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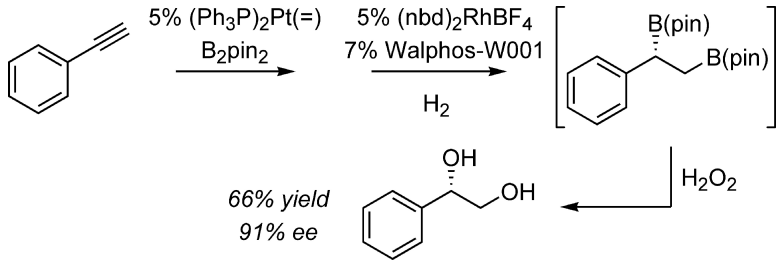

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Catalytic Enantioselective Hydrogenation of Vinyl Bis(boronates)

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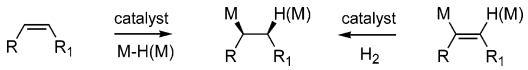
New catalytic methods for the generation of reactive enantiomerically enriched molecules are important for chemical synthesis. Of particular interest are methods that enable domino reaction sequences for the introduction of functional group complexity. In this respect, reactions that furnish reactive and stereogenic carbon−metal bonds are particularly useful for the generation of stereochemically intricate structures. While processes such as alkene hydrometalation[1] and bismetalation[2] have been developed to create such intermediates, these processes are often plagued with low substrate scope and, for hydrometalation, may provide regioisomer mixtures.[3] An alternative method for generating stereogenic carbon−metal bonds is the hydrogenation of prochiral vinylmetallic species (Scheme 1).[4] This reaction may circumvent many of the problems inherent in alkene metalation reactions, and since vinyl−metal compounds are readily available, asymmetric hydrogenation may provide an attractive complement to current methods for the synthesis of enantioenriched sp^3 hybridized organometallics. Herein, we report the first highly enantioselective hydrogenation of vinylmetallic substrates which, in this case, provides access to enantiomerically enriched alkyl 1,2-bis(boronates).[5]

Scheme 1

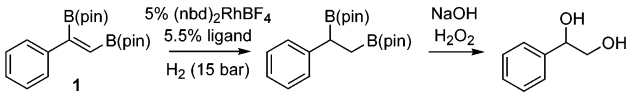


Recently, our laboratory reported the preparation of enantiomerically enriched alkyl 1,2-bis(boronates) by the catalytic asymmetric diboration of alkenes.[6] Although this reaction is highly selective with most *trans*-alkene substrates, the majority of monosubstituted olefins do not provide high asymmetric induction. Since a number of reaction sequences, such as tandem diboration/Suzuki coupling/oxidation,[7] may be enabled by the sequential transformation of sterically differentiated C−B bonds, the selective diboration of 1-alkenes is a particularly attractive goal. While current efforts are directed at solving this problem, as suggested above, an alternate approach to the product alkyl-1,2-bis(boronates) is the hydrogenation of vinyl 1,2-bis(boronates). These prochiral substrates are readily available by diboration of alkyne precursors using commercially available catalysts and reagents.[8]

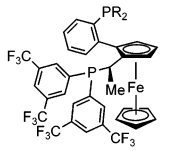
Initial experiments probed the reactivity of vinyl bis(boronates) toward group 9 hydrogenation catalysts. In these experiments, *E*-1,2-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)styrene (**1**) was subject to asymmetric hydrogenation with 5 mol % catalyst at 15 bar H_2 in dichloroethane (DCE), followed by basic peroxide oxidation. In general, it was found that rhodium complexes were superior to their iridium analogues. The most promising ligands are depicted in Table 1 wherein (*R*,*R*)-Walphos-W001[9] provided the most selective catalyst and afforded 73% ee and 82% yield in DCE. Upon examination of other solvents, it was found that toluene provides significantly higher selectivity (93% ee) with comparable yields.

Under optimized conditions, excellent yields and high enantioselectivities are obtained with an in situ generated catalyst composed of 2 mol % of rhodium salt and 4 mol % Walphos (Table 2). While Walphos-W001 ligand leads to high asymmetric induction for aromatic substrates, lower enantioselectivity is observed with aliphatic substituents on the diborylalkene. Accordingly, the family of Walphos ligands was reevaluated with aliphatic substrates

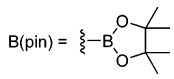
Table 1. Asymmetric Hydrogenation of Vinyl Bis(boronate) **1**



entry	ligand[a]	solvent	% yield[b]	% ee
1	Binap	DCE	61	43
2	Phanephos	DCE	50	47
3	xylyl-Binap	DCE	56	9
4	BoPhoz	DCE	58	33
5	Walphos-W001	DCE	82	73
6	Walphos-W001	THF	77	48
7	**Walphos-W001**	**toluene**	**85**	**93**
8	Walphos-W008	DCE	n.d.	32

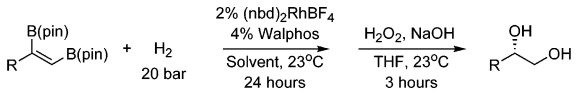


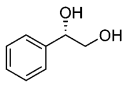
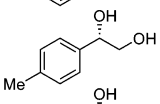
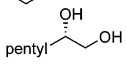
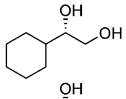
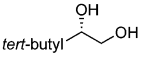
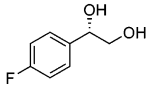
R=Ph Walphos-W001
R=Cy Walphos-W008



[a] See Supporting Information for ligand structures. [b] Isolated yield of purified material.

