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Rhodium-catalyzed asymmetric hydroformylation of vinylarenes with novel chiral P,N-ligands derived from 1,2:5,6-di-*O*-cyclohexylidene-D-mannitol

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Abstract—Several new chiral P,N-ligands were prepared from 1,2:5,6-di-*O*-cyclohexylidene-D-mannitol, 1,1′-binaphthol, and phenyl isocyanate derivatives. Their Rh(I) complexes were applied as catalyst precursors in the asymmetric hydroformylation of vinylarenes. The steric and electronic properties of the phenylcarbamate substituents and the chiral binaphthyl moiety showed remarkable effects on the enantioselectivity and regioselectivity of the reaction. The matching combination of phenylcarbamate and the binaphthyl moiety of the ligand 1,2:5,6-di-*O*-cyclohexylidene-3-phenylcarbamate-4-[(*S*)-1,1′-binaphthyl-2,2′-diyl]phosphite-D-mannitol gave 50% ee and an 89/11 b/n ratio (branch-to-normal ratio). A synergic effect between the chiralities of mannitol and the binaphthol moieties was observed. Hydroformylation of the styrene gave the product in 75% ee when 1,2:5,6-di-*O*-cyclohexylidene-3,4-bis[(*R*)-1,1′-binaphthyl-2,2′-diyl]phosphite-D-mannitol was used as the chiral ligand.

1. Introduction

Asymmetric hydroformylation is a useful method for the preparation of optically active aldehydes, which are important intermediates for synthesizing biologically active compounds and new materials such as biodegradable polymers and liquid crystals,[1] The asymmetric hydroformylation with rhodium and platinum/tin catalytic systems bearing phosphine ligands have been widely investigated in this type of reaction.[1] However, the enantioselectivity of the asymmetric hydroformylation of styrene for rhodium systems[2] and the activity and chemoselectivity for platinum/tin systems[3] were generally poor. Over the last decade, asymmetric hydroformylation using Rh-diphosphite[4] and Rh-phosphine-phosphite (BINAPHOS) catalyst systems[5] gave better activities and selectivities than the phosphine-based ones. To date, the Rh-BINAPHOS system is the only catalyst applicable to the asymmetric hydroformylation of a wide variety of substrates although the synthesis of the ligand BINAPHOS was somewhat difficult. The catalytic systems had some disadvantages such as high CO pressure,[5] and its regioselectivity was not completely satisfactory.[6] Therefore, the design and synthesis of new chiral ligands for the asymmetric hydroformylation continues to be an active area of research.

The use of carbohydrates as starting materials for the synthesis of chiral ligands has several advantages: the raw materials are highly enantiomerically pure and are readily available, and the multifunctional property makes it possible to design various structures through a series of modifications. Chiral diphosphite ligands starting from D-mannitol and L-diethyl tartrate have been used in the asymmetric hydroformylation of styrene, while the catalytic activity of the diphosphites strongly depends on the bulkiness of the introduced substituents.[7] Chiral diphosphite ligands derived from an axially chiral biphenyl and D-galactopyranoside backbone have been used in the asymmetric hydroformylation of styrene, with up to 64% ee at 14% conversion being obtained using hydridorhodium diphosphite

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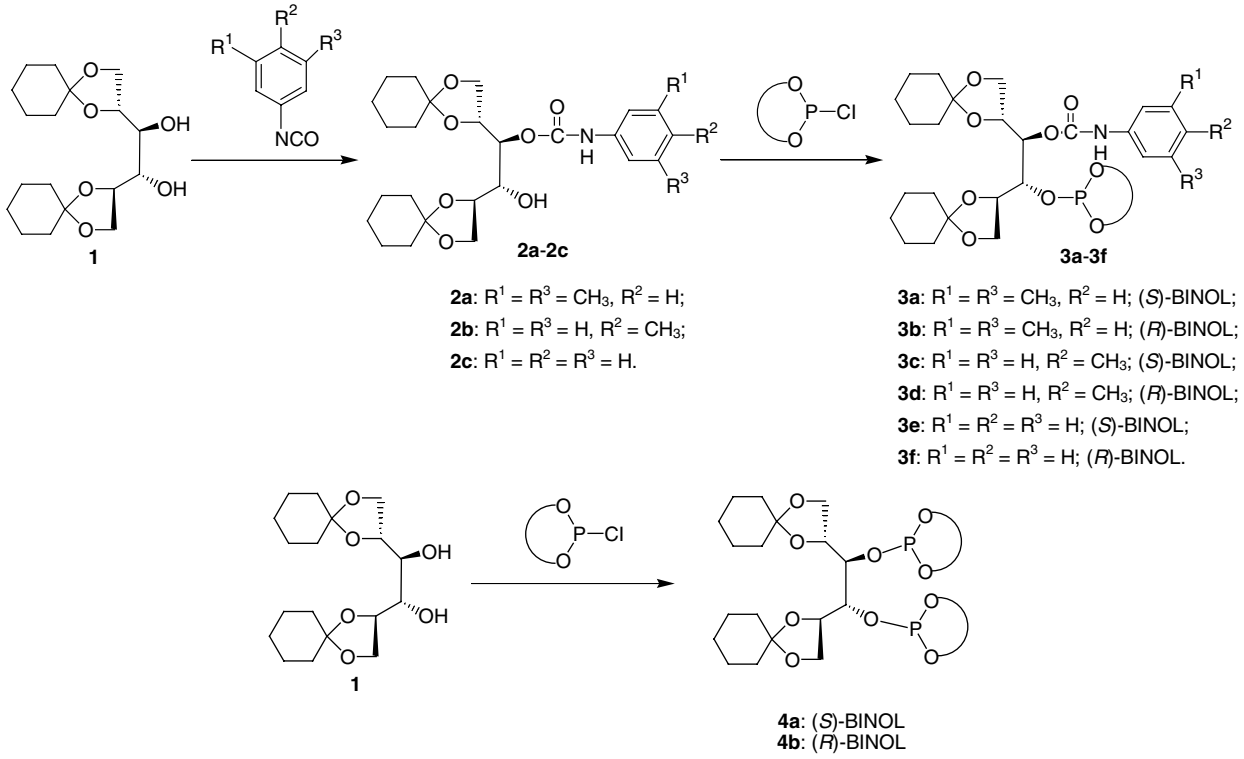


