Cross-Coupling

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Rhodium-Catalyzed Cross-Coupling of Organoboron Compounds with Vinyl Acetate**

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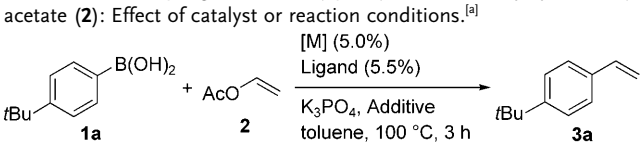
Transition-metal-catalyzed cross-coupling of organometallics with organohalogen compounds is a powerful approach for connecting two molecules by a carbon–carbon bond.[1] In organic synthesis, either organobromine or organoiodine compounds are typically used as the coupling partners with an organometallic compound. The chloro[2] or sulfonate[3] group is occasionally chosen as the leaving group of the electrophilic substrate. Furthermore, the organometallic compounds can couple with an electrophilic substrate bearing a phosphate,[4] alkoxy,[5] thio,[6] siloxy,[7] diazonium,[8] ammonium,[9] sulfonium,[10] chlorosulfonyl,[11] triazene,[12] azole,[13] or phosphonium group.[14]

The usability and environmental friendliness of the cross-coupling may be enhanced if an acetoxy group functions as the leaving group of the electrophilic substrate. The acetate substrates are readily available from commercial sources, or the esterification of alcohols with acetic anhydride in general. The acetate compounds are easier to handle in air than the corresponding sulfonates or phosphates. The acetoxy group itself does not have a serious impact on animals. Furthermore, cross-coupling using acetate electrophiles will release an acetate salt as the sole stoichiometric by-product, and this salt is readily metabolized by microbes in the natural environment. However, the acetoxy group is an unusual leaving group for metal-catalyzed cross-couplings, because the catalyst generally cleaves the acyl C–O bond in preference to another C–O bond.[15] Use of the acetate leaving group had been limited to the reaction of allylic[16] or benzylic substrates.[17] Very recently, the groups of Shi and Garg independently developed the Suzuki–Miyaura[18] or Negishi coupling[19] of aryl or alkenyl pivalates using a [$NiCl_2${P(cC_6H_{11})$_3$}$_2$] catalyst.

The cross-coupling of organometallic species with vinyl chloride or bromide allows access to terminal alkenes,[2a,20] which are widely used as substrates in many organic reactions and also as monomers in polymer synthesis. However, the boiling points of the vinyl halides are lower than ambient temperature, which impairs their use in laboratory-scale experiments. Vinyl tosylate can also be used for vinylation, although it is inferior to halides in terms of availability.[21] Therefore, vinyl acetate has emerged as an ideal coupling partner with organometallic compounds in vinylation[22] because it is easy to handle owing to its moderate boiling point. Moreover, the vinylic electrophile is comparable in cost to vinyl chloride. Herein, we report the cross-coupling of organoboron compounds with vinyl acetate using a rhodium complex as a catalyst.

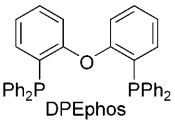
We attempted the reaction of 4-*tert*-butylphenylboronic acid (**1a**) with vinyl acetate (**2**) in the presence of various metal complexes (Table 1). The desired cross-coupling scarcely occurred in the presence of palladium or nickel complexes that are commonly used for catalytic cross-

Table 1: Cross-coupling of 4-*tert*-butylphenylboronic acid (**1a**) with vinyl acetate (**2**): Effect of catalyst or reaction conditions.[a]



$Ph_2P(CH_2)_nPPh_2$

DPPP (n = 3)
DPPB (n = 4)
DPPPent (n = 5)



