Chiral Synthesis via Organoboranes. 1.[1] A Simple Procedure To Achieve Products of Essentially 100% Optical Purity in Hydroboration of Alkenes with Monoisopinocampheylborane. Synthesis of Boronic Esters and Derived Products of Very High Enantiomeric Purities

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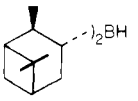
Abstract: Several optically pure isopinocampheylalkylboranes were prepared from readily available prochiral olefins and monoisopinocampheylborane of 100% ee. Simple crystallization converts the optically impure dialkylboranes obtained on hydroboration to optically pure dialkylboranes. Thus, the isopinocampheyl moiety is used both for optical induction and for upgrading the dialkylboranes to essentially 100% ee. These dialkylboranes readily eliminate α-pinene on treatment with acetaldehyde to give boronic esters and acids, $R^*B(OR)_2$ and $R^*B(OH)_2$, of very high enantiomeric purities. Upon oxidation, these dialkylboranes afford the corresponding alcohols in essentially 100% optical purity. Since it is now possible to transfer chiral organic groups from boron to practically all other elements of chemical interest, this development opens the door to the simple synthesis of practically all chiral compounds in essentially 100% ee.

Asymmetric hydroboration, discovered in 1961,[3] marked the beginning of a practical, nonenzymatic asymmetric synthesis. Prior to this time, asymmetric synthesis had been very inefficient and hardly of practical utility. Diisopinocampheylborane (Ipc_2BH, **1**)[4] is currently one of the most versatile chiral reagents readily



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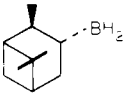
available for laboratory use.[5] Numerous applications of this reagent have appeared in the literature over the past 2 decades. It has been applied for asymmetric hydroboration of prochiral olefins to provide chiral products, such as alcohols, amines, halides, hydrocarbons, and ketones.[5] It has also been used for the asymmetric synthesis of natural products such as prostaglandin $F_{2\alpha}$,[5] loganin,[5] and the carotenoid zeaxanthin.[6] A major advantage of Ipc_2BH is the ready availability of both enantiomers of α-pinene. Consequently, chiral centers of opposite configuration can be generated by using Ipc_2BH derived from the appropriate antipode of α-pinene.

Ipc_2BH is an excellent chiral hydroborating agent for cis-disubstituted alkenes such as *cis*-2-butene and *cis*-3-hexene, achieving asymmetric hydroboration as high as 98.4% with *cis*-2-butene.[7] Later, the development of new reagents and procedures enabled the preparation of the first chiral monoalkylborane, monoisopinocampheylborane ($IpcBH_2$, **2**).[4,8,9] It achieves con-



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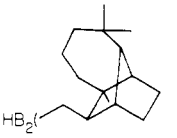
siderable asymmetric induction in the hydroboration of trans-substituted and trisubstituted olefins.[10] More recently, dilongifolylborane (Lgf_2BH, **3**)[11] has been successfully utilized for



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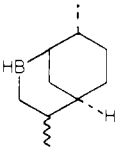
asymmetric hydroboration of cis-substituted and trisubstituted olefins. Limonylborane (LimBH, **4**),[12] the first chiral borahetero-cyclane, was prepared by the cyclic hydroboration of limonene, followed by hydridation. This reagent was also used for the asymmetric hydroboration of prochiral olefins.



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Unfortunately, in spite of all of these chiral hydroborating agents, only in two instances has very high, enzyme-like, asymmetric induction been achieved. Thus, hydroboration of *cis*-2-butene with Ipc_2BH gives a trialkylborane containing the chiral 2-butyl group with >98% ee.[7] Hydroboration of 1-phenyl-1-cyclopentene with $IpcBH_2$ gave a dialkylborane containing the *trans*-2-phenylcyclopentyl group with 100% ee. In these two cases, the intermediate organoboranes can be converted to alkylboronic esters of high optical purity.[13]

Alkylboronic esters are esthetically appealing intermediates for carbon–carbon bond-forming reactions.[14] These reactions are

