Hydroboration. 92. Investigation of Practical Methods for the Synthesis of Optically Pure Isopinocampheylchloroborane for the Asymmetric Hydroboration of Representative Prochiral Alkenes

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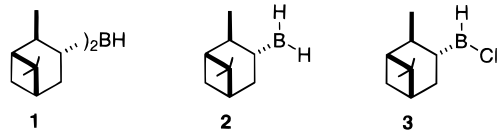
A quantitative study was made of the preparation of the optically pure borane reagent, isopinocampheylchloroborane (IpcBHCl), potentially valuable for asymmetric hydroboration. IpcBHCl (87−90%) in equilibrium with 5−6.5% of $IpcBCl_2$ and $IpcBH_2$, respectively, can be prepared conveniently by a number of relatively simple operations: (1) the reaction of isopinocampheylborane ($IpcBH_2$) with anhydrous hydrochloric acid (HCl) in ethyl ether (EE); (2) the reaction of stoichiometric amounts of $IpcBH_2$ with isopinocampheyldichloroborane ($IpcBCl_2$) in EE; and (3) the reduction of $IpcBCl_2$ with trimethylsilane (Me_3SiH) or lithium aluminum hydride (LAH) in EE. The reduction of $IpcBCl_2$ with Me_3SiH in pentane proceeds extremely slowly to provide the desired reagent, IpcBHCl. However, in EE, the reduction proceeds much faster, providing an equilibrium mixture of 90% IpcBHCl, 5% $IpcBH_2$, and 5% $IpcBCl_2$. We also investigated the reduction of $IpcBCl_2$ with Me_3SiH in pentane and dichloromethane (CH_2Cl_2) in the presence of known amounts of EE, tetrahydrofuran (THF), and dimethyl sulfide (SMe_2), solvents which coordinate with the dichloroboranes. A comparative study of the rate of hydroboration of the alkene, 2-methyl-2-butene, with $IpcBH_2$ and IpcBHCl, obtained as described above, was made in representative solvents, such as pentane, CH_2Cl_2, EE, and THF, at 0 °C and, in many cases, also at 25 °C. This study revealed that the rate of hydroboration is faster in THF for $IpcBH_2$, while for IpcBHCl, the rate is faster in EE. Asymmetric hydroboration of prochiral alkenes was achieved by two methods, *viz.*, IpcBHCl, produced by the reaction of $IpcBH_2$ with HCl in EE (method A), and the reduction−hydroboration reaction of $IpcBCl_2$ with LAH (0.25 equiv) in the presence of the prochiral alkene (method B) in EE. In both methods, the temperature of the reaction mixture was maintained at −25 °C. Almost identical results were realized in these two procedures, with the enantiomeric excess (ee) realized with IpcBHCl, in some cases, considerably better than that achieved with $IpcBH_2$. Although, IpcBHCl was obtained in only 87−90% purity along with $IpcBH_2$ and $IpcBCl_2$ as side products, the presence of the latter compound had no observable effect on the chiral outcome of the asymmetric hydroboration.

Chiral synthesis has become a major focus of interest to achieve the synthesis of optically active compounds of interest. As a result, much emphasis is being given to the synthesis of improved, easily accessible chiral auxiliaries and reagents. The increase in the synthetic methodologies available for chiral syntheses is exemplified by the numerous reviews that have appeared in the literature.[2] We have been pursuing research on chiral syntheses *via* optically pure organoboranes derived from terpenes.[3] The efficacy of a terpene, α-pinene, to provide a general asymmetric synthesis *via* organoboranes is noteworthy.[3] The hydroboration of α-pinene can provide either the chiral dialkylborane (Ipc_2BH, **1**)[4] or the monoalkylborane ($IpcBH_2$, **2**),[5] depending upon the reaction conditions.



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The former reagent (**1**) has been shown to hydroborate sterically less demanding prochiral *cis*-alkenes, providing product alcohols in ≥90% ee.[4] The latter reagent, $IpcBH_2$ (**2**), now in which one of the Ipc groups of Ipc_2BH is replaced by a hydrogen atom, handles hindered prochiral *trans*- and trisubstituted alkenes to give optical inductions ranging from 53 to ≥99%, with the higher values obtained with aryl-substituted alkenes.[5] These results indicate that the effectiveness of these two complimentary reagents depends on their steric requirements. This is also supported by literature reports,[6] based on theoretical calculations, suggesting that the steric bulk and environment around the boron atom in the pinene-based borane reagents are critical for achieving a high degree of stereoselection in asymmetric hydroboration. This has

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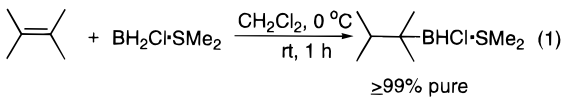
been very well illustrated by the application of the sterically bulkier chiral auxiliaries, readily derived from easily accessible α-pinene, namely 2-ethyl-,[7] 2-*n*-propyl-,[8] and 2-isopropylapopinenes[9] in asymmetric reduction and hydroboration reactions. Thus, these observations and the broad scope of the chiral borane reagents for asymmetric syntheses prompted us to explore the effect of modifying the hydroborating agent by introducing a halogen atom in the BH_2 moiety of the $IpcBH_2$ (**2**) for the asymmetric hydroboration of prochiral alkenes in the hope of optimizing the steric fit between the olefin and the reagent.

This objective initiated research on the synthesis of isopinocampheylchloroborane, (IpcBHCl, **3**), readily produced from the α-pinene by simple reactions to be discussed. Gratifyingly, optically pure IpcBHCl reagent, prepared *in situ* from the reduction of $IpcBCl_2$ with trimethylsilane, proved to be an excellent choice for the asymmetric cyclic hydroboration of 1-allyl-1-cyclohexene providing *trans*-1-decalone in ≥99% ee.[10] Interestingly, hydroboration of 1-allyl-1-cyclohexene with IpcBHCl·EE, obtained from the reaction of equivalent amounts of $IpcBH_2$ with HCl in EE, provided *trans*-1-decalone in only 84% ee.[10] However, preliminary results in the asymmetric hydroboration of bromocycloalkenes with optically pure IpcBHCl reagent provided improved enantioselectivities for the synthesis of bicyclic amines.[11] Moreover, we have recently established that racemic IpcBHCl (**3**) is an effective stepwise hydroborating reagent for the synthesis of unsymmetrical ketones.[12] In order to further understand the chemistry of the IpcBHCl reagent, we decided to study in detail methods of its synthesis and its behavior in asymmetric hydroboration. Thus, in this paper, we report, for the first time, a critical investigation of practical methods for the synthesis of optically pure IpcBHCl (**3**) and its utility as an improved chiral chloroborane reagent for the asymmetric hydroboration of prochiral alkene substrates.

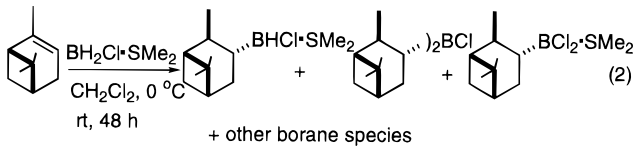
Results and Discussion

Recently, Cha *et al.*[13] have reported the hydroboration of α-pinene with methyl sulfide complexes of monohaloboranes ($BH_2X{\cdot}SMe_2$; X = Cl, Br, and I) to provide methyl sulfide complexes of isopinocampheylhaloboranes ($IpcBHX{\cdot}SMe_2$; X = Cl, Br, and I). However, there is no mention of the purity of these reagents, or their applicability for asymmetric hydroboration. In view of our program in asymmetric synthesis *via* organoboranes using sterically varied pinene-based chiral auxiliaries[7−9] and also the potential of IpcBHCl (**3**) for further synthetic manipulations, we undertook a systematic study of its synthesis by various promising approaches: (1) by the direct hydroboration of α-pinene with monochloroborane dimethyl sulfide ($BH_2Cl{\cdot}SMe_2$);[13] (2) the reaction of $IpcBH_2$ with HCl; (3) exchange of $IpcBH_2$ with $IpcBCl_2$; (4) reduction of $IpcBCl_2$ with Me_3SiH; and (5) reduction of $IpcBCl_2$ with 1/4 equiv of LAH. We also examined the effect of solvents, such as pentane, CH_2Cl_2, EE, and THF, in methods (3) and (4) to provide pure IpcBHCl. We have also examined its rate of reaction with the representative alkene, 2-methyl-2-butene, in typical hydroborating solvents, such as pentane, CH_2Cl_2, EE, and THF. We also examined the effectiveness of IpcBHCl reagent for the asymmetric hydroboration of representative prochiral alkenes.

