Supporting Information

Palladium(II) Acetate Catalyzed Reductive Heck Reaction of Enones; A Practical Approach


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Palladium(II) Acetate Catalyzed Reductive Heck reaction of Enones; a Practical Approach

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Supporting Information

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Experimental Section:
All experiments were carried out in oven-dried glassware, in an atmosphere of nitrogen, unless specified otherwise, by standard Schenk techniques. All the solvents used for extraction, filtration and flash chromatography were used without further purification. All reagents were purchased from Sigma-Aldrich or Acros and were used without further purification. Flash column chromatography was performed on 230-430 mesh silica gel. $^1$H-, $^{13}$C-, NMR spectroscopy was performed on Varian AMX400 spectrometers. Chemical shifts were determined relative to the residual solvent peaks (CHCl$_3$, $\delta$ = 7.26 ppm for $^1$H NMR, $\delta$ = 77.0 ppm for $^{13}$C NMR). The mass spectra were recorded on a Thermoscientific LTQ OrbitrapXL spectrometer. Pd(OAc)$_2$, Pd(0)-NHC, DIPEA, and NMP were purchased from Sigma Aldrich and used. The starting materials, ($E$)-4-methyl-1-phenylpent-2-en-1-one$^{[1]}$ and $^5$$^{[2]}$ were prepared according to literature procedure.

Procedure for the preparation of ($E$)-4-phenylbut-3-en-2-one-4-$d$ (1a-$d_1$)

![Chemical structure]

To a solution of Diethyl(2-oxopropyl)phosphonate 6 (0.90 g) in THF (20 ml) at 0 °C was added $n$-BuLi in hexane (2.9 ml) slowly and stirred for 30 min. Then $d$-benzaldehyde 5 (0.50 g) was added and the resultant mixture was allowed to stir at room temperature for 3 h. After completion of reaction, the reaction mixture was quenched with water and extracted with ethylacetate (50 ml x 2). The resultant organic layer was and dried with MgSO$_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography using ether/pentane (1/4) as eluent affording the title compound in 80% yield. The compound has been previously described in literature$^{[3]}$

Spectroscopic data:

4-(4-Methoxyphenyl)-4-phenylbutan-2-one (3a)
Yellow solid; mp: 61-62 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.31 – 7.12 (m, 7H), 6.83 (d, J = 8.4 Hz, 2H), 4.55 (t, J = 7.6 Hz, 1H), 3.77 (d, J = 0.9 Hz, 3H), 3.16 (d, J = 7.6 Hz, 2H), 2.08 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 207.0, 158.1, 144.2, 135.9, 128.6, 128.5, 127.5, 126.3, 113.9, 55.1, 49.8, 45.2, 30.6; HRMS calculated for C$_{17}$H$_{19}$O$_2$ [M+H]$^+$: 255.1379, found: 255.1380; Purification: Flash chromatography; Eluent: ether/pentane = 1/4

4-Phenyl-4-(p-tolyl)butan-2-one (3b)

Colorless solid: mp: 44-45 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.31 – 7.08 (m, 9H), 4.57 (t, J = 7.6 Hz, 1H), 3.18 (d, J = 7.5 Hz, 2H), 2.31 (s, 3H), 2.09 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 206.9, 144.0, 140.8, 135.9, 129.2, 128.5, 127.6, 127.5, 126.3, 49.7, 45.7, 30.6, 20.9; HRMS calculated for C$_{17}$H$_{19}$O [M+H]$^+$: 239.1430, found: 239.1429; Purification: Flash chromatography; Eluent: ether/toluene = 3/97

4,4-Diphenylbutan-2-one (3e)

Colorless oil: $^1$H NMR (400 MHz, CDCl$_3$) δ 7.31 – 7.15 (m, 10H), 4.59 (t, J = 7.6 Hz, 1H), 3.18 (d, J = 7.5 Hz, 2H), 2.08 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 206.8, 143.8, 128.6, 127.7, 126.4, 49.7, 46.0, 30.6; HRMS calculated for C$_{16}$H$_{17}$O$_1$ [M+H]$^+$:
225.1273, found: 225.1272; Purification: Flash chromatography; Eluent: ether/toluene = 3/97

Methyl 4-(3-oxo-1-phenylbutyl)benzoate (3d)

![Chemical structure of methyl 4-(3-oxo-1-phenylbutyl)benzoate (3d)]

