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Regio- and Stereoselective Ni-Catalyzed 1,4-Hydroboration of 1,3-Dienes: Access to Stereodefined (*Z*)-Allylboron Reagents and Derived Allylic Alcohols

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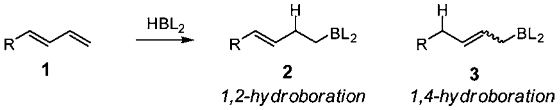
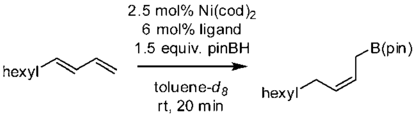
Since its first demonstration by Manning and Noth,[1] catalytic hydroboration has become a powerful tool for organic synthesis.[2] While this reaction is often applied to the transformation of alkenes and alkynes, the hydroboration of other hydrocarbon substrates such as dienes,[3] allenes,[4] and enynes[5] remains relatively unexplored. Selective reaction of diene substrates, in particular, is remarkably useful; these reactions convert simple hydrocarbon building blocks into alkene-containing organoboranes, compounds which are versatile intermediates in organic synthesis.[6] In this regard, only a few examples of catalytic diene hydroboration have been described with none able to effectively convert terminally substituted dienes such as **1** to allylboronates **3**. Both Ni(II)/dppe[3a] and Rh(I)/dppe[3c] were found to catalyze the hydroboration of dienes and, similar to the noncatalyzed reaction with 9-BBN,[7] furnish the 1,2-addition product (**2**, Scheme 1) selectively. Suzuki and Miyaura found that 1,4-hydroboration can be accomplished with Pd and Rh catalysis. This is an excellent reaction with 2-substituted and 2,3-disubstituted butadienes, but for terminally substituted dienes is limited to cyclic substrates (i.e., cyclohexadiene).[3b] Recently, Ritter described an iron catalyst that exhibits remarkable selectivity in the 1,4-hydroboration of 2-substituted dienes.[3d] This is a powerful method for the regio- and stereoselective synthesis of many useful allyl boronates, but it is less general for terminally substituted diene substrates that lack substitution at the 2-position.[8] In this report, we describe a catalytic 1,4-hydroboration of 1-substituted dienes that is highly regio- and stereoselective and is an effective complement to the above-described methods. Significantly, this reaction provides synthetically useful allylboronates in an operationally convenient fashion and, upon oxidation, it delivers stereodefined substituted allylic alcohols which are often difficult to access through single-step synthesis routes.[9]

Scheme 1

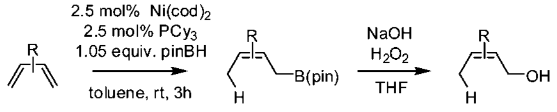


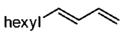
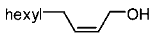
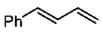
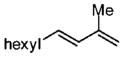
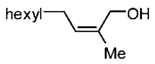
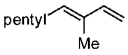
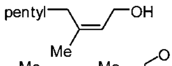
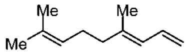
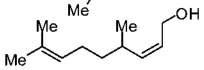
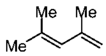
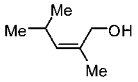
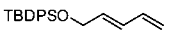
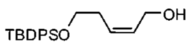
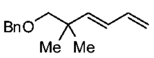
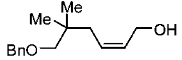
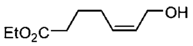
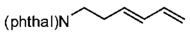
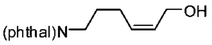
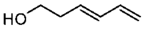
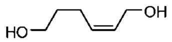
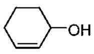
Scheme 2



ligand	% conv
none	<5
PCy$_3$	>95
P(NMe$_2$)$_3$	>95
PPh$_3$	30
dppb (2.5%)	<5

Table 1. Ni-Catalyzed 1,4-Hydroboration of Simple 1,3-Dienes[a]



entry	substrate	product	yield (%)[b]
1			85
2			91[c]
3			93
4			81
5			29[d]
6			63[e]
7			56
8			89
9			81[f]
10			61[f]
11			72[g]
12			60

