Organometallics **2004,** *23,* 1991−1996 1991

Synthesis of Enantiopure Planar Chiral Bisferrocenes Bearing Sulfur or Nitrogen Substituents

Ramón Gómez Arrayás, Inés Alonso, Olga Familiar, and Juan Carlos Carretero*

Departamento de Química Orgánica, Facultad de Ciencias, Universidad Autónoma de Madrid, 28049 Madrid, Spain

Received January 29, 2004

A new procedure for the preparation of enantiopure planar chiral bisferrocenes bearing potentially metal-coordinating sulfur or nitrogen substituents is reported. The diastereoselective *ortho*-lithiation of enantiopure sulfinyl- or oxazolidinylferrocenes followed by treatment with nonenolizable esters leads in a one-pot operation to the corresponding bisferrocenyl carbinols. Due to the presence of a strong hydrogen bond between the hydroxyl group and one of the sulfinyl moieties, the pyrolysis of the bis(sulfinyl)bisferrocene **3a** in toluene at 110 °C takes place by selective removal of the non-hydrogen-bonded sulfoxide to afford in good yield a tetraferrocene disulfide derivative. Interesting structural information for these novel bi- and tetraferrocenes, deduced by NMR and X-ray crystallography, is also discussed.

Introduction

Since the pioneering work of Hayashi and Kumada in 1974 on the synthesis of the first chiral ferrocenyl phosphine,[1] the planar chiral 1,2-disubstituted ferrocene unit has become one of the most useful backbones in the design of new ligands for enantioselective catalysis.[2] More recently this interest has been extended to the synthesis of enantiopure species with bisferrocene structure. Among these, the diphosphine PhTRAP, developed by Ito et al.,[3] the triphosphine Pigiphos, described by Togni et al.,[4] the bis azaferrocene **I**, developed by Fu et al.,[5] and the bisPPFOMe reported by Hayashi[6] have proved to be very efficient ligands in a variety of metal-mediated enantioselective processes[7,8] (Figure 1).

We report herein that enantiopure hydroxymethyl bisferrocenes having potentially metal-coordinating sulfur or nitrogen substituents at the cyclopentadienyl ring are readily synthesized in a one-step procedure by diastereoselective *ortho*-lithiation of enantiomerically pure sulfinylferrocenes or oxazolidinyl ferrocenes, followed by addition of a nonenolizable ester.

Results and Discussion

In 1993 Kagan et al. described that the *ortho*-lithiation of the readily available (*R*)-*tert*-butylsulfinylferrocene (**1**) is controlled by the sulfinyl group, occur-

---

* Corresponding author. Fax: +34 91 4973966. E-mail: juancarlos.carretero@uam.es.

(1) For recent reviews, see: (a) Hayashi, T.; Yamamoto, K.; Kumada, M. *Tetrahedron Lett.* **1974**, 4405. See also: (b) Hayashi, T.; Mise, T.; Fukushima, M.; Kagotani, M.; Nagashima, N.; Hamada, Y.; Matsumoto, A.; Kawakami, S.; Konishi, M.; Yamamoto, K.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1138.

(2) (a) Dai, L.-X.; Tu, T.; You, S.-L.; Deng, W.-P.; Hou, X.-L. *Acc. Chem. Res.* **2003**, *36*, 659. (b) Togni, A.; Bieler, N.; Burckhardt, U.; Köllner, C.; Pioda, G.; Schneider, R.; Schnyder, A. *Pure Appl. Chem.* **1999**, *71*, 1531. (c) Togni, A. In *Metallocenes*; Togni, A., Halterman, R. L., Eds.; Wiley-VCH: Weinheim, Germany, 1998; Vol. 2, Chapter 10. (d) Richards, C. J.; Locke, A. J. *Tetrahedron: Asymmetry* **1998**, *9*, 2377. (e) Hayashi, T. In *Ferrocenes*; Togni, A., Hayashi, T., Eds.; VCH: Weinheim, Germany, 1995; Chapter 2.

(3) For a review, see: (a) Ito, Y.; Kuwano, R. *Phosphorus, Sulfur Silicon Relat. Elem.* **1999**, *144−146*, 469. See also: (b) Kuwano, R.; Sato, K.; Kurokawa, T.; Karube, D.; Ito, Y. *J. Am. Chem. Soc.* **2000**, *122*, 7614. (c) Kuwano, R.; Uemura, T.; Saitoh, M.; Ito, Y. *Tetrahedron Lett.* **1999**, *40*, 1327. (d) Sawamura, M.; Sudo, M.; Ito, Y. *J. Am. Chem. Soc.* **1996**, *118*, 3309. (e) Goeke, A.; Sawamura, M.; Kuwano, R.; Ito, Y. *Angew. Chem., Int. Ed.* **1996**, *35*, 662. (f) Sawamura, M.; Kuwano, R.; Ito, Y. *J. Am. Chem. Soc.* **1995**, *117*, 9602. (g) Sawamura, M.; Hamashima, H.; Shinoto, H.; Ito, Y. *Tetrahedron Lett.* **1995**, *36*, 6479. (h) Sawamura, M.; Hamashima, H.; Ito, Y.; *Tetrahedron* **1994**, *50*, 4439. (i) Sawamura, M.; Hamashima, H.; Ito, Y. *J. Am. Chem. Soc.* **1992**, *114*, 8295.

(4) (a) Fadini, L.; Togni, A. *Chem. Commun.* **2003**, 30. (b) Barbaro, P.; Togni, A. *Organometallics* **1995**, *14*, 3570. See also: (c) Barbaro, P.; Bianchini, C.; Togni, A. *Organometallics* **1997**, *16*, 3004.

(5) (a) Shintani, R.; Fu, G. C. *Angew. Chem., Int. Ed.* **2003**, *42*, 4082. (b) Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 4572. (c) Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 10270. (d) Lo, M. M.-C.; Fu, G. C. *Tetrahedron* **2001**, *57*, 2621.

(6) (a) Han, J. W.; Tokunaga, N.; Hayashi, T. *Helv. Chim. Acta* **2002**, *85*, 3848. (b) Han, J. W.; Tokunaga, N.; Hayashi, T. *J. Am. Chem. Soc.* **2001**, *123*, 12915.

