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The synthesis of new chiral phosphine–phosphinites, phosphine–phosphoramidite, and phosphine–phosphite ligands and their applications in asymmetric hydrogenation

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Abstract—New chiral phosphine–phosphinite, phosphine–phosphoramidite ligands and phosphine–phosphite **1a**, **1b**, **2** and **3** have been synthesized and examined in the enantioselective hydrogenation of dehydroamino acid derivatives and α-aryl enamides. The results demonstrate that both rhodium-**1b** and rhodium-**2** complexes were highly efficient catalysts in asymmetric hydrogenation reactions (up to 99.6% ee was obtained).

1. Introduction

Chiral organophosphorus ligands play an important role in metal-catalyzed asymmetric reactions. The seminal work by Knowles and Sabacky in 1968 on the application of a rhodium chiral phosphine catalyst in asymmetric hydrogenation essentially started a new era of study of asymmetric catalysis.[1] In 1971, Kagan and co-workers reported the synthesis of DIOP, the first chiral bisphosphine ligand and its application in the Rh-catalyzed asymmetric hydrogenation.[2] Prompted by this development, Knowles et al. further developed their original monodentate phosphine ligand PAMP (phenylanisylmethylphosphine) to a C_2-symmetric chelating bisphosphine ligand DIPAMP and used it in industrial scale asymmetric hydrogenation for the commercial production of L-dopa. Following these important contributions, synthetic organic chemists from around the world have developed thousands of chiral phosphorus ligands with diverse structures and have used them in metal-catalyzed asymmetric synthesis over the last three decades.[3] High enantioselectivities were obtained in the asymmetric hydrogenation of prochiral olefins using rhodium catalysts containing chiral diphosphine ligands such as Chiraphos,[4] Norphos,[5] BPPM,[6] BDPP,[7] BINAP,[8] Duphos,[9] BICP,[10] P-Phos, etc.[11] However, many effective phosphine ligands are quite difficult to prepare and the search for easily prepared new chiral ligands with high effectiveness is still of high interest.

In recent years, new series of phosphorus ligands such as phosphinite,[12] phosphite,[13] phosphonite,[14] and phosphoroamidite,[15] have been shown to have high efficiency in catalytic asymmetric reactions. Chiral phosphinites can be easily prepared in high yields through the reaction of the corresponding alcohols with chlorophosphines in the presence of an organic base. Mixed chiral phosphorus ligands have also been found to have unique properties in asymmetric catalytic reactions. For example, (*R*,*S*)-BINAPHOS, a chiral phosphine–phosphite ligand derived from BINOL, is highly effective in the rhodium-catalyzed asymmetric hydroformylations of prochiral olefins.[16]

A subclass of chiral ligands derived from ferrocene have been found to be very effective in many transition-metal-

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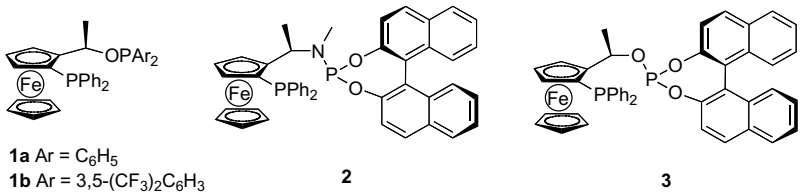


Figure 1. The structures of new chiral ligands derived from ferrocene.

