(−)-Sparteine-Mediated Directed *ortho*-Metalation of *N*-Cumyl-*N*-ethylferrocenecarboxamide. Versatile Routes to Functionalized Planar Chiral Ferrocenecarboxamides, Amines, Esters and Phosphines

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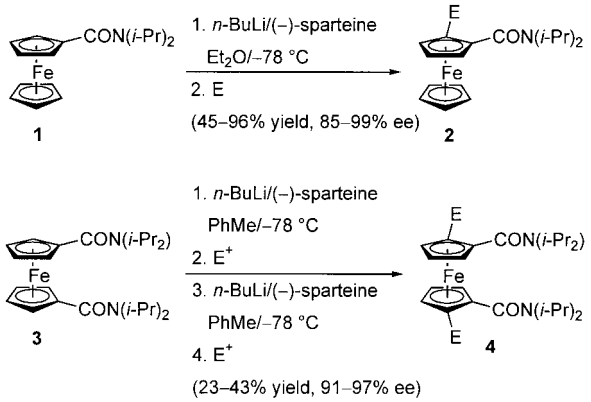
Received: September 16, 2002; Accepted: November 5, 2002

Abstract: *N*-Cumyl-*N*-ethylferrocenecarboxamide **5** provides planar chiral carboxamides **6** in high yield and % ee *via* (−)-sparteine-mediated directed *ortho*-metalation. Mild decumylation affords secondary amides **7**, which serve as intermediates for a convenient and general route to the venerable Ugi planar chiral ferrocenylamines **13** and as versatile precursors for the preparation of novel chiral ferrocenes **15** and **20**. The chiral TMS-ferrocenyl derivative **7c** is used to prepare the enantiomeric (*S*)-**7f**, circumventing the lack of availability of (+)-sparteine.

Keywords: cumyl; enantioselective; Heck reaction; metalation; planar chiral ferrocene, ring-closing metathesis

Introduction

Axially chiral BINOLs[1a] and planar chiral ferrocenes[1b] are evolving as premier classes of chiral ligands for new enantioselective catalytic processes. Recently, we established a highly enantioselective synthesis of substituted planar chiral ferrocenyl-amides **1** → **2**, and ferrocenyl-bisamides **3** → **4** (Scheme 1), using (−)-sparteine-mediated directed *ortho*-metalation (D*o*M) chemistry.[2] This constituted the first general and direct synthetic method to planar chiral ferrocenes which avoids the need for directed metalation groups (DMGs) containing stereogenic centres.[1b]



Scheme 1. (−)-Sparteine-mediated D*o*M of *N,N*-diisopropyl-ferrocenecarboxamides **1** and **3**.

As noted by Kagan,[3] "a major limitation of all the previous methods is that the *ortho*-directing group of the substrate seldom allows functional group modification." In addition, Togni[1b] has advised the need to "overcome the disadvantage of the single enantiomeric form of (−)-sparteine." We have addressed these points and demonstrate herein that the *N*-cumyl-*N*-ethylferrocenecarboxamide **5**[4] is well behaved in (−)-sparteine mediated D*o*M, providing planar chiral ferrocenes **6** in high % ee and that, in contrast to previously used amides **1** and **3**,[2] the products are open to new modes of manipulation as follows:

a) products **6** may be decumylated under mild conditions to furnish 2-substituted *N*-ethylferrocenecarboxamides (**7**) (quantitative yield and high % ee) which are unavailable otherwise;[5]
b) secondary amides **7** may be readily converted to methyl esters using the Charette esterification[6] or, by alkylation, to new tertiary amides (**12a, b**, **18**) which are not otherwise accessible via (−)-sparteine-mediated metalation. Amide **12a** may be reduced to allow direct access to Ugi-type planar chiral ferrocenylamines **13** without chiral auxiliary assistance;
c) 2-TMS-*N*-ethylferrocenecarboxamide **7c** undergoes C-5 rather than the C-1′ deprotonation and thereby allows a latent silicon protection route[7] to the valuable enantiomeric ferrocene (*S*)-**7f**;

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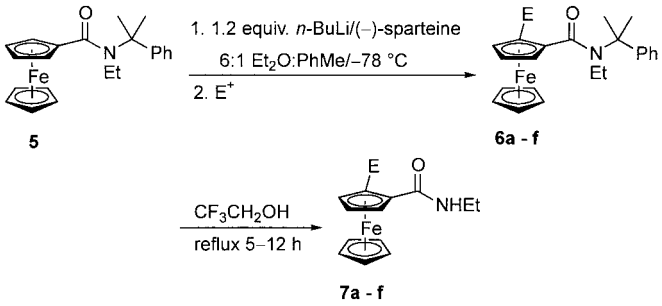
d) manipulation according to a) and b) modes allows access to new, only planar chiral ferrocenes and Hayashi-like ferrocenylphosphine ligands.[8]

Results and Discussion

A priori, the new cumylferrocenecarboxamide **5** was required to perform within two known constraints of the metalation reaction: a) possess sufficient steric bulk in order to achieve high enantioinduction in the (−)-sparteine-mediated D*o*M reaction[9] and b) maintain good solubility in diethyl ether at low temperatures.[10] Compound **5** met both of these criteria (Scheme 2).

Thus, metalation of **5** under optimized conditions (1.2 equiv. *n*-BuLi/(−)-sparteine/6:1 Et_2O:PhMe/ − 78 °C) gave, after quench with a variety of electrophiles, products **6** in good yields (Table 1). The absolute stereochemistry was established by single crystal X-ray analysis of the iodide **6f** as the (*R*)-enantiomer (Figure 1).[11] Decumylation [2,2,2-trifluoroethanol (TFE)/reflux/5 – 12 h] of products **6** led to 2-substituted *N*-ethylferrocenecarboxamides **7** smoothly and usually in quantitative yields.

The mildness of this deprotection method is underscored by the specific case **6b** in which the major



Scheme 2. (−)-Sparteine-mediated D*o*M of **5**, and decumylation of products **6** to secondary amides **7**.

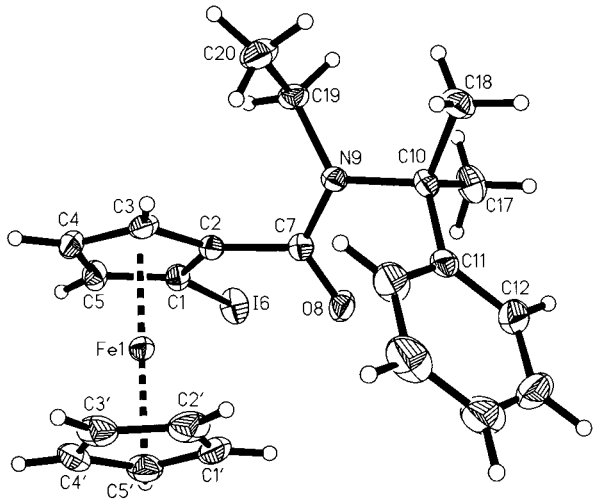


Figure 1. X-ray crystal structure of iodide **6f**.

product, **7b**, is accompanied by only minor amounts (9%) of the trifluoroethyl ether **7g**, E = $CH_2OCH_2CF_3$ whose formation would be expected to be greater under more acidic conditions based on the rapid generation of the α-ferrocenylmethyl carbocation.[12] Alternatively, glacial AcOH at rt was used to decumylate intermediate phosphine **6d** to provide **7d** in 61% overall yield. X-Ray crystallographic analysis of **7d**[11] showed it to have the same relative and absolute (*R*)-stereochemistry as **6f**.[13]

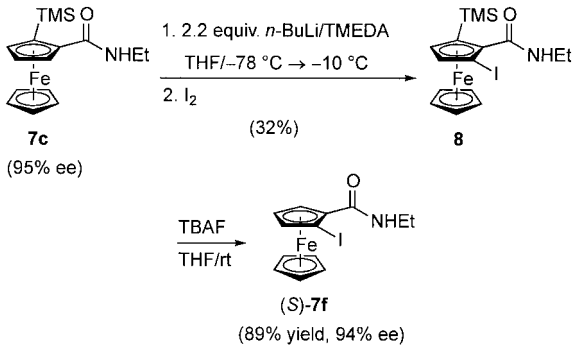
Possibly as a result of the smaller size of the secondary amide compared to the corresponding *N,N*-diisopropylamide,[2a] the trimethylsilyl derivative **7c** underwent metalation in the same ring and, following quench with I_2, afforded the trisubstituted ferrocene **8** as the only isolable product (Scheme 3). Desilylation furnished (*S*)-**7f**, the enantiomer of **7f** (Table 1), with minimal loss of enantiomeric excess thus overcoming, in principle, the unavailability of (+)-sparteine for the synthesis of enantiomeric series of planar chiral ferrocenyl amides.

Conversion of the secondary amides **7a**, **7c**, **7f** (Scheme 4) into the methyl esters **9a**, **9b** and **9c**,

Table 1. Preparation of planar chiral secondary *N*-ethylferrocenecarboxamides **7**.

E^+	E	**6**	Yield [%], **6**	**7**	Yield [%], **7**	ee [%], **7**[c]
MeI	Me	**6a**	87	**7a**	99	96
DMF	CH_2OCH_3[a]	**6b**	75[b]	**7b**	80[f]	95
TMSCl	TMS	**6c**	69	**7c**	99	95
Ph_2PCl	Ph_2P	**6d**	N.D.	**7d**	61[d]	N.D.[e]
$(MeS)_2$	MeS	**6e**	89	**7e**	99	88
ICH_2CH_2I	I	**6f**	72	**7f**	99	96

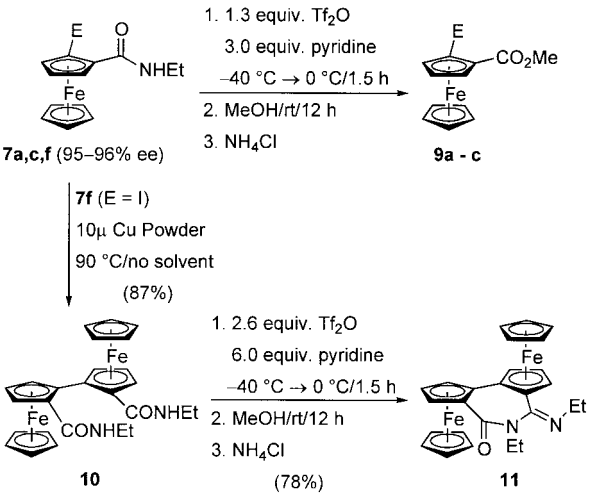
[a] Product aldehyde was reduced with $NaBH_4$ to give the corresponding alcohol, which was methylated using NaH/MeI.
[b] Overall yield.
[c] Determined on a Chiralcel OD column and compared to racemic material.
[d] Decumylated using AcOH/rt/90 min; overall yield from **5**.
[e] Compound underwent racemization rapidly during HPLC analysis. It was recrystallized and subjected to X-ray analysis (see Experimental Section).
[f] The trifluoroethyl ether (**7g**, 9%) was obtained as a by-product.



