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Ni(0)-Catalyzed 1,4-Selective Diboration of Conjugated Dienes

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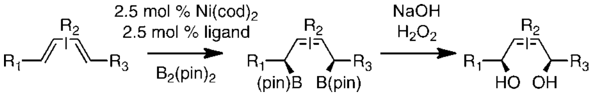
ABSTRACT



A catalytic stereoselective 1,4-diboration of conjugated dienes with $B_2(pin)_2$ was accomplished with $Ni(cod)_2$ and PCy_3 as the catalyst. This reaction broadens the substrate scope of current methods for catalytic diene diboration by including internal and sterically hindered dienes, and it proceeds efficiently at low catalyst loadings. The intermediate allylboronate was oxidized to the stereodefined allylic 1,4-diol.

The catalytic diboration of unactivated unsaturated hydrocarbons can be accomplished with many transition metals including Pt, Pd, Rh, Cu, Au, and Ag.[1] The 1,4-diboration of 1,3-dienes, in particular, allows for the transformation of simple hydrocarbons to synthetically useful allylic diboronate intermediates.[2] Recently, we developed the first catalytic enantioselective version of this type of diboration. This reaction employs a platinum catalyst in conjunction with chiral TADDOL-derived phosphonite ligands and delivers the 1,4-diborylated product in high enantiomeric excess.[3] The resultant bis(boronate) esters can be utilized in carbonyl allylation and, through appropriate oxidation strategies, can be converted to butenolides and 2-alkene-1,4-diols. A current limitation of both the enantioselective and the nonenantioselective processes is that they have only been demonstrated with terminal dienes or cyclic dienes and require the use of moderately expensive catalyst precursors. In this publication, we address these issues and describe a convenient, inexpensive catalytic diene diboration that operates on an expanded substrate scope.

During development of the Ni-catalyzed borylative coupling of dienes and aldehydes,[4] we found that $Ni(cod)_2$, in the presence of tricyclohexylphosphine, promotes the 1,4-diboration of a 1,3-diene by bis(pinacolato)diboron ($B_2(pin)_2$). The fact that the reaction delivered a single regio- and stereoisomer of product and that it employed a simple inexpensive catalyst and reagents prompted us to further study this transformation. Our investigation of the reaction began with a brief analysis of ligand effects in the reaction. As depicted in Scheme 1, the diboration of *trans*-1,3-decadiene was examined in the presence of 2.5 mol % $Ni(cod)_2$ and a near-stoichiometric quantity of $B_2(pin)_2$. This survey revealed that strongly donating monodentate phosphine ligands, including both PCy_3 and hexamethylphosphorous triamide (HMPT),[5] are highly effective in the reaction and after only 15 min catalyze complete conversion to the 1,4-bis(boronate) product; oxidation delivered the (*Z*)-2-alkene-1,4-diol in good yield.

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[1] (a) For a review of Pt- and Rh-catalyzed diboration: Norman, N. C.; Marder, T. B. *Top. Catal.* **1998**, *5*, 63. For Pd: (b) Yang, F. Y.; Cheng, H. *J. Am. Chem. Soc.* **2001**, *123*, 761. (c) Woodward, A. R.; Burks, H. E.; Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 16328. (d) Lillo, V.; Mas-Marzá, E.; Segarra, A.; Carbó, J. J.; Bo, C.; Peris, E.; Fernandez, E. *Chem. Commun.* **2007**, 3380. For Cu: (e) Lillo, V.; Fructos, M. R.; Braga, A. A. C.; Maseras, F.; Reguejo, M. M.; Pérez, P. J.; Fernandez, E. *Chem.—Eur. J.* **2007**, *13*, 2614. (f) Lee, Y.; Jang, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 16630. For Au: (g) Baker, R. T.; Nguyen, P.; Marder, T. B.; Westcott, S. A. *Angew. Chem., Int. Ed.* **1995**, *34*, 1336. (h) Corberan, R.; Ramirez, J.; Sanau, M.; Peris, E.; Fernandez, E. *Tetrahedron: Asymmetry* **2006**, *17*, 1759. (i) Ramirez, J.; Sanau, M.; Fernandez, E. *Angew. Chem., Int. Ed.* **2008**, *47*, 5194. For Ag: (j) Corberan, R.; Ramirez, J.; Poyatos, M.; Peris, E.; Fernandez, E. *Chem. Commun.* **2005**, 3056.

