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NEW CHIRAL BOROHYDRIDES. 3. PREPARATION AND ASYMMETRIC REDUCING PROPERTIES OF POTASSIUM 9-*O* -(1,2-ISOPROPYLIDENE-5-DEOXY-α-D-XYLOFURANOSYL)-9-BORATA-BICYCLO[3.3.1]NONANE[1,2]

Byung Tae Cho* and Yu Sung Chun

Department of Chemistry, Hallym University, Chunchon 200-702, Republic of Korea

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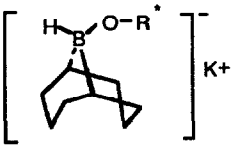
Abstract: A stable, new chiral borohydride, potassium 9-*O* - (1,2-*O*-isopropylidene-5 - deoxy-α-D-xylofuranosyl)-9-boratabicyclo[3.3.1]nonane (K xylide, **1D**) using a xylose derivative as a chiral auxiliary was prepared by the treatment of the corresponding borinic ester **3D** with potassium hydride in THF. The reagent provided high optical induction for asymmetric reduction of prochiral ketones, such as relatively hindered ketones, alkyl aromatic ketones, and α-haloketones. Thus, the reduction of 4-methyl-2-pentanone, 3,3-dimethyl-2-butanone, and 2,2-dimethylcyclopentanone provided the corresponding alcohols in 65 % ee, 76 % ee, and 80 % ee, respectively. The optical induction for unhindered aliphatic ketones was low, such as 36 % ee for 2-heptanone, 46 % ee for 3-methyl-2-butanone. The reductions of alkyl aromatic ketones provide high optical inductions, such as 70 % ee for acetophenone, 82 % ee for butyrophenone, 89 % ee for isobutyrophenone, 99 % ee for pivalophenone, and 93 % ee for 2'-methylacetophenone. For some functionalized ketones, the reduction of 2-chloroacetophenone yields the corresponding alcohol in 92 % ee, whereas the reduction of 3-acetylpyridine, methyl benzoylformate, and 4-phenyl-3-butyn-2-one provide the corresponding alcohols in 62 % ee, 60 % ee and 52 % ee, respectively.

Introduction

Recently we have established the synthesis of chiral dialkylmonoalkoxyborohydrides (**1**) consisting of well defined, single reducing species and possessing chirality on alkoxy group.[3] The syntheses of these chiral borohydrides involve the reaction of 9-borabicyclo[3.3.1]nonane (9-BBN, **2**) with chiral alcohols, followed by conversion of the resulting chiral borinic esters (**3**) (eq 1) into the corresponding potassium dialkylmonoalkoxyborohydrides (**1**) by treatment with excess potassium hydride (eq 2).[3a] Of these chiral hydride reagents, potassium 9-*O* - (1,2:5,6 - di-*O* - isopropylidene-α-D - glucofuranosyl) - 9 - boratabicyclo[3.3.1]nonane (K glucoride, **1B**) using a α - D - glucose



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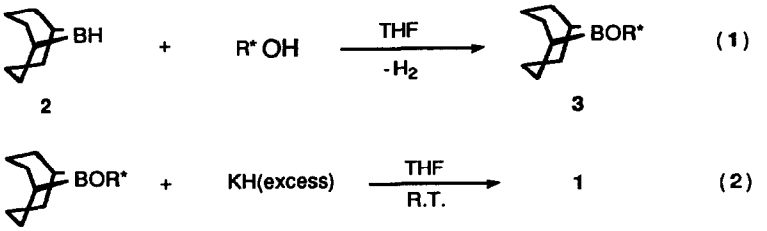
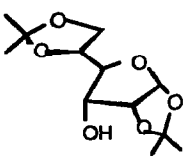
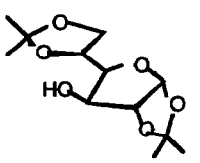


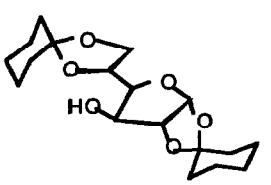
Where R*OH = chiral alcohols



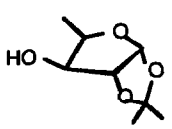
DIPAF, **A**



DIPGF, **B**



DCHGF **C**



IPDXF, **D**

derivative, 1,2:5,6-di-*O*- isopropylidene-α-D-glucofuranose (DIPGF, **B**) as a chiral auxiliary alcohol proved to be one of the most promising asymmetric reducing agents for the reduction of ketones.[5] Especially this reagent is highly effective for the asymmetric reductions of highly hindered aromatic ketones and α-keto esters.[5a,b] However, the reagent is inefficient for the reduction of prochiral unhindered aliphatic ketones.

