

Modular Phosphine-Aminophosphine Ligands Based on Chiral 1,2,3,4-Tetrahydro-1-naphthylamine Backbone: A New Class of Practical Ligands for Enantioselective Hydrogenations

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Abstract: A series of new chiral phosphine-amino-phosphine ligands [(*R*)-HW-Phos] has been prepared from (*R*)-1,2,3,4-tetrahydro-1-naphthylamine through a two-step procedure, and successfully applied in the rhodium-catalyzed asymmetric hydrogenation of various functionalized olefins such as α -enol ester phosphonates, α -enamido phosphonates, (*Z*)- β -(acylamino)acrylates and so on. Excellent enantioselectivities have been achieved in the hydrogenation of most substrates tested, demonstrating the high potential of these newly developed phosphine-amino-phosphine ligands in asymmetric catalysis. The present research also discloses that these newly developed phosphine-amino-phosphine ligands are more efficient than that derived from (*S*)-1-phenylethylamine, suggesting that the increased rigidity conferred by a cyclohexyl fragment in these phosphine-amino-phosphine ligands has a positive effect in the asymmetric induction.

Keywords: asymmetric catalysis; hydrogenation; phosphine-amino-phosphine ligands; rhodium; 1,2,3,4-tetrahydro-1-naphthylamine

Catalytic asymmetric hydrogenation is one of the most powerful and practical tools to access optically active compounds in contemporary synthetic organic chemistry, in which the development of new chiral phosphorus-containing ligands has played a significant role.^[1] Although many excellent phosphorus-containing ligands have been reported for highly enantioselective hydrogenations in the past decades, the quest for new efficient ligands remains a major challenge. A

recent strategy in this area relies upon the use of unsymmetrical hybrid bidentate phosphorus ligands.^[2] Because of holding two chemically distinct phosphorus binding sites, these ligands can offer the unique electronic environment around the metal centre, different from that provided by the ubiquitous C_2 -symmetrical ligands. Among the various unsymmetrical hybrid bidentate phosphorus ligands, a combination of phosphine and aminophosphine fragments was found to be an effective arrangement for the construction of new unsymmetrical hybrid bidentate phosphorus ligands.^[3] The first successful phosphine-amino-phosphine ligand was known as BoPhoz, reported by Boaz et al in 2002, which showed excellent enantioselectivities in the Rh-catalyzed asymmetric hydrogenation of α -dehydroamino acid derivatives, itaconate derivatives and α -keto esters.^[3a] However, the results in the Rh-catalyzed asymmetric hydrogenation of α -enamides with these BoPhoz ligands were less satisfactory. By use of the fluorinated BoPhoz-type ligands, Yip and Chan et al. found that the enantioselectivity for the hydrogenation of this substrate class could be dramatically increased.^[3d] Chen et al. introduced a stereogenic phosphorus atom into Bophoz-type ligands, and the comparative results demonstrate that *P*-chirality improves the enantioselectivity when acting cooperatively with the planar chirality and the chirality at the carbon centre.^[3g] Although significant progress has been made in the past few years, it should be noted that all of these phosphine-amino-phosphine ligands are based on a chiral 1-ferrocenylethylamine backbone, and few other phosphine-amino-phosphine skeletons were found to be effective in asymmetric catalysis. Moreover, the substrate scope with these ligands in catalytic hydrogenation is still limited, whereby some of the more

challenging substrate classes such as β -dehydroamino acid esters could not be hydrogenated in satisfactory enantioselectivities. Therefore, the search for more practical and efficient phosphine-aminophosphine ligands in terms of ease of preparation and wide substrate scope remains an interesting and important goal.

