

Supporting Information

Copper(II)-Catalyzed *ortho*-Functionalization of 2-Arylpyridines with Acyl Chlorides

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1. General experimental details

Chemicals were purchased without special instructions. ^1H NMR and ^{13}C NMR spectra were measured on a 300 MHz or 500 MHz Bruker spectrometer using CDCl_3 as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. Chemical shifts (δ) are given in ppm relative to TMS, the coupling constants J are given in Hz. All reactions were conducted under air atmosphere. Column chromatography was performed using EM Silica gel 60 (300-400 mesh).

1.1 General Procedure for Copper-Catalyzed *ortho*-Benzylation of 2-Arylpyridines C-H Bond using the Acyl Chlorides:

Under O_2 atmosphere, a sealed tube was charged with 2-aryl pyridine (0.2 mmol), acyl chloride (0.4 mmol), $\text{Cu}(\text{OAc})_2$ (7.3 mg, 20 mol %), $t\text{-BuOK}$ (44.8 mg, 0.4 mmol), and dry toluene (2 mL). The mixture was stirred at 145 $^\circ\text{C}$ for 48 h. After the completion of the reaction, as monitored by TLC, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel to give the product.

1.2 General Procedure for *ortho*-Chlorination of 2-arylpyridines with acyl chlorides :

Under O_2 atmosphere, a sealed tube was charged with 2-aryl pyridine (0.2 mmol), acyl chloride (0.6 mmol), $\text{Cu}(\text{OAc})_2$ (7.3 mg, 20 mol %), Li_2CO_3 (29.6 mg, 0.4 mmol), and dry toluene (2 mL). The mixture was stirred at 145 $^\circ\text{C}$ for 48 h. After the completion of the reaction, as monitored by TLC, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel to give the product.

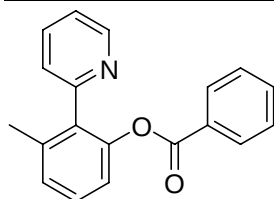
1.3 Preparation of 2-aryl pyridines¹:

Under air atmosphere, a reaction tube was charged with 2-bromopyridine (78.5 mg, 0.5 mmol), arylboronic acid (0.75 mmol), PdCl_2 (4.4 mg, 0.025 mmol), $\text{K}_3\text{PO}_4 \cdot 3\text{H}_2\text{O}$ (399 mg, 1.5 mmol) and toluene (3 mL). After the mixture was heated at 100 $^\circ\text{C}$ for 8 h, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel to give the product.

1. C. Pan, M. Liu, L. Zhang, H. Wu, J. Ding, J. Cheng, *Catal. Comm.*, 2008, **9**, 508.

2. Experimental characterization data for compounds

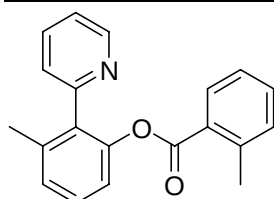
3-methyl-2-(pyridin-2-yl)phenyl benzoate(3aa)²



¹H NMR (CDCl₃, 500 MHz): δ 8.56 (d, *J* = 4.5 Hz, 1H), 7.78-7.76 (m, 2H), 7.57-7.53 (m, 1H), 7.44-7.41 (m, 1H), 7.30-7.22 (m, 4H), 7.15-7.06 (m, 3H), 2.11 (s, 3H).

¹³C NMR (CDCl₃, 125 MHz): δ 165.1, 155.7, 149.3, 148.7, 138.3, 136.3, 133.5, 133.3, 129.9, 129.3, 129.0, 128.3, 128.0, 124.9, 122.2, 120.1, 19.9.

3-methyl-2-(pyridin-2-yl)phenyl 2-methylbenzoate (3ab)



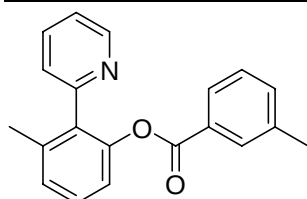
¹H NMR (CDCl₃, 500 MHz): δ 8.68 (d, *J* = 4.5 Hz, 1H), 7.67-7.64 (m, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.38-7.31 (m, 3H), 7.25-7.11 (m, 5H), 2.43 (s, 3H), 2.18 (s, 3H).

