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Preparation of New, Optically Active 1,2-Ferrocenyldiamine Ligands and Their Application to Ruthenium-Catalyzed Asymmetric Transfer Hydrogenation of Ketones

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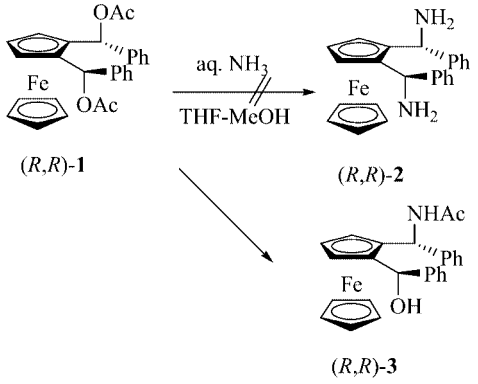
The treatment of (*R*,*R*)-1,2-bis(1-acetoxy-1-phenylmethyl)-ferrocene (**1**) with azidotrimethylsilane in CH_2Cl_2 in the presence of a catalytic amount of a Lewis acid such as $Cu(OTf)_2$ or $Sc(OTf)_3$, at –40 °C for 24 h, gives a mixture of two diastereomeric ferrocenyl diazides **4** and **5** in an 80:20 ratio. The major isomer (*R*,*R*)-**4** is formed with retention of configuration at both benzylic chiral centers whereas the minor isomer *meso*-(*R*,*S*)-**5** is formed with inversion of configuration at one of the two chiral centers. After a shorter reaction time (12 h), the (*R*,*R*)-ferrocenylazido acetate **6** was isolated as a single diastereomer, which gave **4** and **5** under the same conditions with almost the same ratio as with the longer reaction time. These results show that the first step of the reaction is the substitution, with retention of configuration, of the *exo* acetate of **1** by means of an iron-assisted ionization, i.e., neighboring-group participation, then the *endo* acetate is replaced by the azide ion with retention or inversion of configuration to give **4** or **5**, respectively. The optically active complex **4** could be converted into the corresponding ferrocenyldiamine **2** by reduction with $LiAlH_4$, and its ditosylamide **8a** and diacetamide **8b** were isolated as stable compounds. The ferrocenyldiamine and both diamides were used as ligands in the ruthenium-catalyzed asymmetric transfer hydrogenation of aryl ketones, and the complex with **2** gave 1-arylethanols in good yields with up to 75% *ee*.

Introduction

Chiral ferrocenes and half-sandwich metallocenes are of interest especially in asymmetric catalysis as chiral ligands.[1] Ferrocenylphosphanes, for example, have become popular and effective ligands for transition metal complexes that catalyze the asymmetric reaction, often with a high enantioselectivity. On the other hand, ferrocenyl alcohols and amines have rarely been employed as ligands in asymmetric reactions even though many chiral alcohols and amines are known to be good ligands in chiral catalysis.[2] Ikeda et al. have attempted to use a C_2-symmetrical 1,1′-ferrocenyldiol as a ligand for the titanium-catalyzed hydrosilylation of alkenes, although they isolated only the racemic product.[3] We have also succeeded in the scandium-catalyzed asymmetric Diels–Alder reaction using a chiral 1,2-ferrocenyldiol ligand with a high enantioselectivity.[4] The success of this new ferrocenyldiol as a chiral ligand for asymmetric synthesis prompted us to prepare the corresponding 1,2-ferrocenyldiamine ligand. We previously tried to prepare the ferrocenyldiamine **2** by the direct displacement of the (*R*,*R*)-ferrocenyl diacetate **1** by aqueous ammonia; however, the regioselective and stereospecific displacement of the *exo* acetate produced the ferrocenyl acetamido alcohol **3** as the sole product (Scheme 1).[5] Here we report the reaction of diacetate (*R*,*R*)-**1** with azide and subsequent reduction of the intermediate diazido derivative **4** to obtain the desired diamine **2**. Moreover, we report on the use of **2** as a ligand for the ruthenium-catalyzed transfer hydrogenation of ketones.



