Enolization of Thioesters by Chx_2BCl/Et_3N. A representative example of enolization of *S-tert*-butyl thioacetate is described as follows. To a stirred solution of Chx_2BCl (1.2 mL, 5.5 mmol) and Et_3N (0.77 mL, 5.5 mmol) in CCl_4 (15 mL) cooled at 0 °C was added an internal standard, benzene (0.5 mmol), followed by the slow addition of *S-tert*-butyl thioacetate (0.78 mL, 5 mmol). The molarity of the solution was adjusted to 0.3 M. The reaction mixture was stirred for 1 h and worked up as described for ketones. Analysis of the olefinic proton by ^1H NMR suggests >95% enolization.

Enolization of β-Keto Ester by Chx_2BCl/Et_3N. The enolization of ethyl acetoacetate is described as follows. To a stirred solution of Chx_2BCl (1.2 mL, 5.5 mmol) and Et_3N (0.77 mL, 5.5 mmol) in CCl_4 (15 mL) cooled at 0 °C was added an internal standard, benzene (0.5 mmol), followed by the slow addition of ethyl acetoacetate (0.64 mL, 5 mmol). The molarity of the solution was adjusted to 0.3 M. The reaction mixture was stirred for 1 h and worked up as described previously for ketones. Analysis by ^1H NMR showed 94% enolization.

General Procedure for the Aldolization with Benzaldehyde. To a solution of enolborinate in diethyl ether generated from 5 mmol of the carbonyl compound using Chx_2BCl/Et_3N as described above was added benzaldehyde (0.51 mL, 5 mmol) dropwise at -78 °C, and the mixture was stirred for 2-3 h. Then the reaction mixture was allowed to warm up overnight slowly to attain the room temperature. (Later we discovered that the reaction is essentially complete in 2-3 h at -78 °C, so that the slow warmup to 25 °C is unneccessary. Both procedures give the same results.) Then 10 mL of methanol was added to dissolve the precipitate (Et_3NHCl), 1.7 mL of H_2O_2 (30%) was added at 0 °C, and the mixture was stirred for 5-6 h at 25 °C. The solvent was then removed by water aspirator and the reaction mixture was extracted with ether, washed with dilute HCl and water, and dried over anhyd Na_2SO_4. The solvent was removed and the products were analyzed as such by ^1H NMR to determine the syn/anti ratio.

In the case of carboxylic acids, after the aldolization, 5 mL of H_2O was added to the reaction mixture at 25 °C, and the resulting mixture was stirred for 30 min. The products were then extracted with aqueous $NaHCO_3$, neutralized with 20% HCl, extracted with ether, dried over anhyd Na_2SO_4, concentrated, and analyzed by ^1H NMR.

Acknowledgment. We gratefully acknowledge financial support from the United States Office of Naval Research, which made this research possible.

Registry No. 1, 22086-34-6; 2, 137495-66-0; 3, 137495-67-1; 4, 36140-19-9; 5, 58335-30-1; 6, 137495-68-2; BMS, 13292-87-0; 9-BBN, 280-64-8; CH_3COCH_3, 67-64-1; $CH_3COCH_2CH_3$, 78-93-3; $CH_3CH_2COCH_2CH_3$, 96-22-0; $PhCOCH_2CH_3$, 93-55-0; $CH_3CH_2CH_2CHO$, 123-72-8; $PhCH_2CHO$, 122-78-1; $(CH_3)_2CHCHO$, 78-84-2; c-$C_6H_{11}CHO$, 2043-61-0; CH_2=$C(OBChx_2)CH_3$, 137495-69-3; CH_2=$C(OBChx_2)CH_2CH_3$, 137495-70-6; (*E*)-CH_3CH=$C(OBChx_2)CH_2CH_3$, 120312-96-1; (*E*)-CH_3CH=$C(OBChx_2)Ph$, 120312-92-7; CH_3CH_2CH=$CH(OBChx_2)$, 137495-71-7; (*Z*)-$PhCH$=$CH(OBChx_2)$, 137495-72-8; $(CH_3)_2C$=$CH(OBChx_2)$, 137495-73-9; c-C_6H_{10}=$CH(OBChx_2)$, 137495-74-0; $ClBH_2{\cdot}SMe_2$, 63348-81-2; CH_3CH_2COOH, 79-09-4; $CH_3(CH_2)_4COOH$, 142-62-1; $PhCH_2COOH$, 103-82-2; $(CH_3CH_2CO)_2O$, 123-62-6; $CH_3COSC(CH_3)_3$, 999-90-6; CH_3COSPh, 934-87-2; $CH_3COCH_2CO_2C_2H_5$, 141-97-9; CH_3CH=$C(OBChx_2)_2$, 137495-75-1; $CH_3(CH_2)_3CH$=$C(OBChx_2)_2$, 137495-76-2; $PhCH$=$C(OBChx_2)_2$, 137495-77-3; CH_3CH=$C(OBChx_2)OCOC_2H_5$, 137495-78-4; CH_2=$C(OBChx_2)SC(CH_3)_3$, 137495-79-5; CH_2=$C(OBChx_2)SPh$, 137495-80-8; (*Z*)-$CH_3C(OBChx_2)$=$CHCO_2C_2H_5$, 137495-81-9; PhCHO, 100-52-7; (*E*)-$PhCH$=$CH(OBChx_2)$, 137495-82-0; cyclohexene, 110-83-8.

Chiral Synthesis via Organoboranes. 33. The Controlled Reaction of *B*-Alkyldiisopinocampheylboranes with Aldehydes Providing a Convenient Procedure for the Enantiomeric Enrichment of the Boronic Ester Products through Kinetic Resolution

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Controlled treatment of *B*-alkyldiisopinocampheylborane (**3a**), Ipc_2BR*, obtained by asymmetric hydroboration of appropriate olefin, with aldehydes produces chiral boronate esters (**5**) having enantiomeric purities markedly higher than those of the substrate. A systematic study of the reaction revealed that the intermediate borinic esters (**4**) are being kinetically resolved. Since asymmetric hydroboration of alkenes with diisopinocampheylborane (**1**) provides predominantly the diastereomer that reacts faster with aldehydes, the reaction furnishes in situ enantiomeric enrichment of the products. Thus, *B*-alkyldiisopinocampheylboranes (**3a**) possessing 81-96% ee are readily converted into borinic esters (**5**) including 2-butyl, 3-hexyl, and *exo*-norbornyl derivatives of ≥99% ee. Successful efforts were also made to extend the scope of asymmetric hydroboration-kinetic resolution to representative cyclic dienes making available pure enantiomers of *exo*-5-norbornenyl- and 3-cyclohexenylboronic esters.

