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Asymmetric hydrogenation reactions with Rh and Ru complexes bearing phosphine–phosphites with an oxymethylene backbone

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ABSTRACT

Phosphine–phosphites **3a** and **3b**, derived from diphenylhydroxymethyl phosphine have been prepared. From these ligands [Rh(COD)(**3a**)]BF_4 **5a** and $RuCl_2$(**3b**)[(*S*,*S*)-DPEN] **6b** (DPEN = 1,2-diphenylethylenediamine) were synthesized and their structure determined by X-ray diffraction. Ligands **3** are characterized by a small bite angle of 83°. In addition, **5a** led to an active catalyst for the hydrogenation of olefins, giving enantioselectivities of up to 96% ee. Likewise, compound **6b** showed good activity and enantioselectivity in the hydrogenation of *N*-1-phenyl ethylidene aniline and a completed reaction at S/C = 500 in 24 h with 83% ee.

1. Introduction

Chiral phosphine–phosphite ligands are an important class of ligands for asymmetric catalysis.[1] From the initial application of BINAPHOS in the asymmetric hydroformylation of olefins,[2] a broad range of ligands have been prepared and tested in diverse catalytic reactions, exhibiting a wide scope.[3–9] Regarding hydrogenation, the application of phosphine–phosphites has led to efficient Rh,[10] Ir[11] or Ru[12] catalysts being developed for the reduction of C=C and C=N bonds, suitable not only for test substrates, but for more synthetically relevant ones as well.[13]

Considering the potential for ligand tuning that phosphine–phosphites allow, studies on the influence of the main ligand features in a catalytic reaction would be important with regard to the catalyst optimization process. In recent years we have prepared a library of phosphine–phosphites which possess a C–C–O backbone as a common feature. Thus, ligands **1** and **2** (Fig. 1) are characterized by oxyphenylene and oxyethylene bridge substituents, respectively. The nature of the backbone in these phosphine–phosphites greatly influences the conformational mobility of the coordinated ligand and the orientation of the phosphine substituents, which may have a profound influence on the catalysis.[14] In connection with this, Bakos et al. reported on the influence of the length of the backbone in rhodium catalyzed olefin hydrogenations using BINOL and H_8-BINOL based ligands with oxymethylene to oxybutylene bridges.[15] We have also observed that the use of bulkier, *tert*-butyl based phosphite fragments, has a profound effect on the enantioselectivity in diverse olefin and imine hydrogenations.[10g,12b] In a continuation of this and as a complement to our previous work with ligands of types **1** and **2**, we herein report a study dealing with oxymethylene bridged ligands **3**. These compounds are particularly appealing from a synthetic perspective, since the corresponding hydroxyphosphine, which is the most demanding component in the synthesis of phosphine–phosphites, can easily be prepared in one step and high yield from diphenylphosphine and formaldehyde.[16] Thus, we have also reported on the synthesis and performance of ligands **3** in several representative enantioselective hydrogenation reactions, while complementary structural information has also been obtained by X-ray crystallography studies on their coordination complexes.

2. Results and discussion

Initially, phosphine–phosphites **3a** and **3b** were obtained by condensation of diphenylhydroxymethylphosphine with chlorophosphites **4a** and **4b**, respectively (Scheme 1). These compounds were characterized by the usual analytical and spectroscopic techniques and the data obtained are in accordance with the proposed structures. Among the characterization data it should be highlighted that ligands **3** are characterized by two doublets in the $^{31}P\{^1H\}$ NMR with a small $^2J_{PP}$ coupling constant of ca. 4 Hz.

Research from our laboratory has shown that chiral phosphine–phosphites have broad application in the rhodium catalyzed hydrogenation of olefins, while achiral counterparts are also of interest in the hydrogenation of imines catalyzed by ruthenium catalysts bearing a chiral diamine as an ancillary ligand.[12b] Based upon these precedents, catalyst precursors of formula [Rh(COD)(**3a**)]BF_4 **5a** and $RuCl_2$(**4a**)[(*S*,*S*)-DPEN] **6b** were prepared (Scheme 2).

