Synthesis of a New Class of Chiral 1,5-Diphosphanylferrocene Ligands and Their Use in Enantioselective Hydrogenation

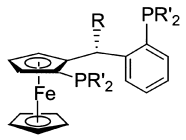
Tania Ireland,[b] Katja Tappe,[a] Gabi Grossheimann,[c] and Paul Knochel*[a]

Abstract: A new family of ferrocenylphosphane ligands has been prepared. Their flexible synthesis allows many structural modifications. The asymmetric induction of these ligands was examined in the hydrogenation of functionalized C=C, C=O, and C=N bonds. The enantioselectivity of the reaction was strongly dependent on the substituent R at the position α to the ferrocene moiety. In many cases, both enantiomeric β-hydroxyesters of the reduction product can be obtained by simply replacing a dimethylamino group in the ligand with a methyl group.

Keywords: asymmetric catalysis · ferrocene · hydrogenation · iron · metallocenes · ligands

Introduction

Asymmetric catalysis is a powerful tool for producing enantiomerically enriched compounds. In particular, asymmetric hydrogenations can be conducted on large scale without producing intrinsic by-products by using hydrogen as a cheap reducing agent.[1] Many chiral phosphanes proved to give excellent activities and enantioselectivities in several metal-catalyzed hydrogenations.[1, 2] However, since careful matching of the chiral ligand, the reaction type, the catalyst, and the substrate is usually necessary, there is still a demand for easily accessible, air-stable chiral diphosphanes whose structure allows convenient modification of steric and electronic properties. Their synthesis must be highly flexible to allow simple fine-tuning and rapid optimization of ligand–substrate matches. We recently described a new class of chiral 1,5-diphosphanylferrocene ligands of type **1** that have these characteristics.[3]



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[a] Prof. Dr. P. Knochel, K. Tappe
Department Chemie, Ludwig-Maximilians Universität München
Butenandtstrasse 5-13, 81377 München (Germany)
Fax: (+49) 89-2180-7680
E-mail: Paul.Knochel@cup.uni-muenchen.de

[b] Dr. T. Ireland
RHODIA Recherches, Centre de Recherche de Lyon
Groupe Catalyse 85
avenue des Frères Perret, 69192 Saint Fons (France)
Fax: (+33) 4-72-89-68-90

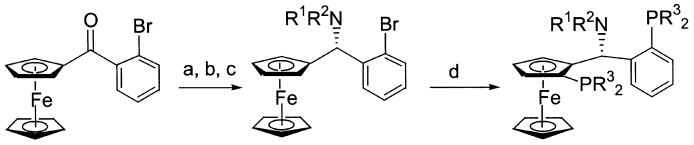
[c] Dr. G. Grossheimann
Bayer AG, IS-SSS-HLS, Geb. 2978
51368 Leverkusen (Germany)

Supporting information for this article (NMR spectra of the ferrocenyl compounds) is available on the WWW under http//wiley-vch.de/home/chemistry/ or from the author.

Although few examples of efficient chiral 1,5-diphosphanes are known,[4] we envisioned that the partial rigidity of the diphosphane backbone of **1** should allow good transfer of chiral information. Furthermore, the ligand structure should be easily optimizable by introducing various R groups at the α-position of the ferrocene unit or by modifying the electronic properties of the phosphane moieties. Here we report on the synthesis of phosphanes **1** and their application in enantioselective hydrogenation.

Results and Discussion

Ligand design: The phosphanes **1** are readily prepared in five steps starting from ferrocene (Scheme 1). Friedel–Crafts acylation of ferrocene with 2-bromobenzoyl chloride furnished the ketone **2** in 80% yield. Corey–Bakshi–Shibata (CBS) reduction of the ketone **2** afforded the corresponding alcohol **3** in 95% yield and 96% *ee*.[5] The alcohol **3** was obtained in almost enantiomerically pure form (99.5% *ee*) after recrystallization from heptane. Acylation of **3** gave quantitatively the intermediate acetate, which was converted to the corre-



2 **4** **1**

Scheme 1. Synthesis of the phosphanes **1**. a) CBS catalyst (0.3 equiv), $BH_3 \cdot Me_2S$, 0 °C, 2 h; b) Ac_2O, pyridine, 12 h; c) HNR^1R^2, CH_3CN or THF, H_2O, 12 h; d) *t*BuLi (3.5 equiv), −78 °C to room temperature, 1 h; then $ClPR^3_2$ (2.5 equiv).

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sponding ferrocenylamine **4** with retention of configuration by treatment with an amine.[6] Finally, diastereoselective dilithiation[7] of the amine **4** followed by reaction with a chlorophosphane gave the corresponding diphosphane **1**. This flexible synthetic pathway allowed us to easily introduce various substituents R^1, R^2, and R^3. Variations of the phosphorus and nitrogen substituents of the ligands **1** are summarized in Table 1.

Table 1. Variations of the phosphorus and the nitrogen substituents of the ligands of type **1**.

R^1R^2N-	R^3_2P-	Product **4**	[%]	Product **1**	Yield [%]
Me_2N-	Ph_2P-	**4a**	90	**1a**	88
Me_2N-	$(3,5\text{-xylyl})_2P$-	**4a**	90	**1b**	33
$(CH_2CH_2)_2N$-	Ph_2P-	**4b**	94	**1c**	64
(*R*)-PhCH(Me)MeN-	Ph_2P-	**4c**	99	**1d**	41
(*S*)-PhCH(Me)MeN-	Ph_2P-	**4d**	77	**1e**	58
$Me_2NCH_2CH_2MeN$-	Ph_2P-	**4e**	98	**1f**	41
Et_2N-	Ph_2P-	**4f**	93	**1g**	62
nPr_2N-	Ph_2P-	**4g**	90	**1h**	53
nBu_2N-	Ph_2P-	**4h**	90	**1i**	46
iBu_2N-	Ph_2P-	**4i**	88	**1j**	36

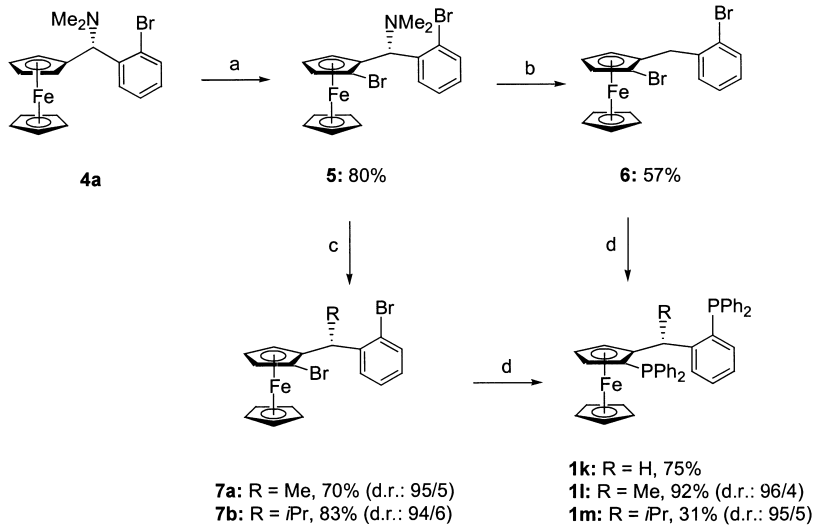
Variation of the phosphorus substituents: Different PR^3_2 were introduced by dilithiation of the ferrocenylamine **4a** followed by treatment with $ClPPh_2$ or ClP(3,5-xylyl)$_2$ to give **1a** and **1b** in about 80 and 30 % yield, respectively, for two steps. The moderate yield of **1b** is probably due to the steric hindrance of the xylyl substituents on the phosphorus atoms.

Variation of the nitrogen substituents: Different substituents R^1 and R^2 on the nitrogen atom were introduced by straightforward substitution of the intermediate acetate with various amines. Thus, the diphosphanes **1c–j** bearing alkyl, cyclic, functionalized, and chiral amino groups at the position α to the ferrocene moiety were prepared in moderate to good yields depending on the steric bulk of the amine (see Table 1).

Introduction of hydrogen and alkyl substituents at the position α to ferrocene: To investigate further the influence of the stereocenter at the position α to ferrocene on the ligand properties, the diphosphane **1k** bearing no substituent and **1l,m** bearing alkyl substituents were prepared. The amine **4a** was dilithiated in situ with *t*BuLi and treated with $Cl_4Br_2C_2$ to give the dibrominated product **5** as a single diastereomer in 80 % yield. Reduction of the benzylic amino group of **5** with triethylsilane in trifluoroacetic acid gave the deaminated product **6** in 57 % yield and 97 % *ee*. Starting from the amine **5**, alkyl substituents were readily introduced at the position α to ferrocene by substituting the amino group with organozinc reagents. This substitution is known to proceed with retention of the configuration.[8] Thus, reaction of the ferrocenylamine **5** with Me_2Zn or iPr_2Zn in the presence of acetyl chloride as a promoter led to the products **7a**,**b** in 70–83 % yield with high retention of configuration (d.r. = 94:6). Finally, double bromine–lithium exchange by reaction of **6, 7a**, and **7b** with *n*BuLi followed by quenching with $ClPPh_2$ afforded the phosphanes **1k, 1l**, and **1m** in 75, 92, and 31 % yield, respectively (Scheme 2). Steric hindrance due to the isopropyl substituent might explain the low yield of **1m**, and mixtures of monophosphanes were identified as side products.

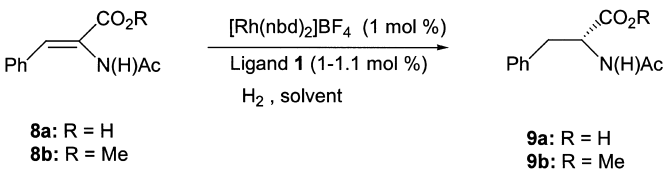
The highly flexible synthesis of the ferrocenylphosphanes **1** allowed us to rapidly modify the ligand structure. The influence of substituents on the phosphorus atom and in the position α to ferrocene on the ligand properties, as well as the efficiency and selectivity of these ligands were examined in asymmetric catalysis.

Enantioselective hydrogenation of C=C bonds: Rhodium-catalyzed asymmetric hydrogenation of α-(acylamino)acrylic



Scheme 2. Synthesis of the diphosphanes **1k–m**. a) *t*BuLi (3.5 equiv), –78 °C to room temperature, 1 h; then $Cl_4Br_2C_2$ (2.2 equiv), 1 h; b) Et_3SiH (10 equiv), TFA, room temperature, 72 h; c) CH_3COCl (2 equiv), R_2Zn (4 equiv), THF, –78 °C to room temperature, 12 h; d) *n*BuLi 2.2 equiv), –78 °C, 15 min; then $ClPPh_2$ (2.3 equiv), –78 °C to room temperature, 1 H. TFA = trifluoroacetic acid.

acids and esters to produce the corresponding amino acid derivatives has been extensively studied[9] and affords a good starting point for comparing the effectiveness of a new chiral ligand.[10] Asymmetric hydrogenation of α-acetamidocinnamic acid (**8a**) and its methyl ester **8b** (Scheme 3) was performed



Scheme 3. Rhodium-catalyzed asymmetric hydrogenation of α-acetamidocinnamic acid (**8a**) and its methyl ester **8b** with the 1,5-diphosphane ligands **1a–m**. nbd = norbornadiene.

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in MeOH or MeOH/toluene (1/1) with 1 mol% of the catalyst prepared in situ from $[Rh(nbd)_2]BF_4$ (1 mol%) and the ligand (1 mol%). The results are summarized in Table 2.

Table 2. Hydrogenation of α-acetamidocinnamic acid derivatives **8a**,**b**.

Entry	Ligand	Substrate	Solvent	Pressure [bar]	Reaction time [h]	Conversion [%][a]	*ee* [%][a]
1	**1a**	**8a**[b]	MeOH	1	14	17	83 (*R*)
2	**1c**	**8a**[b]	MeOH	1	21	traces	rac.
3	**1k**	**8a**[b]	MeOH	5	1	quant.	76 (*R*)
4	**1a**	**8b**	MeOH/Tol.	1	0.5	quant.	95 (*R*)
5	**1c**	**8b**	MeOH/Tol.	5	3	quant.	92 (*R*)
6	**1d**	**8b**	MeOH/Tol.	1	16	90	70 (*R*)
7	**1e**	**8b**	MeOH/Tol.	1	1.5	quant.	95 (*R*)
8	**1f**	**8b**	MeOH/Tol.	1	20	traces	–
9	**1k**	**8b**	MeOH	5	2.5	90	77 (*R*)
10	**1l**	**8b**	MeOH	1	0.6	quant.	52 (*S*)
11	**1m**	**8b**	MeOH/Tol.	1	4	quant.	96.6 (*R*)

[a] Determined by GC analysis (Chirasil L-Val). [b] The hydrogenation product **9a** was esterified with trimethylsilyldiazomethane before the GC measurements.

