Supporting Information

Maleimides-assisted *Anti*-Markovnikov Wacker-type Oxidation of Vinylenaires Using Molecular Oxygen as a Terminal Oxidant

Sonoe Nakaoka, Yuka Murakami, Yasutaka Kataoka, and Yasuyuki Ura*

*Department of Chemistry, Faculty of Science, Nara Women's University, Kitauoyanishi-machi, Nara 630-8506, Japan

ura@cc.nara-wu.ac.jp

General Information S2

General Procedure for the Synthesis of Aldehydes 2a–2o and Their NMR Data S2

Synthesis of Pd(η²-mah)₂(η²-cyclopentene) S6

Pd(0) Complex-catalyzed *Anti*-Markovnikov Wacker-type Oxidation S7

Table S1 Effect of Amounts of CuCl, H₂O, and t-AmylOH on the Maleimide-assisted *Anti*-Markovnikov Wacker-type Oxidation S8

¹H and ¹³C NMR Spectra for 2a–2o S9
General Information

Unless otherwise indicated, all reactions were performed under an oxygen atmosphere (1 atm). PdCl$_2$(MeCN)$_2$, Pd$_2$(dba)$_3$, and Pd($\eta^2$-mah)$_2(\eta^2$-cyclopentene) were prepared as described in the literature. $t$-AmylOH was purchased from Wako Pure Chemical Industries and Tokyo Chemical Industry Co. Ltd. and was degassed by carrying out three freeze-pump-thaw cycles. Other chemicals including styrene derivatives were also commercially available and were used without further purification. Flash column chromatography was performed using silica gel SILICYCLE SiliaFlash F60 (40–63μm, 230–400 mesh). NMR spectra were recorded on either a JEOL AL-400 (400 MHz ($^1$H), 376 MHz ($^{19}$F), 100 MHz ($^{13}$C)) or a Bruker AV-300N (300 MHz ($^1$H), 282 MHz ($^{19}$F)) spectrometer. Chemical shift values ($\delta$) were expressed relative to SiMe$_4$. GC analyses were performed on a Shimadzu GC-14B gas chromatograph with a capillary column (Shinwa Chemical Industries, ULBON HR-1701, 0.25 mm i.d. × 25 m). HPLC was performed on a Japan Analytical Industry Co., Ltd. LC-908 with columns (Japan Analytical Industry Co., Ltd., JAIGEL-1H and JAIGEL-2H, 20 mm i.d. × 6 m). Infrared spectra were measured on a JASCO FT/IR-6100 spectrophotometer. Mass spectra were recorded on a SHIMADZU GCMS-QP5050 spectrometer.

General Procedure for the Synthesis of Arylacetaldehydes 2a-2o from Vinylarenes 1a-1o

To a reaction vessel, PdCl$_2$(MeCN)$_2$ (13.0 mg, 0.050 mmol), maleimide (4.9 mg, 0.050 mmol), and CuCl (9.9 mg, 0.10 mmol) were added. Vinylarene (0.50 mmol), H$_2$O (45.1 μL, 2.5 mmol), $t$-AmylOH (5.0 mL) were then added, and the reaction mixture was stirred at 40 °C for 0.8–72 h under 1 atm of O$_2$ (an O$_2$ balloon was equipped). The reaction mixture was cooled to room temperature and was quenched by the addition of hexane (1.5 mL). After filtration of the precipitates, the solution was passed through a short silica gel column (eluent: hexane to hexane/ethyl acetate) to remove $t$-AmylOH. The solvents were removed and the residue was purified by flash column chromatography (eluent: hexane/ethyl acetate) (for 2e–2o) or by HPLC (for 2c and 2d). Compounds 2a and 2b were derivatized to 2,4-dinitrophenylhydrazones using literature procedures.

Determination of the GC yields: Mesitylene (69.8 μL, 0.50 mmol) was added to the reaction mixture as an internal standard. A portion of the reaction mixture was sampled and diluted with Et$_2$O. The sample solution was passed through a short silica gel column to remove metal complexes, and was analyzed by GC.