Accordingly, with the hope of development of improved chiral hydride reagents, we prepared a chiral borohydride, potassium 9-*O* - (1,2: 5,6 - di-*O*-isopropylidene- α -D-allofuranosyl)-9-boratabicyclo [3.3.1]nonane (**1A**) modified with an allose derivative, C-3 epimer of DIPGF **B**, 1,2:5,6-di-*O* - isopropylidene-α- D-allofuranose (DIPAF, **A**) using the same methodology shown in eq 1 and 2. Unfortunately, in a preliminary experiment, we found that this reagent provided low optical inductions, such as 57 % ee for acetophenone and 3 % ee for 3-methyl-2-butanone, although the products alcohols gave the opposite configurations (S isomers) as compared to those produced by **1B**.[4] Subsequently, it occurs to us that one of asymmetric inducing factors of the chiral borohydrides utilizing monosaccharide derivatives as chiral auxiliaries might be the steric effect of the attaching group at the 4-position as well as the configuration of hydroxyl group at the 3-position of the furanose ring moiety of monosaccharide derivatives. In this regard, we prepared potassium 9-*O*-(1,2:5,6-di-*O*-cyclohexylidene-α-D-glucofuranosyl)-9- boratabicyclo[3.3.1]nonane (**1C**) utilizing 1,2:5,6 - di -*O*-cyclohexylidene-α-D-glucofuranose (DCHGF, **C**) bearing a bulkier group at the 4-position of the furanose ring moiety as compared to that of DIPGF, **B** and examined its enantioselectivity for the reduction of our representative classes of ketones.[6] In this study, we found that this hydride reagent gave almost the same optical inductions as compared to those afforded by **1B**.[7] The results revealed that at least the steric effect of the attaching group at the 4-position of the furanose ring moiety in **1B** and **1C** did not make a significant role on the optical inductions for ketone reductions.

Accordingly, to gain a better understanding of the factors for asymmetric reduction and with the hope of development of improved chiral hydride reagents, we undertook a study on synthesis of a new chiral borohydride (**1D**) modified with 1,2-isopropylidene-5-deoxy-α-D-xylofuranose(IPDXF, **D**) derived from α-D-xylose, possessing a small substituent group, methyl group at the 4-position of the furanose ring moiety and its asymmetric reducing characteristics for ketones.

Results and Discussion

A monosaccharide derivative, IPDXF, **D** was prepared by reductive cleavage of 1,2-isopropylidene-3,5-anhydro-α-D-xylofuranose obtained from α-D-xylose with lithium aluminum hydride according to the literature.[8] A new chiral dialkylmonoalkoxyborohydride, potassium 9-*O*-(1,2-*O*-isopropylidene-5-deoxy-α-D-xylofuranosyl)-9-boratabicyclo[3.3.1]nonane (K xylide,[9] **1D**) was prepared by treatment of excess potassium hydride with the corresponding borinic ester **3D**, which in turn was prepared by the reaction of 9-BBN and IPDXF, **D** (eq 1 and 2).

The stability of the reagent was examined by ^{11}B NMR spectra and by measuring the number of moles of hydrogen evolved by hydrolysis of aliquots of the supernatant solution at appropriate time intervals.

The reductions were carried out at -78 ℃ or -50 ℃ in tetrahydrofuran (THF) by using a 10 % excess of the reagent.

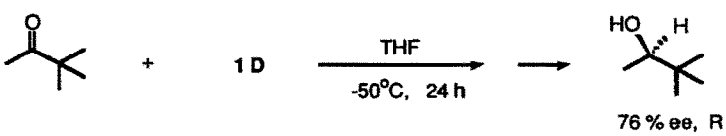
Optical purities of the products alcohols were determined by capillary Gc analyses of (+) - α -

methoxy-α-(trifluoromethyl)phenylacetates (MTPA esters)[10] or (-)-menthyl chloroformate (MCF)[11] derivatives of the corresponding alcohols, using a methyl silicone capillary column (50 m) or a FFAP capillary column (50 m).

