Supporting Information for

Catalytic Amination of 2-Substituted Pyridines with Hydrazine Derivatives

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Complete experimental procedures and
spectral data for compounds **5a-d**, and **7a-d**.

General Considerations. All experiments were performed in an efficient fume hood. Solvents and reagents were used without further purification. All the reagents were transferred in a dry-box, and the reactions were carried out under argon atmosphere. $Pd(OAc)_2$, $Pd_2(dba)_3$, BINAP, and DPPF were purchased from Strem Chemical Company. All other chemicals were purchased from Sigma-Aldrich. Silica gel 60, 70-230 mesh was used for column chromatography. Deuterated solvents were purchased from Aldrich or Norell, and were used without further purification.

NMR spectra were acquired at ambient temperatures (18 ± 2 ^{o}C), unless otherwise noted, using a Varian Gemini 200 Fourier transform spectrometer. The ^{1}H NMR spectra in $CDCl_3$ were referenced to TMS. The $^{13}C\{^{1}H\}$ NMR spectra were recorded at 50 MHz and referenced relative to the $^{13}C\{^{1}H\}$ peaks of the solvent. Spectra are reported as δ (ppm), (multiplicity, coupling constants (Hz), and number of hydrogens). Melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 1720X FTIR as KBr pellets, and are reported in cm^{-1}. HRMS and FAB MS were carried out at University of Maryland.

General Procedure A:

A Schlenk tube was charged with benzophenone hydrazone **1** (157 mg, 0.8 mmol), palladium acetate (5 mg, 2 mol %), 2,2'-*bis*(diphenylphosphanyl)-1,1'-binaphthyl (BINAP) (13 mg, 2 mol %), and sodium *t*-butoxide (135 mg, 1.4 mmol) in a dry box. The tube was purged with argon, then toluene (2 mL), and pyridyl substrate (1 mmol) were added. The reaction mixture was heated at 100 ^{0}C with stirring until the hydrazine derivative had been consumed as judged by TLC. The reaction mixture was cooled, diluted with CH_2Cl_2, washed with water and concentrated under vacuum. The crude residue was purified by silica gel chromatography with an eluent of hexanes and ethylacetate.

General Procedure B:

A Schlenk tube was charged with $Pd_2(dba)_3$ (37 mg, 0.04 mmol, 8 mol %), 1,1'-*bis*-(diphenylphosphanyl) ferrocene (DPPF) (67 mg, 0.12 mmol, 12 mol %), Cs_2CO_3 (352 mg, 1 mmol), and di-*tert*-butyl hydrazodiformate **3** (186 mg, 0.8 mmol) in a dry box. The tube was purged with argon, then toluene (2 mL), and pyridyl substrate (1 mmol) were added. The reaction mixture was heated at 100 ^{0}C with stirring until the hydrazine derivative had been consumed, as judged by TLC. The reaction mixture was cooled, diluted with CH_2Cl_2, washed with water and concentrated under vacuum. The crude residue was purified by silica gel chromatography with an eluent of hexanes and ethylacetate.

2-(Benzophenonehydrazono) pyridine, 5a (Table 1, Entry 2): General procedure **A** was followed with 2-bromopyridine **4b** (316 mg, 2 mmol), **1** (314 mg, 1.6 mmol), palladium acetate (9 mg, 0.04 mmol, 2 mol %), BINAP (25 mg, 0.04 mmol, 2 mol %), and sodium ^{t}butoxide (270 mg, 2.8 mmol). Column purification with 20% ethylacetate / hexane as eluent gave 520 mg (95% yield) of the coupled product **5a** as a light yellow solid, m.p.: 92-94 ^{o}C. ^{1}H NMR: 8.17 (s, 1H), 8.03 (d, J = 6 Hz, 1H), 7.65-7.44 (m, 8H), 7.36-7.24 (m, 4H), 6.71 (t, J = 6Hz, 1H); ^{13}C NMR: 156.34, 147.35, 145.94, 137.82, 137.76, 132.27, 129.48, 129.15, 128.65, 128.23, 127.98, 126.50, 115.56, 107.32; IR (KBr, cm^{-1}): 3333, 1597, 1490, 1443, 1296, 766; HRMS calcd for $C_{18}H_{15}N_3$: 273.1266. Found: 273.1271.

