COMMUNICATIONS

Asymmetric Dihydroxylation of 2-Substituted 1-Vinylferrocenes: The First Non-Enzymatic Kinetic Resolution of Planar-Chiral Ferrocenes

Agustí Bueno,[a] Malgorzata Rosol,[a] Jasón García,[a] and Albert Moyano[a,*]

[a] Unitat de Recerca en Síntesi Asimètrica, Departament de Química Orgànica, Universitat de Barcelona. Facultat de Química, C. Martí i Franquès 1–11, 08028-Barcelona, Catalonia, Spain
Phone: (+34)-93-402-1245; Fax: (+34)-93-339-7878; e-mail: amoyano@ub.edu

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Abstract: The first non-enzymatic kinetic resolution of planar chiral ferrocenes has been achieved by the Sharpless catalytic asymmetric dihydroxylation (AD) of a set of racemic 2-substituted 1-ethenylferrocenes **1a–d**. The enantioselectivity factor k_{rel} varies from 20 to 62 [for $(DHQD)_2PYR$ ligands], and from 5 to 27 [for $(DHQ)_2PYR$ ligands]. The stereochemical outcome of the resolution can be easily predicted by the mnemonic device for AD, with the additional hypothesis that in the preferred transition state the olefin group and the upper cyclopentadiene ring of vinylferrocenes exhibit an essentially coplanar geometry.

**Keywords:** asymmetric catalysis; dihydroxylation; ferrocene ligands; kinetic resolution; metallocenes

More than fifty years after its discovery, ferrocene and its derivatives are still the object of unabated interest in several areas of science.[1] In particular, much effort has been devoted to the enantioselective preparation of planar-chiral 1,2-disubstituted ferrocenes, which have played a key role in the development of efficient ligands for asymmetric catalysis.[2] Up to date, the vast majority of synthetic approaches towards these compounds rely on the directed metallation of suitably functionalized ferrocene precursors. The metallation of enantiopure ferrocenes bearing chiral, *ortho*-directing auxiliary groups such as alkylamines,[3] oxazolines,[4] sulfoxides,[5] or acetals[6] is the most widely used strategy, together with Snieckus' enantioselective *ortho*-metallation of achiral ferrocenecarboxamides[7] by the butyllithium-sparteine system.

Recent research from our laboratory has been focused on the synthesis of β-ferrocenyl-β-amino alcohols, a new class of central chiral ferrocene derivatives, and on the study of their synthetic applications.[8] In the course of these studies, we have made extensive use of the Sharpless asymmetric dihydroxylation[9] (AD) of 1-ferrocenylethenes.[10] We have found that in most instances this reaction takes place with good to excellent enantioselectivity, and that the ferrocenyl moiety has a strong affinity for the SW binding pocket of PYR-based ligands. In spite of the considerable controversy about the detailed mechanism of the AD process,[9] there is a general agreement on the importance of π-stacking interactions in the stabilization of the transition state (TS) complex for aryl-substituted alkenes. Theoretical calculations on the AD of styrene and of stilbene show that in the TS the phenyl and the alkene moieties present a coplanar geometry.[11] We reasoned that a similar coplanarity requirement should be operative in the AD of vinylferrocenes. If this is the case, the presence of a bulky substituent adjacent to the vinyl group would strongly destabilize one of the two limiting planar conformations of the molecule, so that for a given enantiomer of a 2-substituted 1-vinylferrocene one face of the olefin would be much more reactive than the other (see Figure 1).
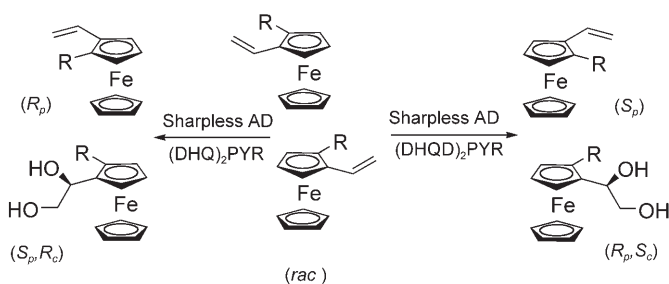
Thus, for the (R_p)-enantiomer of a 2-substituted 1-vinylferrocene, dihydroxylation would take place preferentially on the *si*-face of the alkene, so that the $(DHQD)_2PYR$-catalyzed reaction would be much faster than the $(DHQ)_2PYR$-catalyzed one; the reverse situation [fast dihydroxylation of the *re*-face with $(DHQ)_2PYR$ ligand, slow reaction for the $(DHQD)_2PYR$ ligand] would take place for the (S_p)-enantiomer. In other words, the AD reaction should be capable of effecting the catalytic kinetic resolution (KR) of racemic 2-substituted 1-vinylferrocenes (Scheme 1).

