Chiral Synthesis via Organoboranes. 3. Conversion of Boronic Esters of Essentially 100% Optical Purity to Aldehydes, Acids, and Homologated Alcohols of Very High Enantiomeric Purities

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Abstract: 2-Alkyl-1,3,2-dioxaborinanes, $R^*BO_2(CH_2)_3$, of essentially 100% optical purity can be prepared by the asymmetric hydroboration of readily available prochiral olefins with subsequent removal of the chiral auxiliary. Homologation of 2-alkyl-1,3,2-dioxaborinanes to α-methoxyalkyl derivatives, $R^*CH(OMe)BO_2(CH_2)_3$, of essentially 100% ee is achieved by reaction with LiCH(OMe)SPh, followed by treatment with $HgCl_2$. The intermediates, $R^*CH(OMe)BO_2(CH_2)_3$, are smoothly oxidized with H_2O_2 in a pH 8 buffer to give the corresponding aldehydes, R^*CHO, in very high optical purity. Consequently, it is now possible to synthesize a wide variety of optically active aldehydes, R^*CHO, either (+) or (−), in essentially 100% ee. The aldehydes can be reduced and oxidized by using borane–methyl sulfide (BMS) and aqueous chromic acid, respectively. Consequently, β-chiral alcohols, R^*CH_2OH, and α-chiral acids, R^*CO_2H, both of very high optical purity, are also available by this method.
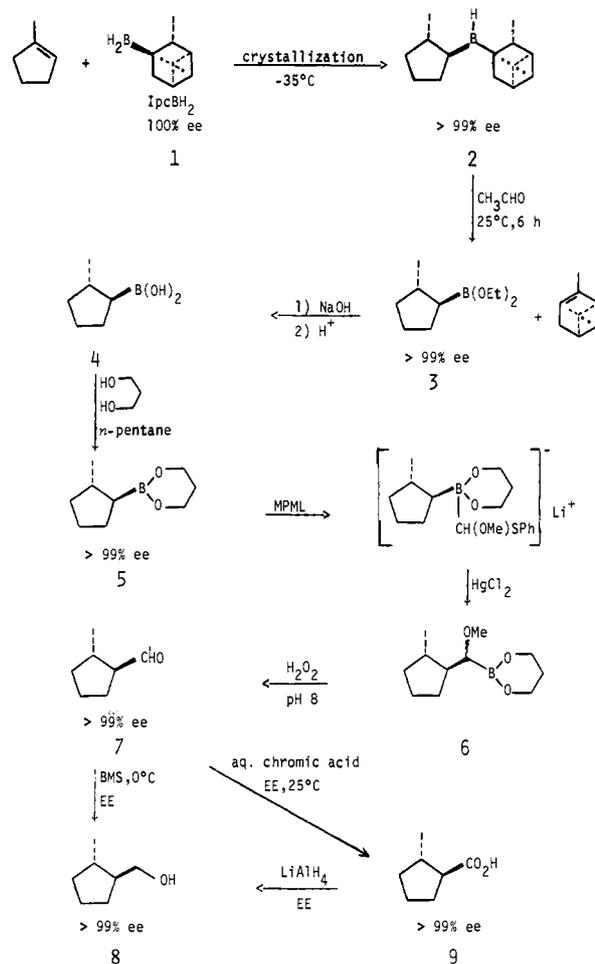
Optically active aldehydes bearing a chiral center at the α-position are important building blocks in organic synthesis.[2] A promising method among others for preparing these aldehydes is the enantioselective α-alkylation of aldehydes through chiral hydrazone derivatives[3] or chiral imines.[4] A highly enantioselective synthesis of 2-phenyl- and 2-vinylcycloalkanecarboxaldehydes has also been achieved by Michael addition of Grignard reagents to chiral imine derivatives of 1-cycloalkenecarboxaldehydes.[5] On the other hand, asymmetric hydroformylation of alkenes by a chiral Rh catalyst has not yet achieved high enantioselectivity.[6]

