Supporting information

Silver(I)-Mediated Oxidative C(sp³)−H Amination of Ethers with Azoles Derivatives Under Mild Conditions

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1. General Information

All reactions were carried out with magnetic stirring and in dried glassware. Standard syringe techniques were applied for transfer of dry solvents. All solvents before used were dried and distilled under standard methods. All other commercially available reagents were used as received. Proton (^1H NMR) and carbon (^13C NMR) nuclear magnetic resonance spectra were recorded at 400 MHz and 100 MHz, respectively. The chemical shifts are given in parts per million (ppm) on the delta (δ) scale. The solvent peak was used as a reference value, for ^1H NMR: TMS = 0.00 ppm, for ^13C NMR: CDCl₃ = 77.00 ppm. The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. Analytical TLC was performed on precoated silica gel plates. High-resolution mass spectra (HRMS) were obtained on an Agilent mass spectrometer using ESI-TOF (electrospray ionization-time of flight).

2. Experimental Section

2.1 General procedure for the N-alkylation of azoles

\[
\begin{align*}
\text{R}^1 & \quad \text{X} & \quad \text{Y} \\
\text{H} & \quad \text{Z} & \quad \text{H} \\
\text{ Ag}_2\text{CO}_3 \text{(1.0 equiv)} & \quad \text{i-C}_3\text{F}_7\text{I} \text{(1.5 equiv)} \quad \text{100 °C, 10 h}
\end{align*}
\]

In a 15 mL tube, the corresponding azoles 1 (0.2 mmol, 1.0 equiv), Ag₂CO₃ (0.2 mmol, 1.0 equiv), i-C₃F₇I (0.3 mmol, 1.5 equiv), and ethers 2 (2.0 mL) were added under air. The tube was sealed and the resulting solution was heated in a 100 °C oil bath with vigorous stirring for 10 h. Then the reaction mixture was cooled to room temperature. The mixture was extracted with ethyl acetate (20 mL × 3), and the combined organic layer was dried over anhydrous Na₂SO₄, filtered and the solvent was evaporated under vacuum. The residue was purified by flash chromatography using methanol/dichloromethane (1:10) as eluent to afford the products.

1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazole (3a)

^1H NMR (400 MHz, CDCl₃) δ 8.26 (s, 1H), 7.85 – 7.77 (m, 1H), 7.57 – 7.45 (m, 1H), 7.34 – 7.25 (m, 2H), 5.67 (t, J = 4Hz, 1H), 4.19 – 4.01 (m, 2H), 3.95 – 3.55 (m, 4H); ^13C NMR (100 MHz, CDCl₃) δ 143.27, 141.43, 132.93, 123.29, 122.63, 120.18, 110.45, 78.26, 67.81, 66.22,
1-(1,4-dioxan-2-yl)-2-methyl-1H-benzo[d]imidazole (3b)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.71 – 7.58 (m, 2H), 7.26 – 7.16 (m, 2H), 5.66 (dd, $J = 9.7, 3.2$ Hz, 1H), 4.15 – 4.06 (m, 2H), 4.05 – 3.95 (m, 1H), 3.90 – 3.79 (m, 3H), 2.66 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 150.53, 142.35, 133.45, 122.49, 122.30, 119.07, 111.59, 80.76, 67.53, 67.21, 65.67, 14.70; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{12}$N$_2$O$_2$ [M+H]$^+$: 205.0972, found: 205.0983.

1-(1,4-dioxan-2-yl)-2-ethyl-1H-benzo[d]imidazole (3c)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.72 – 7.49 (m, 2H), 7.20 – 7.05 (m, 2H), 5.57 (dd, $J = 9.8, 2.8$ Hz, 1H), 4.08 – 3.95 (m, 2H), 3.94 – 3.86 (m, 1H), 3.78 – 3.67 (m, 3H), 2.91 – 2.77 (m, 2H), 1.36 (t, $J = 7.5$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 154.97, 142.67, 133.39, 122.25, 122.00, 119.25, 111.82, 80.43, 67.47, 67.21, 65.55, 21.41, 11.80; HRMS (ESI-TOF) m/z Calcd for C$_{13}$H$_{16}$N$_2$O$_2$ [M+H]$^+$: 233.1285, found: 233.1304.

2-chloro-1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazole (3d)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.82 – 7.63 (m, 2H), 7.37 – 7.17 (m, 2H), 5.87 (dd, $J = 9.6, 3.2$ Hz, 1H), 4.19 – 3.96 (m, 3H), 3.97 – 3.77 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 141.87, 139.06, 133.50, 123.51, 123.11, 119.63, 112.27, 81.22, 67.34, 67.20, 65.70; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{11}$ClN$_2$O$_2$ [M+H]$^+$: 239.0582, found: 239.0589.
1-(1,4-dioxan-2-yl)-2-nonyl-1H-benzo[d]imidazole (3e)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.68 – 7.55 (m, 2H), 7.18 – 7.11 (m, 2H), 5.59 (dd, $J$ = 9.8, 3.0 Hz, 1H), 4.11 – 3.99 (m, 2H), 3.98 – 3.89 (m, 1H), 3.80 – 3.69 (m, 3H), 2.83 (t, $J$ = 4Hz, 2H), 1.83 – 1.71 (m, 2H), 1.41 – 1.16 (m, 12H), 0.80 (t, $J$ = 6.8 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 154.20, 142.72, 133.32, 122.32, 122.15, 119.33, 111.99, 80.64, 67.63, 67.36, 65.68, 31.74, 29.35, 29.33, 29.21, 29.15, 28.18, 27.90, 22.55, 14.01; HRMS (ESI-TOF) m/z Calcd for C$_{20}$H$_{30}$N$_2$O$_2$ [M+H]$^+$: 331.2380, found: 331.2397.

4-bromo-1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazole (3f)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.31 (s, 1H), 7.53 – 7.40 (t, $J$ = 8 Hz, 2H), 7.16 (t, $J$ = 7.9 Hz, 1H), 5.67 (t, $J$ = 3.6 Hz, 1H), 4.19 – 4.07 (m, 2H), 3.91 – 3.79 (m, 2H), 3.76 – 3.68 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 141.85, 133.46, 125.61, 124.23, 113.45, 109.95, 78.41, 67.54, 66.18, 62.80; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{11}$BrN$_2$O$_2$ [M+H]$^+$: 283.0077, found: 283.0083.

