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New unsymmetrical hybrid ferrocenylphosphine-phosphoramidite ligands derived from H_8-BINOL for highly efficient Rh-catalyzed enantioselective hydrogenation

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Received 10 January 2005; accepted 2 February 2005

Abstract—A series of new H_8-BINOL-derived unsymmetrical hybrid ferrocenylphosphine-phosphoramidite ligands have been synthesized and successfully used in Rh-catalyzed asymmetric hydrogenations. The same or higher enantioselectivities (99.9% ee) were achieved in the hydrogenation of dimethyl itaconate and α-dehydroamino acid esters as those obtained with BINOL-derived analogues. However, slightly lower enantioselectivities (99.0% ee) were obtained in the hydrogenation of enamides.

1. Introduction

Catalytic asymmetric hydrogenation is one of the most powerful tools for obtaining a wide range of enantiomerically pure or enriched compounds.[1] Many historically successful ligands used in this reaction are bidentate *P*-chelate ligands, and most have a C_2-symmetrical structure or at least two closely related binding sites.[2] Therefore, C_2-symmetry remains a popular principle for ligand design. However, some recent reports have demonstrated the potential of unsymmetrical bidentate phosphorus ligands in the catalytic asymmetric hydrogenation, challenging the need for C_2-symmetry in asymmetric hydrogenation ligand design.[3] For example, Hoge et al. reported that a three-hindered quadrant motif of Rh-catalysts derived from *tert*-butylmethylphosphino-di-*tert*-butylphosphinomethane can provide enantioselectivities equal to the current state of the art with C_2-symmetrical ligands during asymmetric hydrogenation. Recently, we[4a] and Chan and co-workers[4b] independently reported that the unsymmetrical hybrid phosphine-phosphoramidite ligands (S_c,R_p,S_a)-**1** combining a planar-chiral ferrocene backbone with an axial-chiral binaphthyl moiety displayed excellent enantioselectivities in the Rh-catalyzed asymmetric hydrogenation of enamides, dimethyl itaconate and α-dehydroamino acid derivatives, and that the binaphthyl moiety was able to play a crucial role in the enantioselectivity and control of the chirality of the hydrogenation products. Therefore, replacing the binaphthyl moiety with other groups, such as H_8-binaphthyl, may have an important influence on the catalytic activity and selectivity. Despite the chiral binaphthyl framework being extensively used in asymmetric catalysis,[5] the partially hydrogenated binaphthyl framework (such as H_8-binaphthyl) has not yet attained the same popularity as its parent binaphthyl structure in asymmetric catalysis.[6] In a few cases, the partially hydrogenated binaphthyl framework has shown improved chiral induction over its parent structure due to the increased steric interaction between the two partially hydrogenated naphthalene rings in H_8-binaphthyl. Stimulated by our recent success in the development of efficient unsymmetrical hybrid ligands and the effectiveness of the octahydrobinaphthyl backbone in asymmetric catalysis, we wished to develop some new unsymmetrical hybrid phosphine-phosphoramidite ligands based on H_8-BINOL for the Rh-catalyzed asymmetric hydrogenation. As a result, we herein report a series of new H_8-BINOL-derived ferrocenylphosphine-phosphoramidite ligands (S_c,R_p,S_a)-**2a**–**c** and (R_c,S_p,S_a)-**2d**, exhibiting the same or higher enantioselectivity in the hydrogenation of

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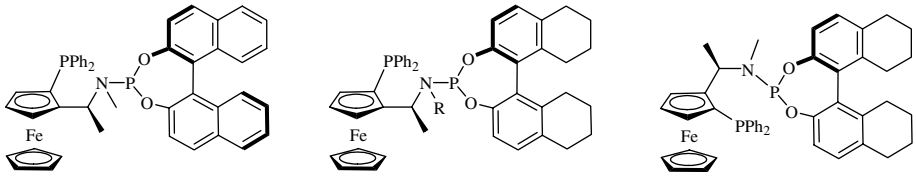
doi:10.1016/j.tetasy.2005.02.003



(S_c,R_p,S_a)-**1** (S_c,R_p,S_a)-**2a**: R = Me; (S_c,R_p,S_a)-**2b**: R = H; (S_c,R_p,S_a)-**2c**: R = Et (R_c,S_p,S_a)-**2d**

α-dehydroamino acid derivatives and dimethyl itaconate in comparison with its BINOL-derived parent ligands.