Scheme 3. Preparation of the antipode of **7f**.

respectively, by application of the very useful Charette conditions[6] was achieved in low to moderate yields (Table 2); however, in all cases, starting material was recovered, without loss of enantio-integrity, and recycled. This route represents a new and mild two-step hydrolysis protocol[14] from **6** for access to the scarcely known class of planar chiral ferrocenyl esters.[15]

Ullmann homocoupling of iodo amide **7f** (Scheme 4) provided efficiently the C_2-symmetric biferrocene diamide **10**.[16] Attempted double Charette esterification of (*R,R*)-**10** gave the structurally interesting and crystallographically verified[11] azepanone-bridged biferrocene **11**[17] (Figure 2), presumably by nucleophilic attack of



Scheme 4. Charette esterification of secondary ferrocenecarboxamides.

Table 2. Synthesis of planar chiral ferrocenyl esters.

E	**9**	yield [%], **9**[a]	ee [%], **9**
Me	**9a**	50(92)	96
TMS	**9b**	49(92)	93
I	**9c**	26(94)	96

[a] Yields in brackets are based on recovered starting material.

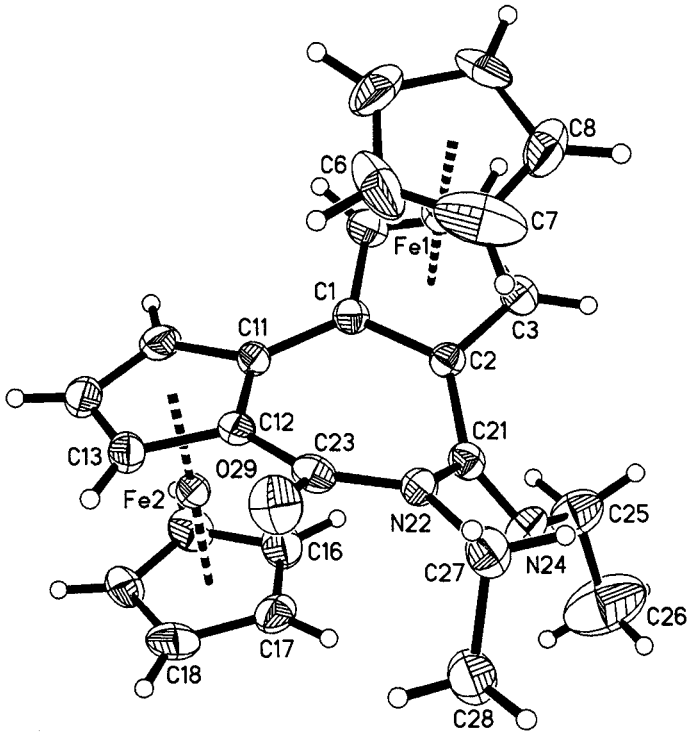
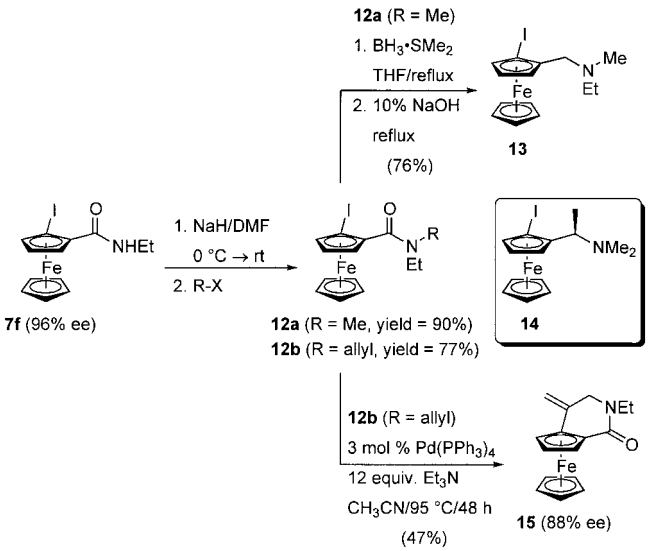


Figure 2. X-ray crystal structure of azepanone **11**.

one secondary amide group onto a monoimminium triflate intermediate.

The key secondary iodoferrocenylamide[18] (*R*)-**7f** (Scheme 5) also provided, by alkylation, a facile route to new planar chiral tertiary ferrocenecarboxamides which are inaccessible by direct (–)-sparteine-mediated metalation owing to predicted or potential competing deprotonation at alternate sites.[19] Thus, treatment of **7f** with NaH in DMF, followed by the addition of the



Scheme 5. Products derived from *N*-alkylation of **7f**.

requisite alkyl halide furnished new tertiary amides **12a, b** in good yields. The simplest case, *N*-ethyl-*N*-methylcarboxamide **12a**, underwent smooth reduction with $BH_3 \cdot SMe_2$ to the amine **13** which represents the *only planar chiral* constitutional isomer of the well known amine **14**.[20] Generalization of this procedure to other Ugi-type amines[21] is anticipated. More interestingly, the *N*-allylamide **12b** served as an excellent substrate for intramolecular Heck reaction. Exposure of **12b** to typical Heck conditions[22] provided the structurally unique annulated ferrocenyl piperidinone **15** in moderate yield and good enantiomeric excess.

Although simple olefinic ferrocenes are currently generating considerable interest as substrates for Grubbs metathesis,[23] only one report which takes advantage of this powerful reaction to prepare ferrocenes with planar chirality (albeit racemic) has appeared.[24] With the availability of the *N*-functionalized derivatives, this opportunity transparently presented itself. Thus, the formylferrocene **16** (Scheme 6) was subjected to excess $TMSCH_2MgCl$ to afford the intermediate carbinol which, without purification,[25] was treated with NaH/THF to furnish the vinylferrocene **17**. Decumylation (CF_3CH_2OH) gave the corresponding secondary amide in excellent (99%) yield, the mildness of the deprotection conditions having no effect on the acid-sensitive vinyl substituent.[26] Allylation (NaH/DMF/allyl bromide) gave the required Grubbs reaction precursor **18**. Application of widely used ring-closing metathesis (RCM) conditions and hydrogenation of the resulting double bond gave the Cp ring fused azepinone **19** in good yield and enantiomeric excess.

In order to derive potential chiral ligands of such systems, lactam **19** was subjected to further D*o*M chemistry. Deprotonation using standard conditions for tertiary benzamides, followed by quench with Ph_2PCl, gave the structurally novel phosphine **20**. Although originating from (−)-sparteine-mediated metalation of **5**, compound **20** showed opposite relative stereochemistry compared to the phosphine **7d**, but the same relative stereochemistry as the iodide (*S*)-**7f** prepared by the silyl deprotection route (Scheme 3).[27]

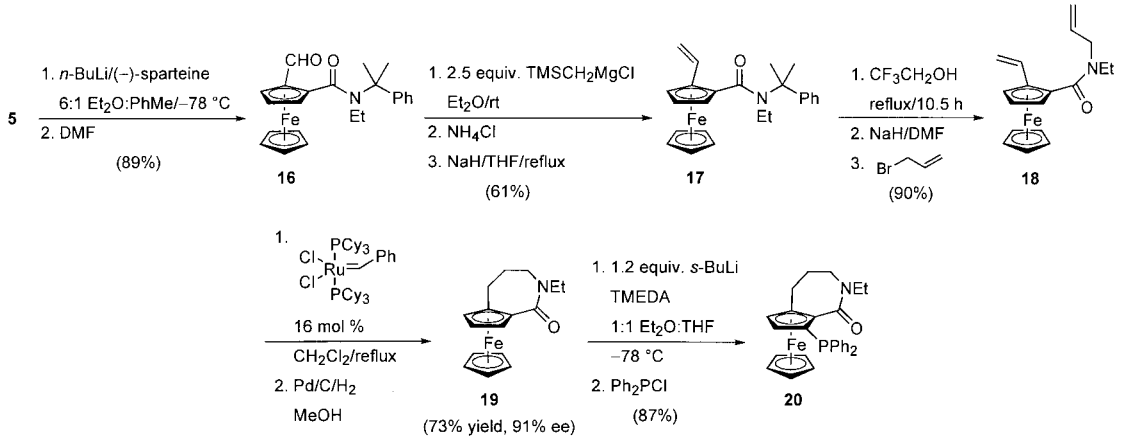
Conclusions

In conclusion, we have demonstrated that the *N*-cumyl-*N*-ethylferrocenecarboxamide **5** serves as a pivotal source for the (−)-sparteine-mediated, highly enantioselective, and general synthesis of new planar chiral ferrocenylamides **6** (Scheme 2). In contrast to the previously described **2**,[2a, b] amides **6** are easily manipulated under mild conditions. Thus conversion to secondary amides, **6** → **7**, and hence to esters, **7** → **9** and Ugi-type amines **12a** → **13** (Schemes 4 and 5), is readily achieved. Furthermore, (*R*)-**7c**, unlike the corresponding **2**, E = TMS,[28] may be converted, *via* silicon trickery (**8**), into (*S*)-**7f**. Finally, formylferrocene **16** serves as an intermediate for the preparation of the structurally novel phosphine **20** for which the key step is an unprecedented RCM reaction to afford a ferrocene with a Cp ring-fused azepinone. The utility of ferrocenyl amides **7** as precursors to new planar chiral ferrocene ligands and their exploration in asymmetric catalysis are under study in our laboratories.

Experimental Section

General Remarks

^{1}H NMR spectra were recorded on either Bruker AC-200, Avance-300 or Avance-400 instruments with tetramethylsilane (TMS) as an internal standard. Chemical shifts (δ) are reported in parts per million (ppm) relative to TMS. When peak multiplicities are given, the following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublet; m, multiplet; b, broad; brs, broad singlet. ^{13}C NMR spectra were proton decoupled and recorded on Bruker AC-200, Avance-300 or Avance-400 spectrometers using the carbon



Scheme 6. Ring-closing metathesis route to a novel ferrocenylphosphine, **20**.

signal of the deuterated solvent as the internal standard. ^{31}P NMR spectra were proton decoupled and recorded on an Avance-300 or Avance-400 instrument using H_3PO_4 as an external standard. ^{19}F NMR spectra were recorded on an Avance-400 instrument using $ClCF_3$ as an external standard. Melting points were determined on a Fisher Scientific hot-stage melting point apparatus and are uncorrected. IR spectra were recorded on a BOMEM MB-100, MB-120 or MB-Series FT-infrared spectrophotometer as liquid films on NaCl plates or as KBr discs. Electron impact mass spectra (EIMS) were performed on Kratos MS890 (4 kV, 35 eV, 220 °C), Hewlett-Packard 5890 Series II/5971A MSD, Varian Saturn 2000, Fisons VG-Quattro or Autospec instruments. Elemental analyses were obtained from Canadian Microanalytical Service, Ltd., Delta, BC. If microanalyses are not reported, the purity of the compounds were judged to be >90% by ^1H NMR and ^{13}C NMR analyses, and the molecular ion was confirmed by high resolution mass spectrometry (HRMS). All reported yields are isolated yields.

Stereoselectivities of the reactions were determined using a Waters HPLC system consisting of a 600E multi-solvent delivery system, a Waters 486 UV detector ($\lambda = 254$ nm), a Waters 746 integrator/recorder and a Chiracel OD column at rt. Enantiopurity assays were completed with both racemic and enantioenriched materials and repeated at least once in order to ensure the accuracy of the method used. Specific rotations were measured on a Rudolph Research Autopol II automatic polarimeter at the sodium D-line.

