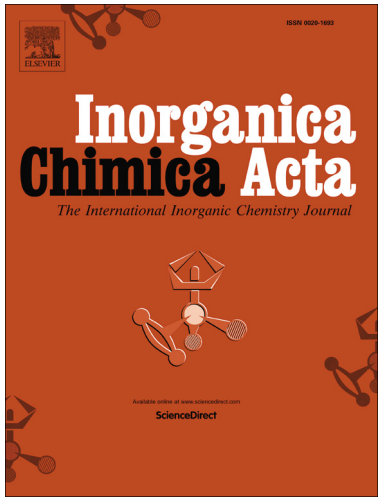

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The First Application of C_2-Symmetric Ferrocenyl Phosphinite Ligands for Rhodium-Catalyzed Asymmetric Transfer Hydrogenation of Various Ketones

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Abstract

Homogeneous catalysis has been responsible for many major recent developments in synthetic organic chemistry. The combined use of organometallic and coordination chemistry has produced a number of new and powerful synthetic methods for important classes of compounds in general and for optically active substances in particular. For this aim, a new class of chiral modular C_2-symmetric ferrocenyl phosphinite ligands has been prepared in good yields by using the inexpensive 1,1'-ferrocenedicarboxyaldehyde and various ferrocene based-amino alcohols as starting materials, and applied in the rhodium(I)-catalyzed asymmetric transfer hydrogenation (ATH) of aromatic ketones to give corresponding secondary alcohols with excellent enantioselectivities and reactivities using *iso*PrOH as the hydrogen source (up to 99% conversion and 98% ee). The substituents on the backbone of the ligands are found to exhibit a remarkable effect on both the activity and % ee. The structures of these ligands and their complexes have been elucidated by a combination of multinuclear NMR spectroscopy, IR spectroscopy and elemental analysis.

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***Keywords*:** Asymmetric Catalysis; C_2-symmetric Ferrocenyl phosphinite; Asymmetric Transfer Hydrogenation; Aromatic Ketones; Rhodium(I)

1. Introduction

Ferrocene based ligands have gained much attention due to their peculiar chemical features, diastereoselective metallation on the cyclopentadienyl ring [i] and retentive nucleophilic displacement on the benzylic position [ii], which allow the preparation of a broad range of substituted derivatives [iii]. Ferrocene derivatives have recently attracted renewed interest for modern ligand design due to their promise for widespread applications both on a laboratory scale and in industry [iv,v]. The interest is due to some exceptional features of ferrocene chemistry, which include the replacement of heteroatomic α-substituents with full retention of configuration and possibility of diastereoselective directed metallation [vi]. Especially, the ferrocene moiety has been extensively explored as a backbone of chiral P based ligands due to its easy modifiability and highly electron donating property. The excellent structure of ferrocenes enables us to design a variety of chiral ferrocenyl P based ligands, which are useful tools in metal-catalyzed asymmetric reactions [vii]. In addition, the ferrocene-derived ligands generally crystallize readily and are relatively air stable compared to their nonferrocenyl analogues. These features are beneficial for purification and usage of the ligands [viii].

In the past decades, a large number of chiral bidendate phosphorus containing ligands (P,P') having a C_2-symmetrical structure or holding two closely related bindings sites were widely studied [ix,x]. C_2-symmetry reduces the number of possible catalyst-substrate arrangements and, consequently, the number of competing reaction pathways by a factor of 2, which can be an important factor in enantioselectivity [xi]. Among the recently developed efficient transition-metal-based chiral reduction catalysts, the C_2-symmetric ferrocenyl phosphines were notably reported [xii,xiii,xiv,xv]. Because of its great success in catalytic asymmetric reactions [xvi], chiral ferrocenyl-phosphine ligands have attracted considerable attention in recent years [xvii,xviii]. These ligands are very efficient for a wide range of reactions, such as hydrogenation [xix], hydrosilylation [xx], allylic alkylation [xxi], palladium catalyzed cross-coupling reactions [xxii,xxiii,xxiv,xxv,xxvi] and cyclopropanation [xxvii]. Although ferrocenyl phosphine ligands have found widespread applications in transition metal catalyzed asymmetric transfer hydrogenations [xxviii,xxix,xxx], the analogous phosphinites have different chemical, electronic and structural advantages compared to phosphines. For instance, the metal-phosphorus bond is often stronger in phosphinites compared to the related phosphine due to the presence of electron-withdrawing P-OR group. In addition, the empty σ*-orbital of the phosphinite $P(OR)R_2$ is stabilized, making the phosphinite a better acceptor [xxxi]. Moreover, the most important advantage of chiral phosphinite ligands over the corresponding *P*-based ligands is their facile preparation, which leads to a substantial interest to develop highly effective chiral phosphinite ligands for asymmetric catalysis [xxxii,xxxiii,xxxiv].

Asymmetric Transfer Hydrogenation using 2-propanol as a hydrogen source offers an attractive route for reducing simple unfunctionalized ketones to chiral alcohols [xxxv,xxxvi,xxxvii]. The reaction uses inexpensive reagents and is usually easy to perform. Furthermore, considering

advantage of both C_2-symmetrical ligands and phosphinites often give high levels enantioselectivity in asymmetric reactions [xxxviii], in recent years our research group has reported the synthesis [xxxix,xl,], characterization and coordination properties of this kind of ligands [xli,xlii,xliii]. Inspired by the excellent results obtained with some of the chiral phosphinite ligands [xliv,xlv,xlvi and references therein], we have developed a new class of C_2-symmetric ferrocenyl phosphinite ligands that allow good control of enantiselectivites via facile structural manipulation. Herein, we report our preliminary results on the full synthesis and characterization of ferrocenyl phosphinite ligands and their rhodium(I) complexes. As far as we know, there are not many reports on asymmetric transfer hydrogenation of ketones by using chiral rhodium C_2-symmetric ferrocenyl phosphinites as catalyst. These C_2-symmetric ferrocenyl phosphinites have been employed successfully as ligands in rhodium(I)-promoted asymmetric transfer hydrogenation of various ketones.

2. Experimental Section

2.1. Materials and methods

Unless otherwise mentioned, all reactions were carried out under an atmosphere of argon using conventional Schlenk glass ware, solvents were dried using established procedures and distilled under argon just prior to use. Analytical grade and deuterated solvents were purchased from Merck. The starting materials ferrocene, L-phenyl alaninol, L-phenyl glycinol, L-leucinol, L-isoleucinol, (*S*)-(+)-1-amino-2-propanol, (*R*)-(-)-2-amino-1-phenylethanol, (*R*)-(-)-2-amino-1-butanol, (1S,2*R*)-(+)-2-amino-1,2-diphenylethanol, PPh_2Cl and Et_3N were purchased from Fluka and used as received. 1,1'-ferrocenedicarboxyaldehyde, [xlvii] and $[Rh(\mu\text{-}Cl)(cod)]_2$ [xlviii] were prepared according to the literature procedures. ^1H (at 400.1 MHz), ^{13}C (at 100.6 MHz) and ^{31}P-

{^{1}H} NMR (at 162.0 MHz) spectra were recorded on a Bruker AV 400 spectrometer, with TMS (tetramethylsilane) as an internal reference for ^{1}H NMR and ^{13}C NMR or 85% H_3PO_4 as an external reference for ^{31}P-{^{1}H} NMR. The IR spectra were recorded on a Mattson 1000 ATI UNICAM FT-IR spectrometer as KBr pellets. Specific rotations were taken on a Perkin-Elmer 341 model polarimeter. Elemental analysis was carried out on a Fisons EA 1108 CHNS-O instrument. Melting points were recorded by a Gallenkamp Model apparatus with open capillaries. GC analyses were performed on a Shimadzu GC 2010 Plus Gas Chromatograph equipped with a cyclodex-B (Agilent) capillary column (30 m x 0.32 mm I.D. x 0.25 μm film thickness). Racemic samples of alcohols were obtained by reduction of the corresponding ketones with $NaBH_4$ and used as the authentic samples for % ee determination. The GC parameters for asymmetric transfer hydrogenation of ketones were as follows; initial temperature, 50 ºC; initial time 1.1 min; solvent delay, 4.48 min; temperature ramp 1.3 ºC/min; final temperature, 150 ºC; initial time 2.2 min; temperature ramp 2.15 ºC/min; final temperature, 250 ºC; initial time 3.3 min; final time, 44.33 min; injector port temperature, 200 ºC; detector temperature, 200 ºC, injection volume, 2.0 μL.

2.2. General procedure for the transfer hydrogenation of ketones

Typical procedure for the catalytic hydrogen-transfer reaction: a solution of the Rh(I)-complexes **17-24**, (0.01mmol), NaOH (0.05 mmol) and the corresponding ketone (1mmol) in degassed *iso*PrOH (10 mL) was refluxed until the reaction completed. Then, a sample of the reaction mixture is taken off, diluted with acetone and analyzed immediately by GC, conversions obtained are related to the residual unreacted ketone.

2.3. General procedures for the synthesis of C_2-symmetric ferrocenyl amino alcohols

***Method A, for compound,* 1-4** and **8:** A mixture of ferrocenedicarboxaldehyde (1.00 g, 4.13 mmol) and amino alcohol (12.4 mmol) in previously dried CH_2Cl_2 (250 ml) containing molecular sieves (4Å, 5.00 g) was refluxed under argon for 10 h. The mixture was filtered through Celite 545. The solvent was removed under reduced pressure and the residue was re-dissolved in dry methanol (150 ml). Solid $NaBH_4$ (0.79 g, 20.8 mmol) was added in small portions at 0 ºC. After stirring for 1h, the reaction was quenched by addition of a saturated solution of NH_4Cl (250 ml) and extracted with CH_2Cl_2 (3 x 30ml). The combined organic extracts were dried over Na_2SO_4 and evaporated. The subsequent purification by column chromatography yielded the desired ferrocenyl amino alcohols.

***Method B, for compound, 5-7*:** The procedure for the preparation of ferrocenyl-substituted β-amino alcohols was used for **5-7**. A mixture of ferrocenedicarboxaldehyde (484 mg, 2 mmol) and amino alcohol (4.2 mmol) were dissolved in dry chloroform (25 ml) and the solution was refluxed under argon for 1.5 h. Then, the solution was allowed to cooling to room temperature and the solvent was evaporated under reduced pressure. The residue was re-dissolved in dry methanol (40 ml). The methanolic solution was cooled to 0 ºC and solid $NaBH_4$ (0.79 g, 20.8 mmol) was added in small portions. After stirring for further 1 h at 0 ºC and 1.5 h at room temperature, the reaction was terminated by addition of 10 % aqueous NaOH (40 ml) and extracted with CH_2Cl_2 (2 x 25 ml). The combined organic layers were dried over $MgSO_4$, evaporated and the residue was chromatographed over a silica column.

