Tetrahedron Vol. 40, No. 8, pp. 1325 to 1332, 1984
Printed in Great Britain.

0040-4020/84 $3.00 + .00
Pergamon Press Ltd.

ORGANOBORANES—34

GENERAL SYNTHESIS OF CHIRAL BORONIC AND BORINIC ESTERS VIA ASYMMETRIC HYDROBORATION-DISPLACEMENT. CARBENOIDATION OF CHIRAL BORINIC ESTERS TO ACYCLIC KETONES OF HIGH ENANTIOMERIC PURITIES

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(*Received in USA* 23 *May* 1983)

Abstract—Asymmetric hydroboration of appropriate alkenes with diisopinocampheylborane (Ipc_2BH) or monoisopinocampheylborane ($IpcBH_2$) produces intermediates that readily eliminate α-pinene on treatment with acetaldehyde, providing a direct, convenient route to chiral boronic esters of high enantiomeric purities. Mixed chiral trialkylboranes, readily prepared by stepwise hydroboration of appropriate alkenes with $IpcBH_2$, eliminate α-pinene on treatment with acetaldehyde under very mild conditions. The procedure makes readily available chiral borinic esters of high enantiomeric purities. The synthetic utility of chiral borinic esters is demonstrated by converting them into acyclic ketones including an alarm pheromone of the ant *Manica mutica*.

Chiral hydroboration is one of the most valuable reactions in asymmetric synthesis.[1] Asymmetric hydroboration, discovered in 1961, is the first efficient non-enzymatic asymmetric synthesis.[2] Since that time, numerous, highly efficient, asymmetric syntheses have been reported, particularly in the last decade.[3] There are now four chiral hydroborating agents, *viz* diisopinocampheylborane (Ipc_2BH),[4] monoisopinocampheylborane ($IpcBH_2$),[5] dilongifolylborane (Lgf_2BH),[6] and limonylborane (LimBH),[7] available for asymmetric hydroboration. These reagents are effective for three of the four major classes of prochiral alkenes.

The intermediate chiral boranes, obtained by asymmetric hydroboration, have been transformed into chiral alcohols[4-7] by oxidation with alkaline hydrogen peroxide, chiral iodides[8] by base-induced iodination, and chiral amines[9] by amination with hydroxylamine-O-sulfonic acid. However, these intermediates have not been converted into other chiral products utilizing carbon-carbon bond-forming reactions. Several such reactions are known for achiral organoboranes.[10]

The C–C bond-forming reactions of organoboranes are believed to proceed through an organoborate anion, which undergoes a facile 1,2-migration of an alkyl group from B to an adjacent atom containing an appropriate leaving group. In many of these reactions, only one of the three alkyl groups are utilized. In some cases, 9-borabicyclo[3.3.1]nonyl (9-BBN)[11] and thexyl[12] groups circumvent this difficulty. However, in other cases, these derivatives are not effective.[13] In some cases, alkoxy has been effectively used as a non-migrating "blocking" group.[14]

Interestingly, the situation in the case of chiral organoboranes is different where the chiral auxiliary is attached to B, making the boranes mixed. In order to successfully use these intermediates for C–C bond-forming reactions, the chiral auxiliary groups should (1) have minimum migratory aptitude, or (2) be capable of selective removal prior to the C–C bond-forming reaction.

In the case of chiral boranes derived from Ipc_2BH and $IpcBH_2$, the 3-pinanyl group, although tested in limited cases, does have considerable migratory aptitude, therefore making the synthesis less efficient.[15] Consequently, the second alternative appeared more attractive.

It is known that trialkylboranes react with aldehydes to generate the starting alkenes with the formation of borinates or boronates.[16] This reaction has been successfully used for asymmetric reduction of deuterated aldehydes,[17] acetylenic ketones[18] and simple ketones.[19] The rate of elimination of an alkene from the trialkylborane depends on the degree of substitution at the β-position to the B (i-Bu > 1-Bu ≫ Et) and on the ability of the group to form a *syn*-planar B–C–C–H conformation (cyclopentyl ≳ norbornyl > *sec*-butyl ≫ cyclohexyl). Fortunately, the elimination of the first alkyl group is much faster than that of the second group, permitting selective elimination of one alkyl group.[16]

Based on these considerations, we surmised that the trialkylboranes derived from Ipc_2BH and $IpcBH_2$ on treatment with aldehyde might selectively eliminate α-pinene to provide chiral boronic and borinic esters. In practice, this proved successful. A portion of our study has appeared in the form of preliminary communications.[20,21] We now describe in full the results of our study on the synthesis of chiral boronic esters, borinic esters, and acyclic ketones.

