# Highly Enantioselective Rh-Catalyzed Hydrogenation Based on Phosphine−Phosphite Ligands Derived from Carbohydrates

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A new class of efficient catalysts was developed for the asymmetric hydrogenation of α,β-unsaturated carboxylic acid derivatives by synthesizing a series of novel phosphine−phosphite ligands (**4a**−**d**) derived from readily available D-(+)-xylose. Excellent enantioselectivities (>99%) were achieved under very mild reaction conditions (1 bar $H_2$ and 20 °C). Varying the biphenyl substituents in the phosphite moiety greatly affected the enantioselectivity in the hydrogenation reactions. The results also indicate that the sense of enantioselectivity is mainly controlled by the configuration of the phosphite moiety. $^{31}P\{^1H\}$ NMR and kinetic studies on intermediates of the catalytic cycle show that the $[Rh(P_1-P_2)(enamide)]BF_4$ species is the resting state and that the rate dependence is first order in rhodium and hydrogen pressure and zero order in enamide concentration.

## Introduction

The asymmetric hydrogenation of functionalized prochiral olefins is one of the most important applications of asymmetric catalysis. Over many years, the scope of this reaction has been gradually extended both in reactant structure and catalyst efficiency.[1] Chiral bidentate phosphorus ligands have played a dominant role in the success of asymmetric hydrogenation.[1,2] Many chiral diphosphines[1,2] and diphosphinites[3] have therefore been synthesized as ligands for enantioselective transition-metal catalyzed hydrogenations. Recent reports on the use of chiral phosphite[4] and phosphoroamidite[5] ligands in asymmetric hydrogenation have demonstrated their potential utility. Nevertheless, the search for new highly efficient ligand systems derived from readily available simple starting materials is still of great importance in catalysis research.

Chiral ligands from the chiral pool have recently attracted a great deal of interest because they are easily available from nature at a reasonable price and because they make tedious optical resolution procedures unnecessary. Moreover, carbohydrates are particularly advantageous because they are highly functionalized compounds with several stereogenic centers, which easily allows the regio- and stereoselective introduction of different functionalities.[6] Their modular nature therefore allows the synthesis of a systematic series of ligands[3a−c,4,7] that can be screened in the search for high activities and enantioselectivities and, at the same time, can provide information about the origin of the stereoselectivity of the reaction.[7j]

In previous studies, different types of phosphorus ligands with a xylofuranoside backbone have been applied to asymmetric hydrogenation with varying degrees of success. Brunner et al. reported moderate enantioselectivities (up to 35%) with phosphine−phosphinite and diphosphinite ligands.[8] More recently, we reported moderate-to-good enantiomeric excesses with diphosphite (ee up to 35%)[4b] and diphosphine (ee up to 91%)[7e] at room temperature, but in both cases the activities were low.

Following our interest in using carbohydrates as an available chiral source for ligands, and bearing in mind Achiwa's idea that two different donor sites can a priori match the intermediates better and so influence their reactivity and enantioselectivity,[9] we have designed a

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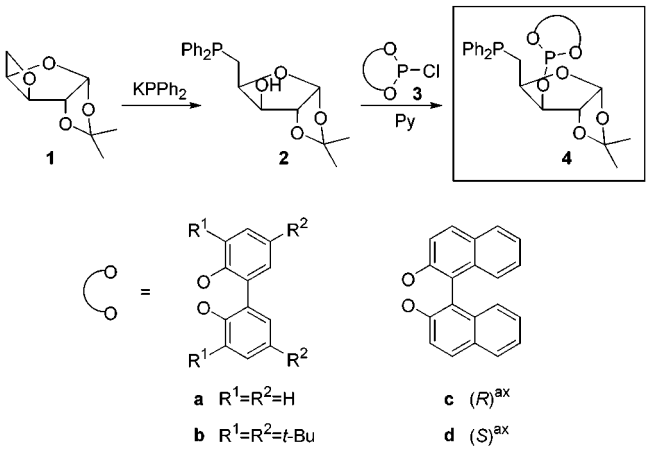
**Scheme 1. Synthesis of Phosphine−Phosphite Ligands 4a−d**




new family of chiral bidentate phosphine−phosphite ligands with xylofuranoside backbone. These ligands combine the advantages of both types of ligand. We also synthesized their cationic Rh(I) precursors and investigated their use in the highly active and enantioselective rhodium-catalyzed asymmetric hydrogenation of α,β-unsaturated carboxylic acid derivatives.[10] To the best of our knowledge, this is the first example of phosphine−phosphite ligands applied to hydrogenation.[11] We also carried out a kinetic study and investigated the reactivity of some key intermediates.

## Results and Discussion

**Synthesis of Phosphine−Phosphite Ligands.** Scheme 1 shows the sequence for the synthesis of the ligands. The new ligands **4a**−**d** were synthesized very efficiently in two steps from oxetane **1**, which is easily prepared on a large scale from D-(+)-xylose.[12] The key step is the oxetane ring opening using a slight excess of potassium diphenylphosphide in DMF to afford phosphine−alcohol intermediate **2**. The yield was considerably higher than with the method of Brunner et al., which prepared **2** from related 5-tosylate derivative.[13] Subsequently treating **2** with 1 equiv of the corresponding in situ formed phosphorochloridite **3a**−**d**[14] in the presence of base provided easy access to the desired phosphine−phosphite ligands **4a**−**d**. These were isolated in good yields as air-stable solids.

