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Chiral diphosphites derived from (1*R*,2*R*)-*trans*-1,2-cyclohexanediol: a new class of ligands for asymmetric hydrogenations

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ABSTRACT

A series of novel chiral diphosphite ligands was easily prepared in a few steps from commercial (1*R*,2*R*)-*trans*-1,2-cyclohexanediol as the chiral source, and successfully employed in the Rh-catalyzed asymmetric hydrogenation of α,β-unsaturated carboxylic acid derivatives and enamides with up to 99% ee for dimethyl itaconate and enamides and with up to 94% ee for α-dehydroamino acid esters. The stereochemically matched combination of (1*R*,2*R*)-*trans*-1,2-cyclohexanediol backbone and (*S*)-binaphthyl in the ligand (1*R*,2*R*)-bis[(*S*)-1,1′-binaphthyl-2,2′-diyl]phosphitecyclohexanediol, was essential for inducing high enantioselectivity. Moreover, the sense of enantiodiscrimination of the products was mainly determined by the configuration of the binaphthyl moieties.

1. Introduction

In recent years, the industrial demand for optically active compounds in the production of chiral drugs, agrochemicals, flavor, and advanced materials has increased remarkably.[1] Asymmetric hydrogenation with transition-metal complex bearing chiral ligands is a powerful approach to synthesize chiral substances from unsaturated starting materials, and thus the design and development of new catalysts, which provide high activity and enantioselectivity for asymmetric hydrogenation reactions remain appealing challenges.[2] In this context, chiral P-donor ligands (phosphines,[3] phosphites,[4] phosphoroamidites[5]) have gathered much attention in recent decades. Among the aforementioned ligands, phosphites, which are attractive due to their high efficiency, facile synthesis, and less sensitivity to air, have emerged as suitable ligands for Rh-catalyzed enantioselective hydrogenations.[6] Despite the tremendous advance of this field, many research groups are still focused on the search for new catalytic systems that can be easily prepared and which can catalyze a wide range of substrates with good activity and good enantioselectivity.[5b]

1,2-Cyclohexanediol is widely used in preparing polyester, epoxy resin thinner, *o*-dihydroxybenzene, and so on. As an important organic intermediate, 1,2-cyclohexanediol has enjoyed great success over the years in the field of medicine, pesticide, spice, and organic synthesis.[7] For example, RajanBabu et al.[8] found that ligands **1a** and **1b** (Fig. 1), derived from (1*S*,2*S*)-*trans*-1,2-cyclohexanediol and the corresponding diarylchlorophosphines proved to be effective for the hydrogenation of dimethyl itaconate with good enantiomeric excesses (up to 79% ee) in 1999. Recently, Arena et al.[9] used (1*R*,2*R*)-diaminocyclohexane as the backbone, and prepared enantiopure diphosphoramidite ligand **2** (Fig. 2), which was successfully employed in Rh-catalyzed asymmetric hydrogenations of dimethyl itaconate, methyl 2-acetamidoacrylate, and (*Z*)-methyl-2-acetamido-3-phenylacrylate with up to 88% ee. To the best of our knowledge, although a number of chiral, phosphorus-donor ligands have been synthesized for transition-metal-catalyzed asymmetric transformations, chiral phosphite ligands derived from cyclohexanediol have been rarely studied, hence we designed and synthesized novel diphosphite ligands **5a**–**5d** by changing the electron density at the phosphorus atom and the configuration of the biaryl moieties of the ligands. These ligands were successfully applied to Rh-catalyzed asymmetric hydrogenations of α,β-unsaturated carboxylic acid derivatives and enamides. It

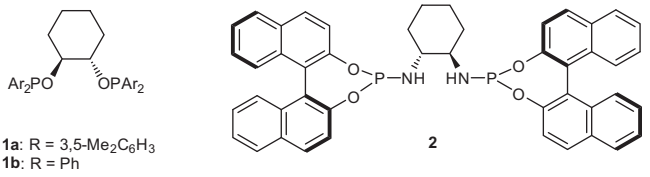

Figure 1. The representative examples of the application of *trans*-1,2-cyclohexanediol and (1*R*,2*R*)-diaminocyclohexane.