¹³C NMR (CDCl₃, 125 MHz): δ 165.8, 155.9, 149.4, 148.6, 140.7, 138.2, 136.2, 133.7, 132.3, 131.5, 130.8, 128.9, 128.4, 127.8, 125.6, 124.9, 122.1, 120.2, 21.4, 19.8.

IR (prism, cm⁻¹): ν 3075, 1732, 1503, 1242, 1216.

HRMS (EI) Calcd for C₂₀H₁₈NO₂ (M+H)⁺ 304.1338, found 304.1298.

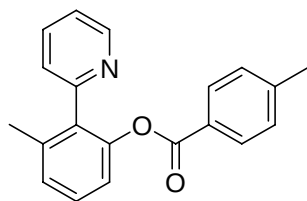
3-methyl-2-(pyridin-2-yl)phenyl 3-methylbenzoate(3ac)²



¹H NMR (CDCl₃, 500 MHz): δ 8.58 (s, 1H), 7.58-7.55 (m, 3H), 7.30-7.23 (m, 3H), 7.18-7.06 (m, 4H), 2.24 (s, 3H), 2.11 (s, 3H).

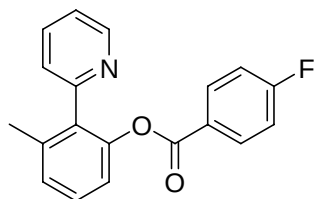
¹³C NMR (CDCl₃, 125 MHz): δ 165.2, 155.6, 149.1, 148.6, 138.12, 138.05, 136.3, 134.0, 133.2, 130.4, 129.1, 128.9, 128.1, 127.8, 127.0, 124.9, 122.1, 120.0, 21.1, 19.8.

3-methyl-2-(pyridin-2-yl)phenyl 4-methylbenzoate(3ad)²



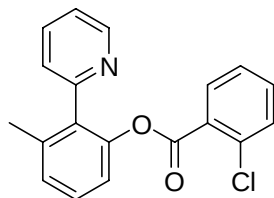
^1H NMR (CDCl_3 , 300 MHz): δ 8.56 (d, J = 4.4 Hz, 1H), 7.65 (d, J = 8.2 Hz, 2H), 7.54-7.51 (m, 1H), 7.29-7.20 (m, 2H), 7.13-7.05 (m, 5H), 2.27 (s, 3H), 2.10 (s, 3H).
 ^{13}C NMR (CDCl_3 , 125 MHz): δ 165.1, 155.7, 149.2, 148.6, 144.0, 138.1, 136.1, 133.4, 129.9, 129.0, 128.8, 127.8, 126.5, 124.8, 122.0, 120.1, 21.5, 19.8.

3-methyl-2-(pyridin-2-yl)phenyl 4-fluorobenzoate (3ae)



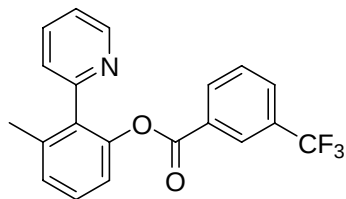
^1H NMR (CDCl_3 , 300 MHz): δ 8.55 (d, J = 4.6 Hz, 1H), 7.80-7.75 (m, 2H), 7.551-7.545 (m, 1H), 7.28-7.19 (m, 2H), 7.15-7.04 (m, 3H), 6.96-6.90 (m, 2H), 2.10 (s, 3H).
 ^{13}C NMR (CDCl_3 , 125 MHz): δ 165.9 (d, $J_{\text{C-F}}$ = 253.1 Hz), 164.0, 155.6, 149.3, 148.5, 138.2, 136.1, 133.4, 132.4 (d, $J_{\text{C-F}}$ = 9.4 Hz), 128.9, 128.0, 125.5 (d, $J_{\text{C-F}}$ = 2.9 Hz), 124.8, 122.1, 120.0, 115.5 (d, $J_{\text{C-F}}$ = 21.9 Hz), 19.8.
IR (prism, cm^{-1}): ν 3087, 1737, 1507, 1263, 1218.
HRMS (EI) Calcd for $\text{C}_{19}\text{H}_{15}\text{FNO}_2$ ($\text{M}+\text{H}$) $^+$ 308.1087, found 308.1070.

