On the Mechanism of Oxazoline-Directed Metalations: Evidence for Nitrogen-Directed Reactions

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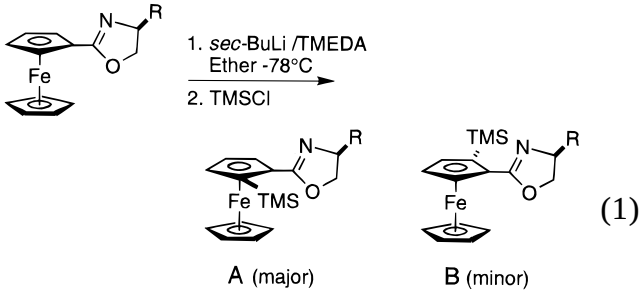
We recently described a method for the synthesis of ferrocene complexes possessing planar chirality which relies on the asymmetric deprotonation of chiral ferrocenyloxazolines. The unexpected stereochemical outcome of these reactions led us to examine whether the metalation is directed by the oxygen or the nitrogen of the oxazoline. In this paper, we describe the synthesis of a constrained ferrocenyloxazoline (compound **13**) in which oxygen- and nitrogen-directed metalations provide different stereochemical outcomes. Our results show that nitrogen is responsible for the directive effects of the oxazoline when alkyllithium reagents are used to deprotonate the ferrocene. The implications of this result on the origin of asymmetric induction in the metalation of the unconstrained ferrocenyloxazolines **19** and **20** are discussed.

The use of ferrocene derivatives possessing planar chirality in asymmetric synthesis is well-known.[1] The preparation of these compounds in nonracemic form has typically relied on classical resolution;[2] however, more practical and versatile methods for their asymmetric synthesis have recently been developed.[3] We have described one such method which relies on the diastereotopic group selective deprotonation of chiral ferrocenyloxazolines (eq 1).[4] The magnitude of the asymmetric



(1)

induction observed with our process depends to a large extent on the conditions employed in the metalation (e.g., solvent, additive, base) and to a lesser extent on the size of the substituent attached to the oxazoline. Larger substituents lead to higher selectivity, and no change is observed in either the sense (which is as shown in eq 1) or magnitude of asymmetric induction upon introducing oxygen or sulfur heteroatoms into the alkyl substituent of the oxazoline.

The stereochemical results of this study prompted us to investigate the origin of asymmetry operating in the metalation. Oxazoline-directed metalations can, in principle, occur via nitrogen or oxygen coordination. In our system, in order to produce the observed stereochemical outcome via a nitrogen-directed reaction, the oxazoline must adopt a rotomer in which the alkyl group of the oxazoline is placed in the more hindered position at the transition state (toward the iron and other cyclopentadienyl ring, see structure C, Figure 1). However, if the metalation is directed by oxygen, the oxazoline assumes a rotomer in which the alkyl group points in the less hindered direction (structure D, Figure 1). Surprisingly, there is little data on the mechanism of oxazoline-directed lithiations in the literature, and both nitrogen and oxygen have been suggested to direct metalations.[5] Recent studies by Collum suggest that oxygen can compete favorably with nitrogen for coordination to some organolithium species[6] and, consequently, that it is not unreasonable to consider an oxygen-directed reaction. We have therefore prepared a ferrocenyloxazoline in which the conformation of the oxazoline is restricted such that the heteroatoms are directed toward different ortho protons of the cyclopentadienyl ring. Metalation of this species and trapping with an electrophile provides different products depending on which heteroatom is directing the reaction, thereby enabling us to distinguish between these modes of coordination. This paper describes our synthesis of this compound, as well as our metalation studies which show that in the case of metalations using alkyllithium reagents it is the nitrogen of the oxazoline that directs the incoming base.

Figure 1.

The desired conformational constraint was achieved via the bridged ferrocenyloxazoline derivative **13**, which contains a tether linking the oxazoline to the other

[⊗] Abstract published in *Advance ACS Abstracts,* February 1, 1996.

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(3) (a) Riant, O.; Samuel, O.; Kagan, H. B. *J. Am. Chem. Soc.* **1993**, *115*, 5835. (b) Rebiere, F.; Riant, O.; Ricard, L.; Kagan, H. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 568. (c) Richards, C. J.; Damalidis, T.; Hibbs, D. E.; Hursthouse, M. B. *Synlett* **1995**, 74. (d) Nishibayashi, Y.; Uemura, S. *Synlett* **1995**, 79. (e) Ratajczak, A.; Misterkiewicz, B. *J. Organomet. Chem.* **1975**, *91*, 73. (f) Hayashi, T.; Mise, T.; Kumada, M. *Tetrahedron Lett.* **1976**, *48*, 4351. (g) Wang, Y.-F.; Lalonde, J. J.; Momongan, M.; Bergbreiter, D. E.; Wong, C.-H. *J. Am. Chem. Soc.* **1988**, *110*, 7200. (h) Boaz, N. W. *Tetrahedron Lett.* **1989**, *30*, 2061.

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(6) Collum, D. B. *Acc. Chem. Res.* **1992**, *25*, 448. Collum, D. B. *Acc. Chem. Res.* **1993**, *26*, 227. These articles review the work of the author as well as others in this field.

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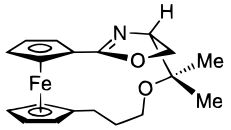

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Figure 2.

cyclopentadienyl ring of the ferrocene (Figure 2).[7] Many attempts to prepare this compound by further functionalization of a suitable ferrocenyloxazoline failed. We therefore chose to synthesize this compound from ferrocene, a strategy which requires the differential substitution of the two cyclopentadienyl rings and elaboration of these substituents to an oxazoline on one ring and the linking chain on the other. This was accomplished by preparing the 1,1′-bis(tributylstannyl) derivative followed by sequential transmetalation of the tributyltin groups[8] and trapping with suitable precursors for the oxazoline or linking chain (Scheme 1). Thus, bislithiation of ferrocene using 3 equiv of *n*-butyllithium and TMEDA in ether at room temperature[9] followed by trapping with tributyltin chloride provided 1,1′-bis(tributyltin)ferrocene (**1**) in 80% yield. Treatment of **1** with *n*-butyllithium in THF provided the monolithio species which was trapped with acrolein to provide allylic alcohol **2** in 60% yield. Compound **2** underwent isomerization to the conjugated allylic alcohol upon treatment with Amberlyst-15 in wet THF. The hydroxyl group was then protected as a *tert*-butyldimethylsilyl ether to provide **4** in 71% overall yield from **2**. Treatment of **4** with *n*-butyllithium in THF provided the corresponding lithioferrocene derived from transmetalation of the remaining tributyltin moiety, which was trapped with methyl chloroformate to provide the carbomethoxy-substituted ferrocene **5** in 73% yield. This sequence enables us to synthesize gram quantities of a ferrocene derivative with an oxazoline precursor (carbomethoxy group) on one ring and a three-carbon tether on the other. Hydrolysis of methyl ester **5** proved difficult, largely because the product is sensitive to oxidative decomposition. However, we found that if the hydrolysis is performed in the presence of sodium borohydride, a reducing environment is maintained and the reaction provides an 87% yield of acid **6**. Activation of the carboxylate was accomplished by preparation of the pentafluorophenyl ester, which upon treatment with (*S*)-2-amino-3-methyl-1,3-butanediol[10] provided amide **8** in 91% yield from **6**. Conversion of **8** to oxazoline **9** was accomplished by selective activation of the primary alcohol via the tosylate followed by *in situ* cyclization to the oxazoline in 90% yield. The allylic alcohol was then unmasked by treatment with TBAF. Attempted tosylation of the allylic alcohol resulted in extensive decomposition, presumably due to the propensity of the allylic, ferrocenyl tosylate to ionize to the conjugated ferrocenyl cation. The olefin was therefore hydrogenated and the primary alcohol selectively activated as the tosylate (**12**), setting the stage for the macrocyclization. This reaction proved difficult to accomplish in high yield, and a variety of conditions were examined. The optimum conditions involved treatment of **12** with NaH and 18-crown-6 in DMSO at room temperature. In this way, a 30% yield of the desired product was obtained.