Formation and Stability of 1D. The chiral borinic esters **3D** was prepared by treatment of 9-BBN with 1,2-isopropylidene-5-deoxy - α - D-xylofuranose (IPDXF, **D**). The reactions proceeded smoothly in THF at 25 ℃ with the evolution of 1 equiv of hydrogen within 2 h (eq 1). The ^{11}B NMR spectra of the resulting solution revealed complete disappearance of 9-BBN (δ 28.0 ppm) with the appearance of only the desired borinic esters (δ 58.7 ppm). The borinic ester **3D** was isolated as a viscous oil by distillation in high yield. When **3D** was treated with a modest excess of potassium hydride (1.2-1.3 equiv) in THF at room temperature (ca. 25 ℃), slightly exothermic reaction was observed, after a short induction period (ca. 30 min). The hydride uptake reaction was complete within 4 h to give the desired corresponding hydride **1D**. The reagent **1D** exhibits chemical shift at δ - 0.36 ppm(br. s) in the ^{11}B NMR spectra and characteristic strong absorption at 2073 cm^{-1} attributed to B-H stretching vibration in the IR spectrum. The stoichiometric ratio of K : B: H in **1D** was defined as 1 : 1 : 1 by analysis of the supernatant solution of **1D** in THF.

The stability of **1D** was examined by utilizing the ^{11}B NMR spectra and measuring the number of moles of hydrogen evolved by hydrolysis of aliquots of the supernatant solution at appropriate time intervals. Thus, we found that the hydride solution of **1D** could be stored over excess potassium hydride under a positive pressure of nitrogen at room temperature for at least 3 months without disproportionation and loss of hydride activity.

Asymmetric Reduction of Aliphatic Ketones. Under the standard conditions (in THF, at -78 ℃), the reduction of unhindered ketones, such as 2-heptanone and 3-methyl-2-butanone, was complete in 20 h to give the corresponding alcohols in 36 % ee and 46 % ee, respectively. For the reduction of relatively hindered aliphatic ketones, such as 4-methyl-2-butanone, 3,3-dimethyl-2-butanone and 2,2-dimethylcyclopentanone, however, the optical inductions of products alcohols obtained were much favorable, although the reaction is slow. Thus, the reduction of 4-methyl-2-butanone was complete in 36 h to give 4-methyl-2-butanol in 65 % ee. The reduction of 3,3-dimethyl-2-butanone provided the product alcohol in 76 % ee, requiring 24 h at - 50 ℃ for complete reduction(eq 3). The reduction of 2,2-dimethylcyclopentanone was more slowly to give the corresponding alcohol in 92 %



(3)

yield at -50 ℃ for 4 days, achieving the optical induction of 80 % ee (eq 4). In this reaction, all of the alcohols obtained were consistently enriched in the R enantiomers. The results were summarized in Table 1.

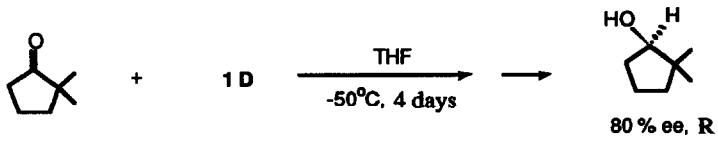


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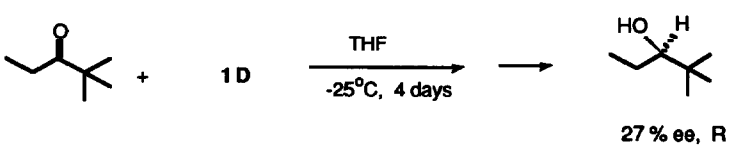
Table 1. Asymmetric Reduction of Representative Aliphatic Ketones with 1D in THF at -78 °C.[a]

