(–)-Sparteine-mediated stereoselective directed ortho metalation of ferrocene diamides[1]

Radoslaw Laufer, Ulrich Veith, Nicholas J. Taylor, and Victor Snieckus

Abstract: The utility of (–)-sparteine-mediated directed ortho metalation (D*o*M) has been investigated in stereoselective preparation of planar chiral ferrocenes derived from 1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**5**). In the synthesis of C_2-symmetric analogs of **5**, the protocol (base, solvent, and two-step D*o*M) was found to be crucial for obtaining high enantio- and diastereo-selectivities of the products. A variety of highly enantioenriched mono and doubly functionalized derivatives of **5** have been synthesized. The synthetic applications of these compounds as chiral ligands in asymmetric alkylation of aldehydes and asymmetric palladium-catalyzed allylic substitutions have been demonstrated.

Key words: directed ortho metalation, stereoselective deprotonation, ferrocene ligands, asymmetric catalysis.

Résumé : On a étudié l'utilité de l'ortho métallation dirigée (*o*MD) orientée par la (–)-spartéine, dans la préparation stéréosélective de ferrocènes chiraux planaires dérivés du 1,1′-*N*,*N*,*N*′,*N*′-tétraisopropylferrocènedicarboxamide (**5**). Dans la synthèse d'analogues de symétrie C_2 du composé **5**, on a trouvé que le protocole expérimental (base, solvant et *o*MD en deux étapes) est crucial si on veut obtenir des valeurs élevées d'énantio- et de diastéréo-sélectivités des produits. On a pu synthétiser avec un degré d'énantioenrichissement élevé une grande variété de dérivés du composé **5** mono- et di-fonctionnalisés avec un degré d'énantioenrichissement élevé. On a démontré l'utilité synthétique de ces composés, en particulier comme ligands chiraux dans l'alkylation asymétrique d'aldéhydes et dans les substitutions allyliques asymétriques catalysées par le palladiium.

Mots clés : ortho métallation dirigée, déprotonation stéréosélective, ligands ferrocènes, catalyse asymétrique.

[Traduit par la Rédaction]

The disclosure, with an interesting socio-chemical history, of the correct structure of ferrocene over half a century ago constituted a landmark achievement that heralded an entirely new theme of organometallic chemistry (1). The continuing significance of the field of ferrocene chemistry (2) is attested by research in areas of asymmetric catalysis (3, 4), enantioselective synthesis (2, 5), diverse material science (2), and biological (6) areas and, most spectacularly, industrial applications (7). Shortly after the excellent summary of the field by Schlőgl (8), Ugi and co-workers (9) reported the effective preparation of optically active planar chiral ferrocenes, which proceeds by diastereoselective directed ortho metalation (D*o*M) and subsequent reaction with electrophiles and which relies on a chiral auxiliary directed metalation group (DMG) for the central to planar chirality transfer. Following these pioneering studies, Kagan and co-workers (10) demonstrated a high diastereoselective D*o*M reaction using chiral sulfoxide DMGs, which was followed by rapid accumulation of reports using other DMGs, providing convincing evidence for the generality of the diastereoinduction process (11, 12) (Scheme 1).

In 1996, stimulated by the results of Hoppe and Hense (13) and Beak et al. (14), we reported on the highly enantioselective synthesis of planar chiral ferrocenecarboxamides **1a** → **2a** by (–)-sparteine-mediated D*o*M chemistry (Scheme 2) (15). This constituted the first general and direct synthetic method to enantiomerically pure ferrocenyls that avoids substrate-specific resolution (9*a*, 16) and chiral auxiliary introduction and removal (10, 17). In subsequent work, we addressed a limitation of the diethyl amide DMG of "seldom allow(ing) functional group modification" (10*b*) by introducing the *N*-cumyl-*N*-ethylferrocenecarboxamide (**1b**), which behaved equally well in sparteine-mediated D*o*M chemistry to afford planar chiral ferrocenes in high yields and % ee, and served, after mild decumylation, as convenient syntheses of optically active Ugi amines, little-known esters, and new phosphines (18). Another limitation, "the disadvantage of the (availability of a) single enantiomeric form of (–)-sparteine" (19) was addressed by showing that 2-TMS-*N*-ethylferrocenecarboxamide (**3**, E = TMS) undergoes C-5 rather than C-1′ deprotonation and thereby allows a latent silicon protec-

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Dedicated to friend and former colleague, Arthur Carty, in recognition of his forefront and continuing contributions to organometallic chemistry and chemistry in Canada, and for early fruitful collaboration in diazepine irontricarbonyl chemistry.

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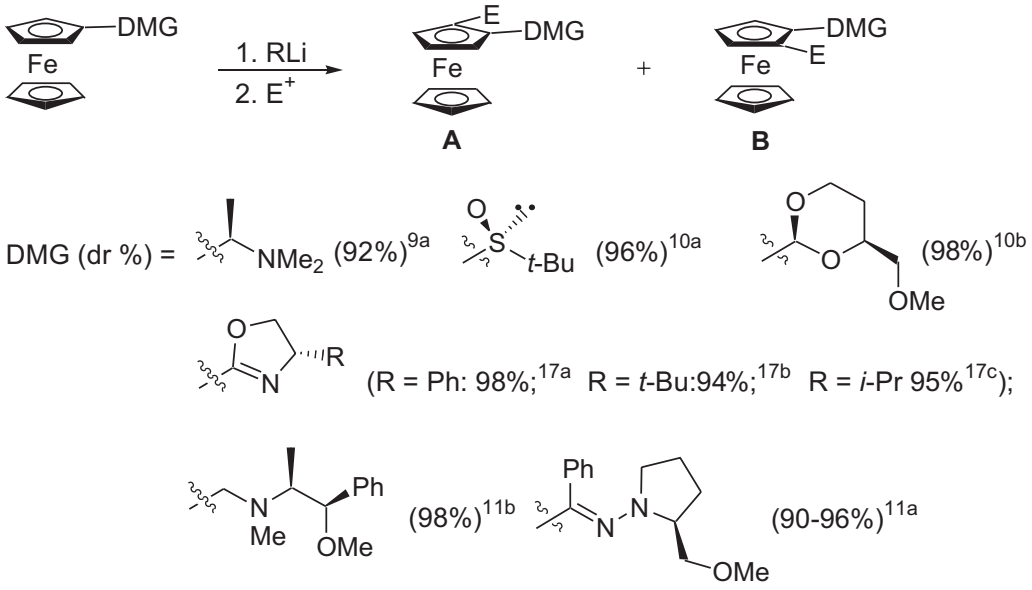
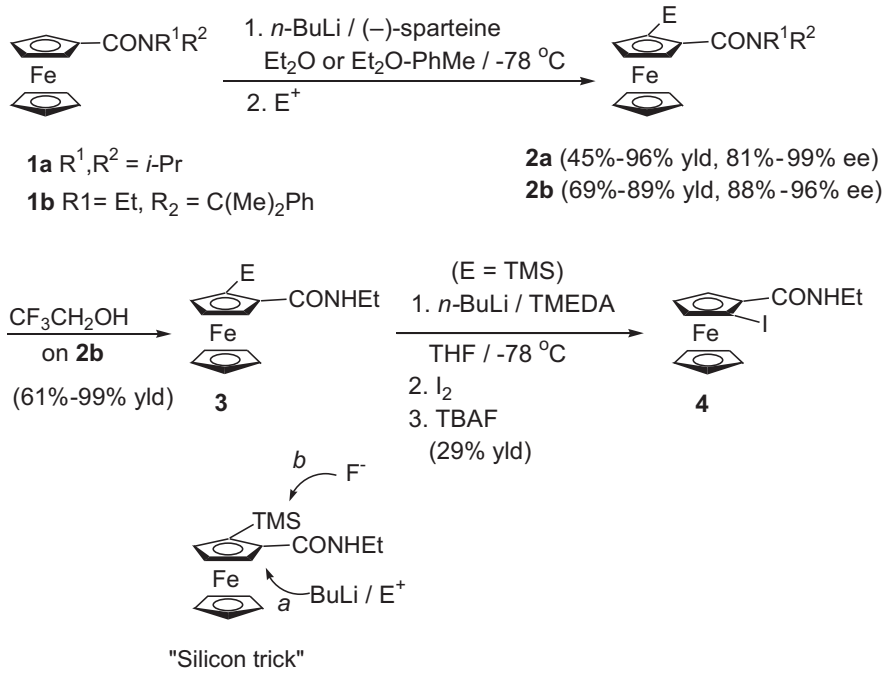
Scheme 1.



Scheme 2.



tion route (4, 20, 21) to the valuable enantiomeric ferrocene (*S*) series (Scheme 2).

As part of efforts to expand the scope of the (–)-sparteine-mediated enantioinduction of planar chirality, we recently reported (22) on the synthesis of highly enantioenriched mono- and double-functionalized derivatives of ferrocenyl 1,1′-bisamides, **6** and **7** (Scheme 3) by combined D*o*M–Pd-catalyzed Suzuki–Miyaura and Stille cross-coupling reactions (23). Herein we present the full details of our studies.

At the outset of our initial investigation, we attempted to establish the optimal reaction conditions for D*o*M of ferrocenyldiamide **5** in Et_2O using chlorotrimethylsilane (TMSCl) as the electrophilic partner. Only later, we discovered that application of TMSCl led to exceptional results. As gleaned from the results in Table 1, use of more than 2 equiv. of both *n*-BuLi and (–)-sparteine led to effective electrophilic trapping of doubly deprotonated **5** (Table 1, entries 2 and 3) in very good yields, however, with unsatisfactory levels of both diastereoselectivity (dr meso:dl, 2:1, **7a**: E = TMS) and optical activity (54% optical purity).[4] Application of *s*-BuLi and (–)-sparteine allowed for quantitative conversions of **5** into **7a** (Table 1, entry 5), but the reaction

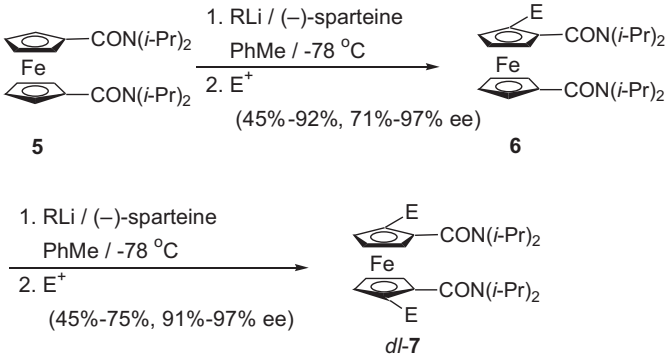
[4] Neither (±)-**6a** nor (±)-**7a** could be resolved on chiral HPLC. The requisite homochiral crystals of (+)-**7a** were obtained by recrystallizations of the enantioenriched **7a** from hexanes.

Table 1. Metalation of 1,1′-ferrocenyldiamide **5** in Et_2O (E^+ = TMSCl).

