Electronic Supplementary Information

for

Palladium Catalyzed Direct Ortho C-H Acylation of 2-Arylpyridines

Using Toluene Derivatives as Acylation Reagents

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Experimental Section General

All reactions were run in oven-dried flasks under air. Unless otherwise noted, reagents were commercially available and were used without purification. ¹H NMR (400MHz) and ¹³C NMR (100 MHz) spectra were recorded on a Bruker Avance 400 spectrometers in CDCl₃ [using (CH₃)₄Si (for ¹H, $\delta = 0.00$; for ¹³C, $\delta = 77.00$) as internal standard]. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet. High-resolution mass spectra were obtained with a Waters Q-TOF mass spectrometer. Melting points were recorded on a Buchi B-54 melting point apparatus and are uncorrected.

General Experimental Procedures and Characterizations

2-arylprydine (0.5 mmol), toluene derivatives (1.0 mmol), $Pd(OAc)_2$ (0.01 mmol), TBHP (1.5 mmol, 70% aq.) and DMSO (0.5 mL) were added in a 25 mL seal tube with a Teflon lined cap. The mixture was heated at 90 °C (oil bath temperature) for 24 h. After cooling to room temperature, the volatiles were removed under reduced pressure, and the residue was purified by a flash column chromatography on silica gel using hexane/ethyl acetate as eluent to give the corresponding product.



3aa¹

Pale yellow solid, m.p. 107-109 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.39 (d, *J* = 4.8 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 7.2 Hz, 2H), 7.52-7.65 (m, 4H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.04 (t, *J* = 4.8 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 198.6, 156.4, 148.9, 139.4, 139.1, 138.6, 136.6, 136.4, 130.7, 130.4, 129.0, 128.7, 128.6, 128.4, 122.5, 122.1.

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3ba²

Pale yellow solid, m.p. 103-105 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.35 (d, J = 4.8 Hz, 1H), 7.67-7.70 (m, 3H), 7.54 (dt, J_1 = 7.6 Hz , J_2 = 2.4 Hz, 1H), 7.36-7.50 (m, 4H), 7.25-7.28 (m, 2H), 6.68 (t, J = 4.8 Hz, 1H), 2.46 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 192.0, 156.7, 148.9, 139.5, 138.7, 138.0, 136.7, 136.3, 132.2, 130.9, 129.6, 129.4, 128.6, 128.0, 122.4, 121.7, 21.2.



3ca³

Pale yellow solid, m.p. 101-103; ¹H NMR (CDCl₃, 400 MHz): δ 8.39 (d, *J* = 4.4 Hz, 1H), 7.68 (d, *J* = 7.2 Hz, 2H), 7.58 (s, 1H), 7.51-7.56 (m, 1H), 7.24-7.48 (m, 4H), 7.26 (t, *J* = 7.6 Hz, 2H), 7.00 (t, *J* = 4.8 Hz, 1H), 2.51 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 198.1, 157.4, 149.3, 139.2, 137.9, 137.0, 136.3, 132.2, 131.2, 130.2, 129.6, 128.6, 128.0, 127.0, 123.1, 121.2, 21.2.



3ea³

Pale yellow solid, m.p. 111-113 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.33 (d, J = 4.4 Hz, 1H), 7.70-7.75 (m, 3H), 7.54 (t, J = 8.0 Hz, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 7.2 Hz, 1H), 7.25-7.29 (m, 2H), 7.14 (dd, J_1 = 8.0 Hz, J_2 = 2.8 Hz, 1H), 7.06 (d, J = 2.8 Hz, 1H), 6.97 (t, J = 4.8 Hz, 1H), 3.89 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 197.0, 159.9, 156.2, 148.7, 140.9, 137.8, 136.3, 132.3, 131.8, 129.9, 129.3, 128.0, 122.0, 121.4, 116.1, 114.0, 55.6.