Entry	[M]	Ligand	Additive	Yield [%][b]
1	[Ni(cod)$_2$]	–	–	8
2[c]	[$NiCl_2${P(c-C_6H_{11})$_3$}$_2$]	–	–	17
3	[Pd(dba)$_2$]	–	–	0
4	[{$RuCl_2$(p-cymene)}$_2$]	–	–	16
5	[{IrCl(cod)}$_2$]	–	–	36
6	[{RhCl(cod)}$_2$]	–	–	26
7	[{IrCl(cod)}$_2$]	DPPB	–	0
8	[{RhCl(cod)}$_2$]	DPPB	–	34
9	[{RhCl(cod)}$_2$]	DPPB	*t*AmOH	75[d]
10	[{RhCl(cod)}$_2$]	DPPB	*i*PrOH	63
11	[{RhCl(cod)}$_2$]	DPPB	EtOH	54
12	[{RhCl(cod)}$_2$]	DPPB	Et_2NH	55
13	[{RhCl(cod)}$_2$]	P($c$$C_6H_{11}$)$_3$	*t*AmOH	21
14	[{RhCl(cod)}$_2$]	DPPP	*t*AmOH	54
15	[{RhCl(cod)}$_2$]	DPPPent	*t*AmOH	0
16	[{RhCl(cod)}$_2$]	DPEphos	*t*AmOH	36

[a] Reactions were conducted in toluene (1.0 mL). **1a** (0.20 mmol)/**2** K_3PO_4/additive/[M]/ligand 100:1000:300:150:5.0:5.5. [b] GC yield (average of two runs). [c] The reaction was conducted in dioxane at 110°C. [d] **3a** was isolated in 75% yield when the reaction was conducted in 0.5 mmol scale for 3 h. See the Supporting Information for details. cod = cycloocta-1,5-diene, dba = dibenzylideneacetone, DPPB = 1,4-bis(diphenylphosphino)butane, DPPP = 1,3-bis(diphosphino)propane, DPPPent = 1,5-bis(diphenylphosphino)pentane, DPEphos = 2,2′-bis(diphenylphosphino)diphenyl ether, *t*Am = 1,1-dimethylpropyl.

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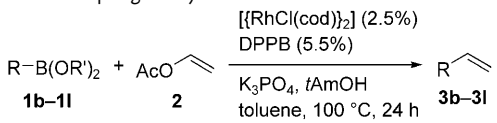
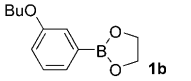
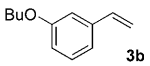
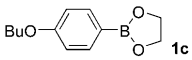
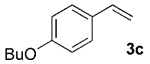
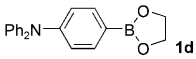
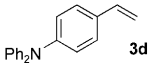
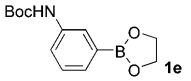
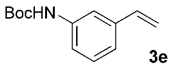
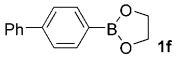
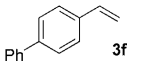
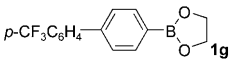
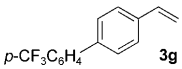
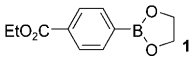
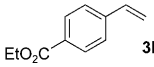
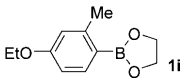
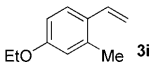
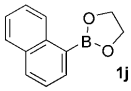
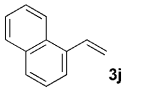
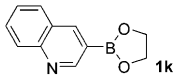
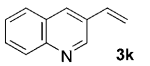
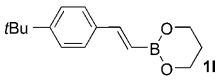
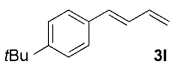
coupling reactions (Table 1, entries 1–3). Even [$NiCl_2${P(cC_6H_{11})$_3$}$_2$], which is the most effective catalyst for the cross-coupling of aryl pivalates,[18,19] failed to produce the desired vinylarene **3a** in high yield. A certain amount of **3a** was obtained from the reaction with [{IrCl(cod)}$_2$] or [{RhCl(cod)}$_2$] (cod = cycloocta-1,5-diene; Table 1, entries 5 and 6); however, the cross-coupling was accompanied by the formation of *tert*-butylbenzene (25–40%). This undesirable side-reaction was suppressed by using a bisphosphine ligand, DPPB (Table 1, entry 8). Furthermore, the addition of a stoichiometric protic compound improved the rhodium-catalyzed carbon–carbon bond formation remarkably (Table 1, entries 9–12). In particular, *tert*-amyl alcohol is effective for the production of **3a**; the vinylated product was isolated in 75% yield. However, the yield of **3a** significantly decreased when the alcohol was used as a reaction solvent. DPPB is the ligand of choice: the use of other phosphine ligands caused a decrease in the yield of **3a** (Table 1, entries 13–16).