Compound **13** was metalated with *sec*-butyllithium in THF at −78 to 0 °C and trapped with iodomethane or TMSCl to provide the corresponding substituted products (**14** and **15**) in 70% and 82% yields, respectively. In each case, only one isomer was detected by NMR and HPLC, indicating that the metalation proceeds with a very high level of diastereoselectivity (>100:1).[11] *The structure of the product of alkylation with iodomethane was determined by X-ray crystallography and was found to contain the methyl group proximal to the nitrogen of the oxazoline, consistent with a nitrogen-directed reaction (Figure 3).*

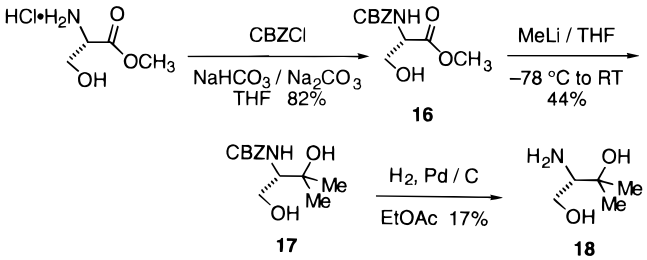
This result indicates that metalation of our unconstrained oxazolines[4] (e.g., **19** and **20**) proceeds by nitrogen coordination via the rotomer where the alkyl group of the oxazoline is pointing toward the more hindered side of the ferrocene (structure C, Figure 1).[12] The predominance of this transition state cannot be due to an intrinsic preference of the alkyl group on the oxazoline to be in the more hindered position but must be due to some other interaction forcing it to adopt that conformation. We speculate that this interaction involves the incoming alkyllithium reagent and the substituent on the oxazoline. A model for the transition structure which would lead to the major and minor products is shown in Figure 4. In this model, butyllithium[13] is coordinated to the nitrogen of the oxazoline and is undergoing what is formally a σ-bond metathesis reaction[14] with the C−H of the cyclopentadienyl ring. This mechanism allows the lithium to interact with the cyclopentadienyl carbon during deprotonation, thereby avoiding the formation of a free carbanion, a species which we feel is unlikely in

(7) For examples of directed metalation of ferrocene compounds, see: (a) Slocum, D. W.; Rockett, B. W.; Hauser, C. R. *J. Am. Chem. Soc.* **1965**, *87*, 1241. (b) Bolton, E. S.; Pauson, P. L.; Sandhu, M. A.; Watts, W. E. *J. Chem. Soc. C* **1969**, *17*, 2260. (c) Marr, G. *J. Organomet. Chem.* **1967**, *9*, 141. (d) Schmitt, G.; Klein, P.; Ebertz, W. *J. Organomet. Chem.* **1982**, *234*, 63. For reviews of directed metalation of aryl compounds, see: (e) Gilman, H.; Morton, J. W., Jr. *Org. React.* **1954**, *8*, 258. (f) Reuman, M.; Meyers, A. I. *Tetrahedron* **1985**, *41*, 837. (g) Gschwend, H.; Rodriguez, H. R. *Org. React.* **1979**, *26*, 1. (h) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879.

(8) Wright, M. E. *Organometallics* **1990**, *9*, 853.

(9) Rausch, M. D.; Ciappenelli, D. J. *J. Oraganomet. Chem.* **1967**, *10*, 127.

(10) (*S*)-2-Amino-3-methyl-1,3-butanediol (**18**) was prepared in three steps from L-serine methyl ester by protecting the nitrogen as the CBZ derivative, followed by addition of MeLi to the ester and finally deprotecting the nitrogen by hydrogenation:



(11) Similar results were obtained using *tert*-butyllithium in THF.

(12) We do not feel that the oxygen on the tether is playing a significant role in the reaction. If any chelate structure were formed, we would expect to see a difference in the stereochemical outcome of the metalation of unconstrained oxazolines containing heteroatoms at this position as compared to those that do not. However, we have prepared five different oxazolines with an oxygen in the corresponding position and they behave analogously to their nonoxygenated counterparts (i.e., no change in either the sense or magnitude of asymmetric induction). See ref 4b for details.

(13) We have chosen to ignore the aggregation state of the butyllithium because it is difficult to know with certainty what the reactive aggregate is, especially in coordinating solvents such as THF. In hexanes in the presence of TMEDA, we speculate that it is a monomer.

(14) This type of reaction is well known for d^0 early transition metal complexes. For a discussion, see: Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; pp 295−298.

Scheme 1

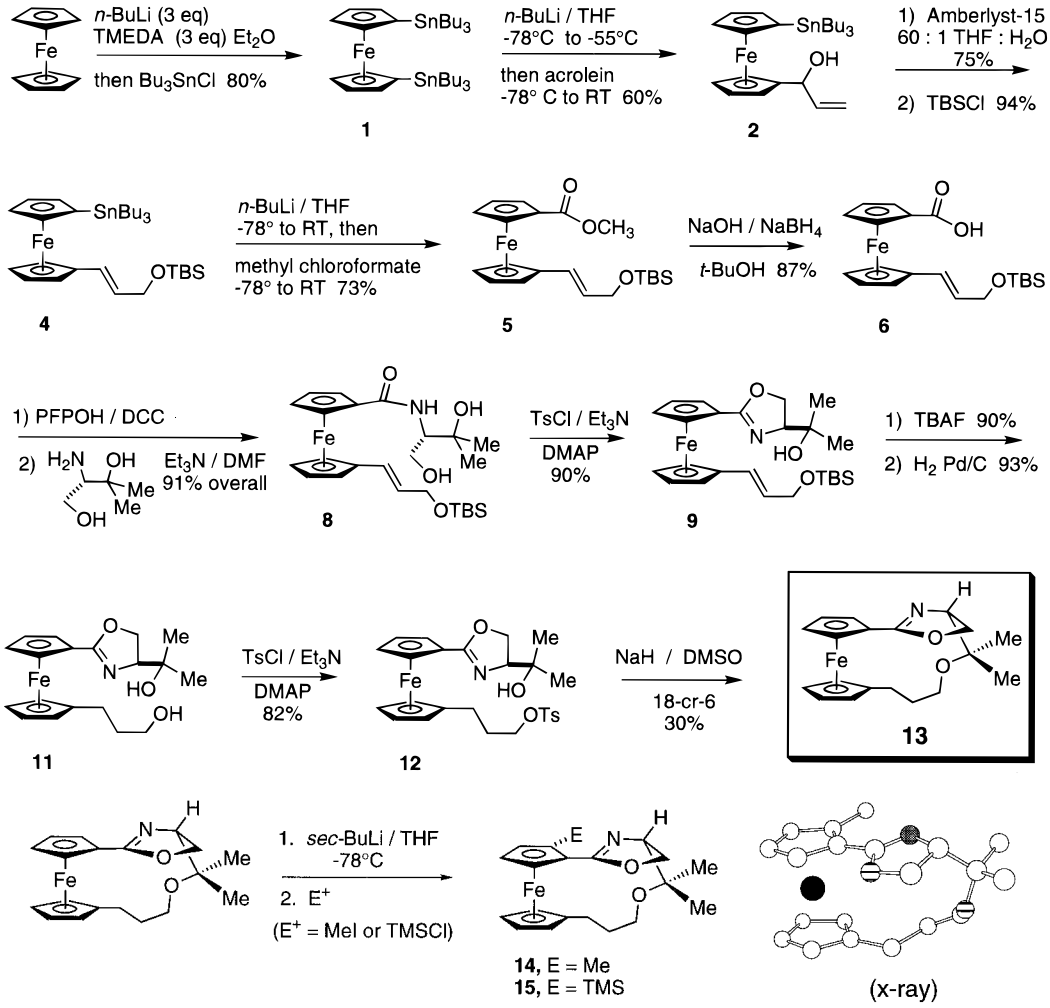


Figure 3.