5-Bromo-2-(benzophenonehydrazono)pyridine, 5b (Table 1, Entry 3): General procedure **A** was followed with 2,5-dibromopyridine **4c** (474 mg, 2 mmol), **1**(314 mg, 1.6 mmol), palladium acetate (9 mg, 0.04 mmol, 2 mol %), BINAP (25 mg, 0.04 mmol, 2 mol %), and sodium ^{t}butoxide (270 mg, 2.8 mmol). Column purification with 10% ethylacetate / hexane as eluent gave 450 mg (80% yield) of the 2-coupled product **5b** as a white solid, m.p.: 42-44 ^{o}C. ^{1}H NMR: 8.17 (s, 1H), 8.06 (d, J = 2 Hz , 1H), 7.66 (dd, J1= 8 Hz, J2 = 2 Hz, 1H), 7.60 - 7.44 (m, 6H), 7.39 (d, J = 8 Hz, 1H), 7.35 - 7.23 (m, 4H); ^{13}C NMR: 155.07, 147.99, 146.87, 140.23, 137.54, 132.10, 129.57, 129.36, 128.62, 128.54, 128.08, 126.65, 109.74, 108.84; IR (KBr, cm^{-1}): 3300, 1584, 1489, 1385, 1292, 769; HRMS calcd. for $C_{18}H_{14}BrN_{3}$: 353.0350. Found: 353.0346.

Pentachlorophenyl-6-(benzophenonehydrazono) nicotinate, 5c (Table 1, Entry 4): General procedure **A** was followed with pentachlorophenyl-6-chloro-nicotinate **4d** (405 mg, 1 mmol), **1** (160 mg, 0.8 mmol), palladium acetate (5 mg, 0.02 mmol, 2 mol %), BINAP (13 mg, 0.02 mmol, 2 mol %), and sodium ^{t}butoxide (135 mg, 1.4 mmol). Column purification with 10% ethylacetate / hexane as eluent gave 216 mg (45% yield) of the coupled product **5c** as a white solid, m.p.: 202-204 ^{o}C. ^{1}H NMR: 8.91 (d, J = 2 Hz , 1H), 8.64 (s , 1H), 8.36 (dd , J1 = 8Hz , J2 = 2Hz , 1H), 7.75 – 7.50 (m, 5H), 7.45 – 7.30 (m, 6H);^{13}C NMR: 161.34, 159.51, 151.95, 149.93, 144.17, 139.77, 137.07, 131.80, 131.70, 131.30, 129.75, 129.70, 129.24, 128.55, 128.21, 127.91, 127.08, 114.86, 106.84; IR (KBr, cm^{-1}): 3324, 1784, 1596, 1520, 1240, 1048, 768; FAB (M+1) calcd. for $C_{25}H_{14}Cl_{5}N_{3}O_{2}$: 565.9577. Found: 565.9592.

