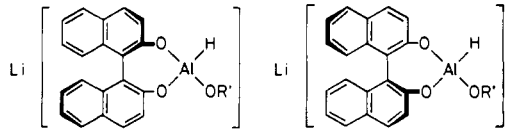
Synthetic Applications of the Enantioselective Reduction by Binaphthol-Modified Lithium Aluminum Hydride Reagents[1]

R. Noyori,* I. Tomino, M. Yamada, and M. Nishizawa

Contribution from the Department of Chemistry, Nagoya University, Chikusa, Nagoya 464, Japan. *Received January 24, 1984*

Abstract: The reduction of prochiral carbonyl substrates with the chiral binaphthol-modified lithium aluminum hydride reagents provides an effective means for preparing alcoholic products of high optical purity. The reaction is applicable to a variety of structurally diverse unsaturated carbonyl compounds such as aromatic ketones, acetylenic ketones, olefinic ketones and aldehydes, etc. Either of the antipodes is obtainable in a predictable manner by choosing the handedness of the auxiliary binaphthol ligand. The utility is exemplified by the efficiently stereocontrolled synthesis of prostaglandin intermediates, some insect pheromones, chiral primary terpenic alcohols, optically active styrene oxide, etc.

Nature is characterized by a highly chiral constitution. High levels of asymmetric reactions mimic the strictly stereocontrolled bioconversions and further provide the most effective way to produce the valuable constituents or their synthetic precursors possessing chiral structures.[2] The asymmetric transformation of simple acyclic substrates is particularly significant, because current only a limited number of methods are available for controlling the stereochemistry of acyclic systems.[3] The bina-

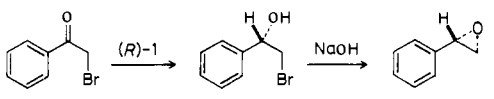


(*R*)-1 (*S*)-1

phthol-modified lithium aluminum hydride reagents (BINAL-Hs) of type **1**,[1] which have been devised through rational stereochemical engineering, offer promise of an asymmetric reduction of carbonyl functions with defined absolute stereochemistry. This paper demonstrates the utility of the highly efficient reduction procedure.

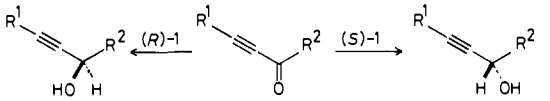
Results

Synthesis of Optically Active Styrene Oxide. The chiral BINAL-H reagent, (*R*)- or (*S*)-**1**, was prepared in situ in tetrahydrofuran (THF) by mixing lithium aluminum hydride ($LiAlH_4$) with equivalent amounts of a simple alcohol (R'OH) and optically pure (*R*)- or (*S*)-binaphthol.[1] Since this reagent has very high enantioface-differentiating ability in the reduction of aromatic ketones, we anticipated the possibility of a simple synthesis of chiral aryloxiranes[4] via the enantioselective reduction. Indeed the reduction of phenacyl bromide (**2**) with 3 equiv of (*R*)-**1** (R^1O = C_2H_5O) at −78 °C gave the bromohydrin **3**,[5] which without purification was treated with aqueous NaOH to form (*S*)-styrene oxide [(*S*)-**4**] in 97% yield and 95% ee.[4i,6]



2 (*S*)-3 (*S*)-4

Enantioselective Reduction of Acetylenic Ketones. Reduction of simple prochiral alkynyl ketones (**5**) with 3 equiv of (*R*)- or (*S*)-**1**[7] at −100 to −78 °C gave after aqueous workup the corresponding propargylic alcohols (**6**) in generally high chemical and optical yields.[8] The results are summarized in Table I. Absolute configurations of the products was determined by the sign of rotation. The optical purities were assayed by high-performance liquid chromatography (HPLC) after conversion of the products to the diastereomeric (*S*)-β,β,β-trifluoro-α-methoxy-α-phenylpropionates (MTPA esters).[9] The most satisfactory results were obtained by using the BINAL-H reagents which contain a simple R'O group such as CH_3O or C_2H_5O. The ketonic substrates bearing an ethynyl group and a longer alkynyl substituent are equally employable. As has been observed in the enantioselective reduction of aromatic ketones,[1] the reaction with (*R*)-BINAL-H tends to produce the *R* propargylic alcohols predominantly, whereas the *S* reducing agent affords the *S* enantiomers as the major product.



(*R*)-6 5 (*S*)-6

a. R^1 = H; R^2 = n-C_5H_{11}
b. R^1 = H; R^2 = n-C_8H_{17}
c. R^1 = H; R^2 = n-$C_{11}H_{23}$
d. R^1 = H; R^2 = $CH(CH_3)_2$
e. R^1 = n-C_4H_9; R^2 = CH_3
f. R^1 = n-C_4H_9; R^2 = n-C_5H_{11}

The optically active propargylic alcohols thus obtained have been recognized as important synthetic intermediates. For example, reaction of (*S*)-**6a** with lithium dimethyl cuprate leads to (*R*)-2,3-nonadiene.[10] A variety of natural products can be derived from the chiral alcohols as well.[11,12] (*S*)-**6a** is a building block

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(5) Brown, H. C.; Pai, G. G. *J. Org. Chem.* **1983**, *48*, 1784.

(6) Use of 1 equiv of **1** resulted in marked decrease in the reaction rate and stereoselectivity.

(7) The hydride attack takes place in the normal stereochemical sense, but the notation of the absolute configuration differs because of peculiarities in the priority assignment.

(8) Preliminary report: Nishizawa, M.; Yamada, M.; Noyori, R. *Tetrahedron Lett.* **1981**, *22*, 247.

(9) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(10) Luche, J. L.; Barreiro, E.; Dollat, J. M.; Crabbé, P. *Tetrahedron Lett.* **1975**, 4615.

(11) For the synthesis of corticoids, see: Johnson, W. S.; Brinkmeyer, R. S.; Kapoor, V. M.; Yarnell, T. M. *J. Am. Chem. Soc.* **1977**, *99*, 8341. Johnson, W. S.; Frei, B.; Gopalan, A. S. *J. Org. Chem.* **1981**, *46*, 1512.

(12) For the synthesis of dendrobatid toxin 251D via (*S*)-1-heptyn-3-ol, see: Overman, L. E.; Bell, K. L. *J. Am. Chem. Soc.* **1981**, *103*, 1851.

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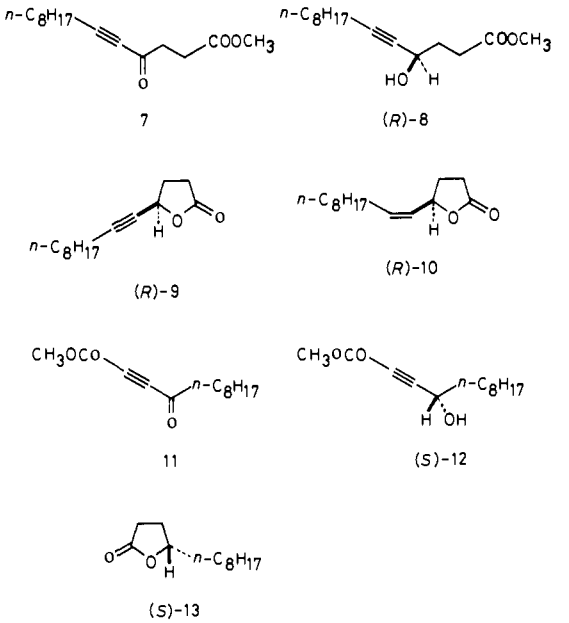
Table I. Enantioselective Reduction of Acetylenic Ketones with BINAL-H (1)[a]

		BINAL-H		carbinol product 6		
entry	ketone 5	R'O	binaphthol confign	chemical yield, %[b]	% ee[c]	confign
1	CH≡CCO-*n*-C_5H_{11}	CH_3O	*S*	87	84	*S*
2	CH≡CCO-*n*-C_5H_{11}	C_2H_5O	*S*	71	84	*S*
3	CH≡CCO-*n*-C_8H_{17}	CH_3O	*S*	80	96	*S*
4	CH≡CCO-*n*-C_8H_{17}	CH_3O	*R*	69	94	*R*
5	CH≡CCO-*n*-C_8H_{17}	C_2H_5O	*S*	74	90	*S*
6	CH≡CCO-*n*-C_8H_{17}	AlO	*R*	64	92	*R*
7	CH≡CCO-*n*-$C_{11}H_{23}$	CH_3O	*S*	90	92	*S*
8	CH≡CCOCH$(CH_3)_2$	CH_3O	*S*	84[d]	57	*S*
9	*n*-C_4H_9C≡CCOCH$_3$	CH_3O	*R*	79	84	*R*
10	*n*-C_4H_9C≡CCO-*n*-C_5H_{11}	CH_3O	*S*	85	90	*S*

[a] Reaction was carried out in THF by using 3 equiv of **1** at −100 °C for 1 h and at −78 °C for 2 h. [b] Isolated yield. [c] Based on HPLC analysis of the derived MTPA esters. [d] GC yield.

for prostaglandin synthesis.[13] (*S*)-**6b** has been used as a key intermediate for the preparation of avenaciolide,[14] an antifungal metabolite, and the pheromone of the dried bean beetle.[15] (*S*)- or (*R*)-**6c** is known to be the synthetic intermediate of the pheromone of the *Vespa orientalis*.[16]

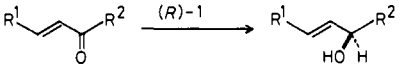
We have further applied the enantioselective reduction to the preparation of some insect pheromones. The reduction of the ynone **7** with (*R*)-**1** (R'O = CH_3O) afforded the acetylenic alcohol (*R*)-**8** in 84% ee (^{1}H NMR analysis of the MTPA derivative[9] in the presence of Eu(fod)$_3$) in 80% yield in addition to a few percent of the lactone derivative **9**. The absolute stereochemistry was substantiated by converting it to the lactone (*R*)-**9** by treatment with *p*-toluenesulfonic acid. The acetylenic bond in (*R*)-**9** was then subjected to the partial hydrogenation over the Lindlar catalyst to give the Japanese beetle pheromone, (*R*)-**10**, in 97% yield.[17] The optical purity of the product was estimated to be



73%, indicating the occurrence of some racemization during the catalytic hydrogenation.

Although the rove beetle pheromone **13** has been synthesized by two groups,[18,19] correlation between the absolute configuration and sign of rotation is still in controversy. When the acetylenic ketone **11** was reduced with (*S*)-BINAL-H [(*S*)-**1**, R'O = CH_3O], there was obtained (*S*)-**12** (87% ee based on HPLC analysis of the 3β-acetoxyetienic acid ester) (80% yield).[21] The absolute configuration was confirmed by its conversion to known levorotatory 2-acetoxydecanoic acid[20] by acetylation followed by ozonolysis. Diimide reduction[22] of (*S*)-**12** followed by exposure to *p*-toluenesulfonic acid gave the *S* lactone **13** in 86[18] or 76% ee[19a] (based on optical rotation using reported literature values) in 57% yield. Thus although the absolute stereochemistry of the natural rove beetle pheromone is still unclear,[23] it must possess an (*S*)-(−) or a (*R*)-(+) relationship.[19a]

Enantioselective Reduction of Olefinic Ketones. Although some high-yield asymmetric reductions have been reported with aromatic[24] and acetylenic ketone substrates,[25] there exist only a limited number of chiral reagents capable of reducing olefinic ketones with high enantioselectivity.[26] We found that reduction of simple prochiral alkenyl ketones of type **14** with the chiral BINAL-H, (*R*)-**1** (R'O = C_2H_5O), proceeds smoothly at low temperature to form the *R* allylic alcohols [(*R*)-**15**] in substantially high en-



14 (R)-15

a, R^1 = *n*-C_4H_9; R^2 = CH_3

b, R^1 = *n*-C_4H_9; R^2 = *n*-C_5H_{11}

c, R^1 = cyclopentyl; R^2 = *n*-C_5H_{11}

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(20) Authentic (*R*)-(+)-2-acetoxydecanoic acid, $[\alpha]_D^{23}$ +7.25° (*c* 1.44, chloroform), was prepared from (*R*)-(+)-3-hydroxy-1-undecyne (**6b**) by an analogous procedure.

