Chiral [$RuCl_2$(dipyridylphosphane)(1,2-diamine)] Catalysts: Applications in Asymmetric Hydrogenation of a Wide Range of Simple Ketones

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Abstract: The dipyridylphosphane/diamine – Ru complex combined with *t*BuOK in 2-propanol acts as a very effective catalyst system for the enantioselective hydrogenation of a diverse range of simple ketones including heteroaromatic ketones, substituted benzophenones, alkenyl ketones, and cyclopropyl ketones. The combination of desirable features, such as quantitative chemical yields within hours, broad substrate scope, excellent enantioselectivities (up to 99%), and high substrate-to-catalyst ratios, among others, makes the present catalyst system of high practical interest.

Keywords: asymmetric catalysis · enantioselectivity · hydrogentation · P ligands · ruthenium

Introduction

Since many enantiomerically pure secondary alcohols are very valuable intermediates for the manufacture of structurally interesting and biologically active compounds, the development of highly effective systems for the synthesis of chiral alcohols is not only of interest to the academic world but also of substantial interest to industrial scientists. Accordingly, a number of strategies for the asymmetric reduction of prochiral ketones to single enantiomer alcohols have been developed.[1] From both scientific and commercial points of view, asymmetric hydrogenation is more efficient and beneficial than either stoichiometric[2] or other catalytic reduction systems.[3–5] Ru – phosphane complexes, especially the Ru-binap catalyst system, have been demonstrated to be highly enantioselective in the hydrogenation of various functionalized ketones[1, 6] and industrial processes for the synthesis of the key intermediates of antibiotic carbapenems[7] and antibacterial Levofloxacin[8] have been well established. However, these catalysts often fail to give good results with simple ketones that lack neighboring heteroatoms to enable the substrate to anchor strongly to the metal center. Recently, a significant breakthrough in this area was achieved by Noyori and co-workers, who discovered that an appropriate diphosphane/Ru/chiral diamine/inorganic base catalyst system exhibited high efficiency and steroselectivities for the asymmetric hydrogenation of a wide range of unfunctionalized prochiral ketones in 2-propanal.[9] Among these catalysts, *trans*-$RuCl_2$[(*S*)-Xylbinap][(*S*)-daipen][10] or its enantiomer gave the best results.[11, 12] Another catalyst system Phane-Phos/ruthenium/diamine[13] also showed high activity and enantioselectivity in the asymmetric hydrogenation of simple ketones.

We have recently prepared a new family of chiral dipyridylphosphane ligands P-Phos (**1a**),[14a] Tol-P-Phos (**1b**),[14b] and Xyl-P-Phos (**1c**),[14c] and have established their effectiveness in many catalytic asymmetric hydrogenation reactions. We found their Ru/diamine complexes **2a**–**2c** to be highly effective in the asymmetric hydrogenation of a variety of aromatic ketones. In particular, with the use of the *trans*-[$RuCl_2${(*R*)-**1c**}{(*R*,*R*)-dpen}] ((*R*,*RR*)-**2c**, dpen = 1,2-diphenylethylenediamine) in combination with *t*BuOK in 2-propanol, various *ortho*-, *meta*-, and *para*-substituted acetophenones were hydrogenated quantitatively under mild conditions in consistently excellent enantioselectivities (up to > 99.9%), even with very high substrate-to-catalyst ratios (S/C up to 100000).[14d] Unlike the Ru – binap catalyst system, which often needs an expensive diamine daipen[12a] for good results, the Ru – (P-Phos) catalyst system can be used in combination with a substantially less expensive diamine, dpen, to give excellent results. In addition, catalysts **2a**–**2c** are air-stable even in solution. The combination of these desirable features makes them of high practical interest and prompts us to explore their applications in the asymmetric hydrogenation of a wide scope of simple ketones.

