Supporting Information

Palladium-Catalyzed Cyanation of Aryl Bromides Promoted by Low-level Organotin Compounds

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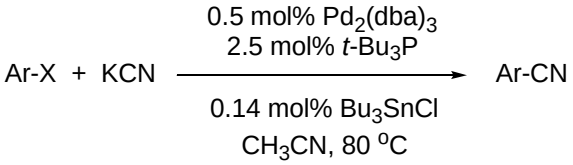

General Considerations: All reactions were carried out under a nitrogen atmosphere in dried glassware. All aryl halides, heteroaryl halides and the aryl triflate were purchased from commercial sources and were used without further purification. Potassium cyanide, tri-*n*-butyltin chloride and tris(dibenzylideneacetone) dipalladium(0) were purchased from Aldrich Chemical Co. and were used directly. Acetonitrile was purchased from Fisher Scientific Company and contained less than 80 μg/mL water. Tri-*tert*-butylphosphine (10 wt% in hexanes) and Xantphos were purchased from Strem Chemicals. Tri-*n*-butyltin chloride solution (14 μL/mL) was prepared by addition of 0.14 mL of tri-*n*-butyltin chloride into 10 mL of heptane. Conversion was determined by HPLC assay. ^{1}H NMR and ^{13}C NMR were obtained with a Bruker DPX-400 in $CDCl_3$.

General Procedures for table 1 compounds:

Condition a:

Entry 1

To a dry 50 mL flask was added KCN (0.8 g, 12 mmol), acetonitrile (7.5 mL) and 1-bromonaphthalene (1.1 mL, 8 mmol). The suspension was degassed three times (vacuum / nitrogen), and then a solution of Bu_3SnCl in heptane (0.24 mL, 0.011 mmol), *t*-Bu_3P (10 wt% in hexanes, 0.63 mL, 0.2 mmol) and $Pd_2(dba)_3$ (38 mg, 0.04 mmol) were added. The suspension was degassed three times and stirred at ambient temperature for 30 min. The mixture was degassed again, and then heated at 80 °C for 17 h. Reaction conversion was determined by HPLC. The reaction mixture was diluted with ethyl acetate or MTBE (20 mL), and result was washed with water (10 mL) twice. The organic solution was dried with Na_2SO_4 and concentrated. The residue was purified with a silica gel column (hexanes/ethyl acetate 8/1) to afford the title compound with a yield of 97%.

^{1}H NMR: δ 8.26 (*dd*, *J* = 8.4 Hz, 0.8 Hz, 1 H), 8.10 (*d*, *J* = 8.4 Hz, 1 H), 7.96-7.92 (*m*, 2 H), 7.74-7.70 (*m*, 1 H), 7.66-7.62 (*m*, 1 H), 7.56-7.53 (*m*, 1 H).

^{13}C NMR δ 133.3, 133.0, 132.7, 132.5, 128.7, 128.7, 127.6, 125.3, 125.0, 117.9, 110.3.

Entry 2
The residue was purified with a silica gel column (hexanes/MTBE 4/1) to afford the title compound with a yield of 90%.
^{1}H NMR: δ 7.68-7.64 (*m*, 2 H), 7.64-7.60 (*m*, 1 H), 7.51-7.27 (*m*, 2 H).
^{13}C NMR δ 132.8, 132.2, 129.2, 118.9, 112.6.

Entry 3
The residue was purified with a silica gel column (hexanes/ethyl acetate 8/1) to afford the title compound with a yield of 90%.
^{1}H NMR: δ 7.56 (*d*, *J* = 8.2 Hz, 2 H), 7.27 (*d*, *J* = 8.2 Hz, 2 H), 2.43 (*s*, 3 H).
^{13}C NMR δ 143.7, 132.1, 129.9, 119.2, 109.4, 21.9.

Entry 4
The residue was purified with a silica gel column (hexanes/ethyl acetate 8/1) to afford the title compound with a yield of 93%.
^{1}H NMR: δ 7.75-7.69 (*m*, 4 H), 7.62-7.59 (*m*, 2 H), 7.52-7.48 (*m*, 2 H), 7.46-7.27 (*m*, 1 H)
^{13}C NMR δ 145.6, 139.1, 132.5, 129.0, 128.6, 127.6, 127.1, 118.8, 110.8.

