Alkenylation of allylic alcohols using alkenylboron dihalides: a formal transition-metal free Suzuki reaction†

George W. Kabalka,* Min-Liang Yao, Scott Borella and Zhongzhi Wu

Carbon–carbon bond formation *via* substitution of an allylic hydroxide with stereodefined alkenyl groups using alkenylboron dihalides in the absence of transition metals.

Transition-metal catalyzed allylic alkylation (especially asymmetric alkylation, AAA) of allylic halides, carbonates, and carboxylates is a very active topic in organic synthesis.[1] Numerous studies have been reported describing ligands[2] and transition metal complexes[3] designed to enrich the regio- and/or enantioselectivities of these reactions. In this context, reactions with soft nucleophiles have been well-studied. However, reactions involving hard nucleophiles have not been developed as well due to the stability of the carbon–metal bond in the transient π-allyl intermediates.[4] To achieve allylic substitution using hard nucleophiles, the transmetallation of Grignard or organozinc reagents to the more reactive copper reagents is often required.[5,6] For organoboron nucleophiles, transformation of boronic acids to more reactive lithium borates[7] or zinc borates[8] is generally required. Until now, only the coupling of arylboronic acids with allylic halides,[9] and carbonates[9a,10] has been described. For example, the RuCl₃ catalyzed coupling of allylic alcohols with arylboronic acids was recently achieved.[11] Subsequently a successful sealed tube, Pd(PPh₃)₄ catalyzed reaction was reported.[12] Recently, Genet reported a [Rh(cod)Cl]₂ catalyzed reaction of Baylis–Hillman adducts with arylboronic acids.[13] The reaction afforded formal Suzuki coupling products through an unusual 1,4-addition/β-hydroxy elimination sequence. Interestingly, the coupling of a vinyl group to an alcohol in the absence of a transition metal has never been reported. Herein, we wish to report the first transition metal free, formal Suzuki-type[14] allylic alkenylation using allylic alcohols and alkenylboron dihalides. From the point of organic synthesis, this novel allylic alkenylation is quite attractive because it allows the attachment of stereodefined alkenyl groups to an existing carbon skeleton. The direct use of allylic alcohols as electrophiles makes the reaction atom-efficient and more environmentally friendly.

We have focused on the chemistry of boron halide derivatives for many years and have developed a number of novel reactions.[15] Examples include the Grignard-like alkylation of aryl aldehydes using alkylboron dihalides, and the BX₃/PhBX₂ mediated reactions of styrene and aryl aldehydes leading to either 1,3-dihalo-1,3-diarylpropanes or 3-halo-1,3-diarylpropanols. Recently we reported a BX₃ mediated reaction between aryl acetylenes and aryl aldehydes (Scheme 1).[16] Stereodefined 1,3,5-triaryl-1,5-dichloro-1,4-pentadienes were isolated. At that time we proposed

that the reaction proceeded through a 2-halovinyl(allyloxy)boron halide intermediate **A**. The migration of the 2-halovinyl group from boron to carbon then generated the final product. This led us to investigate whether the migration of alkenyl groups could, indeed, occur under these reaction conditions.[17]

The reaction shown in Scheme 2 was designed to probe the feasibility of such an alkenyl group migration. Reaction of allylic alcohol **1** and alkenylboron dihalide **2** in the presence of base (BuLi or NaH) would generate intermediate **B** which is similar in structure to the earlier proposed intermediate **A**. Based on the suggested migration, Scheme 1, intermediate **B** should rearrange to the desired product **3**. It is well-known that the reaction of terminal alkynes with one equivalent of boron trihalide generates the stereodefined (Z)-2-halo-1-alkenylboron dihalide, **2**, in quantitative yield.[18] Due to its readily availability 1,3-diphenyl-prop-2-en-1-ol (**1**, R = R₁ = Ph) was chosen as a model compound to evaluate the feasibility of the proposed alkenylation reaction. Fortunately, in the presence of base (BuLi or NaH), the reaction proceeded smoothly using (Z)-2-chloro-2-phenyl-1-alkenylboron dichloride at room temperature[19] and the desired product (Z,E)-1-chloro-1,3,5-triphenyl-1,4-pentadiene (**3a**) was isolated in 83% yield. The reaction is highly stereoselective. The resonances observed at 4.94 ppm (dd) in the ¹H NMR spectrum and at 48.5 ppm in the ¹³C NMR spectrum demonstrate that only a single isomer forms in the reaction.[20]

The method provides stereodefined 1,4-pentadienes starting from readily available allylic alcohols. To evaluate the scope of this new allylic alkenylation reaction, a variety of allylic alcohols **1** and alkenylboron dihalides **2** were prepared and subjected to the reaction. The results are presented in Table 1. For both alkenylboron dichlorides and alkenylboron dibromides derived from aryl alkynes, the reactions produce the expected products in moderate to high yields. The isolated yields are somewhat lower when alkenylboron dibromides are utilized. For alkenylboron dihalides derived from aliphatic alkynes, the allylic alkenylation reaction requires the use of alkenylboron dibromides. Unsymmetrical allylic alcohols also produce pure products; no regioisomers were detected by NMR analysis. Transition-metal catalyzed allylic substitution reactions often afford mixtures of regioisomers from the π-allylic intermediates.[9,10] Further investigation revealed that substituents R and R₁ are not limited to aryl groups. In this respect, the new allylic alkenylation reaction is more general than the reaction shown in Scheme 1. Interestingly, we found that monosubstituted allylic alcohols do not lead to the desired products.

