

Diastereoselective Construction of Functionalized Homoallylic Alcohols by Ni-Catalyzed Diboron-Promoted Coupling of Dienes and Aldehydes

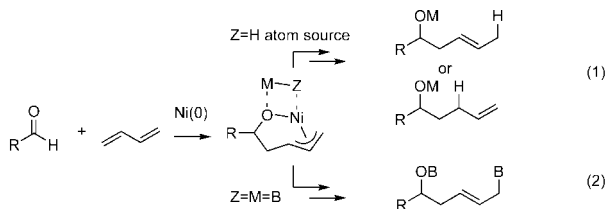
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The dimetalation of unsaturated substrates is an effective tool for enriching the functional and stereochemical complexity of simple hydrocarbon substrates.¹ In the particular case of diboration, reaction of alkenes,² dienes,^{2b,3} allenes,⁴ and enones⁵ provides reactive intermediates that may participate in stereoselective cascade reaction sequences. In general, these reactions are energetically highly favored with the addition of bis(ethyleneglycolato)diboron to ethylene calculated to be exothermic by 41.7 kcal/mol.⁶ A useful extension of this methodology would arise if the reactivity inherent in diboration reactions could be used to promote multicomponent coupling processes. Considering the oxophilic nature of boron, an attractive starting point for these studies is the reductive coupling of unsaturated hydrocarbons and carbonyls, a transition-metal catalyzed process that is enabled by the use of metal hydrides, molecular hydrogen, or their equivalents, to facilitate C–C bond formation.⁷ In particular, the coupling of simple dienes and carbonyls, a Ni-promoted process first discovered by Wilke⁸ with subsequent pioneering studies in catalysis by Mori⁹ and Tamaru,¹⁰ was targeted.¹¹ In the context of diboron-promoted coupling, we considered that this transformation might be a very effective tool for the preparation of synthetically versatile allylboronates.¹²

Mechanistic studies by Ogoshi have provided the first structural evidence that the Ni-promoted reductive (and alkylative) coupling of dienes and aldehydes is initiated by cyclometalation of the substrates.¹³ In the presence of a metal hydride, subsequent σ -bond metathesis and reductive elimination generate the unsaturated reaction product (eq 1). Here, we demonstrate that diboron reagents may participate in a similar σ -bond metathesis reaction, thereby providing access to organoboronic esters as the reaction product (eq 2). A notable aspect of this reaction is that the products are obtained with excellent levels of stereoselectivity and with regioselectivity that complements the stepwise diene diboration/carbonyl allylation reaction.^{12b} A unique and particularly useful feature of this process is that oxidative workup directly provides a functionally and stereochemically enriched product whose synthesis would otherwise require multiple steps.



Initial experiments surveyed the Ni-catalyzed, room temperature reaction of bis(pinacolato)diboron, *trans*-1,3-pentadiene, and benzaldehyde. After extensive optimization of reaction parameters (ligand, solvent, temperature, concentration), the optimal set of reaction conditions was found to include PCy₃ as the ligand, THF as the solvent, at room temperature, and a substrate concentration

Table 1. Ni-Catalyzed Coupling of Dienes, Aldehydes, and B₂(pin)₂

entry	aldehyde	diene	product	d.r. ^a	yield ^b
1				>20:1	66
2				>20:1	63
3				>20:1	63
4				>20:1	62
5				>20:1	53
6				>20:1	70 ^c
7				>20:1	65 ^c
8				N/A	34 ^c
9				N/A	68 ^d
10				>20:1	47 ^c
11				>20:1	24 ^c
12				>20:1	57