Although poor activities and moderate enantioselectivities were observed for the hydrogenation of the free acid **8a** (Table 2, entries 1–3), hydrogenation of (*Z*)-methyl α-acetamidocinnamate (**8b**) proceeded smoothly to give reduction product **9b** with enantioselectivities of up to 96.6% with the isopropyl-substituted ligand **1m** (Table 2, entry 11). The substituent in the position α to the ferrocene moiety appeared to play an essential role in the efficiency of the ligand and the enantioselectivity of the reaction. Using the phosphane **1k** without a substituent in the α position gave **9b** with only 77% *ee*, and a hydrogen pressure of 5 bar was necessary (Table 2, entry 9), whereas **9b** was obtained in 95% *ee* with the dimethylamino-substituted ligand **1a** (Table 2, entry 4). Surprisingly, **9b** with the opposite configuration was obtained with the methyl-substituted ligand **1l** (Table 2, entry 10). Replacing the dimethylamino group (**1a**) by a pyrrolidyl substituent (**1c**) led to a slight decrease in the activity and enantioselectivity of the reaction (Table 2, entry 5). Of special interest is the marked difference in the enantioselectivity and reactivity for **1d** and **1e** (Table 2, entries 6 and 7), which bear chiral amino substituents with opposite configurations. An internal cooperativity exists between the stereocenter at the position α to the ferrocene moiety and that of the *N*-methyl-*N*-phenylethyl substituent, analogous to the principle of matched and mismatched (external cooperativity) introduced by Masamune et al.[11] No hydrogenation occurred with the ligand **1f** bearing a second coordination site (Table 2, entry 8). The enantioselectivities obtained for the hydrogenation of **8b** are quite encouraging since they are comparable with those described in the literature with known ligands.[12]

Ligands **1** proved to be also very efficient for the rhodium-catalyzed hydrogenation of dimethyl itaconate (**10**). Hydrogenation of **10** was performed in MeOH or MeOH/toluene (1/1) under 1 bar of hydrogen pressure with 1 mol% of the catalyst prepared in situ from $[Rh(nbd)_2]BF_4$ (1 mol%) and the ligand (1 mol%). The results are summarized in Table 3.

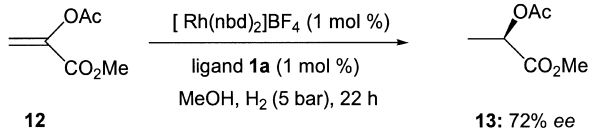
Table 3. Hydrogenation of dimethyl itaconate **10**.

Entry	Ligand	Solvent	Pressure [bar]	Reaction time [h]	Conversion [%][a]	*ee* [%][a]
1	**1a**	MeOH	1	14	quant.	91 (*S*)
2	**1b**	EtOH	1	17	0	–
3	**1c**	MeOH/Tol	1	14	quant.	81 (*S*)
4	**1d**	MeOH	1	16	91	74 (*S*)
5	**1e**	MeOH	1	1.5	quant.	98.2 (*S*)
6	**1f**	MeOH	1	20	0	–
7	**1k**	MeOH	10[c]	3	quant.	75 (*S*)
8	**1l**	MeOH/Tol	1	1	quant.	19 (*R*)
9	**1m**	MeOH	1	4	quant.	97.9 (*S*)

[a] Determined by ^1H NMR spectroscopy. [b] Determined by HPLC analysis (Daicel Chiracel OD). [c] No conversion was observed using 1 bar of hydrogen pressure.

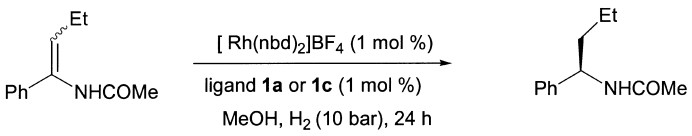
Enantioselectivities of up to 98.2% (Table 3, entry 5) were obtained with **1e**. The same trend as described above was observed for the influence of the ligand structure on the enantioselectivity of the reaction.

Enol esters and enamides are interesting substrates for asymmetric hydrogenation since the reduction products can be easily converted to optically active alcohols or amines. Hydrogenation of the enol ester **12** with ligand **1a** afforded the acetate **13** with 72% *ee* (Scheme 4). Hydrogenation of the enamide **14** afforded the amide **15** in 68% *ee* with ligand **1a** and 76% *ee* with ligand **1c** (Scheme 5). Unlike the preceeding examples, use of the pyrrolidyl-substituted ligand **1c** led to better enantioselectivities than with **1a**, and this confirms the importance of ligand–substrate matching.



12 **13:** 72% *ee*

Scheme 4. Hydrogenation of the enol ester **12** with the ligand **1a**.

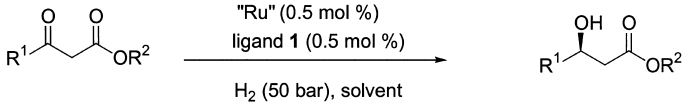


14 **15**

with ligand **1a**: 68% *ee*
with ligand **1c**: 76% *ee*

Scheme 5. Hydrogenation of the enamide **14** with ligands **1a** and **1c**.

Enantioselective hydrogenation of C=O bonds: The ferrocenylphosphanes of type **1** are also highly efficient for the ruthenium-catalyzed asymmetric hydrogenation of various 1,3-ketoesters (Scheme 6).[1, 10] All the ruthenium-catalyzed hydrogenation reactions were performed with 0.5 mol% of the catalyst formed in situ from $[Ru(cod)(C_4H_7)_2]$/HBr ("Ru", cod = 1,5-cyclooctadiene; 0.5 mol%) and the ligand (0.5 mol%).[13] The results obtained for the hydrogenation of various 1,3-ketoesters **16** are summarized in Table 4. Whereas the reduction product **17a** was obtained with the same configuration with **1a**, **1k**, or **1m**, the α-hydroxyester **17a** with the opposite configuration was obtained with **1l**



16a: $R^1 = R^2 = Me$ **16d:** R^1 = propyl; $R^2 = Et$ **17a-f**
16b: R^1 = Me; $R^2 = Et$ **16e:** R^1 = isopropyl; $R^2 = Et$
16c: R^1 = Ph; $R^2 = Et$ **16f:** R^1 = chloromethyl; $R^2 = Et$

Scheme 6. Ruthenium-catalyzed asymmetric hydrogenation of the 1,3-ketoesters **16a–f**.

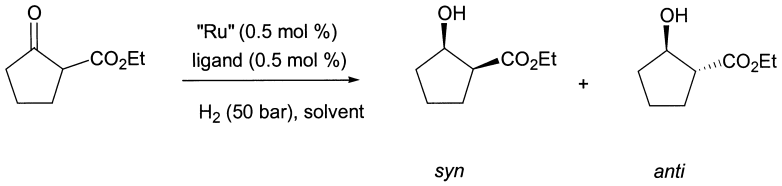
(Table 4, entry 3). Similarly, both enantiomers of **17b–f** could be obtained by using either **1a** or **1l**. These results are consistent with those obtained previously for the hydrogenation of C=C bonds. Remarkably, whereas changing the substituents on the nitrogen atom from methyl to propyl led to a decrease in enantioselectivity for the reduction of **16b** (Table 4, entries 5, 9–11), ligand **1j** bearing a diisobutylamino group in the position α to ferrocene gave the reduction product **17b** with the opposite configuration and 98.6% *ee* (Table 4, entry 12). Reduction of the chloromethyl-substituted α-ketoester **16f** led to the corresponding α-hydroxyester **17f** with moderate enantioselectivities (Table 4, entries 23–26). Lower enantioselectivities for the reduction of **16f** were also observed by Burk et al. (76% *ee*) with the DuPHOS ligand.[14] Higher reaction rates and better enantioselectivities for the hydrogenation of **16a** with ligand **1a** were obtained by increasing the hydrogen pressure from 10 to 100 bar (10 bar: 16 h, 95.6% *ee*; 100 bar: 1 h, 96.9% *ee*). It is noteworthy that the reduction of **16b** could be performed with a substrate/catalyst ratio of 5000 to give the α-hydroxyester **17b** with 93.2% *ee* in 62 h.

Hydrogenation was also successful for cyclic ketoesters such as ethyl 2-oxocyclopentanecarboxylate (**18**; Scheme 7 and Table 5) and ethyl 2-oxocyclohexanecarboxylate (**20**; Scheme 8 and Table 6). Depending on the ligand **1** and the reaction conditions, high diastereoselectivities and enantioselectivities were observed for the hydrogenation of **18** (Table 5, entries 1 and 4). Although poor diastereoselectivities were observed for the

Table 4. Hydrogenation of various 1,3-ketoesters.

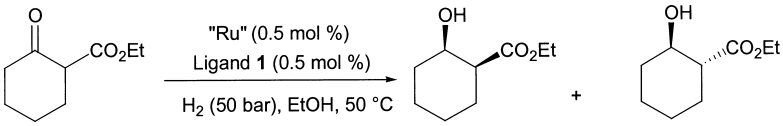
Entry	Substrate[a]	Ligand	Temp [°C]	Time [h]	Conversion [%][b]	*ee* [%][c]
1	**16a**	**1a**	50	14	quant.	96.3 (*R*)
2	**16a**	**1k**	room temperature	10	quant.	78 (*R*)
3	**16a**	**1l**	50	8	quant.	86 (*S*)
4	**16a**	**1m**	50	9	quant.	93.3 (*R*)
5	**16b**	**1a**	50	8	quant.	95.5 (*R*)
6	**16b**	**1b**[d]	50	17	quant.	93.4 (*R*)
7	**16b**	**1d**	50	9	90	84 (*R*)
8	**16b**	**1e**[d]	50	16	quant.	59 (*R*)
9	**16b**	**1g**[d]	50	15	quant.	84.6 (*R*)
10	**16b**	**1h**[d]	50	19	quant.	76.9 (*R*)
11	**16b**	**1i**[d]	50	16	quant.	70.4 (*R*)
12	**16b**	**1j**[d]	50	19	quant.	98.6 (*S*)
13	**16b**	**1l**	50	6	75	69 (*S*)
14	**16b**	**1m**	50	9	quant.	95.9 (*R*)
15	**16c**	**1a**	50	12	quant.	95.0 (*S*)
16	**16c**	**1d**	50	9	quant.	86.0 (*S*)
17	**16c**	**1l**	50	8	quant.	93.7 (*R*)
18	**16c**	**1m**	50	8	quant.	96.0 (*S*)
19	**16d**	**1a**	50	9	quant.	96.5 (*R*)
20	**16d**	**1l**	50	10	quant.	92.7 (*S*)
21	**16e**	**1a**	50	12	quant.	95.9 (*R*)
22	**16e**	**1l**	50	10	quant.	96.5 (*S*)
23	**16f**	**1a**	50	23[e]	82	75 (*S*)
24	**16f**	**1d**	50	22	quant.	74 (*S*)[d]
25	**16f**	**1e**	50	17	quant.	79 (*S*)[d]
26	**16f**	**1l**	50	8	quant.	46 (*R*)

[a] MeOH was used as a solvent for methylesters and EtOH for ethylester. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by HPLC analysis (Daicel Chiracel OD). [d] "Ru": 0.8 mol%, ligand 0.9 mol%. [e] Reaction performed at 90 °C in CH_2Cl_2.



18 **19**

Scheme 7. Ruthenium-catalyzed hydrogenation of ethyl 2-oxocyclopentanecarboxylate (**18**) with the 1,5-diphosphane ligands **1a, 1b**, and **1l**.



20 **21**

Scheme 8. Ruthenium-catalyzed hydrogenation of ethyl 2-oxocyclohexanecarboxylate (**20**).

Table 5. Hydrogenation of ethyl 2-oxocyclopentanecarboxylate **18**.

Entry[a]	Ligand	Solvent	Temp. [°C]	Time [h]	*de* [%][b,c]	*ee* [%][d]
1	**1a**	EtOH/CH_2Cl_2 (1/10)	50	63	98.2	90.9 (1*R*,2*R*)
2	**1a**	EtOH	50	22	67	81 (1*R*,2*R*)[c]
3	**1b**	EtOH	50	16	38.3	51.7 (1*R*,2*R*)[c]
4	**1l**	EtOH	room temperature	21	90.5	91.6 (1*S*,2*S*)

[a] Results determined after complete conversion. [b] The major diastereomer is the *anti* product. [c] Determined by HPLC analysis (Daicel Chiracel OD). [d] 0.8 mol% "Ru", 0.9 mol% ligand.

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Table 6. Hydrogenation of ethyl 2-oxocyclohexanecarboxylate **20**.

