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Palladium-catalysed coupling reaction of allenic alcohols with aryl- and alkenylboronic acids

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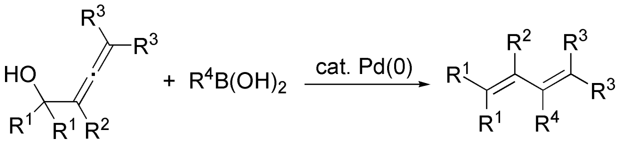
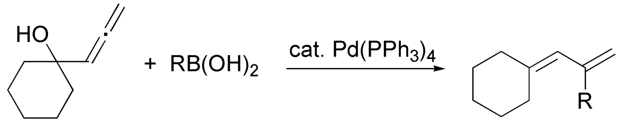
The direct coupling of aryl- and alkenylboronic acids with allenic alcohols has been achieved using a palladium catalyst to yield various substituted dienes and trienes in high yields.

Organoboronic acids are widely used reagents in organic synthesis because of their commercial availability, stability and nontoxicity. Various kinds of reactions using organoboronic acids have been developed to construct a carbon–carbon bond.[1] Among them, palladium-catalysed coupling reactions of organoboronic acids with allylic,[2] propargylic[3] and allenic[4] compounds are one of the useful reactions to produce a variety of synthetically useful unsaturated compounds. In these reactions, halides, esters and carbonates are used as a leaving group of the substrates, which are normally prepared by conversion from the corresponding alcohols. The ability to use the alcohol itself in the coupling reactions would be highly beneficial from the viewpoint of atom economy although hydroxide is generally regarded as having poor reactivity as a leaving group.[5] Recently, the direct coupling reaction of boronic acids with allylic alcohols catalysed by a rhodium complex has been reported, in which the allylic alcohol can be effectively activated by carrying out the reaction in ionic liquids.[5f] However, to the best of our knowledge, direct coupling of allenic alcohols with boronic acids has not been reported. During the course of our studies of transition metal-catalysed reactions using allenic alcohols,[6] we found the palladium-catalysed direct coupling with boronic acids (Scheme 1). We wish to report here our preliminary results describing this coupling reaction.



Scheme 1

Table 1 Palladium-catalysed coupling of allenic alcohol **1a** with boronic acids **2a–2j**[a]



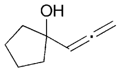
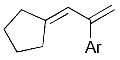
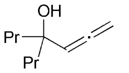
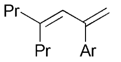
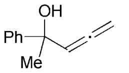
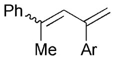
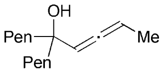
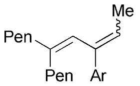
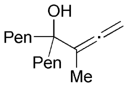
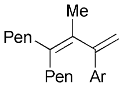
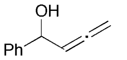
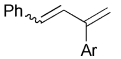
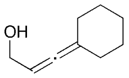
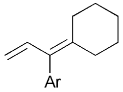
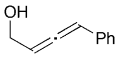
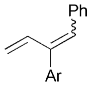
1a **2a-2j** **3aa-3aj**

Entry	Boronic acid	Product	Yield (%)
1	2-methylphenylboronic acid (**2a**)	**3aa**	99
2[b]	**2a**	**3aa**	99
3[c]	**2a**	**3aa**	88
4	4-methylphenylboronic acid (**2b**)	**3ab**	87
5	2-methoxyphenylboronic acid (**2c**)	**3ac**	99
6	4-methoxyphenylboronic acid (**2d**)	**3ad**	90
7	phenylboronic acid (**2e**)	**3ae**	83
8	1-naphthaleneboronic acid (**2f**)	**3af**	97
9	4-acetylphenylboronic acid (**2g**)	**3ag**	67
10	3-nitrophenylboronic acid (**2h**)	**3ah**	63
11	*trans*-1-hexenylboronic acid (**2i**)	**3ai**	84
12	*trans*-2-phenylvinylboronic acid (**2j**)	**3aj**	93

[a] Reactions were carried out using $Pd(PPh_3)_4$ (10 mol%) in dioxane at 80 °C for 1 h. [b] 2 mol% of $Pd(PPh_3)_4$ was used. [c] 0.5 mol% of $Pd(PPh_3)_4$ was used.

Initial attempts were made using 1-(1,2-propadienyl)cyclohexanol (**1a**) as a substrate (Table 1). When **1a** was subjected to reaction with 2-methylphenylboronic acid (**2a**) in the presence of 10 mol% $Pd(PPh_3)_4$ in dioxane at 80 °C, the reaction was completed within 1 h to afford a coupled diene **3aa** in 99% yield (entry 1 in Table 1).† The reaction can be performed in the presence of 2 mol% palladium catalyst without loss of the reactivity (entry 2), and the product is efficiently obtained even in the presence of 0.5 mol% of catalyst (88% yield, entry 3). A series of substituted boronic acids were then subjected to the reaction (entries 4–12). Similar reactivity has been observed in the reactions with other methyl- and methoxy-substituted phenylboronic acids **2b–2d** to lead to the corresponding products **3ab–3ad** in high yields (entries 4–6). Phenyl- and 1-naphthaleneboronic acids (**2e** and **2f**) also give good results (entries 7 and 8). Arylboronic acids **2g** and **2h** having an electron-withdrawing group tolerate the reaction to produce the products **3ag** and **3ah** in moderate yields (entries 9 and 10). When the reactions with alkenylboronic acids **2i** and **2j** are carried out, the correspond-

Table 2 Reactions of various substituted allenic alcohols **1b–1i** with 2-methylphenylboronic acid **2a**[a]

