Ferrocene-Based Chiral Phosphine-Triazines: A New Family of Highly Efficient P,N Ligands for Asymmetric Catalysis

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Abstract: The presence of the additional heterocyclic nitrogen atoms in chiral P,N ligands has an important influence on the asymmetric catalysis, and a clear trend was observed in the present research that the enantioselectivity and reactivity were significantly increased by raising the number of heterocyclic nitrogen atoms in these P,N ligands. Through finely tuning the number of heterocyclic nitrogen atoms, a new family of ferrocene-based chiral phosphine-triazine ligands with three heterocyclic nitrogen atoms has been developed and successfully applied in Pd-catalyzed asymmetric allylic substitution. Up to 99% ee with 99% yield of allylic alkylation products and 94% ee of allylic amination products have been obtained by the use of ligand (R_c,S_p)-**1f** with a 4,6-diphenoxy-1,3,5-triazine moiety.

Keywords: allylic alkylation; asymmetric catalysis; palladium; phosphine-triazine ligands; P,N ligands

Introduction

In the past decade, much interest has been devoted to the development of highly efficient chiral P,N ligands for asymmetric catalysis, and a great number of chiral P,N ligands have been synthesized and successfully applied in a variety of catalytic asymmetric reactions with impressive enantioselectivity.[1] The most important and widely used P,N ligands so far are those bearing a phosphorus and a heterocyclic N atom as their donor atoms, e.g., PHOX,[2] QUINAP[3] and some ferrocene-based ligands.[4] To the best of our knowledge, however, just a limited example of chiral P,N ligands with two or more heterocyclic N donors corresponding to one P donor have been reported to exhibit high enantioselectivity in catalytic asymmetric reactions[5] and, with the exception of a quite recent work of Guiry et al.,[6] no reports have been focused on the investigation of the influence of additional heterocyclic N atoms on the catalytic activity and selectivity. In our recent research,[7] we have reported that ferrocene-based phosphine-imine ligands with an additional pyridine N donor exhibited extremely different activity in Pd-catalyzed asymmetric allylic alkylation upon changing the position of the N atom in the pyridine moiety. Thus, the Pd complex derived from the ligand with a 3-pyridine N atom turned out to be an efficient catalyst, affording an allylic alkylation product with an ee value of up to 98%, while the Pd complex derived from the ligand with a 2-pyridine N atom surprisingly showed no activity (Figure 1).

This interesting result suggested that the presence of an additional heterocyclic N atom in an appropriate position could dramatically promote the enantioselective induction of P,N ligands. Following these observations, we therefore wanted to know what would happen when the number of heterocyclic N atoms in the appropriate position increased, and whether it would be a new

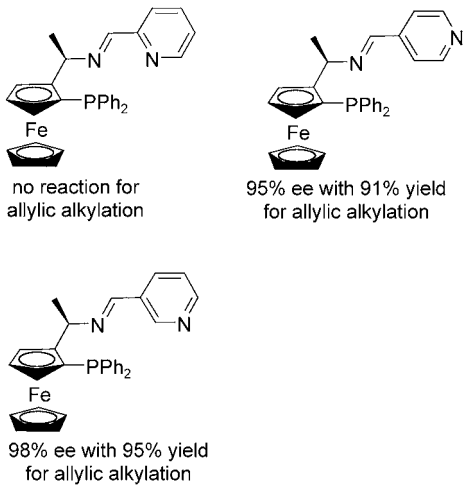

Figure 1. Influence of the pyridine N atom on Pd-catalyzed asymmetric allylic alkylation.

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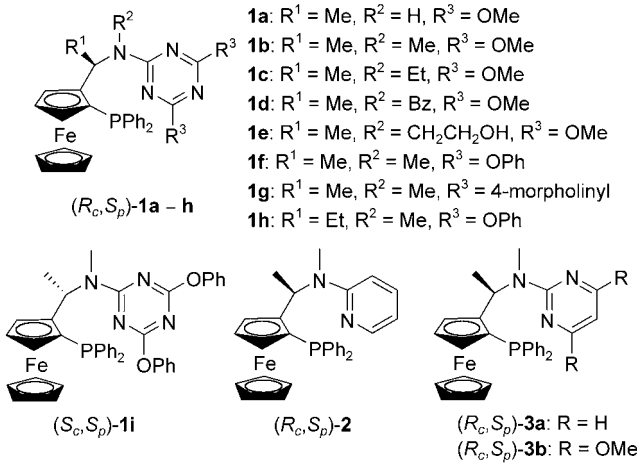
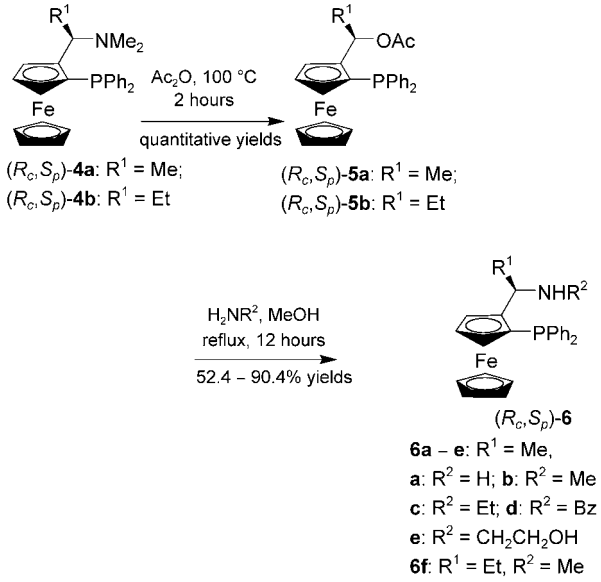


