JOC Articles

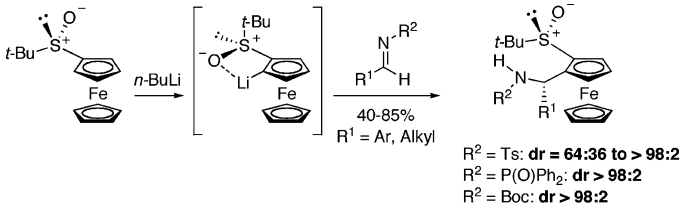
Diastereoselective Addition of Enantiopure Lithium *tert*-Butylsulfinylferrocene to Imines

Guillaume Grach,[†] Jana Sopkova-de Oliveira Santos,[‡] Jean-François Lohier,[†] Ljubica Mojovic,[§] Nelly Plé,[§] Alain Turck,[§] Vincent Reboul,*[,†] and Patrick Metzner*[,†]

Laboratoire de Chimie Moléculaire et Thio-organique, UMR CNRS 6507, ENSICAEN, Université de Caen, 14050 Caen, France, Centre d'Etudes et de Recherche sur le Médicament de Normandie, Université de Caen, 14032 Caen, France, and Laboratoire de Chimie Organique Fine et Hétérocyclique, UMR CNRS 6014, IRCOF, INSA, B.P. 08, 76131 Mont Saint Aignan, France

vincent.reboul@ensicaen.fr

Received June 30, 2006



(*S*)-*tert*-Butylsulfinylferrocene was submitted to ortho-metalation, and the corresponding lithium derivative was trapped by alkyl or aryl imines bearing various electron-withdrawing groups on the nitrogen atom (Ts, Dpp, Boc). New aminosulfoxides were obtained with complete diastereocontrol when Dpp or Boc groups were used. The absolute configuration (S_S,S_{Fc},*S*) has been determined by single-crystal X-ray analysis and chemical correlation. An unusual pseudocyclic boatlike transition state has been proposed to explain the stereochemical course of this reaction.

Introduction

Since the first diastereoselective ortho-lithiation of *N*,*N*-dimethyl-1-ferrocenylethylamine **(1)** was reported[1] by Ugi in 1970, alternative ortho-directing groups[2] have been used with success and allowed the preparation of enantiopure 1,2-disubstituted ferrocene derivatives with planar and central chirality.[3] Among them, the stereogenic sulfinyl group has emerged recently with the methodology developed by Kagan[4] and Hua,[5] using enantiopure *p*-tolylsulfinylferrocene (**3**) and *tert*-butylsulfinylferrocene (**4**). This interest was largely due to the easy preparation of the starting material (two enantiomers available in only one step from ferrocene). Moreover, the sulfoxide moiety may be transformed into other functional groups or may be removed.[6] The resulting lithium sulfinylferrocene **5** derivatives were trapped with electrophiles leading to 1,2-substitution (Scheme 1).[7]

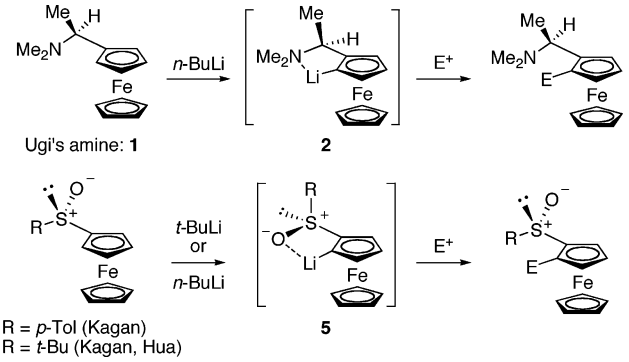
Only a few prochiral electrophiles have been used with **5**, probably as the result of the very low asymmetric induction observed.[8,9] For example, in the arylsulfinyl series, Knochel described the use of 2-(diphenylphosphine)-benzaldehyde with the lithio derivative **5** (R = *p*-Tol) leading to a 55:45 mixture of diastereoisomers, which were not easily separable. No

* To whom correspondence should be addressed.
[†] Laboratoire de Chimie Moléculaire et Thio-organique.
[‡] Centre d'Etudes et de Recherche sur le Médicament de Normandie.
[§] Laboratoire de Chimie Organique Fine et Hétérocyclique.

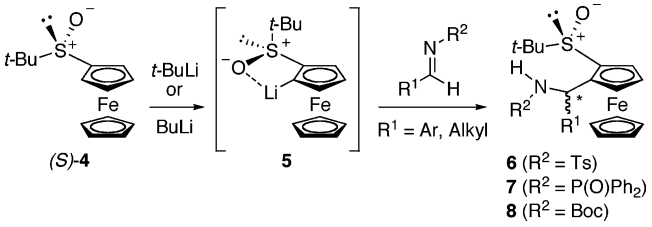
(1) Marquading, D.; Klusacek, H.; Gokel, G. W.; Hoffmann, P.; Ugi, I. K. *J. Am. Chem. Soc.* **1970**, *92*, 5389−5393.
(2) Last example to date: Vinci, D.; Mateus, N.; Wu, X.; Hancock, F.; Steiner, A.; Xiao, J. *Org. Lett.* **2006**, *8*, 215−218 and references therein.
(3) (a) Atkinson, R. C. J.; Gibson, V. C.; Long, N. J. *Chem. Soc. Rev.* **2004**, *33*, 313−328. (b) Colacot, T. J. *Chem. Rev. (Washington, DC, U.S.)* **2003**, 3101−3118. (c) Richards, C. J.; Locke, A. J. *Tetrahedron: Asymmetry* **1998**, *9*, 2377−2407.
(4) (a) Riant, O.; Argouarch, G.; Guillaneux, D.; Samuel, O.; Kagan, H. B. *J. Org. Chem.* **1998**, *63*, 3511−3514. (b) Rebière, F.; Riant, O.; Ricard, L.; Kagan, H. B. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 568−570.
(5) (a) Lagneau, N. M.; Yi, C.; Robben, P. M.; Sin, H.-S.; Takasu, K.; Chen, J.-S.; Robinson, P. D.; Hua, D. H. *Tetrahedron* **1998**, *54*, 7301−7334. (b) Hua, D. H.; Lagneau, N. M.; Chen, Y.; Robben, P. M.; Clapham, G.; Robinson, P. D. *J. Org. Chem.* **1996**, *61*, 4508−4509.
(6) (a) See ref 4a. (b) Pedersen, H. L.; Johannsen, M. *Chem. Commun.* **1999**, 2517−2518. (c) Lotz, M.; Polborn, K.; Knochel, P. *Angew. Chem., Int. Ed.* **2002**, *41*, 4708−4711.

10.1021/jo061360t CCC: $33.50
Published on Web 11/23/2006

SCHEME 1. Diastereoselective Ortho-Lithiation



SCHEME 2. Diastereoselective Ortho-Lithiation Followed by Aldimine Addition



induction was obtained with unsubstituted benzaldehyde. Surprisingly, imines were not previously used as prochiral electrophiles.

Our very recent observation of a diastereocontrolled addition of benzenesulfinyl carbanions and analogues with imines[10] prompted us to investigate ferrocenesulfinyl carbanions, with respect to the attractive synthesis of new ligands for asymmetric catalysis.

Here, we wish to report the reaction of alkyl- and arylaldimines bearing various electron-withdrawing groups on the nitrogen atom with the lithium derivative of (*S*)-*tert*-butylsulfinylferrocene (Scheme 2).