Synthesis of chiral boronic esters

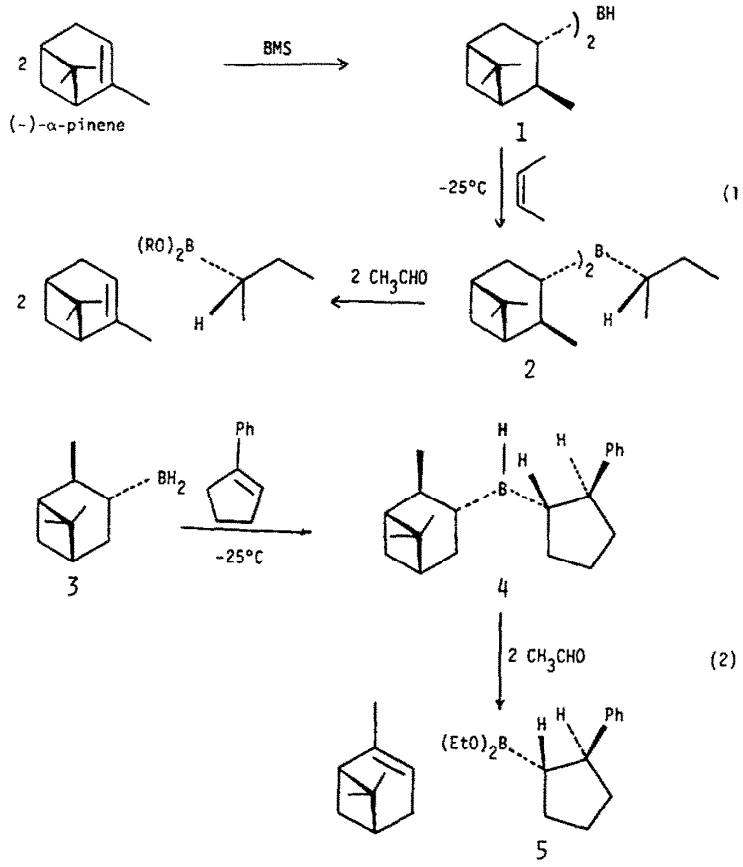
Alkylboronic esters, containing only one alkyl group attached to boron, are esthetically appealing and economical organoboron intermediates for C–C bond-forming reactions. No loss of the alkyl groups

result in such transformations. Consequently, several unsuccessful attempts were previously made to use these derivatives for homologation. Until the discovery of Matteson and Majumdar[22] and our own recent contribution,[23] there had been no effective means for homologation of boronic esters.

Recently Matteson and Ray[24] reported an elegant synthesis of chiral boronic esters using *cis*-pinanediol and Grignard reagents. We sought an alternative, convenient route to these intermediates *via* asymmetric hydroboration-displacement.

Accordingly, we prepared 2-butyldiisopinocampheylborane **2** by hydroboration of *cis*-2-butene with (+)-Ipc_2BH, **1**. The trialkylborane **2** contains the chiral 2-Bu group with > 98% ee. The problem was to find a convenient method to remove 3-pinanyl groups from **2** for the targeted synthesis of 2-butylboronic ester. It is known that 3-methyl-2-butyl eliminates faster than the 2-Bu group on treatment of the corresponding trialkylboranes with aldehyde. Consequently, it appeared that 3-pinanyl might eliminate faster than 2-Bu on treatment of **2** with an aldehyde.

The present method is also applicable to the dialkylboranes derived from monoisopinocampheylborane ($IpcBH_2$). Monoisopinocampheylborane is an excellent chiral hydroborating agent for trisubstituted and *trans*-alkenes.[5] Accordingly, 1-phenylcyclopentene was hydroborated with $IpcBH_2$, **3**, to provide the dialkyl-borane, **4**. The intermediate **4** on treatment with 100% excess acetaldehyde quantitatively liberated α-pinene to furnish the desired boronic ester, **5** (eqn 2). The progress of the reaction was readily monitored by ^{11}B NMR of the aliquot samples (boronate $\delta + 32$). It is interesting to note that in the case of **4** both alkyl groups have similar structural features (derived from trisubstituted cyclic alkene); however, only the 3-pinanyl group participates in the elimination process. This fact is evident from the GC analysis of the oxidation product of the boronate, which indicated α-pinene and *trans*-2-phenylcyclopentanol to be the sole products. (1*S*, 2*S*)-(+)-Diethyl *trans*-(2-phenylcyclopentyl)boronate **5** was readily isolated by distillation under reduced pressure. The optical purity of **5** was estimated to be

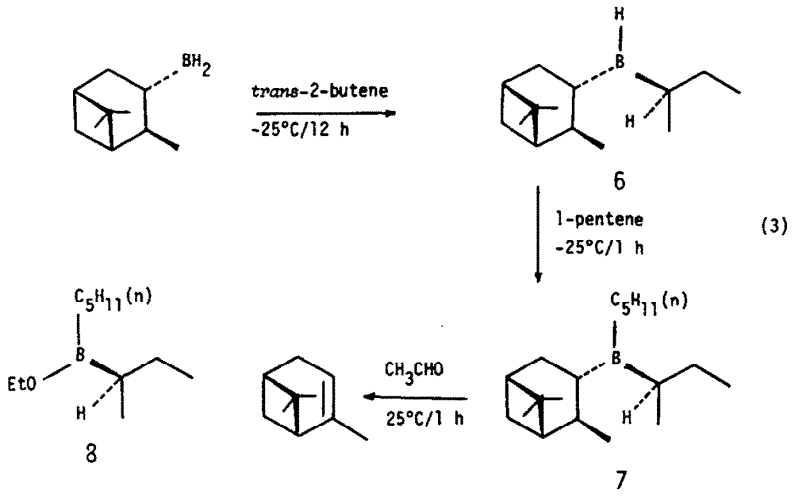


Thus, treatment of **2** with 100% excess acetaldehyde at 25° selectively and quantitatively liberated α-pinene to provide diethyl 2-butyl-boronate. This intermediate is readily separated from α-pinene by extraction with aqueous sodium hydroxide and converted into 2-butylboronic acid by acidification with acid. Reesterification of the acid with methanol provided (*S*)-(+)-dimethyl-2-butylboronate (eqn 1). The enantiomeric purity of the boronate was estimated to be 97% by its oxidation to (*S*)-(+)-2-butanol with alkaline hydrogen peroxide. 100% by its oxidation to *trans*-2-phenylcyclopentanol.