2. Results and discussions

2.1. Synthesis of H_8-BINOL-derived ferrocenylphosphine-phosphoramidite ligands 2

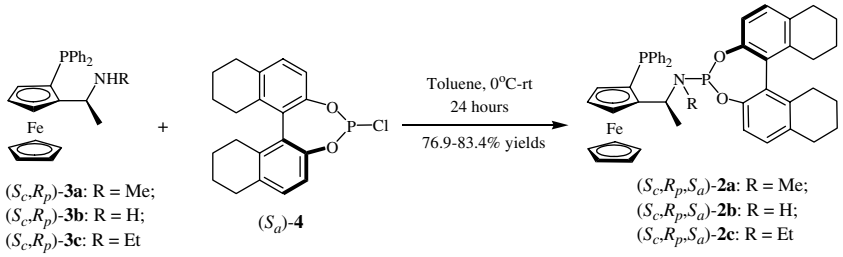
The synthesis of these unsymmetrical hybrid phosphine-phosphoramidite ligands is straightforward. By the reaction of ferrocenylphosphine-amines (S_c,R_p)-**3a**–**c**[7] with H_8-BINOL-derived (S_a)-chlorophosphite **4**[8] in toluene at 0 °C to rt, ligands (S_c,R_p,S_a)-**2a**–**c** were easily prepared in 76.9–83.4% yields, as outlined in Scheme 1. In the same procedure, ligand (R_c,S_p,S_a)-**2d** was synthesized from the corresponding (R_c,S_p)-**3a** in 81.3% yields. Similar to its BINOL analogue (S_c,R_p,S_a)-**1**, ligand (S_c,R_p,S_a)-**2a** also exhibits an extraordinary stability towards air and moisture, and tolerance of various hydrogenation conditions, which make this ligand highly practical for general laboratory preparations as well as scale-up operations.

2.2. Rh-catalyzed asymmetric hydrogenation of α-dehydroamino acid derivatives 5

In the first set of experiments, we used the Rh-catalyzed asymmetric hydrogenation of α-dehydroamino acid derivatives to benchmark the potential of these H_8-BINOL derived phosphine-phosphoramidite ligands for asymmetric catalysis. Hydrogenation was conducted at room temperature under an H_2 pressure of 10 bar in the presence of 1 mol% of catalysts prepared in situ from $Rh(COD)_2BF_4$ and 1.1 equiv of chiral ligand, with full conversions were observed in all cases. As shown in Table 1, the H_8-BINOL-derived ligands exhibited higher enantioselectivities than their BINOL analogues. Thus, excellent enantioselectivity (99.9% ee) were achieved in the Rh-catalyzed asymmetric hydrogenation of methyl (*Z*)-acetamidocinnamate **5a** by using 1.1 equiv of H_8-BINOL-derived ligand (S_c,R_p,S_a)-**2a** to Rh, while the corresponding BINOL-derived ligand (S_c,R_p,S_a)-**1** only gave the hydrogenation product in 97.6% ee under the same hydrogenation conditions (entry 1 vs entry 3). The reaction was not solvent dependent and proceeded smoothly in all of the solvents tested to give the product with >99% ee (entries 4 and 5). Lowering the H_2 pressure to 1 bar, gave similar enantioselectivities (entry 6). Other listed ligands were also used in this reaction to examine the substitutent effect in the enantioselectivity, and the results showed that there are no substantial differences between (S_c,R_p,S_a)-**2b** and (S_c,R_p, S_a)-**2c** with (S_c,R_p,S_a)-**2a**, indicated few influence of the substitutent in amino moiety in the enantioselective induction of ligands (entries 7 and 8 vs entry 3). However, (R_c,S_p,S_a)-**2d** only gave a hydrogenation product with 50.0% ee with the same configuration as that obtained with (S_c,R_p,S_a)-**2a**, suggesting that a (S_c)-central chirality, (R_p)-planar chirality and (S_a)-axial chirality were matched configurations in these H_8-BINOL-derived phosphine-phosphoramidites for asymmetric hydrogenation (entry 9). Considering the relatively simple preparation of (S_c,R_p,S_a)-**2a**, we then selected (S_c,R_p,S_a)-**2a** for further study of this reaction. A variety of α-dehydroamino acid esters were undertaken to examine the efficiency of this catalyst system. The results demonstrate that the Rh/(S_c,R_p,S_a)-**2a** complex was very efficient for this type of substrates. Excellent enantioselectivities were obtained in each case regardless of the electronic properties of the aryl group on the substrates **5** and all the substrates were hydrogenated in over 99.5% ee even at low catalyst loadings (entries 10–16).

