Supporting Information

A greener borrowing hydrogen methodology: palladium-catalyzed dehydrative N-benzylation of 2-aminopyridines in water

Hidemasa Hikawa,* Hirokazu Imamura, Shoko Kikkawa, and Isao Azumaya*

Faculty of Pharmaceutical Sciences, Toho University, Funabashi, Chiba 274-8510, Japan
hidemasa.hikawa@phar.toho-u.ac.jp and isao.azumaya@phar.toho-u.ac.jp

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S1
**General procedure:** A mixture of aminopyridines 1 (1 mmol), palladium(II) acetate (12 mg, 0.05 mmol), sodium diphenylphosphinobenzene-3-sulfonate (TPPMS, 36 mg, 0.1 mmol) and benzyl alcohol 2 (5-10 mmol) in H$_2$O (4 mL) was heated for 16 h in a sealed tube under air. After cooling, the reaction mixture was poured into water and extracted with EtOAc. The organic layer was washed with brine, dried over MgSO$_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexanes/EtOAc) to give desired product 3.

**N-Benzylpyridin-2-amine 3a**

Yield 165 mg (90%) as a white solid; mp 90-91 °C; IR (KBr) (cm$^{-1}$) 3226, 3029, 1600, 1575; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 4.50 (d, $J$=5.7 Hz, 2H), 4.95 (brs, 1H), 6.36 (dt, $J$=8.5, 0.9 Hz, 1H), 6.58 (ddd, $J$=7.1, 5.0, 0.9 Hz, 1H), 7.23-7.36 (m, 4H), 7.39 (dd, $J$=8.7, 7.1, 1.8 Hz, 1H), 8.09 (ddd, $J$=5.0, 1.8, 0.9 Hz, 2H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 46.3, 106.8, 113.1, 127.2, 127.4, 128.6, 137.5, 139.2, 148.2, 158.6; MS (FAB): m/z 185 [M+H]$^+$.

**N-Benzyl-5-methylpyridin-2-amine 3b**

Yield 158 mg (80%) as a pale yellow solid; mp 105-107 °C; IR (KBr) (cm$^{-1}$) 3234, 3027, 1610, 1535; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 2.17 (s, 3H), 4.47 (d, $J$=5.5 Hz, 2H), 4.77 (brs, 1H), 6.31 (d, $J$=8.2 Hz, 1H), 7.20-7.29 (m, 2H), 7.29-7.39 (m, 4H), 7.92 (d, $J$=2.3 Hz, 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 46.3, 106.8, 113.1, 127.2, 127.4, 128.6, 138.5, 139.4, 147.7, 156.9; MS (FAB): m/z 199 [M+H]$^+$.

**N-Benzyl-3-methylpyridin-2-amine 3c**

Yield 163 mg (82%) as a colorless oil; IR (KBr) (cm$^{-1}$) 3443, 1601; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 2.09 (s, 3H), 4.35 (brs, 1H), 4.69 (d, $J$=5.5 Hz, 2H), 6.56 (dd, $J$=6.9, 5.0 Hz 1H), 7.22-7.26 (m, 1H), 7.28 (tt, $J$=6.9, 1.8 Hz 1H), 7.32-7.42 (m, 3H), 8.05 (dd, $J$=4.8, 1.4 Hz 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 46.3, 106.4, 121.9, 127.1, 127.4, 128.6, 138.5, 139.4, 147.7, 156.9; MS (FAB): m/z 199 [M+H]$^+$.

**N-Benzyl-5-fluoropyridin-2-amine 3d**

Yield 113 mg (56%) as a white solid; mp 95-97 °C; IR (KBr) (cm$^{-1}$) 3239, 3031, 1618, 1585; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 4.47 (d, $J$=6.0 Hz 2H), 4.80 (brs, 1H), 6.33 (dd, $J$=9.1, 3.2 Hz 1H), 7.18 (d, $J$=9.2, 7.8, 2.8 Hz 1H), 7.24-7.38 (m, 5H), 7.97 (d, $J$=2.8 Hz 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 46.8, 107.1 (d, $J_{CF}$=3.8 Hz), 125.2 (d, $J_{CF}$=21.1 Hz), 127.3, 127.4, 128.7, 134.8 (d, $J_{CF}$=24.9 Hz), 139.0, 153.5 (d, $J_{CF}$=242 Hz), 155.3; MS (FAB): m/z 203 [M+H]$^+$.

