Addition Compounds of Alkali Metal Hydrides. 31. Preparation and Properties of Chiral Dialkoxymonoalkylborohydrides. A New Class of Asymmetric Reducing Agents

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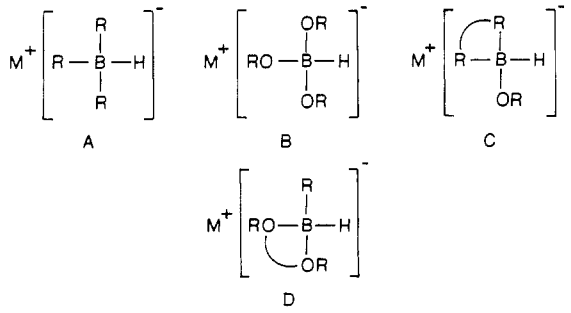
A series of new chiral cyclic boronic esters possessing chirality on alkyl and/or diol moieties, such as methylboronic acid ester **10**, thexylboronic acid esters **11–13**, (+)- or (−)-monoisopinocampheylboronic acid esters **15–19**, and phenylboronic acid ester **14**, were prepared and characterized. As representative chiral diols, (2*R*,3*R*)-(−)-butanediol, (+)-pinanediol, and 1,2;5,6-di-*O*-isopropylidene-D-mannitol were selected. Of these chiral boronic esters, [2*R*,3*R*]-(−)-butanediol thexylboronate (**11**), 1,2;5,6-di-*O*-isopropylidene-D-mannitol thexylboronate (**13**), (+)-pinanediol phenylboronate (**14**), and ethanediol (+)-monoisopinocampheylboronate (**15**) were readily converted into the corresponding chiral dialkoxymonoalkylborohydrides **11′**, **13′**, **14′**, and **15′**, respectively, by treatment of excess potassium hydride in THF at 25 °C. The chiral borohydrides thus formed are all stable at 25 °C and can be stored over potassium hydride under a positive pressure of nitrogen for several months. The asymmetric reductions of representative prochiral ketones, acetophenone, and 3-methyl-2-butanone with these reagents were examined in THF at −78 °C. They gave optical inductions in the range of 5–74% ee for acetophenone and 13–44% ee for 3-methyl-2-butanone. Among the borohydrides examined, potassium 1,2;5,6-di-*O*-isopropylidene-D-mannitol thexylhydridoborate (**13′**) provides the best results, giving 74% ee for acetophenone and 44% ee for 3-methyl-2-butanone. By use of this reagent, the asymmetric reductions of several representative classes of ketone were examined. Thus, 2,2-dimethylcyclopentanone, 3-acetylpyridine, 2-chloroacetophenone, methyl benzoylformate, 4-phenyl-3-buten-2-one, 2-cyclohexen-1-one, and 4-phenyl-3-butyn-2-one were reduced to the corresponding alcohols with 0.3% ee, 56% ee, 16% ee, 25% ee, 15% ee, 71% ee, and 35% ee, respectively, in THF at −78 °C.

Recently we have established the general syntheses of a series of trisubstituted borohydrides, such as trialkylborohydrides[2] A, trialkoxyborohydrides[2] B, dialkylmonoalkoxyborohydrides[4] C, and dialkoxymonoalkylborohydrides[5] D. Among these trisubstituted borohydrides,



A B C D

the general syntheses of "mixed" trisubstituted borohydrides C and D have been accomplished by using cyclic moieties, such as 9-BBN in C and glycols in D, to stabilize the products toward disproportionation.

In the recent past, classes A and C have been applied to the syntheses of chiral borohydrides,[6] providing highly effective reducing agents, NB-Enantride[6b] and potassium 9-[(1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranosyl)oxy]-9-boratabicyclo[3.3.1]nonane (K9-*O*-DIPGF-9-BBNH, K-Glucoride).[8]

Class D reagent appeared to be highly attractive for chiral borohydrides since various chiral diols are readily available, and, moreover, chiral diols containing a C_2 axis of symmetry can be incorporated.[9] However, no work has been done on exploring the possible utilities of these dialkoxymonoalkylborohydrides D, as asymmetric reducing agents.

Therefore, we undertook the study of the syntheses of various chiral dialkoxymonoalkylborohydrides and their asymmetric reducing characteristics toward selected prochiral ketones.

