Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 18 (2007) 1893–1898

[5]Ferrocenophane based ligands for stereoselective Rh-catalyzed hydrogenation and Cu-catalyzed Michael addition

Ambroz Almássy,[a] Katalin Barta,[b] Giancarlo Franciò,[b] Radovan Šebesta,[a,*] Walter Leitner[b,*] and Štefan Toma[a]

[a]*Department of Organic Chemistry, Faculty of Natural Sciences, Comenius University, Mlynska dolina, 84215 Bratislava, Slovakia*
[b]*Institute for Technical and Macromolecular Chemistry, RWTH Aachen, Worringerweg 1, 52074 Aachen, Germany*

Received 8 May 2007; accepted 10 August 2007

Abstract—A series of homochiral [5]ferrocenophane based N/P, N/S, N/Se, Se/P and P/P ligands was prepared from (*R*)-*N*,*N*-dimethylamino[5]ferrocenophane. These ligands were tested in the Rh-catalyzed hydrogenation of dimethyl itaconate and in Cu-catalyzed Michael addition of Et_2Zn to cyclohex-2-enone. The best results in terms of conversion and enantioselectivity in the Rh-catalyzed hydrogenation provided bis(diphenylphosphine) ligand **2h** (100% conversion and 95% ee) and aminophosphine **2a** in the Cu-catalyzed conjugate addition (100% conversion 84% ee). The enantioselectivity of the Rh-catalyzed hydrogenation of methyl 2-acetamidoacrylate was lower (41% ee).

1. Introduction

Ferrocenyl derivatives represent one of the most prominent classes among chiral ligands. The structure of these compounds allows the incorporation of different elements of chirality in the molecule.[1] Since the first synthesis of a homochiral bidentate P/N ligand by Hayashi and Kumada[2] these have found numerous applications in a variety of transition metal-catalyzed asymmetric reactions. Several comprehensive reviews cover their utility in asymmetric catalysis.[3–7] In particular, ferrocenyl phosphines were successfully applied in Rh-catalyzed asymmetric hydrogenation reactions.[8–11] Ferrocenyl diphosphines and amino phosphines were also recently found to be suitable ligands for the Cu-catalyzed conjugate addition of organometallic reagents to α,β-unsaturated carbonyl compounds.[12–15] Josiphos-type diphosphines (Fig. 1), introduced by Togni[16] are the most outstanding exponents of ferrocene ligands because of their high versatility as well as efficiency and have been included in the selection of privileged ligand structures.[17] Josiphos-type ligands have also found application in the industrial production of Metolachlor, dihydrojasmonate and biotin.[18]

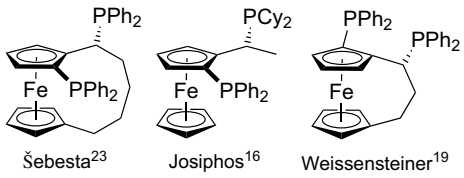


Figure 1.

Ligand tuning was pursued by systematic variation of the substituents at the phosphorus atoms. A different approach for modifying such compounds was suggested by Weissensteiner, who introduced additional three membered homo- and heteroannular bridges[19] leading to an increased conformational rigidity of the ligand backbone. These ligands show good enantioselectivities in Rh and Ir-catalyzed hydrogenations of olefins, ketones and imines althouth heteroannularly-bridged derivatives were inferior to Josiphos in the above mentioned reactions. Erker introduced similar [3]ferrocenophane diphosphines with an additional methyl group on the bridge and used them in the Rh-catalyzed hydrogenation.[20] Besides the well-known P/P and P/N ligands, bidentate sulfur and selenium ferrocene derivatives can also be useful in some catalytic reactions.[21,22] Recently, we published the synthesis of new [5]ferrocenophane-based diphosphine, **2h**, which proved to be a valuable ligand for Pd-catalyzed allylic substitution.[23]

* Corresponding authors. Tel.: +421 2 60296376; fax: +421 2 60296337 (R.Š.); tel.: +49 241 8026480; fax: +49 241 8022177 (W.L.); e-mail addresses: sebesta@fns.uniba.sk; leitner@itmc.rwth.aachen.de

0957-4166/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2007.08.011

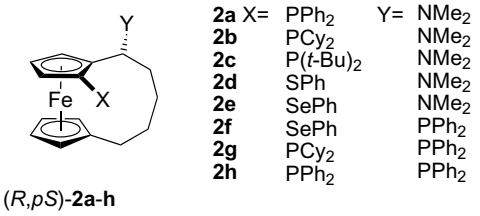
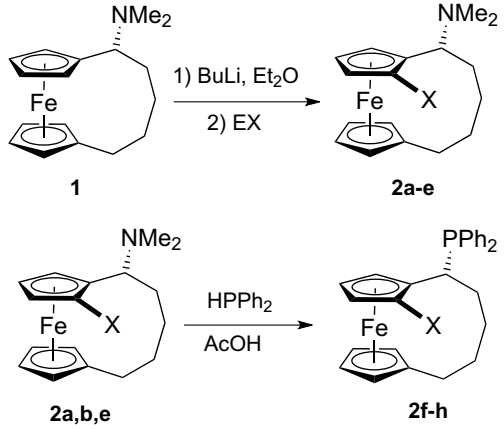


Figure 2.

Herein we report a series of new heteroannularly-bridged [5]ferrocenophane ligands **2a**–**h** bearing a variety of combinations of donor groups (Fig. 2). These novel ligands have been used in Rh-catalyzed asymmetric hydrogenation as well as in Cu-catalyzed conjugate addition.

