A Versatile New Catalyst for the Enantioselective Isomerization of Allylic Alcohols to Aldehydes: Scope and Mechanistic Studies

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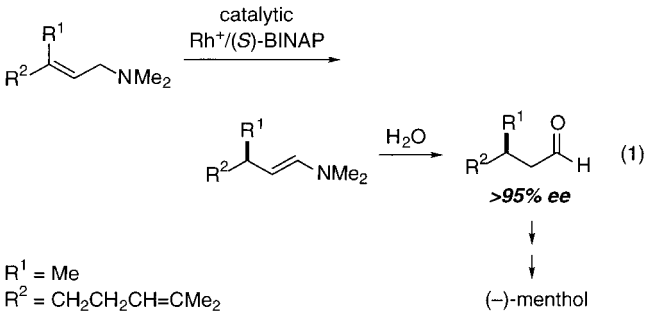
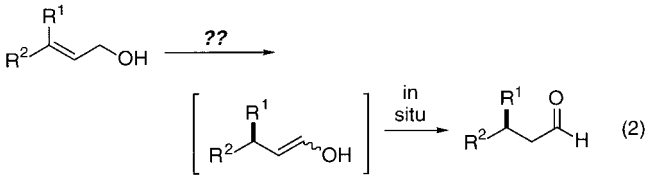
A new planar-chiral bidentate phosphaferrocene ligand (**2**) has been synthesized and structurally characterized. The derived rhodium complex, [Rh(cod)(**2**)]BF_4, serves as an effective catalyst for asymmetric isomerizations of allylic alcohols to aldehydes, furnishing improved yields, scope, and enantioselectivities relative to previously reported methods. The catalyst is air-stable and can be recovered at the end of the reaction. Mechanistic studies establish that the isomerization proceeds via an intramolecular 1,3-hydrogen migration and that the catalyst differentiates between the enantiotopic C1 hydrogens.

Introduction

The catalytic enantioselective isomerization of olefins (e.g., allylic amines,[1] allylic ethers,[2] and unfunctionalized alkenes[3,4]) has been the subject of a number of investigations. Indeed, one of the landmark accomplishments in asymmetric catalysis is the industrial-scale application of a Rh^+/BINAP-catalyzed isomerization of geranylamine to produce (−)-menthol and related terpenes (eq 1).[5]



In contrast to the remarkable progress that has been achieved for reactions of allylic amines, comparable success has not been realized for the corresponding asymmetric isomerizations of readily available allylic alcohols (eq 2), due in part to difficulty in effecting catalysis of even the nonasymmetric reaction.[6] At the time that we initiated our studies of this process, the best enantioselectivity that had been reported was 53% ee (eq 2; 47% yield).[7,8]



Several years ago, we decided to pursue the possibility that, because ligands that are based on planar-chiral aromatic heterocycles possess novel structural and bonding features[9] relative to more conventional ligands such

(1) (a) Kumobayashi, H.; Akutagawa, S.; Otsuka, S. *J. Am. Chem. Soc.* **1978**, *100*, 3949−3950. (b) Tani, K.; Yamagata, T.; Otsuka, S.; Akutagawa, S.; Kumobayashi, H.; Taketomi, T.; Takaya, H.; Miyashita, A.; Noyori, R. *J. Chem. Soc., Chem. Commun.* **1982**, 600−601. (c) Tani, K.; Yamagata, T.; Akutagawa, S.; Kumobayashi, H.; Taketomi, T.; Takaya, H.; Miyashita, A.; Noyori, R.; Otsuka, S. *J. Am. Chem. Soc.* **1984**, *106*, 5208−5217. (d) Tani, K.; Yamagata, T.; Tatsuno, Y.; Yamagata, Y.; Tomita, K.-I.; Akutagawa, S.; Kumobayashi, H.; Otsuka, S. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 217−219. (e) For an overview, see Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994; Chapter 3. Akutagawa, S.; Tani, K. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley-VCH: New York, 2000; Chapter 3.

(2) (a) Frauenrath, H.; Philipps, T. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 274. (b) Frauenrath, H.; Kaulard, M. *Synlett* **1994**, 517−518. (c) Hiroya, K.; Kurihara, Y.; Ogasawara, K. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2287−2289. (d) Hiroya, K.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1995**, 2205−2206. (e) Kamikubo, T.; Hiroya, K.; Ogasawara, K. *Tetrahedron Lett.* **1996**, *37*, 499−502. (f) Frauenrath, H.; Reim, S.; Wiesner, A. *Tetrahedron: Asymmetry* **1998**, *9*, 1103−1106. (g) Brunner, H.; Prommesberger, M. *Tetrahedron: Asymmetry* **1998**, *9*, 3231−3239. (h) Faitg, T.; Soulié, J.; Lallemand, J.-Y.; Mercier, F.; Mathey, F. *Tetrahedron* **2000**, *56*, 101−104. (i) Frauenrath, H.; Brethauer, D.; Reim, S.; Maurer, M.; Raabe, G. *Angew. Chem., Int. Ed.* **2001**, *40*, 177−179.

(3) (a) Carlini, C.; Politi, D.; Ciardelli, F. *J. Chem. Soc., Chem. Commun.* **1970**, 1260−1261. (b) Giacomelli, G.; Bertero, L.; Lardicci, L.; Menicagli, R. *J. Org. Chem.* **1981**, *46*, 3707−3711. (c) Chen, Z.; Halterman, R. L. *J. Am. Chem. Soc.* **1992**, *114*, 2276−2277. (d) Halterman, R. L.; Chen, Z.; Khan, M. A. *Organometallics* **1996**, *15*, 3957−3967.

(4) For a general review, see: Akutagawa, S. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 1999; Chapter 23.

(5) Takasago International Corp. manufactures thousands of tons per year of (−)-menthol and related terpenes through the Rh^+/BINAP-catalyzed enantioselective isomerization of allylic amines: (a) Akutagawa, S. In *Chirality in Industry*; Collins, A. N., Sheldrake, G. N., Crosby, J., Eds.; Wiley: New York, 1992. (b) Akutagawa, S. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 1999; Chapter 41.4.

(6) For a discussion of difficulties encountered in catalyzing the isomerization of allylic alcohols to aldehydes, see: Bianchini, C.; Meli, A.; Oberhauser, W. *New J. Chem.* **2001**, *25*, 11−12 and references therein.

(7) (a) Tani, K. *Pure Appl. Chem.* **1985**, *57*, 1845−1854. (b) Otsuka, S.; Tani, K. *Synthesis* **1991**, 665−680.

(8) See also: (a) Botteghi, C.; Giacomelli, G. *Gazz. Chim. Ital.* **1976**, *106*, 1131−1134. (b) Kitamura, M.; Manabe, K.; Noyori, R.; Takaya, H. *Tetrahedron Lett.* **1987**, *28*, 4719−4720. (c) Bergens, S. H.; Bosnich, B. *J. Am. Chem. Soc.* **1991**, *113*, 958−967. (d) Reference 2c. (e) Wiles, J. A.; Lee, C. E.; McDonald, R.; Bergens, S. H. *Organometallics* **1996**, *15*, 3782−3784.

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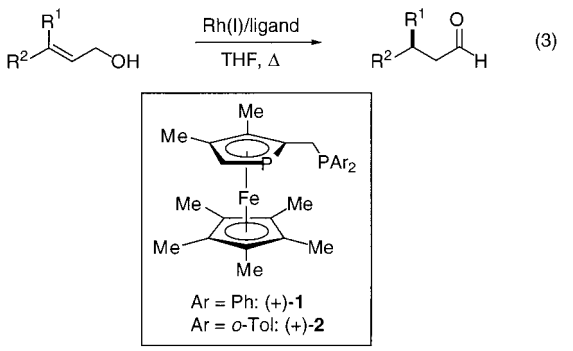
as tertiary phosphines and amines, they might provide distinctive reactivity and stereoselection.[10−12] As part of this program, we reported last year that planar-chiral phosphaferrocene **1** furnishes the highest enantioselectivity described to date for the catalytic asymmetric isomerization of allylic alcohols to aldehydes (eq 3; 64−86% ee, 55−91% yield; all *Z* olefins, with one exception).[13]



In this article, we provide the synthesis of a new planar-chiral phosphaferrocene, di(*o*-tolyl) phosphine **2**, that is markedly more robust than **1** and that affords significantly improved scope, enantioselectivity, and yield in rhodium-catalyzed asymmetric isomerizations of allylic alcohols. Furthermore, we describe mechanistic studies that furnish useful insight into the reaction pathway.

Results and Discussion

Synthesis of Phosphaferrocene Ligand 2. As illustrated in eq 4, it is straightforward to vary the structure of the tertiary phosphine portion of these bidentate phosphaferrocene-based ligands. Thus, di(*o*-tolyl) phosphine (+)-**2** is readily prepared from the previously reported alcohol (+)-**3**.[13,14] Relative to ligand **1**, the more sterically encumbered **2** exhibits significantly higher stability toward air (e.g., no decomposition during flash chromatography[15]).

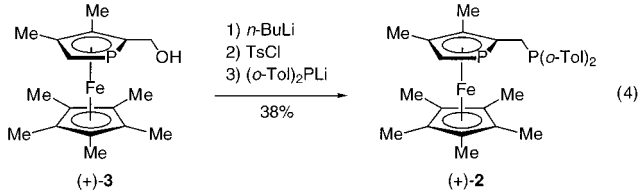
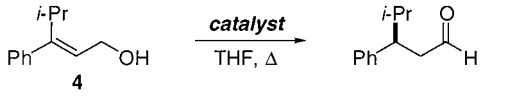


Table 1. Optimization of Enantioselectivity



Entry	Catalyst	Temp	Yield	ee
1	[Rh((+)-**1**)]BF_4[a]	70 °C	81%	**78%**
2	[Rh((+)-**2**)]BF_4[b]	70 °C	95%	**82%**
3	[Rh(cod)((+)-**2**)]BF_4	100 °C	97%	**93%**

[a] Prepared in situ from $[Rh(cod)_2]BF_4$, ligand, and H_2 (1 atm) in THF. [b] Prepared in situ from [Rh(cod)((+)-**2**)]BF_4 and H_2 (1 atm) in THF.

Catalytic Enantioselective Isomerizations. With new planar-chiral phosphaferrocene ligand **2** in hand, we turned our attention to the rhodium-catalyzed asymmetric isomerization of a representative test substrate, allylic alcohol **4** (Table 1). As reported earlier, we obtain aldehyde in 78% ee when we employ ligand **1** in this process (entry 1).[13] We were pleased to discover that, under the same conditions, di(*o*-tolyl) phosphine **2** furnishes both improved yield and stereoselection (entry 2).