Figure 2. Structures of ferrocenylphosphine-heterocycle ligands **1**, **2** and **3**.



Scheme 1. Synthesis of ferrocenylphosphine-amines (R_c,S_p)-**6a** – **f**.

strategy for developing efficient ligands by tuning the number of heterocyclic N atoms in the appropriate positions. As a result, herein we describe the first example of the easily accessible P,N ligands **1** (Figure 2), which contain a planar chiral ferrocenyl backbone and a triazine unit, as a highly efficient chiral ligands for Pd-catalyzed asymmetric allylic substitutions. By comparing the catalytic activity of P,N ligands **1**, **2** and **3** with different numbers of heterocyclic N atoms, the role of the additional heterocyclic N atoms in the Pd-catalyzed asymmetric allylic alkylation was also investigated.

Results and Discussion

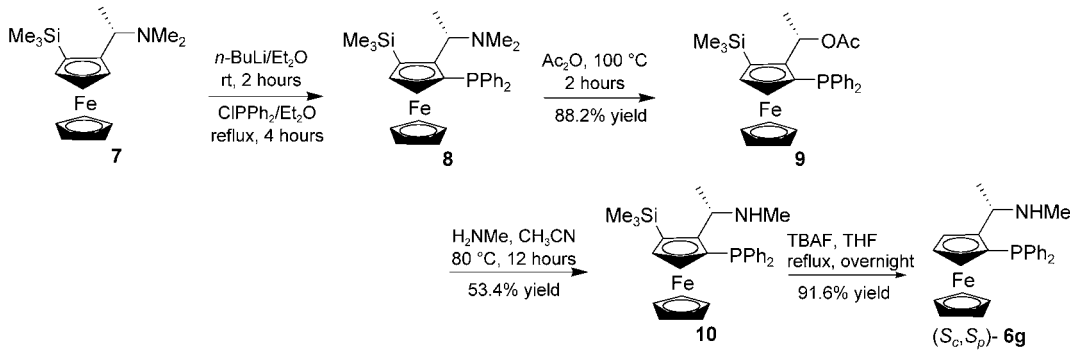
Synthesis of Ferrocene-Based Phosphine-Heterocycle Ligands 1, 2 and 3

The P,N ligands **1**, **2** and **3** can be easily prepared from (R_c,S_p)-PPFA **4** through a three-step transformation. The initial step involved the synthesis of the key intermediate amines (R_c,S_p)-**6a**–**f**, which were prepared from the corresponding dimethylamino species **4** through the intermediacy of actetate **5** according to the procedure reported by our and other groups as outlined in Scheme 1.[8,9] By the reaction of actetate **5** with a variety of amines in refluxing methanol, primary and secondary amines (R_c,S_p)-**6a**–**f** were prepared in 52.4–90.4% yields. In contrast to the distereomers (R_c,S_p)-**6a**–**f**, however, the synthesis of (S_c,S_p)-**6g** is somewhat more difficult.[10] Through the initial introduction of a trimethylsilyl-protected group and final deprotection by TBAF (tetrabutylammonium fluoride), (S_c,S_p)-**6g** was synthesized in enantiomeric purity in a total yield of 43.1% as outlined in Scheme 2. By the reaction of a series of ferrocenylphosphine-amines (R_c,S_p)-**6a** – **f** or (S_c,S_p)-**6g** with various 4,6-disubstituted 2-chloropyrimidines or 2-chloro-1,3,5-triazines in refluxing ethanol in the presence of $NaHCO_3$, the targeted P,N ligands **1** and **3** with the different heterocycles were easily prepared in 47.2 to 86.2% yields as outlined in Scheme 3. The synthetic protocol described herein allows the preparation of a series of ferrocenylphosphine-heterocycle ligands, which can differ in the nature of the heterocycles, as well as the steric and electronic properties, covering a wide structural diversity for ligand optimization. An exception is ligand (R_c,S_p)-**2** with a pyridine moiety, which cannot be prepared under the above-described reaction conditions for **1** and **3**. However, by the reaction of acetate **5a** with 2-(methylamino)pyridine in refluxing ethanol in the presence of a catalytic amount of DMAP, ligand (R_c,S_p)-**2** was synthesized although the yield of 37.8% was rather low.