Scheme 1. The synthesis of chiral ligands.

dicarbonyl catalysts.[8] A new series of phosphite–phosphoroamidite ligands based on a furanoside backbone from glucose gave high regioselectivities and moderate enantioselectivities (up to 65% ee) in the asymmetric hydroformylation of styrene.[9a] Recently, new chelating diphosphite ligands with the furanoside backbone from glucose and axially chiral biphenyl or binaphthyl moieties have been applied to the asymmetric hydroformylation of vinylarenes; up to 91% ee and 97/3 b/n ratio were achieved under mild conditions.[9b,c]

Herein, we report the preparation and application of several new chiral P,N-ligands derived from 1,2:5,6-di-*O*-cyclohexylidene-D-mannitol, 1,1′-binaphthol and phenylisocyanate derivatives. The ligands have the axially chiral binaphthyl moiety and the phenylcarbamate substituents at either the 3- or 4-position of D-mannitol (Scheme 1). These Rh(acac)$(CO)_2$–ligand complexes were applied as catalyst precursors in the asymmetric hydroformylation of vinylarenes. The effect of the steric and electronic properties of phenylcarbamate substituents, and chiral binaphthyl moiety on the enantioselectivity and regioselectivity of the reaction was studied. A synergic effect between the stereogenic centers of D-mannitol and the chiral binaphthol substituents was observed.

2. Results and discussion

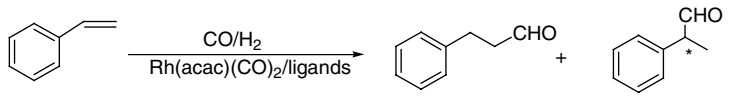
2.1. Synthesis of the chiral P,N-ligands

Chiral P,N-ligands **3a**–**f** were synthesized stereospecifically in two steps from 1,2:5,6-di-*O*-cyclohexylidene-D-mannitol **1**. The reaction of **1** with phenyl isocyanate derivatives produced the expected compounds **2a**–**c** in moderate yields. Reactions of compounds **2a**–**c** with 1.1 equiv of the desired phosphorochloride synthesized in situ[10] afforded the corresponding chiral P,N-ligands **3a**–**f** (Scheme 1). Chiral diphosphite ligands **4a** and **4b** were synthesized from compound **1** and the desired phosphorochloride synthesized in situ[10] (Scheme 1). All the ligands were stable on silica gel during the purification procedure under a nitrogen atmosphere. These ligands were white solids and were stable to air at room temperature.

2.2. Asymmetric hydroformylation of vinylarenes

The results of asymmetric hydroformylation of styrene[11] are summarized in Table 1. It is interesting to note that the chirality match between the mannitol backbone and the binaphthyl functional group could significantly influence the stereochemical outcome of the reaction. The use of ligand **3a** gave high regioselectivity (b/n = 93/7) but low enantioselectivity (34% ee) (Table 1, entry 1). In contrast, the use of ligand **3b** bearing the same 3,5-dimethyl-phenylcarbamate substituent and the axially chiral binaphthyl with a configuration opposite to that of ligand **3a** gave low regioselectivity (b/n = 87/13), the opposite sense of enantioselectivity with 6.7% ee (Table 1, entry 2). The use of ligand **3c** gave high regioselectivity (b/n = 91/9) and 19% ee (Table 1, entry 3). In contrast, the use of ligand **3d** bearing the same 4-methyl-phenylcarbamate substituent and the axially chiral binaphthyl with a configuration opposite to that of ligand **3c** gave low regioselectivity (b/n = 83/17) and racemic product (Table 1, entry 4). The use of ligands