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(22) The catalytic hydrogenation over 10% Pd/C resulted in partial racemization to give **13** in 66% ee. It is unlikely to consider the possibility of racemization during diimide reduction. Therefore the discrepancy in the optical purity of **12** and **13** would be mainly ascribed to the uncertainty of rotation measurement.

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Table II. Enantioselective Reduction of Olefinic Ketones with BINAL-H (**1**, R'O = C_2H_5O)[a]

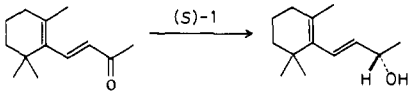
entry	ketone **14**	binaphthol confign in **1**	carbinol product **15** chemical yield, %[b]	% ee	confign
1	(*E*)-*n*-C_4H_9CH=$CHCOCH_3$	*R*	47[c]	79	*R*
2	(*E*)-*n*-C_4H_9CH=$CHCO$-*n*-C_5H_{11}	*R*	91	91	*R*
3	(*E*)-*cyclo*-C_5H_9CH=$CHCO$-*n*-C_5H_{11}	*R*	91	92	*R*

[a] Reaction was carried out in THF using 3 equiv of **1** at −100 °C for 1 h and then at −78 °C for 2 to 15 h. [b] Isolated yield. [c] This low yield probably depends on volatility of the product. GC analysis of the crude extract showed the existence of neither starting material nor any by-products.

antiomeric excess (Table II). Diimide reduction of the unsaturated alcohol (*R*)-**15a** gave 2-octanol possessing the known absolute configuration and optical rotation.[27] The products (*R*)-**15b** and (*R*)-**15c** werre transformed to (*R*)-2-acetoxyheptanal by acetylation and subsequent ozonolysis, and compared with an authentic sample by ^{1}H NMR with the aid of a chiral lanthanide shift reagent, tris[3-heptafluorobutyryl-(+)-camphorato]europium(III) [Eu(hfbc)$_3$]. In the reduction of the β-substituted alkenones **14a–c**, no 1,4-addition, forming after aqueous workup the saturated ketones, was observed. However, this undesired pathway became significant with β-unsubstituted enones such as 1-octen-3-one. Such behavior of olefinic ketones is in contrast to that of acetylenic ketone substrates which produce only secondary alcohols leaving the triple bond intact. It should be added that simple cyclic enones such as 2-cyclohexenone, 3-methyl-2-cyclohexenone, 2-isopropylidenecyclohexanone, etc., resisted BINAL-H reduction under standard reaction conditions.

The optically active allylic alcohols are important compounds in their own right and also serve as versatile intermediates for construction of chiral organic frameworks through, for example, the Claisen rearrangement,[28,29] the Pd(II)-assisted sigmatropic reaction,[30] or intramolecular S_N2' displacement of the derivatives.[31] The BINAL-H reduction of an enone was successfully applied to the stereoselective introduction of a hydroxyl group into the cholesterol sidechain at C-24, -25, and -26 positions.[32]

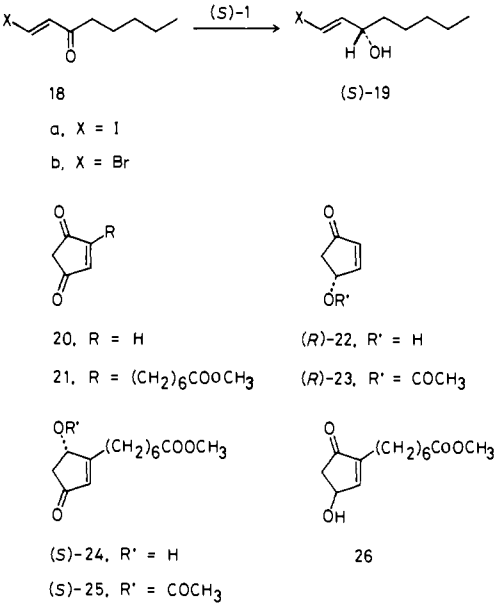
When β-ionone (**16**), a conjugated dienone, was exposed to 3 equiv of (*S*)-**1** (R'O = C_2H_5O) at −100 to −78 °C, smooth reaction took place to produce (*S*)-β-ionol (**17**)[33] in nearly 100% ee (based



16 (S)-17

on the Eu(hfbc)$_3$-aided ^{1}H NMR analysis of the acetate) in 87% yield. The absolute stereochemistry was established by the chemical correlation with 2-isobutyroxypropanal of known absolute configuration.[34]

The BINAL-H reduction provides an extremely powerful tool for prostaglandin (PG) synthesis.[35] First, this procedure allows the efficiently enantioselective preparation of building units for the conjugate addition approaches.[36] When the iodovinyl ketone **18a** was treated with 3 equiv of (*S*)-**1** (R'O = C_2H_5O) at −100 to −78 °C, there was produced the PG ω-chain alcohol possessing *S* configuration, (*S*)-**19a**, in 95% yield (97% enantiomerically pure[37d]). In a like manner, the highly selective reduction was achieved with the bromovinyl ketone **18b**, forming (*S*)-**19b** in 96% ee and in 96% yield.[38] The carbinols (*S*)-**19a** and (*S*)-**19b** exhibited similar CD patterns and showed positive Cotton effects in the 215- to 224-nm region. This straightforward chemical transformation appears to be much more effective than the microbiological reduction of **19a** (10% chemical yield and 77% optical yield)[37c] or classical resolution of a racemate.[37d] The requisite



cyclopentenone block is also obtainable in optically active form by this method. Thus when 4-cyclopentene-1,3-dione (**20**) was exposed to 1.5 equiv of (*S*)-**1** (R'O = C_2H_5O) at −100 °C, rapid reaction took place to give (*R*)-4-hydroxy-2-cyclopentenone [(*R*)-**22**][39] accompanied by some unidentified polymeric material.

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(38) Optically pure (*S*)-**19a** and (*S*)-**19b** were prepared by optical resolution according to the Fried's procedure.[37d]

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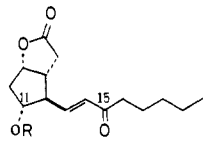
Acetylation of **22** by acetic anhydride and pyridine led to the acetate, (*R*)-**23**, in 94% ee (65% yield based on **20**), which was evaluated by the Eu(hfbc)$_3$-aided NMR analysis. The (*S*)-BINAL-H reduction of the related cyclopentenedione **21** proceeded only sluggishly but, interestingly, gave regio- and enantioselectively the hydroxy ketone, (*S*)-**24** (91% ee as estimated by Eu(hfbc)$_3$-shifted NMR of the acetate (*S*)-**25**; 26% yield, or 76% yield after correction for the recovery of **21**). Only a trace amount of the regioisomer **26** was formed.[40] The BINAL-H reduction has played a key role in recent realization of the convergent entry to PGs via three-component coupling processes; the combination of the (*R*)-4-hydroxy-2-cyclopentenone unit with the *S* vinylic halides via the organocopper intermediates[41] followed by aldol trapping technique leads to various primary PGs and prostacyclin having the correct natural configurations.[42]

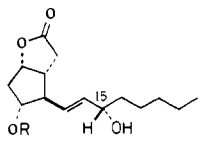
The BINAL-H asymmetric reduction also brought the Corey PG synthesis[43] to completion. A characteristic feature of this widely used route is the complete stereochemical control of the functionalized cyclopentane framework achieved by utilizing the bicyclic lactone intermediates such as **27–29**. The only remaining problem was the stereoselective conversion of the ω-enone side chain to the allylic alcohols of the correct 15*S* (PG numbering) configuration. Despite tremendous efforts so far made, any perfect solution has not yet been offered. Previous attempts to differentiate the carbonyl α and β faces rely mainly on the diastereo-directing effects of the C-11 functional group, and most reactions have been tried with *bulky* reducing agents.[44] On the other hand, in light



27, R = $COCH_3$

28, R = THP

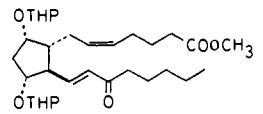
29, R = H



30, R = $COCH_3$

31, R = THP

32, R = H



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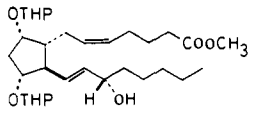

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of the excellent enantioselectivity, as high as 92%, observed in the reaction of the model substrate **14c**, we anticipated that the use of the *chiral* BINAL-H reagent could solve this long-standing problem. Indeed the reduction of the lactonic enones, **27–29**, with 3 equiv of (*S*)-**1** (R'O = C_2H_5O)[1] at −100 to −78 °C was effected with exceptionally high stereoselectivity (>99%) to afford the desired 15*S* alcohols **30–32**. In a similar manner, the reaction of the monocyclic substrate **33** led to the PG $F_{2\alpha}$ derivative **34**. The stereoisomeric ratios were determined by the standard HPLC analysis. The results are summarized in Table III. The general tendency is not affected by the nature of the 11-hydroxy blocking groups or whether the hydroxyl group is blocked or not.

Table III. Diastereoselective Reduction of PG Intermediates by BINAL-H (**1**, R'O = C_2H_5O)[a]

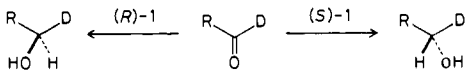
			alcoholic product	
entry	ketone	binaphthol confign in **1**	% yield[b]	15*S*/15*R* ratio[c]
1	**27**	*S*	95	99.4:0.6
2	**28**	*S*	96	99.5:0.5
3	**28**	*R*	93	32:68
4	**29**	*S*	97[d]	100:0
5	**33**	*S*	88[e]	100:0

[a] Reaction was carried out in THF using the optically active ketone and 3 equiv of **1** at −100 °C for 2 h and at −78 °C for 2 h. [b] Isolated yield. [c] Determined by HPLC analysis. [d] Yield based on 42% conversion. [e] Yield based on 62% conversion.