THF and Et_2O were freshly distilled from sodium benzophenone ketyl under nitrogen prior to use. PhMe was distilled from Na. CH_2Cl_2, DMF and CH_3CN were distilled from CaH_2 (under reduced pressure for DMF). *n*-BuLi and *s*-BuLi were purchased from FMC Corporation or Aldrich, as solutions in hexanes or cyclohexanes, respectively, and were titrated against *s*-butanol-1,10-phenanthroline.[29] *N,N,N′,N′*-Tetramethylethylenediamine (TMEDA), (−)-sparteine and pyridine were dried and distilled over CaH_2 and stored under argon. Cu powder was freshly purified[30] before use. All commercial materials were purchased from Aldrich Chemical Co., Lancaster Synthesis Ltd. or Strem Chemicals, Inc.

All the reactions were performed in flame- or oven-dried glassware under argon, using syringe-septum cap techniques. The −78 °C, −40 °C and 0 °C designations are approximate and refer to dry ice in acetone or ice/water slush. The phrase "standard work-up" refers to addition of water or saturated aqueous NH_4Cl, extraction with Et_2O or EtOAc, washing the organic extract with saturated brine solution, drying over $MgSO_4$, filtration, and evaporation to dryness under vacuum. Flash chromatography was carried out using Selecto silica gel 60 (0.032–0.063 mm).

Standard Method for the Lithiation of *N*-Cumyl-*N*-ethylferrocenecarboxamide (5)

A solution of (−)-sparteine (0.41 mL, 1.8 mmol, 1.2 equiv.) in Et_2O (24 mL, 16 mL/mmol of **5**) was stirred at rt (1 min), cooled to −78 °C, and treated with *n*-BuLi (1.8 mmol, 1.2 equiv.). After stirring (20 or 30 min) at −78 °C, a solution of **5** (0.563 g, 1.5 mmol) in PhMe (4 mL, 2.7 mL/mmol of **5**) was added dropwise *via* a syringe pump (~1 h). Any remaining starting material in the syringe was rinsed with Et_2O (1 mL) and was also added to the reaction mixture (over ~2 min). After stirring for 2 h at −78 °C, the reaction mixture was quenched by the addition of an electrophile (1.8 mmol, 1.2 equiv., except for the iodide), and the whole was allowed to warm slowly to rt (over at least 3 h, except for the iodide), or stirred for an additional 1 h at −78 °C before treatment with saturated aqueous NH_4Cl solution. The resulting mixture was subjected to standard work-up to afford the crude product.

N-Cumyl-*N*-ethylferrocenecarboxamide (5)

A stirred suspension of ferrocenecarboxylic acid (10.6 g, 46.1 mmol) in PhMe (79 mL) under a $CaCl_2$ drying tube was treated with oxalyl chloride (8.4 mL, 96.3 mmol) and a catalytic amount of DMF (0.95 mL, 13.8 mmol), and the whole was stirred for 1.5 h at rt. The PhMe and excess oxalyl chloride were removed under vacuum, and the residue was taken up in Et_2O (150 mL) and cooled to 0 °C. The mixture was treated with a solution of Et_3N (19.5 mL, 140 mmol) and cumylamine (7.48 g, 55.3 mmol) in Et_2O (20 mL) and the whole was stirred for 12 h at rt. The mixture was treated with saturated aqueous NH_4Cl solution, extracted with CH_2Cl_2 ($\times 3$), and the organic extract was washed with water ($\times 2$), brine, dried (anhydrous $MgSO_4$), and thoroughly dried under high vacuum. The crude orange-brown product was dissolved in dry THF (200 mL), cooled to 0 °C and treated with NaH (7.93 g, 60% dispersion in mineral oil, 0.198 mol), and the reaction mixture was stirred at rt for 20 min. The solution was treated with EtI (5.29 mL, 66.1 mmol) and the reaction mixture was heated at reflux for 6 h (**NB**: reflux for more than 8 h leads to decomposition), cooled to 0 °C and subjected to standard work-up. Column chromatography of the pre-adsorbed product (hexanes:EtOAc, 80:20) afforded **5** as a red-orange solid; yield: 8.62 g (50%); mp 103–106 °C (heptane); IR (KBr): $\nu_{max} = 3106, 3083, 3052, 3000, 2963, 2923, 2870, 1619$ cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.43–7.17$ (m, 5H), 4.64 (t, 2H, $J = 2.0$ Hz), 4.26 (t, 2H, $J = 2.0$ Hz), 4.08 (s, 5H), 3.77 (q, 2H, $J = 6.9$ Hz), 1.74 (s, 6H), 1.36 (t, 3H, $J = 6.9$ Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 171.0, 149.7, 128.0, 125.5, 124.0, 80.7, 70.3, 69.8, 69.1, 61.8, 40.6, 28.4, 18.5$; EIMS: *m/z* (%) = 375 (M^+, 27), 257 (76), 121 (39), 119 (60), 91 (100); HRMS (EI): calcd. for $C_{22}H_{25}NOFe$: 375.1286; found: 375.1284; anal. calcd. for $C_{22}H_{25}NOFe$: C 70.41, H 6.71, N 3.73; found: C 70.30, H 6.89, N 3.86.

(*S*)-2-Methyl-*N*-cumyl-*N*-ethylferrocenecarboxamide (6a)

According to the Standard Method, a stirred solution of (−)-sparteine (0.41 mL, 1.8 mmol) and *n*-BuLi (0.73 mL, 2.47 M, 1.8 mmol) in Et_2O (24 mL) was treated with a solution of **5** (0.563 g, 1.5 mmol) in PhMe (4 mL), and after 2 h, the reaction mixture was quenched with MeI (0.11 mL, 1.8 mmol). Standard work-up followed by column chromatography (hexanes:EtOAc, 9:1) afforded **6a** as an orange oil; yield: 0.510 g (87%); IR (NaCl, neat): $\nu_{max} = 3092, 2978, 1641$ cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.40–7.11$ (m, 5H), 4.28 (s, 1H), 4.08 (s, 1H), 3.99 (s, 6H), 3.66–3.31 (m, 2H), 2.05 (s, 3H), 1.75 (s, 3H), 1.66 (s, 3H), 1.05 (t, 3H, $J = 6.9$ Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta =$ 170.4, 149.3, 127.7, 125.3, 124.0, 85.3, 84.6, 70.2, 69.2, 66.5, 65.2, 61.0, 41.0, 29.5, 27.4, 17.4, 13.2; EIMS: *m/z* (%) = 389 (M^+, 45), 271 (100), 198 (32), 133 (58); HRMS (EI): calcd. for $C_{23}H_{27}NOFe$: 389.1442; found: 389.1428.

(*S*)-2-Hydroxymethyl-*N*-cumyl-*N*-ethylferrocenecarboxamide (*pre*-6b) and (*S*)-2-Methoxymethyl-*N*-cumyl-*N*-ethylferrocenecarboxamide (6b)

According to the Standard Method, a stirred solution of (−)-sparteine (0.41 mL, 1.8 mmol) and *n*-BuLi (0.73 mL, 2.47 M, 1.8 mmol) in Et_2O (24 mL) was treated with a solution of **5** (0.563 g, 1.5 mmol) in PhMe (4 mL), and after 2 h, the reaction mixture was quenched with DMF (0.14 mL, 1.8 mmol). Addition of water and standard work-up afforded the crude aldehyde as a dark red-orange oil, which was dissolved in MeOH (23 mL), treated with $NaBH_4$ (0.170 g, 3.0 mmol) and stirred for 12 h at rt. The mixture was poured carefully into ice-cooled saturated aqueous NH_4Cl solution, and the whole was extracted with Et_2O ($\times 2$), and the combined organic layer was dried (anhydrous $MgSO_4$) and concentrated under vacuum. Column chromatography (hexanes:EtOAc 1:1) afforded the methyl carbinol ***pre*-6b** as an orange oil; yield: 0.493 g (81%); IR (NaCl, neat): $\nu_{max} = 3392, 3089, 2975, 1602\ cm^{-1}$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.38-7.11$ (m, 5H), 4.65 (b, 1H), 4.41 (s, 1H), 4.28 (s, 1H), 4.25 (s, 1H), 4.30–4.19 (m, 2H), 4.12 (s, 5H), 4.04–3.89 (m, 1H), 3.61–3.44 (m, 1H), 1.78 (s, 3H), 1.62 (s, 3H), 1.20 (t, 3H, $J = 7.2$ Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 172.3, 148.9, 127.6, 125.2, 123.6, 91.8, 80.5, 70.6, 69.9, 67.5, 66.5, 61.6, 58.8, 41.0, 29.7, 26.6, 17.9$; EIMS: *m/z* (%) = 405.2 (M^+, 35), 322 (31), 222 (100), 204 (40), 132 (34), 119 (83); HRMS (EI): calcd. for $C_{23}H_{27}NO_2Fe$: 405.1390; found: 405.1390.

NaH (0.146 g, 60% dispersion in mineral oil, ~3.7 mmol) was washed with hexanes (4 mL), and the solvent was carefully removed by syringe and replaced with DMF (8 mL). A solution of carbinol ***pre*-6b** (0.493 g, 1.22 mmol) in DMF (6 mL) was added by cannula to the stirred suspension of NaH in DMF at 0 °C. Additional DMF (6 mL) was added to rinse the flask containing ***pre*-6b**, and this was also transferred to the reaction mixture. The reaction mixture was stirred at rt (30 min) before MeI (0.10 mL, 1.6 mmol) was added. After 3.5 h, the mixture was cooled to 0 °C, and saturated aqueous NH_4Cl solution and water were sequentially added slowly. The product was extracted with Et_2O ($\times 2$) and the combined organic extract was washed water ($\times 2$), brine, dried (anhydrous $MgSO_4$) and concentrated under vacuum. Column chromatography (hexanes:EtOAc 3:1) afforded **6b** as a viscous orange oil; yield: 0.472 g (92%); IR (NaCl, neat): $\nu_{max} = 3087, 2978, 1640\ cm^{-1}$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.41-7.13$ (m, 5H), 4.53 (d, 1H, $J = 11.0$ Hz), 4.39 (b, 1H), 4.30 (b, 1H), 4.20 (d, 1H, $J = 11.0$ Hz), 4.14–4.12 (m, 1H), 4.04 (s, 5H), 3.73–3.37 (m, 2H), 3.30 (s, 3H), 1.76 (s, 3H), 1.67 (s, 3H), 1.14 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 169.8, 149.5, 127.9, 125.4, 123.9, 85.3, 85.2, 70.2, 69.7, 68.8, 67.2, 66.4, 61.3, 57.9, 41.3, 29.9, 27.2, 17.6$; EIMS: *m/z* (%) = 419 (M^+, 41), 354 (17), 322 (30), 236 (57), 119 (85), 105 (100); HRMS (EI): calcd. for $C_{24}H_{29}NO_2Fe$: 419.1548; found: 491.1542.

