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Asymmetric synthesis catalyzed by chiral ferrocenylphosphine-transition metal complexes

IX *. Preparation of chiral ferrocenylbisphosphines containing an aminoalkyl side chain **

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Abstract

New optically active ferrocenylbisphosphines containing an aminoalkyl pendant side chain were prepared. They are (*R*)-*N*-methyl-*N*-(2-piperidino)ethyl-1-[(*S*)-1′,2-bis(diarylphosphino)ferrocenyl]ethylamines, where aryl groups on the phosphorus atoms are 4-$CF_3C_6H_4$, 3-$CF_3C_6H_4$, 4-FC_6H_4, 4-$MeOC_6H_4$, and 3,5-Me_2-4-$MeOC_6H_2$.

Introduction

Asymmetric synthesis catalyzed by chiral phosphine-metal complexes is an area of research that has attracted a great deal of interest due to its utility in the synthesis of optically active compounds [1]. Design and preparation of effective chiral phosphine ligands is one of the most significant subjects in this area. Chiral ferrocenylphosphines which we have been developing [2] are superior to others in that structural modification can be readily carried out by introduction of a functional group (X) on the ferrocenylmethyl position by nucleophilic substitution reactions. The functional group, which is controlled by the substituents on the chiral carbon center to direct towards the reaction site of the metal catalysts [2], has been proposed to interact attractively with functional groups on reaction substrates to bring about high stereoselectivity in various types of catalytic asymmetric reactions [3–7]. Among the chiral ferrocenylphosphines we have prepared, those containing 2-(dialkylamino)ethylamino groups on the side chain are particularly useful since they have been demonstrated to be highly effective for rhodium(I)-catalyzed asym-

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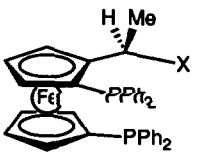
metric hydrogenation of olefins [3] and gold(I)-catalyzed asymmetric aldol-type reaction of isocyanoacetate [4]. Here we report procedures for the preparation of new ferrocenylbisphosphines containing a 2-(dialkylamino)ethylamino group on the side chain and substituted phenyl groups on the phosphorus atoms.



