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New efficient synthesis of Taniaphos ligands: application in ruthenium- and rhodium-catalyzed enantioselective hydrogenations

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Abstract—A third generation of Taniaphos 1,5-diphosphine ferrocene ligands with the new and interesting (S_{Fc},3*S*)- and (R_{Fc},3*R*)-configurations has been prepared. With these ligands, the ruthenium-catalyzed hydrogenation of C=O bonds proceeded with high diastereo- and enantioselectivity (up to >99% de and 97% ee). Good results were also obtained for the rhodium-catalyzed hydrogenation of C=C (up to 96% ee) and C=N bonds (up to 65% ee).

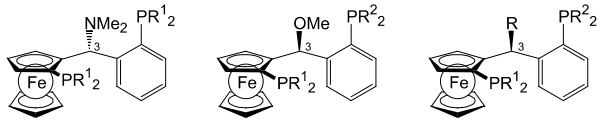
1. Introduction

Metal-catalyzed asymmetric hydrogenation is an important method for preparing chiral molecules such as α-amino acids, 1,3-diols or aldol products.[1] The choice of an appropriate chiral ligand for each class of substrate is essential for achieving high enantioselectivities. Although many chiral diphosphines have been reported, there is still a need for preparing readily available diphosphines, which have a broad application range in asymmetric reductions.[2] Recently, we have reported a new class of chiral 1,5-diphosphine ferrocene ligands of type **1** (Taniaphos), which gave exceptionally high enantioselectivities for various metal-catalyzed asymmetric reactions (Scheme 1).[3]

The 1,5-diphosphine unit present in all Taniaphos ligands is essential for the high catalytic activity of these ligands. Although forming an eight-membered chelate ring with metallic salts, the presence of the ferrocenyl and the aryl rings assures a moderate flexibility (only a few degrees of freedom are possible) of this large ring system allowing excellent enantiodifferentiation.[4] The configuration of the substituent of position 3 (Scheme 1) in the Taniaphos ligands of type **1** proves to be especially important for achieving high enantioselectivities.

In the original Taniaphos ligands **1**, we had prepared diastereomeric 1,5-diphosphines with the relative (S_{Fc},3*R*)- or (R_{Fc},3*S*)-configurations. The control of the stereochemistry at position 3 proved to be essential. Thus, the second generation of catalysts of type **2** bearing a methoxy group in position 3 with a (3*S*)-configuration instead of (3*R*) as in the diphosphines **1** proved in many cases to be superior.[5] To prepare ligands of type **2** we have used a different synthetic approach to that for the original Taniaphos ligands of type **1**. This new synthesis[5] had the advantage of allowing the preparation of 1,5-diphosphines with two different groups R^1 and R^2, but it had also the disadvantage that a tedious separation of diastereomers **4** and **5** was required (Scheme 2).

Herein, we report another synthetic approach related to the original Taniaphos-ligand synthesis avoiding the separation of diastereomers as well as the need to use the chiral sulfoxide **6**.[6] We demonstrate also the utility of these new ligands **3** in asymmetric catalysis.



1: Taniaphos **2** **3**

R^1 = Ph; Xyl
R^2 = Ph

Scheme 1. Taniaphos **1** and the related ligands **2** and **3**.

Keywords: Enantioselective hydrogenation; Ferrocene ligands.
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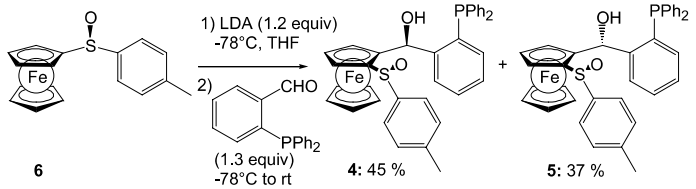


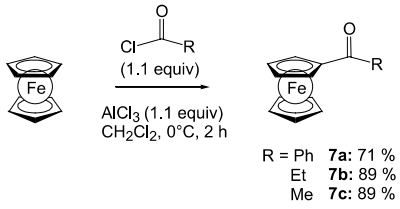
Scheme 2. Preparation of the diastereomeric alcohols **4** and **5**.

2. Results and discussion

2.1. Synthesis of the ligands of type 3

The synthesis of the new Taniaphos ligands with a 3*S* configuration starts by connecting the group R to the ferrocene moiety via *Friedel–Crafts* acylation (Scheme 3).[7]

Then, the resulting ferrocenyl ketones **7a**–**c** were converted into the amines **8a**–**c** and **9a**,**b** in three steps. The CBS-reduction was performed either with the (*R*)-CBS catalyst or the (*S*)-CBS catalyst.[8] Thus, CBS-reduction of the ketones **7a**–**c** with the (*R*)-CBS catalyst afforded the ferrocenyl alcohols **10a**,**b** whereas with the (*S*)-CBS catalyst the alcohols **11a**,**b** were obtained with high enantioselectivity.[9] Acylation gave quantitatively the intermediate acetates, which were converted to the corresponding ferrocenylamines **12a**,**b** and **13a**,**b** with retention of configuration by treatment with dimethylamine.[10] Diastereoselective lithiation afforded the planar chiral amines **8a**–**c** and **9a**,**b** (Scheme 4).[11]



Scheme 3. Preparation of the ketones **7a**–**c**.

Substitution of the dimethylamino groups with *o*-bromophenylzinc bromide **14** in the presence of acetyl chloride and subsequent recrystallization from Et_2O led to the diastereomeric pure ligand precursors **15a**–**c** and **16a**,**b** in high yields.[12] Double halogen–lithium exchange followed by the reaction with $ClPPh_2$ gave the corresponding diphosphines **17a**,**b** and **18a**,**b** (Scheme 5).

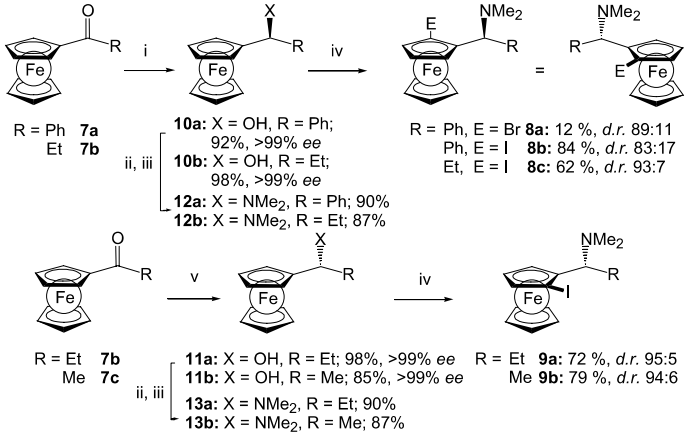
2.2. Asymmetric catalysis

The efficiency and selectivity of the new 1,5-diphosphines **17a**,**b** and **18a**,**b** as well as the influence of the group R were examined in ruthenium- and rhodium-catalyzed hydrogenation reactions. The stereoselectivity of the new ligands were compared with Taniaphos (**19**, first generation)[3] and Taniaphos **20** (second generation)[5] (Scheme 6).

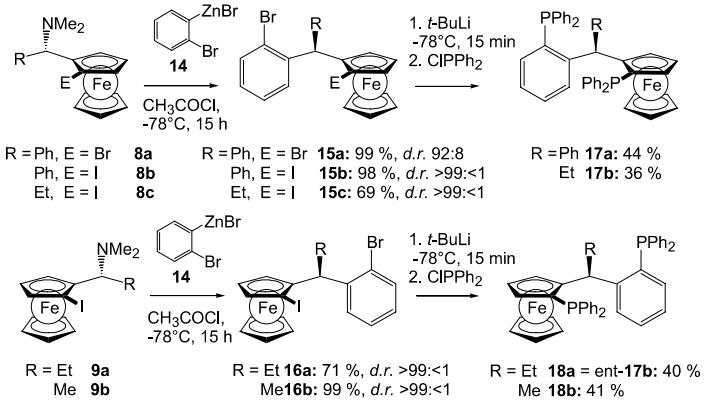
2.2.1. Enantioselective hydrogenation of C=O bonds.[1,13]

Taniaphos-analogous ferrocenyl phosphines are highly efficient for the ruthenium-catalyzed asymmetric hydrogenation of various 1,3-ketoesters (Scheme 7).[3,5] All 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%).[14] The results obtained for the hydrogenation of various 1,3-ketoesters **21** are summarized in Table 1.

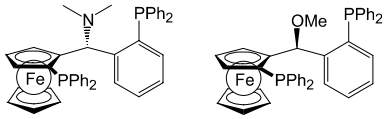
In the case of the 1,3-ketoester **21a**, the enantioselectivity could be improved by maximizing the steric hin-



Scheme 4. Synthesis of the amines **8a**–**c** and **9a**,**b**. Reagents and conditions: (i) (*R*)-CBS catalyst (0.3 equiv), $BH_3{\cdot}SMe_2$ (1 equiv), THF, 0 °C, 2 h; (ii) Ac_2O, pyridine, rt, 12 h; (iii) $HNMe_2$, CH_3CN or MeOH, H_2O; (iv) *t*-BuLi (1.5 equiv), Et_2O, 0 °C, 1 h; then $C_2Cl_4Br_2$ or I_2 (2 equiv); (v) (*S*)-CBS catalyst (0.3 equiv), $BH_3{\cdot}SMe_2$ (1 equiv), THF, 0 °C, 2 h.

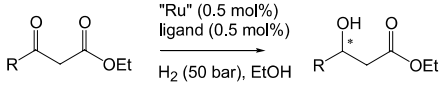


Scheme 5. Synthesis of the diphosphines **17a**,**b** and **18a**,**b**.