(*R*,*R*)-**1** (*R*,*R*)-**2** (*R*,*R*)-**3**

Scheme 1.

Results and Discussion

We postulated that the retentive substitution of both acetoxy groups in (*R*,*R*)-**1** by the azide ion could be carried out

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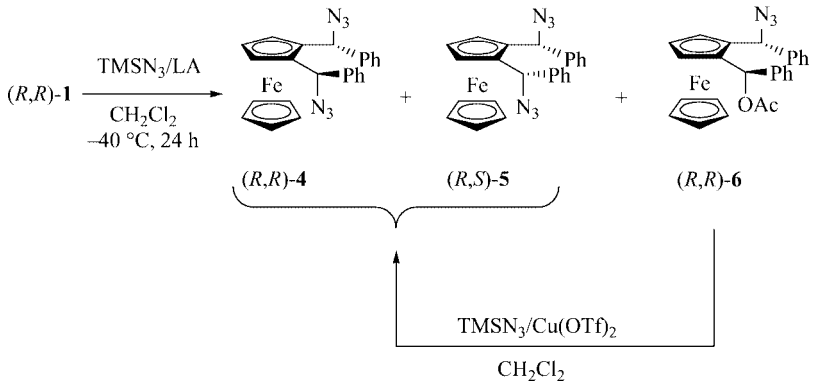


Scheme 2.

with azidotrimethylsilane ($TMSN_3$) (Scheme 2).[6] However, the expected diazide was not obtained and almost all of the starting complex **1** was recovered after 24 h at room temperature. We then carried out the reaction in the presence of a catalytic amount (10 mol-%) of a Lewis acid at –40 °C for 24 h and using three equivalents of $TMSN_3$. The obtained results are reported in Table 1. $Cu(OTf)_2$ (entry 2) promoted the reaction and the starting **1** was almost totally consumed after 24 h; the acetoxy groups completely disappeared in the ^1H NMR spectrum. The introduction of the azide group to the ferrocenyl compound was confirmed by the IR spectrum in which the azide group is observed at 2200 cm^{-1}. The ^1H NMR spectrum shows the presence of the two diastereomeric diazides. Two cyclopentadienyl signals are observed, with a major signal at δ = 4.14 ppm and a minor one at δ = 3.78 ppm. Separation of the diastereomers by preparative TLC (SiO_2) gave each diastereomer in a pure form: the major product was identified as the (*R*,*R*)-diazide **4** based on its ^1H NMR spectrum, which has two benzylic signals at δ = 5.48 and 5.75 ppm as singlets, and the minor one was identified as *meso*-**5**, which has only one benzylic signal at δ = 5.67 ppm as a singlet. The optical rotation of each compound supported its identification: the diazide **4** is optically active whereas **5** is optically inactive. We further confirmed the structure of **4** by an X-ray crystallographic analysis (vide infra), which confirmed that both acetates had been replaced by an azide group with retention of configuration in the production of **4**.

When the reaction was quenched after a shorter reaction time, i.e. after 12 h, the (*R*,*R*)-ferrocenylazido acetate **6** was obtained as the major product (Table 1, entry 3). Its structure was confirmed by comparing the ^1H NMR spectrum of the acetamido alcohol, which was derived from **6**, with the ^1H NMR spectrum of an authentic sample of **3** obtained by aminolysis of **1**.[5] The azido acetate **6** could be converted into **4** and **5** upon treatment with $Cu(OTf)_2$ under the same conditions (isomer ratio of **4/5** = 80:20), showing that **6** is an intermediate of the reaction.

