# Scope and Mechanism of the Pt-Catalyzed Enantioselective Diboration of Monosubstituted Alkenes

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S Supporting Information

ABSTRACT: The Pt-catalyzed enantioselective diboration of terminal alkenes can be accomplished in an enantioselective fashion in the presence of chiral phosphonite ligands. Optimal procedures and the substrate scope of this transformation are fully investigated. Reaction progress kinetic analysis and kinetic isotope effects suggest that the stereodefining step in the catalytic cycle is olefin migratory insertion into a Pt−B bond. Density functional theory analysis, combined with other experimental data, suggests that the insertion reaction positions platinum at the internal carbon of the substrate. A stereochemical model for this reaction is advanced that is in line both with these features and with the crystal structure of a Pt−ligand complex.
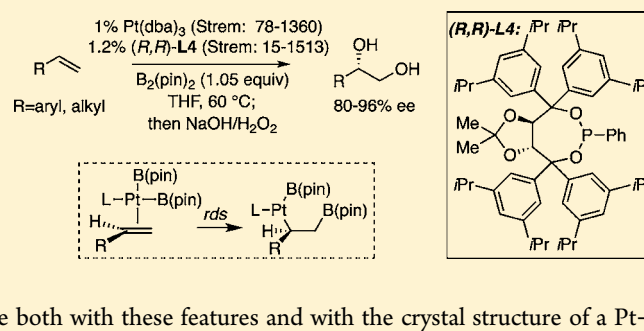
1. INTRODUCTION

The catalytic enantioselective reactions of terminal alkenes offer singular opportunities for strategic chemical synthesis. Such reactions can facilitate both hydrocarbon chain extension and functional group installation simultaneously and in a stereoselective fashion. Given these features, it is unfortunate that few catalytic processes apply to terminal olefins in a highly enantioselective manner. Indeed, other than substrate-specific reactions that only apply to electronically biased alkenes (e.g., styrenes, dienes, and vinyl acetates) or to those that bear adjacent directing groups,[1] the range of asymmetric transformations that apply to simple aliphatic α-olefins is limited.[2] To address this shortcoming, we initiated studies on the catalytic enantioselective diboration of terminal alkene substrates.[3] From the outset, it was anticipated that one could engage the diboration product in a range of transformations that apply to organoboronate intermediates[4] and therefore expand the range of strategically useful enantioselective reactions that apply to 1-alkenes.

The Pt-catalyzed diboration of alkynes was first reported by Miyaura and subsequently studied by Marder and Smith.[5] A general feature of these reactions is that they occur by oxidative addition of $B_2(pin)_2$ to Pt(0) leading to a bis(boryl)platinum intermediate that then reacts by olefin insertion and reductive elimination. Further study of these reactions led to the development of alkene[6] and diene diborations[6c,7] with the latter reaction being accomplished in an enantioselective fashion.[8] We reported the discovery of a Pt-catalyzed enantioselective diboration that applies to terminal olefins[9] and a contemporaneous report by Hoveyda[10] documented a similar class of reaction products obtained by catalytic and enantioselective, copper-catalyzed, double borylation of alkynes. The enantioselective alkene diboration reaction was
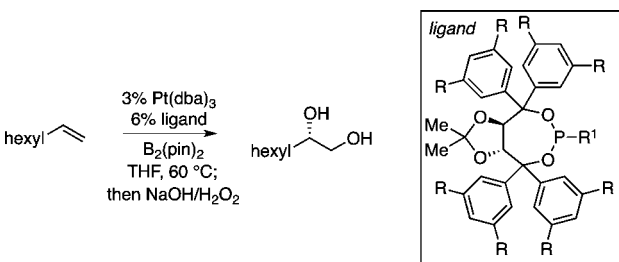
accomplished with a Pt(0) catalyst in the presence of a readily available taddol-derived phosphonite ligand.[11] These initial studies revealed an effective transformation useful enough to be adopted for asymmetric natural product syntheses (*vide infra*); however, significant improvements regarding the scope and selectivity were clearly warranted. Moreover, a lack of mechanistic details about the inner working of this reaction hampered the design of improved processes. In this report, we describe an improved catalyst and conditions for the enantioselective diboration and its application to a broad range of olefinic substrates. We also provide experimental insight that suggests olefin migratory insertion to give an internal C−Pt intermediate is the rate-limiting and stereocontrolling step of the reaction. This information is used to develop an understanding of the stereoselection in this transformation.

2. RESULTS AND DISCUSSION

2.1. Identification of the Optimal Ligand. An optimization of ligand structures for the enantioselective diboration of 1-octene focused on a set of *meta*-substituted, taddol-derived, phosphonite and phosphoramidites.[12] A sample of ligands were examined in tetrahydrofuran (THF) and toluene solvents and the selectivity was found to be relatively insensitive to the medium. As depicted in Table 1, 3,5-diisopropylphenyltaddol-PPh (**L4**) was found to be comparable to the previously reported ligand, 3,5-diethylphenyltaddol-PPh (**L3**) under the conditions of Table 1.[13] A direct correlation between ligand size and enantioselectivity can also be observed, with the selectivity increasing as the size of the meta substituent

Table 1. Ligand Optimization for Diboration of 1-Octene[a]

entry	ligand	R	R[1]	solvent	yield (%)[b]	er[c]
1	L1	H	Ph	tol	24	80:20
2	L2	Me	Ph	THF	84	95:5
3	L2	Me	Ph	tol	81	92:8
4	L3	Et	Ph	tol	83	96:4
5	L4	i-Pr	Ph	THF	82	97:3
6	L4	i-Pr	Ph	tol	84	97:3
7	L5	t-Bu	Ph	tol	74	90:10
8	L6	OMe	Ph	tol	69	90:10
9	L7	H	NMe$_2$	tol	68	84:16
10	L8	H	NEt$_2$	tol	35	70:30
11	L9	Me	NMe$_2$	THF	73	89:11
12	L9	Me	NMe$_2$	tol	77	90:10
13	L10	Me	N(CH$_2$)$_4$	tol	76	91:9
14	L11	t-Bu	NMe$_2$	THF	34	88:12
15	L11	t-Bu	NMe$_2$	tol	40	78:22

[a]Reactions were conducted at 0.1 M substrate concentration for 12 h as described in the text. [b]Yield refers to isolated yield of the purified reaction product. [c]Enantiomeric ratio determined on the derived acetonide by chromatography with a chiral stationary phase.

is varied (H < Me < Et ≅ i-Pr). However, when the size of the ligand is enhanced past **L4**, enantioselectivities and yields diminish (i.e., selectivity is diminished with t-Bu substituted ligands). Subsequent experiments revealed that, at lower catalyst loadings and lower ligand−metal ratio, **L4** reproducibly provides high selectivity, whereas selectivity with **L3** is lower and more variable (i.e., with 1 mol % Pt(dba)$_3$ and 1.2 mol % **L3**, reaction with 1-octene occurs in 72−90% ee). Thus, **L4** was employed for the remainder of this study.