Vinylations of arylboronic acids other than **1a** with vinyl acetate were conducted under the optimized conditions, but owing to the protodeboration of the boronic acids, in most cases the yields of the coupling products were low or moderate. The reaction of 3-butoxyphenylboronic acid afforded 3-butoxystyrene (**3b**) in 48% yield of isolated product along with a significant amount of butoxybenzene (ca. 2:1 ratio determined by GC). The side reaction was successfully avoided by using ethylene glycol ester **1b** in place of the arylboronic acid. The vinylation of **1b** gave the desired product **3b** in 88% yield (Table 2, entry 1). A range of aryl boronates were coupled with **2** in the presence of the DPPB–rhodium catalyst and were transformed into the corresponding substituted styrenes. Neither an electron-donating nor an electron-withdrawing group on the aromatic ring of **1** caused significant inhibition of the rhodium catalysis (Table 2, entries 1–7). The catalytic vinylation was compatible with Boc-protected amino or alkoxycarbonyl groups (Table 2, entries 4 and 7). Ortho-substituted styrene **3i** was obtained from **1i** in good yield (Table 2, entry 8). As with monocyclic aryl boronates, polycyclic or heterocyclic aryl boronates acted as coupling partners with **2** (Table 2, entries 9 and 10). Furthermore, the rhodium-catalyzed reaction is applicable to the synthesis of 1,3-dienes. (*E*)-1-Aryl-1,3-butadiene **3l** was obtained from the reaction of alkenylboronate **1l** with **2** in moderate yield (Table 2, entry 11). No formation of the *Z* isomer was detected during the course of the rhodium-catalyzed carbon–carbon bond formation.

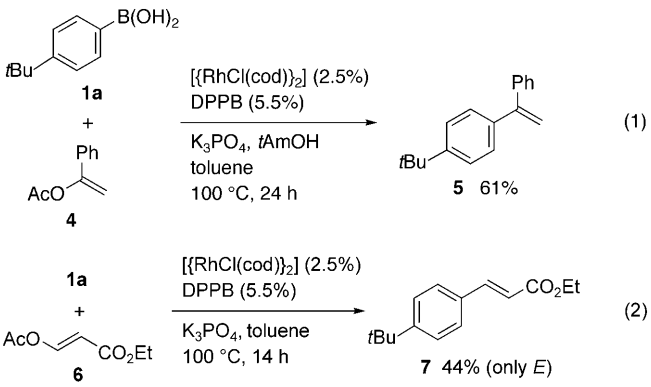
Reactions of some substituted vinyl acetates were attempted with the present rhodium catalyst system. α-Acetoxystyrene **4** reacted with **1a**, affording 1,1-diarylethene **5** in moderate yield [Eq. (1)]. Furthermore, (*E*)-β-acetoxyacrylate **6** was converted into (*E*)-cinnamate **7** with no formation of its *Z* isomer [Eq. (2)]. The absence of *tert*-amyl alcohol improved the yield of **7** because the alcohol additive caused the solvolysis of the acetate. However, the DPPB–rhodium catalyst failed to effectively couple arylboron compounds to other substituted vinyl acetates, such as β-acetoxystyrene and 2-propenyl acetate (16% and 0% yield, respectively).

Table 2: Cross-coupling of arylboronates **1** with **2**.[a]

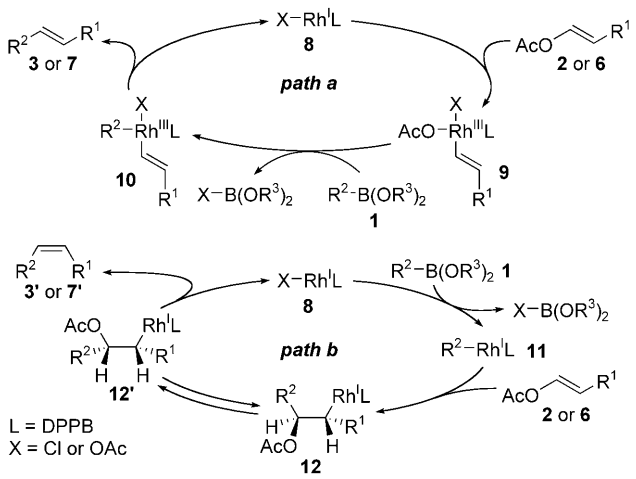


Entry	1	Product (3)	Yield [%][b]
1[c]			88
2			91
3			77
4[c]			51
5			77
6			68
7[d]			57
8[e]			79
9			85
10			43
11[c,f]			49

