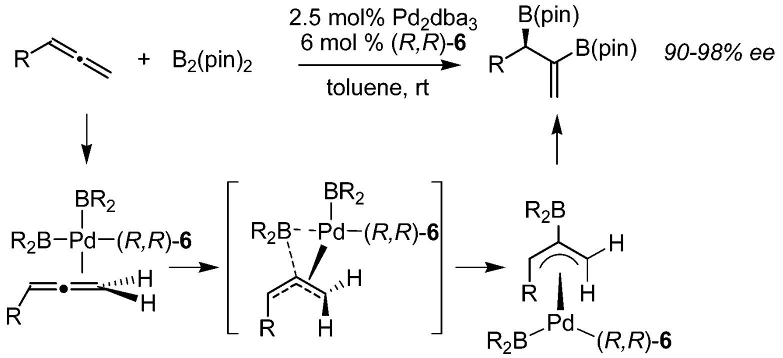
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Article

Development, Mechanism, and Scope of the Palladium-Catalyzed Enantioselective Allene Diboration

Heather E. Burks, Shubin Liu, and James P. Morken

J. Am. Chem. Soc., **2007**, 129 (28), 8766-8773• DOI: 10.1021/ja070572k • Publication Date (Web): 23 June 2007



J|A|C|S
ARTICLES

Development, Mechanism, and Scope of the Palladium-Catalyzed Enantioselective Allene Diboration

Heather E. Burks,[†] Shubin Liu,*[,‡] and James P. Morken*[,†]

Contribution from the Department of Chemistry, Merkert Chemistry Center, Boston College, Chestnut Hill, Massachusetts 02467, and Division of Research Computing, Information Technology Services, University of North Carolina, Chapel Hill, North Carolina 27599

Received January 25, 2007; E-mail: shubin@email.unc.edu; morken@bc.edu

Abstract: In the presence of a chiral phosphoramidite ligand, the palladium-catalyzed diboration of allenes can be executed with high enantioselectivity. This reaction provides high levels of selectivity with a range of aromatic and aliphatic allene substrates. Isotopic-labeling experiments, stereodifferentiating reactions, kinetic analysis, and computational experiments suggest that the catalytic cycle proceeds by a mechanism involving rate-determining oxidative addition of the diboron to Pd followed by transfer of both boron groups to the unsaturated substrate. This transfer reaction most likely occurs by coordination and insertion of the more accessible terminal alkene of the allene substrate, by a mechanism that directly provides the η^3 π-allyl complex in a stereospecific, concerted fashion.

1. Introduction

Addition of element−element bonds across unsaturated substrates such as alkenes, alkynes, dienes, and allenes can be a powerful technique for organic synthesis, particularly because such transformations may enable multicomponent reaction sequences.[1] Dimetalation of allenes is especially versatile because the vinylic and allylic metal groups in the product often exhibit orthogonal reactivity. In 1981, Watanabe and co-workers first demonstrated the dimetalation of allenes by employing $R_3Si-SiR_3$ reagents in conjunction with Pd catalysts.[2] Addition of distannyl,[3] silylstannyl,[4] and stannylgermyl[5] reagents are also known to be catalyzed by group 10 metal catalysts.[6] More recently, silylboron[7] and stannylboron[8] reagents have been added to allenes under Pd and Pt catalysis, and the addition of Si−B reagents has been rendered enantioselective.[9] Because of the Lewis acidic character of trivalent organoboron compounds, the diboration of allenes[10] should provide addition products that have unique reactivity relative to analogous silicon and tin derivatives. In this regard, we recently developed an enantioselective diboration of prochiral allenes, a transformation which is catalyzed by tris(dibenzylideneacetone)dipalladium(0) (Pd_2dba_3) and (*R*,*R*)-(TADDOL)$PNMe_2$ (**1**, Scheme 1).[11] This reaction is operative for a wide range of monosubstituted allenes, affording 1,2-bis(boronate)esters in good yield with high levels of enantiomeric excess. Importantly, this reaction can initiate a number of single-pot enantioselective C−C bond-forming sequences. For instance, the intermediate diboron compounds (**2**, Scheme 1) engage in allylation of both aldehydes[12] and imines[13] providing high levels of chirality transfer. The chiral homoallylic amines and alcohols which are generated by this diboration/allylation sequence can be engaged in a range of subsequent transformations providing an array of chiral products from a single allene precursor. In addition to allylation reactions, the intermediate diboron may be reacted with 9-BBN and the

---

[†] Boston College.

[‡] University of North Carolina.

(1) For review, see: (a) Suginome, M.; Ito, Y. *Chem. Rev.* **2000**, *100*, 3221. (b) Beletskaya, I.; Moberg, C. *Chem. Rev.* **2006**, *106*, 2320.

(2) (a) Watanabe, H.; Saito, M.; Sutou, N.; Nagai, Y. *J. Chem. Soc., Chem. Commun.* **1981**, 617. (b) Watanabe, H.; Saito, M.; Sutou, N.; Kishimoto, K.; Inose, J.; Nagai, Y. *J. Organomet. Chem.* **1982**, *225*, 343.

(3) (a) Killing, H.; Mitchell, T. *Organometallics* **1984**, *3*, 1318. (b) Mitchell, T. N.; Kwetkat, K.; Rutschow, D.; Schneider, U. *Tetrahedron* **1989**, *45*, 969. (c) Kwetkat, K.; Riches, B. H.; Rossett, J.-M.; Brecknell, D. J.; Byriel, K.; Kennard, C. H. L.; Young, D. J.; Schneider, U.; Mitchell, T. N.; Kitching, W. *Chem. Commun.* **1996**, 773.

(4) (a) Mitchell, T. N.; Killing, H.; Dicke, R.; Wickenkamp, R. *J. Chem. Soc., Chem. Commun.* **1985**, 354. (b) Koerber, K.; Gore, J.; Vatele, J.-M. *Tetrahedron Lett.* **1991**, *32*, 1187. (c) Jeganmohan, M.; Shanmugasundaram, M.; Chang, K.-J.; Cheng, C.-H. *Chem. Commun.* **2002**, 2552.

(5) Mitchell, T. N.; Schneider, U.; Fröhling, B. *J. Organomet. Chem.* **1990**, *384*, C53.

(6) For a review of Sn−M additions, see: Mitchell, T. N. *Synthesis* **1992**, 803.

(7) (a) Suginome, M.; Ohmori, Y.; Ito, Y. *Synlett* **1999**, 1567. (b) Suginome, M.; Ohmori, Y.; Ito, Y. *J. Organomet. Chem.* **2000**, *611*, 403. (c) Chang, K.-J.; Rayabarapu, D. K.; Yang, F.-Y.; Cheng, C.-H. *J. Am. Chem. Soc.* **2005**, *127*, 126.

(8) Onozawa, S.; Hatanaka, Y.; Tanaka, M. *Chem. Commun.* **1999**, 1863.