[2] (a) Ishiyama, T.; Yamamoto, M.; Miyaura, N. *Chem. Commun.* **1996**, 2073. (b) Clegg, W.; Thorsten, J.; Marder, T. B.; Norman, N. C.; Orpen, A. G.; Peakman, T. M.; Quayle, M. J.; Rice, C. R.; Scott, A. J. *J. Chem. Soc., Dalton Trans.* **1998**, 1431.

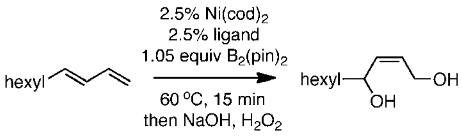
[3] Burks, H. E.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 9134.

[4] Cho, H. Y.; Morken., J. P. *J. Am. Chem. Soc.* **2008**, *130*, 16140.

[5] For an excellent description of the electronic properties of HMPT, see: Moloy, K. G.; Petersen, J. L. *J. Am. Chem. Soc.* **1995**, *117*, 7696.

10.1021/ol101797f

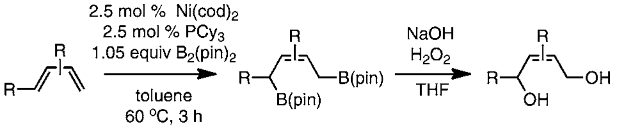
Scheme 1. Effect of Ligands on Ni-Catalyzed Diene Diboration

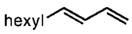
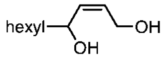
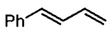
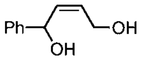
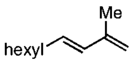
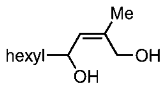
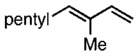
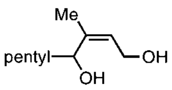
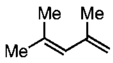
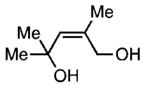
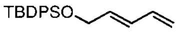
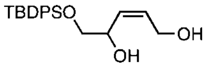
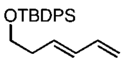
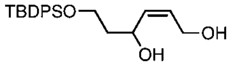
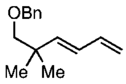
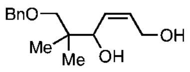
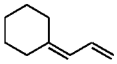
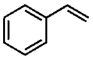


ligand	yield (%)
none	<5
PCy$_3$	83
P(NMe$_2$)$_3$	83
PPh$_3$	8
P(OEt)3	<5

The substrate scope of the Ni/PCy$_3$-catalyzed diboration reaction was investigated with a series of conjugated diene substrates (Table 1). To ensure complete conversion, the reactions were generally allowed to proceed for 3 h. As represented in entries 1 and 2, substrates with aromatic and alkyl substitution were converted to the derived 1,4-diol product in high yield and stereoselectivity. Multiply substituted dienes react to provide trisubstituted alkenes with high levels of olefin stereocontrol (entries 3−5). Remarkably, the highly substituted diene in entry 5 was efficiently converted to the derived 1,4-diol in good yield. Notably, silyl ethers and more Lewis basic benzyl ethers are tolerated in the reaction (entries 7 and 8), although an allylic silyl ether was incompatible with the reaction conditions (entry 6). The refractory nature of the allylic ether may arise from the known proclivity for allyl ethers to furnish π-allyl complexes in the presence of Ni(0) complexes.[6] Impressively and in contrast to Pt-catalyzed diboration, there is no decrease in regioselectivity when a quaternary carbon is adjacent to the diene; the 1,4-diol is obtained in high yield and high regioselectivity (entry 8; a 1:1 mixture of 1,4- and 1,2-products is observed in the Pt-catalyzed reaction).[3]

Table 1. Ni-Catalyzed 1,4-Diboration of Conjugated Dienes[a]