[a] Reactions were conducted in toluene (2.0 mL). The ratio of **1** (0.50 mmol)/**2** K$_3$PO$_4$/*t*AmOH/[{RhCl(cod)}$_2$]/DPPB was 100:500:300:300:2.5:5.5. [b] Yield of isolated product. [c] The ratio of **1**/*t*AmOH was 1:2. [d] The ratio of **1**/*t*AmOH was 1:1.1. [e] The reaction was conducted for 36 h. [f] The reaction was conducted for 48 h. Boc = *tert*-butoxycarbonyl.



We consider that the rhodium-catalyzed vinylation proceeds through a pathway similar to a typical mechanism of palladium-catalyzed Suzuki–Miyaura reaction (path a in Scheme 1).[23] The DPPB-ligated rhodium(I) species **8** under-



Scheme 1. Two possible reaction pathways of the rhodium-catalyzed cross-coupling of alkenyl acetates with organoboron compounds **1**.

goes oxidative addition of the olefinic C–O bond of alkenyl acetate to yield the (alkenyl)rhodium(III) complex **9**. Transmetalation of **9** with **1**, and the subsequent reductive elimination from **10**, produces the desired coupling product. Although there has been no report on the oxidative addition of alkenyl acetate to rhodium(I), some (vinyl)-(acetato)ruthenium(II) complexes have been isolated from the reactions of **2** with ruthenium(0) by Komiya et al.[24]

Another possible pathway, path b, can be conceived for the catalytic transformation. The catalytic cycle starts from the transmetalation of **1** with the rhodium(I) species **8**. The resulting Rh–C bond of **11** adds to the carbon–carbon double bond of **2** to form the (β-acetoxyalkyl)rhodium(I) complex **12**. β-Acetoxy elimination from **12** produces the desired coupling product and regenerates the (acetato)rhodium(I) **8**.[25] The process from **8** to **12** has been reported in the mechanistic studies on the rhodium-catalyzed 1,4-addition of organoboron compounds to electron-deficient olefins.[26] If the rhodium-catalyzed cross-coupling proceeded through path b, a *Z* alkene would be obtained as the sole product from *E*-alkenyl acetate. The stereochemistry of the reaction in Equation (2) thus rules out the possibility that the rhodium-catalyzed cross-coupling proceeds through path b.[27]

In summary, we have demonstrated that vinyl acetate is usable as an electrophilic substrate for the catalytic cross-coupling with organoboron compounds. The substitution of the acetoxy group with an aryl or alkenyl group was enabled by using a bisphosphine-ligated rhodium catalyst, whereas conventional palladium[28] and nickel catalysts are unsuitable for the cross-coupling. It is noteworthy that the rhodium-catalyzed cross-coupling can be conducted under halogen-free conditions,[29] which may open a new environmentally benign methodology for connecting two molecules through a newly formed carbon–carbon bond.

Experimental Section

General procedure: Under nitrogen atmosphere, a mixture of an arylboron compound **1** (0.50 mmol), [{RhCl(cod)}$_2$] (6.2 mg, 13 μmol), DPPB (11.7 mg, 28 μmol), and K_3PO_4 (320 mg, 1.5 mmol) was diluted with toluene (2.0 mL). Alkenyl acetate (1.1 or 2.5 mmol) and *tert*-amyl alcohol (0.55–1.5 mmol) were added into the resulting suspension at room temperature. The mixture was stirred at 100 °C for 24 h and then diluted with hexane (2.0 mL) or EtOAc (2.0 mL). After the filtration through a Celite pad, solvent was removed from the filtrate under reduced pressure. The residue was purified with a flash column chromatography (EtOAc/hexane) to give the desired product **3**.

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Keywords: acetates · boranes · cross-coupling · homogeneous catalysis · rhodium

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