2.3.1.(*S*)-bis[*N*-(2-hydroxy-1-benzyl)ethyl]-1,1'-ferrocenylmethyldiamine, (1)

(*S*)-bis[*N*-(2-hydroxy-1-benzyl)ethyl]-1,1'-ferrocenylmethyldiamine was obtained from (*S*)-phenyl alaninol and 1,1'-ferrocenedicarboxyaldehyde. The crude product was purified through

column chromatography (SiO_2, eluent: CH_3OH/Et_3N: 20/0.5). Yield: 1.65 g, yellow oil (77%). $[\alpha]_D^{20}$ +42.8 (c 1.2, MeOH)]; ^{1}H NMR ($CDCl_3$, ppm): δ 7.21-7.35 (m, 10H, CH_2**Ph**), 3.71-4.03 (m, 8H, C_5**H**$_4$), 3.68 (m, 2H, -C**H**$_2$OH (a)), 3.38-3.42 (m, 2H, C**H**$_2$OH (b) and 4H, C**H**$_2$NH), 3.02 (m, 2H, C**H**NH), 2.80 (m, 4H, C**H**$_2$Ph), 2.34 (br, 4H, NH and OH). ^{13}C NMR ($CDCl_3$, ppm): δ 138.55 (*i*-**C**$_6$H$_5$), 129.19, 128.65, 126.55 (**C**$_6$H$_5$), 87.36 (*i*-C_5H_4), 68.22, 68.15, 68.13, 68.00 (**C**$_5$H$_4$), 62.63 (**C**H$_2$OH), 60.05 (**C**HNH), 45.88 (**C**H$_2$NH), 38.14 (**C**H$_2$Ph). IR (KBr pellet in cm^{-1}) υ(O-H): 3418, (N-H): 3291, (C=C-Cp): 1450, (C-H): 2861, 2906, 3025, 3078. Anal. calcd. for $C_{30}H_{36}N_2O_2Fe$, C, 70.30; H, 7.09; N, 5.47, found: C, 70.17; H, 6.94; N, 5.32 %.

2.3.2. (*S*)-bis[*N*-(2-hydroxy-1-phenyl)ethyl]-1,1'-ferrocenylmethyldiamine, (2)

(*S*)-bis[*N*-(2-hydroxy-1-phenyl)ethyl]-1,1'-ferrocenylmethyldiamine was obtained from (*S*)-phenylglycinol and 1,1'-ferrocenedicarboxyaldehyde. The crude product was purified through column chromatography (SiO_2, eluent: $CHCl_3/CH_3CN$: 7/3). Yield: 1.40 g, yellow crystals (70%). Mp: 130-132 ºC. $[\alpha]_D^{20}$ +31.6 (c 1.2, MeOH)]; ^{1}H NMR ($CDCl_3$, ppm) δ:7.28-7.40 (m, 10H, C_6**H**$_5$), 3.98-4.33 (m, 8H, C_5**H**$_4$), 3.96 (m, 2H, C**H**N), 3.78-3.82 (m, 2H, C**H**$_2$OH (a)), 3.66-3.71 (m, 2H, C**H**$_2$OH (b)), 3.42 (d, *J*=12.7 Hz, 2H, C**H**$_2$NH (a)), 3.16 (d, *J*=12.7 Hz, 2H, C**H**$_2$NH (b)), 2.98 (br, 4H, N**H** and O**H**). ^{13}C NMR ($CDCl_3$, ppm): δ 139.73 (*i*-C_6H_5), 128.71, 127.75, 127.48 (**C**$_6$H$_5$), 87.96 (*i*-C_5H_4), 68.86, 68.16, 67.90 (**C**$_5$H$_4$), 67.01 (**C**H$_2$OH), 65.13 (**C**HN), 46.08 (**C**H$_2$NH). IR (KBr pellet in cm^{-1}) υ(O-H): 3420, (N-H): 3283, (C=C-Cp): 1451, (C-H): 3081, 3027, 2915, 2839. Anal. calcd. for $C_{28}H_{32}N_2O_2Fe$, C, 69.41; H, 6.67; N, 5.78, found: C, 69.12; H, 6.48; N, 5.63 %.

2.3.3. (S)-bis[*N*-(2-hydroxy-1-*iso*-butyl)ethyl]-1,1'-ferrocenylmethyldiamine, (3)

(*S*)-bis[*N*-(2-hydroxy-1-*iso*-butyl)ethyl]-1,1'-ferrocenylmethyldiamine was obtained from (*S*)-leucinol and 1,1'-ferrocenedicarboxyaldehyde. The crude product was purified through column chromatography (SiO_2, eluent: CH_3OH/Et_3N: 20/0.5).Yield: 1.32 g, yellow crystals (72%). Mp: 92-94 ºC. $[\alpha]_D^{20}$ +56.6 (c 1.2, MeOH)]; ^{1}H NMR ($CDCl_3$, ppm): δ 4.14-4.27 (m, 8H, $C_5\underline{\mathbf{H}}_4$), 3.71-3.74 (m, 2H, $C\underline{\mathbf{H}}_2OH$ (a)), 3.61-3.64 (m, 2H, $C\underline{\mathbf{H}}_2NH$ (a) and 4H, NH and OH), 3.48 (d, 2H, *J*= 12.8 Hz, $C\underline{\mathbf{H}}_2NH$ (b)), 3.37-3.42 (m, 2H, $C\underline{\mathbf{H}}_2OH$ (b)), 2.83 (br, 2H, C**H**N), 1.61-1.67 (m, 2H, C**H**CH_3), 1.36-1.43 (m, 2H, $CHC\underline{\mathbf{H}}_2$ (a)), 1.27-1.34 (m, 2H, $CHC\underline{\mathbf{H}}_2$ (b)), 0.90-0.93 (m, 12H, $CHC\underline{\mathbf{H}}_3$). ^{13}C NMR ($CDCl_3$, ppm): δ 86.54 (*i*-$\underline{\mathbf{C}}_5H_4$), 69.00, 68.61, 68.52, 68.33 ($\mathbf{C}_5H_4$), 63.05 ($\underline{\mathbf{C}}H_2OH$), 56.96 (**C**HN), 45.57 ($\underline{\mathbf{C}}H_2NH$), 40.33 ($\underline{\mathbf{C}}HCH_2$), 24.99 ($\underline{\mathbf{C}}HCH_3$), 23.24, 22.51 ($CH\underline{\mathbf{C}}H_3$). IR (KBr pellet in cm^{-1}) υ(O-H): 3425, (N-H): 3290, (C=C-Cp): 1455, (C-H): 2956, 2919, 2870, 2824. Anal. calcd. for $C_{24}H_{40}N_2O_2Fe$: C, 64.85; H, 9.09; N, 6.30, found: C, 64.70; H, 8.96; N, 6.21 %.

2.3.4. (*S*)-bis[*N*-(2-hydroxy-1-*sec*-butyl)ethyl]-1,1'-ferrocenylmethyldiamine, (4)

(*S*)-bis[*N*-(2-hydroxy-1-*sec*-butyl)ethyl]-1,1'-ferrocenylmethyldiamine was obtained from (*S*)-isoleucinol and 1,1'-ferrocenedicarboxyaldehyde. The crude product was purified through column chromatography (SiO_2, eluent: CH_3OH/Et_3N: 20/0.5). Yield: 1.25 g, yellow crystals (68%). Mp: 64-66 ºC. $[\alpha]_D^{20}$ +53.9 (c 1.2, MeOH)]; ^{1}H NMR ($CDCl_3$, ppm): δ 4.11-4.21 (m, 8H, $C_5\underline{\mathbf{H}}_4$), 3.63 (dd, 2H, *J*= 4.0 and 10.7 Hz, $C\underline{\mathbf{H}}_2OH$ (a)), 3.55 (d, 2H, *J*=12.8 Hz, $C\underline{H}_2NH$ (a)), 3.36-3.41 (m, 2H, $C\underline{\mathbf{H}}_2OH$ (b) and 2H, $C\underline{\mathbf{H}}_2NH$ (b)), 2.62 (m, 2H, C**H**N), 2.48 (br, 4H, N**H** and O**H**), 1.61-1.67 (m, 2H, C**H**CH_3), 1.44-1.50 (m, 2H, $C\underline{\mathbf{H}}_2CH_3$ (a)), 1.18-1.27 (m, 2H, $C\underline{\mathbf{H}}_2CH_3$ (b)), 0.95 (t, 6H, *J*=7.4 Hz, $CH_2C\underline{\mathbf{H}}_3$), 0.89 (d, 6H, *J* = 6.9 Hz, $CHC\underline{\mathbf{H}}_3$). ^{13}C NMR ($CDCl_3$, ppm): δ 87.84 (*i*-$C_5H_4$), 68.49, 68.42, 68.29, 68.06 ($\underline{\mathbf{C}}_5H_4$), 62.56 (**C**HN), 60.34 ($\underline{\mathbf{C}}H_2OH$), 46.20 ($\underline{\mathbf{C}}H_2NH$), 35.33 ($\underline{\mathbf{C}}HCH_3$), 26.45 ($\underline{\mathbf{C}}H_2CH_3$), 14.39 ($CH\underline{\mathbf{C}}H_3$), 11.87 ($CH_2\underline{\mathbf{C}}H_3$). IR (KBr pellet

in cm^{-1}) υ (O-H): 3416, (N-H): 3279, (C=C-Cp): 1456, (C-H): 2958, 2929, 2871, 2830. Anal. calcd. for $C_{24}H_{40}N_2O_2Fe$: C, 64.85; H, 9.09; N, 6.30, found: C, 64.79; H, 8.96; N, 6.24 %.

2.3.5. (*S*)-bis[*N*-(2-hydroxypropyl)ethyl]-1,1'-ferrocenylmethyldiamine (5)

(*S*)-bis[*N*-(2-hydroxypropyl)ethyl]-1,1'-ferrocenylmethyldiamine was obtained from (*S*)-1-amino-2-propanol and 1,1'-ferrocenedicarboxyaldehyde. The crude product was purified through column chromatography (SiO_2, eluent: CH_2Cl_2/CH_3OH: 10/1).Yield: 640 mg, yellow oil (88%). $[\alpha]_D^{20}$ +46.0 (c 1.2, MeOH)]; ^{1}H NMR ($CDCl_3$, ppm): δ 4.19 (s, 2H, $C_5\underline{\mathbf{H}}_4$), 4.16 (s, 2H, $C_5\underline{\mathbf{H}}_4$), 4.12 (br, 4H, $C_5\underline{\mathbf{H}}_4$), 3.87 (br, 2H, C**H**OH), 3.56 (d, 2H, *J*=13.1 Hz, C$\underline{\mathbf{H}}_2$NH (a)), 3.46 (d, 2H, *J*= 13.1 Hz, C$\underline{\mathbf{H}}_2$NH (b)), 3.20 (br, 4H, N**H** and O**H**), 2.75 (dd, 2H, *J* = 2.1 and 11.9 Hz, C$\underline{\mathbf{H}}_2$CH (a)), 2.50 (m, 2H, C$\underline{\mathbf{H}}_2$CH (b)), 1.53 (dd, 6H, *J*= 6.1 and 25.6 Hz, CHC$\underline{\mathbf{H}}_3$). ^{13}C NMR ($CDCl_3$, ppm): δ 86.83 (*i*-$\underline{\mathbf{C}}_5H_4$), 68.89, 68.66, 68.36, 68.25 ($\underline{\mathbf{C}}_5H_4$), 65.43 (**C**HOH), 56.65 (**C**H_2CH), 48.26 (**C**H_2NH), 20.74 (CH**C**H_3). IR (KBr pellet in cm^{-1}) υ (O-H): 3405, (N-H): 3270, (C=C-Cp): 1475, (C-H): 2946, 2919, 2850, 2814. Anal. calcd. for $C_{18}H_{28}N_2O_2Fe$: C, 60.01; H, 7.85; N, 7.78, found: C, 59.90; H, 7.72; N, 7.63 %.