**Ethyl 2-(benzylamino)nicotinate 3e**

Yield 113 mg (56%) as a white solid; mp 95-97 °C; IR (KBr) (cm$^{-1}$) 3239, 3031, 1618, 1585; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 4.47 (d, $J$=6.0 Hz 2H), 4.80 (brs, 1H), 6.33 (dd, $J$=9.1, 3.2 Hz 1H), 7.18 (d, $J$=9.2, 7.8, 2.8 Hz 1H), 7.24-7.38 (m, 5H), 7.97 (d, $J$=2.8 Hz 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$: 46.8, 107.1 (d, $J_{CF}$=3.8 Hz), 125.2 (d, $J_{CF}$=21.1 Hz), 127.3, 127.4, 128.7, 134.8 (d, $J_{CF}$=24.9 Hz), 139.0, 153.5 (d, $J_{CF}$=242 Hz), 155.3; MS (FAB): m/z 203 [M+H]$^+$.
Yield 213 mg (83%) as a colorless oil; IR (KBr) (cm\(^{-1}\)) 3367, 1686, 1594; \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 1.37 (t, \(J\) = 6.9 Hz, 3H), 4.31 (q, \(J\) = 7.3 Hz, 2H), 4.76 (d, \(J\) = 5.5 Hz, 2H), 6.55 (dd, \(J\) = 7.8, 4.6 Hz, 1H), 7.22-7.28 (m, 1H), 7.30-7.40 (m, 3H), 8.15 (dd, \(J\) = 7.8, 1.8 Hz, 1H), 8.29 (dd, \(J\) = 4.6, 1.8 Hz, 1H), 8.32 (brs, 1H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 14.4, 45.0, 60.9, 106.3, 111.3, 127.1, 127.6, 128.7, 139.7, 140.0, 153.7, 158.6, 167.6; MS (FAB): \(m/z\) 257 \([\text{M+H}]^+\).

**Methyl 6-(benzylamino)nicotinate 3f**

Yield 208 mg (86%) as a white solid; mp 147-149 \(^\circ\)C; IR (KBr) (cm\(^{-1}\)) 3222, 1706, 1601; \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.87 (s, 3H), 4.58 (d, \(J\) = 6.0 Hz, 2H), 5.41 (brs, 1H), 6.36 (d, \(J\) = 8.7 Hz, 1H), 7.27-7.38 (m, 5H), 7.99 (d, \(J\) = 8.7, 2.3 Hz, 1H), 8.76 (d, \(J\) = 1.8 Hz, 1H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 46.1, 51.7, 105.7, 115.5, 127.4, 127.6, 128.8, 138.1, 138.6, 151.5, 160.8, 166.4; MS (FAB): \(m/z\) 243 \([\text{M+H}]^+\); Anal. Calcd for C\(_{14}\)H\(_{14}\)N\(_2\)O\(_2\): C, 69.41; H, 5.82; N, 11.56. Found: C, 69.41; H, 5.93; N, 11.45.

**N-Benzyl-5-(trifluoromethyl)pyridin-2-amine 3g**

Scale-up experiment (see Scheme 8): A mixture of 5-(trifluoromethyl)pyridin-2-amine (1b) (1.13 g, 7 mmol), Pd(OAc)\(_2\) (78.6 mg, 0.35 mmol), sodium diphenylphosphinobenzene-3-sulfonate (TPPMS, 255.0 mg, 0.7 mmol) and benzyl alcohol (2a) (3.4 mL, 35 mmol) in H\(_2\)O (28 mL) was heated at 100 \(^\circ\)C for 16 h under air. After cooling, the reaction mixture was poured into water and extracted with EtOAc. The organic layer was washed with brine, dried over MgSO\(_4\) and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexanes/EtOAc) to give desired product 3g (1.27 g, 5.0 mmol, 72%) as a white solid; mp 148-150 \(^\circ\)C; IR (KBr) (cm\(^{-1}\)) 3233, 1616; \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 4.57 (d, \(J\) = 6.0 Hz, 2H), 5.20 (brs, 1H), 6.40 (d, \(J\) = 8.7 Hz, 1H), 7.25-7.40 (m, 5H), 7.58 (d, \(J\) = 8.7, 2.8 Hz, 1H), 8.36 (s, 1H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 46.1, 106.1, 115.8 (q, \(J\)\(_{CF}\) = 32.6 Hz), 124.6 (q, \(J\)\(_{CF}\) = 270.3 Hz), 127.4, 127.6, 128.8, 138.1, 138.6, 151.5, 160.8, 166.4; MS (FAB): \(m/z\) 253 \([\text{M+H}]^+\); Anal. Calcd for C\(_{14}\)H\(_{14}\)N\(_2\): C, 69.41; H, 5.82; N, 11.56. Found: C, 69.41; H, 5.93; N, 11.45.

