# Hydroboration. 96. Synthesis and Chemistry of Sterically Modified α-Pinene-Related 2-Organylapoisopinocampheylchloro- and -bromoboranes, Potentially Valuable for Asymmetric Hydroboration

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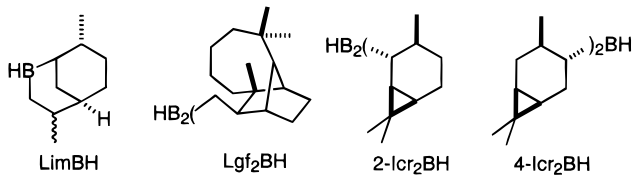
Optically pure and sterically varied 2-organylapoisopinocampheylchloro- and -bromoboranes (RapBHX; X = Cl and Br; R = Et (EapBHX), Pr (PraBHX), *i*-Bu (*i*-BapBHX), Ph (PapBHX), and *i*-Pr (*i*-PraBHX)), potentially valuable for asymmetric hydroboration of prochiral alkenes, are conveniently prepared by a number of simple approaches from the corresponding 2-organylapoisopinocampheyldihaloboranes ($RapBX_2$) and 2-organylapoisopinocampheylboranes ($RapBH_2$). All of these reagents can be readily obtained from 2-organylapopinenes (2-R-apopinenes). Increasing the steric bulk at the 2-position of the apopinene moiety significantly influences the formation of the desired RapBHCl. Thus, when R = *i*-Pr, a significantly lower amount of the sterically bulkier alkylchloroborane reagent, *i*-PraBHCl (47−52%), is formed in equilibrium with *i*-$PraBH_2$ (22−23%) and *i*-$PraBCl_2$ (22−23%). Surprisingly, a higher equilibrium composition for PapBHCl (84−86%), a sterically demanding borane reagent, is observed in equilibrium with 7−8% each of $PapBH_2$ and $PapBCl_2$. This result closely resembles the values realized in the formation of IpcBHCl, the least sterically hindered reagent among the organylchloroboranes examined in this study. However, it is possible to shift this equilibrium conveniently to achieve an increased concentration of RapBHCl (>95%) in ethyl ether ($Et_2O$) in the presence of known amounts (1−4 equiv) of strongly coordinating solvents (CS), such as dimethyl sulfide ($SMe_2$) and tetrahydrofuran (THF), solvents which readily coordinate with the chloroborane intermediates. Interestingly, irrespective of the bulk at the 2-position of the apopinene structure, the mere replacement of chloride in the RapBHCl reagents by bromide provides essentially pure RapBHBr·CS (>95%, R = Me, Et, Pr, *i*-Bu, Ph, and *i*-Pr; CS = $Et_2O$, THF, and $SMe_2$) reagents.



Asymmetric syntheses to achieve the preparation of chiral compounds of interest is well-reviewed in the literature.[2] Currently, much emphasis is being given to the synthesis of easily accessible, improved chiral auxiliaries and reagents. We have been actively pursuing research on chiral syntheses via enantiomerically pure organoboranes conveniently obtained from terpenes.[3]

Although diisopinocampheylborane ($Ipc_2BH$), derived from α-pinene, provides high ee's with the less sterically hindered *cis*-alkenes, it failed to achieve high optical induction for the more hindered trans and trisubstituted alkenes.[4,5] However, isopinocampheylborane ($IpcBH_2$) provides moderate to excellent optical purities (54% to ≥99%) in the hydroboration of trans and trisubstituted alkenes, with the higher values realized with phenyl-substituted alkenes.[6] Later, a number of terpene-based borane reagents, obtained from abundant low-cost terpenes, e.g., limonene, longifolene, and (+)-2- and (+)-3-carenes, were developed and applied to the hydroboration of prochiral alkenes.[5,7] Regrettably, these reagents provided less satisfactory results in asymmetric hydroboration.




Therefore, with the growing importance of organoboranes for asymmetric synthesis, the search for new chiral reagents continues. Over the years of our research involving α-pinene as a chiral director, as well

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(2) (a) *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1983; Vols. 1−5. (b) Crosby, J. *Tetrahedron* **1991**, *47*, 4789. (c) Duhamel, P. *Bull. Soc. Chim. Fr.* **1996**, *133*, 457. (d) Noyori, R.; Hashiguchi, S. *Appl. Homogeneous Catal. Organomet. Compd.* **1996**, *1*, 552. (c) Davies, I. W.; Reider, P. J. *Chem. Ind.* **1996**, *11*, 412.