In this study, we have found that catalyst (*R*,*RR*)-**2c** acted as a very efficient catalyst precursor for highly enantioselective hydrogenation of a diverse range of simple ketones including heteroaromatic ketones, substituted benzophe-

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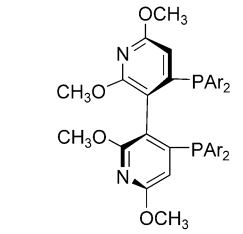
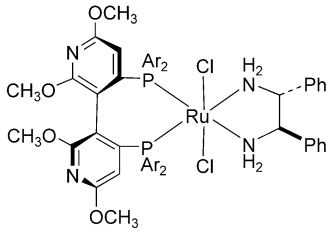


(*R*)-**1a**, Ar = C_6H_5, (*R*)-P-Phos

(*R*)-**1b**, Ar = 4-$CH_3C_6H_4$, (*R*)-Tol-P-Phos

(*R*)-**1c**, Ar = 3,5-$(CH_3)_2C_6H_3$, (*R*)-Xyl-P-Phos



(*R,RR*)-**2a**, Ar = C_6H_5

(*R,RR*)-**2b**, Ar = 4-$CH_3C_6H_4$

(*R,RR*)-**2c**, Ar = 3,5-$(CH_3)_2C_6H_3$

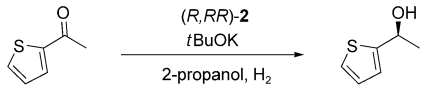
nones, alkenyl ketones, and cyclopropyl ketones. To our knowledge, no other catalyst has so far been reported, which approaches the effectiveness of the Xylbinap-Ru-daipen system in the hydrogenation of simple ketones with such a wide variety of substrates.[12]

Results and Discussion

Asymmetric hydrogenation of heteroaromatic ketones and 1′-acetonaphthone: The asymmetric hydrogenation of heteroaromatic ketones offers an especially attractive route to chiral alcoholic products, which serve as valuable intermediates and building blocks for a variety of biologically active compounds and chiral ligands.[15] For example, (*R*)-1-(3-pyridyl)ethanol is an intermediate in the synthesis of heteroyohimbine alkaloids such as reserpinin and arcin[15a] and the synthetically useful chiral α-hydroxy aldehydes can be obtained from alkyl(2-thiazolyl)methanol products.[16] Other examples include (*S*)-duloxetine,[15c] an inhibitor of serotonin and norepinephrine uptake carriers, and Singulair for treatment of chronic asthma.[17]

Our study began with 2-acetylthiophone (**3a**), and the results are summarized in Table 1. The catalytic activity of catalyst **2** was not disturbed by the sulfur-containing heterocycle. When the hydrogenation was conducted in 2-propanol containing (*R,RR*)-**2c** and *t*BuOK with S/C = 4000 and a substrate-to-base (S/B) molar ratio of 200 under 350 psi of H_2 at ambient temperature, the corresponding alcohol (*S*)-**4a** was obtained in quantitative yield and 98.3 % *ee* (Table 1, entry 3). Consistent with the results observed in the (*R,RR*)-**2c** catalyzed hydrogenation of acetophenone,[14d] the presence of a base and the substrate-to-base ratio were crucial for the high activity of the catalyst. For instance, no desirable product was detected after 12 h when **3a** was hydrogenated without the addition of *t*BuOK or with an S/B ratio of 100 (Table 1, entries 1 and 2). In contrast, when the S/B varied from 200 to 700, complete conversions were observed within 12 h and the *ee* values of the desired product (*S*)-**4a** were essentially identical (Table 1, entries 3–5). The hydrogen pressure was found to have almost no effect on the enantioselectivity (Table 1, entries 3, 6, and 7) but lower pressure resulted in a somewhat slower rate (Table 1, entry 6 versus entry 7). In addition, the enantioselectivity was markedly influenced by the structure of the chiral dipyridylphosphane ligands. The use of Xyl-P-Phos (**1c**) provided far superior ee to those obtained with the parent ligand P-Phos (**1a**) or Tol-P-Phos (**1b**) (Table 1, entry 3 versus entries 8 and 9).