We believe that the synthesis of chiral boronic esters *via* displacement of the 3-pinanyl group, although tested only for these limited cases, must be quite general and should be applicable to other chiral organoboranes readily available by asymmetric hydroboration with Ipc_2BH and $IpcBH_2$.

Synthesis of chiral borinic esters

Optically inactive borinic esters have been pre-



pared and used in C–C bond-forming reactions. However, there was no method available for the synthesis of chiral borinic esters. Accordingly, we undertook to see whether asymmetric hydroboration might provide a route to these synthetically useful derivatives.

The strategy of the present method depends upon the successful synthesis of chiral mixed trialkylboranes, followed by selective elimination of the starting chiral auxiliary, the 3-pinanyl group, from the boron intermediate. The chiral mixed trialkylboranes were readily prepared by stepwise hydroboration of prochiral alkenes, followed by nonprochiral alkenes, with $IpcBH_2$. Thus, hydroboration of *trans*-2-butene with $IpcBH_2$ in the molar ratio of 1:1 results in the formation of 3-pinanyl-2-butylborane, **6**, which then rapidly hydroborates 1-pentene at −25° to provide the trialkylborane, **7**. Reaction of the resulting trialkylborane with 100% excess acetaldehyde under very mild conditions (25°, 1 hr) occurs with selective, facile elimination of the 3-pinanyl group to provide 2-butyl-*n*-pentylborinate, **8**, and α-pinene (eqn 3).

The α-pinene liberated is readily removed by distillation under vacuum. It may be noted that the α-pinene thus recovered is optically pure, $[\alpha]^{23}D$-51.5° (neat). Distillation of the residue yields (*R*)-(−)-ethyl-2-butyl-*n*-pentylborinate in 73% ee as estimated by its oxidation to (*R*)-(−)-2-butanol. Similarly, we have prepared ethyl *trans*-(2-methylcyclohexyl)-*n*-pentylborinate and ethyl *trans*-(2-phenylcyclopentyl)ethylborinate in 75 and 100% ee, respectively (Table 1).

Synthesis of chiral acyclic ketones

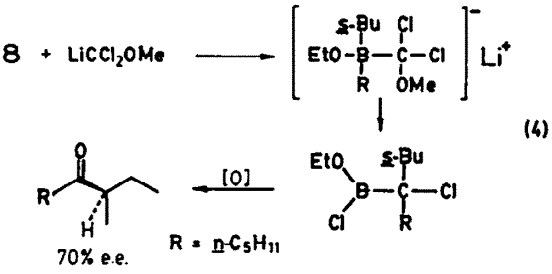
The asymmetric synthesis of ketones has been extensively studied in the past decade.[25,26] Excellent success has been achieved in the enantioselective alkylation of appropriate ketones. In the case of acyclic ketones,[26] highly favorable results are realized only in the alkylation of symmetrical ketones, thereby severely limiting the generality of the method. We have developed a new, more general approach involving asymmetric hydroboration-carbenoidation for the synthesis of acyclic ketones.

The carbenoidation of trialkylboranes[27] and borinic esters[14d] with α,α-dichloromethyl methyl ether (DCME) in the presence of hindered base is known

Table 1. Synthesis of chiral borinic esters *via* asymmetric hydroboration displacement[a]

Olefin-A	Olefin-B	Borinate Ester	Yield, % (Isolated)	Bp °C (mm Hg)	$[\alpha]^{23}D$ °C	ee %	Config.
trans-2-butene	1-pentene	ethyl 2-butyl-*n*-pentylborinate	75	47(1)	-4.7 (c 7.4, THF)	73	*R*
1-methylcyclohexene	1-pentene	ethyl *trans*-(2-methylcyclohexyl)-*n*-pentylborinate	72	65(0.01)	-24.7 (c 8.6, THF)	75	1*R*,2*R*
1-phenylcyclopentene	ethylene	ethyl *trans*-(2-phenylcyclopentyl)-ethylborinate	67	85(0.01)	-26.6 (c 11.8, THF)	100	1*R*,2*R*

[a] $IpcBH_2$, prepared from (-)-α-pinene, was used for asymmetric hydroboration.



to give, after oxidation of the intermediate boranes, trialkylcarbinols and ketones respectively. Application of this reaction to chiral borinic esters provides a convenient route to chiral ketones. Thus, treatment of ethyl 2-butyl-*n*-pentylborinate, **8**, with DCME and lithium triethylcarboxide, followed by oxidation of the intermediate with alkaline hydrogen peroxide, furnished (*R*)-(−)-3-methyl-4-nonanone in 70% ee (eqn 4).

