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SYNTHESIS OF 1',2',3',4',5'-PENTAMETHYL-3,4-DIPHENYL- AZAFERROCENE AND ITS ENANTIOSELECTIVE C-2 FUNCTIONALIZATION VIA (-)-SPARTEINE-MEDIATED LITHIATION

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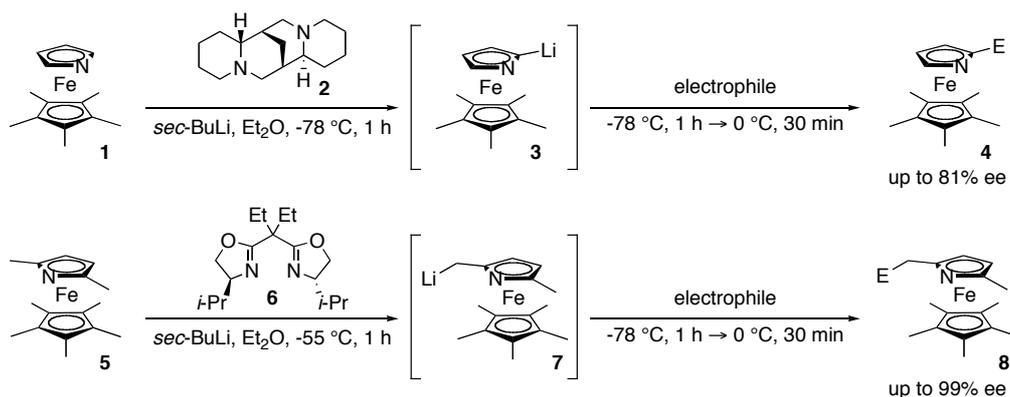
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Abstract – Lithiation of 1',2',3',4',5'-pentamethyl-3,4-diphenylazaferrocene (**9**) with *sec*-BuLi/(-)-sparteine (**2**) in Et₂O at -78 °C followed by quenching with electrophiles gave the C-2 functionalized azaferrocenes (**17**) in good enantioselectivities (up to 79% ee). In contrast, treatment of **9** with *tert*-BuLi/(-)-sparteine (**2**) led to lateral lithiation at the methyl group of cyclopentadienyl ring.

INTRODUCTION

Planar chiral 2-substituted azaferrocene have attracted considerable attention as chiral catalysts or ligands in asymmetric synthesis.¹ The synthesis of chiral azaferrocenes has been effected by conventional resolution technique² or by direct HPLC separation on a chiral stationary phase.^{1a,1d} Recently, however, more attractive asymmetric syntheses *via* organolithium intermediates have been developed by two groups. Johansen et al. generated chiral 2-azaferrocenyllithium by ligand exchange of optically pure 2-azaferrocenyl *p*-tolyl sulfoxides.³ On the other hand, we successfully employed chiral ligand-mediated enantioselective lithiation technique to generate **3** and **7** (Scheme 1).⁴ Anderson et al. extended our method to the synthesis of a broad range of chiral 2-substituted 1',2',3',4',5'-pentamethyl-azaferrocene derivatives.⁵

The application of chiral azaferrocenes to catalytic asymmetric reactions has been relatively unexplored compared to that of the parental chiral ferrocene derivatives.⁶ The reason may be explained, in part, by difficulty of handling the azaferrocene derivatives due to their thermal and chemical instability. In fact, azaferrocenes **4** and **8** prepared by ourselves are found to be too unstable to use for the further reactions. Efraty et al. have reported that azaferrocene changes to ferrocene under reflux in benzene and undergoes

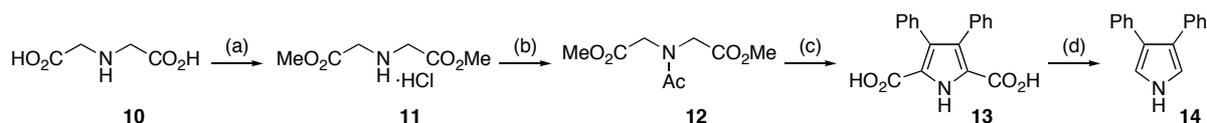


Scheme 1

facile reactions with π -acidic and σ -donor ligands.⁷ These results suggested us that the stability of azaferrrocenes could be improved if the reactive iron center was protected from the attack of π -acidic or σ -donor ligands by introducing bulky substituents on the pyrrolyl ring. Based upon this working hypothesis, we designed 1',2',3',4',5'-pentamethyl-3,4-diphenylazaferrocene (**9**) as a stable azaferrrocene. In this paper, we report a synthesis of 1',2',3',4',5'-pentamethyl-3,4-diphenylazaferrocene (**9**) and its enantioselective C-2 functionalization *via* chiral ligand-mediated lithiation.