Results and Discussion

The *tert*-butylsulfinyl ferrocene (**4**) is readily available in enantiopure form from ferrocene and Ellman's (*S*)-*tert*-butyl *tert*-butanethiosulfinate[11] (**9**) in one step as shown by Carretero and his group.[12] Using the procedure of Mueller-Wersterhoff[13] (to obtain monolithiated ferrocene), we prepared sulfoxide (*S*)-**4** on a multigram scale in 66% yield (Scheme 3).

We chose imines bearing electron-withdrawing groups, incorporating an oxygen atom susceptible to coordination with the lithium atom, leading to potentially ordered transition states. The reaction was first tested and optimized with *N*-tosyl imines **11**. Other electron-withdrawing groups, easier to cleave, were

SCHEME 3. Preparation of Enantiopure Sulfoxide 4

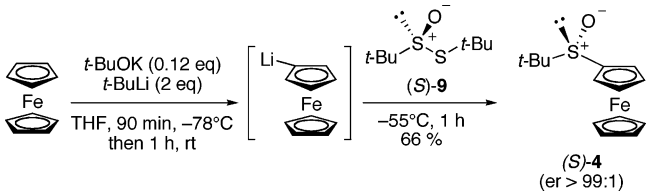


TABLE 1. Synthesis of 6b by Metalation of Sulfoxide 4 and Addition of Isopropyl-*N*-tosylimine 11b

entry	alkyllithium (equiv)	temp, time	conversion[a] (%)	dr[b]
1	*t*-BuLi (1.5)	−78 °C, 1.5 h	43	85:15
2	*n*-BuLi (1.1)	−78 °C, 1.5 h	56	89:11
3	*n*-BuLi (1.1)	−78 °C, 10 min	56	90:10
4	*n*-BuLi (1.1)	−40 °C, 1.5 h	51	80:20
5	*n*-BuLi (1.1)	rt, 1.5 h	55	70:30
6	*n*-BuLi (1.1) + TMEDA (1)	−78 °C, 1.5 h	52	88:12

[a] Measured by ^{1}H NMR on δ of *t*-Bu of sulfinyl groups. [b] Measured by ^{1}H NMR on δ of CH*Me*$_2$ groups.

then employed: *N*-phosphinoyl[14] (**13**; R^2 = $POPh_2$) and *N*-carbamoyl (**12**; R^2 = Boc).

N-Tosyl imines **11** were prepared from corresponding commercial aldehydes in two steps according to Chemla's procedure[15] (for **11a**−**c,e**) or in one step (for **11d**) according to Proctor's protocol (BF_3·Et_2O, MS, reflux).[16] A similar method was used for the synthesis of aromatic *N*-Boc imines **12** (Scheme 4).[17] The alkyl *N*-Boc imines could not be prepared using this methodology (formation of enamine[18] instead of imine during the deprotonation step). They were generated in situ from sulfone **10**.[19] Two *N*-phosphinoyl imines **13** have been synthesized according to Jennings's protocol (NEt_3, $TiCl_4$, 0 °C).[20]

Ferrocenyl sulfoxide (**4**) was first lithiated with *t*-BuLi (THF, −78 °C, 1.5 h; entry 1), as indicated in a earlier paper[21] and reacted at −78 °C with *N*-tosyl imine **11b** (R^1 = *i*-Pr) as a model (Table 1). Conversion and dr were easily determined on the crude product by ^{1}H NMR, from the respective chemical shifts of sulfinyl *t*-Bu and *i*-Pr methyl groups. Pleasingly, the anticipated tosylamino-sulfoxides **6b** were obtained but with moderate conversion. These two diastereoisomers (**6b**) can be easily separated by chromatography on silica gel. The yield was improved using *n*-BuLi (THF, 0 °C then rt, 2 h; Table 1 entries 2−6). The reaction time can be reduced to 10 min (entry 3) instead of 1.5 h. Surprisingly, the reactions seem to stall at ≈50% conversion, with the remainder of the material being unreacted sulfinyl ferrocene. It might be the result of the formation of an 1:1 organo-lithium heteroaggregate of the desired lithiated product **5** with the starting material **4** (in the presence of THF).[22] However, the addition of TMEDA did not

(7) For recent examples of 1,2-disubstituted sulfinylferrocenes: Kloetzing, R. J.; Knochel, P. *Tetrahedron: Asymmetry* **2006**, *17*, 116−123. Seitzberg Jimmi, G.; Dissing, C.; Sotofte, I.; Norrby, P.-O.; Johannsen, M. *J. Org. Chem.* **2005**, *70*, 8332−8337. Raghunath, M.; Gao, W.; Zhang, X. *Tetrahedron: Asymmetry* **2005**, *16*, 3676−3681.

(8) See ref 6c.

(9) See ref 5a.

(10) Le Fur, N.; Mojovic, L.; Plé, N.; Turck, A.; Reboul, V.; Metzner P. *J. Org. Chem.* **2006**, *71*, 2609−2616.

(11) Weix, D. J.; Ellman, J. A. *Org. Lett.* **2003**, *5*, 1317−1320.

(12) Priego, J.; Mancheño, O. G.; Cabrera, S.; Carretero, J. C. *J. Org. Chem.* **2002**, *67*, 1346−1353.

(13) Sanders, R.; Mueller-Westerhoff, U. T. *J. Organomet. Chem.* **1996**, *512*, 219−224.

(14) For a recent review: Weinreb, S. M.; Orr, R. K. *Synthesis* **2005**, 1205−1227.

(15) Chemla, F.; Hebbe, V.; Normant, J.-F. *Synthesis* **2000**, 75−77.

(16) McKay, W. R.; Proctor, G. R. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2435−2442.

(17) (a) Kanazawa, A. M.; Denis, J.-N.; Greene, A. E. *J. Org. Chem.* **1994**, *59*, 1238−1240. (b) Wenzel, A. G.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 12964−12965.

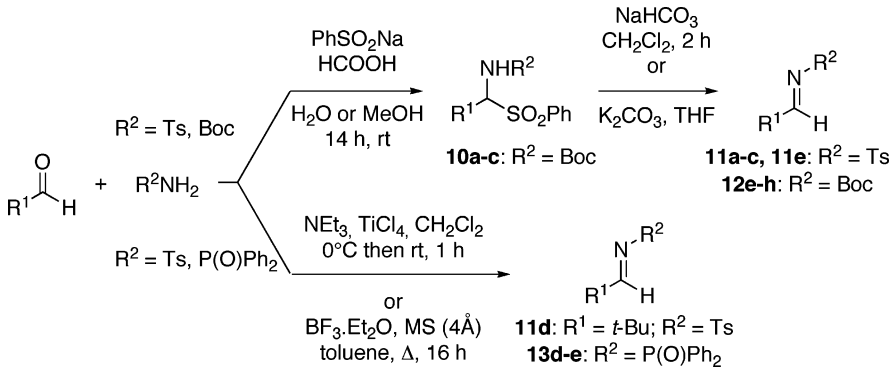
(18) Mecozzi, T.; Petrini, M. *Synlett* **2000**, 73−74.

(19) Petrini, M. *Chem. Rev.* **2005**, *105*, 3949−3977.

(20) Jennings, W. B.; Lovely, C. J. *Tetrahedron* **1991**, *47*, 5561−5568.

(21) Minière, S.; Reboul, V.; Metzner, P. *ARKIVOC (Gainesville, FL, U.S.)* **2005**, (xi), 161−177.

