Palladium-Catalyzed Acetoxylation of sp³ C-H Bonds Using Molecular Oxygen

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A. General method

$^1$H and $^{13}$C NMR spectra were recorded on BRUKER DRX-400 or BRUKER DRX-600 spectrometer using CDCl$_3$ as solvent and TMS as an internal standard. Gas chromatograph mass spectra were obtained with a SHIMADZU model GCMS –QP 5000 spectrometer. HRMS was carried out on a MAT 95XP (Thermo).

B. General Procedure

The reaction was carried out in a HF-10 autoclave. Pd(OAc)$_2$ (11.2 mg, 0.05 mmol), CuI (1 mmol), acetic acid (3 mL), substrate (1 mmol) were added into a 10 mL autoclave in sequence. O$_2$ were pumped into the autoclave by a cooling pump to reach the desired pressure, then the autoclave was heated by oil bath under magnetic stirring for the desired reaction time. After the reaction finished, the autoclave was allowed to cool to 0 °C. O$_2$ was vented and the resulting crude oil was dissolved in ethyl acetate (20 mL) and washed with water (1×20 mL) and saturated aqueous NaHCO$_3$ (2×20 mL). The organic layer was dried over MgSO$_4$, filtered, and concentrated to afford a crude product, which was purified by chromatography on a silica gel column using light petroleum ether/ethyl acetate as eluent.

C. Analytical data for 2a-2l

\[
\begin{align*}
\text{2-(1-Acetoxyethyl)-pyridine (2a):} \\
\text{1H NMR (CDCl$_3$, 400 MHz) $\delta$ 1.59 (d, 3 H), 2.11 (s, 3 H), 5.92 (q, 1 H), 7.25-7.26 (m, 1 H), 7.36 (d, 1 H), 7.74 (dd, $J = 1.2$, 1.2, 1.6 Hz 1 H), 8.59 (d, 1 H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 20.7, 21.2, 72.5, 130.1, 120.8, 123.0, 137.8, 159.8, 170.2 ppm; MS (EI, 70 eV) $m/z$ (%): 165 (M$^+$, 4), 122 (100), 106 (100), 78 (28), 43 (28), 28 (22).}
\end{align*}
\]
2-(1-Acetoxymethyl)-pyridine (2b) \(^1\)

\(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) 2.14 (s, 3 H), 5.21 (s, 2 H), 7.21-7.22 (m, 1 H), 7.34 (d, 1 H), 7.69 (ddd, \(J = 1.6, 1.6, 1.6\) Hz, 1 H), 8.57 (m, 1 H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) 20.3, 66.2, 121.4, 122.4, 136.5, 148.7, 155.2, 170.1 ppm; MS (EI, 70 eV) \(m/\text{z}\) (%): 151 (M\(^+\), 3), 108 (62), 92 (9), 78 (12), 43 (14), 28 (100).

![2-(1-Acetoxymethyl)-pyridine (2b)](image)

2-(1-Acetoxypentyl)-pyridine (2c) \(^1\)

\(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) 0.84 (s, 3 H), 1.23-1.32 (m, 4 H), 1.88-1.94 (q, 2 H), 2.09 (s, 3 H), 5.75 (t, 1 H), 7.16 (ddd, \(J = 0.8, 0.8, 0.8\) Hz, 1 H), 7.26 (d, 1 H), 7.65 (ddd, \(J = 1.6, 2.0, 1.6\) Hz, 1 H), 8.55 (d, 1 H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) 13.8, 21.1, 22.4, 27.4, 34.5, 76.6, 121.9, 122.6, 136.8, 149.1, 159.6, 170.4 ppm; MS (EI, 70 eV) \(m/\text{z}\) (%): 207 (M\(^+\), 3), 164 (16), 151 (38), 108 (100), 93 (18), 78 (16), 43 (22), 28 (49); HRMS Calculated for C\(_{12}\)H\(_{17}\)NO\(_2\) (M) 207.1255, found: 207.1259.

