

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  $\mu\text{m}$ .  $^1\text{H}$  NMR and  $^{13}\text{C}$  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:**

$\text{PdCl}_2$  (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 °C. 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):**

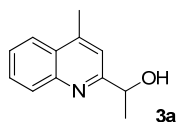
$\text{PdCl}_2$  (0.01 mmol), (*rac*)-Binap (0.01 mmol) and dicumyl peroxide (0.7 mmol) were placed in a dry sealable tube. To this, butyraldehyde (1.0 mL) and isoquinoline (0.2 mmol) (**1c**) were added. The tube was sealed, and stirred for 16 hours at 120 °C. The reaction mixture was cooled to room temperature and flushed through a short column of silica gel with ethyl acetate. The presence/absence of alcohol (**3l**) was determined by  $^1\text{H}$  NMR, as was the yield of ketone (**5l**) using mesitylene as the internal standard. Compound **5l** is a known compound.<sup>1</sup>

### **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  $\mu\text{L}$  mechanical pipette with plastic pipette tip was used to transfer 10  $\mu\text{L}$  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.

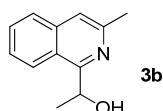
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<sup>1</sup> Khusnutdinov, R. I.; Baiguzina, A. R.; Mukminov, R. R. *Russ. J. Org. Chem.*, **2010**, 46, 1399.



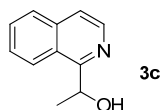
$R_f = 0.4$  (3: 1, Hexanes: Ethyl Acetate)

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , 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):  $m/z$ :  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{12}\text{H}_{14}\text{ON}$ : 188.1070; found: 188.1051.



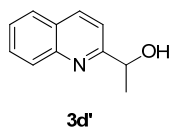
$R_f = 0.4$  (4: 1, Hexanes: Ethyl Acetate)

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , 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):  $m/z$ :  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{12}\text{H}_{14}\text{ON}$ : 188.1070; found: 188.1084.



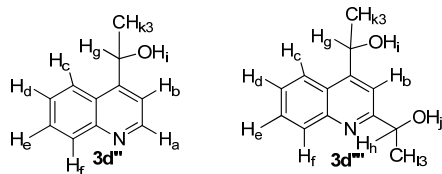
$R_f = 0.4$  (3: 1, Hexanes: Ethyl Acetate)

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , 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):  $m/z$ :  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{11}\text{H}_{12}\text{ON}$ : 174.0913; found: 174.0896.



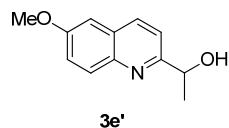
$R_f = 0.2$  (2: 1, Hexanes: Ethyl Acetate)

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , 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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , 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):  $m/z$ :  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{11}\text{H}_{12}\text{ON}$ : 174.0913; found: 174.0924.



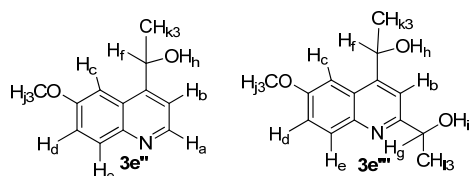
R<sub>f</sub> = 0.1 (2: 1, Hexanes: Ethyl Acetate), isolated as a mixture (3d'': 3d''' = 1: 1.6)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, ppm) δ 8.88 (d, *J* = 4.7 Hz, 1H) [*H<sub>a</sub>*], 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) [*H<sub>g</sub>*], 5.12-5.05 (s, 1H) [*H<sub>j</sub>*], 5.05-4.97 (m, 1H) [*H<sub>h</sub>*], 2.45-2.30 (m, 2H) [*H<sub>i</sub>*], 1.66-1.64 (m, 6H) [*H<sub>k</sub>*], 1.57 (d, *J* = 6 Hz, 3H) [*H<sub>l</sub>*]; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, 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, 125.6, 124.8, 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]<sup>+</sup> calculated for C<sub>11</sub>H<sub>12</sub>ON: 174.0917; found: 174.0924; HRMS (ESI): *m/z*: [M+H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>16</sub>O<sub>2</sub>N: 218.1176; found: 218.1187.