Determination of the NMR yields: After the reaction, the mixture was cooled to room temperature and was quenched by the addition of hexane (1.5 mL). 1,1,2,2-Tetrachloroethene (52.9 μL, 0.50 mmol) was added as an internal standard. The mixture was sampled and mixed with CDCl$_3$, and the sample was analyzed by $^1$H NMR. Integrations of the characteristic triplet peaks which appear at around 9.7 ppm for arylacetaldehydes 2a-2o, those of the singlet peaks which appear at around 2.6 ppm for acetophenone derivatives 3a–3o, and those of the singlet peaks which appear at around 9.9 ppm for acetaldehyde derivatives 3a–3o, were used to determine the yields.
ppm for benzaldehyde derivatives were compared to those of the peaks for the internal standard to
calculate the NMR yields of the products.
The spectral data for $2a$ (2,4-dinitrophenylhydrazone derivative), $5 \quad 2b$ (2,4-dinitrophenylhydrazone
derivative), $4 \quad 2g$, $6 \quad 2k$, $7 \quad 2l$, and $21$ were in accordance with those reported in the literature. The $^1H$ and
$^{13}C$ NMR data for $2c$–$2f$, $2h$–$2j$, and $2m$–$2o$ are listed below.

(3-Methylphenyl)acetaldehyde ($2c$). Compound $2c$ was purified by HPLC (solvent: CHCl$_3$) and
was obtained as a mixture with 3-methylacetophenone ($3c$). $^1H$ NMR for $2c$ (400 MHz, CDCl$_3$): d
9.71 ($t, J = 2.4$ Hz, 2H, $H^a$), 7.25 ($t, J = 7.6$ Hz, 1H, $H^d$), 7.10 ($d, J = 8.0$ Hz, 1H, $H^c$ or $H^e$), 7.02 ($s$, 1H, $H^f$), 7.00 ($d, J = 8.4$ Hz, 1H, $H^c$ or $H^e$), 3.62 ($d, J = 2.4$ Hz, 2H, $H^b$), 2.34 (s, 3H, Me). $^{13}C$ NMR
for $2c$ (100 MHz, CDCl$_3$): $\delta$ 199.6 (C$_1$), 138.6 (C$_3$ or C$_7$), 131.6 (C$_3$ or C$_7$), 130.3 (arom.), 128.8
(arom.), 128.3 (arom.), 126.5 (arom.), 50.4 (C$_2$), 26.5 (Me). IR spectrum (CH$_2$Cl$_2$ solution): 3061,
3022, 2924, 2826, 2731, 1723, 1683, 1608, 1589, 1489, 1274, 1259, 1042, 784 cm$^{-1}$. MS (El) m/z
134 (M$^+$), 105 ([M-CHO$^+$]).

(4-Methylphenyl)acetaldehyde ($2d$). Compound $2d$ was purified by HPLC (solvent: CHCl$_3$) and
was obtained as a mixture with 2-methylacetophenone ($3d$). The $^1H$ NMR spectral data for $2d$ were
in accordance with that reported in the literature.$^9$ $^{13}C$ NMR for $2d$ (100 MHz, CDCl$_3$): $\delta$ 199.6 (C$_1$),
137.0 (C$_3$ or C$_6$), 129.6 (C$_4$ or C$_5$), 129.4 (C$_4$ or C$_5$), 128.7 (C$_3$ or C$_7$), 50.1 (C$_2$), 21.6 (Me). IR
spectrum (CH$_2$Cl$_2$ solution): 3054, 3026, 2925, 2826, 2730, 1724, 1605, 1515, 1414, 1386, 1269,
1210, 1170, 1113, 1041, 810 cm$^{-1}$. MS (El) m/z 134 (M$^+$), 105 ([M-CHO$^+$]).
(2,5-Dimethylphenyl)acetaldehyde (2e). Compound 2e was purified by flash column chromatography (eluent: hexane/ethyl acetate = 20:1). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.67 (t, $J = 2.4$ Hz, 1H, H$^a$), 7.08 (d, $J = 7.8$ Hz, 1H, H$^d$ or H$^e$), 7.02 (d, $J = 7.8$ Hz, 1H, H$^d$ or H$^e$), 6.96 (s, 1H, H$^c$), 3.63 (d, $J = 2.4$ Hz, 2H, H$^b$), 2.30 (s, 3H, Me), 2.21 (s, 3H, Me). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 199.2 (C1), 135.9 (arom.), 133.8 (arom.), 131.2 (arom.), 130.4 (arom.), 130.3 (arom.), 48.6 (C2), 20.7 (Me), 19.1 (Me). IR spectrum (CH$_2$Cl$_2$ solution): 3062, 3003, 2925, 2824, 2729, 1724, 1616, 1505, 1456, 1383, 1315, 1261, 1182, 1156, 1117, 1042, 881, 816 cm$^{-1}$. MS (EI) $m/z$ 148 (M$^+$), 119 ([M-CHO]$^+$).