Table 2. Rh-Walphos-Catalyzed Asymmetric Hydrogenation of Vinyl Bis(boronates)[a]



entry	product[a]	ligand	solvent	% yield[b]	% ee[c]
1		W001	toluene	90	93
2		W001	toluene	92	86
3		W001 W008	toluene DCE	86 81	77 85
4		W008	DCE	72	89
5[d]		W008	DCE	89	93
6		W001	toluene	60	90

[a] Identity of major enantiomer determined by correlation to authentic materials. [b] Isolated yield of purified material. [c] Enantiomeric excess determined by chiral GC analysis. [d] Experiment at 30 bar H_2.

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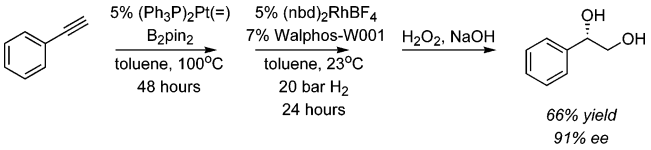
wherein it was found that Walphos-W008 in DCE solvent provided increased selectivity with these compounds.

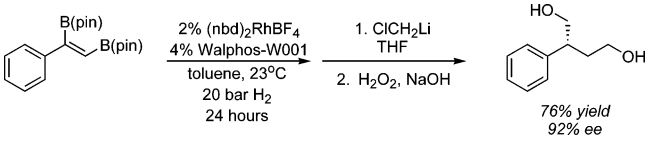
Platinum-catalyzed diboration of terminal alkynes provides ready access to 1,2-bis(boryl)alkenes which were used as substrates in Table 2.[8c−e] To minimize both solvent consumption and the number of manipulations required to obtain the saturated 1,2-bis(boryl)-alkane, we attempted a domino one-pot alkyne diboration/hydrogenation sequence (Scheme 2). Since platinum complexes are well-known as hydrogenation catalysts, an elevated loading of the Rh-Walphos catalyst was employed in the hydrogenation step to minimize competitive nonselective hydrogenation by the achiral platinum-based diboration catalyst. In addition, $(Ph_3P)_2Pt$(ethylene) was used instead of $(Ph_3P)_4Pt$ for the diboration step to minimize superfluous achiral phosphine in the reaction vessel.[10] Upon subjection of the alkyne to catalytic diboration, followed by catalytic hydrogenation and oxidation, styrenediol was isolated in 66% yield based on diboron and 91% ee. This level of selectivity is only slightly lower than that observed for the reduction of the purified vinyl bis(boronate).

Scheme 2. Single-Pot Diboration/Hydrogenation/Oxidation of Phenylacetylene



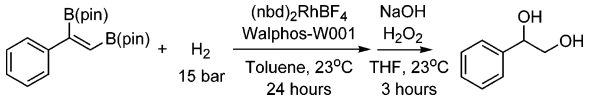
As alluded to above, an attractive feature of stereogenic carbon-metal bonds is the diversity of functional groups that may be obtained simply by altering reaction "workup" sequences. While oxidative workup conveniently delivers 1,2-diols from 1,2-bis-(boronate) intermediates, a homologation/oxidation workup was found to deliver optically active 1,4-diols.[11] This transformation was accomplished by treatment of the intermediate saturated 1,2-bis(boronate) with chloromethyllithium followed by $NaOH/H_2O_2$ (Scheme 3). The derived chiral butanediol was obtained with excellent levels of asymmetric induction. Notably, this reaction can be accomplished in a single-reaction pot with only a single solvent swap (THF for toluene) in the reaction sequence.

Scheme 3. Single-Pot Hydrogenation/Homologation/Oxidation of Vinyl Bis(boronate) **1**



Preliminary observations suggest that a simple 1:1 ligand:metal complex is not the sole participating entity in the hydrogenation reaction. As depicted in Table 3, the reaction selectivity is remarkably dependent on the ligand:metal ratio. A catalyst derived from an equimolar ratio of Walphos-W001 and rhodium salt provided the product in low enantioselection (entry 2). Surprisingly, the product obtained from this reaction possessed the configuration opposite to that obtained in the initial ligand survey. It was found that addition of excess ligand is required for optimal enantioselectivity (entry 3), whereas a substoichiometric amount of ligand (entry 1) allows access to the opposite enantiomer with a modest level of asymmetric induction. ^{31}P NMR experiments directed at understanding precatalyst stoichiometry remain inconclusive.

Table 3. Effect of Ligand:Metal Ratio on Asymmetric Hydrogenation of **1**



entry	mol % ligand	mol % Rh	% yield	% ee	configuration
1	1.6	2.0	90	52	*R*
2	2.0	2.0	83	37	*R*
3	4.0	2.0	84	93	*S*

In conclusion, we have described the asymmetric hydrogenation of prochiral vinyl bis(boronates). The reaction products are versatile intermediates which should prove useful in the assembly of a number of functional substructures.

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Supporting Information Available: Procedures, characterization data, enantiomeric purity data, and structure proofs. This material is available free of charge via the Internet at http://pubs.acs.org.

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