Hydroboration of α-Pinene with $BH_2Cl{\cdot}SMe_2$ in Dichloromethane. There has been extensive research reported on the hydroboration of unsaturated compounds with ether complexes of monochloroboranes ($BH_2Cl{\cdot}$THF or EE) and also with the methyl sulfide complexes of BH_2-Br and BH_2I.[14] There are some advantages and disadvantages associated with these reagents.[14] However, it has been shown that hydroboration of tetrasubstituted alkene, *i.e.*, 2,3-dimethyl-2-butene (thexylene, Thx), with $BH_2Cl{\cdot}SMe_2$ in dichloromethane at room temperature essentially furnished the monohydroboration product, *i.e.*, the methyl sulfide complex of thexylchloroborane ($ThxBHCl{\cdot}SMe_2$) as a monomeric species (eq 1).[15]



Thus, on the basis of this result, α-pinene was added to an equimolar amount of $BH_2Cl{\cdot}SMe_2$ in CH_2Cl_2 at 0 °C. The rate of the reaction was monitored by the ^1H NMR spectrum of the olefinic proton of the residual α-pinene, using benzene as an internal standard.[9a] The reaction was complete in 10 min at room temperature. However, the desired $IpcBHCl{\cdot}SMe_2$ was formed in only 47%, along with substantial amounts of other boron derivatives of α-pinene and other borane species.[16,17] Even after 48 h at 25 °C, no appreciable change in the composition of the reaction mixture was noticed (eq 2).



Therefore, this unfavorable result led us to examine other systems for the preparation of the IpcBHCl reagent.

Reaction of $IpcBH_2$ with HCl in EE. Optically pure $IpcBH_2$ was prepared in EE according to the literature procedure.[5] Equimolar amounts of $IpcBH_2$ and HCl were allowed to react in EE at −5 °C, and the H_2 rapidly (∼5 min) liberated was measured. The ^{11}B NMR spectrum of the reaction mixture showed a mixture of IpcBHCl·EE (90%) along with 5% each of $IpcBH_2$ and $IpcBCl_2$·

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(15) Brown, H. C.; Sikorski, J. A. *Organometallics* **1982**, *1*, 28.
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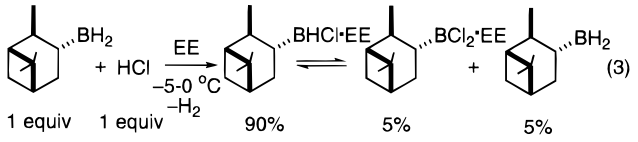
(17) By ^{11}B NMR spectrum: the reaction mixture contained $IpcBHCl{\cdot}SMe_2$ (∼47%) along with considerable amounts of Ipc_2BCl (∼23%), $BH_3{\cdot}SMe_2$(∼7%), $BHCl_2{\cdot}SMe_2$ (∼3%), and ∼10% each of $IpcBCl_2{\cdot}SMe_2$ and $BH_2Cl{\cdot}SMe_2$.

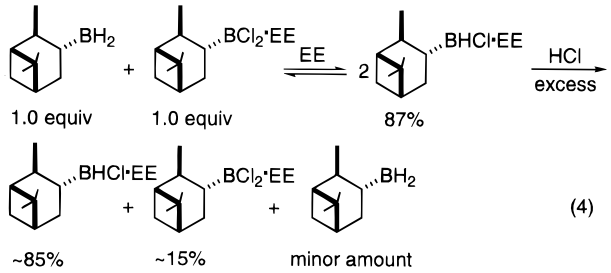
EE; the ^{11}B NMR spectrum[16] indicated no change in the composition of the reaction mixture even after 12 h at 0 °C (eq 3).



(3)

The active hydride was conveniently determined by analysis for hydride.[18] This result led us to examine the reaction of $IpcBH_2$ with $IpcBCl_2$ for the preparation of IpcBHCl.

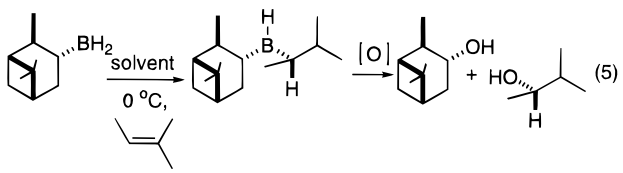
Reaction of $IpcBH_2$ in EE with $IpcBCl_2$·EE at 0 °C. Optically pure $IpcBCl_2$ was prepared by the reaction of boron trihalide, Me_3SiH, and α-pinene (**1a**−**f**).[19] Mixing equimolar amounts of $IpcBH_2$ and $IpcBCl_2$ in EE at 0 °C gave a mixture of IpcBHCl (87%) along with 6.4% of each reactants. The composition of the reaction mixture was almost the same even after 24 h at 0 °C (eq 4).



(4)

This result was almost identical with that obtained in the previous experiment, probably representing an equilibrium mixture of these species. Further, addition of ethereal HCl to this equilibrium mixture reduced the $IpcBH_2$ signal until it did not appear in the ^{11}B NMR spectrum, providing IpcBHCl·EE in ~85% chemical yield along with $IpcBCl_2$·EE.

It is apparent from these results that the reaction of $IpcBH_2$ with HCl or $IpcBCl_2$ provides IpcBHCl (87−90%) in equilibrium with $IpcBH_2$ and $IpcBCl_2$ in EE in about 5−10 min. Therefore, it was of interest to investigate the effect of representative solvents, such as pentane, CH_2Cl_2, and THF on the reaction of $IpcBH_2$ with $IpcBCl_2$ to provide IpcBHCl and on its rate of its reaction with the alkene, 2-methyl-2-butene, at 0 and 24 °C. Prior to this study, for the purpose of comparison, the rate of hydroboration of 2-methyl-2-butene with $IpcBH_2$ was examined in pentane, CH_2Cl_2, EE, and THF at 0 °C. The reaction was followed by the ^{11}B NMR spectra of methanolyzed aliquots taken after definite time intervals.[9a,16] It is well known that the hydroboration of moderately hindered alkenes such as 2-methyl-2-butene with $IpcBH_2$ provides dialkylborane cleanly (eq 5).



(5)

Therefore, for this reaction, except for that in EE, the EE was removed under reduced pressure and replaced by pentane, CH_2Cl_2, or THF. The ^{11}B NMR spectral value for $IpcBH_2$ in pentane and CH_2Cl_2 is δ 22−24 (br), and $IpcBH_2$ exists predominantly as a dimer (Table 1).[16] However, in THF, ~32−34% monomeric $IpcBH_2$·THF complex is observed. This is attributed to the higher Lewis basicity of THF, which causes the dissociation of dimeric $IpcBH_2$ to an equilibrium concentration of monomeric $IpcBH_2$ coordinated with THF, $IpcBH_2$·THF (^{11}B NMR spectrum, δ 11.7).

Table 1. ^{11}B NMR Spectrum Chemical Shifts of $IpcBH_2$, $IpcBCl_2$, and IpcBHCl in Representative Solvents at 24 °C

	^{11}B NMR spectrum values (δ)		
solvent	$IpcBH_2$	$IpcBCl_2$	IpcBHCl[b]
pentane	22−24 (br)	62	42
CH_2Cl_2	22−24 (br)	62	41
EE	22.5−24 (br)	18	13−14
THF[a]	24 (br) and 11.7 (br)	16.3	13−14
SMe_2	−2.9−3.0[b]	12.4	5.5−6.5[b]

[a] The ^{11}B NMR spectra reveal that $IpcBH_2$ in THF (~1.0 M) exists as a dimer (δ 23−24, ~66−68%) and the $IpcBH_2$·THF exists as a monomer (δ 10.5−12.0, ~32−34%). [b] Proton-decoupled ^{11}B NMR spectrum.