Colorless oil: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.95 (d, $J = 8.3$ Hz, 2H), 7.31 – 7.26 (m, 4H), 7.20 (d, $J = 7.3$ Hz, 3H), 4.65 (t, $J = 7.5$ Hz, 1H), 3.88 (s, 3H), 3.20 (d, $J = 7.5$ Hz, 2H), 2.09 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 206.1, 166.7, 149.0, 142.9, 129.8, 128.6, 128.3, 127.7, 127.6, 126.6, 51.9, 49.2, 45.8, 30.5; HRMS calculated for C$_{18}$H$_{19}$O$_3$ [M+H]: 283.1328, found: 283.1330; Purification: Flash chromatography; Eluent: ether/pentane = 1/6

4-(4-Fluorophenyl)-4-phenylbutan-2-one (3f)

![Chemical structure of 4-(4-Fluorophenyl)-4-phenylbutan-2-one (3f)]

Pale yellow solid: mp: 35-36 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.32 – 7.26 (m, 2H), 7.23 – 7.16 (m, 5H), 7.00 – 6.93 (m, 2H), 4.59 (t, $J = 7.5$ Hz, 1H), 3.17 (d, $J = 7.9$ Hz, 2H), 2.09 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 206.5, 161.3 (d, $J_{C,F} = 245.4$ Hz), 143.6, 139.6 (d, $J = 3.0$ Hz), 129.1 (d, $J = 10.1$ Hz), 128.6, 127.5, 126.5, 115.3 (d, $J = 20.2$ Hz), 49.7, 45.1, 30.6; HRMS calculated for C$_{16}$H$_{15}$FONa [M+Na]$^+$: 265.0999, found: 265.0998; Purification: Flash chromatography; Eluent: ether/toluene = 3/97

4-(4-Chlorophenyl)-4-phenylbutan-2-one (3g)
Yellow oil: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.32 – 7.12 (m, 9H), 4.58 (t, $J = 7.5$ Hz, 1H), 3.17 (d, $J = 7.5$ Hz, 2H), 2.09 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 206.3, 143.3, 142.4, 132.1, 129.0, 128.6, 128.6, 127.6, 126.6, 49.4, 45.2, 30.6; HRMS calculated for C$_{16}$H$_{15}$ClONa [M+Na]$^+$: 281.0703, found: 281.0703; Purification: Flash chromatography; Eluent: ether/toluene = 3/97

4-(4-Bromophenyl)-4-phenylbutan-2-one (3h)

Pale yellow oil: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.44 – 7.36 (m, 2H), 7.33 – 7.24 (m, 2H), 7.24 – 7.15 (m, 3H), 7.14 – 7.06 (m, 2H), 4.56 (t, $J = 7.5$ Hz, 1H), 3.16 (d, $J = 7.5$ Hz, 2H), 2.09 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 206.3, 143.2, 142.9, 131.6, 129.4, 128.7, 127.6, 126.6, 120.2, 49.4, 45.3, 30.6; HRMS calculated for C$_{16}$H$_{15}$BrONa [M+Na]$^+$: 325.0198, found: 325.0197; Purification: Flash chromatography; Eluent: ether/toluene = 3/97

4-Phenyl-4-(m-tolyl)butan-2-one (3i)

Colorless oil: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.31 – 7.25 (m, 2H), 7.25 – 7.21 (m, 2H), 7.17 (tq, $J = 7.3$, 2.3, 1.9 Hz, 2H), 7.09 – 6.92 (m, 3H), 4.55 (t, $J = 7.6$ Hz, 1H), 3.17 (d, $J = 7.5$ Hz, 2H), 2.30 (s, 3H), 2.08 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$
206.9, 143.9, 143.7, 138.1, 128.5, 128.4, 127.7, 127.2, 126.4, 124.6, 49.7, 46.0, 30.6, 21.5; HRMS calculated for C_{17}H_{18}ONa [M+Na]^+: 261.1249, found: 261.1248; Purification: Flash chromatography; Eluent: ether/toluene = 3/97

4-Phenyl-4-(o-tolyl)butan-2-one (3j)

[Diagram]

