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Synthesis of (−)-(4*R*,5*R*)-4,5-bis[di-3′-(2′,6′-dimethoxypyridyl)-phosphinomethyl]-2,2-dimethyl-1,3-dioxolane and its application in the Rh-catalyzed asymmetric hydrogenation reactions

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Abstract

The chiral ligand (−)-(4*R*,5*R*)-4,5-bis[di-3′-(2′,6′-dimethoxypyridyl)phosphinomethyl]-2,2-dimethyl-1,3-dioxolane **3** [(*R*,*R*)-Py*-DIOP] was synthesized via a key intermediate bis[3-(2,6-dimethoxypyridyl)]phosphine-borane **9**. The asymmetric hydrogenation of prochiral olefins was investigated using a rhodium catalyst containing **3**. For the hydrogenation of amidoacrylic acids, enols and itaconic acid, while the enantioselectivity of [Rh-(*R*,*R*)-Py*-DIOP] was similar to that of [Rh-(*R*,*R*)-DIOP] the absolute configurations of the products from the two catalyst systems were found to be opposite. © 1998 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Transition metal–organophosphine complexes have been extensively studied and widely used for catalytic organic synthesis in the past three decades. Tremendous success has been achieved in the use of chiral arylphosphine ligands in Rh- and Ru-catalyzed asymmetric hydrogenation reactions. In contrast, chiral phosphine ligands containing heterocyclic moieties such as pyridyl groups have been relatively unexplored even though the expansion of metal–phosphine chemistry with the rich chemistry of heterocyclic functionalities is quite obvious. In an examination of the catalytic properties of transition metal complexes containing heterocyclic organophosphines, Rh and Ru catalysts containing pyridylphosphine ligands have been previously prepared and studied.[1] Unfortunately, they were found to be inactive in homogeneous catalytic hydrogenation reactions.[1a] The inactivity of the catalysts was attributed to the pyridyl group which coordinated to the metal center and rendered the complex coordinately saturated. Recently, we have prepared a substituted pyridylphosphine ligand **1** and found

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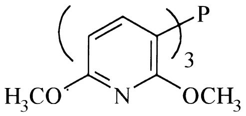
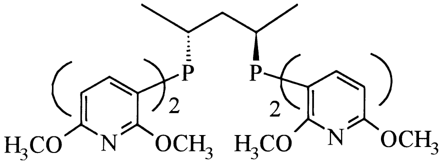
that by preventing the coordination of the pyridyl group to the metal center, the resulting complexes were active for the hydrogenation of olefins, aldehydes, and imines.[2] Furthermore, separation of the catalyst from the reaction product in a water-immiscible organic solvent was achieved by extracting the catalyst with aqueous hydrochloric acid.[2] This work prompted us to carry out the synthesis of chiral diphosphines with noncoordinating pyridyl groups and to examine the use of the new chiral ligands in catalytic asymmetric synthesis.

Two convenient targets in an initial study are the synthesis and application of novel pyridyl diphosphine ligands Py*-Skewphos **2** and Py*-DIOP **3** in which the corresponding PPh_2 moieties of Skewphos and DIOP are replaced by PPy_2* (Py*=2,6-dimethoxypyridine). Since the catalytic properties of Rh(Skewphos) and Rh(DIOP) have been extensively studied, the study of Rh(Py*-Skewphos) and Rh(Py*-DIOP) in comparison with Rh(Skewphos) and Rh(DIOP) is expected to offer an excellent opportunity to examine the difference between pyridyl phosphine ligands and their regular arylphosphine analogs in Rh-catalyzed asymmetric hydrogenation reactions. In a recent publication we reported the synthesis of **2** and its unique properties in catalytic asymmetric hydrogenation.[3] In this paper we wish to report the synthesis of **3** and its unexpected property in the catalytic asymmetric hydrogenation of prochiral olefins.