Table 1. Asymmetric hydrogenation of 2-acetylthiophene **3a** catalyzed by **2**.[a]



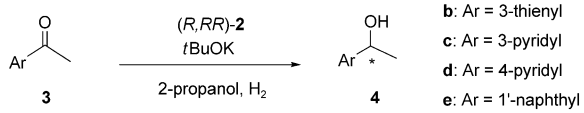
3a **4a**

Entry	Catalyst	S/B [M/M]	P_{H_2} [psi]	Time [h]	Conv. [%][b]	*ee* [%][b]
1[c]	(*R,RR*)-**2c**	–	350	12	–	–
2	(*R,RR*)-**2c**	100	350	12	2.4	–[d]
3	(*R,RR*)-**2c**	200	350	12	> 99.9	98.3 (*S*)
4	(*R,RR*)-**2c**	500	350	12	> 99.9	98.2 (*S*)
5	(*R,RR*)-**2c**	700	350	12	> 99.9	98.1 (*S*)
6	(*R,RR*)-**2c**	200	150	12	98.8	97.8 (*S*)
7	(*R,RR*)-**2c**	200	600	12	> 99.9	98.1 (*S*)
8	(*R,RR*)-**2a**	200	350	12	87.2	71.0 (*S*)
9	(*R,RR*)-**2b**	200	350	12	> 99.9	71.5 (*S*)

[a] Reaction conditions: 46 mg substrate, substrate concentration = 1.5 M, S/C (M/M) = 4000, 25–28 °C. [b] The conversions were determined by NMR and GC analysis. The *ee* values were determined by chiral GC with a 25 m × 0.25 mm Chrompack Chirasil-DEX CB column. The absolute configuration was determined by comparing the retention times with those in reference [12c)]. [c] The reaction was performed without the addition of *t*BuOK and no product was detected. [d] The *ee* value could not be determined accurately because of the low conversion.

Similarly excellent results were obtained in the hydrogenation of some other heteroaromatic ketones (Table 2). The hydrogenation of 3-thienyl ketone **3b** gave (*S*)-**4b** quantitatively in 98.9 % *ee* after 5 h (Table 2, entry 1) under the same conditions as those for the hydrogenation of 2-thienyl ketone **3a**. The enantioselectivity remained consistently high (99.0 % *ee*, Table 2, entry 2), even when the S/C ratio was increased to 10000. The rate of the hydrogenation of 3-pyridyl ketone **3c** was faster than that of 4-pyridyl ketone **3d**. For example, **3c** was hydrogenated with an S/C of 4000 under 350 psi H_2 to provide (*S*)-**4c** in 99.2 % conversion and with 97.0 % *ee* after 10 h (Table 2, entry 4). In contrast, under otherwise identical conditions, the hydrogenation of **3d** offered (*S*)-**4d** in only 50.8 % conversion within 12 h (Table 2, entry 5) and the reaction was completed in 24 h with 97.9 % *ee* (Table 2, entry 6). In a manner similar to the Ru-binap catalyst system,[12c] the hydrogenation of 2-acetylpyridine was very sluggish (2.4 % conversion after 24 h) with catalyst (*R,RR*)-**2c**, probably as a result of the tight coordination of the pyridyl functionality causing saturation of the catalyst and leading to the diminution of activity.

Table 2. Asymmetric hydrogenation of heteroaromatic ketones and 1′-acetonaphthone.[a]



Entry	Ketone	Catalyst	S/C [M/M]	S/B (M/M)	P_{H_2} [psi]	Time [h]	Conv. [%][b]	*ee* [%][b,c]
1	**3b**	(*R*,*RR*)-**2c**	4000	200	350	5	>99.9	98.9(*S*)
2	**3b**	(*R*,*RR*)-**2c**	10000	200	500	16	>99.9	99.0 (*S*)
3[d]	**3c**	(*R*,*RR*)-**2c**	2000	100	350	5	>99.9	97.2 (*S*)
4[d]	**3c**	(*R*,*RR*)-**2c**	4000	100	350	10	99.2	97.0 (*S*)
5[d]	**3d**	(*R*,*RR*)-**2c**	4000	100	350	12	50.8	97.9 (*S*)
6[d]	**3d**	(*R*,*RR*)-**2c**	4000	100	350	24	>99.9	97.9 (*S*)
7	**3e**	(*R*,*RR*)-**2a**	4000	200	300	8	64.8	91.9 (*S*)
8	**3e**	(*R*,*RR*)-**2b**	4000	200	300	8	>99.9	93.1 (*S*)
9	**3e**	(*R*,*RR*)-**2c**	4000	200	300	8	>99.9	98.6 (*S*)

[a] Reaction conditions: 50–100 mg substrate, substrate concentration = 1.0–2.5 M, 25–28 °C. [b] The conversions were determined by NMR and GC analysis. The *ee* values were determined by chiral GC with a 25 m × 0.25 mm Chrompack Chirasil-DEX CB column. [c] The absolute configuration was determined by comparison of the sign of optical rotation or the retention times with those in references [9e, 12c)]. [d] The conversion was determined by NMR and GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column. The *ee* values were determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OB-H column.

