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Highly Diastereoselective *ortho*-Lithiation of 1,1'-Bis-(oxazolinyl)ferrocene Directed to C_2-Symmetric Chiral Ligands

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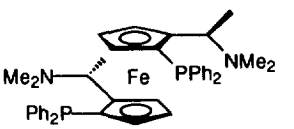
Abstract: C_2-Symmetric 1,1',2,2'-tetrasubstituted ferrocene derivatives are prepared in high yields from chiral 1,1'-bis(oxazolinyl)ferrocenes *via* diastereoselective *o,o'*-dilithiation with *sec*-butyllithium followed by nucleophilic substitution. 1,1'-Bis(oxazolinyl)ferrocenes were prepared from 1,1'-ferrocenedicarbonyl dichloride and enantiomerically pure aminoalcohols *via* the corresponding bis(β-hydroxylamide)s and dimesylates as intermediates.

Planar chirality of ferrocene has found increasing importance for metal-catalyzed asymmetric organic synthesis in recent years.[1] For the purpose of developing novel ferrocene ligands with planar chirality, several research groups have recently studied the diastereoselective *ortho*-lithiation of ferrocenyl methyl amine,[1] ferrocenyl acetals,[2] ferrocenyl sulfoxides,[3] and especially ferrocenyl oxazolines.[4] However, C_2-symmetric ferrocene ligand with planar chirality has not received much attention until now. Hayashi and co-workers reported an example of C_2-symmetric 1,1',2,2'-tetrasubstituted ferrocene chiral ligand **1** with which an excellent enantiomeric excess was achieved for the coupling reaction of vinyl bromide and 1-phenylethylzinc chloride.[5] For the preparation of **1**, however, a resolution procedure was needed.

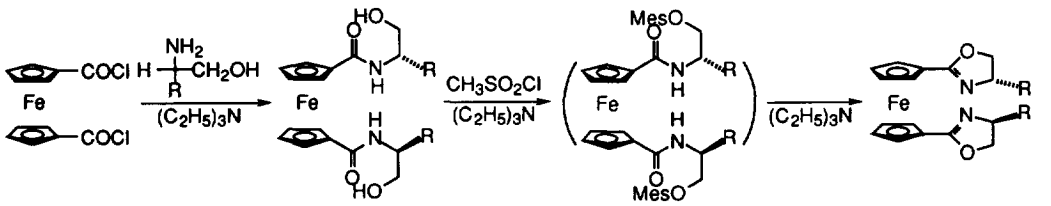


1

We here report the highly diastereoselective *o,o'*-dilithiation of 1,1'-bis(oxazolinyl)ferrocene **5**, leading to the synthesis of novel C_2-symmetric 1,1',2,2'-tetrasubstituted ferrocene, as well as the preparation of 1,1'-bis(oxazolinyl)ferrocene **5**. Thus, by the dilithiation of bis(oxazolinyl)ferrocene with *sec*-butyllithium followed by the reaction with electrophiles, novel C_2-symmetric 1,1',2,2'-tetrasubstituted ferrocene derivatives were obtained in high yields with ease, only requiring purification using silica gel column chromatography, rather than by resolution. Park and co-workers[6] have recently published very similar work but with different results

from ours.

1,1'-Bis(oxazolinyl)ferrocenes **5a-c** were readily synthesized from 1,1'-ferrocenedicarbonyl dichloride **2** and enantiomerically pure aminoalcohols by a convenient and effective method *via* the corresponding bis(β-hydroxylamide)s **3a-c** and dimesylates **4a-c** as intermediates (Scheme 1). This method was also reported very

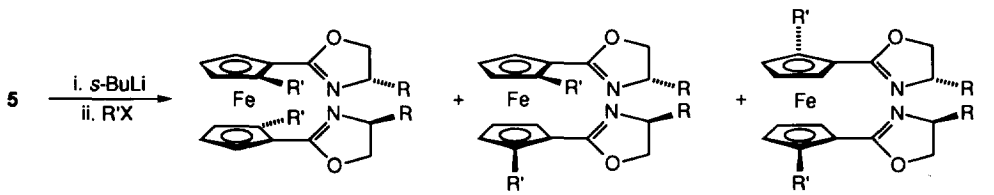


2 **3a~c** **4a~c** **5a~c**

Scheme 1 **a**, R = *i*-Pr; **b**, R = *t*-Bu; **c**, R = Ph

recently by Denmark and co-workers for the preparation of other kinds of oxazoline compounds.[7] Bis(β-hydroxylamide)s **3a-c** were prepared in over 85% yields from 1,1'-ferrocenedicarbonyl dichloride **2** and enantiomerically pure aminoalcohols (2.2 equiv.) in the presence of triethylamine (4.0 equiv.). Then the amides **3a-c** were treated with methanesulfonyl chloride (2.3 equiv.) and triethylamine (4.0 equiv.) at room temperature for 3 h to afford directly 1,1'-bis(oxazolinyl)ferrocenes **5a-c** in about 90% yield without isolation of dimesylates **4a-c**.

