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Novel atropisomeric bisphosphine ligands with a bridge across the 5,5′-position of the biphenyl for asymmetric catalysis

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Abstract—A new type of atropisomeric bisphosphine ligand **2** with a bridge across the 5,5′-position of the biphenyl has been developed. The axial chirality of this type of ligands can be retained by macrocyclic ring strain produced from 5,5′-linkage of the biphenyl even without 6,6′-substituents on the biphenyls. Ligand (*R*)-**2a** showed good catalytic activity and enantioselectivity for Rh(I)-catalyzed asymmetric hydrogenation of (*Z*)-α-acetamidocinnamic acid **11**.

1. Introduction

The design and synthesis of chiral phosphine ligands has played a significant role in the development of transition-metal catalyzed asymmetric reactions, and have attracted a great deal of attention from both academia and industry.[1] Since Noyori et al. developed the axially chiral bisphosphine ligand BINAP in the early 1980s,[2] many bisphosphine ligands supported by an atropisomeric scaffold have been developed and applied successfully in various asymmetric catalytic reactions.[3] It was found that modulation of the steric and electronic properties of the atropisomeric scaffold of the ligand could remarkably influence their efficiency in asymmetric catalytic reactions. Recently, the steric design of the biaryl core has been extensively explored with ligands such as BIPHEMP,[4] MeO-BIPHEP,[4] TunePhos,[5] SEGPHOS,[6] SYNPHOS,[7] and DIFLUORPHOS.[8] It was demonstrated that the ligands display a narrow dihedral angle of biaryl backbone and showed better enantioselectivities in the Ru(II)-catalyzed asymmetric hydrogenation of β-keto esters. Recently, we have developed a novel atropisomeric framework **1** (Fig. 1),[9] in which the biphenyl has only two coordinating groups next to the axis, and the axial chirality of the ligands can be retained by steric hindrance of two bulky coordinating groups and macrocyclic ring strain produced from the 5,5′-linkage of the biphenyls even without 6,6′-substituents. The modulation of the length of the backbone carbon chain could control the conformational flexibility of the metal chelate rings formed with atropisomeric ligands to provide a more suitable chiral environment for asymmetric catalysis. When the coordinating groups are chiral oxazolines, they display stable axial chirality, and their palladium complexes as catalysts show high catalytic activity and enantioselectivity in the asymmetric Wacker-type cyclization of allylphenols.[9]

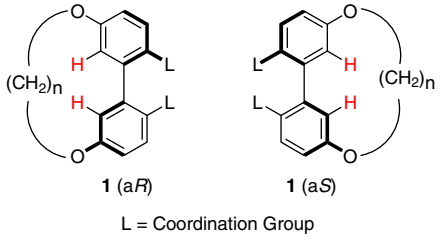

Figure 1. Atropisomeric ligands with a bridge across the 5,5′-positions of the biphenyl.

In contrast with atropisomeric BINAP-type ligands, their simple analog NAPHOS (Fig. 2), which forms a nine-membered ring with metals, is not so effective for asymmetric hydrogenation.[10] It is generally believed that the low enantioselectivities with NAPHOS-type atropisomeric phosphines are largely due to the formation of conformationally flexible nine-membered metal-chelate rings. Thus, a transfer of the backbone chirality through an additional methylene group before the phenyl group on the phosphine may not be efficient. Significantly, high enantioselectivities were achieved for the Rh(I)-catalyzed asymmetric

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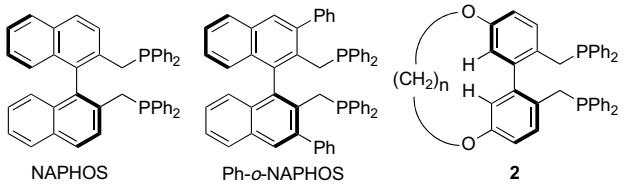
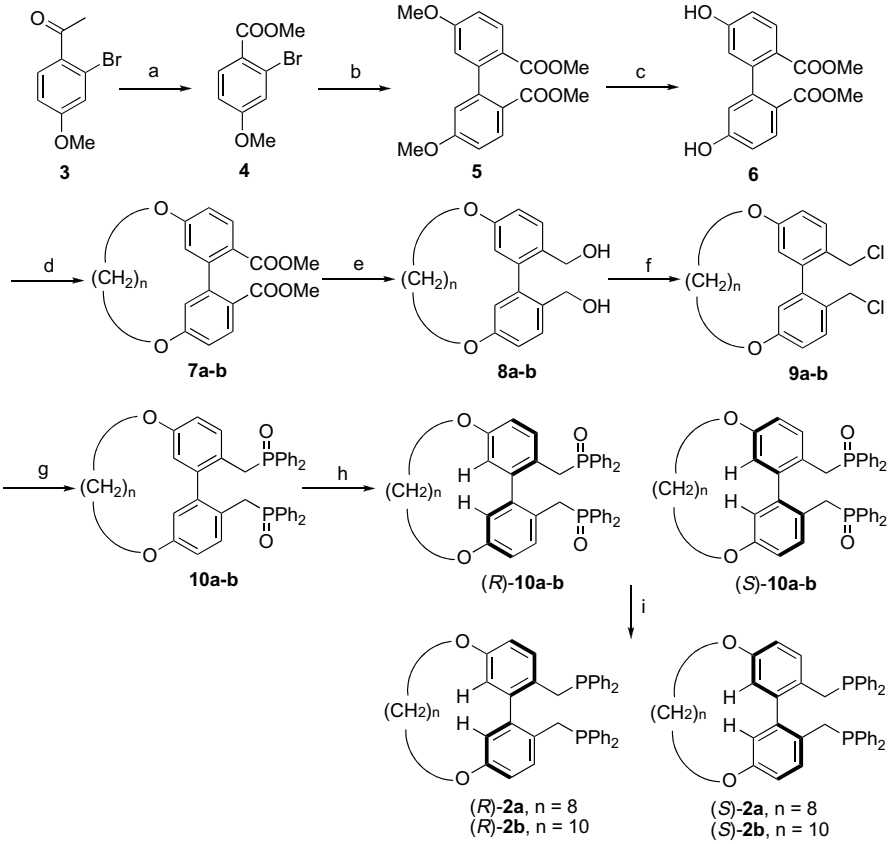