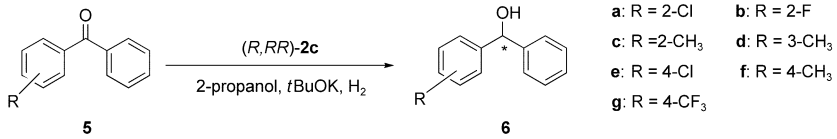
Under the standard conditions, other aromatic ketones such as 1′-acetonaphthone (**3e**) were hydrogenated smoothly in high enantioselectivity, irrespective of the use of **1a**, **1b**, or **1c** as the chiral ligand (Table 2, entries 7–9) and **1c** was found to be the best choice again (entry 9).

Asymmetric hydrogenation of substituted benzophenones: Benzhydrol and its derivatives are widely used in the synthesis of pharmaceuticals.[18] The current industrial processes for producing benzhydrols mainly rely on stoichiometric reduction using $NaBH_4$ or through the addition of arylmetals to benzaldehydes. From a practical standpoint, it is highly desirable to develop effective catalytic asymmetric hydrogenation methods for the economical synthesis of chiral benzhydrols from substituted benzophenones. Noyori and co-workers reported the highly enantioselective hydrogenation of a range of unsymmetrical diaryl ketones using a Ru-Xylbinap-daipen system.[12b] To our best knowledge, no other catalyst system reported so far can attain the effectiveness of the Ru-Xylbinap-daipen catalyst in this type of hydrogenation reaction.

In this study, we discovered that the present catalyst (*R*,*RR*)-**2c** with a much less expensive diamine, dpen, exhibited comparable or even higher efficiency and enantioselectivity than Ru-Xylbinap-daipen in the hydrogenation of a variety of substituted benzophenones (Table 3). This hydrogenation can be performed with an S/C molar ratio as high as 10000 (Table 3, entry 2). In the presence of (*R*,*RR*)-**2c**, *ortho*-substituted substrates **5a**–**5c** were hydrogenated to the desired products with high *ee* values (Table 3, entries 1–4). For instance, the hydrogenation of *o*-flurobenzophenone (**5b**) at ambient temperature under 300 psi of initial hydrogen pressure was completed in 15 h to give the desired product in 97.6% *ee* (Table 3, entry 3). The substrate **5c**, which has an electron-donating methyl substituent, provided the *R* alcohol in 95.9% *ee* (Table 3, entry 4). Simple *meta*- and *para*-substituted benzophenones were converted to the corresponding alcohols with moderate enantioselectivity, as expected (Table 3, entries 5–8). The results compared favorably with those obtained from the use of Ru-Xylbinap-daipen complex. For example, using (*R*,*RR*)-**2c**, *p*-trifluoromethyl benzophenone **5g** was hydrogenated to (*R*)-**6g** in 77.2% *ee* (Table 3, entry 8); whereas the Ru-Xylbinap complex afforded **6g** in only 47% *ee* under similar conditions.[12b]

Asymmetric hydrogenation of alkenyl ketones to chiral allylic alcohols: The effectively selective asymmetric hydrogenation of alkenyl ketones to chiral allylic alcohols has long remained difficult because most existing homogeneous or heterogeneous catalysts tend to catalyze the hydrogenation of the C=C bond preferentially over a coexisting C=O bond.[19] In addition, some simple enones are very sensitive to basic conditions. Noyori and co-workers recently resolved this enduring problem by using Ru-Xylbinap-daipen in combination with K_2CO_3, a weak base, in place of conventional KOH or *t*BuOK.[12a]

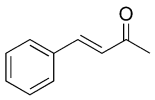
Table 3. Asymmetric hydrogenation of substituted benzophenones catalyzed by (*R*,*RR*)-**2c**.[a]