	1D				% ee	
ketones	time(h)	yield[b]	% ee[c]	config.[d]	1B[e]	1C[f]
2-heptanone	20	98	36	R	26	38
3-methyl-2-butanone	20	97	46	R	39	58
4-methyl-2-pentanone	36	98	65	R		51
3,3-dimethyl-2-butanone	24[g]	98	76	R	70	58
2,2-dimethyl-3-pentanone	4 d[h]	95	27	R		
2,2-dimethylcyclopentanone	4 d[g]	92	80	R[i]	84	80

[a] [Hydride / compound] = 1.1, [ketones] = 0.3 M. [b] By Gc analysis. [c] Determined by capillary Gc analysis of MTPA esters.[10] [d] By the comparison of elution orders of MTPA esters or menthyl carbonate of the known compounds. [e] The values taken from ref. 5a. [f] The values taken from ref. 4. [g] At -50 °C. [h] At -25 °C. [i] Determined by capillary Gc analysis of (-)-menthyl carbonates.

From Table 1, it was realized that this reagent provided a slight improvement in optical inductions as compared to those achieved by **1B** or **1C** for acyclic aliphatic ketones, such as 2-heptanone, 3-methyl-2-butanone, 4-methyl-2-pentanone, and 3,3-dimethyl-2-butanone. The results are surprising, indicating that the steric effect of a substituting group at the 4-position of the furanose ring moiety in **1B**, **1C** or **1D** is not significant for optical induction in the reduction of aliphatic ketones. Interestingly, the reduction of an ethyl alkyl ketone (RCOEt), 2,2-dimethyl-3-pentanone resulted in sharp decrease in the optical induction to give 27 % ee, R, as compared to 76 % ee, R, realized in the reduction of a methyl alkyl ketone (RCOMe), 3,3-dimethyl-2-butanone (eq 5). The reason for the decrease of optical induction is not fully understood, but presumably, it seems to be attributed to the steric effect of ethyl group of the ketone in the transition state.



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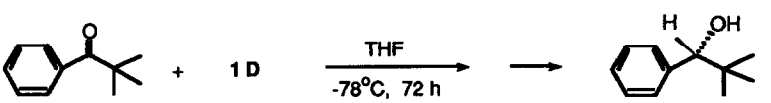
Asymmetric Reduction of Alkyl Aromatic Ketones. As shown in Table 2, most of a representative series of alkyl aromatic ketones examined were reduced smoothly to the corresponding alcohols with high optical yields in THF at -78 °C. When steric size of R in PhCOR was varied from Me ⟶ Pr ⟶ *i*-Pr ⟶ *t*-Bu, the optical inductions of the products alcohols obtained increased

Table 2. Asymmetric Reduction of Representative Alkyl Aromatic Ketones with 1D in THF at -78 °C.[a]

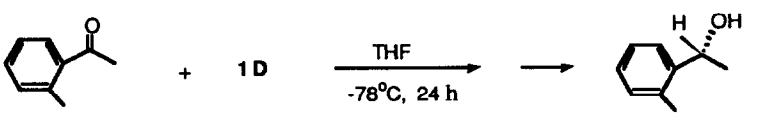
	1D				% ee	
ketones	time(h)	yield[b]	% ee[c]	config.[d]	1B[e]	1C[f]
acetophenone	24	96	70	R	78	70
propiophenone	30	97	86	R	92	
butyrophenone	36	98	82	R	87	
isobutyrophenone	48	98	89	R	87	
pivalophenone	72	95	99	R	100(97)	
2'-methylacetophenone	24	95	93	R	91	

[a-f] See the corresponding footnotes in Table 2.

remarkably except in the case of butyrophenone (R=Pr), such as 70 % ee for acetophenone, 86 % ee for propiophenone, 82 % ee for butyrophenone, 89 % ee for isobutyrophenone, and 99 % ee for pivalophenone. Especially, it is noteworthy that the reduction of pivalophenone provides essentially optically pure (R)-(+)-2,2-dimethyl-1-phenylpropanol (eq 6). Changing the phenyl group in acetophenone to the *o* -tolyl group, a dramatic increase of optical induction was observed. Thus, the



99 % ee, R (6)



93 % ee, R (7)

reduction of 2'-methylacetophenone provided the product alcohol in 93 % ee as compared to 70 % ee for acetophenone (eq 7). Again, all of the alcohols obtained are consistently enriched in the R enantiomers.