Table 1. Asymmetric hydroformylation of styrene catalyzed by $Rh(acac)(CO)_2$/ligands[a]



5a **6a**, (n) **7a**, (b)

Entry	L	Conv.[b]	b/n[b]	%ee[c] (conf.)
1	**3a**	25	93/7	34% (*R*)
2	**3b**	32	87/13	6.7% (*S*)
3	**3c**	27	91/9	19% (*R*)
4	**3d**	30	83/17	Racemic
5	**3e**	22	89/11	50% (*S*)
6	**3f**	28	84/16	3.1% (*S*)
7	**4a**	0	0	0
8	**4b**	2.4	72/28	75% (*S*)

[a] Reaction conditions: styrene, 0.04 mL, 3.64 mg, 0.35 mmol; 0.5 mL of Toluene; S/C = 200, $Rh(acac)(CO)_2$, 0.45 mg, 0.00175 mmol; L/Rh = 4; CO, 800 psi, H_2, 800 psi; *T*, room temperature; *t*, 20 h.

[b] The data on the conversion and b/n ratio were determined by GC–MS analysis of styrene, 2-phenylpropanal, and 3-phenylpropanal.

[c] The ee was determined by GC analysis using a chiral capillary column (Chrompack Chirasil-Dex CB column, 50 m × 0.25 mm I.D.) of the corresponding methyl-2-phenylpropionate derived by esterification and Jones oxidation of the product. The absolute configuration was determined by methyl-2-phenylpropionate and the comparison of retention time with an authentic (*R*)-sample.

3e and **3f** bearing the same phenylcarbamate substituents but opposite in the configuration of binaphthyl moiety gave the same sense of enantioselectivity. However, ligand **3e** gave higher regioselectivity (b/n = 89/11) and better enantioselectivity (50% ee) (Table 1, entries 5 and 6). Comparison of these results clearly indicated that the steric and electronic properties of the phenylcarbamate substituent and the axially chiral binaphthyl moiety had a remarkable effect on the regioselectivity and enantioselectivity of the reaction. No reaction occurred when **4a** was used as the ligand (Table 1, entry 7). These results were very similar to those previously reported using 1,2:5,6-diisopropylidene-3,4-di(2,2′-bisphenoxyphosphinoxy)-D-mannitol as the ligand.[7] In contrast, the use of ligand **4b**, in which the chirality of the binaphthyl moiety was opposite to that in ligand **4a**, gave moderate enantioselectivity (75% ee) and regioselectivity (b/n, 72/28) even though the conversion was low (Table 1, entry 8). These results clearly indicated the existence of a synergic effect between the stereogenic centers of mannitol and the chiral binaphthol substituents.

As shown in Table 1, only **3e** and **4b** gave notable results in the asymmetric hydroformylation of styrene, and **3e** was used for the optimization of the reaction conditions as it gave better conversion and regioselectivity although the enantioselectivity was not high. A profound solvent effect on the enantioselectivity of the reaction was observed, although the solvent had little effect on the regioselectivity of the reaction. The results are summarized in Table 2. The use of dichloromethane or *n*-hexane gave comparable results (Table 2, entries 1 and 2), but ether solvents (ether and THF, Table 2, entries 3 and 4) seemed to be detrimental to the enantioselectivity. Contrary to the common notion that the use of trimethylorthoformate is effective in the reactions,[3b,12] a lower enantioselectivity (27% ee) was observed when trimethylorthoformate as a solvent was used (Table 2, entry 5). In methanol, most of the product aldehydes were obtained as the corresponding dimethyl acetals (Table 2, entry 6), indicating that the reaction conditions were fairly acidic in methanol.[5]

Table 2. The effect of solvents on asymmetric hydroformylation of styrene catalyzed by $Rh(acac)(CO)_2$/ligand **3e**[a]

Entry	L	Conv.[b]	b/n[b]	%ee[c] (conf.)
1	CH_2Cl_2	20	88/12	47% (*S*)
2	*n*-Hexane	30	86/14	54% (*S*)
3	Et_2O	32	85/15	28% (*S*)
4	THF	41	81/19	25% (*S*)
5[c]	Trimethylortho-formate ($C_4H_{10}O_3$)	11	89/11	27% (*S*)
6	Methanol	18	87/13[d]	34% (*S*)

[a] Reaction conditions: styrene, 0.04 mL, 3.64 mg, 0.35 mmol; 0.5 mL of solvent; S/C = 200, $Rh(acac)(CO)_2$, 0.45 mg, 0.00175 mmol; CO, 800 psi, H_2, 800 psi; *T*, room temperature; *t*, 20 h.