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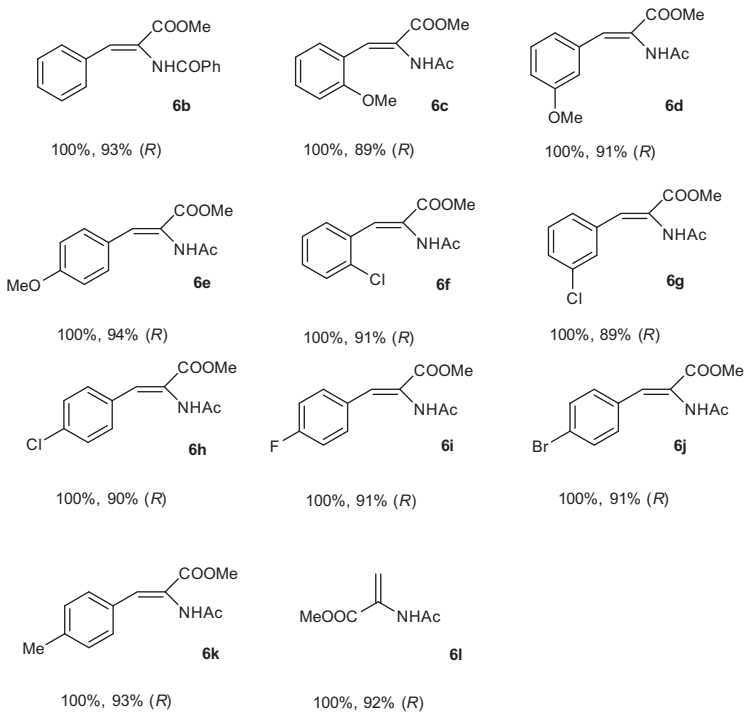


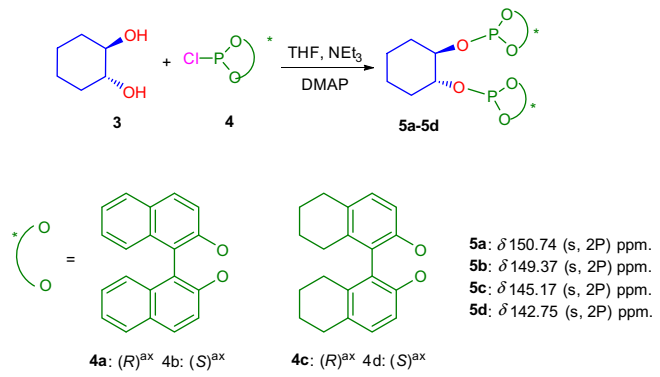
Figure 2. Selected results for the asymmetric Rh-catalyzed hydrogenation of substrates **6b**–**6l** using the $[Rh(cod)_2]BF_4$/**5b** catalytic system.

was found that the sense of enantiodiscrimination of the products was mainly determined by the configuration of the binaphthyl moieties.

2. Results and discussion

2.1. Synthesis of chiral phosphite ligands 5a–5d

As shown in Scheme 1, ligands **5a**–**5d** were synthesized in one step from commercially available (1*R*,2*R*)-*trans*-1,2-cyclohexanediol **3** (99% ee) and the corresponding diarylchlorophosphines **4**, which were derived from 2,2′-dihydroxy-1,1′-binaphthol (binaphthol), and 2,2′-dihydroxy-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthol (H_8-binaphthol) by procedures reported previously[10] (Scheme 1). In the ^{31}P NMR spectrum of **5a**, a singlet at 150.74 ppm was observed for the two equivalent phosphorus atoms. However, the chemical shift of **5c** moved to high field (145.17 ppm) when the biaryl moieties changed to H_8-binaphthol. Similarly, in the ^{31}P NMR spectrum of **5b**, the two phosphorus atoms appeared as a sharp singlet at 149.37 ppm. As expected,



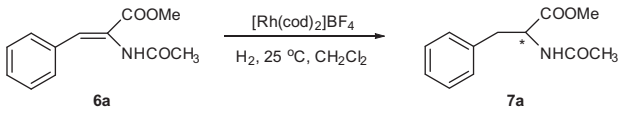
Scheme 1. The synthesis of diphosphite ligands derived from (1*R*,2*R*)-*trans*-1,2-cyclohexanediol.

