Diastereoselective additions of organometallic reagents to (S_{Fc})-2-*p*-tolylsulfanylferrocene carboxyaldehyde and to (S_{Fc})-2-*p*-tolylsulfanyl ferrocenyl imines. Synthesis of new central and planar chiral ferrocenyl alcohols and amines

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Dedicated to Professor Binne Zwanenburg on his 70th birthday

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Abstract

Enantiomerically pure 2-hydroxyalkyl, 2-aminoalkyl and 2-iminoalkyl ferrocenyl *p*-tolylsulfides are easily prepared in good yields and with complete diastereocontrol from (*S*)-(2-*p*-tolylthio)ferrocencarboxyaldehyde. This aldehyde provides also an easy access to the first enantiomerically pure planar chiral ferrocenyl cyanohydrin. The absolute configuration of the new stereocenters has been determined by single-crystal X-ray analysis.

Keywords: Planar chiral ferrocenyl aldehyde, planar chiral ferrocenyl imines, organometallic reagents

Introduction

The design and the synthesis of new ferrocenyl derivatives possessing planar and/or central chirality are of great importance in the development of new versatile and effective ligands as well as of useful chiral auxiliaries and building blocks[1] for asymmetric synthesis. It is noteworthy that planar chiral ferrocenes have also found considerable applications in industrial processes.[2]

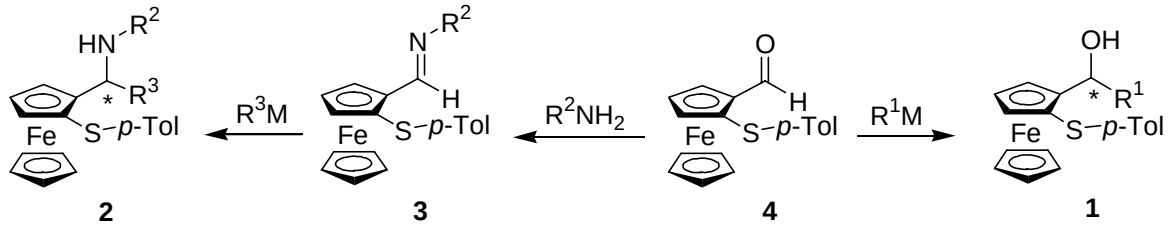
In general, the synthesis of enantiopure or enantiomerically enriched 1,2-disubstituted ferrocenes involves either a traditional resolution of racemic intermediates[3] or a stereoselective

ortho-metallation step. The stereoselective *ortho*-metallation methods reported to date rely on a diastereoselective lithiation of ferrocenyl sulfoxides,[4] acetals,[5] amines,[6] oxazolines,[7] hydrazones,[8] sulfoximines,[9] azepines,[10] methylethers,[11] methoxymethylpyrrolidines[3b,12] and *O*-methylephedrines[13] or on an enantioselective lithiation of achiral ferrocenyl phosphinoxides,[14] amides[15] or amines[16] using a chiral lithium amide or external chiral auxiliaries such as (-)-sparteine or cyclohexanediamine.

1,2-Disubstituted enantiomerically pure planar chiral ferrocenylaldehydes have been recently employed as precursors of more complex molecules,[17] in particular the formyl group could be stereoselectively alkylated[18] by reaction with organometallic reagents. Asymmetric additions of organometallic reagents to the C=N functional group are of great interest for the preparation of chiral amines and derivatives.[19] Only few examples have been reported so far on the 1,2-addition of organometallic reagents to ferrocenyl imines. In particular chiral ferrocenyl amines possessing central chirality have been obtained *via* highly stereoselective additions of organolithium[20] or organozinc[21] reagents to chiral ferrocenyl imines deriving from enantiomerically pure amines or by enantioselective addition of dialkylzinc reagents to achiral ferrocenyl imines in the presence of chiral ligands.[22] Moreover, new planar chiral ferrocenyl diamines have been synthesized starting from 2-(*N*,*N*-dimethylaminomethyl) ferrocencarboxaldehyde *via* the corresponding imine.[23]

As a part of our ongoing interest in sulfur containing compounds[24] and in molecules bearing the sulfur and the ferrocene moiety,[25] we have recently synthesized enantiomerically pure β-hydroxyalkyl, β-aminoalkyl and β-iminoalkyl ferrocenyl sulfides having only the central chirality. Some of these derivatives were successfully employed as ligands in palladium-catalyzed allylic substitution with asymmetric induction up to 99%.[26]

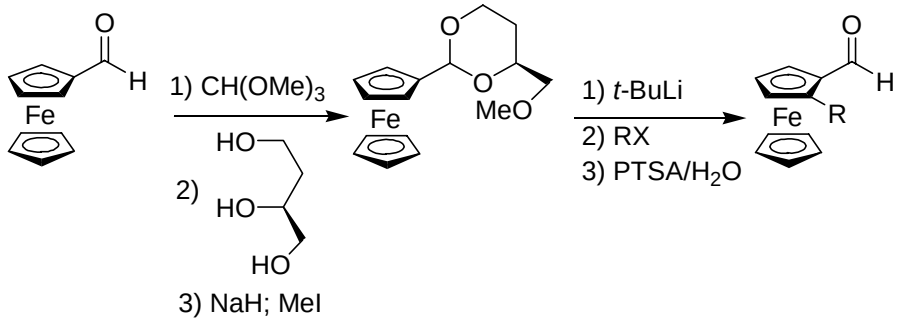
Herein we wish to report our results on the synthesis of 2-(hydroxyalkyl)- **1**, 2-(aminoalkyl)-ferrocenyl *p*-tolylsulfides **2** with planar and central chirality, and 2-(iminoalkyl)-ferrocenyl *p*-tolylsulfides **3** with planar chirality taking advantage of (*S*)-(2-*p*-tolylthio) ferrocencarboxyaldehyde **4**[5b] as the key compound (Scheme 1). The enantiomerically pure **4** can react with organometallic reagents affording **1** and with amines allowing the preparation of ferrocenyl imines **3**, which in turn may be converted into **2** by reaction with organometallic reagents thus introducing a new stereogenic center beside the planar chirality.



Scheme 1

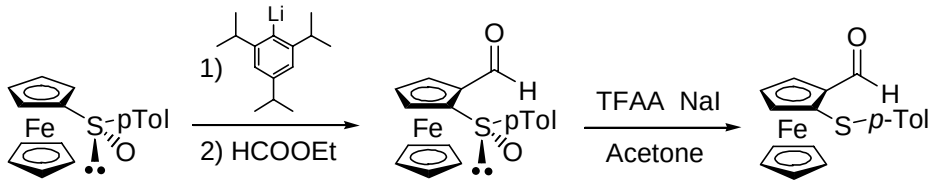
Results and Discussion

(*S*)-(2-*p*-Tolylthio)ferrocencarboxyaldehyde **4**[5b] has been synthesized, beside a wide range of enantiopure α-substituted ferrocenyl aldehydes, by Kagan et al. starting from ferrocencarboxyaldehyde that could be readily transformed into the acetal of (*S*)-1,2,4-butantriol. The enantio- and diastereomerically pure ferrocenyl acetal behaves as *ortho*-lithiation guide and the deprotonation can be stereoselectively directed to a single diastereotopic *ortho*-hydrogen (Scheme 2).