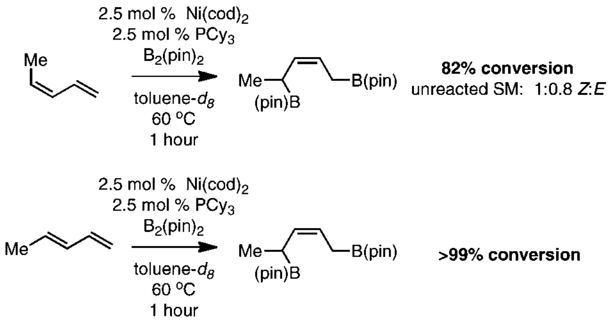
entry	substrate	product	yield (%)[b]
1			84
2			84[c]
3			88
4			94
5			71
6			-
7			95
8			88
9		no reaction	-
10		no reaction	-

[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] 1 mol % catalyst Ni(cod)$_2$ and 1 mol % PCy$_3$ employed for this experiment.

Similar to Pt-catalyzed diboration, only dienes able to adopt the *S*-*cis* conformation participate in 1,4-diboration.[3] As seen in entry 9 (Table 1), an A(1,3) interaction destabilizes the *S*-*cis* conformation of the substrate, and this is likely the reason the reaction does not proceed. However, the more hindered diene in entry 5 contains offsetting A(1,3) interactions in the *S*-*cis* and *S*-*trans* conformers, and this reaction proceeds efficiently. Unlike Pt-catalyzed diboration,[7] however, simple alkenes do not react at all under these conditions (entry 10).

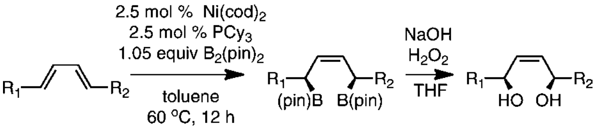
To further test the hypothesis that the *S*-*cis* conformation is the reactive one, diborations of *cis*-and *trans*-1,3-pentadiene were compared by ^{1}H NMR as the reaction progressed (Scheme 2). After 1 h of reaction, *trans*-pentadiene was completely converted to the derived 1,4-bis(boronate) ester. In contrast, the reaction of *cis*-pentadiene was incomplete (82% conversion). Further, the remaining starting material was found to consist of a roughly equal mixture of the *trans* and *cis* isomer. Thus while *cis*-dienes can participate in the 1,4-diboration, they appear to do so at a slower rate and the reactive pathway may involve prior isomerization to the *trans* diene isomer.

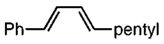
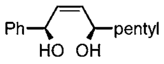
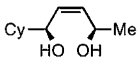
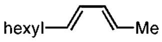
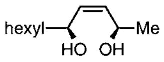
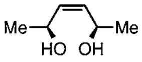
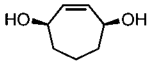
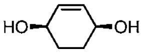
Scheme 2. Comparison of the Diboration of *cis*- and *trans*-1,3-Pentadiene



Recent examples of catalytic diene diboration have surrounded terminal dienes and cyclic substrates; internal dienes have not been studied. To learn whether Ni catalysts might effectively expand the scope of diene diboration, a series of internal dienes was examined under the above-described reaction conditions. Preliminary experiments suggested that longer reaction times are required, but with this modification, internal acyclic dienes were found to be willing participants in the diboration (Table 2).

Table 2. Ni-Catalyzed 1,4-Diboration of Internal Dienes[a]



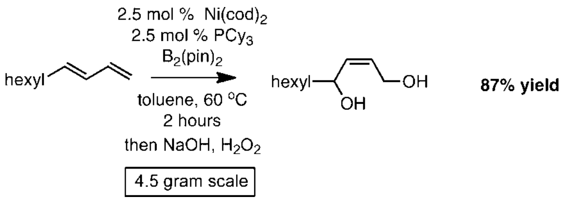
entry	substrate	product	yield (%)[b]
1			77
2			66
3			74
4			72
5			44
6			47

[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.

Generally, the internal dienes react efficiently and provide the internal *Z*-*syn*-1,4-diol after oxidation. As depicted in Table 2, both aryl and alkyl substituents are tolerated (entries 1−4). Cyclic dienes also participate in the Ni-catalyzed diboration, but with somewhat inferior yields (entries 5 and 6).