(7) For other bisferrocene-based chiral ligands in asymmetric catalysis, see: (a) Xiao, L.; Weissensteiner, W.; Mereiter, K.; Widhalm, M. *J. Org. Chem.* **2002**, *67*, 2206. (b) Tanaka, Y.; Taniguchi, N.; Kimura, T.; Uemura, M. *J. Org. Chem.* **2002**, *67*, 9227. (c) You, S.-L.; Hou, X.-L.; Dai, L.-X.; Zhu, X.-Z. *Org. Lett.* **2001**, *2*, 149. (d) Xiao, L.; Mereiter, K.; Spindler, F.; Weissensteiner, W. *Tetrahedron: Asymmetry* **2001**, *12*, 1105. (e) Nettekoven, U.; Widhalm, M.; Kalchhauser, H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Lutz, M.; Spek, A. L. *J. Org. Chem.* **2001**, *66*, 759. (f) Longmire, J. M.; Wang, B.; Zhang, X. *Tetrahedron Lett.* **2000**, *41*, 5435. (g) You, S.-L.; Hou, X.-L.; Dai, L.-X.; Cao, B.-X.; Sun, J. *Chem. Commun.* **2000**, 1933. (h) Kim, S.-G.; Cho, C.-W.; Ahn, K. H. *Tetrahedron* **1999**, *55*, 10079. (i) Larsen, A. O.; Taylor, R. A.; White, P. S.; Gagné, M. R. *Organometallics* **1999**, *18*, 5157. (j) Song, J.-H.; Cho, D.-J.; Jeon, S.-J.; Kim, Y.-H.; Kim, T.-J.; Jeong, J. H. *Inorg. Chem.* **1999**, *38*, 893. (k) Cho, D.-J.; Jeon, S.-J.; Kim, H.-S.; Cho, C.-S.; Shim, S.-C.; Kim, T.-J. *Tetrahedron: Asymmetry* **1999**, *10*, 3833. (l) Kim, S.-G.; Cho, C.-W.; Ahn, K. H. *Tetrahedron: Asymmetry* **1997**, *8*, 1023. (m) Riant, O.; Sammuel, O.; Flenner, T.; Taudien, S.; Kagan, H. B. *J. Org. Chem.* **1997**, *62*, 6733. For recent examples on nonchiral bisferrocene-based ligands, see: (n) Dong, T.-Y.; Huang, B.-R.; Lin, M.-C.; Chiang, M. Y. *Polyhedron* **2003**, 1199. (o) Salo, E. V.; Guan, Z. *Organometallics* **2003**, *22*, 5033. (p) Horikoshi, R.; Mochida, T.; Torigoe, R.; Yamamoto, Y. *Eur. J. Inorg. Chem.* **2002**, 3197.

(8) For chiral triferrocenes as ligands in enantioselective catalysis, see: (a) Ganter, C.; Kaulen, C.; Englert, U. *Organometallics* **1999**, *18*, 5444. See also: (b) Ganter, C.; Glinsböckel, C.; Ganter, B. *Eur. J. Inorg. Chem.* **1998**, 1163.

10.1021/om049924b CCC: $27.50

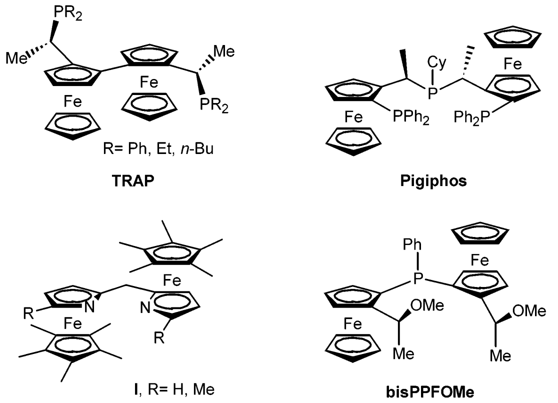
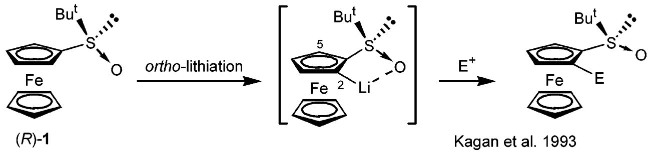


Figure 1. Relevant bisferrocenes used in enantioselective catalysis.

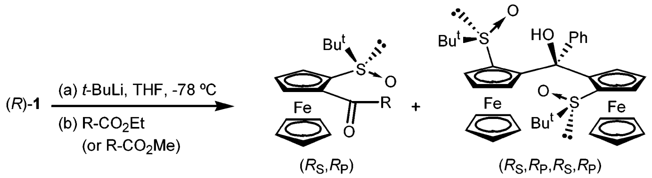
Scheme 1



ring with complete selectivity at C-2 (and not at C-5).[9] After addition of an appropriate electrophile, planar chiral 1,2-disubstituted ferrocenes were isolated in high yields (Scheme 1). By using this methodology several groups,[10] including ours,[11] have reported a variety of new types of planar chiral ferrocenes. Surprisingly, however, the reaction of lithiated sulfinyl ferrocenes with esters, which could be a quite simple alternative to the synthesis of chiral bisferrocene structures, to our best knowledge, has not been previously described.

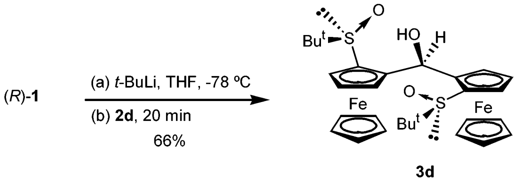
Gratifyingly, deprotonation of (*R*)-**1** with *t*-BuLi (1.2 equiv) in THF at −78 °C, followed by addition of ethyl benzoate (1.2 equiv, −78 °C), afforded cleanly the hydroxymethyl bisferrocene **3a** as an air-stable red crystalline solid in 88% yield with ee > 99.5% (HPLC, Chiralcel OD column). The intermediate ketone **2a** was not detected in the ^{1}H NMR spectrum of the crude reaction mixture. To examine the influence of the electronic nature of the aromatic ester in this bisferrocene synthesis,[12] we extended the reaction to both electron-rich and electron-deficient substituted benzoates (Scheme 2). Interestingly, while the methyl *p*-methoxybenzoate provided the bisferrocene **3b** as the only product in 72% isolated yield, the ethyl *p*-nitrobenzoate afforded exclusively the intermediate ketone **2c**

Scheme 2



R = Ph,	**2a**, ---	**3a**, 85%
R = (*p*-OMe)C$_6$H$_4$,	**2b**, ---	**3b**, 72%
R = (*p*-NO$_2$)C$_6$H$_4$,	**2c**, 78%	**3c**, ---
R = H,	**2d**, 71%	**3d**, ---
R = Et	----	----

Scheme 3



3d

(78% yield). On the other hand, in the case of using ethyl formate as an example of an unhindered ester, the corresponding carbonyl intermediate, which is the aldehyde **2d**, was also selectively obtained as previously reported by Hua.[10d] These results from ethyl *p*-nitrobenzoate and ethyl formate suggest that in both cases the sp^3 hemiketal intermediate, resulting from the initial addition of the *ortho*-lithiated ferrocene, is not able to evolve into the carbonyl derivative under these very mild conditions (THF, −78 °C). However, the bisferrocenyl carbinol **3d** was cleanly obtained by further addition of *ortho*-lithiated (*R*)-**1** to the aldehyde **2d** (Scheme 3). Not unexpectedly the acylation reaction failed in the case of esters having acidic hydrogens at the α-position such as ethyl acetate, which provided a complex reaction mixture.