(4-Acetoxyphenyl)acetaldehyde (2f). N-methylmaleimide was used in place of maleimide as an additive for better separation. Compound 2f was purified by flash column chromatography (eluent: hexane/ethyl acetate = 5:1). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.74 (t, $J = 2.1$ Hz, 1H, H$^a$), 7.21 (d, $J = 8.4$ Hz, 2H, arom.), 7.10 (d, $J = 8.4$ Hz, 2H, arom.), 3.88 (s, 2H, H$^b$). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 199.0 (C1), 169.3 (C7), 149.9 (C3 or C6), 130.5 (C4 or C5), 129.3 (C3 or C6), 122.1 (C4 or C5), 49.7 (C2), 21.0 (Me). IR spectrum (KBr disk): 2923, 2895, 2824, 2728, 1749, 1726, 1509, 1378, 1371, 1222, 1207, 1195, 1167, 1019, 1012, 915, 858 cm$^{-1}$. MS (EI) $m/z$ 178 (M$^+$), 136 ([M-COCH$_3$+H]$^+$), 107 ([M-COCH$_3$+H-CHO]$^+$).

(2,3,4,5,6-Pentafluorophenyl)acetaldehyde (2h). Compound 2h was purified by flash column chromatography (eluent: hexane/ethyl acetate = 1:20). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.76 (s, 1H, H$^a$), 3.88 (s, 2H, H$^b$). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 194.1 (C1), 145.2 (m, C4), $J_{CF} = 243.3$ Hz ,
140.7 (m, $C^6$, $J_{CF} = 252.6$ Hz), 137.6 (m, $C^5$, $J_{CF} = 253.9$ Hz), 37.0 (C).

$^{19}$F NMR (282 MHz, CDCl$_3$): $\delta$ -150.8 (dd, $J = 8.5$, 22.6 Hz, 2F, F$_a$), -163.4 (t, $J = 19.7$ Hz, 1F, F$_c$), -171.0 – -170.7 (m, 2F, F$_b$). IR spectrum (CH$_2$Cl$_2$ solution): 2837, 2736, 1726, 1658, 1523, 1508, 1384, 1323, 1269, 1258, 1126, 1052, 990, 956, 909 cm$^{-1}$. MS (EI) $m/z$ 210 (M$^+$), 181 ([M-CHO]$^+$).

(2-Chlorophenyl)acetaldehyde (2i). Compound 2i was purified by flash column chromatography (eluent: hexane/ethyl acetate = 10:1 to 7:1). The $^1$H NMR spectral data was in accordance with that reported in the literature. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 198.1 (C$_1$), 134.5 (C$_7$), 149.9 (C$_3$ or C$_6$), 130.5 (C$_4$ or C$_5$), 129.3 (C$_3$ or C$_6$), 122.1 (C$_4$ or C$_5$), 49.7 (C$_2$), 21.0 (Me). IR spectrum (CH$_2$Cl$_2$ solution): 3064, 3024, 2907, 2829, 2732, 1724, 1595, 1574, 1475, 1444, 1407, 1387, 1318, 1266, 1187, 1129, 1055, 1039, 933, 808 cm$^{-1}$. MS (EI) $m/z$ 154 (M$^+$), 125 ([M-CHO]$^+$).

(4-Chlorophenyl)acetaldehyde (2j). Compound 2j was purified by flash column chromatography (eluent: hexane/ethyl acetate =11:1 to 7:1). The $^1$H NMR spectral data were in accordance with that reported in the literature. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 198.6 (C$_1$), 133.3 (C$_3$ or C$_6$), 130.9 (C$_4$ or C$_6$), 130.2 (C$_3$ or C$_6$), 129.0 (C$_4$ or C$_5$), 49.7 (C$_2$). IR spectrum (KBr disk): 2899, 2847, 2472, 1703, 1494, 1405, 1385, 1319, 1089, 1017, 935, 793, 752 cm$^{-1}$. MS (EI) $m/z$ 154 (M$^+$), 125 ([M-CHO]$^+$).

(4-Bromophenyl)acetaldehyde (2m). Compound 2m was purified by flash column chromatography (eluent: hexane/ethyl acetate = 14:1 to 9:1). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.73 (t, $J = 2.4$ Hz, 1H, H$_a$), 7.48 (d, $J = 8.4$ Hz, 2H arom.), 7.09 (t, $J = 8.4$ Hz, 2H, arom.), 3.65 (d, $J = 2.4$ Hz, 2H, H$_b$). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 198.4 (C$_1$), 132.0 (C$_4$ or C$_5$), 131.2 (C$_4$ or C$_5$), 130.7 (C$_3$ or C$_6$), 121.4
(C₃ or C₆), 49.7 (C₂).