3fa⁴

Pale yellow solid, m.p. 110-111 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.43 (d, *J* = 4.4 Hz, 1H), 7.67 (d, *J* = 7.6 Hz, 2H), 7.53-7.59 (m, 2H), 7.36-7.42 (m, 2H), 7.26-7.28 (m, 3H), 7.04 (m, 2H), 3.96 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 197.2, 161.2, 157.1, 149.0, 138.3, 136.3, 132.1, 131.8, 131.6, 129.6, 128.0, 126.6, 123.4, 122.0, 114.6, 113.8, 55.6; HRMS(ESI): calcd for C₁₉H₁₅NO₂[H] 290.1181, found 290.1178.



3ga³

Pale yellow solid, m.p. 109-110 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.34 (d, J = 4.4 Hz, 1H), 7.68-7.74 (m, 3H), 7.57 (d, J = 8.0 Hz, 2H), 7.48-7.53 (m, 2H), 7.41 (t, J = 7.6 Hz, 1H), 7.27-7.29 (m, 2H), 7.03 (t, J = 4.8 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 196.2, 155.5, 149.0, 141.0, 137.9, 137.3, 136.5, 134.9, 132.6, 130.2, 130.0, 129.4, 129.0, 128.2, 122.4, 122.2.



3ha³

Pale yellow solid, m.p. 114-115 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.36 (d, J = 4.4 Hz, 1H), 7.66-7.76 (m, 5H), 7.57-7.60 (m, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.42 (t, J = 7.2 Hz, 1H), 7.28-7.32 (m, 2H), 7.05 (t, J = 4.8 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 197.7, 155.6, 149.0, 141.2, 138.3, 137.3, 136.6, 133.1, 132.6, 131.6, 130.2, 129.4, 128.2, 123.0, 122.4, 122.3.



3ia

Pale yellow solid, m.p. 103-105 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.39 (d, *J* = 4.4 Hz, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 8.21 (s, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.58-7.64 (m, 2H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 8.0 Hz, 2H), 7.07 (t, *J* = 4.8 Hz, 1H), 4.42 (q, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 197.2, 165.7, 155.7, 149.1, 143.3, 139.8, 137.5, 136.6, 132.6, 131.1, 130.6, 130.1, 129.4, 128.8, 128.2, 122.8, 122.6, 61.4, 14.3; HRMS(ESI): calcd for C₂₁H₁₇NO₃[H] 2332.1287, found 332.1310.



3ja

Pale yellow solid, m.p. 97-98 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.39 (d, *J* = 4.8 Hz, 1H), 7.91 (d, *J* = 2.4 Hz, 2H), 7.82 (s, 1H), 7.64-7.68 (m, 3H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.6, 1H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.11 (t, *J* = 4.8 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 195.7, 154.7, 149.3, 143.5, 140.6, 136.9, 136.8, 133.4, 133.0, 132.6, 129.4, 129.4, 128.4, 123.0, 122.8, 117.9,

112.5; HRMS(ESI): calcd for $C_{19}H_{12}N_2O[H]$ 285.1028, found 285.1045.



3ab²

Pale yellow solid, m.p. 107-108 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.45 (d, *J* = 4.8 Hz, 1H), 7.52-7.68 (m, 5H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.17-7.20 (m, 2H), 7.10 (d, *J* = 7.6 Hz, 1H), 7.04 (t, *J* = 4.8 Hz, 1H), 6.96 (t, *J* = 4.8 Hz, 1H), 2.59 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 199.7, 157.4, 148.7, 140.8, 140.1, 139.1, 138.1, 136.3, 131.2, 130.9, 130.5, 129.8, 129.1, 128.5, 124.8, 122.6, 122.1, 121.8, 20.9.



3ac⁵

Pale yellow solid, m.p. 100-102 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.40 (d, *J* = 4.8 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.47-7.80 (m, 7H), 7.15-7.23 (m, 2H), 7.04 (t, *J* = 4.8 Hz, 1H), 2.30 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 198.4, 156.9, 149.0, 139.7, 137.8, 136.4, 133.2, 131.2, 130.0, 129.1, 128.9, 128.5, 128.3, 128.0, 127.0, 124.0, 122.8, 122.0, 21.2.



3ad³

Pale yellow solid, m.p. 103-104 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.41 (d, *J* = 4.3 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.56-7.63 (m, 4H), 7.49-7.53 (m, 3H), 7.09 (d, *J* = 8.0 Hz, 2H), 7.04 (t, *J* = 4.8 Hz, 1H), 2.33 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 192.3, 157.1, 149.0, 140.6, 139.9, 138.0, 136.7, 136.2, 132.2, 129.7, 129.5, 129.4, 129.1, 128.0, 123.0, 121.8, 21.5.