(1) Hydroboration. 68.
(2) Postdoctoral research associate on Grant CHE-79-18881 of the National Science Foundation.
(3) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 486.
(4) These organoboranes actually exist in the solution as the dimers, that is, as derivatives of the diborane molecule. However, it is convenient to refer to them as simple borane derivatives.
(5) For a recent review on "Asymmetric Syntheses via Chiral Organoborane Reagents", see: Brown, H. C.; Jadhav, P. K.; Mandal, A. K. *Tetrahedron* **1981**, *37*, 3547.
(6) Rüttimann, A.; Mayer, H. *Helv. Chim. Acta* **1980**, *63*, 1456.
(7) Brown, H. C.; Yoon, N. M. *Isr. J. Chem.* **1977**, *15*, 12.
(8) Brown, H. C.; Yoon, N. M. *J. Am. Chem. Soc.* **1977**, *99*, 5514.
(9) Brown, H. C.; Schwier, J. R.; Singaram, B. *J. Org. Chem.* **1978**, *43*, 4395.
(10) Brown, H. C.; Jadhav, P. K.; Mandal, A. K. *J. Org. Chem.* **1978**, *43*, 5074.
(11) Jadhav, P. K.; Brown, H. C. *J. Org. Chem.* **1981**, *46*, 2988.
(12) Jadhav, P. K.; Kulkarni, S. U. *Heterocycles* **1982**, *18*, 169.
(13) Brown, H. C.; Jadhav, P. K.; Desai, M. C. *J. Am. Chem. Soc.* **1982**, *104*, 4303.
(14) (a) Matteson, D. S.; Majumdar, D. S. *J. Am. Chem. Soc.* **1980**, *102*, 7588. (b) Brown, H. C.; Imai, T. *Ibid.* **1983**, *105*, 6285.

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Table I. IpRBH Compounds Available in ~100% ee

olefin	borane IpcRBH	alcohol ROH	method of purification[g]	% ee[a] before purification	% ee[a] after purification	yield, %	config of ROH
cis-2-butene	9	2-butanol	A	97	99[b]	78	*S*
2-methyl-2-butene	8	3-methyl-2-butanol	B	53	100[c]	51	*S*
1-methylcyclopentene	5	*trans*-2-methylcyclopentanol	C	62	100[d]	65	1*S*,2*S*
1-methylcyclohexene	7	*trans*-2-methylcyclohexanol	D	72	≥99[e]	75	1*S*,2*S*
1-phenylcyclopentene	*f*	*trans*-2-phenylcyclopentanol	E		100[f]	72	1*S*,2*R*
(*Z*)-3-phenyl-2-pentene	6	*erythro*-3-phenyl-2-pentanol	C	85	100[f]	77	2*S*,3*S*

[a] Optical purity was determined by measuring the rotations of the alcohols and comparing the vlues with the maximum reported rotations (see footnotes *b-e*). [b] Leroux, P. J., Lucas, H. J. *J. Am. Chem. Soc.* **1951**, *73*, 41. $\alpha^{25}D$ + 10.67° (neat, *l* 1.0) for 2-butanol. [c] Sanderson, W. A.; Mosher, H. S. *Ibid.* **1966**, *88*, 4185. $\alpha^{27}D$ +8.12° (neat, *l* 2.0) for 3-methyl-2-butanol. [d] Partridge, J. J.; Chadha, N. K.; Uskoković, M. R. *Ibid.* **1973**, *95*, 532. $[\alpha]^{25}D$ +43.9° (*c* 1.0, CH_3OH) for *trans*-2-methylcyclopentanol. [e] Bäckström, R.; Sjöbers, B. *Ark. Kemi* **1967**, *26*, 549. $[\alpha]^{25}D$ +42.9° (*c* 1.0, CH_3OH) for *trans*-2-methylcyclohexanol. [f] See ref 10. [g] A, prepared by indirect method. See Experimental Section. B, aging the crystalline dialkylborane in THF at −35 °C. C, selective crystallization of the dialkylborane from EE. D, aging the crystalline dialkylborane in THF at 0 °C. E, prepared by direct hydroboration using $IpcBH_2$.[10]