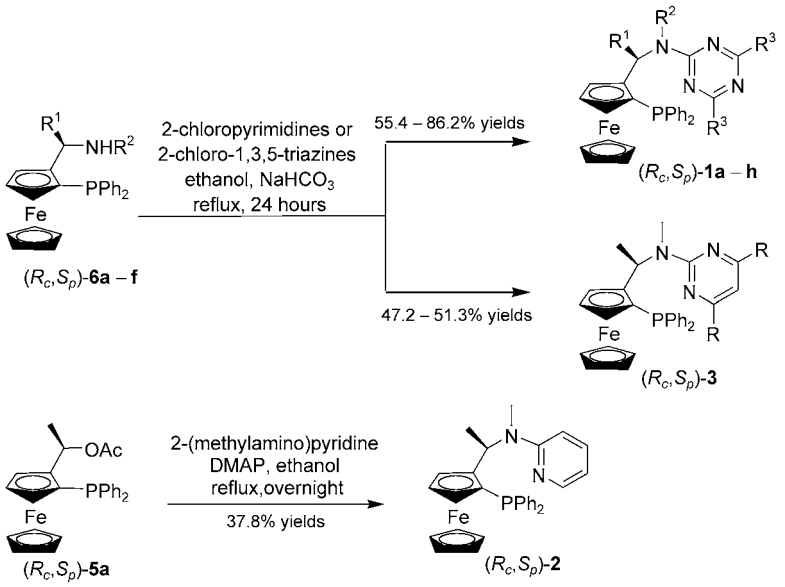
Influence of the Number of Heterocyclic N Atoms on Pd-Catalyzed Asymmetric Allylic Alkylation

With these ligands in hand, we then examined their efficiency in catalytic asymmetric reactions. A model reaction of the Pd-catalyzed asymmetric allylic alkylation of 1,3-diphenylprop-2-en-1-yl esters **11** with dimethyl malonate (**12a**) was then chosen to benchmark the potential use of these ferrocenylphosphine-heterocycle ligands for asymmetric catalysis.[11] In a first set of experiments, we examined the influence of the heterocycle moiety on the catalytic reaction by the use of ligands (R_c,S_p)-**1b**, (R_c,S_p)-**2**, (R_c,S_p)-**3** with a similar structure but different number of heterocyclic N atoms (Figure 3).

The reaction was carried out at room temperature using CH_2Cl_2 as solvent in the presence of 2.0 mol % of



Scheme 2. Synthesis of ferrocenylphosphine-amines (S_c,S_p)-**6g**.



Scheme 3. Synthesis of ferrocene-based phosphine-heterocycle ligands **1, 2** and **3**.

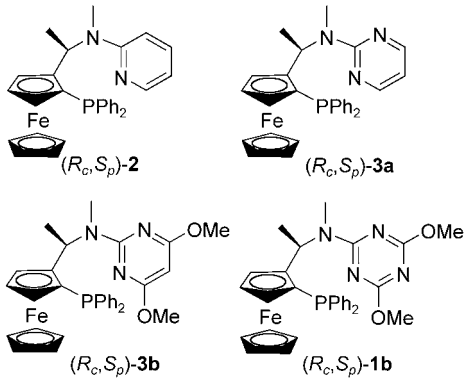


Figure 3. Structures of ligands (R_c,S_p)-**1b**, (R_c,S_p)-**2** and (R_c,S_p)-**3**.

$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$, 5.0 mol % of chiral ligand, and a mixture of *N,O*-bis(trimethylsilyl)acetamide (BSA) and a catalytic amount of KOAc. As shown in Table 1, the reactivity and enantioselectivity strongly depended on the kind of heterocyclic moiety, and a very interesting phenomenon was observed in that the catalytic activity and enantioselectivity significantly increased with an increasing number of N atoms in the heterocycle. As a comparison, ligand (R_c,S_p)-PPFA **4a** without a heterocycle was first used in the tested reaction, and an ee value of 48% was obtained (entry 1). By the use of ligand (R_c,S_p)-**2** containing a pyridine unit, an inspiring increase in enantioselectivity to 81% ee was achieved (entry 2), which indicated that the introduction of a heterocycle into the nitrogen moiety was very advantageous to promote the enantioselective induction of these P,N ligands. Ligand (R_c,S_p)-**3a**, incorporating a pyrimidine moiety with two sp^2 heterocyclic N atoms, brought about a high asymmetric induction (92% ee) (entry 3). Introducing two methoxy groups into the 4,6-positions of pyrimidine unit further increased the enantioselectivity and catalytic activity (93% ee and 91% yields) (entry 4). Replacing the pyrimidine unit with a triazine moiety containing three heterocyclic N atoms, resulting in ligand (R_c,S_p)-**1b**, exhibited even higher enantioselectivity and reactivity, giving the allylic product with an ee value of up to 98% and 99% yield at room temperature within 12 hours (entry 5). The above results reveal the impor-