The hydroboration of 2-methyl-2-butene with $IpcBH_2$ in THF was faster than that observed in EE, pentane, and CH_2Cl_2. This may be explained by the fact that $IpcBH_2$·THF, a reactive monomeric species, undergoes a relatively fast dissociation into $IpcBH_2$, which reacts relatively rapidly with alkene, resulting in further dissociation of the $IpcBH_2$−dimer to the reactive $IpcBH_2$·THF complex, readily available for hydroboration.[20] This reaction was essentially complete in 1 h, while 3 h were required for the reaction in EE. The reaction was even slower in pentane and CH_2Cl_2, the rate of hydroboration requiring almost 4 h to be completed. From these observations, the following trend for the rate of hydroboration of 2-methyl-2-butene with $IpcBH_2$ in these solvents is evident: pentane ≅ CH_2Cl_2 < EE < THF. These results are shown graphically in Figure 1. The enantiomeric excess of the product alcohol, 3-methyl-2-butanol, was determined by the usual procedure.[7,9b] The enantiomeric excess of the alcohols was almost the same in all cases (37−40%).

After this study, we turned our attention to the reaction of $IpcBH_2$ with $IpcBCl_2$ in pentane, CH_2Cl_2, EE, and THF. Thus, $IpcBH_2$ was prepared as described previously in these solvents and treated with an equivalent amount of $IpcBCl_2$ at 0 °C. The reaction was analyzed by the ^{11}B NMR spectrum,[9a,16] indicating the formation of 87% of IpcBHCl·EE in equilibrium with $IpcBH_2$ and $IpcBCl_2$·EE. However, in THF, essentially quantitative formation of IpcBHCl·THF was observed, while in pentane and CH_2Cl_2, the reaction did not provide the desired IpcBHCl cleanly.

Further, IpcBHCl obtained by these methods was examined for the rate of hydroboration with 2-methyl-

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(20) We predict that $IpcBH_2$·THF undergoes dissociation to provide THF and $IpcBH_2$, which then hydroborates the alkene. This is based on the fact that the hydroboration of reactive alkenes with 9-BBN-dimer proceeds significantly faster in THF than in EE (in which 9-BBN predominantly exists as a dimer) because of the presence of the monomeric 9-BBN·THF complex. This complex dissociates rapidly into THF and 9-BBN, which then reacts with alkene (Brown, H. C.; Chandrasekharan, J.; Wang, K. K. *Pure Appl. Chem.* **1983**, *55*, 1387).

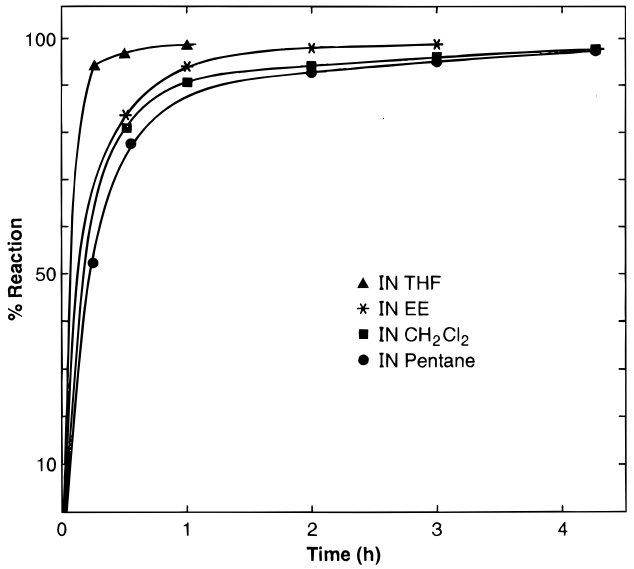


Figure 1. Hydroboration of 2-methyl-2-butene (2.0 M) with $IpcBH_2$ (1.0 M) in pentane, CH_2Cl_2, EE, and THF at 0 °C.

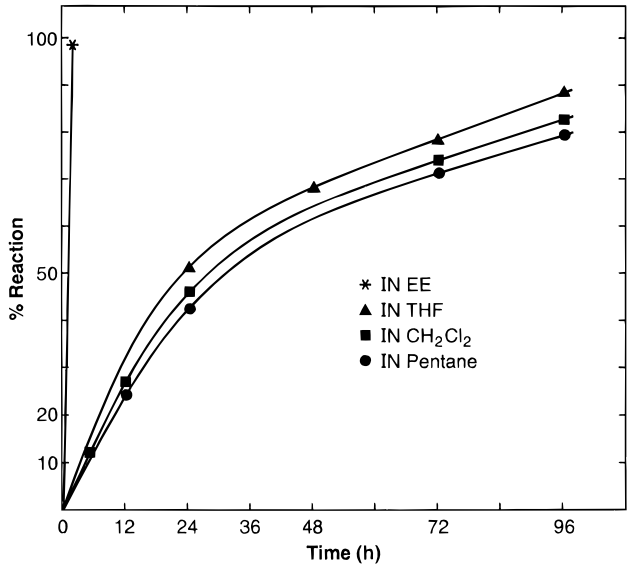


Figure 2. Hydroboration of 2-methyl-2-butene (1.0 M) with IpcBHCl (1.0 M) obtained from the reaction of $IpcBH_2$ with $IpcBCl_2$ in pentane, CH_2Cl_2, EE, and THF at 0 °C.

2-butene at 0 °C as described above and at 24 °C by measuring the dialkylchloroborane formed by the ^{11}B NMR spectrum recorded at fixed time intervals. Unlike $IpcBH_2$, IpcBHCl coordinates with EE and THF to provide the coordinated monomeric species in these solvents. However, IpcBHCl forms a weaker complex with EE than with THF. As a result, IpcBHCl·EE, a reactive hydroborating species, hydroborates 2-methyl-2-butene at a faster rate than does IpcBHCl·THF. In EE, hydroboration is complete in less than 0.25 h at 0 °C. However, the rate of hydroboration in pentane, CH_2Cl_2, and THF is very slow at 0 °C, with only 79%, 83%, and 86% completion indicated after 4 days. The slower rate observed in pentane and CH_2Cl_2 may be attributed to the lower concentration (5−7%) of the reactive hydroborating species; *i.e.*, IpcBHCl formed, probably, due to the very slow exchange of dimeric $IpcBH_2$ with $IpcBCl_2$. On the other hand, the formation of strong IpcBHCl·THF complex must be responsible for the slower rate in

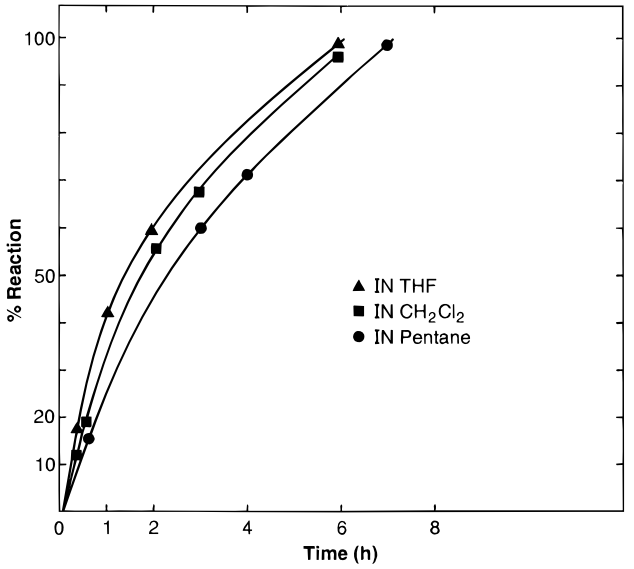


Figure 3. Hydroboration of 2-methyl-2-butene (1.0 M) with IpcBHCl (1.0 M) obtained from the reaction of $IpcBH_2$ with $IpcBCl_2$ in pentane, CH_2Cl_2, and THF at 24 °C.

