# Palladium-Catalyzed Reduction of Acid Chlorides to Aldehydes with Hydrosilanes

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**Abstract:** An efficient synthesis of aldehydes from acid chlorides with hydrosilanes as a reducing agent in the presence of a palladium catalyst has been achieved. A simple mixture of commercially available $Pd(dba)_2$ and $Mes_3P$ as a catalyst realized the reduction of various acid chlorides including aliphatic acid chlorides and α,β-unsaturated acid chlorides to the corresponding aldehydes in good to high yields under mild reaction conditions.

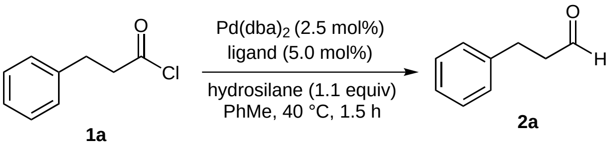
**Key words:** acid chloride, aldehyde, hydrosilane, palladium, phosphine

The transformation of carboxylic acid derivatives to aldehydes is one of the most classical and essential reactions in organic synthesis.[1] Among them, conversion of acid chlorides into the corresponding aldehydes has been intensively investigated. The reduction of acid chlorides with molecular hydrogen over supported palladium catalysts (Pd–$BaSO_4$) is well-known as the Rosenmund reduction.[2] However, during the reaction the uptake of hydrogen must be monitored to avoid over-reduction. Furthermore, various reducing agents such as aluminum hydrides,[3] sodium hydrides,[4] and tin hydrides[5] were also employed in the reduction of acid chlorides to aldehydes.

On the other hand, hydrosilanes, which are stable, easy-to-handle, and efficient reducing reagents,[6] were also known as possible reducing agents for the conversion of acid chlorides into aldehydes.[7] Recently, aroyl chlorides were effectively converted into the corresponding aldehydes employing polymethylhydrosiloxane (PMHS) in the presence of palladium catalysts.[8] However, in the reaction, aliphatic acid chlorides could not be used as substrates.[8] Very recently, the reduction of aliphatic acid chlorides and aroyl chlorides with $HSiMe_2Ph$ has been reported in the presence of $\{Cp[(i\text{-}Pr)_3P]Ru(NCMe)_2\}[PF_6]$ as catalyst.[9] However, in this Ru-catalyzed reaction, α,β-unsaturated acid chlorides could not be employed as substrates. Therefore, it is highly desirable to develop a simple and effective catalyst system to cover a wide variety of substrates.

Recently, we have reported an iridium-catalyzed addition reaction of acid chlorides to terminal alkynes.[10] Importantly, aliphatic acid chlorides as well as aroyl chlorides could be used in the addition reaction[10a] with suppression of decarbonylation and β-hydrogen elimination which have been two major intrinsic problems in transition-metal-catalyzed reactions.[11] During the course of these studies, we found that a palladium complex successfully catalyzes the reduction of acid chlorides with hydrosilanes to the corresponding aldehydes in good to high yields. In the reaction, a simple mixture of commercially available[12] $Pd(dba)_2$[13] and $Mes_3P$[13] shows high catalytic activity, and various acid chlorides including aliphatic acid chlorides and aroyl chlorides can be used as sub-

**Table 1** Effect of Ligands and Hydrosilanes on the Palladium-Catalyzed Reduction of 3-Phenylpropionyl Chloride (**1a**)[a]



| Entry | Ligand | Hydrosilane | Yield (%)[b] |
|---|---|---|---|
| 1 | none | $HSiEt_3$ | 0 |
| 2 | $Ph_3P$ | $HSiEt_3$ | trace |
| 3 | $(2\text{-}Tol)_3P$ | $HSiEt_3$ | trace |
| 4 | $Mes_3P$ | $HSiEt_3$ | 99 (77)[c] |
| 5 | $Cy_3P$ | $HSiEt_3$ | 12 |
| 6 | dppe[d] | $HSiEt_3$ | 0 |
| 7 | dppf[d] | $HSiEt_3$ | 0 |
| 8 | *rac*-BINAP[d] | $HSiEt_3$ | trace |
| 9 | $Mes_3P$ | $HSiMe_2Ph$ | 97 |
| 10 | $Mes_3P$ | $HSiMePh_2$ | 94 |
| 11 | $Mes_3P$ | $HSi(i\text{-}Pr)_3$ | 65 |
| 12 | $Mes_3P$ | $HSi(OEt)_3$ | 7 |
| 13 | $Mes_3P$ | $H_2SiPh_2$ | 57 |
| 14 | $Mes_3P$ | $H_3SiPh$ | trace |