the ^{31}P NMR spectrum of **5d** contains a singlet for the two equivalent phosphorus atoms and moved to a high field (142.75 ppm). This rule also applies to our previous literature data.[11]

2.2. Asymmetric hydrogenation of α-dehydroamino acid esters

The asymmetric hydrogenation of α-dehydroamino acid derivatives is considered to be one of the most important approaches for the preparation of various chiral α-amino acids, which are of great synthetic importance in the preparation of chiral drugs and natural products.[12] In the first set of experiments, we evaluated the diphosphite ligands **5a**–**5d** in the Rh-catalyzed asymmetric hydrogenation of (*Z*)-methyl 2-acetamido-3-phenylacrylate **6a**, which was used as a model substrate. The catalysts were prepared in situ by adding the corresponding ligands to the catalyst precursor $[Rh(cod)_2]BF_4$. The reaction proceeded smoothly at room temperature using CH_2Cl_2 as the solvent under 10 atm of H_2, and the results are summarized in Table 1. It was found that the catalysts showed high activities, and all catalysts completed the reactions under the conditions specified. Ligand **5a** give 22% ee (*S*) for methyl 2-acetamido-3-phenylpropanoate **7a** (Table 1, entry 1), and ligand **5b**, which bore (*S*)-binaphthyl in comparison with ligand **5a**, gave 92% ee (*R*) (Table 1, entry 2). However, only 5% ee (*S*) was achieved when using $[Rh(cod)_2]BF_4$/**5c** as the catalyst (Table 1, entry 3). In contrast, the configuration of the H_8-binaphthyl moiety was opposite to that of **5c** and gave 86% ee (*R*) (Table 1, entry 4) when **5d** was used as the ligand. It is noteworthy that ligand **5b** was the most efficient ligand in this reaction. The results indicated that the matching combination of the stereogenic centers of the cyclohexanediol backbone and the (*S*)-binaphthyl of ligand **5b** was fundamental to obtain higher enantioselectivity. By comparing entries 1–4 of Table 1, it can be seen that the sense of enantioselectivity was mainly determined by the configuration of the binaphthyl or H_8-binaphthyl moiety of ligands **5a**–**5d**, and an (*S*)-binaphthyl fragment gives an (*R*)-product and conversely an (*S*)-product for an (*R*)-binaphthyl.

Table 1
The effect of ligand structures and solvents on the enantioselectivity for the hydrogenation of α-dehydroamino acid esters[a]



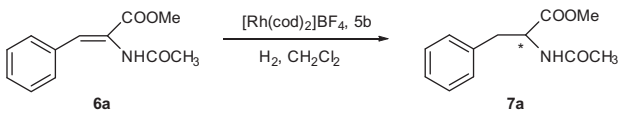
Entry	Ligands	Solvent	Conv.[b] (%)	ee[b] (%) (conf.)
1	**5a**	CH_2Cl_2	100	22 (*S*)
2	**5b**	CH_2Cl_2	100	92 (*R*)
3	**5c**	CH_2Cl_2	100	5 (*S*)
4	**5d**	CH_2Cl_2	100	86 (*R*)
5	**5b**	THF	41	8 (*R*)
6	**5b**	Et_2O	6	92 (*R*)
7	**5b**	Toluene	80	90 (*R*)
8	**5b**	Hexane	n.d.	n.d.

[a] $[Rh(cod)_2]BF_4$ (0.0025 mmol), ligand/Rh = 1.1, substrate/Rh = 100, $p(H_2)$ 10 atm, CH_2Cl_2 (3 mL), 25 °C, t = 6 h.
[b] The data on the conversion and enantiomeric excess were measured by GC with a Chirasil-L-Val column (25 m × 0.25 mm × 0.25 μm film thickness). The absolute configuration of the products was determined by comparison with authentic samples.

In addition, an obvious effect of the solvent on the reaction was observed. Using THF as the solvent gave poor enantioselectivity (Table 1, entry 5). Up to 92% ee (*R*) but only 6% conversion for **7a** was achieved when the reaction was carried out in Et_2O, and the poor solubility in Et_2O of substrate **6a** may give rise to this result (Table 1, entry 6). Both good activity and enantioselectivity were received when using toluene as the solvent (Table 1, entry 7). Hexane was proven to be the worst solvent for this reaction (Table 1, entry 8). In conclusion, CH_2Cl_2 was screened as the most appropriate solvent in terms of both conversion and selectivity in our cases.