In the reduction of the PG intermediates, the sense and degree of the stereoselection proved to depend on the configuration of the BINAL-H reducing agent **1**. The *S* reagent reduces the *optically active, chiral* enone **28** (a mixture of diastereomers due to the THP group), for example, with very high stereoselectivity, 15*S*/15*R* = 99.5:0.5 (Table III, entry 2), whereas reduction of the same substrate with the *R* reagent exhibited only moderate 15*R* selection, 15*S*/15*R* = 32:68 (entry 3). These values are to be compared with the enantioselectivity, 96:4, observed in the reduction of the prototype, *achiral* enone **14c** (Table II). The normal *S*/*S* or *R*/*R* reagent/product configurational correlation indicates that the reduction of **28** is fundamentally enantioselective in nature, but the level of the differentiation is profoundly affected by the chiral lactone moiety. The energy difference of the diastereomeric transition states ($\Delta\Delta G^{\ddagger}$) in the enantioselective reduction of the prochiral enone **14c** is 1.1 kcal/mol at −100 °C. The chiral cyclopentane assembly in **28** decreases the kinetic energy difference by 0.8 kcal/mol in the (*R*)-BINAL-H reduction and increases the bias by 0.7 kcal/mol in the reduction with the *S* reagent. Thus the successful generation of the 15*S* configuration is a result of the double stereodifferentiation.[45,46]

Enantioselective Synthesis of Chiral Primary Alcohols. Isotopically labeled chiral primary alcohols serve as key substances in mechanistic studies of various chemical and biochemical transformations.[47] The BINAL-H reduction of deuterium-labeled aldehydes allows simple synthesis of such compounds.[48,49]

When geranial-*1-d* (**35a**)[50] in THF was exposed to 3 equiv of (*S*)-**1** (R'O = C_2H_5O) at −100 °C, rapid reaction took place to afford dextrorotatory geraniol-*1-d* (**36a**) in 91% yield. The



(*R*)-36 35 (*S*)-36

a, R = (*E*)-CH=C(CH_3)CH_2CH_2CH=C(CH_3)$_2$

b, R = (*Z*)-CH=C(CH_3)CH_2CH_2CH=C(CH_3)$_2$

c, R = (*E,E*)-CH=C(CH_3)CH_2CH_2CH=C(CH_3)CH_2CH_2CH=C(CH_3)$_2$

d, R = (*Z,E*)-CH=C(CH_3)CH_2CH_2CH=C(CH_3)CH_2CH_2CH=C(CH_3)$_2$

e, R = C_6H_5

absolute configuration of the dominant enantiomer was unambiguously substantiated to be *S* by comparison with the authentic

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(44) A 15*S*/15*R* ratio of 92:8 was recorded in the reaction of the enone possessing a *p*-phenylphenylcarbamoyl blocking group and a bulky trialkylborohydride reagent [Corey, E. J.; Becker, K. B.; Varma, R. K. *J. Am. Chem. Soc.* **1972**, *94*, 8616] or reduction of 11-unprotected hydroxy enone **29** with diisobutylaluminum 2,6-di-*tert*-butyl-4-methylphenoxide [Iguchi, S.; Nakai, H.; Hayashi, M.; Yamamoto, H. *J. Org. Chem.* **1979**, *44*, 1363].

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(46) For a similar double asymmetric differentiation see ref 29a.

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Table IV. Enantioselective Reduction of Deuterium-Labeled Aldehydes with BINAL-H (**1**, R'O = C_2H_5O)[a]

entry	aldehyde **35**	binaphthol confign in **1**	carbinol product **36**[b] chemical yield, %[c]	% ee[d]	confign
1	geranial-*1-d*	*S*	91	91,[e] 84	*S*
2	neral-*1-d*	*S*	90	72	*S*
3	(*E*,*E*)-farnesal-*1-d*	*R*	91	88	*R*
4	(*Z*,*E*)-farnesal-*1-d*	*R*	93	82	*R*
5	benzaldehyde-*1-d*	*R*	59, 100[f]	87	*R*

[a] Reaction was carried out in THF using 2.5 equiv of **1** at −100 °C for 2 to 3 h. The reaction was rapid and the starting aldehyde was consumed readily (100% conversion). [b] Deuterium content was <99%. [c] Isolated yield. [d] Based on ^1H NMR in the presence of $Eu(hfbc)_3$. [e] Based on optical rotation. [f] GC yield.

S alcohol, prepared by reduction of the deuterio aldehyde **35a** with yeast alcohol dehydrogenase and NADH.[51] The relationship between the absolute configuration and optical properties of chiral geraniol-*1-d* was thus clarified for the first time. The optical purity of the synthetic product was assayed to be 91% by optical rotation measurement or 84% by ^1H NMR analysis with $Eu(hfbc)_3$.

Similarly the BINAL-H asymmetric reduction was successfully applied to the synthesis of optically active deuterium-labeled nerol (**36b**), stereoisomeric farnesols (**36c** and **36d**), and benzyl alcohol (**36e**).[52] The results are summarized in Table IV. The absolute configurations of **36b–d** were deduced from the sign of rotation and behavior of ^1H NMR signals due to the C-1 protons in the presence of the $Eu(hfbc)_3$ shift reagent, where signals due to the pro-*S* protons are assumed to move downfield faster as is observed in the spectrum of **36a**.[53] Thus the *S* reducing agent affords the alcohols enriched by the *S* enantiomer, and the *R* reagent produces the *R* alcohols preferentially. Although the optical purities of the synthetic products are lower than those of the enzymatically derived alcohols, the chemical method is even more convenient for the preparation of the chiral alcohols in large quantity.

Conclusion

The BINAL-H reduction is applicable to a wide range of unsaturated carbonyl substrates and proceeds in satisfactory chemical and optical yields. The procedure is operationally simple. In addition, both enantiomers of binaphthol are easily available in optically pure form, and, therefore, this method allows the synthesis of either the *S* or *R* carbonols with equal ease from the corresponding carbonyl compounds by choosing handedness of the chiral ligand. The chiral auxiliary ligand can be recovered from the reaction mixture in high yield (>90%) in reusable form without any racemization. Thus this newly introduced method fully satisfies the requirements of being a valuable asymmetric reduction. The examples described above would sufficiently display the general utility.

Experimental Section

General. Infrared (IR) spectra were recorded on a JASCO IRA-1 grating spectrometer. Mass spectra were performed on a JEOLCO JMS-D10 spectrometer. Proton nuclear magnetic resonance (^1H NMR) spectra were determined on a JEOLCO JNM-PMX-60 (60 MHz), Varian NV-21 (90 MHz), Varian HA-100 (100 MHz), or JEOLCO FX-100 (100 MHz, Fourier transform mode) instrument. The chemical shifts are expressed in parts per million downfield fron internal tetramethylsilane (δ = 0), and signal patterns are indicated as s, single; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak. Melting-point determinations were performed by using a Yanagimoto micro melting-point apparatus and the data are uncorrected. Optical rotations were recorded on a JASCO DIP-4 digital polarimeter as neat sample in a 0.01-dm cell or as a solution in a 1-dm cell. For thin-layer chromatography (TLC) analysis precoated silica gel plates (E. Merck 60 F_{254}, 0.2 mm) were used. Volatile products were purified by bulb-to-bulb distillation using a Büchi Kugelrohr apparatus and preparative gas chromatography (GC) on a Varian 1700 instrument with a column of 5% FFAP on Chromosorb (9.5 × 2000 mm) using helium as carrier gas. Preparative column chromatography was done on E. Merck Art 7734 (70–230 mesh) or Fuji-Devison BW-80 (80–200 mesh) silica gel. High-performance liquid chromatgraphy (HPLC) analyses were carried out on a Waters 6000A instrument with a JASCO UVIDEC-100 UV detector and a JASCOSIL SS-05 column or a JASCO trirotor instrument with a Waters μ-Porasil column and a Shodex RI detector.

Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl. Lithium aluminum hydride ($LiAlH_4$, Metallogesellschaft) was used as a clear THF solution, and its concentration was determined by measuring the quantity of hydrogen gas evolved by dropwise addition of water. Methanol and ethanol for the modification of $LiAlH_4$ were distilled from magnesium. Optically pure (*S*)-(−)-2,2'-dihydroxy-1,1'-binaphthyl or (*S*)-(−)-binaphthol was prepared according to the Cram's procedure:[54] mp 207–208 °C; $[\alpha]^{21}_D$ −38.0° (*c* 1.00, THF). The *R* enantiomer had mp 207–208 °C; $[\alpha]^{21}_D$ +37.1° (*c* 1.00, THF). Binaphthol is optically stable under neutral or aprotic conditions but may racemize upon exposure to an acid or base in protic media.[54] Therefore, one should be careful in the workup of the reaction mixture to recover the auxiliary in reusable form. The deuterium-labeled aldehydes **35a–e** were prepared by the reported procedure[50] and purified by preparative GC. Since the ^1H NMR spectra showed no signals due to the aldehydic protons, the deuterium content was considered to be 100% within the limits of NMR accuracy.

All asymmetric reductions werre conducted under argon atmosphere in a flame-dried, long-necked flask equipped with a rubber septum. (*R*)- or (*S*)-BINAL-H reagents [(*R*)- or (*S*)-**1** (R'O = CH_3O or C_2H_5O)] were prepared in THF as described previously.[1] *If a large quantity of precipitate separates out, one should repeat the preparation from the beginning.* The freshly prepared reagent was stirred for 30 min at room temperature before use. Identification of the known products was done by IR and ^1H NMR analyses. In order to determine the optical purity, in some cases, the alcoholic products were converted to the (*S*)-β,β,β-trifluoro-α-methoxy-α-phenylpropionates (MTPA esters) according to Mosher's procedure[9] by using (*S*)-MTPA supplied from Aldrich (99%+) or to 3β-acetoxyetienate according to Woodward's procedure.[21] A chiral NMR shift reagent, tris[heptafluorobutyryl-(+)-camphorato]europium-(III) [$Eu(hfbc)_3$] (Aldrich), was also employed for deterimining optical purity of the products.

Asymmetric Synthesis of Optically Active Styrene Oxide (4). α-Bromoacetophenone (**2**) (360 mg, 1.81 mmol) in THF (4 mL) was added dropwise over a period of 3 min at −78 °C to the BINAL-H reagent, (*R*)-**1** (R'O = C_2H_5O), prepared by mixing $LiAlH_4$ (1.17 M THF solution, 4.60 mL, 5.38 mmol), ethanol (1.00 M THF solution, 5.38 mL, 5.38 mmol), and (*R*)-(+)-binaphthol (1.54 g, 5.38 mmol) in THF (8 mL). The mixture was stirred for an additional 2 h at this temperature and quenched by addition of methanol (1 mL) at −78 °C. The mixture was stirred with ether (10 mL) and water (0.5 mL) at room temperature for 10 min, treated with anhydrous magnesium sulfate, and filtered through a cotton–Celite pad. The filtrate was evaporated, dissolved in benzene (30 mL), and washed by 3 N NaOH solution (30 mL × 3) to remove binaphthol. The organic layer was mixed with 3 N NaOH (30 mL) and stirred for 2 h at room temperature. The organic layer was dried, filtered, and concentrated. Bulb-to-bulb distillation [80–90 °C (18 mmHg)] gave pure (*S*)-(−)-styrene oxide [(*S*)-**4**] (211 mg, 97%) as a colorless oil: α^{23}_D −0.335° (neat, *l* = 0.01), 95% ee based on the known maximum rotation (lit.[4i] $[\alpha]^{25}_D$ +35.17° (neat)).