Ethyl-6-(benzophenonehydrazono) nicotinate, 5d (Table 1, Entry 6): General procedure **A** was followed with ester triflate **4f** (150 mg, 0.5 mmol), **1** (79 mg, 0.4 mmol), palladium acetate (3 mg, 0.01 mmol, 2 mol %), BINAP (7 mg, 0.01 mmol, 2 mol %), and sodium ^{t}butoxide (68 mg, 0.7 mmol). Column purification with 10% ethylacetate / hexane as eluent gave 100 mg, 72% yield of the coupled product **5d** as a white solid, m.p.: 155-157 ^{o}C. ^{1}H NMR: 8.71 (d, J = 2Hz, 1H), 8.43 (s, 1H), 8.21 (dd, J1 = 8 Hz, J2 = 2Hz , 1H), 7.60 – 7.50 (m, 7H), 7.40-7.25 (m, 4H), 4.35 (q, J = 8 Hz, 2H), 1.38 (t, J=8 Hz, 3H); ^{13}C NMR: 165.43, 158.65, 150.45, 148.51, 139.01, 137.33, 131.91, 129.62, 129.53, 128.86, 128.58, 128.11, 126.86, 118.22, 106.36, 60.51, 14.21; IR (KBr, cm^{-1}): 3332; 1704, 1604, 1524, 1404, 1256, 776; HRMS calcd for $C_{21}H_{19}N_3O_2$: 345.1447. Found: 345.1502.

2-Hydrazinopyridine, 6 (Scheme 1): A Schlenk tube was charged with $Pd_2(dba)_3$ (75 mg, 0.08 mmol, 8 mol %), DPPF (134 mg, 0.24 mmol, 12 mol %), Cs_2CO_3 (704 mg, 2 mmol), and *t*-butyl carbazate **2** (265 mg, 2 mmol) in a dry box. The tube was purged with argon, then toluene (4 mL) and 2-bromopyridine **4b** (316 mg, 2 mmol) were added and the reaction mixture was heated at 100 ^{0}C for 16 h. The reaction mixture was cooled, diluted with CH_2Cl_2, washed with water and concentrated under vacuo. The crude material was dissolved in 20%HCl/EtOH and stirred at room temperature for 6 h. The solvent was evaporated under vacuum, and the residue was washed with 10% sodium hydroxide. Extraction with ethyl ether gave 98 mg (45% yield) of 2-hydrazino pyridine **6** as a brown solid, which was identical to a commercial sample (Aldrich).

2-(1,2-di-*tert*-butoxycarbonyl-hydrazino)pyridine, 7a (Table 2, Entry 5): General procedure **B** was followed with 2-bromopyridine **4b** (474 mg, 3 mmol), **3** (560 mg, 2.4 mmol), $Pd_2(dba)_3$ (109 mg, 0.12 mmol, 8 mol %), DPPF (200 mg, 0.36 mmol, 12 mol %), Cs_2CO_3 (1.05 g, 3 mmol). Column purification with 20% ethylacetate / hexane as eluent gave 630 mg (85% yield) of the coupled product **7a** as a white solid, m.p.: 80-82 ^{o}C. ^{1}H NMR: 8.58 (s, 1H), 8.34 (d, J = 4 Hz, 1H), 7.62 (m, 2H), 7.00 (dd, J1 = 8 Hz, J2 = 4 Hz, 1H), 1.40 (s, 9H), 1.36 (s, 3H); ^{13}C NMR: 154.98, 153.50, 153.05, 147.33, 137.28, 120.31, 118.68, 82.12, 80.65, 27.94, 27.82; IR (KBr, cm^{-1}): 3171, 2975, 1731, 1595, 855, 771; FAB MS (M+1) calcd. for $C_{15}H_{23}N_3O_4$: . 310.1766 Found: 310.1766.

5-Bromo-2-(1,2-di-*tert*-butoxycarbonyl-hydrazino) pyridine, 7b (Table 2, Entry 7): General procedure **B** was followed with 2,5-dibromopyridine **4c** (711 mg, 3 mmol), **3** (560 mg, 2.4 mmol), $Pd_2(dba)_3$ (109 mg, 0.12 mmol, 8 mol %), DPPF (200 mg, 0.36 mmol, 12 mol %), Cs_2CO_3 (1.05 g, 3 mmol). Column purification with 10% ethylacetate / hexane as eluent gave 792 mg (85 % yield) of the coupled product **7b** as a white solid, m.p.: 75-77 ^oC. ^1H NMR: 8.44 (d, J = 2 Hz, 1H), 7.95 (s, 1H), 7.78 (dd, J_1 = 8 Hz, J_2 = 2 Hz, 1H), 7.71 (d, J = 8 Hz, 1H), 1.52 (s, 9H), 1.47 (s, 9H); ^{13}C NMR: 154.73, 152.82, 152.22, 148.32, 139.80, 119.45, 115.94, 82.87, 81.27, 27.98, 27.91; IR (KBr, cm^{-1}): 3212, 1730, 1582, 1462, 1156, 838; FAB MS (M+1) calcd for $C_{15}H_{22}BrN_3O_4$: 388.0871. Found: 388.0853.