Results and Discussion

The general synthesis of D involves the preparation of boronic esters from the corresponding diols with monoalkylboranes[5] or boronic acids[16,17] or monoalkyldibromoboranes,[17] followed by treatment of the boronic esters with

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(9) A C_2 axis often may lead to a high asymmetric induction: for example, diisopropyl tartrate in Sharpless' epoxidation,[10] 2,5-dimethylborolane in Masamune's asymmetric hydroboration and reduction,[11] 2,5-dimethylpyrrolidine in Whitesell's asymmetric alkylation of enamine,[12] Katsuki's asymmetric alkylation of carboxylic acid derivatives,[13] 2,3-butanediol in Matteson's homologation reaction using chiral organoboranes,[14] and diisopropyl tartrate in Roush's chiral allylboration.[15]

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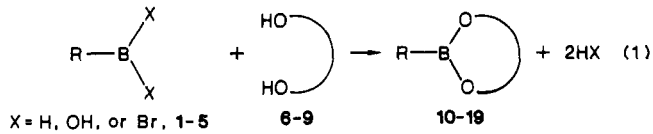
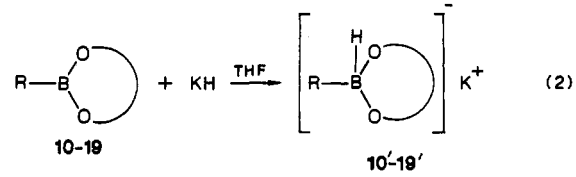
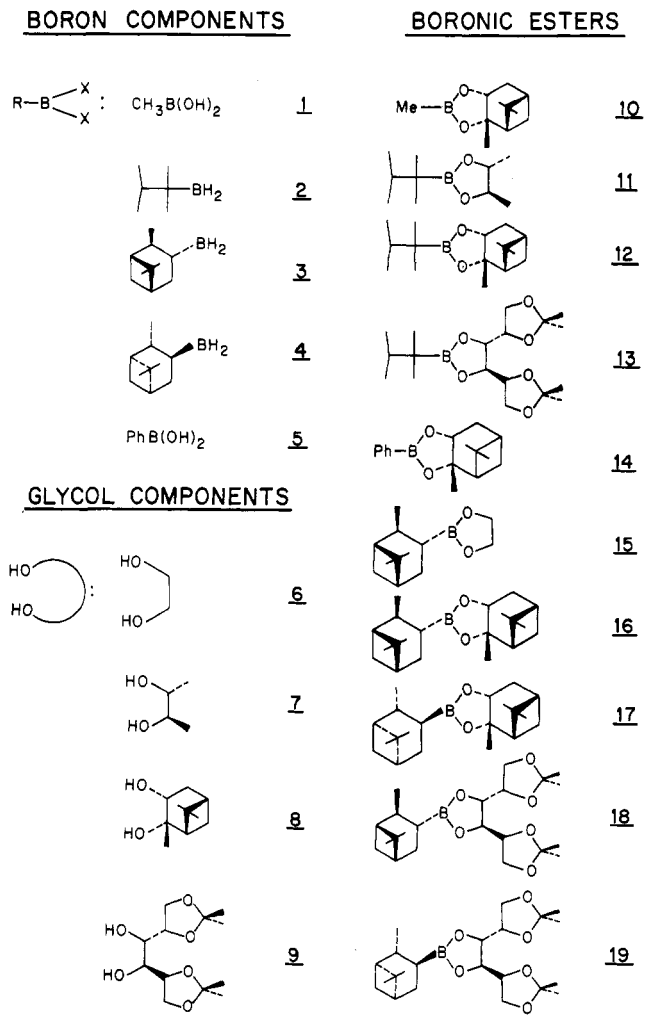
excess potassium hydride in THF[5] (eq 1 and 2).





Accordingly, we decided to prepare new chiral dialkoxymonoalkylborohydrides by using the same methodology aforementioned. As representative R groups, methyl, thexyl, (+)- or (−)-isopinocampheyl, and phenyl groups were selected. To incorporate these alkyl groups into the products, methylboronic acid (**1**), thexylborane (**2**), (+)- or (−)-monoisopinocampheylborane (**3** or **4**), and phenylboronic acid (**5**), respectively were used. As representative diols, ethylene glycol (**6**), (2*R*,3*R*)-(−)-butanediol (**7**), (1*S*,2*S*,3*R*,5*S*)-(+)-pinanediol (**8**), and 1,2;5,6-di-*O*-isopropylidene-D-mannitol (**9**) were selected.



The chiral boronic esters **10–19** obtained were then treated with excess potassium hydride in THF to prepare the corresponding chiral dialkoxymonoalkylborohydride **10′–19′**.

