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Walphos versus Biferrocene-Based Walphos Analogues in the Asymmetric Hydrogenation of Alkenes and Ketones

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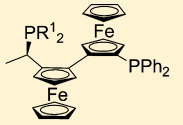
Supporting Information

ABSTRACT: Two representative Walphos analogues with an achiral 2,2″-biferrocenediyl backbone were synthesized. These diphosphine ligands were tested in the rhodium-catalyzed asymmetric hydrogenation of several alkenes and in the ruthenium-catalyzed hydrogenation of two ketones. The results were compared with those previously obtained on using biferrocene ligands with a C_2-symmetric 2,2″-biferrocenediyl backbone as well as with those obtained with Walphos ligands. The application of one newly synthesized ligand in the hydrogenation of 2-methylcinnamic acid gave (*R*)-2-methyl-3-phenylpropanoic acid with full conversion and with 92% ee. The same ligand was used to transform 2,4-pentanedione quantitatively and diastereoselectively into (*S*,*S*)-2,4-pentanediol with 98% ee.

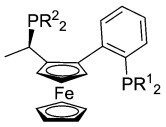


R^1 = 3,5-$(CF_3)_2C_6H_3$, Ph

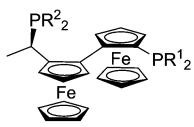
INTRODUCTION

About 10 years ago we reported on the synthesis of a group of diphosphine ligands, the so-called Walphos ligand family, and their application in the asymmetric hydrogenation of alkenes, ketones, and imines.[1] All of these ligands are based on a phenylferrocenylethyl backbone, and they vary only in the substituents on their phosphino units (R^1 and R^2; Chart 1).

Chart 1



Walphos



Walphos-analogues

SL-W001	R^1 = Ph, R^2 = 3,5-$(CF_3)_2C_6H_3$	(*R*,S_p,R_p)-**1**
SL-W002	R^1 = R^2 = Ph	(*R*,S_p,R_p)-**2**

Originally, these derivatives were developed and used as ligands for hydrogenation catalysts, but a variety of additional applications have subsequently been reported.[2]

On the basis of the success of these ligands, we very recently investigated Walphos analogues with a biferrocene instead of a ferrocenylaryl backbone (Chart 1).[3] In these ligands the aryl ring of the Walphos backbone is replaced by a ferrocenyl unit. In asymmetric hydrogenations the Walphos ligands and their analogous biferrocene compounds showed significantly different performances with respect to both product ee values and absolute configuration.

The backbone of Walphos analogues such as **1** and **2** with an *R*,S_p,R_p absolute configuration were constructed by a Negishi coupling between (*R*)-1-(*N*,*N*-dimethylamino)ethylferrocene ((*R*)-**3**) and (*S*)-2-bromoiodoferrocene ((*S*)-**4**) (analogous to the reaction of (*R*)-**3** and *rac*-**4** shown in Scheme 1). This reaction resulted in the intermediate (*R*,S_p,R_p)-**5**, which was converted into the final ligands with a C_2-symmetric biferrocene-2,2″-diyl backbone. It is clear, however, that a coupling reaction between (*R*)-**3** and (*R*)-**4** would lead to the diastereomeric intermediate (*R*,S_p,S_p)-**5** with an achiral biferrocene-2,2″-diyl backbone. Substitution of such an achiral biferrocene backbone with two nonidentical substituents would also lead to chiral derivatives, and we were therefore curious as to how Walphos analogues with an *R*,S_p,S_p absolute configuration would perform in asymmetric catalysis.

We report here the synthesis of two biferrocene-based Walphos analogues (**1** and **2**) with an *R*,S_p,S_p configuration and their application in the rhodium-catalyzed hydrogenation of alkenes and the ruthenium-catalyzed hydrogenations of two ketones. The results obtained with these biferrocene ligands are compared with those of their *R*,S_p,R_p-configured diastereomers and those of the corresponding Walphos ligands.

RESULTS AND DISCUSSION

Synthesis of Ligands and Complexes. Ligands (*R*,S_p,S_p)-**1** and (*R*,S_p,S_p)-**2** were prepared in a way analogous to that for their *R*,S_p,R_p-configured diastereomers. However, racemic

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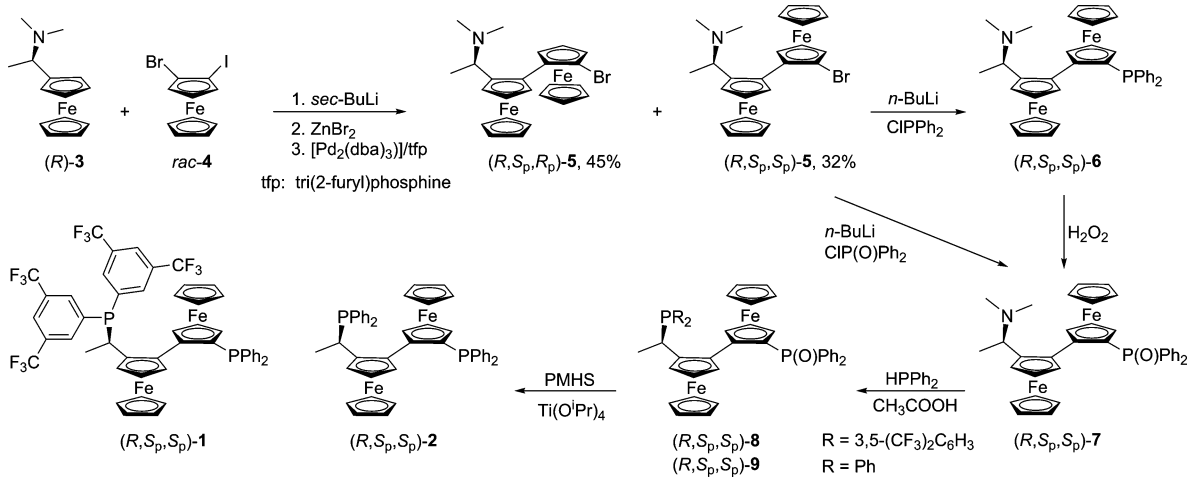
Scheme 1. Synthesis of Ligands (R,S_p,S_p)-1 and (R,S_p,S_p)-2



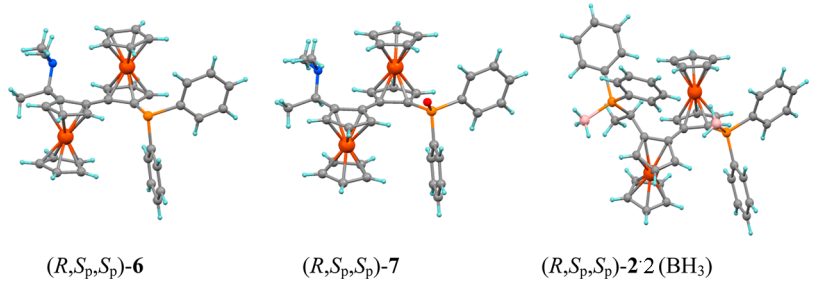


Figure 1. Structural features of (R,S_p,S_p)-**6**, (R,S_p,S_p)-7, and (R,S_p,S_p)-**2**·2BH_3.

2-bromoiodoferrocene (*rac*-**4**) was used instead of (*R*)-2-bromoiodoferrocene ((*R*)-**4**). A Negishi coupling[4] of (*R*)-1-(*N*,*N*-dimethylamino)ethylferrocene with *rac*-**4**[5] gave both diastereomers of **5** with an overall yield of 77% ((R,S_p,R_p)-**5**, 45%; (R,S_p,S_p)-**5**, 32%). The two diastereomers could be separated by chromatography, and the diastereomer (R,S_p,S_p)-**5**[6] was reacted with *n*-BuLi and subsequently quenched with chlorodiphenylphosphine. Oxidation of the resulting aminophosphine (R,S_p,S_p)-**6** with H_2O_2 resulted in the formation of the phosphine oxide (R,S_p,S_p)-7 (52% based on **5**), which can also be obtained directly from **5**. Reaction of (R,S_p,S_p)-**5** with *n*-BuLi followed by treatment with diphenylphosphinyl chloride gave the phosphine oxide (R,S_p,S_p)-7 in 77% yield. X-ray diffraction studies on the aminophosphine (R,S_p,S_p)-**6** and the aminophosphine oxide (R,S_p,S_p)-7 confirmed their structural integrity as well as their absolute configurations (Figure 1; for the crystallographic data see the Experimental Section).

Further reaction of phosphine oxide **7** with bis[3,5-bis(trifluoromethyl)phenyl]phosphine or diphenylphosphine in acetic acid at 70 °C gave the phosphine−phosphine oxides (R,S_p,S_p)-**8** (60%) and (R,S_p,S_p)-**9**.[1b] In solution the side-chain phosphorus of (R,S_p,S_p)-**9** was found to be rather sensitive to oxidation and the crude product **9** was therefore used in the last step. Reduction of phosphine oxides **8** and **9** with polymethylhydrosiloxane/titanium isopropoxide[7] gave the desired ligands (R,S_p,S_p)-**1** (92%) and (R,S_p,S_p)-**2** (70% based on **7**). A small amount of (R,S_p,S_p)-**2** was then reacted with BH_3·THF to give the bis(borane) complex (R,S_p,S_p)-**2**·2BH_3 (99%). The molecular structure of this compound was determined by X-ray diffraction (Figure 1 and Experimental Section). In addition, ligand (R,S_p,S_p)-**2** was reacted with $[PdCl_2(CH_3CN)_2]$ to give the palladium dichloride complex $[PdCl_2((R,S_p,S_p)$-**2**$)]$ in 99% yield.

