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. $^1$H 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 ($\delta$) 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-Benzoxylolation 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), Cu(OAc)$_2$ (7.3 mg, 20 mol %), $t$-BuOK (44.8 mg, 0.4 mmol), and dry toluene (2 mL). The mixture was stirred at 145 °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-arylpirdines with acyl chlorides:

Under O$_2$ atmosphere, a sealed tube was charged with 2-aryl pyridine (0.2 mmol), acyl chloride (0.6 mmol), Cu(OAc)$_2$ (7.3 mg, 20 mol %), Li$_2$CO$_3$ (29.6 mg, 0.4 mmol), and dry toluene (2 mL). The mixture was stirred at 145 °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 pyridines:

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), K$_3$PO$_4$·3H$_2$O (399 mg, 1.5 mmol) and toluene (3 mL). After the mixture was heated at 100 °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.

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2. Experimental characterization data for compounds

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

\[
\begin{align*}
\text{δ} & \text{8.56 (d, } J = 4.5 \text{ Hz, 1H), 7.78-7.76 (m, 2H), 7.57-7.53 (m, 1H), 7.44-7.41 (m, 1H), 7.30-7.22 (m, 4H), 7.15-7.06 (m, 3H), 2.11 (s, 3H).}
\end{align*}
\]

\[
\begin{align*}
\text{N} & \text{O} \\
1H NMR (CDCl₃, 500 MHz) & \text{δ} \\
13C NMR (CDCl₃, 125 MHz) & \text{δ}
\end{align*}
\]

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 2-methylbenzoate (3ab)

\[
\begin{align*}
\text{δ} & \text{8.68 (d, } J = 4.5 \text{ Hz, 1H), 7.67-7.64 (m, 1H), 7.60 (d, } J = 8.0 \text{ Hz, 1H), 7.38-7.31 (m, 3H), 7.25-7.11 (m, 5H), 2.43 (s, 3H), 2.18 (s, 3H).}
\end{align*}
\]

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)

\[
\begin{align*}
\text{δ} & \text{8.58 (s, 1H), 7.58-7.55 (m, 3H), 7.30-7.23 (m, 3H), 7.18-7.06 (m, 4H), 2.24 (s, 3H), 2.11 (s, 3H).}
\end{align*}
\]

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 4-methylbenzoate (3ad)

\[
\begin{align*}
\text{δ} & \text{8.58 (s, 1H), 7.58-7.55 (m, 3H), 7.30-7.23 (m, 3H), 7.18-7.06 (m, 4H), 2.24 (s, 3H), 2.11 (s, 3H).}
\end{align*}
\]

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 4-fluorobenzoate (3ae)

\[ \text{IR (prism, cm}^{-1}\text{): } \nu = 3087, 1737, 1507, 1263, 1218. \]

\[ \text{HRMS (EI) Calcd for C}_{19}\text{H}_{15}\text{FNO}_{2} (M+H)^+ 308.1087, \text{found 308.1070.} \]

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

\[ \text{IR (prism, cm}^{-1}\text{): } \nu = 3065, 1746, 1460, 1435, 1242, 1216. \]

\[ \text{HRMS (EI) Calcd for C}_{19}\text{H}_{14}\text{ClNO}_{2} (M)^+ 323.0713, \text{found 323.0718.} \]

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

\[ \text{IR (prism, cm}^{-1}\text{): } \nu = 3065, 1746, 1460, 1435, 1242, 1216. \]

\[ \text{HRMS (EI) Calcd for C}_{19}\text{H}_{14}\text{ClNO}_{2} (M)^+ 323.0713, \text{found 323.0718.} \]
\[^{1}\text{H NMR (CDCl}_3, 500 MHz): \delta 8.66 (s, 1H), 8.05-8.04 (m, 2H), 7.78-7.67 (m, 2H), 7.53-7.50 (m, 1H), 7.41-7.19 (m, 5H), 2.21 (s, 3H). \]

\[^{13}\text{C NMR (CDCl}_3, 125 MHz): \delta 163.6, 155.2, 149.1, 148.4, 138.3, 136.6, 133.1, 132.9, 131.0 (q, J_{C,F} = 32.9 Hz), 130.2, 129.8, 129.7, 129.1, 129.0, 128.2, 126.8, 125.0, 123.5 (q, J_{C,F} = 271.0 Hz), 119.9, 19.8. \]

IR (prism, cm\(^{-1}\)): \( \nu 3079, 1741, 1463, 1241, 1217. \)

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)

\[
\begin{align*}
\text{N} & \quad \text{O} \\
& \quad \text{OCH}_2\text{CH}_3
\end{align*}
\]

\[^{1}\text{H NMR (CDCl}_3, 300 MHz): \delta 8.61 (d, J = 4.1 Hz, 1H), 7.584-7.580 (m, 1H), 7.33-7.25 (m, 4H), 7.13-7.05 (m, 2H), 6.82-6.74 (m, 2H), 3.95 (q, J = 7.0 Hz, 2H), 2.10 (s, 3H), 1.30 (t, J = 7.0 Hz, 3H). \]

\[^{13}\text{C NMR (CDCl}_3, 125 MHz): \delta 164.9, 157.9, 155.9, 149.2, 148.6, 138.1, 136.2, 133.7, 133.6, 131.6, 128.9, 127.8, 125.0, 122.0, 120.3, 119.8, 119.3, 113.2, 19.8, 14.6. \]