We report here the experimental implementation of these ideas, showing that in fact the AD-mediated
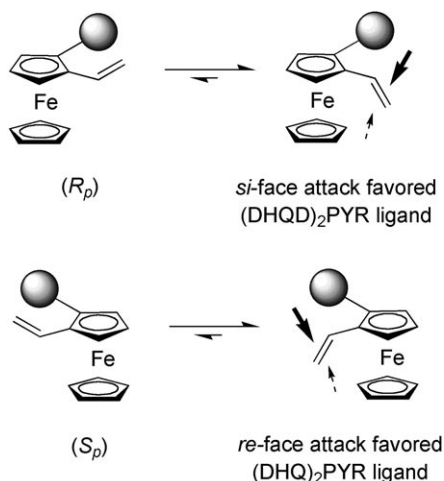
Figure 1. Predicted enantiomer and face-selectivities in the Sharpless asymmetric dihydroxylation of 2-substituted-1-vinylferrocenes.


Scheme 1. Predicted stereochemical outcome of the kinetic resolution of 2-substituted-1-vinylferrocenes by asymmetric dihydroxylation.

KR of a set of racemic 2-substituted 1-vinylferrocenes takes place with moderate to good enantioselectivity factors (k_{rel} values up to 62). Moreover, the absolute configurations of the products completely agree with the mechanistic hypothesis depicted in Scheme 1.

Ferrocenylethenes **1a** and **1b** (see reaction in Table 1) were easily obtained in racemic form from *N,N*-diisopropylferrocenecarboxamide[7] and from 4,4-dimethyl-2-ferrocenyl-1,3-oxazoline,[14] respectively, by a two-step procedure involving *ortho*-lithiation (*n*-BuLi-TMEDA, Et$_2$O or *n*-BuLi, THF), addition of acetaldehyde and dehydration (MsCl, NEt$_3$, DCM) of the intermediate alcohol. On the other hand, both **1c** and **1d** were prepared by metallation (*s*-BuLi, THF) of 2-ferrocenyl-1,3-dioxane,[15] trapping with the adequate electrophile (Me$_3$SiCl or I$_2$), acetal hydrolysis (aqueous *p*-TsOH, THF), addition of methylmagnesium bromide and alumina-promoted dehydration.

Table 1. Asymmetric dihydroxylation of racemic 2-substituted-1-vinylferrocenes.[a]

R = CON(*i*-Pr)$_2$ (**a**); 4,4-dimethyl-1,3-oxazolin-2-yl (**b**);TMS (**c**); I (**d**)
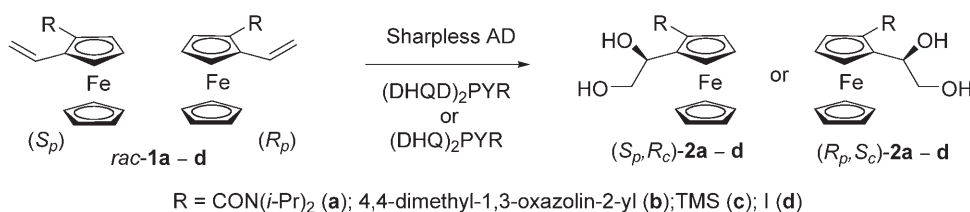
Entry	Starting alkene	Ligand (% mol equivs.)	Time (min)	Recovered alkene (% yield,[b] er[c])	Diol product (% yield,[b] er[c])	k_{rel}
1	(±)-**1a**	(DHQD)$_2$PYR (2.4)	30	(+)-(S_p)-**1a** (52, n.d.[d])	(+)-(R_p,S_c)-**2a** (31, 93:7)	n.d.[d]
2	(±)-**1a**	(DHQD)$_2$PYR (5)	10	(+)-(S_p)-**1a** (16, 96:4)	(+)-(R_p,S_c)-**2a** (44, 95:5)	62.3
3	(±)-**1a**	(DHQ)$_2$PYR (5)	52	(−)-(R_p)-**1a** (28, 18:82)	(−)-(S_p,R_c)-**2a** (44, 10:90)	17.3
4	(±)-**1b**	(DHQD)$_2$PYR (5)	30	(+)-(S_p)-**1b** (16, n.d.[d])	(−)-(R_p,S_c)-**2b** (35, 90:10)	n.d.[d]
5[e]	(±)-**1b**	(DHQD)$_2$PYR (5)	30	(+)-(S_p)-**1b** (36, 88:12)	(−)-(R_p,S_c)-**2b** (47, 93:7)	30.3
6[e]	(±)-**1b**	(DHQ)$_2$PYR (5)	60	(−)-(R_p)-**1b** (23, 15:85)	(+)-(S_p,R_c)-**2b** (44, 7:93)	27.7
7	(±)-**1c**	(DHQD)$_2$PYR (5)	25	(+)-(S_p)-**1c** (23, 93:7[f])	(−)-(R_p,S_c)-**2c** (47, 94:6)	43.3
8	(±)-**1c**	(DHQ)$_2$PYR (5)	20	(−)-(R_p)-**1c** (31, 23:77[f])	(+)-(S_p,R_c)-**2c** (48, 18:82)	7.7
9	(±)-**1d**	(DHQD)$_2$PYR (5)	60	(+)-(S_p)-**1d** (27, 89:11)	(+)-(R_p,S_c)-**2d** (43, 90:10)	21.1
10	(±)-**1d**	(DHQD)$_2$PYR (10)	110	(+)-(S_p)-**1d** (19, 97:3)	(+)-(R_p,S_c)-**2d** (45, 85:15)	19.4
11	(±)-**1d**	(DHQ)$_2$PYR (10)	105	(−)-(R_p)-**1d** (20, 14:86)	(−)-(S_p,R_c)-**2d** (48, 16:84)	11.1

[a] *General reaction conditions:* 1.5 mol equivs. K$_3$[Fe(CN)$_6$], 1.5 mol equivs. K$_2$CO$_3$, ligand-K$_2$OsO$_2$(OH)$_4$ ratio = 1.3:1, 0.5 mmol alkene in 30 mL 1:1 CH$_3$CN-H$_2$O, room temperature.
[b] Yield of isolated product after chromatographic purification.
[c] By HPLC (Chiralcel® OD column).
[d] Not determined.
[e] Reactions performed at 0 °C.
[f] By polarimetry.