RESULTS AND DISCUSSION

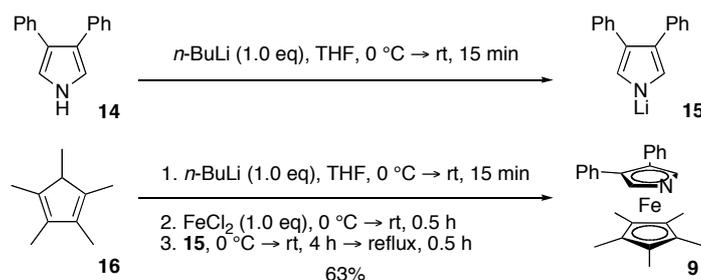
The synthesis of 3,4-diphenylpyrrole (**14**) which is required for the preparation of azaferrrocene (**9**) was carried out at first (Scheme 2). Commercially available iminodiacetic acid (**10**) was treated with thionyl chloride in methanol to give dimethyl iminodiacetate hydrochloride (**11**). Acetylation of **11** with acetic anhydride in the presence of triethylamine afforded acetamide (**12**). Conversion of **12** to 3,4-diphenylpyrrole (**14**) was carried out by using the modified procedure of Friedman.⁸ Treatment of **12** with benzil and sodium methoxide in refluxing methanol followed by hydrolysis gave **13** in 69% yield. Decarboxylation of **13** in refluxing ethanolamine produced 3,4-diphenylpyrrole (**14**).



Scheme 2 *Reagents and conditions*: (a) SOCl_2 , MeOH, $-10\text{ }^\circ\text{C}$ then rt, 3 d (94%); (b) Ac_2O , Et_3N , $0\text{ }^\circ\text{C}$, 0.5 h then rt, 4 h (91%); (c) (1) benzil (0.5 equiv.), NaOMe (10 equiv.), MeOH, reflux, 0.5 h, (2) H_2O , reflux, 0.5 h (69%); (d) ethanolamine, reflux, 1 h (92%).

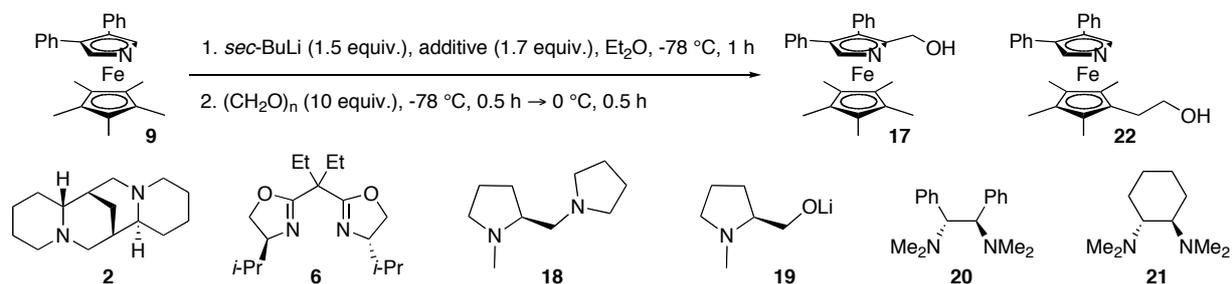
The synthesis of 1',2',3',4',5'-pentamethyl-3,4-diphenylazaferrocene (**9**) is shown in Scheme 3. Pyrrole (**14**) was deprotonated by *n*-BuLi to give lithium pyrrolide (**15**) which was used for the next reaction as it

stands. Deprotonation of 1,2,3,4,5-pentamethylcyclopentadiene (Cp^{*}-H) (**16**)⁹ with *n*-BuLi followed by successive treatment with FeCl₂ and lithium pyrrolide (**15**) afforded the desired azaferrocene (**9**) in 63% yield. Although we have not carried out precise comparison, the azaferrocene (**9**) was found to be somewhat more stable than parental **1**.



