A New Atropisomeric P,N Ligand for Rhodium-Catalyzed Asymmetric Hydroboration

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A new optically active and large dihedral angle atropisomeric P,N ligand, pyphos, which contains a tertiary phosphine and pyridine moiety, was prepared and resolved through diastereomeric complexation with chiral palladium amine complexes. The hexafluorophosphate salt of the diastereomers were found to be separable by fractional recyrstallization, while the corresponding chloride salt did not. [Rh(COD)pyphos]PF_6 complex was synthesized by metalation of pyphos with $[Rh(COD)Cl]_2$ followed by anion exchange with NH_4PF_6 in excellent yield, and the target rhodium complex was characterized by single-crystal X-ray crystallography. The chiral cationic rhodium complex was utilized in the enantioselective hydroboration of vinylarenes. Excellent regioselectivity and good enantioselectivity were observed, and the ee values were found to be dependent on the electronic properties of para-substituted styrenes.

Introduction

The discovery of the oxidative addition of Wilkinson's catalyst ($Rh(PPh_3)_3Cl$) with boron hydrides such as catecholborane has led to the development of metal-catalyzed hydroboration.[1,2] The hydroboration reaction is markedly accelerated in the presence of the rhodium catalyst[2] and has a significant effect on the regiochemistry of the reaction.[3−8] This invention also demonstrated that the catalyzed and the uncatalyzed reactions can display complementary functional group and diastereoselectivity.[9] Apart from the regio- and chemoselectivity of hydroboration, the most interesting application is the enantioselective version of this reaction which can be aplied to the natural product and drug synthesis.[10] The first asymmetric hydroboration was reported by Burgess using norborene and chiral Rh-DIOP catalyst to give 55% ee at −40 °C.[11−13] A highly enantioselective hydroboration reaction (up to 96% ee, −78 °C) was then reported by Hayashi's group, who employed a cationic rhodium-BINAP catalyst for the reaction of styrenes.[14,15] Subsequently, other catalysts for asymmetric hydroboration have been developed; Togni,[16,17] Brown,[18−21] Chung,[22] Fleet,[23] and Guiry[24] employed Rh complexes of chiral

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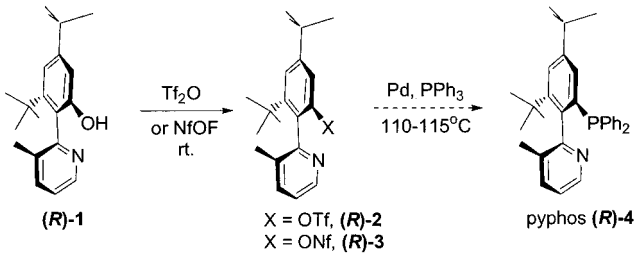
heterotopic P,N ligands to give moderate to high enantioselectivity in the hydroboration of vinylarenes. However, the reported examples of axially chiral P,N ligands are limited.[25] Recently, Zhang et al. reported that the dihedral angles of chiral biaryl ligands influenced the enantioselectivities of the asymmetric hydrogenation apart from the steric and/or electronic properties of the ligands.[26,27] To access axially tunable advantage in optimizing the enantioselectivity of a reaction, we envision that a strategy to incorporate a *tert*-butyl and a methyl group in a biaryl ligand for the restriction of sp^2-sp^2 biaryl rotation and for the generation of a large dihedral angle in the chiral ligand. The substitution of pyridine moiety for one of the aryl rings in the biaryl ligand would further add an attractive feature for the phase separation of the ligand from the reaction mixture by extracting them with hydrochloric acid.[28,29] Herein, we report the preparation of optically active atropisomeric P,N ligand **4**, X-ray characterization of the corresponding Rh−pyphos complex, and the first application of pyphos in rhodium-catalyzed asymmetric hydroboration of vinylarenes.

Results and Discussion

Synthesis of Atropisomeric P,N Ligand, pyphos, by Using Optically Active Pyridylphenol 1. The synthesis of optically active pyphos **4** was initially attempted from the optically active pyridylphenol **1**.[30] The optically pure **1** was transformed to its triflate derivative **2** in excellent yield[31] without racemization, as confirmed by chiral HPLC analysis (Scheme 1). Triflate (*R*)-**2** was then subjected to palladium-catalyzed phosphination at 110−115 °C (Scheme 1).[32] Nevertheless, the phosphine ligand **4** was found to be a racemic mixture.[33] Racemization studies revealed that the chiral triflate (*R*)-**2** started to racemize at about 100 °C and was configurationally stable at/or below 90 °C even after extensive reaction. As no phosphination occurred below 110 °C and other phosphination methods proved to be ineffective,[34] the synthesis of chiral P,N ligand **4** from its corresponding optically active triflate precursor is not possible. The more sterically bulky and reactive triflate analogue, nonaflate, was then prepared.[35] The optically pure nonaflate (*R*)-**3** was synthesized in 85% yield from optically pure pyridylphenol (*R*)-**1** using perfluorobutanesulfonic fluoride in the presence of sodium hydride in dry ether at room temperature (Scheme 1). Nonaflate (*R*)-**3** was subjected to palladium-catalyzed phosphination to yield chiral P,N ligand **4**. Though (*R*)-**3** had a higher racemization temperature (105 °C) than that of triflate (*R*)-**2**, it was still not high enough to achieve the phosphination. Therefore, an alternative synthetic pathway was chosen, and pyphos **4** was prepared from **1** in racemic form and its optical resolution was carried out using diastereomeric complexation with chiral palladium amine complexes (Scheme 2).

Scheme 1. Synthesis of Chiral Atropisomeric P,N Ligand



(*R*)-**1** X = OTf, (*R*)-**2** X = ONf, (*R*)-**3** pyphos (*R*)-**4**

Resolution of pyphos by Fractional Crystallization of Diastereomeric Palladium Complexes. The failure in the preparation of chiral pyphos **4** from optically pure precursor **1** led to the resolution of pyphos in later stage. The chiral palladium amine complex was synthesized from the reaction of (*R*)-*N*,*N*-dimethyl-α-methylbenzylamine with palladium(II) dichloride in methanol to form the optically active palladium amine dimer **5** in 88% yield (Scheme 2).[36] This μ-chloro dimer **5** was reacted with pyphos **4** to form the diastereomers (*R*,*R*)-**6** and (*R*,*S*)-**6** (Scheme 2). Initial attempts by fractional recrystallization of the diastereomers was unsuccessful using chloroform, dichloromethane, acetone, toluene, and a mixture of solvents.[37]

The alternative (*R*)-*N*,*N*-dimethyl-α-methylnaphthylamine resolving agent was recently found to be more effective than its phenyl derivative, (*R*)-*N*,*N*-dimethyl-

(21) For hydroboration/amination, see: Fernandez, E.; Maeda, K.; Hooper, M. W.; Brown, J. M. *Chem. Eur. J.* **2000**, *6*, 1840−1846. Brown et al. also reported double asymmetric induction in enantioselective hydroboration using matched pair of Rh−BINAP complexes with chiral borane which derived from ephedrine, see: Brown, J. M.; Lloyd-Jones, G. C. *Tetrahedron*: *Asymmetry* **1990**, *1*, 869−872.

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(33) The ee (%) determination of pyphos ligand was accomplished by its pyphos oxide derivative 2-(2′-diphenylphosphinyl-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine **9** using chiral HPLC (chiralpak AD column, hexane:2-propanol = 975:25, flow rate = 1.0 mL/min, UV = 254 nm).

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(37) Chloroform (13% de), dichloromethane (10% de), acetone (2% de), toluene (2% de), chloroform/butanol (8% de). The diastereomeric excesses were estimated by ^{1}H NMR integration.