[a] Reactions conducted at [substrate] = 0.25 M and oxidized with 30% H_2O_2 and 3 M NaOH. [b] Isolated yield of purified material. Values are an average of two experiments. [c] Catalyst Ni(cod)$_2$ (1 mol %) and PCy$_3$ (1 mol %) employed for the experiment. [d] Reaction 12 h at 60 °C. Product isolated with an equimolar quantity of 4,8-dimethyl-3,7-nonadien-2-ol. [e] Reaction for 12 h at 25 °C. [f] Oxidation with buffered (pH = 7) H_2O_2. [g] pinBH (2.1 equiv) employed.

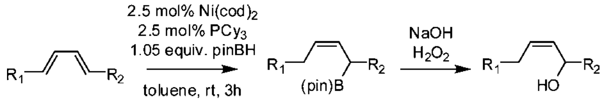
During our studies on the Pt-catalyzed enantioselective 1,4-diboration of dienes,[10] we considered that a borane, used in place of $B_2(pin)_2$, might deliver substituted allylboronates as the reaction product. An initial survey examined the reaction of 1,3-decadiene and pinacolborane at room temperature (Scheme 2). While the Pt-based catalysts were ineffective (as were Pd-based catalysts), 2.5 mol % Ni(cod)$_2$ combined with PCy$_3$ provides a particularly effective catalyst that efficiently converts 1,3-decadiene to the primary *(Z)*-allylic boronate ester in just 20 min.[11] Subsequent to this finding, a survey of the substrate scope was undertaken to address parameters that might influence the reaction. Several conclusions can be drawn from these experiments (Table 1). First, substrates with aromatic substituents were found to react equally as well as substrates containing simple alkyl groups (entries 1 and 2). Second, multiply substituted dienes react with high levels of stereocontrol (entries 3−6) and can provide products with difficult-to-access substitution patterns. Third, as suggested by the product alkene configuration, the reactive diene conformer is likely the *S-cis* arrangement and, accordingly, substrates less able to adopt

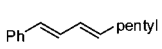
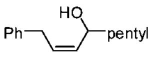
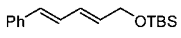
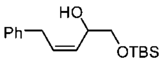
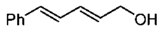
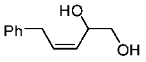
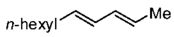
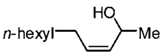
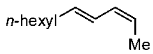
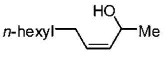
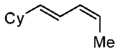
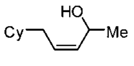
10.1021/ja910750b

this conformation are less reactive. For example, the *S*-cis conformer for entry 5 suffers an A(1,3) interaction and this substrate requires higher temperature (60 °C) for reaction; the more hindered example in entry 6 possesses offsetting A(1,3) interactions in the *S-cis* and *S-trans* rotamers and this reaction proceeds efficiently at room temperature. Lastly, a variety of synthetically common functional groups are tolerated. For instance, the reaction tolerates the presence of silyl ethers, benzyl ethers, pthalimides, esters and unprotected alcohols (entries 7−11).

The Ni-catalyzed diene hydroboration is sufficiently sensitive to diene substituents that internal dienes react in a highly regioselective fashion. As revealed by the oxidation products in Table 2, borylation occurs primarily at the less hindered carbon and, notably, the regiocontrol is high even when the required discrimination is between a methyl and an *n*-alkyl group (entry 4). Also of note, high stereo- and regioselection are obtained even when mixtures of diene stereoisomers are employed in the reaction (entries 5 and 6).