Very recently, we have developed a readily accessible phosphine-aminophosphine ligand, (*S*)-HH-Phos, which was prepared through a two-step transformation from inexpensive and commercially available (*S*)-1-phenylethylamine (Figure 1).^[4] Although *ee* values of 93–97% were achieved in the Rh-catalyzed asymmetric hydrogenation of dimethyl α -benzyloxyethenephosphonates and *N*-benzyloxycarbonyl α -enamido phosphonates, the asymmetric induction of this ligand class still needs to be improved. Moreover, (*S*)-HH-Phos is less efficient for the hydrogenation of other functionalized olefins, normally giving the hydrogenation products in *ee* values of <90%. We reasoned that the flexible nature of the chiral phenylethylamine backbone should be responsible for these unsatisfactory results, and ligands with an appropriate rigid structure might have a better asymmetric induc-

tion than that derived from (*S*)-1-phenylethylamine. On the basis of this assumption, we therefore envisioned that chiral 1,2,3,4-tetrahydro-1-naphthylamine-derived phosphine-aminophosphine species might be an excellent ligand class since the increased rigidity conferred by a cyclohexyl fragment may result in high enantioselectivities. Herein we report the synthesis of this new phosphine-aminophosphine ligand class and their applications in highly efficient rhodium-catalyzed asymmetric hydrogenation of α -enol ester phosphonates, α -enamido phosphonates, (*Z*)- β -(acylamino)acrylates and so on.

These new phosphine-aminophosphine ligands **1** can be easily prepared from commercially available, optically active 1,2,3,4-tetrahydro-1-naphthylamine **2** through a two-step transformation, which is shown in Scheme 1. The key to the synthesis of these target compounds is the direct *ortho*-functionalization of the primary amine, which can be easily carried out by a direct and experimentally convenient one-pot protocol. Thus, (*R*)-1,2,3,4-tetrahydro-1-naphthylamine **2** was treated with *n*-BuLi at 0 °C, following by slow addition of neat ClSiMe₃, which *in situ* generated a monosilylated product, *N*-(trimethylsilyl)-1,2,3,4-tetrahydro-1-naphthylamine. The latter was further dilithiated by addition of 3 equiv. of *n*-BuLi at –25 °C, and then *ortho*-phosphinated with ClPPh₂. After work-up and crystallization from *n*-hexane, the key intermediate (*R*)-THNANH₂ **3** was obtained in 52% overall yields. (*R*)-THNANH₂ **3** was then converted into the corresponding phosphine-aminophosphine ligand (*R*)-HW-Phos **1a** in high yield by the reaction with ClPPh₂ in CH₂Cl₂ at 0 °C in the presence of Et₃N as a scav-

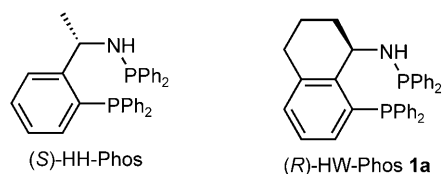
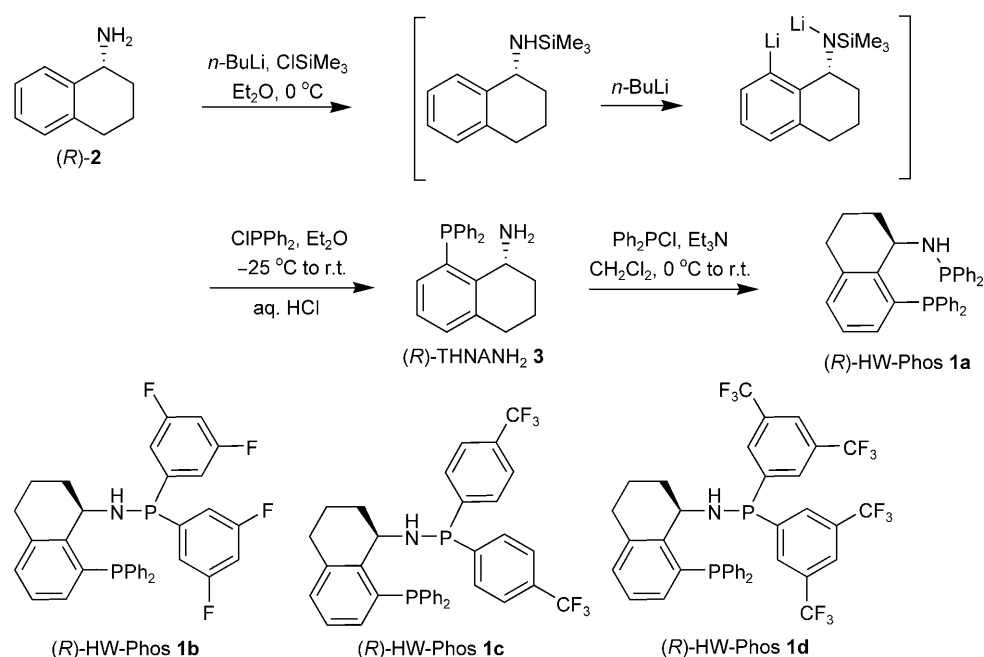
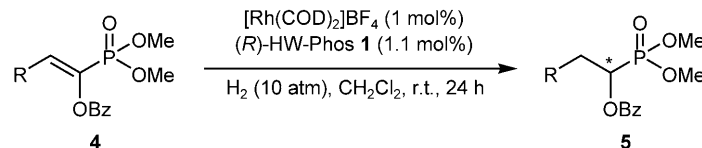