Hydroboration is one of the fundamentally novel reactions in organic chemistry. In recent times a variety of procedures have become available for the enantioselective version of this reaction. They include chiral organoboranes derived from terpenes,[2] Masamune's reagent,[3] and a modestly successful catalytic procedure involving chiral transition metal complexes.[4] All of these routes transform prochiral alkenes to the corresponding chiral alcohols. However, the reagents derived from (+)- and (-)-α-pinene

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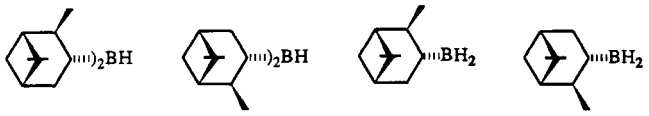
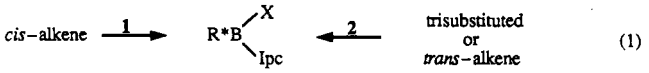
have given a new dimension to the scope of asymmetric hydroboration, making accessible chiral organoboranes which are readily transformed into an array of pure enantiomers.[5]



d_1 l_1 d_2 l_2

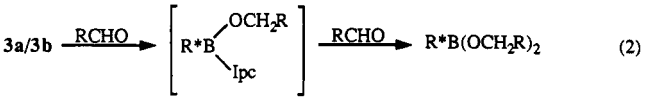
The discovery of the first enantioselective hydroborating reagent,[6a] diisopinocampheylborane (Ipc_2BH, **1**) marked the beginning of a practical nonenzymatic asymmetric synthesis. The reagent provided 51–87% enantiomeric excess (ee) in the hydroboration of *cis*-disubstituted alkenes. Later on, the availability of enantiomerically pure **1**[6b] and modified reaction conditions significantly improved the results.[6c] The reaction of **1** with more hindered olefins, however, is sluggish and proceeds with partial displacement of α-pinene from the reagent. These difficulties prompted us to explore monoisopinocampheylborane ($IpcBH_2$, **2**). The moderate steric requirement of **2** permitted smooth hydroboration of *trans*-disubstituted as well as trisubstituted alkenes in 53–100% ee.[7a-c]



cis-alkene —1→ R*B(X)Ipc ←2— trisubstituted or *trans*-alkene (1)

3a, X = Ipc **3b**, X = H

We subsequently discovered[8] that treatment of the intermediates **3a** and **3b** with an aldehyde regenerated the chiral auxiliary, α-pinene (eq 2). The resulting boronic esters (**5**) could be easily converted into the corresponding chiral monoalkylboranes which proved to be the starting point for a variety of transformations.[9a-c]

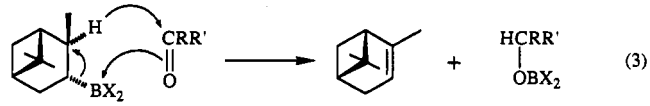


3a/3b —RCHO→ [R*B(OCH$_2$R)Ipc] (**4**) —RCHO→ R*B(OCH$_2$R)$_2$ (**5**) (2)

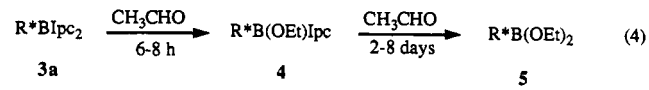
With the growing synthetic utility of chiral organoboranes, we learned to upgrade the enantiomeric purity of the key intermediates, **5**, to ≥99% ee. In the case of the products arising from **2**, direct crystallization of **3b** itself proved to be the method of choice.[7c] The enantiomeric enrichment of the product from **1**, however, was achieved tediously at the later stages.[10] An additional problem encountered with **3a** was the sluggish reaction with aldehydes. The present study was undertaken to overcome these difficulties and also to understand the reaction between **3a** and aldehydes. The investigation provided us with some unexpected observations regarding the reaction mechanism. The most gratifying aspect was the finding that the intermediate diastereomeric borinic esters (**4**) were kinetically resolved, thereby leading to a simple in situ procedure for enantiomeric enrichment of the products, viz. boronic esters (**5**). A part of the present study was also devoted to extending the scope of asymmetric hydroboration for hitherto unreported cyclic dienes.

Results and Discussion

Isopinocampheylboranes react with aldehydes and ketones liberating the 3-pinyl group as α-pinene, presumably via a cyclic mechanism (eq 3). In the case of *B*-alkyldiisopinocampheylboranes (**3a**), the reaction with simple aldehyde proceeds stepwise, giving successively borinic (**4**) and boronic (**5**) esters. The first step of the reaction is relatively fast, whereas the second one is comparatively slow (eq 4).



(3)



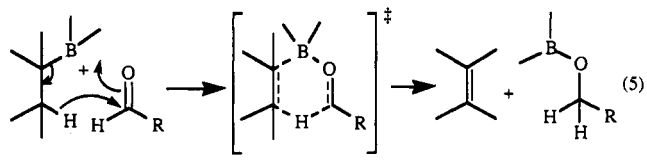
R*BIpc$_2$ —CH$_3$CHO, 6-8 h→ R*B(OEt)Ipc —CH$_3$CHO, 2-8 days→ R*B(OEt)$_2$ (4)

3a **4** **5**

R* = 2-butyl, 3-hexyl, *exo*-norbornyl, etc.

In order to investigate the structural effects of representative aldehydes in the reaction, **3a** (R* = 2-butyl) was selected as the substrate. A standard solution of the organoborane in THF was obtained by hydroboration[6c] of *cis*-2-butene with $^d Ipc_2BH$ (derived from (+)-α-pinene) in THF at −25 °C. Portions of the stock solution were treated with 2 equiv of selected aldehydes at ambient temperature, and progress of the reactions was monitored by ^{11}B NMR. It was found that the reaction was slowest with CH_3CHO. There was a small, but significant, difference in the reactivity of $(CH_3)_2CHCHO$ and PhCHO. Remarkably, the reaction with CCl_3CHO was much faster than that with other aldehydes examined!

Mikhailov proposed a cyclic mechanism for the reduction of benzaldehyde by reaction with trialkylboranes (eq 5).[11a] In the present investigation, our results can also be



(5)

rationalized in terms of a concerted mechanism similar to that involved in the Diels–Alder reaction. In the Diels–Alder reaction, the presence of electron-withdrawing groups in the dienophile favors the cycloaddition. Alternatively, the presence of electron-donating groups on the dienophile hinders the reaction. The opposite effect is generally observed by introducing such groups into the

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(10) (a) Brown, H. C.; Vara Prasad, J. V. N. *J. Org. Chem.* **1986**, *51*, 4526. (b) Enantiomeric upgradation by crystallization: boronic acid of ≥90% ee was dissolved in a minimum volume of EtOH and then diluted with twice the volume of degassed water. The resulting suspension was warmed (50–70 °C) until a clear solution was obtained and allowed to stand at ambient temperature to obtain crystalline boronic acid of ≥99% ee. The product was dried at water aspirator until constant weight (60–70% recovery); Joshi, N. N. unpublished results.

(11) (a) Mikhailov, B. M.; Bubnov, Yu. N.; Kieselev, V. G. *J. Gen. Chem. USSR* **1966**, *36*, 65. (b) Midland, M. M.; Zderic, S. A. *J. Am. Chem. Soc.* **1982**, *104*, 525. (c) For an examination of the rates of reaction of Ipc_2BCl and Ipc_2Balk with benzaldehyde; see: Brown, H. C.; Ramachandran, P. V.; Chandrasekharan, J. *Organometallics* **1986**, *5*, 2138.

