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Substitution with retention in organoboranes and utilization of the phenomenon for a general synthesis of pure enantiomers

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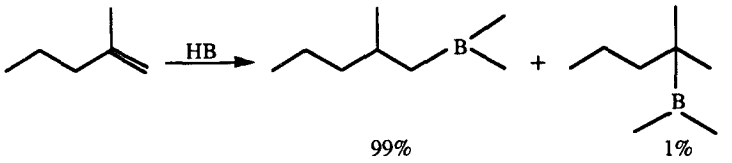
Abstract. Organoboranes, readily available via the hydroboration of unsaturated organic compounds, exhibit a remarkable versatility in their reactions. The boron atom in these organoboranes can be readily converted into a wide variety of organic groups under very mild conditions, providing simple versatile syntheses of organic compounds. Exploration of these substitution reactions reveal that, with rare exceptions, the organoboranes transfer the alkyl group to other elements of synthetic interest with complete retention of stereochemistry. Recently we have discovered a method of synthesizing essentially optically pure organoborane intermediates. These optically active alkyl groups attached to boron can also be transferred with complete retention of optical activity. Consequently, it is now possible to achieve by a rational synthesis the preparation of almost any optically active compound with a chiral center, either R- or S-, in essentially 100% enantiomeric excess.

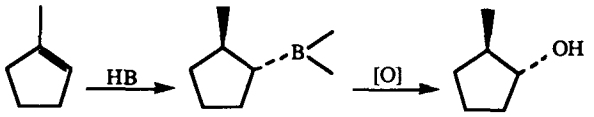
Keywords. Substitution with retention; organoboranes; synthesis of pure enantiomers; retention of stereochemistry.

The ether-catalyzed addition of diborane to unsaturated organic molecules – the hydroboration reaction – made organoboranes readily available (Brown and Subba Rao 1957; Brown *et al* 1975). A systematic study of the scope and characteristics of the hydroboration reaction revealed that the addition of borane to unsaturated organic molecules is essentially quantitative and proceeds in an *anti*-Markonikov manner (1).



(1)

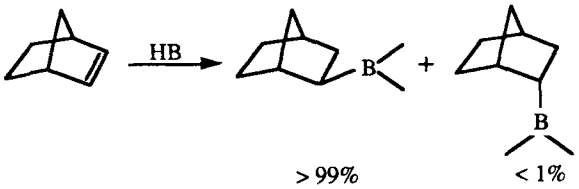
The reaction involves a *cis*-addition of the H–B bond (2).



(2)

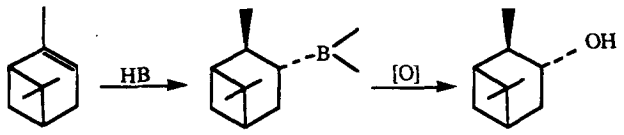
* For correspondence.

The addition takes place preferentially from the less hindered side of the double bond (3).



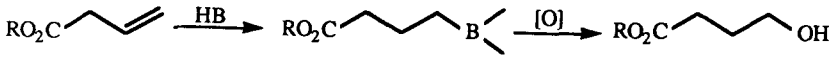
(3)

No rearrangements of the carbon skeleton have been observed, even in molecules as labile as α-pinene (4).



(4)

Most functional groups can tolerate the hydroboration reaction (5).



(5)

Initially, the hydroboration reaction did not attract much attention as a synthetically useful reaction. After all, hydroboration produces organoboranes. At the time we started, only three things were really known about organoboranes: (1) they were oxidized by air; (2) they were stable to water; (3) they formed addition compounds with bases. Our research program has taken this exotic group of chemicals, diborane and organoboranes from unknown materials of little interest to important reagents with major synthetic importance. Exploration of the chemistry of organoboranes, with emphasis on reactions of synthetic utility, has revealed their exceptional versatility (Brown *et al* 1975). An unexpected characteristic of these reactions of organoboranes is the fact that organoboranes transfer the alkyl group to essentially most of the other elements of synthetic and biological interest with complete maintenance of stereochemical integrity. Typical transformations are indicated in figure 1.

Protonolysis

As mentioned earlier, the organoboranes are remarkably stable to water, aqueous bases, and aqueous mineral acids. However, they undergo protonolysis by carboxylic acid. Protonolysis of organoboranes proceeds with retention of configuration (Brown and Murray 1986). Thus one can take advantage of the unique properties of the hydroboration reaction to achieve stereospecific hydrogenations (figure 2) (Zweifel and Brown 1964).

Protonolysis of organoboranes also makes possible the stereospecific synthesis of deuterium derivatives (figure 3).

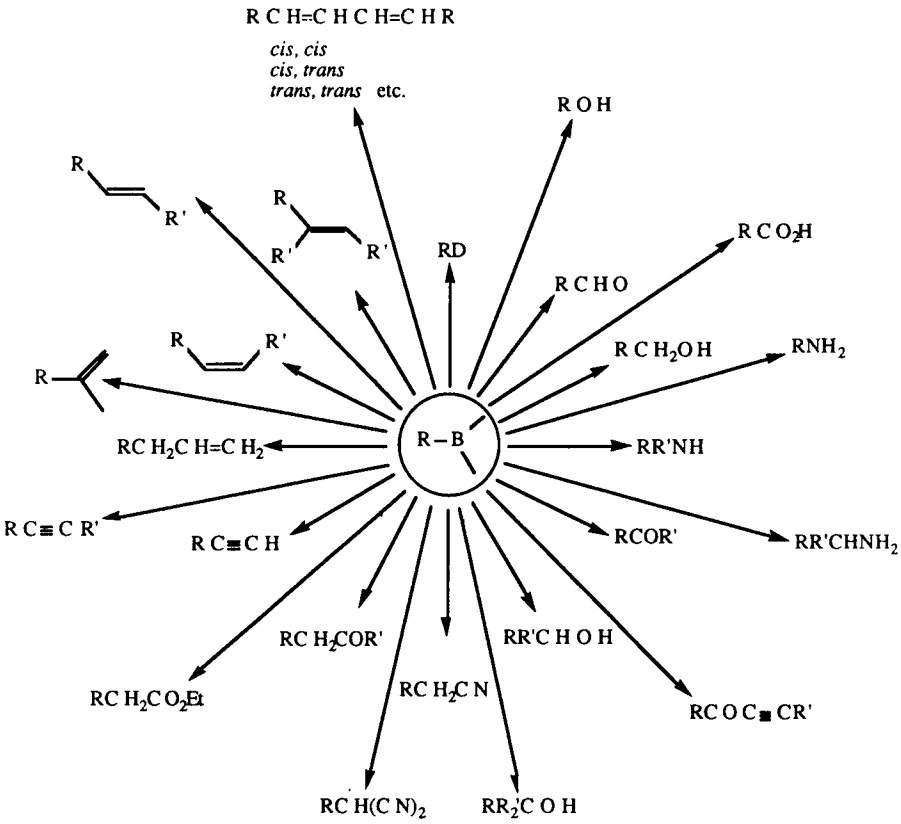


Figure 1. Chart summarizing representative substitution reactions of organoboranes.

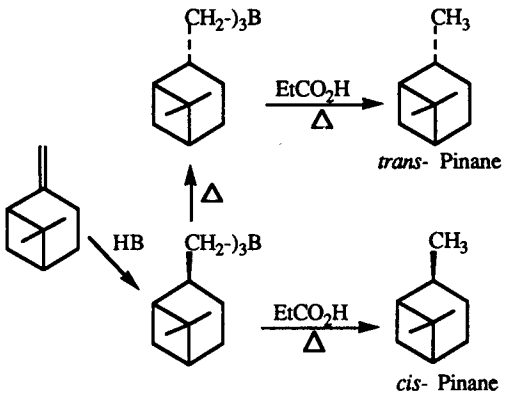


Figure 2. Hydroboration-protonolysis of β-pinene to provide either *cis*- or *trans*-pinane as desired.

Oxidation

Similarly, oxidation of organoboranes with alkaline hydrogen peroxide produces the alcohols in essentially quantitative yield with complete retention of configuration (figure 4) (Brown and Zweifel 1961b).

