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Tetrahedron
Tetrahedron 62 (2006) 12220–12226

Chiral ferrocenyl amidophosphine ligand for highly enantioselective addition of diethylzinc to *N*-diphenylphosphinoylimines

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Received 15 August 2006; revised 1 October 2006; accepted 8 October 2006
Available online 30 October 2006

Abstract—The asymmetric addition of diethylzinc to *N*-diphenylphosphinoylimines afforded *N*-diphenylphosphinoylamides with enantioselectivity of up to 90% ee in the presence of a catalytic amount of chiral ligand (*S*)-*N*-ferrocenoyl-2-[(diphenylphosphino)methyl]-pyrrolidine **13** (7 mol %) and $Cu(OTf)_2$ (15 mol %). The remarkable improvement of enantioselectivities, as compared with the same type of chiral ligand **6**, could be explained by the unique structure of ferrocenyl amidophosphine ligand combining with the reactive intermediate of this addition reaction.

1. Introduction

The efficient and enantioselective synthesis of chiral amines is of primary importance due to their extensive utilization in organic synthesis as resolving agents,[1] raw materials or intermediates in the production of some biologically active substances[2] and chiral auxiliaries for asymmetric synthesis.[2,3] The catalytic asymmetric addition of organometallic reagents to imines is one of the most efficient approaches to chiral amines.[3,4] Due to the good tolerance of various functionalities with respect to organolithiums and Grignard reagents, the enantioselective addition of dialkylzinc reagents to C=N double bonds has attracted much attention,[5] although stoichiometric amounts of ligands were usually required to obtain high yields and enantioselectivities. Recently, catalytic systems[6–12] were developed for highly enantioselective addition of diorganozincs to activated *N*-arylimines **1**,[6] *N*-acylimines **2**,[7,8] *N*-sulfonylimines **3**[9,10,11a] and *N*-phosphinoylimines **4**,[11b,12] in the presence of *a small number* of catalytic amounts of chiral catalysts or ligands (Fig. 1). More recently, we reported the enantioselective addition of diethylzinc to the *N*-diphenylphosphinoylimines **4** with up to 97% ee in the presence of 6 mol % of *N*,*P*-ferrocenyl ligands.[13] This is in great contrast to the catalytic asymmetric alkylation of carbonyl compounds with dialkyzinc reagents, which has become a very effective and general method.[14] Not surprisingly, the asymmetric addition of dialkyzincs to C=N bond in the presence of a catalytic amount of chiral ligands is at the infant stage in spite of its great potential in organic synthesis.

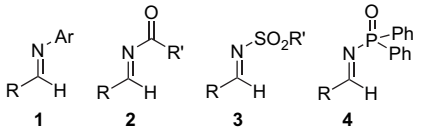

Figure 1. The structure of activated imines.

In transition-metal-mediated asymmetric catalytic additions, the nature of the starting imines plays a critical role for the success of these reactions. That is, strong substrate dependence is very obvious, especially in transition-metal-mediated catalytic asymmetric alkylation of imines either by means of stoichiometric or catalytic amounts of chiral ligands. For instance, the asymmetric addition of diethylzinc to *N*-diphenylphosphinoylimines **4** afforded the corresponding addition product with up to 94% ee in the presence of a stoichiometric amount of chiral ligand **5**,[5b] while the addition of diethylzinc to imine **3** with a different electron-withdrawing group on the nitrogen led to a racemic product under the same conditions and identical ligand **5** (Fig. 2). Similar phenomena were also observed in the asymmetric addition of diethylzinc to *N*-sulfonylimines **3** and *N*-phosphinoylimines **4** in the presence of a catalytic amount of chiral ligands **6**,[9b,12a] **7**,[11a,b] or **8**,[11a,b] respectively (Fig. 2). To the best of our knowledge, there has been no report on highly enantioselective addition of diorganozincs to the C=N bond of different types of imines, such as *N*-sulfonylimines and *N*-phosphinoylimines, by means of the same chiral ligand.

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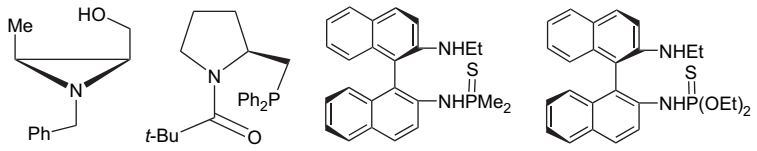
doi:10.1016/j.tet.2006.10.015



N-sulfonylimines **3**	0% ee[5b]	63% ee[9b]	90% ee[11a]	34% ee[11a]
N-phosphinoylimines **4**	94% ee[5b]	23% ee[12a]	13% ee[11b]	85% ee[11b]

Figure 2.