Figure 1. Structure of phosphine-aminophosphine ligands (*S*)-HH-Phos and (*R*)-HW-Phos **1a**.



Scheme 1. Synthesis of (*R*)-HW-Phos ligands **1a–d**.

Table 1. Rh-catalyzed asymmetric hydrogenation of α -enol ester phosphonates **4**.^[a]

Entry	Ligand	Substrate	Conversion [%]	<i>ee</i> [%] (Configuration) ^[b]
1	(<i>S</i>)-HH-Phos	4a : R = H	100	93.1 (<i>S</i>)
2	1a	4a : R = H	100	96.5 (<i>R</i>)
3	1b	4a : R = H	100	97.7 (<i>R</i>)
4	1c	4a : R = H	100	98.7 (<i>R</i>)
5	1d	4a : R = H	100	99.4 (<i>R</i>)
6	1d	4b : R = Me	100	99.2 (<i>R</i>)
7	1d	4c : R = Et	100	99.6 (<i>R</i>)
8	1d	4d : R = Ph	100	99.2 (<i>R</i>)
9	1d	4e : R = 4-Cl-C ₆ H ₄	100	99.0
10	1d	4f : R = 3-Cl-C ₆ H ₄	100	99.1
11	1d	4g : R = 2-Cl-C ₆ H ₄	100	98.5
12	1d	4h : R = 4-F-C ₆ H ₄	100	99.8
13	1d	4i : R = 4-NO ₂ -C ₆ H ₄	100	98.7
14	1d	4j : R = 4-CH ₃ O-C ₆ H ₄	100	99.1
15	1d	4k : R = 3-CH ₃ OC ₆ H ₄	100	98.9
16	1d	4l : R = O- <i>i</i> -Pr	100	99.7

^[a] All reactions were performed with 0.25 mmol of substrate at room temperature under an H₂ pressure of 10 atm in 2 mL of CH₂Cl₂ for 24 h. Substrate/[Rh(COD)₂]BF₄/ligand = 1/0.01/0.011. Full conversions were achieved in all reactions.

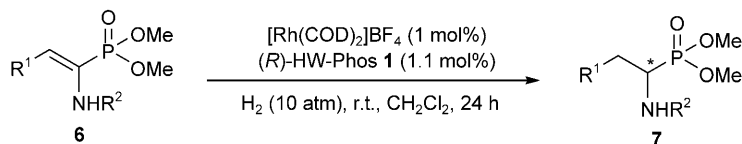
^[b] The *ee* values were determined by HPLC on a chiral column. The absolute configuration was determined by comparing the optical rotation with the reported data.

enger for the HCl eliminated. Because two phosphorus groups are introduced sequentially in two separate steps, the electronic and steric properties of these ligands can be easily varied by replacing the diphenylphosphino group in the aminophosphino moiety with various diarylphosphino groups. Thus, a series of (*R*)-HW-Phos **1b–d** was prepared in good yields by a same procedure.

As we have reported, the (*S*)-HH-Phos ligand derived from (*S*)-phenylethylamine displayed 93–97% *ee* for the Rh-catalyzed asymmetric hydrogenation of α -enol ester phosphonates **4**. For a comparison in the asymmetric induction between (*S*)-HH-Phos and (*R*)-HW-Phos, in the first set of experiments, we used the Rh-catalyzed asymmetric hydrogenation of α -enol ester phosphonates **4** to benchmark the potential of these newly developed phosphine-aminophosphine ligands **1** in asymmetric catalysis. The reaction was performed in CH₂Cl₂ at room temperature under an H₂ pressure of 10 atm in the presence of 1 mol% of catalysts prepared *in situ* from [Rh(COD)₂]BF₄ and 1.1 equiv. of chiral ligands, and the results are summarized in Table 1.