Similarly, we have prepared several chiral borinic esters and converted them without isolation into the ketones (Table 2), including an alarm pheromone of the ant *Manica mutica*[28] (Table 2, Entry 1).

Organoboranes bearing alkyl groups such as methyl and aryl are not available by hydroboration. These boranes, however, are readily prepared by using Grignard or organolithium reagents. In order to demonstrate the utility of the present method, we prepared *trans*-2-phenylcyclopentyl methyl ketone as a representative example.

Thus, the dialkylborane, obtained by the hydroboration of 1-phenylcyclopentene with $IpcBH_2$, was methanolyzed and the borinate ester in *n*-pentane was treated with MeLi at −78°.[29] The trialkylborane, obtained by warming the "ate" complex to room temperature, on successive treatment with acetaldehyde, DCME and oxidation, provided the desired ketone in 90% ee.

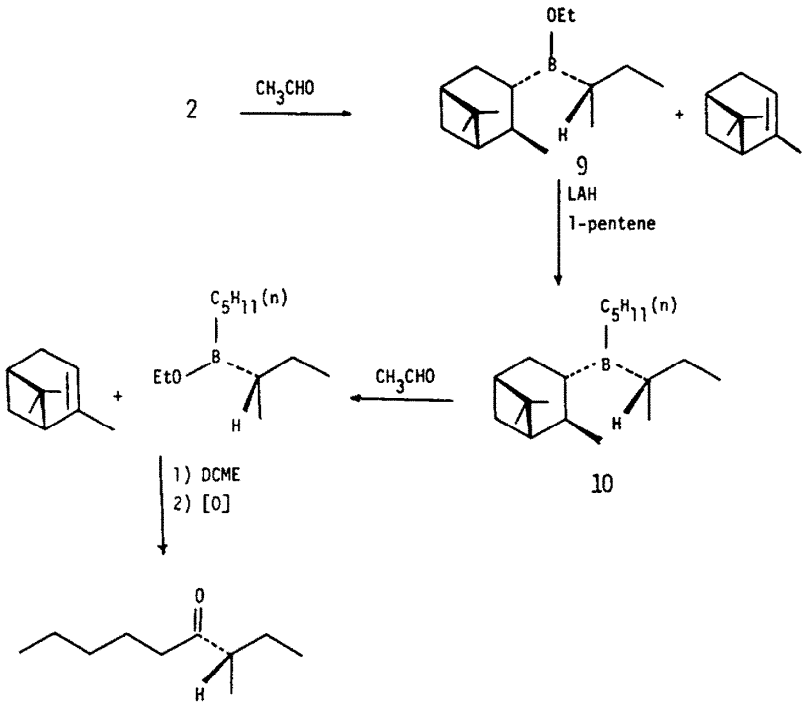
Ipc_2BH is an excellent chiral hydroborating agent for *cis*-alkenes, whereas, $IpcBH_2$ fails with such alkenes. Consequently, we explored use of Ipc_2BR for the synthesis of acyclic ketones. To achieve our goal, it was important to realize precise control over the elimination process. We successfully achieved the desired selectivity by controlling both the quantity of acetaldehyde and the reaction time. Thus, intermediate **2**, on treatment with 100% excess (for one elimination) acetaldehyde at 25°, furnished ethyl 2-butyl-3-pinanylborinate, **9**, after 6 hr. The excess acetaldehyde and liberated α-pinene were removed under reduced pressure. The removal of α-pinene was monitored by ^1H NMR of the aliquot samples. The borinate was then reduced with lithium aluminum hydride in the presence of 1-pentene.[30] The dialkylborane, generated *in situ*, hydroborated 1-pentene to furnish the trialkylborane, **10**. It was then converted into (*S*)-(+)-3-methyl-4-nonanone in 95% ee (Scheme 1).

Similarly, (*S*)-(+)-4-methyl-3-hexanone, an alarm pheromone of the ant *Manica mutica*, was prepared in 83% optical purity.

Table 2. Asymmetric synthesis of representative acyclic ketones *via* asymmetric hydroboration[a]-carbenoidation

Olefin-A	Olefin-B	Product Ketones: Ketone	Yield, % (Isolated)	$[\alpha]^{23}D$ Deg	% ee	Config.
trans-2-butene	ethylene	4-methyl-3-hexanone	78[b]	-19.2(c 3.67, Et_2O)	60[c]	*R*
trans-2-butene	1-pentene	3-methyl-4-nonanone	66	-15.7(c 5, Et_2O)	70[d]	*R*
trans-2-butene	5-hexenylacetate	8-methyl-7-one-1-decanol[e]	65	-11.92(c 5.11, EtOH)	—[f]	*R*
1-methylcyclohexene	1-pentene	*trans*-(2-methylcyclohexyl)-*n*-pentyl ketone	70	-14.7(c 5.2, EtOH)	75[g]	1*R*,2*R*
1-phenylcyclopentene	1-pentene	*trans*-(2-phenylcyclopentyl)-*n*-pentyl ketone	78	-103.8(c 5.2, EtOH)	90[g]	1*R*,2*S*
1-phenylcyclopentene	—[h]	*trans*-(2-phenylcyclopentyl)-methyl ketone	66	-106.8(c 5, EtOH)	90[g]	1*R*,2*S*