With this set of racemic 2-substituted 1-vinylferrocenes (**1a–d**) in our hands, we proceeded to study their catalytic asymmetric dihydroxylation, using the (DHQD)$_2$PYR and (DHQ)$_2$PYR ligands.[16] The reactions were performed at room temperature or at 0°C in acetonitrile-water (1:1), followed by work-up and ^{1}H NMR analysis of the product mixture, and the enantiomeric purities of both the diols and the recovered olefins were generally evaluated by HPLC. The absolute stereochemistry of the reaction products was established by chemical correlation with known or independently prepared compounds, as well as by chromatographic and chiroptical methods (see Supporting Information). The k_{rel}[17] values were calculated from the enantiomeric purity data of the resolution products, and checked for internal consistency with the conversions estimated from the yields of the diols **2a–d**. The results of this study are summarized in Table 1.

Clear-cut kinetic resolutions were achieved in all instances, although the k_r values were dependent both on the nature of the 2-substituent and on the AD ligand. Several conclusions can be drawn from the data in Table 1. The (DHQD)$_2$PYR ligand is more selective, for a given olefin, than the (DHQ)$_2$PYR one. This fact can be correlated with our previous results on the AD of 1-ferrocenylethenes, that indicate a generally higher enantioselectivity for dihydroquinidine ligands.[8] Also, for the (DHQD)$_2$PYR ligand, the enantioselectivity factor of the resolution decreases along the following sequence: **1a** > **1c** > **1b** > **1d**. For the (DHQ)$_2$PYR ligand, the differences in enantioselectivity are less pronounced, and decrease along the sequence **1b** > **1a** > **1d** > **1c**. Although this different behaviour can be attributed to the quasi-enantiomeric relationship between both kinds of ligands, the general trend is that the ferrocenylethenes with the bulkiest substituents (**1a**, **1b**) are superior substrates for the KR than those having the less bulky ones (**1c**, **1d**). Most importantly, and according to our mechanistic hypothesis, the (DHQD)$_2$PYR ligands react preferentially with the (R_p) enantiomers of planar-chiral ferrocenylethenes **1a–d**, leading to (R_p,S_c) diols and to unreacted alkenes of major (S_p) stereochemistry, while the (DHQ)$_2$PYR ligands show the opposite behaviour. In an isolated experiment, we have shown that the stereochemical course of the resolution of (±)-**1a**

does not change with the use of the (DHQD)$_2$PHAL ligand, although the enantioselectivity factor (k_{rel} = 34.7) is somewhat smaller.

The dihydroxylation products **2a–d** were always isolated in high diastereochemical purity (>95:5 dr, checked both by NMR and by HPLC), independently both of the nature of the 2-substituent and of the AD ligand. It is worth noting here that the KR of racemic alkenes *via* AD has been successful only in a small number of examples,[17b] and in most instances leads to the diol products as diastereomeric mixtures.[18] Since in every case the yield of the recovered olefin is smaller than that calculated from conversion, we could not exclude *a priori* that this unprecedented diastereoselectivity was not due to the selective destruction of the "mismatched" diastereomer.

In order to gain some more insight into this question, highly enantiopure (97:3 er) olefin (S_p)-**1c** [obtained *via* diastereoselective *ortho*-lithiation of (S)-4-tert-butyl-2-ferrocenyl-1,3-oxazoline[4b]] was submitted to AD with the "matched" (DHQ)$_2$PYR ligand; we were pleased to find that the reaction was complete in less than 20 min at room temperature, and that the expected diol (S_p,R_c)-**2c** was isolated in an excellent 93% yield and with a 99.4:0.6 er (Scheme 2).

On the other hand, AD of the same olefin with the "mismatched" (DHQD)$_2$PYR ligand took place much more slowly, and after 1 h minor amounts of the starting vinylferrocene were still present in the reaction mixture (TLC analysis). Interestingly enough, the only diol product (isolated in 6% yield after chromatographic purification) formed in the reaction was again (+)-**2c**, obtained in moderate enantiomeric purity (80:20 er). We propose that with the "mismatched" ligand **1c** undergoes slow oxidation to a ferricinium cation.[19] The most likely cause for the diminished yields of recovered olefins is therefore the oxidative degradation of the less reactive enantiomer in the reaction medium, a phenomenon that we had previously observed during the AD of slow-reacting vinylferrocenes.[8]

The reaction shown in Scheme 2 also showcases another potential use of the present findings, i.e., the totally stereocontrolled preparation of ferrocene derivatives exhibiting both central and planar stereogenicity elements by AD of scalemic planar chiral vinylferro-