The effect of other reaction parameters, such as pressure of H_2, the ratio of L./Rh, reaction temperature, and catalyst loading, was also investigated. No obvious change of enantioselectivity was seen when increasing the pressure of H_2 from 5 atm to 30 atm (Table 2, entries 1 and 2 vs Table 1, entry 2). The addition of one fold excess of ligand did not affect the outcome of the reaction (Table 2, entry 3). There was no change in the enantioselectivity when lowering the reaction temperature to 5 °C (Table 2, entry 4). Up to 90% ee was also achieved when the catalyst loading was decreased to 0.02 mol % (TON = 5000), which indicates that no decomposition of catalyst took place (Table 2, entry 8).[5b] For practical terms, this allowed us to perform the reaction at lower catalyst concentration without loss in activity or enantioselectivity.

Table 2
Effect of other factors on the enantioselectivity for the hydrogenation of α-dehydroamino acid esters[a]



Entry	Sub./Rh	L./Rh	$p(H_2)$ (atm)	t (h)	Conv.[b] (%)	ee[b] (%) (conf.)
1	100	1.1	5	6	100	92 (*R*)
2	100	1.1	30	6	100	91 (*R*)
3	100	2	10	6	100	90 (*R*)
4[c]	100	1.1	10	6	100	92 (*R*)
5	100	1.1	10	2	100	91 (*R*)
6	50	1.1	10	6	100	91 (*R*)
7	1000	1.1	30	12	100	91 (*R*)
8	5000	1.1	30	24	100	90 (*R*)

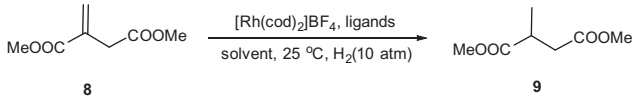
[a] $[Rh(cod)_2]BF_4$ (0.0025 mmol), CH_2Cl_2 (3 mL).
[b] The data on conversion, the enantiomeric excess, and the absolute configuration of the product were determined by the same condition as noted in Table 1.
[c] Reaction carried out at 5 °C.

With the optimized reaction conditions in hand, the hydrogenation of a variety of α-dehydroamino acid esters were carried out using $[Rh(cod)_2]BF_4$/**5b** as the catalyst. As shown in Figure 2, it can be seen that methyl 2-benzamido-3-phenylpropanoate was obtained with 93% ee. The hydrogenation appeared to be insensitive to the position of the substituent on the phenyl ring, and good enantioselectivities (mostly over 90% ee) were observed for the hydrogenation of substrates **6c**–**6h**. Moreover, the enantioselectivity was also hardly affected by the presence of either electron-donating or electron-withdrawing groups on the phenyl ring, for example see substrates **6e**, **6h**–**6k**. Methyl 2-acetamidoacrylate **6l** was also examined and up to 92% ee was achieved.

2.3. Asymmetric hydrogenation of dimethyl itaconate

In order to further investigate the catalytic performance of this catalytic system, we tested it in the Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate. The results are summarized in Table 3. In general the results followed the same trend as

Table 3
Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate[a]



Entry	Ligands	Sub./Rh	$p(H_2)$ (atm)	t (h)	Conv.[b] (%)	ee[b] (%) (conf.)
1	**5a**	100	10	6	100	48 (*R*)
2	**5b**	100	10	6	100	99 (*S*)
3	**5c**	100	10	6	100	3 (*R*)
4	**5d**	100	10	6	100	99 (*S*)
5	**5b**	100	2.5	1	100	99 (*S*)
6	**5b**	5000	30	6	100	99 (*S*)
7	**5b**	10,000	30	24	100	97 (*S*)

[a] $[Rh(cod)_2]BF_4$ (0.0025 mmol), ligand/Rh = 1.1, substrate/Rh = 100, $p(H_2)$ 10 atm, CH_2Cl_2 (3 mL), 25 °C, t = 6 h.
[b] The data on the conversion and enantiomeric excess were measured by GC with a gamma-DEX 225 column (30 m × 0.25 mm × 0.25 μm film thickness). The absolute configuration of the products was determined by comparison with authentic samples.