3-methyl-2-(pyridin-2-yl)phenyl 2-chlorobenzoate (3af)



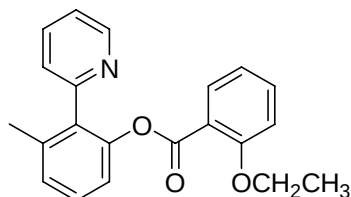
^1H NMR (CDCl_3 , 500 MHz): δ 8.70 (s, 1H), 7.71-7.68 (m, 1H), 7.44-7.34 (m, 5H), 7.26-7.15 (m, 4H), 2.19 (s, 3H).
 ^{13}C NMR (CDCl_3 , 125 MHz): δ 163.8, 155.6, 149.3, 148.3, 138.3, 136.5, 134.1, 133.4, 132.8, 131.4, 131.0, 129.09, 129.07, 128.2, 126.4, 125.1, 122.3, 120.0, 19.9.
IR (prism, cm^{-1}): ν 3065, 1746, 1460, 1435, 1242, 1216.
HRMS (EI) Calcd for $\text{C}_{19}\text{H}_{14}\text{ClNO}_2$ (M) $^+$ 323.0713, found 323.0718.

3-methyl-2-(pyridin-2-yl)phenyl 3-(trifluoromethyl)benzoate (3ag)



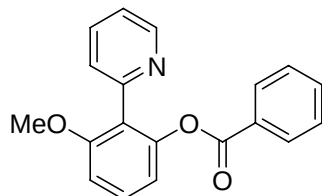
^1H NMR (CDCl_3 , 500 MHz): δ 8.66 (s, 1H), 8.05-8.04 (m, 2H), 7.78-7.67 (m, 2H), 7.53-7.50 (m, 1H), 7.41-7.19 (m, 5H), 2.21 (s, 3H).
 ^{13}C NMR (CDCl_3 , 125 MHz): δ 163.6, 155.2, 149.1, 148.4, 138.3, 136.6, 133.1, 132.9, 131.0 (q, $J_{\text{C-F}} = 32.9$ Hz), 130.2, 129.8, 129.7, 129.1, 129.0, 128.2, 126.8, 125.0, 123.5 (q, $J_{\text{C-F}} = 271.0$ Hz), 119.9, 19.8.
IR (prism, cm^{-1}): ν 3079, 1741, 1463, 1241, 1217.
HRMS (EI) Calcd for $\text{C}_{20}\text{H}_{14}\text{F}_3\text{NO}_2$ (M) $^+$ 357.0977, found 357.0970.

3-methyl-2-(pyridin-2-yl)phenyl 2-ethoxybenzoate (3ah)



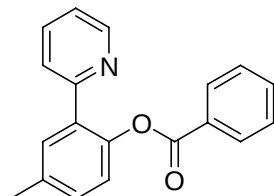
^1H NMR (CDCl_3 , 300 MHz): δ 8.61 (d, $J = 4.1$ Hz, 1H), 7.584-7.580 (m, 1H), 7.33-7.25 (m, 4H), 7.13-7.05 (m, 3H), 6.82-6.74 (m, 2H), 3.95 (q, $J = 7.0$ Hz, 2H), 2.10 (s, 3H), 1.30 (t, $J = 7.0$ Hz, 3H).
 ^{13}C NMR (CDCl_3 , 125 MHz): δ 164.3, 158.9, 155.9, 149.2, 148.6, 138.1, 136.2, 133.7, 133.6, 131.6, 128.9, 127.8, 125.0, 122.0, 120.3, 119.8, 119.3, 113.2, 19.8, 14.6.
IR (prism, cm^{-1}): ν 3065, 1739, 1451, 1242, 1213.
HRMS (EI) Calcd for $\text{C}_{21}\text{H}_{19}\text{NO}_3$ (M) $^+$ 333.1365, found 333.1359.