Asymmetric Reduction of Alknynyl Ketones. A. 1-Octyn-3-one (5a). A solution of 1-octyn-3-one (**5a**) (100 mg, 0.807 mmol) in THF (1 mL) was added dropwise over a period of 10 min at −100 °C to (*S*)-**1** (R'O

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= CH_3O) prepared by mixing $LiAlH_4$ (0.79 M THF solution, 3.06 mL, 2.42 mmol), methanol (1.00 M THF solution, 2.42 mL, 2.42 mmol), and (*S*)-(−)-binaphthol (629 mg, 2.42 mmol) in THF (4.5 mL). The mixture was maintained at −100 °C for 1 h and at −78 °C for 2 h. The excess reducing agent was destroyed by addition of methanol (0.2 mL) at −78 °C, and to this was added water (0.2 mL) and ether (10 mL). The mixture was stirred for 10 min at room temperature. The whole mixture was treated with anhydrous magnesium sulfate and filtered through a cotton–Celite pad, and the filtrate was concentrated in vacuo. Column chromatography on silica gel (20 g) using a 5:1 mixture of pentane and ether as eluent gave oily 1-octyn-3-ol (**6a**) (88 mg, 87%) and recovered crystalline (−)-binaphthol (620 mg). Bulb-to-bulb distillation [120–130 °C (25 mmHg)] of **6a** followed by preparative GC (130 °C) provided a pure sample: $[\alpha]^{21}_D$ −18.8° (*c* 1.30, ether), 84% ee based on HPLC analysis of the MTPA esters. Analysis (99.5:0.5 petroleum ether–acetonitrile, flow rate 3 mL/min) gave peaks due to the ester of (*S*)-**6a** (t_R 4.3 min) and the ester of (*R*)-**6a** (t_R 5.1 min) in 92.2: 7.8 ratio.

B. 1-Undecyn-3-one (5b). A solution of the ketone **5b** (50 mg, 0.3 mmol) in THF (2 mL) was treated at −100 °C for 1 h and at −78 °C for 2 h with (*S*)-**1** (R′O = CH_3O) prepared from $LiAlH_4$ (0.79 M THF solution, 1.14 mL, 0.90 mmol), methanol (1.00M THF solution, 0.90 mL, 0.90 mmol), and (*S*)-(−)-binaphthol (258 mg, 0.90 mmol) in THF (3 mL). Quenching with methanol followed by extractive workup and column chromatography on silica gel gave (*S*)-(−)-1-undecyn-3-ol [(*S*)-**6b**] (40 mg, 80%) and binaphthol (240 mg). An analytical sample of (*S*)-**6b** was obtained by bulb-to-bulb distillation [130–140 °C (5 mmHg)] followed by preparative GC (170 °C): $[\alpha]^{23}_D$ −16.5° (*c* 0.86, ether), 96% ee based on HPLC analysis of the MTPA esters (99.5:0.5 petroleum ether–acetonitrile, flow rate 3 mL/min) which afforded peaks of the esters of (*S*)-**6b** (t_R 3.6 min, 97.8%) and (*R*)-**6b** (t_R 4.1 min, 2.2%). Anal. ($C_{11}H_{20}O$) C, H.

C. 1-Tetradecyn-3-one (5c). A solution of the ketone **5c** (100 mg, 0.48 mmol) in THF (2 mL) was treated at −100 °C for 1 h and at −78 °C for 2 h with (*S*)-**1** (R′O = CH_3O) prepared from $LiAlH_4$ (0.79 M THF solution, 1.83 mL, 1.44 mmol), methanol (1.00 M THF solution, 1.44 mL, 1.44 mmol), and (*S*)-(−)-binaphthol (412 mg, 1.44 mmol) in THF (4 mL). Quenching with methanol followed by extractive workup and column chromatography on silica gel gave (*S*)-(−)-1-tetradecyn-3-ol [(*S*)-**6c**] (91 mg, 90%) and binaphthol (390 mg). Bulb-to-bulb distillation [135–145 °C (3 mmHg)] of the former followed by preparative GC (195 °C) gave an analytical sample: $[\alpha]^{23}_D$ −13.8° (*c* 0.76, ether). HPLC analysis of the MTPA esters (99.5:0.5 petroleum ether–acetonitrile, flow rate 3 mL/min) exhibited peaks due to the esters of (*S*)-**6c** (t_R 3.4 min, 96.0%) and (*R*):-**6c** (t_R 3.9 min, 4.0%) indicating 92% optical purity. Anal. ($C_{14}H_{26}O$) C, H.

D. 4-Methyl-1-pentyn-3-one (5d). A solution of **5d** (288 mg, 3.00 mmol) in THF (3 mL) was treated at −100 °C for 1 h and at −78 °C for 2 h with (*S*)-**1** (R′O = CH_3O) generated by mixing $LiAlH_4$ (1.32 M THF solution, 6.82 mL, 9.00 mmol), methanol (1.03 M THF solution, 8.74 mL, 9.00 mmol), and (*S*)-(−)-binaphthol (2.57 g, 9.00 mmol) in THF (12 mL). Quenching with methanol followed by workup gave a crude product, from which binaphthol (2.55 g) was recovered by recrystallization from pentane. The mother liquor was concentrated to give an oil (271 mg) which contained (*S*)-(−)-4-methyl-1-pentyn-3-ol [(*S*)-**6d**] as the major component (84% yield by GC analysis with added methyl decanoate as internal standard). Preparative GC (140 °C) afforded an analytical sample: $[\alpha]^{23}_D$ −15.4° (*c* 0.81, ether), −9.1° (*c* 0.11, dioxane). HPLC analysis of the MTPA esters (99:1 petroleum ether–acetonitrile, flow rate 3 mL/min) gave peaks arising from the esters of (*S*)-**6d** (t_R 4.1 min, 78.5%) and (*R*)-**6d** (t_R 3.5 min, 21.5%), indicating optical purity of 57%.

E. 3-Octyn-2-one (5e). A solution of the ynone **5e** (124 mg, 1.00 mmol) was treated at −100 °C for 1 h and at −78 °C for 20 h with (*R*)-**1** (R′O = CH_3O) generated by mixing $LiAlH_4$ (0.66 M THF solution, 4.55 mL, 3.00 mmol), methanol (1.03 M THF solution, 2.93 mL, 3.00 mmol), and (*R*)-(+)-binaphthol (858 mg, 3.00 mmol). Quenching with methanol followed by workup gave a crude material, from which binaphthol (805 mg) was recovered by recrystallization from pentane. The mother liquor was concentrated and chromatographed on a silica gel column to afford (*R*)-(+)-3-octyn-2-ol [(*R*)-**6e**] (100 mg, 79%). Bulb-to-bulb distillation [140–150 °C (30 mmHg)] afforded an analytical sample: $[\alpha]^{23}_D$ +33.0° (*c* 1.62, ether). HPLC analysis of the MTPA esters (99.5:0.5 petroleum ether–acetonitrile, flow rate 1 mL/min) giving peaks of the esters of (*R*)-**6e** (t_R 6.6 min, 92%) and (*S*)-**6e** (t_R 6.0 min, 8%) indicating an optical purity of 84%. Anal. ($C_8H_{14}O$) C, H.

F. 5-Dodecyn-7-one (5f). A solution of **5f** (100 mg, 0.56 mmol) in THF (1 mL) was treated at −100 °C for 1 h and at −78 °C for 2 h with (*S*)-**1** (R′O = CH_3O) formed from $LiAlH_4$ (0.79 M THF solution, 2.11 mL, 1.67 mmol), methanol (1.00 M THF solution, 1.67 mL, 1.67 mmol), and (*S*)-(−)-binaphthol (477 mg, 1.67 mmol) in THF (5 mL). Column chromatography of the crude product on silica gel afforded (*S*)-(−)-5-dodecyn-7-ol [(*S*)-**6f**] (86 mg, 85%). Bulb-to-bulb distillation [120–135 °C (2 mmHg)] gave an oily analytical sample: $[\alpha]^{21}_D$ −12.3° (*c* 1.35, ether), −2.6° (*c* 0.50, chloroform). HPLC analysis of the MTPA esters (99.5:0.5 petroleum ether–acetonitrile, flow rate 1 mL/min) showing peaks arising from the esters of (*S*)-**6f** (t_R 8.6 min, 95%) and (*R*)-**6f** (t_R 9.9 min, 5%) indicated the optical purity to be 90%. Anal. ($C_{12}H_{22}O$) C, H.

Synthesis of the Japanese Beetle Pheromone [(*R*)-10]. A. Asymmetric Reduction of Methyl 4-Oxo-5-tetradecynoate (7). A solution of the ynone **7** (252 mg, 1.00 mmol) in THF (4 mL) was treated at −100 °C for 1 h and at −78 °C for 2 h with (*R*)-**1** (R′O = CH_3O) prepared from $LiAlH_4$ (0.79 M THF solution, 3.80 mL, 3.00 mmol), methanol (1.00 M THF soluiton, 3.00 mL, 3.00 mmol), and (*R*)-(+)-binaphthol (858 mg, 3.00 mmol). Methanol quenching, extractive workup, and column chromatography on silica gel (20 g) using a 2:1 mixture of petroleum ether and either gave binaphthol (844 mg) and (*R*)-methyl 4-hydroxy-5-tetradecyn-4-olide [(*R*)-**8**] (208 mg, 80%) which contained ca. 10% of the corresponding lactonic product: IR (neat) 3400 (OH), 2230 (C≡C), 1740 (C=O) cm^{-1}; ^1H NMR (CCl_4) 0.91 (t, *J* = 7 Hz, CH_3CH_2), 3.63 (s, OCH_3), 4.33 (t, *J* = 7 Hz, *CH*OH). The optical purity was estimated to be 84% on the basis of ^1H NMR analysis of the MTPA esters; the spectrum taken with 0.3 equiv of $Eu(fod)_3$ in $CDCl_3$ showed the methoxyl signal of the (*R*)-**8** ester at δ 4.32 (92%) and that of the *S* ester at δ 4.20 (8%). This crude hydroxy ester was subjected directly to the subsequent lactonization.

B. (*R*)-(−)-5-Tetradecyn-4-olide [(*R*)-9]. A mixture of (*R*)-**8** (84% ee) (254 mg, 1.00 mmol) and *p*-toluenesulfonic acid (10 mg) in benzene was heated at reflux for 1 h. The concentrated material was chromatographed on a silica gel column (20 g) using a 15:1 mixture of dichloromethane and ether and distilled by a Kugelrohr apparatus [170–180 °C (4 mmHg)] to give (*R*)-(−)-**9** (203 mg, 92%) as a colorless oil: $[\alpha]^{26}_D$ −3.5° (*c* 0.86, chloroform), 84% ee (lit.[17c] $[\alpha]^{22}_D$ −4.1° (*c* 1.66, chloroform)). The IR and ^1H NMR data were identical with those reported.[17c]

C. (*R*,*Z*)-(−)-5-Tetradecen-4-olide [(*R*)-10]. A solution of (*R*)-**9** (84% ee) (82 mg, 0.36 mmol) in ether (20 mL) was stirred with Lindlar catalyst (40 mg) under atmospheric pressure of hydrogen at room temperature for 12 h. The concentrated filtrate was subjected to column chromatography on silica gel (10 g, dichloromethane) and subsequent bulb-to-bulb distillation [160–170 °C (4 mmHg)] to give (*R*)-(−)-**10** (81 mg, 97%) as a colorless oil: $[\alpha]^{20}_D$ −51.2° (*c* 3.00 chloroform), 73% ee based on the highest reported value of optical rotation (lit.[17a–c,18] $[\alpha]^{25}_D$ −70.0° (*c* 6.4, chloroform)).

