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Synthesis and Application of Arylmonophosphinoferrocene Ligands: Ultrafast Asymmetric Hydrosilylation of Styrene†

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A short and efficient synthetic route to a novel class of atropisomeric and planar chiral 2-aryl-1-diphenylphosphanylferrocene ligands is presented. The modular design of the ligands allows a synthetic approach in which both the aromatic moiety and the phosphino substituent can be varied easily. This permits fine-tuning of steric and electronic properties. The ligands have been tested in the asymmetric hydrosilylation of styrene where enantioselectivities up to 90% are obtained. Optimization of the palladium-to-ligand ratio resulted in hitherto unparalleled turnover frequencies (TOF) exceeding 180 000 h^{-1}. The absolute stereochemistry of the ligands was determined from an X-ray structure. 2D NMR experiments in combination with ab initio calculations were used to assign the conformation of the atropisomeric biarylic scaffold.

Introduction

Asymmetric catalysis is a continuously expanding field where the development of novel chiral ligands is essential for ensuring an elaboration of the nearly unendless possibilities that lie within this area. The ultimate goal within this field seems to be construction of a universal ligand, i.e., one that is broadly applicable and substrate independent. However, a consideration of the diversity of the ligands unveiled so far and of the reactions in which they are effective suggests this task to be unrealizable. Thus, the focus of research is shifted toward design of modular ligand classes that are easily synthesized and modified to meet the demands of a particular substrate and reaction.

Among the selection of chiral ligands, optically pure tertiary phosphines have emerged as extremely versatile due to their outstanding ability to form highly active and selective complexes with late-transition metals in particular. Hence, efficient catalysts have been achieved for a large number of reactions where the products are provided in excellent yields and with high enantiomeric excess. Since the development of the DIOP ligand by Kagan and co-workers, the design of chiral phosphines has for a long period been dominated by chelating bisphosphine derivatives possessing a chiral scaffold.[1] Prominent examples are the BINAP,[2] ferrocene,[3] Trost,[4] and Duphos[5] ligands (Figure 1).

In spite of the enormous potential of bidentate phosphines, the past decades of research have revealed some limitations imparted in this ligand type. The problems arise in reactions where a vacant site on the metal is needed for substrate coordination in the course of the catalytic cycle. Due to the strong preference for bidentate coordination, bisphosphines are in some instances unable to provide the required coordination site, and hence, they either inhibit the reaction or give low turnover.[6]

Consequently, chiral monophosphine ligands are highly important since they show activity and selectivity in catalytic reactions where the bidentate phosphine-based ligands have failed. Recent examples have also shown that easily accessible monophosphine derivatives can display reactivity and selectivity comparable to or exceeding bidentate ligands.[7] A distinguished reaction exemplifying the significance of monophosphines is the palladium-catalyzed asymmetric hydrosilylation of alkenes. Herein, palladium−bisphosphine complexes display no catalytic activity, whereas monophosphine ligands

† Synthesis and Application of Arylferrocenyl (Pseudo-Biarylic) Complexes. 2. For part 1, see ref 13a.

(1) (a) Dand, T. P.; Kagan, H. B. *Chem. Commun.* **1971**, 481. (b) Kagan, H. B.; Dang, T. P. *J. Am. Chem. Soc.* **1972**, *94*, 6429.

(2) For the first contribution, see: (a) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932. For an account, see e.g.: (b) Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345.

(3) For important contributions to this area, see: (a) Marquarding, D.; Klusacek, H.; Gokel, G.; Hoffmann, P.; Ugi, I. *J. Am. Chem. Soc.* **1970**, *92*, 5389. (b) Hayashi, T.; Yamamoto, K.; Kumada, M. *Tetrahedron Lett.* **1974**, *15*, 4405. (c) Hayashi, T.; Mise, T.; Fukushima, M.; Kagotani, M.; Nagashima, M.; Hamada, Y.; Matsumoto, A.; Kawakami, S.; Konishi, M.; Yamamoto, K.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1138. (d) Togni, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Landert, H.; Tijani, A. *J. Am. Chem. Soc.* **1994**, *116*, 4062. For reviews and accounts, see e.g.: (e) Hayashi, T.; Kumada, M. *Acc. Chem. Res.* **1982**, *15*, 395. (f) Hayashi, T. *Pure Appl. Chem.* **1988**, *60*, 7. (g) *Ferrocenes. Homogeneous Catalysis, Organic Synthesis, Materials Science*; Togni, A., Hayashi, T., Eds.; VCH: Weinheim, Germany, 1995. (i) Sawamura, M.; Ito, Y. *Chem. Rev.* **1992**, *92*, 857.

(4) For early contributions, see: (a) Trost, B. M.; Van Vranken, D. L. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 228. (b) Trost, B. M.; Van Vranken, D. L.; Bingel, C. *J. Am. Chem. Soc.* **1992**, *114*, 9327. For overviews, see: (c) Trost, B. M. *Acc. Chem. Res.* **1996**, *29*, 355. (d) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395.

(5) For early contributions, see: (a) Burk, M. J.; Feaster, J. E.; Harlow, R. L. *Organometallics* **1990**, *9*, 2653. (b) Burk, M. J.; Feaster, J. E.; Harlow, R. L. *Tetrahedron: Asymmetry* **1991**, *2*, 569. (c) Burk, M. J.; Harlow, R. L. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1462. (d) Burk, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 8518. For a historical review and an account, see: (e) Burk, M. J. *ChemTracts: Org. Chem.* **1998**, *11*, 787. (f) Burk, M. J. *Acc. Chem. Res.* **2000**, *33*, 363.

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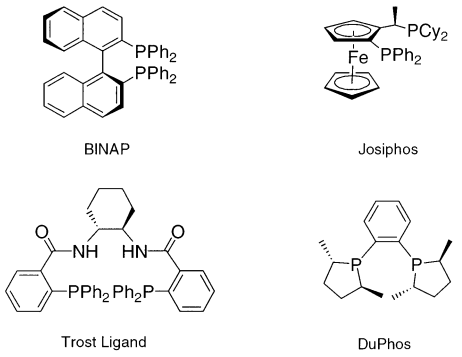


FIGURE 1. Bisphosphine ligands.

create active palladium species able to afford the product in high yield.[6a]

Despite the versatility of chiral monophosphines, the reports on novel ligands of this types are still limited. The most efficient chiral monophosphine ligands reported up to this point are based on either a planar chiral ferrocene scaffold or an axially chiral biaryl scaffold. The planar chiral ferrocenyl monophosphines developed by Kumada and Hayashi[4,8] stems from stereoselective derivatization of Ugi's amine[4a] and hence contain a chiral center adjacent to the 1,2-disubstituted ferrocene. The original dimethyl amino substituent from Ugi's amine can be replaced by a variety of heteroatomic nucleophiles or removed entirely. Consequently, a variety of ligands with different coordinating ability and steric requirements can be attained via this synthetic strategy (Figure 2).

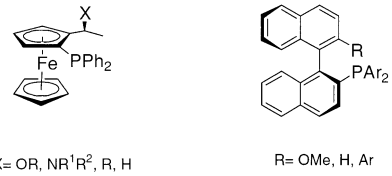


FIGURE 2. Monophosphine ligands.

Among axially chiral monophosphines, the MOP ligands developed by Hayashi and co-workers are outstanding in terms of reactivity and enantioselectivity.[9] Undoubtedly, the axially chiral binaphthylic scaffold found in, e.g.,

(6) Some of the most prominent examples of this are as follows: (a) The asymmetric hydrosilylation: Uozumi, Y.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 9887. (b) The asymmetric hydrovinylation: RajanBabu, T. V.; Nomura, N.; Jin, J.; Radetich, B.; Park, H.; Nandi, M. *Chem. Eur. J.* **1999**, *5*, 1963. (c) The asymmetric arylation of imines: Hayashi, T.; Ishigedani, M. *J. Am. Chem. Soc.* **2000**, *122*, 976. (d) The asymmetric Grignard cross-coupling: Hayashi, T.; Hayashizaki, K., Kiyoi, T.; Ito, J. *J. Am. Chem. Soc.* **1988**, *110*, 8153. See also: (e) Matsumoto, Y.; Naito, M.; Uozumi, Y.; Hayashi, T. *Chem. Commun.* **1993**, 1468. (f) Tsuji, Y.; Kusui, T.; Kojima, T.; Sugiura, Y.; Yamada, N.; Tanaka, S.; Ebihara, M.; Kawamura, T. *Organometallics* **1998**, *17*, 4835. (g) Imada, Y.; Fujii, M.; Kubota, Y.; Murahashi, S.-I. *Tetrahedron Lett.* **1997**, *38*, 8227. (h) Stará, I. G.; Stary, I.; Kollárovic, A.; Teply, F.; Vyskocil, S.; Saman, D. *Tetrahedron Lett.* **1999**, *40*, 1993. (i) Sato, Y.; Nishiyama, T.; Mori, M. *J. Org. Chem.* **1994**, *59*, 6133. (j) Oppolzer, W.; Kuo, D. L.; Hutzinger, M. W.; Léger, R.; Durand, J.-O.; Leslie, C. *Tetrahedron Lett.* **1997**, *38*, 6213. (k) Hanzawa, Y.; Tabuchi, N.; Saito, K.; Noguchi, S.; Taguchi, T. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 2395. (l) Hayashi, T. *J. Organomet. Chem.* **2002**, *653* (1−2), 41. (m) Han, J. W.; Tokunaga, N.; Hayashi, T. *Synlett* **2002**, 871. (n) For the asymmetric arylation of aldehydes, see: Sakai, M.; Ueda, M.; Miyaura, N. *Angew. Chem., Int. Ed.* **1998**, *37*, 3279.

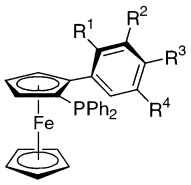
(7) For examples where monophosphines give higher selectivity than the usual bisphosphines, see e.g.: (a) Feringa, B. L.; Pineschi, M.; Arnold, L. A.; Imbos, R.; de Vries, A. H. M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2620. For examples where monophosphines give similar selectivities as bisphosphines, see e.g.: (b) Reetz, M. T.; Mehler, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 3889 (c) Kitayama, K.; Uozumi, Y.; Hayashi, T. *Chem. Commun.* **1995**, 1533. (d) Tye, H.; Smyth, D.; Eldred, C.; Wills, M. *Chem. Commun.* **1997**, 1053. (e) Graf, C. D.; Malan, C.; Harms, K.; Knochel, P. *J. Org. Chem.* **1999**, *64*, 5581. (f) Zhu, G.; Chen, Z.; Jiang, Q.; Xiao, D.; Cao P.; Zhang, X. *J. Am. Chem. Soc.* **1997**, *119*, 3836. (g) Bartels, B.; Helmchen, G. *Chem. Commun.* **1999**, 741. For examples where monophosphines display superior reactivity, see e.g.: (h) Old, D. V.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 9722. (i) Wolfe, J. P.; Buchwald, S. L. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 2413. (j) Aranyos, A.; Old, D. W.; Kiyomori, A.; Wolfe, J. P.; Sadighi, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 4369. (k) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550. (l) Fox, J. M.; Huang, X.; Chieffi, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 1360.

(8) (a) Hayashi, T.; Tajika, M.; Tamao, K.; Kumada, M. *J. Am. Chem. Soc.* **1976**, *98*, 3718. (b) Hayashi, T.; Tamao, K.; Katsuro, Y.; Nakae, I.; Kumada, M. *Tetrahedron Lett.* **1980**, *21*, 1871. (c) Hayashi, T.; Konishi, M.; Hioki, T.; Kumada, M.; Ratajczak, A.; Niedbala, H. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3615. (d) Hayashi, T.; Konishi, M.; Fukushima, M.; Mise, T.; Kagotani, M.; Tajika, M.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 180. (e) Hayashi, T.; Konishi, M.; Ito, H.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4962. (f) Hayashi, T.; Hagihara, T.; Katsuro, Y.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 363. (g) Hayashi, T.; Kabeta, K.; Yamamoto, T.; Tamao, K.; Kumada, M. *Tetrahedron Lett.* **1983**, *24*, 5661. (h) Hayashi, T.; Kabeta, K. *Tetrahedron Lett.* **1985**, *26*, 3023. (i) Hayashi, T.; Konishi, M.; Okamoto, Y.; Kabeta, K.; Kumada, M. *J. Org. Chem.* **1986**, *51*, 3772. (j) Hayashi, T.; Hayashizaki, K.; Kiyoi, T.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 8153. (k) Hayashi, T.; Matsumoto, Y.; Morikawa, I.; Ito, Y. *Tetrahedron*: *Asymmetry* **1990**, *1*, 151. (l) Han, J. W.; Tokunaga, N.; Hayashi, T. *J. Am. Chem. Soc.* **2001**, *123*, 12915.