1-(1,4-dioxan-2-yl)-5-methyl-1H-benzo[d]imidazole (3g) and 1-(1,4-dioxan-2-yl)-6-methyl-1H-benzo[d]imidazole (3g')

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.23 (d, $J$ = 5.8 Hz, 2H), 7.68 (d, $J$ = 8.3 Hz, 1H), 7.60 (s, 1H), 7.40 (d, $J$ = 8.3 Hz, 1H), 7.31 (s, 1H), 7.15 (t, $J$ = 16 Hz, 2H), 5.74 – 5.63 (m, 2H), 4.19 – 4.09 (m, 4H), 3.94 – 3.72 (m, 8H), 2.49 (d, $J$ = 7.5 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 143.55, 141.48, 141.07, 133.54, 133.23, 132.55, 131.05, 124.93, 124.41, 119.96, 119.72, 110.37, 110.05, 78.47, 78.36, 67.96, 66.35, 63.32, 21.74, 21.41; HRMS (ESI-TOF) m/z Calcd for C$_{12}$H$_{14}$N$_2$O$_2$ [M+H]$^+$: 219.1128, found: 219.1140.
5-chloro-1-(1,4-dioxan-2-yl)-1\text{H}-benzo[d]imidazole (3h) and 6-chloro-1-(1,4-dioxan-2-yl)-1\text{H}-benzo[d]imidazole (3h')

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.32 (d, $J = 8.2$ Hz, 2H), 7.79 (s, 1H), 7.71 (d, $J = 8.6$ Hz, 1H), 7.53 (s, 1H), 7.43 (d, $J = 8.6$ Hz, 1H), 7.27 (d, $J = 8.6$ Hz, 2H), 5.73 – 5.62 (m, 2H), 4.23 – 4.08 (m, 4H), 3.94 – 3.68 (m, 8H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 143.82, 142.67, 142.20, 141.58, 133.52, 131.54, 129.22, 128.38, 123.85, 123.49, 120.87, 119.79, 111.51, 110.94, 78.45, 67.58, 67.50, 66.24, 62.96; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{11}$N$_2$O$_2$ [M+H]$^+$: 239.0582, found: 239.0584.

5-bromo-1-(1,4-dioxan-2-yl)-1\text{H}-benzo[d]imidazole (3i) and 6-bromo-1-(1,4-dioxan-2-yl)-1\text{H}-benzo[d]imidazole (3i')

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.15 (d, $J = 7.0$ Hz, 2H), 7.85 (s, 1H), 7.60 – 7.57 (m, 1H), 7.55 (s, 1H), 7.34 – 7.27 (m, 3H), 5.59 – 5.51 (m, 2H), 4.11 – 3.98 (m, 4H), 3.82 – 3.71 (m, 4H), 3.68 – 3.61 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.56, 142.47, 142.25, 142.08, 134.00, 131.91, 126.25, 125.93, 122.91, 121.37, 116.54, 115.55, 113.75, 111.83, 78.25, 78.23, 67.50, 67.45, 66.18, 62.84; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{11}$BrN$_2$O$_2$ [M+H]$^+$: 283.0077, found: 283.0083.

1-(1,4-dioxan-2-yl)-6-fluoro-1\text{H}-benzo[d]imidazole (3j)

and 1-(1,4-dioxan-2-yl)-5-fluoro-1\text{H}-benzo[d]imidazole (3j')

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.31 (s, 1H), 8.27 (s, 1H), 7.74 (dd, $J = 8.8$, 4.8 Hz, 1H), 7.53 – 7.40 (m, 2H), 7.22 (dd, $J = 8.6$, 2.4 Hz, 1H), 7.07 (qd, $J = 9.3$, 2.4 Hz, 2H), 5.72 – 5.67 (m, 1H), 5.67 – 5.62 (m, 1H), 4.23 – 4.10 (m, 4H), 3.96 – 3.84 (m, 4H), 3.83 – 3.72 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 159.92 (d, $J_{C,F} = 240.7$ Hz), 159.53 (d, $J_{C,F} = 238.4$ Hz), 143.81 (d, $J_{C,F} = 12.7$ Hz), 142.91, 142.10 (d, $J_{C,F} = 2.7$ Hz), 139.69, 133.24 (d, $J_{C,F} = 13.2$ Hz), 129.57, 121.06 (d, $J_{C,F} = 10.0$ Hz), 111.87 (d, $J_{C,F} = 26.0$ Hz), 111.27 (d, $J_{C,F} = 25.4$ Hz), 111.09 (d, $J_{C,F} = 10.7$ Hz), 106.05 (d, $J_{C,F} = 24.1$ Hz), 97.59 (d, $J_{C,F} = 28.0$ Hz), 78.56, 78.53, 67.80, 67.67, 66.37, 63.11; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{11}$FN$_2$O$_2$ [M+H]$^+$: 223.0877, found: 223.0890.
1-(1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazol-5-yl)ethan-1-one (3k) and 1-(1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazol-6-yl)ethan-1-one (3k′)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.43 (s, 1H), 8.33 (s, 1H), 8.28 (s, 1H), 8.17 (s, 1H), 7.98 – 7.87 (m, 2H), 7.73 (d, $J$ = 8.5 Hz, 1H), 7.45 (d, $J$ = 8.6 Hz, 1H), 5.69 (t, $J$ = 3.8 Hz, 1H), 5.65 (t, $J$ = 3.8 Hz, 1H), 4.17 – 4.01 (m, 4H), 3.86 (s, 6H), 3.84 – 3.62 (m, 8H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 167.18, 167.06, 146.70, 144.04, 143.11, 143.02, 136.24, 132.72, 125.21, 124.92, 124.78, 124.05, 122.52, 119.86, 112.82, 110.31, 78.38, 78.34, 67.74, 67.67, 66.26, 63.09, 63.06, 52.06, 51.99; HRMS (ESI-TOF) m/z Calcd for C$_{13}$H$_{14}$N$_2$O$_3$ [M+H]$^+$: 266.1061, found: 266.1089.

1-(1,4-dioxan-2-yl)-5-nitro-1H-benzo[d]imidazole (3l) and 1-(1,4-dioxan-2-yl)-6-nitro-1H-benzo[d]imidazole (3l′)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.56 (d, $J$ = 2.1 Hz, 1H), 8.46 (s, 1H), 8.42 – 8.37 (m, 2H), 8.14 – 8.05 (m, 2H), 7.76 (d, $J$ = 8.9 Hz, 1H), 7.53 (d, $J$ = 8.9 Hz, 1H), 5.76 (t, $J$ = 3.5 Hz, 1H), 5.72 (t, $J$ = 3.6 Hz, 1H), 4.26 – 4.08 (m, 4H), 3.92 – 3.75 (m, 4H), 3.73 – 3.66 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 174.58, 146.11, 144.95, 143.73, 143.69, 142.66, 137.16, 132.36, 120.16, 118.78, 118.18, 116.57, 110.82, 107.75, 78.45, 78.42, 67.30, 67.29, 66.22, 66.20, 62.73, 62.67; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{11}$N$_3$O$_4$ [M+H]$^+$: 250.0822, found: 250.0837.

1-(1,4-dioxan-2-yl)-7-methyl-1H-benzo[d]imidazole (3m)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.27 (s, 1H), 7.33 (d, $J$ = 8Hz, 1H), 7.22 (t, $J$ = 7.5 Hz, 1H), 7.11 (d, $J$ = 6.9 Hz, 1H), 5.68 (m, 1H), 4.18 – 4.07 (m, 2H), 3.91 – 3.66 (m, 4H), 2.69 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 142.50, 140.57, 132.66, 130.26, 123.41, 123.17, 107.98, 78.55, 68.05, 66.35, 63.43, 16.59; HRMS (ESI-TOF) m/z Calcd for C$_{12}$H$_{14}$N$_2$O$_2$ [M+H]$^+$: 219.1128, found: 219.1141.
1-(1,4-dioxan-2-yl)-5,6-dimethyl-1H-benzo[d]imidazole (3n)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.20 (s, 1H), 7.58 (s, 1H), 7.29 (s, 1H), 5.71 – 5.63 (t, $J = 8$ Hz, 1H), 4.21 – 4.09 (m, 2H), 3.95 – 3.73 (m, 4H), 2.39 (d, $J = 7.2$ Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 141.66, 140.66, 132.83, 131.89, 131.50, 120.22, 110.70, 78.51, 68.04, 66.42, 63.38, 20.55, 20.22; HRMS (ESI-TOF) m/z Calcd for C$_{13}$H$_{16}$N$_2$O$_2$ [M+H]$^+$: 233.1285, found: 233.1296.

