Supplementary Information

Direct C–H alkylation and indole formation of anilines with diazo compounds under rhodium catalysis

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General methods

Commercially available reagents were used without additional purification, unless otherwise stated. Sealed tubes (13 × 100 mm²) were purchased from Fischer Scientific and dried in oven for overnight and cooled under a stream of nitrogen prior to use. Thin layer chromatography was carried out using plates coated with Kieselgel 60F₂₅₄ (Merck). For flash column chromatography, E. Merck Kieselgel 60 (230-400 mesh) was used. Nuclear magnetic resonance spectra (¹H and ¹³C NMR) were recorded on a Bruker Unity 500 MHz and 700 MHz spectrometer for CDCl₃ solutions and chemical shifts are reported as parts per million (ppm) relative to, respectively, residual CHCl₃ δ_H (7.24 ppm) and CDCl₃ δ_C (77.23 ppm) as internal standards. Resonance patterns are reported with the notations s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). In addition, the notation br is used to indicate a broad signal. Coupling constants (J) are reported in hertz (Hz). IR spectra were recorded on a Varian 2000 Infrared spectrophotometer and are reported as cm⁻¹. High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-600 spectrometer.
General procedure for the synthesis of pyrimidyl arylamines:¹⁻³ To an oven-dried flask charged with aniline (977.8 mg, 10.5 mmol, 150 mol %), 2-chloropyrimidine (801.7 mg, 7.0 mmol, 100 mol %) and acetic acid (7 mL) in 1,4-dioxane (19 mL) was added. The reaction mixture was stirred at 110 °C for 24 h and monitored by TLC. Upon completion, the mixture was extracted with CH₂Cl₂ (3 × 20 mL) and washed with brine. The organic layer was dried over MgSO₄ and concentrated in vacuo. The residue was purified by flash column chromatography (n-hexanes/EtOAc) to give N-phenylpyrimidin-2-amine 1a (990.6 mg) in 82% yield.

General procedure for the synthesis of pyridinyl arylamines:¹⁻³ To an oven-dried flask charged with aniline (1.4 g, 15 mmol, 100 mol %), 2-bromopyridine (2.4 g, 15 mmol, 100 mol %) was added. The reaction mixture was stirred at 160 °C for 7 h and monitored by TLC. Upon completion, saturated NaHCO₃ was added and the mixture was extracted with EtOAc (3 × 15 mL). The combined organic phase was washed with brine and dried over MgSO₄. The solid was filtered off and the filtrate was evaporated in vacuum. The crude product was purified by flash column chromatography (n-hexanes/EtOAc) to give N-phenylpyridin-2-amine 4a (2.44 g) in 95% yield.

General procedure for the synthesis of diazo substrates: Diazo substrates were prepared according to the previous literature.⁴

References:
Typical procedure for the alkylation of $N$-phenylpyrimidin-2-amines (3a–3u)

To an oven-dried sealed tube charged with $N$-phenylpyrimidin-2-amine (1a) (34.2 mg, 0.2 mmol, 100 mol %), [RhCp*Cl$_2$]$_2$ (3.1 mg, 0.005 mmol, 2.5 mol %), and AgOAc (5 mg, 0.03 mmol, 15 mol %) in MeOH (1 mL) was added dimethyl 2-diazomalonate (2a) (37.9 mg, 0.24 mmol, 120 mol %) under air. The reaction mixture was allowed to stir at 60 °C for 24 h, and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography ($n$-hexanes/EtOAc: 3:1) to afford 3a (37.2 mg) in 62% yield.
Characterization data for alkylated products (3a–3u)

Dimethyl 2-(2-(pyrimidin-2-ylamino)phenyl)malonate (3a)

\[
\text{MeO}_2C-\text{CO}_2\text{Me}
\]

\[
3a
\]

\(^1\text{H NMR (500 MHz, CDCl}_3\) \(\delta\): 8.34 (d, \(J = 4.5\) Hz, 2H), 7.99 (br s, 1H), 7.67 (d, \(J = 8.0\) Hz, 1H), 7.39–7.35 (m, 2H), 7.18 (d, \(J = 7.6\) Hz, 1H), 6.67 (t, \(J = 4.5\) Hz, 1H), 4.79 (s, 1H), 3.64 (s, 6H); \(^{13}\text{C NMR (125 MHz, CDCl}_3\) \(\delta\): 169.1, 160.7, 158.1, 137.6, 130.9, 129.1, 127.7, 126.5, 125.4, 112.4, 55.4, 52.9, 29.6; IR (KBr) \(\nu\): 3359, 2953, 2924, 1728, 1577, 1509, 1438, 1404, 1246, 1149, 1024, 799, 755 cm\(^{-1}\); HRMS (EI) calcd for C\(_{15}\)H\(_{15}\)N\(_3\)O\(_4\) [M]\(^+\) 301.1063, found 301.1058.

Diethyl 2-(2-(pyrimidin-2-ylamino)phenyl)malonate (3b)

\[
\text{EtO}_2C-\text{CO}_2\text{Et}
\]

\[
3b
\]

\(^1\text{H NMR (700 MHz, CDCl}_3\) \(\delta\): 8.34 (d, \(J = 4.9\) Hz, 2H), 8.16 (br s, 1H), 7.72 (d, \(J = 8.4\) Hz, 1H), 7.38–7.35 (m, 2H), 7.16 (d, \(J = 7.7\) Hz, 1H), 6.65 (t, \(J = 4.9\) Hz, 1H), 4.72 (s, 1H), 4.17–4.13 (m, 2H), 4.11–4.06 (m, 2H), 1.17 (t, \(J = 7.0\) Hz, 6H); \(^{13}\text{C NMR (175 MHz, CDCl}_3\) \(\delta\): 168.7, 160.6, 158.0, 137.7, 131.0, 128.9, 127.4, 125.9, 125.0, 112.3, 62.0, 56.0, 13.8; IR (KBr) \(\nu\): 3350, 2981, 2927, 1724, 1577, 1513, 1439, 1402, 1300, 1245, 1148, 1029, 799, 754 cm\(^{-1}\); HRMS (EI) calcd for C\(_{17}\)H\(_{19}\)N\(_3\)O\(_4\) [M]\(^+\) 329.1376, found 329.1375.

Diisopropyl 2-(2-(pyrimidin-2-ylamino)phenyl)malonate (3c)

\[
\text{iPrO}_2C-\text{CO}_2\text{iPr}
\]

\[
3c
\]

S5
1H NMR (700 MHz, CDCl3) δ 8.34 (d, J = 4.9 Hz, 2H), 8.31 (br s, 1H), 7.77 (d, J = 7.7 Hz, 1H), 7.35–7.41 (m, 2H), 7.13 (d, J = 7.7 Hz, 1H), 6.64 (t, J = 4.5 Hz, 1H), 5.01–4.97 (m, 2H), 4.67 (s, 1H), 1.21 (d, J = 6.3 Hz, 6H), 1.13 (d, J = 6.3 Hz, 6H); 13C NMR (175 MHz, CDCl3) δ 168.3, 160.5, 158.0, 137.8, 131.1, 128.8, 127.1, 125.2, 124.6, 112.3, 69.8, 56.5, 21.4, 21.3; IR (KBr) ν 3342, 2978, 2930, 1712, 1578, 1519, 1441, 1367, 1247, 1131, 799, 754 cm⁻¹; HRMS (EI) calcd for C19H23N3O4 [M]+ 357.1689, found 357.1691.