(9) For the first contribution, see: (a) Uozumi, Y.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 9887. For later papers on the use of MOP-ligands, see e.g.: (b) Uozumi, Y.; Tanahashi, A.; Lee, S.-Y.; Hayashi, T. *J. Org. Chem.* **1993**, *58*, 1945. (c) Uozumi, Y.; Suzuki, N.; Ogiwara, A.; Hayashi, T. *Tetrahedron* **1994**, *50*, 4293. (d) Hayashi, T.; Niizuma, S.; Kamikawa, T.; Suzuki, N.; Uozumi, Y. *J. Am. Chem. Soc.* **1995**, *117*, 9101. (e) Uozumi, Y.; Kitayama, K.; Hayashi, T.; Yanagi, K.; Fukuyo, E. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 713. (f) Hayashi, T.; Iwamura, H.; Naito, M.; Matsumoto, Y.; Uozumi, Y.; Miki, M.; Yanagi, K. *J. Am. Chem. Soc.* **1994**, *116*, 775. (g) Uozumi, Y.; Lee, S.-Y.; Hayashi, T. *Tetrahedron Lett.* **1992**, *33*, 7185. (h) Uozumi, Y.; Hayashi, T. *Tetrahedron Lett.***1993**, *34*, 2335. (i) Kitayama, K.; Uozumi, Y.; Hayashi, T. *J. Chem. Soc., Chem. Commun.* **1995**, 1533. (j) Kitayama, K.; Tsuji, H.; Uozumi, Y.; Hayashi, T. *Tetrahedron Lett.* **1996**, *37*, 4169. (k) Hayashi, T.; Iwamura, H.; Uozumi, Y. *Tetrahedron Lett.* **1994**, *35*, 4813. (l) Hayashi, T.; Kawatsura, M.; Iwamura, H.; Yamaura, Y.; Uozumi, Y. *J. Chem. Soc., Chem. Commun.* **1996**, 1767. (m) Kawatsura, M.; Uozumi, Y.; Ogasawara, M.; Hayashi, T. *Tetrahedron* **2000**, *56*, 2247. (n) Hayashi, T.; Kawatsura, M.; Uozumi, Y. *Chem. Commun.* **1997**, 561. (o) Hayashi, T.; Kawatsura, M.; Uozumi, Y. *J. Am. Chem. Soc.* **1998**, *120*, 1681. (p) Matsumoto, Y.; Naito, M.; Hayashi, T. *Organometallics* **1992**, *11*, 2732. (q) Matsumoto, Y.; Naito, M.; Uozumi, Y.; Hayashi, T. *J. Chem. Soc., Chem. Commun.* **1993**, 1468. (r) Tsuji, Y.; Kusui, T.; Kojima, T.; Sugiura, Y.; Yamada, N.; Tanaka, S.; Ebihara, M.; Kawamura, T. *Organometallics* **1998**, *17*, 4835. (s) Imada, Y.; Fujii, M.; Kubota, Y.; Murahashi, S.-I. *Tetrahedron Lett.* **1997**, *38*, 8227. (t) Oppolzer, W.; Kuo, D. L.; Hutzinger, M. W.; Le'ger, R.; Durand, J.-O.; Leslie, C. *Tetrahedron Lett.* **1997**, *38*, 6213. (u) Hanzawa, Y.; Tabuchi, N.; Saito, K.; Noguchi, S.; Taguchi, T. *Angew. Chem., Int. Ed.* **1999**, *38*, 2395. (v) RajanBabu, T. V.; Nomura, N.; Jin, J.; Radetich, B.; Park, H.; Nandi, M. *Chem. Eur. J.* **1999**, *5*, 1963. (w) Sato, Y.; Nishiyama, T.; Mori, M. *J. Org. Chem.* **1994**, *59*, 6133. (x) Stara', I. G.; Stary, I.; Kolla'rovic, A.; Teply, F.; Vyskocil, S.; Saman, D. *Tetrahedron Lett.* **1999**, *40*, 1993. (y) Sakai, M.; Ueda, M.; Miyaura, N. *Angew. Chem., Int. Ed.***1998**, *37*, 3279. (z) Hayashi, T.; Ishigedani, M. *J. Am. Chem. Soc.* **2000**, *122*, 976. (a′) Hayashi, T.; Hirate, S.; Kitayama, K.; Tsuji, H.; Torii, A.; Uozumi, Y. *Chem. Lett.* **2000**, 1272. (b′) Hayashi, T. *Catal. Today* **2000**, *62*, 3. (c′) Hayashi, T.; Hirate, S.; Kitayama, K.; Tsuji, H.; Torii, A.; Uozumi, Y. *J. Org. Chem.* **2001**, *66*, 1441. (d′) Hayashi, T.; Han, J. W.; Takeda, A.; Tang, J.; Nohmi, K.; Mukaide, K.; Tsuji, H.; Uozumi, Y. *Adv. Synth. Catal.* **2001**, *343* (3), 279. (e′) Han, J. W.; Hayashi, T. *Chem. Lett.* **2001**, 976. (g′) Shimada, T.; Mukaise, K.; Shinohara, A.; Han, J. W.; Hayashi, T. *J. Am. Chem. Soc.* **2002**, *124*, 1584. (h′) Han, J. W.; Hayashi, T. *Tetrahedron*: *Asymmetry* **2002**, *13*, 325. For review and accounts on the use of MOP ligands, see: (a) Hayashi, T. *Acta Chem. Scand.* **1996**, *50*, 259. (b) Hayashi, T. *Acc. Chem. Res.* **2000**, *33*, 354.

BINOL,[10] BINAP, and MOP ligands creates chiral surroundings that are highly efficient exemplified by their application in a range of catalytic reactions covering most of the field of asymmetric synthesis.[11] The elaboration of this ligand class from diol over bisphosphine to monophosphine elegantly exemplifies how modifications on the chiral scaffold can lead to ligands that meet the demands of different reaction types. Within the MOP ligands, variation of the substituent in the 2′-position and on the phosphorus atom demonstrates a spectacular fine-tuning of the ligands toward a variety of substrates in the palladium-catalyzed asymmetric hydrosilylation[9a′−h′] (Figure 2).

Herein, we wish to present a class of monophosphine ligands **1** containing a novel pseudo-biarylic scaffold, which is constituted of an arylferrocene framework (Figure 3). The phosphino moiety is attached to the ferrocene adjacent to the aryl group rendering the ligands planar chiral. Depending on the substitution pattern on the aryl group restricted rotation around the arylferrocene bond can lead to atropisomery (pseudoaxial chirality), consequently adding to the steric diversity of the ligands.[12]



1

FIGURE 3. General structure of (*S*)-aryl-MOPF ligands.

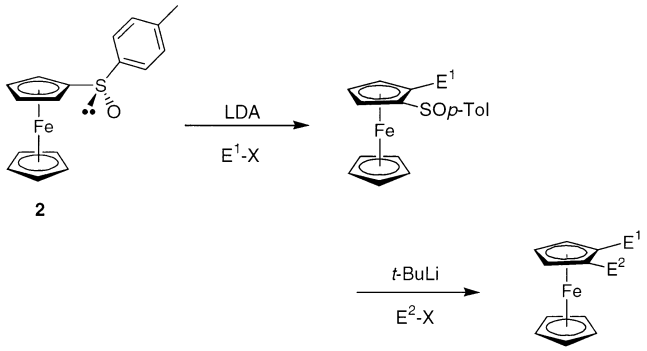
Although the efficiency of both planar chiral and axially chiral ligands is well established, the combination of those two systems is still unexplored.[13] We envisioned that having an aryl substituent directly linked to a monophosphinoferrocene could lead to ligands that display reactivity and selectivity similar to other biarylic systems. However, opposed to axially chiral binaphthylic derivatives, the chirality of the ligands presented here does not rely on restricted rotation around the biarylic bond and virtually any aromatic group can be introduced, retaining the inherent planar chirality of the 1,2-disubstituted ferrocene. Consequently, derivatization in the pseudo-biarylic system can easily be accomplished. The short synthetic routes described facilitate preparation of arrays of ligands, rendering this approach highly useful for fine-tuning reactivity and selectivity. Furthermore, it should be noted that the modular design imparts the possibility of constructing families of ligands with varying coordination number and atoms in two to three steps, e.g., P−N, P−O, and P−P derivatives.

Here, the methodology has been applied to the synthesis of the aryl-monophosphinoferrocene (MOPF) ligands. Within this particular ligand array, the steric and electronic properties of the aryl moiety have been varied. The importance of these modifications has been examined in the palladium-catalyzed asymmetric hydrosilylation of styrene. The ligands are shown to be extremely efficient with respect to rate and afford enantioselectivities comparable to the best results previously reported.

Ligand Synthesis

The modular approach to the MOPF ligands requires a common ferrocene scaffold that by simple operations can be modified into an array of different ligands. Additionally, the chiral auxiliary on the ferrocene should be removed entirely to allow for direct attachment of both the aromatic moiety and the phosphino group onto the ferrocene. A suitable precursor for this purpose was found in the easily accessible ferrocenyl sulfoxide **2**.[14] By diastereoselective ortho-lithation of **2** and concomitant *tert*-butyllithium-mediated sulfoxide cleavage, the optically pure arylferrocenylmonophosphines should be available in two steps (Scheme 1).

SCHEME 1



2

To construct the pseudo-biarylic system, we chose to focus on the Negishi cross-coupling. None of the aryl groups introduced in the reaction sequence are sensitive toward the rather basic reaction conditions present in this reaction. Furthermore, the Negishi cross-coupling does not require the synthesis of a precursor and the ferrocenyl sulfoxide can be used directly, hence lowering the number of synthetic steps. The initial attempts to synthesize the aryl-MOPF ligands involved the known intermediate **3** (Scheme 2).[14a] Treatment of this with *tert*-butyllithium removed the sulfoxide quantitatively, but all attempts to use the lithiated species in a Negishi cross-coupling failed and only the hydrolyzed cleavage product was isolated. Apparently, the steric bulk of the

(10) For early contributions, see: (a) Kyba, E. B.; Koga, K.; Sousa, L. R.; Siegel, M. G.; Cram, D. J. *J. Am. Chem. Soc.* **1973**, *95*, 2692. (b) Norori, R.; Tomino, I.; Tanimoto, Y. *J. Am. Chem. Soc.* **1979**, *101*, 3129. For overviews, see e.g.: (c) Pu, L. *Chem. Rev.* **1998**, *98*, 2405. (d) Rosini, C.; Franzini, L.; Raffaelli, A.; Salvadori, P. *Synthesis* **1992**, 503.

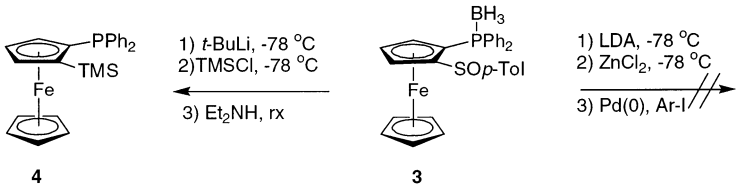
(11) *Asymmetric Synthesis*; Hayashi, T., Tomioka, K., Yonemitsu, O., Eds.; Gordon and Breach Science Publishers: Tokyo, 1998. See also refs 2, 9, and 10.

(12) The term axial chiral should preferably be avoided in this context since these compounds are not axial chiral but rather rotational diastereomers. Note that the two conformers of the fragment containing the naphthyl and ferrocene molecule with, e.g., the naphthyl group in an exo and endo position are not enantiomorphic, e.g., super imposable mirror images of each other.

(13) Part of this work has been communicated: (a) Pedersen, H. L.; Johannsen, M. *Chem. Commun.* **1999**, 2517. For the synthesis of another chiral arylferrocenyl derivative, see: (b) Bringmann, G.; Hinrichs, J.; Peters, K.; Peters, E.-V. *J. Org. Chem.* **2001**, *66*, 629.

(14) This ortho-lithiation chemistry was originally developed by Kagan et al.: (a) Riant, O.; Argourch, G.; Guillaneux, D.; Samuel, O.; Kagan, H. B. *J. Org. Chem.* **1998**, *63*, 3511. See also: (b) Hua, D. H.; Lagneau, N. M.; Chen, Y.; Robben, P. M.; Clapham, G.; Robinson, P. D. *J. Org. Chem.* **1996**, *61*, 4508.

