Bromide-Mediated *ortho*-Deprotonation in the Synthesis of Chiral, Nonracemic Ferrocene Derivatives

Marianne Steurer,[†] Yaping Wang,[†] Kurt Mereiter,[‡] and Walter Weissensteiner*,[†]

Faculty of Chemistry, University of Vienna, Währinger Strasse 38, A-1090 Vienna, Austria, and Faculty of Chemistry, Vienna University of Technology, Getreidemarkt 9/162SC, A-1060 Vienna, Austria

Received April 4, 2007

Bromide-mediated methods for the synthesis of 1,2,3- and 1,3-substituted ferrocenes are described. Starting from monosubstituted ferrocene derivatives {Fc-R^1, R^1 = 1-dimethylaminoethyl [$CH(NMe_2)$-Me], *p*-tolylsulfinyl [4-$MeC_6H_4S(O)$], (2-methoxymethylpyrrolidin-1-yl)methyl [2-$MeOCH_2(C_4H_7N)CH_2$], ephedrine derivative $CH_2N(Me)CH(Me)CH(Ph)OMe$, and dimethylaminomethyl [$CH_2(NMe_2)$]} achiral, racemic and chiral, nonracemic 1,2,3-trisubstituted ferrocene derivatives are accessible through two consecutive *ortho*-lithiations. In the first deprotonation step bromide is introduced stereoselectively into position 2. In the second step, the use of Li-TMP (TMP = 2,2,6,6-tetramethylpiperidine) as the base leads to deprotonation of the *ortho*-position next to bromide, and subsequent reaction with different electrophiles gives a variety of 1,2,3-trisubstituted ferrocene derivatives. Removal of the central bromide substituent leads to 1,3-disubstituted derivatives, including pincer-type ferrocene ligands.

Introduction

At present, enantiopure ferrocene derivatives are mainly used as ligands for homogeneous enantioselective catalysts,[1] but these compounds have also found applications in a number of other fields including polymer chemistry,[2] liquid crystal chemistry,[3] electrochemistry,[4] and bioorganometallic chemistry.[5] Most of the ferrocene-based catalyst ligands in use are 1,2-disubstituted derivatives. In addition, several higher substituted ferrocenes such as 1,1′,2-tri-, 1,2,3-tri-, or 1,1′,2,2′-tetrasubstituted derivatives have been found to give excellent performance as catalyst ligands in asymmetrically catalyzed reactions. Almost all ligands with these substitution patterns have been prepared using routes involving either one or two enantio- or diastereoselective lithiations of appropriate mono- or 1,1′-disubstituted precursors.[6,7] For example, most enantiopure 1,2-di- and 1,2,3-trisubstituted ferrocenes have been prepared starting from a monosubstituted derivative Fc-R^c, where R^c is a stereogenic directing group (Scheme 1, route 1). After a diastereoselective *ortho*-lithiation and reaction with an electrophile, 1,2-disubstituted derivatives are obtained. A number of such directing groups can also promote a second *ortho*-lithiation, and this provides access to 1,2,3-trisubstituted derivatives. In many cases, a further step can be carried out in which the stereogenic directing group R^c is replaced by a third substituent R^3.

Interestingly, applications of chiral, nonracemic 1,3-disubstituted ferrocenes are very rare, a situation that might be due to the fact that until very recently suitable methods for the synthesis of both achiral and chiral 1,3-disubstituted derivatives were severely lacking.[2c,3,5d] However, in 2002 Koridze[8]—as well as Brown, van Koten, and co-workers[9]—extended the concept of aryl-based pincer ligands to the ferrocene backbone[10] and a search for short and facile routes to chiral, nonracemic 1,3-disubstituted ferrocenes was initiated. Originally, highly enantiomerically enriched 1,3-disubstituted ferrocenes were obtained

* Corresponding author. E-mail: walter.weissensteiner@univie.ac.at.
[†] University of Vienna.
[‡] Vienna University of Technology.

(1) (a) Gomez Arrayás, R.; Adrio, J.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2006**, *45*, 7674−7715. (b) Barbaro, P.; Bianchini, C.; Giambastiani, G.; Parisel, S. L. *Coord. Chem. Rev.* **2004**, *248*, 2131−2150. (c) Colacot, T. J. *Chem. Rev.* **2003**, *103*, 3101−3118. (d) Dai, L.-X.; Tu, T.; You, S.-L.; Deng, W.-P.; Hou, X.-L. *Acc. Chem. Res*. **2003**, *36*, 659−667. (e) *Catalytic Asymmetric Synthesis*; Ojima, I., Ed., Wiley-VCH: New York, 2000.

(2) (a) Abd-El-Aziz, A. S.; Shipman, P. O. In *Frontiers in Transition Metal-Containing Polymers*; Abd-El-Aziz, A. S., Manners, I., Eds.; Wiley: New York, 2007; pp 45−133. (b) Hida, N.; Takei, F.; Onitsuka, K.; Shiga, K.; Asaoka, S.; Iyoda, T.; Takahashi, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 4349−4352. (c) Plenio, H.; Hermann, J.; Sehring, A. *Chem.−Eur. J.* **2000**, *6*, 1820−1829. Dendrimers: (d) Mery, D.; Astruc, D. *Coord. Chem. Rev.* **2006**, *250*, 1965−1979. (e) Routaboul, L.; Vincendeau, S.; Turrin, C.-O.; Caminade, A.-M.; Majoral, J.-P.; Daran, J.-C.; Manoury, E. *J. Organomet. Chem*. **2007**, *692*, 1064−1073. (f) Kollner, C.; Togni, A. *Can. J. Chem*. **2001**, *79*, 1762−1774.

(3) Brettar, J.; Bürgi, T.; Donnio, B.; Guillon, D.; Klappert, R.; Scharf, T.; Deschenaux, R. *Adv. Funct. Mater*. **2006**, *16*, 260−267.

(4) (a) Lopez, J. L.; Tárraga, A.; Espinosa, A.; Velasco, M. D.; Molina, P.; Lloveras, V.; Vidal-Gancedo, J.; Rovira, C.; Veciana, J.; Evans, D. J.; Wurst, K. *Chem.−Eur. J.* **2004**, *10*, 1815−1826. (b) Sutcliffe, O. B.; Bryce, M. R.; Batsanov, A. S. *J. Organomet. Chem*. **2002**, *656*, 211−216. (c) Takeuchi, M.; Mizuno, T.; Shinkai, S.; Shirakami, S.; Itoh, T. *Tetrahedron: Asymmetry* **2000**, *11*, 3311−3322.

(5) (a) van Staveren, D. R.; Metzler-Nolte, N. *Chem. Rev.* **2004**, *104*, 5931−5985. (b) James, P.; Neudörfl, J.; Eissmann, M.; Jesse, P.; Prokop, A.; Schmalz, H.-G. *Org. Lett.* **2006**, *8*, 2763−2766. (c) Chowdhury, S.; Schatte, G.; Kraatz, H.-B. *Angew. Chem., Int. Ed. Engl*. **2006**, *45*, 6882−6884. (d) Ferber, B.; Top, S.; Vessieres, A.; Welter, R.; Jaouen, G. *Organometallics* **2006**, *25*, 5730−5739.

(6) (a) Atkinson, R. C. J.; Gibson, V. C.; Long, N. J. *Chem. Soc. Rev.* **2004**, *33*, 313−328. (b) *Ferrocenes: Homogeneous Catalysis, Organic Synthesis, Materials Science*; Togni, A., Hayashi, T., Eds.; VCH: Weinheim, 1995.

(7) Clayden, J. In *Chemistry of Organolithium Compounds*; Rappoport, Z., Marek, I., Eds.; Wiley: Chichester, 2004; pp 495−646.

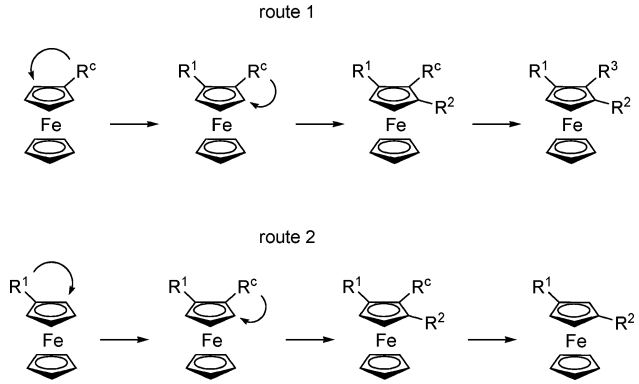
(8) Koridze, A. A.; Sheloumov, A. M.; Kuklin, S. A.; Lagunova, V. Y.; Petukhova, I. I.; Dolgushin, F. M.; Ezernitskaya, M. G.; Petrovskii, P. V.; Macharashvili, A. A.; Chedia, R. V. *Russ. Chem. Bull.* **2002**, *51*, 1077−1078.

(9) Farrington, E. J.; Martinez Viviente, E.; Williams, B. S.; van Koten, G.; Brown, J. M. *Chem. Commun.* **2002**, 308−309.

(10) For achiral ferrocene-based pincer ligands see also: (a) Kuklin, S. A.; Sheloumov, A. M.; Dolgushin, F. M.; Ezernitskaya, M. G.; Peregudov, A. S.; Petrovskii, P. V.; Koridze, A. A. *Organometallics* **2006**, *5*, 5466−5476. (b) Koridze, A. A.; Kuklin, S. A.; Sheloumov, A. M.; Dolgushin, F. D.; Lagunova, V. Y.; Petukhova, I. I.; Ezernitskaya, M. G.; Peregudov, A. S.; Petrovskii, P. V.; Vorontsov, E. V.; Baya, M.; Poli, R. *Organometallics* **2004**, *23*, 4585−4593.

10.1021/om7003282 CCC: $37.00
Publication on Web 06/19/2007

Scheme 1. General Reaction Schemes for the Synthesis of 1,2-Di-, 1,2,3-Tri-, and 1,3-Disubstituted Ferrocenes



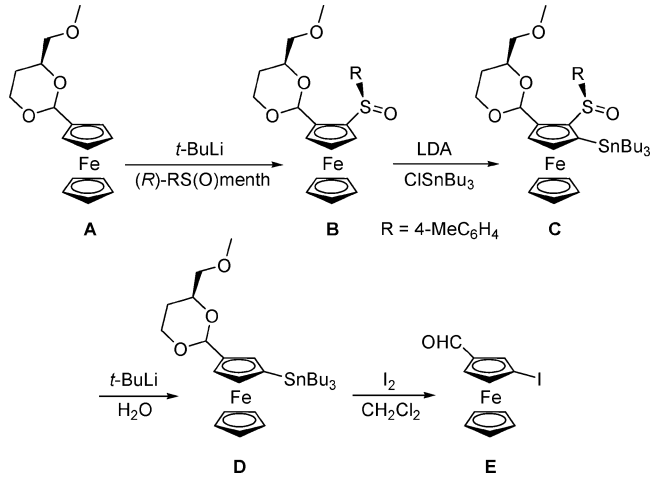
from racemates[11] by separating the enantiomers using different resolution methods.[12] However, the lack of both general methods for the synthesis of the racemates and efficient resolution methods meant that pure enantiomers were obtained only on a rather small scale.