2.3. Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate 7

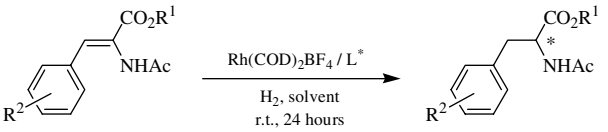
Similar to its BINOL analogue (S_c,R_p,S_a)-**1**, remarkable enantioselectivities were also obtained in the Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate



(S_c,R_p)-**3a**: R = Me; (S_c,R_p)-**3b**: R = H; (S_c,R_p)-**3c**: R = Et (S_a)-**4** (S_c,R_p,S_a)-**2a**: R = Me; (S_c,R_p,S_a)-**2b**: R = H; (S_c,R_p,S_a)-**2c**: R = Et

Scheme 1. Synthesis of H_8-BINOL-derived ferrocenylphosphine-phosphoramidite ligands (S_c,R_p,S_a)-**2a**–**c**.

Table 1. Rh-catalyzed asymmetric hydrogenation of α-dehydroamino acid derivatives **5** using H_8-BINOL-derived ligands (S_c,R_p,S_a)-**2a**–**2c** and (R_c,S_p,S_a)-**2d**[a]



5a: R^1 = Me, R^2 = H; **5b**: R^1 = Et, R^2 = H; **5c**: R^1 = Me, R^2 = 2-Cl; **5d**: R^1 = Me, R^2 = 4-Cl; **5e**: R^1 = Et, R^2 = 4-Cl; **5f**: R^1 = Me, R^2 = 2-MeO; **5g**: R^1 = Me, R^2 = 4-MeO

6a: R^1 = Me, R^2 = H; **6b**: R^1 = Et, R^2 = H; **6c**: R^1 = Me, R^2 = 2-Cl; **6d**: R^1 = Me, R^2 = 4-Cl; **6e**: R^1 = Et, R^2 = 4-Cl; **6f**: R^1 = Me, R^2 = 2-MeO; **6g**: R^1 = Me, R^2 = 4-MeO

Entry	Ligand	Substrate	Solvent	[Rh/L] (mol%)	Ee (%)[b] config.[c]
1	(S_c,R_p,S_a)-**1**	**5a**	CH_2Cl_2	1/1.1	97.6 (*R*)
2	(S_c,R_p,S_a)-**1**	**5a**	CH_2Cl_2	1/2.2	99.0 (*R*)
3[b]	(S_c,R_p,S_a)-**2a**	**5a**	CH_2Cl_2	1/1.1	99.9 (*R*)
4	(S_c,R_p,S_a)-**2a**	**5a**	CH_3OH	1/1.1	99.7 (*R*)
5	(S_c,R_p,S_a)-**2a**	**5a**	Toluene	1/1.1	99.5 (*R*)
6	(S_c,R_p,S_a)-**2a**	**5a**	CH_3OH	1/1.1	99.8 (*R*)[d]
7	(S_c,R_p,S_a)-**2b**	**5a**	CH_2Cl_2	1/1.1	99.8 (*R*)
8	(S_c,R_p,S_a)-**2c**	**5a**	CH_2Cl_2	1/1.1	99.9 (*R*)
9	(R_c,S_p,S_a)-**2d**	**5a**	CH_2Cl_2	1/1.1	50.0 (*R*)
10	(S_c,R_p,S_a)-**2a**	**5b**	CH_2Cl_2	1/1.1	99.7 (*R*)
11	(S_c,R_p,S_a)-**2a**	**5c**	CH_2Cl_2	1/1.1	99.8 (*R*)
12	(S_c,R_p,S_a)-**2a**	**5d**	CH_2Cl_2	1/1.1	99.7 (*R*)
13	(S_c,R_p,S_a)-**2a**	**5e**	CH_2Cl_2	1/1.1	99.5 (*R*)
14	(S_c,R_p,S_a)-**2a**	**5f**	CH_2Cl_2	1/1.1	99.8 (*R*)
15	(S_c,R_p,S_a)-**2a**	**5g**	CH_2Cl_2	1/1.1	99.7 (*R*)
16	(S_c,R_p,S_a)-**2a**	**5a**	CH_2Cl_2	0.1/0.11	99.8 (*R*)