Scheme 3

Next, we examined the enantioselective C-2 lithiation of azaferrocene (**9**). The results were summarized in Table 1. Since C-2 lithiation of azaferrocene (**9**) has not been reported, we initially tested the feasibility of this reaction under achiral conditions. Treatment of azaferrocene (**9**) with *sec*-BuLi (1.5 equiv.) in the presence of TMEDA in Et₂O at -78 °C for 1 h followed by quenching with paraformaldehyde produced racemic **17** in 61% yield (entry 1). The lithiations of **9** with *sec*-BuLi in the presence of chiral bidentate ligands (**2**, **6**, and **18-21**) were examined next (entries 2-7). Similar to the case of the parental azaferrocene (**1**),⁴ enantioselective lithiation of **9** was effected most satisfactory by using (-)-sparteine (**2**)¹⁰ as a chiral ligand (entry 2). Other chiral ligands such as *S*-valine-derived bis(oxazoline) (**6**),¹¹ *S*-proline-derived ligand (**18**) and (**19**),¹² *N,N,N',N'*-tetramethyl-(1*R*,2*R*)-1,2-diphenylethylenediamine (**20**),¹³ and *N,N,N',N'*-tetramethyl-(1*R*,2*R*)-1,2-diaminocyclohexane (**21**)¹⁴ were found to be less effective than (-)-sparteine (**2**) (entries 3-7). In order to improve the chemical yield and enantioselectivity, we further surveyed other bases in the presence of **2** (entries 8 and 9). The lithiation proceeded smoothly by using *n*-BuLi as a base, however, enantiomeric excess of **17** was decreased considerably (entry 8). In contrast to the previous results, when *tert*-BuLi was used as a base, the lithiation occurred at the methyl group of 1,2,3,4,5-pentamethylcyclopentadienyl (Cp^{*}) ring selectively (entry 9).¹⁵ Therefore, we examined the effect of chiral ligands on regioselectivity of the lithiation using *tert*-BuLi as a base (entries 10-12). When chiral ligands (**6**) and (**21**) were used, only azaferrocene (**17**) was obtained in good yields and low enantiomeric excesses (entries 10 and 12). The lithiation in the presence of **18** resulted in non-regioselective reaction at C-2 and Cp^{*} methyl group (entry 11). These results suggested that the lithiation at the Cp^{*} methyl group might occur in the presence of bulky ligand such as **2** and **18**.

Table 1. Enantioselective lithiation of azaferrocene (**9**)

entry	BuLi	ligand	17		22 (%) ^a
			yield (%) ^a	% ee ^b	
1	<i>sec</i> -	TMEDA	61	-	-
2	<i>sec</i> -	2	74	78	-
3	<i>sec</i> -	6	63	10	-
4	<i>sec</i> -	18	69	8	-
5	<i>sec</i> -	19	30	2	-
6	<i>sec</i> -	20	20	33	-
7	<i>sec</i> -	21	70	34	-
8	<i>n</i> -	2	69	47	-
9	<i>tert</i> -	2	-	-	80
10	<i>tert</i> -	6	72	18	-
11	<i>tert</i> -	18	31	11	41
12	<i>tert</i> -	21	72	53	-

^a Isolated yield.

^b Enantiomeric excess was determined by HPLC analysis (Daicel Chiralpak AD).

In order to enrich the enantiomeric purity of **17**, recrystallization of **17** from diethyl ether was conducted. Unfortunately, the crystals thus obtained were found to be racemate. On the other hand, the enantiomeric purity of the filtrate was increased. However, we could not obtain enantiomerically pure crystalline **17** from the filtrate. The X-ray crystal structure of the racemic azaferrocene (**17**) is shown in Figure 1. The iron atom has a sandwich-like coordination with the planar Cp* and pyrrolyl rings. Both rings are equi-distant from Fe atom (the mean Fe-ring plane distance is 1.66 Å) but are slightly deviate from parallel (interplanar angle: ca. 4.3 °) due to steric repulsion between phenyl groups of pyrrolyl ring and methyl groups of Cp*.^{3a,16}

Since we have established the best conditions for the enantioselective C-2 lithiation of **9**, we next carried out enantioselective C-2 functionalization of **9** with other electrophiles. The results were summarized in Table 2. The lithiation of **9** using *sec*-BuLi/(-)-sparteine (**2**) followed by quenching with electrophiles