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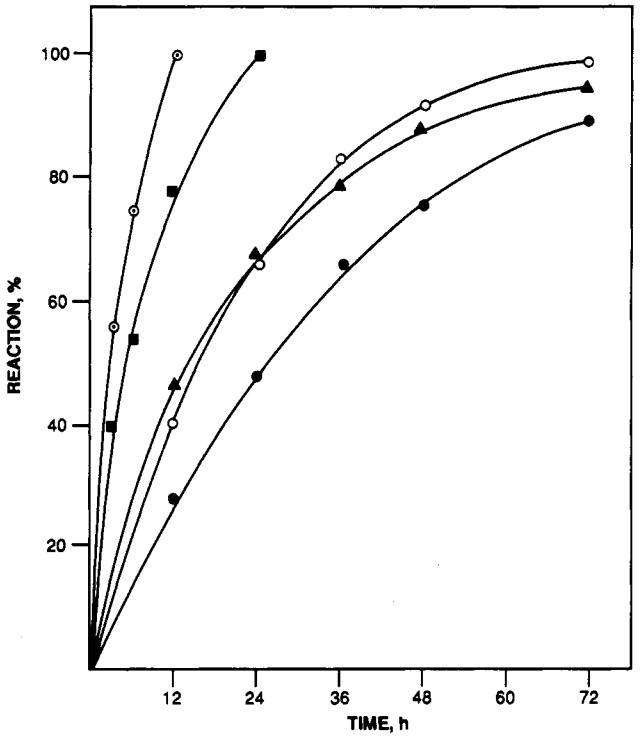
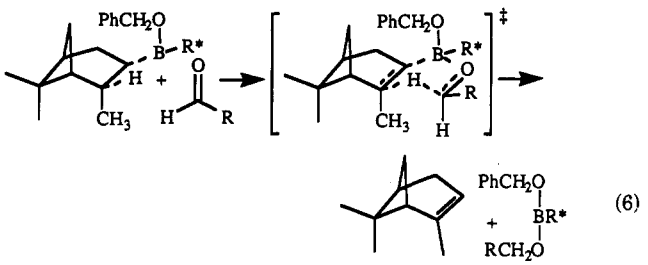


Figure 1. Rate study of the reaction between (2-Bu)BIpc$_2$ and representative aldehydes; 1.0 M THF, 25 ± 1 °C. (●) CH_3CHO, (▲) $(CH_3)_2CHCHO$, (■) CCl_3CHO, (○) PhCHO, (◎) PhCHO + 5 mol % BF_3·Et_2O.

diene. Finally, the introduction of Friedel–Craft catalysts into the reaction mixture results in electronic shifts, which can markedly alter the reaction rate.

In the reaction of aldehydes with the alkylisopinocampheylborinic esters, R*IpcBOEt, that produces the optical upgrade that is the subject of this study, we must go through a similar transition state (eq 6).



(6)

Factors which increase the electrophilicity of the boron atom, such as a chlorine substituent on boron, should favor the rate of reaction. Factors which increase the electron deficiency on the carbonyl carbon should enhance the rate of transfer of the β-hydrogen and favor the reaction. This provides a simple interpretation which rationalizes the phenomena we have observed of the factors which influence the rate of the reaction leading to the enantiomeric enrichment of the boronic ester products.

For example, as pointed out above, the reaction of chloral with R*IpcBOEt is much faster than the rate with benzaldehyde. Similarly, the rate of reaction of benzaldehyde–BF_3 is considerably greater than the reaction with free benzaldehyde. Finally, the reaction of Ipc_2BCl with ketones is far faster than the corresponding reactions with B-Ipc-9-BBN.[11c] The rate study of a related derivative, 2-butyldiisopinocampheylborane (2-BuBIpc$_2$), with representative aldehydes is summarized in Figure 1.

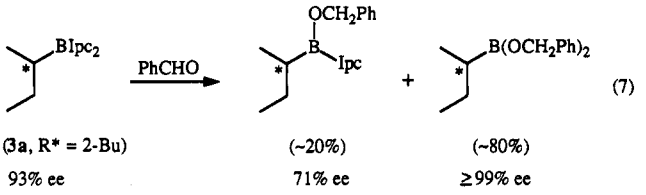
Kinetic Resolution. The routine procedure[8] for preparing chiral boronate esters (5) from the hydroboration products (3) involves a simple treatment with an excess of aldehyde. During the above-mentioned rate study, however, we inadvertently worked up one of the reaction mixtures involving the treatment of 2-BuBIpc$_2$ with PhCHO after ~90% completion. At that stage of the reaction, ^{11}B NMR indicated a ~1:4 mixture of the unreacted intermediate (benzylborinate, δ 53 ppm) and the product (dibenzylboronate, δ 31 ppm). The reaction mixture was therefore extracted with 3 N NaOH to isolate boronic acid from the reaction mixture. Oxidation of the isolated boronic acid with alkaline H_2O_2 provided optically active 2-butanol. The enantiomeric excess (% ee) of the product was determined by capillary GC analysis of its MTPA ester. To our surprise, the % ee of 2-butanol was significantly higher than that of the starting material, 2-BuBIpc$_2$! To confirm the results, the borinic acid remaining in the organic phase following the extraction of the boronic acid with 3 N NaOH was isolated and oxidized. Indeed, the % ee of 2-butanol from the borinic acid was very much lower (eq 7).

Table I. Enantiomeric Purities of the Boronic Esters (5) Obtained by the Treatment of *B*-Alkyldiisopinocampheylboranes (3a) with PhCHO

$$\underset{\mathbf{3a}}{R^*BIpc_2} \xrightarrow{PhCHO} \underset{\mathbf{4}}{R^*B(OCH_2Ph)Ipc} \xrightarrow{PhCHO} \underset{\mathbf{5}}{R^*B(OCH_2Ph)_2}$$

entry	R*	time,[a] d	ratio[b] 4	ratio[b] 5	% ee[c] of 5
1	2-butyl	4[d]	0	100	93[d]
2		3	20	80	>99
3	3-hexyl	9[d]	0	100	91[d]
4		6	20	80	>99[d]
5	*exo*-norbornyl	3[d]	0	100	81[d]
6		2	20	80	90
7		1.5	30	70	93

[a] All reactions were carried out as 1.0 M in THF and at ambient temperature. [b] Approximate, established by ^{11}B NMR. [c] Of the corresponding R*OH obtained by the oxidation of 5. [d] Represents the initial induction. 4 and 5 were not separated prior to oxidation.



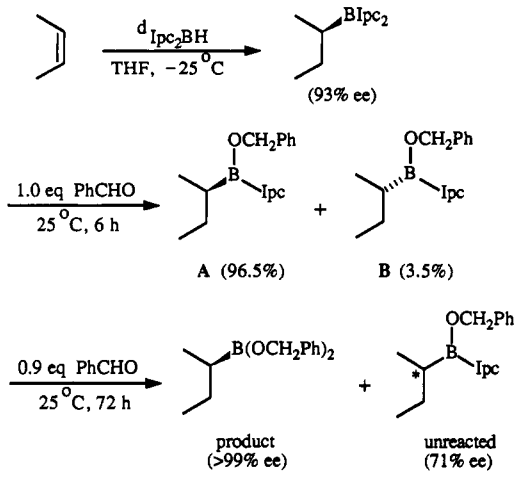
(7)

It appeared that we had encountered kinetic resolution during the displacement reaction. This unexpected finding appeared to be a promising procedure for an in situ enantiomeric enrichment of boronic esters. The reaction was therefore examined for a few other diisopinocampheylborane derivatives (3a) and appeared to be generally applicable (Table I). It appeared that the two diastereomers (A and B) of the intermediate borinic ester react with an aldehyde at different rates. To examine this hypothesis, we proceeded to prepare the two diastereomers by independent methods and to study separately their reaction with PhCHO.