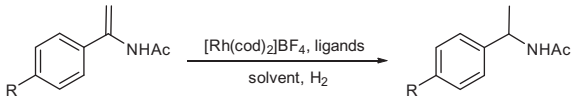
observed for the hydrogenation of **6a**. Again, the highest enantioselectivity (ee values up to 99%) was obtained when $[Rh(cod)_2]BF_4$/**5b** was used (Table 3, entry 2). Ligand **5d** also showed excellent asymmetric induction ability as compared to ligand **5b** (Table 3, entry 4). In fact, this reaction can be completely reacted within 1 h under 2.5 atm of H_2. Moreover, up to 97% ee was still attained although the value of TON reached 10,000 (Table 3, entry 7). It is worth mentioning that compared with substrates **6a**–**6k**, products with the opposite configuration were synthesized when substrate **8** was used.

2.4. Asymmetric hydrogenation of enamides

Enamides are important substrates for synthesis of optically active secondary amines, which are useful building blocks for the synthesis of fine chemicals.[5b] We subsequently applied ligands **5a**–**5d** in the Rh-catalyzed asymmetric hydrogenation of several enamides. Ligand **5b** also proved to be effective for this reaction using *N*-(1-phenylvinyl)acetamide **10a** as the substrate (Table 4, entries 1–4).

No significant changes in catalytic performance were observed when changing the hydrogen pressure and reaction temperature (Table 4, entries 7–9). The Rh-catalyzed asymmetric hydrogenation of other enamides was also assessed. Up to 99% ee for

Table 4
The Rh-catalyzed asymmetric hydrogenation of enamides[a]



10a: R=H
10b: R=F
10c: R=Cl
10d: R=Br
10e: R=Me

11a: R=H
11b: R=F
11c: R=Cl
11d: R=Br
11e: R=Me

Entry	Ligands	Substrates	Solvents	$p(H_2)$ (atm)	Conv.[b] (%)	ee[c] (%) (conf.)
1	**5a**	**10a**	CH_2Cl_2	10	100	33 (*S*)
2	**5b**	**10a**	CH_2Cl_2	10	100	91 (*R*)
3	**5c**	**10a**	CH_2Cl_2	10	100	15 (*S*)
4	**5d**	**10a**	CH_2Cl_2	10	100	87 (*R*)
5	**5b**	**10a**	Toluene	10	100	17 (*R*)
6	**5b**	**10a**	THF	10	18	78 (*R*)
7	**5b**	**10a**	CH_2Cl_2	5	100	91 (*R*)
8	**5b**	**10a**	CH_2Cl_2	30	100	91 (*R*)
9[d]	**5b**	**10a**	CH_2Cl_2	10	100	91 (*R*)
10	**5b**	**10b**	CH_2Cl_2	10	100	99 (*R*)
11	**5b**	**10c**	CH_2Cl_2	10	100	99 (*R*)
12	**5b**	**10d**	CH_2Cl_2	10	100	99 (*R*)
13	**5b**	**10e**	CH_2Cl_2	10	100	81 (*R*)

[a] $[Rh(cod)_2]BF_4$ (0.0025 mmol), ligand/Rh = 1.1, substrate/Rh = 100, solvent (3 mL), 25 °C, *t* = 6 h.
[b,c] The data on the conversion were measured by GC with a AT FFAP column (30 m × 0.25 mm × 0.25 μm film thickness), and enantiomeric excess was measured by GC with a CP-Chirasil-DEX CB column (25 m × 0.25 mm × 0.25 μm film thickness). The absolute configuration of the products was determined by comparison with authentic samples.
[d] Reaction carried out at 5 °C.

N-[1-(4-fluorophenyl)ethyl]acetamide **11b**, *N*-[1-(4-chlorophenyl) ethyl]acetamide **11c** and *N*-[1-(4-bromophenyl)ethyl]acetamide **11d** were obtained (Table 4, entries 10–12). These results show that the enantioselectivity is affected by the presence of electron-withdrawing groups at the *para* positions of the aryl group.