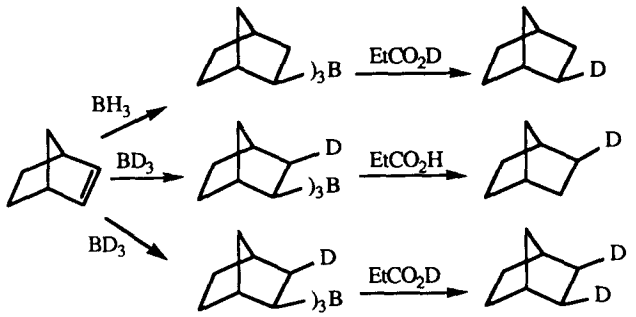


Figure 3. Hydroboration-protonolysis of norbornene to demonstrate protonolysis with retention.

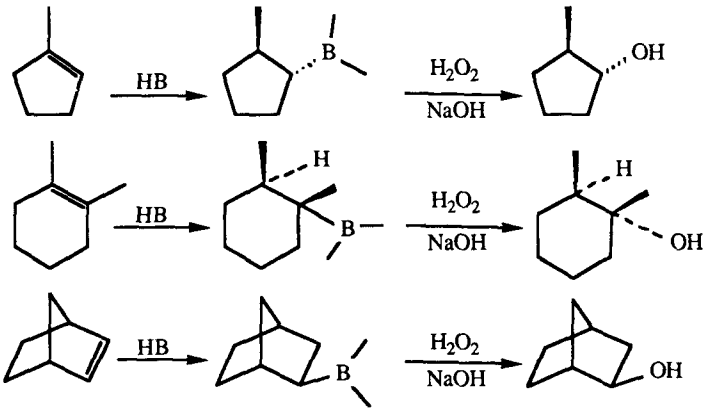


Figure 4. Representative hydroborations-oxidations which establish retention in the oxidation stage.

Amination

Organoboranes are readily converted by chloramine or O-hydroxylamine sulfonic acid to primary amines (Rathke *et al* 1966). The use of dimethylalkylboranes, prepared from lithium dimethylborohydride, is especially effective in permitting essentially complete utilization of the alkyl groups (Brown *et al* 1987a). Here also the reaction proceeds with retention (figure 5).

The reaction of organoboranes, such as monoalkyldichloroboranes, with organic azides provides a convenient route to secondary amines (Brown *et al* 1973). This procedure provides a simple route to pure N-*exo*-norbornylaniline, corresponding to retention in the reaction of the *exo*-norbornyl boron moiety produced in the hydroboration (figure 6).

Formylation

In the presence of hydride reducing agents (MH), carbonylation of organoboranes proceeds readily to provide an intermediate which is oxidized to the aldehyde or hydrolyzed to the methylol derivative. The use of *B*-alkyl-9-BBN derivatives is

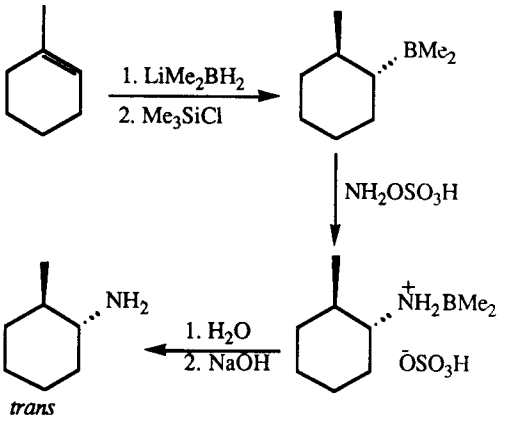


Figure 5. Amination of organoborane intermediates with retention of configuration.

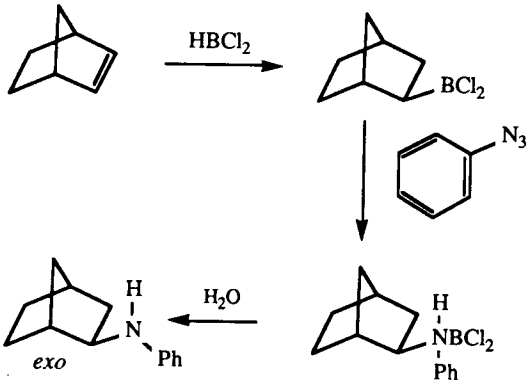


Figure 6. Synthesis of secondary amines with retention from organoborane intermediates and organic azides.

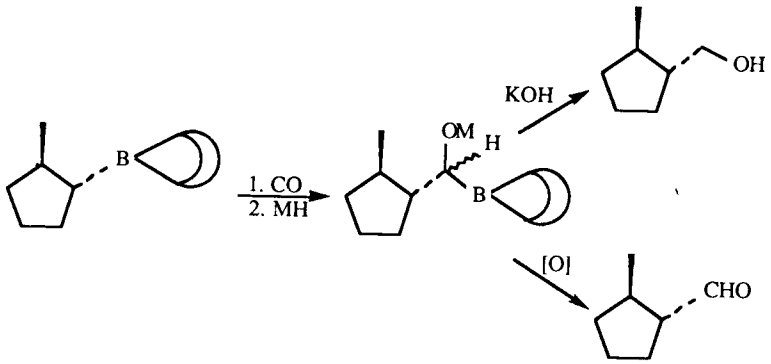


Figure 7. Conversion of R-B-9BBN via carbonylation into aldehydes or methylol derivatives with retention of configuration.

especially effective in permitting essentially complete utilization of the alkyl group (Brown and Knights 1969; Brown *et al* 1979). The stereospecificity realized in the hydroboration reaction is retained during the reaction (figure 7) (Brown *et al* 1969b).

Alkylboronate esters are also converted into the corresponding aldehydes by successive treatment with methoxy(phenylthio)methyllithium (MPML), mercuric chloride and buffered hydrogen peroxide (Brown and Imai 1983). This reaction also proceeds with retention of configuration, as observed in other related reactions of organoboranes. Thus, the *trans*-geometry obtained by hydroboration of 1-methylcyclohexene is retained in the product (figure 8).

Homologation

Reaction of alkylboronic esters with dichloromethyllithium, followed by reduction of the intermediate with potassium triisopropoxyborohydride (KIPBH), gives the corresponding one-carbon homologated boronic esters. Oxidation provides methylol derivatives (figure 9) (Brown *et al* 1985c).

Ketone synthesis

Yet another reaction of organoboranes that proceeds with retention of stereochemistry is the synthesis of ketones via the DCME reaction. Dialkylborinic acid

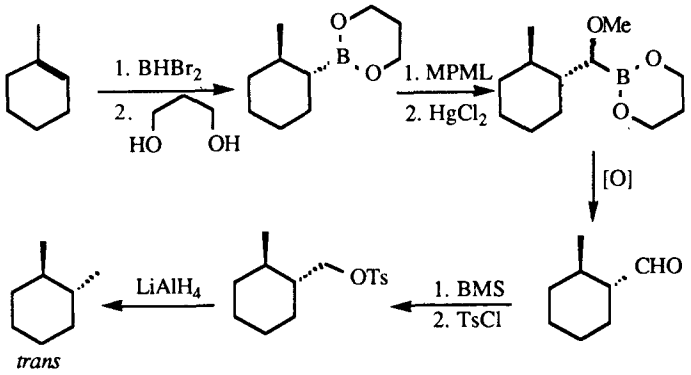


Figure 8. Transformation of the hydroboration product from 1-methylcyclohexene into *trans*-2-methylcyclohexane carboxaldehyde with complete retention of configuration.

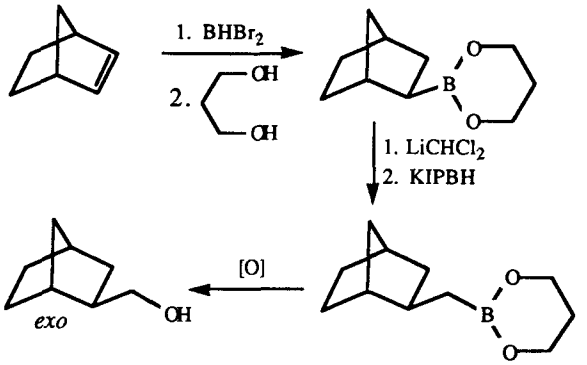


Figure 9. Homologation of boronic esters into the higher boronic esters with retention.

esters, now readily available via hydroboration with chloroborane-ethyl etherate, react with α,α-dichloromethyl methyl ether (DCME), in the presence of sterically hindered base, to transfer the alkyl groups from boron to carbon under remarkable mild conditions. Oxidation of the intermediate provides the corresponding ketone (figure 10) (Carlson and Brown 1973).