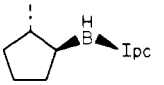
especially promising for chiral synthesis proceeding through boron intermediates. Recently the dialkylboranes, obtained by hydroboration of prochiral olefins with $IpcBH_2$, were converted into valuable synthetic intermediates and were utilized in reactions involving the formation of asymmetric carbon–carbon bonds.[15] The intermediate dialkylboranes are potential chiral hydroborating agents, a possibility not yet explored. These promising applications make it desirable to have available isopinocampheylalkylboranes (IpcRBH)[4] in high optical purity (if possible, purities approaching 100%). Since most of the IpcRBH reaction products are solids, we undertook to see whether selective crystallization of the dialkylboranes might provide a convenient route for upgrading the optical purity of the IpcRBH intermediates.

Results and Discussion

Monoisopinocampheylborane reacts readily with 1-methyl-1-cyclopentene to give a dialkylborane containing the *trans*-2-methylcyclopentyl group of 66% ee.[8] The dialkylborane is a solid and in part crystallizes from the reaction mixture. We established that the crystalline dialkylborane was optically more pure than the dialkylborane in the supernatant solution. Encouraged by this finding, we studied this reaction in selected solvents [tetrahydrofuran (THF), diglyme (DG), ethyl ether (EE), and *n*-pentane] in order to find the most favorable solvent for selective crystallization of the dialkylborane.

In this study we consistently used monoisopinocampheylborane (100% ee) from 91.6% ee (+)-α-pinene. A stock solution of monoisopinocampheylborane in EE was prepared by the reaction of TMED·$2BH_2Ipc$[9] with boron trifluoride etherate (EE·BF_3) in EE. The EE solution of $IpcBH_2$ thus prepared can be stored without any isomerization or loss of hydride activity for at least 20 days at 0 °C. The ethyl ether was evaporated at 12 mmHg and the neat $IpcBH_2$ was dissolved to obtain a standard solution of $IpcBH_2$ in the other solvents (THF, DG, and *n*-pentane). Among the solvents studied, EE emerged as the best solvent to achieve the selective crystallization of optically pure IpcRBH.

For example, 1-methylcyclopentene was added to $IpcBH_2$ in EE at −35 °C and left at −35 °C, without stirring, for 12 h. The isopinocampheyl-*trans*-(2-methylcyclopentyl)borane (**5**) crystallized in a well-defined form in 65% yield. The crystalline dialkylborane on oxidation produced *trans*-2-methylcyclopentanol same alcohol in 12% optical purity. It is evident that the major isomer becomes incorporated in the crystalline solid, leaving the minor isomer in solution.



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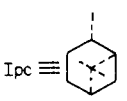
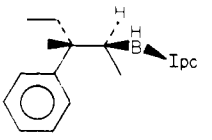


Hydroboration of (*Z*)-3-phenyl-2-pentene with $IpcBH_2$ in EE gave the dialkylborane isopinocampheyl(3-phenyl-2-pentyl)borane (**6**). This dialkylborane behaved differently. Optically impure material crystallized as an amorphous solid, leaving the optically pure erythro isomer in solution (77%).



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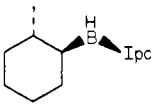
Under similar experimental conditions, 1-methylcyclohexene gave the crystalline isopinocampheyl-trans-(2-methylcyclohexyl)borane (**7**) of 89% ee in 85% isolated yield. The optical purity of the dialkylborane was further upgraded by suspending the solid dialkylborane in THF and allowing the reaction mixture to age for 12 h at 0 °C. The crystalline IpcRBH (**7**) thus obtained was ≥99% optically pure.



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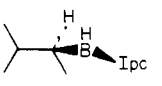
Similary, hydroboration of 2-methyl-2-butene gave isopinocampheyl(3-methyl-2-butyl)borane (**8**) of 89% ee in 65% isolated yield. The crystalline dialkylborane was suspended in THF and was allowed to age for 12 h at -35 °C. The solid IpcRBH (**8**) thus obtained was 100% optically pure. The optical purity of all of these dialkylboranes was determined by measuring the rotations of the alcohols obtained following alkaline hydrogen peroxide oxidation and comparing the values with the maximum reported rotations.