From Table 2, it is observed that this reagent provides similar optical inductions as compared to those realized by **1B** for the reduction of the same ketones. Again, in the reduction of alkyl aromatic ketones, it shows that the steric effect of an attaching group at position 4 of the furanose ring moiety in **1D** or **1B** is not a significant factor for the asymmetric induction.

Asymmetric Reduction of Functionalized Ketones. Additionally, the reduction of some functionalized ketones were carried out in THF at -78 °C. As the representative functionalized ketones, we selected 2-chloroacetophenone for α-haloketones, methyl benzoylformate for α-keto esters, 3-acetylpyridine for heterocyclic ketones, and 4-phenyl-3-butyn-2-one for acetylenic ketones. Most of the ketones examined were reduced smoothly to the corresponding alcohols in high yields, although the reaction of methyl benzoylformate was somewhat slow, requiring 50 h at -78 °C to be complete. Among the functionalized ketones examined, this reagent is the most effective for the reduction of 2-chloroacetophenone, giving 1-phenyl-2-chloroethanol in 92 % ee (eq 8). The value of % ee exhibits the much improved optical yield as compared to 77 % ee obtained by **1B** or **1C**. For methyl benzoylformate, 3-acetylpyridine, and 4-phenyl-3-butyn-2-one, the reductions afforded the corresponding alcohols in 60 % ee, 62 % ee, and 52 % ee, respectively. The results and a direct comparison of those achieved by **1B** or **1C** for the same ketones are summarized in Table 3. In the reduction of 2-chloroacetophenone and methyl benzoylformate, the opposite configurational notations of the product alcohols are due to the sequence rule.

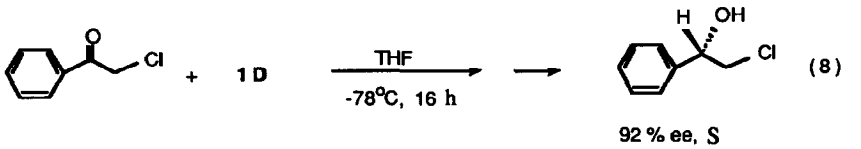


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Table 3. Asymmetric Reduction of Representative Functionalized Ketones with 1D in THF at -78 °C. [a]

	1D				% ee	
ketones	time(h)	yield [b]	% ee [c]	config. [d]	1B [e]	1C [f]
2-chloroacetophenone	16	99	92	S	77	78
methyl benzoylformate	50	96	60	S	92	92
3-acetylpyridine	36	98	62	R	70	55
4-phenyl-3-butyn-2-one	22	98	52	R	61	62

[a-f] See the corresponding footnotes in Table 1.

Conclusion

The synthesis of a stable, new chiral monoalkoxyborohydride, K xylide,**1D** utilizing a xylose derivative as a chiral auxiliary was studied. This reagent is highly effective in achieving optical inductions for the reduction of prochiral ketones, such as hindered aliphatic ketones, alkyl aromatic ketones, and α-haloketone. In particular, the reduction of pivalophenone yields the essentially optical pure corresponding alcohol. Moreover, the directions of the asymmetric induction are consistent, providing the R isomers by *si* facial addition of hydride for both aliphatic and alkyl aromatic ketones. For both α-halo ketone and α-keto ester, the S isomers produced by *Re* facial addition of hydride are obtained. In a direct comparison of the reduction for the same ketones, the asymmetric reducing properties of this reagent very closely resemble to those of K glucoride (**1B**).

Experimental Section

General Methods. All glassware was dried at 140 ℃ overnight, assembled hot, and cooled to room temperature in a stream of nitrogen. The experimental technique for handling air-sensitive compounds have been previously described.[12] ^{11}B NMR spectra were recorded on Brucker AC-80 spectrometer and the chemical shifts were in δ (ppm) relative to BF_3OEt_2. ^1H NMR spectra were scanned on a Varian T-60A spectra with Me_4Si as an internal standard. IR measurements were conducted on a Shimadzu IR-435 equipped with a Shimadzu DRR-1 data station. Gc analyses were carried out with a Shimadzu 7A having a flame ionization detector and integrated with a Shimadzu CR-1B intergrator. The yields of products alcohols were determined by Gc analysis using internal standard methods using columns (3 mm x 4 m) of 10 % carbowax 20 M or 10 % OV-1 on chromosorb W (80- 100 mesh). Optical purities were determined by capillary Gc analysis of MTPA esters or MCF derivatives. The analysis was done on a Hewlett- Packard 5890 gas chromatograph using a methyl silicone capillary column (50 m) or a FFAP capillary column (50 m) and integrated with a Hewlett- Packard 3390 A intergrator. Mass spectra was conducted on a VG-70-VSEQ high resolution mass spectrometer.

