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# Mizoroki–Heck type arylation of alkenes using aroyl chlorides under base-free conditions

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**Abstract**—The Mizoroki–Heck type arylation of alkenes with aroyl chlorides accompanied by decarbonylation efficiently proceeds in the presence of a palladium catalyst system, $PdCl_2(PhCN)_2/(PhCH_2)Bu_3NCl$, even without adding any base. The products can be isolated by a very simple procedure.

The palladium-catalyzed arylation of alkenes with aryl halides (ArX) is well known as the Mizoroki–Heck (MH) reaction and is now recognized to be of genuine synthetic utility for preparing aromatic fine chemicals.[1] Besides the halides, various synthetic equivalents including ArOTf and ArCOX can also be employed as the arylating reagents. Aroyl chlorides are among the practically useful aryl sources, as they are relatively reactive and a wide range of aromatic carboxylic acids as their precursors are available.[2]

One of the early significant examples of the decarbonylative MH type reaction using aroyl chlorides was reported by Blaser and Spencer, in which an amine base, typically *N*,*N*-dimethylbenzylamine, for trapping HCl evolved was employed in a less polar solvent such as *p*-xylene.[3] Under the conditions, however, the undesirable direct reaction of the chlorides, especially electron-deficient ones, with the amine competitively takes place to a considerable extent, which diminishes the product yield.

On the other hand, we demonstrated that the arylation of alkenes using aroyl chlorides as well as arenesulfonyl chlorides can be effectively carried out by employing an inorganic base such as potassium carbonate together with an appropriate quaternary ammonium salt.[4] Both the electron-deficient and -rich chlorides can act as the effective arylating reagents under the phase-transfer conditions.

In our recent study of the catalytic transformation reactions of aroyl chlorides, we observed that a rhodium–ethylene complex, $[RhCl(C_2H_4)_2]_2$, also catalyzes effectively the MH type decarbonylative arylation.[5] In this case, it was found that the addition of a base as well as a phosphine ligand can be omitted. This appears to have a significant synthetic advantage, since the formation of stoichiometric amount of a salt can be avoided with enabling the recovery of HCl evolved.[6] Consequently, we have further undertaken to develop an effective protocol for the MH type arylation under base-free conditions using less expensive palladium in place of rhodium,[7] which is reported herein.

In an initial attempt, benzoyl chloride (**1a**) (1 mmol) was treated with styrene (**2a**) (1.2 mmol) in a batch reactor with an $N_2$ balloon in the presence of $PdCl_2(PhCN)_2$ (0.01 mmol) in refluxing *o*-xylene for 6 h, (*E*)-stilbene (**3a**) being formed in only 16% yield (Table 1, entry 1).

While use of LiCl (0.04 mmol) as an additive did not affect the reaction at all, the same amount of quaternary ammonium chlorides significantly enhanced the reaction (entries 3–6).[4–6] Among those examined, the relatively more lipophilic $(PhCH_2)Bu_3NCl$ was found to be most effective. Thus, using the ammonium salt without adding any base, **3a** was obtained in 95% yield along with a minor amount of 1,1-diphenylethylene (**4a**) (entry 6). The reaction in refluxing toluene was sluggish (entry 7).

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*Keywords*: Alkenes; Aroyl chlorides; Arylation; Palladium and compounds.

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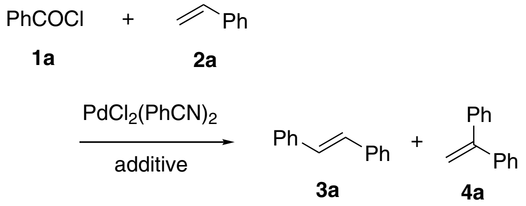
**Table 1.** Reaction of benzoyl chloride (**1a**) with styrene (**2a**)[a]



| Entry | Additive | Time (h) | Yield (%)[b] 3a | Yield (%)[b] 4a |
|---|---|---|---|---|
| 1 | — | 6 | 16 | — |
| 2 | LiCl | 6 | 17 | — |
| 3 | (PhCH$_2$)Et$_3$NCl | 6 | 51 | 2 |
| 4 | Bu$_4$NCl | 3 | 87 | 5 |
| 5 | Me(Octyl)$_3$NCl | 3 | 89 | 5 |
| 6 | (PhCH$_2$)Bu$_3$NCl | 3 | 95 (85) | 5 |
| 7[c] | (PhCH$_2$)Bu$_3$NCl | 6 | 37 | tr |

[a] Reaction conditions: **1a** (1 mmol), **2a** (1.2 mmol), PdCl$_2$(PhCN)$_2$ (0.01 mmol), additive (0.04 mmol) in refluxing *o*-xylene (5 mL) under N$_2$ (1 atm).