(+)-(S_p)-**1c**
(97:3 er)

(+)-(S_p,R_c)-**2c**
(93% yield, >99:1er)
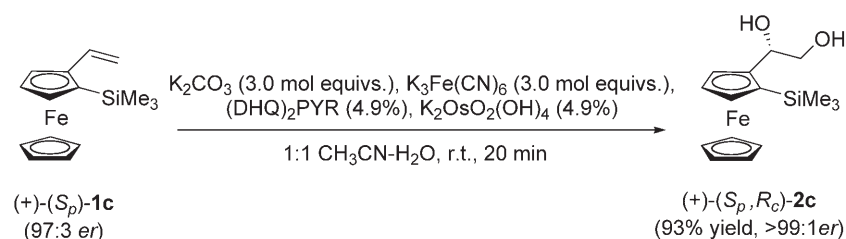
Scheme 2. Asymmetric dihydroxylation of (+)-(S_p)-**1c** with the "matched" (DQH)$_2$PYR ligand.

cenes with the "matched" ligands. In order to test the generality of this concept, we submitted (+)-(R_p)-1-vinyl-2-methylferrocene **1e** (97:3 *er*, easily prepared from ferrocenecarbaldehyde by means of Kagan's chiral acetal procedure;[6] note the change in the priority of the substituents with respect to vinylferrocenes **1a–d**) to the same reaction conditions of Scheme 2. According to our expectations, essentially enantiopure (>99:1 *er*, according to HPLC) (+)-(R_p,R_c)-1-(2-methylferrocenyl)ethane-1,2-diol was obtained in 81% yield after chromatographic purification.

The AD of 2-substituted 1-vinylferrocenes appears therefore to be a fairly general process, exhibiting several unique features. a) It constitutes the first non-enzymatic KR of a planar-chiral ferrocene, and one of the scarce examples of successful application of the AD reaction to the KR of acyclic, conformationally-unrestricted alkenes.[17b,18] b) The stereochemical course of the dihydroxylation can be easily accommodated within the Sharpless' mnemonic device for AD,[9,20] and gives further support to previous results consistent with an early, reactant-like transition state for the product-determining step in the AD reaction.[11,21] c) Apart from its interest on a mechanistic level, the process may be of preparative value, since it allows the direct access, from relatively inexpensive starting materials, to new planar- and central-chiral ferrocene derivatives, with high degrees of stereochemical control. Finally, the present findings pave the way to the discovery of other non-enzymatic catalytic kinetic resolutions of planar-chiral ferrocenes, an issue that is being currently addressed in our laboratory.

Experimental Section

Synthesis of Racemic 2-Substituted 1-Ethenylferrocenes; (±)-*N,N*-Diisopropyl-2-vinylferrocenecarboxamide (1a)

To a cold (−78°C), stirred solution of TMEDA (0.90 mL, 6.0 mmol) in anhydrous diethyl ether (20 mL) a 1.6 M solution of *n*-butyllithium in hexanes (3.75 mL, 6.0 mmol) was added dropwise. The reaction mixture was stirred at −78°C for 15 min and a solution of *N,N*-diisopropylferrocenecarboxamide (**1**) (1.56 g, 5.0 mmol) in diethyl ether (15 mL) was added with the aid of a cannula. After stirring for 80 min at the same temperature, a solution of freshly distilled acetaldehyde (2.9 mL, 52 mmol) in diethyl ether (15 mL) was added slowly; 15 min after the end of the addition, the cooling bath was removed and the progress of the reaction was monitored by TLC. After 45 min, the solution was poured over aqueous saturated ammonium chloride (50 mL) and extracted with diethyl ether (3×10 mL). The combined organic phases were washed with brine (10 mL), dried over magnesium sulfate, and evaporated under reduced pressure. The crude product was purified by column chromatography

on silica gel, using hexanes-ethyl acetate mixtures as eluents, to give (±)-*N,N*-diisopropyl-2-(1-hydroxyethyl)ferrocenecarboxamide (mixture of diastereomers) as an orange-colored solid; yield: 1.38 g (77%).

To a stirred solution of this alcohol mixture (1.61 g, 4.52 mmol) and triethylamine (6.8 mL, 48.8 mmol) in dry dichloromethane (13.5 mL) methanesulfonyl chloride (0.54 mL, 7.0 mmol) was added in one portion at room temperature. The mixture was heated to reflux, and the progress of the reaction was followed by TLC. After 35 min, an additional portion of methanesulfonyl chloride (0.17 mL, 2.2 mmol) was added, and stirring was maintained for 20 min. The resulting mixture was poured over aqueous saturated sodium bicarbonate (25 mL) and the aqueous phase was extracted with dichloromethane (3×10 mL). The combined organic phases were washed with brine (10 mL), dried over magnesium sulfate, and evaporated under vacuum. The crude product was purified by column chromatography on silica gel, using hexanes-ethyl acetate mixtures as eluents, to give the title compound as an orange-colored solid; yield: 1.06 g (70%).