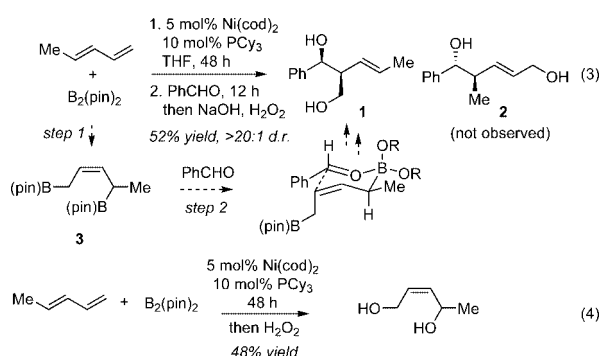
^a Determined by analysis of unpurified reaction. ^b Isolated yield of purified material. ^c Run using 10 mol % Ni(cod)₂, 10 mol % PCy₃, and a reaction time of 14 h. ^d Run using 10 mol % Ni(cod)₂, 10 mol % P(OEt)₃. With PCy₃ this reaction provides 10% yield. Purification was aided by acetylation.

of 0.2 M. With these conditions, benzaldehyde, *trans*-1,3-pentadiene, and B₂(pin)₂ were effectively coupled and, after oxidative workup, the allylic alcohol product was obtained in good yield and stereoselectivity (Table 1, entry 1).

A number of other aldehydes and dienes participate in the stereoselective diboron-promoted diene-aldehyde coupling. As

depicted in Table 1, aromatic aldehydes tend to be effective substrates with $B_2(\text{pin})_2$ and *trans*-piperylene (Table 1, entries 1–5). With the more encumbered 3-methylpentadiene (entries 6, 7) a versatile trisubstituted alkene was furnished; within the limits of detection, this product was obtained as a single stereoisomer with respect to the stereocenters and the alkene. With butadiene (entry 8) reaction yields suffered, even with further optimization of reaction conditions. In contrast to butadiene, isoprene (entry 9) reacted with comparable efficiency as compared to 1,3-pentadiene and furnished a single alkene stereoisomer as determined by ^1H NMR analysis of the oxidation product. With this substrate, the use of $\text{P}(\text{OEt})_3$ as the ligand was critical—with PCy_3 , significant amounts of a double allylation product, incorporating 2 equiv of the aldehyde, were obtained. Entries 10 and 11 document that the reaction is not necessarily limited to aromatic aldehydes; both saturated and α,β -unsaturated aldehydes engaged in the reaction, although yields were diminished with these substrates (entries 10, 11). Lastly, entry 12 shows that with *cis*-1,3-pentadiene the same stereoisomer was favored as when the *trans* diene was employed (cf. entry 1). Here, it merits mention that when the *cis* diene was subjected to the catalyst, in the absence of the other reactants, rapid *cis/trans* isomerization resulted (data not shown). Thus, it is plausible that diene isomerization occurred during the course of the reaction, and the *trans* alkene was more rapidly incorporated into the product.

To probe features of the mechanism that might be important for further reaction design, exploratory experiments were carried out. When *trans*-1,3-pentadiene and $B_2(\text{pin})_2$ were allowed to react with the catalyst for 48 h, prior to the addition of benzaldehyde, addition product **1** was obtained (eq 3; with 6 h reaction time for the first step, a mixture of **1** and **2** resulted). This addition product is regioisomeric with respect to the products in Table 1 and appears most likely to result from sequential Ni-catalyzed 1,4 diene diboration to give **3**, followed by selective aldehyde allylation (see eq 3). This conjecture was supported by the outcome in eq 4.¹⁴ The fact that the three-component reaction in Table 1 takes a different course than the process in eq 3 suggests that a sequential diene diboration followed by aldehyde allylation does not operate in Table 1; a more likely mechanism is related to that in eq 2.



In conclusion, we have demonstrated that diboron reagents can be used to facilitate stereoselective intermolecular coupling of dienes and aldehydes. The reaction products are particularly well suited for the construction of polyketide natural products and other useful chiral materials. Studies in asymmetric catalysis and in alternate transformations of the allyl boron product are underway.

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Supporting Information Available: Characterization and procedures. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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