Colorless oil: ^1H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.26 – 7.06 (m, 9H), 4.78 (t, \(J = 7.5\) Hz, 1H), 3.15 (d, \(J = 7.5\) Hz, 2H), 2.30 (s, 3H), 2.08 (s, 3H); ^13C NMR (101 MHz, CDCl\textsubscript{3}) \(\delta\) 206.9, 143.5, 141.5, 136.4, 130.8, 128.5, 127.9, 126.4, 126.3, 126.2, 126.0, 50.0, 41.9, 30.7, 19.8; HRMS calculated for C_{17}H_{18}ONa [M+Na]^+: 261.1249, found: 261.1249; Purification: Flash chromatography; Eluent: ether/toluene = 3/97

4-Phenyl-4-(thiophen-3-yl)butan-2-one (3k)

[Diagram]

Pale yellow oil: ^1H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.32 – 7.17 (m, 6H), 6.97 – 6.93 (m, 1H), 6.89 (dd, \(J = 5.0, 1.3\) Hz, 1H), 4.64 (t, \(J = 7.5\) Hz, 1H), 3.25 – 3.04 (m, 2H), 2.08 (s, 3H); ^13C NMR (101 MHz, CDCl\textsubscript{3}) \(\delta\) 206.7, 144.7, 143.5, 128.6, 127.7, 127.5, 126.6, 125.8, 120.4, 50.1, 41.8, 30.6; HRMS calculated for C_{14}H_{14}OSNa [M+Na]^+: 253.0657, found: 253.0657; Purification: Flash chromatography; Eluent: ether/pentane = 1/9

4-(1H-indol-5-yl)-4-phenylbutan-2-one (3l)
Reddish brown oil: $^1$H NMR (400 MHz, CDCl$_3$) δ 8.12 (s, 1H), 7.53 - 7.49 (m, 1H), 7.30 - 7.24 (m, 5H), 7.20 - 7.13 (m, 2H), 7.05 (dd, $J$ = 8.4, 1.7 Hz, 1H), 6.49 (s, 1H), 4.70 (t, $J$ = 7.6 Hz, 1H), 3.35 - 3.12 (m, 2H), 2.08 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 207.6, 144.8, 135.3, 134.5, 128.5, 128.0, 127.7, 126.2, 124.5, 122.4, 119.1, 111.2, 102.6, 50.3, 46.3, 30.7; HRMS calculated for C$_{18}$H$_{17}$ONa [M+Na]$^+$: 286.1202, found: 286.1203; Purification: Flash chromatography; Eluent: ether/pentane = 2/3

3-(4-Methoxyphenyl)-1,3-diphenylpropan-1-one (3m)

Pale yellow solid: mp: 91-92 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.95 (d, $J$ = 8.4 Hz, 2H), 7.56 (t, $J$ = 7.2 Hz, 1H), 7.50 - 7.38 (m, 2H), 7.35 - 7.24 (m, 4H), 7.25 - 7.14 (m, 3H), 6.83 (dd, $J$ = 8.7, 1.8 Hz, 2H), 4.80 (t, $J$ = 7.3 Hz, 1H), 3.76 (s, 3H), 3.73 (d, $J$ = 7.3 Hz, 2H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 198.1, 158.0, 144.5, 137.0, 136.2, 133.0, 128.7, 128.5, 128.0, 127.7, 126.2, 113.9, 55.1, 45.1, 44.9; HRMS calculated for C$_{22}$H$_{21}$O$_2$ [M+H]$^+$: 317.1536, found: 317.1535; Purification: Flash chromatography; Eluent: ether/pentane = 1/4

4-(4-Methoxyphenyl)-4-(p-tolyl)butan-2-one (3n)
Pale yellow solid: mp: 73-74 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.19 – 7.07 (m, 6H), 6.86 – 6.78 (m, 2H), 4.52 (td, $J = 7.6$, 2.9 Hz, 1H), 3.77 (d, $J = 1.3$ Hz, 3H), 3.14 (dd, $J = 7.7$, 2.4 Hz, 2H), 2.31 (d, $J = 2.3$ Hz, 3H), 2.08 (d, $J = 1.7$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 207.2, 158.0, 141.2, 136.2, 135.9, 129.2, 128.6, 127.4, 113.9, 55.2, 50.0, 44.9, 30.6, 20.9; HRMS calculated for C$_{18}$H$_{21}$O$_2$ [M+H]$: 269.1536$, found: 269.1534; Purification: Flash chromatography; Eluent: ether/pentane = 1/4