3. Conclusion

In conclusion, we have described the application of novel diphosphite ligands in the asymmetric hydrogenation reaction. These ligands can be easily prepared in a few steps from commercial (1*R*,2*R*)-*trans*-1,2-cyclohexanediol as a chiral source and the NMR data were consistent with the expectation for these ligands. Regarding both the good activity and the excellent enantioselectivity (up to 99% ee) obtained in the Rh-catalyzed asymmetric hydrogenations of α,β-unsaturated carboxylic acid derivatives and enamides, it can be demonstrated that the stereochemically matched combination of (1*R*,2*R*)-*trans*-cyclohexanediol backbone and (*S*)-binaphthyl in the ligand (1*R*,2*R*)-bis[(*S*)-1,1′-binaphthyl-2,2′-diyl]phosphitecyclohexane-diol was essential for inducing high enantioselectivity. The sense of enantiodiscrimination of products was predominately determined by the configuration of the biaryl moieties of ligands **5a**–**5d**. The application of these ligands to other transition metal-catalyzed asymmetric reactions is ongoing in our laboratory.

4. Experimental section

4.1. General

NMR spectra were recorded on Bruker 300 MHz or Bruker 400 MHz spectrometers. ^1H and ^{13}C NMR spectra were reported in parts per million with TMS (δ = 0.00 ppm) as an internal standard. ^{31}P NMR spectra were reported in parts per million with 85% H_3PO_4 as an external reference. Proton chemical shifts (δ) and coupling constants (*J*) are reported in ppm and Hz, respectively. Spin multiplicities were given as s (singlet), d (doublet), t (triplet), and m (multiplet). HRMS were recorded on a Bruker microTOF-QII mass instrument. All the melting points were determined on an X-4 melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin–Elmer 241 MC polarimeter at 20 °C.

All non-aqueous reactions and manipulations were performed under an N_2 atmosphere with standard Schlenk techniques. Reactions were monitored by thin layer chromatography (TLC, silica gel GF254 plates). Column chromatography separations were conducted on silica gel (200–300 mesh). NEt_3, THF, Et_2O, hexane, and toluene were distilled with Na and benzophenone as an indicator, and CH_2Cl_2 was dried over CaH_2 before use. H_8-binaphthol was prepared according to a literature procedure.[13] All the other chemicals were obtained commercially and used without further purification.

4.2. Synthesis of ligands 5a–5d

4.2.1. (1*R*,2*R*)-Bis[(*R*)-1,1′-binaphthyl-2,2′-diyl]phosphitecyclohexanediol 5a

To a 100 mL Schlenk flask equipped with a condenser were added 2.0 g of (*R*)-binaphthol, 20 mL of toluene, and 12 mL of PCl_3. Under a nitrogen atmosphere, the mixture was refluxed for 20 h. After removal of the excess PCl_3 and toluene, the residue was dissolved in 20 mL of toluene, and then was transferred to another Schlenk flask, and toluene was removed in vacuo to obtain (*R*)-1,1′-binaphthyl-2,2′-diyl-chlorophosphite **4a** as a white powder, which was used directly in the following step without further purification. To a stirred solution of compound **3** (77.6 mg, 0.67 mmol), compound **4a** (507.5 mg, 1.45 mmol), and 4-dimethylaminopyridine (DMAP) (17.7 mg, 0.15 mmol) in THF (10 mL) at −15 °C, NEt_3 (0.32 mL) was slowly added using a syringe over 2 min, after which the solution was stirred for 0.5 h at −15 °C. The mixture was then stirred at room temperature for 1 h. Next, THF was distilled off in vacuo, and toluene (20 mL) was added. The solid was removed by filtration through a pad of silica gel, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (R_f = 0.48, *n*-hexane/THF = 3:1), to furnish ligand **5a** as a white foamy solid (223.2 mg, 44.77% yield). $[\alpha]_D^{20}$ = −499 (*c* 0.15, CH_2Cl_2); mp 132–133 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 8.14 (d, *J* = 8.8 Hz, 2H, Ar), 8.06 (d, *J* = 8.2 Hz, 4H, Ar), 7.99 (d, *J* = 8.8 Hz, 2H, Ar), 7.47–7.57 (m, 6H, Ar), 7.44 (d, *J* = 8.8 Hz, 2H, Ar), 7.35 (dd, *J* = 15.6, 8.0 Hz, 4H, Ar), 7.25–7.29 (m, 2H, Ar), 7.22 (s, 2H, Ar), 4.17 (m, 2H, CH), 2.14 (t, *J* = 12.0 Hz, 2H, CH_2), 1.62 (s, 2H, CH_2), 1.47 (d, *J* = 10.0 Hz, 2H, CH_2), 1.17–1.27 (m, 2H, CH_2) ppm. ^{13}C NMR (101 MHz, DMSO-d_6) δ 147.94, 147.34, 132.46, 132.17, 131.58, 131.28, 131.09, 130.36, 129.08, 128.93, 127.13, 126.98, 126.39, 126.34, 125.72, 125.68, 124.02, 123.97, 122.45, 121.95, 77.56, 77.39, 32.75, 23.30 ppm. ^{31}P NMR (162 MHz, DMSO-d_6) δ 150.74 ppm. HRMS (ESI^+): calcd for $C_{46}H_{34}NaO_6P_2$ $[M+Na]^+$ 767.1723; found: 767.1725.