Figure 2. NAPHOS-type ligands forming nine-membered metal chelate rings.

hydrogenation of functional olefins using modified NAPHOS (Ph-*o*-NAPHOS) in which two phenyl groups were introduced at the 3,3′-positions of NAPHOS to improve the conformational rigidity of the nine-membered metal chelate ring.[11] Based on this knowledge, if the phosphinomethyl groups were introduced at the 2,2-positions on our atropisomeric framework **1**, the conformational flexibility of nine-membered metal chelate rings could be controlled by a macrocyclic ring strain of the 5,5′-linkage of the biphenyls to lead to an improvement of enantioselectivities for Rh(I)-catalyzed asymmetric hydrogenation of functional olefins. Thus, we report herein the synthesis of a new type of atropisomeric bisphosphine ligand with a bridge across the 5,5′-positions of that biphenyl, 2,2′-bis(diphenylphosphinomethyl)-5,5′-(polymethylenedioxy)-1,1′-biphenyls **2**, the evaluation of their stability of axial configurations, and their application in Rh(I)-catalyzed asymmetric hydrogenation of a model functional olefin.

2. Results and discussion

The enantiomerically pure bisphosphine ligands **2** were readily prepared from 2-bromo-4-methoxyacetophenone **3**[12] as illustrated in Scheme 1. Bromoform reaction of starting material **3** followed by esterification afforded carboxylic ester **4** in 86% yield.[13] Ullman coupling of methyl 2-bromo-4-methoxybenzoate **4** with activated copper powder furnished the biphenyl skeleton **5** in 61% yield. Demethylation of **5** with aluminum chloride and 1-dodecanethiol afforded a mixture of the corresponding diphenol diester **6**, diphenol monoacid, and diphenol diacid. This mixture was further converted to diphenol diester **6** by esterification with $SOCl_2$ in methanol with 81% yield from **5**. Cyclization of **6** with 1,8-dibromooctane and 1,10-dibromodecane led to key intermediates **7a** and **7b** in 41% and 39% yields, respectively. Straightforward reduction of **7a** to the hydroxymethyl-biphenyl **8a** with $LiAlH_4$ and subsequent reaction of **8a** with thionyl chloride led to chloromethylbiphenyl **9a** in 76% yield from **7a**. Nucleophilic attack of compound **9a** with lithium diphenylphosphine oxide produced the



Scheme 1. Reagents and conditions: (a) (i) Br_2, NaOH; (ii) $SOCl_2$, MeOH, 86%; (b) Cu, 61%; (c) (i) $AlCl_3$, 1-dodecanethiol, CH_2Cl_2; (ii) $SOCl_2$, MeOH, 81%; (d) $Br(CH_2)_nBr$, K_2CO_3, DMF; for **7a**, 41%; for **7b**, 39%; (e) $LiAlH_4$, THF; for **8a**, 98%; for **8b**, 99%; (f) $SOCl_2$, CH_2Cl_2; for **9a**, 78%; for **9b**, 76%; (g) *n*-BuLi, $HP(O)Ph_2$, THF; for **10a**, 93%; for **10b**, 91%; (h) chiral preparative HPLC, a Daicel Chiralcel OD-H column, for **10a**, 88%; for **10b**, 86%; (i) $HSiCl_3$, Et_3N, toluene; for **2a**, 61%; for **2b**, 59%.

desired 2,2′-bis(diphenylphosphinomethyl)-5,5′-(octamethylenedioxy)-1,1′-biphenyl dioxide **10a** in 93% yield. The resolution of racemic **10a** by chiral preparative HPLC using a Daicel Chiralcel OD-H column obtained enantiomerically pure (>99% ee) (+)-**10a** and (−)-**10a**, respectively, in 88% yield. Reduction of the resolved bisphosphine oxide **10a** with trichlorosilane in toluene at 90 °C produced enantiomerically pure bisphosphine ligand **2a** without racemization during the reduction process, which was in accordance with the enantiomeric purities determined by HPLC. In the same way, the enantiomerically pure bisphosphine ligand **2b** was prepared from dimethyl 5,5′-decamethylenedioxybiphenyl-2,2′-dicarboxylate **7b** in 35% overall yield. The sense of the axial chirality of **10a** was determined by the major Cotton effects (CE) in the CD spectra. The CD curve of (−)-**10a** displayed a positive CE at 310.6 nm. This signed feature is the characteristic of (*R*)-configuration at the chiral axis, which was in contrast with the spectra in the literature of axially chiral biphenyl compounds.[14]