**6-(Benzylamino)nicotinonitrile 3h**

Yield 178 mg (85%) as a white solid; mp 118-120 \(^\circ\)C; IR (KBr) (cm\(^{-1}\)) 3227, 2219, 1604; \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 4.56 (d, \(J\) = 5.5 Hz, 2H), 5.63 (brs, 1H), 6.38 (d, \(J\) = 9.2 Hz, 1H), 7.27-7.39 (m, 4H), 7.56 (dd, \(J\) = 8.7, 2.3 Hz, 1H), 8.29 (d, \(J\) = 1.8 Hz, 1H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 46.0, 97.3, 106.6, 118.5, 127.5, 127.8, 128.9, 137.6, 139.8, 153.2, 159.7; MS (FAB): \(m/z\) 210 \([\text{M+H}]^+\).

**6-(Benzylamino)nicotinamide 3i**

Yield 205 mg (90%) as a white solid; mp 168-170 \(^\circ\)C; IR (KBr) (cm\(^{-1}\)) 3411, 3178, 1648, 1603; \(^1\)H-NMR (400 MHz, DMSO-\(d_6\)) \(\delta\) 4.53 (d, \(J\) = 6.0 Hz, 2H), 6.51 (d, \(J\) = 8.7 Hz, 1H), 7.06 (brs, 1H), 7.18-7.27 (m, 1H), 7.28-7.35 (m, 4H), 7.60 (t, \(J\) = 6.0 Hz, 1H), 7.67 (brs, 1H), 7.82 (dd, \(J\) = 8.7, 2.3 Hz, 1H), 8.52 (d,
$J=2.3 \text{ Hz, 1H)}$; $^{13}$C-NMR (100 MHz, DMSO-$d_6$) $\delta$ 44.5, 107.6, 118.4, 127.2, 127.8, 128.8, 136.6, 140.6, 149.1, 160.6, 167.5; MS (FAB): $m/z$ 228 [M+H]$^+$.  

$N$-Benzylypyridin-3-amine 3j  
Yield 166 mg (90%) as a pale brow solid; mp 87-89 °C; IR (KBr) (cm$^{-1}$) 3263, 1591; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 4.14 (brs, 1H), 4.34 (d, $J=5.0$ Hz, 2H), 6.87 (dd, $J=8.2, 1.4$ Hz, 1H), 7.06 (dd, $J=3.2$ Hz, 1H), 7.26-7.40 (m, 5H), 7.97 (dd, $J=4.6, 1.4$ Hz, 1H), 8.01 (d, $J=3.2$ Hz, 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 47.9, 118.6, 123.8, 127.5, 127.6, 128.9, 136.3, 138.6, 139.0, 144.1; MS (FAB): $m/z$ 185 [M+H]$^+$.  

$N$-Benzylypyrimidin-2-amine 3k  
Yield 130 mg (70%) as a white solid; mp 78-80 °C; IR (KBr) (cm$^{-1}$) 3236, 1600; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 4.64 (d, $J=5.5$ Hz, 2H), 5.84 (brs, 1H), 6.52 (t, $J=4.6$ Hz, 1H), 7.24-7.38 (m, 5H), 8.22 (brd, $J=4.1$ Hz, 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 45.5, 110.9, 127.3, 127.6, 128.7, 139.2, 158.2, 162.4; MS (FAB): $m/z$ 186 [M+H]$^+$.  