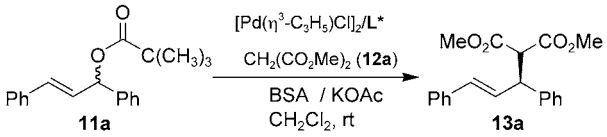
tant role of the presence of the additional heterocyclic N atoms in the Pd-catalyzed asymmetric allylic alkylation, and a clear trend was that the enantioselectivity and reactivity were significantly increased with an increasing number of heterocyclic N atoms, which is of great importance for the design and optimization of new efficient P,N ligands. In order to gain a deeper insight into the origin of the efficiency of ligand (R_c,S_p)-**1b**, we focused our efforts on investigating the difference in π-electron populations between the N atoms of pyridine, pyrimidine and triazine.[12] The comparison was encouraged by the fact that the enantioselectivity and reactivity of ligands was closely related with π-electron populations of heterocycle N atom, and ligands with larger electron populations of N atom gave the allylic alkylation product in higher enantiomeric excess and chemical yield (Table 1). Thus, the triazine N atom has the largest electron populations among these heterocyclic N atoms, and the corresponding phosphine-triazine ligand (R_c,S_p)-**1b** exhibited the highest enantioselectivity. The ^{31}P NMR spectrum of the Pd complex of the phosphine-triazine ligand (R_c,S_p)-**1b** shows a single signal at 6.30 ppm, indicated that only one mode of (R_c,S_p)-**1b** complexing to the central metal occurred in spite of the presence of the multi-N-donor atoms.

Pd-Catalyzed Asymmetric Allylic Alkylation using Phosphine-Triazine Ligands 1

The above experiments disclosed that the triazine moiety was the most important fragment for constructing this kind of phosphine-heterocycle ligands. We then synthesized a series of phosphine-triazine ligands **1**, and investigated their efficiency in Pd-catalyzed asymmetric allylic substitution. Initially, optimization of the reaction conditions was performed by the use of ligand (R_c,S_p)-**1b**, and the results are summarized in Table 2. Initially, the effects of base additives in the catalytic reaction were evaluated using toluene as solvent and 1,3-diphenylprop-2-en-1-yl pivalate (**11a**) as substrate (entries 1–4). The reaction using lithium acetate as base additives provided 89% ee with 94% yield of allylic alkylation product (entry 1). Using sodium acetate, potassium acetate or cesium acetate instead of lithium acetate led to higher enantioselectivities (entries 2–4 *vs.* entry 1). When potassium acetate was used, the highest enantioselectivity was found to be 95% ee (entry 3). Next, the effect of solvents on this reaction was investigated. The reaction was not strongly solvent-dependent, and gave good results in each solvent used (entries 5–8). When the reaction was carried out in CH_2Cl_2, up to 98% ee with 99% yield was obtained (entry 8). Lowering the reaction temperature to 10 °C could further improve the enantioselectivity to 99% ee, but a longer time was required to complete the reaction (entry 9). However, further lowering the reaction temperature to 0 °C caused a decrease of the enantioselectivity to 92% ee with 81% yield (entry 10). When the catalyst loadings were decreased to 0.5 mol %, high enantioselectivity was maintained (entry 11). Replacing pivalate **11a** with acetate **11b** as substrate resulted in a slightly decreased reactivity and enantioselectivity (entry 12). The reaction of pivalate **11a** with bulkier nucleophiles such as diethyl methylmalonate (**12b**) also gave the corresponding product **13b** in the satisfactory enantiomeric excess (98% ee) (entry 13).

Under the optimized reaction conditions (CH_2Cl_2 as solvent, pivalate **11a** as substrate, BSA-KOAc as base, and completing the reaction at room temperature), the efficiency of these ferrocenylphosphine-triazine ligands

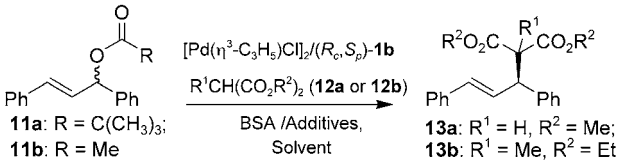
Table 1. Influence of the number of heterocyclic N atoms on the Pd-catalyzed asymmetric allylic alkylation of 1,3-diphenylprop-2-en-1-yl pivalate (**11a**) with dimethyl malonate (**12a**).[a]



Entry	Ligand	Heterocyclic moiety	π-Electron population of heterocyclic N atom[b]	Yield [%][c]	ee [%][d] (config.)[e]
1	(R_c,S_p)-**4a**	-	–	85	48 (*S*)
2	(R_c,S_p)-**2**	Pyridine	1.426	53	81 (*S*)
3	(R_c,S_p)-**3a**	Pyrimidine	1.449	87	92 (*S*)
4	(R_c,S_p)-**3b**	Pyrimidine	1.449	91	93 (*S*)
5	(R_c,S_p)-**1b**	Triazine	1.467	99	98 (*S*)