2.2. Identification of the Optimal Pt(0) Source, Catalyst Composition, and Catalyst Activation. Among the complexes that apply to the Pt-catalyzed diboration, Pt(0) precursors are employed almost exclusively. In terms of practical utility, dibenzylideneacetone complexes are simple to prepare and have the ideal features of being thermally stable and insensitive to air and moisture. Notably, dibenzylideneacetone−platinum complexes are prepared in a single-step synthesis from dba and K$_2$PtCl$_4$ in an aqueous medium and without drybox techniques.[14] The identity of the product that arises from this synthesis depends upon the conditions and the isolation procedure; simple washing of the solid precipitate with methanol gives Pt(dba)$_3$, whereas recrystallization from THF/methanol gives Pt$_2$(dba)$_3$.

Using 1-tetradecene as a probe substrate for the enantioselective diboration, we undertook a comparison of different Pt(0) precursors (Figure 1). This survey showed that there is very little dependence of enantioselectivity on the nature of the precatalyst, with dba complexes proving equally effective as Pt(nbe)$_3$. Analysis of reaction rates by calorimetry (Figure 1) also indicated that all three complexes provide equally reactive catalysts: at 1.0 M concentration, all three
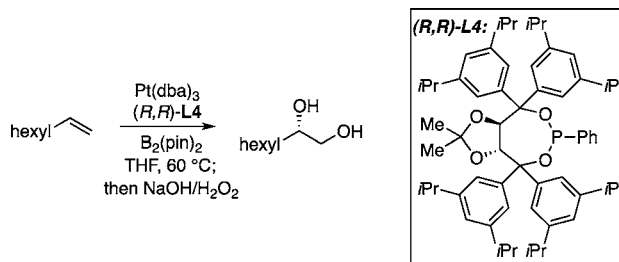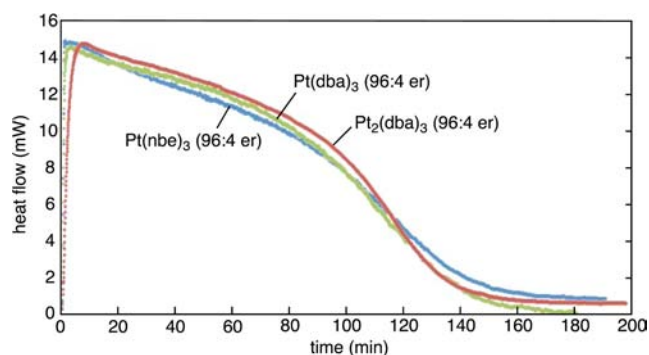

Figure 1. Reaction rates with Pt(nbe)$_3$, Pt$_2$(dba)$_3$, and Pt(dba)$_3$. Reactions employed 1 mol % platinum, 1.2 mol % (R,R)-**L4**, and 1.2 equiv B$_2$(pin)$_2$. initial [tetradecene] = 1.0 M.

reactions are complete in 3 h. Considering that Pt(dba)$_3$ is the most conveniently prepared complex of the three, it was selected for all further studies.

The effect of the catalyst loading and the ligand−metal ratio is depicted in Table 2. Relative to initially described conditions

Table 2. Impact of Catalyst Loading and Ligand−Metal Ratio on the Diboration of 1-Octene[a]

| entry	Pt(dba)$_3$ (mol %)	(R,R)-L4 (mol %)	[octene] (M)	time (h)	yield (%)	er
1	3.0	6.0	0.1	3	89	97:3
2	0.5	1.0	1.0	11	88	96:4
3	0.2	0.4	1.0	28	60	96:4
4	3.0	3.6	0.1	1	88	98:2
5	1.0	1.2	1.0	3	82	97:3
6	3.0	3.0	0.1	3	75	86:14
7	1.0	1.0	1.0	3	66	94:6
8	1.0	0.75	1.0	3	39	80:20
9	1.0	0.5	1.0	3	30	64:36

[a]Yield refers to isolated yield of the purified reaction product. Enantiomeric ratio determined on the derived acetonide by chromatography with a chiral stationary phase.

(entry 1), the reaction could be run at higher substrate concentration (1.0 M versus 0.1 M) and the catalyst loading could be decreased from 3 to 0.5 mol % without a significant effect on enantioselectivity (entry 2); however, the yield is diminished at 0.2 mol % catalyst loading (entry 3). A close analysis of ligand−metal ratio shows that a 1:1 ratio is also effective (entry 7), although at the price of decreased yield relative to higher ligand loading (entry 5). When the ligand−metal ratio is less than 1:1, enantioselectivity also begins to suffer (entries 8 and 9), likely from competitive diboration by a phosphonite-free Pt complex. Considering that 1 mol % of a 1.2:1 phosphonite−Pt complex provided reproducibly high yield and selectivity (entry 5), this catalyst loading/composition was adopted for subsequent studies. Importantly, employing a

1.2:1 ligand−metal ratio ensures an optimum outcome even if the ligand batch is slightly oxidized during the course of its synthesis (up to 4 mol % ligand oxidation is common).

Experiments by Pringle reveal that addition of phosphites to Pt(nbe)$_3$ results in rapid displacement of the norbornene ligand (<1 h at rt).[15] In contrast, we have found that addition of either (R,R)-**L3** or (R,R)-**L4** to Pt(dba)$_3$ does not lead to a substantial change in the ^{31}P NMR after 1 h at room temperature. To understand the chemistry that allows Pt(dba)$_3$ to provide a catalyst with equal activity to Pt(nbe)$_3$ in alkene diborations, the chemistry of the activation step was studied. In the procedure employed above for catalytic alkene diboration, a catalyst "activation step" precedes addition of substrate and involves treating 1 mol % of Pt(dba)$_3$ with 1.2 mol % of the phosphonite ligand in the presence of 1.05 equiv of B$_2$(pin)$_2$ at 80 °C for 20−30 min. Without pre-complexation at this elevated temperature, lower yields (due to olefin isomerization and hydroboration byproducts) and reduced levels of enantioselectivity are observed. As depicted in Scheme 1,