1



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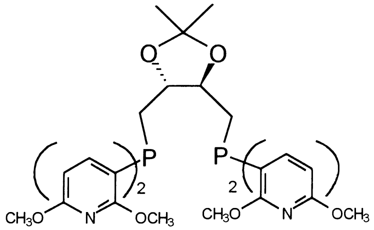

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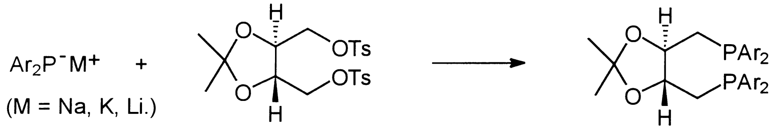
2. Results and discussion

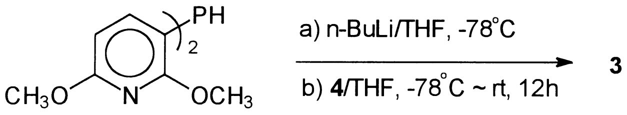
The standard method for the synthesis of DIOP involves a reaction between the diphenyl phosphide anion and the tosylate of the backbone (Eq. 1).[4]



4 **5**

(1)

However, adoption of this method for the synthesis of **3** was less successful in our initial experiments. After quenching the reaction (Eq. 2), a small amount of **3** was isolated (<5% yield) accompanied by unexpected side reactions.

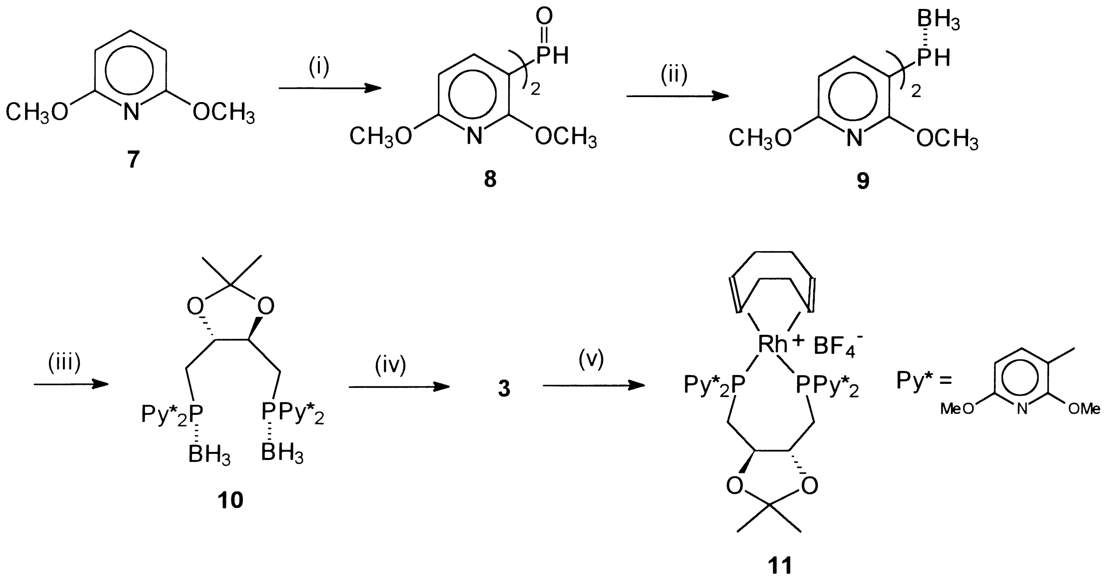


6

(2)

However, by following the phosphine–borane route for the synthesis of chiral diphosphine ligands,[5,6] we were able to synthesize **3** in moderate yield (Scheme 1).

In this route, bis[3-(2,6-dimethoxypyridyl)]phosphine-borane **9** was prepared in good yield through the reduction of the phosphine oxide **8** with $LiAlH_4/CeCl_3/NaBH_4$.[7] Deprotonation of **9** with



(i) a) n-BuLi/THF, -40°C, b) $(EtO)_2POLi$. 80% yield.

(ii) a) $LiAlH_4$-$NaBH_4$-$CeCl_3$/THF, b) 2N HCl. 54% yield.

(iii) a) n-BuLi/THF, -78°C, b)(*2R, 4R*)-1,4-ditosyl-2,3-O-isopropylidenethreitol, rt, 12 h. 70% yield.

(iv) DABCO/toluene, 40°C, 4 h. 87% yield.

(v) $[Rh(COD)_2]BF_4$/THF. 83% yield.

