Chiral Synthesis via Organoboranes. 43. Selective Reductions. 58. Reagent-Controlled Diastereoselective Reduction of (+)- and (−)-α-Chiral Ketones with (+)- and (−)-*B*-Chlorodiisopinocampheylborane

P. Veeraraghavan Ramachandran, Guang-Ming Chen,[1] and Herbert C. Brown*

H. C. Brown and R. B. Wetherill Laboratories of Chemistry, Purdue University, West Lafayette, Indiana 47907

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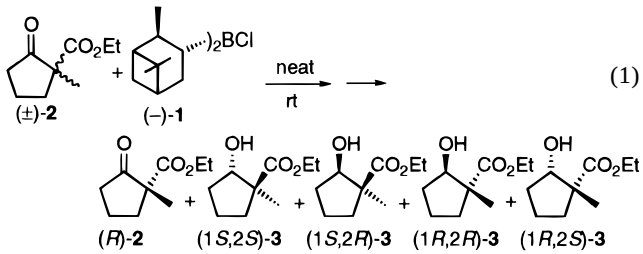
Asymmetric reduction of (+)- and (−)-α-chiral ketones with (+)- and (−)-*B*-chlorodiisopinocampheylborane provides the product alcohols in very high diastereomeric excess, with the matched pairs providing >100:1 selectivity and the mismatched pairs showing 4:1−15:1 selectivity. The high selectivity achieved even in the mismatched pairs reveals the power of the reagent to control the stereochemical outcome. The rates of the reaction of the matched pairs are faster than those of the mismatched pairs. In all the cases studied thus far, the (−)-reagent (^{d}Ipc$_2$BCl) and (*S*)-ketone or the (+)-reagent (^{l}Ipc$_2$BCl) and (*R*)-ketone constitute matched pairs and the (−)-reagent and (*R*)-ketone or the (+)-reagent and (*S*)-ketone constitute mismatched pairs. A possible mechanism for the reductions is discussed.

Introduction

A decade ago, Masamune and co-workers reviewed double asymmetric synthesis as a strategy for stereochemical control in organic synthesis.[2] They proposed a rule which relates the results of single asymmetric reactions with the outcome of double asymmetric reactions. Since the introduction of the concept of matched and mismatched pairs in double asymmetric reactions,[2] organic chemists have exploited the matched interactions of two optically active reactants in multistep synthesis.[3] In our program of chiral synthesis via organoboranes,[4] we have studied the effectiveness of our α-pinene-based reagents in double asymmetric synthetic situations and demonstrated the excellent control of diastereofacial selectivity in acyclic carbon−carbon bond-forming reactions using pinane-based allyl- and crotylborane reagents,[5] making possible several valuable applications for key steps in important syntheses.[3] Similar success was exhibited by pinane-based reagents in enolboration−aldolizations also.[6] Though we had introduced (+)- and (−)-*B*-chlorodiisopinocampheylboranes (^{l}- and ^{d}Ipc$_2$BCl; Aldrich, (+)- and (−)-DIP-Chloride, (+)- and (−)-**1**) as successful reagents for the asymmetric reduction of several classes of prochiral ketones,[7] these reagents have not been tested for double asymmetric reductions.

Recently, we carried out the kinetic resolution of several α-tertiary ketones with (+)- and (−)-**1**, as a means of preparing optically pure carbonyl compounds with an α-quaternary carbon atom.[8] The reduction of ethyl 1-methyl-2-oxocyclopentanecarboxylate (**2**) with 0.50 equiv of (−)-**1** at rt provided the unreacted (*R*)-keto ester in 75% enantiomeric excess (ee) (eq 1). The product ethyl 1-methyl-2-hydroxycyclopentanecarboxylate (**3**) obtained was shown to be 91% [(1*S*,2*S*)-*trans*]-**3**, 2% [(1*R*,2*R*)-*trans*]-**3**, and 7% [(1*R*,2*S*)-*cis*]-**3**. When the reagent used for the reduction was increased to 0.60 equiv, the % ee of the recovered ketone improved to 96%, and with 0.65 equiv of the reagent, essentially optically pure ketone was recovered. The product alcohol now had a composition of 80% [(1*S*,2*S*)-*trans*]-**3**, 5% [(1*R*,2*R*)-*trans*]-**3**, and 15% [(1*R*,2*S*)-*cis*]-**3**. This clearly shows that while the ee of the ketone improved, the extent of the diastereomeric excess achieved in the alcohol decreased with increasing amounts of the reagent. The reduction of the racemic ketone with 1.1 equiv of (−)-**1** provided an isomeric ratio of 51% [(1*S*,2*S*)-*trans*]-**3**, 8% [(1*R*,2*R*)-*trans*]-**3**, and 41% [(1*R*,2*S*)-*cis*]-**3** (eq 1). This ratio reveals that in asymmetric reductions using (−)- or (+)-**1** the opposite isomers of the ketone provide one of the diastereomers of the product alcohol, either predominantly or exclusively.