Scheme 2. Resolution of Pyphos by Diastereomeric Complexation

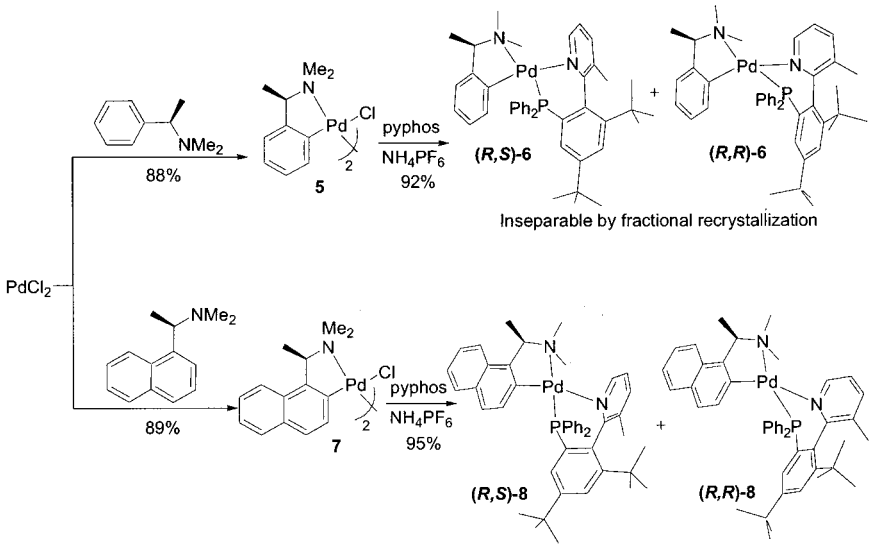


Table 1. Results of Diastereomeric Crystallization of pyphos−Amine−Palladium Complex

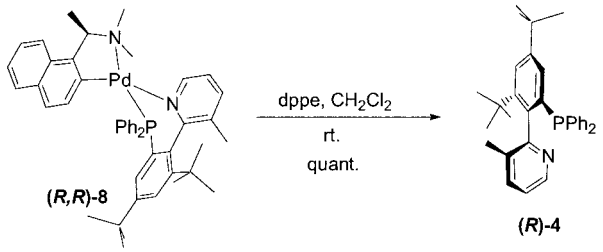
entry	X^-	solvent	de[a] (%)
1	Cl	$CHCl_3$	2
2	Cl	CH_{2Cl2}	5
3	PF_6	$CHCl_3$	>99
4	PF_6	$CHCl_3$/ether	>99
5	PF_6	CH_{2Cl2}	13

[a] Determined by ^{1}H NMR integration.

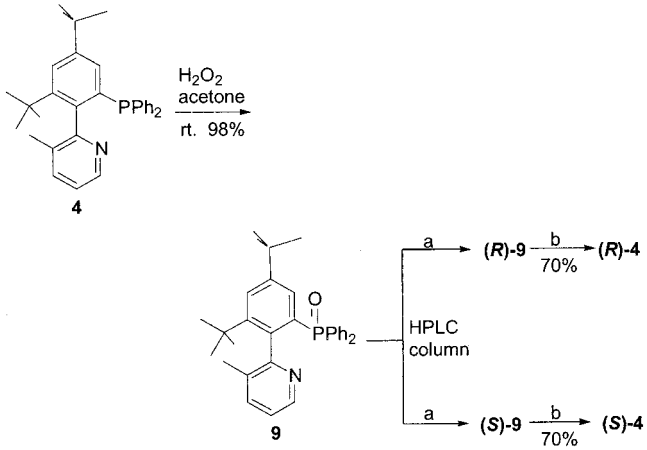
α-methylbenzylamine.[38] The μ-chloro bridge palladium dimer **7** was then prepared in 89% yield (Scheme 2), which subsequently reacted with pyphos **4** to yield the diastereomers (*R*,*R*)-**8** and (*R*,*S*)-**8** as the chloride salt or hexafluorophosphate salt after anion exchange with NH_4PF_6 in dichloromethane (Scheme 2). The diastereomers of **8** were then fractionally crystallized using different solvents (Table 1). Interestingly, the chloride salts of **8** were inseparable using chloroform, but the PF_6 salts were found to have excellent diastereomeric crystallization upon using the same solvent (Table 1, entries 1 and 3). However, dichloromethane proved to be inferior for diastereomeric crystallization in either Cl or PF_6 salts of **8** (Table 1, entries 2 and 5). The addition of diethyl ether to chloroform only enhanced the rate of crystallization of (*R*,*R*)-**8** but had no deleterious effect on the diastereomeric excess (Table 1, entry 4). The optically active pyphos (*R*)-**4** was obtained by the decomplexation of (*R*,*R*)-**8** by using dppe (1,2-bis(diphenylphosphino)-ethane) in dichloromethane in quantitative yield (Scheme 3).

Resolution of Biaryl P,N Ligand by Chiral HPLC. The alternative resolution method was accomplished by chiral HPLC. The direct resolution of pyphos **4** using a Daicel OD, OD-H, OJ, or AD chiral column was unsuccessful. To our delight, the corresponding more polar pyphos oxide **9**, which was prepared by oxidation of pyphos **4** in excellent yield (Scheme 4), could be resolved using a Daicel AD column to afford the optically active pyphos oxide (*R*)-**9** and (*S*)-**9**.[39] The chiral P,N ligand **4** was then obtained by reduction of the corresponding

Scheme 3. Decomplexation of Chiral Complex



Scheme 4. Resolution of Pyphos by Chiral HPLC



phosphine oxide using trichlorosilane[40] in toluene at 90 °C for 2 days in 70% yield without racemization (Scheme 4). The racemization temperature of pyphos **4** was found to be 130 °C in dodecane.

Synthesis and Structural Characterization of Rh−P,N Complex. The Rh complex of **4** was prepared by mixing $[Rh(COD)Cl]_2$ with **4** in dichoromethane at room temperature for 5 min, followed by anion exchange with NH_4PF_6 in 82% yield after crystallization in dichloromethane (Scheme 5). A single crystal of rhodium complex **10** was obtained after recrystallization in layered mixtures of dichloromethane/diethyl ether. Table 2 lists the crystal and data collection parameters. The structure of the rhodium−pyphos complex is shown in Figure 1.

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(39) HPLC conditions: Hex/^{i}PrOH = 9/1, flow rate = 0.6 mL/min, T_R = 14.66 min, t_S = 21.99 min.

(40) For reduction of phosphine oxide, see: Naumann, K.; Zon, G.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 7012−7023.

Scheme 5. Preparation of Rhodium−P,N Complex 10

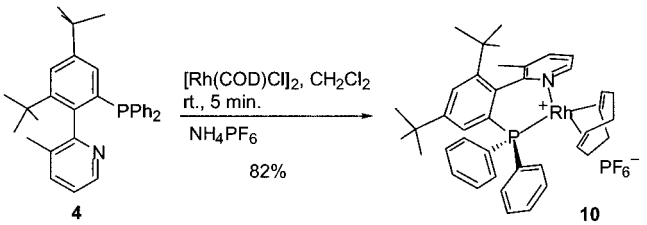

Table 2. Crystal Data and Structure Refinement Details of 10

empirical formula	$C_{41}H_{50}Cl_2F_6NP_2Rh$
formula weight	906.57
T (K)	293(2)
wavelength (Å)	0.71073
crystal system	orthorhombic
space group	$P2_12_12_1$
unit cell dimensions	$a = 10.5493(6)$ Å
	$b = 14.9952(8)$ Å
	$c = 25.9098(1)$ Å
	$\alpha = 90.0°$
	$\beta = 90.0°$
	$\gamma = 90.0°$
volume (Å^3)	4098.5(4)
Z	4
density (calcd) (Mg/m^3)	1.469
absorption coefficient (mm^{-1})	0.683
F(000)	1864
crystal size (mm)	0.41 × 0.38 × 0.34
θ range for data collection (deg)	1.57−26.00
limiting indices	$-11 \le h \le 13$
	$-18 \le k \le 16$
	$-31 \le l \le 20$
reflections collected	24 697
independent reflections	8014 ($R_{int} = 0.0343$)
absorption correction	empirical
max transmission	1.000
min transmission	0.8776
refinement method	full-matrix least-squares on F^2
data/restraints/parameters	8014/49/474
goodness-of-fit on F^2	0.997
final R Indices [$I > 2\sigma(I)$]	R1 = 0.0437, wR2 = 0.1114
R indices (all data)	R1 = 0.0554, wR2 = 0.1195
absolute structure parameter	−0.03 (3)
extinction coefficient	0.00000 (5)
largest diff peak and hole (e Å^{-3})	0.495 and −0.537

The X-ray crystal structure of **10** showed both the tertiary phosphine P and pyridine N atom are well coordinated to the rhodium center. The Rh(1)−N(1) bond distance is 2.130 Å, which is similar to that in Togni's ferrocenyl phosphine/pyrazole ligand−Rh complex (Table 3).[41] However, the Rh(1)−P(1) bond distance (2.2995(12) Å) of pyphos showed a shorter distance than the rhodium complex of ferrocenyl phosphine/pyrazole ligand (2.311-(4) Å),[41] which demonstrated that the P moiety in pyphos ligand coordinated closer to rhodium. This may have better chiral induction in asymmetric catalysis. The dihedral angle between the C(7)−C(8)−C(9)−C(10)−C(11)−C(12) aryl and pyridyl ring was 72° [for free pyphos ligand, the dihedral angle is 87° and 89° from ChemDraw 3D calculations and the X-ray single-crystal structure (the quality of crystal was poor), respectively]. Some distortion of the chiral axis C(5)−C(7) was observed, which may be due to the steric hindrance of the adjacent *tert*-butyl group (Figure 1).