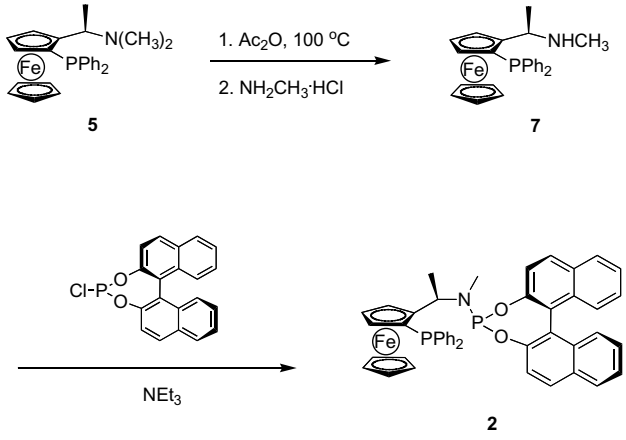
catalyzed asymmetric reactions.[17] Hayashi and co-workers prepared a series of chiral ferrocenylphosphine ligands starting from Ugi's chiral α-dimethyl aminoethylferrocene and successfully used them in the asymmetric hydrosilylation, hydrogenation, and Grignard cross coupling.[18] Togni et al. have developed a series of highly effective bisphosphanes, as exemplified by Josiphos, which was used in the Rh-catalyzed asymmetric hydrogenation on an industrial scale as well as in Pd-catalyzed allylic alkylation.[19] Kagan and co-workers investigated some ferrocene-based 1,3-bis(phosphanes) with planar chirality for hydrogenation, with up to 98% ee being observed.[20] Heller and co-workers obtained high ee's in the asymmetric hydrogenation of β-aryl-substituted β-acylaminoacrylates using Et-FerroTANE as a ligand.[21] Knochel and co-workers prepared a number of ferrocenyl ligands with two phosphanyl substituents and successfully used them in hydrogenation and Pd(0)-catalyzed allylic substitution reactions.[22] Spindler and co-workers described a ligand family based on the phenylferrocenylethyl backbone and achieved up to 95% ee in the hydrogenation of a 2-isopropylcinnamic acid derivative to give a product of high industrial interest.[23] Recently, Boaz et al. reported the preparation of phosphinoferrocenylaminophosphines and the application of them in the rhodium-catalyzed asymmetric hydrogenation.[24]

One of the targets in our study of catalytic asymmetric synthesis is the development of effective chiral ligands that can be easily prepared and successfully applied in asymmetric synthesis. Herein we report the synthesis of new mixed chiral phosphine–phosphinites, phosphine–phosphoramidite ligands, and phosphine–phosphite **1**, **2**, and **3**, respectively, based on a ferrocene framework (Fig. 1). The results of using these ligands in the asymmetric hydrogenation of dehydroamino acids and enamides are also discussed.

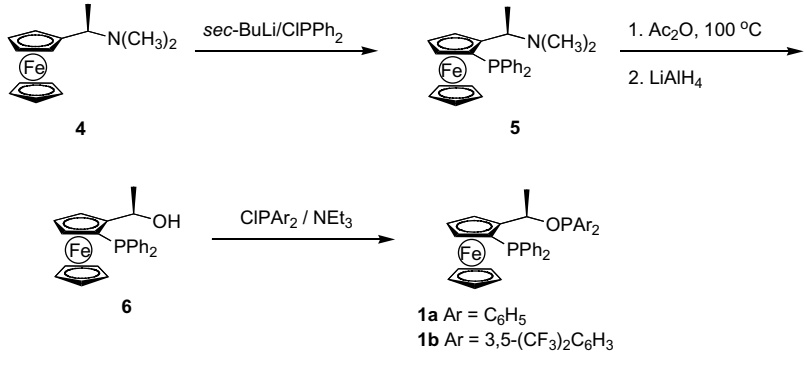
2. Results and discussion

The chiral phosphine–phosphinites ligands can be conveniently prepared from Ugi's amine, *N*,*N*-dimethyl-1-ferrocenylethylamine (Scheme 1). Amine **4** can be readily converted to phosphine **5** using *sec*-butyl lithium instead of the *n*-butyl lithium with the yield of the product increasing from 60% to over 80%. Phosphine **5** was reacted with acetic anhydride at 100 °C for 3 h to afford the acetate with retention of configuration, which was then reduced with $LiAlH_4$ to give the corresponding alcohol **6** in 90% yield. The reaction of **6** with a suitable chlorophosphine in the presence of DMAP and triethylamine afforded ligands **1a** or **1b**.

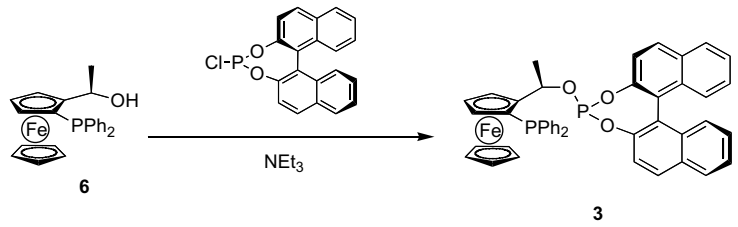
In order to exploit the unique properties of a binaphthyl moiety, two new chiral ligands (**2** and **3**) were then synthesized using synthetic procedures similar to that for ligand **1**. The reaction of the acetate intermediate



Scheme 2. The synthetic route of chiral phosphine–phosphoramidite ligand **2**.