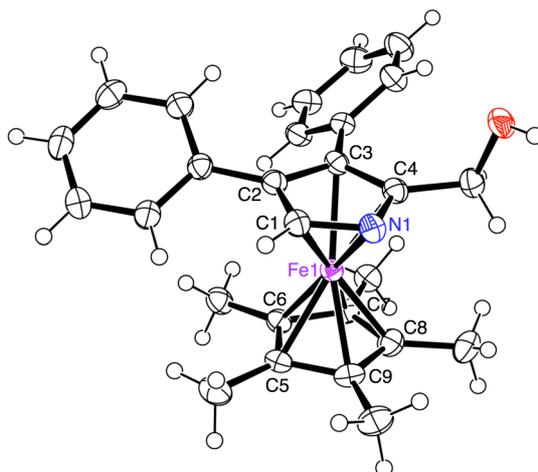
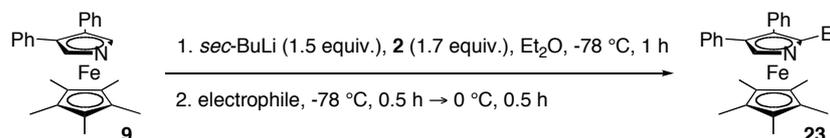


Figure 1 X-Ray crystal structure of racemic azaferrocene (**17**). The thermal ellipsoids are at a 50% probability level. Selected bond distances (Å): Fe1-N1 2.0311(18), Fe1-C1 2.010(2), Fe1-C2 2.092(2), Fe1-C3 2.094(2), Fe1-C4 2.036(2), Fe1-C5 2.062(2), Fe1-C6 2.061(2), Fe1-C7 2.071(2), Fe1-C8 2.053(2), Fe1-C9 2.064(2).

such as iodine, chlorotrimethylsilane, chlorodiphenylphosphine, and diphenyl disulfide produced the corresponding products (**23**) in modest to good yields. The enantiomeric excesses of the products were comparable to that obtained in the reaction with paraformaldehyde.

Finally, we would like to propose a plausible mechanistic explanation for the enantio- and regioselectivities of the lithiation of azaferrocene (**9**) in the presence of (–)-sparteine (**2**) (Scheme 4). When the lithiation is carried out using *sec*- or *n*-BuLi as a base, the nitrogen atom on pyrrolyl ring may coordinate to the BuLi/(–)-sparteine complex and then butyl anion deprotonates the adjacent C-2 proton *via* complex-induced proximity effect (CIPE)¹⁷ to give the lithio species (**25**) (route 1). Compared to the *n*-BuLi/(–)-sparteine/**9** complex (**24**), the rotation around a nitrogen-lithium bond in

Table 2. Enantioselective C-2 functionalization of azaferrocene (**9**)

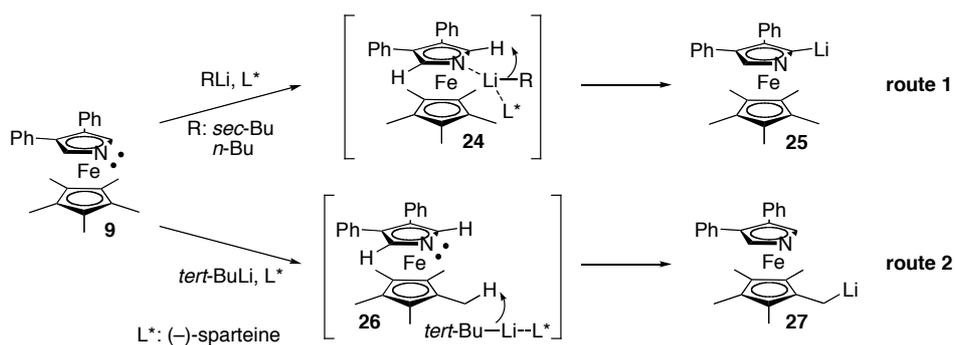


entry	electrophile	E	product	yield (%) ^a	% ee ^b
1	I ₂	I	23a	84	79
2	TMSCl	TMS	23b	61	75
3	Ph ₂ PCl	PPh ₂	23c	39	77
4	PhSSPh	SPh	23d	88	76

^a Isolated yield.

^b Enantiomeric excess was estimated by HPLC analysis (Daicel Chiralpak AD).

sec-BuLi/(–)-sparteine/**9** complex (**24**) is more restricted due to bulkiness of *sec*-butyl group. Thus, enantioselectivity of C-2 deprotonation using *sec*-BuLi would be superior to that using *n*-BuLi. In the reaction with *tert*-BuLi, a *tert*-BuLi/(–)-sparteine complex¹⁸ may be too bulky to interact with the pyrrolyl nitrogen of **9**. Therefore, the complex could not lithiate at C-2 by an assistance of CIPE but deprotonate more easily accessible methyl protons of Cp* to produce **27** (route 2).