[a] Reactions were performed in the presence of substrate/$Rh(COD)_2BF_4$/ligand = 100:1:1.1 under 10 bar of H_2 in the indicated solvent at room temperature for 24 h. Full conversions were achieved in all of reactions.

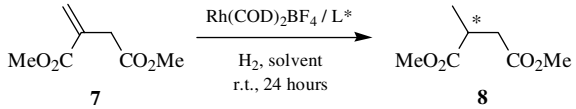
[b] Enantiomeric excesses were determined by GC using a CP-Chiralsil-L-Val capillary (0.25 mm × 30 m) column.

[c] The absolute configuration was determined by comparing the GC retention times with the GC data in the literature.

[d] The reaction was performed under an H_2 pressure of 1 bar.

7 by the use of these new H_8-BINOL-derived phosphine-phosphoramidite ligands, with the results summarized in Table 2. In all cases, full conversions were obtained. Among these ligands, (S_c,R_p,S_a)-**2a** and (S_c,R_p,S_a)-**2b** showed the highest enantioselectivity, and gave the hydrogenation product in 99.9% ee (entries 2 and 3 vs entry 1). However, when ligand (S_c,R_p,S_a)-**2c** was used in this reaction, an observable decrease in the ee value of the hydrogenation product to 94.0% was observed (entry 4). This is probably attributable to the larger steric environment due to the presence of an ethyl group in the amino moiety. When the unmatched ligand (R_c,S_p,S_a)-**2d** was used in the reaction, an expectedly low enantioselectivity was achieved (entry 5). Excellent enantioselectivity was also obtained when the reaction was performed in CH_3OH and toluene, indicating that the reaction was not solvent dependent (entries 6 and 7). The H_2 pressure had little influence in the reactivity and enantioselectivity. When the reaction was carried out under an H_2 pressure of 1 bar, the same enantioselectivity (99.9% ee) was obtained (entry 8).

Table 2. Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate **7** using H_8-BINOL-derived ligands (S_c,R_p,S_a)-**2a**–**2c** and (R_c,S_p,S_a)-**2d**[a]



Entry	Ligand	Solvent	Ee (%)[b] config.[c]
1	(S_c,R_p,S_a)-**1**	CH_2Cl_2	99.9 (*S*)
2	(S_c,R_p,S_a)-**2a**	CH_2Cl_2	99.9 (*S*)
3[b]	(S_c,R_p,S_a)-**2b**	CH_2Cl_2	99.9 (*S*)
4	(S_c,R_p,S_a)-**2c**	CH_2Cl_2	94.0 (*S*)
5	(S_c,R_p,S_a)-**2d**	CH_2Cl_2	19.0 (*S*)
6	(S_c,R_p,S_a)-**2a**	CH_3OH	99.9 (*S*)
7	(S_c,R_p,S_a)-**2a**	Toluene	99.3 (*S*)
8	(S_c,R_p,S_a)-**2a**	CH_3OH	99.9 (*S*)[d]

[a] Reactions were performed in the presence of substrate/$Rh(COD)_2BF_4$/ligand = 100:1:1.1 under 10 bar of H_2 in the indicated solvent at room temperature for 24 h. Full conversions were achieved in all of the reactions.

[b] Enantiomeric excesses were determined by GC using a γ-DEX-225 capillary (0.25 mm × 30 m) column.

[c] The absolute configuration was determined by comparing the GC retention times with GC data in the literature.

[d] The reaction was performed under an H_2 pressure of 1 bar.