To our delight, these newly developed phosphine-aminophosphine ligands **1a–d** displayed extraordinarily high enantioselectivities (96.5–99.4% *ee*) in the rhodium-catalyzed asymmetric hydrogenation of dimethyl α -benzoyloxyethenephosphonate **4a** (entries 2–5,

Table 1), significantly higher than that obtained with the phosphine-aminophosphine ligand [(*S*)-HH-Phos] derived from (*S*)-1-phenylethylamine (entry 1, Table 1). These results suggested that the increased rigidity in these phosphine-aminophosphine ligands has a positive effect in the asymmetric induction. As it is deduced from the data in Table 1, (*R*)-HW-Phos **1d**, bearing two CF₃ groups in the 3,5-positions of the phenyl ring of the aminophosphino moiety, was the most efficient ligand with regard to asymmetric induction and afforded the hydrogenation product with an *ee* value of 99.4% (entry 5, Table 1). With the optimal ligand **1d**, we next examined the enantioselectivity of the hydrogenation of β -alkyl substituted α -benzoyloxyethenephosphonates **4b** and **c**. The results indicated that the β -alkyl substituent in the substrate has little effect on the enantioselectivity. Thus, **4b** with a methyl group and **4c** with an ethyl group were hydrogenated in 99.2% *ee* and 99.6% *ee*, respectively (entries 6 and 7, Table 1). To further broaden the synthetic interest of this highly enantioselective procedure, a set of structurally diverse β -aryl substituted substrates **4d–k** was submitted to the optimized Rh-catalyzed asymmetric hydrogenation. The catalytic asymmetric hydrogenation of β -aryl substituted α -enol ester phosphonates remains a challenging task.^[5] It is only very recently that some unsymmetrical hybrid bidentate phosphorus ligands have been found to show good to

Table 2. Rh-catalyzed asymmetric hydrogenation of α -enamido phosphonates **6**.^[a]

Entry	Ligand	Substrate	Conversion [%]	<i>ee</i> [%] (Configuration) ^[b]
1	(<i>S</i>)-HH-Phos	6a : R ¹ = H, R ² = Cbz	100	96.2 (<i>S</i>)
2	1a	6a : R ¹ = H, R ² = Cbz	100	98.7 (<i>R</i>)
3	1b	6a : R ¹ = H, R ² = Cbz	100	99.5 (<i>R</i>)
4	1c	6a : R ¹ = H, R ² = Cbz	100	99.5 (<i>R</i>)
5	1d	6a : R ¹ = H, R ² = Cbz	100	99.6 (<i>R</i>)
6	1d	6b : R ¹ = H, R ² = Ac	100	99.9
7	1d	6c : R ¹ = Me, R ² = Cbz	— ^[c]	— ^[c]
8	1d	6d : R ¹ = Ph, R ² = Cbz	100	99.1 (<i>R</i>)

^[a] All reactions were performed with 0.25 mmol of substrate at room temperature under an H₂ pressure of 10 atm in 2 mL of CH₂Cl₂ for 24 h. Substrate/[Rh(COD)₂]BF₄/ligand = 1/0.01/0.011. Full conversions were achieved in all reactions.

^[b] The *ee* values were determined by HPLC on a chiral column. The absolute configuration was determined by comparing the optical rotation with the reported data.

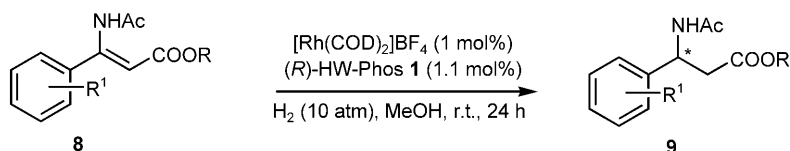
^[c] Not determined because of low conversion.

