Supporting information for:

Palladium Catalyzed Minisci Reaction with Simple Alcohols

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General Information:
All experiments were carried out under air. Flash column chromatography was performed over SiliCycle silica gel 40-63 μm. 1H NMR and 13C NMR spectra were acquired by Varian Mercury-500 MHz. High-resolution mass spectra (HRMS) were obtained from a JEOL JMS-700 instrument (EI). Commercially available chemicals were used without further purification. Commercially available absolute ethanol was dried over 4Å molecular sieves before use.

Typical procedure:
PdCl₂ (0.01 mmol), (rac)-Binap (0.01 mmol) and dicumyl peroxide (0.7 mmol) were placed in a dry sealable tube. To this, dried ethanol (1.0 mL) and lepidine (0.2 mmol) (1a) were added. The tube was sealed, and stirred for 16 hours at 120 oC. The reaction mixture was cooled to room temperature and flushed through a short column of silica gel with ethyl acetate. The solvent was removed under vacuum. The product (3a) was isolated from the dark crude reaction mixture by flash column chromatography.

Reaction of isoquinoline with butyraldehyde (in the presence of peroxide):
PdCl₂ (0.01 mmol), (rac)-Binap (0.01 mmol) and dicumyl peroxide (0.7 mmol) were placed in a dry sealable tube. To this, butyraldehyde (1.0 mL) and isoquinoline (0.2 mmol) (1c) were added. The tube was sealed, and stirred for 16 hours at 120 oC. The reaction mixture was cooled to room temperature and flushed through a short column of silica gel with ethyl acetate. The presence/absence of alcohol (3l) was determined by 1H NMR, as was the yield of ketone (5l) using mesitylene as the internal standard. Compound 5l is a known compound.1

Reactions with 10 mol% HCl:
For reactions on a 0.2 mmol scale (with respect to N-heterocycle): a solution of 1 mL EtOH : 10 mol % HCl (0.02 mmol) was first prepared. A BIOHIT Proline 2-20 μL mechanical pipette with plastic pipette tip was used to transfer 10 μL of concentrated HCl (12 M) to 6 mL EtOH. The solution was mixed thoroughly and 1 mL of this solution was used for each reaction requiring 10 mol % HCl.

R\text{f} = 0.4 (3: 1, Hexanes: Ethyl Acetate)

$^1$H NMR (500 MHz, CDCl$_3$, ppm) $\delta$ 8.06 (d, $J = 8.5$ Hz, 1H), 7.97 (d, $J = 8.0$ Hz, 1H), 7.71 (t, $J = 8.0$ Hz, 1H), 7.55 (t, $J = 8.1$ Hz, 1H), 7.18 (s, 1H), 5.52-5.51 (s, 1H); 4.98 (q, $J = 6.5$ Hz, 1H), 2.71 (s, 3H), 1.57 (d, $J = 6.5$ Hz, 3H); $^1$C NMR (125 MHz, CDCl$_3$, ppm) $\delta$ 162.5, 146.1, 145.3, 129.4, 129.3, 127.4, 126.1, 123.7, 118.5, 68.6, 24.1, 18.9; HRMS (ESI): $m/z$: [M+H]$^+$ calculated for C$_{12}$H$_{14}$ON: 188.1070; found: 188.1051.

R\text{f} = 0.4 (4: 1, Hexanes: Ethyl Acetate)

$^1$H NMR (500 MHz, CDCl$_3$, ppm) $\delta$ 8.00 (d, $J = 8.5$ Hz, 1H), 7.76 (d, $J = 8.3$ Hz, 1H), 7.64 (dd, $J = 1.0$, 6.9 Hz, 1H), 7.53 (dd, $J = 1.0$, 6.9 Hz, 1H), 7.40 (s, 1H), 5.56-5.42 (m, 2H), 2.68 (s, 3H), 1.59 (d, $J = 7.0$ Hz, 3H); $^1$C NMR (125 MHz, CDCl$_3$, ppm) $\delta$ 161.4, 149.2, 137.4, 130.1, 126.9, 126.2, 124.1, 122.7, 118.3, 65.7, 25.5, 23.9; HRMS (ESI): $m/z$: [M+H]$^+$ calculated for C$_{12}$H$_{14}$ON: 188.1070; found: 188.1084.