$N$-(4-Methylbenzyl)pyridin-2-amine 3l  
Yield 149 mg (75%) as a white solid; mp 72-74 °C; IR (KBr) (cm$^{-1}$) 3235, 1609; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 2.34 (s, 3H), 4.45 (d, $J=5.5$ Hz, 2H), 4.83 (brs, 1H), 6.37 (d, $J=8.9$ Hz, 1H), 6.58 (dd, $J=7.3, 5.0, 0.7$ Hz, 1H), 7.15 (d, $J=7.8$ Hz, 2H), 7.25 (d, $J=8.2$ Hz, 2H), 7.39 (ddd, $J=8.7, 7.3, 1.8$ Hz, 1H), 8.10 (dd, $J=5.0, 1.4$ Hz, 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 21.1, 46.1, 106.7, 113.0, 127.4, 129.3, 136.1, 136.9, 137.4, 148.2, 158.7; MS (FAB): $m/z$ 199 [M+H]$^+$.  

$N$-(3-Methylbenzyl)pyridin-2-amine 3m  
Yield 159 mg (80%) as a white solid; mp 95-97 °C; IR (KBr) (cm$^{-1}$) 3240, 1608; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 2.37 (s, 3H), 4.47 (d, $J=5.5$ Hz, 2H), 4.64 (brs, 1H), 6.38 (dt, $J=8.2, 0.9$ Hz, 1H), 6.60 (ddd, $J=6.9, 5.0, 0.9$ Hz, 1H), 7.15-7.23 (m, 3H), 7.32 (d, $J=6.9$ Hz, 1H), 7.41 (ddd, $J=9.2, 7.3, 1.8$ Hz, 1H), 8.11 (ddd, $J=5.0, 1.8, 0.9$ Hz, 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 19.1, 44.5, 106.9, 113.1, 126.2, 127.5, 128.1, 130.5, 136.4, 136.9, 137.5, 148.3, 158.7; MS (FAB): $m/z$ 199 [M+H]$^+$.  

$N$-(2-Methylbenzyl)pyridin-2-amine 3n  
Yield 159 mg (80%) as a white solid; mp 74-76 °C; IR (KBr) (cm$^{-1}$) 3223, 1601; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 2.34 (s, 3H), 4.46 (d, $J=6.0$ Hz, 2H), 4.84 (brs, 1H), 6.37 (d, $J=8.2$ Hz, 1H), 6.59 (dd, $J=7.3, 5.5$ Hz, 1H), 7.08 (d, $J=7.3$ Hz, 1H), 7.13-7.20 (m, 2H), 7.23 (t, $J=7.3$ Hz, 1H), 7.40 (dd, $J=6.9, 1.8$ Hz, 1H), 8.11 (dt, $J=5.0, 0.9$ Hz, 1H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 21.4, 46.3, 106.7, 113.1, 124.4, 128.0, 128.1, 128.5, 137.4, 138.3, 139.1, 148.2, 158.7; MS (FAB): $m/z$ 199 [M+H]$^+$.  

S4
**N-(3-Methylbenzyl)-4-(trifluoromethyl)aniline 3o**

Yield 178 mg (67%) as a white solid; mp 110-112 °C; IR (KBr) (cm⁻¹) 3245, 1620; H-NMR (400 MHz, CDCl₃) δ 2.35 (s, 2H), 4.51 (d, J=5.5 Hz, 2H), 5.27 (brs, 1H), 6.39 (d, J=9.2 Hz, 1H), 7.08-7.18 (m, 3H), 7.24 (t, J=7.8 Hz, 1H), 7.57 (dd, J=8.7, 2.3 Hz, 1H), 8.33 (s, 1H); C-NMR (100 MHz, CDCl₃) δ 21.4, 46.1, 105.9, 115.6 (q, J_CF=33.6 Hz), 124.5, 124.6 (q, J_CF=270.3 Hz), 128.2, 128.4, 128.7, 134.5 (q, J_CF=2.9 Hz), 138.1, 138.6, 146.1 (q, J_CF=4.8 Hz), 160.3; MS (FAB): m/z 267 [M+H]+; HRMS-FAB: m/z (M⁺) calcd for C₁₄H₁₃F₃N₂ 267.1109, found 267.1109.