SCHEME 2

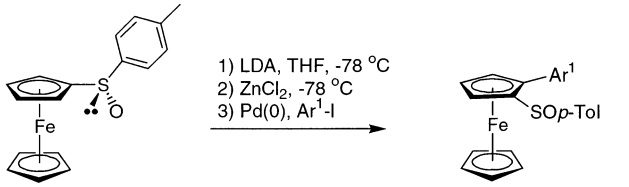


4 **3**

borane-protected diphenylphosphino group prevents trans-metalation to palladium. In one case, the anion was trapped with chlorotrimethylsilane giving, after removal of the borane protecting group, ligand **4**. Attempts to introduce more bulky silyl electrophiles at this stage were unsuccessful, confirming the reduced access to this position when situated adjacent to the sterically demanding borane adduct.

To overcome this obstacle, the order of events was reversed. First, the biarylic scaffold was constructed by a palladium-catalyzed Negishi cross-coupling between the metalated ferrocenyl sulfoxide and an aryl iodide. Successfully, a range of electron-rich and -poor aromatics could be introduced in high yields and with complete diastereo- and atroposelectivity (Table 1). No other diastereoisomer or rotamer could be detected according to ^{1}H NMR, indicating a diastereoselectivity of >98% (vide infra). Examination of different phosphine ligands for palladium revealed that 2-trifurylphosphine gave the highest yield in the coupling although the difference was not decisive.

TABLE 1. Diastereoselective Ortho-Lithiation−Negishi Arylation of (*S*)-2 Yielding (S_P,S_S)-5a−e



2

5a: Ar^1=Ph
5b: Ar^1=3,5-CF_3-C_6H_3
5c: Ar^1=*o*-MeO-C_6H_4
5d: Ar^1=*p*-MeO-C_6H_4
5e: Ar^1=1-Naphthyl

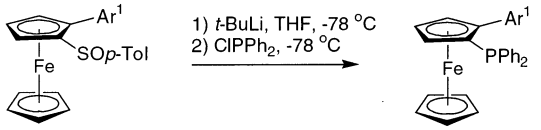
entry	product	stereochemistry of product[a]	reaction time/h	T[b]/°C	yield/%
1	**5a**	S_P,S_S	48	rt	77
2	**5b**	S_P,S_S	96	rt	60
3	**5c**	S_P,S_S	48	reflux	90
4	**5d**	S_P,S_S	96	rt	95
5	**5e**	S_P,S_S	96	rt	88

[a] The subscripts "P" and "S" designate the descriptor of planar chirality and the chirality at sulfur, respectively. [b] Ortho-lithiation and trans-metalation were carried out at −78 °C.

To complete the synthesis of the aryl-MOPF ligands, the phosphino group had to be introduced in the second step. Three approaches were evaluated. Direct entrapment of the ferrocenyl anion with chlorodiphenylphosphine would give immediate access to the desired product (Table 2). However, knowing that phosphines are extremely prone to oxidation, in situ protection with borane could be necessary to afford stable adducts that could be purified and then deprotected prior to use (Table 3). Finally, a third approach based on electrophilic addition of chloro diphenylphosphine oxide and reduction was examined (Table 4).

As seen in Table 2 (entries 1 and 2), chlorodiphenylphosphine reacted smoothly with the quantitatively formed lithiated ferrocenyl species, and using strictly anhydrous workup procedures the phosphines **1a** and **1b** could be isolated in good yields without oxidation to the corresponding phosphine oxide. Introduction of an *o*- or *p*-methoxy substituent on the aromatic moiety resulted in a more sensitive reaction with varying amounts of oxidized byproduct (Table 2, entries 3 and 4). Surprisingly, the reaction with **5e** was very prone to oxidation, and the corresponding phosphine oxide was the major product in all instances. On the basis of these results, it seems that the oxidation potential of the phosphino moiety in the aryl-MOPF ligands is strongly influenced by the electronic and steric properties of the aryl substituent on the ferrocene.

TABLE 2. Direct Synthesis of the Phosphines (*S*)-1a−d



5a: Ar^1=Ph
5b: Ar^1=3,5-CF_3-C_6H_3
5c: Ar^1=*o*-MeO-C_6H_4
5d: Ar^1=*p*-MeO-C_6H_4

1a: Ar^1=Ph
1b: Ar^1=3,5-CF_3-C_6H_3
1c: Ar^1=*o*-MeO-C_6H_4
1d: Ar^1=*p*-MeO-C_6H_4

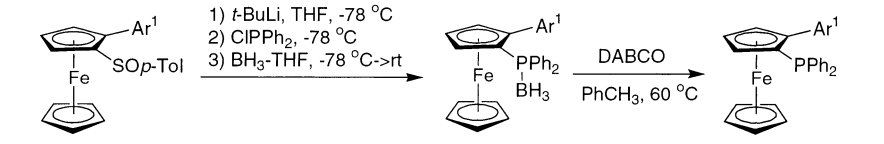
entry	sulfoxide	MOPF ligand	stereochemistry of ligand[a]	yield/%
1	**5a**	**1a**	*S*	77
2	**5b**	**1b**	*S*	70
3	**5c**	**1c**	*S*	34−76[b]
4	**5d**	**1d**	*S*	38

[a] The stereochemistry is based on an X-ray structure of **1a** and by chemical correlation with **2** (vide infra). [b] The yield is dependent on the amount of phosphine oxide formed.

Next, the approach where the phosphines were protected in situ as the borane adducts was examined. This procedure turned out to be the most efficient for the synthesis of most of the ligands. After the in situ protection, the derivatives **6b**−**e** could be isolated in good yields (Table 3).

Interestingly, the borane group in adduct **6b** was relatively labile due to the moderately more electron poor phosphino moiety. The borane group was partly released during aqueous work up of **6b** affording 44% of the desired product in combination with 32% of the deborated and oxidized derivative (Table 3, entry 1). More electron rich aryl groups on the ferrocene led to good yields of the desired products (Table 3, entries 2−4). After facile deprotection with DABCO, the pure phosphines could be

TABLE 3. Synthesis of MOPF Ligands 1b−e via the Borane Adducts



5b: Ar^1=3,5-CF_3-C_6H_3
5c: Ar^1=*o*-MeO-C_6H_4
5d: Ar^1=*p*-MeO-C_6H_4
5e: Ar^1=1-Naphthyl

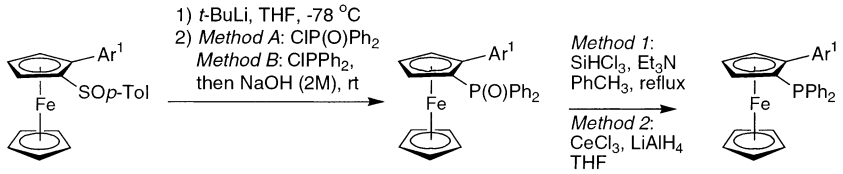
6b: Ar^1=3,5-CF_3-C_6H_3
6c: Ar^1=*o*-MeO-C_6H_4
6d: Ar^1=*p*-MeO-C_6H_4
6e: Ar^1=1-Naphthyl

1b: Ar^1=3,5-CF_3-C_6H_3
1c: Ar^1=*o*-MeO-C_6H_4
1d: Ar^1=*p*-MeO-C_6H_4
1e: Ar^1=1-Naphthyl

entry	sulfoxide	MOPF ligand	stereochemistry of ligand[a]	yield of **6b−e**/%	yield of **1b−e**/%
1	**5b**	**1b**	*S*	44 (76)[b]	93
2	**5c**	**1c**	*S*	73	75
3	**5d**	**1d**	*S*	63	96
4	**5e**	**1e**	*S*	86	88

[a] The stereochemistry is based on an X-ray structure of **1a** and by chemical correlation with **2** (vide infra). [b] 32% of the deborated and oxidized compound was also isolated.

TABLE 4. Synthesis of (*S*)-1a, (*S*)-1c, and (*S*)-1e via the Phosphine Oxides



5a: Ar^1=Ph
5c: Ar^1=*o*-MeO-C_6H_4
5e: Ar^1=1-Naphthyl

7a: Ar^1=Ph
7c: Ar^1=*o*-MeO-C_6H_4
7e: Ar^1=1-Naphthyl

1a: Ar^1=Ph
1c: Ar^1=*o*-MeO-C_6H_4
1e: Ar^1=1-Naphthyl

entry	sulfoxide	MOPF ligand	method	stereochemistry of ligand[a]	yield of **7**/%	yield of **1**/%
1	**5a**	**1a**	A, 1	*S*	82	73
2	**5c**	**1c**	B, 1	*S*	75	71
3	**5e**	**1e**	B, 2	*S*	67	85

[a] The stereochemistry is based on an X-ray structure of **1a** and by chemical correlation with **2** (vide infra).

isolated in high yields. This procedure also turned out to be efficient for the synthesis of aryl-MOPF ligand **1e**, with an acceptable overall yield of 76%.

Finally, synthesis of the phosphine oxides followed by reduction was tested (Table 4). Potentially, this method could improve the yield since chlorodiphenylphosphine oxide is expected to be a more reactive electrophile. This was, however, only the case for the simple phenyl derivative **7a** (compare entry 1 in Tables 2 and 4). In the case of the two substrates **7c** and **7e**, the reactivity of the electrophile was overruled by the steric properties of the biarylic system, and the sterically more demanding phosphine oxide electrophile afforded low yields (<50%) in both reactions. The most effective way to synthesize the phosphine oxides finally turned out to be the in situ oxidation of the initially formed phosphine. This could easily be accomplished by entrapment of the ferrocenyl anion with chlorodiphenylphosphine and basic workup affording the phosphine oxides **7c** and **7e** in good yields (Table 4, entries 2 and 3). Reduction of **7a** and **7c** under standard conditions furnishes the MOPF ligands **1a** and **1c** in 60% and 53% overall yield, respectively. The naphthyl-substituted phosphine oxide **7e** was reduced slowly in the presence of $SiHCl_3$ and Et_3N providing only small amount of the product. Prolonged reaction times led to decomposition of the substrate making optimization of this procedure difficult. An alternative reduction protocol applying $CeCl_3$ in combination with $LiAlH_4$ turned out to be successful for this particular phosphine oxide affording the product **1e** in 85% yield corresponding to an overall yield of 57% starting from **5e**.[15] Although the phosphines **1a**, **1c**, and **1e** can be synthesized in acceptable yields via reduction of the corresponding phosphine oxides, the reaction sequence involving the borane adduct was preferable due to the easy handling and purification of these compounds.

The phosphines **1a−e** are all stable when stored cold and in the dark. Exposure to a diluted basic reaction media though leads to various amounts of oxidation.

Structural and Conformational Analysis

The assigned stereochemistry for ligand **1a** is confirmed by an X-ray crystal structure (Figure 4). It is revealed from this structure that the dihedral angle between the substituted Cp-ring and the phenyl substituent is 38°.

(15) (a) Henson, P. D.; Naumann, K.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 5645. (b) Imamoto, T.; Kikuchi, S.; Miura, T.; Wada, Y. *Org. Lett.* **2001**, *3*, 87. (c) Imamoto, T.; Takeyama, T.; Kusumoto, T. *Chem. Lett.* **1985**, 1491. (d) Johnson, C. R.; Imamoto, T. *J. Org. Chem.* **1987**, *52*, 2170. (e) Koide, Y.; Sakamoto, A.; Imamoto, T. *Tetrahedron Lett.* **1991**, *32*, 3375. (f) Imamoto, T.; Hikosaka, T. *J. Org. Chem.* **1994**, *59*, 6753.

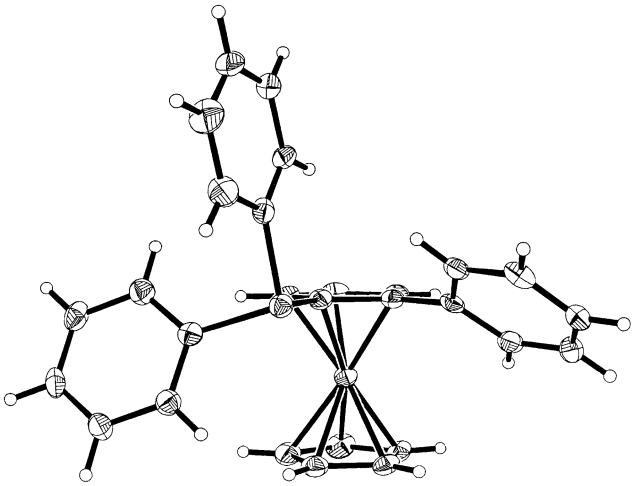


FIGURE 4. View of phenyl-MOPF (*S*)-**1a**. Displacement ellipsoids are drawn at the 50% probability level.[16]

To clarify the behavior of these novel ligands in solution and possibly get some valuable help to design novel ligands, a study of the ligands dynamic behavior was undertaken.