19 **20**

Scheme 6. Taniaphos **19** (first generation)[3] and Taniaphos **20** (second generation).[4]



21a: R = Me
21b: R = Ph

22a,b

Scheme 7. Ruthenium-catalyzed asymmetric hydrogenation of the 1,3-ketoesters **21a**,**b**.

drance of the group R in position 3 from methyl [90% ee (*S*), entry 9] to phenyl [92% ee (*R*), entry 5]. Hydrogenation of the ketoester **21b** showed the opposite dependency. By minimizing the steric hindrance of the group R, the enantioselectivity could be raised from 87% ee (*S*) (entry 11) for the phenyl-substituted ligand **17a** to 96% ee (entry 16) for the methyl-substituted **18b**. With this result, **18b** showed better selectivity for the hydrogenation of the ketoester **21b** than Taniaphos **19**. In all cases, the ligands **17a**,**b** and **18a**,**b** gave good conversion and the enantioselectivities could be improved up to 11% (entries 6 and 7) by lowering the temperature from 50 to 30 °C.

Hydrogenation was also successful for cyclic ketoesters such as ethyl 2-oxocyclopentanecarboxylate (**23**, Scheme 8, Table 2).

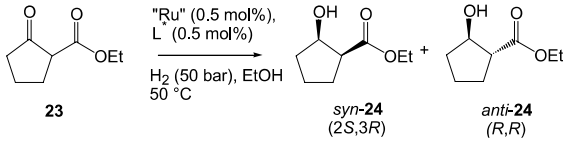
Depending on the group R, excellent diastereoselectivities and good enantioselectivities were observed for the hydrogenation of the ketoester **23** (Table 2, entry 4).

Hydrogenation of symmetrical 1,3-diketones such as bis-benzoylmethane **25** led to the corresponding diol **26** in favor of the *anti*-product (Scheme 9, Table 3).

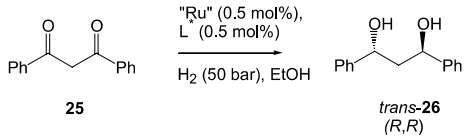
Table 1. Ruthenium-catalyzed asymmetric hydrogenation of the 1,3-ketoesters **21a**,**b**

Entry	Substr.	Ligand	Temp. (°C)	Time (h)	Conv. (%)[a]	Ee (%)[b]
1	**21a**	**19**	50	8	100	96 (*R*)[3]
2	**21b**	**19**	50	12	100	95 (*S*)[3]
3	**21b**	**20**	50	20	100	98 (*R*)[5]
4	**21a**	**17a**	50	17	100	92 (*R*)
5	**21a**	**17a**	30	21.5	100	92 (*R*)
6	**21a**	**17b**	50	13	100	80 (*R*)
7	**21a**	**17b**	30	14.5	91	91 (*R*)
8	**21a**	**18b**	50	16.5	100	83 (*S*)
9	**21a**	**18b**	30	16.5	100	90 (*S*)
10	**21b**	**17a**[c]	50	23	100	84 (*S*)
11	**21b**	**17a**[c]	30	23	100	87 (*S*)
12	**21b**	**17b**	50	14	100	88 (*S*)
13	**21b**	**17b**	30	21	100	91 (*S*)
14	**21b**	**18a** = *ent*-**17b**	50	13	100	88 (*R*)
15	**21b**	**18b**	50	13	100	94 (*R*)
16	**21b**	**18b**	30	18	100	96 (*R*)

[a] Determined by ^{1}H NMR spectroscopy.
[b] Determined by HPLC analysis (Daicel Chiracel OD).
[c] 'Ru': 1 mol%, ligand: 1 mol%.



Scheme 8. Ruthenium-catalyzed hydrogenation of ethyl 2-oxocyclopentanecarboxylate **23**.



Scheme 9. Ruthenium-catalyzed hydrogenation of the symmetrical 1,3-diketone **25**.

The results obtained for the hydrogenation of the diketone **25** showed the strongest dependency on the steric hindrance of the group R in the ligands **17a** and **18b**. Unfortunately, using the phenyl-substituted ligand **17a** afforded the diol **26** with moderate diastereoselectivity and practically no enantiodifferentiation [60% de, 3% ee (*R*,*R*), entry 3]. Instead, the product *trans*-**26** could be obtained with good selectivity using the methyl-substituted ligand **18b** [>99% de, 97% ee (*R*,*R*), entry 4].

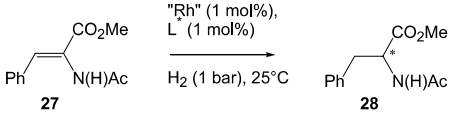
2.2.2. Enantioselective hydrogenation of C=C bonds. The ligands **17a**,**b** and **18a**,**b** have been tested in the rhodium-catalyzed asymmetric hydrogenation of α-(acylamino)acrylic ester **27**, since it is an important way to produce the corresponding amino acid (Scheme 10).[15] All the rhodium-catalyzed hydrogenations were performed with 1 mol% of the catalyst prepared in situ from $[Rh(cod)_2]BF_4$ ('Rh'; 1 mol%) and the ligand (1 mol%). The results are summarized in Table 4.

In all cases using the ligands **17a**,**b** and **18a**,**b**, the conversion and the enantioselectivity could be improved by using a mixture of MeOH/CH_2Cl_2 (1:10) instead of MeOH/toluene (1:1). The best result could be obtained with the methyl-substituted ligand **18b** [94% ee (*S*), entry 9].

The new diphosphine ligands were also tested in the rhodium-catalyzed hydrogenation of dimethyl itaconate **29** (Scheme 11). The hydrogenation reactions of **29** were performed in MeOH or MeOH/toluene (1:1), at rt and 1 bar of hydrogen pressure. The results are summarized in Table 5.

In comparison with Taniaphos **19** [91% ee (*R*), entry 1], the enantioselectivity could be improved by using ligand **18b** [96% ee (*S*), entry 5]. In all cases, after short reaction times (less than 4.5 h) and mild reaction conditions, complete conversion was observed.

2.2.3. Enantioselective hydrogenation of C=N bonds. The preparation of optically pure amines by catalytic asymmetric hydrogenation of imines is still a very challenging task.[16] The new ligands **17a**,**b** and **18a**,**b** were tested in the hydrogenation of the *N*-benzoyl hydrazone **31**[17] by using MeOH as solvent in the presence of 1 mol% of the catalyst prepared in situ from



Scheme 10. Rhodium-catalyzed hydrogenation of α-(acylamino)-acrylic ester **27**.

Table 2. Ruthenium-catalyzed hydrogenation of ethyl 2-oxocyclopentanecarboxylate **23**

Entry	Ligand	Solvent	Time (h)	Conv. (%)[a]	De (%)[b,c]	Ee (%)[b]
1	**19**	EtOH/CH_2Cl_2 (1:10)	63	100	98	91 (*R*,*R*)[3]
2	**17a**	EtOH	20.5	100	96	80 (*R*,*R*)
3	**17b**	EtOH	14	100	98	86 (*R*,*R*)
4	**18b**	EtOH	13	100	99	85 (*S*,*S*)

[a] Determined by ^1H NMR spectroscopy.
[b] Determined by HPLC analysis (Daicel Chiracel OD).
[c] The major diastereomer is the *anti*-product.

Table 3. Ruthenium-catalyzed hydrogenation of the symmetrical 1,3-diketone **25**

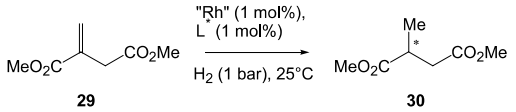
Entry	Ligand	Temp. (°C)	Time (h)	Conv. (%)[a]	De (%)[b,c]	Ee (%)[b]
1	**19**	25	12	100	98	98 (*S*,*S*)[3]
2	**20**	50	36	100	>99	>99 (*R*,*R*)[5]
3	**17a**	50	13.5	100	60	3 (*R*,*R*)
4	**18b**	50	16.5	100	>99	97 (*R*,*R*)

[a] Determined by ^1H NMR spectroscopy.
[b] Determined by HPLC analysis (Daicel Chiracel OD).
[c] The major diastereomer is the *anti*-product.

Table 4. Rhodium-catalyzed hydrogenation of α-(acylamino)acrylic ester **27**

Entry	Ligand	Solvent	Time (h)	Conv. (%)[a]	Ee (%)[b]
1	**19**	MeOH/toluene (1:1)	0.5	100	95 (*R*)[3]
2	**20**	MeOH/toluene (1:1)	1.5	100	99 (*S*)[5]
3	**17a**	MeOH/toluene (1:1)	16.5	16	64 (*R*)
4	**17a**	MeOH/CH_2Cl_2 (1:10)	3.5	100	90 (*R*)
5	**17b**	MeOH/toluene (1:1)	4	Traces	50 (*R*)
6	**17b**	MeOH/CH_2Cl_2 (1:10)	3.5	100	86 (*R*)
7	**18a** = *ent*-**17b**	MeOH/CH_2Cl_2 (1:10)	6	100	88 (*S*)
8	**18b**	MeOH/toluene (1:1)	4	50	86 (*S*)
9	**18b**	MeOH/CH_2Cl_2 (1:10)	4	100	94 (*S*)

[a] Determined by ^{1}H NMR spectroscopy.
[b] Determined by GC analysis (Chirasil-L-Val).

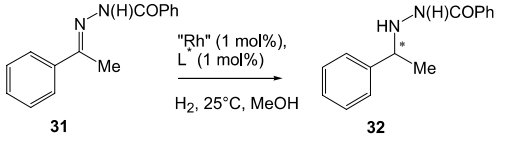


Scheme 11. Rhodium-catalyzed hydrogenation of dimethyl itaconate **29**.

Table 5. Rhodium-catalyzed hydrogenation of dimethyl itaconate **29**

Entry	Ligand	Solvent	Time (h)	Conv. (%)[a]	Ee (%)[b]
1	**19**	MeOH	14	100	91 (*R*)[3]
2	**20**	MeOH/toluene	0.5	100	98 (*S*)[5]
3	**17a**	MeOH	4.5	100	85 (*R*)
4	**17b**	MeOH	2.5	100	91 (*R*)
5	**18b**	MeOH	4	100	96 (*S*)

[a] Determined by ^{1}H NMR spectroscopy.
[b] Determined by HPLC analysis (Daicel Chiracel OD).