SCHEME 4. Preparation of Imines and Sulfones



a : R^1 = Me; **b**: R^1 = *i*-Pr; **c**: R^1 = Cy; **d**: R^1 = *t*-Bu; **e**: R^1 = Ph; **f**: R^1 = *m*-BrC_6H_4; **g**: R^1 = 3-Pyr; **h**: R^1 = *p*-$NO_2C_6H_4$.

TABLE 2. Diastereoselective Addition of Aldimines on Lithiated (*S*)-4

Entry	Imine or sulfone	R^1	Conversion[a] (%)	Yield (%)	Product	dr[b]
1		Me (**11a**)	60	59	**6a**	>98:2
2		*i*-Pr (**11b**)	56	55	**6b**	90:10
3	R^2 = Ts	Cy (**11c**)	n.d.	58	**6c**	89:11[c]
4		*t*-Bu (**11d**)	77	54	**6d**	64:36
5		Ph (**11e**)	80	65	**6e**	75:25
6		*t*-Bu (**13d**)	41	-	**7d**	>98:2
7	R^2 = P(O)Ph_2	Ph (**13e**)	42	41	**7e**	>98:2
8		Me (**10a**)[d]	70[e]	63[f]	**8a**	>98:2
9	R^2 = Boc	*i*-Pr (**10b**)[d]	80[e]	76[f]	**8b**	>98:2
10		Cy (**10c**)[d]	85[e]	85[f]	**8c**	>98:2
11		Ph (**12e**)	81	78	**8e**	>98:2
12		*m*-BrC_6H_4(**12f**)	n.d.	40	**8f**	>95:5[c]
13	R^2 = Boc	3-Pyr (**12g**)	45	41	**8g**	>98:2
14		*p*-$NO_2C_6H_4$ (**12h**)	54	49	**8h**	>98:2

[a] Measured by ^{1}H NMR on δ of *t*-Bu of sulfoxide groups. [b] Determined by ^{1}H NMR on crude product. [c] Calculated from the mass of each diastereoisomer. [d] The reaction was carried out with 2 equiv of sulfinylferrocene, 2.2 equiv of *n*-butyllithium, and 1 equiv of sulfone. [e] Measured by ^{1}H NMR on δ of *t*-Bu of sulfoxide groups and based on sulfone. [f] Isolated yield based on sulfone.

have any beneficial effect on conversion (entry 6) or dr. The best asymmetric induction (90:10 ratio; Table 1, entry 3) was obtained when the addition was performed at −78 °C. These optimized conditions were used for the following reactions.

Using the optimized conditions, we were able to prepare a variety of amino sulfoxide derivatives **6** using other aliphatic *N*-tosylimines (Table 2; entries 1−4). The reaction yields were all around 55%.[23]

Surprisingly, the more hindered imine (R^1 = *t*-Bu; **11d**) led to the lowest dr (Table 2, entry 4) and the less hindered imine (R^1 = Me; **11a**) led to only one diastereoisomer (Table 2, entry 1). In the aromatic series (Table 2, entry 5), a slightly better conversion and yield were obtained, but a modest dr was observed and we could not separate the two diastereoisomers on silica gel. Two *N*-phosphinoylimines **13d**−**e** were also tested (Table 2, entries 6 and 7). They led to a single diastereoisomer, according to the ^{1}H NMR spectrum, with lower conversions and yields. Compound **7d** was especially unstable and could not be fully characterized. Such phosphorylated imines are very sensitive to hydrolysis;[24] consequently, other aromatic or alkyl groups were not tested and we decided to use another oxygenated group on the nitrogen atom: the carbamoyl moiety (Boc).

(22) Gossage, R. A.; Jastrzebski, J. T. B. H.; van Koten, G. *Angew. Chem., Int. Ed.* **2005**, *44*, 1448−1454.

(23) Amino sulfoxides have been surmised to be good ligands for any metals present in the silica gel, leading to low yields: Pedersen, B.; Rein, T.; Sotofte, I.; Norrby, P.-O.; Tanner, D. *Collect. Czech. Chem. Commun.* **2003**, *68*, 885−898.

(24) Arini, L. G.; Sinclair, A.; Szeto, P.; Stockman, R. A. *Tetrahedron Lett.* **2004**, *45*, 1589−1591.

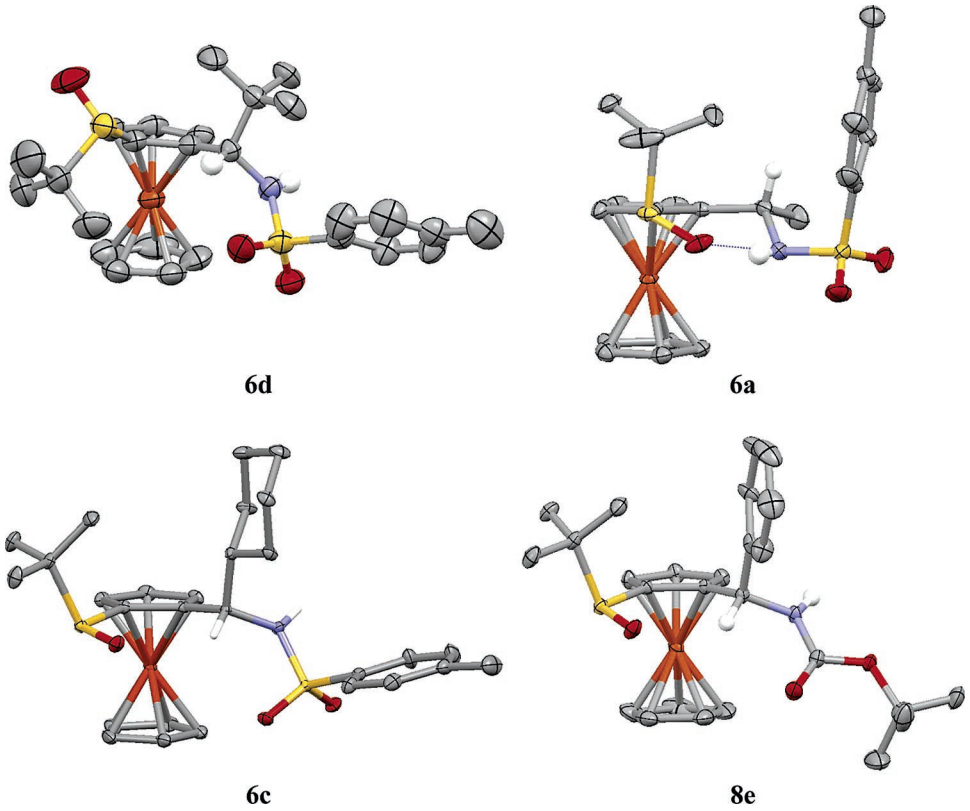


FIGURE 1. X-ray crystal structure for **6d**, **6a**, **6c**, and **8e** (50% thermal ellipsoids). For clarity hydrogen atoms are omitted except in the cases of C*H and NH.