Entry[a]	Ligand	Time [h]	*de* [%][b,c]	*ee* [%][c] of *syn*-**21**	*ee* [%][c] of *anti*-**21**
1	**1a**	63	11	96.5 (1*S*,2*R*)	89.6 (1*R*,2*R*)
2	**1b**	19	84.6	>99 (1*S*,2*R*)	>99 (1*R*,2*R*)[c]
3	**1d**	24	79.7	>99 (1*S*,2*R*)	>99 (1*R*,2*R*)[c]
4	**1e**	24	41.1	99.5 (1*S*,2*R*)	>99 (1*R*,2*R*)[c]
5	**1l**	31	6	82.7 (1*R*,2*S*)	50.8 (1*R*,2*R*)

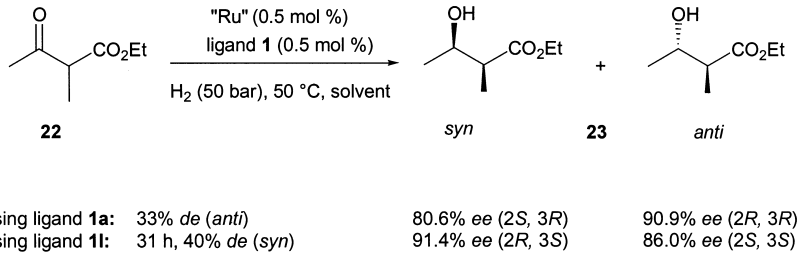
[a] Results determined after complete conversion. [b] In both cases the *anti* diastereomer was the major product. [c] Determined by HPLC analysis (Daicel Chiracel OD). [d] 0.8 mol% "Ru", 0.9 mol% ligand.

reduction of **20** with **1a** and **1l**, the *anti* product **21** was obtained with up to 84.6% *de* and greater than 99% *ee* with the bulkier ligands **1b** and **1d** (Table 6, entries 2 and 3).

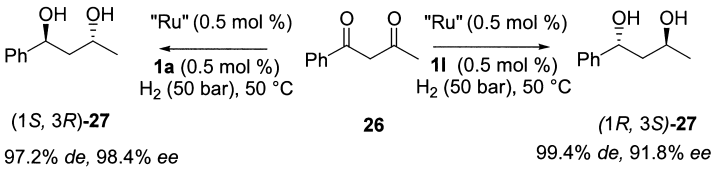
Hydrogenation of the α-ketoester **22** with ligand **1a** (in CH_2Cl_2 for 65 h) or with ligand **1l** (in EtOH/CH_2Cl_2 10/1 for 31 h) led after complete conversion to the α-hydroxyester **23** not only with the opposite topicity but also with the opposite diastereoselectivity (Scheme 9).

Hydrogenation of symmetrical 1,3-diketones RC=OCH$_2$C=OR **24** (**a**: R = Me; **b**: R = Ph) under the same reaction conditions led to the corresponding diols RC(OH)CH$_2$C(OH)R **25** (**a**: R = Me; **b**: R = Ph) with high diastereoselectivities in favor of the *anti* products and with high enantioselectivities (up to 98.9% *de* and 98.8% *ee*; Table 7, entry 5).

High diastereoselectivities and enantioselectivities were also obtained in the hydrogenation of the unsymmetrical 1,3-diketone **26** (Scheme 10). Once again, both enantiomers of the *anti*-diol **27** could be obtained by using ligands **1a** or **1l**.

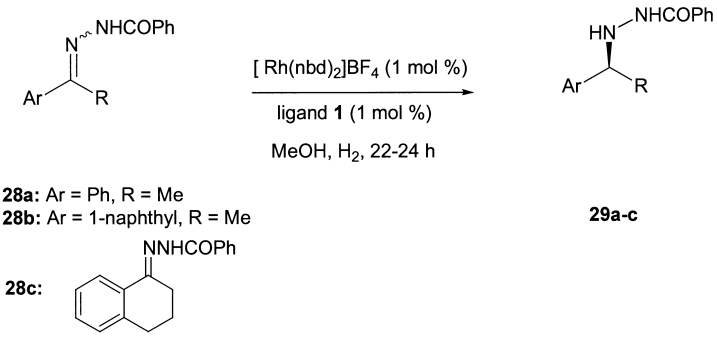


Scheme 9. Hydrogenation of ethyl 2-methyl-3-oxobutyrate (**22**).



Scheme 10. Hydrogenation of unsymmetrical 1,3-diketone **26**.

Enantioselective hydrogenation of C=N bonds: Preparation of optically pure amines by catalytic asymmetric hydrogenation of imines is still a challenging task, although promising methodologies have been developed.[15] The efficiency of the ligands **1** was first examined for the hydrogenation of hydrazones.[16] These substrates have the advantage of possessing a second coordination site. Hydrogenation of various *N*-benzoylhydrazones **28a–c** (Scheme 11) was performed in MeOH in the presence of 1 mol% of the catalyst prepared in situ from [Rh(nbd)$_2$]BF$_4$ (1 mol%) and **1** (1 mol%). The results are summarized in Table 8.



Scheme 11. Hydrogenation of the *N*-benzoylhydrazones **30a–c**.

Moderate enantioselectivities were generally observed with all ligands **1**. Surprisingly, the best enantioselectivity was obtained with the unsubstituted ligand **1k** (Table 8, entry 9). Furthermore, the methyl-substituted ligand **1l** gave **29a**,**b** with the same configuration that was obtained with the other ligands, and **29c** with the opposite configu-

Table 7. Hydrogenation of symmetrical 1,3-diketones of type **24**.

Entry	Substrate	Ligand	Time [h]	*de* [%][a,b]	*ee* [%][b]
1	**24a:** R = Me	**1a**	8	95.9	96.7 (*R*,*R*)
2	**24a**	**1l**	8	84.0	78.0 (*S*,*S*)
3	**24a**	**1m**	9	94.4	98.6 (*R*,*R*)
4	**24b:** R = Ph	**1a**	8	98.0	98.2 (*S*,*S*)
5	**24b**	**1l**	12	98.9	98.8 (*R*,*R*)

[a] The major diastereomer is the *anti* product. [b] Determined by GC (Chirasil-DexCB) or HPLC analysis (Daicel Chiracel OD).

Table 8. Hydrogenation of the *N*-benzoylhydrazones **28a–c**.

Entry	Substrate	Ligand	Pressure [bar]	Conversion [%]	*ee* [%][a]
1	**28a**	**1a**	30	71	41 (*S*)
2	**28a**	**1b**[b]	30	quant.	21.7 (*S*)
3	**28a**	**1c**	10	53	36 (*S*)
4	**28a**	**1k**	30	quant.	53 (*S*)
5	**28a**	**1l**	30	quant.	43 (*S*)
6	**28b**	**1a**	30	90	57 (*S*)
7	**28b**	**1b** [b,c]	50	quant.	28.7 (*S*)
8	**28b**	**1c**	10	32	56 (*S*)
9	**28b**	**1k**[d]	30	>95	65 (*S*)
10	**28b**	**1l**	30	quant.	45 (*S*)
11	**28c**	**1a**	50	53	65 (−)[e]
12	**28c**	**1b**[b]	50	quant.	15,2 (−)[e]
13	**28c**	**1c**	50	59	67 (−)[e]
14	**28c**	**1k**	30	86	8 (−)[e]
15	**28c**	**1l**	30	>95	17 (+)[e]

[a] Determined by HPLC analysis (Daicel Chiracel OJ). [b] [Rh(cod)$_2$]BF$_4$ 0.8 mol%, ligand 0.8 mol%. [c] 40 °C, 14 h. [d] EtOH was used as solvent. [e] The absolute configuration of **29c** has not been determined yet.

ration. The results obtained for the hydrogenation of **28c** are somewhat different. Ligand **1c** led to the hydrazine **29c** with the best enantioselectivity (Table 8, entry 13), and **1l** gave hydrazine **29c** with the opposite configuration (Table 8, entry 15). Ligand–substrate matching appears to be even more important for the hydrogenation of C=N bonds than for C=O or C=C bonds.

Conclusion

In summary, we have developed a new family of ferrocenyl phosphanes **1** whose synthesis is highly flexible and offers many possibilities for variation. This allowed us to rapidly modify the structure of phosphanes **1** to optimize ligand–substrate matching. Ligands **1** proved to be very efficient ligands and led to excellent enantioselectivities in the hydrogenation of various functionalized double bonds and 1,3-dicarbonyl compounds. Furthermore, the two opposite configurations of the reduced products could be obtained by merely modifying the substituent in the position α to the ferrocene moiety.

Experimental Section

General: Melting points are uncorrected. NMR spectra were recorded at room temperature in $CDCl_3$ on Bruker ARX 200, AC 300, AM 400 or AMX 500 instruments. Chemical shifts are given relative to the residual solvent peak. Signals of the minor diastereomer that differ from those of the major isomer are given for sake of comparison. Optical rotations were measured on a Perkin Elmer 241 polarimeter. IR spectra were recorded on a Nicolet 510 FT-IR spectrometer. Electron impact (EI) mass spectra were recorded on a Varian CH 7A. Enantiomeric excesses were determined by HPLC analysis (Chiralcel OD and OJ columns, Daicel Chemical Industries with *n*-heptane/2-propanol as mobile phase and detection by a diode array UV/Vis detector) or by GC analysis (Chirasil-DEX CB or Chiralsil-L-Val columns, Chrompak, with hydrogen as carrier gas). Racemic compounds were used to choose the operating conditions for the resolution of the enantiomer and diastereomer peaks. Organic layers were dried over anhydrous $MgSO_4$. Column chromatography was carried out on silica gel 60 (70–230 mesh, ASTM). Hydrogenations were performed in 100 or 200 mL stainless steel autoclaves or in a Schlenk tube with a hydrogen-filled balloon for the reactions under 1 bar pressure.

Materials: Tetrahydrofuran (THF), diethyl ether, methyl *tert*-butyl ether (MTBE), and toluene were distilled from sodium/benzophenone; CH_2Cl_2 was distilled from CaH_2; acetone from $CaCl_2$; and MeOH and *i*PrOH were distilled from Mg turnings. Pyridine was dried over KOH. Commercial reagents were used without further purification. The following starting materials were prepared according to literature procedures: $[\{Rh(nbd)Cl\}_2]$,[17] $[Rh(nbd)_2]BF_4$,[2a] (*S*,*S*)-diphenylprolinolmethyloxazaborolidine (CBS catalyst).[18]

Synthesis of *o*-bromobenzoylferrocene (2): A solution of aluminum(III) chloride (7.88 g, 59.10 mmol) and *o*-bromobenzoyl chloride (12.40 g, 7.40 mL, 56.51 mmol) in CH_2Cl_2 (50 mL) was added dropwise to a solution of ferrocene (10.00 g, 53.75 mmol) in CH_2Cl_2 (50 mL) at 0 °C. The mixture was warmed to room temperature and stirred for 2 h. Hydrolysis was then performed at 0 °C by addition of ice-cold water. The reaction mixture was diluted with CH_2Cl_2 and washed twice with saturated aqueous K_2CO_3. After conventional workup, the crude product was purified by chromatography (pentane/MTBE 4/1) to give the ketone **2** (16.09 g, 43.60 mmol, 81% yield) as a dark red solid. M.p. 102 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.64-7.61$ (m, 1H), 7.52–7.45 (m, 1H), 7.42–7.26 (m, 2H), 4.73–4.71 (m, 2H), 4.59–4.58 (m, 2H), 4.29 (s, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 199.4, 141.3, 133.4, 130.8, 128.7, 126.7, 119.5, 78.2, 72.9, 71.1, 70.1$; MS: *m/z* (%): 370 (100) $[M+1]^+$, 369 (56) $[M]^+$, 368 (98) $[M-1]^+$; elemental analysis (%) calcd for $C_{17}H_{13}BrFeO$ (369.0): C 55.33, H 3.55; found: C 55.12, H 3.77.

Synthesis of (*R*)-(α-hydroxy-*o*-bromophenylmethyl)ferrocene (3): Ketone **2** (4.00 g, 10.80 mmol) was dissolved in THF (20 mL) and treated with $BH_3 \cdot SMe_2$ (1M in THF, 11 mL, 11 mmol) and CBS catalyst (0.90 g, 3.25 mmol, 0.3 equiv) in THF (10 mL) according to the procedure described in the literature (addition time: 2 h, reaction time: 30 min).[5a] Chromatography (pentane/MTBE 4/1) of the crude product afforded the alcohol **2** (3.80 g, 10.26 mmol, 95% yield, 96–97% *ee*) as an orange solid: m.p. 71 °C. Recrystallization from heptane gave the alcohol in enantiomerically pure form. $[\alpha]^{20}_{(kap)d(/kap)} = -159.7$ ($c = 0.41$ in $CHCl_3$); HPLC (OD, heptane/*i*PrOH 92/8, 0.6 mL/min): t_r/min = 15.9 (*R*), 18.4 (*S*); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.65-7.07$ (m, 4H), 5.81 (s, 1H), 4.41 (m, 1H), 4.26 (s, 5H), 4.20 (m, 1H), 4.16 (m, 2H), 2.74 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): $\delta = 142.4, 132.5, 128.8, 127.8, 127.4, 122.3, 93.6, 70.2, 68.4, 68.1, 67.7, 67.5, 66.2$; MS: *m/z* (%): 372 (21) $[M+1]^+$, 371 (4) $[M]^+$, 370 (22) $[M-1]^+$; elemental analysis (%) calcd for $C_{17}H_{15}BrFeO$ (371.1): C 55.03, H 4.07; found: C 54.86, H 3.95.