5,6-dichloro-1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazole (3o)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.28 (s, 1H), 7.90 (s, 1H), 7.65 (s, 1H), 5.65 (t, $J = 3.6$ Hz, 1H), 4.28 – 4.10 (m, 2H), 3.98 – 3.82 (m, 2H), 3.81 – 3.66 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 143.42, 142.84, 132.35, 127.62, 127.00, 121.53, 112.33, 78.55, 67.53, 66.41, 62.88; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{10}$N$_2$O$_2$ [M+H]$^+$: 273.0192, found: 273.0195.

5,6-dichloro-1-(1,4-dioxan-2-yl)-2-methyl-1H-benzo[d]imidazole (3p)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.68 (s, 1H), 7.62 (s, 1H), 5.51 (dd, $J = 9.4$, 3.2 Hz, 1H), 4.09 – 3.96 (m, 1H), 3.96 – 3.84 (m, 2H), 3.82 – 3.70 (m, 3H), 2.54 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 152.52, 141.95, 132.56, 126.10, 120.08, 113.19, 80.65, 67.29, 66.98, 65.54, 14.59; HRMS (ESI-TOF) m/z Calcd for C$_{12}$H$_{12}$Cl$_2$N$_2$O$_2$ [M+H]$^+$: 287.0349, found: 287.0368.

1-(1,4-dioxan-2-yl)-1H-indazole (3q)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.06 (s, 1H), 7.73 (d, $J = 8.1$ Hz, 1H), 7.59 (d, $J = 8.5$ Hz, 1H), 7.42 (t, $J = 7.6$ Hz, 1H), 7.20 (t, $J = 7.5$ Hz, 1H), 5.85 (dd, $J = 8.1$, 2.8 Hz, 1H), 4.49 (dd, $J = 11.7$, 8.2 Hz, 1H), 4.11 (dd, $J = 11.7$, 2.8 Hz, 1H), 4.03 – 3.93 (m, 2H), 3.88 – 3.79 (m, 2H); $^{13}$C NMR
(100 MHz, CDCl$_3$) δ 139.84, 134.92, 126.88, 124.48, 121.53, 121.12, 109.58, 81.36, 67.87, 65.92; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{12}$N$_2$O$_2$ [M+H]$^+$: 205.0972, found: 205.0985.

1-(1,4-dioxan-2-yl)-5-methyl-1H-indazole (3r)
$^1$H NMR (400 MHz, CDCl$_3$) δ 7.91 (s, 1H), 7.45 – 7.38 (m, 2H), 7.21 – 7.20 (m, 0.55H), 7.19 – 7.17 (m, 0.45H), 5.75 (dd, $J$ = 8.2, 2.8 Hz, 1H), 4.40 (dd, $J$ = 11.7, 8.2 Hz, 1H), 4.03 (dd, $J$ = 11.7, 2.8 Hz, 1H), 3.94 – 3.85 (m, 2H), 3.82 – 3.71 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 138.52, 134.47, 131.06, 128.97, 124.87, 120.20, 109.21, 81.35, 67.92, 65.95, 21.24; HRMS (ESI-TOF) m/z Calcd for C$_{12}$H$_{14}$N$_2$O$_2$ [M+H]$^+$: 219.1128, found: 219.1140.

5-chloro-1-(1,4-dioxan-2-yl)-1H-indazole (3s)
$^1$H NMR (400 MHz, CDCl$_3$) δ 7.92 (s, 1H), 7.62 (s, 1H), 7.46 (d, $J$ = 8.9 Hz, 1H), 7.29 (dd, $J$ = 8.9, 1.9 Hz, 1H), 5.73 (dd, $J$ = 7.8, 2.9 Hz, 1H), 4.42 – 4.31 (m, 1H), 4.04 (dd, $J$ = 11.8, 2.9 Hz, 1H), 3.94 – 3.83 (m, 2H), 3.81 – 3.71 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 138.27, 134.12, 127.52, 127.14, 125.31, 120.29, 110.87, 81.50, 67.66, 65.89, 65.70; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{11}$ClN$_2$O$_2$ [M+H]$^+$: 239.0582, found: 239.0603.

1-(1,4-dioxan-2-yl)-1H-benzo[d][1,2,3]triazole (3t)
$^1$H NMR (400 MHz, CDCl$_3$) δ 8.07 (d, $J$ = 8.2 Hz, 1H), 7.75 (d, $J$ = 8.1 Hz, 1H), 7.51 (t, $J$ = 7.3 Hz, 1H), 7.39 (t, $J$ = 7.4 Hz, 1H), 6.09 (d, $J$ = 4.8 Hz, 1H), 4.59 – 4.47 (m, 1H), 4.22 (d, $J$ = 11.0 Hz, 1H), 4.03 – 3.81 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 145.90, 132.45, 127.75, 124.22, 119.86, 110.53, 81.82, 67.14, 65.79, 65.23; HRMS (ESI-TOF) m/z Calcd for C$_{10}$H$_{11}$N$_3$O$_2$ [M+H]$^+$: 206.0924, found: 206.0932.

2-(1,4-dioxan-2-yl)-5-methyl-2H-benzo[d][1,2,3]triazole (3u)
1H NMR (400 MHz, CDCl$_3$) $\delta$ 7.70 (d, $J = 8.8$ Hz, 1H), 7.55 (s, 1H), 7.16 (dd, $J = 8.8$, 1.4 Hz, 1H), 6.00 (dd, $J = 6.7$, 2.9 Hz, 1H), 4.41 (dd, $J = 11.9$, 6.7 Hz, 1H), 4.12 (dd, $J = 11.9$, 2.9 Hz, 1H), 4.03 – 3.96 (m, 1H), 3.93 – 3.86 (m, 1H), 3.83 – 3.77 (m, 2H), 2.41 (s, 3H); 13C NMR (100 MHz, CDCl$_3$) $\delta$ 144.77, 142.97, 137.27, 130.11, 117.83, 116.54, 86.22, 67.69, 65.83, 65.24, 22.06; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{13}$N$_3$O$_2$ [M+H]$^+$: 220.1081, found: 220.1081.

1-(1,4-dioxan-2-yl)-5-methyl-1H-benzo[d][1,2,3]triazole (3u') and 1-(1,4-dioxan-2-yl)-6-methyl-1H-benzo[d][1,2,3]triazole (3u'')

1H NMR (400 MHz, CDCl$_3$) $\delta$ 7.83 (d, $J = 8.5$ Hz, 1H), 7.71 (s, 1H), 7.52 (d, $J = 8.5$ Hz, 1H), 7.40 (s, 1H), 7.23 (d, $J = 8.5$ Hz, 1H), 7.11 (d, $J = 8.5$ Hz, 1H), 5.98 – 5.91 (m, 2H), 4.45 – 4.35 (m, 2H), 4.10 (dt, $J = 11.9$, 2.4 Hz, 2H), 3.91 – 3.68 (m, 8H), 2.43 (s, 3H), 2.40 (s, 3H); 13C NMR (100MHz, CDCl$_3$) $\delta$ 146.39, 144.44, 138.48, 134.26, 132.84, 130.85, 129.85, 126.47, 119.19, 118.66, 109.97, 109.59, 81.74, 81.62, 67.09, 65.74, 65.29, 65.16, 21.79, 21.23; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{13}$N$_3$O$_2$ [M+H]$^+$: 220.1081, found: 220.1099.