As a starting point, ab initio calculations on the simple phenyl-substituted ferrocene (Figure 5) were performed. The energy of activation for rotation around the phenyl−ferrocene bond was found to be less than for ethane (E_a = 10 vs 12 kJ/mol). This corresponds to completely free rotation around the biarylic bond and indicates that the repulsion between the lower Cp-ring and the phenyl group is negligible. In the calculated lowest energy conformation, the dihedral angle was found to be 35°, which is close to the value found in the solid state.

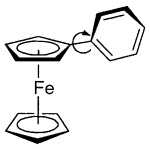
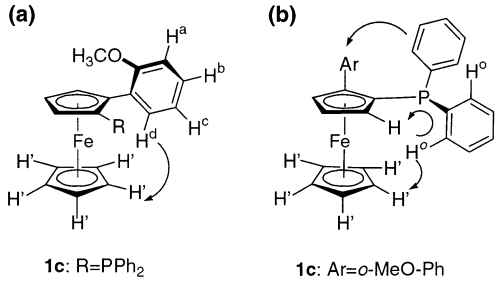


FIGURE 5.

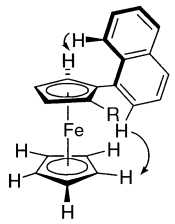
Introduction of the 1-diphenylphosphino substituent on the ferrocene scaffold might lead to restricted rotation around the biarylic bound, due to steric interactions between the two substituents. If the phenyl group were incapable of rotating freely within the NMR time scale, the protons on the phenyl substituent located above the upper Cp-ring would no longer be chemically equivalent to the protons located below the upper Cp-ring. The protons located below the Cp-ring should be relatively more deshielded due to anisotropic effects from the cyclopentadienide ligand and the iron atom. The actual ^{1}H NMR shows a complex higher order spectrum where two equivalent protons are deshielded relative to the three remaining protons. Based on the coupling pattern and correlation with ^{13}C NMR, we assign the least shielded signal in the spectrum to the two ortho protons on the phenyl group. Accordingly, *no* restricted rotation around the phenyl−ferrocene bond is indicated, and we expect the aryl group in the simple MOPF ligand **1a** to rotate with a low barrier of activation.

In contrary to the ligand **1a**, the ligands **1c** and **1e** carrying the *o*-MeO phenyl and 1-naphthyl substituent



1c: R=PPh_2 **1c**: Ar=*o*-MeO-Ph

FIGURE 6.



1e: R=PPh_2
7e: R=P(O)Ph_2

FIGURE 7.

respectively could be expected to have a higher barrier to rotation, which might give rise to atropisomers (Figures 6 and 7). A favored orientation would, in turn, be revealed in the NMR spectra of the ligands. The ^{1}H NMR spectrum of **1c** showed that one proton is considerably more deshielded compared to the rest of the spin system. Assignment by 1D-TOCSY and NOE difference established that this absorption stems from H^d (Figure 6a). An orientation of H^d below the upper Cp-ring would lead to a downfield shift (vide supra).[17] A NOESY experiment confirms this orientation since dipolar coupling is observed between H^d and the lower Cp-ring protons (H′). The methoxy protons on the other hand did not show any dipolar coupling to H′, indicating no close proximity to the lower Cp-ring.

The phenyl groups on phosphorus are believed to be positioned similar to the orientation seen in the crystal structure of **1a** (Figure 6b). The phenyl group pointing out of the plane has NOE between the ortho protons (H^o) and protons on both Cp rings, verifying the conformation in Figure 6b. The other phenyl group is coupled through space to ring protons of the anisole substituent.

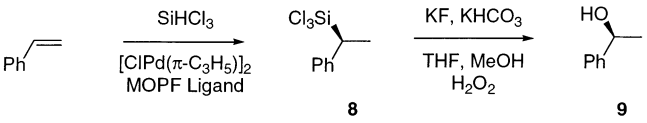
The same series of experiments were conducted for **1e** and **7e**. For both derivatives, the NOESY experiment verified the rotamer depicted in Figure 7. Moreover, the phenyl groups on phosphorus showed the same dipolar coupling found for **1c** corresponding to an orientation similar to **1c** (Figure 6b) and the solid-state structure of **1a**.

The NMR data obtained for the ligands **1c** and **1e** heavily suggest that they exist as an atropisomer with

(16) **Crystal data:** $C_{28}H_{23}FeP$, M = 446.28, monoclinic, a = 9.332(2) Å, b = 11.638(2) Å, c = 10.114(2) Å, β = 106.22(3)°, U = 1054.6(4) Å^3, T = 120(2) K, space group $P2_1$ (no. 4), Z = 2, μ(Mo Kα) = 0.803 mm^{-1}, 7514 reflections measured, 4770 unique (R_{int} = 0.041) and 3720 reflections with $I > 2\sigma(I)$ that were used in all calculations. The Flack factor was −0.05(2), indicating that the absolute configuration is correct. The final R1 was 0.0496 and wR(F^2) was 0.1138 (all data).

(17) For a related observation, see: Uemura, M. *J. Org. Chem.* **1996**, *61*, 1375.

SCHEME 3. Hydrosilylation and Oxidation of Styrene

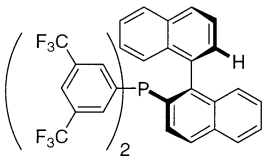


the sterically demanding ortho substituent located above the ferrocene system. This implies a more rigid biarylic system where the rotational freedom of the aryl subtituent is restricted compared to ligand **1a**.

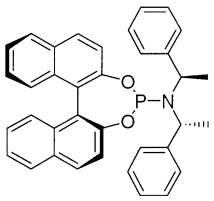
Asymmetric Hydrosilylation of Styrene

Catalytic asymmetric functionalization of alkenes is an important task in organic chemistry. The palladium-catalyzed asymmetric hydrosilylation of double bonds is a highly potent hydrometalation reaction that displays excellent regioselectivity for aryl-substituted olefins. Among the various transformations organosilanes can undergo, the Tamao−Flemming oxidation is extremely important.[18] This stereospecific oxidation converts chiral silanes into alcohols with complete retention of stereochemistry. Hence, the overall reaction sequence of hydrosilylation and oxidation is equivalent to an enantioselective Markovnikov hydration of an olefin (Scheme 3).

Until recently, only Hayashi's MOP ligands have displayed high efficiency with respect to reactivity and selectivity in the hydrosilylation of olefins. Thus, the palladium-catalyzed hydrosilylation of styrene with MOP ligand **10** affords upon oxidation 1-phenylethanol with 98% enantiomeric excess.[9a′,c′] Earlier this year, we disclosed the palladium-catalyzed hydrosilylation of aromatic alkenes with Feringa's chiral phosphoramidite ligand **11**.[19] Here, hydrosilylation and oxidation of styrene affords 1-phenylethanol with 99% enantiomeric excess, which is the highest ever reported.



(*R*)-**10**



(*S*$_A$, *R*$_C$, *R*$_C$)-**11**

The aryl-MOPF ligands were screened in the palladium-catalyzed asymmetric hydrosilylation of styrene in order to explore the influence of the aromatic moiety on the reactivity and selectivity. Commencing with 1 mol % palladium and 2 mol % aryl-MOPF ligand **1a**−**e** styrene was smoothly hydrosilylated in the presence of excess of trichlorosilane (Table 5). In all cases, 100% conversion to 1-phenyl(trichlorosilyl)ethane was observed within a short time (0.5−8 h). The *o*-MeO-Ph-MOPF **1c** results in the highest conversion rate (Table 5, entry 3), whereas 3,5-(CF_3)-Ph-MOPF **1b** gives the lowest (Table 5, entry 2), indicating that a relative electron-rich aryl substituent is beneficial for the reactivity. However, a comparison with the reaction rate for the electronically similar *p*-MeO-Ph-MOPF **1d** (Table 5, entry 4) reveals that the electronic properties are not exclusively decisive for the conversion rate. Apparently, the steric requirements of the ligands likewise influence the reactivity.

TABLE 5. Asymmetric Hydrosilylation of Styrene with Ligand 1a−e

entry	ligand	mol % Pd/ mol % ligand	reaction temp/°C	reaction time/h	conversion to **8**[a]/%	ee of **9**[b,c]/%
1	**1a**	1/2	rt	1.5	100	76 (*S*)
2	**1b**	1/2	rt	8	100	25 (*S*)
3	**1c**	1/2	rt	0.5	100	68 (*S*)
4	**1d**	1/2	rt	1.6	100	86 (*S*)
5	**1e**	1/2	rt	1.5	100	79 (*S*)

[a] Conversion determined by ^{1}H NMR. [b] ee determined by HPLC on a DAICEL OD-H column. [c] Absolute configuration determined by optical rotation.

TABLE 6. Asymmetric Hydrosilylation of Styrene with Ligands 1c−e

entry	ligand	mol % Pd/ mol % ligand	reaction temp/°C	reaction time/h	conversion to **8**[a]/%	ee of **9**[b,c]/%
1	**1c**	0.1/0.2	rt	4	100	71 (*S*)
2	**1d**	0.1/0.2	rt	5.5	100	90 (*S*)
3	**1e**	0.1/0.2	rt	3.5	100	85 (*S*)

[a] Conversion determined by ^{1}H NMR. [b] ee determined by HPLC on a DAICEL OD-H column. [c] Absolute configuration determined by optical rotation.

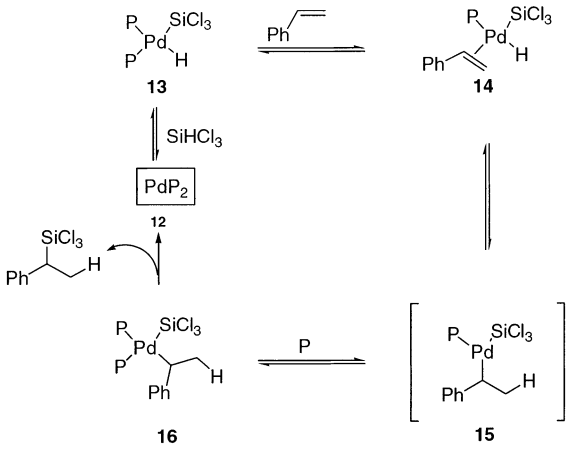
Tamao oxidation of the organosilanes affords (*S*)-1-phenylethanol with an enantiomeric excess ranging from 25% to 86%. The 3,5-(CF_3)-Ph-MOPF ligand **1b** only induces a small selectivity, and combined with the relatively low reactivity of this ligand, it seems that this aromatic moiety is a poor second component for the pseudo-biarylic scaffold in the ligands (Table 5, entry 2). As seen in entries 1, 3, 4, and 5 in Table 5, there is no obvious correlation between the observed enantioselectivies and the electronic and steric properties of the aromatic moiety in aryl-MOPF ligands **1a**, **c**, **d**, and **e**. The presumed rigidity of the pseudo-biarylic scaffold in *o*-MeO-Ph-MOPF **1c** seems to be unfavorable providing (*S*)-1-phenylethanol with only 68% ee. Similarly, the relatively rigid biarylic scaffold in 1-Naph-MOPF **1e** has only a slightly positive effect on the selectivity compared to the simple and more flexible Ph-MOPF **1a**, 79% ee and 76% ee, respectively. The highest enantioselectivity is provided by *p*-MeO-Ph-MOPF **1d**, hence suggesting that a combination of an electron-rich aryl substituent with steric flexibility is optimal.

Prompted by the initial results, the investigation of the aryl-MOPF ligands was continued. In the following experiments, the catalyst loading was decreased to 0.1 mol % palladium and 0.2 mol % of ligand **1c**, **d**, or **e** (Table 6). Again, all the catalyses proceeded efficiently. A 2−8-fold increase in reaction times and a noteworthy increase in asymmetric induction was observed. The highest selectivity was observed for ligand **1d**, where (*S*)-1-phenylethanol was obtained with 90% ee upon oxidation (Table 6, entry 2). Remarkably, the reaction time in the catalysis with **1e** is increased only by approximately

(18) Tamao, K. Oxidative Cleavage of the Silicon−Carbon Bond: Development, Mechanism, Scope and Limitations. In *Advances in Silicon Chemistry*; Larson, G. L., Ed.; JAI Press: Greenwich, CT, 1996; Vol. 3, pp 1−62.

(19) Jensen, J. F.; Svendsen, B. Y.; la Cour, T. V.; Pedersen, H. L.; Johannsen, M. *J. Am. Chem. Soc.* **2002**, *124*, 4558.

SCHEME 4. Chalk−Harrod Mechanism for the Hydrosilylation of Styrene



a factor 2 when the catalyst loading is decreased by a factor 10 (Table 6, entry 3).

