

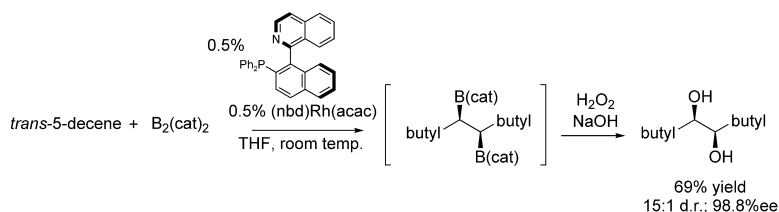
Communication

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Rhodium-Catalyzed Enantioselective Diboration of Simple Alkenes

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Catalytic enantioselective reactions that convert simple inexpensive alkenes to functionalized chiral products hold an important place in the production of fine chemicals, pharmaceuticals, and materials.¹ Efforts to develop such processes have been intense and have resulted in the introduction of a number of catalytic asymmetric alkene transformations. We expected that it might be possible to introduce a variety of such processes simultaneously by developing a catalytic asymmetric alkene dimetalation reaction (Scheme 1). This process would provide a reactive 1,2-dimetalated intermediate that could be useful for the synthesis of a variety of optically active 1,2-difunctional compounds. In this report, we describe the first example of a catalytic enantioselective diboration reaction which operates on simple alkene substrates. We also describe initial experiments aimed at converting these compounds to optically active synthetic building blocks.

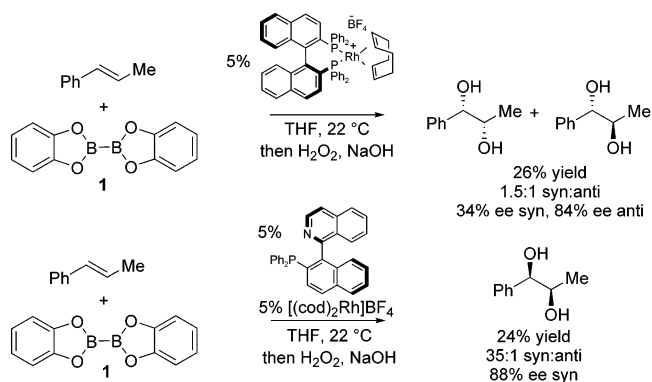
Scheme 1



A number of metal–metal bonded species have been added across unfunctionalized alkenes in a catalytic fashion; however, these processes have not been subject to asymmetric catalysis.² Due to the synthetic utility of the carbon–boron bond in organic synthesis,³ we were attracted to diboron reagents for use in enantioselective alkene dimetalation reactions.⁴ On the basis of the observations of Marder, Baker, and Westcott that Rh(I) complexes are effective for alkene diboration,^{5,6} we decided to examine several chiral group 9 transition metal complexes for the catalytic diboration of *trans*- β -methylstyrene. As shown in Scheme 2, two catalysts that exhibited enantioselection in the transformation were [(*S*)-binapRh(cod)]BF₄ and (*S*)-quinap/[(cod)₂Rh]BF₄, which are both known for the rhodium-catalyzed enantioselective hydroboration of styrenes.^{7,8} At 5 mol % catalyst loading in THF solvent at room temperature, both of these catalysts facilitated addition of bis-(catechol)diboron (1) to *trans*- β -methylstyrene, and after oxidative workup, the derived 1,2-diols were isolated with significant levels of enantioenrichment. While the catalyst with binap as the chiral ancillary ligand provided a 1.5:1 mixture of syn:anti diastereomers, the quinap-derived catalyst provided significantly higher diastereo- and enantioselection. The quinap-derived catalyst was therefore selected for further development.