Scheme 1
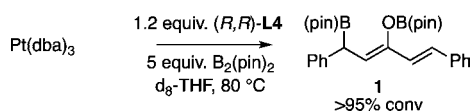
when a similar "activation" reaction was analyzed by ^{1}H NMR in d_8−THF, diboration of dba was found to occur in >95% conversion. This reactivity is in line with the Pt−phosphine catalyzed conjugate borylation of activated alkenes reported by Marder.[16] Notably, according to studies by a number of investigators[17] on the binding of alkenes to related d^{10} Pd complexes, one would anticipate that the conjugate borylation product **1** would bind less effectively to Pt(0) than does dba such that the conjugate borylation of dba may provide a mechanism for removing the coordinating enone from the metal complex. Analysis of the catalyst activation reaction by ^{31}P NMR shows formation of a new phosphorus-containing structure with broad resonances and coupling to platinum: ^{31}P{^{1}H} NMR (THF) δ 200.0 ppm ($^1J_{P−Pt}$ = 1980 Hz); **L4** δ = 158.1 ppm (s). Broadening of the phosphorus resonance is consistent with the ligand bound to a Pt−boryl complex.[18] Addition of 1-tetradecene to this mixture at room temperature results in disappearance of the resonance at 200 ppm and formation of a new Pt−boryl complex with broadened resonances in the ^{31}P NMR: ^{31}P{^{1}H} NMR (THF) δ 152.3 ppm ($^1J_{P−Pt}$ = 2715 Hz).

2.2.1. Substrate Scope: Procedures and Oxidation Efficiency. Purified taddol-derived phosphonite ligands are stable in air for extended time periods. For example, when purified solid **L4** was exposed to air for >1 month, <3% decomposition was detected by ^{31}P NMR spectroscopy. Note that **L4** is prone to more rapid oxidation when dissolved in solution (**L4** was 12% oxidized after being dissolved in ether for 1 h). Similarly, Pt(dba)$_3$ and B$_2$(pin)$_2$ are also stable to air and moisture. Accordingly, the following drybox-free diboration/ oxidation procedure was employed to study the substrate scope in the following sections: in the open atmosphere, 1 mol % Pt(dba)$_3$, 1.2 mol % **L4**, and 1.05 equiv B$_2$(pin)$_2$ were weighed into a vial that was then sealed with a septum cap and purged with N$_2$. THF was then added by syringe, the vial was then sealed, placed behind a blast shield,[19] and heated to 80 °C for

30 min. The vial was then cooled to room temperature and charged with the alkene by syringe, purged once more with N$_2$, then stirred at 60 °C for 3 h. Finally, oxidative workup (generally treatment with NaOH and H$_2$O$_2$) delivered the derived 1,2-diol.
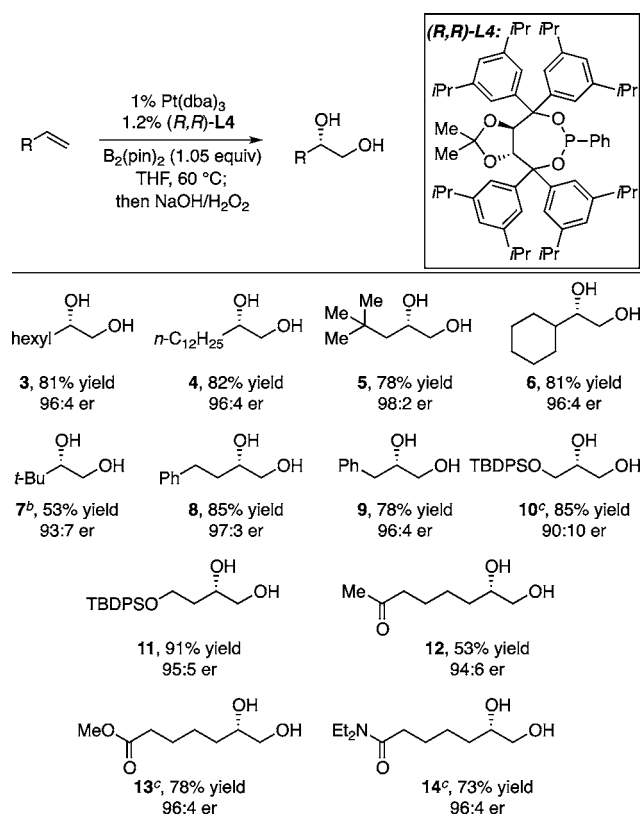
Analysis of diboration reactions is most conveniently accomplished by subjecting the intermediate 1,2-bis(boronate) intermediate to in situ oxidation to the derived 1,2-diol. The efficiency of this oxidation step was examined to determine how well the yield of the 1,2-diol reflects to the overall efficiency of diboration reactions. As depicted in Scheme 2 (eq 1), when

Scheme 2
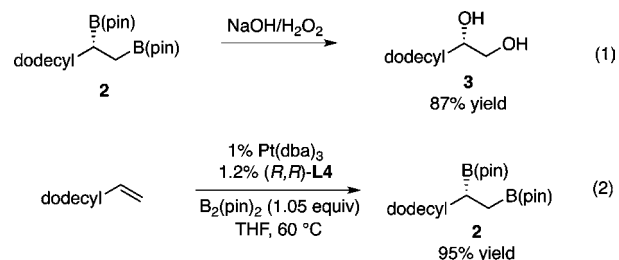
isolated, purified 1,2-bis(boronate) **2** is subjected to oxidation with excess H$_2$O$_2$ in the presence of 3.0 M NaOH, the derived 1,2-diol **3** is obtained in 87% yield. The isolated yield for this transformation is higher than that obtained for the single-pot diboration/oxidation (82% yield, Table 3 compound **4**) but is not quantitative. This outcome suggests that the yield for the diboration step is somewhat higher than that for the two-step diboration/oxidation sequence. Indeed, when the intermediate 1,2-bis(boronate) **2** derived from the diboration of 1-tetradecene was isolated and purified by column chromatography, it was obtained in 95% yield (Scheme 2, eq 2). Some loss in yield can be attributed to the oxidative workup sequence. However, considering the ease of isolation and characterization of the derived 1,2-diols, the two-step procedure was employed to survey the reaction scope.

2.2.2. Substrate Scope: Aliphatic Alkenes. To learn about the scope of enantioselective diborations with ligand **L4**, a number of aliphatic alkenes were examined and the collected data shown in Table 3. In general, high enantioselectivities were observed regardless of the size of the substituent adjacent to the olefin: 1-octene, vinylcyclohexane and *t*-butylethylene furnish the derived 1,2-diols **3**, **6**, and **7** in 96:4, 96:4, and 93:7 enantiomeric ratios, respectively. The size of the olefin substituent does have an impact on reactivity, with large substituents appearing to diminish reactivity. Although 1-octene and vinyl cyclohexane react efficiently with 1 mol % catalyst, *t*-butylethylene required 3 mol % Pt catalyst to deliver a product yield of 53%. Substrates bearing a variety of functional groups were also surveyed. With elevated catalyst loading, TBDPS-protected allyl alcohol was transformed to **10** efficiently but in slightly diminished enantioselectivity. Oxygenation at the homoallylic position appeared inconsequential and high yields and selectivity for **11** were observed. Potentially reactive and coordinating functional groups were also surveyed: carbonyls are known to participate in some diboration reactions[20] but were not affected by the diboration of adjacent alkenes (product **12**). Similarly, olefinic substrates bearing ester and amide functional groups were tolerated during the construction of **13** and **14**.

