## **Rhodium-Catalyzed Double 1,4-Addition of Arylboronic Acids to** β-Aryloxyacrylates Involving β-Oxygen Elimination

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**Abstract:** The rhodium-catalyzed addition reaction of arylboronic acids to  $\beta$ -aryloxyacrylates gives 3,3diarylpropanoates in good yields. The double arylation reaction proceeds *via* the intermediate cinnamates generated by  $\beta$ -oxygen elimination.

**Keywords:** 1,4-addition; boron; esters;  $\beta$ -oxygen elimination; rhodium

The rhodium-catalyzed carbon–carbon bond-forming reactions of organoboron compounds have become an indispensable tool in organic syntheses.<sup>[1]</sup> In particular, the rhodium-catalyzed 1,4-addition reactions to electron-deficient alkenes have been extensively studied.<sup>[2]</sup> However, the 1,4-additions to  $\alpha,\beta$ -unsaturated carbonyl compounds with oxygen functionality at the  $\beta$  position have been limited to cyclic substrates.<sup>[3]</sup> Herein, we report a rhodium-catalyzed reaction of  $\beta$ -aryloxyacrylates and arylboronic acids that leads to the formation of 3,3-diarylpropanoates. The double arylation proceeds *via* intermediate formation of cinnamates by  $\beta$ -oxygen elimination.

Methyl (*E*)- $\beta$ -aryloxyacrylates were readily prepared from the reaction between methyl propiolate and the corresponding phenols (1.1 equiv.) in THF in the presence of a catalytic amount of 1,4-diazabicyclo-[2.2.2]octane.<sup>[4]</sup> Initially, the reaction of  $\beta$ -aryloxyacrylates **1a–c** and 4-methylphenylboronic acid (**2a**) was performed in the presence of catalytic amounts of [Rh(OH)(cod)]<sub>2</sub> (cod=cycloocta-1,5-diene; Table 1). When the reaction of phenoxyacrylate **1a** with **2a** (5 equiv. to **1a**) was conducted with 3 mol% [Rh(OH)(cod)]<sub>2</sub> (6 mol% Rh) at room temperature in MeOH for 2 h, methyl 3,3-bis(4-methylphenyl)propanoate (**3a**) was isolated in 88% yield (entry 1).<sup>[5-7]</sup> The expected product [i.e., methyl 3-(4-methylphenyl)-3-phenoxypropanoate] was not observed; double arylation occurred exclusively. An analogous double arylation was previously observed as a side reaction in the rhodium-catalyzed arylation of some acrylates.<sup>[8]</sup> When the reaction was performed with one equivalent of **2a**, a 56:44 mixture of **3a** and methyl (*E*)-3-(4-methylphenyl)acrylate (**4a**) was obtained in a combined yield of 19% along with 74% of recovered **1a** (entry 2). Acrylate **1b** bearing an electron-donating aryloxy group provided **3a** in 83% yield (entry 3),

**Table 1.** Rhodium-catalyzed reaction of  $\beta$ -aryloxyacrylates **1a–c** with 4-methylphenylboronic acid (**2a**).<sup>[a]</sup>



[a] Reaction conditions: 1, 2 (1 or 5 equiv.), [Rh(OH)(cod)]<sub>2</sub>
 (1.5 or 3 mol%), MeOH (0.1 M), room temperature, 2 h.

- <sup>[b]</sup> Isolated yield by preparative TLC.
- <sup>[c]</sup> Isolated along with 4a (8%) and 1a (74%).
- <sup>[d]</sup> Isolated along with 4a (18%).
- <sup>[e]</sup> 4-Methylphenylboronic acid pinacol ester was used instead of 2a, and the reaction was performed in refluxing MeOH.

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whereas when 4-acetylphenoxy derivative 1c was employed, **3a** was obtained in 99% yield (entry 4). A catalyst loading of 3 mol% Rh resulted in incomplete conversion after 2 h, and the product **3a** was obtained in 32% yield along with **4a** (18%; entry 5). When 4-methylphenylboronic acid pinacol ester was used as the arylating agent, a higher temperature was required to facilitate the reaction (entry 6).

Based on the finding that cinnamate **4** was formed as a by-product under certain conditions, the mechanism for the formation of double arylation product **3** appears to follow a tandem sequence involving 1,4-addition/ $\beta$ -oxygen elimination<sup>[9-11]</sup> forming **4** followed by 1,4-addition/protonation (Scheme 1). The absence of the usual 1,4-addition product in the reaction mixture indicates that  $\beta$ -oxygen elimination occurred so smoothly that the possible protonation of intermediate **A** was completely suppressed. The present reaction stands in stark contrast to the rhodium(I)-phosphane-catalyzed reaction of a  $\beta$ -acetoxyacrylate and an arylboronic acid that formed a cinnamate as the cross-coupling product.<sup>[12]</sup>

The reaction of methyl  $\beta$ -benzyloxyacrylate (1d) afforded a mixture of double arylation product 3a (11%) and methyl 3-benzyloxy-3-(4-methylphenyl)propanoate (5, 16%) (Scheme 2). The reactivity and eliminating ability of the benzyloxy group of 1d are comparatively poorer than those of the aryloxy counterparts.

A control experiment revealed that the reaction of methyl propiolate with **2a** failed to form the double arylation product **3a** under the present reaction conditions, demonstrating the potential utility of  $\beta$ -aryloxyacrylates for the synthesis of 3,3-diarylpropanoates.



Scheme 1. Possible mechanism.



Scheme 2. Reaction of 1d with 2a.