excellent enantioselectivities in this transformation.^[6] Therefore, the search of new chiral ligands with the properties superior to their predecessors for this transformation is still highly desirable. Gratifyingly, we found that all β -aryl substituted substrates **4d–k** were hydrogenated in excellent enantioselectivity (98.5–99.8% *ee*) with the present catalytic system, regardless of the substitution pattern and electronic properties of the substituent in the phenyl ring of the substrates (entries 8–15, Table 1). High enantioselectivity was also observed in the hydrogenation of the β -alkoxy-substituted substrate **4l**, for which 99.7% *ee* was obtained (entry 16, Table 1). These results demonstrate that the present catalytic system is highly enantioselective in the hydrogenation of α -enol ester phosphonates, comparable to the best results reported so far.^[5,6] However, an attempt to lower the catalyst loadings to 0.1 mol% failed, under the optimized hydrogenation conditions, <50% conversions were achieved.

To further demonstrate the scope and flexibility of the present catalytic system, we decided to apply the phosphine-aminophosphine ligands **1** to the hydrogenation of α -enamido phosphonates **6**. Although the catalytic asymmetric hydrogenation of α -dehydroamino acid derivatives is one of the most studied and widely applied methods for the enantioselective preparation of α -amino acids, there are only a few catalytic hydrogenation methods available to access optically active α -aminophosphonic acid derivatives, partly due to the difficult accessibility of a variety of substituted enamido phosphonates.^[7] Some *N*-protected α -enamido phosphonates **6a–d** were prepared in moderate yields by the condensation reaction between acyl

phosphonates and amides as described in the literature.^[8] However, the synthesis of other substituted substrates using the same method failed. The subsequent hydrogenation was performed under the optimized conditions (CH₂Cl₂ as the reaction media, H₂ pressure of 10 atm, and room temperature for 24 h) as employed in the hydrogenation of α -enol ester phosphonates. The results in Table 2 disclose that these newly developed phosphine-aminophosphine ligands [(*R*)-HW-Phos **1a–d**] are also highly efficient for the hydrogenation of dimethyl α -benzyloxycarbonylaminoethenephosphonate (**6a**), providing higher enantioselectivities than that obtained with (*S*)-HH-Phos. Again, (*R*)-HW-Phos **1d**, bearing two CF₃ groups in the 3,5-positions of the phenyl ring of the aminophosphino moiety, was found to be the most efficient ligand with regard to asymmetric induction and afforded the hydrogenation product with an *ee* value of 99.6% (entry 5, Table 2). Protective groups on the nitrogen had little impact on the enantioselectivity, normally giving *ee* values of over 99% (entries 5 and 6, Table 2). The β -substituent in the substrates had an significant effect in the enantioselectivity. For the hydrogenation of the substrate **6c** with a β -methyl substituent, a low conversion was observed even in an elevated H₂ pressure (entry 7, Table 2). In sharp contrast, the substrate **6d** with a β -phenyl substituent was hydrogenated in full conversion and 99.1% *ee* (entry 8, Table 2).

We continued our investigation on the use of these new phosphine-aminophosphine ligands **1a–d** in the hydrogenation of (*Z*)- β -aryl- β -(acylamino)acrylates **8a–h**. The asymmetric hydrogenation of β -(acylamino)acrylates, in particular those bearing an aryl group

Table 3. Rh-catalyzed asymmetric hydrogenation of (*Z*)- β -aryl- β -(acylamino)acrylates **8**.^[a]

Entry	Ligand	Substrate	Conversion [%]	ee [%] (Configuration) ^[b]
1	(<i>S</i>)-HH-Phos	8a : Ar = Ph, R = Et	0	–
2	1a	8a : Ar = Ph, R = Et	100	93.5 (<i>R</i>)
3	1b	8a : Ar = Ph, R = Et	100	92.1 (<i>R</i>)
4	1c	8a : Ar = Ph, R = Et	100	94.9 (<i>R</i>)
5	1d	8a : Ar = Ph, R = Et	100	92.1 (<i>R</i>)
6	1c	8b : Ar = 4-Me-C ₆ H ₄ , R = Me	100	95.7
7	1c	8c : Ar = 3-Me-C ₆ H ₄ , R = Me	100	95.0
8	1c	8d : Ar = 2-Me-C ₆ H ₄ , R = Me	100	96.5
9	1c	8e : Ar = 4-MeO-C ₆ H ₄ , R = Me	100	96.8
10	1c	8f : Ar = 4-MeO-C ₆ H ₄ , R = Et	100	96.3
11	1c	8g : Ar = 4-Me-C ₆ H ₄ , R = Et	100	96.2
12	1c	8h : Ar = 3-MeO-C ₆ H ₄ , R = Et	100	96.8

^[a] All reactions were performed with 0.25 mmol of substrate at room temperature under an H₂ pressure of 10 atm in 2 mL of MeOH for 24 h. Substrate/[Rh(COD)₂]BF₄/ligand = 1/0.01/0.011.