(9) (a) Suginome, M.; Ohmura, T.; Miyake, Y.; Mitani, S.; Ito, Y.; Murakami, M. *J. Am. Chem. Soc.* **2003**, *125*, 11174. (b) Ohmura, T.; Suginome, M. *Org. Lett.* **2006**, *8*, 2503. (c) Ohmura, T.; Taniguchi, H.; Suginome, M. *J. Am. Chem. Soc.* **2006**, *128*, 13682.

(10) (a) Ishiyama, T.; Kitano, T.; Miyaura, N. *Tetrahedron Lett.* **1998**, *39*, 2357. (b) Yang, F.-Y.; Cheng, C.-H. *J. Am. Chem. Soc.* **2001**, *123*, 761. For a review of catalytic diboration, see: (c) Marder, T. B.; Norman, N. C. *Top. Catal.* **1998**, *5*, 63. (d) Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2000**, *611*, 392. (e) Ishiyama, T.; Miyaura, N. *Chem. Rec.* **2004**, *3*, 271.

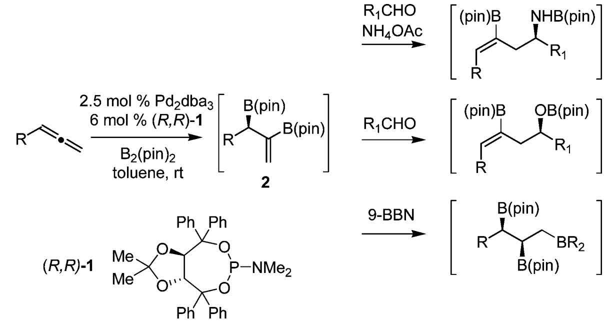
(11) (a) Pelz, N. F.; Woodward, A. R.; Burks, H. E.; Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 16328. For enantioselective diboration of alkenes, see: (b) Morgan, J. B.; Miller, S. P.; Morken, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 8702. (c) Miller, S. P.; Morgan, J. B.; Nepveux, F. J.; Morken, J. P. *Org. Lett.* **2004**, *6*, 131. (d) Trudeau, S.; Morgan, J. B.; Shrestha, M.; Morken, J. P. *J. Org. Chem.* **2005**, *70*, 9538. (e) Ramírez, J.; Segarra, A. M.; Fernández, E. *Tetrahedron: Asymmetry* **2005**, *16*, 1289.

(12) Woodward, A. R.; Burks, H. E.; Chan, L. M.; Morken, J. P. *Org. Lett.* **2005**, *7*, 5505.

(13) Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2006**, *128*, 74.

10.1021/ja070572k CCC: $37.00

Scheme 1



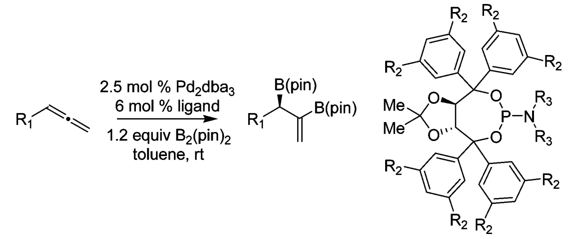
resulting triboron employed in sequential cross-coupling oxidation sequences.[14]

As concerns the allene diboration reaction, platinum catalysis was described by Miyaura and co-workers and was proposed to proceed by oxidative addition of Pt(0) to the diboron, followed by insertion of the allene into a Pt−B bond.[10a] Subsequent reductive elimination was suggested to provide the product and release the Pt catalyst in the original oxidation state. Although it might be anticipated that a Pd-catalyzed reaction would operate by the same mechanism, oxidative addition of Pd(0) to a boron−boron bond is virtually unknown; only a single example of Pd-catalyzed alkyne diboration exists, and it proceeds in 8% yield.[15] The unusual oxidative addition that was posited in the Pd-catalyzed allene diboration reaction, combined with the observation that the allene diboration product is one wherein bond formation occurs by addition to the more substituted alkene in the 1,2-diene substrate, provides a compelling reason to study the mechanism of this reaction. A clearer picture of this process may also aid in further refinement of this transformation and serve as a guide for the development of related catalytic processes. In this article, we describe experiments directed toward ligand development and substrate scope; additionally, experimental and computational experiments that shed light on the mechanism of the Pd-catalyzed enantioselective allene diboration reaction are described.

2. Results and Discussion

2.1. Reaction Development. Preliminary experiments revealed that Lewis basic phosphine ligands accelerate the Pd-catalyzed allene diboration reaction and that phosphoramidite ligands can influence the product enantiopurity. To improve upon initially observed levels of selectivity that were garnered with ligand (*R*,*R*)-**1**, various substituted TADDOL-derived phosphoramidites[16] were analyzed in the catalytic reaction (Table 1). Phosphoramidites derived from TADDOL offer elements of variability at the nitrogen site as well as at the aryl ring and the dioxolane protecting group. Alteration of the nitrogen substituents led to inferior stereoselectivity in all reactions examined. Replacement of the methyl groups with ethyl groups or incorporation of a cyclic amine significantly lowered the enantioselectivity (ligands **3**−**5**, Table 1). These permutations can be generalized as alterations that enhance the size of the nitrogen groups, and this might be the source of stereochemical erosion. However, a phosphoramidite derived from methyl amine also afforded products of diminished enantioselection (data not shown). This brief analysis appeared to suggest that the nitrogen appendage in (*R*,*R*)-**1** is already optimal for the allene diboration.

Table 1. Effect of Ligand on Enantioselective Diboration of Allenes[a]



ligand	R_2	R_3	R_1 = decyl % yield (% ee)	R_1 = Cy % yield (% ee)	R_1 = Ph % yield (% ee)
1	H	Me	61 (91)[b]	62 (89)[b]	75 (87)[b]
3	H	Et	42 (48)[b]	18 (52)	38 (30)
4	H	$(CH_2)_4$	80 (86)	80 (85)	53 (72)
5	H	$(CH_2)_5$	58 (47)	29 (46)	50 (30)
6	Me	Me	72 (98)[b]	92 (93)	72 (97)
7	*t*Bu	Me	34 (63)[b]	39 (66)	26 (51)
8	CF_3	Me	24 (38)[b]	61 (39)	38 (36)

[a] Reaction carried out at a substrate concentration of 0.15 M for 24 h unless noted. Isolated yield determined after silica gel chromatography. Enantiomeric excess determined for the diastereomeric diols prepared by sequential diimide reduction and oxidation of the diboration product. [b] Reaction time of 12 h.