[a] The reactions were carried out in CH_2Cl_2 in the present of 2.0 mol % $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$, 5.0 mol % of chiral ligand, 3.0 equivs. of dimethyl malonate, 3.0 equivs. of BSA and a catalytic amount of KOAc at room temperature for 12 hours.
[b] The data were reported by Wiberg et al.[12]
[c] Isolated yields.
[d] Determined by HPLC analysis using a Chiralpak AD column (eluent: hexane:2-propanol = 90:10, 1.0 mL/min).
[e] The *S* configuration was confirmed by comparing the specific rotation with the literature value.[14]

Table 2. Optimization of the reaction conditions of Pd-catalyzed asymmetric allylic alkylation using ferrocenylphosphine-triazine ligand (R_c,S_p)-**1b**.[a]

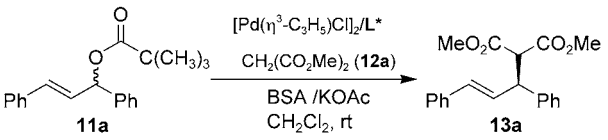


Entry	Substrate	Nu^-	Solvent	Additives	T [°C]	Yield [%][b]	ee [%][c] (config.)[d]
1	**11a**	**12a**	Toluene	LiOAc	25	94	89 (*S*)
2	**11a**	**12a**	Toluene	NaOAc	25	91	93 (*S*)
3	**11a**	**12a**	Toluene	KOAc	25	97	95 (*S*)
4	**11a**	**12a**	Toluene	CsOAc	25	90	91 (*S*)
5	**11a**	**12a**	Benzene	KOAc	25	99	94 (*S*)
6	**11a**	**12a**	Et_2O	KOAc	25	94	95 (*S*)
7	**11a**	**12a**	THF	KOAc	25	97	96 (*S*)
8	**11a**	**12a**	CH_2Cl_2	KOAc	25	99	98 (*S*)
9	**11a**	**12a**	CH_2Cl_2	KOAc	10	93	99 (*S*)[e]
10	**11a**	**12a**	CH_2Cl_2	KOAc	0	81	92 (*S*)[e]
11	**11a**	**12a**	CH_2Cl_2	KOAc	25	95	97 (*S*)[f]
12	**11b**	**12a**	CH_2Cl_2	KOAc	25	93	97 (*S*)
13	**11a**	**12b**	CH_2Cl_2	KOAc	25	96	98 (*R*)[g, h]

[a] The reactions were carried out in the present of 2.0 mol % $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$, 5.0 mol % of chiral ligand, 3.0 equivs. of nucleophile, 3.0 equivs. of BSA and a catalytic amount of metal acetate at indicated temperature for 12 hours.
[b] Isolated yields.
[c] Determined by HPLC analysis using a Chiralpak AD column (eluent: hexane:2-propanol = 90:10, 1.0 mL/min).
[d] The *S* configuration was confirmed by comparing the specific rotation with the literature value.[14]
[e] The reaction was carried out for 24 hours.
[f] Using 0.5 mol % of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ as precatalyst.
[g] Determined by HPLC analysis using a Chiralcel OD + OB column (eluent: hexane:2-propanol = 199:1, 1.0 mL/min).
[h] The *R* configuration was confirmed by comparing the specific rotation with the literature value.[15]

1 was then investigated. The results are summarized in Table 3. The enantioselectivity was strongly dependent on the nitrogen substituent. Ligand (R_c,S_p)-**1a** with an N–H proton showed extremely low reactivity, and no allylic alkylation product **13a** was detected even after 24 hours (entry 1). This result was very unexpected since some reports in the past few years have demonstrated that the presence of an N–H proton in the ligand could significantly promote the enantioselectivity of Pd-catalyzed asymmetric allylic alkylation probably due to a second interaction between the N–H proton in the ligand and the nucleophile.[13] However, the reason for this phenomenon is still unclear. When the N–H proton was replaced with a methyl group, the reaction proceeded in very good reactivity (99% yield) and enantioselectivity (98% ee) (entry 2 *vs.* entry 1). When the N substituent was ethyl, benzyl or 2-hydroxyethyl, ligands (R_c,S_p)-**1c**–**e** showed slightly lower enantioselectivities compared with ligand (R_c,S_p)-**1b** (entries 3–5 *vs.* entry 2). After having demonstrated the presence of a methyl group as the N substituent in ligands **1** tended to give higher enantioselectivity, we then investigated the influence of the substituent in the triazine moiety on the catalytic asymmetric reaction. The use of ligand (R_c,S_p)-**1f** with 4,6-diphenoxy groups in the triazine moiety resulted in the highest enantioselectivity of 99% ee with 99%

Table 3. Asymmetric allylic alkylation of allylic pivalate **11a** using ligands **1**.[a]



Entry	Ligand	Yield [%][b]	ee [%][c] (config.)[d]
1	(R_c,S_p)-**1a**	No reaction	No reaction
2	(R_c,S_p)-**1b**	99	98 (*S*)
3	(R_c,S_p)-**1c**	97	95 (*S*)
4	(R_c,S_p)-**1d**	95	96 (*S*)
5	(R_c,S_p)-**1e**	99	97 (*S*)
6	(R_c,S_p)-**1f**	99	99 (*S*)
7	(R_c,S_p)-**1g**	79	62 (*S*)
8	(R_c,S_p)-**1h**	98	96 (*S*)
9	(S_c,S_p)-**1i**	81	83 (*S*)