Synthesis of the Rove Beetle Pheromone [(*S*)-13]. A. Asymmetric Recution of Methyl 4-Oxo-2-dodecynoate (11). A solution of the ynone **11** (224 mg, 1.00 mmol) in THF (3 mL) was treated at −100 °C for 2 h and at −78 °C for 1 h with (*S*)-**1** (R′O = CH_3O) formed from $LiAlH_4$ (0.66 M THF solution, 2.83 mL, 3.00 mmol), methanol (1.03 M THF solution, 2.91 mL, 3.00 mmol), and (*S*)-(−)-binaphthol (858 mg, 3.00 mmol) and quenched by methanol. Workup and recrystallization from hexane gave back binaphthol (811 mg) as crystals. The mother liquor was subjected to column chromatography on silica gel (20 g) using a 3:1 mixture of petroleum ether and ether to give (*S*)-(−)-methyl 4-hydroxy-3-dodecynoate [(*S*)-**12**] (180 mg, 80%) as a colorless oil. Bulb-to-bulb distillation [150–160 °C (0.5 mmHg)] afforded a pure sample: $[\alpha]^{21}_D$ −6.1° (*c* 1.08, ether); IR (neat) 3400 (OH), 2250 (C≡C), 1740 (C=O) cm^{-1}; ^1H NMR (CCl_4) 0.90 (t, *J* = 7 Hz, CCH_3), 3.65 (s, OCH_3), 4.40 (t, *J* = 5 Hz, *CH*OH).

A solution of (*S*)-**12** (12 mg) in CCl_4 was added to a solution of 3β-acetoxyetienoyl chloride (25 mg) and triethylamine (20 mg) in CCl_4 (1 mL), and the mixture was stirred at room temperature for 1 h.[21] Aqueous workup followed by silica gel column chromatography using a 3:1 mixture of petroleum ether and ether gave a diastereomeric mixture of the 3β-acetoxyetienate derivatives. HPLC analysis of this mixture (25:1 hexane–THF, flow rate 2 mL/min) gave peaks of the esters of (*S*)-**12** and (*R*)-**12** (t_R 8.3 min and 10.1 min, respectively) in 93.5:6.5 ratio.

B. Determination of the Absolute Configuration of (−)-Methyl 4-Hydroxy-2-dodecynoate (12). This hydroxy ester ($[\alpha]^{21}_D$ −6.1° (*c* 1.08, ether), 87% ee, 50 mg) was converted to its acetate by treatment with acetic anhydride (0.15 mL) and pyridine (0.2 mL). To this acetate in dichloromethane (1 mL) kept at −78 °C was added a cooled (−78 °C), saturated solution of ozone in dichloromethane (0.04 M, 11.5 mL, 0.46 mmol), and the mixture was stirred at 0 °C for 1 h. The acidic products were extracted by 5% sodium hydrogen carbonate solution (20 mL × 3) and the combined aqueous extracts were acidified by concentrated HCl. The concentrated ether extracts were dried and chromatographed on a silica gel column using a 1:2 mixture of petroleum ether and ether to afford (−)-2-acetoxydecanoic acid (14 mg, 32%) as a colorless syrup,

$[\alpha]^{23}_D$ −7.79° (*c* 0.68, chloroform).

Authentic (*R*)-(+)-1-undecyn-3-ol [(*R*)-**6b**] (94% ee, 50 mg) was formed through acetylation followed by ozonolysis, $[\alpha]^{23}_D$ +7.25° (*c* 1.44, chloroform). Thus the absolute configuration of (−)-**12** was established to be *S*.

C. **Rove Beetle Pheromone [(*S*)-13].** To a stirred suspension of potassium azodicarboxylate (86 mg, 0.44 mmol) and (*S*)-**12** (87% ee, 20 mg, 0.089 mmol) in methanol (6 mL) was dropwise added acetic acid (132 mg, 2.5 mmol) at room temperature. After stirring for 3 h, the mixture was evaporated at reduced pressure to removal methanol. After addition of sodium carbonate solution, the mixture was extracted with ether. The concentrated extract was dissolved in benzene (20 mL) containing *p*-toluenesulfonic acid (4 mg) and heated at reflux for 1 h. The concentrated material was chromatographed on a silica gel column (10 g, dichloromethane)e to give (*S*)-(−)-**13** (10 mg, 57%) as a colorless oil. Bulb-to-bulb distillation [150–160 °C (3 mmHg)] provided an analytical sample: $[\alpha]^{22}_D$ −28.7° (*c* 0.30, methanol), 86% ee (lit.[18] $[\alpha]^{22.5}_D$ +33.3° (*c* 0.73, methanol)) or 76% ee (lit.[19a] *R* isomer, $[\alpha]^{25}_D$ +37.7° (*c* 1.0, methanol)); IR (neat) 1780 cm^{-1} (C=O); ^1H NMR (CCl_4) 0.90 (t, *J* = 7 Hz, CH_3), 1.1–1.9 (m, CH_2), 2.1–2.6 (m, CH_2), 4.38 (m, >CHO–).

Asymmetric Reduction of Alkenyl Ketones. A. (*E*)-1-Cyclopentyl-1-octen-3-one (14c). A solution of the enone **14c** (200 mg, 1.00 mmol) in THF (2 mL) was added dropwise at −100 °C to (*R*)-**1** (R'O = C_2H_5O) prepared from $LiAlH_4$ (1.99 M THF solution, 1.00 mL, 1.99 mmol), ethanol (1.00 M THF solution, 2.00 mL, 2.00 mmol), and (*R*)-(+)-binaphthol (572 mg, 2.00 mmol) in THF (3 mL). The mixture was stirred for an additional 1 h at −100 °C and at −78 °C for 2 h. Methanol (0.2 mL) and water (1 mL) were added at −78 °C, and the mixture was warmed to room temperature. This was stirred with ether for 1 h and then treated with anhydrous magnesium sulfate and filtered. When the filtrate was evaporated and then diluted by hexane, binaphthol (510 mg) was recovered as crystals. Chromatography of the mother liquor on a silica gel column (40 g) using a 4:1 mixture of petroleum ether and ether as eluent gave (*R*)-(−)-**15c** (138 mg, 91%) as a colorless oil. Bulb-to-bulb distillation [140 °C (2 mmHg)] afforded an analytical sample: $[\alpha]^{24}_D$ −9.0° (*c* 0.79, methanol); IR (neat) 3320 (OH), 1670 (C=C), 970 (=C–H) cm^{-1}; ^1H NMR (CCl_4) 0.90 (t, *J* = 7 Hz, CH_3), 1.2–1.8 (m, CH_2), 2.40 (s, OH), 3.90 (m, C*H*OH), 5.50 (m, =CH). Anal. ($C_{13}H_{24}O$)C, H.

The absolute configuration and optical purity (92%) were determined after oxidative degradation to (+)-2-acetoxyheptanal: The above-mentioned carbinol (106 mg) was treated with pyridine (1 mL) and acetic anhydride (1 mL) to give the acetate (125 mg, 97%) as a colorless oil. A cooled (−78 °C) solution of ozone in dichloromethane (0.04 M, 40 mL, 1.6 mmol) was added to this acetate in dichloromethane (10 mL) at −78 °C, and the resulting solution was stirred at −78 °C for 1 h. Dimethyl sulfide (0.3 mL, 4 mmol) was added, and the mixture was warmed to room temperature and stirred for an additional 3 h. The volatile materials were evaporated in vacuo. Column chromatography of the residual oil on silica gel (10 g) with a 4:1 mixture of hexane and ether gave after bulb-to-bulb distillation [135–140 °C (20 mmHg)] (*R*)-(+)-2-acetoxyheptanal (73 mg, 80%), $[\alpha]^{20}_D$ +33.9° (*c* 1.35, chloroform). ^1H NMR analysis in the presence of 0.7 equiv of $Eu(hfbc)_3$ showed signals due to the acetyl methyl of the *R* and *S* enantiomers at δ 4.87 (96%) and 5.14 (4%), respectively, indicating the 92% optical purity. The absolute configuration was established by comparison with the authentic (*S*)-(−) isomer prepared from commercial prostaglandin E_2 by an analogous degradation procedure: $[\alpha]^{20}_D$ −37.8° (*c* 0.5, chloroform), 100% ee based on the ^1H NMR analysis ($CDCl_3$) in the presence of $Eu(hfbc)_3$ (0.7 equiv) which exhibited only one acetoxyl methyl signal at δ 5.14.

B. (*E*)-3-Octen-2-one (14a). The enone **14a** (700 mg, 5.56 mmol) was treated at −100 °C for 1 h and at −78 °C for 15 h with (*R*)-**1** (R'O = C_2H_5O) generated from $LiAlH_4$ (1.99 M THF solution, 8.4 mL, 16.7 mmol), ethanol (1.00 M THF solution, 16.7 mL, 16.7 mmol), and (*R*)-(+)-binaphthol (4.85 g, 16.7 mmol) in THF (25 mL). Quenching with methanol followed by extractive workup formed crude material, from which binaphthol (4.20 g) was recovered by recrystallization from hexane. Column chromatography of the mother liquor on silica gel (20 g) using a 5:1 mixture of pentane and ether followed by bulb-to-bulb distillation [105–115 °C (18 mmHg)] gave (*R,E*)-3-octen-2-ol [(*R*)-**15a**] (333 mg, 47%) as a colorless oil, $[\alpha]^{24}_D$ +1.50° (*c* 1.80, methanol). The optical purity (79%) as well as the absolute configuration was determined on the basis of rotation value of the saturated derivative. The above-obtained alcohol (30 mg, 0.23 mmol) was reduced by treatment with potassium azodicarboxylate (452 mg, 2.3 mmol) and acetic acid (140 mg, 2.3 mmol) in methanol (3 mL). Column chromatography of the crude product on silica gel (5 g) using a 4:1 mixture of pentane and ether followed by bulb-to-bulb distillation [105–110 °C (25 mmHg)] gave (*R*)-(−)-2-octanol (22 mg, 74%) as a colorless oil: $[\alpha]^{21}_D$ −8.00° (*c* 0.70, ethanol), 79% ee (lit.[27] *S* enantiomer, $[\alpha]^{21}_D$ +10.1° (*c* 5.57, ethanol)).