(1)

2:1 ::						
1:0.5	75% ee	91%	0%	2%	7%
1:0.6	96% ee	86%	0%	3%	9%
1:0.65	≥99% ee	80%	0%	5%	15%
1:1.1	–	51%	0%	8%	41%

Analysis of the kinetic resolution of racemic 1-methylnorcamphor (**4**) reveals the same phenomenon. We

(1) Postdoctoral Research Associate on a Grant from the U.S. Army Research Office.

(2) Masamune, S.; Choy, W.; Peterson, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1.

(3) For example: Wang, Z.; Deschenes, D. *J. Am. Chem. Soc.* **1992**, *114*, 1090.

(4) Brown, H. C.; Ramachandran, P. V. *J. Organomet. Chem.* **1995**, *500*, 1.

(5) Brown, H. C.; Bhat, K. S.; Randad, R. S. *J. Org. Chem.* **1987**, *52*, 3701.

(6) (a) Paterson, I.; Cumming, J. G.; Smith, J. D.; Ward, R. A. *Tetrahedron Lett.* **1994**, *35*, 441. (b) Paterson, I.; Lister, M. A. *Tetrahedron Lett.* **1988**, *29*, 585.

(7) (a) Brown, H. C.; Chandrasekharan, J.; Ramachandran, P. V. *J. Am. Chem. Soc.* **1988**, *110*, 1539. DIP-Chloride is a trademark of the Aldrich Chemical Co. (b) The superscripts *d* and *l* refer to (+)- and (−)-α-pinene, respectively, used to prepare the corresponding (−)- and (+)-DIP-Chloride, respectively.

(8) Ramachandran, P. V.; Chen, G. M.; Brown, H. C. J. Org. Chem. **1996**, *61*, XXX.

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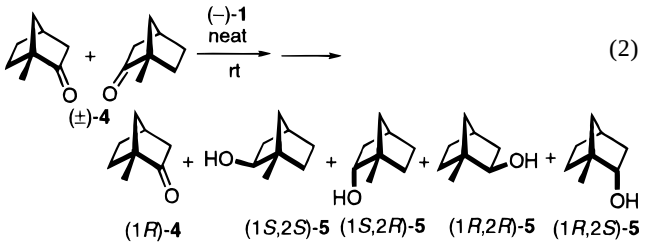
Table 1. Asymmetric Reduction of α-Chiral Ketones with (−)- and (+)-1 under Neat Conditions at Room Temperature

ketone	reagent	reactn time, h	isol yield, %	exo,[a] %	*endo*,[a] %	product alcohol,[b] % (1*S*,2*S*)	(1*S*,2*R*)	(1*R*,2*R*)	(1*R*,2*S*)
(*S*)-ethyl 1-methyl-2-oxo-cyclopentanecarboxylate	(−)-**1**	1	70	≥99 (*t*)[c]	0 (*c*)[c]	≥99	0		
(*S*)-ethyl 1-methyl-2-oxo-cyclopentanecarboxylate	(+)-**1**	72	69	19 (*t*)[c]	81 (*c*)[c]	19	81		
(*R*)-ethyl 1-methyl-2-oxo-cyclopentanecarboxylate	(−)-**1**	72	72	18 (*t*)[c]	82 (*c*)[c]			19	81
(*R*)-ethyl 1-methyl-2-oxo-cyclopentanecarboxylate	(+)-**1**	1	66	≥99 (*t*)[c]	0 (*c*)[c]			≥99	0
(1*S*)-1-methylnorcamphor	(−)-**1**	0.5	91	≥99	0	≥99	0		
(1*S*)-1-methylnorcamphor	(+)-**1**	2	90	11	89	11	89		
(1*R*)-1-methylnorcamphor	(−)-**1**	2	88	12	88			12	88
(1*R*)-1-methylnorcamphor	(−)-**1**	48[d]	98	7	93			7	93
(1*R*)-1-methylnorcamphor	(+)-**1**	0.5	89	≥99	0			≥99	0
(1*S*)-camphenilone	(−)-**1**	1	86	0	≥99	≥99	0		
(1*S*)-camphenilone	(+)-**1**	12	91	94	6	6	94		
(1*R*)-camphenilone	(−)-**1**	12	83	93	7			7	93
(1*R*)-camphenilone	(+)-**1**	1	97	0	≥99			≥99	0
(1*S*)-camphor	(−)-**1**	0.5	95	≥99[e]	≤1	≥99	≤1		
(1*S*)-camphor	(+)-**1**	10	97	32	68	32	68		
(1*S*)-camphor	(+)-**1**	96[d]	97	21	79	21	79		
(1*R*)-camphor	(−)-**1**	10	95	34	66			34	66
(1*R*)-camphor	(+)-**1**	0.5	95	≥99[e]	1			≥99	1

[a] Determined by direct analysis on a SPB-5 capillary column. [b] Determined as a derivative on a capillary column. [c] (*t*) = *trans* and (*c*) = *cis*. [d] At −25 °C. [e] Crystallization from hexane gave essentially pure *exo*-**9**.