Synthesis of (*R*)-[α-(*N*,*N*-dimethylamino)-*o*-bromophenylmethyl]ferrocene (4a): Alcohol **3** (3.50 g, 9.43 mmol) was treated with acetic anhydride (2 mL) and pyridine (5 mL), and the solution was stirred for 12 h at room temperature. Volatile matter was removed in vacuo. The crude acetate was dissolved in acetonitrile (50 mL) and treated with dimethylamine (40% in H_2O, 16 mL) at room temperature overnight. The reaction mixture was then concentrated and poured into saturated aqueous NH_4Cl and extracted with diethyl ether. After conventional workup, the crude product was purified by chromatography (pentane/Et_2O 4/1 to pure Et_2O) to give the amine **4a** (3.56 g, 8.96 mmol, 95% yield) as an orange solid. M.p. 73 °C; $[\alpha]^{20}_{(kap)d(/kap)} = -72.8$ ($c = 1.02$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.73-7.70$ (m, 1H), 7.64–7.61 (m, 1H), 7.39–7.31 (m, 1H), 7.16–7.06 (m, 1H), 4.47 (s, 1H), 4.25–4.24 (m, 1H), 4.20–4.19 (m, 1H), 4.16–4.14 (m, 1H), 4.11–4.09 (m, 1H), 3.76 (s, 5H), 2.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 142.9, 132.3, 129.5, 128.1, 127.1, 124.8, 89.7, 70.6, 68.5, 68.3, 66.1, 44.0$; MS: *m/z* (%): 399 (62) $[M+1]^+$, 398 (15) $[M]^+$, 397 (64) $[M-1]^+$; elemental analysis (%) calcd for $C_{19}H_{20}BrFeN$ (398.1): C 57.32, H 5.06, N 3.52; found: C 57.03, H 5.37, N 3.43.

Synthesis of (*R*)-[α-(1-pyrrolidyl)-*o*-bromophenylmethyl]ferrocene (4b): After acetylation of the alcohol **3** (1.20 mmol), the resulting acetate was treated with pyrrolidine (0.5 mL, 6.0 mmol, 5 equiv) in acetonitrile (15 mL) and H_2O (2.5 mL) as described above. After chromatography (pentane/Et_2O 3/1 to pure Et_2O) of the crude product, the amine **4b** (0.48 g, 1.13 mmol, 94% yield) was obtained as an orange solid. M.p. 83 °C; $[\alpha]^{20}_{(kap)d(/kap)} = -59.7$ ($c = 1.03$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.81-7.78$ (m, 1H), 7.64–7.61 (m, 1H), 7.38–7.31 (m, 1H), 7.15–7.12 (m, 1H), 4.49 (s, 1H), 4.25–4.23 (m, 2H), 4.16–4.13 (m, 1H), 4.10–4.08 (m,1H), 3.84 (s, 5H), 2.37–2.27 (m, 4H), 1.69–1.65 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 143.8, 132.4, 130.0, 128.1, 127.3, 124.1, 90.8, 70.2, 68.6, 68.3, 67.3, 66.08, 66.1, 53.3, 23.2$; MS: *m/z* (%): 425 (42) $[M+1]^+$, 424 (13) $[M]^+$, 423 (45) $[M-1]^+$; elemental analysis (%) calcd for $C_{21}H_{22}BrFeN$ (424.2): C 59.47, H 5.23, N 3.30; found: C 59.22, H 5.21, N 3.58.

Synthesis of (*R*)-[α-{(*R*)-*N*-methyl-1-phenylethylamino}-*o*-bromophenylmethyl]ferrocene (4c): After acetylation of the alcohol **3** (1.35 mmol), the resulting acetate was treated with (*R*)-*N*-methyl-1-phenylethylamine (0.6 mL, 4.1 mmol, 3.0 equiv) in acetonitrile (18 mL) and H_2O (2.5 mL) as described above. After conventional workup and removal of the solvent and the excess reagents in vacuo, the pure amine **4c** (657 mg, 1.35 mmol, 99.8% yield) was obtained as an orange oil. Purification of the crude product by column chromatography on silica gel led to decomposition. $[\alpha]^{20}_{(kap)d(/kap)} = +227$ ($c = 0.48$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.21-8.13$ (m, 1H), 7.82–7.79 (m, 1H), 7.66–7.26 (m, 7H), 5.13 (s, 1H), 4.45–4.43 (m, 2H), 4.35–4.33 (m, 1H), 4.29–4.28 (m, 1H), 4.02–3.94 (m, 6H), 1.94 (s, 3H), 1.51 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 144.2, 143.9, 132.5, 129.9, 128.3, 127.7, 127.5, 126.2, 124.9, 90.5, 71.1, 68.7, 68.7, 68.5, 66.4, 66.1, 64.1, 56.4, 32.8, 10.2$; MS: *m/z* (%): 489 (29) $[M+1]^+$, 488 (10) $[M]^+$, 487 (30) $[M-1]^+$.

Synthesis of (*R*)-[α-{(*S*)-*N*-methyl-1-phenylethylamino}-*o*-bromophenylmethyl]ferrocene (4d): After acetylation of the alcohol **3** (1.48 mmol), the resulting acetate was treated with (*S*)-*N*-methyl-1-phenylethylamine (0.65 mL, 4.50 mmol, 3 equiv) in acetonitrile (20 mL) and H_2O (2.7 mL)

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as described above. Filtration of the reaction mixture and drying of the precipitate afforded the amine **4d** (558 mg, 1.43 mmol, 77% yield) as an orange solid. Purification of the crude product by column chromatography on silica gel led to decomposition. M.p. 135 °C; $[\alpha]^{20}_{(kap)d(/kap)} = -39.8$ ($c = 0.47$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.78$ (dd, $J = 7.8$, 1.7 Hz, 1H), 7.56 (dd, $J = 8.0$, 1.0 Hz, 1H), 7.37–7.03 (m, 7H), 4.84 (s, 1H), 4.19–4.17 (m, 2H), 4.07–4.06 (m, 1H), 4.02–4.01 (m, 1H), 3.80 (q, $J = 6.8$ Hz, 1H), 3.68 (s, 5H), 1.70 (s, 3H), 1.12 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 144.0$, 143.9, 132.6, 130.0, 128.2, 127.9, 127.7, 127.4, 126.2, 125.1, 90.5, 70.6, 68.7, 68.5, 66.5, 66.2, 64.4, 55.7, 33.2, 11.8; MS: *m/z* (%): 489 (43) $[M+1]^+$, 488 (30) $[M]^+$, 487 (45) $[M-1]^+$; elemental analysis (%) calcd for $C_{26}H_{26}BrFeN$ (488.2): C 64.06, H 5.38, N 2.88; found: C 63.90, H 5.46, N 2.83.

Synthesis of (*R*)-[α-{*N*-methyl(2-*N*′,*N*′-dimethylamino)ethylamino}-*o*-bromophenylmethyl]ferrocene (4e): After acetylation of the alcohol **3** (1.35 mmol), the resulting acetate was treated with *N*,*N*,*N*′-trimethylethylenediamine (0.77 mL, 6.73 mmol, 5 equiv) in acetonitrile (18 mL) and H_2O (2.5 mL) as described above. After chromatography (pentane/Et_2O 3/1 to Et_2O with 2% NEt_3) of the crude product, the amine **4e** (601 mg, 1.32 mmol, 98% yield) was obtained as an orange oil. $[\alpha]^{20}_{(kap)d(/kap)} = -33.4$ ($c = 1.07$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.62-7.53$ (m, 2H), 7.32–7.23 (m, 1H), 7.10–7.00 (m, 1H), 4.70 (s, 1H), 4.21–4.20 (m, 1H), 4.07–4.02 (m, 3H), 3.74 (s, 5H), 2.37–2.16 (m, 4H), 2.02 (s, 6H), 1.98 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 142.6$, 132.5, 129.9, 128.2, 127.1, 125.2, 89.6, 70.7, 68.6, 68.2, 67.3, 66.8, 66.5, 57.3, 52.5, 45.7, 40.1; MS: *m/z* (%): 456 (10) $[M+1]^+$, 455 (10) $[M]^+$, 454 (9) $[M-1]^+$; elemental analysis (%) calcd for $C_{22}H_{27}BrFeN_2$ (455.2): C 58.05, H 5.98, N 6.15; found: C 57.81, H 5.88, N 6.27.

Synthesis of (*R*)-[α-(*N*,*N*-diethylamino)-*o*-bromophenylmethyl]ferrocene (4f): After acetylation of the alcohol **3** (2.60 mmol), the resulting acetate was dissolved in THF (10 mL) and H_2O (8 mL) and treated with *N*,*N*-diethylamine (1.4 mL, 13.2 mmol, 5 equiv) as described above. After chromatography (pentane/Et_2O 4/1) of the crude product, the amine **4f** (1.00 g, 2.50 mmol, 93% yield) was obtained as an orange oil. $[\alpha]^{20}_{(kap)d(/kap)} = -24.9$ ($c = 1.51$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.63$ (d, $J = 7.5$ Hz, 1H), 7.54 (dd, $J = 8.0$, 1.2 Hz, 1H), 7.28 (t, $J = 7.3$ Hz, 1H), 7.05 (td, $J = 7.6$, 1.5 Hz, 1H), 4.92 (s, 1H), 4.21–4.20 (m, 1H), 4.07–4.02 (m, 3H), 3.71 (s, 5H), 2.35 (q, $J = 7.0$ Hz, 4H), 0.80 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 144.2$, 132.9, 130.6, 128.5, 127.6, 125.6, 91.0, 71.0, 69.1, 68.5, 67.3, 66.6, 63.7, 43.2, 11.7; MS: *m/z* (%): 427 (31) $[M+1]^+$, 425 (34) $[M-1]^+$; elemental analysis (%) calcd for $C_{21}H_{24}BrFeN$ (426.2): C 59.18, H 5.68, N 3.29; found: C 59.00, H 5.69, N 3.13.

Synthesis of (*R*)-[α-(*N*,*N*-di-*n*-propylamino)-*o*-bromophenylmethyl]ferrocene (4g): After acetylation of the alcohol **3** (3.20 mmol), the resulting acetate was dissolved in THF (11 mL) and H_2O (9 mL) and treated with di-*n*-propylamine (2.2 mL, 16.04 mmol, 5 equiv) as described above. After chromatography (pentane/Et_2O 4/1) of the crude product, the amine **4g** (1.29 g, 2.84 mmol, 90% yield) was obtained as an orange oil. $[\alpha]^{20}_{(kap)d(/kap)} = -6.9$ ($c = 1.54$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.55-7.51$ (m, 2H), 7.25 (t, $J = 7.4$ Hz, 1H), 7.08–7.02 (m, 1H), 5.11 (s, 1H), 4.27 (s, 1H), 4.03 (s, 2H), 3.97 (s, 1H), 3.80 (s, 5H), 2.36–2.19 (m, 4H), 0.66 (t, $J = 7.4$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 143.2$, 132.9, 131.0, 128.5, 127.2, 125.9, 90.7, 70.9, 69.1, 68.2, 67.9, 66.9, 64.1, 52.1, 20.6, 12.2; MS: *m/z* (%): 455 (71) $[M+1]^+$, 453 (78) $[M-1]^+$; elemental analysis (%) calcd for $C_{23}H_{28}BrFeN$ (454.2): C 60.82, H 6.21, N 3.08, Br 17.59; found: C 60.91, H 6.25, N 3.02, Br 17.28.