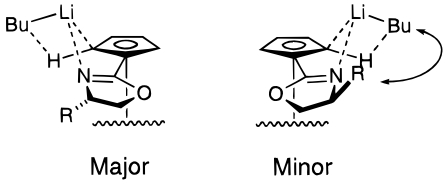


Figure 4.

nonpolar solvents at −78 °C.[15] Furthermore, it is reasonable to assume that the metalating agent approaches the cyclopentadienyl ring away from the iron and the bulk of the ferrocene molecule. In the transition state leading to the minor diastereomer, there is a steric interaction between the alkyl group on the oxazoline and the butyllithium. This interaction is relieved in the transition state leading to the major diastereomer since the alkyl group points toward the iron and away from the incoming base. The stereoselectivity of the reaction is therefore not governed by an interaction between the oxazoline substituent and the ferrocene but by the interaction of this substituent with the metalating agent.[16,17] This model predicts that as this interaction becomes more severe, the selectivity in the metalation should increase. To test this prediction, we have metalated oxazolines **19** and **20** with *n*-BuLi, *s*-BuLi, and *t*-BuLi in THF at −78 °C and measured the diastereoselectivity. In the case of oxazoline **19**, we observe that the selectivity increases as the alkyl group of the base increases in size (Table 1). This trend is also observed with substrate **20** for *n*-BuLi- and *s*-BuLi-promoted reactions, but not with *t*-BuLi. We suspect that this is due to severe steric hindrance between the *tert*-butyl group of the oxazoline and the alkyllithium preventing reaction via a nitrogen-directed pathway, resulting in reaction via an undirected or an oxygen-directed pathway.[18]

In conclusion, this study provides evidence that reactions involving alkyllithium reagents and oxazolines proceed via a nitrogen-directed pathway. This indicates that the metalation of our unconstrained oxazolines (e.g., **19** and **20**) proceeds by a rotamer in which the alkyl group of the oxazoline is pointing toward the iron and the bottom cyclopentadienyl ring. This conformation is adopted because it minimizes the interaction between the alkyl group of the oxazoline and the incoming alkyllithium reagent, as confirmed by the selectivities ob-

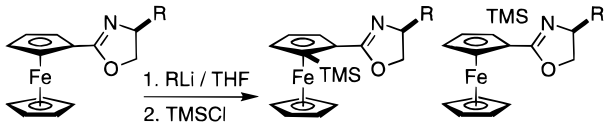
(15) For example, metalation of the valine-derived oxazoline with *sec*-butyllithium in hexanes containing 1 equiv of TMEDA proceeds in excellent yields and stereoselectivities. See ref 4a.

(16) For a related transition structure proposal, see ref 3c.

(17) For a related transition structure hypothesis in an addition reaction, see: Kundig, E. P.; Ripa, A.; Liu, R.; Amurrio, D.; Bernardelli, G. *Organometallics* **1993**, *12*, 3737.

(18) For further evidence of this, see ref 4a.

Table 1



19, R=*i*-Pr
20, R=*t*-Bu

A B

Entry	Oxazoline	RLi	A : B
1	19	*n*-BuLi	3:1
2	19	*sec*-BuLi	8:1
3	19	*tert*-BuLi	16:1
4	20	*n*-BuLi	6:1
5	20	*sec*-BuLi	36:1
6	20	*tert*-BuLi	6:1

served upon metalating **19** and **20** with alkyllithium species bearing different sized alkyl groups.

Experimental Section

General. All reactions were conducted under a nitrogen atmosphere in oven-dried glassware using solvents purified according to standard procedures. ^{1}H NMR spectra were obtained at 400 MHz and ^{13}C NMR spectra at 100 MHz in chloroform-*d*, with chemical shifts reported in ppm referenced to residual chloroform (7.24 ppm for ^{1}H and 77.0 ppm for ^{13}C). Representative NMR spectra are included in the supporting information. Infrared spectra were recorded as thin films on NaCl plates. Optical rotations were obtained at 589 nm. Concentrations for optical rotations are reported in g/mL. FAB mass spectra were obtained using a matrix of 3-nitrobenzyl alcohol. Melting points are uncorrected. Elemental analyses were performed by Supersun Technology Analytical Laboratory, Stony Brook, NY. The diastereomeric excesses of the metalation reactions were determined by integration of the downfield cyclopentadienyl *ortho*-proton resonances, which were base-line resolved in the ^{1}H NMR spectra. Spectroscopic data are provided for the major diastereomer only.

1,1′-Bis(tributylstannyl)ferrocene (1). *n*-Butyllithium (1.58 M in hexanes, 306 mL, 0.484 mol, 3.0 equiv) was added to a solution of TMEDA (distilled over CaH_2, 73.0 mL, 0.484 mol, 3.0 equiv) in ether (150 mL) at room temperature, and the resulting solution was allowed to stir for 5 min. This solution was then added to a suspension of ferrocene (30.0 g, 0.161 mol, 1.0 equiv) in ether (150 mL) at room temperature, and the reaction mixture was allowed to stir for 12 h. The reaction mixture was then cooled to −78 °C, and tributyltin chloride (91.9 mL, 0.339 mol, 2.1 equiv) was added via cannula. The reaction mixture was allowed to warm to room temperature, and the reaction was quenched with water (200 mL). The organic phase was washed with 1 M HCl (2 × 200 mL), water (200 mL), a saturated aqueous solution of sodium bicarbonate (200 mL), and brine (200 mL),and was then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography[19] on silica gel (hexanes) followed by Kugelrohr distillation (230 °C at 0.01 mmHg) provided 99.6 g of **1** (81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.28 (br, 4H), 4.01 (br, 4H), 1.62 (m, 12H), 1.40 (m, 12H), 1.07 (m, 12H), 0.96 (m, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 74.21, 70.46, 67.89, 29.24, 27.45, 13.73, 10.25. IR (thin film): 3087.5 cm^{-1}. R_f = 0.7 (hexanes).