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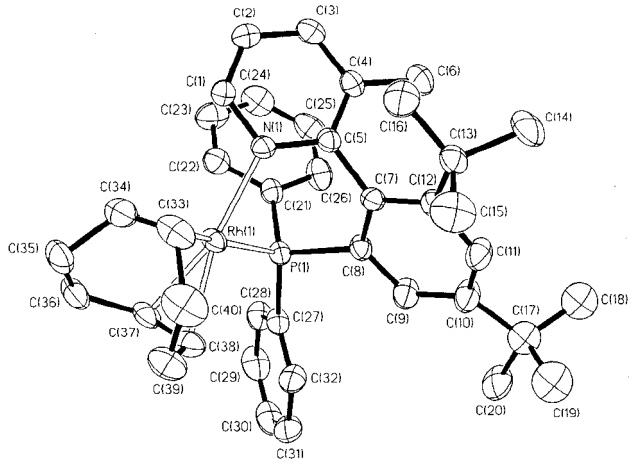
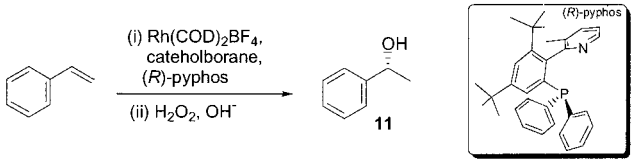


Figure 1. X-ray crystal structure of Rh-pyphos **10**.

Table 3. Selected Bond Distances (Å) and Angles (deg) for Complex 10

Bond Distances			
Rh(1)−N(1)	2.130(4)	Rh(1)−C(37)	2.135(4)
Rh(1)−C(38)	2.154(5)	Rh(1)−C(33)	2.211(4)
Rh(1)−C(34)	2.242(5)	Rh(1)−P(1)	2.2995(12)
P(1)−C(21)	1.817(5)	P(1)−C(8)	1.834(4)
P(1)−C(27)	1.835(5)	N(1)−C(1)	1.354(6)
N(1)−C(5)	1.370(6)		
Bond Angles			
N(1)−Rh(1)−P(1)	81.77(9)	C(21)−P(1)-C(8)	107.0(2)
C(21)−P(1)−C(27)	105.2(2)		

Table 4. Results of Asymmetric Hydroboration of Styrene

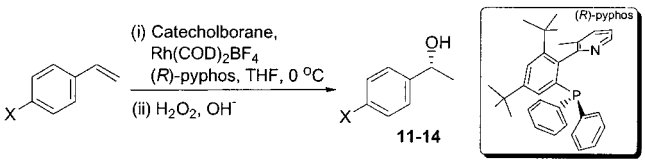


entry	catalyst, mol %	solvent	T (°C)	time[a] (h)	% yield[b]	% ee[c]
1	1 mol % $Rh(COD)_2BF_4$, pyphos	THF	rt	12	70	69
2	1 mol % $Rh(COD)_2BF_4$, pyphos	THF	rt	12	72	70
3	1 mol % $Rh(COD)_2BF_4$, pyphos	THF	0	18	72	90
4	1 mol % $[Rh(COD)Cl]_2$, pyphos	THF	0	48	trace	
5	1 mol % $Rh(COD)_2BF_4$, pyphos	DME	0	24	55	89
6	1 mol % $Rh(COD)_2BF_4$, pyphos	CH_2Cl_2	0	24	65	85

[a] Monitored by GC. [b] Isolated yield. [c] Determined by HPLC using a Daicel OD-H column. Average at least two runs for entries 1 and 3.

Catalytic Asymmetric Hydroboration. The chiral atropisomeric P,N ligand **4** was applied in asymmetric hydroboration (Table 4). In the presence of a catalytic amount (1 mol %) of $Rh(COD)_2BF_4$ and (*R*)-pyphos **4**, styrene reacted completely with catecholborane in THF at room temperature for 12 h. The corresponding 1-phenylethanol was obtained in 70% yield with 69% ee (Table 4, entry 1). Excellent regioselectivity was observed as the formation of side product, benzyl alcohol, was less than 1% as determined by GC−MS. When the catalyst loading was increased to 2 mol %, identical rates, yield, and enantioselectivity were obtained (Table 4, entry 2).

Table 5. Results of Asymmetric Hydroboration of Para-Substituted Styrenes



entry	X	ee[c] (%)	confign	log (*R*/*S*)	σ_p
1	OMe	94[a]	*R*	1.51	−0.26
2	Me	93[b]	*R*	1.44	−0.17
3	H	90[b]	*R*	1.27	0.00
4	Cl	79[b]	*R*	0.93	+0.23

[a] Determined by GCD. [b] Determined by HPLC using a Daicel OD-H column. [c] % ee were reported in average over at least two runs (entries 1, 3, and 4).

Lowering the temperature to 0 °C increased the enantiomeric excess of the *sec*-alcohol **11** up to 90% ee without affecting the regioselectivity (Table 4, entry 3). The neutral complex, $[Rh(COD)Cl]_2$/(*R*)-pyphos system, did not catalyze the hydroboration reaction (Table 4, entry 4). The stereoselectivity was relatively insensitive to solvent change; however, a lower product yield was obtained when DME or CH_2Cl_2 solvent was used (Table 4, entries 5 and 6). The enantioselectivity of the *sec*-alcohol versus time was also investigated.[42] The enanatiomeric excess of **11** was found to be 82% at the beginning of the first 2 h and the ee value remained constant at 90% ee until the end of the reaction.

The optimized Rh-catalyzed asymmetric hydroboration conditions were applied to para-substituted styrenes with different electronic properties. The regioselectivity forming 1-arylethylborane was excellent (>98:2 to 99:1) for all the styrenes examined, irrespective of the electron-releasing or electron-withdrawing nature of the substitutent group on the phenyl ring. The *p*-methoxystyrene showed the highest enantioselectivity with 94% ee of the 1-(4-methoxyphenyl)ethanol **12** formed (Table 5, entry 1). The less electron-donating *p*-methylstyrene with reference to *p*-methoxystyrene gave slightly lower enantiomeric excess of the alcohol **13** compared with **12** (Table 5, entries 1 and 2). However, much lower enantiomeric excess of *p*-chlorophenylethanol **14** was observed in the electron-deficient *p*-chlorostyrene (Table 5, entry 4).

The enantioselectivity in this catalyzed hydroboration of para-substituted styrenes depends on the electronic effect of styrene.[43] The results showed that the ee ranged from 79% ee for the *p*-chloro substituent to 94% ee for *p*-methoxy substituent. A plot of log(*R*/*S*) of the hydroboration product versus Hammett constant σ_p gave a modestly straight line with R^2 equal to 0.984 (Figure 2).[44] A linear free energy relationship was obeyed.

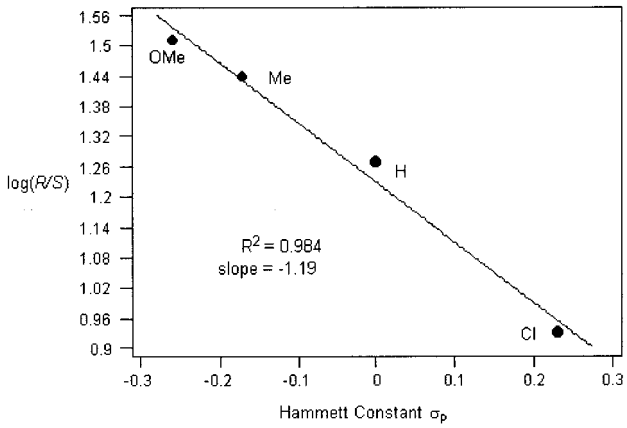


Figure 2. Hammett plot of the ee value of hydroboration products with Hammett constants.