were initially surprised to observe that the reduction of (±)-**4** with 0.50 equiv of (−)-**1** provides the contrathermodynamic[9] (1*S*,2*S*)-*exo*-1-methyl-2-norbornanol as the major product (86%) (eq 2). But a close examination



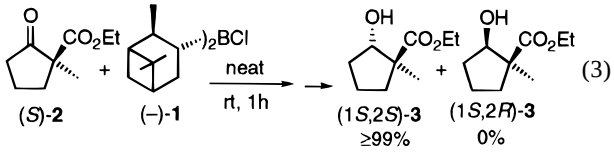
(2)

	(1*R*)-**4**	(1*S*,2*S*)-**5**	(1*S*,2*R*)-**5**	(1*R*,2*R*)-**5**	(1*R*,2*S*)-**5**
4:**1** :: 1:0.5	63% ee	86%	0%	5%	9%
1:0.6	88% ee	84%	0%	3%	13%
1:0.7	≥99% ee	80%	0%	4%	16%
1:1.1	–	52%	0%	7%	41%

revealed that when the (1*S*)-ketone is preferentially reduced, with (−)-**1**, the reagent that produces predominantly (*S*)-alcohols,[7] we obtain (1*S*,2*S*)-1-methyl-2-norbornanol. Reduction of (±)-**4** with a stoichiometric amount of (−)-**1** produces 52% (1*S*,2*S*)-**5** (*exo*), 7% (1*R*,2*R*)-**5** (*exo*), and 41% (1*R*,2*S*)-**5** (*endo*), i.e., 41% of the *endo*-product and 59% of the *exo*-alcohol. This predicts that the reaction of optically pure (1*S*)-**4** with (−)-**1** should provide (1*S*,2*S*)-**5** (*exo*) exclusively, whereas (1*R*)-**4** with (−)-**1** should provide (1*R*,2*S*)-**5** (*endo*) predominantly. As a corollary, the reduction of (1*R*)-**4** and (1*S*)-**4** with (+)-**1** should provide (1*R*,2*R*)-**5** (*exo*) exclusively and (1*S*,2*R*)-**5** (*endo*) predominantly, respectively. To test the validity of these predictions, in the hope of better understanding the capability of DIP-Chloride for double asymmetric reductions, we undertook an examination of the reaction of representative optically pure ketones with optically pure antipodes of the reagent. The results of this study are presented and discussed here.

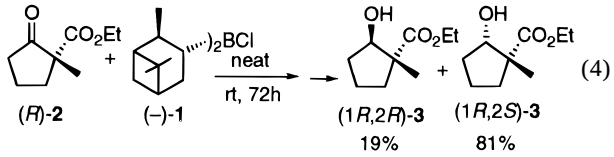
Results and Discussion

The reduction of (*S*)-**2** with (−)-**1** under neat condition at rt is complete in 1 h, and the usual diethanolamine workup provides the hydroxy ester, analyzed as the trifluoroacetate with a Chiraldex-GTA capillary column[10] to be exclusively ethyl [(1*S*,2*S*)-*trans*]-1-methyl-2-hydroxycyclopentanecarboxylate [(1*S*,2*S*)-**3**] (eq 3). On the



(3)

contrary, the reduction of (*R*)-**2** with (−)-**1** is slower, complete only after 72 h, producing a mixture of hydroxy esters, 81% [(1*R*,2*S*)-*cis*]-**3** and 19% [(1*R*,2*R*)-*trans*]-**3** (eq 4). The difference in the rate of reduction is in accord with the kinetic resolution experiments described previ-



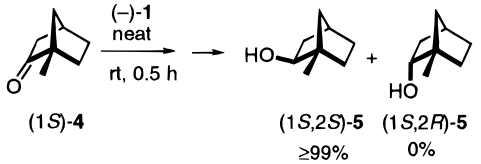
(4)

ously, when (±)-**2** was resolved with (−)-**1** to provide (*R*)-**2** and with (+)-**1** to obtain (*S*)-**2**.[8] The combination of (*S*)-**2** and (−)-**1**, the reagent that produces predominantly (*S*)-alcohols, appears to constitute a matched pair, whereas the combination of (*R*)-**2** and (−)-**1** constitutes a mismatched pair. As can be expected from the foregoing result, the antipode of the reagent, (+)-**1**, with (*R*)-**2** provides the *trans*-hydroxy ester [(1*R*,2*R*)-*trans*]-**3** essentially exclusively, whereas the reaction of (+)-**1** with (*S*)-**2** gives 81% of the *cis*-hydroxy ester [(1*S*,2*R*)-*cis*]-**3** predominantly (Table 1).

The double asymmetric reduction of optically pure 1-methyl-2-norbornanones, (1*R*)- and (1*S*)-**4**, with (+)- and (−)-**1** reveals similar control by the reagent. Reduction of (1*S*)-1-methyl-2-norbornanone with the matching reagent, (−)-**1**, results in a complete reaction in only 0.5 h, and the usual workup provides (1*S*,2*S*)-1-methyl-2-norbornanol ((1*S*,2*S*)-**5** (*exo*)) as the exclusive product (eq 5).

