

Published in final edited form as:

J Am Chem Soc. 2010 March 3; 132(8): 2534–2535. doi:10.1021/ja910750b.

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

Robert J. Ely and James P. Morken*

Department of Chemistry, Merkert Chemistry Center, Boston College, Chestnut Hill, MA 02467

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 enynes⁵ 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)/dpe^{3a} and Rh(I)/dpe^{3c} were found to catalyze the hydroboration of dienes and, similar to the non-catalyzed reaction with 9-BBN,⁷ furnish the 1,2-addition product (**2**; Scheme 1) selectively. Suzuki and Miyaoura found that 1,4-hydroboration product 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

During our studies on the Pt-catalyzed enantioselective 1,4-diboration of dienes,¹⁰ we considered that a borane, used in place of B₂(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 PCy₃ provides a particularly effective catalyst that efficiently converts 1,3-decadiene to the primary (*Z*)-allylic boronate ester in just 20 minutes.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

* morken@bc.edu .

 Supporting Information Available: Characterization and procedures. This information is available free of charge through the internet at <http://pubs.acs.org>.

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 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 off-setting 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, phthalimides, 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 exclusively 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).

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 η^4 -diene complex **4** or nickelacycle **5**. While coordination of an L₂Ni(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.

In addition to its utility as a method for allylic alcohol synthesis, the diene hydroboration reaction provides convenient access to allylboron reagents which 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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

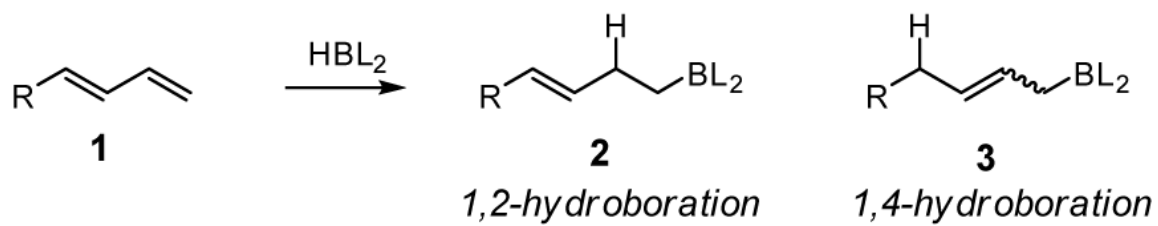
Acknowledgments

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

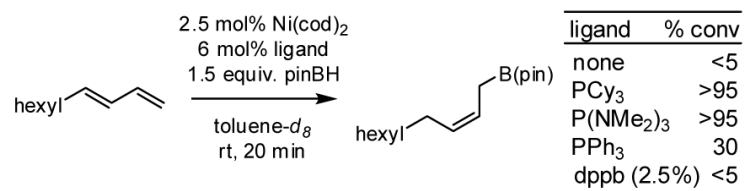
References

- (1). Männig D, Nöth H. *Angew. Chem. Int. Ed. Engl* 1985;24:878.
- (2)(a). Reviews: Crudden CM, Edwards D. *Eur. J. Org. Chem* 2003:4695. (b) Beletskaya I, Pelter A. *Tetrahedron* 1997;53:4957. (c) Burgess K, Ohlmeyer MJ. *Chem. Rev* 1991;91:1179.
- (3)(a). Zaidlewicz M, Meller J. *Tetrahedron Lett* 1997;38:7279. (b) Satoh M, Nomoto Y, Miyaura N, Suzuki A. *Tetrahedron Lett* 1989;30:3789. (c) Matsumoto Y, Hayashi T. *Tetrahedron Lett*