[a] Reaction conditions: 3-phenylpropionyl chloride (**1a**, 0.50 mmol), hydrosilane (0.55 mmol), $Pd(dba)_2$ (0.0125 mmol, 2.5 mol%), ligand (0.025 mmol, 5.0 mol%, P/Pd = 2) in toluene (1.0 mL) at 40 °C for 1.5 h.
[b] Yield based on the GC internal standard technique.
[c] Isolated yield employing $HSiMePh_2$ as a hydrosilane.
[d] A mixture of $Pd(dba)_2$ (0.0125 mmol) and bidentate phosphine (0.0125 mmol) was used.

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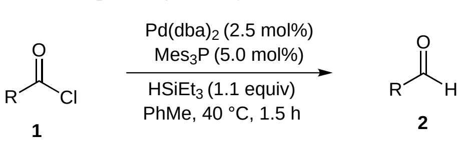
strates with suppression of decarbonylation and β-hydrogen elimination. Noteworthy is that α,β-unsaturated acid chlorides successfully afford the corresponding aldehydes in high yields.

First, the reaction of 3-phenylpropionyl chloride (**1a**) with $HSiEt_3$ was carried out in the presence of a catalytic amount of Pd(dba)$_2$ with a ligand in toluene at 40 °C (Table 1).[14] Without a ligand, **1a** did not convert at all (Table 1, entry 1). With an addition of a monodentate phosphine ligand such as $Ph_3P$ and (2-Tol)$_3$P,[13] only a trace amount of 3-phenylpropanal (**2a**) was afforded with low conversion of **1a** (Table 1, entries 2 and 3). In contrast, the use of $Mes_3P$ as a ligand dramatically improved the catalytic activity, giving **2a** quantitatively (Table 1, entry 4). A bulky and basic phosphine, $Cy_3P$,[13] was not so efficient (Table 1, entry 5). Bidentate phosphines such as dppe,[13] dppf,[13] and *rac*-BINAP[13] were not effective at all (Table 1, entries 6–8). As for hydrosilanes, $HSiMe_2Ph$ and $HSiMePh_2$ were effective (Table 1, entries 9 and 10), while HSi(*i*-Pr)$_3$, HSi(OEt)$_3$, $H_2SiPh_2$, and $H_3SiPh$ were less efficient (Table 1, entries 11–14). As a solvent, the reaction in $CH_2Cl_2$ provided **2a** in 97% yield, but in THF the yield of **2a** decreased considerably to 62%.[14] $PdCl_2(PhCN)_2$ can be used as a palladium precursor giving **2a** in 97% yield, while Pd(OAc)$_2$ decreased the yield of **2a** to 24%.[14]

Efficacy of the present catalyst system was confirmed employing various acid chlorides (Tables 2 and 3). Acid chlorides **1b**–**p** listed in Table 2 were smoothly converted into the corresponding aldehydes **2b**–**p** in good to high yields (Table 2, entries 1–15). Among them, sterically more congested substrates **1f** and **1g** gave the products smoothly (Table 2, entries 5 and 6). 3-Arylpropionyl chlorides **1h**–**l** would afford thermodynamically stable conjugated alkenes after decarbonylation followed by β-hydrogen elimination (Table 2, entries 7–11). However, in these cases, the desired aldehydes **2h**–**l** were obtained in good yield. Furthermore, ester (**1m**) and ketone (**1n**) functionalities were tolerated in the reaction (Table 2, entries 12 and 13).