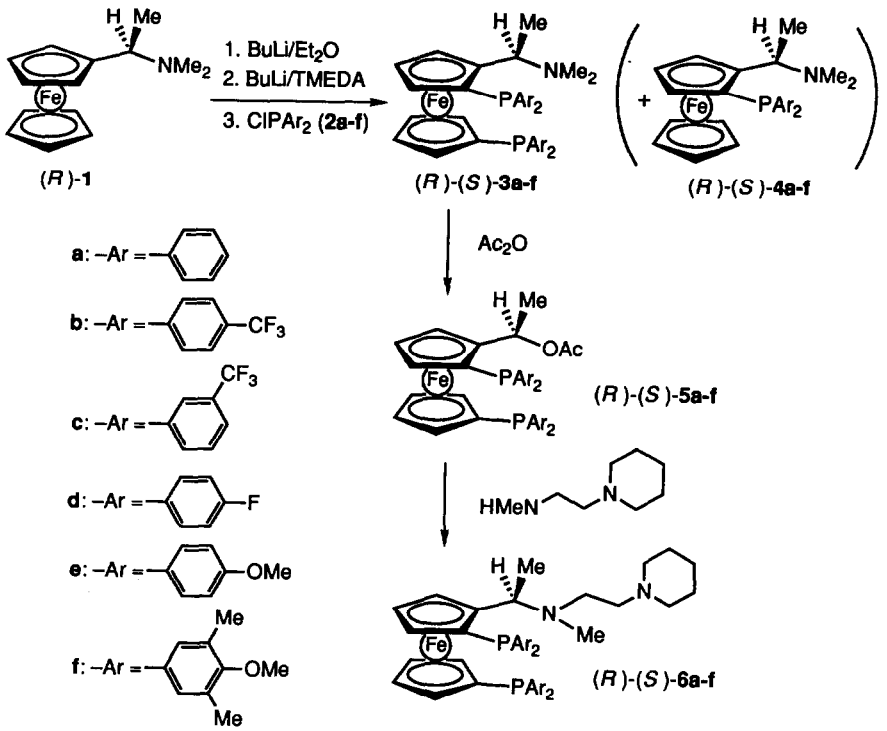
(*R*)-(*S*)-BPPF-X

Results and discussion

We have previously reported [8] the procedure for the preparation of optically active ferrocenylbisphosphine, (*R*)-*N*,*N*-dimethyl-1-[(*S*)-1′,2-bis(diphenylphosphino)ferrocenyl]ethylamine ((*R*)-(*S*)-BPPFA (**3a**)) by diphenylphosphination of the stereoselectively dilithiated ferrocene which was generated by stepwise lithiation of (*R*)-*N*,*N*-dimethyl-1-ferrocenylethylamine (**1**) with butyllithium in ether and then with butyllithium and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA). The yield of **3a** was improved from 58%, which was reported in the previous paper [8], to 70% by prolonging the reaction time of the dilithiation step. Several di(substituted phenyl)phosphino groups were introduced into (*R*)-**1** by addition of chlorodiarylphosphines **2b–f** [9–11] to the dilithiated ferrocene (Scheme 1). Ferrocenylbisphosphines (*R*)-(*S*)-**3** were isolated in over 60% yields for **3b–d** by silica gel column chromatography. Monophosphines (*R*)-(*S*)-**4b–d** were also isolated from the reaction mixture as by-products. Recently, Werz and coworkers [11] have also reported the preparation of bisphosphines **3b–e**, though the yields were not generally so high.

Ferrocenylphosphines containing the 1-acetoxyethyl group are key intermediates to a variety of functionalized ferrocenylphosphine ligands [2]. The replacement of the dimethylamino group on the ferrocenylmethyl position on **3** by an acetoxy group was effected by treatment of **3** with a large excess of acetic anhydride. The reaction temperature was found to be important for the selective conversion. Acetates **5b** and **5c**, which have an electron-withdrawing group on the diphenylphosphino groups, were obtained in high yields by reaction at 100°C, the reaction conditions being the same as those reported [8] for the conversion of BPPFA (**3a**) into acetate **5a**. On the other hand, the reaction of **3e** and **3f**, both of which have electron-releasing groups on the phenyl, at the same temperature gave a complex mixture of products including polymeric materials. Werz and coworkers [11] have also reported unsuccessful attempts to prepare acetate **5e**. It turned out that a lower reaction temperature is required for the substitution reaction of **3e** and **3f**. Reaction at 70 or 80°C for 1 h gave acetates **5e** and **5f** in good yields. Acetate **5e** was found to undergo partial decomposition during a chromatographic work-up, but a crude material obtained by removal of excess acetic anhydride from the reaction mixture was used conveniently for the next step.

Nucleophilic substitution of the acetoxy group of **5** with a 2-(piperidino)ethylamino group was carried out by treatment of acetate **5** with 10–20 equivalents of



Scheme 1

1-(2-methylaminoethyl)piperidine in refluxing methanol or ethanol. The reaction time was dependent on the substituents on the diphenylphosphino group. The substitution of acetates **5b** and **5c**, which contain a trifluoromethyl group, requires a longer reaction time than that of others. All acetates **5a–f** and diamines **6a–f** obtained here are diastereomerically pure and the substitution reactions are assumed to proceed with retention of configuration as is usually observed for the reactions at the 1-ferrocenylethyl position [12]. Some of the ferrocenylbisphosphinediamines **6b–f** which are substituted on the diphenylphosphino group have been found to be more effective than the unsubstituted one (**6a**) for the asymmetric aldol-type reaction of isocyanoacetate; this will be reported in due course.

Experimental

Optical rotations were recorded on a JASCO DIP-370 digital polarimeter. ^{1}H and ^{31}P NMR spectra were obtained with a JEOL EX-90 (90 MHz for ^{1}H and 36 MHz for ^{31}P). Chemical shifts are given in ppm relative to internal $SiMe_4$ for ^{1}H NMR and to external 85% H_3PO_4 for ^{31}P NMR spectra.