1-[1′-(Tributylstannyl)ferrocenyl]-2-propen-1-ol (2). *n*-Butyllithium (1.58 M in hexanes, 29 mL, 45.3 mmol, 1.1 equiv) was added dropwise to a solution of **1** (30.0 g, 39.3 mmol, 1.0 equiv) in tetrahydrofuran (80 mL) cooled to −78 °C. The reaction mixture was allowed to warm to −55° C and then recooled to −78° C. Freshly distilled acrolein (3.0 mL, 44.9, 1.1 equiv) was added to the reaction mixture, which was then warmed to room temperature and diluted with pentane (100 mL) and water (150 mL). The organic phase was washed with brine (150 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexanes and then 15:1 hexanes:ethyl acetate) provided 12.5 g of **2** (60%). 1H NMR (400 MHz, $CDCl_3$): δ 6.08 (ddd, J = 17.0 Hz, 10.3 Hz, 6.0 Hz, 1H), 5.32 (dt, J = 17.0 Hz, 1.4 Hz, 1H), 5.16 (dt, J = 10.3 Hz, 1.4 Hz, 1H), 4.84 (m, 1H), 4.35 (br, 2H), 4.16 (br, 1H), 4.14 (br, 1H), 4.09 (br, 2H), 4.04 (br, 2H), 2.05 (br, 1H), 1.56 (m, 6H), 1.36 (m, 6H), 1.02 (m, 6H), 0.91 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.60, 114.87, 91.49, 74.84, 74.70, 70.72, 70.72, 70.71, 69.60, 68.23, 68.18, 66.44, 66.39, 29.13, 27.35, 13.67, 10.18. IR (thin film): 3413.7 (br), 3086.4 cm^{-1}. R_f = 0.4 (5:1 hexanes:ethyl acetate).

(*E*)-3-[1′-(Tributylstannyl)ferrocenyl]-2-propen-1-ol (3). Amberlyst-15 ion-exchange resin (3.0 g) was added to a solution of **2** (8.5 g, 16.0 mmol, 1.0 equiv) in 3:1 THF:H_2O (32 mL), and the reaction was allowed to stir for 11 h. The reaction mixture was filtered, and the filtrate was diluted with ether, washed with brine, dried over $MgSO_4$, filtered, and concentrated. Purification by flash chromatography (hexanes and then 20:1 hexanes:ethyl acetate) provided 6.4 g of **3** (75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.33 (d, J = 15.7 Hz, 1H), 5.93 (dt, J = 15.7 Hz, 6.0 Hz, 1H), 4.26 (br, 4H), 4.15 (d, J = 6.0 Hz, 2H), 4.13 (br, 2H), 3.92 (br, 2H), 1.56 (m, 6H), 1.36 (m, 6H), 1.03 (m, 6H), 0.91 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 129.47, 125.76, 82.19, 75.39, 75.39, 72.04, 72.04, 69.19, 68.73, 68.73, 66.72, 66.72, 63.97, 29.15, 27.38, 13.69, 10.21. IR (thin film): 3329.7 (br), 3086.6 cm^{-1}. R_f = 0.2 (5:1 hexanes:ethyl acetate).

(*E*)-3-[1′-(Tributylstannyl)ferrocenyl]-1-(*tert*-butyldimethylsiloxy)-2-propene (4). *tert*-Butyldimethylsilyl chloride (7.24 g, 48.1 mmol, 1.05 equiv) and imidazole (7.24 g, 106.3 mmol, 2.3 equiv) were added to a solution of **3** (24.3 g, 45.8 mmol, 1.0 equiv) in dichloromethane (90 mL) at room temperature. The reaction mixture was allowed to stir for 0.5 h and then diluted with pentane (100 mL) and water (150 mL). The organic phase was washed with water (150 mL), 1 M copper sulfate solution (2 × 150 mL), and brine (150 mL), dried over $MgSO_4$, filtered, and concentrated at reduced pressure to give 27.8 g of **4** (94%) which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.31 (br d, J = 15.6 Hz, 1H), 5.89 (dt, J = 15.6 Hz, 5.4 Hz, 1H), 4.29 (br, 2H), 4.28 (br, 2H), 4.23 (dd, J = 5.4 Hz, 1.4 Hz, 2H), 4.14 (br, 2H), 3.96 (br, 2H), 1.60 (m, 6H), 1.40 (m, 6H), 1.05 (m, 6H), 0.98 (s, 9H), 0.96 (m, 9H), 0.14 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 127.39, 126.45, 82.84, 75.28, 75.28, 71.91, 71.91, 68.98, 68.48, 68.48, 66.60, 66.60, 64.15, 29.16, 27.38, 25.97, 18.38, 13.71, 10.19, −5.06. IR (thin film): 3088.1 cm^{-1}. R_f = 0.9 (5:1 hexanes:ethyl acetate).

(*E*)-1′-[3-(*tert*-Butyldimethylsiloxy)-2-propenyl]ferrocene 1-Methyl Ester (5). *n*-Butyllithium (1.42 M in hexanes, 20.3 mL, 28.8 mmol, 1.5 equiv) was added dropwise to a solution of **4** (12.4 g, 19.2 mmol, 1.0 equiv) in tetrahydrofuran (100 mL) cooled to −78 °C. The reaction mixture was allowed to warm to room temperature and then recooled to −78 °C. Methyl chloroformate (14.8 mL, 192 mmol, 10 equiv) was added, and the reaction mixture was warmed to room temperature and diluted with pentane (100 mL) and water (150 mL). The organic phase was washed with brine (150 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexanes, then 40:1 hexanes:ethyl acetate, and then 20:1 hexanes:ethyl acetate) provided 5.8 g of **5** (73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.16 (d, J = 15.7 Hz, 1H), 5.87 (dt, J = 15.7 Hz, 5.2 Hz, 1H), 4.71 (br, 2H), 4.30 (br, 4H), 4.19 (br, 4H), 3.76 (s, 3H), 0.91 (s, 9H), 0.08 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.38, 128.31, 125.02, 84.84, 72.20, 72.20, 72.09, 70.90, 70.90, 70.06, 70.06, 67.98, 67.98, 63.91, 51.42, 25.96, 18.41, −5.14. IR (thin film): 1717.0 cm^{-1}. R_f = 0.4 (10:1 hexanes:ethyl acetate). Anal. Calcd for $C_{21}H_{30}FeO_3Si$: C, 60.87; H, 7.3. Found: C, 60.83; H, 7.29.

(*E*)-1′-[3-(*tert*-Butyldimethylsiloxy)-2-propenyl]ferrocene-1-carboxylic Acid (6). Methyl ester **5** (0.050 g, 0.121 mmol, 1.0 equiv) was dissolved in 10:1 *tert*-butyl alcohol:H_2O

(19) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(1 mL). Concentrated NaOH (50% by wt, 0.158 g, 1.98 mmol, 16.4 equiv) and $NaBH_4$ (0.011 g, 0.30 mmol, 2.5 equiv) were added, and the reaction mixture was heated to reflux for 5 h. The reaction mixture was then cooled to room temperature and diluted with pentane (10 mL), and the reaction was quenched with water (5 mL). The aqueous phase was isolated, then neutralized with 3 M HCl (10 mL), and extracted with dichloromethane (3 × 15 mL). The combined organic extracts were washed with brine (50 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexanes and then 5:1 hexanes:ethyl acetate) provided 0.042 g of **6** (87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.71 (br, 1H), 6.16 (d, J = 15.7 Hz, 1H), 5.90 (dt, J = 15.7 Hz, 5.6 Hz, 1H), 4.78 (br, 2H), 4.37 (br, 4H), 4.24 (br, 2H), 4.19 (d, J = 5.6 Hz, 2H), 0.92 (s, 9H), 0.09 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.26, 127.83, 125.88, 84.06, 72.68, 72.68, 71.40, 70.41, 70.41, 68.24, 68.24, 64.27, 64.27, 64.27, 25.99, 18.47, −5.16. IR (thin film): 2928.6 (br) cm^{-1}. R_f = 0.6 (1:1 hexanes:ethyl acetate). Anal. Calcd for $C_{20}H_{28}FeO_3Si$: C, 60.0; H, 7.05. Found: C, 60.54; H, 7.03.