No.	Base	Equiv.	Yield (%)			
			6a	**7a**	**7a** dr[a] dl:meso	Op[b] (*dl*-**7a**)
1	*n*-BuLi–(–)-sparteine	2.1	10	Trace	46:54	—
2	*n*-BuLi–(–)-sparteine	3.1	3	88	30:70	54
3	*n*-BuLi–(–)-sparteine	4.2	Trace	87	37:63	—
4	*n*-BuLi–TMEDA	4.2	38	46	49:51	—
5	*s*-BuLi–(–)-sparteine	4.2	—	99	4:96	15
6	*s*-BuLi–TMEDA	4.2	—	99	25:75	—

Note: Conditions: RLi–(–)-sparteine or TMEDA; Et_2O at –78 °C for 2 h then excess TMSCl; –78 °C → rt.
[a]Determined by GC analysis of crude reaction mixtures.
[b]Op (optical purity); homochiral **7a**: $[\alpha]^{23}_{578}$ +49.2° (*c* 0.24, $CHCl_3$).

Scheme 3.



exhibited prohibitively strong preference for the meso diastereomer and very low optical induction for *dl*-**7a** (15% optical purity). Interestingly, in all cases D*o*M-trimethylsilylation of **5** utilizing *n*-BuLi or *s*-BuLi together with TMEDA led to modestly (Table 1, entries 3 vs. 4 and 5 vs. 6) improved contents of racemic *dl*-**7a**.

For electrophilies other than TMSCl, the reactions of 1,1′-ferrocenyldiamide (**5**) with 4.2 equiv. of *n*-BuLi–(–)-sparteine in Et_2O at –78 °C are markedly different. As illustrated in Table 2, the protocol furnished, almost exclusively, products from electrophilic trapping of monolithium anion in good yields but with moderate enantioselectivities. At present, the high yields for the double D*o*M of **5** in the reactions involving TMSCl are difficult to rationalize. Related reactions, involving deprotonation of hindered lithium dialkylamides and in situ TMSCl as the electrophilic trap, have been shown to give superior yields and stereoselectivities. Effects of the in situ generated LiCl has been suggested as the causative agent (24). Despite the apparent incompatibility of *n*-BuLi with TMSCl, we have observed a modest LiCl effect on D*o*M of **5**. Under unchanged reaction conditions, D*o*M of **5** with 4.2 equiv. of *n*-BuLi–(–)-sparteine in the presence of 2.0 equiv. of LiCl followed by a quench with an excess of MeI led to improved yields and greatly enhanced stereoselectivities for both the mono-**6b** (61% yield, 79% ee vs. Table 2, entry 1) and dimethylated **7b**. Compound **7b** was obtained in 16% yield (3:1 dr dl:meso, 80% ee), compared with only trace amounts observed under LiCl-free conditions.

Although double D*o*M–electrophile quench was effected much more efficiently with *s*-BuLi–(–)-sparteine, the same general trend for the unfavorable diastereoselectivities and low enantioinductions was observed with a number of different electrophiles (Table 3). Under these reaction conditions, monocarbinol **6d** was isolated as the only product in low yield and low enantiomeric excess (Table 3, entry 6). Interestingly, unlike 2,2′-bis(diphenylphosphine) (**7c**), which was obtained in respectable yield either directly from **5** utilizing *s*-BuLi (Table 3, entry 5) or stepwise, with *n*-BuLi via **6g** (vide infra, Table 4), all attempts to prepare the 2,2′-bis(diphenylhydroxymethyl) derivative by D*o*M of **5** or monocarbinol **6d** were unsuccessful.

Table 2. Monometalation of **5** in Et_2O (base is *n*-BuLi).

No.	E+	Product (E)	Yield (%)	ee (%)
1	MeI	**6b** (Me)	56	68
2	I_2	**6c** (I)	53	59
3	$Ph_2C{=}O$	**6d** (Ph_2C-OH)	77	64

Note: Conditions: 4.2 equiv. *n*-BuLi–(–)-sparteine; Et_2O; –78 °C for 2 h then 6 equiv. E^+, –78 °C → rt for 4 h.

Gratifyingly, use of solvents of lower coordinating abilities (Table 5, entries 1–3) allowed the preparation of 1,1′,2-trisubstituted derivatives (**6b**–**6i**) in augmented optical and chemical yields. Toluene was found to give the optimal balance between the level of enantioinduction and chemical yield, e.g., the diphenylphosphine derivative **6g** was obtained in 53% yield and 97% ee without a recrystallization (Table 5, entry 9). Interestingly, the opposite solvent effect on the entantioselectivty of (–)-sparteine-assisted D*o*M was observed in applications of *N*,*N*-diisopropylferrocenylcarboxamide (15). Reduction of the amount of *n*-BuLi–(–)-sparteine to 2.2 equiv. caused a slight decline in the chemical yield of the product **6d** (Table 5, entry 5 vs. 6), but did not lead to the erosion of ee. Again, utilization of TMSCl as the electrophile afforded 2,2′-disilylated product **7a** as the major product (71% yield, dr dl:meso, 3:1, 97% optical purity) when 4.2 equiv. of base was used (Table 5, entry 12). Lesser amount of the base (2.2 equiv.) resulted in formation of the monosilylated **6a** as the major product with **7a** isolated as a minor component (16% yield, dr dl:meso, 68:32, 99% optical purity) (Table 5, entry 13).

The enantiomeric excess for stannane **6f** (Table 5, entry 8) was determined by its transformation into carbinol **6d** in a sequence involving a lithiodestannylation–benzophenone quench. Under these unoptimized conditions, the relatively lower ee of **6d** (82% ee) derived from **6f** may be the result of partial racemization, occurring via an intermolecular Li-H

Table 3. Double D*o*M of **5** in Et_2O using *s*-BuLi and TMEDA or (–)-sparteine.

No.	E^+	Diamine	Product (E)	Yield (%)[a]	*dl*-**7**:*meso*-**7**	ee (%)
1	MeI	(–)-Sparteine	**7b** (Me)	70	24:76[b]	53[b]
2	MeI	TMEDA	**7b**	19	21:79[b]	—
3	TMSCl	(–)-Sparteine	**7a** (TMS)	99	4:96[c]	15[d]
4	TMSCl	TMEDA	**7a**	99	25:75[c]	—
5	PPh_2Cl	(–)-Sparteine	**7c** (PPh_2)	49	<5:>95[e]	—
6	$Ph_2C{=}O$	(–)-Sparteine	**6d** (Ph_2C-OH)	36[f]	NA	32[b]
7	Ph_2S_2	TMEDA	**7d** (PhS)	51	31:69[b]	—

Note: Conditions: 4.2 equiv. *s*-BuLi–(–)-sparteine or TMEDA; Et_2O at –78 °C for 2 h then 6 equiv. E^+ at –78 °C → rt for 4 h.
[a]Combined yields.
[b]Determined by chiral HPLC.
[c]Determined by GC analysis of crude reaction mixtures.
[d]As optical purity.
[e]Determined by ^{31}P NMR.
[f]Only the mono derivative **6d** was isolated.

Table 4. *n*-BuLi–(–)-sparteine-induced monometalation of 2-substituted derivatives, **6a**, **6g**, and **6h**.

(SM) ee (%)	E^+	Product	Yield (%)	dl:meso	ee (%)
(**6a**) 0	TMSCl[a]	**7a**	86	51:49	72[b]
(**6a**) —[c]	TMSCl[d]	**7a**	75	84:16	91[b]
(**6g**) 97	Ph_2PCl[e]	**7c**	45	>95:<5[f]	98[b]
(**6h**) 89	$(PhS)_2$[a]	**7d**	60	99:1[g]	97[g]

[a]2.1 equiv. of *n*-BuLi–(–)-sparteine were used.
[b]Determined as optical purity.
[c]$[\alpha]^{23}_{578}$ +67.5° (*c* 0.54, $CHCl_3$).
[d]4.2 equiv. of *n*-BuLi–(–)-sparteine were used.
[e]1.5 equiv. of *n*-BuLi–(–)-sparteine were used.
[f]Determined by ^{31}P NMR.
[g]Determined by chiral HPLC.

exchange. The heteroatom-tethered phenyl derivatives (thioether, diphenylphosphine, and phenylselenide) **6g**–**6i** (Table 5, entries 9–11) were found to surrender their optical integrity on standing in solution. For example, 2-(phenylthio)-1,1′-ferrocenediamide derivative **6h** undergoes racemization in a mixture of hexanes and *i*-PrOH at a faster rate ($t_{1/2} \approx 9$ h) (25) compared with the corresponding derivative of *N*,*N*-diisopropylferrocenylcarboxamide ($t_{1/2} \approx 24$ h) (15). Noteworthy is the fact that the solution of C_2-symmetric analog, chiral 2,2′-bis(diphenylthio)-1,1′-ferrocenediamide (**7d**), exhibited a very low tendency towards isomerization losing ~30% ee and de on standing at room temperature (rt) for 19 days (25).

Highly diastereo- and enantio-enriched, tetrasubstituted ferrocenyldiamides *dl*-**7** were prepared by subjecting 1,2,1′-trisubstituted ferrocenes **6** to a further asymmetric D*o*M (Table 4). This constituted the first reported preparation of C_2-symmetric ferrocenes outfitted exclusively with the element of planar chirality (26). Quench with electrophiles furnished products **7a**, **7c**, and **7d** with diastereoselective amplification of enantioselectivity as demonstrated by converting **6h** (89% ee) into optically active, 2,2′-bis(diphenylthio)-1,1′-ferrocenediamide (**7d**, 97% ee, 99:1 dl:meso) (27).

To demonstrate the combined potential of D*o*M-cross coupling strategy (28) as a route to aryl-substituted ferrocenes, the iodo (**6c**) and stannane (**6f**) ferrocenediamides were subjected to Suzuki–Miyaura and Gronowitz-modified Stille (29) cross-coupling conditions (Scheme 4). Thus, the reaction of **6c** (89% ee) with (2,4-dimethoxyphenyl)boronic acid afforded the aryl derivatives **6k** in a modest yield (20% yield, 89% ee) together with recovered **6c** (70% yield). Palladium coupling of **6f** and bromobenzene led to a formation of **6l** (35% yield) along with destannylated product **5** (51% yield).

X-ray crystallographic analysis of compounds 7a and 6d

The (*S*) absolute configuration (8), established by single crystal X-ray crystallography analysis of carbinol **6d** (Fig. 1),[5] was provisionally assigned to all of the 2-substituted ferrocenediamides **6a**–**6l**. This is the same sense of enantioinduction as previously seen in (–)-sparteine-assisted D*o*M of *N*-cumyl-*N*-ethyl and *N*,*N*-diisolpropyl ferrocenyl monoamides (15, 18). The (*R*,*R*) absolute configuration of the C_2-symmetric derivatives of **5** (**7a**, **7c**, and **7d**,

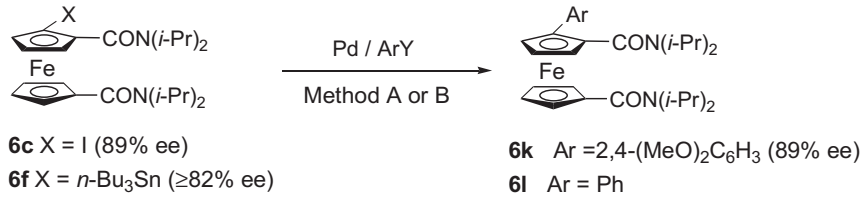
[5] Supplementary data for this article are available on the journal Web site (http://canjchem.nrc.ca) or may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0R6, Canada. DUD 5008. For more information on obtaining material refer to http://cisti-icist.nrc-cnrc.gc.ca/irm/unpub_e.shtml. CCDC 295149 and 602324 contain the crystallographic data for this manuscript. These data can be obtained, free of charge, via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax +44 1223 336033; or deposit@ccdc.cam.ac.uk).