(*R*)-2-Trimethylsilyl-*N*-cumyl-*N*-ethylferrocenecarboxamide (6c)

According to the Standard Method, a stirred solution of (−)-sparteine (0.28 mL, 1.2 mmol) and *n*-BuLi (0.48 mL, 2.50 M, 1.2 mmol) in Et_2O (16 mL) was treated with a solution of **5** (0.375 g, 1.0 mmol) in PhMe (2.7 mL), and after 2 h, the reaction mixture was quenched with TMSCl (0.15 mL, 1.2 mmol). Standard work-up followed by column chromatography (hexanes: EtOAc, 19:1) afforded **6c** as an orange oil; yield: 0.307 g (69%); IR (NaCl, neat): $\nu_{max} = 3089, 2974, 1642\ cm^{-1}$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.41-7.14$ (m, 5H), 4.52–4.51 (m, 1H), 4.30–4.28 (m, 1H), 4.14 (s, 5H), 4.12–4.11 (m, 1H), 3.68–3.49 (m, 1H), 3.40–3.22 (m, 1H), 1.80 (s, 3H), 1.67 (s, 3H), 1.09 (t, 3H, $J = 6.9$ Hz), 0.21 (s, 9H); ^{13}C NMR (50.3 MHz, $CDCl_3$); $\delta =$ 170.6, 149.3, 128.0, 125.5, 124.3, 91.7, 73.8, 70.2, 69.8, 69.1, 61.4, 41.5, 30.1, 27.2, 17.6, 0.6; EIMS: *m/z* (%) = 447 (M^+, 14), 314 (100), 151 (83), 135 (47), 123 (46); HRMS (EI): calcd. for $C_{25}H_{33}NOSiFe$: 447.1681; found: 447.1687.

(*R*)-2-Thiomethyl-*N*-cumyl-*N*-ethylferrocenecarboxamide (6e)

According to the Standard Method, a stirred solution of (−)-sparteine (0.28 mL, 1.2 mmol) and *n*-BuLi (0.48 mL, 2.48 M, 1.2 mmol) in Et_2O (16 mL) was treated with a solution of **5** (0.375 g, 1.0 mmol) in PhMe (2.7 mL), and after 2 h, the reaction mixture was quenched with $(MeS)_2$ (0.11 mL, 1.2 mmol). Standard work-up followed by column chromatography (hexanes: EtOAc, 17:1) afforded **6e** as an orange oil; yield: (0.375 g (89%); IR (NaCl, neat): $\nu_{max} = 3092, 2978, 1644\ cm^{-1}$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.49-7.45$ (m, 2H), 7.35–7.28 (m, 2H), 7.20–7.13 (m, 1H), 4.42 (b, 1H), 4.32 (b, 1H), 4.14 (s, 6H), 3.59-3.36 (m, 2H), 2.30 (s, 3H), 1.76 (s, 6H), 1.07 (t, 3H, $J = 7.1$ Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 168.4, 148.8, 127.5, 125.2, 124.2, 86.7, 85.2, 70.9, 69.6, 68.3, 66.2, 61.2, 41.2, 28.8, 28.0, 18.8, 17.2$; EIMS: *m/z* (%) = 421 (M^+, 89), 303 (73), 245 (44), 217 (51), 165 (72), 119 (100); HRMS (EI): calcd. for $C_{23}H_{27}NOSFe$: 421.1163; found: 421.1194.

(*R*)-2-Iodo-*N*-cumyl-*N*-ethylferrocenecarboxamide (6f)

According to the Standard Method, a stirred solution of (−)-sparteine (1.66 mL, 7.2 mmol) and *n*-BuLi (2.77 mL, 2.60 M, 7.2 mmol) in Et_2O (98 mL) was treated with a solution of **5** (2.25 g, 6.0 mmol) in PhMe (16 mL), and after 2 h, the reaction mixture was quenched with a solution of ICH_2CH_2I (2.37g, 8.4 mmol) in Et_2O (20 mL), added over 45 min. Stirring was continued at −78 °C for 2 h, the mixture was treated with saturated aqueous NH_4Cl solution and warmed quickly to rt. The solution was extracted with Et_2O ($\times 3$), and the combined organic extract was washed with saturated aqueous $Na_2S_2O_3$ solution, dried (anhydrous $MgSO_4$) and concentrated under vacuum. Column chromatography (hexanes:EtOAc, 88:12) afforded **6a** as an orange solid; yield: 2.16 g (72%); mp 126–127 °C (heptane); $[\alpha]^{23}_D$: +11.5 (*c* 0.52, $CHCl_3$); CSP HPLC analysis (Chiralcel OD; eluent: hexanes:*i*-PrOH, 99:1, flow 0.4 mL/min) determined 96% ee [t_R(major) = 31.06 min, t_R(minor) = 32.78 min]; X-ray (CCDC 163407): $C_{22}H_{24}FeINO$, $M = 501.20$, orthorhombic, $P2_12_12_1$, $a = 10.2948(8)$ Å, $b = 12.8470(12)$ Å, $c =$ 14.8854(11) Å, $V = 1968.7(3)$ Å^3, $Z = 4$; $D_c = 1.691$ g/cm^3, $F(000) = 1000$, $T = 180$K. Data were collected on a Siemens P4 diffractometer system with graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å); 5198 data were collected. The structure was solved by Patterson and Fourier (SHELXTL IRIS), corrected for Lorentz-polarization effects and refined by full-matrix least squares on F^2 resulting in final R, R_w, and

GOF (for 4754 data with $F > 2\sigma(F)$ of 0.0179, 0.0408 and 1.773, respectively, for solution using the (*R*) model. The corresponding values for the (*S*) model were 0.0266, 0.0622 and 2.703; IR (NaCl, neat): $\nu_{max} = 3088, 2978, 1644\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.48-7.46$ (m, 2H), 7.35 – 7.30 (m, 2H), 7.22 – 7.17 (m, 1H), 4.46 – 4.42 (m, 1H), 4.41 – 4.40 (m, 1H), 4.19 – 4.17 (m, 1H), 4.16 (s, 5H), 3.53 – 3.31 (m, 2H), 1.78 (s, 3H), 1.74 (s, 3H), 1.04 (t, 3H, $J = 7.1$ Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta =$ 168.0, 148.9, 127.9, 125.7, 124.6, 89.4, 74.4, 72.9, 68.1, 68.0, 61.6, 41.7, 41.4, 29.2, 28.3, 17.3; EIMS: *m/z* (%) = 501 (M^+, 11), 255 (47), 183 (42), 119 (100); HRMS (EI): calcd. for $C_{22}H_{24}NOIFe$: 501.0212; found: 501.0247.

(*S*)-2-Methyl-*N*-ethylferrocenecarboxamide (7a)

A stirred solution of **6a** (0.510 g, 1.31 mmol) in TFE (14 mL) was heated at reflux for 11 h. Evaporation of the solvent under vacuum and column chromatography (hexanes:EtOAc, 2:3) afforded **7a** as an orange oil that slowly crystallized; yield: 0.350 g (99%); mp 78 – 80 °C (CH_2Cl_2); $[\alpha]_D^{23}$: − 74.1 (*c* 1.16, $CHCl_3$); CSP HPLC analysis (Chiralcel OD; eluent: hexanes:*i*-PrOH, 90:10, flow 1.0 mL/min) determined 96% ee [t_R(major) = 9.64 min, t_R(minor) = 20.94 min]; IR (NaCl, neat): $\nu_{max} = 3364$, 3315, 3070, 2974, 1628, 1537 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 6.23$ (brt, 1H), 4.51 – 4.50 (m, 1H), 4.20 (m, 1H), 4.12 (m, 1H), 4.10 (s, 5H), 3.43-3.33 (m, 2H), 2.28 (s, 3H), 1.19 (t, 3H, $J = 6.9$ Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 170.7$, 85.2, 74.7, 72.3, 69.9, 67.2, 67.1, 33.9, 15.0, 14.4; EIMS: *m/z* (%) = 271 (M^+, 100), 133 (92), 121 (51), 105 (45); HRMS (EI): calcd. for $C_{14}H_{17}NOFe$: 271.0660; found: 271.0662; anal. calcd. for $C_{14}H_{17}NOFe$: C 62.02, H 6.32, N 5.17; found: C 62.12, H 6.31, N 5.08.

(*S*)-2-Methoxymethyl-*N*-ethylferrocenecarboxamide (7b) and (*S*)-2-trifluoroethoxymethyl-*N*-ethylferrocenecarboxamide (7g)

A stirred solution of amide **6b** (0.461 g, 1.10 mmol) in TFE (11 mL) was heated at reflux for 5 h. Evaporation of the solvent under vacuum and column chromatography (hexanes:EtOAc, 1:1) afforded, in order, trifluoroethyl ether **7g** (0.036 g, 9%) and methyl ether **7b** (0.263 g, 80%).

7g: Viscous orange oil; CSP HPLC analysis (Chiralcel OD; eluent: hexanes:*i*-PrOH, 90:10, flow 1.0 mL/min) determined 91% ee [t_R(major) = 10.28 min, t_R(minor) = 28.91 min]; IR (NaCl, neat): $\nu_{max} = 3324$, 3094, 2976, 2932, 2875, 1628, 1544 cm^{-1}; ^{19}F NMR (376.4 MHz, $CDCl_3$): $\delta = -174.9$ (t, 3F, $^3J_{(^{19}F-^1H)} = 9.1$ Hz); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 6.60$ (b, 1H), 4.97 (d, 1H, $J = 11.8$ Hz), 4.79 – 4.77 (m, 1H), 4.51 (d, 1H, $J = 11.8$ Hz), 4.36 – 4.29 (m, 2H), 4.20 (s, 5H), 4.03 – 3.80 (m, 2H), 3.47 – 3.32 (m, 2H), 1.19 (t, 3H, $J = 7.1$ Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 169.4, 123.4$ (q, $^1J_{(^{13}C-^{19}F)} = 279.0$ Hz), 80.0, 78.1, 77.2, 72.8, 71.5, 71.2, 70.3, 69.6, 68.9, 66.8 (q $^2J_{(^{13}C-^{19}F)} = 34.9$ Hz), 34.4, 14.9; EIMS: *m/z* (%) = 369 (M^+, 26), 304 (12), 224 (93), 105 (100); HRMS (EI): calcd. for $C_{16}H_{18}NO_2F_3Fe$: 369.0639; found: 369.0640.

7b: Orange oil; CSP HPLC analysis (Chiralcel OD; eluent: hexanes:*i*-PrOH, 90:10, flow 1.0 mL/min) determined 95% ee [t_R(major) = 10.92 min, t_R(minor) = 29.50 min]; IR (NaCl, neat): $\nu_{max} = 3329$, 3091, 2974, 1638, 1541 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.35$ (b, 1H), 4.86 (s, 1H), 4.69 (d, 1H, $J =$ 11.5 Hz), 4.28 (s, 1H), 4.25 – 4.19 (m, 2H), 4.17 (s, 5H), 3.44 – 3.28 (m, 2H), 3.36 (s, 3H), 1.18 (t, 3H, $J = 7.3$ Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 169.2$, 80.2, 78.0, 72.3, 71.5, 69.7, 69.6, 67.9, 57.0, 33.8, 14.5; EIMS: *m/z* (%) = 301 (M^+, 76), 269 (19), 236 (44), 206 (60), 178 (40), 135 (100), 121 (43), 105 (86); HRMS (EI): calcd. for $C_{15}H_{19}NO_2Fe$: 301.0765; found: 301.0762.