In 2004, Brown and co-workers reported a broadly applicable method for the synthesis of achiral or racemic 1,3-disubstituted ferrocene derivatives, with the key step in this reaction sequence being a selective *meta*-lithiation of ferrocenyl-tolyl sulfide.[13] The use of this methodology enabled the synthesis of a variety of 1,3-disubstituted ferrocenes on a larger scale. However, attempts to run this and other reactions enantioselectively proved unsuccessful and, in addition, methods for separating the enantiomers of racemic mixtures are still available only to a very limited extent. As a result, we and others became interested in the development of general and preparatively useful methods for the diastereoselective synthesis of chiral, nonracemic 1,3-disubstituted ferrocenes.

As suggested several years ago by Kagan, the preparation of 1,2,3-trisubstituted precursors according to reaction route 1 (Scheme 1) and subsequent removal of the central substituent should lead to chiral, nonracemic 1,3-disubstituted ferrocenes.[14] However, this sequence requires a central substituent that can direct sequentially and diastereoselectively to both *ortho*-positions and can finally be replaced by a proton. Sulfinyl and, to a lesser extent, sulfonyl groups might be considered for this purpose. For a racemic derivative this sequence had already been carried out in 1974 by Slocum and co-workers, who used chloride as the central *ortho*-directing group R^c.[15]

Alternatively, a second reaction sequence (Scheme 1, route 2) seems to be suitable to build up chiral, nonracemic ferrocene derivatives diastereoselectively: starting from an appropriate monosubstituted ferrocene derivative (Fc-R^1), 1,2,3-trisubstituted

Scheme 2. Sulfoxide-Mediated Synthesis of 1,3-Disubstituted Ferrocenes (from ref 19)



intermediates are obtained in two steps, both of which involve *ortho*-deprotonation reactions. Subsequent removal of the central substituent (R^c) gives 1,3-disubstituted ferrocenes. In this case the central substituent R^c must be both *ortho*-directing *and* removable, although stereogenicity is not required. This allows for a broader range of possible candidates for R^c, including the halides (chloride and bromide) as well as sulfinyl and sulfonyl groups.

In preliminary studies we evaluated this reaction sequence by using chloride, bromide,[16] and the *p*-tolylsulfinyl group[17] as the central substituent R^c. In our opinion bromide was best suited for this purpose, since the removal of chloride from the ferrocene backbone (in comparison to bromide) requires much more vigorous reaction conditions, while the stereogenic *p*-tolylsulfinyl group must be introduced with the appropriate relative configuration to allow for the second *ortho*-deprotonation step. This can be achieved, for example, by diastereoselective oxidation of sulfides[12a,18] or, as reported very recently by Jaouen, Top, and co-workers, by transferring the *p*-tolylsulfinyl group with use of a chiral reagent (Scheme 2, step **A** → **B**).[19] The use of the latter approach gave 1,3-disubstituted ferrocene derivatives in good yields, but this methodology requires two stereogenic *ortho*-directing groups.

Our approach to chiral, nonracemic 1,3-disubstituted ferrocenes also follows reaction route 2 (Scheme 1) but with bromide as the central substituent. In a recent communication we reported that (i) bromide can be used in combination with a number of stereogenic *ortho*-directing groups R^1, (ii) *ortho*-deprotonation next to bromide can be achieved in high yield, and (iii) bromide can be easily exchanged by other electrophiles.[20] In addition, we realized that in several cases in the second *ortho*-lithiation step the original *ortho*-directing group R^1 competed with bromide, and deprotonation next to bromide as well as next to R^1 was observed. In such cases R^1 had to be transformed into a nondirecting substituent R′ (Scheme 3). We now describe in detail bromide-mediated synthesis routes to

(11) (a) Bonini, B. F.; Capitò, E.; Comes-Franchini, M.; Fochi, M.; Ricci, A. *ARKIVOC* **2006**, 85−96. (b) Lindsell, W. E.; Xinxin, L. *J. Chem. Res.* **1998**, (S) 62−63; (M) 423−433. (c) Bickert, P.; Hildebrandt, B.; Hafner, K. *Organometallics* **1984**, *3*, 653−657. (d) Leigh, T. *J. Chem. Soc.* **1964**, 3294−3302. (e) Rosenblum, M.; Woodward, R. B. *J. Am. Chem. Soc.* **1958**, *80*, 5443−5449.

(12) (a) D'Antona, N.; Lambusta, D.; Morrone, R.; Nicolosi G.; Secundo, F. *Tetrahedron: Asymmetry* **2004**, *15*, 3835−3840. (b) Chuard, T.; Cowling, S. J.; Fernandez-Ciurleo, M.; Jauslin, I.; Goodby, J. W.; Deschenaux, R. *Chem. Commun.* **2000**, *21*, 2109−2110. (c) Izumi, T.; Hino, T. *J. Chem. Technol. Biotechnol.* **1992**, *55*, 325−331. (d) Yamazaki, Y.; Uebayasi, M.; Hosono, K. *Eur. J. Biochem.* **1989**, *184*, 671−80. (e) Haller, G.; Schlögl, K. *Monatsh. Chem.* **1967**, *98*, 603−618.

(13) Pichon, C.; Odell B.; Brown, J. M. *Chem. Commun.* **2004**, 598−599.

(14) Rebiere, F.; Riant, O.; Ricard, L.; Kagan, H. B. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 568−570.

(15) Slocum, D. W.; Marchal R. L.; Jones, W. E. *Chem. Commun.* **1974**, 967−968.

(16) Steurer, M. Diploma Thesis, University of Vienna, 2005.

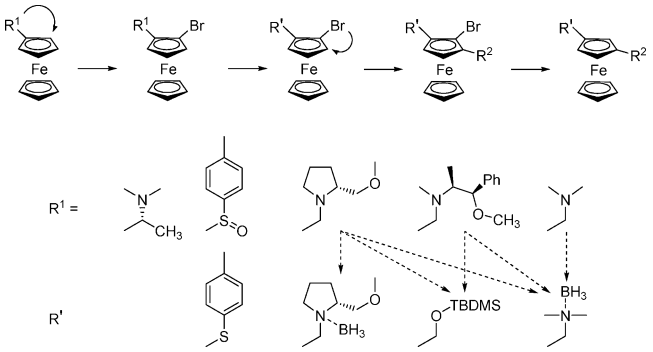
(17) Tiedl, K. Diploma Thesis, University of Vienna, 2005.

(18) (a) Lagneau, N. M.; Chen, Y.; Robben, P. M.; Sin, H.-S.; Takasu, K.; Chen, J.-S.; Robinson, P. D.; Hua, D. H. *Tetrahedron* **1998**, *54*, 7301−7334. (b) Glahsl, G.; Herrmann, R. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1753−1757. (c) Herrmann, R.; Hübener, G.; Ugi, I. *Tetrahedron* **1985**, *41*, 941−947.

(19) Ferber, B.; Top, S.; Welter, R.; Jaouen, G. *Chem.−Eur. J.* **2006**, *12*, 2081−2086.

(20) Steurer, M.; Tiedl, K.; Wang, Y.; Weissensteiner, W. *Chem. Commun.* **2005**, 4929−4931.

Scheme 3. Bromide-Mediated Synthesis of 1,2,3-Tri- and 1,3-Disubstituted Ferrocenes



1,2,3-tri- and 1,3-disubstituted ferrocenes that make use of different *ortho*-directing groups R^1 and report how some of these groups can be transformed easily into nondirecting functional groups in order to prevent interference in the second *ortho*-deprotonation step. Furthermore, the use of a number of different electrophiles to introduce substituents R^2 is described along with two methods for the removal of bromide. Finally, synthetic procedures for a few potential pincer ligands are given.

Results

The aromatic halides fluoride, chloride, and bromide are well known to direct metalation—mostly lithiation—to the *ortho*-positions of their aromatic backbone.[21] In the case of chloroferrocene this was investigated by Huffman et al. as early as 1965[22] and later on by Slocum and co-workers.[23] As with bromobenzenes, bromo-substituted ferrocenes can be *ortho*-deprotonated using lithium diisopropylamide (LDA), and this was described in several papers by Butler and co-workers.[24]

On the basis of these and our preliminary results we tested bromide as the central substituent R^c in combination with four stereogenic substituents (R^1), 1-dimethylaminoethyl [$CH(NMe_2)$-Me], the *p*-tolylsulfinyl [4-$MeC_6H_4S(O)$] unit, (2-methoxymethylpyrrolidin-1-yl)methyl [2-$MeOCH_2(C_4H_7N)CH_2$], and the ephedrine derivative $CH_2N(Me)CH(Me)CH(Ph)OMe$, as well as the nonstereogenic dimethylaminomethyl [$CH_2(NMe_2)$] group (Scheme 3).

Sequence 1, R^1 = CH(NMe$_2$)Me. In the first reaction sequence [R^1 = $CH(NMe_2)Me$ (Scheme 4)] commercially available (*R*)-*N*,*N*-(1-dimethylaminoethyl)ferrocene [Ugi's amine, (*R*)-**1**] was reacted according to a published procedure with *s*-BuLi and $BrCF_2CF_2Br$ to give (R,S_p)-**2** in 88% yield.[25] In order to optimize the subsequent deprotonation step with respect to temperature and the amount of base, different conditions were applied to the reaction of (R,S_p)-**2** with Li-TMP (TMP = 2,2,6,6-tetramethylpiperidine) as the base and $ClSiMe_3$ as the electrophile. The use of these optimized conditions gave (R,R_p)-**3** exclusively (83%).

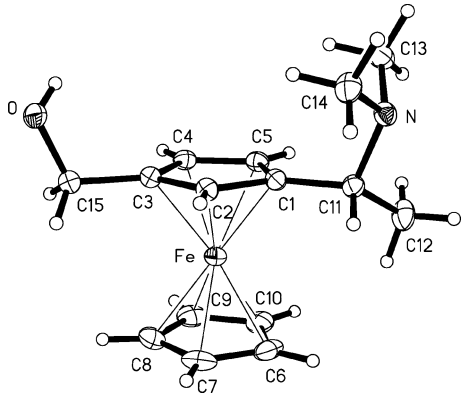


Figure 1. Molecular structure of (R,S_p)-**8**. Selected bond lengths (Å): Fe−C(1−5)$_{av}$ = 2.044(1), Fe−C(6−10)$_{av}$ = 2.046(1), C(1)−C(11) = 1.509(1), C(3)−C(15) = 1.500(2), N−C(11) = 1.493(1), N−C(13) = 1.458(2), N−C(14) = 1.463(1), C(15)−O = 1.422(1).