Synthesis of (*R*)-[α-(*N*,*N*-di-*n*-butylamino)-*o*-bromophenylmethyl]ferrocene (4h): After acetylation of the alcohol **3** (4.06 mmol), the resulting acetate was dissolved in THF (14 mL) and H_2O (11 mL) and treated with di-*n*-butylamine (3.4 mL, 20.3 mmol, 5 equiv) as described above. After chromatography (pentane/Et_2O 4/1) of the crude product, the amine **4h** (1.76 g, 3.65 mmol, 90% yield) was obtained as an orange oil. $[\alpha]^{20}_{(kap)d(/kap)} = -14.2$ ($c = 1.47$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.53$ (d, $J = 8.0$ Hz, 2H), 7.25 (t, $J = 7.6$ Hz, 1H), 7.07–7.01 (m, 1H), 5.06 (s, 1H), 4.25–4.24 (m, 1H), 4.03–4.02 (m, 2H), 3.99 (s, 1H), 3.78 (s, 5H), 2.28–2.21 (m, 4H), 1.27–1.20 (m, 4H), 1.14–1.03 (m, 4H), 0.73 (t, $J = 7.2$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 143.4$, 132.9, 130.9, 128.5, 127.3, 125.8, 111.2, 90.8, 71.0, 69.1, 68.3, 67.8, 66.8, 64.1, 50.1, 29.4, 20.9, 17.9, 14.5; MS: *m/z* (%): 483 (52) $[M+1]^+$, 481 (56) $[M-1]^+$; elemental analysis (%) calcd for $C_{25}H_{32}BrFeN$ (482.3): C 62.26, H 6.69, N 2.90, Br 16.57; found: C 62.34, H 6.69, N 2.87, Br 16.46.

Synthesis of (*R*)-[α-(*N*,*N*-diisobutylamino)-*o*-bromophenylmethyl]ferrocene (4i): After acetylation of the alcohol **3** (2.70 mmol), the resulting acetate was dissolved in THF (10 mL) and H_2O (10 mL) and treated with diisobutylamine (2.36 mL, 13.52 mmol, 5 equiv) as described above. After chromatography (pentane/Et_2O 4/1) of the crude product, the amine **4i** (1.15 g, 2.38 mmol, 88% yield) was obtained as an orange solid. M.p. 77–78 °C; $[\alpha]^{20}_{(kap)d(/kap)} = -10.1$ ($c = 1.11$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.56$ (dd, $J = 8.0$, 1.2 Hz, 1H), 7.38 (dd, $J = 7.7$, 1.7 Hz, 1H), 7.22 (td, $J = 7.5$, 1.0 Hz, 1H), 7.04 (td, $J = 7.6$, 1.5 Hz, 1H), 5.41 (s, 1H), 4.45–4.44 (m, 1H), 4.06–4.05 (m, 1H), 3.98–3.97 (m, 1H), 3.94 (s, 5H), 3.84–3.83 (m, 1H), 2.01–1.98 (m, 4H), 1.65 (sept, $J = 6.7$ Hz, 2H), 0.79 (d, $J = 6.5$ Hz, 6H), 0.69 (d, $J = 6.6$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 140.5$, 133.1, 131.7, 128.7, 126.7, 89.8, 71.1, 69.1, 69.0, 67.6, 64.2, 60.2, 27.5, 21.4, 21.1; MS: *m/z* (%): 483 (14) $[M+1]^+$, 481 (16) $[M-1]^+$; elemental analysis (%) calcd for $C_{25}H_{32}BrFeN$ (482.3): C 62.26, H 6.69, N 2.90, Br 16.57; found: C 62.26, H 6.65, N 2.84, Br 16.18.

Synthesis of 1-(S_{Fc})-diphenylphosphanyl-2-[(*R*)-α-(*N*,*N*-dimethylamino)-*o*-diphenylphosphanylphenylmethyl]ferrocene (1a): The amine **4a** (502 mg, 1.26 mmol) was dissolved in Et_2O (5 mL) under argon and cooled to −78 °C. Then *t*BuLi (1.45 M in pentane, 3.05 mL, 4.41 mmol, 3.5 equiv) was added dropwise. The mixture was warmed to room temperature and stirred for 1 h at room temperature. $ClPPh_2$ (0.58 mL, 3.15 mmol, 2.5 equiv) was then added dropwise at −78 °C, and the mixture was stirred for 1 h at room temperature. After hydrolysis and conventional workup, the crude product was purified by flash chromatography (pentane/Et_2O 5/1) to give the phosphane **4a** (763 mg, 1.11 mmol, 88% yield) as an orange solid. M.p. 84 °C; $[\alpha]^{20}_{(kap)d(/kap)} = +297$ ($c = 1.06$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.52-7.42$ (m, 2H), 7.32–6.66 (m, 22H), 6.00 (d, $J = 10.1$ Hz, 1H), 4.54 (s, 1H), 4.28–4.26 (m, 1H), 3.87 (s, 1H), 3.82 (s, 5H), 2.02 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 146.93$ (d, $J = 24.3$ Hz), 139.46–126.42 (m), 98.47 (d, $J = 24.7$ Hz), 73.21 (d, $J = 14$ Hz), 71.46 (d, $J = 4.5$ Hz), 71.17 (d, $J = 5.4$ Hz), 70.14, 68.63, 64.55–64.07 (m), 43.17; ^{31}P NMR (81 MHz, $CDCl_3$, 25 °C): $\delta = -16.7$ (d, $J = 19.1$ Hz), −23.2 (d, $J = 19.1$ Hz); MS: *m/z* (%): 687 (37) $[M]^+$; elemental analysis (%) calcd for $C_{43}H_{39}FeNP_2$ (687.6): C 75.11, H 5.72, N 2.04; found: C 74.87, H 5.64, N 1.97.

Synthesis of 1-(S_{Fc})-bis(3,5-xylyl)phosphanyl-2-[(*R*)-α-(*N*,*N*-dimethylamino)-*o*-bis(3,5-xylyl)phosphanylphenylmethyl]ferrocene (1b): The amine **4a** (1.00 g, 2.50 mmol) in Et_2O (12 mL) was treated with *t*BuLi (1.5 M in pentane, 7.4 mL, 12.6 mmol, 3.5 equiv) and $ClP(3,5\text{-xylyl})_2$ (2.42 g, 8.73 mmol, 2.5 equiv) according to the procedure described for **1a**. After flash chromatography (pentane/Et_2O 4/1), the diphosphane **1b** (0.65 g, 0.82 mmol, 33% yield) was obtained as an orange solid. M.p. 84–85 °C; $[\alpha]^{20}_{(kap)d(/kap)} = +208.8$ ($c = 1.09$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.35-6.45$ (m, 12H), 6.38 (s, 1H), 6.18–6.16 (m, 2H), 5.81–5.78 (m, 1H), 4.30 (s, 1H), 4.08 (s, 1H), 3.72 (s, 1H), 3.65 (s, 5H), 2.06 (s, 7H), 1.99 (s, 12H), 1.86 (s, 5H), 1.79 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 137.7$ (d, $J = 7.3$ Hz), 137.4 (d, $J = 8.7$ Hz), 136.8 (d, $J = 12.7$ Hz), 136.7 (d, $J = 7.3$ Hz), 135.2, 133.4 (d, $J = 24.6$ Hz), 132.3 (d, $J = 3.7$ Hz), 132.1 (d, $J = 3.7$ Hz), 131.9 (d, $J = 20.9$ Hz), 130.9–130.1 (m), 129.2, 74.7 (d, $J = 15.1$ Hz), 72.1, 71.4, 70.5, 43.6, 21.8, 21.5; ^{31}P NMR (81 MHz, $CDCl_3$, 25 °C): $\delta = -16.9$ (d, $J = 16.6$ Hz), −23.7 (d, $J = 16.6$ Hz); MS: *m/z* (%): 799 (34) $[M]^+$; elemental analysis (%) calcd for $C_{51}H_{54}FeNP_2$ (798.8): C 76.98, H 6.84, N 1.80; found: C 77.17, H 7.16, N 1.62.

Synthesis of 1-(S_{Fc})-diphenylphosphanyl-2-[(*R*)-α-(1-pyrrolidyl)-*o*-diphenylphosphanylphenyl)methyl]ferrocene (1c): The amine **4b** (335 mg, 0.81 mmol) in Et_2O (15 mL) was treated with *t*BuLi (1.45 M in pentane, 1.96 mL, 2.84 mmol, 3.5 equiv) and $ClPPh_2$ (0.37 mL, 2.02 mmol, 2.5 equiv) according to the procedure described for **1a**. After flash chromatography (pentane/Et_2O 5/1), the diphosphane **1c** (370 mg, 0.52 mmol, 64% yield) was obtained as an orange solid. M.p. 94 °C; $[\alpha]^{20}_{(kap)d(/kap)} = +232$ ($c = 1.14$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.72-7.64$ (m, 1H), 7.59–7.52 (m, 2H), 7.37–6.76 (m, 21H), 6.10–5.84 (m, 1H), 4.62–4.52 (m, 1H), 4.30 (s, 1H), 3.92 (s, 1H), 3.78 (s, 5H), 2.50–2.32 (m, 4H), 1.38–1.10 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 148.6$ (d, $J = 25$ Hz), 139.4–126.1 (m), 99.3 (d, $J = 23$ Hz), 76.4, 72.4 (d, $J = 14.9$ Hz), 71.1 (d, $J = 4.5$ Hz), 69.7, 68.1, 62.5 (m), 51.5, 22.9; ^{31}P NMR (81 MHz, $CDCl_3$, 25 °C): $\delta = -17.1$ (d, $J = 20.3$ Hz), −22.4 (d, $J = 20.3$ Hz); MS: *m/z* (%): 713 (62) $[M]^+$; elemental analysis (%) calcd for $C_{45}H_{41}FeNP_2$ (713.6): C 75.74, H 5.79, N 1.96; found: C 75.61, H 5.97, N 1.68.

Synthesis of 1-(S_{Fc})-diphenylphosphanyl-2-[(*R*)-α-{*N*-(*R*)-methyl-1-phenylethylamino}-*o*-diphenylphosphanylphenylmethyl]ferrocene (1d): The amine **4c** (500 mg, 1.02 mmol) in Et_2O (10 mL) was treated with *t*BuLi (1.35 M in pentane, 2.60 mL, 3.57 mmol, 3.5 equiv) and $ClPPh_2$ (0.47 mL, 2.55 mmol, 2.5 equiv) according to the procedure described for **1a**. After flash chromatography (pentane/Et_2O 25/1 with 2% Et_3N), the diphosphane **1d** (325 mg, 0.48 mmol, 41% yield) was obtained as an orange solid. M.p. 105 °C; $[\alpha]^{20}_{(kap)d(/kap)} = +227$ ($c = 0.48$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.09-7.91$ (m, 1H), 7.60–7.45 (m, 2H), 7.40–6.75 (m, 26H), 6.19 (d, $J = 10.6$ Hz, 1H), 4.48–4.47 (m, 1H), 4.24–4.22 (m, 1H), 4.03–3.93 (m, 2H), 3.56 (s, 5H), 1.75 (s, 3H), 0.80 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 150.2$ (d, $J = 27.1$ Hz), 144.3, 135.5–126.0 (m), 101.5 (d, $J = 26.1$ Hz), 72.6 (d, $J = 15.9$ Hz), 71.9–71.7 (m), 69.9, 68.6, 63.1 (d, $J = 23.8$ Hz), 56.4, 35.7 (d, $J = 1.5$ Hz), 16.1 (d, $J = 5.4$ Hz); ^{31}P NMR (81 MHz, $CDCl_3$, 25 °C): $\delta = -18.0$ (d, $J = 17.8$ Hz), −23.4 (d, $J = 17.8$ Hz); elemental analysis (%) calcd for $C_{50}H_{45}FeNP_2$ (777.7): C 77.22, H 5.83, N 1.80; found: C 76.87, H 5.74, N 1.60.

Synthesis of 1-(S_{Fc})-diphenylphosphanyl-2-[(*R*)-α-{*N*-(*S*)-methyl-1-phenylethylamino}-*o*-diphenylphosphanylphenylmethyl]ferrocene (1e): The amine **4d** (1.20 g, 2.46 mmol) in Et_2O (15 mL) was treated with *t*BuLi (1.57 M in pentane, 5.0 mL, 7.8 mmol, 3.2 equiv) and $ClPPh_2$ (1.0 mL, 5.4 mmol, 2.2 equiv) according to the procedure described for **1a**. After flash chromatography (pentane/Et_2O 25/1 with 2% Et_3N), the diphosphane **1e** (1.11 g, 1.43 mmol, 58% yield) was obtained as an orange solid. M.p. 104–108 °C; $[\alpha]^{20}_{(kap)d(/kap)} = +261$ ($c = 0.5$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.46-7.45$ (m, 2H), 7.32–6.92 (m, 20H), 6.90–6.61 (m, 6H), 6.58–6.49 (m, 2H), 5.27–5.06 (m, 1H), 4.82 (br s, 1H), 4.39–4.38 (m, 1H), 4.00 (s, 1H), 3.74 (s, 5H), 1.59 (s, 3H), 1.41 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 148.6$ (d, $J = 26.1$ Hz), 145.9, 139.9–125.9 (m), 97.9 (d, $J = 26.4$ Hz), 72.7 (d, $J = 16.0$ Hz), 71.4 (d, $J = 4.0$ Hz), 71.0 (br), 70.1, 69.1, 60.7 (br), 59.6, 33.5, 19.9; ^{31}P NMR (81 MHz, $CDCl_3$, 25 °C): $\delta = -18.3$ (d, $J = 31.2$ Hz), −23.3 (d, $J = 31.2$ Hz); elemental analysis (%) calcd for $C_{50}H_{45}FeNP_2$ (777.7): C 77.22, H 5.83, N 1.80; found: C 76.91, H 6.29, N 1.97.