Scheme 2

An alternative procedure, developed by us, for synthesizing aldehyde (*S*)-**4** is based on the diastereoselective *ortho*-lithiation of (*S*)-ferrocenyl *p*-tolyl sulfoxide **5**[4c] (Scheme 3) with a sterically hindered base such as 2,4,6-triisopropylphenyllithium,[4b] followed by electrophilic trapping with ethyl formate. The obtained (S_{Fc},S_S)-2-*p*-tolylsulfinyl ferrocenecarboxy aldehyde **6** was directly reduced to the corresponding aldehyde (*S*)-**4** by treatment with sodium iodide and trifluoroacetic anhydride in acetone.[27] The enantiopure aldehyde (*S*)-**4** was obtained in 45% overall yield and showed spectroscopic and optical properties identical with the product obtained following the Kagan's procedure.



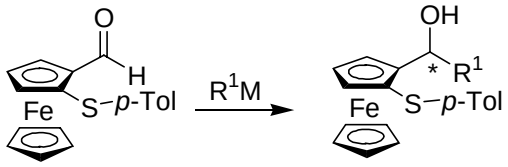
5 **6** **4**

Scheme 3

The reaction of aldehyde (*S*)-**4** with organometallic reagents, namely Grignard reagents, organolithium derivatives, tetraallyltin, and with diethylaluminiumcyanide and trimethylsilyl cyanide afforded the corresponding secondary alcohols **1** in very good yields, very short reaction time (only few minutes) and high diastereoselectivity as determined by ^{1}H-NMR spectra of the crude reaction mixture. Only one set of signals was detected in the reactions with methylmagnesium bromide (entry 1), vinylmagnesiumbromide (entry 3), tetraallyltin (entry 6),

diethylaluminiumcyanide (entry 7) and trimethylsilyl cyanide (entry 8). On the contrary the reaction with phenylmagnesiumbromide (entry 4), methyllithium (entry 2) and *n*-butyllithium (entry 5) showed two sets of signals. In these cases the two diastereoisomers could be separated by preparative thin layer chromatography.

Table 1. Reaction of aldehyde (*S*)-**4** with organometallic reagents



4 **1**

Entry	R^1M	T (°C)	Solvent	**1**	Yield of **1** (%)[a]	d.e.[b]
1	CH_3MgBr	-78	THF	**a**	87	> 98
2	CH_3Li	- 78	THF	**a**	82	86
3	CH_2=CHMgBr	-78	THF	**b**	76	> 98
4	PhMgBr	-78	THF	**c**	89	96
5	BuLi	-78	THF	**d**	85	82
6[c]	$Sn(\swarrow\!\!\!\!\searrow)_4$	0	CH_2Cl_2	**e**	86	> 98
7	Et_2AlCN	-78	THF	**f**	98	> 98
8[d]	TMSCN	-50	CH_2Cl_2	**g**	98	> 98

[a] Isolated yield.
[b] Determined by ^{1}H-NMR on the crude reaction mixture.
[c] In the presence of 10 mol% of $Sc(OTf)_3$.
[d] In the presence of 10 mol% of ZnI_2.

Although (*R*)-(+)-ferrocenecyanohydrin acetate has been previously obtained[28] by Lipase catalyzed acylation of the racemic ferrocenecyanohydrin and (*R*)-(+)-ferrocenecyanohydrin has been synthesized from formyl ferrocene employing the hydroxynitrile lyase from *Hevea brasiliensis*,[29] products **1f** and **1g** represent the first enantiomerically pure ferrocenecyanohydrins containing both the central and the planar chirality.

The absolute configuration of the new stereocenters has been determined by single-crystal X-ray analysis on the major diastereoisomer of product **1c**[30] indicating (*S*)-configuration (Figure 1). We could therefore assign the (S,S_{Fc}) configuration to products **1**. This stereochemical outcome can be rationalized by an *exo* attack of the organometallic species on the less congested *Si*-face of the aldehyde away from the sterically hindered lower cyclopentadienyl ring (Figure 2). These results are in agreement with the assumption of Ugi[31] and of Kagan.[32]

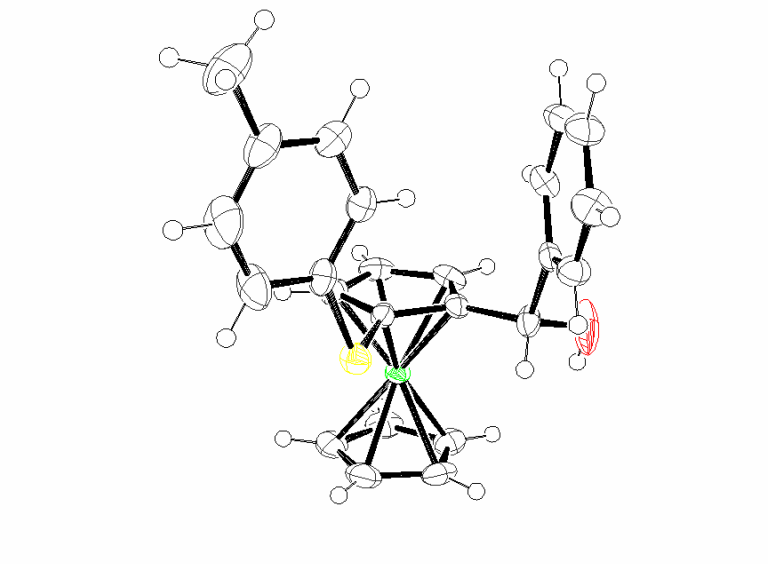


Figure 1. X-ray crystal structure of (S,S_{Fc})-**1c**.

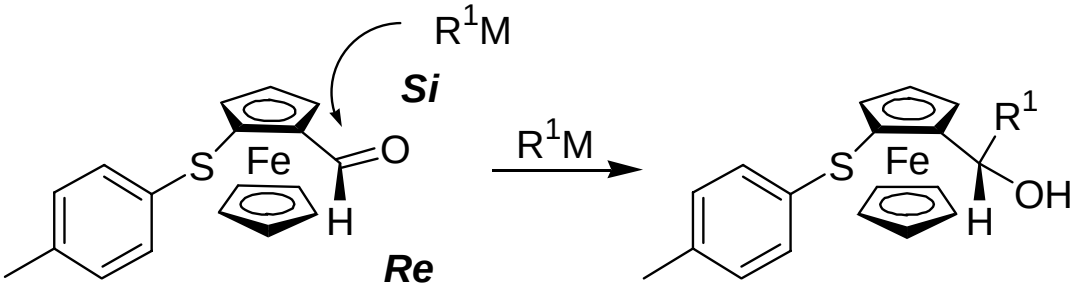
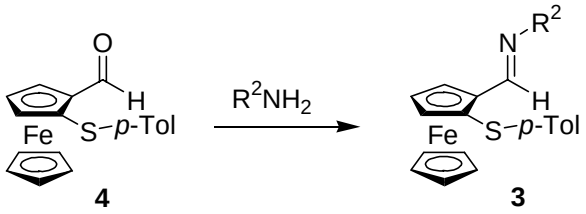


Figure 2. *Exo* attack of the organometallic species on aldehyde (*S*)-**4**.