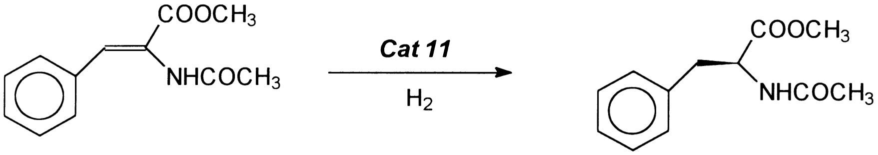
Scheme 1.

BuLi at low temperature followed by the addition of a THF solution of (2*R*,3*R*)-1,4-ditosyl-2,3-*O*-isopropylidenethreitol **4** gave a high yield of Py*-DIOP·BH_3 **10**. The pyridyldiphosphine ligand **3** was obtained by the deboranation of **10** with DABCO.[6] The rhodium complex **11** was prepared by mixing ligand **3** with 1 equivalent of $[Rh(COD)_2]BF_4$ in THF.

The Rh-(*R*,*R*)-Py*-DIOP complex **11** was found to be an effective catalyst for the asymmetric hydrogenation of α-amidoacrylic acid and derivatives. The hydrogenation of methyl α-acetamidocinnamate proceeded smoothly at ambient temperature and under 500 psi of H_2 for 1 h, leading to *N*-acetyl-phenylalanine in 100% yield and 57% enantiomeric excess (*S*). The rate and enantioselectivity of the reaction were affected by the choice of solvent, H_2 pressure and reaction temperature (Table 1). Higher H_2 pressure and reaction temperature gave a higher rate of reaction at the expense of enantioselectivity (Table 1, entries 3–8). When the reaction was carried out in methanol at 0°C and under 100 psi of H_2 for 8 h, the product was formed in 100% yield and 64% *ee* (*S*). In comparison, 55% *ee* (*R*) of *N*-acetyl-phenylalanine was obtained from the same reaction using Rh-(*R*,*R*)-DIOP as catalyst.[8] Quite interestingly, the hydrogenation products from the two systems were found to be of opposite configurations. This phenomenon cannot be explained simply in terms of steric effects. For example, use of hindered DIOP analogue **5b** (**5**: Ar=3,5-dimethyl phenyl) in the hydrogenation of α-acetamidocinnamic acid gave *N*-acetyl-phenylalanine with 39% *ee* but still with *R* configuration.[8]

It is of interest to note that while the Rh(DIOP) catalyst generally gives a higher *ee* in the hydrogenation of amidoacrylic acids than the corresponding methyl esters,[8] the reverse is true when using catalyst **11**. For example, while the hydrogenation of α-benzamidocinnamic acid catalyzed by **11** gave only 66% *ee*, the same catalyst under otherwise identical conditions gave 83% *ee* in the hydrogenation of methyl α-benzamidocinnamate (Table 2, entries 2, 3). In contrast, the hydrogenation of methyl α-

Table 1
The effects of solvent, hydrogen pressure and reaction temperature on the Rh(Py*-DIOP)-catalyzed asymmetric hydrogenation of methyl α-acetamidocinnamate[a]



Entry	*solvent*	*P H_2 (psi)*	*temp.(C)*	*time(h)*	*conv.(%)*	*ee [b](%)*	*config.*
1	THF	500	25	3	17	44	*S*
2	*i*-PrOH	500	25	3	90	40	*S*
3	MeOH	500	25	1	100	57	*S*
4	MeOH	1500	25	1	100	50	*S*
5	MeOH	100	25	1	97	60	*S*
6	MeOH	50	25	1	71	61	*S*
7	MeOH	100	50	1	100	55	*S*
8	MeOH	100	0	8	100	64	*S*

[a] The reactions were carried out using a substrate to catalyst molar ratio of 100. [b] The ee's were determined by gas chromatography using a 25-m Chirasil L-Val capillary column.