α-Alkylation

α-Halo esters can be alkylated readily by organoboranes in the presence of suitable bases. This reaction is applicable to a wide variety of α-halo derivatives, such as ethyl bromoacetate, bromoacetone, chloroacetonitrile, etc (Brown *et al* 1969a). The use of B-alkyl-9-BBN derivatives provides more economical utilization of the organic groups. In this reaction also, the transfer of the alkyl group from boron to carbon proceeds with stereochemical integrity (figure 11) (Brown *et al* 1969b).

Acetylene synthesis

The ate complex formed by the reaction of an organoborane with lithium acetylide-ethylene diamine reacts with iodine at −78°C to give the corresponding

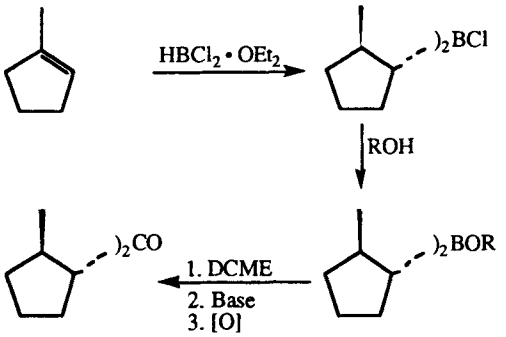


Figure 10. Ketone synthesis via DCME reaction proceeds with retention.

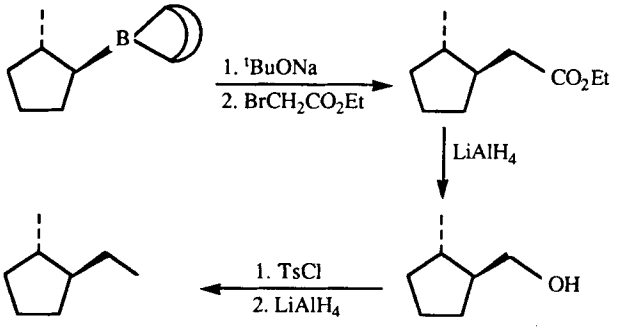


Figure 11. α-Alkylation reaction of organoboranes proceeds with retention of stereochemistry.

terminal acetylene (Midland *et al* 1974). Application of the reaction to 1-methylcyclopentene established that the reaction proceeds with complete retention of configuration (figure 12).

Whereas the great majority of the substitution reactions of organoboranes proceed with complete retention, a few reactions are known which proceed with loss of stereochemical purity or with inversion.

Oxidation with oxygen

Organoboranes can be converted into alcohols by controlled treatment with air or molecular oxygen. This oxidation apparently proceeds through free radical intermediates, resulting in a loss of stereochemical purity of the product (figure 13) (Brown *et al* 1986b).

Halogenolysis

Simple treatment of the organoborane with halogen in the presence of a suitable base produces the desired organic halide. Surprisingly, the bromination of *exo*-norbornyl boron derivatives proceeds with predominant inversion to yield *endo*-norbornyl bromide (figure 14) (Brown and Lane 1970, 1971).

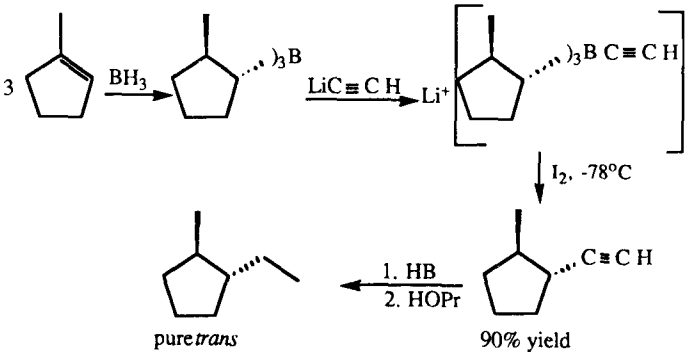


Figure 12. Acetylene synthesis proceeds with retention.

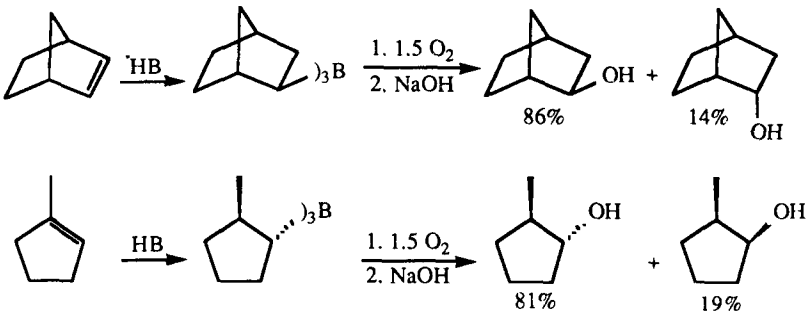


Figure 13. Oxidation of organoboranes by molecular oxygen proceeds with loss of stereochemical identity.

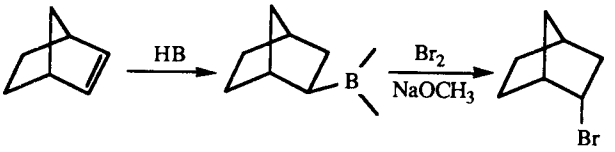


Figure 14. Inversion in the conversion of *exo*-norbornyl boron intermediated into the norbornyl bromide.

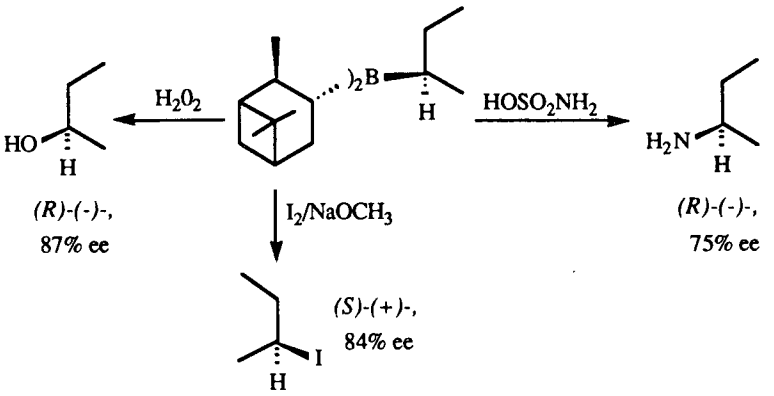


Figure 15. An example of inversion as contrasted to predominant retention in the substitution reactions of organoboranes.

It should be pointed out that the chiral intermediate, 2-butyldiisopinocampheylborane, is readily converted into optically active 2-butanol (Brown and Zweifel 1961a) and optically active 2-aminobutane (Verbit and Heffron 1967), both with complete retention of configuration, but into 2-iodobutane (Brown *et al* 1976) with complete inversion of configuration (figure 15).

In recent years the chemical literature has reflected the growing popularity of chiral reagents for the construction of optically active organic molecules. The realization that the great majority of the substitution reactions of organoboranes proceed with retention made it evident that if we could learn to achieve the synthesis of optically active groups attached to boron, we could transfer those groups to carbon and other elements to permit a general synthesis of optically pure enantiomers.

Asymmetric hydroboration – diisopinocampheylborane

Our initial interest in chiral organoborane chemistry stemmed from the ready availability of naturally occurring terpenes needed to prepare the chiral organoborane reagents. We selected α-pinene, primarily, to demonstrate the mildness of the hydroboration reaction (*vide supra*). The product, diisopinocampheylborane (Ipc_2BH) (Brown and Zweifel 1961a), was the first asymmetric hydroboration reagent. It was of interest to ascertain the degree of asymmetric induction achieved by hydroboration with Ipc_2BH. Indeed, the hydroboration-oxidation of *cis*-2-butene with Ipc_2BH (from (+)-α-pinene of 93% ee) provided [R]-(−)-2-butanol of

87% ee (Zweifel and Brown 1964)! Accordingly we had achieved the first truly successful, remarkably high, non-enzymatic, asymmetric synthesis. Another major advantage of Ipc_2BH is the ready availability of both (+)- and (−)-α-pinenes. Consequently, chiral centers of opposite configuration can be generated using Ipc_2BH derived from the appropriate enantiomers of α-pinene.