Although *n*-butyllithium had been successfully used for the lithiation of mono(oxazolinyl)ferrocene,[4a] it was not strong enough for dilithiation of 1,1'-bis(oxazolinyl)ferrocene **5a,b**. When the stronger base, *sec*-butyllithium was used, excellent results were obtained. Thus, 1,1'-bis(oxazolinyl)ferrocene **5a** or **5b** in THF was treated with 2.6 equiv. of *sec*-butyllithium at -78 ℃ for a period of 3 h and then 10 min at 0 ℃ to ensure complete dilithiation. The dilithiated species was then trapped with 2.6 equiv. of an electrophile such as methyl iodide, chlorodiphenylphosphine, and trimethylsilyl chloride at 0 ℃. After stirred at room temperature over night, the corresponding tetrasubstituted ferrocene was obtained in high yield (Scheme 2). The



6a~e **7a~e** **8a~e**

a: R = *i*-Pr, R' = CH_3; **b**: R = *t*-Bu, R' = CH_3; **c**: R = *i*-Pr, R' = PPh_2;
d: R = *t*-Bu, R' = PPh_2; **e**: R = *i*-Pr, R' = $Si(CH_3)_3$

Scheme 2 *Reagents*: ii, R'X = CH_3I, Ph_2PCl, $(CH_3)_3SiCl$

diastereoselectivity of *o,o'*-dilithiation of **5a,b** was revealed to be high by ^{1}H-NMR of the crude products with

the main product being the C_2-symmetric one **6a-e**. When the substituent is isopropyl, the ratio of the major product (**6a,c,e**) to minor *meso*-product (**7a,c,e**) was 78 : 22, regardless of the kind of electrophile. As the substituent is the bulkier, *tert*-butyl group, the ratio of major product (**6b,d**) to minor *meso*-product (**7b,d**) was 85 : 15. In both cases product **8a-e** could not be detected. The enantiomerically pure main C_2-symmetric products **6a,b,e** and minor *meso*-products **7a,b,e** were easily isolated by silica gel column chromatography. However, diphosphine **6c,d** were prone to be oxidized to the corresponding phosphine oxide during purification with the normal treatment, perhaps due to the presence of a trace amount of decomposition products from ferrocene derivatives. But they could be isolated in high yields by silica gel column chromatography with degassed eluent under argon atmosphere. The purified products are now stable to air.

Park and co-workers also obtained C_2-symmetric product **6c,d** in a yield of less than 7% by the lithiation and phosphorylation of **5a,b**, using *n*-butyllithium,[6] but the spectroscopic data of their **6c,d** were different from ours. By using *tert*-butyllithium (or *sec*-butyllithium) they obtained *meso*-products **7c,d** as the main products.

We did not examine the effect of *tert*-butyllithium as lithiation agent, but *sec*-butyllithium proved to be strong enough to generate dilithiated species with high diastereoselectivity and to give C_2-symmetric products **6a-e** in high yields.

The molecular structure of main product **6b** was fully characterized by X-ray crystallography as shown in Figure 1 which indicates not only a C_2-symmetric configuration as the whole molecule but also a (*S*)-planar

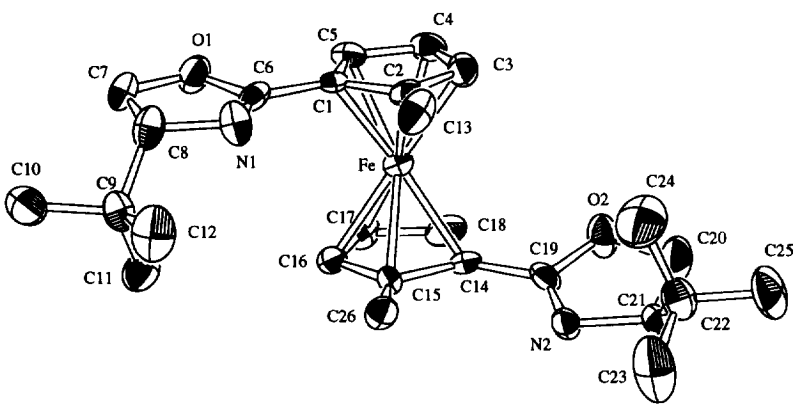


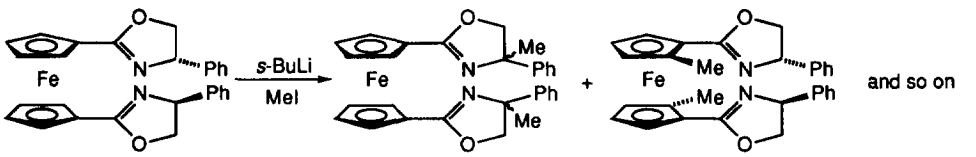
Figure 1 Crystal structure of **6b** (ORTEP, ellipsoids at the 30% probability level). Selected bond length [Å] and bond and torsion angle [°]: C(1)-C(2) 1.42 (1), C(2)-C(13) 1.49 (2), C(1)-C(6) 1.51 (1), O(1)-C(6) 1.39 (1), N(1)-C(6) 1.24 (1), O(1)-C(7) 1.45 (2), N(1)-C(8) 1.47 (1), C(7)-C(8) 1.52 (2), C(8)-C(9) 1.52 (2); C(1)-C(2)-C(13) 127 (1), C(2)-C(1)-C(6) 123 (1), O(1)-C(6)-N(1) 118 (1), O(1)-C(6)-C(1) 110 (1), N(1)-C(6)-C(1) 130 (1), C(5)-C(1)-C(6) 126 (1); N(1)-C(6)-C(1)-C(2) -5(1), C(1)-C(6)-O(1)-C(7) -179.2(9), C(1)-C(6)-N(1)-C(8) -178 (1), C(6)-N(1)-C(8)-C(9) 122 (1), C(6)-C(1)-C(2)-C(13) -5 (1).

