Hz, 1H), 7.48-7.43 (m, 3H), 7.24 (d, $J$ = 8.4 Hz, 2H), 4.11 (q, $J$ = 7.2 Hz, 2H), 3.99 (t, $J$ = 4.5 Hz, 4H), 3.51 (t, $J$ = 4.6 Hz, 4H), 1.02 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 167.3, 159.7, 140.9, 136.2, 134.7, 134.2, 133.7, 131.6, 131.3, 128.7, 128.6, 126.7, 124.7, 122.7, 67.0, 61.4, 51.8, 13.9; IR (KBr): 3020, 2961, 2920, 2851, 1736, 1573, 1562, 1543, 1445, 1267, 782 cm$^{-1}$; HRMS: calcd for C$_{22}$H$_{20}$Cl$_2$N$_2$O$_3$ (M+H$^+$) 431.0924; found 431.0928; mp: 89-91 °C.

Ethyl 4-methyl-1-morpholinoisoquinoline-3-carboxylate (5e)

Prepared from (Z)-ethyl 2-isocyano-3-phenylbut-2-enolate (21.5 mg, 0.10 mmol, 1.0 equiv) and morpholino benzoate (31.05 mg, 0.15 mmol, 1.5 equiv) according to the general procedure. Column chromatography purification (EtOAc : petroleum ether = 1 : 8) furnished the product 5e as a light yellow oil (10 mg, 0.031 mmol, 31% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.14 (d, $J$ = 8.1 Hz, 1H), 8.04 (d, $J$ = 8.4 Hz, 1H), 7.71 (t, $J$ = 8.4 Hz, 1H), 7.59 (t, $J$ = 8.1 Hz, 1H), 4.46 (q, $J$ = 7.1 Hz, 2H), 3.96 (t, $J$ = 4.5 Hz, 4H), 3.42 (t, $J$ = 4.7 Hz, 4H), 2.69 (s, 3H), 1.44 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR
(125 MHz, CDCl₃): δ 168.3, 159.2, 140.3, 138.2, 130.1, 127.2, 125.8, 124.9, 122.9, 122.1, 67.2, 61.4, 51.9, 14.4, 14.0; IR (KBr): 3073, 2959, 2921, 2850, 1721, 1615, 1579, 1504, 1441, 1273, 767 cm⁻¹; HRMS: calcd for C₁₇H₂₀N₂O₃ (M+H⁺) 301.1547; found 301.1549.
IV. Copies of $^1$H and $^{13}$C NMR Spectra

3a
3c
$3n$
3q
3s
5b
$5e$
V. Deuteration Studies

To provide preliminary insight into the reaction mechanism, 2,6-diphenyl aryl isocyanide 6 with one of the phenyl rings fully deuterated was used in an intramolecular competition study. An obvious kinetic isotope effect (KIE) $k_H/k_D = 4.9$ was observed (eqn. 1).

$$k_H/k_D = 4.9$$
determined by the $^1$HNMR ratio of 7 to 8