The bisferrocene structure of compounds **3** was firmly established by NMR and mass spectrometry studies and unequivocally confirmed by X-ray diffraction analysis of **3a** (Figure 2).[13] Single crystals of **3a** were obtained at 4 °C by slow evaporation of a dichloromethane solution of this compound in a hexane bath. Relevant information from the crystal structure of **3a** is the presence of a seven-membered hydrogen bond between the hydroxyl group and one of the sulfinylic oxygens. The SO···H distance is 1.87(4) Å, remarkably shorter than the sum of the van der Waals radii[14] for H and O. The O···H−O angle (θ) is near-linear (171°), and the directionality at the atom acceptor is appropriate[15] (S−O···H angle (ϕ) = 115°). The length of the S−O bond that participates in the hydrogen bond (S(1)−O(1) distance = 1.502(2) Å) agrees with those reported for similar cases[16] and is only slightly longer than that of

---

[9] (a) Rebière, F.; Riant, O.; Ricard, L.; Kagan, H. B. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 568. See also: (b) Riant, O.; Argouarch, G.; Guillaneux, D.; Samuel, O.; Kagan, H. B. *J. Org. Chem.* **1998**, *63*, 3511. (c) Diter, P.; Samuel, O.; Taudien, S.; Kagan, H. B. *Tetrahedron: Asymmetry* **1994**, *5*, 549.

[10] (a) Pedersen, H. L.; Johannsen, M. *J. Org. Chem.* **2002**, *67*, 7982. (b) Lotz, M.; Polborn, K.; Knochel, P. *Angew. Chem., Int. Ed.* **2002**, *41*, 4708. (c) Bolm, C.; Kuhn, T. *Isr. J. Chem.* **2002**, *41*, 263. (d) 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.

[11] (a) García Mancheño, O.; Priego, J.; Cabrera, S.; Gómez Arrayás, R.; Llamas, T.; Carretero, J. C. *J. Org. Chem.* **2003**, *68*, 3679. (b) Priego, J.; García Mancheño, O.; Cabrera, S.; Carretero, J. C. *J. Org. Chem.* **2002**, *67*, 1346.

[12] For the synthesis of bis(sulfinyl)bisferrocene using a different approach, see: (a) Jensen, J. F.; Søtofte, I.; Sørensen, H. O.; Johannsen, M. *J. Org. Chem.* **2003**, *68*, 1258. (b) Cotton, H. K.; Huerta, F. F.; Backvall, J.-E. *Eur. J. Org. Chem.* **2003**, 2756. (c) Xiao, L.; Mereiter, K.; Spindler, F.; Weissensteiner, W. *Tetrahedron: Asymmetry* **2001**, *12*, 1105.

[13] Crystal structure data for $C_{35}H_{40}Fe_2O_3S_2$ (**3a**): crystal size 0.18 × 0.12 × 0.08 mm^3, orthorhombic, space group $P2_12_12_1$, $a = 12.09610(10)$ Å, $b = 16.29880(10)$ Å, $c = 16.5371(2)$ Å, $V = 3260.32(5)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.394$ Mg m^{-3}, $\mu = 8.591$ mm^{-1}, $2\theta_{max} = 140.8°$, 6035 reflections collected. Refinement on F^2 for 6035 reflections and 527 parameters gave GOF = 1.041, R1 = 0.0281 and wR2 = 0.0699 for $I > 2\sigma(I)$. Absolute structure parameter = −0.006(3). Residual electron density $-0.215 < \Delta\rho < 0.346$ eÅ^{-3}.

[14] Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441 (van der Waals radii values: H = 1.20 Å, O = 1.52 Å, S = 1.80 Å).

[15] (a) Platts, J. A.; Howard, S. T.; Bracke, B. R. F. *J. Am. Chem. Soc.* **1996**, *118*, 2726. (b) Hay, B. P.; Dixon, D. A.; Bryan, J. C.; Moyer, B. A. *J. Am. Chem. Soc.* **2002**, *124*, 182.

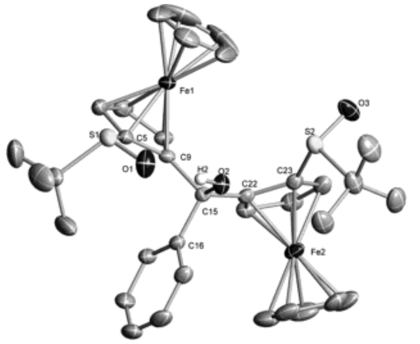


Figure 2. ORTEP plot for **3a** (30% thermal ellipsoids) showing the atomic numbering of selected atoms. The hydrogen atoms, except H(2), have been omitted for clarity. Selected bond lengths (Å) and angles (deg): C(15)−O(2), 1.412(3); C(15)−C(9), 1.539(3); C(15)−C(22), 1.523(3); S(1)−O(1), 1.502(2); S(2)−O(3) 1.495(2); O(2)−C(15)−C(9), 112.24(17); O(2)−C(15)−C(22), 105.36(18); O(1)−H(2)−O(2), 172(4); O(1)−S(1)−C(5)−C(9), 0.3(3); O(3)−S(2)−C(23)−C(22), −134.3(2).