The trisubstituted derivatives (R,R_p)-**4** (82%) and (R,S_p)-**6** (81%) were obtained on using the electrophiles dimethylformamide (DMF) and $ClSnBu_3$. Reduction of aldehyde **4** with $LiAlH_4$ gave alcohol (R,R_p)-**5** in 92% yield. Further reaction of **3** and **5** with *n*-BuLi (**3**, 1.5 equiv; **5**, 2.5 equiv) and H_2O removed the bromide substituent and resulted in the 1,3-trisubstituted ferrocenes (R,S_p)-**7** (84%) and (R,S_p)-**8** (88%). Single crystals of **8** suitable for an X-ray diffraction study could be obtained. The molecular structure of **8** depicted in Figure 1 confirms not only the 1,3-substitution pattern but also its (R,S_p) absolute configuration.

It is interesting to note that—like a *p*-tolylsulfinyl group (Scheme 2, step **C** → **D**)—the bromide substituent of **6** located adjacent to a tributylstannyl substituent can be removed selectively. Reaction of **6** with 1.5 equiv of *tert*-BuLi and H_2O gave (R,S_p)-**9** (97%) exclusively. Further transformation of the tributylstannyl group was achieved by treating **9** with 1.2 equiv of *n*-BuLi. Subsequent reaction with electrophile DMF or I_2 resulted in aldehyde (R,S_p)-**10** (87%) and iodo derivative (R,S_p)-**11** (72%). It should be mentioned that attempts to replace the tributylstannyl group of **9** by iodide under standard conditions (I_2/CH_2Cl_2, Scheme 2, step **D** → **E**) resulted in product mixtures, since under these reaction conditions the dimethylamino group is partially oxidized to an acetyl group. As an example for a further functional group transformation, we synthesized aminophosphine (R,S_p)-**12** (67%).[26] In summary, reaction sequence 1 provides a facile, high-yielding route to a number of differently substituted chiral, nonracemic 1,3-disubstituted ferrocenes. For example, amino alcohol (R,S_p)-**8** was obtained in four steps from (*R*)-**1** in 58% overall yield.

Sequence 2, R^1 = 4-MeC$_6$H$_4$S(O). In the second reaction sequence, the use of bromide as the central substituent was combined with the *ortho*-directing *p*-tolylsulfinyl substituent [R^1 = 4-$MeC_6H_4S(O)$ (Scheme 5)]. It was anticipated that this sequence could complement the methodology recently reported by Brown and co-workers for the synthesis of racemic derivatives.[13] Bromide (R,S_p)-**14** was prepared according to literature

(21) (a) Clayden, J. *Organolithiums: Selectivity for Synthesis*; Pergamon: Amsterdam, 2002; pp 58−59. (b) Mongin, F.; Schlosser, M. *Tetrahedron Lett.* **1996**, *37*, 6551−6554.

(22) Huffman, J. W.; Keith, L. H.; Asbury, R. L. *J. Org. Chem.* **1965**, *30*, 1600−1604.

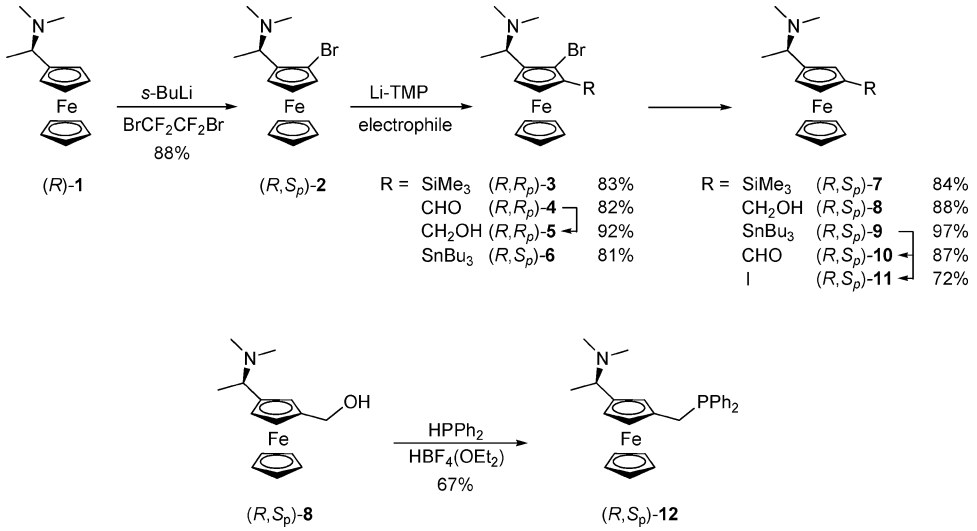
(23) (a) Slocum, D. W.; Jennings, C. A.; Engelmann, T. R.; Rockett, B. W.; Hauser, C. R. *J. Org. Chem.* **1971**, *36*, 377−381. (b) Slocum, D. W.; Koonsvitsky, B. P.; Ernst, C. R. *J. Organomet. Chem.* **1972**, *38*, 125−132.

(24) (a) Butler, I. R.; Drew, M. G. B. *Inorg. Chem. Commun.* **1999**, *2*, 234−237. (b) Butler, I. R.; Müssig, S; Plath, M. *Inorg. Chem. Commun.* **1999**, *2*, 424−427. (c) Butler, I. R.; Drew, M. G. B.; Greenwell, C. H.; Lewis, E.; Plath, M.; Müssig, S.; Szewczyk, J. *Inorg. Chem. Commun.* **1999**, *2*, 576−580.

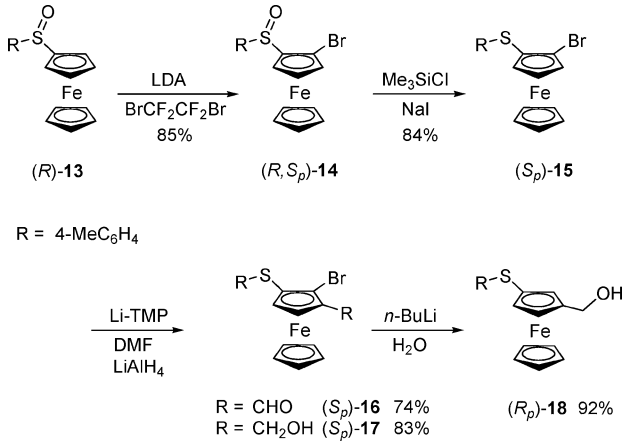
(25) (a) Han, J. W.; Tokunaga, N.; Hayashi, T. *Helv. Chim. Acta* **2002**, *85*, 3848−3854. For alternative methods see: (b) Taylor, C. J.; Roca, F. X.; Richards, C. J. *Synlett* **2005**, 2159−2162. (c) Barbaro, P.; Bianchini, C.; Giambastiani, G.; Togni, A. *Tetrahedron Lett.* **2003**, *44*, 8279−8283. (d) Pugin, B.; Landert, H.; Pioda, G. (Novartis A.-G., Switz.) PCT Int. Appl. WO 9815565, 1998.

(26) For the synthesis methodology see: Cabou, J.; Brocard, J.; Pélinski, L. *Tetrahedron Lett.* **2005**, *46*, 1185−1188.

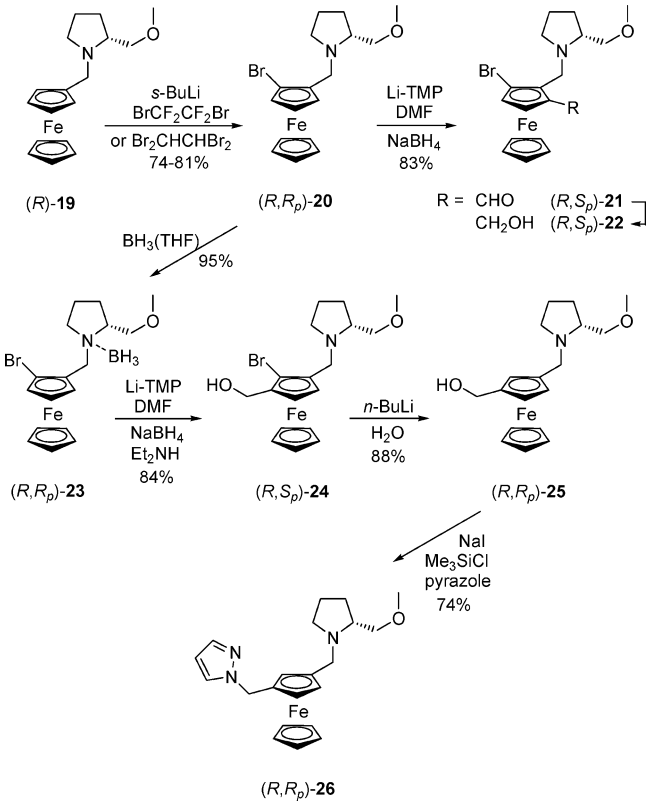
Scheme 4. Synthesis of 1,3-Disubstituted Ferrocenes, Sequence 1



Scheme 5. Synthesis of 1,3-Disubstituted Ferrocenes, Sequence 2



Scheme 6. Synthesis of 1,3-Disubstituted Ferrocenes, Sequence 3



procedures by reacting *p*-tolyl-ferrocenyl sulfoxide (*R*)-**13**[27] with LDA and $BrCF_2CF_2Br$ (85%),[24a] and the product was subsequently reduced with sodium iodide and chlorotrimethylsilane[28] to give sulfide (S_p)-**15** (84%). On using Li-TMP *ortho*-deprotonation occurred selectively adjacent to the bromide substituent, and subsequent reaction with DMF gave aldehyde (S_p)-**16** in 74% yield. Reduction with $LiAlH_4$ resulted in alcohol (S_p)-**17** (83%), which on reaction with *n*-BuLi and H_2O led to the desired 1,3-disubstituted ferrocene derivative (R_p)-**18** (92%). Overall, **18** is accessible from **13** in 40% yield, and as recently reported for its racemate,[13] **18** can easily be functionalized and can therefore serve as a valuable starting material for a variety of chiral, nonracemic 1,3-disubstituted ferrocene derivatives.

Sequence 3, R^1= 2-MeOCH$_2$(C$_4$H$_7$N)CH$_2$. The third reaction sequence involves the use of bromide as the central substituent together with the (2-methoxymethylpyrrolidin-1-yl)-methyl substituent [2-$MeOCH_2(C_4H_7N)CH_2$] as the *ortho*-directing group R^1 (Scheme 6). Bromide (R,R_p)-**20** was prepared by reacting (*R*)-**19**[29] with *s*-BuLi and either $BrCF_2CF_2Br$ (81%) or $Br_2CHCHBr_2$ (74%).[30] However, when **20** was treated with Li-TMP followed by DMF as the electrophile, a mixture of aldehydes was obtained in which (R,S_p)-**21** was the main component. Reduction of this mixture with $NaBH_4$ led to the isolation of alcohol (R,S_p)-**22** in 83% yield.