2.3.6. (*R*)-bis[*N*-(2-hydroxy-2-phenyl)ethyl]-1,1'-ferrocenylmethyldiamine (6)

(*R*)-bis[*N*-(2-hydroxy-2-phenyl)ethyl]-1,1'-ferrocenylmethyldiamine was obtained from (R)-2-amino-1-phenylethanol and 1,1'-ferrocenedicarboxyaldehyde. The crude product was purified through column chromatography (SiO_2, eluent: $CHCl_3/CH_3CN$: 7/3).Yield: 140 mg, yellow crystals (83%). Mp: 163-165 ºC. $[\alpha]_D^{20}$ -23.5 (c 1.2, MeOH)]; ^{1}H NMR ($CDCl_3$, ppm): δ 7.19-7.39 (m, 10H, CH**Ph**), 4.91 (d, 2H, *J*=7.6 Hz, C**H**OH), 4.45 (br, 4H, N**H** and O**H**), 4.10-4.35 (m, 8H, $C_5\underline{\mathbf{H}}_4$), 3.67 (q, 4H, *J* =13.8 Hz, C$\underline{\mathbf{H}}_2C_5H_4$), 2.94 (d, 2H, *J*=10.2 Hz, C$\underline{\mathbf{H}}_2$NH (a)), 2.84 (t, 2H, *J*=10.6 Hz, C$\underline{\mathbf{H}}_2$NH (b)). ^{13}C NMR ($CDCl_3$, ppm): δ 142.24 (*i*-$\mathbf{C}_6H_5$), 128.45, 127.63, 125.90

($CH_2\underline{C}_6H_5$), 84.80 (*i*-$\underline{C}_5H_4$), 71.08 (<u>C</u>HOH), 69.38, 69.26, 68.77, 68.69 ($\underline{C}_5H_4$), 56.02 ($\underline{C}H_2NH$), 47.46 ($\underline{C}H_2C_5H_4$). IR (KBr pellet in cm^{-1}) υ (O-H): 3390, (N-H): 3253, (C=C-Cp): 1460, (C-H): 3091, 3035, 2920, 2840. Anal. calcd. for $C_{28}H_{32}N_2O_2Fe$: C, 69.41; H, 6.67; N, 5.78, found: C, 69.21; H, 6.54; N, 5.65 %.

2.3.7. (*R*)-bis[*N*-(2-hydroxy-1-ethyl)ethyl]-1,1'-ferrocenylmethyldiamine (7)

(*R*)-bis[*N*-(2-hydroxy-1-ethyl)ethyl]-1,1'-ferrocenylmethyldiamine was obtained from (R)-2-amino-1-butanol and 1,1'-ferrocenedicarboxyaldehyde. The crude product was purified through column chromatography (SiO_2, eluent: CH_2Cl_2/CH_3OH: 10/1).Yield: 700 mg, yellow oil (90%). $[\alpha]_D^{20}$ -36.8 (c 1.2, MeOH)]; ^{1}H NMR ($CDCl_3$, ppm): δ 4.24 (s, 2H, $C_5\underline{H}_4$), 4.17 (s, 2H, $C_5\underline{H}_4$), 4.12 (s, 4H, $C_5\underline{H}_4$), 3.70 (dd, 2H, *J*= 3.4 and 10.8 Hz, $C\underline{H}_2OH$ (a)), 3.54 (d, 2H, *J* = 12.7 Hz, $C\underline{H}_2NH$ (a)), 3.36-3.41 (m, 4H, $C\underline{H}_2OH$ and $C\underline{H}_2NH$ (b)), 2.63 (br, 2H, C<u>H</u>NH; 2H, N<u>H</u> and 2H, O<u>H</u>), 1.53-1.60 (m, 2H, $C\underline{H}_2CH_3$ (a)), 1.39-1.46 (m, 2H, $C\underline{H}_2CH_3$ (b)), 0.94 (t, 6H, *J* = 7.5 Hz, $CH_2\underline{C}H_3$). ^{13}C NMR ($CDCl_3$, ppm): δ 84.74 (*i*-$\underline{C}_5H_4$), 68.68, 68.30, 68.24, 68.01 ($\underline{C}_5H_4$), 62.84 ($\underline{C}H_2OH$), 60.61 (<u>C</u>HN), 45.72 ($\underline{C}H_2NH$), 24.04 ($\underline{C}H_2CH_3$), 10.42 ($CH_2\underline{C}H_3$). IR (KBr pellet in cm^{-1}) υ(O-H): 3435, (N-H): 3280, (C=C-Cp): 1475, (C-H): 2966, 2939, 2860, 2834. Anal. calcd. for $C_{20}H_{32}N_2O_2Fe$: C, 61.85; H, 8.32; N, 7.21, found: C, 61.70; H, 8.20; N, 7.09 %.

2.3.8. (1*S*,2*R*)-bis[N-(2-hydroxy-1,2-diphenyl)ethyl]-1,1'-ferrocenylmethyldiamine, (8)

(1*S*, 2*R*)-bis[*N*-(2-hydroxy-1,2-diphenyl)ethyl]-1,1'-ferrocenylmethyldiamine was obtained from (1S, 2*R*)-2-amino-1,2-diphenyl ethanol and 1,1'-ferrocenedicarboxyaldehyde. The crude product was purified through column chromatography (SiO_2, eluent: CH_3OH/Et_3N: 20/0.5). Yield: 1.62 g, yellow crystals (65%). Mp: 121-123 ºC. $[\alpha]_D^{20}$ +24.7 (c 1.2, MeOH)]; ^{1}H NMR ($CDCl_3$, ppm): δ 7.21-7.31 (m, 20H, $C_6\underline{H}_5$), 4.77 (d, 2H, *J* = 5.8 Hz, C<u>H</u>OH), 4.19 (d, 2H, *J*= 5.9 Hz, C<u>H</u>NH),

3.84-3.93 (m, 8H, $C_5\underline{\mathbf{H}}_4$), 3.28 (d, 2H, J = 13.1 Hz, $C\underline{\mathbf{H}}_2NH$, (a)), 3.15 (d, 2H, J = 13.1 Hz, $C\underline{\mathbf{H}}_2NH$, (b)), 1.71 (br, 4H, N**H** and O**H**). ^{13}C NMR ($CDCl_3$, ppm): δ 140.62, 139.54 (*i*-$\underline{\mathbf{C}}_6H_5$), 128.36, 128.30, 128.20, 127.91, 127.71, 127.61 ($\underline{\mathbf{C}}_6H_5$), 87.08 (*i*-$\mathbf{C}_5H_4$), 78.31 ($\underline{\mathbf{C}}$HOH), 68.52, 68.18, 68.03, 67.97 ($\underline{\mathbf{C}}_5H_4$), 61.88 ($\underline{\mathbf{C}}$HNH), 45.96 ($\underline{\mathbf{C}}H_2NH$). IR (KBr pellet in cm^{-1}) υ (O-H): 3332, (N-H): 3281, (C=C-Cp): 1453, (C-H): 3078, 3027, 2890, 2826. Anal. calcd. for $C_{40}H_{40}N_2O_2Fe$, C, 75.46; H, 6.35; N, 5.40; found: C, 75.32; H, 6.21; N, 4.28 %.

2.4. General procedure for synthesis of ferrocene based C_2-symmetric phosphinites (9-16)

To a solution of ferrocenylaminoalcohol (1 equiv.) in dry toluene (20 ml) was added triethylamine (2 equiv.) and the mixture was stirred for 10 min under argon atmosphere. To this solution was added dropwise monochlorodiphenylphosphine, PPh_2Cl (2 equiv.). The mixture was then stirred at room temperature until all the reactions were completed. A white precipitate of triethylamine hydrochloride was removed by filtration under argon and the remaining organic phase was evaporated under reduced pressure to produce a yellow viscous oily product.

2.4.1. (*S*)-bis[*N*-2-diphenylphosphinite-1-benzyl)ethyl]-1,1'-ferrocenylmethyldiamine, (9)

Yield: 100 mg, (83%). $[\alpha]_D^{20}$ +37.2 (c 1.2, MeOH)]; ^{1}H NMR ($CDCl_3$, ppm): δ 7.15-7.56 (m, 30 H, $C_6\underline{\mathbf{H}}_5$ and $C_6\underline{\mathbf{H}}_5P$), 3.81-3.99 (m, 8H, $C_5\underline{\mathbf{H}}_4$ and 4H, $C\underline{\mathbf{H}}_2OP$), 3.50 (d, 2H, J =12.9 Hz, $C\underline{\mathbf{H}}_2NH$ (a)), 3.43 (d, 2H, J=12.9 Hz, $C\underline{\mathbf{H}}_2NH$ (b)), 3.13 (m, 2H, C**H**N), 2.89 (m, 2H, $C\underline{\mathbf{H}}_2Ph$ (a)), 2.80 (m, 2h, $C\underline{\mathbf{H}}_2Ph$ (b)). ^{13}C NMR ($CDCl_3$, ppm): δ 141.87 (d, J=18.1 Hz, *i*-$\underline{\mathbf{C}}_6H_5P$), 138.68 (*i*-$\underline{\mathbf{C}}_6H_5$), 130.62 (d, J= 11.1, *o*-$\underline{\mathbf{C}}_6H_5PO$), 129.45, 129.38, 129.32, 129.06, 128.51 (*p*-$\underline{\mathbf{C}}_6H_5PO$, *m*-$\underline{\mathbf{C}}_6H_5PO$, *o-, m-, p*-$\underline{\mathbf{C}}_6H_5$), 87.15 (*i*-$\underline{\mathbf{C}}_5H_4$), 71.19 (d, J= 18.0, $\underline{\mathbf{C}}H_2OP$), 68.58, 68.50, 68.37, 68.31 ($\underline{\mathbf{C}}_5H_4$), 59.52 (d, J=8.1 Hz, $\underline{\mathbf{C}}$HN), 46.41 ($\underline{\mathbf{C}}H_2NH$), 38.09 ($\underline{\mathbf{C}}H_2Ph$). ^{31}P-{^{1}H} NMR ($CDCl_3$, ppm): δ 114.66 (s, O$\underline{\mathbf{P}}Ph_2$). IR (KBr pellet in cm^{-1}) υ (N-H): 3330, (C=C-Cp): 1454, (O-P): 1027,

(C-H): 3036, 3025, 2923, 2864. Anal. calcd. for $C_{54}H_{54}N_2O_2P_2Fe$: C, 73.62; H, 6.19; N, 3.18, found: C, 73.46; H, 6.05; N, 3.08 %.

2.4.2. (*S*)-bis[*N*-2-diphenylphosphinite-1-phenyl)ethyl]-1,1'-ferrocenylmethyldiamine, (10)

Yield: 95 mg, (77%). $[\alpha]_D^{20}$ +56.1 (c 1.2, MeOH)];^{1}H NMR ($CDCl_3$, ppm): δ 7.28-7.65 (m, 30 H, $C_6\underline{\mathbf{H}}_5PO$ and $C_6\underline{\mathbf{H}}_5$), 4.02-4.07 (m, 8H, $C_5\underline{\mathbf{H}}_4$ and 2H, C**H**N), 3.93 (m, 4H, C$\underline{\mathbf{H}}_2$OP), 3.41 (d, 2H, *J*=13.1 Hz, C$\underline{\mathbf{H}}_2$NH (a)), 3.22 (d, 2H, *J*=13.1 Hz, **C**$\underline{\mathrm{H}}_2$NH (b)), 2.42 (br, 2H, N$\underline{\mathrm{H}}$). ^{13}C NMR ($CDCl_3$, ppm): δ 141.76 (d, *J*=18.6 Hz, *i*-$\underline{\mathbf{C}}_6H_5PO$), 140.11 (*i*-$\underline{\mathbf{C}}_6H_5$), 130.61, 130.47, 130.39, 129.44, 128.51, 128.45, 128.38, 127.92, (*o*-$\underline{\mathbf{C}}_6H_5PO$, *p*-$\underline{\mathbf{C}}_6H_5PO$, *m*-$\underline{\mathbf{C}}_6H_5PO$, *o-, p-, m*-$\underline{\mathbf{C}}_6H_5$), 87.06 (*i*-$\underline{\mathbf{C}}_5H_4$), 74.74 (d, *J*=18.1 Hz, ($\underline{\mathbf{C}}H_2OP$), 68.68, 68.49, 68.42, 68.18 ($\underline{\mathbf{C}}_5H_4$), 63.39 (d, *J*=8.0 Hz, **C**HN), 46.18 (($\underline{\mathbf{C}}H_2NH$). ^{31}P-{^{1}H} NMR ($CDCl_3$, ppm): δ 116.76 (s, O**P**Ph_2). IR (KBr pellet in cm^{-1}) υ(N-H): 3331, (C=C-Cp): 1436, (O-P): 1020, (C-H): 3068, 3028, 2922, 2862. Anal. calcd. for $C_{52}H_{50}N_2O_2P_2Fe$: C, 73.23; H, 5.92; N, 3.29, found: C, 73.11; H, 5.82; N, 3.18 %.