C. (*E*)-7-Dodecen-6-one (14b). A solution of the enone **14b** (80 mg, 0.44 mmol) was treated at −100 °C for 1 h and at −78 °C for 4 h with (*R*)-**1** (R'O = C_2H_5O) prepared from $LiAlH_4$ (1.99 M THF solution, 0.44 mL, 0.88 mmol), ethanol (1.00 M THF solution, 0.88 mL, 0.88 mmol), and (*R*)-(+)-binaphthol (252 mg, 0.88 mmol) in THF (2 mL). Quenching with methanol (0.5 mL) and water (0.5 mL) followed by usual workup afforded a crude product, dilution of which resulted in recovery of binaphthol (220 mg) as crystals. The mother liquor was chromatographed on a silica gel column (10 g) using a 10:1 mixture of hexane and ether to give (*R,E*)-(−)-7-dodecen-6-ol [(*R*)-**15b**] (74 mg, 91%) as a colorless oil: $[\alpha]^{23}_D$ −6.00° (*c* 0.75, methanol); IR (neat) 3300 (OH), 1660 (C=C) cm^{-1}; ^1H NMR (CCl_4) 0.90 (t, *J* = 7 Hz, CH_3), 1.1–1.7 (br, CH_2), 2.00 (br, CH_2), 3.90 (m, –C*H*OH), 5.41 (m, –CH=). The optical purity and absolute configuration were determined after conversion to 2-acetoxyheptanol. The allylic alcohol (40 mg) was treated with acetic anhydride (0.5 mL) and pyridine (0.5 mL) to give the acetate (40 mg). Ozonolysis (ozone-saturated dichloromethane solution, 23 mL, 0.92 mmol) at −78 °C followed by treatment with dimethyl sulfide (0.1 mL) and usual workup gave a crude oil. Column chromatography and subsequent bulb-to-bulb distillation afforded (*R*)-(+)-2-acetoxyheptanal (22 mg, 73%) as a colorless oil, $[\alpha]^{22}_D$ +34.9° (*c* 1.1, chloroform). ^1H NMR analysis with added 0.7 equiv of $Eu(hfbc)_3$ showed signals due to the acetoxyl methyl of the *R* and *S* enantiomers at δ 4.87 (95.5%) and 5.1 (4.5%), respectively, indicating the optical purity of 91%.

Asymmetric Reduction of β-Ionone (16). A solution of β-ionone (**16**) (140 mg, 0.78 mmol) in THF (1.5 mL) was exposed at −100 °C for 1 h and at −78 °C for 2 h to (*S*)-**1** (R'O = C_2H_5O) formed from $LiAlH_4$ (0.79 M THF solution, 2.73 mL, 2.18 mmol), ethanol (1.00 M THF solution, 2.18 mL, 2.18 mmol), and (*S*)-(−)-binaphthol (624 mg, 2.18 mmol) in THF (4 mL). Methanol (0.2 mL) was added at −78 °C to destroy the excess reducing agent and the mixture was warmed to room temperature. After addition of water (0.2 mL) and ether (20 mL), stirring was continued for an additional 30 min. To this was added anhydrous magnesium sulfate and the mixture was filtered through a cotton–Celite pad and concentrated in vacuo. Binaphthol (585 mg) was recovered as crystals by addition of hexane. The mother liquor was chromatographed on a silica gel column (30 g) using a 3:1 mixture of petroleum ether and ether and distillation [90–95 °C (2 mmHg)] to give (*S*)-(−)-β-ionol [(*S*)-**17**] (128 mg, 87%) as a colorless oil, $[\alpha]^{24}_D$ −8.22° (*c* 1.01, chloroform). This sample was optically pure within the limits of ^1H NMR accuracy; the spectrum of (±)-β-ionol with added $Eu(hfbc)_3$ (0.5 equiv) under irradiation at the terminal methyl protons (δ 5.38) exhibited a pair of doublets with equal intensities at δ 11.98 and 12.25 due to $CH_3CH(OH)$–proton.

The (*R*)-(+) or (*S*)-(−) configurational relationship was established by transformation to 2-isobutyryloxypropanal. To a solution of (*R*)-(+)-β-ionol [(*R*)-**17**], $[\alpha]^{24}_D$ +8.5° (*c* 2.80, chloroform, ~100% ee) (99 mg, 0.51 mmol) in pyridine (1 mL) at 0 °C was added isobutyroyl chloride (200 mg, 1.90 mmol); the mixture was stirred at 0 °C for 1 h. Quenching by water, ether extraction, and silica gel column chromatography (20 g) using a 20:1 mixture of petroleum ether and ether afforded the isobutyric acid ester (112 mg) as a colorless oil. A cooled solution of this oil in dichloromethane was treated with ozone-saturated dichloromethane (25 mL) at −78 °C for 10 min. To this was added dimethyl sulfide (0.1 mL) and the mixture was stirred at room temperature for 1 h. Silica gel column chromatography of the crude product using a 15:1 mixture of dichloromethane and ether followed by bulb-to-bulb distillation [110–130 °C (25 mmHg)] gave (*R*)-(+)-2-isobutyryloxypropanal (35 mg), $[\alpha]^{24}_D$ +28° (*c* 1.00, chloroform). The authentic (*R*)-(+) isomer (51 mg) was prepared from (*R,E*)-(+)-3-octen-2-ol [(*R*)-**15a**], $[\alpha]^{24}_D$ +1.50° (*c* 1.80, methanol, 79% ee)[27] (97 mg), by the acetylation–ozonolysis sequence, $[\alpha]^{24}_D$ +15.1° (*c* 1.01, chloroform). The low rotation value may in part be due to contamination of some chemical impurities, which exhibited some ^1H NMR signals in δ 1.2–1.5 region.

Asymmetric Reduction of Prostaglandin Intermediates. A. (*E*)-1-Iodo-1-octen-3-one (18a). A solution of the enone **18a** (150 mg, 0.60 mmol) in THF (1 mL) was treated at −100 °C for 2 h and at −78 °C for 1 h with (*S*)-**1** (R'O = C_2H_5O) prepared from $LiAlH_4$ (0.97 M THF solution, 1.84 mL, 1.80 mmol), ethanol (1.00 M THF solution, 1.79 mL, 1.79 mmol), and (*S*)-(−)-binaphthol (510 mg, 1.80 mmol) in THF (5 mL). The excess reducing agent was destroyed by addition of methanol (0.5 mL) at −78 °C and the mixture was warmed to room temperature. Water (1 mL) and ether (40 mL) were added, and the mixture was stirred for 30 min. The whole mixture was treated with anhydrous magnesium sulfate and filtered. The filtrate was evaporated and diluted with hexane to give back binaphthol (465 mg) as crystals. Column chromatography of the mother liquof on silica gel (40 g) using a 4:1 mixture of petroleum ether and ether afforded (*S,E*)-(+)-1-iodo-1-octen-3-ol [(*S*)-**19a**] (143 mg, 95%) as a colorless oil. Bulb-to-bulb distillation [135–140 °C (2mmHg)] gave an analytical sample: $[\alpha]^{24}_D$

+9.53° (*c* 1.56, methanol). The optical purity was determined to be 97% by comparison of the rotation value with that of the authentic sample prepared by our hands according to the reported procedure,[37d] $[\alpha]^{24}_D$ +9.87° (*c* 1.57, methanol). Anal. ($C_8H_{15}OI$) C, H.

B. (*E*)-1-Bromo-1-octen-3-one (18b). A solution of **18b** (130 mg, 0.65 mmol) in THF (2 mL) was treated at −100 °C for 2 h and at −78 °C for 1 h with (*S*)-**1** (R′O = C_2H_5O) generated from $LiAlH_4$ (0.97 M THF solution, 1.99 mL, 1.94 mmol), ethanol (1.00 M THF solution, 1.94 mL, 1.94 mmol), and (*S*)-(−)-binaphthol (554 mg, 1.94 mmol), quenched by methanol, and worked up. Binaphthol (502 mg) was recovered by recrystallization from hexane. The mother liquor was chromatographed on a silica gel column (30 g) with a 3:1 mixture of petroleum ether and ether to give (*S*,*E*)-(+)-1-bromo-1-octen-3-ol [(*S*)-**19b**] (128 mg, 96%). Bulb-to-bulb distillation [140–145 °C (3 mmHg)] afforded an analytical sample as a colorless oil: $[\alpha]^{24}_D$ +12.6° (*c* 1.39, methanol). The optical purity was assayed to be 96% on the basis of the rotation value of the authentic sample, $[\alpha]^{24}_D$ +13.1° (*c* 1.39, methanol), obtained by optical resolution. The absolute configuration was deduced by comparison of the CD spectrum showing positive Cotton effect at 208 nm with those of (*S*)-**18a** which exhibited positive Cotton effect at 212 nm: IR (neat) 3320 (OH), 1620 (C=C), 935 (=CH) cm^{-1}; ^1H NMR (CCl_4) 0.92 (t, *J* = 7 Hz, CH_3), 1.2–1.6 (br, CH_2), 1.80 (s, OH), 4.08 (m, C*H*OH), 6.0–6.4 (br, CH=). Anal. ($C_8H_{15}OBr$) C, H.

C. 2-Cyclopentene-1,4-dione (20). To a solution of the diketone **20** (202 mg, 2.05 mmol) in THF (10 mL) at −100 °C was added the BINAL-H reagent, (*S*)-**1** (R′O = C_2H_5O), formed from $LiAlH_4$ (1.99 M THF solution, 1.57 mL, 3.12 mmol), ethanol (1.00 M THF solution, 3.12 mL, 3.12 mmol), and (*S*)-(−)-binaphthol (893 mg, 3.12 mmol) in THF (6 mL). After 5-min stirring, the mixture was quenched with methanol (0.5 mL) and water (0.5 mL), and worked up. Extraction with ether and subsequent chromatography of the crude product on a silica gel column (30 g) using a 1:1 mixture of dichloromethane and ether gave binaphthol (830 mg) and a fraction (196 mg) containing (*R*)-(+)-4-hydroxy-2-cyclopentenone [(*R*)-**22**] and some binaphthol (TLC). Bulb-to-bulb distillation [98–105 °C (0.1 mmHg)] afforded pure material of (*R*)-**22** (130 mg, 65%) as a colorless oil, $[\alpha]^{24}_D$ +83.1° (*c* 1.70, methanol).

Acetylation of **22** was conduced by dissolving it in a mixture of pyridine (0.3 mL) and acetic anhydride (0.15 mL) at 0 °C. Stirring at room temperature was continued for 40 min. Quenching by 2 N HCl (15 mL) was followed by extration with ether. The combined extracts were washed with saturated sodium hydrogen carbonate solution and dried. The concentrated filtrate was distilled in vacuo [58–60 °C (0.1 mmHg)] to give (*R*)-(+)-4-acetoxy-2-cyclopentenone [(*R*)-**23**] (190 mg, 95%) as a colorless oil, $[\alpha]^{22}_D$ +86.5° (*c* 3.00, methanol), +90.6° (*c* 0.01, methanol). The optical purity was determined to be 94% on the basis of ^1H NMR spectrum ($CDCl_3$) taken with 0.65 equiv of Eu(hfbc)$_3$ which exhibited the acetoxyl methyl signals of the *R* and *S* enantiomers at δ 5.43 (97%) and 5.27 (3%), respectively. Anal. ($C_7H_8O_3$) C, H.

D. 2-(6-Carbomethoxyhexyl)cyclopentene-1,4-dione (21). A solution of the diketone **21** (150 mg, 0.63 mmol) in THF (1 mL) was treated at −100 °C for 1 h and at −78 °C for 2 h with (*R*)-**1** (R′O = C_2H_5O) prepared from $LiAlH_4$ (1.10 M THF solution, 1.7 mL, 1.89 mmol), ethanol (1.00 M THF solution, 1.89 mL, 1.89 mmol), and (*R*)-(+)-binaphthol (540 mg, 1.89 mmol) in THF (5 mL), quenched with methanol, and worked up. Column chromatography of the crude product on silica gel (40 g) using a 3:2 mixture of benzene and ethyl acetate gave recovered dione **21** (98 mg), binaphthol (520 mg), and (*S*)-(+)-4-hydroxy-(6-carbomethoxyhexyl)cyclopenten-2-one [(*S*)-**24**] (41 mg, 26%) as a crystalline solid: mp 46–48 °C; $[\alpha]^{24}_D$ +12.1° (*c* 1.6, methanol); CD $[\theta]^{24}_{227}$ −68 700 (*c* 4.8 × 10^{-6}, methanol); $[\theta]^{24}_{315}$ +11 800 (*c* 9.6 × 10^{-5}, methanol); IR ($CHCl_3$) 3500 (OH), 1710 (C=O), 1620 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 1.2–2.0 (br, CH_2), 2.43 (m, CH_2), 2.88 (dd, *J* = 20, 3 Hz, C(5)H), 2.90 (dd, *J* = 20, 6 Hz, C(5)H), 3.75 (s, OCH_3), 4.90 (m, C*H*OH), 6.00 (br, =CH).