In the complex (R,S_p,S_p)-**2**·2BH_3, as well as in precursors **6** and **7** (Figure 1), the two ferrocene units adopt an *anti* arrangement with Fe1−C1−C11−Fe2 dihedral angles of −178.5 and −177.3° (**6**), 176.8° (**7**), and 150.8° (**2**·2BH_3). In this conformation the diphenylphosphino units of **2** are oriented *trans* to each other (torsion angles C2−C1−C11−C12 of 178.0 and 180.0° (**6**), 178.4° (**7**), and 158.4° (**2**·2BH_3). The ligand (R,S_p,S_p)-**2** is not very well preoriented for *cis* coordination, but it could easily be transformed into the palladium dichloride complex $[PdCl_2((R,S_p,S_p)$-**2**$)]$.

Asymmetric Hydrogenations. Both of the newly synthesized Walphos analogues **1** and **2** with an R,S_p,S_p absolute configuration were tested as ligands in the asymmetric hydrogenation of several alkenes and two ketones (Chart 2). All catalysts for the hydrogenation of alkenes were formed in situ by reacting the ligands with the metal precursor $[Rh(NBD)_2]BF_4$ (NBD = norbornadiene). The catalysts for the hydrogenation of ketones were prepared by reaction of the ligands with the precursor $[RuI_2(p\text{-cymene})]_2$. The results obtained with ligands **1** and **2** of R,S_p,S_p configuration are summarized in Table 1 together with our previously reported data for ligands **1** and **2** of R,S_p,R_p configuration and those for the original Walphos ligands SL-W001 and SL-W002.[1,3]

The use of ligands (R,S_p,S_p)-**1** and (R,S_p,S_p)-**2** in the hydrogenation of all substrates (Chart 2) resulted in quantitative or nearly quantitative conversion. The standard test substrates (*Z*)-methyl α-acetamidocinnamate (MAC), methyl acetamidoacrylate (MAA), dimethyl itaconate (DMI), and 2-phenylcinnamic acid (PCA) gave only moderate enantiomeric excesses of up to 84% ee (Table 1, entries 1−8). For these substrates the corresponding Walphos ligands SL-W001-1 and SL-W002-1 show significantly better performance (Table 1,

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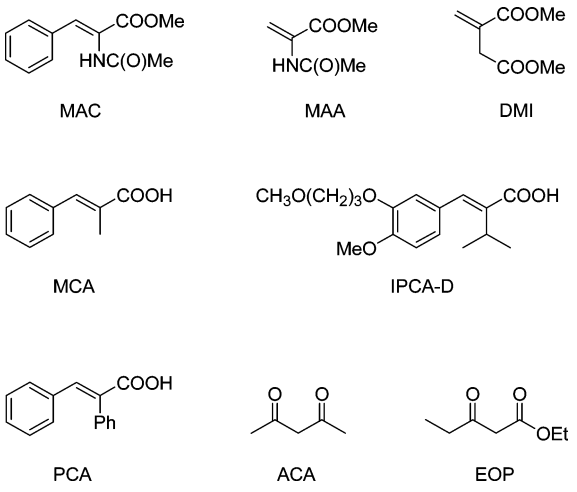
Chart 2. Substrates Used for Catalyst Screening



entries 2, 3, 6, and 8). Surprisingly, with 2-methylcinnamic acid (MCA) the opposite trend was observed. In this case, the use of ligands (R,S_p,S_p)-**1** and (R,S_p,S_p)-**2** gave products with 89% and 92% ee, respectively, while the corresponding Walphos ligands resulted in only 62% and 83% ee (Table 1, entries 9 and 10).[8,9]

Given the results obtained for MCA, it seemed of interest to investigate the performance of ligands (R,S_p,S_p)-**1** and (R,S_p,S_p)-**2** in the hydrogenation of the structurally related and commercially interesting cinnamic acid derivative IPCA-D.[1a,7] The use of the original Walphos ligands SL-W001-1 and SL-W002-1 in the rhodium-catalyzed hydrogenation of IPCA-D gave products with 94% and 74% ee after isolation (Table 1, entries 11 and 12). For this sterically much more demanding substrate, both values are higher than those obtained with MCA (83% and 62% ee). However, when their biferrocene analogues (R,S_p,S_p)-**1** and (R,S_p,S_p)-**2** were applied in the hydrogenation of IPCA-D the opposite trend was seen. In comparison to MCA, the product ee values dropped from 89% and 92% ee to 77% and 88% ee, respectively.

The biferrocene ligands (R,S_p,S_p)-**1** and (R,S_p,S_p)-**2** were used in the ruthenium-catalyzed hydrogenations of diketone acetylacetone (ACA) and the β-keto ester ethyl 3-oxopentanoate (EOP). High enantiomeric excesses were obtained (ACA, 98% ee; EOP, 92% ee; Table 1, entries 13−16), but in these cases the corresponding Walphos ligands also performed very well (ACA, 96% ee; EOP, 93% ee).

In brief, the hydrogenation of substrates MCA, ACA, and EOP with biferrocene ligands (R,S_p,S_p)-**1** and (R,S_p,S_p)-**2** led to products with enantiomeric excesses of ≥92%. Furthermore, the value obtained for MCA (92%) was significantly higher than that achieved with either of the two Walphos ligands (83% and 62% ee).

A comparison of the ee values listed in Table 1 shows that, overall, the Walphos ligands gave the best performance of the systems tested. Four out of the eight substrates (MAA, IPCA-D, ACA, and EOP) could be hydrogenated with enantiomeric excesses greater than 90% (93−97% ee). On using the ligands (R,S_p,S_p)-**1** and (R,S_p,S_p)-**2**, which are both based on the achiral 2,2″-biferrocenediyl backbone, three of the substrates (MCA, ACA, and EOP) gave product ee values greater than 90% (92−98% ee). However, on using ligands (R,S_p,R_p)-**1** and (R,S_p,R_p)-**2**, which are based on the C_2-symmetrical 2,2″-biferrocenediyl backbone, only one substrate (MAC) gave a product with such a high enantiomeric excess (91% ee) (Table 1, entry 2). It appears that, in asymmetric hydrogenations, Walphos ligands and their biferrocene analogues show significantly different performances.

This finding becomes even more apparent when, in addition to ee values, the absolute configurations of the products are considered. This comparison is based on the fact that the side-chain-substituted ferrocene unit of all ligands used has the R,S_p absolute configuration. For the substrates MAC, MAA, and DMI the product absolute configurations obtained with ligands (R,S_p,S_p)-**1** and (R,S_p,S_p)-**2** are identical with those obtained with their Walphos analogues (MAC, MAA, *S*; DMI, *R*), while those achieved with ligands (R,S_p,R_p)-**1** and (R,S_p,R_p)-**2** vary with the substitution pattern of the phosphine substituents. The product with an *S* configuration was obtained with (R,S_p,R_p)-**1**,

Table 1. Hydrogenation Results Obtained with Walphos Ligands and Their Biferrocene Analogues[a]

entry	substrate	biferrocene ligand	conversn, %	ee, % (confign)	biferrocene ligand	conversn, %	ee, % (confign)	Walphos ligand[b]	conversn, %	ee, % (confign)
1	MAC	(R,S_p,S_p)-**1**	100	61 (*S*)	(R,S_p,R_p)-**1**	100	21 (*S*)	SL-W001-1	100	63 (*S*)
2	MAC	(R,S_p,S_p)-**2**	100	80 (*S*)	(R,S_p,R_p)-**2**	100	**91** (*R*)	SL-W002-1	100	88 (*S*)
3	MAA	(R,S_p,S_p)-**1**	100	65 (*S*)	(R,S_p,R_p)-**1**	100	51 (*S*)	SL-W001-1	100	**97** (*S*)
4	MAA	(R,S_p,S_p)-**2**	100	75 (*S*)	(R,S_p,R_p)-**2**	100	89 (*R*)	SL-W002-1	100	**96** (*S*)
5	DMI	(R,S_p,S_p)-**1**	100	77 (*R*)	(R,S_p,R_p)-**1**	99	26 (*R*)	SL-W001-1	100	52 (*R*)
6	DMI	(R,S_p,S_p)-**2**	100	59 (*R*)	(R,S_p,R_p)-**2**	100	77 (*S*)	SL-W002-1	100	87 (*R*)
7	PCA	(R,S_p,S_p)-**1**	100	80 (*S*)	(R,S_p,R_p)-**1**	100	44 (*R*)	SL-W001-1	100	82 (*R*)
8	PCA	(R,S_p,S_p)-**2**	100	84 (*S*)	(R,S_p,R_p)-**2**	100	29 (*R*)	SL-W002-1	77	89 (*R*)
9	MCA	(R,S_p,S_p)-**1**	100	89 (*R*)	(R,S_p,R_p)-**1**	100	40 (*R*)	SL-W001-1	99	83 (*S*)
10	MCA	(R,S_p,S_p)-**2**	100	**92** (*R*)	(R,S_p,R_p)-**2**	100	46 (*S*)	SL-W002-1	100	62 (*S*)
11	IPCA-D	(R,S_p,S_p)-**1**	100	77 (*S*)	(R,S_p,R_p)-**1**	100	34 (*R*)	SL-W001-1	100	**94** (*R*)
12	IPCA-D	(R,S_p,S_p)-**2**	99	88 (*S*)	(R,S_p,R_p)-**2**	100	54 (*R*)	SL-W002-1	100	74 (*R*)
13	ACA	(R,S_p,S_p)-**1**	100	**96** (*S,S*)	(R,S_p,R_p)-**1**	100	85 (*S,S*)	SL-W001-1	100	**96** (*S,S*)
14	ACA	(R,S_p,S_p)-**2**	100	**98** (*S,S*)	(R,S_p,R_p)-**2**	100	80 (*S,S*)	SL-W002-1	100	85 (*R,R*)
15	EOP	(R,S_p,S_p)-**1**	99	68 (*S*)	(R,S_p,R_p)-**1**	100	75 (*S*)	SL-W001-1	100	**93** (*S*)
16	EOP	(R,S_p,S_p)-**2**	100	**92** (*S*)	(R,S_p,R_p)-**2**	94	33 (*S*)	SL-W002-1	100	76 (*S*)