Synthesis of 1-(S_{Fc})-diphenylphosphanyl-2-[(*R*)-α-{*N*-methyl(2-*N*′,*N*′-dimethylamino)ethylamino}-*o*-diphenylphosphanylphenylmethyl]ferrocene (1f): The amine **4e** (170 mg, 0.37 mmol) in Et_2O (2 mL) was treated with *t*BuLi (1.56 M in pentane, 0.8 mL, 1.3 mmol, 3.5 equiv) and $ClPPh_2$ (0.2 mL, 0.9 mmol, 2.5 equiv) according to the procedure described for **1a**. After flash chromatography (Et_2O with 3% Et_3N), the diphosphane **1f** (132 mg, 0.18 mmol, 48% yield) was isolated as an orange solid. $[\alpha]^{20}_{(kap)d(/kap)} = +232.4$ ($c = 0.45$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.55-7.44$ (m, 2H), 7.35–7.18 (m, 12H), 7.00–6.58 (m, 10H), 6.29 (d, $J = 10.6$ Hz, 1H), 4.51 (br s, 1H), 4.32 (br s, 1H), 3.95 (br s, 1H), 3.86 (s, 5H), 2.62–2.57, (m, 2H), 2.27 (s, 3H), 2.09–1.93 (m, 7H), 1.74–1.62 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 147.5$ (d, $J = 26.5$ Hz), 139.9–126.3 (m), 98.6 (d, $J = 25.2$ Hz), 73.2 (d, $J = 14.2$ Hz), 71.5 (d, $J = 4.8$ Hz), 71.2 (m), 70.1, 68.6, 64.7 (dd, $J = 24.5$ and 6.8 Hz), 58.2, 52.9, 45.7, 39.9; ^{31}P NMR (81 MHz, $CDCl_3$, 25 °C): $\delta = -16.8$ (d, $J = 14.0$ Hz), −24.0 (d, $J = 14.0$ Hz); elemental analysis (%) calcd for $C_{46}H_{46}FeN_2P_2$ (744.7): C 74.19, H 6.23, N 3.76; found: C 73.84, H 6.10, N 3.56, HRMS: calcd 744.2485; found 744.2496.

Synthesis of 1-(S_{Fc})-diphenylphosphanyl-2-[(*R*)-α-(*N*,*N*-diethylamino)-*o*-diphenylphosphanylphenylmethyl]ferrocene (1g): The amine **4f** (685 mg, 1.61 mmol) in Et_2O (10 mL) was treated with *t*BuLi (1.5 M in pentane, 3.8 mL, 5.6 mmol, 3.5 equiv) and $ClPPh_2$ (0.63 mL, 3.5 mmol, 2.2 equiv) according to the procedure described for **1a**. After flash chromatography (pentane/Et_2O 4/1), the diphosphane **1g** (0.71 g, 0.99 mmol, 62% yield) was obtained as an orange solid. M.p. 206–207 °C; $[\alpha]^{20}_{(kap)d(/kap)} = +296.3$ ($c = 1.21$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.50-7.47$ (m, 2H), 7.35–7.18 (m, 13H), 6.95–6.86 (m, 5H), 6.81–6.75 (m, 2H), 6.66 (td, $J = 7.4$, 1.4 Hz, 1H), 6.59–6.54 (m, 1H), 6.45 (d, $J = 10.6$ Hz, 1H), 4.56 (s, 1H), 4.31–4.29 (m, 1H), 3.95 (s, 1H), 3.80 (s, 5H), 2.65–2.54 (m, 2H), 2.41–2.29 (m, 2H), 0.68 (t, $J = 7.0$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 148.7$ (d, $J = 27.1$ Hz), 140.4–139.6 (m), 138.0 (d, $J = 12.1$ Hz), 136.2–135.7 (m), 134.4 (d, $J = 19.5$ Hz), 134.1 (d, $J = 4.2$ Hz), 133.9 (d, $J = 3.9$ Hz), 132.8 (d, $J = 18.9$ Hz), 131.2, 129.1 128.6–127.4 (m), 126.6, 100.0 (d, $J = 25.8$ Hz), 73.2 (d, $J = 14.5$ Hz), 72.1–71.8 (m), 70.4, 68.9, 45.3, 14.9; ^{31}P NMR (81 MHz, $CDCl_3$, 25 °C): $\delta = -17.04$ (d, $J = 17.3$ Hz), −24.61 (d, $J = 17.3$ Hz); MS: *m/z* (%): 715 (11) $[M+1]^+$; elemental analysis (%) calcd for $C_{45}H_{43}FeNP_2$ (715.6): C 75.53, H 6.06, N 1.96; found: C 75.29, H 6.10, N 1.87.

Synthesis of 1-(S_{Fc})-diphenylphosphanyl-2-[(*R*)-α-(*N*,*N*-di-*n*-propylamino)-*o*-diphenylphosphanylphenylmethyl]ferrocene (1h): The amine **4g** (706 mg, 1.55 mmol) in Et_2O (10 mL) was treated with *t*BuLi (1.5 M in pentane, 3.6 mL, 5.4 mmol, 3.4 equiv) and $ClPPh_2$ (0.61 mL, 3.42 mmol, 2.2 equiv) according to the procedure described for **1a**. After flash chromatography (pentane/Et_2O 4/1 and pentane/Et_2O = 20/1), the diphosphane **1h** (375 mg, 0.83 mmol, 53% yield) was obtained as a bright orange solid. M.p. 159–160 °C; $[\alpha]^{20}_{(kap)d(/kap)} = +315.3$ ($c = 1.15$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.45-7.41$ (m, 2H), 7.30–7.17 (m, 13H), 6.95–6.85 (m, 4H), 6.74 (t, $J = 6.9$ Hz, 3H), 6.62 (td, $J = 7.4$, 1.0 Hz, 1H), 6.52 (d, $J = 11.0$ Hz, 1H), 6.44 (t, $J = 7.0$ Hz, 1H), 4.66 (s, 1H), 4.31–4.29 (m, 1H), 3.95 (s, 1H), 3.84 (s, 5H), 2.46–2.39 (m, 2H), 2.34–2.25 (m, 2H), 1.23–1.19 (m, 2H), 1.07–1.00 (m, 2H), 0.59 (t, $J = 7.3$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 148.2$ (d, $J = 28.9$ Hz), 140.4 (d, $J = 12.9$ Hz), 139.7 (d, $J = 11.7$ Hz), 138.2 (d, $J = 11.1$ Hz), 136.0–132.7 (m), 129.1, 128.5–126.6 (m), 99.8 (d, $J = 24.7$ Hz), 73.0 (d, $J = 14.5$ Hz), 72.2–72.0 (m), 70.4, 68.8, 54.4, 22.8, 12.1; ^{31}P NMR (81 MHz, $CDCl_3$, 25 °C): $\delta = -17.0$ (d, $J = 17.4$ Hz), −25.1 (d, $J = 17.4$ Hz); MS: *m/z* (%): 743 (10) $[M]^+$; elemental analysis (%) calcd for $C_{47}H_{47}FeNP_2$ (743.7): C 75.91, H 6.37, N 1.88; found: C 75.63, H 6.40, N 1.82.

Synthesis of 1-(S_{Fc})-diphenylphosphanyl-2-[(*R*)-α-(*N*,*N*-di-*n*-butylamino)-*o*-diphenylphosphanylphenyl)methyl]ferrocene (1i): The amine **4h** (687 mg, 1.42 mmol) in Et_2O (10 mL) was treated with *t*BuLi (1.5 M in pentane, 3.3 mL, 5.0 mmol, 3.6 equiv) and $ClPPh_2$ (0.56 mL, 3.13 mmol, 2.2 equiv) according to the procedure described for **1a**. After flash chromatography (pentane/Et_2O 20/1), the diphosphane **1i** (509 mg, 0.66 mmol, 46% yield) was obtained as a bright orange solid. M.p. 68–69 °C; $[\alpha]^{20}_{(kap)d(/kap)} = +300.1$ ($c = 1.23$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.48-7.39$ (m, 4H), 7.30–7.17 (m, 11H), 6.95–6.85 (m, 4H), 6.79–6.74 (m, 3H), 6.62 (td, $J = 7.4$, 1.2 Hz, 1H), 6.51–6.44 (m, 2H), 4.63 (s, 1H), 4.30–4.29 (m, 1H), 3.95 (s, 1H), 3.82 (s, 5H), 2.53–2.43 (m, 2H), 2.36–2.28 (m, 2H), 1.18–0.9 (m, 8H), 0.69 (t, $J = 7.0$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 148.4$ (d, $J = 28.8$ Hz), 140.4 (d, $J = 12.9$ Hz), 139.7 (d, $J = 10.3$ Hz), 138.0–133.9 (m), 132.8 (d, $J = 19.4$ Hz), 131.1, 129.0–126.6 (m), 73.0 (d, $J = 14.4$ Hz), 72.1 (d, $J = 4.7$ Hz), 70.4, 63.2–62.8 (m), 52.3, 32.0, 20.9, 14.6; ^{31}P NMR (81 MHz, $CDCl_3$, 25 °C): $\delta = -17.0$ (d, $J = 16.8$ Hz), −25.0 (d, $J = 16.8$ Hz); MS: *m/z* (%): 771 (11) $[M]^+$; elemental analysis (%) calcd for $C_{49}H_{51}FeNP_2$ (771.7): C 76.26, H 6.66, N 1.81; found: C 75.68, H 6.60, N 1.63.

Synthesis of 1-(S_{Fc})-diphenylphosphanyl-2-[(*R*)-α-(*N*,*N*-diisobutylamino)-*o*-diphenylphosphanylphenylmethyl]ferrocene (1j): The amine **4i** (603 mg, 1.25 mmol) in Et_2O (10 mL) was treated with *t*BuLi (1.5 M in pentane, 2.9 mL, 4.4 mmol, 3.5 equiv) and $ClPPh_2$ (0.49 mL, 2.75 mmol, 2.2 equiv) according to the procedure described for **1a**. After flash chromatography (pentane/Et_2O 20/1), the diphosphane **1j** (346 mg, 0.45 mmol, 36% yield) was obtained as a bright orange solid. M.p. 84–85 °C; $[\alpha]^{20}_{(kap)d(/kap)} = +366.3$ ($c = 1.05$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.69-7.63$ (m, 2H), 7.33–7.17 (m, 13H), 7.02–6.87 (m, 4H), 6.72–6.50 (m, 5H), 6.23 (t, $J = 7.0$ Hz, 1H), 5.03 (s, 1H), 4.30 (s, 1H), 3.93–3.92 (m, 1H), 3.82 (s, 5H), 2.25–2.09 (m, 4H), 1.75–1.70 (m, 2H), 0.88 (d, $J = 6.5$ Hz, 6H), 0.55 (d, $J = 6.5$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 46.7$ (d, $J = 27.1$ Hz), 140.2–138.9 (m), 136.0–134.7 (m), 134.0 (d, $J = 17.9$ Hz), 132.8 (d, $J = 18.9$ Hz), 132.1, 128.6–126.7 (m), 99.1 (d, $J = 25.8$ Hz), 72.9–72.4 (m), 70.5, 68.7, 62.9 (d, $J = 30.2$ Hz), 60.6, 27.7, 21.5 (d, $J = 15.1$ Hz); ^{31}P NMR (81 MHz, $CDCl_3$, 25 °C): $\delta = -16.6$ (d, $J = 14.1$ Hz), −26.6 (d, $J = 14.2$ Hz); MS: *m/z* (%): 771 (10) $[M]^+$; elemental analysis (%) calcd for $C_{49}H_{51}FeNP_2$ (771.7): C 76.26, H 6.66, N 1.81; found: C 75.77, H 6.76, N 1.72.