**Table 2** The Palladium-Catalyzed Reduction of Acid Chlorides to the Corresponding Aldehydes[a]



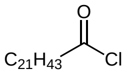
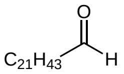
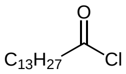
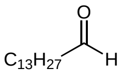
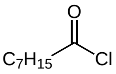
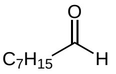
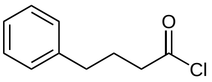
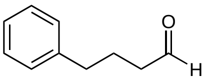
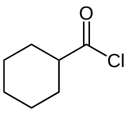
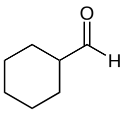
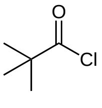
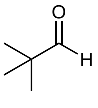
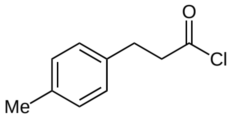
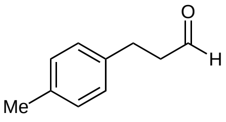
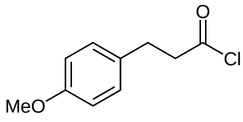
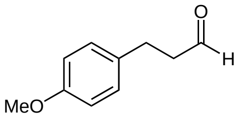
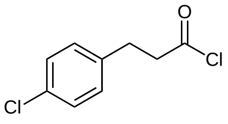
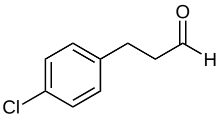
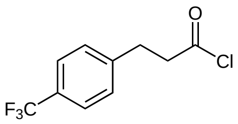
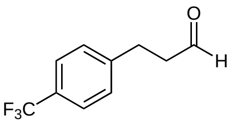
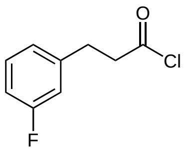
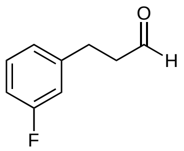
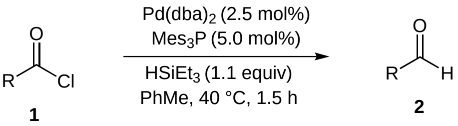
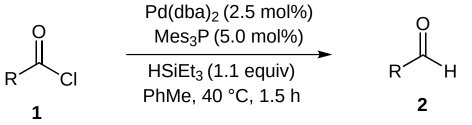
| Entry | Acid chloride | Aldehyde | Yield (%)[b] |
|---|---|---|---|
| 1 |  **1b** |  **2b** | 90 |
| 2 |  **1c** |  **2c** | 68 |
| 3[c] |  **1d** |  **2d** | (91)[d] |
| 4[e] |  **1e** |  **2e** | 74 |
| 5[e] |  **1f** |  **2f** | (88)[d] |
| 6 |  **1g** |  **2g** | (85)[d] |
| 7 |  **1h** |  **2h** | 72 |
| 8 |  **1i** |  **2i** | 70 |
| 9[e,f] |  **1j** |  **2j** | 76 |
| 10[e] |  **1k** |  **2k** | 79 |
| 11[e] |  **1l** |  **2l** | 77 |

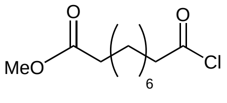
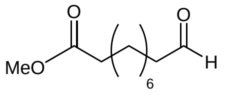
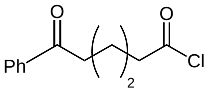
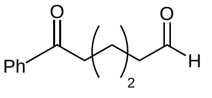
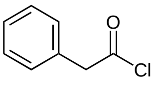
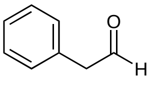
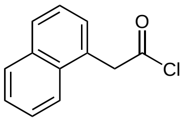
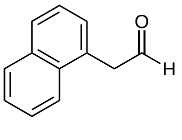
**Table 2** The Palladium-Catalyzed Reduction of Acid Chlorides to the Corresponding Aldehydes[a] (continued)



Entry Acid chloride Aldehyde Yield (%)[b]