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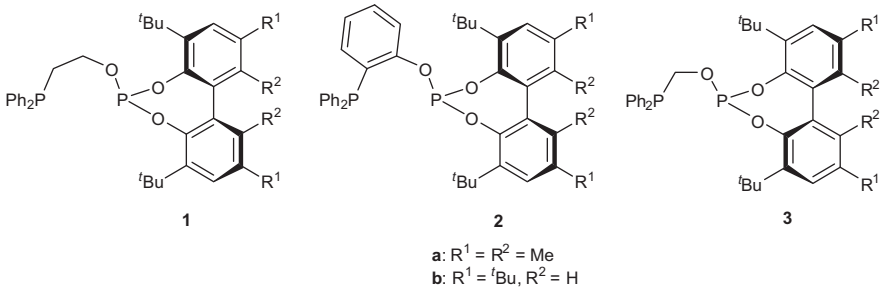
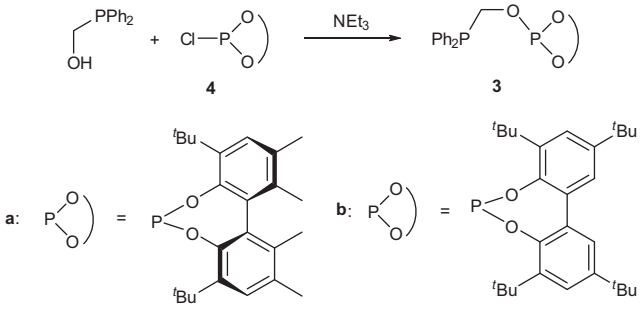
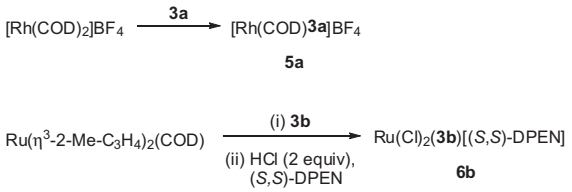


Figure 1. Structure of the phosphine–phosphite ligands.



Scheme 1. Synthesis of oxymethylene bridged ligands **3**.



Scheme 2. Preparation of complexes **5a** and **6b**.

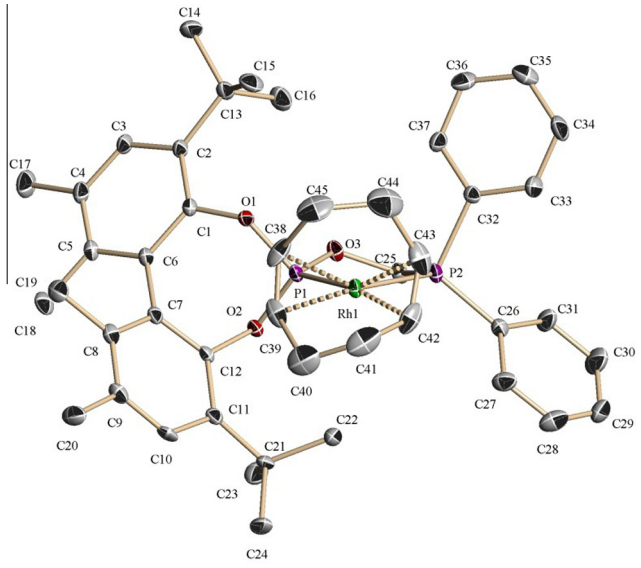


Figure 2. ORTEP view of complex **5a**.

With the intention of obtaining information about the structure of coordinated ligands **3**, complexes **5a** and **6b** were characterized by X-ray diffraction. The Rh compound **5a** has a square-planar structure (Fig. 2). The calculation of the distance from the rhodium atom to the olefin bond centroids gave values of 2.209 and 2.171 Å, thus reflecting the expected higher *trans*-influence of the phosphite fragment.[17] These distances are relatively high considering the range for diphosphine derivatives, which typically oscillate between 2.10 and 2.17 Å.[18] In contrast to the typical clockwise/counterclockwise turn observed for the COD derivatives of chiral diphosphines that minimize the steric interactions,[18] the coordination of COD in **5a** showed a displacement of both olefin centroids above the coordination plane. Thus the C(39) and C(42) olefinic carbons nearly lie in the equatorial plane. This structural feature, enabled by the C_1 symmetry of the chiral ligand, as well as the relatively long Rh–olefin bonds, can be attributed to the high steric hindrance caused by both of the phosphorus functionalities of the phosphine–phosphite ligand, particularly below the coordination plane by the aryl ring of the biphenyl defined by C(11) and the edge oriented phenyl substituent defined by C(26). Moreover, as observed before in the structures of ligands **1a** and **2a**, the PPh_2 fragment displays a typical propeller-like arrangement of the phenyl substituents with that above the coordination plane in a pseudoaxial position and the phenyl below the plane in a pseudoequatorial position. The structure is characterized by a bite angle of 82.6 degrees, which is in the range observed for ethane

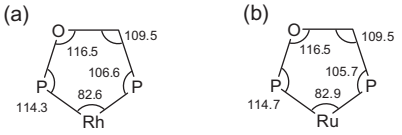


Figure 3. Angles (degrees) found in the metallacycles formed by **5a** (a) and **6b** (b).

bridged diphosphines, while being substantially smaller than those observed for complexes of ligands **1** and **2**. The latter typically range around 90 degrees (e.g. 90.9° in [Ir(COD)(**1b**)]BF_4 and 88.6 in Rh(Cl)(CO)(**2a**)). In addition, the adoption of the five membered metallacycle produces values for O-P-Rh and C-P-Rh angles of 114.3° and 106.6°. These values are smaller than those found for the six membered metallacycle of the aforementioned Ir compound, which show values of 115° and 121°, respectively. Comparison with five membered metallacycles (Fig. 3) defined by diphosphines indicates the similar values of the angles with the exception of the P(1)–O(3)–C(25) angle of 116.5° (Fig. 3a), which is wider than the typical value of 107° for P–C–C fragments in diphosphines.