Then we turned our attention to the preparation of planar chiral ferrocenyl imines **3** that was readily achieved by treatment of the aldehyde (*S*)-**4** with the appropriate amine in the presence of powdered molecular sieves (4 Å) in toluene. The 2-iminoalkyl ferrocenyl *p*-tolyl sulfides **3a** and **3b** were obtained in excellent yields (Table 2) and were purified by crystallization from MeOH. The yield of product **3c** was increased by reacting (*S*)-**4** with $TsNH_2$ in the presence of $TiCl_4$ and Et_3N using CH_2Cl_2 as the solvent.[33] Imines **3** were obtained as geometrically (*E*)-homogeneous compounds according to the ^{1}H-NMR spectra. Moreover, they are very stable and in particular **3c** could also be purified by column chromatography on silica gel.

Table 2. Synthesis of 2-iminoalkyl ferrocenyl *p*-tolylsulfides **3**



4 **3**

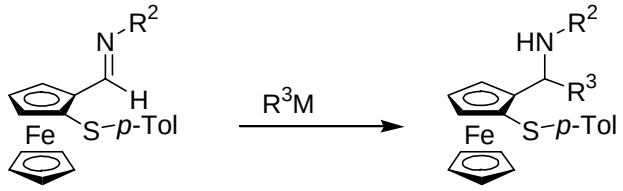
Entry	R^2	**3**	T (°C)	Yield (%)[a]	*E:Z*[b]
1	PMP	**a**	50	90	> 98:2
2	CH_2Ph	**b**	50	93	> 98:2
3	Ts	**c**	110[c]	41	> 98:2
4	Ts	**c**	r.t.[d]	98	> 98:2

[a] Isolated yield.
[b] Determined by ^{1}H-NMR on the crude reaction mixture.
[c] In the presence of a catalytic amount of *p*-toluensulfonic acid.
[d] Reaction performed with $TiCl_4$ in the presence of Et_3N using CH_2Cl_2 as the solvent.

The reactivity of ferrocenyl imines **3** with organometallic reagents and the possibility of obtaining 2-aminoalkyl ferrocenyl *p*-tolylsulfides **2** were tested upon derivatives **3a** and **3c** as model compounds.

As can be deduced from the results reported in Table 3 both imines **3a** and **3c** can be successfully allylated with tetraallyltin in the presence of catalytic amount of $Sc(OTf)_3$ affording the corresponding homoallylic amines **2a** and **2b** in good yields and very goods diastereoselectivity (entries 1 and 2). The *N*-PMP ferrocenyl imine **3a** does not react with Grignard reagents even in the presence of a Lewis acid as LiCl, $MgBr_2$ or $Sc(OTf)_3$ (entries 4-7); the reaction of **3a** with MeLi occurs in very low yield (10%) and with 58% d.e. (entry 3). The *N*-tosyl ferrocenyl imine **3c** shows a different behavior and readily reacts with methylmagnesium bromide, vinylmagnesium bromide and phenylmagnesiumbromide, in the presence of $MgBr_2$ or LiCl, the latter giving a very fast reaction and better results in term of yields. The amines **2e, 2f** and **2g** (entries 8, 10, 11, 13) bearing the central and the planar chirality were indeed obtained in good yields and good to very good diastereoselectivity. Product **2e** was also obtained by reaction of **3c** with MeLi (entry 9), but in lower yield reproducing the same behavior as observed in the case of the aldehyde **4**.

Table 3. Synthesis of 2-aminoalkyl ferrocenyl *p*-tolylsulfides **2**



3 **2**

Entry	**3**	R^2	R^3M	L. A.	Reaction Conditions	**2**	Yield of **2** (%)[a]	d.e.[b]
1	**a**	PMP	$Sn(\sim\!\!=\!\!\sim)_4$	$Sc(OTf)_3$	CH_2Cl_2/0 °C/18h	**a**	72	>98
2	**c**	Ts	$Sn(\sim\!\!=\!\!\sim)_4$	$Sc(OTf)_3$	CH_2Cl_2/0 °C/18h	**b**	88	>98
3	**a**	PMP	MeLi	-	THF/r.t./24h	**c**	10	58
4	**a**	PMP	MeMgBr	-	THF/r.t./24h	**c**	-	-
5	**a**	PMP	MeMgBr	$MgBr_2$	THF/r.t./24h	**c**	-	-
6	**a**	PMP	MeMgBr	$Sc(OTf)_3$	CH_2Cl_2/r.t./24h	**c**	-	-
7	**a**	PMP	MeMgBr	LiCl	Et_2O/0 °C/	**c**	-	-
8	**c**	Ts	MeMgBr	$MgBr_2$	THF/0 °C/18h	**e**	78	>98
9	**c**	Ts	MeLi	-	THF/0 °C /18h	**e**	43	>98
10	**c**	Ts	CH_2=CHMgBr	$MgBr_2$	THF/r.t./48h	**f**	36[c]	>98
11	**c**	Ts	CH_2=CHMgBr	LiCl	Et_2O/0 °C/2 min	**f**	97	96
12	**c**	Ts	PhMgBr	$MgBr_2$	THF/r.t./48h	**g**	-	-
13	**c**	Ts	PhMgBr	LiCl	Et_2O/0 °C/10 min	**g**	97	77

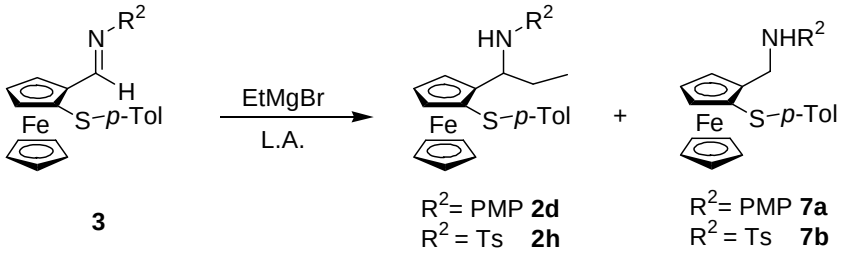
[a] Isolated yield.