Table 5. *n*-BuLi–(–)-sparteine-induced monolithiation of **5**.

No.	E+	Product (E)	Solvent	Yield (%)	ee (%)
1	I_2	**6c** (I)	Et_2O	53	59
2	I_2	**6c**	*t*-BuOMe	77	70
3	I_2	**6c**	PhMe	70	89
4	MeI	**6b** (Me)	PhMe	71	92
5	Ph_2C=O	**6d** (Ph_2C-OH)	PhMe	92	94
6	Ph_2C=O	**6d**	PhMe	72[a]	96
7	Et_2C=O	**6e** (Et_2C-OH)	PhMe	45	91
8	Bu_3SnCl	**6f** (Bu_3Sn)	PhMe	58	≥82[b]
9	Ph_2PCl	**6g** (Ph_2P)	PhMe	53	97[c]
10	$(PhS)_2$	**6h** (PhS)	PhMe	71	89[c]
11	$(PhSe)_2$	**6i** (PhSe)	PhMe	82	71[c]
12	TMSCl	**6a** (TMS)	PhMe	16	—[d]
13	TMSCl	**6a**	PhMe	68[a]	—[e]

Note: Conditions: 4.2 equiv. *s*-BuLi–(–)-sparteine, solvent at –78 °C for 2 h then 6 equiv. E^+ at –78 °C → rt for 4 h.
[a]2.1 equiv. of both *n*-BuLi and (–)-sparteine were used.
[b]ee was determined after conversion into **6d** (1, *n*-BuLi; 2, Ph_2C=O).
[c]ee determination was carried out immediately after purification.
[d]$[\alpha]^{23}_{578}$ +64.3° (*c* 0.11, $CHCl_3$); **7a** was also isolated in 71% yield (dr dl:meso, 72:28); 97% optical purity.
[e]$[\alpha]^{23}_{578}$ +67.5° (*c* 0.54, $CHCl_3$); also **7a** was isolated in 16% yield (dr dl:meso, 68:32); 99% optical purity.

Scheme 4.



6c X = I (89% ee)
6f X = *n*-Bu_3Sn (≥82% ee)

6k Ar =2,4-$(MeO)_2C_6H_3$ (89% ee)
6l Ar = Ph

Methods: A. on **6c**: 2,4-$(MeO)_2C_6H_3B(OH)_2$ / $Pd(PPh_3)_4$ / 2 mol/L aq. Na_2CO_3 / DME / 85 °C / 5 d (20% yld)
B. on **6f**: PhBr / $PdCl_2$(dppf) / CuO / DMF /150 °C / 18 h (35% yld)

Table 4) must be derived from (*R*) stereochemistry of the corresponding chiral precursors (**6a**, **6g**, and **6h**). The formation of *meso*-**7** products necessitates that the second deprotonation occurs with the opposite stereoselectivity, which may be the result of a cooperative effect of the two DMGs.

In the crystal structure of **6d**, the Cp rings are almost eclipsed with respect to each other, deviating by 14.0° from a fully eclipsed conformation. A hydrogen bond between the carbonyl group of carboxamide and the proximal hydroxyl group (O16—H16, 1.94 Å) is evident. Presumably, owing to packing effects, the two carboxylamides remain in a relative proximity.

Compound *meso*-**7a** proved amenable to X-ray analysis and its crystal structure is shown in Fig. 1.[5] The center of inversion structure entails the staggered conformation for both Cp rings with minimum interactions among the four substituents.

Applications of the ferrocenediamides

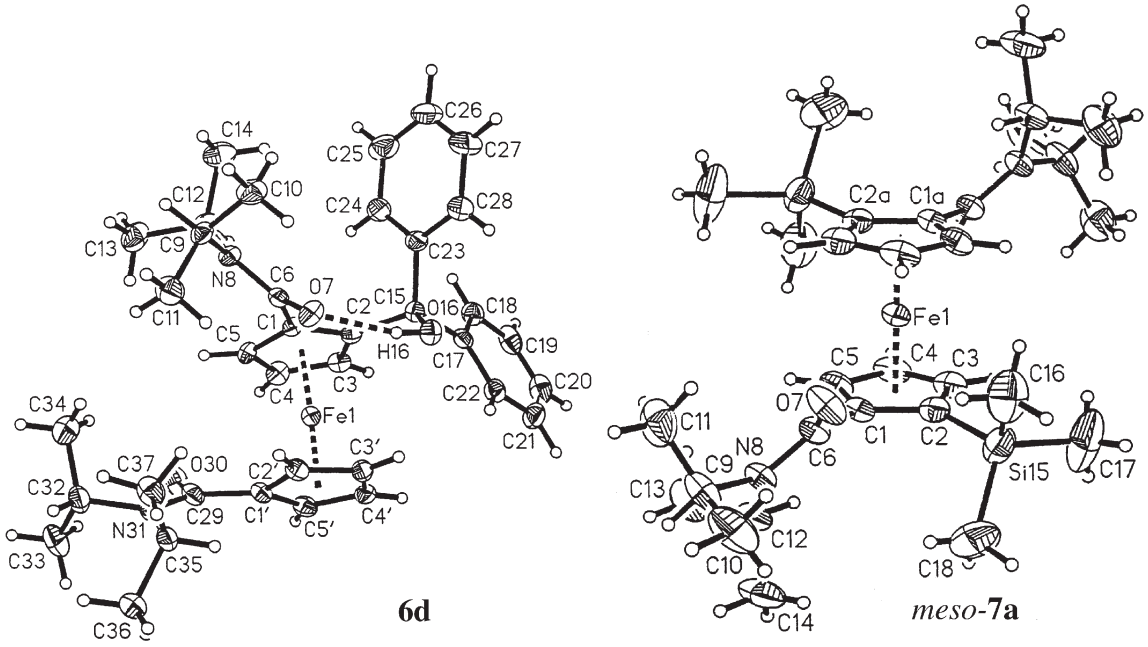
In an initial study of utility the new planar chiral ferrocenes in asymmetric synthesis, 1,1′-bis(diphenylphosphino)-2,2′-ferrocenyldiamide (**7c**, 98% ee) was tested as an auxiliary ligand for enantioselective Pd-catalyzed allylic substitution of (±)-phenylcinnamyl acetate (Scheme 5) (30).

The reactions were conducted using palladium allyl chloride dimer (2.5 mol%) as the Pd source utilizing the Trost alkylation conditions (31) or sodiodimethylmalonate. In both cases, alkylated product **8** was obtained in essentially quantitative yield and with good enantiocontrol (96% yield, 84% ee (*R*)). The enantiomeric excess was determined by chiral HPLC and the absolute configuration of the product was assigned by comparison of the optical rotation with literature values (32).

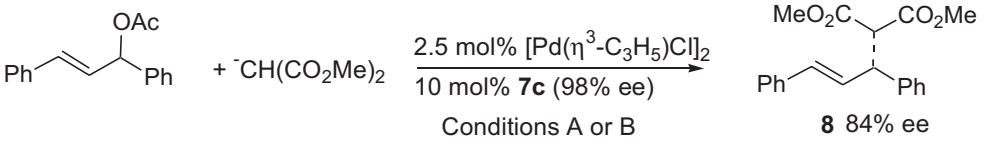
In an additional classic test for enantioinduction, the 1,1′,2-ferrocenyldiamides (**6d**, **6e**, and **6k**) were shown to exhibit moderate to good catalytic activities in the reaction of diethylzinc with benzaldehyde (Scheme 6, Table 6) (33).

Thus, in a typical reaction, a stirred solution of benzaldehyde (1 mmol) and chiral additive (**6d**, **6e**, **6k**) (5 mol%) in either hexane or PhMe under argon, was treated with diethylzinc (1.6 equiv.) and the resultant mixture was stirred at rt for 48–72 h. The crude product was analyzed by chiral HPLC, purified by flash chromatography, and the absolute configuration was determined by a comparison of its

Fig. 1. X-ray crystallographic structures of **6d** and *meso*-**7a**.

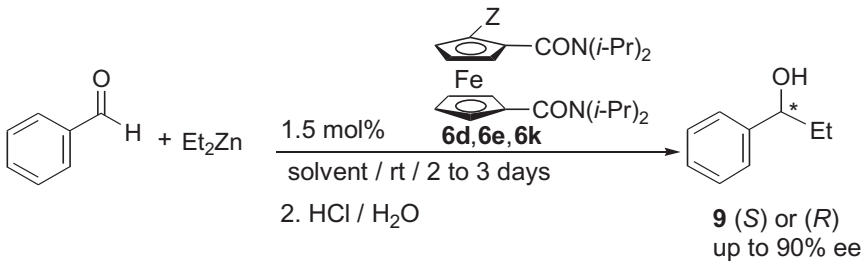


Scheme 5.



Conditions:
A. *N,O*-bis(trimethylsilyl)acetamide / AcOK / $CH_2(CO_2Me)_2$ / CH_2Cl_2 / rt / 10 h
B. $NaCH(CO_2Me)_2$ / THF / rt / 36 h

Scheme 6.



optical rotation with the literature values (34). The results are summarized in Table 6. Ethylations of benzaldehyde in hexanes catalyzed by carbinols **6d** and **6e** proceed with the same degree of enantioinduction; however, for **6e**, the chemical yield is greatly diminished, presumably as a consequence of the lower solubility of the catalyst (Table 6, entries 1 and 4). Quite unusual and, to our knowledge, previously unobserved, is the variation in the enantiotopicity of the reaction as a function of the solvent (Table 6, entry 1 vs. entry 2) and use of lithium salt of carbinol **6d** (Table 6, entry 2 vs. entry 3). The lithium salt of the **6d**-catalyzed reaction proceeded in PhMe with greater optical efficiency (47% ee) than the free carbinol **6d** (12% ee) and with a reversal of enantioselection (Table 6, entries 2 and 3). The best optical yield (90% ee) was observed for a nonprotic ligand **6k** (Table 6, entry 5). Attempts to lower the temperature of the process led to prohibitively long reaction times. These variations in the entantiotopiciy of the reaction are currently not understood.

In summary, direct and highly efficient enantioselective syntheses of mono- (**6a**–**6i**) and C_2-symmetric, homoleptic (**7a**, **7c**, and **7d**) ferrocene diamides from achiral ferrocenyldicarboxamide **5** using (–)-sparteine-mediated D*o*M and combined D*o*M-cross coupling (**6k**, and **6l**) have been demonstrated. The preliminary encouraging results in asymmetric synthesis and the current intense activity in ferrocene-

Table 6. 2-Substituted derivatives (**6d**, **6e**, **6k**) (catalyzed Et_2Zn addition to PhCHO).

No.	*Z*	Ligand (ee, %)	Solvent	Yield (%)	ee (%)[a]
1	$Ph_2C(OH)$	**6d** (96)	Hexanes	98	61 (*S*)
2	$Ph_2C(OH)$	**6d** (96)	PhMe	98	12 (*R*)
3	$Ph_2C(OLi)$	**6d**·Li (95)	PhMe	70	47 (*S*)[b]
4	$Et_2C(OH)$	**6e** (90)	Hexanes	37	60 (*S*)
5	2,4-$(MeO)_2C_6H_3$	**6k** (89)	PhMe	43	90 (*S*)

[a]Determined on a Chiracel OD column and compared to racemic material.
[b]$[\alpha]^{23}_D$ –21.7° (*c* 3.43, $CHCl_3$).

based catalysis (4, 35) may stimulate continuing efforts in the design, synthesis, and application of similar planar chiral ferrocenyl ligands.