On the other hand, the Ru complex shows a distorted octahedral structure with a *cis*-arrangement of the chloro ligands. Thus, the phosphite and one of the chloro ligands occupy the axial positions while the amine nitrogens, the remaining chloro and the phosphine occupy the equatorial plane (Fig. 4). As mentioned in the

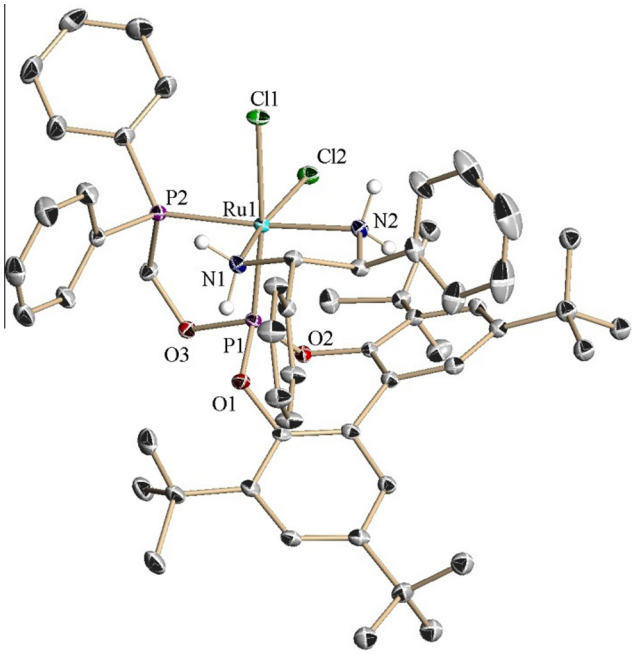


Figure 4. ORTEP view of complex **6b**.

structure of **5a**, **6b** also displays a narrow bite angle of 82.1 degrees (Fig. 3b). This contrasts, for instance, with the value of ethane bridged $RuCl_2$(**1a**)[(*R*,*R*)-DPEN], which displays a bite angle of 92.3 degrees. In addition, the structure shows the significant *trans*-influence of the phosphite group with the Ru-Cl(1) distance being appreciably longer than that of the Ru-Cl(2) distance (2.461 and 2.404 Å, respectively). It is noticeable that despite complexes **5a** and **6b** having different natures, the parameters of the metallacycle are very similar.

Complexes **5a** and **6b** show in the $^{31}P\{^1H\}$ NMR spectra $^2J_{PP}$ coupling constants, of 39 Hz and 47 Hz, respectively. These values are significantly lower than constants found in complexes with a longer backbone. For the sake of comparison, this coupling constant is 61 Hz in [Rh(COD)(**1a**)]BF_4[10g] and 69 Hz in $RuCl_2$(**1a**)[(*S*,*S*)-DPEN].[12b]

We were also interested in comparing the performance of the catalyst precursor **5a** with those based on phosphine–phosphite ligands **1** in the asymmetric hydrogenation of several representative olefins (Fig. 5). First, complex **5a** showed full conversion and a 91% ee in the hydrogenation of methyl *N*-acetyl-2-aminoacrylate **7b** under mild conditions (Table 1). In the case of methyl *N*-acetyl-2-aminocinnamate **7a** the reaction was slower under these conditions (70% conversion), but a higher enantioselectivity of 96% ee was observed. In addition, the hydrogenation of dimethyl itaconate also proceeded smoothly with a good enantioselectivity of 89% ee. Comparison of these results with those obtained with the

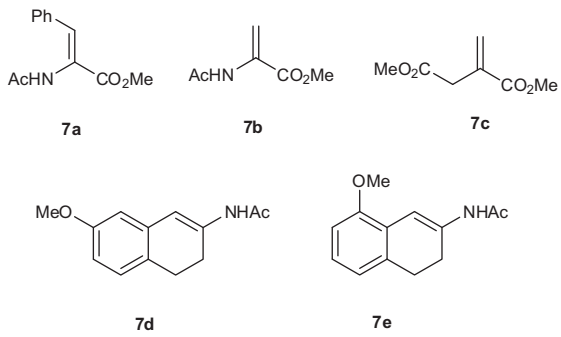


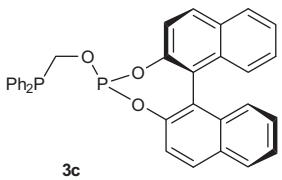
Figure 5. Olefin substrates considered in this study.