Table 2. Percentage of Enantiomeric Excess of 3-Methyl-2-butanol Obtained in the Asymmetric Hydroboration of 2-Methyl-2-butene with $IpcBH_2$ and IpcBHCl in Representative Organic Solvents

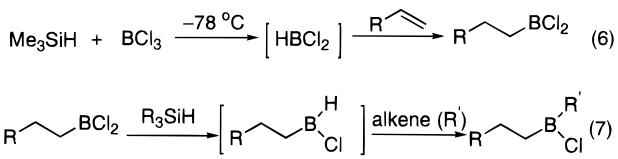
	% ee of 3-methyl-2-butanol[a]		
		$IpcBH_2$ + $IpcBCl_2$	
solvent	$IpcBH_2$, 0°C	0 °C	24 °C
pentane	39	56	34
CH_2Cl_2	37	40	33
EE	40	55	
THF	40	56	50

[a] Percent ee determined by capillary GC analysis of the menthyl carbonate derivative on an SPB-5 column.

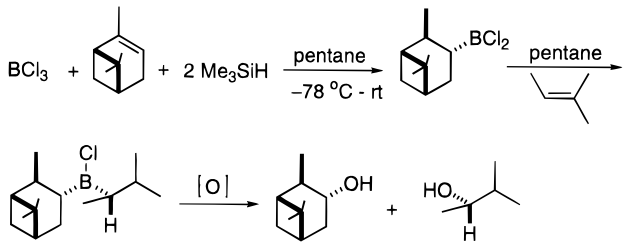
THF. At 24 °C, in CH_2Cl_2 and THF, >95% of hydroboration to provide the desired dialkylchloroborane was complete in 6 h, while 7 h were required in pentane. From these observations, the following increasing trend is indicated for the rate of hydroboration of 2-methyl-2-butene with IpcBHCl in these solvents: pentane < CH_2Cl_2 < THF ≪ EE. These results are graphically depicted in Figures 2 and 3.

The enantiomeric excess of the product alcohol, 3-methyl-2-butanol, observed at 0 °C in THF and EE, was almost the same (55−56%), while it was 50% in THF at 24 °C. However, in pentane and CH_2Cl_2 at 0 °C, enantioselectivity was lower (33−34%) since in these solvents a small amount of $BHCl_2$, an achiral borane, was formed that also hydroborated the alkene (Table 2).

Reaction of a Mixture of α-Pinene and Me_3SiH with Boron Trichloride (BCl_3) in Representative Solvents. Matteson[19a,b] reported that a mixture of alkene and trialkylsilane react with BCl_3 at −78 °C to give $RBCl_2$ in about 5 min. A second equivalent of trialkylsilane slowly reduces $RBCl_2$ in the presence of an alkene to give dialkylchloroborane at 25 °C (eqs 6 and 7).

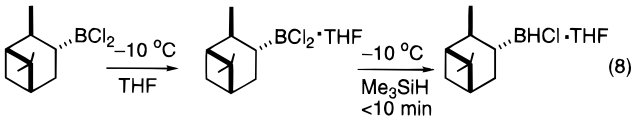


Scheme 1

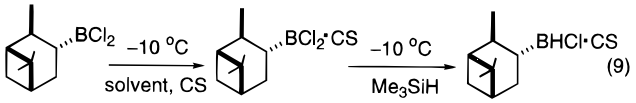


Therefore, it was anticipated that the reaction of 2 equiv of Me_3SiH, 1.0 equiv each of α-pinene, and BCl_3 in pentane at −78 °C would provide the required IpcBHCl. However, this reaction provided $IpcBCl_2$ (δ 62) in quantitative yield. But trace amounts of IpcBHCl (∼1−2%) were noticed at 0 °C after 24 h. Identical results were obtained in the reduction of freshly distilled $IpcBCl_2$ with Me_3SiH in pentane at −78 or 0 °C for 24 h. However, the reduction of $IpcBCl_2$ took place in the presence of 2-methyl-2-butene to provide IpcBHCl, which immediately hydroborated the alkene to give the dialkylchloroborane at 0 °C in 24 h. The enantiomeric excess of product alcohol was 55%. The same reaction was almost complete in 5 days at −25 °C, and the optical purity of the product alcohol was increased to 67%, almost identical with that realized in the hydroboration of this alkene with the preformed IpcBHCl·EE in EE at −25 °C (see Table 5 for comparative results) (Scheme 1).

From these results, it is evident that the reduction of $IpcBCl_2$ with Me_3SiH is extremely slow in pentane, probably proceeding to the formation of a small equilibrium concentration of IpcBHCl, and could not be used to prepare pure IpcBHCl. Therefore, it was decided to examine this reaction in the other representative solvents, such as CH_2Cl_2, EE, and THF. Moreover, our previous experiments had revealed that EE and THF are better solvents for the preparation of IpcBHCl. Indeed, a highly remarkable acceleration in the reduction of $IpcBCl_2$ with Me_3SiH was observed when EE was used as a solvent.[21] The reaction in this case was complete in <10 min even at −10 °C to provide the same equilibrium mixture of IpcBHCl·EE (∼90%), $IpcBH_2$ (∼5%), and $IpcBCl_2$·EE (∼5%),[16] unaltered after 24 h at 0 °C, whereas, in THF, a more basic solvent than EE, the reduction of $IpcBCl_2$·THF with Me_3SiH also proceeded rapidly to provide IpcBHCl·THF of >98% purity in <10 min. Therefore, the use of THF as the solvent shifted the reaction from the equilibrium mixture achieved previously in EE to essentially pure IpcBHCl·THF (eq 8).



The equilibrium distribution observed for the reduction of $IpcBCl_2$ by Me_3SiH in EE was similar to that observed for the alternative procedures used to prepare preformed IpcBHCl·EE (eqs 3 and 4). Moreover, the hydroboration of 2-methyl-2-butene in EE was over in less than 15 min at 0 °C to provide IpcR*BCl, readily oxidized to alcohol in 55% ee, the same as that realized by other methods (Table 2). Interestingly, in CH_2Cl_2 the *in situ* reduction and concurrent hydroboration reaction with stoichiometric amounts of $IpcBCl_2$, Me_3SiH, and 2-methyl-2-butene at 0 °C was much faster than the reaction in pentane, more than 90% of the reaction being over in 1 h, while only 3 h were required for complete reaction. This is a remarkable effect of the solvent. In pentane, both reduction of $IpcBCl_2$ with Me_3SiH and concurrent hydroboration of alkene is extremely slow. The best solvents appear to be coordinating solvents (CS), such as EE and THF, which exert a major effect on the reduction−hydroboration reaction of $IpcBCl_2$. Therefore, it was interesting and essential to investigate systematically the effect of *known amounts* of coordinating solvents, such as EE, THF, and dimethyl sulfide (SMe_2), all of which coordinate readily with dichloroboranes, on the reduction of $IpcBCl_2$ with Me_3SiH in pentane, CH_2Cl_2, and EE solvents to produce the pure addition compounds, IpcBHCl·CS (eq 9).



solvent = pentane, CH_2Cl_2, and EE
coordinating solvent (CS) = EE, DMS, and THF

Thus, to the solution of $IpcBCl_2$ in pentane, CH_2Cl_2, or EE, an equivalent amount of solvents such as EE or THF or SMe_2 was added in stepwise fashion at −10 °C, followed by a stoichiometric amount of Me_3SiH, and the reaction monitored by the ^{11}B NMR spectra of the aliquots taken at definite time intervals. In pentane and CH_2Cl_2 at 0 °C, a total of 6 equiv of EE was required to obtain an equilibrium mixture[16] of 87−89% of IpcBHCl·EE, 5−6.5% of $IpcBCl_2$·EE, and $IpcBH_2$. However, >98% of IpcBHCl·THF was obtained in EE and CH_2Cl_2 when 2 and 3 equiv, respectively, of THF was used.[22] Similarly, to obtain >98% of IpcBHCl·SMe_2 in CH_2Cl_2 and EE, only 1.0 equiv of SMe_2 was required at 24 °C. On the other hand, at 24 °C, the reduction of $IpcBCl_2$ to form desired the IpcBHCl·SMe_2 was very slow in pentane, even in the presence of 2 equiv of SMe_2. Only after 12 h was IpcBHCl·SMe_2 formed in 90−91% along with 8−9% of BH_2Cl·SMe_2. The later species was probably formed by a dehydroboration of the former. These results are summarized in Table 3.