**Di-tert-butyl 2-(2-(pyrimidin-2-ylamino)phenyl)malonate (3d)**

![3d](image)

1H NMR (500 MHz, CDCl3) δ 8.43 (br s, 1H), 8.36 (d, J = 5.0 Hz, 2H), 7.72 (d, J = 8.0 Hz, 1H), 7.36–7.32 (m, 2H), 7.11 (d, J = 7.7 Hz, 1H), 6.41 (t, J = 5.0 Hz, 1H), 4.58 (s, 1H), 1.39 (s, 18H); 13C NMR (125 MHz, CDCl3) δ 168.0, 160.6, 158.0, 137.8, 131.2, 128.5, 127.2, 124.9, 124.4, 112.2, 82.6, 58.3, 27.7; IR (KBr) ν 3342, 2978, 2930, 1712, 1578, 1519, 1441, 1367, 1247, 1131, 799, 754 cm⁻¹; HRMS (EI) calcd for C21H27N3O4 [M]+ 385.2002, found 385.2002.

**Dibenzyl 2-(2-(pyrimidin-2-ylamino)phenyl)malonate (3e)**

![3e](image)

1H NMR (700 MHz, CDCl3) δ 8.28 (d, J = 4.9 Hz, 2H), 8.03 (br s, 1H), 7.69 (d, J = 8.4 Hz, 1H), 7.41–7.38 (m, 2H), 7.30–7.29 (m, 6H), 7.26–7.25 (m, 4H), 7.19 (d, J = 7.7 Hz, 1H), 6.63 (t, J = 4.9 Hz, 1H), 5.15 (d, J = 11.9 Hz, 2H), 5.04 (d, J = 12.6 Hz, 2H), 4.90 (s, 1H); 13C NMR (175 MHz, CDCl3) δ 168.4, 160.6, 158.0, 137.6, 135.0, 130.9, 129.1, 128.4, 128.3, 128.2, 127.6, 126.1, 125.3, 112.4, 67.6, 55.4; IR (KBr) ν 3358, 2957, 2924, 1725, 1577, 1440, 1218, 1136, 1002, 799, 748, 697 cm⁻¹; HRMS (EI) calcd for C27H32N3O4 [M]+ 453.1689, found 453.1683.
Methyl 2-(phenylsulfonyl)-2-(2-(pyrimidin-2-ylamino)phenyl)acetate (3f)

\[
\begin{align*}
\text{MeO}_2\text{C} & \quad \text{SO}_{\text{Ph}} \\
\text{N} & \quad \text{N}
\end{align*}
\]

\(3f\)

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.39 (d, \(J = 4.5\) Hz, 2H), 7.94 (br s, 1H), 7.72–7.71 (m, 3H), 7.62 (t, \(J = 7.5\) Hz, 1H), 7.45 (t, \(J = 7.5\) Hz, 2H), 7.40 (t, \(J = 9.0\) Hz, 1H), 7.29 (d, \(J = 8.0\) Hz, 1H), 7.05 (t, \(J = 8.0\) Hz, 1H), 6.74 (d, \(J = 4.5\) Hz, 1H), 5.69 (s, 1H), 3.65 (s, 3H); \(^{13}\)C NMR (175 MHz, CDCl\(_3\)) \(\delta\) 165.3, 160.6, 158.1, 138.6, 135.8, 134.3, 130.3, 130.2, 130.1, 128.5, 126.1, 125.2, 121.9, 112.9, 69.9, 53.0; IR (KBr) \(\nu\) 3354, 2954, 2923, 1743, 1577, 1513, 1440, 1405, 1322, 1309, 1144, 1080, 799, 758, 686 cm\(^{-1}\); HRMS (EI) calcd for C\(_{19}\)H\(_{17}\)N\(_3\)O\(_4\)S [M]+ 383.0940, found 383.0949.

Ethyl 2-(diethoxyphosphoryl)-2-(2-(pyrimidin-2-ylamino)phenyl)acetate (3g)

\[
\begin{align*}
\text{EtO}_2\text{C} & \quad \text{P(O)(Et)}_2 \\
\text{N} & \quad \text{N}
\end{align*}
\]

\(3g\)

\(^1\)H NMR (700 MHz, CDCl\(_3\)) \(\delta\) 8.63 (br s, 1H), 8.38 (br s, 2H), 7.74 (d, \(J = 7.7\) Hz, 1H), 7.61 (d, \(J = 7.7\) Hz, 1H), 7.34 (t, \(J = 7.7\) Hz, 1H), 7.16 (t, \(J = 7.7\) Hz, 1H), 6.68 (t, \(J = 4.9\) Hz, 1H), 4.57 (d, \(J = 2.8\) Hz, 1H), 4.16–3.99 (m, 6H), 1.25 (t, \(J = 7.0\) Hz, 3H), 1.21 (t, \(J = 7.0\) Hz, 3H), 7.15 (t, \(J = 7.0\) Hz, 3H); \(^{13}\)C NMR (175 MHz, CDCl\(_3\)) \(\delta\) 167.5, 160.3, 158.0, 137.5 (d, \(J_{\text{C-P}} = 5.6\) Hz), 130.1 (d, \(J_{\text{C-P}} = 5.0\) Hz), 128.5 (d, \(J_{\text{C-P}} = 2.8\) Hz), 125.5, 125.0 (d, \(J_{\text{C-P}} = 2.1\) Hz), 124.5 (d, \(J_{\text{C-P}} = 8.5\) Hz), 112.2, 64.0 (d, \(J_{\text{C-P}} = 7.0\) Hz), 63.3 (d, \(J_{\text{C-P}} = 7.0\) Hz), 61.8, 48.1 (d, \(J_{\text{C-P}} = 137.3\) Hz), 16.3 (d, \(J_{\text{C-P}} = 5.6\) Hz), 16.2 (d, \(J_{\text{C-P}} = 5.9\) Hz), 13.8; IR (KBr) \(\nu\) 3262, 2981, 2926, 1730, 1577, 1517, 1439, 1405, 1237, 1016, 962, 797, 751 cm\(^{-1}\); HRMS (EI) calcd for C\(_{18}\)H\(_{20}\)N\(_3\)O\(_3\)P [M]+ 393.1454, found 393.1452.