The formation and stability of the resulting borohydrides were examined by ^{11}B NMR spectra and by measuring the number of moles of H_2 evolved by hydrolysis of aliquots of the supernatant solution at appropriate time intervals. The stable chiral dialkoxymonoalkylborohydrides were characterized by ^{11}B NMR and IR spectroscopy and their enantioselectivities as reducing agents examined with acetophenone and 3-methyl-2-butanone. Then the asymmetric reduction of various classes of ketones were studied with the chiral borohydride (**13′**) selected on the basis of the results for the two ketones. The enantiomeric excesses of the alcohols obtained were determined by capillary GC analysis of their MTPA ester derivatives[18] or 1-menthyl carbonate derivatives.[19]

Synthesis of Chiral Cyclic Boronic Esters. The chiral cyclic boronic esters possessing chirality on dialkoxy moieties, such as a methylboronic acid ester (**10**), thexylboronic acid esters (**11–13**), and a phenylboronic acid ester (**14**) were prepared by reaction of **1**, **2**, and **5**, respectively, with the corresponding chiral diols in *n*-pentane or in THF at 25 °C. Thus, the reaction of boronic acids **1** and **5** with (+)-pinanediol (**8**) was carried out in *n*-pentane at 25 °C. The reactions are complete within 2 h to give the corresponding boronic esters **10** and **14**, respectively. In this reaction, methyl boronic acid (**1**) was prepared by carbonylation of borane–methyl sulfide complex, followed by hydrolysis of the resulting methylboroxin.[16] Phenylboronic acid (**5**) and (+)-pinanediol (**8**) are commercially available. Thexylboronic acid esters **11–13** were prepared from thexylborane (**2**) and the corresponding chiral diols **7–9**. The reaction proceeded smoothly in THF at 25 °C with the evolution of 2 equiv of H_2 within 3 h.

On the other hand, a chiral boronic ester (**15**), possessing chirality on the alkyl moiety, and chiral boronic esters (**16–19**), possessing chirality on both alkyl and dialkoxy moieties, were prepared by using (+)- or (−)-monoisopinocampheylborane[20] (**3** and **4**) with the corresponding diols (**8** and **9**). The reaction proceeded smoothly to give the desired boronic esters with the evolution of 2 equiv of H_2 within 2 h at 0 or 25 °C. The (+)- or (−)-monoisopinocampheylborane (**3** or **4**) was prepared by hydroboration of (−)- or (+)-α-pinene with borane–methyl sulfide, followed by treatment with tetramethylethylenediamine (TMEDA), providing enantiomerically pure crystals, followed by liberation of the pure reagent with $BF_3{\cdot}OEt_2$.[20] All of the chiral boronic esters obtained exhibit ^{11}B NMR chemical shifts in the range of δ 30.2–35.7 downfield relative to $BF_3{\cdot}OEt_2$ as the reference. The results are summarized in Table I.

Formation and Stability of Chiral Dialkoxymonoalkylborohydrides. To obtain the chiral dialkoxymonoalkylborohydrides, all of the chiral boronic esters shown in Table I were treated with a slight excess of potassium hydride in THF at 25 °C. Following a short induction time of 0.5–1.0 h, the chiral boronic esters, such as **11**, **13**, **14**, and **15**, take up hydride readily, slightly exothermically, to form the corresponding borohydrides (**11′**, **13′**, **14′**, and **15′**) within 5 h. The course of the reaction was monitored by withdrawing aliquots of the mixture at appropriate time intervals and observing their ^{11}B NMR spectra. The chiral boronic esters exhibited signals between δ 30.2 and 35.7 in ^{11}B NMR, whereas the corresponding borohydrides exhibit signals between δ 4.5 and 8.7. Consequently, the reactions could be easily followed by the disappearance of the boronic ester signal with the concurrent appearance of the borohydride signal. ^{11}B

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Table I. ^{11}B NMR Spectra and Physical Properties of Chiral Boronic Esters

chiral boronic ester	bp, °C (mmHg) [mp, °C]	n^{20}_D	^{11}B NMR (THF), δ	$[\alpha]^{22}_D$, deg (c, THF)
10	78–81 (0.06)	1.4608	32.9 (s)	+43.3 (4.04)
11	72–73 (17)	1.4196	34.9 (s)	+7.95 (3.8)
12	110–112 (0.15)	1.4649	34.4 (s)	+30.3 (5.07)
13	162–164 (0.45)	1.4433	34.9 (s)	+14.87 (9.17)
14	[74–76][a]		30.2 (s)	+6.91 (5.04)
15	96–98 (0.15)	1.4755	34.95 (s)	−13.6 (4.85)
16	[66–68]		34.2 (s)	+7.19 (11.2)
17	164–166 (0.25)	1.4932	34.5 (s)	+21.66 (3.5)
18	226–228 (0.3)	1.4703	34.9 (s)	+15.82 (2.13)
19	215–216 (0.4)	1.4690	35.7 (s)	+6.61 (2.80)

[a] Lit. mp 74.5–75.5 °C: Matteson, D. S.; Ray, R.; Rocks, R. R.; Tsai, D. J. *Organometallics* **1983**, *2*, 1536.

Table II. Formation and Physical Properties of Stable Chiral Dialkoxymonoalkylborohydrides[a]

chiral borohydride	formation temp, °C	formation time, h	^{11}B NMR (THF), δ	IR ν_{B-H}, cm^{-1} (THF)
11′	25	1.0	8.7 (br s)	2010
13′	25	5.0	8.2 (br s)	2020
14′	25	3.0	6.9 (br s)	2030
15′	25	1.0	4.5 (br s)	2120

[a] By the reaction of the chiral boronic esters with excess potassium hydride in THF.

