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Concise Synthesis of β,β-Diaryl Esters and Ketones from Ethynylcarbonyl Compounds by Rhodium-catalyzed Double Arylation with Arylboroxins

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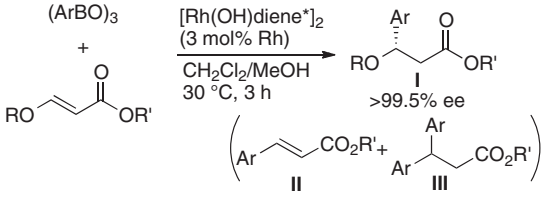
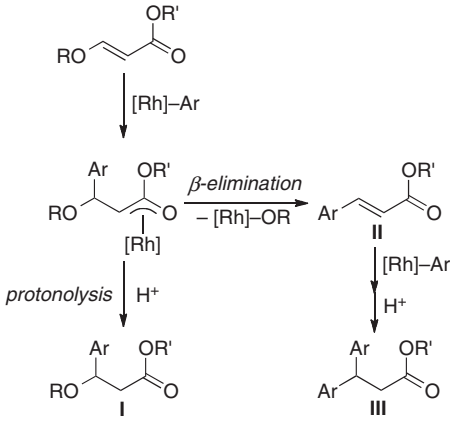
3,3-Diarylpropanoate esters were prepared from *tert*-butyl propiolate and arylboroxins in high yields through the rhodium-catalyzed double arylation of β-alkoxyacrylate, which was generated in situ from *tert*-butyl propiolate and 2,2,2-trifluoroethanol. The present method was also successfully applied to the double arylation of ethynyl ketones.

A symmetrically substituted diarylmethine unit is an important structural component found in natural products.[1] One convenient method for the synthesis of compounds bearing the diarylmethine unit is the transition-metal-catalyzed 1,4-addition of arylmetal reagents to cinnamate-type esters giving 3,3-diarylpropanoates.[2–4] A variety of aromatic groups substituted with electron-donating and -withdrawing functionalities can be introduced under mild conditions, but to construct the symmetric diarylmethine units, the appropriate cinnamate esters having the same aromatic groups as arylmetal reagents are required to prepare. An introduction of two aromatic groups in a single operation has been realized by use of a palladium catalysis. The palladium-catalyzed double arylation of acrylate esters with arenediazonium salts (the Heck–Matsuda reaction)[5] has been reported to prepare symmetric diarylacrylates, which were subjected to hydrogenation giving 3,3-diarylpropanoates.[6,7] The Horner–Wadsworth–Emmons reaction of diaryl ketones with phosphonium ylides giving diarylacrylates followed by reduction is another approach to 3,3-diarylpropanoates.[8] The synthesis of 3,3-diarylpropanoic acid derivatives has also been reported in the reaction of benzhydrols bearing two electron-donating aromatic rings with malonic acid.[9] Such approaches are still limited in terms of substrate scope.[10]

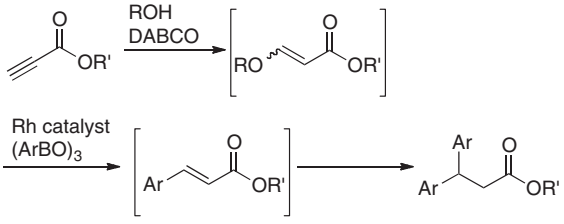
Recently, we reported rhodium-catalyzed asymmetric addition of arylboroxins to β-alkoxyacrylate esters (Scheme 1).[11] The reaction was successfully catalyzed by a hydroxorhodium/chiral diene complex, and β-aryl-β-alkoxypropanoate esters **I** were isolated in high yields with very high enantioselectivity. During this study, we observed the formation of cinnamate esters **II** and 3,3-diarylpropanoates **III** depending on the reaction conditions.[12] Their formation is explained as shown in Scheme 2: (1) β-Elimination of the alkoxy group[13] from the oxa-π-allylrhodium intermediate,[14] which is formed by the reaction of an arylrhodium species with the acrylate ester, gives the substitution product **II**; (2) the hydroarylation of **II** gives a double arylation product **III**. We focused on the 3,3-diarylpropanoates in the arylation of β-alkoxyacrylates because the readily available arylboron reagents offer access to a wide variety of 3,3-diarylpropanoates. Here we report concise synthesis of symmetric 3,3-diarylpropanoates by rhodium-catalyzed addition of arylboroxins. Very recently, Matsuda and co-workers independently reported a similar rhodium-catalyzed double arylation giving 3,3-diarylpropanoates, which was realized by use of isolated β-aryloxyacrylates.[15]



Scheme 1. Rhodium-catalyzed asymmetric addition of arylboroxins to β-alkoxyacrylate esters.