Commercial α-pinene is only 92% optically pure. However, we have learned to prepare Ipc_2BH of high enantiomeric purity from such α-pinene. The crystalline Ipc_2BH formed on hydroboration of α-pinene (92% ee) is allowed to stand at 0°C in the presence of a slight excess of α-pinene. The major isomer becomes incorporated into the crystalline reagent, leaving the "unwanted" isomer in solution (figure 16) (Brown and Yoon 1977; Brown and Singaram 1984b).

Treatment of Ipc_2BH with benzaldehyde liberates α-pinene of ~100% ee. Thus the two reactions provide a convenient procedure for upgrading commercial α-pinene to an enantiomeric purity of essentially 100% ee (figure 17) (Brown *et al* 1982b, p. 4583).

Better asymmetric inductions were realized in the hydroboration of *cis*-olefins with this Ipc_2BH of high optical purity (figure 18) (Brown *et al* 1982b, p. 5065).

Similarly, the asymmetric hydroboration of heterocyclic olefins is both highly regio- and enantioselective. Thus hydroboration of 2,3-dihydrofuran with Ipc_2BH, followed by oxidation, provides 3-hydroxyfuran in essentially 100% ee (figure 19) (Brown and Vara Prasad 1986).

Several synthetic intermediates have been made using asymmetric hydroboration with Ipc_2BH, followed by oxidation. An example is the prostaglandin precursor

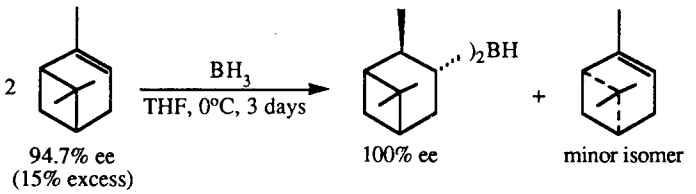


Figure 16. Preparation of pure diisopinocampheylborane.

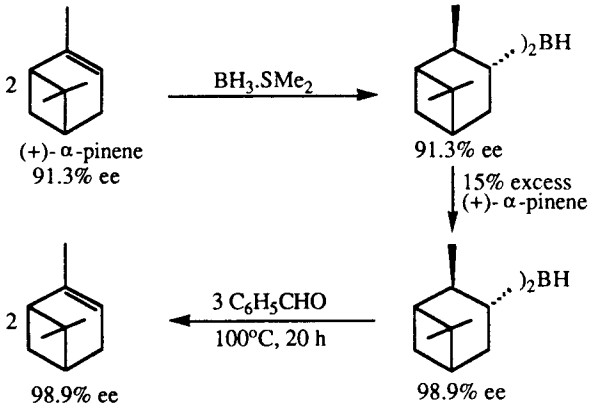


Figure 17. Preparation of α-pinene of high optical purity.

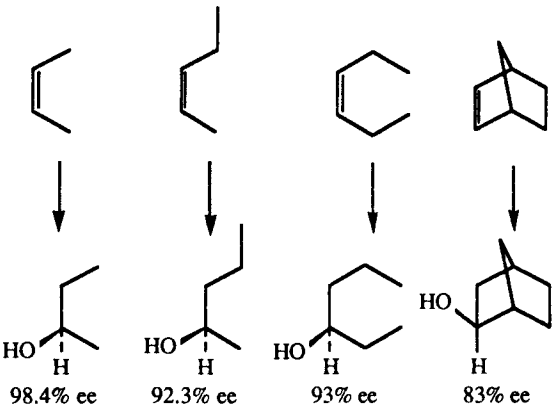


Figure 18. Asymmetric hydroboration of *cis*-alkenes with Ipc_2BH.

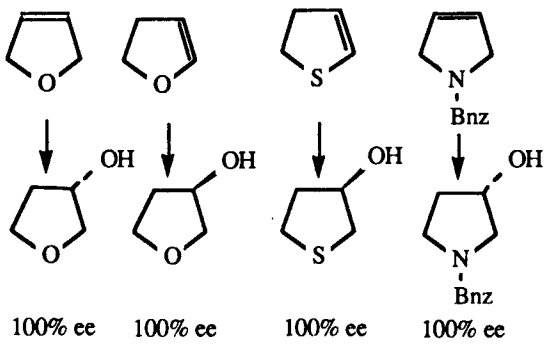


Figure 19. Asymmetric hydroboration of some heterocyclic alkenes.

obtained from the asymmetric hydroboration-oxidation reaction of methyl cyclopentadiene-5-acetate (figure 20) (Patridge *et al* 1973, p. 532). Useful intermediates for the synthesis of loganin and zeaxanthin have been obtained by asymmetric hydroboration-oxidation of 5-methyl cyclopentadiene (Patridge *et al* 1973, p. 7171) and safranol ether (Rüttimann and Mayer 1980) respectively (figure 20).

Diisopinocampheylborane handles *cis*-alkenes very effectively. However, it is not an effective asymmetric hydroborating agent for 2-substituted-1-alkenes. Although simple 2-methyl-1-alkenes yield alcohols of $\leq 30\%$ ee, very high selectivities have been achieved when one of the two substituents was very bulky. Thus, the tylonolide precursor was obtained from the asymmetric hydroboration-oxidation reaction of the complex 2-methyl-1-olefinic compound with $(-)$-Ipc_2BH and the isomeric ratio was at least 50:1. Asymmetric hydroboration-oxidation of the complex olefin using $(+)$-Ipc_2BH gave the epimeric alcohol with a selectivity of at least 50:1 (figure 21) (Masamune *et al* 1982).

Diisopinocampheylborane is also not an effective asymmetric hydroborating agent for *trans*-alkenes and trisubstituted alkenes. Evidently the steric requirements of 2-methyl-1-alkenes are too low to provide a good steric fit with the reagent. On the other hand, the steric requirements of *trans*- and trisubstituted alkenes are, apparently, too large for the reagent (figure 22).

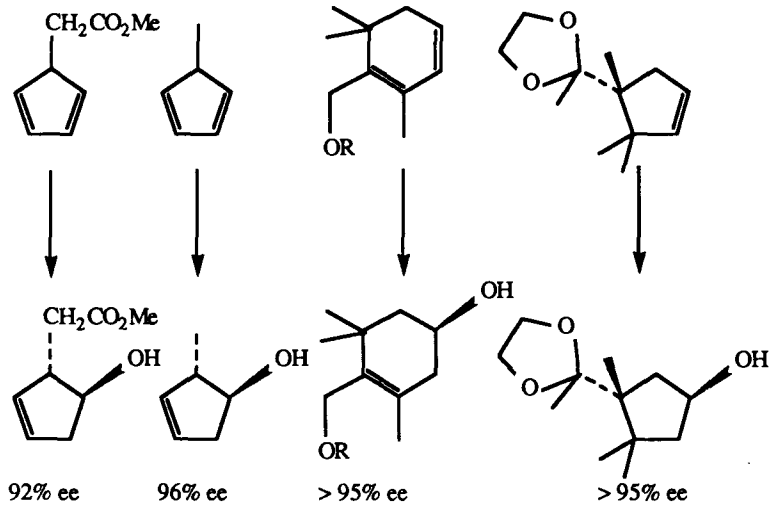


Figure 20. Preparation of synthetic intermediates by asymmetric hydroboration-oxidation procedure.

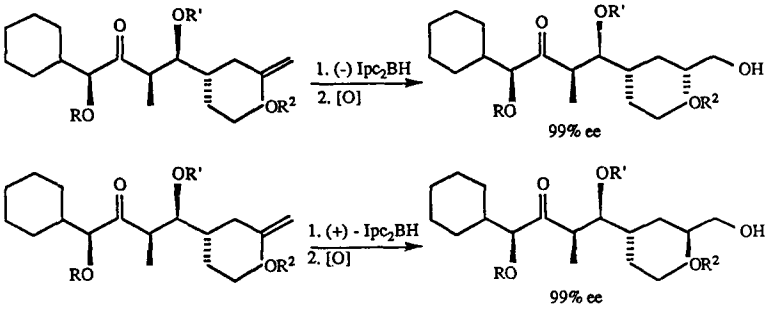


Figure 21. Synthesis of tylonolide precursor by asymmetric hydroboration-oxidation method.