Pentachlorophenyl-6-(1,2-di-*tert*-butoxycarbonyl-hydrazino) nicotinate, 7c (Table 2, Entry 8): General procedure **B** was followed with pentachlorophenyl-6-chloro-nicotinate **4d** (405 mg, 1 mmol), **3** (186 mg, 0.8 mmol), $Pd_2(dba)_3$ (37 mg, 0.04 mmol, 8 mol %), DPPF (67 mg, 0.12 mmol, 12 mol %), Cs_2CO_3 (352 mg, 1 mmol). Column purification with 10% ethylacetate / hexane as eluent gave 216 mg (45% yield) of the coupled product **7c** as a light yellow solid, m.p.: 99-101 ^oC. ^1H NMR: 9.22 (d, J = 2 Hz, 1H), 8.44 (dd, J1 = 8 Hz, J2 = 2Hz, 1H), 8.11 (d, J = 8 Hz, 1H), 7.56 (s, 1H), 1.59 (s, 9H), 1.51 (s, 9H);^{13}C NMR: 160.87, 157.53, 154.61, 152.49, 150.51, 143.85, 139.38, 131.99, 131.70, 127.76, 119.41, 116.22, 83.72, 81.69, 28.05, 27.92; IR (KBr, cm^{-1}): 2980, 1758, 1599, 1247, 1153, 1063; FAB MS (M+1) calcd. for $C_{22}H_{22}Cl_5N_3O_6$: 602.0000. Found: 601.9957.

Ethyl-6-(1,2-di-*tert*-butoxycarbonyl-hydrazino) nicotinate, 7d (Table 2, Entry 10): General procedure **B** was followed with ester triflate **4f** (300 mg, 1 mmol), **3** (186 mg, 0.8 mmol), $Pd_2(dba)_3$ (37 mg, 0.04 mmol, 8 mol %), DPPF (67 mg, 0.12 mmol, 12 mol %), Cs_2CO_3 (352 mg, 1 mmol). Column purification with 10% ethylacetate / hexane as eluent gave 174 mg (57% yield) of the coupled product **7d** as a white solid, m.p.118-120 ^{o}C. ^{1}H NMR: 8.91 (d, J = 2 Hz, 1H), 8.22 (dd, J1 = 8 Hz, J2 = 2 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 6.80 (s, 1H), 4.38 (q, J = 8 Hz, 2H), 1.44 (s, 18H), 1.39 (t, J = 8 Hz, 3H); ^{13}C NMR: 164.83, 157.76, 155.64, 149.19, 138.47, 120.87, 113.04, 81.78, 80.96, 60.76, 27.87, 14.03; IR (KBr, cm^{-1}): 3338, 1718, 1592, 1263, 778.

Hydrolysis of 7a (Scheme 2): 2-(1,2-di-*tert*-butoxycarbonyl-hydrazino) pyridine, **7a** (140 mg, 0.45 mmol) was dissolved in 5 mL of 20% HCl/EtOH and stirred at room temperature for 6h, during which time, the starting material was consumed completely. The volume of the reaction mixture was reduced under vacuum. The hydrazine dihydrochloride precipitate was filtered, washed with ether, and dried under vacuum to yield the product 62 mg (75% yield) as a light tan solid, which was identical to a commercial sample (Aldrich).