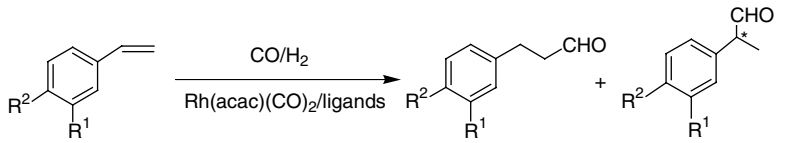
[b] The data on the conv., b/n ratio, and ee were determined using the same conditions as noted in Table 1.

[c] 0.5 mL of trimethylorthoformate ($C_4H_{10}O_3$).

[d] The product: 2-phenylpropanal, 3-phenylpropanal, dimethyl acetal of 2-phenylpropanal, and dimethyl acetal of 3-phenylpropanal.

Biologically active compounds bearing a trifluoromethyl or pentafluorophenyl group may possess unique physiological activities.[13] Hydroformylation of fluorinated olefins would be a convenient method to synthesize the intermediates of such compounds. 3-Fluorostyrene **5b** and 4-fluorostyrene **5c** were tested for asymmetric hydroformylation with $Rh(acac)(CO)_2$ in the presence of ligands **3e** and **4b**, respectively. As shown in Table 3, the reaction of substrate **5b** in *n*-hexane gave 40% ee when ligand **3e** was used (Table 3, entry 1), while the use of ligand **4b** gave the product with 17% ee (Table 3, entry 2). The reaction of substrate **5c** in *n*-hexane gave the product in 27% ee when ligand **3e** was used (Table 3, entry 3), while the use of ligand **4b** gave the product in 15% ee (Table 3, entry 4). It should be noted that the reaction of substrates **5b** and **5c** showed significantly

Table 3. Asymmetric hydroformylation of 3-fluorostyrene and 4-fluorostyrene catalyzed by Rh(acac)$(CO)_2$/ligand **3e** or **4b** complex[a]



5b, R^1 = F, R^2 = H
5c, R^1 = H, R^2 = F

6b, R^1 = F, R^2 = H
6c, R^1 = H, R^2 = F

7b, R^1 = F, R^2 = H
7c, R^1 = H, R^2 = F

Entry	Sub	L	Conv.[b]	b/n[b]	%ee[c] (conf.)[d]
1	**5b**	**3e**	25	90/10	40% (*S*)
2	**5b**	**4b**	70	80/20	17% (*R*)
3	**5c**	**3e**	68	74/26	27% (*S*)
4	**5c**	**4b**	99	80/20	15% (*R*)

[a] Reaction conditions: substrate **5b** or **5c**, 0.35 mmol; 0.5 mL of solvent, *n*-C_6H_{14}; S/C = 200, Rh(acac)$(CO)_2$, 0.45 mg, 0.00175 mmol; L/Rh = 4; CO, 800 psi, H_2, 800 psi; *T*, room temperature; *t*, 20 h.

[b] The data on the conversion and b/n ratio were determined using the same conditions as noted in Table 1.

[c] The ee of the product of **5b** was determined using the same conditions as noted in Table 1. The ee of the product of **5c** was determined by HPLC analysis of the corresponding methyl-2-(4-fluorophenyl)propionate derived by esterification and Jones oxidation of the product using a chiral column (Chiralcel OJ 25 × 0.46 cm I.D.).

[d] The absolute configurations of compounds **7b** and **7c** were assigned from their chromatographic behavior.

different enantioselectivity in the presence of ligand **3e** (Table 3, entries 1 and 3). This possibly indicates that the effect of the steric and electronic properties of substrates **5b** and **5c** on the enantioselectivity was very important when **3e** was used as a chiral ligand.

3. Conclusion

New chiral P,N-ligands were prepared from 1,2:5,6-di-*O*-cyclohexylidene-D-mannitol, 1,1′-binaphthol, and phenyl isocyanate derivatives. The ligands had the axially chiral binaphthyl moiety and the phenylcarbamate substituent at the 3- or 4-position of D-mannitol. The Rh(acac)$(CO)_2$–ligand complexes were applied as catalyst precursors in the asymmetric hydroformylation of vinylarenes. The steric and electronic properties of the phenylcarbamate substituent and the axially chiral binaphthyl moiety revealed a remarkable effect on the b/n ratio and ee of the reaction. Ligand **3e** gave 50% ee and regioselectivity 89/11 (b/n). A synergic effect between the stereogenic centers C-3 and C-4 of mannitol and the chiral binaphthol substituents was also observed. Up to 75% ee using ligand **4b** was obtained.