(*E*)-1′-[3-(*tert*-Butyldimethylsiloxy)-2-propenyl]ferrocene-1-Pentafluorophenyl Ester (7). To a solution of **6** (0.95 g, 2.37 mmol, 1.0 equiv) in THF (5 mL) at room temperature was added a solution of pentafluorophenol (0.655 g, 3.56 mmol, 1.5 equiv) in THF (5 mL) followed by a solution of dicyclohexylcarbodiimide (0.539 g, 2.61 mmol, 1.1 equiv) in THF (5 mL). The reaction mixture was allowed to stir for 0.5 h, and the solution was then concentrated. The residue was dissolved in hexanes (5 mL), and the dicyclohexylurea that precipitated was filtered. The filtrate was washed with 1 M NaOH (5 mL), water (5 mL), and brine (5 mL), dried over $MgSO_4$, and concentrated under reduced pressure to provide 1.32 g of **7** (98%) which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.25 (d, J = 15.7 Hz, 1H), 5.94 (dt, J = 15.7 Hz, 5.1 Hz, 1H), 4.85 (br, 2H), 4.50 (br, 2H), 4.42 (br, 2H), 4.34 (br, 2H), 4.17 (dd, J = 5.1 Hz, 1.7 Hz, 2H), 0.91 (s, 9H), 0.08 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.73, 143 (m), 140 (m), 139 (m), 137 (m), 128.99, 124.90, 85.62, 74.07, 71.94, 70.98, 68.68, 67.42, 63.79, 25.92, 18.40, −5.18. IR (thin film): 1756.2 cm^{-1}. R_f = 0.7 (5:1 hexanes:ethyl acetate).

(*E*)-(*S*)-*N*-[1-(Hydroxymethyl)-2-hydroxy-2-methylpropyl]-1′-[3-(*tert*-butyldimethylsiloxy)-2-propenyl]ferrocene-1-carboxamide (8). Triethylamine (443 μL, 3.2 mmol, 4.0 equiv) was added via syringe to a solution of **7** (0.450 g, 0.794 mmol, 1.0 equiv) and (*S*)-2-amino-3-methyl-1,3-butanediol[10] (0.347 g, 2.9 mmol, 3.7 equiv) in dimethylformamide (4 mL) at room temperature. The reaction mixture was warmed to 85° C over a period of 50 min and then cooled to room temperature and concentrated at reduced pressure. Purification by flash chromatography (hexanes and then 2:1 hexanes: ethyl acetate) provided 0.370 g of **8** (93%). 1H NMR (400 MHz, $CDCl_3$): δ 6.62 (d, J = 7.7 Hz, 1H), 6.25 (d, J = 15.8 Hz, 1H), 5.87 (dt, J = 15.8 Hz, 5.3 Hz, 1H), 4.66 (br, 1H), 4.54 (br, 1H), 4.32 (br, 1H), 4.30 (br, 2H), 4.27 (br, 2H), 4.21 (br, 1H), 4.19 (d, J = 5.3 Hz, 2H), 4.03 (m, 1H), 3.84 (m, 2H), 3.65 (br, 1H), 3.54 (br, 1H), 1.36 (s, 3H), 1.24 (s, 3H), 0.91 (s, 9H), 0.10 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.61, 127.85, 126.06, 84.58, 73.13, 73.13, 71.56, 71.39, 70.33, 70.01, 69.42, 69.28, 68.74, 67.86, 64.19, 63.32, 56.86, 27.72, 27.31, 25.98, 18.53, −5.12, −5.15. IR (thin film): 3382.0, 1634.0, 1538.2 cm^{-1}. $[\alpha]^{24}_D$ = 2.0° (*c* 0.0069 g/mL, ethanol). R_f = 0.1 (5:1 hexanes: ethyl acetate).

(*E*)-(*S*)-2-[1′-[3-(*tert*-Butyldimethylsiloxy)-1-propenyl]-ferrocenyl]-4,5-dihydro-4-(1-hydroxy-1-methylethyl)oxazole (9). *p*-Toluenesulfonyl chloride (0.165 g, 0.87 mmol, 1.3 equiv), a catalytic amount of 4-(dimethylamino)pyridine (0.8 mg, 6.7 μmol, 1%), and **8** (0.334 g, 0.67 mmol, 1.0 equiv) were dissolved in dichloromethane (3.3 mL) at room temperature. Triethylamine (0.28 mL, 2.0 mmol, 3 equiv) was then added, and the reaction mixture was allowed to stir for 12 h. The reaction mixture was diluted with ether (10 mL), and the reaction was quenched with a saturated aqueous solution of sodium bicarbonate (10 mL). The organic phase was washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated at reduced pressure. Purification by flash chromatography (hexanes and then 2:1 hexanes:ethyl acetate) provided 0.29 g of **9** (90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.20 (d, J = 6.2 Hz, 1H), 5.86 (dt, J = 15.7 Hz, 5.1 Hz, 1H), 4.67 (br, 1H), 4.65 (br, 1H), 4.32 (m, 3H), 4.26 (br, 2H), 4.19 (m, 5H), 4.05 (dd, J = 9.9 Hz, 8.1 Hz, 1H), 2.00 (br, 1H), 1.30 (s, 3H), 1.15 (s, 3H), 0.91 (s, 9H), 0.08 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.14, 127.87, 125.46, 84.78, 75.61, 71.51, 71.45, 71.25, 70.79, 70.04, 70.04, 70.04, 69.81, 68.34, 67.99, 67.91, 64.02, 26.96, 25.98, 24.92, 18.44, −5.11. IR (thin film): 3409.9 (br), 1651.6 cm^{-1}. $[\alpha]^{24}_D$ = 1.9° (*c* 0.01345 g/mL, ethanol). R_f = 0.4 (1:1 hexanes:ethyl acetate).

(*E*)-(*S*)-2-[1′-(3-Hydroxy-1-propenyl)ferrocenyl]-4,5-dihydro-4-(1-hydroxy-1-methylethyl)oxazole (10). Tetrabutylammonium fluoride hydrate (0.46 g, 1.75 mmol, 3 equiv) was added to a solution of **9** (0.282 g, 0.58 mmol, 1.0 equiv) in THF (1.2 mL) at room temperature. The reaction mixture was allowed to stir for 1 h and then was diluted with ether, and the reaction was quenched with a saturated aqueous solution of sodium bicarbonate. The organic phase was washed with brine, dried over $MgSO_4$, filtered, concentrated under reduced pressure, and purified by flash chromatography (hexanes and then 5:1 ethyl acetate:triethylamine) to provide 0.193 g of **10** (90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.22 (d, J = 15.7 Hz, 1H), 5.94 (dt, J = 15.7 Hz, 5.8 Hz, 1H), 4.64 (br, 1H), 4.63 (br, 1H), 4.27 (m, 5H), 4.19 (m, 3H), 4.06 (m, 3H), 3.58 (br, 1H), 2.59 (br, 1H), 1.29 (s, 3H), 1.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.43, 127.82, 126.92, 84.29, 75.42, 71.25, 71.16, 71.16, 70.81, 70.33, 70.25, 69.96, 69.87, 68.45, 68.20, 68.16, 63.33, 26.93, 25.03. IR (thin film): 3353.7 (br), 1643.9 cm^{-1}. $[\alpha]^{24}_D$ = −3.6° (*c* 0.0111 g/mL, ethanol). R_f = 0.1 (1:1 hexanes: ethyl acetate).