(*R*)-2-Trimethylsilyl-*N*-ethylferrocenecarboxamide (7c)

A stirred solution of amide **6c** (0.307 g, 0.69 mmol) in TFE (10 mL) was heated at reflux for 6 h. Evaporation of the solvent under vacuum and column chromatography (hexanes:EtOAc, 85:15) gave **7c** as an orange oil which slowly solidified; yield: 0.226 g (99%); mp 104 – 106 °C; $[\alpha]_D^{23}$: − 89.8 (*c* 0.33, $CHCl_3$); CSP HPLC analysis (Chiralcel OD; eluent: hexanes:*i*-PrOH, 90:10, flow 1.0 mL/min) determined 95% ee [t_R(major) = 6.35 min, t_R(minor) = 13.04 min]; IR (KBr): $\nu_{max} = 3298$, 2950, 1627, 1549 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 5.78$ (b, 1H), 4.62 – 4.60 (m, 1H), 4.41 – 4.39 (m, 1H), 4.28 – 4.26 (m, 1H), 4.18 (s, 5H), 3.50 – 3.28 (m, 2H), 1.22 (t, 3H, $J = 7.3$ Hz) 0.33 (s, 9H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 170.5$, 82.2, 76.7, 73.7, 71.4, 70.7, 69.5, 34.4, 15.3, 0.4; EIMS: *m/z* (%) = 329 (M^+, 18), 314 (100), 204 (25), 149 (25); HRMS (EI): calcd. for $C_{16}H_{23}NOSiFe$: 329.0898; found: 329.0900.

(*R*)-2-Diphenylphosphino-*N*-ethylferrocenecarboxamide (7d)

To a solution of (−)-sparteine (1.61 mL, 7.0 mmol) in Et_2O (50 mL) at − 78 °C was added *n*-BuLi (2.80 mL, 2.50 M, 7.0 mmol). The solution was stirred (0.5 h) and treated dropwise with a solution of **5** (1.876 g, 5.0 mmol) in a mixture of PhMe (5mL) and Et_2O (100 mL) over a period of 1.5 h. Stirring was continued (1.5 h) before a solution of Ph_2PCl (1.35 mL, 7.5 mmol) in Et_2O (20 mL) was added dropwise. The suspension was stirred (1 h) at − 78 °C and allowed to warm to − 50 °C over 4 h. Saturated NH_4Cl was added and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layer was dried over anhydrous Na_2SO_4, and concentrated under vacuum. The crude product (**6d**) was dissolved in glacial acetic acid (50 mL) and stirred for 2.5 h at rt. After concentration under vacuum, the residue was purified by column chromatography (hexanes:EtOAc, 10:1) to afford **7d** as a yellow solid which could be recrystallized to enantiomeric purity from CH_2Cl_2; yield: 1.33 g (61%); mp 63 – 65 °C (CH_2Cl_2); X-ray (CCDC 163409) $C_{25}H_{24}FeNOP$, $M = 441.27$, monoclinic, $P2_1$, $a = 9.813(2)$ Å, $b = 9.7356(19)$ Å, $c =$ 11.703(2) Å, $\beta = 100.341(4)°$; $V = 1099.8(4)$ Å^3, $Z = 2$; $D_c =$ 1.332 g/cm^3, $F(000) = 460$, $T = 296$ K. Data were collected on a CCD-detector-equipped SMART system with graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å); 4343 data were collected. The structure was solved by direct method (SHELXTL version 5.0), corrected for Lorentz-polarization effects and refined by full-matrix least squares on F^2 resulting in final R, R_w, and GOF (for 2478 data with $F > 4\sigma(F)$ of 0.0346, 0.0503 and 0.861, respectively, for solution using the (*R*) model. The corresponding values for the (*S*) model were 0.0863, 0.1011 and 0.848; IR (KBr): $\nu_{max} = 3423$, 3410, 3343, 3067, 3051, 2967,

2926, 2870, 2855, 1632, 1534, cm^{-1}; ^{31}P NMR (121.5 MHz, CD_2Cl_2): δ = − 19.27; ^1H NMR (300 MHz, CD_2Cl_2): δ = 7.61 – 7.56 (m, 2 H), 7.47 – 7.45 (m, 3 H), 7.32 – 7.31 (m, 3 H), 7.23 – 7.19 (m, 2 H), 7.04 (brs, 1 H), 5.07 – 5.05 (m, 1 H), 4.48 (t, 1H, J = 2.4 Hz), 4.16 (s, 5H), 3.82 – 3.81 (m, 1H), 3.37 – 3.32 (m, 2H, J = 7.2 Hz), 1.14 (t, 3H, J = 7.2 Hz); ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ = 169.7, 139.0 (d, $J_{^{31}P-^{13}C}$ = 8.1 Hz), 137.0 (d, $J_{^{31}P-^{13}C}$ = 8.4 Hz), 135.4 (d, $J_{^{31}P-^{13}C}$ = 21.1 Hz), 132.5 (d, $J_{^{31}P-^{13}C}$ = 18.3 Hz), 129.9, 128.7, 128.6, 128.6, 128.5, 81.7 (d, $J_{^{31}P-^{13}C}$ = 18.4 Hz), 76.0 (d, $^1J_{^{31}P-^{13}C}$ = 10.7 Hz), 74.6 (d, $^1J_{^{31}P-^{13}C}$ = 4.0 Hz), 73.1 (d, $^1J_{^{31}P-^{13}C}$ = 2.6 Hz), 71.5, 71.1, 34.7, 15.3; EIMS: *m/z* (%) = 441 (M^+, 25), 376 (17), 226 (22), 215 (10), 201 (98), 183 (27), 170 (47), 141 (12), 133 (19), 129 (13), 121 (100), 115 (14), 109 (14), 107 (16), 104 (11); HRMS (EI): calcd. for $C_{25}H_{24}NOPFe$: 441.0945; found: 441.0956.

(*R*)-2-Thiomethyl-*N*-ethylferrocenecarboxamide (7e)

A stirred solution of amide **6e** (0.375 g, 0.89 mmol) in TFE (9 mL) was heated at reflux for 10 h. Evaporation of the solvent under vacuum and column chromatography (hexanes:EtOAc, 1:1) gave **7e** as an orange oil that slowly crystallized; yield: 0.268 g (99%); mp 71 – 74 °C; $[\alpha]_D^{23}$: − 10.2 (*c* 0.59, $CHCl_3$); CSP HPLC analysis (Chiralcel OD; eluent: hexanes:*i*-PrOH, 90:10, flow 1.0 mL/min) determined 88% ee [t_R(major) = 6.75 min, t_R(minor) = 10.33 min]; IR (NaCl, neat): ν_{max} = 3318, 3091, 2973, 1640, 1535 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 5.04 – 5.02 (m, 1H), 4.48 – 4.46 (m, 1H), 4.37 – 4.35 (m, 1H), 4.19 (s, 5H), 3.53 – 3.38 (m, 2H), 2.23 (s, 3H), 1.25 (t, 3H, J = 7.2 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 169.2, 79.0, 76.6, 76.1, 71.5, 70.7, 69.6, 33.8, 21.3, 14.9; EIMS: *m/z* (%) = 303 (M^+, 100), 245 (52), 217 (42), 152 (46), 121 (32); HRMS (EI): calcd. for $C_{14}H_{17}NOSFe$: 303.0380; found: 303.0397.

(*R*)-2-Iodo-*N*-ethylferrocenecarboxamide (7f)

A stirred solution of amide **6f** (2.15 g, 4.29 mmol) in TFE (43 mL) was heated at reflux for 12 h. Evaporation of the solvent under vacuum and column chromatography (hexanes:EtOAc, 1:1) gave **7f** as a viscous orange oil; yield: 1.64 g (99%); $[\alpha]^{23}_D$: + 53.5 (*c* 0.64, $CHCl_3$); CSP HPLC analysis (Chiralcel OD; eluent: hexanes:*i*-PrOH, 85:15, flow 1.0 mL/min) determined 96% ee [t_R(major) = 13.20 min, t_R(minor) = 15.73 min]; [**NB: 7f** was observed to racemize slowly in this solvent system. A sample prepared by dissolving **7f** in hexanes:EtOAc (85:15) before injection was found not to undergo racemization. The purified compound is configurationally and chemically stable for at least one month in the dark at rt]; IR (NaCl, neat): ν_{max} = 3307, 3080, 2967, 1633, 1533 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 6.50 (b, 1H), 4.89 – 4.87 (m, 1H), 4.59 – 4.57 (m, 1H), 4.38 (t, 1H, J = 2.2 Hz), 4.22 (s, 5H), 3.48 (quintet, 2H, J = 6.8 Hz), 1.26 (t, 3H, J = 6.9 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 168.2, 78.2, 76.9, 72.7, 71.0, 69.5, 39.5, 34.5, 15.0; EIMS: *m/z* (%) = 383 (M^+, 46), 255 (56), 184 (74), 128 (100); HRMS (EI): calcd. for $C_{13}H_{14}NOIFe$: 382.9470; found: 382.9495.

(*S*)-2-Iodo-5-trimethylsilyl-*N*-ethylferrocenecarboxamide (8)

A stirred solution of trimethylsilane **7c** (0.165 g, 0.5 mmol) and TMEDA (0.17 mL, 1.1 mmol) in THF (5 mL) at 78 °C, was treated with *s*-BuLi (0.82 mL, 1.34 M, 1.1 mmol), and the reaction mixture was warmed to − 10 °C and stirred for 2 h. The mixture was cooled back to − 78 °C and a solution of I_2 (0.305 g, 1.2 mmol, 2.4 equiv.) in THF (3 mL) was added slowly and the whole was allowed to warm to rt. Standard work-up (including washing once with saturated aqueous $Na_2S_2O_3$ solution), followed by column chromatography (hexanes: EtOAc, 90:10) afforded **8** as an orange oil; yield: 72 mg (32%); IR (NaCl, neat): ν_{max} = 3415, 3092, 2958, 1652, 1519 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 6.40 (b, 1H), 4.65 – 4.63 (m, 1H), 4.30 – 4.28 (m, 1H), 4.20 (s, 5H), 3.47 (m, 2H), 1.28 (t, 3H, J = 7.3 Hz), 0.29 (s, 9H); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 168.6, 85.7, 78.8, 76.5, 74.0, 72.5, 43.8, 34.7, 15.1, 0.1; EIMS: *m/z* (%) = 455 (M^+, 7), 440 (65), 256 (18), 121 (56), 69 (100); HRMS (EI): calcd. for $C_{15}H_{19}NOSiIFe$ ($M^+ - CH_3$): 439.9630; found: 439.9616.

(*S*)-2-Iodo-*N*-ethylferrocenecarboxamide [(*S*)-7f]

A solution of **8** (72 mg, 0.16 mmol) in THF (2 mL) was treated with TBAF (0.5 mL, 1.0 M in THF, 0.5 mmol) and the reaction mixture was stirred at rt for 3 h. Evaporation of the solvent under vacuum followed by column chromatography (hexanes: EtOAc, 1:1) afforded (*S*)-**7f** as an orange oil; yield: 54 mg (89%). CSP HPLC analysis (Chiralcel OD; eluent: hexanes: *i*-PrOH, 85:15, flow 1.0 mL/min) determined 94% ee [t_R(minor) = 13.20 min, t_R(major) = 15.68 min]. [**NB:** (*S*)-**7f** was observed to racemize slowly in this solvent system. A sample prepared by dissolving (*S*)-**7f** in hexanes:EtOAc (85:15) before injection was found not to undergo racemization]. The compound showed ^1H NMR spectral data in agreement with that reported above for (*R*)-**7f**.