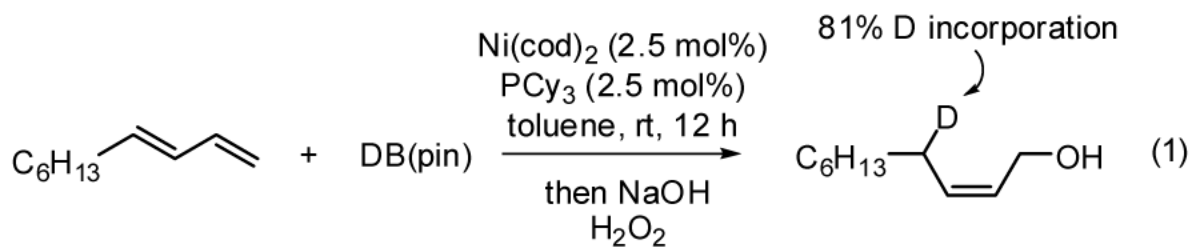
- 1991;32:3387. (d) Wu JY, Moreau B, Ritter T. *J. Am. Chem. Soc.* 2009;131:12915. [PubMed: 19702262]
- (4). Yamamoto Y, Fujikawa R, Yamada A, Miyaura N. *Chem. Lett.* 1999;1069.
- (5). Matsumoto Y, Naito M, Hayashi T. *Organometallics* 1992;11:2732.
- (6). For an excellent review of the allylboration reaction, see: Lachance, H.; Hall, DG. *Organic Reactions*. Denmark, SE., editor. Vol. Vol. 73. Wiley; New York: 2009.
- (7). Brown HC, Liotta R, Kramer GW. *J. Org. Chem.* 1978;43:1058.
- (8). Cyclohexadiene and nopadiene react well whereas both 1,2- and 1,4 hydroboration occur with 1,3-decadiene. See supporting info, ref. ^{3d}.
- (9). For a recent synthesis of (*Z*) allylic alcohols along with a comprehensive survey of other methods, see: Kerrigan MH, Jeon S-J, Chen YK, Salvi L, Carroll PJ, Walsh PJ. *J. Am. Chem. Soc.* 2009;131:8434. [PubMed: 19476375]
- (10). Burks HE, Kliman LT, Morken JP. *J. Am. Chem. Soc.* 2009;131:9134. [PubMed: 19505078]
- (11)(a). For Ni-catalyzed hydroboration of alkynes, see: Gridnev ID, Miyaura N, Suzuki A. *Organometallics* 1993;12:589. For a review of Ni-catalyzed reactions of dienes, see: (b) Kimura, M.; Tamaru, Y. *Modern Organonickel Chemistry*. Tamaru, Y., editor. Wiley-VCH; Weinheim, Germany: 2005. p. 137-170.
- (12). Benn R, Betz P, Goddard R, Jolly PW, Kokel N, Kruger C, Topalovic I. *Z. Naturforsch.* 1991;46:1395.
- (13). Karsch HH, Leithe AW, Reisky M, Witt E. *Organometallics* 1999;18:90.
- (14). Shirakawa E, Takahashi G, Tsuchimoto T, Kawakami Y. *Chem Commun* 2002:2210.



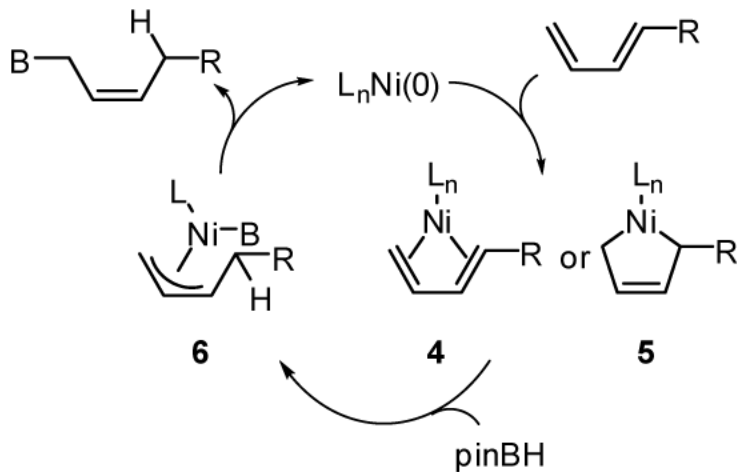
Scheme 1.