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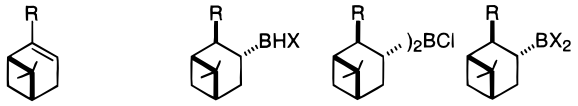
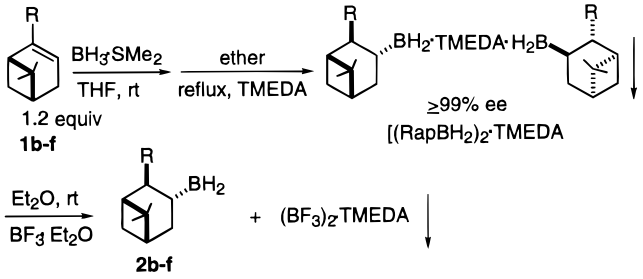
as theoretical calculations based on α-pinene-derived borane reagents,[8] suggest that the success of these reagents probably has its origin in the steric influence of the 2-methyl group of α-pinene (Ipc), as well as the steric and electronic environment around the boron atom. Therefore, we decided to modify the 2-position of the α-pinene structure. Consequently, we synthesized 2-ethyl- (Eap, **1b**),[9] 2-*n*-propyl- (Pra, **1c**),[10] 2-isobutyl- (*i*-Bap, **1d**),[11] 2-phenyl- (Pap, **1e**),[12] and 2-isopropylapopinenes (*i*-Pra, **1f**)[11] (2-organylapopinenes, 2-R-apopinenes, **1a**−**f**).




**1a** R = Me **1d** R = *i*-Bu **2** X = H **5a,b** **6** X = Cl
**1b** R = Et **1e** R = Ph **3** X = Cl **7** X = Br
**1c** R = Pr **1f** R = *i*-Pr **4** X = Br **8** X = I

Representative borane reagents derived from these chiral auxiliaries (**1b**−**f**) are achieving greatly improved stereochemical results in their reactions. For example, $EapBH_2$ (**2b**)[9] and *i*-$PraBH_2$ (**2f**),[13] derived from terpenes **1b** and **1f**, respectively, achieve higher asymmetric results than the parent $IpcBH_2$ (**2a**).[6] An improvement in asymmetric reduction of prochiral ketones is evident with the diorganylchloroborane ($Eap_2BCl$, **5b**), derived from 2-ethylapopinene (**2b**), in comparison with $Ipc_2BCl$ (**5a**).[14] A new asymmetric hydroborating agent, isopinocampheylchloroborane (IpcBHCl, **3a**)[15] proved to be excellent for the asymmetric cyclic hydroboration of 1-allyl-1-cyclohexene, achieving ≥99% enantiomeric excess for the product *trans*-1-decalone.[16] Finally, we discovered that the corresponding isopinocampheylbromoborane (IpcBHBr) achieved improved asymmetric induction in the hydroboration of prochiral alkenes at −78 °C, compared with those realized with IpcBHCl.[17] It is interesting, however, to note that asymmetric hydroboration of prochiral alkenes with IpcBHCl prepared in situ from the reduction of $IpcBCl_2$ with $Me_3SiH$ in pentane at −25 °C requires several days for completion.[15] However, under similar conditions, a major improvement in the reactivity of $IpcBBr_2$ with $Me_3SiH$ in pentane is observed. Thus, in situ generated IpcBHBr, from the reduction of $IpcBBr_2$ with $Me_3SiH$, hydroborates olefins in pentane in 4−6 h, even at −78 °C.[17] Therefore, in this context, it was of interest to investigate the chemistry of the IpcBHBr system. It was also desirable to systematically study the chemistry and synthesis of the higher analogues of IpcBHX (X = Cl, Br) reagents, such as the 2-organylapoisopinocampheylchloroborane reagents (**3**) and their bromo (**4**) counterparts, potentially useful for the asymmetric hydroboration of prochiral alkenes. Thus, in this paper we wish to report a systematic study of the formation of RapBHX (**3**, **4**) (R = Et, Pr, *i*-Bu, Ph, and *i*-Pr; X = Cl, Br) reagents.

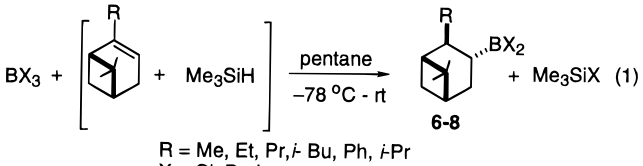
**Scheme 1**




## Results and Discussion

The synthesis of 2-R-apopinenes (**1b**−**f**) has been reported in our earlier papers.[9−12] The desired $RapBH_2$ (**2a**−**f**) can be readily obtained in quantitative yields through hydroboration of these apopinenes, reaction with TMEDA, followed by removal of the TMEDA from the resultant bis(2-organylapoisopinocampheylborane)·TMEDA adducts by treatment with boron trifluoride−etherate ($BF_3$·$Et_2O$) (Scheme 1).[18]

The formation of alkyldichloroborane from the reaction of boron trichloride with a mixture of the alkene and trialkylsilane has been reported by Matteson.[19] We investigated the utility of this remarkable reaction by synthesizing the sterically demanding $RapBX_2$ (X = Cl (**6**), Br (**7**), and I (**8**)) in quantitative yields from the reaction of 2-R-apopinenes (**1a**−**f**) with boron trihalides ($BX_3$) and trialkylsilane (eq 1).[20]