**Scheme 2. Synthesis of Rhodium(I)−Cationic Complexes 5a−d**

$$[Rh(cod)_2]BF_4 + \underset{\textbf{4a-d}}{P_1\text{-}P_2} \longrightarrow \underset{\textbf{5a-d}}{[Rh(P_1\text{-}P_2)(cod)]BF_4} + cod$$

**Table 1. Selected Spectroscopic NMR Data for Complexes 5a−d[a]**

| | $P_1$ = phosphine | | $P_2$ = phosphite | | |
|---|---|---|---|---|---|
| compd | $\delta$ ($P_1$) | $J_{P1-Rh}$ | $\delta$ ($P_2$) | $J_{P2-Rh}$ | $J_{P1-P2}$ |
| **5a** | 13.9 | 145.2 | 135.1 | 260.5 | 43.3 |
| **5a** (55%)[b] | 18.6 | 148.3 | 132.8 | 266.8 | 45.6 |
| **5a** (45%)[b] | 7.5 | 142.0 | 143.7 | 253.2 | 41.6 |
| **5b** | 15.3 | 144.3 | 131.4 | 260.8 | 40.2 |
| **5b** (60%)[b] | 19.7 | 147.9 | 130.4 | 268.2 | 43.9 |
| **5b** (40%)[b] | 8.8 | 141.9 | 141.0 | 248.9 | 42.1 |
| **5c** | 14.9 | 141.3 | 141.3 | 262.2 | 48.2 |
| **5d** | 15.2 | 140.7 | 140.7 | 260.6 | 49.0 |

[a] NMR measured in $CD_2Cl_2$ at 25 °C, chemical shift ($\delta$) in ppm, coupling constants ($J$) in hertz. [b] NMR measured at −80 °C, relative abundance in brackets.

The $^1H$ and $^{13}C$ NMR spectra were as expected for these xylofuranoside ligands. Two doublets, one for each phosphorus moiety, were observed in the $^{31}P$ NMR spectra. The $J_{P-P}$ values of 12−33 Hz are similar to those reported for other phosphine−phosphite ligands.[11a] Due to the axial chirality of the biphenyl group, two pairs of signals were expected for ligands **4a** and **4b**. However, the existence of a single doublet for each phosphorus atom in the variable-temperature $^{31}P$ NMR suggested rapid ring inversions (atropoisomerization) in the bisphenol−phosphorus moieties on the NMR time scale.[15]

**Synthesis of Rhodium(I) Complexes.** The olefinic cationic Rh(I) complexes were prepared in high yields by reacting stoichiometric amounts of chiral phosphine ($P_1$)−phosphite ($P_2$) ligands **4a**−**d** with $[Rh(cod)_2]BF_4$ in dichloromethane (Scheme 2).

Complexes **5a**−**d** were isolated as a yellow, moderately air-stable powder by adding hexane. The elemental analysis of C and H matched the stoichiometry $[Rh(cod)(P_1-P_2)]_n(BF_4)_n$. The FAB mass spectra showed the highest ion at $m/z$ values that correspond to the cationic mononuclear species.

The $^1H$ NMR spectra of complexes **5a**−**d** were in agreement with the expected coordinated pattern for the xylofuranoside protons. Also as expected for these $C_1$-symmetrical complexes, there were four signals for the olefinic carbon atoms of the coordinated cyclooctadiene. However, the eight methylenic protons appeared as a unique broad signal. This phenomenon has also been reported for related asymmetric compounds with a similar ligand backbone.[4b,7c,16]

The VT-$^{31}P$ NMR spectra for complexes **5c** and **5d**, which contain a binaphthyl moiety, showed two sharp double doublets due to the $^{31}P/^{31}P$ and $^{31}P/^{103}Rh$ couplings (Table 1). These results are consistent with the presence of a single isomer in solution. At room temperature, the $^{31}P$ NMR spectra for complexes **5a** and **5b** showed a sharp double doublet in the phosphite region and a broad doublet in the phosphine region (Table 1). This suggested fluxional processes on the NMR time scale, and these were confirmed by measuring a VT-$^{31}P$ NMR. At 193 K, the $^{31}P$ NMR spectra therefore showed two sets of signals

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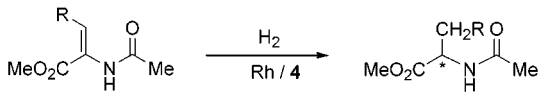
**Table 2. Asymmetric Hydrogenation of Methyl (*N*)-Acetamidoacrylate 6 and Methyl (*Z*)-(*N*)-Acetamidocinnamate 7 with $[Rh(cod)_2]BF_4$/4[a]**




**6** R = H
**7** R = Ph

| entry | substrate | solvent | ligand | TOF[b] | % convn[c] (time/min) | % ee[d] |
|---|---|---|---|---|---|---|
| 1 | **6** | MeOH | **4b** | 85 | 100 (75) | 91 (*R*) |
| 2 | **6** | $CH_2Cl_2$ | **4b** | 40 | 100 (150) | >99 (*R*) |
| 3 | **6** | Toluene | **4b** | 12 | 100 (600) | 97 (*R*) |
| 4 | **6** | THF | **4b** | 64 | 100 (120) | 92 (*R*) |
| 5[e] | **6** | $CH_2Cl_2$ | **4b** | 41 | 100 (150) | >99 (*R*) |
| 6[f] | **6** | $CH_2Cl_2$ | **4b** | 40 | 100 (150) | >99 (*R*) |
| 7[g] | **6** | $CH_2Cl_2$ | **4b** | 43 | 100 (150) | >99 (*R*) |
| 8 | **6** | $CH_2Cl_2$ | **4a** | >1200 | 100(<5) | 88.2 (*S*) |
| 9 | **6** | $CH_2Cl_2$ | **4c** | 318 | 100 (20) | 97.6 (*R*) |
| 10 | **6** | $CH_2Cl_2$ | **4d** | 330 | 100 (20) | 98.3 (*S*) |
| 11 | **7** | $CH_2Cl_2$ | **4a** | 653 | 100 (10) | 84.1 (*S*) |
| 12 | **7** | $CH_2Cl_2$ | **4b** | 31 | 100 (180) | 98.8 (*R*) |
| 13 | **7** | $CH_2Cl_2$ | **4c** | 212 | 100 (30) | 94.3 (*R*) |
| 14 | **7** | $CH_2Cl_2$ | **4d** | 245 | 100 (30) | 91 (*S*) |

[a] $[Rh(cod)_2]BF_4$ = 0.01 mmol. **4**/Rh =1.1. Substrate/Rh = 100. P = 1 atm. $CH_2Cl_2$ = 6 mL. *T* = 25 °C. [b] TOF in mol product × mol $Rh^{-1}$ × $h^{-1}$ measured by GC after 5 min. [c] Percent conversion measured by GC. [d] Percent enantiomeric excess measured by GC using an L-Chiralsil-Val column. [e] Using preformed complex **5b** (0.01 mmol). [f] **4b**/Rh = 2. [g] Using preformed [Rh(nbd)(**4b**)]$BF_4$ (0.01 mmol).