6-chloro-1-(1,4-dioxan-2-yl)-1H-benzo[d][1,2,3]triazole (3v)

1H NMR (400 MHz, CDCl$_3$) $\delta$ 7.89 (d, $J = 8.8$ Hz, 1H), 7.69 (s, 1H), 7.26 (dd, $J = 8.8$, 1.8 Hz, 1H), 5.96 (dd, $J = 6.7$, 2.9 Hz, 1H), 4.39 (dd, $J = 12.0$, 6.7 Hz, 1H), 4.15 (dd, $J = 12.0$, 2.9 Hz, 1H), 3.89 – 3.70 (m, 4H); 13C NMR (100 MHz, CDCl$_3$) $\delta$ 144.37, 134.25, 133.03, 125.58, 120.73, 110.65, 82.04, 66.95, 65.81, 64.99; HRMS (ESI-TOF) m/z Calcd for C$_{10}$H$_{10}$N$_3$O$_2$ [M+H]$^+$: 240.0534, found: 240.0553.

5-chloro-1-(1,4-dioxan-2-yl)-1H-benzo[d][1,2,3]triazole (3v')

1H NMR (400 MHz, CDCl$_3$) $\delta$ 7.97 (s, 1H), 7.63 (d, $J = 8.8$ Hz, 1H), 7.39 (dd, $J = 8.8$, 1.8 Hz, 1H), 6.00 (dd, $J = 6.7$, 2.9 Hz, 1H), 4.42 (dd, $J = 12.0$, 6.7 Hz, 1H), 4.16 (dd, $J = 12.0$, 2.8 Hz, 1H), 3.94 – 3.70 (m, 4H); 13C NMR (100MHz, CDCl$_3$) $\delta$ 146.56, 131.23, 130.20, 128.77, 119.28, 111.77, 82.12, 67.07, 65.87, 65.04; HRMS (ESI-TOF) m/z Calcd for C$_{10}$H$_{10}$N$_3$O$_2$ [M+H]$^+$: 240.0534, found: 240.0546.
3-(1,4-dioxan-2-yl)-3\textit{H}[1,2,3]triazolo[4,5-b]pyridine (3w)

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.65 (dd, $J = 4.5$, 1.4 Hz, 1H), 8.33 (dd, $J = 8.3$, 1.4 Hz, 1H), 7.32 (dd, $J = 8.3$, 4.5 Hz, 1H), 6.26 (dd, $J = 8.4$, 2.9 Hz, 1H), 4.63 (dd, $J = 11.6$, 8.4 Hz, 1H), 4.10 (dd, $J = 11.7$, 2.9 Hz, 1H), 4.05 – 3.94 (m, 2H), 3.89 – 3.79 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 150.78, 145.70, 136.90, 128.90, 120.35, 79.78, 67.26, 66.30, 65.87; HRMS (ESI-TOF) m/z Calcd for C$_9$H$_{10}$N$_4$O$_2$ [M+H]$^+$: 207.0877, found: 207.0900.

2-(1,4-dioxan-2-yl)-2\textit{H}[1,2,3]triazolo[4,5-b]pyridine (3w')

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.78 (dd, $J = 4.2$, 1.6 Hz, 1H), 8.20 (dd, $J = 8.6$, 1.6 Hz, 1H), 7.31 (dd, $J = 8.6$, 4.2 Hz, 1H), 6.07 (dd, $J = 6.0$, 2.9 Hz, 1H), 4.46 (dd, $J = 12.0$, 6.0 Hz, 1H), 4.14 (dd, $J = 12.0$, 2.9 Hz, 1H), 4.12 – 4.06 (m, 1H), 3.94 – 3.87 (m, 1H), 3.87 – 3.78 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 155.31, 152.89, 136.58, 127.60, 122.78, 86.96, 67.58, 65.89, 64.99; HRMS (ESI-TOF) m/z Calcd for C$_9$H$_{10}$N$_4$O$_2$ [M+H]$^+$: 207.0877, found: 207.0891.

1-(1,4-dioxan-2-yl)-1\textit{H}[1,2,3]triazolo[4,5-b]pyridine (3w'')

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.68 (dd, $J = 4.3$, 1.2 Hz, 1H), 8.13 (dd, $J = 8.4$, 1.5 Hz, 1H), 7.39 (dd, $J = 8.4$, 4.4 Hz, 1H), 6.07 (dd, $J = 6.5$, 3.0 Hz, 1H), 4.39 (dd, $J = 12.0$, 6.5 Hz, 1H), 4.20 (dd, $J = 12.0$, 3.0 Hz, 1H), 4.01 – 3.70 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 157.59, 148.53, 124.96, 122.57, 120.22, 82.77, 67.03, 65.90, 64.97; HRMS (ESI-TOF) m/z Calcd for C$_9$H$_{10}$N$_4$O$_2$ [M+H]$^+$: 207.0877, found: 207.0899.

1-(1,4-dioxan-2-yl)-1\textit{H}-pyrazolo[3,4-b]pyridine (3x)

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.50 (dd, $J = 4.6$, 1.5 Hz, 1H), 8.01 (s, 1H), 7.99 (dd, $J = 8.0$, 1.5 Hz, 1H), 7.10 (dd, $J = 8.0$, 4.6 Hz, 1H), 6.22 (dd, $J = 9.0$, 2.8 Hz, 1H), 4.44 (dd, $J = 11.5$, 9.0 Hz, 1H), 4.06 – 3.86 (m, 3H), 3.83 – 3.71 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 150.65, 149.12,
134.11, 130.21, 117.79, 115.87, 78.53, 67.88, 66.57, 65.79; HRMS (ESI-TOF) m/z Calcd for C_{10}H_{11}N_{3}O_{2} [M+H]^{+}: 206.0924, found: 206.0955.

1-(1,4-dioxan-2-yl)-3-methyl-1H-pyrazolo[3,4-b]pyridine (3y)

$^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.46 (dd, $J = 4.6$, 1.5 Hz, 1H), 7.91 (dd, $J = 8.0$, 1.5 Hz, 1H), 7.06 (dd, $J = 8.0$, 4.6 Hz, 1H), 6.15 (dd, $J = 9.5$, 2.8 Hz, 1H), 4.41 (dd, $J = 11.5$, 9.5 Hz, 1H), 4.10 – 3.85 (m, 3H), 3.83 – 3.67 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 151.44, 148.98, 143.09, 129.55, 117.06, 115.77, 78.46, 68.08, 66.91, 65.73, 12.49; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{13}$N$_3$O$_2$ [M+H]^{+}: 220.1081, found: 220.1103.