The distribution of the products depends on the Lewis acid catalyst (Table 1). The use of $Cu(OTf)_2$, $In(OTf)_3$, and $Sc(OTf)_3$ afforded the desired optically active **4** as the main product (entries 2,9, and 10), whereas the intermediate **6** was the major product when $Mg(ClO_4)_2$ and $Y(OTf)_3$ were used as the Lewis acid catalyst (entries 5 and 11). $Yb(OTf)_2$ gave almost a 1:1 mixture of **4** and the unwanted *meso*-**5** (entry 12).

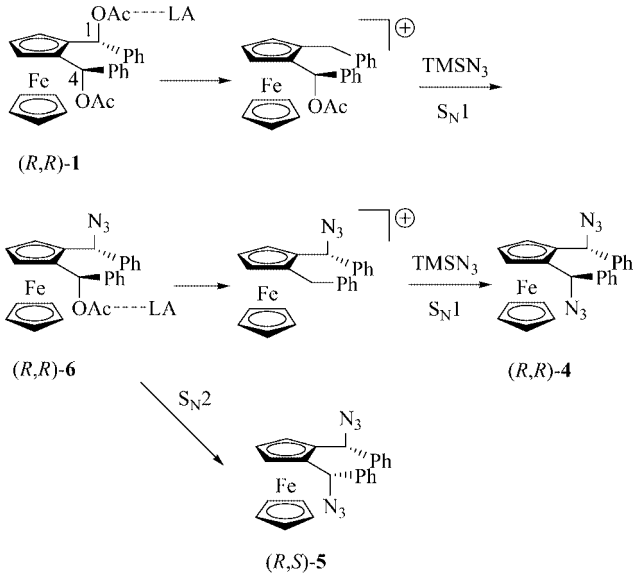
Table 1. Reaction of (*R*,*R*)-ferrocenyl diacetate **1** with $TMSN_3$.[a]

Entry	Lewis acid	Conversion [%]	Product distribution[b] **4/5/6**
1	none	0	–
2	$Cu(OTf)_2$	95	80:20:0
3[c]	$Cu(OTf)_2$	95	26:4:70
4	$CuOTf{\cdot}C_6H_6$	95	77:23:0
5	$Mg(ClO_4)_2$	95	1:4:95
6	$Al(O\textit{i}Pr)_3$	<1	–
7	$Ti(O\textit{i}Pr)_4$	2	–
8	$BF_3{\cdot}Et_2O$	95	70:30:0
9	$In(OTf)_3$	94	77:23:0
10	$Sc(OTf)_3$	96	80:20:0
11[d]	$Y(OTf)_3$	96	0:0:100
12	$Yb(OTf)_3$	95	58:42:0

[a] Reaction conditions: **1** (0.1 mmol), $TMSN_3$ (0.3 mmol), Lewis acid (0.01 mmol), CH_2Cl_2 (10 mL) at –40 °C for 24 h. [b] The product distribution was determined by ^1H NMR spectroscopy. [c] The reaction was quenched after 12 h. [d] Reaction time of 48 h.

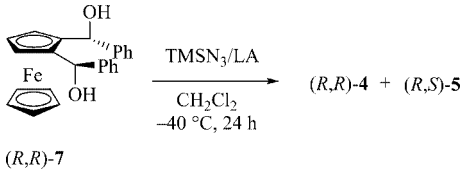
A plausible reaction mechanism is illustrated in Scheme 3. The acetoxy group of C-1 is first displaced by $TMSN_3$ to give **6**, with retention of the configuration, by an S_N1 mechanism similar to the previous aminolysis of the diacetate **1**.[5] As discussed in a preceding paper, one of the acetoxy groups at C-1 (*exo* to the ferrocenyl group) is suitably aligned for the iron-assisted ionization (neighboring-group participation) to proceed efficiently. The second acetoxy group at C-4 (*endo* to the ferrocenyl group) is not suitably aligned, but can undergo a conformational change to adopt the appropriate orientation for ionization to occur in the presence of $Cu(OTf)_2$. The retentive replacement by a second azide ion via the carbocation (S_N1 mechanism) gives the major product **4** with the participation of the iron group, while the backside attack of the azide ion on the *endo* acetate (S_N2 inversion mechanism) might produce the minor product **5**.[7]