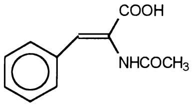
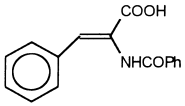
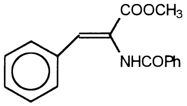
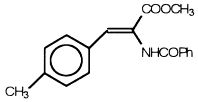
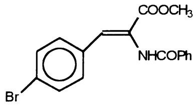
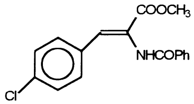
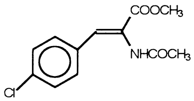
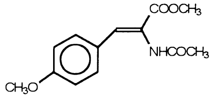
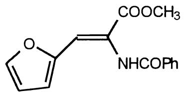
benzamidocinnamate with Rh(DIOP) catalyst gave only 14% *ee*.[9] The asymmetric hydrogenation of other amidoacrylic acid esters using **11** as catalyst has also been studied. Similar *ee* values have been obtained in the hydrogenation of benzamides of substituted cinnamates (Table 2, entries 4–6).

The opposite product configurations using **3** (as compared to DIOP) as a chiral ligand have also been observed in the hydrogenation of other prochiral olefins such as enol esters and itaconic acid, and the results are shown in Table 3. For comparison purposes, some hydrogenation results of the Rh(DIOP) system from the literature are also listed in Table 3. Rh-(*R*,*R*)-DIOP generally gave products in *R* configuration in the hydrogenation of prochiral olefins such as amidoacrylic acids and enols, while Rh-(*S*,*S*)-DIOP gave the products in *S* configuration.[9–11] Itaconic acid was an exception to this trend and the *S* product was obtained with Rh-(*R*,*R*)-DIOP catalyst. In our study, it was found that in the hydrogenation of amidoacrylic acids and enols catalyzed by Rh-(*R*,*R*)-Py*-DIOP, all products were of *S* configurations (Table 3, entries 1–3), while the hydrogenation of itaconic acid gave a product of *R* configuration (Table 3, entry 4). The modification of the DIOP ligand has been widely investigated because of the ready availability of the chiral source. The use of the modified chiral DIOP analogs resulted in diverse *ee* values in the hydrogenation of prochiral olefins.[8,9,11,12]

It is worth noting that good *ee* values have been obtained in the hydrogenation of enamides (Table 3, entries 5–9). Compared with DIOP, a higher *ee* value was obtained in the hydrogenation of a β-unsubstituted enamide using Py*-DIOP as the chiral ligand (Table 3, entry 5). In particular, *ee* values over 80% have been obtained even using *Z/E* mixtures of the *N*-acetyl α-aryl-1-propenylamines as substrates (Table 3, entries 6–8). Since in many cases the separation of *Z/E* isomers are extremely difficult, it is highly desirable to develop catalyst systems which can give high *ee* values in the hydrogenation of the mixture of *Z/E* isomers.[13] To the best of our knowledge, very few ligands have been reported to give promising results in the hydrogenation of *Z/E* mixtures of enamides.[13,14]

In conclusion, we have synthesized a novel chiral pyridyl diphosphine (*R*,*R*)-Py*-DIOP **3** and its Rh complex **11**. Moderate to good enantiomeric excesses have been obtained in the asymmetric hydrogenation of methyl α-benzamidocinnamate and other enamides by using **11** as catalyst precursor. A

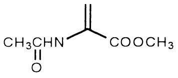
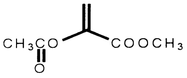
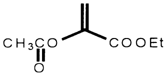
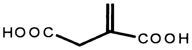
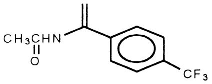
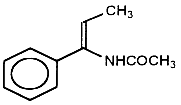
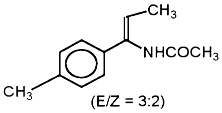
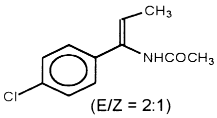
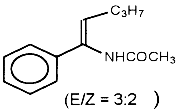
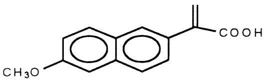
Table 2
The asymmetric hydrogenation of aromatic α-(acylamino)acrylic acids catalyzed by **11**[a]

Entry	*Substrate*	*Ee*[b] *(config.)*
1		33 % *(S)*
2		66% *(S)*
3		83% *(S)*
4		80% *(S)*
5		78% *(S)*
6		79% *(S)*
7		57% *(S)*
8		62% *(S)*
9		55% *(S)*

[a] The reactions were carried out in methanol under 100psi H_2 at ambient temperature for 1 h; substrate/catalyst = 100 (M/M); 100% conversion was achieved in all cases. [b] The ee's were determined by gas chromatography using a 25-m Chirasil L-Val capillary column.

comparison of the experimental results with those obtained from the use of the DIOP system reveals that the products of the two systems are of opposite configurations in the hydrogenation of amidoacrylic acids, enols and itaconic acid. Therefore, the optically active products of both *R* and *S* configurations can be obtained by using Rh catalysts containing chiral ligands derived from the readily available L-tartric acid.