Materials. THF was distilled over benzophenone ketyl and stored under a nitrogen atmosphere in an ampule. 9-Borabicyclo[3.3.1]nonane (9-BBN) and potassium hydride were purchased from Aldrich Chemical Company. Commercially available ketones were obtained from Aldrich or Wiley and used without further purification. Pivalophenone was prepared by Grignard reaction of trimethylacetonitrile according to the literature.[13] 1,2-isopropylidene-5-deoxy-α-D-xylofuranose (IPDXF, D) was prepared by the known method[8] from α-D-xylose. (R)-(+)-MTPA[14] was purchased from Aldrich Chemical Company and was converted to the acid chloride[10] and distilled. (-)-menthyl chloroformate (MCF) was obtained from Aldrich Chemical Company and used without further purification.

Preparation of 9-*O* - (1,2 - isopropylidene - 5 - deoxy - α - D - xylofuranosyl) - 9-borabicyclo[3.3.1]nonane (9-O-IPDXF-9-BBN, 3D). An oven dried, 200-mL, round-bottom flask with a side arm, a condenser, and an adaptor attached to a mercury bubbler was flushed with nitrogen and cooled to room temperature. Into the flask were charged 12.2 g (100 mmol) of 9-BBN and 30 mL of THF. To the slurry of 9-BBN in THF was added 17.4 g (100 mmol) of IPDXF (**D**) dissolved in 60 mL of THF dropwise via a double-ended needle with vigorous stirring at room temperature. Hydrogen evolved immediately. After the reaction mixture was stirred for 2 h, the mixture was refluxed for additional 1 h to ensure completion of the reaction. ^{11}B NMR of the solution showed a broad singlet at δ 58.7. Evaporation of the solvent, followed by distillation under vacuum, provided 25.7 g (87 % yield) of **3D** as a viscous oil : bp 133-135 °C/0.25 mmHg; ^{11}B NMR δ 58.7 (s); HRMS(CI), calcd MH^+ for $C_{16}H_{27}BO_4$ 295.2102, found 295.2087.

Preparation of potassium 9-*O* - (1,2 - isopropylidene - 5 - deoxy - α -D - xylofuranosyl)-9-boratabicyclo[3.3.1]nonane (K xylide, 1D). An oil suspension of potassium hydride , transferred to a flask, was allowed to settle and most of the oil removed with a double-ended needle. Then the potassium hydride was washed with n-pentane (3 x 30 mL). After evaporation of n-pentane in a vacuo, the oil-free potassium hydride was suspended in THF. To this suspension of potassium hydride (3.6 g, 90 mmol) in 50 mL of THF was added the THF solution (90 mL) of **3D** (20.6 g, 70 mmol) via a double-ended needle with vigorous stirring. The reaction became slightly exothermic after a 10-30 min induction period. The reaction was monitored both by hydrolysis of centrifuged aliquots and by ^{11}B NMR. It was complete within 4 h, producing the desired compound, **1D**. After the reaction was complete, the excess of potassium hydride was allowed to settle for 48 h. An aliquot of the clear solution was hydrolyzed in a THF-glycerine-2 N HCl mixture (1:1:1) and the hydrogen evolved was measured, indicating the concentration of **1D** as 0.48 M (96 % yield): ^{11}B NMR δ - 0.36 ppm (br. s): IR υ_{B-H} 2073 cm^{-1}. The content of potassium was measured as KOH produced by hydrolysis, indicating $[K^+]$ = 0.49 M by titration of a standard acid. The concentration of boron was estimated by Gc analysis of 1,5-cyclooctanediol following oxidation of an aliquot with alkaline hydrogen peroxide. The concentration was 0.48 M. Therefore, a stoichiometry of K : B : H as 1 :1 : 1 was established. The hydride solution of **1D** in THF can be stored over excess potassium hydride under positive nitrogen pressure at room temperature for at least 3 months without disproportionation or loss of hydride activity.