The alcohol (*S*)-**24** (23 mg) was treated with a mixture of pyridine (0.3 mL) and acetic anhydride (0.2 mL) at 0 °C for 2 h. The product was chromatographed on a silica gel column (10 g) using a 4:1 mixture of benzene and ethyl acetate to give acetate (*S*)-**25** (26 mg) as a syrup: $[\alpha]^{24}_D$ +26.4° (*c* 0.91, chloroform), 91% ee on the basis of the ^1H NMR spectrum ($CDCl_3$) taken with 2.0 equiv of Eu(hfbc)$_3$ which exhibited the acetoxyl methyl signals of the *S* and *R* enantiomers at δ 8.00 (95.5%) and 8.23 (4.5%), respectively. The absolute configuration was deduced by comparison of the CD spectrum, $[\theta]^{24}_{214}$ −41 600 (*c* 2.58 × 10^{-4}, methanol), $[\theta]^{24}_{315}$ +6700 (*c* 2.58 × 10^{-3}, methanol), with the spectrum of (*R*)-**25**, $[\theta]^{25}_{205}$ +80 000 (*c* 1.03 × 10^{-3}, methanol), $[\theta]^{25}_{320}$ −5965 (*c* 1.03 × 10^{-2}, methanol).

E. (1*S*,5*R*,6*R*,7*R*)-7-Acetoxy-6-[(*E*)-3-oxo-1-octenyl]-2-oxabicyclo[3.3.0]octan-3-one (27). A solution of the lactonic enone **27** (140 mg, 0.45 mmol) in THF (3 mL) was treated at −100 °C for 2 h and at −78 °C for 2 h with (*S*)-**1** (R′O = C_2H_5O) formed from $LiAlH_4$ (1.17 M THF solution, 1.20 mL, 1.40 mmol), ethanol (1.00 M THF solution, 1.40 mL, 1.40 mmol), and (*S*)-(−)-binaphthol (403 mg, 1.41 mmol) in THF (4 mL), and quenced with methanol. Ordinary workup followed by column chromatography of the ether extracts on silica gel (50 g) using ether gave binaphthol (388 mg) and almost pure (1*S*,5*R*,6*R*,7*R*,15*S*)-7-acetoxy-6-[(*E*)-3-hydroxy-1-octenyl]-2-oxabicyclo[3.3.0]octan-3-one (**30**) (134 mg, 95%). HPLC analysis (1:1 ethyl acetate–dichloromethane as eluent, flow rate 3 mL/min) indicated the ratio of **30** (t_R 7.6 min) to the 15*R* isomer (t_R 8.4 min) to be 99.4:0.6.

F. (1*S*,5*R*,6*R*,7*R*)-7-(Tetrahydro-2-pyranyloxy)-6-[(*E*)-3-oxo-1-octenyl]-2-oxabicyclo[3.3.0]octan-3-one (28). A solution of the enone **28** (158 mg, 0.45 mmol) in THF (3 mL) was treated at −100 °C for 2 h and at −78 °C for 2 h with (*S*)-**1** (R′O = C_2H_5O) prepared from $LiAlH_4$ (1.17 M THF solution, 1.20 mL, 1.40 mmol), ethanol (1.00 M THF solution, 1.40 mL, 1.40 mmol), and (*S*)-(−)-binaphthol (403 mg, 1.41 mmol), quenched with methanol, and worked up. Column chromatography of the crude extract on silica gel (15 g) using ether gave crystalling binaphthol (345 mg) and (1*S*,5*R*,6*R*,7*R*,15*S*)-7-(tetrahydro-2-pyranyloxy)-6-[(*E*)-3-hydroxy-1-octenyl]-2-oxabicyclo[3.3.0]octan-3-one (**31**) (159 mg, 96%) as a syrup. HPLC analysis (1:1 ethyl acetate–dichloromethane) indicated the ratio of **31** (t_R 8.4 and 8.6 min) to the 15*R* isomer (t_R 9.8 and 10.1 min) to be 99.5:0.5.

In a similar manner, a solution of the enone **28** (158 mg, 0.45 mmol) in THF (3 mL) was treated at −100 °C for 1 h and at −78 °C for 2 h with (*R*)-**1** (R′O = C_2H_5O) prepared from $LiAlH_4$ (1.17 M THF solution, 1.20 mL, 1.40 mmol), ethanol (1.00 M THF solution, 1.40 mL, 1.40 mmol), and (*R*)-(+)-binaphthol (403 mg, 1.41 mmol). Quenching with methanol followed by extractive workup with ether and column chromatography on silica gel (10 g, ether) gave binaphthol (350 mg) and the alcoholic product (154 mg, 93%). HPLC analyses indicated the ratio of **31** to the 15*R* isomer to be 32:68.

G. (1*S*,5*R*,6*R*,7*R*)-7-Hydroxy-6-[(*E*)-3-oxo-1-octenyl]-2-oxabicyclo[3.3.0]octan-3-one (29). A solution of the enone **29** (120 mg, 0.45 mmol) in THF (3 mL) was treated at −100 °C for 1 h and at −78 °C for 2 h with (*S*)-**1** (R′O = C_2H_5O) prepared from $LiAlH_4$ (1.17 M THF solution, 1.20 mL, 1.40 mmol), ethanol (1.00 M THF solution, 1.40 mL, 1.40 mmol), and (*S*)-(−)-binaphthol (403 mg, 1.41 mmol) in THF (2 mL). Quenching with methanol followed by workup and column chromatography on silica gel (40 g) using a 4:1 mixture of ethyl acetate and benzene and then ethyl acetate gave binaphthol (377 mg), unreacted enone **29** (70 mg, 58%), and (1*S*,5*R*,6*R*,7*R*,15*S*)-7-hydroxy-6-[(*E*)-3-hydroxy-1-octenyl]-2-oxabicyclo[3.3.0]octan-3-one (**32**) (50 mg, 42%, or 97% based on consumed **29**). HPLC analysis (ethyl acetate) gave only a single peak due to **32** (t_R 6.0 min); the 15*R* isomer (t_R 5.1 min) was not detected.

H. (5*Z*,13*E*)-9α,11α-Bis(tetrahydro-2-pyranyloxy)-15-oxaprosta-5,13-dienoic Acid Methyl Ester (33). A solution of the enone **33** 240 mg, 0.45 mmol) in THF (3 mL) was treated at −100 °C for 1 h and at −78 °C for 2 h with (*S*)-**1** (R′O = C_2H_5O) prepared from $LiAlH_4$ (1.17 M THF solution, 1.20 mL, 1.40 mmol), ethanol (1.00 M THF solution, 1.40 mL, 1.40 mmol), and (*S*)-(−)-binaphthol (403 mg, 1.41 mmol) in THF (2 mL). Quenching by methanol followed by extractive workup with ether and column chromatography on silica gel (10 g) using a 2:1 mixture of dichloromethane and ethyl acetate gave binaphthol (370 mg), unreacted enone **33** (92 mg, 38%), and the desired alcohol, (5*Z*,13*E*)-9α,11α-bis(tetrahydro-2-pyranyloxy)-15*S*-hydroxyprosta-5,13-dienoic acid methyl ester (**34**) (134 mg, 55%, or 88% based on consumed starting material). HPLC analysis (1:1 dichloromethane and ethyl acetate) gave a single peak arising from the 15*S* isomer **34** (t_R 7.0 min). The 15*R* isomer (t_R 8.2 min) was not detected.

Asymmetric Reduction of Deuterium-Labeled Aldehydes. A. Enzymatic Reduction of Geranial-*1-d* (35a).[51] Geranial-*1-d* (62 mg; no ^1H NMR signal at δ 9.88) was dispersed in a pH 7.4 phosphate buffer (130 mL) by ultrasonic vibration. Nictotinamide adenine dinucleotide phosphate (271 mg, 0.41 mmol) and yeast alcohol dehydrogenase (1.2 mg, 400 units, Sigma) were added, and the mixture was allowed to stand at room temperature for 60 h. The ether extracts were dried and concentrated. Preparative GC (170 °C) of the crude product (65 mg) afforded pure (*S*)-(+)-geraniol-*1-d* [(*S*)-**36a**] (21 mg) as a colorless oil: $[\alpha]^{24}_D$ +1.51° (*c* 1.06, cyclopentane); IR (neat) 3360 (OH), 2160 (CD), 1660 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) 1.67 (s, CH_3), 1.76 (s, CH_3), 2.11 (m, CH_2), 4.16 (br d, *J* = 6 Hz, C*H*DOH), 5.17 (m, =CH), 5.48 (br d, *J* = 6 Hz, =C*H*CHD). ^1H NMR of a mixture of this alcohol and Eu(hfbc)$_3$ (0.4 equiv) in $CDCl_3$, upon irradiation at the vinylic proton (δ 12.80), gave a single peak at δ 15.90 due to the C(1) proton; no signal due to (*R*)-**36a** was seen at δ 16.05.

B. BINAL-H Reduction of 35a. A solution of **35a** (77 mg, 0.50 mmol) was treated at −100 °C for 2 h with (*S*)-**1** (R′O = C_2H_5O) prepared from $LiAlH_4$ (0.79 M THF solution, 1.60 mL, 1.26 mmol), ethanol (1.00 M THF solution, 1.26 mL, 1.26 mmol), and (*S*)-(−)-bi-

naphthol (360 mg, 1.26 mmol) in THF (2 mL). Methanol (0.2 mL) and water (0.4 mL) were added at this temperature and the mixture was warmed to room temperature, diluted with ether (20 mL), stirred for 30 min, and then treated with magnesium sulfate. The filtrate was evaporated and then diluted with pentane to give back binaphthol (335 mg) as crystals. Column chromatography of the mother liquor on silica gel (25 g) using a 3:1 mixture of petroleum ether and ether gave (*S*)-(+)-gerniol-*1-d* [(*S*)-**36a**] (71 mg, 91%) as a colorless oil. Bulb-to-bulb distillation [125–130 °C (19 mmHg)] afforded pure material, $[\alpha]^{24}_D$ +1.38° (*c* 1.70, cyclopentane). The optical purity was assayed to be 91% by comparison of the rotation value with that of the enzymatically derived product. ^{1}H NMR analysis ($CDCl_3$) in the presence of Eu(hfbc)$_3$ (0.4 equiv) indicated 84% optical purity; irradiation of the vinylic proton (δ 12.80) gave signals due to the C(1) protons of the (*S*)-**36a** and (*R*)-**36a** at δ 15.90 and 16.05, respectively, in 92:8 ratio.