3-methoxy-2-(pyridin-2-yl)phenyl benzoate² (3ba)

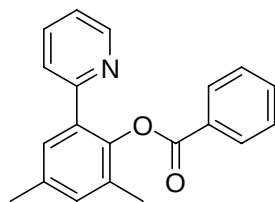


^1H NMR (CDCl_3 , 300 MHz): δ 8.51 (d, $J = 4.4$ Hz, 1H), 7.82-7.79 (m, 2H), 7.55-7.41 (m, 2H), 7.37-7.25 (m, 4H), 7.051-7.046 (m, 1H), 6.89-6.84 (m, 2H), 3.70 (s, 3H).
 ^{13}C NMR (CDCl_3 , 125 MHz): δ 164.9, 157.9, 152.9, 149.5, 148.9, 135.9, 133.2, 129.9, 129.7, 129.2, 128.2, 125.9, 123.2, 122.0, 115.3, 108.9, 56.1.

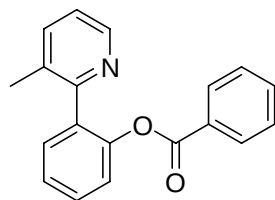
4-methyl-2-(pyridin-2-yl)phenyl benzoate³ (3ca)



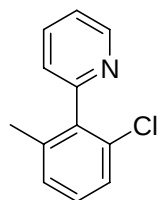
^1H NMR (CDCl_3 , 300 MHz): δ 8.54 (d, $J = 4.5$ Hz, 1H), 8.01-7.98 (m, 2H), 7.55-7.47 (m, 4H), 7.39-7.34 (m, 2H), 7.22-7.18 (m, 1H), 7.12-7.09 (m, 2H), 2.36 (s, 3H).
 ^{13}C NMR (CDCl_3 , 125 MHz): δ 165.3, 155.3, 149.2, 146.0, 136.5, 136.1, 133.4, 132.4, 131.3, 130.5, 130.1, 129.5, 128.4, 123.9, 123.0, 122.2, 20.9.

2,4-dimethyl-6-(pyridin-2-yl)phenyl benzoate² (3da)

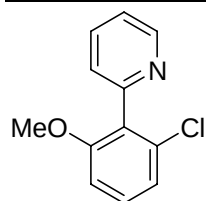
¹H NMR (CDCl₃, 500 MHz): δ 8.59 (d, *J* = 4.6 Hz, 1H), 8.10 (d, *J* = 7.9 Hz, 2H), 7.61-7.52 (m, 3H), 7.47-7.38 (m, 3H), 7.16-7.12 (m, 2H), 2.40 (s, 3H), 2.24 (s, 3H).
¹³C NMR (CDCl₃, 125 MHz): δ 164.8, 156.0, 149.2, 144.7, 136.3, 135.8, 133.3, 132.2, 131.1, 130.1, 129.4, 128.9, 128.4, 128.3, 123.6, 122.0, 20.8, 16.5.

2-(3-methylpyridin-2-yl)phenyl benzoate (3ea)

¹H NMR (CDCl₃, 500 MHz): δ 8.37 (d, *J* = 3.0 Hz, 1H), 7.82-7.80 (m, 2H), 7.47-7.40 (m, 3H), 7.36-7.28 (m, 5H), 7.05-7.03 (m, 1H), 2.15 (s, 3H).
¹³C NMR (CDCl₃, 125 MHz): δ 164.5, 155.3, 148.3, 146.4, 138.0, 133.3, 132.3, 130.4, 129.9, 129.34, 129.29, 128.3, 125.9, 122.8, 122.5, 19.0.
IR (prism, cm⁻¹): ν 2959, 1732, 1450, 1252, 1195.
HRMS (EI) Calcd for C₁₉H₁₆NO₂ (M+H)⁺ 290.1181, found 290.1169.