Table 2. Ni-Catalyzed 1,4-Hydroboration of Functionalized Dienes[a]

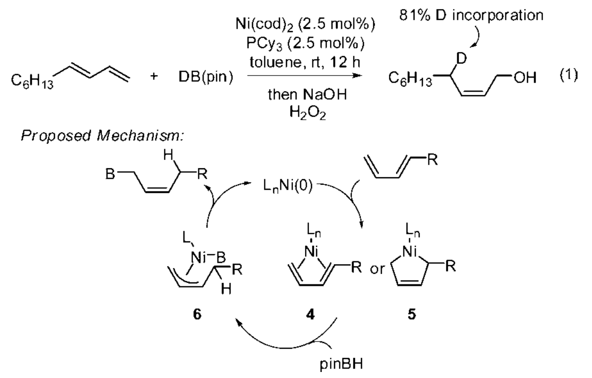


entry	substrate	product	regioselection	yield (%)[b]
1			10:1	84[c]
2			>20:1	91[d]
3			>20:1	54[d,e]
4			5:1	61[c]
5	 10:1 *E,Z*:*E,E*		>20:1	82[c]
6	 4:1 *E,Z*:*E,E*		>20:1	83[c]

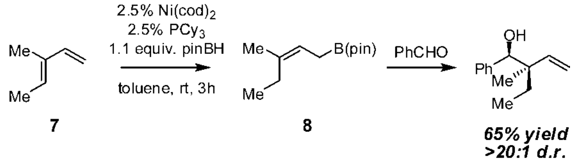
[a] Reactions conducted at [substrate] = 0.25 M and oxidized with 30% H_2O_2 and 3 M NaOH. [b] Isolated yield. Values are an average of two experiments. [c] Reaction for 12 h. [d] $Ni(cod)_2$ (1 mol %) and PCy_3 (1 mol %) employed for the experiment. [e] pinBH (2.1 equiv) employed.

To probe mechanistic features, the hydroboration of 1,3-decadiene was conducted with DB(pin) and the oxidation product analyzed spectroscopically (Scheme 3, eq 1). The deuterium atom was observed only at the C4 site in the product. This outcome, combined with the observations that the hydroboration reaction is ineffective with styrene and that an effective reaction appears to require access to the *S-cis* diene conformation, suggests that this process may proceed through a mechanism such as that depicted in Scheme 3. Initial association of Ni(0) and the diene is anticipated to furnish either η4-diene complex **4** or nickelacycle **5**. While coordination of an $L_2Ni(0)$ fragment to butadiene has been shown to result in the former structure,[12] the later bonding mode is observed in the reaction of heterobutadienes with Ni(0)[13] and was proposed to account for the Ni-catalyzed coupling of 1,3-dienes and organoboronates.[14] Subsequent reaction with HB(pin) furnishes the least hindered π-allyl complex **6** which provides the product.

Scheme 3



Scheme 4



In addition to its utility as a method for allylic alcohol synthesis, the diene hydroboration reaction provides convenient access to allylboron reagents that would be difficult to prepare otherwise. For example, as depicted in Scheme 4, hydroboration of commercially available 3-methyl-1,3-pentadiene (**7**) provides allylboronate **8**. As might be expected, addition of benzaldehyde to the unquenched hydroboration mixture furnishes the quaternary center-containing allylation product in a highly stereoselective fashion and in good yield. Further development of this reaction and study of its mechanism are in progress.

Acknowledgment. Support provided by the NIGMS (R01 GM-64451) and the NSF (DBI-0619576; BC Mass Spec Center).

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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(11) For Ni-catalyzed hydroboration of alkynes, see: (a) Gridnev, I. D.; Miyaura, N.; Suzuki, A. *Organometallics* **1993**, *12*, 589. For a review of Ni-catalyzed reactions of dienes, see: (b) Kimura, M.; Tamaru, Y. In *Modern Organonickel Chemistry*; Tamaru, Y., Ed.; Wiley-VCH: Weinheim, Germany, 2005; pp 137−170.
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JA910750B