Entry	Substrate		Product[b]		Yield (%) (*E* : *Z*)
1		**1b**		**3ba**	95
2		**1c**		**3ca**	97
3[c]		**1d**		**3da**	98 (1.5 : 1)
4[d]		**1e**		**3ea**	99 (9 : 1)
5		**1f**		**3fa**	91
6		**1g**		**3ga**	96 (16 : 1)
7		**1h**		**3ha**	91
8[e]		**1i**		**3ia**	97 (> 20 : 1)

[a] Reactions were carried out in the presence of 10 mol% $Pd(PPh_3)_4$ in dioxane at 80 °C for 1–2 h. [b] Ar = 2-methylphenyl. [c] The stereochemistry of each product was tentatively assigned by the ^{1}H-NMR shift of the methyl proton on the dienyl group. [d] The stereochemistry of each product was determined by using the NOESY technique. [e] The stereochemistry of each product was tentatively assigned by comparison with the known 1,2-diphenylbutadiene.

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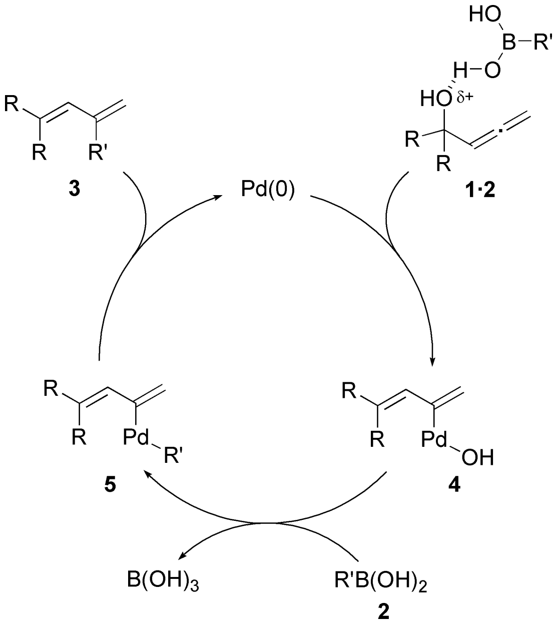
ing coupled trienes **3ai** and **3aj** are produced in good yields (entries 11 and 12).

Some results of palladium-catalysed reactions of various allenic alcohols **1b–1i** with 2-methylphenylboronic acid **2a** are summarized in Table 2. The reactions of **1b**–**1d**, which have a cyclopentyl, dipropyl and methylphenyl substituent, respectively, successfully proceed to afford the corresponding products **3ba–3da** in high yields (entries 1–3). When substrates **1e** and **1f** possessing a methyl group on the allenyl group are subjected to the reactions, the substituted dienes **3ea** and **3fa** are obtained in 99% and 91% yield, respectively (entries 4 and 5). A substrate **1g** containing a secondary hydroxyl group is uneventfully transformed to the product **3ga** in 96% yield (entry 6). Furthermore, it is clear that the reactions of primary allenic alcohols **1h** and **1i** also proceed to produce the dienes **3ha** and **3ia** in 91% and 97% yields (entries 7 and 8). All coupled products **3ba–3ia** are obtained in over 90% yields, and the corresponding (*E*)-products are predominantly produced with moderate to high stereoselectivities from the reactions of the unsymmetrical substrates **1d**, **1e**, **1g** and **1i** (entries 3, 4, 6 and 8).

A plausible mechanism for the reaction is shown in Scheme 2. It is proposed that the substrate **1** is activated by a hydrogen bond interaction with boronic acid **2** to form the reactive species **1·2**. S_N2' attack of palladium on **1·2** affords the allylpalladium hydroxide **4**, which is subsequently subjected to transmetalation with boronic acid **2** to lead to the intermediate **5**. Reductive elimination of palladium from **5** produces the coupled product **3** and regenerates palladium catalyst.



Scheme 2 Proposed reaction mechanism.

In conclusion, we have developed a palladium-catalysed coupling reaction of allenic alcohols with aryl- and alkenylboronic acids. Various aryl- and alkenyl-substituted dienes can be directly synthesized from the corresponding allenic alcohols, and neither carbonates nor esters are required as a leaving group. Synthetic applications of the obtained dienes are being investigated and further studies of this type of reaction are now in progress.

Notes and references

† Typical procedure: To a stirred solution of **1a** (50.0 mg, 0.362 mmol) in 1,4-dioxane (3.6 mL) was added 2-methylphenylboronic acid (**2a**) (98.4 mg, 0.724 mmol), $Pd(PPh_3)_4$ (41.8 mg, 0.036 mmol) at rt, and stirring was continued for 1 h at 80 °C. After filtration of the reaction mixture using AcOEt with a small amount of silica gel followed by evaporation of the eluate, the residue was chromatographed on silica gel with hexane as eluent to give **3aa** (76.1 mg, 99%) as a colorless oil; R_f = 0.49 (in hexane); IR (neat) 2926, 2853, 1639, 1448 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.18–7.12 (4H, m), 5.86 (1H, s), 5.21 (1H, m), 4.99 (1H, d, *J* = 2.8 Hz), 2.23 (3H, s), 2.14 (2H, t, *J* = 5.8 Hz), 1.96 (2H, t, *J* = 5.8 Hz), 1.61–1.33 (6H, m); ^{13}C-NMR (400 MHz, $CDCl_3$) δ 146.9, 143.3, 142.8, 135.2, 129.8, 128.6, 126.8, 125.5, 123.2, 117.0, 38.2, 29.3, 28.8, 27.6, 26.7, 20.1; MS *m*/*z* 212 (M^+); HRMS *m*/*z* calcd for $C_{16}H_{20}$ 212.1565 (M^+), found 212.1568.

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