2. Results and discussion

Using a previously described procedure,[23] key intermediate (*R*)-dimethylamino[5]ferrocenophane **1** was synthesized. Amine **1** was then lithiated diastereoselectively using *n*-BuLi in Et_2O and quenched with various electrophiles to introduce different donor groups (Scheme 1).



Scheme 1.

In this way, three homochiral [5]ferrocenophane amino phosphines **2a**–**c**, sulfur/N **2d** and selenium/N **2e** derivatives were prepared (Fig. 2). The overall reaction proceeded with high diastereoselectivities (⩾90%) and was only slightly affected by the nature of the electrophile. Ligands **2a**–**e** were purified by column chromatography. Selectivities and yields are summarized in Table 1.

The structure of ligand **2e** was determined by X-ray crystallographic analysis (Fig. 3) confirming the expected absolute stereochemistry.

Further structural diversification was achieved by nucleophilic substitution of the dimethylamino with a diphenylphosphino group. This reaction is known to proceed with retention of configuration at the stereogenic centre

Table 1. Diastereoselectivity of the reaction of *ortho*-lithiated (*R*)-**1** with electrophiles

Product	Reagent	ds (%)	Yield (%)
2a	PPh_2Cl	93	58[a]
2b	PCy_2Cl	93	48[a]
2c	$P(t\text{-}Bu)_2Cl$	100	40[a]
2d	PhSSPh	90	62[b]
2e	PhSeSePh	93	68[b]

[a] Determined by ^{31}P NMR.
[b] Determined by ^{1}H NMR.

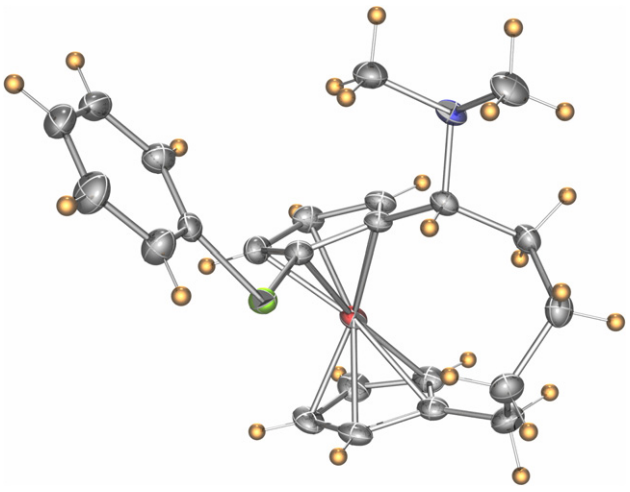
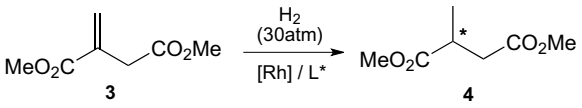


Figure 3.

(Scheme 1).[16] In this way, ligands **2f**, **2g** and **2h** were prepared starting from **2e**, **2b** and **2a**, respectively. Ligands **2g** and **2h** could be obtained in pure form by crystallization from hot ethanol, whereas ligand **2f** was purified by column chromatography in the form of its BH_3-adduct. The free ligand **2f** was obtained by treatment with Et_2NH. It should be noted that all these ligands are, to a certain extent, air- and acid-sensitive.

The Rh-catalyzed hydrogenation of dimethyl itaconate **3** was chosen as a benchmark reaction for the first evaluation of ligands **2a**–**h** in catalysis (Scheme 2). The catalysts were preformed in situ by mixing equimolar amounts of the ligand and $[Rh(cod)_2]BF_4$ in CH_2Cl_2 or methanol. The hydrogenation reactions were carried out within a standard reaction time of 14 h at a catalyst loading of 1 mol %. Conversions and enantiomeric excesses were determined by GC analysis. The results are summarized in Table 2.



Scheme 2.

Full conversion of the starting material was achieved in all the reactions. Good enantioselectivity (72% ee) was obtained in the presence of diphenylphosphino/N-ligand

2a, whereas using ligands **2b** and **2c** containing the more basic and sterically demanding dicyclohexyl and di-*t*-butyl phosphine groups resulted in the formation of diester **4** as a racemic mixture. (Table 2, entries 3 and 4). A sharp decrease in enantioselectivity was observed when 2 equiv of **2a** per [Rh] were used, suggesting that the catalytic species, which imparts enantioinduction is bearing only one (chelating) ligand (Table 2, entry 2 vs 1). The reactions with **2b** and **2c** were also carried out in methanol but the change in solvent did not improve the enantioselectivity (Table 2, entries 5 and 6). Almost no enantioinduction was observed for S/N **2d**, Se/N **2e** and Se/P **2f** ligands (Table 2, entries 7–9).

Table 2. Rh-catalyzed hydrogenation of dimethyl itaconate

Entry	Ligand	L:Rh[a]	Solvent	Time (h)	ee[b] (%)
1	**2a**	1:1	CH_2Cl_2	14	72 (*S*)
2	**2a**	2:1	CH_2Cl_2	14	7 (*S*)
3	**2b**	1:1	CH_2Cl_2	14	0
4	**2c**	1:1	CH_2Cl_2	14	0
5	**2b**	1:1	MeOH	1	0
6	**2c**	1:1	MeOH	1	0
7	**2d**	1:1	CH_2Cl_2	14	4 (*S*)
8	**2e**	1:1	CH_2Cl_2	14	0
9	**2f**	1:1	CH_2Cl_2	14	4 (*R*)
10	**2h**	1:1	CH_2Cl_2	14	95 (*S*)
11	**2g**	1:1	CH_2Cl_2	14	58 (*S*)

[a] Ratio [Rh]/3 1:100 and $p(H_2) = 30$ atm in all cases. Full conversion was achieved in all reactions.
[b] Determined by GC on Lipodex E column, isotherm. 85 °C.