attributed to different isomers in solution (Table 1). The formation of different isomers may have been caused by two diastereoisomers obtained from the atropisomerism of the bisphenol in the phosphite moiety, different conformers for the six-membered chelate ring, or a combination of both. Although several conformers of the six-membered chelate ring have been observed in similar complexes with furanoside ligands,[4b,7,16] the presence of a single species in solution for complexes **5c** and **5d** indicates that interconversion in the biphenyl is responsible for the different isomers in solution for complexes **5a** and **5b**. This behavior contrasts with the inhibition biphenyl interconversion upon coordination to the metal center that is usually observed with diphosphites and other phosphine−phosphite ligands.[4b,11,17]

**Asymmetric Hydrogenation**. In a first set of experiments, we used the rhodium-catalyzed hydrogenation of methyl (*N*)-acetamidoacrylate **6** to scope the potential of ligands **4a**−**d** for asymmetric catalysis. The reaction proceeded smoothly at 1 bar of $H_2$ at room temperature. In general, the catalysts were prepared in situ by adding the corresponding phosphine−phosphite ligand to $[Rh(cod)_2]BF_4$ as a catalyst precursor. The results are summarized in Table 2.

The effects of different reaction parameters (e.g., solvent, catalyst preparation, and ligand-to-rhodium ratio) were investigated for the catalytic precursor containing ligand **4b**. The results showed that the efficiency of the process was affected by the nature of the solvent (Table 2, entries 1−4). Although rhodium-catalyzed asymmetric hydrogenation reactions are usually performed in methanol, the reaction in this solvent showed the lowest enantioselectivity (Table 2, entry 1). Moreover, when methanol was used as a solvent, enantioselectivity decreased slightly over time, which suggests that, due to the partial decomposition of the ligand in methanol, the catalyst evolved over time.[18] The best catalyst performance (in terms of activity and enantioselectivity) was obtained when dichloromethane was used as a solvent (Table 2, entry 2).

As expected, the efficiency of the process was not affected when preformed catalyst precursor **5b** was used (Table 2, entry 5) or when a 1-fold excess of ligand was added (Table 2, entry 6). Heller et al. recently showed that when norbornadiene (nbd) is used as a counter ligand in the cationic Rh-Duphos asymmetric hydrogenation, the reaction is faster than with related cyclooctadiene complexes.[19] We therefore compared the cod precatalyst **5b** with the corresponding nbd complex, but the activity and enantioselectivity of the two catalyst precursors were similar (Table 2, entry 7 vs 5).

The rest of the ligands were therefore tested under "standard" conditions, i.e., dichloromethane as a solvent and a ligand-to-rhodium ratio of 1. Ligand **4a**, with the nonsubstituted biphenyl moiety at the phosphite, resulted in higher activity than ligand **4b**, although the enantioselectivity was lower (Table 2, entry 8 vs 2). The presence of bulky *tert*-butyl groups in the ortho positions of the biphenyl moiety therefore had an extremely positive effect on enantioselectivity. Interestingly, the sense of the enantioselectivity was reversed: the (*S*)-enantiomer was obtained with ligand **4a** whereas the (*R*)-enantiomer was obtained with ligand **4b**.

Ligands **4c** and **4d**, which contain a stereogenic binaphthyl moiety, produced a high reaction rate and high enantioselectivity (Table 2, entries 9 and 10). Thus, ligand **4c**, which has an (*R*)-binaphthyl moiety, led to an ee of 97.6% (*S*), whereas diastereomer **4d**, which has an (*S*)-binaphthyl moiety, resulted in an ee of 98.3% (*R*). This indicates that the sense of the enantiodiscrimination is predominantly controlled by the conformation of the binaphthyl at the phosphite moiety.

To verify the generality of these results, we performed the Rh-catalyzed asymmetric hydrogenation of methyl (*Z*)-(*N*)-acetylaminocinnamate **7** (Table 2, entries 11−14). As expected, the results followed the same trend as those of methyl (*N*)-acetamidoacrylate **6**, but the enantiomeric excesses were somewhat smaller and the reaction rates were slightly slower. The configuration of the hydrogenated product was not affected by the phenyl group in **7**. The catalyst precursor with ligand **4b** produced the highest enantiomeric excess (98.8%; Table 2, entry 12).

**Mechanistic Considerations.** The commonly accepted mechanism of asymmetric diphosphine−Rh(I)-catalyzed hydrogenation, first proposed by Landis and Halpern, involves the reversible binding of the substrate to the catalysts, followed by enantio- and rate-determining activation of $H_2$ and subsequent fast reductive elimination of the hydrogenated product (Scheme 3).[20]

In the past few years, this mechanism has proved valid for other phosphorus ligands. Thus, RajanBabu et al.[3b,c,21]

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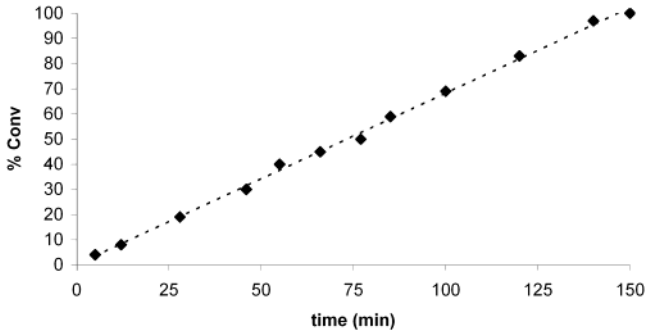



**Figure 1.** Variation of the conversion over time. Conditions: $T = 25$ °C, $pH_2 = 1$ bar, [**5b**] = 1.67 mM, $[\mathbf{6}]_o = 0.17$ M.