R\text{f} = 0.4 (3: 1, Hexanes: Ethyl Acetate)

$^1$H NMR (500 MHz, CDCl$_3$, ppm) $\delta$ 8.42 (d, $J = 5.8$ Hz, 1H); 8.02 (d, $J = 8.5$ Hz, 1H), 7.83 (d, $J = 8.3$ Hz, 1H), 7.68 (t, $J = 8.0$ Hz, 1H), 7.593-7.554 (m, 2H), 5.58 (q, $J = 6.1$ Hz, 1H), 5.33 (s, 1H), 1.59 (d, $J = 6.4$ Hz, 3H); $^1$C NMR (125 MHz, CDCl$_3$, ppm) $\delta$ 162.0, 140.3, 136.3, 130.1, 127.4, 127.2, 124.5, 124.0, 120.3, 65.9, 25.3; HRMS (ESI): $m/z$: [M+H]$^+$ calculated for C$_{11}$H$_{12}$ON: 174.0913; found: 174.0896.

R\text{f} = 0.2 (2: 1, Hexanes: Ethyl Acetate)

$^1$H NMR (500 MHz, CDCl$_3$, ppm) $\delta$ 8.16 (d, $J = 8.3$ Hz, 1H), 8.08 (d, $J = 8.6$ Hz, 1H), 7.83 (d, $J = 8.0$ Hz, 1H) 7.75-7.71 (m, 1H), 7.57-7.53 (m, 1H), 7.36 (d, $J = 8.5$ Hz, 1H), 5.08-4.98 (m, 2H); 1.58 (d, $J = 6.6$ Hz, 3H); $^1$C NMR (125 MHz, CDCl$_3$, ppm) $\delta$ 162.7, 146.3, 137.0, 129.8, 129.4, 128.7, 127.5, 127.3, 126.3, 126.0, 123.3, 117.9, 68.7, 25.2, 24.1; HRMS (ESI): $m/z$: [M+H]$^+$ calculated for C$_{11}$H$_{12}$ON: 174.0913; found: 174.0924.
Rf = 0.1 (2: 1, Hexanes: Ethyl Acetate), isolated as a mixture (3d''': 3d''' = 1: 1.6)

1H NMR (500 MHz, CDCl3, ppm) δ 8.88 (d, J = 4.7 Hz, 1H) [Hₘ], 8.14-8.8.08 (m, 2H), 8.02 (d, J = 8.6 Hz, 1H), 7.98 (dd, J = 3.2, 8.3 Hz, 1H), 7.72 (m, 2H), 7.60 (d, J = 4.4 Hz, 1H), 7.58-7.53 (m, 3H), 5.69-5.64 (m, 2H) [Hₙ], 5.12-5.05 (s, 1H) [Hₚ], 5.05-4.97 (m, 1H) [Hₚ'], 2.45-2.30 (m, 2H) [Hₚ''], 1.66-1.64 (m, 6H) [Hₚ'''], 1.57 (d, J = 6 Hz, 3H) [Hₚ'''']; 13C NMR (125 MHz, CDCl3, ppm) [mixture of 3d'' and diastereomers of 3d'''] δ 163.1, 163.0, 153.1, 150.2, 147.7, 146.2, 130.0, 129.79, 129.76, 129.6, 129.52, 129.50, 126.9, 126.6, 125.8, 123.2, 123.1, 116.9, 113.73, 113.66, 69.0, 66.5, 66.3, 24.96, 24.92, 24.8, 24.3, 24.2; HRMS (ESI): m/z: [M+H]+ calculated for C11H12ON: 174.0917 ; found: 174.0924; HRMS (ESI): m/z: [M+H]+ calculated for C13H16O2N: 218.1176; found: 218.1187.