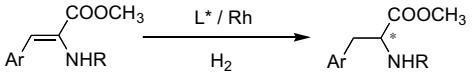


Scheme 1. The synthetic route for chiral phosphine–phosphinite ligands **1a** and **1b**.



Scheme 3. The synthetic route of chiral phosphine–phosphinite ligand **3**.

Table 1. The asymmetric hydrogenation of α-dehydroamino acid derivatives catalyzed by Rh-**1a** and Rh-**1b**[a]



8a-j

Entry	Ligand	Substrate		Solvent	*T* (°C)	Ee (%)[b]
1	**1a**	**8a**	Ar = Ph, R = Ac	CH_2Cl_2	rt	59.4
2	**1b**	**8a**	Ar = Ph, R = Ac	CH_2Cl_2	rt	86.3
3	**1b**	**8a**	Ar = Ph, R = Ac	THF	rt	79.6
4	**1b**	**8a**	Ar = Ph, R = Ac	MeOH	rt	20.0
5	**1b**	**8a**	Ar = Ph, R = Ac	Toluene+CH_2Cl_2	rt	90.0
6	**1b**	**8a**	Ar = Ph, R = Ac	*i*-PrOH	rt	67.9
7	**1b**	**8a**	Ar = Ph, R = Ac	Toluene+CH_2Cl_2	5	96.5
8	**1b**	**8b**	Ar = *p*-CF_3–Ph, R = Ac	Toluene+CH_2Cl_2	5	99.0
9	**1b**	**8c**	Ar = *p*-Cl–Ph, R = Ac	Toluene+CH_2Cl_2	5	97.0
10	**1b**	**8d**	Ar = *p*-MeO–Ph, R = Ac	Toluene+CH_2Cl_2	5	97.8
11	**1b**	**8e**	Ar = *m*-Cl–Ph, R = Ac	Toluene+CH_2Cl_2	5	96.1
12	**1b**	**8f**	Ar = *p*-Br–Ph, R = Ac	Toluene+CH_2Cl_2	5	99.1
13	**1b**	**8g**	Ar = *p*-Me–Ph, R = Ac	Toluene+CH_2Cl_2	5	95.3
14	**1b**	**8h**	Ar = H, R = Ac	Toluene+CH_2Cl_2	5	95.8
15	**1b**	**8i**	Ar = *p*-F–Ph, R = benzoyl	Toluene+CH_2Cl_2	5	98.3
16	**1b**	**8j**	Ar = *p*-Cl–Ph, R = benzoyl	Toluene+CH_2Cl_2	5	**99.6**

[a] The catalyst was prepared in situ. Hydrogen pressure was 150 psi in all reactions; substrate/catalyst (mol/mol) = 100.
[b] The ee values were determined by GC analysis using a Chrompack chiral fused silica 25 m × 0.25 mm chirasil-L-VAL column. All products were in (*S*)-configuration based on the comparison with published data.

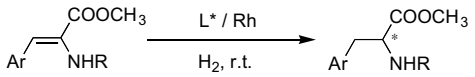
with the methylammonium chloride led to the secondary amines **7**. Reaction of **7** or **6** with chlorobinaphthoxyphosphine afforded ligands **2** or **3**, respectively (Schemes 2 and 3).

Ligands **1a** and **1b** were first examined in the Rh-catalyzed asymmetric hydrogenation of (*Z*)-2-acetamidocinnamic acid methyl ester. Common factors governing the enantioselectivities of the reaction were examined. The results shown in Table 1 clearly indicate that the enantioselectivity of the catalyst containing **1b** is substantially better to the catalyst containing **1a**. The enantioselectivity was sensitive to the choice of solvents; a mixed solvent of dichloromethane and toluene was found to give the best result. The reaction temperature was also an important factor. A significant increase in enantioselectivity was observed at lower reaction temperatures. When the reaction temperature was lowered to 5 °C from ambient temperature, the ee value was found to increase from 90% to 96.5% (entry 7 vs 5). On the other hand, hydrogen pressure had relatively little effect on the enantioselectivity. The use of **1b** in the Rh-catalyzed hydrogenation of the methyl ester of other α-acylamidocinnamic acids was further studied. All of the substrates tested gave over 95% ee (entries 9–16) with the highest ee being 99.6% (entry 16).