To evaluate the stability of the axial configuration of bisphosphine ligands **2**, two enantiomerically pure ligands (*S*)-**2a** and (*S*)-**2b** were dissolved, respectively, in toluene, and stirred at 90 °C for 18 h. As a result, no racemization had occurred by the determination by HPLC. However, when the temperature was increased to 100 °C, the ligands underwent racemization in toluene. As illustrated in Figure 3, the axial configuration of ligand **2a** with octamethylenedioxy bridge is more stable than that of ligand **2b**. The enantiomeric purity of (*S*)-**2a** dropped to 64% ee, whereas the ee value of (*S*)-**2b** dropped to 43% after 32 h at 100 °C. When the temperature was increased to 110 °C, ligands (*S*)-**2a** and (*S*)-**2b** were completely converted to a racemic mixture after 24 h. Nevertheless, these results clearly showed that the atropisomeric bisphosphine ligands **2** could be applied in general transition-metal catalyzed asymmetric reactions due to their stable axial chirality at 90 °C. In addition, the axial configuration could be further stabilized through the chelation of the ligand with a metal to form a metal chelate ring in catalytic reactions.

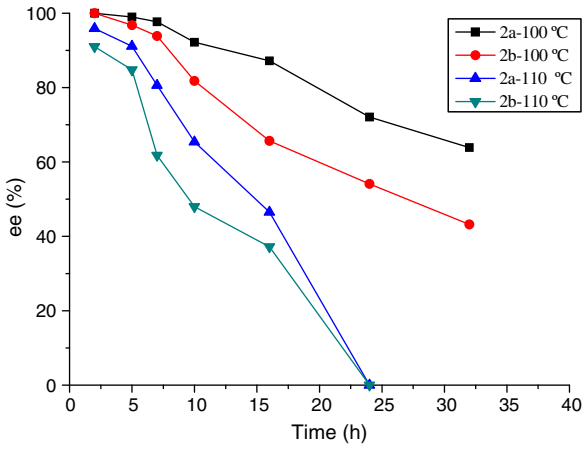
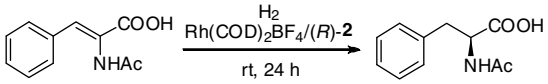


Figure 3. Rate of racemization for atropisomeric bisphosphines **2** in toluene at 100 °C and 110 °C (determined by HPLC using a Daicel Chiralcel AD-H column).

To evaluate the effectiveness of our atropisomeric bisphophine ligands **2** in Rh(I)-catalyzed asymmetric hydrogenation, typically, (*Z*)-α-acetamidocinnamic acid **11a** was used as a model substrate for the hydrogenation. The hydrogenation reaction was catalyzed by 1 mol % of the Rh(I)-(*R*)-**2a** complex generated in situ by mixing $Rh(COD)_2BF_4$ with bisphosphine (*R*)-**2a** in methanol at room temperature. It was found that the catalytic efficiency largely depended on the hydrogen pressure. As shown in Table 1, the hydrogenation reaction showed higher catalytic activity with the hydrogen pressure being increased (entries 1–5). The enantioselectivity was also enhanced with the hydrogen pressure being increased from 1 to 10 atm (from 51% to 84% ee, entries 1–3). However, by further increasing the hydrogen pressure, the enantioselectivity decreased remarkably (entries 4 and 5). With (*R*)-**2b** as a ligand, which has a decamethylenedioxy bridge, the enantioselectivity decreased to 81% ee under 10 atm of hydrogen pressure (entry 6). The reaction medium also affects the catalytic activity and the enantioselectivity of the product (entries 7–12). The highest enantioselectivity (86% ee) was obtained in acetone under 10 atm of hydrogen pressure (entry 12). It is noteworthy that the enantioselectivity obtained with our atropisomeric ligands **2** is much higher than that obtained with NAPHOS ligand (54% ee).[10a]

Table 1. Rh(I)-catalyzed asymmetric hydrogenation of (*Z*)-α-acetamidocinnamic acid using atropisomeric bisphosphines **2** as a ligand[a]



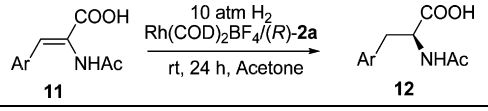
11a **12a**

Entry	Ligand	H_2 pressure (atm)	Solvent	Conv.[b] (%)	ee[c] (%)
1	**2a**	1	MeOH	63	51
2	**2a**	5	MeOH	78	71
3	**2a**	10	MeOH	80	84
4	**2a**	20	MeOH	100	45
5	**2a**	40	MeOH	100	41
6	**2b**	10	MeOH	85	81
7	**2a**	10	THF	86	78
8	**2a**	10	CH_2Cl_2	65	51
9	**2a**	10	Toluene	40	66
10	**2a**	10	EtOH	75	83
11	**2a**	10	*i*-PrOH	75	81
12	**2a**	10	Acetone	78	86

[a] All reactions were carried out at room temperature for 24 h. The catalyst was prepared in situ from $Rh(COD)_2BF_4$ and ligand (substrate:Rh: ligand = 100:1:1.1).
[b] Determined by ^1H NMR analysis.
[c] The enantiomeric excesses were determined by chiral HPLC using a Daicel Chiralcel OD-H column. The (*S*)-absolute configurations were assigned by comparison of specific rotations with the known reported data.[15]

The scope of the asymmetric hydrogenation reaction with different substrates is shown in Table 2. A series of (*Z*)-α-acetamido-β-arylacrylic acids **11** were hydrogenated with Rh(I)-(*R*)-**2a** complex as a catalyst in acetone under 10 atm of hydrogen pressure. All the reactions were not completely accomplished under these reaction conditions. Only a small electronic effect of the aryl ring was observed on the enantioselectivity (82–86% ee).