In our recent paper, we did a quantitative study of the preparation of optically pure IpcBHCl.[15] This reagent is made by four possible approaches: (1) the reaction of stoichiometric amounts of $IpcBH_2$ with $IpcBCl_2$ in $Et_2O$; (2) the reduction of $IpcBCl_2$ with $Me_3SiH$ in $Et_2O$; (3) the reduction of $IpcBCl_2$ with lithium aluminum hydride (LAH) in $Et_2O$; (4) the reaction of $IpcBH_2$ with anhydrous hydrogen chloride (HCl) in $Et_2O$. The first and second approaches were also



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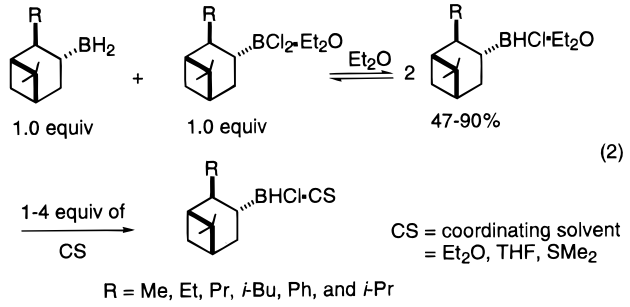
**Table 1. $^{11}$B NMR Chemical Shifts of the RapBH$_2$, RapBHCl, RapBCl$_2$, RapBBr$_2$, and RapBHBr Derivatives in Various Representative Solvents at 24 °C**

| | | $^{11}$B NMR values ($\delta$) | | | |
|---|---|---|---|---|---|
| solvent | RapBH$_2$ | RapBCl$_2$[a] | RapBHCl[b] | RapBBr$_2$ | RapBHBr |
| pentane | 22−23 (br) | 62 | 42 | 65 | 41−42 (br) |
| Et$_2$O | 22.5−23.0 (br) | 18−19 | 14−16 | 14 | 12.8[b,c] |
| THF | 22 (br) and 10.3 (br) | 16−17 | 12−14 | 12.5[d] | 11.5[b,d] |
| SMe$_2$ | −2.9 to −3.0[b] | 12−13 | 5.0−7.0[b] | 6.8 | 3.0−3.5[b] |

[a] *i*-PraBCl$_2$ loosely complexed with Et$_2$O (∼0.8−1.0 M solution) ($^{11}$B NMR: $\delta$ 50−55). [b] Proton-decoupled $^{11}$B NMR. [c] Cleaves Et$_2$O slowly at 0 °C. [d] Cleaves THF slowly in less than 2 h ($^{11}$B NMR: $\delta$ 32 br singlet).

investigated in tetrahydrofuran (THF) and in nonethereal solvents, such as pentane and dichloromethane ($CH_2Cl_2$). We decided to extend these procedures to understand the chemistry involved in the preparation of RapBHCl (**3b**−**f**) and RapBHBr (**4a**−**f**) from RapBH$_2$ (**2b**−**f**) and RapBBr$_2$ (**7a**−**f**), respectively.

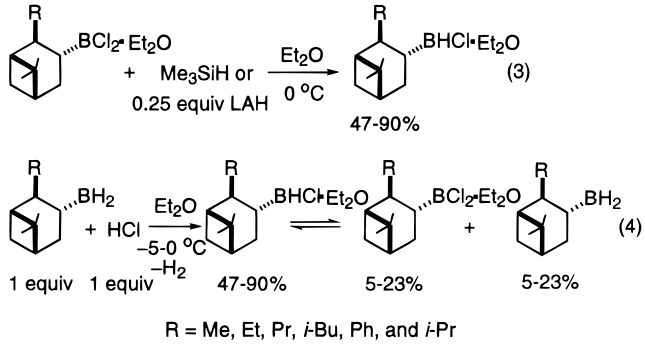
**Preparation and Chemistry of 2-Organylapoisopinocampheylchloroborane (RapBHCl, 3b−f) Reagents. Approach 1:** Optically pure RapBCl$_2$ (**6b**−**f**) were prepared as described in eq 1.[20] The reaction was monitored by $^{11}$B NMR spectroscopy.[15,21] The $^{11}$B NMR spectral chemical shifts for RapBH$_2$, RapBCl$_2$, and RapBHCl in representative solvents at 24 °C are given in Table 1. Mixing equimolar amounts of RapBH$_2$ and RapBCl$_2$ in Et$_2$O at 0 °C gave an equilibrium mixture containing a major amount of the desired RapBHCl·Et$_2$O, along with almost equal percentages of RapBH$_2$ and RapBCl$_2$·Et$_2$O (eq 2). The reaction was complete