Thus, IpcBHCl·CS prepared by these methods was allowed to hydroborate an equivalent amount of 2-methyl-2-butene. The relative rate of reaction at 0 °C and, in most cases, at 24 °C was followed by the ^{11}B NMR spectral examination of aliquots, as described previously. Although a total of 6 equiv of EE was required to produce the desired IpcBHCl·EE (87−89%) in pentane and CH_2Cl_2, only 1.0 equiv of EE was required to achieve the *in situ* reduction−hydroboration of 2-methyl-2-butene in pentane and CH_2Cl_2 with stoichiometric amounts of $IpcBCl_2$ and Me_3SiH. In these solvents, the reaction was complete in 15 min at 0 °C. In comparison with the rates of reaction of IpcBHCl·EE, the rates of hydroboration of 2-methyl-2-butene by IpcBHCl·THF are appreciably slower

(21) In EE as solvent, synthesis of the efficient reducing agent, ^{d}Ipc$_2$BCl (≥99% ee),[3] was achieved in essentially quantitative yield by carrying out the reaction of equimolar amounts of optically pure $IpcBCl_2$, Me_3SiH and (+)-α-pinene (≥99% ee). The reaction was complete in less than 15 min at 0 °C. Dhokte, U. P.; Brown, H. C. unpublished results.

(22) The $IpcBCl_2$·THF precipitated when 1.0 equiv of THF was added to $IpcBCl_2$ in pentane. Therefore, this mixture was not used in reduction.

Table 3. Composition of the Equilibrium Mixture[a] in the Formation of IpcBHCl By Various Methods at 0 °C

entry	source	$IpcBH_2$ (%)	$IpcBCl_2$ (%)	IpcBHCl (%)
1[b]	$IpcBH_2$ + HCl	5.0	5.0	90[d]
2[b]	$IpcBH_2$ + $IpcBCl_2$	6.4	6.4	87[d]
3[c]	α-Pinene + BCl_3 + $2Me_3SiH$ or $IpcBCl_2$ + Me_3SiH			trace
4[b]	$IpcBCl_2$ + Me_3SiH	5.0	5.0	90[d]
5[c]	$IpcBCl_2$ + Me_3SiH + EE (6 equiv)	5.0	6.0	89[d]
6[e]	$IpcBCl_2$ + Me_3SiH + EE (6 equiv)	6.5	6.5	87[d]
7[e]	$IpcBCl_2$ + Me_3SiH + THF (3 equiv)			>98[f]
8[b]	$IpcBCl_2$ + Me_3SiH + THF (2 equiv)			>98[f]
9[b,e]	$IpcBCl_2$ + Me_3SiH + DMS (1 equiv)			>98[g]
10[b]	$IpcBCl_2$ + 0.25 equiv LAH	6.6		88[d]

[a] By ^{11}B NMR spectrum. [b] Reaction in EE. [c] Reaction in pentane; in absence of EE only trace amounts of IpcBHCl are formed. [d] IpcBHCl·EE complex. [e] Reaction in CH_2Cl_2. [f] IpcBHCl·THF complex. [g] IpcBHCl·DMS complex.

in EE and CH_2Cl_2. The reaction was complete to the extent of 50% in 2−3 h, with >95% of the reaction over after 24 h at 0 °C. Even at 24 °C, the reaction took longer in EE, 45 min, and in CH_2Cl_2, 1 h, than the 15 min required by IpcBHCl·EE at 0 °C.

It is probable that the presence of the excess THF, 2 equiv in EE and 3 equiv in CH_2Cl_2, required to prepare IpcBHCl·THF (>98% chemical yield) in EE and CH_2Cl_2, respectively, was responsible for lowering the rate of hydroboration. On the other hand, only 1 equiv of SMe_2 was required for the preparation of IpcBHCl·SMe_2 (>98%) in EE and CH_2Cl_2. As a result, the rate of hydroboration of 2-methyl-2-butene was relatively faster with IpcBHCl·SMe_2 (not containing excess CS) than with IpcBHCl·THF (containing excess CS) in EE and CH_2Cl_2.[20,23] Thus, at 0 °C, more than 50% hydroboration with IpcBHCl·SMe_2 was complete in less than 30 min, while 4 and 6 h were required to complete the reaction in EE and CH_2Cl_2, respectively. These results are graphically represented in Figure 4.

Reduction of 1.0 Equiv of $IpcBCl_2$ with 0.25 Equiv of Lithium Aluminum Hydride (LAH) at −5 °C. It is reported in the literature that the reduction of the methyl sulfide complex of alkyldibromoborane with 0.25 equiv of LAH cleanly provides the methyl sulfide complex of alkylmonobromoborane, which upon hydroboration with 1 equiv of alkene furnishes dialkylbromoborane dimethyl sulfide complex (eq 10).[24]

$$BHBr_2{\cdot}SMe_2 + \text{alkene} \rightarrow RBBr_2{\cdot}SMe_2 \xrightarrow[\text{LAH}]{\text{0.25 equiv}} \xrightarrow{\text{alkene } (R^1)} RR^1BBr{\cdot}SMe_2 \quad (10)$$

Therefore, it was of interest to examine the usefulness of LAH as a reducing agent for the reduction of $IpcBCl_2$ to prepare IpcBHCl. Thus, the reduction of $IpcBCl_2$·EE in EE with LAH (0.25 equiv) in EE at −5 °C provided an equilibrium mixture[16] of IpcBHCl·EE (88%) along with 6.6% each of $IpcBCl_2$·EE and $IpcBH_2$. The composition

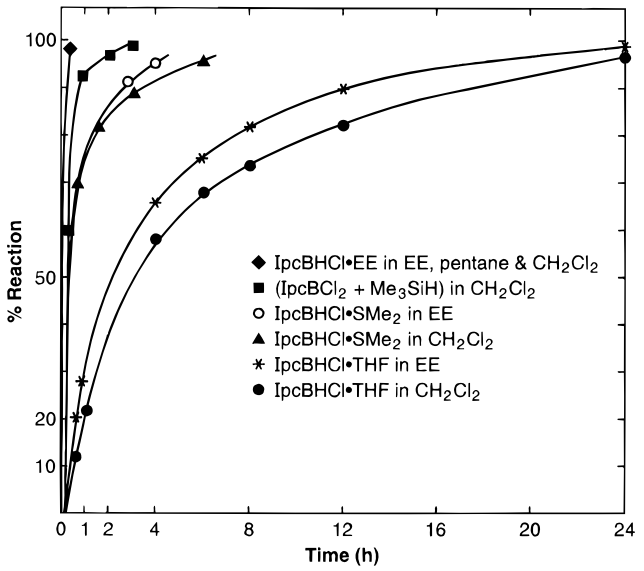
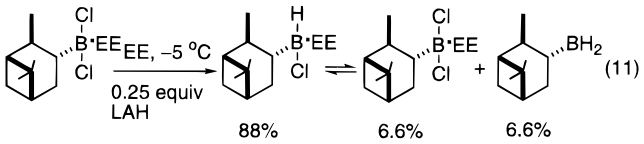


Figure 4. Reaction (reduction-hydroboration) of $IpcBCl_2$, Me_3SiH, and 2-methyl-2-butene (1:1:1) in the presence or absence of coordinating solvents (THF or SMe_2) in CH_2Cl_2 or EE at 0 °C.

of the reaction mixture was unchanged even after 6 h at 0 °C (eq 11).