2.4. Rh-catalyzed asymmetric hydrogenation of enamides 9

To explore further the utility of these Rh-complexes in the asymmetric hydrogenation, we then applied ligands **2** in the Rh-catalyzed asymmetric hydrogenation of α-enamides **9**, with the results summarized in Table 3. In contrast to higher enantioselectivities in the hydrogenation of α-dehydroamino acid esters, H_8-BINOL-derived ligands (S_c,R_p,S_a)-**2a**–**c** exhibited somewhat lower enantioselectivities than their BINOL analogue (S_c,R_p,S_a)-**1**. Thus, Rh/(S_c,R_p,S_a)-**1** hydrogenated

Table 3. Rh-catalyzed asymmetric hydrogenation of α-enamides **9** using H_8-BINOL-derived ligands (S_c,R_p,S_a)-**2a**–**c** and (R_c,S_p,S_a)-**2d**[a]

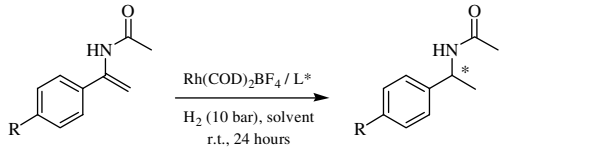
Entry	Ligand	Substrate	Solvent	Ee (%)[b] config.[c]
1	(S_c,R_p,S_a)-**1**	**9a**	CH_2Cl_2	99.6 (*R*)
2	(S_c,R_p,S_a)-**2a**	**9a**	CH_2Cl_2	96.7 (*R*)
3[b]	(S_c,R_p,S_a)-**2b**	**9a**	CH_2Cl_2	96.9 (*R*)
4	(S_c,R_p,S_a)-**2c**	**9a**	CH_2Cl_2	90.5 (*R*)
5	(R_c,S_p,S_a)-**2d**	**9a**	CH_2Cl_2	59.1 (*R*)
6	(S_c,R_p,S_a)-**2b**	**9b**	CH_2Cl_2	96.4 (*R*)
7	(S_c,R_p,S_a)-**2b**	**9c**	CH_2Cl_2	95.5 (*R*)
8	(S_c,R_p,S_a)-**2b**	**9d**	CH_2Cl_2	96.0 (*R*)
9	(S_c,R_p,S_a)-**2b**	**9e**	CH_2Cl_2	98.3 (*R*)
10	(S_c,R_p,S_a)-**2b**	**9f**	CH_2Cl_2	97.1 (*R*)
11	(S_c,R_p,S_a)-**2b**	**9g**	CH_2Cl_2	99.0 (*R*)
12	(S_c,R_p,S_a)-**2b**	**9a**	CH_3OH	95.8 (*R*)
13	(S_c,R_p,S_a)-**2b**	**9a**	Toluene	96.1 (*R*)

[a] Reactions were performed in the presence of substrate/$Rh(COD)_2BF_4$/ligand = 100:1:1.1 under 10 bar of H_2 in the indicated solvent at room temperature for 24 h. Full conversions were achieved in all of reactions.

[b] Enantiomeric excesses were determined by GC using a chiral Select 1000 capillary (0.25 mm × 30 m) column.

[c] The absolute configuration was determined by comparing the GC retention times with GC data in the literature.

N-(1-phenylethenyl)acetamide **9a** in 99.6% ee, while the corresponding H_8-BINOL-derived (S_c,R_p,S_a)-**2a** only gave the hydrogenation product in 96.7% ee (entry 2 vs entry 1). We propose that such a phenomenon probably results from the larger torsional dihedral angle in the H_8-binaphthyl moiety, which has the negative effect in the asymmetric hydrogenation of enamides. Among ligands (S_c,R_p,S_a)-**2a**–**c**, (S_c,R_p, S_a)-**2b** showed the highest enantioselective induction and gave the hydrogenation product of *N*-(1-phenylethenyl)acetamide **9a** in 96.9% ee (entries 2–4) while the unmatched ligand (R_c,S_p,S_a)-**2d** only showed low enantioselectivities of 59.1% ee (entry 5). We then selected (S_c,R_p,S_a)-**2b** for further study of this reaction. A series of substituted enamides **9b**–**g** were then tested in this reaction, and all of them were hydrogenated in high enantioselectivity. The highest ee values of 99.0% were achieved in the hydrogenation of *N*-[1-(3-methoxyphenyl)ethenyl]acetamide **9g** (entries 6–11). However, in all cases, slightly lower enantioselectivities were observed in comparison with those obtained with Rh/(S_c,R_p,S_a)-**1** reported by us recently.[4a] When the reaction was carried out in CH_3OH or toluene, a slightly lower enantioselectivities were observed (entries 12 and 13).