Scheme 4

In conclusion, we have succeeded in the synthesis of new chiral azaferrocenes **17** and **23** via (–)-sparteine-mediated enantioselective lithiation of **9**. During the course of this study, we found out that **9** could be deprotonate selectively at the methyl group of Cp* with *tert*-BuLi/(–)-sparteine. Proper combination of these enantio- and regioselective lithiations may be useful in the synthesis of new types of planar chiral azaferrocene.

EXPERIMENTAL

Melting points were determined with a Yanagimoto micro melting points apparatus and are uncorrected. IR spectra were obtained with a Perkin-Elmer System 2000 instrument. NMR spectra were recorded on a JEOL JNM-AL400 instrument (400 MHz for ^1H and 100 MHz for ^{13}C) using tetramethylsilane as an internal standard. High resolution mass spectra were recorded on a JEOL JMS-700N spectrometer. HPLC analyses were performed on a Shimadzu LC-6A apparatus. Optical rotations were measured on a JASCO P-1020 digital polarimeter at ambient temperature. X-Ray crystal structure analysis was carried out with a Rigaku FR-E SuperBright at Institute for Materials Chemistry and Engineering (IMCE), Kyushu University. Flash chromatography was conducted on Silica Gel 60N, 40–50 μm (Kanto Chemical Co., Inc.). Column chromatography was conducted on Silica Gel 60N, 63–210 μm (Kanto Chemical Co., Inc.) or Chromatorex NH-DM1020 silica gel (Fuji Silysia Chemical Ltd.). *sec*- and *tert*-Butyllithiums were purchased from Kanto Chemical Co., Inc. *n*-Butyllithium was purchased from Aldrich Chemical Co., Inc. The alkyllithiums were used after titration with 2,5-dimethoxybenzyl

alcohol. Dry diethyl ether and THF were distilled from Na-benzophenone ketyl under argon immediately before use.

Dimethyl iminodiacetate hydrochloride (**11**)

Thionyl chloride (82.3 mL, 1.13 mol) was added dropwise to MeOH (500 mL) at $-10\text{ }^{\circ}\text{C}$. After being stirred for 10 min, iminodiacetic acid (50.0 g, 376 mmol) was added portionwise to the solution at $-10\text{ }^{\circ}\text{C}$ and the suspension was allowed to warm to rt. After being stirred for 3 d, the reaction mixture was evaporated under reduced pressure. The residue was purified by recrystallization from MeOH to give **11** as colorless needles (69.8 g, 94%). Mp $180\text{--}183\text{ }^{\circ}\text{C}$ (decomp); IR (KBr): 1761, 1436, 1345, 1237, 1071, 983 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6): δ 3.75 (s, 6H), 4.01 (s, 4H), 10.11 (br s, 2H); ^{13}C NMR (100 MHz, DMSO- d_6): δ 46.18, 52.52, 166.75. *Anal.* Calcd for $\text{C}_6\text{H}_{12}\text{ClNO}_4$: C, 36.47; H, 6.12; N, 7.09. Found: C, 36.45; H, 6.08; N, 6.95.

Dimethyl *N*-acetylaminodiacetate (**12**)

Under an argon atmosphere, acetic anhydride (26.3 mL, 278 mmol) was added dropwise to a mixture of dimethyl iminodiacetate hydrochloride (**11**) (50.0 g, 253 mmol) and triethylamine (74.1 mL, 531 mmol) in CH_2Cl_2 (800 mL) at $0\text{ }^{\circ}\text{C}$. After being stirred for 20 min, the mixture was allowed to warm to rt and stirred for additional 4 h. The mixture was quenched with water and the product was extracted with CH_2Cl_2 . The extract was washed successively with water and brine, dried over Na_2SO_4 , and evaporated under reduced pressure. The residue was purified by recrystallization from CH_2Cl_2 -hexane to give **12** as colorless granules (46.7 g, 91%). Mp $82\text{--}83\text{ }^{\circ}\text{C}$; IR (KBr): 1743, 1663, 1467, 1431, 1225, 998 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 2.12 (s, 3H), 3.73 (s, 3H), 3.78 (s, 3H), 4.16 (s, 2H), 4.20 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.04, 47.64, 50.76, 52.18, 52.54, 169.33, 169.77, 171.13. *Anal.* Calcd for $\text{C}_8\text{H}_{13}\text{NO}_5$: C, 47.29; H, 6.45; N, 6.89. Found: C, 47.51; H, 6.37; N, 6.82.