Increasing steric requirements	2-METHYL-1-ALKENE	~ 20% ee
	cis-ALKENES	~ 100% ee
	trans-ALKENES	~ 20% ee
	TRISUBSTITUTED ALKENES	~ 20% ee
	Will $IpcBH_2$ handle more hindered classes?	

Figure 22. Ipc_2BH handles only one class effectively.

Asymmetric hydroboration – monoisopinocampheylborane

We shifted to monoisopinocampheylborane, $IpcBH_2$, for the asymmetric hydroboration of *trans*-alkenes and trisubstituted alkenes. It is difficult to halt the hydroboration of α-pinene at the monoalkylborane stage. The reaction commonly proceeds rapidly to the dialkylborane stage. However, treatment of Ipc_2BH with

one-half equivalent of *N,N,N',N'*-tetramethylethylenediamine (TMED) provides the 1 : 2 adduct, TMED·2BH_2Ipc, with the liberation of one equivalent of α-pinene. The adduct crystallizes out in enantiomerically and diastereomerically pure form. The reagent, IpcBH_2, is readily liberated by treating the adduct with boron trifluoride etherate (figure 23) (Brown *et al* 1978).

Asymmetric hydroboration of *trans*-olefins with monoisopinocampheylborane is very effective (figure 24) (Brown *et al* 1982c).

Monoisopinocampheylborane is also very effective for the asymmetric hydroboration of trisubstituted alkenes (figure 25) (Brown *et al* 1982c).

Considerably improved asymmetric inductions are realized in the hydroboration of the phenyl derivatives of the trisubstituted alkenes with IpcBH_2. Thus, 1-phenylcyclohexene provides the hydroboration product in 97% ee (figure 26) (Brown *et al* 1982c, 1987c).

Apparently Ipc_2BH and IpcBH_2 are complementary to each other. These two reagents handle three of the four major classes of alkenes. There remains a need for a reagent which will provide access to products of high optical purity from alkenes of relatively low steric requirements such as the 2-methyl-1-alkenes (figure 27). However, as discussed later, we have developed an alternative solution to this problem.

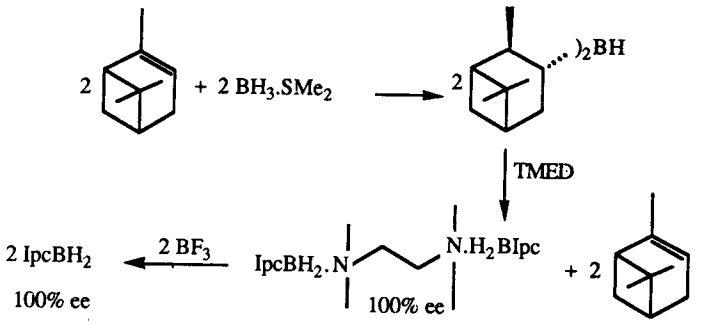


Figure 23. Synthesis of IpcBH_2 in 100% ee.

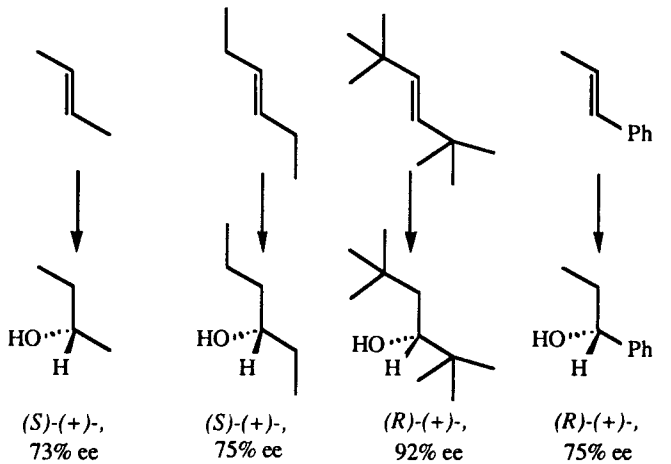


Figure 24. Asymmetric hydroboration of *trans*-alkenes with IpcBH_2.

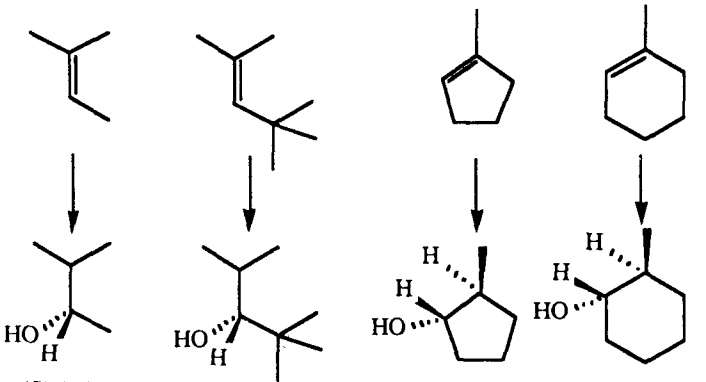


Figure 25. Asymmetric hydroboration of trisubstituted alkenes with $IpcBH_2$.

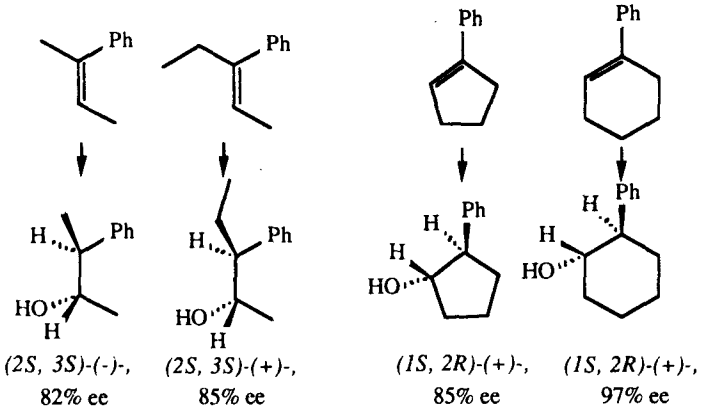


Figure 26. Asymmetric hydroboration of trisubstituted alkenes with a phenyl substituent by $IpcBH_2$.

	CLASS	Ipc_2BH	$IpcBH_2$
Increasing steric requirements ↓	2-METHYL-1-ALKENE	~ 20% ee	~ 1%
	cis-ALKENES	~ 100% ee	~ 25%
	trans-ALKENES	~ 20% ee	70-90% ee
	TRISUBSTITUTED ALKENES	~ 20% ee	60-100% ee

Figure 27. Range of applicability of Ipc_2BH and $IpcBH_2$.

Recently, Masamune and coworkers have reported the synthesis and resolution of a new asymmetric hydroborating agent, *trans*-2,5-dimethylboralane (Masamune *et al* 1985). The C_2 symmetry, which makes both faces of the boron atom equivalent, is an important feature of this reagent.

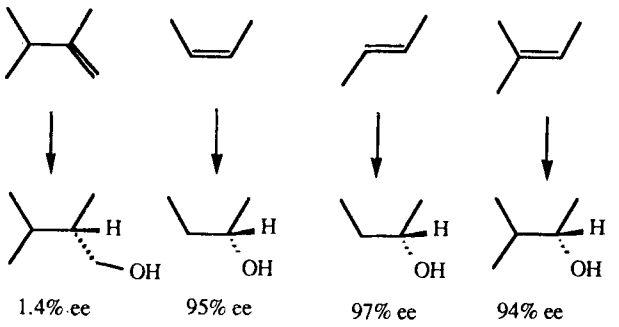


Figure 28. Asymmetric hydroboration with the Masamune reagent.

This reagent yielded excellent results in the asymmetric hydroboration of three of the four representative classes of olefins. However, the 2-substituted-1-alkenes proved resistant and gave nearly racemic product (figure 28).

It is not yet clear whether this reagent can be recycled. Consequently, until it becomes commercially available at a reasonable cost, its use will involve considerable effort.