[a] $IpcBH_2$, prepared from (-)-α-pinene, was used for asymmetric hydroboration. [b] GC yield. [c] D. Enders and H. Eichenauer, *Angew. Chem., Int. Ed. Engl.* 18, 397 (1979) report $[\alpha]^{23}D$ +30.2 (c 3.7, Et_2O) for 94% ee 4-methyl-3-hexanone. [d] D. Seebach and D. Steinmüller, *Ibid.* 7, 619 (1968) report maximum rotation for 3-methyl-4-nonanone $[\alpha]^{23}D$ +22.4 (c 5, Et_2O). [e] The acetoxy group is hydrolyzed under DCME-oxidation conditions. [f] Attempts to determine % ee by ^1H NMR in the presence of chiral shift reagent $Eu(hfc)_3$ were unsuccessful. [g] As determined by ^1H NMR in the presence of chiral shift reagent $Eu(hfc)_3$ using Varian XL-200 spectrometer. [h] Methyl lithium is used to prepare the trialkylborane containing methyl as one of the alkyl groups.



Scheme 1.

CONCLUSION

It is evident from the present study that chiral hydroboration of appropriate alkenes with either diisopinocampheylborane or monoisopinocampheylborane of high optical purity provide chiral organoboranes from which α-pinene can be readily displaced with acetaldehyde. The selectivity of elimination of the 3-pinanyl group over other alkyl groups on B is remarkable and the number of 3-pinanyl groups eliminated can be precisely controlled. The products formed are readily isolated as boronic esters or borinic esters of high optical purity. In these displacement reactions, the chiral auxiliary, α-pinene, is readily recovered without loss of optical activity for recycle in the synthesis, Moreover, the products with chiral centers of opposite configuration can be readily synthesized using the appropriate enantiomer of α-pinene to prepare the reagents.

The chiral borinic esters are converted into acyclic ketones of high optical purities. The high asymmetric induction realized in the chiral hydroboration is retained in the C–C bond-forming reaction. Even though the chiral center is in the α position to the keto group, there is only 2–6% racemization under alkaline conditions utilized for the hydrogen peroxide oxidation. Acyclic ketones containing two chiral ketones (Table 2, Entries 3–6) are readily prepared by the present method. However, synthesis of such ketones by the known enantioselective procedures is not possible. The present study demonstrates the versatility and utility of chiral organoboranes in asymmetric synthesis.

EXPERIMENTAL

All operations were carried out under N_2, with oven-dried glassware.[31] GLC analyses were carried out with a Hewlett-Packard 5750 chromatograph using (a) 6 ft × 0.25 in column packed with 10% Carbowax 20M on Chromosorb W (60–80 mesh) or (b) a 6 ft × 0.25 in column packed with 10% SE-30 on Chromosorb W (60–80 mesh). For preparative GLC, either (c) a 6 ft × 0.5 in column packed with 10% Carbowax 20M on Chromosorb W (60–80 mesh) or (d) a 6 ft × 0.5 in column packed with 20% SE-30 on Chromosorb W (60–80 mesh) was used. Rotations were measured on a Rudolph Polarimeter Autopol III.

Materials. Tetrahydrofuran (THF) was distilled from a small excess of lithium aluminum hydride (LAH) and stored under N_2. (+)-α-Pinene, $[\alpha]^{23}D + 47.1°$ (neat), 91.3% ee and (−)-β-pinene, $[\alpha]^{23}D - 21.0°$ (neat) were purchased from Aldrich Chemical Co. and distilled from a small excess of LAH. (−)-α-Pinene, $[\alpha]^{23}D - 47.4°$ (neat), 92% ee, was prepared by isomerization of β-pinene with KAPA.[32] Acetaldehyde and the alkenes used for this study were commercial products of the highest purity available and they were used as received.

Spectra. The ^{11}B NMR spectra were obtained on a Varian FT-80A instrument. The chemical shifts are in δ values relative to $BF_3 \cdot OEt_2$. ^1H NMR spectra were recorded on a Perkin–Elmer R-32 instrument.

(S)-(+)-*Dimethyl 2-butylboronate.* 2-Butyldiisopinocampheylborane, **2**, (50 mmol) was prepared from (−)-α-pinene, BMS and *cis*-2-butene following the reported procedure.[4c] It was treated with acetaldehyde (11 ml, 200 mmol) and stirred at 25° for 36 hr. Excess acetaldehyde and THF were pumped off (25°, 14 mm, 1 hr) and pentane (50 ml) was added. The resulting mixture of α-pinene and diethyl 2-butylboronate was stirred with 3 M NaOH (3 × 50 ml, each portion was stirred for 1 hr). The combined aqueous phase was acidified with HCl aq and extracted with ether (3 × 50 ml) and dried ($MgSO_4$). Ether was removed to give 2-butylboronic acid, which was dried under vacuum (0.5 mm, 10 hr). It was then converted into methyl ester by refluxing it with the mixture of MeOH–$CHCl_3$ (1:2.4, 200 ml) using Soxhlet apparatus filled with molecular sieves—4Å type for 20 hr. At the end of this period, after the removal of $CHCl_3$ and MeOH, (*S*)-(+)-dimethyl 2-butylboronate was isolated by distillation (4.6 g, 71%), b.p. 38°/30 mm, $[\alpha]^{23}D + 9.1°$ (*c* 11.7, THF).