4-(4-Chlorophenyl)-4-(4-methoxyphenyl)butan-2-one (3o)

Pale yellow oil: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.27 – 7.21 (m, 2H), 7.16 – 7.06 (m, 4H), 6.82 (d, $J = 8.8$ Hz, 2H), 4.52 (t, $J = 7.5$ Hz, 1H), 3.77 (s, 3H), 3.12 (d, $J = 7.5$ Hz, 2H), 2.08 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 206.6, 158.2, 142.8, 135.4, 132.1, 129.0, 128.6, 128.6, 114.0, 55.2, 49.7, 44.5, 30.7; HRMS calculated for C$_{17}$H$_{17}$ClO$_2$Na [M+Na]$^+$: 311.0809, found: 311.0808; Purification: Flash chromatography; Eluent: ether/toluene = 1/4

3-(4-Methoxyphenyl)-1-phenylbutan-1-one (3p)

White solid: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.92 (d, $J = 8.3$ Hz, 2H), 7.54 (t, $J = 7.3$ Hz, 1H), 7.44 (dd, $J = 8.3$, 7.0 Hz, 2H), 7.19 (d, $J = 8.6$ Hz, 2H), 6.84 (d, $J = 8.6$ Hz,
2H), 3.78 (s, 3H), 3.54 – 3.37 (m, 1H), 3.27 (dd, \( J = 16.3, 5.9 \) Hz, 1H), 3.15 (dd, \( J = 16.3, 8.1 \) Hz, 1H), 1.32 (d, \( J = 6.9 \) Hz, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 199.2, 158.0, 138.6, 137.2, 132.9, 128.0, 127.7, 113.9, 55.2, 47.3, 34.8, 22.1; HRMS calculated for \( \text{C}_{17}\text{H}_{19}\text{O}_2 \) [M+H]\(^{+}\): 255.1379, found: 255.1381; Purification: Flash chromatography; Eluent: ether/pentane = 1/9

3-(4-Methoxyphenyl)-4-methyl-1-phenylpentan-1-one (3r)

Colorless oil: \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.87 (d, \( J = 7.5 \) Hz, 2H), 7.52 (t, \( J = 7.3 \) Hz, 1H), 7.42 (t, \( J = 7.6 \) Hz, 2H), 7.08 (d, \( J = 8.5 \) Hz, 2H), 6.79 (d, \( J = 8.8 \) Hz, 2H), 3.76 (s, 3H), 3.38 – 3.26 (m, 2H), 3.11 (q, \( J = 7.2 \) Hz, 1H), 1.99 – 1.82 (m, 1H), 0.97 (s, 3H), 0.79 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 199.6, 157.8, 137.4, 135.5, 132.7, 129.2, 128.4, 128.0, 113.4, 55.1, 47.1, 42.7, 33.3, 21.0, 20.2; HRMS calculated for \( \text{C}_{19}\text{H}_{23}\text{O}_2 \) [M+H]\(^{+}\): 283.1692, found: 283.1694; Purification: Flash chromatography; Eluent: ether/pentane = 1/9

3-(4-Methoxyphenyl)cyclohexan-1-one (3s)

Yellow oil: \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.14 (d, \( J = 8.6 \) Hz, 2H), 6.87 (d, \( J = 8.7 \) Hz, 2H), 3.79 (s, 3H), 3.03 – 2.89 (m, 1H), 2.61 – 2.31 (m, 4H), 2.18 – 2.02 (m, 2H), 1.88 – 1.70 (m, 2H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 211.1, 158.3, 136.3, 127.5, 114.0, 55.3, 49.2, 44.0, 41.2, 33.0, 25.5; HRMS calculated for \( \text{C}_{13}\text{H}_{17}\text{O}_2 \) [M+H]\(^{+}\): 205.1223, found: 205.1221. Purification: Flash chromatography; Eluent: ether/pentane = 1/4

4,4'-(2-Nitroethane-1,1-diyl)bis(methoxybenzene) (3t)
Brownish yellow oil; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.14 (d, $J = 8.7$ Hz, 4H), 6.85 (d, $J = 8.7$ Hz, 4H), 4.91 (d, $J = 8.1$ Hz, 2H), 4.84 – 4.77 (m, 1H), 3.78 (s, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 158.8, 131.5, 128.6, 114.3, 79.7, 55.2, 47.5; HRMS calculated for C$_{16}$H$_{17}$NO$_4$Na [M+Na$^+$]: 310.1049, found: 310.1052; Purification: Flash chromatography; Eluent: ether/pentane = 1/5