(11)

The result of this experiment was identical with the observations noted in the previous experiments. Asymmetric hydroboration with stoichiometric amounts of $IpcBCl_2$ (≥99% ee), 2-methyl-2-butene, and 0.25 equiv of LAH in EE at −25 °C provided the product alcohol of 65% ee (see Table 5 for comparative results).

Asymmetric Hydroboration of Representative Prochiral Alkenes with Isopinocampheylchloroborane in EE at −25 °C. In order to allow for the direct comparison of IpcBHCl with $IpcBH_2$, the standard set of alkenes was examined,[7,9b] *i.e.*, representative terminal, *cis*-, *trans*-, and trisubstituted alkenes. Equimolar amounts of alkenes were hydroborated at −25 °C with IpcBHCl in EE. The IpcBHCl (85−90%) used in these reactions was obtained by the reaction of $IpcBH_2$ (99% ee) with excess HCl in EE (method A). Alternatively, $IpcBCl_2$ (99% ee) was utilized to generate IpcBHCl (**3**) for the hydroboration of prochiral alkenes at −25 °C in the presence of 0.25 equiv of LAH[25] in EE (method B) (Scheme 2).

The progress of each reaction was monitored by the ^{11}B NMR spectrum of an aliquot after methanolysis.[7,9b] The reaction time ranged from 24−30 h. The intermediate, mixed dialkylchloroborane, was treated with methanol at −25 °C and oxidized with alkaline peroxide[7,9b] to provide the product alcohol and (−)-isopinocampheol. The two alcohols were easily separated by short-path distillation. These two methods gave almost identical results within experimental error.

(23) Wang, K. K.; Brown, H. C. *J. Am. Chem. Soc.* **1982**, *104*, 7148.
(24) Brown, H. C.; Basavaiah, Kulkarni, S. U. *Organometallics* **1982**, *1*, 212.

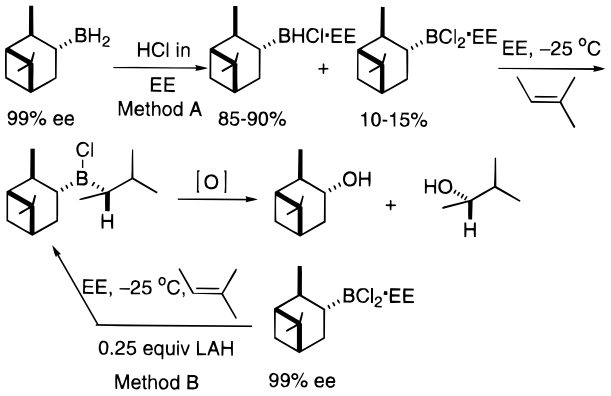
(25) Similar results were realized with trimethylsilane as the reducing agent.

Table 4. Asymmetric Hydroboration of Representative Alkenes with Optically Pure IpcBHCl[a] in EE at −25 °C and Its Comparison with Optically Pure $IpcBH_2$[a]

alkene	alcohol	yield (%)	absolute confign	optical purity (% ee) methods[b] A	B	$IpcBH_2$ (% ee)
2-methyl-1-butene	2-methyl-1-butanol[c]	73	*S*	11		1.5
cis-2-butene	2-butanol[d]	64	*S*	44		24
trans-2-butene	2-butanol[d]	61−66	*S*	67	64	73
2-methyl-2-butene	3-methyl-2-butanol[e]	69−77	*S*	67	65	53
1-methylcyclopentene	*trans*-2-methylcyclopentanol[e]	65−72	1*S*,2*S*	44	45	66
1-methylcyclohexene	*trans*-2-methylcyclohexanol[e]	62−68	1*S*,2*S*	79	79	72

[a] Synthesized from (+)-α-pinene. [b] Methods A: ($IpcBH_2$ + HCl + alkene) and B: ($IpcBCl_2$ + 0.25 equiv of LAH + alkene). [c] Percent ee determined by comparison with highest reported rotation.[29] [d] Percent ee determined by capillary GC as the MTPA ester on an SPB-5 column. [e] Percent ee determined by capillary GC as the menthyl carbonate derivative on an SPB-5 column.

Scheme 2



The asymmetric induction achieved for the terminal alkene, 2-methyl-1-butene, was poor, providing (−)-2-methyl-1-butanol in only 11% ee. The hydroboration/oxidation of *cis*-butene with IpcBHCl gave (+)-2-butanol in 44% ee, less satisfactory than Ipc_2BH, but better than $IpcBH_2$. The *trans*-2-butene was converted into the same alcohol in 67% ee (Scheme 2), while 1-methylcyclopentene was converted into *trans*-2-methyl-1-cyclopentanol in 44−46% ee. The enantiomeric excess realized in these two examples was lower in comparison with $IpcBH_2$.[5] However, significantly better optical yields were realized, *viz.*, 67% and 79% for the asymmetric hydroboration of 2-methyl-2-butene and 1-methylcyclohexene, respectively, in comparison with the $IpcBH_2$.[5] The results from methods A and B are summarized in Table 4.

We also confirmed that there is no effect of modest amounts of excess $IpcBCl_2$ (≥99% ee, 25 or 50 mol %) on the enantioselection of the product in the asymmetric hydroboration of 2-methyl-2-butene using optically pure IpcBHCl (85−90% pure) containing $IpcBCl_2$ in EE at −25 °C. The enantiomeric excess of product alcohol realized in these experiments was 70% and 68%, respectively. These results are summarized in Table 5 and are compared with the other results.

Conclusions

This paper describes our detailed study of the synthesis of IpcBHCl, a promising asymmetric hydroborating agent, by direct and indirect strategies and its usefulness for the asymmetric hydroboration of prochiral alkenes. This study has revealed a number of simple relationships between the various possible methods for the synthesis of IpcBHCl and its hydroboration properties. These results are summarized as follows.

(1) Direct method of generation of IpcBHCl from the reaction of α-pinene with $BH_2Cl{\cdot}SMe_2$ gives an undesired mixture of products.

Table 5. Summary of the Results of Asymmetric Hydroboration of 2-Methyl-2-butene with IpcBHCl (≥99% ee), in EE at −25 °C, Obtained by Various Methods

entry	source	purity of IpcBHCl (%)	time (h)	% ee[a]
1	$IpcBH_2$ + HCl	85−90	24	67
2	$IpcBH_2$ + $IpcBCl_2$	85	24	68
3[b]	α-Pinene + BCl_3 + $2Me_3SiH$ or $IpcBCl_2$ + Me_3SiH		5 days	67
		24[c]	57[c]	
4	$IpcBCl_2$ + 1/4 LAH	∼90	24	65
5	$IpcBH_2$ + HCl + $IpcBCl_2$ (25 mol %)	85−90	24	70
6	$IpcBH_2$ + HCl + $IpcBCl_2$ (50 mol %)	85−90	24	68

[a] Percent ee determined by capillary GC analysis of the menthyl carbonate derivative on an SPB-5 column. [b] Reaction was carried out in pentane. [c] Reaction at 0 °C.

(2) The reaction of $IpcBH_2$ with HCl or with $IpcBCl_2$ and the reduction of $IpcBCl_2$ with LAH (0.25 equiv) or with Me_3SiH in EE all give an equilibrium mixture of IpcBHCl·EE (87−90%) along with 5−6.5% each of $IpcBH_2$ and $IpcBCl_2$ (see Table 3). For the first time, we have shown that the reduction of alkylchloroboranes, such as $IpcBCl_2$, with Me_3SiH can be highly accelerated with EE as solvent. In THF as well, the reduction is very fast to provide essentially pure IpcBHCl·THF in quantitative yield.

(3) The reduction−hydroboration using $IpcBCl_2$, Me_3SiH, and alkene in pentane is extremely slow. This reaction is relatively faster in CH_2Cl_2 alone, which is over in 3 h at 0 °C. However, reduction−hydroboration can be accelerated in the pentane and CH_2Cl_2 solvents by the addition of 1−2 equiv of EE.