In summary, we have developed a novel method to prepare stereodefined 1-halo-1,3,5-substituted-1,4-pentadienes using readily

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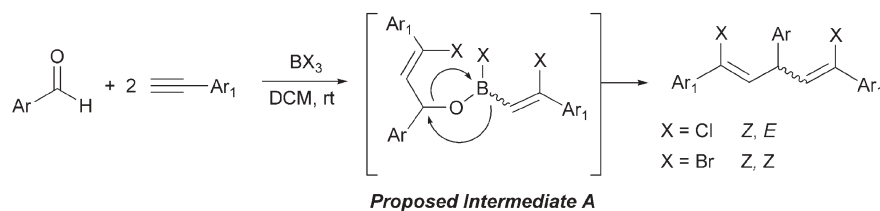
Scheme 1 Preparation of 1,4-dienes *via* boronate rearrangement.
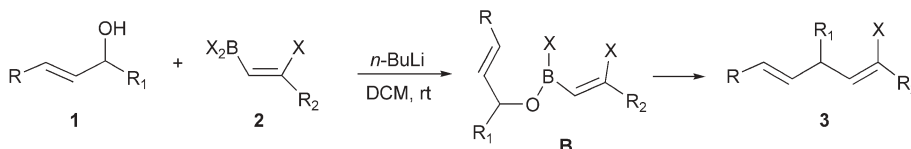
Scheme 2 Preparation of 1,4-dienes *via* reaction of vinylboron dihalides with allyl alcohols.

Table 1 Allylic alkenylation of allylic alcohols[a]

R	R_1	R_2	X	Product[b]	Yield[c](%)
Ph	Ph	Ph	Cl	3a	83
Ph	Ph	p-MePh	Cl	3b	81
Ph	Ph	m-FPh	Cl	3c	78
Ph	Ph	p-ClPh	Cl	3d	79
Ph	Ph	p-BrPh	Cl	3e	65
Ph	Ph	o-FPh	Cl	3f	61
Ph	Ph	Ph	Br	3g	71
Ph	Ph	p-MePh	Br	3h	68
Ph	Ph	n-C_4H_9	Br	3i	62
Ph	Ph	n-C_8H_{17}	Br	3j	65
Ph	Me	m-FPh	Cl	3k	77
Ph	Me	m-FPh	Br	3l	58[d]
Ph	Me	Ph	Br	3m	53[d]
(E)-PhCH=CH–	Ph	Ph	Cl	3n	66
1-Naphthyl	Ph	Ph	Cl	3o	47[e]
H	p-ClPh	Ph	Cl	—	Trace
Ph	H	Ph	Cl	—	Trace

[a] Reaction carried out in dry DCM at room temperature with *n*-BuLi as base. [b] All products were characterized by NMR spectra and elemental analyses (or HRMS). [c] Isolated yields based on alkynes. [d] NaH used as base. [e] Approximately 15% of 1-(3-chloro-3-phenylpropenyl)napthalene was isolated.

available allylic alcohols and alkynes (the precursor to the (Z)-alkenylboron dihalides). The reaction conditions are mild and the reaction is highly stereo- and regioselective. Because the reaction involves alkenylboron dihalides and the products are identical to those obtained in Suzuki coupling reactions, this new reaction can be viewed as a formal transition metal free Suzuki reaction.

George W. Kabalka,* Min-Liang Yao, Scott Borella and Zhongzhi Wu
Departments of Chemistry and Radiology, The University of Tennessee, Knoxville, TN 37996-1600, USA. E-mail: kabalka@utk.edu; Fax: +1-865-974-2997; Tel: +1-865-974-3260

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19 Typical reaction procedure: boron trihalide (1.5 mmol), alkyne (1.5 mmol), and dry dichloromethane (8 mL) were combined in a 25 mL flask under a nitrogen atmosphere and stirred for 1 hour. In a separate flask, the allylic alcohol (1.6 mmol) in dry dichloromethane (8 mL) was treated with *n*-butyllithium (1.0 mL of a 1.6 M solution in hexanes) at 0 °C and stirred at room temperature for 1 hour. The second solution was then transferred to the first flask and the mixture allowed to stir at room temperature overnight. Water (20 mL) was added and the reaction mixture was extracted with ethyl acetate and dried over anhydrous MgSO$_4$. The solvents were removed *in vacuo* and the product purified by silica gel column chromatography using hexane as an eluent.

20 At this time, the experimental evidence cannot be used to identify whether the migration of the vinyl group to the allylic center occurs with inversion, retention, or racemization. Analogous studies involving chiral benzylic alcohols (unpublished results) strongly support the formation of cationic intermediates which would lead to epimerization at the migration terminus. Further studies using chiral allylic alcohols are underway.