Scheme 12. Rhodium-catalyzed hydrogenation of the *N*-benzoyl hydrazone **31**.

Table 6. Rhodium-catalyzed hydrogenation of the *N*-benzoyl hydrazone **31**

Entry	Ligand	Pressure (bar)	Time (h)	Conv. (%)[a]	Ee (%)[b]
1	**19**	50	22–24	40	45 (*S*)[18]
2	**17a**	30	22	100	65 (*S*)
3	**17b**	30	22	100	59 (*S*)
4	**18b**	30	22	100	59 (*R*)

[a] Determined by ^{1}H NMR spectroscopy.
[b] Determined by HPLC analysis (Daicel Chiracel OJ).

$[Rh(cod)_2]BF_4$ ('Rh'; 1 mol%) and the ligand (1 mol%) (Scheme 12, Table 6).

The new 1,5-diphosphine ferrocene ligands **17a**,**b** and **18b** showed in all cases better reactivity and enantioselectivity than Taniaphos **19** by using milder reaction conditions (entries 2–4). Interestingly, the best result could be obtained using the phenyl-substituted ligand **17a** [65% ee (*S*), entry 2].

3. Conclusion

In summary, we have developed a stereoselective synthesis of a third generation of Taniaphos-analogous 1,5-diphosphine ferrocene ligands with the interesting (S_{Fc},3*S*)- and (R_{Fc},3*R*)-configurations, which offers many possibilities for variation. The new ligands could successfully be applied to ruthenium- and rhodium-catalyzed hydrogenations of C=O, C=C and C=N bonds. Generally, we found that ligand **18b** (R = Me) gave the best enantioselectivities. The increase of steric hindrance at position 3 had a rather detrimental effect. Further modifications of the R group are under investigation.

4. Experimental

All reactions were carried out under argon using standard Schlenk techniques. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX 300 instrument. ^{31}P NMR spectra were recorded on a Varian Mercury 200 instrument. Chemical shifts (δ) are given as ppm relative to the residual solvent peak. IR spectra were recorded on a Perkin–Elmer 1420 IR spectrometer. Mass spectra were recorded on a Finnigan MAT 95 Q spectrometer. Optical rotations were measured on a Perkin–Elmer 241 polarimeter. Column chromatography was performed on Merck silica gel 60 (230–400 mesh ASTM). Thin layer chromatography was performed on Merck TLC-plates silica gel 60 F-254. Enantiomeric excesses were determined by HPLC analysis (Chiralcel OD-H, OD an OJ, Daicel Chemical Industries, *n*-heptane/isopropanol as mobile phase and detection by a diode array UV–vis detector) or GC analysis (Chirasil-L-Valin, Chrompak, with hydrogen as carrier gas). Racemic compounds were used for calibration in each case for the separations.

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.

4.1. Acylation of ferrocene

4.1.1. Benzoylferrocene, 7a. Aluminum(III) chloride (16.4 g, 123 mmol) was added to a solution of benzoyl chloride (14 mL, 123 mmol) in CH_2Cl_2 (110 mL) at 0 °C. This solution was added to a solution of ferrocene (20.8 g, 112 mmol) in CH_2Cl_2 (110 mL) at 0 °C over 30 min. The reaction mixture was stirred at rt and after 1.5 h, the mixture was quenched by adding it to ice cold water. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3×100 mL). The organic layers were washed with saturated K_2CO_3 solution, water, and brine and dried over $MgSO_4$. The crude material was purified by column chromatography (*n*-pentane/Et_2O 4:1). Benzoylferrocene **7a** was obtained as a red solid (22.9 g, 79 mmol, 71%); mp 106–107 °C (lit.[7] 108 °C); IR (KBr): *v* 3436 (br, m), 3114 (w), 3092 (w), 3066 (w), 1627 (vs), 1598 (m), 1578 (m), 1451 (m), 1440 (m), 1376 (m), 1290 (s), 1167 (m), 1057 (m), 1026 (m); ^{1}H NMR ($CDCl_3$): δ 7.82–7.79 (m, 2H), 7.47–7.34 (m, 3H), 4.81 (t, $J = 2.0$ Hz, 2H), 4.48 (t, $J = 1.8$ Hz, 2H), 4.11 (s, 5H); ^{13}C NMR ($CDCl_3$): δ 199.5, 140.2, 131.9, 128.6, 128.5, 78.6, 73.0, 71.9, 70.6; MS (EI, 70 eV) *m*/*z* (%): 291 (M^++1, 29), 290 (M^+, 100), 288 (9), 197 (6), 133 (6); HRMS calcd for $C_{17}H_{14}FeO$: 290.0394. Observed: 290.0395.

4.1.2. Propionylferrocene, 7b. Prepared according to the procedure described above from ferrocene (17.1 g, 92 mmol), aluminum(III) chloride (13.5 g, 10 mmol), and propionyl chloride (8.8 mL, 101 mmol) with a reaction time of 1.5 h and isolated as a red oil (19.7 g, 81.5 mmol, 89%); (mp lit.[19] 67–68 °C); IR (KBr): *v* 3930 (br, w), 3097 (m), 2975 (m), 2936 (m), 1669 (vs), 1454 (s), 1413 (m), 1378 (m), 1248 (s), 1106 (m), 1098 (m), 1050 (m), 1026 (m), 1002 (m); ^{1}H NMR ($CDCl_3$): δ 4.71 (s, 2H), 4.40 (s, 2H), 4.11 (s, 5H), 2.66 (q, $J = 7.2$ Hz, 2H), 1.13 (t, $J = 7.4$ Hz, 3H); ^{13} C NMR ($CDCl_3$): δ 205.3, 79.3, 72.4, 70.1, 69.6, 33.1, 8.9; MS (EI, 70 eV) *m*/*z* (%): 243 (M^++1, 25), 242 (M^+, 100), 240 (10), 213 (60), 186 (19), 185 (87), 129 (59), 128 (16), 121 (32), 56 (14); CHN calcd for $C_{13}H_{14}FeO$: C, 64.50; H, 5.83. Observed: C, 64.29; H, 5.80.

4.1.3. Acetylferrocene, 7c. Prepared according to the procedure described above from ferrocene (10.6 g, 57 mmol), aluminum(III) chloride (8.4 g, 63 mmol), and acetyl chloride (4.5 mL, 63 mmol) with a reaction time of 1 h and isolated as a red solid (11.6 g, 51 mmol, 89%); mp 85–86 °C (lit.[20] 84–86 °C); IR (KBr): *v* 3436 (br, w), 3096 (w), 1662 (vs), 1457 (m), 1376 (m), 1281 (m), 1115 (w), 1102 (w), 1005 (w); ^{1}H NMR ($CDCl_3$): δ 4.70 (t, $J = 2.0$ Hz, 2H), 4.43 (t, $J = 2.0$ Hz, 2H), 4.13 (s, 5H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 202.5, 79.7, 72.7, 70.3, 70.0, 27.8; MS (EI, 70 eV) *m*/*z* (%): 229 (M^++1, 15), 228 (M^+, 100), 213 (11), 186 (11), 185 (61), 129 (12); CHN calcd for $C_{12}H_{12}FeO$: C, 63.20; H, 5.30. Observed: C, 63.15; H, 5.31.

4.2. Reduction of the ferrocenyl ketones 7a–c

4.2.1. (*S*)-(3-Hydroxyphenylmethyl)ferrocene, 10a. A solution of borane dimethyl sulfide complex (4.3 mL, 45 mmol) in THF (45 mL) was prepared. The (*R*)-CBS catalyst (methyl oxazaborolidine; 3.7 g, 13.5 mmol, 0.3 equiv) was dissolved in 20% of this solution. A solution of benzoylferrocene **7a** (13.1 g, 45 mmol) in THF (45 mL) and the remaining borane dimethyl sulfide complex solution were added simultaneously at 0 °C over 45 min. The disappearance of the red colored ketone indicated the reaction progress. After complete reduction, methanol (4 mL, **CAUTION:** gas evolution) was added dropwise. The reaction mixture was quenched with saturated NH_4Cl solution and extracted with Et_2O (150 mL). The organic layers were washed with water and brine and dried over $MgSO_4$. The crude product was purified by column chromatography (*n*-pentane/Et_2O 4:1). The alcohol **10a** was isolated as a yellow solid [12.1 g, 41 mmol, 92%, >98% ee (*S*)]. HPLC analysis (OD-H, 92% *n*-heptane, 8% isopropanol, 0.6 mL/min): retention time (min) 23.3 (*R*), 37.2 (*S*); mp 88–89 °C; $[\alpha]_D = +132.2$ (*c* 0.79, $CHCl_3$); IR (KBr): *v* 3566 (m), 3401 (br, m), 3082 (m), 3028 (w), 2855 (w), 1652 (br, w), 1494 (m), 1453 (m), 1410 (w), 1320 (w), 1182 (m), 1104 (m), 1048 (m), 1018 (m), 1000 (m); ^{1}H NMR ($CDCl_3$): δ 7.31–7.13 (m, 5H), 5.35 (d, $J = 2.7$ Hz, 1H), 4.11 (s, 5H), 4.07 (s, 4H), 2.46 (d, $J = 3.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 142.3, 127.1, 126.4, 125.2, 93.1, 71.0, 67.5, 67.1, 67.0, 66.4, 65.0; MS (EI, 70 eV) *m*/*z* (%): 293 (M^++1, 21), 292 (M^+, 98), 291 (M^+−1, 14), 290 (62), 277 (16), 276 (81), 275 (73), 274 (27), 273 (10), 227 (51), 209 (13), 186 (12), 154 (52), 153 (100), 152 (56), 151 (10), 138 (25), 121 (40), 56 (17); CHN calcd for $C_{17}H_{16}FeO$: C, 69.89; H, 5.52. Observed: C, 69.95; H, 5.54.