(1S, 2S)-(+)-*Diethyl* trans-(2-*phenylcyclopentyl*)*boronate* (5). Monoisopinocampheylborane was prepared from (+)-α-pinene, as described earlier.[3d] A 0.867 M soln of $IpcBH_2$ in THF (40.3 ml, 35 mmol) was cooled to −25°, treated with 1-phenylcyclopentene (5 ml, 35 mmol) and the contents further stirred at −25° for 48 hr while the dialkylborane precipitated out of the soln. The mixture was then treated with acetaldehyde (7.8 ml), 140 mmol) at −25° and it was allowed to stir at 25° for 6 hr. Excess acetaldehyde and THF were pumped off (25°, 14 mm, 1hr) and then α-pinene (25°, 0.2 mm, 8 hr). The residue was distilled under high vacuum to afford (1*S*, 2*S*)-(+)-diethyl *trans*-(2-phenylcyclopentyl)boronate: (8 g, 66%), b.p. 92°/0.02 mm, $(\alpha)^{23}D$ +25.4 (*c* 9.65, THF). The boronate (3.65 g, 14.8 mmol) was dissolved in 15 ml THF and treated with 3 N NaOH (6 ml, 18 mmol), followed by dropwise addition of 30% H_2O_2 (3 ml, 24 mmol) and stirred at 55° for 1 hr. The distillation of the residue after the usual workup provided *trans*-2-phenylcyclopentanol: (2.02 g, 84%), b.p. 130°/6 mm, $[\alpha]^{23}D$ +71.2 (*c* 11.9, EtOH), 100% ee.

(R)-(−)-*Ethyl* 2-*butyl*-n-*pentylboronate* (8). *trans*-2-Butene (2.8 g, 50 mmol) was added to a stirred soln of 0.89 M $IpcBH_2$ in THF (56 ml), 50 mmol) at −25° and the mixture was further stirred for 12 hr at −25° while the dialkylborane precipitated out of the soln. It was then treated with 1-pentene (3.5 g, 50 mmol) and stirred at −25° for 1 hr. At this point, the solid disappeared and the ^{11}B NMR of the resulting clear soln indicated the formation of trialkylborane (δ +82). It was then treated with acetaldehyde (5.6 ml, 100 mmol) at −25° and was allowed to stir at 25° for 1 hr. The resulting borinate (^{11}B NMR δ +54) was made free of excess acetaldehyde, THF and α-pinene (25°, 14 mm, 1 hr; 25°, 0.05 mm, 8 hr). The volatile portions collected in Dry Ice·acetone traps were combined and distilled to provide α-pinene: (4.5 g, 67%), b.p. 155°/745 mm, $[\alpha]^{23}D$ −51.5 (neat), 99.8% ee. The residue on distillation afforded (*R*)-(−)-ethyl 2-butyl-n-pentylborinate (6.9 g, 75%), b.p. 47°/1 mm, $[\alpha]^{23}D$ +4.7° (*c* 7.4, THF). It was oxidized in the usual manner to provide (*R*)-(−)-2-butanol, $[\alpha]^{23}D$ −9.85 (neat), 73% ee.

(1R, 2R)-(−)-*Ethyl* trans-(2-*methylcyclohexyl*)-n-*pentylborinate*. To a stirred 0.95 M soln of $IpcBH_2$ in THF (53 ml, 50 mmol) at −25°, 1-methylcyclohexene (4.8 g, 50 mmol) was added and further stirred at −25° for 6 hr. To the resulting dialkylborane was added 1-pentene (3.5 g, 50 mmol) and stirred at 0° for 6 hr. At this point the formation of trialkylborane was complete (^{11}B NMR δ + 83). The trialkylborane was then treated with acetaldehyde (5.6 ml, 100 mmol) and stirred at 25° for 6 hr to furnish the desired borinate (^{11}B NMR δ + 53). The residue after removal of excess acetaldehyde, THF and α-pinene was distilled to afford (1*R*, 2*R*)-(−) Ethyl *trans*-(2-methylcyclohexyl)-n-pentylborinate: (8 g, 72%), b.p. 65°/0.01 mm, $[\alpha]^{23}D$ −24.7 (*c* 8.6, THF).

(1R, 2R)-(−)-*Ethyl* trans-(2-*phenylcyclopentyl*)*ethylborinate*. To a stirred 0.95 M soln of $IpcBH_2$ in THF (31.6 ml, 30 mmol) at −25° was added 1-phenylcyclopentene (4.32 g, 30 mmol) and the mixture stirred for 48 hr at −25°. To the solid dialkylborane at −25° was passed ethylene gas until the solid dialkylborane disappeared (1 hr) to provide clear soln of the desired trialkylborane (^{11}B NMR δ + 82). The mixture was warmed up to 0° and was treated with acetaldehyde (3.4 ml, 60 mmol) and stirred for an additional 3 hr at 0°. The residue, after removal of excess acetaldehyde, THF and α-pinene, on distillation gave (1*R*, 2*R*)-(−)-ethyl *trans*-(2-phenylcyclopentyl)ethylborinate (4.62 g, 67%), b.p. 83°/0.01 mm, $[\alpha]^{23}D$ −26.6° (*c* 11.8, THF). It was oxidized in the usual manner to yield *trans*-2-phenylcyclopentanol, $[\alpha]^{23}D$ 71.2° (*c* 11.9, EtOH), 100% ee.

