On Titanium-Promoted Hydroborations of Alkenes by Borohydride and by Catecholborane

Kevin Burgess* and Wilfred A. van der Donk

Department of Chemistry, Texas A&M University, College Station, Texas 77843

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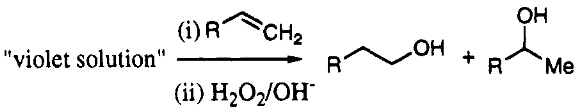
Some literature reports of "catalyzed" hydroborations of alkenes by the borohydride anion and by catecholborane were investigated to probe the actual mode of hydroboration. Reactions involving both $TiCl_3$ and $Ti(O^iPr)_4$ seems to involve predominantly formation of BH_3 *in situ*, although there is some evidence that the metal may be directly involved in a few cases. Ambiguity arises because it is shown that alkyl boronate esters can be formed by exchange between catecholborane and alkylboranes, so formation of these esters is not firm evidence of catalysis.

Introduction

There have been several reports of "catalyzed hydroborations of alkenes" mediated by titanium complexes. For instance, in previous work we have investigated the puzzling set of reactions previously reported to be Cp_2TiCl_2-catalyzed hydroborations of alkenes by borohydride.[1,2] We now envisage them as the Lewis acid promoted decomposition of borohydride to diborane, conventional (uncatalyzed) hydroboration, then, under some circumstances, titanium-to-boron alkyl transfer to give tetraalkylborates (Scheme 1).

Additions of borohydride to alkenes also have been reported to be promoted by $TiCl_3$ (eq 1).[3] We were curious about the nature of this reaction, particularly with respect to the similarities with the series of events shown in Scheme 1. In this manuscript we describe some experiments to characterize the role of the metal salt in these, and related,[4−6] reactions.

$$0.2\,TiCl_3 + 0.2\ \text{18-crown-6} + 1.0\,NaBH_4 \xrightarrow[1\ h]{THF,\ 30\ °C}$$

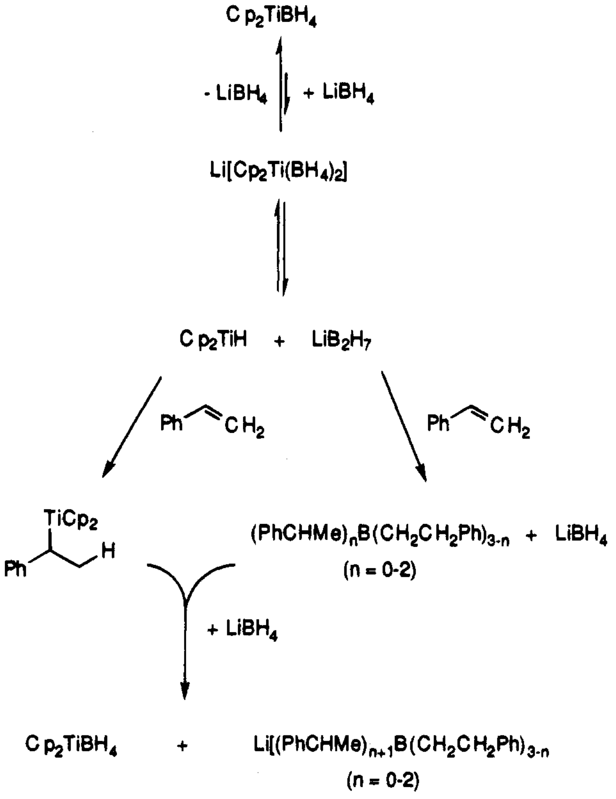


(1)

Hydroboration Systems from Titanium(3+) Chloride and Borohydride

This work began with a ^{11}B NMR study of the reaction of $TiCl_3$ with lithium borohydride. Titanium complexes formed in this reaction are paramagnetic and NMR inconspicuous, so only the noncomplexed boron containing products were evident (eq 2). Nevertheless, this experiment was informative since it showed that $BH_3·THF$ (with $B_2H_7^-$ and BH_4^-; all peaks broadened by exchange processes) was formed after 3.5 h at 30 °C.