Until this point, we had been employing Rh/cod (cod = cyclooctadienyl) complexes as precatalysts, which we treated with hydrogen to reduce the cod.[16] We have determined that we can simplify this experimental procedure through the direct use of [Rh(cod)((+)-**2**)]BF_4, an air-stable crystalline solid, as the catalyst; at 100 °C, this complex effects isomerization without the need to hydrogenate the remaining cod. As shown in entry 3 of Table 1, [Rh(cod)((+)-**2**)]BF_4 is not only more convenient to use, but also is more enantioselective.[17]

[Rh(cod)((+)-**2**)]BF_4 has in fact proved to be an effective catalyst for the asymmetric isomerization of a range of allylic alcohols.[18] Both the yields and the ee's are higher for *E* allylic alcohols (Table 2) than for the *Z* isomers (Table 3).[19] In contrast, for enantioselective isomerizations catalyzed by Rh/**1**, higher stereoselection is observed for *Z* allylic alcohols.[13]

As shown in Table 2, [Rh(cod)((+)-**2**)]BF_4-catalyzed asymmetric isomerizations of *E* allylic alcohols proceed in uniformly good yield. The enantiomeric excess is dependent on the steric demand of the alkyl substituent; unbranched groups (entries 1 and 2) furnish lower selectivities than does a branched group, which provides excellent ee (entries 3−6). On the other hand, the stereoselection appears to be independent of the steric demand (entries 3 and 4), as well as the electronic nature (entries 3, 5, and 6), of the aromatic substituent.

As for *E* allylic alcohols (Table 2), the enantioselectivity for [Rh(cod)((+)-**2**)]BF_4-catalyzed isomerizations of *Z* allylic alcohols is dependent on the steric demand of the alkyl group (Table 3, entries 1−4),[20] but not the aromatic group (entries 3 and 5). However, in contrast to *E* allylic alcohols, for *Z* allylic alcohols the electronic nature of the aromatic substituent appears to have a modest impact

(9) For leading references, see: (a) Deschamps, B.; Ricard, L.; Mathey, F. *J. Organomet. Chem.* **1997**, *548*, 17−22. (b) Deschamps, B.; Ricard, L.; Mathey, F. *J. Organomet. Chem.* **1997**, *548*, 17−22.

(10) For our studies of phosphorus-based heterocycles, see: (a) Qiao, S.; Fu, G. C. *J. Org. Chem.* **1998**, *63*, 4168−4169. (b) Shintani, R.; Lo, M. M.-C.; Fu, G. C. *Org. Lett.* **2000**, *2*, 3695−3697.

(11) Independently, Ganter has also been exploring applications of planar-chiral phosphorus heterocycles in asymmetric catalysis: Ganter, C.; Kaulen, C.; Englert, U. *Organometallics* **1999**, *18*, 5444−5446. See also: Ganter, C.; Glinsböckel, C.; Ganter, B. *Eur. J. Inorg. Chem.* **1998**, 1163−1168.

(12) For our studies of nitrogen-based heterocycles, see: (a) Dosa, P. I.; Ruble, J. C.; Fu, G. C. *J. Org. Chem.* **1997**, *62*, 444−445. (b) Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 10270−10271. (c) Rios, R.; Liang, J.; Lo, M. M.-C.; Fu, G. C. *Chem. Commun.* **2000**, 377−378. (d) Lo, M. M.-C.; Fu, G. C. *Tetrahedron* **2001**, *57*, 2621−2634.

(13) Tanaka, K.; Qiao, S.; Tobisu, M.; Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 9870−9871.

(14) Several other diaryl derivatives of **1**, prepared similarly, were less effective than ligand **2** in rhodium-catalyzed asymmetric isomerization reactions (lower yields, lower enantioselectivities).

(15) In contrast, purification of parent diphenyl ligand **1** by flash chromatography in the air leads to appreciable decomposition.

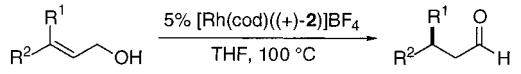
(16) See footnote 12 of reference 13.

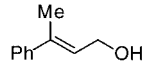
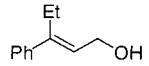
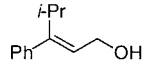
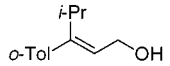
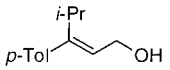
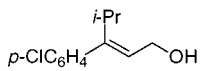
(17) We have not been able to isolate [Rh(cod)((+)-**1**)]BF_4 in pure form.

(18) Under the same conditions, allylic methyl ethers and homoallylic alcohols do not undergo isomerization.

(19) At partial conversion, we see no evidence for *E*/*Z* isomerization of either the *E* or the *Z* allylic alcohol.

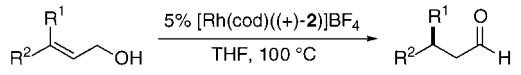
Table 2. Catalytic Enantioselective Isomerization of *E* Allylic Alcohols to Aldehydes

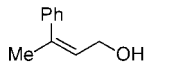
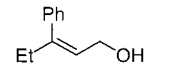
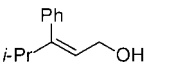
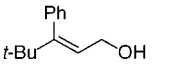
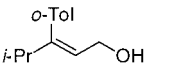
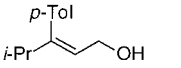
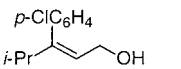


Entry	Allylic Alcohol	Yield (%)[a,b]	ee (%)[a]
1		91 (82)	75 (56)
2		96	76
3		98 (81)	92 (78)
4[c]		86 (8)	92 (87)
5		90 (85)	91 (64)
6		86 (79)	92 (73)

[a] Average of two runs (first run, new catalyst; second run, catalyst recovered from the previous reaction); the values in parentheses are for Rh/**1**. [b] Isolated yields. [c] Reaction was carried out at 150 °C.

Table 3. Catalytic Enantioselective Isomerization of *Z* Allylic Alcohols to Aldehydes

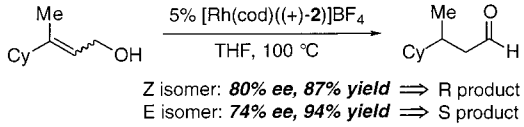


Entry	Allylic Alcohol	Yield (%)[a,b]	ee (%)[a]
1		80	59
2		78	57
3		82	82
4		90	90
5[c]		60	81
6		83	77
7		83	85

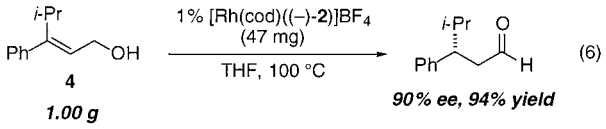
[a] Average of two runs (first run, new catalyst; second run, catalyst recovered from the previous reaction, except for entry 6). [b] Isolated yields. [c] Reaction was carried out at 150 °C.

on stereoselection (more electron-poor ⟹ higher ee; entries 3, 6, and 7).

An aromatic group is not required to obtain enantioselectivity in this catalytic asymmetric isomerization process. Thus, [Rh(cod)((+)-**2**)]BF_4 cleanly converts the illustrated cyclohexyl/methyl substituted allylic alcohols to the desired aldehydes in good ee (eq 5).[21,22]



Practical Issues. For the isomerizations described above (Table 2, Table 3, and eq 5), we chose to develop a general protocol, rather than to individually optimize the reaction conditions for each substrate (e.g., minimizing the reaction temperature or the catalyst loading). To demonstrate that the use of a lower catalyst loading is possible, as well as to provide an example of a preparative-scale process, we carried out a 1 g isomerization of allylic alcohol **4** with 1% [Rh(cod)((−)-**2**)]BF_4 (eq 6).



It is worth noting that we can reuse the catalyst for these enantioselective isomerizations. Thus, [Rh(cod)((−)-**2**)]BF_4 can be crystallized directly from the reaction mixture simply by adding pentane. For the isomerization depicted in eq 6, this process affords 32 mg (68%) of [Rh(cod)((−)-**2**)]BF_4,[23] which furnishes 91% ee and 96% yield in a subsequent isomerization of allylic alcohol **4**. In fact, most of the reactions illustrated in Tables 2 and 3 were run once with recovered catalyst, with no erosion in enantioselectivity or yield.[24]

Thus, relative to ligand **1**, new planar-chiral phosphaferrocene ligand **2** provides a substantially more practical and versatile catalyst for asymmetric isomerizations of allylic alcohols. From the standpoints of yield and ee, the advantage is particularly clear for *E* olefins (see Table 2).

Mechanistic Studies. With regard to the issue of mechanism, Takaya and Noyori have proposed that the Rh^+/BINAP-catalyzed isomerizations of allylic amines proceed through the pathway outlined in eq 7.[25] We have conducted related studies, which afford data that are consistent with an analogous sequence of steps for the [Rh(cod)(**2**)]BF_4-catalyzed isomerization of allylic alcohols.[26]

Through the use of a 1,1-dideuterated allylic alcohol, we have determined that our isomerizations follow a

(20) New phosphaferrocene ligand **2** is much more effective than ligand **1** for isomerizations of hindered substrates. For example, for the allylic alcohol depicted in entry 4 of Table 3, ligand **2** provides an 88% yield of the desired product after 22 h at 100 °C, whereas ligand **1** furnishes a 12% yield after 48 h at 100 °C. Entry 4 of Table 2 affords an additional example of greatly enhanced reactivity in the presence of ligand **2**, relative to ligand **1**.

(21) Use of first-generation phosphaferrocene ligand **1** for the isomerization of the *E* allylic alcohol illustrated in eq 5 furnishes the aldehyde in 57% ee and 83% yield.

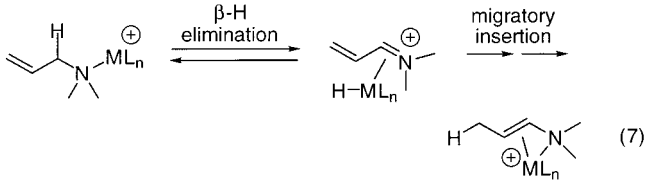
(22) Under these conditions, geraniol is isomerized in good yield (91%) and modest enantioselectivity (52% ee). Previous to this work, the best result that had been reported for geraniol was 37% ee and 70% yield (ref 7).

(23) For isomerizations that are run with 5% catalyst, we typically recover >80% of the catalyst.

(24) For details, see the Experimental Section.

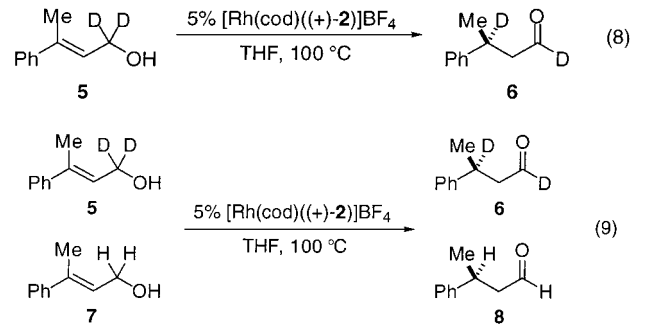
(25) Inoue, S.-I.; Takaya, H.; Tani, K.; Otsuka, S.; Sato, T.; Noyori, R. *J. Am. Chem. Soc.* **1990**, *112*, In4897−4905.

(26) (a) For a study of rhodium-catalyzed isomerizations of allylic alcohols to enols, see: ref 8c. (b) For a study of ruthenium-catalyzed isomerizations of allylic alcohols to aldehydes, see: Trost, B. M.; Kulawiec, R. J. *J. Am. Chem. Soc.* **1993**, *115*, 2027−2036.