4.2.2. (*S*)-(3-Hydroxypropyl)ferrocene, 10b. Prepared according to the procedure described above from propionylferrocene **7b** (19.2 g, 79 mmol) with borane dimethyl sulfide complex (7.5 mL, 79 mmol) and the (*R*)-CBS catalyst (6.6 g, 24 mmol, 0.3 equiv). **10b** was isolated as an orange oil [18.9 g, 78 mmol, 98%, >98% ee (*S*)]. HPLC analysis (OD, 92% *n*-heptane, 8% isopropanol, 0.6 mL/min): retention time (min) 12.6 (*R*), 13.2 (*S*); $[\alpha]_D = +56.9$ (*c* 1.55, $CHCl_3$); IR (KBr): *v* 3927 (br, w), 3434 (br, m), 3094 (m), 2963 (s), 2932 (m), 2875 (m), 2376 (w), 1643 (br, m), 1463 (m), 1455 (m), 1411 (m), 1385 (m), 1105 (vs), 1090 (m), 1035 (s), 1001 (s); ^{1}H NMR ($CDCl_3$): δ 4.16–4.08 (m, 9H), 1.91 (d, $J = 3.3$ Hz, 1H), 1.63–1.55 (m, 2H), 0.88 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 94.6, 71.5, 68.6, 68.2, 68.1, 67.7, 65.6, 31.4, 10.8; MS (EI, 70 eV) *m*/*z* (%): 244 (M^+, 41), 227 (18), 226 (100), 225 (20), 224 (13), 186 (12), 161 (21), 138 (37), 134 (19), 121 (29), 56 (15); HRMS calcd for $C_{13}H_{16}FeO$: 244.0551. Observed: 244.0560.

4.2.3. (*R*)-(3-Hydroxypropyl)ferrocene, 11a. Prepared according to the procedure described above from propionylferrocene **7b** (10.8 g, 45 mmol) with borane dimethyl sulfide complex (4.2 mL, 45 mmol) and the (*S*)-CBS catalyst (4.3 g, 16 mmol, 0.3 equiv). **10b** was isolated as an orange oil [10.6 g, 43.6 mmol, 98%, >98% ee (*R*)]; $[\alpha]_D = -83.6$ (*c* 0.45, $CHCl_3$).

4.2.4. (*R*)-(3-Hydroxyethyl)ferrocene, 11b. Prepared according to the procedure described above from acetylferrocene **7c** (17.5 g, 77 mmol) with borane dimethyl sulfide complex (7.3 mL, 77 mmol) and the (*S*)-CBS catalyst (6.4 g, 23 mmol, 0.3 equiv). **10b** was isolated as a yellow solid [14.9 g, 65 mmol, 85%, >98% ee (*R*)]. HPLC analysis (OD-H, 99% *n*-heptane, 1% isopropanol, 0.6 mL/min): retention time (min) 40.6 (*S*), 42.6 (*R*); mp 77 °C (lit.[10] 72–73 °C); $[\alpha]_D = -41.2$ (*c* 0.26, $CHCl_3$); IR (KBr): *v* 3922 (w), 3393 (br, s), 3086 (m), 2972 (m), 2959 (m), 2922 (m), 1642 (br, w), 1456 (m), 1433 (m), 1410 (m), 1364 (m), 1309 (m), 1234 (m), 1105 (s), 1093 (vs), 1071 (m), 1036 (m), 1024 (m), 1011 (m), 1002 (m); ^{1}H NMR ($CDCl_3$): δ 4.51–4.44 (m, 1H), 4.15–4.08 (m, 9H), 1.86 (d, $J = 4.8$ Hz, 1H), 1.37 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 95.1, 68.7, 68.3, 68.2, 66.5, 66.0, 24.1; MS (EI, 70 eV) *m*/*z* (%): 213 (M^+−OH, 16), 212 (100), 121 (20); CHN calcd for $C_{12}H_{14}FeO$: C, 62.64; H, 6.13. Observed: C, 62.88; H, 6.18.

4.3. Synthesis of the amines 12a,b and 13a,b

4.3.1. (*S*)-[3-(*N*,*N*-Dimethylamino)phenylmethyl]ferrocene, 12a. (*S*)-(3-Hydroxyphenylmethyl)ferrocene **10a** (11.8 g, 40 mmol) was dissolved in pyridine (40 mL) and acetic anhydride (36 mL) and stirred 12 h at rt. Solvents were removed under vacuum and the resulting acetate was dissolved in acetonitrile (200 mL) without further purification. Dimethylamine (45 mL, 40% solution in water) was added and the reaction mixture again stirred for 12 h at rt. Solvents were removed under reduced pressure and the crude product dissolved in Et_2O (150 mL). The organic phase was washed with saturated NH_4Cl solution, water and brine and dried over $MgSO_4$. The crude product was purified by column chromatography (*n*-pentane/Et_2O 1:1 + 0.5% NEt_3) and afforded the amine **12a** as an orange solid (10.8 g, 34 mmol, 85%); mp 63–64 °C; $[\alpha]_D = -135.2$ (*c* 0.84, $CHCl_3$); IR (KBr): *v* 3436 (br, w), 3088 (w), 2985 (m), 2962 (m), 2942 (m), 2858 (m), 2812 (m), 2762 (m), 1492 (m), 1465 (m), 1453 (m), 1430 (m), 1294 (m), 1202 (m), 1147 (m), 1106 (m), 1038 (m), 1006 (m); ^{1}H NMR ($CDCl_3$): δ 7.43–7.39 (m, 2H), 7.34–7.28 (m, 2H), 7.25–7.18 (m, 1H), 4.12–4.09 (m, 2H), 4.07–4.05 (m, 1H), 4.02–4.00 (m, 1H), 3.70 (s, 1H), 3.66–3.63 (m, 4H), 2.00 (s, 6H); ^{13}C NMR ($CDCl_3$): δ 143.9, 128.9, 128.4, 127.5, 90.8, 72.8, 70.9, 69.1, 68.9, 67.7, 66.8, 44.9; MS (EI, 70 eV) *m*/*z* (%): 319 (M^+, 29), 276 (28), 275 (100), 153 (10), 121 (15); HRMS calcd for $C_{19}H_{21}FeN$: 319.1023. Observed: 319.1035.

4.3.2. (*S*)-[3-(*N*,*N*-Dimethylamino)propyl]ferrocene, 12b. Prepared according to the procedure described above from (*S*)-(3-hydroxypropyl)ferrocene **10b** (110 mg, 0.5 mmol) with pyridine (0.6 mL) and acetic acid anhydride (0.4 mL), the resulting acetate was reacted with acetonitrile (2 mL) and dimethylamine (2 mL, 40% solution in water) in a sealed tube at 60 °C for 20 h. After purification by acid–base workup, the amine **12b** was obtained as a yellow solid (106 mg, 0.4 mmol, 87%); mp 66–67 °C; $[\alpha]_D = +54.8$ (*c* 1.39, $CHCl_3$); IR (KBr): *v* 3464 (br, w), 3102 (m), 3088 (m), 2960 (s), 2931 (vs), 2884 (m), 2870 (m), 2851 (m), 2818 (m), 2776 (m), 1768 (w), 1738 (w), 1636 (w), 1472 (m), 1446 (m), 1264 (m), 1255 (m), 1228 (m), 1105 (s), 1024 (m), 1002 (m); ^{1}H NMR ($CDCl_3$): δ 4.06–3.99 (m, 8H), 3.94–3.93 (m, 1H), 3.18 (dd, $J = 11.0$, 3.5 Hz, 1H), 2.03–1.93 (m, 7H), 1.73–1.57 (m, 1H), 1.03 (t, $J = 1.4$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 86.1, 69.7, 68.9, 67.8, 67.5, 67.2, 65.3, 40.9, 24.8, 12.7; MS (EI, 70 eV) *m*/*z* (%): 271 (M^+, 23), 243 (15), 242 (100), 227 (18), 226 (18); CHN calcd for $C_{15}H_{21}FeN$: C, 66.44; H, 7.81; N, 5.17. Observed: C, 66.23; H, 7.70; N, 5.09.

4.3.3. (*R*)-[3-(*N*,*N*-Dimethylamino)ethyl]ferrocene, 13a. $[\alpha]_D = -57.1$ (*c* 0.50, $CHCl_3$).

4.3.4. (*R*)-[3-(*N*,*N*-Dimethylamino)ethyl]ferrocene, 13b.[21] Prepared according to the procedure described above from (*R*)-(3-hydroxyethyl)ferrocene **11b** (14.7 g, 64 mmol) with pyridine (100 mL) and acetic anhydride (44 mL), the resulting acetate was reacted with MeOH (220 mL) and dimethylamine (44 mL, 40% solution in water). The crude product was purified by column chromatography (*n*-pentane/Et_2O 1:1 + 0.5% NEt_3) and afforded the amine **13b** as an orange oil (5.5 g, 21.4 mmol, 34%); $[\alpha]_D = +8.3$ (*c* 2.65, $CHCl_3$); IR (KBr): *v* 3928 (w), 3094 (m), 2972 (s), 2935 (s), 2897 (m), 2856 (m), 2819 (s), 2777 (s), 1642 (br, w), 1472 (m), 1455 (s), 1367 (m), 1299 (m), 1261 (m), 1230 (m), 1215 (m), 1181 (m), 1156 (m), 1106 (s), 1083 (m), 1071 (m), 1040 (s), 1001 (m); ^{1}H NMR ($CDCl_3$): δ 4.08–4.03 (m, 9H), 3.54 (q, $J = 6.9$ Hz, 1H), 2.02 (s, 6H), 1.38 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 87.5, 69.8, 69.0, 67.8, 67.6, 67.3, 59.1, 41.0, 16.5; MS (EI, 70 eV) *m*/*z* (%): 258 (M^++1, 13), 257 (M^+, 95), 243 (13), 242 (100), 227 (10), 214 (22), 213 (100), 212 (40), 186 (38), 121 (41), 72 (12), 56 (11); HRMS calcd for $C_{14}H_{19}FeN$: 257.0867. Observed: 257.0845.