4.2.2. (1*R*,2*R*)-Bis[(*S*)-1,1′-binaphthyl-2,2′-diyl]phosphitecyclohexanediol 5b

(*S*)-1,1′-Binaphthyl-2,2′-diyl-chlorophosphite **4b** was synthesized by the same procedure as that of **4a**, and was used directly without further purification. Treatment of compound **3** (77.6 mg, 0.67 mmol), **4b** (507.5 mg, 1.45 mmol), and DMAP (17.7 mg, 0.15 mmol) as described for the synthesis of ligand **5a** afforded ligand **5b**, which was purified by flash chromatography (R_f = 0.53, *n*-hexane/THF = 3:1) to produce a white solid (175.1 mg, 49.13% yield). $[\alpha]_D^{20}$ = +180 (*c* 0.18, CH_2Cl_2); mp 138–139 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 8.14 (d, *J* = 8.8 Hz, 2H, Ar), 8.06 (d, *J* = 8.2 Hz, 2H, Ar), 7.99 (t, *J* = 8.0 Hz, 4H, Ar), 7.57 (d, *J* = 8.8 Hz,

2H, Ar), 7.52–7.41 (m, 6H, Ar), 7.30 (t, J = 7.6 Hz, 4H, Ar), 7.22–7.18 (m, 4H, Ar), 4.28 (s, 2H, CH), 1.89 (d, J = 12.2 Hz, 2H, CH_2), 1.59–1.36 (m, 4H, CH_2), 1.20 (s, 2H, CH_2) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.06, 147.31, 132.45, 132.16, 131.56, 131.20, 131.08, 130.44, 129.04, 128.92, 127.08, 126.95, 126.40, 126.34, 125.67, 125.49, 123.87, 123.82, 122.10, 122.02, 77.12, 76.98, 31.95, 22.61 ppm. ^{31}P NMR (161 MHz, DMSO-d_6) δ 149.37 ppm. HRMS (ESI$^+$): calcd for $C_{46}H_{34}NaO_6P_2$ [M+Na]$^+$ 767.1723; found: 767.1732.

4.2.3. (1*R*,2*R*)-Bis[(*R*)-1,1′-H_8-binaphthyl-2,2′-diyl]phosphitecyclohexanediol 5c