(7)

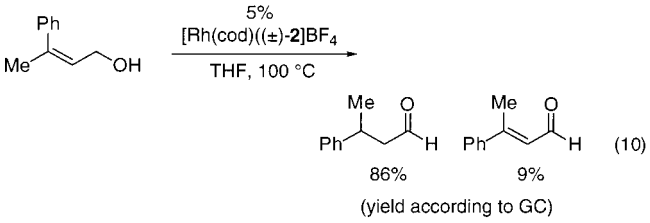
clean 1,3-migration pathway (eq 8).[27] Furthermore, we have established that the migration is an intramolecular process; thus, treatment of a 1:1 mixture of 1,1-dideuterated allylic alcohol **5** and nondeuterated allylic alcohol **7** with [Rh(cod)((+)-**2**)]BF_4 furnishes dideuterated **6** and nondeuterated **8**, with no monodeuterated aldehyde detectable by high-resolution mass spectrometry (eq 9).



(8)

(9)

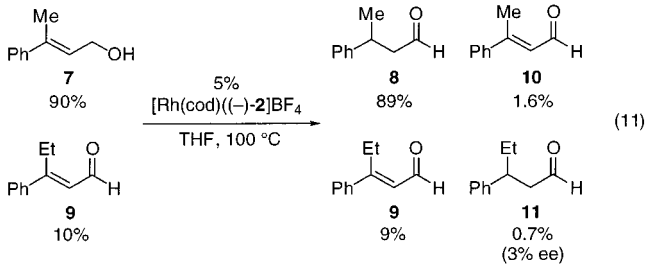
For the [Rh(cod)(**2**)]BF_4-catalyzed enantioselective isomerizations depicted in Tables 2 and 3, the α,β-unsaturated aldehyde, formed through oxidation of the allylic alcohol, is the major sideproduct (e.g., eq 10). The pathway outlined in eq 7 readily accounts for the generation of this compound.



(10)

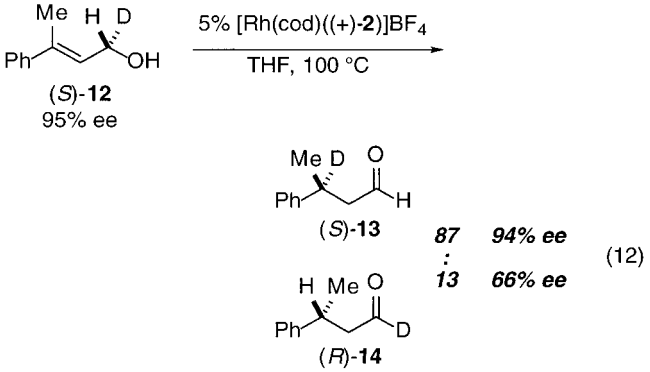
To determine if the unbound α,β-unsaturated aldehyde is an important intermediate on the route to formation of the desired saturated aldehyde, we carried out the reaction illustrated in eq 11. If a significant portion of the desired product is formed through dissociation/reassociation of the α,β-unsaturated aldehyde, then under these conditions a substantial fraction of **9** should be converted to **11**. The small amount of **11** that is generated, along with its low enantiomeric excess, indicates that the free α,β-unsaturated aldehyde is not a critical intermediate in our isomerization processes.[28]

To gain insight into the origin of the stereoselectivity, we examined the asymmetric isomerization of allylic alcohol (*S*)-**12** (95% ee) by each enantiomer of the catalyst (eqs 12 and 13). With (+)-**2**, the deuterium of (*S*)-**12** migrates preferentially to generate (*S*)-**13** in high ee; with (−)-**2**, the hydrogen of (*S*)-**12** migrates predominantly to furnish (*R*)-**14** with excellent stereoselection. These data establish that differentiation between the enantiotopic

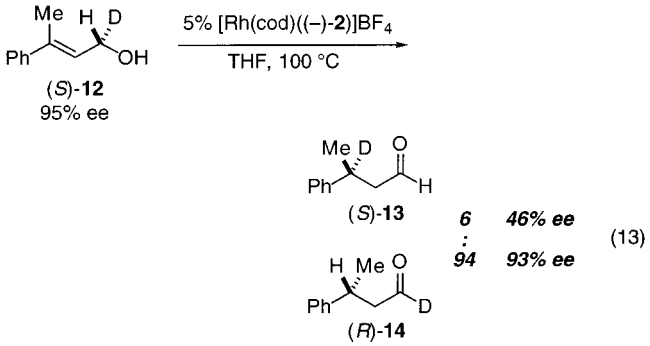


(11)

H/D's during the C−H activation step is an important element of the catalyst's stereocontrol. The differing ratios of D versus H migration for the two enantiomers of the catalyst (87:13 in eq 12; 94:6 in eq 13) are due to an H/D isotope effect that diminishes the enantiotopic-group selectivity of the chiral catalyst in eq 12, but amplifies it in eq 13.



(12)



(13)

Conclusions

In summary, we have synthesized a new planar-chiral bidentate phosphaferrocene ligand (**2**), and we have applied it to rhodium-catalyzed asymmetric isomerizations of allylic alcohols to aldehydes. In terms of yield, scope, and enantioselectivity, this ligand is significantly more effective than phosphaferrocene **1**, which provides the basis for the only other reasonably general and stereoselective method for accomplishing this useful transformation. The isomerization catalyst derived from ligand **2**, [Rh(cod)(**2**)]BF_4, is air-stable and can readily be recovered from the reaction and reused. Mechanistic work has established that these asymmetric isomerizations proceed through an intramolecular 1,3-hydrogen migration pathway and that the chiral catalyst preferentially activates one of the enantiotopic C1 hydrogens.

Experimental Section

General. ^{31}P NMR spectra were recorded with complete proton decoupling on a Varian Mercury 300 spectrometer (121 MHz) at ambient temperature and are referenced to external

(27) The ee of the product (76%) is essentially identical to that observed for the nondeuterated compound (75% ee; Table 3, entry 1).

(28) The result of the crossover experiment illustrated in eq 9 is consistent with this conclusion.

85% H_3PO_4 (δ 0). ^{19}F NMR spectra were recorded on a Varian Mercury 300 spectrometer (282 MHz) at ambient temperature and are referenced to external CCl_3F (δ 0).

Analytical chiral GC was performed on either a Chiraldex G-TA column (20 m × 0.25 mm) or a Chiraldex B-PH column (20 m × 0.25 mm).

THF and Et_2O were distilled from sodium benzophenone ketyl. CH_2Cl_2 was distilled from CaH_2. Hexanes were distilled from sodium. Grade V hydrogen (Boc Gases) and 4 Å molecular sieves (Fluka) were used as received.

$[Rh(cod)_2]BF_4$,[29] (+)- and (−)-**3**,[30] phosphaferrocene (+)-**1**,[30] and $(o\text{-tol})_2PH$[31] were prepared according to literature procedures.

(*Z*)- and (*E*)-3-phenyl-2-buten-1-ol[32] were prepared according to literature procedures, and the olefin configuration was confirmed by NOE experiments.

(*Z*)- and (*E*)-phenyl-2-penten-1-ol[33] and (*E*)-3-cyclohexyl-2-buten-1-ol[34] were prepared according to literature procedures.

All reactions were carried out under an atmosphere of nitrogen or argon in oven-dried glassware with magnetic stirring, unless otherwise indicated.

(*Z*)- and (*E*)-4-Methyl-3-phenyl-2-penten-1-ol. *n*-BuLi (31 mL, 50 mmol; 1.6 M in hexane) was added to a stirred solution of triethylphosphonoacetate (11.2 g, 50.0 mmol) in hexanes (50 mL) at 0 °C, and the resulting mixture was stirred for 0.5 h at 0 °C. Isobutyrophenone (7.4 g, 50 mmol) was added, and the reaction was refluxed for 3 h. The mixture was then cooled to room temperature, quenched by the addition of saturated aqueous Na_2CO_3, and extracted with Et_2O. The organic layer was washed with water, dried over Na_2SO_4, and concentrated. The resulting residue was purified by flash chromatography (hexanes:EtOAc = 20:1) to give ethyl (*E*)-4-methyl-3-phenyl-2-pentenoate[35] (first fraction: 3.8 g, 17 mmol, 34%) and ethyl (*Z*)-4-methyl-3-phenyl-2-pentenoate[35] (second fraction: 2.5 g, 12 mmol, 23%) as colorless oils (not optimized).

Ethyl (*E*)-4-methyl-3-phenyl-2-pentenoate (200 mg, 0.916 mmol) in Et_2O (2 mL) was added to a stirred mixture of $LiAlH_4$ (38 mg, 1.0 mmol) in Et_2O (5 mL) at 0 °C. The reaction was stirred for 10 min at 0 °C and then quenched at 0 °C with H_2O (0.1 mL). After stirring for 10 min at room temperature, the mixture was dried over $MgSO_4$, filtered through Celite, and concentrated. The resulting residue was purified by flash chromatography (hexanes:Et_2O = 5:2) to give (*E*)-4-methyl-3-phenyl-2-penten-1-ol (142 mg, 0.806 mmol, 88%) as a colorless oil. The configuration of (*E*)-4-methyl-3-phenyl-2-penten-1-ol was confirmed by an NOE experiment.

FTIR (neat): 3320, 2963, 2929, 2872, 1492, 1464, 1442, 1362, 1087, 1012 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.17−7.34 (m, 5H), 5.50 (t, J = 6.9 Hz, 1H), 4.38 (d, J = 6.9 Hz, 2H), 3.05 (heptet, J = 6.9 Hz, 1H), 1.07 (d, J = 6.9 Hz, 6H). ^{13}C NMR ($CDCl_3$) δ: 150.1, 142.3, 128.5, 127.7, 127.4, 126.7, 59.2, 30.0, 22.3. HRMS (EI): calcd for $C_{12}H_{16}O$ (M^+), 176.1201; found, 176.1197.

Ethyl (*Z*)-4-methyl-3-phenyl-2-pentenoate (215 mg, 0.985 mmol) was treated with $LiAlH_4$ (40 mg, 1.0 mmol) as described above to give (*Z*)-4-methyl-3-phenyl-2-penten-1-ol (147 mg, 0.837 mmol, 85%) as a colorless oil. The configuration of (*Z*)-4-methyl-3-phenyl-2-penten-1-ol was confirmed by an NOE experiment.

FTIR (neat): 3316, 3055, 2961, 2929, 2871, 1652, 1600, 1493, 1465, 1441, 1382, 1360, 1310, 1073, 1024, 985 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.23−7.35 (m, 3H), 7.05−7.09 (m, 2H), 5.64 (dt, J = 1.2 and 6.9 Hz, 1H), 3.96 (dd, J = 0.6 and 6.9 Hz, 2H), 2.60 (heptet, J = 6.6 Hz, 1H), 1.04 (d, J = 6.6 Hz, 6H). ^{13}C NMR ($CDCl_3$) δ: 151.1, 140.3, 128.7, 128.1, 127.0, 123.3, 60.8, 36.0, 21.9. HRMS (EI): calcd for $C_{12}H_{16}O$ (M^+), 176.1201; found, 176.1198.