(R,R)-isomer, A *(S,R)*-isomer, B

The *R,R* diasteromer (A) of 93% ee was obtained by asymmetric hydroboration[6c] of *cis*-2-butene with $^dIpc_2BH$,

Scheme I. *R,R* Diastereomer Reacts Faster, Leading to the Optical Upgradation of Boronic Ester



followed by treatment with 1 equiv of PhCHO. This is a relatively fast reaction. Subsequent reaction of A with an additional 0.9 equiv of PhCHO and analysis of the reaction mixture was carried out as described above. The enantiomeric excess of the borinic ester produced was ≥99% and that of the unreacted borinic ester was only 70%. The results implied that the major diastereomer A in the experiment was the faster reacting component, thereby enhancing the enantiomeric purity of the product, i.e., boronic ester (Scheme I).

To confirm the above results further, the reation of the *S,R* diasteromer (B) with PhCHO was examined. This diastereomer could be easily prepared[7b,c] from *trans*-2-butene. Hydroboration of *trans*-2-butene with $^{d}IpcBH_2$ (from (+)-α-pinene) gave a dialkylborane, 2-Bu(BH)Ipc, which upon treatment with $PhCH_2OH$ provided B of 80% ee. The reaction of B with PhCHO was significantly slower than that of A. Separation of the product (boronic ester) from the unreacted borinic ester, oxidation of each component, and determination of % ee of the resulting 2-butanol was carried out as usual. As expected, the product boronic ester had been downgraded (to 78% ee) and the unreacted borinic ester upgraded (to 91% ee). Here the major isomer, *S,R* reacts slower than the minor isomer, *R,R*, thereby upgrading the unreacted borinic ester. However, the extent of upgradation is only moderate due to the fact that the *R,R* diastereomer, though being faster reacting, is present as a minor impurity in the mixture. This confirms our earlier conclusion that *R,R* is the faster reacting diastereomer (Scheme II).

Optimization of the Reaction Parameters. Having established the above kinetic resolution as a valuable tool for upgrading the enantiomeric purity of boronic esters from hydroboration of appropriate alkenes with Ipc_2BH, we sought to optimize the procedure. A study was undertaken for evaluating the solvent effect, the structure of the aldehyde, and the stoichiometry of the reactants.

To begin with, it was observed that enantioselection can be slightly improved (3–4%) by performing the hydroboration with Ipc_2BH in Et_2O rather than in THF. This finding is in accord with an earlier observation[6a] that better results are realized by performing hydroboration in diglyme rather than in THF. The use of Et_2O as the solvent proved additionally advantageous in our study since the subsequent step (i.e., treatment with aldehyde) could be carried out in the same solvent. In fact, the reaction of **3a** with PhCHO was faster in Et_2O than in THF. The optimization of the kinetic resolution was studied in detail using **3a** (R* = *exo*-norbornyl) because norbornene provides a product with lower % ee than is achieved with the other *cis*-alkenes. A 0.5 M solution of *exo*-NrbBIpc$_2$ was treated with 2 equiv of representative aldehydes, and the reaction was monitored until ~90% complete. The product (boronic ester) was extracted with 3 N NaOH and oxidized with H_2O_2, and the % ee of the resulting *exo*-norborneol determined. All the aldehydes tested, with the exception of CCl_3CHO, provided significant kinetic resolution. Best results were realized with PhCHO, which converted *exo*-NrbBIpc$_2$ of 81% ee to *exo*-NrbB(OCH$_2$Ph)$_2$ of 93% ee (entry 4, Table II).

Scheme II. *S,R* Diastereomer Reacts Slower, Leading to the Optical Downgradation of Boronic Ester

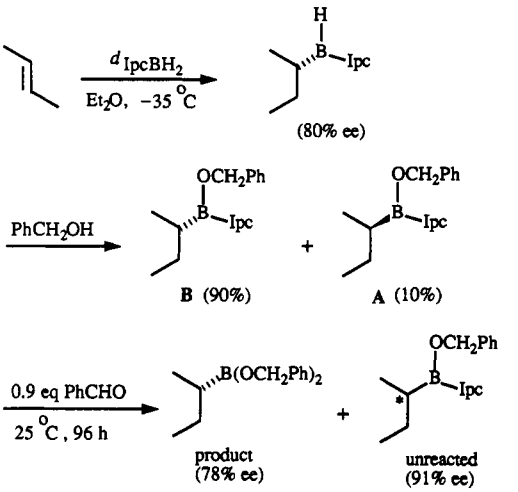
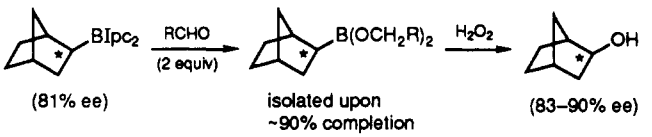


Table II. Examination of Representative Aldehydes for Kinetic Resolution



entry	RCHO	time,[a,b] h	% ee[c]
1	CH_3CHO	48	86
2	$(CH_3)_2CHCHO$	36	87
3	CCl_3CHO	12	83
4	PhCHO	36	90

[a] All reactions were carried out as 1.0 M in THF and at ambient temperature. [b] Based on approximate estimation by ^{11}B NMR. [c] Determined by the capillary GC analysis of the corresponding MCF derivative.

Our next task was to establish the optimal stoichiometry of R*BIpc$_2$ and PhCHO and also to examine the effect of $BF_3{\cdot}Et_2O$ as a catalyst in the reaction. As expected, a decreased amount of PhCHO provided improved enantiomeric enrichment of the boronic ester (Table III). In fact it was possible to obtain ≥99% ee for *exo*-NrbB(OCH$_2$Ph)$_2$, albeit with a modest 50% conversion. Keeping in view the sluggish reaction rates of other R*BIpc$_2$ with aldehydes, the effect of $BF_3{\cdot}Et_2O$ as the catalyst was also examined. The use of 1 mol % of the catalyst significantly enhanced the reaction rate as well as the chemical conversion. Interestingly though, the addition of $BF_3{\cdot}Et_2O$ at the beginning of the reaction proved detrimental for the kinetic resolution (entry 5, Table III). The desired result was achieved, however, if the catalyst was added at the second stage of the reaction, that is, after the formation of the borinic ester (entry 6, Table III). An explanation for the difference could be derived from our earlier observation during the reactions involving CCl_3CHO. Whereas the reaction of R*BIpc$_2$ with simple aldehyde

proceeds in two stages (that is, sequential elimination of each of the two isopinocampheyl groups), the same reaction with CCl_3CHO or in the presence of BF_3-Et_2O provides random distribution of products (eq 8). In other words,

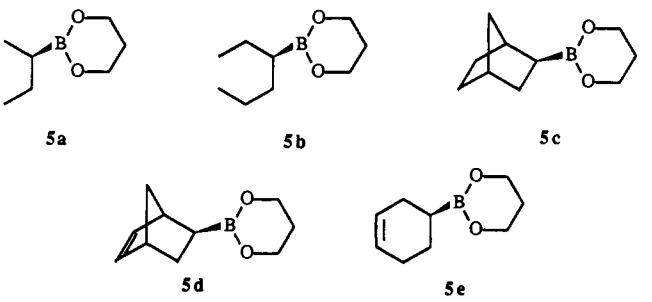
$$\underset{\textbf{3a}}{R^*BIpc_2} \xrightarrow[\text{or } CH_3CHO + 1\text{ mol \% } BF_3]{CCl_3CHO\ (1\text{ equiv})} R^*BIpc_2 + R^*B(OCH_2R)Ipc + R^*B(OCH_2R)_2 \quad (8)$$

the much faster reactions involving CCl_3CHO or CH_3CHO + 1 mol % BF_3 are much less selective than the slower reactions with simple aldehydes.