Table 2. Rh(I)-catalyzed asymmetric hydrogenation of (*Z*)-α-acetamido-β-arylacrylic acids using atropisomeric bisphosphine (*R*)-**2a** as a ligand[a]



Entry	Substrate	Ar	Conv.[b] (%)	ee[c] (%)
1	**11a**	Ph	78	86
2	**11b**	*p*-Me-Ph	57	82
3	**11c**	*p*-F-Ph	61	85
4	**11d**	*p*-Cl-Ph	45	85
5	**11e**	*o*-Cl-Ph	71	86
6	**11f**	*p*-Br-Ph	75	86

[a] All reactions were carried out at room temperature under 10 atm of H_2 for 24 h. The catalyst was prepared in situ from $Rh(COD)_2BF_4$ and ligand (substrate:Rh:ligand = 100:1:1.1).

[b] Determined by ^1H NMR analysis.

[c] The enantiomeric excesses were determined by chiral HPLC using a Daicel Chiralcel OD-H column. The (*S*)-absolute configurations were assigned by comparison of specific rotations with the known reported data.[15]

3. Conclusion

In conclusion, we have developed a new type of atropisomeric bisphosphine ligand **2** with a bridge across the 5,5′-position of the biphenyl. It was demonstrated that the axial chirality of this type of ligands can be retained by macrocyclic ring strain produced from the 5,5′-linkage of the biphenyl. For the Rh(I)-catalyzed asymmetric hydrogenation of (*Z*)-α-acetamido-β-arylacrylic acids **11**, ligand (*R*)-**2a** showed good catalytic activity and enantioselectivity. Further studies will focus on the development and application of this class of atropisomeric ligands.

4. Experimental

4.1. General experimental conditions

All air- and moisture-sensitive manipulations were carried out with standard Schlenk techniques under nitrogen. The reaction solvents were distilled prior to use (toluene and dichloromethane were distilled from CaH_2, THF was distilled from Na). The commercially available reagents were used without further purification. Column chromatography was run on silica gel (100–200 mesh). Melting points were uncorrected. ^1H NMR spectra and ^{13}C NMR spectra were recorded on a Varian MERCURY plus-400 spectrometer. The ee values were determined by HPLC using a Daicel Chiralcel OD-H column or a Daicel Chiralpak AD-H column. Optical rotations (concentration *c* given as g/100 mL) and CD spectrum were measured at the Shanghai Institute of Organic Chemistry, Chinese Academy of Science. Elemental analysis was performed at the Instrumental Analysis Center of Shanghai Jiao Tong University. HRMS was performed on a Micromass LCTTM at the Analysis and Research Center of East China University of Science and Technology.

4.2. Methyl 2-bromo-4-methoxybenzoate 4

Sodium hypobromite solution was freshly prepared by adding bromine (46.0 mL, 0.90 mol) to 20% sodium hydroxide solution (585 mL) at 0–10 °C. To a rapidly stirred sodium hypobromite solution at room temperature, 2-bromo-4-methoxyacetophenone **3** (58.0 g, 0.25 mol) was added over a 25-min period. Stirring was continued at 35–38 °C for 24 h. Unreacted sodium hypobromite was destroyed by sodium bisulfite solution, and extracted with ether to remove the unreacted ketone. The aqueous layer was acidified with concentrated hydrochloric acid to give a white precipitate, which was filtered to obtain a white solid (53.5 g, 92%). Mp 197–198 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, $J = 8.8$ Hz, 1H, ArH), 7.23 (d, $J = 2.4$ Hz, 1H, ArH), 6.90 (dd, $J = 2.8$, 8.8 Hz, 1H, ArH), 3.87 (s, 3H, OCH_3). Thionyl chloride (105 mL, 1.44 mol) was added dropwise to the solution of 2-bromo-4-methoxybenzoic acid (99.2 g, 0.4 mol) in methanol (150 mL) at 0 °C. The mixture was stirred at reflux temperature for 14 h. Excess $SOCl_2$ and methanol was removed by distillation. The residue was dissolved in ethyl acetate, washed with water and 5% sodium hydroxide solution (70 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo to give product **4** (100.1 g, 95%). Mp 25–26 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, $J = 8.8$ Hz, 1H, ArH), 7.19 (d, $J = 2.4$ Hz, 1H, ArH), 6.86 (dd, $J = 2.4$, 8.8 Hz, 1H, ArH), 3.89 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.55, 162.13, 133.09, 123.36, 123.01, 119.71, 112.74, 55.53, 51.95.