The hydrosilylation of styrene in the presence of a palladium−monophosphine complex is assumed to proceed via the Chalk−Harrod mechanism depicted in Scheme 4.[20]

Presumably, the first step in the catalysis with ligand **1e** where a phosphine needs to dissociate to open a coordination site on palladium for the incoming substrate is a rate-limiting process. Lowering the concentration of palladium and phosphine ligand should affect this equilibrium, pushing it toward the alkene-coordinated palladium complex **14**. Hence, a decrease in catalyst loading can be revealed in an increase in turnover frequency. The origin of the enhanced selectivity could probably be found in the same relative rate enhancement. Background reactions leading to racemic 1-phenyl(trichlorosilyl)-ethane, 2-phenyl-1-(trichlorosilyl)ethane, and ethylbenzene will be suppressed when the monophosphine−palladium complex is the dominating catalyst. Consequently, a relative decrease of the inactive period in the catalytic system decreases the relative amount of product formed via unwanted side reactions. The consequences of lowering the catalyst loading are most profound for ligand **1e**, although the catalyses applying **1d** and **1c** show similar tendencies.

To gain more information on the relative rate enhancement observed when decreasing the palladium and ligand concentration, a series of experiments were conducted where the palladium/ligand quotient was varied (Table 7). A palladium concentration of 0.1 mol % was retained, but the concentration of the phosphine ligand was varied. The first experiment performed with 0.16 mol % **1e** revealed a highly interesting observation (Table 7, entry 1). ^{1}H NMR after 2 min showed only traces of styrene, and after 5 min, full conversion was obtained. This indicates that the palladium-to-ligand ratio is a decisive factor for the conversion time. Further lowering the amount of ligand **1e** to 0.14 and 0.12 mol %, respectively, gave the fastest turnover observed (entries 2 and 3, Table 7). In both experiments, the addition of trichlorosilane led to a profound color change within the first 30 s, furnishing a bright red solution. A typical hydrosilylation

(20) Chalk, A. J.; Harrod, J. F. *J. Am. Chem. Soc.* **1965**, *87*, 16.

TABLE 7. Hydrosilylation of Styrene with Ligands 1d,e and PPh_3

entry	ligand	mol % Pd/ mol %ligand	reaction temp/°C	reaction time	conversion to **8**[a] (%)	ee of **9**[b,c]/%
1	**1e**	0.1/0.16	rt	5 min	100	63 (*S*)
2	**1e**	0.1/0.14	rt	20 s[d]	100	69 (*S*)
3	**1e**	0.1/0.12	rt	20 s[d]	100	62 (*S*)
4	**1e**	0.1/∼0.10	rt	18 h	100	80 (*S*)
5	**1e**	0.1/0.06	rt	25 h	100	79 (*S*)
6	**1d**	0.1/0.14	rt	15 min	100	79 (*S*)
7	**1d**	0.1/∼0.1	rt	24 h	100	86 (*S*)
8	PPh_3	1/2	rt	1 h	54	
9	PPh_3	1/1.5	rt	1 h	84	
10	PPh_3	1/1.2	rt	1 h	94	
11	PPh_3	1/∼1	rt	1 h	35	

[a] Conversion determined by ^{1}H NMR. [b] ee determined by HPLC on a DAICEL OD-H column. [c] Absolute configuration determined by optical rotation. [d] The reaction proceeds for 20 s, but the total time from addition of silane to precipitation of Pd is 2 min.

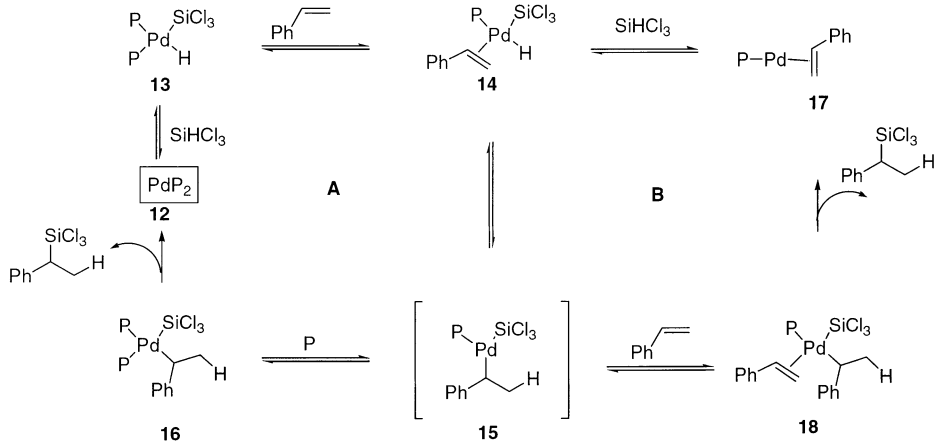
of styrene with 2 equiv of aryl-MOPF ligand per palladium is a yellow homogeneous solution, and no color change is observed upon addition of the reagents. The observed color change might indicate the formation of a different Pd-species in the reactions where only a slight excess of the ligand is applied. Immediately after the color change, a highly exothermic reaction is initiated. This is maintained for ∼20 s, after which time palladium black precipitates. ^{1}H NMR of the reaction before formation of the red complex shows only small amounts of the product, whereas complete conversion is observed after precipitation of palladium. This strongly indicates that the reaction mainly takes place in the period between the color change and the precipitation. Due to lack of precise kinetic measurements no absolute TOF number can be calculated, but based solely on the reaction time of 20 s the catalyst must turn over with a frequency of at least 180 000 h^{-1}.[21] Importantly, the enantioselectivity is largely maintained during the ultrafast reactions, and only a small decrease is affected. This is properly due to the highly exothermic nature of the reaction.

The reaction becomes more problematic when approaching a 1:1 ratio of palladium and ligand **1e**. Due to oxidation of small amounts of the phosphine in the reaction media, it is not possible to have exactly one phosphine per palladium. Consequently, either a fast reaction indicating a slight excess of the phosphine or a heterogeneous reaction indicating an excess of palladium is attained. Surprisingly, the latter reaction proceeds, although slowly, and full conversion to the product is observed after 18 h (Table 7, entry 4). Even with a 0.1: 0.06 ratio of palladium and **1e**, a catalytically active species is generated affording 100% conversion to the product after 25 h (Table 7, entry 5).

To explore the generality of the observed rate enhancement, we examined the aryl-MOPF ligand **1d** as well as PPh_3 under similar conditions. An analogous behavior was observed when applying 0.14 mol % of **1d** and 0.1

(21) At present, we can only give an underestimate of the actual turnover frequency based on the complete reaction time, i.e., 20 s for each catalytically active species to turn over 1000 molecules (0.1 mol % catalyst) (i.e., 180 000 turnovers per hour). The closest match we have found is in a recently published paper by Hayashi et al. By modifying the standard MOP ligand to a fluoro derivative they increased the TOF from 83 at 0 °C to around 1000 at −24 °C. See: Hayashi, T.; Hirate, S.; Kitayama, K.; Tsuji, H.; Torii, A.; Uozumi, Y. *J. Org. Chem.* **2001**, *66*, 1441.

SCHEME 5



mol % Pd. Although not as fast as Pd−**1e** catalyst, the reaction still finished within 15 min (Table 7, entry 6). A lower activity of the Pd−**1d** complex compared to Pd−**1e** was already established in the catalysis under standard conditions (entries 2 and 3, Table 6). Palladium−PPh_3 complexes display a profound lower activity in the hydrosilylation of styrene, and the catalyses are conducted with 1 mol % palladium. Applying 2 mol % PPh_3 affords 54% conversion within 1 h (Table 7, entry 8). As demonstrated by entries 9 and 10 (Table 7), lowering the amount of phosphine ligand to 1.5 and 1.2 mol %, respectively, did indeed increase the reaction rate, although the rates still are far from those obtained with the aryl-MOPF ligands. A conversion of 84% and 94%, respectively, was attained within 1 h (Table 7, entries 9 and 10). The catalysis with a 1:1 palladium triphenylphosphine ratio provided the lowest rate with 35% conversion after 1 h, which is similar to the effect observed for the aryl-MOPF ligands although not as profound (Table 7, entry 11).

Consequently, it seems like a general observation that simply lowering the phosphine-to-palladium ratio enhances the rate of hydrosilylation. A large difference in absolut reaction rate between the different Pd−ligand complexes, however, persists, stating that the rate also is greatly influenced by the electronic and steric properties of the ligand.

To account for the drastic effect observed upon decreasing the amount of phosphine, we invoke the competitive action of two catalytic cycles (A and B, Scheme 5). Cycle A commences with the oxidative addition of trichlorosilane to the $Pd(0)P_2$ species **12**, affording the 16-electron complex **13** having two coordination sites occupied by phosphine ligands. A ligand exchange reaction must follow, allowing coordination of the alkene. This equilibrium is expected to be far to the left due to the high affinity of palladium for coordinating phosphines, thereby favoring complex **13** over **14**.[22] It is well-known that bisphosphines are poor ligands for the palladium-catalyzed hydrosilylation. The lack of reactivity can be explained by their reluctance to liberate a vacancy on the metal for the incoming alkene. Migratory insertion from **14** affords the transient 14-electron complex **15**, which upon coordination of a phosphine forms **16**. Finally, reductive elimination releases the silane, and regenerates $Pd(0)P_2$. In cycle B, an alkene is coordinated to complex **15**, yielding complex **18**. Reductive elimination from **18** again reduces palladium, this time in the form of complex **17**. Oxidative addition of trichlorosilane to **17** reinitiates the catalytic cycle by forming **14**. Contemplating, that phosphines are superior to alkenes as ligands for palladium, it appears reasonable, that cycle A will dominate when the palladium-to-phosphine ratio is 1:2. Accordingly, **16** will be the prevailing species formed from **15**, trapping the catalyst in cycle A. Lowering the amount of phosphine facilitates the generation of complex **18**, favoring cycle B. Furthermore, it has been postulated, that reductive elimination occurs faster from a palladium complex bearing only one phosphine ligand, which could add to the speed of cycle B, if this step turned out to be rate determining under these conditions.[23]

Summarizing the above, two factors could influence the observed relative rate of the hydrosilylation. The first factor is the unfavored ligand exchange between complex **13** and **14** when 2 equiv of phosphine ligand is present (slow A cycle) vs the generation of complex **18** when less than 2 equiv of phosphine is used (fast B cycle). With similar reasoning, we expect the aryl-MOPF ligands to be superb in terms of stabilizing low-valent palladium intermediates as, e.g., **17**, thereby facilitating turnovers via the fast cycle B. This stabilization could be steric or due to pseudo-bidentate coordination to the aryl group and the phosphine in the ligand. The second factor could be the presumed faster reductive elimination from complex **18** compared to the reductive elimination from complex **16**. It should be stressed that the mechanistic considerations presented here is our working hypothesis. At present we do not have kinetic measurements or any exact knowledge about the rate-determining step to support our conclusions.

Conclusion

A class of novel arylmonophosphinoferrocene ligands has been introduced to the field of catalytic asymmetric synthesis. The modular design of the ligands was demonstrated to be highly successful for the construction of

(22) For other data supporting the importance of monophosphine complexes in hydrosilylations, see: Marinetti, A. *Tetrahedron Lett.* **1994**, *35*, 5861.

(23) Gillie, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4937.

an array of aryl-MOPF ligands with different electronic and steric properties. The short syntheses—two to three steps starting from the optically pure ferrocenyl sulfoxide **2**—makes the design outstandingly effective for accessing a wide variety of ligands.

We have shown that the new class of aryl-MOPF ligands disclosed in this paper is among the best ligands so far developed for the asymmetric hydrosilylation of styrene affording products with up to 90% ee. Furthermore, the extremely high turn over frequency effectuated by the MOPF ligands brings the hydrosilylation in to a new era where industrial application becomes an option.[24]

We are currently pursuing the extension of our design to other ligand types as well as the optimization of the MOPF ligands. Initial experiments show that the aryl group on the ferrocene scaffold has significant influence on the rate of β-elimination contra the rate of reductive elimination. This is currently being explored in the hydrosilylation of aliphatic terminal alkenes. Due to the excellent reactivity displayed by the MOPF ligands, we expect them to show interesting results in a variety of palladium-catalyzed bond-constructing reactions and are currently pursuing this task. This work will be reported in due course.