Table 3. Diboration of Aliphatic 1-Alkenes with Pt(dba)$_3$ and (R,R)-L4^a

3, 81% yield, 96:4 er (hexyl)
4, 82% yield, 96:4 er (n-C$_{12}$H$_{25}$)
5, 78% yield, 98:2 er
6, 81% yield, 96:4 er (cyclohexyl)

7^b, 53% yield, 93:7 er (t-Bu)
8, 85% yield, 97:3 er (Ph)
9, 78% yield, 96:4 er (Ph)
10^c, 85% yield, 90:10 er (TBDPSO)

11, 91% yield, 95:5 er (TBDPSO)
12, 53% yield, 94:6 er

13^c, 78% yield, 96:4 er (MeO)
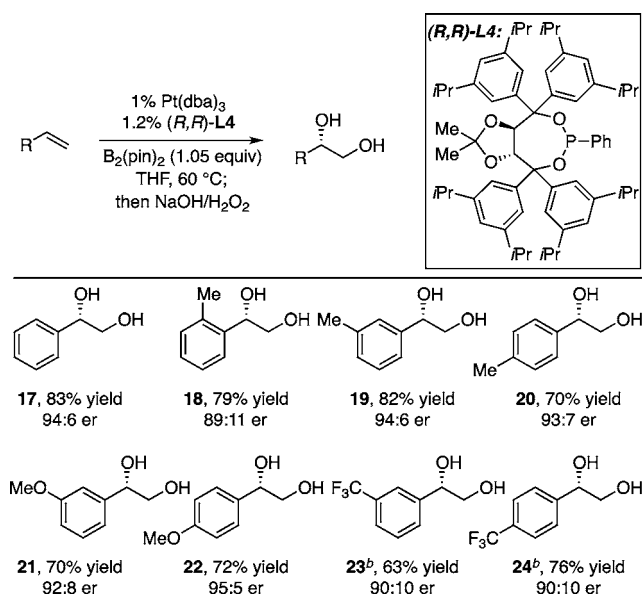**14^c**, 73% yield, 96:4 er (Et$_2$N)

^{a}Conditions: [alkene] = 1.0 M, reaction time = 3 h. Yield refers to isolated yield of the purified reaction product. Enantiomeric ratio determined on the derived acetonide by chromatography with a chiral stationary phase. ^{b}3.0% Pt(dba)$_3$ and 3.6% (R,R)-L4 was employed for 12 h. ^{c}Oxidation with H$_2$O$_2$ at pH = 7.

In terms of olefin oxidation transformations, the diboration/oxidation is complementary to osmium-catalyzed dihydroxylation. The osmium-catalyzed reaction is accelerated with more electron-rich substrates such that more substituted alkenes generally react faster than less substituted substrates. In contrast, Pt-catalyzed diboration is highly sensitive to steric effects such that added substitution on the alkene leads to marked diminution in reaction rate. This feature can be used advantagously with polyolefin substrates. For example, the 1,1-disubstituted alkene in **15** is selectively oxidized (5:1 regioselectivity) under conditions for Sharpless' asymmetric dihydroxylation to provide a moderate yield of the derived 1,2-diol (Scheme 3, eq 4).[21] In contrast, Pt-catalyzed diboration/oxidation leads to selective and high yield conversion to 1,2-diol

Scheme 3
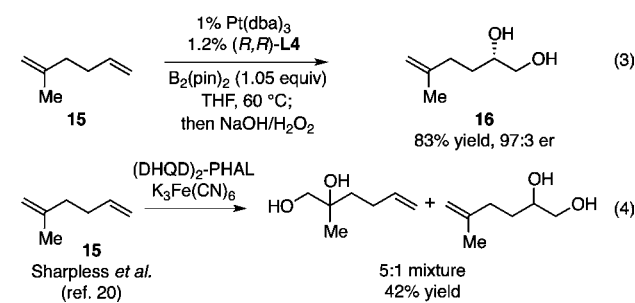
16 wherein the less substituted alkene is oxidized without detectable transformation of the 1,1-disubstitued olefin (eq 3).

2.2.3. Substrate Scope: Aromatic Alkenes. In many transition-metal-catalyzed processes, π-benzyl stabilization can alter the regiochemistry of olefin migratory insertion reactions for aromatic relative to aliphatic alkene substrates.[22] If such a turnover applied to Pt-catalyzed diboration, it would be expected to dramatically alter the stereochemical outcome of diborations of styrenes relative to aliphatic alkenes. To examine whether such a divergent reaction manifold operates in diborations, a variety of substituted styrenes were examined (Table 4). Under the optimized conditions, *ortho, meta,* and

Table 4. Diboration of Styrenes with Pt(dba)$_3$ and (R,R)-L4^a

17, 83% yield, 94:6 er
18, 79% yield, 89:11 er (Me, ortho)
19, 82% yield, 94:6 er (Me, meta)
20, 70% yield, 93:7 er (Me, para)

21, 70% yield, 92:8 er (MeO, meta)
22, 72% yield, 95:5 er (MeO, para)
23^b, 63% yield, 90:10 er (F$_3$C, meta)
24^b, 76% yield, 90:10 er (F$_3$C, para)

^{a}Reactions conducted at [alkene] = 1.0 M for 3 h. Yield refers to isolated yield of the purified reaction product. Enantiomeric ratio determined on the derived acetonide by chromatography with a chiral stationary phase. ^{b}3.0% Pt(dba)$_3$ and 3.6% (R,R)-L4 was employed with reaction at 60 °C for 12 h.

para-substituted styrenes undergo effective diboration, affording moderate to good yields and enantioselectivities. Electron-rich styrenes provided high enantiopurity (product **22**), whereas electron-deficient styrenes required longer reaction times, a higher catalyst loading, and their reactions occurred with slightly diminished enantiocontrol (products **23** and **24**). Collectively, however, the consistently high levels of enantioselectivity and identical sense of facial selectivity suggests that both aliphatic and aromatic alkene substrates react by similar insertion modes.