in 0.25−0.50 h. Interestingly, in the formation of EapBHCl·Et$_2$O and PraBHCl·Et$_2$O, there was not much difference in the constitution of the equilibrium mixture. Thus, 79−80% of RapBHCl·Et$_2$O (R = Et, Pr) was obtained along with 10−11% each of RapBH$_2$ (R = Et, Pr) and RapBCl$_2$·Et$_2$O (R = Et, Pr).[21] Under similar experimental conditions, a further decrease in the major product, RapBHCl·Et$_2$O (R = *i*-Bu, *i*-Pr), was observed in the equilibrium mixtures involving the bulkier 2-R groups, 2-isobutyl (**3d**) and 2-isopropyl (**3f**).[21] In these cases, *i*-BapBHCl·Et$_2$O was formed in 66−70% yield while a significantly lower percentage of *i*-PraBHCl·Et$_2$O (only 47−52%) was observed. Apparently, 6−7% of dimeric (*i*-PraBHCl)$_2$ was formed in this reaction.[21] In contrast to these results, interestingly, the reaction of PapBH$_2$ (**2e**), the 2-phenyl derivative, with PapBCl$_2$ (**6e**) in Et$_2$O at 0 °C provided a much higher equilibrium concentration of the major component, i.e., 84−86% of PapBHCl·Et$_2$O along with 7−8% each of **2e** and **6e**;[21] values comparable with those obtained for the formation of IpcBHCl·Et$_2$O.[15]

We further investigated the effect of addition of known amounts of tetrahydrofuran (THF) and SMe$_2$ to the above equilibrium mixtures to provide RapBHCl·CS (CS = coordinating solvent = THF, SMe$_2$). Thus, addition of 2 and 1 equiv of THF and SMe$_2$, respectively, to the equilibrium mixture, except for R = *i*-Pr, of RapBHCl·Et$_2$O, RapBH$_2$, and RapBCl$_2$·Et$_2$O provided RapBHCl·THF (∼98% purity) and RapBHCl·SMe$_2$ (∼95% pure), produced in ∼1 and ∼12 h, respectively at 0 °C (eq 2). When 1 equiv of SMe$_2$ was added to the equilibrium mixture containing *i*-PraBHCl·Et$_2$O (47−52%), the desired *i*-PraBHCl·SMe$_2$ was formed in 75−80% purity, along with other undesirable haloborane derivatives at 0 °C in ∼12%, while 4 equiv of THF was required to provide the desired *i*-PraBHCl·THF in >95% purity at 0 °C in ∼2 h (eq 2).[21]

The results obtained in approach 1 were further substantiated by the other approaches. Thus, RapBHCl were prepared by the reduction of RapBCl$_2$ (**6b**−**f**) with Me$_3$SiH (approach 2) or 0.25 equiv of LAH (approach 3) in Et$_2$O at 0 °C (eq 3).[15] Similarly, in approach 4, RapBH$_2$ (**2b**−**f**) were allowed to react with an equivalent amount of HCl in Et$_2$O at 0 °C (eq 4). All of these




reactions were followed by $^{11}$B NMR spectroscopy.[21] Results comparable to those realized in approach 1 were obtained (Table 2). To better understand the effect of Et$_2$O in stabilizing RapBHCl·Et$_2$O formation, we decided to examine the effect of more basic solvents, such as THF and SMe$_2$, introduced as coordinating solvents (CS = THF and SMe$_2$) in Et$_2$O and pentane, on the reduction of RapBCl$_2$ with either Me$_3$SiH or 0.25 equiv of LiAlH$_4$ (eq 5).

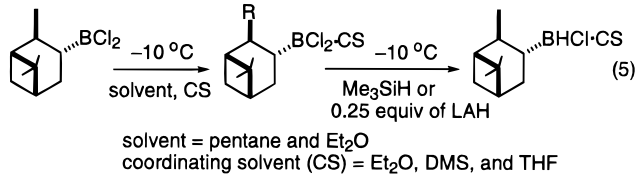
Thus, the reduction of RapBCl$_2$·THF with Me$_3$SiH (or 0.25 equiv of LiAlH$_4$) in THF was smooth and over in 0.25−0.5 h to provide the desired RapBHCl·THF (R = Et, Pr, *i*-Bu, Ph, and *i*-Pr) in quantitative yield. However, the reaction in Et$_2$O required 2−3 equiv of THF to achieve the clean formation of the desired RapBHCl·

(21) All borane species mentioned in this paper showed distinct $^{11}$B NMR signals adequate for their approximate percentage determination. Srebnik, M.; Cole, T. E.; Ramachandran, P. V.; Brown, H. C. *J. Org. Chem.* **1989**, *54*, 6085.