(±)-2-(2-Vinylferrocenyl)-4,4-dimethyl-1,3-oxazoline (1b)

To a cold (−78°C), stirred solution of 2-ferrocenyl-4,4-dimethyl-1,3-oxazoline (1.0 g, 3.5 mmol) in anhydrous tetrahydrofuran (42 mL) a 1.6 M solution of *n*-butyllithium in hexanes (3.3 mL, 5.3 mmol) was added dropwise. The reaction mixture was stirred at −78°C for 90 min. After raising the temperature to 0°C, freshly distilled acetaldehyde (0.4 mL, 7.1 mmol) was added slowly; 15 min after the end of the addition, the cooling bath was removed and the progress of the reaction was monitored by TLC. After 16 h, the solution was poured over aqueous saturated ammonium chloride (45 mL) and extracted with ethyl acetate (3×10 mL). The organic phase was dried over magnesium sulfate, and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel, using hexanes-ethyl acetate (45%-50%) mixtures as eluents, to give (±)-2-(1-hydroxyethyl)ferrocenyl-4,4-dimethyl-1,3-oxazoline (mixture of diastereomers) as a reddish oil; yield: 1.1 g (95%).

To a stirred solution of this alcohol mixture (1.0 g, 3.0 mmol) and triethylamine (4.4 mL, 32 mmol) in dry dichloromethane (9 mL) methanesulfonyl chloride (0.34 mL, 4.4 mmol) was added in one portion at room temperature. The mixture was heated to reflux, and the progress of the reaction was followed by TLC. After 60 min, an additional portion of methanesulfonyl chloride (0.10 mL, 1.3 mmol) was added. Stirring was continued for 60 min, and the resulting mixture was poured over aqueous saturated sodium bicarbonate (20 mL). The aqueous phase was extracted with dichloromethane (5×15 mL). The combined organic phases were dried over magnesium sulfate, and evaporated under vacuum. The crude product was purified by column chromatography on alumina, using hexanes-ethyl acetate (5–10%) mixtures as eluents, to give the title compound as an orange-colored solid; yield: 0.80 g (87%).

(±)-1-Trimethylsilyl-2-vinylferrocene (1c)

a) To a cold (−78°C), stirred solution of 2-ferrocenyl-1,3-dioxane (0.27 g, 1.0 mmol) in anhydrous tetrahydrofuran

(7 mL) a 1.15 M solution of *sec*-butyllithium in hexanes (1.3 mL, 1.5 mmol) was added dropwise. The reaction mixture was stirred at −78 °C for 30 min and at 0 °C for 60 min. After cooling again to −78 °C, freshly distilled trimethylchlorosilane (0.4 mL, 7.1 mmol) was added slowly; 30 min after the end of the addition, the cooling bath was removed and the progress of the reaction was monitored by TLC. After 1 h, the solution was poured over brine (20 mL). The organic phase was washed with brine (20 mL), dried over magnesium sulfate, and evaporated under reduced pressure. The crude product was purified by column chromatography on triethylamine-pretreated silica gel (10% v/v), using an hexane-triethylamine (10%) mixture as eluent, to give a *ca.* 3:1 mixture of (±)-2-(2-trimethylsilylferrocenyl)-1,3-dioxane and (±)-2-[1′,2-bis(trimethylsilyl) ferrocenyl]-1,3-dioxane as a red-colored oil; yield: 0.35 g (quantitative).

To a solution of the above mixture (0.34 g, 1.0 mmol) in tetrahydrofuran (7 mL), *p*-toluenesulfonic acid (0.27 g, 1.4 mmol) and water (3 mL) were added sequentially, and the resulting solution was heated to reflux for 2 h (TLC monitoring). After cooling to room temperature, diethyl ether (10 mL) was added, and the reaction mixture was poured over aqueous saturated sodium bicarbonate (20 mL). The organic phase was washed with aqueous saturated sodium bicarbonate (10 mL) and with water (10 mL), dried over magnesium sulfate, and evaporated under reduced pressure. The crude product was purified by column chromatography silica gel, using hexane-ethyl acetate mixtures as eluents, to afford a *ca.* 3:1 mixture of (±)-2-trimethylsilylferrocenecarbaldehyde and (±)-1′,2-bis(trimethylsilyl)ferrocenecarbaldehyde as a red-colored oil; yield: 0.26 g. Spectral data for (±)-2-trimethylsilylferrocenecarbaldehyde coincided with those described in the literature for the optically active compound.[22]

b) To a cold (0 °C), stirred solution of the mixture of (±)-2-trimethylsilylferrocenecarbaldehyde and (±)-1′,2-bis(trimethylsilyl)ferrocenecarbaldehyde obtained above (0.22 g, *ca.* 0.54 + 0.18 mmol) in anhydrous tetrahydrofuran (5 mL) a 3 M solution of methylmagnesium bromide in tetrahydrofuran (0.40 mL, 1.2 mmol) was added dropwise. After 25 min of stirring at 0 °C (TLC monitoring), the reaction mixture was poured over brine (20 mL), and extracted with diethyl ether (3×10 mL). The organic phase was washed with brine (15 mL), dried over magnesium sulfate, and evaporated under reduced pressure. The crude product was purified by column chromatography silica gel, using hexane-ethyl acetate mixtures as eluents, to afford (±)-1-[1′,2-bis(trimethylsilyl)ferrocenyl]ethanol (yield: 57 mg, (18%) and (±)-1-(2-trimethylsilylferrocenyl)ethanol (yield: 134 mg, 53%), as red-colored oils.