Diisopropyl 2-(2-(pyridin-2-ylamino)phenyl)malonate (3h)
\[ \text{Diisopropyl 2-}(5\text{-methoxy-2-(pyrimidin-2-ylamino)phenyl})\text{malonate (3i)} \]

\[ \text{Diisopropyl 2-}(5\text{-methyl-2-(pyrimidin-2-ylamino)phenyl})\text{malonate (3j)} \]
Diisopropyl 2-(5-butyl-2-(pyrimidin-2-ylamino)phenyl)malonate (3k)

\[ \text{3k} \]

\[^{1}\text{H NMR (400 MHz, CDCl}_3\text{) \delta 8.32 (d, } J = 4.8 \text{ Hz, 2H), 8.07 (br s, 1H), 7.57 (d, } J = 6.8 \text{ Hz, 1H), 7.16 (d, } J = 6.4 \text{ Hz, 2H), 6.62 (t, } J = 4.8 \text{ Hz, 1H), 5.02-4.96 (m, 2H), 4.64 (s, 1H), 2.33 (s, 3H), 1.21 (d, } J = 6.4 \text{ Hz, 6H), 1.13 (d, } J = 6.4 \text{ Hz, 6H); }^{13}\text{C NMR (175 MHz, CDCl}_3\text{) \delta 168.3, 160.8, 158.0, 134.9, 134.7, 131.6, 129.5, 127.5, 125.7, 112.0, 69.7, 56.2, 21.5, 21.4, 20.8; IR (KBr) } \nu 3347, 2980, 2925, 1723, 1581, 1517, 1444, 1410, 1242, 1163, 1097, 987, 905, 800 \text{ cm}^{-1}; \text{HRMS (EI) calcd for } C_{20}H_{25}N_3O_4 [M]^+ 371.1845, \text{found } 371.1843. \]

Diisopropyl 2-(5-chloro-2-(pyrimidin-2-ylamino)phenyl)malonate (3l)

\[ \text{3l} \]

\[^{1}\text{H NMR (500 MHz, CDCl}_3\text{) \delta 8.34 (d, } J = 4.5 \text{ Hz, 2H), 8.26 (br s, 1H), 7.75 (d, } J = 8.5 \text{ Hz, 1H), 7.34 (s, 1H), 7.30 (dd, } J = 8.5, 2.5 \text{ Hz, 1H), 6.66 (t, } J = 5.0 \text{ Hz, 1H), 5.02-4.97 (m, 2H), 4.61 (s, 1H), 1.21 (d, } J = 6.5 \text{ Hz, 6H), 1.13 (d, } J = 6.0 \text{ Hz, 6H); }^{13}\text{C NMR (125 MHz, CDCl}_3\text{) \delta 167.8, 160.4, 158.0, 136.6, 131.0, 129.4, 128.8, 128.4, 126.4, 112.7, 70.1, 56.2, 21.4, 21.3; IR (KBr) } \nu 3341, 2981, 2933, 1720, 1577, 1508, 1444, 1407, 1245, 1165, 1095, 976, 903, 798 \text{ cm}^{-1}; \text{HRMS (EI) calcd for } C_{19}H_{22}ClN_3O_4 [M]^+ 391.1299, \text{found } 391.1299. \]
Diisopropyl 2-(2-(pyrimidin-2-ylamino)-5-(trifluoromethyl)phenyl)malonate (3m)

\[
\begin{array}{c}
\text{H NMR (500 MHz, CDCl}_3\text{) }\delta 8.70\ (s, 1H), 8.40\ (d, J = 4.5\ Hz, 2H), 8.08\ (d, J = 8.5 \\
\text{Hz, 1H), 7.60–7.57 (m, 2H), 6.73 (t, J = 5.0\ Hz, 1H), 5.04–5.00 (m, 2H), 4.68 (s, 1H), 1.22 (d,} \\
\text{J = 6.0 Hz, 6H), 1.14 (d, J = 6.5 Hz, 6H); }\text{C NMR (125 MHz, CDCl}_3\text{) }\delta 167.9, 160.0, 158.1, \\
141.5, 128.5 \ (q, J_{CF} = 3.6\ Hz), 126.0, 125.9 \ (q, J_{CF} = 3.6\ Hz), 125.4 \ (q, J_{CF} = 32.6\ Hz), \\
125.1, 124.2, 122.9, 113.3, 56.9, 21.4, 21.3; }\text{IR (KBr) }\nu 3353, 2984, 2936, 1722, 1578, 1525, \\
1447, 1423, 1330, 1303, 1163, 1101\ cm}^{-1}; \text{HRMS (EI) calcd for C}_{20}H_{22}F_3N_3O_4 [M]^+ \\
425.1562, \text{found 425.1565.}
\end{array}
\]

Diisopropyl 2-(5-(ethoxycarbonyl)-2-(pyrimidin-2-ylamino)phenyl)malonate (3n)

\[
\begin{array}{c}
\text{H NMR (500 MHz, CDCl}_3\text{) }\delta 8.87\ (s, 1H), 8.40\ (d, J = 5.0\ Hz, 2H), 8.10\ (d, J = 8.5 \\
\text{Hz, 1H), 7.96 (s, 1H), 6.70 (t, J = 5.0\ Hz, 1H), 5.05–5.00 (m, 2H), 4.69 (s, 1H), 4.35 (q, J =} \\
7.0\ Hz, 2H), 1.37 (t, J = 7.5\ Hz, 3H), 1.22 (d, J = 6.0\ Hz, 6H), 1.12 (d, J = 6.0\ Hz, 6H); }\text{C NMR (125 MHz, CDCl}_3\text{) }\delta 168.2, 166.0, 160.0, 158.0, 142.7, 133.2, 130.3, 125.2, 125.0, \\
123.0, 113.2, 70.2, 60.8, 57.4, 21.4, 21.3, 14.3; }\text{IR (KBr) }\nu 3335, 2980, 2923, 1711, 1576, \\
1519, 1444, 1415, 1278, 1171, 1095, 1017, 988, 913, 797, 766\ cm}^{-1}; \text{HRMS (EI) calcd for C}_{22}H_{27}N_3O_6 [M]^+ \\
429.1900, \text{found 429.1902.}
\end{array}
\]

Diisopropyl 2-(4-methoxy-2-(pyrimidin-2-ylamino)phenyl)malonate (3o)

S10
Diisopropyl 2-(4-methyl-2-(pyrimidin-2-ylamino)phenyl)malonate (3p)

\[
\begin{array}{c}
\text{Pr}_2\text{O} & \text{CO}_2\text{Pr} \\
\text{Me} & \text{N} & \text{N} & \text{Me}
\end{array}
\]

\(^1\text{H NMR (500 MHz, CDCl}_3\text{)} \delta 8.36–8.35 \text{ (m, 3H), 7.44 (d, } J = 2.5 \text{ Hz, 1H), 7.24 (d, } J = 8.5 \text{ Hz, 1H), 6.68–6.64 \text{ (m, 2H), 5.02–4.97 \text{ (m, 2H), 4.60 (s, 1H), 3.80 (s, 3H), 1.21 (d, } J = 6.0 \text{ Hz, 6H), 1.14 (d, } J = 6.0 \text{ Hz, 6H); } ^{13}\text{C NMR (125 MHz, CDCl}_3\text{)} \delta 168.6, 160.4, 159.8, 158.0, 138.8, 131.9, 118.9, 112.4, 110.5, 110.0, 69.7, 55.9, 55.2, 21.5, 21.4; \text{ IR (KBr)} \nu 3345, 2980, 2925, 1720, 1577, 1520, 1442, 1254, 1165, 1098, 800 \text{ cm}^{-1}; \text{ HRMS (EI) calcd for } C_{20}H_{25}N_3O_5 [M]^+ 387.1794, \text{ found } 387.1793.\]