**Table 2. Equilibrium Formation of RapBHCl·$Et_2O$, with $RapBCl_2$ and $RapBH_2$, in the Reactions of $RapBCl_2$·$Et_2O$ with $RapBH_2$ or with $Me_3SiH$ (TMS)[a] and $RapBH_2$ with HCl in $Et_2O$ at 0 °C**

| | approximate percentage formation from analysis by $^{11}B$ NMR | | |
|---|---|---|---|
| R | RapBHCl·$Et_2O$ | $RapBCl_2$ | $RapBH_2$ |
| Me | 87−90 | 5−6.5 | 5−6.5 |
| Et[b,c] | 79−80 | 10−11 | 10−11 |
| *n*-Pr | 79−80 | 10−11 | 10−11 |
| *i*-Bu | 66−70 | 15−17 | 15−17 |
| Ph | 84−86 | 7−8 | 7−8 |
| *i*-Pr[c−e] | 47−52 | 22−23 | 22−23 |

[a] Identical results were obtained when 0.25 equiv of LAH was used as the reducing agent. [b] Equilibrium was shifted to clean EapBHCl·THF (>98% pure in ∼1 h) by adding 2 equiv of THF, while EapBHCl·$SMe_2$ (∼95% pure formed after 12 h at 0 °C) was obtained by adding 1 equiv of $SMe_2$. [c] Reduction of $RapBCl_2$ (R = Et and *i*-Pr) with $Me_3SiH$ was possible in pentane in the presence of 1 equiv of $SMe_2$ at 24 °C providing RapBHCl·$SMe_2$ (R = Et and *i*-Pr; >95% pure) in 6 h. [d] Approximately 6−7% dimeric *i*-PraBHCl was seen by $^{11}B$ NMR at ca. $\delta$ 40−45. [e] Equilibrium was shifted to *i*-PraBHCl·$SMe_2$ (75−80% pure along with other haloborane derivatives in ∼12 h at 0 °C) in the presence of 1 equiv of $SMe_2$, while 4 equiv of THF was used to obtain *i*-PraBHCl·THF (>95% pure in ∼2 h at 0 °C).




THF (R = Et, Pr, *i*-Bu, Ph, and *i*-Pr). Similarly, we observed that the reduction of $RapBCl_2$ (R = Et and *i*-Pr) with $Me_3SiH$ was possible in pentane in the presence of 1 equiv of $SMe_2$ at 24 °C to provide RapBHCl·$SMe_2$ (R = Et and *i*-Pr; >95% pure) in 6 h. All of these results are summarized in Table 2.

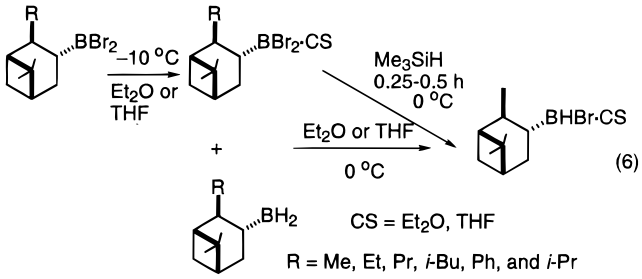
These results imply that as the 2-R group of RapBHCl·$Et_2O$ increases in steric requirements from Me to Et ≅ Pr to *i*-Bu and to *i*-Pr, decreasing amounts of RapBHCl·$Et_2O$ (R = Me ≅ Ph, Et ≅ Pr, *i*-Bu, and *i*-Pr) exist in equilibrium, along with almost equal larger amounts of $RapBH_2$ (**2a**−**f**) and $RapBCl_2$ (**6a**−**f**). However, 2-Ph in PapBHCl·$Et_2O$ (**3e**) provides an exception. We previously noted that the behavior of the 2-phenyl derivative was anomalous.[12] Clearly, the electronic effect of the phenyl substituent is quite different from those of the alkyl substituents examined. Interestingly, the synthesis of RapBHCl·THF is possible in $Et_2O$ or pentane as solvent, provided an adequate amount of THF (2−3 equiv) is present.

These observations suggested the desirability of examining the effect of introducing a bromine atom in place of the chlorine atom on the boron atom of the reagents RapBHCl to achieve the synthesis of RapBHBr exclusively.

**Preparation and Chemistry of 2-Organylapoisopinocampheylbromoboranes (RapBHBr, 4b−f).** The synthesis of $RapBBr_2$ (**7a**−**f**) was carried out as described earlier (eq 1). The $^{11}B$ NMR spectral chemical shifts for $RapBBr_2$ (**7a**−**f**) and RapBHBr (**4a**−**f**) are shown in Table 1. The equilibration of $RapBH_2$ (**2a**−**f**) with $RapBBr_2$ (**7a**−**f**) in a 1:1 molar ratio was performed in $Et_2O$ at 0 °C as described previously (eq 2). Similarly, the reduction of $RapBBr_2$ was performed with $Me_3SiH$ in $Et_2O$ at 0 °C, as shown in eq 3. The critical investigation for the formation of IpcBHBr·CS (CS = $Et_2O$, THF, and $SMe_2$) is described. The reaction progress was monitored by $^{11}B$ NMR spectroscopy.[21] Unlike the equilibrium formation of IpcBHCl·$Et_2O$, IpcBHBr·$Et_2O$ is formed in 0.25−1.0 h in >98% purity by the methods described in eqs 3 and 5.[21] The IpcBHBr·$Et_2O$ kept at 0 °C for 12 h did not show any appreciable change in $^{11}B$ NMR spectrum. The addition of 1 equiv of $SMe_2$ to IpcBHBr·$Et_2O$ in $Et_2O$ provided IpcBHBr·$SMe_2$ ($^{11}B$ NMR signal at $\delta$ 3.34) quantitatively in ∼10 min at 24 °C. This compound kept at 0 °C for 48 h showed unchanged $^{11}B$ NMR spectrum in comparison with the freshly prepared sample.