4.4. Diastereoselective lithiation of the amines 12a,b and 13a,b

4.4.1. (R_{Fc})-1-Bromo-2-[3-(*S*)-(*N*,*N*-dimethylamino)phenylmethyl]ferrocene, 8a. A solution of (*S*)-[3-(*N*,*N*-dimethylamino)phenylmethyl]ferrocene **12a** (6.2 g, 20 mmol) in Et_2O (138 mL) was cooled to 0 °C. *t*-BuLi (16.8 mL, 29 mmol, 1.74 M solution in pentane, 1.5 equiv) was added, the mixture stirred for 1 h at 0 °C and a solution of dibromotetrachloroethane (12.7 g, 39 mmol, 2 equiv) in Et_2O (50 mL) added. After warming up to rt, a saturated solution of $Na_2S_2O_5$ was added. The organic phase was washed with water and brine and

dried over $MgSO_4$. The crude product was purified by column chromatography (CH_2Cl_2/Et_2O 1:1 + 0.5% NEt_3) and afforded the amine **8a** as an orange solid (960 mg, 2.4 mmol, 12%, dr 89:11); mp 94–97 °C; $[\alpha]_D = -74.3$ (*c* 0.90, $CHCl_3$); IR (KBr): *v* 3437 (br, m), 3067 (w), 3033 (w), 2978 (m), 2952 (m), 2858 (m), 2813 (m), 2767 (vs), 1641 (br, w), 1489 (m), 1465 (m), 1452 (m), 1374 (w), 1288 (m), 1242 (m), 1188 (m), 1106 (m), 1008 (m); ^{1}H NMR ($CDCl_3$): δ 7.54–7.50 (m, 2H), 7.38–7.33 (m, 2H), 7.28–7.22 (m, 1H), 4.36–4.34 (m, 1H), 4.24–4.23 (m, 1H), 4.10–4.08 (m, 1H), 3.91 (s, 1H), 3.57 (s, 1H), 2.02 (s, 6H); ^{13}C NMR ($CDCl_3$): δ 144.9, 128.7, 128.6, 127.7, 89.9, 81.5, 71.6, 71.3, 69.7, 69.1, 67.2, 66.0, 44.9; MS (EI, 70 eV) *m*/*z* (%): 399 (M^++1, 14), 397 (M^+−1, 16), 356 (13), 355 (54), 354 (12), 353 (62), 309 (14), 275 (21), 274 (22), 273 (100), 217 (29), 216 (14), 215 (41), 203 (11), 202 (33), 154 (46), 153 (73), 134 (75), 121 (29), 56 (19), 43 (41); CHN calcd for $C_{19}H_{20}BrFeN$: C, 57.32; H, 5.06; N, 3.52; Br, 20.07. Observed: C, 57.59; H, 5.14; N, 3.44; Br, 19.44.

4.4.2. (R_{Fc})-1-Iodo-2-[3-(*S*)-(*N*,*N*-dimethylamino)phenylmethyl]ferrocene, 8b. Prepared according to the procedure described above from (*S*)-[3-(*N*,*N*-dimethylamino)phenylmethyl]ferrocene **12a** (614 mg, 1.92 mmol) with *t*-BuLi (3.6 mL, 2.9 mmol, 0.8 M solution in pentane, 1.5 equiv) and iodine (976 mg, 3.9 mmol, 2 equiv) in Et_2O (14 mL). The crude product was purified by column chromatography (*n*-pentane/Et_2O 1:1 + 0.5% NEt_3) and afforded the amine **8b** as an orange solid (716 mg, 1.6 mmol, 84%, dr 83:17); mp 94–96 °C; $[\alpha]_D = -72.9$ (*c* 0.77, $CHCl_3$); IR (KBr): *v* 3436 (br, vs), 2935 (m), 2856 (m), 2810 (m), 1636 (br, m), 1450 (m), 1366 (w), 1186 (m), 1106 (m), 1006 (m); ^{1}H NMR ($CDCl_3$): δ 7.54–7.50 (m, 2H), 7.39–7.33 (m, 2H), 7.27–7.21 (m, 1H), 4.37–4.35 (m, 1H), 4.29–4.27 (m, 1H), 4.21–4.19 (m, 1H), 3.81 (s, 1H), 3.52–3.50 (m, 5H), 2.02 (s, 6H); ^{13}C NMR ($CDCl_3$): δ 145.2, 128.7, 128.6, 127.7, 92.3, 73.6, 72.1, 71.4, 69.8, 66.5, 45.0; MS (EI, 70 eV) *m*/*z* (%): 445 (M^+, 34), 402 (24), 401 (100), 275 (14), 274 (17), 273 (60), 217 (16), 215 (16), 202 (15), 153 (20), 152 (29), 134 (32), 121 (15); HRMS calcd for $C_{19}H_{20}FeIN$: 444.9990. Observed: 444.9971.

4.4.3. (R_{Fc})-1-Iodo-2-[3-(*S*)-(*N*,*N*-dimethylamino)propyl]ferrocene, 8c. Prepared according to the procedure described above from (*S*)-[3-(*N*,*N*-dimethylamino)propyl]ferrocene **12b** (4.1 g, 15 mmol) with *t*-BuLi (14.1 mL, 23 mmol, 1.6 M solution in pentane, 1.5 equiv) and iodine (5.7 g, 23 mmol, 1.5 equiv) in Et_2O (100 mL). The crude product was purified by column chromatography (*n*-pentane/Et_2O 1:1 + 0.5% NEt_3) and afforded the amine **8c** as an orange solid (3.7 g, 9.3 mmol, 62%, dr 93:7); mp 95–97 °C; $[\alpha]_D = +26.2$ (*c* 1.14, $CHCl_3$); IR (KBr): *v* 3436 (br, w), 3090 (w), 2963 (s), 2929 (s), 2818 (m), 2778 (m), 1644 (w), 1470 (m), 1449 (m), 1366 (m), 1259 (m), 1230 (m), 1198 (m), 1154 (m), 1106 (s), 1043 (m); ^{1}H NMR ($CDCl_3$): δ 4.39 (s, 1H), 4.17 (s, 1H), 4.05 (s, 5H), 3.97 (s, 1H), 3.3 (dd, $J = 10.5$, 3.3 Hz, 1H), 2.09–2.01 (m, 7H), 1.85–1.70 (m, 1H), 1.08 (t, $J = 1.7$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 89.1, 74.5, 72.1, 68.5, 66.4, 63.2, 45.7, 41.5, 26.4, 12.8; MS (EI, 70 eV) *m*/*z* (%): 397 (M^+, 42), 369 (22), 368 (100), 353 (20), 312 (12), 226 (20), 184 (11), 121 (16), 86 (27), 56 (10); HRMS calcd for $C_{15}H_{20}FeIN$: 396.9990. Observed: 397.0005.

4.4.4. (S_{Fc})-1-Iodo-2-[3-(*R*)-(*N*,*N*-dimethylamino)propyl]ferrocene, 9a. Prepared according to the procedure described above from (*R*)-[3-(*N*,*N*-dimethylamino)propyl]ferrocene **13a** (1.3 g, 4.8 mmol) with *t*-BuLi (3.5 mL, 5.3 mmol, 1.5 M solution in pentane, 1.1 equiv) and iodine (1.4 g, 5.5 mmol, 1.15 equiv) in Et_2O (100 mL). The crude product was purified by column chromatography (*n*-pentane/Et_2O 1:1 + 0.5% NEt_3) and afforded the amine **9a** as an orange solid (1.4 g, 3.4 mmol, 72%, dr 95:5); mp 101–102 °C; $[\alpha]_D = -29.7$ (*c* 0.89, $CHCl_3$); IR (KBr): *v* 3436 (br, m), 3090 (m), 2978 (m), 2063 (s), 2928 (s), 2882 (m), 2817 (m), 2778 (m), 1637 (br, w), 1470 (m), 1449 (m), 1366 (m), 1354 (m), 1259 (m), 1230 (m), 1198 (m), 1154 (m), 1106 (s); ^{1}H NMR ($CDCl_3$): δ 4.40–4.38 (m, 1H), 4.17 (t, $J = 2.4$ Hz, 1H), 4.05 (s, 5H), 3.97–3.96 (m, 1H), 3.30 (dd, $J = 10.5$, 3.6 Hz, 1H), 2.12–2.00 (m, 7H), 1.87–1.70 (m, 1H), 1.08 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 89.1, 74.5, 72.1, 68.5, 66.4, 63.2, 45.7, 41.5, 26.4, 12.8; MS (EI, 70 eV) *m*/*z* (%): 397 (M^+, 41), 369 (14), 368 (100), 353 (24), 352 (17), 226 (32), 184 (18), 184 (10), 169 (11), 154 (10), 153 (13), 141 (13), 121 (35), 86 (53), 77 (15), 56 (20), 42 (18); CHN calcd for $C_{15}H_{20}FeIN$: C, 45.37; H, 5.08; N, 3.53; I, 31.96. Observed: C, 45.30; H, 5.00; N, 3.44; I, 31.93.