4.3. 5,5′-Dimethoxy-diphenic acid dimethyl ester (5)

A mixture of compound **4** (61.3 g, 0.3 mol) and activated copper powder (55.9 g, 0.9 mol) was stirred at 160–180 °C for 24 h. The residue was cooled, and CH_2Cl_2 (200 mL) was added. It was then filtered and washed with CH_2Cl_2 (40 mL × 5), and the filtrate was concentrated. The obtained residue was recrystallized with ethyl acetate and petroleum ether to give white solid **5** (25.2 g, 61%). mp 166–167 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, $J = 8.8$ Hz, 2H, ArH), 6.91 (dd, $J = 2.8$, 9.2 Hz, 2H, ArH), 6.69 (d, $J = 3.2$ Hz, 2H, ArH), 3.84 (s, 6H, OCH_3), 3.61 (s, 6H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.74, 161.97, 146.04, 132.17, 121.57, 115.54, 112.36, 55.51, 51.68. Anal. Calcd for $C_{18}H_{18}O_6$: C, 65.45; H, 5.49. Found: C, 65.21; H, 5.90.

4.4. Dimethyl 5,5′-dihydroxybiphenyl-2,2′-dicarboxylate 6

A solution of biphenyl diester **5** (10.0 g, 30.0 mmol) in CH_2Cl_2 (20 mL) was added dropwise to a mixture prepared from 1-dodecanethiol (40.5 g, 0.2 mol) and aluminum trichloride (13.4 g, 0.1 mol) in CH_2Cl_2 (50 mL) at room temperature. The mixture was stirred overnight at room temperature, and then poured into ice-water, extracted with CH_2Cl_2. The organic layer was washed with water, and then basified by the addition of a solution of sodium hydroxide (3.0 M, 40 mL). The aqueous layer was washed with CH_2Cl_2, acidified with concentrated hydrochloric acid, and then extracted with ethyl acetate. The organic layer was dried over $MgSO_4$, and concentrated in vacuo

to gain demethylated compounds. Thionyl chloride (22 mL, 0.3 mol) was added dropwise at 0 °C to a solution of demethylated compounds in methanol (50 mL) and the mixture was refluxed for 14 h. Excess $SOCl_2$ and methanol was removed by distillation. The residue was dissolved in ethyl acetate, then washed with water, dried over $MgSO_4$, then concentrated in vacuo, recrystallized with ethyl acetate and petroleum ether to give **6** (7.4 g, 81%) as a white solid. Mp 224–225 °C. ^{1}H NMR (400 MHz, acetone-d_6): δ 9.02 (s, 2H, OH), 7.87 (d, $J = 8.4$ Hz, 2H, ArH), 6.88 (dd, $J = 2.0$, 8.4 Hz, 2H, ArH), 6.64 (d, $J = 3.2$ Hz, 2H, ArH), 3.52 (s, 6H, OCH_3); ^{13}C NMR (100 MHz, acetone-d_6): δ 167.09, 160.89, 147.03, 132.85, 121.80, 117.78, 114.50, 51.41. Anal. Calcd for $C_{16}H_{14}O_6$: C, 63.57; H, 4.67. Found: C, 63.23; H, 4.87.

4.5. Dimethyl 5,5′-(octamethylenedioxy)-biphenyl-2,2′-dicarboxylate 7a

To a suspension of anhydrous potassium carbonate (7.76 g, 56.2 mmol) in DMF (50 mL) was added dropwise a solution of compound **6** (5.7 g, 18.7 mmol) and 1,8-dibromooctane (5.1 g, 18.7 mmol) in DMF (20 mL) at 80 °C for 5 h. The mixture was stirred further at 80 °C for 24 h. The reaction mixture was filtered, and the filtrate was concentrated in vacuo. The resulting residue was dissolved in CH_2Cl_2 (50 mL), washed with water and brine, dried over $MgSO_4$, concentrated in vacuo, then purified by chromatography on silica gel to give product **7a** as white crystals (3.2 g, 41%). Mp 124–125 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, $J = 8.8$ Hz, 2H, ArH), 6.90 (dd, $J = 2.4$, 8.8 Hz, 2H, ArH), 6.76 (d, $J = 2.4$ Hz, 2H, ArH), 4.38 (ddd, $J = 6.8$, 6.8, 12.0 Hz, 2H, OCH), 4.10 (ddd, $J = 4.8$, 7.2, 12.8 Hz, 2H, OCH), 3.62 (s, 6H, OCH_3), 1.97–1.92 (m, 2H, CH), 1.62–1.53 (m, 2H, CH), 1.47–1.25 (m, 8H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.96, 161.45, 146.00, 132.00, 121.57, 116.66, 113.49, 65.97, 51.70, 28.69, 28.39, 24.73. Anal. Calcd for $C_{24}H_{28}O_6$: C, 69.88; H, 6.84. Found: C, 69.83; H, 6.28.

4.6. Dimethyl 5,5′-(decamethylenedioxy)-biphenyl-2,2′-dicarboxylate 7b

Compound **7b** was obtained as a white crystal in 39% yield following the procedure for the synthesis of **7a**. Mp 104–105 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, $J = 9.2$ Hz, 2H, ArH), 6.89 (dd, $J = 3.2$, 8.8 Hz, 2H, ArH), 6.71 (d, $J = 2.0$ Hz, 2H, ArH), 4.24 (ddd, $J = 6.0$, 8.0, 11.2 Hz, 2H, OCH), 4.09 (ddd, $J = 6.4$, 7.2, 13.6 Hz, 2H, OCH), 3.61 (s, 6H, OCH3), 1.87–1.80 (m, 2H, CH), 1.70–1.63 (m, 2H, CH), 1.42–1.25 (m, 12H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.88, 161.25, 146.06, 132.00, 121.53, 115.61, 114.84, 68.07, 51.64, 28.58, 28.51, 27.66, 25.13. Anal. Calcd for $C_{26}H_{32}O_6$: C, 70.89; H, 7.32. Found: C, 70.85; H, 7.22.