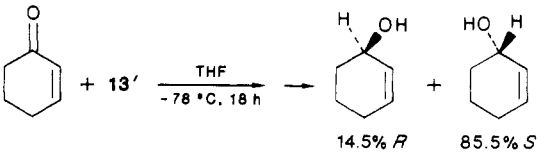
NMR spectra of the chiral borohydrides exhibit broad singlet peaks like those of achiral dialkoxymonoalkylborohydrides.[5]

IR spectra of solutions of the chiral borohydrides in THF displayed characteristically strong absorptions around 2000 cm^{-1}, attributed to the B–H stretching vibrations.

The stabilities of the resulting borohydrides were examined by utilizing the ^{11}B NMR spectra and measuring the number of moles of hydrogen evolved by hydrolysis of clear aliquots of the supernatant solution at appropriate time intervals. The hydride solutions of **11′**, **13′**, **14′**, and **15′** in THF can be stored over excess potassium hydride under a positive pressure of nitrogen at 25 °C for at least 6 months without disproportionation or loss of hydride activity. The results are summarized in Table II.

In contrast, the hydridations of the other chiral boronic esters **10**, **12**, **16**, **17**, **18**, and **19** with potassium hydride were not successful. Of these chiral boronic esters, the relatively hindered boronic ester **12** did not react with potassium hydride, even at 65 °C for 4 days, revealing the presence of the boronic ester itself (δ 34.4) in the ^{11}B NMR spectra. All other boronic esters formed thick precipitates slowly and the whole mixture gelled when the boronic esters were treated with excess potassium hydride in THF at 25 °C. In these cases, the ^{11}B NMR spectra revealed only a decrease of the boronic ester, without formation of the desired borohydride. To explore the preparation of the borohydrides, therefore, we selected the typical chiral boronic ester **16** and attempted hydridation by several different methods, such as reaction of the boronic esters with *tert*-butyllithium at −78 °C[22] or with lithium aluminum hydride in the presence of triethylenediamine at 0 °C[21] or with lithium trimethoxy aluminum hydride at 25 °C.[23] However, disappointingly, all attempts failed to produce the desired borohydride. Such results are probably attributable to the extreme instability of the desired addition products, the corresponding chiral borohydrides.

Asymmetric Reduction of Representative Ketones. Two representative prochiral ketones, acetophenone and 3-methyl-2-butanone, were selected to test the reactivities and the effectiveness of the asymmetric reduction by the new chiral dialkoxymonoalkylborohydrides **11′**, **13′**, **14′**, and **15′**. The reduction proceeded smoothly to give the corresponding alcohols with >90% yields within 24 h for acetophenone and within 12 h for 3-methyl-2-butanone. The chiral borohydrides reduced acetophenone with 9–74% ee and 3-methyl-2-butanone with 13–44% ee. The results are summarized in Table III. Of these reagents **13′** containing a bulky diol moiety with a C_2 axis of symmetry provides the best results. Accordingly, we examined the asymmetric reduction of the other types of ketones, such as 2,2-dimethylcyclopentanone, 3-acetylpyridine, 2-chloroacetophenone, 4-phenyl-3-buten-2-one, 2-cyclohexen-1-one, and 4-phenyl-3-butyn-2-one, with this reagent in THF at −78 °C. As shown in Table IV, reduction of the carbonyl compounds examined, with the exception of 2,2-dimethylcyclopentanone, are complete within 24 h, providing 56% ee for 3-acetylpyridine, 16% ee for 2-chloroacetophenone, 25% ee for methyl benzoylformate, 15% ee for 4-phenyl-3-buten-2-one, 71% ee for 2-cyclohexen-1-one and 35% ee for 4-phenyl-3-butyn-2-one. In the case of 2,2-dimethylcyclopentanone, the reduction proceeded very slowly, giving only 0.3% ee optical induction. It is noteworthy that 2-cyclohexen-1-one is regioselectively reduced to the corresponding allylic alcohol with high optical induction. Most of the trisubstituted



borohydrides[24] including K-Glucoride[25] and NB-Enantride[6b] failed to give the corresponding allylic alcohols. They gave preferentially the 1,4-reduction products, cyclohexanone and cyclohexanol.[26] However, in other cases, the results realized do not appear to be competitive with those produced by K-Glucoride.[8]

Conclusion

In this study, a series of new chiral cyclic boronic esters possessing chirality on the alkyl and/or diol moieties were prepared and characterized. Moreover, the present study provides a convenient synthesis of new chiral dialkoxymonoalkylborohydrides with general structures **20** and **21**

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(24) (a) Ganem, B. *J. Org. Chem.* **1975**, *40*, 146. (b) Fortunato, J. M.; Ganem, B. *Ibid.* **1976**, *41*, 2194.
(25) K-Glucoride: Potassium 9-[(1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranosyl)oxy]-9-boratabicyclo[3.3.1]nonane. See ref 8.
(26) Our unpublished results for K-Glucoride and NB-Enantride.