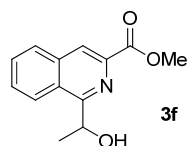
R<sub>f</sub> = 0.1 (1: 1, Hexanes: Ethyl Acetate)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, 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); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, 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]<sup>+</sup> calculated for C<sub>12</sub>H<sub>14</sub>O<sub>2</sub>N: 204.1019; found: 204.0999.



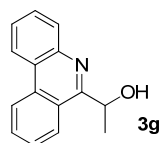
R<sub>f</sub> = 0.1 (1: 1, Hexanes: Ethyl Acetate), isolated as a mixture (3e'': 3e''' = 1: 1)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, ppm) δ 8.72 (d, *J* = 4.6 Hz, 1H) [*H<sub>a</sub>*], 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) [*H<sub>f</sub>*], 5.01-4.93 (m, 2H) [*H<sub>g</sub>* and *H<sub>i</sub>*], 3.94 (s, 6H) [*H<sub>j</sub>*], 2.50-2.30 (m, 2H) [*H<sub>h</sub>*], 1.65 (d, *J* = 6.7 Hz, 6H) [*H<sub>k</sub>*], 1.56 (d, *J* = 6.6 Hz, 3H) [*H<sub>l</sub>*]; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, 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]<sup>+</sup> calculated for C<sub>12</sub>H<sub>14</sub>O<sub>2</sub>N: 204.1019; found: 204.0997; HRMS (ESI): *m/z*: [M+H]<sup>+</sup> calculated for C<sub>14</sub>H<sub>18</sub>O<sub>3</sub>N: 248.1281; found: 248.1253.



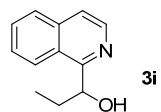
R<sub>f</sub> = 0.1 (2: 1, Hexanes: Ethyl Acetate)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, ppm) δ 8.50 (s, 1H), 8.13 (d, *J* = 8.3 Hz, 1H), 8.01 (d, *J* = 8.8 Hz, 1H), 7.81-7.74 (m, 2H), 5.62 (m, 1H), 5.22 (d, *J* = 6.8 Hz, 1H), 4.03 (s, 3H), 1.63 (d, *J* = 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): *m/z*: [M+H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>14</sub>O<sub>3</sub>N: 232.0968; found: 232.0948.



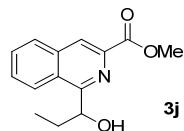
R<sub>f</sub> = 0.3 (2: 1, Hexanes: Ethyl Acetate)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, ppm) δ 8.65 (d, *J* = 8.3 Hz, 1H), 8.55 (d, *J* = 8.1 Hz, 1H), 8.15 (d, *J* = 8 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.86 (dd, *J* = 1.2, 7.1 Hz, 1H), 7.76-7.65 (m, 3H), 5.68-5.60 (m, 2H), 1.66 (d, *J* = 6.1 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): *m/z*: [M+H]<sup>+</sup> calculated for C<sub>15</sub>H<sub>14</sub>ON: 224.1070; found: 224.1047.



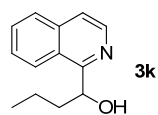
R<sub>f</sub> = 0.2 (3: 1, Hexanes: Ethyl Acetate)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, ppm) δ 8.45 (d, *J* = 5.6 Hz, 1H); 8.04 (d, *J* = 8.5 Hz, 1H); 7.87 (d, *J* = 8.1 Hz, 1H); 7.71 (dd, *J* = 1.3, 6.9 Hz, 1H); 7.64-7.61 (m, 1H), 7.59 (d, *J* = 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, *J* = 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): *m/z*: [M+H]<sup>+</sup> calculated for C<sub>12</sub>H<sub>14</sub>ON: 188.1070; found: 188.1080.