configuration around the ferrocene axis for each ferrocene ring. There are some experimental evidences on the stereochemistry of *ortho*-lithiation of oxazoline compounds, that is, the chelation of lithium with the oxazoline nitrogen is more favorable than with the oxazoline oxygen.[8] And, on lithiation of mono(oxazolinyl)ferrocene, the substituent on oxazoline ring is reported to prefer the *syn* orientation with respect to ferrocenyl iron atom.[4c]

In our case, bis(oxazolinyl)ferrocene was lithiated twice by the same process as that for mono(oxazolinyl)ferrocene to give C_2-symmetric products. This chelation structure is different from those reported for ferrocenyl sulfoxides[3] and ferrocenyl amine[9] in which a bulky group in a chiral substituent prefers the *anti* orientation to ferrocenyl iron atom.

It is interesting that the X-ray crystallography of tetrasubstituted product **6b** has the same conformation as the chelation structure during lithiation process (Figure 1).

Phenyl substituted mono(oxazolinyl)ferrocene was *ortho*-lithiated on the ferrocene ring with *sec*-butyllithium in high yield.[4b,c] For the *ortho*-lithiation of bis(phenyloxazolinyl)ferrocene, however, the expected result was not obtained (Scheme 3). When 2.6 equiv. of *sec*-butyllithium was used as a lithiation agent, followed by trapping



5c **9** not isolated

Scheme 3

with methyl iodide, a very complicated mixture was given. From ^{1}H-NMR evidence, lithiation was shown to occur not only at the ferrocene rings (several signals by methyl protons at about δ = 2.2), but also at the oxazoline rings (several signals by methyl protons at about δ = 3.1). On use of 1.3 equiv. of *sec*-butyllithium and 1.3 equiv. of methyl iodide, ^{1}H-NMR of the reaction mixture indicated that lithiation partly took place on ferrocene rings, but compound **9** from lithiation at oxazoline rings was the main product which was isolated in 21% yield with silica gel column chromatography. The structure of **9** was confirmed by NOE measurement (Figure 2). Since the specific rotation of **9** is very low ($[\alpha]_D^{18}$ = -5.2 (c 0.48, $CHCl_3$)), racemization on lithiation had probably occurred. However, the ^{1}H-NMR of compound **9** showed a simple spectrum, and the proof to show the racemization of disubstituted oxazoline ring was not obtained.

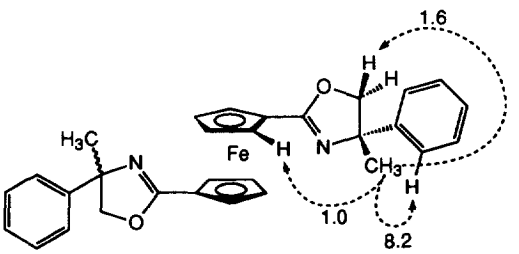


Figure 2 Nuclear Overhauser Enhancement (%) in **9**

In summary, a convenient method has been established for the synthesis of 1,1'-bis(oxazolinyl)ferrocene

compounds from ferrocenedicarbonyl dichloride and enantiomerically pure aminoalcohol *via* the corresponding bis(β-hydroxylamide) and dimesylate as intermediates. The *ortho*-lithiation of 1,1'-bis(oxazolinyl)ferrocene with *sec*-butyllithium followed by trapping with electrophiles revealed that the oxazoline ring having isopropyl or *tert*-butyl substituent afforded high diastereoselectivity. The C_2-symmetric 1,1',2,2'-tetrasubstituted ferrocene derivatives as main products were obtained in high yields simply by silica gel chromatographic purification. When the substituent was a phenyl group, complicated mixtures were obtained. Thus, lithiation occurred not only at ferrocene rings but also at oxazoline rings and the expected product could not be isolated.

The C_2-symmetric tetrasubstituted ferrocene derivatives obtained in this work can be used as ligands for asymmetric synthesis. Furthermore, the oxazoline moiety can also be derivatized further to lead to novel C_2-symmetric chiral ferrocene derivatives. The investigation in this area is being carried out in our laboratory.

Experimental

General methods

Melting points were measured on a Yanagimoto micromelting point apparatus and have not been corrected. Optical rotations were measured on a DIP-181 digital polarimeter. ^{1}H-NMR spectra were recorded on a Bruker AM-600 (600 MHz) spectrometer and the chemical shifts were referenced to $CHCl_3$ (δ 7.27) in $CDCl_3$. ^{31}P-NMR spectra were recorded on a JEOL GSX-400 spectrometer operating at 162 MHz and the chemical shifts were referenced to external $P(OMe)_3$ (δ 0.00). IR spectra were obtained on a HITACHI 260-10 infrared spectrophotometer. The fast atom bombardment mass spectra were obtained on a JEOL JMS-DX303HF spectrometer. Elemental analyses were performed on a Yanagimoto CHN-Corder. The X-ray crystallography was performed on a Rigaku AFC5R diffractometer.

THF was freshly distilled from sodium, CH_2Cl_2 from P_2O_5, and triethylamine from CaH_2 before use. Ferrocenedicarbonyl dichloride was prepared from ferrocene dicarboxylic acid and oxalyl chloride with normal method and aminoalcohols were prepared by reduction of the corresponding commercially available amino acids with $LiAlH_4$ as reducing agent.[10] Merck 70 ~ 230 mesh silica gel was used for column chromatography. All of the other chemicals used in synthetic procedures were of reagent grade or better.