[b] Determined by ^{1}H-NMR on the crude reaction mixture.

[c] Beside 39 % of recovered starting material.

The reaction of **3c** with EtMgBr in the presence of $MgBr_2$ or LiCl furnished the alkylation product **2h** together with the amine **7b** deriving from the reduction of the C-N double bond (Table 4 entries 3 and 4) whereas imine **3a** was found unreactive (entry 1) . Recently, Szymoniak[34] and Takahashi[35] have shown that imines undergo Zr-catalyzed addition with ethylmagnesium reagents whereas the same imines are inert towards the same reagents in the absence of the zirconium catalyst. These papers prompted us to perform the same reaction on imine **3a** and **3c**, but also in this case imine **3a** was found unreactive (entry 2) and a mixture of the amino derivatives **2h** and **7b** was obtained from imine **3c**. This mixture was enriched in the alkylation product **2h** by increasing the amount of the Grignard reagent (entries 3-5).

Table 4. Reaction with EtMgBr



3

R^2= PMP **2d**
R^2 = Ts **2h**

R^2= PMP **7a**
R^2 = Ts **7b**

Entry	**3**	Reaction conditions	L.A.	Yield of **2** (%)[a]	d.e.[b]	Yield of **7** (%)[a]	Ratio **2h**:**7b**
1	**a**	EtMgBr 3 equiv /THF/r.t./48 h	$MgBr_2$	-	-	-	-
2	**a**	EtMgBr 3 equiv /THF/r.t./48 h	Cp_2ZrCl_2	-	-	-	-
3	**c**	EtMgBr 3 equiv /THF/r.t./48 h	$MgBr_2$	9	>98	26	1:3
4	**c**	EtMgBr 3 equiv /Et_2O/r.t./16 h	LiCl	31[e]	>98	31	1:1
5	**c**	EtMgBr 3 equiv /THF/r.t./30 min	Cp_2ZrCl_2	21	>98	67	1:3
6	**c**	EtMgBr 10 equiv THF/r.t./30 min	Cp_2ZrCl_2	30	>98	60	1:2
7	**c**	EtMgBr 25 equiv THF/r.t./30 min	Cp_2ZrCl_2	48	>98	42	1.2:1

The absolute configuration of the new stereocenters of amino derivatives **2** has been determined by single-crystal X-ray analysis on the major diastereoisomer of product **2g**[36] indicating an (*S*)-configuration (Figure 3). We could therefore assign the (S,S_{Fc}) configuration to products **2**. This result implies a similar behavior of the imine (*S*)-**3** and the aldehyde (*S*)-**4** toward the addition of organometallic reagents.

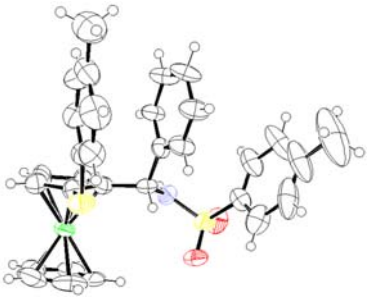


Figure 3. X-ray crystal structure of (S,S_{Fc})-**2g**.

Conclusions

(S)-(2-*p*-Tolylthio)ferrocencarboxyaldehyde was found to be a very versatile compound that allowed the synthesis of a large variety of enantiomerically pure sulfur containing ferrocenyl derivatives. 2-Hydroxyalkyl, 2-aminoalkyl and 2-iminoalkyl ferrocenyl *p*-tolylsulfides were easily prepared in good yields and with complete diastereocontrol. Moreover *(S)*-(2-*p*-tolylthio)ferrocencarboxyaldehyde provides an easy access to the first enantiomerically pure planar chiral cyanohydrin. All these derivatives bear several functional groups, that make them attractive from a synthetic point of view, and contain different heteroatoms, useful for the coordination to a metal centers and for the preparation of new ligands for asymmetric catalysis.

Experimental Section

General Procedures. Melting points (uncorrected) were determined with a Büchi melting point apparatus. ^{1}H NMR and ^{13}C NMR spectra were recorded with a Varian Gemini 300 at 300 and 75 MHz, or a Varian Gemini 400 at 400 and 100 MHz respectively, using $CDCl_3$ solutions of the samples. Chemical shifts (δ) are reported in ppm relative to $CHCl_3$ (δ = 7.26 for ^{1}H and δ = 77.0 for ^{13}C). *J* values are given in Hz. ^{13}C NMR spectral assignments were made by DEPT experiments. IR spectra were recorded on a Perkin-Elmer model 257 grating spectrometer. Mass spectra were obtained using a VG 7070-E spectrometer at an ionizing voltage of 70 eV or with an electrospray ionization source (ESIMS). All the ESIMS spectra were performed using MeOH as the solvent. $[\alpha]_D$ values were measured with Perkin Elmer Polarimeter 341 and are given in 10^{-1}degcm^{2}g^{-1}. The originality of all compounds was checked by a CAS-on-line structure search. Reactions were conducted in oven-dried (120 °C) glassware under a positive Ar atmosphere. Transfer of anhydrous solvents or mixtures was accomplished with oven-dried syringes/septum techniques. THF was distilled from sodium/benzophenone prior to use and stored under Ar. CH_2Cl_2 was passed through basic alumina and distilled from CaH_2 prior to use. Other solvents were purified by standard procedures. Light petroleum ether refers to the fraction with a bp 40-60 °C. The reactions were monitored by TLC, using silica gel plates (Baker-flex IB2-F). Column chromatography was performed with Merck silica gel 60 (70-230 mesh). Preparative thick layer chromatography was carried out on glass plates using a 1 mm layer of Merck silica gel 60 Pf 254. All chemicals were used as obtained or purified by distillation as needed. (*S*)-ferrocenyl *p*-tolyl sulfoxide **5**[4c] and (S)-(2- *p*-tolylsulfanyl)ferrocenecarboxaldehyde **4**[5b] were prepared following the literature procedure.

($S_{Fc}S_S$)-2-(*p*-Tolylsulfinyl)-ferrocenecarboxaldehyde (6). A solution of of (*S*)-ferrocenyl *p*-tolyl sulfoxide **5** (0.2 g, 0.6 mmol) in dry THF (5 mL) cooled at-78 °C under argon atmosphere was transferred *via cannula* into a cooled solution of 2,4,6-triisopropylphenyllithium[4b] (1.2 mmol) in THF (5 mL) prepared from 1-bromo-2,4,6-triisopropylbenzene and *t*-BuLi at –

78 °C for 2.5 h. The resulting solution was warmed to –40 °C over 1.5h and then stirred at –40 °C for another 1.5h. The solution was cooled again to –78 °C and freshly distilled ethyl formate was added. After 10 min the reaction was quenched with acetic acid and the mixture was concentrated under reduced pressure. The crude was diluted with Et_2O, washed with water, dried ($MgSO_4$) and concentrated. Column chromatography (Light petroleum / Et_2O = 1:1) afforded **6** in 68% yield (140 mg). δ_H ($CDCl_3$, 300MHz) 2.37 (3H, s, CH_3), 4.60 (5H, s, FcH), 4.71 (H br s, FcH), 4.76 (1H, bs, FcH), 5.02 (1H, bs, FcH), 7.27 (2H, d, J = 8.0 Hz, ArH), 7.51 (2H, d, J = 8.4 Hz, ArH), 10.49 (H, s, CHO).