[a]Reaction conditions: for alkenes, 1 mmol of substrate in 2.5 mL of MeOH, reaction time 16 h, 20 °C, hydrogen pressure MAC, MAA, DMI 1 bar, MCA 20 bar, and PCA, IPCA-D 50 bar, metal precursor $[Rh(NBD)_2]BF_4$ (NBD = norbornadiene); for ketones, 2.53 mmol of ACA or 1 mmol of EOP in 10 mL of MeOH, reaction time 16 h, 80 °C, hydrogen pressure 80 bar, additive HCl(aq), metal precursor $[RuI_2(p\text{-cymene})]_2$. [b]Absolute configuration R,S_p.

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whereas (R,S_p,R_p)-**2** resulted in the product with an *R* configuration (Table 1, entries 1−6). The hydrogenation of substrates PCA, MCA, and IPCA-D with ligands (R,S_p,S_p)-**1** and (R,S_p,S_p)-**2**, however, resulted in products that had absolute configurations opposite to those obtained with the corresponding Walphos ligands SL-W001-1 and SL-W002-1 (Table 1, entries 7−12). The hydrogenation results for ketones ACA and EOP are more consistent since, with one exception (ACA and ligand SL-W002-1; Table 1, entry 14), the same product configuration was detected in all cases (ACA, *S*,*S*; EOP, *S*).

In summary, the original Walphos ligands appear to have a broader scope of applicability than their biferrocene-based analogues. The replacement of the backbone phenyl ring of Walphos-type ligands gave derivatives with either an S_p,R_p- or S_p,R_p-configured biferrocene backbone. In the hydrogenation of alkenes and ketones these diastereomeric ligands show significantly different performances in comparison to each other and also in comparison to the corresponding Walphos ligand. From the experimental results it is clear that the changes in the ligand backbone are so pronounced that not only do the ee values change significantly but also, in several cases, the product absolute configuration of the predominant enantiomer is reversed (for a comparison of the molecular structures of complexes [$PdCl_2$(SL-W002-1)], [$PdCl_2$((R,S_p,R_p)-**1**)], and [$PdCl_2$((R,S_p,S_p)-**1**)] see Figure S4, in the Supporting Information).

CONCLUSION

The newly synthesized ligands (R,S_p,S_p)-**1** and (R,S_p,S_p)-**2** perform very well in the rhodium-catalyzed hydrogenation of 2-methylcinnamic acid (MCA) to give products with enantiomeric excesses of 89% and 92%, respectively. In the ruthenium-mediated hydrogenation of acetylacetone (ACA) and ethyl 3-oxopentanoate (EOP) even higher enantiomeric excesses could be achieved (ACA, 98%; EOP, 92% ee). However, for the commercially interesting substrate IPCA-D the Walphos ligand SL-W001-1 still gives the best results.

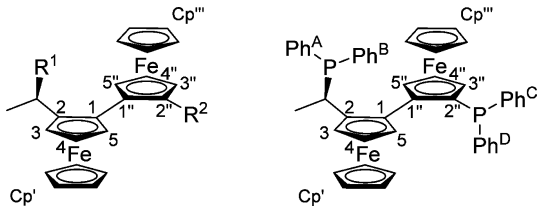
The performance of the original R,S_p-configured Walphos ligands SL-W001-1 and SL-W002-1 in the rhodium-catalyzed asymmetric hydrogenation of several alkenes and the ruthenium-catalyzed hydrogenation of two ketones was compared to that of their analogous biferrocene-based ligands **1** and **2** of R,S_p,S_p and R,S_p,R_p absolute configuration, respectively. The newly synthesized ligands (R,S_p,S_p)-**1** and (R,S_p,S_p)-**2** perform particularly well in the hydrogenation of MCA, ACA, and EOP, but in general they do not match the performance of the original Walphos ligands. In a number of cases products with opposite absolute configuration were formed. The use of the ligands (R,S_p,S_p)-**1** and (R,S_p,S_p)-**2**, with one exception (MAC, 91% ee), only gave moderate product ee values. For the diastereomeric biferrocene ligands the R,S_p,S_p configuration clearly matches much better than the R,S_p,R_p configuration.

The replacement of the Walphos ferrocenylphenyl backbone with a biferrocene unit of either S_p,S_p or S_p,R_p absolute configuration seems to result in marked structural changes in the ligands and complexes. These changes are reflected in the catalysis results, which in most cases differ significantly not only in product ee values but also in product absolute configurations.

Nevertheless, for each series of ligands matching substrate/catalyst pairs were identified that gave the corresponding product with reasonably high enantiomeric excess: i.e., MCA/(R,S_p,S_p)-**2**, 92% ee; ACA/(R,S_p,S_p)-**2**, 98% ee; MAC/(R,S_p,R_p)-**2**, 91% ee; MAA/SL-W002-1, 97% ee; DMI/SL-W001-1, 87% ee; IPCA-D/SL-W002-1, 94% ee; EOP/SL-W001-1, 93% ee. Overall, it seems that for the development of efficient catalytic systems the search for matching catalyst/substrate pairs is at least as important as the search for novel catalyst backbones and structures.

EXPERIMENTAL SECTION

General Details. All reactions except oxidations with H_2O_2 were carried out under an argon atmosphere using standard Schlenk techniques and dry solvents. Solvents were dried according to standard procedures under an argon atmosphere and were freshly distilled prior to use. Tetrahydrofuran (THF) was dried over sodium/benzophenone, dichloromethane (DCM) and acetone were dried over P_2O_5, Et_2O was dried over $LiAlH_4$, MeOH was dried over magnesium methoxide, and toluene was dried over sodium. Column chromatography was performed either on silica gel (Merck, 40−63 μm) or on aluminum oxide (Merck, aluminum oxide 90). Petroleum ether (PE, boiling range 60−80 °C), ethyl acetate (EA), and triethylamine (TEA) were used as the eluents. NMR spectra were recorded either in $CDCl_3$ or in CD_2Cl_2. Chemical shifts are referenced to $CHCl_3$ (^{1}H, 7.26 ppm) and $CDCl_3$ (^{13}C, 77.0 ppm) and to $CDHCl_2$ (^{1}H, 5.32 ppm) and CD_2Cl_2 (^{13}C, 53.7 ppm). ^{31}P NMR spectra are referenced to 85% H_3PO_4 (^{31}P, 0 ppm). For the assignment of peaks, the following abbreviations were used: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet. Coupling constants in ^{13}C NMR spectra are due to ^{31}P−^{13}C or ^{19}F−^{13}C coupling. High-resolution mass spectra were recorded on an ESI-Qq aoTOF MS system. Optical rotations were measured in $CHCl_3$. Conversion and ee values were measured by GC and HPLC.



General Atom Numbering Schemes for NMR Assignment.