Scheme 1. Proposed Mechanism for the Formation of Tetraalkylborates in the $Cp_2Ti(\mu\text{-}H)_2BH_2$-Mediated Hydroboration of Phenylethene



$$0.2\,TiCl_3 + 1.0\,LiBH_4 \xrightarrow{THF,\ 30\ °C,\ 3.5\ h} \underbrace{BH_3 + B_2H_7^- + BH_4^-}_{\text{observed by }^{11}B\text{ NMR}} \quad (2)$$

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(2) Burgess, K.; van der Donk, W. A. *Tetrahedron Lett.* **1993**, *34*, 6817.

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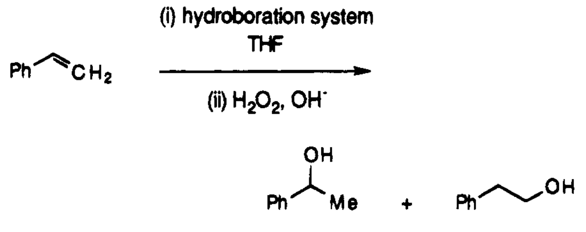
Borane was therefore implicated as the active hydroborating agent.

Further experiments were performed to identify the organoboron products formed in the $TiCl_3$-promoted reactions, to check that they were derived from BH_3 as asserted above. Titanium trichloride (0.2 equiv) was treated with 1.1 equiv of $LiBH_4$ in THF, for 1 h at 30 °C; phenylethene (1.0 equiv) then was added, and the ^{11}B NMR was recorded after 12 h at 30 °C. Trace amounts of tetraalkylborates were observed, but the only other signal was an extremely broad peak corresponding to BH_4^-. The fact that alkylboranes were not observed was of little consequence because exchange processes can cause a disappearance of the appropriate ^{11}B NMR peaks for these compounds.[1] However, alkylboranes that are hidden by such exchange processes can be converted to alkylborohydrides *in situ* by adding $LiAlH_4$, and thereby visualized.[1] Indeed, when the mixture described above was "quenched" with $LiAlH_4$/DABCO,[7,8] the ^{11}B NMR was identical to that of BH_3 reacted with phenylethene when quenched with $LiAlH_4$/DABCO. Furthermore, the ratio of the two regioisomeric alcohols formed after oxidation ($PhCH_2CH_2OH$ and PhCH(OH)Me) was 4:1, very close to that observed for the conventional hydroboration of phenylethene with BH_3 (eq 3). On the basis of these observations, it seems extremely likely that BH_3 is the active hydroborating agent.



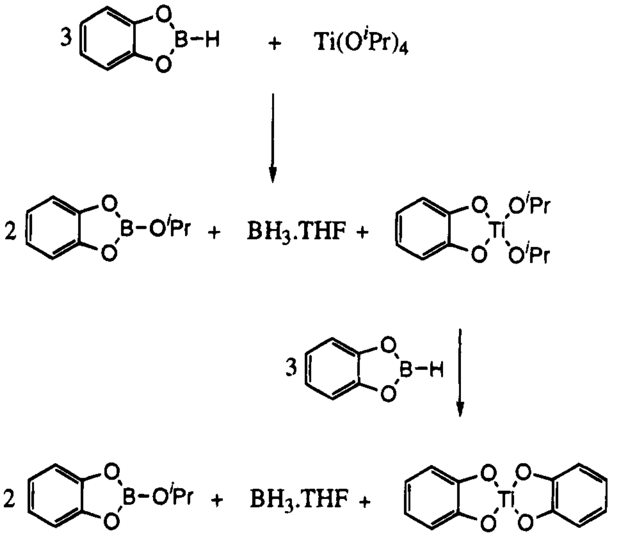
(3)

hydroboration system	*2':1'*
20 mol % $TiCl_3$, 1.1 $LiBH_4$, 30 C, 12 h	20:80
BH_3, THF, 0 °C, 3 h	17:83