4. Experimental

4.1. Reagents and materials

All experiments were carried out under a nitrogen atmosphere. Phenyl isocyanate, 3-methylphenyl isocyanate, and 3,5-dimethylphenyl isocyanate were purchased from Acros and used without further purification. Styrene, 3-fluorostyrene, and 4-fluorostyrene were purchased from Aldrich, distilled, and degassed with dry nitrogen before use. Toluene, ether, methanol, and THF were distilled from sodium. Dichloromethane and *n*-hexane were distilled over calcium hydride. The other commercially available reagents were used as received without further purification. ^{1}H NMR, ^{13}C NMR, and ^{31}P NMR were recorded on a Varian AS 500 at room temperature. ^{1}H NMR spectra are reported in parts per million with TMS as an internal standard ($\delta = 0$ ppm). ^{31}P NMR spectra are reported in parts per million with 85% H_3PO_4 as an external reference.

4.2. 1,2:5,6-Di-*O*-cyclohexylidene-3-[(3,5-dimethyl)phenylcarbamate]-D-mannitol 2a, 1,2:5,6-di-*O*-cyclohexylidene-3-[(3-methyl)phenylcarbamate]-D-mannitol 2b, and 1,2:5,6-di-*O*-cyclohexylidene-3-phenyl-carbamate-D-mannitol 2c

1,2:5,6-Di-*O*-cyclohexylidene-D-mannitol **1** (1.0 g, 2.92 mmol) was dissolved in 20 mL of dichloromethane, and mixed at room temperature with 4-*N*,*N*-dimethylaminopyridine (DMAP, 0.025 g, 0.205 mmol) and 3,5-dimethylphenyl isocyanate (0.43 g, 2.92 mmol). The reaction mixture was stirred for 12 h at room temperature, and the dichloromethane was distilled off under reduced pressure at room temperature. The residue was purified by column chromatography (eluent: CH_2Cl_2/EA = 10) to produce **2a** as white powder (0.805 g, 58%). ^{1}H NMR ($CDCl_3$): $\delta = 1.30$–1.59 (m, 20H), 2.21 (s, 6H), 3.85 (m, 1H), 3.96 (m, 3H), 4.06 (m, 2H), 4.37 (dd, $J = 6.5$ and 12.0 Hz, 1H), 5.00 (d, $J = 5.5$ Hz, 1H), 6.65 (s, NH), 6.90–6.94 (m, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 21.5$, 23.9, 24.1, 24.2, 25.1, 25.2, 34.7, 34.8, 36.3, 36.7, 65.6, 66.2, 71.0, 73.4, 75.0, 75.3, 77.0, 77.2, 77.4, 77.5, 109.9, 110.6, 116.5, 125.6, 137.6, 139.0, 152.8 ppm.

Treatment of compound **1** and 3-methylphenyl isocyanate as described for compound **2a** yielded compound **2b** as a white powder (0.62 g, 45%). ^{1}H NMR ($CDCl_3$): $\delta = 1.38$–1.66 (m, 20H), 2.30 (s, 3H), 3.90–4.14 (m, 6H), 4.44 (dd, $J = 6.0$ and 12.0 Hz, 1H), 5.07 (d, $J = 5.0$ Hz, 1H), 6.84 (s, NH), 7.26–7.27 (m, 4H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 20.7$, 23.7, 23.9, 24.0, 25.0,

25.1, 30.9, 34.5, 34.6, 36.1, 36.5, 65.5, 66.0, 70.9, 75.1, 76.7, 77.0, 77.3, 77.5, 110.0, 110.7, 119.0, 129.9, 133.6, 135.2, 152.9 ppm.

Treatment of compound **1** and phenyl isocyanate as described for compound **2a** yielded compound **2c** as a white powder (0.51 g, 39%). ^{1}H NMR ($CDCl_3$): $\delta = 1.53$–1.66 (m, 20H), 2.8 (d, 1H), 3.93 (dd, 1H), 4.05 (m, 2H), 4.13 (m, 2H) ppm, 4.47 (dd, $J = 6.5$ and 12.5 Hz, 1H), 5.10 (d, $J = 5.5$ Hz, 1H), 6.81 (s, 1H), 7.26–7.27 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 19.7$, 22.7, 23.8, 24.1, 25.0, 30.8, 34.4, 34.6, 35.8, 36.5, 65.4, 66.1, 71.9, 74.1, 75.7, 76.0, 76.3, 76.5, 109.0, 110.8, 118.0, 128.9, 133.6, 134.2, 150.9 ppm.