Boranes derived from α-pinene exhibit great potential for converting commercially available prochiral olefins into optically active derivatives. A recent development offers promise of providing both chiral organoborane intermediates and all organic compounds containing a chiral center in essentially 100% optical purity in both (+)- and (−)-isomers.[7] Thus, asymmetric hydroboration of prochiral olefins with monoisopinocampheylborane, $IpcBH_2$ (**1**), in the molar ratio of 1:1, followed by crystallization, provides the chiral isopinocampheylalkylboranes, IpcR*BH (e.g., **2**), in essentially 100% optical purity. Treatment of these dialkylboranes with acetaldehyde under mild conditions results in the selective, facile elimination of the 3-pinanyl group, providing the corresponding boronic ester (e.g., **3**) in very high optical purity (Scheme I). Recently this reaction has been applied for the synthesis of various monoalkylboranes and borohydrides of very high optical purity.[8]

Matteson and his co-workers have also described a highly promising alternative route to optically active boronic esters.[9]

Chiral alkylboronic acids and esters are exceptionally promising intermediates for carbon–carbon bond-forming reactions.[9,10] These reactions are especially promising for chiral synthesis proceeding through boron intermediates. We have reported recently an effective means of converting alkylboronic esters into aldehydes through the intermediate formation of α-methoxy de-

Scheme I

rivatives by successive treatment with methoxy(phenylthio)-methyllithium, LiCH(OMe)SPh (MPML), and $HgCl_2$[10] (e.g., **5**, **6**).

With the ready availability of alkylboronic esters of very high optical purities, we applied the above reaction to these essentially optically pure boronic esters to test the possibility of synthesizing α-chiral aldehydes of comparably high optical purities.

Results and Discussion

The optically active 2-alkyl-1,3,2-dioxaborinanes were prepared by esterification[11] of the corresponding boronic acids with 1,3-

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Table I. 2-Alkyl-1,3,2-dioxaborinanes of High Optical Purity[a]

boronic esters R*BO$_2$(CH$_2$)$_3$ R*	yield, % (isolated)	bp, °C (mmHg)	$[\alpha]^{23}$D, deg (c, THF)	% ee[b]	config of R*BO$_2$(CH$_2$)$_3$
1-methylpropyl	80	70–72 (20)	−4.8 ± 0.02 (6)	99[c]	R
1-ethylbutyl	85	92–94 (15)	+0.87 ± 0.012 (15)	>99.7[d,e]	R
1,2-dimethylpropyl	75	90–92 (17)	+5.71 ± 0.01 (9)	>99[c,f]	S
trans-2-methylcyclopentyl	80	108–110 (15)	+37.84 ± 0.02 (9)	>99.6[c,e]	1S,2S
trans-2-methylcyclohexyl	85	80–82 (2.5)	+24.16 ± 0.02 (7)	>99[c,e]	1S,2S
trans-2-phenylcyclopentyl	80	104–106 (0.01)	+80.37 ± 0.02 (9)	>99.7[g]	1S,2S

[a] (+)-α-Pinene was used for asymmetric hydroboration. [b] Optical purity was determined by measuring the rotation of the alcohols obtained on oxidation and comparing the value with maximum reported rotations (see footnotes c–g). [c] See ref 7. [d] Oxidation of the ester gave 3-hexanol, which exhibited $[\alpha]^{23}$D −7.53° ± 0.04 (neat, *l* 1). See ref 20. [e] Analyzed by ^{31}P NMR. [f] Analyzed by ^{19}F NMR. [g] See ref 21.

Table II. α-Chiral Aldehydes of Very High Optical Purity

R*CHO	yield, % (isolated)	bp, °C (mmHg)	$[\alpha]^{23}$D, deg	% ee[a]	config of R*CHO
2-methyl-1-butanal	60	80–82 (745)	−33.2 ± 0.2 (c 2, acetone)	99[b]	R
2-ethyl-1-pentanal	75	78–80 (110)	−5.54 ± 0.04 (c 6, CHCl$_3$)	>99[c]	R
2,3-dimethyl-1-butanal	70	68–70 (160)	+71.4 ± 0.1 (neat)	99[d]	S
trans-2-methylcyclopentanecarboxaldehyde	70	88–90 (110)	+30.57 ± 0.04 (c 4, benzene)	>99[c]	1S,2S
trans-2-methylcyclohexanecarboxaldehyde	80	72–74 (20)	+35.08 ± 0.02 (c 6, CHCl$_3$)	99[c]	1S,2S
trans-2-phenylcyclopentanecarboxaldehyde	80	92–94 (0.05)	+82.97 ± 0.2 (c 1, benzene)	>99[e]	1S,2S