Materials. Chlorodiarylphosphines ($ClPAr_2$, **2b–e**) [9,10] were prepared by the reaction of Et_2NPCl_2 with 2 equivalents of corresponding arylmagnesium bromides (for **2c,d,e**) or aryllithium (for **2b**) followed by treatment of the resulting Et_2NPAr_2 with dry hydrogen chloride in hexane [9]. Overall yields of **2b**, **2c**, **2d**, and **2e** based

on Et_2NPCl_2 were 65%, 91%, 76%, and 45%, respectively. Chlorodiarylphosphine **2f** was prepared according to the reported procedure [10].

1-(2-Methylaminoethyl)piperidine

A mixture of 9.89 g (77 mmol) of 1-(2-aminoethyl)piperidine and 50 ml (0.62 mol) of ethyl formate was refluxed for 3 h, and low boiling compounds, excess ethyl formate and ethanol, were removed under reduced pressure. The resulting crude formamide was dissolved in 20 ml of THF, and was added dropwise to a mixture of 2.7 g (71 mmol) of lithium aluminium hydride and 100 ml of THF at 0°C with stirring. The mixture was refluxed for 8 h, and hydrolyzed at 0°C by slow successive addition of 2.7 ml of water, 2.7 ml of 15% of aqueous sodium hydroxide, and 5.4 ml of water. The precipitates formed were removed by filtration and washed with THF. The filtrate and washings were combined and concentrated under reduced pressure. Distillation of the residue gave 8.70 g (80% yield) of 1-(2-methylaminoethyl)piperidine: B.p. 70–72°C/10 mmHg (162–168°C [13]). ^1H NMR ($CDCl_3$): δ 1.3–1.8 (m, 7H), 2.2–2.8 (m, 8H), 2.46 (s, 3H).

(R)-N,N-Dimethyl-1-[(S)-1',2-bis(diarylphosphino)ferrocenyl]ethylamines (3)

The procedure we have previously reported [8] for the preparation of (*R*)-(*S*)-**3a** was improved as follows (a typical procedure is given for the preparation of (*R*)-(*S*)-**3d**):

To a solution of 2.36 g (9.16 mmol) of (*R*)-**1** in 12 ml of dry ether was added 7.1 ml of 1.58 M butyllithium (11.2 mmol) in hexane over a period of 7 min at room temperature. After stirring at room temperature for 3 h, 7.5 ml of 1.58 M butyllithium (11.9 mmol) in hexane and 1.8 ml (11.9 mmol) of TMEDA were added successively. The mixture was stirred at room temperature for 19 h and then it was cooled to −78°C with a dry ice–acetone bath. A solution of 6.35 g (24.7 mmol) of chlorodi(4-fluorophenyl)phosphine (**2d**) in 7 ml of ether was added, the mixture was slowly warmed up to room temperature, and then it was refluxed for 1 h. The mixture was hydrolyzed with aqueous sodium carbonate at 0°C and extracted with ether. The ether extracts were dried over anhydrous sodium sulfate and evaporated *in vacuo*. The resulting red residue was chromatographed on silica gel to give 5.11 g (80% yield) of (*R*)-(*S*)-**3d** (eluent: benzene/ethyl acetate = 5/1) together with 0.32 g (7% yield) of (*R*)-(*S*)-**4d** (eluent: benzene/ethyl acetate = 1/1) as a side product. Diastereomeric isomers of **3d** and **4d** were not detected by ^1H or ^{31}P NMR spectroscopy.

(*R*)-(*S*)-**3a**: Yield 70% (58% [8]). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −23.4 (s), −17.4 (s). No attempt was made to isolate monophosphine **4a**.