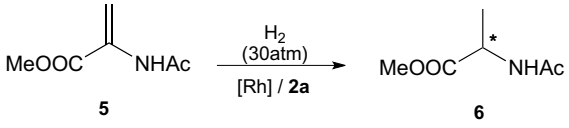
High enantioselectivity (95% ee) was obtained in the presence of bis-diphenylphosphino ligand **2h** (Table 2, entry 10). This result compares very well with the enantioselectivity obtained with the corresponding Josiphos ligand (PPh_2) (96% ee).[24] In contrast, moderate enantioselectivity (58% ee) was achieved with dicyclohexylphosphino-diphenylphosphino derivative **2g** (Table 2, entry 11). This result is surprising taking into account the very high enantioselectivity obtained with similar not-bridged Josiphos ligand (PCy_2) (99% ee).[16] On the other hand, a similar considerable decrease in enantioselectivity was observed when **2b** was used instead of **2a** (Table 2, cf. entries 1 and 3 vs entries 10 and 11), indicating that the [5]ferrocenophane backbone is more sensitive to steric/electronic variation than the more adaptive Josiphos-type ligands. In the same reaction, [3]ferrocenophane derivatives led to an enantioselectivity of up to 43%.[19] It should be pointed out, however, that no direct comparison can be made between [3]- and [5]ferrocenophane-based ligands because of the different relative position of the phosphine substituents.

Our further investigation concentrated on the most effective ligand **2h** (Table 3). The hydrogenation of dimethyl itaconate **3** proceeded with the same high enantioselectivity (95% ee) even at a substrate to catalyst (S/C) ratio of 1000:1 with an average turnover frequency (TOF_{av}) of 60 h^{-1} (Table 3, entry 2). Hydrogenation of methyl 2-acetamido-acrylate **5** (Scheme 3) under standard reaction conditions resulted in the full conversion of the starting material and an enantioselectivity of 41% (Table 3, entry 3). By increasing the S/C ratio to 500:1, the enantioselectivity dropped to 17% while conversion remained quantitative (Table 3, entry 4).

Table 3. Rh/**2h**-catalyzed hydrogenation of **3** and **5**

Entry	Subst.	[Rh]/subst.	Conversion (%)	ee (%)
1	**3**	1:100	100	95 (*S*)[a]
2	**3**	1:1000	84	95 (*S*)[a]
3	**5**	1:100	100	41 (*R*)[b]
4	**5**	1:500	100	17 (*R*)[b]

Reaction was carried out at $p(H_2) = 30$ atm, during 14 h.
[a] Determined by GC on Lipodex E column, isotherm. 85 °C.
[b] Determined by GC on Lipodex E column, gradient 80–150 °C, 3 °C/min.



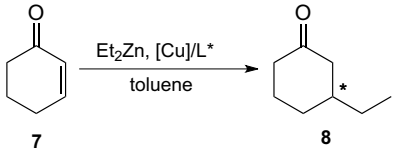
Scheme 3.

Next we decided to examine ligands **2a**, **2b**, **2d**, **2e** and **2g** in the Cu-catalyzed conjugate addition of Et_2Zn to cyclohex-2-enone. Copper(I) triflate was chosen as the Cu-source and the reaction was carried out under typical conditions.[25] The results are summarized in Table 4. A promising enantioselectivity of 78% ee at −15 °C was obtained with P/N ligand **2a** (Table 4, entry 1), which could be further increased to 84% ee at −35 °C (Table 4, entry 2). Again, a dramatic drop in enantioselectivity was observed using the dicyclohexylphosphino derivative **2b** instead of **2a**. The product was obtained almost quantitatively, albeit as a racemic mixture (Table 4, entry 3). A very low enantioselectivity (up to 2% ee) was achieved with the other ligands (Table 4, entries 4–6) (Scheme 4).

Table 4. Cu-catalyzed conjugate addition of Et_2Zn to enone **7**

Entry	Ligand	Temperature	Conversion (%)	ee[a] (%)
1	**2a**	−15	100	78 (*R*)
2	**2b**	−15	95	0
3	**2d**	−15	42	2 (*R*)
4	**2e**	−15	73	0
5	**2a**	−35	100	84 (*R*)
6	**2g**	−35	80	0

Lig/Cu 1:1, [Cu]/subst. 1:80.
[a] Determined by GC on Lipodex E column, isotherm. 100 °C.



Scheme 4.

3. Conclusion

Novel heteroannular bridged, homochiral bidentate [5]ferrocenophane based ligands **2a**–**h** have been synthesized. Depending on the substituents at the phosphorus moiety, different results in the catalysis were obtained when compared to the corresponding non-bridged Josiphos type ligands. In the hydrogenation of dimethyl itaconate **3**, bidentate bis-diphenylphosphino derivative **2h** led to high enantioselectivities (95% ee vs 96% ee with corresponding Josiphos), while only modest ee was obtained with **2g** (58% ee vs 98% ee for the corresponding Josiphos). In the same reaction, good enantioselectivities were observed also for P/N derivative **2a** (72% ee). Lower enantioselectivity was achieved in the hydrogenation of methyl 2-acetamidoacrylate **5** using **2h** as the ligand. Moreover, amino phosphine **2a** turned out to be useful for the Cu-catalyzed Michael addition of Et_2Zn to cyclohex-2-enone **7** (84% ee at −35 °C). Further investigations on the ligand structure and possibilities of their utilization in other asymmetric reactions are currently underway in our laboratory.