(*S*)-2-[1′-(3-Hydroxy-1-propenyl)ferrocenyl]-4,5-dihydro-4-(1-hydroxy-1-methylethyl)oxazole (11). A mixture of **10** (0.082 g, 0.217 mmol, 1.0 equiv) and Pd / C (10% Pd, 0.5 g) in ethyl acetate (2 mL) was allowed to stir for 1.5 h under an atmosphere of H_2 (balloon pressure) and was then filtered through Celite and concentrated. The crude product was purified by flash chromatography (hexanes and then 1:1 ethyl acetate:triethylamine) to provide 0.075 g of **11** (93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.65 (br, 2H), 4.32 (dd, J = 10.1 Hz, 8.5 Hz, 1H), 4.28 (br, 2H), 4.21 (t, J = 8.5 Hz, 1H), 4.06 (m, 5H), 3.63 (t, J = 6.2 Hz, 2H), 2.66 (br, 1H), 2.36 (dd, J = 8.0 Hz, 7.5 Hz, 2H), 1.74 (m, 2H), 1.31 (s, 3H), 1.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.80, 90.03, 75.55, 71.19, 70.87, 70.82, 70.26, 69.71, 69.71, 69.57, 68.77, 68.72, 68.38, 62.15, 33.68, 27.02, 25.07, 24.80. IR (thin film): 3355.7 (br), 1646.0 cm^{-1}. $[\alpha]^{24}_D$ = 53.1° (*c* 0.01185 g/mL, ethanol). R_f = 0.1 (1:1 hexanes: ethyl acetate). Anal. Calcd for $C_{19}H_{25}FeNO_3$: C, 61.47; H, 6.79; N, 3.77. Found: C, 61.25; H, 7.03; N, 3.90.

(*S*)-2-[1′-[4-(*p*-Tolylsulfonyl)-4-oxabutyl]ferrocenyl]-4,5-dihydro-4-(1-hydroxy-1-methylethyl)oxazole (12). Compound **11** (0.075 g, 0.202 mmol, 1.0 equiv), *p*-toluenesulfonyl chloride (0.042 g, 0.222 mmol, 1.1 equiv), and a catalytic amount of 4-(dimethylamino)pyridine were dissolved in dichloromethane (2.0 mL) at room temperature. Triethylamine (84.5 μL, 0.606 mmol, 3 equiv) was added, and the reaction mixture was allowed to stir 5 h. At this time the reaction mixture was diluted with pentane (5 mL), ethyl acetate (5 mL), and water (10 mL). The organic phase was washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated at reduced pressure. The crude product was purified by flash chromatography (hexanes and then ethyl acetate) to provide 0.087 g of **12** (82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.2 Hz, 2H), 4.63 (br, 1H), 4.62 (br, 1H), 4.31 (A of ABX, J = 10.0 Hz, 8.5 Hz, 1H), 4.24 (br, 2H), 4.20 (X of ABX, J = 8.5 Hz, 1H), 4.06 (B of ABX, J = 10.0 Hz, 8.5 Hz, 1H), 4.03 (br, 2H), 3.98 (m, 4H), 2.42 (s, 3H), 2.31 (m, 2H), 1.77 (m, 2H), 1.30 (s, 3H), 1.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.23, 144.72, 132.99, 129.81, 127.84, 88.42, 75.54, 71.20, 70.85, 70.81, 70.47, 69.86, 69.61, 69.56, 69.53, 69.53, 68.98, 68.96, 68.32, 30.20, 26.88, 25.04, 24.50, 21.59. IR (thin film): 3380.6, 1651.4, 1358.8, 1175.9 cm^{-1}. $[\alpha]^{24}_D$ = 25.0° (*c* 0.00525 g/mL, ethanol). R_f = 0.4 (ethyl acetate). Anal. Calcd for $C_{26}H_{31}FeNO_5S$: C, 59.43; H, 5.95; N, 2.67. Found: C, 59.71; H, 6.01; N, 2.67.

(*S*)-1-[2-(4,5-Dihydro-4,1′-(1,1-dimethyl-2-oxa-1,5-pentanediyl)oxazolyl)][8]ferrocenophane (13). Dry sodium

hydride powder (6.8 mg, 0.284 mmol, 1.5 equiv), 18-cr-6 (75.1 mg, 0.284 mmol, 1.5 equiv), and **12** (99.5 mg, 0.189 mmol, 1.0 equiv) were dissolved in DMSO (1.9 mL), and the reaction mixture was allowed to stir at room temperature for 24 h. The reaction mixture was then diluted with ethyl acetate (10 mL) and washed with brine (10 mL). The aqueous phase was washed with ethyl acetate (2 × 10 mL), and then the combined organic phases were washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexanes and then 15:1 hexanes:ethyl acetate) provided 20 mg of **13** (30%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.79 (br, 1H), 4.60 (X of ABX, J = 7.8 Hz, 1H), 4.60 (br, 1H), 4.30 (br, 1H), 4.28 (br, 1H), 4.26 (A of ABX, J = 10.3 Hz, 7.8 Hz, 1H), 4.20 (br, 1H), 4.14 (br, 1H), 4.03 (br, 1H), 3.99 (br, 2H), 3.97 (B of ABX, J = 10.3 Hz, 7.8 Hz, 1H), 3.85 (m, 2H), 3.54 (m, 2H), 2.56 (m, 2H), 2.13 (m, 2H), 1.82 (m, 2H), 1.63 (m, 2H), 1.52 (s, 3H), 1.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.40, 91.61, 76.38, 74.31, 72.40, 69.92, 69.46, 69.17, 68.82, 68.61, 67.79, 67.76, 66.82, 66.71, 63.61, 28.64, 28.37, 22.54, 22.19. IR (thin film): 1656.1 cm^{-1}. $[\alpha]^{24}_D$ = 526.9° (*c* 0.0089 g/mL, ethanol). R_f = 0.7 (ethyl acetate). Anal. Calcd for $C_{19}H_{23}FeNO_2$: C, 64.6; H, 6.56; N, 3.97. Found: C, 64.41; H, 6.49; N, 4.05.