The electronic effect of asymmetric hydroboration could probably be explained by a series of metal−alkene complexes where electron-rich styrenes coordinate more strongly trans to the pyridine than the electron-poor analogues (Figure 3).[45−49] Hence, we suggest that in the transition state the more electron-rich styrene may coordinate closer to the rhodium center, resulting in improved stereochemical communication and thus gives rise to a higher enantioselectivity (Figure 3, model A). However, for the electron-poor styrene, it has a greater possibility to coordinate to the rhodium center in two modes as it is far from the chiral environment in the transition state (Figure 3, model B).[46] Therefore, a lower ee of the product is observed.

A comparison of dihedral angle and steric effect with other atropisomeric ligands is shown in Table 6. The pyphos ligand probably lies into the optimal board range of dihedral angle (see QUINAP, 67°; pyphos 87°) in catalytic asymmetric hydroboration as the ee values are similar. In contrast with asymmetric hydrogenation, the optimal range is rather sharp and the ee values versus dihedral angles changed dramatically.[26] The steric effects of the ligands also play an important role in determining the stereoselectivity of the reaction. A six-membered ring metal−ligand (Rh−pyphos) coordination was found to be better than a seven-member ring (Rh−BINAP) coordina-

(42) Table 4, entry 3 conditions were used without modification. Samples were taken from the reaction mixture in intervals of 30 min, 1 h, 2 h, 4, 16, and 18 h. After oxidation of the product by alkaline hydrogen peroxide, the organic extract was diluted, filtered over Celite and analyzed by chiral HPLC using OD-H column.

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(44) For the values of Hammett constants, see: Gordon, A. J.; Ford, R. A. *The Chemist's Companion*; John Wiley: New York, 1972.

(45) Kurosawa, H.; Ikeda, I. *J. Organomet. Chem.* **1992**, *428*, 289−301.

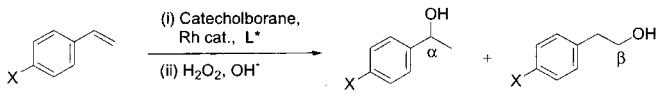
(46) For evidences for the role of dπ−pπ bonding in rhodium-mediated hydroboration, see: (a) Burgess, K.; van der Donk, W. A.; Jarstfer, M. B.; Ohlmeyer, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 6139−6144. For a review in metal-alkene binding, see: (b) Gladysz, J. A.; Boone, B. J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 551−583.

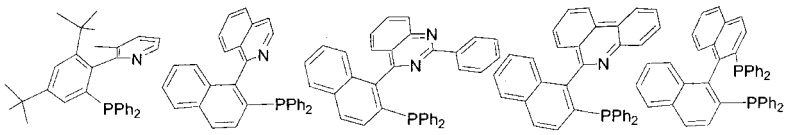
(47) Burgess has proposed a transition structure model for the catalyzed hydroboration of 1,1-disubstituted allylic alcohol derivatives: (a) Burgess, K.; Ohlmeyer, M. J. *Tetrahedron Lett.* **1989**, *30*, 5861−5864. (b) Moser, W. R., Slocum, D. W., Eds. *Homogeneous Transition Metal Catalyzed Reactions*; Advances in Chemistry Series 230; American Chemical Society: Washington, DC, 1992; pp 163−177. This model assumes that complexation of the olefin to the metal is the rate stereochemical-determining step of the reaction.

(48) For selected reference in hydroboration mechanistic studies, see: (a) Evans, D. A.; Fu, G. C. *J. Org. Chem.* **1990**, *55*, 2280−2282. (b) Evans, D. A.; Fu, G. C.; Anderson, B. A. *J. Am. Chem. Soc.* **1992**, *114*, 6679−6685. (c) Burgess, K.; Van der Donk, W. A.; Westcott, S. A.; Marder, T. B.; Baker, R. T. Calabrese, J. C. *J. Am. Chem. Soc.* **1992**, *114*, 9350−9393. (d) Westcott, S. A.; Blom, H. P.; Marder, T. B.; Baker, R. T. *J. Am. Chem. Soc.* **1992**, *114*, 8863−8869.

(49) For other mechanistic studies of steric and electronic effects in insertion of olefin, see: Burger, B. J.; Santarsiero, B. D.; Trimmer, M. S.; Bercaw, J. E. *J. Am. Chem. Soc.* **1988**, *110*, 3134−3146.

Table 6. Comparison of Dihedral Angles and Steric Effects of Atropisomeric Ligands





	pyphos	QUINAP[18]	2-Ph-quinazolinap[24]	PHENAP[19]	BINAP[14]
Dihedral angle[a]	87°	67°	65°	66°	72°
%ee, *p*-H (α:β)	90 (99:1)	88 (97:3)	79 (80:20)	67 (94:6)	57 (99:1)
p-OMe	94 (98:2)	94 (95:5)	81 (77:23)		
p-Cl	79 (99:1)	78 (98:2)	49 (83:17)		

[a] The dihedral angles were estimated by ChemDraw 3D calculation of the free ligands.

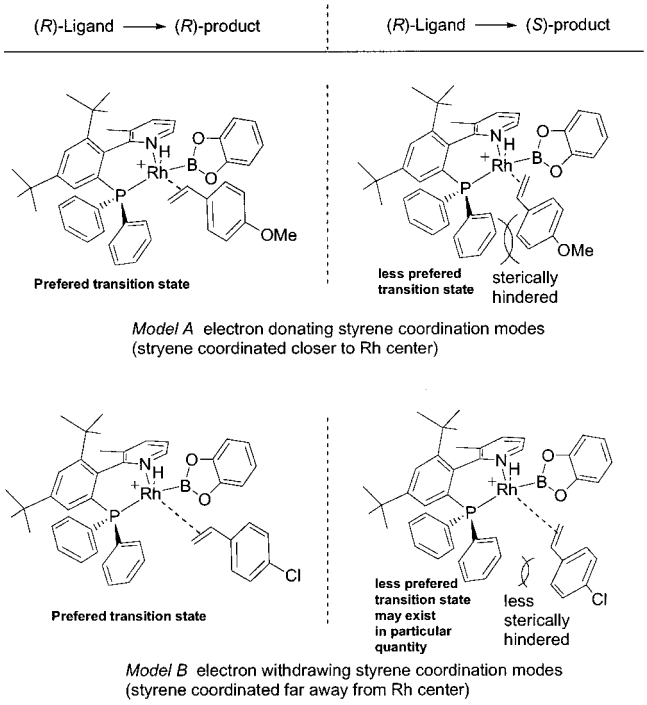


Figure 3. Suggested transition-state models for electronically controlled asymmetric hydroboration.

tion mode (Table 6). This trend was probably caused by the closer ligand to rhodium distance.

Recovery of P,N Ligand Using an Aqueous Extraction Process. Pyphos **4** is configurationally stable in acidic medium. The pyridine moiety of the P,N ligand allows the facile acid/aqueous extraction of ligand for recycling of the catalyst. The partition coefficient of pyphos ligand in layered diethyl ether and 12 N hydrochloric acid was found to be 9:91, respectively. Thus, the acid layer was separated and neutralized by sodium hydroxide solution to pH 8 and extracted with dichloromethane to afford 91% of recovery of P,N ligand **4**. The % ee of the aqueous extracted ligand was >99% as verified by chiral HPLC. This characteristic serves as another basis for the development of a new generation of chiral ligands and the application of other catalyst-recyclable asymmetric reactions.

Conclusion

A new optically active atropisomeric P,N ligand, pyphos, with a large dihedral angle containing a tertiary phosphine and pyridine moiety was prepared and resolved through diastereomeric complexation with chiral palladium naphthylamine complexes in a hexafluorophosphate salt other than chloride salt. The [Rh(COD)-pyphos]PF_6 complex was synthesized in excellent yield, and the single crystal of rhodium−PN complex was characterized by X-ray crystallography. The cationic chiral rhodium complex was applied to enantioselective hydroboration of vinylarenes. Excellent regioselectivities and good enantioselectivities were observed, and the ee values were found to be obeyed a linear free energy relationship with the Hammett constants.