**N-(4-Methoxybenzyl)pyridin-2-amine 3p**

Yield 176 mg (82%) as a white solid; mp 118-120 °C; IR (KBr) (cm⁻¹) 3234, 1604; H-NMR (400 MHz, CDCl₃) δ 3.80 (s, 3H), 4.43 (d, J=6.0 Hz, 2H), 4.78 (brs, 1H), 6.37 (d, J=8.2 Hz, 1H), 6.59 (ddd, J=7.3, 5.0, 0.9 Hz, 1H), 6.88 (d, J=8.7 Hz, 2H), 7.29 (d, J=8.7 Hz, 2H), 7.40 (d, J=8.7, 6.9, 1.8 Hz, 1H), 8.11 (dd, J=5.0, 1.4 Hz, 1H); C-NMR (100 MHz, CDCl₃) δ 45.8, 55.3, 106.8, 113.1, 114.0, 128.7, 131.1, 137.4, 148.2, 158.6, 158.8; MS (FAB): m/z 215 [M+H]+.

**N-(4-Butoxybenzyl)pyridin-2-amine 3q**

Yield 208 mg (81%) as a white solid; mp 83-85 °C; IR (KBr) (cm⁻¹) 3229, 1606; H-NMR (400 MHz, CDCl₃) δ 0.97 (t, J=7.3 Hz, 1H), 1.48 (sext, J=7.8 Hz, 1H), 1.76 (quin, J=7.3 Hz, 1H), 3.95 (t, J=6.9 Hz, 2H), 4.42 (d, J=5.5 Hz, 2H), 4.77 (brs, 1H), 6.37 (d, J=8.7 Hz, 1H), 6.58 (dd, J=7.3, 5.0 Hz, 1H), 6.86 (d, J=8.0 Hz, 2H), 7.26 (d, J=8.0 Hz, 2H), 7.40 (dd, J=6.9, 1.8 Hz, 1H), 8.10 (dt, J=5.0, 0.9 Hz, 1H); C-NMR (100 MHz, CDCl₃) δ 13.9, 19.3, 31.3, 45.9, 67.7, 106.8, 113.1, 114.6, 128.7, 130.9, 137.4, 148.2, 158.4, 158.6; MS (FAB): m/z 257 [M+H]+; Anal. Calcd for C₁₆H₂₀N₂O: C, 74.97; H, 7.86; N, 10.93. Found: C, 74.73; H, 7.90; N, 10.79.

**N-[1-(4-Methoxyphenyl)ethyl]pyridin-2-amine 3r**

Yield 139 mg (61%) as a white solid; mp 89-91 °C; IR (KBr) (cm⁻¹) 3263, 2978, 1610; H-NMR (400 MHz, CDCl₃) δ 1.53 (d, J=6.9 Hz, 3H), 3.79 (s, 3H), 4.68 (quint, J=6.6 Hz, 1H), 4.88 (brd, J=5.5 Hz, 1H), 6.19 (d, J=8.7 Hz, 1H), 6.54 (dd, J=6.9, 5.0 Hz, 1H), 6.86 (d, J=8.7 Hz, 2H), 7.29 (d, J=8.7 Hz, 2H), 7.32 (dd, J=6.4, 2.3 Hz, 1H); C-NMR (100 MHz, CDCl₃) δ 24.4, 51.3, 55.3, 106.7, 113.0, 114.0, 126.9, 136.7, 137.4, 148.2, 158.1, 158.6; MS (FAB): m/z 229 [M+H]+.

**N-(Naphthalen-2-ylmethyl)pyridin-2-amine 3s**

Yield 176 mg (75%) as a white solid; mp 110-112 °C; IR (KBr) (cm⁻¹) 3228, 1600; H-NMR (400 MHz, CDCl₃) δ 4.67 (d, J=5.8 Hz, 2H), 4.98 (brs, 1H), 6.40 (d, J=8.2 Hz, 1H), 6.60 (dd, J=6.9, 5.0, 0.9 Hz, S5
1H), 7.36-7.52 (m, 3H), 7.76-7.86 (m, 4H), 8.13 (dd, J=5.0, 1.8, 0.9 Hz, 1H); 13C-NMR (100 MHz, CDCl3) δ 46.5, 106.8, 113.3, 125.7, 125.8, 126.2, 127.7, 128.4, 132.7, 133.4, 136.7, 137.5, 148.3, 158.6; MS (FAB): m/z 235 [M+H]+.