Asymmetric Reduction of Prochiral Ketones with K xylide, 1D. General Procedure . An oven-dried 25-mL, long necked, round-bottom flask equipped with a septum-capped side arm, a magnetic stirring bar, and a stopcock adaptor was cooled to room temperature under a stream of nitrogen. 5.5 mmol of a solution of **1D** in THF was transferred to the flask. The solution was cooled to -78 °C . To this was added 5 mmol of a THF solution of the prochiral ketone precooled to -78 °C via a double-ended needle.[12] The reaction mixture was stirred at -78 °C. The concentration of the ketone compound was made to be 0.3 M. At appropriate time intervals, the reaction mixture was quenched by the addition of anhydrous methanol or anhydrous HCl in ethyl ether at -78 °C to make sure of complete reduction.

Reduction of Aliphatic Ketones. The reduction of 3,3-dimethyl-2-butanone is described as representative. According to the general procedure, 5 mmol of 3,3-dimethyl-2-butanone (1.0 M, 5 mL) was reacted with 5.5 mmol of **1D** in THF (0.48 M, 11.5 mL) at - 50 ℃ for 24 h. The reaction mixture was treated with 10 mmol of anhydrous HCl or methanol precooled to -50 ℃. The mixture was stirred at - 50 °C for 1 h to destroy unreacted hydride and then warmed to room temperature. The solvents were pumped off in a vacuo (20 mmHg, 27 ℃). The residue was dissolved in 15 mL of ethyl ether and treated with 3 N NaOH (3 mL) and then oxidized with 30 % hydrogen peroxide (2 mL) at room temperature for 3 h. The ether layer was separated and the aqueous layer was saturated with potassium carbonate and extracted with ethyl ether (5 mL x 3). The combined ether layer was washed with brine (5 mL x 3), dried over anhydrous magnesium sulfate, and filtered. Gc analysis (10 % carbowax 20 M, 4 m, 60 °C, isothermal) showed the formation of 3,3-dimethyl-2-butanol in 98 % yield. The product was isolated by fractional distillation. The optical purity was determined by capillary Gc analysis (methyl silicone, 50 m, 150 °C, isothermal) of MTPA esters prepared by the reaction of the product alcohol (0.1 mmol) and (R)-(+)-MTPA acid chloride (0.2 mmol) in carbon tetrachloride (0.4 mL) in the presence of pyridine (0.1 mL) for 24 h at 27 ℃.[10] The Gc analysis indicated a composition of 12 % of S isomer (t_R : 41.90 min) and 88 % of R isomer (t_R : 42.65 min) of the product alcohol (i.e., 76 % ee, R). Similarly, the reduction and the determination of optical purity for the other aliphatic ketones were carried out. For 3-methyl-2-butanone, the unreacted hydride was destroyed with methanol. The optical purity of 2,2-dimethylcyclopentanol was determined by capillary Gc analysis (FFAP, 50 m, 160 °C, isothermal) of (-)-menthyl carbonates of the alcohol prepared from (-)-menthyl chloroformate and the product alcohol.[11] The results are summarized in Table 1.

Reduction of Alkyl Aromatic Ketones. The reduction of pivalophenone is representative. The reaction of pivalophenone (5 mmol) with **1D** (5.5 mmol) was carried out in THF at -78 ℃. After 72 h, the reaction mixture was quenched with anhydrous HCl in ethyl ether precooed to -78 °C. The work-up procedure was followed by the same procedure as described in the previous experiment. Gc analysis (10 % carbowax 20 M, 4 m, 180 °C, isothermal) revealed the formation 2,2-dimethyl-1-phenylpropanol in 95 % yield. The product alcohol was isolated by bulb-to-bulb distillation (bp 115-120 ℃/18 mmHg). Capillary Gc analysis (methyl silicone, 50 m, 180 ℃, isothermal) of MTPA esters of the product alcohol showed a composition of 99.5 % of R isomer (t_R : 76.21 min) and 0.5 % of S isomer (t_R : 76.91 min), i.e., 99 % ee, R. The results for the other alkyl aromatic ketones are summarized in Table 2.