Experimental Section

General Information. All moisture- and air-sensitive manipulations were carried out under an argon atmosphere using standard Schlenk techniques. Glassware was flame- or oven-dried prior to use. Argon gas was dried by passage through P_2O_5. THF was distilled from sodium/benzophenone under nitrogen. Benzene, dichloromethane, and toluene were distilled from CaH_2. *t*-BuLi (1.5 or 1.7 M solution in pentane), *n*-BuLi (1.6 M solution in hexane), $ZnCl_2$ (0.5 M solution in THF), BH_3·THF (1 M solution in THF), and $SiHCl_3$ were used as received without further purification. LDA (0.5 M THF solution) was prepared immediate prior to use.

TLC analyses were performed on Merck silica gel 60 F_{254} plates, using UV light and a 5% solution of phosphormolybdic acid in ethanol for visualization. Ferrocenes could be seen directly as yellow-brown spots. Purification by flash chromatography was performed using Merck silica gel 60 (0.035−0.070 mm or 0.040−0.063 mm).

^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded at 30 °C. ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz), and ^{31}P NMR (202 MHz) spectra were recorded at 30 °C. Chemical shifts are reported in ppm using $CHCl_3$ (δ 7.27) and $CDCl_3$ (δ 77.0) as internal standard for ^{1}H and ^{13}C, respectively. H_3PO_4 (85%) was used as external standard for ^{31}P. Coupling constants are reported in hertz.

General Procedure: Synthesis of (S_P,S_S)-2-Phenyl-1-(*p*-tolylsulfinyl)ferrocene (5a) by Diastereoselective Ortho-Metalation and Concomitant Negishi Cross-Coupling of Ferrocenyl Sulfoxide (*S*)-2. To a stirred suspension of sulfoxide (*S*)-**2** (1.34 g, 4.13 mmol) in anhyd THF (15 mL, 0.3 M) at −78 °C under argon was added LDA (9.90 mL, 0.5 M, 4.95 mmol) dropwise via syringe. The resulting orange-red solution was stirred at −78 °C for 30 min before $ZnCl_2$ (9.10 mL, 0.5 M, 4.54 mmol) was added slowly via syringe. After being stirred for 30 min at −78 °C, the reaction was slowly warmed to rt over 1 h. To the resulting yellow solution of the trans-metalated ferrocenyl sulfoxide was added iodobenzene (2.11 g, 10.32 mmol) followed by a preformed solution of $Pd_2(dba)_3$·$CHCl_3$ (0.09 g, 0.09 mmol, 4 mol % Pd) and 2-trifurylphosphine (0.09 g, 0.38 mmol, 9.25 mol %) in anhyd THF (3 mL). The reaction was stirred at rt for 48 h, and after acidic workup the crude reaction mixture was purified by flash chromatography (pentane/ethyl acetate/dichloromethane 69/22/9) to afford 1.28 g (3.19 mmol, 77%) of (S_P,S_S)-**5a** as a yellow amorphous powder together with 0.29 g (0.88 mmol, 21%) of recovered (*S*)-**2**: ^{1}H NMR (300 MHz) δ 7.80 (d, J = 7.5 Hz, 2H), 7.71 (d, J = 7.5 Hz, 2H), 7.33 (m, 5H), 4.71 (m, 1H), 4.43 (m, 1H), 4.16 (s + m, 5H + 1H), 2.43 (s, 3H); ^{13}C NMR (75 MHz) δ 141.5 (2C), 136.0, 130.0 (2C), 129.5 (2C), 128.4 (2C), 127.4, 125.9 (2C), 90.0, 72.4 (2C), 71.4 (5C), 69.7 (2C), 21.8; MS (EI) *m*/*z* 400 [M$^+$]; HRMS (ES, *m*/*z*) calcd for $C_{23}H_{20}FeOS$ (M$^+$) 400.0584, found 400.0584.

(S_P,S_S)-2-[3,5-Bis(trifluoromethyl)phenyl-1-(*p*-tolylsulfinyl)ferrocene (5b). Compound **5b** was prepared according to the general procedure. Purification by flash chromatography (pentane/ethyl acetate 88/12) afforded 60% of (S_P,S_S)-**5b** as a red amorphous powder: ^{1}H NMR (500 MHz) δ 8.16 (bs, 2H), 7.69 (s, 1H), 7.41 (d, J = 7.5 Hz, 2H), 7.15 (d, J = 7.5 Hz, 2H), 4.73 (m, 1H), 4.61 (m, 1H), 4.57 (m, 1H), 4.34 (s, 5H), 2.33 (s, 3H); ^{13}C NMR (75 MHz) δ 141.0, 140.3, 139.5, 131.2 (q, J = 33 Hz, 2C), 130.1 (2C), 129.4 (2C), 124.9 (2C), 123.5 (q, J = 273 Hz, 2C), 120.6, 94.4, 85.4, 72.8, 71.9 (5C), 70.0 (2C), 21.4; MS (EI) 536 [M$^+$]; HRMS (ES, *m*/*z*) calcd for $C_{25}H_{18}F_6FeOS$ (M$^+$) 536.0332, found 536.0325.

(S_P,S_S)-2-(*o*-Anisole)-1-(*p*-tolylsulfinyl)ferrocene (5c). Compound **5c** was prepared according to the general procedure. Purification by flash chromatography (pentane/ethyl acetate 67/33) afforded 90% of (S_P,S_S)-**5c** as a red-orange amorphous powder: ^{1}H NMR (300 MHz) δ 8.02 (dd, J^1 = 7.4 Hz, J^2 = 1.1 Hz, 1H), 7.64 (d, J = 8.0 Hz, 2H), 7.29 (m, 3H), 7.06 (dd, J^1 = J^2 = 7.4 Hz, 1H), 6.85 (d, J = 8.2 Hz, 1H), 4.77 (m, 1H), 4.44 (m, 1H), 4.23 (m, 1H), 4.18 (s, 5H), 3.73 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (75 MHz) δ 157.6, 141.1, 141.0, 133.9, 129.3 (2C), 128.9, 125.6 (2C), 123.8, 120.4, 111.1, 94.1, 86.3, 74.1, 71.2 (5C), 69.2, 68.4, 55.6, 21.7; MS (EI) *m*/*z* 430 [M$^+$]; HRMS (ES, *m*/*z*) calcd for $C_{24}H_{22}FeO_2S$ (M$^+$) 430.0609, found 430.0609.

(S_P,S_S)-2-(*p*-Anisole)-1-(*p*-tolylsulfinyl)ferrocene (5d). Compound **5d** was prepared according to the general procedure. Purification by flash chromatography (pentane/diethyl ether 50/50) afforded 95% of (S_P,S_S)-**5d** as a yellow amorphous powder: $[\alpha]^{20}_D$ = −29 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.69 (m, 4H), 7.29 (d, J = 6.0 Hz, 2H), 6.87 (d, J = 6.0 Hz, 2H), 4.63 (m, 1H), 4.35 (m, 1H), 4.11 (s, 5H), 4.07 (m, 1H), 3.81 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (75 MHz) δ 159.1, 141.5 (2C), 131.1 (2C), 129.5 (2C), 128.1, 125.9 (2C), 113.9 (2C), 90.2, 72.1 (2C), 71.3 (5C), 69.3 (2C), 55.5, 21.7; MS (EI) *m*/*z* 430 [M$^+$]; HRMS (ES, *m*/*z*) calcd for $C_{24}H_{22}FeO_2S$ (M$^+$) 430.0609, found 430.0609.

(S_P,S_S)-2-(1-Naphthyl)-1-(*p*-tolylsulfinyl)ferrocene (5e). Compound **5e** was prepared according to the general procedure. Purification by flash chromatography (pentane/ethyl acetate 75/25) affords 88% of (S_P,S_S)-**5e** as a yellow amorphous powder: $[\alpha]^{20}_D$ = 41 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz) δ 8.24 (d, J = 7.3 Hz, 1H), 7.82 (d, J = 8.1, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.56 (dd, J^1 = 8.1 Hz, J^2 = 7.3 Hz, 1H), 7.45 (d, J = 8.1 Hz, 1H), 7.35 (dd, J^1 = 8.1 Hz, J^2 = 7.3 Hz, 1H), 7.26 (d, J = 7.9 Hz, 2H), 7.20 (ddd, J^1 = 8.1 Hz, J^2 = 7.3 Hz, J^3 = 1.3 Hz, 1H), 6.92 (d, J = 7.9 Hz, 2H), 4.64 (m, 1H), 4.57 (m, 1H), 4.53 (m, 1H), 4.38 (s, 5H), 2.19 (s, 3H); ^{13}C NMR (75 MHz) δ 140.6, 140.4, 133.5, 133.4, 131.5, 131.4, 128.9 (2C), 128.3, 128.1, 125.9, 125.8, 125.5, 125.0, 124.6 (2C), 96.5, 89.7, 74.1, 71.3 (5C), 69.1, 68.7, 21.4; MS (EI): *m*/*z*= 450 [M$^+$]; HRMS (ES, *m*/*z*) calcd for $C_{27}H_{22}FeOS$ (M$^+$) 450.0741, found 450.0741.

Synthesis of (*S*)-2-Phenyl-1-(diphenylphosphanyl)ferrocene (1a) by Selective Removal of the Sulfoxide and Direct Introduction of the Phosphino Group. To a stirred solution of (S_P,S_S)-**5a** (0.10 g, 0.25 mmol) in anhyd THF (5 mL, 0.05 M) under argon at −78 °C was added *t*-BuLi (0.18 mL, 1.7 M, 0.30 mmol) dropwise. The reaction was stirred for 5

(24) To make a reaction industrially relevant, TOF of at least 10 000 is required: Blaser, H.-U.; Spindler, F. In *Comprehensive Asymmetric Catalysis*; Jacobsen, N. J., Pfaltz, A., Yamamoto, H., Eds.; Springer: Heidelberg, 1999; Chapter 41.1

min at −78 °C before Ph_2PCl (122 mg, 0.55 mmol) was added dropwise to the dark red solution of the lithiated ferrocene. After being stirred for 30 min at −78 °C, the reaction was heated quickly to rt, diluted with 5 mL of diethyl ether, filtered through silica gel, and concentrated under reduced pressure. The resulting residue was flash chromatographed (pentane/diethyl ether 98/2) to afford 0.09 g (1.93 mmol, 77%) of the product as a yellow amorphous powder: ^{1}H NMR (500 MHz) δ 7.65 (d, J = 7.0 Hz, 2H), 7.60 (m, 2H), 7.41 (m, 3H), 7.25−7.16 (m, 8 H), 4.76 (m, 1H), 4.42 (m, 1H), 4.03 (s, 5H), 3.83 (m, 1H); ^{13}C NMR (125 MHz) δ 140.7 (d, J_{C-P} = 11.4 Hz, 1C), 138.8, 138.7 (d, J_{C-P} = 12.4 Hz, 1C), 136.1 (d, J_{C-P} = 21.4 Hz, 2C), 132.9 (d, J_{C-P} = 17.4 Hz, 2C), 130.0 (d, J_{C-P} = 6.9 Hz, 2C), 129.8, 128.8 (m, 4C), 128.5 (2C), 128.4, 127.1, 94.0 (d, J_{C-P} = 21.4 Hz, 1C), 75.4 (d, J_{C-P} = 11.5 Hz, 1C), 73.0 (m, 2C), 71.3 (bs, 5C), 70.5; ^{31}P NMR (202 MHz) δ −20.3; MS (EI) m/z 446 $[M]^+$; HRMS (ES, m/z) calcd for $C_{28}H_{23}FePNa$ (M^+) 469.0784, found 469.0786.

(*S*)-2-[3,5-Bis(trifluoromethyl)phenyl]-1-(diphenylphosphanyl)ferrocene (1b). Compound **1b** was synthesized according to the procedure described for **1a** Purification by flash chromatography (pentane/diethyl ether 98/2) afforded the product as a yellow amorphous powder: yield 70%; ^{1}H NMR (300 MHz) δ 7.95 (bs, 2H), 7.57 (s, 1H), 7.55 (m, 2H), 7.38 (m, 3H), 7.16 (m, 5H), 4.71 (m, 1H), 4.42 (m, 1H), 3.98 (s, 5H), 3.86 (m, 1H); ^{13}C NMR (75 MHz) δ 141.7, 138.8 (d, J_{C-P} = 10.0 Hz, 1C), 137.0 (d, J_{C-P} = 10.1 Hz, 1C), 135.3 (d, J_{C-P} = 21.5 Hz, 2C), 132.7 (d, J_{C-P} = 19.1 Hz, 2C), 131.1 (q, J_{C-F} = 32.6 Hz, 2C), 129.6, 129.2 (bs, 2C), 128.6 (d, J_{C-P} = 7.3 Hz, 4C), 123.6 (q, J_{C-F} = 272.2 Hz, 2C), 120.0 (bs, 2C), 89.8 (d, J_{C-P} = 21.0 Hz, 1C), 76.4 (d, J_{C-P} = 12.3 Hz, 1C), 73.5 (d, J_{C-P} = 3.9 Hz, 1C), 72.6 (d, J_{C-P} = 2.9 Hz, 1C), 71.2 (5C), 70.7; HRMS (ES) m/z calcd for $C_{30}H_{21}F_6FePNa$ (M^+) 605.0532, found 605.0533.