Ligand **1b**, with two CF_3 groups at the 3 and 5 positions of the phenyl, afford excellent results in comparison to those obtained using **1a** as the ligand in asymmetric hydrogenation reactions. This positive result can be explained as a consequence of the *meta*-dialkyl effect, which widely exists in Ru, Pd, Rh, and Ir chemistry. 3,5-Dialkylphenyl groups used as P-substituents increase the rigidity of the chiral pocket, with the ee values increased as a result.[25–28]

The new phosphine–phosphoramidite ligand **2** and phosphine–phosphinites **3** were also tested in the rhodium-catalyzed asymmetric hydrogenation of α-dehydroamino acid derivatives. The results of the asymmetric hydrogenation of (*Z*)-2-acetamidocinnamic acid methyl ester catalyzed by Rh-**2** and Rh-**3** complexes under different conditions are summarized in Table 2. Chiral ligand **2** was found to give remarkable enantioselectivity in this reaction. An excellent ee value of the desired product was obtained at room temperature with THF as solvent. It is noteworthy that the enantioselectivity of

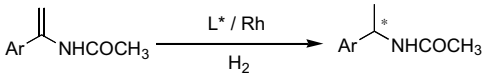
Table 2. The asymmetric hydrogenation of α-dehydroamino acid derivatives catalyzed by Rh-**2** or Rh-**3**[a]



Entry	Ligand	Substrate	Pressure (psi)	Solvent	Ee (%)[b]
1	**3**	Ar = Ph, R = CH_3CO	300	CH_2Cl_2	85
2	**3**	Ar = Ph, R = CH_3CO	300	THF	89
3	**2**	Ar = Ph, R = CH_3CO	300	CH_2Cl_2	96
4	**2**	Ar = Ph, R = CH_3CO	300	CH_3OH	87
5	**2**	Ar = Ph, R = CH_3CO	200	THF	98
6	**2**	Ar = Ph, R = CH_3CO	300	THF	99
7	**2**	Ar = Ph, R = CH_3CO	500	THF	99
8	**2**	Ar = *p*-NO_2–Ph, R = CH_3CO	300	THF	**99.6**
9	**2**	Ar = *p*-CH_3–Ph, R = CH_3CO	300	THF	97.4
10	**2**	Ar = *p*-F–Ph, R = PhCO	300	THF	99
11	**2**	Ar = *p*-Br–Ph, R = CH_3CO	300	THF	99
12	**2**	Ar = *p*-Cl–Ph, R = PhCO	300	THF	99

[a] The catalyst was prepared in situ. All reactions were carried out at room temperature; substrate/catalyst (mol/mol) = 100.
[b] The ee values were determined by GC with a Chrompack chiral fused silica 25 m × 0.25 mm chirasil-L-VAL column. All products were in (*S*)-configuration based on the comparison with published data.

Table 3. The enantioselective hydrogenation of enamides catalyzed by Rh-**1** and Rh-**2** complex[a]



Entry	Ligand	Aryl	Solvent	Temperature (°C)	Ee (%)[b]
1	**1a**	Ph	CH_2Cl_2	rt	72
2	**1b**	Ph	CH_2Cl_2	rt	83
3	**1b**	*p*-CF_3–Ph	CH_2Cl_2	0	91
4	**2**	Ph	CH_2Cl_2	rt	73
5	**2**	Ph	THF	rt	77
6	**2**	Ph	*i*-PrOH	rt	76
7	**2**	Ph	THF	0	87.5

[a] The catalyst was prepared in situ. Hydrogen pressure was 300 psi in all reactions. All the reactions were carried out at room temperature; substrate/catalyst (mol/mol) = 100.
[b] The ee values were determined by GC analysis with a Chrompack chiral fused silica 25 m × 0.25 mm chirasil-L-VAL column. All products were in (*S*)-configuration based on the comparison with published data.

the catalyst is sensitive to the solvent used. Higher ee values of the products were achieved in THF (99% ee) while only 87% ee was observed when methanol was used as solvent (entry 4). In contrast, the hydrogen pressure had very little effect on the enantioselectivities (Table 2, entries 5–7).