![2-(1-Acetoxypentyl)-pyridine (2c)](image)

2-(1-Acetoxybenzyl)-pyridine (2d) \(^2\)

\(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) 2.20 (s, 3 H), 6.89 (s, 1 H), 7.18 (t, 1 H), 7.27 (d, 1 H), 7.32-7.36 (m, 3 H), 7.41-7.44 (m, 2 H), 7.68 (t, 1 H), 8.58 (d, 1 H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) 20.7, 77.4, 120.5, 122.2, 126.9, 127.7, 128.1, 136.4, 138.5, 148.9, 158.7, 169.4 ppm; MS (EI, 70 eV) \(m/\text{z}\) (%): 227 (M\(^+\), 6), 184 (100), 167 (88), 106 (23), 78 (30), 43 (24), 28 (6).

![2-(1-Acetoxybenzyl)-pyridine (2d)](image)

7-Acetoxy-6,7-dihydro-1,5-pyridine (2e)

\(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) 2.07-2.10 (m, 1 H), 2.13 (s, 3 H), 2.64-2.66 (m, 1 H),
2.90-2.92 (m, 1H), 3.05-3.08 (m, 1H), 6.14 (dd, $J = 4.8, 5.2$ Hz, 1 H), 7.20 (dd, $J = 4.8$ Hz, 1 H), 7.62(d, 1H), 8.51 (d, 1 H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 20.6, 27.3, 30.3, 76.6, 122.9, 132.8, 137.0, 148.1, 159.9, 170.2 ppm; MS (EI, 70 eV) $m/z$ (%): 177 (M$^+$, 6), 134 (100), 117 (40), 106 (25), 78 (10), 43 (13), 28 (39).

![2-(1-acetoxy-4-chlorobenzyl)-pyridine(2f)](image)

2-(1-acetoxy-4-chlorobenzyl)-pyridine(2f) $^3$

$^1$H NMR (CDCl$_3$, 600 MHz) $\delta$ 2.19 (s, 3 H), 6.84 (s, 1 H), 7.19(t, 1 H), 7.30 (d, 2 H), 7.37(d, 2 H), 7.41 (d, 1 H), 7.69 (t, 1 H), 8.57 (d, 1 H); $^{13}$C NMR (CDCl$_3$, 150 MHz) $\delta$ 21.1, 77.1, 120.8, 122.8, 128.7, 134.1, 136.9, 137.5, 149.5, 158.6, 169.7 ppm; MS (EI, 70 eV) $m/z$ (%): 261 (M$^+$, 9), 218 (100), 201 (28), 167 (50), 78 (28), 43 (18), 28 (8);

![2-(1-Acetoxyethyl)-pyrazine (2g)](image)

2-(1-Acetoxyethyl)-pyrazine (2g)

$^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 1.61 (d, 3 H), 2.13 (s, 3 H), 5.96 (q, 1 H), 8.53 (d, 2 H), 8.65 (s, 1 H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 20.0, 20.8, 70.9, 142.4, 143.6, 143.7, 155.5, 169.9 ppm; MS (EI, 70 eV) $m/z$ (%): 166 (M$^+$, 8), 124 (100), 107 (30), 80 (18), 52 (11), 43 (69), 32 (18), 28 (70); HRMS Calculated for C$_8$H$_{10}$N$_2$O$_2$ (M) 166.0740, found: 166.0742.

![2-(1-Acetoxyethyl)-pyrazine (2h)](image)

2-(1-Acetoxyethyl)-pyrazine (2h)

$^1$H NMR (CDCl$_3$, 600 MHz) $\delta$ 2.19 (s, 3 H), 5.27 (s, 2 H), 8.65 (d, 2 H), 8.81 (s, 1 H); $^{13}$C NMR (CDCl$_3$, 150 MHz) $\delta$ 20.8, 64.7, 143.8, 144.1, 144.2, 151.4, 170.5 ppm; MS (EI, 70 eV) $m/z$ (%): 152 (M$^+$, 3), 109 (26), 43 (20), 32 (62), 28 (100); HRMS Calculated for C$_7$H$_8$N$_2$O$_2$ (M) 152.0582, found: 152.0586
2-(1-Acetoxypentyl)-pyrazine (2i)

$^1$H NMR (CDCl$_3$, 600 MHz) $\delta$ 0.90 (t, 3 H), 1.33-1.37 (m, 4 H), 1.94-1.20 (m, 2 H), 2.14 (s, 3 H), 5.83 (dd, $J$ = 4.0, 4.0 Hz, 1 H), 8.55 (d, 2 H), 8.64 (s, 1 H); $^{13}$C NMR (CDCl$_3$, 150 MHz) $\delta$ 13.9, 21.0, 22.4, 27.3, 34.2, 74.7, 143.1, 143.8, 144.1, 155.3, 170.4 ppm; MS (EI, 70 eV) m/z (%): 208 (M$^+$, 8), 165 (13), 152 (18), 133 (14), 122 (33), 110 (100), 43 (29), 28 (10); HRMS Calculated for C$_{11}$H$_{16}$N$_2$O$_2$ (M) 208.1210, found: 208.1212.