2.4.3. (*S*)-bis[*N*-2-diphenylphosphinite-1-*iso*-butyl)ethyl]-1,1'-ferrocenylmethyldiamine, (11)

Yield: 110 mg, (85%). $[\alpha]_D^{20}$ +35.3 (c 1.2, MeOH)];^{1}H NMR ($CDCl_3$, ppm): δ 7.55 (m, 8H, o-$C_6\underline{\mathbf{H}}_5P$), 7.38-7.42 (m, 12H, *m*- and *p*-$C_6\underline{\mathbf{H}}_5P$), 4.02-4.16 (m, 8H, $C_5\underline{\mathbf{H}}_4$), 3.89 (m, 4H, C$\underline{\mathbf{H}}_2$OP), 3.58 (br, 4H, C$\underline{\mathbf{H}}_2$NH), 2.96 (br, 2H, C**H**N), 1.64-1.71 (m, 2H, C$\underline{\mathbf{H}}CH_3$), 1.38-1.45 (m, 4H, CHC$\underline{\mathbf{H}}_2$), 0.91 (d, 6H, *J*=6.6 Hz, CHC$\underline{\mathbf{H}}_3$, (a)), 0.86 (d, 6H, *J*=6.5 Hz, CHC$\underline{\mathbf{H}}_3$, (b)). ^{13}C NMR ($CDCl_3$, ppm): δ 141.84 (d, *J*= 19.2 Hz, *i*-$\underline{\mathbf{C}}_6H_5P$), 130.47 (d, *J*= 20.1 Hz, *o*-$\underline{\mathbf{C}}_6H_5P$), 129.47 (s, *p*-$\underline{\mathbf{C}}_6H_5P$), 128.42 (d, *J*=6.0 Hz, *m*-$\underline{\mathbf{C}}_6H_5P$), 87.15 (*i*-$C_5H_4$), 71.48 (d, *J*=16.1 Hz, $\underline{\mathbf{C}}H_2OP$), 69.24, 69.14, 68.73, 68.66 ($\underline{\mathbf{C}}_5H_4$), 55.81 (d, *J*=7.0 Hz, **C**HN), 45.90 ($\underline{\mathbf{C}}H_2NH$), 40.46 (CH$\underline{\mathbf{C}}H_2$), 24.90

(**C**HCH$_3$), 22.80 (CH**C**H$_3$, (a)), 22.98 (CH**C**H$_3$, (b)). ^{31}P-{^{1}H} NMR (CDCl$_3$, ppm): δ 114.26 (s, O**P**Ph$_2$). IR (KBr pellet in cm^{-1}) υ(N-H): 3332, (C=C-Cp): 1435, (O-P): 1023, (C-H): 3069, 2953, 2867. Anal. calcd. for $C_{48}H_{58}N_2O_2P_2Fe$: C, 70.92; H, 7.21; N, 3.45, found: C, 70.76; H, 7.06; N, 3.32 %.

2.4.4. (*S*)-bis[*N*-2-diphenylphosphinite-1-*sec*-butyl)ethyl]-1,1'-ferrocenylmethyldiamine, (12)

Yield: 105 mg, (82%). $[\alpha]_D^{20}$ +66.2 (c 1.2, MeOH)];^{1}H NMR (CDCl$_3$, ppm): δ 7.53 (m, 8H, *o*-C$_6$**H**$_5$P), 7.38-7.46 (m, 12H, *m*- and *p*- C$_6$**H**$_5$P), 4.02-4.18 (m, 8H, C$_5$**H**$_4$), 3.92 (m, 4H, C**H**$_2$OP), 3.52 (br, 4H, C**H**$_2$NH), 2.81 (br, 2H, C**H**N), 1.68 (br, 2H, C**H**CH$_3$), 1.53 (m, 2H, C**H**$_2$CH$_3$ (a)), 1.24 (m, 2H, C**H**$_2$CH$_3$ (b)), 0.88-0.95 (m, 12H, CHC**H**$_3$, (a) and CH$_2$C**H**$_3$, (b)). ^{13}C NMR (CDCl$_3$, ppm): δ 142.00 (d, *J*=17.1 Hz, *i*-**C**$_6$H$_5$PO), 130.41 (d, *J*=21.5Hz, *o*-**C**$_6$H$_5$PO), 129.36 (s, *p*-**C**$_6$H$_5$PO), 128.39 (s, *J*=5.1 Hz, *m*-**C**$_6$H$_5$PO), 87.06 (*i*-**C**$_5$H$_4$), 69.67, 69.49, 68.97, 68.88, 68.40 (**C**H$_2$OP, **C**$_5$H$_4$), 61.83 (**C**HN), 46.70 (**C**H$_2$NH), 35.79 (**C**HCH$_3$), 26.07 (**C**H$_2$CH$_3$), 14.82 (CH**C**H$_3$, (a)), 12.14 (CH$_2$**C**H$_3$, (a)). ^{31}P-{^{1}H} NMR (CDCl$_3$, ppm): δ 115.66 (s, O**P**Ph$_2$). IR (KBr pellet in cm^{-1}) υ (N-H): 3332, (C=C-Cp): 1437, (O-P): 1026, (C-H): 3069, 2960, 2926, 2873. Anal. calcd. for $C_{48}H_{58}N_2O_2P_2Fe$: C, 70.92; H, 7.21; N, 3.45, found: C, 70.75; H, 7.06; N, 3.30 %.

2.4.5. (*S*)-bis[*N*-2-diphenylphosphinite propyl]-1,1'-ferrocenylmethyldiamine, (13)

Yield: 100 mg, (92%). $[\alpha]_D^{20}$ +53.4 (c 1.2, MeOH)]; ^{1}H NMR (CDCl$_3$, ppm): δ 7.25-7.83 (m, 20 H, C$_6$**H**$_5$PO), 4.23 (m, 2H, C**H**OP), 4.00-4.06 (m, 8H, C$_5$**H**$_4$), 3.39-3.49 (m, 4H, C**H**$_2$NH), 2.84 (m, 2H, C**H**$_2$CH (a)), 2.75 (m, 2H, CHC**H**$_2$ (b)), 1.31 (d, 6H, *J*= 4.1 Hz, CHC**H**$_3$). ^{13}C NMR (CDCl$_3$, ppm): δ 142.87 (d, *J*=16.9 Hz, *i*-**C**$_6$H$_5$P), 130.11 (d, *J*=21.3 Hz, *o*-**C**$_6$H$_5$P), 129.05 (s, *p*-

C$_6$H$_5$P), 128.51 (d, *J*= 10.5 Hz, *m*-**C**$_6$H$_5$P), 86.46 (*i*-**C**$_5$H$_4$), 76.65 (s, **C**HOP), 68.88, 68.86, 68.33, 68.30 (**C**$_5$H$_4$), 55.97 (d, *J*=5.0 Hz, **C**H$_2$CH), 48.61 (**C**H$_2$NH), 20.48 (d, *J* = 6.4 Hz, CH**C**H$_3$). ^{31}P-{^{1}H} NMR (CDCl$_3$, ppm): δ 107.12 (s, O**P**Ph$_2$). IR (KBr pellet in cm^{-1}) υ(N-H): 3343, (C=C-Cp): 1438, (O-P): 1024, (C-H): 3057, 2968, 2928, 2884. Anal. calcd. for $C_{42}H_{46}N_2O_2P_2Fe$: C, 69.23; H, 6.38; N, 3.85, found: C, 69.10; H, 6.25; N, 3.68 %.

2.4.6. (*R*)-bis[*N*-2-diphenylphosphinite-2-phenyl]-1,1'-ferrocenylmethyldiamine, (14).

Yield: 125 mg. (91%). $[\alpha]_D^{20}$ -56.3 (c 1.2, MeOH)];^{1}H NMR (CDCl$_3$, ppm): δ 7.84-7.28 (m, 30H, C$_6$**H**$_5$ and C$_6$**H**$_5$PO), 5.05 (m, 2H, C**H**OP), 4.08-3.94 (m, 8H, **C**$_5$H$_4$), 3.46-3.38 (m, 4H, C**H**$_2$Cp), 3.18-3.12 (m, 2H, C**H**$_2$NH (a)), 2.97-2.89 (m, 2H, C**H**$_2$NH (b)). ^{13}C NMR (CDCl$_3$, ppm): δ 142.15 (*J* = 14.8 Hz, *i*-**C**$_6$H$_5$PO), 141.93 (*i*-**C**$_6$H$_5$), 129.49, 129.05, 128.58, 128.49, 128.42, 128.39 (**C**$_6$H$_5$ and **C**$_6$H$_5$PO), 86.03 (*i*-**C**$_5$H$_4$), 81.92 (d, *J*= 20.6 Hz, **C**HOP), 68.67, 68.62, 68.51, 68,24 (**C**$_5$H$_4$), 56.66 (**C**H$_2$NH), 48.48 (**C**H$_2$Cp). ^{31}P-{^{1}H} NMR (CDCl$_3$, ppm): δ 112.79 (s, O**P**Ph$_2$). IR (KBr pellet in cm^{-1}) υ (N-H): 3360, (C=C-Cp): 1448, (O-P): 1014, (C-H): 3087, 3030, 2937, 2874. Anal. calcd. for $C_{52}H_{50}N_2O_2P_2Fe$: C, 73.23; H, 5.92; N, 3.29, found: C, 73.10; H, 5.75; N, 3.18 %.

2.4.7. (*R*)-bis[*N*-2-diphenylphosphinite-1-ethyl]-1,1'-ferrocenylmethyldiamine, (15).

Yield: 95 mg, (90%). $[\alpha]_D^{20}$ -42.8 (c 1.2, MeOH)]; ^{1}H NMR (CDCl$_3$, ppm): δ 7.80-7.27 (m, 20 H, C$_6$**H**$_5$PO), 3.89-4.09 (m, 8H, C$_5$**H**$_4$), 3.81-3.88 (m, 4H, C**H**$_2$OP), 3.53 (m, 4H, C**H**$_2$NH), 2.81(m, 2H, C**H**N), 1.59 (m, 4H, C**H**$_2$CH$_3$), 0.92 (t, 6H, *J*=7.4 Hz, CH$_2$C**H**$_3$). ^{13}C NMR (CDCl$_3$, ppm): δ 141.75 (d, *J*= 9.0 Hz, *i*-**C**$_6$H$_5$P), 130.54, 130.35, 130.32 (*o*-, *m*-, *p*- **C**$_6$H$_5$), 86.59 (*i*-**C**$_5$H$_4$), 71.21 (d, *J*= 18.1 Hz, **C**H$_2$OP), 68.91, 68.86, 68.45, 68.44 (**C**$_5$H$_4$), 59.32 (d, *J*= 8.0 Hz, **C**HN), 46.09 (**C**H$_2$NH), 24.03 (**C**H$_2$CH$_3$), 10.28 (CH$_2$**C**H$_3$). ^{31}P-{^{1}H} NMR (CDCl$_3$, ppm): δ

114.38 (s, O**P**Ph_2). IR (KBr pellet in cm^{-1}) υ (N-H): 3378, (C=C-Cp): 1438, (O-P): 1030, (C-H): 3072, 2959, 2928, 2873. Anal. calcd. for $C_{44}H_{50}N_2O_2P_2Fe$: C, 69.83; H, 6.67; N, 3.70, found: C, 69.70; H, 6.50; N, 3.58 %.