A variety of (*Z*)-2-acetamido-3-arylacrylic acids were hydrogenated using the Rh-**2** catalyst and in all cases the desired products were found to have 99% ee or higher, except for the product from the hydrogenation of (*Z*)-2-acetamido-3-[(*o*-methyl)-phenyl]-acrylic acid methyl ester having an electron donor group on the phenyl ring. Again, these results compared favorably with those obtained with the best known chiral phosphine, phosphinite, phosphite, phosphonite or phosphoroamidite-rhodium catalysts.

The asymmetric catalytic hydrogenation of enamides with Rh-**1** and Rh-**2** were also tested with the results summarized in Table 3. Moderate to good enantioselectivities were obtained.

It is well known that the drawback of chiral phosphinite ligands is their moisture-sensitivity. In our experiment, we found that chiral ligands **1b** were relatively air and water stable when compared to other chiral phosphinite ligands.[3,12c] The ease of preparation, high enantioselectivity and relative air and water stabilities make the mixed chiral phosphorus ligands extensively useful in asymmetric synthesis.

3. Conclusion

In conclusion, new chiral phosphine–phosphinite, phosphine–phosphoramidite ligands, and phosphine–phosphite **1a**, **1b**, **2**, and **3** have been synthesized and examined for the enantioselective hydrogenation of dehydroamino acid derivatives and α-aryl enamides. The results demonstrated that both Rh-**1b** and Rh-**2** complexes are highly efficient catalysts in asymmetric hydrogenation reactions.

4. Experimental

4.1. General handling and materials

All manipulations were carried out under a dry nitrogen atmosphere using standard Schlenk techniques or in a nitrogen atmosphere glove-box unless otherwise stated. All solvents were distilled and degassed prior to use.

4.2. Preparation of chiral ligand 1a

A solution of triethylamine (0.29 mL, 2.1 mmol) and diphenylphosphinous chloride (0.25 g, 1.1 mmol) in toluene (5 mL) was transferred via a syringe into a 100 mL round-bottomed flask containing compound (1*R*,2*S*)-**6** (0.41 g, 1.0 mmol) and DMAP (20 mg) in toluene (15 mL) at 0 °C under a nitrogen atmosphere. After the mixture has been stirred 6 h, the resulting mixture was purified through a Al_2O_3-packed column with toluene as an eluent. The eluates were concentrated in vacuo to afford the solid phosphoramidite (0.19 g, 31% yield).[1] H NMR (500 MHz, $CDCl_3$): δ 7.79–7.13 (m, 20H), 5.05–5.03 (m, 1H), 4.73 (s, 1H), 4.34 (s, 1H), 4.01 (s, 5H), 3.72 (s, 1H), 1.64 (d, 3H, $J = 7.0$ Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.3, 144.9, 144.3, 144.1, 139.2, 138.1, 137.9, 135.4, 135.1, 132.2, 131.8, 131.6, 131.0, 129.1, 128.2, 127.5, 125.4, 124.3, 123.2, 122.1, 121.9, 94.4, 94.2, 94.2, 94.1, 76.5, 76.4, 73.1, 52.5, 51.7, 18.7. ^{31}P NMR (200 MHz, $CDCl_3$): δ 37.6, −20.8. HRMS (EI) m/z calcd for $C_{36}H_{32}FeOP_2$ (M^+) 598.1278, found 598.1269.