(S_p)-2-{(*R*)-1-Bis[3,5-bis(trifluoromethyl)phenyl]phosphinoethyl}-(S_p)-2″-diphenylphosphino-1,1″-biferrocene ((R,S_p,S_p)-1). To a degassed solution of phosphine oxide (R,S_p,S_p)-**8** (500 mg, 0.474 mmol) in THF (10 mL) were added PMHS (0.408 mL, 4.74 mmol) and Ti(O-*i*Pr)$_4$ (0.719 mL, 2.37 mmol). The resulting mixture was heated under reflux under argon at 75 °C for 3 h. The resulting dark green solution was cooled to room temperature and transferred to the top of a column (aluminum oxide, PE/EA/EtOH = 90/10/1) without prior workup. Elution and subsequent removal of the solvents gave the crude product as an orange solid. In order to remove excess PMHS, the crude product was again purified by chromatography (aluminum oxide, PE/EA = 10/1) to give the pure product as an orange solid (yield: 457 mg, 0.436 mmol, 92%). Mp: 74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.46 (dd, J_1 = 7.1 Hz, J_2 = 9.8 Hz, 3H, CH_3CH), 3.60 (dd, J_1 = 1.5 Hz, J_2 = 2.3 Hz, 1H, H3/H5), 3.62−3.62 (m, 1H, CH_3CH), 3.84 (s, 5H, Cp‴), 4.12 (s, 5H, Cp′), 4.19−4.20 (m, 2H, H4 + H3″), 4.30−4.35 (m, 2H, H4″ + H5″), 4.79−4.82 (m, 1H, H3/H5), 7.16−7.24 (m, 3H, Ph$^{C/D}$-*meta* + Ph$^{C/D}$-*para*), 7.29−7.37 (m, 2H, Ph$^{C/D}$-*ortho*), 7.38−7.44 (m, 3H, Ph$^{C/D}$-*meta* + Ph$^{C/D}$-*para*), 7.45 (bd, J = 4.7 Hz, 2H, Ph$^{A/B}$-*ortho*), 7.56 (bd, J = 5.9 Hz, 2H, Ph$^{A/B}$-*ortho*), 7.65−7.75 (m, 2H, Ph$^{C/D}$-*ortho*), 7.77 (bs, 1H, Ph$^{A/B}$-*para*), 7.89 (bs, 1H, Ph$^{A/B}$-*para*). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 18.2 (d, J = 6.8 Hz, CH_3CH), 29.6 (dd, J_1 = 6.3 Hz, J_2 = 19.1 Hz, CH_3CH), 66.4 (d, J = 8.8 Hz, C3/C5), 66.8 (C4), 69.9 (C4″), 70.26 (5C, Cp′/Cp‴), 70.28 (5C, Cp′/Cp‴), 71.0 (d, J = 12.5 Hz, C3/C5), 73.1 (d, J = 4.3 Hz, C3″), 73.5 (d, J = 5.1 Hz, C5″), 74.4 (d, J = 16.8 Hz, C1″), 83.4 (bs, C1), 88.8 (d, J = 18.2 Hz, C2), 90.4 (d, J = 28.4 Hz, C2″), 123.0 (q, J = 273.1 Hz, 2C, CF_3), 123.1 (q, J = 273.5 Hz, 2C, CF_3), 122.1−122.3 (m, Ph$^{A/B}$-*para*), 123.3−123.6 (m, Ph$^{A/B}$-*para*), 127.9−128.1 (m, 4C, Ph^{C}-*meta* + Ph^{D}-*meta*), 128.1 (Ph$^{C/D}$-*para*), 129.3 (Ph$^{C/D}$-*para*), 131.7−132.1 (m, 2C, Ph$^{A/B}$-*ortho*), 132.3 (d, J = 17.7 Hz, 2C,

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Ph$^{C/D}$-*ortho*), 134.6−135.1 (m, Ph$^{A/B}$-*ortho*), 135.6 (q, J = 22.9 Hz, 2C, Ph$^{C/D}$-*ortho*), 137.8, 138.1, 140.1, 140.3 (2C, Ph$^{A/B}$-*ipso*), 139.4, 139.5, 141.1, 141.2 (2C, Ph$^{C/D}$-*ipso*). Ph$^{A/B}$-*meta* not observed. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ −21.7 (bs, CH_3CHPR_2), 9.0 (d, J = 3.9 Hz, Fc-PPh_2). HR-MS (ESI, MeOH/MeCN): m/z [M]$^+$ calcd 1038.0799 for $C_{50}H_{36}F_{12}Fe_2P_2$, found 1038.0806. $[\alpha]^{20}_{\lambda}$ (nm): −488° (589) (c 0.235, $CHCl_3$).

(S_p)-2-[(*R*)-1-Diphenylphosphinoethyl]-(S_p)-2″-diphenylphosphino-1,1″-biferrocene ((*R*,S_p,S_p)-2). To a degassed solution of crude (*R*,S_p,S_p)-**9** (500 mg, 0.626 mmol) in THF (5 mL) were added PMHS (0.430 mL) and Ti(O-*i*Pr)$_4$ (711.9 mg, 2.50 mmol). The resulting mixture was heated under reflux under argon at 75 °C for 4 h. The resulting dark green solution was cooled to room temperature and transferred to the top of a column (aluminum oxide, PE/EA/EtOH = 85/15/1) without prior workup. Elution and subsequent removal of the solvents gave the crude product as an orange solid. In order to remove excess PMHS, the crude product was suspended in PE/EA (95/5) and filtered. The product was washed several times with the same solvent mixture and was dried in vacuo (yield: 340 mg, 4.38 mmol, 70%). Mp: 89 °C. ^{1}H NMR (600 MHz, CD_2Cl_2): δ 1.50 (dd, J_1 = 7.1 Hz, J_2 = 12.2 Hz, 3H, CH_3CH), 3.26−3.33 (m, 1H, CH_3CH), 3.85 (s, 5H, Cp‴), 4.13−4.15 (m, 1H, H3/H5), 4.14 (s, 5H, Cp′), 4.19−4.21 (m, 3H, H3″ + H5″ + H4), 4.48 (dt, J_1 = 0.6 Hz, J_2 = 2.6 Hz, 1H, H4″), 4.57−4.59 (m, 1H, H3/H5), 7.02−7.07 (m, 2H, Ph^B-*ortho*), 7.10−7.16 (m, 2H, Ph^D-*ortho*), 7.17−7.21 (m, 2H, Ph^B-*meta*), 7.22−7.28 (m, 3H, Ph^D-*meta* + Ph$^{B/D}$-*para*), 7.33−7.38 (m, 4H, Ph^A-*meta* + Ph^A-*para* + Ph$^{B/D}$-*para*), 7.38−7.41 (m, 3H, Ph^C-*meta* + Ph^C-*para*), 7.47−7.52 (m, 2H, Ph^A-*ortho*), 7.65−7.70 (m, 2H, Ph^C-*ortho*). ^{13}C{^{1}H} NMR (150.9 MHz, CD_2Cl_2): δ 20.2 (d, J = 9.9 Hz, CH_3CH), 28.6 (dd, J_1 = 3.2 Hz, J_2 = 7.8 Hz, CH_3CH), 66.8 (C4), 67.7 (d, J = 10.9 Hz, C3/C5), 69.9 (C4″), 70.0 (d, J = 11.5 Hz, C3/C5), 70.45 (5C, Cp′/Cp‴), 70.47 (5C, Cp′/Cp‴), 72.7 (d, J = 4.3 Hz, C3″/C5″), 73.5 (d, J = 15.4 Hz, C1″), 75.1 (bs, C3″/C5″), 83.6 (bs, C1), 91.1 (d, J = 29.0 Hz, C2″), 91.9 (C2), 128.2−128.8 (10C, 8Ph-*meta* + 2Ph-*para*), 129.4 (Ph-*para*), 129.8 (bs, Ph-*para*), 132.9 (d, J = 14.1 Hz, 2C, Ph^B-*ortho*), 133.0 (d, J = 17.5 Hz, 2C, Ph^A-*ortho*), 135.2 (d, J = 19.5 Hz, 2C, Ph^D-*ortho*), 135.78 (d, J = 23.1 Hz, 2C, Ph^C-*ortho*), 139.7 (d, J = 11.7 Hz, Ph^C-*ipso*), 141.5 (d, J = 10.9 Hz, Ph^A-*ipso*), Ph^B-*ipso* and Ph^D-*ipso* not observed. ^{31}P{^{1}H} NMR (243 MHz, CD_2Cl_2): δ −24.5 (Fc-PPh_2), 7.1 (CH_3CH-PPh_2). HR-MS (ESI, MeOH/MeCN): m/z [M]$^+$ calcd 766.1304 for $C_{46}H_{40}Fe_2P_2$, found 766.1308. $[\alpha]^{20}_{\lambda}$ (nm): −481° (589) (c 0.245, $CHCl_3$).

(S_p)-2-[(*R*)-1-Diphenylphosphinoethyl]-(S_p)-2″-diphenylphosphino-1,1″-biferrocene−*P*,*P*-bis(borane) ((*R*,S_p,S_p)-2·2BH$_3$). The derivative (*R*,S_p,S_p)-**2** (100 mg, 0.126 mmol) was dissolved in THF (2 mL), and the solution was degassed. To the resulting solution was added dropwise at 0 °C a solution of BH_3 in THF (1 M, 0.38 mL, 0.38 mmol), and the mixture was stirred for 16 h at room temperature The reaction mixture was quenched at 0 °C with water (15 mL) and extracted twice with DCM. The combined organic phases were washed with water, dried over $MgSO_4$, and filtered, and the solvents were evaporated. The desired product was obtained as an orange foam (yield: 100.9 mg, 0.125 mmol, >99%). Single crystals suitable for X-ray structure determination were grown from CH_2Cl_2/ethyl acetate by slow evaporation of the solvent. Mp: >180 °C dec. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86-1.90 (6H, BH_3), 2.19 (dd, J_1 = 7.2 Hz, J_2 = 17.4 Hz, 3H, CH_3CH), 3.77 (s, 5H, Cp′), 3.80 (t, J = 2.6 Hz, H4), 3.86−3.89 (m, 1H, H3″), 3.96 (s, 5H, Cp‴), 4.00−4.04 (m, 1H, H3), 4.05−4.16 (m, 1H, CH_3CH), 4.36−4.42 (m, 1H, H3), 4.44 (t, J = 2.6 Hz, H4″), 4.64−4.68 (m, 1H, H5″), 7.34−7.87 (m, 20H, Ph). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 23.7 (d, J = 5.4 Hz, CH_3CH), 29.6 (d, J = 29.9 Hz, CH_3CH), 65.9 (C4), 66.4 (d, J = 15.4 Hz, C1″), 68.2 (bs, C5), 70.0 (d, J = 6.8 Hz, C4″), 70.2 (5C, Cp′), 70.5 (5C, Cp‴), 72.4 (C3), 72.9 (d, J = 4.3 Hz, C3″), 74.7 (d, J = 7.8 Hz, C5″), 78.9 (d, J = 3.9 Hz, C1), 89.6 (d, J = 13.4 Hz, C2″), 91.4 (d, J = 2.2 Hz, C2), 128.1−129.1 (8C, Ph-*meta*), 130.3−131.4 (4C, Ph-*para*), 132.9 (d, J = 9.2 Hz, 2C, Ph-*ortho*), 133.8−134.2 (6C, Ph-*ortho*), 128.5, 130.0, 130.5, 131.8, 132.4 (Ph-*ipso*). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 17.4 (bs, Fc-PPh_2), 29.4 (bs, CH_3CH-PPh_2). HR-MS (ESI, MeOH/MeCN): m/z [M + Na]$^+$ calcd 817.1857 for $C_{46}H_{40}Fe_2P_2Na$, found 817.1833; $[\alpha]^{20}_{\lambda}$ (nm): +371° (589) (c 0.265, $CHCl_3$).