We explored the scope of the reaction first with alkyl groups for R^1 (entries 8−10). These alkyl *N*-Boc-imines were prepared in situ from sulfones **10a**−**c** by the action of an extra amount of base (e.g., LiHMDS,[25] NaH[26]) or by an excess of carbon nucleophile.[27] We first tried the following conditions: 2 equiv of *n*-BuLi in the presence of **4** and subsequent addition of sulfone **10b**. Unfortunately, only the addition of *n*-BuLi to the imine, formed in situ, was obtained. The same reaction was observed with LDA as a base leading to the amidation adduct.[28] Consequently, we chose to use only 1 equiv of *n*-BuLi with compound **4** and then to use 2 equiv of the lithio derivative **5** with 1 equiv of sulfone **10a**−**c** (Table 2, entries 8−10). The corresponding aliphatic adducts **8a**−**c** were obtained in good yields (based on the sulfone) as single diastereoisomer. It is important to note that the unreacted (S_S)-*tert*-butylsulfinylferrocene (**4**) can be recovered after chromatography on silica gel (50−62% yield) and reused (er > 98/2). Various aromatic (Table 2, entries 11, 12, and 14) and heteroaromatic (entry 13) imines **12e**−**h** were then used with success. As previously noted, only one diastereoisomer was isolated in each case. The highest yield was obtained with imine **12e** (78%; Table 2, entry 11).

For compound **6d** (R^1 = *t*-Bu, R^2 = Ts), we were able to unambiguously establish the (S_S,S_{Fc},*S*) absolute configuration of the stereocenters by X-ray diffraction analysis of a single crystal[29] of the major isomer (Figure 1).[30] We observed that the more hindered group, the *tert*-butyl on the asymmetric carbon center, is positioned above the Cp ring, and it is interesting to note that the sulfinyl *tert*-butyl group is thus directed toward the iron atom. Consequently, a high tilting of the sulfoxide substituent relative to the Cp plane ($Cp_{Centroid}$−C−S = 18.68° or 0.565 Å out of the plane of Cp ring[31]) was observed and can be associated with this 1,2-substitution. To our knowledge, it constitutes the largest angle observed in the sulfurated ferrocene derivative series so far.[32] For the same reasons, the two Cp rings are not parallel and an unusual tilt angle of 10.4° was observed.[31]

We assume that the same configuration (S_S,S_{Fc},*S*) was obtained for the other aliphatic derivatives **6**. In order to see if this congested conformation for **6** was similar in solution, we decided to compare, for each diastereoisomer, the chemical shifts of two protons: N*H* and C**H*. They are in proximity to the

(25) Liao, W.-W.; Deng, X.-M.; Tang, Y. *Chem. Commun.* **2004**, 1516−1517.
(26) Zawadzki, S.; Zwierzak, A. *Tetrahedron Lett.* **2004**, *45*, 8505−8506.
(27) Pesenti, C.; Bravo, P.; Corradi, E.; Frigerio, M.; Meille, S. V.; Panzeri, W.; Viani, F.; Zanda, M. *J. Org. Chem.* **2001**, *66*, 5637−5640.
(28) For a recent example of an imine amidation reaction: Rowland, G. B.; Zhang, H.; Rowland, E. B.; Chennamadhavuni, S.; Wang, Y.; Antilla, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 15696−15697.
(29) Single crystals suitable for X-ray crystal analysis were obtained from a concentrated solution of ethanol and by the slow diffusion of pentane.
(30) Crystal structure data for $C_{26}H_{35}FeNO_3S_2$: crystal size 0.6 × 0.1 × 0.1 mm^3, orthorhombic, space group $P2_12_12_1$, a = 16.2321(3) Å, b = 17.8126(4) Å, c = 18.5205(4) Å, V = 5354.94(19) Å^3, Z = 8, μ = 0.746 mm^{-1}. 63 931 reflections collected. Refinement for 14 170 reflections and 655 parameters gave GOF = 1.139, R1 = 0.0349, and wR2 = 0.1121. Absolute structure parameter = −0.011(10). Selected bond lengths (Å) and angles (deg) on the first molecule of the asymmetric unit: C*−C_{Cp}, 1.510; S−O, 1.490; S−C_{Cp}, 1.779; C*−N, 1.477; N−C*−C_{Cp}, 110.8; O−S−C_{Cp}−C_{Cp}, 125.5.
(31) Measured on the first molecule of the asymmetric unit.
(32) 61 ferrocene derivatives with one adjacent sulfur atom were found in the CSD (version 5.27; Nov, 2005) including 12 sulfinylferrocenes. Among them, a similar case was observed with bis(sulfinyl)bisferrocene (0.54 Å out of the plane of the Cp ring): Arrayás, R. G.; Alonso, I.; Familiar, O.; Carretero, J. C. *Organometallics* **2004**, *23*, 1991−1996.

TABLE 3. Chemical Shift of Characteristic Protons of 6, 7, and 8 Derivatives

		δ NH (ppm)			δ C*H (ppm)		
entry	product (dr)	major	minor	Δδ	major	minor	Δδ
1	**6a** (>98/2)	8.28[a]			4.03[a]		
2	**6b** (90/10)	5.54[a]	8.48[a]	2.94	4.77[a]	3.84[a]	0.93
3	**6c** (89/11)	5.36[a]	8.38[a]	3.02	4.79−4.87[a]	3.90−3.94[a]	0.89−0.93
4	**6d** (64/36)	5.07[a]	8.80[a]	3.73	4.44−4.48[a]	4.47[a]	0.01−0.03
5	**7e** (>98/2)	5.80−5.83[b]			5.67−5.71[b]		
6	**8a** (>98/2)	7.19[b]			4.85[b]		
7	**8b** (>98/2)	6.22[b]			5.49[b]		
8	**8c** (>98/2)	6.14[b]			5.50[b]		
9	**8e** (>98/2)	6.98−7.00[b]			6.48−6.50[b]		
10	**8f** (>98/2)	7.12−7.14[b]			6.47[b]		
11	**8g** (>98/2)	7.13−7.16[b]			6.48−6.57[b]		
12	**8h** (>98/2)	7.31−7.33[b]			6.57[b]		

[a] In $CDCl_3$. [b] In acetone-d_6

sulfinyl group, which is known to exert a strong anisotropic effect.[33] The values are summarized in Table 3.

In the aliphatic series of **6** (Table 3, entries 1−4), the chemical shifts are consistent for each diastereoisomer (NH δ 5.07−5.54; C*H δ 4.44−4.77) except for **6a** (entry 1), whose N*H* appeared significantly deshielded: 8.28 ppm as compared to ≈ 5.5 ppm. Due to the low steric hindrance of the methyl group, we suspected that this shielding was the consequence of a conformation change. It was confirmed by X-ray diffraction analysis of **6a** (Figure 1).[29,34] As expected, the (S_S,S_{Fc},*S*) absolute configuration was observed. The *tert*-butyl group of the sulfoxide is now located above the Cp ring. Surprisingly, the carbon atom of the methyl group is almost in the plane of the Cp ring (C−C*−C_{Cp}−C_{Cp}, 171.0°). This conformational preference can be understood by two weak bondings: (i) a hydrogen one between the N*H* and the sulfinyl oxygen (S(*O*)---N*H*, 2.053 Å; N−H---O angle, 168.2°); (ii) and a CH-π stabilizing electrostatic interaction[35] between the phenyl ring of the tosyl group and the C−H bond of the *tert*-butyl group (d = 2.72 Å). On the other hand, the N*H* group seems to be far away from the iron atom (N*H*---*Fe*, 3.409 Å).[36]

Unfortunately, we were not able to obtain the X-ray structure of the minor isomer of **6**. In all of the cases (**6b**−**d**), the two isomers exhibited a spectacular difference of N*H* chemical shifts (up to 3.73 ppm). To explain this, we propose the existence of hydrogen bonding between the N*H* and the sulfinyl oxygen atom (Figure 2) for the minor isomer.