Asymmetric Hydroboration of Cyclic Dienes. Whereas the hydroboration of acyclic dienes is simple and predictable, the hydroboration of cyclic diene is intricately goverened by the structure of the diene and the reagent. Hydroboration of 2,5-norbornadiene with a hindered (e.g. Sia_2BH)[13a] as well as an unhindered reagent (e.g. 9-BBN)[13b] provides a statistical mixture of monohydroborated, dihydroborated, and unreacted diene. On the other hand, 1,3- and 1,4-cyclohexadienes can be hydroborated with either reagent to obtain predominantly the monohydroboration product. Surprisingly, the hydroboration of 1,5-cyclooctadiene yields predominant dihydroboration with Sia_2BH as well as 9-BBN. Thus, these three dienes exhibit three different behavior patterns in hydroboration.

Before we began the present study, only the chiral boronate esters from simple alkenes were accessible. Except for 1,3-cyclohexadiene,[14] the asymmetric hydroboration of cyclic dienes has been neglected, partly due to the difficulties encountered during such attempts. Asymmetric monohydroboration of nonconjugated cyclic dienes could provide very valuable bifunctional molecules that could be further manipulated via a variety of optically active intermediates. The first part of our study, therefore, dealt with the hydroboration of these three representative cyclic dienes viz. 2,5-norbornadiene, 1,4-cyclohexadiene, and 1,5-cyclooctadiene. Each one of these dienes, upon treatment with 1 equiv of $^dIpc_2BH$ in Et_2O at −25 °C, gave varying amounts of white amorphous solid insoluble in the most commonly used solvents. Careful characterization revealed the products to be symmetrically substituted dihydroboration products. Analysis of the reaction mixtures following oxidation revealed that norbornadiene gave a statistical mixture of mono- and dihydroborated products, cyclohexadiene was monohydroborated predominantly, and cyclooctadiene was dihydroborated almost exclusively. Changing the solvent (Et_2O, THF, or n-Bu_2O) did not alter the product distribution significantly. The only option left for improving the yield of the desired monohydroborated product was to employ an excess of the diene. To obtain a high degree of monohydroboration for norbornadiene, at least a 400% excess of the diene was desirable. A 200% excess was sufficient to realize almost quantitative monohydroboration of the cyclohexadiene. The resulting cycloalkenylboronic esters were of 81% and 89% ee, respectively. As described for other boronic esters, the enantiomeric enrichment of the cycloalkenylboronic esters was also achieved via kinetic resolution. The use of a large excess of dienes was not a serious disadvantage since the excess is easily recovered from the reaction mixture. In the case of cyclooctadiene, a 400% excess of the diene provided 35% yield of the monohydroborated product with 43% ee. Although the yield could doubtless be improved by using even larger excesses of the diene, we did not explore this because of the low optical induction realized (Table IV).

The boronic esters were conveniently isolated as the corresponding acids which were easily reesterified with 1,3-propanediol to obtain very stable cyclic esters viz. 1,3,2-dioxaborinanes (**5a–c**). Needless to emphasize, the use of $^lIpc_2BH$ (derived from (−)-α-pinene) would provide the opposite enantiomers of all of the products obtained in the present study (Table V).



Conclusions

A careful study of the reaction between *B*-alkyldiisopinocampheylboranes (**3a**) and representative aldehydes revealed several interesting aspects of the reaction. Interestingly, the aldehydes with an electron-deficient carbonyl group reacted faster than the simple aldehydes. Accordingly, external activation of the aldehydes with a Lewis acid was proposed and then proved by employing BF_3-Et_2O as the catalyst for the reaction. The most fruitful aspect of the study was the observation that the intermediate borinic esters (**4**) were kinetically resolved during the reaction with aldehydes. The finding was developed into a simple and efficient in situ procedure for converting the initial hydroboration products (**3a**) of 81–96% ee to the corresponding boronic esters (**5a–e**) of ≥99% ee.

Experimental Section

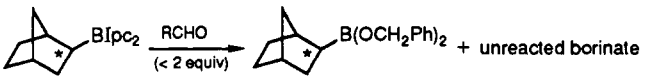
All moisture- and air-sensitive reactions were carried out under nitrogen atmosphere using oven-dried glassware. ^{11}B NMR, ^1H NMR and ^{13}C NMR chemical shifts are in δ relative to BF_3-Et_2O and Me_4Si, respectively. Capillary gas chromatographic analyses were carried out on a 30 m × 0.25 mm SPB-5 column.

Materials. Tetrahydrofuran (THF) was freshly distilled over sodium benzophenone ketyl. Anhydrous ether (Et_2O) was purchased from Mallinckrodt Inc. and was used directly. The alkenes as well as the aldehydes used were commercial products of highest purity available and were used without further purification. (−)-Menthyl chloroformate (MCF)[15] and (+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPAA) were purchased from Aldrich Chemical Co. The latter was converted to the corresponding acid chloride as described.[16]

Rate Study of the Reaction between R^*BIpc_2 (3a) and Aldehydes. (*R*)-2-Butyldiisopinocampheylborane was chosen as the representative R^*BIpc_2, and a 1.0 M stock solution of the compound in THF was obtained by hydroboration of *cis*-2-butene with $^dIpc_2BH$ as described earlier.[6c] Five 25-mL flasks equipped with rubber septa, N_2 supply, and magnetic stirring bars were each charged with portions (10 mL, 10 mmol) of the above solution. To the stirred solution (maintained at 25 ± 1 °C by external cooling), the appropriate aldehyde (20 mmol) was added dropwise. The four aldehydes selected for the study were CH_3CHO (flask 1), $(CH_3)_2CHCHO$ (flask 2), CCl_3CHO (flask 3), and PhCHO (flask 4). To the fifth flask BF_3-Et_2O (60 μL, 0.5 mmol) was added, followed by PhCHO (2 mL, 20 mmol) added dropwise. After stirring at 25 ± 1 °C for 1 h, the reaction mixtures

(13) (a) Zweifel, G.; Nagase, K.; Brown, H. C. *J. Am. Chem. Soc.* **1962**, *84*, 190. (b) Liotta, R.; Brown, H. C. *J. Org. Chem.* **1977**, *42*, 2836.
(14) Brown, H. C.; Jadhav, P. K.; Bhat, K. S. *J. Am. Chem. Soc.* **1985**, *107*, 2564.
(15) Westley, J. W.; Halpern, B. *J. Org. Chem.* **1968**, *33*, 3978.
(16) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

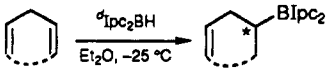
Table III. Enantiomeric Upgradation of Boronic Esters by Kinetic Resolution



entry	PhCHO, equiv	time,[a] h	ratio[b] borinate	ratio[b] boronate	% ee[c]
1	1.9[d]	48[d]	0	100	85 (81)[e]
2	1.9	36	20	80	93
3	1.8	36	30	70	97
4	1.7	24	50	50	99
5	1.7[f]	6[g]	20	70	87
6	1.7[h]	12	30	70	97

[a] The reactions were carried out as 0.5 M in Et_2O and at ambient temperature. [b] Approximate, established by ^{11}B NMR. [c] Of (1*S*,2*S*)-*exo*-norborneol obtained by the oxidation of the boronic acid extracted from the reaction mixture with 3 N NaOH. [d] The entire reaction mixture was oxidized after 48 h and represents initial induction. [e] The figure in the parentheses corresponds to the hydroboration. [f] 1 mol % BF_3·Et_2O was added at the beginning of the reaction. [g] The final reaction mixture still had ~10% of the unreacted R*$BIpc_2$. [h] 1 mol % BF_3·Et_2O was added after the removal of the first isopinocamphenyl group.