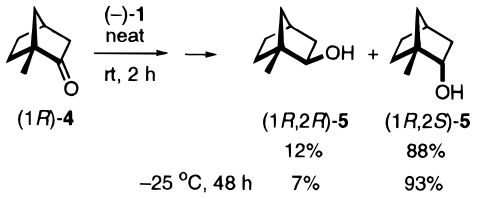
(9) Rei, M. H. *J. Org. Chem.* **1979**, *44*, 2760.

(10) Chiraldex-GTA is a trademark of Alltech Associates, Inc.



(5)

The reduction of the mismatched ketone, (1*R*)-**4** with (−)-**1** is slower, requiring 2 h for completion, and provides 88% of (1*R*,2*S*)-1-methyl-2-norbornanol ((1*R*,2*S*)-**5** (*endo*)) and 12% of (1*R*,2*R*)-**5** (*exo*) (eq 6). The *endo* product increases to 93% when the reaction is conducted at −25 °C. The fact that there is not a large difference in the

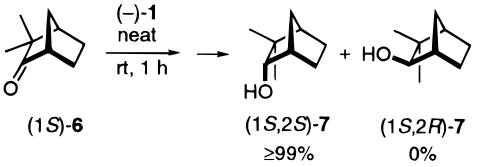


(6)

rate of reduction of the matched and mismatched pair of the reagent and the ketone in this case provides an explanation for our observation that we are forced to use 1.4 equiv of the reagent at 0 °C for the kinetic resolution of (±)-**4**.[8]

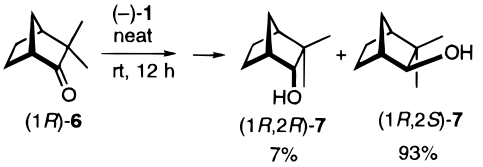
The results are identical for the reduction of (1*R*)-**4** and (1*S*)-**4** with the antipode of the reagent, (+)-**1** (Table 1).

While the (1*S*,2*S*)-product is *exo* for 1-methyl-2-norbornanol, a similar product from the reduction of 3,3-dimethyl-2-norbornanone (camphenilone, **6**), (1*S*,2*S*)-3,3-dimethyl-2-norbornanol (**7**), is *endo*. This provides an excellent opportunity to demonstrate control by the reagent in this double asymmetric reduction. On the basis of the reductions of **2** and **4** with (+)- and (−)-**1** described above, if the (1*S*)-ketone and (−)-reagent are the matched pair, and assuming that the product is formed depending on the proven capability of the (−)-reagent to form the (*S*)-alcohol, it is anticipated that the reduction would produce the *endo*-alcohol from this combination, whereas the *exo*-alcohol should be obtained from the mismatched pair. Indeed, treatment of (1*S*)-**6** with (−)-**1** results in a relatively rapid reaction at rt (1 h), and the product is exclusively (1*S*,2*S*)-**7** (*endo*) (eq 7).



(7)

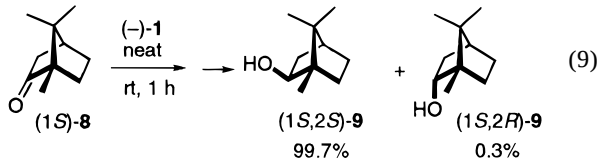
The reaction of the mispatched pair (1*R*)-**6** with (−)-**1** requiring 12 h at rt for complete reduction, reveals a better selectivity than the product from the reduction of (1*R*)-**4**, 93% (1*R*,2*S*)-**7** (*exo*) and 7% (1*R*,2*R*)-**7** (*endo*) (eq 8).



(8)

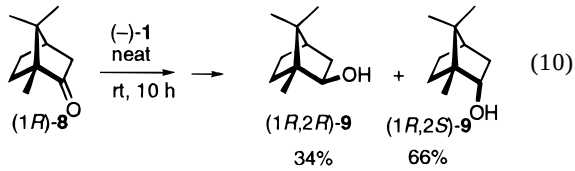
In comparison, the reduction of (1*R*)-**6** with (+)-**1** gives ≥99% (1*R*,2*R*)-**7** (*endo*) and the reaction of (1*S*)-**6** with (+)-**1** gives 94% (1*S*,2*R*)-**7** (*exo*) and 6% (1*S*,2*S*)-**7** (*endo*) (Table 1), thus displaying the control of the reagent over the stereochemical outcome in the mismatched cases also.

The reduction of camphor (**8**) using hydride reagents provides a classic example of the role of steric effects on the course of the reductions. The extreme steric requirements of the camphor structure control the *endo*-approach of the hydride, even with the least sterically demanding reagent, sodium borohydride, providing the *exo*-product almost exclusively (98%). Accordingly, the reduction of camphor provides a major test for **1**. As expected, the reduction of (1*S*)-**8** with (−)-**1** provides 99.7% of [(1*S*)-*exo*]isoborneol and 0.3% of [(1*S*)-*endo*]-borneol (eq 9). The slower reacting mismatched pair



(9)

(1*R*)-**8** and (−)-**1** gave a product ratio of 66% [(1*R*)-*endo*]-borneol and 34% [(1*R*)-*exo*]isoborneol (eq 10).