An interesting issue arises from the reaction studied above: in the presence of excess borohydride, most of the BH_3 produced by disproportionation would exist as $B_2H_7^-$, yet it was not clear that this is a hydroborating agent. An experiment therefore was undertaken to test if LiB_2H_7 could hydroborate alkenes in the absence of other additives. It was shown that LiB_2H_7 (formed *in situ* from BH_3 and excess borohydride) does indeed hydroborate phenylethene. Presumably, trace BH_3 is the active hydroborating agent, formed in small amounts *via* disproportionation of $B_2H_7^-$ in an equilibrium process which shifts to compensate for consumption of BH_3.

Appreciable amounts of tetraalkylborates and trialkylborohydrides were formed in the $TiCl_3$-mediated reactions after 36 h at 65 °C if excess phenylethene was added. This behavior is reminiscent of the Cp_2TiCl_2 promoted hydroborations of phenylethene (Scheme 1)[1] and may involve alkyl transfer reactions similar to those observed in zirconium chemistry.[9] Formation of tetraalkylborates in the $TiCl_3$-promoted reaction of phenylethene with borohydride at 65 °C, but not at 30 °C, indicates that similar processes involving alkyl transfer form titanium to boron occur only at elevated temperatures in these reactions.

Scheme 2. Possible Formation of $Ti(O_2C_6H_4)_2$ from Catecholborane and $Ti(O^iPr)_4$



Hydroboration Systems from Titanium Tetraisopropoxide and Catecholborane

Disproportionation reactions involving catecholborane are a major obstacle to development of systems for highly stereoselective rhodium-catalyzed hydroborations of alkenes.[10] Screening experiments to identify alternative systems for accelerating addition of catecholborane to alkenes showed that $Ti(O^iPr)_4$ gave alcohols after oxidation, whereas control experiments without this metal alkoxide gave no observable hydroboration products.

Experiments were performed to investigate the origin of hydroboration in catecholborane additions promoted by $Ti(O^iPr)_4$. When $Ti(O^iPr)_4$ was treated with catecholborane in THF, the solution rapidly turned deep red, and a red solid could be isolated after removal of solvent and excess catecholborane under reduced pressure. The ^{13}C NMR spectrum of this material corresponded to that published previously for $Ti(O_2C_6H_4)_2$,[11] although resolutions in these spectra were poor due to paramagnetism caused by electron transfer from the aromatic catechol moieties to the metal center.

The ^{11}B NMR spectrum of the reaction mixture from $Ti(O^iPr)_4$ and catecholborane showed that, besides $Ti(O_2C_6H_4)_2$, $BH_3{\cdot}THF$ and $^iPrOBO_2C_6H_4$ were also formed (the latter borate was prepared by reaction of catecholborane with ^iPrOH for comparison). A possible rationale for these results is the disproportionation reaction shown in Scheme 2.

Further evidence for the postulate shown in Scheme 2 was obtained by monitoring the progress of the reaction by multinuclear NMR. The ^{13}C NMR spectrum