2.2.4. Substrate Scope: Chiral Substrates. The impact of substrate chirality is critical to applications in asymmetric synthesis. As depicted in Table 5, diboration of alkenes containing β-hydrocarbon stereocenters resulted in highly diastereoselective reactions, regardless of the enantiomer of ligand employed (product **25** and **26**). Catalyst control is also the primary stereochemical influence when a methylated hydrocarbon stereocenter is situated adjacent to the reacting alkene (compounds **27** and **28**). However, there is a small level of double diastereodifferentiation such that a mismatched pairing provided a 12:1 dr of **27**, whereas the matched case provides **28** with 20:1 dr. Substrates bearing oxygenated α-

Table 5. Diastereoselective Diboration of Chiral Substrates[a]
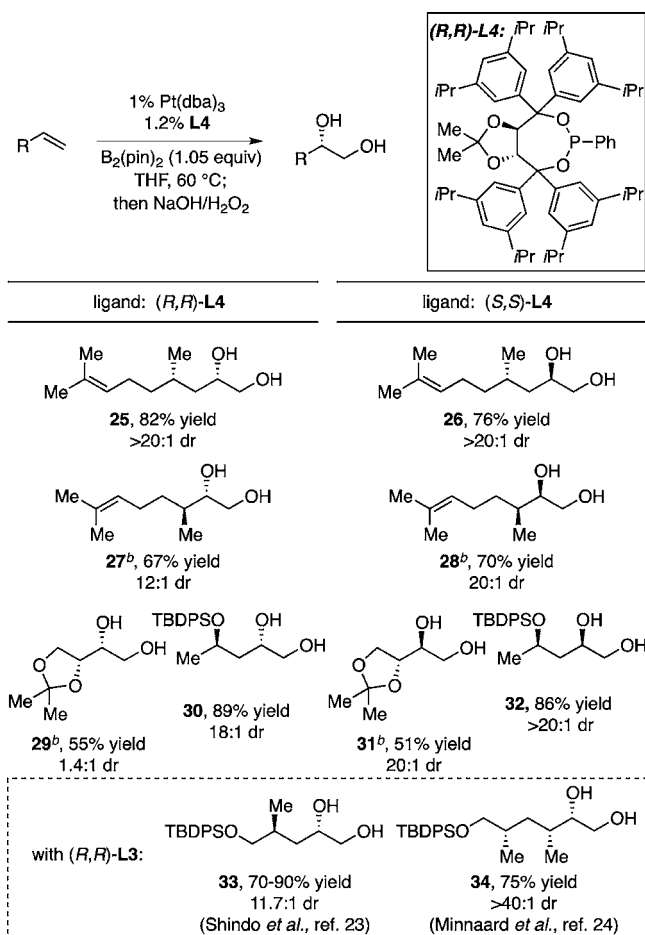
[a]Unless otherwise stated, reactions were conducted at 1.0 M substrate concentration for 3 h as described in the text. Yield refers to isolated yield of the purified reaction product. Diastereomer ratio (dr) determined by ^1H NMR analysis. [b]3.0% Pt(dba)$_3$ and 3.6% (R,R)- or (S,S)-**L4** was employed with reaction at 60 °C for 12 h.

stereocenters exhibited much more pronounced differences between matched and mismatched stereoisomers (products **29** and **31**). However, the influence of oxygenated stereocenters is diminished as the stereocenter is more remote from the alkene such that the stereochemistry in products **30** and **32** is largely controlled by the catalyst. Compounds **33** and **34** depict examples reported in total synthesis efforts from the laboratories of Shindo[23] and Minnaard,[24] respectively, that indicate that high levels of stereoinduction can be obtained with other oxygenated chiral substrates.

2.2.5. Substrate Scope: Unreactive Substrates. A list of unreactive substrates is provided in Figure 2. Addition of a single additional alkene substituent is sufficient to prevent
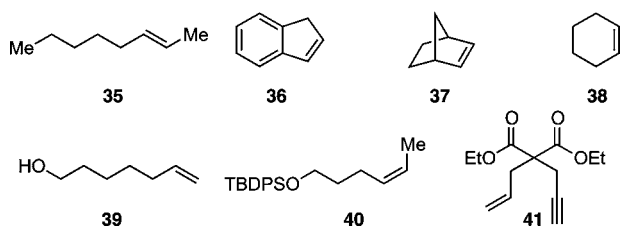

Figure 2. Unreactive diboration substrates.

alkene diboration, even with increased heating and catalyst concentration. This effect occurred for both *cis*-and *trans*-alkenes and those that are strained or aromatic. Interestingly, terminal alkynes do not undergo diboration and the presence of an alkyne is sufficient to poison the reaction of terminal alkenes. This effect operates whether the alkyne is tethered to the alkene (**41**) or simply present in solution (i.e., a 1:1 mixture of 1-tetradecyne and 1-tetradecene yielded no diboration of either substrate). It is reasonable to conclude that the more π-acidic alkyne may bind tightly to the catalyst, preventing either oxidative addition of B$_2$(pin)$_2$ or alkene binding. Lastly, it should be noted that the presence of an unprotected alcohol caused the reaction to take a different course with the alkene undergoing hydroboration.

2.3. Mechanistic Analysis. To provide a general understanding of the outcome of Pt-catalyzed enantioselective alkene diboration reactions and to provide directions for reaction modification when the need arises, a study of the reaction mechanism was undertaken. Our analysis makes the assumption that, like other Pt-catalyzed diborations, the catalytic cycle includes the following steps: insertion of a Pt(0) complex into the B—B bond of B$_2$(pin)$_2$,[5,25] olefin insertion into a Pt—B bond, and reductive elimination to furnish the product.[26]

2.3.1. Reaction Progress Kinetic Analysis. To learn how the reaction rate responds to changes in reaction conditions, experiments involving the diboration of 1-tetradecene were analyzed. The reaction rates were monitored by calorimetry and followed over the entire course of the reaction.[27] Under standard initial reaction conditions ([substrate] = 1 M, [B$_2$(pin)$_2$] = 1.05 M, 1 mol % Pt(dba)$_3$, 1.2 mol % **L4**) the diboration of 1-tetradecene was complete in 3 h with a heat flow/time profile as depicted above in Figure 1. Reaction rate data from the calorimeter was corroborated by GC analysis versus an internal standard. When the data in Figure 1 is integrated (see Figure 3A; plot of reaction rate versus substrate concentration), it becomes apparent that, although not quite zero order, the rate does not change substantially over the first ∼60% of the reaction. Also depicted in Figure 3A, when the initial concentrations of both B$_2$(pin)$_2$ and 1-tetradecene are increased to 1.5 M, the reaction rates were largely unaffected and critically, the rate of this reaction, when at 1 M substrate concentration (i.e., at 33% conversion), is nearly identical to the rate of the reaction initiated at 1 M substrate concentration. This feature suggests that catalyst decomposition and product inhibition are not significant complicating features to this process.