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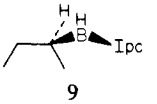
Preparation of isopinocampheyl-2-butylborane (**9**) of high optical purity posed a problem. Hydroboration of *trans*-2-butene



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with $IpcBH_2$ at -35 °C gave the corresponding crystalline dialkylborane of 79% ee in 85% isolated yield. All attempts to upgrade its optical purity were futile. However, we successfully

(15) Brown, H. C.; Jadhav, P. K.; Desai, M. C. *J. Am. Chem. Soc.* **1982**, *104*, 6844.

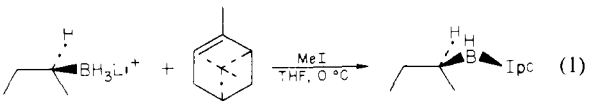
(16) Singaram, B.; Cole, T. E.; Brown, H. C., to be submitted for publication.

Table II. Dimethyl Alkylboronates of High Optical Purity

boronic esters $RB(OMe)_2$	yield, %	bp, °C (mmHg)	$[\alpha]^{23}_D$ (*c*, THF)	% ee[a]	config of $RB(OMe)_2$	^{11}B NMR chemical shift (δ)[d]
dimethyl 2-butylboronate	71	38 (30)	+9.1° (11.7)	97[b]	*S*	+31.3
dimethyl (3-methyl-2-butyl)boronate	69	42–44 (15)	+7.1° (9.9)	99	*S*	+31.5
dimethyl *trans*-(2-methylcyclopentyl)boronate	70	72–74 (16)	+51.5° (17.1)	≥99	1*S*,2*S*	+31.2
dimethyl *trans*-(2-methylcyclohexyl)boronate	63	80–81 (15)	+41.5° (15.4)	99	1*S*,2*S*	+30.7
dimethyl *trans*-(2-phenylcyclopentyl)boronate	66	85 (0.05)	+32.9° (7.8)	100[c]	1*S*,2*S*	+31.5
dimethyl *erythro*-(3-phenyl-2-pentyl)boronate	68	90–92 (0.02)	−8.5° (5.5)	100	2*S*,3*R*	+31.7

[a] See footnote *a* in Table I. [b] The result taken from an earlier study.[13] [c] Brown, H. C.; Desai, M. C., unpublished results. [d] Relative to $EE{\cdot}BF_3$ (δ 0).

synthesized this dialkylborane by an indirect method. (*S*)-(+)-Dimethyl 2-butylboronate[13] of 97% ee was converted to lithium 2-butylborohydride with use of lithium aluminum hydride.[16] This borohydride, in the presence of 1 equiv of (+)-α-pinene (100% ee), reacted with methyl iodide to afford crystalline IpcRBH (**9**) of 99% optical purity (eq 1). The results are summarized in Table I.



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Treatment of these optically pure dialkylboranes with acetaldehyde[13] at 25 °C liberated α-pinene quantitatively and provided the corresponding diethyl alkylboronates in high optical purity. These intermediates were readily separated from α-pinene by extraction with aqueous sodium hydroxide and converted by reesterification to dimethyl alkylboronates of high optical purity (Table II).

Implications

The present procedure provides a simple method for resolving *sym*-diisopinocampheyldialkylboranes, readily synthesized by hydroboration, into products of essentially 100% ee. The resolution procedure does not require the preparation of intermediates which are then treated with optically active acids or bases, as in the usual resolutions. Moreover, the characteristics of the reaction make it applicable to relatively large scale preparations.