The X-ray structure of **6c** (major diastereoisomer) was also obtained (Figure 1).[37] With a more hindered alkyl group than methyl, the cyclohexyl is now located on the same side of the *tert*-butyl of the sulfinyl group. Unusually weak hydrogen bonding between the C*H* and the sulfinyl oxygen (S(*O*)---C**H*, 2.529 Å; C−H---O angle, 124.8°) could be responsible for this conformational preference.[38]

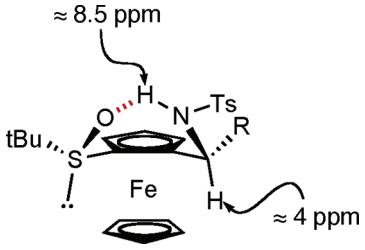


FIGURE 2. Proposed conformation of the minor isomer of **6**.

In the Boc series (compounds **8**), the chemical shifts of N*H* and C**H* were also consistent and seemed to be in agreement with chemical shifts for the major isomer of the tosyl series (Table 3, entries 6−12). Consequently, we suppose that the same asymmetric induction of the sulfinyl group took place leading to the (S_S,S_{Fc},*S*) configuration. This was verified by chemical correlation. The Boc group of compound **8b** was easily[39] deprotected by TFA.[40] The reprotection by a tosyl group of the resulting primary amine **14** can be readily accomplished in good yield without compromising the integrity of the stereocenter since the same ^{1}H NMR spectrum of the major isomer of **6b** was obtained (Scheme 5).[41]

Single crystals of compound **8e** were obtained, and the expected (S_S,S_{Fc},*S*) configuration was confirmed by X-ray diffraction analysis (Figure 1).[42] The phenyl group is on the

(33) Green, C. H.; Helleir, D. G. *J. Chem. Soc., Perkin Trans. 2* **1972**, 458−463.

(34) Crystal structure data for $C_{23}H_{29}FeNO_3S_2$: crystal size 0.603 × 0.424 × 0.337 mm^3, monoclinic, space group *P*21, a = 9.7869(4) Å, b = 11.2474(4) Å, c = 10.5714(4) Å, V = 1135.78(8) Å^3, Z = 2, μ = 0.872 mm^{-1}. 37 257 reflections collected. Refinement for 15 183 reflections and 300 parameters gave GOF = 1.081, R1 = 0.0351, and wR2 = 0.1029. Absolute structure parameter = 0.000(7). Selected bond lengths (Å) and angles (deg): C*−C_{Cp}, 1.5152(18); S−O, 1.5123(12); S−C_{Cp}, 1.7600(13); C*−N, 1.483(2); N−C*−C_{Cp}, 109.59(10); O−S−C_{Cp}−C_{Cp}, −1.3.

(35) Nishio, M. *Tetrahedron* **2005**, *61*, 6923−6950.

(36) According to DFT-based conformational analyses of a number of ferrocene containing alcohols, the Fe−H distance was between 2.61 and 2.95 Å: Vrcek, V.; Bühl, M. *Organometallics* **2006**, *25*, 358−367.

(37) Crystal structure data for $C_{28}H_{37}FeNO_3S_2$: crystal size 0.557 × 0.110 × 0.091 mm^3, tetragonal, space group *P*4(1), a = 11.8067(4) Å, b = 11.8067(4) Å, c = 19.3721(7) Å, V = 2700.43(16) Å^3, Z = 4, μ = 0.743 mm^{-1}. 11 5827 reflections collected. Refinement for 18 377 reflections and 464 parameters gave GOF = 1.035, R1 = 0.0271, and wR2 = 0.0616. Absolute structure parameter = 0.001(4). Selected bond lengths (Å) and angles (deg): C*−C_{Cp}, 1.5214(10); S−O, 1.5048(6); S−C_{Cp}, 1.7777(7); C*−N, 1.4702(9); N−C*−C_{Cp}, 110.38(6); O−S−C_{Cp}−C_{Cp}, −1.3.

(38) Desiraju, G. R. *Acc. Chem. Res.* **1996**, *29*, 441−449.

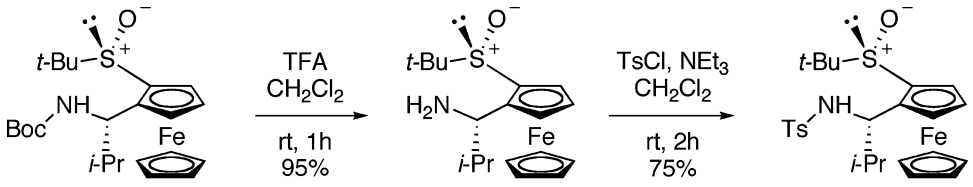
(39) No reaction occurred with H_2SO_4, and the starting material was recovered: Strazzolini, P.; Misuri, N.; Polese, P. *Tetrahedron Lett.* **2005**, *46*, 2075−2078.

(40) Shendage, D. M.; Froehlich, R.; Haufe, G. *Org. Lett.* **2004**, *6*, 3675−3678.

(41) Pallavicini, M.; Valoti, E.; Villa, L.; Piccolo, O. *Tetrahedron: Asymmetry* **2001**, *12*, 1071−1075.

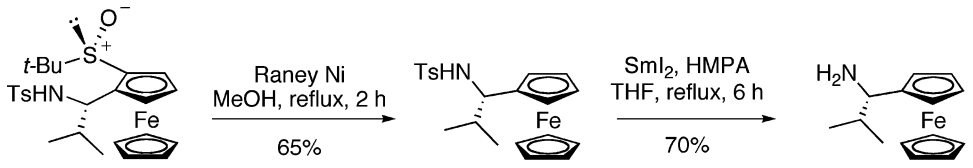
(42) Crystal structure data for $C_{26}H_{33}FeNO_3S$: crystal size 0.521 × 0.199 × 0.142 mm^3, orthorhombic, space group $P2_12_12_1$, a = 17.7483(14) Å, b = 19.5715(16) Å, c = 22.6086(18) Å, V = 7853.3(11) Å^3, Z = 12, μ = 0.681 mm^{-1}. 247 864 reflections collected. Refinement for 27 904 reflections and 884 parameters gave GOF = 1.080, R1 = 0.0320, and wR2 = 0.0855. Absolute structure parameter = −0.021(5). Selected bond lengths (Å) and angles (deg) on the first molecule of the asymmetric unit: C*−C_{Cp}, 1.519; S−O, 1.502; S−C_{Cp}, 1.766; C*−N, 1.465; N−C*−C_{Cp}, 111.1; O−S−C_{Cp}−C_{Cp}, −6.82.