Both products were obtained as *ca.* 1:1 diastereomer mixtures. A solution of (±)-1-(2-trimethylsilylferrocenyl)ethanol (0.13 g, 0.42 mmol) in dry toluene (4.5 mL) was heated to reflux in a Dean–Stark apparatus in the presence of neutral alumina (0.27 g) for 140 min. After cooling to room temperature, solvent was eliminated under vacuum to give the pure racemic olefin **1c** as a red-colored oil; yield: 0.10 g (86%).

(±)-1-Iodo-2-vinylferrocene (1d)

a) To a cold (−78 °C), stirred solution of 2-ferrocenyl-1,3-dioxane (0.27 g, 1.0 mmol) in anhydrous tetrahydrofuran (6 mL) a 1.15 M solution of *sec*-butyllithium in hexanes (1.3 mL, 1.5 mmol) was added dropwise. The reaction mixture was stirred at −78 °C for 20 min and at 0 °C for 60 min. After cooling again to −78 °C, a solution of iodine (0.51 g, 2.0 mmol) in anhydrous tetrahydrofuran (3 mL) was added with the aid of a cannula; 15 min after the end of the addition, the cooling bath was removed and the solution was poured over a 10% aqueous solution of sodium thiosulphate (20 mL). The organic phase was treated again with sodium thiosulphate (2×10 mL), and the combined aqueous phases were extracted with diethyl ether (20 mL). The combined organic phases were washed with brine (20 mL), dried over magnesium sulfate, and evaporated under reduced pressure. The crude product was purified by column chromatography on triethylamine-pretreated silica gel (10% v/v), using a hexane-triethylamine (10%) mixture as eluent, to give (±)-2-(2-iodoferrocenyl)-1,3-dioxane as a red-colored oil; yield: 0.39 g (97%).

To a solution of the above compound (0.35 g, 0.9 mmol) in tetrahydrofuran (5 mL), *p*-toluenesulfonic acid (0.17 g, 0.9 mmol) and water (0.3 mL) were added sequentially, and the resulting solution was heated to reflux for 100 min (TLC monitoring). After cooling to room temperature, diethyl ether (10 mL) was added, and the reaction mixture was poured over aqueous saturated sodium bicarbonate (20 mL). The organic phase was washed with aqueous saturated sodium bicarbonate (20 mL) and with water (20 mL), dried over magnesium sulfate, and evaporated under reduced pressure. The crude product was purified by column chromatography silica gel, using hexane-ethyl acetate mixtures as eluents, to afford the title compound, as a red-colored oil; yield: 0.27 g (90%). Spectral data for (±)-2-iodoferrocenecarbaldehyde coincided with those described in the literature for the optically active compound.[22]

b) To a cold (0 °C), stirred solution of (±)-2-iodoferrocenecarbaldehyde (0.24 g, 0.70 mmol) in anhydrous tetrahydrofuran (7 mL) a 3 M solution of methylmagnesium bromide in tetrahydrofuran (0.35 mL, 1.1 mmol) was added dropwise. After 20 min of stirring at 0 °C (TLC monitoring), the reaction mixture was poured over brine (30 mL), and extracted with diethyl ether (3×10 mL). The organic phase was washed with brine (15 mL), dried over magnesium sulfate, and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel, using hexane-ethyl acetate mixtures as eluents, to afford (±)-1-(2-iodoferrocenyl)ethanol as an orange-colored oil; yield: 0.20 g (81%). This product was obtained as a *ca.* 1:1 diastereomer mixture.

A solution of (±)-1-(2-iodoferrocenyl)ethanol (0.17 g, 0.49 mmol) in dry toluene (10 mL) was heated to reflux in a Dean–Stark apparatus in the presence of neutral alumina (0.26 g) for 4 h. After cooling to room temperature, solvent was eliminated under vacuum to give a crude product that was purified by column chromatography on silica gel, using hexane as eluent, to afford the racemic olefin **1d** as a red-colored oil; yield: 0.12 g (71%).

Representative Procedure for Kinetic Resolution under the Sharpless Dihydroxylation Conditions: Asymmetric Dihydroxylation of (±)-1a

To a stirred solution of $K_3[Fe(CN)_6]$ (0.24 g, 0.72 mmol) and potassium carbonate (0.10 g, 0.72 mmol) in 1:1 acetonitrile-water (24 mL), were added (DHQD)$_2$PYR (22 mg, 0.024 mmol) and $K_2OsO_2(OH)_4$ (6.9 mg, 0.019 mmol), with stirring maintained at room temperature until complete dissolution of the osmate. At this point, a solution of (±)-2-*N,N*-diisopropyl-2-vinylferrocenecarboxamide (**1a**) (164 mg, 0.48 mmol) in acetonitrile (3 mL) was added dropwise, followed by the addition of water (3 mL). After 10 min of stirring at room temperature, sodium sulfite (0.90 g, 7 mmol) was added and stirring maintained for 20 min. The reaction mixture was extracted with ethyl acetate (5×7 mL); the organic extracts were washed with brine (10 mL), dried over magnesium sulfate and the solvents removed at reduced pressure. Column chromatography of the crude product (silica gel, hexane-ethyl acetate mixtures as eluents) afforded optically active olefin (+)-**1a** (yield: 26 mg, 16%; *er* = 96:4, HPLC), and (+)-2-(1,2-dihydroxyethyl)-*N,N*-diisopropylferrocenecarboxamide **2a** (yield: 80 mg, 44%; *er* = 95:5, HPLC) as a yellow semi-solid.