(*R*)-(*S*)-**3b**: Yield 63%. Orange glassy solid, $[\alpha]_D^{20}$ −217° (*c* 0.63, chloroform) ($[\alpha]_D^{20}$ +183° (*c* 0.55, chloroform) for (*S*)-(*R*)-**3b** [11]). ^1H NMR ($CDCl_3$): δ 1.11 (d, *J* 7 Hz, 3H), 1.70 (s, 6H), 3.48–3.62 (m, 2H), 3.91–4.17 (m, 4H), 4.34–4.48 (m, 2H), 7.08–7.68 (m, 16H). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −23.4 (s), −17.4 (s). Anal. Found: C, 56.60; H, 3.87; N, 1.42. $C_{42}H_{33}NF_{12}P_2Fe$ calc.: C, 56.21; H, 3.71; N, 1.56%. (*R*)-(*S*)-**4b**: Yield 18%. Orange glassy solid, $[\alpha]_D^{20}$ −254° (*c* 0.56, chloroform). ^1H NMR ($CDCl_3$): δ 1.22 (d, *J* 7 Hz, 3H), 1.72 (s, 6H), 3.78 (m, 1H), 3.96 (s, 5H), 4.15 (dq, *J* 3 and 7 Hz, 1H), 4.29 (t, *J* 3 Hz, 1H), 4.43 (broad s, 1H), 7.15–7.71 (m, 8H). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −22.3 (s). Anal. Found: C, 58.60; H, 4.57; N, 2.36. $C_{28}H_{26}NF_6PFe$ calc.: C, 58.25; H, 4.54; N, 2.43%.

(*R*)-(*S*)-**3c**: Yield 62%. Orange viscous oil, $[\alpha]_D^{20}$ −225° (*c* 0.57, chloroform) ($[\alpha]_D^{20}$ +183° (*c* 0.55, chloroform) for (*S*)-(*R*)-**3c** [11]). ^{1}H NMR ($CDCl_3$): δ 1.11 (d, *J* 7 Hz, 3H), 1.67 (s, 6H), 3.45–3.58 (m, 2H), 3.92–4.23 (m, 4H), 4.34–4.47 (m, 2H), 7.22–7.95 (m, 16H). ^{31}P {^{1}H} NMR ($CDCl_3$): δ −22.7 (s), −16.9 (s). Anal. Found: C, 56.26; H, 3.80; N, 1.47. $C_{42}H_{33}NF_{12}P_2Fe$ calc.: C, 56.21; H, 3.71; N, 1.56%. (*R*)-(*S*)-**4c**: Yield 18%. Orange viscous oil, $[\alpha]_D^{20}$ −247° (*c* 0.52, chloroform). ^{1}H NMR ($CDCl_3$): δ 1.21 (d, *J* 7 Hz, 3H), 1.70 (s, 6H), 3.73 (m, 1H), 3.97 (s, 5H), 4.14 (dq, *J* 3 and 7 Hz, 1H), 4.27 (t, *J* 3 Hz, 1H), 4.42 (m, 1H), 7.27–7.73, 7.90–8.10 (m, 8H). ^{31}P{^{1}H} NMR ($CDCl_3$): δ −21.3 (s). Anal. Found: C, 58.65; H, 4.57; N, 2.39. $C_{28}H_{26}NF_6PFe$ calc.: C, 58.25; H, 4.54; N, 2.43%.

(*R*)-(*S*)-**3d**: Yield 80%. Orange glassy solid, $[\alpha]_D^{20}$ −273° (*c* 0.73, chloroform) ($[\alpha]_D^{20}$ −270° (*c* 0.49, chloroform) [11]). ^{1}H NMR ($CDCl_3$): δ 1.12 (d, *J* 7 Hz, 3H), 1.70 (s, 6H), 3.35–3.51 (m, 2H), 3.88–4.20 (m, 4H), 4.24–4.43 (m, 2H), 6.74–7.66 (m, 16H). ^{31}P{^{1}H} NMR ($CDCl_3$): δ −26.1 (t, *J* 4 Hz), −20.1 (t, *J* 4 Hz). Anal. Found: C, 65.32; H, 4.76; N, 1.96. $C_{38}H_{33}NF_4P_2Fe$ calc.: C, 65.44; H, 4.76; N, 1.95%. (*R*)-(*S*)-**4d**: Yield 7%. Orange crystals (recrystallized from methanol), m.p. 82°C, $[\alpha]_D^{20}$ −287° (*c* 0.70, chloroform). ^{1}H NMR ($CDCl_3$): δ 1.22 (d, *J* 7 Hz, 3H), 1.73 (s, 6H), 3.78 (m, 1H), 3.94 (s, 5H), 4.13 (dq, *J* 3 and 7 Hz, 1H), 4.25 (t, *J* 3 Hz, 1H), 4.38 (m, 1H), 6.78–7.68 (m, 8H). ^{31}P{^{1}H} NMR ($CDCl_3$): δ −25.2 (t, *J* 4 Hz). Anal. Found: C, 65.23; H, 5.47; N, 2.92. $C_{26}H_{26}NF_2PFe$ calc.: C, 65.43; H, 5.49; N, 2.93%.