**Table 2** The Palladium-Catalyzed Reduction of Acid Chlorides to the Corresponding Aldehydes[a] (continued)



| Entry | Acid chloride | Aldehyde | Yield (%)[b] |
|---|---|---|---|
| 12[g] | <br>**1m** | <br>**2m** | 73 |
| 13[e] | <br>**1n** | <br>**2n** | 65 |
| 14[g,h] | <br>**1o** | <br>**2o** | (99)[d] |
| 15[e] | <br>**1p** | <br>**2p** | 83 |

[a] Reaction conditions: acid chloride (**1**, 0.50 mmol), $HSiEt_3$ (0.55 mmol), $Pd(dba)_2$ (0.0125 mmol, 2.5 mol%), $Mes_3P$ (0.025 mmol, 5.0 mol%) in toluene (1.0 mL) at 40 °C for 1.5 h.

[b] Isolated yield.

[c] For 3 h.

[d] Yield based on the GC internal standard technique.

[e] $HSiMePh_2$ was used in place of $HSiEt_3$.

[f] At 60 °C.

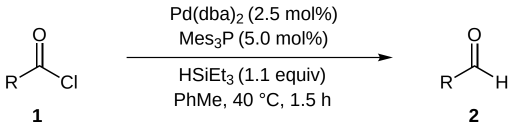
[g] $HSiMe_2Ph$ was used in place of $HSiEt_3$.

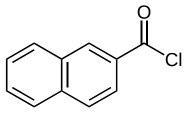
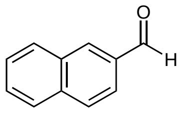
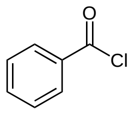
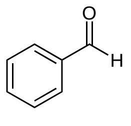
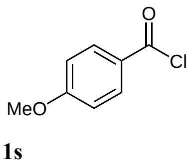
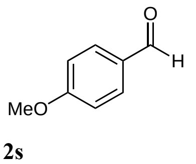
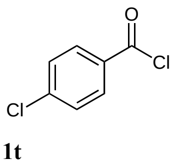
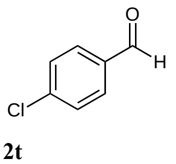
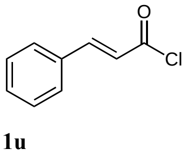
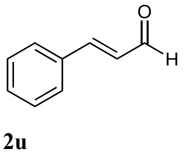
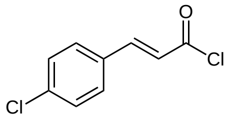
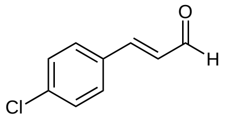
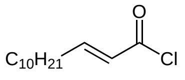
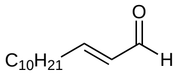
[h] For 5 h.

In addition, aroyl chlorides **1q**–**t** also afforded the corresponding aldehydes in good yields (Table 3, entries 1–4). It is noteworthy that the reactions of α,β-unsaturated acid chloride **1u**–**w** were selectively converted into the corresponding aldehyde **2u**–**w** in good to high yield (Table 3, entries 5–7). In the recent ruthenium-catalyzed reaction,[9] **2u** was obtained in low yield (18%) due to considerable 1,4-hydrosilylation of **2u** in 82% yield.

Next, the present method was applied to synthesize aldehyde-$d_1$. Compared to former procedures,[15] our method is efficient to provide the aldehydes-$d_1$. In Scheme 1, aliphatic, aromatic, and α,β-unsaturated aldehydes-$d_1$ **3b**,**q**,**u** were easily synthesized employing the corresponding acid chlorides **1b**,**q**,**u** with $DSiEt_3$[16a] (for **1b** and **1q**) or $DSiMePh_2$[16b] (for **1u**) under the standard reaction conditions.[14,17]