Synthesis of 1-(S_{Fc})-bromo-2-[(*R*)-α-(*N*,*N*-dimethylamino)-*o*-bromophenylmethyl]ferrocene (5): The amine **4a** (270 mg, 0.68 mmol) in Et_2O (3 mL) was treated with *t*BuLi (1.45 M in pentane, 1.65 mL, 2.39 mmol, 3.5 equiv) and $C_2Br_2Cl_4$ (487 mg, 1.49 mmol, 2.2 equiv) in Et_2O (2 mL) according to the procedure described for **1a**. After flash chromatography (pentane/Et_2O 5/1), the amine **4a** (260 mg, 0.54 mmol, 80% yield, 97.5% *ee*) was obtained as an orange solid. M.p. 84 °C; $[\alpha]^{20}_{(kap)d(/kap)} = +125.5$ ($c = 0.71$ in $CHCl_3$); HPLC (OJ, heptane/*i*PrOH 95/5, 0.6 mL/min): t_r/min = 7.11 ($1S_{Fc}$, αR), 10.65 ($1R_{Fc}$, αS); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.56-7.54$ (m, 1H), 7.20–7.18 (m, 2H), 7.07–7.00 (m, 1H), 5.06 (s, 1H), 4.47–4.46 (m, 1H), 4.37–4.36 (m, 1H), 4.18–4.13 (m, 1H), 4.12 (s, 5H), 2.43 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 141.0$, 132.4, 131.0, 128.2, 127.1, 126.2, 90.2, 77.3, 71.7, 70.0, 67.5, 67.2, 65.3, 44.4; MS: *m/z* (%): 479 (30) $[M+2]^+$, 477 (61) $[M]^+$, 475 (33) $[M-2]^+$; elemental analysis (%)

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calcd for $C_{19}H_{19}Br_2FeN$ (477.0): C 47.84, H 4.01, N 2.94; found: C 47.72, H 3.94, N 2.79.

Synthesis of 1-(S_{Fc})-bromo-2-(*o*-bromophenylmethyl)ferrocene (6): The amine **5** (295 mg, 0.62 mmol) was dissolved in trifluoroacetic acid (2 mL), and Et_3SiH (1 mL, 6.20 mmol, 10 equiv) was added. The mixture was stirred for 72 h at room temperature and then extracted with Et_2O. The organic layer was washed with saturated K_2CO_3 solution and brine and dried over $MgSO_4$. After removal of the solvent, the crude product was purified by flash chromatography (pentane/Et_2O 20/1) to give **6** (152 mg, 0.35 mmol, 57% yield, 97% *ee*) as an orange oil. $[\alpha]^{20}_{(kap)d(/kap)} = -28.5$ ($c = 1.04$ in $CHCl_3$); HPLC (OJ, heptane/*i*PrOH 98/2, 0.6 mL/min): t_r/min = 12.78 (S_{Fc}), 15.66 (R_{Fc}); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.56-7.53$ (m, 1H), 7.21–7.16 (m, 1H), 7.11–7.04 (m, 2H), 4.45 (m, 1H), 4.20 (s, 5H), 4.15 (m, 1H), 4.09 (m, 1H), 3.93 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 14.0$, 132.5, 130.1, 127.8, 127.3, 124.2, 85.2, 80.3, 71.3, 69.8, 67.7, 66.0, 34.5; MS: *m/z* (%): 436 (24) $[M+2]^+$, 434 (44) $[M]^+$, 432 (25) $[M-2]^+$; elemental analysis (%) calcd for $C_{17}H_{14}Br_2Fe$ (434.0): C 47.05, H 3.25; found: C 47.31, H 3.45.

Synthesis of 1-(S_{Fc})-bromo-2-[1′-(*R*)-*o*-bromophenylethyl]ferrocene (7a): Me_2Zn (2 M in THF, 1.7 mL, 4.2 mmol) was added to a solution of the amine **5** (400 mg, 1.05 mmol) in dry THF (6 mL) under argon at −78 °C, followed by CH_3COCl (0.12 mL, 1.68 mmol). The reaction mixture was allowed to warm to room temperature overnight. After hydrolysis and conventional workup, the crude product was purified by flash chromatography (pentane/Et_2O 50/1) to give **7a** (330 mg, 0.73 mmol, 70% yield, d.r. = 95/5, 98.5% *ee*) as a sticky orange solid. $[\alpha]^{20}_{(kap)d(/kap)} = +78.9$ ($c = 0.45$ in $CHCl_3$); HPLC (OD, 99.7% heptane/0.3% *i*PrOH, 0.6 mL/min): t_r/min = 12.97 ($1R_{Fc}$, $1'S$), 16.88 ($1S_{Fc}$, $1'R$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.57-7.54$ (m, 1H), 7.41–7.48 (m, 1H), 7.35–7.31 (m, 1H), 7.05–7.00 (m, 1H), 4.52 (q, $J = 7.1$ Hz, 1H), 4.33–4.32 (m, 1H), 4.14 (s, minor diastereomer), 3.97–3.96 (m, 1H), 3.94–3.83 (m, 6H), 1.50 (d, $J = 7.1$ Hz, minor diastereomer), 1.39 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 144.9$, 132.90, 129.0, 127.9, 127.4, 124.2, 91.4, 79.2, 71.0, 69.8, 66.0, 64.7, 23.8; minor diastereomer, separate signals: 132.4, 128.1, 127.5, 71.3, 70.3, 65.5, 65.4, 38.2, 20.6; MS: *m/z* (%): 450 (59) $[M+2]^+$, 448 (100) $[M]^+$, 446 (70) $[M-2]^+$; elemental analysis (%) calcd for $C_{18}H_{16}Br_2Fe$ (448.0): C 48.26, H 3.60; found: C 48.01, H 3.62.

Synthesis of 1-(S_{Fc})-bromo-2-[1′-(*R*)-*o*-bromphenyl-2′-methylpropyl]ferrocene (7b): The amine **5** (230 mg, 0.48 mmol) in dry THF (3 mL) was treated with *i*Pr_2Zn (2 M in THF, 1.0 mL, 2.00 mmol) and CH_3COCl (0.07 mL, 1.00 mmol) according to the procedure described for **7a**. The crude product was purified by flash chromatography (pentane/Et_2O 50/1) to give **7b** (190 mg, 0.40 mmol, 83% yield, *d.r.* = 95/5, 98.5% *ee*) as an orange oil. $[\alpha]^{20}_{(kap)d(/kap)} = +119$ ($c = 0.51$ in $CHCl_3$); HPLC (OD, 99.5% heptane/0.5% *i*PrOH, 0.6 mL/min): t_r/min = 8.61 ($1S_{Fc}$, $1'R$), 9.66 ($1R_{Fc}$, $1'S$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.70-7.66$ (m, minor diastereomer), 7.54–7.51 (m, 1H), 7.16–7.10 (m, 1H), 7.01–6.95 (m, 2H), 4.39–4.35 (m, 1H), 4.33–4.30 (m, 1H), 4.13–4.09 (m, 6H), 3.71 (s, minor diastereomer), 2.52–2.41 (m, 1H), 2.04–1.90 (m, minor diastereomer), 1.25 (d, 3H, $J = 7.5$ Hz), 0.83 (d, 3H, $J = 6.8$ Hz), 0.79 (d, $J = 6.6$ Hz, minor diastereomer), 0.75 (d, $J = 6.6$ Hz, minor diastereomer); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 143.6$, 132.3, 130.4, 127.2, 127.0, 91.6, 78.9, 71.5, 70.2, 67.1, 65.2, 48.9, 32.5, 23.1, 20.8; minor diastereomer, separate signals: 128.5, 127.5, 126.5, 71.0, 55.8, 21.5; MS: *m/z* (%): 478 (64) $[M+2]^+$, 476 (100) $[M]^+$, 474 (64) $[M-2]^+$, 433 (40), 215 (80), 152 (82); elemental analysis (%) calcd for $C_{20}H_{20}Br_2Fe$ (476.0): C 50.46, H 4.23; found: C 50.26, H 4.23.

Synthesis of 1-(S_{Fc})-diphenylphosphanyl-2-(*o*-diphenylphosphanylphenylmethyl)ferrocene (1k): *n*BuLi (1.6 M in hexane, 0.37 mL, 0.59 mmol, 2.2 equiv) was added dropwise to a solution of the ferrocenyl compound **6** (120 mg, 0.27 mmol) in dry THF (2 mL), at −78 °C. The mixture was stirred for 15 min and then $ClPPh_2$ (0.12 mL, 0.66 mmol, 2.4 equiv) was added. The solution was then warmed to room temperature and stirred for 1 h. After hydrolysis and conventional workup, the crude product was purified by flash chromatography (pentane/Et_2O 20/1) to give **1k** (130 mg, 0.20 mmol, 75% yield) as an orange solid. M.p. 82 °C; $[\alpha]^{20}_{(kap)d(/kap)} = +46.4$ ($c = 0.59$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta ? = 7.66-7.56$ (m, 2H), 7.45–7.15 (m, 18H), 7.02–6.91 (m, 3H), 6.84–6.74 (m, 1H), 4.35–4.31 (m, 1H), 4.27–4.17 (m, 3H), 3.94 (s, 5H), 3.79–3.78 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 145.5$ (d, $J = 25.1$ Hz), 139.4 (d, $J = 10.0$ Hz), 137.8–127.6 (m), 126.0, 93.2 (d, $J = 27.6$ Hz), 75.7 (d, $J = 1.9$ Hz), 72.7–72.5 (m), 70.7 (d, $J = 4.1$ Hz), 69.8, 68.9, 33.0 (dd, $J = 23.1$, 9.9 Hz); ^{31}P NMR (81 MHz, $CDCl_3$, 25 °C): $\delta = -13.6$ (d, $J = 5.7$ Hz), −21.9 (d, $J = 5.7$ Hz); MS: *m/z* (%): 644 (56) $[M]^+$; HRMS calcd for $C_{41}H_{34}FeP_2$: 644.1485; found: 644.1478.

Synthesis of 1-(S_{Fc})-diphenylphosphanyl-2-[1′-(*R*)-(*o*-diphenylphosphanylphenyl)ethyl]ferrocene (1l): Compound **7a** (285 mg, 0.63 mmol) in dry THF (4 mL) was treated with *n*BuLi (1.6 M in hexane, 0.87 mL, 1.40 mmol, 2.2 equiv) and $ClPPh_2$ (0.30 mL, 1.52 mmol, 2.4 equiv) according to the procedure described for **1k**. After flash chromatography (pentane/Et_2O 20/1), the diphosphane **1l** (384 mg, 0.58 mmol, 92.6% yield, *d.r.* = 96/4) was obtained as an orange solid. $[\alpha]^{20}_{(kap)d(/kap)} = +354.5$ ($c = 0.55$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.58-7.50$ (m, 2H), 7.38–6.96 (m, 21H), 6.84–6.81 (m, 1H), 4.95–4.88 (m, 1H), 4.24–4.22 (m, 1H), 4.13–4.12 (m, 1H), 3.95 (s, minor diastereomer), 3.69–3.68 (m, 6H), 1.24 (d, $J = 7.1$ Hz, minor diastereomer), 0.85 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 151.1$ (d, $J = 23.5$ Hz), 140.7–127.6 (m), 126.2, 99.7 (d, $J = 25.4$ Hz), 75.9 (d, $J = 12.1$ Hz), 70.8 (d, $J = 4.3$ Hz), 69.7, 69.7, 69.5, 69.4 (m), 36.3 (dd, $J = 25.0$, 9.7 Hz), 25.2 (d, $J = 5.4$ Hz); ^{31}P NMR (81 MHz, $CDCl_3$, 25 °C): $\delta = -12.9$ (d, $J = 18.4$ Hz), −22.4 (d, $J = 18.4$ Hz); minor diastereomer, separate signals: −18.3 (d, $J = 33.0$ Hz), −21.7 (d, $J = 33.0$ Hz); MS: *m/z* (%): 658 (43) $[M]^+$; HRMS calcd: 658.1642; found: 658.1636; elemental analysis (%) calcd for $C_{42}H_{36}FeP_2$ (658.5): C 76.60, H 5.51; found: C 76.41, H 5.42.

Synthesis of 1-(S_{Fc})-diphenylphosphanyl-2-[1′-(*R*)-(*o*-diphenylphosphanylphenyl)-2′-methylpropyl]ferrocene (1m): Compound **7b** (190 mg, 0.40 mmol) in dry THF (2 mL) was treated with *n*BuLi (1.6 M in hexane, 0.55 mL, 0.88 mmol, 2.2 equiv) and $ClPPh_2$ (0.18 mL, 0.96 mmol, 2.4 equiv) according to the procedure described for **1k**. After flash chromatography (pentane), the diphosphane **1m** (85 mg, 0.12 mmol, 31% yield, *d.r.* = 95/5) was obtained as an orange solid. M.p. 98 °C; $[\alpha]^{20}_{(kap)d(/kap)} = +315.5$ ($c = 0.45$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.57-7.46$ (m, 2H), 7.38–7.11 (m, 17H), 6.96–6.82 (m, 3H), 6.75–6.62 (m, 2H), 5.24–5.19 (m, 1H), 4.55 (br s, 1H), 4.84–3.69 (m, minor diastereomer), 4.28–4.26 (m, 1H), 3.68 (s, 5H), 3.14 (s, minor diastereomer), 2.49–2.48 (m, 1H), 0.75 (d, $J = 6.7$ Hz, 3H), 0.51 (d, $J = 6.7$ Hz, 3H), 0.26 (d, $J = 6.6$ Hz, minor diastereomer); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 150.9$ (d, $J = 27.5$ Hz), 139.8–126. 8 (m), 125.4, 101.4 (d, $J = 27.1$ Hz), 74.0 (d, $J = 16.6$ Hz), 71.6 (d, $J = 4.4$ Hz), 69.8, 69.6, 68.8, 47.6 (d, $J = 20.4$ Hz), 33.4, 23.5, 21.5; ^{31}P NMR (81 MHz, $CDCl_3$, 25 °C): $\delta = -17.8$ (d, $J = 26.7$ Hz), −22.8 (d, $J = 26.7$ Hz); minor diastereomer, separate signals: −17.6 (d), −25.8 (d, $J = 44.5$ Hz); MS: *m/z* (%): 686 (11) $[M]^+$; HRMS calcd for $C_{44}H_{40}FeP_2$: 686.1950; found: 686.1955.