3,4-Diphenylpyrrole-2,5-dicarboxylate (**13**)

Under an argon atmosphere, sodium (23.0g, 1.00 mol) was added portionwise to MeOH (250 mL) at rt. After successive addition of a solution of dimethyl *N*-acetylaminodiacetate (**12**) (20.3 g, 100 mmol) in MeOH (125 mL) and benzil (10.5 g, 50 mmol), the reaction mixture was refluxed for 0.5 h. After being cooled to rt, water (500 mL) was added and the mixture was refluxed for 0.5 h again. After being cooled to rt, the mixture was evaporated under reduced pressure to remove MeOH. The residual solution was washed with Et_2O and acidified with 6 M aqueous HCl. The precipitate thus formed was collected by filtration, washed with water, and dried under reduced pressure. Recrystallization from EtOH gave **13** as pale brown powder (10.6 g, 69%). Mp $273\text{--}293\text{ }^{\circ}\text{C}$ (decomp); IR (KBr): 3030, 1691, 1493, 1408,

1257 cm^{-1} ; ^1H NMR (400 MHz, DMSO-d_6): δ 7.01-7.08 (m, 4H), 7.10-7.18 (m, 6H), 11.82 (s, 1H), 12.63 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 122.16, 126.23, 126.96, 129.85, 130.58, 133.76, 161.28. *Anal.* Calcd for $\text{C}_{18}\text{H}_{13}\text{NO}_4$: C, 70.35; H, 4.26; N, 4.56. Found: C, 70.20; H, 4.25; N, 4.49.

3,4-Diphenylpyrrole (14)

Under an argon atmosphere, ethanolamine (40 mL) was heated to reflux. To this was added portionwise 3,4-diphenylpyrrole-2,5-dicarboxylate (**13**) (5.00 g, 16.3 mmol) under reflux. After being refluxed for 1 h, the reaction mixture was cooled to rt, and poured into ice-cold water. The product was extracted with CH_2Cl_2 , and the extract was washed with water, dried over Na_2SO_4 , and evaporated under reduced pressure. The residue was purified by bulb-to-bulb distillation (180-185 $^\circ\text{C}/0.5$ mmHg) to give **14** as pale yellow liquid (3.27 g, 92%), which on standing solidified. Mp 96.5-97.5 $^\circ\text{C}$; IR (KBr): 3446, 1602, 1536, 1487, 1435, 1083, 1059, 768, 706 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 6.88 (d, $J=2.6$ Hz, 2H), 7.15-7.30 (m, 10H), 8.21 (br s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 117.42, 123.61, 125.72, 128.17, 128.56, 135.78. *Anal.* Calcd for $\text{C}_{16}\text{H}_{13}\text{N}$: C, 87.64; H, 5.98; N, 6.39. Found: C, 87.49; H, 6.10; N, 6.29.

Lithium 3,4-Diphenylpyrrolide (15)

Under an argon atmosphere, 3,4-diphenylpyrrole (**14**) (2.00 g, 9.12 mmol) was dissolved in THF (28 mL) and the mixture was cooled to 0 $^\circ\text{C}$. To the solution was added dropwise a hexane solution of *n*-BuLi (1.49 M, 6.12 mL, 9.12 mmol) at 0 $^\circ\text{C}$ and the mixture was allowed to warm to rt. After being stirred for 15 min, the mixture was cooled to 0 $^\circ\text{C}$. The mixture thus obtained was used for the next reaction as it stands.

1',2',3',4',5'-Pentamethyl-3,4-diphenylazaferrocene (9)

Under an argon atmosphere, a hexane solution of *n*-BuLi (1.49 M, 6.73 mL, 10.0 mmol) was added dropwise to a solution of $\text{Cp}^*\text{-H}$ (**16**) (1.37 g, 10.0 mmol) in THF (28 mL) at 0 $^\circ\text{C}$ and the suspension was allowed to warm to rt. After being stirred for 15 min, the suspension was cooled to 0 $^\circ\text{C}$ and added by cannula to a vigorously stirring suspension of FeCl_2 , which was prepared by treatment of $\text{FeCl}_2\cdot 4\text{H}_2\text{O}$ (1.99 g, 10.0 mmol) under reduced pressure at 100 $^\circ\text{C}$ overnight, in THF (41 mL) at 0 $^\circ\text{C}$. The resulting forest green solution was allowed to warm to rt, stirred for 0.5 h, and cooled to 0 $^\circ\text{C}$. A mixture of potassium pyrrolide (**15**) in THF was added by cannula at 0 $^\circ\text{C}$ and the reaction mixture was allowed to warm to rt. After being stirred for 4 h, the mixture was refluxed for 0.5 h, cooled to rt, and passed through a pad of Silica Gel 60. The filtrate was evaporated under reduced pressure. The residue was purified by flash chromatography over Silica Gel 60N (hexane-EtOAc=3:1~EtOAc) to give **9** as orange