A general asymmetric synthesis

As discussed earlier, our studies have established that organoboranes transfer the alkyl group to essentially most of the other elements of synthetic and biological interest with complete maintenance of stereochemical integrity. Consequently, organoboranes derived from α-pinene exhibit great potential in converting commercially available prochiral olefins into various optically active derivatives. Initially, the application of asymmetric hydroboration was limited primarily to the synthesis of optically active alcohols (Brown *et al* 1981). Recently, the chiral organoboranes, obtained from asymmetric hydroboration, have been utilized to synthesize optically active amines, halides, ketones and hydrocarbons (Brown *et al* 1981, 1984). However, the optical purity of these compounds were less satisfactory, only in the range of 60–90% ee. One reason for this is, in the past, chiral organoborane intermediates were difficult to prepare, except in few cases, in an optically pure form. Additionally, the optically active compounds thus obtained were contaminated with isopinocampheyl migrated product and made further purification necessary (C A Brown *et al* 1986).

Chiral organoborane chemistry experienced a major renaissance in the past few years. Three recent developments, in our laboratories, have proven of major importance and offer promise of a general synthesis of essentially any organic compound containing an asymmetric center in 100% ee. Either of the two enantiomers can be produced at will. Consequently, it would appear that for the first time we have within our grasp a rational synthesis of almost any organic compound with an asymmetric center in 100% ee.

First, we discovered that treatment of the asymmetric hydroboration products with acetaldehyde removes the isopinocampheyl group as α-pinene, yielding the optically active boronic esters. In this way, 2-butyldiisopinocampheylborane is readily converted into diethyl 2-butylboronate in 97% ee (figure 29) (Brown *et al* 1982a).

Similarly, diethyl *trans*-2-phenylcyclohexylboronate can be obtained in 97% ee (Brown *et al* 1987c). The elimination of the isopinocampheyl group is highly selective and in all cases we have studied thus far, this group is eliminated in preference to the desired chiral group (figure 30).

The α-pinene displaced could be readily recovered for recycling.

Second, the reaction product from $IpcBH_2$ and prochiral olefin, IpcR*BH, are often crystalline solids and readily crystallize from the reaction mixture. We have now discovered that such simple crystallization provides product of essentially 100% ee (figure 31) (Brown and Singaram 1984a).

We could now readily prepare many chiral boronic esters of essentially 100% optical purity (figure 32) (Brown and Singaram 1984a).

Recently Matteson *et al* (1985) have achieved an alternative synthesis of optically active boronic esters by a homologation procedure (figure 33).

Third, treatment of these optically active boronic esters with lithium aluminum hydride converts these relatively unreactive boronic esters into very reactive lithium monoalkylborohydrides, LiR^*BH_3. By an appropriate choice of the ester group, the aluminum by-product, $HAl(OR)_2$, readily precipitates from solution.

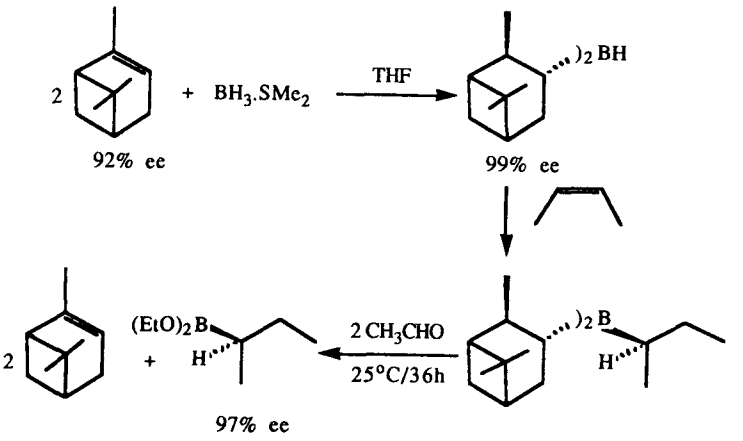


Figure 29. Asymmetric hydroboration with Ipc_2BH with regeneration of the α-pinene.

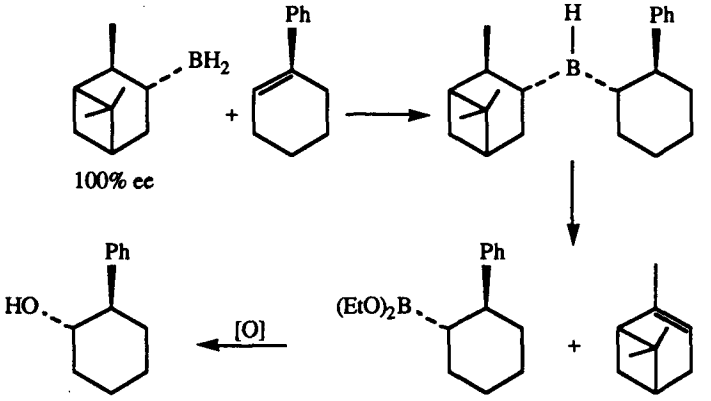


Figure 30. Asymmetric hydroboration with $IpcBH_2$ with regeneration of α-pinene.

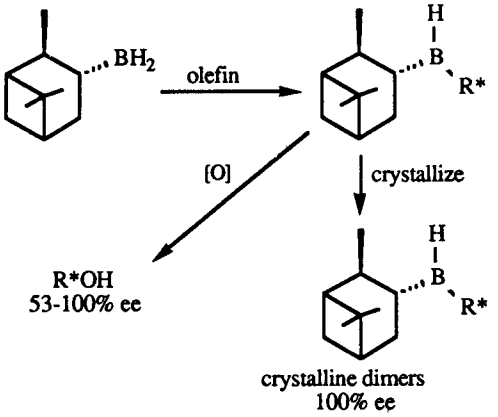


Figure 31. Major improvement in optical purity afforded by recrystallization of the hydroboration product.

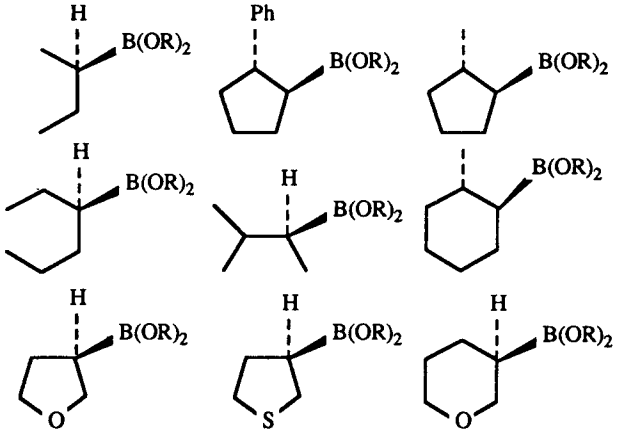


Figure 32. Representative boronic esters of 100% ee.

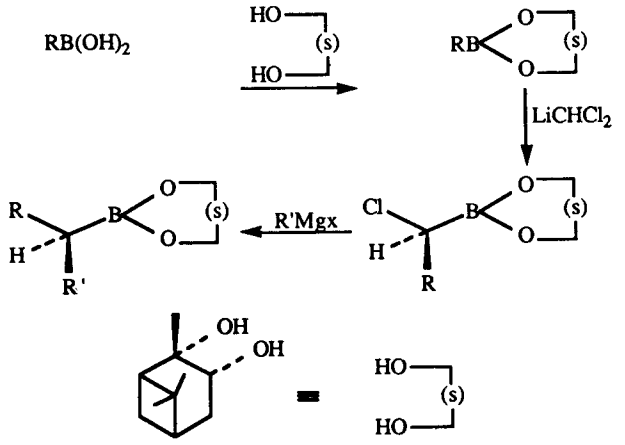


Figure 33. Matteson procedure for the synthesis of optically active boronate esters.

Simple treatment of the monoalkylborohydride with acid gives the optically active monoalkylborane and other substituted borane derivatives (figure 34) (Brown *et al* 1985d).

We can now make all of the boron reagents, such as thexylmonoalkylborane and B-alkyl-9-borabicyclononane, we had previously found valuable to achieve synthesis via organoboranes in very high optical purity (figure 35) (Brown *et al* 1988a, b).