IR spectrum (KBr disk): 2898, 2844, 2741, 1702, 1488, 1404, 1382, 1318, 1070, 1013, 935, 789, 741 cm⁻¹. MS (EI) m/z 198 (M⁺), 169 ([M-CHO]⁺).

(3-Trifluoromethylphenyl)acetaldehyde (2n). Compound 2n was purified by flash column chromatography (eluent: hexane/ethyl acetate = 10:1 to 7:1). ¹H NMR (400 MHz, CDCl₃): δ 9.78 (t, J = 2.0 Hz, 1H, Hₐ), 7.57 (d, J = 7.6 Hz, 1H, Hₖ or Hₘ), 7.50 (t, J = 7.6 Hz, 1H, Hₖ), 7.48 (s, 1H, Hₙ), 7.40 (d, J = 7.6 Hz, 1H, Hₖ or Hₘ), 3.78 (d, J = 2.0 Hz, 2H, H₃). ¹³C NMR (100 MHz, CDCl₃): δ 198.2 (C₁), 133.0 (q, J₄CF = 4 Hz, C₅), 132.8 (C₃), 131.3 (q, J₂CF = 128.8 Hz, C₇), 129.4 (C₄), 126.3 (q, J₆CF = 15.2 Hz, C₆ or C₈), 124.3 (q, J₈CF = 15.2 Hz, C₆ or C₈), 123.9 (q, J₉CF = 270.9 Hz, C₉), 50.1 (C₂). ¹⁹F NMR (376 MHz, CDCl₃): δ -71.8. IR spectrum (CH₂Cl₂ solution): 3064, 2962, 2926, 2831, 2733, 1728, 1493, 1451, 1335, 1268, 1247, 1168, 1127, 1098, 1075, 1041, 946, 902, 802 cm⁻¹. MS (EI) m/z 188 (M⁺), 159 ([M-CHO]⁺).

(3-Nitrophenyl)acetaldehyde (2o). Compound 2o was purified by flash column chromatography (eluent: hexane/ethyl acetate = 3:1). ¹H NMR (300 MHz, CDCl₃): δ 9.85 (t, J = 2.0 Hz, 1H, Hₐ), 8.17 (td, J = 4.9, 2.2 Hz, 1H, Hₖ), 8.11 (br s, 1H, Hₖ), 7.57 (d, J = 4.9 Hz, 2H, Hₖ and Hₘ), 3.91 (d, J = 2.0 Hz, 2H, H₃). ¹³C NMR (100 MHz, CDCl₃): δ 197.5 (C₁), 135.8 (arom.), 135.0 (arom.), 133.8 (arom.), 129.7 (arom.), 124.5 (arom.), 122.4 (arom.), 49.6 (C₂). IR spectrum (KBr disk): 2841, 2738, 1725, 1527, 1351, 1086, 1033, 804, 736 cm⁻¹. MS (EI) m/z 165 (M⁺), 136 ([M-CHO]⁺).

Synthesis of Pd(η²-mah)(η²-cyclopentene)

Pd(η²-mah)(η²-cyclopentene) was prepared as described in the literature. IR spectrum (KBr disk): 1820, 1765 cm⁻¹ [v(CO)]. Anal. Calcd for C₁₃H₁₂O₆Pd: C, 42.13; H, 3.26. Found: C, 41.78; H, 3.32. Because of the instability in solution, satisfactory NMR data were not obtained as reported previously.
**Pd(0) Complex-catalyzed Anti-Markovnikov Wacker-type Oxidation**

To a reaction vessel, Pd(\(\eta^2\)-mah)\(_2\)(\(\eta^2\)-cyclopentene) (0.05 mmol) or Pd\(_2\)(dba)\(_3\)·CHCl\(_3\) (0.025 mmol), CuCl\(_2\) (0.10 mmol), and \(t\)-AmyIOH (5.0 mL) were added under argon, and the reaction mixture was stirred at room temperature for 30 min. Oxygen was then introduced to the reaction mixture. Styrene (0.50 mmol) and H\(_2\)O (2.5 mmol) were added to the mixture, and the reaction mixture was stirred at 60 °C. After 1 h, mesitylene (0.50 mmol) was added as an internal standard. A portion of the reaction mixture was sampled and diluted with Et\(_2\)O. The sample solution was passed through a short silica gel column to remove metal complexes, and was analyzed by GC.
Table S1 Effect of amounts of CuCl, H₂O, and t-AmylOH on the maleimide-assisted anti-Markovnikov Wacker-type oxidation