Experiments directed toward tuning the aryl groups of ligand **1** were focused on analysis of the meta substituents. The enhanced steric bulk associated with substitution at this site has led to enhanced enantioselection with other TADDOL-derived catalysts.[17] In fact, attachment of methyl groups at the meta positions of TADDOL-derived phosphoramidite (Table 1, ligand **6**) provided the greatest enantioselectivity enhancement. Further increases in the steric encumbrance of the ligand (3,5-di-*tert*-butylphenyl) were not beneficial. Ultimately, (*R*,*R*)-xylylTADDOLPNMe$_2$ (**6**) was found to be the optimal ligand for the palladium-catalyzed diboration of prochiral allenes and exhibited high selectivity with a linear alkyl substituent on the allene, as well as a branched alkyl group and a phenyl group.

2.2. Substrate Scope. Several substrates that were examined in the Pd-catalyzed diboration with phosphoramidite ligand (*R*,*R*)-**1** were re-examined with (*R*,*R*)-**6**. Gratifyingly, the enantiopurity of the 1,2-vinyl(boronate)esters increased in all cases. The diboration adduct from decyl allene was obtained in 98% ee (Table 2, entry 1) with (*R*,*R*)-**6** versus 91% ee with (*R*,*R*)-**1**. Allenes bearing alkyl substituents such as methyl, cyclohexyl, and 2-phenylethyl afforded 1,2-bis(boronate)esters in *slightly* lower levels of enantiomeric purity (entries 2−4). Allenes bearing benzyl- and silyl-protected oxygen atoms also reacted with high levels of enantioselection (entries 5 and 6). Analysis of the reaction with substituted aromatic allenes

---

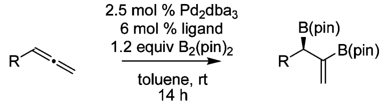
(14) Pelz, N. F.; Morken, J. P. *Org. Lett.* **2006**, *8*, 4557.

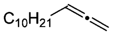
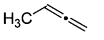
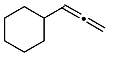
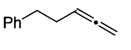
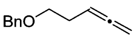
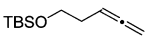
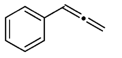
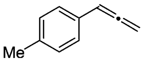
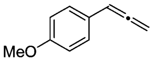
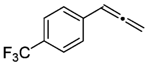
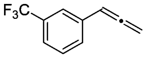
(15) Ishiyama, T.; Matsuda, N.; Murata, M.; Ozawa, F.; Suzuki, A.; Miyaura, N. *Organometallics* **1996**, *15*, 713.

(16) Review of these ligands in catalysis: (a) Feringa, B. L. *Acc. Chem. Res.* **2000**, *33*, 346. Select examples, hydrogenation: (b) ven den Berg, M.; Minnard, A. J.; Schudde, E. P.; van Esch, J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *J. Am. Chem. Soc.* **2000**, *122*, 11539. (c) Hydrosilation: Jensen, J. F.; Svendsen, B. Y.; la Cour, T. V.; Pedersen, H. L.; Johannsen, M. *J. Am. Chem. Soc.* **2002**, *124*, 4558. (d) Hydroboration: Ma, M. F. P.; Li, K.; Zhou, Z.; Tang, C.; Chan, A. S. C. *Tetrahedron: Asymmetry* **1999**, *10*, 3259.

(17) (a) Boele, M. D. K.; Kamer, P. C. J.; Lutz, M.; Spek, A. L.; de Vries, J. G.; van Leeuwen, P. W. N. M.; van Strijdonck, G. P. F. *Chem. Eur. J.* **2004**, *10*, 6232. (b) Corey, E. J.; Matsumura, Y. *Tetrahedron Lett.* **1991**, *32*, 6289.

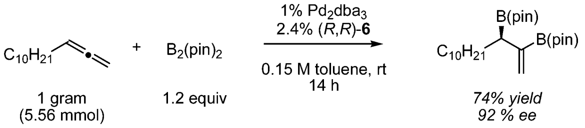
Table 2. Enantioselective Diboration with (R,R)-**6** versus (R,R)-**1**[a]



entry	substrate	ligand: (R,R)-**1**		ligand: (R,R)-**6**	
		% yield[b]	% ee[c]	% yield[b]	% ee[c]
1		61	91	72	98
2		68	92	77	95
3		62	89	92	93
4		73	90	76	97
5		57	91	85	97
6				68	97
7		75	87	71	97
8				71	95
9				68	94
10[d]				52	94
11[d]				52	90

[a] Reaction carried out at a substrate concentration of 0.15 M. [b] Isolated yield of purified product. [c] Enantiomeric purity determined for the diastereomeric diols prepared by sequential diimide reduction and oxidation of the reaction product. [d] 0.3 M [substrate], 3 equiv of $B_2(pin)_2$, 24 h.

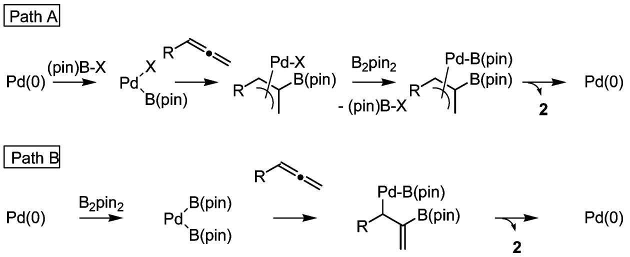
Scheme 2



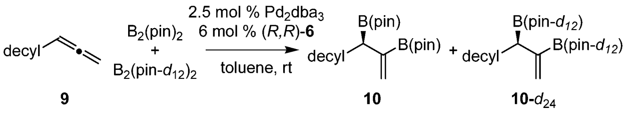
suggests that that there is not a significant impact of substrate electronic properties on enantioselection. For example, when phenyl allene was used in the reaction, the product was obtained in 97% ee (Table 2, entry 7). Substituting the para position with a more electron-donating methyl or methoxy group (entries 8 and 9) provided comparable levels of yield and selectivity. Similarly, substrates possessing a trifluoromethyl group at either the para or meta positions provided product of undiminished enantiopurity. However, the electron-poor substrates required more forcing reaction conditions (3 equiv of $B_2(pin)_2$; [substrate] = 0.3 M, 24 h) and p-nitrophenyl allene did not react, even with the more reactive catalyst generated from PCy_3 and Pd_2dba_3.

To ascertain whether the Pd-catalyzed allene diboration reaction may be run on larger scale, the experiment in Scheme 2 was undertaken. With decreased catalyst loading (1 mol % Pd_2dba_3 and 2.4 mol % (R,R)-**6**), 1 g of decyl allene was converted to the 1,2-bis(boronate)ester in 74% yield with slightly diminished enantioselectivity (98% ee → 92% ee).