Table 1
Olefin hydrogenation with [Rh(COD)(P-OP)]BF_4 complexes[a]

Entry	Substrate	P–OP	Conv.	% ee (conf.)[d]
1	**7a**	(*R*)-**3a**	70	96 (*S*)
2	**7b**	(*R*)-**3a**	100	91 (*S*)
3	**7c**	(*R*)-**3a**	100	89 (*R*)
4[c]	**7b**	(*S*)-**3c**	100	54 (*R*)
5[c]	**7c**	(*S*)-**3c**	100	87 (*S*)
6[b,c]	**7d**	(*R*)-**3a**	50	57 (*R*)
7[b,c]	**7e**	(*R*)-**3a**	20	21 (*R*)
8[b]	**7d**	(*S*)-**1a**	54	75 (*S*)
9[b]	**7e**	(*S*)-**1a**	100	83 (*S*)

[a] Reactions were carried out at room temperature with an initial hydrogen pressure of 4 bar, in methylene chloride at a S/C = 100 unless otherwise noted. Reaction time 24 h. Conversion was determined by chiral GC.
[b] Reactions performed at 20 bar.
[c] Reactions performed with the precatalyst prepared in situ.
[d] Configurations were determined as previously reported.[10c,16b]

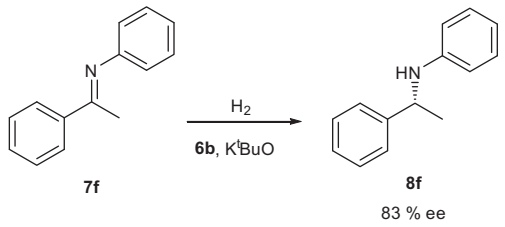
analogous catalyst of the longer ligand backbone **1a** showed that the proximity between the two phosphorus functionalities in ligand **3a** is detrimental for these hydrogenations, since in the three cases the catalyst bearing ligand **1a** provided higher enantioselectivities (99% ee) for the three olefins. In addition, we were interested in investigating the influence of the size of the phosphite fragment in oxymethylene bridged ligands. In this regard, it should be mentioned that literature data indicate that a catalyst bearing a BINOL based ligand **3c**, showed a 64% ee in the hydrogenation of methyl *N*-acetyl-2-aminocinnamate.[15] For the sake of completion we have generated complex [Rh(COD)(**3c**)]BF_4 in situ and performed the hydrogenations of methyl *N*-acetyl-2-aminoacrylate and dimethyl itaconate under standard conditions. Both reactions showed full conversion and enantioselectivities of 54% and 87% ee, respectively (entries 4 and 5). Overall, these values indicate a better performance of the catalyst bearing the bulkier phosphite in the hydrogenation of the enamides, while similar results for catalysts based on **3a** and **3c** were obtained in the case of dimethylitaconate. However, the bulky phosphite group, along with the short backbone, should render a rather congested metal center that should be detrimental for catalyst activity, as shown in the uncompleted hydrogenation of methyl *N*-acetyl-2-aminocinnamate.



3c

Compound **5a** was also tested against more challenging enamides derived from β-tetralone.[19,20] Thus, reactions performed with **5a** were slow, giving conversions of 50% and 20% for **7d** and **7e**, respectively (entries 6 and 7). For comparative purposes, we also performed hydrogenations of these substrates using [Rh(COD)(**1a**)]BF_4. It should be worth noting that this complex provided a moderate conversion and a respectable 75% ee for substrate **7d** (entry 8), while it provided full conversion and a higher enantioselectivity of 83% ee for the 8-methoxy substituted substrate **7e** (entry 9). Therefore, as observed for the previous substrates, the shortening of the backbone is accompanied by a decrease in enantioselectivity. Bakos et al. have observed a similar trend for catalysts based on less sterically demanding BINOL based phosphine–phosphites.[15]

On the other hand, the performance of Ru complex **6b** in the hydrogenation of representative imine **7f** (Scheme 3) in the presence of base has also been examined. The reaction performed at a S/C = 100, following the usual conditions for these reactions



Scheme 3. Hydrogenation of imine **7f**.