The reaction of equivalent amounts of $IpcBH_2$ (**2a**) with $IpcBBr_2$ (**7a**) in THF and $SMe_2$ at 0 °C provided the desired IpcBHBr·THF and IpcBHBr·$SMe_2$ quantitatively in 0.25 and 12 h, respectively. However, IpcBHBr·THF reacted slowly with the cleavage of THF at 0 °C to give possible species, such as IpcBHO$(CH_2)_4$-Br ($^{11}B$ NMR, $\delta$ 21−22 br) and IpcB[O$(CH_2)_4$Br]$_2$ ($\delta$ 31 br). At 0 °C, after 48 h, approximately 24% and 30% (by $^{11}B$ NMR) of the former and the latter species, respectively, were observed. In contrast, at 0 °C, the exchange reaction between $IpcBH_2$ and $IpcBBr_2$ in noncoordinating solvents, such as pentane and dichloromethane ($CH_2Cl_2$), was extremely slow, providing equilibrium mixtures in which the required IpcBHBr was only 3−4%. The reaction mixture, maintained at 0 °C for 24 h, showed a complex mixture of boron components.

Unlike the reduction of IpcBCl$_2$·$Et_2O$ with $Me_3SiH$, the reduction of IpcBBr$_2$·$Et_2O$ with $Me_3SiH$ provided clean IpcBHBr·$Et_2O$ in less than 0.5 h. Under similar conditions, this reaction in THF provided IpcBHBr·THF in >99% purity in 0.5 h (eq 6).




After critically investigating the formation of IpcBHBr, we decided to carry out the exchange reactions between $RapBH_2$ (**2b**−**f**) and $RapBBr_2$ (**7b**−**f**) in $Et_2O$ at 0 °C. Thus, by mixing stoichiometric quantites of $RapBBr_2$ and $RapBH_2$ in $Et_2O$, the sterically bulkier RapBHBr·$Et_2O$ derivatives (R = Me, Et, Pr, *i*-Bu, Ph, and *i*-Pr) were formed in 0.25−1.0 h in >95% purity.[21] Similar results were obtained for the reduction of $RapBBr_2$ (**7b**−**f**) with $Me_3SiH$ in $Et_2O$ at 0 °C. The reduction was complete in 0.5−1 h.[21] All of these reagents cleave THF slowly at 0 °C, and even $Et_2O$, albeit very slowly.

## Conclusions

This paper describes a detailed quantitative study of the preparation and chemistry of sterically and elec-

tronically varied RapBHX (X = Cl, Br; R = Me, Et, *i*-Pr, Bu, Ph, *i*-Pr) reagents. These reagents can be prepared conveniently in a number of simple operations. In the preparation of RapBHX, all of these procedures provide almost the same results. It is quite evident from these results that the steric and electronic environment around the boron atom of these reagents plays a significant role in their formation. Thus, increasing the bulk of R in the 2-position of apopinene from Me to Et to *i*-Bu to *i*-Pr lowers the equilibrium percentage of RapBHCl for the reactions in $Et_2O$. However, there is no significant difference between the steric effects of the ethyl- (Et) and the propyl- (Pr) groups. Consequently, equal equilibrium amounts of the corresponding RapBHCl (R = Et and Pr) in $Et_2O$ is observed in their reaction. Interestingly, the 2-phenyl group provides a higher equilibrium concentration of PapBHCl in $Et_2O$, which closely resembles the results realized in the formation of IpcBHCl.[15] The addition of known amounts of coordinating solvents (CS) such as THF and $SMe_2$, which are known to coordinate chloroboranes, helps to shift the equilibrium in $Et_2O$ in favor of the desired RapBHCl·CS. Similarly, carrying out all of these reactions in THF provides exclusively the desired RapBHCl·THF in >95%.

Interestingly, unlike the preparation of RapBHCl, irrespective of the 2-organyl group in RapBHCl, replacement of the chlorine atom by bromine provides RapBHBr·$Et_2O$ exclusively (>95%). However, the formation of the bulkier RapBHBr·THF is complicated by the concurrent cleavage of THF. Fortunately, this can be circumvented easily by substituting THF with $Et_2O$ or $SMe_2$. Now that we can control the formation of essentially pure RapBHCl·CS and RapBHBr·CS, we are exploring the possibility of achieving even higher enantioselectivities in applying these reagents to the asymmetric hydroboration of prochiral alkenes.