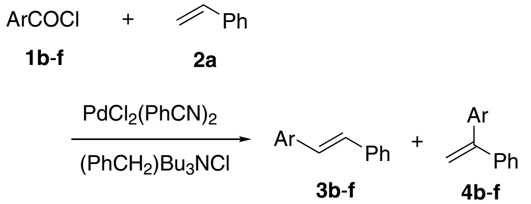
[b] GC yield. Value in parenthesis indicates isolated yield.

[c] Reaction in refluxing toluene.

Table 2 summarizes the results of the reactions using various aroyl chlorides **1b**–**f** with **2a**. In the presence of the catalyst system, PdCl$_2$(PhCN)$_2$/(PhCH$_2$)Bu$_3$NCl, both the electron-rich (**1b**,**c**,**f**) and -deficient aroyl chlorides (**1d**,**e**) reacted to give the corresponding stilbene derivatives **3b**–**f** in satisfactory yields. As in the reaction using the rhodium catalyst, the solid products were isolated in essentially pure states by a simple workup procedure; that is, only filtration, evaporation and washing with an appropriate solvent such as methanol.[5,8]

The aroyl chlorides also reacted with butyl acrylate (**2b**) in place of **2a** (Table 3). Thus, treatment of **1a**–**f** with **2b** afforded butyl (*E*)-cinnamate and its derivatives **5a**–**f** in 79–95% yields. In contrast to the reactions with **2a**, no regio-isomeric products were detected. As expected, the reactions of 4-bromobenzoyl chloride (**1d**) with *N*,*N*-dimethylacrylamide (**2c**) and acrylonitrile (**2d**) gave the corresponding coupling products **6** and **7** (entries 7 and 8). The latter was a mixture of the *E* and *Z* isomers.

**Table 2.** Reaction of aroyl chlorides **1b**–**f** with styrene (**2a**)[a]

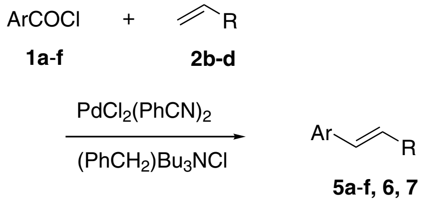


| Entry | 1 | Ar | Product(s), yield (%)[b] |
|---|---|---|---|
| 1 | **1b** | 4-MeC$_6$H$_4$ | **3b**, 88 (81); **4b**, 4 |
| 2 | **1c** | 4-MeOC$_6$H$_4$ | **3c**, 87 (75); **4c**, 4 |
| 3 | **1d** | 4-BrC$_6$H$_4$ | **3d**, 87 (84); **4d**, 7 |
| 4 | **1e** | 4-O$_2$NC$_6$H$_4$ | **3e**, 87 (80) |
| 5 | **1f** | 2-Naphthyl | **3f**, 73 (69); **4f**, 4 |

[a] Reaction conditions: **1** (1 mmol), **2a** (1.2 mmol), PdCl$_2$(PhCN)$_2$ (0.01 mmol), (PhCH$_2$)Bu$_3$NCl (0.04 mmol) in refluxing *o*-xylene (5 mL) under N$_2$ (1 atm) for 3 h.

[b] GC yield. Value in parenthesis indicates isolated yield.