4.4.5. (S_{Fc})-1-Iodo-2-[3-(*R*)-(*N*,*N*-dimethylamino)ethyl]ferrocene, 9b. Prepared according to the procedure described above from (*R*)-[3-(*N*,*N*-dimethylamino)ethyl]ferrocene **13b** (1.69 g, 6.6 mmol) with *t*-BuLi (4.8 mL, 7.2 mmol, 1.5 M solution in pentane, 1.1 equiv) and iodine (2.0 g, 7.9 mmol, 1.2 equiv) in Et_2O (50 mL). The crude product was purified by column chromatography (CH_2Cl_2/Et_2O 1:1 + 0.5% NEt_3) and afforded the amine **9b** as an orange oil (2.0 g, 5.2 mmol, 79%, dr 94:6); $[\alpha]_D = -0.33$ (*c* 0.61, $CHCl_3$); IR (KBr): *v* 3094 (m), 2971 (s), 2935 (vs), 2856 (m), 2817 (s), 2773 (s), 1642 (br, w), 1451 (s), 1373 (m), 1262 (m), 1194 (m), 1156 (m), 1106 (m), 1089 (m), 1057 (m), 1002 (m); ^{1}H NMR ($CDCl_3$): δ 4.40–4.38 (m, 1H), 4.18–4.16 (m, 1H), 4.09–4.07 (m, 1H), 4.05 (s, 5H), 3.55 (q, $J = 6.8$ Hz, 1H), 2.08 (s, 6H), 1.43 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 90.6, 74.7, 72.1, 68.6, 66.0, 58.0, 45.9, 41.6, 16.3; MS (EI, 70 eV) *m*/*z* (%): 384 (M^++1, 19), 383 (M^+, 100), 369 (14), 368 (79), 340 (18), 339 (97), 338 (72), 337 (12), 336 (10), 312 (41), 213 (16), 212 (18), 211 (12), 208 (10), 184 (13), 155 (20), 154 (13), 153 (30), 152 (12), 128 (11), 121 (28), 72 (21), 56 (16); HRMS calcd for $C_{14}H_{18}FeIN$: 382.9833. Observed: 382.9846.

4.5. Substitution of the amino function

4.5.1. (R_{Fc})-1-Bromo-2-[3-(*S*)-(*o*-bromophenyl)phenylmethyl]ferrocene, 15a. *o*-Bromoiodobenzene (0.16 mL, 1.26 mmol, 1.5 equiv) was dissolved in THF (4 mL) and cooled to −30 °C. *i*-PrMgCl (0.67 mL, 1.3 mmol, 1.95 M

solution in THF, 1.55 equiv) was added and the reaction mixture stirred for 30 min. $ZnBr_2$ solution (0.92 mL, 1.6 mmol, 1.7 M solution in THF, 1.8 equiv) was added and after stirring for 30 min at −30 °C the reaction mixture was cooled to −78 °C. A solution of (R_{Fc})-1-bromo-2-[3-(*S*)-(*N*,*N*-dimethylamino)phenylmethyl]ferrocene **8a** (334 mg, 0.8 mmol) in THF (4 mL) was added and the resulting solution stirred at rt overnight. Et_2O (5 mL) was added and the organic phase washed with water and brine and dried over $MgSO_4$. The crude product was purified by column chromatography (*n*-pentane/CH_2Cl_2 20:1) and afforded **15a** as an orange solid (423 mg, 0.8 mmol, 99%, dr 92:8); mp 116–117 °C; $[\alpha]_D = -79.6$ (*c* 0.73, $CHCl_3$); IR (KBr): *v* 3431 (br, m), 3056 (w), 3027 (w), 1638 (br, w), 1563 (w), 1492 (w), 1462 (m), 1106 (m), 1022 (m), 1001 (m); ^{1}H NMR ($CDCl_3$): δ 7.40–7.37 (m, 1H), 7.32–7.25 (m, 4H), 7.22–7.17 (m, 1H), 7.11–7.06 (m, 1H), 6.96–6.91 (m, 1H), 6.86–6.83 (m, 1H), 5.58 (s, 1H), 4.42 (s, 1H), 4.05–4.03 (m, 6H), 3.75 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 141.9, 139.2, 131.8, 129.1, 128.5, 127.0, 126.8, 126.1, 125.6, 123.9, 89.9, 78.2, 70.3, 70.0, 69.6, 66.7, 64.7, 49.2; MS (EI, 70 eV) *m*/*z* (%): 512 (M^++2, 12), 511 (M^++1, 48), 510 (M^+, 25), 509 (M^+−1, 100), 508 (14), 507 (55), 465 (10), 350 (12), 230 (14), 229 (79), 228 (87), 227 (32), 226 (52), 215 (19), 203 (10), 202 (32), 165 (10), 152 (23), 120 (15); HRMS calcd for $C_{23}H_{18}Br_2Fe$: 507.9125. Observed: 507.9127.

4.5.2. (R_{Fc})-1-Iodo-2-[3-(*R*)-(*o*-bromophenyl)phenylmethyl]ferrocene, 15b. Prepared according to the procedure described above from (R_{Fc})-1-iodo-2-[3-(*S*)-(*N*,*N*-dimethylamino)phenylmethyl]ferrocene **8b** (570 mg, 1.3 mmol) with *o*-bromoiodobenzene (0.25 mL, 1.9 mmol, 1.5 equiv), *i*-PrMgCl (1.02 mL, 2.0 mmol, 1.95 M solution in THF, 1.55 equiv), $ZnBr_2$ (1.28 mL, 2.31 mmol, 1.7 M solution in THF, 1.8 equiv), and acetyl chloride (0.13 mL, 1.5 mmol, 1.2 equiv) in THF (12 mL). The crude product was purified by column chromatography (*n*-pentane/Et_2O 9:1), recrystallized from Et_2O and afforded **15b** as an orange solid (699 mg, 1.3 mmol, 98%, dr >99:<1); mp 121–122 °C; $[\alpha]_D = -92.1$ (*c* 2.55, $CHCl_3$); IR (KBr): *v* 3436 (br, vs), 3084 (w), 3058 (w), 3028 (w), 1629 (br, w), 1493 (w), 1463 (m), 1107 (m), 1024 (m), 1002 (m); ^{1}H NMR ($CDCl_3$): δ 7.39 (d, $J = 8.1$ Hz, 1H), 7.30–7.25 (m, 4H), 7.21–7.16 (m, 1H), 7.10–7.05 (m, 1H), 6.96–6.91 (m, 1H), 6.80 (d, $J = 7.8$ Hz, 1H), 5.47 (s, 1H), 4.42 (d, $J = 1.5$ Hz, 1H), 4.13–4.12 (m, 1H), 4.00 (s, 5H), 3.80 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 143.4, 140.6, 133.2, 130.6, 130.2, 128.4, 128.2, 127.5, 127.0, 125.6, 93.9, 75.5, 72.2, 68.9, 68.5, 52.3, 45.0; MS (EI, 70 eV) *m*/*z* (%): 559 (M^++2, 24), 558 (M^++1, 96), 557 (M^+, 26), 556 (100), 229 (55), 228 (65), 227 (24), 226 (35), 215 (15), 202 (22), 152 (14), 121 (10); HRMS calcd for $C_{23}H_{18}BrFeI$: 555.8986. Observed: 555.9005.

4.5.3. (R_{Fc})-1-Iodo-2-[3-(*R*)-(*o*-bromophenyl)propyl]ferrocene, 15c. Prepared according to the procedure described above from (R_{Fc})-1-iodo-2-[3-(*S*)-(*N*,*N*-dimethylamino)propyl]ferrocene **8c** (2.07 g, 5.2 mmol) with *o*-bromoiodobenzene (1.01 mL, 7.8 mmol, 1.5 equiv), *i*-PrMgCl (4.15 mL, 8.1 mmol, 1.95 M solution in THF, 1.55 equiv), $ZnBr_2$ (5.53 mL, 9.4 mmol, 1.7 M solution in THF, 1.8 equiv), and acetyl chloride (0.56 mL, 6.3 mmol, 1.2 equiv) in THF (40 mL). The crude product was purified by column chromatography (*n*-pentane/CH_2Cl_2 20:1), recrystallized from Et_2O and afforded **15c** as an orange solid (1.82 g, 3.6 mmol, 69%, dr >99:<1); mp 95–96 °C; $[\alpha]_D = +95.2$ (*c* 2.51, $CHCl_3$); IR (KBr): *v* 3436 (br, m), 3092 (w), 3054 (w), 2963 (m), 2926 (m), 1641 (br, w), 1466 (s), 1428 (m), 1370 (m), 1106 (m), 1019 (m), 1001 (m); ^{1}H NMR ($CDCl_3$): δ 7.43 (d, $J = 8.1$ Hz, 1H), 7.02 (t, $J = 7.5$ Hz, 1H), 6.89 (t, $J = 7.5$ Hz, 1H), 6.74 (d, $J = 7.8$ Hz, 1H), 4.33 (s, 1H), 4.29 (s, 1H), 4.23 (dd, $J = 9.9$, 4.2 Hz, 1H), 4.15–4.11 (m, 5H), 2.35–2.22 (m, 1H), 1.81–1.66 (m, 1H), 0.96 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 144.3, 132.7, 129.6, 127.8, 127.7, 126.2, 94.9, 75.3, 72.2, 68.2, 66.7, 45.5, 44.8, 30.1, 12.4; MS (EI, 70 eV) *m*/*z* (%): 510 (M^++1, 15), 509 (M^+, 3), 508 (M^+−1, 100), 217 (4), 215 (4), 152 (5); CHN calcd for $C_{19}H_{18}BrFeI$: C, 44.83; H, 3.56; Br, 15.70; I, 24.93. Observed: C, 45.01; H, 3.38; Br, 16.39; I, 25.08.