the non-hydrogen-bonded sulfoxide [S(2)−O(3) distance = 1.495(2) Å], also lengthened with respect to typical aryl alkyl sulfoxides.[9a,17] On the other hand, the O(2)···S(2) distance (2.90 Å) is shorter than the sum of the van der Waals radii[14] for O and S, which suggests the presence of a stabilizing donor−acceptor interaction between them. This kind of interaction had been previously proposed from conformational studies on β-oxygenated sulfoxides[18] and has also been observed in the solid state of other hydroxy sulfoxides.[19] This interaction, along with the hydrogen bond, imposes **3a** to adopt a very congested conformation in the solid state (the sulfinyl group on Fc(2) is 0.54 Å out of the plane of the cyclopentadienyl ring), in which both ferrocene units are oriented opposite each other. This can be easily quantified by measuring the improper dihedral angle (T) formed by the centroids of each cyclopentadienyl ring. The usual value for this angle in related Fc−C−Fc systems[20] is in the range 80−110°, while in **3a** this angle is much higher (147°). Interestingly, both ferrocene units are surrounded by quite different environments. Thus, the phenyl ring at C15 is placed just in front of one of the ferrocene moieties [Fe(2)], but in nearly *anti* arrangement with regard to the other one [Fe(1)]. On the other hand, the *tert*-butyl group on Fc(1) is pointed away from the Fe(1), whereas the equivalent group on Fc(2) is directed toward the Fe(2) atom.

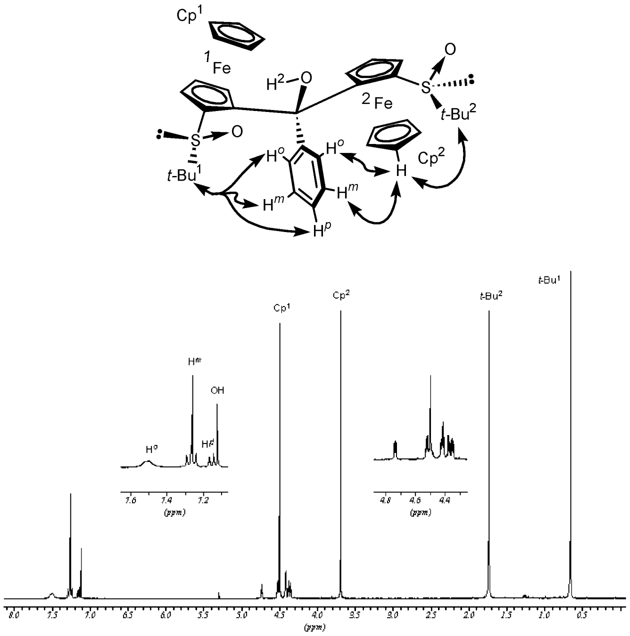


Figure 3. ^{1}H NMR spectrum of bisferrocene **3a** and significant NOE cross-peaks.

To establish whether the conformation of the bisferrocene **3a** in solution is similar to that observed in the solid state, we investigated compound **3a** by one- and two-dimensional NMR in CDCl$_3$. The quite outstanding differences in the chemical shifts of the two *tert*-butyl groups (singlets at 0.62 and 1.70 ppm) and the unsubstituted Cp rings (singlets at 3.68 and 4.48 ppm) indicate that both ferrocene units are in very different environments (Figure 3). In good accordance with the X-ray structure, the protons of the *tert*-butyl group of ferrocene 1 (t-Bu^1, 0.62 ppm) and those of the unsubstituted Cp-ring of ferrocene 2 (Cp^2, 3.68 ppm) appear greatly shielded compared to the expected chemical shifts of such protons in related systems (typically around 1.0 and 4.5 ppm, respectively). This remarkable effect, likely caused by the cone anisotropy effect of the phenyl ring, suggests that complex **3a** adopts in solution a major conformation with the phenyl group situated between t-Bu^1 and Cp^2. Similarly, the high deshielding of the *tert*-butyl group of ferrocene 2 (t-Bu^2, 1.70 ppm), which is above the aromatic ring, can also be explained invoking the same cone anisotropy effect of the phenyl moiety. The intramolecular hydrogen bond between the hydroxyl group and the sulfinylic oxygen at ferrocene 1 is also evident in the ^{1}H NMR spectra by the presence of a singlet at 7.12 ppm. In full agreement with the previous discussion, 2D NOESY experiments revealed strong NOE cross-peaks of the protons on t-Bu^1 with the *ortho*-, *metha*-, and *para*-protons of the phenyl group (H^o, H^m, and H^p) and the hydroxyl proton H^2, while t-Bu^2 showed NOE contacts with the *ortho* protons H^o (not with H^m or H^p), H^2 and Cp^2. The NOE cross signals of Cp^2 with H^o and H^m, along with the absence of NOE between the protons on the phenyl group and Cp^1, were also structurally relevant. All these NMR spectroscopic data strongly support for **3a** a conformation in solution very similar to that observed in the crystal.

The presence of the S−O(1)···H(2) hydrogen bond produced also some unexpected chemical consequences. Thus, when compound **3a** was treated under typical

---

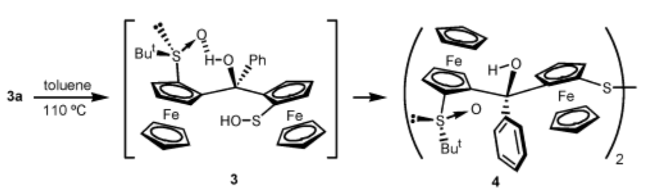
(16) For an example of an intramolecular hydrogen bond involving a sulfoxide and a hydroxy group in a seven-membered ring see: Aversa, M. C.; Baratucci, A.; Bonaccorsi, P.; Bonini, B. F.; Giannetto, P.; Nicolo, F. *Tetrahedron: Asymmetry* **1999**, *10*, 3919.

(17) See for example: (a) Banziger, M.; Klein, S.; Rihs, G. *Helv. Chim. Acta* **2002**, *85*, 1399. (b) Alonso, I. López-Solera, I. Raithby, P. R. *Acta Crystallogr., Sect. C* **1996**, *52*, 1548. (c) Casarini, D.; Lunazzi, L.; Gasparrini, F.; Villani, C.; Cirilli, M.; Gavuzzo, E. *J. Org.Chem.* **1995**, *60*, 97.

(18) Carreño, M. C.; Carretero, J. C.; García Ruano, J. L.; Rodríguez, J. H. *Tetrahedron* **1990**, *46*, 5649, and references therein.

(19) Abe, H.; Tsuchida, D.; Kashino, S.; Takeuchi, Y.; Harayama. T. *Chem. Pharm. Bull.* **1999**, *47*, 833.