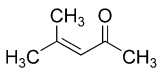
Entry	Ketone	S/C [M/M]	S/B [M/M]	P_{H_2} [psi]	Time [h]	Conv. [%][b]	*ee* [%][c]
1	**5a**	2000	100	300	15	>99.9	97.2 (*R*)
2	**5a**	10000	75	500	35	>99.9	97.4 (*R*)
3	**5b**	2000	100	300	15	99.7	97.6 (*R*)
4	**5c**	2000	100	300	13	98.6	95.9 (*R*)
5	**5d**	2000	100	300	48	>99.9	43.2 (+)
6	**5e**	2000	50	300	15	99.0	47.3 (*R*)
7	**5f**	2000	75	300	15	99.3	3.9 (*R*)
8	**5g**	2000	50	300	15	>99.9	77.2 (*R*)

[a] Reaction conditions: 30–60 mg substrate, substrate concentration = 1.0 M, 25–28 °C. [b] The conversion was determined by NMR and GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column. [c] The *ee* values were determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OB-H or 25 cm × 4.6 mm Daicel Chiralcel OD column. The absolute configuration was determined by comparison of the sign of optical rotation or the retention times with those in reference [12b)].

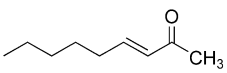
To further explore the scope of substrates, we also investigated the effectiveness of catalyst (*R*,*RR*)-**2c** for chemoselective hydrogenation of the carbonyl group of three α,β-unsaturated ketones (**7a**–**7c**). In the presence of either



7a



7b



7c

K_2CO_3 or *t*BuOK, the hydrogenation reaction of benzalacetone **7a** in 2-propanol containing (*R*,*RR*)-**2c** with an S/C ratio of 10000 furnished the corresponding allylic alcohol **8a** in 97.0% *ee* and 97.1% *ee*, respectively (Table 4, entries 2 and 4). No over-reduction of the C=C functionality was detected. With the S/C ratio of up to 12000, both mesityl oxide **7b** and highly base-sensitive 3-nonen-2-one **7c** were transformed to allylic alcohols (**8b** and **8c**) in 93.3% and 90.3% *ee* (Table 4, entries 5–7), respectively.

Asymmetric hydrogenation of cyclopropyl ketones: The cyclopropyl group is of interest in synthetic methodologies.[20] Takaya and co-workers[21] and Noyori and co-workers[12a] have reported the hydrogenation of cyclopropyl phenyl ketone **9a**. To our knowledge, the hydrogenation of substituted phenyl cyclopropyl ketones such as **9b**–**9d** have not been reported so far, although the enantioselective cyclopropylation of aldehydes using dicycolpropylzinc to provide substituted phenyl cyclopropyl alcohols has been studied.[22]

By using (*R*,*RR*)-**2c** as catalyst, **9a** was hydrogenated smoothly in the presence of *t*BuOK with an S/C ratio of 5000 under 350 psi H_2 to give (*S*)-**10a** in 97.6% *ee* (Table 5, entry 1) without cleavage of the three-membered ring. Similarly high enantioselectivities were observed in the hydrogenation of various substituted phenyl cyclopropyl ketones (Table 5, entries 2–4 and 6). The substrate possessing an electron-withdrawing group in the para position of the phenyl group was more reactive than that with an electron-donating substituent. For example, with an S/C ratio of 2000, the hydrogenation of cyclopropyl 4-chlorophenyl ketone (**9b**) was complete in 14 h (Table 5, entry 2), whereas the reaction rate was substantially lower (33.5% conversion after 24 h) in the case of cyclopropyl 4-methoxyphenyl ketone (**9d**, Table 5, entry 5).

Conclusion

In summary, the chiral $RuCl_2$(dipyridylphosphane)(1,2-diamine) complex **2c**, combined with an appropriate inorganic base in 2-propanol, is a highly effective catalyst system for the enantioselective hydrogenation of a wide range of simple ketones, such as heteroaromatic, alkenyl, and cyclopropyl ketones, as well as substituted benzophenones. The present catalyst system is of high practical potential because of its high efficacy, enantioselectivity, and flexibility.