Table III. Asymmetric Reduction of Representative Ketones with Chiral Dialkoxymonoalkylborohydrides in THF at -78 °C[a]

chiral dialkoxymono-alkylborohydride	acetophenone			3-methyl-2-butanone		
	time, h	yield,[b] %	% ee[c] (config)[d]	time, h	yield,[b] %	% ee[c] (config)[d]
11′	24	98	9 (*S*)	12	96	13 (*R*)
13′	24	96	74 (*R*)	12	95	44 (*R*)
14′	24	95	5 (*R*)	12	89	14 (*S*)
15′	24	99	14 (*S*)	12	97	18 (*R*)

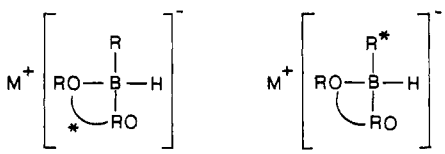
[a] $[H^-]/[ketone]$ = 1.1:1.0, [ketone] = 0.3 M. [b] By GC analysis. [c] By capillary GC analysis of MTPA ester. [d] By comparing the elution order of diastereomeric MTPA esters with those from the corresponding authentic alcohols in capillary GC analysis, unless otherwise indicated.

Table IV. Asymmetric Reduction of Representative Classes of Ketones with Potassium 1,2;5,6-Di-*O*-isopropylidene-D-mannitol Thexylhydridoborate (13′) in THF at -78 °C[a]

ketones	time	alcohol products		
		yield,[b] %	% ee[c]	config[d]
3-methyl-2-butanone	16 h	98	44	*R*
2,2-dimethylcyclopentanone	4 days	98	0.3[e]	*R*
acetophenone	24 h	97	74	*R*
3-acetylpyridine	16 h	96	56	*R*
methyl benzoylformate	12 h	70	25	*S*
2-chloroacetophenone	20 h	81[f]	16[f]	*S*
2-cyclohexen-1-one	18 h	90	71	*S*
4-phenyl-3-buten-2-one	16 h	92	15[g]	*R*
4-phenyl-3-butyn-2-one	16 h	93	35	*S*

[a-d] See corresponding footnotes in Table III. [e] By capillary GC analysis of menthyl carbonate derivatives of the corresponding alcohol. [f] By conversion to styrene oxide. Measured $[\alpha]^{23}_D$ -7.53° (*c* 1.22, benzene). Based on calculated $[\alpha]^{18}_D$ 46.84° (*c* 1.08, benzene), *R*, ref 28. [g] $[\alpha]^{23}_D$ 5.87° (*c* 5.59, $CHCl_3$), based on calculated $[\alpha]^{20}_D$ 39.6° (*c* 5.26, $CHCl_3$), *R*, ref 29.

by reaction of the chiral cyclic boronic esters with excess potassium hydride in THF. Asymmetric reduction of two



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representative prochiral ketones, acetophenone and 3-methyl-2-butanone, with these chiral borohydrides was examined. Of these borohydrides examined, potassium 1,2;5,6-di-*O*-isopropylidene-D-mannitol thexylhydridoborate (13′) affords the best results. With this reagent, asymmetric reduction of the other classes of ketones was also examined. This reagent gives 71% ee optical induction, particularly for the cyclic enone, 2-cyclohexen-1-one with high chemical yield (>90%).

Experimental Section

General Procedure. All glassware was dried at 140 °C overnight, assembled hot, and cooled to room temperature in a stream of nitrogen. All reactions involving air-sensitive materials were carried out under a static pressure of nitrogen. The liquids were transferred with dry syringes or double-ended needles. ^{11}B NMR spectra were recorded on a Varian FT-80 spectrometer, and all ^{11}B chemical shifts were reported in δ (ppm) relative to $BF_3{\cdot}OEt_2$. ^1H NMR spectra were scanned on a Varian T-60A spectrometer with Me_4Si as an internal standard, and all of the chemical shifts were reported in δ (ppm) relative to Me_4Si. IR spectra were recorded on a Perkin-Elmer 1420 spectrophotometer equipped with a Perkin-Elmer 3600 IR data station. Gas chromatographic analyses were carried out with a Hewlett-Packard 5730A instrument attached with a Hewlett-Packard 3390A integrator/plotter using 6 ft × 0.125 in column of 10% Carbowax 20M on Chromosorb W and an internal standard. Capillary gas chromatographic analyses were carried out with a Hewlett-Packard 5890 chromatograph attached with a Hewlett-Packard 3390A integrator/plotter using 15 M Supelcowax or 50 M methyl silicone capillary column. Optical rotations were measured on a Rudolph Polarimeter Autopol III.