4. Experimental

Homochiral amine (*R*)-**1**, ligands (*R*,*pS*)-**2a** and (*R*,*pS*)-**2h** were prepared following a procedure developed by our research group.[23] All reactions were carried out under an argon atmosphere using standard Schlenk technique. The solvents were degassed. Column chromatography was performed on 40/100 mesh silica gel columns. GC analysis was performed on Sichromat 1-4 Gas Chromatograph equipped with FID detector. The NMR spectra were recorded on a Varian Gemini 2000 spectrometer and Bruker NMR at 300 MHz for ^{1}H, 75 MHz for ^{13}C and 121 MHz for ^{31}P NMR. TMS was used as an internal standard. The chemical shift values are given in ppm and listed coupling constants are in Hz. The IR spectra were recorded on a Mettler-Toledo ReactIR instrument with the scale in cm^{-1}. Elemental analyses were performed on a Carlo Erba Instrumentazione analyzer. HR-MS was measured on Finnigan Mat 95. Melting points were measured on a Barnstead Electrothermal IA9200 apparatus and are uncorrected.

4.1. (*R*,*pS*)-1-(Dicyclohexylphosphanyl)-2,1′-[1-(dimethylamino)pentan-1,5-diyl]ferrocene 2b

To a stirred solution of amine (*R*)-**1** (288 mg, 0.94 mmol) in anhydrous Et_2O (10 mL) *n*-BuLi (0.90 mL, 1.44 mmol, 1.6 M hexane soln) was added dropwise. The mixture was stirred at ambient temperature for 2.5 h and then cooled to 0 °C. A solution of $ClPCy_2$ (380 mg, 1.60 mmol) in Et_2O (5 mL) was added dropwise. The reaction mixture was stirred overnight. Then H_2O (10 mL) was added, the layers separated and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with H_2O (4 × 10 mL), dried over Na_2SO_4 and the solvent vacuum evaporated. The crude product was purified by column chromatography (SiO_2, hexane/Et_2O 1:1 + 1% Et_3N). Pure phosphine **2b** (222 mg, 48%) was isolated as an orange oil. Compound decomposes in chloroform solution. $[\alpha]_D = -207$ (*c* 0.70, acetone). ^{1}H NMR (acetone-d_6, 300 MHz): δ 4.34 (dd, 1H, $J = 2.5$, 2.5 Hz, H CFc), 4.30 (ddd, 1H, $J = 2.5$, 1.5, 1.3 Hz, HCFc), 4.14 (dd, 1H, $J = 2.4$, 1.3 Hz, HCFc), 4.12 (ddd, 1H, $J = 2.4$, 2.4, 1.3 Hz, HCFc), 4.02 (ddd, 1H, $J = 2.4$, 1.4, 1.4 Hz, HCFc), 3.97 (ddd, 1H, $J = 2.4$, 1.3, 1.3 Hz, HCFc), 3.81–3.84 (m, 1H, HCFc), 3.63 (dddd, 2H, $J = 12.3$, 6.6, 2.5, 2.4 Hz), 2.24–2.46 (m, 2H), 2.10 (s, 6H, $(CH_3)_2N$), 2.05–2.17 (m, 2H), 1.16–1.96 (m, 24H). ^{13}C NMR (acetone-d_6, 75 MHz): 96.8 (d, $J = 22.3$ Hz), 91.1, 79.7 (d, $J = 20.0$ Hz), 69.7 (d, $J = 2.2$ Hz), 69.3 (d, $J = 3.3$ Hz), 68.8 (d, $J = 5.0$ Hz), 68.0 (d, $J = 4.8$ Hz), 67.9, 67.1, 66.6, 60.0 (d, $J = 11.2$ Hz), 43.9, 39.7, 35.8 (d, $J = 14.5$ Hz), 35.1 (d, $J = 12.7$ Hz), 33.3 (d, $J = 24.8$ Hz), 31.6 (d, $J = 14.5$ Hz), 30.1 (d, $J = 5.8$ Hz), 29.8, 27.8 (d, $J = 4.9$ Hz), 27.6 (d, $J = 8.8$ Hz), 27.4, 27.3 (d, $J = 15.0$ Hz), 27.2 (d, $J = 6.4$ Hz), 26.3 (d, $J = 2.6$ Hz), 25.2, 24.0 (d, $J = 6.4$ Hz), 22.0. ^{31}P NMR (acetone-d_6, 121 MHz): −12.6. IR (neat) *v*: 2922.0, 2852.5, 2775.3, 1447.5, 1262.2, 1084.7, 1019.0, 802.9, 752.7 cm^{-1}. HR-MS: calcd for $C_{29}H_{45}FeNP$, 494.2634; found 494.2639.