4-chloro-1-(1,4-dioxan-2-yl)-1H-pyrazolo[3,4-b]pyridine (3z)

$^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.47 (d, $J = 5.0$ Hz, 1H), 8.18 (s, 1H), 6.27 (dd, $J = 8.8$, 2.9 Hz, 1H), 4.51 (dd, $J = 11.6$, 8.9 Hz, 1H), 4.12 – 3.99 (m, 3H), 3.90 – 3.84 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 151.55, 149.51, 138.05, 132.59, 117.87, 115.83, 78.92, 67.77, 66.54, 65.82; HRMS (ESI-TOF) m/z Calcd for C$_{10}$H$_{10}$ClN$_3$O$_2$ [M+H]^{+}: 240.0534, found: 240.0563.

5-bromo-1-(1,4-dioxan-2-yl)-1H-pyrazolo[3,4-b]pyridine (3aa)

$^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.61 (d, $J = 2.1$ Hz, 1H), 8.22 (d, $J = 2.1$ Hz, 1H), 8.06 (s, 1H), 6.25 (dd, $J = 8.9$, 2.9 Hz, 1H), 4.50 (dd, $J = 11.6$, 8.9 Hz, 1H), 4.13 – 3.99 (m, 3H), 3.89 – 3.82 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 150.06, 149.12, 133.33, 132.04, 117.31, 113.46, 78.73, 67.79, 66.57, 65.83; HRMS (ESI-TOF) m/z Calcd for C$_{10}$H$_{10}$BrN$_3$O$_2$ [M+H]^{+}: 284.0029, found: 284.0007.
1-(1,4-dioxan-2-yl)-1H-imidazole (3ab)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.71 (s, 1H), 7.06 (d, $J = 28.3$ Hz, 2H), 5.37 (s, 1H), 4.13 – 3.56 (m, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 136.26 , 129.06 , 117.57 , 79.34 , 68.31 , 65.84 , 63.75; HRMS (ESI-TOF) m/z Calcd for C$_7$H$_{10}$N$_2$O$_2$ [M+H]$^+$: 155.0815, found: 155.0825.

1-(1,4-dioxan-2-yl)-2-methyl-1H-imidazole (3ac)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.11 (d, $J = 1.3$ Hz, 1H), 6.86 (d, $J = 1.2$ Hz, 1H), 5.28 (dd, $J = 6.2$, 3.0 Hz, 1H), 3.91 (dd, $J = 11.9$, 3.0 Hz, 1H), 3.85 – 3.64 (m, 5H), 2.38 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 145.07 , 127.15 , 117.13 , 78.27 , 68.41 , 66.05 , 64.19 , 13.12; HRMS (ESI-TOF) m/z Calcd for C$_8$H$_{12}$N$_2$O$_2$ [M+H]$^+$: 169.0972, found: 169.0981.

1-(1,4-dioxan-2-yl)-3-phenyl-1H-pyrazole (3ad)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.80 – 7.71 (m, 2H), 7.64 (d, $J = 2.5$ Hz, 1H), 7.36 – 7.27 (m, 2H), 7.26 – 7.20 (m, 1H), 6.55 (d, $J = 2.5$ Hz, 1H), 5.52 (dd, $J = 6.0$, 4.1 Hz, 1H), 4.06 – 4.01 (m, 2H), 3.89 – 3.68 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 152.20 , 132.89 , 130.20 , 128.49 , 127.87 , 125.76 , 103.55 , 83.39 , 68.41 , 65.92 , 65.05; HRMS (ESI-TOF) m/z Calcd for C$_{13}$H$_{14}$N$_2$O$_2$ [M+H]$^+$: 231.1128, found: 231.1151.

2-(1,4-dioxan-2-yl)-2H-1,2,3-triazole (3ae)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.63 (s, 2H), 5.76 (dd, $J = 7.3$, 2.9 Hz, 1H), 4.25 (dd, $J = 11.8$, 7.3 Hz, 1H), 4.01 (dd, $J = 11.8$, 2.9 Hz, 1H), 3.94 – 3.81 (m, 2H), 3.79 – 3.69 (m, 2H); $^{13}$C NMR (100
MHz, CDCl$_3$ δ 135.20, 84.77, 67.48, 65.83, 65.40; HRMS (ESI-TOF) m/z Calcd for C$_6$H$_9$N$_3$O$_2$ [M+H]$^+$: 156.0768, found: 156.0781.

1-(1,4-dioxan-2-yl)-1H-1,2,3-triazole (3ae$^*$)
$^1$H NMR (400 MHz, CDCl$_3$) δ 7.83 (d, $J = 1.0$ Hz, 1H), 7.67 (d, $J = 0.9$ Hz, 1H), 5.83 (dd, $J = 5.9$, 3.0 Hz, 1H), 4.10 (dd, $J = 12.0$, 3.0 Hz, 1H), 3.99 (dd, $J = 12.0$, 5.9 Hz, 1H), 3.84 – 3.67 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 133.73, 122.74, 81.79, 68.09, 66.02, 64.35; HRMS (ESI-TOF) m/z Calcd for C$_6$H$_9$N$_3$O$_2$ [M+H]$^+$: 156.0768, found: 156.0783.

1-(1,4-dioxan-2-yl)-1H-1,2,4-triazole(3af)
$^1$H NMR (400 MHz, CDCl$_3$) δ 8.39 (s, 1H), 7.93 (s, 1H), 5.71 – 5.47 (m, 1H), 4.09 – 3.97 (m, 2H), 3.85 – 3.70 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 151.64, 142.94, 81.15, 67.48, 65.73, 63.71; HRMS (ESI-TOF) m/z Calcd for C$_6$H$_9$N$_3$O$_2$ [M+H]$^+$: 156.0768, found: 156.0779.

1-(1,4-dioxan-2-yl)-5-methyl-1H-tetrazole (3ag)
$^1$H NMR (400 MHz, CDCl$_3$) δ 6.02 (dd, $J = 6.0$, 2.9 Hz, 1H), 4.35 (dd, $J = 12.0$, 6.0 Hz, 1H), 4.13 (dd, $J = 12.0$, 2.9 Hz, 1H), 4.08 – 4.03 (m, 1H), 3.96 – 3.85 (m, 3H), 2.59 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 163.21, 83.57, 66.98, 65.80, 64.79, 10.87; HRMS (ESI-TOF) m/z Calcd for C$_6$H$_{10}$N$_4$O$_2$ [M+H]$^+$: 171.0877, found: 171.0885.

9-(1,4-dioxan-2-yl)-9H-purine (3ah)
$^1$H NMR (400 MHz, CDCl$_3$) δ 9.11 (s, 1H), 8.95 (s, 1H), 8.47 (s, 1H), 6.01 (dd, $J = 5.6$, 3.0 Hz, 1H), 4.15 (dd, $J = 12.0$, 3.0 Hz, 1H), 4.06 (dd, $J = 12.0$, 5.6 Hz, 1H), 3.90 – 3.78 (m, 4H); $^{13}$C
NMR (100 MHz, CDCl$_3$) $\delta$ 152.90 , 150.98 , 148.80 , 143.69 , 133.70 , 77.07 , 68.25 , 66.19 , 64.14; HRMS (ESI-TOF) m/z Calcd for C$_9$H$_{10}$N$_4$O$_2$ [M+H]$^+$: 207.0877, found: 207.0882.