In contrast to bromide **2**, in this case deprotonation occurred predominantly next to the stereogenic *ortho*-directing group rather than next to the bromide substituent. In order to circumvent this problem, we reasoned that protection of the nitrogen lone pair could reverse the direction of *ortho*-deprotonation. Hence, (R,R_p)-**20** was reacted with BH_3(THF)

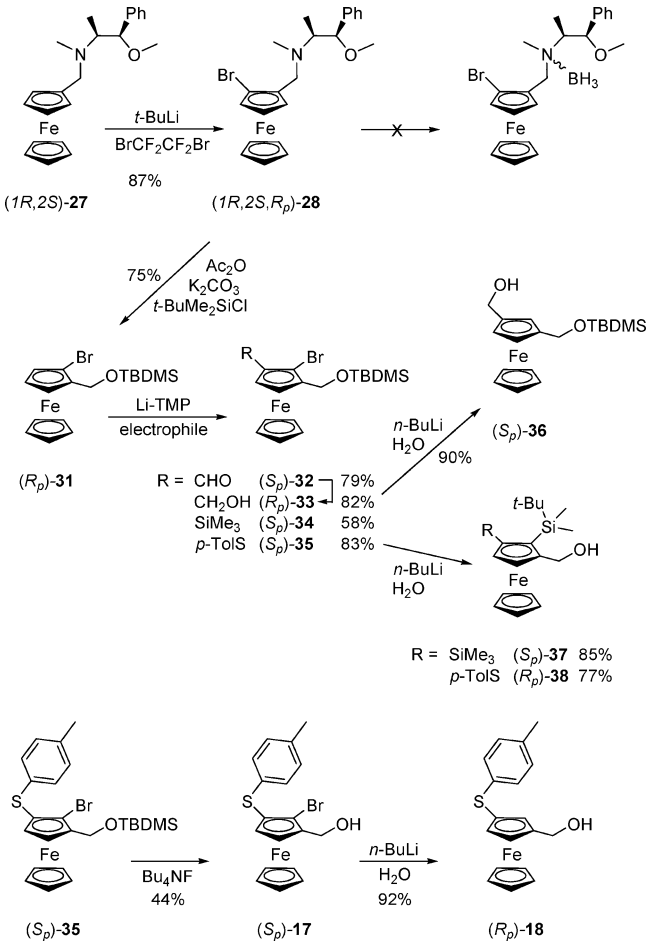
(27) (a) Guillaneux, D.; Kagan, H. B. *J. Org. Chem.* **1995**, *60*, 2502−2505. (b) Riant, O.; Argouarch, G.; Guillaneux, D.; Samuel, O.; Kagan, H. B. *J. Org. Chem.* **1998**, *63*, 3511−3514. (c) Rebiere, F.; Samuel, O.; Kagan, H. B. *Tetrahedron Lett.* **1990**, *31*, 3121−3124. (d) Cotton, H. K.; Huerta, Fernando F.; Bäckvall, J.-E. *Eur. J. Org. Chem.* **2003**, 2756−2763.

(28) For the synthesis methodology see: Olah, G. A.; Narang, S. C.; Gupta, B. G. B.; Malhotra, R. *Synthesis* **1979**, 61−62.

(29) Ganter, C.; Wagner, T. *Chem. Ber.* **1995**, *128*, 1157−1161.

(30) Pugin, B.; Feng, X. (Solvias A.-G., Switz.) PCT Int. Appl. WO 2006114438, 2006.

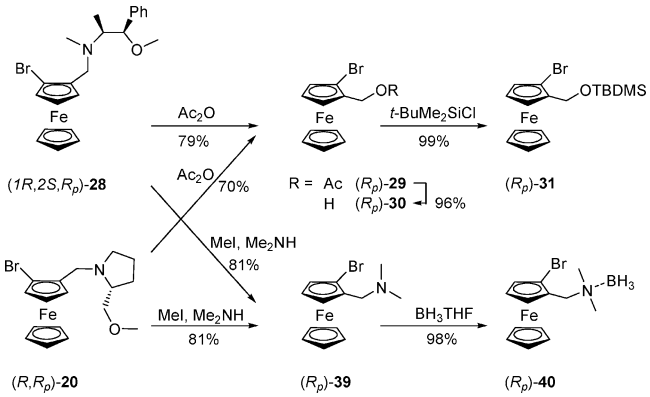
Scheme 7. Synthesis of 1,3-Disubstituted Ferrocenes, Sequence 4



and boron complex **23** was obtained in 95% yield. It should be mentioned that, in principle, complexation of **20** might be expected to give two diastereomers with opposite absolute configuration at the nitrogen. However, only one diastereomer was observed. Chromatography of the product led to partial deprotection, and it was therefore used for the next reaction without further purification. As in the case of **2**, complex **23** could be deprotonated with Li-TMP next to bromide, and reaction with DMF as the electrophile gave the desired aldehyde. However, this intermediate aldehyde proved to be rather unstable and was therefore reacted immediately after workup. Reduction with $NaBH_4$ and deprotection with diethylamine resulted in (R,S_p)-**24** in 84% yield (based on **23**). Removal of bromide with *n*-BuLi and H_2O led to enantiopure 1,3-disubstituted ferrocene (R,R_p)-**25** (88%). Based on **19** the 1,3-disubstituted derivative **25** was prepared in 52−57% overall yield and, as an example of an application, was subsequently transformed into pincer ligand (R,R_p)-**26** (74%).[31]

Sequence 4, R^1 = $CH_2N(Me)CH(Me)CH(Ph)OMe$. The fourth reaction sequence starts from the *O*-methylephedrine-substituted ferrocene derivative (1*R*,2*S*)-**27** [R^1 = $CH_2N(Me)$-CH(Me)CH(Ph)OMe, (Scheme 7)], which is easily accessible from *N*-ferrocenylmethyl-*N*,*N*,*N*-trimethylammonium iodide and *O*-methylephedrine.[32]

Scheme 8



Reaction of **27** with *t*-BuLi and $BrCF_2CF_2Br$ gave (1*R*,2*S*,R_p)-**28** in 87% yield.[32a] All attempts to selectively *ortho*-deprotonate bromide **28** led to product mixtures. In addition, unlike in the case of **20**, reaction of **28** with BH_3(THF) resulted in diastereomeric boron complexes that showed a high tendency for deprotection in THF. To overcome this problem, we decided to transform the *ortho*-directing *O*-methylephedrine unit into nondirecting functional groups, and we suspected that a silyl-protected hydroxyl or a boron-protected dimethylamino group would be appropriate.

As depicted in Scheme 8, bromide (1*R*,2*S*,R_p)-**28** was reacted with acetic anhydride to give acetate (R_p)-**29** (79%),[33] and after saponification to alcohol (R_p)-**30** (96%),[34] the hydroxyl group was protected as a *tert*-butyldimethylsilyl ether [(R_p)-**31**, 99%]. On the other hand, reaction of **28** with CH_3I followed by Me_2NH gave amine (R_p)-**39** (81%),[32a,35] which on reaction with BH_3(THF) resulted in the very stable boron complex (R_p)-**40** (98%). It is important to note that (R_p)-**29** and (R_p)-**39** are also accessible from (R,R_p)-**20** in 81% and 70% yield, respectively (Scheme 8).

After transforming the *O*-methylephedrine unit of **28** into the *tert*-butyldimethylsilyl-protected hydroxyl group (**31**, 75% overall yield, based on **28**), the reaction conditions optimized for **2** (Li-TMP, DMF) were used for the selective transformation of bromide (R_p)-**31** (Scheme 7) into aldehyde (S_p)-**32** (79%), which, after reduction with $LiAlH_4$, gave alcohol (R_p)-**33** (82%). Finally, reaction with *n*-BuLi and H_2O removed the bromide and gave the 1,3-disubstituted ferrocene derivative (S_p)-**36** in 90% yield (44% overall, based on **28**). When the *ortho*-substitution reaction of (R_p)-**31** was carried out with electrophile $ClSiMe_3$ or $(4\text{-}MeC_6H_4S)_2$ the 1,2,3-trisubstituted derivatives (S_p)-**34** (58%) and (S_p)-**35** (83%) were obtained. Interestingly, reaction of **34** and **35** with *n*-BuLi and H_2O not only removed the bromide substituent but also induced a retro-Brook rearrangement,[36] which led to the undesired derivatives (S_p)-**37** and (R_p)-**38** in 85% and 77% yield, respectively. In order to avoid this problem, (S_p)-**35** was deprotected with tetrabutylammonium fluoride, and this provided another route to (S_p)-**17**, which as described above (Scheme 5) can be debrominated to the 1,3-disubstituted derivative (R_p)-**18**.

Sequence 5, R^1= CH_2NMe_2. Next we investigated whether (R_p)-**39**, which is easily accessible from (1*R*,2*S*,R_p)-**28**, (R,R_p)-

(31) For the synthesis methodology see: Šebesta, R.; Toma, Š; Sališová, M. *Eur. J. Org. Chem.* **2002**, 692−695.

(32) (a) Xiao, L.; Kitzler, R.; Weissensteiner, W. *J. Org. Chem.* **2001**, *66*, 8912−8919. (b) Kitzler, R.; Xiao, L.; Weissensteiner, W. *Tetrahedron: Asymmetry* **2000**, *11*, 3459−3462. (c) Fleischer, I.; Toma, Š. *Coll. Czech. Chem. Commun.* **2004**, *69*, 330−338.

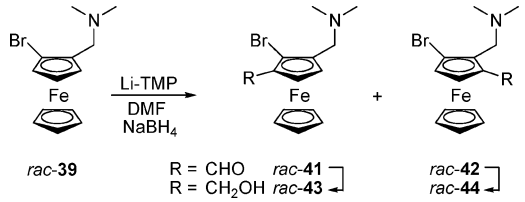
(33) For an alternative synthesis method see: Widhalm, M.; Nettekoven, U.; Mereiter, K. *Tetrahedron: Asymmetry* **1999**, *10*, 4369−4391.

(34) For alternative synthesis methods see: (a) Refs 12c and 33. (b) Pickett, T. E.; Roca, F. X.; Richards, C. J. *J. Org. Chem.* **2003**, *68*, 2592−2599.

(35) For an alternative synthesis see: Xiao, L.; Mereiter, K.; Weissensteiner, W.; Widhalm, M. *Synthesis* **1999**, 1354−1362.

(36) Tomooka, K. In *Chemistry of Organolithium Compounds*; Rappoport, Z., Marek, I., Eds.; Wiley: Chichester, 2004; pp 749−828.