(R)-(−)-4-*Methyl*-3-*hexanone from* $IpcBH_2$. *trans*-2-Butene (2.8 g, 50 mmol) was added to a stirred 0.75 M soln of $IpcBH_2$ in THF (56.1 ml, 50 mmol) at −25° and the mixture was further stirred at −25° for 12 hr while the dialkylborane precipitated out of the soln. Ethylene gas was then bubbled through the mixture at −25° for 2 hr. The resulting trialkylborane (^{11}B NMR δ + 80) was treated with acetaldehyde (5.6 ml, 100 mmol) and stirred for 1 hr at 25°. Excess acetaldehyde and THF were pumped off (25°, 14 mm, 1 hr) and the borinate in THF (40 ml) was cooled to 0°. To the mixture was added DCME (6.3 g, 55 mmol), followed by dropwise addition of 1.185 M Et_3COLi (84.3 ml, 100 mmol). The ice bath was removed and the contents allowed to stir at room temp. for 2 hr. The resulting organoborane was then treated with 95% EtOH (20 ml), solid NaOH (4 g, 100 mmol), followed by dropwise addition of 30% H_2O_2 (25 ml). The mixture was stirred at 55° for 1 hr, poured into water (30 ml) and extracted with ether (3 × 30 ml). The combined organic extract was washed with water (30 ml), brine (30 ml) and dried over $MgSO_4$. (*R*)-(−)-4-Methyl-3-hexanone was found to be 78% by GC analysis, using an internal standard. A GC pure sample was obtained by careful distillation, followed by separation on preparative GC: $[\alpha]^{23}D$ −19.2° (*c* 3.67, Et_2O), 60% ee.

(R)-(−)-3-*Methyl*-4-*nonanone from* $IpcBH_2$. A 0.864 M soln of $IpcBH_2$ in THF (57.8 ml, 50 mmol) was cooled to −25° and treated with *trans*-2-butene (2.8 g, 50 mmol). The contents were stirred at −25° for 12 hr while the dialkylborane separated out of the soln. 1-Pentene (3.5 g, 50 mmol) was then added and the contents stirred at −25° for 1 hr. At this point, the solid disappeared and ^{11}B NMR of the soln indicated formation of the desired trialkylborane (^{11}B NMR δ + 82). It was then treated with acetaldehyde (5.6 ml, 100 mmol) at 25° and the mixture stirred for an additional hr. Excess acetaldehyde, THF and α-pinene were pumped off (25°, 14 mm, 1 hr; 25°, 0.2 mm, 8 hr). The borinate (^{11}B NMR δ + 55) was dissolved in THF (40 ml), cooled to 0° and treated with DCME (6.3 g, 55 mmol), followed by dropwise addition of 1.185 M Et_3COLi (84.3 ml, 100 mmol). The ice bath was removed and the contents stirred at 25° for 2 hr. The resulting organoborane was then treated with 95% EtOH (20 ml), solid NaOH (4 g, 100 mmol), followed by dropwise addition of 30% H_2O_2 (25 ml). The mixture was stirred at 55° for 1 hr, poured into 30 ml water and extracted with ether (3 × 30 ml). The combined organic extract was washed with water (30 ml), brine (30 ml), and dried over $MgSO_4$. The organic extract was distilled to remove solvents and Et_3COH, b.p. 141–142°. The residue then distilled under vacuum to provide (*R*)-(−)-3-methyl-4-nonanone: (5.1 g, 66%), b.p. 96°/14 mm. A GC pure sample was obtained by preparative GC, $[\alpha]^{23}D$ − 15.7° (*c* 5, Et_2O), 70% ee.

(R)-(−)-8-*Methyl*-7-*one*-1-*decanol*. To a stirred suspension of 2-butyl-3-pinanylborane (50 mmol), prepared as described above, was added 5-hexenyl acetate (7.2 g, 50 mmol) and the contents stirred for 3 hr at −25°. The resulting trialkylborane (^{11}B NMR δ + 82) was converted into the desired ketone, as described under procedure for 3-methyl-4-nonanone. The keto alcohol was distilled: (6.1 g, 65%), b.p. 98°/0.25 mm. It was purified by "Flash Chromatography" to get GC pure sample, $[\alpha]^{23}D$ − 11.92° (*c* 5.115, EtOH). The attempts to determine % ee by chiral shift reagent, Eu(hfc)$_3$, were unsuccessful. However, it should be close to 70%.

(1R, 2R)-(−)-trans-2-*Methylcyclohexyl*-n-*pentyl ketone*. Ethyl *trans*-(2-methylcyclohexyl)-n-pentylborinate (50 mmol) was prepared following the procedure described. The borinate was converted without isolation into the ketone following the procedure described under 3-methyl-4-nonanone. The ketone was isolated: (6.85 g, 70%), b.p. 80–85°/0.6 mm. A GC pure sample was obtained by preparative GC, $[\alpha]^{23}D$ − 14.7° (*c* 5.2, EtOH). ^1H NMR in the presence of Eu(hfc)$_3$ indicated it to be 75% enantiomerically pure.