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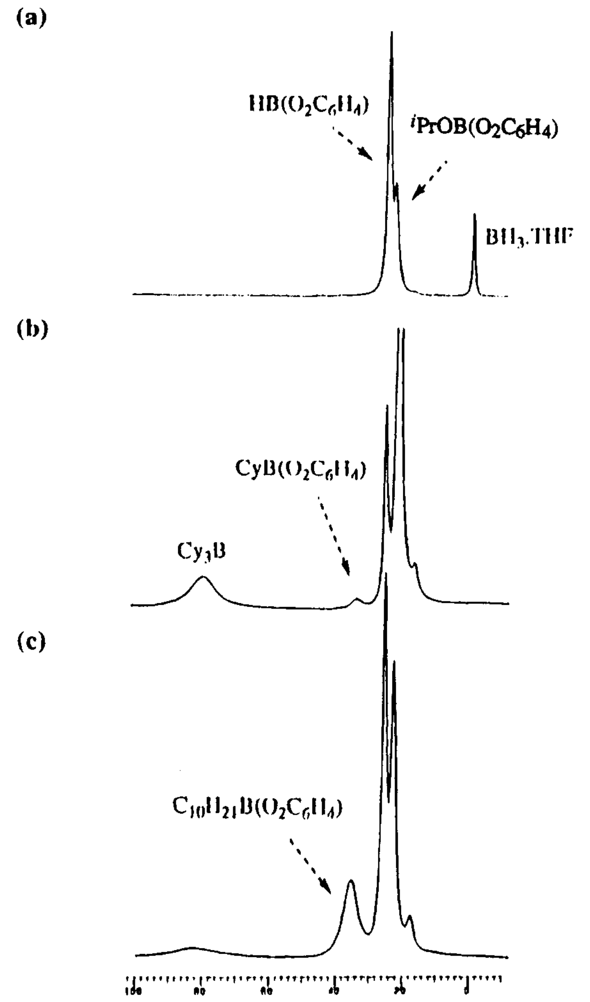
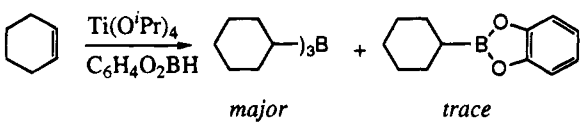


Figure 1. Proton–boron decoupled ^{11}B NMR spectra from (a) 1.0 equiv of Ti(O^{i}Pr)$_4$ and 6.0 equiv of catecholborane after 6 h, (b) 0.1 equiv of Ti(O^{i}Pr)$_4$, 1.5 equiv of catecholborane, and 1.0 equiv of cyclohexene after 12 h, and (c) 0.1 equiv of Ti(O^{i}Pr)$_4$, 1.5 equiv of catecholborane, and 1.0 equiv of 1-decene after 12 h.

revealed immediate consumption of Ti(O^{i}Pr)$_4$ and initial formation of ^{i}PrOBO$_2$C$_6$H$_4$ and a species that produces two new signals (δ 24.8 and 68.1 ppm). The intensities of the two unassigned signals in the ^{13}C NMR decreased with time, eventually fading into the baseline after 6 h. This unknown reaction intermediate was only observed in the ^{13}C NMR. It could be (^{i}PrO)$_2$Ti(O$_2$C$_6$H$_4$), the initial product from redistribution of the ligands on boron and titanium; however, we were unable to check this easily because mixtures of Ti(O^{i}Pr)$_4$ and (HO)$_2$C$_6$H$_4$ did not provide a convenient route to an authentic sample of this complex. During the same time period, the ^{11}B NMR of this reaction in THF showed signals for ^{i}PrOBO$_2$C$_6$H$_4$ (23.1 ppm), catecholborane (doublet, 26.0 ppm), and BH$_3$·THF (quartet, 0.2 ppm) (Figure 1a). The intensity of the resonance corresponding to BH$_3$·THF slowly increased and an additional signal with a relatively low intensity corresponding to B$_2$(O$_2$C$_6$H$_4$)$_3$ was observed also.

A series of reactions were performed to identify the organoboron products of the catecholborane additions accelerated by Ti(O^{i}Pr)$_4$. ^{11}B NMR spectra recorded 12 h after 1.5 equiv of catecholborane was added to a mixture of 1.0 equiv of cyclohexene and 0.1 equiv of Ti(O^{i}Pr)$_4$ indicated that the major product of this reaction was Cy$_3$B, with only a very minor trace of CyB(O$_2$C$_6$H$_4$)$_2$ (eq 4, Figure 1b). However, when the same procedure



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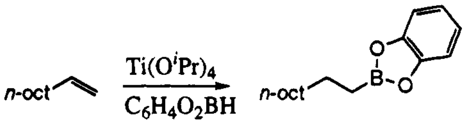