(*Z*)- and (*E*)-4-Methyl-3-(4-methylphenyl)-2-penten-1-ol. These were prepared from 4′-methylisobutyrophenone[36] by the same procedure described for (*Z*)- and (*E*)-4-methyl-3-phenyl-2-penten-1-ol. The configurations of (*Z*)- and (*E*)-4-methyl-3-(4-methylphenyl)-2-penten-1-ol were assigned by analogy with the ^1H NMR spectra of (*Z*)- and (*E*)-4-methyl-3-phenyl-2-penten-1-ol.

Z isomer. Colorless oil. FTIR (neat): 3355, 2959, 1608, 1510, 1464, 1286, 1245, 1178, 1033, 984 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.12−7.15 (m, 2H), 6.95−6.99 (m, 2H), 5.63 (dt, J = 1.2 and 6.9 Hz, 1H), 3.97 (d, J = 6.9 Hz, 2H), 2.58 (m, 1H), 2.35 (s, 3H), 1.03 (d, J = 6.9 Hz, 6H). ^{13}C NMR ($CDCl_3$) δ: 151.0, 137.4, 136.7, 128.9, 128.6, 123.2, 60.7, 35.9, 21.8, 21.4. HRMS (EI): calcd for $C_{13}H_{18}O$ (M^+), 190.1358; found, 190.1355.

E isomer. Colorless oil. FTIR (neat): 3316, 2963, 2927, 2871, 2362, 1510, 1456, 1362, 1022, 816 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.06−7.12 (m, 4H), 5.48 (t, J = 6.6 Hz, 1H), 4.36 (d, J = 6.6 Hz, 2H), 3.03 (heptet, J = 6.9 Hz, 1H), 2.35 (s, 3H), 1.06 (d, J = 6.9 Hz, 6H). ^{13}C NMR ($CDCl_3$) δ: 150.1, 139.5, 136.4, 128.6, 128.5, 127.3, 59.2, 30.0, 22.2, 21.3. HRMS (EI): calcd for $C_{13}H_{18}O$ (M^+), 190.1358; found, 190.1353.

(*Z*)- and (*E*)-4-Methyl-3-(4-chlorophenyl)-2-penten-1-ol. These were prepared starting from 4′-chloroisobutyrophenone[36] by the same procedure described for (*Z*)- and (*E*)-4-methyl-3-phenyl-2-penten-1-ol. The configurations of (*Z*)- and (*E*)-4-methyl-3-(4-chlorophenyl)-2-penten-1-ol were assigned by analogy with the ^1H NMR spectra of (*Z*)- and (*E*)-4-methyl-3-phenyl-2-penten-1-ol.

Z isomer. Colorless oil. FTIR (neat): 3314, 2962, 2872, 1651, 1593, 1489, 1466, 1384, 1361, 1305, 1241, 1090, 1030, 1014, 985 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.27−7.34 (m, 2H), 7.00−7.05 (m, 2H), 5.67 (dt, J = 1.2 and 6.9 Hz, 1H), 3.96 (dd, J = 0.9 and 6.6 Hz, 2H), 2.57 (heptet, J = 6.9 Hz, 1H), 1.04 (d, J = 6.9 Hz, 6H). ^{13}C NMR ($CDCl_3$) δ: 149.8, 138.6, 132.9, 130.0, 128.3, 123.8, 60.5, 35.9, 21.8. HRMS (EI): calcd for $C_{12}H_{15}ClO$ (M^+), 210.0811; found, 210.0814.

E isomer. Colorless oil. FTIR (neat): 3334, 2963, 2362, 1646, 1592, 1488, 1464, 1363, 1090, 1015 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.25−7.29 (m, 2H), 7.09−7.13 (m, 2H), 5.47 (t, J = 6.6 Hz, 1H), 4.37 (d, J = 6.6 Hz, 2H), 3.02 (heptet, J = 6.9 Hz, 1H), 1.05 (d, J = 6.9 Hz, 6H). ^{13}C NMR ($CDCl_3$) δ: 148.9, 140.6, 132.7, 129.9, 128.0, 127.9, 59.1, 29.9, 22.2. HRMS (EI): calcd for $C_{12}H_{15}ClO$ (M^+), 210.0811; found, 210.0816.

(*Z*)- and (*E*)-4-Methyl-3-(2-methylphenyl)-2-penten-1-ol. These were prepared starting from 2′-methylisobutyrophenone[37] by the same procedure described for (*Z*)- and (*E*)-4-methyl-3-phenyl-2-penten-1-ol. The configurations of (*Z*)- and (*E*)-4-methyl-3-(2-methylphenyl)-2-penten-1-ol were assigned by analogy with the ^1H NMR spectra of (*Z*)- and (*E*)-4-methyl-3-phenyl-2-penten-1-ol.

Z isomer. Colorless oil. FTIR (neat): 3304, 2961, 1460, 1028, 985, 761, 732 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.12−7.20 (m, 3H), 6.93−6.96 (m, 1H), 5.69 (dt, J = 1.5 and 6.6 Hz, 1H), 3.83 (ddd, J = 0.9, 3.0, and 6.6 Hz, 2H), 2.45 (m, 1H), 2.19 (s, 3H), 1.09 (d, J = 6.9 Hz, 3H), 1.05 (d, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 149.8, 140.1, 135.5, 130.0, 128.9, 127.0, 125.4, 123.2, 60.9, 35.7, 21.8, 21.5, 19.9. HRMS (EI): calcd for $C_{13}H_{18}O$ (M^+), 190.1352; found, 190.1348.

E isomer. Colorless oil. FTIR (neat): 3322, 2962, 2871, 1648, 1487, 1461, 1380, 1361, 1101, 1011, 762, 732 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.08−7.21 (m, 3H), 6.99−7.02 (m, 1H), 5.36 (t, J = 6.6 Hz, 1H), 4.39 (d, J = 6.6 Hz, 2H), 3.03 (heptet, J = 6.9 Hz, 1H), 2.26 (s, 3H), 1.00 (d, J = 6.9 Hz, 6H). ^{13}C NMR ($CDCl_3$) δ: 130.2, 129.4, 127.7, 126.7, 124.7, 59.2, 30.7, 22.1, 20.7. HRMS (EI): calcd for $C_{13}H_{18}O$ (M^+), 190.1352; found, 190.1350.

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(*Z*)-4,4-Dimethyl-3-phenyl-2-penten-1-ol. Ethyl (*Z*)-4,4-dimethyl-3-phenyl-2-pentenoate[35] (416 mg, 1.79 mmol) in Et_2O (2 mL) was added to a stirred mixture of $LiAlH_4$ (68 mg, 1.8 mmol) in Et_2O (10 mL) at 0 °C. The reaction was stirred for 10 min at 0 °C and then quenched at 0 °C with H_2O (0.1 mL). After stirring for 10 min at room temperature, the mixture was dried over $MgSO_4$, filtered through Celite, and concentrated. The resulting residue was purified by flash chromatography (hexanes:Et_2O = 5:2) to give (*Z*)-4,4-dimethyl-3-phenyl-2-penten-1-ol (325 mg, 1.71 mmol, 95%) as a colorless solid.

mp 36−38 °C. FTIR (neat): 3316, 2985, 2905, 2868, 1479, 1482, 1357, 1025, 981, 770, 709 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.23−7.34 (m, 3H), 6.99−7.02 (m, 2H), 5.76 (t, J = 6.6 Hz, 1H), 3.75 (d, J = 6.6 Hz, 2H), 1.08 (s, 9H). ^{13}C NMR ($CDCl_3$) δ: 153.7, 139.5, 129.5, 127.8, 126.6, 123.3, 61.1, 36.3, 29.7. HRMS (EI): calcd for $C_{13}H_{18}O$ (M^+), 190.1352; found, 190.1337.

(*Z*)-3-Cyclohexyl-2-buten-1-ol.[34] Cp_2TiCl_2 (30 mg, 0.12 mmol) was added to a stirred 0 °C solution of isobutylmagnesium bromide (1.4 mL, 2.8 mmol; 2.0 M in Et_2O) in Et_2O (2 mL), and the resulting mixture was stirred for 5 min at 0 °C. A solution of 3-cyclohexyl-2-propyn-1-ol[38] (163 mg, 1.18 mmol) in Et_2O (2 mL) was added, and the reaction was stirred for 2 h at room temperature. It was then concentrated, and the residue was dissolved in THF (4 mL). MeI (454 mg, 3.20 mmol) was added to the 0 °C solution, which was then stirred for 2 h at room temperature. The reaction was quenched (dilute aqueous HCl) and extracted with Et_2O. The organic layer was washed with saturated aqueous Na_2CO_3, dried over Na_2SO_4, and concentrated. The resulting residue was purified by flash chromatography (hexanes:Et_2O = 4:1) to give (*Z*)-3-cyclohexyl-2-buten-1-ol (108 mg, 0.700 mmol, 59%).

^1H NMR ($CDCl_3$) δ: 5.34 (dt, J = 3.9 and 0.9 Hz, 1H), 4.15 (dq, J = 7.2 and 0.9 Hz, 2H), 2.39−2.50 (m, 1H), 1.67 (dd, J = 1.5 and 0.9 Hz, 3H), 1.22−1.77 (m, 10H).

Synthesis of (+)-2 (eq 4). *n*-BuLi (140 μL, 0.22 mmol; 1.6 M in hexane) was added dropwise to a stirred solution of (+)-**3** (74 mg, 0.22 mmol; >99% ee) in THF (7 mL), and the resulting mixture was stirred for 10 min at room temperature. A solution of *p*-toluenesulfonyl chloride (43 mg, 0.23 mmol) in THF (1 mL) was added dropwise, and the reaction mixture was stirred for 10 min at room temperature. (*o*-Tol)$_2$PLi, prepared by mixing (*o*-tol)$_2$PH (95 mg, 0.44 mmol) in THF (2 mL) with *n*-BuLi (277 μL, 0.44 mmol; 1.6 M in hexane), was added dropwise, and the resulting solution was stirred for 2 h at room temperature. The reaction was quenched by the addition of H_2O (0.2 mL), dried ($MgSO_4$), and filtered through Celite. The solvent was evaporated, and the residue was purified by flash chromatography (hexanes:benzene = 4:1) to give (+)-**2** (45 mg, 0.0852 mmol, 38%) as an amorphous yellow compound.