7-(1,4-dioxan-2-yl)-7H-purine (3ah')
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.10 (s, 1H), 9.04 (s, 1H), 8.52 (s, 1H), 5.78 (t, $J = 3.5$ Hz, 1H), 4.28 – 4.10 (m, 2H), 3.94 – 3.78 (m, 2H), 3.77 – 3.64 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 160.73 , 153.75 , 146.86 , 141.32 , 124.55 , 79.25 , 67.21 , 66.37 , 62.83; HRMS (ESI-TOF) m/z Calcd for C$_9$H$_{10}$N$_4$O$_2$ [M+H]$^+$: 207.0877, found: 207.0880.

N-(2-(1-(1,4-dioxan-2-yl)-1H-tetrazol-5-yl)-4-oxo-4H-chromen-8-yl)-4-(4-phenylbutoxy)benzamide (3ai)
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.93 – 8.82 (m, 2H), 7.98 (d, $J = 8.8$ Hz, 2H), 7.87 (dd, $J = 8.0$, 1.4 Hz, 1H), 7.44 (t, $J = 8.0$ Hz, 1H), 7.35 – 7.24 (m, 3H), 7.25 – 7.17 (m, 3H), 6.98 (m, 2H), 6.23 – 6.14 (m, 1H), 4.59 – 4.45 (m, 1H), 4.26 (dd, $J = 12.4$, 2.8 Hz, 1H), 4.15 – 4.01 (m, 3H), 4.00 – 3.84 (m, 3H), 2.72 (t, $J = 7.1$ Hz, 2H), 1.96 – 1.76 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 177.04 , 164.41 , 162.40 , 159.17 , 151.07 , 145.36 , 141.96 , 129.02 , 128.35 , 128.31 , 128.14 , 125.95 , 125.82 , 125.72 , 123.97 , 123.95 , 119.30 , 114.51 , 111.22 , 84.84 , 68.00 , 66.60 , 65.86 , 63.93 , 35.47 , 28.61 , 27.73; HRMS (ESI-TOF) m/z Calcd for C$_{31}$H$_{29}$N$_5$O$_6$ [M+H]$^+$: 568.2191, found: 568.2209.

3-((2'-(1-(1,4-dioxan-2-yl)-1H-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl)methyl)-2-butyl-1,3-diazaspiro[4.4]non-1-en-4-one (3aj)
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.89 (dd, $J = 7.6$, 1.3 Hz, 1H), 7.57 – 7.46 (m, 2H), 7.43 (dd, $J = 7.5$, 1.2 Hz, 1H), 7.20 – 7.14 (m, 2H), 7.08 (m, 2H), 5.94 (dd, $J = 5.4$, 2.9 Hz, 1H), 4.68 (s, 2H), 4.16 (dd, $J = 12.1$, 5.4 Hz, 1H), 4.01 (dd, $J = 12.1$, 2.9 Hz, 1H), 3.93 – 3.74 (m, 4H), 2.37 – 2.29
(m, 2H), 2.03 – 1.92 (m, 6H), 1.87 – 1.78 (m, 2H), 1.65 – 1.53 (m, 2H), 1.40 – 1.29 (m, 2H), 0.88 (t, J = 7.3 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ 186.46, 165.15, 161.89, 141.40, 140.41, 135.17, 130.67, 130.40, 130.18, 129.76, 127.66, 126.16, 125.75, 83.75, 76.37, 66.87, 65.78, 64.35, 43.23, 37.34, 28.70, 27.71, 26.02, 22.27, 13.68; HRMS (ESI-TOF) m/z Calcd for C29H34N6O3 [M+H]+: 515.2765, found: 515.2797.

**9-(tetrahydrofuran-2-yl)-9H-purin-6-amine (3ak)**

1H NMR (400 MHz, CDCl3) δ 8.35 (s, 1H), 7.93 (s, 1H), 6.30 (dd, J = 6.3, 3.1 Hz, 1H), 6.24 (s, 2H), 4.34 – 4.20 (m, 1H), 4.12 – 4.01 (m, 1H), 2.65 – 2.39 (m, 2H), 2.23 – 2.06 (m, 2H); 13C NMR (100 MHz, CDCl3) δ 155.43, 152.61, 149.17, 138.46, 120.18, 85.84, 69.59, 32.43, 24.19; HRMS (ESI-TOF) m/z Calcd for C9H11N5O [M+H]+: 206.1036, found: 206.1048.

**1-(tetrahydrofuran-2-yl)-1H-benzo[d]imidazole (4a)**

1H NMR (400 MHz, CDCl3) δ 7.93 (s, 1H), 7.75 – 7.67 (m, 1H), 7.39 – 7.33 (m, 1H), 7.23 – 7.14 (m, 2H), 6.06 (m, 1H), 4.12 – 4.01 (m, 1H), 3.98 – 3.88 (m, 1H), 2.39 – 2.24 (m, 2H), 2.09 – 1.91 (m, 2H); 13C NMR (100 MHz, CDCl3) δ 144.14, 140.13, 132.44, 122.88, 122.26, 120.17, 110.33, 85.84, 68.77, 31.65, 24.08; HRMS (ESI-TOF) m/z Calcd for C11H12N2O [M+H]+: 189.1022, found: 189.1001.

**1-(tetrahydro-2H-pyran-2-yl)-1H-benzo[d]imidazole (4b)**

1H NMR (400 MHz, CDCl3) δ 8.00 (s, 1H), 7.76 – 7.67 (m, 1H), 7.49 – 7.39 (m, 1H), 7.28 – 7.11 (m, 2H), 5.40 (dd, J = 9.8, 2.5 Hz, 1H), 4.11 – 3.96 (m, 1H), 3.75 – 3.59 (m, 1H), 2.20 – 1.93 (m, 3H), 1.76 – 1.52 (m, 3H); 13C NMR (100 MHz, CDCl3) δ 143.72, 140.31, 132.90, 123.06, 122.44, 120.24, 110.77, 83.29, 67.93, 30.65, 24.87, 22.63; HRMS (ESI-TOF) m/z Calcd for C12H14N2O [M+H]+: 203.1179, found: 203.1156.
1-(1,3-dioxolan-2-yl)-1H-benzo[d]imidazole (4c)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.06 (s, 1H), 7.85 – 7.77 (m, 1H), 7.61 – 7.54 (m, 1H), 7.37 – 7.29 (m, 2H), 6.25 (dd, $J$ = 5.7, 2.1 Hz, 1H), 5.45 (s, 1H), 5.08 (s, 1H), 4.44 (dd, $J$ = 9.7, 2.1 Hz, 1H), 4.22 (dd, $J$ = 9.7, 5.7 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.07, 141.23, 132.01, 123.56, 122.85, 120.55, 110.17, 96.39, 81.31, 69.43; HRMS (ESI-TOF) m/z Calcd for C$_{10}$H$_{10}$N$_2$O$_2$ [M+H]$^+$: 191.0815, found: 191.0822.

1-(benzo[d][1,3]dioxol-2-yl)-1H-benzo[d]imidazole (4d)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.11 (s, 1H), 7.85 (s, 1H), 7.82 (m, 1H), 7.37 – 7.29 (m, 1H), 7.28 – 7.25 (m, 2H), 7.05 – 6.96 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 145.27, 144.25, 140.10, 131.03, 124.12, 123.45, 122.94, 120.71, 111.04, 109.06, 107.36; HRMS (ESI-TOF) m/z Calcd for C$_{14}$H$_{10}$N$_2$O$_2$ [M+H]$^+$: 239.0815, found: 239.0824.