(*S*)-2-(*o*-Anisole)-1-(diphenylphosphanyl)ferrocene (1c). Compound **1c** was synthesized according to the procedure described for **1a**. Purification by flash chromatography (pentane/diethyl ether 98/2) afforded the product as an orange amorphous powder: yield 34−76%; ^{1}H NMR (300 MHz) δ 8.00 (d, J = 8.0 Hz, 1H), 7.61 (m, 2H), 7.39 (m, 3H), 7.16 (m, 6H), 6.96 (ddd, $J^1 = J^2$ = 8.0 Hz, J^3 = 1.0 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 4.71 (m, 1H), 4.45 (m, 1H), 4.03 (s, 5H), 3.92 (m, 1H), 3.49 (s, 3H); ^{13}C NMR (75 MHz) δ 157.8, 140.6 (d, J_{C-P} = 9.8 Hz, 1C), 139.1 (d, J_{C-P} = 9.8 Hz, 1C), 135.6 (d, J_{C-P} = 21.8 Hz, 2C), 133.7 (d, J_{C-P} = 6.7, 1C), 132.4 (d, J_{C-P} = 17.5 Hz, 2C), 129.2, 128.3 (d, J_{C-P} = 4.1 Hz, 2C), 128.2, 127.8 (d, J_{C-P} = 5.8 Hz, 2C), 127.4, 125.8, 120.0, 110.6, 91.7 (m, 2C), 74.3 (d, J_{C-P} = 3.5 Hz, 1C), 71.2 (d, J_{C-P} = 4.3 Hz, 1C), 70.5 (5C), 69.6, 55.1; ^{31}P NMR (202 MHz) δ −20.3; MS (EI) m/z 476 $[M]^+$; HRMS (ES, m/z) calcd for $C_{29}H_{25}FeOPNa$ (M^+) 499.0890, found 499.0890.

(*S*)-2-(*p*-Anisole)-1-(diphenylphosphanyl)ferrocene (1d). Compound **1d** was synthesized according to the procedure described for **1a**. Purification by flash chromatography (pentane/diethyl ether 98/2) afforded the product as a yellow amorphous powder: yield 38%; ^{1}H NMR (300 MHz) δ 7.61−7.54 (m, 2H), 7.56 (d, J = 8.7 Hz, 2H), 7.41−7.38 (m, 3H), 7.22−7.13 (m, 5H), 6.78 (d, J = 8.7 Hz, 2H), 4.70 (m, 1H), 4.38 (m, 1H), 4.01 (s, 5H), 3.79 (m, 1H), 3.77 (s, 1H); ^{13}C NMR (75 MHz) δ 158.5, 140.3 (d, J_{C-P} = 10.1 Hz, 1C), 138.2 (d, J_{C-P} = 10.8 Hz, 1C), 135.6 (d, J_{C-P} = 20.6 Hz, 2C), 132.4 (d, J_{C-P} = 17.7 Hz, 2C), 130.5 (d, J_{C-P} = 6.2 Hz, 2C), 130.3, 129.3, 128.3 (d + s, J_{C-P} = 6.2 Hz, 2C + 2C), 127.9, 113.5 (2C), 93.6 (d, J_{C-P} = 22.1 Hz, 1C), 74.6 (d, J_{C-P} = 10.9 Hz, 1C), 72.2 (d, J_{C-P} = 3.6 Hz, 1C), 72.1 (d, J_{C-P} = 4.1 Hz, 1C), 70.7 (5C), 69.8, 55.4; ^{31}P NMR (202 MHz) δ −20.4; MS (EI) m/z 476 $[M^+]$; HRMS (ES, m/z) calcd for $C_{29}H_{25}FeOPNa$ (M^+) 499.0890, found 499.0889.

Synthesis of (*S*)-2-[3,5-Bis(trifluoromethyl)phenyl]-1-[diphenylphosphanyl(borane)]ferrocene (6b). To a stirred solution of (S_P,S_S)-**5b** (0.39 g, 0.72 mmol) in anhyd THF (14 mL, 0.05 M) under argon at −78 °C was added *t*-BuLi (0.55 mL, 1.7 M, 1.20 mmol) dropwise. The reaction was stirred for 5 min at −78 °C before Ph_2PCl (0.40 g, 1.81 mmol) was added dropwise to the dark red solution of the lithiated ferrocene. After the mixture was stirred at −78 °C for 30 min, BH_3·THF (3.60 mL, 1.0 M, 3.60 mmol) was added slowly to the reaction via syringe. The reaction was heated quickly to rt and stirred at that temperature for 1 h followed by quenching with 2 M NaOH and extraction with diethyl ether. The organic layer was washed with saturated brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was filtered through a short column of silica gel to afford 0.19 g (0.32 mmol, 44% yield) of the product as an orange amorphous powder together with 0.05 g (0.25 mmol) of $Ph_2P(BH_3)H$: ^{1}H NMR (300 MHz) δ 7.71−7.63 (m, 4H), 7.60 (bs, 1H), 7.53−7.40 (m, 6H), 7.38−7.26 (m, 2H), 4.68 (m, 1H), 4.60 (m, 1H), 4.40 (s, 5H), 4.19 (m, 1H), 1.40−1.18 (m, 3H); ^{13}C NMR (75 MHz) δ 139.4, 133.1 (d, J_{C-P} = 9.2 Hz, 2C), 131.9 (2C), 131.4, (d, J_{C-P} = 11.8 Hz, 2C), 130.9 (2C), 130.0 (d, J_{C-P} = 64.4 Hz, 1C), 129.3 (d, J_{C-P} = 70.4 Hz, 1C), 129.2 (d, J_{C-P} = 10.4 Hz, 2C), 128.7 (d, J_{C-P} = 9.6 Hz, 2C), 120.8, 91.0 (d, J_{C-P} = 10.0 Hz, 1C), 75.5 (m, 2C), 71.6 (s, 5C), 70.9 (d, J_{C-P} = 7.2 Hz, 1C), 70.6 (d, J_{C-P} = 61.5 Hz, 1C).

(*S*)-2-(*o*-Anisole)-1-[diphenylphosphanyl(borane)]ferrocene (6c). The compound was synthesized from (S_P,S_S)-**5c** according to the procedure described for **6b**. Purification by flash chromatography (pentane/diethyl ether 95/5) afforded the product as a yellow amorphous powder: yield 73%; $[\alpha]^{20}_D$ = −47 (c = 0.92, $CHCl_3$); ^{1}H NMR (300 MHz) δ 7.67−7.60 (m, 2H), 7.50−7.30 (m, 7H), 7.23−7.10 (m, 3H), 6.70 (ddd, $J^1 = J^2$ = 7.5 Hz, J^3 = 0.9 Hz, 1H), 6.56 (d, J = 7.5 Hz), 4.58 (m, 1H), 4.54 (m, 1H), 4.44 (m, 1H), 4.33 (s, 5H), 3.44 (s, 3H), 1.53−0.93 (m, 3H); ^{13}C NMR (75 MHz) δ 158.1, 134.5, 133.3 (d, J_{C-P} = 5.5 Hz, 2C), 133.2 (d, J_{C-P} = 5.7 Hz, 2C), 132.1 (d, J_{C-P} = 59.2 Hz, 1C), 130.7 (d, J_{C-P} = 58.0 Hz, 1C), 130.6 (d, J_{C-P} = 1.2 Hz, 1C), 130.5 (d, J_{C-P} = 0.8 Hz, 1C), 128.8, 128.2 (d, J_{C-P} = 10.1 Hz, 2C), 128.0 (d, J_{C-P} = 10.7 Hz, 2C), 124.2, 119.7, 109.4, 92.0 (d, J_{C-P} = 9.4 Hz, 1C), 76.3 (d, J_{C-P} = 6.7 Hz, 1C), 74.1 (d, J_{C-P} = 10.6 Hz, 1C), 71.1 (5C), 70.3 (d, J_{C-P} = 7.4 Hz, 1C), 69.1 (d, J_{C-P} = 64.5 Hz, 1C), 54.5; MS (EI) m/z 490 $[M]^+$, 476 $[M^+ - BH_3]$.

(*S*)-2-(*p*-Anisole)-1-[diphenylphosphanyl(borane)]ferrocene (6d). The compound was synthesized from (S_P,S_S)-**5d** according to the procedure described for **6b**. Purification by flash chromatography (pentane/diethyl ether 95/5) afforded the product as a yellow amorphous powder: yield 63%; ^{1}H NMR (500 MHz) δ 7.59 (m, 2H), 7.42 (m, 6H), 7.26 (m, 2H), 7.11 (m, 2H), 6.58 (m, 2H), 4.59 (m, 1H), 4.51 (m, 1H), 4.31 (s, 5H), 4.21 (m, 1H), 3.74 (s, 3H), 1.51−1.20 (m, 3H); ^{13}C NMR (125 MHz) δ 159.3, 134.0 (d, J_{C-P} = 9.1 Hz, 2C), 133.6 (d, J_{C-P} = 9.9 Hz, 2C),132.7 (2C), 131.9 (d, J_{C-P} = 57.8 Hz, 1C), 131.4 (d, J_{C-P} = 3.0 Hz, 1C), 131.3 (d, J_{C-P} = 2.3 Hz, 1C), 131.0 (d, J_{C-P} = 57.0 Hz, 1C), 128.9 (d, J_{C-P} = 4.5 Hz, 2C), 128.8 (d, J_{C-P} = 4.5 Hz, 2C), 128.7, 113.4 (2C), 94.6 (d, J_{C-P} = 8.4 Hz, 1C), 75.8 (d, J_{C-P} = 6.9 Hz, 1C), 75.3 (d, J_{C-P} = 9.9 Hz, 1C), 71.6 (5C), 70.7 (d, J_{C-P} = 7.6 Hz, 1C), 69.4 (d, J_{C-P} = 61.4 Hz, 1C), 55.9; MS (EI) m/z = 476 $[M - BH_3^+]$.

(*S*)-2-(1-Naphthyl)-1-[diphenylphosphanyl(borane)]ferrocene (6e). The compound was synthesized from (S_P,S_S)-**5e** according to the procedure described for **6b**. Purification by flash chromatography (pentane/diethyl ether 98/2) afforded the product as a yellow amorphous powder: yield 86%; ^{1}H NMR (300 MHz) δ 7.61−7.51 (m, 3H), 7.46−7.39 (m, 3H), 7.26−7.16 (m, 4H), 7.13−7.00 (m, 5H), 6.90−6.84 (m, 2H), 4.61 (m, 1H), 4.56 (m, 1H), 4.53 (m, 1H), 4.40 (s, 5 H), 1.5−1.0 (m, 3H); ^{13}C NMR (75 MHz) δ 133.6 (d, J_{C-P} = 10.4 Hz, 2C), 132.7 (d, J_{C-P} = 9.2 Hz, 2C), 132.5 (d, J_{C-P} = 84.2 Hz, 1C), 130.7, 130.2 (d, J_{C-P} = 154.1 Hz, 1C), 128.3−127.6 (m, 9C), 126.0, 125.4 (d, J_{C-P} = 8.3 Hz, 2C), 125.1, 93.5 (d, J_{C-P} = 6.4 Hz, 1C), 76.2 (d, J_{C-P} = 5.8 Hz, 1C), 74.6 (d, J_{C-P} = 12.0 Hz, 1C), 71.4 (d, J_{C-P} = 63.0 Hz, 1C), 74.3 (5C), 70.4 (d, J_{C-P} = 7.8 Hz, 1C); MS (EI) m/z 510 $[M]^+$, 496 $[M - BH_3^+]$.

Synthesis of (*S*)-2-[3,5-Bis(trifluoromethyl)phenyl]-1-(diphenylphosphanyl)ferrocene (1b) via Deboration of 6b. A 0.19 g (0.317 mmol) portion of **6b** was dissolved in anhyd toluene (19 mL, 0.02 M). DABCO (0.18 g, 1.59 mmol) was added, and the mixture was heated to 60 °C for 30 min. After concentration under reduced pressure, the crude residue was purified by flash chromatography (pentane/diethyl ether 98/2) to afford 0.17 g (0.30 mmol, 93%) of (*S*)-**1b** as a red-orange amorphous powder.

