

Rhodium-Catalyzed Mizoroki–Heck-Type Arylation of Alkenes with Aryl Chlorides under Phosphane- and Base-Free Conditions

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The arylation of alkenes with aryl halides (ArX) is well-known as the Mizoroki–Heck 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. One of the substantial problems in the reaction comes from an acidic by-product (HX), which requires the addition of stoichiometric amounts of base. Recently, the use of aromatic carboxylic acid anhydrides^[2] and aryl esters^[3] allowed the reaction to be conducted under base-free conditions. Although these methods are useful, additional workup procedures such as fractional distillation and acid–base extraction are required to obtain pure coupling products owing to the corresponding organic by-products.

Aryl and aroyl halides are also capable of undergoing oxidative addition toward certain rhodium(I) complexes to form aryl rhodium(III) species, and a number of useful catalytic processes involving this step have been developed.^[4,5] We previously demonstrated that aroyl chlorides efficiently react with terminal and internal alkynes in the presence of a rhodium–phosphane catalyst to produce the corresponding vinyl chloride and indenone derivatives, accompanied by decarbonylation and dehydrochlorination, respectively.^[5a] The coupling with alkenes in place of alkynes was successful when norbornenes were used in the presence of a disilane, giving aroylarylation products.^[5b] Herein we report our new findings that styrene and acrylate ester can also be arylated by using an appropriate phosphane-free rhodium catalyst.^[6] Thus, the alkenes efficiently undergo Mizoroki–Heck-type coupling with aroyl chlorides in the absence of any base and phosphane ligand; the by-products (CO and HCl) are readily removed.^[7] The simple conditions make the product-isolation procedure significantly simple, as described below.

In an initial attempt, benzoyl chloride (**1a**) was treated with styrene (**2**; 1 equiv) in a batch reactor with an N₂ balloon under conditions similar to those employed for the reaction with internal alkynes. In the presence of [{RhCl(cod)}₂] (1 mol %), PPh₃ (2 mol %), and Na₂CO₃ (1 equiv) in refluxing *o*-xylene for 24 h,^[5a] (*E*)-stilbene (**3a**) was formed in only 7 %

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yield (Table 1, entry 1). Fortunately, it was found that an ethylene complex $[\{\text{RhCl}(\text{C}_2\text{H}_4)_2\}_2]$ exhibits significantly higher activity than $[\{\text{RhCl}(\text{cod})\}_2]$. Thus, the yield of **3a** was improved to 69%; a minor amount of 1,1-diphenylethylene (**4a**) was detected, as was the case in the palladium-catalyzed Mizoroki–Heck reaction (Table 1, entry 2).^[2,3] Interestingly, the reaction proceeded much more smoothly in the absence of the phosphane ligand and base. As a result, **3a** was obtained in 82% yield within 4 h (Table 1, entry 4). Under the same conditions, $[\{\text{Rh}(\text{acac})(\text{cod})\}_2]$ and $[\{\text{RhCl}(\text{nbd})\}_2]$ showed lower activities (Table 1, entries 5 and 6). In the latter case, however, prolonged reaction time led to a satisfactory product yield (Table 1, entry 7). Although a decrease in the amount of $[\{\text{RhCl}(\text{C}_2\text{H}_4)_2\}_2]$ to 0.25 mol% resulted in a slight decrease in the product yield (Table 1, entry 8), **3a** was obtained in 87% yield within 2 h when 1.2 equivalents of **2** was used (Table 1, entry 9).

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

$\text{PhCOCl} + \text{Ph-CH=CH}_2 \xrightarrow[\text{o-xylene}]{\text{Rh cat.}}$		$\text{Ph-CH=CH-Ph} + \text{Ph}_2\text{C=CH}_2$	
Entry	Rh cat. (mol%)	Time [h]	Yield [%] ^[b]
			3a 4a
1 ^[c]	$[\{\text{RhCl}(\text{cod})\}_2]$ (1)/PPh ₃ (2)	24	7
2 ^[c]	$[\{\text{RhCl}(\text{C}_2\text{H}_4)_2\}_2]$ (1)/PPh ₃ (2)	23	69
3	$[\{\text{RhCl}(\text{C}_2\text{H}_4)_2\}_2]$ (1)/PPh ₃ (2)	23	69
4	$[\{\text{RhCl}(\text{C}_2\text{H}_4)_2\}_2]$ (1)	4	82
5	$[\{\text{Rh}(\text{acac})(\text{cod})\}_2]$ (1)	26	36
6	$[\{\text{RhCl}(\text{nbd})\}_2]$ (1)	4	33
7	$[\{\text{RhCl}(\text{nbd})\}_2]$ (1)	18	88
8	$[\{\text{RhCl}(\text{C}_2\text{H}_4)_2\}_2]$ (0.25)	4	72
9 ^[d]	$[\{\text{RhCl}(\text{C}_2\text{H}_4)_2\}_2]$ (0.25)	2	87
10 ^[d,e]	$[\{\text{RhCl}(\text{C}_2\text{H}_4)_2\}_2]$ (0.25)	8	75

[a] Unless noted, the reaction of **1a** (1 mmol) with **2** (1 mmol) was conducted in refluxing *o*-xylene (5 mL) under N₂ (balloon). [b] Yield determined by GC based on the amount of **1a** used. [c] With Na₂CO₃ (1 mmol). [d] **2** (1.2 mmol) was used. [e] With LiCl (0.04 mmol).