Scheme 3



Scheme 4



2.3. Reaction Mechanism. 2.3.1. Crossover Experiments. Two prospective mechanisms for the Pd-catalyzed addition of diborons to allenes are depicted in Scheme 3. Pathway A is modeled after a mechanism that was suggested by Yang and Cheng, who found that small amounts of added vinyl halide could initiate Pd(0)-catalyzed allene diboration reactions by facilitating the production of a minor amount of haloboronate.[10b] If a small amount of adventitious boron halide was already present, then it might be anticipated that the mechanism in pathway A (oxidative addition, insertion, transmetalation, and reductive elimination) could account for the observed reactivity. As posited above, the Pd-catalyzed allene diboration might also be considered to initiate by oxidative addition of Pd(0) directly to $B_2(pin)_2$ as depicted in pathway B.[18]

A crossover experiment was undertaken to differentiate among possible modes of oxidative addition during the allene diboration reaction. In this experiment, allene **9** was subjected to diboration with an equimolar mixture of $B_2(pin\text{-}d_{12})_2$[19] and unlabeled $B_2(pin)_2$ with 2.5 mol % Pd_2dba_3 and 6 mol % phosphoramidite ligand (R,R)-**6** as the catalyst (Scheme 4). Analysis of the isolated diboration product by electrospray mass spectrometry revealed only **10** and **10**-d_{24} as the reaction products; **10**-d_{12} could not be detected. This experimental outcome is inconsistent with a pathway involving σ-bond metathesis as invoked for pathway A and suggests that allene diboration is initiated by oxidative addition of $B_2(pin)_2$ to a Pd(0) complex.

2.3.2. Ligand Analysis. DFT calculations by Morokuma and co-workers, and by Sakaki and Kikuno, suggest that oxidative addition of $B_2(pin)_2$ to Pd complexes is energetically unfavorable: although the barrier for oxidative addition of $B_2(OH)_4$ to $Pd(PH_3)_2$ is smaller than for the analogous Pt complex (8.6 kcal/

---

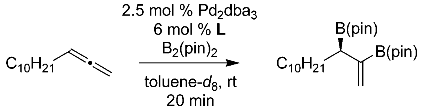
(18) Oxidative addition of diboron reagents to d^8 metals: (a) Iverson, C. N.; Smith, M. R., III. *J. Am. Chem. Soc.* **1995**, *117*, 4403. (b) Ishiyama, T.; Matsuda, N.; Murata, M.; Ozawa, F.; Suzuki, A.; Miyaura, N. *Organometallics* **1996**, *15*, 713. (c) Lesley, G.; Nguyen, P.; Taylor, N. J.; Marder, T. B.; Scott, A. J.; Clegg, W.; Norman, N. C. *Organometallics* **1996**, *15*, 5137. (d) Nguyen, P.; Lesley, G.; Taylor, N. J.; Marder, T. B.; Picket, N. L.; Clegg, W.; Elsegood, M. R. J.; Norman, N. C. *Inorg. Chem.* **1994**, *33*, 4623. (e) Clegg, W.; Lawlor, F. J.; Lesley, G.; Marder, T. B.; Norman, N. C.; Orpen, A. G.; Quayle, M. J.; Rice, C. R.; Scott, A. J.; Souza, F. E. S. *J. Organomet. Chem.* **1998**, *550*, 183.

(19) Pinacol-d_{12} was prepared by modification of literature procedures and used for the synthesis of $B_2(pin\text{-}d_{12})_2$. Preparation of pinacol-d_{12}: (a) Boller, T. M.; Murphy, J. M.; Hapke, M.; Ishiyama, T.; Miyaura, N.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 14263. (b) Binks, J.; Lloyd, D. *J. Chem. Soc. C* **1971**, 2641. Preparation of $B_2(pin\text{-}d_{12})_2$: (c) Ishiyama, T.; Murata, M.; Ahiko, T.-A.; Miyaura, N. *Org. Synth.* **2000**, *77*, 176.

(20) Cui, Q.; Musaev, D. G.; Morokuma, K. *Organometallics* **1998**, *17*, 742.

(21) Sakaki, S.; Kikuno, T. *Inorg. Chem.* **1997**, *36*, 226.

Table 3. Correlation between Ligand Basicity and Reactivity

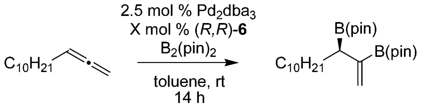


entry	L	% conv^a	ν_{CO} (cm^{-1})^b	pK_a^{c}
1	none	0		
2	P(tBu)$_3$	0		11.4
3	PCy$_3$	100	1943	9.7
4	P(NMe$_2$)$_3$	100	1964	
5	P(OEt)$_3$	80	1996	3.31
6	PPh$_3$	<3	1979	2.73
7	(R,R)-**1**	28	1984	
8	(R,R)-**6**	19	1984	
9	P(OPh)$_3$	<3	2016	−2.00
10	dppe	4		

^{a} Determined by ^{1}H NMR spectroscopy. ^{b} Values are in CH_2Cl_2 solvent. See ref 24 for 3−6, 8, and 9. See Supporting Information for the determination of ν_{CO} in entries 7 and 8. Note that entries 3 and 6 were repeated as a check for technique. ^{c} Values are in nitromethane. Data from ref 25.

mol vs 14.0 kcal/mol), the reaction is endothermic for Pd but exothermic for Pt. The $(PH_3)_2Pd[B(OH)_2]_2$ complex resides 15.9 kcal/mol higher in energy than the analogous Pt complex, and this energy difference persists for all the catalytic intermediates that are in the +2 oxidation state. Accordingly, Pd complexes are less effective catalysts for alkyne diboration reactions than analogous Pt complexes. According to these calculations, it can be anticipated that electron-donating ligands would stabilize diboration intermediates that are in higher oxidation states and thus might facilitate Pd catalysis.[22,23] Comparison of the reactivity exhibited in the presence of various phosphorus ligands supports this contention (Table 3). Although a rough correlation exists between reactivity and the CO stretching frequency of derived *trans*-**L**$_2$Rh(CO)Cl complexes,[24] there are significant outlying data points. For instance, the CO stretching frequency of *trans*-[(R,R)-**1**]$_2$Rh(CO)Cl was measured and found to be higher than that for the PPh$_3$ derivative, suggesting that **1** may be a weaker donor than PPh$_3$. However, the phosphoramidite ligand provides higher reactivity than PPh$_3$. Similarly, P(OEt)$_3$ provides higher reactivity than anticipated based on the CO stretching frequency of its *trans*-**L**$_2$Rh(CO)Cl derivative. With the exception of P(tBu)$_3$, a sterically encumbered ligand, a better correlation appears to exist between diboration reactivity and pK_a of the derived R_3PH^+ ion.[25] The acidity measurement is insensitive to back-bonding and has been noted to correlate with the rate of oxidation of LPd(0) complexes to phenyl iodide.[26] Although the pK_a for phosphoramidite ligands is not known, experiments by Pregosin, Albinati, and co-workers suggest that a binol-derived phosphoramidite may be only a slightly weaker donor to a Pd(II) allyl as compared to PCy$_3$.[27]

Table 4. Enantioselective Allene Diboration with Varied M/L Ratio



entry	(R,R)-**6**/Pd	% yield	% ee
1	1.2:1	72	98
2	1.08:1	78	96
3	0.5:1	71	90
4	0.1:1	54	53
5	0	10% conv	0

In the context of asymmetric catalysis, the ligand acceleration observed above can have significant practical advantages. Enantioselective reactions that benefit from ligand-accelerated catalysis may retain a high level of selectivity even when the ligand/metal ratio is less than one.[28] The data in Table 4 indicates that the Pd-catalyzed allene diboration reaction is in this class of reactions, and useful levels of selectivity may result even when the ligand loading is less than that of the transition metal (entry 3). For instance, with 0.5 equiv of ligand relative to palladium, synthetically useful levels of selectivity can result. However, for optimal levels of stereoinduction, a slight excess of ligand relative to Pd is required.