4.3. 1,2:5,6-Di-*O*-cyclohexylidene-3-[(3,5-dimethyl)phenylcarbamate]-4-[(*S*)-1,1′-binaphthyl-2,2′-diyl]phosphite-D-mannitol 3a and 1,2:5,6-di-*O*-cyclohexylidene-3-[(3,5-dimethyl)phenylcarbamate]-4-[(*R*)-1,1′-binaphthyl-2,2′-diyl]phosphite-D-mannitol 3b

(*S*)-1,1′-Binaphthyl-2,2′-diyl-chlorophosphine (0.87 mmol) was synthesized in situ[10] and dissolved in toluene (10 mL). Compound **2a** (0.381 g, 0.8 mmol) was azeotropically dried with toluene (3×10 mL) and then dissolved in triethylamine (4 mL) to which DMAP (0.01 g, 0.083 mmol) had been added. A solution of phosphorochloridite was transferred slowly to a solution of compound **2a** at 0 °C. The reaction mixture was stirred overnight at room temperature, and the formed triethylamine salts were removed by filtration. Evaporation of the solvent gave a white foam, which was purified by flash chromatography (CH_2Cl_2/Et_2O, 9/1, $R_f = 0.86$) to produce **3a** as white powder (0.42 g, 66%). ^{31}P NMR (202 MHz, $CDCl_3$), $\delta = 153.7$ ppm. ^{1}H NMR ($CDCl_3$): $\delta = 1.61$–1.86 (m, 20H), 2.30 (s, 6H), 3.94–4.14 (m, 3H), 4.29 (s, 2H), 4.53 (d, $J = 7.0$ Hz, 1H), 4.92 (s, 1H), 5.22 (d, $J = 7.5$ Hz, 1H), 6.74 (s, NH), 7.01–8.02 (m, 15H, Ar–H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 21.6$, 21.7, 24.0, 24.3, 25.5, 33.9, 35.3, 35.9, 36.8, 64.1, 66.9, 72.9, 74.3, 75.1, 75.6, 77.1, 77.3, 77.6, 110.0, 110.6, 116.6, 122.0, 122.3, 123.2, 124.7, 125.3, 125.6, 125.9, 126.3, 126.5, 127.3, 128.5, 128.6, 129.3, 130.2, 130.6, 131.4, 131.8, 132.9, 133.1, 137.3, 138.1, 139.1, 147.3, 147.6, 148.6, 152.3 ppm.

Treatment of the in situ formed[10] (*R*)-1,1′-binaphthyl-2,2′-diyl-chlorophosphine (0.87 mmol) and compound **2a** afforded ligand **3b**, which was purified by flash chromatography (CH_2Cl_2/Et_2O, 9/1, $R_f = 0.87$) to produce a white powder (0.30 g, 47%). ^{31}P NMR (202 MHz, $CDCl_3$), $\delta = 156.6$ ppm. ^{1}H NMR ($CDCl_3$): $\delta = 1.32$–1.71 (m, 20H), 2.31 (s, 6H), 3.87 (s, 1H), 4.08 (d, $J = 22$ Hz, 2H), 4.23 (s, 1H), 4.34 (d, $J = 4.5$ Hz, 1H), 4.46 (s, 1H), 5.06 (d, $J = 7.0$ Hz, 1H), 5.15 (d, $J = 6.5$ Hz, 1H), 6.56 (s, NH), 6.75–8.01 (m, 15H, Ar–H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 21.0$, 21.7, 24.0, 24.3, 26.5, 33.9, 35.3, 36.8, 64.1, 66.9, 73.9, 74.3, 75.1, 75.3, 75.9, 77.1, 77.3, 77.6, 110.0, 110.6, 116.6, 122.0, 122.8, 123.2, 124.7, 125.1, 125.3, 125.6, 125.9, 126.4, 126.5, 127.3, 128.5, 128.6, 129.3, 130.2, 130.6, 131.1, 131.8, 132.9, 133.1, 137.3, 138.1, 139.1, 147.2, 147.6, 148.9 ppm.

4.4. 1,2:5,6-Di-*O*-cyclohexylidene-3-[(4-methylphenylcarbamate)]-4-[(*S*)-1,1′-binaphthyl-2,2′-diyl]phosphite-D-mannitol 3c and 1,2:5,6-di-*O*-cyclohexylidene-3-[(4-methylphenylcarbamate)-4-[(*R*)-1,1′-binaphthyl-2,2′-diyl]phosphite-D-mannitol 3d

Treatment of the in situ formed[10] (*S*)-1,1′-binaphthyl-2,2′-diyl-chlorophosphine (0.87 mmol) and compound **2b** afforded ligand **3c**, which was purified by flash chromatography (CH_2Cl_2/Et_2O, 9/1, $R_f = 0.85$) to produce a white powder (0.25 g, 40%). ^{31}P NMR (202 MHz, $CDCl_3$), $\delta = 154.5$ ppm. ^{1}H NMR ($CDCl_3$): $\delta = 1.32$–1.74 (m, 20H), 2.23 (s, 3H), 3.86 (m, 1H), 3.95 (m, 1H), 4.13 (m, 3H), 4.40 (d, $J = 6.0$ Hz, 1H), 4.78 (d, $J = 12.5$ Hz, 1H), 5.08 (d, $J = 7.0$ Hz, 1H), 6.49 (s, NH), 6.91–7.91 (m, 16H, Ar–H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 21.5$, 23.9, 24.3, 25.6, 33.0, 35.5, 35.8, 36.6, 64.7, 65.9, 71.9, 76.6, 76.9, 77.0, 77.9, 109.0, 110.8, 117.9, 121.0, 122.1, 122.2, 123.2, 124.6, 124.7, 125.0, 125.1, 125.3, 126.3, 126.5, 127.0, 127.2, 128.3, 128.6, 129.8, 130.1, 130.5, 131.2, 131.8, 132.9, 133.1, 133.6, 134.8, 147.6, 148.3, 148.6, 151.3 ppm.