As depicted in Figure 3B, doubling the catalyst loading leads to a 2-fold increase in the reaction rate indicating first-order dependence of the rate on catalyst concentration. Heat flow versus time profiles for reactions that employ excess alkene and excess B$_2$(pin)$_2$ are depicted in parts C and D of Figure 3. From the data in Figure 3C, it appears that the reaction rate exhibits slight positive order dependence on B$_2$(pin)$_2$ concentration. Increased alkene concentration (Figure 3D) appears to be inconsequential to the reaction rate at early stages of the reaction. At later stages of the reaction, the heat flow is enhanced with excess alkene and the reaction provides higher overall heat output. This feature may be an artifact of exothermic isomerization of the terminal alkene to internal alkenes, a process that begins to occur as B$_2$(pin)$_2$ is consumed (in the absence of B$_2$(pin)$_2$ isomerization of 1-tetradecene to 2-tetradecene occurs in >95% conversion). When the initial alkene concentration is reduced to 0.7 M, the overall heat
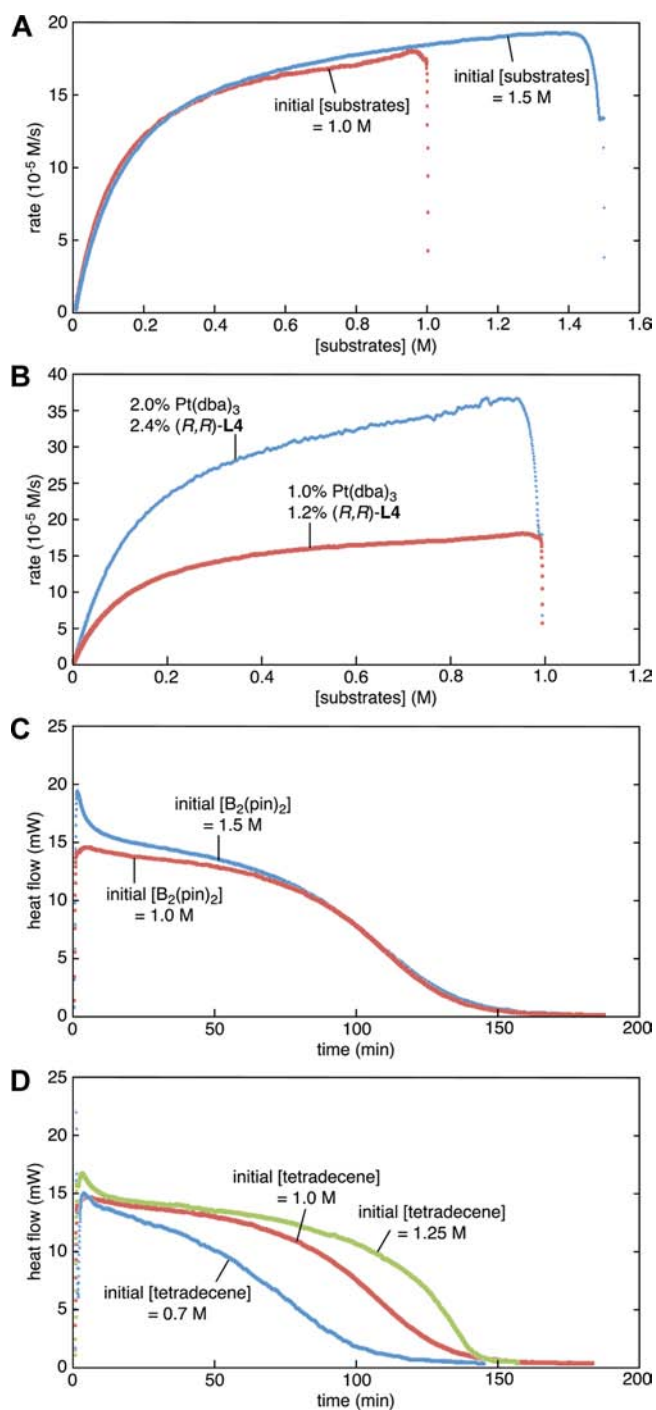
Figure 3. Reaction progress kinetic analysis of the catalytic enantioselective diboration of 1-tetradecene. (A) Reaction rate versus substrate concentrations. [Alkene]= [$B_2(pin)_2$] for both 1.0 M (red) and 1.5 M (blue) reactions, with (R,R)-**L4**: Pt(dba)$_3$ = 1.2: 1.0. (B) Absolute reaction rate versus [alkene], employing 1.2 mol % (R,R)-**L4** and 1.0 mol % Pt(dba)$_3$ (red), 2.4 mol % (R,R)-**L4** and 2.0 mol % Pt(dba)$_3$ (blue). (C) Heat flow versus time of normal diboration reaction conditions (red) and with excess $B_2(pin)_2$ (blue). (D) Heat flow versus time of normal diboration reaction conditions (red), with excess alkene (green), and with 0.7 M alkene (blue).

output is 70% of the stoichiometric experiment whereas the initial rate is comparable.

Collectively, the kinetic data suggests that over most of the reaction course, alkene diboration catalyzed by Pt(dba)$_3$ and **L4**

is close to zero-order in both substrates. This feature of the reaction suggests that the most significant step kinetically is likely an elementary transformation that, in some manner, involves a Pt complex that is already loaded with $B_2(pin)_2$ and the alkene. Although a number of mechanisms would give rise to these observations, a scenario that is consistent with reported computational and experimental studies is depicted in Scheme 4. In this proposal, oxidative addition of $B_2(pin)_2$ to an L$_n$Pt(0)

Scheme 4
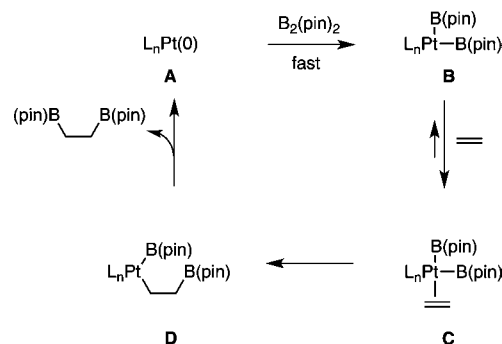
complex (**A** → **B**) is fast and followed by alkene association to give **C**. With this sequence of steps, the reaction would exhibit near zero-order dependence on substrate concentration if the turnover-limiting step was either **C**→**D** (i.e., reversible alkene binding strongly favors the olefin complex and migratory insertion is rate-limiting) or **D**→**A** (reversible migratory insertion precedes rate limiting reductive elimination). An equally tenable hypothesis would arise from a cycle where olefin coordination precedes oxidative addition.