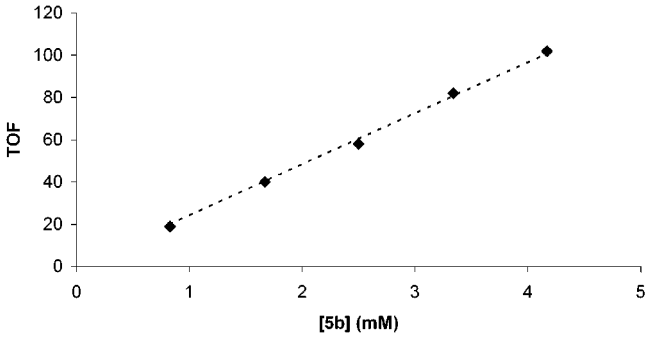
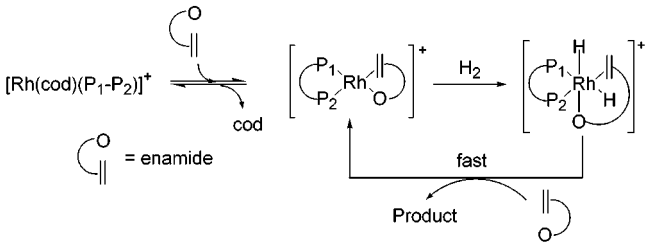



**Figure 2.** Variation of the rhodium concentration. Conditions: $T = 25$ °C, $pH_2 = 1$ bar, $[\mathbf{6}]_o = 0.17$ M.

**Scheme 3**




and we[4b] recently provided experimental support for a similar pathway using cationic Rh(I) diphosphinite and diphosphite precursors, respectively. However, the presence of two different functionalities in these Rh(I) phosphine−phosphite catalysts may affect the catalytic sequence. To learn more about the catalytic cycle, we made a kinetic study and investigated the species formed with catalyst precursor **5b** under hydrogenation conditions.

The rate-controlling steps of the hydrogenation reaction of methyl (*N*)-acetamidoacrylate **6** using catalyst precursor **5b** were determined by a kinetic study in which we investigated the concentration dependency of the reaction rates of all the reactants (e.g., substrate and rhodium concentration and hydrogen pressure). The substrate concentration dependency was established by following the conversion over time. The graph of conversion versus time clearly shows a zero-order dependency on substrate concentration (Figure 1).

To study the effect of rhodium concentration on reaction rate, we varied this concentration between 0.83 and 4.17 mM (Figure 2). The rate (TOF) of hydrogenated product formation is linearly proportional to the rhodium concentration, which indicates a first-order dependency.

The hydrogen pressure was varied between 1 and 3 bar. The results in Table 3 show a first-order dependency.

**Table 3. Hydrogen Pressure Dependency on the Hydrogenation Reaction Rate[a]**

| $P_{H2}$ (atm) | [**5b**] (mM) | TOF[b] |
|---|---|---|
| 1 | 1.67 | 40 |
| 2 | 1.67 | 74 |
| 3 | 1.67 | 115 |

[a] Conditions: $T = 25$ °C, $[\mathbf{6}]_o = 0.17$ M. [b] TOF in mol product × mol $Rh^{-1}$ × $h^{-1}$ measured by GC after 5 min.

This kinetic study indicates that the rate-determining step is the activation of hydrogen. This feature matches with the expected Landis−Halpern mechanism. However, the so-called "dihydride mechanism",[22] in which the substrate coordination takes place after the activation of hydrogen, cannot be excluded because the same kinetic pattern would be obtained if the addition of hydrogen were the rate-determining step.

To obtain more insight into the sequence of the catalytic cycle, we studied the species formed under hydrogenation conditions. First we investigated the reactivity of catalyst precursor **5b** with molecular hydrogen. The VT-$^1$H NMR spectra did not show the formation of hydride species when catalyst precursor **5b** was dissolved in dichoromethane-$d_2$ and pressurized with 1.1 bar of $H_2$. Also, the VT-$^{31}$P NMR spectra did not show any new signal, which indicated that catalyst precursor **5b** did not react with molecular hydrogen under these conditions. After dehydroamino acid derivative **6** was added, two new double doublets at 145.8 ($P_2$) and 16.3 ($P_1$) ppm were observed in the $^{31}P\{^1H\}$ NMR spectrum. These new signals were assigned to the cationic rhodium complex [Rh (**4b**)(**6**)]$^+$. The $P_1-P_2$ coupling constant is 63 Hz, whereas $J\{P_1-Rh\}$ and $J\{P_2-Rh\}$ are 158 and 236 Hz, respectively. VT-$^{31}P\{^1H\}$ NMR spectra between +25 and −80 °C showed that there was only one diastereomer. Also, neither the [Rh(**4b**)(**6**)$H_2$]$BF_4$ species nor the [Rh(**4b**)(alkyl)H]$BF_4$ species were observed under hydrogenation conditions.

The NMR results using Rh−phosphine−phosphite catalyst precursor **5b** agreed with the well-established Landis−Halpern mechanism via Rh enamide species (Scheme 3). However, this evidence is not conclusive because species [Rh(**4b**)(**6**)$H_2$]$BF_4$ may have been present in amounts that were below the detection limit of the NMR equipment.

The origin of the enantioselectivity can be explained by analyzing the structure of the square-planar enamide intermediates and their reactivity toward hydrogen.[23] The coordination mode of the enamide is based on both electronic and steric properties, so we investigated whether it is affected by the different steric properties of ligands **4a** and **4b**. Thus, when complex **5a** was treated with enamide **6** in the same way as complex **5b** (vide supra), two new double doublets at 146.3 ($P_2$) and 15.1 ($P_1$) ppm attributed to [Rh(**4a**)(**6**)]$^+$ were observed in the $^{31}P\{^1H\}$ NMR. The chemical shifts and the coupling constants ($J\{P_1-P_2\}$= 61.2 Hz, $J\{P_1-Rh\}$= 154.6 Hz, $J\{P_2-Rh\}$= 237.4 Hz) are similar to those for complex [Rh(**4b**)(**6**)]$^+$. Also, VT-$^{31}P\{^1H\}$ NMR showed that only one diasteroi-

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somer was present. This suggests that for our Rh−phosphine−phosphite, the coordination mode of the enamide is mainly controlled by the electronic properties of the ligand. In summary, the formation of the diastereomeric Rh(III)−dihydride complexes, and therefore that of the hydrogenated product, is mainly controlled by the steric hindrance of the phosphite moiety, which controls the rotation of the substrate with respect to the ligand that follows the oxidative addition of $H_2$. This agrees with our hydrogenation results, which indicated that the sense of the enantioselectivity was controlled by the phosphite moiety (vide supra).