In a similar way, the asymmetric dihydroxylation of (±)-**1a** (169 mg, 0.50 mmol) using (DHQ)$_2$PYR (22 mg, 0.025 mmol) as the chiral ligand gave, after 52 min of stirring at room temperature, (−)-**1a** (yield: 47 mg, 28%; *er* = 82:18, HPLC) and (−)-**2a** (yield: 81 mg, 44%; *er* = 90:10, HPLC).

Independent Synthesis of (+)-(S_p)-1-Trimethylsilyl-2-vinylferrocene

To a cold (0°C), stirred solution of (−)-(S_p)-2-trimethylsilyl-ferrocenecarbaldehyde[4a,22] (1.58 g, 5.60 mmol) in anhydrous tetrahydrofuran (38 mL) a 3M solution of methylmagnesium bromide in tetrahydrofuran (2.80 mL, 8.40 mmol) was added dropwise. After 15 min of stirring at 0°C (TLC monitoring), the reaction mixture was poured over brine (40 mL), and extracted with diethyl ether (3×30 mL). The organic phase was washed with brine (40 mL), dried over magnesium sulfate, and evaporated under reduced pressure, to afford the intermediate (S_p)-1-(2-trimethylsilylferrocenyl)-ethanol as a *ca.* 1:1 diastereomer mixture; yield: 1.46 g (88%).

Without further purification, a solution of this product in dry toluene (50 mL) was heated to reflux in a Dean–Stark apparatus in the presence of neutral alumina (6.0 g) for 4 h. After cooling to room temperature, solvent was eliminated under vacuum to give a crude product that was purified by column chromatography on alumina, using hexane as eluent, to afford the highly enantiopure (*er* = 97:3)[4a] olefin (+)-(S_p)-**1c** as a red-colored oil; yield: 1.12 g (84%).

Catalytic Asymmetric Dihydroxylation of (+)-(S_p)-1-Trimethylsilyl-2-vinylferrocene (1c)

To a stirred solution of $K_3[Fe(CN)_6]$ (4.42 g, 13.4 mmol) and potassium carbonate (1.85 g, 13.4 mmol) in 1:1 acetonitrile-water (400 mL), were added (DHQ)$_2$PYR (0.20 g, 0.22 mmol) and $K_2OsO_2(OH)_4$ (83 mg, 0.22 mmol), with stirring maintained at room temperature until complete dissolu-

tion of the osmate. At this point, a solution of (+)-(S_p)-**1c** (1.27 g, 4.45 mmol) in acetonitrile (10 mL) was added dropwise, followed by the addition of water (10 mL). After 60 min of stirring at room temperature, sodium sulfite (10 g, 78 mmol) was added and stirring maintained for 20 min. The reaction mixture was extracted with ethyl acetate (3× 30 mL); the organic extracts were washed with brine (30 mL), dried over magnesium sulfate and the solvents removed at reduced pressure. Column chromatography of the crude product (silica gel, hexane-ethyl acetate mixtures as eluents) afforded (+)-1-(2-trimethylsilylferrocenyl)ethan-1,2-diol; yield: 1.32 g (93%); *er* = 99.4:0.6 (HPLC).

Note Added in Proof

After submission of this article, a paper reporting the kinetic resolution of planar-chiral ferrocenes by enantioselective metathesis appeared in the literature.[23]

References

[1] a) *Ferrocenes*, (Eds.: T. Hayashi, A. Togni), VCH, Weinheim, **1995**; b) D. R. vanStaveren, N. Metzler-Nolte, *Chem. Rev.* **2004**, *104*, 5931–5985; c) P. D. Beer, *Adv. Inorg. Chem.* **1992**, *39*, 79–157.

[2] a) A. Togni, in: *Metallocenes – Synthesis Reactivity, Applications*, Vol. 2, (Eds.: A. Togni, R. L. Halterman), Wiley-VCH, Weinheim, **1998**, pp. 685–718; b) C. J. Richards, A. J. Locke, *Tetrahedron: Asymmetry* **1998**, *9*, 2377–2407; c) O. B. Sutcliffe, M. R. Bryce, *Tetrahedron: Asymmetry* **2003**, *14*, 2297–2325.

[3] a) D. Marquarding, H. Klusacek, G. Gokel, P. Hoffmann, I. Ugi, *J. Am. Chem. Soc.* **1970**, *92*, 5389–5393; b) T. Hayashi, M. Kumada, *Acc. Chem. Res.* **1982**, *15*, 395–401; c) M. Sawamura, Y. Ito, Y. *Chem. Rev.* **1992**, *92*, 857–871.

[4] a) T. Sammakia, H. A. Latham, D. R. Schaad, *J. Org. Chem.* **1995**, *60*, 10–11; b) C. J. Richards, T. Damalidis, D. E. Hibbs, M. B. Hursthouse, *Synlett* **1995**, 74–76; c) Y. Nishibayashi, S. Uemura, *Synlett* **1995**, 79–81.