$[\alpha]^{20}_D$ +37.4° (*c* 0.46, THF; >99% ee). FTIR (neat): 3629, 2963, 2911, 1451, 1375, 1231, 1159, 1029, 861, 746 cm^{-1}. ^1H NMR (CD_2Cl_2) δ: 7.08−7.31 (m, 8H,), 3.18 (d, J = 35.7 Hz, 1H), 2.76−2.80 (m, 2H), 2.20 (s, 3H), 2.15 (s, 3H), 2.01 (s, 3H), 1.81 (s, 15H), 1.75 (s, 3H). ^{13}C NMR (CD_2Cl_2) δ: 143.4 (d, J = 25.7 Hz), 142.5 (d, J = 24.8 Hz), 138.1 (dd, J = 17.6 Hz), 137.3 (d, J = 16.1 Hz), 131.9 (d, J = 2.9 Hz), 131.3, 130.0 (d, J = 4.3 Hz), 129.7 (d, J = 4.7 Hz), 128.6, 128.3, 126.1, 126.0, 94.4 (d, J = 6.5 Hz), 93.7 (dd, J = 55.1 and 18.4 Hz), 90.5 (dd, J = 5.0 and 2.1 Hz), 82.2, 80.9 (dd, J = 56.9 and 1.4 Hz), 28.4 (dd, J = 19.7 and 14.6 Hz), 21.6, 21.3, 14.5, 11.0 (d, J = 3.8 Hz), 10.7. ^{31}P NMR (CD_2Cl_2) δ: −60.1 (d, 22.0 Hz), −34.2 (d, 22.0 Hz). HRMS (EI): calcd for $C_{31}H_{38}FeP_2$ (M^+), 528.1793; found, 528.1827.

Synthesis of [Rh(cod)((+)-2)]BF_4. In a N_2-filled glovebox, a solution of (+)-**2** (41 mg, 0.078 mmol, >99% ee) in THF (2 mL) was added to a stirred suspension of [Rh(cod)$_2$]BF_4 (30 mg, 0.074 mmol) in THF (6 mL), and the resulting dark-red solution was stirred for 10 min at room temperature. The reaction mixture was filtered through an acrodisc, concentrated to 1 mL, and then added dropwise to pentane (15 mL; stirring) at room temperature. The resulting orange suspension was filtered, and the crystals were dried under vacuum to give [Rh(cod)((+)-**2**]BF_4 (58 mg, 0.070 mmol, 95%) as orange crystals.

mp >250 °C. FTIR (neat): 2918, 1451, 1378, 1261, 1055, 802, 761 cm^{-1}. ^1H NMR (CD_2Cl_2) δ: 8.82 (br, 1H), 7.14−7.65 (m, 8H), 6.98 (br, 1H), 5.90 (br, 1H), 5.81 (br, 1H), 4.76 (br, 1H), 3.76 (br, 1H), 3.34 (d, J = 32.4 Hz, 1H), 2.81−2.95 (m, 2H), 2.36−2.74 (m, 6H), 2.32 (s, 3H), 2.28 (s, 3H), 2.08 (s, 3H), 1.98 (s, 3H), 1.50 (s, 15H). ^{31}P NMR (CD_2Cl_2) δ: 33.9 (dd, J = 178.2 and 28.7 Hz), 63.2 (dd, J = 138.5 and 25.0 Hz). ^{19}F NMR (CD_2Cl_2) δ: 23.5 (s). HRMS (ESI): calcd for $C_{39}H_{50}FeP_2Rh$ (M^+), 739.1787; found, 739.1800. Anal. Calcd for $C_{39}H_{50}BF_4FeP_2Rh$: C, 56.69; H, 6.10. Found: C, 56.67; H, 6.14.

Table 1, Entry 1. In a N_2-filled glovebox, a solution of (+)-**1** (6.7 mg, 0.013 mmol) in THF (2 mL) was added dropwise to a stirred suspension of [Rh(cod)$_2$]BF_4 (5.4 mg, 0.013 mmol) in THF (4 mL), resulting in a bright-red solution. After 5 min, the reaction mixture was filtered through an acrodisc, which was washed with THF (1 mL). The filtrate was placed into a 100 mL Schlenk tube, which was removed from the glovebox and cooled with liquid nitrogen. After three vacuum/H_2-refill cycles, the valve to the Schlenk tube was closed, and the solution was stirred for 1 h at room temperature, giving a dark-brown mixture. The mixture was filtered through an acrodisc in a glovebox, providing a dark-brown solution. The filtrate was placed into a Schlenk tube and concentrated to dryness. Then, a solution of (*E*)-4-methyl-3-phenyl-2-penten-1-ol (47.2 mg, 0.268 mmol) in THF (3 mL) was added to the residue in the Schlenk tube, and the reaction mixture was stirred for 24 h at 70 °C. The solution was then concentrated, and the product was purified by silica gel column chromatography (hexanes:Et_2O = 10:1) to give (*R*)-4-methyl-3-phenylpentanal (40.6 mg, 0.231 mmol, 86%; 77% ee; the value in Table 1 is the average of two runs) as a colorless oil. The enantiomeric excess of 4-methyl-3-phenylpentanal was analyzed on a Chiraldex G-TA column (105 °C; isothermal).

Table 1, Entry 2. In a N_2-filled glovebox, [Rh(cod)((+)-**2**)]BF_4 (7.0 mg, 0.0085 mmol) and THF (3 mL) were placed into a 100 mL Schlenk tube. The Schlenk tube was taken out of the glovebox and cooled with liquid nitrogen. After three vacuum/H_2-refill cycles, the valve to the Schlenk tube was closed, and the solution was stirred for 1 h at room temperature, giving a dark-brown mixture. The mixture was filtered through an acrodisc in a glovebox, providing a dark-brown solution. The filtrate was placed into a Schlenk tube and concentrated to dryness. Then, (*E*)-4-methyl-3-phenyl-2-penten-1-ol (30.0 mg, 0.170 mmol) in THF (3 mL) was added to the residue in the Schlenk tube, and the reaction mixture was stirred for 24 h at 70 °C. The solution was then concentrated, and the product was purified by silica gel column chromatography (pentane:Et_2O = 4:1) to give (*R*)-4-methyl-3-phenylpentanal (28.6 mg, 0.163 mmol, 95%; 82% ee).

Table 1, Entry 3. In a N_2-filled glovebox, [Rh(cod)((+)-**2**)]BF_4 (8.2 mg, 0.010 mmol), (*E*)-4-methyl-3-phenyl-2-penten-1-ol (35.0 mg, 0.199 mmol), and THF (3 mL) were added to a Schlenk tube, and the resulting dark-red solution was stirred for 26 h at 100 °C. The reaction mixture was then cooled to room temperature and added to pentane (6 mL; stirred). The resulting slurry was filtered, and the crystals were washed with pentane, dissolved in THF, and concentrated to furnish the recovered catalyst, [Rh(cod)((+)-**2**)]BF_4 (7.4 mg, 0.0090 mmol, 90%), as a red solid. The filtrate was concentrated, and the product was purified by silica gel column chromatography (pentane:Et_2O = 4:1) to give (*R*)-4-methyl-3-phenylpentanal (33.8 mg, 0.192 mmol, 97%; 93% ee).

Tables 2 and 3: General Procedure 1 (With a Glovebox; Table 2, Entry 1). In a N_2-filled glovebox, [Rh(cod)((+)-**2**)]BF_4 (9.8 mg, 0.012 mmol), (*E*)-3-phenyl-2-buten-1-ol (35.0 mg, 0.237 mmol), and THF (3 mL) were added to a Schlenk tube, and the resulting dark-red solution was stirred for 22 h at 100 °C. The reaction mixture was then cooled to room temperature and added to pentane (10 mL). The resulting slurry was filtered, providing orange crystals. The crystals were washed with pentane, dissolved in THF, and the solvent

(38) Borne, R. F.; Forrester, M. L.; Waters, I. W. *J. Med. Chem.* **1977**, *20*, 771−776.

was removed, affording the recovered catalyst, [Rh(cod)((+)-**2**)]BF_4 (8.4 mg, 0.010 mmol, 86%), as a red solid. The filtrate was concentrated, and the product was purified by silica gel column chromatography (pentane:Et_2O = 4:1) to give (*S*)-3-phenylbutanal (31.8 mg, 0.215 mmol, 91%; 74% ee) as a colorless oil.

Tables 2 and 3: General Procedure 2 (Without a Glovebox, With Recycled Catalyst; Table 2, Entry 6). In the air, the recovered catalyst, [Rh(cod)((+)-**2**)]BF_4 (5.8 mg, 0.0070 mmol), was placed into a Schlenk tube, which was then filled with argon. Under a positive pressure of argon, a solution of (*E*)-3-(4-chlorophenyl)-4-methyl-2-penten-1-ol (29.5 mg, 0.140 mmol) in THF (3 mL) was added via a Pasteur pipet. The Schlenk tube was closed, and the dark-red solution was stirred for 21 h at 100 °C. The reaction mixture was then cooled to room temperature and added to pentane (10 mL; stirred). The resulting slurry was filtered, providing orange crystals. The crystals were washed with pentane, dissolved in THF, and the solvent was removed, affording the recovered catalyst, [Rh(cod)((+)-**2**)]BF_4 (5.3 mg, 0.0064 mmol, 91%), as a red solid. The filtrate was concentrated and purified by silica gel column chromatography (pentane:Et_2O = 4:1) to give (*R*)-3-(4-chlorophenyl)-4-methylpentanal (24.4 mg, 0.116 mmol, 83%; 91% ee) as a colorless oil.

Although the twice-used catalyst appeared to be pure by NMR (^1H and ^{31}P), an elemental analysis showed a lower than expected carbon and hydrogen content. Anal. Calcd for $C_{39}H_{50}BF_4FeP_2Rh$: C, 56.69; H, 6.10. Found: C, 54.01; H, 5.82.

Table 2, Entry 1. The first run was carried out as described in Procedure 1.

A second run was carried out according to Procedure 1, using the recovered catalyst. Reaction time: 22 h. (*S*)-3-Phenylbutanal was obtained in 91% isolated yield with 76% ee.

(*S*)-3-Phenylbutanal.[39] Colorless oil. $[\alpha]^{20}_D$ +21.3° (*c* 1.50, CH_2Cl_2; 74% ee). ^1H NMR ($CDCl_3$) δ: 9.71 (t, J = 2.1 Hz, 1H), 7.19−7.35 (m, 5H), 3.32−3.43 (m, 1H), 2.77 (ddd, J = 16.8, 6.9, and 2.1 Hz, 1H), 2.66 (ddd, J = 16.8, 7.5, and 2.1 Hz, 1H), 1.33 (d, J = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 202.0, 145.6, 128.9, 127.0, 126.7, 52.1, 34.6, 22.5. Chiraldex G-TA column, retention time = 16.1 min (90 °C; isothermal).

Table 2, Entry 2. Procedure 1 was followed, using 8.9 mg of [Rh(cod)((+)-**2**)]BF_4 and 35.0 mg of (*E*)-3-phenyl-2-penten-1-ol. Reaction time: 21 h. (*S*)-3-Phenylpentanal was obtained in 97% isolated yield with 76% ee.

A second run was carried out according to Procedure 2, using the recovered catalyst. Reaction time: 24 h. (*S*)-3-Phenylpentanal was obtained in 94% isolated yield with 75% ee.

(*S*)-3-Phenylpentanal. Colorless oil. $[\alpha]^{20}_D$ +11.8° (*c* 1.26, benzene; 56% ee). ^1H NMR ($CDCl_3$) δ: 9.67 (t, J = 2.1 Hz, 1H), 7.16−7.34 (m, 5H), 3.04−3.14 (m, 1H), 2.72 (dd, J = 16.8 and 2.1 Hz, 2H), 1.56−1.79 (m, 2H), 0.81 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 202.4, 143.9, 128.9, 127.8, 126.8, 50.5, 42.0, 29.7, 12.1. Chiraldex G-TA column, retention time = 23.8 min (90 °C; isothermal).