(10)

The enantiomers are produced in the reduction of the antipodes of **8** with (+)-**1**. The reduction of (1*S*)-**8** with (+)-**1** was also carried out at −25 °C when the reaction was decelerated (4 d for completion), but improves the *endo*:*exo* ratio to 79:21 (Table 1).

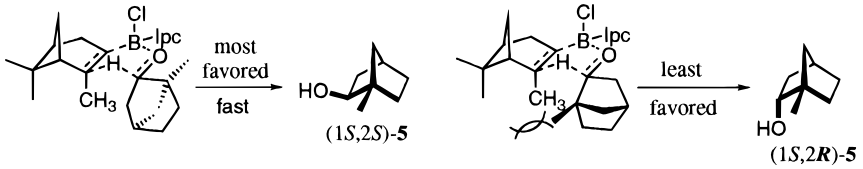
For convenience, all of the results of the double asymmetric reductions with (+)- and (−)-**1** are summarized in Table 1.

Mechanism of Reduction. The tentative model of the transition state that we proposed earlier to explain and predict the configuration of products from reductions using **1**[7] can be utilized to rationalize the differences in the rate of the reduction and the control of the stereochemistry by the reagent. For example, for the reduction of (1*S*)-(+)- and (1*R*)-(−)-**4** with (−)-**1** ($^{d}Ipc_2BCl$), four transition state models are possible that will provide each of the four diastereomers [Scheme 1, parts a−d]. In the favored transition state for both (1*S*)- and (1*R*)-ketones, the ketone approaches the reagent with its quaternary carbon atom having the 1-methyl group away from the methyl group at the 2-position of the apopinane structure of the reagent [Scheme 1, parts a and c. As can be seen from the model, under favored situations, (1*S*)-ketone produces the *exo*-alcohol and (1*R*)-ketone produces the *endo*-alcohol. Strong steric interactions between the two methyl groups allow the reagent to control the stereo outcome.

Of the two disfavored models, the interactions between the 2-methyl group of the reagent and the 1-methyl group of the (1*S*)-ketone (Scheme 1, part b seems to be very prominent, making this the least favored transition state. This leads to the exclusive formation of (1*S*,2*S*)-**5** (*exo*). However, the model in Scheme 1, part d, for (1*R*)-ketone is not as hindered as part b and contributes to the partial formation of (1*R*,2*R*)-**5** (*exo*).

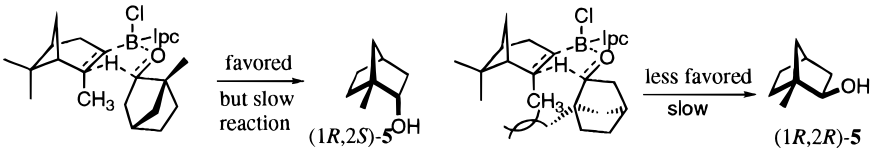
This model probably can be used to account for the differences in the rates of the reduction for the two

Scheme 1



(**a**). Favored transition state model for the interaction of $^{d}Ipc_2BCl$ and (1*S*)-**4**

(**b**). Disfavored transition state model for the interaction of $^{d}Ipc_2BCl$ and (1*S*)-**4**



(**c**). Favored transition state model for the interaction of $^{d}Ipc_2BCl$ and (1*R*)-**4**

(**d**). Disfavored transition state model for the interaction of $^{d}Ipc_2BCl$ and (1*R*)-**4**

isomers of the ketone. A comparison of the favored transition state models [Scheme 1 parts a and c] shows that there could be a larger interaction between the bridge methylene group of the ketone and the 2-methyl group of the reagent in part c as compared to part a which causes a slower reaction rate for the (1*R*)-ketone. Such an interaction in the disfavored model might also be contributing to the complete absence of (1*S*,2*R*)-**5** (*endo*) from the (1*S*)-ketone.

Conclusions

In conclusion, we have demonstrated that the predictable nature of the reduction of prochiral ketones with DIP-Chloride can be extended for the reagent-controlled reduction of chiral ketones where the matched pairs show ≥99% diastereoselectivity and the mismatched pairs show a diastereoselectivity of 68−94%. The rates of the reactions of the matched pairs are faster than those of the mismatched pairs. In all the cases studied, the (−)-reagent and (*S*)-ketone or the (+)-reagent and (*R*)-ketone constitute matched pairs and the (−)-reagent and (*R*)-ketone or the (+)-reagent and (*S*)-ketone constitute mismatched pairs. We believe that this capability of our versatile reagent should find further applications in organic synthesis. We are continuing to study the scope and limitations of this double asymmetric reduction.