4.2. (*R*,*pS*)-1-(Di-*tert*-butylphosphanyl)-2,1′-[1-(dimethylamino)pentan-1,5-diyl]ferrocene 2c

Same procedure as in previous except that $ClP(t\text{-}Bu)_2$ (290 mg, 1.60 mmol) was used. Yield: 166 mg (40%) of a red crystalline compound. Compound decomposes in chloroform solution. Mp: 66–69 °C. $[\alpha]_D = -395$ (*c* 0.45, methanol). ^{1}H NMR (acetone-d_6, 300 MHz): δ 4.56 (ddd, 1H, $J = 2.5$, 2.5, 1.2 Hz, HCFc), 4.50–4.53 (m, 1H, HCFc), 4.31 (dd, 1H, $J = 2.4$, 1.2 Hz, HCFc), 4.20 (ddd, 1H, $J = 2.4$, 2.4, 1.4 Hz, HCFc), 4.08 (ddd, 1H, $J = 2.5$, 1.3, 1.2 Hz, HCFc), 4.04 (ddd, 1H, $J = 2.4$, 2.4, 1.3 Hz, HCFc), 3.86 (ddd, 1H, $J = 2.5$, 1.3, 1.3 Hz, HCFc), 3.57 (ddd, 1H, $J = 6.0$, 4.1, 4.1 Hz, HC(1)), 2.13–2.42 (m, 3H), 2.09 (s, 6H, $(CH_3)_2N$), 1.69–1.92 (m, 5H), 1.52 (d, 9H, $J = 12.0$ Hz, *t*-Bu–P), 0.94 (d, 9H, $J = 11.0$ Hz, *t*-Bu–P). ^{13}C NMR (acetone-d_6, 75 MHz): δ 88.7, 77.4, 75.2, 71.4 (d, $J = 4.6$ Hz), 70.7 (d, $J = 5.4$ Hz), 68.6, 67.5, 66.6, 66.4, 62.5 (d, $J = 14.2$ Hz), 44.4, 33.6 (d, $J = 19.7$ Hz), 31.8 (d, $J = 17.3$ Hz), 30.9 (d, $J = 13.0$ Hz), 30.7 (d, $J = 12.2$ Hz), 28.5, 26.9, 23.4, 22.4, 19.3. ^{31}P NMR (acetone-d_6, 121 MHz): δ 15.6. IR (neat) *v*: 2925.9, 2860.3, 2817.8, 2771.5, 1455.2, 1362.6, 1262.2, 1173.4, 1030.6, 814.5, 756.6 cm^{-1}. Elem. Anal. Calcd for $C_{25}H_{40}FeNP$ (441.4): C, 68.02; H, 9.13; N, 3.17. Found: C, 69.35; H, 9.74; N, 3.10. HR-MS: calcd for $C_{25}H_{41}FeNP$, 442.2321; found 442.2328.

4.3. (*R*,*pS*)-1-(Phenylsulfanyl)-2,1′-[1-(dimethylamino)pentan-1,5-diyl]ferrocene 2d

To a stirred solution of (*R*)-**1** (250 mg, 0.84 mmol) *n*-BuLi (790 μL, 1.26 mmol, 1.6 M hexane soln) was added dropwise and the mixture stirred for 2.5 h. The reaction mixture was cooled in ice-salt bath, solid PhSSPh (312 mg, 1.43 mmol) was added during 45 min and the mixture was stirred overnight. The reaction was quenched with H_2O (10 mL). The layers were separated and aqueous layer extracted with Et_2O (2 × 10 mL). The combined organic extracts were washed with H_2O (3 × 10 mL), dried over

Na_2SO_4 and the solvent was vacuum evaporated. The crude product was purified by column chromatography (SiO_2, PhH/Et_3N 99:1). Thioether **2d** (210 mg, 62%) was isolated as a yellow crystalline solid. Analytical sample was recrystallized from Et_2O. Mp: 85–88 °C. $[\alpha]_D = -155$ (*c* 0.79, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.10–7.21 (m, 4H, HCPh), 7.00–7.06 (m, 1H, HCPh), 4.52 (dd, 1H, $J = 2.4$, 1.4 Hz, HCFc), 4.39 (dd, 1H, $J = 2.6$, 2.6 Hz, HCFc), 4.34 (dd, 1H, $J = 2.6$, 1.3 Hz, HCFc), 4.27 (dd, 1H, $J = 2.5$, 2.4, 1.3 Hz, HCFc), 4.11 (ddd, 1H, $J = 2.4$, 2.4, 1.3 Hz, HCFc), 3.99 (ddd, 1H, $J = 2.4$, 1.3, 1.2 Hz, HCFc), 3.89 (ddd, 1H, $J = 2.5$, 1.3, 1.2 Hz, HCFc), 3.30 (dd, 1H, $J = 6.5$, 2.1 Hz, HC(1)), 2.44 (ddd, 1H, $J = 15.8$, 8.2, 3.9 Hz), 1.81-2.16 (m, 7H), 1.90 (s, 6H, $(CH_3)_2N$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 140.3, 128.5, 126.3, 124.9, 94.1, 93.4, 75.7, 74.5, 71.7, 69.7, 68.9, 68.6, 68.3, 67.4, 61.5, 42.6, 29.9, 26.8, 24.6, 24.3. IR (neat): 3080.3, 2929.7, 2856.4, 2821.7, 2771.5, 1582.6, 1474.5, 1443.6, 1262.2, 1080.8, 1022.9, 853.1, 814.5, 737.3, 690.9 cm^{-1}. Elem. Anal. Calcd for $C_{23}H_{27}FeNS$ (405.4): C, 68.15; H, 6.71; N, 3.46. Found: C, 68.40; H, 6.49; N, 3.56.