As the optically active 1,2-ferrocenyldiol **7** is a good ligand for the $Sc(OTf)_3$-catalyzed asymmetric Diels–Alder reaction,[4] the hydroxy groups may correctly coordinate to



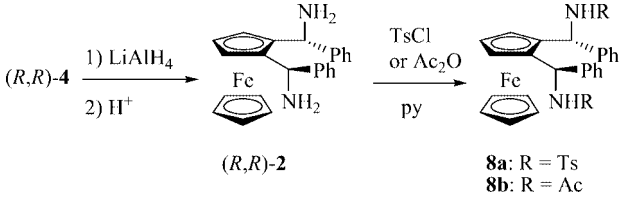
Scheme 3.

the scandium atom. If both hydroxy groups were to be adequately activated by scandium due to the coordination, the replacement by the azide ion would be smoother than the acetoxy groups. However, the reaction of the diol with $TMSN_3$ under the same conditions resulted in the predominant formation of *meso*-**5**. The use of a stoichiometric amount of $Cu(OTf)_2$ in place of $Sc(OTf)_3$ gave an almost 1:1 mixture of **4** and **5** (Scheme 4).



Scheme 4.

The desired 1,2-ferrocenyldiamine **2** could be quantitatively obtained by reduction of **4** with $LiAlH_4$; its ditosylamide **8a** and diacetamide **8b** were isolated as stable forms and could be kept in air at room temperature for a long time (Scheme 5). The X-ray crystallographic analysis of the structure of **8a** confirmed its stereochemistry to be (*R*,*R*) (Figure 1).[8]



Scheme 5.

We applied **2**, **4**, and **8a**,**b** as ligands for the ruthenium-catalyzed asymmetric transfer hydrogenation of ketones **9**.[9] The preliminary results are summarized in Table 2. The reaction was carried out with 0.5 mol-% of $[Ru(p\text{-cymene})_2]_2$ and 2 mol-% of **2**, **4**, or **8a**,**b** in *i*PrOH (hydrogen source) at

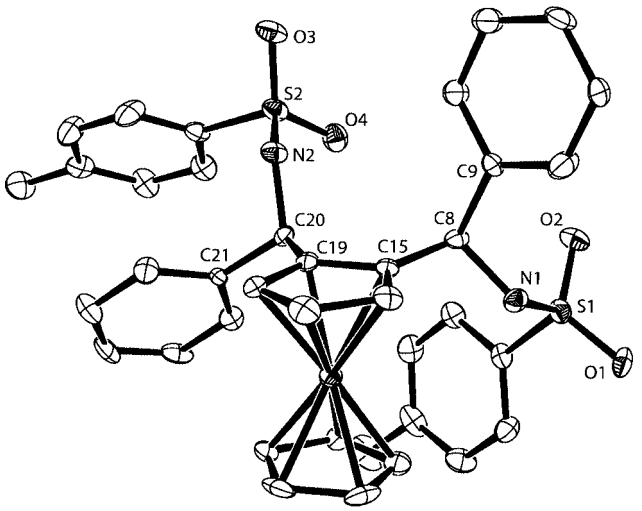
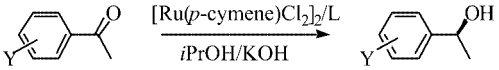


Figure 1. Molecular structure of **8a** (ORTEP plot). Selected bond lengths [Å]: C(8)–C(15) 1.51, N(1)–C(8) 1.48, C(19)–C(20) 1.49, N(2)–C(20) 1.49. Selected torsion angles [°]: N(1)–C(8)–C(15)–C(19)–129.6, C(9)–C(8)–C(15)–C(19) 107.6, C(15)–C(19)–C(20)–N(2) –89.3, C(15)–C(19)–C(20)–C(21) 143.1.