9a: R = H; **9b**: R =4-Me;
9c: R = 4-Cl; **9d**: R = 4-Br;
9e: R = 4-CF_3; **9f**: R = 4-OMe;
9g: R = 3-OMe

10a: R = H; **10b**: R =4-Me;
10c: R = 4-Cl; **10d**: R = 4-Br;
10e: R = 4-CF_3; **10f**: R = 4-OMe;
10g: R = 3-OMe

3. Conclusion

In conclusion, we have developed a series of new H_8-BINOL-derived ferrocenylphosphine-phosphoramidite ligands for highly efficient Rh-catalyzed asymmetric hydrogenation. In comparison to its BINOL analogues, the same or higher enantioselectivities in the hydrogenation of dimethyl itaconate and α-dehydroamino acid derivatives were observed, although, slightly lower enantioselectivities were achieved in the hydrogenation of α-enamides. Thus, by the use of ligand (S_c,R_p,S_a)-**2**, up to 99.9% ee, 99.9% ee and 99.0% ee were obtained in the hydrogenation of α-dehydroamino acid derivatives, dimethyl itaconate and α-enamides, respectively. Further investigations of other catalytic asymmetric reactions with these H_8-BINOL-derived phosphine-phosphoramidite ligands are underway and progress will be reported in due time.

4. Experimental

4.1. General

All synthetic reactions and manipulations were performed in a nitrogen or argon atmosphere using standard Schlenk techniques. Hydrogenations were carried out in a stainless steel autoclave. Solvents were reagent grade, dried and distilled before use following the standard procedures. (S_a)-H_8-BINOL,[9] (S_c,R_p)-**3a**–**c** and (R_c,S_p)-**3a**[7] were prepared according to the literature procedure. (S_a)-Chlorophosphite **4**[8] was synthesized following a modified method for the corresponding BINOL analogues. α-Dehydroamino acid esters **5**[10] and enamides **9**[11] were known compounds, which were synthesized according to the literature procedure. Dimethyl itaconate **7** was purchased from Acros. All other chemicals were obtained commercially. Optical rotations were measured on a JASCO P-1020 high sensitive polarimeter. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a BRUKER DEX 400 (400 MHz) spectrometer. Chemical shifts were determined relative to the residual solvent peaks. Enantiomeric excesses were determined by capillary GC analysis with a CP-Chiralsil-L-Val column (0.25 mm × 30 m) for **6**, γ-DEX-225 capillary column (0.25 mm × 30 m) for **8**, and a chiral Select 1000 column (0.25 mm × 30 m) for **10**.

4.2. General procedure for the synthesis of H_8-BINOL-derived ferrocenylphosphine-phosphoramidite ligands 2

A suspension of (S_a)-H_8-BINOL (1.03 g, 3.5 mmol) and 1-methyl-2-pyrrolidone (0.001 g, 0.01 mmol) in PCl_3 (7.21 g, 52.5 mmol) was warmed to 75 °C and then stirred for 5 min. After this time, a clear solution was obtained. The bulk of the excess PCl_3 was removed under reduced pressure and then the final traces were removed by azeotropic distillation with toluene (10 mL) in vacuo. A white solid corresponding to the title compound (S_a)-chlorophosphite **4** was obtained, which can be further purified by recrystallization from *n*-hexane. The resulting (S_a)-chlorophosphite **4** (358.5 mg, 1.0 mmol) was then dissolved in 4.0 mL of dried toluene, which was cooled to 0 °C. A solution of (S_c,R_p)-**3a**–**c** or (R_c,S_p)-**3a** (1.0 mmol) and Et_3N (303 mg, 3.0 mmol) in 4.0 mL of toluene was added to above solution for 30 min. The resulting mixture was left standing at room temperature overnight. The precipitate was filtered, and the solid washed with toluene (5 mL × 1). The filtrate was collected, and concentrated under reduced pressure. Adding the *n*-hexane to the filtrate gave the yellow powder **2**, which was sufficiently pure for further use. An analytic sample was obtained by column chromatography purification following recrystallization from *n*-hexane/CH_2Cl_2 to give yellow powder **2** in high yields.