(*R*)-1,1′-H_8-Binaphthyl-2,2′-diyl-chlorophosphite **4c** was synthesized by the same procedure as that of **4a**, and was used directly without further purification. Treatment of compound **3** (77.6 mg, 0.67 mmol), **4c** (530.0 mg, 1.48 mmol), and DMAP (17.7 mg, 0.15 mmol) as described for the synthesis of ligand **5b** afforded ligand **5c**, which was purified by flash chromatography (R_f = 0.77, *n*-hexane/toluene = 1:1) to produce a white solid (185.1 mg, 46.34% yield). $[\alpha]_D^{20} = -153$ (*c* 0.11, CH_2Cl_2); mp 91–92 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 7.13 (d, J = 8.0 Hz, 2H, Ar), 7.06 (d, J = 8.0 Hz, 2H, Ar), 6.98 (d, J = 8.0 Hz, 2H, Ar), 6.84 (d, J = 8.0 Hz, 2H, Ar), 4.04 (s, 2H, CH), 2.85–2.70 (m, 8H, CH_2), 2.69–2.56 (m, 4H, CH_2), 2.13 (ddd, J = 28.0, 16.8, 8.2 Hz, 6H, CH_2), 1.81–1.67 (m, 12H, CH_2), 1.63 (s, 2H, CH_2), 1.57–1.30 (m, 8H, CH_2) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 146.32, 145.82, 137.30, 135.01, 133.83, 129.87, 129.41, 127.76, 119.38, 119.07, 77.17, 76.97, 32.78, 28.86, 27.72, 27.59, 23.41, 22.50, 22.41, 22.39, 22.28 ppm. ^{31}P NMR (161 MHz, DMSO-d_6) δ 145.17 ppm. HRMS (ESI$^+$): calcd for $C_{46}H_{50}NaO_6P_2$ [M+Na]$^+$ 783.2975; found: 767.2947.

4.2.4. (1*R*,2*R*)-Bis[(*S*)-1,1′-H_8-binaphthyl-2,2′-diyl]phosphitecyclohexanediol 5d

(*S*)-1,1′-H_8-Binaphthyl-2,2′-diyl-chlorophosphite **4d** was synthesized by the same procedure as that of **4a**, and was used directly without further purification. Treatment of compound **3** (64.9 mg, 0.56 mmol), **4d** (500.0 mg, 1.40 mmol), and DMAP (17.1 mg, 0.14 mmol) as described for the synthesis of ligand **5b** afforded ligand **5d**, which was purified by flash chromatography (R_f = 0.45, *n*-hexane/toluene = 2:1) to produce a white solid (132.7 mg, 41.16% yield). $[\alpha]_D^{20}$ = +170 (*c* 0.10, CH_2Cl_2); mp 105–106 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 7.13 (s, 2H, Ar), 7.06 (dd, J = 17.6, 8.2 Hz, 4H, Ar), 6.89 (d, J = 7.4 Hz, 2H, Ar), 4.16 (s, 2H, CH), 2.77 (s, 8H, CH_2), 2.59 (s, 4H, CH_2), 2.11 (d, J = 10.6 Hz, 6H, CH_2), 1.72 (s, 16H, CH_2), 1.47 (s, 6H, CH_2) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 146.37, 145.87, 137.35, 135.06, 133.88, 129.92, 129.46, 127.81, 119.43, 119.12, 77.22, 77.02, 32.83, 28.91, 27.77, 27.64, 23.46, 22.55, 22.46, 22.44, 22.33 ppm. ^{31}P NMR (161 MHz, DMSO-d_6) δ 142.75 ppm. HRMS (ESI$^+$): calcd for $C_{46}H_{50}NaO_6P_2$ [M+Na]$^+$ 783.2975; found: 767.3002.

4.3. Representative procedure for the Rh-catalyzed hydrogenation

After stirring a solution of $[Rh(cod)_2]BF_4$ (0.0025 mmol) and ligand **5b** (0.00275 mmol) in degassed CH_2Cl_2 (1 mL) at room temperature for 1 h, a solution of the corresponding substrate (0.25 mmol) in degassed CH_2Cl_2 (2 mL) was added. The mixture was transferred via syringe into a stainless autoclave that had been previously purged with argon. The hydrogenation was carried out in the autoclave at room temperature for 6 h. After releasing H_2, the reaction mixture was passed through a short silica gel column to remove the catalyst. After evaporation of the solvent under reduced pressure, the residue was purified by flash chromatography on silica gel. The data on conversion and enantiomeric excess of the product were determined by GC with a gamma-DEX 225 column (30 m × 0.25 mm × 0.25 μm film thickness) or Chirasil-L-Val column (25 m × 0.25 mm × 0.25 μm film thickness) or CP-Chirasil-DEX CB column (25 m × 0.25 mm × 0.25 μm film thickness) or AT FFAP (30 m × 0.25 mm × 0.25 μm film thickness). The absolute configuration was determined by comparison with authentic samples.

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