C. Neral-*1-d* (35b). A solution of **35b** (72 mg, 0.47 mmol) was treated at −100 °C for 2 h with (*S*)-**1** (R′O = C_2H_5O) prepared from $LiAlH_4$ (0.79 M THF solution, 1.50 mL, 1.18 mmol), ethanol (1.00 M THF solution, 1.18 mL, 1.18 mmol), and (*S*)-(−)-binaphthol (338 mg, 1.18 mmol), quenched with methanol, and worked up. Binaphthol (290 mg) was recovered by recrystallization from hexane. Column chromatography of the mother liquor on silica gel (20 g) using a 3:1 mixture of petroleum ether and ether gave (*S*)-(+)-nerol-*1-d* [(*S*)-**36b**] (64 mg, 90%). Preparative GC (170 °C) followed by bulb-to-bulb distillation [120–122 °C (20 mmHg)] afforded pure material: $[\alpha]^{24}_D$ +1.21° (*c* 1.41, cyclopentane); IR (neat) 3320 (OH), 2150 (CD), 1660 (C=C) cm^{-1}; ^{1}H NMR ($CDCl_3$) 1.67 (s, CH_3), 1.76 (s, CH_3), 1.80 (s, OH), 1.83 (s, CH_3), 2.16 (m, CH_2), 4.12 (br d, *J* = 6 Hz, CHD), 5.17 (m, =CH), 5.50 (d, *J* = 6 Hz, =C*H*CHD). ^{1}H NMR analysis ($CDCl_3$) with added Eu(hfbc)$_3$ (0.4 equiv) indicated 72% optical purity; under irradiation of the vinylic proton (δ 12.60), signals due to the C(1) protons of (*S*)-**36b** and (*R*)-**36b** appeared at δ 14.80 and 14.96, respectively, in 86:14 ratio. Signals of the pro-*S* protons are assumed to move downfield faster, as has been observed in geraniol-*1-d*.[53]

D. (*E*,*E*)-Farnesal-*1-d* (35c). A solution of **35c** (160 mg, 0.72 mmol) in THF (1 mL) was treated at −100 °C for 2 h with (*R*)-**1** (R′O = C_2H_5O) prepared from $LiAlH_4$ (0.79 M THF solution, 2.76 mL, 2.17 mmol), ethanol (1.00 M THF solution, 2.17 mL, 2.17 mmol), and (*R*)-(+)-binaphthol (621 mg, 2.17 mmol) in THF (4 mL). Standard workup gave back binaphthol (520 mg). Column chromatography of the mother liquor on silica gel (50 g) using a 3:1 mixture of petroleum ether and ether gave (*R*,*E*,*E*)-(−)-farnesol-*1-d* [(*R*)-**36c**] (145 mg, 91%). Bulb-to-bulb distillation [100–105 °C (2 mmHg)] afforded the analytical sample: $[\alpha]^{24}_D$ −0.80° (*c* 4.0, cyclopentane); IR (neat) 3300 (OH), 2150 (CD), 1670 (C=C) cm^{-1}; ^{1}H NMR ($CDCl_3$) 1.50 (s, OH), 1.60 (s, 2 CH_3), 1.67 (s, 2 CH_3), 4.10 (br d, *J* = 6 Hz, CHD), 5.10 (m, =CH), 5.34 (d, *J* = 6 Hz, =C*H*CHD). ^{1}H NMR analysis ($CDCl_3$) with added Eu(hfbc)$_3$ (0.4 equiv) indicated 88% optical purity; irradiation of the vinylic proton (δ 12.10) gave signals due to the C(1) protons of (*R*)-**36c** and (*S*)-**36c** at δ 15.31 and 15.10, respectively, in 94:6 ratio. Anal. ($C_{15}H_{25}DO$) C, H.

E. (*E*,*Z*)-Farnesal-*1-d* (35d). A solution of **35d** (134 mg, 0.61 mmol) was treated at −100 °C for 2 h with (*R*)-**1** (R′O = C_2H_5O) formed from $LiAlH_4$ (0.79 M THF solution, 2.75 mL, 2.17 mmol), ethanol (1.00 M THF solution, 2.17 mL, 2.17 mmol), and (*R*)-(+)-binaphthol (620 mg, 2.17 mmol) in THF (4 mL) and followed by standard workup. Binaphthol (530 mg) was recovered by recrystallization from hexane. Column chromatography of the mother liquor on silica gel (50 g) using a 3:1 mixture of petroleum ether and ether gave (*R*,*E*,*Z*)-(+)-farnesol-*1-d* [(*R*)-**36d**] (126 mg, 93%), whose bulb-to-bulb distillation [100–105 °C (2 mmHg)] afforded the analytical sample: $[\alpha]^{24}_D$ −0.72° (*c* 2.50, cyclohexane); IR (neat) 3320 (OH), 2150 (CD), 1670 (C=C) cm^{-1}; ^{1}H NMR ($CDCl_3$) 1.33 (s, OH), 1.63 (s, CH_3), 1.70 (s, CH_3), 1.77 (s, CH_3), 4.10 (br d, *J* = 6 Hz, CHD), 5.10 (m, =CH), 5.42 (d, *J* = 6 Hz, =C*H*CHD). ^{1}H NMR analysis ($CDCl_3$) in the presence of Eu(hfbc)$_3$ (0.4 equiv) indicated the optical purity of 82%; the signals due to the C(1) protons of (*R*)-**36d** and (*S*)-**36d** appeared at δ 14.82 and 14.61, respectively, in 91:9 ratio upon irradiation of the vinylic proton (δ 12.00).[53] Anal. ($C_{15}H_{25}DO$) C, H.

F. Benzaldehyde-α-*d* (35e). A solution of **35e** (260 mg, 2.43 mmol) in THF (2 mL) was treated at −100 °C for 3 h with (*R*)-**1** (R′O = C_2H_5O) prepared from $LiAlH_4$ (1.63 M THF solution, 5.10 mL, 8.31 mmol), ethanol (2.00 M THF solution, 4.20 mL, 8.40 mmol), and (*R*)-(+)-binaphthol (2.41 g, 8.43 mmol) in THF (15 mL). The reaction proceeded rapidly and GC analysis indicated that the conversion was 100%. Standard workup followed by bulb-to-bulb distillation [120–140 °C (50 mmHg)] gave (*R*)-(−)-benzyl-α-*d* alcohol [(*R*)-**36e**] (156 mg, 59%). Preparative GC (150 °C) afforded pure sample (105 mg), $[\alpha]^{26}_D$ −1.32° (*c* 6.34, cyclopentane), 87% ee based on the highest reported value of rotation (lit.[24c] (*S*)-**36e** $[\alpha]^{20}_D$ +1.58° (*c* 7.07, cyclopentane)).

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Registry No. (*R*)-**1** (R′ = Et), 70945-91-4; (*S*)-**1** (R′ = Et), 70981-93-0; (*R*)-**1** (R′ = Me), 70945-92-5; (*S*)-**1** (R′ = Me), 75766-18-6; **2**, 70-11-1; (*S*)-**4**, 20780-54-5; **5a**, 27593-19-7; **5b**, 76291-85-5; **5c**, 73501-40-3; **5d**, 13531-82-3; **5e**, 1119-58-0; **5f**, 28884-88-0; (*S*)-**6a**, 32556-71-1; (*S*)-**6a** MTPA ester, 32556-74-4; (*R*)-**6a** MTPA ester, 32556-75-5; (*S*)-**6b**, 70095-33-9; (*S*)-**6b** MTPA ester, 77889-10-2; (*R*)-**6b**, 74364-80-0; (*R*)-**6b** MTPA ester, 74327-00-7; (*S*)-**6c**, 77889-04-4; (*S*)-**6c** MTPA ester, 91410-88-7; (*R*)-**6c**, 91410-89-8; (*S*)-**6d**, 77943-78-3; (*S*)-**6d** MTPA ester, 91410-90-1; (*R*)-**6d** MTPA ester, 91410-91-2; (*R*)-**6e**, 77889-05-5; (*R*)-**6e** MTPA ester, 91410-92-3; (*S*)-**6e** MTPA ester, 91410-93-4; (*S*)-**6f**, 77889-06-6; (*S*)-**6f** MTPA ester, 91410-94-5; (*R*)-**6f** MTPA ester, 91410-95-6; **7**, 77889-02-2; (*R*)-**8**, 77889-07-7; (*R*)-**8** MTPA ester, 77889-12-4; (*S*)-**8** MTPA ester, 91410-96-7; (*R*)-**9**, 72151-69-0; (*R*)-(*Z*)-**10**, 64726-91-6; **11**, 77889-03-3; (*S*)-**12**, 77889-08-8; (*S*)-**12** MTPA ester, 91410-97-8; (*R*)-**12** MTPA ester, 91410-98-9; (*S*)-**12** acetate, 91410-99-0; (*S*)-**13**, 69830-92-8; (*R*)-**13**, 69830-91-7; (*E*)-**14a**, 18402-82-9; (*E*)-**14b**, 81791-67-5; (*E*)-**14c**, 81791-68-6; (*R*)-**15a**, 81801-15-2; (*R*)-**15b**, 81801-16-3; **16**, 79-77-6; (*S*)-**17**, 81801-17-4; (*R*)-**17**, 83348-85-0; (*R*)-**17** isobutyrate, 91411-00-6; **18a**, 39178-64-8; **18b**, 52418-89-0; (*S*)-**19a**, 39647-93-3; (*S*)-**19b**, 72243-93-7; **20**, 930-60-9; **21**, 91411-01-7; (*R*)-**22**, 59995-47-0; (*R*)-**23**, 59995-48-1; (*S*)-**23**, 59995-50-5; (*S*)-**24**, 91411-02-8; (*S*)-**25**, 91411-03-9; (*R*)-**25**, 91411-04-0; **27**, 26054-68-2; **28** *(THP-(*R*)), 91465-57-5; **28** *(THP-(*S*)), 91465-58-6; **29**, 60623-67-8; **30**, 37863-05-1; (15*R*)-**30**, 38539-37-6; **31**, 72243-94-8; (15*R*)-**31**, 75766-77-7; **32**, 26054-67-1; **33**, 62648-92-4; **34**, 72204-57-0; **35a**, 76192-44-4; **35b**, 76192-47-7; **35c**, 76192-48-8; **35d**, 76207-92-6; **35e**, 3592-47-0; (*S*)-**36a**, 64543-50-6; (*R*)-**36a**, 91464-58-3; (*S*)-**36b**, 76248-02-7; (*R*)-**36b**, 91464-59-4; (*S*)-**36c**, 91411-05-1; (*R*)-**36c**, 76192-45-5; (*S*)-**36d**, 91411-06-2; (*R*)-**36d**, 76192-46-6; (*R*)-**36e**, 4181-90-2; $(CH_3)_2CHC(O)Cl$, 79-30-1; (−)-$CH_3(CH_2)_7CH(OAc)CO_2H$, 77889-09-9; $LiAlH_4$, 16853-85-3; EtOH, 64-17-5; MeOH, 67-56-1; (*S*)-2-octanol, 6169-06-8; (*R*)-2-acetoxyheptanal, 84711-24-0; (*S*)-2-acetoxyheptanal, 75584-25-7; (*R*)-(+)-1,1′-bi-2-naphthol, 18531-94-7; (*S*)-(−)-1,1′-bi-2-naphthol, 18531-99-2.