SCHEME 5. Chemical Correlation



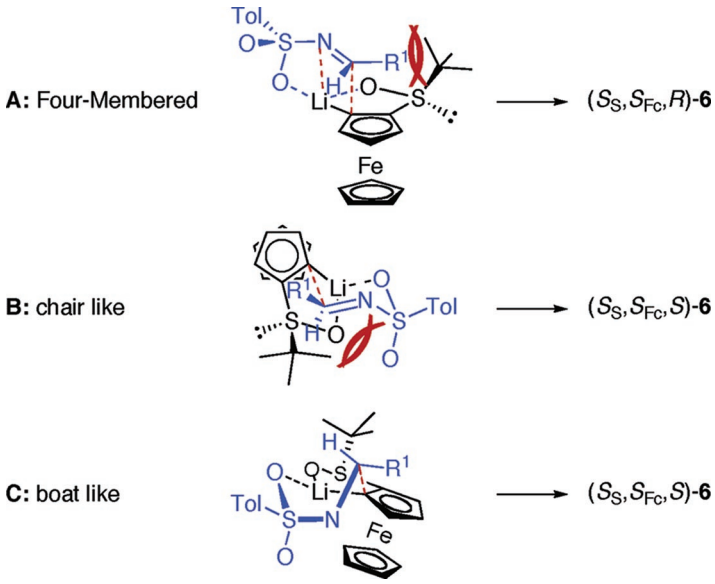
8b **14** **(S_S,S_{Fc},*S*)-6b**

SCHEME 6. Synthesis of α-Ferrocenylalkylamine



(S_S,S_{Fc},*S*)-6b **(*S*)-15** (er > 99:1) **(*S*)-16** (er: 99:1)

SCHEME 7. Four-Membered (A), Pseudocyclic Chairlike (B), and Pseudocyclic Boatlike (C) Transition States in Tosyl Series



exo side of the ferrocene, but comparable to structure **6d**, the *tert*-butyl sulfinyl function is also located on the exo side of the ferrocene. As in the **6c** structure, this X-ray analysis showed weak hydrogen bonding between the C**H* and the sulfinyl oxygen (S(*O*)---C**H*, 2.288 Å; S−O---H angle, 135.85°).[35]

Other transformations have been performed in order to synthesize an enantiopure α-ferrocenylalkylamine. An example was given with the synthesis of amine (*S*)-**16** in two steps (Scheme 6): reductive cleavage of the stereogenic sulfur moiety with Raney nickel[43] and then deprotection of the tosyl group by SmI_2.[44] The enantiopurity of **15** and **16**,[45] er 99:1 (chiral HPLC), confirmed that no epimerization occurred during this process.[46]

To explain the homogeneous stereochemical sense (all S_S,S_{Fc},*S* configurations), we tried to build transition states. We supposed the following: (i) The sulfoxide and the lithium atom form a flat five-membered ring, coplanar with the Cp ring. (ii) One of the ring faces is clearly hindered by the iron atom, which is linked to the second Cp ring. Consequently, the approach of the imine from the exo side of the ferrocene will be preferred. (iii) The imine has an (*E*)-configuration in which the tolyl group is anti to the N=C bond (along the N−S bond).[47]

Examination of possible approaches of the sulfinyl carbanion and the imine led us to consider a concerted four-membered transition state **A**, as first proposed by Garcia Ruano's group[48] and then by us (Scheme 7).[10] It cannot be applied in the ferrocene series. Indeed, when a coordination of the lithium atom with both the *tert*-butylsulfinyl oxygen atom and one of the two sulfonylimine oxygen (or Boc oxygen) atoms takes place, the

(43) D'Antona, N.; Lambusta, D.; Morrone, R.; Nicolosi, G.; Secundo, F. *Tetrahedron: Asymmetry*, **2004**, 3835−3840.

(44) Kuriyama, M.; Soeta, T.; Hao, X.; Chen, Q.; Tomioka, K. *J. Am. Chem. Soc.* **2004**, *126*, 8128−8129.

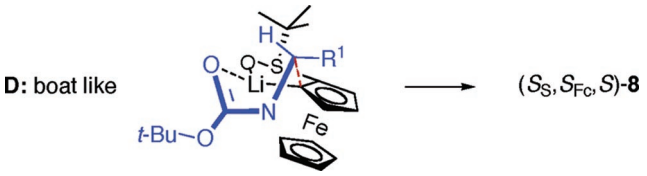
(45) Racemic **16** was prepared in four steps according to an adapted procedure from: Woltersdorf, M.; Kranich, R.; Schmalz, H.-G. *Tetrahedron* **1997**, *53*, 7219−7230.

(46) (a) Herrmann, R.; Huebener, G.; Siglmueller, F.; Ugi, I. *Liebigs Ann. Chem.* **1986**, 251−268. (b) Cushman, M.; Chen, J. K. *J. Org. Chem.* **1987**, *52*, 1517−1521.

(47) Charette, A. B.; Giroux, A. *Tetrahedron Lett.* **1996**, *37*, 6669−6672.

(48) (a) Garcia, Ruano, J. L.; Alemán, J.; Soriano, J. F. *Org. Lett.* **2003**, *5*, 677−680. (b) Garcia Ruano, J. L.; Alemán J. *Org. Lett.* **2003**, *5*, 4513−4516.

SCHEME 8. Pseudocyclic Boatlike Transition States in the Boc Series



model does not lead to the observed configuration. It appears that this approach is disfavored by a strong steric interaction between the R^1 and *t*-Bu groups.

We excluded a pseudocyclic chairlike transition state **B** (Scheme 7) due to severe electrostatic and steric interactions between the *tert*-butylsulfinyl and the sulfonyl groups.

Another model allowed us to remove all of the preceding interactions by placing the tolylsulfonyl group and sulfinyl groups far apart. Coordination of the lithium atom to the oxygen atoms of both the sulfinyl and sulfonyl groups may force the transition state to adopt a pseudocyclic **boatlike** transition state **C**. It leads to the (S_S,S_{Fc},*S*) diastereoisomer, in agreement with the experiment (Scheme 7). When the R^1 group was hindered (R^1 = Cy, *i*-Pr, *t*-Bu), a possible steric interaction with the Cp ring could have counterbalanced the previous effect and explained the lower selectivity.

In the Boc series, the same type of model **D** can be proposed, involving a coordination between the carbonyl of the Boc group and the lithium atom (Scheme 8). According to the sp^2 hybridization of the carbonyl group, instead of the sp^3 arrangement of the sulfonyl function, the steric interaction between the Cp ring and the R^1 group should be lower and explain the better asymmetric induction.

Conclusion

The results reported here provide a nice entry to new 2-aminoalkyl or aminoaryl ferrocenyl *tert*-butylsulfoxides **(6**−**8)**. The sequence is rather straightforward, only two steps from ferrocene, and it is very practical. Though the yields were moderate, the unreacted (S_S)-*tert*-butylsulfinylferrocene (**4**) was recovered after purification.

The closest precedent for structures **6**−**8** in literature was from the Bonini group[49] who investigated the asymmetric synthesis of aminoalkyl-ferrocenyl sulfides by the reaction of enantiomerically pure (*S*)-2-iminoalkyl-ferrocenyl *p*-tolylsulfide with organometallic reagents in the presence of a Lewis acid. A very nice asymmetric induction was observed (in favor of *S*,S_{Fc}). However, this method required the synthesis of the starting material in three steps and, moreover, partial reduction of the imine was observed.

Compared to the Ugi's methodology leading to (S_S,R_{Fc},*S*) configurations,[50] our method allowed the synthesis of the other diastereoisomer.

Compounds **6**−**8** are potential precursors of a range of new ferrocene derivatives. Enantiopure 1-ferrocenylalkyl- (in particular with an alkyl group different from methyl) and 1-ferrocenylaryl-amines are not easy to prepare.[51] These derivatives were used as ligands in asymmetric synthesis[52] and were demonstrated to be better enantioselective ligands for some reactions.[53] Also, this opens the way to a growing class of bidentate ligands with both nitrogen and sulfur coordination sites for asymmetric catalysis.[54]

Further application can also be undertaken. In particular, the synthesis of 1,1′,2-trisubstituted ferrocene derivatives via a second metalation−alkylation sequence with compounds **8** bearing a Boc group.[55]

Experimental Section

General Procedure for Addition of Imines on (S_S)-*tert*-Butylsulfinylferrocene (4). To a cold solution (0 °C) of (S_S)-*tert*-butylsulfinylferrocene (**4**) (1 equiv) in dry THF (2 mL for 50 mg of **4**) was added *n*-BuLi (in hexanes; 1.1 equiv). The mixture was stirred for 2 h at room temperature, and the solution was cooled at −78 °C. The imine (1 equiv) in dry THF (1.5 mL for 50 mg of imine) was added slowly. The reaction mixture was stirred at −78 °C. After completion, a 10% water solution in THF (2 mL for 50 mg of **4**) was added at −78 °C. The reaction mixture was warmed at room temperature, then water (2 mL for 50 mg of **4**) was added. The aqueous layer was extracted with Et_2O (2 mL for 50 mg of **4**). The combined organic layers were dried over $MgSO_4$ and then evaporated to dryness.