[a] Optical purity was determined by measuring the rotation of the alcohols obtained on reduction and comparing the value with the maximum reported rotations.[22] See Table III. [b] Banno, K.; Mukaiyama, T. *Chem. Lett.* **1976**, 279; $[\alpha]^{20}$D −31.4° (c 2.73, acetone) for (R)-2-methyl-1-butanal. [c] Not previously reported. [d] Rsuda, K.; Kishida, Y.; Hayatsu, R. *J. Am. Chem. Soc.* **1960**, 82, 3396; $[\alpha]^{25}$D −65.2° (neat) for (R)-2,3-dimethyl-1-butanal. [e] See ref 5. These authors predicted a maximum rotation of $[\alpha]^{20}$D −76.8° (benzene) for (1S,2S)-*trans*-2-phenylcyclopentanecarboxaldehyde.

Table III. β-Chiral Alcohols of Very High Optical Purity

| R*CH$_2$OH	yield, % (isolated)	bp, °C (mmHg)	$[\alpha]^{23}$D, deg	% ee[b]	config of R*CH$_2$OH
2-methyl-1-butanol	90	126–127 (750)	+4.8 (neat, *l* 1)[a]	99[c]	R
2-ethyl-1-pentanol	95	78–80 (20)	−3.36 ± 0.01 (neat, *l* 1)	>99[d,e]	R
2,3-dimethyl-1-butanol	94	64–66 (25)	+4.8 (neat, *l* 1)[a]	99[d,f]	S
trans-2-methylcyclopentylmethanol	95	110–112 (80)	+54.9 ± 0.1 (c 1, MeOH)	>99[d,g]	1S,2S
trans-2-methylcyclohexylmethanol	95	106–108 (20)	+41.7 ± 0.1 (c 1, MeOH)	99[d,h]	1S,2S
trans-2-phenylcyclopentylmethanol	95	92–94 (0.01)	+52.3 ± 0.1 (c 1, MeOH)	>99[d,g]	1S,2S

[a] Observed rotation. [b] On the basis of maximum reported rotations (see footnotes c–h). [c] Vogler, K.; Chopard-dit-Jean, L. H. *Helv. Chim. Acta* **1960**, 43, 279; α^{23}D −4.84° (neat, *l* 1) for (S)-2-methyl-1-butanol. [d] See ref 22. [e] Levene, P. A.; Rothen, A.; Meyer, G. M.; Kuna, M. *J. Biol. Chem.* **1936**, 115, 401. These authors predicted a maximum rotation of $[\alpha]^{25}_{5876}$ +3.34° (neat, *l* 1) for (S)-2-ethyl-1-pentanol. [f] Rsuda, K.; Kishida, Y.; Hayatsu, R. *J. Am. Chem. Soc.* **1960**, 82, 3396; α^{23}D −4.52° (neat, *l* 1) for (R)-2,3-dimethyl-1-butanol. [g] Analyzed by ^{31}P NMR. [h] Analyzed by ^{19}F NMR.

propanediol (e.g., **4 → 5**). In this study, we prepared the optically active boronic acids using diisopinocampheylborane, Ipc$_2$BH (>-99% ee),[12] and IpcBH$_2$ (100% ee),[13] prepared from (+)-α-pinene. The optical purity of all of these 2-alkyl-1,3,2-dioxaborinanes was determined by measuring the rotations of the alcohols obtained following alkaline hydrogen peroxide oxidation and comparing the values with the maximum reported rotations. The enantiomeric excess of most of these alcohols was also determined by ^{19}F NMR of their MTPA esters[14] and/or by ^{31}P NMR with use of the Anderson and Shapiro reagent[15] (Table I).[16]

Methoxymethyl phenyl sulfide[17] was lithiated with s-BuLi at −50 °C.[10] To the thus generated MPML, 1 equiv of (1S',2S')-(+)-2-(*trans*-2'-methylcyclopentyl)-1,3,2-dioxaborinane (**5**) of >99% ee was added and the mixture allowed to come to 25 °C. The alkyl migration was readily induced by adding mercury(II) chloride to give the α-methoxy derivative. Oxidation of the α-methoxy derivative with H$_2$O$_2$ proceeded smoothly in a pH 8 phosphate buffer medium, being complete in 1.5 h at 25 °C. The (1S,2S)-(+)-*trans*-2-methylcyclopentanecarboxaldehyde

(**7**) of >99% ee was isolated by steam distillation and purified by distillation.

