Stereoselective synthesis of trisubstituted alkenylboranes by palladium-catalysed reaction of alkynyltriarylborates with aryl halides†

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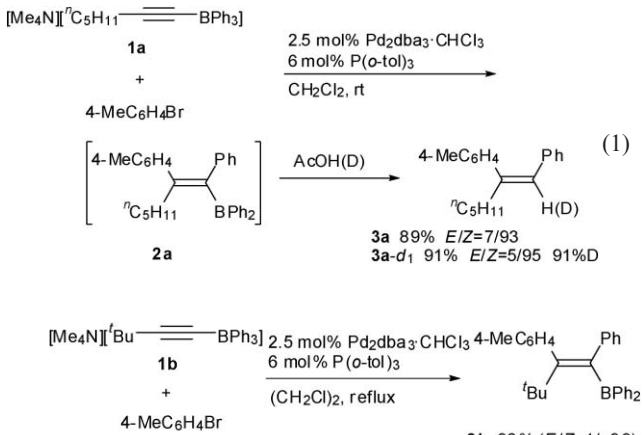
The palladium-catalysed reaction of alkynyltriarylborates with aryl halides afforded trisubstituted alkenylboranes, in which two different aryl groups were installed across the carbon–carbon double bond in a *cis* arrangement.

Organoboron compounds are valuable reagents in organic synthesis, especially for carbon–carbon bond forming reactions such as Suzuki–Miyaura coupling reaction.[1] In addition, recent studies on boron-containing compounds have demonstrated their potential as functional materials.[2] Therefore, efficient methods to prepare organoboranes in a stereo-defined form are of significant interest.[3] Di- and trisubstituted alkenylboranes can be synthesised by the reaction of alkynyltriorganylborates with electrophiles,[4] such as a proton,[5] alkyl halides,[6] acyl halides,[7] (π-allyl)palladium species,[8] carbon dioxide,[9] oxiranes,[10] chlorophosphanes,[11] sulfenyl chlorides[12] and metal halides,[5a,13] which attack the β-position of the alkynyl group to induce 1,2-migration of the organyl group from boron to the α-position. However, an analogous reaction using aryl halides or pseudohalides has not been reported, although such an arylative reaction would significantly reinforce the potential of the 1,2-migration protocol for the synthesis of π-conjugated organic materials. Herein, we report the palladium-catalysed reaction of alkynyltriarylborates with aryl halides, which affords trisubstituted alkenylboranes in a highly stereoselective manner.

Alkynytriarylborate **1a**[14] (1.0 equiv.) was reacted with 4-bromotoluene (1.0 equiv.) for 3 h at room temperature in the presence of a catalyst generated from $Pd_2dba_3{\cdot}CHCl_3$ and $P(o\text{-tol})_3$. Subsequent treatment of the reaction mixture with acetic acid afforded trisubstituted alkene **3a** in 89% yield (*E*/*Z* = 7/93, eqn (1)).[15] The ^{1}H NMR spectrum of the reaction mixture showed that no 4-(hept-1-ynyl)toluene was formed[16] and that only a trace amount (less than 5%) of 4-methylbiphenyl was produced.

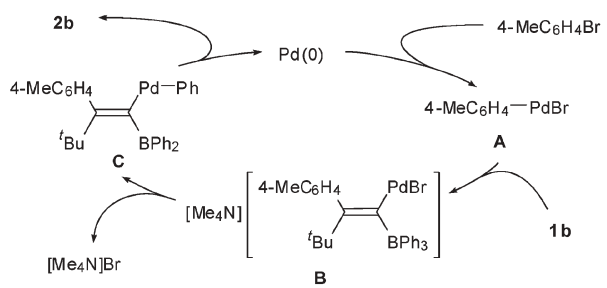
When deuterated acetic acid was employed for hydrolysis, **3a**-d_1 was obtained in 91% yield (91% incorporation of D), indicating that the alkenylborane **2a** was likely the precursor to **3a**. Although attempts to isolate **2a** failed due to the lability of the carbon–boron linkage, the alkenylborane **2b** (*E*/*Z* = 1/>99), generated from **1b** at reflux in 1,2-dichloroethane, was stable enough to be isolated by column chromatography on silica gel (eqn (2)). The *tert*-butyl group located *cis* to boron may have provided steric protection for the labile carbon–boron linkage.



A possible mechanism for the formation of **2b** from **1b** is shown in Scheme 1. Initially, oxidative addition of 4-bromotoluene to palladium(0) occurs, giving *p*-tolylpalladium species **A**. Regioselective carbopalladation across the carbon–carbon triple bond of **1b** forms the intermediate **B**. Then, a phenyl group migrates from boron to *palladium*, replacing the bromide anion. Finally, the alkenylborane **2b** is released by reductive elimination with regeneration of palladium(0).[17]

A minor pathway leading to the formation of (*E*)-**3a** from **1a** may arise from 1,2-phenyl migration from boron to the α-*carbon*, displacing palladium(0) and the bromide anion. Such a substitutive 1,2-phenyl migration can occur with inversion of the α-carbon stereochemistry.[18]

Intramolecular transfer of the aryl group on boron was confirmed by a crossover experiment (eqn (3)). When a mixture of **1c** and **1d** was subjected to the reaction with 4-bromotoluene (2.0 equiv.), **3c** and **3d** were obtained in 91 and 86% yield, respectively. No crossover products were detected by ^{1}H NMR



Scheme 1 Proposed mechanism.