4.5.4. (S_{Fc})-1-Iodo-2-[3-(*S*)-(*o*-bromophenyl)propyl]ferrocene, 16a. Prepared according to the procedure described above from (S_{Fc})-1-iodo-2-[3-(*R*)-(*N*,*N*-dimethylamino)propyl]ferrocene **9a** (217 mg, 0.6 mmol) with *o*-bromoiodobenzene (0.10 mL, 0.8 mmol, 1.4 equiv), *i*-PrMgCl (0.43 mL, 0.8 mmol, 1.95 M solution in THF, 1.5 equiv), $ZnBr_2$ (0.57 mL, 1.0 mmol, 1.72 M solution in THF, 1.8 equiv), and acetyl chloride (0.05 mL, 0.7 mmol, 1.3 equiv) in THF (8 mL). The crude product was purified by column chromatography (*n*-pentane/CH_2Cl_2 20:1), recrystallized from Et_2O and afforded **16a** as an orange solid (196 mg, 0.4 mmol, 71%, dr >99:<1); mp 101.5–102 °C; $[\alpha]_D = -118.4$ (*c* 0.44, $CHCl_3$); IR (KBr): *v* 3436 (br, vs), 3092 (w), 2957 (m), 2927 (m), 1636 (br, m), 1564 (w), 1467 (m), 1106 (m), 1022 (m); ^{1}H NMR ($CDCl_3$): δ 7.43 (dd, $J = 8.1$, 1.2 Hz, 1H), 7.02 (td, $J = 7.6$, 1.3 Hz, 1H), 6.92–6.86 (m, 1H), 6.74 (dd, $J = 7.7$, 1.7 Hz, 1H), 4.33 (dd, $J = 1.2$, 2.4 Hz, 1H), 4.30–4.29 (m, 1H), 4.23 (dd, $J = 10.1$, 4.4 Hz, 1H), 4.15–4.13 (m, 1H), 4.13–4.10 (m, 5H), 2.35–2.22 (m, 1H), 1.81–1.66 (m, 1H), 0.96 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 144.3, 132.7, 129.6, 127.9, 127.7, 126.2, 94.9, 75.3, 72.2, 68.2, 66.7, 45.5, 44.8, 30.1, 12.4; MS (EI, 70 eV) *m*/*z* (%): 511 (M^++2, 20), 510 (M^++1, 90), 509 (M^+, 22), 508 (100), 481 (10), 479 (11), 273 (11), 217 (48), 216 (21), 215 (37), 202 (46), 180 (10), 179 (14), 178 (12), 166 (17), 165 (40), 153 (14), 152 (61), 151 (14), 121 (16); CHN calcd for $C_{19}H_{18}BrFeI$: C, 44.83; H, 3.56; Br, 15.70; I, 24.93. Observed: C, 44.79; H, 3.32; Br, 15.48; I, 24.91.

4.5.5. (S_{Fc})-1-Iodo-2-[3-(*S*)-(*o*-bromophenyl)ethyl]ferrocene, 16b. Prepared according to the procedure described above from (S_{Fc})-1-iodo-2-[3-(*R*)-(*N*,*N*-dimethylamino)ethyl]ferrocene **9b** (1.87 g, 4.9 mmol) with *o*-bromoiodobenzene (0.92 mL, 7.3 mmol, 1.5 equiv), *i*-PrMgCl (3.9 mL, 7.6 mmol, 1.95 M solution in THF, 1.55 equiv), $ZnBr_2$ (5.1 mL, 8.8 mmol, 1.72 M solution in

THF, 1.8 equiv), and acetyl chloride (0.51 mL, 5.86 mmol, 1.2 equiv) in THF (60 mL). The crude product was purified by column chromatography (*n*-pentane/CH_2Cl_2 20:1), recrystallized from Et_2O and afforded **16b** as an orange solid (2.41 g, 4.9 mmol, 99%, dr >99:<1); mp 103–104 °C; $[\alpha]_D = -52.1$ (*c* 1.65, $CHCl_3$); IR (KBr): *v* 3436 (br, m), 2967 (m), 1628 (br, w), 1468 (m), 1458 (m), 1373 (w), 1251 (w), 1240 (w), 1106 (m), 1022 (s); ^{1}H NMR ($CDCl_3$): δ 7.43 (dd, $J = 8.0$, 1.4 Hz, 1H), 7.00 (td, $J = 7.6$, 3.9 Hz, 1H), 6.90 (td, $J = 7.6$, 1.7 Hz, 1H), 6.65 (dd, $J = 7.7$, 1.7 Hz, 1H), 4.39–4.32 (m, 3H), 4.19 (t, $J = 2.4$ Hz, 1H), 4.12 (s, 5H), 1.51 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 144.5, 131.4, 127.3, 126.5, 126.4, 123.0, 92.7, 74.0, 70.7, 66.8, 65.3, 43.9, 38.8, 19.6; MS (EI, 70 eV) *m*/*z* (%): 497 (M^++2, 20), 496 (M^++1, 88), 495 (M^+, 21), 494 (100), 288 (15), 273 (12), 217 (36), 216 (17), 215 (29), 202 (28), 167 (53), 166 (56), 165 (83), 153 (13), 152 (69), 151 (13), 121 (25), 115 (11), 58 (13), 56 (12), 43 (37); HRMS calcd for $C_{18}H_{16}$BrFeI: 493.8829. Observed: 493.8860.

4.6. Synthesis of the diphosphines 17a,b and 18a,b

4.6.1. (R_{Fc})-1-Diphenylphosphino-2-[3-(*R*)-(*o*-diphenylphosphino)phenylmethyl]ferrocene, 17a. (R_{Fc})-1-Bromo-2-[3-(*R*)-(*o*-bromophenyl)phenylmethyl]ferrocene **15a** (254 mg, 0.5 mmol) was dissolved in THF (4 mL) and cooled to −78 °C. *n*-BuLi (0.73 mL, 1.1 mmol, 1.5 M solution in hexane, 2.2 equiv) was added and the resulting solution stirred 15 min at −78 °C. Chlorodiphenylphosphine (0.21 mL, 1.2 mmol, 2.4 equiv) was added and the reaction mixture stirred overnight and warmed up to rt. Water was added and the organic phase washed with water and brine and dried over $MgSO_4$. The crude product was purified by column chromatography (*n*-pentane/Et_2O 20:1), recrystallized from Et_2O and afforded the diphenylphosphine **17a** as an orange solid (155 mg, 0.2 mmol, 44%, dr >99:<1); mp 170 °C; $[\alpha]_D = +26.4$ (*c* 0.58, $CHCl_3$); IR (KBr): *v* 3436 (br, vs), 3054 (w), 1630 (br, m), 1480 (w), 1436 (m), 1159 (w), 1108 (w); ^{1} H NMR ($CDCl_3$): δ 7.55–7.54 (m, 2H), 7.29–7.12 (m, 10H), 6.99–6.77 (m, 13H), 6.69–6.61 (m, 3H), 6.51–6.47 (m, 1H), 4.28 (s, 2H), 3.88 (s, 1H), 3.77 (s, 5H); ^{13}C NMR ($CDCl_3$): δ 150.0 (d, $J = 26.0$ Hz), 142.4, 139.6 (d, $J = 10.0$ Hz), 139.1 (d, $J = 11.2$ Hz), 138.7 (d, $J = 9.1$ Hz), 136.4–135.2 (m), 133.9–133.4 (m), 132.6 (d, $J = 18.4$ Hz), 130.7, 129.3–126.0 (m), 99.9–99.6 (m), 75.3 (d, $J = 9.7$ Hz), 72.1 (d, $J = 4.9$ Hz), 71.7 (d, $J = 2.9$ Hz), 70.1, 69.5; ^{31}P NMR ($CDCl_3$): δ −17.1 (d, $J = 18.7$ Hz), −23.1 (d, $J = 19.0$ Hz); MS (EI, 70 eV) *m*/*z* (%): 721 (M^++1, 10), 720 (M^+, 19), 655 (26), 654 (44), 653 (13), 537 (10), 536 (46), 535 (100), 469 (12), 468 (10), 458 (16), 414 (13), 413 (27), 337 (24), 259 (16), 257 (15), 183 (24), 120 (11); HRMS calcd for $C_{47}H_{38}FeP_2$: 720.1798. Observed: 720.1781.

4.6.2. (R_{Fc})-1-Diphenylphosphino-2-[3-(*R*)-(*o*-diphenylphosphinophenyl)propyl]ferrocene, 17b. Prepared according to the procedure described above from (R_{Fc})-1-iodo-2-[3-(*R*)-(*o*-bromophenyl)propyl]ferrocene **15c** (198 mg, 0.4 mmol) with *t*-BuLi (1.0 mL, 1.6 mmol, 1.6 M solution in pentane, 4.2 equiv) and chlorodiphenylphosphine (0.16 mL, 0.9 mmol, 2.3 equiv) in THF (5 mL). The crude product was purified by column chromatography (*n*-pentane/Et_2O 20:1), recrystallized from Et_2O and afforded the diphenylphosphine **17b** as an orange solid (91 mg, 0.1 mmol, 36%, dr >99:<1); mp 150–151 °C; $[\alpha]_D = +313.1$ (*c* 0.19, $CHCl_3$); IR (KBr): *v* 3436 (br, vs), 2927 (w), 1629 (br, m), 1479 (w), 1434 (w); ^{1}H NMR ($CDCl_3$): δ 7.54–7.48 (m, 2H), 7.27–7.20 (m, 8H), 7.09–6.95 (m, 7H), 6.88–6.70 (m, 5H), 6.51–6.45 (m, 2H), 6.26 (br s, 1H), 4.48 (br s, 1H), 4.23 (s, 1H), 3.90 (s, 5H), 3.78 (br s, 1H), 2.32–2.34 (m, 1H), 1.79–1.76 (m, 1H), 0.53–0.49 (m, 3H); ^{13}C NMR ($CDCl_3$): δ 150.3 (d, $J = 27.6$ Hz), 139.2 (d, $J = 8.3$ Hz), 138.3 (d, $J = 12.3$ Hz), 138.0–137.8 (m), 136.9 (d, $J = 41.7$ Hz), 134.7 (d, $J = 30.0$ Hz), 134.0, 133.1 (d, $J = 19.9$ Hz), 132.2 (d, $J = 17.5$ Hz), 127.9, 127.2 (d, $J = 3.7$ Hz), 127.1, 126.8 (d, $J = 7.1$ Hz), 126.5, 126.1 (d, $J = 5.3$ Hz), 125.5, 124.5, 100.3 (d, $J = 30.0$ Hz), 73.7 (d, $J = 12.4$ Hz), 70.3 (d, $J = 4.3$ Hz), 69.0 (d, $J = 3.2$ Hz), 68.7, 67.9, 41.2–40.8 (m), 29.5, 11.7; ^{31}P NMR ($CDCl_3$): δ −19.2 (d, $J = 37.0$ Hz), −21.7 (d, $J = 36.6$ Hz); MS (EI, 70 eV) *m*/*z* (%): 672 (M^+, 20), 488 (38), 487 (100), 410 (16), 337 (18), 183 (19); HRMS calcd for $C_{43}H_{38}FeP_2$: 672.1798. Observed: 672.1788.