1,1'-Bis[(*S*)-N-(1-isopropyl-2-hydroxyethyl)-amido]-ferrocene 3a: To a solution of (*S*)-(+)-valinol (4.54 g, 44.0 mmol) and triethylamine (11.2 ml, 80.0 mmol) in 80 ml of dichloromethane was added dropwise ferrocenedicarbonyl dichloride (6.22 g, 20 mmol) in 60 ml of dichloromethane under argon atmosphere at 0 ℃, and then the reaction mixture was stirred at room temperature for 24 h. The resulting mixture was washed with saturated $NaHCO_3$ aqueous solution and then brine. The organic solution was dried over Na_2SO_4 and the solvent was evaporated in vacuo. After purified with short column chromatography eluted with ethylacetate, **3a** (7.64 g, 86% yield) was isolated as a red solid. mp 156-157 ℃ (dec.). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 1.00 (d, *J* 6.9 Hz, 6H, CH_3), 1.02 (d, *J* 6.6 Hz, 6H, CH_3), 1.96 (m, 2H, Me_2CH), 3.75 (dd, *J* 6.0, 11.6 Hz, 2H, OCH), 3.88 (dd, *J* 3.0, 11.6 Hz, 2H, OCH), 3.93 (m, 2H, NCH), 4.38 (brs, 2H, FcH), 4.47 (brs, 2H, FcH), 4.50 (brs, 2H, FcH), 4.76 (brs, 2H, FcH), 6.34 (d, *J* 8.5 Hz, 2H, NH). IR (KBr, cm^{-1}): 2960, 2872, 1629, 1628, 1542, 1465, 1377, 1314, 1260, 1183, 1073, 1026, 820. FAB-MS (m/z): 444.

1,1'-Bis[(*S*)-N-(1-*tert*-butyl-2-hydroxyethyl)-amido]-ferrocene 3b: Following the same procedure as described above, **3b** (4.25 g, 90% yield) was obtained from ferrocenedicarbonyl dichloride (3.11

g, 10 mmol) and (*S*)-(+)-*tert*-leucinol (2.58 g, 22.0 mmol). mp 195-197 ℃ (dec.). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 0.99 (s, 18H, CH_3), 3.69 (dd, *J* 7.7, 11.6 Hz, 2H, OCH), 3.96 (dd, *J* 3.8, 11.6 Hz, 2H, OCH), 4.01 (ddd, *J* 3.8, 7.7, 9.4 Hz, 2H, NCH), 4.39 (brs, 2H, FcH), 4.46 (brs, 2H, FcH), 4.56 (brs, 2H, FcH), 4.84 (brs, 2H, FcH), 6.18 (d, *J* 9.4 Hz, 2H, NH). IR (KBr, cm^{-1}): 2960, 2880, 1618, 1550, 1475, 1370, 1305, 1180, 1108, 1055. FAB-MS (m/z): 472.

1,1'-Bis[(*S*)-N-(1-phenyl-2-hydroxyethyl)-amido]-ferrocene 3c: Following the same procedure as described above, **3c** (6.53 g, 85% yield) was prepared from ferrocenedicarbonyl dichloride (4.67 g, 15 mmol) and (*S*)-(+)-phenylglycinol (4.53 g, 33 mmol). mp 198-200 ℃ (dec.). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 3.86 (dd, *J* 7.6, 11.8 Hz, 2H, OCH), 4.01 (dd, *J* 3.9, 11.8 Hz, 2H, OCH), 4.34 (brs, 2H, FcH), 4.43 (brs, 2H, FcH), 4.48 (brs, 2H, FcH), 4.77 (brs, 2H, FcH), 5.24 (ddd, *J* 3.9, 7.0, 7.6 Hz, 2H, NCH), 7.02 (d, *J* 7.0 Hz, 2H, NH), 7.29-7.37 (m, 10H, PhH). IR (KBr, cm^{-1}): 2950, 2855, 1650, 1520, 1455, 1380, 1295, 1182, 1075, 1035, 835, 760, 700. FAB-MS (m/z): 513.

1,1'-Bis[(*S*)-4-isopropyloxazolin-2-yl]-ferrocene 5a: To a solution of **3a** (4.44 g, 10.0 mmol) and triethylamine (5.6 ml, 40 mmol) in 100 ml of dichloromethane was added dropwise methanesulfonyl chloride (2.64 g, 23.0 mmol) in 20 ml of dichloromethane for a period of 30 min at 0 ℃ under argon atmosphere, and then the solution was stirred at 0 ℃ for 1 h and then at room temperature for 2 h. The resulting solution was washed with chilled water (5 ℃) and then brine. The organic layer was dried over Na_2SO_4 and then the solvent was evaporated in vacuo. By recrystallization from hexane, **5a** (3.76 g, 92% yield) was obtained as reddish crystals. mp 112-113 ℃. $[\alpha]_D^{25}$ = -106.5 (c 0.5, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 0.94 (d, *J* 6.6 Hz, 6H, CH_3), 1.02 (d, *J* 6.7 Hz, 6H, CH_3), 1.86 (m, 2H, Me_2CH), 3.98 (m, 2H, NCH), 4.06 (t, *J* 7.9 Hz, 2H, OCH), 4.31 (dd, *J* 7.9, 10.1 Hz, 2H, OCH), 4.35 (brs, 4H, FcH), 4.74 (brs, 2H, FcH), 4.77 (brs, 2H, FcH). IR (KBr, cm^{-1}): 2957, 2888, 1662, 1485, 1460, 1375, 1285, 1248, 1144, 1121, 1102, 1026, 962, 832. FAB-MS (m/z): 409. Anal. calcd. for $C_{22}H_{28}N_2O_2Fe$: C, 64.71; H, 6.91; N, 6.86. Found: C, 64.53; H, 7.03; N, 6.81.