Materials. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl prior to use. (+)-Pinanediol, (2*R*,3*R*)-(-)-butanediol, phenylboronic acid, and all prochiral ketones except 2,2-dimethylcyclopentanone were purchased from Aldrich Chemical Company and used without further purification. 1,2;5,6-Di-*O*-isopropylidene-D-mannitol and 2,2-dimethylcyclopentanone were purchased from Fluka Chemical Company and Wiley Organics, respectively. Potassium hydride (Aldrich Chemical Company) was used in oil-free form. (*R*)-α-Methoxy-α-(trifluoromethyl)phenylacetic acid, (*R*)-MTPA, was purchased from Aldrich Chemical Company and converted to the acid chloride and distilled. Methylboronic acid,[16] thexylborane,[27] and (+)- or (-)-monoisopinocampheylboranes[20] were prepared by the established methods.

Preparation of Chiral Cyclic Boronic Esters. The preparations of the following compounds are representative.

(+)-Pinanediol Methylboronate (10). An oven-dried, 200-mL, round-bottom flask with a side arm, magnetic stirring bar, and stopcock adaptor was cooled to room temperature under a stream of nitrogen. In the flask were placed 5.98 g of methylboronic acid[16] (100 mmol), 17.03 g of (+)-pinanediol (100 mmol), and 80 mL of *n*-pentane. The reaction mixture was stirred at 25 °C for 1 h. Water separated was removed via a double-ended needle, and the pentane layer was dried over anhydrous $MgSO_4$, filtered, and concentrated. The pure boronic ester **10** was obtained by vacuum distillation: yield, 15.76 g, 81%; bp 78–81 °C (0.06 mmHg); n^{20}_D 1.4608; $[\alpha]^{22}_D$ 43.3° (*c* 4.04, THF); ^{11}B NMR δ 32.9 (s) (THF); MS, M^+ 183/184. With the same procedure, (+)-pinanediol phenylboronate (**14**) was prepared.

1,2;5,6-Di-*O*-isopropylidene-D-mannitol Thexylboronate (13). With the usual experimental setup, 39.35 g of 1,2;5,6-di-*O*-isoproylidene-D-mannitol (**9**, 150 mmol) in 150 mL of THF was slowly added to thexylborane (150 mmol) at 10–20 °C (a separate small-scale experiment exhibited evolution of 2 equiv of H_2). Then the mixture was warmed to 25 °C and stirred for 6 h. After the THF was evaporated under reduced pressure (14 mmHg, 25 °C), the product **13** was isolated by distillation [162–164 °C (0.45 mmHg)]: yield, 41.7 g, 78%; n^{20}_D 1.4433; $[\alpha]^{22}_D$ 14.87° (*c* 9.17, THF); ^{11}B NMR δ 34.9 (s) (THF): MS, M^+ 355/356. With the same procedure, **11** and **12** were prepared.

(+)-Pinanediol (+)-Monoisopinocampheylboronate (16). (+)-Monoisopinocampheylborane (76 mL of 0.79 M; 60 mmol) in ethyl ether (EE) was added to 10.22 g of (+)-pinanediol (60 mmol) in 30 mL of EE at 25 °C. ^{11}B NMR spectra indicated the reaction was complete in 0.5 h to form the corresponding boronic ester (a separate small-scale experiment indicated evolution of 2 equiv of H_2). The solvent was evaporated under reduced pressure, and the product **16** was isolated as a white solid: yield, 18.2 g, 96%; mp 66–68 °C; $[\alpha]^{22}_D$ 7.19° (*c* 11.2, THF); ^{11}B NMR δ 34.2 (s) (THF); MS, M^+ 315/316. With the same procedure, **15**, **17**, **18**, and **19** were obtained. The results are summarized in Table I.

Preparation of Chiral Dialkoxymonoalkylborohydrides. The following procedure for the preparation of 13′ is representative. With the usual experimental setup, potassium hydride as an oil suspension (14.4 g) was transferred to the flask by a double-ended needle. The potassium hydride was allowed to settle and most of the oil decanted with a double-ended needle. Then