Asymmetric hydrogenation: **general procedure**: *In situ preparation of rhodium catalyst*: The rhodium complex (0.01 mmol) and the ligand **1** (1.05–1.1 equiv) were placed in a dried Schlenk tube under an argon atmosphere and the indicated solvent (4 mL) was added. The mixture was then stirred for 10–20 min at room temperature.

In situ preparation of ruthenium catalyst:[12] [Ru(cod)(2-methallyl)$_2$] (0.01 mmol) and the ligand **1** (1.05–1.1 equiv) were placed in a dried Schlenk tube under an argon atmosphere and acetone (2 mL) was added. A solution of HBr in MeOH (0.1 mL, 0.3 M) was added dropwise to this solution. An orange precipitate formed. After 10–20 min of stirring, the solvent was removed under vacuum, and the indicated solvent (4 mL) was added.

Hydrogenation in Schlenk tubes: The catalyst solution was added to the substrate under an argon atmosphere. The Schlenk tube was then briefly connected to vacuo and purged with hydrogen from a balloon.

Hydrogenation in an autoclave: The substrate was placed in a glass tube equipped with a stirring bar in the autoclave. After three cycles of vacuum–argon, the catalyst solution was added to the substrate by syringe under an argon stream. Volatile substrates were added directly to the catalyst solution before introduction to the autoclave under argon. The autoclave was then purged three times with hydrogen, heated to the desired temperature, and placed under the indicated H_2 pressure.

Hydrogenation products: **determination of enantiomeric excess**: The substrates used for hydrogenation are commercially available or were prepared according to literature procedures. Most of the hydrogenation products have been previously described. *N*-acetylphenylalanine methyl ester (**9b**):[2d] GC (Chiralsil L-Val) 140 °C isotherm: t_r/min = 10.1 (*R*), 11.7 (*S*); dimethyl 2-methylsuccinate (**11**):[2e] HPLC (OJ, 20 °C, 5% *i*PrOH in heptane, 0.6 mL/min): t_r/min = 9.9 (*R*), 15.2 (*S*); methyl 2-acetoxypropa-

noate (**13**):[19] HPLC (OD, 20 °C, 1 % *i*PrOH in heptane, 0.6 mL/min): t_r/min = 13.4 (*S*), 15.6 (*R*); acetyl 1-phenylbutylamide (**15**):[20] GC (Chiralsil L-Val) 115 °C isotherm: 23.5 (*R*), 24.9 (*S*); methyl 3-hydroxybutanoate (**17a**):[21] HPLC (OD, 20 °C, 5 % *i*PrOH in heptane, 0.9 mL/min): t_r/min = 9.2 (*R*), 13.3 (*S*); ethyl 3-hydroxybutanoate (**17b**):[21] HPLC (OD, 20 °C, 5 % *i*PrOH in heptane, 0.9 mL/min): t_r/min = 7.3 (*R*), 10.2 (*S*); ethyl 3-hydroxy-3-phenylpropanoate (**17c**):[21] HPLC (OD, 30 °C, 5 % *i*PrOH in heptane, 0.9 mL/min): t_r/min = 11.3 (*S*), 15.9 (*R*); ethyl 3-hydroxyhexanoate (**17d**):[21] HPLC (OD, 20 °C, 5 % *i*PrOH in heptane, 0.5 mL/min): t_r/min = 12.0 (*R*), 16.4 (*S*); ethyl 3-hydroxy-4-methylpentanoate (**17e**):[21] HPLC (OD, 20 °C, 5 % *i*PrOH in heptane, 0.5 mL/min): t_r/min = 10.8 (*R*), 15.9 (*S*); ethyl 3-hydroxy-4-chlorobutanoate (**17f**):[21] HPLC (OD, 30 °C, 2 % *i*PrOH in heptane, 0.6 mL/min): t_r/min = 10.6 (*S*), 15.6 (*R*); ethyl 2-hydroxycyclopentane carboxylate (**19**):[21] HPLC (OD, 40 °C, 2 % *i*PrOH in heptane, 0.32 mL/min): t_r/min = 19.7 (1*R*,2*S*), 25.7 (1*S*,2*R*), 27.4 (1*R*,2*R*), 31.1 (1*S*,2*S*); ethyl 2-hydroxycyclohexane carboxylate (**21**):[21] HPLC (OD, 35 °C, 2 % *i*PrOH in heptane, 0.3 mL/min): t_r/min = 18.0 (1*R*,2*S*), 19.3 (1*S*,2*R*), 23.0 (1*S*,2*S*), 23.8 (1*R*,2*R*); ethyl 2-methyl-3-hydroxybutanoate (**23**):[21] GC (Chiralsil L-Val) 74 °C isotherm: 14.4 (2*S*,3*S*), 15.2 (2*R*,3*S*), 15.7 (2*S*,3*R*), 16.4 (2*R*,3*R*); 2,4-pentanediol (**24a**):[21] GC (Chiralsil L-Val) 88 °C isotherm: 5.3 (*S*,*S*), 6.2 (*R*,*R*), 8.6 (*R*,*S*); 1,3-diphenyl-1,3-propanediol (**24b**):[21] HPLC (OD, 30 °C, 10 % *i*PrOH in heptane, 0.6 mL/min): t_r/min = 16.5 (*S*,*S*), 19.2 (*R*,*R*), 23.3 (*S*,*R)*; 1-phenyl-1,3-butanediol (**27**): HPLC (OD, 30 °C, 5 % *i*PrOH in heptane, 0.7 mL/min): t_r/min = 22.0 (1*S*,3*R*), 25.2 (1*S*,3*S*), 32.8 (1*R*,3*R)*; 1-phenyl-1-(2-benzoylhydrazino)ethane (**29a**):[16b] HPLC (OJ, 30 °C, 10 % *i*PrOH in heptane, 0,6 mL/min): t_r/min = 14.3 (*R*), 19.9 (*S*); 1-(2-naphthyl)-1-(2-benzoylhydrazino)ethane (**29b**):[16b] HPLC (OJ, 40 °C, 10 % *i*PrOH in heptane, 0.8 mL/min): t_r/min = 20.6 (*R*), 23.0 (*S*); 1-(2-benzoylhydrazino)tetralone (**29c**): HPLC (OD, 40 °C, 10 % *i*PrOH in heptane, 0.6 mL/min): t_r/min = 16.9 (+), 22.5 (−).

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[1] a) R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1994**; b) *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), VCH, Weinheim, **1993**.

[2] a) M. D. Fryzuk, B. Bosnich, *J. Am. Chem. Soc.* **1977**, *99*, 6262; b) W. S. Knowles, *Acc. Chem. Res.* **1983**, *16*, 106; c) R. Noyori, H. Takaya, *Acc. Chem. Res.* **1990**, *23*, 345; d) M. J. Burk, J. E. Feaster, W. A. Nugent, R. L. Harlow, *J. Am. Chem. Soc.* **1993**, *115*, 10125; e) A. Togni, C. Breutel, A. Schnyder, F. Spindler, H. Landert, T. Tijani, *J. Am. Chem. Soc.* **1994**, *116*, 4062.

[3] a) T. Ireland, G. Grossheimann, C. Wieser-Jeunesse, P. Knochel, *Angew. Chem.* **1999**, *111*, 3397; *Angew. Chem*, *Int. Ed*. **1999**, *38*, 3212; b) Degussa-Huels: Patent application WO/0037478.

[4] G. Descotes, D. Lafont, D. Sinou, *J. Organomet. Chem*. **1978**, 150 (1), C14 – C16.

[5] a) L. Schwink, P. Knochel, *Chem. Eur. J.* **1998**, *4*, 95; b) J. Wright, L. Framkes, P. Reeves, *J. Organomet. Chem*. **1994**, *476*, 215; c) E. J. Corey, R. K. Bakshi, S. Shibata, *J. Am. Chem. Soc*. **1987**, *109*, 7925.

[6] I. K. Ugi, D. Marquarding, G. W. Gokel, *J. Org. Chem*. **1972**, *37*, 3052.

[7] I. K. Ugi, L. F. Batelle, R. Bau, G. W. Gokel, *J. Am. Chem. Soc*. **1973**, *95*, 482.

[8] M. Lotz, T. Ireland, J. J. Almena, P. Knochel, *Tetrahedron: Asymmetry* **1999**, *10*, 1839.

[9] a) T. V. RajanBabu, T. A. Ayers, A. L. Casalnuovo, *J. Am. Chem. Soc.* **1994**, *116*, 4101; b) C. R. Landis, J. Halpern, *J. Am. Chem. Soc.* **1987**, *109*, 1746; c) W. S. Knowles, *Acc. Chem. Res.* **1983**, *16*, 106; d) A. S. C. Chan, J. J. Pluth, J. Halpern, *J. Am. Chem. Soc.* **1980**, *102*, 5952; e) J. M. Brown, *Chem. Soc. Rev.* **1993**, 25; f) M. J. Burk, J. E. Feaster, W. A. Nugent, R. L. Harlow, *J. Am. Chem. Soc.* **1993**, *115*, 10125.

[10] For reviews, see: a) K. E. Koenig in *Asymmetric Synthesis* (Ed.: J. D. Morrison), Academic Press, Orlando, FL, **1985**, p. 71; b) H. Takaya, T. Ohta, R. Noyori in *Catalytic Asymmetric Synthesis* (Ed.: I. Ojima), VCH, New York, **1993**, p. 1; c) R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1994**, p. 16.

[11] S. Masamune, W. Choy, J. S. Petersen, L. R. Sita, *Angew. Chem.* **1985**, *97*, 1; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 1.

[12] J. J. Almena Perea, A. Börner, P. Knochel, *Tetrahedron Lett*. **1998**, *39*, 8073, and references therein.

[13] a) J. P. Genêt, C. Pinel, S. Mallart, S. Jugé, S.Thorimbert, J. Laffitte, A. *Tetrahedron: Asymmetry* **1991**, *2*, 555; b) J. P. Genêt, C.Pinel, V. Ratovelomanana-Vidal, S. Mallart, X. Pfister, L. Bischoff, S. Darses, C. Galopin, J. A. Laffitte, *Tetrahedron: Asymmetry* **1994**, *5*, 675.

[14] M. J. Burk, M. F. Gross, T. G. Harper, P. C. S. Kalberg, J. R. Lee, J. P. Martinez, *Pure Appl. Chem*. **1996**, *68*, 37.

[15] Recent review: S. Kobayashi, H. Ishitani, *Chem. Rev.* **1999**, *99*, 1069.

[16] a) M. J. Burk, J. E. Feaster, *J. Am. Chem. Soc.* **1992**, *114*, 6266; b) M. J. Burk, J. P. Martinez, J. E. Feaster, *Tetrahedron* **1994**, *50*, 4399.

[17] E. W. Abel, M. A. Bennett, G. Wilkinson, *J. Chem. Soc*. **1959**, 3178.

[18] D. J. Mathre, T. K. Jones, L. C. Xavier, T. J. Blackblock, R. A. Reamer, J. J. Mohan, T. T. Jones, K. Hoogsteen, M. W. Baum, E. J. J. Grabowski, *J. Org. Chem*. **1991**, *56*, 751.

[19] M. J. Burk, C. S. Kalberg, A. Pizzano, *J. Am. Chem. Soc*. **1998**, *120*, 4345.

[20] M. J. Burk, Y. M. Wang, J. R. Lee, *J. Am. Chem. Soc*. **1996**, *118*, 5142.

[21] K. Mashima, K. H. Kusano, N. Sato, Y. Matsumura, K. Nozaki, H. Kumobayashi, N. Sayo, Y. Hori, T. Ishizaki, S. Akutagawa, H. Takaya, *J. Org. Chem*. **1994**, *59*, 3064.

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