(R,S_p,S_p)- and (R,S_p,R_p)-2″-Bromo-2-[1-(*N*,*N*-dimethylamino)ethyl]-1,1″-biferrocene ((R,S_p,S_p)-5 and (R,S_p,R_p)-5). To a degassed solution of (*R*)-**3** (584 mg, 2.27 mmol) in THF (3 mL) was added dropwise at −78 °C *sec*-BuLi (1.4 M in cyclohexane, 1.8 mL, 2.52 mmol). The resulting deep red solution was stirred for 1 h at −78 °C and for 2 h at 0 °C. A solution of $ZnBr_2$ in THF (1.3 M, 2.3 mL, 2.99 mmol) was added, and the reaction mixture was stirred for a further 40 min at 0 °C. A solution of $[Pd_2(dba)_3]\cdot CHCl_3$ (118 mg, 0.114 mmol) and tris(2-furyl)phosphine (212 mg, 0.913 mmol) in THF was prepared. The mixture was degassed and stirred for 20 min at room temperature to give a dark green clear solution. To this catalyst solution were transferred a degassed solution of *rac*-**4** (577 mg, 1.476 mmol) in THF (2 mL) and the freshly prepared ferrocenylzinc compound. The resulting solution was heated under argon at 75 °C for 19 h. The reaction mixture was cooled to room temperature, quenched with 5 M NaOH (5 mL), diluted with water, and extracted with Et_2O (3 × 70 mL). The combined organic phases were washed with water (3 × 50 mL) and brine (2 × 50 mL) and dried over $MgSO_4$. The mixture was filtered, the solvents were evaporated, and the crude products were separated by column chromatography on aluminum oxide. PE eluted excess tfp and PE/Et_2O/NEt_3 60/1/3 eluted the first diastereomer (R,S_p,S_p)-**5** and excess **3**, while PE/Et_2O/NEt_3 5/5/1 gave the second diastereomer (R,S_p,R_p)-**3**. Diastereomer (R,S_p,R_p)-**5**: yield 32% (249 mg, 0.749 mmol). Derivative (R,S_p,R_p)-**5**: yield 45% (344 mg, 0.661 mmol). (R,S_p,S_p)-**5**: mp 113−115 °C; ^{1}H NMR (500.1 MHz, $CDCl_3$) δ 1.39 (d, 3H, J = 6.7 Hz, CH_3CH), 2.09 (s, 6H, N(CH_3)$_2$), 3.78 (q, J = 6.7 Hz, 1H, CH_3CH), 4.09 (s, 5H, Cp‴), 4.10−4.12 (bs, 6H, Cp′ + H4″), 4.21−4.22 (m, 1H, H3), 4.26 (dd, J_1 = J_2 = 2.6 Hz, 1H, H4), 4.49−4.51 (m, 1H, H3″), 4.87−4.89 (dd, J_1 = 1.5 Hz, J_2 = 2.5 Hz, 1H, H5), 5.01−5.03 (m, 1H, H5″); ^{13}C{^{1}H} NMR (125.8 MHz, $CDCl_3$) δ 11.5 (CH_3CH), 39.8 (2C, N(CH_3)$_2$), 56.0 (CH_3CH), 66.3 (C4″), 66.5 (C4), 67.0 (C3), 69.1 (C5″), 69.5 (C5), 70.2 (5C, Cp′), 71.6 (C3″), 71.8 (5C, Cp‴), 79.0 (C_q), 82.3 (C_q), 82.6 (C_q), 88.8 (C_q); HR-MS (ESI, MeOH/MeCN) m/z [M + H]$^+$ calcd 520.0026 for $C_{24}H_{27}BrFe_2N$, found 520.0027; $[\alpha]^{23}_{\lambda}$ (nm): −850 (589) (c 0.725, $CHCl_3$). (R,S_p,R_p)-**5**: Mp: 89−94 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.51 (d, J = 6.9 Hz, 3H, CH_3CH), 1.70 (s, 6H, N(CH_3)$_2$), 3.42 (q, J = 6.9 Hz, 1H, CH_3CH), 4.18 (dd, J_1 = 1.4 Hz, J_2 = 2.5 Hz, 1H, H3), 4.26 (dd, J_1 = J_2 = 2.6 Hz, 1H, H4″), 4.28 (s, 5H, Cp′), 4.36 (bs, 6H, Cp‴ + H4), 4.39 (dd, J_1 = 1.5 Hz, J_2 = 2.6 Hz, 1H, H5″), 4.45 (dd, J_1 = 1.5 Hz, J_2 = 2.6 Hz, 1H, H3″), 4.60 (dd, J_1 = 1.4 Hz, J_2 = 2.5 Hz, 1H, H5); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 20.1 (CH_3CH), 41.1 (2C, N(CH_3)$_2$), 55.3 (CH_3CH), 66.1 (C4″), 66.5 (C4), 67.0 (C3), 69.6 (5C, Cp′), 69.8 (C3″), 70.1 (C5″), 71.5 (5C, Cp‴), 71.6 (C5), 82.6 (C_q), 82.7 (C_q), 85.7 (C_q), 88.7 (C2); HR-MS (ESI, MeOH/MeCN) m/z [M + H]$^+$ calcd 520.0026 for $C_{24}H_{27}BrFe_2N$, found 520.0022; $[\alpha]^{20}_{\lambda}$ (nm) −950° (589), −1062° (578), −1631° (546) (c 0.283, $CHCl_3$).

(R,S_p,S_p)-2-[1-(*N*,*N*-Dimethylamino)ethyl]-2″-diphenylphosphino-1,1″-biferrocene ((R,S_p,S_p)-6). To a degassed solution of (R,S_p,S_p)-**5** (2.43 g, 4.67 mmol) in THF (30 mL) was added dropwise at −40 °C a solution of *sec*-BuLi (1.3 M in cyclohexane, 4.3 mL, 5.6 mmol). The resulting dark red mixture was stirred for 40 min at −40 °C and warmed to room temperature, and subsequently chlorodiphenylphosphine (1.1 mL, 6.4 mmol) was added. The mixture was stirred for 18 h at room temperature and for 1 h at 35 °C. The reaction was quenched at room temperature with 5 mL of saturated aqueous $NaHCO_3$, the product was extracted twice with ethyl acetate, and the combined organic phases were washed with water and brine. After drying over $MgSO_4$, filtration, and evaporation of the solvents, the crude product was obtained as an orange solid. After chromatography (aluminum oxide, PE/EE/NEt_3 = 100/1/3) the pure product was obtained as an orange foam (yield: 1.69 g, 2.70 mmol, 58%). Single crystals suitable for X-ray structure determination were grown from ethyl acetate by slow evaporation of the solvent. Mp: 196−201 °C. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 1.34 (d, J = 6.6 Hz, 3H, CH_3CH), 2.19 (s, 6H, N(CH_3)$_2$), 3.69 (s, 5H, Cp′), 3.80 (s, 5H, Cp‴), 3.88 (q, J = 6.6 Hz, 1H, CH_3CH), 3.92 (bs, 1H, H3″), 4.18−4.21 (m, 2H, H3 + H4), 4.39 (dd, J_1 = J_2 = 2.5 Hz, 1H, H4″), 5.34−5.36 (m, 1H, H5″), 5.39−5.42 (m, 1H, H5), 7.26−7.30 (m, 1H,

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Ph^B-*para*), 7.31−7.36 (m, 2H, Ph^B-*meta*), 7.36−7.40 (m, 3H, Ph^A-*meta* + Ph^A-*para*), 7.45−7.49 (m, 2H, Ph^B-*ortho*), 7.59−7.63 (m, 2H, Ph^A-*ortho*); Ph^A pointing toward Cp‴. $^{13}C\{^1H\}$ NMR (125.6 MHz, $CDCl_3$): δ 10.2 (CH_3CH), 39.9 (2C, $N(CH_3)_2$), 56.6 (CH_3CH), 65.7 (C3/C4), 66.4 (C3/C4), 67.5 (5C, Cp′), 69.7 (C4″), 70.3−70.7 (6C, Cp‴ + C5), 72.8 (bs, C5″), 73.0−73.3 (2C, C3″ + C1″), 83.8 (C1), 88.0 (C2), 89.6 (d, J = 22.6 Hz, C2″), 127.9 (d, J = 7.5 Hz, 2C, Ph^A-*meta*), 128.2 (bs, 3C, Ph^B-*meta* + Ph^B-*para*), 128.8 (Ph^A-*para*), 133.1 (d, J = 19.3 Hz, 2C, Ph^B-*ortho*), 135.4 (d, J = 22.0 Hz, 2C, Ph^A-*ortho*), 139.0 (d, J = 11.3 Hz, Ph^A-*ipso*), 140.2 (d, J = 11.3 Hz, Ph^B-*ipso*). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ −20.0. HR-MS (ESI, MeOH/MeCN): m/z $[M + H]^+$ calcd 626.1362 for $C_{36}H_{37}Fe_2NP$, found 626.1351; $[\alpha]^{23}_{\lambda}$ (nm): −554 (589) (c 0.232, $CHCl_3$).