Experimental section

General procedures

Melting points were determined on a Buchi SMP-20 or a Fisher hot stage melting point apparatus and were uncorrected. IR spectra were recorded on a BOMEM MB-100 and PerkinElmer 1600 FT-IR spectrophotometer as either neat film, a CH_2Cl_2 solution, or a KBr pellet. ^1H NMR and ^{13}C NMR spectra were recorded on either a Bruker AM-250 or an AC-200 instrument with tetramethylsilane or $CDCl_3$ as an internal standard. ^{31}P NMR spectra were recorded on an AC-200 instrument with H_3PO_4 as an external standard.

Mass spectra (MS) were determined on a high-resolution Varian MAT-CH7 instrument at 70 eV (Monsanto Co., St. Louis, Missouri and Guelph Centre for Mass Spectrometry Service, University of Waterloo Mass Spectrometry Service). Elemental analyses were performed by Chemisar Laboratories, Guelph, Ontario. Stereoselectivities of the reactions were determined using and a Waters HPLC system consisting of a 600E multisolvent delivery system, a Waters 486 UV detector (λ = 254 nm), and a Waters 746 integrator/recorder. The columns used were: Chiralpak, Chiracel OD, and Whelk-O1. Optical rotations were determined using a PerkinElmer 241 polarimeter at λ = 578 or 589 nm at rt. All dry solvents used were purified according to Perrin and Armarego (36): THF and Et_2O were freshly distilled from sodium benzophenone ketyl under nitrogen prior to use. Hexane and PhMe were distilled from CaH_2 and Na, respectively.

n-BuLi and *s*-BuLi were purchased from Sigma-Aldrich Chemical Co., as solutions in hexanes and cyclohexane, respectively. They were stored in resealable containers and titrated periodically against 2,5-dimethoxybenzyl alcohol (37) or *s*-butanol-1,10-phenanthroline (38). *N*,*N*,*N*′,*N*′-Tetramethylenethylenediamine (TMEDA) and (–)-sparteine were dried and distilled over CaH_2 and stored under argon. All commercial materials were purchased from Sigma-Aldrich Chemical Co. or Lancaster Synthesis Ltd. $Pd(PPh_3)_4$ was prepared following a literature procedure (39).

All the reactions were performed in oven-dried glassware under argon, using syringe-septum cap techniques. The –78 °C temperature designation is approximate and achieved by a dry ice – acetone bath. The phrase "standard workup" refers to addition of water or satd. aq. NH_4Cl, extraction with Et_2O, washing the organic extracts (brine), drying ($MgSO_4$), filtration, and concentration under reduced pressure. Flash column chromatography was carried out using Merck silica gel 60 (0.040–0.063 mm).

Standard methods

*(A) Lithiation of 1,1′-*N,N,N′,N′*-tetraisopropylferrocenedicarboxamide (5)*

A solution of (–)-sparteine (0.91 mL, 4.20 mmol) or TMEDA (0.64 mL, 4.20 mmol) in PhMe or Et_2O (20 mL) under Ar was stirred at rt (5 min), cooled to –78 °C, and treated with either *n*-BuLi or *s*-BuLi (4.20 mmol). After stirring (10 min) at –78 °C, a solution of **5** (0.44 g, 1.0 mmol) in either PhMe (4.5 mL) or Et_2O (10 mL) was added dropwise (ca. 1 drop / 10 s). After stirring for 2 h at –78 °C, the reaction mixture was quenched by an addition of electrophile (6 mmol) and then allowed to warm to rt over 4 h. Standard workup afforded the crude product.

*(B) Lithiation of 2-substituted derivatives of 1,1′-*N,N,N′,N′*-tetraisopropylferrocenedicarboxamide (6a, 6g, 6h)*

A solution of (–)-sparteine (0.45–0.91 mL, 2.1–4.2 mmol) in PhMe (20 mL) under Ar was stirred at rt (5 min), cooled to –78 °C, and treated with *n*-BuLi (4.2 mmol). After stirring (10 min) at –78 °C, a solution of a **6** (1.0 mmol) in PhMe (2.5 mL) was added slowly. After stirring for 2 h at –78 °C, the reaction mixture was quenched by addition of the electrophile (3.0–6.0 mmol), allowed to warm to rt over 4 h, and then subjected to standard workup to afford the crude product.

Experimental procedures

1,1′-Ferrocenedicarboxylic acid

A solution of *n*-BuLi (72.2 mL, 1.66 mol/L solution in hexane, 120 mmol) was added to a solution of ferrocene (10.1 g, 53.7 mmol) and TMEDA (20.0 mL, 132 mmol) in hexane (150 mL) under Ar at 0 °C. The reaction mixture was stirred for 12 h at rt. The hexane supernatant solution was removed via cannula and THF (150 mL) was added to dissolve the precipitate. The resultant solution was cooled to –78 °C and purged with carbon dioxide for 1 h. Later the reaction mixture was allowed to warm to rt and treated with H_2O (50 mL). THF was removed under reduced pressure. The aqueous residue was extracted with Et_2O (2 × 100 mL) and acidified with 2 N aq. HCl. The precipitate (bright yellow) was collected by filtration, dried in vacuo, and used without further purification (10.6 g, 72%); mp > 300 °C

(dec). IR (KBr) ν_{max}: 915, 1029, 1167, 1292, 1372, 1403, 1487, 1675, 2825 (br). ^{1}H NMR (DMSO-d_6) δ: 4.30 (s, 4H, Cp-*H*), 4.78 (s, 4H, Cp-*H*), 10.75–11.60 (br, 2H, COO*H*). ^{13}C NMR (DMSO-d_6) δ: 71.2, 72.5, 73.4, 171.0. MS *m*/*z* (rel intensity) (FAB): 274.2 (M^+, 8), 257.1 (11), 231.2 (8). HRMS calcd. for $C_{12}H_{10}{}^{56}FeO_4$: 273.9929; found: 273.9969.

1,1′-N,N,N′,N′-*Tetraisopropylferrocenedicarboxamide (5)*

To a stirred solution of 1,1′-ferrocenedicarboxylic acid (10.0 g, 36.2 mmol) in PhMe (100 mL) at rt, DMF (1.10 mL, 14.1 mmol) and oxalyl chloride (12.8 mL, 149 mmol) were added sequentially. The reaction mixture was stirred for 1 h at rt before PhMe and the excess of oxalyl chloride were removed under reduced pressure. The residue was dissolved in Et_2O (250 mL), cooled to 0 °C, and treated with an excess of HN(*i*-Pr)$_2$ (28.4 mL, 217 mmol). The reaction mixture was stirred for 8–12 h at rt. Standard workup followed by column chromatography (EtOAc–hexane, 1:2) and crystallization gave **5** as an orange solid (11.1 g, 80%); mp 133 to 134 °C (Et_2O–hexane) (lit. value (40) mp 127 to 128 °C). IR (KBr) ν_{max}: 1000, 1050, 1105, 1162, 1198, 1225, 1289, 1377, 1458, 1561, 1684, 2803, 2957, 3091. ^{1}H NMR ($CDCl_3$) δ: 1.05–1.70 (br, 24H, CH(C*H*$_3$)$_2$), 3.30–3.58, 4.35–4.55 (br, 2H, C*H*(CH$_3$)$_2$), 4.37 (t, *J* = 2.0 Hz, 4H, C$_5$*H*$_4$), 4.58 (t, *J* = 2.0 Hz, 4H, C$_5$*H*$_4$). ^{13}C NMR ($CDCl_3$) δ: 21.0, 70.9, 71.3, 83.2, 167.1. MS *m*/*z* (rel intensity) (EI): 440 (M^+, 100), 340 (16), 312 (9), 270 (6), 248 (20), 213 (10), 186 (11), 177 (5), 156 (12), 146 (9), 121 (19), 92 (10), 65 (7). HRMS calcd. for $C_{24}H_{36}{}^{54}FeN_2O_2$: 438.2169; found: 438.2173.

2-(Trimethylsilyl)-1,1′-N,N,N′,N′-*tetraisopropylferrocenedicarboxamide (6a)*

According to Standard method A, a solution of (–)-sparteine (0.49 mL, 2.2 mmol) and *n*-BuLi (1.4 mL, 1.65 mol/L solution in hexane, 2.2 mmol) was sequentially treated with a solution of **5** (0.47 g, 1.1 mmol) in PhMe and TMSCl (0.34 mL, 2.7 mmol). Standard workup followed by column chromatography (EtOAc–hexane, 1:30) afforded compound **6a** as an orange solid (0.42 g, 68%); mp 107.0–107.5 °C (hexanes). $[\alpha]^{23}_{578}$ +67.5° (*c* 0.54, $CHCl_3$). IR (KBr) ν_{max}: 2962, 2883, 1624, 1449, 1325, 1204, 1149, 1040, 829, 754. ^{1}H NMR ($CDCl_3$) δ: 0.23 (s, 9H, Si(C*H*$_3$)$_3$), 0.80–1.60 (br, 24H, CH(C*H*$_3$)$_2$)), 3.2–4.1 (br, 4H, C*H*(CH$_3$)$_2$), 4.20, 4.38, 4.43, 4.49, 4.57, 4.67 (m, 7H, Cp-*H*). ^{13}C NMR ($CDCl_3$) δ: 0.5, 20.7, 21.2, 71.0, 72.03, 72.23, 75.7, 82.4, 93.5, 168.6. MS *m*/*z* (rel intensity) (EI): 512 (M^+, 51), 510 (4), 497 (100), 439 (7), 220 (9), 149 (14), 73 (14). HRMS calcd. for $C_{27}H_{44}{}^{54}FeN_2O_2Si$: 510.2568; found: 510.2551. Two other isolated fractions contained *dl*-**4a** (0.032g, 5%), $[\alpha]^{23}_{578}$ +49.2° (*c* 0.49, $CHCl_3$), 99% op (optical purity) and *meso*-**4a** (0.015 g, 2%).

2-Methyl-1,1′-N,N,N′,N′-*tetraisopropylferrocenedicarboxamide (6b)*

According to Standard method A, a solution of (–)-sparteine (0.91 mL, 4.1 mmol) and *n*-BuLi (2.35 mL, 1.75 mol/L solution in hexane, 4.12 mmol) was sequentially treated with a solution of **5** (0.437 g, 0.98 mmol) in PhMe and MeI (0.37 mL, 5.9 mmol). Standard workup followed by column chromatography (EtOAc–hexane, 1:4) afforded **6b** as an orange solid (0.32 g, 71%); mp 123 to 124 °C. CSP HPLC analysis (Chiralcel OD; eluent: *n*-hexane–*i*-PrOH–Et_2NH (99:1:0.01, flow 0.75 mL/min) determined 92% ee (t_R(major *dl*) = 26.95 min, t_R(minor) = 29.35 min). $[\alpha]^{23}_{578}$ +63.2° (*c* 0.66, $CHCl_3$). IR (KBr) ν_{max}: 1025, 1044, 1111, 1137, 1157, 1204, 1316, 1372, 1453, 1615, 2954, 3001, 3086. ^{1}H NMR ($CDCl_3$) δ: 0.65–1.82 (br, 24H, CH(C*H*$_3$)$_2$)), 2.02 (s, 3H, CpC*H*$_3$), 3.25–3.55 and 3.70–4.05 (br, 4H, C*H*(CH$_3$)$_2$), 4.18 (m, 2H, Cp-*H*), 4.39 (m, 2H, Cp-*H*), 4.57 (m, 2H, Cp-H), 4.67 (br, 1H, Cp-*H*). ^{13}C NMR ($CDCl_3$) δ: 12.7, 20.1, 20.7, 20.9, 21.0, 45.3, 50.2, 67.8, 68.2, 70.8, 71.3, 71.4, 71.6, 72.0, 82.1, 85.1, 88.2, 169.2. MS *m*/*z* (rel intensity) (EI): 454 (27), 426 (4), 169 (6). HRMS calcd. for $C_{25}H_{38}{}^{56}FeN_2O_2$: 454.2283; found: 454.2242.

