SUPPORTING INFORMATION

Catalytic Coupling of C-H and C-I Bonds Using Pyridine As a Directing Group

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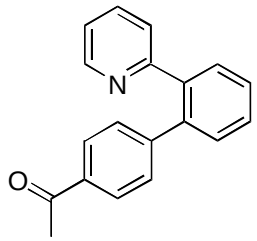
Experimental Section

General considerations. The coupling reactions were performed without special precautions in 6-dram screw-cap vials. Flash chromatography was performed on 60Å silica gel (Sorbent Technologies). GC analyses were performed on a Shimadzu CG-2010 chromatograph equipped with a Restek column (Rtx®-5, 15 m, 0.25 mm ID). The ^{1}H and ^{13}C NMR spectra were recorded on a GE QE-300 spectrometer using TMS peak as an internal standart. Melting points were measured on a Mel-Temp apparatus and are uncorrected. Elemental analyses were performed by Atlantic Microlab Inc. of Norcross, GA. IR-spectra were obtained using a ThermoNicolet Avatar 370 FT-IR instrument.

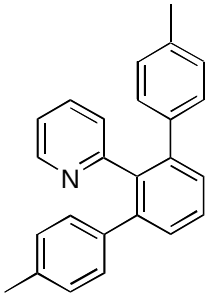
Materials. Acetic acid (EMC), propionic acid (Acros), *t*-BuOH (Acros), AgOAc purified (Fisher), $Pd(OAc)_2$ (J&J Materials), 2-phenylpyridine (Lancaster), 2-ethylpyridine (Eastman Kodak) were used as obtained. 8-Methylquinoline, 1-phenylpyrazole, 7,8-benzoquinoline, 4-methyliodobenzene, 4-iodoacetophenone, 5-iodo-m-xylene are available from Acros, 4-iodo-1-bromobenzene and 4-iodobenzotrifluoride are available from Aldrich. Methyl 4-iodobenzoate and methyl 3-iodobenzoate are known.[1]

General procedure: A 6-dram screw-cap vial was charged with $Pd(OAc)_2$ (3-5 mol%), AgOAc (1.1-3.1 eq), iodide (3-5 eq) and substrate. The appropriate solvent (AcOH, EtCOOH or *t*-BuOH) was added and resulting mixture was stirred at 130^{o}C. The convertion was monitored by GC. After completion of reaction ethyl acetate was added to reaction mixture followed by filtration through a pad of Celite. The filtrate was evaporated under reduced pressure and residue was dried under vacuum to remove solvent. The residue was purified by flash chromatography.

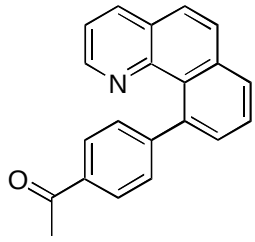


2-(2-(4-Acetylphenyl)-phenyl)-pyridine: 2-Phenylpyridine (155 mg, 1.0 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), AgOAc (350 mg, 2.1 mmol) and 4-iodoacetophenone

(1.23 g, 5 mmol) were mixed with acetic acid (5 ml) and heated at 130^{o}C for 116h. Purification by flash chromatography (EtOAc/hexanes) gave 200 mg (73%) of a white solid, mp 100.5-101.5^{o}C (hexanes/ethyl acetate), R_f=0.08 (EtOAc/hexanes 1/4); ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.62 (dd, 1H, *J*= 5.0, 1.6 Hz) 7.86-7.82 (2H, m) 7.73-7.68 (1H, m) 7.54-7.40 (4H, m) 7.28-7.23 (2H, m) 7.13 (1H, ddd, *J* = 5.0, 5.0, 1.1 Hz) 6.93 (1H, d, *J*= 7.8 Hz) 2.59 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 198.1, 152.4, 149.7, 146.7, 139.9, 139.7, 135.8, 135.6, 130.8, 130.5, 130.1, 128.9, 128.5, 128.4, 125.4, 121.8, 26.8. FT-IR (neat, cm^{-1}) 1673. Anal. Calcd. for $C_{19}H_{15}NO$: C 83.49, H 5.53, N 5.12. Found C 83.25, H 5.52, N 5.07.

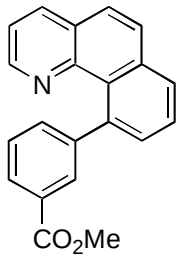


2-(2,6-Di-(4-methylphenyl))-phenylpyridine: 2-Phenylpyridine (155 mg, 1.0 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), AgOAc (350 mg, 2.1 mmol) and 4-methylphenyliodide (1.09 g, 5 mmol) were mixed with acetic acid (5 ml) and heated at 130^{o}C for 165h. Purification by flash chromatography (EtOAc/hexanes) gave 268 mg (80%) of white crystals. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.34 (1H, dd, *J*= 4.9, 1.4 Hz) 7.53-7.38 (3H, m) 7.32 (1H, ddd, *J*= 7.7, 7.7, 1.6 Hz) 7.01-6.86 (10H, m) 2.26 (6H, s). This compound has been reported previously.[2]