Entry 5
The residue was purified with a silica gel column (hexanes/ethyl acetate 8/1) to afford the title compound with a yield of 54%.
^{1}H NMR: δ 7.71-7.67 (*m*, 2 H), 7.19-7.17 (*m*, 2 H).
^{13}C NMR: δ 165.1 (*d*, *J* = 256.4 Hz), 134.7 (*d*, *J* = 9.5 Hz), 118.0, 116.9 (*d*, *J* = 22.7 Hz), 117.7 (*d*, *J* = 3.5 Hz).

Entry 6
The residue was purified with a silica gel column (hexanes/MTBE 8/1) to afford the title compound with a yield of 81%.
^{1}H NMR: δ 7.92-7.81 (*m*, 4H).
^{13}C NMR δ 134.6 (*q*, *J* = 33.6 Hz), 132.7, 126.2 (*q*, *J* = 3.7 Hz), 123.1 (*q*, *J* = 273.0 Hz), 117.4, 116.1.

Entry 7
The residue was purified with a silica gel column (hexanes/ethyl acetate 8/1) to afford the title compound with a yield of 93%.
^{1}H NMR: δ 8.10 (*d*, *J* = 8.5 Hz, 2 H), 7.78 (*d*, *J* = 8.4 Hz, 2 H), 2.65 (*s*, 3H).
^{13}C NMR δ 196.5, 140.0, 132.6, 128.7, 117.9, 116.5, 26.8.

Entry 8
The residue was purified with a silica gel column (hexanes/MTBE 8/1) to afford the title compound with a yield of 91%.
^{1}H NMR: δ 8.15 (*d*, *J* = 8.4, 2H), 7.75 (*d*, *J* = 8.6, 2 H), 4.43 (*q*, *J* = 7.2, 2 H), 1.42 (*t*, 7.2, 3 H).

^{13}C NMR δ 165.0, 134.4, 132.2, 130.1, 118.0, 116.4, 61.9, 14.3.

Entry 9
The residue was purified with a silica gel column (hexanes/MTBE 8/1) to afford the title compound with a yield of 50%.
^{1}H NMR: δ 7.59-7.57 (*m*, 2 H), 6.96-6.94 (*m*, 2 H), 3.86 (*s*, 3 H).
^{13}C NMR δ 162.9, 134.0, 119.2, 114.8, 104.1, 55.6.

Entry 12
The reaction was carried out at 22 ^{o}C for 3 h. The residue was purified with a silica gel column (hexanes/MTBE 8/1) to afford the title compound with a yield of 96%.
^{1}H NMR: δ 7.56 (*d*, *J* = 8.2 Hz, 2 H), 7.27 (*d*, *J* = 8.2 Hz, 2 H), 2.43 (*s*, 3 H).
^{13}C NMR δ 143.7, 132.1, 129.9, 119.2, 109.4, 21.9.

Entry 13
The residue was purified with a silica gel column (hexanes/MTBE 8/1) to afford the title compound with a yield of 92%.
^{1}H NMR: δ 7.65 (*dd*, *J* = 1.9 Hz, 1.8 Hz, 1 H), 7.60 (*ddd*, *J* = 8.1 Hz, 2.0 Hz, 1.1 Hz, 1 H), 7.56 (*ddd*, *J* = 7.8 Hz, 1.4 Hz, 1.4 Hz, 1 H), 7.42 (*dd*, *J* = 7.8 Hz, 7.8 Hz, 1 H).
^{13}C NMR: δ 135.4, 133.3, 132.0, 130.5, 130.3, 117.5, 114.1.

Entry 14
The residue was purified with a silica gel column (hexanes/ethyl acetate 2/1) to afford the title compound with a yield of 89%.
^{1}H NMR: δ 7.67 (*s*, 1 H), 7.61-7.55 (*m*, 2 H), 7.46 (*dd*, *J* = 7.7 Hz, 7.6 Hz, 1 H), 4.74 (*s*, 2 H), 2.22 (*br*, 1 H).
^{13}C NMR δ 142.4, 131.1, 131.0, 130.2, 129.3, 118.8, 112.4, 63.9.

Entry 15
The amount of Bu_3SnCl solution was reduced to 0.12 mL. The residue was purified with a silica gel column (hexanes/MTBE 8/1) to afford the title compound with a yield of 90%.