2-Iodo-1,1′-N,N,N′,N′-*tetraisopropylferrocenedicarboxamide (6c)*

According to Standard method A, a solution of (–)-sparteine (0.97 mL, 4.20 mmol) and *n*-BuLi (2.47 mL, 1.70 mol/L solution in hexane, 4.20 mmol) was sequentially treated with solutions of **5** (0.44 g, 1.0 mmol) and iodine (1.52 g, 6.00 mmol) in PhMe (4.5 mL and 14 mL, respectively). Standard workup followed by column chromatography (EtOAc–hexane, 1:10) afforded **6c** as a slowly solidifying orange oil (0.37 g, 70%); mp 113–115 °C. CSP HPLC analysis ((*S*,*S*)-Whelk-O1; eluent: *n*-hexane–*i*-PrOH (96:4, flow 0.5 mL/min) determined 89% ee (t_R(major) = 25.84 min, t_R(minor) = 21.68 min). $[\alpha]^{23}_D$ +33.2 (*c* 0.47, $CHCl_3$). IR (neat) ν_{max}: 807, 1037, 1206, 1316, 1369, 1460, 1635, 2931, 2966. ^{1}H NMR ($CDCl_3$) δ: 0.92–1.72 (m, 24H, CH(C*H*$_3$)$_2$), 3.38–3.70 (m 4H, C*H*(CH$_3$)$_2$), 4.26–6.60 and 4.82–4.88 (m, 7H, Cp*H*). ^{13}C NMR ($CDCl_3$) δ: 20.41, 20.54, 40.64, 45.6, 50.4, 68.9, 70.3, 72.8, 74.1, 74.7, 75.1, 83.7, 92.8, 165.6, 168.0. MS *m*/*z* (rel intensity) (EI): 566 (M^+, 0.5), 502 (8), 414 (6), 219 (25), 131 (40), 69 (100). HRMS calcd. for $C_{24}H_{35}{}^{56}FeIN_2O_2$: 566.1092; found: 566.1103.

2-(Diphenylhydroxymethyl)-1,1′-N,N,N′,N′-*tetraisopropylferrocenedicarboxamide (6d)*

Method 1

According to Standard method A, a solution of (–)-sparteine (0.91 mL, 4.1 mmol) and *n*-BuLi (2.36 mL, 1.75 mol/L solution in hexane, 4.1 mmol) was sequentially treated with solutions of **5** (0.433 g, 0.98 mmol) and benzophenone (1.07 g, 5.90 mmol) in PhMe (4.5 mL and 10.0 mL, respectively). Standard workup followed by column chromatography (EtOAc–hexane, 1:15) afforded the title compound (**6d**) as an orange solid (0.56 g, 92%); mp 179–182 °C (Et_2O). CSP HPLC analysis ((*S*,*S*)-Whelk-O1; eluent: *n*-hexane–*i*-PrOH 92:8, flow 0.75 mL/min) determined 94% ee (t_R(major) = 12.06 min, t_R(minor) = 15.15 min). $[\alpha]^{23}_D$ +161.1° (*c* 0.54, $CHCl_3$). IR (KBr) ν_{max}: 704, 752, 765, 818, 832, 1031, 1047, 1134, 1161, 1202, 1320, 1368, 1456, 1594, 2875, 2932, 2966, 3066, 3204. ^{1}H NMR ($CDCl_3$) δ: 0.65–1.48 (br, 24H, CH(C*H*$_3$)$_2$), 2.87, 3.15, 3.44, 4.20 (m, 4H, C*H*(CH$_3$)$_2$), 3.67, 4.29, 4.56, 4.63, 4.92 (m, 7H, Cp-*H*), 5.81 (s, 1H, O*H*), 7.06–7.40, 7.55 (m, 10H, Ph*H*), 7.94 (s, 1H, C*H*(OH)Ph$_2$). ^{13}C NMR ($CDCl_3$) δ: 20.4, 20.5, 40.6, 45.6, 50.4, 68.9, 70.3, 72.8, 74.07, 74.7, 75.1, 83.7, 92.8, 165.6, 168.0. MS *m*/*z* (rel intensity) (EI): 622 (M^+, 2), 614 (8), 502

(50), 414 (42), 354 (3), 218 (78), 131 (100), 70 (98). HRMS calcd. for $C_{37}H_{46}{}^{56}FeN_2O_3$: 622.2858; found: 622.2836.

Method 2

By Sn-Li exchange from 2-(tributylstannyl)-1,1′-N,N,N′,N′-tetraisopropylferrocenedicarboxamide (6f).

n-BuLi (0.09 mL, 1.67 mol/L solution in hexane, 0.15 mmol) was added to a cold (–78 °C), stirred solution of 2-(tributylstannyl)-1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**6f**) (0.10 g, 0.14 mmol) in PhMe (5 mL). The resulting solution was stirred for 15 min, benzophenone (0.052 g, 0.28 mmol) in PhMe (0.5 mL) was added, and stirring was continued for 40 min at –78 °C before the reaction mixture was allowed to warm to rt. Standard workup and flash chromatography (EtOAc–hexane, 8:1) afforded pure **6d** (0.022 g, 25%) and also **5** (3 mg, 5%) and unreacted 2-(tributylstannyl)-1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**6f**) (51 mg, 49%). The crude product was analysed by CSP HPLC ((*S*,*S*)-Whelk-O1; eluent: *n*-hexane–*i*-PrOH 97:3, flow 0.5 mL/min) and found to be 82% ee (t_R(major) = 22.88 min, t_R(minor) = 35.98 min).

2-(Diethylhydroxymethyl)-1,1′-N,N,N′,N′-tetraisopropylferrocenedicarboxamide (6e)

According to Standard method A, a solution of (–)-sparteine (0.97 mL, 4.4 mmol) and *n*-BuLi (2.31 mL, 1.90 mol/L solution in hexane, 4.40 mmol) was sequentially treated with solutions of **5** (0.459 g, 1.04 mmol) and 3-pentanone (0.63 mL, 6.2 mmol) in PhMe (4.5 and 5.0 mL, respectively). Standard workup followed by column chromatography (EtOAc–hexane, 1:6) afforded **6e** as an orange solid (0.25 g, 45%); mp 121 to 122 °C. CSP HPLC analysis (Chiralcel OD; eluent: *n*-hexane–*i*-PrOH 98:2, flow 0.15 mL/min) determined 90% ee (t_R(major) = 37.02 min, t_R(minor) = 39.18 min). $[\alpha]^{23}{}_{578}$ –31.2° (*c* 0.34, $CHCl_3$). IR (KBr) ν_{max}: 814, 970, 1038, 1038, 1113, 1135, 1157, 1200, 1340, 1453, 1604, 2939, 3343. ^{1}H NMR ($CDCl_3$) δ: 0.47 (t, *J* = 7.5 Hz, 3H, CH_2CH_3), 0.72–1.98 (m, 31H, $CH(CH_3)_2$, CH_2CH_3, CH_2CH_3, 3.29–3.55 (br, 4H, $CH(CH_3)_2$), 4.10–4.32 (m, 3H, Cp*H*), 4.47 (s, 1H, Cp*H*), 4.60 (s, 2H, Cp*H*), 4.73 (s, 1H, Cp*H*), 6.10 (s, 1H, O*H*). ^{13}C NMR ($CDCl_3$) δ: 7.6, 9.2, 20.3, 20.7, 20.9, 29.6, 33.9, 46.2, 50.8, 67.7, 69.5, 71.7, 72.2, 72.6, 82.0, 83.1, 101.4, 168.9, 171.4. MS *m*/*z* (rel intensity) (EI): 526 (M^+, 18), 508 (100), 446 (3), 338 (4), 316 (12), 306 (5), 265 (5), 231 (5), 161 (7), 105 (9), 91 (8), 86 (7). HRMS calcd. for $C_{29}H_{46}{}^{56}FeN_2O_3$: 526.2858; found: 526.2893. Anal. calcd. for $C_{29}H_{46}FeN_2O_3$: C 66.15, H 8.80, N 5.22; found: C 66.17, H 8.65, N 4.93.

2-(Tributylstannyl)-1,1′-N,N,N′,N′-tetraisopropylferrocenedicarboxamide (6f)

According to Standard method A, a solution of (–)-sparteine (0.92 mL, 4.2 mmol) and *n*-BuLi (5.17 mL, 1.68 mol/L solution in hexane, 8.69 mmol) was sequentially treated with a PhMe (4.5 mL) solution of **5** (0.903 g, 1.00 mmol) and neat tributyltin chloride (3.51 mL, 12.41 mmol). Standard workup followed by column chromatography (EtOAc–hexane, 1:10) afforded **6f** as a red oil, which was purified by Kugelrohr distillation (0.86 g, 58%). $[\alpha]^{23}{}_{578}$ +90.4° (*c* 0.44, $CHCl_3$). IR (neat) ν_{max}: 1039, 1158, 1204, 1280, 1323, 1372, 1457, 1614, 2930. ^{1}H NMR ($CDCl_3$) δ: 0.79–1.83 (br, 51H, $CH(CH_3)_2$, Bu-*H*), 3.19–3.68 (br, 4H, $CH(CH_3)_2$)), 4.22–4.33 (m, 3H, Cp- *H*), 4.30–4.52 (m, 2H, Cp-*H*), 4.52–4.68 (m, 2H, Cp-*H*). ^{13}C NMR ($CDCl_3$) δ: 11.22, 13.7, 14.6, 14.8, 21.0, 26.8, 27.4, 28.0, 29.2, 46.1, 50.0, 69.9, 70.4, 71.1, 71.5, 72.0, 74.2, 76.1, 82.3, 88.4, 168.9, 169.4. MS *m*/*z* (rel intensity) (FAB): 730 (M^+, 7), 673 (100), 630 (9), 558 (28), 495 (28), 426 (16), 368 (20). Anal. calcd. for $C_{36}H_{62}FeN_2O_2Sn$: C 59.28, H 8.57, N 3.84; found: C 58.99, H 8.49, N 3.80.