(R,S_p,S_p)-2-[1-(*N,N*-Dimethylamino)ethyl]-2″-diphenylphosphinyl-1,1″-biferrocene ((R,S_p,S_p)-7). *Method A: From (R,S_p,S_p)-6 with H_2O_2.* To a solution of (R,S_p,S_p)-**6** (649 mg, 1.04 mmol) in acetone (150 mL) was added an aqueous solution of H_2O_2 (30%, 5 mL). The reaction mixture was stirred for 50 min at room temperature and was then quenched with saturated aqueous $Na_2S_2O_3$. The organic material was extracted with EtOAc, the combined organic phases were washed with water and brine, dried over $MgSO_4$ and filtered, and the solvents were evaporated. The crude product was purified by chromatography (aluminum oxide, PE/EA/TEA = 5/1/1), and the pure product was obtained as a red-orange solid (yield: 608 mg, 0.948 mmol, 91%).

Method B: From (R,S_p,S_p)-5 with ClP(O)Ph$_2$. Synthesis procedure as described for (R,S_p,S_p)-**6**: (R,S_p,S_p)-**5** (1.220 g, 2.346 mmol) in THF (26 mL), *n*-BuLi (1.6 M in hexane, 1.76 mL, 2.815 mmol), and diphenylphosphinyl chloride (0.6 mL, 3.167 mmol). Purification by column chromatography (aluminum oxide, PE/EE/NEt_3 10/10/1) yielded 1.164 g (1.815 mmol, 77%) of the pure product as an orange foam. Single crystals suitable for X-ray structure determination were grown from ethyl acetate by slow evaporation of the solvent.

Mp: 201−203 °C. ^1H NMR (500.1 MHz, $CDCl_3$): δ 1.36 (d, J = 6.1 Hz, 3H, CH_3CH), 2.28 (s, 6H, $N(CH_3)_2$), 3.42 (bs, 5H, Cp′), 3.78 (bs, 1H, H3″), 4.06 (s, 5H, Cp‴), 4.10 (q, J = 6.1 Hz, 1H, CH_3CH), 4.14 (dd, J_1 = J_2 = 2.6 Hz, 1H, H4), 4.18 (bs, 1H, H3), 4.42−4.45 (m, 1H, H4″), 5.53 (bs, 1H, H5″), 5.91 (bs, 1H, H5), 7.44−7.47 (m, 2H, Ph^B-*meta*), 7.48−7.54 (m, 4H, Ph^A-*meta* + Ph^A-*para* + Ph^B-*para*), 7.77−7.83 (m, 2H, Ph^B-*ortho*), 7.85−7.91 (m, 2H, Ph^A-*ortho*); Ph^B pointing toward Cp‴. $^{13}C\{^1H\}$ NMR (125.8 MHz, $CDCl_3$): δ 8.7 (CH_3CH), 39.5 (2C, $N(CH_3)_2$), 57.3 (CH_3CH), 67.1 (C4), 68.6 (C3), 69.5 (5C, Cp′), 71.0 (d, J = 12.2 Hz, C4″), 71.2 (5C, Cp‴), 71.8 (C5), 73.8 (d, J = 8.2 Hz, C5″), 76.3 (d, J = 16.6 Hz, C3″), 81.8 (C1), 87.1 (C2), 89.0 (d, J = 9.4 Hz, C2″), 127.8 (d, J = 11.7 Hz, 2C, Ph^B-*meta*), 128.5 (d, J = 11.9 Hz, 2C, Ph^A-*meta*), 131.1 ($Ph^{A/B}$-*para*), 131.7 ($Ph^{A/B}$-*para*), 132.0 (d, J = 9.4 Hz, 2C, Ph^A-*ortho*), 132.1 (d, J = 10.0 Hz, 2C, Ph^B-*ortho*), 134.7, 135.0, 135.5, 135.9 (2C, Ph^A-*ipso* + Ph^B-*ipso*); 1 C_q (C1″) not observed. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 31.9. HR-MS (ESI, MeOH/MeCN): m/z $[M + H]^+$ calcd 642.1311 for $C_{36}H_{37}Fe_2NOP$, found 642.1311. $[\alpha]^{23}_{\lambda}$ (nm): −272° (589) (c 0.258, $CHCl_3$).

(S_p)-2-{(*R*)-1-Bis[3,5-bis(trifluoromethyl)phenyl]phosphinoethyl}-(S_p)-2″-diphenylphosphinyl-1,1″-biferrocene ((R,S_p,S_p)-8). In a Schlenk flask, phosphine oxide (R,S_p,S_p)-7 (800 mg, 1.25 mmol) and bis-(3,5-trifluoromethyl)phenylphosphine (0.86 g, 1.88 mmol) were dissolved under Ar in freshly distilled acetic acid (20 mL) through which Ar had been bubbled for several hours. The resulting solution was again degassed and subsequently heated under Ar at 75 °C for 18 h. The mixture was cooled to room temperature, the acetic acid was removed under vacuum, the residue was taken up in DCM (15 mL), and saturated aqueous $NaHCO_3$ was added. The phases were separated, and the aqueous phase was extracted with DCM. The combined organic phases were washed with water and brine and dried over $MgSO_4$. After filtration and evaporation of the solvents, the crude product was purified by column chromatography under inert conditions with deoxygenated solvents on aluminum oxide. The solvent mixture PE/DEE 20/1 removed the excess diphenylphosphine and PE/EE 2/1 eluted the title compound as an orange foam (yield: 797 mg, 0.749 mmol, 60%). Mp: 123 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 1.47 (bt, J = 6.5 Hz, 3H, CH_3CH), 3.21 (bs, 1H, Cp), 3.64 (s, 5H, Cp), 3.95−4.09 (m, 3H, CH_3CH + 2 Cp), 4.14 (s, 5H, Cp), 4.50 (bs, 1H, Cp), 5.00 (bs, 1H, Cp), 5.64 (bs, 1H, Cp), 7.42−7.60 (m, 6H, Ph), 7.68−7.75 (d, J = 6.3 Hz, 2H, Ph), 7.77−7.81 (m, 2H, Ph), 7.82−7.93 (m, 5H, Ph), 7.98 (bs, 1H, Ph). $^{13}C\{^1H\}$ NMR (150.9 MHz, $CDCl_3$): δ 17.5 ($CHCH_3$), 29.7 (d, J = 19.5 Hz, $CHCH_3$), 66.9 (Cp), 67.3 (Cp), 69.8 (5C, Cp), 70.8 (d, J = 17.4 Hz, Cp), 71.2 (5C, Cp), 72.6 (Cp), 73.4 (Cp), 75.7 (Cp), 80.2 (Cp), 86.6−87.1 (m, Cp), 121.0−139.5 (Ph), 2 Fc-C_q not observed. $^{31}P\{^1H\}$ NMR (243 MHz, $CDCl_3$): δ 7.8 (CH_3CHPR_2), 30.8 (Fc-*P*(O)Ph_2). HR-MS (ESI, MeOH/MeCN): m/z $[M]^+$ calcd 1054.0748 for $C_{50}H_{46}F_{12}Fe_2OP_2$, found 1054.0766. $[\alpha]^{20}_{\lambda}$ (nm): −116° (589) (c 0.19, $CHCl_3$).

(S_p)-2-[(*R*)-1-Diphenylphosphinoethyl]-(S_p)-2″-diphenylphosphinyl-1,1″-biferrocene ((R,S_p,S_p)-9). In a Schlenk flask, phosphine oxide (R,S_p,S_p)-7 (800 mg, 1.25 mmol) was dissolved under Ar in freshly distilled acetic acid (20 mL) through which Ar had been bubbled for several hours. The resulting solution was again degassed. Subsequently diphenylphosphine (929.5 mg, 4.99 mmol) was added and the resulting mixture was heated under Ar at 75 °C for 18 h. After the mixture was cooled to room temperature, the acetic acid was removed under vacuum, the residue was taken up in DCM (15 mL), and saturated aqueous $NaHCO_3$ was added. The phases were separated, and the aqueous phase was extracted with DCM. The combined organic phases were washed with water and brine and dried over $MgSO_4$. After filtration and evaporation of the solvents, the crude product was used in the next step without further purification. ^1H NMR (400 MHz, $CDCl_3$): δ 2.24 (d, J = 6.4 Hz, 3H, CH_3CH), 3.58 (s, 5H, Cp′), 3.66−3.71 (m, 1H, Cp), 3.86 (q, J = 6.4 Hz, 1H, CH_3CH), 3.91−3.94 (m, 1H, Cp), 4.01 (t, J = 2.6 Hz, 1H, Cp), 4.11 (s, 5H, Cp), 4.42−4.45 (m, 1H, Cp), 5.05−5.09 (m, 1H, Cp), 5.36 (dd, J_1 = 1.5 Hz, J_2 = 2.6 Hz, 1H, Cp), 7.72−7.94 (m, 20H, Ph). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 5.8 (Fc-PPh_2), 29.9 (CH_3CH-P(O)Ph_2). Bisphosphine oxide: $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 28.6 (Fc-P(O)Ph_2), 36.0 (CH_3CH-P(O)Ph_2).