Scheme 9

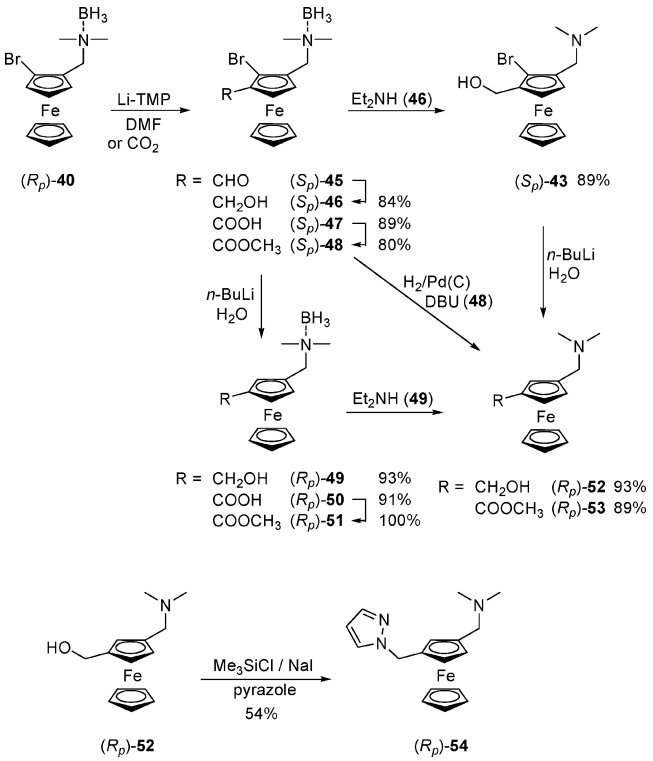


20[32a] (Scheme 8), and other sources,[35] and its boron complex (R_p)-**40** could be selectively *ortho*-deprotonated adjacent to the bromide substituent, since this would provide another route for the exclusive formation of ferrocene-stereogenic 1,3-disubstituted derivatives. Furthermore, it was anticipated that the use of racemic bromide derivative **39**, which can be easily obtained from commercially available *N*,*N*-dimethyl-*N*-ferrocenylmethyl amine,[35,37] would enable the scope of this methodology to be extended to achiral and racemic 1,3-disubstituted ferrocenes.

In order to ascertain whether *ortho*-deprotonation next to the bromide can be carried out selectively in the presence of a dimethylaminomethyl substituent, *rac*-**39** was reacted under the conditions optimized for **2** with Li-TMP and DMF as the electrophile. In this case *ortho*-lithiation took place next to bromide as well as adjacent to the dimethylaminomethyl substituent, and a mixture of aldehydes **41** and **42** in a ratio of 70:30 (84% conversion) was obtained (Scheme 9). For the sake of better characterization these compounds were reduced with $NaBH_4$ to the alcohols **43** and **44**. We noted with interest that in a very recent communication Butler and co-workers reported that the use of modified reaction conditions and Eschenmoser's salt as the electrophile gave 1-bromo-2,5-bis(dimethylaminomethyl)ferrocene from *rac*-**39** in 86% yield.[38] We therefore applied these modified reaction conditions to *rac*-**39**, but with DMF as the electrophile aldehydes **41** and **42** were obtained only in a slightly better isomer ratio (79:21), albeit with a decrease in conversion from 84% to 61%. However, treatment of **39** with BH_3(THF) and subsequent reaction of the resulting boron complex, *rac*-**40**, with Li-TMP and different electrophiles led to exclusive *ortho*-lithiation adjacent to bromide.

Consequently, for the next reaction sequence boron complex **40** in both its racemic and enantiopure forms was used as the starting material. In almost all cases identical reaction conditions were used for the racemic and enantiopure compounds, and therefore the following discussion concerns only the synthesis of chiral, nonracemic derivatives (Scheme 10; reaction details for racemic derivatives are given in the Supporting Information). Lithiation of (R_p)-**40** and further treatment with DMF led to aldehyde (S_p)-**45**, which is stable enough for characterization but on standing at room temperature tends to deprotect to (S_p)-**41** and reacts further on to alcohols **43** and **46**. Aldehyde **45** was therefore reduced immediately after workup with BH_3(THF) to alcohol (S_p)-**46** (84% based on **40**), which on deprotection with Et_2NH gave amino alcohol (S_p)-**43** (89%). Optimization of this reaction sequence allowed the transformation of (R_p)-**40** into (S_p)-**43** without isolating the intermediates **45** and **46** and gave an overall yield of 87%. Finally, when **43** was reacted with *n*-BuLi and H_2O, the 1,3-disubstituted ferrocene (R_p)-**52** (93%) was obtained.[39] In a similar way to **43**, compound **46** can also be debrominated with *n*-BuLi and H_2O, which leads to the 1,3-disubstituted boron complex (R_p)-**49** (93%). Decomplexation of this derivative with Et_2NH also resulted in amino alcohol (R_p)-**52** (93%).

Scheme 10. Synthesis of 1,3-Disubstituted Ferrocenes, Sequence 5



In this sequence, CO_2 was tested as the electrophile in addition to DMF. Reaction of (R_p)-**40** with Li-TMP and CO_2 gave the very stable carbonic acid (S_p)-**47** (89%), which when treated with a solution of CH_2N_2 in diethyl ether, resulted in the methyl ester (S_p)-**48** (80%). A search for a suitable debromination method revealed that hydrogenation under basic conditions with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as the base and Pd on charcoal as the catalyst was best suited. The use of these conditions led to debromination of **48** and, at the same time, deprotection to the 1,3-disubstituted ester (R_p)-**53** in 89% yield.[40] Furthermore, carbonic acid **47** reacted with *n*-BuLi (2.2 equiv) and H_2O to give the 1,3-disubstituted boron complex (R_p)-**50** (91%), which was reacted with CH_2N_2 in diethyl ether to give ester (R_p)-**51** quantitatively.

In this case the pincer ligand (R_p)-**54**, which bears a pyrazole substituent, was prepared in one step from (R_p)-**52** (54%).[31]

Overall, depending on whether starting material **39** is used in its racemic or enantiopure form, this sequence provides easy access to achiral, racemic and chiral, nonracemic 1,2,3-tri- and 1,3-disubstituted ferrocene derivatives. Under optimized conditions, 1,3-disubstituted amino alcohol (R_p)-**52** was prepared from (R_p)-**39** in 79% overall yield without isolating intermediates **45** and **46**.

Concluding Remarks

In this study we have evaluated five bromide-mediated reaction sequences for the synthesis of 1,2,3-tri- and 1,3-

(37) Marr, G.; Moore, R. E.; Rockett, B. W. *J. Chem. Soc.* (*C*) **1968**, 24−27.

(38) Butler, I. R.; Woldt, B.; Oh, M.-Z.; Williams, D. J. *Inorg. Chem. Commun.* **2006**, *9*, 1255−1258.

(39) For *rac*-**52** see also: Koridze A. A.; Sheloumov, A. M.; Kuklin, S. A.; Lagunova, V. Y.; Petukhova, I. I.; Dolgushin, F. M.; Ezernitskaya, M. G.; Petrovskii, P. V.; Macharashvili, A. A.; Chedia, R. V. *Russ. Chem. Bull.* **2002**, *51*, 1077−1078.

(40) For an analogous procedure see: Sajiki, H.; Kume, A.; Hattori, K.; Hirota, K. *Tetrahedron Lett.* **2002**, *43*, 7247−7250.

disubstituted ferrocenes. All sequences start from a monosubstituted ferrocene derivative Fc-R^1, bearing either a stereogenic or a nonstereogenic *ortho*-directing group (R^1), and involve two consecutive *ortho*-deprotonation steps. In the first step, 2-bromo-substituted derivatives (1-R^1,2-Br-Fc) are prepared, while in the second step the use of Li-TMP as the base enables deprotonation of the position adjacent to the bromo substituent. The use of appropriate electrophiles provides access to a variety of 1,2,3-trisubstituted ferrocenes (1-R^1,2-Br,3-R^3-Fc) using these routes. In some cases, in order to prevent interference of *ortho*-directing groups R^1 in the second deprotonation step, these groups had to be transformed into nondirecting substituents. This could, for example, be achieved by transforming amino functionalities (R^1) into their amine-trihydroboron complexes.

Since bromide can be easily removed from trisubstituted ferrocenes (1-R^1,2-Br,3-R^3-Fc) either by bromide−lithium exchange or by catalytic hydrogenation, 1,3-disubstituted ferrocene derivatives (1-R^1,3-R^3-Fc) become accessible in high overall yield, and this includes pincer-type derivatives.

In general, (i) bromide as an *ortho*-directing group can be used in combination with a number of stereogenic and nonstereogenic functional groups, (ii) with Li-TMP as the base *ortho*-deprotonation next to bromide can be achieved in high yield and in most cases with very high stereoselectivity, and (iii) bromide can be easily exchanged by other electrophiles.

Experimental Section

General Methods. Melting points were determined on a Kofler melting point apparatus and are uncorrected. ^{1}H (400.132 MHz), ^{13}C NMR (100.624 MHz), and ^{31}P (161.975 MHz) spectra were recorded in $CDCl_3$. Chemical shifts (δ) are reported in ppm relative to $CHCl_3$ (7.26, ^{1}H), $CDCl_3$ (77.0, ^{13}C), and 85% H_3PO_4 (0.0, ^{31}P). In ^{1}H NMR data br s, d, t, and q refer to broad singlet, doublet, triplet, and quartet, respectively, and C_q in ^{13}C NMR data stands for quaternary carbon atom. Mass spectra were measured on a Finnigan MAT 900S or Finnigan MAT 8230 (EI, 70 eV) spectrometer. Optical rotations were measured on a Perkin-Elmer 241 polarimeter at 20 °C. All reactions were carried out under Ar using standard Schlenk techniques. Pentane and Et_2O were distilled from lithium aluminum hydride, acetonitrile and dichloromethane were distilled from calcium hydride, and THF was distilled from sodium and benzophenone under Ar prior to use. Acetic acid and acetic anhydride were freshly distilled, and Ar was bubbled through each for 12 h prior to use. Chromatographic separations were performed under gravity on either silica gel (Merck, 40−63 μm) or alumina (Merck, aluminum oxide 90, 0.063−0.200 mm). Petroleum ether with a boiling range of 55−65 °C was used for chromatography.

Typical Procedures. (R,R_p)-1-Bromo-5-[1-(*N*,*N*-dimethylamino)ethyl]-2-formylferrocene, (R,R_p)-4. To a degassed solution of (R,S_p)-**2**[25a] (500 mg, 1.488 mmol) in THF (5 mL) was added dropwise at −78 °C Li-TMP in THF/hexane (0.7 M, 4.25 mL, 2.98 mmol). The reaction mixture was subsequently stirred for 30 min at −78 °C followed by 3 h at −30 °C. The temperature was again lowered to −78 °C, and dimethylformamide (350 μL, 4.52 mmol) was added. The temperature was raised to 0 °C, and stirring was continued for 16 h. The reaction was quenched with saturated aqueous Na_2CO_3 (15 mL) before diethyl ether was added, and the phases were separated. The aqueous phase was extracted three times with diethyl ether. The combined organic phases were washed with brine. After drying over $MgSO_4$ and removal of the solvents under reduced pressure, the residue was chromatographed on alumina. A mixture of petroleum ether, ethyl acetate, and triethylamine in a ratio of 30:10:1 eluted (R,R_p)-**4** (442 mg, 1.214 mmol, 82% yield) as a red oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.47 (d, J = 6.9 Hz, 3H, CHCH_3), 2.17 (s, 6H, N(CH_3)$_2$), 3.87 (q, J = 6.9 Hz, 1H, CHCH$_3$), 4.25 (s, 5H, Cp′), 4.61 (d, J = 2.8 Hz, 1H, Cp-H4), 4.90 (d, J = 2.8 Hz, 1H, Cp-H3), 10.22 (s, 1H, CHO). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.8 (*C*H$_3$CH), 41.0 (2C, N(CH_3)$_2$), 55.7 (*C*HCH$_3$), 65.6 (Cp-C3), 69.6 (Cp-C4), 72.8 (5C, Cp′), 75.3, 92.9 (2 Cp-C_q), 193.9 (CHO), 1 Cp-C_q not observed. MS (60 °C) m/z (%): 365/363 (30) [M^+], 321/319 (6), 268 (28), 239 (54), 212 (16). HRMS: calcd for $C_{15}H_{18}$BrFeNO 362.9923, found 362.9928. [α]$_\lambda^{20}$ (nm): −720 (589), −806 (578), −1334 (546) (*c* 0.128, $CHCl_3$).