(i.e. 20 bar of hydrogen, 60 °C and [KOBu^t]/[Ru] = 100), showed full conversion and a good enantioselectivity of 83% ee. The catalyst showed a remarkable activity and was able to complete a reaction performed at a S/C = 500 in 24 h, without a decrease in the enantioselectivity. Most interestingly, this catalyst outperformed ethylene bridged complex $RuCl_2$(**1a**)[(*S*,*S*)-DPEN], which showed 72% conversion and 73% ee at S/C = 100.[12b]

3. Conclusion

Phosphine–phosphite ligands **3a** and **3b** have been prepared and applied in representative olefin and imine asymmetric hydrogenation reactions. These ligands are characterized by a narrow bite angle which brings the substituents of both phosphorus functionalities closer thus producing a rather congested metal environment. The Rh catalyst generated from **5a** gave moderate to high enantioselectivities in the hydrogenation of methyl *N*-acetyl-2-aminocinnamate, methyl *N*-acetyl-2-aminoacrylate, and dimethyl itaconate, but it did not improve the results provided by the oxyethylene counterpart catalyst. In contrast, the Ru complex bearing the achiral **3b** outperformed the catalyst bearing an oxyethylene fragment. These results along with the very simple preparation of diphenylhydroxymethylphosphine, contribute to the interest of phosphine–phosphites **3** in asymmetric hydrogenation reactions.

4. Experimental

4.1. General

All reactions and manipulations were performed under an atmosphere of nitrogen or argon, either in a Braun Labmaster 100 glovebox or using standard Schlenk-type techniques. All solvents were distilled under nitrogen with the following desiccants: sodium-benzophenone-ketyl for diethyl ether (Et_2O) and tetrahydrofuran (THF); sodium for hexanes and toluene; CaH_2 for dichloromethane (CH_2Cl_2); and NaO^{i}Pr for isopropanol (^{i}PrOH). Ru(COD)(2-methylallyl)$_2$ was prepared as described previously.[21] All other reagents were purchased from commercial suppliers and used as received. IR spectra were recorded on a Bruker Vector 22 spectrometer. NMR spectra were obtained on Bruker DPX-300, DRX-400, or DRX-500 spectrometers. $^{31}P\{^1H\}$ NMR shifts were referenced to external 85% H_3PO_4, while $^{13}C\{^1H\}$ and ^1H shifts were referenced to the residual signals of deuterated solvents. All data are reported in ppm downfield from Me_4Si. All NMR measurements were carried out at 25 °C. HPLC analyses were performed by using a Waters 2691. HRMS data were obtained on a JEOL JMS-SX 102A mass spectrometer in the General Services of Universidad de Sevilla (CITIUS). Optical rotations were measured on a Perkin–Elmer Model 341 polarimeter.

4.2. Compound 3a

A solution of diphenylhydroxymethyl phosphine (0.103 g, 0.48 mmol) dissolved in toluene (10 mL) was added dropwise over a solution of chlorophosphite **4a** (0.201 g, 0.48 mmol) and triethylamine (0.058 g, 0.57 mmol) in toluene (10 mL). Reaction mixture was stirred for 15 h, the resulting suspension filtered and the solution obtained evaporated under reduced pressure. The oil obtained was dissolved in diethyl ether and filtered through a short pad of neutral alumina. The solution was evaporated to yield **3a** as a white solid (0.228 g, 80% yield). $[\alpha]_D^{20} = -392$ (*c* 1.0, THF); ^1H NMR ($CDCl_3$, 400 MHz): δ 1.32 (s, 9H, CMe_3), 1.42 (s, 9H, CMe_3), 2.96 (s, 3H, Me), 1.84 (s, 3H, Me), 2.22 (s, 3H, Me), 2.24 (s, 3H, Me), 3.70 (ddd, J_{HP} = 4.1, 7.0 Hz, J_{HH} = 12.8 Hz, 1H, PC*H*H), 4.69 (ddd, J_{HP} = 5.0, 7.4 Hz, J_{HH} = 12.8 Hz, 1H, PC*H*H), 7.08 (s, 1H, Ar-H), 7.14 (s, 1H, Ar-H), 7.27–7.43 (m, 10H, PPh_2); $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ −14.0 (d, J_{PP} = 4 Hz; PC), 125.4 (d, J_{PP} = 4 Hz; PO); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 16.6 (Me), 16.8 (Me), 20.5 (Me), 20.6 (Me), 31.1 (*C*Me_3), 31.5 (d, J_{CP} = 5 Hz, *C*Me_3), 34.7 (2 *C*Me_3), 63.3 (dd, J_{CP} =15, 3 Hz, PCH_2O), 127.9 (CH arom), 128.3 (CH arom), 128.4 (CH arom), 128.5 (CH arom), 128.5 (CH arom), 128.5 (CH arom), 128.7 (CH arom), 129.1 (CH arom), 130.9 (d, J_{CP} = 2 Hz, C_q arom), 131.7 (d, J_{CP} = 5 Hz, C_q arom), 131.8 (C_q arom), 132.5 (C_q arom), 132.8 (CH arom), 133.0 (CH arom), 133.7 (CH arom), 133.8 (CH arom), 134.6 (C_q arom), 135.1 (C_q arom), 135.6 (d, J_{CP} = 11 Hz, C_q arom), 136.1 (d, J_{CP} = 11 Hz, C_q arom), 136.9 (C_q arom), 138.3 (C_q arom), 145.7 (d, J_{CP} = 3 Hz, C_q arom), 145.9 (d, J_{CP} = 3 Hz, C_q arom); HRMS (EI): *m*/*z* 598.2755, $[M]^+$ (exact mass calcd for $C_{37}H_{44}O_3P_2$: 598.2766).