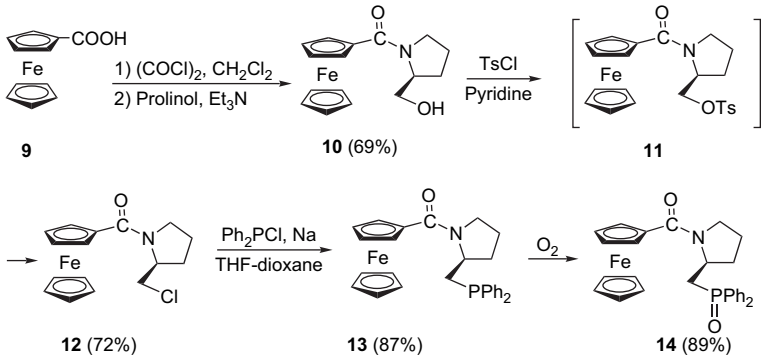
The development of new chiral ligands plays a key role for overcoming this substrate limitation because subtle changes in conformational, steric and/or electronic properties of the chiral ligands can often result in dramatic variation of the enantioselectivity and reactivity. In a previous article, we reported the synthesis of chiral ferrocenyl amidophosphine ligand **13** and its application in the copper-catalyzed enantioselective addition of diethylzinc to the C═N bond of *N*-sulfonylimines **3**.[15] In order to examine the generality of chiral ferrocenyl amidophosphine ligand towards other imine substrates, herein we report the chiral ferrocenyl amidophosphine–$Cu(OTf)_2$-catalyzed enantioselective addition of diethylzinc to *N*-diphenylphosphinoylimines **4** with enantioselectivity of up to 90% ee.

2. Results and discussion

The chiral ferrocenyl amidophosphine ligand **13** was easily synthesized from the reaction of ferrocenecarboxylic acid with L-proline. The preparation of **13** is outlined in Scheme 1. The reaction of ferrocenecarboxylic acid **9** with oxalyl chloride in CH_2Cl_2 gave ferrocenoyl chloride, which was combined with (*S*)-prolinol in the presence of Et_3N to produce (*S*)-*N*-ferrocenoyl prolinol **10** in 69% yield.[16] We planned to prepare (*S*)-*N*-ferrocenoyl prolinol tosylate **11** by the reaction of (*S*)-*N*-ferrocenoyl prolinol **10** with TsCl in the presence of pyridine, but after work-up, an unexpected chlorine-substituted product **12** was obtained in 72% yield and confirmed by HRMS, ^1H NMR, ^{13}C NMR and IR analyses. Treatment of **12** with $NaPPh_2$ in the presence of THF/dioxane afforded the chiral ferrocenyl amidophosphine ligand **13** in 84% yield according to the reported procedure.[17]

The chiral ferrocenyl amidophosphine ligand **13** was easily oxidized, due to its instability in air, to afford the corresponding (*S*)-*N*-ferrocenoyl diphenylphosphinoylmethylpyrroline **14** after being exposed to air for some hours (Scheme 1). The single crystal growth of **14** was performed in EtOAc at room temperature, and orange red crystals were obtained. The absolute configuration of chiral compound **14** was confirmed by X-ray diffraction (Fig. 3).[18] X-ray structural analysis revealed that the nitrogen atom on pyrrolidine ring has a planar structure with the sum of the three bond angles being 359.9°. This is not a trigonal-pyramidal structure because the nitrogen atom (sp^2) on pyrrolidine ring forms a conjugated system with carbonyl (CO) group and Cp ring moiety (Fig. 3). The C(11)–N(1)–C(15), C(11)–N(1)–C(12) and C(15)–N(1)–C(12) bond angles in **14** are 119.6°, 128.4° and 111.9°, respectively.[18]

At the outset of our study, we examined the effects of the ratio of $Cu(OTf)_2$ to ligand **13** on yields and enantioselectivities of the reaction of diethylzinc with *N*-diphenylphosphinoylimines derived from benzaldehyde at −5 to 0 °C, and the results are summarized in Table 1 (entries 1–8). When 4 mol % of ligand **13** equivalent to imine **15** was used, yields and enantioselectivities of the reaction increased with increase in the amounts of $Cu(OTf)_2$ (Table 1 entries 1–4). The use of 15 mol % of $Cu(OTf)_2$ gave the best yield (53%) and enantioselectivity (70% ee, Table 1 entry 4). When 7 mol % of ligand **13** was used in the presence of 15 mol % of $Cu(OTf)_2$, the enantioselectivity increased to 78% (entry 7). Increasing the amount of the catalyst did not result in higher asymmetric induction (Table 1 entries 7 and 8). So, the combination of 7 mol % of chiral ligand **13** and 15 mol % of $Cu(OTf)_2$ seemed the most suitable catalyst for the alkylation of imines. Raising the reaction



Scheme 1. Synthesis of ligand **13**.