2.3.2. Natural Abundance ^{13}C Kinetic Isotope Effects. We have been unable to gain useful information about catalytic intermediates by NMR spectroscopy. As an alternative approach to determine whether migratory insertion might be rate-limiting and stereochemistry-determining or whether reductive elimination controls the product configuration, ^{13}C kinetic isotope effects for the alkene substrate were examined. These experiments were conducted using methods developed by Singleton for natural abundance kinetic isotope effect (KIE) analysis.[28] With allylbenzene as a probe substrate, two diborations were conducted on a 1.5 g scale using standard conditions and stopped at 81 ± 3 and 83 ± 3% conversion. After recovery of starting material, ^{13}C NMR analysis with a 125 s relaxation delay was conducted and the integrations relative to C-4 found to be as depicted in Scheme 5. Although the ^{12}C/^{13}C KIEs for the allylic carbon and aromatic carbons are negligible, a substantial isotope effect is observed at both olefinic carbons. This observation appears most consistent with olefin migratory insertion being the first irreversible step in the cycle and suggests that addition of a Pt—boryl across the π-system is the stereochemistry-determining step of the reaction. Were migratory insertion reversible[29] with the reductive elimination controlling the rate (and therefore stereochemistry) of the reaction, a sizable KIE at only one carbon would be expected. It merits mention that the magnitude of the ^{12}C/^{13}C KIEs are comparable to those measured by Landis for Ziegler—Natta polymerization of 1-hexene.[30] In the Landis study, it was argued that olefin migratory insertion into a Zr—alkyl is the turnover-limiting step.
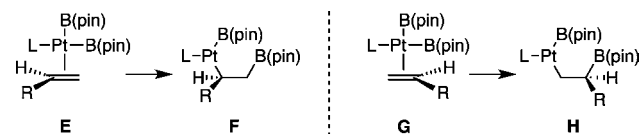
2.3.2.1. Regioselectivity of Olefin Insertion: Experiments. The studies above suggest that olefin insertion is likely the

Scheme 5

Scheme 6

Scheme 7
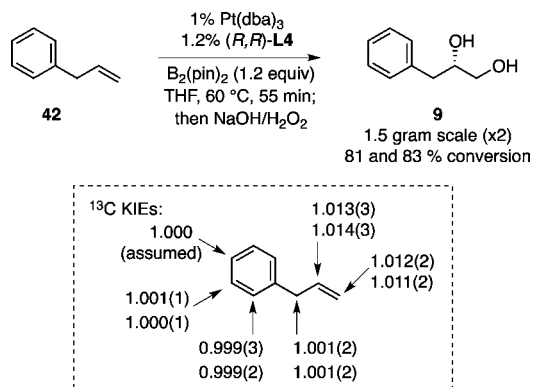
stereocontrolling step of alkene diborations. Development of a stereochemical model for this reaction will therefore depend on understanding the regioselectivity of this step. Although an olefin insertion that positions Pt at the internal carbon (**E → F**, Scheme 6) would appear to be more hindered than the alternative pathway (**G → H**), it explains two features: first, this insertion mode positions the prochiral carbon of the alkene much closer to the chiral ligand and can more easily explain the high enantioselectivity for the diboration process; second, if **G → H** were the favored insertion mode for aliphatic alkenes, then one might expect significantly different selectivity with aromatic alkenes where π-benzyl stabilization in **F** might increase the extent of reaction through this alternate mode.

An experiment consistent with the conjecture that olefin insertion positions Pt at the internal position is depicted in Scheme 7. When vinyl cyclopropane **43** was subjected to
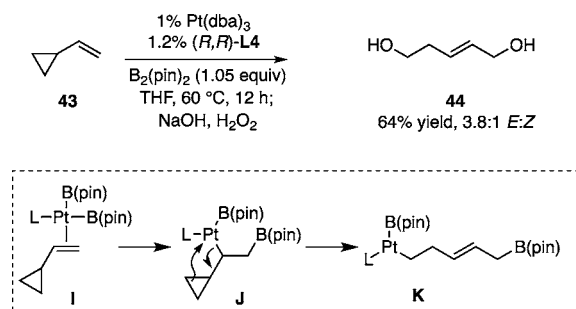
conditions for catalytic enantioselective diboration, ring-opened bis(boronate) **44** was obtained as the exclusive reaction product. As shown in the inset, a reasonable pathway for production of **44** involves borylplatination of the alkene in a manner that gives the internal C−Pt bond (**I → J**, Scheme 7 inset) subsequent rupture of the adjacent cyclopropane (**J → K**) and reductive elimination would deliver **44**. An analogous ring-opening was observed by Miyaura in the diboration of methylene cyclopropanes and was attributed to rupture of an α-

cyclopropyl organoplatinum complex.[31] Cyclopropane ring-opening pathways involving similar intermediates have also been previously reported by Lautens in the palladium-catalyzed hydrostannation[32] and by Beletskaya using rhodium-catalyzed hydrosilation.[33] Importantly, the proposed internal insertion mode is not without precedent in group 10 metal-catalyzed reactions.[34]

2.3.2.2. Regioselectivity of Olefin Insertion: Computations. Further evidence suggesting that olefin migratory insertion in the (alkene)Pt[B(pin)]$_2$ complex occurs to give an internal C−Pt bond was gained by density functional theory (DFT) calculations on a simplified system. As depicted in Figure 4, the
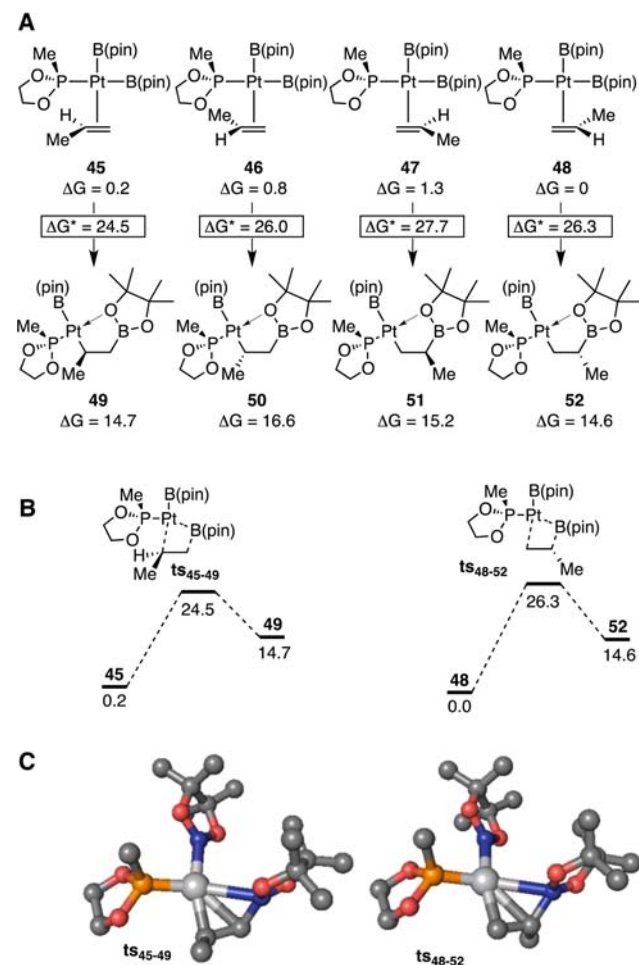