Experimental Section

General Considerations. Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under nitrogen immediately prior to use. Dichloromethane, pyridine, styrene and triethylamine were distilled from calcium hydride under nitrogen atmosphere before use. *N*,*N*-Dimethylformamide was distilled from magnesium sulfate under reduced pressure. $Rh(COD)_2BF_4$ and $[Rh(COD)Cl]_2$ were prepared according to literature method without modification.[50] Thin-layer chromatography was performed on precoated silica gel 60 F_{254} plates. Silica gel (70−230 and 230−400 mesh) was used for column chromatography. ^1H NMR spectra were recorded on a 300 MHz spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm) or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) on a δ scale downfield from TMS. ^{13}C NMR spectra were recorded on a 75 MHz spectrometer and referenced to $CDCl_3$ (δ 77.00 ppm). ^{31}P NMR spectra were recorded on a 162 MHz and referenced to 85% H_3PO_4 externally. Coupling constants (J) are reported in hertz (Hz). HPLC analyses were conducted on a Waters 486 system with a UV detector at 254 nm, using a Daicel OD column (0.46 × 25 cm), Daicel OD-H column (0.46 × 15 cm) and Daicel AD column (0.46 × 25 cm). GC-MS analysis was conducted on a HP G1800C GCD system using a HP5MS column (30 m × 0.25 mm) or Alltech β-cyclodextrin chiral column (50 m × 0.25 mm). The Hammett plot was generated using MacCurve Fit version 1.1, Kevin Raner Software 1994.

(50) Fryzuk, M. D.; Bosnich, B. *J. Am. Chem. Soc.* **1977**, *99*, 6262−6267.

(*R*)-3,5-Di-*tert*-butyl-2-(3′-methyl-2′-pyridyl)phenyl Trifluoromethanesulfonate (2). (*R*)-3,5-Di-*tert*-butyl-2-(3′-methyl-2′-pyridyl)phenol[30,43a] (*R*)-(**1**) (297 mg, 1.0 mmol) was dissolved in dry dichloromethane (5 mL) under nitrogen at room temperature in a three-necked round-bottom flask. Pyridine (0.26 mL, 3.0 mmol) and trifluoromethanesulfonic anhydride (triflic anhydride) (0.18 mL, 1.1 mmol) in dry dichloromethane (3 mL) were then added slowly to the reaction mixture. White fumes evolved, and the color of the solution was changed from yellow to orange. The reaction mixture was stirred at room temperature for 2 h. Water (5 mL) was added, and the aqueous phase was extracted with dichloromethane (20 mL × 3). The combined organic extract was washed with water and brine, dried over $MgSO_4$, and rotary-evaporated. The resultant brown residue was purified by column chromatography on silica gel using a solvent mixture (hexane/ethyl acetate = 5:1) as the eluent to afford (*R*)-3,5-di-*tert*-butyl-2-(3′-methyl-2′-pyridyl)phenyl trifluoromethanesulfonate (*R*)-(**2**) (408 mg, 95%) as white solids: $R_f = 0.6$ (hexane/ethyl acetate = 4:1); mp 96−98 °C; HPLC (column: analytical Daicel OD-H, solvent, hexane/2-propanol = 995:5; UV lamp, 254 nm; flow rate, 0.3 mL/min) t_R = 11.20 min; $[\alpha]^{20}_D = +2.3$ (c = 0.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (s, 9 H), 1.36 (s, 9 H), 2.12 (s, 3 H), 7.20 (s, 1 H), 7.23 (dd, 1 H, J = 7.8 Hz, 4.8 Hz), 7.57 (d, 1 H, J = 8.0 Hz), 7.63 (d, 1 H, J = 0.8 Hz), 8.53 (d, 1 H, J = 4.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 29.7, 31.1, 35.1, 37.5, 115.4, 118.2 (q, J_{CF} = 317.6 Hz), 124.4, 132.7, 133.1, 138.3, 146.4, 148.2, 150.5, 152.1, 152.5; MS (EI) *m*/*z* (relative intensity) 430 ($M^+ + 1$, 74), 414 (52), 296 (19), 281 (100), 266 (22); HRMS (ESIMS) calcd for $C_{21}H_{26}F_3NO_3SH^+$ 430.1658, found 430.1647.

(*S*)-3,5-Di-*tert*-butyl-2-(3′-methyl-2′-pyridyl)phenyl Trifluoromethanesulfonate (*S*)-(2). (*S*)-3,5-Di-*tert*-butyl-2-(3′-methyl-2′-pyridyl)phenol[30,43a] (*S*)-(**1**) (65 mg, 0.22 mmol) was used to yield the (*S*)-3,5-di-*tert*-butyl-2-(3′-methyl-2′-pyridyl)-phenyl trifluoromethanesulfonate (*S*)-(**2**) (85 mg, 90%, 100%*ee*) according to the above procedure. HPLC (column: analytical Daicel OD-H, solvent, hexane/2-propanol = 995:5; UV lamp, 254 nm; flow rate, 0.3 mL/min) t_R = 9.82 min; $[\alpha]^{20}_D = -2.2$ (c = 0.6, $CHCl_3$).

(*R*)-(3,5-Di-*tert*-butyl-2-(3′-methyl-2′-pyridyl)phenyl Nonafluorobutanesulfonate (*R*)-(3). (*R*)-3,5-Di-*tert*-butyl-2-(3′-methyl-2′-pyridyl)phenol[30,43a] (*R*)-(**1**) (594 mg, 2.0 mmol) in anhydrous ether (3 mL) was added to NaH (120 mg, 2.7 mmol) in anhydrous ether (7 mL) at 0 °C. Nonafluorobutanesulfonyl fluoride (1.2 g, 4.0 mmol) was then added under nitrogen at 0 °C. After complete addition, the reaction mixture was heated to reflux for 2 h. The reaction mixture was then cooled and added with water (20 mL). The aqueous phase was extracted by diethyl ether (50 mL × 2). The combined organic phase was washed with water and brine and dried over $MgSO_4$. The solvent was removed by rotary evaporation, and the residue was purified by column chromatography on silica gel using a solvent mixture (hexane/ethyl acetate = 5:1) as the eluent to yield the (*R*)-3,5-di-*tert*-butyl-2-(3′-methyl-2′-pyridyl)phenyl nonafluorobutanesulfonate (*R*)-(**3**) (984 mg, 85%) as light yellow solids: $R_f = 0.6$ (hexane/ethyl acetate = 5:1); mp 48−50 °C; HPLC (column: analytical Daicel OD-H, solvent, hexane/2-propanol = 99:1; UV lamp, 254 nm; flow rate, 0.4 mL/min) t_R = 6.67 min; $[\alpha]^{20}_D = +2.2$ (c = 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (s, 9 H), 1.36 (s, 9 H), 2.11 (s, 3 H), 7.22 (d, 1 H, J = 0.9 Hz), 7.24 (dd, 1 H, J = 3.8 Hz, 7.4 Hz), 7.55 (d, 1 H, J = 7.5 Hz), 7.63 (d, 1 H, J = 1.6 Hz), 8.52 (d, 1 H, J = 3.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.2, 31.1, 32.3, 35.1, 37.1, 109.2−118.9 (m), 115.1, 123.1, 124.5, 129.3, 133.9, 137.6, 146.0, 148.0, 150.4, 152.7, 155.2; MS (FAB) *m*/*z* (relative intensity) 580 ($M^+ + 1$, 60), 564 (10), 297 (30), 282 (100), 266 (33); HRMS (ESIMS) calcd for $C_{24}H_{26}F_9NO_3SH^+$ 580.1562, found 580.1536.

General Procedures for Racemization Experiment: For (*R*)-2. A 5 mL Telfon stopcock flask was charged with (*R*)-**2** (5 mg, 11 μmol) and dodecane (2 mL) under nitrogen. The solution was heated to a specific temperature and monitored by HPLC: HPLC (column: analytical Daicel OD-H, solvent, hexane/2-propanol = 995:5; UV lamp, 254 nm; flow rate, 0.3 mL/min) t_R = 9.82 min, t_S =11.20 min. **For (*R*)-3:** HPLC (column: analytical Daicel OD-H, solvent, hexane/2-propanol = 99:1; UV lamp, 254 nm; flow rate, 0.4 mL/min) t_R = 6.41 min, t_S = 7.28 min.