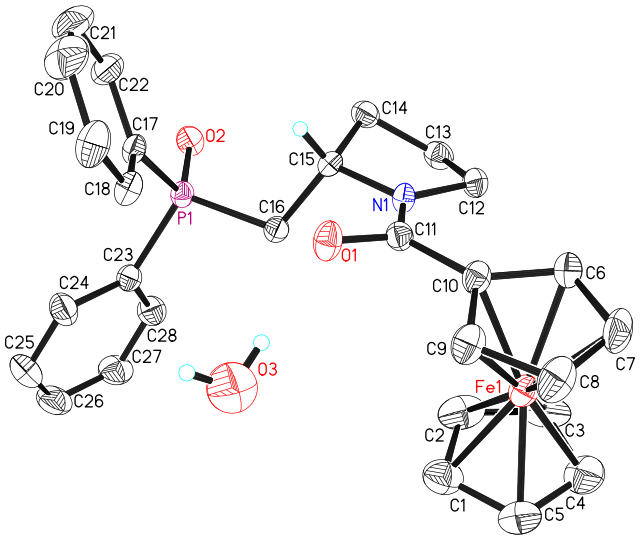


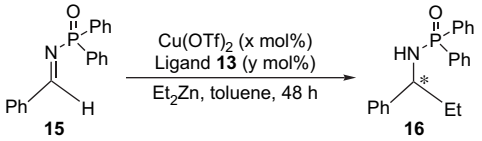
Figure 3. X-ray crystal structure of compound **14** including one H_2O molecule. Selected bond distances (Å) and angles (°) are: O(1)–C(11), 1.248(4); N(1)–C(11), 1.343(4); C(10)–C(11), 1.480(5); N(1)–C(15), 1.478(4); C(15)–C(16), 1.527(4); P(1)–C(16), 1.813(3); P(1)–O(2), 1.488(2); P(1)–C(17), 1.798(3); P(1)–C(23), 1.804(4); N(1)–C(15)–C(16), 111.1(3); O(1)–C(11)–N(1), 119.1(3); N(1)–C(11)–C(10), 122.2(3); O(1)–C(11)–C(10), 118.7(3); C(11)–N(1)–C(15), 119.6(3); C(11)–N(1)–C(12), 128.4(3); C(15)–N(1)–C(12), 111.9(3); C(15)–C(16)–P(1), 113.4(2); O(2)–P(1)–C(16), 112.79(14); O(2)–P(1)–C(17), 112.60(15); C(17)–P(1)–C(23), 108.76(16).

temperature from −5 to 0 °C to room temperature (20–25 °C) resulted in a drop in the addition selectivity from 78% to 73% (Table 1 entries 9 and 6). Addition of 4 Å molecular sieves (MS) to the reaction system did not benefit the enantioselectivities and the yields of the products (Table 1, entries 10 vs 6). In contrast, Gong and other groups have reported that the use of 4 Å MS very obviously affects the reaction product both in terms of yields and enantiomeric excesses.[19] Addition of CuI (4 mg) did not affect the chemical yield and enantioselectivity of the reaction (Table 1, entry 11).

Recently, Charette and Boezio reported the same type of chiral ligands **6** for the addition of diethylzinc to *N*-diphenylphosphinoylimine **15** with low enantioselectivity of 23% ee.[12a] Comparison of our results (up to 78% ee) with those of Boezio and Charette demonstrates that the replacement of the pivaloyl group on the pyrrolidine nitrogen atom by a ferrocenoyl unit results in a remarkable improvement in the enantioselectivity. These results also suggest that the hindrance of rigid, bulky ferrocenyl unit and the electron-donating conjugated effect of the Cp ring possessing a partial negative charge play an important role in the enantioselection in the addition of diethylzinc to *N*-diphenylphosphinoylimine. The high enantioselectivity by **13** is understandable: (a) because the nitrogen atom (sp^2) on pyrrolidine ring forms an extended conjugated system with carbonyl (CO) group and Cp ring moiety (Fig. 3), the rotation about the N–CO and Cp–CO sigma bonds is retarded and the structure of ligand **13** is also made more rigid; (b) steric repulsion between the rigid, bulky ferrocenyl unit and Ph_2P group makes the carbonyl oxygen atom point towards Ph_2P group (Fig. 3), which is helpful to form a chelate with copper or zinc; (c) the electron-donating conjugated effect of the Cp ring with a partial negative charge strengthens further the coordinating ability of carbonyl oxygen atom and increases the possibility of formation of a zinc cuprate–oxygen phosphine complex,[9b] which is the reactive intermediate of 1,4-conjugate addition;[20] (d) the rigid, bulky ferrocenyl substituent effectively shields one face of the chelate, which may prohibit the approach of *N*-diphenylphosphinoylimine **15** from this face and is responsible for the high enantioselectivity.

Chartte et al.[12d] reported that the level of asymmetric induction was greatly dependent upon the order of addition of reagents in the Cu(II)–Me-DuPHOS-catalyzed asymmetric ethylation of *N*-diphenylphosphinoylimine **15**. We also investigated the effect of the order of addition of reagents on enantioselectivity (Table 2). A slight improvement in product ee was observed when $Cu(OTf)_2$ was mixed with

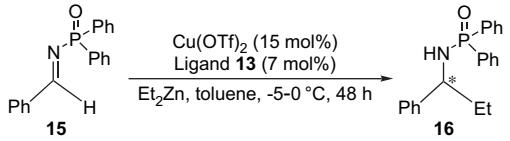
Table 1. Optimization of the reaction conditions of the enantioselective ethylation of imines[a]



Entry	Ligand (%)	$Cu(OTf)_2$ (%)	Temp (°C)	Yield (%)[b]	ee (%)[c]	Config.[d]
1	4	3	−5 to 0	30	60	*R*
2	4	6	−5 to 0	45	67	*R*
3	4	10	−5 to 0	52	69	*R*
4	4	15	−5 to 0	53	70	*R*
5	4	20	−5 to 0	51	70	*R*
6	7	15	−5 to 0	60	78	*R*
7	10	15	−5 to 0	60	78	*R*
8	15	15	−5 to 0	60	78	*R*
9	7	15	20 to 25	54	73	*R*
10[e]	7	15	−5 to 0	55	76	*R*
11	7	15	−5 to 0	61	78	*R*

[a] All reactions were carried out in toluene with the 0.3 mmol of imine and the order of addition of the reagents was $Cu(OTf)_2$–L-imine–Et_2Zn.
[b] The isolated yield.
[c] The ee was determined by HPLC with Daicel Chiralcel OD: 2-propanol/hexane (10/90), 0.5 mL/min: t_R=12.9 min, t_S=16.6 min.
[d] The absolute configuration was assigned as *R* by comparing retention time of HPLC with the literature value.[12,13]
[e] MS (4 Å) was added.