Experimental Section

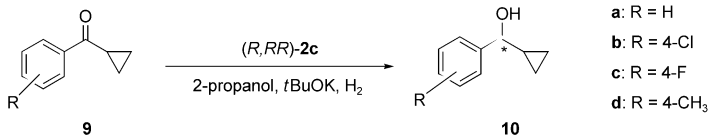
General methods: All manipulations with air-sensitive reagents were carried out under a dry nitrogen atmosphere using standard Schlenk techniques or in a nitrogen-filled MBRAUN Lab Master 130 glovebox. The hydrogenation reactions were performed in a 50 mL stainless-steel autoclave from Parr company. ^{1}H NMR and ^{31}P NMR spectra were

Table 4. Asymmetric hydrogenation of alkenyl ketones catalyzed by (*R*,*RR*)-**2c**.[a]

Entry	Ketone	S/C[M/M]	Base	S/B [M/M]	P_{H2} [psi]	Time [h]	Conv. [%][b]	*ee* [%][c]
1	**7a**	2000	K_2CO_3	20	350	10	>99.9	97.0 (*S*)
2	**7a**	10000	K_2CO_3	20	500	15	>99.9	97.1 (*S*)
3	**7a**	2000	*t*BuOK	500	350	10	>99.9	96.9 (*S*)
4	**7a**	10000	*t*BuOK	500	500	15	>99.9	97.0 (*S*)
5	**7b**	2000	*t*BuOK	250	350	8	99.2	90.2 (*S*)[d]
6	**7b**	12000	*t*BuOK	250	500	16	99.1	90.3 (*S*)[d]
7	**7c**	2000	K_2CO_3	250	350	15	91.8	93.4 (*S*)[d]

[a] Reaction conditions: 20–50 mg substrate, substrate concentration = 0.1–1.0 M, 25–28 °C. [b] The conversion was determined by NMR and GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column. [c] The *ee* values were determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OD column. The absolute configuration was determined by comparison of the sign of optical rotation or the retention times with those in reference [12a)]. [d] The *ee* values were determined by chiral GC with a 25 m × 0.25 mm Chrompack Chirasil-DEX CB column.

Table 5. Asymmetric hydrogenation of cyclopropyl ketones catalyzed by (*R*,*RR*)-**2c**.[a]



9 **10**

Entry	Ketone	S/C [M/M]	S/B [M/M]	P_{H_2} [psi]	Time [h]	Conv. [%][b]	*ee* [%]
1	**9a**	5000	250	350	18	>99.9	97.6 (*S*)[c]
2	**9b**[d]	2000	250	350	14	>99.9	92.3 (+)
3	**9b**	5000	250	500	24	87.2	92.3 (+)
4	**9c**[d]	2000	250	350	24	86.3	92.0 (+)
5	**9d**	2000	250	350	24	33.5	-[e]
6	**9d**	1000	100	350	48	>99.9	96.1 (−)[f]

[a] Reaction conditions: 30 mg substrate, substrate concentration = 1.0 M, 25–28 °C. [b] The conversion was determined by NMR and GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column. [c] The *ee* values were determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OD column. The absolute configuration was determined by comparison of the retention times with those in reference [12a)]. [d] The conversions were determined by NMR and GC analysis. The *ee* values were determined by chiral GC with a 25 m × 0.25 mm Chrompack Chirasil-DEX CB column. [e] The *ee* value has not been determined. [f] The *ee* value was determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel AD column.

recorded in $CDCl_3$ on a Varian AS 500 at room temperature, and the chemical shifts were expressed in ppm. Gas chromatographic analyses were conducted on an HP 4890A or HP 5890 series II system. Optical rotations were measured on a Perkin-Elmer Model 341 polarimeter. The ketone substrates were stirred over CaH_2 to remove acidic impurities and distilled prior to use. DMF and 2-propanol were freshly distilled over CaH_2 before use. Other commercial reagents were used as received without further purification unless otherwise stated. Optically pure P-Phos (**1a**), Tol-P-Phos (**1b**), and Xyl-P-Phos (**1c**) were synthesized according to previously reported procedures.[14a–c] Catalysts **2a**–**2c** were prepared and characterized by our reported method.[14d]