## Conclusions

A series of novel phosphine−phosphite ligands **4a**−**d** that contain a furanoside as a simple but highly effective chiral backbone was reported. These ligands, which are easily prepared in a few steps from the readily available D-(+)-xylose, are very effective in the Rh(I)-catalyzed asymmetric hydrogenation of α,*β*-unsaturated carboxylic acid derivatives. The results show that the presence of bulky *tert*-butyl groups in the ortho positions of the biphenyl moiety or the presence of a stereogenic binaphthyl moiety had an extremely positive effect on enantioselectivity. The absolute configuration of the major enantiomer of the hydrogenated product is mainly controlled by the configuration of the phosphite moiety. Kinetic studies indicates that the rate dependence is first order in rhodium and hydrogen pressure and zero order in enamide concentration. NMR studies on the intermediates formed under hydrogenation conditions indicate that the $[Rh(P_1-P_2)(enamide)]BF_4$ species is the resting state. The combination of high enantioselectivities and activities under mild conditions (room temperature, 1 bar of $H_2$) open up a new class of ligands for asymmetric hydrogenation.

## Experimental Section

**General Remarks.** All reactions and purifications were carried out under dry argon atmosphere in oven-dried glassware. Solvents were purified by standard procedures. Compounds $[Rh(cod)_2]BF_4$,[24] oxetane **1**,[12] and phosphorochloridites **3a**−**d**[14] were prepared by previously described methods. Elemental analyses were performed on a Carlo Erba EA-1108 instrument. $^1H$, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR spectra were recorded on a Varian Gemini 300 MHz spectrometer. Chemical shifts were relative to $SiMe_4$ ($^1H$ and $^{13}C$) as internal standard or $H_3PO_4$ ($^{31}P$) as external standard. All assignments in NMR spectra were determined by COSY and HETCOR spectra. Hydrogenation reactions were performed in a previously described hydrogen vacuum line.[25] Gas chromatographic analyses were run on a Hewlett-Packard HP 5890A instrument (split/splitless injector, Permabond L-Chirasil-Val, 25 m column, internal diameter 0.25 mm, carrier gas: 150 kPa He, F.I.D. detector) equipped with a Hewlett-Packard HP 3396 series II integrator.

**5-Deoxy-1,2-*O*-isopropylidene-5-diphenylphosphine-α-D-xylofuranose (2).** Potassium diphenylphosphine (2.2 mmol) was added to a solution of oxetane **1** (0.35 g, 2 mmol) in dimethylformamide (8 mL). The mixture was stirred overnight at room temperature. Water (50 mL) was then added, and the product was extracted with dichloromethane (3 × 50 mL). The organic phase was then evaporated, and the residue was purified by column chromatography (eluent: ether, $R_f$ 0.90). Yield: 590 mg (80%) of a white solid. $^{31}P$ NMR, $\delta$ ($CDCl_3$): −22.3 (s).

**3-(1,1′-Biphenyl-2,2′-diyl)phosphite-5-deoxy-1,2-*O*-isopropylidene-5-diphenylphosphine-α-D-xylofuranose (4a).** In situ formed phosphorochloridite **3a** (1 mmol) was dissolved in toluene (8 mL), to which pyridine (0.25 mL, 6 mmol) was added. 5-Deoxy-1,2-*O*-isopropylidene-5-diphenylphosphine-α-D-xylofuranose **2** (0.25 g, 0.7 mmol) was azeotropically dried with toluene (3 × 1 mL) and dissolved in toluene (8 mL), to which pyridine (0.25 mL, 6 mmol) was added. This solution was added in 30 min to the solution of **3a** at room temperature. The reaction mixture was stirred overnight at room temperature, and the pyridine salts were removed by filtration. Evaporation of the solvent gave a white foam, which was purified by flash column chromatography (eluent: toluene, $R_f$ 0.23). Yield: 244 mg (61%) of a white solid. Anal. Calcd for $C_{32}H_{30}O_6P_2$: C, 67.13; H, 5.28. Found: C, 67.45; H, 5.42. $^{31}P$ NMR, $\delta$ ($CDCl_3$): −18.3 (d, 1P, $J_{P-P}$ = 17 Hz), 148.2 (d, 1P, $J_{P-P}$ = 17 Hz). $^1H$ NMR, $\delta$ ($CDCl_3$): 1.22 (s, 3H, $CMe_2$), 1.30 (s, 3H, $CMe_2$), 2.38 (dd, 1H, H-5′, $^3J_{5'-4}$ = 8.1 Hz, $^2J_{5'-5}$ = 13.2 Hz), 2.57 (dd, 1H, H-5, $^3J_{5-4}$ = 6.6 Hz, $^2J_{5-5'}$ = 13.2 Hz), 4.12 (m, 1H, H-4), 4.62 (d, 1H, H-2, $^3J_{2-1}$ = 3.2 Hz), 4.73 (dd, 1H, H-3, $^3J_{3-4}$ = 2.2 Hz, $^3J_{3-P}$ = 9.6 Hz), 5.87 (d, 1H, H-1, $^3J_{1-2}$ = 3.2 Hz), 7.0−7.5 (m, 13H, Ar). $^{13}C$ NMR, $\delta$ ($CDCl_3$): 26.2 (C*Me*$_2$), 26.4 (C*Me*$_2$), 27.1 (d, C-5, $J_{C-P}$ = 14.8 Hz), 77.5 (dd, C-4, $J_{C-P}$ = 4.5 Hz, $J_{C-P}$ = 19.4 Hz), 78.1 (dd, C-3, $J_{C-P}$ = 5.2 Hz, $J_{C-P}$ = 11.4 Hz), 84.6 (d, C-2, $J_{C-P}$ = 2.3 Hz), 105.1 (C-1), 111.8 (*C*Me$_2$), 122.0, 125.4, 128.5, 128.6, 128.7, 128.9, 129.3, 130.0, 130.1, 132.8, 133.9 (Ar).