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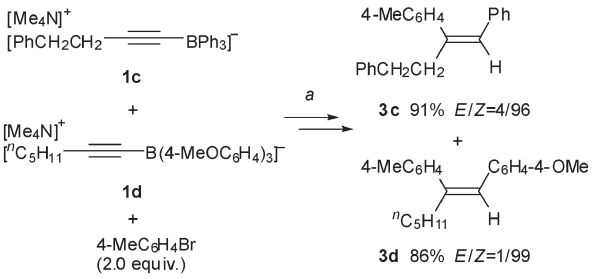
and GC-MS.



[a] 5.0 mol% $Pd_2dba_3{\cdot}CHCl_3$, 12 mol% P(*o*-tol)$_3$, CH_2Cl_2, rt, 3 h; then AcOH, rt, 3 h.

(3)

Trisubstituted alkenes **3** were synthesised by the reaction of **1a** with various aryl halides (Table 1). The reaction of 4-iodotoluene was complete within 1 h, yielding the product **3a** stereoselectively in 89% yield (entry 1). The corresponding chloride and triflate gave only a trace amount of the product. Aryl bromides having electron-donating and -withdrawing groups at the 4-positions both successfully participated in the reaction (entries 3 and 4). Ester, phthalimide and chloro groups remained intact under the reaction conditions (entries 5–7). Although 3-bromotoluene reacted smoothly (entry 8), the reaction with 2-bromotoluene was sluggish, probably due to steric reasons.

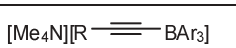
The use of other alkynyltriarylborates in the reaction with 4-bromotoluene was also examined (Table 2). Alkynylborates

Table 1 Reaction of **1a** with various aryl halides[a]

Entry	Aryl halide	Product	Yield[b] (%)	*E*/*Z*[c]
1[d]	4-MeC_6H_4I	**3a**	89	7/93
2	PhBr	**3e**	88	5/95
3	4-$MeOC_6H_4Br$	**3f**	93	7/93
4	4-$CF_3C_6H_4Br$	**3g**	90	4/96
5	4-$EtO_2CC_6H_4Br$	**3h**	93	7/93
6	4-$PhthNC_6H_4Br$	**3i**	84	6/94
7	4-ClC_6H_4Br	**3j**	88	5/95
8	3-MeC_6H_4Br	**3k**	93	5/95

[a] *Reaction conditions*: 1.0 equiv. **1a**, 1.0 equiv. aryl halide, 2.5 mol% $Pd_2dba_3{\cdot}CHCl_3$, 6 mol% P(*o*-tol)$_3$, CH_2Cl_2, rt, 3 h; then AcOH, rt, 3 h. [b] Isolated yield. [c] Determined by ^{1}H NMR. [d] Reaction time: 1 h.

Table 2 Reaction of various alkynylborates **1** with 4-bromotoluene[a]



Entry	**1** (R, Ar)	Product	Yield[b] (%)	*E*/*Z*[c]
1	**1e** (Et, Ph)	**3l**	85	6/94
2	**1f** (^{i}Bu, Ph)	**3m**	86	6/94
3	**1g** (^{i}Pr, Ph)	**3n**	74	1/>99
4	**1h** (^{n}C_5H_{11}, 4-MeC_6H_4)	**3o**	88	6/94
5	**1i** (^{n}C_5H_{11}, 3-MeC_6H_4)	**3p**	89	4/96
6	**1j** (^{n}C_5H_{11}, 4-FC_6H_4)	**3q**	86	6/94
7	**1k** (^{n}C_5H_{11}, 2-thienyl)	**3r**	82	9/91

[a] *Reaction conditions*: 1.0 equiv. **1**, 1.0 equiv. 4-bromotoluene, 2.5 mol% $Pd_2dba_3{\cdot}CHCl_3$, 6 mol% P(*o*-tol)$_3$, CH_2Cl_2, rt, 3 h; then AcOH, rt, 3 h. [b] Isolated yield. [c] Determined by ^{1}H NMR.