(4) We have demonstrated the use of known amounts of THF and SMe_2 solvents in the reduction of $IpcBCl_2$ with Me_3SiH to provide IpcBHCl·CS, a monomer, in the solvents such as EE and CH_2Cl_2, respectively. The desired IpcBHCl·CS can be obtained in quantitative yield.

(5) The rate of hydroboration of a representative alkene, 2-methyl-2-butene, with $IpcBH_2$ is faster in THF in comparison with other representative solvents. However, with IpcBHCl·THF, the rate is slower in THF than with IpcBHCl·EE in EE. In general, the rate of hydroboration is slower in pentane and CH_2Cl_2 solvents.

(6) It is evident that, irrespective of the methods used for the asymmetric hydroboration of prochiral alkenes either *via* preformed IpcBHCl (obtained from the reaction of $IpcBH_2$ with HCl, method A) or *in situ* reduction−hydroboration of $IpcBCl_2$ with LAH (0.25 equiv) (method B), almost the same optical induction is realized. In some cases, better enantiomeric excess of the product alcohol is obtained using IpcBHCl as compared to $IpcBH_2$. The

presence of $IpcBCl_2$ in the asymmetric hydroboration of prochiral alkenes has no significant effect on the chiral outcome of the reaction (Table 5).

In conclusion, we have demonstrated that the IpcBHCl reagent can be conveniently synthesized by a number of simple methods. However, for practical purposes, we recommend method B for the asymmetric hydroboration since $IpcBCl_2$ can be prepared conveniently in almost quantitative yield and stored at room temperature for considerable periods of time without noticeable change.[26] The present study will help in developing practical procedures for the synthesis of structurally varied chiral hindered 2-organylapoisopinylhaloboranes of considerable promise in the area of asymmetric synthesis *via* chiral organoboranes. Our preliminary results for asymmetric hydroboration with 2-ethylapoisopinylchloroborane (EapBHCl) and with IpcBHBr reagents are quite promising.[27] This research is in progress and will be reported shortly.

Experimental Section

All glassware was dried overnight at 140 °C, assembled hot, and cooled to ambient temperature in a stream of nitrogen.[18] All reactions were performed under static pressure of dry nitrogen. The ^{11}B NMR spectra were recorded at 96 MHz and were referenced to BF_3·EE.

Materials. $IpcBH_2$[5] and $IpcBCl_2$[19a,b] were prepared using literature procedures. Trimethylsilane, dry EE, DMS, and pentane were used as obtained. Dichloromethane and THF were distilled from phosphorous pentoxide and sodium benzophenone ketyl, respectively, prior to use.

Hydroboration of α-Pinene with BH_2Cl·SMe_2 in CH_2Cl_2. A cold (0 °C) solution of CH_2Cl_2, containing BH_2Cl·SMe_2 (10 mmol) and benzene in CH_2Cl_2 (1.0 M, 2.0 mL, 2.0 mmol) as an internal standard, was stirred at 0 °C, and α-pinene (1.36 g, 10 mmol) was added *via* syringe. The rate of the reaction was followed by ^1H NMR spectra of aliquots (~0.1 mL) taken in $CDCl_3$ (0.6 mL) at 24 °C.[9a,16] The reaction was over in less than 10 min, and at that point, the ^{11}B NMR spectrum of an aliquot showed a mixture of products.[17]

Reaction of $IpcBH_2$ with HCl in EE. $IpcBH_2$ in EE was prepared from the reaction of BF_3·EE with $IpcBH_2$·TMEDA adduct (≥99% ee), obtained from (+)-α-pinene of ≥91% ee.[5] To the solution of optically pure $IpcBH_2$ (1.15 M, 8.7 mL, 10 mmol) in EE cooled at −5 °C was added HCl in EE (2.38 M, 4.20 mL, 10 mmol) slowly, and the liberated H_2 was measured (9.5 mmol, 95% in 5 min). The ^{11}B NMR spectrum of the solution indicated a mixture of 90% IpcBHCl·EE, and 5% each of $IpcBCl_2$·EE and $IpcBH_2$. The molarity of the solution was conveniently determined by hydride analysis.[18] The hydrolysis of a 1.0 mL aliquot produced 19.2 mL of H_2, which corresponds to 0.77 M. The chloride content was estimated by hydrolyzing an aliquot and titrating the HCl produced with a standard aqueous solution of NaOH using phenolphthalein as an indicator. The solution was 0.79 M in chloride.

Reaction of $IpcBH_2$ with $IpcBCl_2$·EE in EE. To EE (2.70 mL) cooled at −10 °C was slowly added optically pure $IpcBCl_2$ (3.11 mmol) (^{11}B NMR spectrum of $IpcBCl_2$·EE is a singlet at δ 17−18). This solution was added to a cold (0 °C) solution of $IpcBH_2$ (1.15 M, 2.70 mL, 3.11 mmol) in EE and stirred for 15 min. At that point, the ^{11}B NMR spectrum of the reaction showed a mixture of IpcBHCl (87%) and 6.4% each of $IpcBCl_2$ and $IpcBH_2$. After 24 h, HCl in EE (2.39 M, 0.30 mL, 0.71 mmol) was added at 0 °C. The ^{11}B NMR spectrum of the reaction mixture showed 85% of IpcBHCl and 15% of $IpcBCl_2$. The solution was 0.83 M in hydride and 1.10 M in chloride.

Typical Procedure for the Examination of the Rate and Enantiomeric Excess for the Hydroboration of 2-Methyl-2-butene with $IpcBH_2$ in EE. Optically pure $IpcBH_2$ (1.20 M, 8.3 mL, 10 mmol) in EE was made according to the literature procedure.[5] For reactions other than in EE, solvent EE was removed (13 mmHg, 25 °C, 20−30 min) and replaced by the same volume of either pentane, CH_2Cl_2, or THF (8.3 mL). The ^{11}B NMR spectrum was recorded (Table 1) and the solution analyzed for hydride content.[18] The solution was cooled to 0 °C, and 2-methyl-2-butene (10 mmol) was added at that temperature. The rate of the reaction was followed at fixed time intervals by the ^{11}B NMR spectrum of an aliquot (~0.10−0.20 mL) after methanolysis with cold (−10 °C) methanol (~0.40−0.50 mL).[9a,16] At the end of the reaction, the mixture was methanolyzed and subjected to alkaline peroxide oxidation.[7,9b] The resultant product alcohol, 3-methyl-2-butanol, was separated from the isopinocampheol by a short-path distillation, derivatized as the menthyl carbonate,[28a] and analyzed on the capillary GC (SPB-5 column, 30 m at 140 °C isothermal temperature) for its percentage enantiomeric excess (Table 2). The results of these reactions are graphically represented in Figure 1. These results are also provided in Table 6 (supporting information).

Typical Procedure for the Examination of Rate and Enantiomeric Excess for the Hydroboration of 2-Methyl-2-butene with IpcBHCl, Obtained from the Reaction of $IpcBH_2$ with $IpcBCl_2$ at 0 °C in Representative Solvents. To a cold (0 °C) solution of optically pure $IpcBH_2$ (1.20 M, 4.2 mL, 5.0 mmol), prepared in 9.0 mL of pentane or CH_2Cl_2 or THF as mentioned above, was added neat, optically pure $IpcBCl_2$ (5.0 mmol) *via* syringe. The reaction mixture was stirred for 5 min, and the ^{11}B NMR spectrum of an aliquot was recorded[16] (results are given in Table 7, supplementary information). The active hydride (~1.00 M) and chloride contents of the solution were determined.[18] To the reaction mixture was added 2-methyl-2-butene (10 mmol) at 0 °C, and the rate of the reaction was followed at that temperature as described in the preceding experiment. The rate of hydroboration at 24 °C was determined by the direct measurement of dialkylchloroborane (δ 72−74) evident in the ^{11}B NMR spectrum. The results of these reactions are graphically shown in Figures 2 and 3. The results are given in Table 8 (supporting information).