**3-(3,3′,5,5′-Tetra-*tert*-butyl-1,1′-biphenyl-2,2′-diyl)phosphite-5-deoxy-1,2-*O*-isopropylidene-5-diphenylphosphine-α-D-xylofuranose (4b).** Treatment of in situ formed phosphorochloridite **3b** (1 mmol) and 5-deoxy-1,2-*O*-isopropylidene-5-diphenylphosphine-α-D-xylofuranose **2** (0.25 g, 0.7 mmol) as described for compound **4a** afforded compound **5b**, which was purified by flash chromatography (eluent: toluene, $R_f$ 0.50). Yield: 435 mg (78%) of a white solid. Anal. Calcd for $C_{48}H_{62}O_6P_2$: C, 72.34; H, 7.84. Found: C, 71.98; H, 7.94. $^{31}P$ NMR, $\delta$ ($CDCl_3$): −21.5 (d, 1P, $J_{P-P}$ = 11.9 Hz), 144.7 (d, 1P, $J_{P-P}$ = 11.9 Hz). $^1H$ NMR, $\delta$ ($CDCl_3$): 1.11 (s, 3H, $CMe_2$), 1.23 (s, 3H, $CMe_2$), 1.33 (s, 9H, $CH_3$, *t*-Bu), 1.35 (s, 9H, $CH_3$, *t*-Bu), 1.43 (s, 9H, $CH_3$, *t*-Bu), 1.51 (s, 9H, $CH_3$, *t*-Bu), 2.32 (ddd, 1H, H-5′, $^3J_{5'-4}$ = 7.2 Hz, $^2J_{5'-5}$ = 13.5 Hz, $J_{5'-P}$ = 5.2 Hz), 2.52 (ddd, 1H, H-5, $^3J_{5-4}$ = 7.5 Hz, $^2J_{5-5'}$ = 13.5 Hz, $J_{5-P}$ = 1.8 Hz), 4.02 (m, 1H, H-4), 4.12 (d, 1H, H-2, $^3J_{2-1}$ = 3.6 Hz), 4.62 (dd, 1H, H-3, $^3J_{3-4}$ = 2.6 Hz, $^3J_{3-P}$ = 8.4 Hz), 5.65 (d, 1H, H-1, $^3J_{1-2}$ = 3.6 Hz), 7.1−7.5 (m, 9H, Ar). $^{13}C$ NMR, $\delta$ ($CDCl_3$): 26.2 (C*Me*$_2$), 26.4 (C*Me*$_2$), 27.4 (d, C-5, $J_{C-P}$ = 14.8 Hz), 31.2 ($CH_3$, *t*-Bu), 31.4 ($CH_3$, *t*-Bu), 31.5 ($CH_3$, *t*-Bu), 34.5 (C, *t*-Bu), 35.3 (C, *t*-Bu), 77.4 (dd, C-4, $J_{C-P}$ = 5.1 Hz, $J_{C-P}$ = 18.4 Hz), 77.8 (d, C-3, $J_{C-P}$ = 5.8 Hz), 84.3 (d, C-2, $J_{C-P}$ = 2.3 Hz), 104.3 (C-1), 111.4 (*C*Me$_2$), 124.3, 126.6, 128.4, 128.6, 128.8, 132.6, 132.8, 133.0, 133.2, 138.3, 138.6, 140.1, 140.4, 145.6, 146.8 (Ar).

**3-[(*R*)-1,1′-Binaphthyl-2,2′-diyl)phosphite-5-deoxy-1,2-*O*-isopropylidene-5-diphenylphosphine-α-D-xylofuranose (4c).** Treatment of in situ formed phosphorochloridite **3c** (1 mmol) and 5-deoxy-1,2-*O*-isopropylidene-5-diphenylphosphine-α-D-xylofuranose **2** (0.25 g, 0.7 mmol) as described for compound **4a** afforded compound **5c**, which was purified by flash chromatography (eluent: toluene, $R_f$ 0.17). Yield: 279 mg (59%) of a white solid. Anal. Calcd for $C_{40}H_{34}O_6P_2$: C, 71.42; H, 5.09. Found: C, 72.02; H, 4.89. $^{31}P$ NMR, $\delta$ ($CDCl_3$): −22.5 (d, 1P, $J_{P-P}$ = 33 Hz), 150.7 (d, 1P, $J_{P-P}$ = 33 Hz). $^1H$ NMR, $\delta$ ($CDCl_3$): 1.30 (s, 3H, $CMe_2$), 1.32 (s, 3H, $CMe_2$), 2.37 (ddd, 1H, H-5′, $^3J_{5'-4}$ = 8.4 Hz, $^2J_{5'-5}$ = 13.5 Hz, $J_{5'-P}$ = 5.1 Hz), 2.55 (ddd, 1H, H-5, $^3J_{5-4}$ = 6.6 Hz, $^2J_{5-5'}$ = 13.5 Hz, $J_{5-P}$ = 3.6 Hz), 4.11 (m, 1H, H-4), 4.72 (d, 1H, H-2, $^3J_{2-1}$ = 3.6 Hz), 4.76 (dd, 1H, H-3, $^3J_{3-4}$ = 2.4 Hz, $^3J_{3-P}$ = 10.1 Hz), 5.88 (d, 1H, H-1, $^3J_{1-2}$ = 3.6 Hz), 7.0−7.5 (m, 15H, Ar). $^{13}C$ NMR, $\delta$ ($CDCl_3$): 26.4 (C*Me*$_2$), 26.5 (C*Me*$_2$), 26.9 (d, C-5, $J_{C-P}$ = 14.3 Hz), 77.6 (dd, C-4, $J_{C-P}$ = 5.0, 20.6 Hz), 78.3 (dd, C-3, $J_{C-P}$ = 5.1, 15.9 Hz), 84.6 (d, C-2, $J_{C-P}$ = 3.4 Hz), 104.4 (C-1), 112.0 (*C*Me$_2$), 121.4, 121.7, 125.0, 125.2, 126.3, 127.0, 128.4, 128.5, 128.6, 129.0, 129.9, 130.4, 132.5, 132.7, 132.9, 133.2 (Ar).