Condition b:
Entry 17
To a dry 50 mL flask was added KCN (0.8 g, 12 mmol), acetonitrile (7.5 mL) and 3-bromopyridine (0.78 mL, 8 mmol). The suspension was degassed three times (vacuum / nitrogen), and then a solution of Bu_3SnCl in heptane (0.43 mL, 0.021 mmol), XANTPHOS (23 mg, 0.04 mmol) and $Pd_2(dba)_3$ (38 mg, 0.04 mmol) were added. The suspension was degassed three times and stirred at ambient temperature for 30 min. The mixture was degassed again, and then heated at 80 °C for 17 h. Reaction conversion was determined by HPLC. The reaction mixture was diluted with ethyl acetate or MTBE (20 mL), and result was washed with water (10 mL) twice. The organic solution was dried

with Na_2SO_4 and concentrated. The residue was purified with a silica gel column (hexanes/MTBE 8/1) to afford the title compound with a yield of 93%.
^{1}H NMR: δ 8.90 (*dd J* = 2.0 Hz, 0.7 Hz, 1 H), 8.83 (*dd, J* = 5.0 Hz, 1.7 Hz, 1 H), 7.98 (*ddd, J* = 8.1 Hz, 1.7 Hz, 1.7 Hz, 1 H), 7.45 (*ddd, J* = 8.0 Hz, 4.0 Hz, 0.7 Hz, 1 H).
^{13}C NMR δ 153.0, 152.5, 139.2, 123.6, 116.5, 110.2.

Entry 10
The residue was purified with a silica gel column (hexanes/MTBE 8/1) to afford the title compound with a yield of 78%.
^{1}H NMR: δ 8.38-8.36 (*m*, 2 H), 7.91-7.89 (*m*, 2 H).
^{13}C NMR δ 133.5, 124.3, 118.4, 116.8.

Entry 11
The residue was purified with a silica gel column (hexanes/MTBE 8/1) to afford the title compound with a yield of 88%.
^{1}H NMR: δ 8.38-8.36 (*m*, 2 H), 7.91-7.89 (*m*, 2 H).
^{13}C NMR δ 133.5, 124.3, 118.4, 116.8.

Entry 16
The amount of Bu_3SnCl solution was reduced to 0.24 mL. DPPF (23 mg) was used as a catalyst ligand. The residue was purified with a silica gel column (hexanes/ethyl acetate 2/1) to afford the title compound with a yield of 88%.
^{1}H NMR: δ 8.72 (dt, J = 4.8 Hz, 1 H), 7.85 (dt, J = 8.0 Hz, 1.8 Hz, 1 H), 7.70 (dt, J = 7.8 Hz, 1 H), 7.54 (ddd, J = 7.8 Hz, 4.8 Hz, 3.8 Hz, 1 H)
^{13}C NMR δ 151.2, 137.1, 134.1, 128.6, 127.0, 117.2.

Entry 18
The reaction was carried out at 22 ^{o}C for 3 h. The residue was purified with a silica gel column (hexanes/ethyl acetate 8/1) to afford the title compound with a yield of 95%.
^{1}H NMR: δ 8.90 (*dd J* = 2.0 Hz, 0.7 Hz, 1 H), 8.83 (*dd, J* = 5.0 Hz, 1.7 Hz, 1 H), 7.98 (*ddd, J* = 8.1 Hz, 1.7 Hz, 1.7 Hz, 1 H), 7.45 (*ddd, J* = 8.0 Hz, 4.0 Hz, 0.7 Hz, 1 H).
^{13}C NMR δ 153.0, 152.5, 139.2, 123.6, 116.5, 110.2.

Entry 19
The residue was purified with a silica gel column (hexanes/ethyl acetate 8/1) to afford the title compound with a yield of 96%.
^{1}H NMR: δ 9.03 (*d, J* = 1.7 Hz, 1 H), 8.53 (*d, J* = 2.0 Hz, 1 H), 8.17 (*d, J* = 8.9 Hz, 1 H). 7.91-7.88 (m, 2 H), 7.69 (*dt, J* = 8.0 Hz, 1.1 Hz, 1 H)
^{13}C NMR δ 149.8, 148.9, 141.5, 132.8, 129.9, 128.5, 128.3, 126.3, 117.1, 106.7,

NMR studies:

To a NMR tube was added CD_3CN (0.8 mL), Bu_3SnCl (54 μL). After recorded ^1H and ^{13}C NMR spectra, KCN (13 mg) was added, and then sonicated for 30 seconds. ^1H and ^{13}C NMR spectra was recorded.
^1H and ^{13}C NMR spectra of Bu_3SnCN (60 mg) and Bu_3SnCN with KCN (13 mg) were separately recorded in CD_3CN (0.8 mL).