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

the potassium hydride was washed with *n*-pentane (3 × 70 mL). To this oil-free potassium hydride (4.8 g, 120 mmol) suspended in THF (50 mL) was added the THF solution (150 mL) of **13** (35.5 g, 100 mmol) with vigorous stirring. The reaction was monitored both by hydrolysis of centrifuged aliquots and ^{11}B NMR. The reaction was complete within 5 h at 25 °C, producing the addition compound **13′**. The excess potassium hydride was allowed to settle. Then an aliquot of the supernatant clear solution was hydrolyzed in a THF–glycerol–2 N HCl (1:1:1) solution, and the hydrogen evolved was measured. Concentration of the solution of **13′** was found to be 0.48 M (96% yield): ^{11}B NMR δ 8.2 (br, s) (THF); IR ν_{B-H} 2020 cm^{-1}. The concentration of boron was estimated in the form of 2,3-dimethyl-2-butanol obtained by alkaline hydrogen peroxide oxidation of an aliquot, indicating [B] 0.49 M by GC analysis. The content of potassium was measured as KOH following hydrolysis of an aliquot, indicating [K^+] 0.5 M by titration with standard acid. Therefore, a stoichiometry of K/B/H as 1:1:1 was established. Similarly, chiral dialkoxymonoalkylborohydrides **11′**, **14′**, and **15′** were obtained. These hydride solutions in THF stored over excess potassium hydride under a positive pressure of nitrogen at 25 °C revealed no change in hydride activity and no disproportionation in ^{11}B NMR spectra for at least 6 months. The results are summarized in Table II.

Asymmetric Reduction of Prochiral Ketones. The procedures for asymmetric reduction of the following compounds with **13′** are representative.

Acetophenone. To the solution of **13′** in THF (0.48 M, 11.5 mL, 5.5 mmol) precooled to −78 °C was added the solution of acetophenone in THF (1.0 M, 5 mL, 5 mmol) precooled to −78 °C via a double-ended needle. After 24 h, the unreacted hydride was quenched by addition of anhydrous HCl in ethyl ether (5 mmol) precooled to −78 °C. Then the reaction mixture was raised to 25 °C and the solvent evaporated. The reduction product was extracted with *n*-pentane (15 mL × 3) after hydrolysis of the residue with dilute HCl, followed by conversion of the boronic acid moiety into the "ate" complex[8] using aqueous NaOH. The pentane layer was washed with brine (15 mL × 3), dried over anhydrous $MgSO_4$, filtered, and analyzed by GC. The GC analysis indicated the presence of 97% of the product alcohol, 1-phenylethanol. The product was isolated by bulb-to-bulb distillation after evaporation of the solvent and treated with (*R*)-(+)-MTPA acid chloride. The capillary GC analysis of the resulting MTPA ester using 15 M Supelcowax capillary column (160 °C, isothermal) revealed a composition of 87% *R* and 13% *S* (i.e., 74% ee, *R*). Similarly, 3-acetylpyridine and 2,2-dimethylcyclopentanone were reduced to the corresponding alcohols with 35% ee *R* and 0.3% ee *R*, respectively. The optical purity of 2,2-dimethylcyclopentanol was determined by capillary GC analysis of the *l*-menthyl carbonate[19] of the alcohol.

3-Methyl-2-butanone. After the reduction was carried out on a 10-mmol scale for 6 h at −78 °C, unreacted hydride was destroyed by addition of anhydrous methanol (10 mmol) and stirring for 1 h at −78 °C. All of the solvent was evaporated under reduced pressure (14 mmHg, 25 °C) after the temperature was raised to 25 °C. The residue was dissolved in *n*-pentane and hydrolyzed with dilute HCl. The pentane layer was worked up by the same procedure as before. The product alcohol was separated by fractional distillation using a Widmer column. Capillary GC analysis of MTPA esters of product alcohols indicated a composition of 72% *R* and 28% *S* (i.e., 44% ee, *R*).

Methyl Benzoylformate. The keto ester (5 mmol) was treated with **13′** (5.5 mmol) in THF at −78 °C as described in the previous experiment. After 12 h, unreacted hydride was destroyed by the addition of anhydrous methanol and then the solvent evaporated. The residue was dissolved in EE (15 mL). To this was added pH 7 buffer solution (2 mL) at 0 °C, and the mixture was oxidized with 30% hydrogen peroxide (2 mL) for 3 h at 0 °C. The aqueous layer was saturated with sodium chloride and extracted with ethyl ether (15 mL × 2). The combined ethereal solution was dried over anhydrous $MgSO_4$. GC analysis showed the formation of 70% methyl mandelate. After evaporation of the solvent, the product α-hydroxy ester was isolated by bulb-to-bulb distillation and treated directly with (*R*)-MTPA acid chloride. Capillary GC analysis of the resulting MTPA ester using 15 M Supelcowax capillary column (200 °C, isothermal) indicated a composition of 62.5% *S* and 37.5% *R* (i.e., 25% ee, *S*).