(*R*)-(*S*)-**3e**: Yield 30%. Orange glassy solid, $[\alpha]_D^{20}$ −312° (*c* 0.56, chloroform) ($[\alpha]_D^{20}$ +250° (*c* 0.51, chloroform) for (*S*)-(*R*)-**3e** [11]). ^{1}H NMR ($CDCl_3$): δ 1.15 (d, *J* 7 Hz, 3H), 1.74 (s, 6H), 3.72 (s, 3H), 3.76 (s, 3H), 3.78 (s, 6H), 3.45–4.38 (m, 8H), 6.64–7.53 (m, 16H). ^{31}P{^{1}H} NMR ($CDCl_3$): δ −27.0 (s), −21.1 (s). Anal. Found: C, 67.44; H, 6.15; N, 1.89. $C_{42}H_{45}NP_2Fe$ calc.: C, 67.66; H, 6.08; N, 1.89%. (*R*)-(*S*)-**4e**: Yield 20%. Orange glassy solid, $[\alpha]_D^{20}$ −301° (*c* 0.51, chloroform). ^{1}H NMR ($CDCl_3$): δ 1.27 (d, *J* 7 Hz, 3H), 1.77 (s, 6H), 3.74 (s, 3H), 3.81 (s, 3H), 3.93 (s, 5H), 3.83–4.41 (m, 4H), 6.66–7.63 (m, 8H). ^{31}P{^{1}H} NMR ($CDCl_3$): δ −26.5 (s). Anal. Found: C, 67.36; H, 6.53; N, 2.57. $C_{28}H_{32}NO_2PFe$ calc.: C, 67.08; H, 6.43; N, 2.79%.

(*R*)-(*S*)-**3f**: Yield 27%. Orange glassy solid, $[\alpha]_D^{20}$ −258° (*c* 0.48, chloroform). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.05–1.15 (broad s, 3H), 1.76 (broad s, 6H), 2.15 (s, 6H), 2.21 (s, 6H), 2.23 (s, 6H), 2.27 (s, 6H), 3.66 (s, 3H), 3.70 (s, 3H), 3.71 (s, 6H), 3.6–4.4 (m, 8H), 6.80 (d, *J* 7 Hz, 2H), 6.92 (d, *J* 8 Hz, 2H), 6.95 (d, *J* 8 Hz, 2H), 7.23 (d, *J* 8 Hz, 2H). ^{31}P{^{1}H} NMR ($CDCl_3$): δ −24.9 (s), −19.6 (s). Anal. Found: C, 70.00; H, 7.33; N, 1.79. $C_{50}H_{61}O_4NP_2Fe$ calc.: C, 70.01; H, 7.17; N, 1.79%. (*R*)-(*S*)-**4f**: Yield 4%. Orange crystals (recrystallized from methanol), m.p. 146°C, $[\alpha]_D^{20}$ −286° (*c* 0.51, chloroform). ^{1}H NMR ($CDCl_3$): δ 1.26 (d, *J* 7 Hz, 3H), 1.78 (s, 6H), 2.16 (s, 6H), 2.29 (s, 6H), 3.66 (s, 3H), 3.73 (s, 3H), 3.92 (s, 5H), 3.8–4.4 (m, 4H), 6.81 (d, *J* 8 Hz, 2H), 7.25 (d, *J* 8 Hz, 2H). ^{31}P{^{1}H} NMR ($CDCl_3$): δ −24.4 (s). Anal. Found: C, 68.94; H, 7.23; N, 2.51. $C_{32}H_{40}NO_2PFe$ calc.: C, 69.18; H, 7.39; N, 2.51%.

(R)-1-[(S)-1',2-Bis(diarylphosphino)ferrocenyl]ethyl acetates (5)

Preparation of (*R*)-(*S*)-**5a** (^{31}P{^{1}H} NMR ($CDCl_3$): δ −25.5 (s), −17.9(s)) in 90% yield has been previously reported [8].