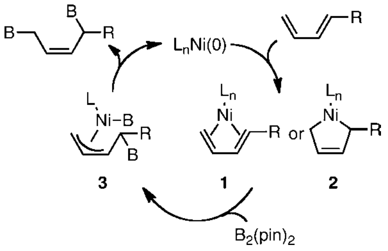
To examine the synthetic utility of the subsequent diboration, a large scale Ni-catalyzed diboration of 1,3-decadiene was examined (Scheme 3). Noteworthy is that this substrate and other terminal dienes are readily prepared on multigram scale by the Wittig methylenation of enals. In the case of 1,3-decadiene, it was found that on 4.5 g scale the Ni-catalyzed reaction proceeded effectively and delivered the derived 1,4-diol in 87% yield. It should be noted that purification of the product, on large scale, is greatly aided by subjection of the crude reaction mixture to 3 equiv of $NaIO_4$; this effectively removes pinacol which is the only byproduct of this reaction.

Scheme 3. Large Scale Diboration of 1,3-Decadiene



The commonly accepted mechanism for diboration of dienes with group 10 metals involves oxidative addition of the boron species to the metal followed by coordination of the alkene. Subsequent insertion into the M-B bond with concomitant π-allyl formation, followed by reductive elimination provides the product.[2] However, the observation that styrene is unreactive suggests that this mechanism may not be operative.[8] An alternate possibility involves initial association of Ni(0) with the diene to form complex **1** or **2** (Scheme 4).[9] Subsequent reaction with $B_2(pin)_2$ would provide the least hindered Ni−C bond that provides the product after reductive elimination. Current studies are aimed at elucidating these features of this reaction.

Scheme 4. Proposed Catalytic Cycle for Diene Diboration



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(6) For early examples: (a) Eisch, J. J.; Im, K. R. *J. Organomet. Chem.* **1977**, *139*, C45. (b) Hayashi, T.; Konishi, M.; Yokota, K.; Humada, M. *Chem. Commun.* **1981**, 313. (c) Yamamoto, T.; Ishizu, J.; Yamamoto, A. *J. Am. Chem. Soc.* **1981**, *103*, 6863.

(7) Pt-catalyzed alkene diboration: (a) Ishiyama, T.; Yamamoto, M.; Miyaura, N. *Chem. Commun.* **1997**, 689. (b) Iverson, C. N.; Smith, M. R., III. *Organometallics* **1997**, *16*, 2757. (c) Marder, T. B.; Norman, N. C.; Rice, C. R. *Tetrahedron Lett.* **1998**, *39*, 155. (d) Mann, G.; John, K. D.; Baker, R. T. *Org. Lett.* **2000**, *2*, 2105. (e) Lillo, V.; Mata, J.; Ramirez, J.; Peris, E.; Fernandez, E. *Organometallics* **2006**, *25*, 5829.

(8) Similarly, reaction of 2-vinylnaphthalene occurs with <25% conversion to a mixture of compounds, none of which appear to be a diboration product.

(9) (a) Benn, R.; Betz, P.; Goddard, R.; Jolly, P. W.; Kokel, N.; Kruger, C.; Topalovic, I. *Z. Naturforsch.* **1991**, *46*, 1395. (b) Karsch, H. H.; Leithe, A. W.; Reisky, M.; Witt, E. *Organometallics.* **1999**, *18*, 90. (c) Shirakawa, E.; Takahashi, G.; Tsuchimoto, T.; Kawakami, Y. *Chem. Commun.* **2002**, 2210.

In summary, we have developed a novel Ni-catalyzed 1,4-diboration of conjugated dienes. This system expands the scope of dienes to provide internal 1,4-bis(boronate)esters, provides more reliable 1,4-selectivity with sterically hindered dienes, and requires short reaction times. Further studies on the mechanism and synthetic utility are underway in our laboratory.

Acknowledgment. This work was supported by the National Institutes of Health (GM 64451).

Supporting Information Available: Complete experimental procedures and characterization data (^{1}H and ^{13}C NMR, IR, and mass spectrometry). This material is available free of charge via the Internet at http://pubs.acs.org.

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