[5] F. Rebière, O. Riant, L. Ricard, H. B. Kagan, *Angew. Chem. Int. Engl. Ed.* **1993**, *32*, 568–570.

[6] O. Riant, O. Samuel, H. B. Kagan, *J. Am. Chem. Soc.* **1993**, *115*, 5835–5836.

[7] M. Tsukazaki, M. Tinkl, A. Roglans, B. J. Chapell, N. J. Taylor, V. Snieckus, *J. Am. Chem. Soc.* **1996**, *118*, 685–686.

[8] a) R. M. Moreno, A. Bueno, A. Moyano, *J. Organomet. Chem.* **2002**, *660*, 62–70; b) A. Moyano, M. Rosol, R. M. Moreno, C. López, M. A. Maestro, *Angew. Chem. Int. Ed.* **2005**, *44*, 1865–1869; c) R. M. Moreno, A. Bueno, A. Moyano, *J. Org. Chem.* **2006**, *71*, 2528–

2531; d) R. M. Moreno, A. Moyano, *Tetrahedron: Asymmetry* **2006**, *17*, 1104–1110, and references cited therein.

[9] a) H. C. Kolb, M. S. Van Nieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483–2547; b) I. E. Markó, J. S. Svendsen, in: *Comprehensive Asymmetric Catalysis*, Vol. 2, (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer Verlag, Berlin, **1999**, pp. 713–787.

[10] For a precedent, see: W. G. Jary, J. Baumgartner, *Tetrahedron: Asymmetry* **1998**, *9*, 2081–2085.

[11] a) P.-O. Norrby, T. Rasmussen, J. Haller, T. Strassner, K. N. Houk, *J. Am. Chem. Soc.* **1999**, *121*, 10186–10192; b) G. Ujaque, F. Maseras, A. Lledós, *J. Org. Chem.* **1997**, *62*, 7892–7894.

[12] a) T. Izumi, S. Aratani, *J. Chem. Tech. Biotechnol.* **1992**, *57*, 33–36; b) T. Izumi, F. Tamura, K. Sasaki, *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2784–2788, and references cited therein.

[13] a) A. Patti, D. Lambusta, M. Piatelli, G. Nicolosi, P. McArdle, D. Cunningham, M. Walsh, *Tetrahedron* **1997**, *53*, 1361–1368; b) A. Patti, D. Lambusta, M. Piatelli, G. Nicolosi, *Tetrahedron: Asymmetry* **1998**, *9*, 3073–3080, and references cited therein.

[14] C. Bolm, K. Muñiz-Fernández, A. Seger, G. Raabe, K. Günther, *J. Org. Chem.* **1998**, *63*, 7860–7867.

[15] W. Steffen, M. Laskoski, G. Collins, U. H. F. Bunz, *J. Organomet. Chem.* **2001**, *630*, 132–138.

[16] G. A. Crispino, K.-S. Jeong, H. C. Kolb, Z.-M. Wang, D. Xu, K. B. Sharpless, *J. Org. Chem.* **1993**, *58*, 3785–3786.

[17] a) H. B. Kagan, J.-C. Fiaud, *Top. Stereochem.* **1988**, *18*, 249–330; b) J. M. Keith, J. F. Larrow, E. N. Jacobsen, *Adv. Synth. Catal.* **2001**, 5–26; c) Calculations were effected by means of the *Selectivity*® program, version Mac 1.0 and Win 1.0, © 1994 by K. Faber and A. Kleewein.

[18] The KR of racemic alkenes *via* AD leads in most instances to the diol products as diastereomeric mixtures: a) M. S. VanNieuwenhze, K. B. Sharpless, *J. Am. Chem. Soc.* **1993**, *115*, 7864–7865; b) T. Yokomatsu, T. Yamagishi, T. Sada, K. Suemune, S. Shibuya, *Tetrahedron* **1998**, *54*, 781–790; c) R. Rios, C. Jimeno, P. J. Carroll, P. J. Walsh, *J. Am. Chem. Soc.* **2002**, *124*, 10272–10273; d) W.-M. Dai, Y. Zhang, Y. Zhang, *Tetrahedron: Asymmetry* **2004**, *15*, 525–535.

[19] For an excellent review on divergent reactions on a racemic mixture, see: H. B. Kagan, *Tetrahedron* **2001**, *57*, 2449–2468.

[20] K. B. Sharpless, W. Amberg, Y. L. Bennani, G. A. Crispino, J. Hartung, K.-S. Jeong, H.-L. Kwong, K. Morikawa, Z.-M. Wang, D. Xu, X.-L. Zhang, *J. Org. Chem.* **1992**, *57*, 2768–2771.

[21] H. S. Christie, D. P. G. Hamon, K. L. Tuck, *Chem. Commun.* **1999**, 1989–1990.

[22] O. Riant, O. Samuel, T. Flessner, S. Taudien, H. B. Kagan, *J. Org. Chem.* **1997**, *62*, 6733–6745.

[23] M. Ogasawara, S. Wanatabe, L. Fan, K. Nakaima, T. Takahashi, *Organometallics* **2006**, *25*, 5201.