Table 2 summarizes the results for the syntheses of stilbenes **3a–i** and cinnamate **6** by the reactions of 4-substituted benzoyl chlorides **1a–g**, 2-naphthoyl chloride (**1h**), or anthraquinone-2-carbonyl chloride (**1i**) with **2** and of **1a** with *n*-butyl acrylate (**5**). The reactions were carried out under a slow stream of N₂ to effectively remove HCl and CO evolved. It can be seen from Table 2 that various functional groups are tolerated under the present conditions.^[8] It should be emphasized that essentially pure stilbenes **3** were isolated after a simple workup procedure, that is, only filtration, evaporation, and washing with an appropriate solvent such as methanol (see Experimental Section). The cinnamate **6** was isolated by Kugelrohr distillation.^[9] The reactions in Table 2, entries 1, 2, 4, 6, and 13 were carried with use of 10 mmol of **1**. Even on a relatively larger scale and with a higher substrate/catalyst ratio (**1**/Rh = 2000), the products were obtained with good yields after reasonable reaction times.

The initial step of the present reaction appears to involve oxidative addition of **1** to a Rh^ICl species to generate

Table 2: Reaction of aryl chlorides with styrene or *n*-butyl acrylate.^[a]

<div><div><div><div><div>ArCOCl</div><div>1a-i</div></div><div>+</div><div><div><div><div><div></div><div></div></div><div>R</div></div><div>2: Ph 5: CO₂nBu</div></div><div><div>[[RhCl(C₂H₄)₂]₂]</div><div>o-xylene</div></div><div><div><div>Ar</div><div></div><div>R</div></div><div>3a-i, 6</div></div></div></div></div></div>								
Entry	1	Ar	[mmol]	Alkene	[mmol]	t [h]	Product	Yield [%] ^[b]
1	a	Ph	10	2	15	6	3a	86
2	b	4-MeC ₆ H ₄	10	2	15	7	3b	79
3	c	4-MeOC ₆ H ₄	1	2	1.2	4	3c	51
4	d	4-BrC ₆ H ₄	10	2	15	6	3d	81
5	e	4-NCC ₆ H ₄	1	2	1.5	6	3e	73
6	f	4-O ₂ NC ₆ H ₄	10	2	15	10	3f	75
7	g	4-MeO ₂ CC ₆ H ₄	1	2	1.5	24	3g	75
8	h	2-naphthyl	1	2	1.2	3	3h	83
9	i	2-AQ ^[c]	1	2	1.2	12	3i	69
10 ^[d]	a	Ph	1	5	1.2	7	6	(73) ^[e]
11 ^[d,g]	a	Ph	1	5	1.2	9	6	(95:5) ^[f]
12 ^[d,h]	a	Ph	1	5	1.2	9	6	(81) (93:7) ^[f]
13 ^[h]	a	Ph	10	5	12	48	6	(98) (96:4) ^[f]
								72 (93:7) ^[f]

[a] Unless noted, the reaction was carried out with $[\{\text{RhCl}(\text{C}_2\text{H}_4)_2\}_2]$ (2.5 μmol) in refluxing *o*-xylene (5 mL) under a slow stream of N₂. [b] Yield of isolated product based on the amount of **1** used. Value in parenthesis is determined by GC. [c] 2-AQ-COCl = Anthraquinone-2-carbonyl chloride. [d] With $[\{\text{RhCl}(\text{C}_2\text{H}_4)_2\}_2]$ (0.01 mmol). [e] No increase in the yield after 24 h. [f] *E/Z* ratio. [g] With Me(*n*-C₈H₁₇)₃NCl (0.04 mmol). [h] With LiCl (0.04 mmol).

$[\text{ArCORh}^{\text{III}}\text{Cl}_2]$, which then undergoes decarbonylation to give $[\text{ArRh}^{\text{III}}\text{Cl}_2]$ as the key intermediate.^[5,10] The subsequent insertion of the alkene and β-hydride elimination as in the Mizoroki–Heck reaction affords the coupling product and Rh^{III}(H)Cl₂. The latter may release HCl, regenerating Rh^ICl. Dienes such as cod and nbd on the catalyst precursors may retard the reaction by their stronger coordination ability relative to that of the alkene substrates. The success with the bromide **1d** seems to be due to the fact that oxidative addition of aryl halides under the present conditions is difficult to take place. Notably, the addition of a chloride source such as an alkylammonium chloride or lithium chloride considerably improved the reaction efficiency with the acrylate ester (Table 2, entry 10 vs. entries 11 and 12), whereas no positive effect was observed in the case of styrene (Table 1, entry 10). Thus, it is possible that the enhancement is due to the generation of anionic rhodium species by the coordination of chloride. The electron-poor alkene may preferably interact with the metal center.

In summary, we have demonstrated that the Mizoroki–Heck-type arylation of alkenes can be performed using benzoyl chlorides in the presence of a rhodium catalyst without the addition of any phosphane ligand and base. Not only does the reaction proceed efficiently, but also the workup procedure is significantly simple. Thus, this protocol seems to provide a new, convenient route to vinyl-substituted aromatic compounds.

Experimental Section

Typical procedure: A mixture of **1a** (10 mmol, 1.41 g), **2** (15 mmol, 1.56 g), and $[\{\text{RhCl}(\text{C}_2\text{H}_4)_2\}_2]$ (2.5 μmol, 1 mg) in refluxing *o*-xylene (5 mL) was stirred under N₂ flow (in a draft chamber). The effluent

gas was led to water during the reaction, so that HCl could be recovered as hydrochloric acid. After 6 h, the mixture was cooled to room temperature, Et₂O (30 mL) was added, and a small amount of insoluble material was removed by filtration through filter paper. After evaporation of the solvents under vacuum, MeOH (10 mL) was added, and the resulting mixture was filtered to give white crystals of **3a** (1.54 g, 86%). Characterization data of products are summarized in the Supporting Information.

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