4.3. Compound 3b

An ampoule was charged with diphenylhydroxymethylphosphine (0.096 g, 0.44 mmol) and chlorophosphite **4b** (0.209 g, 0.44 mmol). The solids were dissolved in toluene (15 mL) and triethylamine was added (0.089 g, 0.88 mmol). The mixture was stirred for 24 h, filtered, and brought to dryness. The residue was dissolved in diethyl ether, passed through a short pad of neutral alumina and brought to dryness. Ligand **3b** was obtained as a white foamy solid (0.203 g, 70% yield). ^1H NMR (CD_2Cl_2, 500 MHz): δ 1.33 (s, 18H, CMe_3), 1.42 (s, 18H, CMe_3), 4.43 (t, J_{HP} = 5.7 Hz, 2H, PCH_2), 7.15 (d, J_{HH} = 2.5 Hz, 2H, Ar-H), 7.27–7.38 (m, 10H, Ar-H), 7.43 (d, J_{HH} = 2.5 Hz, 2H, Ar-H); $^{31}P\{^1H\}$ NMR (CD_2Cl_2, 162 MHz): δ −15.5 (d, J_{PP} = 6 Hz, PC), 135.6 (d, J_{PP} = 6 Hz, PO); $^{13}C\{^1H\}$ NMR (CD_2Cl_2, 125 MHz): δ 31.3 (2 *C*Me_3), 31.8 (2 *C*Me_3), 35.1 (2 *C*Me_3), 35.8 (2 *C*Me_3), 64.4 (d, J_{CP} = 13 Hz, PCH_2O), 124.8 (2CH arom), 126.8 (2CH arom), 128.8 (d, J_{CP} = 7 Hz, 4CH arom), 129.3 (2C_q arom), 132.9 (2C_q arom), 133.4 (d, J_{CP} = 18 Hz, 4CH arom), 136.0 (d, J_{CP} = 12 Hz, 2C_q arom), 140.3 (2C_q arom), 146.5 (d, J_{CP} = 5 Hz, 2C_q arom), 147.3 (2C_q arom); HRMS (EI): *m*/*z* 655.3451, $[M]^+$ (exact mass calcd for $C_{41}H_{53}O_3P_2$: 654.3392); Elem. Anal. Calcd for $C_{41}H_{53}O_3P_2$ (%): C, 75.20; H, 8.00. Found: C, 75.21; H, 8.09.

4.4. Compound [Rh(COD)(3a)]BF_4 5a

A solution of phosphine–phosphite **3a** (0.125 g, 0.21 mmol) in CH_2Cl_2 (5 mL) was slowly added over a solution of [Rh(COD)$_2$]BF_4 (0.081 g, 0.20 mmol) in CH_2Cl_2 (5 mL) cooled at 0 °C. The reaction mixture was stirred for 3 h at room temperature, concentrated to approximately half of the initial volume, and filtered. The resulting solution was evaporated under reduced pressure and the resulting solid was purified by recrystallization from a CH_2Cl_2/Et_2O 1:1 mixture, yielding **5a** as orange crystals (0.088 g, 47% yield). ^1H NMR (CD_2Cl_2, 500 MHz): δ 1.39 (s, 9H, CMe_3), 1.44 (s, 9H, CMe_3), 1.76 (s, 3H, Me), 1.86 (s, 3H, Me), 2.01 (m, 1H, C*H*H, COD), 2.15 (m, 1H, C*H*H, COD), 2.28 (s, 3H, Me), 2.31 (s, 3H, Me), 2.39 (m, 5H, C*H*H, COD), 2.58 (m, 1H, C*H*H, COD), 4.32 (m, 1H, =CH COD), 4.60 (m, 2H, =CH COD), 5.27 (m, 1H, =CH COD), 7.27 (s, 1H, Ar-H), 7.28 (s, 1H, Ar-H), 7.63 (m, 10H, PPh_2); $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz): δ 63.7 (dd, J_{RhP} = 153 Hz, J_{PP} = 39 Hz, PC), 156.9 (dd, J_{RhP} = 255 Hz, J_{PP} = 40 Hz, PO); $^{13}C\{^1H\}$ NMR (CD_2Cl_2, 125 MHz): δ 16.6 (Me), 16.8