2.3.3. Stereodifferentiation. Subsequent to oxidative addition, the allene substrate may insert into one of the Pd−B bonds. This transformation can occur in a manner that provides a vinyl palladium compound or a regioisomeric allyl palladium intermediate. Although insertion reactions that involve allenes usually occur in a manner that provides allyl palladium intermediates,[29] allene insertion reactions that produce vinyl metallic intermediates have been implicated in catalytic reactions,[30] and a vinyl−metal species has been isolated from a stoichiometric allene insertion into an osmium hydride.[31] In accord with these mechanistic possibilities, it was considered that paths B−D in Scheme 5 might be operative in the allene diboration. Paths B and C proceed by addition of the bis(boryl)palladium intermediate to the more substituted allene double bond and provide either allyl or vinyl palladium intermediates, respectively. Alternatively, path D involves addition across the less substituted alkene, followed by isomerization and reductive elimination from an intermediate palladium allyl complex. This pathway has been proposed for allene silaboration.[7b]

To distinguish pathways B−D a stereodifferentiating experiment was undertaken that employed optically active, deuterium-labeled substrate (R)-**9**-d_1 in a catalytic diboration reaction with chiral ligand (R,R)-**6**. As depicted in Scheme 6, diastereomeric products are expected if either pathway B or C operates as opposed to pathway D. If pathway D operates, addition to the

---

(22) For the accelerating effect of basic phosphines on diboration, see: Alkynes: (a) Thomas, R. L.; Souza, F. E.; Marder, T. B. *J. Chem. Soc., Dalton Trans.* **2001**, 1650. Allenes: (b) ref 10a.

(23) For a review that describes the accelerating effect in a number of Pd-catalyzed reactions, see: Bedford, R. B.; Cazin, C. S. J.; Holder, D. *Coord. Chem. Rev.* **2004**, *248*, 2283.

(24) For the values in Table 3, see: (a) Otto, S.; Roodt, A. *Inorg. Chim. Acta* **2004**, *357*, 1. (b) Vastag, S.; Heil, B.; Markó, L. *J. Mol. Catal.* **1979**, *5*, 189.

(25) For a compilation of pK_a values, see: Rahman, M. M.; Liu, H.-Y.; Eriks, K.; Prock, A.; Giering, W. P. *Organometallics* **1989**, *8*, 1.

(26) Amatore, C.; Carré, E.; Jutland, A.; M'Barki, M. A. *Organometallics* **1995**, *14*, 1818.

(27) Filipuzzi, S.; Pregosin, P. S.; Albinati, A.; Rizzato, S. *Organometallics* **2006**, *25*, 5955.

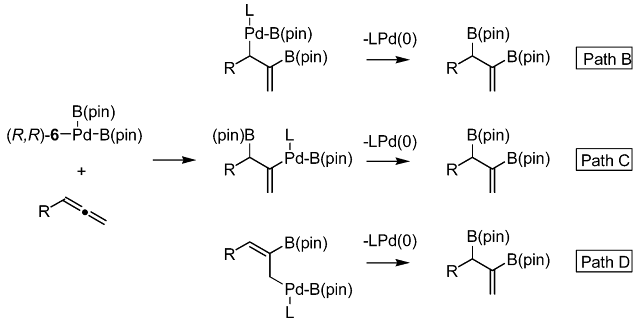
(28) Berrisford, D. J.; Bolm, C.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **1995**, *34*, 1059.

(29) Reviews: (a) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067. (b) Cazes, B. *Pure Appl. Chem.* **1990**, *62*, 1867.

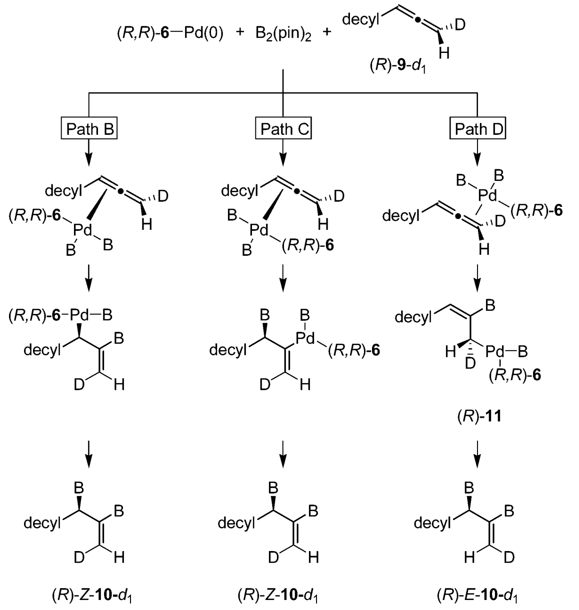
(30) Carbopalladation, see: (a) Fu, C.; Ma, S. *Org. Lett.* **2005**, *7*, 1605. Intramolecular hydroamination: (b) Arredondo, V. M.; McDonald, F. E.; Marks, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 4871. (c) Arredondo, V. M.; McDonald, F. E.; Marks, T. J. *Organometallics* **1999**, *18*, 1949.

(31) Xue, P.; Zhu, J.; Hung, H. S. Y.; Williams, I. D.; Lin, Z.; Jia, G. *Organometallics* **2005**, *24*, 4896.

Scheme 5



Scheme 6



terminal alkene is expected to occur anti to the decyl substituent at C3. Such an approach path is well-documented in carbopalladation of allenes.[32] With (*R*)-**9**-d_1 as substrate, the η^1 intermediate (*R*)-**11** is expected as an initial adduct. Chiral ligand (*R*,*R*)-**6** favors the *R* configuration in the diboration product, and this configuration may only be obtained by a bond rotation in (*R*)-**11** that also furnishes the *E* configuration of the alkene. Thus, pathway D is expected to furnish diastereomer (*R*)-*E*-**10**-d_1 from (*R*)-**9**-d_1 if ligand (*R*,*R*)-**6** is employed. If pathways B or C operate, they would both proceed by addition of the palladium bis(boryl) complex to the *Re* face of allene carbon 3 when (*R*,*R*)-**6** is used as the chiral ligand. This approach path provides the *Z*-configured alkene, and therefore these pathways would produce diastereomer (*R*)-*Z*-**10**-d_1 when (*R*,*R*)-**6** is the ligand and (*R*)-**9**-d_1 is the substrate.