4.7. 2,2′-Bis(hydroxymethyl)-5,5′-(octamethylenedioxy)-1,1′-biphenyl 8a

To a suspension of lithium aluminum hydride (1.7 g, 44.8 mmol) in THF (30 mL) was added dropwise a solution of diester **7a** (3.7 g, 9.0 mmol) in dry THF (20 mL) at 0 °C for 1 h. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was quenched with saturated aqueous Na_2SO_4 at 0 °C until the gray color of unreacted lithium aluminum hydride became white. The resulting residue was acidified with 1 M HCl, extracted with EtOAc, washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo to give product **8a** as a white solid (3.1 g, 98%). Mp 187–189 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, $J = 8.4$ Hz, 2H, ArH), 6.92 (dd, $J = 8.4$, 2.8 Hz, 2H, ArH), 6.70 (d, $J = 2.8$ Hz, 2H, ArH), 4.21–4.36 (m, 6H, OCH_2 and CH_2OH), 4.05 (m, 2H, OCH_2), 3.42 (br s, 2H, OH), 1.89 (m, 2H, CH_2), 1.52 (m, 2H, CH_2), 1.45–1.16 (m, 8H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.00, 141.75, 131.62, 130.84, 118.61, 113.83, 65.87, 62.14, 28.93, 28.45, 24.92. Anal. Calcd for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 72.15; H, 8.07.

4.8. 2,2′-Bis(hydroxymethyl)-5,5′-(decamethylenedioxy)-1,1′-biphenyl 8b

Product **8b** was obtained as a white solid in 99% yield following the procedure for the synthesis of **8a**. Mp 164–165 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, $J = 8.8$ Hz, 2H, ArH), 6.91 (dd, $J = 8.8$, 2.4 Hz, 2H, ArH), 6.67 (d, $J = 2.4$ Hz, 2H, ArH), 4.20–4.29 (m, 6H, OCH_2 and CH_2OH), 4.06 (m, 2H, OCH_2), 3.42 (s, 2H, OH), 1.82 (m, 2H, CH_2), 1.56 (m, 2H, CH_2), 1.36–1.20 (m, 12H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.91, 141.82, 131.54, 131.20, 117.10, 115.19, 68.15, 62.07, 28.85, 28.65, 27.77, 24.95. Anal. Calcd for $C_{24}H_{32}O_4$: C, 74.97; H, 8.39. Found: C, 73.85; H, 8.42.

4.9. 2,2′-Bis(chloromethyl)-5,5′-(octamethylenedioxy)-1,1′-biphenyl 9a

Thionyl chloride (3.2 mL) was added to a solution of 2,2′-bis(hydroxymethyl)-5,5′-(octamethylenedioxy)-1,1′-biphenyl **8a** (3.1 g, 8.7 mmol) in dichloromethane (50 mL) under ice-cooling, and then the resulting mixture was stirred at rt for 12 h. The excess $SOCl_2$ was destroyed slowly by the dropwise addition of ice-water. The organic layer was washed with water and dried over $MgSO_4$, and concentrated in vacuo. Finally, the residue obtained was purified by column chromatography (eluent: ethyl acetate and petroleum ether) to give white solid **9a** (2.7 g, 78%). Mp 114–115 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, $J = 8.4$ Hz, 2H, ArH), 6.96 (dd, $J = 8.4$, 2.8 Hz, 2H, ArH), 6.74 (d, $J = 2.8$ Hz, 2H, ArH), 4.46 (d, $J = 11.6$ Hz, 2H, CH_2Cl), 4.41 (d, $J = 11.6$ Hz, 2H, CH_2Cl), 4.36–4.29 (m, 2H, OCH_2), 4.10–4.04 (m, 2H, OCH_2), 1.92 (m, 2H, CH_2), 1.59 (m, 2H, CH_2), 1.46–1.16 (m, 8H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.74, 141.15, 131.85, 127.17, 118.71, 114.05, 65.97, 44.33, 28.97, 28.66, 24.94. Anal. Calcd for $C_{22}H_{26}O_2$: C, 67.18; H, 6.66. Found: C, 65.98; H, 6.75.

4.10. 2,2′-Bis(chloromethyl)-5,5′-(decamethylenedioxy)-1,1′-biphenyl 9b

Product **9b** was obtained as a white solid in 76% yield following the procedure for the synthesis of **9a**. Mp 76–78 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d,

$J = 8.4$ Hz, 2H, ArH), 6.96 (dd, $J = 2.8$, 8.4 Hz, 2H, ArH), 6.74 (d, $J = 2.8$ Hz, 2H, ArH), 4.38 (d, $J = 11.2$ Hz, 2H, CH_2Cl), 4.34 (d, J = 11.2 Hz, 2H, CH_2Cl), 4.25–4.19 (m, 2H, OCH_2), 4.13–4.06 (m, 2H, OCH_2), 1.88–1.78 (m, 2H, CH_2), 1.62–1.41 (m, 2H, CH_2), 1.37–1.1 (m, 12H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.52, 141.20, 131.79, 127.54, 117.76, 115.37, 68.10, 44.53, 28.86, 28.60, 27.88, 24.97. Anal. Calcd for $C_{24}H_{30}O_2$: C, 68.40; H, 7.18. Found: C, 67.96; H, 7.22.