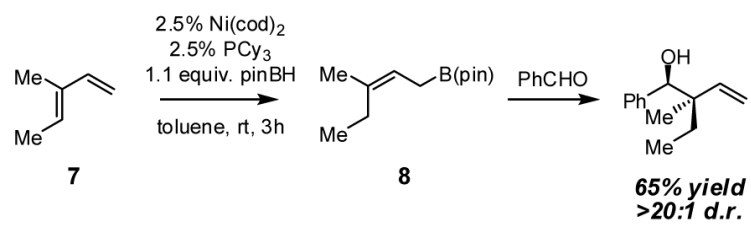
Scheme 2.



Proposed Mechanism:



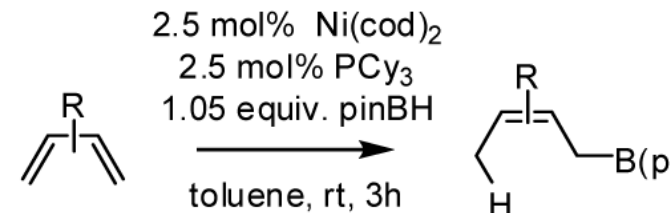
Scheme 3.

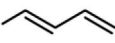
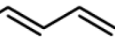
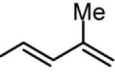


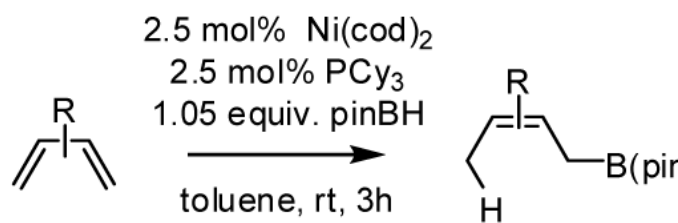
Scheme 4.

Table 1

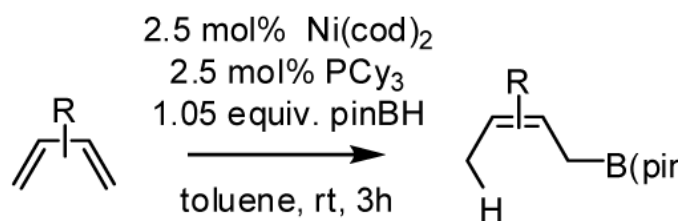
Ni-Catalyzed 1,4-Hydroboration of Simple 1,3-Dienes^a



| entry | substrate |
|-------|---|
| 1 | hexyl  |
| 2 | Ph  |
| 3 | hexyl  |

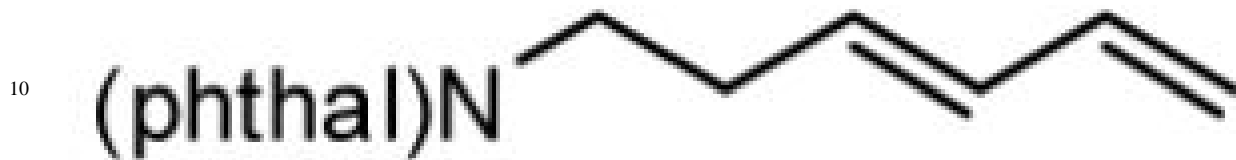


| entry | substrate |
|-------|-----------|
| 4 | |
| 5 | |
| 6 | |
| 7 | |
| 8 | |



entry

substrate





entry

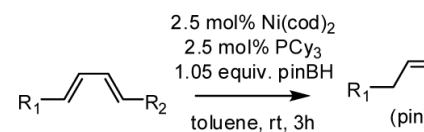
substrate

12



- (a) Reactions conducted at [substrate]=0.25M and oxidized with 30% H₂O₂ and 3M NaOH.
- (b) Isolated yield of purified material. Values are an average of two experiments.
- (c) 1 mol% catalyst Ni(cod)₂ and 1 mol% PCy₃ employed for this 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) H₂O₂.
- (g) 2.1 equiv. pinBH employed.