2.4.8. (1*S*,2*R*)-bis[*N*-2-diphenylphosphinite-1,2-diphenyl)ethyl]-1,1'-ferrocenylmethyldi-amine, (16).

Yield: 95 mg, (86 %). $[\alpha]_D^{20}$ +17.6 (c 1.2, MeOH)]; ^{1}H NMR ($CDCl_3$, ppm): δ 7.03-7.44 (m, 40H, C_6**H**$_5$P and C_6**H**$_5$), 4.94-4.86 (m, 2H, C**H**N), 4.09 (m, 2H, C**H**OP), 3.60-3.90 (m, 8H, C_5**H**$_4$), 3.18 (m, 2H, C**H**$_2$NH (a)), 2.98 (m, 2H, C**H**$_2$NH (b)), 1.35 (br, 2H, N**H**). ^{13}C NMR ($CDCl_3$, ppm): δ 141.65 (d, *J*= 19.4 Hz, *i*-**C**$_6$$H_5$PO), 139.87, 140.82 (*i*-C_6H_5,(a) and *i*-C_6H_5, (b)), 130.63, 130.41, 129.67, 128.86, 128.73, 128.60, 128.46, 128.38, 128.28 (**C**$_6$$H_5$PO and *i*-**C**$_6$$H_5$,(a) and *i*-**C**$_6$$H_5$), 87.35 (*i*-**C**$_5$$H_4$), 86.31 (d, *J*=19.1 Hz, (**C**HOP), 68.11, 67.99, 67.78, 67.72 (**C**$_5$$H_4$), 67.65 (s, **C**HN), 45.86 (**C**H_2NH). ^{31}P-{^{1}H} NMR ($CDCl_3$, ppm): δ 112.54 (s, O**P**Ph_2). IR (KBr pellet in cm^{-1}) υ(N-H): 3319, (C=C-Cp): 1451, (O-P): 1015, (C-H): 3068, 3057, 3027, 2925. Anal. calcd. for $C_{64}H_{58}N_2O_2P_2Fe$: C, 76.48; H, 5.83; N, 2.79, found: C, 76.38; H, 5.71; N, 2.72 %.

2.5. Synthesis of Rhodium complexes of the ferrocene based *C*$_2$-symmetric phosphinites (17-24)

2.5.1. (*S*)-bis[[*N*-2-diphenylphosphinite-1-benzyl)ethyl]-1,1'-ferrocenylmethyldiamine (chloro η^4-1,5-cyclooctadiene rhodium(I))], (17)

A solution of (*S*)-bis[*N*-2-diphenylphosphinite-1-benzyl)ethyl]-1,1'-ferrocenylmethyl diamine, **9** (176 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) was added dropwise to the solution of $[Rh(COD)Cl]_2$

(99 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) at -78 °C. The reaction mixture was warmed slowly to room temperature within 30 min, and stirred at this temperature for an additional 10 min. The resulting yellow solution was concentrated to 2 ml under reduced pressure, and addition of hexane (30 ml) caused the precipitation of a dark yellow solid. The supernatant solution was decanted, the solid was washed with hexane: diethylether (1:1) and dried by vacuum, yielding rhodium complex, **17**. Yield: 230 mg, 84%, m.p: 105-107 ^{o}C. ^{31}P-{^{1}H} NMR ($CDCl_3$, 162.0 MHz, ppm): 119.65 (d, J_{RhP} = 179.8 Hz). IR (KBr pellet in cm^{-1}): υ (NH): 3330, (CH): 3070, 3038, 2925, 2850, (C-C-Cp): 1457, (O-P): 1031; Anal. Calc. for [$C_{70}H_{78}N_2O_2P_2FeRh_2Cl_2$] (1373.88 g/mol): C 61.87, N 2.04, H 5.73; found: C 61.74, N 1.90, H 5.60 %.

2.5.2. (*S*)-bis[[*N*-2-diphenylphosphinite-1-phenyl)ethyl]-1,1'-ferrocenylmethyldiamine (chloro η^4-1,5-cyclooctadiene rhodium(I))], (18)

A solution of (*S*)-bis[*N*-2-diphenylphosphinite-1-phenyl)ethyl]-1,1'-ferrocenylmethyl diamine, **10** (171 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) was added dropwise to the solution of $[Rh(COD)Cl]_2$ (99 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) at -78 °C. The reaction mixture was warmed slowly to room temperature within 30 min, and stirred at this temperature for an additional 15 min. The resulting yellow solution was concentrated to 2 ml under reduced pressure, and addition of hexane (30 ml) caused the precipitation of a dark yellow solid. The supernatant solution was decanted, the solid was washed with hexane : diethylether (1:1) and dried by vacuum, yielding rhodium complex, **18**. Yield: 245 mg, 90%, m.p: 120-122 ^{o}C. ^{31}P-{^{1}H} NMR ($CDCl_3$, 162.0 MHz, ppm): 120.02 (d, J_{RhP} = 179.8 Hz). IR (KBr pellet in cm^{-1}): υ (N H): 3313, (CH): 3054, 3015, 2907, 2855, (C-C-Cp): 1426, (O-P): 1008; Anal. Calc. for

$[C_{68}H_{74}N_2O_2P_2FeRh_2Cl_2]$ (1345.82 g/mol): C 60.68, N 2.08, H 5.55; found: C 60.53, N 1.96, H 5.40 %.

2.5.3. (*S*)-bis[[*N*-2-diphenylphosphinite-1-*iso*-butyl)ethyl]-1,1'-ferrocenylmethyldiamine (chloro η^4-1,5-cyclooctadiene rhodium(I))], (19)

A solution of (*S*)-bis[*N*-2-diphenylphosphinite-1-*iso*-butyl)ethyl]-1,1'-ferrocenyl methyldiamine, **11** (163 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) was added dropwise to the solution of $[Rh(COD)Cl]_2$ (99 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) at -78 °C. The reaction mixture was warmed slowly to room temperature within 30 min, and stirred at this temperature for an additional 20 min. The resulting yellow solution was concentrated to 2 ml under reduced pressure, and addition of hexane (30 ml) caused the precipitation of a dark yellow solid. The supernatant solution was decanted, the solid was washed with hexane:diethylether (1:1) and dried by vacuum, yielding rhodium complex, **19**. Yield: 215 mg, 82%, m.p: 115-117 °C. $^{31}P-\{^1H\}$ NMR ($CDCl_3$, 162.0 MHz, ppm): 119.03 (d, J_{RhP}=179.8 Hz). IR (KBr pellet in cm^{-1}): υ (N-H): 3335, (CH): 3075, 2966, 2960, 2872, (C-C-Cp): 1441, (O-P): 1026; Anal. Calc. for $[C_{64}H_{82}N_2O_2P_2FeRh_2Cl_2]$ (1305.84 g/mol): C 58.86, N 2.15, H 6.34; found: C 58.72, N 2.08, H 6.20 %.

2.5.4. (*S*)-bis[[*N*-2-diphenylphosphinite-1-*sec*-butyl)ethyl]-1,1'-ferrocenylmethyldiamine (chloro η^4-1,5-cyclooctadiene rhodium(I))], (20)

A solution of (*S*)-bis[*N*-2-diphenylphosphinite-1-*sec*-butyl)ethyl]-1,1'-ferrocenylmethyldiamine, **12** (163 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) was added dropwise to the solution of $[Rh(COD)Cl]_2$ (99 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) at -78 °C. The reaction mixture was warmed slowly to room temperature within 30 min, and stirred at this temperature for an

additional 20 min. The resulting yellow solution was concentrated to 2 ml under reduced pressure, and addition of hexane (30 ml) caused the precipitation of a dark yellow solid. The supernatant solution was decanted, the solid was washed with hexane : diethylether (1:1) and dried by vacuum, yielding rhodium complex, **20**. Yield: 230 mg, 87%, m.p: 112-114 ^{o}C. ^{31}P {^{1}H}-NMR ($CDCl_3$, 162.0 MHz, ppm): 119.64 (d, J_{RhP}=178.2 Hz). IR (KBr pellet in cm^{-1}): υ (N-H): 3327, (CH): 3070, 2964, 2915, 2876, (C-C-Cp): 1455, (O-P): 1020; Anal. Calc. for [$C_{64}H_{82}N_2O_2P_2FeRh_2Cl_2$] (1305.84 g/mol): C 58.86, N 2.15, H 6.34; found: C 58.68, N 2.02, H 6.15 %.

2.5.5. (*S*)-bis[[*N*-2-diphenylphosphinite propyl]-1,1'-ferrocenylmethyldiamine(chloro η^4-1,5-cyclooctadiene rhodium(I))], (21)

A solution of (*S*)-bis[*N*-2-diphenylphosphinite propyl]-1,1'-ferrocenylmethyldiamine, **13** (146 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) was added dropwise to the solution of $[Rh(COD)Cl]_2$ (99 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) at -78 °C. The reaction mixture was warmed slowly to room temperature within 30 min, and stirred at this temperature for an additional 10 min. The resulting yellow solution was concentrated to 2 ml under reduced pressure, and addition of hexane (30 ml) caused the precipitation of a dark yellow solid. The supernatant solution was decanted, the solid was washed with hexane : diethylether (1:1) and dried by vacuum, yielding rhodium complex, **21**. Yield: 208 mg, 85%, m.p: 121-123 ^{o}C. ^{31}P-{^{1}H} NMR ($CDCl_3$, 162.0 MHz, ppm): 118.2 (d, J_{RhP} = 174.96 Hz). IR (KBr pellet in cm^{-1}): υ (N H): 3328, (CH): 3080, 2974, 2945, 2876, (C-C-Cp): 1455, (O-P): 1030; Anal. Calc. for [$C_{58}H_{70}N_2O_2P_2FeRh_2Cl_2$] (1221.68 g/mol): C 57.01, N 2.29, H 5.79; found: C 56.78, N 2.10, H 5.55 %.

2.5.6. (*R*)-bis[[*N*-2-diphenylphosphinite-2-phenyl]-1,1'-ferrocenylmethyldiamine(chloro η^4-1,5-cyclooctadiene rhodium(I))], (22)

A solution of (*R*)-bis[*N*-2-diphenylphosphinite-2-phenyl]-1,1'-ferrocenylmethyl diamine, **14** (171 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) was added dropwise to the solution of $[Rh(COD)Cl]_2$ (99 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) at -78 °C. The reaction mixture was warmed slowly to room temperature within 30 min, and stirred at this temperature for an additional 20 min. The resulting yellow solution was concentrated to 2 ml under reduced pressure, and addition of hexane (30 ml) caused the precipitation of a dark yellow solid. The supernatant solution was decanted, the solid was washed with hexane : diethylether (1:1) and dried by vacuum, yielding rhodium complex, **22**. Yield: 240 mg, 89%, m.p: 130-132 °C. $^{31}P-\{^1H\}$ NMR ($CDCl_3$, 162.0 MHz, ppm): 119.94 (d, J_{RhP} = 178.2 Hz). IR (KBr pellet in cm^{-1}): υ (NH): 3325, (CH): 3074, 2974, 2918, 2876, (C-C-Cp): 1445, (O-P): 1030; Anal. Calc. for $[C_{68}H_{74}N_2O_2P_2FeRh_2Cl_2]$ (1345.82 g/mol): C 60.68, N 2.08, H 5.55; found: C 60.48, N 1.86, H 5.36 %.