4-(4-Methoxyphenyl)-4-phenylbutan-2-one-4-$d$ (3a-d$_1$)

Yellow solid; mp: 62-63 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.30 – 7.11 (m, 7H), 6.84 – 6.78 (m, 2H), 3.76 (s, 3H), 3.14 (s, 2H), 2.07 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 207.0, 158.1, 144.2, 135.9, 128.6, 128.6, 127.6, 126.4, 113.9, 55.2, 49.8, 30.7; HRMS calculated for C$_{17}$H$_{17}$DO$_2$Na [M+Na$^+$]: 278.1261, found: 278.1263; Purification: Flash chromatography; Eluent: ether/pentane = ¼

References:
HRMS Spectra for 3a

Observed

Expected

NL:
2.87E3

SMN_Pd1#10-31
RT: 0.25-0.85 AV:
22 T: FTMS + p ESI
Full ms
[50.00-550.00]
HRMS for 3b

Observed

Expected
HRMS for 3c

Observed

Expected
HRMS for 3d

Observed

Expected

NL:
1.78E6
SMN Pd_999-22
RT: 0.21-0.57 AV:
14 T FTMS + p ESI
Full ms
[50.00-550.00]
HRMS for 3f

Observed

Expected

C_{16} H_{15} F ONa
C_{16} H_{15} F O Na
pa Chrg 1
HRMS for 3g

Observed

Expected
HRMS for 3h

**Observed**

**Expected**

NL: 4.78E5
SMN: Pd17#10-25
RT: 0.25-0.68 AV: 16 T: FTMS + p ESI
Full ms [50.00-550.00]
HRMS for 3i

Observed

Expected

C_{17}H_{18}O
C_{17}H_{18}O; Na_{1}

NL:
1.46E6
SMN_Pd2097-34
RT: 5.16-0.94 AV:
28 T: FTMS + p ESI
Full ms [50.00-550.00]
HRMS for 3j

[Chemical structure image]

Observed

Expected

NL: 8.99E5
SMN_Pd2288-30
RT: 0.19-0.83 AV:
23 T: FTMS + p ESI
Full ms
[50.00-550.00]
3k-C13 NMR

The image contains a chemical structure and an NMR spectrum. The structure shows a thiazole ring with a ketone group attached to a phenyl ring and a methyl group. The NMR spectrum displays chemical shifts indicating the presence of various protons and nuclei at different ppm values.
HRMS for 3k

C_{14}H_{12}NaOS^+
Expected Mass: 253.06576

C_{19}H_{17}OS:
C_{19}H_{17}O_1S_1
pa Chrg 1

C_{19}H_{16}OSNa:
C_{19}H_{16}O_1S Na_1
pa Chrg 1
HRMS for 3l

\[ \text{C}_{18}\text{H}_{17}\text{NNaO}^+ \]
Expected Mass: 286.12024
HRMS for 3n

Observed

Expected

SMN_Pd15#11-30
RT: 0.28-0.82 AV:
20 T: FTMS + p ESI
Full ms
[50.00-550.00]

C_{18} H_{21} O_2
C_{18} H_{21} O_2
pa Chrg 1
HRMS for 3o

Observed

Expected
HRMS for 3p

Observed

Expected
HRMS for 3r

Observed

Expected

NL:
8.25E5
SMN_Pd_28#8-32
RT: 0.18-0.85 AV:
25 T: FTMS + p ESI
Full ms
[50.00-550.00]

NL:
8.09E5
C_{19}H_{23}O_{2}:
C_{19}H_{23}O_{2}:
aChrg 1
3s-C13 NMR
HRMS for 3s

Observed

Expected

SMN: Pd27#6-27
RT: 0.13-0.74 AV:
22 T: FTMS + p ESI
Full ms
[50.00-550.00]
HRMS for 3t

Observed

Expected

C_{16}H_{17}NO_3Na;
C_{16}H_{17}N_2O_4Na
pa Chrg 1

7.99E4
SMN_Pd_2#9-23
RT: 0.21-0.60 AV:
15 T: FTMS + p ESI
Full ms
[50.00-550.00]
HRMS for 3a-d1

Observed

Expected