Table 2

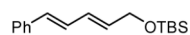
Ni-Catalyzed 1,4-Hydroboration of Functionalized Dienes^a

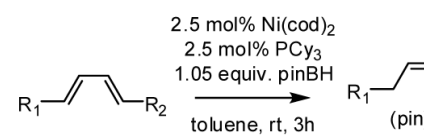
| entry | substrate |
|-------|-----------|
|-------|-----------|

1



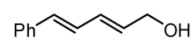
2



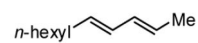


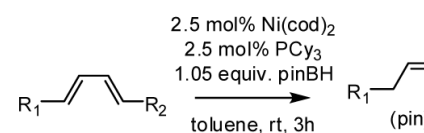
| entry | substrate |
|-------|-----------|
|-------|-----------|

3



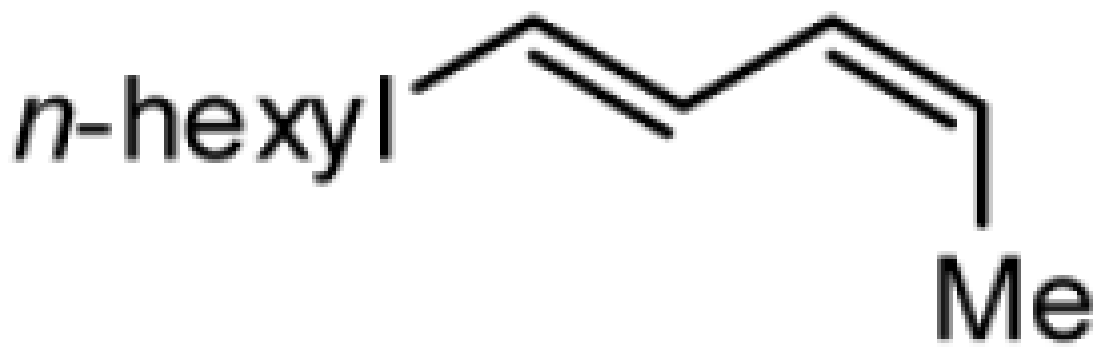
4



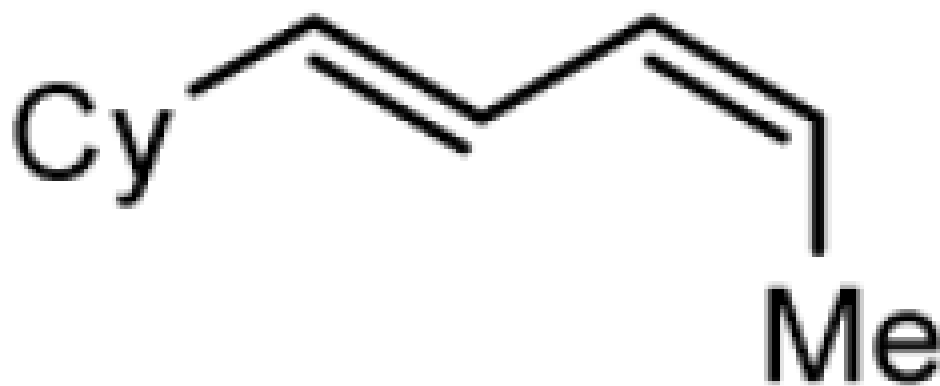


entry

substrate



10:1 *E*, *Z*:*E*, *E*



4:1 *E*, *Z*:*E*, *E*

^(a) See footnote a, Table 1.

^(b) Isolated yield. Values are an average of two experiments.

(c) Reaction for 12 h.

(d) 1 mol% Ni(cod)₂ and 1 mol% PCy₃ employed for this experiment.

(e) 2.1 equivalents pinBH employed.