Now the remarkable synthetic versatility of organoboranes takes over. For the first time, we have a wide variety of procedures available for the synthesis of both (+)- and (−)-isomers, optically pure boronic esters and other boron intermediates. It appears as if we have been building up organoborane chemistry primarily for this moment. Now we can use all of the knowledge previously gained in developing syntheses via achiral organoboranes to produce optically pure enantiomers (figure 36).

There are now a number of reactions which can be applied to the, relatively unreactive, boronic esters. Thus they are readily converted into α-chiral aldehydes, R*CHO, and these can either be reduced to β-chiral alcohols, R^*CH_2OH, or oxidized to α-chiral acids, R^*CO_2H (figure 37) (Brown *et al* 1985a).

We can adopt the Matteson homologation reaction to achieve the synthesis of optically pure β-chiral boronic esters which are difficult to prepare by the asymmetric hydroboration of 2-substituted-1-olefins. A second operation provides the γ-chiral boronic ester (figure 38) (Brown *et al* 1985b).

Optically pure boronic esters can be converted into optically active ketones of very high optical purity through the intermediate formation of the corresponding borinic esters (figure 39) (Brown *et al* 1987b).

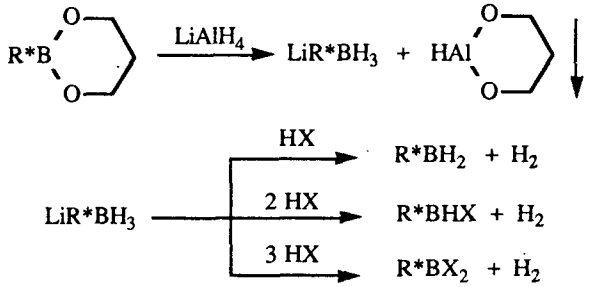


Figure 34. Conversion of optically active boronic acids into optically active borohydrides and derived boranes.

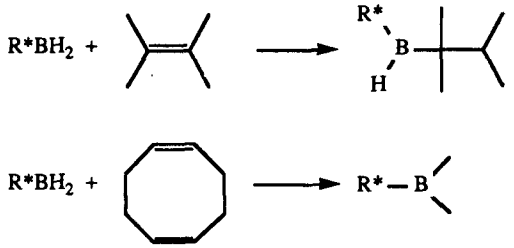


Figure 35. Synthesis of optically active thexyl and 9-BBN derivatives.

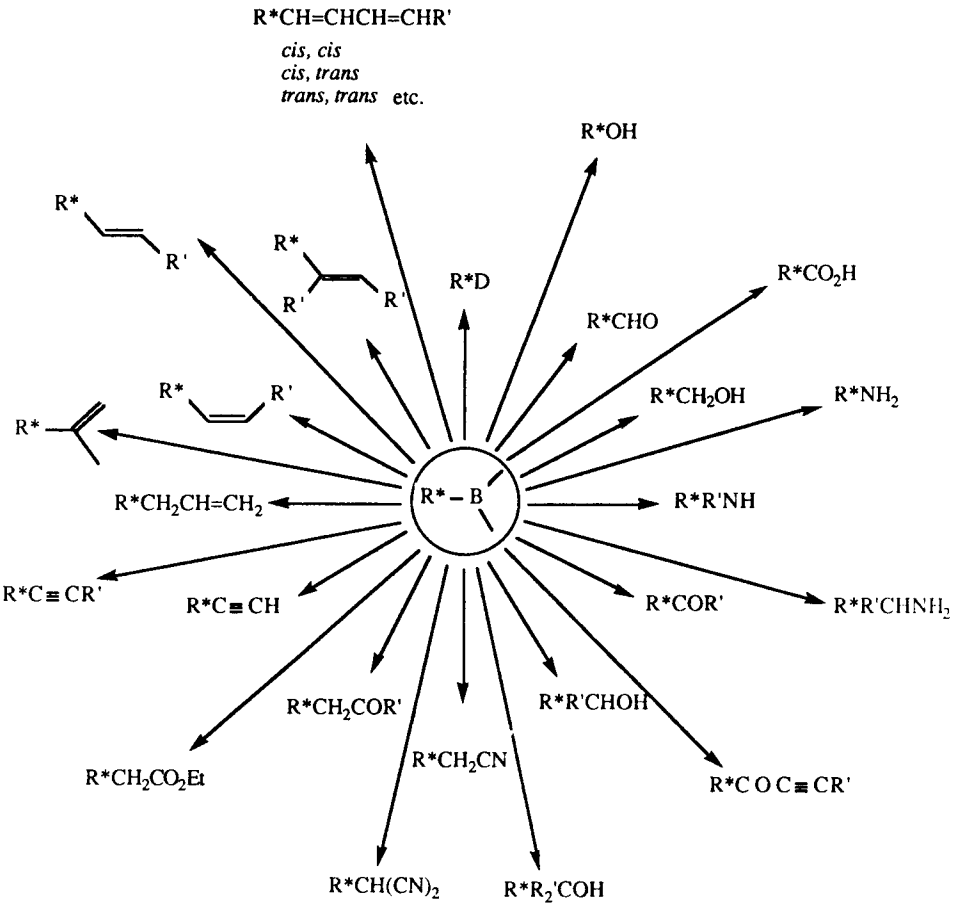


Figure 36. Borane chemistry makes possible a general synthesis of optically pure enantiomers.

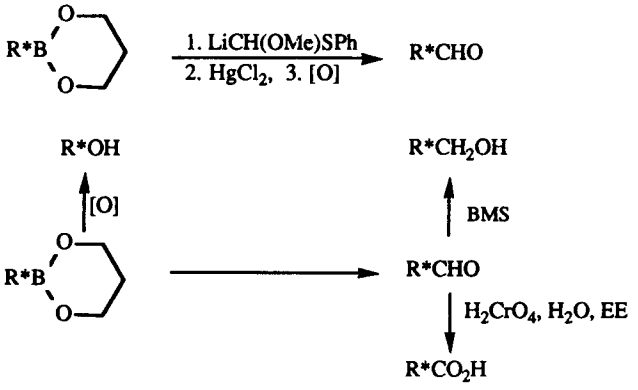


Figure 37. Conversion of optically active boronic esters into optically active aldehydes, acids and methylol derivatives of essentially 100% ee.

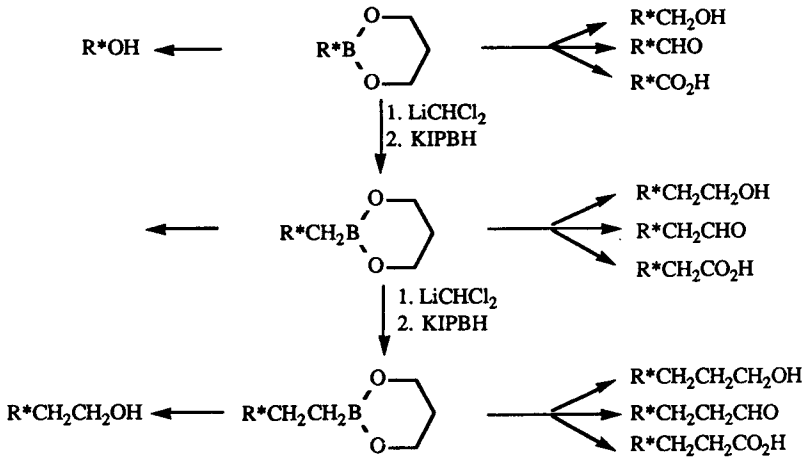


Figure 38. Synthesis of optically active derivatives via successive homologations.

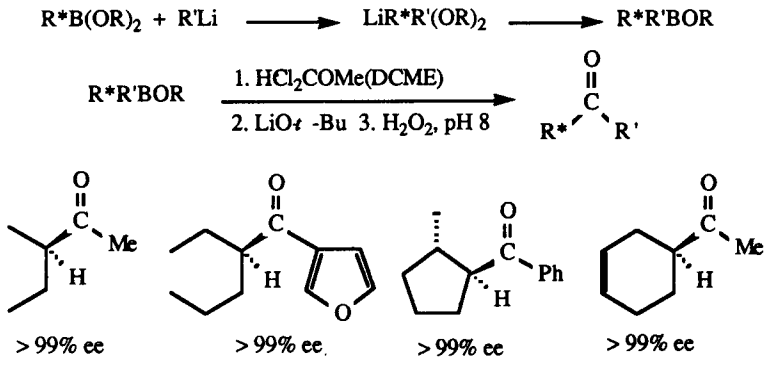


Figure 39. Synthesis of optically active ketones of essentially 100% ee.