(20) (a) Diferrocenyl(phenyl)methanol: Glidewell, C.; Klar, R. B.; Lightfoot, P.; Zakaria, C. M.; Ferguson, G. *Acta Crystallogr., Sect.* B: Struct. Sci. **1996**, *52*, 110. (b) 1,1′-Bis(ferrocenyl)-2,2′-dimethylpropan-1-ol: Sharma, H. K.; Cervantes-Lee, F.; Pannell, K. H. *J. Organomet. Chem.* **1992**, *438*, 183. (c) Diferrocenylmethanol: Ferguson, G.; Glidewell, C.; Opromolla, G.; Zakaria, C. M.; Zanello, P. *J. Organomet. Chem.* **1996**, *517*, 183.



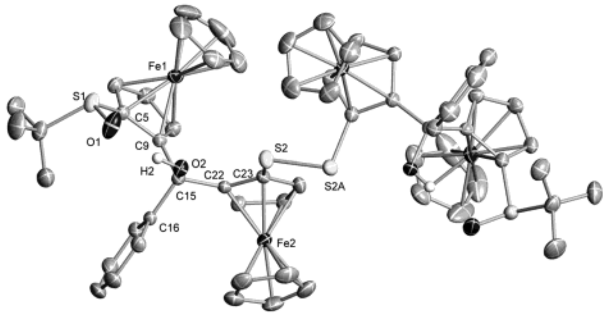


Figure 4. ORTEP plot for **4** (30% thermal ellipsoids) showing the atomic numbering of selected atoms. The hydrogen atoms, except H(2), have been omitted for clarity. Selected bond lengths (Å) and angles (deg): C(15)−O(2), 1.408(3); C(15)−C(22), 1.520(3); C(15)−C(9), 1.544(3); S(1)−O(1), 1.495(2); S(2)−S(2A), 2.0538(13); O(2)−C(15)−C(22), 105.51(18); O(2)−C(15)−C(9), 112.33(18); O(1)−H(2)−O(2), 167.6; O(1)−S(1)−C(5)−C(9), 5.5(3); C(22)−C(23)−S(2)−S(2A), 164.31(19).

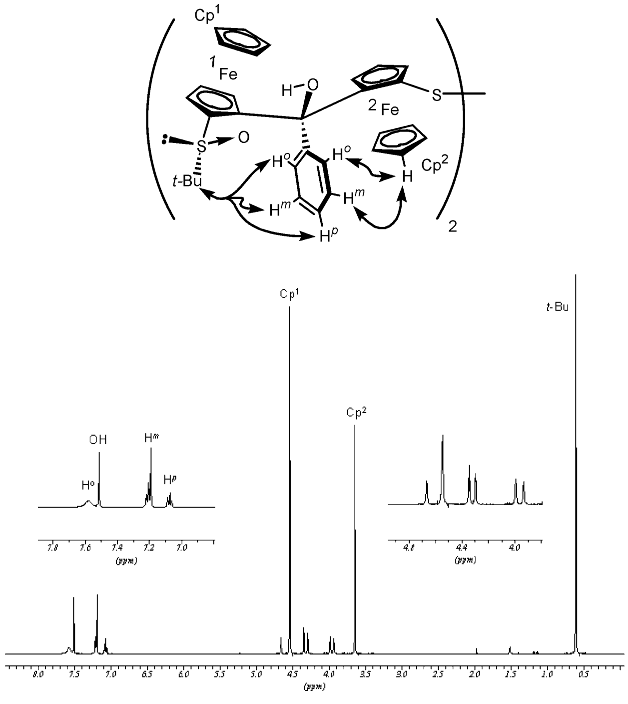
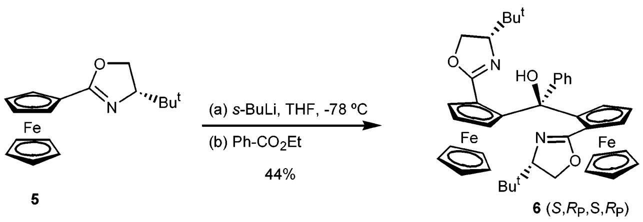


Figure 5. ^{1}H NMR spectrum of **4** and relevant NOE cross-peaks.

sulfoxide-pyrolysis conditions (heating in toluene at 110 °C for 2.5 h), only the nonassociated sulfinyl group reacted, affording in reasonable yield (64%) the tetraferrocenyl disulfide **4**, resulting presumably from the dimerization of the unstable sulfenic acid intermediate **3** (Scheme 4). The structure of **4** was elucidated by ^{1}H NMR and mass spectrometry [(M^+) + H = 1222, determined by FAB] and unequivocally confirmed by X-ray crystallography (Figure 4).[21] As shown in Figure 4 compound **4** shows a C_2 axis (there is only half a structure in the asymmetric crystallographic unit) and the ferrocene units adopt a conformation very similar to that of the precursor **3a**.

Scheme 4



In accordance with this crystal structure, the ^{1}H NMR spectrum of **4** (Figure 5) shows the disappearance of the deshielded signal of the *tert*-butyl group at ferrocene 2 (*t*-Bu^2 in the precursor **3a**) and the presence of shielded singlets for the remaining *tert*-butyl group of the sulfoxide at ferrocene 1 and the unsubstituted Cp at ferrocene 2 (0.62 and 3.68 ppm, respectively). The intramolecular hydrogen bond between the hydroxyl group and the sulfinylic oxygen is also detected by a deshielded singlet at 7.51 ppm. On the other hand, the ^{1}H−NOESY spectra of **4** clearly shows the spatial closeness of the phenyl group to both *t*-Bu and Cp^2 groups (see Figure 5). As far as we know, this is the first example of an enantiopure tetraferrocene reported to date.[22]

Interestingly, this simple procedure for the synthesis of bisferrocenes can also be applied to compounds containing chiral nitrogen substituents, such as oxazolidines, which constitute one of the most popular chiral moieties currently used in enantioselective catalysis.[23] Thus, the synthesis of the (S,R_p,S,R_p)-bis(oxazolidinyl)-bisferrocene **6** was accomplished in a manner similar to that for bisferrocenes **3**. Starting from (*S*)-*tert*-butyloxazolidinylferrocene **5**, which was readily obtained from ferrocenecarboxylic acid[24] according to reported procedures,[25] its diastereoselective *ortho*-lithiation with *s*-BuLi (THF, −78 °C) followed by in situ treatment with ethyl benzoate afforded the bis(oxazolidinyl)bisferrocene **6** as the main product (44% yield), along with 20% of the starting oxazolidine. In this *ortho*-lithiation process the use of *s*-BuLi as base seems to be essential, since attempts of *ortho*-lithiation with the