2.5.7. (*R*)-bis[[*N*-2-diphenylphosphinite-1-ethyl]-1,1'-ferrocenylmethyldiamine(chloro η^4-1,5-cyclooctadiene rhodium(I))], (23)

A solution of (*R*)-bis[*N*-2-diphenylphosphinite-1-ethyl]-1,1'-ferrocenylmethyldiamine, **15** (151 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) was added dropwise to the solution of $[Rh(COD)Cl]_2$ (99 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) at −78 °C. The reaction mixture was warmed slowly to room temperature within 30 min, and stirred at this temperature for an additional 10 min. The resulting yellow solution was concentrated to 2 ml under reduced pressure, and addition of hexane (30 ml) caused the precipitation of a dark yellow solid. The supernatant solution was decanted, the solid was washed with hexane : diethylether (1:1) and dried by vacuum, yielding rhodium complex, **23**

Yield: 220 mg, 88%; m.p:124-126 °C. ^{31}P-{^{1}H} NMR ($CDCl_3$, 162.0 MHz, ppm): 119.21 (d, J_{RhP}=175.0 Hz). IR (KBr pellet in cm^{-1}): υ (N H): 3320, (CH): 3090, 2954, 2935, 2879, (C C-Cp): 1454, (O-P): 1022; Anal. Calc. for [$C_{60}H_{74}N_2O_2P_2FeRh_2Cl_2$] (1249.74 g/mol): C 57.65, N 2.24, H 5.98; found: C 57.40, N 1.96, H 5.58 %.

2.5.8. (1*S*,2*R*)-bis[[*N*-2-diphenylphosphinite-1,2-diphenyl)ethyl]-1,1'-ferrocenylmethyldi-amine(chloroη^4-1,5-cyclooctadiene rhodium(I))], (24)

A solution of (1*S*,2*R*)-bis[*N*-2-diphenylphosphinite-1,2-diphenyl)ethyl]-1,1'-ferrocenyl methyldiamine, **16** (201 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) was added dropwise to the solution of $[Rh(COD)Cl]_2$ (99 mg, 0.20 mmol) in CH_2Cl_2 (15 ml) at -78 °C. The reaction mixture was warmed slowly to room temperature within 60 min, and stirred at this temperature for an additional 30 min. The resulting yellow solution was concentrated to 2 ml under reduced pressure, and addition of hexane (30 ml) caused the precipitation of a dark yellow solid. The supernatant solution was decanted, the solid was washed with hexane : diethylether (1:1) and dried by vacuum, yielding rhodium complex, **24**. Yield: 270 mg, 90%, m.p:136-138 °C. ^{31}P-{^{1}H} NMR ($CDCl_3$, 162.0 MHz, ppm): 117.72 (d, J_{RhP}= 176.6 Hz). IR (KBr pellet in cm^{-1}): υ (NH): 3367, (CH):3078, 3008, 2917, 2870, (C-C-Cp): 1458, (O-P): 1023; Anal. Calc. for [$C_{80}H_{82}N_2O_2P_2FeRh_2Cl_2$] (1498.02 g/mol): C 64.13, N 1.87, H 5.53; found: C 63.74, N 1.60, H 5.35 %.

3. Results and discussion

3.1. Synthesis and characterization of the amino alcohols, C_2-symmetric ferrocenyl-phosphinites and their rhodium(I) complexes

The synthetic strategy and reaction conditions adopted in this work are described in Scheme 1. We first established an easy methodology for the synthesis of ferrocene-1,1'-dicarboxyaldehyde based, in part, on conditions reported by Pelinski and Mueller-Westerhoff [xlix]. Following the references, tetramethylethylenediamine (TMEDA) (5.32 ml, 35.4 mmol) was added to a solution of ferrocene (3.00 g., 16.2 mmol) in dry *n*-hexane and the suspension was stirred for 5 min under argon. *n*-BuLi (22 ml, 35.4 mmol, 1.7 M in hexane) was added dropwise with a syringe. The mixture was left to stirring at room temperature overnight. After stirring at -78 ºC for 15 min, THF followed by anhydrous DMF were added to the reaction mixture. The solution was quenched with brine and CH_2Cl_2. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 30ml). The combined organic layers were dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified through column chromatography giving the ferrocene-1,1'-dicarboxaldehyde as bright red crystalline solid in third fraction (Scheme 1). Subsequently, in separate experiments, ferrocene-1,1'-dicarboxyaldehyde was reacted with commercially available L-phenyl alaninol, L-phenyl glycinol, L-leucinol, L-isoleucinol, (*S*)-(+)-1-amino-2-propanol, (*R*)-(-)-2-amino-1-phenylethanol, (*R*)-(-)-2-amino-1-butanol or (1S,2*R*)-(+)-2-amino-1,2-diphenylethanol in the presence of molecular sieves, and reduction of the crude reactions mixtures with $NaBH_4$ in methanol provided the corresponding enantimerically pure ferrocene based amino alcohols, **1-8** in good yields (60-88 %). The ^1H NMR spectra of compounds **1-8** show characteristic features: the α- and β-cyclopentadienyl (Cp) protons in the amino alcohols with relatively small non-resolved multiplets appear approximately at δ 4.00 ppm The magnetic non-equivalence of the monosubstituted Cp ring was observed, which is caused by their planar structure. The ^{13}C-{^1H} NMR spectra also exhibit the typical signals for substituted ferrocenes. All ^1H NMR and ^{13}C NMR spectra were given in SI (for

details see experimental section and supporting information). The structures for these ferrocene based chiral amino alcohols are consistent with the data obtained from IR spectroscopy and elemental analysis.

Insert Scheme 1 Here

The synthetic procedure for the preparation of the ligands is shown in Scheme 1. Chiral C_2-symmetric phosphinite ligands based on ferrocenyl group, **9-16** were synthesized by hydrogen abstraction from the described ferrocene based chiral amino alcohols **1-8**, by a base (Et_3N) and the subsequent reaction with two equivalents of Ph_2PCl, in anhydrous toluene under inert argon atmosphere. The progress of these reactions was conveniently followed by ^{31}P-{^1H} NMR spectroscopy. The signal of the starting material PPh_2Cl at δ 81.0 ppm disappeared and new singlets appeared downfield due to the C_2-symmetric ferrocenyl phosphinite ligands. Both of the phosphorus atoms are equivalent in each ligand and exhibit singlets approximately at 107-114 ppm, and the ^{31}P-{^1H} NMR spectra of the free ligands are [l] in line with the values previously observed for similar compounds [li,lii,liii]. Solution of the ligands in $CDCl_3$ and in air, prepared under anaerobic condition, is stable (up to 36 h) and decomposes very slowly gradually to give oxide and the hydrolysis product diphenylphosphinous acid, $Ph_2P(O)H$ [liv]. Furthermore, the ^{31}P-{^1H} NMR spectrum also displays formation of PPh_2PPh_2 and $P(O)Ph_2PPh_2$, as indicated by signals at about δ -15.6 ppm as singlet and δ 35.4 ppm and δ -21.8 ppm as doublets with $^1J_{(PP)}$ 220 Hz, respectively, after the 72 h [lv]. The assignment of the ^1H chemical shifts was derived

from 2D HH-COSY spectra and the appropriate assignment of the ^{13}C chemical shifts from DEPT and 2D HMQC spectra. Furthermore, IR spectra and C, H, N elemental analyses are in agreement with the proposed structures for C_2-symmetric ferrocenyl phosphinite ligands. Typical spectra of these ligands are illustrated in SI.

Rhodium complexes of these new ligands were prepared as indicated in experimental section and illustrated in Scheme 1. Complexation reactions were straightforward, with coordination to rhodium being carried out at room temperature. All the rhodium complexes were readily synthesized in good yields and the whole reactions resulting **17-24** are depicted in Scheme 1. Treatment of $[Rh(\mu\text{-}Cl)(cod)]_2$ with C_2-symmetric ferrocenyl phosphinite ligands **9-16** in 1:1 molar ratio in toluene resulted in the formation of dinuclear complexes **17-24** as crystalline air stable solids. The C_2-symmetric ferrocenyl phosphinites were expected to cleave the $[Rh(\mu\text{-}Cl)(cod)]_2$ dimer to give the corresponding complexes, **17-24** via monohapto coordination of the phosphinite group. Furthermore, the reactions between rhodium(I) precursor and ferrocenyl-phosphinites are not affected by the molar ratio of $[Rh(\mu\text{-}Cl)(cod)]_2$ as well as the steric and electronic properties of the donor phosphorus atoms. The initial color change was attributed to the dimer cleavage most probably by the C_2-symmetric ferrocenyl phosphinite ligand. All the complexes were isolated as indicated by doublets in the $^{31}P\text{-}\{^1H\}$ NMR spectra at approximately δ 120 ppm (d, $^1J_{RhP}$: 178-180 Hz), in line with the values previously observed for similar compounds [lvi,[lvii]] with a coordination shift of approximately δ 8.0 ppm (see SI) attributed to formation of the corresponding C_2-symmetric ferrocenyl phosphinites. Interestingly, ^1H NMR spectra of these complexes are featured by very broad signals at room temperature. Upon lowering the temperature to -80 ºC, the signals remain unresolved; hence their clear assignment cannot be accomplished. Elemental analyses of the complexes are also consistent with the

suggested molecular formulas. The absorption bands corresponding to Rh(I)-C_2-symmetric ferrocenyl phosphinite complexes in the IR spectra do not exhibit significant differences with respect to those of free ligands (see SI and experimental section).

3.2. Rh(I)-catalyzed asymmetric transfer hydrogenation of ketones using *iso*PrOH and base

In the studies of Asymmetric Transfer Hydrogenation, the *iso*PrOH/base [lviii,lix,lx,lxi] and formic acid/triethylamine [lxii,lxiii] system has long been used as a source of hydrogen. We preferred to examine the asymmetric transfer hydrogenation of simple ketones by using a *iso*PrOH/base system in the presence of a catalytic amount of Rh(I)-C_2-symmetric ferrocenyl ligands (**17-24**). In a preliminary study, complexes **17-24** were tested as precursors for the catalytic asymmetric transfer hydrogenation of acetophenone and the results are summarized in Table 1. A typical procedure using acetophenone as substrate was as follows. 0.01 mmol of the complex and 1 mmol of acetophenone were added to a solution of NaOH in *iso*PrOH (0.05 mmol of NaOH in 10 mL *iso*PrOH) and refluxed at 82 ºC, while the reaction was monitored by GC. In all reactions, these complexes catalyzed the reduction of ketones to the corresponding alcohols via hydrogen transfer from *iso*PrOH. A comparison of complexes **17-24** as precatalysts for the asymmetric hydrogenation of acetophenone by *iso*PrOH is given in Table 1. Catalytic experiments were carried out under inert (Ar) atmosphere using standard Schlenk-line techniques. These systems catalyzed the reduction of acetophenone to corresponding alcohol ((*S*)-, (*R*)-1-phenylethanol) in the presence of NaOH.