4.3. Preparation of chiral ligand 1b

Triethylamine (0.29 mL, 2.1 mmol) and bis-[3,5-bis-(trifluoromethyl)phenyl]phosphinous chloride (0.5 g, 1.0 mmol) in toluene (5 mL) were transferred via a syringe into a 100 mL round-bottomed flask containing alcohol (1*R*,2*S*)-**6** (0.41 g, 1.0 mmol) and DMAP (20 mg) in toluene (15 mL) at 0 °C under a nitrogen atmosphere. After the mixture had been stirred for 6 h, the resulting mixture was purified through a pre-dried neutral Al_2O_3-packed column with toluene as an eluent. The eluates were concentrated in vacuo to afford the solid phosphoramidite (0.69 g, 79% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96–6.88 (m, 16H), 5.81 (m, 1H), 4.77 (s, 1H), 4.56 (s, 1H), 4.15 (s, 1H), 4.02 (s, 5H), 1.81 (d, 3H, $J = 2.5$ Hz), 1.79 (d, 3H, $J = 7$ Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.5, 146.2, 145.0, 144.9, 139.3, 139.2, 138.0, 137.9, 137.9, 135.5, 135.4, 132.2, 132.1, 131.9, 131.9, 131.7, 131.6, 131.5, 131.5, 131.3, 131.2, 129.7, 129.4, 129.2, 128.4, 128.3, 128.2, 127.7, 127.7, 127.6, 125.4, 124.4, 124.3, 123.4, 123.2, 123.2, 122.2, 122.2, 94.3, 94.2, 94.0, 94.0, 76.6, 76.5, 76.4, 76.3, 72.6, 72.6, 70.58, 70.5, 70.0, 69.9, 69.2, 69.2, 22.4, 22.3, 21.5. ^{31}P NMR (200 MHz, $CDCl_3$): δ 96.49 (d, $J = 26.0$ Hz), −25.21 (d, $J = 26$ Hz). HRMS (EI) m/z calcd for $C_{40}H_{28}F_{12}FeOP_2$ (M^+) 870.0773, found 870.0794.

4.4. Preparation of chiral ligand 2

Phosphorus trichloride (0.1 mL, 1.1 mmol) and triethylamine (0.4 mL, 2.9 mmol) were transferred via a syringe into a 100 mL round-bottomed flask containing (R)-BINOL (0.3 g, 1.0 mmol) in toluene (20 mL) at 0 °C under a nitrogen atmosphere. After the mixture had been stirred for 6 h, the volatiles were removed under vacuum. A solution of amine **7** (1.0 mmol) and triethylamine (0.3 mL, 2.1 mmol) in toluene (15 mL) was added to the flask and the mixture allowed to react overnight. The resulting mixture was purified through a pre-dried neutral Al_2O_3-packed column with toluene as an eluent. The eluates were concentrated in vacuo to afford the solid phosphoramidite product (0.61 g, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95–7.10 (m, 22H), 6.75–6.73 (d, 1H, $J = 8.5$ Hz), 5.36–5.30 (m, 1H), 4.44 (s, 1H), 4.31 (s, 1H), 3.98 (s, 5H), 3.89 (s, 1H), 1.74–1.73 (d, 3H), 1.69 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.6, 150.6, 149.6, 140.7, 140.6, 138.5, 138.4, 137.9, 135.8, 135.6, 132.6, 132.7, 132.6, 132.2, 132.0, 131.2, 130.6, 129.8, 129.7, 129.2, 129.104, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.5, 127.0, 127.0, 125.8, 125.8, 125.4, 124.5, 124.3, 123.7, 123.7, 122.9, 122.3, 121.9, 94.8, 94.6, 94.6, 94.4, 75.6, 75.5, 72.0, 51.1, 50.7, 24.7, 18.8. ^{31}P NMR (200 MHz, $CDCl_3$): δ 149.5 (d, $J = 53.2$ Hz), −23.7 (d, $J = 53.2$ Hz). HRMS (EI) m/z calcd for $C_{45}H_{37}FeNO_2P_2$ (M^+) 741.1649, found 741.1668. $[\alpha]_D^{20} = -208$ (c 0.48, toluene).

4.5. Preparation of chiral ligand 3

With the same procedure as the preparation of ligand **2** except using alcohol (1*R*,2*S*)-**6** as reactant 0.29 g (40% yield) of the solid product was obtained. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20–6.90 (m, 22H), 5.45 (m, 1H), 4.42 (s, 1H), 4.25 (s, 1H), 3.99 (s, 5H), 3.92 (s, 1H), 1.81 (d, 3H, $J = 7.0$Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.4, 150.4, 149.4, 141.3, 141.2, 138.7, 138.6, 137.9, 135.7, 135.7, 132.4, 132.3, 132.3, 132.0, 131.9, 130.9, 130.2, 129.4, 129.1, 128.9, 128.7, 127.9, 127.9, 127.6, 127.4, 127.3, 126.9, 125.6, 125.6, 124.3, 123.7, 122.7, 122.1, 94.8, 94.7, 94.6, 94.5, 76.2, 76.1, 72.2, 51.3, 50.9, 19.6. ^{31}P NMR (200 MHz, $CDCl_3$): δ 151.5, −21.3. HRMS (EI) m/z calcd for $C_{44}H_{34}FeO_3P_2$ (M^+) 728.1333, found 728.1325.