Experimental Section

General Methods. Techniques for handling air-sensitive compounds have been previously described.[11] Analyses of the menthyl chloroformate (MCF) derivatives[12] were performed on a gas chromatograph (GC) using a SPB-5 capillary column (30 m), at appropriate temperatures. Some of the product alcohols were converted to the trifluoroacetates and analyzed on a Chiraldex-GTA capillary column (23 m).

Materials. Ethyl ether (EE) (Mallinckrodt) was used as such. (+)- and (−)-camphor, trifluoroacetic anhydride, (+)- and (−)-DIP-Chloride, diethanolamine, and menthyl chloroformate were all obtained from Aldrich Chemical Co. Enantiomerically pure isomers of ethyl 1-methylcyclopentanecarboxylate, 1-methylnorcamphor, and camphenilone were prepared by the kinetic resolution of their racemates using appropriate enantiomers of DIP-Chloride.[8]

(11) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Syntheses via Boranes;* Wiley-Interscience: New York, 1975; Chapter 9.

(12) Westley, J. W.; Halpern, B. *J. Org. Chem.* **1968**, *33*, 3978.

Reduction of Ketones with 1. General Procedure. An oven-dried 50 mL round bottom flask equipped with a septum-capped side arm, magnetic stirring bar, and a connecting tube was cooled to rt in a stream of nitrogen. The ketone (10 mmol) and DIP-Chloride (12 mmol) were transferred to the flask in a glovebag. The reaction mixture was stirred at appropriate temperatures until the reaction was complete as shown by the ^{11}B NMR spectrum of a methanolyzed aliquot (δ 32). EE (25 mL) was added, followed by diethanolamine (24 mmol), and the mixture was stirred for 2 h when the boron components precipitated as a complex. This precipitate was filtered and washed with pentane. The combined filtrates were concentrated and chromatographed using vacuum liquid chromatography on silica gel. α-Pinene was eluted with pentane, followed by elution of the alcohol with pentane:EE (1:1). The *cis*/*trans* or *exo*/*endo* ratio of the alcohols was determined by comparing them with the product obtained from the reduction of the ketone with $NaBH_4$. The reactions of individual ketones are presented below.

Reduction of Ethyl (*S*)-(+)-1-Methyl-2-oxocyclopentanecarboxylate ((*S*)-2). (a) With (−)-1. (*S*)-(+)-**2** (5.2 mmol, 0.89 g) was treated with 2.02 g (6.3 mmol) of (−)-**1** at rt as described in the general procedure. The reaction was complete in 1 h. Workup and chromatography provided 0.63 g (70%) of the product hydroxy ester **3**. Analysis of the TFA derivative of this product on a Chiraldex-GTA column revealed a composition of ≥99% [(1*S*,2*S*)-*trans*]-**3**. The other diastereomer could not be detected by GC. $[\alpha]^{25}_D = +24.80$ (*c* 3.2, $CHCl_3$). ^1H NMR δ (ppm) ($CDCl_3$): 1.21 (s, 3H), 1.24−1.29 (t, J = 7.1 Hz, 3H), 1.53−2.08 (m, 6H), 2.09−2.10 (d, J = 3.7 Hz, 1H), 4.12−4.19 (q, J = 7.1 Hz, 2H), 4.31−4.37 (m, 1H). ^{13}C NMR δ (ppm) ($CDCl_3$): 14.09, 17.16, 19.02, 30.86, 33.79, 52.00, 60.48, 76.79, 177.75. Anal. Calcd for $C_9H_{16}O_3$: C, 62.75; H, 9.37. Found: C, 62.42; H, 9.63.

(b) With (+)-1. (*S*)-(+)-**2** (3.1 mmol, 0.52 g) was treated with 1.18 g (3.7 mmol) of (+)-**1** at rt as described in the general procedure. The reaction was complete in 72 h. Workup and chromatography provided 0.37 g (69%) of the product hydroxy ester which showed a composition of 81% [(1*S*,2*R*)-*cis*]-**3** and 19% [(1*S*,2*S*)-*trans*]-**3**.

Reduction of Ethyl (*R*)-(−)-1-Methyl-2-oxocyclopentanecarboxylate ((*R*)-2). (a) With (−)-1. (*R*)-(−)-**2** (3.0 mmol, 0.51 g) was treated with 1.18 g (3.7 mmol) of (−)-**1** at rt as described in the general procedure. The reaction was complete in 72 h. Workup and chromatography provided 0.37 g (72%) of the product hydroxy ester **3** which showed an isomeric composition of 82% [(1*R*,2*S*)-*cis*]-**3** and 18% [(1*R*,2*R*)-*trans*]-**3**.