1,1'-Bis[(*S*)-4-*tert*-butyloxazolin-2-yl]-ferrocene 5b: Following the same procedure as described above, **5b** (3.18 g, 91% yield) was obtained from **3b** (3.78 g, 8 mmol), triethylamine (4.5 ml, 32 mmol) and methanesulfonyl chloride (2.11 g, 18.4 mmol) and purified from ether as red crystals. mp 171.5-172.5 ℃. $[\alpha]_D^{25}$ = -183.1 (c 0.5, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 0.97 (s, 18H, CH_3), 3.90 (dd, *J* 7.8, 9.9 Hz, 2H, OCH or NCH), 4.16 (dd, *J* 7.8, 8.7 Hz, 2H, OCH or NCH), 4.26 (dd, *J* 8.7, 9.9 Hz, 2H, OCH or NCH), 4.35 (brs, 4H, FcH), 4.73 (brs, 2H, FcH), 4.79 (brs, 2H, FcH). IR (KBr, cm^{-1}): 2960, 2875, 1660, 1355, 1305, 1262, 1110, 1015, 963, 818. FAB-MS (m/z): 437. Anal. calcd. for $C_{24}H_{32}N_2O_2Fe$: C, 66.06; H, 7.39; N, 6.42. Found: C, 66.25; H, 7.33; N, 6.43.

1,1'-Bis[(*S*)-4-phenyloxazolin-2-yl]-ferrocene 5c: Following the same procedure described above, **5c** (4.19 g, 88% yield) was obtained from **3c** (5.13g, 10 mmol), triethylamine (5.6 ml, 40 mmol) and methanesulfonyl chloride (2.64 g, 23 mmol) and purified from hexane as red crystals. mp 118-119 ℃. $[\alpha]_D^{25}$ = -157.4 (c 0.5, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$) δ 4.20 (t, *J* 8.2 Hz, 2H, OCH), 4.45 (brs, 2H, FcH), 4.47 (brs, 2H, FcH), 4.71 (dd, *J* 8.2, 9.8 Hz, 2H, OCH), 4.87 (brs, 2H, FcH), 4.89 (brs, 2H, FcH), 5.24 (dd, *J* 8.2, 9.8 Hz, 2H, NCH), 7.28-7.38 (m, 10H, PhH). IR (KBr, cm^{-1}): 2965, 2900, 1650, 1480, 1455, 1375, 1350, 1295, 1240, 1110, 1018, 948, 910, 825, 755, 700. FAB-MS (m/z): 477. Anal. calcd. for

$C_{28}H_{24}N_2O_2Fe$: C, 70.60; H, 5.08; N, 5.88. Found: C, 70.59; H, 5.13; N, 5.89.

1,1'-Bis[(*S*)-4-isopropyloxazolin-2-yl]-(*R*)-(*R*)-2,2'-dimethylferrocene 6a and 1,1'-Bis[(*S*)-4-isopropyloxazolin-2-yl]-(*S*)-(*R*)-2,2'-dimethylferrocene 7a: To a solution of **5a** (0.408 g, 1.0 mmol) in 20 ml of THF was added dropwise 1.3 M solution of *sec*-butyllithium in cyclohexane (2.0 ml, 2.6 mmol) at -78 ℃ under argon atmosphere. The reaction solution was stirred at the temperature for 3 h and then at 0 ℃ for 10 min to ensure complete dilithiation. Methyl iodide (0.37 g, 2.6 mmol) was added with a syringe to the solution of dilithiated species at 0 ℃ and then the reaction mixture was stirred at room temperature over night. The solvent was removed in vacuo and the residue was dissolved in 60 ml of dichloromethane. The solution was washed with water and brine, dried over Na_2SO_4, and then the solvent was evaporated in vacuo to give an oil (0.46 g). According to the ^{1}H-NMR of the crude product, it is revealed that the ratio of **6a** to **7a** is 78 : 22.[11] Enantiomerically pure **6a** (0.24 g, 54% yield) and **7a** (0.057g, 13% yield) were isolated by silica gel column chromatography eluted with ethylacetate-benzene (1 : 7).

6a: Rf = 0.075 (ethylacetate-benzene, 1 : 7). oil. $[\alpha]_D^{23}$ = +81.3 (c 0.47, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 0.95 (d, *J* 6.7 Hz, 6H, CH_3), 1.05 (d, *J* 6.8 Hz, 6H, CH_3), 1.81 (m, 2H, Me_2CH), 2.16 (s, 6H, $FcCH_3$), 3.94 (m, 2H, NCH), 4.03 (dd, *J* 7.3, 8.2 Hz, 2H, OCH), 4.11 (dd, *J* 1.6, 2.2 Hz, 2H, FcH), 4.15 (dd, *J* 2.2, 2.6 Hz, 2H, FcH), 4.27 (dd, *J* 7.3, 9.5 Hz, 2H, OCH), 4.61 (dd, *J* 1.6, 2.6 Hz, 2H, FcH). IR (neat, cm^{-1}): 2950, 2875, 1648, 1475, 1460, 1420, 1375, 1358, 1258, 1207, 1170, 1145, 1060, 1005, 970, 948, 810. FAB-MS (m/z): 436. Anal. calcd. for $C_{24}H_{32}N_2O_2Fe$: C, 66.06; H, 7.39; N, 6.42. Found: C, 65.99, H, 7.27; N, 6.47.