Table 3
The asymmetric hydrogenation of prochiral olefins catalyzed by **11**[a]

Entry	*Substrate*	*ee (config.) with ligand **9***	*ee (config.) with Rh-DIOP systems*
1		48% *(S)*[b]	60% *(S)* *Rh-(S,S)-DIOP*[9]
2		28% *(S)*[b]	
3		42% *(S)*[b]	27% *(R)* *Rh-(R,R)-DIOP*[10]
4		32% *(R)*[b]	62% *(S)* *Rh-(R,R)-DIOP*[11]
5		76% *(S)*[c]	36% (*R*)[e] *Rh-(S,S)-DIOP*
6	 (E/Z = 2:1)	84% *(S)*[c]	87% (*R*)[e] *Rh-(S,S)-DIOP*[f]
7	 (E/Z = 3:2)	81% *(S)*[c]	
8	 (E/Z = 2:1)	81% *(S)*[c]	
9	 (E/Z = 3:2)	40% *(S)*[c]	
10		32% *(S)*[d]	

[a] The reactions (except entry 10) were carried out in methanol under 100psi H_2 at ambient temperature for 1 h; substrate/catalyst = 100 (M/M); 100% conversion was achieved in all cases. [b] The ee's were determined by gas chromatography using a 25-m CP Chirasil-DEX-CB capillary column. [c] The ee's were determined by gas chromatography using a 25-m Chirasil L-Val capillary column. [d] The hydrogenation was carried out in methanol under 1000psi H_2 at 50°C for 10 h with a substrate/catalyst = 100 (M/M); 100% conversion; the ee was determined by HPLC using a SUMI CHIRAL OA-2500 column. [e]This work, catalyst: [Rh(*S*,*S*)-DIOP(COD)]ClO$_4$, reactions conditions: same as Rh(Py*-DIOP). [f]92% ee (*R*) was reported by Kagan *et al* using the same catalyst, however, the *E/Z* ratio was not mentioned.[9]

3. Experimental

Unless otherwise noted, all reactions were carried out under dry nitrogen atmosphere. Melting points were determined using an Electrothermal 9100 apparatus. Optical rotations were measured on a Perkin–Elmer Model 341 polarimeter. NMR spectra were recorded on a Bruker DPX-400 spectrometer. Mass analyses were performed by a Finnigan Model Mat 95 ST mass spectrometer. HPLC analyses were performed using a Hewlett–Packard Model HP 1050 LC interfaced to an HP 1050 Series workstation.

*3.1. Bis[3-(2,6-dimethoxypyridyl)]phosphine oxide **8***[3]

A solution of *n*-butyllithium (62.5 mL of a 1.6 M hexane solution, 100 mmol) was added to a solution of 2,6-dimethoxypyridine (13.9 g, 100 mmol) in 200 mL of THF at −40°C with magnetic stirring over a period of 1 h. The resulting mixture was stirred for another 1 h at −40°C and for 4 h at ambient temperature. A THF solution (100 mL) of lithium diethylphosphide (50 mmol), which was prepared in situ by adding *n*-butyllithium (31.3 mL of a 1.6 M hexane solution, 50 mmol) to a THF solution (20 mL) of diethylphosphite (6.7 mL, 50 mmol), was added dropwise to the above solution over a period of 1 h. After stirring for 24 h at room temperature, the reaction was quenched by adding 5 mL of water. The solvent was removed under reduced pressure with a rotary evaporator and the residue was redissolved in 300 mL of ethyl acetate. The ethyl acetate solution was washed with brine (2×50 mL) and dried over anhydrous sodium sulfate. The solution was concentrated to 50 mL and then cooled in a refrigerator overnight. A light yellow solid was collected, which upon recrystallization from ethyl acetate afforded a white powdery product (12.9 g, 80% theoretical yield). Mp: 139–140°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.90 (s, 6H), 3.95 (s, 6H), 6.40 (d, J=8.1 Hz, 2H), 7.84 (dd, $J_{P\text{–}H}$=13.5 Hz, $J_{H\text{–}H}$=8.1 Hz, 2H), 8.06 (d, $J_{P\text{–}H}$=515.2 Hz, 1H); ^{31}P NMR (160 MHz, $CDCl_3$) δ: 4.8 ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 53.5, 53.6, 101.9 (d, $J_{P\text{–}C}$=9.9 Hz), 102.9 (d, $J_{P\text{–}C}$=113.0 Hz), 144.6 (d, $J_{P\text{–}C}$=9.0 Hz), 163.4 (d, $J_{P\text{–}C}$=6.2 Hz), 166.1; IR (KBr): 2997, 2947, 2400, 1593, 1481, 1375, 1333, 1186, 1095, 1010, 933, 807cm^{-1}; MS (30 ev): *m/z* 325 (M^++1), 294, 152.