When the above procedure was used, the following α-chiral aldehydes were prepared in very high optical purities (Table II).

99% ee   > 99% ee   99% ee

> 99% ee   99% ee   > 99% ee
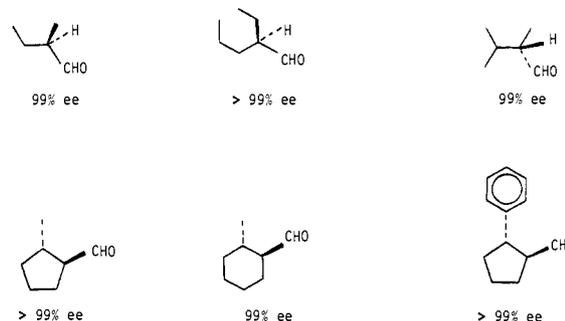
These aldehydes were reduced with use of borane–methyl sulfide (BMS) to the corresponding β-chiral alcohols without any detectable racemization or epimerization (e.g., **8**). The optical purity of these alcohols was determined by ^{19}F NMR of their MTPA esters and also by ^{31}P NMR with use of the Anderson and Shapiro reagent.[16] The optical purity and absolute configuration of these β-chiral alcohols were also determined by measuring the rotations and comparing the values with the maximum reported rotations (Table III). From these data, the optical purities of the corresponding aldehydes were determined. It should be pointed out that β-chiral alcohols, such as 2-methyl-1-butanol and 2,3-di-

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(16) Racemic alcohols give two signals, which are well resolved.
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methyl-1-butanol, are difficult to prepare in high optical purity by asymmetric hydroboration of the corresponding alkenes[18] (eq 1).

$$R = H \quad \sim 21\% \text{ ee}$$
$$R = CH_3 \quad \sim 30\% \text{ ee}$$
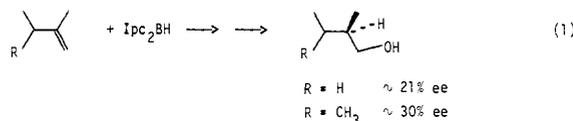
We also tested the possibility of oxidizing optically active aldehydes to optically active carboxylic acids by the two-phase chromic acid procedure.[19] Indeed, (1*S*,2*S*)-*trans*-2-methylcyclopentanecarboxylic acid (9) was obtained in >99% ee. The (1*S*,2*R*)-isomer could not be detected by gas chromatographic analyses on a 50-m Methylsilicone capillary column or on a 20-m Carbowax 20M capillary column.[20] The ^{1}H NMR (470 MHz) spectrum of 9 also showed the absence of the (1*S*,2*R*)-isomer. The acid was reduced, using LiAlH$_4$, to the alcohol 8, which exhibited $[\alpha]^{23}_D$ +53.4° (*c* 1, MeOH), suggesting epimerization during the reduction. No attempt was made to minimize the epimerization.

Conclusion

The present study provides a convenient and simple procedure for the synthesis of a wide variety of α-chiral aldehydes of essentially 100% ee. It also provides a method for synthesizing optically active aldehydes that cannot be prepared by currently available procedures.[3-5] Both (+)- and (−)-α-pinenes are readily available. Consequently, both enantiomers are readily synthesized.