4.6. A typical procedure for the hydrogenation of enamides

The catalyst was made in situ by mixing $[Rh(COD)_2]BF_4$ (2.0 mg, 0.005 mmol) and ligand **1b** (5.0 mg, 5.5 μmol) in THF (1 mL) for 10 min. A small portion of the catalyst solution (0.2 mL) was transferred into a 50 mL glass-lined stainless steel autoclave, which contained an enamide substrate (0.1 mmol) and a magnetic stirring bar. The reactor was charged with hydrogen gas and the solution stirred at the required temperature for a predetermined period of time. After the reaction was complete, the hydrogen gas was released and the ee value of the product determined by

GC analysis with a Chrompack chiral fused silica 25 m × 0.25 mm chirasil-L-VAL column.

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References and notes

1. Knowles, W. S.; Sabacky, M. J. *J. Chem. Soc., Chem. Commun.* **1968**, L1445.
2. (a) Kagan, H. B.; Dang, T. P. *J. Chem. Soc., Chem. Commun.* **1971**, 481; (b) Kagan, H. B.; Dang, T. P. *J. Am. Chem. Soc.* **1972**, *94*, 6429; (c) Kagan, H. B.; Langlois, N.; Dang, T. P. *J. Organomet. Chem.* **1975**, *90*, 353.
3. For a review, please see: Tang, W.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029.
4. Fryzuk, M. D.; Bosnich, B. *J. Am. Chem. Soc.* **1977**, *99*, 6262.
5. Brunner, H.; Pieronczyk, W.; Schönhammer, B.; Streng, K.; Bernal, I.; Korp, J. *Chem. Ber.* **1981**, *114*, 1137.
6. Achiwa, K. *J. Am. Chem. Soc.* **1976**, *98*, 8265.
7. McNeil, P. A.; Roberts, N. K.; Bosnich, B. *J. Am. Chem. Soc.* **1981**, *103*, 2280.
8. Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932.
9. (a) Burk, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 8158; (b) Burk, M. J.; Feaster, J. E.; Nugent, W. A.; Harlow, R. L. *J. Am. Chem. Soc.* **1993**, *115*, 10125; (c) Burk, M. J.; Gross, M. F.; Martinez, J. P. *J. Am. Chem. Soc.* **1995**, *117*, 9375.
10. Zhu, G.; Cao, P.; Jiang, Q.; Zhang, X. *J. Am. Chem. Soc.* **1997**, *119*, 1799.
11. (a) Riley, D. P.; Shumate, R. E. *J. Org. Chem.* **1980**, *45*, 5187; (b) Bergstein, W.; Kleemann, A.; Martens, J. *Synthesis* **1981**, 76.
12. (a) Chan, A. S. C.; Hu, W. H.; Pai, C. C.; Lau, C. P.; Jiang, Y. Y.; Mi, A. Q.; Yan, M.; Sun, J.; Lou, R. L.; Deng, J. G. *J. Am. Chem. Soc.* **1997**, *119*, 9570;; (b) RajanBabu, T. V.; Ayers, T. A.; Halliday, G. A.; You, K. K.; Calabrese, J. C. *J. Org. Chem.* **1997**, *62*, 60124; (c) Chen, Y. X.; Li, X. S.; Tong, S. K.; Choi, M. C. K.; Chan, A. S. C. *Tetrahedron Lett.* **1999**, *40*, 957; (d) Selke, R.; Ohff, M.; Riepe, A. *Tetrahedron* **1996**, *52*, 15079; (e) Zhou, Y. G.; Zhang, X. *Chem. Commun.* **2002**, 1124; (f) Zhou, Y. G.; Tang, W.; Wang, W. B.; Li, W.; Zhang, X. *J. Am. Chem. Soc.* **2002**, *124*, 4952.