3ae

Pale yellow solid, m.p. 111-112 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.41 (d, *J* = 4.4 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.63-7.47 (m, 5H), 7.34 (s, 2H), 7.02-7.05 (m, 2H), 2.25 (s, 6H); ¹³C NMR (CDCl₃, 100 MHz): δ 198.3, 157.1, 149.0, 139.8, 139.7, 137.3, 137.6, 136.2, 134.2, 130.1, 129.1, 129.0, 128.3, 127.5, 122.8, 121.9, 21.1; HRMS(ESI): calcd for C₂₀H₁₇NO[H] 288.1388, found 288.1392.



3ag²

Pale yellow solid, m.p. 95-96 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.43 (d, *J* = 4.4 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 8.8 Hz, 2H), 7.55-7.70 (m, 2H), 7.47-7.52 (m, 3H), 7.05 (t, *J* = 4.8 Hz, 1H), 6.77 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 197.0, 163.0, 157.1, 149.1, 139.7, 136.3, 132.0, 130.8, 130.0, 129.0, 128.8, 128.6, 128.4, 123.0, 121.9, 113.3, 55.4.



3ah

Pale yellow solid, 99-101 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.41 (d, *J* = 4.8 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.59-7.64 (m, 2H), 7.51-7.56 (m, 3H), 7.35 (s, 1H), 7.14-7.20 (m, 2H), 6.97 (t, *J* = 4.8 Hz, 1H), 6.95 (d, *J* = 4.8 Hz, 1H), 3.79 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 197.6, 159.4, 156.7, 148.9, 139.6, 139.5, 139.2, 136.5, 130.2, 129.1, 129.0, 128.7, 128.6, 122.7, 122.6, 122.0, 119.1, 113.1, 55.4; HRMS(ESI): calcd for C₁₉H₁₅NO₂[H] 290.1181, found 290.1186.



3ai

Pale yellow solid, m.p. 116-118 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.52 (d, J = 4.4 Hz, 1H), 7.53-7.72 (m, 5H), 7.46 (d, J = 8.0 Hz, 1H), 7.17-7.32 (m, 3H), 7.03-7.08 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz): δ 197.3, 157.1, 148.9, 139.3, 137.9, 136.4, 132.7, 131.6, 131.2, 131.1, 130.5, 130.2, 129.2, 128.7, 126.6, 126.0, 122.8, 121.9; HRMS(ESI): calcd for C₁₈H₁₂NCl[H] 294.0686, found 294.0718.



3ag

Pale yellow solid, m.p. 115-116 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.35 (d, *J* = 4.4 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.53-7.68 (m, 7H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 7.05 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 196.3, 156.3, 146.7, 139.7, 139.5, 138.9, 136.6, 134.3, 132.1, 130.5, 129.4, 129.1, 129.1, 128.7, 128.6, 127.5, 122.3, 122.1; HRMS(ESI): calcd for C₁₈H₁₂NOCl[H] 294.0686, found 294.0704.



3ak³

Pale yellow solid, m.p. 117-119 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.36 (d, *J* = 4.8 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.60-7.65 (m, 4H), 7.54-7.55 (m, 3H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.06 (t, *J* = 4.8 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 196.8, 156.6, 148.8, 139.6, 139.4, 137.9, 136.6, 132.3,

130.3, 129.4, 129.0, 128.7, 128.3, 128.1, 122.7, 122.0.



3al³

Pale yellow solid, m.p. 115-117 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.37 (d, *J* = 4.8 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.64-7.66 (m, 2H), 7.62-7.65 (m, 5H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.08 (t, *J* = 4.8 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 196.3, 156.3, 148.8, 139.2, 139.1, 136.9, 136.6, 131.3, 130.8, 130.4, 129.0, 128.7, 128.6, 127.3, 122.4, 122.2.