(*S*)-2-Methyl(methoxycarbonyl)ferrocene (9a)

A stirred solution of **7a** (0.334 g, 1.23 mmol) and pyridine (0.30 mL, 1.6 mmol) in CH_2Cl_2 (6 mL) at − 40 °C was treated with Tf_2O (0.27 mL, 1.6 mmol) over 20 min. The reaction mixture was allowed to warm slowly to 0 °C (2 h) and maintained at 0 °C for an additional 10 h. Absolute MeOH (2.5 mL, 61 mmol) was added, and stirring was continued for an additional 12 h at rt before saturated aqueous NH_4Cl solution was added. The whole was extracted with CH_2Cl_2 (× 2), and the combined organic extract was dried (anhydrous $MgSO_4$) and concentrated under vacuum. Column chromatography (hexanes:EtOAc, 25:2) afforded **9a** as an orange oil; yield: 0.159 g (50%). CSP HPLC analysis (Chiralcel OD; eluent: hexanes:*i*-PrOH, 96:4, flow 1.0 mL/min) determined 96% ee [t_R(major) = 6.17 min, t_R(minor) = 7.24 min]; IR (NaCl, neat): ν_{max} = 3093, 2988, 1713 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 4.70 – 4.69 (m, 1H), 4.30 – 4.29 (m, 1H), 4.22 (brt, 1H), 4.11 (s, 5H), 3.80 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 172.9, 86.9, 73.4, 70.2, 70.1, 69.2, 68.7, 51.2, 14.5; EIMS: *m/z* (%) = 258 (M^+, 6), 195 (13), 149 (12), 122 (13), 85 (46), 57 (100); HRMS (EI): calcd. for $C_{13}H_{14}O_2Fe$: 258.0343; found: 258.0365.

(*R*)-2-Trimethylsilyl(methoxycarbonyl)ferrocene (9b)

A stirred solution of **7c** (0.166 g, 0.5 mmol) and pyridine (0.12 mL, 1.5 mmol) in CH_2Cl_2 (5 mL) at -40 °C was treated with Tf_2O (0.11 mL, 0.65 mmol) over 20 min. The reaction mixture was allowed to warm slowly to 0 °C (2 h) and maintained at 0 °C for an additional 10 h. Absolute MeOH (1 mL, 25 mmol) was added, and stirring was continued for an additional 12 h at rt before saturated aqueous NH_4Cl solution was added. The product was extracted with CH_2Cl_2 ($\times 2$) and the combined organic extract was dried (anhydrous $MgSO_4$) and concentrated under vacuum. Column chromatography (hexanes: EtOAc, 19:1) afforded **9b** as an orange oil; yield: 77 mg (49%). CSP HPLC analysis (Chiralcel OD; eluent: hexanes: *i*-PrOH, 99:1, flow 0.35 mL/min) determined 93% ee [t_R(major) = 14.06 min, t_R(minor) = 16.38 min]; IR (NaCl, neat): $\nu_{max} = 3096$, 2952, 1715, 1447 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 5.00-4.99$ (m, 1H), 4.52–4.50 (m, 1H), 4.35–4.33 (m, 1H), 4.20 (s, 5H), 3.79 (s, 3H), 0.31 (s, 9H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 172.6$, 78.1, 75.5, 74.5, 74.4, 78.2, 69.6, 51.3, 0.3; EIMS: *m/z* (%) = 316 (M^+, 100), 301 (72), 286 (40), 271 (37), 243 (52), 149 (71), 135 (54), 121 (65); HRMS (EI): calcd. for $C_{15}H_{20}O_2SiFe$: 316.0582; found: 316.0571.

(*R*)-2-Iodo(methoxycarbonyl)ferrocene (9c)

A stirred solution of **7f** (0.155 g, 0.40 mmol) and pyridine (0.10 mL, 1.2 mmol) in CH_2Cl_2 (3 mL) at -40 °C was treated with Tf_2O (0.09 mL, 0.53 mmol) over 20 min. The reaction mixture was allowed to warm slowly to 0 °C (2 h) and maintained at 0 °C for an additional 10 h. Absolute MeOH (2.5 mL, 61 mmol) was added, and stirring was continued for an additional 12 h at rt before saturated aqueous NH_4Cl solution was added. The product was extracted with CH_2Cl_2 ($\times 2$) and the combined organic extract was dried (anhydrous $MgSO_4$) and concentrated under vacuum. Column chromatography (hexanes: EtOAc, 9:1) gave **9a** as an orange oil; yield: 39 mg (26%). CSP HPLC analysis (Chiralcel OD; eluent: hexanes:*i*-PrOH, 90:10, flow 0.8 mL/min) determined 96% ee [t_R(major) = 7.13 min, t_R(minor) = 9.14 min]; IR (NaCl, neat): $\nu_{max} = 3100$, 2992, 2948, 2851, 1719, 1447 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): $\delta =$ 4.85–4.83 (m, 1H), 4.70–4.68 (m, 1H), 4.44 (brt, 1H), 4.22 (s, 5H), 3.84 (s, 3H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 170.7$, 79.7, 72.7, 72.2, 70.9, 70.1, 51.6, 39.6; EIMS: *m/z* (%) = 370 (M^+, 21), 183 (17), 156 (100), 128 (80), 122 (44), 119 (22); HRMS (EI): calcd. for $C_{12}H_{11}O_2FeI$: 369.9153; found: 369.9161.

(*R,R*)-2,2′′-Bis[(*N*-ethylamino)carbonyl]-1,1′′-biferrocene (10)

To a solution of **7f** (1.08 g, 2.82 mmol) in CH_2Cl_2 (10 mL) was added purified Cu powder (8.96 g, < 10 μ, 141 mmol) and the solvent was immediately removed under vacuum. The solid mixture was placed under argon and heated to 80 °C for 28 h. The mixture was diluted with CH_2Cl_2, passed through Celite, and silica gel was added to pre-adsorb the crude compound under vacuum. Column chromatography (EtOAc:MeOH, 24:1) afforded **10** as a crystalline red-orange solid; yield: 0.630 g (87%); mp 223–225 °C (EtOH) (decomp); $[\alpha]_D^{23}$: +646 (*c* 0.39, $CHCl_3$); IR (KBr): $\nu_{max} = 3328$, 3106, 2963, 1634, 1538 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 5.30$ (b, 2H), 5.11–5.09 (m, 2H), 4.75–4.73 (m, 2H), 4.52–4.49 (m, 2H), 4.35 (s, 10H), 3.26–2.98 (m, 4H), 0.91 (t, 6H, $J = 7.3$ Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 168.5$, 81.7, 78.2, 75.6, 71.8, 70.8, 68.8, 34.2, 14.5; EIMS: *m/z* (%) = 512 (M^+, 83), 447 (57), 376 (65), 305 (56), 163 (52), 105 (100); HRMS (EI): calcd. for $C_{26}H_{28}N_2O_2Fe_2$: 512.0850; found: 512.0848; anal. calcd. for $C_{26}H_{28}N_2O_2Fe_2$: C 60.97, H 5.51, N 5.47; found: C 61.04, H 5.47, N 5.36.

1-Ethyl-3,4-[(*R*)-1,2-ferrocenyl]-5,6-[(*R*)-1,2-ferrocenyl]-7-(ethylimino)-2-azepanone (11)

A stirred solution of **10** (0.256 g, 0.5 mmol) and pyridine (0.24 mL, 3 mmol) in CH_2Cl_2 (5 mL) under argon at -40 °C was treated with Tf_2O (0.22 mL, 1.3 mmol) over 20 min. The reaction mixture was allowed to warm slowly to 0 °C (2 h) and maintained at 0 °C for an additional 10 h. Absolute MeOH (2 mL, 50 mmol) was added, and stirring was continued for an additional 12 h at rt before saturated aqueous NH_4Cl solution was added. The product was extracted with CH_2Cl_2 ($\times 2$) washed with 1.2 N HCl and saturated aqueous $KHCO_3$ solution, dried (anhydrous $MgSO_4$) and concentrated under vacuum. Column chromatography (hexanes:EtOAc, 4:1) gave **11** as a red-orange solid; yield: 0.193 g (78%); mp 163–165 °C (heptane); X-ray (CCDC 163408): $C_{26}H_{26}Fe_2N_2O$, $M = 494.19$, monoclinic, $P2_1$, $a = 17.863(2)$ Å, $b = 9.2794(13)$ Å, $c =$ 21.735(3) Å, $V = 3370.6(8)$ Å^3, $Z = 6$; $D_c = 1.461$ g/cm^3, $F(000) = 1536$, $T = 180$K. Data were collected on a Siemens P4 diffractometer system with graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å); 4907 data were collected. The structure was solved by Patterson and Fourier (SHELXTL IRIS), corrected for Lorentz-polarization effects and refined by full-matrix least squares on F^2 resulting in final R, R_w, and GOF (for 4733 data with $F > 2\sigma(F)$) of 0.0281, 0.0560 and 1.807, respectively, for solution using the (*R*) model. The corresponding values for the (*S*) model were 0.0301, 0.0600 and 1.936; IR (KBr): $\nu_{max} = 3106$, 3092, 2966, 2930, 2866, 2846, 1637, 1609, 1448 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 4.92-4.91$ (m, 1H), 4.53–4.51 (m, 1H), 4.50–4.48 (m, 1H), 4.39–4.25 (m, 4H), 4.11–4.01 (m, 1H), 3.99 (s, 5H), 3.96 (s, 5H), 3.61–3.45 (m, 2H), 1.55 (t, 3H, $J = 7.1$ Hz), 1.30 (t, 3H, $J = 7.3$ Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 169.6$, 156.7, 83.4, 82.6, 79.7, 75.9, 70.5, 70.0, 69.7, 68.5, 67.5, 67.1, 66.4, 65.6, 47.2, 44.2, 16.4, 14.4; EIMS: *m/z* (%) = 494 (M^+, 49), 452 (32), 208 (23), 179 (38), 149 (37), 121 (100); HRMS (EI): calcd. for $C_{26}H_{26}N_2OFe_2$: 494.0744; found: 494.0735.

(*R*)-2-Iodo-*N*-ethyl-*N*-methylferrocenecarboxamide (12a)

NaH (0.332 g, 60% dispersion in mineral oil, ~8.3 mmol) was washed with hexanes (5 mL), and the solvent was carefully removed by syringe and replaced with DMF (10 mL). A solution of **7f** (1.06 g, 2.77 mmol) in DMF (10 mL) was added by cannula to the suspension of NaH in DMF at 0 °C with stirring. Additional DMF (5 mL) was added to rinse the flask containing **7f**, and this was also transferred to the reaction mixture. The mixture was stirred at rt (30 min) before MeI (0.34 mL, 5.5 mmol) was added. After 7.5 h, the mixture was cooled to 0 °C and treated sequentially, by slow addition, with

saturated aqueous NH_4Cl solution and water. The product was extracted with EtOAc (× 2) and the combined organic extract was washed with water (× 2), brine, dried (anhydrous $MgSO_4$) and concentrated under vacuum. Column chromatography (hexanes:EtOAc, 3:1) afforded **12a** as an orange oil; yield: 0.99 g (90%); IR (NaCl, neat): $\nu_{max} = 3092$, 2971, 2930, 2875, 1636, 1487 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 223 K, 1:1 mixture of rotamers): $\delta = 4.52$ (s, 1H), 4.42 – 4.39 (m, 1H), 4.37 (s, 5H), 4.27 (s, 1H), 3.72 – 3.65 (m, 0.5H), 3.43 – 3.35 (m, 0.5H), 3.26 – 3.13 (m, 1H), 3.04 (s, 1.5H), 2.80 (s, 1H), 1.21 (t, 1.5H, J = 7.3 Hz), 1.05 (t, 1.5H, $J = 7.0$ Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$, 223 K): $\delta = 167.6$, 167.3, 88.4, 87.7, 74.0, 73.9, 72.7, 72.6, 68.2, 67.4, 45.8, 42.2, 41.1, 40.1, 36.2, 32.5, 13.7, 12.0; EIMS: *m/z* (%) = 397 (M^+, 5), 269 (6), 184 (12), 148 (18), 128 (25), 119 (100), 105 (58); HRMS (EI): calcd. for $C_{14}H_{16}NOIFe$: 396.9626; found: 396.9634.