Rf = 0.1 (1: 1, Hexanes: Ethyl Acetate)

1H NMR (500 MHz, CDCl3, ppm) δ 8.05 (d, J = 8.3 Hz, 1H), 7.97 (d, J = 9.3 Hz, 1H); 7.38 (dd, J = 2.7, 6.4 Hz, 1H), 7.31 (d, J = 8.5 Hz, 1H), 7.10 (d, J = 2.7 Hz, 1H), 5.01 (q, J = 5.9 Hz, 1H), 4.95 (s, 1H), 3.94 (s, 3H), 1.57 (d, J = 6.6 Hz, 3H); 13C NMR (125 MHz, CDCl3, ppm) δ 160.4, 157.7, 142.4, 135.8, 130.8, 130.1, 128.3, 122.3, 118.2, 105.3, 68.6, 55.5, 24.1; HRMS (ESI): m/z: [M+H]+ calculated for C12H14O2N: 204.1019; found: 204.0999.

Rf = 0.1 (1: 1, Hexanes: Ethyl Acetate), isolated as a mixture (3e''': 3e''' = 1: 1)

1H NMR (500 MHz, CDCl3, ppm) δ 8.72 (d, J = 4.6 Hz, 1H) [Hₙ], 8.02 (d, J = 9 Hz, 1H), 8.00-7.98 (m, 1H), 7.53-7.47 (m, 2H), 7.38-7.33 (m, 2H), 7.26-7.22 (m, 2H), 5.58-5.52 (m, 2H) [Hₖ], 5.01-4.93 (m, 2H) [Hₗ and Hₗ'], 3.94 (s, 6H) [Hₖ'], 2.50-2.30 (m, 2H) [Hₖ], 1.65 (d, J = 6.7 Hz, 6H) [Hₖ'], 1.56 (d, J = 6.6 Hz, 3H) [Hₖ]; 13C NMR (125 MHz, CDCl3, ppm) [mixture of 3e''' and diastereomers of 3e'''''] δ 160.6, 160.5, 157.9, 157.8, 147.8, 132.33, 132.25, 132.19, 132.17, 131.5, 130.9, 128.8, 128.7, 126.6, 125.7, 121.9, 121.68, 121.65, 117.9, 114.0, 113.0, 101.9, 101.6, 68.9, 66.7, 66.6, 55.8, 24.4, 24.34, 24.32, 24.3, 24.2; HRMS (ESI): m/z: [M+H]+ calculated for C13H16O2N: 204.1019 ; found: 204.0997; HRMS (ESI): m/z: [M+H]+ calculated for C14H18O3N: 248.1281; found: 248.1253.
R<sub>f</sub> = 0.1 (2: 1, Hexanes: Ethyl Acetate)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, ppm) δ 8.50 (s, 1H), 8.13 (d, <i>J</i> = 8.3 Hz, 1H), 8.01 (d, <i>J</i> = 8.8 Hz, 1H), 7.81-7.74 (m, 2H), 5.62 (m, 1H), 5.22 (d, <i>J</i> = 6.8 Hz, 1H), 4.03 (s, 3H), 1.63 (d, <i>J</i> = 7.0, Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, ppm) δ 165.9, 162.8, 139.3, 136.2, 131.0, 129.6, 129.1, 126.1, 124.5, 123.9, 66.3, 52.6, 25.3; HRMS (ESI): <i>m/z</i>: [M+H]+ calculated for C<sub>13</sub>H<sub>14</sub>O<sub>3</sub>N: 232.0968; found: 232.0948.