2-(Diphenylphosphino)-1,1′-N,N,N′,N′-tetraisopropylferrocenedicarboxamide (6g)

According to Standard method A, a solution of (–)-sparteine (1.04 mL, 4.20 mmol) and *n*-BuLi (2.40 mL, 1.75 mol/L solution in hexane, 4.20 mmol) was sequentially treated with a PhMe (4.5 mL) solution of **5** (0.440 g, 1.00 mmol) and neat chlorodiphenylphosphine (1.1 mL, 6.0 mmol). After stirring for 1 h at –78 °C, the reaction mixture was allowed to warm to 0 °C and quenched with satd. aq. NH_4Cl. Standard workup followed by column chromatography (SiO_2 deactivated by additon of 2% Et_3N, EtOAc–hexane 1:10) afforded **6g** as an orange solid (0.335 g, 54%); mp 142–144 °C (dec). CSP HPLC analysis (Chiracel OD; eluent: *n*-hexane–*i*-PrOH 98:2, flow 0.25 mL/min) determined 97% ee (t_R(major) = 31.31 min, t_R(minor) = 34.24 min). $[\alpha]^{23}{}_D$ +225.5° (*c* 0.31, CH_2Cl_2). IR (KBr) ν_{max}: 2963, 1624, 1449, 1336, 1206, 820, 751, 701. ^{1}H NMR ($CDCl_3$) δ: 0.32–1.75 (br, 24 $CH(CH_3)_2$), 3.03–3.48 (br, 4H, $CH(CH_3)_2$), 3.90, 4.26, 4.34, 4.37, 4.45, 4.51, 4.58, 4.65, 4.80 (m, 7H, Cp*H*), 7.18–7.62 (br, 10H, C_6H_5). ^{13}C NMR ($CDCl_3$) δ: 20.3, 21.4, 31.6, 71.7, 72.2, 73.4, 74.7, 76.9, 80.3, 82.7, 86.0, 98.3, 128.1, 128.2, 128.7, 133.0, 133.4, 134.1, 134.6, 137.9, 139.2, 166.7. MS *m*/*z* (rel. intensity) (EI): 625 (M^+, 62), 539 (71), 423 (100), 346 (84), 245 (69). HRMS calcd. for $C_{36}H_{46}{}^{56}FeN_2O_2P$: 625.2674; found: 625.2646.

2-(Phenylthio)-1,1′-N,N,N′,N′-tetraisopropylferrocenedicarboxamide (6h)

According to Standard method A, a solution of (–)-sparteine (0.93 mL, 4.2 mmol) and *n*-BuLi (2.76 mL, 1.52 mol/L solution in hexane, 4.2 mmol) was sequentially treated with solutions of **5** (0.440 g, 1.00 mmol) and Ph_2S_2 (1.30 g, 5.95 mmol) in PhMe (4.5 mL and 10.0 mL, respectively). Standard workup followed by column chromatography (EtOAc–hexane, 1:6) afforded **6h** (0.39 g, 71%); mp 135–137 °C. CSP HPLC analysis (Chiralcell OD; eluent: *n*-hexane–*i*-PrOH (0.1% solution of Et_2NH of 99.1:0.9, flow mL/min) determined 89% ee (t_R(major) = 17.54 min, t_R(minor) = 21.21 min). $[\alpha]^{23}{}_{578}$ +97.7° (*c* 1.41, $CHCl_3$). IR (KBr) ν_{max}: 738, 814, 814, 840, 1041, 1143, 1205, 1337, 1453, 1611, 2935. ^{1}H NMR ($CDCl_3$) δ: 0.33–1.61 (br, 24H, $CH(CH_3)_2$), 3.12–3.78 (br, 4H, $CH(CH_3)_2$), 4.35–4.98 (m, 7H, Cp-*H*), 7.01–7.37 (m, 5H, C_6H_5). ^{13}C NMR ($CDCl_3$) δ: 19.99, 20.4, 20.7, 20.9, 45.8, 50.5, 70.6, 71.7, 72.6, 72.9, 73.7, 73.9, 77.7, 79.0, 83.7, 92.8, 125.4, 127.3, 128.7, 139.7, 165.5, 168.6. MS *m*/*z* (rel intensity) (FAB): 548 (M^+, 45), 460 (62), 372 (72), 328 (31), 185 (100), 132 (88). Anal. calcd. for $C_{30}H_{40}FeN_2O_2S$: C 65.67, H 7.35, N 5.11; found: C 65.80, H 7.28, N 5.05.

2-(Phenylselenyl)-1,1′-N,N,N′,N′-tetraisopropylferrocenedicarboxamide (6i)

According to Standard method A, a solution of (–)-sparteine (0.92 mL, 4.2 mmol) and *n*-BuLi (2.49 mL, 1.68 mol/L solution in hexane, 4.19 mmol) was sequentially treated with solutions of **5** (0.439 g, 1.00 mmol) and Ph_2Se_2 (1.87 g, 5.98 mmol) in PhMe (4.5 and 2.5 mL, respectively). Standard workup followed by column chromatography (EtOAc–hexane, 1:4) afforded **6i** (0.36 g, 82%); mp 126 to 127 °C. CSP HPLC analysis (Chiralcel OD; eluent: *n*-hexane–*i*-PrOH 99:1, flow 0.3 mL/min) determined 71% ee (t_R(major) = 32.92 min, t_R(minor) = 35.90 min). $[\alpha]^{23}_{578}$ +216° (*c* 0.23, $CHCl_3$). IR (CH_2Cl_2) ν_{max}: 1037, 1135, 1160, 1205, 1266, 1322, 1372, 1463, 1475, 1621, 2971, 2934, 3053. ^{1}H NMR ($CDCl_3$) δ: 0.37–1.60 (br, 24H, $CH(CH_3)_2$)), 3.11–3.76 (br, 4H, $CH(CH_3)_2$)), 4.40 (dd, *J* = 2.8, 1.3 Hz, 1H, Cp-*H*), 4.48–4.70 (m, 3H, Cp-*H*), 4.68 (dt, *J* = 1.3, 2.6 Hz, 1H, Cp-*H*), 4.90 (dt, *J* = 1.3, 2.6 Hz, 1H, Cp*H*), 7.08–7.19 (m, 3H, C_6H_5), 7.27–7.35 (m, 2H, C_6H_5). ^{13}C NMR ($CDCl_3$) δ: 14.1, 21.0, 22.6, 31.5, 45.8, 49.8, 50.4, 71.1, 71.2, 72.2, 72.6, 73.4, 73.2, 74.2, 77.3, 83.4, 92.4, 126.1, 128.8, 130.3, 133.7, 166.0, 168.5. MS *m*/*z* (rel intensity) (FAB): 597 (M^+, 9), 553 (8), 517 (6), 461 (11), 369 (32), 356 (5), 277 (100), 241 (8). HRMS calcd. for $C_{30}H_{41}{}^{56}FeN_2O_2Se$: 597.1683; found: 597.1678.

2-(2,4-Dimethoxyphenyl)-1,1′-N,N,N′,N′-tetraisopropylferrocenedicarboxamide (6k)

A mixture of $Pd(PPh_3)_4$ (0.070 g, 0.06 mmol), 2-iodo-1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**6c**) (0.34 g, 0.61 mmol, 89% ee), degassed aq. Na_2CO_3 solution (1.80 mL, 2 mol/L, 3.66 mmol), and 2,4-dimethoxyphenylboronic acid (0.18 g, 0.97 mmol) in freshly distilled DME (15 mL) was refluxed for 5 days. The crude material was passed through Celite, and the filtrate was subjected to standard workup. Purification by column chromatography (EtOAc–hexane, 1:8) afforded **6k** as a brown-red solid (0.069 g, 20%); mp 161–163 °C. CSP HPLC analysis (Chiralcel OD; eluent: *n*-hexane–*i*-PrOH 98.5:1.5, flow 0.20 mL/min) determined 89% ee (t_R(major) = 67.93 min, t_R(minor) = 75.04 min). $[\alpha]^{23}_{578}$ +8.9° (*c* 0.18, $CHCl_3$). IR (KBr) ν_{max}: 817, 1036, 1151, 1205, 1317, 1370, 1454, 1533, 1619, 2936. ^{1}H NMR ($CDCl_3$) δ: 0.25–1.75 (br, 24H, $CH(CH_3)_2$), 3.05–3.65 (b, 2H, $CH(CH_3)_2$), 3.72 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 4.32–4.44 (m, 3H, Cp*H*), 4.54 (m, 2H, Cp*H*), 4.67–4.70 (m, 1H, Cp*H*), 4.76–4.79 (m, 1H, Cp*H*), 6.38 (d, *J* = 2.6 Hz, 1H, H(3)-C_6H_3), 6.45 (dd, *J* = 2.6, 8.4 Hz, 1H, H(5)-C_6H_3), 7.70 (d, *J* = 8.4 Hz, 1H, H(6)-C_6H_3). ^{13}C NMR ($CDCl_3$) δ: 19.5, 19.9, 20.9, 21.0, 45.5, 50.4, 55.4, 69.3, 69.8, 71.5, 71.7, 73.0, 73.4, 74.7, 81.4, 82.4, 90.0, 98.2, 104.2, 117.7, 127.9, 128.1, 130.4, 132.6, 134.7, 134.9, 157.9, 159.8, 167.7, 169.3. MS *m*/*z* (rel intensity) (CI): 577 (MH^+, 46), 576 (42), 476 (9), 441 (17), 349 (6), 330 (13), 309 (6), 253 (16), 233 (13), 194 (16), 145 (22), 131 (15), 117 (100), 100 (14), 86 (19), 71 (10). HRMS calcd. for $C_{32}H_{44}{}^{56}FeN_2O_4$: 576.2650; found: 576.2675.

2-Phenyl-1,1′-N,N,N′,N′-tetraisopropylferrocenedicarboxamide (6l)

A mixture of $PdCl_2$(dppf) (37 mg, 0.051 mmol), CuO (95 mg, 1.2 mmol), and PhBr (0.02 mL, 0.19 mmol) in DMF (3 mL) was heated to 150 °C for 30 min and treated with a solution of 2-(tributylstannyl)-1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**6f**) (0.107 g, 0.15 mmol, $[\alpha]^{23}_{578}$ +90.4° (*c* 0.44, $CHCl_3$), i.e., ≥82% ee) in DMF (0.3 mL). The resulting reaction mixture was stirred for 18 h at 100 °C, cooled to rt, passed through Celite, concentrated and subjected to standard workup followed by column chromatography (hexane–EtOAc, 6:1) to afford **6l** as a brown oil (27 mg, 35%) and separately 1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**5**) (24 mg, 51%). Compound **6l**: $[\alpha]^{23}_{578}$ –266.1° (*c* 0.17, $CHCl_3$). IR (neat) ν_{max}: 764, 815, 1038, 1111, 1135, 1159, 1207, 1261, 1318, 1372, 1457, 1508, 1623, 2926, 2964. ^{1}H NMR ($CDCl_3$) δ: 0.24–1.72 (br, 24H, $CH(CH_3)_2$), 3.13–3.60 (br, 4H, $CH(CH_3)_2$), 4.25–4.92 (br, 7H, Cp*H*), 7.25 (m, 3H, C_6H_5), 7.56 (m, 2H, C_6H_5). ^{13}C NMR ($CDCl_3$) δ: 19.5, 19.8, 20.8, 20.9, 21.0, 22.7, 29.7, 45.7, 50.6, 68.6, 70.0, 70.9, 72.0, 72.9, 73.4, 74.3, 82.4, 85.6, 90.1, 126.6, 128.1, 137.5, 167.5, 168.9. MS *m*/*z* (rel intensity) (FAB): 517 (MH^+, 22), 416 (5), 330 (3), 277 (8), 185 (100), 116 (5). HRMS calcd. for $C_{30}H_{41}{}^{56}FeN_2O_2$ (MH^+): 517.2518; found: 517.2495.