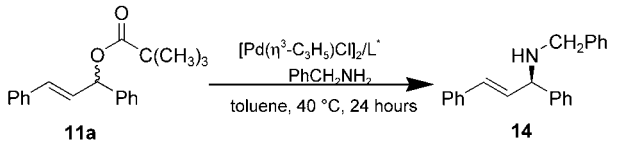
[a] The reactions were carried out in CH_2Cl_2 in the present of 2.0 mol % $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$, 5.0 mol % of chiral ligand, 3.0 equivs. of dimethyl malonate, 3.0 equivs. of BSA and a catalytic amount of KOAc at room temperature for 12 hours.
[b] Isolated yields.
[c] Determined by HPLC analysis using a Chiralpak AD column (eluent: hexane:2-propanol = 90:10, 1.0 mL/min).
[d] The *S* configuration was confirmed by comparing the specific rotation with the literature value.[14]

yields (entry 6). However, a dramatic decrease in the enantioselectivity to 62% ee was observed by the use of ligand (R_c,S_p)-**1 g** with 4,6-dimorpholino substituents (entry 7). When an ethyl group was introduced into the ferrocenylmethyl position, a slightly decreased enantioselectivity (96% ee) was observed (entry 8). In order to investigate the diastereomeric impact of ferrocenylphosphine-triazine ligands in Pd-catalyzed asymmetric allylic alkylation, (S_c,S_p)-**1i** was also used in the tested reaction. However, in comparison with its highly efficient diastereomer (R_c,S_p)-**1f**, (S_c,S_p)-**1i** exhibited lower enantioselectivity but gave the alkylation product **13a** with the same configuration (entry 9). This result indicated that (R_c)-central chirality and (S_p)-planar chirality were matched in these ferrocenylphosphine-triazine ligands for Pd-catalyzed asymmetric allylic alkylation. The configuration of allylic alkylation product **13a** from these reactions was proved to be *S* by comparing the specific rotation with literature values.[14]

Pd-Catalyzed Asymmetric Allylic Amination using Phosphine-Heterocycle Ligands 1, 2 and 3

In order to show the validity of the developed phosphine-heterocycle ligands, their application in the Pd-catalyzed asymmetric allylic amination of 1,3-diphenylprop-2-en-1-yl pivalate (**11a**) with benzylamine was then investigated. The reaction was performed at room temperature using toluene as solvent in the presence of 2.0 mol % of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and 6.0 mol % of chiral ligand. We found that the quality of the benzylamine is very important to carry out the reaction smoothly, therefore it must be dried and evaporated before use. As shown in Table 4, phosphine-heterocycle ligands **1**, **2** and **3** exhibited somewhat lower reactivity and selectivity in the allylic amination in comparison to the results obtained in allylic alkylation (entries 1–4). Again, phosphine-triazine ligand (R_c,S_p)-**1b** exhibited higher enantioselectivity, and an ee value of 86% with 55% yield was obtained (entry 4). The effect of solvents on this reaction was then investigated and a significant variation in the catalytic activity was observed (entries 4–6). Et_2O proved to be an inferior solvent for the reaction, and only 61% ee with 37% yield was obtained (entry 5). Using CH_2Cl_2 as solvent, the enantioselectivity decreased observably with a slight decrease in the yield (entry 6). The reaction was sensitive to temperature. When the reaction was carried out at 40 °C, a similar enantioselectivity was obtained with a marked increase of yield (entry 7). However, increasing the temperature further to 50 °C caused a decrease in enantioselectivity to 81% ee with 96% yield (entry 8). A series of phosphine-triazine ligands was then tested in this reaction under the optimized reaction conditions (entries 9–14). Among them, ligand (R_c,S_p)-**1f** showed the highest enantioselectivity and reactivity, and an ee value of 94% with 82% yield was obtained (entry 13).

Table 4. Asymmetric allylic amination of allylic pivalate **11a** using ligands **1**, **2** and **3**.[a]



11a **14**

Entry	Ligand	Solvent	Temp. [°C]	Yield [%][b]	ee [%][c]
1	(R_c,S_p)-**2**	Toluene	25	51	43
2	(R_c,S_p)-**3a**	Toluene	25	44	67
3	(R_c,S_p)-**3b**	Toluene	25	61	70
4	(R_c,S_p)-**1b**	Toluene	25	55	86
5	(R_c,S_p)-**1b**	Et_2O	25	37	61
6	(R_c,S_p)-**1b**	CH_2Cl_2	25	54	71
7	(R_c,S_p)-**1b**	Toluene	40	80	86
8	(R_c,S_p)-**1b**	Toluene	50	96	81
9	(R_c,S_p)-**1a**	Toluene	40	–	–
10	(R_c,S_p)-**1c**	Toluene	40	79	80
11	(R_c,S_p)-**1d**	Toluene	40	71	78
12	(R_c,S_p)-**1e**	Toluene	40	83	90
13	(R_c,S_p)-**1f**	Toluene	40	82	94
14	(R_c,S_p)-**1h**	Toluene	40	80	88

[a] The reactions were carried out in toluene in the present of 2.0 mol % $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$, 6.0 mol % of chiral ligand, 3.0 equivs. of benzylamine at the indicated temperature for 24 hours.
[b] Isolated yields.
[c] Determined by HPLC analysis using a Chiralcel OD column (eluent: hexane:2-propanol = 200:1, 0.6 mL/min).