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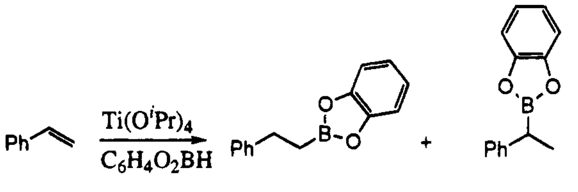

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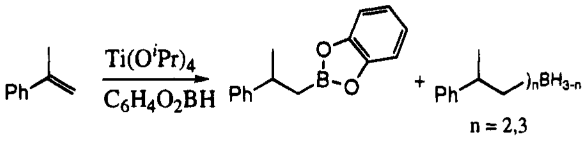

(7)

was repeated with 1-decene as the substrate, the major product appeared to be n-C$_{10}$H$_{21}$B(C$_6$H$_4$O$_2$) and some B(n-C$_{10}$H$_{21}$)$_3$ (*ca.* 82 ppm) was observed (eq 5, Figure 1c). Two more substrates were subjected to the reaction conditions: phenylethene showed predominant formation of the boronic ester product, and 2-phenylpropene produced about equal quantities of alkyl boronates and tri- and dialkylboranes (eqs 6 and 7).

Data from eqs 4–7 suggest a competition between titanium-catalyzed addition of catecholborane to alkenes and hydroboration of the substrates by BH$_3$·THF, produced *via* redistribution of boron and titanium ligands. For fast reacting monosubstituted alkenes such as 1-decene and phenylethene the predominant products appear to be formed *via* addition of catecholborane, while reactions with the less reactive, disubstituted alkenes 2-phenylpropene and cyclohexene result in significant quantities of alkylboranes from BH$_3$ hydroboration.

Experiments were undertaken to check that trialkylboranes were not formed from alkyl boronate esters under the Ti(O^{i}Pr)$_4$-mediated reaction conditions. This was a particular concern because, if this exchange occurred, observation of trialkylboranes would not prove that hydroboration of the substrates occurred *via* BH$_3$ formed *in situ*. Thus, cyclohexene was hydroborated at 100 °C with catecholborane,[12,13] the crude product was purified by vacuum distillation, and 1.0 mmol of this compound was added to 0.1 mmol of Ti(O^{i}Pr)$_4$ in 2 mL of THF. Catecholborane was then introduced and the reaction mixture was analyzed by ^{11}B NMR after 12 h at 25 °C. This spectrum showed signals corresponding to BH$_3$·THF, catecholborane, ^{i}PrOB(O$_2$C$_6$H$_4$), and CyB(O$_2$C$_6$H$_4$). No trialkylboranes were observed, indicating that Cy$_3$B produced in Ti(O^{i}Pr)$_4$-mediated hydroboration of cyclohexene was not derived from the initially formed boronate ester CyB(O$_2$C$_6$H$_4$) (eq 8).

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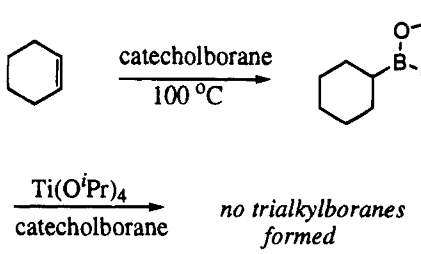
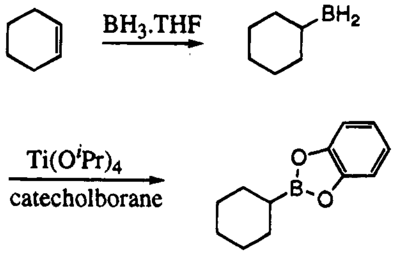


(8)

In contrast to the results in eq 8, it was shown that alkyl boronate esters can be formed from BH_3-derived hydroboration products. Thus, cyclohexene and 1-decene were separately hydroborated with an excess of BH_3, and then, after complete consumption of the substrate (GC), 0.1 equiv of Ti(O^{i}Pr)$_4$ and 1.5 equiv of catecholborane were added. The crude reaction mixtures were analyzed by ^{11}B NMR after 11 h at 25 °C. The monoalkylboranes RBH_2 formed after the hydroboration were cleanly converted into the corresponding boronate esters (eqs 9 and 10).