![Chemical reaction diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>CuCl (mol%)</th>
<th>H₂O (eq)</th>
<th>t-AmylOH (mL)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>2a</th>
<th>3a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>5.0</td>
<td>2.0</td>
<td>1</td>
<td>60</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>5.0</td>
<td>2.0</td>
<td>1</td>
<td>63</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>1.0</td>
<td>2.0</td>
<td>4</td>
<td>61</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>3.0</td>
<td>2.0</td>
<td>2</td>
<td>63</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>10.0</td>
<td>2.0</td>
<td>3</td>
<td>45</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>20</td>
<td>5.0</td>
<td>3.0</td>
<td>2</td>
<td>66</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>7</td>
<td>20</td>
<td>5.0</td>
<td>5.0</td>
<td>3</td>
<td>74</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

*a Reaction conditions: 1a (0.50 mmol), PdCl₂(MeCN)₂ (0.05 mmol), maleimide (0.05 mmol), CuCl (0.05–0.10 mmol), H₂O (0.50–5.0 mmol), t-AmylOH (2.0–5.0 mL), 40 °C, O₂ (1 atm), 1–4 h. b GC yields. c NMR yields.
Phenylacetaldehyde (2a). Compound 2a was isolated as a 2,4-dinitrophenylhydrazone derivative.

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
(2-Methylphenyl)acetaldehyde (2b). Compound 2b was isolated as a 2,4-dinitrophenylhydrazone derivative.

$\text{^1H NMR (400 MHz, CDCl}_3\text{)}$

$\text{^13C NMR (100 MHz, CDCl}_3\text{)}$
(3-Methylphenyl)acetaldehyde (2c). Compound 2c was obtained as a mixture with 3c.

$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{13}C$ NMR (100 MHz, CDCl$_3$)
(4-Methylphenyl)acetaldehyde (2d). Compound 2d was obtained as a mixture with 3d.

\[ \text{H NMR (400 MHz, CDCl}_3\text{)} \]

\[ \text{C NMR (100 MHz, CDCl}_3\text{)} \]

\(^1\text{H NMR (400 MHz, CDCl}_3\text{)}\)

\(^{13}\text{C NMR (100 MHz, CDCl}_3\text{)}\)
(2,5-Dimethylphenyl)acetaldehyde (2e).

$\begin{align*}
\text{H}^a & \quad 1\text{H} \\
\text{arom.} & \quad 3\text{H} \\
\text{H}^b & \quad 2\text{H}
\end{align*}$

$\begin{align*}
\text{C}^1 + \text{C}^5 + \text{C}^8 & \\
\text{C}^2 & \\
\text{C}^4 + \text{C}^6 + \text{C}^7 & \\
\text{C}^9 + \text{C}^{10}
\end{align*}$

$\overset{1}{\text{H}} \text{ NMR (400 MHz, CDCl}_3)$

$\overset{13}{\text{C}} \text{ NMR (100 MHz, CDCl}_3)$
(4-Acetoxyphenyl)acetaldehyde (2f).

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
(4-Fluorophenyl)acetaldehyde (2g). Compound 2g was purified by flash column chromatography (eluent: hexane/ethyl acetate =10:1 to 7:1).

**1H NMR (400 MHz, CDCl₃)**

**13C NMR (100 MHz, CDCl₃)**
(2,3,4,5,6-Pentafluorophenyl)acetaldehyde (2h).

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
(2-Chlorophenyl)acetaldehyde (2i).

**1H NMR (400 MHz, CDCl₃)**

**13C NMR (100 MHz, CDCl₃)**
(4-Chlorophenyl)acetaldehyde (2j).

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
(2-Bromophenyl)acetaldehyde (2k). Compound 2k was purified by flash column chromatography (eluent: hexane/ethyl acetate = 20:1).

\[ \begin{align*}
\text{H}^a & : 1.00 \\
\text{H}^b & : 1.00, 3.06, 2.25 \\
\text{arom.} & : 7.00 \\
\end{align*} \]

\[ \begin{align*}
\text{C}^4 + \text{C}^5 + \text{C}^6 + \text{C}^7 & : 120 \\
\text{C}^2 & : 150 \\
\text{C}^1 & : 30 \\
\text{C}^3 + \text{C}^8 & : 80 \\
\end{align*} \]
(3-Bromophenyl)acetaldehyde (2l). 2l was purified by flash column chromatography (eluent: hexane/ethyl acetate = 10:1).

\[ \text{\textbf{1H NMR (400 MHz, CDCl}_3\text{)}} \]

\[ 13\text{C NMR (100 MHz, CDCl}_3\text{)}} \]
(4-Bromophenyl)acetaldehyde (2m).

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
(3-Trifluoromethylphenyl)acetaldehyde (2n).

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
(3-Nitrophenyl)acetaldehyde (2o).

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
References