**Table 3** The Palladium-Catalyzed Reduction of Aroyl Chlorides and α,β-Unsaturated Acid Chlorides[a]



| Entry | Acid chloride | Aldehyde | Yield (%)[b] |
|---|---|---|---|
| 1 | <br>**1q** | <br>**2q** | 84 |
| 2[c] | <br>**1r** | <br>**2r** | (79)[d] |
| 3[c] | <br>**1s** | <br>**2s** | 73 |
| 4[c,e] | <br>**1t** | <br>**2t** | 73 |
| 5[f] | <br>**1u** | <br>**2u** | 86 |
| 6[f] | <br>**1v** | <br>**2v** | 76 |
| 7[f] | <br>**1w** | <br>**2w** | 71 |

[a] Reaction conditions: acid chloride (**1**, 0.50 mmol), $HSiEt_3$ (0.55 mmol), $Pd(dba)_2$ (0.0125 mmol, 2.5 mol%), $Mes_3P$ (0.025 mmol, 5.0 mol%) in toluene (1.0 mL) at 40 °C for 1.5 h.

[b] Isolated yield.

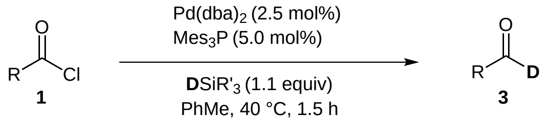
[c] A mixture of $Pd(dba)_2$ (0.025 mmol), $Mes_3P$ (0.050 mmol), and $HSiEt_3$ (1.1 mmol) in toluene (2.0 mL) was used.

[d] Yield based on the GC internal standard technique.

[e] For 3 h.

[f] $HSiMePh_2$ was used in place of $HSiEt_3$.

In conclusion, we have developed the palladium-catalyzed reduction of acid chlorides with hydrosilanes to the corresponding aldehydes. A mixture of a commercially available palladium precursor and a phosphine ligand shows high catalytic activity. Noteworthy is that a wide variety of acid chlorides including aliphatic acid chlorides, aroyl chlorides, and α,β-unsaturated acid chlorides can be employed in the reaction.



**1b** R = $C_{21}H_{43}$ with $DSiEt_3$ — **3b** 92% yield (99% D)
**1q** R = Naph with $DSiEt_3$ — **3q** 74% yield (98% D)
**1u** R = (*E*)-CH=CHPh with $DSiMePh_2$ — **3u** 80% yield (97% D)

**Scheme 1** Synthesis of aldehydes-$d_1$ from acid chlorides and $DSiEt_3$

**Typical Procedure for the Palladium-Catalyzed Reduction of 3-Phenylpropionyl Chloride (1a) with $HSiEt_3$ (Table 1, Entry 4)**
$Pd(dba)_2$ (7.2 mg, 0.0125 mmol) and $Mes_3P$ (9.7 mg, 0.025 mmol) were added to a 10 mL Schlenk flask with a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then, toluene (1.0 mL) was added to the flask, and the resultant solution was stirred at r.t. for 10 min. $HSiEt_3$ (88 μL, 0.55 mmol) and **1a** (74 μmL, 0.50 mmol) were added to the flask in this order, and the reaction mixture was stirred at 40 °C for 1.5 h under an argon atmosphere. After cooling to r.t., the reaction mixture was diluted with diethyl ether (5.0 mL), and tetradecane (50 μL, 0.19 mmol) as an internal standard was added. The yield of 3-phenylpropanal (**2a**; 99%) was analyzed by GC. When **2a** was isolated, $HSiMePh_2$ (110 μL, 0.55 mmol) was employed as the hydrosilane. After the reaction mixture was cooled to r.t., **2a** was isolated by silica gel column chromatography (hexane–EtOAc = 13: 1). A colorless oil (52 mg) was obtained in 77% yield.

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**Supporting Information** for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

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(12) $Pd(dba)_2$ and $Mes_3P$ are commercially available from TCI and Aldrich.
(13) Abbreviations: dba: dibenzylideneacetone, $Mes_3P$: tris(2,4,6-trimethylphenyl)phosphine, $(2\text{-Tol})_3P$: tri-*ortho*-tolylphosphine, $Cy_3P$: tricyclohexylphosphine, dppe: 1,3-bis(diphenylphosphino)ethane, dppf: 1,1′-bis(diphenylphosphino)ferrocene, *rac*-BINAP: 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl.
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