Diisopropyl 2-(4-ethyl-2-(pyrimidin-2-ylamino)phenyl)malonate (3q)

\[
\begin{array}{c}
\text{Pr}_2\text{O} & \text{CO}_2\text{Pr} \\
\text{Et} & \text{N} & \text{N}
\end{array}
\]

\(^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 8.36 \text{ (d, } J = 4.8 \text{ Hz, 2H), 8.26 (br s, 1H), 7.57 \text{ (s, 1H), 7.28 (d, } J = 2.8 \text{ Hz, 1H), 6.98 (d, } J = 7.6 \text{ Hz, 1H), 6.66 (t, } J = 4.8 \text{ Hz, 1H), 5.05–4.99 \text{ (m, 2H), 4.67 (s, 1H), 2.37 (s, 3H), 1.23 (d, } J = 6.4 \text{ Hz, 6H), 1.15 (d, } J = 6.0 \text{ Hz, 6H); } ^{13}\text{C NMR (175 MHz, CDCl}_3\text{)} \delta 168.4, 160.5, 157.9, 138.8, 137.3, 130.9, 125.9, 125.8, 124.4, 112.1, 69.6, 56.0, 21.5, 21.4, 21.3; \text{ IR (KBr)} \nu 3354, 2980, 2927, 1723, 1576, 1524, 1444, 1253, 1165, 1099, 801 \text{ cm}^{-1}; \text{ HRMS (EI) calcd for } C_{20}H_{25}N_3O_4 [M]^+ 371.1845, \text{ found } 371.1843.\]

Diisopropyl 2-(4-ethyl-2-(pyrimidin-2-ylamino)phenyl)malonate (3q)

\[
\begin{array}{c}
\text{Pr}_2\text{O} & \text{CO}_2\text{Pr} \\
\text{Et} & \text{N} & \text{N}
\end{array}
\]

\(^1\text{H NMR (700 MHz, CDCl}_3\text{)} \delta 8.35 \text{ (d, } J = 4.9 \text{ Hz, 2H), 8.23 (br s, 1H), 7.54 \text{ (s, 1H), 7.29 (d, } J = 7.7 \text{ Hz, 1H), 7.00 (d, } J = 7.7 \text{ Hz, 1H), 6.65 (t, } J = 4.9 \text{ Hz, 1H), 5.02–4.98 \text{ (m, 2H), 4.65 (s, 1H), 2.68 (q, } J = 7.7 \text{ Hz, 2H), 1.23–1.21 \text{ (m, 9H), 1.14 (d, } J = 6.3 \text{ Hz, 6H); } ^{13}\text{C NMR (175 MHz, CDCl}_3\text{)} \delta 168.4, 160.4, 158.0, 145.0, 137.2, 130.9, 125.0, 124.8, 124.7, 112.1, 69.7, 55.8, 28.5, 21.5, 21.4, 15.0; \text{ IR (KBr)} \nu 3350, 2978, 2932, 1721, 1574, 1523, 1445,
Diisopropyl 2-(4-fluoro-2-(pyrimidin-2-ylamino)phenyl)malonate (3r)

\[
\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 8.76 (s, 1H), 8.37 (d, J = 4.8 Hz, 2H), 7.70 (d, J = 8.0 Hz, 1H), 7.34–7.28 (m, 1H), 6.87 (t, J = 8.8 Hz, 1H), 6.68 (t, J = 4.8 Hz, 1H), 5.08 (s, 1H), 5.02–4.96 (m, 2H), 1.22 (d, J = 6.4 Hz, 6H), 1.11 (d, J = 6.4 Hz, 6H); \] ^13C NMR (175 MHz, CDCl\text{3}) \delta 168.2, 160.9 (d, J_{C-F} = 243.9 Hz), 160.0, 157.9, 138.8, 129.4 (d, J_{C-F} = 10.1 Hz), 120.2, 114.6, 112.7, 110.6 (d, J_{C-F} = 22.9 Hz), 70.2, 48.7, 21.4, 21.3.; IR (KBr) v 3337, 2982, 2926, 1721, 1575, 1517. 1438, 1401, 1235, 1171, 1098, 798 cm^{-1}; HRMS (EI) calcd for C_{19}H_{22}FN_{3}O_{4} [M]^+ 375.1594, found 375.1595.

Diisopropyl 2-(4-chloro-2-(pyrimidin-2-ylamino)phenyl)malonate (3s)

\[
\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 8.46 (s, 1H), 8.37 (d, J = 4.8 Hz, 2H), 7.92 (d, J = 2.0 Hz, 1H), 7.27 (d, J = 8.0 Hz, 1H), 7.08 (dd, J = 8.0, 2.0 Hz, 1H), 6.70 (t, J = 4.8 Hz, 1H), 5.04–4.98 (m, 2H), 4.63 (s, 1H), 1.21 (d, J = 6.4 Hz, 6H), 1.13 (d, J = 6.4 Hz, 6H); \] ^13C NMR (175 MHz, CDCl\text{3}) \delta 168.0, 160.0, 158.0, 139.0, 134.3, 132.1, 124.7, 124.6, 124.3, 112.9, 70.0, 56.1, 21.4, 21.3.; IR (KBr) v 3272, 2980, 2924, 1576, 1519, 1446, 1417, 1240, 1098, 994, 935, 796, 772 cm^{-1}; HRMS (EI) calcd for C_{19}H_{22}ClN_{3}O_{4} [M]^+ 391.1299, found 391.1300.

Diisopropyl 2-(3-(pyrimidin-2-ylamino)naphthalen-2-yl)malonate (3t)
$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.30 (br s, 1H), 8.22 (br s, 2H), 8.02 (d, $J$ = 8.0 Hz, 1H), 7.89–7.86 (m, 2H), 7.74 (d, $J$ = 8.5 Hz, 1H), 7.50–7.44 (m, 2H), 6.58 (t, $J$ = 5.0 Hz, 1H), 5.16 (s, 1H), 5.04–4.99 (m, 2H), 1.24 (d, $J$ = 6.5 Hz, 6H), 1.15 (d, $J$ = 6.5 Hz, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 167.8, 162.1, 158.3, 134.1, 133.1, 131.1, 129.4, 128.2, 127.4, 127.0, 126.5, 126.3, 123.6, 111.9, 69.3, 54.4, 21.6, 21.5; IR (KBr) $\nu$ 3199, 2980, 2933, 1726, 1585, 1519, 1446, 1374, 1263, 1162, 1100, 995, 904, 801 cm$^{-1}$; HRMS (EI) calcd for C$_{23}$H$_{25}$N$_3$O$_4$ [M]$^+$ 407.1845, found 407.1840.