(*R*)-2-[(*N*-Ethyl-*N*-methylamino)methyl]-1-iodoferrocene (13)

A stirred solution of **12a** (0.97 g, 2.4 mmol) in THF (40 mL) was treated with $BH_3 \cdot SMe_2$ (0.93 mL, 9.8 mmol), and the reaction mixture was heated at reflux for 2 h. After cooling to 0 °C, 10% NaOH (40 mL) was added slowly, and the mixture was heated at reflux for an additional 3 h. Standard work-up followed by column chromatography (EtOAc:Et_3N, 97:3) afforded **13** as an orange oil; yield: 0.711 g (76%); IR (NaCl, neat): $\nu_{max} = 3093$, 2969, 2934, 2874, 2837, 2786, 1453 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) $\delta = 4.42 – 4.41$ (m, 1H), 4.30 – 4.29 (m, 1H), 4.20 (t, 1H, $J = 2.5$ Hz), 4.11 (s, 5H), 3.46 (d, 1H, $J = 13.2$ Hz), 3.38 (d, 1H, $J = 13.2$ Hz), 2.44 (q, 2H, $J = 6.9$ Hz), 2.18 (s, 3H), 1.08 (t, 3H, $J = 6.5$ Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$) $\delta = 85.1$, 74.7, 71.5, 69.0, 68.8, 56.4, 51.0, 46.4, 41.3, 12.7; EIMS: *m/z* (%) = 383 (M^+, 10), 325 (12), 199 (12), 141 (15), 121 (100); HRMS (EI): calcd. for $C_{14}H_{18}NIFe$: 382.9833; found: 383.9859.

(*R*)-2-Iodo-*N*-allyl-*N*-ethylferrocenecarboxamide (12b)

NaH (0.306 g, 60% dispersion in mineral oil, ~7.65 mmol) was washed with hexanes (4 mL), and the solvent was carefully removed by syringe and replaced with DMF (10 mL). A solution of **7f** (0.977 g, 2.55 mmol) in DMF (7 mL) was added by cannula to the suspension of NaH in DMF at 0 °C with stirring. Additional DMF (3 mL) was added to rinse the flask containing **7f**, and this was also transferred to the reaction mixture. The mixture was stirred at rt (30 min) and treated with allyl bromide (0.44 mL, 5.1 mmol). After 12 h, the mixture was cooled to 0 °C and sequentially treated with saturated aqueous NH_4Cl solution and water, and the product was extracted with EtOAc (× 2). The combined organic layer was washed with water (× 2), brine, dried (anhydrous $MgSO_4$) and concentrated under vacuum. Column chromatography (hexanes:EtOAc, 9:1) afforded **12b** as an orange oil; yield: 0.83 g (77%); IR (NaCl, neat): $\nu_{max} = 3087$, 2974, 2929, 1640 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 230 K, 1:1 mixture of rotamers): $\delta = 5.90 – 5.82$ (0.5H), 5.69 – 5.62 (0.5H), 5.33 – 5.11 (m, 2H), 4.51 (s, 1H), 4.45 – 4.36 (m, 7H), 4.25 (m, 1H), 3.91 – 3.64 (m, 2H), 3.12 – 3.01 (m, 1H), 1.20 (t, 1.5H, $J = 6.9$ Hz), 0.99 (t, 1.5H, $J = 7.0$ Hz); ^{13}C NMR (100.6 MHz, 230 K, $CDCl_3$): $\delta = 167.6$, 167.4, 133.3, 132.6, 116.7, 88.8, 87.6, 73.9, 73.8, 72.6, 68.1, 67.4. 67.1, 50.4, 46.5, 42.6, 41.3, 41.0, 39.7, 13.7, 12.4; EIMS: *m/z* (%) = 423 (M^+, 49), 294 (20), 280 (30), 210 (33), 183 (50), 128 (100), 121 (89); HRMS (EI): calcd. for $C_{16}H_{18}NOIFe$: 422.9783; found: 422.9771.

1-Ethyl-3,4-[(*S*)-1,2-ferrocenyl]-5-methylene-2-piperidinone (15)

A sealed tube apparatus capped with a rubber septum under argon was charged with a solution of iodide **12b** (140 mg, 0.33 mmol) in CH_3CN (4.2 mL). To the stirred solution was added Et_3N (0.56 mL, 4.0 mmol) and solid $Pd(PPh_3)_4$ (11.4 mg, 3 mol %) by quickly removing the septum, adding the catalyst, and sealing the tube with a screw-top. The resulting mixture was heated with stirring at an external temperature of 95 °C for 48 h. After cooling to rt, the tube was opened and the reaction mixture worked up by the addition of saturated aqueous $NaHCO_3$ solution. The product was extracted with EtOAc (× 3), and the combined organic layer was washed with water (× 2), brine, dried (anhydrous Na_2SO_4) and concentrated under vacuum. Column chromatography (hexanes:EtOAc, 1:1) afforded **15** as an orange glass; yield: 46 mg (47%). CSP HPLC analysis (Chiralcel OD; eluent: hexanes:*i*-PrOH, 90:10, flow 1.0 mL/min) determined 88% ee [t_R(minor) = 10.46 min, t_R(major) = 11.98 min]; IR (NaCl, neat): $\nu_{max} = 3090$, 2971, 2931, 2872, 1638 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 5.20$ (d, 1H, $J = 2.0$ Hz), 5.11 (s, 1H), 4.93 (s, 1H), 4.60 – 4.59 (m, 1H), 4.55 – 4.49 (m, 1H), 4.44 (t, 1H, $J = 2.3$ Hz), 4.18 (s, 5H), 4.00 – 3.93 (m, 1H), 3.79 – 3.67 (m, 1H), 3.44 – 3.32 (m, 1H), 1.23 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 168.0$, 137.1, 106.8, 82.7, 73.1, 70.6(2C), 68.0, 64.3, 52.8, 41.2, 12.5; EIMS: *m/z* (%) = 295 (M^+, 2), 247 (6), 220 (6), 149 (36), 121 (93), 119 (100), 105 (67); HRMS (EI): calcd. for $C_{16}H_{17}FeNO$: 295.0659; found: 295.0659.

(*S*)-2-Formyl-*N*-cumyl-*N*-ethylferrocenecarboxamide (16)

According to the Standard Method, a solution of (−)-sparteine (0.41 mL, 1.8 mmol) and *n*-BuLi (0.71 mL, 2.53 M, 1.8 mmol) in Et_2O (24 mL) was treated with a solution of **5** (0.563 g, 1.5 mmol) in PhMe (4 mL), and after 2 h, the reaction mixture was quenched with DMF (0.14 mL, 1.8 mmol), added dropwise over 5 min. Standard work-up followed by column chromatography (hexanes:EtOAc, 70:30) afforded **16** as an unstable red-orange oil which darkened quickly in air; yield: 0.542 g (89%). The compound was used immediately for the preparation of **17**; IR (NaCl, neat): $\nu_{max} = 2979$, 2873, 1672, 1635 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 10.13$ (s, 1H), 7.43 – 7.19 (m, 5H), 4.89 (s, 1H), 4.82 (s, 1H), 4.62 (s, 1H), 4.21 (s, 5H), 3.60 – 3.52 (m, 2H), 1.76 (s, 6H), 1.13 (t, 3H, $J = 7.2$ Hz).

(*S*)-2-[1-Hydroxy-2-(trimethylsilyl)ethyl]-*N*-cumyl-*N*-ethylferrocenecarboxamide (*pre*-17)

A solution of aldehyde **16** (90.5 mg, 0.224 mmol) in Et_2O (2 mL) under argon at rt was treated with a solution of $TMSCH_2MgCl$ (0.56 mL, 1.0 M in ether, 0.56 mmol), added over 50 min. The mixture was stirred for 2 h at rt and cooled to

0 °C. Standard work-up followed by column chromatography (hexanes:EtOAc, 90:10) afforded ***pre*-17** as an orange oil; yield: 50 mg (45%); IR (NaCl, neat): $\nu_{max} = 3337, 2974, 2952, 1605, 1440\ cm^{-1}$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.42-7.18$ (m, 5H), 5.71 (d, 1H, $J = 9.1$ Hz), 4.45 – 4.43 (m, 3H), 4.10 (s, 5H), 4.09 (s, 1H), 4.04 – 3.93 (m, 1H), 3.65 – 3.54 (m, 1H), 1.87 (s, 3H), 1.65 (s, 3H), 1.27 (t, 3H, $J = 7.0$ Hz), 1.14 – 0.76 (m, 2H), – 0.10 (s, 9H); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 174.3, 149.3, 128.1, 125.8, 124.1, 100.9, 78.3, 70.7, 70.6, 67.5, 67.3, 65.8, 62.0, 41.8, 30.7, 29.2, 26.2, 18.5, -1.0$; EIMS: *m/z* (%) = 491 (M^+, 5), 473 (18), 282 (18), 218 (28), 145 (55), 119 (100); HRMS (EI): calcd. for $C_{27}H_{37}NO_2SiFe$: 491.1943; found: 491.1926.

(*S*)-2-Vinyl-*N*-cumyl-*N*-ethylferrocenecarboxamide (17)

Crude carbinol ***pre*-17**, prepared as described above from aldehyde **16** (449 mg, 1.11 mmol), was dissolved in a round-bottomed flask in THF (12 mL) under argon and the solution was cooled to 0 °C with stirring. NaH (88 mg, 60% dispersion in mineral oil, ~2.2 mmol) was added, and the mixture was heated at reflux for 5 h. After cooling to 0 °C, water was added and the product was extracted with Et_2O followed by CH_2Cl_2 ($\times 2$) and the combined organic extract was dried (anhydrous $MgSO_4$) and concentrated under vacuum. Column chromatography (hexanes:EtOAc, 88:12) afforded **17** as an orange oil that slowly solidified; yield: 0.272 g (61% overall from aldehyde **16**); mp 105 – 107 °C; IR (NaCl, neat): $\nu_{max} = 3087, 3057, 2978, 2932, 1639, cm^{-1}$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.43-7.19$ (m, 5H), 6.69 (dd, 1H, $J = 17.6$ Hz, 10.6 Hz), 5.37 (dd, 1H, $J = 17.7$ Hz, 1.5Hz), 5.07 (dd, 1H, $J = 10.6$ Hz, 1.5Hz), 4.49 – 4.48 (m, 1H), 4.45 – 4.44 (m, 1H), 4.21 (t, 1H, $J = 2.7$ Hz), 4.04 (s, 5H), 3.57-3.38 (m, 2H), 1.77 (s, 3H), 1.71 (s, 3H), 1.07 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$) $\delta = 169.9, 149.4, 133.3, 128.0, 125.6, 124.3, 112.0, 85.3, 84.3, 71.2, 68.6, 67.1, 64.4, 61.5, 41.4, 29.6, 27.8, 17.6$; EIMS: *m/z* (%) = 401 (M^+, 42), 283 (54), 145 (45), 119 (53), 91 (100); HRMS (EI): calcd. for $C_{24}H_{27}NOFe$: 401.1442; found: 401.1443.