4.11. 2,2′-Bis(diphenylphosphinomethyl)-5,5′-(octamethylenedioxy)-1,1′-biphenyl dioxide 10a

n-BuLi (5.1 mL, 9.5 mmol, 1.86 M in hexane) was added dropwise to a solution of diphenylphosphine oxide (1.9 g, 9.5 mmol) in dry THF at −78 °C after which the resulting mixture was stirred for 1 h. To this mixture, a solution of 2,2′-bis(chloromethyl)-5,5′-(octamethylenedioxy)-1,1′-biphenyl **9a** (1.5 g, 3.8 mmol) in THF was added dropwise over 20 min. The solution was allowed to stir overnight at room temperature. The reaction mixture was quenched by saturated aqueous NH_4Cl, and THF was concentrated in vacuo, and the aqueous layer extracted twice with EtOAc. The combined organic solution was washed twice with water and dried over $MgSO_4$. The organic solvent was evaporated, and the resulting residue was recrystallized from EtOAc to give white solid **10a** (2.6 g, 93%). Mp 245–246 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.61 (dd, $J = 8.4$ Hz, 1.6 Hz, 2H, ArH), 7.55–7.47 (m, 6H, ArH), 7.43–7.36 (m, 6H, ArH), 7.23–7.18 (m, 4H, ArH), 7.16–7.11 (m, 4H, ArH), 6.85 (dd, $J = 8.4$ Hz, 2.8 Hz, 2H, ArH), 5.54 (d, $J = 2.8$ Hz, 2H, ArH), 3.86 (m, 4H), 3.55–3.47 (m, 4H, $PhCH_2$), 1.64 (m, 2H, CH_2), 1.49 (m, 2H, CH_2), 1.15–1.28 (m, 8H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.42, 157.39, 141.72, 141.65, 133.42, 132.59, 132.45, 132.06, 132.01, 131.97, 131.61, 131.52, 131.49, 131.43, 131.20, 131.12, 128.83, 128.72, 128.22, 128.11, 120.51, 117.91, 117.89, 114.15, 66.66, 34.07, 33.41, 28.58, 27.56, 24.57; ^{31}P NMR (161 MHz, $CDCl_3$) δ 30.80. Anal. Calcd for $C_{46}H_{46}O_4P_2$: C, 76.23; H, 6.40. Found: C, 75.69; H, 6.30. HRMS (Micromass LCT) calcd for $C_{46}H_{47}O_4P_2$: 725.2986; found: 725.2950.

4.12. (*R*)-(−)-2,2′-Bis(diphenylphosphinomethyl)-5,5′-(octamethylenedioxy)-1,1′-biphenyl dioxide (*R*)-(−)-10a

$[\alpha]_D^{25} = -34.1$ (*c* 1, $CHCl_3$); mp 113–117 °C; all other analytical data were identical to those of **10a**.

4.13. (*S*)-(+)-2,2′-Bis(diphenylphosphinomethyl)-5,5′-(octamethylenedioxy)-1,1′-biphenyl dioxide (*S*)-(+)-10a

$[\alpha]_D^{25} = +33.8$ (*c* 1, $CHCl_3$); mp 113–117 °C; all other analytical data were identical to those of **10a**.

4.14. 2,2′-Bis(diphenylphosphinomethyl)-5,5′-(decamethylenedioxy)-1,1′-biphenyl dioxide 10b

Compound **10b** was obtained as a white solid in 91% yield following the procedure for the synthesis of **10a**. Mp 219–222 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.60 (dd, $J = 8.8$ Hz, 2.4 Hz, 2H, ArH), 7.55–7.52 (m, 6H, ArH), 7.40–7.36 (m, 6H, ArH), 7.25–7.16 (m, 8H, ArH), 6.82 (dd, $J = 8.4$ Hz, 2.4 Hz, 2H, ArH), 5.76 (d, $J = 2.8$ Hz, 2H, ArH), 3.86 (m, 4H, OCH_2), 3.47–3.35 (m, 4H, $PhCH_2$), 1.66 (m, 2H, CH_2), 1.52 (m, 2H, CH_2), 1.29–1.14 (m, 12H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.53, 141.89, 141.66, 133.57, 132.59, 131.97, 131.83, 131.65, 131.42, 131.33, 131.20, 131.11, 128.84, 128.73, 128.39, 128.28, 120.91, 120.84, 116.64, 116.42, 68.09, 33.88, 33.22, 28.70, 28.62, 27.47, 25.17; ^{31}P NMR (161 MHz, $CDCl_3$) δ 31.21. Anal. Calcd for $C_{48}H_{50}O_4P_2$: C, 76.58; H, 6.69. Found: C, 75.85; H, 6.58. HRMS (Micromass LCT) calcd for $C_{48}H_{51}O_4P_2$: 753.3286; found: 753.3263.

4.15. (*R*)-(−)-2,2′-Bis(diphenylphosphinomethyl)-5,5′-(decamethylenedioxy)-1,1′-biphenyl dioxide (*R*)-(−)-10b

$[\alpha]_D^{25} = -37.5$ (*c* 1.1, $CHCl_3$); mp 86–90 °C; all other analytical data were identical to those of **10b**.