4.2.1. *N*-Methyl-*N*-{(*S*)-1-[(*R*)-2-(diphenylphosphino)ferrocenyl]ethyl}-(*S*)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-bi-2-naphthyl phosphoramidite (S_c,R_p,S_a)-2a. The general procedure was followed with (S_c,R_p)-**3a** as starting material to give a foam solid (S_c,R_p,S_a)-**2a**. Yield: 76.9%. $[\alpha]_D^{25} = +161$ (*c* 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.49–1.51 (m, 2H), 1.65 (d, *J* = 3.2 Hz, 3H), 1.72–1.78 (m, 9H), 2.14–2.21 (m, 2H), 2.50–2.60 (m, 2H), 2.72–2.82 (m, 4H), 3.86 (s, 1H), 3.96 (s, 5H), 4.30 (s, 1H), 4.43 (s, 1H), 5.17–5.21 (m, 1H), 6.27–6.29 (m, 1H), 6.77–6.79 (m, 1H), 6.88–6.94 (m, 2H), 7.07–7.11 (m, 2H), 7.17–7.21 (m, 3H), 7.36–7.37 (m, 3H), 7.56–7.57 (m, 2H); ^{13}C NMR (400 MHz,

$CDCl_3$): δ 18.3, 22.1, 22.2, 27.1, 27.2, 28.6, 68.6, 69.2, 69.8, 71.3, 117.7, 118.3, 126.9, 127.2, 127.4, 128.4, 128.5, 131.7, 135.0, 135.2. ^{31}P NMR (400 MHz, $CDCl_3$): δ 24.9 (d, $J = 124$ Hz), 142.4 (d, $J = 124$ Hz). HRMS calcd for $C_{45}H_{45}FeNO_2P_2 + H$: 750.2353, found: 750.2337.

4.2.2. *N*-{(*S*)-1-[(*R*)-2-(Diphenylphosphino)ferrocenyl]-ethyl}-(*S*)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-bi-2-naphthyl phosphoramidite (S_c,R_p,S_a)-2b. The general procedure was followed with (S_c,R_p)-**3b** as starting material to give a foam solid (S_c,R_p,S_a)-**2b**. Yield: 83.4%. $[\alpha]_D^{25} = +238$ (*c* 0.3, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.51–1.53 (m, 2H), 1.65 (d, $J = 8.0$ Hz, 3H), 1.74–1.77 (m, 6H), 2.19–2.24 (m, 2H), 2.50–2.66 (m, 2H), 2.74–2.81 (m, 4H), 3.15–3.21 (m, 1H), 3.83 (s, 1H), 3.96 (s, 5H), 4.25 (s, 1H), 4.38 (s, 1H), 4.62–4.68 (m, 1H), 6.46–6.48 (m, 1H), 6.73–6.75 (m, 1H), 6.92–7.19 (m, 7H), 7.36–7.53 (m, 3H), 7.54–7.55 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 22.1, 22.3, 25.2, 27.3, 28.7, 68.0, 68.5, 69.2, 69.4, 71.1, 118.1, 118.9, 127.1, 127.5, 127.9, 128.5, 128.6, 131.9, 132.1, 134.8, 135.0, 137.0, 148.1. ^{31}P NMR (400 MHz, $CDCl_3$): δ 23.9, 144.3 (d, $J =$ 48.8 Hz). HRMS calcd for $C_{44}H_{43}FeNO_2P_2 + H$: 736.2197, found: 736.2243.