(Me), 20.4 (Me), 20.5 (Me), 28.7 (CH_2), 29.8 (CH_2), 30.5 (CH_2), 31.7 (CMe_3), 31.9 (CH_2), 32.2 (CMe_3), 35.2 (CMe_3), 35.3 (CMe_3), 68.4 (dd, J_{CP} = 18, 30 Hz; PCH_2O), 97.9 (dd, J_{CP} = 10, 6 Hz, =CH COD), 109.3 (m, 2 =CH COD), 112.2 (dd, J_{CP} = 10, 6 Hz, =CH COD), 126.6 (d, J_{CP} = 43 Hz; C_q arom), 128.8 (d, J_{CP} = 46 Hz; C_q arom), 129.1 (CH arom), 129.2 (C_q arom), 129.5 (CH arom), 129.7 (C_q arom), 130.3 (CH arom), 130.4 (CH arom), 130.5 (CH arom), 130.6 (CH arom), 132.8 (CH arom), 132.9 (2CH arom), 133.0 (CH arom), 133.1 (CH arom), 133.2 (CH arom), 134.8 (C_q arom), 135.0 (C_q arom), 136.1 (C_q arom), 136.7 (C_q arom), 137.2 ($2C_q$ arom), 144.2 (d, J_{CP} = 6 Hz; C_q arom), 144.7 (d, J_{CP} = 14 Hz; C_q arom); Elem. Anal. Calcd for $C_{45}H_{56}BF_4O_3P_2Rh$ (%): C, 60.28; H, 6.30. Found: C, 60.05; H, 6.47

4.5. Compound [$RuCl_2$(3b)[(*S,S*)-DPEN)] 6b

A solution of Ru(COD)(η^3-2-MeC_3H_4)$_2$ (0.072 g, 0.20 mmol) and **3b** (0.078 g, 0.12 mmol) in *n*-hexane (5 mL) was heated at reflux for 5 h. The mixture was evaporated under reduced pressure and the residue was dissolved in CH_2Cl_2 (3 mL). The solution was added dropwise over a solution of (*S,S*)-DPEN (0.043 g, 0.20 mmol) and HCl (8 mL, 0.05 M in Et_2O) cooled at −20 °C. The resulting mixture was stirred for 30 min at room temperature, evaporated under vacuum, and the residue was purified by column chromatography using a cyclohexane/Et_2O 1:1 mixture to give a yellow solid (0.057 g, 25%). ^{1}H NMR (CD_2Cl_2, 500 MHz): δ 1.06 (s, 9H, CMe_3), 1.12 (s, 9H, CMe_3), 1.30 (s, 9H, CMe_3), 1.37 (s, 9H, CMe_3), 2.99 (m, 1H, N*H*H), 3.16 (m, 1H, NH*H*), 3.96 (m, 1H, N*H*H), 4.11 (m, 1H, NH*H*), 4.26 (ddd, J_{HH} = 11.8 Hz, J_{HH} = 4.5 Hz, J_{HH} = 4.5 Hz, 1H, *CH*NH_2), 4.40 (ddd, J_{HH} = 11.8 Hz, J_{HH} = 4.3 Hz, J_{HH} = 4.3 Hz, 1H, C*H*NH_2), 4.94 (m, 2H, PCH_2), 6.95 (m, 3H, 3H arom), 7.07 (m, 4H, 4H arom), 7.13 (m, 6H, 6H arom), 7.31 (m, 3H, 3H arom), 7.36 (m, 4H, 4H arom), 7.72 (m, 4H, 4H arom); ^{31}P NMR (CD_2Cl_2, 202.5 MHz,): δ 69.7 (d, PC, J_{PP} = 47 Hz), 171.9 (d, PO); ^{13}C NMR (CD_2Cl_2, 125 MHz): δ 30.2 (*C*Me_3), 31.4 (C*Me*$_3$), 31.5 (C*Me*$_3$), 31.8 (C*Me*$_3$), 32.2 (C*Me*$_3$), 34.7 (d, J_{CP} = 4 Hz, *C*Me_3), 36.6 (*C*Me_3), 36.8 (*C*Me_3), 63.3 (s, 2CH, *C*HNH_2), 67.8 (dd, J_{CP} = 34 Hz, J = 14 Hz, PCH_2), 125.9 (CH arom), 126.2 (CH arom), 127.4 (CH arom), 127.7 (CH arom), 127.8 (2CH arom), 127.9 (2CH arom), 128.5 (2CH arom), 128.6 (CH arom), 128.6 (CH arom), 128.7 (2CH arom), 129.3 (2CH arom), 129.5 (2CH arom), 130.3 (2CH arom), 131.1 (C_q arom), 131.8 (d, J_{CP} = 3 Hz, C_q arom), 133.6 (CH arom), 133.7 (2CH arom), 133.8 (CH arom), 134.7 (C_q arom), 134.8 (C_q arom), 135.0 (C_q arom), 135.1 (C_q arom), 140.1 (C_q arom), 140.2 ($2C_q$ arom), 140.5 (C_q arom), 146.6 (d, J_{CP} = 38 Hz, C_q arom), 146.7 (d, J_{CP} = 33 Hz, C_q arom). Elem. Anal. Calcd for $C_{55}H_{68}Cl_2N_2O_3P_2Ru$ (%): C, 63.58; H, 6.60; N, 2.70. Found: C, 63.51; H, 6.81; N, 2.76.