(*R*)-(*S*)-**5b**: A mixture of 0.90 g (1.0 mmol) of (*R*)-(*S*)-**3b** and 1.9 ml (20 mmol) of acetic anhydride was stirred at 100°C for 2 h. Excess acetic anhydride was removed at the same temperature *in vacuo* and the residual red oil was chromatographed on silica gel (benzene) to give 0.77 g (84% yield) of (*R*)-(*S*)-**5b**. Orange glassy solid, $[\alpha]_D^{20}$ −219° (*c* 0.57, chloroform) ($[\alpha]_D^{20}$ +207° (*c* 0.39, chloroform) for (*S*)-(*R*)-**5b** [11]). ^{1}H NMR ($CDCl_3$): δ 1.22 (s, 3H), 1.52 (d, *J* 6.5 Hz, 3H), 3.51–3.60 (m, 1H), 3.63–3.73 (m, 1H), 4.10–4.28 (m, 3H), 4.46–4.65 (m, 2H), 6.10 (dq, *J* 3 and 6.5 Hz, 1H), 7.1–7.7 (m, 16H). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −24.9 (s), −18.0 (s). Anal. Found: C, 55.25; H, 3.57. $C_{42}H_{30}O_2F_{12}P_2Fe$ calc.: C, 55.29; H, 3.31%.

(*R*)-(*S*)-**5c**: A mixture of 3.13 g (3.49 mmol) of (*R*)-(*S*)-**3c** and 6.6 ml (70 mmol) of acetic anhydride was stirred at 100°C for 7 h. Excess acetic anhydride was removed at the same temperature *in vacuo* and the residual red oil was chromatographed on silica gel (benzene/ethyl acetate = 5/1) to give 2.90 g (91% yield) of (*R*)-(*S*)-**5c** as orange glassy solid. It was dissolved in hexane and the solution was allowed to stand overnight at room temperature to give yellow crystals. M.p. 81°C. $[\alpha]_D^{20}$ −195° (*c* 0.59, chloroform) ($[\alpha]_D^{20}$ +202° (*c* 0.55, chloroform) for (*S*)-(*R*)-**5c** [11]). ^{1}H NMR ($CDCl_3$): δ 1.18 (s, 3H), 1.52 (d, *J* 6.5 Hz, 3H), 3.49–3.66 (m, 2H), 4.06–4.29 (m, 3H), 4.43–4.66 (m, 2H), 6.08 (dq, *J* 3 and 6.5 Hz, 1H), 7.18–7.89 (m, 16H). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −24.1 (s), −17.5 (s). Anal. Found: C, 55.68; H, 3.38. $C_{42}H_{30}O_2F_{12}P_2Fe$ calc.: C, 55.29; H, 3.31%.

(*R*)-(*S*)-**5d**: A mixture of 1.71 g (2.45 mmol) of (*R*)-(*S*)-**3d** and 4.7 ml (50 mmol) of acetic anhydride was stirred at 100°C for 4 h. Excess acetic anhydride was removed at the same temperature *in vacuo* and the residual red oil was chromatographed on silica gel (benzene/ethyl acetate = 5/1) to give 1.00 g (57% yield) of (*R*)-(*S*)-**5d**. Orange glassy solid, $[\alpha]_D^{20}$ −248° (*c* 0.62, chloroform) ($[\alpha]_D^{20}$ −267° (*c* 0.5, chloroform) [11]). ^{1}H NMR ($CDCl_3$): δ 1.23 (s, 3H), 1.53 (d, *J* 6.5 Hz, 3H), 3.42–3.58 (m, 2H), 4.06–4.60 (m, 5H), 6.08 (dq, *J* 3 and 6.5 Hz, 1H), 6.80–7.54 (m, 16H). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −27.7 (t, *J* 4 Hz), −20.6 (t, *J* 4 Hz). Anal. Found: C, 64.43; H, 4.30. $C_{38}H_{30}O_2F_4P_2Fe$ calc.: C, 64.06; H, 4.24%.