(R,R_p)-1-Bromo-5-[1-(*N*,*N*-dimethylamino)ethyl]-2-hydroxymethylferrocene, (R,R_p)-5. A suspension of $LiAlH_4$ (35 mg, 0.923 mmol) in THF (3 mL) was flushed with Ar and cooled to 0 °C before a degassed solution of (R,R_p)-**4** (261 mg, 0.717 mmol) in THF (5 mL) was added dropwise at 0 °C. The reaction mixture was subsequently stirred for 30 min at 0 °C followed by 16 h at rt. The reaction was cooled to 0 °C and then quenched with ethanol (10 mL) followed by water (20 mL). Diethyl ether was added, and the phases were separated. The aqueous phase was extracted three times with diethyl ether. The organic phases were combined and washed with brine. After drying over $MgSO_4$ and removal of the solvents under reduced pressure, the residue was chromatographed on alumina. A mixture of petroleum ether, ethyl acetate, and triethylamine (30:30:1) eluted nonpolar impurities, while ethanol eluted product (R,R_p)-**5** (241 mg, 0.658 mmol, 92% yield, yellow powder).

Mp: 139−146 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.50 (d, J = 6.9 Hz, 3H, CHCH_3), 1.74 (br s, 1H, OH), 2.15 (s, 6H, N(CH_3)$_2$), 3.78 (q, J = 6.9 Hz, 1H, CHCH$_3$), 4.13 (s, 5H, Cp′), 4.15 (d, J = 2.8 Hz, 1H, Cp-H4), 4.31 (d, J = 2.8 Hz, 1H, Cp-H3), 4.45, 4.46 (AB, J = 12.4 Hz, 2H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.9 (*C*H$_3$CH), 41.0 (2C, N(CH_3)$_2$), 56.3 (*C*HCH$_3$), 60.2 (CH_2), 64.9 (Cp-C4), 65.9 (Cp-C3), 71.6 (5C, Cp′), 81.6, 85.2, 88.4 (3 Cp-C_q). MS (80 °C) m/z (%): 367/365 (77) [M^+], 352/350 (9), 323/321 (41), 296/295 (21), 214/212 (37), 121 (18). HRMS: calcd for $C_{15}H_{20}$BrFeNO 365.0079, found 365.0085. [α]$_\lambda^{20}$ (nm): +16.7 (589), +18.4 (578), +28.8 (546) (*c* 0.576, $CHCl_3$).

(R,S_p)-3-[1-(*N*,*N*-Dimethylamino)ethyl]-1-hydroxymethylferrocene, (R,S_p)-8. To a degassed solution of (R,R_p)-**5** (70 mg, 0.191 mmol) in THF (3 mL) was added dropwise at −78 °C *n*-BuLi in hexane (1.6 M, 300 μL, 0.48 mmol). After stirring for 30 min at 0 °C the reaction was quenched with water (10 mL) before diethyl ether was added, and the phases were separated. The aqueous phase was extracted three times with diethyl ether. The organic phases were combined and washed with brine. After drying over $MgSO_4$ and removal of the solvents under reduced pressure, the residue was chromatographed on alumina. A mixture of petroleum ether, ethyl acetate, and triethylamine (30:30:1) eluted nonpolar impurities, while ethanol eluted product (R,S_p)-**8** (48 mg, 0.167 mmol, 88% yield, yellow powder).

Crystals for the X-ray structure determination were grown by crystallization from dichloromethane/petroleum ether.

Mp: 113−117 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (d, J = 6.9 Hz, 3H, CHCH_3), 1.71 (br s, 1H, OH), 2.09 (s, 6H, N(CH_3)$_2$), 3.57 (q, J = 6.9 Hz, 1H, CHCH$_3$), 4.11 (m, 1H, Cp-H), 4.12 (s, 5H, Cp′), 4.21 (m, 1H, Cp-H), 4.25 (t, J = 1.4 Hz, 1H, Cp-H2), 4.33 (s, 2H, CH_2OH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.6 (CH*C*H$_3$), 40.6 (2C, N(CH_3)$_2$), 58.5 (*C*HCH$_3$), 60.9 (CH_2OH), 66.96 (Cp-CH), 66.99 (Cp-CH), 69.0 (5C, Cp′), 69.1 (Cp-C2), 87.8, 87.9 (2 Cp-C_q). MS (70 °C) m/z (%): 287 (81) [M^+], 272 (25), 243 (90), 225 (27), 134 (100). HRMS: calcd for $C_{15}H_{21}$FeNO 287.0973, found 287.0980. [α]$_\lambda^{20}$ (nm): −1.2 (589), −1.6 (578), −7.9 (546) (*c* 0.674, $CHCl_3$).

(R,R_p)-1-Bromo-2-[(2-methoxymethylpyrrolidin-1-yl)methyl]-ferrocene, (R,R_p)-20. To a degassed solution of (*R*)-*N*-ferrocenylmethyl-2-methoxymethylpyrrolidine, (*R*)-**19**[29] (2 g, 6.385 mmol), in diethyl ether (32 mL) was added dropwise at −78 °C *s*-BuLi in cyclohexane (1.3 M, 5.9 mL, 7.67 mmol). The reaction mixture was stirred for 1.5 h at −78 °C and 1.5 h at −30 °C before the

temperature was lowered to −78 °C, and a degassed solution of $Br_2CHCHBr_2$ (6.22 g, 23.94 mmol) in diethyl ether (20 mL) was added dropwise within 30 min. Stirring was continued for an additional 30 min at −78 °C and 16 h at rt. The reaction was quenched with water (20 mL), and the phases were separated. The aqueous phase was extracted with dichloromethane (3 × 10 mL), and the organic phases were combined and washed with an aqueous solution of $Na_2S_2O_5$, NaOH (0.05 M), and brine. The organic phases were extracted with an aqueous solution of citric acid (10%, 3 × 50 mL), and the combined aqueous phases were extracted with diethyl ether (3 × 30 mL). The aqueous phases were basified at 0 °C with NaOH (2 M, pH 9) and subsequently extracted with diethyl ether. After drying over $MgSO_4$ and removal of the solvents under reduced pressure, the residue was chromatographed on alumina. A mixture of petroleum ether, diethyl ether, and triethylamine (80:20:1) was used as the eluent to give (*R*,*R*$_p$)-**20** (1.85 g, 4.718 mmol, 74% yield) as a dark orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54−1.78 (m, 3H, NCH_2CH_2 + NCHCH*H*), 1.80−1.91 (m, 1H, NCHC*H*H), 2.21−2.31 (m, 1H, NCH*H*CH$_2$), 2.69−2.78 (m, 1H, NC*H*CH$_2$), 2.99−3.01 (m, 1H, NC*H*HCH$_2$), 3.25, 3.44 (AB-part of an ABX system, J_{AB} = 9.3 Hz, J_{AX} = 6.3 Hz, J_{BX} = 4.8 Hz, 2H, $CHCH_2OCH_3$), 3.36 (s, 3H, OCH_3), 3.47, 3.98 (AB, J = 13.4 Hz, 2H, $CpCH_2N$), 4.08 (t, J = 2.5 Hz, 1H, Cp-H4), 4.14 (s, 5H, Cp′), 4.20−4.23 (m, 1H, Cp-H3), 4.39−4.42 (m, 1H, Cp-H5). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.8 (NCH_2CH_2), 28.6 (NCH*C*H$_2$), 52.0 ($CpCH_2N$), 54.4 (NCH_2CH_2), 59.1 (OCH_3), 61.9 (N*C*HCH$_2$), 66.2 (Cp-C4), 68.3 (Cp-C3), 70.2 (Cp-C5), 71.02 (5C, Cp′), 71.03 (Cp-C$_q$), 76.5 ($CHCH_2OCH_3$) 80.8 (Cp-C$_q$). MS (100 °C) *m*/*z* (%): 393/391 (8) [M$^+$], 348/346 (7), 294/292 (27), 279/277 (48), 212 (56), 184 (24), 128 (57), 84 (23), 56 (100). HRMS: calcd for $C_{17}H_{22}BrFeNO$ 391.0236, found 391.0230. $[\alpha]_\lambda^{20}$ (nm): +28.8 (589), +27.7 (578), +17.8 (546) (*c* 0.534, $CHCl_3$).

{(*R*,*R*$_p$)-1-Bromo-2-[(2-methoxymethylpyrrolidin-1-yl)methyl]ferrocene}trihydroboron, (*R*,*R*$_p$)-23. To a degassed solution of (*R*,*R*$_p$)-**20** (1 g, 2.55 mmol) in THF (13 mL) was added dropwise at 0 °C BH_3(THF) in THF (1.0 M, 7.6 mL, 7.6 mmol). The reaction mixture was subsequently stirred for 3 h at rt. The reaction was quenched with water (20 mL), and diethyl ether was added. The phases were separated, and the aqueous phase was extracted three times with diethyl ether. The organic phases were combined and washed with brine. After drying over $MgSO_4$ and removal of the solvents under reduced pressure (*R*,*R*$_p$)-**23** (1.05 g, 95% chemical purity as determined by ^{1}H NMR) was obtained as a highly viscous orange oil. Since (*R*,*R*$_p$)-**23** tends to deprotect on chromatography, it was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.4−1.8 (br s, 3H, BH_3), 1.73−1.83 (m, 3H, NCH_2CH_2 + NCHCH*H*), 2.03−2.14 (m, 1H, NCHC*H*H), 2.58−2.68 (m, 1H, NCH*H*CH$_2$), 3.05−3.12 (m, 1H, NC*H*HCH$_2$), 3.13−3.22 (m, 1H, NC*H*CH$_2$), 3.43 (s, 3H, OCH_3), 3.48, 4.02 (AB-part of an ABX system, J_{AB} = 10.2 Hz, J_{AX} = 4.3 Hz, J_{BX} = 7.6 Hz, 2H, $CHCH_2OCH_3$), 4.19, 4.44 (AB, J = 14.4 Hz, 2H, $CpCH_2N$), 4.19 (s, 5H, Cp′), 4.21 (t, J = 2.6 Hz, 1H, Cp-H4), 4.51 (dd, J_1 = 2.6 Hz, J_2 = 1.5 Hz, 1H, Cp-H), 4.57 (dd, J_1 = 2.6 Hz, J_2 = 1.5 Hz, 1H, Cp-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.8 (NCH_2CH_2), 25.7 (NCH*C*H$_2$), 57.2 ($CpCH_2N$), 59.1 (OCH_3), 59.5 (NCH_2CH_2), 62.8 (N*C*HCH$_2$), 67.7 (Cp-CH), 71.4 (2 Cp-CH), 71.6 (5C, Cp′), 72.3 ($CHCH_2OCH_3$), 82.4 (Cp-C$_q$), 1 Cp-C$_q$ not observed.