Table IV. Asymmetric Monohydroboration of Cyclic Nonconjugated Dienes



entry	diene	% excess of diene	% yield[a]	% ee[b]
1	2,5-norbornadiene	0	27	
2		100	55	
3		200	74	
4		400	85	83
5	1,4-cyclohexadiene	0	55	
6		100	81	
7		200	97	89
8	1,5-cyclooctadiene	0	<5	
9		200	14	
10		400	35	43

[a] Of monohydroboration, estimated by GC. [b] Of the corresponding 3-alkenols obtained by oxidizing the hydroboration product.

were allowed to stand at ambient temperature (and under a positive pressure of N_2). The reactions were periodically monitored by ^{11}B NMR, which revealed the transformation of R*$BIpc_2$ (δ ~83) to R*$B(OCH_2R)Ipc$ (δ ~54) and then to R*$B(OCH_2R)_2$ (δ 31). The rates of the reactions were in the following order: PhCHO + 5 mol % BF_3·Et_2O > CCl_3CHO ≫ PhCHO ≥ $(CH_3)_2CHCHO$ > CH_3CHO. The results are summarized graphically in Figure 1.

Enantiomeric Purities of the Boronic Esters (5) Obtained by the Treatment of *B*-Alkyldiisopinocampheylboranes (3a) with PhCHO. The reaction with (*R*)-2-butyldiisopinocampheylborane is representative. A 1.0 M solution of the compound in THF (50 mL, 50 mmol) was treated with PhCHO (10 mL, 100 mmol), and the reaction was monitored as described above.

(a) From the Incomplete Reaction. At ~90% completion (occurring after 3 days), the reaction mixture was found to contain the boronic and borinic esters in ~4:1 ratio. At that stage, 50 mL of the reaction mixture was transferred to another flask and treated with MeOH (2 mL) followed by water (2 mL). Most of the solvent was pumped off under water aspirator. The reaction mixture was diluted with Et_2O (50 mL), and the boronic acid was extracted with 3 N NaOH (3 × 15 mL). A small portions (5 mL) of the extract was treated with 30% H_2O_2 (2 mL) and worked up as usual.[17] The resulting (*R*)-2-butanol was derivatized with MTPACl as described in the literature[16] and analyzed by capillary GC, which revealed ≥99% ee for the product.

(b) From the Completed Reaction. The remaining portion of the above reaction mixture (10 mL, ~8 mmol) containing boronic ester (>95%) and borinic ester (<5%) after 4 days was directly oxidized by treatment with 3 N NaOH (3 mL) and 30% H_2O_2 (3 mL). Capillary GC analysis indicated 93% ee for the resulting (*R*)-2-butanol. Since the treatment of R*$BIpc_2$ with an aldehyde as well as the oxidation of organoboranes proceeds with total retention of the configuration, the % ee of 2-butanol from this experiment reflects the initial induction.

The % ee of other optically active alcohols obtained by the oxidation of the corresponding boronic acids are summarized in Table I.

Kinetic Resolution of the Borinic Ester (A) with PhCHO. A 1.0 M solution of 2-$BuBIpc_2$ (20 mL, 20 mmol) in THF was treated with PhCHO (2 mL, 20 mmol), and the reaction was monitored as described above. After stirring at ambient temperature for 6 h, the formation of A (δ 54) was complete. At that stage, an additional amount of PhCHO (1.8 mL, 18 mmol) was added and the reaction mixture was allowed to stand (for 72 h) until ^{11}B NMR indicated no additional change in the ratio (~4:1) of the product, boronic ester (δ 32), and the unreacted A. The reaction was treated with MeOH (1 mL) followed by water (1 mL) and concentrated under water aspirator. The residue was dissolved in Et_2O (30 mL) and extracted with 3 N NaOH (2 × 10 mL) to recover the boronic acid. The aqueous portion was treated with 30% H_2O_2 (6 mL) and worked up as usual.[17] A small portion (~10 μL) of the resulting (*R*)-2-butanol was converted to MTPA ester and analyzed by capillary GC, which revealed ≥99% ee for the product.

The organic phase of the above reaction mixture contained the unreacted portion of A. It was concentrated, redissolved in Et_2O (5 mL), and oxidized by the treatment with 3 N NaOH (2 mL) and 30% H_2O_2 (2 mL). The resulting (*R*)-2-butanol had 70% ee.

Kinetic Resolution of the Borinic Ester (B) with PhCHO. Hydroboration of *trans*-2-butene (2.8 mL, 30 mmol) with $^dIpcBH_2$ (3 mL of 0.9 M in Et_2O, 28 mmol) was carried out as described in the literature.[7c] The resulting dialkylborane (80% ee) was isolated (3.8 g, 64% yield), suspended in cold THF (15 mL), and treated with $PhCH_2OH$ (1.6 mL, 18 mmol). An immediate evolution of H_2 was observed, and the resulting clear solution was examined by ^{11}B NMR, which showed a single peak at δ 54, corresponding to the borinic ester. PhCHO (1.6 mL, 16 mmol) was then added, and the reaction mixture was allowed to stand at ambient temperature (96 h). Monitoring of the reaction, isolation of the product, and determination of the enantiomeric purity was carried out as described above. (*S*)-2-Butanol from the boronic acid and from unreacted B was found to be of 78% and 91% ee, respectively.

Examination of Representative Aldehydes for the Kinetic Resolution. A 1.0 M solution of *exo*-$NrbBIpc_2$ of 81% ee was obtained as described,[6c] and its reaction with CH_3CHO is representative. A solution of the organoborane (20 mL, 20 mmol) was treated with CH_3CHO (2.2 mL, 40 mmol). The reaction was found to be ~90% complete after 48 h, and ^{11}B NMR at that stage revealed the boronic and borinic esters in a ~4:1 ratio. Following the details provided in the previous experiments, the reaction was worked up to obtain the boronic acid, which was then oxidized with alkaline H_2O_2. Capillary GC analysis of the MCF derivative of the resulting (1*S*,2*S*)-*exo*-norborneol indicated it to be of 86% ee.

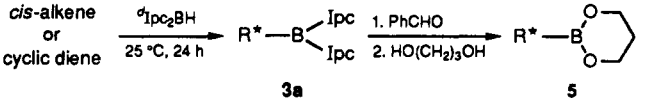
The above procedure was repeated using $(CH_3)_2CHCHO$, CCl_3CHO, and PhCHO. The results are summarized in Table II.

Boronic Esters (5a–e) of Very High Enantiomeric Purity via Asymmetric Hydroboration Followed by Kinetic Resolution. 1. From *cis*-Alkenes. The reported procedure[6c] for asymmetric hydroboration of *cis*-alkenes was modified and is illustrated for the preparation of the 2-butyl derivative (**5a**) as follows. Freshly prepared[18] $^dIpc_2BH$ (28.6 g, 100 mmol) of 99% ee was crushed, placed in a 250-mL flask equipped with the usual assembly, and covered with anhydrous Et_2O (50 mL). The re-

(17) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Synthesis via Boranes*; Wiley-Interscience: New York, 1975.

(18) Brown, H. C.; Joshi, N. N. *J. Org. Chem.* **1988**, *53*, 4059.