Chiral allene (*R*)-**9**-d_1[33] was subjected the diboration conditions with (*R*,*R*)-**6** as the chiral ligand, and the course of the reaction was monitored by ^{1}H NMR analysis (Figure 1). After 60 min of reaction, the major reaction product exhibited a singlet at 5.8 ppm corresponding to the hydrogen atom trans to boron (chemical shift assignments were made by NOESY analysis of unlabeled bis(boronate)). A minor compound consistent with the other alkene stereoisomer exhibited a singlet resonance at 6.2 ppm (ratio = 7:1 *E*/*Z*). In addition to these two compounds, non-deuterated material was also present. Unexpectedly, the alkene stereoisomer ratio diminished over time, and at 10 h a 3:1 diastereomer ratio was observed. Two experiments suggest that this diastereochemical erosion is not the result of product equilibration. First, resubjection of the 3:1 *E*/*Z* mixture to the catalyst did not lead to further diminution of the stereoisomer ratio. Concerned that the 3:1 *E*/*Z* ratio might represent an equilibrium isotope effect, the diboration of (*R*)-**9**-d_1 was conducted with ligand (*S*,*S*)-**6**. As opposed to the reaction with ligand (*R*,*R*)-**6**, when ligand (*S*,*S*)-**6** is employed a 1:3 *E*/*Z* ratio of alkene stereoisomers is observed.

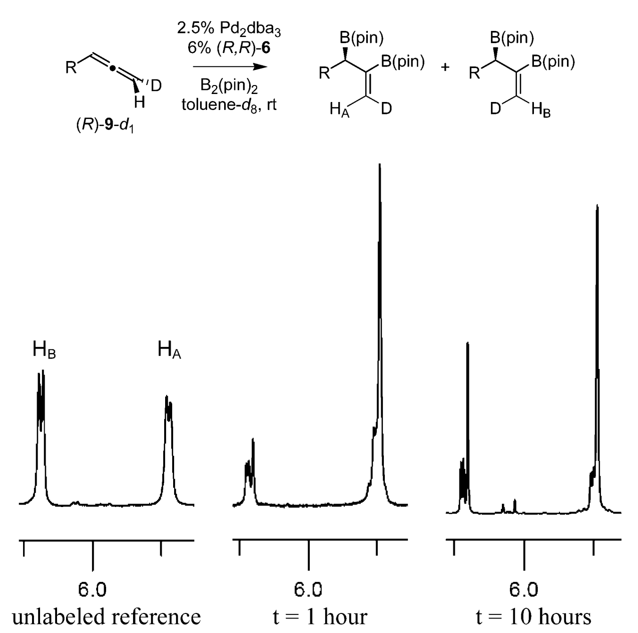
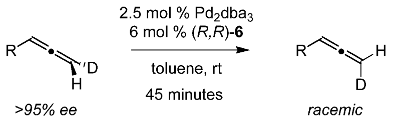


Figure 1. Diboration of enantiomerically enriched substrate (*R*)-**9**-d_1 with catalyst prepared from (*R*,*R*)-**6**. Reaction monitored by in situ NMR.

Scheme 7

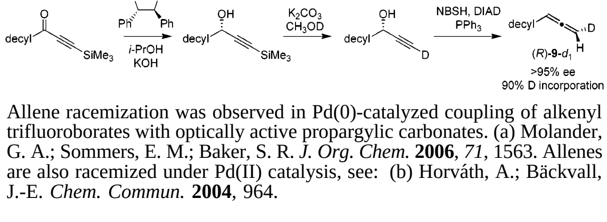


Importantly, when the above-described experiment was repeated and halted at 90 min, the recovered starting material was found to be racemic. Moreover, when (*R*)-**9**-d_1 was subjected to Pd_2dba_3 and (*R*,*R*)-**6**, in the absence of $B_2(pin)_2$, the allene was completely racemized after 45 min of reaction (Scheme 7). ^{13}C NMR analysis of the recovered allene shows a triplet resonance only for C1, suggesting that the deuterium label remains exclusively attached to C1 and that it has not scrambled between substrate molecules.[34]

---

(32) (a) Hiroi, K.; Kato, F.; Yamagata, A. *Chem. Lett.* **1998**, 397. (b) Gamez, P.; Ariente, C.; Goré, J.; Cazes, B. *Tetrahedron* **1998**, *54*, 14835.

(33) Synthesis of substrate (*R*)-**9**-d_1 was accomplished as shown below, and its optical purity was established by ^{1}H and ^{2}H NMR analysis of the Yb(hfc)$_3$/Ag(fod) complex. See the Supporting Information for complete details.



(34) Allene racemization was observed in Pd(0)-catalyzed coupling of alkenyl trifluoroborates with optically active propargylic carbonates. (a) Molander, G. A.; Sommers, E. M.; Baker, S. R. *J. Org. Chem.* **2006**, *71*, 1563. Allenes are also racemized under Pd(II) catalysis, see: (b) Horváth, A.; Bäckvall, J.-E. *Chem. Commun.* **2004**, 964.

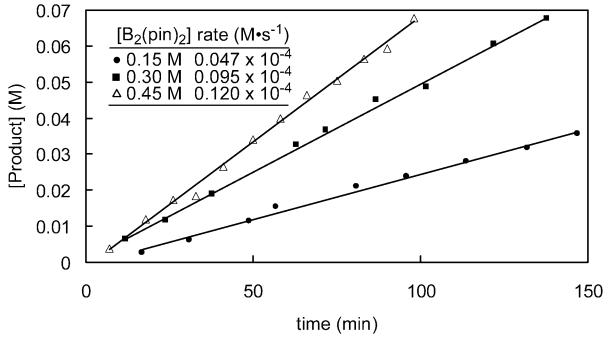
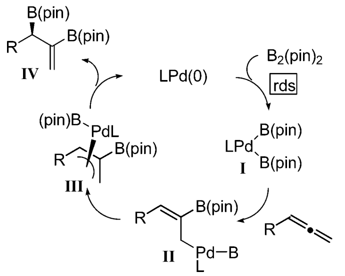


Figure 2. Formation of product vs time in the presence of 0.15 M $B_2(pin)_2$ (●), 0.30 M $B_2(pin)_2$ (■), and 0.45 M $B_2(pin)_2$ (Δ). Catalyst loading: 0.2 mol % Pd_2dba_3 and 0.48 mol % (*R*,*R*)-**6**.