4.16. (*S*)-(+)-2,2′-Bis(diphenylphosphinomethyl)-5,5′-(decamethylenedioxy)-1,1′-biphenyl dioxide (*S*)-(+)-10b

$[\alpha]_D^{25} = +36.8$ (*c* 1.1, $CHCl_3$); mp 86–90 °C; all other analytical data were identical to those of **10b**.

4.17. (*R*)-(−)-2,2′-Bis(diphenylphosphinomethyl)-5,5′-(octamethylenedioxy)-1,1′-biphenyl (*R*)-(−)-2a

Trichlorosilane (5.6 mL, 56 mmol) was added to a solution of 2,2′-bis(diphenylphosphinomethyl)-5,5′-(octamethylenedioxy)-1,1′-biphenyl dioxide **10a** (2.0 g, 2.8 mmol) and triethylamine (8.0 mL, 56 mmol) in toluene (50 mL) at 0 °C. The reaction mixture was stirred at 90 °C for 12 h. After cooling to room temperature, degassed aqueous sodium hydroxide (10 M) was added to quench the reaction until the organic and aqueous layers became clear, and was extracted twice with degassed EtOAc. The combined organic layer was washed with 2 M hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and brine, and then dried over anhydrous sodium sulfate. Removal of the solvent and flash column chromatography on silica gel (eluent: ethyl acetate and petroleum ether) gave **2a** as a white solid (1.2 g, 61%). Mp 134–138 °C; $[\alpha]_D^{25} = -28.6$ (*c* 1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.27 (m, 14H, ArH), 7.22–7.16 (m, 8H, ArH), 6.78 (dd, $J = 8.8$ Hz, 2.8 Hz, 2H, ArH), 6.11 (d, $J = 2.8$ Hz, 2H, ArH), 4.15–4.05 (m, 2H, OCH_2), 4.00–3.90 (m, 2H, OCH_2), 3.40–3.20 (m, 4H), 1.84 (m, 2H, CH_2), 1.56 (m, 2H, CH_2), 1.48–1.29 (m, 8H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.04, 134.00, 133.36, 133.18, 133.01, 132.83, 132.07, 130.99, 130.79, 130.03, 129.17, 129.03, 128.93, 128.83, 128.76, 128.71, 128.58, 128.27, 128.10, 128.04, 117.23, 65.80, 32.07, 30.51, 28.67, 27.96, 24.85; ^{31}P NMR (161 MHz, $CDCl_3$) δ −8.27; HRMS (Micromass LCT) calcd for $C_{46}H_{46}O_2P_2Na$: 715.2871; found: 715.2876.

4.18. (*R*)-(−)-2,2′-Bis(diphenylphosphinomethyl)-5,5′-(decamethylenedioxy)-1,1′-biphenyl (*R*)-(−)-2b

Compound **2b** was obtained as a white solid in 56% yield following the procedure for the synthesis of **2a**. Mp 112–116 °C; $[\alpha]_D^{25} = -31.5$ (*c* 1, $CHCl_3$); ^1H NMR (400 MHz,

$CDCl_3$): δ 7.49–7.16 (m, 14H, ArH), 7.06–7.04 (m, 8H, ArH), 6.71 (dd, $J = 8.8$ Hz,1.6 Hz, 2H, ArH), 6.33 (d, $J = 1.6$ Hz, 2H, ArH), 4.11–4.03 (m, 2H, OCH_2), 4.00–3.92 (m, 2H, OCH_2), 3.21 (s, 4H, $PhCH_2$), 1.76 (m, 2H, CH_2), 1.63 (m, 2H, CH_2), 1.48–1.26 (m, 12H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.54, 144.00, 140.23, 134.20, 134.03, 133.30, 133.10, 132.94, 128.75, 128.73, 128.70, 128.61, 128.49, 128.43, 128.26, 128.20, 116.29, 68.10, 29.86, 29.82, 28.68, 28.64, 27.84, 25.09; ^{31}P NMR (161 MHz, $CDCl_3$) δ −9.38; HRMS (Micromass LCT) calcd for $C_{48}H_{50}O_2P_2Na$: 743.3188; found: 743.3184.

4.19. General procedure for Rh(I)-catalyzed asymmetric hydrogenation of (*Z*)-α-acetamidocinnamic acid 11a

$[Rh(COD)_2]BF_4$ (0.01 mmol) and (*R*)-**2a** (0.011 mmol) were dissolved in degassed MeOH (2 mL) and stirred for 20 min to form a solution of [Rh(COD)(*R*)-**2a**]BF_4 catalyst for the asymmetric hydrogenation. Then a solution of substrate **11a** (1 mmol) in MeOH (2 mL) was added to a catalyst solution prepared above. The hydrogenation was performed in a stainless steel autoclave at room temperature under 10 atm of hydrogen for 24 h. The resulting solution was passed through a short silica gel column to remove the catalyst. The ee value and conversion of the product were measured by chiral HPLC and ^1H NMR spectroscopy without any further purification. The products were converted to the corresponding methyl ester for the determination of their ee value using chiral HPLC (a Daicel Chiralcel OD-H column, flow rate = 0.5 mL/min, hexane/2-propanol (75:25), UV detector, 254 nm).

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