(b) With (+)-1. (*R*)-(−)-**2** (1.4 mmol, 0.23 g) was treated with 0.53 g (1.7 mmol) of (+)-**1** at rt as described in the general procedure. The reaction was complete in 1 h. Workup and chromatography provided 0.16 g (66%) of the product hydroxy ester which showed a composition of ≥99% [(1*R*,2*R*)-*trans*]-**3**. The other diastereomer could not be detected by GC. $[\alpha]^{25}_D =$

−24.52 (*c* 3.1, $CHCl_3$). The ^1H and ^{13}C NMR spectra were identical to those obtained from (1*S*,2*S*)-*trans*]-**3**. Anal. Calcd for $C_9H_{16}O_3$: C, 62.75; H, 9.37. Found: C, 62.38; H, 9.60.

Reduction of (1*S*)-(+)-1-Methylnorcamphor ((1*S*)-4). (a) With (−)-1. (1*S*)-(+)-**4** 7.6 mmol, 0.94 g) was treated with 2.93 g (9.1 mmol) of (−)-**1** at rt as described in the general procedure. The reaction was complete in 0.5 h. Workup and chromatography provided 0.87 g (91%) of the product alcohol, mp 75−76 °C. Analysis of the MCF derivative of the alcohol on a SPB-5 capillary column showed an isomeric composition of ≥99% (1*S*,2*S*)-**5**. The other diastereomer could not be detected by GC. $[\alpha]^{25}_D = -0.81$ (*c* 2.95, $CHCl_3$).[13] ^1H NMR δ (ppm) ($CDCl_3$): 1.14 (s, 3H), 1.40−1.41 (d, J = 4.2 Hz, 1H), 0.95−1.82 (m, 8H), 2.13−2.18 (m, 1H), 3.44−3.50 (m, 1H). ^{13}C NMR δ (ppm) ($CDCl_3$): 16.05, 30.26, 32.98, 35.89, 40.05, 43.01, 47.39, 77.40. Anal. Calcd for $C_8H_{14}O$: C, 76.13; H, 11.19. Found: C, 75.88; H, 11.40.

(b) With (+)-1. (1*S*)-(+)-**4** (3.9 mmol, 0.48 g) was treated with 1.49 g (4.6 mmol) of (+)-**1** at rt as described in the general procedure. The reaction was complete in 2 h. Workup and chromatography provided 0.44 g (90%) of the product alcohol which showed an isomeric composition of 89% (1*S*,2*R*)-**5** and 11% (1*S*,2*S*)-**5**.

Reduction of (1*R*)-(−)-1-Methylnorcamphor ((1*R*)-4). (a) With (−)-1. (1*R*)-(−)-**4** (5.8 mmol, 0.72 g) was treated with 2.23 g (7.0 mmol) of (−)-**1** at rt as described in the general procedure. The reaction was complete in 2 h. Workup and chromatography provided 0.64 g (88%) of the product which showed a composition of 88% (1*R*,2*S*)-**5** and 12% (1*R*,2*R*)-**5**.

At −25 °C, the reaction was complete in 48 h and workup provided 98% of the product alcohol which showed an isomeric composition of 93% (1*R*,2*S*)-**5** and 7% (1*R*,2*R*)-**5**.

(b) With (+)-1. (1*R*)-(−)-**4** (8.3 mmol, 1.03 g) was treated with 3.2 g (9.9 mmol) of (+)-**1** at rt as described in the general procedure. The reaction was complete in 0.5 h. Workup and chromatography provided 0.93 g (89%) of the product alcohol, mp 75−76 °C, which showed an isomeric composition of ≥99% (1*R*,2*R*)-**5**. The other diastereomer could not be detected by GC. $[\alpha]^{25}_D = +0.82$ (*c* 4.76, $CHCl_3$).[13] The ^1H and ^{13}C NMR spectra were identical to those obtained from (1*S*,2*S*)-**5**. Anal. Calcd for $C_8H_{14}O$: C, 76.13; H, 11.19. Found: C, 75.88; H, 11.56.

Reduction of (1*S*)-(+)-Camphenilone ((1*S*-6)). (a) With (−)-1. (1*S*)-(+)-**6** (4.9 mmol, 0.67 g) was treated with 1.88 g (5.9 mmol) of (−)-**1** at rt as described in the general procedure. The reaction was complete in 1 h. Workup and chromatography provided 0.59 g (86%) of the product alcohol, mp 74−75 °C. Analysis of the MCF derivative of the alcohol on a SPB-5 capillary column showed it to be exclusively (1*S*,2*S*)-**7**. The other diastereomer could not be detected by GC. $[\alpha]^{25}_D$ = +21.4 (*c* 3.45, $CHCl_3$). ^1H NMR δ (ppm) ($CDCl_3$): 0.86 (s, 3H, *endo*-CH_3), 0.98 (s, 3H), 1.12−1.70 (m, 6H), 1.37 (s, 1H), 1.75−1.80 (m, 1H), 2.24−2.30 (m, 1H,), 3.63−3.68 (d, 1H). ^{13}C NMR δ (ppm) ($CDCl_3$): 18.12, 19.92, 24.54, 30.52, 33.74, 37.90, 43.90, 48.25, 80.36. Anal. Calcd for $C_9H_{16}O$: C, 77.08; H, 11.51. Found: C, 77.11; H, 11.70.