Dichloro{(S_p)-2-[(*R*)-1-diphenylphosphinoethyl-κP]-(S_p)-2″-diphenylphosphino-κP-1,1″-biferrocene}palladium(II) ([$PdCl_2$(R,S_p,S_p)-(2)]). To a mixture of (R,S_p,S_p)-**2** (60 mg, 0.078 mmol) and bis(acetonitrile)dichloropalladium(II) (20.28 mg, 0.065 mmol) was added degassed DCM (3 mL). The dark red solution was stirred under argon at room temperature for 16 h. The solution was filtered under inert conditions over a pad of Celite. The solvent was removed, and the dark red solid residue was dried in vacuo (yield: 73 mg, 0.077 mmol, 99%). Mp: >200 °C (unsolvated complex). ^1H NMR (400 MHz, $CDCl_3$): δ 1.76 (dd, J_1 = 7.2 Hz, J_2 = 12.2 Hz, 3H, CH_3CH), 3.30−3.33 (m, 1H, H3), 3.44 (dd, J_1 = 1.5 Hz, J_2 = 2.5 Hz, 1H, H5), 3.65−3.68 (m, 1H, H3″), 3.86 (t, J = 2.6 Hz, 1H, H4), 4.16 (s, 5H, Cp′), 4.45 (s, 5H, Cp‴), 4.50 (t, J = 2.6 Hz, 1H, H4″), 4.77−4.80 (m, 1H, H5″), 5.23−5.31 (m, 1H, CH_3CH), 7.10−7.18 (m, 2H, Ph^D-*meta*), 7.19−7.25 (m, 1H, Ph^D-*para*), 7.29−7.36 (m, 2H, Ph^C-*meta*), 7.36−7.48 (m, 5H, Ph^A-*meta* + Ph^D-*ortho* + $Ph^{A/C}$-*para*), 7.49−7.62 (m, 4H, Ph^B-*meta* +Ph^B-*para* + $Ph^{A/C}$-*para*), 7.73−7.85 (m, 4H, Ph^A-*ortho* + Ph^C-*ortho*), 8.26−8.35 (m, 2H, Ph^B-*ortho*). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 22.9 (d, J = 4.8 Hz, CH_3CH), 31.5 (d, J = 5.8 Hz, CH_3CH), 66.2 (C4), 67.2 (d, J = 2.3 Hz, C3), 69.5 (5C, Cp′), 70.1 (d, J = 5.2 Hz, C4″), 70.4 (5C, Cp‴), 73.0 (C5), 74.2 (bs, C5″), 75.5 (d, J = 6.0 Hz, C3″), 81.1 (bs, C1), 89.6 (d, J = 7.7 Hz, C2), 89.9 (d, J = 14.2 Hz, C2″), 127.0 (d, J = 11.5 Hz, 2C, $Ph^{A/D}$-*meta*), 127.1 (d, J = 12.3 Hz, 2C, $Ph^{A/D}$-*meta*), 127.7 (d, J = 11.4 Hz, 2C, Ph^C-*meta*), 128.8 (d, J = 10.0 Hz, 2C, Ph^B-*meta*), 129.92 ($Ph^{A/C/D}$-*para*), 129.94 ($Ph^{A/C/D}$-*para*), 131.0 (d, J = 2.3 Hz, $Ph^{B/C/D}$-*para*), 131.1 (d, J = 3.0 Hz, $Ph^{B/C/D}$-*para*), 132.0 (d, J = 10.0 Hz, 2C, $Ph^{A/C}$-*ortho*), 133.3 (d, J = 129.6 Hz, Ph^D-*ipso*), 133.5 (d, J = 9.2 Hz, 2C, Ph^B-*ortho*), 134.8 (d, J = 13.1 Hz, 2C, Ph^D-*ortho*), 127.4, 128.5, 129.0, 129.7, 130.6, and 132.1 Ph^A-*ipso*, Ph^B-*ipso*, Ph^C-*ipso* not distinguishable. C1″ not observed. $^{31}P\{^1H\}$ NMR (162 MHz, CD_2Cl_2): δ 28.5 (Fc-PPh_2), 48.1 (CH_3CH-PPh_2). HR-MS (ESI, MeOH/MeCN): m/z $[M - Cl]^+$ calcd 907.0027 for $C_{46}H_{52}ClFe_2P_2Pd$, found 907.0050; $[\alpha]^{20}_{\lambda}$ (nm): +636 (589) (c 0.115, $CHCl_3$).

Hydrogenations. The substrate (1 mmol) was dissolved under argon in a degassed solvent (2.5 mL). The catalyst was formed in situ by stirring a mixture of the ligand and metal precursor in a degassed solvent (2.5 mL) for 30 min at room temperature The catalyst and the

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substrate solutions were transferred through a stainless steel capillary into either a glass or a steel autoclave. The argon gas was then replaced by hydrogen gas (3−5 cycles) and the pressure was set. After completion of the reaction, the reaction mixture was filtered through a plug of silica. Conversions and ee values of the product were determined by either gas chromatography or HPLC. In an effort to ensure consistency and reproducibility, all hydrogenations were carried out at least twice.

The following reaction conditions and methods were applied. MAC: MAC (219.2 mg, 1 mmol); $[Rh(NBD)_2][BF_4]$ + 1.1 equiv of ligand; S/C = 25; solvent MeOH (5 mL); $p(H_2)$ 1 bar; 20 °C; reaction time 16 h. Analysis data for MAC: GC, column PERMABOND-L-Chirasil-Val (25 m); 160 °C isothermal; MAC 11.1 min, *R* 25.4 min, *S* 28.6 min. MAA: MAA (143.1 mg, 1 mmol); $[Rh(NBD)_2][BF_4]$ + 1.1 equiv of ligand; S/C = 25; solvent MeOH (5 mL); $p(H_2)$ 1 bar; 20 °C; reaction time 16 h. Analysis data for MAA: GC, column PERMABOND-L-Chirasil-Val (25 m); 110 °C isothermal; MAA 5.3 min, *R* 8.8 min, *S* 10.9 min. DMI: DMI (158.2 mg, 1 mmol); $[Rh(NBD)_2][BF_4]$ + 1.1 equiv of ligand; S/C = 25; solvent MeOH (5 mL); $p(H_2)$ 1 bar; 20 °C; reaction time 16 h. Analysis data for DMI: GC, column LIPODEX-E (50 m); 85 °C isothermal; DMI 46.2 min, *S* 29.5 min, *R* 30.7 min. MCA: MCA (162.2 mg, 1 mmol); $[Rh(NBD)_2][BF_4]$ + 1.1 equiv of ligand; S/C = 25; solvent MeOH (5 mL); $p(H_2)$ 20 bar; 20 °C; reaction time 20 h. Workup for MCA: after removal of the solvent under reduced pressure, the crude product was dissolved in DCM and extracted with NaOH (2 M). The organic phase was discarded. The aqueous phase was made acidic by addition of aqueous HCl (to pH 1) and was extracted twice with DCM (2 × 25 mL). The combined organic phases were washed with brine and dried over $MgSO_4$, and the solvent was removed under reduced pressure. Subsequently, the residue was transformed into the corresponding methyl ester. The residue was dissolved in MeOH, and diazomethane in Et_2O was added until the solution turned pale yellow and remained this color. After the mixture was stirred for 20 min at room temperature, the solvent was removed carefully under reduced pressure and the residue was filtered through a short plug of silica, which had been wetted with MeOH. Analysis data for MCA: HPLC, column Daicel, Chiraldex OB-H; temperature 25 °C; eluent hexane/*i*PrOH 97:3; flow rate 0.5 mL/min; detector DAD; Sig 230 nm; substrate 15.8 min, *R* 10.7 min, *S* = 11.6 min. PCA: PCA (224.2 mg, 1 mmol); $[Rh(NBD)_2][BF_4]$ + 1.1 equiv of ligand; S/C = 100; solvent MeOH (5 mL); $p(H_2)$ 50 bar; 20 °C; reaction time 19 h; esterification to the methyl ester see MCA. Analysis data for MCA: HPLC, column Daicel, Chiraldex OD-H; temperature 25 °C, eluent hexane/*i*PrOH 97:3, flow rate 0.5 mL/min; detector DAD; Sig 230 nm; substrate 20 min, *R* 18 min, *S* 18.7 min. IPCA-D: IPCA-D (308.4 mg, 1 mmol); $[Rh(NBD)_2][BF_4]$ + 1.1 equiv of ligand; S/C = 25; solvent MeOH (5 mL); $p(H_2)$ 50 bar; 20 °C; reaction time 20 h. Analysis data for IPCA-D: HPLC, column Chiralpak IC; temperature 25 °C; solvent heptane/EtOH/TFA = 90/10/0.1; flow rate 1.0 mL/min; detector DAD; Sig 230 nm; IPCA-D 5.6 min, *S* 8.7 min, *R* 10.3 min. ACA: ACA (253.3 mg, 2.53 mmol); $[RuI_2(p\text{-cymene})]_2$ + 1.1 equiv of ligand; S/C = 500; solvent MeOH (10 mL); additive HCl(aq) (240 μL, 1 N); $p(H_2)$ 80 bar; 80 °C; reaction time 17 h. Analysis data for ACA: GC, column PERMABOND-L-Chirasil-Val (25 m); 88 °C isothermal; ACA 2.0 min, *R* 8.3 min, *S* 9.1 min. EOP: EOP (144.2 mg, 1 mmol); $[RuI_2(p\text{-cymene})]_2$ + 1.1 equiv of ligand; S/C = 100; solvent EtOH (10 mL); additive HCl(aq) (47.4 μL, 1 N); $p(H_2)$ 80 bar; 80 °C; reaction time 16 h. Formation of trifluoroacetate derivative: after removing the solvent and drying under reduced pressure, to the remaining residue was added trifluoroacetic anhydride (2 mL). After stirring for 20 min, the excess trifluoroacetic anhydride was removed by blowing argon over the solution and the residue was filtered through a short plug of silica, which had been wetted with MeOH. Analysis data for EOP: GC, column LIPODEX-E (50 m); 80 °C isothermal; substrate 15.6 min; *R* 26.6 min; *S* 29.7 min.