Table V. Preparation of 2-Alkyl-1,3,2-dioxaborinanes of Very High Enantiomeric Purity via Asymmetric Hydroboration Followed by Kinetic Resolution



3a 5

R*	% ee[a] of 3a	PhCHO, equiv	time, h	% yield	% ee[a] of 5	config
2-butyl	96 (93)[b]	1.9	24[c]	74	≥99	*R*[d]
3-hexyl	91	1.8	48[c]	67	≥99	*R*[d]
exo-norbornyl	85 (81)[b]	1.8	36	54	97 (≥99)[e]	1*S*,2*S*[f]
exo-5-norbornen-2-yl	83	1.8	36	48	96 (≥99)[e]	1*R*,2*S*[f]
3-cyclohexen-1-yl	89	1.7	12	60	≥99	*S*[g]

[a] Based on the corresponding alcohol obtained by oxidation with alkaline H_2O_2. A small descripancy with the values published earlier, may arise from the use of optical rotation to establish % ee in those studies. [b] The figures in parentheses correspond to the hydroboration performed in THF instead of Et_2O as the solvent. [c] The reaction was catalyzed by 1 mol % BF_3·Et_2O. [d] Reference 6a. [e] The figures in parentheses correspond to the boronic acid crystallized from H_2O–EtOH (2:1), see ref 10b. [f] Reference 20. [g] By analogy.

action flask was immersed in a cryobath maintained at −25 °C, and the Et_2O layer covering the $^dIpc_2BH$ was removed using a double-ended needle. This washing ensures removal of any impurity arising from hydrolysis, oxidation, or dissociation of Ipc_2BH. A precooled solution of *cis*-2-butene (10 mL, 110 mmol) in Et_2O (100 mL) was then introduced into the flask, and the reaction mixture was vigorously stirred until a clear solution resulted. At times, certain R*$BIpc_2$ derivatives crystallize out during the reaction, thereby making it difficult to assess the progress of the reaction. In such cases, stirring was continued for 24 h at −25 °C.

After the completion of hydroboration, the reaction mixture was gradually warmed to 0 °C and the resulting clear solution was treated with PhCHO (19.3 mL, 190 mmol). Thereafter, the reaction mixture was allowed to stand at ambient temperature. ^{11}B NMR indicated complete conversion of the trialkylborane (**3a**) to the corresponding borinic ester (**4**) within 6 h. At that stage, a catalytic amount (120 μL, 1 mmol) of BF_3·Et_2O was added, and the reaction was allowed to proceed until no additional change in the ratio of boronate and borinate was seen. It was then treated with MeOH (4 mL, to facilitate the cleavage of the benzyl ester), and after 1 h extracted with 3 N NaOH (3 × 30 mL). The NaOH extract was washed once with Et_2O (25 mL) to remove any dissolved $PhCH_2OH$, cooled in an ice bath, and acidified with 6 N HCl. The resulting thick white precipitate was extracted with Et_2O (3 × 100 mL), dried over anhydrous Na_2SO_4, and concentrated at water aspirator to obtain (*R*)-2-butylboronic acid (9.3 g), which was esterified with 1,3-propanediol by the known procedure[19] to obtain (*R*)-(−)-2-butyl-1,3,2-dioxaborinane, **5a**, 10.5 g (74%, based on $^dIpc_2BH$): bp 81–82 °C (25 Torr) [lit.[21] bp 70–72 °C (20 Torr)]; $[\alpha]^{23}_D$ −4.2° (*c* 3.6, CCl_4) [lit.[21] $[\alpha]^{23}_D$ −4.8° (*c* 6, THF)].

(*R*)-2-(+)-(3-Hexyl)-1,3,2-dioxaborinane (5b): bp 90–91 °C (20 Torr) [lit.[21] bp 92–94 °C (20 Torr)]; $[\alpha]^{23}_D$ +0.9° (*c* 3.5, CCl_4) [lit.[21] $[\alpha]^{23}_D$ +0.87 (*c* 15, THF)].

(1*S*,2*S*)-2-(+)-*exo*-Norbornyl-1,3,2-dioxaborinane (5c): bp 119–120 °C (20 Torr); $[\alpha]^{23}_D$ +18.6° (*c* 4, CCl_4); ^{11}B NMR ($CDCl_3$) δ +30 (s); ^1H NMR ($CDCl_3$) δ 0.70–0.87 (m, 1 H), 1.05–1.55 (m, 8 H), 1.90 (q, *J* = 6 Hz, 4 H), 2.20 (bd, 2 H), 3.96 (t, *J* = 7 Hz, 4 H); ^{13}C NMR ($CDCl_3$) δ 27.9, 29.8, 32.5, 32.8, 37.0, 38.4, 39.0, 62.0, 96.7. Anal. Calcd for $C_{10}H_{17}O_2B$: C, 66.70; H, 9.52; B, 6.00. Found: C, 66.33; H, 9.67; B, 5.83.

A small portion of **5c** was oxidized[17] with alkaline H_2O_2 and the resulting (1*S*,2*S*)-(−)-*exo*-norborneol was purified by preparative GC. The product revealed $[\alpha]^{23}_D$ −4.9° (*c* 7, $CHCl_3$) [lit.[6c] $[\alpha]^{23}_D$ −4.2° (*c* 7.5, EtOH) for 83% ee], and 97% ee by the capillary GC analysis of its MCF derivative.

2. From Nonconjugated Cyclic Dienes. Following the procedure detailed above, $^dIpc_2BH$ (14.3 g, 50 mmol) was used to hydroborate 2,5-norbornadiene (27 mL, 250 mmol, 400% excess). After being stirred for 24 h at −25 °C, the reaction mixture was warmed to 0 °C and treated with PhCHO (9.1 mL, 90 mmol). It was then allowed to stand undisturbed so that the white precipitate of dihydroboration product settles down in the flask and does not react with PhCHO. ^{11}B NMR indicated completion of the reaction in 36 h. The usual procedure was followed to isolate the boronic acid, which was converted into the cyclic ester viz. (1*S*,2*S*)-(+)-(*exo*-5-norbornen-2-yl)-1,3,2-dioxaborinane, **5d**, 4.3 g (48%, based on $^dIpc_2BH$): bp 120–122 °C (20 Torr); $[\alpha]^{23}_D$ +25.3° (*c* 3.9, CCl_4); ^{11}B NMR ($CDCl_3$) δ +31 (s); ^1H NMR ($CDCl_3$) δ 0.55–0.60 (m, 1 H), 1.00–1.20 (m, 3 H), 1.62–2.02 (m, 3 H), 2.80–2.90 (m, 2 H), 3.98 (q, *J* = 7 Hz, 4 H), 3.88–3.92 (m, 1 H), 6.04–6.08 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 27.7, 42.4, 44.3, 47.6, 61.9, 96.5, 134.7, 137.9. Anal. Calcd for $C_{10}H_{15}O_2B$: C, 67.46; H, 8.49; B, 6.07. Found: C, 67.18; H, 8.78; B, 5.89.

Oxidation of **5d** with alkaline H_2O_2 provided (1*R*,2*S*)-(+)-*exo*-5-norbornen-2-ol which was purified by preparative GC. The product showed $[\alpha]^{23}_D$ +7.5° (*c* 8, $CHCl_3$) [lit.[6c] $[\alpha]^{23}_D$ +6.2° (*c* 8.7, $CHCl_3$) for 79% ee], and 96% ee by the capillary GC analysis of its MCF derivative.

(+)-α-Pinene and the excess diene were recovered from the organic phase left after the extraction of boronic acid with 3 N NaOH.