2-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine[32] (pyphos) (4). Racemic 3,5-di-*tert*-butyl-2-(3′-methyl-2′-pyridyl)phenyl trifluoromethanesulfonate **(1)** (1.07 g, 2.5 mmol), palladium(II) acetate (56 mg, 0.25 mmol), and triphenylphosphine (1.51 g, 5.8 mmol) were dissolved in dry DMF (10 mL) under nitrogen. The solution was heated to 110−115 °C for 4.5 days, and the color of the solution was changed from yellow to red. The reaction was cooled, and DMF was removed under reduced pressure. The residue was purified by column chromatography on silica gel using a solvent mixture of (hexane/ethyl acetate = 6:1, $R_f = 0.6$) as eluent to obtain the crude product. This crude product was then purified by column chromatography on silica gel with eluent (toluene/ethyl acetate = 20:1) to afford the pure 2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (pyphos) **(4)** (790 mg, 68%) as a white solid: mp 135−136 °C; $R_f = 0.6$ (toluene/ethyl acetate = 15:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.13 (s, 9 H), 1.17 (s, 9 H), 1.94 (s, 3 H), 7.04−7.30 (m, 13 H), 7.60 (d, 1 H, J = 2.0 Hz), 8.34 (d, 1 H, J = 4.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.9, 31.1, 32.4, 34.8, 37.2, 125.8, 127.9, 128 (d, J_{CP} = 8.0 Hz), 128.2 (d, J_{CP} = 4.6 Hz), 130.1, 131.2 (d, J_{CP} = 7.6 Hz), 131.1 (d, J_{CP} = 7.5 Hz), 133.4 (d, J_{CP} = 19.3 Hz), 134.0 (d, J_{CP} = 20.0 Hz), 137.1 (d, J_{CP} = 8.7 Hz), 138.0 (d, J_{CP} = 9.3 Hz), 138.2, 145.1, 147.1 (d, J_{CP} = 5.6 Hz), 149.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.60; MS (EI) *m*/*z* (relative intensity) 465 (M^+, 80), 450 (88), 408 (100), 388 (82), 374 (22), 358 (35), 342 (23); HRMS (ESIMS) calcd for $C_{32}H_{36}NPH^+$ 466.2658, found 466.2622.

Di-μ-chlorobis[(*R*)-dimethyl(1-phenylethyl)aminato-*C*^{2},*N*]dipalladium(II) (5).[36] Palladium(II) dichloride (618 mg, 3.5 mmol) and lithium chloride (348 mg, 7.0 mmol) were dissolved in methanol (15 mL) at 60 °C. The solution was then stirred for 1 h until a deep red solution was obtained. The solution was filtered and treated with (*R*)-*N*,*N*-dimethylphenylethylamine (1.2 g, 8.1 mmol). The yellow precipitate formed was filtered at room temperature, washed with methanol, and dried under reduced pressure to obtain di-μ-chlorobis[(*R*)-dimethyl(1-phenylethyl)aminato-*C*^{2},*N*]dipalladium(II) (885 mg, 88%) as yellow solid: MS (FAB) *m*/*z* (relative intensity) 581 (M^+, 20), 544 (22), 391 (70), 307 (100); $[\alpha]^{20}_D = -53.2$ (c = 0.5, CH_2Cl_2).

(*R*,*R*)- and (*R*,*S*)-[Dimethyl(1-phenylethyl)aminato-*C*^{2},*N*]-[2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine]palladium(II) Hexafluorophosphate ((*R*,*R*)-6 and (*R*,*S*)-6). Di-μ-chlorobis[(*R*)-dimethyl(1-phenylethyl)aminato-*C*^{2},*N*]dipalladium(II) **(5)** (290 mg, 0.5 mmol) and 2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine **(4)** (465 mg, 1.0 mmol) were dissolved in degassed methanol (20 mL) under nitrogen and stirred until a clear solution was obtained. Ammonium hexafluorophosphate (163 mg, 1.0 mmol) in degassed water (15 mL) was then added. After a half portion of NH_4PF_6 was added, white precipitate formed. The suspension was stirred vigorously at room temperature for 1 h. The precipitate was filtered, washed with water and methanol, and dried under reduced pressure to yield the (*R*,*S*)- and (*R*,*R*)-[dimethyl(1-phenylethyl)aminato-*C*^{2},*N*]-[2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine]palladium(II) hexafluorophosphate (800 mg, 92%) as white solid: mp 230 °C dec; $[\alpha]^{20}_D = +100.5$ (c = 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.10 (s, 18 H), 1.22 (s, 18 H), 1.41 (d, 3 H, J = 6.6 Hz), 1.58 (s, 3 H), 1.62 (s, 3 H), 1.75 (d, 3 H, J = 6.6 Hz), 2.61 (d, 3 H, J = 2.4 Hz), 2.79 (d, 3 H, J = 3.3 Hz), 2.86 (d, 3 H, J = 2.1 Hz), 3.02 (d, 3 H, J = 3.3 Hz), 3.57 (q, 1 H, J = 6.6 Hz), 4.87 (q, 1 H, J = 6.6 Hz), 6.07−6.13 (m, 2 H), 6.38−6.42 (m, 2 H), 6.81−6.99 (m, 10 H), 7.13 (s, 1 H), 7.16 (s, 1 H), 7.25−7.65 (m, 18 H), 7.75 (s, 2 H), 8.68 (dd, 2 H, J = 9.7, 4.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.19, 19.8, 19.9, 25.1, 30.8, 32.8, 32.9, 34.9, 38.1, 38.2, 42.0, 47.9, 48.7, 51.6, 72.1, 76.1, 122.0, 123.2, 123.8 (d, J_{CP} = 11.0 Hz), 124.3 (d, J_{CP} = 11.1 Hz), 124.6 (d, J_{CP} = 10.9 Hz), 125.2, 125.7 (d, J_{CP} = 5.4 Hz), 126.4, 127.2 (d, J_{CP} = 5.4 Hz), 127.5 (d, J_{CP} =

5.5 Hz), 128.0−129.1 (m), 131.8, 132.3, 135.3 (d, J_{CP} = 7.9 Hz), 136.5 (d, J_{CP} = 10.0 Hz), 139.0 (d, J_{CP} = 24.7 Hz), 139.1, 139.7, 146.3 (d, J_{CP} = 10.5 Hz), 149.4, 149.6 (d, J_{CP} = 8.2 Hz), 150.9, 151.9 (d, J_{CP} = 22.4 Hz), 152.0, 152.6, 154.8, 157.2; ^{31}P (162 MHz, $CDCl_3$) δ −40.45, 40.19, −143.23 (heptet, J_{PF} = 712.8 Hz); MS (FAB) *m*/*z* (relative intensity) 705 ($M^+ - PF_6$, 22), 465 (100); HRMS (ESIMS) calcd for $C_{43}H_{45}NPPd^+$ 706.2374, found 706.2377.

(*R*,*R*)-[Dimethyl(1-phenylethyl)aminato-*C*^{2},*N*]-[2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine]palladium(II) Hexafluorophosphate ((*R*,*R*)-8). Di-μ-chlorobis[(*R*)-dimethyl(1-naphthylethyl)aminato-*C*^{2},*N*]dipalladium(II) **(7)** (340 mg, 0.5 mmol) and 2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (pyphos) **(4)** (465 mg, 1.0 mmol) were dissolved in degassed methanol (20 mL) under nitrogen and stirred until clear solution was obtained. Ammonium hexafluorophosphate (163 mg, 1.0 mmol) in degassed water (15 mL) was then added. The suspension was stirred vigorously at room temperature for 1 h. The precipitate was filtered, washed with water and methanol, and dried under reduced pressure to yield a mixture of diastereomers. The (*R*,*R*)-[dimethyl(1-phenylethyl)aminato-*C*^{2},*N*]-[2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine]palladium(II) hexafluorophosphate (*R*,*R*)-**8** was obtained from fractional crystallization using layering chloroform/diethyl ether mixture as white solids (830 mg, 92%): mp 250 °C dec; $[\alpha]^{20}_D$ = +120.5 (*c* = 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.11 (s, 9 H), 1.16 (s, 9 H), 1.63 (s, 3 H), 1.88 (d, 2 H, *J* = 6.3 Hz), 2.88 (s, 6 H), 4.39 (m, 1 H), 6.32 (dd, 1 H, *J* = 5.8 Hz, 2.7 Hz), 6.85−6.93 (m, 4 H), 7.14 (d, 2 H, *J* = 9.2 Hz), 7.33−7.49 (m, 8 H), 7.66 (dd, 2 H, *J* = 5.9 Hz, 2.8 Hz), 7.75 (d, 1 H, *J* = 1.1 Hz), 8.74 (d, 1 H, *J* = 4.8 Hz); ^{13}C NMR (300 MHz, $CDCl_3$) δ 19.9, 23.8, 30.9, 32.7, 32.9, 35.0, 38.3, 48.3, 51.9, 73.1, 123.0, 123.7, 124.6, 125.3 (d, J_{PC} = 10.2 Hz), 126.1, 128.4−128.9 (m), 131.4, 131.9, 132.4, 135.0−135.2 (m), 136.5 (d, J_{PC} = 11.1 Hz), 136.7 (d, J_{PC} = 10.9 Hz), 139.8, 147.0, 148.9, 149.3, 149.7 (d, J_{PC} = 10.2 Hz), 152.1 (d, J_{PC} = 10.3 Hz); ^{31}P (162 MHz, $CDCl_3$) δ 38.90, −143.23 (heptet, J_{PF} = 712.8 Hz); MS (FAB) *m*/*z* (relative intensity) 756 ($M^+ - PF_6$, 20), 465 (90); HRMS (ESIMS) calcd for $C_{47}H_{47}NPPd^+$ 756.2973, found 756.2980.