Conclusion

In conclusion, we have prepared a new family of ferrocene-based chiral phosphine-heterocycle ligands **1**–**3** and successfully applied them to Pd-catalyzed asymmetric allylic substitution. A clear trend was that the enantioselectivity and reactivity were significantly increased by increasing the number of heterocyclic N atoms in these P,N ligands, and the most efficient were those bearing a triazine moiety with three heterocyclic N atoms. By the use of (R_c,S_p)-**1f** with a 4,6-diphenoxy-1,3,5-triazine moiety in the tested reaction, an ee value of up to 99% ee with 99% yields in allylic alkylation and an ee value of 94% ee with 82% yield in allylic amination were achieved. Further investigations of other catalytic asymmetric reactions with these phosphine-triazine ligands are underway and progress will be reported in due time.

Experimental Section

General Remarks

See Supporting Information for general experimental details as well as procedures for the preparation and characterization of all precursors and ligands.

General Procedure for the Preparation of Ferrocenylphosphine-Amine Intermediates (R_c,S_p)-6a–f

(R_c,S_p)-PPFA **4** (5.0 mmol) was sealed in an air-free tube with acetic anhydride (3.0 mL). The tube was heated to 100 °C for 2 hours. After being cooled to room temperature, the reaction mixture was poured into 150 mL of 10% aqueous potassium carbonate with vigorous stirring. The oily material obtained solidified about 10 minutes later, and the solution was extracted with Et_2O (50 mL × 2). The combined ether extract was washed with 2 N HCl (25 mL × 1), 5% K_2CO_3 (25 mL × 1), and water (25 mL × 1), and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was dissolved in a mixture of amine (25 mmol) and 50 mL of MeOH. The mixture was then placed in a 100-mL of round-bottomed Schlenk flask and heated at reflux temperature for 12 hours. The reaction mixture was diluted with 50 mL of CH_2Cl_2, washed with water (25 mL × 2), and then dried over Na_2SO_4. The solvent was evaporated, and the residue was purified by silica gel column chromatography (modified by 2% Et_3N) to give the targeted product.

General Procedure for the Preparation of *N*-Methyl-(*S*)-1-[(*S*)-2-(diphenylphosphino)-ferrocenyl]ethylamine [(S_c,S_p)-6g]

(*S*)-*N*,*N*-Dimethyl-1-[(*R*)-2-trimethylsilyl-(*S*)-5-(diphenylphosphino)ferrocenyl]ethylamine (**8**; 1.03 g, 2.0 mmol) was sealed in an air-free tube with acetic anhydride (2.0 mL). The tube was heated to 100 °C for 2 hours. After being cooled to the room temperature, the reaction mixture was poured into 150 mL of 15% aqueous potassium carbonate with vigorous stirring. The resultant oily material was extracted with Et_2O (30 mL × 2). The ether extract was washed with 5.0% HCl (20 mL × 2), 5.0% K_2CO_3 (20 mL × 2), and brine (50 mL × 1), and then dried over Na_2SO_4. The solvent was removed under reduced pressure, the residue was purified by column chromatography (silica gel, hexanes/ethyl acetate = 30/1) to give an orange oil. The resulting oil was dissolved in a solution of 10 mL of 33% aqueous H_2NMe in 20 mL of CH_3CN. The mixture was then placed in a 100-mL autoclave and heated at 70–80 °C for 8 hours. The reaction mixture was diluted with 50 mL of CH_2Cl_2, washed with water (25 mL × 1), and dried over anhydrous Na_2SO_4. The solvent was evaporated, and the residue was purified by silica gel column chromatography with hexanes/EtOAc (10:1 to 4:1 v/v) as eluent to give an orange viscous liquid, which was solidified on standing; yield: 0.75 g. This solid was further recrystallized from 2-propanol to give *N*-methyl-(*S*)-1-[(*R*)-2-trimethylsilyl-(*S*)-5-(diphenylphosphino)ferrocenyl]-ethylamine (**10**) as a brown solid; yield: 0.47 g.

The resulting **10** (125 mg, 0.25 mmol) was then dissolved in 5.0 mL of a 1.0 mol/L solution of tetrabutylammonium fluoride (TBAF) in THF. After 3 hours at reflux, the mixture was concentrated under vacuum to afford a brown oil, which was extracted with Et_2O (10 mL × 2). The resulting organic layer was washed with water (10 mL × 2), and then dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (modified by 2% Et_3N) with hexanes/EtOAc/Et_3N (50:10:1 to 20:10:1 v/v/v) as eluent to give (S_c,S_p)-**6 g** as an orange crystals; yield: 98 mg (91.6%).