^[b] The *ee* values were determined by GC or HPLC on a chiral column. The absolute configuration was determined by comparing the optical rotation with the reported data.

at β -position, remains much less successful compared to the hydrogenation of their α -analogues. Although some chiral monodentate and bidentate phosphorus-containing ligands have recently been reported to show good to excellent enantioselectivities,^[9] phosphine-aminophosphine ligands have proved to be an inferior ligand for this transformation and displayed only low to moderate enantioselectivities.^[10] Initially, we examined the influence of the ligand structure on the reactivity and enantioselectivity. Hydrogenation was conducted in MeOH at room temperature under an H₂ pressure of 10 bar in the presence of 1.0 mol% catalysts prepared *in situ* from [Rh(COD)₂]BF₄ and 1.1 equiv. of chiral ligand. As shown in Table 2, phenylethylamine-derived phosphine-aminophosphine ligand [(*S*)-HH-Phos] surprisingly showed no activity in the hydrogenation of (*Z*)- β -phenyl- β -(acylamino)acrylates **8a** (entry 1, Table 3). In sharp contrast, the corresponding (*R*)-HW-Phos **1a** exhibited satisfactory results, providing the hydrogenation product in full conversion with 93.5% *ee* (entry 2, Table 3). The subsequent experiments disclosed that all of the chiral 1,2,3,4-tetrahydro-1-naphthylamine-derived phosphine-aminophosphine ligands **1a–d** were efficient for the hydrogenation of (*Z*)- β -phenyl- β -(acylamino)acrylates **8a**, giving the hydrogenation products in full conversions with good enantioselectivities (92.1–94.9% *ee*, entries 2–5, Table 3). However, different from that in the hydrogenation of α -enol ester phosphonates, (*R*)-HW-Phos **1c** with a CF₃ group in the 4-position of the phenyl ring of the aminophosphino moiety exhibited the highest enantioselectivity

(94.9% *ee*, entry 4, Table 3). With the optimal ligand **1c**, a variety of (*Z*)- β -aryl- β -(acylamino)acrylates **8b–h** were hydrogenated in excellent enantioselectivities (95.0–96.8% *ee*, entries 6–12, Table 3), which represented the best result in the hydrogenation of β -(acylamino)acrylates with phosphine-aminophosphine ligands.

We also investigated the efficiency of these newly developed phosphine-aminophosphine ligands **1** in the hydrogenation of some other functionalized olefins such as α -dehydroamino acid esters, α -enamides and itaconate (Figure 2), and the results are summarized in Table 4. For the hydrogenation α -dehydroamino acid esters **10**, (*R*)-HW-Phos **1d** proved to be the best ligand and provided the hydrogenation products in good enantioselectivities (entries 1–4, Table 4). Unexpectedly, this kind of ligands was inefficient in the hydrogenation of dimethyl itaconate **11** in terms of asymmetric induction, in which an *ee* value of only

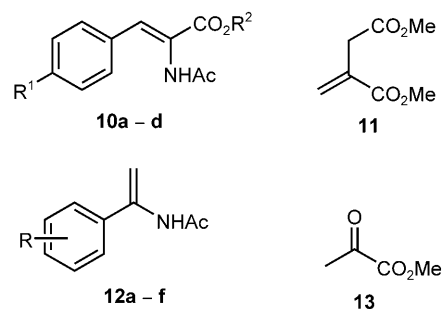
**Figure 2.**

Table 4. Rh-catalyzed asymmetric hydrogenation of functionalized olefins and ketones **10–13**.^[a]