(*S*)-2-Vinyl-*N*-ethylferrocenecarboxamide (*pre*-18)

A solution of amide **17** (0.314 mg, 0.782 mmol) in TFE (8 mL) was heated at reflux for 10.5 h. Evaporation of the solvent under vacuum and column chromatography (hexanes:EtOAc, 1:1) afforded ***pre*-18** as an orange oil that slowly solidified; yield: 0.218 g (99%); mp 113.5 – 115 °C; IR (KBr): $\nu_{max} = 3310, 3089, 2975, 2931, 1632, 1542\ cm^{-1}$; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 7.20$ (dd, 1H, $J = 17.8, 11.3$ Hz), 6.01 (b, 1H), 5.45 (dd, $J = 17.8, 1.3$ Hz), 5.17 (dd, $J = 11.3, 1.3$ Hz), 4.63 – 4.58 (m, 2H), 4.31 (t, 1H, $J = 2.5$ Hz), 4.14 (s, 5H), 3.44-3.36 (m, 2H), 1.21 (t, 3H, $J = 6.9$ Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 170.1, 133.3, 113.5, 84.6, 75.5, 70.8, 68.9, 68.7, 67.6, 34.3, 15.1$; EIMS: *m/z* (%) = 283 (M^+, 100), 145 (12), 121 (27); HRMS (EI): calcd. for $C_{15}H_{17}NOFe$: 283.0660; found: 283.0634.

(*S*)-2-Vinyl-*N*-allyl-*N*-ethylferrocenecarboxamide (18)

NaH (92 mg, 60% dispersion in mineral oil, ~2.3 mmol) was washed with hexanes (4 mL), and the solvent was carefully removed by syringe and replaced with DMF (3 mL). A solution of ***pre*-18** (0.218 g, 0.77 mmol) in DMF (2 mL) was added by cannula to the suspension of NaH in DMF at 0 °C with stirring. Additional DMF (1 mL) was added to rinse the flask containing ***pre*-18**, and this was also transferred to the reaction mixture. The mixture was stirred at rt (30 min) and treated with allyl bromide (0.13 mL, 1.5 mmol). After 2 h, the mixture was cooled to 0 °C and treated sequentially with saturated aqueous NH_4Cl solution and water. The product extracted with EtOAc ($\times 2$) and the combined organic layer was washed with water ($\times 2$), brine, dried (anhydrous $MgSO_4$) and concentrated under vacuum. Column chromatography (hexanes:EtOAc, 85:15) afforded **18** as an orange oil; yield: 0.226 g (91%); IR (NaCl, neat): $\nu_{max} = 3092, 2971, 2928, 1621, 1476\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$, 225 K, 1:1 mixture of rotamers): $\delta = 6.79-6.61$ (m, 1H), 5.89 – 5.82 (m, 0.5H), 5.74 – 5.66 (m, 0.5H), 5.40 (d, 1H, $J = 17.4$ Hz), 5.22 – 5.10 (m, 3H), 4.58 (s, 1H), 4.45 (s, 1H), 4.29 – 4.25 (m, 6H), 3.93 – 3.74 (m, 2H), 3.25 – 3.09 (m, 2H), 1.18 – 1.15 (m, 1.5H), 1.02 – 1.00 (m, 1.5H); ^{13}C NMR (100.6 MHz, $CDCl_3$, 225 K): $\delta = 169.0, 168.7, 133.5, 132.8, 132.7, 132.6, 116.7, 116.6, 112.2, 112.1, 83.8, 83.3, 83.2, 81.8, 70.8, 68.5, 68.4, 67.6, 67.4, 64.4, 63.9, 50.4, 46.7, 42.6, 39.8, 13.8, 12.1$; EIMS: *m/z* (%) = 323 (M^+, 16), 212 (13), 121 (100); HRMS (EI): calcd. for $C_{18}H_{21}NOFe$: 323.0973; found: 323.0953.

1-Ethyl-3,4-[(*S*)-1,2-ferrocenyl]-2,7-dihydro-1*H*-2-azepinone (*pre*-19)

A solution of vinylferrocene **18** (226 mg, 0.70 mmol) in CH_2Cl_2 (14 mL) was transferred by cannula to a flame-dried 2-necked flask under argon equipped with a reflux condenser. The stirred solution was treated with Grubbs' catalyst [bis(tricyclohexylphosphine)benzylidene ruthenium(IV) dichloride] (46 mg, 8 mol %) and the reaction mixture was heated at reflux for 3.5 h at which time additional Grubbs' catalyst was added (46 mg, 8 mol %) and the mixture was refluxed for an additional 18 h. The solvent was removed under vacuum and the residue was subjected to column chromatography (hexanes:EtOAc, 55:45) to give ***pre*-19** as an orange oil; yield: 0.181 g (88%). CSP HPLC analysis (Chiralcel OD; eluent: hexanes: *i*-PrOH, 90:10, flow 1.0 mL/min) determined 93% ee [t_R(minor) = 8.56 min, t_R(major) = 13.23 min]; IR (NaCl, neat): $\nu_{max} = 3092, 2971, 2928, 1621, 1476\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.66$ (d, 1H, $J = 9.5$ Hz), 5.95 – 5.90 (m, 1H), 5.13 (s, 1H), 4.40 (s, 1H), 4.36 (s, 1H), 4.14 (s, 5H), 3.86 – 3.80 (m, 1H), 3.72 – 3.67 (m, 1H), 3.61 – 3.56 (m, 1H), 3.45 – 3.42 (m, 1H), 1.19 (*t*, 3H, $J = 7.0$ Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 170.8, 132.6, 123.2, 81.6, 77.6, 73.9, 70.9, 70.3, 69.8, 45.1, 43.2, 13.9$; EIMS: *m/z* (%) = 295 (M^+, 19), 146 (39), 121 (100); HRMS (EI): calcd. for $C_{16}H_{17}NOFe$: 295.0660; found: 295.0650.

1-Ethyl-3,4-[(*S*)-1,2-ferrocenyl]-2,5,6,7-tetrahydro-1*H*-2-azepinone (19)

A stirred mixture of unsaturated azepinone ***pre*-19** (189 mg, 0.64 mmol) and 10% Pd/C (34 mg, 0.0032 mmol, approx. 5 mol %) in MeOH (20 mL) was prepared. The flask was purged and filled with hydrogen ($\times 4$) and stirred at rt for 12 h. The mixture was passed through Celite and the filtrate was concentrated under vacuum. The residue was dissolved in EtOAc and the resulting solution was passed through silica gel using EtOAc as

eluent. Concentration under vacuum afforded pure **19** as an orange oil which slowly solidified; yield: 172 mg (91%); mp 88.5 – 91.5 °C; CSP HPLC analysis (Chiralcel OD; eluent: hexanes:*i*-PrOH 90:10, flow 1.0 mL/min) determined 91% ee [t_R(minor) = 9.52 min, t_R(major) = 11.83 min]; IR (KBr): ν_{max} = 3079, 2969, 2952, 1606 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 4.94 (s, 1H), 4.28 – 4.26 (m, 2H), 4.14 (s, 5H), 3.70 – 3.65 (m, 1H), 3.50 – 3.25 (m, 3H), 2.93 – 2.84 (m, 1H), 2.62 – 2.52 (m, 1H), 2.06 – 2.00 (m, 2H), 1.19 (t, 3H, J = 6.8 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 171.2, 85.8, 76.4, 72.5, 70.5, 70.3, 68.8, 48.6, 44.1, 28.6, 28.1, 13.3; EIMS: *m/z* (%) = 297 (M^+, 41), 201 (13), 149 (25), 142 (47), 121 (100); HRMS (EI): calcd. for $C_{16}H_{19}NOFe$: 297.0816; found: 297.0805.

1-Ethyl-3,4-[(*S*)-5-diphenylphosphino-1,2-ferrocenyl]-2,5,6,7-tetrahydro-1*H*-2-azepinone (20)

A stirred solution of **19** (114 mg, 0.384 mmol) and TMEDA (0.07 mL, 0.46 mmol) in Et_2O (4 mL) and THF (3 mL) under argon at − 78 °C was treated with *s*-BuLi (0.37 mL, 1.25 M, 0.46 mmol) by dropwise addition. After 2 h, PPh_2Cl (0.09 mL, 0.5 mmol) was added dropwise and the reaction mixture was allowed to warm slowly to rt. A solution of saturated aqueous NH_4Cl was added and the product was extracted with CH_2Cl_2 (× 2), dried (anhydrous Na_2SO_4) and concentrated under vacuum. Column chromatography (hexanes:EtOAc:Et_3N, 68:30:2, product was collected under argon) afforded **20** as an orange foam; yield: 162 mg (87%); mp 53 – 55 °C; IR (KBr): ν_{max} = 3062, 2929, 2861, 1611 cm^{-1}; ^{31}P NMR (162.0 MHz, $CDCl_3$): δ = − 18.13; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.50 – 7.46 (m, 2H), 7.33 – 7.30 (m, 3H), 7.24 – 7.18 (m, 5H), 4.23 (d, 1H, J = 2.3 Hz), 4.13 (s, 5H), 3.59 (d, J = 2.3 Hz), 3.44 – 3.31 (m, 2H), 3.21 – 3.18 (m, 2H), 2.89 – 2.80 (m, 1H), 2.60 – 2.50 (m, 1H), 2.03 – 1.97 (m, 1H), 1.78 – 1.70 (m, 1H), 0.90 (t, 3H, J = 6.9 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 170.2, 140.3 (d, $J^{31}_{P-}{}^{13}_{C}$ = 14.2 Hz), 138.9 (d, $J^{31}_{P-}{}^{13}_{C}$ = 16.6 Hz), 134.5 (d, $J^{31}_{P-}{}^{13}_{C}$ = 21.8 Hz); 132.3 (d, $J^{31}_{P-}{}^{13}_{C}$ = 19.0 Hz), 128.3, 127.8, 127.7, 127.6, 127.5, 127.4, 87.7 (d, $J^{31}_{P-}{}^{13}_{C}$ = 1.8 Hz), 83.3 (d, $^1J^{31}_{P-}{}^{13}_{C}$ = 13.9 Hz), 80.2 (d, $^1J^{31}_{P-}{}^{13}_{C}$ = 14.5 Hz), 71.4, 70.7 (d, $^1J^{31}_{P-}{}^{13}_{C}$ = 3.3 Hz), 70.0, 46.6, 42.4, 28.4, 25.8, 12.9; EIMS: *m/z* (%) = 481 (M^+, 17), 452 (23), 404 (10), 183 (35), 129 (28) 121 (100); HRMS (EI): calcd. for $C_{28}H_{28}NOPFe$: 481.1258; found: 481.1248.

Acknowledgements

We are grateful to NSERC Canada for support under the Research Grant program, to Dr. Françoise Sauriol for impeccable assistance with NMR spectroscopic determinations, and to Dr. Yousheng Zhang for the X-ray crystallographic analysis of ***7d****. CM is a grateful recipient of an Ontario Graduate Scholarship (2000 – 2001) and HS warmly acknowledges the Humboldt Foundation for a Fyodor Lynen Fellowship.*

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[11] Crystallographic data (excluding structure factors) for **6f**, **7d** and **11** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-163407, 163409 and 163408, respectively. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk].

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