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Pt-Catalyzed Enantioselective Diboration of Terminal Alkenes with $B_2(pin)_2$

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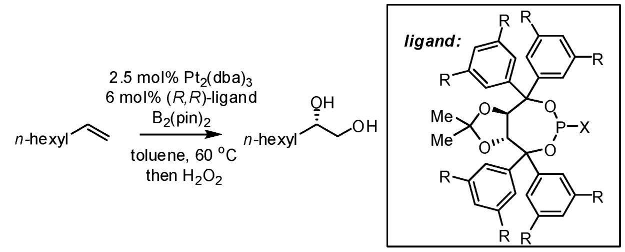
The transition-metal-catalyzed diboration is an enabling method for the conversion of simple olefins to functionally and stereochemically enriched products.[1,2] Of the substrate classes that might be considered for this reaction, terminal alkenes are among the most attractive. 1,2-Diboration of a terminal olefin provides a reactive intermediate with both primary and secondary boronate groups, and the different environments of these elements cause them to exhibit differential reactivity in subsequent transformations.[3] To employ these strategies in asymmetric synthesis, the issue of enantioselectivity in alkene diborations is critical. This has been addressed in our laboratory[4] where it was determined that enantioselective diboration could be accomplished with bis(catecholato)diboron in the presence of Rh(I) and the chiral ligand Quinap.[5] Unfortunately, this process is not only impractical with respect to reaction cost (both $B_2(cat)_2$ and the catalyst are expensive) but also suffers from the fact that low enantioselectivity is observed for most 1-alkene substrates. In this report we describe a practical and economical enantioselective alkene diboration reaction that is highly effective with terminal olefins, occurring with good yield and excellent enantioselectivity.

Recently, we described the Pt-catalyzed enantioselective 1,4-diboration of 1,3-dienes in the presence of taddol-derived phosphonite ligands; after oxidation, the net 1,4-dihydroxylation product is obtained.[6] Of interest was the observation that enantioselective 1,2-diboration occurs as a side reaction with some 1,3-diene substrates. This feature prompted us to examine the asymmetric diboration of 1-alkene substrates under the influence of platinum complexes. Initial experiments with 1-octene showed that this process can be enantioselective and that taddol-derived phosphonite and phosphoramidite ligands[7] can provide elevated levels of enantioselection (Table 1). Ligand **L2** appeared optimal and was selected for further fine-tuning. Subsequent experiments suggested that several parameters are important for obtaining the highest enantioselectivity. First, ^{31}P NMR analysis revealed that preheating $Pt_2(dba)_3$ and the phosphonite ligand at 80 °C for 30 min is required to achieve complete complexation of the metal and ligand and that the presence of $B_2(pin)_2$ aids in this complexation step; without this pretreatment, diminished enantioselectivity is observed in the diboration. Second, a ligand loading of 1.2 equiv, relative to platinum, results in optimal selectivity and yield; with 2 equiv of ligand precomplexed to Pt, only 9% yield of product is obtained.[8] Lastly, fine-tuning of the R substituent on **L2** revealed that the ethyl derivative (**L8**, Table 2) is more selective than the methyl derivative and leads to the derived 1,2-diol in 92% enantiomeric excess when combined with the above-described modifications.

Table 1. Effect of Chiral Ligand on the Catalytic Enantioselective Diboration of 1-Octene[a]



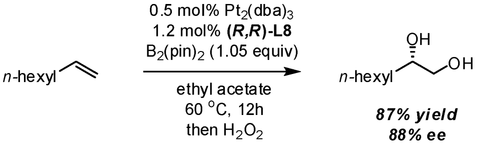
ligand	R	X	yield (%)[b]	ee (%)[c]
L1	H	Ph	24	60
L2	Me	Ph	81	83
L3	*t*-Bu	Ph	74	80
L4	H	NMe_2	35	40
L5	Me	NMe_2	77	80
L6	*t*-Bu	NMe_2	40	57
L7	Me	NMe_2	35	40

[a] Reaction carried out at 60 °C for 12 h, followed by oxidation with 30% H_2O_2 and 3 M NaOH for 3 h. [b] Percent yield of purified material. [c] Enantiopurity of the derived acetonide determined by GC analysis employing a chiral stationary phase.