(*S*$_{Fc}$)-2-(*p*-Tolylsulfanyl)-ferrocenecarboxaldehyde (4). To a stirred solution of **6** (100 mg, 0.28 mmol) and NaI (105 mg, 0.70 mmol) in acetone (1.0 mL) at 0 °C under argon atmosphere, a solution of trifluoroacetic anhydride (0.16 ml, 1.12 mmol) in acetone (1.0 mL) was slowly added. After stirring for 30 min at 0 °C, the reaction mixture was concentrated *in vacuo* and water (4 mL) was added. The mixture was extracted with $CHCl_3$ (3 x 5 mL) and the organic layer was washed with a 10% solution of $Na_2S_2O_3$, dried and concentrated. The residue was purified by chromatography on silica gel (light petroleum/EtOAc 2:3) giving **4** as a red solid (62 mg, 65%).

General procedure for the reaction with Grignard reagents

To a solution of (*S*)-**4** (0.5 mmol) in dry THF cooled at –78 °C under argon atmosphere, a solution of the Grignard reagent (1.5 mmol) was slowly added. The colour of the solution immediately change from red to yellow/orange and a TLC analysis (hexane/EtOAc 4:1) showed the complete disappearance of the starting aldehyde. The reaction mixture was quenched at –78 °C with saturated NH_4Cl solution and extracted with Et_2O. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure. The diastereomeric ratio was determined by ^1H and ^{13}C NMR spectra on the reaction mixture and then the final derivative was isolated by column chromatography eluent (eluent hexane/EtOAc 4:1).

(1*S*)-1-[(*S*$_{Fc}$)-2-(*p*-Tolylsulfanyl)-ferrocenyl]ethanol (1a). Following the general procedure and using a 3.0 M solution in THF of MeMgBr, the final product was obtained after chromatography as a yellow solid in 87 % yield. M.p. 93 – 95 (Et_2O) (dec). δ_H ($CDCl_3$, 300MHz) 1.17 (3H, d, J = 6.3 Hz, CH_3), 2.25 (3H, s, CH_3), 2.34 (1H, s, OH), 4.36 (6H, br s, FcH + CHOH), 4.53 (2H br s, FcH), 4.64 (1H, br s, FcH), 6.91 (2H, d, J = 8.4 Hz, ArH), 6.99 (2H, d, J = 8.4 Hz, ArH). δ_C ($CDCl_3$, 75MHz) 21.4, 22.7 (CH_3), 64.5, 68.2, 69.2, 69.75, 70.55 (CH), 90.6, 93.9 (C), 125.0, 129.8 (ArCH), 140.5, 141.5 (ArC). ν_{max}(CCl_4) 3437 cm^{-1}. ESI-MS *m/z* 352 (M^+); 375 (M^+ +Na). $[\alpha]^{20}_D$ +19.5 (c 0.645 $CHCl_3$). Anal. Calcd. for $C_{19}H_{20}FeOS$ (352.06): C, 64.76; H, 5.72. Found: C, 65.01; H, 5.61.

(1*S*)-1-[(*S*$_{Fc}$)-2-(*p*-Tolylsulfanyl)-ferrocenyl]-2-propen-1-ol (1b). Following the general procedure and using a 1.0 M solution in THF of vinylMgBr, the final product was obtained after chromatography as a yellow solid in 81% yield. M.p. 112 –114 °C (Et_2O). δ_H ($CDCl_3$, 300MHz) 2.25 (3H, s, CH_3), 2.50 (1H, s, OH) 4.31 (5H, s, FcH), 4.40 (1H, m, FcH), 4.47 (2H, m, FcH), 4.92 (1H, dt, m, J = 10.3, J = 1.4 Hz, H_a-CH_2=), 5.02 (1H, bd, J = 6.3 Hz, CHOH), 5.07 (1H, dt,

J = 17.0, *J* = 1.4 Hz, H_b-CH_2=), 5.54 (1H, 4d, *J* = 17.0, *J* = 10.3, J = 6.3 Hz, CH=), 6.95 (4H, m, ArH). δ_C ($CDCl_3$, 75MHz) 20.8 (CH_3), 67.5, 68.7, 69.2, 70.0, 75.5 (CH) 115.0 (CH_2), 126.5, 129.3 (ArCH), 135.0 (ArC), 138.9 (CH). ν_{max}(CCl_4) 3611 cm^{-1}. ESI-MS *m/z* 387 (M^++Na). $[\alpha]^{20}_D$ +108 (c 0.51 in $CHCl_3$). Anal. Calcd. for $C_{20}H_{20}FeOS$ (364.06): C, 65.92; H, 5.53. Found: C, 65.78; H, 5.62.

(1*S*)-1-[(*S*$_{Fc}$)-2-(*p*-Tolylsulfanyl)-ferrocenyl](phenyl)methanol (1c). Following the general procedure and using a 1.0 M solution in THF of PhMgBr, the final product was obtained as a mixture of two diastereoisomers with a d.e. 96% (calculated by ^{1}H-NMR on the crude mixture). The two diastereoisomers could be isolated by preparative TLC (hexane/EtOAc = 15:1.). The major diastereoisomer was fully characterized and crystallized by MeOH affording crystals suitable for X-ray analysis.

(1*S*)-1c. M.p. 107 – 108 °C (MeOH). δ_H ($CDCl_3$, 300MHz) 2.21 (3H, s, CH_3), 2.64 (1H, br s, OH) 4.39 (5H, s, FcH), 4.46 (1H, m, FcH), 4.51 (2H, m, FcH), 5.61 (1H, br s, CH), 6.69 (2H, d, *J* = 8.0 Hz, ArH), 6.82 (2H, d, *J* = 8.0 Hz, ArH), 7.12 (2H, m, ArH), 7.19 (3H, m, ArH). δ_C ($CDCl_3$, 75MHz) 20.8 (CH3), 67.7, 68.8, 70.3, 70.45, 75.6, (CH), 77.2, 97.6 (FcC), 126.4, 126.5, 127.2, 127.95, 129.1 (ArCH), 134.7, 135.4, 142.2, 142.3 (ArC). ν_{max}(CCl_4) 3577 cm^{-1}. ESI-MS *m/z* 437 (M^++Na). $[\alpha]^{20}_D$ +38 (c 0.51 in $CHCl_3$). Anal. Calcd. for $C_{24}H_{22}FeOS$ (414.07): C, 69.55; H, 5.35. Found: C, 65.69; H, 5.22.