---

(21) Crystal structure data for $C_{62}H_{62}Fe_4O_4S_4$ (**4**): crystal size 0.20 × 0.16 × 0.14 mm^3, orthorhombic, space group $P2_12_12$, $a = 14.87200(10)$ Å, $b = 23.0986(2)$ Å, $c = 7.93910(10)$ Å, $V = 2727.26(5)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.489$ Mg m^{-3}, $\mu = 10.172$ mm^{-1}, $2\theta_{max} = 140.94°$, 17 645 reflections collected, 4994 independent. Refinement on F^2 for 4994 reflections and 338 parameters gave GOF = 1.056, R1 = 0.0277 and wR2 = 0.0734 for $I > 2\sigma(I)$. Absolute structure parameter = −0.012(3). Residual electron density $-0.182 < \Delta\rho < 0.259$ e Å^{-3}.

(22) For achiral or racemic tetraferrocenes, see for instance: (a) Denifl, P.; Hradsky, A.; Bildstein, B.; Wurst, K. *J. Organomet. Chem.* **1996**, *523*, 79. (b) Bildstein, B.; Schweiger, M.; Kopacka, H.; Wurst. K. *J. Organomet. Chem.* **1998**, *553*, 73. (c) Bildstein, B.; Skibar, W.; Schweiger, M.; Kopacka, H.; Wurst, K. *J. Organomet. Chem.* **2001**, *622*, 135.

(23) For recent reviews, see: (a) Rechari, D.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 3467. (b) Johnson, J. S.; Evans, D. A. *Acc. Chem. Res.* **2000**, *33*, 325. (c) Fache, F.; Schultz, E.; Tommasino, M. L.; Lemaire, M. *Chem. Rev.* **2000**, *100*, 2159. (d) Helmchen, G.; Pfaltz, A. *Acc. Chem. Res.* **2000**, *33*, 336. For chiral bis(oxazolidinyl)bisferrocenes in enantioselective catalysis, see refs 7g and 7k.

(24) Although ferrocenecarboxylic acid is commercially available, it can be readily prepared by carboxylation of lithiated ferrocene. See, for instance: Sorensen, H. S.; Larsen, J.; Rasmussen, B. S.; Laursen, B.; Hansen, S. G.; Skrysdstrup, T.; Amatore, C.; Jutand, A. *Organometallics* **2002**, *21*, 5243.

(25) Bolm, C.; Hermanns, N.; Kesselgruber, M.; Hildebrand, J. P. *J. Organomet. Chem.* **2001**, *624*, 157.

bulky *t*-BuLi resulted in the main recovery of the starting material. The structure of **6** was established by NMR and mass spectrometry, and its planar (*R*) configuration was inferred according to the reported stereoselectivity for *ortho*-lithiation of oxazolidinylferrocenes.[26]

In summary, enantiopure chiral planar bisferrocenes substituted with sulfur or nitrogen groups are readily prepared by selective *ortho*-lithiation of chiral sulfinylferrocenes and oxazolidinylferrocenes followed by reaction with nonenolizable esters. The study of these compounds and derivatives as chiral ligands in enantioselective catalysis is underway and will be reported in due course.

Experimental Section

NMR spectra were recorded on a Bruker AMX-300 spectrometer [300 MHz (^{1}H), 75 MHz (^{13}C)] at room temperature in $CDCl_3$ with internal $CHCl_3$ as the reference (7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C). NOESY spectra of **3a** and **4** were recorded at 27 °C on a Bruker AMX-300 and a Bruker DMX-500 MHz, respectively, the data being collected in phase applying the method noesytp. Mixing time for both NOESY spectra was 500 ms. IR spectra were recorded on a Bruker Vector 22 using KBr pellets. Picks are reported with the following intensities: s (strong, 67−100%), m (medium, 40−67%), w (weak, 20−40%), and br (broad). Melting points were taken in open capillary tubes on a Gallenkamp melting point apparatus. Optical rotations were measured at 25 °C with a Perkin-Elmer 241 MC polarimeter. THF, toluene, and dichloromethane were dried over microwave-activated 4 Å molecular sieves (1 week) before use. Esters were purchased from commercial sources and used as received. Single crystals of both compounds were grown by slow diffusion of hexane onto dichloromethane solutions. Data collections were carried out at room temperature on a Bruker Smart CCD diffractometer using graphite-monochromated Cu Kα (λ = 1.54178 Å) and the $2\theta/\omega$ scan method. Absorption correction method SADABS (v. 2.03) was applied. Both structures were solved by direct methods (SHELXS-97),[27] and the refinement was made by full-matrix least-squares on F^2 (SHELXL-97). Anisotropic parameters were used in the last cycle of refinement for all non-hydrogen atoms. For compound **3a** most of the hydrogen atoms have been found in the difference Fourier map. Only three of them [H(10), H(11), and H(12)] were included in calculated positions and refined riding on their respective carbon atoms with the thermal parameter related to the bonded atoms. For compound **4** all hydrogen atoms were included in calculated positions and refined riding on their respective bonded atoms with the related thermal parameter.

General Procedure for the Reaction of (*R*)-1 with Esters. To a solution of (*R*)-*tert*-butylsulfinyl ferrocene (*R*)-**1** (1.85 g, 6.39 mmol) in THF (60 mL), cooled to −78 °C, was added dropwise a 1.7 M solution of *t*-BuLi in pentane (4.5 mL, 7.41 mmol). The reaction mixture was stirred at −78 °C for 1.5 h, and then a solution of the corresponding ester (8.05 mmol) in THF (1 mL) was added and the reaction mixture was kept at −78 °C. Once the reaction was complete or no evolution was observed (monitored by TLC), brine was added (10 mL). The aqueous layer was extracted with AcOEt (2 × 20 mL). The combined organic layers were dried ($MgSO_4$), and the solvent was evaporated. The residue was purified by flash chromatography (element indicated below for each case).