As depicted in Table 2, Pt-catalyzed diboration of many 1-alkene substrates occurs in a highly enantioselective fashion. Generally, only 1.05 equiv of the diboron reagent are required and the products can be isolated in good yield. In addition to 1-octene, other aliphatic α-olefins undergo selective diboration.[9] Notably, the reaction is insensitive to the nature of the alkyl substituent with large groups (entries 5 and 6) and small groups (entry 1) equally tolerated. Also of note, substrates bearing protected oxygen functionality undergo clean diboration with excellent levels of enantioselection. Surprisingly, substrates with allylic oxygenation do not suffer from competing π-allyl chemistry as has been documented in related catalyzed reactions between diboron reagents and allylic ethers.[4b,10] *Remarkably, the catalytic diboration of allylic ethers (i.e., entry 9) only occurs in the presence of ligand* **(R,R)-L8***; in the absence of* **(R,R)-L8** *or with* PCy_3 *as the ligand, the diboration/oxidation product cannot be detected.* Also of note is that styrene reacts with useful levels of enantioselectivity; in Rh-Quinap catalyzed diboration, this substrate reacts with anomalously low selectivity (33% ee).[4a]

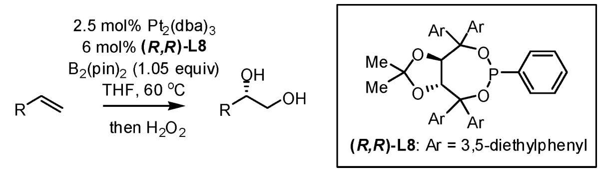
Operation of the Pt-catalyzed asymmetric diboration on a large scale would be most practical with reaction conditions that employ diminished catalyst loading and benign reaction solvent.[11] As depicted in Scheme 1, ethyl acetate can also be employed as the reaction solvent, although in this solvent the product is furnished with slightly diminished enantiomeric purity relative to THF.

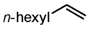
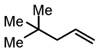
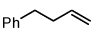
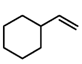
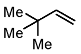
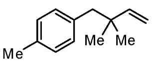
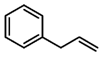
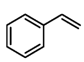
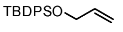
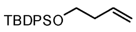
Scheme 1



10.1021/ja9047762 CCC: $40.75

Table 2. Catalytic Enantioselective Diboration of 1-Alkenes[a]



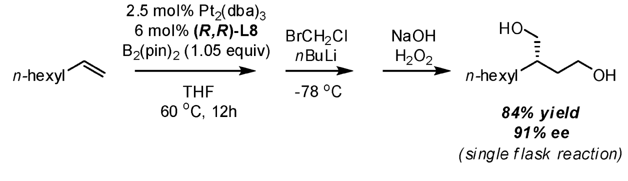
entry	substrate	yield (%)[b]	ee (%)[c]
1		83	92
2		77	94
3		80	94
4		87	94
5		46	90
6		52	87
7		86	93
8		84	86
9		93	90[d]
10		92	90

[a] Unless otherwise indicated, **(*R*,*R*)-L8** was employed with reaction at 60 °C for 12 h, followed by oxidation with 30% H_2O_2 and 3 M NaOH for 3 h. [b] Percent yield of purified material. Value is an average of two experiments. For entries 2, 5, and 10 product coelutes with pinacol. [c] Determined by GC or SFC analysis employing a chiral stationary phase. [d] Oxidation carried out with H_2O_2 in a buffer at pH = 7. Racemization by silyl transfer occurs under basic conditions.

Importantly, the catalyst loading can also be decreased to 0.5 mol % of the Pt dimer and 1.2 mol % ligand. With these conditions the reaction still occurs efficiently and in a reasonable time frame.

An attractive feature of the Pt-catalyzed asymmetric diboration is that the reaction conditions are compatible with many subsequent transformations of the chiral bis(boronate) ester and, thereby, enable single-flask transformations *without an intermediate reaction workup*. An example of this strategy is depicted in Scheme 2 where 1-octene is subjected to catalytic asymmetric diboration. After 12 h of reaction at 60 °C, the reaction mixture is cooled to −78 °C and treated with 2 equiv of $ClCH_2Li$. Under these conditions, clean methylene insertion[12] into each carbon−boron bond occurs and oxidative workup provides the derived 1,4-diol in good yield and excellent enantiomeric purity.

Scheme 2



In conclusion, we have described the first highly enantioselective asymmetric diboration of simple terminal alkenes. In addition to the oxidation and homologation reactions described here, many other transformations should be available to the diboron intermediate. Additional studies in this regard, and on further development of the catalytic reaction, 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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(9) With these conditions, *trans*-2-octene and α-methyl styrene are unreactive. Reaction of 1-octene with $B_2(cat)_2$ occurred in 17% yield and 62% ee. Lower yields in Table 2 reflect a lack of conversion; hydroboration products are not detected.

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