Stereoselective synthesis of vinyl-substituted (*Z*)-stilbenes by rhodium-catalysed addition of arylboronic acids to allenic alcohols†

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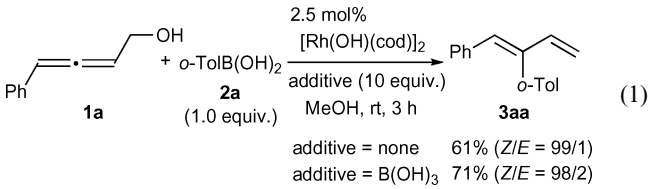
Vinyl-substituted (*Z*)-stilbenes are stereoselectively synthesised on treatment of 4-arylbuta-2,3-dien-1-ols with arylboronic acids in the presence of a rhodium(I) catalyst. The reaction proceeds through the regioselective addition of organorhodium(I) species across the aryl-substituted carbon–carbon double bond of the allene moiety and subsequent δ-elimination of Rh(I)–OH.

Rhodium-catalysed addition reactions of organoboronic acids to unsaturated functionalities have rapidly expanded as a powerful tool for the construction of carbon–carbon bonds.[1] Mechanistically, an organorhodium(I) species is generated by transmetalation between Rh(I)–OR species (OR = hydroxy or alkoxy) and organoboronic acids. It undergoes intermolecular addition to various unsaturated organic compounds and, for the next part of the catalytic cycle, the Rh(I)–OR species is regenerated typically by two types of termination steps. One is protodemetalation with H_2O or ROH,[2] and the other is β-elimination with an OR group located β to rhodium(I) of an organorhodium(I) intermediate.[3] We have developed a variety of rhodium-catalysed reactions which proceed through a sequential addition/β-OR elimination pathway.[4] For example, the addition reaction of arylboroxines onto *cis*-allylic diols gave 2-arylalk-3-en-1-ols.[5] Herein, we report a new addition reaction of organoboronic acids to allenic alcohols, in which δ-elimination of an Rh(I)–OH species occurs with an organorhodium(I) adduct to give vinyl-substituted (*Z*)-stilbenes stereoselectively.[6,7]

A solution of 4-phenylbuta-2,3-dien-1-ol (**1a**), *o*-tolylboronic acid (**2a**, 1.0 equiv.) and a catalytic amount of $[Rh(OH)(cod)]_2$ (5 mol% Rh, cod = cycloocta-1,5-diene) in MeOH (0.1 M) was stirred for 3 h at room temperature. The allenic alcohol **1a** was consumed and chromatographic isolation afforded (*Z*)-vinyl-(2′-methyl)stilbene (**3aa**) in 61% yield with high stereoselectivity (*Z*/*E* = 99 : 1, eqn (1)). The stereochemistry of the double bond was confirmed by a difference NOE study. When the reaction was carried out in the presence of ten equivalents of $B(OH)_3$ as an additive,[8] the yield of **3aa** was improved to 71%.‡ It is of interest that the stereochemical outcome is opposite to that of the reaction of **1a** with **2a** using a palladium catalyst; (*E*)-isomer **3aa** was selectively produced in the presence of $Pd(PPh_3)_4$.[9]

The stereoselective formation of (*Z*)-isomer **3aa** can be explained by assuming a reaction pathway involving δ-elimination of Rh(I)–OH, as depicted in Scheme 1.[10] Initially, *o*-tolylrhodium(I) species **A** is generated by transmetalation between Rh(I)–OH and **2a**. Regioselective *syn* addition of **A** across the phenyl-substituted carbon–carbon double bond of **1a** occurs from the less-hindered side (*a-side*) to give the alkylrhodium(I) intermediate **B**.[11] We assume that attachment of rhodium(I) to the benzylic position is favoured for the carborhodation of **A**, as with the case of the rhodium-catalysed hydroarylation of styrene.[12] Then, intramolecular coordination of the hydroxy group to rhodium(I) forms a six-membered ring rhodium(I) intermediate, for which two half-chair conformations (**C** and **D**) are available. The intermediate **C** having the phenyl substituent at the pseudo-equatorial position is more stable than the other conformer **D**. The more stable conformer **C** undergoes δ-elimination of Rh(I)–OH with a double bond shift to afford (*Z*)-isomer **3aa** together with the catalytically active Rh(I)–OH species.



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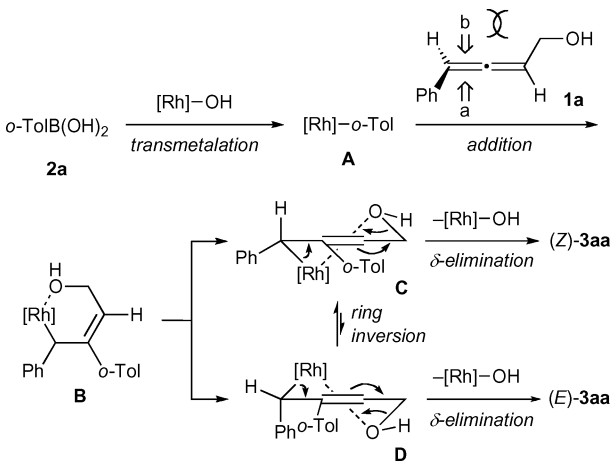

Scheme 1 Proposed reaction pathway

A variety of aryl- and alkenylboronic acids **2** were subjected to the addition reaction to **1a** (Table 1). The two other isomeric tolylboronic acids **2b** and **2c** both afforded the corresponding vinylstilbenes **3ab–3ac** with high stereoselectivities (*Z*/*E* = >95 : 5, entries 1 and 2). Not only electron-donating and -withdrawing arylboronic acids **2e–2h** but also heteroarylboronic acids **2i** and **2j** were suitably reactive (entries 4–9). In addition, even alkenylboronic acids **2k** and **2l** could participate in the addition reaction (entries 10 and 11).