(*S*)-2-(−)-(3-Cyclohexen-1-yl)-1,3,2-dioxaborinane (5e). 1,4-Cyclohexadiene (14.2 mL, 150 mmol, 200% excess) was hydroborated with $^dIpc_2BH$ (14.3 g, 50 mmol) and worked up as described above to obtain **5e**, 4.9 g (60%, based on $^dIpc_2BH$): bp 114–116 °C (20 Torr); $[\alpha]^{23}_D$ −71.5° (*c* 4, CCl_4); ^{11}B NMR ($CDCl_3$) δ +31 (s); ^1H NMR ($CDCl_3$) δ 1.02–1.12 (m, 1 H), 1.35–1.50 (m, 1 H), 1.70–1.80 (m, 1 H), 1.90–2.05 (m, 6 H), 3.97 (q, *J* = 7 Hz, 4 H), 5.65 (bq, 2 H); ^{13}C NMR ($CDCl_3$) δ 24.2, 25.8, 26.5, 27.7, 61.8, 96.5, 127.4, 128.5. Anal. Calcd for $C_9H_{15}O_2B$: C, 65.11; H, 9.11; B, 6.51. Found: C, 64.98; H, 9.32; B, 6.32. Oxidation of **5e** gave (*S*)-(−)-3-cyclohexen-1-ol which exhibited $[\alpha]^{23}_D$ −77.9° (*c* 10, $CHCl_3$) [lit.[22] $[\alpha]^{23}_D$ −5.13° (*c* 0.6, $CHCl_3$) for 19% ee] and ≥99% ee by the capillary GC analysis of its MTPA ester.

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Registry No. 1, 21932-54-7; **3a** (R* = 2-butyl), 137627-66-8; **3a** (R* = 3-hexyl), 137627-67-9; **3a** (R* = *exo*-norbornyl), 137627-68-0; **3a** (R* = *exo*-norbornen-2-yl), 137627-69-1; **3a** (R* = 3-cyclohexen-1-yl), 137627-70-4; **4** (R* = 2-butyl), 137627-73-7; **4** (R* = 2-hexyl), 137627-74-8; **4** (R* = *exo*-norbornyl), 137627-75-9; **5a**, 97235-22-8; **5b**, 97235-23-9; **5c**, 137694-54-3; **5d**, 137627-71-5; **5e**, 137627-72-6; B, 137627-76-0; PhCHO, 100-52-7; $HO(CH_2)_3OH$, 504-63-2; CH_3CHO, 75-07-0; $(CH_3)_2CHCHO$, 78-84-2; CCl_3CHO, 75-87-6; (*R*)-$H_3CCH(CH_2CH_3)B(OCH_2Ph)_2$, 137627-77-1; (*R*)-$H_3CCH_2CH(OH)CH_2CH_2CH_3$, 13421-42-6; (*R*)-(*exo*-norbornyl)$B(OEt)_2$, 137627-78-2; (*R*)-(*exo*-norbornyl)B-(OBu-*i*)$_2$, 137627-79-3; (*R*)-(*exo*-norbornyl)$B(OCH_2CCl_3)_2$, 137627-80-6; (*R*)-(*exo*-norbornyl)$B(OCH_2Ph)_2$, 137627-81-7; (cycloocten-4-yl)$BIpc_2$, 137627-82-8; *cis*-2-butene, 590-18-1; *cis*-3-

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hexene, 7642-09-3; bicyclo[2.2.1]hept-2-ene, 498-66-8; bicyclo-[2.2.1]hepta-2,5-diene, 121-46-0; 1,4-cyclohexadiene, 628-41-1; *trans*-2-butene, 624-64-6; (*R*)-2-butanol, 14898-79-4; 1,5-cyclo-octadiene, 111-78-4; (*R*)-*exo*-norbornyl alcohol, 61277-93-8; (1*R*,2*S*)-(+)-*exo*-5-norbornen-2-ol, 71030-15-4; (*R*)-2-butylboronic acid, 92116-84-2.

Supplementary Material Available: ^{11}B NMR, ^{1}H NMR, and ^{13}C NMR spectra for compounds **5c-e** (9 pages). Ordering information is given on any current masthead page.

Preparation, Reactions, and Stereochemistry of 4-Methyl-4-phosphatetracyclo[3.3.0.0^{2,8}.0^{3,6}]octane 4-Oxide and Derivatives

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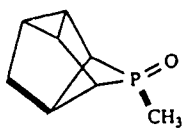
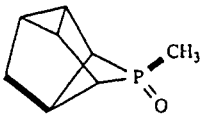
The cis isomer **1b** of the title compound was observed for the first time. It was prepared as a mixture with the previously reported trans isomer **1a**. Reduction of the latter under sterically controlled conditions enabled selective formation of either the cis or trans tetracyclic phosphine **7**. Although oxidation of the phosphine gave none of the expected phosphine oxide, stereoselective reactions with sulfur or selenium gave the cis and trans sulfides and selenides. Likewise, each phosphine isomer was transformed into several phosphonium salts by quaternization with methyl bromide, benzyl bromide, and *p*-nitro- and *p*-fluorobenzyl bromide. Stereochemical assignments for **1a** and **1b** were based on NMR lanthanide shift experiments. Corresponding assignments for the phosphines, sulfides, selenides, and phosphonium salts were based on both ^{1}H and ^{13}C NMR spectral data and the expected outcome of the reaction by literature precedent. For **1a**, **1b** and a series of derivatives, the ^{31}P-^{13}C coupling constants were found to be much larger than those observed in less rigid heterocyclic systems. They were consistent with previously reported Karplus relationships, provided a multiple-coupling path correction was made and coupling through nonbonded interactions was considered. Differences in the P-C coupling constants between the cis and trans isomers are also discussed. The $^{2}J_{PC}$ coupling constants were dependent upon the geometry about phosphorus in the phosphines and in the oxides. Several reactions of the title compound and the salt derivatives are described. These include reaction of the dimethyl salt **13** with methyllithium to give norbornylene and trimethylphosphine as well as a ring-opened product **22**. With the exception of the *p*-nitrobenzylphosphonium salt **12** which exhibited exocyclic P-C cleavage on treatment with aqueous NaOH, all of the salts led to ring opening. Treatment of both **1a** and salt **13** with aqueous sodium deuteroxide gave ring opening with selective deuterium incorporation at the syn-C-7 position.

Introduction

Four-membered phosphorus-containing rings, or phosphetanes, have received extensive study during the last two decades and have proven to be a class of compounds rich in unusual chemical reactivity, stereochemistry, and physical properties.[1] Earlier reports[2] on the synthesis of 4-methyl-4-phosphatetracyclo[3.3.0.0^{2,8}.0^{3,6}]octane 4-oxide[3] (**1**) were of special interest to us,[4] because oxide **1** possesses a conformationally rigid four-membered phosphorus heterocycle. The fixed and symmetrical geometry of the



1a (trans)



1b (cis)

tetracyclic skeleton provides a useful model to test the generality of stereospecific ^{31}P-^{13}C coupling constants which we[5] and others[6-8] previously observed. In the original reports[2] only one isomeric oxide with unspecified geometry was isolated. We anticipated from work with monocyclic phosphetanes[1a] that alteration of the reaction workup would provide both isomers, **1a** and **1b**, whose cis vs trans configuration[9] about phosphorus could be estab-

† This paper is dedicated in memory of John M. Cowles, deceased Jan 12, 1990.

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