R<sub>f</sub> = 0.3 (2: 1, Hexanes: Ethyl Acetate)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, ppm) δ 8.65 (d, <i>J</i> = 8.3 Hz, 1H), 8.55 (d, <i>J</i> = 8.1 Hz, 1H), 8.15 (d, <i>J</i> = 8 Hz, 1H), 8.11 (d, <i>J</i> = 8 Hz, 1H), 7.86 (dd, <i>J</i> = 1.2, 7.1 Hz, 1H), 7.76-7.65 (m, 3H), 5.68-5.60 (m, 2H), 1.66 (d, <i>J</i> = 6 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, ppm) δ 162.1, 142.1, 133.3, 130.8, 129.4, 128.8, 127.3, 126.9, 125.2, 124.1, 122.9, 122.7, 122.0, 65.9, 25.1; HRMS (ESI): <i>m/z</i>: [M+H]+ calculated for C<sub>15</sub>H<sub>14</sub>ON: 224.1070; found: 224.1047.

R<sub>f</sub> = 0.2 (3: 1, Hexanes: Ethyl Acetate)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, ppm) δ 8.45 (d, <i>J</i> = 5.6 Hz, 1H); 8.04 (d, <i>J</i> = 8.5Hz, 1H); 7.87 (d, <i>J</i> = 8.1 Hz, 1H); 7.71 (dd, <i>J</i> = 1.3, 6.9 Hz, 1H); 7.64-7.61 (m, 1H), 7.59 (d, <i>J</i> = 5.9 Hz, 1H), 5.48-5.38 (m, 1H), 5.20-5.08 (s, 1H), 2.11-2.03 (m, 1H), 1.76-1.67 (m, 1H), 1.01 (t, <i>J</i> =7.5 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, ppm) δ 161.2, 140.3, 136.4, 130.2, 127.5, 127.2, 124.8, 124.2, 120.4, 70.6, 32.0, 9.7; HRMS (ESI): <i>m/z</i>: [M+H]+ calculated for C<sub>12</sub>H<sub>14</sub>ON: 188.1070; found: 188.1080.

R<sub>f</sub> = 0.1 (3: 1, Hexanes: Ethyl Acetate)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, ppm) δ 8.48 (s, 1H); 8.11 (d, <i>J</i> = 8.3 Hz, 1H); 7.99 (d, <i>J</i> = 7.8 Hz, 1H); 7.80-7.73 (m, 2H), 5.38-5.46 (m, 1H), 5.08 (d, <i>J</i> = 6.6 Hz, 1H), 4.02 (s, 3H), 2.09-2.01 (m, 1H), 1.77-1.68 (m, 1H); 1.04 (t, <i>J</i> = 7.6 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, ppm) δ 165.9, 161.9, 139.2, 136.1, 130.9, 129.5, 129.0, 126.3, 124.4, 123.8, 71.0, 52.6, 31.9, 9.9; HRMS (ESI): <i>m/z</i>: [M+H]+ calculated for C<sub>14</sub>H<sub>16</sub>O<sub>3</sub>N: 246.1151; found: 246.1139.
Rf = 0.5 (4: 1, Hexanes: Ethyl Acetate)

$^1$H NMR (500 MHz, CDCl$_3$, ppm) $\delta$ 8.45 (d, $J = 5.9$ Hz, 1H), 8.04 (d, $J = 8.4$ Hz, 1H); 7.87 (d, $J = 8.3$ Hz, 1H), 7.59 (d, $J = 5.8$ Hz, 1H); 7.61-7.64 (m, 1H), 7.71 (dd, $J = 1.0$, 8.1 Hz, 1H), 5.49-5.46 (m, 1H), 5.09 (d, $J = 7.1$ Hz, 1H); 1.98-1.90 (m, 1H); 1.70-1.59 (m, 2H); 1.45-1.55 (m, 1H), 0.96 (t, $J = 7.3$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$, ppm) $\delta$ 161.5, 140.4, 136.4, 130.2, 127.5, 127.2, 124.8, 124.1, 120.3, 69.4, 41.4, 18.8, 14.0; HRMS (ESI): m/z: [M+H]$^+$ calculated for C$_{13}$H$_{16}$ON: 202.1226; found: 202.1238.