2,2′-Bis(trimethylsilyl)-1,1′-N,N,N′,N′-tetraisopropylferrocenedicarboxamide (7a)

Method 1

From 1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**5**). According to Standard method A, a solution of (–)-sparteine (0.51 mL, 2.30 mmol) and *n*-BuLi (1.36 mL, 1.69 mol/L solution in hexane, 2.30 mmol) in PhMe (20 mL) was sequentially treated with a solution of 1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**5**) (0.24 g, 0.55 mmol) PhMe (4.5 mL) and then TMSCl (0.42 mL, 3.3 mmol). Standard workup followed by column chromatography (EtOAc–hexane, 1:30) gave separately *dl*-**7a** (0.153 g, 50%), *meso*-**7a** (0.065 g, 21%), and 2-(trimethylsilyl)-1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**6a**) (0.043 g, 16%, $[\alpha]^{23}_{578}$ +64.3° (*c* 0.11, $CHCl_3$)) as orange solids.

dl-*2,2′-Bis(trimethylsilyl)-1,1′-N,N,N′,N′-tetraisopropylferrocenedicarboxamide (7a):* $[\alpha]^{23}_{578}$ +48.0° (*c* 0.51, $CHCl_3$). Optical purity: 97%; mp 192–194 °C (hexanes). IR (KBr) ν_{max}: 833, 1041, 1069, 1120, 1155, 1207, 1246, 1279, 1330, 1371, 1455, 1627, 2934. ^{1}H NMR ($CDCl_3$) δ: 0.25 (s, 18H, $Si(CH_3)_3$), 0.77–1.12 (br, 24H, $CH(CH_3)_2$), 3.15–3.50, 3.80–4.06 (br, 4H, $CH(CH_3)_2$), 4.15 (s, 2H, Cp-*H*), 4.60 (s, 4H, Cp-*H*). ^{13}C NMR ($CDCl_3$) δ: 0.6, 20.7, 45.9, 50.1, 73.0, 73.5, 74.0, 74.4, 92.6, 168.9. MS *m*/*z* (rel intensity) (EI): 585 (M^+, 76), 442 (26), 312 (16), 220 (22), 128 (17), 73 (95). Anal. calcd. for $C_{30}H_{52}{}^{56}FeN_2O_2Si_2$: C 61.62, H 8.96, N 4.79; found: C 61.50, H 8.73, N 4.79.

meso-*2,2′-Bis(trimethylsilyl)-1,1′-N,N,N′,N′-tetraisopropylferrocenedicarboxamide (7a):* mp 192–194 °C (Et_2O–hexane). IR (KBr) ν_{max}: 904, 1040, 1067, 1127, 1156, 1207, 1279, 1349, 1454, 1623, 2963, 3088. ^{1}H NMR ($CDCl_3$) δ: 1.32 (s, 18H, $Si(CH_3)_3$), 0.75–1.70 (br, 24H, $CH(CH_3)_2$), 3.15–3.44, 3.73–4.05 (br, 4H, $CH(CH_3)_2$), 4.34 (s, 2H, Cp-*H*), 4.43 (s, 2H, Cp-*H*), 4.52 (s, 2H, Cp-*H*). ^{13}C NMR ($CDCl_3$) δ: 0.0, 20.7, 45.7, 50.1, 70.5, 72.6, 74.8, 92.2, 168.7. MS (EI) *m*/*z* (rel intensity): 585 (M^+, 5), 370 (2), 204 (3), 100 (5), 73 (100). Anal. calcd. for $C_{30}H_{52}{}^{56}FeN_2O_2Si_2$: C 61.62, H 8.96, N 4.79; found: C 61.80, H 8.85, N 4.79.

Method 2

From 2-(trimethylsilyl)-1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**6a**). According to Standard method B, a solution of (–)-sparteine (0.71 mL, 3.23 mmol), and *n*-BuLi (1.96 mL, 1.65 mol/L solution in hexane, 3.23 mmol) in PhMe (20 mL) was sequentially treated with a solution of 2-(trimethylsilyl)-1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**6a**, 0.39 g, 0.76 mmol, $[\alpha]^{23}_{578}$ +67.5° (*c* 0.54, $CHCl_3$)) in PhMe (2.5 mL) and then TMSCl (0.60 mL, 4.6 mmol). Standard workup followed by column chromatography (EtOAc–hexane, 1:30) gave the title compounds (**7a**) as orange solids; *dl*-**7a** (0.336 g, 75%) and *meso*-**7a** (0.056 g, 12%), *dl*-**7a** ($[\alpha]^{23}_{578}$ +44.8° (*c* 0.42, $CHCl_3$)); 91% optical purity.

2,2′-Dimethyl-1,1′-N,N,N′,N′-*tetraisopropylferrocenedicarboxamide (7b)*

Method 1

From 1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**5**) using *s*-BuLi. According to Standard method A, a solution of (–)-sparteine (0.90 mL, 4.1 mmol) and *s*-BuLi (3.44 mL, 1.18 mol/L solution in cyclohexane, 4.06 mmol) in Et_2O (20 mL) was sequentially treated with a solution of 1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**5**) (0.447 g, 1.02 mmol) in Et_2O (10 mL) followed by MeI (0.38 mL, 6.1 mmol). Standard workup followed by column chromatography (EtOAc–hexane, 1:15) afforded a mixture of *meso*-**7b** and *dl*-**7b** diastereomers (0.33 g, 70%) as an orange solid. CSP HPLC analysis (Chiralcel OD; eluent: *n*-hexane–*i*-PrOH 99.4:0.6, flow 1.0 mL/min) determined dr (meso:dl, 76:24) and 52% ee (t_R(major dl) = 5.74 min, t_R(minor dl) = 6.96 min, t_R(meso diastereomer) = 9.30 min). IR (KBr) ν_{max}: 815, 1022, 1037, 1076, 1134, 1156, 1210, 1314, 1346, 1371, 1455, 1629, 2937, 3088. ^{1}H NMR ($CDCl_3$) δ: 0.62–1.78 (br, 24H, $CH(CH_3)_2$), 2.02 (s, 6H, $CpCH_3$), 3.18–4.00 (br, 4H, $CH(CH_3)_2$), 4.15 (m, 2H, Cp-*H*), 4.36 (m, 2H, Cp-*H*), 4.52 (m, 1H, Cp-*H*), 4.66 (m, 1H, Cp-*H*). ^{13}C NMR ($CDCl_3$) δ: [12.06], 12.44, 20.75, [20.48], 45.35, 49.85, [68.50], 69.41, [69.98], 72.11, 84.76, [86.76], 87.10, 167.90. MS *m*/*z* (rel intensity) (FAB): 468 (M^+, 100), 396 (2), 368 (35), 262 (26), 213 (5), 134 (13), 55 (11). HRMS calcd. for $C_{26}H_{40}{}^{56}FeN_2O_2$: 468.2439; found: 468.2390. Values in square parentheses indicate resonances assigned to the dl-diastereomer.

Method 2

From 1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**5**) using *n*-BuLi in the presence of LiCl. According to Standard method A, a solution of (–)-sparteine (0.49 mL, 2.2 mmol), vacuum-dried LiCl (0.048 g, 2.1 mmol), and *n*-BuLi (1.32 mL, 1.69 mol/L solution in hexane, 4.2 mmol) in Et_2O (10 mL) was sequentially treated with a solution of 1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**5**) (0.23 g, 0.53 mmol) in Et_2O (5 mL) and MeI (0.37 mL, 6.0 mmol). Standard workup followed by column chromatography (EtOAc–hexane, 1:15) afforded a mixture of *dl*-**7b** and *meso*-**7b** diastereomers (0.040 g, 16%). CSP HPLC analysis determined 80% ee and dr = 72:28 (dl:meso); 2) and separately 2-methyl-1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**6b**) (0.15 g, 61%), 79% ee by CSP HPLC analysis, as well as the starting material 1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**5**) (0.018 g, 8%).

2,2′-Bis(diphenylphosphino)-1,1′-N,N,N′,N′-*tetraisopropylferrocenedicarboxamide (7c)*

Preparation of *dl*-**7c** from 2-(diphenylphosphino)-1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**6g**). According to Standard method B, a solution of (–)-sparteine (0.30 mL, 1.4 mmol) and *n*-BuLi (0.67 mL, 2.00 mol/L solution in hexane, 1.3 mmol) in PhMe (20 mL) was sequentially treated with a solution of 2-(diphenylphosphino)-1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**6g**) (0.400 g, 0.91 mmol, 97% ee) in PhMe (2.5 mL) and Ph_2PCl (0.36 mL, 1.9 mmol). The reaction mixture was quenched with satd. aq. NH_4Cl and extracted with CH_2Cl_2. The organic extract was washed with brine and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2 pretreated with 2% Et_3N, EtOAc–hexane 1:6) to give compound **7c** as a bright yellow solid (0.29 g, 45%); dr(dl:meso) >95:<5 by ^{31}P NMR; mp 233–236 °C (dec) (lit. value (41) mp 228–230 °C). $[\alpha]^{20}_D$ +277° (*c* 0.76, CH_2Cl_2), 98% optical purity. IR (KBr) ν_{max}: 3088, 2938, 1625, 1531, 1454, 1371, 1333, 1279, 1244, 1204, 1154, 1039. ^{1}H NMR ($CDCl_3$) δ: 0.34–1.53 (br, 24H, $CH(CH_3)_2$), 3.04–3.26 and 3.92–4.13 (br, 4H, $CH(CH_3)_2$), 3.53 (s, 2H, Cp-*H*), 4.78–4.82 (m, 4H, Cp-*H*), 7.12–7.43 (br, 20H, C_6H_5). ^{13}C NMR ($CDCl_3$) δ: 13.7, 19.0, 20.3, 50.0, 72.7, 74.8, 76.7, 81.1, 90.5, 127.9, 128.0, 128.1, 128.2, 129.1, 130.0, 130.4, 132.7, 133.1, 133.5, 133.6, 133.9, 137.9, 138.1, 139.0, 167.0. ^{31}P NMR($CDCl_3$) δ: –22.27. Anal. calcd. for $C_{48}H_{54}{}^{56}FeN_2O_2P_2$: C 71.28, H 6.73, N 3.46: found: C 71.36, H 6.75, N 3.51.

Preparation of meso-**7c** *from 1,1′*-N,N,N′,N′-*tetraisopropylferrocenedicarboxamide (**5**) using* s-*BuLi*

According to Standard method A, a solution of (–)-sparteine (1.9 mL, 8.4 mmol) and *s*-BuLi (7.1 mL, 1.18 mol/L solution in cyclohexane, 8.4 mmol) in Et_2O (40 mL) was sequentially treated with a solution of 1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**5**) (0.883 g, 2.01 mmol) in Et_2O (20 mL) and Ph_2PCl (2.16 mL, 12.0 mmol). The reaction mixture was quenched with satd. aq. NH_4Cl and extracted with excess CH_2Cl_2. The organic extract was washed with brine and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2 pretreated with 2% Et_3N, EtOAc–hexane 1:6) to give *meso*-**7c** as a bright yellow solid (0.79 g, 49%). The diastereomeric composition was determined by ^{31}P NMR dr(meso:dl) >95:<5; mp 235–237 °C (dec). IR (KBr) ν_{max}: 3063, 2924, 1629, 1451, 1373, 1330, 1205, 1159, 1093, 822. ^{1}H NMR ($CDCl_3$) δ: 0.34–1.68 (br, 24H, $CH(CH_3)_2$), 2.92–3.25 and 3.43–3.96 (br, 4H, $CH(CH_3)_2$), 4.20 and 4.76 (m, 6H, Cp-*H*), 7.12–7.67 (br, 20H, C_6H_5). ^{13}C NMR ($CDCl_3$) δ: 20.3, 72.8, 81.1, 90.8, 91.2, 128.0, 128.0, 128.2, 128.9, 132.8, 133.1, 134.5, 134.9, 139.6, 139.9, 166.3. ^{31}P NMR ($CDCl_3$) δ: –22.68. MS *m*/*z* (rel intensity) (FAB): 808 (M^+, 3), 766 (8), 639 (16), 625 (47). Anal. calcd. for $C_{48}H_{54}{}^{56}FeN_2O_2P_2$: C 71.28, H 6.73, N 3.46; found: C 71.39, H 6.79, N 3.52.