**Diisopropyl 2-(3-methyl-2-(pyrimidin-2-ylamino)phenyl)malonate (3u)**

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.31 (d, $J$ = 4.8 Hz, 2H), 7.54 (br s, 1H), 7.32 (dd, $J$ = 7.2, 1.6 Hz, 1H), 7.27–7.20 (m, 2H), 6.63 (t, $J$ = 4.8 Hz, 1H), 4.97–4.90 (m, 2H), 4.77 (s, 1H), 2.23 (s, 3H), 1.21 (d, $J$ = 6.4 Hz, 6H), 1.15 (d, $J$ = 6.4 Hz, 6H); $^{13}$C NMR (175 MHz, CDCl$_3$) $\delta$ 168.0, 160.7, 158.1, 136.9, 135.4, 131.5, 130.9, 128.1, 127.0, 111.6, 69.4, 55.2, 21.5, 18.9; IR (KBr) $\nu$ 3216, 2979, 2932, 1725, 1580, 1445, 1228, 1157, 1097, 994, 913, 800 cm$^{-1}$; HRMS (EI) calcd for C$_{20}$H$_{25}$N$_3$O$_4$ [M]$^+$ 371.1845, found 371.1844.
**Typical procedure for the synthesis of indoles (5a–5p)**

To an oven-dried sealed tube charged with N-phenylpyridin-2-amine (4a) (34.0 mg, 0.2 mmol, 100 mol %), [RhCp*Cl₂]₂ (3.1 mg, 0.005 mmol, 2.5 mol %), and AgOAc (5 mg, 0.03 mmol, 15 mol %) in MeOH (1 mL) was added ethyl 2-diazo-3-oxobutanoate (2h) (37.5 mg, 0.24 mmol, 120 mol %) under air. The reaction mixture was allowed to stir at 60 °C for 24 h, and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (n-hexanes/EtOAc: 5:1) to afford 5b (52.8 mg) in 94% yield.
Characterization data for indole products (5a–5p)

Ethyl 2-methyl-1-(pyrimidin-2-yl)-1H-indole-3-carboxylate (5a)

1H NMR (400 MHz, CDCl3) δ 8.89 (d, J = 4.8 Hz, 2H), 8.17 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 7.6 Hz, 1H), 7.32 (t, J = 4.8 Hz, 1H), 7.29–7.22 (m, 2H), 4.44 (q, J = 7.2 Hz, 2H), 2.95 (s, 3H), 1.48 (t, J = 7.2 Hz, 3H); 13C NMR (175 MHz, CDCl3) δ 165.9, 158.5, 157.3, 145.5, 135.9, 127.1, 123.2, 122.9, 121.3, 118.8, 112.4, 108.3, 59.8, 14.5, 14.3; IR (KBr) ν 2978, 2929, 1659, 1564, 1456, 1418, 1399, 1193, 1094, 1024, 748 cm\(^{-1}\); HRMS (EI) calcd for C\(_{16}\)H\(_{18}\)N\(_2\)O\(_2\) [M]\(^{+}\) 281.1164, found 281.1167.

Ethyl 2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5b)

1H NMR (700 MHz, CDCl3) δ 8.81 (br s, 1H), 8.28 (d, J = 8.0 Hz, 1H), 8.03 (t, J = 7.7 Hz, 1H), 7.52–7.48 (m, 2H), 7.36–7.34 (m, 1H), 7.30–7.25 (m, 2H), 4.53 (q, J = 7.1 Hz, 2H), 2.80 (s, 3H), 1.56 (t, J = 7.1 Hz, 3H); 13C NMR (175 MHz, CDCl3) δ 166.0, 150.0, 149.9, 145.0, 138.6, 136.5, 126.7, 123.3, 122.7, 122.3, 122.1, 121.4, 110.2, 106.2, 59.6, 14.5, 13.1; IR (KBr) ν 2924, 1691, 1588, 1543, 1468, 1436, 1397, 1268, 1178, 1115, 1078, 784, 747 cm\(^{-1}\); HRMS (EI) calcd for C\(_{17}\)H\(_{16}\)N\(_2\)O\(_2\) [M]\(^{+}\) 280.1212, found 280.1215.

Methyl 2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5c)
1H NMR (500 MHz, CDCl₃) δ 8.75 (d, J = 5.0 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H), 7.98 (td, J = 8.5, 2.0 Hz, 1H), 7.48–7.43 (m, 2H), 7.32–7.26 (m, 1H), 7.24–7.21 (m, 2H), 4.01 (s, 3H), 2.75 (s, 3H); 13C NMR (125 MHz, CDCl₃) δ 166.4, 150.1, 150.0, 145.1, 138.6, 136.6, 126.6, 123.3, 122.7, 122.3, 122.1, 121.4, 110.3, 106.1, 50.8, 13.1; IR (KBr) ν 3055, 2946, 2974, 2928, 1685, 1588, 1541, 1468, 1435, 1391, 1364, 1276, 1201, 1159, 1113, 1098, 1079, 1022, 993, 785, 740 cm⁻¹; HRMS (EI) calcd for C₁₆H₁₄N₂O₂ [M]⁺ 266.1055, found 266.1057.

tert-Butyl 2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5d)

1H NMR (500 MHz, CDCl₃) δ 8.78 (br s, 1H), 8.22 (d, J = 8.0 Hz, 1H), 8.00 (td, J = 8.5, 2.0 Hz, 1H), 7.50–7.45 (m, 2H), 7.32–7.26 (m, 1H), 7.24–7.21 (m, 2H), 2.75 (s, 3H), 1.74 (s, 9H); 13C NMR (125 MHz, CDCl₃) δ 165.4, 150.3, 150.0, 144.5, 138.5, 136.5, 126.8, 123.2, 122.6, 122.2, 121.1, 121.4, 110.2, 107.5, 80.0, 28.7, 13.2; IR (KBr) ν 2974, 2928, 1685, 1588, 1541, 1468, 1435, 1391, 1364, 1276, 1201, 1159, 1113, 1098, 1079, 1022, 993, 785, 740 cm⁻¹; HRMS (EI) calcd for C₁₉H₂₀N₂O₂ [M]⁺ 308.1525, found 308.1524.