At room temperature, transfer hydrogenation of acetophenone occurred very slowly [lxiv], with low conversions (up to 52 %, 48 h) and moderate to high enantioselectivities (up to 96 % ee) in

the reactions (Table 1, entries 1-8). Because of the reversibility at room temperature the prolonging the reaction time (96 h) led to a slight decreasing of enantioselectivity, as indicated by the catalytic results collected with catalyst, **22** (Entry 6, [b]) [lxv,lxvi]. Furthermore, as can be inferred from the Table 1 (Entries 9-16), the presence of base is necessary to observe appreciable conversions. It is well-known that the base facilitates the formation of rhodium alkoxide by abstracting proton of the alcohol and subsequently alkoxide undergoes *β*-elimination to give metal hydride, which is an active species in this reaction [lxvii,lxviii,lxix,lxx]. Namely, role of the base is to generate a more nucleophilic alkoxide ion which would rapidly attack the rhodium complex responsible for dehydrogenation of *iso*PrOH. In addition, the choice of base, such as KOH and NaOH, had little influence on the conversion and enantioselectivity (Table 1, entry 22,[e]) and with a catalyst/NaOH ratio of 1/5, the complexes are very active leading to a quantitative transformation of the acetophenone (Table 1, entries 25-28,[f]).

Insert Table 1 Here

Insert Table 2 Here

Reduction of acetophenone into (*S*)- or (*R*)-1-phenylethanol could be achieved in high yield by increasing the temperature up to 82 ^{o}C (Table 1, entries 17-24). Furthermore, the conversions

gradually decreased with increasing the mole ratios of [acetophenone]/[Rh] from 250/1 to 500/1 or 1000/1, except the time lengthened, the enantioselectivities were still high (up to 92% ee, table 2, entries 1-9). Namely, the ee's remained unchanged when the molar ratios of substrate to catalyst were increased and these C_2-phosphinite ligands with ferrocenyl moiety show much higher activity and high enantioselectivity. Similar tendency was reported in earlier studies [lxxi,lxxii], indicating that these kind of ligands play an important role in metal-ligand catalytic system [lxxiii,lxxiv]. Furthermore, it is noteworthy that the catalytic systems, **17-24** display the differences in reactivity. These results indicate that the structural difference of the C_2-ferrocenyl phosphinite ligands is a crucial factor for catalytic activity. It was seen that when the chiral center is near the rhodium center, the % ee is high. So, from the results, one can say that complexes **21**, **22** and **24** were effective catalysts for the hydrogenation of acetophenone, yielding products up to 96% ee. It has also been shown that the catalytic activities in the studied hydrogen transfer reactions were generally much higher for Rh(I)-(*R*)-bis[*N*-2-diphenylphosphinite-2-phenyl]-1,1'-ferrocenylmethyldiamine, **22** than for the other complexes. Furthermore, aryl moiety (complex **22** and **24**) is more responsible for high activity than alkyl moiety (complexes **17-20** and **23**). This different behavior in enantioselectivity can be explained on the basis of aromatic moiety (phenyl) attaches to chiral carbon center in the ligand backbone enabling the optimization molecular rigidity. These results have also shown that enantiomeric purity of the product can be affected by electronic factors, and steric factors of the substituents on the ligands. As seen from Tables, the catalytic activities in the studied hydrogen transfer reactions were generally much higher for the **21, 22** and **24** than those for the other complexes

Insert Table 3 Here

In order to check the application range of the rhodium-catalyzed transfer hydrogenation, acetophenone derivatives were subjected to asymmetric reduction using the conditions optimized for acetophenone. Table 3 illustrates conversions of the reduction performed in a 0.1 M of *iso*PrOH solution containing **21, 22** and **24** and NaOH (Ketone:Cat.:NaOH = 100:1:5). The results demonstrate that a range of acetophenone derivatives can be hydrogenated with high enantioselectivities. Substitution of the phenyl ring of the acetophenone substrate led to a marked decrease in the catalytic activity and % ee. That's to say, electronic properties (the nature and position) of the substituents on the phenyl ring of the ketone caused the changes in the reduction rate. The introduction of electron withdrawing substituents to the *para* position of the aryl ring of the ketone decreased the electron density of the C=O bond so that the activity was improved resulting in easier hydrogenation [lxxv,lxxvi] As expected, the lowest enantioselectivity was observed in transfer hydrogenation of *p*-methoxyacetophenone. From the results, it is obvious that the introduction of an electron-donating group such as methoxy group to the *p*-position decelerates the reaction, but that to the *o*-position increases the rate and improves the enantioselectivity. On the contrary, the introduction of electron-withdrawing substituents, such as F or NO_2, to the *para* positions of the aryl ring of the ketone, resulted in improved activity with good enantioselectivity (Table 3, entries 1-3 and 10-12). The examination of the results indicates clearly that with each of the tested complexes, the highest enantioselectivity was found for *o*-methoxyacetophenone (99% ee) when Rh(I)-(*R*)-bis[*N*-2-diphenylphosphinite-2-phenyl]-1,1'-ferrocenylmethyldiamine, **22** was used as the catalyst precursor.

4. Conclusions

In summary, we have developed a new class of C_2-symmetric ferrocenyl phosphinite ligands, which exhibited excellent enantiselectivities in the rhodium(I)-catalyzed asymmetric transfer hydrogenation of aromatic ketones (up to 97% ee). This type of ligands has salient features such as cheap starting materials and facile preparation, structural tunability, as well as remote stereocontrol capability of backbone substituents. The chirality of carbon center in the ligand backbone is of particular importance for asymmetric induction offering an obvious target for further optimization. The simplicity and efficiency clearly make it an excellent choice of catalyst for practical preparation of invaluable alcohols via catalytic asymmetric transfer hydrogenation of aromatic ketones. Furthermore, the development of a practical synthesis of C_2-symmetric ferrocenyl phosphinites and demonstration that they are competent auxiliaries for catalysis open up a neglected vein in the rich chemistry of phosphorus ligands. Further work on modifying the ligand structure for improvement of the enantioselectivity as well as broadening the substrate scope of the asymmetric transfer hydrogenation (ATH) is undergoing in this lab.

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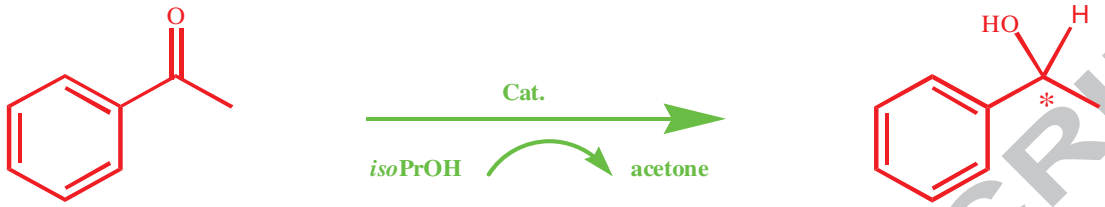
Captions

Scheme 1 *Reagents and conditions (i) n*-BuLi, TMEDA, - 78 °C, THF, DMF; *(ii)* L-phenyl alaninol, L-phenyl glycinol, L-leucinol, L-isoleucinol, (*S*)-(+)-1-amino-2-propanol, (*R*)-(-)-2-amino-1-phenylethanol,

(*R*)-(-)-2-amino-1-butanol or (1S,2*R*)-(+)-2-amino-1,2-diphenylethanol*;* $NaBH_4$, MeOH for **1-8**; *(iii)* 2 equiv. Ph_2PCl, 2 equiv. Et_3N, for **9-16** *(iv)* 1 equiv. $[Rh(\mu\text{-}Cl)(cod)]_2$, for **17-24**.

Table 1. Asymmetric Transfer hydrogenation of acetophenone with *iso*PrOH catalyzed by Rh-C_2-symmetric ferrocenyl monodendate phosphinite complexes (**17-24**).



Entry	Complex	S/C/Base	Time	Conv.(%)[g]	% ee[h]	Config.[i]	TOF(h^{-1})[k]
1	17[a]	100:1:5	48 h	48	64	*R*	<3
2	18[a]	100:1:5	48 h	44	71	*S*	<3
3	19[a]	100:1:5	48 h	50	52	*R*	<3
4	20[a]	100:1:5	48 h	52	55	*S*	<3
5	21[a]	100:1:5	48 h	41	80	*S*	<3
6	22[a]	100:1:5	48 h (96 h)[b]	32(36)[b]	96(92)[b]	*R*	<3
7	23[a]	100:1:5	48 h	45	57	*R*	<3
8	24[a]	100:1:5	48 h	30	88	*R*	<3
9	17[c]	100:1	24 h	<10	...	...	trace
10	18[c]	100:1	24 h	<10	...	...	trace
11	19[c]	100:1	24 h	<10	...	...	trace
12	20[c]	100:1	24 h	<10	...	...	trace
13	21[c]	100:1	24 h	<10	...	...	trace
14	22[c]	100:1	24 h	<10	...	...	trace

15	**23[c]**	**100:1**	**24 h**	**<10**	**…**	**…**	**trace**
16	**24[c]**	**100:1**	**24 h**	**<10**	**…**	**…**	**trace**
17	**17[d]**	**100:1:5**	**1 h**	**98**	**67**	***R***	**98**
18	**18[d]**	**100:1:5**	**1 h**	**97**	**73**	***S***	**97**
19	**19[d]**	**100:1:5**	**1 h**	**95**	**56**	***R***	**95**
20	**20[d]**	**100:1:5**	**1 h**	**96**	**58**	***S***	**96**
21	**21[d]**	**100:1:5**	**2 h**	**97**	**84**	***S***	**49**
22	**22[d]**	**100:1:5**	**3 h (3 h)[e]**	**98(96)[e]**	**98(93)[e]**	***R***	**33(32)**
23	**23[d]**	**100:1:5**	**1 h**	**98**	**60**	***R***	**98**
24	**24[d]**	**100:1:5**	**3 h**	**99**	**91**	***R***	**33**
25	**22[f]**	**100:1:3**	**3 h**	**99**	**94**	***R***	**33**
26	**22[f]**	**100:1:5**	**3 h**	**98**	**98**	***R***	**33**
27	**22[f]**	**100:1:7**	**3 h**	**98**	**93**	***R***	**33**
28	**22[f]**	**100:1:9**	**3 h**	**97**	**92**	***R***	**32**

Reaction conditions

[a] At room temperature; acetophenone/Rh/NaOH,100:1:5,

[b] At room temperature; acetophenone/Rh/NaOH, 100:1:5, (96 h)

[c] Refluxing in *iso*-PrOH; acetophenone/Rh, 100:1, in the absence of base,

[d] Refluxing in *iso*-PrOH; acetophenone/Rh/NaOH, 100:1:5,

[e] Refluxing in *iso*-PrOH; acetophenone/Rh/KOH, 100:1:5,

[f] Refluxing in *iso*-PrOH; acetophenone/Rh/NaOH, 100:1:5,

[g] Determined by GC (three independent catalytic experiments),

[h] Determined by capillary GC analysis using a chiral cyclodex B (Agilent) capillary column,

[i] Determined by comparison of the retention times of the enantiomers on the GC traces with literature values, (*S)* or (*R)* configuration was obtained in all experiments,

[k] TOF = (mol product/mol Cat.) x h^{-1}.

Table 2 Transfer hydrogenation of acetophenone with *iso*PrOH catalyzed by Rh-ferrocenyl based C_2-symmetric monodendate phosphinite complexes (**21, 22** and **24**).

Entry	Catalyst	S/C/KOH	Time	Conv.(%)[b]	% ee[c]	Config.[d]	TOF(h^{-1})[e]
1	21	250:1:5	4 h	98	81	*S*	25

2	**22**	**250:1:5**	**5 h**	**99**	**95**	***R***	**20**
3	**24**	**250:1:5**	**5 h**	**99**	**90**	***R***	**20**
4	**21**	**500:1:5**	**6 h**	**99**	**79**	***S***	**17**
5	**22**	**500:1:5**	**8 h**	**98**	**93**	***R***	**12**
6	**24**	**500:1:5**	**8 h**	**98**	**88**	***R***	**12**
7	**21**	**1000:1:5**	**10 h**	**99**	**78**	***S***	**10**
8	**22**	**1000:1:5**	**12 h**	**99**	**94**	***R***	**<10**
9	**24**	**1000:1:5**	**13 h**	**98**	**89**	***R***	**<10**

Reaction conditions

[a] Refluxing in *iso*PrOH; acetophenone/Rh/NaOH, 250, 500 or 1000:1:5.