Table 2, Entry 3. Procedure 1 was followed, using 8.2 mg of [Rh(cod)((+)-**2**)]BF_4 and 35.0 mg of (*E*)-4-methyl-3-phenyl-2-penten-1-ol. Reaction time: 26 h. (*R*)-4-Methyl-3-phenylpentanal was obtained in 97% isolated yield with 93% ee.

A second run was carried out according to Procedure 1, using the recovered catalyst. Reaction time: 22 h. (*R*)-4-Methyl-3-phenylpentanal was obtained in 99% isolated yield with 92% ee.

(*R*)-4-Methyl-3-phenylpentanal. Colorless oil. $[\alpha]^{20}_D$ −17.3° (*c* 1.38, CH_2Cl_2; 93% ee). Chiraldex G-TA column, retention time = 14.2 min (105 °C; isothermal).

Table 2, Entry 4. Procedure 1 was followed, using 7.6 mg of [Rh(cod)((+)-**2**)]BF_4 and 35.0 mg of (*E*)-4-methyl-3-(2-methylphenyl)-2-penten-1-ol. Reaction time: 24 h. Reaction temperature: 150 °C. (*R*)-4-Methyl-3-(2-methylphenyl)pentanal was obtained in 85% isolated yield with 91% ee.

A second run was carried out according to Procedure 2, using the recovered catalyst. Reaction time: 48 h. (*R*)-4-Methyl-3-(2-methylphenyl)pentanal was obtained in 87% isolated yield with 92% ee.

(*R*)-4-Methyl-3-(2-methylphenyl)pentanal. Colorless oil. $[\alpha]^{20}_D$ −14.2° (*c* 1.49, CH_2Cl_2; 91% ee). Chiraldex G-TA column, retention time = 20.2 min (105 °C; isothermal).

Table 2, Entry 5. Procedure 1 was followed, using 7.6 mg of [Rh(cod)((+)-**2**)]BF_4 and 35.0 mg of (*E*)-4-methyl-3-(4-methylphenyl)-2-penten-1-ol. Reaction time: 22 h. (*R*)-4-Methyl-3-(4-methylphenyl)pentanal was obtained in 89% isolated yield with 91% ee.

A second run was carried out according to Procedure 1, using the recovered catalyst. Reaction time: 21 h. (*R*)-4-Methyl-3-(4-methylphenyl)pentanal was obtained in 90% isolated yield with 91% ee.

(*R*)-4-Methyl-3-(4-methylphenyl)pentanal. Colorless oil. $[\alpha]^{20}_D$ −23.0° (*c* 0.81, CH_2Cl_2; 91% ee).

The aldehyde was reduced ($LiAlH_4$), acylated (trifluoroacetic anhydride), and then analyzed on a Chiraldex B-PH column, retention time = 13.7 min (90 °C; isothermal).

Table 2, Entry 6. Procedure 1 was followed, using 6.9 mg of [Rh(cod)((+)-**2**)]BF_4 and 35.0 mg of (*E*)-3-(4-chlorophenyl)-4-methyl-2-penten-1-ol. Reaction time: 22 h. (*R*)-3-(4-Chlorophenyl)-4-methylpentanal was obtained in 88% isolated yield with 92% ee.

The second run was carried out as described in Procedure 2.

(*R*)-3-(4-Chlorophenyl)-4-methylpentanal. Colorless oil. $[\alpha]^{20}_D$ −15.3° (*c* 1.04, CH_2Cl_2; 92% ee).

The aldehyde was reduced ($LiAlH_4$), acylated (trifluoroacetic anhydride), and then analyzed on a Chiraldex B-PH column, retention time = 47.4 min (90 °C; isothermal).

Table 3, Entry 1. Procedure 1 was followed, using 9.8 mg of [Rh(cod)((+)-**2**)]BF_4 and 35.0 mg of (*Z*)-3-phenyl-2-buten-1-ol. Reaction time: 22 h. (*R*)-3-Phenylbutanal was obtained in 79% isolated yield with 58% ee.

A second run was carried out according to Procedure 2, using the recovered catalyst. Reaction time: 45 h. (*R*)-3-Phenylbutanal was obtained in 81% isolated yield with 60% ee.

(*R*)-3-Phenylbutanal.[39] Colorless oil. $[\alpha]^{20}_D$ −15.5° (*c* 1.29, CH_2Cl_2; 58% ee), −12.0° (*c* 1.20, Et_2O; 58% ee) [lit. $[\alpha]^{25}_D$ −38.5° (*c* 0.2, Et_2O; >95% ee)]. Chiraldex G-TA column, retention time = 17.3 min (90 °C; isothermal).

Table 3, Entry 2. Procedure 1 was followed, using 8.9 mg of [Rh(cod)((+)-**2**)]BF_4 and 35.0 mg of (*Z*)-3-phenyl-2-penten-1-ol. Reaction time: 23 h. (*R*)-3-phenylpentanal was obtained in 75% isolated yield with 56% ee.

A second run was carried out according to Procedure 2, using the recovered catalyst. Reaction time: 24 h. (*R*)-3-Phenylpentanal was obtained in 80% isolated yield with 58% ee.

(*R*)-3-Phenylpentanal.[40] Colorless oil. $[\alpha]^{20}_D$ −18.4° (*c* 1.56, benzene; 76% ee) [lit. $[\alpha]^{20}_D$ −15.9° (*c* 1.27, benzene; 82% ee)]. Chiraldex G-TA column, retention time = 27.1 min (90 °C; isothermal).

Table 3, Entry 3. Procedure 1 was followed, using 8.2 mg of [Rh(cod)((+)-**2**)]BF_4 and 35.0 mg of (*Z*)-4-methyl-3-phenyl-2-penten-1-ol. Reaction time: 46 h. (*S*)-4-Methyl-3-phenylpentanal was obtained in 81% isolated yield with 83% ee.

A second run was carried out according to Procedure 1, using the recovered catalyst. Reaction time: 46 h. (*S*)-4-Methyl-3-phenylpentanal was obtained in 82% isolated yield with 81% ee.

(*S*)-4-Methyl-3-phenylpentanal.[40] Colorless oil. $[\alpha]^{20}_D$ +14.9° (*c* 1.04, CH_2Cl_2; 83% ee), +24.6° (*c* 2.26, benzene; 83% ee) [lit. $[\alpha]^{20}_D$ +23.1° (*c* 0.94, benzene; 86% ee)]. ^1H NMR ($CDCl_3$) δ: 9.71 (t, J = 2.1 Hz, 1H), 7.24−7.43 (m, 5H), 3.07 (ddd, J = 9.3, 7.5, and 5.7 Hz, 1H), 2.93 (ddd, J = 16.2, 5.7, and 2.1 Hz, 1H), 2.86 (ddd, J = 16.2, 9.3, and 2.7 Hz, 1H), 1.99 (d of septet, J = 6.6 and 7.5 Hz, 1H), 1.07 (d, J = 6.6 Hz, 3H), 0.89 (d, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 202.3, 142.5, 128.3, 128.1, 126.4, 47.2, 46.9, 33.5, 20.6, 20.3. Chiraldex G-TA column, retention time = 16.2 min (105 °C; isothermal).

(39) Lee, T.; Jones, J. B. *J. Am. Chem. Soc.* **1996**, *118*, 502−508.

(40) Ahlbrecht, H.; Enders, D.; Santowski, L.; Zimmermann, G. *Chem. Ber.* **1989**, *122*, 1995−2004.

Table 3, Entry 4. Procedure 1 was followed, using 5.8 mg of [Rh(cod)((+)-**2**)]BF_4 and 26.7 mg of (*Z*)-4,4-dimethyl-3-phenyl-2-penten-1-ol. Reaction time: 22 h. (*S*)-4,4-Dimethyl-3-phenylpentanal was obtained in 88% isolated yield with 90% ee.

A second run was carried out according to Procedure 1, using the recovered catalyst. Reaction time: 51 h. (*S*)-4,4-Dimethyl-3-phenylpentanal was obtained in 92% isolated yield with 91% ee.

(*S*)-4,4-Dimethyl-3-phenylpentanal.[41] Colorless oil. $[\alpha]^{20}_D$ +44.0° (*c* 1.29, CH_2Cl_2; 91% ee). ^1H NMR ($CDCl_3$) δ: 9.53 (dd, J = 2.7 and 1.8 Hz, 1H), 7.13−7.30 (m, 5H), 3.03 (dd, J = 7.2 and 5.1 Hz, 1H), 2.88 (ddd, J = 16.5, 10.2, and 5.1 Hz, 1H), 2.79 (ddd, J = 16.2, 4.8, and 2.1 Hz, 1H), 0.91 (s, 9H). ^{13}C NMR ($CDCl_3$) δ: 202.9, 141.3, 129.6, 128.1, 126.8, 50.6, 44.9, 34.1, 28.2. Chiraldex G-TA column, retention time = 19.0 min (*S* isomer) and 21.3 min (*R* isomer) (105 °C; isothermal).

The absolute configuration of (+)-4,4-dimethyl-3-phenylpentanal was determined to be *S* by converting it to (*S*)-4,4-dimethyl-3-phenylpentanoic acid (CrO_3/aqueous H_2SO_4).[42] $[\alpha]^{20}_D$ −20.4° (*c* 2.2, $CHCl_3$; 91% ee), $[\alpha]^{20}_D$ −13.9° (*c* 1.0, EtOH; 91% ee) [lit. $[\alpha]_D$ −15.8° (*c* 0.820, EtOH)].

Table 3, Entry 5. Procedure 1 was followed, using 7.6 mg of [Rh(cod)((+)-**2**)]BF_4 and 35.0 mg of (*Z*)-4-methyl-3-(2-methylphenyl)-2-penten-1-ol. Reaction time: 48 h. Reaction temperature: 150 °C. (*S*)-4-Methyl-3-(2-methylphenyl)pentanal was obtained in 63% isolated yield with 83% ee.

A second run was carried out according to Procedure 2, using the recovered catalyst. Reaction time: 47 h. (*S*)-4-Methyl-3-(2-methylphenyl)pentanal was obtained in 58% isolated yield with 79% ee.

(*S*)-4-Methyl-3-(2-methylphenyl)pentanal. Colorless oil. $[\alpha]^{20}_D$ +13.0° (*c* 1.11, CH_2Cl_2; 83% ee). FTIR (neat): 2958, 1724, 1464, 1385, 1035, 758, 730 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 9.56 (t, J = 2.1 Hz, 1H), 7.05−7.19 (m, 4H), 3.23 (ddd, J = 9.6, 8.1, and 5.4 Hz, 1H), 2.83 (ddd, J = 16.5, 5.4, and 2.1 Hz, 1H), 2.72 (ddd, J = 16.5, 9.6, and 2.1 Hz, 1H), 2.37 (s, 3H), 1.88 (m, 1H), 0.99 (d, J = 6.6 Hz, 3H), 0.80 (d, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 202.6, 142.0, 136.4, 130.6, 126.5, 126.4, 126.2, 47.8, 41.7, 34.1, 21.1, 20.58, 20.56. HRMS (EI): calcd for $C_{13}H_{18}O_2$ (M^+), 190.1352; found, 190.1356. Chiraldex G-TA column, retention time = 21.0 min (105 °C; isothermal).