X-ray Crystallography. Single crystal X-ray diffraction data for (R,S_p,S_p)-**2**·2BH_3, (R,S_p,S_p)-**6**, and (R,S_p,S_p)-**7** were collected on a Bruker Kappa APEX-2 CCD diffractometer at T = 100 K using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) and φ- and ω-scan fine-sliced frames covering complete Ewald spheres with θ_{max} = 30°. The data were integrated with the program SAINT, and corrections for absorption and $\lambda/2$ effects were applied with the program SADABS.[10a] The structures were solved by direct methods with the program SHELXS97, and refinement on F^2 was carried out with the program SHELXL97.[10b] Non-hydrogen atoms were refined anisotropically. All H atoms were placed in calculated positions and thereafter refined as riding. The absolute structures of all compounds could be unambiguously determined by anomalous dispersion effects and the Flack absolute structure parameter. Important crystallographic data are provided below.

(R,S_p,S_p)-**2**·2BH_3: compound crystallized as a solvate with a mixture of disordered CH_2Cl_2 and ethyl acetate in an estimated 60/40 ratio. The chemical formula was idealized to (R,S_p,S_p)-**2**·2BH_3·CH_2Cl_2, $C_{47}H_{48}B_2Cl_2Fe_2P_2$, M_r = 879.01, orange prism, 0.60 × 0.07 × 0.05 mm, monoclinic, space group $P2_1$ (No. 4), a = 11.3173(3) Å, b = 9.5521(3) Å, c = 20.2125(5) Å, β = 93.674(2)°, V = 2180.56(10) Å^3, Z = 2, μ = 0.893 mm^{-1}, ρ_{calcd} = 1.339 g cm^{-3}, 55105 reflections collected and merged to 12614 independent data (R_{int} = 0.039); after squeezing the disordered solvent with program PLATON[10c] final *R* indices (all data) were R1 = 0.0342, wR2 = 0.0679, 472 parameters, Flack absolute structure parameter −0.020(6), excursions in difference Fourier map between −0.23 and 0.43 e Å^{-3}.

(R,S_p,S_p)-**6**: $C_{36}H_{36}Fe_2NP$, M_r = 625.33, orange block from ethyl acetate, 0.28 × 0.16 × 0.10 mm, monoclinic, space group $P2_1$ (No. 4), a = 7.3616(3) Å, b = 18.1714(7) Å, c = 22.4087(9) Å, β = 99.319(2)°, V = 2958.1(2) Å^3, Z = 4 (Z' = 2), μ = 1.061 mm^{-1}, ρ_{calcd} = 1.404 g cm^{-3}, 70046 reflections collected and merged to 17172 independent data (R_{int} = 0.090); final *R* indices (all data) were R1 = 0.0472, wR2 = 0.0847, 727 parameters, Flack absolute structure parameter 0.017(8), excursions in difference Fourier map between −0.52 and 0.73 e Å^{-3}.

(R,S_p,S_p)-**7**: $C_{36}H_{36}Fe_2NOP$, M_r = 641.33, orange block from ethyl acetate, 0.45 × 0.42 × 0.32 mm, monoclinic, space group $P2_1$ (No. 4), a = 10.4728(4) Å, b = 8.1019(3) Å, c = 17.7567(6) Å, β = 100.508(2)°, V = 1481.38(9) Å^3, Z = 2, μ = 1.064 mm^{-1}, ρ_{calcd} = 1.438 g cm^{-3}, 32255 reflections collected and merged to 8638 independent data (R_{int} = 0.028); final *R* indices (all data) were R1 = 0.0197, wR2 = 0.0516, 373 parameters, Flack absolute structure parameter −0.004(5), excursions in difference Fourier map between −0.26 and 0.37 e Å^{-3}.

■ ASSOCIATED CONTENT

Supporting Information

Figures, tables with geometric data, and CIF files for the crystal structures of (R,S_p,S_p)-**2**·2BH_3 (R,S_p,S_p)-**6**, and (R,S_p,S_p)-**7** text and figures with information on a comparison of the structural features of complexes [$PdCl_2$(SL-W002-1)], [$PdCl_2$((R,S_p,R_p)-**2**)], and [$PdCl_2$((R,S_p,S_p)-**2**)]. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Sturm, T.; Weissensteiner, W.; Spindler, F. *Adv. Synth. Catal.* **2003**, *345*, 160−164. (b) Wang, Y.; Sturm, T.; Steurer, M.; Arion, V. B.; Mereiter, K.; Spindler, F.; Weissensteiner, W. *Organometallics* **2008**, *27*, 1119−1127.

(2) Blaser, H.-U.; Lotz, M. In *Asymmetric Catalysis*; Dai, L.-X., Hou, X.-L., Eds.; Wiley-VCH: Weinheim, Germany, 2010; pp 73−95.
(3) Zirakzadeh, A.; Groß, M. A.; Wang, Y.; Mereiter, K.; Spindler, F.; Weissensteiner, W. *Organometallics* **2013**, *32*, 1075−1084.
(4) (a) Negishi, E.-I.; Hu, Q.; Huang, Z.; Qian, M.; Wang, G. *Aldrichim. Acta* **2005**, *38*, 71. (b) Negishi, E.-I.; Zeng, X.; Tan, Z.; Qian, M.; Hu, Q.; Huang, Z. In *Metal-Catalyzed Cross-Coupling Reactions*; De Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, Germany, 2004; Vol. *2*, pp 815−889.
(5) (a) Butler, I. R. *Inorg. Chem. Commun.* **2008**, *11*, 15−19. (b) Dayaker, G.; Sreeshailam, A.; Chevallier, F.; Roisnel, T.; Krishna, P. R.; Mongin, F. *Chem. Commun.* **2010**, *46*, 2862−2864.
(6) For an X-ray diffraction study of (R,S_p,S_p)-**5**·BH_3 see: Wang, Y.; Zirakzadeh, A.; Weissensteiner, W.; Mereiter, K. *Acta Crystallogr., Sect. E* **2011**, *67*, m1806−m1807.
(7) Coumbe, T.; Lawrence, N. J.; Muhammad, F. *Tetrahedron Lett.* **1994**, *35*, 625−628.
(8) (a) Boogers, J. A. F.; Sartor, D.; Felfer, U.; Kotthaus, M.; Steinbauer, G.; Dielemans, B.; Lefort, L.; de Vries, A. H. M.; de Vries, J. G. In *Asymmetric catalysis on industrial scale*; Blaser, H.-U., Federsel, H.-J., Eds.; Wiley-VCH: Weinheim, Germany, 2010; pp 127−150. (b) Woodmansee, D. H.; Müller, M.-A.; Tröndlin, L.; Hörmann, E.; Pfaltz, A. *Chem. Eur. J.* **2012**, *18*, 13780−13786. (c) Li, S.; Zhu, S.-F.; Zhang, C.-M.; Song, S.; Zhou, Q.-L. *J. Am. Chem. Soc.* **2008**, *130*, 8584−8585. (d) Andrushko, N.; Andrushko, V.; Thyrann, T.; König, G.; Börner, A. *Tetrahedron Lett.* **2008**, *49*, 5980−5982.
(9) For additional asymmetric hydrogenation results for 2-methylcinnamic acid see: (a) Li, J.-Q.; Quan, X.; Andersson, P. G. *Chem. Eur. J.* **2012**, *18*, 10609−10616. (b) Zhu, S.-F.; Yu, Y.-B.; Li, S.; Wang, L.-X.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2012**, *51*, 8872−8875.
(10) (a) *APEX2, SAINT, and SADABS*; Bruker AXS Inc., Madison, WI, 2012. (b) Sheldrick, G. M. *Acta Crystallogr., Sect. A* **2008**, *A64*, 112−122. (c) Spek, A. L. *J. Appl. Crystallogr.* **2003**, *36*, 7−13.