*3.2. Bis[3-(2,6-dimethoxypyridyl)]phosphine **6***[3]

A toluene solution (100 mL) of **8** (5 g, 15.4 mmol), triethylamine (10 mL, 72 mmol) and trichlorosilane (7.2 mL, 72 mmol) was stirred at reflux temperature for 12 h. The reaction mixture was allowed to cool to room temperature. A 15% NaOH solution (20 mL) was added and the mixture was stirred at reflux temperature for 4 h. The aqueous layer was separated from the organic phase and was extracted with 2×20 mL toluene. The combined organic solution was dried over anhydrous sodium sulfate. The solvent was evaporated in vacuo to give a white solid which was washed with methanol (2×15 mL) to afford **6** (3.6 g, 76% theoretical yield). Mp: 113–114°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.91 (s, 6H), 3.95 (s, 6H), 5.05 (d, $J_{P\text{–}H}$=229.5 Hz, 1H), 6.26 (d, J=7.9 Hz, 2H), 7.48 (dd, $J_{P\text{–}H}$=6.4 Hz, $J_{H\text{–}H}$=7.9 Hz, 2H); ^{31}P NMR (160 MHz, $CDCl_3$) δ: −78.8 ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 54.2, 54.3, 102.0, 105.5 (d, $J_{P\text{–}C}$=112.4 Hz), 147.5 (d, $J_{P\text{–}C}$=12.5 Hz), 164.3 (d, $J_{P\text{–}C}$=10.0 Hz), 164.8; IR (KBr): 3006, 2960, 2914, 2315, 2256, 1578, 1485, 1460, 1420, 1380, 1189, 1275, 1249, 1189, 1104, 887, 814 cm^{-1}; MS (30 ev): *m/z* 309 (M^++1).

*3.3. Bis[3-(2,6-dimethoxypyridyl)]phosphine-borane **9***

Anhydrous cerium chloride (5.0 g, 20.2 mmol) was quickly pulverized in a mortar and was placed in a 100 mL two-necked flask. Tetrahydrofuran (50 mL) was then added and the mixture was stirred for 0.5 h. $NaBH_4$ (0.76 g, 20.2 mmol) was added and the stirring was continued for another 1 h. The flask was immersed in an ice bath and **8** (2.2 g, 6.8 mmol) was added in portions. The ice bath was removed and the mixture was stirred at ambient temperature for 12 h. The reaction mixture was carefully poured into ice–water containing 2 N HCl (50 mL) under stirring and the final mixture was then extracted with ethyl acetate (3×50 mL). The combined extracts were washed with brine (20 mL), dried over Na_2SO_4 and evaporated to about 2 mL. The concentrated extract was subjected to column chromatography on silica gel using hexane:ethyl acetate (4:1) as eluent. The product was recrystallized from hexane–benzene to afford a white crystalline solid **9** (1.2 g, 54% theoretical yield). Mp: 120–121°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.91 (s, 12H), 6.37 (d, J=8.2 Hz, 2H), 6.46 (dq, $J_{P\text{–}H}$=407.7 Hz, $J_{BH3\text{–}H}$=6.7 Hz, 1H), 7.46 (dd, $J_{P\text{–}H}$=11.8 Hz, $J_{H\text{–}H}$=8.2 Hz, 2H); ^{31}P NMR (160 MHz, $CDCl_3$) δ: −29.4 (broad) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 54.4, 54.5, 98.5 (d, $J_{P\text{–}C}$=62.7 Hz), 103.0 (d, $J_{C\text{–}P}$=9.0 Hz), 146.4 (d, $J_{P\text{–}C}$=12.5 Hz), 164.1, 166.6; MS: *m/z* 308 ($M^+ - BH_3$).