(S_{Fc},S_S)-2-(*N*-Tosyl-1-amino-2-methylpropyl)-1-*tert*-butylsulfinylferrocene (6b). The reaction was performed on 250 mg (0.86 mmol) of (S_S)-*t*-butylsulfinylferrocene (**4**) and 194 mg (0.86 mmol)

(49) Bernardi, L.; Bonini, B. F.; Capitò, E.; Dessole, G.; Femoni, C.; Fochi, M.; Comes-Franchini, M.; Mincio, A.; Ricci, A. *ARKIVOC (Gainesville, FL, U.S.)* **2004**, (*ii*), 72−90.

(50) (a) Wang, C.-H.; Brubaker, C. H. J. *J. Mol. Catal. A: Chem.* **1992**, *75*, 221−223. (b) Okoroafor, M. O.; Ward, D. L.; Brubaker, C. H. *Organometallics* **1988**, *7*, 1504−1511. (c) Herrmann, R.; Hübener, G.; Ugi, I. *Tetrahedron* **1985**, *40*, 941−947.

(51) (a) Yasuike, S.; Kofink, C. C.; Kloetzing, R. J.; Gommermann, N.; Tappe, K.; Gavryushin, A.; Knochel, P. *Tetrahedron: Asymmetry* **2005**, *16*, 3385−3393. (b) Fukuda, T.; Takehara, A.; Haniu, N.; Iwao, M. *Tetrahedron: Asymmetry* **2000**, *11*, 4083−4091.

(52) (a) Dai, H.; Hu, X.; Chen, H.; Bai, C.; Zheng, Z. *J. Mol. Catal. A: Chem.* **2004**, *211*, 17−21. (b) Hu, X.; Dai, H.; Bai, C.; Chen, H.; Zheng, Z. *Tetrahedron: Asymmetry* **2004**, *15*, 1065−1068. (c) Tappe, K.; Knochel, P. *Tetrahedron: Asymmetry* **2004**, *15*, 91−102.

(53) (a) Hu, X.; Chen, H.; Dai, H.; Hu, X.; Zheng, Z. *Tetrahedron: Asymmetry* **2003**, *14*, 2073−2080. (b) Hu, X.; Chen, H.; Dai, H.; Zheng, Z. *Tetrahedron: Asymmetry* **2003**, *14*, 3415−3421. (c) Hu, X.; Dai, H.; Hu, X.; Chen, H.; Wang, J.; Bai, C.; Zheng, Z. *Tetrahedron: Asymmetry* **2002**, *13*, 1687−1693. (d) Hu, X.; Chen, H.; Hu, X.; Dai, H.; Bai, C.; Wang, J.; Zheng, Z. *Tetrahedron Lett.* **2002**, *43*, 9179−9182. (e) Fukuda, T.; Takehara, A.; Iwao, M. *Tetrahedron: Asymmetry* **2001**, *12*, 2793−2799. (f) Dubner, F.; Knochel, P. *Tetrahedron Lett.* **2000**, *41*, 9233−9237. (g) Schwink, L.; Knochel, P. *Chem.*−*Eur. J.* **1998**, *4*, 950−968. (h) Schwink, L.; Ireland, T.; Puntener, K.; Knochel, P. *Tetrahedron: Asymmetry* **1998**, *9*, 1143−1163. (i) Ohno, A.; Yamane, M.; Hayashi, T.; Oguni, N.; Hayashi, M. *Tetrahedron: Asymmetry* **1995**, *6*, 2495−2502.

(54) (a) Gerard, S.; Pressel, Y.; Riant, O. *Tetrahedron: Asymmetry* **2005**, *16*, 1889−1891. (b) Anderson, J. C.; Osborne, J. *Tetrahedron: Asymmetry* **2005**, *16*, 931−934. (c) Cabrera, S.; Gomez, Arrayas, R.; Alonso, I.; Carretero, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 17938−17947. (d) Mancheno, O. G.; Arrayas, R. G.; Carretero, J. C. *Organometallics* **2005**, *24*, 557−561. (e) Hu, X.; Bai, C.; Dai, H.; Chen, H.; Zheng, Z. *J. Mol. Catal. A: Chem.***2004**, *218*, 107−112. (f) Tu, T.; Zhou, Y.-G.; Hou, X.-L.; Dai, L.-X.; Dong, X.-C.; Yu, Y.-H.; Sun, J. *Organometallics* **2003**, *22*, 1255−1265. (g) Dai, L.-X.; Tu, T.; You, S.-L.; Deng, W.-P.; Hou, X.-L. *Acc. Chem. Res.* **2003**, *36*, 659−667. (h) Karlström, A. S. E.; Huerta, F. F.; Meuzelaar, G. J.; Bäckvall, J.-E. *Synlett* **2001**, 923−926. (i) You, S.-L.; Zhou, Y.-G.; Hou, X.-L.; Dai, L. X. *Chem. Commun.* **1998**, 2765−2766.

(55) Chong, J. M.; Hegedus, L. S. *Organometallics* **2004**, *23*, 1010−1014.