7a: Rf = 0.10 (ethylacetate-benzene, 1 : 7). oil. $[\alpha]_D^{23}$ = -167.4 (c 0.57, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 0.92 (d, *J* 6.7 Hz, 3H, CH_3), 0.96 (d, *J* 6.7 Hz, 3H, CH_3), 1.03 (d, *J* 6.7 Hz, 3H, CH_3), 1.05 (d, *J* 6.7 Hz, 3H, CH_3), 1.82 (m, 2H, Me_2CH), 2.19 (s, 3H, $FcCH_3$), 2.20 (s, 3H, $FcCH_3$) 3.94 (m, 2H, NCH), 4.03 (m, 2H, OCH), 4.11 (brs, 1H, FcH), 4.13 (brs, 2H, FcH), 4.16 (brs, 1H, FcH), 4.27 (m, 2H, OCH), 4.53 (brs, 2H, FcH). IR (neat, cm^{-1}): 2950, 2880, 1650, 1480, 1465, 1425, 1375, 1365, 1265, 1212, 1060, 1010, 976, 957, 812. FAB-MS (m/z): 436.

1,1'-Bis[(*S*)-4-*tert*-butyloxazolin-2-yl]-(*R*)-(*R*)-2,2'-dimethylferrocene 6b and 1,1'-Bis[(*S*)-4-*tert*-butyloxazolin-2-yl]-(*S*)-(*R*)-2,2'-dimethylferrocene 7b: Following the same procedure as described above, the crude mixture (0.47 g) of **6b** and **7b** was obtained from **5b** (0.436 g, 1.0 mmol). ^{1}H-NMR analysis revealed that the ratio of **6b** to **7b** is 85 : 15.[12] Enantiomerically pure **6b** (0.218 g, 47% yield) and **7b** (0.023 g, 5% yield) were isolated by silica gel column chromatography eluted with ethylacetate-benzene (3 : 7).

6b: Rf = 0.38 (ethylacetate-benzene, 3 : 7). mp 118-119 ℃. $[\alpha]_D^{18}$ = -157.7 (c 0.5, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 0.99 (s, 18H, CH_3), 2.22 (s, 6H, $FcCH_3$), 3.91 (dd, *J* 7.7, 9.9 Hz, 2H, NCH or OCH), 4.08 (brs, 2H, FcH), 4.13 (dd, *J* 7.7, 8.7 Hz, 2H, NCH or OCH), 4.14 (brs, 2H, FcH), 4.20 (dd, 2H, *J* 8.7, 9.9 Hz, 2H, NCH or OCH), 4.61 (brs, 2H, FcH). IR (KBr, cm^{-1}): 2945, 2860, 1645, 1475, 1420, 1360, 1295, 1255, 1207, 1070, 1008, 815. FAB-MS (m/z): 465. Anal. calcd. for $C_{26}H_{36}N_2O_2Fe$: C, 67.24; H, 7.81; N, 6.03. Found: C, 66.91; H, 7.72; N, 5.86.

7b: Rf = 0.46 (ethylacetate-benzene, 3 : 7). oil. $[\alpha]_D^{20}$ = -150.6 (c 0.50, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 0.92 (s, 9H, CH_3), 0.99 (s, 9H, CH_3), 2.21 (s, 3H, $FcCH_3$), 2.23 (s, 3H, $FcCH_3$), 3.91 (m, 2H, NCH or OCH), 4.07 (brs, 1H, FcH), 4.09 (brs, 1H, FcH), 4.11 (dd, *J* 7.8, 8.3 Hz, 1H, NCH or OCH), 4.14 (dd, *J* 7.8, 8.3 Hz, 1H, NCH or OCH), 4.16 (brs, 1H, FcH), 4.19 (brs, 1H, FcH), 4.22 (m, 2H, NCH or OCH), 4.50 (brs, 1H, FcH), 4.52 (brs, 1H, FcH). IR (KBr, cm^{-1}): 2945, 2850, 1650, 1470, 1357, 1290, 1255, 1200, 1065, 1000, 810. FAB-MS (m/z): 465.

2,2'-Bis[(*S*)-4-isopropyloxazolin-2-yl]-(*S*)-(*S*)-1,1'-bis(diphenylphosphino)-ferrocene 6c and 2,2'-Bis[(*S*)-4-isopropyloxazolin-2-yl]-(*S*)-(*R*)-1,1'-bis(diphenylphosphino)-ferrocene 7c: 2.6 equiv. of chlorodiphenylphosphine (0.86 g, 3.9 mmol) was dropped at 0 ℃ to the solution containing dilithiated species generated from **5a** (0.613 g, 1.5 mmol) and 1.3 M solution of *sec*-butyllithium in cyclohexane (3.0 ml, 3.9 mmol) as described above, and then the solution was stirred at room temperature over night. After the solvent was evaporated in vacuo, the residue was isolated directly by silica gel column chromatography eluted with degassed ethylacetate-benzene (1 : 7) under argon and **6c** (0.74 g, 63% yield) and **7c** (0.16 g, 14% yield) were obtained as enantiomerically pure red solids.