(1*S*) and (1*R*)-1-[(*S*$_{Fc}$)-2-(*p*-Tolylsulfanyl)-ferrocenyl]-1-pentanol ((1*S*)-1d and (1*R*)-1d). To a solution of (*S*)-**4** (170 mg, 0.5 mmol) in dry THF cooled at –78 °C under argon atmosphere, a solution of *n*-BuLi (1.6M, 0.5 mL, 0.75 mmol) was slowly added. The colour of the solution immediately change from red to yellow and a TLC analysis (light petroleum/Et_2O = 3/1) showed the complete disappearance of the starting aldehyde. The reaction mixture was quenched at –78 °C with water and extracted with Et_2O. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure. The ^{1}H and ^{13}C NMR spectra of the crude reaction mixture showed the presence of a mixture of diastereoisomers in a 10:1 ratio (de =82%). Chromatography of the crude yielded as the major R_f product the major diastereoisomer in 78 % yield (155 mg) as orange/yellow viscous oil and as the second R_f product the minor diastereoisomer in 7 % yield (15 mg) as a yellow oil.

(1*S*)-1d. δ_H ($CDCl_3$, 300MHz) 0.70 (3H, t, *J* = 7.1 Hz, CH_3), 1.00 – 1.47 (6H, m, $(CH_2)_3$), 2.10 (1H, br s, OH), 2.24 (3H, s, CH_3) 4.30 (5H, s, FcH), 4.34 (1H, m, FcH), 4.46 (1H, m, FcH), 4.51 (1H, m, FcH), 4.58 (1H, brd, *J* = 7.0 Hz, CHOH), 6.93 (2H, d, *J* = 8.0 Hz, ArH), 6.98 (2H, d, *J* = 8.0 Hz, ArH). δ_C ($CDCl_3$, 75MHz) 13.8 (CH_3), 20.8. 22.35, 27.8 (CH_2), 37.6 (CH), 68.75, 67.8, 68.4, 69.8, 75.4 (CH), 126.4, 129.3 (ArCH), 134.9, 136.0 (ArC). ν_{max}(CCl_4) 3590 cm^{-1}. ESI-MS *m/z* 417 (M^++Na). $[\alpha]^{20}_D$ +5.7 (c 0.51 in $CHCl_3$). Exact mass Calcd. for $C_{22}H_{26}FeOS$: 394.1054. Found: 394.1078.

(1*R*)-1d. δ_H ($CDCl_3$, 300MHz) 0.90 (3H, t, *J* = 7.0 Hz, CH_3), 1.20 – 1.80 (6H, m, $(CH_2)_3$), 1.98 (1H, brd, *J* = 4.3 Hz, OH), 2.24 (3H, s, CH_3) 4.23 (5H, s, FcH), 4.33 (1H, m, FcH), 4.38 (1H, m, FcH), 4.45 (1H, m, FcH), 4.64 (1H, m, CHOH), 6.69 (4H, m, ArH). δ_C ($CDCl_3$, 75MHz) 14.0 (CH_3), 22.5, 28.7, 30.2 (CH_2), 35.6 (CH), 68.6, 68.7, 69.1, 70.1, 75.75 (CH), 125.9,

129.6(ArCH), 136.4, 138.7 (ArC). ν_{max}(CCl_4) 3588 cm^{-1}; ESI-MS *m/z* 417 (M^++Na). $[\alpha]^{20}_D$ –7.4 (c 0.50 in $CHCl_3$).

(1*S*)-1-[(*S*$_{Fc}$)-2-(*p*-Tolylsulfanyl)-ferrocenyl]-3-buten-1-ol (1e). To a solution of (*S*)-**4** (170 mg, 0.5 mmol) in dry CH_2Cl_2 and of catalytic amounts of $Sc(OTf)_3$ (28 mg, 0.05 mmol) cooled at 0 °C under argon atmosphere, tetraallyltin (0.13 mL, 0.55 mmol) was added. The reaction was stirred at 0°C per 0.5 h and then quenched by adding water at the same temperature. The organic layer was separated, dried over magnesium sulfate and concentrated under reduced pressure. The ^1H and ^{13}C NMR spectra of the crude reaction mixture showed the presence of a single diastereoisomer. Chromatography on silica gel yielded the desired compound in 86% yield as a yellow viscous oil. δ_H (C_6D_6, 300MHz) 1.85 (3H, s, CH_3), 2.01 (1H, s, OH) 2.15 (2H, m, CH_2), 3.86 (1H, m, FcH), 3.98 (5H, s, FcH), 4.24 (1H, m, FcH), 4.26 (1H, m, FcH), 4.80 (2H, m, CH_2= + CHOH), 5.80 (1H, m, CH=) 6.68 (2H, d, *J* = 8.0 Hz, ArH), 7.00 (2H, d, *J* = 8.0 Hz, ArH). δ_C (C_6D_6, 75MHz) 20.55 (CH_3), 43.25 (CH_2), 67.4, 67.9, 68.5, 70.2, 75.6 (CH), 74.8, 96.7 (FcC), 117.2 (CH_2), 126.5, 129.5 (ArCH), 134.8 (ArC), 135.1 (CH), 137.1 (ArC). ν_{max}(CCl_4) 3577 cm^{-1}. ESI-MS *m/z* 378 (M^+), 401 (M^++Na). $[\alpha]^{20}_D$ +33.7 (c 0.55 in $CHCl_3$). Exact mass Calcd. for $C_{21}H_{22}FeOS$: 378.0741. Found: 378.0721.

(*S*)-[(*S*$_{Fc}$)-2-*p*-Tolylsulfanyl]ferrocene cyanohydrin (1f). To a solution of (*S*)-**4** (170 mg, 0.5 mmol) in dry THF cooled at –78 °C under argon atmosphere, a solution of the Et_2AlCN (1.0 M in Toluene, 2.5 mL, 2.5 mmol) was slowly added. The colour of the solution immediately changed from red to yellow. The reaction mixture was quenched at –78 °C with water and extracted with Et_2O. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure. The ^1H and ^{13}C NMR spectra of the crude reaction mixture showed the presence of a single diastereoisomer and a chemical purity major of 97%. M.p. 80 °C (dec) (EtOAc). δ_H (C_6D_6, 300MHz) 1.78 (3H, s, CH_3), 2.40 (1H, s, OH), 3.69 (1H, m, FcH), 3.90 (5H, s, FcH), 4.03 (1H, m, FcH), 4.07 (1H, m, FcH), 4.76 (1H, s, CH), 6.63 (2H, d, *J* = 8.4 Hz, ArH), 6.92 (2H, d, *J* = 8.4 Hz, ArH). δ_C (C_6D_6, 75MHz) 20.6 (CH_3), 60.0, 69.3, 69.4, 70.9, 76.2 (CH), 88.4, 88.7 (FcC), 118.6 (CN), 127.0, 130.0 (ArCH), 135.6, 135.7 (ArC). ν_{max}(CCl_4) 3440 cm^{-1}. ESI-MS *m/z* 386 (M^++Na). $[\alpha]^{20}_D$ +394 (c 0.50 $CHCl_3$). Anal. Calcd. for $C_{19}H_{17}FeNOS$ (363.04): C, 62.80; H, 4.72; N, 3.86. Found: C, 62.69; H, 4.89; N 3.91.