A typical procedure of asymmetric hydrogenation: A 1.56×10^{-3} M solution of (*R*,*RR*)-**2c** in 2-propanol (59 μL, 9.20×10^{-5} mmol), 2-acetylthiophene (**3a**, 40 μL, 0.368 mmol), 2-propanol (130 μL), and a 0.1 M *t*BuOK solution in *t*BuOH (18.5 μL, 1.85×10^{-3} mmol) were added to a 50 mL autoclave under a nitrogen atmosphere. Hydrogen was initially introduced into the autoclave at a pressure of 300 psi before being reduced to 10–20 psi by carefully releasing the stop valve. After this procedure was repeated three times, the vessel was pressurized to 350 psi. The reaction mixture was stirred at room temperature for 12 h before releasing the H_2. The conversion and the enantiomeric excess of the product (*S*)-1-(2-thienyl)ethanol [(*S*)-**4a**] were determined by NMR spectroscopy and chiral GC analysis to be >99.9% and 98.3%, respectively (column, Chirasil-DEX CB; 25 m × 0.25 mm, CHROMPACK, carrier gas, N_2).

1-(2-Thienyl)ethanol (4a): Capillary GC, Chirasil-DEX CB column; 120 °C; isothermal; t_R(**3a**) = 5.45 min; $t_R(R)$ = 10.46 min; $t_R(S)$ = 11.34 min.

1-(3-Thienyl)ethanol (4b): Capillary GC, Chirasil-DEX CB column; 120 °C; isothermal; t_R(**3b**) = 6.60 min; $t_R(R)$ = 12.92 min; $t_R(S)$ = 13.79 min.

1-(3-Pyridyl)ethanol (4c): The conversion was determined by capillary GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column; 160 °C; isothermal; t_R(**3c**) = 7.11 min; t_R(**4c**) = 18.08 min. The *ee* value was determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OB-H column (eluent, 2-propanal/hexane 10:90; flow rate = 1.0 mL min^{-1}; detection: 254 nm light); $t_R(S)$ = 8.40 min; $t_R(R)$ = 13.42 min.

1-(4-Pyridyl)ethanol (4d): The conversion was determined by capillary GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column; 160 °C; isothermal; t_R(**3d**) = 6.49 min; t_R(**4d**) = 19.38 min. The *ee* value was determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OB-H column (eluent, 2-propanal/hexane 10:90; flow rate = 1.0 mL min^{-1}; detection: 254 nm light); $t_R(S)$ = 10.05 min; $t_R(R)$ = 12.94 min.

1-(1′-Naphthyl)ethanol (4e): Capillary GC, Chirasil-DEX CB column; 170 °C; isothermal; t_R(**3e**) = 7.43 min; $t_R(S)$ = 13.89 min; $t_R(R)$ = 14.87 min.

***o*-Chlorobenzhydrol (6a)**: The conversion was determined by capillary GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column; 230 °C; isothermal; t_R(**5a**) = 9.85 min; t_R(**6a**) = 17.12 min. The *ee* value was determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OD column (eluent, 2-propanal/hexane 10:90; flow rate = 1.0 mL min^{-1}; detection: 254 nm light); $t_R(R)$ = 7.86 min; $t_R(S)$ = 9.81 min.

***o*-Fluorobenzhydrol (6b)**: The conversion was determined by capillary GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column; 230 °C; isothermal; t_R(**5b**) = 6.18 min; t_R(**6b**) = 9.83 min. The *ee* value was determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OD column (eluent, 2-propanal/hexane 4:96; flow rate = 0.5 mL min^{-1}; detection: 254 nm light); $t_R(R)$ = 22.71 min; $t_R(S)$ = 25.99 min.

***o*-Methylbenzhydrol (6c)**: The conversion was determined by capillary GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column; 230 °C; isothermal; t_R(**5c**) = 6.10 min; t_R(**6c**) = 11.65 min. The *ee* value was determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OD column (eluent, 2-propanal/hexane 4:96; flow rate = 0.8 mL min^{-1}; detection: 254 nm light); $t_R(R)$ = 18.98 min; $t_R(S)$ = 21.22 min.

***m*-Methylbenzhydrol (6d)**: The conversion was determined by capillary GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column; 230 °C; isothermal; t_R(**5d**) = 7.48 min; t_R(**6d**) = 11.70 min. The *ee* value was determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OB-H column (eluent, 2-propanal/hexane 10:90; flow rate = 1.0 mL min^{-1}; detection: 254 nm light); t_R = 13.48 min (minor) and 23.37 min (major).