General Procedure for the Preparation of Ferrocenylphosphine-Triazine Ligands 1a–i

(R_c,S_p)-**6** (1.0 mmol), 2-chloro-4,6-disubstituted-1,3,5-triazine (1.0 mmol) and $NaHCO_3$ (84 mg, 1.0 mmol) were placed in a 25-mL round-bottomed Schlenk flask. After the air in the flask was replaced by argon, dried and degassed ethanol (10 mL) was added. The mixture was stirred overnight under an argon atmosphere at reflux temperature. After being cooled to room temperature, the solution was diluted by 10 mL of ethanol. The solvent was evaporated under vacuum. The residue was purified with silica gel column chromatography and recrystallized from *n*-hexane to afford **1**.

General Procedure for the Preparation of Ferrocenylphosphine-Pyridine Ligands (R_c,S_p)-2

(R_c,S_p)-PPFOAc (**5a**; 456 mg, 1.0 mmol), 2-(methylamino)pyridine (216 mg, 2.0 mmol), and a catalytic amount of DMAP were placed in a 25-mL round-bottomed Schlenk flask. After the air in the flask was replaced by argon, dried and degassed ethanol (10 mL) was added. The mixture was stirred overnight under an argon atmosphere at reflux temperature. The solvent was evaporated under vacuum. The residue was purified by silica gel column chromatography with hexanes/acetate/Et_3N (4:1:0.1 v/v/v), and recrystallized from *n*-hexane to afford the targeted product (R_c,S_p)-**2** as a brown solid.

General Procedure for the Preparation of Ferrocenylphosphine-Pyrimidine Ligands (R_c,S_p)-3

(R_c,S_p)-**6b** (427 mg, 1.0 mmol), 2-chloropyrimidine or 2-chloro-4,6-dimethoxypyrimidine (1.0 mmol) and $NaHCO_3$ (84 mg, 1.0 mmol) were placed in a 25-mL round-bottomed Schlenk flask. After the air in the flask was replaced by argon, dried and degassed ethanol (10 mL) was added. The mixture was stirred overnight under argon atmosphere at reflux temperature. After the solution was cooled to room temperature, the solution was diluted by 10 mL of ethanol. The solvent was evaporated under vacuum. The residue was purified by silica gel column chromatography and recrystallized from *n*-hexane to afford the targeted product.

General Procedure for the Preparation of the Pd Complex of Ferrocenylphosphine-Triazine (R_c,S_p)-1b

(R_c,S_p)-**1b** (5.5 mmol) and $Pd(CH_3CN)_2Cl_2$ (5.0 mmol) were placed in a 10-mL Schlenk tube. After the air in the tube was replaced by argon, dried and degassed CH_2Cl_2 (2.0 mL) was added. The resulting solution was stirred under argon atmosphere at room temperature for 4 hours. Ether (4 mL) was added, and the resulting precipitate was collected and dried to afford the Pd complex.

General Procedure for Asymmetric Allylic Alkylations

A solution of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (3.7 mg, 0.01 mmol) and chiral phosphine-triazine **1** (0.025 mmol) in CH_2Cl_2 (1.5 mL) was stir-

red at room temperature for one hour under an argon atmosphere. To this Pd catalyst was added allylic pivalate **11a** (0.50 mmol) in CH_2Cl_2 (1.5 mL), followed by dimethyl malonate (**12a**; 170 μL, 1.5 mmol), *N,O*-bis(trimethylsilyl)-acetamide (BSA, 0.37 mL, 1.5 mmol), and a catalytic amount of KOAc sequentially. After stirring for 12 hours, the reaction mixture was quenched with saturated aqueous NH_4Cl solution and diluted with CH_2Cl_2. The organic layer was separated, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate, 8:1) to afford a pure product **13a**. The enantiomeric excess was determined by HPLC (Chiralpak AD, hexanes:2-propanol = 90:10, 1.0 mL/min). The absolute configuration was determined by comparison of the specific rotation with the literature value.[14]

General Procedure for Asymmetric Allylic Amination

A solution of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (3.7 mg, 0.01 mmol) and chiral ligand (0.03 mmol) in toluene (1.5 mL) was stirred at indicated temperature for one hour under an argon atmosphere. To this Pd catalyst was added allylic pivalate **11a** (0.50 mmol) in toluene (1.5 mL), followed by benzylamine (1.5 mmol). After stirring for 24 hours, the reaction mixture was quenched with saturated aqueous NH_4Cl solution and diluted with CH_2Cl_2. The organic layer was separated, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography (hexane:ethyl acetate, 20:1) to afford a pure product **14**. The enantiomeric excess was determined by HPLC (Chiralcel OD, hexanes:2-propanol = 200:1, 0.6 mL/min).

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