4.2.3. *N*-Ethyl-*N*-{(*S*)-1-[(*R*)-2-(diphenylphosphino)ferrocenyl]ethyl}-(*S*)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-bi-2-naphthyl phosphoramidite (S_c,R_p,S_a)-2c. The general procedure was followed with (S_c,R_p)-**3c** as starting material to give a foam solid (S_c,R_p,S_a)-**2c**. Yield: 77.1%. $[\alpha]_D^{25} = +180$ (*c* 0.3, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 0.28–0.32 (m, 3H), 1.46–1.48 (m, 2H), 1.72–1.81 (m, 9H), 2.17–2.73 (m, 10H), 3.93 (s, 5H), 4.04 (s, 1H), 4.35 (s, 1H), 4.52 (s, 1H), 5.14–5.18 (m, 1H), 6.45–6.47 (m, 1H), 6.63–6.65 (m, 1H), 6.89–6.95 (m, 2H), 7.25–7.36 (m, 8H), 7.62–7.63 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 16.6, 20.6, 22.3, 27.1, 27.2, 28.5, 28.7, 35.4, 68.0, 68.8, 69.2, 69.3, 71.4, 117.9, 118.4, 127.4, 128.2, 128.5, 132.4, 132.6, 133.0, 134.9, 135.1, 148.5. ^{31}P NMR (400 MHz, $CDCl_3$): δ 26.0 (d, $J = 102.4$ Hz), 145.2 (d, $J = 102.4$ Hz). HRMS calcd for $C_{46}H_{47}FeNO_2P_2 + H$: 764.2510, found: 764.2544.

4.2.4. *N*-Methyl-*N*-{(*R*)-1-[(*S*)-2-(diphenylphosphino)ferrocenyl]ethyl}-(*S*)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-bi-2-naphthyl phosphoramidite (R_c,S_p,S_a)-2d. The general procedure was followed with (R_c,S_p)-**3a** as starting material to give a foam solid (R_c,S_p,S_a)-**2d**. Yield: 81.3%. $[\alpha]_D^{25} = -254$ (*c* 0.3, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 1.46–1.49 (m, 2H), 1.65 (d, $J = 7.2$ Hz, 3H), 1.71–1.75 (m, 6H), 1.90–1.91 (d, 3H), 2.11–2.19 (m, 2H), 2.53–2.55 (m, 2H), 2.68–2.77 (m, 4H), 3.86 (s, 5H), 4.08 (s, 1H), 4.37–4.38 (m, 1H), 4.50 (s, 1H), 5.03–5.05 (m, 1H), 6.68–6.70 (m, 1H), 6.85–6.87 (m, 1H), 6.99–7.01 (m, 1H), 7.23–7.28 (m, 6H), 7.35–7.36 (m, 3H), 7.56–7.61 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 18.9, 22.0, 22.2, 27.1, 28.5, 68.8, 69.3, 69.8, 71.3, 118.3, 126.9, 127.5, 128.1, 128.6, 131.9, 132.1, 134.8, 135.1. ^{31}P NMR (400 MHz, $CDCl_3$): δ 26.2, 144.7. HRMS calcd for $C_{45}H_{45}FeNO_2P_2 + H$: 750.2353, found: 750.2402.

4.3. General procedure for asymmetric hydrogenation

In a nitrogen-filled glovebox, a stainless steel autoclave was charged with $Rh(COD)_2BF_4$ (4.0 mg, 1×10^{-2} mmol) and H_8-BINOL-derived ferrocenylphosphine-phosphoramidite ligands **2** (1.1×10^{-2} mmol) in 1 mL of a degassed CH_2Cl_2. After stirring for 10 min at room temperature. A substrate (10 mmol) in 1 mL of the same solvents was added to the reaction mixture, and then the hydrogenation performed at room temperature under an H_2 pressure of 10 bar for 24 h. The reaction mixture was passed through a short silica gel column to remove the catalyst. After evaporating the solvent, the crude reaction mixture was subjected to GC to determine the enantiomeric excesses and yields of hydrogenation products. Enantiomeric excesses were determined by capillary GC analysis with a CP-Chiralsil-L-Val column (0.25 mm × 30 m) for **6**, γ-DEX-225 capillary column (0.25 mm × 30 m) for **8**, and a chiral Select 1000 column (0.25 mm × 30 m) for **10**.

Acknowledgements

The authors would like to thank the National Natural Science Foundation of China (20472083) for financial support of this work.

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