Benzyl 2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5e)
Ethyl 2-propyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5e)

\[ \text{Et}_2\text{N} \text{IR} (\text{KBr}) \nu: 3362, 2980, 2929, 1692, 1587, 1532, 1467, 1436, 1321, 1273, 1180, 1069, 993, 746, 696 \text{ cm}^{-1} \]

\[ \text{IR} (\text{KBr}) \nu: 3056, 2980, 2931, 1693, 1587, 1541, 1469, 1437, 1400, 1267, 1177, 1115, 1075, 1025, 995, 783, 748, 698 \text{ cm}^{-1} \]

\[ \text{HRMS (EI)} \text{ calcd for C}_{22}\text{H}_{18}\text{N}_2\text{O}_2 [\text{M}^+] 342.1368, \text{ found 342.1370} \]

Ethyl 2-propyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5f)

\[ \text{Et}_2\text{N} \text{IR} (\text{KBr}) \nu: 3362, 2961, 2929, 1692, 1587, 1532, 1467, 1436, 1321, 1273, 1180, 1069, 993, 746, 696 \text{ cm}^{-1} \]

\[ \text{IR} (\text{KBr}) \nu: 3056, 2980, 2931, 1693, 1587, 1541, 1469, 1437, 1400, 1267, 1177, 1115, 1075, 1025, 995, 783, 748, 698 \text{ cm}^{-1} \]

\[ \text{HRMS (EI)} \text{ calcd for C}_{19}\text{H}_{20}\text{N}_2\text{O}_2 [\text{M}^+] 308.1525, \text{ found 308.1523} \]

Ethyl 5-methoxy-2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5h)
$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.69 (s, 1H), 7.92 (dt, $J = 8.5, 1.5$ Hz, 1H), 7.71 (d, $J = 2.5$ Hz, 1H), 7.41–7.37 (m, 2H), 7.10 (d, $J = 9.0$ Hz, 1H), 6.80 (dd, $J = 9.0, 2.5$ Hz, 1H), 4.42 (q, $J = 7.0$ Hz, 2H), 3.89 (s, 3H), 2.69 (s, 3H), 1.46 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 166.0, 156.0, 150.3, 149.9, 145.0, 138.5, 131.6, 127.7, 123.2, 121.9, 112.3, 111.1, 106.1, 103.6, 59.5, 55.7, 14.5, 13.3; IR (KBr) $\nu$ 2980, 2927, 1688, 1581, 1539, 1469, 1434, 1399, 1270, 1186, 1160, 1078, 1032, 851, 780, 747 cm$^{-1}$; HRMS (EI) calcd for C$_{18}$H$_{18}$N$_2$O$_3$ [M]$^+$ 310.1317, found 310.1312.

**Ethyl 2,5-dimethyl-1-(pyridin-2-yl)-1$H$-indole-3-carboxylate (5i)**

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.70 (d, $J = 3.5$ Hz, 1H), 7.98 (s, 1H), 7.92 (dt, $J = 8.5, 2.0$ Hz, 1H), 7.41–7.37 (m, 2H), 7.09 (d, $J = 8.0$ Hz, 1H), 6.99 (d, $J = 8.5$ Hz, 1H), 4.43 (q, $J = 7.0$ Hz, 2H), 2.69 (s, 3H), 2.48 (s, 3H), 1.47 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 166.1, 150.3, 149.9, 144.8, 138.5, 135.0, 131.7, 127.0, 124.1, 123.1, 122.0, 121.2, 109.9, 105.9, 59.5, 21.6, 14.6, 13.2; IR (KBr) $\nu$ 2976, 2923, 1687, 1588, 1541, 1469, 1434, 1397, 1268, 1197, 1150, 1132, 1075, 1035, 993, 883, 782 cm$^{-1}$; HRMS (EI) calcd for C$_{18}$H$_{18}$N$_2$O$_2$ [M]$^+$ 294.1368, found 294.1363.

**Ethyl 2-methyl-1-(pyridin-2-yl)-5-(trifluoromethoxy)-1$H$-indole-3-carboxylate (5j)**
**Ethyl 5-chloro-2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5k)**

1H NMR (500 MHz, CDCl₃) δ 8.70 (d, J = 3.5 Hz, 1H), 8.15 (s, 1H), 7.95 (dt, J = 8.5, 1.5 Hz, 1H), 7.45–7.43 (m, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.11 (s, 1H), 4.43 (q, J = 7.0 Hz, 2H), 3.89 (s, 3H), 2.69 (s, 3H), 1.47 (t, J = 7.0 Hz, 3H); 13C NMR (125 MHz, CDCl₃) δ 165.0, 150.1, 149.8, 146.1, 138.7, 128.1, 127.8, 123.5, 122.9, 122.0, 121.1, 111.4, 106.0, 59.8, 14.5, 13.2; IR (KBr) ν 3062, 2978, 2926, 1692, 1587, 1541, 1435, 1396, 1183, 1085, 877, 780, 746 cm⁻¹; HRMS (EI) calcd for C_{17}H_{15}ClN_{2}O_{2} [M]⁺ 314.0822, found 314.0821.

**Ethyl 6-methoxy-2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5l)**
Ethyl 2,6-dimethyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5m)

Ethyl 6-fluoro-2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5n)
1H NMR (500 MHz, CDCl₃) δ 8.72 (d, J = 3.5 Hz, 1H), 7.95 (td, J = 9.0, 2.0 Hz, 1H), 7.46–7.44 (m, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.10–7.06 (m, 1H), 6.95–6.89 (m, 2H), 4.40 (q, J = 7.0 Hz, 2H), 2.61 (s, 3H), 1.43 (t, J = 7.0 Hz, 3H); 13C NMR (125 MHz, CDCl₃) δ 165.2, 155.7 (d, J_C-F = 250.0 Hz), 150.1 (d, J_C-F = 8.6 Hz), 144.2, 139.3 (d, J_C-F = 10.0 Hz), 138.7, 123.6, 123.3 (d, J_C-F = 8.0 Hz), 122.3, 114.7 (d, J_C-F = 19.0 Hz), 108.5 (d, J_C-F = 21.8 Hz), 106.4 (q, J_C-F = 3.8 Hz), 105.8 (d, J_C-F = 3.0 Hz), 60.1, 14.3, 13.0; IR (KBr) ν 3056, 2980, 2929, 1692, 1587, 1542, 1468, 1434, 1398, 1219, 1154, 1079, 766, 726 cm⁻¹; HRMS (EI) calcd for C₁₇H₁₅FN₂O₂ [M]⁺ 298.1118, found 298.1121.

Ethyl 6-chloro-2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5o)

1H NMR (500 MHz, CDCl₃) δ 8.72 (d, J = 4.5 Hz, 1H), 8.07 (d, J = 8.5 Hz, 1H), 7.96 (td, J = 8.5, 2.0 Hz, 1H), 7.47–7.43 (m, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.22–7.20 (m, 2H), 4.42 (q, J = 7.5 Hz, 2H), 2.68 (s, 3H), 1.46 (t, J = 7.5 Hz, 3H); 13C NMR (125 MHz, CDCl₃) δ 165.6, 150.1, 149.6, 145.5, 138.8, 136.9, 128.6, 125.3, 123.6, 122.8, 122.4, 122.0, 110.4, 106.3, 59.7, 14.5, 13.1; IR (KBr) ν 3055, 2978, 2930, 1693, 1587, 1545, 1470, 1437, 1396, 1262, 1196, 1125, 1063, 813, 786, 747 cm⁻¹; HRMS (EI) calcd for C₁₇H₁₅ClN₂O₂ [M]⁺ 314.0822, found 314.0821.