Reduction of 2-Chloroacetophenone. Following the general procedure, 5 mmol of 2-chloroacetophenone was treated with 5.5 mmol of **1D** in THF at -78 ℃. After 16 h, the unreacted hydride was destroyed by addition of anhydrous HCl in ethyl ether precooled to -78 ℃. And then solvent was pumped off under reduced pressure (20 mmHg, 27 ℃). The residue was dissolved in ethyl ether (15 mL) and treated with 3 N HCl (3 mL). The aqueous layer was extracted with ethyl ether (5 mL x 3). The combined extract was washed with brine , dried over anhydrous magnesium sulfate, and concentrated. The formation of the product alcohol in 99 % yield was realized by Gc analysis (methyl silicone, 50 m, 150 °C, isothermal). The product alcohol was isolated by bulb - to - bulb

distillation (bp 110-115 °C/5 mmHg). The distilled product was directly derivatized with (R)-MTPA acid chloride and the MTPA ester was analyzed by capillary Gc (methylsilicon, 50 m, 190 °C, isothermal). The analysis indicated the formation of the product alcohol in 92 % ee, S, providing a composition of 96 % of R isomer (t_R : 59.12 min) and 4 % of S isomer (t_R : 60.10 min) of the product alcohol.

Reduction of Methyl benzoylformate. According to the general procedure, the reaction of 5 mmol of methyl benzoylformate with 5.5 mmol of **1D** was carried out in THF at -78 °C for 50 h. After the unreacted hydride was quenched by the addition of anhydrous methanol (10 mmol), the solvent was pumped off in vacuo. The residue was dissolved in ethyl ether (15 mL) and oxidized with 30 % hydrogen peroxide (2 mL) in the presence of pH 7 phosphate buffer solution (2 mL) at 0 °C for 3 h. The aqueous layer was extracted with ethyl ether (5 mL x 3). The combined extract was washed with brine and dried over anhydrous sodium sulfate. Gc analysis (methyl silicone, 50 m, 160 °C, isothermal) revealed the formation of the product alcohol methyl mandelate in 96 % yield. The alcohol was isolated by bulb-to-bulb distillation (125-135 °C/10 mmHg) and directly converted to the MTPA ester. Analysis of the MTPA ester on capillary Gc (methyl silicone, 50 m, 210 °C, isothermal) indicated 60 % ee, S, showing the formation of 20 % of R isomer (t_R : 32.72 min) and 80 % of S isomer (t_R : 33.88 min).

Reduction of 3-Acetylpyridine. 5 mmol of 3-Acetylpyridine was reacted with 5.5 mmol of **1D** in THF at -78 °C for 36 h. The reaction mixture was quenched by the addition of anhydrous HCl in ethyl ether, followed by addition of 3 N HCl (3 mL) at room temperature. The solvent was evaporated under reduced pressure. The residue was dissolved in ethyl ether (15 mL). The aqueous layer was basified with 6 N NaOH, saturated with potassium carbonate, and extracted with ethyl ether (5 mL x 3). The ether extract was washed with brine, dried over anhydrous potassium carbonate, and concentrated. Gc analysis showed the presence of the product alcohol in 98 % yield. The optical purity of the alcohol was determined by capillary Gc analysis (methy l-silicone, 50 m, 200 °C, isothermal) of its MTPA ester, providing 62 % ee, R, with a composition of 81 % of R isomer (t_R : 30.24 min) and 19 % of S isomer (t_R : 30.89 min).

Reduction of 4-Phenyl-3-butyn-2-one. The reaction and the work-up procedures were carried out with the same as described in the reduction of alkyl aromatic ketones. After 22 h, Gc analysis (10 % carbowax 20 M, 4 m, 170 °C, isothermal) indicated the formation of the product alcohol in 98 % yield. Capillary Gc analysis (methyl silicone, 50 m, 210 °C, isothermal) of MTPA ester of the product alcohol indicated the formation of 76 % of R isomer (t_R : 37.18 min) and 24 % of S isomer (t_R : 38.16 min), i.e., 52 % ee, R.

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References and Notes

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