(*R*,*S*$_p$)-1-Bromo-2-hydroxymethyl-5-[(2-methoxymethylpyrrolidin-1-yl)methyl]ferrocene, (*R*,*S*$_p$)-24. To a degassed solution of (*R*,*R*$_p$)-**23** (1 g, 2.46 mmol) in THF (12 mL) was added dropwise at −78 °C Li-TMP in THF/hexane (0.7 M, 7.0 mL, 4.9 mmol). The reaction mixture was stirred for 30 min at −78 °C and 3 h at −30 °C. After lowering the temperature again to −78 °C dimethylformamide (570 μL, 7.36 mmol) was added dropwise, and the reaction mixture was subsequently stirred for 30 min at −78 °C and 1 h at 0 °C. The reaction was quenched with water (1 mL), and diethyl ether was added. The phases were separated, and the aqueous phase was extracted three times with diethyl ether. The organic phases were combined and washed with brine. After drying over $MgSO_4$ and removal of the solvents under reduced pressure, the residue was dissolved in ethanol (15 mL). To this solution was added at rt $NaBH_4$ (140 mg, 3.70 mmol) in three portions, and the resulting mixture was stirred for 16 h at rt. The reaction was quenched with water (10 mL), and ethanol was removed under reduced pressure. The aqueous phase was extracted with dichloromethane (3 × 5 mL), and the combined organic phases were washed with brine. After drying over $MgSO_4$ and removal of the solvents under reduced pressure, the residue was dissolved in diethylamine and stirred for 16 h at rt. Diethylamine was removed under reduced pressure immediately before the residue was purified by chromatography on alumina. A mixture of petroleum ether and ethyl acetate (5:1) removed a mixture of byproducts, while petroleum ether and ethyl acetate (3:1) eluted (*R*,*S*$_p$)-**24** (869 mg, 0.206 mmol, 84% yield) as an orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54−1.77 (m, 4H, NCH_2CH_2 + NCHCH*H* + OH), 1.81−1.92 (m, 1H, NCHC*H*H), 2.20−2.30 (m, 1H, NCH*H*CH$_2$), 2.69−2.77 (m, 1H, NC*H*CH$_2$), 3.01−3.07 (m, 1H, NC*H*HCH$_2$), 3.29, 3.47 (AB-part of an ABX system, J_{AB} = 9.4 Hz, J_{AX} = 6.1 Hz, J_{BX} = 4.8 Hz, 2H, $CHCH_2OCH_3$), 3.37 (s, 3H, OCH_3), 3.43, 4.02 (AB, J = 13.4 Hz, 2H, $CpCH_2N$), 4.12 (s, 5H, Cp′), 4.26 (s, 2H, 2 Cp-H), 4.40, 4.57 (AB, J = 12.3 Hz, 2H, $CpCH_2OH$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.7 (NCH_2CH_2), 28.5 (NCH*C*H$_2$), 52.1 ($CpCH_2N$), 54.4 (NCH_2CH_2), 59.2 (OCH_3), 60.1 ($CpCH_2OH$), 62.1 (N*C*HCH$_2$), 66.4, 68.0 (2 Cp-*C*H), 71.4 (5C, Cp′), 76.6 ($CHCH_2O$), 82.6, 83.7, 85.9 (3 Cp-C$_q$). MS (90 °C) *m*/*z* (%): 423/421 (4) [M$^+$], 378/376 (5), 309/307 (96), 171/169 (24), 155 (100), 138 (24), 121 (17). HRMS: calcd for $C_{18}H_{24}BrFeNO_2$ 421.0342, found 421.0350. $[\alpha]_\lambda^{20}$ (nm): +34.6 (589), +34.4 (578), +30.7 (546) (*c* 0.596, $CHCl_3$).

(*R*,*R*$_p$)-1-Hydroxymethyl-3-[(2-methoxymethylpyrrolidin-1-yl)methyl]ferrocene, (*R*,*R*$_p$)-25. To a degassed solution of (*R*,*S*$_p$)-**24** (700 mg, 1.658 mmol) in THF (2 mL) was added dropwise at −78 °C *n*-BuLi in hexane (1.6 M, 2.6 mL, 4.16 mmol). After stirring for 1 h at 0 °C the reaction was quenched with water (10 mL). Diethyl ether was added, and the phases were separated. The aqueous phase was extracted three times with diethyl ether. The organic phases were combined and washed with brine. After drying over $MgSO_4$ and removal of the solvents under reduced pressure, the residue was chromatographed on alumina. A mixture of petroleum ether and ethyl acetate (1:1) eluted starting material, while elution with petroleum ether, ethyl acetate, and ethanol (15:30:1) gave product (*R*,*R*$_p$)-**25** (500 mg, 1.457 mmol, 88% yield) as an orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.44−1.68 (m, 3H, NCH_2CH_2 + NCHCH*H*), 1.70−1.82 (m, 1H, NCHC*H*H), 2.12−2.22 (m, 1H, NCH*H*CH$_2$), 2.53−2.61 (m, 1H, NC*H*CH$_2$), 2.72 (br s, 1H, OH), 2.81−2.89 (m, 1H, NC*H*HCH$_2$), 3.20, 3.32 (AB-part of an ABX system, J_{AB} = 9.4 Hz, J_{AX} = 6.0 Hz, J_{BX} = 5.0 Hz, 2H, $CHCH_2OCH_3$), 3.27, 3.68 (AB, J = 13.1 Hz, 2H, $CpCH_2N$), 3.30 (s, 3H, OCH_3), 4.05 (s, 5H, Cp′), 4.07−4.12 (s, 2H, 2 Cp-H), 4.21 (br s, 3H, Cp-H + CH_2OH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.4 (NCH_2CH_2), 28.3 (NCH*C*H$_2$), 53.6 ($CpCH_2N$), 53.9 (NCH_2CH_2), 58.9 (OCH_3), 60.3 ($CpCH_2OH$), 61.5 (N*C*HCH$_2$), 67.6 (Cp-*C*H), 68.6 (5C, Cp′), 69.9 (Cp-*C*H), 70.0 (Cp-*C*H), 76.1 ($CHCH_2O$), 83.8, 88.1 (2 Cp-C$_q$). MS (80 °C) *m*/*z* (%): 343 (24) [M$^+$], 229 (100), 211 (14), 135 (10), 91 (39). HRMS: calcd for $C_{18}H_{25}FeNO_2$ 343.1235, found 343.1241. $[\alpha]_\lambda^{20}$ (nm): +63.0 (589), +64.5 (578), +67.8 (546) (*c* 1.066, $CHCl_3$).

(*R*,*R*$_p$)-1-[(Pyrazol-1-yl)methyl]-3-[(2-methoxymethylpyrrolidin-1-yl)methyl]ferrocene, (*R*,*R*$_p$)-26. To a degassed solution of (*R*,*R*$_p$)-**25** (250 mg, 0.728 mmol) and sodium iodide (220 mg, 1.47 mmol) in acetonitrile (10 mL) was added dropwise at rt chloro-

trimethylsilane (230 μL, 1.80 mmol). The resulting suspension was stirred for 5 min before pyrazole (139 mg, 2.04 mmol) was added. After stirring the reaction mixture at rt for 16 h, water (10 mL) was added and the pH was adjusted with aqueous NaOH to about 10. The aqueous phase was extracted with dichloromethane (3 × 20 mL), and the combined organic phases were washed with brine and dried over $MgSO_4$. The solvents were removed under reduced pressure, and the residue was purified by chromatography. A mixture of petroleum ether and ethyl acetate in a ratio of 1:1 eluted byproducts, while elution with petroleum ether, ethyl acetate, and ethanol (45:45:10) gave product (*R*,R_p)-**26** (213 mg, 0.542 mmol, 74% yield) as an orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.52−1.73 (m, 3H, NCH_2CH_2 + NCHCH*H*), 1.78−1.89 (m, 1H, NCHC*H*H), 2.17−2.26 (m, 1H, NCH*H*CH_2), 2.57−2.65 (m, 1H, NC*H*CH_2), 2.91−2.97 (m, 1H, NC*H*HCH_2), 3.22, 3.32 (AB-part of an ABX system, J_{AB} = 9.3 Hz, J_{AX} = 6.3 Hz, J_{BX} = 5.2 Hz, 2H, $CHCH_2OCH_3$), 3.30 (s, 3H, OCH_3), 3.34, 3.72 (AB, *J* = 13.4 Hz, 2H, Cp(C3)CH_2N), 4.10 (s, 5H, Cp′), 4.18−4.20 (m, 1H, Cp-H4), 4.20−4.22 (m, 1H, Cp-H5), 4.32 (br t, 1H, Cp-H2), 5.00, 5.04 (AB, *J* = 14.4 Hz, 2H, Cp-(C1)CH_2N), 6.21 (dd, J_1 = J_2 = 2.0 Hz, 1H, NNCHC*H*), 7.34 (d, *J* = 2.0 Hz, 1H, NNCHCHC*H*), 7.48 (d, *J* = 2.0 Hz, 1H, NNCH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.7 (NCH_2CH_2), 28.5 ($NCHCH_2$), 51.6 (Cp(C1)CH_2N), 54.1 (Cp(C3)CH_2N), 54.5 (NCH_2CH_2), 59.1 (OCH_3), 62.1 ($NCHCH_2$), 68.7 (Cp-C5), 69.3 (5C, Cp′), 70.5 (Cp-C4), 70.9 (Cp-C2), 76.4 ($CHCH_2O$), 83.0 (Cp-C_q), 105.3 (NNCHCH), 128.3 (NNCHCHCH), 138.8 (NNCH), 1 Cp-C_q not observed. MS (80 °C) *m*/*z* (%): 393 (10) [M^+], 279 (100), 236 (34), 211 (46), 121 (32), 91 (43). HRMS: calcd for $C_{21}H_{27}FeN_3O$ 393.1504, found 393.1512. $[\alpha]_\lambda^{20}$ (nm): +44.3 (589), +45.1 (578), +46.5 (546) (*c* 0.548, $CHCl_3$).