IR (prism, cm\(^{-1}\)): \( \nu 3065, 1739, 1451, 1242, 1213. \)

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 benzoate (3ba)

\[
\begin{align*}
\text{MeO} & \quad \text{N} \\
& \quad \text{O} \\
& \quad \text{O}
\end{align*}
\]

\[^{1}\text{H NMR (CDCl}_3, 300 MHz): \delta 8.51 (d, J = 4.4 Hz, 1H), 7.82-7.79 (m, 2H), 7.55-7.41 (m, 2H), 7.37-7.25 (m, 4H), 7.051-7.046 (m, 1H), 6.89-6.84 (m, 2H), 3.70 (s, 3H). \]

\[^{13}\text{C NMR (CDCl}_3, 125 MHz): \delta 164.9, 157.9, 152.9, 149.5, 148.9, 135.9, 133.2, 129.9, 129.7, 129.2, 128.2, 125.9, 123.2, 122.0, 115.3, 108.9, 56.1. \]

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

\[
\begin{align*}
\text{N} & \quad \text{O} \\
& \quad \text{O}
\end{align*}
\]

\[^{1}\text{H NMR (CDCl}_3, 300 MHz): \delta 8.54 (d, J = 4.5 Hz, 1H), 8.01-7.98 (m, 2H), 7.55-7.47 (m, 4H), 7.39-7.34 (m, 2H), 7.22-7.18 (m, 1H), 7.12-7.09 (m, 2H), 2.36 (s, 3H). \]

\[^{13}\text{C NMR (CDCl}_3, 125 MHz): \delta 165.3, 155.3, 149.2, 146.0, 136.5, 136.1, 133.4, 132.4, 131.3, 130.5, 130.1, 129.5, 128.4, 123.9, 123.0, 122.2, 20.9. \]

2,4-dimethyl-6-(pyridin-2-yl)phenyl benzoate\(^2\) (3da)

\[
\begin{align*}
\text{\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz):} &\quad \delta 8.59 (d, J = 4.6 \text{ Hz}, 1\text{H}), 8.10 (d, J = 7.9 \text{ Hz}, 2\text{H}), \\
&\quad 7.61-7.52 (m, 3\text{H}), 7.47-7.38 (m, 3\text{H}), 7.16-7.12 (m, 2\text{H}), 2.40 (s, 3\text{H}), 2.24 (s, 3\text{H}). \\
\text{\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 125 MHz):} &\quad \delta 164.8, 156.0, 149.2, 144.7, 136.3, 135.8, 133.3, 132.2, 131.1, 130.1, 129.4, 128.9, 128.4, 128.3, 123.6, 122.0, 20.8, 16.5.
\end{align*}
\]

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

\[
\begin{align*}
\text{\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz):} &\quad \delta 8.37 (d, J = 3.0 \text{ Hz}, 1\text{H}), 7.82-7.80 (m, 2\text{H}), 7.47-7.40 (m, 3\text{H}), 7.36-7.28 (m, 5\text{H}), 7.05-7.03 (m, 1\text{H}), 2.15 (s, 3\text{H}). \\
\text{\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 125 MHz):} &\quad \delta 164.5, 155.3, 148.3, 146.4, 138.0, 133.3, 132.3, 130.4, 129.9, 129.34, 129.29, 128.3, 125.9, 122.8, 122.5, 19.0. \\
\text{IR (prism, cm\textsuperscript{-1}}): &\quad \nu 2959, 1732, 1450, 1252, 1195. \\
\text{HRMS (EI) Calcd for C\textsubscript{19}H\textsubscript{16}NO\textsubscript{2} (M+H\textsuperscript{+}):} &\quad 290.1181, \text{ found 290.1169.}
\end{align*}
\]

2-(2-chloro-6-methylphenyl)pyridine\(^4\) (4aa)

\[
\begin{align*}
\text{\textsuperscript{1}H NMR (CDCl\textsubscript{3}, 500 MHz):} &\quad \delta 8.66 (d, J = 3.5 \text{ Hz}, 1\text{H}), 7.72 (td, J = 7.5, 1.5 \text{ Hz}, 1\text{H}), \\
&\quad 7.24-7.22 (m, 3\text{H}), 7.19-7.09 (m, 2\text{H}), 2.01 (s, 3\text{H}). \\
\text{\textsuperscript{13}C NMR (CDCl\textsubscript{3}, 125 MHz):} &\quad \delta 157.3, 149.3, 138.9, 138.5, 136.5, 133.0, 129.0, 128.5, 126.9, 125.0, 122.3, 20.3.
\end{align*}
\]

2-(2-chloro-6-methoxyphenyl)pyridine\(^5\) (4ba)

\[
\begin{align*}
\end{align*}
\]

$^1$H 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)

$^1$H 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).


IR (prism, cm$^{-1}$): ν 2923, 1732, 1588, 1458.

HRMS (EI) Calcd for C$_{13}$H$_{12}$ClN (M$^+$) 217.0658, found 217.0666.

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

$^1$H 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)pyridine (4fa)

$^1$H 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 $^1$H NMR and $^{13}$C NMR