The absolute configuration of (+)-4-methyl-3-(2-methylphenyl)pentanal was determined to be *S* by converting it to an oxazolidine and analyzing the oxazolidine by ^{13}C NMR (ephedrine method).[40] For the racemic aldehyde and (−)-ephedrine, ^{13}C NMR ($CDCl_3$) δ: 97.2 (C-2, *R*), 96.0 (C-2, *S*), 81.8 (C-5, *S*), 81.4 (C-5, *R*), 64.4 (C-4, *R* and *S*), 15.5 (4-CH_3, *R*), 15.2 (4-CH_3, *S*).

Table 3, Entry 6. Procedure 1 was followed, using 7.6 mg of [Rh(cod)((+)-**2**)]BF_4 and 35.0 mg of (*Z*)-4-methyl-3-(4-methylphenyl)-2-penten-1-ol. Reaction time: 22 h. (*S*)-4-Methyl-3-(2-methylphenyl)pentanal was obtained in 84% isolated yield with 77% ee.

A second run was carried out according to Procedure 1, using the recovered catalyst. Reaction time: 21 h. (*S*)-4-Methyl-3-(4-methylphenyl)pentanal was obtained in 82% isolated yield with 77% ee.

(*S*)-4-Methyl-3-(4-methylphenyl)pentanal. Colorless oil. $[\alpha]^{20}_D$ +16.1° (*c* 0.89, CH_2Cl_2; 77% ee). FTIR (neat): 2960, 1726, 1671, 1514, 1466, 1386, 1036, 810 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 9.59 (dd, J = 2.4 and 1.8 Hz, 1H), 7.02−7.11 (m, 4H), 2.93 (ddd, J = 9.6, 7.5, and 5.4 Hz, 1H), 2.79 (ddd, J = 16.2, 5.4, and 2.1 Hz, 1H), 2.72 (ddd, J = 16.2, 9.6, and 2.4 Hz, 1H), 2.32 (s, 3H), 1.84 (d of septet, J = 6.6 and 6.6 Hz, 1H), 0.94 (d, J = 6.6 Hz, 3H), 0.78 (d, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 202.9, 139.6, 136.2, 129.2, 128.3, 47.5, 46.9, 33.8, 21.4, 20.9, 20.6. HRMS (EI): calcd for $C_{13}H_{18}O_2$ (M^+), 190.1352; found, 190.1355.

The aldehyde was reduced ($LiAlH_4$), acylated (trifluoroacetic anhydride), and then analyzed on a Chiraldex B-PH column, retention time = 14.1 min (90 °C; isothermal).

The absolute configuration of (+)-4-methyl-3-(4-methylphenyl)pentanal was determined to be *S* by converting it to an oxazolidine and analyzing the oxazolidine by ^{13}C NMR (ephedrine method).[40] For the racemic aldehyde and (−)-ephedrine, ^{13}C NMR ($CDCl_3$) δ: 96.8 (C-2, *R*), 96.0 (C-2, *S*), 82.0 (C-5, *S*), 81.6 (C-5, *R*), 64.6 (C-4, *R*), 64.4 (C-4, *S*), 15.6 (4-CH_3, *R*), 15.3 (4-CH_3, *S*).

Table 3, Entry 7. Procedure 1 was followed, using 6.9 mg of [Rh(cod)((+)-**2**)]BF_4 and 35.0 mg of (*Z*)-3-(4-chlorophenyl)-4-methyl-2-penten-1-ol. Reaction time: 21 h. (*S*)-3-(4-Chlorophenyl)-4-methylpentanal was obtained in 86% isolated yield with 84% ee.

A second run was carried out according to Procedure 1, using the recovered catalyst. Reaction time: 20 h. (*S*)-3-(4-Chlorophenyl)-4-methylpentanal was obtained in 80% isolated yield with 86% ee.

(*S*)-3-(4-Chlorophenyl)-4-methylpentanal. Colorless oil. $[\alpha]^{20}_D$ +12.8° (*c* 1.20, CH_2Cl_2; 84% ee). FTIR (neat): 2960, 1725, 1491, 1092, 1013, 819 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 9.60 (dd, J = 2.4 and 1.8 Hz, 1H), 7.23−7.28 (m, 2H), 7.06−7.10 (m, 2H), 2.94 (ddd, J = 9.6, 7.5, and 5.1 Hz, 1H), 2.81 (ddd, J = 16.5, 5.1, and 1.8 Hz, 1H), 2.71 (ddd, J = 16.5, 9.6, and 2.4 Hz, 1H), 1.83 (d of septet, J = 6.6 and 6.6 Hz, 1H), 0.93 (d, J = 6.6 Hz, 3H), 0.75 (d, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 202.0, 141.3, 132.4, 129.8, 128.7, 47.5, 46.5, 33.7, 20.9, 20.5. HRMS (EI): calcd for $C_{12}H_{15}ClO$ (M^+), 210.0811; found, 210.0808.

The aldehyde was reduced ($LiAlH_4$), acylated (trifluoroacetic anhydride), and then analyzed on a Chiraldex B-PH column.

(*S*)-3-(4-Chlorophenyl)-4-methylpentan-1-ol. Colorless oil. $[\alpha]^{20}_D$ −11.4° (*c* 0.70, CH_2Cl_2; 84% ee). FTIR (neat): 3332, 2953, 1489, 1471, 1411, 1386, 1092, 1045, 1014 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.24−7.29 (m, 2H), 7.05−7.10 (m, 2H), 3.45−3.53 (m, 1H), 3.33−3.41 (m, 1H), 2.43 (ddd, J = 11.7, 7.8, and 3.9 Hz, 1H), 2.03−2.14 (m, 1H), 1.73−1.86 (m, 2H), 0.97 (d, J = 6.6 Hz, 3H), 0.73 (d, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 142.3, 131.8, 129.8, 128.4, 61.6, 49.0, 36.0, 33.7, 21.2, 20.8. HRMS (EI): calcd for $C_{12}H_{15}ClO$ (M^+), 212.0968; found, 212.0972. Chiraldex B-PH column, retention time = 48.7 min (trifluoroacetate; 90 °C; isothermal).

The absolute configuration of (−)-3-(4-chlorophenyl)-4-methylpentan-1-ol was determined to be *S* by converting it to (*S*)-4-methyl-3-phenylpentan-1-ol[40] (10% Pd/C, 25% aqueous NaOH, EtOH, 1 atm H_2, rt, 3 h). Chiraldex G-TA column, retention times = 26.88 min [*R* isomer, minor], 27.35 min [*S* isomer, major] (105 °C; isothermal). An authentic sample of (*S*)-4-methyl-3-phenylpentan-1-ol was prepared by reducing (*S*)-4-methyl-3-phenylpentanal with $LiAlH_4$.

Equation 5 (*Z* isomer). Procedure 1 was followed, using 9.4 mg of [Rh(cod)((+)-**2**)]BF_4 and 35.0 mg of (*Z*)-3-cyclohexyl-2-buten-1-ol. Reaction time: 21 h. (*R*)-3-Cyclohexylbutanal was obtained in 86% isolated yield with 80% ee.

A second run was carried out according to Procedure 1, using the recovered catalyst. Reaction time: 19 h. (*R*)-3-Cyclohexylbutanal was obtained in 88% isolated yield with 80% ee.

(*R*)-3-Cyclohexylbutanal.[43] Colorless oil. $[\alpha]^{20}_D$ −13.9° (*c* 0.65, CH_2Cl_2; 80% ee). Chiraldex G-TA column, retention time = 42.2 min (70 °C; isothermal).

The aldehyde was reduced ($LiAlH_4$), acylated (trifluoroacetic anhydride), and then analyzed on a Chiraldex G-TA column, retention time = 21.4 min (80 °C; isothermal).

Equation 5 (*E* isomer). Procedure 1 was followed, using 9.4 mg of [Rh(cod)((+)-**2**)]BF_4 and 35.0 mg of (*E*)-3-cyclohexyl-2-buten-1-ol. Reaction time: 21 h. (*S*)-3-Cyclohexylbutanal was obtained in 91% isolated yield with 74% ee.

A second run was carried out according to Procedure 1, using the recovered catalyst. Reaction time: 19 h. (*S*)-3-Cyclohexylbutanal was obtained in 97% isolated yield with 75% ee.

(*S*)-3-Cyclohexylbutanal.[43] Colorless oil. $[\alpha]^{20}_D$ +7.4° (*c* 1.1, CH_2Cl_2; 75% ee). ^1H NMR ($CDCl_3$) δ: 9.75 (dd, J = 3.0 and 1.8 Hz, 1H), 2.46 (ddd, J = 15.9, 4.8, and 1.8 Hz, 1H), 2.19 (ddd, J = 15.9, 9.0, and 3.0 Hz, 1H), 1.89−2.02 (m, 1H), 1.62−1.78 (m, 5H), 0.83−1.29 (m, 6H), 0.91 (d, J = 6.9 Hz, 3H). ^{13}C

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NMR ($CDCl_3$) δ: 203.7, 48.8, 43.1, 33.4, 30.6, 29.5, 26.99, 26.94, 26.89, 17.3. Chiraldex G-TA column, retention time = 40.9 min (70 °C; isothermal).

The aldehyde was reduced ($LiAlH_4$), acylated (trifluoroacetic anhydride), and then analyzed on a Chiraldex G-TA column, retention time = 22.4 min (80 °C; isothermal).

The absolute configuration of (+)-3-cyclohexylbutanal was determined to be *S* by converting (*S*)-3-phenylbutanal to (*S*)-3-phenylbutan-1-ol ($LiAlH_4$) and then to (*S*)-3-cyclohexylbutan-1-ol (5% Rh/C, H_2, AcOH)[44] and comparing it to the product of the $LiAlH_4$ reduction of (+)-3-cyclohexylbutanal.

Preparative-Scale Isomerization of (*E*)-4-Methyl-3-phenyl-2-penten-1-ol (eq 6). In the air, [Rh(cod)((−)-**2**)]BF_4 (47.0 mg, 0.057 mmol) was placed into a Schlenk tube, which was then filled with argon. Under a positive pressure of argon, a solution of (*E*)-4-methyl-3-phenyl-2-penten-1-ol (1.00 g, 5.68 mmol) in THF (50 mL) was added via a Pasteur pipet. The Schlenk tube was closed, and the dark-red solution was stirred for 67 h at 100 °C. The reaction mixture was then cooled to room temperature, concentrated to ∼10 mL, and added to pentane (30 mL; stirred). The resulting slurry was filtered, providing orange crystals. The crystals were washed with pentane, dissolved in THF, and the solvent was removed, affording the recovered catalyst, [Rh(cod)((+)-**2**)]BF_4 (32.0 mg, 0.0387 mmol, 68%), as a red solid.