Ethyl 2,7-dimethyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5p)
$^1$H NMR (500 MHz, CDCl$_3$) δ 8.68 (d, $J = 3.5$ Hz, 1H), 8.09 (d, $J = 8.0$ Hz, 1H), 7.88 (td, $J = 8.5, 2.0$ Hz, 1H), 7.48–7.46 (m, 1H), 6.91 (d, $J = 7.0$ Hz, 1H), 4.42 (q, $J = 7.0$ Hz, 2H), 2.50 (s, 3H), 1.78 (s, 3H), 1.46 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 166.0, 152.1, 149.4, 145.5, 138.1, 135.6, 127.2, 125.3, 124.3, 124.2, 122.0, 119.4, 105.5, 59.5, 18.8, 14.5, 12.6; IR (KBr) ν 3048, 2978, 2927, 1692, 1587, 1551, 1469, 1438, 1399, 1245, 1201, 1098, 792, 744 cm$^{-1}$; HRMS (EI) calcd for C$_{18}$H$_{18}$N$_2$O$_2$ [M]$^+$ 294.1368, found 294.1363.
General procedure and characterization for C7-alkylation of indole 5b

To an oven-dried sealed tube charged with ethyl 2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5b) (56.1 mg, 0.2 mmol, 100 mol %), [RhCp*Cl₂]₂ (3.1 mg, 0.005 mmol, 2.5 mol %), and AgSbF₆ (6.8 mg, 0.02 mmol, 10 mol %) in EtOH (1 mL) was diisopropyl 2-diazaomalonate (2c) (64.2 mg, 0.24 mmol, 150 mol %). The reaction mixture was allowed to stir at room temperature for 24 h. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (n-hexanes/EtOAc: 4:1) to afford 3a (83.7 mg) in 90% yield.

Diisopropyl 2-(3-(ethoxycarbonyl)-2-methyl-1-(pyridin-2-yl)-1H-indol-7-yl)malonate (7a)

![Chemical Structure of 7a]

¹H NMR (500 MHz, CDCl₃) δ 8.69 (d, J = 5.0 Hz, 1H), 8.20 (d, J = 7.5 Hz, 1H), 7.91 (t, J = 8.0 Hz, 1H), 7.50–7.48 (m, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.26–7.21 (m, 2H), 4.92–4.87 (m, 2H), 4.42 (q, J = 7.0 Hz, 2H), 3.96 (s, 1H), 2.42 (s, 3H), 1.43 (t, J = 7.5 Hz, 3H), 1.14 (d, J = 6.5 Hz, 6H), 1.12 (t, J = 6.5 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 167.4, 165.8, 151.7, 150.4, 146.1, 138.9, 135.0, 128.0, 124.5, 124.3, 124.2, 122.1, 121.5, 116.4, 106.0, 69.2, 59.6, 52.7, 21.5, 21.4, 14.5, 12.6; IR (KBr) ν 3051, 2980, 2933, 1726, 1695, 1467, 1438, 1241, 1167, 1097, 993, 801, 747 cm⁻¹; HRMS (EI) calcd for C₂₆H₃₀N₂O₆ [M]+ 466.2104, found 466.2104.
General procedure and characterization for C7-cyanation of indole 5b

To an oven-dried sealed tube charged with ethyl 2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5b) (56.1 mg, 0.2 mmol, 100 mol %), [RhCp*Cl₂]₂ (6.2 mg, 0.01 mmol, 5 mol %), AgSbF₆ (13.7 mg, 0.04 mmol, 20 mol %), and NaOAc (4.9 mg, 0.06 mmol, 30 mol %) in DCE (1 mL) was added N-cyano-N-phenyl-p-methylbenzenesulfonamide (NCTS) (6a) (108.9 mg, 0.4 mmol, 200 mol %). The reaction mixture was allowed to stir at 110 °C for 24 h, and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (n-hexanes/EtOAc = 4:1) to afford 7b (28.1 mg) in 46% yield.

Ethyl 7-cyano-2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (7b)

![Chemical structure of 7b](image)

¹H NMR (500 MHz, CDCl₃) δ 8.76 (d, J = 5.5 Hz, 1H), 8.45 (d, J = 8.0 Hz, 1H), 8.01 (td, J = 9.0, 2.0 Hz, 1H), 7.60–7.57 (m, 1H), 7.49 (d, J = 7.5 Hz, 1H), 7.45 (d, J = 7.5 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 4.43 (q, J = 7.0 Hz, 2H), 2.59 (s, 3H), 1.46 (t, J = 7.0 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 165.1, 150.2, 148.9, 146.9, 138.8, 135.7, 128.9, 128.0, 126.8, 125.4, 124.3, 121.9, 116.0, 106.2, 94.8, 60.0, 14.5, 12.7; IR (KBr) ν 3054, 2923, 2853, 1698, 1468, 1443, 1258, 1087, 799, 740 cm⁻¹; HRMS (EI) calcd for C₁₈H₁₃N₃O₂ [M]+ 305.1164, found 305.1168.
General procedure and characterization for C7-amidation of indole 5b

To an oven-dried sealed tube charged with ethyl 2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5b) (56.1 mg, 0.2 mmol, 100 mol %), [RhCp*Cl₂]₂ (6.2 mg, 0.01 mmol, 5 mol %) and AgSbF₆ (13.7 mg, 0.04 mmol, 20 mol %) was added n-butyl isocyanate (6b) (67.5 µL, 0.6 mmol, 300 mol %) and DCE (1 mL) under N₂ atmosphere. The reaction mixture was allowed to stir at 100 °C for 24 h and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (n-hexanes/EtOAc = 2:1) to afford 7c (46.2 mg) in 61% yield.

Ethyl 7-(butylcarbamoyl)-2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (7c)

![Chemical structure of 7c]

¹H NMR (500 MHz, CDCl₃) δ 8.57 (d, J = 4.5 Hz, 1H), 8.32–8.29 (m, 1H), 7.94 (td, J = 9.0, 2.0 Hz, 1H), 7.43–7.40 (m, 2H), 7.27–7.25 (m, 2H), 5.75 (t, J = 5.0 Hz, 1H), 4.43 (q, J = 7.0 Hz, 2H), 2.88 (q, J = 6.0 Hz, 2H), 2.61 (s, 3H), 1.48 (t, J = 7.0 Hz, 3H), 1.37–1.28 (m, 4H), 0.91 (t, J = 7.5 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 167.8, 165.7, 151.3, 149.0, 146.4, 138.7, 132.5, 128.3, 123.7, 123.6, 123.2, 122.4, 121.8, 121.7, 106.3, 59.8, 39.5, 31.2, 20.0, 14.5, 13.7, 13.0; IR (KBr) v 3325, 2956, 2926, 1698, 1630, 1553, 1468, 1250, 1184, 1091, 744 cm⁻¹; HRMS (EI) calcd for C₂₂H₂₅N₃O₃ [M]⁺ 379.1896, found 379.1889.
General procedure and characterization for the transformation of 3a

To an oven-dried sealed tube charged with dimethyl 2-(2-(pyrimidin-2-ylamino)phenyl)malonate (3a) (60.2 mg, 0.2 mmol, 100 mol %) in toluene (5 mL) was added DBU (121.7 mg, 0.8 mmol, 400 mol %). The reaction mixture was allowed to stir at 110 °C for 12 h. Upon completion, the solvent was removed under vacuum. The mixture was extracted with EtOAc (3 × 10 mL) and washed with brine. The organic layer was dried over MgSO₄ and concentrated in vacuo. The residue was purified by flash column chromatography (n-hexanes/EtOAc = 1:1.5) to afford 8a (23.9 mg) in 42% yield.