[(R_S,R_P)-2-(*tert*-Butylsulfinyl)ferrocenyl] (*p*-Nitrophenyl) Ketone (2c). Following the general procedure, (*R*)-**1** (100 mg, 0.34 mmol) was treated with *t*-BuLi (1.7 M in pentane, 260 μL, 0.45 mmol) and ethyl *p*-nitrophenyl benzoate (67 mg, 0.34 mmol), affording after chromatographic purification (*n*-hexanes−EtOAc, 1:4) **2c** (118 mg, 78%) as a red solid: $[\alpha]_D$ +134 (*c* 0.03, $CHCl_3$); mp 135−136 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.28 (d, J = 8.6 Hz, 2H), 7.94 (d, J = 9.1 Hz, 2H), 4.86 (s, 1H), 4.68 (s, 2H), 4.48 (s, 5H), 1.19 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.0, 149.3, 144.9, 131.7, 130.9, 75.5, 74.4, 72.4, 71.9, 71.4, 65.8, 60.3, 56.8, 23.9. IR (cm^{-1}): 3094 (w), 3063 (w), 1657 (s), 1554 (s), 1474 (s), 1458 (m), 1346 (s), 1321 (s), 1062 (s), 898 (s), 882 (s), 868 (s), 778 (s). MS (FAB+): *m/z* 440 [M$^+$ + H, 22], 383 [M$^+$ + H − OH,13]. HRMS (FAB+): calcd for $C_{21}H_{23}NO_4S(^{56}Fe)$ [M$^+$ + H] 440.0619, found 440.0609. Anal. Calcd for $C_{21}H_{22}NO_4SFe$: C, 57.41; H, 4.82. Found: C, 57.21; H, 4,84.

[(R_S,R_P)-1-(*tert*-Butylsulfinyl)-2-formylferrocene (2d).[10d] Following the general procedure, (*R*)-**1** (100 mg, 0.34 mmol) was treated with *t*-BuLi (1.7 M in pentane, 260 μL, 0.45 mmol) and ethyl formate (36 μL, 0.45 mmol), affording after chromatographic purification (*n*-hexanes−diethyl ether, 1:5) **2d**[10d] (78 mg, 71%) as a yellow solid.

Bis[(R_S,R_P)-2-(*tert*-butylsulfinyl)ferrocenyl](phenyl)methanol (3a). Following the general procedure, (*R*)-**1** (1.85 g, 6.39 mmol) was treated with *t*-BuLi (1.7 M in pentane, 4.5 mL, 7.41 mmol) and ethyl benzoate (1.5 mL, 8.05 mmol) to afford, after chromatographic purification (*n*-hexanes−EtOAc, 4:1), **3a** (3.92 g, 90%) as a red solid; $[\alpha]_D$ +236 (*c* 0.09, $CHCl_3$); mp 144−145 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49 (bs, 2H), 7.26 (m, 2H), 7.14 (m, 1H), 7.12 (s, 1H, OH), 4.72 (s, 1H), 4.66 (s, 1H), 4.49 (s, 5H), 4.42 (d, J = 2.42 Hz, 2H), 4.36 (d, J = 6.5 Hz, 2H) 3.68 (s, 5H), 1.73 (s, 9H), 0.65 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.5, 127.1, 126.4, 102.0, 96.3, 95.0, 78.0, 75.1, 73.4, 72.9, 72.5, 72.3, 72.0, 71.5, 70.2, 69,6, 69.4, 68.9, 68.7, 68.5, 57.3, 56.4, 23.8, 23.7, 23.2, 22.9. IR (cm^{-1}): 3343 (br), 3121 (s), 3070 (s), 1644 (w), 1597 (w), 1489 (s), 1460 (s), 1445 (s), 1412 (s), 1387 (m), 1205 (s), 1062 (vs), 702 (vs). MS (FAB+): *m/z* 685 [M$^+$ + H, 10], 368 [M$^+$ + H − OH, 8]. HRMS (FAB+): calcd for $C_{35}H_{41}O_3S_2(^{56}Fe)_2$ [M$^+$ + H] 685.1196, found 685.1188. The ee was determined to be >99.9% by HPLC analysis on a Daicel Chiralpark AD, *i*-PrOH/hexanes, 1:99, flow rate 1 mL/min (t_R = 27.3 min for the (−) enantiomer and 29.4 min for the (+) enantiomer).

Bis[(R_S,R_P)-2-(*tert*-butylsulfinyl)ferrocenyl](*p*-methoxyphenyl)methanol (3b). Following the general procedure, (*R*)-**1** (100 mg, 0.34 mmol) was treated with *t*-BuLi (1.7 M in pentane, 260 μL, 0.45 mmol) and methyl *p*-methoxybenzoate (28.6 mg, 0.17 mmol) to afford, after chromatographic purification (*n*-hexanes−diethyl ether, 1:6), **3b** (89 mg, 72%) as an orange solid; $[\alpha]_D$ +375 (*c* 0.10, $CHCl_3$); mp 140−141 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.13 (s, 1H, OH), 6.83 (d, J = 1.6 Hz, 2H), 6.68 (d, J = 1.6 Hz, 2H), 4.76 (m, 1H), 4.53 (s, 5H), 4.45 (m, 2H), 4.41 (m, 2H), 4.36 (m, 1H), 3.77 (s, 3H), 3.47 (s, 5H), 1.77 (s, 9H), 0.74 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.3, 144.6, 127.8, 112.3, 97.3, 94.7, 77.9, 74.8, 72.4, 72.3, 71.4, 70.2, 69.6, 69.3, 68.6, 68.4, 57.3, 56.4, 55.4, 24.8, 23.8, 23.0. IR (cm^{-1}): 3418 (br), 3122 (m), 3070 (m), 1607 (m), 1507 (s), 1300 (s), 1009 (s), 828 (m), 801 (m). MS (FAB+): *m/z* 715 [M$^+$ + H, 10], 649 (9), 398 (9). HRMS (FAB+): cald for $C_{36}H_{43}O_4S_2(^{56}Fe)_2$ [M$^+$ + H] 715.1301, found 715.1304. Anal. Calcd for $C_{36}H_{42}O_4SFe_2$: C, 60.51; H, 5.92. Found: C, 60.27, H, 6.01.

Bis[(R_S,R_P)-2-(*tert*-butylsulfinyl)ferrocenyl]methanol (3d). To a solution of (*R*)-**1** (53 mg, 0.18 mmol) in THF (2.5 mL), cooled to −78 °C, was added a 1.7 M solution of *t*-BuLi in pentane (139 μL, 0.24 mmol). The mixture was stirred at −78 °C for 2 h, and a solution of **2d** (58 mg, 0.18 mmol) in THF (1 mL) was slowly added. The resulting solution was stirred at −78 °C for 4 h, and it was treated with saturated

---

[26] For a review on diastereoselective *ortho*-lithiation, see: (a) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879. For oxazolines as directing groups in diastereoselective *ortho*-lithiation of ferrocene systems: (b) Richards, C. J.; Mulvaney, A. *Tetrahedron: Asymmetry* **1996**, *7*, 1419. (c) Sammakia, T.; Latham, H. A.; Schaad, D. R. *J. Org. Chem.* **1995**, *60*, 10. (d) Nishibayashi, Y.; Uemura, S. *Synlett.* **1995**, 79.