13. (a) Reetz, M. T.; Neugebauer, T. *Angew. Chem., Int. Ed.* **1999**, *38*, 179; (b) Reetz, M. T.; Mehler, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 3889.
14. (a) Reetz, M. T.; Gosberg, A.; Goddard, R.; Kyung, S. *J. Chem. Soc., Chem. Commun.* **1998**, 2077; (b) Pastor, S. D.; Shum, S. P. Ciba Speciality Chemical Corperation US Patent 5,817,850, 1998; (c) Reetz, M. T.; Sell, T. *Tetrahedron Lett.* **2000**, *41*, 6333.
15. van den Berg, M.; Minnaard, A. J.; Schudde, E. P.; van Esch, J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *J. Am. Chem. Soc.* **2000**, *122*, 11539.
16. (a) Higashizima, T.; Sakai, N.; Nozaki, K.; Takaya, H. *Tetrahedron Lett.* **1994**, *35*, 2023; (b) Nozaki, K.; Sakai, N.; Nanno, T.; Higashijima, T.; Mano, S.; Horiuchi, T.; Takaya, H. *J. Am. Chem. Soc.* **1997**, *119*, 4413; (c) Ewalds, R.; Eggeling, E. B.; Hewat, A. C.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Vogt, D. *Chem. Eur. J.* **2000**, *6*, 1496; (d) Nozaki, K.; Matsuo, T.; Shibahara, F.; Hiyama, T. *Adv. Synth. Catal.* **2001**, *343*, 61.
17. (a) Togni, A.; Halterman, R. L. In *Metallocenes*; Wiley-VCH: Weinheim, 1998; Vol. 2, p 685; (b) Richards, C. J.; Locke, A. J. *Tetrahedron: Asymmetry* **1998**, *9*, 2377.
18. (a) Hayashi, T.; Tajika, M.; Tamao, K.; Kumada, A. A. *J. Am. Chem. Soc.* **1976**, *98*, 3718; (b) Hayashi, T.; Mise, T.; Fukushima, M.; Kagotani, M.; Nagashima, N.; Hamada, Y.; Matsumoto, A.; Kawakami, S.; Konishi, M.; Yamamoto, K.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1138; (c) Ohno, A.; Yamane, M.; Hayashi, T. *Tetrahedron: Asymmetry* **1995**, *6*, 2495–2502; (d) Han, J. W.; Tokunaga, N.; Hayashi, T. *Helv. Chim. Acta* **2002**, *85*, 3848.
19. Togni, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Landert, H.; Tijani, A. *J. Am. Chem. Soc.* **1994**, *116*, 4062–4066.
20. Argouarch, G.; Samuel, O.; Kagan, H. B. *Eur. J. Org. Chem.* **2000**, 2885.
21. You, J.; Drexler, H.-J.; Zhang, S.; Fischer, C.; Heller, D. *Angew. Chem., Int. Ed.* **2003**, *42*, 913.
22. (a) Ireland, T.; Grossheimann, G.; Wieser-Jeunesse, C.; Knochel, P. *Angew. Chem., Int. Ed.* **1999**, *38*, 3112–3115; (b) Lotz, M.; Kramer, G.; Knochel, P. *Chem. Commun.* **2002**, 2546.
23. Sturm, T.; Weissensteiner, W.; Spindler, F. *Adv. Synth. Catal.* **2003**, *345*, 160.
24. Boaz, N. W.; Debenham, S. D.; Mackenzie, E. B.; Large, S. E. *Org. Lett.* **2002**, *4*, 2421.
25. Selvakumar, K.; Valentini, M.; Pregosin, P. S. *Organometallics* **2000**, *19*, 1299.
26. Tschoerner, M.; Pregosin, P. S.; Albinati, A. *Organometallics* **1999**, *18*, 670.
27. Trabesinger, G.; Albinati, A.; Feiken, N.; Kunz, R. W.; Pregosin, P. S.; Tschoerner, M. *J. Am. Chem. Soc.* **1997**, *119*, 6315.
28. RajanBabu, T. V.; Ayers, T. A.; Casalnuovo, A. L. *J. Am. Chem. Soc.* **1994**, *116*, 4101.