***p*-Chlorobenzhydrol (6e)**: The conversion was determined by capillary GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column; 230 °C; isothermal; t_R(**5e**) = 10.09 min; t_R(**6e**) = 22.02 min. The *ee* value was determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OB-H column (eluent, 2-propanal/hexane 10:90; flow rate = 1.0 mL min^{-1}; detection: 254 nm light); $t_R(R)$ = 13.13 min; $t_R(S)$ = 19.02 min.

***p*-Methylbenzhydrol (6f)**: The conversion was determined by capillary GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column; 230 °C; isothermal; t_R(**5f**) = 8.20 min; t_R(**6f**) = 12.35 min. The *ee* value was determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OB-H column (eluent, 2-propanal/hexane 10:90; flow rate = 0.5 mL min^{-1}; detection: 254 nm light). $t_R(R)$ = 19.25 min; $t_R(S)$ = 21.97 min.

***p*-Trifluromethylbenzhydrol (6g)**: The conversion was determined by capillary GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column; 230 °C; isothermal; t_R(**5g**) = 4.48 min; t_R(**6g**) = 9.27 min. The *ee* value was determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OB-H column (eluent, 2-propanal/hexane 10:90; flow rate = 0.8 mL min^{-1}; detection: 254 nm light); $t_R(R)$ = 9.17 min; $t_R(S)$ = 11.95 min.

(*E*)-4-Phenyl-3-buten-2-ol (8a): The conversion was determined by capillary GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column; 180 °C; isothermal; t_R(**7a**) = 9.43 min; t_R(**8a**) = 11.31 min. The *ee* value was determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OD column (eluent, 2-propanal/hexane 10:90; flow rate = 0.5 mL min^{-1}; detection: 254 nm light); $t_R(R)$ = 16.08 min; $t_R(S)$ = 22.38 min.

4-Methyl-3-penten-2-ol (8b): The conversion was determined by capillary GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column; 70 °C; isothermal; t_R(**7b**) = 5.50 min; t_R(**8b**) = 10.17 min. The *ee* value was determined by capillary GC with a 25 m × 0.25 mm Chirasil-DEX CB column; 70 °C; isothermal; $t_R(R)$ = 10.62 min; $t_R(S)$ = 16.26 min.

(*E*)-3-Nonen-2-ol (8c): The conversion was determined by capillary GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column; 100 °C; isothermal; t_R(**7c**) = 12.48 min; t_R(**8c**) = 14.84 min. The *ee* value was determined by capillary GC with a 25 m × 0.25 mm Chirasil-DEX CB column; 80 °C; isothermal; $t_R(R)$ = 41.48 min; $t_R(S)$ = 44.07 min.

Cyclopropyl(phenyl)methanol (10a): The conversion was determined by capillary GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column; 170 °C; isothermal; t_R(**9a**) = 7.67 min; t_R(**10a**) = 11.47 min. The *ee* value was determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel OD column (eluent, 2-propanal/hexane 5:95; flow rate = 0.5 mL min^{-1}; detection: 254 nm light); $t_R(R)$ = 18.06 min; $t_R(S)$ = 21.61 min.

Cyclopropyl(*p*-chlorophenyl)methanol (10b): Capillary GC, Chirasil-DEX CB column; 160 °C; isothermal; t_R(**9b**) = 10.84 min. The retention times of two enantiomers of **10b** are: t_R = 21.27 min (minor) and t_R = 22.10 min (major).

Cyclopropyl(*p*-fluorophenyl)methanol (10c): Capillary GC, Chirasil-DEX CB column; 140 °C; isothermal; t_R(**9c**) = 8.76 min. The retention times of two enantiomers of **10c** are: t_R = 16.47 min (minor) and t_R = 17.24 min (major).

Cyclopropyl(*p*-methylphenyl)methanol (10d): The conversion was determined by capillary GC with a 30 m × 0.25 mm J & W Scientific INNOWAX column; 210 °C; isothermal; t_R(**9d**) = 15.12 min; t_R(**10d**) = 17.46 min. The *ee* value was determined by chiral HPLC analysis with a 25 cm × 4.6 mm Daicel Chiralcel AD column (eluent, 2-propanal/hexane 5:95; flow rate = 0.5 mL min^{-1}; detection: 254 nm light); t_R = 29.85 min (minor) and t_R = 33.60 min (major).

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