4.4. (*R*,*pS*)-1-(Phenylselenyl)-2,1′-[1-(dimethylamino)pentan-1,5-diyl]ferrocene 2e

Same procedure as in previous except that PhSeSePh (446 mg, 1.43 mmol) was used. Yield: 258 mg (68%) of brown crystalline compound. Mp: 76.3–78.9 °C [Et_2O]. $[\alpha]_D = -148$ (*c* 0.85, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): 7.28–7.34 (m, 2H, HCPh), 7.05–7.18 (m, 3H, HCPh), 4.49 (dd, 1H, $J = 2.4$, 1.3 Hz, HCFc), 4.40 (dd, 1H, $J = 2.6$, 2.5 Hz, HCFc), 4.29 (dd, 1H, $J = 2.6$, 1.3 Hz, HCFc), 4.23 (ddd, 1H, $J = 2.5$, 2.4, 1.3 Hz, HCFc), 4.13 (ddd, 1H, $J = 2.4$, 2.4, 1.3 Hz, HCFc), 4.00 (ddd, 1H, $J = 2.5$, 1.3, 1.3 Hz, HCFc), 3.84 (dd, 1H, $J = 2.4$, 1.3, 1.3 Hz, HCFc), 3.33 (dd, 1H, $J = 6.5$, 2.0 Hz, HC(1)), 2.43 (ddd, 1H, $J = 15.9$, 8.3, 3.7 Hz), 2.02–2.14 (m, 2H), 1.79–2.02 (m, 5H), 1.88 (s, 6H, $(CH_3)_2N$). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 134.9, 129.5, 128.5, 125.9, 94.1, 93.3, 75.4, 70.9, 69.4, 69.1, 68.2, 67.4, 62.4, 42.4, 29.8, 27.3, 24.7, 24.4. IR (neat): 3072.6, 2929.7, 2856.4, 2821.7, 2775.3, 1578.7, 1474.5, 1443.6, 1219.8, 1065.4, 1022.9, 814.5, 752.7, 733.4, 690.9, 663.9 cm^{-1}. Elem. Anal. Calcd. for $C_{23}H_{27}FeNSe$ (452.3): C, 61.08; H, 6.02; N, 3.10. Found: C, 61.95 H, 5.71; N, 3.20. HR-MS: calcd for $C_{23}H_{28}FeNSe$, 454.0731; found, 454.0710.

4.5. (*R*,*pS*)-1-(Phenylselenyl)-2,1′-[1-(diphenylphosphanyl)pentan-1,5-diyl]ferrocene, borane complex 2f·BH_3

To a solution of (*R*,*pS*)-**2e** (600 mg, 1.33 mmol) in AcOH (10 mL), $HPPh_2$ (360 mg, 1.73 mmol) was added dropwise. The reaction mixture protected from light was stirred and heated to 85 °C for 15 h. The solvent was vacuum evaporated and the residue was dissolved in anhydrous Et_2O (15 mL) and cooled to 0 °C. $BH_3{\cdot}SMe_2$ (700 μL, 1.40 mmol, 2 M THF soln) was added dropwise and the mixture was stirred for 20 min at 0 °C. Solvents were evaporated under vacuum and the crude mixture was purified by column chromatography (SiO_2, hexane/Et_2O 3:1). Product (*R*,*pS*)-**2f**·BH_3 (474 mg, 59%) was isolated as an orange crystalline compound. Analytical sample was recrystallized from hexane. Mp: 55–59 °C. $[\alpha]_D = -259$ (*c* 0.27, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.82–7.90 (m, 2H, HCAr), 7.43–7.52 (m, 4H, HCAr), 7.04–7.17 (m, 7H, HCAr), 6.83–6.92 (m, 2H, HCAr), 4.90–4.92 (m, 1H, HC(1)), 4.41 (dd, 1H, $J = 2.5$, 1.4 Hz, HCFc), 4.32 (dd, 1H, $J = 2.6$, 2.6 Hz, HCFc), 4.14 (dd, 1H, $J = 4.2$, 2.1 Hz, HCFc), 4.03–4.05 (m, 2H, HCFc), 3.66–3.69 (m, 1H, HCFc), 3.54–3.61 (m, 1H, HCFc), 2.07–2.34 (m, 4H), 1.62–2.03 (m, 4H), 0.40–1.00 (br s, 3H, BH_3). ^{13}C NMR (acetone-d_6, 75 MHz): δ 133.0 (d, $J = 8.1$ Hz), 132.7 (d, $J = 8.6$ Hz), 131.2, 130.3, 128.9, 128.7 (d, $J = 9.5$ Hz), 127.9 (d, $J = 9.9$ Hz), 126.3, 92.7, 73.8, 71.3, 68.8 (d, $J = 4.1$ Hz), 68.4, 66.9, 55.6, 55.0, 34.1, 27.6, 24.1, 23.7, 21.0. ^{31}P NMR ($CDCl_3$, 121 MHz): δ 24.6 (br s). HR-MS: calcd $C_{33}H_{31}FePSe$, 594.0678; found 594.0705.

Free ligand **2f** was liberated from BH_3 just prior to use by treating **2f**·BH_3 with Et_2NH in anhydrous Et_2O followed by high vacuum. **2f**. ^1H NMR ($CDCl_3$, 300 MHz): 7.42–7.61 (m, 2H, HCAr), 7.31–7.36 (m, 2H, HCAr), 7.10–7.16 (m, 5H, HCAr), 7.08–6.95 (m, 4H, HCAr), 6.86–6.94 (m, 2H, HCAr), 4.38–4.44 (m, 2H, HCFc), 4.28 (dd, 1H, $J = 2.4$, 2.4 Hz, HCFc), 4.15–4.19 (m, 1H, HCFc), 4.07–4.10 (m, 1H, HCFc), 4.00–4.03 (m, 1H, HCFc), 3.79–3.82 (m, 1H, HCFc), 3.32 (ddd, 1H, $J = 7.1$, 7.1, 2.5 Hz, HC(1)), 2.32–2.44 (m, 1H), 2.06–2.29 (m, 3H), 1.74–1.96 (m, 4H). ^{31}P NMR (PhH-d_6, 121 MHz): δ −0.5.