3am²

Pale yellow solid, m.p. 119-120 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.91 (d, *J* = 8.8 Hz, 1H), 8.15 (d, *J* = 4.4 Hz, 1H), 7.72-7.79 (m, 4H), 7.65 (t, *J* = 8.0 Hz, 2H), 7.51-7.59 (m, 2H), 7.36-7.42 (m, 3H), 7.18 (t, *J* = 8.0 Hz, 1H), 6.78 (t, *J* = 4.5 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 197.9, 157.0, 148.8, 141.1, 140.2, 136.3, 136.2, 133.6, 132.3, 131.0, 130.7, 130.2, 129.7, 128.9, 128.5, 128.0, 127.6, 126.5, 126.2, 123.8, 122.3, 121.4.



3an²

Pale yellow solid, m.p. 118-120 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.35 (d, *J* = 4.8 Hz, 1H), 8.09 (s, 1H), 7.93 (dd, *J*₁ = 8.8 Hz, *J*₂ = 1.8 Hz, 1H), 7.77-7.85 (m, 4H), 7.67 (dt, *J*₁ = 7.6 Hz, *J*₂ = 1.8 Hz, 1H), 7.58-7.63 (m, 2H), 7.52-7.56 (m, 3H), 7.47 (t, *J* = 8.0 Hz, 1H), 9.95-6.98 (m, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ 198.3, 156.8, 148.9, 139.6, 139.6, 136.4, 135.3, 135.2, 132.2, 131.6, 130.3, 129.5, 129.2, 128.9, 128.6, 128.2, 128.0, 127.6, 126.4, 124.9, 122.7, 121.9.



3ed

Pale yellow solid, m.p. 104-105 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.37 (d, J = 4.4 Hz, 1H), 7.73 (d, J = 8.8 Hz, 1H), 7.61 (d, J = 8.0 Hz, 2H), 7.54 (dt, J_I = 7.6 Hz, J_2 = 2.0 Hz, 1H), 7.44 (d, J = 7.6 Hz, 1H), 7.12 (dd, J_I = 8.8 Hz, J_2 = 2.4 Hz, 1H), 7.07 (d, J = 8.0 Hz, 2H), 7.03 (d, J = 2.4 Hz, 1H), 6.90 (t, J = 4.4 Hz, 1H), 3.89 (s, 3H), 2.32 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 198.1, 159.8, 156.4, 148.7, 143.2, 141.0, 136.4, 135.1, 131.8, 130.1, 129.6, 128.8, 122.3, 121.4, 116.0, 113.8, 55.6, 21.6; HRMS(ESI): calcd for C₂₀H₁₇NO₂[H] 304.1338, found 304.1319.



3ee

Pale yellow solid, m.p. 96-97 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.37 (d, *J* = 4.4 Hz, 1H), 7.73 (d, *J* = 8.8 Hz, 1H), 7.56 (dt, *J*₁ = 8.0 Hz, *J*₂ = 2.0 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.34 (s, 2H), 7.13 (dd, *J*₁ = 8.8 Hz, *J*₂ = 2.8 Hz, 1H), 7.04 (d, *J* = 2.8 Hz, 2H), 7.00 (t, *J* = 4.8 Hz, 1H), 3.89 (s, 3H), 2.25 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 197.2, 159.8, 156.6, 148.7, 141.2, 137.6, 137.6, 136.2, 134.1, 130.1, 127.4, 122.2, 121.4, 115.9, 114.0, 55.6, 21.1; HRMS(ESI): calcd for C₂₁H₁₉NO₂[H] 318.1494, found 318.1483.



3jd

Pale yellow solid, m.p. 102-103 °C; ¹H NMR (CDCl₃, 400 MHz): δ 8.42 (d, J = 4.4 Hz, 1H), 7.87-7.92 (m, 2H), 7.79 (s, 1H), 7.66 (t, J = 8.0 Hz, 1H), 7.54-7.59 (m, 3H), 7.12-7.14 (m, 3H), 2.35 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 197.8, 154.9, 149.4, 144.0, 143.5, 140.8, 136.8, 134.3, 134.0, 133.3, 132.4, 129.7, 129.1, 123.0, 122.9, 118.0, 112.4, 21.7; HRMS(ESI): calcd for C₂₀H₁₄N₂O[H] 299.1184, found 299.1214.

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