Diphenylphosphine derivatives **6g** and **7c** were found to be air-sensitive, but could be stored for months as solids un-

der argon at low temperatures (–20 °C). Purification by column chromatography required deactivation of silica gel with Et_3N.

2,2′-Bis(phenylthio)-1,1′-N,N,N′,N′-tetraisopropylferrocenedicarboxamide (7d)

According to Standard method B, a solution of (–)-sparteine (0.07 mL, 0.31 mmol and *n*-BuLi (0.19 mL, 1.67 mol/L solution in hexane, 0.15 mmol) in PhMe (5 mL) was sequentially treated with a solution of 2-(phenylthio)-1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**6h**) (0.084 g, 0.15 mmol, 89% ee) in PhMe (0.5 mL) and Ph_2S_2 (0.131 g, 0.6 mmol) in PhMe (0.5 mL). Standard workup followed by column chromatography (EtOAc–hexane, 1:10) gave **7d** as an orange solid (0.06 g, 60%). CSP HPLC analysis (Chiralcel OD; eluent: *n*-hexane–*i*-PrOH 99:1, flow 0.4 mL/min) determined dr(dl:meso) = 98.5:1.5 and 97% ee (t_R(major dl) = 15.97 min, t_R(minor dl) = 19.14 min, t_R(meso diastereomer) = 22.00 min).

dl-*2,2′-Bis(phenylthio)-1,1′*-N,N,N′,N′-*tetraisopropylferrocenedicarboxamide (*dl-***7d***)*

mp 200–202 °C (dec). IR (KBr) ν_{max}: 2954, 1628, 1458, 1372, 1325, 1207, 1159, 1127, 1033. ^{1}H NMR ($CDCl_3$) δ: 0.42–1.71 (br, 24H, CH(CH_3)$_2$), 3.24 (sept, *J* = 11 Hz, 2H, C*H*(CH_3)$_2$), 3.72 (sept, *J* = 11 Hz, 2H, C*H*(CH_3)$_2$), 4.71 (s, 4H, Cp-*H*), 4.59 (m, 2H, Cp-*H*), 7.02–7.28 (br, 10H, C_6H_5). ^{13}C NMR ($CDCl_3$) δ: 20.9, 50.6, 74.0, 77.4, 80.6, 92.5, 125.5, 127.6, 128.6, 139.2, 165.3. MS *m*/*z* (rel intensity) (FAB): 657 (MH^+, 98), 656 (M^+, 100), 557 (17), 548 (14), 455 (34), 356 (16), 318 (28), 302 (89), 201 (69), 185 (59), 154 (69), 137 (59). HRMS calcd. for $C_{36}H_{45}{}^{56}FeN_2O_2S_2$ (MH^+): 657.2272; found: 657.2294. Anal. calcd. for $C_{36}H_{44}{}^{56}FeO_2N_2S_2$: C 65.84, H 6.75, N 4.26; found: C 66.02, H 6.68, N 4.32.

meso-*2,2′-Bis(phenylthio)-1,1′*-N,N,N′,N′-*tetraisopropylferrocenedicarboxamide (*meso-***7d***)*

mp 201–203 °C (dec). IR (KBr) ν_{max}: 2949, 1631, 1459, 1372, 1316, 1207, 1034. ^{1}H NMR ($CDCl_3$) δ: 0.26–1.79 (br, 24H, CH(CH_3)$_2$), 3.24 (m, 2H, C*H*(CH_3)$_2$), 3.67 (m, 2H, C*H*(CH_3)$_2$), 4.53, 4.70, 4.90 (m, 6H, Cp-*H*), 6.92–7.38 (br, 10H, C_6H_5). ^{13}C NMR ($CDCl_3$) δ: 20.0, 20.7, 45.8, 50.5, 71.4, 74.2, 79.1, 82.1, 125.5, 127.7, 128.7, 137.0, 165.1. MS *m*/*z* (rel intensity) (FAB): 657 (MH^+, 8), 656 (M^+, 7), 556 (2), 547 (2), 455 (5), 338 (5), 302 (14), 246 (16), 201 (9), 185 (100), 154 (59), 137 (65). HRMS calcd. for $C_{36}H_{45}{}^{56}FeN_2O_2S_2$ (MH^+): 657.2272; found: 657.2292.

Dimethyl 1,3-diphenylprop-2-enylmalonate (8) — Asymetric Pd-catalyzed allylic substitution

Method 1 (utilizing BSA and AcOK)

A solution of 1,3-diphenyl-1-acetoxy-2-propene (0.25 g, 1.0 mmol) (42), 2,2′-bis(diphenylphosphino)-1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**7c**, 0.071 g, 0.1 mmol, 96% ee), and allylpalladium chloride dimer (0.009 g, 0.025 mmol) in CH_2Cl_2 (3.5 mL) was stirred for 15 min at rt before a solution (CH_2Cl_2, 3.5 mL) of BSA (0.74 mL, 3.0 mmol), dimethyl malonate (0.40 g, 3.0 mmol), and AcOK (0.004 g, 0.04 mmol) was added. The reaction mixture was stirred for 10 h at rt, quenched with water, and subjected to the standard workup. Purification by column chromatography (EtOAc–hexane, 1:5) gave compound **8** as a pale yellow solid (0.313 g, 96%). CSP HPLC analysis (eluent: *n*-hexane–*i*-PrOH 99:1, flow 0.2 mL/min) determined 84% ee (t_R(major) = 58.78 min, t_R(minor) = 63.50 min). $[\alpha]^{23}_D$ +15.9° (*c* 0.71, EtOH). IR (neat) ν_{max}: 2995, 1758, 1605, 1493, 1454, 1316, 1259. ^{1}H NMR ($CDCl_3$) δ: 3.52 (s, 3H, CO_2CH_3), 3.70 (s, 3H, CO_2CH_3), 3.95 (d, *J* = 10.9 Hz, 1H, C*H*(CO_2CH_3)$_2$), 4.27 (dd, *J* = 10.9, 8.0 Hz, 1H, Ph-C*H*), 6.32 (dd, *J* = 8.0, 15.7 Hz, 1H, -C*H*=CH-Ph), 6.51 (d, *J* = 15.7 Hz, 1H, Ph-CH=), 7.19–7.33 (m, 10H, C_6H_5). ^{13}C NMR ($CDCl_3$) δ: 48.9, 52.0, 52.2, 57.3, 126.1, 126.9, 127.3, 127.6, 127.9, 128.2, 128.4, 128.9, 131.5, 136.5, 140.0, 167.4, 167.9. MS *m*/*z* (rel intensity) (EI): 324 (M^+, 56), 292 (29), 264 (37), 232 (41), 204 (84), 193 (98), 178 (53), 165 (39), 152 (18), 139 (12), 128 (42), 115 (100), 102 (43), 91 (74), 78 (42), 69 (43). HRMS calcd. for $C_{20}H_{20}O_4$: 324.1361; found: 324.1353.

Method 2 (utilizing NaH)

A solution of 1,3-diphenyl-1-acetoxy-2-propene (0.095 g, 0.38 mmol), 2,2′-bis(diphenylphosphino)-1,1′-*N*,*N*,*N*′,*N*′-tetraisopropylferrocenedicarboxamide (**7c**, 0.027 g, 0.038 mmol, 96% ee), allylpalladium chloride dimer (0.004 g, 0.011 mmol), and THF (2 mL) was stirred for 15 min at rt and then treated with a THF (3 mL) solution of NaCH(CO_2Me)$_2$ (prepared by the addition of NaH (60% in oil, 0.05 g, 1.13 mmol) to dimethylmalonate (0.15 g, 1.13 mmol) in THF (3 mL) at 0 °C) at rt. The reaction reaction mixture was stirred for 36 h at rt, quenched with water, and subjected to the standard workup. Purification by column chromatography afforded compound **8** (0.117 g, 96%), which, as determined by CSP HPLC, was 84% ee (R-enantiomer).

1-Phenylpropan-1-ol (9) (Et_2Zn addition to benzaldehyde)

To a stirred solution of benzaldehyde (0.10 mL, 1.6 mmol) and chiral ferrocenyl ligand (**6d**, **6e**, **6k**, **6l**) (0.05 mmol) in either hexane (15 mL) or PhMe (5 mL) was added a solution of Et_2Zn (1.60 mL, 1.0 mol/L in hexane, 1.60 mmol) at rt and the reaction mixture was further stirred for 1–3 days. The reaction mixture was quenched with excess 0.2 mol/L aq. HCl solution at 0 °C. After standard workup, the crude material was analyzed by CSP HPLC (Chiralcel OD column, eluent: *n*-hexane–isopropyl alcohol 99:1, flow 0.5 mL/min, t_R 29.66 min, t_R 27.20 min) and purified by column chromatography (hexane–EtOAc, 10:1) to yield compound **9** as a colorless oil. IR (CH_2Cl_2) ν_{max}: 700, 756, 1097, 1454, 1493, 2875, 2930, 2966, 3030, 3369. ^{1}H NMR ($CDCl_3$) δ: 0.92 (t, *J* = 7.3 Hz, 3H, CH_2CH_3), 1.81 (m, 2H, CH_2CH_3), 1.90–2.00 (br, 1H, O*H*), 4.59 (t, *J* = 6.6 Hz, 1H, C*H*(OH)CH_2), 7.20–7.40 (m, C_6H_5). ^{13}C NMR ($CDCl_3$) δ: 10.1, 31.8, 76.0, 126.0, 127.4, 128.3. MS *m*/*z* (rel intensity) (EI): 136 (M^+, 32), 117 (2), 107 (100), 97 (0.5). HRMS calcd. for $C_9H_{12}O$: 136.0888; found: 136.0897.

Et_2Zn addition to benzaldehyde catalyzed by the lithium salt of 2-(diphenylhydroxymethyl)-1,1′-N,N,N′,N′-tetraisopropylferrocenedicarboxamide (6d)

A solution of *n*-BuLi (0.05 mL, 1.67 mol/L in hexane, 0.85 mmol) was added to a cold (–78 °C) solution of **6d** (53.4 mg, 0.086 mmol) in PhMe (20 mL). PhCHO (0.19 mL,

0.86 mmol) and Et_2Zn (1.37 mL, 1.0 mol/L in hexane, 1.37 mmol) were added and stirring was continued at rt for 3 days. The reaction mixture was quenched with excess 0.2 mol/L HCl at 0 °C. Standard workup followed by flash chromatography afforded compound **9** (0.082 g, 70%, 47% ee).

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