Treatment of the in situ formed[10] (*R*)-1,1′-binaphthyl-2,2′-diyl-chlorophosphine (0.87 mmol) and compound **2b** afforded ligand **3d**, which was purified by flash chromatography (CH_2Cl_2/Et_2O, 9/1, $R_f = 0.83$) to produce a white powder (0.27 g, 43%). ^{31}P NMR (202 MHz, $CDCl_3$), $\delta = 157.6$ ppm. ^{1}H NMR ($CDCl_3$): $\delta = 1.33$–1.84 (m, 20H), 2.20 (s, 3H), 3.73 (s, 1H), 3.94 (m, 2H), 4.07 (m, 1H), 4.18 (d, $J = 8.0$ Hz, 1H), 4.32 (s, 1H), 4.91 (d, $J = 7.5$ Hz, 1H), 5.01 (d, $J = 6.5$ Hz, 1H), 6.46 (s, NH), 6.99–7.88 (m, 16H, Ar–H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 21.0$, 24.0, 24.3, 25.5, 33.9, 35.2, 35.9, 36.7, 64.0, 66.9, 72.9, 75.6, 77.0, 77.3, 77.5, 109.9, 110.5, 118.9, 122.0, 122.1, 122.2, 123.1, 124.6, 124.7, 125.0, 125.1, 125.3, 126.2, 126.5, 127.2, 127.3, 128.5, 128.6, 129.8, 130.2, 130.5, 131.4, 131.8, 132.9, 133.1, 133.7, 134.9, 147.6, 148.5, 148.6, 150.8 ppm.

4.5. 1,2:5,6-Di-*O*-cyclohexylidene-3-phenylcarbamate-4-[(*S*)-1,1′-binaphthyl-2,2′-diyl]phosphite-D-mannitol 3e and 1,2:5,6-di-*O*-cyclohexylidene-3-phenylcarbamate-4-[(*R*)-1,1′-binaphthyl-2,2′-diyl]phosphite-D-mannitol 3f

Treatment of the in situ formed[10] (*S*)-1,1′-binaphthyl-2,2′-diyl-chlorophosphine (0.87 mmol) and compound **2c** afforded ligand **3e**, which was purified by flash chromatography (CH_2Cl_2/Et_2O, 9/1, $R_f = 0.87$) to produce a white powder (0.26 g, 43%). ^{31}P NMR (202 MHz, $CDCl_3$), $\delta = 154.5$ ppm. ^{1}H NMR ($CDCl_3$): $\delta = 1.32$–1.74 (m, 20H), 2.23 (s, 3H), 3.86 (m, 1H), 3.95 (m, 1H), 4.13 (m, 3H), 4.40 (d, $J = 6.5$ Hz, 1H), 4.78 (d, $J = 7.0$ Hz, 1H), 5.08 (d, $J = 8.0$ Hz, 1H), 6.49 (s, NH), 6.91–7.91 (m, 16H, Ar–H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 24.1$, 24.2, 24.7, 25.3, 25.6, 33.9, 35.2, 35.6, 36.7, 64.0, 66.3, 72.7, 75.0, 77.0, 77.3, 77.5, 109.0, 110.6, 113.3, 118.0, 118.4, 122.1, 122.8, 123.7, 124.0, 124.5, 124.6, 124.9, 125.6, 126.6, 127.0, 127.1, 127.7, 128.0, 128.9, 129.0, 129.3, 129.5, 130.0, 130.6, 131.6, 132.8, 133.1, 133.8, 152.6 ppm.

Treatment of the in situ formed[10] (*R*)-1,1′-binaphthyl-2,2′-diyl-chlorophosphine (0.87 mmol) and compound

2c afforded ligand **3f**, which was purified by flash chromatography (CH_2Cl_2/Et_2O, 9/1, $R_f = 0.84$) to produce a white powder (0.28 g, 46%). ^{31}P NMR (202 MHz, $CDCl_3$), $\delta = 156.1$ ppm. ^1H NMR ($CDCl_3$): $\delta = 1.17$–1.83 (m, 20H), 3.712 (s, 1H), 3.87 (s, 1H), 3.93 (s, 1H), 4.08 (s, 1H), 4.18 (d, $J = 6.5$ Hz, 1H), 4.31 (s, 1H), 4.90 (d, $J = 7.5$ Hz, 1H), 5.01 (d, $J = 7.0$ Hz, 1H), 6.51 (s, NH), 6.94–7.84 (m, 17H, Ar–H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 24.0$, 24.2, 24.3, 25.5, 25.6, 34.0, 35.2, 35.9, 36.8, 64.1, 66.9, 72.9, 75.6, 77.1, 77.3, 77.6, 110.0, 110.6, 111.3, 118.1, 118.8, 122.0, 122.3, 123.2, 124.3, 124.5, 124.6, 124.7, 125.6, 126.6, 127.2, 127.3, 127.7, 128.5, 128.6, 129.1, 129.3, 129.7, 130.2, 130.6, 131.8, 132.9, 133.1, 133.7, 152.3 ppm.