room temperature for 4 h. The reaction with acetophenone and **2** proceeded smoothly to give (*S*)-1-phenylethanol (**10**; Y = H) in good yield with 75% *ee* (entry 1). Performing the reaction at 0 °C for 3 h did not improve the enantioselectivity (entry 2). The *ee* value obtained in the reduction of acetophenone was higher than that of Knochel's chiral 1,1′-ferrocenyldiamine ligand (52% *ee*).[2] The reduction of acetophenone in the presence of **4**, **8a**, and **8b** did not occur (entries 3–5). Next we examined the reduction of various ketones using the ruthenium complex and **2**. *ortho*- and

Table 2. Asymmetric transfer hydrogenation of ketones in the presence of $[Ru(p\text{-cymene})Cl_2]_2$ and our ferrocenyldiamine and diamides.[a]



9 **10**

Entry	Ketone **9**	L	Yield [%][b]	*ee* [%][b] (config.)
1	Y = H	**2**	98	75 (*S*)
2[c]	Y = H	**2**	88	75 (*S*)
3[d]	Y = H	**2**	86	66 (*S*)
3[e]	Y = H	**8a**	0	–
4[e]	Y = H	**8b**	0	–
5[e]	Y = H	**4**	0	–
6[e]	Y = *o*-CH_3	**2**	86	75 (*S*)
7[e]	Y = *o*-Cl	**2**	97	33 (*S*)
8	Y = *p*-F	**2**	96	60 (*S*)
9	Y = *p*-NO_2	**2**	96	14 (*S*)
10	1-acetonaphthone	**2**	96	63 (*R*)
11	2-acetonaphthone	**2**	95	61 (*R*)

[a] Reaction conditions: ketone (1.2 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (0.005 mmol, 0.5 mol-%), **2** (0.02 mmol, 2 mol-%), KOH (0.05 mmol, 5 mol-%), *i*PrOH (23 mL) at 25 °C for 4 h. [b] Yield and *ee* (%) were determined by GC and/or HPLC. [c] At 0 °C for 4 h. [d] 1.2 mol-% of **2** was used. [e] At 25 °C for 24 h.

para-Substituted acetophenones and 1- and 2-acetonaphthones were similarly reduced to the corresponding optically active 1-arylethanols with 14–75% *ee*. The *ee* value in the reduction with *o*-methylacetophenone was as high as that with acetophenone (entry 6), and the reduction with *p*-fluoroacetophenone and 1- and 2-acetonaphthone gave moderate *ee* values (entries 8, 10, and 11). These results show that **2** is a promising chiral ligand for asymmetric synthesis. A detailed study of the design and application of this 1,2-ferrocenyldiamine as a ligand for metal-catalyzed asymmetric syntheses is now in progress.

Experimental Section

General: The ^{1}H and ^{13}C NMR spectra were recorded with a Varian Mercury 300 (300 MHz) spectrometer as solutions in $CDCl_3$. The chemical shifts are reported in δ units downfield from the internal reference ($SiMe_4$). The IR spectra were obtained with a JASCO Herschel FT/IR-230A spectrometer, and the optical rotations were determined with a JASCO DIP-370 instrument. The HPLC analyses were carried out with a Hitachi L-7100 apparatus equipped with a UV detector and using chiral columns (Chiralcel OD-H, AS-H, OB). The GC/MS analyses were carried out on a Hewlett–Packard 5980/5972 instrument equipped with a chiral capillary column (Chiraldex GT-A) using helium as carrier gas. Column chromatography was performed using a Yamazen YFLC-254 and a Michael Miller column equipped with a UV detector using Merck Silica Gel 60. Preparative TLC was conducted using a 20×20 cm^2 glass sheet coated with a 2-mm-thick layer of Merck Kieselgel 60 PF_{254}.