of imine **11b**. The mixture was stirred 15 min at −78 °C. The crude product was purified by column chromatography, using dichloromethane/ethyl acetate (9/1) as eluent, to afford two diastereoisomers (56%, dr = 90:10). The major diastereoisomer (S_{Fc},S_S,*S*)-**6b** was isolated as a yellow solid (226 mg, R_f = 0.50 with dichloromethane/ethyl acetate 9:1): $[\alpha]_D^{20} = -6{,}4$ (c = 1, $CHCl_3$); mp 124 °C; IR (KBr) ν 1462, 1325, 1157 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.86 (d, 2H, J = 8.3 Hz, Ar), 7.29 (d, 2H, J = 8.3 Hz, Ar), 5.54 (d, 1H, J = 6.8 Hz, NH), 4.77 (dd, 1H, J = 6.8, J = 3.1 Hz, CH−N), 4.44 (s, 5H, Cp), 4.31−4.40 (m, 3H, Cp), 2.41 (s, 3H, Me), 2.19−2.25 (m, 1H, CH of *i*-Pr), 1.16 (s, 9H, *t*-Bu), 0.73 (d, 3H, J = 7.0 Hz, Me of *i*-Pr), 0.68 (d, 3H, J = 7.0 Hz, Me of *i*-Pr); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 143.2 (Ar), 139.2 (Ar), 129.8 (2C, Ar), 127.8 (2C, Ar), 93.2 (Cp), 82.0 (Cp), 72.0 (5C, Cp), 69.4 (Cp), 69.0 (Cp), 68.6 (Cp), 57.4 (C_{quat} *t*-Bu), 56.7 (CH−N), 34.0 (CH of *i*-Pr), 24.1 (3C, C *t*-Bu), 21.9 (Me of Ts), 20.0 (Me of *i*-Pr), 16.7 (Me of *i*-Pr); HRMS (ESI) Calcd for $C_{25}H_{34}FeNO_3S_2$ (MH^+): 516.1330. Found: 516.1317. Anal. Calcd for $C_{25}H_{33}FeNO_3S_2$: C, 58.25; H, 6.45; N, 2.72. Found: C, 58.49; H, 6,84; N, 3.10. The minor diastereoisomer (S_{Fc},S_S,*R*)-**6b** was isolated as a yellow oil (27 mg, R_f = 0.85 with dichloromethane/ethyl acetate 9:1): IR (KBr) ν 1458, 1318, 1151 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.48 (d, 1H, J = 8.6 Hz, NH), 7.77 (d, 2H, J = 8.3 Hz, Ar), 7.21 (d, 2H, J = 8.3 Hz, Ar), 4.50 (s, 5H, Cp), 4.26−4.32 (m, 3H, Cp), 3.84 (dd, 1H, J = 10.2, J = 8.6 Hz, CH), 2.32 (s, 3H, Me), 1.59−1.66 (m, 1H, CH of *i*-Pr), 1.12 (s, 9H, *t*-Bu), 0.47 (d, 3H, J = 7.0 Hz, Me of *i*-Pr), 0.43 (d, 3H, J = 7.0 Hz, Me of *i*-Pr); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 141.8 (Ar), 141.4 (Ar), 129.1 (2C, Ar), 126.5 (2C, Ar), 94.1 (Cp), 79.9 (Cp), 73.3 (Cp), 71.8 (5C, Cp), 68.8 (Cp), 68.2 (Cp), 61.3 (CH−N), 57.4 (C_{quat} *t*-Bu), 36.5 (CH of *i*-Pr), 23.7 (3C, C *t*-Bu), 21.7 (Me of Ts), 21.4 (Me of *i*-Pr), 21.0 (Me of *i*-Pr).

General Procedure for Addition of Sulfones (10) on (S_S)-*t*-Butylsulfinylferrocene (4). To a cold solution (0 °C) of (S_S)-*tert*-butylsulfinylferrocene (**4**) (2 equiv) in dry THF (2 mL for 50 mg of **4**) was added *n*-BuLi (in hexanes; 2.2 equiv). The mixture was stirred for 2 h at room temperature, and the solution was cooled at −78 °C. The appropriate sulfone **10** (1 equiv) in dry THF was added dropwise. The reaction mixture was stirred at −78 °C. After completion, a 10% water solution in THF (2 mL for 50 mg of **4**) was added at −78 °C. The reaction mixture was warmed at room temperature, then water (2 mL for 50 mg of **4**) was added. The aqueous layer was extracted with Et_2O (2 mL for 50 mg of **4**). The combined organic layers were dried over $MgSO_4$ and then evaporated to dryness.

(*S*)-1-Ferrocenyl-2-methyl-*N*-tosyl-propylamine (15). To a solution of Raney nickel (1 g, previously rinsed with water, ethanol, and then methanol) in methanol (10 mL) was added (S_{Fc},S_S,*S*)-**6b** (150 mg, 0,29 mmol), and the whole mixture was stirred under reflux for 2 h. The mixture was cooled, filtered off through celite, and rinsed with ethanol. Evaporation of the solvent and purification by column chromatography with *n*-heptane/ethylacetate (8/2) gave (*S*)-**15** as a yellow oil (75 mg, 65%): $[\alpha]_D^{20} = +32.0$ (c = 1, $CHCl_3$); er >99:1 by HPLC (Daicel AD-H column 250 × 4.6 (length × inside diameter)) 5 μm, 95:5 *n*-heptane/propan-2-ol at 1 mL min^{-1}, 203 nm, 20 °C; t_R = 19.97 min (*R*), t_R = 38.37 min (*S*); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.83 (d, 2H, J = 8.4 Hz, Ar), 7.34 (d, 2H, J = 8.4 Hz, Ar), 4.95 (d, 1H, J = 4.8 Hz, NH), 4.00−4.13 (m, 10H, CH−N and Cp), 2.45 (s, 3H, Me), 2.01−2.09 (m, 1H, CH of *i*-Pr), 0.69 (d, 3H, J = 6.8 Hz, Me of *i*-Pr), 0.63 (d, 3H, J = 7.2 Hz, Me of *i-Pr*); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 143.8 (Ar), 138.7 (Ar), 130.1 (2C, Ar), 127.5 (2C, Ar), 88.1 (Cp), 69.3 (5C, Cp), 69.2 (Cp), 68.2 (Cp), 67.9 (Cp), 66.7 (Cp), 59.2 (CH−N), 31.9 (CH of *i*-Pr), 22.0 (Me of Ts), 19.1 (Me of *i*-Pr), 17.3 (Me of *i*-Pr); HRMS (ESI) Calcd for $C_{21}H_{26}FeNO_2S$ (MH^+): 412.1034. Found: 412.1029.

(*S*)-1-Ferrocenyl-2-methyl-propylamine (16). To a 0.1 M THF solution of SmI_2 (8.76 mL, 0.876 mmol) and HMPA (0.58 mL) was added a solution of (*S*)-**15** (30 mg, 0.073 mmol) in THF (0.35 mL) at room temperature. The whole mixture was stirred under reflux for 12 h (the purple color of the solution disappeared). The mixture was quenched with saturated NaCl (10 mL). The aqueous layer was extracted with ether (2 × 10 mL). The combined organic layers were washed with sat. $NaHCO_3$ (10 mL) and sat. NaCl (10 mL) and then dried over $MgSO_4$. Evaporation of the solvent and purification by column chromatography with ethylacetate gave (*S*)-**16** as a yellow oil (13 mg, 70%): $[\alpha]_D^{20} = +89.2$ (c = 0.325, C_6H_6); lit. $[\alpha]_D^{20} = -89.7$ (c = 1.0, C_6H_6) for (*R*)-**16**;[42] er 99:1 by HPLC (Daicel AD column 250 × 4.6 (length × inside diameter)) 10 μm, 100% CH_3CN at 1 mL min^{-1}, 201 nm, 20 °C; t_R = 13.3 min (*R*), t_R = 37.6 min (*S*); ^1H NMR ($CDCl_3$, 400 MHz) δ 4.19−4.21 (m, 1H, Cp), 4.16 (s, 5H, Cp), 4.07−4.13 (m, 3H, Cp), 3.47 (d, J = 5.0 Hz, CH−N), 1.74 (br, 2H, NH_2), 1.57−1.69 (m, 1H, CH of *i*-Pr), 0.85 (d, 3H, J = 8.0 Hz, Me of *i*-Pr), 0.79 (d, 3H, J = 8.0 Hz, Me of *i*-Pr); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 93.8, 68.2, 67.0, 65.2, 56.5, 35.2, 18.9, 18.6.

Acknowledgment. We thank the "PunchOrga" Network (Pôle Universitaire Normand de Chimie Organique), the "Région Haute-Normandie", the "Région Basse-Normandie", the "Ministère de la Recherche", CNRS (Centre National de la Recherche Scientifique), and the European Union (FEDER funding) for financial support. We also thank Aurélie Faliez and Virginie Tronel (IUT−Rouen) for their contribution to this work.

Supporting Information Available: Experimental procedures and characterization for all new compounds described in this work and crystallographic data for the reported structures (CIF format). This material is available free of charge via the Internet at http://pubs.acs.org.

JO061360T