Entry	Ligand	Substrate	Conversion [%]	ee [%] ^[b]
1	1d	10a : R ¹ = H, R ² = Me	100	95.2
2	1d	10b : R ¹ = H, R ² = Et	100	95.4
3	1d	10c : R ¹ = OMe, R ² = Me	100	95.6
4	1d	10d : R ¹ = Cl, R ² = Me	100	94.0
5	1d	11	100	55.0
6	1b	12a : R = H	100	93.4
7	1b	12b : R = 4-Me	100	96.4
8	1b	12c : R = 4-Cl	100	95.8
9	1b	12d : R = 4-Br	100	97.0
10	1b	12e : R = 4-CF ₃	100	96.3
11	1b	12f : R = 3-OMe	100	96.4
12	1d	13	— ^[c]	— ^[c]

^[a] All reactions were performed with 0.25 mmol of substrate at room temperature under an H₂ pressure of 10 atm in 2 mL of CH₂Cl₂ for 24 h. Substrate/[Rh(COD)₂]BF₄/ligand = 1/0.01/0.011.

^[b] The ee values were determined by GC on a chiral column.

^[c] Not determined because of low conversion.

55% ee was achieved (entry 5, Table 4). Different from that in the hydrogenation of α -dehydroamino acid esters, (*R*)-HW-Phos **1b** with two F-atoms in the 3,5-positions of the phenyl ring of the aminophosphino moiety was found to be the most efficient ligand for the hydrogenation of enamides **12**. A variety of enamides **12** was hydrogenated in good enantioselectivities, regardless of the electronic properties of the substrates (entries 6–11, Table 4). The hydrogenation of functionalized ketone **13** with Rh and Ru catalysts proved to be inefficient, only low conversions were achieved (entry 12, Table 4).

In summary, we have developed a new class of readily available, air-stable chiral phosphine-aminophosphine ligands [(*R*)-HW-Phos **1**] and successfully applied them to the enantioselective hydrogenation of various functionalized olefins such as α -enol ester phosphonates, α -enamido phosphonates and (*Z*)- β -aryl- β -(acylamino)acrylates and so on. Excellent enantioselectivities have been achieved in the hydrogenation of most substrates tested, demonstrating the high potential of these phosphine-aminophosphine ligands in the preparation of optically active α -hydroxyphosphonates, α -aminophosphonates, β -aryl- β -amino acid esters and so on. The present research also indicated that the increased rigidity conferred by a cyclohexyl fragment in these phosphine-aminophosphine ligands has a positive effect in the asymmetric induction. Studies to further investigate the scope of these ligands are currently in progress.

Experimental Section

General Procedure for the Synthesis of Phosphine-Aminophosphine Derivatives (*R*)-HW-Phos **1**

Chlorodiphenylphosphine (0.2 mL, 1.1 mmol, 1.1 equiv.) was dissolved in 2.0 mL of dried CH₂Cl₂, which was cooled to 0°C. A solution of amino-phosphine intermediate (*R*)-THNANH₂ **3** (331 mg; 1.0 mmol) and Et₃N (303 mg, 3.0 mmol) in 2.0 mL of CH₂Cl₂ was added dropwise to above solution during 30 min. The resulting mixture was left standing at room temperature overnight. The residue was purified by column chromatography, resulting in (*R*)-HW-Phos **1a** as white solid; yield: 440 mg (85%), mp 128–129°C; [α]_D¹⁵: –118.2 (c 0.504, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 1.54–1.61 (m, 2H), 1.91–1.92 (m, 1H), 2.15–2.18 (m, 1H), 2.29–2.34 (m, 1H), 2.72–2.75 (m, 1H), 2.83–2.87 (m, 1H), 5.05 (m, 1H), 6.81 (m, 1H), 7.05–7.27 (m, 20H), 7.38 (m, 2H); ³¹P NMR (162 MHz, CDCl₃): δ = –16.5, 34.8; ¹³C NMR (100 MHz, CDCl₃): δ = 16.5, 29.5, 30.0, 52.0, 127.4, 127.9, 128.2, 128.3, 128.4, 128.5, 130.7, 131.5, 131.7, 133.0, 133.4, 133.6, 133.8, 134.0, 137.2, 138.7; HR-MS: *m/z* = 516.1991, calcd. for C₃₄H₃₂NP₂ [M+H]: 516.2010.