4.6. Procedure for the asymmetric hydrogenation of olefins 7a–7c

In a glovebox, a solution of **7b** (5.3 mg, 0.037 mmol) and **5a** (0.33 mg, 0.35 μmol) in CH_2Cl_2 (2.0 mL) was placed in an HEL CAT-18 reactor. The reactor was purged with hydrogen and finally pressurized at 4 bar. The reaction was stirred for 24 h, after which the reactor was evacuated and the resulting solution evaporated under vacuum. The remaining residue was analyzed by ^{1}H NMR to determine the conversion. It was then brought to dryness, and dissolved in an *i*-PrOH/*n*-hexane 1:9 mixture and passed through a short pad of silica to remove catalyst impurities. The solution obtained was evaporated and the residue obtained was analyzed by chiral chromatography to determine the enantiomeric excess as follows: *N*-acetyl phenylalanine methyl ester **8a**: HPLC, *n*-hexane/*i*-PrOH 90:10; 1.0 mL/min, $t_1(R)$ = 14.5 min, $t_2(S)$ = 19.1 min; *N*-acetyl alanine methyl ester **8b**: GC, Supelco β-DEX 225, 15 psi He, 150 °C, $t_1(S)$ = 6.9 min, $t_2(R)$ = 7.2 min; dimethyl 2-methylsuccinate **8c**: GC, Supelco β-DEX 225, 15 psi He, 70 °C (5 min), 10 °C/min up to 130 °C, $t_1(S)$ = 12.6 min, $t_2(R)$ = 12.7 min.

4.7. Procedure for the hydrogenation of enamides 7d and 7e

In a glovebox, the appropriate olefin (0.042 mmol), phosphine–phosphite ligand (0.46 μmol), and [$Rh(COD)_2$]BF_4 (0.42 μmol) from freshly prepared stock solutions in CH_2Cl_2 (total volume = 0.5 mL), were added to a 2 mL glass vial. Vials were placed in a steel reaction vessel model HEL CAT18 that held up to eighteen reactions. The reactor was purged three times with H_2 and finally pressurized to the required pressure. In the case of deuteration reactions, the reactor was purged with Ar, partially evacuated under vacuum, and filled with D_2 at 20 atm. After the desired reaction time, the reactor was slowly depressurized, the solutions were evaporated and the conversions were determined by ^{1}H NMR spectroscopy. The resulting mixtures were dissolved in EtOAc, and filtered through a short pad of silica to remove catalyst impurities. Enantiomeric excess was analyzed by chiral HPLC, as follows: *N*-(7-methoxy-1,2,3,4-tetrahydronaphthalen-2-yl)-acetamide **8d**: HPLC, Daicel Chiralcel OJ-H, *n*-hexane/i-PrOH, 90:10, t_1 = 20.6 min, t_2 = 32.9 min; *N*-(8-methoxy-1,2,3,4-tetrahydronaphthalen-2-yl)-acetamide **8e**: HPLC, Daicel Chiralcel OJ-H, *n*-hexane/i-PrOH 90:10, t_1 = 12.1 min., t_2 = 13.5 min.

4.8. Hydrogenation of imine 7f

In a glovebox, an HEL pressure reactor (20 mL) was charged with imine **7f** (0.18 mmol), Ru complex **6b** (1.8 μmol), ^{t}BuOK (22.0 mg, 0.18 mmol), and isopropanol (2.0 mL). The reactor was purged three times with H_2, pressurized at 20 atm, and heated at 60 °C. After 24 h, the reactor was slowly depressurized, the solution was evaporated, and the conversion was determined by ^{1}H NMR. The resulting mixture was dissolved in CH_2Cl_2, treated with 2 mL of HCl (2 M), and stirred for 20 min. A saturated aqueous solution of $NaHCO_3$ (3 mL) was added to the mixture, the organic layer was separated, dried over magnesium sulfate, and concentrated. Enantiomeric excesses were analyzed by chiral HPLC, as follows: *N*-phenyl-1-phenylethylamine **8f**: Chiralcel OJ-H, hexane–^{i}PrOH (93:7), flow 1.0 mL/min, t_1 = 23.0 min (*R*), t_2 = 26.6 min (*S*).

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