(*S*)-[(*S*$_{Fc}$)-2-*p*-Tolylsulfanyl]ferrocene trimethylsilyl cyanohydrin (1g). To a solution of of (*S*)-**4** (170 mg, 0.5 mmol) in dry CH_2Cl_2 at –50°C under argon atmosphere, a catalytic amount of ZnI_2 and TMSCN (60 mg, 0.6 mmol) were added. The colour of the solution immediately changed from red to yellow. The reaction mixture was quenched with water. The organic layer was separated and dried over magnesium sulfate and concentrated under reduced pressure affording a yellow/brown oil. The ^1H and ^{13}C NMR spectra of the crude reaction mixture showed the presence of a single diastereoisomer and a chemical purity major of 97%. δ_H (C_6D_6, 300MHz) 0.06 (9H, s, $SiMe_3$), 1.79 (3H, s, CH_3), 3.77 (1H, m, FcH), 3.98 (5H, s, FcH), 4.13 (1H, m, FcH), 4.14 (1H, m, FcH), 5.14 (1H, s, CH), 6.67 (2H, d, *J* = 8.0 Hz, ArH), 7.01 (2H, d, *J* = 8.0 Hz, ArH). δ_C (C_6D_6, 75MHz) 0.52 ($SiMe_3$), 20.6 (CH_3), 59.2, 69.3, 71.0, 71.2, 76.4 (CH), 87.2, 89.2 (FcC), 119.0 (CN), 127.0, 129.7, 135.2 (ArCH), 136.2 (ArC). ν_{max}(CCl_4) 1250 cm^{-1}.

ESI-MS *m/z* 458 (M^++Na). $[\alpha]^{20}_D$ +12 (c 0.025 $CHCl_3$). Exact mass Calcd. for $C_{22}H_{25}FeNOSSi$: 435.0775. Found: 435.0715.

***N*-(4-Methoxyphenyl)-*N*-{(*E*)-(S_{Fc})-2-[(*p*-tolylsulfanyl)ferrocenyl]methylidene}amine (3a).** To a stirred solution of (*S*)-**4** (340 mmg, 1.0 mmol) and 4-anisidine (135 mg, 1.1 mmol) in dry toluene under argon atmosphere, dry powdered MS (4 Å) (1 g) were added. The mixture was heated at 50°C overnight and then filtered and concentrated under reduced pressure. An ^{1}H-NMR spectrum of the crude showed the complete conversion of the aldehyde(*S*)-**4** and the presence of **3a** with a purity of about 90%. Crystallisation from boiling MeOH afforded **3a** in 85% yield. M.p 133 – 135 °C (MeOH). δ_H (C_6D_6, 300MHz) 1.77 (3H, s, CH_3), 3.12 (3H, s, CH_3), 3.91 (5H, s, FcH), 4.01 (1H, m, FcH), 4.32 (1H, m, FcH), 5.25 (1H, m, FcH), 6.56 (2H, d, *J* = 8.0 Hz, ArH), 6.59 (2H, d, *J* = 8.0 Hz, ArH), 6.97 (2H, d, *J* = 8.0 Hz, ArH), 7.11 (2H, d, *J* = 8.0 Hz, ArH), 8.82 (1H, s, CH). δ_C (C_6D_6, 75MHz) 20.6 55.25 (CH_3), 69.5, 71.2, 71.7, 72.9 (CH), 86.4, 87.7 (FcC), 114.9, 122.1, 127.2, 129.85 (ArCH), 135.6, 146.2 (ArC), 157.2 (CHN). ν_{max}(CCl_4) 1620 cm^{-1}. ESI-MS *m/z* 441 (M^++H), 464 (M^++Na). $[\alpha]^{20}_D$ +910 (c 0.30 $CHCl_3$). Anal. Calcd. for $C_{25}H_{23}FeNOS$ (441.085): C, 68.02; H, 5.25; N, 3.17. Found: C, 68.25; H, 5.15; N 3.41.

***N*-Benzyl -*N*-{(*E*)-(S_{Fc})-2-[(*p*-tolylsulfanyl)ferrocenyl]methylidene}amine (3b).** To a stirred solution of (*S*)-**4** (340 mg, 1.0 mmol) and benzylamine (1.1 mmol) in dry toluene under argon atmosphere, dry powdered MS (4 Å) (1 g) were added. The mixture was heated at 50°C overnight and then filtered and concentrated under reduced pressure. An ^{1}H-NMR spectrum of the crude showed the complete conversion of the aldehyde(*S*)-**4** and the presence of **3b** with a purity of about 93%. Crystallization from boiling MeOH afforded **3b** in 89% yield. M.p 123 – 125 °C (MeOH). δ_H (C_6D_6, 300MHz) 1.79 (3H, s CH_3),3.89 (5H, s, FcH), 4.0 (1H, m, FcH), 4.31 (1H, m, FcH), 4.33 (2H, d, *J* = 13.5 Hz, H_a-CH_2), 4.45 (2H, d, *J* = 13.5 Hz, H_b-CH_2), 5.13 (1H, m, FcH), 6.67 (2H, d, *J* = 8.7 Hz, ArH), 6.63-7.11 (5H, m, ArH), 7.16 (2H, m, ArH), 8.57 (H, s, CHN). δ_C (C_6D_6, 75MHz) 21.4 (CH_3), 66.4 (CH_2), 69.9, 71.7, 72.0, 77.9 (FcCH), 79.2, 84.4 (FcC) 127.2, 127.6, 129.0, 129.3, 130.6 (ArCH), 135.7,138.0, 141.3 (ArC), 160.8 (CHN). ν_{max}(CCl_4) 1641cm^{-1}. ESI-MS *m/z* 426 (M^++H). $[\alpha]^{20}_D$ + 386 (c 0.315 $CHCl_3$). Anal. Calcd. for $C_{25}H_{23}FeNS$ (425.09): C, 70.59; H, 5.45; N, 3.29. Found: C, 70.35; H, 5.35; N 3.38.