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**3-[(*S*)-1,1′-Binaphthyl-2,2′-diyl)phosphite-5-deoxy-1,2-*O*-isopropylidene-5-diphenylphosphine-α-D-xylofuranose (4d).** Treatment of in situ formed phosphorochloridite **3d** (1 mmol) and 5-deoxy-1,2-*O*-isopropylidene-5-diphenylphosphine-α-D-xylofuranose **2** (0.25 g, 0.7 mmol) as described for compound **4a** afforded compound **5d**, which was purified by flash chromatography (eluent: toluene, $R_f$ 0.19). Yield: 212 mg (45%) of a white solid. Anal. Calcd for $C_{40}H_{34}O_6P_2$: C, 71.42; H, 5.09. Found: C, 71.79; H, 4.88. $^{31}$P NMR, $\delta$ ($CDCl_3$): −22.5 (d, 1P, $J_{P-P}$ = 15.5 Hz), 148.4 (d, 1P, $J_{P-P}$ = 15.5 Hz). $^1$H NMR, $\delta$ ($CDCl_3$): 1.19 (s, 3H, $CMe_2$), 1.36 (s, 3H, $CMe_2$), 2.45 (ddd, 1H, H-5′, $^3J_{5'-4}$ = 8.4 Hz, $^2J_{5'-5}$ = 13.5 Hz, $J_{5'-P}$ = 1.8 Hz), 2.63 (ddd, 1H, H-5, $^3J_{5-4}$ = 6.6 Hz, $^2J_{5-5'}$ = 13.5 Hz, $J_{5-P}$ = 2.1 Hz), 4.15 (m, 1H, H-4), 4.45 (d, 1H, H-2, $^3J_{2-1}$ = 3.3 Hz), 4.68 (dd, 1H, H-3, $^3J_{3-4}$ = 2.4 Hz, $^3J_{3-P}$ = 9.0 Hz), 5.79 (d, 1H, H-1, $^3J_{1-2}$ = 3.3 Hz), 7.0−7.5 (m, 15H, Ar). $^{13}$C NMR, $\delta$ ($CDCl_3$): 26.0 (C*Me*$_2$), 26.3 (C*Me*$_2$), 27.1 (d, C-5, $J_{C-P}$ = 14.8 Hz), 77.4 (dd, C-4, $J_{C-P}$ = 5.6 Hz, $J_{C-P}$ = 19.4 Hz), 78.2 (dd, C-3, $J_{C-P}$ = 5.1 Hz, $J_{C-P}$ = 11.4 Hz), 84.5 (d, C-2, $J_{C-P}$ = 2.9 Hz), 104.4 (C-1), 111.7 (*C*Me$_2$), 121.7, 125.0, 125.3, 126.3, 126.4, 128.4, 128.5, 128.6, 128.8, 128.9, 130.2, 130.5, 132.7, 132.9, 134.0 (Ar).

**Preparation of Rhodium Cationic Precursors.** In a general procedure, phosphine−phosphite ligand (0.05 mmol) was added to a solution of $[Rh(cod)_2]BF_4$ (20.2 mg, 0.05 mmol) in dichloromethane (2 mL). After 5 min, the desired products were obtained by precipitation with hexane as yellow solids.

**[Rh(4a)(cod)]$BF_4$ (5a).** Yield: 41 mg (95%). Anal. Calcd for $C_{40}H_{42}O_6P_2BF_4Rh$: C, 55.22; H, 4.83. Found: C, 55.53; H, 4.96. $^{31}$P NMR, $\delta$ ($CD_2Cl_2$): 13.9 (bd, 1P, $P_1$, $J_{P1-Rh}$ = 145.2 Hz), 135.1 (dd, 1P, $P_2$, $J_{P2-P1}$ = 43.3 Hz, $J_{P2-Rh}$ = 260.5 Hz). $^1$H NMR, $\delta$ ($CD_2Cl_2$): 1.12 (s, 3H, $CH_3$), 1.35 (s, 3H, $CH_3$), 2.0−2.5 (m, 8H, $CH_2$, cod), 2.98 (m, 2H, H-5′, H-5), 3.41 (d, 1H, H-2, $^3J_{2-1}$ = 3.6 Hz), 3.79 (m, 1H, H-4), 4.54 (m, 1H, CH═, cod), 5.01 (m, 1H, H-3), 5.17 (m, 1H, CH═, cod), 5.48 (m, 1H, H-1), 5.69(m, 1H, CH═, cod), 5.75 (m, 1H, CH═, cod), 7.0−8.0 (m, 18H, Ar). $^{31}$P NMR, $\delta$ ($CD_2Cl_2$, 193K): Major isomer: 18.6 (dd, 1P, $P_1$, $J_{P1-P2}$ = 45.6 Hz, $J_{P1-Rh}$ = 148.3 Hz), 132.8 (dd, 1P, $P_2$, $J_{P2-P1}$ = 45.6 Hz, $J_{P2-Rh}$ = 266.8 Hz). Minor isomer: 7.5 (dd, 1P, $P_1$, $J_{P1-P2}$ = 41.6 Hz, $J_{P1-Rh}$ = 142.0 Hz), 143.7 (dd, 1P, $P_2$, $J_{P2-P1}$ = 41.6 Hz, $J_{P2-Rh}$ = 253.2 Hz).