4.6.3. (S_{Fc})-1-Diphenylphosphino-2-[3-(*S*)-(*o*-diphenylphosphinophenyl)propyl]ferrocene, 18a, *ent*-17a. Prepared according to the procedure described above from (S_{Fc})-1-iodo-2-[3-(*S*)-(*o*-bromophenyl)propyl]ferrocene **16a** (169 mg, 0.3 mmol) with *t*-BuLi (0.93 mL, 1.4 mmol, 1.5 M solution in pentane, 4.2 equiv) and chlorodiphenylphosphine (0.14 mL, 0.8 mmol, 2.3 equiv) in THF (3 mL). The crude product was purified by column chromatography (*n*-pentane/Et_2O 20:1), recrystallized from Et_2O and afforded the diphenylphosphine **18a** as an orange solid (89 mg, 0.1 mmol, 40%, dr >99:<1); mp 93–94 °C; $[\alpha]_D = -314.7$ (*c* 0.27, $CHCl_3$); IR (KBr): *v* 3436 (br, m), 3051 (m), 2962 (m), 2929 (w), 2872 (w), 1629 (br, w), 1586 (w), 1479 (m), 1465 (m), 1434 (m), 1164 (m), 1107 (m); ^{1}H NMR ($CDCl_3$): δ 7.54–7.49 (m, 2H), 7.29–7.11 (m, 8H), 7.11–6.95 (m, 7H), 6.87–6.72 (m, 5H), 6.51–6.46 (m, 2H), 5.27 (br s, 1H), 4.49 (br s, 1H), 4.25 (s, 1H), 3.91 (s, 5H), 3.79 (br s, 1H), 2.30–2.24 (m, 1H), 1.77 (br s, 1H), 0.51 (t, $J = 6.5$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 139.3 (d, $J = 10.9$ Hz), 138.4 (d, $J = 12.6$ Hz), 137.9 (d, $J = 10.6$ Hz), 136.9 (d, $J = 10.2$ Hz), 134.8 (d, $J = 22.0$ Hz), 134.0 (d, $J = 2.6$ Hz), 133.2 (d, $J = 20.4$ Hz), 132.3 (d, $J = 17.3$ Hz), 130.6 (d, $J = 16.8$ Hz), 127.9–127.1 (m), 126.8 (d, $J = 7.6$ Hz), 126.5–125.4 (m), 124.5, 100.5–100.1 (m), 73.8 (d, $J = 12.7$ Hz), 70.3 (d, $J = 4.7$ Hz), 69.0–68.7 (m), 67.9, 41.1–40.8 (m), 29.6–29.5 (m), 11.7; ^{31}P NMR ($CDCl_3$): δ 19.2 (d, $J = 37.0$ Hz), −21.7 (d, $J = 36.7$ Hz); MS (EI, 70 eV) *m*/*z* (%): 673 (M^+, 11), 489 (43), 488 (100), 458 (10), 421 (11), 337 (21), 183 (17); HRMS calcd for $C_{43}H_{38}FeP_2$: 673.1876 (M^++H). Observed: 673.1887 (M^++H).

4.6.4. (S_{Fc})-1-Diphenylphosphino-2-[3-(*S*)-(*o*-diphenylphosphinophenyl)ethyl]ferrocene, 18b. Prepared accord-

ing to the procedure described above from (S_{Fc})-1-iodo-2-[3-(*S*)-(*o*-bromophenyl)ethyl]ferrocene **16b** with *t*-BuLi (1.4 mL, 2.3 mmol, 1.61 M solution in pentane, 4.2 equiv) and chlorodiphenylphosphine (0.22 mL, 1.3 mmol, 2.3 equiv) in THF (5 mL). The crude product was purified by column chromatography (*n*-pentane/Et_2O 20:1), recrystallized from Et_2O and afforded the diphenylphosphine **18b** as an orange solid (145 mg, 0.2 mmol, 41%, dr >99:<1); mp 194–195 °C; $[\alpha]_D = -209.4$ (*c* 0.57, $CHCl_3$); IR (KBr): *v* 3436 (br, m), 3052 (w), 2962 (w), 2928 (w), 1635 (br, w), 1586 (w), 1479 (m), 1434 (m), 1240 (w), 1164 (w), 1107 (w); ^{1}H NMR ($CDCl_3$): δ 7.50–7.44 (m, 2H), 7.28–7.24 (m, 8H), 7.17–7.07 (m, 3H), 6.96–6.53 (m, 11H), 5.46–5.35 (m, 1H), 4.57–4.56 (m, 1H), 4.27 (t, $J = 2.4$ Hz, 1H), 3.97–3.96 (m, 5H), 3.73–3.72 (m, 1H), 1.26 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 151.3 (d, $J = 26.2$ Hz), 138.6 (d, $J = 10.6$ Hz), 137.6–137.3 (m), 136.5 (d, $J = 11.4$ Hz), 134.6 (d, $J = 21.4$ Hz), 133.3–133.0 (m), 132.3 (d, $J = 18.5$ Hz), 130.8 (d, $J = 17.6$ Hz), 127.9 (d, $J = 3.8$ Hz), 127.5–127.3 (m), 127.0–126.7 (m), 126.3 (d, $J = 4.9$ Hz), 126.1 (d, $J = 5.7$ Hz), 125.5, 124.7, 99.5 (dd, $J = 27.1$, 1.8 Hz), 74.1 (d, $J = 11.1$ Hz), 70.6 (d, $J = 4.8$ Hz), 68.7–68.6 (m), 67.7, 34.9 (dd, $J = 28.2$, 8.3 Hz), 22.1; ^{31}P NMR ($CDCl_3$): δ −18.6 (d, $J = 33.2$ Hz), −21.9 (d, $J = 33.5$ Hz); MS (EI, 70 eV) *m*/*z* (%): 674 (M^++O, 25), 660 (M^++1, 17), 659 (M^+, 69), 658 (49), 657 (21), 609 (12), 93 (13), 581 (23), 475 (12), 474 (44), 473 (100), 443 (12), 409 (14), 351 (26), 337 (17), 331 (19); HRMS calcd for $C_{42}H_{36}FeP_2$: 659.1720 (M^++H). Observed: 659.1736 (M^++H).

4.7. Asymmetric hydrogenation reactions

4.7.1. In situ rhodium catalyst preparation. The rhodium complex (0.01 mmol) and the ligand (1.05–1.1 equiv) are placed in a dried Schlenk tube under an argon atmosphere and the indicated solvent (4 mL) is added. The mixture is then stirred for 10–20 min at rt (see Tables 4–6).

4.7.2. In situ ruthenium catalyst preparation.[22] [Ru(cod)(2-metallyl)$_2$] (0.01 mmol) and the ligand (1.05–1.1 equiv) are placed in a dried Schlenk tube under an argon atmosphere and acetone (2 mL) is added. To this solution is added dropwise a HBr solution (0.1 mL, 0.3 M solution in MeOH). After 10–20 min of stirring, the solvent is removed under vacuo before adding the indicated solvent (4 mL) (see Tables 1–3).

4.7.3. Hydrogenation in Schlenk tubes. The in situ formed catalyst solution is added to the substrate under an argon atmosphere. The Schlenk tube is then shortly connected to vacuo and purged with hydrogen from a balloon.

4.7.4. Hydrogenation in autoclaves. The substrate is placed in a glass tube equipped with a stirring bar in the autoclave. After three cycles of vacuo-argon, the in situ prepared catalyst solution is added to the substrate via a syringe under an argon flow. Volatile substrates are added directly to the catalyst solution before introduction in the autoclave under argon. The autoclave is then purged three times with hydrogen, heated to the desired temperature and placed under the indicated hydrogen pressure.

4.8. Hydrogenation products. Enantiomeric excess determination

The substrates used in hydrogenation are commercially available or were prepared according to literature procedures. Most of the hydrogenation products have been previously described.

4.8.1. Ethyl 3-hydroxybutanoate 22a.[23] HPLC (OD, 20 °C, 95% *n*-heptane, 5% isopropanol, 0.9 mL/min): retention time (min) 7.3 (*R*), 10.2 (*S*).

4.8.2. Ethyl 3-hydroxy-3-phenyl-propanoate 22b.[23] HPLC (OD, 30 °C, 95% *n*-heptane, 5% isopropanol, 0.9 mL/min): retention time (min) 11.3 (*S*), 15.9 (*R*).

4.8.3. Ethyl 2-hydroxycyclopentane carboxylate 24.[23] HPLC (OD, 40 °C, 98% *n*-heptane, 2% isopropanol, 0.32 mL/min): retention time (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*).

4.8.4. 1,3-Diphenyl-1,3-propanediol 26.[23] HPLC (OD, 30 °C, 90% *n*-heptane, 10% isopropanol, 0.6 mL/min): retention time (min) 16.5 (*S*,*S*), 19.2 (*R*,*R*), 23.3 (*S*,*R*).

4.8.5. *N*-Acetylphenylalanine methyl ester 28.[2d] GC (Chiralsil-L-Val) 140 °C isotherm: retention time (min) 10.1 (*R*), 11.7 (*S*).

4.8.6. Dimethyl 2-methylsuccinate 30.[2e] HPLC (OJ, 20 °C, 95% *n*-heptane, 5% isopropanol, 0.6 mL/min): retention time (min) 9.9 (*R*), 15.2 (*S*).

4.8.7. 1-Phenyl-1-(2-benzoylhydrazino)ethane 32.[17b] HPLC (OJ, 30 °C, 90% *n*-heptane, 10% isopropanol, 0,6 mL/min): retention time (min) 14.3 (*R*), 19.9 (*S*).

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