6-(Methoxycarbonyl)-6H-pyrimido[2,1-b]quinazoline-6-carboxylic acid (8a)

![8a](image)

$^1$H NMR (500 MHz, CDCl₃) δ 8.89 (d, $J = 4.5$ Hz, 2H), 7.82 (d, $J = 8.0$ Hz, 1H), 7.43–7.38 (m, 2H), 7.30 (t, $J = 4.9$ Hz, 1H), 7.21 (t, $J = 7.5$ Hz, 1H), 4.42 (br s, 1H), 3.76 (s, 3H); $^{13}$C NMR (125 MHz, CDCl₃) δ 171.8, 170.0, 158.6, 155.6, 142.0, 130.6, 126.0, 124.7, 124.0, 119.1, 113.8, 77.5, 54.1; IR (KBr) ν 3055, 2929, 1693, 1587, 1541, 1468, 1436, 1399, 1267, 1176, 1115, 1074, 995, 782 cm⁻¹; HRMS (EI) calcd for C₁₄H₁₀N₃O₄ [M]+ 285.0750, found 285.0750.
General procedure and characterization for deprotection of 5b

To a stirred solution of ethyl 2-methyl-1-(pyridin-2-yl)-1H-indole-3-carboxylate (5b) (56.1 mg, 0.2 mmol, 100 mol %) in DCM (5 mL) was added dropwise MeOTf (27 µL, 0.24 mmol, 120 mol %) at 0 °C. The reaction mixture was allowed to stir for 24 h at room temperature. The solvent was removed under vacuum, and the residue was dissolved in EtOH (2.5 mL). An aqueous solution of 2 N NaOH (1.2 mL) was added to the reaction mixture, and the resulting mixture was stirred at 60 °C for 12 h and cooled to room temperature. The solvent was removed under reduced pressure and the mixture was diluted with EtOAc and washed with brine. The combined organic layer was dried over MgSO₄ and concentrated in vacuo. The residue was purified by flash column chromatography (n-hexanes/EtOAc = 4:1) to afford 9a (25.7 mg) in 63% yield.

Ethyl 2-methyl-1H-indole-3-carboxylate (9a)

\[ \text{9a} \]

$^1$H NMR (500 MHz, CDCl₃) δ 8.37 (br s, 1H), 8.10 (d, $J = 7.0$ Hz, 1H), 7.29 (d, $J = 7.0$ Hz, 1H), 7.22–7.18 (m, 2H), 4.40 (q, $J = 7.0$ Hz, 2H), 2.74 (s, 3H), 1.45 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl₃) δ 166.0, 143.8, 134.5, 127.2, 122.3, 121.6, 121.3, 110.4, 104.7, 59.4, 14.6, 14.2; IR (KBr) ν 3303, 2922, 1714, 1659, 1550, 1456, 1367, 1271, 1196, 1120, 1091, 1010, 782, 732 cm$^{-1}$; HRMS (EI) calcd for C$_{12}$H$_{13}$NO$_2$ [M]$^+$ 203.0946, 203.0945.
Experimental procedure and characterization for the synthesis of deuterio-4a

To an oven-dried flask charged with 2-bromopyridine (316 mg, 2 mmol, 100 mol %), aniline-d5 (385 mg, 2.4 mmol, 120 mol %), potassium tert-butoxide (449 mg, 4 mmol, 200 mol%), Pd(OAc)$_2$ (22.4 mg, 0.1 mmol, 5 mol%) and (±)-BINAP (62.2 mg, 0.1 mmol, 5 mol%) were taken and the reaction vessel was flushed with N$_2$. Dry toluene (6 mL) was added to it through the septum. The reaction mixture was stirred at 120 °C for 6 h and monitored by TLC. Upon completion, water was added and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic phase was washed with brine and dried over MgSO$_4$. The organic layer was evaporated in vacuum. The crude product was purified by flash column chromatography ($n$-hexanes/EtOAc = 6:1) to give deuterio-4a (297 mg) in 85% yield.

$2',3',4',5',6'$-Pentadeuterium-N-phenylpyridin-2-amine (deuterio-4a)$^{5}$: $^1$H NMR (500 MHz, CDCl$_3$) δ 8.20 (d, $J = 4.5$ Hz, 1H), 7.48 (t, $J = 8.5$ Hz, 1H), 6.98 (br s, 1H), 6.89 (d, $J = 8.5$ Hz, 1H), 6.74-6.71 (m, 1H).

Reference:
Kinetic Isotope Effect (KIE) experiments

To an oven-dried sealed tube charged with N-phenylpyridin-2-amine (4a) (34.0 mg, 0.2 mmol, 100 mol %), [RhCp*Cl2]2 (3.1 mg, 0.005 mmol, 2.5 mol %) and AgOAc (5 mg, 0.03 mmol, 15 mol %) in MeOH (1 mL) was added ethyl 2-diazo-3-oxobutanoate (2h) (37.5 mg, 0.24 mmol, 120 mol %) and cyclohexanemethanol (22.8 mg, 0.2 mmol, 100 mol%) as an internal standard. In another reaction tube, deuterio-4a (35.0 mg, 0.2 mmol, 100 mol %) was used as a substrate under otherwise identical conditions. The two reactions were allowed to stir at 60 °C. An aliquot of each reaction mixture was taken at the time of 10 min, 20 min, 30 min, 40 min, and 50 min. The corresponding yield of each product was determined by GC (cyclohexanemethanol as an internal standard). A kinetic isotope effect value ($k_H/k_D$) of 1.02 was observed.

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\[
y = 0.1682x + 8.1829
\]

\[
y = 0.1714x + 5.6844
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<td>0.168</td>
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$^1$H NMR and $^{13}$C NMR copies of all products
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[Chemical structure image]

SpinWorks 4: NK-599

[Chemical structure image]
SpinWorks 4: NK-629

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transmitter freq: 400.131001 MHz
processed size: 131072 complex points
width: 8012.82 Hz = 20.0255 ppm = 0.122266 Hz/pt
number of scans: 16

SpinWorks 4: NK-629

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SpinWorks 4:
SpinWorks 4:

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LB: 0.300  QF: 0.0000

SpinWorks 4: NK-635-1
SpinWorks 4:

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SpinWorks 4: NK-633

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SpinWorks 4: NK-619

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SpinWorks 4: NK650P

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number of scans: 32
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SpinWorks 4:
SpinWorks 4: NK653P

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SpinWorks 4:
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number of scans: 16