4.6. (*R*,*pS*)-1-(Dicyclohexylphosphanyl)-2,1′-[1-(diphenylphosphanyl)pentan-1,5-diyl]ferrocene, bis(borane) complex 2g·$(BH_3)_2$

To a solution of (*R*,*pS*)-**2b** (75 mg, 0.152 mmol) in anhydrous AcOH (3 mL), $HPPh_2$ (37 mg, 0.20 mmol) was added. The reaction mixture was heated to 85 °C and stirred in darkness for 12 h. The solvent was evaporated under vacuum and the crude product was recrystallized from anhydrous degassed EtOH to yield ligand (*R*,*pS*)-**2g** (45 mg, 47%) as orange crystals. ^1H NMR (acetone-d_6, 300 MHz): δ 7.54–7.66 (m, 3H, HCPh), 7.42–7.50 (m, 3H, HCPh), 7.17–7.24 (m, 4H, HCPh), 4.29–4.35 (m, 2H, HCFc), 4.21–4.25 (m, 1H, HCFc), 4.11–4.16 (m, 1H, HCFc), 4.07–4.11 (m, 1H, HCFc), 3.99–4.06 (m, 2H, HCFc), 3.59–3.68 (m, 1H, HC(1)), 0.80–2.50 (m, 30H). ^{31}P NMR (acetone-d_6, 121 MHz): δ 2.1, −17.6. For analytical purposes, the BH_3 complex was prepared. Mp: 234 °C (dec.). $[\alpha]_D = -204$ (*c* 0.32, $CHCl_3$) ^1H NMR ($CDCl_3$, 300 MHz): δ 8.15 (m, 2H), 7.54 (m, 3H), 7.33 (m, 2H), 7.18 (m, 1H), 7.08 (m, 2H), 5.61 (s, 1H), 4.48 (t, $J = 2.6$ Hz, 1H), 4.40 (m, 1H), 4.18 (m, 1H), 4.14 (m, 2H), 4.09 (m, 2H), 2.83 (m, 1H), 2.39 (m, 4H), 2.19 (td, $J = 16.5$, 3.9 Hz, 1H), 2.04–1.29 (m, 22H), 1.12–0.70 (m, 6H), 0.20 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 131.2 (d, $J = 2.2$ Hz), 133.7 (d, $J = 8.8$ Hz), 133.6 (d, $J = 8.3$ Hz), 130.1 (d, $J = 2.5$ Hz), 129.3 (d, $J = 51.9$ Hz), 128.2 (d, $J = 55.5$ Hz), 128.8 (d, $J = 9.6$ Hz), 127.7 (d, $J = 9.9$ Hz), 96.3 (dd, $J = 14.2$, 6.5 Hz), 91.2, 74.4 (dd, $J = 49.4$, 4.4 Hz), 71.2 (d, $J = 2.7$ Hz), 71.0 (dd, $J = 7.5$, 4.6 Hz), 70.7, 69.1 (d, $J = 5.8$ Hz), 68.4, 67.7, 66.7, 39.6 (d, $J = 33.9$ Hz), 34.5, (d, $J = 35.0$ Hz), 30.8 (d, $J = 32.7$ Hz), 29.3, 29.0 (d, $J = 6.4$ Hz), 27.8 (d,

$J = 12.9$ Hz), 27.7, 27.2 (d, $J = 2.1$ Hz), 27.1 (d, $J = 16.5$ Hz), 26.7 (dd, $J = 22.9$, 11.5 Hz), 26.1, 25.71, 25.67 (d, $J = 3.3$ Hz), 24.0 (d, $J = 12.9$ Hz), 23.4, 22.3. ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ 25.8 (br s), 21.0 (br s). HR-MS: calcd for $C_{39}H_{48}FeP_2$, 634.2581; found, 634.2577.

4.7. Crystal structure data for 2e

Crystallization from Et_2O, red prism with dimensions $0.30 \times 0.27 \times 0.20$ mm, $C_{23}H_{27}FeNS$, M_r 405.37. Monoclinic space group $P2_1$, $a = 7.7639(7)$, $b = 7.898(3)$, $c = 16.130(4)$ Å, $V = 970.7(4)$ Å^3 from 11,785 reflections, $T = 150(2)$ K, $\lambda = 0.71069$ Å, $Z = 2$, $D_x = 1.387$ g cm^{-3}, $\mu = 0.891$ mm^{-1}. The data were collected on KM4 CCD diffractometer with Mo Kα radiation. Maximum θ was 26.55°. The *hkl* ranges were −9/9, −9/9, −20/20. Reflections measured: 12,958, independent reflections: 3986, reflections with $I > 2\sigma(I)$: 3875. The structure was solved with SIR92. Refinement on F^2 was performed with SHELXL-97, $R[F^2 > 2\sigma(F^2)] = 0.0179$, $wR(F2) = 0.0460$, $S = 1.061$, $\Delta\rho_{max} = 0.185$ e Å^{-3}, $\Delta\rho_{min} = -0.293$ e Å^{-3}. Hydrogen atoms were fixed at calculated positions. The crystallographic data have been deposited with the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 644736.

4.8. Rh-catalyzed hydrogenation

A solution of the ligand (0.02 mmol) in CH_2Cl_2 (1 mL) was added to an equimolar solution of $[Rh(cod)_2]BF_4$ (7.8 mg) in the same solvent (1 mL). The mixture was stirred under argon for 1 h at rt. The resulting catalyst solution was transferred under argon into a stainless steel autoclave (10 mL) and the substrate (2.0 mmol) was added. The reaction vessel was pressurized with H_2 (30 atm) and the mixture stirred at ambient temperature for 14 h. The mixture was filtered through a short pad of silica gel. Conversion and enantiomeric excess were determined by GC analysis.