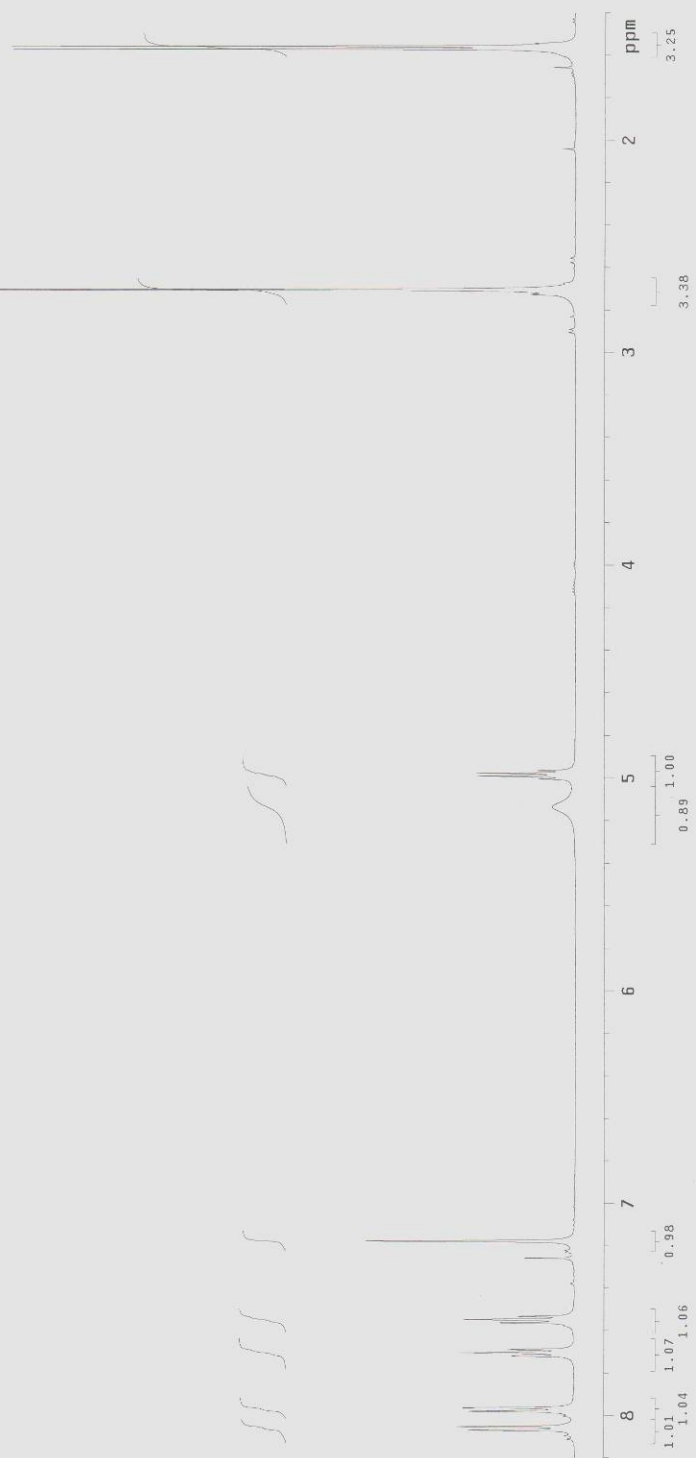
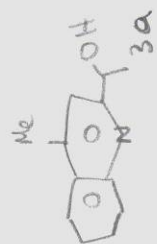
R<sub>f</sub> = 0.1 (3: 1, Hexanes: Ethyl Acetate)

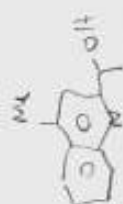
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, ppm) δ 8.48 (s, 1H); 8.11 (d, *J* = 8.3 Hz, 1H); 7.99 (d, *J* = 7.8 Hz, 1H); 7.80-7.73 (m, 2H), 5.38-5.46 (m, 1H), 5.08 (d, *J* = 6.6 Hz, 1H), 4.02 (s, 3H), 2.09-2.01 (m, 1H), 1.77-1.68 (m, 1H); 1.04 (t, *J* = 7.6 Hz, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<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): *m/z*: [M+H]<sup>+</sup> calculated for C<sub>14</sub>H<sub>16</sub>O<sub>3</sub>N: 246.1151; found: 246.1139.



$R_f = 0.5$  (4: 1, Hexanes: Ethyl Acetate)

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





3a