*3.4. (−)-(4R,5R)-4,5-Bis[di-3′-(2′,6′-dimethoxypyridyl)phosphinomethyl]-2,2-dimethyl-1,3-dioxolane-borane **10***

A sample of **9** (0.34 g, 1.2 mmol) was dissolved in dry THF (5 mL), the solution was cooled to −78°C, and *n*-BuLi (0.81 mL of a 1.6 M hexane solution, 1.3 mmol) was added dropwise with vigorous stirring. The lightly yellow solution was allowed to warm to ambient temperature and (2*R*,3*R*)-1,4-ditosyl-2,3-*O*-isopropylidenethreitol in 3 mL of THF was added in a dropwise manner. After stirring for 12 h, the reaction was quenched by adding 1 mL of methanol. The solution was concentrated to about 1 mL, which was then subjected to column chromatography on silica gel using hexane:ethyl acetate (5:1) as the eluent. The pyridylphosphine–borane complex **10** was obtained as a white solid after evaporation of the solvent (0.27 g, 70% theoretical yield). Mp: 103–105°C; $[\alpha]_D^{20}$ +44.1 (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.96 (s, 6H), 2.50 (m, 2H), 2.82 (m, 2H), 3.78 (s, 6H), 3.88 (d, $J_{P\text{–}H}$=3.5 Hz, 6H), 3.90 (s, 6H), 3.94 (m, 2H), 6.26 (d, J=8.0Hz, 2H), 6.31 (d, J=8.0 Hz, 2H), 7.50 (dd, $J_{P\text{–}H}$=11.2 Hz, $J_{H\text{–}H}$=8.0 Hz, 2H), 7.93 (dd, $J_{P\text{–}H}$=11.8 Hz, $J_{H\text{–}H}$=8.0 Hz, 2H); ^{31}P NMR (160 MHz, $CDCl_3$) δ: 6.7 ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.6, 53.2, 53.4, 53.5, 100.1 (d, $J_{P\text{–}C}$=60.9 Hz), 100.9 (d, $J_{P\text{–}C}$=63.7 Hz), 101.4 (d, $J_{P\text{–}C}$=9.6 Hz), 101.8 (d, $J_{P\text{–}C}$=9.7 Hz), 108.2, 145.1 (d, $J_{P\text{–}C}$=10.6 Hz), 147.0 (d, $J_{P\text{–}C}$=13.5 Hz), 163.3, 163.7, 165.2, 165.6; IR (KBr): 2990, 2947, 2856, 2379, 1600, 1481, 1459, 1375, 1312, 1087, 1018, 814, 772 cm^{-1}; MS: *m/z* 742 ($M^+ - 2BH_3$), 435, 307.

*3.5. (−)-(4R,5R)-4,5-Bis[di-3′-(2′,6′-dimethoxypyridyl)phosphinomethyl]-2,2-dimethyl-1,3-dioxolane **3***

Samples of **10** (0.170 g, 0.22mmol) and DABCO (0.066 g, 0.59 mmol) were dissolved in THF (5 mL). The solution was stirred at 40°C for 4 h and then concentrated to about 1 mL under reduced pressure. The concentrated solution was subjected to column chromatography on silica gel using benzene as the eluent to afford **3** as a white solid after evaporation of the solvent (0.142 g, 87% theoretical yield). Mp: 99–101°C; $[\alpha]_D^{20}$ −5.4 (*c* 1.3, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.27 (s, 6H), 2.35 (dd, J_1=13.9 Hz, J_2=4.4 Hz, 1H), 2.48 (dd, J_1=13.4 Hz, J_2=6.4 Hz, 1H), 3.83 (s, 6H), 3.86 (s, 6H), 3.88 (s, 6H), 3.89 (s, 6H), 3.91 (m, 2H), 6.24 (d, J=7.9 Hz, 2H), 6.26 (d, J=7.9 Hz, 2H), 7.43 (dd, $J_{P\text{–}H}$=5.9 Hz, $J_{H\text{–}H}$=7.9