Crystallography: The diffraction data were collected at room temperature using a Rigaku AFC7R four-circle automated diffractometer with graphite-monochromated Mo-K_α radiation and the ω–2θ scan technique to a maximum 2θ value of 50° or 55°. The structure solution and refinements were carried out using the CrystalStructure crystallographic software packages.[10] The positions of the non-hydrogen atoms were determined by Patterson methods (DIRDIF PATTY)[11] and expanded using Fourier techniques (DIRDIF94 or -99).[12] The carbon atoms of the solvate CH_2Cl_2 molecules were refined isotropically.

CCDC-274906 (for **8a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

Reaction of (*R*,*R*)-1,2-Bis(1-acetoxy-1-phenylmethyl)ferrocene (1) with $TMSN_3$ in the Presence of a Lewis Acid. Typical Procedure:[13] A 50-mL Schlenk tube containing a magnetic stirring bar was charged with **1** (50 mg, 0.1 mmol), anhydrous $Cu(OTf)_2$ (4 mg, 0.01 mmol, 10 mol-%), and dry CH_2Cl_2 (10 mL) under a slight pressure of nitrogen. $TMSN_3$ (35 mg, 0.30 mmol) was then added from a syringe, with magnetic stirring, at –40 °C and the resulting mixture was stirred at the same temperature for 24 h. The reaction was subsequently quenched with water and the resulting solution was extracted with CH_2Cl_2 (3×15 mL). The combined extracts were washed (brine), dried ($MgSO_4$), and the solvent was removed on a rotary evaporator to leave a yellow oil. ^{1}H NMR analysis of the crude product revealed the presence of two isomers of the 1,2-ferrocenyldiazides, with **4** as the major product and **5** as the minor product. The isomer ratio was determined by ^{1}H NMR integration of the benzylic protons (**4/5** = 80:20). The crude product was subjected to column chromatography on silica gel (hexane/diethyl ether = 50:1 as eluent) to give pure (*R*,*R*)-1,2-bis(1-azido-1-phenylmethyl)ferrocene (**4**). Total yield of the mixture of **4** and **5**: 42 mg (0.095 mmol, 95%).

Major Isomer 4: Yellow oil. $[\alpha]_D^{25} = -60.3$ ($c = 0.524$, $CHCl_3$). IR (neat): $\tilde{\nu} = 2160$ cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 3.99$ (m, 1 H), 4.14 (s, 5 H), 4.20 (m, 1 H), 4.36 (m, 1 H), 5.48 (s, 1 H), 5.75 (s, 1 H), 7.2–7.3 (m, 10 H) ppm. ^{13}C NMR ($CDCl_3$): $\delta = 64.3$, 64.9, 67.1, 68.3, 68.7, 69.9, 85.3, 87.5, 127.2, 127.6, 128.0, 128.2, 128.3, 128.5, 138.8, 139.2 ppm. $C_{24}H_{20}FeN_6$ (448.30): calcd. C 64.30, H 4.50, N 18.75; found C 64.14, H 4.58, N 18.55.

Minor Isomer *meso*-(*R*,*S*)-5: $[\alpha]_D^{25} = 0$ ($c = 0.884$, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 3.78$ (s, 5 H), 3.99 (m, 1 H), 4.14 (m, 1 H), 4.36 (m, 1 H), 5.68 (s, 1 H), 7.20–7.50 (m, 10 H) ppm. ^{13}C NMR $\delta = 64.5$ 67.9, 68.8, 69.9, 86.8, 127.5, 128.2, 128.5, 139.6 ppm.