Another unique advantage is the ability to correlate the absolute configuration of the aldehydes, R*CHO, to those of the corresponding alcohols R*OH, R*CH$_2$OH, and the acids, R*CO$_2$H (eq 2).
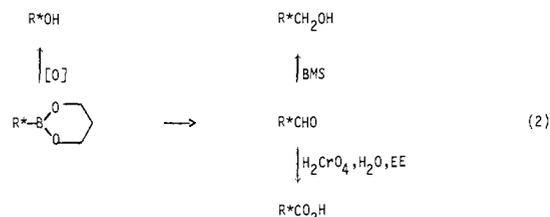
Additionally, trisubstituted alkenes can be hydroborated regio- and stereoselectively and two chiral centers may be generated in one step, then incorporated into the α- and β-positions of the aldehydes (eq 3). This aldehyde synthesis from alkylboronic
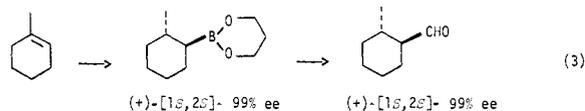
esters, when combined with the asymmetric hydroboration reaction, provides a new method for introducing aldehyde functionality into olefins in a regio-, stereo-, and enantioselective manner (eq 4). Consequently, it is now possible to synthesize
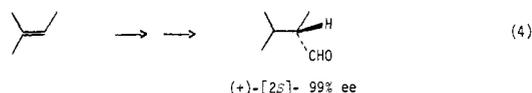
a wide variety of optically active aldehydes, either (+) or (−), in essentially 100% ee. Since these aldehydes can be reduced and oxidized, the corresponding β-chiral alcohols and α-chiral acids are also available by this method.

Experimental Section

All spectral data were obtained by the same instruments reported previously.[10] Chemical shift values are given in ppm relative to Me$_4$Si in ^{1}H and ^{13}C NMR and relative to EE·BF$_3$ in ^{11}B NMR. Purification

of solvents, preparation of reagents, and general reaction equipment have also been described previously.[7,10] In all cases, IpcBH$_2$[13] or Ipc$_2$BH[12] derived from (+)-α-pinene was used for the asymmetric hydroboration. Optical rotations were measured on a Rudolph polarimeter Autopol III. Capillary GC analyses were performed on a Hewlett-Packard 5890 instrument.

Preparation of 2-Alkyl-1,3,2-dioxaborinanes of Very High Optical Purity. General Procedure. Optically active boronic acid (50 mmol)[7] was stirred with *n*-pentane (50 mL) and 1,3-propanediol (4.34 g, 60 mmol) at 25 °C. The boronic acid gradually dissolved (0.5 h) and water separated.[11] The reaction mixture was transferred to a separatory funnel. The reaction flask was washed with *n*-pentane (20 mL), and the washings were transferred to the separatory funnel. The reaction mixture was shaken for a few minutes, and the lower water layer was removed. The *n*-pentane layer was dried over anhydrous MgSO$_4$, and upon removal of the solvent, an almost pure ester was obtained. The 2-alkyl-1,3,2-dioxaborinanes were purified by distillation (Table I).

(*R*)-(−)-2-(1-Methylpropyl)-1,3,2-dioxaborinane was prepared from (*R*)-1-methylpropylboronic acid of 99% ee.[21] ^{11}B NMR +31.2 (singlet); ^{1}H NMR (CDCl$_3$) δ 0.4–1.1 (m, 7 H), 1.1–1.55 (m, 3 H), 1.9 (p, *J* = 7 Hz, 2 H), 3.97 (t, *J* = 7 Hz, 4 H). Oxidation of the ester with alkaline hydrogen peroxide gave (2*R*)-(−)-2-butanol which exhibited α^{23}_D −5.347° (neat, *l* 0.5), suggesting 99% ee for the ester.[7]

(*R*)-(+)-2-(1-Ethylbutyl)-1,3,2-dioxaborinane was prepared from (*R*)-3-hexylboronic acid of >99% ee.[21] ^{11}B NMR +31.3 (singlet); ^{1}H NMR (CDCl$_3$) δ 0.4–1.0 (m, 7 H), 1.0–1.8 (m, 6 H), 1.95 (p, *J* = 6 Hz, 2 H), 3.98 (t, *J* = 6 Hz, 4 H). Oxidation of the ester with alkaline hydrogen peroxide gave (3*R*)-(−)-3-hexanol, which exhibited $[\alpha]^{23}_D$ −7.53 ± 0.04 (neat, *l* 1.0), suggesting >99% ee for the ester.[21] The 3-hexanol thus obtained was derivatized with use of the Anderson and Shapiro reagent. The ^{31}P NMR spectrum showed only a single signal.[16]