Scheme 8

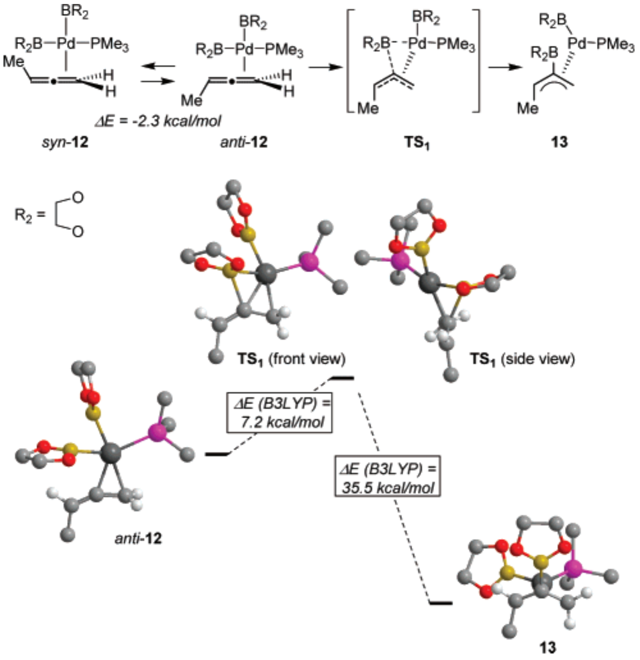


Collectively, isotope-labeling studies suggest that the allene diboration reaction product does not isomerize during the course of the reaction and that the diastereomer ratio is a kinetic one. Apparently, substrate racemization competes with allene diboration such that an initial high level of diastereoselection in the allene diboration is gradually eroded as racemized substrate is produced and participates in the reaction. *The diastereochemical outcome of the diastereodifferentiation experiment described above is only consistent with pathway D being responsible for the Pd-catalyzed allene diboration reaction.*

2.3.4. Catalytic Cycle. The above-described experiments are most consistent with the catalytic cycle depicted in Scheme 8, wherein formation of **I** by oxidative addition of $B_2(pin)_2$ to a Pd(*R*,*R*-**6**)$_n$ complex is the initial step. Subsequent insertion of the allene ultimately provides a π-allyl complex **III**, which then reductively liberates the reaction product. That the bidentate ligand dppe does not exhibit ligand-accelerated catalysis in accord with its basicity may suggest that the allene insertion proceeds by association of the substrate with a three-coordinate Pd center, as is known for other Pd-catalyzed reactions.[18c,35]

Although kinetic experiments would provide a better understanding of the asymmetric allene diboration reaction, catalyst precipitation during the course of the reaction prevents determination of accurate rate constants. However, measurement of initial reaction rates by ^{1}H NMR versus an internal standard was reproducible and revealed that the reaction clearly benefits from added $B_2(pin)_2$ (Figure 2). The apparent first-order dependence on $B_2(pin)_2$ suggests that oxidative addition of the diboron to Pd may be rate-limiting, a contrast with Pt-catalyzed alkyne diboration which is first order in [alkyne].[18c,35a,36] Importantly, these observations also provide a useful method for improving reaction outcome with unreactive substrates (see entries 10 and 11, Table 2).

Scheme 9



2.3.5. Computational Studies. The above reaction mechanism is unusual in that the reductive elimination reaction that releases the diboron product **IV** from an intermediate such as **III** does so in a manner that positions the boron atom on the more hindered carbon of the π-allyl complex. To probe possible reasons for this outcome, a series of high-level DFT calculations using B3LYP[37] was performed for the reaction sequence. The Stuttgart RSC 1997 ECP basis set[38] was used for Pd, and 6-311+G*[39] was used for other elements. Calculations were performed with Gaussian 03 CO2 package with tight SCF convergence and ultrafine integration grids. For transition-state structure searches, a single-point frequency calculation was performed to ensure that the final structure obtained (i) has only one imaginary frequency and (ii) the vibration mode of the negative frequency corresponds to the bond formation that is anticipated. In addition, intrinsic reaction coordinates (IRC) were calculated to verify the relevance of transition-state structures. Calculations were performed with methyl allene as substrate, PMe_3 as the ligand for palladium, and ethylene glycol as the ligand on boron.

Minimization of the putative initial η^2 Pd−olefin complex derived from methyl allene proceeded smoothly, and it was determined that structure *anti*-**12** is more stable than structure *syn*-**12** by 2.3 kcal/mol (Scheme 9), as expected. The allene σ-framework in *anti*-**12** is oriented about 30° out of the palladium square plane. Although this orientation is different than the perpendicular arrangement that is commonly observed for square planar d^8-alkene complexes and was observed for

---

(35) Diboration: (a) Iverson, C. N.; Smith, M. R., III. *Organometallics* **1996**, *15*, 5155. For a review of reactions that are catalyzed by monoligated Pd, see: (b) Christmann, U.; Vilar, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 366.

(36) The same kinetic experiments with varied allene concentration show a slight inverse-order dependence on [allene]. See the Supporting Information.

(37) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(38) Bergner, A.; Dolg, M.; Kuechle, W.; Stoll, H.; Preuss, H. *Mol. Phys.* **1993**, *80*, 1431.

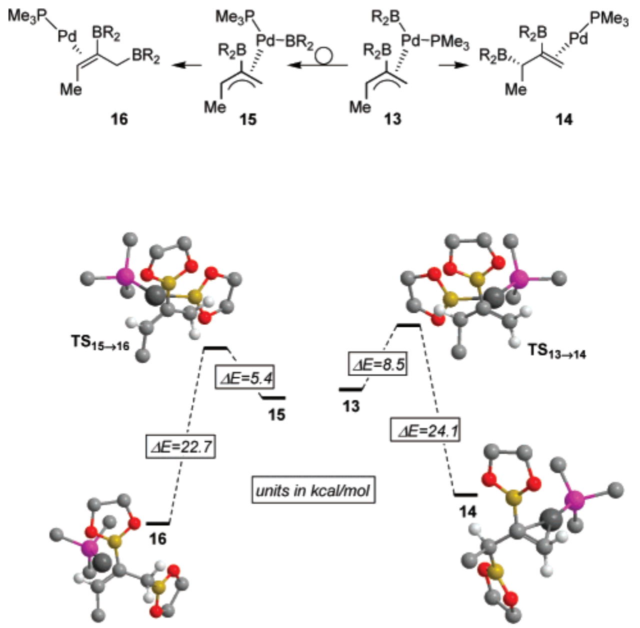
(39) Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650.