2-Chloroacetophenone. After the reduction was carried out on a 10-mmol scale for 20 h, the reaction mixture was quenched by the addition of anhydrous HCl in ethyl ether (10 mmol) and stirring for 1 h at −78 °C. The solvent was evaporated under reduced pressure (14 mmHg, 25 °C). The residue was dissolved in 25 mL of ethyl ether–*n*-pentane (1:1) solution. To this was added 2 N HCl (7 mL), and the mixture was stirred for 0.5 h at 25 °C. Then the organic layer was separated and cooled to 0 °C. To this was added 3 N NaOH (8 mL), and the mixture was stirred for 2 h at 0 °C. The aqueous layer was extracted with ethyl ether (25 mL × 2). The combined organic layer was dried over anhydrous $MgSO_4$. GC analysis revealed the formation of styrene oxide with 81% yield. The distillation product was further purified by column chromatography (silica gel, 60–200 mesh) using cyclohexane–ethyl acetate (9:1) as the eluent. The fraction containing pure styrene oxide was collected, concentrated, and distilled: $[\alpha]^{23}_D$ −7.53 (*c* 1.22, benzene); 16% ee, *S*, based on calculated $[\alpha]^{18}_D$ 46.84 (*c* 1.08, benzene),[28] *R*.

2-Cyclohexen-1-one. The ketone (5 mmol) was treated with **13′** at −78 °C in THF as described above. After 18 h, the unreacted hydride was destroyed by addition of anhydrous methanol at −78 °C and the solvent evaporated. The residue was dissolved in pentane (20 mL) and treated with 2 N HCl (4 mL) at 0 °C for 0.5 h. Then the mixture was made alkaline with 3 N NaOH at 0 °C (5 mL). The organic layer was separated, washed with 3 N NaOH (5 mL × 2), dried over anhydrous $MgSO_4$, and filtered. GC analysis indicated the presence of 2-cyclohexen-1-ol with 90% yield. After evaporation of the solvent, the product alcohol was isolated by bulb-to-bulb distillation and treated directly with (*R*)-MTPA acid chloride. Capillary GC analysis of the resulting MTPA ester using a 50-m methylsilicone capillary column (150 °C, isothermal) revealed a composition of 85.5% *S* and 14.5% *R* (i.e., 71% ee, *S*).

***trans*-4-Phenyl-3-buten-2-one.** The reduction was carried out with exactly the same procedure as described in the previous experiment. After the treatment of anhydrous methanol, the mixture was evaporated. The residue was dissolved in ethyl ether (15 mL) and oxidized with alkaline hydrogen peroxide. The organic layer was separated and the aqueous layer extracted with ethyl ether. The combined solution was dried over anhydrous $MgSO_4$ and filtered. GC analysis revealed the formation of 92% 4-phenyl-3-buten-2-ol. The solvent was evaporated and the product alcohol isolated by bulb-to-bulb distillation. The product was further purified by column chromatography (silica gel 60–200 mesh) using cyclohexane–ethyl acetate (8:2) as the eluent. The fractions containing the pure product alcohol were combined and evaporated. $[\alpha]^{23}_D$ 5.87 (*c* 5.59, $CHCl_3$), 15% ee, *R*, based on calculated $[\alpha]^{20}_D$ 39.6 (*c* 5.26, $CHCl_3$),[29] *R*. With the same procedure, the reduction of 4-phenyl-3-butyn-2-one was carried out. The results are summarized in Tables III and IV.

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Registry No. **1**, 13061-96-6; **2**, 3688-24-2; **3**, 64234-27-1; **4**, 83730-00-1; **5**, 98-80-6; **6**, 107-21-1; **7**, 35007-63-7; **8**, 18680-27-8; **9**, 1707-77-3; **10**, 84110-38-3; **11**, 109583-56-4; **11′**, 109583-59-7; **12**, 109530-51-0; **13**, 109530-52-1; **13′**, 109530-57-6; **14**, 76110-78-6; **14′**, 109530-58-7; **15**, 109530-53-2; **15′**, 109530-59-8; **16**, 109530-54-3; **17**, 109583-57-5; **18**, 109530-55-4; **19**, 109583-58-6; 3-methyl-2-butanone, 563-80-4; 2,2-dimethylcyclopentanone, 4541-32-6; acetophenone, 98-86-2; 3-acetylpyridine, 350-03-8; methyl benzoylformate, 15206-55-0; 2-chloroacetophenone, 532-27-4; 2-cyclohexen-1-one, 930-68-7; 4-phenyl-3-buten-2-one, 1896-62-4; 4-phenyl-3-butyn-2-one, 1817-57-8; (*R*)-3-methyl-2-butanol, 1572-93-6; (*R*)-2,2-dimethylcyclopentanol, 109530-56-5; (*R*)-1-phenylethanol, 1517-69-7; (*R*)-3-(1-hydroxyethyl)pyridine, 7606-26-0; (*S*)-methyl mandelate, 21210-43-5; (*S*)-2-chloro-1-phenylethanol, 70111-05-6; (*S*)-2-cyclohexen-1-ol, 6426-26-2; (*R*)-4-phenyl-3-buten-2-ol, 32271-52-6; (*S*)-4-phenyl-3-butyn-2-ol, 81555-86-4; (*R*)-MTPA acid chloride, 39637-99-5.

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