1-((2-methoxyethoxy)methyl)-1H-benzo[d]imidazole (4e)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.43 (s, 1H), 7.96 (d, $J$ = 7.7 Hz, 1H), 7.59 (d, $J$ = 8 Hz, 1H), 7.42 – 7.30 (m, 2H), 5.68 (s, 2H), 3.64 – 3.53 (m, 2H), 3.51 – 3.44 (m, 2H), 3.33 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 143.82, 141.36, 132.94, 124.45, 122.94, 120.71, 111.04, 109.06, 75.50, 71.51, 68.03, 59.03; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{14}$N$_2$O$_2$ [M+H]$^+$: 207.1128, found: 207.1149.

1-(1,2-dimethoxyethyl)-1H-benzo[d]imidazole (4e')

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.98 (s, 1H), 7.81 – 7.73 (m, 1H), 7.52 – 7.45 (m, 1H), 7.24 (m, 2H), 5.43 (t, $J$ = 5.6 Hz, 1H), 3.83 (dd, $J$ = 10.2, 5.6 Hz, 1H), 3.69 (dd, $J$ = 10.2, 5.5 Hz, 1H), 3.27 (s, 3H), 3.26 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.02, 141.76, 132.64, 123.34, 122.70, 122.64, 121.34, 119.45, 119.45, 75.50, 71.51, 68.03, 59.03; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{14}$N$_2$O$_2$ [M+H]$^+$: 207.1128, found: 207.1149.
120.53, 110.82, 86.83, 73.19, 59.52, 56.57; HRMS (ESI-TOF) m/z Calcd for C_{11}H_{14}N_{2}O [M+H]^+: 207.1128, found: 207.1139.

![Image of 1-(1-butoxybutyl)-1H-benzo[d]imidazole (4f)]

1-(1-butoxybutyl)-1H-benzo[d]imidazole (4f)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.02 (s, 1H), 7.86 – 7.78 (m, 1H), 7.62 – 7.51 (m, 1H), 7.33 – 7.27 (m, 2H), 5.40 ($J$ = 6.6 Hz, 1H), 3.40 – 3.29 (m, 1H), 3.30 – 3.19 (m, 1H), 2.21 – 2.07 (m, 1H), 2.04 – 1.87 (m, 1H), 1.57 – 1.46 (m, 2H), 1.44 – 1.16 (m, 4H), 0.91 ($J$ = 7.4 Hz, 3H), 0.84 ($t$, $J$ = 7.4 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 143.69, 141.28, 132.46, 123.10, 122.53, 120.23, 111.12, 87.18, 68.59, 37.60, 31.28, 19.16, 18.28, 13.69, 13.49; HRMS (ESI-TOF) m/z Calcd for C$_{15}$H$_{22}$N$_2$O [M+H]^+: 247.1805, found: 247.1819.

![Image of 1-((benzyloxy)(phenyl)methyl)-1H-benzo[d]imidazole (4g)]

1-((benzyloxy)(phenyl)methyl)-1H-benzo[d]imidazole (4g)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.06 (s, 1H), 7.85 (d, $J$ = 8.5 Hz, 1H), 7.42 – 7.26 (m, 12H), 7.23 – 7.18 (m, 1H), 6.56 (s, 1H), 4.67 (d, $J$ = 12.0 Hz, 1H), 4.46 (d, $J$ = 12.0 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.18, 142.31, 136.98, 136.05, 132.61, 128.99, 128.65, 128.63, 128.32, 128.05, 125.96, 123.33, 122.70, 120.40, 111.52, 84.45, 70.15; HRMS (ESI-TOF) m/z Calcd for C$_{21}$H$_{18}$N$_2$O [M+H]^+: 315.1492, found: 315.1523.

![Image of 1-(tetrahydrothiophen-2-yl)-1H-benzo[d]imidazole (4h)]

1-(tetrahydrothiophen-2-yl)-1H-benzo[d]imidazole (4h)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.28 (s, 1H), 7.87 – 7.71 (m, 1H), 7.51 – 7.39 (m, 1H), 7.35 – 7.24 (m, 2H), 6.04 (m, 1H), 3.32 – 2.32 (m, 1H), 3.08 – 2.96 (m, 1H), 2.47 – 2.15 (m, 3H), 2.12 – 1.91 (m, 1H), $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.47, 141.74, 133.19, 122.79, 122.34, 120.45, 109.92, 62.92, 38.15, 32.91, 28.60; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{12}$N$_2$S [M+H]^+: 205.0794, found: 205.0770.
1-(phenoxy methyl)-1H-benzo[d]imidazole (4i)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.94 (s, 1H), 7.85 – 7.78 (m, 1H), 7.54 – 7.47 (m, 1H), 7.37 – 7.27 (m, 4H), 7.05 (t, $J = 7.4$ Hz, 1H), 6.94 – 6.86 (m, 2H), 6.02 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 156.04, 143.70, 142.80, 133.25, 129.84, 123.73, 123.38, 122.95, 120.41, 117.08, 110.14, 73.34; HRMS (ESI-TOF) m/z Calcd for C$_{14}$H$_{12}$N$_2$O [M+H]$^+$: 225.1022, found: 225.1019.

2.2 Control experiments

To a mixture of benzimidazole 1a (0.2 mmol, 1.0 equiv.), Ag$_2$CO$_3$ (0.2 mmol, 1.0 equiv.), and 2-iodobutane (0.3 mmol, 1.5 equiv.) was added 1,4-dioxane 2a (2.0 mL) under air. The resultant mixture was heated in a preheated oil bath at 100 °C for 10 h. Then the reaction mixture was cooled to room temperature. The mixture was extracted with ethyl acetate (20 mL $\times$ 3), and the combined organic layer was dried over Na$_2$SO$_4$, filtered and the solvent was evaporated under vacuum. The crude product was obtained by purifying over a column of silica gel and eluted with methanol/dichloromethane (1:10) to give the expected product in 66% yield (3a-1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.98 (s, 1H), 7.87 – 7.76 (m, 1H), 7.47 – 7.39 (m, 1H), 7.33 – 7.27 (m, 2H), 4.48 – 4.20 (m, 1H), 2.16 – 1.80 (m, 2H), 1.61 (d, $J = 6.9$ Hz, 3H), 0.88 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 143.86, 140.88, 133.36, 122.57, 121.99, 120.35, 110.18, 53.78, 29.52, 20.57, 10.71; HRMS (ESI-TOF) m/z Calcd for C$_{11}$H$_{14}$N$_2$ [M+H]$^+$: 175.1230, found: 175.1223.
2.3 Electrospray Ionization-Time-of-Flight-Mass Spectrometry (ESI-TOF-MS) of compound 5

![HRMS spectrum of compound 5](image)

Figure 1. HRMS spectrum of compound 5

2.4 Kinetic isotope effect studies

To a mixture of benzimidazole 1a (0.2 mmol, 1.0 equiv.), Ag$_2$CO$_3$ (0.2 mmol, 1.0 equiv.), and i-C$_3$F$_7$I (0.3 mmol, 1.5 equiv.) was added an equivalent of 1,4-dioxane 2a (1.0 mL) and d$_8$-1,4-dioxane 2a-d (1.0 mL) under air. The resultant mixture was heated in a preheated oil bath at 100 °C for 10 h. Then the reaction mixture was cooled to room temperature. The mixture was extracted with ethyl acetate (20 mL × 3), and the combined organic layer was dried over Na$_2$SO$_4$, filtered and the solvent was evaporated under vacuum. The crude product was obtained by purifying over a column of silica gel and eluted with methanol/dichloromethane (1:10) to give the expected product in 32% yield (3a and 3a-d). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.21 (s, 1H), 7.81 – 7.69 (m, 1H), 7.50 – 7.42 (m, 1H), 7.29 – 7.21 (m, 2H), 5.71 – 5.62 (m, 0.89H), 4.16 – 4.02 (m, 1.78H), 3.91 – 3.65 (m, 3.59H).