## Experimental Section

All glassware was dried at 140 °C overnight, assembled hot, and cooled to ambient temperature in a stream of nitrogen.[22] All reactions involving air- or moisture-sensitive compounds were performed under a static pressure of dry nitrogen.[22] $^{11}B$ NMR spectra were recorded at 96 MHz and were referenced relative to $BF_3$·$Et_2O$. Capillary GC analyses were performed using SPB-5 column (30 m).

**Materials.** Tetrahydrofuran was distilled from sodium benzophenone ketyl and used as required. Commercial anhydrous $SMe_2$ was used as received without any further purification. Solutions (1.0 M) of $BCl_3$ and $BBr_3$ were prepared in dry pentane and stored in a refrigerator. Anhydrous $Et_2O$ was used without purification. The 2-R-apopinenes (**1b**−**f**) were synthesized by the known procedures.[9−12] The 2-R-apopinenes (**1b**−**d**, **f**) were derived from (+)-α-pinene, while (+)-2-phenylapopinene (**1e**)[12] was synthesized from (+)-*β*-pinene.[23] The crystalline bis-adducts of 2-organylapoisopinocampheylboranes with TMEDA ((RapBH$_2$)$_2$·TMEDA, R = Et, Pr, *i*-Bu, Ph, and *i*-Pr) were prepared and transformed into the corresponding mono-2-organylapoisopinylboranes (**2b**−**f**) in higher purity according to the literature procedure.[18] The RapBX$_2$ (X = Cl and Br) derivatives were made according to the literature procedure.[20]

**Typical Procedure for the Preparation of EapBHCl·$Et_2O$ from the Reaction of EapBH$_2$ (2b) with EapBCl$_2$ (6b) in $Et_2O$.** This procedure is representative for the preparation of RapBHCl·$Et_2O$. To $Et_2O$ (8.0 mL) cooled at −10 °C, optically pure EapBCl$_2$ (5.0 mmol) was added slowly ($^{11}B$ NMR spectrum of EapBCl$_2$·$Et_2O$ is a singlet at $\delta$ 17−19). This solution was added to a cold (0 °C) solution of EapBH$_2$ (1.0 M, 5.0 mL, 5.0 mmol) in $Et_2O$ and stirred for 15 min. At that point, the $^{11}B$ NMR spectrum of the reaction showed a mixture of 80% of EapBHCl·$Et_2O$ ($^{11}B$ NMR spectrum, broad doublet $\delta$ 15.5 and 14.3; $^1H$ NMR decoupled $^{11}B$ NMR $\delta$ 14.8 singlet) and 10% each of EapBCl$_2$·$Et_2O$ ($^{11}B$ NMR $\delta$ 17−19 singlet) and EapBH$_2$ dimer ($^{11}B$ NMR $\delta$ 21−22 br singlet). The reaction mixture left at 0 °C for 12 h did not show any appreciable change in the equilibrium composition of these species (by $^{11}B$ NMR spectrum). The molarity of the solution was conveniently determined by hydride analysis.[22] The hydrolysis of a 1.0 mL aliquot produced 23.0 mL of $H_2$, which corresponds to 0.92 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 the indicator. The solution was 1.0 M in chloride. This reaction in THF provided EapBHCl·THF in >98% purity in <10 min ($^{11}B$ NMR, $\delta$ 11.7 broad singlet).

Under similar conditions, RapBHCl·CS (CS = $Et_2O$ and THF) were prepared in $Et_2O$ and THF, respectively, at 0 °C in 0.25−1.0 h. The collective results of these reactions are shown in Table 2. The effect of the addition of known amounts of coordinating solvents (CS = THF and $SMe_2$) to the above equilibrium mixture containing varying amounts of RapBHCl·$Et_2O$ in $Et_2O$ was observed by adding THF or $SMe_2$ in stepwise fashion until the formation of RapBHCl·CS was complete (Table 2). The reaction was followed by a $^{11}B$ NMR spectrum every 0.50 h for 12 h.

The reaction of equimolar amounts of RapBH$_2$ with RapBBr$_2$ in $Et_2O$ was performed as follows. To the solution of RapBH$_2$ (5−10 mmol) in $Et_2O$, cooled to −10 °C, RapBBr$_2$ (5−10 mmol) was added and stirred for 10 min and then stirred for a further 10 min at 0 °C. The reaction period ranged from 0.25 to 0.50 h. The desired RapBHBr·$Et_2O$ derivatives were obtained in >95% purity.