(b) With (+)-1. (1*S*)-(+)-**6** (5.0 mmol, 0.70 g) was treated with 1.94 g (6.0 mmol) of (+)-**1** at rt as described in the general procedure. The reaction was complete in 12 h. Workup and chromatography provided 0.64 g (91%) of the product alcohol which revealed an isomeric composition of 94% (1*S*,2*R*)-**7** and 6% (1*S*,2*S*)-**7**.

(13) Berson reports that a compound of ∼30% optical purity in chloroform (*c* 4.6) showed a rotation that was too small to measure. Berson, J. A.; Walia, J. S.; Remanick, A.; Suzuki, S.; Reynold-Warnhoff, P.; Willner, D. *J. Am. Chem. Soc.* **1961**, *83*, 3986.

Reduction of (1*R*)-(−)-Camphenilone ((1*R*)-6). (a) With (−)-1. (1*R*)-(−)-**6** (3.6 mmol, 0.50 g) was treated with 1.38 g (4.3 mmol) of (−)-**1** at rt as described in the general procedure. The reaction was complete in 12 h. Workup and chromatography provided 0.42 g (83%) of the product which showed a composition of 93% (1*R*,2*S*)-**7** and 7% (1*R*,2*R*)-**7**.

(b) With (+)-1. (1*R*)-(−)-**6** (4.0 mmol, 0.55 g) was treated with 1.55 g (4.8 mmol) of (+)-**1** at rt as described in the general procedure. The reaction was complete in 1 h. Workup and chromatography provided 0.54 g (97%) of the product alcohol, mp 74−75 °C, analyzed to be exclusively (1*R*,2*R*)-**7**. The other diastereomer could not be detected by GC. $[\alpha]^{25}_D = -20.9$ (*c* 3.02, $CHCl_3$). The ^1H and ^{13}C NMR spectra were identical to those obtained from (1*S*,2*S*)-**7**. Anal. Calcd for $C_9H_{16}O$: C, 77.08; H, 11.51. Found: C, 77.27; H, 11.72.

Reduction of (1*S*)-(−)-Camphor ((1*S*)-8). (a) With (−)-1. (1*S*)-(−)-**8** (6.2 mmol, 0.94 g) was treated with 2.40 g (7.5 mmol) of (−)-**1** at rt as described in the general procedure. The reaction was complete in 0.5 h. Workup and chromatography provided 0.91 g (95%) of the product alcohol. Analysis of the alcohol on a SPB-5 capillary column showed an isomeric composition of 99.7% (1*S*,2*S*)-**9** and 0.3% (1*S*,2*R*)-**9**. Crystallization of this material from hexane provided material of ≥99.9% de, mp 212−214 °C. $[\alpha]^{25}_D = +34.6$ (*c* 5.35, EtOH) which corresponds to ≥99% ee on the basis of the maximum rotation reported in the literature.[14]

(b) With (+)-1. (1*S*)-(−)-**8** (7.5 mmol, 1.14 g) was treated with 2.88 g (9.0 mmol) of (+)-**1** at rt as described in the general procedure. The reaction was complete in 10 h. Workup and chromatography provided 1.12 g (97%) of the product alcohol which showed an isomeric composition of 68% (1*S*,2*R*)-**9** and 32% (1*S*,2*S*)-**9**.

At −25 °C, the reaction was complete in 96 h and workup provided 97% of the product alcohol which showed an isomeric composition of 79% (1*S*,2*R*)-**9** and 21% (1*S*,2*S*)-**9**.

Reduction of (1*R*)-(+)-Camphor ((1*R*)-8). (a) With (−)-1. (1*R*)-(+)-**8** (10.1 mmol, 1.55 g) was treated with 3.92 g (12.2 mmol) of (−)-**1** at rt as described in the general procedure. The reaction was complete in 10 h. Workup and chromatography provided 1.48 g (95%) of the product alcohol which when analyzed on a SPB-5 capillary column showed an isomeric composition of 66% (1*R*,2*S*)-**9** and 34% (1*R*,2*R*)-**9**.

(b) With (+)-1. (1*R*)-(+)-**8** (7.2 mmol, 1.10 g) was treated with 2.78 g (8.7 mmol) of (+)-**1** at rt as described in the general procedure. The reaction was complete in 0.5 h. Workup and chromatography provided 1.05 g (95%) of the product alcohol which showed an isomeric composition of 99% (1*R*,2*R*)-**9** and 1% (1*R*,2*S*)-**9**. Crystallization of this material from hexane provided material of ≥99.9% de. $[\alpha]^{25}_D = -34.26$ (*c* 5.64, EtOH) which corresponds to ≥99% ee on the basis of the maximum rotation reported in the literature.[14]

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Supporting Information Available: ^1H and ^{13}C NMR of compounds (1*S*,2*S*)- and (1*R*,2*R*)-**3**, **5**, and **7** (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(14) Pickard, R. H.; Littlebury, W. O. *J. Chem. Soc.* **1907**, *91*, 1973.