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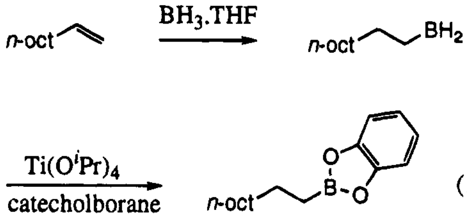

(10)

Conclusion

Any system which promotes hydroboration by degradation of a boron hydride to borane (or any other reactive borane) really provides a method for formation of BH_3 *in situ*, rather than a true "catalyzed hydroboration". Catalyzed hydroborations wherein additions of a boron hydride to an alkene is really metal catalyzed are valuable because they provide different chemo-, regio-, and stereoselectivities to conventional hydroborations using reactive boranes in the absence of any catalyst.[14] The distinction between formation of BH_3 *in situ* and catalyzed hydroboration is therefore important. Reports of new systems for catalyzed hydroborations should be supported by data for the primary organoboron products; formation of alcohols after oxidation of the organoboron products is not a reliable indication of catalysis.[15,16]

We conclude from the results presented above that combination of borohydride with $TiCl_3$ provides BH_3 *in situ*. Some evidence for conversion of trialkylborane to tetraalkylborates was observed in isolated cases; nevertheless, these reactions are of very limited value for organic syntheses. On the basis of these results we expect that combinations of BH_4^- and titanium *tetrachloride* would give very similar results. Indeed, the reaction of borohydride with titanium tetrachloride has been reported to give a titanium–borane complex and diborane (eq 11).[17,18] On the basis of these results we suspect that "new" hydroboration systems formed from $TiCl_4/BH_4^-$ involve, at least in part, reactions of BH_3 *in situ*.[4,5]

$$2\,TiCl_4 + 8\,LiBH_4 \xrightarrow{Et_2O,\ 25\ ^\circ C} 2\,Ti(BH_4)_3 + 8\,LiCl + H_2 + B_2H_6 \quad (11)$$

Hydroborations by catecholborane promoted by Ti(O^{i}Pr)$_4$ appear to proceed predominantly *via* formation of BH_3 *in situ* for slow reacting alkenes, although fast reacting substrates like 1-decene may react *via* a genuine catalytic pathway. Equations 9 and 10 show it is possible that monoalkylboranes can be converted to alkyl boronate esters under the conditions of these reactions; so observation of an alkyl boronate ester is not firm evidence for catalysis in these reactions. Conversely, the ratios of the reagents in the experiments depicted in eqs 9 and 10 were necessarily different from those in the Ti(O^{i}Pr)$_4$ processes; for this reason these observations do not rule out catalysis in the latter transformations. Indeed, if catalysis is not involved in the 1-decene reaction, it is remarkable that the monoalkylborane from 1-decene (which should rapidly hydroborate other 1-decene molecules) undergoes exchange with catecholborane, while $CyBH_2$ (a much less reactive hydroborating agent) does not. On the basis of this observation, it seems Ti(O^{i}Pr)$_4$ may accelerate addition of catecholborane to some (fast reacting) substrates in a process that competes with disproportionation and then conventional hydroboration. A recent paper[6] reported on combinations of catecholborane and Ti(O^{i}Pr)$_4$ with respect to new hydroboration methodology for organic syntheses.[19] We conclude that the value of any catecholborane/Lewis acid combination in new hydroboration methodology is questionable unless supported by extensive mechanistic data.