(*S*)-2-(*o*-Anisole)-1-(diphenylphosphanyl)ferrocene (1c). Compound **6c** was deborated according to the procedure described for **1b**. Purification of the crude residue by flash chromatography (pentane/diethyl ether 98/2) afforded (*S*)-**1c** as a red-orange amorphous powder in 75% yield.

(*S*)-2-(*p*-Anisole)-1-(diphenylphosphanyl)ferrocene (1d). Compound **6d** was deborated according to the procedure described for **1b**. Purification of the crude residue by flash chromatography (pentane/diethyl ether 98/2) afforded (*S*)-**1d** as a yellow amorphous powder in 96% yield.

(*S*)-2-(1-Naphthyl)-1-(diphenylphosphanyl)ferrocene (1e). Compound **6e** was deborated according to the procedure described for **1b**. Purification of the crude residue by flash chromatography (pentane/diethyl ether 98/2) afforded (*S*)-**1e** as a yellow amorphous powder in 88% yield: ^{1}H NMR (500 MHz) δ 8.38 (d, J = 7.3 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.74 (m, 2H), 7.61 (m, 2H), 7.54 (dd, $J^1 = J^2$ = 8.0 Hz, 1H), 7.42 (m, 3H), 7.33 (m, 2H), 7.12 (m, 5H), 4.76 (m, 1H), 4.54 (m, 1H), 4.15 (s, 5H), 3.92 (m, 1H) ^{13}C NMR (75 Mz) δ 139.4 (d, J_{C-P} = 11.2 Hz, 1C), 138.6 (d, J_{C-P} = 10.4 Hz, 1C), 135.3 (d, J_{C-P} = 21.4 Hz, 2C), 133.9, 133.6, 133.5, 132.2 (d, J_{C-P} = 17.4 Hz, 2C), 131.1, 131.0, 129.2, 128.3 (m, 2C), 127.8 (d, J_{C-P} = 6.2 Hz, 2C), 127.6 (d, J_{C-P} = 8.7 Hz, 2C), 126.1, 125.5, 125.4, 125.0, 94.2 (d, J_{C-P} = 23.6 Hz, 1C), 78.9 (d, J_{C-P} = 9.5 Hz, 1C), 74.1 (d, J_{C-P} = 2.9 Hz, 1C), 71.3 (d, J_{C-P} = 4.3 Hz, 1C), 70.8 (5C), 69.6; ^{31}P NMR (202 MHz) δ −21.5; MS (EI) m/z 496 [M$^+$]; HRMS (ES, m/z) calcd for $C_{32}H_{25}FePNa$ (M$^+$) 519.0941, found 519.0941.

(*S*)-2-Phenyl-1-(diphenylphosphinyl)ferrocene (7a). To a stirred solution of (S_P,S_S)-**5a** (0.08 g, 0.20 mmol) in anhyd THF (4 mL, 0.05 M) under argon at −78 °C was added *t*-BuLi (0.16 mL, 1.5 M, 0.24 mmol) dropwise. The reaction was stirred for 5 min at −78 °C before $Ph_2P(O)Cl$ (0.12 g, 0.50 mmol) was added dropwise to the dark red solution of the lithiated ferrocene. After being stirred for 30 min at −78 °C, the reaction was heated quickly to rt, quenched with 1 N HCl, and extracted with diethyl ether. The organic layer was washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by flash chromatography (pentane/ethyl acetate 70/30) to afford 0.08 g (0.17 mmol, 82%) of the product as a yellow amorphous powder: ^{1}H NMR (300 MHz) δ 7.77 (m, 3H), 7.48 (m, 4H), 7.20 (m, 8H), 4.78 (m, 1H), 4.43 (m, 1H), 4.36 (s, 5H), 3.88 (m, 1H); ^{13}C NMR (75 MHz) δ 136.3 (J_{C-P} = 128.3 Hz, 1C), 134.0 (J_{C-P} = 105.4 Hz, 1C), 132.4, 131.9 (J_{C-P} = 1.8 Hz, 2C), 131.8 (J_{C-P} = 2.4 Hz, 2C), 131.5, 131.3, 130.1 (2C), 128.2 (J_{C-P} = 10.8 Hz, 2C), 128.1 (J_{C-P} = 11.7 Hz, 2C), 127.8 (2C), 126.8, 92.5 (J_{C-P} = 9.7 Hz, 1C), 76.5 (J_{C-P} = 15.8 Hz, 1C), 73.4 (J_{C-P} = 111.7 Hz, 1C), 72.8 (J_{C-P} = 9.3 Hz, 1C), 71.3 (5C), 70.4 (J_{C-P} = 11.8 Hz, 1C); ^{31}P (202 MHz) δ 29.8; MS (EI) m/z 462 [M$^+$]; HRMS (ES, m/z) calcd for $C_{28}H_{23}FeOP$ (M$^+$) 462.0836, found 462.0836.

(*S*)-2-(*o*-Anisole)-1-(diphenylphosphinyl)ferrocene (7c). To a stirred solution of (S_P,S_S)-**5c** (0.09 g, 0.21 mmol) in anhyd THF (4 mL, 0.05 M) under argon at −78 °C was added *t*-BuLi (0.17 mL, 1.5 M, 0.25 mmol) dropwise. The reaction was stirred for 5 min at −78 °C before Ph_2PCl (0.12 g, 0.53 mmol) was added dropwise to the dark red solution of the lithiated ferrocene. After being stirred for 30 min at −78 °C, the reaction was heated quickly to rt, and 4 mL of 2 M NaOH was added. The two-phase system was vigorously stirred for 15 min until TLC showed full oxidation to the phosphine oxide. After extraction with diethyl ether, the organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified flash chromatography (pentane/ethyl acetate 50/50) to afford 0.08 g (0.16 mmol, 76%) of the product as an orange-red amorphous powder: ^{1}H NMR (300 MHz) δ 8.04 (d, J = 7.5 Hz, 1H), 7.76 (m, 2H), 7.45 (m, 6H), 7.25 (m, 1H), 7.14 (m, 1H), 7.04 (ddd, $J^1 = J^2$ = 7.5 Hz, J^3 = 1.8 Hz, 1H), 6.54 (d, J = 8.1 Hz, 1H), 4.71 (m, 1H), 4.47 (m, 1H), 4.38 (s, 5H), 4.07 (m, 1H), 3.51 (s, 3H); ^{13}C NMR (75 Mz) δ 157.4, 135.1 (d, J_{C-P} = 105.5 Hz, 1C), 134.7, 134.2 (J_{C-P} = 107.0 Hz, 1C), 131.8 (J_{C-P} = 9.5 Hz, 2C), 131.7 (J_{C-P} = 9.6 Hz, 2C), 131.3 (J_{C-P} = 2.3 Hz, 1C), 130.9 (J_{C-P} = 1.7 Hz, 1C), 128.5, 128.1 (J_{C-P} = 11.7 Hz, 2C), 127.7 (J_{C-P} = 12.2 Hz, 2C), 124.7, 120.0, 109.8, 89.9 (J_{C-P} = 11.2 Hz, 1C), 75.6 (J_{C-P} = 10.2 Hz, 1C), 74.4 (J_{C-P} = 15.1 Hz, 1C), 74.1 (J_{C-P} = 112.7 Hz, 1C), 71.1 (5C), 69.8 (J_{C-P} = 11.3 Hz, 1C), 55.1; ^{31}P NMR (202 MHz) δ 29.1; MS (EI) m/z 492 [M$^+$]; HRMS (ES, m/z) calcd for $C_{29}H_{25}FeO_2P$ (M$^+$) 492.0942, found 492.0942.

(*S*)-2-(1-Naphthyl)-1-(diphenylphosphinyl)ferrocene (7e). Compound **7e** was synthesized according to the procedure described for **7c**. Purification by flash chromatography (pentane/ethyl acetate 60/40) afforded the product as a yellow amorphous powder: yield 68%; ^{1}H NMR (500 MHz) δ 8.34 (dd, J^1 = 7.3 Hz, J^2 = 1.3 Hz, 1H), 7.77 (m, 2H), 7.70 (d, J = 8.5 Hz, 1H), 7.66 (d, J = 7.3, 1H), 7.57 (d, J = 8.1 Hz, 1H), 7.50 (m, 1H), 7.43 (m, 2H), 7.37−7.25 (m, 3H), 7.21 (m, 2H), 6.95 (m, 1H), 6.81 (m, 2H), 4.76 (m, 1H), 4.59 (m, 1H), 4.52 (s, 5H), 4.18 (m, 1H); ^{13}C NMR (75 MHz) δ 134.3 (d, J_{C-P} = 105.2 Hz, 1C), 132.9, 132.7, 132.6 (d, J_{C-P} = 106.7 Hz, 1C), 132.2, 131.6, 131.3 (d, J_{C-P} = 9.3 Hz, 2C), 131.1 (d, J_{C-P} = 3.6 Hz, 1C), 131.0 (d, J_{C-P} = 9.8 Hz, 2C), 130.2 (d, J_{C-P} = 2.6 Hz, 1C), 127.9 (d, J_{C-P} = 4.1 Hz, 2C), 127.8, 127.3, 127.1, 126.9, 125.3, 125.1, 124.8 (d, J_{C-P} = 4.7 Hz, 2C), 92.3 (d, J_{C-P} = 10.8 Hz, 1C), 76.4 (d, J_{C-P} = 111.5 Hz, 1C), 75.1 (d, J_{C-P} = 9.8 Hz, 1C), 74.3 (d, J_{C-P} = 11.4 Hz, 1C), 70.9 (5C), 69.4 (d, J_{C-P} = 10.8 Hz, 1C), 53.3; ^{31}P NMR (202 MHz) δ 27.8; MS (EI) m/z 512 [M$^+$]; HRMS (ES, m/z) calcd for $C_{32}H_{25}FeOP$ (M$^+$) 512.0992, found 512.0993.

Synthesis of (*S*)-2-Phenyl-1-(diphenylphosphanyl)ferrocene (1a) by Reduction of 7a. To a stirred solution of **7a** (0.20 g, 0.43 mmol) in anhyd toluene (22 mL, 0.02 M) were added Et_3N (1.49 mL, 10.75 mmol) and $SiHCl_3$ (5.97 mmol). The reaction was heated to reflux for 24 h. After being cooled to rt, the reaction was diluted with diethyl ether and quenched with a small amount of saturated $NaHCO_3$. The organic layer was separated off, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the crude residue by flash chromatography (pentane/diethyl ether 98/2) afforded 0.07 g (0.146 mmol, 73%) of **1a** as a yellow amorphous powder.

(*S*)-2-(*o*-Anisole)-1-(diphenylphosphanyl)ferrocene (1c). Compound **7c** was reduced according to the procedure described for **1a**. Purification by flash chromatography (pentane/diethyl ether 98/2) afforded **1c** in 83% yield.

(*S*)-2-(1-Naphthyl)-1-(diphenylphosphanyl)ferrocene (1e). $CeCl_3$ (1.5 equiv) was suspended in anhyd THF (0.01 M) under argon. Compound **7e** (1 equiv) dissolved in a small amount of anhyd THF was added followed by slow addition of a THF solution of $LiAlH_4$ (1 M, 4 equiv). The reaction mixture was heated 40 °C for 3 h. After being cooled to rt, the reaction was diluted with toluene and quenched by slow addition of water. The organic layer was washed with water and filtered through a short column of silica gel. Concentration afforded the crude product, which was purified by flash chromatography (pentane/diethyl ether 98/2) to yield 85% of **1e**.

General Procedure for Hydrosilylation of Styrene. The MOPF ligand and $[ClPd(\pi\text{-}C_3H_5)]_2$ were dissolved in styrene (1 equiv) under argon, and the solution was stirred at rt for 30 min before $SiHCl_3$ (1.2 equiv) was added. The reaction was monitored by ^{1}H NMR. The product was purified by Kugelrohr distillation (95 °C/0.5 mm).

General Procedure for Oxidation. The silane (1 equiv) dissolved in anhyd benzene was added slowly to a suspension of KF (6 equiv) and $KHCO_3$ (6 equiv) in MeOH (8 mL/mmol

silane) and THF (8 mL/mmol silane). After the mixture was stirred at rt for 15 min, H_2O_2 (35%, 30 equiv) was added slowly. The reaction mixture was stirred vigorously for 48 h and then quenched with water. The mixture was extracted five times with diethyl ether, and the combined organic phases were washed twice with saturated $Na_2S_2O_3$ and once with saturated $NaHCO_3$, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by flash chromatography (pentane/ethyl acetate 85/15) to afford the alcohol **9** in 75−98% yield.

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Supporting Information Available: Copies of ^1H and ^{13}C spectra of new compounds and X-ray crystal structure data for (*S*)-**1a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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