2-(1-Acetoxyisobuthyl)-pyrazine (2j)

$^1$H NMR (CDCl$_3$, 600 MHz) $\delta$ 0.82 (d, 3 H), 0.91 (d, 3 H), 2.08 (s, 3 H), 2.25-2.31 (m, 1 H), 5.54 (d, 1 H), 8.44 (s, 1 H), 8.53 (s, 2 H); $^{13}$C NMR (CDCl$_3$, 150 MHz) $\delta$ 17.6, 18.6, 20.8, 32.4, 79.2, 143.1, 143.2, 144.1, 154.9, 170.3 ppm; MS (EI, 70 eV) m/z (%): 194 (M$^+$, 6), 152 (15), 133 (38), 110 (100), 94 (54), 52 (6), 43 (55), 28 (13); HRMS Calculated for C$_{10}$H$_{14}$N$_2$O$_2$ (M) 194.1052, found: 194.1055.

2-(1-Acetoxyethyl)-3-methyl-pyrazine (2k)

$^1$H NMR (CDCl$_3$, 600 MHz) $\delta$ 1.52 (d, 3 H), 2.03 (s, 3 H), 2.61 (s, 3H), 5.98 (q, 1 H), 8.34 (s, 1 H), 8.39 (s, 1 H); $^{13}$C NMR (CDCl$_3$, 150 MHz) $\delta$ 18.8, 20.9, 20.9, 69.3, 141.9, 142.3, 151.3, 153.6, 170.3 ppm; MS (EI, 70 eV) m/z (%): 180 (M$^+$, 14), 137 (100), 119 (57), 93 (30), 67 (14), 43 (60), 28 (40); HRMS Calculated for C$_9$H$_{12}$N$_2$O$_2$ (M) 180.0894, found: 180.0899.
**5-Acetoxy-5,6,7,8-tetrahydroquinoxalin (2l)**

$^1$H NMR (CDCl$_3$, 600 MHz) $\delta$ 1.87-1.89 (m, 1 H), 1.98-2.10 (m, 3 H), 2.06 (s, 3 H), 2.86-2.91 (m, 1H), 2.98-3.03 (m, 1H), 5.98 (t, 1 H), 8.38 (s, 2 H); $^{13}$C NMR (CDCl$_3$, 150 MHz) $\delta$ 18.3, 21.1, 28.7, 31.5, 70.3, 142.5, 143.8, 149.7, 153.9, 170.2 ppm; MS (El, 70 eV) $m/z$ (%): 192 (M$^+$, 2), 151 (100), 131 (20), 121 (12), 94 (13 ), 43 (15), 28 (26); HRMS Calculated for C$_{10}$H$_{12}$N$_2$O$_2$ (M) 192.0894, found: 192.0899.

**D. References:**

E. NMR Spectra

2-(1-acetoxyethyl)-pyridine (2a)
13C NMR spectrum of sample CHU-1
2-(1-acetoxyethyl)-pyridine (2b)
2-(1-acetoxypentyl)-pyridine (2c)
2-(1-acetoxybenzyl)-pyridine (2d)
7-Acetoxy-6,7-dihydro-1,5-pyrindine(2e)
2-(1-acetoxy-4-chlorobenzyl)-pyridine(2f)
2-(1-acetoxyethyl)-pyrazine (2g)
2-(1-acetoxymethyl)-pyrazine (2h)
13C of CHJ-Me

BRUKER

144.2 144.0 143.8 ppm

180 160 140 120 100 80 60 40 20 0 ppm
2-(1-acetoxypentyl)-pyrazine (2i)
2-(1-acetoxyisobuthyl)-pyrazine (2j)
13C of chj-10-23-7
2-(1-acetoxyethyl)-3-methyl-pyrazine (2k)
5-acetoxy-5,6,7,8-tetrahydroquinoxalin (2l)

**Supplementary Material (ESI) for Chemical Communications**

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