[27] Sheldrick, G. M. *SHELX-97 Program for Refinement of Crystal Structure*; University of Göttingen: Germany, 1997.

aqueous NH_4Cl (5 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to dryness. The residue was purified by flash chromatography (*n*-hexane−diethyl ether, 1:3) to afford **3d** (72 mg, 66%) as a green solid; $[\alpha]_D$ −158 (*c* 0.1, $CHCl_3$); mp 139−140 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 6.27 (d, *J* = 7.3 Hz, 1H, OH), 5.99 (d, *J* = 6.9 Hz, 1H), 5.32 (s, 1H), 5.08 (s, 1H), 4.46 (s, 5H), 4.40 (s, 5H), 4.30 (m, 4H), 1.12 (s, 9H), 1,11 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 95.0, 93.0, 82.0, 81.7, 77.4, 77.2, 74.3, 72.6, 71.4, 69.3, 69.1, 69.0, 67.5, 63.3, 57.0, 56.7, 23.9. IR (cm^{-1}): 3279 (br), 3095 (m), 3085 (w), 1411 (m), 1076 (s), 1037 (s), 804 (m). MS (FAB+): *m*/*z* 608 [M^+, 24], 591 [M^+ − OH, 64], 543 (25), 292 (42). HRMS (FAB+): cald for $C_{29}H_{36}O_3S_2(^{56}Fe)_2$ 608.0804, found 608.0810.

Synthesis of Tetraferrocenyl Disulfide 4. A solution of bisferrocene **3a** (205 mg, 3.0 mmol) in toluene (3.5 mL) was heated at 100 °C for 2.5 h. Water (5 mL) was added, the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to dryness. The residue was purified by flash chromatography (CH_2Cl_2−EtOAc, 9:1) to afford **4** (236 mg, 64%) as an orange solid; $[\alpha]_D$ +1068 (*c* 0.05, $CHCl_3$); mp 135−136 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 7.57 (m, 4H), 7.51 (s, 2H, OH), 7.20 (m, 4H), 7.07 (m, 2H), 4.66 (s, 2H), 4.54 (s, 12H), 4.35 (s, 2H), 4.30 (s, 2H), 3.99 (s, 2H), 3.93 (s, 2H), 3.65 (s, 10H), 0.61 (s, 18H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.3, 127.1, 126.7, 126.4, 102.4, 95.1, 88.3, 79.2, 76.2, 72.7, 71.9, 71.3, 70.7, 69.1, 68.6, 66.2, 65.7, 57.3, 23.1. IR (cm^{-1}): 3419 (m), 3000 (s), 2980 (w), 2963 (w), 1638 (w), 1487 (m), 1469 (m), 1409 (m), 1375 (m), 1362 (m), 1106 (m), 1072 (m), 1033 (m). MS (FAB+): *m*/*z* 1222 [M^+, 2], 460 (7), 307 (34), 219 (10). HRMS (FAB+): calcd for $C_{62}H_{62}O_4S_4(^{56}Fe)_4$ [M^+ + H] 1222.0928, found 1222.0798.

Bis[*(S,R*$_p$)-(5-*tert*-butyloxazolidinyl)ferrocenyl](phenyl)methanol (6). To a solution of (*S*)-(5-*tert*-butyloxazolidinyl)ferrocene (587 mg, 1.89 mmol) in THF (35 mL), cooled to −78 °C, was added dropwise a 1.3 M solution of *sec*-BuLi in cyclohexane (1.8 mL, 2.29 mmol). The reaction was stirred at −78 °C for 1.5 h, and it was treated with a solution of ethyl benzoate (396 mg, 2.64 mmol) in THF (1.0 mL). The mixture was kept at −78 °C for 2.5 h and then treated with brine (10 mL). The two layers were separated, and the aqueous layer was extracted with AcOEt (2 × 20 mL). The combined organic layers were dried ($MgSO_4$) and evaporated. The residue was purified by flash chromatography (*n*-hexanes−AcOEt, 10:1) to afford **6** as a orange solid (285 mg, 44%); $[\alpha]_D$ +286 (*c* 0.1, $CHCl_3$); mp 110−111 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 9.24 (s, 1H, OH), 7.44 (d, *J* = 7.7 Hz, 2H), 7.24 (t, *J* = 8.1 Hz, 2H), 7.15 (t, *J* = 6.9 Hz, 1H), 4.79 (s, 1H), 4.69 (s, 1H), 4.40 (t, *J* = 8 Hz, 1H), 4.25 (s, 5H), 4.18 (m, 3H), 4.10 (m, 2H), 4.04 (s, 5H), 3.73 (s, 1H), 3.55 (m, 2H), 3.22 (t, *J* = 9.3 Hz, 1H), 1.01 (s, 9H), 0.65 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.2, 166.5, 148.0, 127.6, 126.5, 126.1, 102.5, 99.8, 76.4, 75.3, 74.6, 74.0, 70.9, 70.7, 70.4, 69.7, 69.6, 69.1, 68.8, 68.4, 66.5, 65.5, 53.4, 33.4, 32.8, 26.4, 26.2. IR (cm^{-1}): 3164 (br), 2951 (s), 1652 (s), 1638 (s), 1363 (m), 1295 (m), 1246 (m), 1202 (m), 817 (m). MS (FAB+): *m*/*z* 727 [M^+ + H, 100], 644 (14), 323 (10). HRMS (FAB+): calcd for $C_{41}H_{47}N_2O_3(^{56}Fe)_2$ [M^+ + H] 727.2285, found 727.2304.

Acknowledgment. Support has been provided by the DGCIYT (projects BQU2000-0226 and BQU2003-0508). R.G.A. thanks the MCyT for a “Contrato Ramón y Cajal”. We also acknowledge the Centro de Computación Científica (UAM) for access to CSD.

Supporting Information Available: Tables of atomic coordinates, thermal parameters, all bond distances and angles, and experimental data for X-ray diffraction studies of **3a** and **4**. Copies of ^1H and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OM049924B