**Table 3.** Reaction of aroyl chlorides **1a**–**f** with butyl acrylate (**2b**), *N*,*N*-dimethylacrylamide (**2c**), and acrylonitrile (**2d**)[a]



| Entry | 1 | Ar | 2 | R | Product, yield (%)[b] |
|---|---|---|---|---|---|
| 1 | **1a** | Ph | **2b** | CO$_2$Bu | **5a**, 91 |
| 2 | **1b** | 4-MeC$_6$H$_4$ | **2b** | CO$_2$Bu | **5b**, 92 |
| 3 | **1c** | 4-MeOC$_6$H$_4$ | **2b** | CO$_2$Bu | **5c**, 95 |
| 4 | **1d** | 4-BrC$_6$H$_4$ | **2b** | CO$_2$Bu | **5d**, 82 |
| 5 | **1e** | 4-O$_2$NC$_6$H$_4$ | **2b** | CO$_2$Bu | **5e**, 88 |
| 6 | **1f** | 2-Naphthyl | **2b** | CO$_2$Bu | **5f**, 79 |
| 7 | **1d** | 4-BrC$_6$H$_4$ | **2c** | CONMe$_2$ | **6**, 52 |
| 8[c] | **1d** | 4-BrC$_6$H$_4$ | **2d** | CN | **7**, 87[d] |

[a] Reaction conditions: **1** (1 mmol), **2b** (1.2 mmol), PdCl$_2$(PhCN)$_2$ (0.01 mmol), (PhCH$_2$)Bu$_3$NCl (0.04 mmol) in refluxing *o*-xylene (5 mL) under N$_2$ (1 atm) for 3 h.

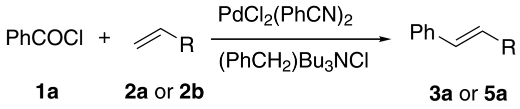
[b] Isolated yield.

[c] **2d** (4 mmol) was used.

[d] *E*:*Z* = 87:13.

As described above, the present reaction under base-free conditions appears to provide a useful synthetic route to arylated alkenes. Subsequently, the arylation was examined in a larger scale as shown in Table 4. Treatment of **1a** (10 mmol) with **2a** (15 mmol) in the presence of PdCl$_2$(PhCN)$_2$ (0.005 mmol) and (PhCH$_2$)Bu$_3$NCl (0.2 mmol) under a slow stream of N$_2$ for 24 h gave **3a** in a moderate yield. However, increasing the amounts of the catalyst and the additive to 0.02 and 1 mmol, respectively, enhanced the product yield up to 85% within 12 h. Interestingly, the reaction of **1a** with **2b** proceeded smoothly even by using 0.005 mmol of the catalyst and cinnamate **5a** was obtained in 84% isolated yield (Kugelrohr distillation). In this case, the formation of a minor amount of the (*Z*)-isomer was detected.

**Table 4.** Synthesis of stilbene (**3a**) and butyl cinnamate (**5a**) in a larger scale[a]



| R | PdCl$_2$(PhCN)$_2$/(PhCH$_2$)Bu$_3$NCl (mmol/mmol) | Yield (%)[b] |
|---|---|---|
| Ph | 0.005/0.2 | 40 |
| Ph[c] | 0.02/1 | 85 (77) |
| CO$_2$Bu[d] | 0.005/0.02 | (84)[e] |

[a] Reaction conditions: **1a** (10 mmol), **2** (15 mmol) in refluxing *o*-xylene (5 mL) under N$_2$ flow for 24 h.

[b] GC yield. Value in parenthesis indicates isolated yield.

[c] Reaction for 12 h.

[d] Reaction with **2b** (12 mmol) for 12 h.

[e] *E*:*Z* = 95:5.

The present reaction may proceed by the mechanism similar to that proposed previously.[3a,5b] The first step involves oxidative addition of an aroyl chloride toward Pd(0) species generated in situ and the subsequent decarbonylation of the resulting aroylpalladium species affords an arylpalladium intermediate. Insertion of an alkene to the intermediate and β-hydrogen elimination give the corresponding arylated alkene along with HPdCl. The refluxing conditions using *o*-xylene is considered to make the elimination of HCl from HPdCl to regenerate Pd(0) facile.[7] The major role of the added lipophilic ammonium chloride in this reaction may be the stabilization of the palladium species in the aromatic solvent.[9]

In summary, we have demonstrated that the MH type arylation of alkenes such as styrene and acrylate ester using aroyl chlorides can be effectively performed in the presence of the palladium catalyst system, $PdCl_2(PhCN)_2/(PhCH_2)Bu_3NCl$, without adding any base. The simple conditions make the product isolation procedure significantly simple. Thus, this protocol appears to provide a practical, convenient route to vinyl-substituted aromatic compounds.

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