(*S,S*)-1-[2-(4,5-Dihydro-4,1′-(1,1-dimethyl-2-oxa-1,5-pentanediyl)oxazolyl)]-2-methyl[8]ferrocenophane (14).[20] *sec*-Butyllithium (40.0 μL, 46.4 μmol, 2.0 equiv) was added to a solution of **13** (8.2 mg, 23.2 μmol, 1.0 equiv) in tetrahydrofuran (0.5 mL) cooled to −78 °C. The reaction was allowed to proceed for 2 h at −78 °C, at which time the reaction mixture was warmed to 0 °C and allowed to stir for 5 min, and then the reaction was quenched with MeI (5 μL, 80.3 μmol, 3.5 equiv). The resulting reaction mixture was allowed to warm to room temperature and then diluted with ether (5 mL), and the reaction was quenched with a saturated aqueous solution of sodium bicarbonate (10 mL). The organic phase was washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give an orange solid which was purified by flash chromatography (hexanes and then 15:1 hexanes:ethyl acetate) to provide 6.0 mg of **14** (70%). Recrystallization by the slow evaporation of a 10:1 hexanes:ethyl acetate solution provided crystals suitable for X-ray diffraction. Mp = 116−120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.55 (X of ABX, J = 7.6 Hz, 1H), 4.55 (br, 1H), 4.23 (br, 1H), 4.17 (A of ABX, J = 10.4 Hz, 7.6 Hz, 1H), 4.12 (br, 1H), 4.11 (br, 1H), 4.08 (br, 1H), 4.02 (B of ABX, J = 10.4 Hz, 7.6 Hz, 1H), 3.95 (br, 1H), 3.86 (m, 1H), 3.73 (br, 1H), 3.54 (m, 1H), 2.61 (m, 1H), 2.33 (s, 3H), 2.15 (m, 1H), 1.79 (m, 1H), 1.65 (m, 1H), 1.54 (s, 3H), 1.10 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.53, 92.07, 85.20, 76.68, 74.34, 71.95, 70.69, 70.34, 69.33, 68.01, 67.15, 66.93, 66.81, 66.45, 63.40, 28.77, 28.36, 22.45, 21.98, 14.76. R_f = 0.9 (ethyl acetate). FAB calcd for $C_{20}H_{25}FeNO_2$ (M^+) 367, found 367.

(*S,R*)-1-[2-(4,5-Dihydro-4,1′-(1,1-dimethyl-2-oxa-1,5-pentanediyl)oxazolyl)]-2-(trimethylsilyl)[8])ferrocenophane (15). This material was prepared from **13** (0.0191 g, 0.054 mmol) following the same procedure as for **14**. The red oil obtained was purified by flash chromatography (hexanes and then 20:1 hexanes:ethyl acetate) to provide 0.0188 g of **15** (82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.81 (br, 1H), 4.48 (t, J = 7.9 Hz, 1H), 4.38 (br, 1H), 4.26 (br, 1H), 4.18 (br, 1H), 4.15 (m, 2H), 3.94 (m, 4H), 3.54 (m, 1H), 2.55 (m, 1H), 2.15 (m, 1H), 1.67 (m, 2H), 1.55 (s, 3H), 1.08 (s, 3H), 0.33 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.95, 91.78, 77.51, 77.39, 76.07, 74.04, 73.64, 73.25, 70.94, 68.96, 68.25, 66.86, 66.71, 66.48, 63.63, 28.98, 28.17, 22.88, 22.12, 0.59. IR (thin film): 1654.6 cm^{-1}. $[\alpha]^{24}_D$ = 257.0° (*c* 0.00875 g/mL, ethanol). R_f = 0.9 (ethyl acetate).

(*S*)-*N*-(Carbobenzyloxy)-L-serine Methyl Ester (16). A saturated solution of sodium bicarbonate adjusted to pH 9 by the addition of solid sodium carbonate (65 mL) was added to a solution of L-serine methyl ester hydrochloride (8.0 g, 51.4 mmol, 1.0 equiv) in THF (130 mL). Benzyl chloroformate (7.7 mL, 54.0 mmol, 1.05 equiv) was added, and the reaction mixture was allowed to stir for 22 h. The aqueous phase was then extracted with dichloromethane (2 × 200 mL), and the combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by Kugelrohr distillation (170 °C at 0.01 mmHg) to provide 10.7 g of **16** (82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (m, 5H), 5.69 (d, J = 6.3 Hz, 1H), 5.11 (s, 2H), 4.44 (m, X of ABX, 1H), 3.99 (A of ABX, J = 11.1 Hz, 3.2 Hz, 1H), 3.91 (B of ABX, J = 11.1 Hz, 2.8 Hz, 1H), 3.77 (s, 3H), 2.18 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.98, 156.20, 135.99, 128.52, 128.23, 128.10, 67.19, 63.21, 55.99, 52.73. IR (thin film): 3398.3 (br), 1718.4, 1522.3 cm^{-1}. $[\alpha]^{24}_D$ = −13.2° (*c* 0.00605 g/mL, ethanol). R_f = 0.7 (ethyl acetate).

(*S*)-*N*-(Carbobenzyloxy)-2-amino-3-methyl-1,3-butanediol (17). A solution of **16** (8.0 g, 31.6 mmol, 1.0 equiv) in THF (60 mL) was cooled to −78 °C, and methyllithium (1.4 M in ether, 113.0 mL, 157.9 mmol, 5.0 equiv) was added via cannula. The reaction mixture was allowed to warm to room temperature and was then diluted with ether (60 mL), and the reaction was quenched with water (100 mL). The organic phase was washed with brine (100 mL), dried over $MgSO_4$, filtered, concentrated under reduced pressure, and purified by Kugelrohr distillation (155−175 °C at 0.01 mmHg) to provide 3.5 g of **17** (44%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 5H), 5.71 (d, J = 8.6 hz, 1H), 5.09 (s, 2H), 4.00 (A of ABX, J = 11.4 Hz, 3.1 Hz, 1H), 3.79 (B of ABX, J = 11.4 Hz, 2.9 Hz, 1H), 3.50 (X of ABX, J = 8.6 Hz, 3.1 Hz, 2.9 Hz, 1H), 2.74 (br, 2H), 1.32 (s, 3H), 1.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.76, 136.32, 128.52, 128.14, 128.02, 73.62, 66.89, 63.30, 58.12, 27.50, 27.42. IR (thin film): 3397.9 (br), 1701.5 cm^{-1}. $[\alpha]^{24}_D$ = 24.9° (*c* 0.0191 g/mL, ethanol). R_f = 0.5 (ethyl acetate).

(*S*)-2-Amino-3-methyl-1,3-butanediol (18). A mixture of **17** (3.35 g, 13.2 mmol, 1.0 equiv) and Pd/C (10%, 1.5 g) in ethyl acetate (12 mL) was allowed to stir for 12 h under 1.2 atm of H_2 and then filtered through Celite. The solids were washed with methanol, and the filtrate was concentrated. The crude product was purified by Kugelrohr distillation (100−120 °C at 0.01 mmHg) to provide 0.275 g of **18** (17%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.74 (A of ABX, J = 10.7 Hz, 3.7 Hz, 1H), 3.55 (B of ABX, J = 10.7 Hz, 7.6 Hz, 1H), 2.68 (X of ABX, J = 7.6 Hz, 3.7 Hz, 1H), 2.12 (br, 4H), 1.21 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 71.77, 63.30, 59.99, 27.12, 25.64. IR (thin film): 3354.2 (br) cm^{-1}. $[\alpha]^{24}_D$ = −14° (*c* 0.0019 g/mL, ethanol). R_f = 0.1 (ethyl acetate).