Pt(II)−allene complexes,[40] it is not unreasonable. The perpendicular orientation is commonly thought to arise from repulsive effects that destabilize the in-plane orientation; when these steric effects are removed there is nothing inherently unfavorable with the in-plane geometry, and in-plane coordination of alkenes has been experimentally observed in Pt(II) and Pd(II) complexes.[41,42] Germane to this topic, the rotational barrier for related bis(boryl)Pt alkene and alkyne complexes, calculated by Morokuma and co-workers, are low (<1 kcal/mol).[43]

Attempted minimization of the anticipated η^1 insertion adduct corresponding to **II** (Scheme 8) resulted in convergence directly on the η^3 intermediate **13** (Scheme 9). This observation is consistent with calculations of Sakaki et al., who found that (allyl)Pd(H)PH_3 adopts an η^3 structure and the higher energy three-coordinate η^1 form faces a barrierless conversion to the η^3 compound.[44] Optimization to a transition state between *anti*-**12** and **13** revealed structure **TS$_1$**, wherein C−B bond formation occurs concomitantly with rotation about the C1−C2 bond; IRC calculations confirm that there are no energy minima on the potential surface that separates *anti*-**12** and **13**. This insertion pathway appears to allow association of the C2−C3 π bond with the Pd center during the transition state such that η^3 bonding develops in concert with alkene insertion. The nature of bonding in this elementary step has been put forward once before in an allene carbopalladation studied by Hughes and Powell[45] and is in contradistinction to the notion that "the more stable η^3 coordination mode can never be formed directly due to orthogonal orbitals."[29a] An important consequence of this mode of insertion is that the position of the remaining boryl and phosphine groups in the initial η^3-Pd−allyl structure is defined by their position in the precursor η^2-alkene complex *anti*-**12**.

Analysis of the reductive elimination from both **13** and its apparent-rotation isomer **15** shows that the barrier for each is small, with that for **15** being 3.1 kcal/mol more favorable than that for **13** (Scheme 10). Given that **15** is also more stable than **13** by 0.7 kcal/mol leads to the conclusion that the barrier for interconversion of **13** and **15** must be high. In fact, conversion of **13** to an η^1-allyl complex, a presumed requirement for isomerization, was found to be energetically uphill with the η^1 structure residing 9.6 kcal/mol above the η^3 compound.[46] This calculation is consistent with calculations by Ariafard and Lin which suggest that the activation barrier for conversion of a neutral η^3-allyl palladium complex to an η^1-allyl complex by association of phosphine is 16.6 kcal/mol.[47] Similarly, recent calculations by Solin and Szabó show a 22.8 kcal/mol barrier for PH_3-induced η^3−η^1 isomerization in cationic palladium allyl complexes,[48] and experiments by Åkermark, Vitagliano, and co-workers indicate that anion-induced η^3−η^1 isomerization faces a minimum barrier of 11.5 kcal/mol.[49] Collectively, these results provide a plausible rationale for regioselectivity: after a site-selective alkene insertion reaction, a low-barrier intramolecular reductive elimination appears able to compete with allyl isomerization and selectively delivers **14** as opposed to **16**.

Scheme 10



3. Conclusion

In the presence of (*R*,*R*)-**6** ligand, the palladium-catalyzed diboration of allenes can be executed with much higher selectivity than with the parent ligand (*R*,*R*)-**1**. This reaction provides similarly high levels of selectivity with both aromatic and aliphatic allenes and with sterically encumbered and unencumbered substrates. The catalytic cycle appears to proceed by a mechanism involving rate-determining oxidative addition of the diboron to Pd followed by transfer of both boron groups to the unsaturated substrate. This transfer reaction most likely occurs by coordination and insertion of the more accessible terminal alkene of the allene substrate, by a mechanism that directly provides the η^3 π-allyl complex in a stereospecific, concerted fashion. According to this mechanistic paradigm, this insertion reaction (*anti*-**12** → **13**, Scheme 9) is most likely the enantiomer-determining step of the allene diboration process. Ongoing studies focused on expanding the scope of the asymmetric diboration reaction, and its application in synthesis, will be reported in due course.

---

(40) (a) Hewitt, T. G.; de Boer, J. J. *J. Chem. Soc. A* **1971**, 817. (b) Clark, H. C.; Dymarski, M. J.; Payne, N. C. *J. Organomet. Chem.* **1979**, *165*, 117. (c) Briggs, J. R.; Crocker, C.; McDonald, W. S.; Shaw, B. L. *J. Chem. Soc., Dalton Trans.* **1981**, 121.

(41) For an analysis of the barrier to rotation in metal−alkene complexes: Albright, T. A.; Hoffmann, R.; Thibeault, J. C.; Thorn, D. L. *J. Am. Chem. Soc.* **1979**, *101*, 3801.

(42) For examples of in-plane alkene coordination to d^8 complexes, see: (a) Musco, A.; Pontellini, R.; Grassi, A.; Meille, S. V.; Rüegger, H.; Ammann, C.; Pregosin, P. S. *Organometallics* **1988**, *7*, 2130. (b) Rakowski, M. H.; Woolcock, J. C.; Wright, L. L.; Green, D. B.; Rettig, M. F.; Wing, R. M. *Organometallics* **1987**, *6*, 1211. (c) Miki, K.; Yamatoya, K.; Kasai, N.; Kurosawa, H.; Emoto, M.; Urabe, A. *J. Chem. Soc., Chem. Commun.* **1984**, 1520. (d) Miki, K.; Kai, Y.; Kasai, N.; Kurosawa, H. *J. Am. Chem. Soc.* **1983**, *105*, 2482.

(43) Cui, Q.; Musaev, D. G.; Morokuma, K. *Organometallics* **1997**, *16*, 1355.

(44) Sakaki, S.; Satoh, H.; Shono, H.; Ujino, Y. *Organometallics* **1996**, *15*, 1713.

(45) Hughes, R. P.; Powell, J. *J. Organomet. Chem.* **1973**, *60*, 409.

(46) Direct interconversion of **13** and **15** by rotation about the metal−allyl axis is generally discounted, see: Pfaltz, A.; Lautens, M. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer-Verlag, Berlin, 1999; Vol. 2, pp 838−839. Consistent with this, we have computed barriers of 19.4 and 29.4 kcal/mol, depending upon the direction of rotation.

(47) Ariafard, A.; Lin, Z. *J. Am. Chem. Soc.* **2006**, *128*, 13010.

(48) Solin, N.; Szabó, K. J. *Organometallics* **2001**, *20*, 5464.

(49) Hannson, S. H.; Norrby, P.-O.; Sjögren, M. P. T.; Åkermark, B.; Cucciolito, M. E.; Giordano, F.; Vitagliano, A. *Organometallics* **1993**, *12*, 4940.

Acknowledgment. This work was supported by the NIH (GM 59417). Financial assistance from Merck Research Laboratories is appreciated, as is AllyChem, Co., Ltd. (www.allychem.com) for a donation of $B_2(pin)_2$. H.E.B. is grateful for a LaMattina Fellowship.

Supporting Information Available: Experimental procedures and physical data (NMR, IR, MS, chiral GC, DFT coordinates). This material is available free of charge via the Internet at http://pubs.acs.org.

JA070572K