The KIE value was calculated as $k_{H}/k_{D} = 8.1$. 
\[
\text{1a} + \text{2a-d} \xrightarrow{\text{Ag}_2\text{CO}_3 (1.0 \text{ equiv.}) / \text{i-C}_3\text{F}_7\text{I} (1.5 \text{ equiv.})} \text{100 }^\circ \text{C, 5 h, Ar} \]

\[k_\text{H}/k_\text{D}=8.1\]
3. $^1$H and $^{13}$C NMR spectra

1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazole (3a)
1-(1,4-dioxan-2-yl)-2-methyl-1H-benzo[d]imidazole (3b)
1-(1,4-dioxan-2-yl)-2-ethyl-1\textit{H}-benzo[d]imidazole (3c)
2-chloro-1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazole (3d)
1-(1,4-dioxan-2-yl)-2-nonyl-1H-benzo[d]imidazole (3e)
4-bromo-1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazole (3f)
1-(1,4-dioxan-2-yl)-5-methyl-1H-benzo[d]imidazole (3g) and 1-(1,4-dioxan-2-yl)-6-methyl-1H-benzo[d]imidazole (3g')
5-chloro-1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazole (3h) and 6-chloro-1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazole (3h')
5-bromo-1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazole (3i) and 6-bromo-1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazole (3i’)}
1-(1,4-dioxan-2-yl)-6-fluoro-1H-benzo[d]imidazole (3j)
And 1-(1,4-dioxan-2-yl)-5-fluoro-1H-benzo[d]imidazole (3j')
1-(1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazol-5-yl)ethan-1-one (3k) and 1-(1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazol-6-yl)ethan-1-one (3k')
1-(1,4-dioxan-2-yl)-5-nitro-1H-benzo[d]imidazole (3l) and 1-(1,4-dioxan-2-yl)-6-nitro-1H-benzo[d]imidazole (3l')
1-(1,4-dioxan-2-yl)-7-methyl-1H-benzo[d]imidazole (3m)
1-(1,4-dioxan-2-yl)-5,6-dimethyl-1H-benzo[d]imidazole (3n)
5,6-dichloro-1-(1,4-dioxan-2-yl)-1H-benzo[d]imidazole (3o)
5,6-dichloro-1-(1,4-dioxan-2-yl)-2-methyl-1H-benzo[d]imidazole (3p)
1-(1,4-dioxan-2-yl)-1H-indazole (3q)
1-(1,4-dioxan-2-yl)-5-methyl-1H-indazole (3r)
5-chloro-1-(1,4-dioxan-2-yl)-1H-indazole (3s)
1-(1,4-dioxan-2-yl)-1H-benzo[d][1,2,3]triazole (3t)
2-(1,4-dioxan-2-yl)-5-methyl-2H-benzo[d][1,2,3]triazole (3u)
1-(1,4-dioxan-2-yl)-5-methyl-1H-benzo[d][1,2,3]triazole(3u’) and 1-(1,4-dioxan-2-yl)-6-methyl-1H-benzo[d][1,2,3]triazole(3u’’)

\[
\begin{align*}
1-(1,4\text{-dioxan-2-yl})-5\text{-methyl-1H-benzo[d][1,2,3]triazole(3u')} & \\
1-(1,4\text{-dioxan-2-yl})-6\text{-methyl-1H-benzo[d][1,2,3]triazole(3u'')} & 
\end{align*}
\]
6-chloro-1-(1,4-dioxan-2-yl)-1H-benzo[d][1,2,3]triazole (3v)
5-chloro-1-(1,4-dioxan-2-yl)-1H-benzo[d][1,2,3]triazole (3v')
3-(1,4-dioxan-2-yl)-3H-[1,2,3]triazolo[4,5-b]pyridine (3w)
2-(1,4-dioxan-2-yl)-2H-[1,2,3]triazolo[4,5-b]pyridine (3w')
1-(1,4-dioxan-2-yl)-1H-[1,2,3]triazolo[4,5-b]pyridine (3w’’

![Chemical Structure](image)

![NMR Spectrum](image)

![1H NMR Spectrum](image)

![13C NMR Spectrum](image)
1-(1,4-dioxan-2-yl)-1H-pyrazolo[3,4-b]pyridine (3x)
1-(1,4-dioxan-2-yl)-3-methyl-1H-pyrazolo[3,4-b]pyridine (3y)
4-chloro-1-(1,4-dioxan-2-yl)-1H-pyrazolo[3,4-b]pyridine (3z)
5-bromo-1-(1,4-dioxan-2-yl)-1H-pyrazolo[3,4-b]pyridine (3aa)
1-(1,4-dioxan-2-yl)-1H-imidazole (3ab)
1-(1,4-dioxan-2-yl)-2-methyl-1H-imidazole (3ac)
1-(1,4-dioxan-2-yl)-3-phenyl-1H-pyrazole (3ad)
2-(1,4-dioxan-2-yl)-2H-1,2,3-triazole (3ae)
1-(1,4-dioxan-2-yl)-1H-1,2,3-triazole (3ae')
1-(1,4-dioxan-2-yl)-1H-1,2,4-triazole (3af)
1-(1,4-dioxan-2-yl)-5-methyl-1H-tetrazole (3ag)
9-(1,4-dioxan-2-yl)-9H-purine (3ah)
7-(1,4-dioxan-2-yl)-7H-purine (3ah')
N-(2-(1-(1,4-dioxan-2-yl)-1H-tetrazol-5-yl)-4-oxo-4H-chromen-8-yl)-4-(4-phenylbutoxy)benzamide (3ai)
3-((2'-(1-(1,4-dioxan-2-yl)-1H-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl)methyl)-2-butyl-1,3-diazaspiro[4.4]non-1-en-4-one (3aj)
9-(tetrahydrofuran-2-yl)-9H-purin-6-amine (3ak)
1-(tetrahydrofuran-2-yl)-1\textit{H}-benzo[d]imidazole(4a)
1-(tetrahydro-2H-pyran-2-yl)-1H-benzo[d]imidazole(4b)
1-(1,3-dioxolan-2-yl)-1H-benzo[d]imidazole (4c)
1-(benzo[d][1,3]dioxol-2-yl)-1H-benzo[d]imidazole(4d)
1-((2-methoxyethoxy)methyl)-1H-benzo[d]imidazole(4e)
1-(1,2-dimethoxyethyl)-1H-benzo[d]imidazole(4e')
1-((benzyloxy)(phenyl)methyl)-1H-benzo[d]imidazole(4g)
1-(tetrahydrothiophen-2-yl)-1H-benzo[d]imidazole(4h)
1-(phenoxymethyl)-1H-benzo[d]imidazole (4i)