Synthesis of 3-hydroxy-1-alkenylboronates *via* phosphine stabilized borylzirconacyclopropenes†‡

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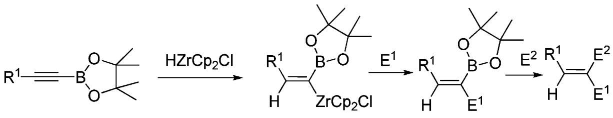
Zirconacyclopropenylboronates can be stabilized to dimerization by complexation with tributylphosphine; the phosphine stabilized zirconacycle boronates react with aliphatic and aromatic ketones and aldehydes at C2 of the triple bond to give the previously unknown 3-hydroxyvinylboronates in 61–80% isolated yields.

Vinylboronates are valuable but relatively inert compounds[1] and can be synthesized by various methods.[2,3] Their utility lies in the ability to transfer the vinyl group from boron to other elements[1] and metals.[4–9] For instance, facile carbon–carbon bond forming reactions between vinylboronates and vinyl/aryl halides occur by palladium catalysis in the presence of base (Suzuki–Miyaura coupling),[10,11] or by transfer to zinc and subsequent reaction with aldehydes.[4] Other methods include intramolecular transfer mediated by halides (Zweifel diene synthesis)[12] or cycloaddition reactions[13] to list but a few reactions. Using highly functionalized vinylboronates enables the synthesis of more complex structures.[14] We have previously prepared vinylboronates by hydrozirconation of 1-alkynylboronates to give 1,1-borazirconocenes and demonstrated that it was possible to selectively react the C_{Sp2}–Zr bond to give highly substituted vinylboronates, which could then be reacted with a different electrophile to provide trisubstituted alkenes in a highly stereo- and regioselective manner (Scheme 1).[15–23]



Scheme 1 Formation and reaction of 1,1-*gem*-borazirconocenes.

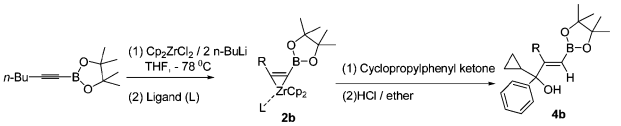
The use of the Negishi reagent ($Cp_2ZrCl_2/2n$-BuLi) with 1-alkynylboronates, on the other hand, leads to mixtures of 1,3-butadienes, the result of homocoupling.[24] It is known that blocking the empty zirconium *d* orbital can stabilize zirconacycles.[25] With this in mind we tried to zirconate 1-2-(hex-1-ynyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane with the Negishi reagent ($Cp_2ZrCl_2/2BuLi$)[26] in the presence of various stabilizing ligands. The results are the subject of this communication.

The best results were obtained with tributylphosphine. Other ligands suh as tri-*n*-octylphosphine and triphenylphosphine gave inferiors results (entries a, b, Table 1). Phosphites (entries d–f), and triethylamine (entry g) were ineffective in stabilizing the borylzirconacylopropenes. Only diborylated 1,3-butadienes were obtained with the latter.

When 1-heptynylboronate was zirconated with the Negishi reagent in the presence of tributylphosphine and worked up with HCl/ether only one product was obtained, **5**. No trace of the homo-coupling product was observed whereas workup with D_2O gave the dideuterio product **6**, indicating that the intermediate zirconacyclopropene was indeed stabilized by the phosphine ligand (Scheme 2).

This is the first time we were able to successfully prepare stable borylzirconacyclopropenes. Phosphine stabilized **2** was then reacted with a series of aldehydes and ketones. Workup of **3** with HCl/ether provided 3-hydroxy-1-alkenylboronates **4** (Scheme 2, Table 2).

Table 1 Ligand effect on the synthesis of **4**



Entry	Ligand	% Yield **4b**
a	$(n\text{-Oct})_3P$	15
b	Ph_3P	17
c	$(Bu)_3P$	81
d	$(MeO)_3P$	—
e	$(EtO)_3P$	—
f	$(EtO)_2POH$	—
g	Et_3N	—

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† Electronic supplementary information (ESI) available: Full analytical and experimental data for **4**. ^1H and ^{13}C NMR spectra for **4**. See DOI: 10.1039/b811287h

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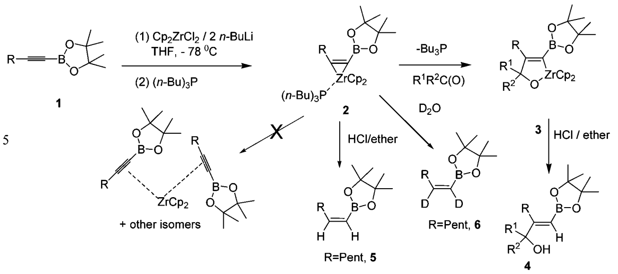


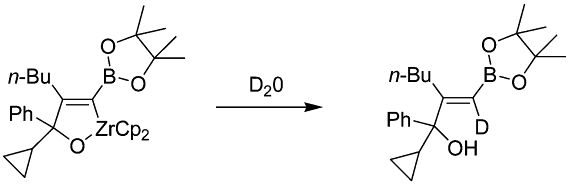
Scheme 2 Mechanism of formation of **4**.