(*R*)-2-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (pyphos) ((*R*)-4). (*R*,*R*)-[Dimethyl(1-phenylethyl)aminato-*C*^{2},*N*]-[2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine]palladium(II) hexafluorophosphate (*R*,*R*)-**8** (450 mg, 0.5 mmol) was dissolved in dichloromethane (10 mL) followed by the addition of 1,2-diphenylphosphinoethane (dppe) (200 mg, 0.5 mmol). The reaction mixture was stirred at room temperature overnight. Water (50 mL) was added, the solution was extracted with dichloromethane (3 × 10 mL), and the combined organic phase was washed with brine and dried over magnesium sulfate. Rotary evaporation of the solvent gave a pale yellow residue that was purified by short column chromatography on silica gel using a solvent mixture of hexane/ethyl acetate (5:1) to afford (*R*)-(**4**) (423 mg, 91%) as white solids.

2-(2′-Diphenylphosphinyl-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (9). 2-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine[32] (pyphos) **4** (300 mg, 0.65 mmol) was dissolved in acetone (15 mL) followed by the addition of hydrogen peroxide (2 mL), and the solution was stirred at room temperature for 5 min. The aqueous phase was extracted by dichloromethane (10 mL × 3), and the combined organic extract was washed with water and brine and dried over $MgSO_4$. The solvent was removed by rotary evaporation, and the residue was purified by short column chromatography on silica gel using a solvent mixture (hexane/ethyl acetate = 1:1) as the eluent to yield 2-(2′-diphenylphosphinyl-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine **9** (306 mg, 98%) as white solids: R_f = 0.2 (hexane/ethyl acetate = 1:1); mp 181−183 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 9 H), 1.19 (s, 9 H), 2.12 (s, 3 H), 8.68 (dd, 1 H, *J* = 8.3 Hz, 4.2 Hz), 7.23−7.49 (m, 10 H), 7.69−7.75 (m, 2 H), 7.80 (d, 2 H, *J* = 2.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.6, 29.6, 31.0, 32.4, 34.7, 37.6, 122.8, 127.7 (d, J_{CP} = 12.2 Hz), 128.0 (d, J_{CP} = 12.1 Hz), 128.4 (d, J_{CP} = 12.2 Hz), 129.2, 129.5 (d, J_{CP} = 13.4 Hz), 130.5, 131.2 (d, J_{CP} = 9.9 Hz), 132.1 (d, J_{CP} = 9.0 Hz), 133.1, 133.6, 134.4, 135.0, 135.8, 136.3, 144.3, 148.2 (d, J_{CP} = 9.6 Hz), 149.0 (d, J_{CP} = 12.3 Hz), 157.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ 30.40; MS (FAB) *m*/*z* (relative intensity) 482 (M^+ + 1, 10), 465 (100), 451 (12), 425 (81), 407 (13), 389 (18), 280 (8), 201 (43); HRMS (ESIMS) calcd for $C_{32}H_{36}NOPH^+$ 482.2607, found 482.2605.

(*R*)-2-(2′-Diphenylphosphinyl-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine ((*R*)-9). (*R*)-**9** was obtained from preparative chiral HPLC with a Daicel AD column using a solvent mixture (hexane/2-propanol = 975:25; UV lamp, 254 nm) as the eluent with a flow rate 1.0 mL/min: t_R = 18.12 min; $[\alpha]^{20}_D$ = +34.5 (*c* = 0.5, $CHCl_3$).

(*S*)-2-(2′-Diphenylphosphinyl-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine ((*S*)-9). (*S*)-**9** was obtained from preparative chiral HPLC with a Daicel AD column using a solvent mixture (hexane/2-propanol = 975:25; UV lamp, 254 nm) as the eluent with a flow rate 1.0 mL/min: t_S = 39.42 min; $[\alpha]^{20}_D$ = −35.2 (*c* = 0.5, $CHCl_3$).

HPLC Method Resolution Method for (*R*)-4 and (*S*)-4: (*R*)-2-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine ((*R*)-4). (*R*)-2-(2′-Diphenylphosphinyl-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (*R*)-**9** (30 mg, 0.06 mmol) was dissolved in dry toluene (3 mL) under nitrogen at room temperature. Trichlorosilane (0.45 mL, 0.6 mmol) and triethylamine (0.88 mL, 0.66 mmol) were then added, and white fumes evolved. After the solution was heated to 95 °C for 2 days, it was cooled to room temperature, and sodium hydroxide solution (2 M, 10 mL) was added. The aqueous phase was extracted by dichloromethane (10 mL × 3), and the combined organic phase was washed with water and brine and dried over magnesium sulfate. The solvent was rotary evaporated off, and the residue was purified by flash column chromatography on silica gel using a solvent mixture (hexane/ethyl acetate = 5:1) as the eluent to afford the (*R*)-2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (pyphos) (*R*)-**4** (20 mg, 70%) as white solids: R_f = 0.6 (hexane/ethyl acetate = 5:1); mp 135−137 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.13 (s, 9 H), 1.17 (s, 9 H), 1.94 (s, 3 H), 7.04−7.30 (m, 13 H), 7.60 (d, 1 H, *J* = 2.0 Hz), 8.34 (d, 1 H, *J* = 4.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.9, 31.1, 32.4, 34.8, 37.2, 125.8, 127.9, 128 (d, J_{CP} = 8.0 Hz), 128.2 (d, J_{CP} = 4.6 Hz), 130.1, 131.2 (d, J_{CP} = 7.6 Hz), 131.1 (d, J_{CP} = 7.5 Hz), 133.4 (d, J_{CP} = 19.3 Hz), 134.0 (d, J_{CP} = 20.0 Hz), 137.1 (d, J_{CP} = 8.7 Hz), 138.0 (d, J_{CP} = 9.3 Hz), 138.2, 145.1, 147.1 (d, J_{CP} = 5.6 Hz), 149.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.60; MS (EI) *m*/*z* (relative intensity) 465 (M^+, 80), 450 (88), 408 (100), 388 (82), 374 (22), 358 (35), 342 (23); $[\alpha]^{20}_D$ = +98.2 (*c* = 0.5, $CHCl_3$).

(*S*)-2-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (pyphos) ((*S*)-4). The general procedure of reduction phosphine oxide for was used. (*S*)-2-(2′-Diphenylphosphinyl-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (*S*)-**9** (30 mg, 0.06 mmol), dry toluene (3 mL), trichlorosilane (0.45 mL, 0.6 mmol), and triethylamine (0.88 mL, 0.66 mmol) were used to afford the (*S*)-2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (pyphos) (*S*)-**4** (20 mg, 70%) as white solids: $[\alpha]^{20}_D$ = −97.0 (*c* = 0.5, $CHCl_3$).