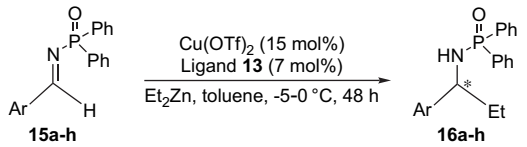
Table 2. The effect of the order of addition

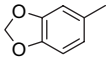


Entry	Method[a]	Yield (%)[b]	ee (%)[c]	Config.[d]
1	A	60	78	*R*
2	B	35	79	*R*

[a] Method A: the order of addition of the reagents was $Cu(OTf)_2$–L-imine–Et_2Zn. The mole ratio of imine/Et_2Zn was 1/3. Method B: the order of addition of the reagents was $Cu(OTf)_2$-Et_2Zn-L-imine. The mole ratio of imine/Et_2Zn was 1/3.
[b] The isolated yield.
[c] The ee was determined by HPLC with Daicel Chiralcel OD: 2-propanol/hexane (10/90), 0.5 mL/min: t_R=12.9 min, t_S=16.6 min.
[d] The absolute configuration was assigned as *R* by comparing retention time of HPLC with the literature value.[12,13]

Table 3. The enantioselective addition of diethylzinc to various *N*-diphenylphosphinoylimines **15**[a]



Entry	Ar	Imine	Yield (%)[b]	ee (%)[c]	Config.[d]
1	C_6H_5	**15a**	60	78	*R*
2	2-$MeOC_6H_4$	**15b**	64	78	*R*
3	4-$MeOC_6H_4$	**15c**	67	84	*R*
4		**15d**	72	78	*R*
5	4-MeC_6H_4	**15e**	78	83	*R*
6	2-ClC_6H_4	**15f**	69	90	*R*
7	4-ClC_6H_4	**15g**	65	73	*R*
8	2-Furyl	**15h**	76	85	*R*

[a] All reactions were carried out in toluene with 0.3 mmol and the order of addition of the reagents was $Cu(OTf)_2$–L-imine–Et_2Zn.
[b] The isolated yield.
[c] Determined by chiral HPLC with a Chiralcel OD or a Chiralpak AD column.[12,13]
[d] Absolute configuration assigned by comparison with known elution order from a Chiralcel OD column and a Chiralpak AD column according to the literature.[12,13]

Et_2Zn prior to the addition of ligand **13**, however, this resulted in a great decrease in chemical yield (Table 2, entry 2).

These reaction conditions were then tested on a variety of other *N*-phosphinoylimines derived from different arylaldehydes in this catalytic system, the results are presented in Table 3. As can be seen from Table 3, good to excellent enantioselectivities (73–90% ee) could be achieved for various aromatic *N*-diphenylphosphinoylimines containing *ortho*-, *para*- or *meta*-substituents on the benzene ring (Table 3, entries 2–7). The presence of electron-donating or electron-withdrawing substituents on the aromatic ring is also compatible with these reaction conditions. The best asymmetric induction (as high as 90% ee) was found by using an imine bearing a 2-ClC_6H_4 group as the substrate in the presence of chiral ligand **13** (Table 3, entry 6). It is advantageous that imine derived from furfural can be converted to an adduct in 76% yield and 85% ee (Table 3, entry 8), because the product is a useful intermediate for the synthesis of biologically active compounds. Until now, chiral ligand **13** is only one example that can afford highly enantioselective addition of diethylzinc to the C=N bond of the different types of imines such as *N*-sulfonylimines[15] and *N*-phosphinoylimines.

3. Conclusion

In conclusion, we have reported copper-catalyzed highly enantioselective addition of diethylzinc to *N*-phosphinoylimines in the presence of catalytic amount of chiral ferrocenyl O,P-ligand **13**. The X-ray structure analysis of derivative **14** of **13** reveals that the nitrogen atom on pyrrolidine ring forms an extended conjugated system with carbonyl (CO) group and Cp ring moiety. The X-ray structure of **14** in combination with proposed reactive intermediate during addition reaction explained that the introduction of a ferrocenyl group into the chiral amidophosphine ligands results in a remarkable improvement in the enantioselectivity, as compared with the same type of chiral ligand **6**. To the best of our knowledge, this is the first case of the highly enantioselective addition of diorganozincs to the C=N bond of the different types of imines such as *N*-sulfonylimines and *N*-phosphinoylimines by means of the identical chiral ligand. Further application of chiral O,P-ligand **13** for asymmetric synthesis is under investigation in our laboratory.