Experimental Section

General Procedures. High field NMR spectra were recorded on a Varian XL 200 (^{11}B at 64.2 MHz, ^{13}C at 50 MHz). ^{11}B chemical shifts are reported in ppm relative to the external standard $BF_3{\cdot}OEt_2$ (0.00 ppm). Quartz NMR tubes for ^{11}B NMR and coaxial inserts were purchased from Wilmad Glass. ^{11}B NMR spectra of crude reaction mixtures were taken with the coaxial insert charged with benzene-d_6 and $BF_3{\cdot}Et_2O$ for locking and reference purposes or after addition of a small amount of degassed, dry benzene-d_6 to the reaction mixture. THF was distilled immediately before use from sodium benzophenone ketyl. Alkenes were purchased from commercial suppliers and distilled prior to use. Solutions of $LiBH_4$ and

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(19) We thank Professor D. A. Evans, Harvard, for informing us that the Ti(O^{i}Pr)$_4$ promoted hydroboration of 1-decene affords an alkylboronate ester.

$LiAlH_4$ in THF, titanium trichloride, titanium tetraisopropoxide, and catecholborane were purchased from Aldrich Chemical Co. The titanium isopropoxide and catecholborane were distilled under reduced pressure before use.

General Procedure for $TiCl_3$-Promoted Hydroboration of Alkenes. A Schlenk tube was charged with 68 mg (0.44 mmol, 0.2 equiv) of $TiCl_3$ inside a glovebox, and the tube was transferred to a vacuum line and placed under an atmosphere of argon. THF (1 mL) was added, followed by 1.1 mL of a 2.0 M solution of $LiBH_4$ in THF. The reaction mixture was stirred for 1 h at 30 °C, and a white fine precipitate was observed. Substrate (2.0 mmol) and internal standard were then introduced in 1.5 mL of THF, and the progress of the reaction was followed by GC. After complete consumption of the substrate half of the crude reaction mixture was analyzed by ^{11}B NMR, while the other half was treated with $LiAlH_4$ and DABCO at −40 °C.[20,21] After standing at 25 °C without stirring for 12 h, the clear supernatant solution was analyzed by ^{11}B NMR.

General Procedure for $Ti(O^iPr)_4$-Catalyzed Hydroboration of Alkenes. A Schlenk tube was evacuated/flushed with argon (3×), 1 mmol of freshly distilled substrate was introduced followed by 3 mL of THF. Distilled titanium isopropoxide (0.1 mmol) was then added by microsyringe, and the colorless reaction mixture was stirred for 10 min at 25 °C prior to the addition of 1.5 mmol of catecholborane. Immediately upon addition, the reaction mixture turned deep red. The solution was stirred for 12 h and then analyzed by ^{11}B NMR.

^{11}B NMR Data for Equations 4–6. In all cases an authentic sample was prepared by hydroborating the appropriate alkene with either BH_3 or catecholborane (at elevated temperature). Chemical shifts δ (ppm) relative to $BF_3{\cdot}OEt_2$: eq 4, BCy_3 81.7, $CyBO_2C_6H_4$ 36.8; eq 5, (n-decene)-$BO_2C_6H_4$ 36.1; eq 6, both isomers of $PhC_2H_5BO_2C_6H_4$ overlap at 36.9.

Note Added in Proof. Just prior to publication, a paper appeared that also described the reactions of catecholborane with $Ti(O^iPr)_4$ (Lindsley, C. W.; DiWare, M. *Tetrahedron Lett.* **1994**, *35*, 5141). It was reported that $HB(O^iPr)_2$ was formed in addition to the products described above, but formation of BH_3 was not observed. It is important that different ratios of starting materials were used in our work and in that by Lindsley *et al.* Nevertheless, the ^{13}C NMR signals at 24.8 and 68.1 ppm observed in early stages of our experiments could be attributed to this $HB(O^iPr)_2$, while the ^{11}B NMR signal for this compound was probably obscured by the relatively large quantities of catecholborane in our reaction mixtures. We speculate that $HB(O^iPr)_2$ is only conspicuous at early time points in the reaction for the ratio of reactants used in our work.

Acknowledgment. We thank Alex Porte for confirming hydroboration of phenylethene with $B_2H_7^-$. Financial support for this work was obtained from the National Science Foundation and The Robert A. Welch Foundation. K.B. is a NIH Research Career Development Awardee and an Alfred P. Sloan Scholar.

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