Scheme 2. Pathways to three products.



Scheme 3. Concise synthesis of symmetric 3,3-diarylpropanoates.

Our approach is focusing on the use of a commercially available propiolate ester as a starting material which generates in situ the corresponding β-alkoxyacrylate ester by the reaction with an alcohol in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO) (Scheme 3).[16] The reaction of propiolates with alcohols in the presence of DABCO was confirmed to be completed within a few minutes to give a quantitative yield of the corresponding β-alkoxyacrylates as a mixture of *E*- and *Z*-isomers. It is desirable that both isomers are used without isolation for the rhodium-catalyzed double arylation. The formal double hydroarylation of a propiolate ester was found to take

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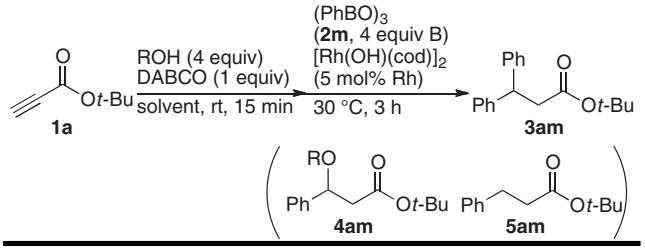
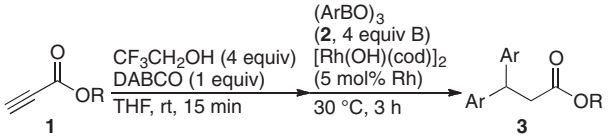
Table 1. Rhodium-catalyzed synthesis of 3,3-diphenylpropanoate **3am**[a]



Entry	ROH	Solvent	Yield[b]/%		
			3am	**4am**	**5am**
1	MeOH	THF	94	3	1
2	EtOH	THF	88	8	2
3	CF_3CH_2OH	THF	95	5	0
4	CF_3CH_2OH	1,4-Dioxane	88	6	3
5	CF_3CH_2OH	CH_2Cl_2	9	0	0
6[c]	CF_3CH_2OH	THF	90	5	0
7[c,d]	—	THF	0	0	0
8[c,d,e]	—	1,4-Dioxane	0	0	0

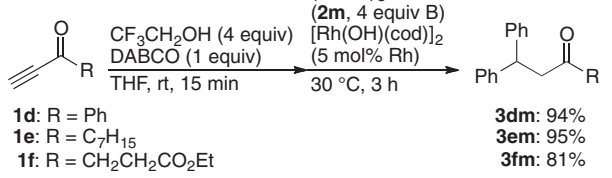
[a]Reaction conditions: **1a** (0.20 mmol), ROH (0.80 mmol), DABCO (0.20 mmol), THF (0.40 mL) at room temperature for 15 min, then **2m** (0.27 mmol), $[Rh(OH)(cod)]_2$ (5.0 μmol, 5 mol % of Rh) at 30 °C for 3 h. [b]Yields (%) determined by ^1H NMR. [c]$PhB(OH)_2$ (0.80 mmol) was used instead of **2m**. [d]Without DABCO. [e]With KOH (2.5 M, 40 μL, 0.5 equiv).

Table 2. Scope of arylboroxins and alkyl popiolates[a]



Entry	R (**1**)	Ar (**2**)	Isolated yield/%
1	*t*-Bu (**1a**)	Ph (**2m**)	93 (**3am**)
2	*t*-Bu (**1a**)	4-MeC_6H_4 (**2n**)	94 (**3an**)
3	*t*-Bu (**1a**)	3-MeC_6H_4 (**2o**)	85 (**3ao**)
4	*t*-Bu (**1a**)	2-MeC_6H_4 (**2p**)	97 (**3ap**)
5	*t*-Bu (**1a**)	4-$MeOC_6H_4$ (**2q**)	99 (**3aq**)
6[b]	*t*-Bu (**1a**)	3,4-$(OCH_2O)C_6H_3$ (**2r**)	96 (**3ar**)
7	*t*-Bu (**1a**)	2-Naphthyl (**2s**)	92 (**3as**)
8	*t*-Bu (**1a**)	4-FC_6H_4 (**2t**)	89 (**3at**)
9[b,c]	*t*-Bu (**1a**)	4-ClC_6H_4 (**2u**)	90 (**3au**)
10[b,c]	*t*-Bu (**1a**)	3,4-$Cl_2C_6H_3$ (**2v**)	71 (**3av**)
11[b,c]	*t*-Bu (**1a**)	4-BrC_6H_4 (**2w**)	95 (**3aw**)
12[b,d]	*t*-Bu (**1a**)	4-$CF_3C_6H_4$ (**2x**)	81 (**3ax**)
13	Me (**1b**)	Ph (**2m**)	88 (**3bm**)
14	Et (**1c**)	Ph (**2m**)	85 (**3cm**)