2-(2-chloro-6-methylphenyl)pyridine⁴ (4aa)

¹H NMR (CDCl₃, 500 MHz): δ 8.66 (d, *J* = 3.5 Hz, 1H), 7.72 (td, *J* = 7.5, 1.5 Hz, 1H), 7.24-7.22 (m, 3H), 7.19-7.09 (m, 2H), 2.01 (s, 3H).
¹³C NMR (CDCl₃, 125 MHz): δ 157.3, 149.3, 138.9, 138.5, 136.5, 133.0, 129.0, 128.5, 126.9, 125.0, 122.3, 20.3.

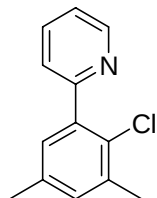
2-(2-chloro-6-methoxyphenyl)pyridine⁵ (4ba)

4. X. Chen, X.-S. Hao, C. E. Goodhue, J.-Q. Yu, *J. Am. Chem. Soc.*, 2006, **128**, 6790.

5. F. Kakiuchi, T. Kochi, H. Mutsutani, N. Kobayashi, S. Urano, M. Sato, S. Nishiyama, T. Tanabe, *J. Am. Chem. Soc.*, 2009, **131**, 11310.

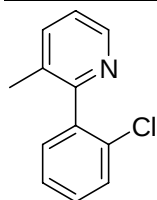
^1H NMR (CDCl_3 , 500 MHz): δ 8.67 (d, J = 4.3 Hz, 1H), 7.72-7.68 (m, 1H), 7.26-7.19 (m, 3H), 7.01 (d, J = 8.1 Hz, 1H), 6.82 (d, J = 8.4 Hz, 1H), 3.65 (s, 3H).
 ^{13}C NMR (CDCl_3 , 125 MHz): δ 158.3, 154.8, 149.3, 136.3, 134.1, 129.9, 128.9, 125.8, 122.4, 121.8, 109.6, 56.1.

2-(2-chloro-3,5-dimethylphenyl)pyridine (4da)



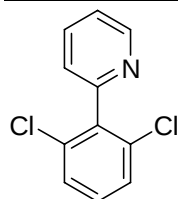
^1H NMR (CDCl_3 , 500 MHz): δ 8.64 (d, J = 4.0 Hz, 1H), 7.71-7.68 (m, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.23-7.11 (m, 2H), 7.04 (s, 1H), 2.34 (s, 3H), 2.26 (s, 3H).
 ^{13}C NMR (CDCl_3 , 125 MHz): δ 157.5, 148.9, 138.8, 136.7, 136.2, 136.1, 131.9, 129.6, 129.2, 125.1, 122.3, 20.7, 20.1.
IR (prism, cm^{-1}): ν 2923, 1732, 1588, 1458.
HRMS (EI) Calcd for $\text{C}_{13}\text{H}_{12}\text{ClN}$ (M) $^+$ 217.0658, found 217.0666.

2-(2-chlorophenyl)-3-methylpyridine⁴ (4ea)



^1H NMR (CDCl_3 , 500 MHz): δ 8.52 (d, J = 4.5 Hz, 1H), 7.60 (d, J = 7.5 Hz, 1H), 7.48-7.46 (m, 1H), 7.36-7.30 (m, 3H), 7.26-7.23 (m, 1H), 2.17 (s, 3H).
 ^{13}C NMR (CDCl_3 , 125 MHz): δ 157.2, 146.7, 139.5, 137.7, 132.8, 132.1, 130.4, 129.5, 129.3, 126.9, 122.8, 18.8.

2-(2,6-dichlorophenyl)pyridine⁴ (4fa)



^1H NMR (CDCl_3 , 500 MHz): δ 8.76 (d, J = 4.5 Hz, 1H), 7.82 (td, J = 7.8, 1.6 Hz, 1H), 7.41 (d, J = 8.0 Hz, 2H), 7.36-7.34 (m, 2H), 7.29-7.26 (m, 1H).
 ^{13}C NMR (CDCl_3 , 125 MHz): δ 155.4, 149.5, 138.3, 136.4, 134.6, 129.8, 128.1, 125.0, 123.0.

3. Copies of product ^1H NMR and ^{13}C NMR