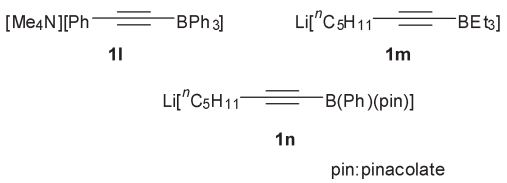
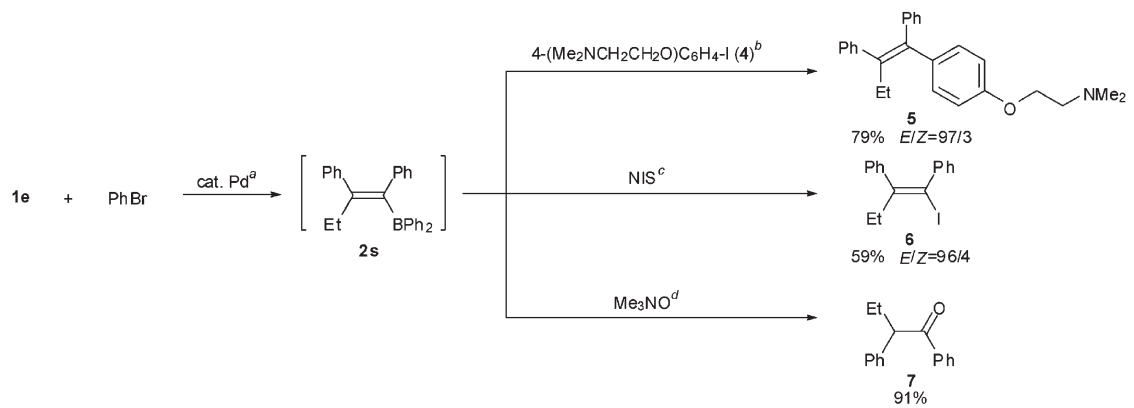


Fig. 1 Other alkynylborates.

possessing a primary alkyl group as the R substituent gave **3l** and **3m** in good yield with high selectivities (entries 1 and 2). In the case where R = isopropyl, (*Z*)-**3n** was formed exclusively (entry 3). Both electron-donating and -withdrawing groups were tolerated as the substituents on the aryl group on boron (entries 4–6, eqn (3)). Furthermore, a 2-thienyl group was efficiently transferred onto the α-carbon (entry 7). In contrast, no or only a trace amount of the corresponding trisubstituted alkenes were obtained when triphenyl(2-phenylethynyl)borate **1l** and triethyl(hept-1-ynyl)borate **1m** were subjected to the reaction with 4-bromotoluene (Fig. 1). Alkynylborates derived from phenyl boronic esters such as **1n** failed to give the corresponding trisubstituted alkenyl boronic esters either.[19]

The synthetic potential of the reaction was demonstrated by the one-pot procedures shown in Scheme 2. The Suzuki–Miyaura coupling reaction was consecutively executed by simply adding aryl iodide **4** and NaOH to a reaction mixture containing the

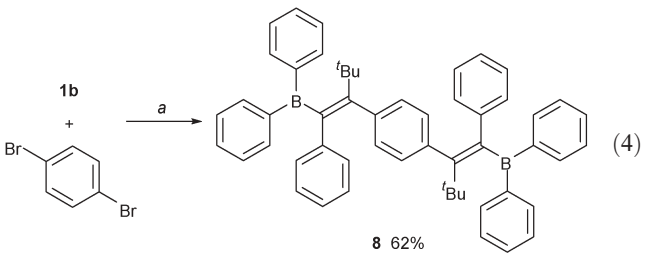


[a] 2.5 mol% $Pd_2dba_3{\cdot}CHCl_3$, 6 mol% P(*o*-tol)$_3$, CH_2Cl_2, rt, 3 h. [b] 3.0 equiv. **4**, NaOH, H_2O, rt, 24 h. [c] NH_3 aq.; then 5.0 equiv NIS, acetone, 0 °C, 1 h. [d] 5.0 equiv Me_3NO, rt, 3 h.

Scheme 2 Reactions of alkenylborane **2s**.

alkenylborane **2s**. (*E*)-Tamoxifen (**5**) was stereoselectively obtained in 79% yield (*E*/*Z* = 97/3).[20] Stereospecific iodination was accomplished by treatment of the ammonia complex of **2s** with NIS, giving the alkenyl iodide **6** in 59% yield (*E*/*Z* = 96/4). An oxidation reaction with trimethylamine *N*-oxide produced the ketone **7** in 91% yield.

Installation of two aryl groups in juxtaposition across a boron-substituted alkene is attractive in terms of the synthesis of boron-containing π-conjugated materials. Thus, the reaction was successfully applied to the construction of diboranyl compound **8** (eqn (4)).



(4)

[a] 2.5 mol% $Pd_2dba_3 \cdot CHCl_3$, 6 mol% P(*o*-tol)$_3$, $(CH_2Cl)_2$, reflux, 1 h.

In summary, a new method for the stereoselective synthesis of trisubstituted alkenylboranes has been developed, in which two different aryl groups were installed across the carbon–carbon double bond in a *cis* arrangement. Application of this method to synthesis of boron-containing functional materials is under way.

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15 No reaction occurred in the absence of the palladium catalyst.

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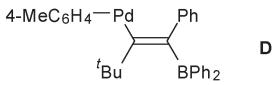
17 An alternative mechanism is also conceivable. The arylpalladium bromide **A** acts as an electrophile such as alkyl halides, giving diorganylpalladium **D**. Subsequent reductive elimination affords the alkenylborane **2b** and palladium(0).



D

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19 Other phenyl boronic esters including catecholate and ethylene glycolate were also subjected to the reaction conditions. However, no desired alkenylboronic esters were formed, presumably due to the instabilities of the corresponding 'ate' complexes under the reaction conditions.

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