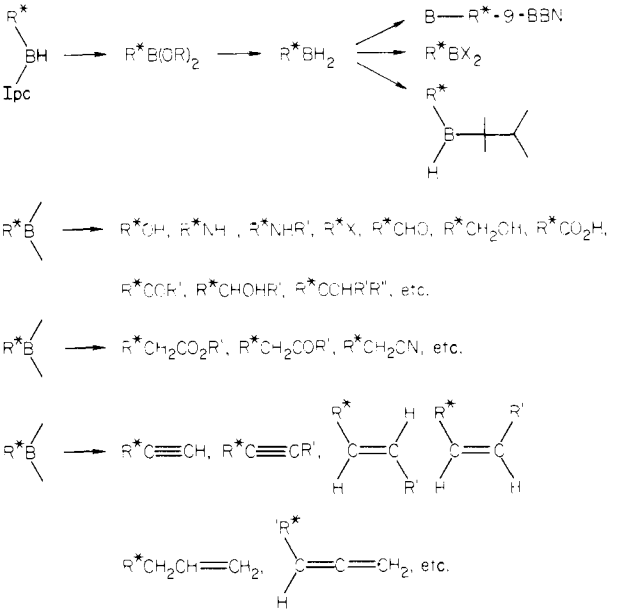
Both (+)- and (-)-α-pinenes are readily available. Consequently, both enantiomers are readily synthesized.

In this development, the resolution has been achieved at the organoborane stage. It is now possible to transfer alkyl groups from boron to essentially all other elements of synthetic interest without observable racemization.[5,15,17] Consider the scope of chiral syntheses which this development opens up.

We are rapidly exploring this new entry into the simple synthesis of chiral derivatives of essentially 100% ee.

Conclusion

The present method provides a convenient procedure for the synthesis of various optically pure isopinocampheylalkylboranes. The isopinocampheyl group is used for optical induction as well as for upgrading the dialkylborane reaction products of lower optical purity. The dialkylboranes are readily converted into the corresponding alkylboronic esters and acids of high enantiomeric purity. These are valuable synthetic intermediates. Oxidation of the dialkylboranes provides the corresponding alcohols of high optical purity. Incidently, the alcohols reported herein were previously prepared by the conventional, relatively tedious route involving resolution of the brucine salts of the corresponding phthalate half-esters. The present method provides a far simpler route to these alcohols in high optical purity. The chiral auxiliary, α-pinene, can be readily recovered and recycled, making this process exceptionally efficient. The chiral dialkylboranes obtained by this procedure are potential asymmetric hydroborating agents. The organyl-boron moiety makes possible a simple synthetic route



(R* is a chiral organic group, both (+) and (−))

to a host of chiral derivatives in essentially 100% ee. We continue to actively explore such asymmetric syntheses via these chiral organoborane intermediates.

Experimental Section

All operations were carried out under a nitrogen atmosphere, with oven-dried glassware.[17] GC analyses were carried out with a Hewlett-Packard 5750 chromatograph using (a) 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 GC, 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. ^{11}B NMR were recorded on a Varian FT-80A instrument. The chemical shifts are in δ relative to $EE{\cdot}BF_3$. Optical rotations were measured on a Rudolph polarimeter Autopol III.

Materials. The bis adduct of monoisopinocampheylborane with tetramethylethylenediamine ($TMED{\cdot}2BH_2Ipc$) was prepared from (+)-α-pinene of 91.6% ee according to the reported procedure.[9] Anhydrous ethyl ether (EE) was available from Mallinckrodt, Inc. and used directly. The alkenes used for this study were commerical products of the highest purity available and were used directly. Lithium aluminum hydride in EE was purachased from Aldrich Chemical Co.

Generation of Monoisopinocampheylborane from $TMED{\cdot}2BH_2Ipc$ in EE. A 250-mL flask with a magnetic stirring bar and septum was charged with 20.85 g of $TMED{\cdot}2BH_2Ipc$ (50 mmol) and EE (67.2 mL). While the slurry was stirred at 25 °C, 12 mL (98 mmol) of $EE{\cdot}BF_3$ was added dropwise, and the reaction mixture was allowed to stir at 25 °C for 2 h. Meanwhile, a 250-mL flask with a septum inlet, magnetic stirring bar, and filtration chamber was assembled under dry nitrogen and cooled to 25 °C. The resulting slurry from the reaction flask was transferred under nitrogen to the filtration chamber. The solid $TMED{\cdot}2BF_3$ was washed with EE (2 × 36 mL). The combined filtrate was analyzed for $IpcBH_2$ by hydrolysis with 1:1:1 glycerol, water, and THF as the hydrolyzing mixture and found to be 0.723 M: 110 mL (79.5 mmol); 79% yield; ^{11}B NMR (decoupled) +22.4 (singlet); $[\alpha]^{23}_D$-39.93 (*c* 11.6, EE). The standard solution of $IpcBH_2$[4] in EE can be stored at 0 °C for at least 20 days without any isomerization or loss of hydride activity.