(*R*)-HW-Phos **1b**: mp 94–95°C; [α]_D¹⁵: –94.3 (c 0.582, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 1.65–1.73 (m, 2H), 1.91 (m, 1H), 2.08–2.12 (m, 1H), 2.32–2.37 (m, 1H), 2.79–2.83 (m, 1H), 2.88–2.90 (m, 1H), 4.97–4.98 (m, 1H), 6.83–6.86 (m, 6H), 7.08–7.72 (m, 13H); ³¹P NMR (162 MHz, CDCl₃): δ = –16.2, 34.5; ¹³C NMR (100 MHz, CDCl₃): δ = 16.7, 29.5, 30.2, 52.0, 103.9, 104.2, 104.5, 104.7, 113.4, 113.7, 113.9, 127.8, 128.7, 130.9, 133.0, 133.5, 133.7, 133.8, 134.0, 136.8, 136.9, 137.1, 137.3, 138.0, 138.1, 161.7; HR-MS: *m/z* = 586.1483, calcd. for C₃₄H₂₆F₄NP₂ [M–H]: 586.1477.

(*R*)-HW-Phos **1c**: mp 88–89°C; [α]_D¹⁵: –90.8 (c 0.526, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 1.63–1.71 (m, 2H), 1.95 (m, 1H), 2.07–2.11 (m, 1H), 2.39–2.44 (m, 1H), 2.78–2.82 (m, 1H), 2.88–2.89 (m, 1H), 4.96–4.97 (m, 1H), 6.76 (m, 1H), 7.00 (m, 2H), 7.09–7.29 (m, 13H), 7.43–8.03 (m, 5H); ³¹P NMR (162 MHz, CDCl₃): δ = –15.8, 34.2; ¹³C NMR (100 MHz, CDCl₃): δ = 16.7, 29.5, 30.4, 52.3, 125.5, 125.6, 127.7, 128.0, 128.6, 128.7, 128.9, 130.9, 132.9, 133.5, 133.7, 133.8, 134.0, 134.5, 134.7, 134.8, 138.2, 143.5; HR-MS: *m/z* = 650.1626, calcd. for C₃₆H₂₈F₆NP₂ [M–H]: 650.1601.

(*R*)-HW-Phos **1d**: mp 164–165°C; [α]_D¹⁵: –65.7 (c 0.504, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 1.69–1.80 (m, 2H), 2.02–2.05 (m, 2H), 2.53–2.58 (m, 1H), 2.81–2.85 (m, 1H), 2.91–2.93 (m, 1H), 4.92–4.93 (m, 1H), 6.72 (m, 1H), 6.87–6.91 (m, 2H), 7.11–7.31 (m, 10H), 7.77–7.84 (m, 6H); ³¹P NMR (162 MHz, CDCl₃): δ = –15.1, 34.0; ¹³C NMR (100 MHz, CDCl₃): δ = 16.8, 29.5, 30.7, 52.6, 123.0, 123.2, 124.7, 128.1, 128.5, 128.6, 128.7, 128.8, 129.0, 130.8, 131.0, 131.5, 131.7, 132.8, 133.5, 133.7, 133.8, 137.4, 144.8, 146.0, 146.2; HR-MS: *m/z* = 786.1326, calcd. for C₃₈H₂₆F₁₂NP₂ [M–H]: 786.1349.

General Procedure for Asymmetric Hydrogenation

In a nitrogen-filled glove-box, [Rh(COD)₂]BF₄ (1.0 mg, 0.0025 mmol) and (*R*)-**1a** (1.4 mg, 0.0028 mmol) were dissolved in degassed CH₂Cl₂ (1 mL) in a 5-mL vial. After stirring at room temperature for 15 min, a solution of dimethyl

α -benzoyloxyethenephosphonate **4a** (64 mg, 0.25 mmol, S/C 100:1) in 1 mL of degassed CH_2Cl_2 was added. The resulting mixture was transferred to an autoclave, which was then charged with H_2 (10 atm). The hydrogenation was performed at room temperature for 24 h. After carefully releasing the hydrogen gas, the reaction mixture was concentrated under reduced pressure. The residue was purified through a plug of silica gel (eluting with a mixture of hexanes/EtOAc, 2/1) to afford **5a**. The enantiomeric excess was determined by chiral GC.

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