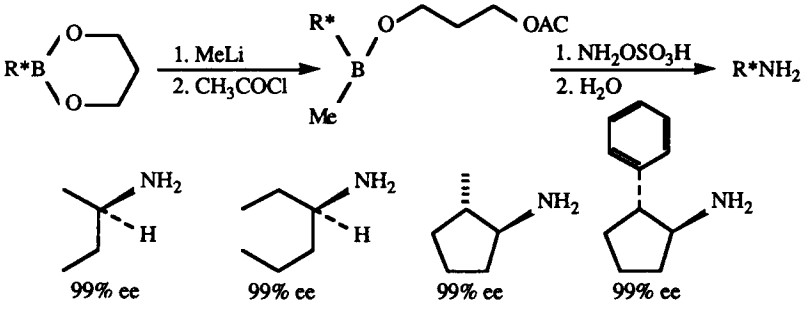


Figure 40. Procedure for the synthesis of primary amines in high enantiomeric purity.

Primary amines of very high optical purity can be obtained from optically active boronic esters through the intermediate formation of alkylmethylborinic esters (figure 40) (Brown *et al* 1986a).

Optically pure thexylmonoalkylboranes, ThxR*BH, are versatile synthetic intermediates. We have utilized these derivatives for various carbon-carbon

bond-forming reactions leading to optically active *trans*-alkenes, *cis*-alkenes, alkynes and ketones (figures 41, 42 and 43) (Brown *et al* 1988a).

Similarly, optically pure B-alkyl-9-borabicyclononane derivatives are converted into homologated esters, nitriles and ketones of very high optical purity (figures 44, 45 and 46) (Brown *et al* 1988b).

In this article we traced major developments, largely in our own research program, which led from the first chiral organoborane, Ipc_2BH, to the present time when we have numerous reagents, methods and applications based on chiral organoboranes for asymmetric synthesis in organic chemistry. Recent developments in our laboratory have greatly expanded the availability of chiral organoboranes and their derivatives with very high optical purity. It should be noted that this process involves an asymmetric synthesis of the desired chiral isomer in approximately 80–90% yield by asymmetric hydroboration. This is followed by crystallization or other purification of the hydroboration product, providing the desired group, R*, attached to boron in essentially 100% optical purity. Simple procedures either are available or envisioned to transfer the optically pure R* to

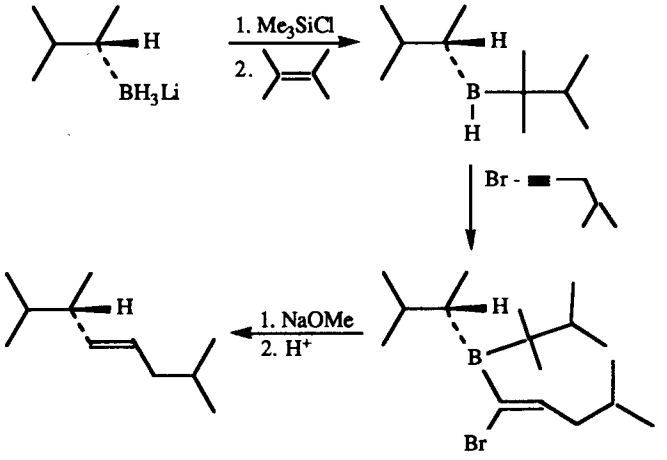


Figure 41. Synthesis of optically active *trans*-alkenes.

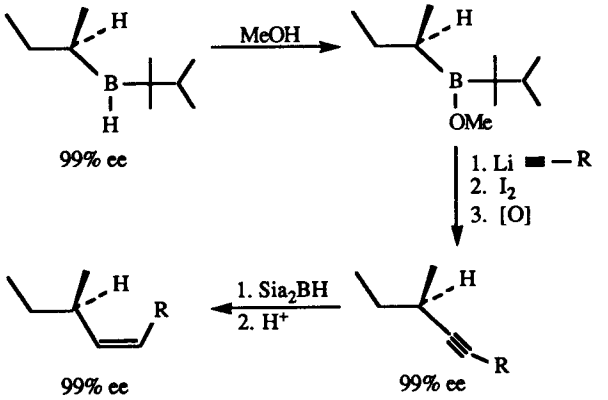


Figure 42. Preparation of optically active alkynes and *cis*-olefins.

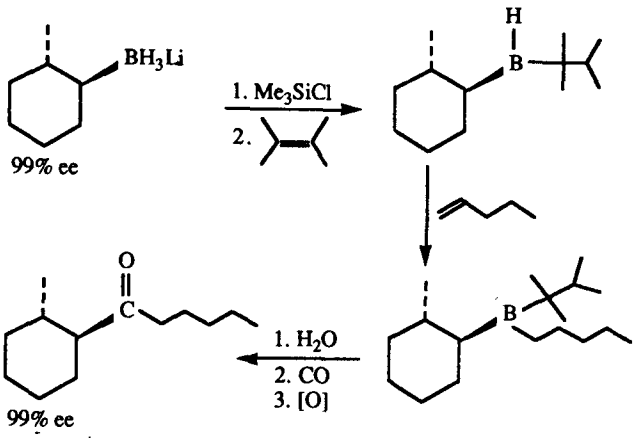


Figure 43. Conversion of optically active ThxR*BH into ketones of essentially 100% ee.

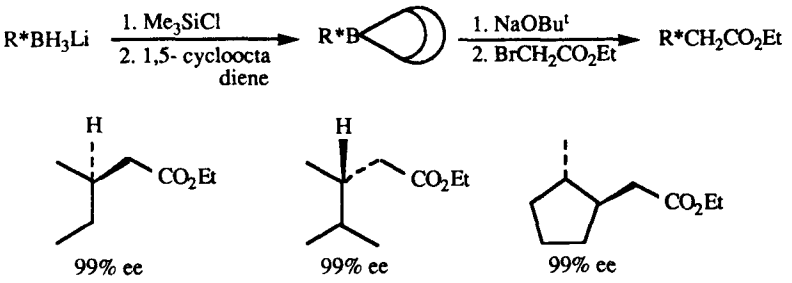


Figure 44. Preparation of optically active homologated esters.

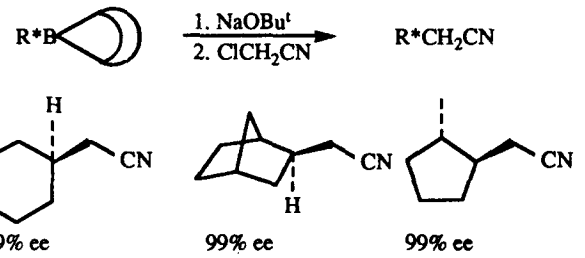


Figure 45. Conversion of optically active B-R*-9BBN into homologated nitriles of essentially 100% ee.

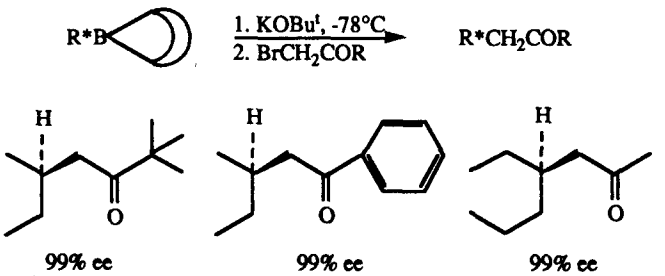


Figure 46. Synthesis of optically active homologated ketones.

the desired organic moiety, providing the desired optically active organic compound in 100% ee. Because both (+)- and (−)-α-pinene are readily available, the process makes it possible to synthesize either enantiomer at will. Finally, the procedure can be controlled to permit the simple recovery and recycling of the chiral auxiliary. For the first time, it appears that we have at hand a rational synthesis of almost any organic compound containing an asymmetric center in enantiomeric purities of essentially 100% ee.

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