4. Experimental

4.1. General

Melting points were determined using YRT-3 melting point apparatus, and were uncorrected. Optical rotations were measured with Perkin Elmer, model 341 Polarimeter at 20 °C in $CHCl_3$. The ee value was determined by HPLC using a chiral column with hexane/2-propanol (ratio as indicated) as the eluent. The chiral HPLC methods were calibrated with the corresponding racemic mixtures. The chromatographic system consisted of a JASCO model PU-1580 intelligent HPLC pump and a JASCO model UV-1575 intelligent UV–vis detector (254 nm). The injection loop had a 20 μL capacity. The column used was a Chiralcel OD or a Chiralpak AD (250×4.6 mm) from Daicel Chemical Ind., Ltd (Japan). The column was operated at ambient temperature. NMR spectra (^1H and ^{13}C) were performed on a Bruker DPX 400 (400 MHz) spectrometer using solutions in $CDCl_3$ (referenced internally to Me_4Si); *J* values are given in hertz. IR spectra were determined on a Therme Nicolet IR 200 spectrophotometer. TLC was performed on dry silica gel plates developed with hexane/ethyl acetate. Mass spectra were obtained using a Waters a-Tof micro™ instrument with an electrospray ionization source (ESIMS). All the ESIMS spectra were performed using MeOH as the solvent.

4.2. Reagents and solvents

Except for diethylzinc purchased from Aldrich and $Cu(OTf)_2$ from Alfa Aesar, all other reagents were purchased in China. Toluene was pre-dried over calcium chloride, and then distilled from sodium before use. Ether was distilled from sodium benzophenone ketyl. All other reagents are commercially available and were used as received. The imines **15a**,[21] **15b**,[22] **15c**,[23] **15d**,[21] **15e**,[12] **15f**,[21] **15g**[12] and **15h**[12] are known compounds and prepared according to the reported procedure.[12,19–21]

4.3. Synthesis of (*S*)-ferrocenoyl prolinol 10

To a solution of ferrocenecarboxylic acid **9** (2.3 g, 10 mmol) in 30 mL of freshly distilled dichloromethane under nitrogen, oxylyl chloride (1.76 mL, 20 mmol) was slowly added via syringe. Gas evolution was accompanied by the formation of a dark red homogeneous solution after 30 min. The reaction mixture was stirred for an additional 30 min, followed by removal of the solvent in vacuo. The resultant crude ferrocenoyl chloride was dissolved in dichloromethane (20 mL) and added slowly to a solution of pyrrolidinol (1.2 g, 12 mmol) and triethylamine (2.7 mL, 20 mmol) in

30 mL of dried dichloromethane at 0 °C under nitrogen. The resulting mixture was allowed to stir at room temperature overnight and then quenched with 40 mL of distilled water. The organic phase was separated, and the aqueous phase was extracted three times with dichloromethane (3×20 mL). After the combined organic phases were dried over Na_2SO_4, the solvent was removed in vacuo. The residue was purified by column chromatography on a silica gel column (eluted with dichloromethane/methanol (93/7)) to afford **10** (2.16 g, 69%) as an orange red solid. Mp 169.1–170.5 °C; $[\alpha]_D^{20}$ 48.6 (*c* 0.4, in CH_3OH); ^1H NMR (400 MHz, $CDCl_3$): δ 1.25–1.59 (m, 1H, $CH_2CH\mathit{H}$), 1.80–1.87 (m, 1H, $CH_2C\mathit{H}H$), 1.95–2.01 (m, 1H, $C\mathit{H}HCH_2$), 2.10–2.14 (m, 1H, $CH\mathit{H}CH_2$), 3.57–3.59 (m, 1H, NC*H*H), 3.61–3.63 (m, 1H, NCH*H*), 3.75–3.80 (m, 1H, NCH), 3.97–4.02 (m, 1H, HO*CH*H), 4.42–4.44 (m, 1H, HO*C*H*H*), 4.23–5.40 (m, 9H, FcH), 5.40 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.3, 28.2, 29.7, 49.7, 62.3, 68.3, 69.4, 69.8, 70.2, 70.5, 71.8, 172.8; IR (KBr pellets): 3335, 2876, 1583, 1464, 1410, 1226, 1099, 1058, 1032, 1006, 819 cm^{-1}; HRMS (ESI): calcd for $C_{16}H_{20}FeNO_2$: 314.0843 (M^++H), found: 314.0844.

4.4. Synthesis of (*S*)-2-(chloromethyl)pyrrolidinocarbonylferrocene 12

To a solution of **10** (666 mg, 2.12 mmol), dry pyridine (2.5 mL) and dimethylaminopyridine (26 mg, 0.21 mmol) in a mixture of dichloromethane (15 mL), TsCl (478 mg, 2.5 mmol) was added slowly at −5 to 0 °C under nitrogen. After stirring for 10 h at the same temperature and 14 h at room temperature, 1 N HCl (10 mL) was added and the aqueous phase was extracted with dichloromethane (3×10 mL). The combined organic phases were dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by preparative TLC (ethyl acetate/petroleum ether (1/2) as developing solvent) to yield the product **12** as an orange red solid (539 mg, 72%). Mp 95.2–96.2 °C; $[\alpha]_D^{20}$ −76.6 (*c* 0.4, in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.83–1.85 (m, 1H, $CH\mathit{H}CH_2$), 2.04–2.09 (m, 3H, $C\mathit{H}HCH_2$, $CH_2C\mathit{H}_2$), 3.59–3.65 (m, 1H, NC*H*H), 3.77–3.80 (m, 1H, ClC*H*H), 3.87–3.89 (m, 1H, ClCH*H*), 3.96–4.01 (m, 1H, NCH*H*), 4.49–4.50 (m, 1H, NCH), 4.21–4.80 (m, 9H, FcH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.21, 27.67, 45.61, 49.61, 58.48, 69.29, 69.77, 70.11, 70.25, 71.70, 169.86; IR (KBr pellets): 3101, 2978, 1607, 1461, 1394, 1160, 1102, 1052, 1000, 816 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{19}ClFeNO$: 354.0504 (M^++H), found: 354.0505.