6c: Rf = 0.33 (ethylacetate-benzene, 1 : 7). mp 75-77 ℃. $[\alpha]_D^{18}$ = -143.5 (c 0.5, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 0.62 (d, *J* 6.8 Hz, 6H, CH_3), 0.82 (d, *J* 6.8 Hz, 6H, CH_3), 1.67 (m, 2H, Me_2CH), 3.48 (brs, 2H, FcH), 3.65 (t, *J* 8.2 Hz, 2H, OCH), 3.87 (m, 2H, NCH), 4.28 (dd, *J* 8.2, 9.7 Hz, 2H, OCH), 4.55 (brs, 2H, FcH), 5.05 (brs, 2H, FcH), 7.16 (m, 4H, PhH), 7.22 (m, 8H, PhH), 7.30 (dd, *J* 7.9, 16.2 Hz, 8H, PhH). ^{31}P-NMR (162 MHz, $CDCl_3$, $(CH_3O)_3P$): δ -159.85. IR (KBr, cm^{-1}): 2950, 2880, 1650, 1478, 1432, 1138, 980, 830, 745, 697. FAB-MS (m/z): 777. Anal. calcd. for $C_{46}H_{46}N_2O_2P_2Fe$: C, 71.14; H, 5.97; N, 3.61. Found: C, 71.20; H, 6.12; N, 3.45.

7c: Rf = 0.28 (ethylacetate-benzene, 1 : 7). mp 185-187 ℃ (dec.). $[\alpha]_D^{18}$ = +114 (c 0.5, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 0.52 (m, 9H, CH_3), 0.74 (d, *J* 6.8 Hz, 3H, CH_3), 1.38 (m, 1H, Me_2CH), 1.50 (m, 1H, Me_2CH), 3.33 (t, *J* 8.5 Hz, 1H, OCH), 3.68 (m, 1H, NCH), 3.77 (m, 1H, NCH), 3.85 (m, 4H, FcH and OCH), 4.02 (t, *J* 8.9 Hz, 1H, OCH), 4.54 (brs, 1H, FcH), 4.57 (brs, 1H, FcH), 4.93 (brs, 1H, FcH), 5.00 (brs, 1H, FcH), 7.16-7.53 (m, 20H, PhH). ^{31}P-NMR (162 MHz, $CDCl_3$, $(CH_3O)_3P$): δ -159.34, -160.18. IR (KBr, cm^{-1}): 2940, 2860, 1650, 1468, 1425, 1130, 970, 825, 735, 685. FAB-MS (m/z): 777.

2,2'-Bis[(*S*)-4-*tert*-butyloxazolin-2-yl]-(*S*)-(*S*)-1,1'-bis(diphenylphosphino)-ferrocene 6d: Following the same procedure as described above, **6d** (0.53 g, 66% yield) was obtained from **5b** (0.436 g, 1.0 mmol) as an enantiomerically pure product. Rf = 0.21 (ethylacetate-benzene, 1 : 30). mp 106-108 ℃. $[\alpha]_D^{18}$ = -272.4 (c 0.32, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 0.78 (s, 18H, CH_3), 3.46 (brs, 2H, FcH), 3.73 (dd, *J* 8.3, 9.9 Hz, 2H, OCH or NCH), 3.84 (t, *J* 8.3 Hz, 2H, OCH or NCH), 4.20 (dd, *J* 8.3, 9.9 Hz, 2H, OCH or NCH), 4.57 (brs, 2H, FcH), 4.99 (brs, 2H, FcH), 7.14-7.28 (m, 20H, PhH). ^{31}P-NMR (162 MHz, $CDCl_3$, $(CH_3O)_3P$): δ -160.08. IR (KBr, cm^{-1}): 2970, 2880, 1670, 1490, 1445, 1155, 995, 755, 708. FAB-MS (m/z): 805. Anal. calcd. for $C_{48}H_{50}N_2O_2P_2Fe$: C, 71.64; H, 6.26; N, 3.48. Found: C, 71.55; H, 6.26; N, 3.45.

2,2'-Bis[(*S*)-4-isopropyloxazolin-2-yl]-(*S*)-(*S*)-1,1'-bis(trimethylsilyl)-ferrocene 6e and 2,2'-Bis[(*S*)-4-isopropyloxazolin-2-yl]-(*S*)-(*R*)-1,1'-bis(trimethylsilyl)-ferrocene 7e: To the solution of dilithiated species generated from **5a** (0.408 g, 1.0 mmol) was added trimethylsilyl chloride (0.283 g,

2.6 mmol) at 0 ℃ as described above, and then the reaction mixture was stirred at room temperature over night. The solvent was evaporated in vacuo and the residue was dissolved in dichloromethane. The solution was washed with water and then brine, dried over Na_2SO_4, and then the solvent was removed in vacuo. By chromatography on silica gel eluted with ethylacetate-benzene (1 : 10), enantiomerically pure **6e** (0.34 g, 61% yield) and **7e** (0.10 g, 18% yield) were obtained as red solids.