(17) For standard procedures for these transformations, see: Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975.

Isopinocampheyl-(1*S*,2*S*)-*trans*-(2-methylcyclopentyl)borane (5). A 50-mL centrifuge vial fitted with a rubber septum and a magnetic stirring bar was charged with 34.6 mL of (−)-IpcBH$_2$ (100% ee) in EE (0.723 M, 25 mmol) and cooled to -35 °C. 1-Methylcyclopentene (3.2 mL, 30 mmol) was added to it. The reactants were mixed together well and the vial was left at -35 °C, without stirring, for 12 h. The supernatant solution was decanted with use of a double-ended needle. The crystalline isopinocampheyl-(1S,2S)-*trans*-(2-methylcyclopentyl)borane (**5**) was washed with cold (-35 °C) EE (2 × 5 mL) and dried at 25 °C under reduced pressure (12 mmHg), 3.79 g (16.3 mmol, 65% yield). The dialkylborane was methanolyzed, oxidized, and worked up following the literature procedure.[10] The (1*S*,2*S*)-*trans*-2-methylcyclopentanol obtained was purified by using column d to furnish a GC-pure material: $[\alpha]^{23}_D$ +46.8 (neat), 100% ee.

Isopinocampheyl-(2*S*,3*R*)-(3-phenyl-2-pentyl)borane (6). with the usual experimental setup, 4 mL (25 mmol) of (*Z*)-3-phenyl-2-pentene was added to 27.2 mL (25 mmol) of 0.92 M IpcBH$_2$ in EE at -35 °C. The final molarity of the reaction mixture was 0.8 M. The reactants were mixed well and allowed to stand at -35 °C, without stirring, for 12 h. The impure dialkylborane crystallized from the solution. The supernatant solution containing the optically pure dialkylborane (**6**) was decanted. The solid was washed with cold EE (2 × 3 mL) and dried, 1.68 g (5.7 mmol, 22.8% yield). The supernatant solution was methanolyzed, oxidized, and worked up according to the published procedure.[10] The (2*S*,3*S*)-3-phenyl-2-pentanol obtained was purified on column d to provide a GC-pure sample: $[\alpha]^{23}_D$ +24.9 (*c* 4, C_2H_5OH), 100% ee.

Isopinocampheyl-(1*S*,2*S*)-*trans*-(2-methylcyclohexyl)borane (7). With the usual experimental setup, 3.5 mL (30 mmol) of 1-methylcyclohexene was added to 34.6 mL (25 mmol) of 0.723 M IpcBH$_2$ in EE at -35 °C. The reactants were mixed together well and left at -35 °C, without stirring, for 12 h. The crystalline dialkylborane was isolated, washed with cold (-35 °C) EE (2 × 5 mL), and dried, 5.24 g (21.3 mmol, 85% yield). The dialkylborane was 89% optically pure. It was suspended in 16 mL of THF so as to give a 1.0 M slurry and allowed to age for 12 h at 0 °C. The supernatant solution was decanted with use of a double-ended needle. The solid isopinocampheyl-(1*S*,2*S*)-trans-(2-methylcyclohexyl)borane (**7**) was washed with cold (0 °C) EE (2 × 3 mL) and dried, 4.66 g (18.9 mmol, 75% yield). The dialkylborane was methanolyzed, oxidized, and worked up following the literature procedure.[10] The (1*S*,2*S*)-*trans*-2-methylcyclohexanol obtained was purified on column d to furnish a GC-pure sample: $[\alpha]^{23}_D$ +42.9 (± 0.1) (*c* 1, MeOH), ≥99% ee.