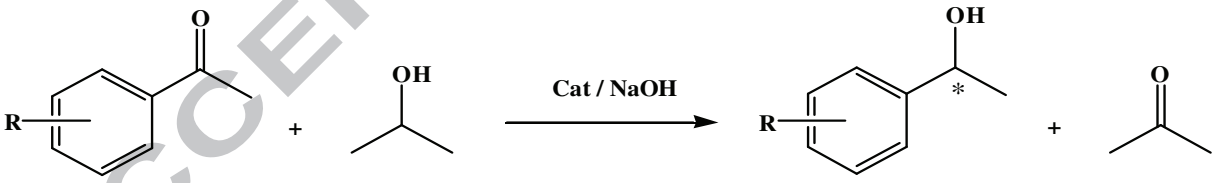
[b] Determined by GC (three independent catalytic experiments),

[c] Determined by capillary GC analysis using a chiral cyclodex B (Agilent) capillary column,

[d] Determined by comparison of the retention times of the enantiomers on the GC traces with literature values, (*S)* or (*R)* configuration was obtained in all experiments,

[e] TOF = (mol product/mol Cat.) x h^{-1}.

Table 3 Asymmetric Transfer Hydrogenation results for substituted acetophenones catalyzed by Rh-ferrocenyl based C_2-symmetric monodendate phosphinite complexes, (1**7-20**).[a]



Entry	Catalyst	R	Time	Conv.(%)[b]	ee (%)[c]	TOF (h^{-1})[d]	Config.[e]
1	21		1/4 h	97	86	388	*S*

2	22	F	1/4 h	98	91	392	*R*
3	24		1/3 h	99	84	297	*R*
4	21		1/3 h	98	84	297	*S*
5	22	Cl	1/3 h	99	90	196	*R*
6	24		1/2 h	98	82	196	*R*
7	21		1/3 h	99	85	297	*S*
8	22	Br	1/3 h	99	89	297	*R*
9	24		1/2 h	98	82	196	*R*
10	21		1/4 h	98	87	392	*S*
11	22	NO_2	1/4 h	99	90	396	*R*
12	24		1/3 h	98	81	294	*R*
13	21		1/2 h	98	93	196	*S*
14	22	2-CH_3O	1/2 h	99	99	198	*R*
15	24		1 h	99	83	99	*R*
16	21		1 h	98	78	98	*S*
17	22	4-CH_3O	1 h	98	85	98	*R*
18	24		2 h	99	77	49	*R*

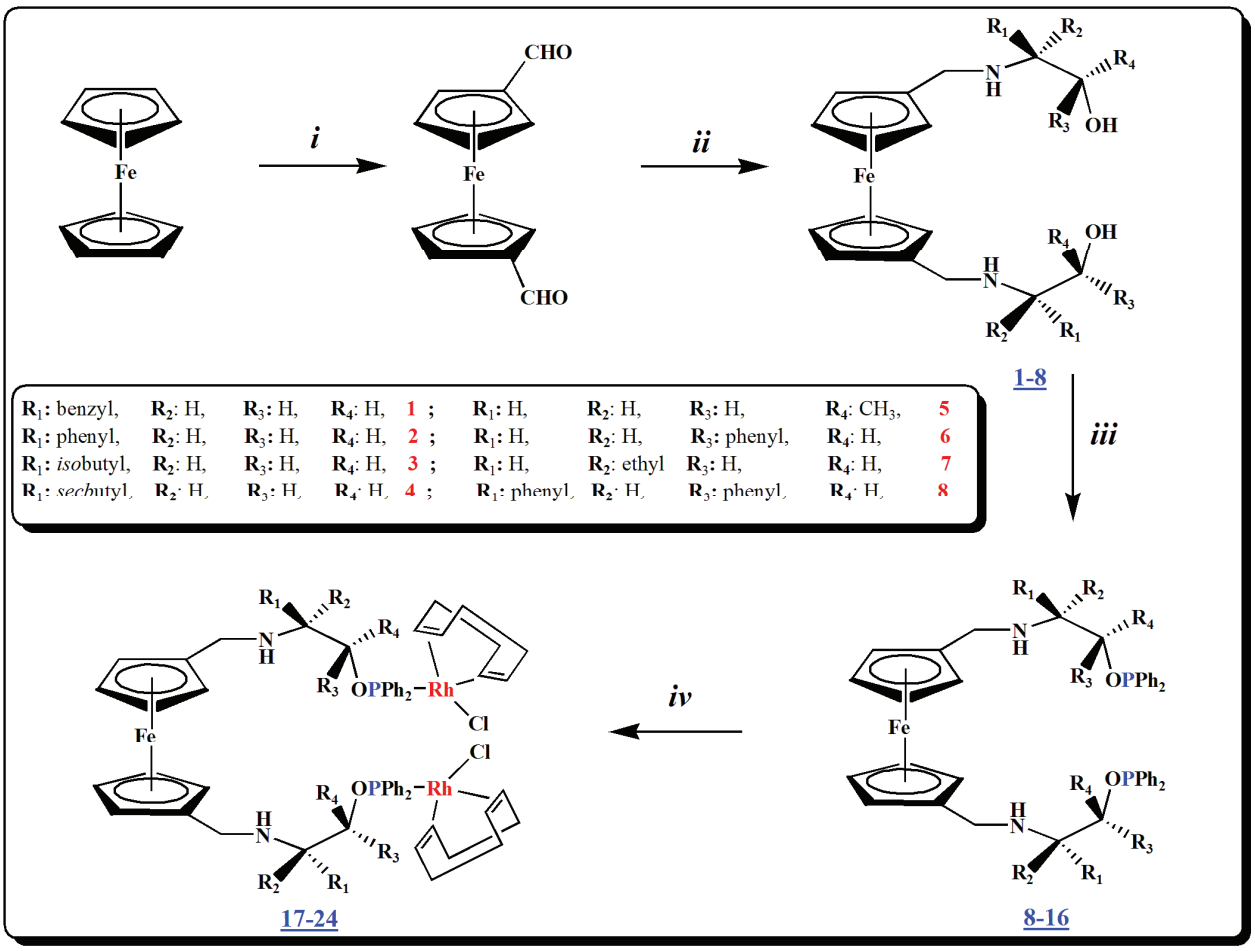
[a] Catalyst (0.005 mmol), substrate (0.5 mmol), *iso*PrOH (5 mL), NaOH (0.025 mmol %), 82 ℃, the concentration of acetophenone derivatives are 0.1 M,

[b] Purity of compounds is checked by ^{1}HNMR and GC (three independent catalytic experiments), yields are based on aryl ketone,

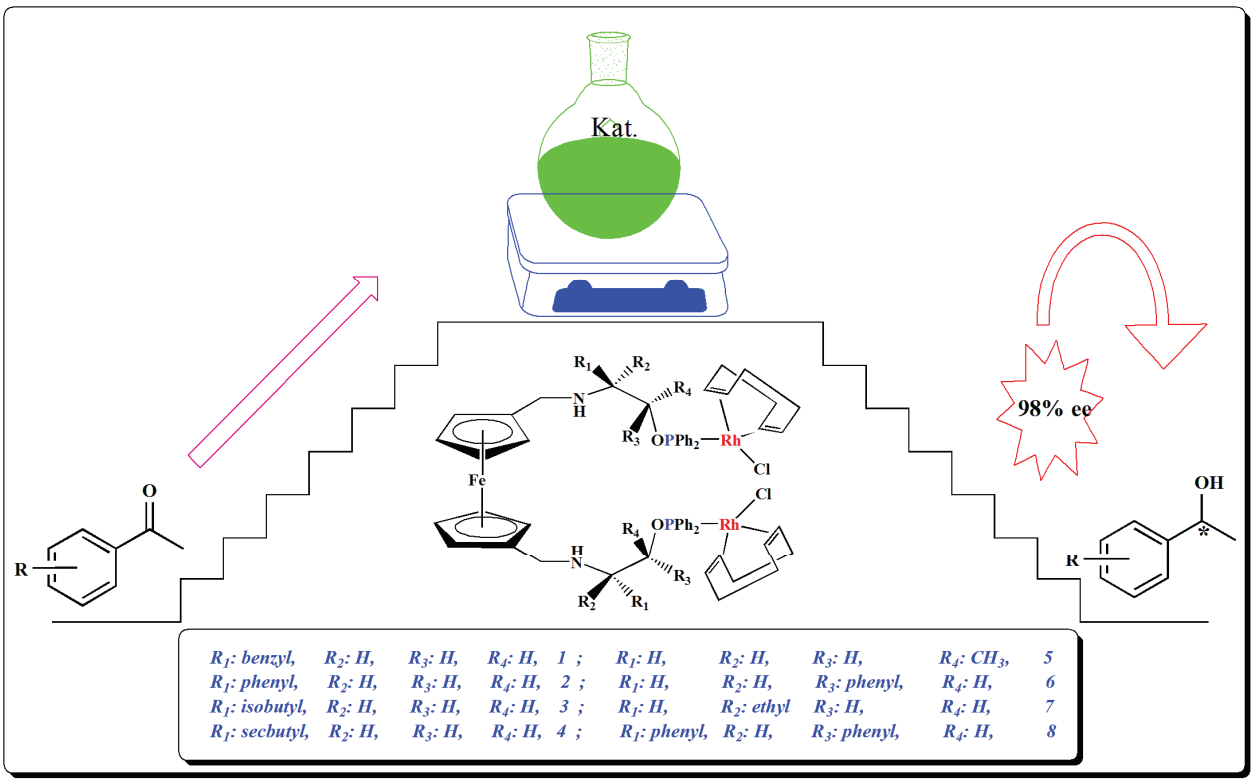
[c] Determined by capillary GC analysis using a chiral cyclodex B (Agilent) capillary column (30 m x 0.32 mm I.D. x 0.25µm film thickness),

[d] TOF = (mol product/mol Cat.) x h^{-1},

[e] Determined by comparison of the retention times of the enantiomers on the GC traces with literature



Scheme 1



Graphical Abstract(pictogram)

A new class of chiral C_2-symmetric ferrocenyl phosphinite ligands has been prepared by using the inexpensive 1,1'-ferrocenedicarboxyaldehyde and various ferrocene based-amino alcohols as starting materials, and applied in the rhodium(I)-catalyzed asymmetric transfer hydrogenation of ketones to give corresponding secondary alcohols using *iso*PrOH as the hydrogen source. Rh complexes of these ligands showed excellent enantioselectivities and reactivities in the transfer hydrogenation of ketones (up to 99% conversion and 99% ee).

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RESEARCH HIGHLIGHTS

- A series of chiral C_2-symmetric ferrocenyl phosphinite ligands was prepared in good yields by using 1,1'-ferrocenedicarboxyaldehyde and ferrocene based-amino alcohols as starting materials.

- They were applied in the rhodium(I)-catalyzed asymmetric transfer hydrogenation (ATH) of aromatic ketones to give corresponding secondary alcohols using *iso*PrOH as the hydrogen source.

- Up to 99% conversion and 99% ee were achieved with these catalytic systems.

- The substituents on the backbone of the ligands exhibit a remarkable effect on both the activity and % ee.