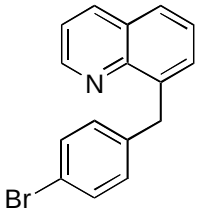


10-(4-Acetylphenyl)-7,8-benzoquinoline: 7,8-Benzoquinoline (179 mg, 1.0 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), AgOAc (183 mg, 1.1 mmol) and 4-iodoacetophenone

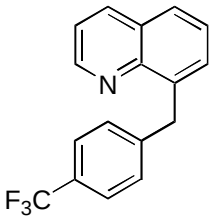
(738 mg, 3 mmol) were mixed with propionic acid (3 ml) and heated at 130°C for 125h. Purification by flash chromatography (EtOAc/hexanes) gave 220 mg (74%) of pale orange needles, mp 111-112°C (hexanes/EtOAc), R_f=0.42 (EtOAc/hexanes 1/4); ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.39 (1H, dd, *J*= 4.4, 2.0 Hz) 8.11 (1H, dd, *J*= 8.1, 1.9 Hz) 8.04-7.99 (2H, m) 7.97 (1H, dd, *J*= 8.1, 1.2 Hz) 7.88 (1H, d, *J*= 8.7 Hz) 7.75-7.68 (2H, m) 7.51 (1H, dd, *J*= 7.4, 1.3 Hz) 7.47-7.42 (2H, m) 7.34 (1H, dd, *J*= 7.9, 4.4 Hz) 2.70 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 198.5, 152.1, 147.1, 146.6, 140.6, 135.5, 135.1, 134.9, 131.1, 129.1, 129.0, 128.7, 128.4, 127.9, 127.5, 127.2, 126.3, 121.4, 26.9. FT-IR (neat, cm^{-1}) 1672. Anal. Calcd. for $C_{21}H_{15}NO$: C 84.82, H 5.08, N 4.71. Found C 84.83, H 5.06, N 4.69.



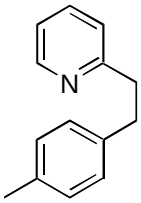
10-(3-Methoxycarbonylphenyl)-7,8-benzoquinoline: 7,8-Benzoquinoline (179 mg, 1.0 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), AgOAc (167 mg, 1 mmol) and methyl 3-iodobenzoate (786 mg, 3 mmol) were mixed with acetic acid (5 ml) and heated at 130°C for 112h. Purification by flash chromatography (EtOAc/hexanes) gave 186 mg (60%) of white crystals, mp 116-117°C (hexanes), R_f=0.40 (EtOAc/hexanes 1/4); ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.37 (1H, dd, *J*= 4.3, 1.8 Hz) 8.12-8.02 (3H, m) 7.96 (1H, d, *J*= 8.1 Hz) 7.87 (1H, d, *J*= 8.8 Hz) 7.73-7.66 (2H, m) 7.58-7.43 (3H, m) 7.32 (1H, dd, *J*= 7.8, 4.4 Hz) 3.89 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 167.8, 147.1, 146.9, 146.8, 140.7, 135.5, 135.2, 133.7, 131.6, 130.1, 129.5, 129.1, 128.6, 128.4, 127.5, 127.25, 127.23, 126.3, 121.4, 52.1. FT-IR (neat, cm^{-1}) 1715. Anal. Calcd. for $C_{21}H_{15}NO_2$: C 80.49, H 4.82, N 4.47. Found C 80.42, H 4.75, N 4.39.



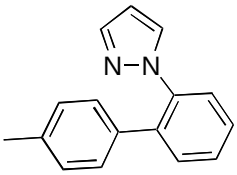
8-(4-Bromobenzyl)-quinoline: 8-Methylquinoline (143 mg, 1.0 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), AgOAc (350 mg, 2.1 mmol) and 4-bromophenyliodide (1.41 g, 5 mmol) were mixed with *t*-butanol (5 ml) and heated at 110^{o}C for 48h. Purification by flash chromatography (EtOAc/hexanes) gave 220 mg (74%) of crystalline material, mp 54-55^{o}C (hexanes/EtOAc), R_f=0.47 (EtOAc/hexanes 1/4). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.95 (1H, dd, *J*= 4.2, 1.7 Hz) 8.15 (1H, dd, *J*= 8.2, 1.8 Hz) 7.70 (1H, dd, *J*= 7.2, 2.4 Hz) 7.49-7.35 (5H, m) 7.22-7.16 (2H, m) 4.62 (2H, s). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 149.8, 146.8, 140.6, 139.7, 136.5, 131.5, 131.2, 129.6, 128.6, 126.8, 126.6, 121.3, 119.9, 36.5. FT-IR (neat, cm^{-1}) 1488, 798. Anal. Calcd. for $C_{16}H_{12}BrN$: C 64.45, H 4.06, N 4.70. Found C 64.22, H 3.91, N 4.49.