(*S*)-(+)-2-(1,2-Dimethylpropyl)-1,3,2-dioxaborinane was prepared from (*S*)-3-methyl-2-butylboronic acid of >99% ee.[7] ^{11}B NMR +31.0 (singlet); ^{1}H NMR (CDCl$_3$) δ 0.87 (d, *J* = 7 Hz, 6 H), 1.5–2.0 (m, 1 H), 1.9 (p, *J* = 6 Hz, 2 H), 3.94 (t, *J* = 6 Hz, 4 H). Oxidation of the ester with alkaline hydrogen peroxide gave (2*S*)-(+)-3-methyl-2-butanol, which exhibited $[\alpha]^{23}_D$ +4.95° (neat, *l* 1.0), suggesting >99% ee for the ester.[7] The Mosher ester of the alcohol showed on ^{19}F NMR analysis a single peak.[16]

(1'*S*,2'*S*)-(+)-2-(*trans*-2'-Methylcyclopentyl)-1,3,2-dioxaborinane (5) was prepared from (1*S*,2*S*)-*trans*-2-methylcyclopentylboronic acid (4) of >99% ee.[7] ^{11}B NMR +31.4 (singlet); ^{1}H NMR (CDCl$_3$) δ 0.4–0.8 (m, 1 H), 1.0 (d, *J* = 7 Hz, 3 H), 1.3–2.1 (m, 8 H), 3.98 (t, *J* = 6 Hz, 4 H). The ester was oxidized with alkaline hydrogen peroxide. The product alcohol, (1*S*,2*S*)-(+)-*trans*-2-≤methylcyclopentanol, exhibited $[\alpha]^{23}_D$ +46.7° (*c* 1, MeOH), suggesting >99% ee for the ester.[7] The above alcohol was derivatized with use of the Anderson and Shapiro reagent. The ^{31}P NMR analysis showed only a single peak.[16]

(1'*S*,2'*S*)-(+)-2-(*trans*-2'-Methylcyclohexyl)-1,3,2-dioxaborinane was prepared from (1*S*,2*S*)-*trans*-2-methylcyclohexylboronic acid of 99% ee.[7] ^{11}B NMR +30.9 (singlet); ^{1}H NMR (CDCl$_3$) δ 0.4–0.7 (m, 1 H), 0.85 (d, *J* = 6.5 Hz, 3 H), 1.1–1.8 (m, 9 H), 1.9 (p, *J* = 6 Hz, 2 H), 3.93 (t, *J* = 6 Hz, 4 H). Oxidation of the ester with alkaline hydrogen peroxide gave (1*S*,2*S*)-(+)-*trans*-2-methylcyclohexanol, which exhibited $[\alpha]^{23}_D$ +42.8° (*c* 1, MeOH), suggesting >99% ee for the ester.[7] The above alcohol was derivatized with use of the Anderson and Shapiro reagent. The ^{31}P NMR analysis showed only a single peak.[16]

(1'*S*,2'*S*)-(+)-2-(*trans*-2'-Phenylcyclopentyl)-1,3,2-dioxaborinane was prepared from (1*S*,2*S*)-*trans*-2-phenylcyclopentylboronic acid of >99% ee.[22] ^{11}B NMR +31.4 (singlet); ^{1}H NMR (CDCl$_3$) δ 0.6–0.8 (m, 1 H), 0.8–2.2 (m, 8 H), 2.67–3.27 (m, 1 H), 3.77 (t, *J* = 6 Hz, 4 H), 7.17 (m, 5 H). Oxidation of the ester gave (1*S*,2*R*)-(+)-*trans*-2-phenylcyclopentanol, which exhibited $[\alpha]^{23}_D$ +71.2° (*c* 12, EtOH), suggesting >99% ee for the ester.[22]

Preparation of Methoxymethyl Phenyl Sulfide. Thiophenol (200 mmol) was dissolved in THF (150 mL) and *n*-BuLi (200 mmol) was added to it at 25 °C with stirring. A clear solution of lithium thiophenoxide was obtained. Chloromethyl methyl ether (250 mmol) was then added with constant stirring. The reaction mixture was stirred for 3 h at 25 °C to ensure complete reaction. The volatiles, THF and *n*-hexane, were evaporated under reduced pressure (12 mmHg), and the residue was taken up in *n*-pentane (200 mL) to precipitate all of the lithium chloride. The *n*-pentane layer was decanted, the *n*-pentane was

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evaporated under reduced pressure (12 mmHg), and the residue was purified by distillation, 80% yield: bp 110–112 °C (17 mmHg); ^{1}H NMR (CDCl$_3$) δ 3.33 (s, 3 H), 4.87 (s, 2 H), 7.11–7.53 (m, 5 H).