6e: Rf = 3.8 (ethylacetate-benzene, 1 : 10). mp 97-98 ℃. $[\alpha]_D^{25}$ = -76.6 (c 0.5, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 0.31 (s, 18H, $SiCH_3$), 0.93 (d, *J* 6.8 Hz, 6H, CH_3), 1.05 (d, *J* 6.7 Hz, 6H, CH_3), 1.81 (m, 2H, Me_2CH), 3.90 (m, 2H, NCH), 3.98 (t, *J* 8.2 Hz, 2H, OCH), 4.29 (brs, 2H, FcH), 4.33 (dd, *J* 8.2, 9.4 Hz, 2H, OCH), 4.39 (brs, 2H, FcH), 4.91 (brs, 2H, FcH). IR (KBr, cm^{-1}): 2960, 2880, 1660, 1470, 1450, 1380, 1360, 1265, 1240, 1142, 1065, 1040, 995, 830. FAB-MS (m/z): 552. Anal. calcd. for $C_{28}H_{44}N_2O_2Si_2Fe$: C, 60.85; H, 8.02; N, 5.07. Found: C, 60.51; H, 8.11; N, 4.93.

7e: Rf = 0.45 (ethylacetate-benzene, 1 : 10). mp 104.5-105.5 ℃. $[\alpha]_D^{25}$ = -98.0 (c 0.5, $CHCl_3$). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 0.32 (s, 9H, $SiCH_3$), 0.34 (s, 9H, $SiCH_3$), 0.93 (d, *J* 6.7 Hz, 3H, CH_3), 0.94 (d, *J* 6.7 Hz, 3H, CH_3), 1.03 (d, *J* 6.8 Hz, 3H, CH_3), 1.04 (d, *J* 6.7 Hz, 3H, CH_3), 1.74 (m, 1H, Me_2CH), 1.81 (m, 1H, Me_2CH), 3.86-4.00 (m, 4H, OCH and NCH), 4.27-4.32 (m, 4H, OCH and FcH), 4.39 (brs, 1H, FcH), 4.40 (brs, 1H, FcH), 4.95 (brs, 1H, FcH), 4.97 (brs, 1H, FcH). IR (KBr, cm^{-1}): 2950, 2900, 1655, 1445, 1390, 1350, 1270, 1248, 1150, 1125, 1060, 1035, 985, 835, 755. FAB-MS (m/z): 552. Anal. calcd. for $C_{28}H_{44}N_2O_2Si_2Fe$: C, 60.85; H, 8.02; N, 5.07; Found: C, 60.48; H, 8.12; N, 5.07.

Dilithiation of 5c: To a solution of **5c** (0.238 g, 0.5 mmol) in 10 ml THF was added 1.3 M solution of *sec*-butyllithium in cyclohexane (0.5 ml, 0.65 mmol) at -78 ℃ under argon atmosphere and then the reaction mixture was stirred at the temperature for 3 h. The temperature was raised to 0 ℃ and methyl iodide (0.093 g, 0.65 mmol) was added. The reaction mixture was stirred at room temperature over night and then the solvent was evaporated in vacuo. By chromatography on silica gel eluted with ethylacetate-benzene (1 : 2), unexpected product **9** (0.053 g, 21% yield) was obtained as a red solid. **9:** Rf = 0.23 (ethylacetate-benzene, 1 : 2). $[\alpha]_D^{18}$ = -5.2 (c 0.48, $CHCl_3$), ^{1}H-NMR (600 MHz, $CDCl_3$): δ 3.13 (s, 6H, CH_3), 4.19 (brs, 4H, FcH), 4.67 (brs, 4H, FcH), 5.00 (s, 2H, OCH), 5.48 (s, 2H, OCH), 7.38 (t, *J* 7.5 Hz, 2H, PhH), 7.43 (t, *J* 7.5 Hz, 4H, PhH), 7.62 (d, *J* 7.5 Hz, 4H, PhH). IR (KBr, cm^{-1}): 2950, 1638, 1490, 1460, 1380, 1350, 1310, 1220, 1180, 1080, 1025, 888, 775, 720, 695. FAB-MS (m/z): 504.

NOE difference experiment of 9 was performed as sequences consisting of two spectra in which the first was obtained off-resonance and the second was obtained with irradiation at the resonance of hydrogen of methyl group (δ = 3.13, 128 scans) on a JEOL GSX-400 spectrometer in $CDCl_3$. The acquisition time was 2.73 second and the pulse delay was 0.1 second. A difference FID was transformed into a frequency-domain spectrum. The NOE result of **9** was illustrated in Figure 2.

X-Ray crystal structure determination of 6b: An orange crystal of **6b** with approximate dimensions of 0.40 x 0.40 x 0.40 mm was mounted on a glass fiber. The measurement was made on a Rigaku AFC5R diffractometer with graphite-monochromated Mo-Kα radiation and a 12kW rotating anode generator. Cell constants and an orientation matrix for data collection were obtained from a least-square refinement using the

setting angles of 25 carefully centered reflections in the range 26.91 < 2θ < 27.45 °corresponded to a primitive orthorhombic cell with dimensions. The data were collected at a temperature of 23 ± 1 ℃ using the ω-2θ scan technique to a maximum 2θ value of 55.0 °. A total of 3262 reflections was collected. The structure was solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 2202 observed reflections (I > 3.00σ(I)) and 281 variable parameters. R = 0.076, R_w = 0.067. Atomic coordinates, bond lengths, angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Center.

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11. The ratio of **6a** to **7a** was determined by comparing the integrals of peaks at δ = 4.61 (**6a**, 2H, FcH) and at δ = 4.53 (**7a**, 2H, FcH) in ^{1}H-NMR.
12. The ratio of **6b** to **7b** was determined by comparing the integrals of peaks at δ = 4.61 (**6b**, 2H, FcH) and at δ = 4.52 and 4.50 (**7b** 2H, FcH) in ^{1}H-NMR.

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