4.5. Synthesis of (*S*)-[2-(diphenylphosphino)methyl]-pyrrolidinocarbonylferrocene 13

In a dried Schlenk tube, small pieces of sodium (184 mg, 8.0 mmol) were added at 0 °C to a solution of Ph_2PCl (0.36 mL, 1.9 mmol, 95% purity) in dried 1,4-dioxane (2 mL) and stirred under reflux for 6 h under a nitrogen atmosphere. The mixture was cooled to 0 °C and a solution of the compound **12** (353 mg, 1.0 mmol) in THF (2 mL) was then added at 0 °C. After stirring for 40 min, the mixture was filtered through Celite and the Celite was washed by THF four times to afford a red filtrate. Concentration and silica gel column chromatography (eluted with ethyl acetate/petroleum ether, (1/4)) gave **13** (418 mg, 87%) as an orange red solid. Mp 114.8–116.0 °C; $[\alpha]_D^{20}$ −38.6 (*c* 0.8, in $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 1.82–1.84 (m, 1H, $CH_2CH\mathit{H}$), 1.85–2.10 (m, 4H, $CH_2C\mathit{H}H$, $C\mathit{H}_2CH_2$, NC*H*), 3.22–3.24 (m, 1H, PC*H*H), 3.56–3.61 (m, 1H, PCH*H*), 3.95–3.97 (m, 1H, NC*H*H), 4.31–4.33 (m, 1H, NCH*H*), 4.18–4.72 (m, 9H, FcH), 7.26–7.57 (m, 10H, 2×PhH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.51, 29.7, 30.7, 32.5, 48.8, 56.3, 56.5, 65.9, 69.5, 69.9, 70.1, 71.1, 128.4, 128.5, 128.7, 128.8, 129.0, 132.6, 132.8, 133.0, 133.2, 136.4, 138.6, 169.4; IR (KBr pellets): 3098, 3053, 2921, 1601, 1462, 1404, 1159, 1099, 823, 747 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{28}FeNOP$: 481.1258 (M^++H), found: 481.1286.

4.6. Synthesis of (*S*)-(−)-*N*-ferrocenoyl-2-[(diphenylphosphinyl)methyl]-pyrrolidine 14

Powdered compound **13** (100 mg, 0.21 mmol) was placed in a glass vessel, and then exposed to air at room temperature, and often stirred with a glass stick. After about 48 h (monitored by thin layer chromatography), purification of the resulting solid by preparative silica gel TLC plate (CH_2Cl_2/acetone=3/1) afforded compound **14** (92 mg) in 89% yield. Compound **14** was recrystallized with EtOAc to afford orange red crystal. Mp 129.4–130.2 °C; $[\alpha]_D^{20}$ +6 (*c* 0.3 in CH_3OH); ^1H NMR (400 MHz, $CDCl_3$): δ 1.8–2.32 (m, 6H, $C\mathit{H}_2C\mathit{H}_2$, $PC\mathit{H}_2$), 3.51–3.60 (m, 1H, NC*H*H), 3.85–3.91 (m, 1H, NCH*H*), 4.30–4.37 (m, 1H, NCH), 4.19–4.74 (m, 9H, FcH), 7.26–8.08 (m, 10H, 2×PhH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.46, 30.42, 33.30, 48.52, 54.83, 69.53, 69.88, 70.06, 70.35, 70.82, 128.51, 128.63, 128.95, 130.29, 130.38, 131.21, 131.31, 131.50, 132.35, 169.75; IR (KBr pellets): 3098, 3053, 2921, 1601, 1462, 1404, 1159, 1115, 1099, 1028, 823 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{29}FeNO_2P$: 498.1285 (M^++H), found: 498.1264.

4.7. General procedure for the asymmetric addition of diethylzinc to *N*-diphenylphosphinoylimines

A solution of $Cu(OTf)_2$ (16.3 mg, 0.045 mmol) and ligand **13** (10.1 mg, 0.021 mmol) in dry toluene (3 mL) was stirred for 1 h at room temperature under a nitrogen atmosphere. *N*-(Diphenylphosphinoyl)imine **15** (0.3 mmol) was added, and the solution was stirred for an additional 10 min; then diethylzinc (1 mol/L in *n*-hexane, 0.9 mL) was added dropwise at 0 °C. The resulting mixture was stirred for 48 h at −5 to 0 °C, and then saturated aqueous NH_4Cl (10 mL) was added. After extraction with CH_2Cl_2 (3×15 mL), the combined organic layers were dried over anhydrous Na_2SO_4. The residue obtained upon removal of volatiles under reduced pressure was purified by the preparative silica gel TLC plate (ethyl acetate) to afford the addition product *N*-(1-arylpropyl)-*P*,*P*-diphenylphosphinic amide **16**.