The filtrate was concentrated and purified by silica gel column chromatography (pentane:Et_2O = 4:1) to give (*S*)-4-methyl-3-phenylpentanal (944 mg, 5.36 mmol, 94%, 90% ee) as a colorless oil.

(*E*)-1,1-Dideuterium-3-phenyl-2-buten-1-ol. Ethyl (*E*)-3-phenyl-2-butenoate[45] (1.00 g, 5.26 mmol) in Et_2O (5 mL) was added to a stirred mixture of $LiAlD_4$ (220 mg, 5.26 mmol) in Et_2O (20 mL) at 0 °C, and the resulting mixture was stirred for 10 min at 0 °C. H_2O (0.1 mL) was added at 0 °C, and the reaction was stirred for 10 min at room temperature. The solution was then dried over $MgSO_4$, filtered through Celite, and concentrated. The resulting residue was purified by flash chromatography (hexanes:Et_2O = 5:2) to give (*E*)-1,1-dideuterium-3-phenyl-2-buten-1-ol (650 mg, 4.33 mmol, 82%) as a colorless oil.

FTIR (neat): 3316, 2360, 2341, 1494, 1445, 1380, 1263, 1147, 1089, 1004, 955, 891, 759, 695 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.26−7.43 (m, 5H), 5.98 (s, 1H), 2.09 (s, 3H). ^2H NMR ($CHCl_3$) δ: 4.31 (s, 2D). HRMS (EI): calcd for $C_{10}H_{10}D_2O$ (M^+), 150.1008; found, 150.1005.

(*S*)-1,3-Dideuterium-3-phenylbutanal (eq 8). In a N_2-filled glovebox, [Rh(cod)((+)-**2**)]BF_4 (5.3 mg, 0.0064 mmol), (*E*)-1,1-dideuterium-3-phenyl-2-buten-1-ol (20.0 mg, 0.133 mmol), and THF (3 mL) were added to a Schlenk tube, and the resulting dark-red solution was stirred for 24 h at 100 °C. The reaction mixture was then cooled to room temperature, concentrated, and purified by silica gel column chromatography (pentane:Et_2O = 4:1) to give (*S*)-1,3-dideuterium-3-phenylbutanal (16.3 mg, 0.109 mmol, 82%; 76% ee) as a colorless oil.

$[\alpha]^{20}_D$ +23.9° (*c* 1.25, CH_2Cl_2; 76% ee). FTIR (neat): 2962, 2069, 1712, 1494, 1447, 1092, 760, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.15−7.34 (m, 5H), 2.76 (d, *J* = 16.8 Hz, 1H), 2.65 (d, *J* = 16.8 Hz, 1H), 1.32 (s, 3H). ^2H NMR ($CDCl_3$) δ: 9.77 (s, 1D), 3.38 (s, 1D). HRMS (EI): calcd for $C_{10}H_{10}D_2O$ (M^+), 150.1008; found, 150.1002. Chiraldex G-TA column, retention times = 15.1 min (*S* isomer), 16.4 min (*R* isomer) (90 °C; isothermal).

Crossover Experiment (eq 9). In a N_2-filled glovebox, [Rh(cod)((+)-**2**)]BF_4 (5.3 mg, 0.0064 mmol), (*E*)-3-phenyl-2-buten-1-ol (10.7 mg, 0.0723 mmol), (*E*)-1,1-dideuterium-3-phenyl-2-buten-1-ol (11.1 mg, 0.0739 mmol), and THF (3 mL) were added to a Schlenk tube, and the resulting dark-red solution was stirred for 24 h at 100 °C. The reaction mixture was then cooled to room temperature, concentrated, and purified by silica gel column chromatography (pentane:Et_2O = 4:1) to give a 1:1 mixture of (*S*)-3-phenylbutanal and (*S*)-1,3-dideuterium-3-phenylbutanal as a colorless oil.

The absence of monodeuterated compounds was confirmed by high-resolution mass spectrometry of the mixture of alcohols generated through treatment of the mixture of aldehydes with $LiAlH_4$.

Equation 11. In a N_2-filled glovebox, [Rh(cod)((−)-**2**)]BF_4 (9.4 mg, 0.11 mmol), (*E*)-3-phenyl-2-buten-1-ol (30.0 mg, 0.203 mmol), (*E*)-3-phenyl-2-pentenal (3.5 mg, 0.022 mmol), and THF (3 mL) were added to a Schlenk tube, and the resulting dark-red solution was stirred for 24 h at 100 °C. The reaction mixture was then cooled to room temperature and concentrated. The catalyst was removed through passage of the residue through a pad of silica gel (Et_2O as the eluant), affording a colorless oil. According to GC, the ratio of 3-phenylbutanal:3-phenyl-2-butenal:3-phenyl-2-pentenal:3-phenylpentanal was 89:1.6:9:0.7.

(*E*)-1-Deuterium-3-phenyl-2-butenal.[46] A mixture of (*E*)-1,1-dideuterium-3-phenyl-2-buten-1-ol (236 mg, 1.57 mmol), Ag_2CO_3 (1.73 g, 6.28 mmol), and benzene (25 mL) was stirred at reflux for 2 h. After cooling to room temperature, the mixture was filtered through Celite and concentrated. The resulting residue was purified by flash chromatography (pentane:Et_2O = 4:1) to give (*E*)-1-deuterium-3-phenyl-2-butenal (154 mg, 1.05 mmol, 67%; not optimized) as a colorless oil, along with recovered (*E*)-1,1-dideuterium-3-phenyl-2-buten-1-ol (73 mg, 0.487 mmol, 31%).

^1H NMR ($CDCl_3$) δ: 7.54−7.56 (m, 2H), 7.41−7.44 (m, 3H), 6.40 (q, *J* = 0.6 Hz, 1H), 2.17 (s, 3H). ^2H NMR ($CHCl_3$) δ: 10.25 (s).

(*S*)-(*E*)-1-Deuterium-3-phenyl-2-buten-1-ol. To a 0 °C solution of (*E*)-1-deuterium-3-phenyl-2-butenal (120 mg, 0.815 mmol) in THF (5 mL) was added (*R*)-Alpine-Borane (2.0 mL, 1.0 mmol). The resulting reaction mixture was stirred for 14 h at room temperature, and then acetaldehyde (0.023 mL, 0.41 mmol) was added. After 15 min of stirring, the mixture was concentrated, and the residue was diluted with Et_2O (30 mL). 2-Aminoethanol (68 mg, 1.1 mmol) was added, and the resulting white suspension was filtered. The filtrate was washed with water, dried over $MgSO_4$, and concentrated. The residue was purified by flash chromatography (pentane:Et_2O = 4:1 → 2:1) to give (*S*)-(*E*)-1-deuterium-3-phenyl-2-buten-1-ol (100 mg, 0.670 mmol, 82%) as a colorless oil. The enantiomeric excess of (*S*)-**5** was determined to be 95% by converting it to the (*S*)-MTPA ester. The absolute configuration of (*S*)-**5** was assigned as *S* by ^1H NMR analysis ($Eu(hfc)_3$).[47]

$[\alpha]^{20}_D$ +0.90° (*c* 3.10, $CHCl_3$; 95% ee). ^1H NMR ($CDCl_3$) δ: 7.24−7.43 (m, 5H), 5.98 (d, *J* = 6.3 Hz, 1H), 4.35 (d, *J* = 6.0 Hz, 1H), 2.09 (s, 3H). ^2H NMR ($CHCl_3$) δ: 4.40 (s).

(*S*)-MTPA ester of (*S*)-(*E*)-1-deuterium-3-phenyl-2-buten-1-ol. ^1H NMR ($CDCl_3$) δ: 7.30−7.54 (m, 5H), 5.93 (dd, *J* = 4.2 and 0.6 Hz, 1H), 5.01 (d, *J* = 4.2 Hz, 0.02H), 4.99 (d, *J* = 4.2 Hz, 0.98H), 3.58 (d, *J* = 0.9 Hz, 3H), 2.13 (d, *J* = 0.3 and 0.3 Hz, 3H). ^2H NMR ($CHCl_3$) δ: 5.06 (s). The enantiomeric excess was determined to be 95% by integration of the ^1H NMR resonances at δ 4.99 and 5.01. A mixture of the diastereomeric (*S*)-MTPA esters of (±)-(*E*)-1-deuterium-3-phenyl-2-buten-1-ol was prepared as a reference.

Equation 12. In a N_2-filled glovebox, [Rh(cod)((+)-**2**)]BF_4 (5.5 mg, 0.0067 mmol), (*S*)-(*E*)-1-deuterium-3-phenyl-2-buten-1-ol (20.0 mg, 0.134 mmol; 95% ee), and THF (2 mL) were added to a Schlenk tube, and the resulting dark-red solution was stirred for 24 h at 100 °C. The reaction mixture was then cooled to room temperature, concentrated, and purified by silica gel column chromatography (pentane:Et_2O = 4:1) to give a mixture of 1-deuterium-3-phenylbutanal and 3-deuterium-3-phenylbutanal (18.7 mg, 0.125 mmol, 93%) as a colorless oil.

According to GC, the ratio of (*S*)-1-deuterium-3-phenylbutanal:(*S*)-3-deuterium-3-phenylbutanal:(*R*)-1-deuterium-3-phenylbutanal:(*R*)-3-deuterium-3-phenylbutanal was 2.3:84.2:

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11.1:2.4. Chiraldex G-TA column, retention times = 48.6 min ((*S*)-3-deuterium-3-phenylbutanal), 50.1 min ((*S*)-1-deuterium-3-phenylbutanal), 53.8 min ((*R*)-3-deuterium-3-phenylbutanal), 54.7 min ((*R*)-1-deuterium-3-phenylbutanal) (80 °C; isothermal).

Equation 13. In a N_2-filled glovebox, [Rh(cod)((−)-**2**)]BF_4 (5.5 mg, 0.0067 mmol), (*S*)-(*E*)-1-deuterium-3-phenyl-2-buten-1-ol (20.0 mg, 0.134 mmol; 95% ee) and THF (2 mL) were added to a Schlenk tube, and the resulting dark-red solution was stirred for 24 h at 100 °C. The reaction mixture was then cooled to room temperature, concentrated, and purified by silica gel column chromatography (pentane:Et_2O = 4:1) to give a mixture of 1-deuterium-3-phenylbutanal and 3-deuterium-3-phenylbutanal (18.6 mg, 0.125 mmol, 93%) as a colorless oil.

According to GC, the ratio of (*S*)-1-deuterium-3-phenylbutanal:(*S*)-3-deuterium-3-phenylbutanal:(*R*)-1-deuterium-3-phenylbutanal:(*R*)-3-deuterium-3-phenylbutanal was 3.5:4.6:90.2:1.7.

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Supporting Information Available: Molecular structure and numbering schemes for [Rh(cod)((−)-**2**)]ClO_4, as well as tables describing crystal data and structure refinement, fractional atomic coordinates, bond distances and angles, anisotropic displacement parameters, hydrogen coordinates, and torsional angles. This material is available free of charge via the Internet at http://pubs.acs.org.

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