[2-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine]-[1,5-cyclootadiene]rhodium(I) Hexafluorophosphate (10). 2-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (pyphos) **(4)** (10 mg, 0.022 mmol) was dissolved in dichloromethane (1 mL) under nitrogen. $[Rh(COD)Cl]_2$ was added, and the color of the solution turned yellow. The solution was stirred for 5 min at room temperature, and ammonium hexafluorophosphate (3.4 mg, 0.022 mmol) was added together with minimal amount of water. The reaction was stirred vigorously at room temperature for 30 min, and the solvent was removed by reduced pressure. The brown solid was washed with a minimal amount of water and dried again. Minimal dichloromethane was added followed by the addition of diethyl ether under nitrogen atmosphere. Orange crystals formed after refrigeration over-

night and were collected by filtration to yield [2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine][1,5-cyclootadiene]rhodium(I) hexafluorophosphate **(10)** (14.5 mg, 82%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.13 (s, 9 H), 1.36 (s, 9 H), 1.43 (s, 3 H), 1.77−1.82 (m, 4 H), 2.43−2.55 (m, 4 H), 3.56−3.58 (m, 1 H), 3.89−3.91 (m, 1 H), 5.20−5.22 (m, 1 H), 5.46−5.48 (m, 1 H), 6.96−7.03 (m, 3 H), 7.27−7.52 (m, 10 H), 7.77 (d, 1 H, J = 1.6 Hz), 8.69 (d, 1 H, J = 5.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.7, 26.1, 28.1, 31.1, 32.2, 32.8, 35.3, 35.7, 38.1, 76.4 (d, J = 13.1 Hz), 78.3 (d, J = 11.9 Hz), 100.5 (d, J = 14.3 Hz), 106.7 (d, J = 14.1 Hz), 123.9, 124.4 (d, J_{CP} = 7.0 Hz), 124.9, 125.5 ((d, J_{CP} = 4.6 Hz), 126.4, 126.6, 127.2, 128.0, 128.7 (d, J_{CP} = 9.6 Hz), 131.5 (d, J_{CP} = 25.7 Hz), 133.2 (d, J_{CP} = 9.4 Hz), 136.3, 138.3 (d, J_{CP} = 19.6 Hz), 139.7, 148.1, 149.8 (d, J_{CP} = 8.4 Hz), 152.5 (d, J_{CP} = 7.1 Hz), 157.6 (d, J_{CP} = 9.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 35.22 (d, J_{PRh} = 143.9 Hz), −143.12 (heptet, J_{PF} = 712.8 Hz); MS (FAB) m/z (relative intensity) 822 (M^+ + 1, 20); HRMS (ESIMS) calcd for $C_{40}H_{48}F_6NP_2RhH^+$ 822.2292, found 822.2285. X-ray crystals were grown under the solvent mixture of dichloromethane/diethyl ether. The X-ray crystal data have been deposited in Cambridge Crystallographic Data Centre (CCDC 179715).

General Procedure for Catalytic Asymmetric Hydroboration. 1-Phenylethanol (11).[51] (*R*)-2-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (pyphos) (*R*)-**4** (1.8 mg, 3.8 μmol) and $Rh(COD)_2BF_4$ (1.5 mg, 3.8 μmol) were dissolved in dry THF (1.5 mL) under nitrogen at room temperature. The solution was stirred for 5 min at room temperature and cooled to 0 °C followed by the addition of styrene (43 μL, 0.38 mmol). The catecholborane (1.0 M in THF, 0.46 mL, 0.46 mmol) was then added, and the color of the solution was changed from yellow to orange. The reaction was stirred for 18 h at 0 °C. Ethanol (2 mL) was added at 0 °C followed by the NaOH solution (3 M, 2.5 mL) and H_2O_2 (35%, 0.5 mL) and stirred vigorously for 0.5 h at room temperature. The reaction mixture was extracted with diethyl ether (10 mL × 3), and the combined organic phase was washed with water and brine and dried over $MgSO_4$. The residue was purified by column chromatography on silica gel using a solvent mixture (hexane/diethyl ether = 1:1) as the eluent to yield the (*R*)-1-phenylethanol **(11)** (34 mg, 72%, 90% ee) as a colorless oil: R_f = 0.5 (hexane/diethyl ether = 1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.49 (d, 3 H, J = 6.4 Hz), 1.91 (brs, 1 H), 4.89 (q, 1 H, J = 6.4 Hz), 7.20−7.40 (m, 5 H); MS (EI): m/z (relative intensity) 122 (M^+, 100), 107 (15), 105 (8), 77 (70); $[\alpha]^{20}_D$ = +45.8 (c = 1.3, CH_2Cl_2); HPLC (solvent, hexane/2-propanol = 975:25; UV lamp, 254 nm; flow rate, 0.5 mL/min) t_R = 16.18 min, t_S = 21.48 min.

1-(4-Methoxyphenyl)ethanol (12).[51] The general procedure of catalytic asymmetric hydroboration was used. (*R*)-2-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (pyphos) (*R*)-**4** (1.8 mg, 3.8 μmol), $Rh(COD)_2BF_4$ (1.5 mg, 3.8 μmol), 4-methoxystyrene (50 μL, 0.38 mmol), catecholborane (1.0 M in THF, 0.46 mL, 0.46 mmol), and dry THF (1.5 mL) were used to yield the (*R*)-1-(4-methoxyphenyl)ethanol **(12)** (43 mg, 74%, 94% ee) as a colorless oil: R_f = 0.4 (hexane/diethyl ether = 1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.47 (d, 3 H, J = 6.4 Hz), 1.87 (brs, 1 H), 3.80 (s, 3 H), 4.84 (q, 1 H, J = 6.4 Hz), 6.90 (d, 2 H, J = 8.6 Hz), 7.31 (d, 2 H, J = 8.6 Hz); MS (EI) m/z (relative intensity) 152 (M^+, 100), 137 (42), 107 (30); $[\alpha]^{20}_D$ = + 45.8 (c = 1.0, $CHCl_3$); GC−MS (column: Alltech β-cyclodextrin chiral column (50 m × 0.25 mm); flow rate, 2 mL/min (helium); temperature program, 120 °C (60 min)) t_R = 42.2 min, t_S = 48.3 min.

1-(4-Methylphenyl)ethanol (13).[51] The general procedure of catalytic asymmetric hydroboration was used. (*R*)-2-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (pyphos) (*R*)-**4** (1.8 mg, 3.8 μmol), $Rh(COD)_2BF_4$ (1.5 mg, 3.8 μmol), 4-methylstyrene (50 μL, 0.38 mmol), catecholborane (1.0 M in THF, 0.46 mL, 0.46 mmol), and dry THF (1.5 mL) were used to yield (*R*)-1-(4-methylphenyl)ethanol **(13)** (38 mg, 74%, 93% ee) as a colorless oil: R_f = 0.5 (hexane/diethyl ether = 1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.47 (d, 3 H, J = 6.5 Hz), 1.86 (brs, 1 H), 2.34 (s, 3 H), 4.85 (q, 1 H, J = 6.5 Hz), 7.19 (d, 2 H, J = 8.2 Hz), 7.29 (d, 2 H, J = 8.2 Hz); MS (EI): m/z (relative intensity) 136 (M^+, 100), 121 (78), 91 (22); $[\alpha]^{20}_D$ = +49.8 (c = 0.5, $CHCl_3$); HPLC (column: analytical Daicel OD-H, solvent, hexane/2-propanol = 99:1; UV lamp, 254 nm; flow rate, 0.6 mL/min) t_R = 21.48 min, t_S = 22.74 min.

1-(4-Chlorophenyl)ethanol (14).[52] The general procedure of catalytic asymmetric hydroboration was used. (*R*)-2-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (pyphos) (*R*)-**4** (1.8 mg, 3.8 μmol), $Rh(COD)_2BF_4$ (1.5 mg, 3.8 μmol), 4-chlorostyrene (46 μL, 0.38 mmol), catecholborane (1.0 M in THF, 0.46 mL, 0.46 mmol), and dry THF (1.5 mL) were used to yield (*R*)-1-(4-chlorophenyl)ethanol **(14)** (42 mg, 70%, 79% ee) as a colorless oil: R_f = 0.5 (hexane/ethyl acetate = 4:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.47 (d, 3 H, J = 6.6 Hz), 1.71 (brs, 1 H), 4.85 (q, 1 H, J = 6.6 Hz), 7.10−7.39 (m, 4 H); MS (EI): m/z (relative intensity) 158 (M^+, 22), 156 (M^+, 100); $[\alpha]^{20}_D$ = +37.8 (c = 0.5, $CHCl_3$); HPLC (column: analytical Daicel OD-H, solvent, hexane/2-propanol = 99:1; UV lamp, 254 nm; flow rate, 0.4 mL/min) t_R = 35.00 min, t_S = 37.38 min.

Absolute Configuration Determination of pyphos. The absolute configuration of pyphos **4** was determined by chemical correlation of the known configuration of pyridylphenol **1**.[30,43a] The optically active pyridylphenol (*R*)-**1** underwent trifluoromethanesulfonation to yield pyridylphenyl triflate (*R*)-**2** without racemization. Though racemization occurred when (*R*)-**2** underwent palladium-catalyzed phosphination,[32] the enantiomeric enriched pyphos **4** was obtained when the reaction was stopped after 1.5 days. The isolated enantiomeric enriched pyphos was then further oxidized by hydrogen peroxide to yield the optically enriched phosphine oxide **9** and analyzed by chiral HPLC using a Daicel OD-H column. The larger peak area of the chromatogram suggested the *R* configuration of pyphos oxide **9**. Thus, its retention time was assigned for (*R*)-**9**.

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