Reaction of a Mixture of α-Pinene and Me_3SiH with BCl_3 in Pentane. BCl_3 (2.34 mL, 20 mmol) was dissolved in pentane (15 mL) at −78 °C. To this cold solution was added a precooled (−78 °C) mixture of α-pinene (2.72 g, 20 mmol) and Me_3SiH (2.96 g, 40 mmol). The progress of the reaction was monitored by the ^{11}B NMR spectrum taken immediately (~1 min); only formation of $IpcBCl_2$ (δ 62) was observed—no formation of IpcBHCl was evident even after 6 h at −78 °C. However, very little (~1−2%) formation of IpcBHCl (br δ 42)[19a,b] was evident at 0 °C after 24 h. The same results were obtained when the reaction was carried out with freshly prepared $IpcBCl_2$ (1.92 g, 8.77 mmol) and Me_3SiH (0.65 g, 8.77 mmol) in pentane (8.0 mL) at −78 °C and also at 0 °C.

In Situ Reduction−Hydroboration of $IpcBCl_2$ with Me_3SiH in the Presence of 2-Methyl-2-butene in Pentane. In this case the reaction was carried out in the presence of 2-methyl-2-butene (9.0 mmol) at 0 and −25 °C. The reaction was over in 24 h at 0 °C and 5 days at −25 °C (as established by the ^{11}B NMR spectrum of the aliquot after methanolysis). The usual workup provided 3-methyl-2-butanol in 57% ee and 67% ee, respectively (Table 5). The same reaction was carried out in CH_2Cl_2 at 0 and 24 °C, and part of the results are presented in Table 9 (supporting information).

In Situ Reduction−Hydroboration of $IpcBCl_2$ with Me_3SiH in EE and THF. To the cold (−10 °C) EE (5.0 mL)

(26) A sample kept at 24 °C for 4 months under N_2 did not show any observable change by $^1H/^{13}C/^{11}B$ NMR spectroscopy. Also, the results from the use of this material in asymmetric hydroborations of alkenes were identical to those obtained with freshly prepared samples. Similarly, alkaline peroxide oxidation of $IpcBCl_2$ gave isopinocampheol of ≥99% ee based on the maximum rotation reported in the literature (Brown, H. C.; Mandal, A. K.; Yoon, N. M.; Schwier, J. R.; Jadhav, P. K. *J. Org. Chem.* **1982**, *47*, 5069).

(27) Dhokte, U. P.; Brown, H. C. Unpublished results.

(28) (a) Westley, J. W.; Halpern, B. *J. Org. Chem.* **1968**, *33*, 3978. (b) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(29) Whitemore, F. C.; Olewine, J. H. *J. Am. Chem. Soc.* **1938**, *60*, 2569.

was slowly added $IpcBCl_2$ (5.0 mmol) followed by precondensed Me_3SiH (5.0 mmol). The ^{11}B NMR spectrum of the solution after ~10 min showed a mixture of IpcBHCl·EE (~90%) and ~5% each of $IpcBH_2$ and $IpcBCl_2$·EE. The same reaction in THF (5.0 mL) provided IpcBHCl·THF (>98%).

Reduction of $IpcBCl_2$ with Me_3SiH in Pentane, CH_2Cl_2, and EE in the Presence of Known Amounts of Coordinating Solvents (CS), Such as EE, THF, and SMe_2. To a cold (−10 °C) solution of pentane or CH_2Cl_2 or EE (4.00−5.00 mL) was slowly added $IpcBCl_2$ (4.50−5.50 mmol). To this solution were added stoichiometric amounts of EE or THF or SMe_2 followed by the addition of condensed and precooled (−78 °C) Me_3SiH (4.50−5.50 mmol). The reaction was followed by a ^{11}B NMR spectrum every 30 min for 12 h. Additional equivalents of coordinating solvents were added in stepwise fashion until complete formation of IpcBHCl·CS was observed (Table 3). To this solution was added 2-methyl-2-butene (4.50−5.50 mmol) at 0 °C, and the rate of the reaction was followed as described above. The % ee results of these reactions are represented in Tables 3 and graphically in Figure 4 (comparative rate data of these reactions are given in Table 9, supporting information).

Reduction of $IpcBCl_2$ (≥99% ee) with 0.25 Equiv of LAH in EE. A cold (−5 °C) solution of $IpcBCl_2$ (6.12 mmol) in EE (5.0 mL) was prepared. To this solution was slowly added 0.25 equiv of LAH in EE (1.05 M, 1.46 mL, 1.53 mmol). The ^{11}B NMR spectrum of the solution after 15 min showed a mixture[16] of 88% IpcBHCl·EE and 6.6% each of $IpcBCl_2$·EE and $IpcBH_2$ (Table 3). The solution was 0.81 M in hydride and 0.84 M in chloride.

Asymmetric Hydroboration of Representative Prochiral Alkenes at −25 °C in EE. Method A: Using IpcBHCl (≥99% ee) Obtained from the Reaction of $IpcBH_2$ (≥99% ee) with HCl in EE. All reactions were performed on a 15−20 mmol scale. Optically pure IpcBHCl was prepared as mentioned earlier and treated with a stoichiometric amount of alkenes at −25 °C for 24−30 h. Usual alkaline peroxide workup[7,9b] provided alcohol, which was derivatized as the menthyl carbonate[28a] or MTPA ester[28b] and analyzed by capillary GC on an SPB-5 column.[7,9b] The results are given in Table 4.

Method B: In Situ Reduction−Hydroboration of $IpcBCl_2$ (≥99% ee) with 0.25 Equiv of LAH[25] in the Presence of Alkene. All reactions were performed on a 5.80−6.00 mmol scale. The procedure for the hydroboration of *trans*-2-butene is representative. To an ethereal solution of optically pure $IpcBCl_2$ (5.85 mmol) at −25 °C was added *trans*-2-butene (5.85 mmol). The reaction mixture was stirred for 15 min, and LAH (1.05 M, 1.39 mL, 1.46 mmol) in EE was added slowly. The reaction was stirred for 30 h and quenched with an excess of cold (−25 °C) methanol. The usual workup procedure[7,9b] provided the alcohol, which was analyzed as described above. The results are given in Table 4.

Asymmetric Hydroboration of 2-Methyl-2-butene Using IpcBHCl (85−90% Pure, ≥99% ee) in the Presence of 25 and 50 Mol % of $IpcBCl_2$ in EE. a: In the Presence of 25 Mol % of $IpcBCl_2$. Optically pure IpcBHCl (86% pure, i.e., 8.6 mmol) was prepared from the reaction of optically pure $IpcBH_2$ (99% ee, 1.15 M, 10 mmol) with HCl in EE (2.39 M, 4.80 mL, 11.4 mmol) at −5 °C. Chemical analysis showed the amount of $IpcBCl_2$ was 14%, *i.e.*, 1.4 mmol, and the solution was 0.85 M in chloride. Therefore, an additional 0.75 mmol of optically pure $IpcBCl_2$ (this makes a total of 25 mol %) was added to the reaction mixture at −25 °C, followed by the addition of 2-methyl-2-butene (8.7 mmol). The reaction was quenched with cold (−25 °C) excess methanol after 24 h. The usual procedure provided 3-methyl-2-butanol (61% yield) of 70% ee (Table 5). **b: In the Presence of 50 Mol % of $IpcBCl_2$ (≥99% ee).** In this experiment, 2.9 mmol of $IpcBCl_2$ (this makes a total of 50 mol %) was added to the above reaction mixture, and the experiment was repeated at −25 °C. Product alcohol, 68% ee, was obtained in 59% yield (Table 5).

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Supporting Information Available: Copies of the ^{11}B NMR spectra for $IpcBCl_2$ in pentane, $IpcBCl_2$·CS (CS = EE, THF, and SMe_2), $IpcBH_2$ in EE and THF, $IpcBH_2$·SMe_2, and IpcBHCl·CS (CS = EE, THF, and SMe_2) and Tables 6−9, which summarize the hydroboration results (14 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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