Figure 4. (A) Relative energetics of migratory insertion involving bis(boryl)platinumpropene complexes. (B) Energy profile for the migratory insertion of **45** and **48** to give **49** and **52**. (C) Calculated transition state structures for conversions to **45 → 49** and **48 → 52**. All free energies (computed at 333K) are in kcal/mol and are relative to **48**.

reactions of four isomeric bis(boryl)Pt·propene complexes (**45−48**, Figure 4A) were examined using DFT.[35] Complexes **45−48** employ an ethylene glycol-derived methyl phosphonite as a model for ligand **L4** and vary by the nature of the alkene coordination: complexes **45** and **48** are rotational isomers with the alkene binding through the *Re* face, whereas isomers **46** and **47** contain the alkene bound through its *Si* face. Of the four complexes, there was no strong preference for any alkene orientation with all four being within 1.3 kcal/mol of each other. Optimization of transition state geometries of each olefin

complex revealed pathways where olefin insertion occurs concomitantly with rotation of the boryl ligand; the rotation allows the pinacol oxygen to begin donating electrons to platinum such that a coordinatively saturated Pt complex is the immediate product of the insertion step in each case (**49**−**52**). These features are analogous to those calculated by Morokuma for the insertion of ethylene.[36] As depicted in Figure 4A, it was found that the two pathways where Pt undergoes bond formation to the internal alkene carbon (**45** → **49** and **46** → **50**) are lower energy paths than those where Pt bonds to the terminal carbon (**47** → **51** and **48** → **52**). The two lowest energy paths for each regioisomer are depicted in Figure 4B along with transition state geometries in Figure 4C. Although the origin of the regiochemical preference is not clear, it is tenable that a larger coefficient of the alkene HOMO resides on the terminal carbon, and overlap between this orbital and the empty p-orbital on boron is relevant during the insertion. Calculations suggest that related interactions operate in palladium-catalyzed alkyne silastannation, a reaction that also occurs by a migratory insertion that provides the internal C−Pd arrangement.[16a,37]

2.4. Model for Stereoselectivity in Alkene Diborations with Pt(dba)₃ and L4. With compelling data indicating that olefin migratory insertion is stereochemistry-determining and provides the internal C−Pt bond, efforts were directed to advance a stereochemical model for this diboration reaction. These studies have been guided by the crystal structure analysis of a *trans*-Cl₂Pt[(*R,R*)-**L2**]₂. This compound was obtained by treatment of PtCl₂ with two equiv of (*R,R*)-**L2** in CDCl₃ at room temperature for 18 h followed by warming to 40 °C for 2 h. ^{31}P NMR analysis showed complete conversion of the ligand (δ = 156.8 ppm) to a new complex (δ = 105.2 ppm). Slow crystallization from CDCl₃ provided crystals suitable for X-ray analysis, an ORTEP representation of which is depicted in Figure 5. The unit cell contains two molecules of the complex in nearly identical conformations, and within each molecule of complex, both ligands adopt a similar conformation. Parts B and C of Figure 5 depict "front" and "top" views of the complex with the substituents from one phosphorus ligand removed. From these views it appears that the platinum atom sits directly on top of one of the taddol aromatic rings.

Should the conformation of the ligand that is represented in Figure 5 persist during the course of the catalytic cycle, it is tenable that subsequent to insertion of Pt into the B−B bond of B₂(pin)₂, alkene coordination may occur in a manner depicted in Figure 6. This orientation is consistent with the hypothesis that insertion provides the internal C−Pt bond, and if interactions with the taddol aryl ring are minimized, it would directly lead to the observed product enantiomer. Additional studies that probe the nuances of these interactions are clearly warranted and will be described in due course.

3. CONCLUSION

In conclusion, we have described the optimization of reaction conditions and the scope of the platinum-catalyzed enantioselective diboration of terminal alkenes. Mechanistic experiments indicate that this reaction occurs by stereochemistry-determining olefin insertion that furnishes an internal C−Pt bond.
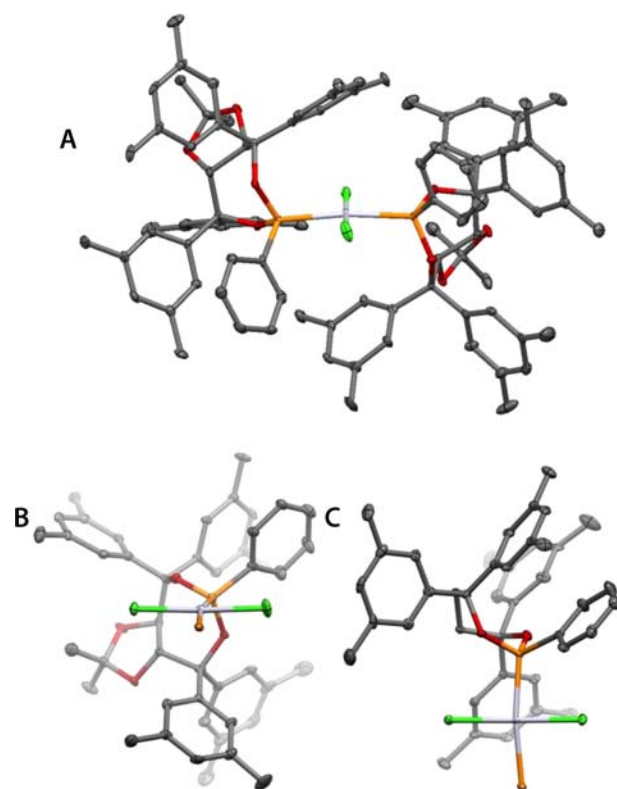

Figure 5. (A) ORTEP of *trans*-Cl₂Pt[(*R,R*)-**L2**]₂ with 50% probability ellipsoids. (B) Front view of complex with substituents from one phosphorus ligand removed. (C) Top view of complex with substituents from one phosphorus ligand and the dioxolane removed for clarity.
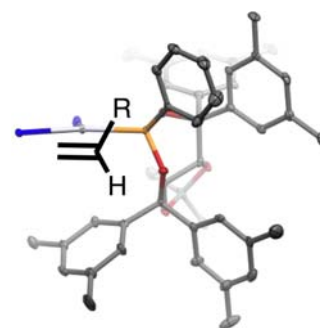

Figure 6. Hypothesis for the stereochemical outcome in enantioselective diborations.

■ ASSOCIATED CONTENT

ⓢ Supporting Information
Procedures, characterization, spectral data, and computational details and crystal data in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes
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