(*R*)-(*S*)-**5e**: A mixture of 0.73 g (0.98 mmol) of (*R*)-(*S*)-**3e** and 1.9 ml (20 mmol) of acetic anhydride was stirred at 70°C for 1 h. Excess acetic anhydride was removed at the same temperature *in vacuo* and the residual red oil, which is a mixture of (*R*)-(*S*)-**5e**, *N*,*N*-dimethylacetamide, and a small amount of acetic anhydride, was used for the next substitution reaction without further purification. Attempts to obtain an analytically pure sample were unsuccessful due to some decomposition during a chromatographic work-up. ^{1}H NMR ($CDCl_3$): δ 1.20 (s, 3H), 1.50 (d, *J* 6.5 Hz, 3H), 3.72 (s, 3H), 3.77 (s, 3H), 3.78 (s, 3H), 3.80 (s, 3H), 3.60–4.55 (m, 7H), 6.13 (dq, *J* 3 and 6.5 Hz, 1H), 6.68–7.50 (m, 16H). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −28.9 (s), −21.6 (s).

(*R*)-(*S*)-**5f**: A mixture of 0.40 g (0.47 mmol) of (*R*)-(*S*)-**3f** and 1.3 ml (14 mmol) of acetic anhydride was stirred at 80°C for 1 h. The mixture was cooled to room temperature. Orange crystals formed were collected on a glass filter, washed with methanol, and dried *in vacuo* to give 0.28 g (68%) of (*R*)-(*S*)-**5f** as orange-yellow needles. M.p. 170°C, $[\alpha]_D^{20}$ −182° (*c* 0.52, chloroform). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.17 (s, 3H), 1.40 (d, *J* 6 Hz, 3H), 2.17 (s, 6H), 2.20 (s, 6H), 2.23 (s, 6H), 2.25 (s, 6H), 3.64 (s, 3H), 3.69 (s, 6H), 3.71 (s, 3H), 3.77 (broad s, 1H), 3.83 (broad s, 1H), 3.90 (broad s, 1H), 4.00 (broad s, 1H), 4.10 (broad s, 1H), 4.44 (broad s, 1H),

4.48 (broad s, 1H), 6.06 (m, 1H), 6.76 (d, *J* 8 Hz, 1H), 6.90 (d, *J* 7 Hz, 1H), 6.97 (d, *J* 8 Hz, 1H), 7.12 (d, *J* 8 Hz, 1H). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −27.4 (s), −20.0 (s). Anal. Found: C, 68.53; H, 6.79. $C_{50}H_{58}O_6P_2Fe$ calc.: C, 68.81; H, 6.70%.

(R)-N-methyl-N-(2-piperidino)ethyl-1-[(S)-1',2-bis(diarylphosphino)ferrocenyl]ethylamines (6)

General procedure for the preparation of (*R*)-(*S*)-**6**: The reported procedure for the replacement of acetate in **5** with nitrogen nucleophiles [8] was slightly modified as follows: A solution of 1.0 mmol of (*R*)-(*S*)-**5** and 1.8 ml of 2-(piperidino)ethylmethylamine in 10 ml of ethanol was refluxed for 3–9 h. The solvent was removed under reduced pressure, and ether was added. The solution was washed successively with aqueous sodium bicarbonate and water, dried over anhydrous magnesium sulfate, and stripped of solvent *in vacuo*. The residue was chromatographed first on a short silica gel column, and a fraction eluted with ethyl acetate/triethylamine (1/1) was collected and evaporated. It was then chromatographed on a short alumina column with ethyl acetate as eluent to give (*R*)-(*S*)-**6** as an orange glassy solid.

(*R*)-(*S*)-**6a**: Yield 80%. $[\alpha]_D^{20}$ −333° (*c* 0.66, chloroform). ^1H NMR ($CDCl_3$): δ 1.14 (d, *J* 7 Hz, 3H), 1.66 (s, 6H), 1.3–2.7 (m, 14H), 3.50 (m, 1H), 3.61 (m, 1H), 3.90–4.25 (m, 4H), 4.35 (m, 2H), 7.1–7.7 (m, 20H). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −24.0 (s), −17.4 (s). Anal. Found: C, 73.28; H, 6.80; N, 4.09. $C_{44}H_{48}N_2P_2Fe$ calc.: C, 73.13; H, 6.69; N, 3.88%.