(1R, 2S)-(−)-trans-2-*Phenylcyclopentyl*-n-*pentyl ketone*. To a stirred soln of 0.75 M $IpcBH_2$ in THF (40 ml, 30 mmol) at −25° was added 1-phenyl-cyclopentene (4.4 ml, 30 mmol) and the mixture was stirred at −25° for 48 hr. To the solid dialkylborane was then added 1-pentene (3.3 ml, 30 mmol)

and the mixture was further stirred for 6 hr at −25°. The trialkylborane (^{11}B NMR δ + 83) was converted into the desired ketone following the procedure described under 3-methyl-4-nonanone. Thus, (1*R*, 2*S*)-(−)-*trans*-2-phenylcyclopentyl-*n*-pentyl ketone was isolated: (5.7 g, 78%), b.p. 112°/0.5 mm, $[\alpha]^{23}$D − 103.8° (*c* 5.2, EtOH). It was found to be 90% optically pure by examination of ^{1}H NMR in the presence of chiral shift reagent Eu(hfc)$_3$.

(1R, 2S)-(−)-trans-2-*Phenylcyclopentylmethyl ketone.* 1-Phenylcyclopentene (7.4 ml, 50 mmol) was added dropwise to 0.9725 M IpcBH$_2$ in THF (51.4 ml, 50 mmol) at −25°. The dialkylborane formed after stirring the mixture at −25° for 48 hr, was treated with MeOH (4 ml, 100 mmol; Caution: H_2 evolution). The resulting borinate (^{11}B NMR δ + 55) was made free of excess MeOH and THF (25°, 14 mm, 2 hr), dissolved in pentane (35 ml), cooled to −78° and treated with 1.43 M soln of MeLi in ethyl ether (34.8 ml, 50 mmol). After stirring the mixture for 15 min at −78°, it was removed from cold bath and allowed to stir at room temp for 6 hr while a white ppt of LiOMe appeared with the formation of the desired trialkylborane (^{11}B NMR δ + 84). The mixture was passed through a filtration chamber and the solid washed with pentane (3 × 25 ml). The filtrate and washings were combined and concentrated to provide the trialkylborane. It was converted into the ketone following the procedure described under 3-methyl-4-nonanone experiment. It was isolated by distillation: (6.23 g, 66%), b.p. 73°/0.1 mm. A GC pure sample was obtained by preparative GC, $[\alpha]^{23}$D − 106.8 (*c* 5, EtOH). ^{1}H NMR in the presence of chiral shift reagent Eu(hfc)$_3$ indicated it to be 90% enantiomerically pure.

(S)-(+)-3-*Methyl*-4-*nonanone from* (+)-*Ipc$_2$BH.* 2-Butyldiisopinocampheylborane, **2**, (50 mmol) was prepared from (−)-α-pinene, BMS and *cis*-2-butene following the reported procedure.[4c] Acetaldehyde was added to the trialkylborane at 0° and the mixture stirred at 25° for 6 hr. The progress of the reaction was monitored by ^{11}B NMR. Excess acetaldehyde, THF and the liberated α-pinene were pumped off under vacuum (25°, 14 mm, 2 hr, 25°, 0.05 mm, 12 hr). The removal of α-pinene was continued until ^{1}H NMR indicated complete disappearance of the signal (at δ + 5.1) due to olefinic proton of α-pinene. The borinate (δ +53) thus obtained was dissolved in THF (25 ml) and 1-pentene (3.5 g, 50 mmol) was added to the borinate followed by dropwise addition of 0.98 M LAH in THF (17 ml, 16.6 mmol). The *in situ* generation of the dialkylborane, followed by hydroboration of 1-pentene, approached near completion after stirring the contents at 25° for 22 hr. To the mixture was then added acetaldehyde (8.4 ml, 150 mmol) at 0° and the contents stirred at 25° for 1 hr. The resulting borinate (δ +53) was converted into the desired ketone following the procedure described under (*R*)-(−)-3-methyl-4-nonanone. Thus, (*S*)-(+)-3-methyl-4-nonanone was isolated: b.p. 96°/14 mm (4.7 g, 60%). A GC pure sample obtained by preparative GC gave rotation: $[\alpha]^{23}$D +21.3 (*c* 5, Et_2O), 95% ee.

(S)-(+)-4-*Methyl*-3-*hexanone from* (+)-*Ipc$_2$BH.* Ethyl 2-butyl-3-pinanylborinate (50 mmol) in THF (25 ml) was prepared as described above and treated with 0.98 M LAH in THF (17 ml, 16.6 mmol) at 25°. Ethylene was then bubbled through the soln for 8 hr. At this point, the formation of the trialkylborane was nearly complete. It was then converted into (*S*)-(+)-4-methyl-3-hexanone following the procedure described above. A GC pure sample obtained by preparative GC gave rotation: $[\alpha]^{23}$D 25.16 (*c* 3.7, Et_2O), 83% ee.

Acknowledgement—We wish to acknowledge our warm appreciation for the steady financial support provided by the National Institutes of Health (GM 10937).

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