Preparation of (*R*,*R*,*S*$_p$)-[1-(1-Acetoxy-1-phenylmethyl)-2-(1-azido-1-phenylmethyl)]ferrocene (6): The title compound was obtained by the $Y(OTf)_3$-catalyzed reaction of **1** with $TMSN_3$ for 48 h. Yield: 44 mg (0.096 mmol, 96%). Yellow oil. $[\alpha]_D^{25} = -31.3$ ($c = 0.16$, $CHCl_3$). IR (neat): $\tilde{\nu} = 2095$, 1734 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 2.23$ (s, 3 H), 4.00 (s, 6 H), 4.21 (m, 1 H), 4.40 (m, 1 H), 5.48 (s, 1 H), 7.06 (s, 1 H), 7.2–7.4 (m, 10 H) ppm. ^{13}C NMR $\delta = 21.2$ 64.5, 67.4, 67.8, 68.3 69.7, 72.3, 85.5, 87.3, 127.4, 127.5, 127.6, 128.1, 128.3, 128.4, 139.3, 140.1, 169.7 ppm. $C_{26}H_{23}FeN_3O_2$ (465.32): calcd. C 67.11, H 4.98, N 9.03; found C 66.97, H 5.13, N 8.96.

Preparation of (*R*,*R*)-1,2-Bis(1-amino-1-phenylmethyl)ferrocene (2): A 50-mL Schlenk tube containing a magnetic stirring bar was charged with **4** (500 mg, 1.12 mmol) and dry diethyl ether (30 mL) under a slight pressure of nitrogen. $LiAlH_4$ (100 mg, 2.8 mmol) was then added in small portions with magnetic stirring at 0 °C. The resulting mixture was stirred at the same temperature for 20 min and then warmed to room temperature over a period of 4 h. The reaction was subsequently quenched with saturated Na_2SO_4 (0.5 mL), the resulting solution was stirred for 10 min, and then diethyl ether (3×20 mL) was added. The ethereal solution was dried (Na_2SO_4), filtered, and then the solvent was removed on a rotary evaporator to leave a brown oil. Crude yield: 420 mg (1.03 mmol, 92%). $[\alpha]_D^{25} = -139.7$ ($c = 0.58$, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.80$ (br. s, 4 H), 4.00 (s, 6 H), 4.13 (m, 1 H), 4.38 (m, 1 H), 4.94 (s, 1 H), 5.17 (s, 1 H), 7.2–7.5 (m, 10 H) ppm. ^{13}C NMR ($CDCl_3$): $\delta = 54.0$, 54.1, 65.8, 66.3. 67.6, 68.9, 91.6 ppm; aromatic signals are not listed here. Compound **3** is not partucularly stable and decomposed into a black oil within a few days, so it was stored as the corresponding ditosylamide **8a**.

Preparation of (*R*,*R*)-1,2-Bis[1-phenyl-1-(*p*-tosylamido)methyl]ferrocene (8a): A mixture of crude **2** (420 mg, 1.03 mmol), tosyl chloride (510 mg, 2.65 mmol), and pyridine (250 mg, 3.20 mmol) in CH_2Cl_2 (30 mL) was stirred at room temperature for 16–20 h. The solvent was then removed under reduced pressure to give crude **8a** as a brown oil. This oil was washed with diethyl ether to give a yellow solid. Yield: 700 mg (0.996 mmol, 98%); m.p. > 167 °C (dec). $[\alpha]_D^{25} = +55.0$ ($c = 0.180$, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 2.29$ (s, 3 H), 2.39 (s, 3 H), 3.90 (s, 5 H), 3.95 (br. s, 1 H), 4.05 (t, $J = 2.60$ Hz, 1 H), 4.11 (br. s, 1 H), 4.56 (d, $J = 5.27$ Hz, 1 H), 5.37 (d, $J = 4.59$ Hz, 1 H), 5.48 (d, $J = 5.27$ Hz, 1 H), 5.68 (d, $J = 4.59$ Hz, 1 H), 6.8–7.3 (m, 14 H), 7.29 (d, $J = 8.20$ Hz, 2 H), 7.61 (d, $J = 8.20$ Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): $\delta = 21.3$, 21.5, 54.6, 56.1, 66.5, 67.5, 67.6, 69.8, 87.3, 91.6 ppm; aromatic signals are not listed here. $C_{38}H_{36}FeN_2O_4S_2$ (704.68): calcd. C 64.77, H 5.15, N 3.98; found C 64.62, H 5.22, N 4.16. Crystals suitable for X-ray analysis were obtained by recrystallization from hexane/CH_2Cl_2.