[a]Reaction conditions: **1** (0.20 mmol), CF_3CH_2OH (0.80 mmol), DABCO (0.20 mmol), THF (0.40 mL) at room temperature for 15 min, then **2** (0.27 mmol), $[Rh(OH)(cod)]_2$ (5.0 μmol, 5 mol % of Rh) at 30 °C for 3 h. [b]Performed with $(ArBO)_3$ (0.40 mmol). [c]At 60 °C for 6 h. [d]Performed using CF_3CH_2OH (1.20 mmol) at 60 °C for 24 h.



Scheme 4. The addition to ethynyl ketones.

place with $[Rh(OH)(cod)]_2$ as a catalyst (Table 1). Thus, *tert*-butyl propiolate was allowed to react with methanol (4 equiv) in THF in the presence of DABCO (1 equiv) at room temperature for 15 min. Then, phenylboroxin (4 equiv of B) and $[Rh(OH)(cod)]_2$ (5 mol % of Rh) were added to the solution of β-methoxyacrylate ($E/Z = 83/17$) and the mixture was stirred at 30 °C for 3 h. The reaction gave *tert*-butyl 3,3-diphenylpropanoate (**3am**) in 94% yield (Entry 1). The formation of a small amount of the addition product **4am** (3%) of the β-methoxyacrylate and 3-phenylpropanoate **5am** (1%) was also observed. The use of ethanol in place of methanol gave a lower yield of **3am** (88%) due to the increased formation of **4am** (8%) (Entry 2). A high chemoselectivity was also observed in the reaction using 2,2,2-trifluoroethanol, which gave **3am** in 95% yield (Entry 3). The solvent had a significant influence on the catalytic activity (Entries 3–5). Thus, the reaction in 1,4-dioxane gave **3am** in 88% yield together with 6% yield of **4am** and 3% yield of **5am** (Entry 4). The use of dichloromethane resulted in a low yield (9%) of **3am**, where the unreacted β-trifluoroethoxyacrylate was observed (Entry 5). Phenylboronic acid can also be used instead of phenylboroxin **2m**, although the yield of **3am** was slightly lower (90%) (Entry 6). It should be noted that the direct reaction of **1a** without formation of the intermediary β-alkoxyacrylate did not give the phenylation products at all (Entry 7). The formation of the addition products was not observed either in the presence of KOH as a base, which is often used in the rhodium-catalyzed 1,4-addition of organoboron reagents (Entry 8).[17]

Table 2 summarizes the results obtained for the reactions of propiolates **1** with arylboroxins **2**. The reaction of several arylboroxins **2m**–**2r** substituted with electron-donating groups gave the corresponding 3,3-diarylpropanoates in high yields (85–99% yields, Entries 1–6). The addition of 2-naphthylboroxin **2s** and (4-fluorophenyl)boroxin **2t** also proceeded under the standard conditions to give **3as** and **3at** in 92% and 89% yield, respectively (Entries 7 and 8). On the other hand, the reactions of arylboroxins bearing electron-withdrawing groups were slow (Entries 9–12). Thus, the addition of 4-chloro- **2u**, 3,4-dichloro- **2v**, 4-bromo- **2w**, and (4-trifluoromethylphenyl)-boroxin **2x** required a higher temperature (60 °C) and a greater amount of boroxins (6 equiv of B) to give **3au**–**3ax** in 71–95% yields (Entries 9–12). Methyl propiolate (**1b**) and ethyl propiolate (**1c**) were also good substrates giving the corresponding double phenylation products in 88% and 85% yield, respectively (Entries 13 and 14).

The present method of the double arylation can also be applied to the reaction of ethynyl ketones (Scheme 4). Thus, the reactions of ethynyl ketones substituted with phenyl (**1d**), heptyl (**1e**), and a functionalized alkyl group (**1f**) at the carbonyl with phenylboroxin **2m** gave the corresponding β,β-diarylketones in 94%, 95%, and 81% yield, respectively.

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In summary, we developed a concise method for the synthesis of symmetric 3,3-diarylpropanoate esters in high yields through the rhodium-catalyzed double arylation of β-alkoxyacrylate esters, which were in situ generated from *tert*-butyl propiolate and 2,2,2-trifluoroethanol. The present method was also successfully applied to the addition to ethynyl ketones giving β,β-diarylketones in high yields.[18]

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