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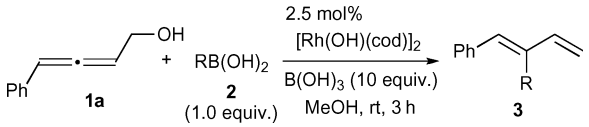
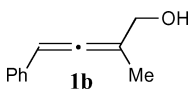
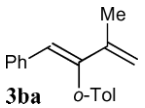
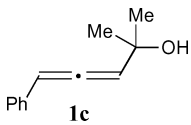
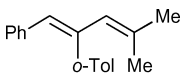
Table 1 Rh(I)-catalysed addition of aryl- and alkenylboronic acids **2** to **1a**[a]



Entry	2	R	3	Yield/%[b]	Z/E[c]
1	**2b**	*m*-Tol	**3ab**	68	>95 : 5
2	**2c**	*p*-Tol	**3ac**	77	>95 : 5
3	**2d**	Ph	**3ad**	68	95 : 5
4	**2e**	*o*-MeO–C_6H_4	**3ae**	76	>95 : 5
5	**2f**	*p*-MeO–C_6H_4	**3af**	68	92 : 8
6	**2g**	*p*-Br–C_6H_4	**3ag**	71	>95 : 5
7	**2h**	*p*-MeO_2C–C_6H_4	**3ah**	73	>95 : 5
8	**2i**	2-thienyl	**3ai**	61	93 : 7[d]
9	**2j**	3-thienyl	**3aj**	71	94 : 6[d]
10	**2k**	β-styryl	**3ak**	52	89 : 11
11	**2l**	(*E*)-hexenyl	**3al**	68	90 : 10

[a] Reactions conducted on a 0.2 mmol scale. [b] Isolated yield. [c] Determined by ^{1}H NMR. [d] In the absence of $B(OH)_3$.

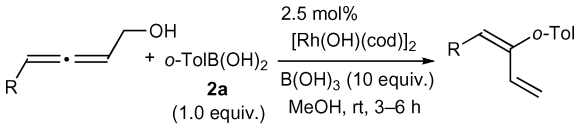
Table 2 Rh(I)-catalysed addition of *o*-tolylboronic acid (**2a**) to α-allenols **1**[a]

Entry	1	3	Yield/%[b]	Z/E[c]
1	 **1b**	 **3ba**	46	>95 : 5[d]
2	 **1c**	 **3ca**	62	91 : 9[d]
3	**1d** Ar = *p*-Cl–C_6H_4	**3da**	68	>95 : 5
4	**1e** Ar = *p*-MeO–C_6H_4	**3ea**	61	86 : 14

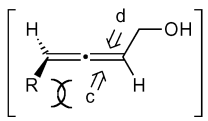
[a] The reaction conditions were the same as those in Table 1. [b] Isolated yield. [c] Determined by ^{1}H NMR. [d] Using 2.5 equiv. of $PhB(OH)_2$ for 24 h.

The use of other allenic alcohols **1** was also examined in the rhodium-catalysed addition reaction of **2a** (Table 2). Trisubstituted allenic alcohol **1b** reacted to produce **3ba** with high stereoselectivity, albeit in low yield (Z/E = >95 : 5, entry 1). Dimethyl-substituted substrate **1c** was also converted to the product **3ca** in 62% yield (Z/E = 91 : 9, entry 2). Both chloro and methoxy substituents were tolerated on the aryl substituent of **1** (entries 3 and 4). The chloro-substituted allenic alcohol **1d** exhibited a higher stereoselectivity than the methoxy-substituted allenic alcohol **1e**.

For comparison, the reaction was carried out using alkyl-substituted allenic alcohols **4**. Much to our surprise, (*E*)-isomers **5** having the opposite stereochemistry were predominantly formed (eqn (2)). The inversion of the stereochemistry is explained by assuming that *o*-tolylrhodium(I) species **A** prefers addition to the hydroxymethyl-substituted carbon–carbon double bond rather than to the cyclohexyl- or *n*-butyl-substituted double bond.[13] *Syn* addition of **A** across the hydroxymethyl-substituted carbon–carbon double bond occurs from the less-hindered side (*d-side*) and β-elimination of Rh(I)–OH immediately follows to give (*E*)-**5**.



4a R = Cy **5aa** 65% (*E*/*Z* = >95/5)
4b R = *n*-Bu **5ba** 56% (*E*/*Z* = 91/9) (2)



In summary, we have developed a rhodium-catalysed addition reaction of arylboronic acids to allenic alcohols, allowing the stereoselective formation of vinyl-substituted (*Z*)-stilbenes. This catalytic process presents a rare example of δ-elimination of Rh(I)–OH.

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Notes and references

‡ **Typical procedure**: An oven-dried flask was charged with **2a** (27.1 mg, 0.20 mmol), $B(OH)_3$ (123.6 mg, 2.0 mmol) and a solution of **1a** (29.4 mg, 0.20 mmol) in MeOH (2.0 mL). Then, $[Rh(OH)(cod)]_2$ (2.3 mg, 5.0 μmol) was added and the flask was flushed with argon. After stirring at room temperature for 3 h, the reaction mixture was diluted with ethyl acetate (10 mL) and passed through a pad of basic silica gel (Fuji Silysia Chemical Ltd., NH-DM1020). The filtrate was concentrated under reduced pressure and the residue was purified by preparative thin-layer chromatography (hexane–ethyl acetate 50 : 1) to give the product **3aa** as a colorless oil (31.6 mg, 0.14 mmol, 71%, Z/E = 98 : 2).

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