Under optimized reaction conditions (increased reaction concentration and alternate Rh salt), 5 mol % of commercial (*S*)-quinap and 5 mol % of commercial (norbornadiene)Rh(acac) were complexed for 5 min and then treated with commercially available unpurified bis(catechol)diboron. After addition of substrate, the reactions were allowed to proceed for 24 h at room temperature.⁹ Upon treatment with alkaline hydrogen peroxide, the resulting 1,2-diols were isolated. Table 1 shows the outcome with a series of prochiral alkene substrates. The reaction appears to be general for *trans* alkenes and, unlike the Rh-quinap-catalyzed hydroboration

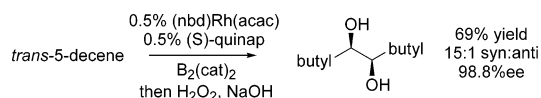
Scheme 2



reaction, does not require the presence of an aromatic group for high reactivity or enantioselectivity (entry 4). The reaction with indene (entry 6) provides the derived syn-1,2-diol in high optical purity; however, the diboration of *cis* alkenes does not appear to be as general as with the *trans* substrate geometry. Surprisingly, dihydronaphthalene and *cis*- β -methylstyrene provide the opposite configuration of product relative to indene (see entries 7 and 8). While the sole trisubstituted alkene in Table 1 reacts in a highly selective fashion, monosubstituted and 1,1-disubstituted alkenes will likely require design/use of new chiral ancillary ligand structures for effective enantiocontrol.

The level of catalyst loading (5 mol %) used in small-scale exploratory experiments might render larger scale experiments overly costly with the precious metal catalyst. To address this issue, we have explored reactions with decreased catalyst loading. As shown in Scheme 3, the diboration of *trans*-5-decene on 1-g scale proceeds in the presence of 0.5 mol % of catalyst and provides yields and levels of stereoselection similar to those described in Table 1.

Scheme 3

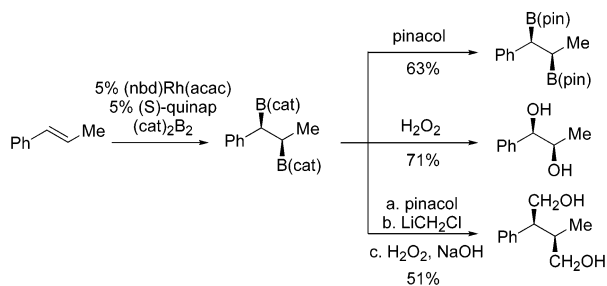


Transformation of 1,2-diboron adducts is not well-described in the literature, likely due to lack of access to these materials in a stereocontrolled fashion in the past. Our preliminary experiments (Scheme 4) indicate that the 1,2-bis(catechol) esters formed in the asymmetric diboration reaction readily undergo transesterification to the bis(pinacol) ester by direct treatment of the crude reaction mixture with pinacol. In addition to this reaction and simple oxidation to the 1,2-diol, we have also found that 1,2-diboron adducts participate in Matteson homologation through the intermediacy of the pinacol ester.¹⁰ In this reaction, the diboron intermediate is subject to chloromethyl lithium and then oxidative workup, thereby providing the derived bis(hydroxymethylation) adduct.

Table 1. Rh-Catalyzed Enantioselective Diboration/Oxidation of Simple Alkenes^a

entry	substrate	product	% yield ^b	% ee
1			71	93
2			71	>98
3			48	98
4			76	98
5			17	93
6			68	88
7			72	49
8			61	49
9			68	33
10			67	46

^a Conditions: 5 mol % of (*S*)-quinap, 5 mol % of (nbd)Rh(acac), 1.1 equiv of B₂(cat)₂, THF, room temperature, 24 h. Oxidative workup with H₂O₂. ^b Isolated yield of purified material. Generally the remainder of mass balance is unconverted starting material.

Scheme 4

In addition to the simple transformations described above, one can envision a variety of other bond constructions involving reactive

1,2-diboron intermediates. Efforts directed toward converting the diboration adducts directly to 1,2-diacids, 1,2-diamines, and other compounds are in progress and will be reported in due course. Additional improvements in catalyst productivity and efforts directed toward the inexpensive production of the commercial diboron reagent¹¹ are in progress and may bring the reaction cost down to the point where it is competitive with other methods for chemical synthesis.

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

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