Preparation of (*R*,*R*)-1,2-Bis(1-acetamido-1-phenylmethyl)ferrocene (8b): A mixture of crude **2** (240 mg, 0.62 mmol), acetic anhydride (140 mg, 1.36 mmol), and DMAP (4.0 mg, 0.03 mmol) in CH_2Cl_2 (20 mL) was stirred at room temperature for 15 h. The solvent was then removed under reduced pressure to give crude **8b** as a brown solid. This solid was recrystallized from hexane/CH_2Cl_2. Yield: 210 mg (4.3 mmol, 70%); m.p. 158 °C (dec). $[a]_D^{25}$ = –26.3 (*c* = 0.45, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.84 (s, 3 H), 2.16 (s, 3 H), 4.1–4.2 (m, 3 H), 4.15 (s, 5 H), 5.94 (d, *J* = 9.37 Hz, 1 H), 5.96 (d, *J* = 7.03 Hz, 1 H), 6.36 (d, *J* = 9.37 Hz, 1 H), 6.97 (d, *J* = 7.03 Hz, 1 H), 6.8–7.26 (m, 10 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 22.6, 23.4, 49.8, 51.7, 66.5, 66.8, 69.3, 69.7, 89.2, 89.3, 168.8 ppm; some aromatic signals are not listed here. $C_{28}H_{28}FeN_2O_2$ (480.38): calcd. C 70.01, H 5.88, N 5.83; found C 69.89, H 6.01, N 5.78.

General Procedure for the Ruthenium/Ferrocenyldiamine-Catalyzed Asymmetric Transfer Hydrogenation of Ketones: A 50-mL Schlenk tube containing a magnetic stirring bar was charged with freshly prepared **2** (10 mg, 23 μmol), [Ru(*p*-cymene)Cl_2]$_2$ (3.6 mg, 5.8 μmol) and dry *i*PrOH (5 mL) under nitrogen. The mixture was stirred and heated at 80 °C for 30 min, during which time the solution became dark red and homogeneous. After cooling to room temperature *i*PrOH (18 mL), acetophenone (144 mg, 1.2 mmol), and KOH (0.1 M in *i*PrOH, 0.58 mL) were added with a syringe, whilst stirring, and the resulting mixture was stirred for 4 h. The mixture was neutralized with dilute HCl and the *i*PrOH was removed under reduced pressure. The residue was diluted with ethyl acetate (25 mL) and the organic solution was washed (brine) and dried ($MgSO_4$). After evaporation of the solvent the residue was subjected to short column chromatography on silica gel (hexane/ethyl acetate as eluent). Chiral GC analysis (Chiraldex GT-A) of the sample revealed the presence of (*S*)-1-phenylethanol as the major enantiomer (75% *ee*).

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[8] Crystal data: crystal dimensions: 0.65 × 0.35 × 0.20 mm^3; crystal system: orthorhombic; lattice type: primitive; detector position: 44.97 mm; pixel size: 0.137 mm; lattice parameters: *a* = 13.797(3), *b* = 13.640(3), *c* = 17.444(4) Å, *V* = 3283.0(12) Å^3; space group: $P2_12_12_1$; *Z* = 4; $D_{calcd.}$ = 1.426 g cm^{-3}; *F*(000) = 1472.00; μ = 6.31 cm^{-1}; final *R* indices [$I > 3\sigma(I)$]: R_1 = 0.058, wR_2 = 0.078.

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[13] Treatment of acetate **1** with inexpensive sodium azide in hot DMF resulted in the formation of **6** in only a trace amount; most of the starting **1** remained unreacted.

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