solid (2.35 g, 63%). Recrystallization from Et₂O gave orange plates. Mp 180-185 °C (decomp) (sealed capillary); IR (KBr): 1600, 1505, 1377, 763, 699 cm⁻¹; ¹H NMR (400 MHz, C₆D₆): δ 1.65 (s, 15H), 5.36 (s, 2H), 7.01-7.12 (m, 6H), 7.40-7.43 (m, 4H); ¹³C NMR (100 MHz, C₆D₆): δ 10.26, 81.22, 89.43, 94.56, 126.67, 128.34, 129.39, 134.98. HREIMS *m/z*. Calcd for C₂₆H₂₇FeN (M⁺): 409.1493. Found: 409.1490.

Enantioselective C-2 lithiation of azaferrocene (9). General procedure

Under an argon atmosphere, azaferrocene (9) (143 mg, 0.350 mmol) and an appropriate chiral ligand (0.595 mmol) were dissolved in Et₂O (10 mL) and the mixture was cooled to -78 °C. A solution of BuLi (0.525 mmol) was added dropwise to the mixture at -78 °C. After being stirred for 1 h, a suspension of paraformaldehyde (105 mg, 3.50 mmol) in Et₂O (2.0 mL) was added dropwise to the mixture at -78 °C. After being stirred for 0.5 h, the mixture was allowed to warm to 0 °C and stirred for an additional 0.5 h. The reaction mixture was quenched with water and the products were extracted with Et₂O. The extract was washed with brine, dried over Na₂SO₄, and evaporated under reduced pressure. The residue was purified by flash chromatography over Silica Gel 60N (hexane-EtOAc=1:1~EtOAc). The results were shown in Table 1.

(+)-2-Hydroxymethyl-1',2',3',4',5'-pentamethyl-3,4-diphenylazaferrocene (17)

According to the general procedure, azaferrocene (9) and paraformaldehyde were reacted under the conditions shown in Table 1, entry 2, to give 17 as orange semisolid (114 mg, 74%). HPLC (Daicel Chiralpak AD, hexane-*i*-PrOH=1:1): 78% ee. IR (KBr): 3208, 1602, 1507, 1019, 763, 700 cm⁻¹; ¹H NMR (400 MHz, C₆D₆): δ 1.63 (s, 15H), 4.48 (br s, 1H), 4.84 (dd, *J* = 7.3 and 12.6 Hz, 1H), 4.97 (dd, *J* = 4.3 and 12.6 Hz, 1H), 5.18 (s, 1H), 6.95-7.23 (m, 8H), 7.62-7.66 (m, 2H). [α]_D²⁴ +252 (c 0.167, benzene). HREIMS *m/z*. Calcd for C₂₇H₂₉FeNO (M⁺): 439.1599. Found: 439.1594.

1'-(2-Hydroxyethyl)-2',3',4',5'-tetramethyl-3,4-diphenylazaferrocene (22)

According to the general procedure, azaferrocene (9) and paraformaldehyde were under the conditions shown in Table 1, entry 9, to give 22 as orange semisolid (123 mg, 80%). IR (KBr): 3245, 1601, 1452, 1049, 764, 699 cm⁻¹; ¹H NMR (400 MHz, C₆D₆): δ 1.27 (s, 6H), 1.80 (s, 6H), 2.15 (t, *J* = 4.9 Hz, 2H), 3.88-3.97 (m, 2H), 5.22 (s, 2H), 5.76 (br s, 1H), 7.02-7.26 (m, 8H), 7.36 (d, *J* = 6.7 Hz, 2H). HREIMS *m/z*. Calcd for C₂₇H₂₉FeNO (M⁺): 439.1599. Found: 439.1589.