Borylzirconacyclopentenes, however, are stable and react with aldehydes and ketones to form 5-hydroxy-1-alkenylboronates.[27] Phosphine stabilized **2** was then reacted with a series of aldehydes and ketones. Workup of **3** with HCl/ether provided 3-hydroxy-1-alkenylboronates **4** (Scheme 2, Table 2). That insertion of an aldehyde or ketone does indeed go through **3** which was demonstrated by working up the reaction of cyclopropylphenyl ketone with D_2O (eqn (1)). The mono deuterated product **7** was obtained, as expected, if **3** was an intermediate.

Both aliphatic (Table 2, **4a–h**) and aromatic alkynylboronates (Table 2, **4i**) may be used. Insertion proceeds well with various ketones and aldehydes as indicated in Table 2. Both aliphatic and aromatic ketones and aldehydes are successfully inserted in satisfactory isolated yields. However, difficulty was encountered with relatively hindered aldehydes or ketones.

For instance, 2-methoxybenzaldehyde and 2,4-dichlorobenzaldehyde gave little product (GC/MS) and these were not isolated) whereas anisaldehyde reacted satisfactorily. Also hindered ketones like benzophenone gave little product (GC/MS) and this was also not isolated.

The regioselectivity of **4** was determined by ^{1}H NMR data. The presence of a singlet in the double bond region is indicative of the coupling of the aldehydes and ketones having occurred on C2. On the other hand, the $^3J_{HH}$ coupling constant (13.5 Hz) of the hydrogens on C1 and C2 to boron in compound **5** demonstrates *cis* stereochemistry. This coupling constant is consistent with the one we obtained by hydrozirconation. Regarding the mechanism (Scheme 1), the tributylphosphine group must first depart. The uncomplexed zirconacyclopropene then reacts faster with the aldehyde or ketone than it dimerizes.

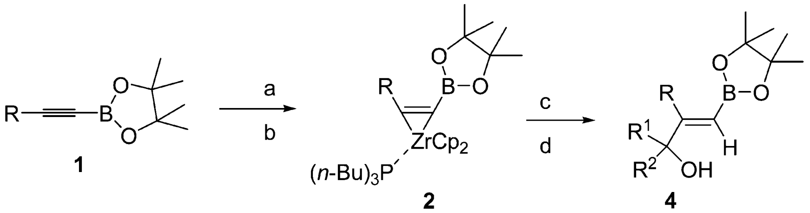


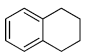
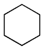
(1)

3h **7**

In conclusion, whereas hydrozirconation places zirconium on the same atom at boron, insertion of aldehydes or ketones into the borylzirconacyclopropenes occurs at the carbon distal to boron, apparently for steric reasons. The two reactions, thus, complement one another and provide access to various substituted vinylboronates useful for subsequent transformations.[28]

Table 2 Formation and isolated yields of **4**



Aldehyde/ketone	4	R	R¹	R²	Yield (%)[e]
Acetone	**a**	*n*-Bu	CH_3	CH_3	75
Cyclopropylphenyl ketone	**b**	*n*-Bu		C_6H_5	73
α-Tetralone	**c**	*n*-Bu			61
Acetone	**d**	*n*-Pent	CH_3	CH_3	76
Cyclopropylphenyl ketone	**e**	*n*-Pent		C_6H_5	81
Cyclohexanone	**f**	*n*-Pent			68
Benzaldehyde	**g**	*n*-Pent	C_6H_5	H	73
Anisaldehyde	**h**	*n*-Pent	4-$MeOC_6H_4$	H	77
Acetone	**i**	C_6H_5	CH_3	CH_3	80

[a] 2 *n*-BuLi, THF, −78 °C. [b]$(n\text{-Bu})_3P$. [c]$R^1R^2C(O)$. [d]HCl/ether. [e] Conversion was >98% as determined by GC/MS and ^{11}B NMR for all reactions.

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