References
A mixture of 2-aminopyridine 1a (94 mg, 1 mmol), Pd(OAc)$_2$ (11 mg, 0.05 mmol), sodium diphenylphosphinobenzene-3-sulfonate (TPPMS, 36 mg, 0.1 mmol), and benzyl alcohol 2a (216 mg, 2 mmol), in H$_2$O (4 mL) was heated at 120 °C for 16 h in a sealed tube under air. After the reaction mixture was cooled, 1,3,5-trimethoxybenzene (168 mg, 1 mmol, internal standard) was added to the reaction mixture, which was extracted with AcOEt. The organic layer was concentrated in vacuo. The residue was analyzed by $^1$H NMR spectroscopy. The conversion yield was calculated by integration.

Conversion yield was calculated by integration.

Table S1, Entry 1 (The yield was determined by $^1$H NMR analysis of the crude product using 1,3,5-trimethoxybenzene as an internal standard.)

<table>
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<th>Signal $\delta$</th>
<th>desired 3a</th>
<th>1,3,5-trimethoxybenzene, internal standard</th>
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<tr>
<td>6.34 (Ar-H)</td>
<td>6.08 (Ar-H)</td>
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<tr>
<td>Integral value</td>
<td>0.72 (1H)</td>
<td>3.00 (3H)</td>
</tr>
<tr>
<td>Calculated ratio</td>
<td>72% from 1a</td>
<td>1 mmol</td>
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Scheme 3S. Crossover experiment.

A mixture of 1b (162 mg, 1 mmol), Pd(OAc)$_2$ (11 mg, 0.05 mmol), sodium diphenylphosphinobenzene-3-sulfonate (TPPMS, 36 mg, 0.1 mmol), benzyl-α,α-d$_2$ alcohol 2a-d$_2$ (5 mmol), and 3-methylbenzyl alcohol 2c (5 mmol) in H$_2$O (4 mL) was heated at 120 °C for 16 h in a sealed tube under air. After cooling, the reaction mixture was poured into water and extracted with EtOAc. The organic layer was washed with brine, dried over MgSO$_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexanes/EtOAc) to give H/D scrambling products $N$-benzyl-5-(trifluoromethyl)pyridin-2-amine (3g-d and 3g-d$_2$ mixture) and $N$-(3-methylbenzyl)-5-(trifluoromethyl)pyridin-2-amine (3o and 3o-d mixture) in 40% and 35% isolated yields, respectively.

$N$-(3-Methylbenzyl)-5-(trifluoromethyl)pyridin-2-amine (3o and 3o-d mixture)

FAB-MS: m/z [M+H]$^+$ 3o, 267, 3o-d, 268.
Scheme 4S. Kinetic isotope effects.

A mixture of 2-aminopyridine 1a (94 mg, 1 mmol), Pd(OAc)$_2$ (11 mg, 0.05 mmol), sodium diphenylphosphinobenzene-3-sulfonate (TPPMS, 36 mg, 0.1 mmol), benzyl alcohol 2a (108 mg, 1 mmol), and 2a-d$_7$ (115 mg, 1 mmol) in H$_2$O (2 mL) was heated at 120 °C for 16 h in a sealed tube under air. After cooling, the reaction mixture was poured into water and extracted with EtOAc. The organic layer was washed with brine, dried over MgSO$_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexanes/EtOAc). The product was analyzed by $^1$H-NMR spectroscopy.

<table>
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<th>Signal $\delta$</th>
<th>7.18-7.40 (Ph-$^5$H and Py-$^1$H)</th>
<th>6.43-6.52 (Py-$^2$H)</th>
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<tr>
<td>Integral value</td>
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<td>2.00</td>
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$4.67 - 1.00 = 3.67$ (Ph-$^5$H), $5.00 - 3.67 = 1.33$ (Ph-$^5$D)  
KIE = $3.67/1.33 = 2.8$

![Authentic sample](image)
Hammett study

A mixture of 2-aminopyridine 1a (94 mg, 1 mmol), 1X (1 mmol), Pd(OAc)$_2$ (11 mg, 0.05 mmol), sodium diphenylphosphinobenzene-3-sulphonate (TPPMS, 36 mg, 0.1 mmol), and benzyl alcohol 2a (310 µL, 2 mmol), in H$_2$O (4 mL) was heated at 120 °C for 16 h in a sealed tube under air. After cooling, the reaction mixture was poured into water and extracted with EtOAc. The organic layer was concentrated in vacuo. The residue was analyzed by $^1$H-NMR spectroscopy.