Enantioselective C-2 functionalization of azaferrocene (9). General procedure

Under an argon atmosphere, azaferrocene (**9**) (143 mg, 0.350 mmol) and (–)-sparteine (**2**) (140 mg, 0.595 mmol) were dissolved in Et₂O (10 mL) and the mixture was cooled to –78 °C. A hexane-cyclohexane solution of *sec*-BuLi (0.525 mmol) was added dropwise to the mixture at –78 °C. After being stirred for 1 h, a mixture of an appropriate electrophile (0.700 mmol) in Et₂O (2.0 mL) was added dropwise to the mixture at –78 °C. After being stirred for 0.5 h, the mixture was allowed to warm to 0 °C and stirred for an additional 0.5 h. The reaction mixture was quenched with water and the products were extracted with Et₂O. The extract was washed with brine, dried over Na₂SO₄, and evaporated under reduced pressure. The residue was purified by flash chromatography over Silica Gel 60N using the following eluents: hexane-EtOAc=3:1 for **23a**, **23b**, and **23c**; hexane-EtOAc=5:1 for **23d**. The results were shown in Table 2.

(+)-2-Iodo-1',2',3',4',5'-pentamethyl-3,4-diphenylazaferrocene (**23a**)

According to the general procedure, iodine (178 mg, 0.700 mmol) was reacted to give **23a** as orange solid (158 mg, 84%). HPLC (Daicel Chiralpak AD, hexane-*i*-PrOH=9:1): 79% ee. IR (KBr): 1601, 1505, 1378, 1202, 888, 766, 700 cm⁻¹; ¹H NMR (400 MHz, C₆D₆): δ 1.62 (s, 15H), 5.31 (s, 1H), 6.92-6.96 (m, 3H), 7.05-7.20 (m, 5H), 7.50 (d, *J*= 7.0 Hz, 2H). [α]_D²⁵ +82.7 (c 0.167, benzene). HREIMS *m/z*. Calcd for C₂₆H₂₆FeIN (M⁺): 535.0459. Found: 535.0439.

(+)-1',2',3',4',5'-Pentamethyl-3,4-diphenyl-2-(trimethylsilyl)azaferrocene (**23b**)

According to the general procedure, chlorotrimethylsilane (88.8 μL, 0.700 mmol) was reacted to give **23b** as orange oil (103 mg, 61%). HPLC (Daicel Chiralpak AD, hexane-*i*-PrOH=100:1): 75% ee. IR (KBr): 1603, 1245, 840, 766, 699 cm⁻¹; ¹H NMR (400 MHz, C₆D₆): δ 0.31 (s, 9H), 1.69 (s, 15H), 5.64 (s, 1H), 6.92-6.99 (m, 3H), 7.04-7.20 (m, 5H), 7.55 (d, *J*= 7.0 Hz, 2H). [α]_D²⁴ +364 (c 0.167, benzene). HREIMS *m/z*. Calcd for C₂₉H₃₅FeNSi (M⁺): 481.1888. Found: 481.1888.

(+)-2-Diphenylphosphino-1',2',3',4',5'-pentamethyl-3,4-diphenylazaferrocene (**23c**)

According to the general procedure, chlorodiphenylphosphine (126 μL, 0.700 mmol) was reacted to give **23c** as orange oil (81.8 mg, 39%). HPLC (Daicel Chiralpak AD, hexane-*i*-PrOH=100:1): 77% ee. IR (KBr): 1602, 1479, 1434, 1028, 765, 741, 696 cm⁻¹; ¹H NMR (400 MHz, C₆D₆): δ 1.54 (s, 15H), 5.67 (s, 1H), 6.70-6.82 (m, 3H), 6.93-7.01 (m, 4H), 7.06-7.26 (m, 9H), 7.77 (d, *J*= 7.5 Hz, 2H), 8.39 (t, *J*= 8.1 Hz, 2H). [α]_D²⁵ +154 (c 0.167, benzene). HREIMS *m/z*. Calcd for C₃₈H₃₆FeNP (M⁺): 593.1935. Found: 593.1922.

(+)-1',2',3',4',5'-Pentamethyl-3,4-diphenyl-2-(phenylthio)azaferrocene (**23d**)

According to the general procedure, diphenyl disulfide (153 mg, 0.700 mmol) was reacted to give **23d** as orange oil (160 mg, 88%). HPLC (Daicel Chiralpak AD, hexane-*i*-PrOH=100:1): 76% ee. IR (KBr): 1478, 1027, 766, 738, 697 cm^{-1} ; ^1H NMR (400 MHz, C_6D_6): δ 1.72 (s, 15H), 5.50 (s, 1H), 6.64-6.80 (m, 3H), 6.90-7.20 (m, 10H), 7.64 (d, J = 6.8 Hz, 2H). $[\alpha]_D^{25}$ +172 (c 0.167, benzene). HREIMS m/z . Calcd for $\text{C}_{32}\text{H}_{31}\text{FeNS}$ (M^+): 517.1527. Found: 517.1537.

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