**Typical Procedure for the Preparation of EapBHCl·$Et_2O$ from the Reaction of EapBH$_2$ (2b) with HCl in $Et_2O$.** This reaction is representative for the preparation of RapBHCl·$Et_2O$. To the solution of optically pure EapBH$_2$ (1.0 M, 10.0 mL, 10 mmol) in $Et_2O$, cooled to −5 °C, HCl in $Et_2O$ (2.38 M, 4.20 mL, 10 mmol) was added slowly and the liberated $H_2$ was measured (9.5 mmol, 95% in ∼10 min). The $^{11}B$ NMR spectrum of the solution indicated an equilibrium mixture of 79% EapBHCl·$Et_2O$ and 10.5% each of EapBCl$_2$·$Et_2O$ and EapBH$_2$. The solution was 0.68 M in hydride and 0.70 M in chloride. Under similar conditions, the RapBHCl·$Et_2O$ derivatives (**3c**−**f**) were prepared in $Et_2O$, in equilibrium with smaller amounts of RapBCl$_2$·$Et_2O$ and RapBH$_2$. However, in the reaction of *i*-PraBH$_2$ with HCl in $Et_2O$, the liberation of $H_2$ was relatively slow at 0 °C and the reaction was complete at ∼5 °C in <10 min, as observed from the measurement of the total $H_2$ liberated. The results of the experiments are the same as those described above and compiled in Table 2.

**Typical Procedure for the Preparation of EapBHCl·$Et_2O$ from the Reduction of EapBCl$_2$ (6b) with Me$_3$SiH in $Et_2O$.** This procedure is representative for the preparation of RapBHCl·$Et_2O$. To cold (−10 °C) $Et_2O$ (5.0 mL), EapBCl$_2$ (5.0 mmol) was added slowly, followed by a solution of Me$_3$SiH (5.0 mmol) in $Et_2O$ (1.0 mL). The $^{11}B$ NMR spectrum of the solution after ∼10 min showed an equilibrium mixture of EapBHCl·$Et_2O$ (∼79%) and ∼10.5% each of EapBH$_2$ and EapBCl$_2$·$Et_2O$. The same reaction in THF (5.0 mL) provided EapBHCl·THF (>98%). Under similar conditions, RapBHCl·$Et_2O$ (**3c**−**f**) were obtained in equilibrium with RapBCl$_2$·$Et_2O$ and RapBH$_2$ in 0.25−1.0 h. The percentage distribution of

(22) Brown, H. C. *Organic Synthesis Via Boranes*; Wiley-Interscience: New York, 1975. A reprinted edition, Vol 1, Aldrich Chemical Co., Inc.: Milwaukee, 1997, is currently available.
(23) Brown, H. C.; Joshi, N. N. *J. Org. Chem.* **1988**, *53*, 4059.

these species is the same as that described previously. The effect of addition of coordinating solvents, such as THF and $SMe_2$, was the same as observed in the earlier experiments. The reduction of $RapBCl_2$ (R = Et, *i*-Pr) with $Me_3SiH$ in pentane in the presence of 1.0 equiv of $SMe_2$ provided >95% $RapBHCl{\cdot}SMe_2$ (R = Et, *i*-Pr) after 6 h at 24 °C (Table 2). However, in THF, the reduction of $RapBCl_2$ with $Me_3SiH$ provided >95% of the desired RapBHCl·THF in ∼0.25−0.5 h.

**Typical Procedure for the Preparation of EapBHCl·$Et_2O$ from the Reduction of $EapBCl_2$ (6b) with 0.25 Equiv of $LiAlH_4$.** To cold (−10 °C) $Et_2O$ (5.0 mL), $EapBCl_2$ (5.0 mmol) was added slowly, followed by a clear solution of LAH (1.0 M, 1.25 mmol) in $Et_2O$. The $^{11}B$ NMR spectrum of the solution after ∼5 min showed an equilibrium mixture of $EapBHCl{\cdot}Et_2O$ (∼80%) and ∼10% each of $EapBH_2$ and $EapBCl_2{\cdot}Et_2O$. The same reaction in THF (5.0 mL) provided EapBHCl·THF (>98%). Under similar conditions, $RapBHCl{\cdot}Et_2O$ (**3c**−**f**) were obtained in equilibrium with $RapBCl_2{\cdot}Et_2O$ and $RapBH_2$ in 0.25−1.0 h. The percentage distribution of these species is the same as that described earlier.

**Typical Procedure for the Preparation of RapBHBr·$Et_2O$ (>95% Pure).** To cold (−10 °C) $Et_2O$ (4.0−9.0 mL), $RapBBr_2$ (5−10 mmol) was added slowly followed by the addition of a solution of $Me_3SiH$ (5−10 mmol) in $Et_2O$ (1.0 mL). The desired $RapBHBr{\cdot}Et_2O$ (>95% purity) was formed in ∼0.25−0.5 h. LAH was not used in this preparation.

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**Supporting Information Available:** $^{11}B$ NMR spectra for $RapBHCl{\cdot}Et_2O$ (**3b**,**c**) and a representative spectrum for RapBHCl·THF and $RapBHBr{\cdot}Et_2O$ (7 pages). Ordering information is given on any current masthead page.

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