2-Ferrocenyl-4,5-dihydro-4-isopropyloxazole (19). *p*-Toluenesulfonyl chloride (0.82 g, 4.29 mmol, 1.3 equiv), a catalytic amount of 4-(dimethylamino)pyridine (0.004 g, 0.03 mmol, 1%), and (2*S*)-*N*-(1-hydroxy-3-methylbutyl)ferrocenamide[4b] (1.0 g, 3.3 mmol, 1.0 equiv) were dissolved in dichloromethane (16 mL) at room temperature. Triethylamine (1.38 mL, 9.9 mmol, 3 equiv) was added, and the reaction mixture was allowed to stir overnight. The reaction mixture was diluted with ether (15 mL), and the reaction was quenched with a saturated aqueous solution of sodium bicarbonate (15 mL). The organic phase was washed with brine (15 mL), dried over $MgSO_4$, filtered, and concentrated at reduced pressure, producing a red solid which was purified by flash chromatography (hexanes and then 10:1 hexanes:ethyl acetate) to provide 0.75 g of **19** (80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.73 (br, 1H), 4.70 (br, 1H), 4.29 (br 2H), 4.25 (A of ABX, J_{AX} = 10 Hz, J_{AB} = 8 Hz, 1H), 4.16 (s, 5H), 4.03 (B of ABX, J_{BX} = 8 Hz, 1H), 3.95 (X of ABX, 1H), 1.82 (m, 1H), 0.97 (d, J = 7 Hz, 3H), 0.90 (d, J = 7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.56, 72.25, 70.57, 70.10, 70.06, 69.51, 69.25, 68.94, 68.90, 32.26, 18.92, 17.75. IR (thin film): 1659.1 cm^{-1}. R_f = 0.7 (ethyl acetate). Anal. Calcd for $C_{16}H_{19}FeNO$: C, 64.67; H, 6.44; N, 4.71. Found: C, 64.72; H, 6.27; N, 4.53.

(20) In the stereochemical designation (*R, S*), the first descriptor (in this example, "*R*") refers to the stereochemistry of the oxazoline substituent while the second descriptor (in this example, "*S*") refers to the stereochemistry of the disubstituted ferrocene. See: Marquarding, D.; Klusacek, H.; Gokel, G.; Hoffmann, P.; Ugi, I. *J. Am. Chem. Soc.* **1970**, *92*, 5389. The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

(*S,S*)-2-(2-Trimethylsilyl)ferrocenyl)-4,5-dihydro-4-isopropyloxazole (19A). General Procedure. The alkyllithium reagent (1.2 equiv) was added to a solution of **19** (0.1−0.2 g, 0.35−0.7 mmol, 1.0 equiv) in tetrahydrofuran (2−5 mL) cooled to −78 °C. The reaction was allowed to proceed for 2 h at −78 °C, at which time the reaction mixture was warmed to 0 °C and allowed to stir for 5 min, and the reaction was then quenched with TMSCl (distilled over CaH_2 under an atmosphere of N_2, 1.3 equiv). The resulting reaction mixture was allowed to warm to room temperature and was then diluted with ether (5 mL), and the reaction was quenched with a saturated aqueous solution of sodium bicarbonate (10 mL). The organic phase was washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a viscous red oil which was purified by flash chromatography (hexanes and then 15:1 hexanes:ethyl acetate) to provide a 3:1−16:1 mixture of diastereomers (85−95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.88 (br, 1H), 4.41 (br, 1H), 4.25 (br, 1H), 4.25 (A of ABX, $J_{AX} = 9$ Hz, $J_{AB} = 8$ Hz, 1H), 4.16 (s, 5H), 3.98 (B of ABX, $J_{BX} = 8$ Hz, 1H), 3.92 (X of ABX, 1H), 1.73−1.85 (m, 1H), 1.01 (d, $J = 7$ Hz, 3H), 0.91 (d, $J = 7$ Hz, 3H), 0.31 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.63, 76.90, 75.35, 73.12, 72.89, 72.83, 71.46, 69.39, 69.27, 32.52, 19.08, 18.02, 0.47. IR (thin film): 1651.5 cm^{-1}. $R_f = 0.5$ (5:1 hexanes:ethyl acetate). Anal. Calcd for $C_{19}H_{27}FeNOSi$: C, 61.78; H, 7.37; N, 3.79. Found: C, 62.04; H, 7.37; N, 3.72.

(*S*)-2-Ferrocenyl-4,5-dihydro-4-*tert*-butyloxazole (20). *p*-Toluenesulfonyl chloride (0.55 g, 2.87 mmol, 1.3 equiv), a catalytic amount of 4-(dimethylamino)pyridine (0.003 g, 0.02 mmol, 1%), and (2*S*)-*N*-(1-hydroxy-3,3-dimethylbutyl)ferrocenamide[4b] (0.70 g, 2.21 mmol, 1.0 equiv) were dissolved in dichloromethane (11 mL) at room temperature. Triethylamine (0.92 mL, 6.62 mmol, 3 equiv) was added, and the reaction mixture was allowed to stir overnight. The reaction mixture was diluted with ether (10 mL), and the reaction was quenched with a saturated aqueous solution of sodium bicarbonate (15 mL). The organic phase was washed with brine (15 mL), dried over $MgSO_4$, filtered, and concentrated at reduced pressure, producing a red solid which was purified by flash chromatography (hexanes and then 10:1 hexanes:ethyl acetate) to provide 0.63 g of **20** (96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.74 (br, 1H), 4.67 (br, 1H), 4.27 (br, 2H), 4.19 (X of ABX, 1H), 4.15 (s, 5H), 4.10 (A of ABX, $J_{AX} = 9$ Hz, $J_{AB} = 8$ Hz, 1H), 3.85 (B of ABX, $J_{BX} = 10$ Hz, 1H), 0.92 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.30, 75.96, 70.71, 69.95, 69.89, 69.35, 68.86, 68.81, 68.13, 33.46, 25.85. IR (thin film): 1663.8 cm^{-1}. $[\alpha]^{24}_D = -150°$ (*c* 0.021 g/mL, CH_2Cl_2). $R_f = 0.8$ (ethyl acetate). Anal. Calcd for $C_{17}H_{21}FeNO$: C, 65.61; H, 6.8; N, 4.5. Found: C, 65.49; H, 6.81; N, 4.38.

(*S,S*)-2-(2-(Trimethylsilyl)ferrocenyl)-4,5-dihydro-4-*tert*-butyloxazole (20A). General Procedure. The alkyllithium reagent (1.2 equiv) was added to a solution of **20** (0.1−0.25 g, 0.34−0.84 mmol, 1.0 equiv) in tetrahydrofuran (2−5 mL) cooled to −78 °C. The reaction was allowed to proceed for 2 h at −78 °C, at which time the reaction mixture was warmed to 0 °C and allowed to stir for 5 min, and then the reaction was quenched with TMSCl (distilled over CaH_2 under an atmosphere of N_2, 1.3 equiv). The resulting reaction mixture was allowed to warm to room temperature and was then diluted with ether (5 mL), and the reaction was quenched with a saturated aqueous solution of sodium bicarbonate (10 mL). The organic phase was washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a viscous red oil which was purified by flash chromatography (hexanes and then 15:1 hexanes:ethyl acetate) to provide a 6:1−36:1 mixture of diastereomers (80−90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.87 (br, 1H), 4.41 (br, 1H), 4.25 (br, 1H), 4.18 (A of ABX, $J_{AX} = 8$ Hz, $J_{AB} = 10$ Hz, 1H), 4.16 (s, 5H), 4.07 (X of ABX, 1H), 3.86 (B of ABX, $J_{BX} = 8$ Hz, 1H), 0.94 (s, 9H), 0.31 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.54, 77.15, 76.68, 75.23, 73.21, 73.04, 71.40, 69.38, 67.82, 33.59, 26.00, 0.53. IR (thin film): 1658.1 cm^{-1}. $R_f = 0.6$ (5:1 hexanes:ethyl acetate). Anal. Calcd for $C_{20}H_{29}FeNOSi$: C, 62.66; H, 7.62; N, 3.65. Found: C, 62.91; H, 7.64; N, 3.62.

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Supporting Information Available: Selected ^{1}H and ^{13}C NMR spectra (9 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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