4.6. 1,2:5,6-Di-*O*-cyclohexylidene-3,4-bis[(*S*)-1,1′-binaphthyl-2,2′-diyl]phosphite-D-mannitol 4a and 1,2:5,6-di-*O*-cyclohexylidene-3,4-bis[(*R*)-1,1′-binaphthyl-2,2′-diyl]phosphite-D-mannitol 4b

Compound **1** (0.206 g, 0.6 mmol) and DMAP (0.015 g, 0.123 mmol) were put in a 50 mL round-bottomed flask. Toluene (5 mL) and dry triethylamine (0.2 mL) were added under dry nitrogen. The mixture was cooled to 0 °C with an ice-bath, (*S*)-1,1′-binaphthyl-2,2′-diyl-chlorophosphine (1.2 mmol) synthesized in situ[10] in toluene (5 mL) was added dropwise in the solution and stirred for 30 min under 0 °C, then left at room temperature overnight. The solvent was removed in vacuo and the residues were purified by flash chromatography (toluene, $R_f = 0.33$) to produce **4a** as white powder (0.47 g, 81%). ^{31}P NMR (202 MHz, CD_2Cl_2), $\delta = 153.4$ ppm. ^1H NMR (CD_2Cl_2): $\delta = 1.49$–1.79 (m, 20H), 4.22–4.27 (m, 4H), 4.61–4.65 (m, 2H), 4.80–4.84 (m, 2H), 7.23–8.06 (m, 12H) ppm. ^{13}C NMR (125 MHz, CD_2Cl_2): $\delta = 24.1$, 24.5, 25.5, 35.1, 37.0, 67.2, 73.9, 76.4, 110.9, 122.0, 122.3, 125.3, 125.5, 125.6, 126.6, 126.7, 127.1, 127.2, 128.5, 128.8, 129.3, 130.1, 130.8, 131.5, 132.0, 132.8, 133.1, 147.5, 148.3 ppm.

Treatment of the in situ formed[10] (*R*)-1,1′-binaphthyl-2,2′-diyl]-chlorophosphine (1.2 mmol) and compound **1** afforded ligand **4b**, which was purified by flash chromatography (toluene, $R_f = 0.34$) to produce a white powder (0.49 g, 84%). ^{31}P NMR (202 MHz, CD_2Cl_2), $\delta =$ 155.1 ppm. ^1H NMR (CD_2Cl_2): $\delta = 1.52$–1.58 (m, 4H), 1.78–1.86 (m, 16H), 4.15–4.18 (m, 2H), 4.28–4.31 (m, 2H), 4.49–4.52 (m, 2H), 4.79–4.82 (m, 2H), 7.30–7.56 (m, 8H), 7.89–8.05 (m, 4H) ppm. ^{13}C NMR (125 MHz, CD_2Cl_2): $\delta = 24.3$, 24.4, 25.6, 34.7, 36.6, 66.5, 74.3, 76.9, 77.1, 110.5, 121.8, 121.9, 122.9, 124.6, 125.2, 125.4, 125.6, 126.4, 126.6, 127.1, 128.5, 128.7, 129.3, 130.3, 130.7, 131.4, 131.9, 132.7, 133.1, 147.5, 148.1 ppm.

4.7. General procedure for the enantioselective hydroformylation of styrene

A 50 mL stainless steel autoclave was charged with styrene, toluene, ligand, and $Rh(acac)(CO)_2$ under a nitrogen atmosphere. The autoclave was pressurized with CO and H_2. The reaction mixture was stirred with a magnetic stirrer at room temperature. After a prescribed reaction time, the residue gas was released. The data on the conversion and b/n ratio were determined by GC–MS analysis of styrene, 2-phenylpropanal, and 3-phenylpropanal on an HPG 1800c GCD system on a Bexs column (30 m × 0.25 mm I.D.). The ee was determined by GC analysis of the corresponding methyl-2-phenylpropionate derived by Jones oxidation and subsequent esterification of the product using an HP5890 gas chromatograph equipped with Chrompack Chirasil-Dex CB column (50 m × 0.25 mm I.D.). The absolute configuration of **7a** was determined by methyl-2-phenylpropionate and the comparison of retention time with an (*R*)-sample. The absolute configurations of compounds **7b/7c** were temporarily assigned from their chromatographic behavior.

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