<table>
<thead>
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<th>R</th>
<th>σ</th>
<th>log($k_r/k_a$)</th>
</tr>
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<tr>
<td>Me</td>
<td>-0.17</td>
<td>0.176</td>
</tr>
<tr>
<td>H</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F</td>
<td>0.06</td>
<td>-0.018</td>
</tr>
<tr>
<td>COOMe</td>
<td>0.45</td>
<td>-0.182</td>
</tr>
<tr>
<td>CN</td>
<td>0.66</td>
<td>-0.44</td>
</tr>
</tbody>
</table>

$R = $ Me: log($k_r/k_a$) = log(1.50/1.00) = 0.176
**Scheme 6(B)**. Control experiments.

A mixture of benzyl alcohol 2a (541 mg, 5 mmol), palladium(II) acetate (11 mg, 0.05 mmol), sodium diphenylphosphinobenzene-3-sulfonate (TPPMS, 36 mg, 0.1 mmol) in H2O (4 mL) was heated for 2 h in sealed tube. After the reaction mixture was cooled, 1,3,5-trimethoxybenzene (168 mg, 1 mmol, internal standard) was added to the reaction mixture, which was extracted with CDCl3 (8 mL), then the organic layer was analyzed by 1H-NMR spectroscopy.

**Conversion yield was calculated by integration.**

<table>
<thead>
<tr>
<th>Signal (δ)</th>
<th>Ph-CHO 4a (1H)</th>
<th>Ph-Me 5a (3H)</th>
<th>1,3,5-trimethoxybenzene, internal standard (3H)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integral value</td>
<td>2.1 (1H)</td>
<td>5.67 (3H)</td>
<td>3.00 (3H)</td>
</tr>
<tr>
<td>Calculated ratio</td>
<td>42% from 2a</td>
<td>38% from 2a</td>
<td>1 mmol</td>
</tr>
</tbody>
</table>
Scheme 6(C)S. Control experiments.

A mixture of benzyl alcohol 2b (152 mg, 1 mmol), palladium(II) acetate (11 mg, 0.05 mmol), sodium diphenylphosphinobenzene-3-sulfonate (TPPMS, 36 mg, 0.1 mmol) in H₂O (4 mL) was heated for 2 h in sealed tube. After the reaction mixture was cooled, 1,3,5-trimethoxybenzene (168 mg, 1 mmol, internal standard) was added to the reaction mixture, which was extracted with CDCl₃ (8 mL), then the organic layer was analyzed by ¹H-NMR spectroscopy. Conversion yield was calculated by integration.

<table>
<thead>
<tr>
<th></th>
<th>4b</th>
<th>5b</th>
<th>1,3,5-trimethoxybenzene, internal standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signal</td>
<td>δ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4b</td>
<td>7.94 (Ar-2H)</td>
<td>1.21 (Ar-CH₂CH₃)</td>
<td>6.09 (Ar-H)</td>
</tr>
<tr>
<td>Integral value</td>
<td>0.98 (2H)</td>
<td>0.94 (3H)</td>
<td>3.00 (3H)</td>
</tr>
<tr>
<td>Calculated ratio</td>
<td>49% from 2b</td>
<td>31% from 2b</td>
<td>1 mmol</td>
</tr>
</tbody>
</table>

A mixture of benzyl alcohol 2b (152 mg, 1 mmol), palladium(II) acetate (11 mg, 0.05 mmol), sodium diphenylphosphinobenzene-3-sulfonate (TPPMS, 36 mg, 0.1 mmol) in H₂O (4 mL) was heated for 2 h in sealed tube. After the reaction mixture was cooled, 1,3,5-trimethoxybenzene (168 mg, 1 mmol, internal standard) was added to the reaction mixture, which was extracted with CDCl₃ (8 mL), then the organic layer was analyzed by ¹H-NMR spectroscopy. Conversion yield was calculated by integration.

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<thead>
<tr>
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<td>0.94 (3H)</td>
<td>3.00 (3H)</td>
</tr>
<tr>
<td>Calculated ratio</td>
<td>49% from 2b</td>
<td>31% from 2b</td>
<td>1 mmol</td>
</tr>
</tbody>
</table>
X: parts per Million: Carbon13

S40
S49