**[Rh(4b)(cod)]$BF_4$ (5b).** Yield: 49 mg (91%). Anal. Calcd for $C_{56}H_{74}O_6P_2BF_4Rh$: C, 61.46; H, 6.78. Found: C, 61.74; H, 6.42. $^{31}$P NMR, $\delta$ ($CD_2Cl_2$): 15.3 (bd, 1P, $P_1$, $J_{P1-Rh}$ = 144.3 Hz), 131.4 (dd, 1P, $P_2$, $J_{P2-P1}$ = 40.2 Hz, $J_{P2-Rh}$ = 260.8 Hz). $^1$H NMR, $\delta$ ($CD_2Cl_2$): 0.90 (s, 3H, $CH_3$), 0.97 (s, 3H, $CH_3$), 1.21 (s, 9H, $CH_3$, *t*-Bu), 1.23 (s, 9H, $CH_3$, *t*-Bu), 1.46 (s, 9H, $CH_3$, *t*-Bu), 1.55 (s, 9H, $CH_3$, *t*-Bu), 2.0−2.5 (m, 8H, $CH_2$, cod), 2.93 (m, 2H, H-5′, H-5), 3.30 (d, 1H, H-2, $^3J_{2-1}$ = 3.9 Hz), 3.82 (m, 1H, H-4), 4.42 (m, 1H, CH═, cod), 4.60 (dd, 1H, H-3, $^3J_{3-4}$ = 2.1 Hz, $J_{3-P}$ = 9.9 Hz), 4.71 (m, 1H, CH═, cod), 5.18 (m, 1H, H-1), 5.41(m, 1H, CH═, cod), 5.53 (m, 1H, CH═, cod), 7.0−7.7 (m, 14H, Ar). $^{31}$P NMR, $\delta$ ($CD_2Cl_2$, 193K): Major isomer: 19.7 (dd, 1P, $P_1$, $J_{P1-P2}$ = 43.9 Hz, $J_{P1-Rh}$ = 147.9 Hz), 130.4 (dd, 1P, $P_2$, $J_{P2-P1}$ = 43.9 Hz, $J_{P2-Rh}$ = 268.2 Hz). Minor isomer: 8.8 (dd, 1P, $P_1$, $J_{P1-P2}$ = 42.1 Hz, $J_{P1-Rh}$ = 141.9 Hz), 141.0 (bd, 1P, $P_2$, $J_{P2-Rh}$ = 248.9 Hz).

**[Rh(4c)(cod)]$BF_4$ (5c).** Yield: 45 mg (94%). Anal. Calcd for $C_{48}H_{46}O_6P_2BF_4Rh$: C, 59.43; H, 4.74. Found: C, 59.68; H, 4.85. $^{31}$P NMR, $\delta$ ($CD_2Cl_2$): 14.9 (dd, 1P, $P_1$, $J_{P1-P2}$ = 48.2 Hz, $J_{P1-Rh}$ = 141.3 Hz), 141.3 (dd, 1P, $P_2$, $J_{P1-P2}$ = 48.2 Hz, $J_{P2-Rh}$ = 262.2 Hz). $^1$H NMR, $\delta$ ($CD_2Cl_2$): 1.19 (s, 3H, $CH_3$), 1.39 (s, 3H, $CH_3$), 1.9−2.6 (m, 8H, $CH_2$), 3.12 (m, 1H, H-5′), 3.50 (m, 1H, H-5), 4.47 (d, 1H, H-2, $^3J_{2-1}$ = 3.6 Hz), 4.71 (m, 1H, H-4), 4.83 (m, 1H, CH═), 4.95 (m, 1H, CH═), 5.28 (m, 1H, CH═), 5.36 (dd, 1H, H-3, $^3J_{3-4}$ = 2.1 Hz, $J_{3-P}$ = 13.9 Hz), 5.72 (d, 1H, H-1, $^3J_{1-2}$ = 3.6 Hz), 5.80 (m, 1H, CH═), 7.0−8.2 (m, 22H, Ar).

**[Rh(4d)(cod)]$BF_4$ (5d).** Yield: 43 mg (90%). Anal. Calcd for $C_{48}H_{46}O_6P_2BF_4Rh$: C, 59.43; H, 4.74. Found: C, 59.14; H, 5.01. $^{31}$P NMR, $\delta$ ($CD_2Cl_2$): 15.2 (dd, 1P, $P_1$, $J_{P1-P2}$ = 49.0 Hz, $J_{P1-Rh}$ = 140.7 Hz), 140.7 (dd, 1P, $P_2$, $J_{P1-P2}$ = 49.0 Hz, $J_{P2-Rh}$ = 260.6 Hz). $^1$H NMR, $\delta$ ($CD_2Cl_2$): 1.17 (s, 3H, $CH_3$), 1.42 (s, 3H, $CH_3$), 1.8−2.6 (m, 8H, $CH_2$), 3.10 (m, 1H, H-5′), 3.39 (m, 1H, H-5), 4.37 (d, 1H, H-2, $^3J_{2-1}$ = 3.2 Hz), 4.64 (m, 1H, H-4), 4.79 (m, 1H, CH═), 4.89 (m, 1H, CH═), 5.31 (m, 1H, CH═), 5.37 (dd, 1H, H-3, $^3J_{3-4}$ = 2.2 Hz, $J_{3-P}$ = 14.4 Hz), 5.63 (d, 1H, H-1, $^3J_{1-2}$ = 3.2 Hz), 5.69 (m, 1H, CH═), 7.2−8.2 (m, 22H, Ar).

**Asymmetric Hydrogenation Reactions.** In a typical run, a Schlenk flask was filled with a dichloromethane solution (6 mL) of substrate (1 mmol), $[Rh(cod)_2]BF_4$ (4.95 mg, 0.01 mmol), and ligand (0.011 mmol). This was then purged three times with $H_2$ and vacuum. The reaction mixture was then shaken under $H_2$ (1 atm) at 298 K. To remove the catalyst, the solution was placed on a short silica gel column and eluted with $CH_2Cl_2$. Conversion and enantiomeric excesses were determined by gas chromatography.

**In Situ NMR Characterization Experiments.** In a typical experiment, a sapphire tube ($\Phi$ = 10 mm) was filled under argon with a solution of [Rh(cod)(**4b**)]$BF_4$ (0.02 mmol) and methyl *N*-acetamidoacrylate **6** (0.30 mmol) in dichloromethane-$d_2$ (1.5 mL). The tube was purged twice and pressurized to 1.2 bar of $H_2$. The reaction was followed under $H_2$ pressure.

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