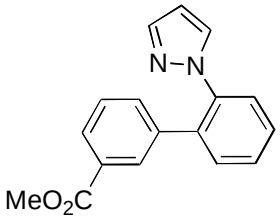
8-(4-Trifluoromethylbenzyl)-quinoline: 8-Methylquinoline (143 mg, 1.0 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), AgOAc (350 mg, 2.1 mmol) and 4-iodobenzotrifluoride (1.36 g, 5 mmol) were mixed with *t*-butanol (5 ml) and heated at 110^{o}C for 42h. Purification by flash chromatography (EtOAc/hexanes) gave 198 mg (69%) of a crystalline material, mp 56-57^{o}C (hexanes/EtOAc), R_f=0.38 (EtOAc/hexanes 1/10). ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.95 (1H, dd, *J*= 4.2, 1.7 Hz) 8.15 (1H, dd, *J*= 8.3, 1.7 Hz) 7.75-7.68 (1H, m) 7.54-7.38 (7H, m) 4.72 (2H, s). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 149.9, 146.8, 145.8, 139.2, 136.5, 130.1, 129.8, 129.7, 128.7, 128.4 (q, $J_{C\text{-}F}$= 31.9 Hz), 126.9, 126.6, 125.4 (br s), 124.6 (q, $J_{C\text{-}F}$= 271.3 Hz), 121.4, 36.9. Anal. Calcd. for $C_{17}H_{12}F_3N$: C 71.07, H 4.21, N 4.88. Found C 71.05, H 4.20, N 4.88.



2-(4-Methylphenylethyl)-pyridinium hydrochloride: 2-Ethylpyridine (64 mg, 0.6 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), AgOAc (210 mg, 1.26 mmol) and 4-methylphenyliodide (654 g, 5 mmol) were mixed with acetic acid (1.5 ml) and heated at 130^{o}C for 47h. Purification by flash chromatography (EtOAc/hexanes) gave 60 mg (51%) of an oil. The hydrochloride salt was obtained by addition of HCl solution in ether, mp 150-151^{o}C. ^{1}H NMR (hydrochloride salt; 300 MHz, $CDCl_3$, ppm) δ 8.73-8.62 (1H, m) 8.24-8.13 (1H, m) 7.77-7.67 (1H, m) 7.47-7.39 (1H, m) 7.10-7.00 (4H, m) 3.63-3.51 (2H, m) 3.27-3.15 (2H, m) 2.30 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 157.2, 145.1, 141.2, 136.5, 135.6, 129.5, 128.6, 127.3, 124.5, 35.3, 35.1, 21.1.



1-(2-(4-Methylphenyl)-phenyl)-pyrazole: 1-Phenylpyrazole (144 mg, 1.0 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), AgOAc (350 mg, 2.1 mmol) and 4-methylphenyliodide (1.09 g, 5 mmol) were mixed with acetic acid (5 ml) and heated at 130^{o}C for 120h. Purification by flash chromatography (EtOAc/hexanes) gave 143 mg (61%) of white crystals, mp 49-50^{o}C (pentane), R_f=0.24 (EtOAc/hexanes 1/10); ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.64 (1H, d, *J*= 1.6 Hz) 7.62-7.57 (1H, m) 7.46-7.41 (3H, m) 7.11-7.06 (3H, m) 7.01-6.97 (2H, m) 6.20 (1H, dd, *J*= 2.2, 2.0 Hz) 2.33 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 140.4, 138.7, 137.4, 136.8, 135.7, 131.5, 131.2, 129.4, 128.5, 128.4, 128.3, 126.7, 106.5, 21.4. Anal. Calcd. for $C_{16}H_{14}N_2$: C 82.02, H 6.02, N 11.96; found C 81.82, H 5.99, N 11.95.



1-(2-(3-Methoxycarbonylphenyl))-phenylpyrazole: 1-Phenylpyrazole (144 mg, 1.0 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), AgOAc (350 mg, 2.1 mmol) and methyl 3-iodobenzoate (1.31 g, 5 mmol) were mixed with acetic acid (5 ml) and heated at 130°C for 160h. Purification by flash chromatography (EtOAc/hexanes) gave 164 mg (59%) of white crystals, mp 77-78°C (hexanes/EtOAc), R_f=0.32 (EtOAc/hexanes 1/4); ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.98-7.94 (1H, m), 7.93-7.91 (1H, m), 7.64-7.59 (2H, m), 7.52-7.48 (3H, m), 7.32 (1H, t, *J*= 7.7 Hz), 7.19-7.15 (1H, m), 7.11 (1H, d, *J*= 2.3 Hz), 6.21 (1H, t, *J*= 1.9 Hz), 3.91 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 167.0, 140.6, 139.0, 138.8, 136.0, 133.1, 131.4, 131.2, 130.8, 129.9, 129.0, 128.8, 128.7, 128.6, 126.9, 106.8, 52.4. FT-IR (neat, cm^{-1}) 1711, 756. Anal. Calcd. for $C_{17}H_{14}N_2O_2$: C 73.37, H 5.07, N 10.07. Found C 73.19, H 5.05, N 9.95.

Additional References:

1 Yasui, S.; Nakamura, K.; Fujii, M.; Ohno, A. *J. Org. Chem.* **1985**, *50*, 3283.

2 Oi, S.; Fukita, S.; Hirata, N.; Watanuki, N.; Miyano, S.; Inoue, Y. *Org. Lett.* **2001**, *3*, 2579.