Hz, 2H), 7.47 (dd, $J_{P\text{–}H}$=5.9 Hz, $J_{H\text{–}H}$=7.9 Hz, 2H); ^{31}P NMR (160 MHz, $CDCl_3$) δ: −43.2 ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.5, 53.1, 53.2, 53.3, 79.9 (d, $J_{P\text{–}C}$=16.6 Hz), 80.8 (d, $J_{P\text{–}C}$=16.6 Hz), 100.8, 100.9, 107.9 (d, $J_{P\text{–}C}$=14.1 Hz), 108.2 (d, $J_{P\text{–}C}$=10.0 Hz), 144.9 (d, $J_{P\text{–}C}$=12.2 Hz), 145.2 (d, $J_{P\text{–}C}$=13.7 Hz), 163.6 (d, $J_{P\text{–}C}$=7.7 Hz), 163.7 (d, $J_{P\text{–}C}$=4.9 Hz), 163.8; IR (KBr): 2980, 2954, 2868, 1591, 1479, 1446, 1413, 1374, 1328, 1275, 1223, 1196, 1012, 801 cm^{-1}; MS: *m/z* 743 (M^++1).

3.6. *(−)-(4*R*,5*R*)-4,5-Bis[di-3′-(2′,6′-dimethoxypyridyl)phosphinomethyl]-2,2-dimethyl-1,3-dioxolane-cyclooctadiene-rhodium(I) tetrafluoroborate* ***11***

Samples of **3** (74 mg, 0.10 mmol) and $[Rh(COD)_2]BF_4$ (46 mg, 0.10 mmol) were dissolved in THF (1 mL). The resulting solution was allowed to stand at ambient temperature for 12 h. The orange crystals thus formed were filtered and washed with THF to afford **10** as brown crystals (86 mg, 83% theoretical yield). Mp: 215–220°C (decomp.); $[\alpha]_D^{20}$ −142.3 (*c* 1.2, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.20 (s, 6H), 2.01 (m, 2H), 2.17 (m, 2H), 2.25–2.45 (m, 4H), 2.52 (m, 2H), 2.94 (m, 2H), 3.16 (m, 2H), 3.86 (s, 6H), 3.93 (m, 2H), 3.97 (s, 6H), 4.09 (s, 6H), 4.13 (s, 6H), 4.21 (m, 2H), 6.27 (d, *J*=8.2 Hz, 2H), 6.84 (d, *J*=8.1 Hz, 2H), 6.95 (dd, $J_{P\text{–}H}$=8.5 Hz, $J_{H\text{–}H}$=8.2 Hz, 2H), 9.26 (dd, $J_{P\text{–}H}$=13.1 Hz, $J_{H\text{–}H}$=8.1 Hz, 2H). ^{31}P NMR (160 MHz, $CDCl_3$) δ: 4.8 (d, $J_{Rh\text{–}P}$=144.2 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.8, 23.3, 26.3, 27.9, 33.1, 54.8, 55.1, 55.2, 68.6, 98.2, 99.2, 99.4, 99.6, 101.4, 101.7, 101.9, 102.4, 103.7, 110, 143.2, 153.7, 162.9, 164.3, 166.1, 168.0; IR (KBr): 2990, 2954, 1600, 1565, 1460, 1375, 1312, 1087, 1004 cm^{-1}; MS (FAB): *m/z* 1041(M^++1), 1011 ($M-OCH_3$), 953 ($M-BF_4$).

3.7. *General procedure for the hydrogenation reaction*

In an inert atmosphere glovebox, a stainless steel reactor was charged with the substrate for hydrogenation (0.1 mmol) and the catalyst **11** (1.0 mg, 0.001 mmol) followed by the addition of methanol (2 mL). The reactor was closed and was pressurized to the pre-determined pressure of H_2 and the mixture was stirred at a pre-set temperature. The conversion and enantiomeric excess of the hydrogenated product were determined by GC or HPLC.

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