4.7.1. (*R*)-*N*-(1-Phenylpropyl)-*P*,*P*-diphenylphosphinoylamide 16a (entry 1 in Table 3). White solid. Mp 117.5–118.5 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 0.79 (t, 3H, *J*=7.4 Hz, $CH_2C\mathit{H}_3$), 1.80–1.89 (m, 1H, $C\mathit{H}HCH_3$), 1.98–2.10 (m, 1H, $CH\mathit{H}CH_3$), 3.23–3.27 (m, 1H, NH), 4.06–4.14 (m, 1H, C*H*NH), 7.14–7.43 (m, 11H, ArH), 7.76–7.87 (m, 4H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.6 (CH_3), 32.5 (CH_2), 57.2 (CHNH), 126.6, 127.1, 128.2,

128.4, 128.4 (Ar), 128.5, 128.5, 131.7, 131.7, 131.8, 131.9, 132.6, 132.7, 143.5 (Ar); IR (KBr pellets): 3141, 1457, 1435, 1190, 1105, 905, 752 cm^{-1}. Enantiomeric excess: 78%, Chiralcel OD, hexane/*i*-PrOH=90/10, 0.5 mL/min, t_R=12.9 min, t_S=16.6 min.

4.7.2. (*R*)-*N*-[1-(2-Methoxylphenyl)propyl]-*P*,*P*-diphenylphosphinoylamide 16b (entry 2 in Table 3). White solid. Mp 118–119.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.77 (t, 3H, J=7.4 Hz, CH_3CH$_2$), 1.87–2.03 (m, 2H, CH$_2$CH$_3$), 3.73 (s, 3H, CH_3O), 3.95–4.00 (m, 1H, NH), 4.13–4.17 (m, CHN), 6.83–6.94 (m, 3H, ArH), 7.21–7.44 (m, 7H, ArH), 7.71–7.84 (m, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.2 (CH_3), 31.1 (CH_2), 55.2 (CH_3O), 55.4 (CHNH), 111.0, 120.6, 128.1, 128.2, 128.3, 128.4, 128.6, 131.3, 131.5, 131.6, 131.8, 131.9, 132.6, 132.7, 157.0 (Ar); IR (KBr pellets): 3185, 3058, 1602, 1494, 1463, 1243, 1192, 1125, 910, 752 cm^{-1}. Enantiomeric excess: 78%, Chiralpak AD, hexane/*i*-PrOH=90/10, 1.0 mL/min, t_R=22.2 min, t_S=27.7 min.

4.7.3. (*R*)-*N*-[1-(4-Methoxylphenyl)propyl]-*P*,*P*-diphenylphosphinoylamide 16c (entry 3 in Table 3). White solid. Mp 130–131 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.76 (t, J=7.3 Hz, 3H, CH$_2$CH_3) 1.86–1.74 (m, 1H, CHHCH$_3$), 2.06–1.94 (m, 1H, CHHCH$_3$), 3.20–3.21 (m, 1H, NH), 3.79 (s, 3H, OCH_3), 4.04–4.06 (m, 1H, CHN), 6.82–7.08 (m, 4H, ArH), 7.33–7.50 (m, 6H, ArH), 7.76–7.86 (m, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.5 (CH_3), 32.3 (CH_2), 55.1 (CH_3O), 56.5 (CHN), 113.6, 127.5, 128.1, 128.3, 131.5, 131.6, 132.0, 132.0, 132.1, 133.2, 135.5, 158.4 (Ar); IR (KBr pellets): 3146, 1513, 1452, 1438, 1247, 1194, 1175, 752 cm^{-1}. Enantiomeric excess: 84%, Chiralpak AD, hexane/*i*-PrOH=80/20, 1.0 mL/min, t_R=11.0 min, t_S=13.5 min.

4.7.4. (*R*)-*N*-[1-Benzo[1,3]dioxol-5-yl-propyl]-*P*,*P*-diphenylphosphinoylamide 16d (entry 4 in Table 3). White solid. Mp 115.2–116.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.78 (t, 3H, J=7.2 Hz, CH_3CH$_2$), 1.74–1.79 (m, 1H, CHHCH$_3$), 1.95–1.99 (m, 1H, CHHCH$_3$), 3.24 (br s, 1H, NH), 4.00–4.03 (m, 1H, CHN), 5.93 (s, 2H, OCH_2O), 6.56–6.70 (m, 3H, ArH), 7.27–7.50 (m, 6H, ArH); 7.74–7.88 (m, 4H ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.6 (CH_3), 32.5 (CH_2), 57.1 (CHNH), 100.9, 106.8, 108.0, 120.1, 128.3, 128.4, 131.7, 131.8, 131.9, 132.5, 132.6, 137.6, 146.5, 147.8 (Ar); IR (KBr pellets): 3148, 1437, 1244, 1178, 1107, 1041, 931, 723 cm^{-1}. Enantiomeric excess: 78%, Chiralpak AD, hexane/*i*-PrOH=80/20, 1.0 mL/min, t_R=9.7 min, t_S=15.0 min.