Preparation of α-Chiral Aldehydes. General Procedure. In a 250-mL round-bottom flask, MPML was prepared by adding at −55 to −50 °C 25 mmol of *sec*-BuLi to a stirred solution of 25 mmol of methoxymethyl phenyl sulfide in 40 mL of freshly distilled THF. After 1 h of stirring at −50 °C, 25 mmol of 2-alkyl-1,3,2-dioxaborinane of 99% ee was added dropwise, but rapidly. The cold bath was allowed to reach −10 to −5 °C in ca. 2 h. Then, under a stream of nitrogen, the top of the flask was opened and 30 mmol of well-powdered HgCl$_2$ was added all at once with vigorous stirring. The flask was recapped and flushed with nitrogen. The mixture was stirred for 0.5 h while the bath temperature reached 25 °C. The bath was removed and the stirring continued for an additional 2 h. The reaction mixture was transferred, using a double-ended needle, into another flask containing 200 mL of *n*-pentane with stirring. The mixture was stirred for 12 h at 25 °C to precipitate most of the metal salts. The *n*-pentane layer was decanted, and evaporation of the *n*-pentane afforded the crude 2-(1-methoxyalkyl)-1,3,2-dioxaborinane in quantitative yield. The α-alkoxyboronic ester was dissolved in diethyl ether (40 mL), and oxidation was done by successive addition of 25 mL of pH 8 phosphate buffer and 50 mmol of hydrogen peroxide. The initial exothermic reaction was controlled by the rate of addition and by water-bath cooling to maintain the temperature below 30 °C. Stirring was continued for 1.5 h, and the organic phase was separated and subjected to steam distillation. Steam was introduced slowly until most of the solvent had been distilled out and then vigorously. The distillation was continued for 15 min. The aqueous phase of the distillate was saturated with sodium chloride and extracted with ether (2 × 20 mL). The ether extract was dried over anhydrous MgSO4 and filtered. Most of the solvent was removed by fractionation under nitrogen at atmospheric pressure with use of a 10-cm Vigreux column. The residue was then purified by distillation to afford the product aldehyde (Table II). In the case of (1*S*,2*S*)-(+)-*trans*-2-phenylcyclopentanecarboxaldehyde, the product was extracted from the nonsteam volatile portion (pot residue) and purified by distillation.

(2*R*)-(−)-2-Methyl-1-butanal. ^{1}H NMR (CDCl$_3$) δ 0.93 (t, *J* = 7 Hz, 3 H), 1.1 (d, *J* = 7 Hz, 3 H), 1.2–2.6 (m, 3 H), 9.67 (d, *J* = 2 Hz, 1 H); ^{13}C NMR (CDCl$_3$) δ 11.2, 12.7, 23.4, 47.6, 205.

(2*R*)-(−)-2-Ethyl-1-pentanal. ^{1}H NMR (CDCl$_3$) δ 0.7–1.2 (m, 6 H), 1.2–1.9 (m, 6 H), 1.9–2.5 (m, 1 H), 9.55 (d, *J* = 3 Hz, 1 H); ^{13}C NMR (CDCl$_3$) δ 11.2, 13.8, 20.1, 21.7, 30.5, 53.1, 204.8.

(2*S*)-(+)-2,3-Dimethyl-1-butanal. ^{1}H NMR (CDCl$_3$) δ 0.87–1.2 (m, 9 H), 1.6–2.6 (m, 2 H), 9.67 (d, *J* = 2 Hz, 1 H); ^{13}C NMR (CDCl$_3$) δ 9.4, 18.5, 20.4, 28.4, 52.3, 205.2.

(1*S*,2*S*)-(+)-*trans*-2-Methylcyclopentanecarboxaldehyde (7). ^{1}H NMR (CDCl$_3$) δ 1.1 (d, *J* = 7 Hz, 3 H), 1.4–2.5 (m, 8 H), 9.6 (d, *J* = 2 Hz, 1 H); ^{13}C NMR (CDCl$_3$) δ 19.5, 24.8, 26.5, 35.0, 36.2, 59.7, 203.8.