4.9. Cu-catalyzed Et_2Zn addition on cyclohex-2-enone

$Cu_2(OTf)_2{\cdot}PhCH_3$ (2.6 mg, 0.005 mmol) was added to a ligand solution (0.011 mmol) in anhydrous toluene (1 mL). The resulting mixture was stirred under argon for 30 min at rt and then cooled in ice-salt bath to −15 °C. Substrate **7** (20 mg, 0.2 mmol) and Et_2Zn (400 μL, 0.4 mmol, 1 M in toluene) were added. The mixture was stirred at −15 °C for 5 h and then quenched with a saturated NH_4Cl solution (2 mL). The organic layer was washed with brine (2 mL), H_2O (2 mL) and dried over Na_2SO_4. Conversion and enantiomeric excess were determined by GC analysis.

Acknowledgements

We gratefully acknowledge support from European project LIGBANK NMP3-2003-505267 and Slovak Grant Agency VEGA, Grant No. 1/3569/06 and Fonds der Chemischen Industrie. NMR measurements provided by Slovak State Programme Project No. 2003SP200280203. We thank Dr. Ivana Císařová (Charles University Prague) for X-ray measurement.

References

1. Togni, A.; Hayashi, T. *Ferrocenes*; VCH: Weinheim, 1995.
2. Hayashi, T.; Tajika, M.; Tamao, K.; Kumada, M. *J. Am. Chem. Soc.* **1976**, *98*, 3718–3719.
3. Colacot, T. *J. Chem. Rev.* **2003**, *103*, 3101–3118.
4. Dai, L. X.; Tu, T.; You, S. L.; Deng, W. P.; Hou, X. L. *Acc. Chem. Res.* **2003**, *36*, 659–667.
5. Barbaro, P.; Bianchini, C.; Giambastiani, G.; Parisel, S. L. *Coord. Chem. Rev.* **2004**, *248*, 2131–2150.
6. Cabrera, S.; Garcia Mancheno, O.; Gomez Arrayas, R.; Alonso, I.; Mauleon, P.; Carretero, J. C. *Pure Appl. Chem.* **2006**, *78*, 257–265.
7. Arrayás, R. G.; Adrio, J.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2006**, *45*, 7674–7715.
8. Marinetti, A.; Labrue, F.; Pons, B.; Jus, S.; Ricard, L.; Genęt, J.-P. *Eur. J. Inorg. Chem.* **2003**, *2003*, 2583–2590.
9. Boaz, N. W.; Mackenzie, E. B.; Debenham, S. D.; Large, S. E.; Ponasik, J. A. *J. Org. Chem.* **2005**, *70*, 1872–1880.
10. Sturm, T.; Weissensteiner, W.; Spindler, F. *Adv. Synth. Catal.* **2003**, *345*, 160–164.
11. Tappe, K.; Knochel, P. *Tetrahedron: Asymmetry* **2004**, *15*, 91–102.
12. Feringa, B. L.; Badorrey, R.; Pena, D.; Harutyunyan, S. R.; Minnaard, A. J. *Proc. Natl. Acad. Sci.* **2004**, *101*, 5834–5838.
13. López, F.; Harutyunyan, S. R.; Meetsma, A.; Minnaard, A. J.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2005**, *44*, 2752–2756.
14. Reetz, M. T.; Gosberg, A.; Moulin, D. *Tetrahedron Lett.* **2002**, *43*, 1189–1191.
15. Liu, L.-T.; Wang, M.-C.; Zhao, W.-X.; Zhou, Y.-L.; Wang, X.-D. *Tetrahedron: Asymmetry* **2006**, *17*, 136–141.
16. Togni, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Lander, H.; Tijani, A. *J. Am. Chem. Soc.* **1994**, *116*, 4062–4066.
17. Yoon, T. P.; Jacobsen, E. N. *Science* **2003**, *299*, 1691–1693.
18. Blaser, H. U.; Brieden, W.; Pugin, B.; Spindler, F.; Studer, M.; Togni, A. *Top. Catal.* **2002**, *19*, 3–16.
19. Sturm, T.; Weissensteiner, W.; Spindler, F.; Mereiter, K.; Lopez-Agenjo, A. M.; Manzano, B. R.; Jalon, F. A. *Organometallics* **2002**, *21*, 1766–1774.
20. Liptau, P.; Tebben, L.; Kehr, G.; Fröhlich, R.; Erker, G.; Hollmann, F.; Rieger, B. *Eur. J. Org. Chem.* **2005**, 1909–1918.
21. Masdeu-Bulto, A. M.; Dieguez, M.; Martin, E.; Gomez, M. *Coord. Chem. Rev.* **2003**, *242*, 159–201.
22. Braga, A. L.; Lutke, D. S.; Vargas, F.; Braga, R. C. *Synlett* **2006**, 1453–1466.
23. Šebesta, R.; Almassy, A.; Císařová, I.; Toma, Š. *Tetrahedron: Asymmetry* **2006**, *17*, 2531–2537.
24. Hems, W. P.; McMorn, P.; Riddel, S.; Watson, S.; Hancock, F. E.; Hutchings, G. *J. Org. Biomol. Chem.* **2005**, *3*, 1547–1550.
25. Alexakis, A.; Benhaim, C.; Rosset, S.; Humam, M. *J. Am. Chem. Soc.* **2002**, *124*, 5262–5263.