(S_p)-1-Bromo-2-hydroxymethyl-5-(*N*,*N*-dimethylamino)methylferrocene, (S_p)-43. From **40**: To a degassed solution of (R_p)-**40** (750 mg, 2.233 mmol) in THF (15 mL) was added dropwise at −78 °C Li-TMP in THF/hexane (0.7 M, 6.4 mL, 4.48 mmol). The reaction mixture was stirred for 30 min at −78 °C and 3 h at −30 °C. After lowering the temperature again to −78 °C dimethylformamide (520 μL, 6.7 mmol) was added dropwise, and the reaction mixture was subsequently stirred for 30 min at −78 °C and 30 min at 0 °C. The reaction was quenched with water (15 mL) before diethyl ether was added. The phases were separated, and the aqueous phase was extracted three times with diethyl ether. The organic phases were combined and washed with brine. After drying over $MgSO_4$ and removal of the solvents under reduced pressure, the residue was dissolved in ethanol (15 mL) and $NaBH_4$ (125 mg, 3.30 mmol) was added at rt. After stirring for 16 h at rt, water (15 mL) was added and ethanol was removed under reduced pressure. The remaining aqueous phase was extracted with diethyl ether (3 ×), the combined organic phases were dried over $MgSO_4$, and the solvents were removed under reduced pressure. The residue was dissolved in diethylamine (10 mL), and the solution was stirred for 16 h at rt. Diethylamine was removed under reduced pressure, and immediately afterward the residue was purified by chromatography on alumina. A mixture of petroleum ether and ethyl acetate (5:1) followed by a mixture of petroleum ether, ethyl acetate, and ethanol (15:5:1) eluted product (S_p)-**43** (681 mg, 1.934 mmol, 87% yield) as an orange oil.

From **46**: A solution of (S_p)-**46** (1.638 g, 4.477 mmol) in diethylamine (40 mL) was stirred at rt for 16 h. Diethylamine was removed under reduced pressure, and immediately afterward the residue was purified by chromatography on alumina. A mixture of petroleum ether and ethyl acetate in a ratio of 1:1 followed by a mixture of petroleum ether, ethyl acetate, and triethylamine (50:50:1) eluted product (S_p)-**43** (1.40 g, 3.977 mmol, 89% yield) as an orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.89 (br s, 1H, OH), 2.23 (s, 6H, $N(CH_3)_2$), 3.36, 3.48 (AB, *J* = 13.1 Hz, 2H, $CH_2N(CH_3)_2$), 4.11 (s, 5H, Cp′), 4.27 (d, *J* = 2.8 Hz, 1H, Cp-H4), 4.29 (d, *J* = 2.8 Hz, 1H, Cp-H3), 4.41, 4.58 (AB, *J* = 12.4 Hz, 2H, CH_2OH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 45.0 (2C, $N(CH_3)_2$), 57.1 ($CH_2N(CH_3)_2$), 60.0 (CH_2OH), 66.7 (Cp-C3), 68.0 (Cp-C4), 71.4 (5C, Cp'), 82.6, 83.0, 85.9 (3 Cp-C_q). MS (30 °C) *m*/*z* (%): 353/351 (40) [M^+], 309/307 (10), 155 (41), 134 (33), 84 (100). HRMS: calcd for $C_{14}H_{18}BrFeNO$ 350.9923, found 350.9945. $[\alpha]_\lambda^{20}$ (nm): −35.7 (589), −38.1 (578), −52.5 (546) (*c* 0.465, $CHCl_3$).

(S_p)-[1-Bromo-2-hydroxycarbonyl-5-(*N*,*N*-dimethylamino)-methylferrocene]trihydroboron, (S_p)-47. To a degassed solution of (R_p)-**40** (1 g, 2.977 mmol) in THF (30 mL) was added dropwise at −78 °C Li-TMP in THF/hexane (0.7 M, 5.1 mL, 3.57 mmol). The reaction mixture was stirred for 30 min at −78 °C and 3 h at −30 °C. The reaction mixture was poured on ground dry ice (30 g) and stirred for 1 h. To this solution was added water (70 mL) and ethyl acetate (100 mL). The phases were separated, and the organic phase was extracted with water. The combined aqueous phases were extracted once with diethyl ether (50 mL) and were acidified with H_3PO_4 (50%) to pH 4. The aqueous phase was extracted with dichloromethane (4 × 50 mL), and the combined dichloromethane phases were washed once with brine (30 mL) and were dried over $MgSO_4$. Removal of the solvents under reduced pressure afforded crude (S_p)-**47** (1.007 g, 2.65 mmol, 89% yield) as a glassy yellow powder, which was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.4−2.2 (br s, 3H, BH_3), 2.51 (s, 3H, $N(CH_3)_2$-A), 2.57 (s, 3H, $N(CH_3)_2$-B), 3.92, 4.22 (AB, *J* = 14.1 Hz, 2H, CH_2), 4.30 (s, 5H, Cp′), 4.77 (d, *J* = 2.9 Hz, 1H, Cp-H4), 5.04 (d, *J* = 2.8 Hz, 1H, Cp-H3), COOH not observed. ^{13}C NMR (100 MHz, $CDCl_3$): δ 49.7 ($N(CH_3)_2$-A), 50.9 ($N(CH_3)_2$-B), 61.2 (CH_2), 71.0 (Cp-C3), 73.3 (Cp-C4), 73.7 (5C, Cp′), 62.2, 81.3, 81.7 (3 Cp-C_q), 175.2 (COOH). MS (80 °C) *m*/*z* (%): 381/379 (35) [M^+], 367/365 (35), 323/321 (15), 255 (27), 241 (23), 169 (38), 57 (100). HRMS: calcd for $C_{14}H_{19}BBrFeNO_2$ 379.0046, found 378.9885. $[\alpha]_\lambda^{20}$ (nm): −4.2 (589), −3.4 (578) (*c* 0.377, $CHCl_3$).

(S_p)-[1-Bromo-2-methoxycarbonyl-5-(*N*,*N*-dimethylamino)-methylferrocene]trihydroboron, (S_p)-48. To a solution of (S_p)-**47** (503 mg, 1.324 mmol) in dichloromethane (20 mL) and methanol (2 mL) was added at rt a solution of CH_2N_2 in diethyl ether (1 M, 2.5 mL, 2.5 mmol), and stirring was continued for 30 min. The solvents were removed under reduced pressure, and the residue was purified by chromatography on alumina. A mixture of petroleum ether and ethyl acetate (7:3) as the eluent afforded (S_p)-**48** (418 mg, 1.061 mmol, 80% yield) as a yellow solid.

Mp: 145−148 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35−2.20 (br s, 3H, BH_3), 2.49 (s, 3H, $N(CH_3)_2$-A), 2.54 (s, 3H, $N(CH_3)_2$-B), 3.88 (s, 3H, OCH_3), 3.90, 4.21 (AB, *J* = 14.0 Hz, 2H, CH_2), 4.24 (s, 5H, Cp'), 4.70 (d, *J* = 2.9 Hz, 1H, Cp-H4), 4.94 (d, *J* = 2.9 Hz, 1H, Cp-H3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 49.6 ($N(CH_3)_2$-A), 50.8 ($N(CH_3)_2$-B), 51.9 (OCH_3), 61.2 (CH_2), 70.4 (Cp-C3), 72.6 (Cp-C4), 73.3 (5C, Cp′), 80.5, 81.4 (2 Cp-C_q), 1 Cp-C_q + CO-C_q not observed. MS (80 °C) *m*/*z* (%): 393/395 (12) [M^+], 381/379 (35), 367/365 (35), 323/321 (15), 255 (27), 241 (23), 169 (38), 57 (100). HRMS: calcd for $C_{15}H_{21}BBrFeNO_2$ 393.0203, found 393.0185. $[\alpha]_\lambda^{20}$ (nm): −2.2 (589), −0.2 (578), +4.2 (546) (*c* 0.499, $CHCl_3$).

(R_p)-1-Methoxycarbonyl-3-(*N*,*N*-dimethylamino)methylferrocene, (R_p)-53. To a solution of (S_p)-**48** (297 mg, 0.754 mmol) in methanol (60 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 420 μL, 2.87 mmol) and palladium on charcoal (10%, 0.015 mmol). The resulting suspension was hydrogenated in a Parr apparatus for 24 h at rt at a hydrogen pressure of 50 psi (3.45 bar). The suspension was flushed with argon, the catalyst was filtered off, and the solvent was removed under reduced pressure. The residue was purified by chromatography on alumina. Ethyl acetate

as the eluent afforded (R_p)-**53** (201 mg, 0.667 mmol, 89% yield) as a yellow solid.

Mp: 52−57 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.18 (s, 6H, $N(CH_3)_2$), 3.25, 3.30 (AB, J = 12.9 Hz, 2H, CH_2), 3.79 (s, 3H, OCH_3), 4.16 (s, 5H, Cp′), 4.41 (dd, J_1 = 2.4 Hz, J_2 = 1.3 Hz, 1H, Cp-H4), 4.77 (dd, J_1 = 2.4 Hz, J_2 = 1.3 Hz, 1H, Cp-H5), 4.82 (br t, J = 1.3 Hz, 1H, Cp-H2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 44.8 (2C, $N(CH_3)_2$), 51.5 (OCH_3), 58.8 (CH_2), 70.1 (Cp-C5), 70.2 (5C, Cp′), 72.0 (Cp-C2), 73.1 (Cp-C4), 70.9, 86.9 (2 Cp-C_q), 172.1 (CO-C_q). MS (50 °C) m/z (%): 301 (100) [M^+] 257 (83), 242 (32), 199 (20), 148 (33), 121 (45), 105 (69). HRMS: calcd for $C_{15}H_{19}FeNO_2$ 301.0765, found 301.0769. $[\alpha]_\lambda^{20}$ (nm): +60 (589), +69 (578), +133 (546) (c 0.124, $CHCl_3$).

X-ray Structure Determination. X-ray data for compound (R,S_p)-**8** were collected on a Bruker Smart APEX CCD area detector diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) and 0.3° ω-scan frames covering a complete sphere of the reciprocal space with θ_{max} = 30°. After data integration with the program SAINT+, corrections for absorption, $\lambda/2$ effects, and crystal decay were applied with the program SADABS.[41] The structure was solved by direct methods and refined on F^2 with the program suite SHELX97.[42] All non-hydrogen atoms were refined anisotropically. Most H atoms were placed in calculated positions and thereafter treated as riding. Crystal data: $C_{15}H_{21}FeNO$, M_r = 287.18, orthorhombic, space group $P2_12_12_1$ (no. 19), T = 173(2) K, a = 6.2478(4) Å, b = 10.4688(6) Å, c = 20.7139(12) Å, V = 1354.83(14) Å^3, Z = 4, μ = 1.101 mm^{-1}. Of 17 488 reflections collected, 3921 were independent; final R indices: R_1 = 0.0208 (all data), wR_1 = 0.0533 (all data). A view of the molecular structure with selected bond distances is shown in Figure 1. The O−H group donates a hydrogen bond to the amino nitrogen, O−N = 2.877(1) Å, thereby linking the molecules to give discrete chains parallel to the b-axis.

Supporting Information Available: Full experimental details for all compounds; CIF file of compound (R,S_p)-**8**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM7003282

(41) Bruker programs: *SMART*, version 5.629; *SAINT+*, version 6.45; *SADABS*, version 2.10; *SHELXTL*, version 6.14; Bruker AXS Inc.: Madison, WI, 2003.

(42) Sheldrick, G. M. *SHELX97*, Program System for Crystal Structure Determination; University of Göttingen: Göttingen, Germany, 1997.