(1*S*,2*S*)-(+)-*trans*-2-Methylcyclohexanecarboxaldehyde. ^{1}H NMR (CDCl$_3$) δ 1.0 (d, *J* = 7 Hz, 3 H), 1.2–2.2 (m, 10 H), 9.6 (d, *J* = 3 Hz, 1 H); ^{13}C NMR (CDCl$_3$) δ 20.3, 24.7, 25.5, 26.0, 31.8, 34.0, 57.2, 204.7.

(1*S*,2*S*)-(+)-*trans*-2-Phenylcyclopentanecarboxaldehyde. ^{1}H NMR (CDCl$_3$) δ 1.5–2.3 (m, 6 H), 2.8 (q, *J* = 8 Hz, 1 H), 3.3 (q, *J* = 8 Hz, 1 H), 7.23 (s, 5 H), 9.62 (d, *J* = 2 Hz, 1 H); ^{13}C NmR (CDCl$_3$) δ 25.2, 26.8, 35.4, 46.7, 59.3, 126.4, 127.2, 128.6, 143.7, 202.7.

Reduction of α-Chiral Aldehydes with BMS. The 2-alkyl-1,3,2-dioxaborinanes were converted into the corresponding aldehydes on a 10-mmol scale reaction by the procedure described above. The aldehydes were steam distilled, extracted with diethyl ether, dried over anhydrous MgSO$_4$, and filtered. The filtrate was cooled to 0 °C and BMS (5 mmol) was added with stirring. Stirring was continued for 0.5 h at 0 °C and

then for 0.5 h at 25 °C. Excess hydride was quenched with water (~20 mmol). Aqueous sodium hydroxide (3 M, 10 mmol) was added and extracted with diethyl ether. The organic layer was dried, and evaporation of the solvent under reduced pressure (12 mmHg) gave the crude product. The β-chiral alcohols thus obtained were distilled and purified further by preparative GC. The optical purity of these β-chiral alcohols was determined by measuring their rotations and comparing the values with the maximum reported rotations.[2] Additionally, these alcohols were analyzed by ^{19}F NMR and/or ^{31}P NMR with use of chiral derivatizing agents. The results are summarized in Table III.

Preparation of (1*S*,2*S*)-(+)-*trans*-2-Methylcyclopentanecarboxylic Acid (9) of Very High Optical Purity. The chromic acid solution used for the oxidation was prepared from the appropriate amount of sodium dichromate and aqueous sulfuric acid, as described previously.[19] To a solution of (1*S*,2*S*)-(+)-*trans*-2-methylcyclopentanecarboxaldehyde (7) of 99% ee (10 mmol) in diethyl ether (4 mL), chromic acid solution (7.5 mL) was added with stirring over 15 min. The temperature was maintained below 30 °C with a water-bath. After 2 h at 25 °C, the reaction mixture was extracted with diethyl ether. The organic layer was washed with 3 M sodium hydroxide (2 × 2 mL). The aqueous alkaline solution was made acidic with 3 M HCl, saturated with NaCl, extracted with diethyl ether, and dried. Evaporation of the solvent afforded 1.15 g of the crude acid, 90% yield. GC analyses on 50-m Methylsilicone and 20-m Carbowax 20M capillary columns showed that the acid was diastereomerically pure. It was purified by preparative GC. ^{1}H NMR (CDCl$_3$) δ 1.07 (d, *J* = 7 Hz, 3 H), 1.2–2.4 (m, 8 H), 11.4 (br s, 1 H); ^{13}C NMR (CDCl$_3$) δ 19.6, 24.6, 30.1, 34.9, 39.5, 51.9, 183.1. $[\alpha]^{23}_D$ +54.2 ± 0.2° (*c* 1, CHCl$_3$). Anal. Calcd for C$_7$H$_{12}$O$_2$: C, 65.59; H, 9.44. Found: C, 65.66; H, 9.54.

Reduction of the crude acid with LiAlH$_4$ in ether gave (1*S*,2*S*)-(+)-*trans*-2-methylcyclopentylmethanol (8), which exhibited $[\alpha]^{23}_D$ +53.4° (*c* 1, MeOH), suggesting epimerization during reduction.