(*R*)-(*S*)-**6b**: Yield 57%. $[\alpha]_D^{20}$ −223° (*c* 0.66, chloroform). ^1H NMR ($CDCl_3$): δ 1.15 (d, *J* 7 Hz, 3H), 1.67 (s, 3H), 1.3–2.6 (m, 14H), 3.43–3.57 (m, 2H), 3.98–4.30 (m, 4H), 4.33–4.51 (m, 2H), 7.05–7.75 (m, 16H). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −24.1 (s), −17.5 (s). Anal. Found: C, 57.97; H, 4.42; N, 2.83. $C_{48}H_{44}N_2F_{12}P_2Fe$ calc.: C, 57.96; H, 4.46; N, 2.82%.

(*R*)-(*S*)-**6c**: Yield 70% (reflux in methanol for 3 days). $[\alpha]_D^{20}$ −194° (*c* 0.32, chloroform). ^1H NMR ($CDCl_3$): δ 1.16 (d, *J* 7 Hz, 3H), 1.57 (s, 3H), 1.2–2.7 (m, 14H), 3.40–3.56 (m, 2H), 4.01–4.25 (m, 4H), 4.33–4.50 (m, 2H), 7.18–7.93 (m, 16H). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −23.4 (s), −17.0 (s). Anal. Found: C, 57.82; H, 4.55; N, 2.79. $C_{48}H_{44}N_2F_{12}P_2Fe$ calc.: C, 57.96; H, 4.46; N, 2.82%.

(*R*)-(*S*)-**6d**: Yield 54%. $[\alpha]_D^{20}$ −241° (*c* 0.84, chloroform). ^1H NMR ($CDCl_3$): δ 1.09 (d, *J* 7 Hz, 3H), 1.57 (s, 3H), 1.2–2.5 (m, 14H), 3.21–3.42 (m, 2H), 3.90–4.36 (m, 6H), 6.7–7.5 (m, 16H). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −26.6 (t, *J* 4 Hz), −20.3 (t, *J* 4 Hz). Anal. Found: C, 66.72; H, 5.68; N, 3.42. $C_{44}H_{44}N_2F_4P_2Fe$ calc.: C, 66.51; H, 5.58; N, 3.53%.

(*R*)-(*S*)-**6e**: Yield 67% (overall yield from (*R*)-(*S*)-**3e**). $[\alpha]_D^{20}$ −287° (*c* 0.37, chloroform). ^1H NMR ($CDCl_3$): δ 1.16 (d, *J* 7 Hz, 3H), 1.69 (s, 3H), 1.3–2.5 (m, 14H), 3.74 (s, 3H), 3.77 (s, 3H), 3.79 (s, 6H), 3.4–4.4 (m, 8H), 6.6–7.5 (m, 16H). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −27.5 (s), −21.2 (s). Anal. Found: C, 68.53; H, 6.73; N, 3.52. $C_{48}H_{56}N_2O_4P_2Fe$ calc.: C, 68.41; H, 6.70; N, 3.32%.

(*R*)-(*S*)-**6f**: Yield 69%. $[\alpha]_D^{20}$ −218° (*c* 0.52, chloroform). ^1H NMR ($CDCl_3$): δ 1.10 (d, *J* 7 Hz, 3H), 1.2–2.6 (m, 14H), 1.61 (s, 3H), 2.16 (s, 6H), 2.20 (s, 6H), 2.22 (s, 6H), 2.25 (s, 6H), 3.66 (s, 3H), 3.68 (s, 3H), 3.69 (s, 3H), 3.70 (s, 3H), 3.88–4.04 (m, 2H), 4.13 (dq, *J* 2 and 7 Hz, 1H), 4.23–4.44 (m, 2H), 6.71 (d, *J* 8 Hz, 2H), 6.91 (d, *J* 8 Hz, 2H), 6.93 (d, *J* 8 Hz, 2H), 7.16 (d, *J* 8 Hz, 2H). $^{31}P\{^1H\}$ NMR

($CDCl_3$): δ −25.6 (s), −19.6 (s). Anal. Found: C, 70.73; H, 7.67; N, 2.81. $C_{56}H_{72}N_2O_4P_2Fe$ calc.: C, 70.43; H, 7.60; N, 2.83%.

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