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Then,  $\beta$ -(4-acetylphenoxy)acrylate **1c** was subjected to the reaction with various arylboronic acids, and the results are summarized in Table 2. Phenyl-, 3-methylphenyl-, and 4-*tert*-butylphenylboronic acids (2b-d) provided the corresponding 3,3-diarylpropanoates (**3b–d**) in high yields (entries 1–3). The reaction of the sterically demanding 2-methylphenylboronic acid (2e) was inefficient at room temperature, and 3,3-diarylpropanoate 3e and cinnamate 4e were formed in 19% and 38% yields, respectively; selective formation of 3e was achieved when the reaction was performed in refluxing MeOH (entry 4). In the case of mesitylboronic acid (2f), the second arylation was hampered, even with reflux, by the severe steric hindrance of the mesityl group, furnishing cinnamate 4f as the sole product in 100% yield (entry 5).<sup>[13]</sup> In contrast to boronic acids 2h and 2i having an electron-donating methoxy group that gave 3,3-diarylpropanoates in good yields at room temperature (entries 7 and 8), the reactions with 2j-m having electron-withdrawing substituents were sluggish at room temperature; low-to-

 Table 2. Double arylation of 1c.<sup>[a]</sup>



Entry	2	Ar	Temp.	3	Yield <sup>[b]</sup>
1	2b	Ph	r.t.	3b	94%
2	2c	$3-MeC_6H_4$	r.t.	3c	95%
3	2d	$4-t-BuC_6H_4$	r.t.	3d	88%
4	2e	$2-MeC_6H_4$	reflux	3e	91%
5	2f	$2,4,6-Me_{3}C_{6}H_{2}$	reflux	3f	0% <sup>[c]</sup>
6	2g	2-naphthyl	r.t.	3g	63% <sup>[d]</sup>
7	2h	$4-MeOC_6H_4$	r.t.	3h	91%
8	2i	$3-MeOC_6H_4$	r.t.	3i	71%
9	2j	$4 - F_3 CC_6 H_4$	reflux	3j	64%
10	2k	$3-AcC_6H_4$	reflux	3k	34%
11	21	$3-O_2NC_6H_4$	reflux	31	22%
12 <sup>[e]</sup>	2m	$4-NCC_6H_4$	reflux	3m	14%
13	2n	$4-FC_6H_4$	r.t.	3n	70%
14	20	$3-BrC_6H_4$	r.t.	30	$28\%^{[f]}$

- [a] Reaction conditions: 1c and arylboronic acid 2 (5 equiv.) were treated in the presence of [Rh(OH)(cod)]<sub>2</sub> (3 mol%) in MeOH at the indicated temperatures for 2 h.
- <sup>[b]</sup> Isolated yield by preparative TLC.
- [c] Methyl (E)-3-mesitylacrylate (**4f**) was obtained in 100% vield.
- <sup>[d]</sup> Isolated along with methyl 3-(2-naphthyl)propanoate (12%).
- <sup>[e]</sup> **1a** was used instead of **1c**.
- <sup>[f]</sup> Isolated along with methyl (*E*)-3-(3-bromophenyl)acrylate (**40**, 9%).

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Scheme 3. Double arylation of 6.



Scheme 4. Synthesis of mixed arylated products.

modest yields of products **3j–m** were obtained when the reaction was performed in refluxing MeOH (entries 9–12). The reaction of 4-fluorophenyl- and 3-bromophenylboronic acids (**2n** and **2o**) afforded the corresponding products (**3n** and **3o**) in 70% and 30% yields, respectively (entries 13 and 14).

In addition to  $\beta$ -aryloxyacrylates,  $\beta$ -phenoxyacrylophenone (6) can also be used as a substrate for the double arylation reaction. The reaction of 6 occurred under the same reaction conditions to produce 3,3-diarylpropiophenones 7 in good yields (Scheme 3).

The observation that bulkier **2f** was reluctant to undergo the second arylation prompted us to examine the introduction of two different aryl groups in **1** by using **2f** and less bulky arylboronic acids. The reaction of **1c** with three equivalents of **2f** at room temperature followed by treatment with three equivalents of **2b** and **2h** at reflux provided a one-pot access to mixed arylated products **8a** and **8b**, respectively, in good yields (Scheme 4).

In conclusion, we have developed a rhodium-catalyzed double 1,4-addition reaction of arylboronic acids to  $\beta$ -aryloxyacrylates and  $\beta$ -phenoxyacrylophenone that leads to the formation of 3,3-diarylpropanoates and 3,3-diarylpropiophenones, respectively. The double arylation was achieved by the regeneration of  $\alpha$ , $\beta$ -unsaturated carbonyl compounds by  $\beta$ -oxygen elimination.

## **Experimental Section**

## General Procedure for the Rhodium(I)-Catalyzed Double Arylation of β-Aryloxyacrylates 1

To a Schlenk tube under nitrogen were added **1c** (43.9 mg, 0.20 mmol), **2a** (136.2 mg, 1.00 mmol), and  $[Rh(OH)(cod)]_2$  (2.8 mg, 6.1 µmol) followed by methanol (2.0 mL). The mixture was stirred at room temperature for 2 h, and then the

solvent was removed under reduced pressure. The crude residue was purified by preparative thin-layer chromatography on silica gel (hexane:AcOEt=5:1) to afforded methyl 3,3-di-*p*-tolylpropanoate (**3a**) as a pale yellow semisolid; yield: 52.8 mg (99%).

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action of **1a** with one equivalent of **2a** was performed in 1,4-dioxane, **3a**, (Z)-3-(4-methylphenyl)acrylate (**4'a**), and **1a** were obtained in 26%, 14%, and 55% yields, respectively (*cf.* Table 1, entry 2).

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