4.7.5. (*R*)-*N*-[1-(4-Methylphenyl)propyl]-*P*,*P*-diphenylphosphinoylamide 16e (entry 5 in Table 3). White solid. Mp 124.5–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.78 (t, J=7.6 Hz, 3H, CH$_2$CH_3) 1.78–1.85 (m, 1H, CHHCH$_3$), 1.96–2.32 (m, 1H, CHHCH$_3$), 2.33 (s, 3H, CH_3), 3.26 (br s, 1H, NH), 4.01–4.05 (m, 1H, CHN), 7.04–7.11 (m, 4H, ArH), 7.32–7.45 (m, 6H, ArH), 7.74–7.86 (m, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.6 (CH_3), 32.3 (CH_2), 55.1 (CH_3Ar), 56.5 (CHNH), 126.5, 128.3, 129.1, 131.6, 131.7, 131.9, 132.6, 133.2, 136.6, 140.6 (Ar); IR (KBr pellets): 3135, 1452, 1435, 1178, 1089, 1060, 931, 722 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{24}NOP$: 348.1517 (M^++H), found: 348.1519. Enantiomeric excess: 83%, Chiralpak AD, hexane/*i*-PrOH=80/20, 1.0 mL/min, t_R=8.7 min, t_S=10.2 min.

4.7.6. (*R*)-*N*-[1-(2-Chlorophenyl)propyl]-*P*,*P*-diphenylphosphinoylamide 16f (entry 6 in Table 3). White solid. Mp 140–141 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (t, J=7.3 Hz, 3H, CH$_2$CH_3) 1.80–2.01 (m, 2H, CH_2CH$_3$), 3.59–3.61 (m, 1H, NH), 4.48–4.50 (m, 1H, CHN), 7.11–7.34 (m, 6H, ArH), 7.36–7.53 (m, 4H, ArH), 7.67–7.76 (m, 2H, ArH), 7.80–7.90 (m, 2H, ArH); IR (KBr pellets): 3059, 1437, 1185, 1124, 1111, 908, 750 cm^{-1}. Enantiomeric excess: 90%, Chiralpak AD, hexane/*i*-PrOH=80/20, 0.7 mL/min, t_R=14.3 min, t_S=19.1 min.

4.7.7. (*R*)-*N*-[1-(4-Chlorophenyl)propyl]-*P*,*P*-diphenylphosphinoylamide 16g (entry 7 in Table 3). White solid. Mp 154.5–155.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.79 (t, J=7.3 Hz, 3H, CH$_2$CH_3) 1.73–1.86 (m, 1H, CHHCH$_3$), 1.92–2.04 (m, 1H, CHHCH$_3$), 3.31 (br s, 1H, NH), 4.05–4.10 (m, 1H, CHN), 7.08 (d, J=8.4 Hz, 2H, ArH), 7.23–7.44 (m, 8H, ArH), 7.70–7.73 (m, 2H, ArH), 7.83–7.86 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.5 (CH_3), 32.4 (CH_2), 56.6 (CHNH), 128.0 (Ar), 128.3, 128.4, 128.5, 128.6, 131.8, 131.9, 132.5, 132.6, 132.8, 142.1 (Ar); HRMS (ESI) calcd for $C_{21}H_{21}ClNOP$: 368.0971 (M^+−H), found: 368.0974. Enantiomeric excess: 73%, Chiralpak AD, hexane/*i*-PrOH=80/20, 1.0 mL/min, t_R=7.2 min, t_S=10.9 min.

4.7.8. (*R*)-*N*-[1-(2-Furyl)propyl]-*P*,*P*-diphenylphosphinoylamide 16h (entry 8 in Table 3). White solid. Mp 96–97.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.82 (t, J=7.4 Hz, 3H, CH$_2$CH_3), 1.83–2.05 (m, 2H, CH_2CH$_3$), 3.30 (br s, 1H, NH), 4.15–4.17 (m, 1H, CHN), 6.04 (d, J=3.2 Hz, 1H), 6.23 (dd, J=3.2, 1.8 Hz, 1H), 7.31 (dd, J=1.8, 0.8 Hz, 1H), 7.34–7.48 (m, 6H, ArH), 7.88 (m, 4H, ArH); IR (KBr pellets): 3182, 1437, 1176, 1124, 1009, 893, 724 cm^{-1}. Enantiomeric excess: 85%, Chiralpak AD, hexane/*i*-PrOH=95/5, 1.0 mL/min, t_R=37.8 min, t_S=41.8 min.

4.8. X-ray crystallographic study

An orange red crystal of approximate dimensions 0.20×0.18×0.18 mm was mounted on a glass fibre. Crystallographic data for **14** were measured on a Rigaku RAXIS-IV imaging plate area detector. The data were collected at 291(2) K using graphite monochromated Mo Kα (λ=0.71073 Å), 2.05°<θ<27.52°. The structures were solved by a direct method and expanded by using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. All calculations were performed using the teXsan crystallographic software package. Crystal data for **14**: monoclinic C_2: a=23.329 [5] Å, α=90°, b=8.1310 [16] Å, β=120.96 [3]°, c=14.925 [3] Å, γ=90°; V=2427.8 (8) Å^3; formula unit $C_{28}H_{29}FeNO_2P$ with Z=4; D_{calcd}=1.385 g cm^{-3}; F (000)=1060; μ(Mo Kα)=0.715 mm^{-1}. Full-matrix least-squares refinement on F^2 based on 3858 independent reflections (R_{int}=0.0233) converged with 303 parameters. Final R indices [I>2 sigma (I)]: R_1=0.0385, wR_2=0.0821; R indices (all data): R_1=0.0385, wR_2=0.0821; GoF=1.052.

Acknowledgements

We are grateful to the National Natural Sciences Foundation of China (NNSFC: 20172047), the Ministry of Education of China, and the Education commission of Henan Province for the financial supports.

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