Isopinocampheyl-(*S*)-(3-methyl-2-butyl)borane (8). With the usual experimental setup, 3.2 mL (30 mmol) of 2-methyl-2-butene was added to 34.6 mL (25 mmol) of 0.723 M IpcBH$_2$ in EE at −35 °C. The reactants were mixed together and left at −35 °C, without stirring, for 12 h. The crystalline dialkylborane was isolated, washed with cold (−35 °C) EE (2 × 3 mL), and dried, 3.97 g (18 mmol, 72% yield). The dialkylborane was 89% optically pure. It was cooled to −35 °C, and 18.5 mL of THF was added to it so as to give a 0.8 M slurry. The reaction mixture was then allowed to age for 12 h at −35 °C. The supernatant solution was decanted with use of a double-ended needle. The solid isopinocampheyl-(*S*)-(3-methyl-2-butyl)borane (**8**) was washed with cold (−35 °C) EE (2 × 2 mL) and dried, 2.82 g (12.8 mmol, 51% yield). The 3-methyl-2-butanol, obtained following alkaline hydrogen peroxide oxidation,[10] was purified on column d to give a GC-pure material: $[a]^{23}_D$ +4.97 ± 0.01 (neat), 100% ee.

Isopinocampheyl-(*S*)-2-butylborane (9). A 50-mL centrifuge vial with a magnetic stirring bar and septum was charged with lithium (*S*)-2-butylborohydride (25 mmol)[16] in 15 mL EE. (+)-α-Pinene (100% ee, 25 mmol) and 6.2 mL of THF were added to it, and the mixture was cooled to 0 °C. Methyl iodide (2 mL, 30 mmol) was added dropwise with stirring. The reaction mixture was stirred for 5 min, and then the stirring was stopped. The dialkylborane crystallized from the solution. It was left at 0 °C for 3 h, and then the supernatant solution was decanted with use of a double-ended needle. The crystalline isopinocampheyl-(*S*)-2-butylborane (**9**) was washed with cold (0 °C) EE (2 × 4 mL) and dried, 4.02 g (19.5 mmol, 78% yield). The 2-butanol, obtained following oxidation,[10] was purified on column d and column c to furnish a GC-pure sample: α^{25}_D +5.348 (neat, *l* 0.5), ≥99% ee.

Preparation of Dimethyl Alkylboronate Esters of High Optical Purity. The following procedure for the preparation of (1*S*,2*S*)-(+)-dimethyl *trans*-(2-methylcyclopentyl)boronate is typical. Acetaldehyde (4 mL, 75 mmol) was added to a suspension of the dialkylborane (5) (25 mmol) in 20 mL of EE at 0 °C. After the vigorous initial reaction, 2 mL of acetaldehyde was added and the reaction mixture was stirred at 25 °C for 6 h. Water (5 mL) was added, and stirring was continued for 0.5 h. Excess acetaldehyde was evaporated (25 °C, 12 mmHg, 1 h), and pentane (30 mL) was added. The boronic acid was extracted with 3 M NaOH (3 × 15 mL) in a separating funnel. The combined aqueous phase was cooled to 0 °C, acidified with 3 M HCl, extracted with EE (3 × 25 mL), and dried over anhydrous $MgSO_4$. Ethyl ether was evaporated, and the boronic acid was reesterified with methanol following the published procedure.[18] The ester was purified by distillation (2.73 g, 70% yield): bp 72−74 °C (16 mmHg); $[\alpha]^{24}_D$ +51.56 (*c* 17.1 THF); ^{11}B NMR +31.2 (singlet). Oxidation of the ester with alkaline hydrogen peroxide gave (1*S*,2*S*)-(+)-*trans*-2-methylcyclopentanol, which exhibited $[\alpha]^{23}_D$ +46.6 (*c* 1, MeOH), suggesting ≥99% ee for the ester.

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