***N*-{(*E*)-[(S_{Fc})-2-(*p*-Tolylsulfanyl)ferrocenyl]methylidene}benzenesulfonamide (3c).**

Method A. To a stirred solution of (*S*)-**4** (340 mmg, 1.0 mmol) and *p*-toluenesulfonamide (171 mg, 1.0 mmol) in dry toluene under argon atmosphere, dry powdered MS (4 Å) (1 g) and a catalytic amount of *p*-toluenesulfonic acid were added. The mixture was heated at reflux overnight and then filtered and concentrated under reduced pressure. Chromatography on silical gel column (Light petroleum/EtOAc 3:1) afforded **3c** in 41% yield. M.p 120 – 123 °C (MeOH). δ_H ($CDCl_3$, 400MHz) 2.27 (3H, s, CH_3), 2.41 (3H, s, CH_3), 4.25 (5H, s, FcH), 4.85 (1H, m, FcH), 4.89 (1H, m, FcH), 5.16 (1H, m, FcH), 6.94 (2H, d, *J* = 8.3 Hz, ArH), 6.99 (2H, d, *J* = 8.3 Hz, ArH), 7.29 (2H, d, *J* = 8.0 Hz, ArH), 7.99 (2H, d, *J* = 8.0 Hz, ArH) 9.29 (1H, s, CH). δ_C ($CDCl_3$, 100MHz) 20.9 21.6 (CH_3), 70.1, 71.8, 74.6, 80.7 (CH), 77.5, 84.0 (FcC), 127.5, 127.7, 129.7 (ArCH), 135.1, 136.0, 144.0 (ArC), 172.4 (CHN). ν_{max}(CCl_4) 1160, 1330, 1581 cm^{-1}. ESI-MS *m/z* 512 (M^++Na). CD λ_{max} ($\Delta\varepsilon$): 293 (25.4), 383 (-3.4), 501 (14.8) (c 1.02 10^{-4} M, $CHCl_3$).

Anal. Calcd. for $C_{25}H_{23}FeNO_2S_2$ (489.05): C, 61.35; H, 4.74; N, 2.86. Found: C, 61.12; H, 4.86; N 2.69.

Method B. $TiCl_4$ (0.5 mL, 0.5 mmol, 1M toluene), was added dropwise to a stirred ice-cooled solution of (*S*)-**4** (340 mg, 1.0 mmol), *p*-toluenesulfonamide (172 mg, 1.0 mmol) and Et_3N (0.4 mL, 3.0 mmol) in dry CH_2Cl_2 (15 mL) under argon atmosphere. The mixture was stirred for 1h at room temperature and then quenched with water. The organic layer was separated dried ($MgSO_4$) and concentrated *in vacuo*. Imine **3c** was obtained in quantitative yield as a red solid (482 mg) and could be used without any further purification. Chromatography on silica gel column (Light petroleum/EtOAc 3:1) for analytical aim afforded **3c** in 85% yield.

***N*-(4-Methoxyphenyl)-*N*-{(1*S*)-1-[2-(*S*$_{Fc}$)-(*p*-tolylsulfanyl)ferrocenyl]-3-butenyl}amine (2a).** (Table 3 entry 1) To a stirred solution of **3a** (110 mg, 0.25 mmol) and of a catalytic amounts of $Sc(OTf)_3$ (14 mg, 0.025 mmol) in dry CH_2Cl_2 cooled at 0°C under argon atmosphere, tetraallyltin (0.07 mL, 0.275 mmol) was added. The reaction was stirred at 0°C per 18 h and then quenched by adding water at the same temperature. The organic layer was extracted washed, dried over magnesium sulfate and concentrated under reduced pressure. The ^1H and ^{13}C NMR spectra of the crude reaction mixture showed the presence of a single diastereoisomer. Chromatography on silica gel yielded the desired compound in 72% yield (70 mg, 0.14 mmol) as a viscous yellow/orange oil. δ_H ($CDCl_3$, 400MHz) 2.11 (1H, m, H_a-CH_2), 2.26 (3H, s, CH_3), 2.33 (1H, m, H_b-CH_2), 3.77 (3H, s, CH_3), 4.17 (5H, s, FcH), 4.33 (2H, m, FcH), 4.49 (2H, m, FcH and CHN), 5.03 (1H, bd, NH) 4.77 (1H, dm, *J* = 17 Hz, H_a-CH_2=), 4.88 (1H, dm, *J* = 10 Hz, H_b-CH_2=), 5.55 (1H, m, CH=), 6.77 (2H, d, *J* = 8.8 Hz, ArH), 6.84 (2H, d, *J* = 8.8 Hz, ArH), 6.96 (2H, d, *J* = 8.4 Hz, ArH), 6.99 (2H, d, *J* = 8.4 Hz, ArH). δ_C ($CDCl_3$, 100MHz) 20.85 (CH_3), 40.73 (CH_2), 51.9 (CHN), 55.8 (CH_3), 67.3, 68.2, 70.2 (FcCH), 74.8 (FcC), 75.4 (FcCH), 95.5 (FcC), 114.99, 115.06 (ArCH), 117.5 (CH_2=), 126.1, 129.4 (ArCH), 134.4 (CH=), 134.8, 136.5, 142.0, 152.2 (ArC). ν_{max}(CCl_4) 3399 cm^{-1}. ESI-MS *m/z* 484 (M^++H) 506 (M^++Na). $[\alpha]^{20}_D$ +85(c 0.40 $CHCl_3$). Exact mass Calcd. for $C_{28}H_{29}FeNOS$: 483.1319. Found: 483.1341.

***N*-{(1*S*)-1-[2-(*S*$_{Fc}$)-(*p*-Tolylsulfanyl)ferrocenyl]-3-butenyl}*p*-toluenesulfonamide (2b).** (Table 3 entry 2) To a stirred solution of **3c** (125 mg, 0.25 mmol) and of a catalytic amounts of $Sc(OTf)_3$ (14 mg, 0.025 mmol) in dry CH_2Cl_2 cooled at –15 °C under argon atmosphere, tetraallyltin (0.07mL, 0.275 mmol) was added. The reaction was stirred at –15 °C for 32 h and then quenched by adding water at the same temperature. The organic layer was extracted washed, dried over magnesium sulfate and concentrated under reduced pressure. The ^1H and ^{13}C NMR spectra of the crude reaction mixture showed the presence of a single diastereoisomer. Chromatography on silica gel yielded the desired compound in 88% yield (93 mg, 0.18 mmol) as a yellow solid. M.p 65 – 67 °C (MeOH). δ_H ($CDCl_3$, 400MHz) 1.89 (2H, m, CH_2), 2.22 (3H, s, CH_3), 2.42 (3H, s, CH_3), 4.21 (1H, m, FcH), 4.27 (5H, s, FcH), 4.32 (1H, m, FcH), 4.47 (1H, m, FcH), 4.54 (1H, dm, *J* = 17 Hz, H_a-CH_2=), 4.63 (1H, m, CHN) 4.86 (1H, dm, *J* = 10 Hz, H_b-CH_2= and 1H, bs, NH) 5.27 (1H, m, CH=), 6.85 (2H, d, *J* = 8.2 Hz, ArH), 6.95 (2H, d, *J* = 8.2 Hz, ArH), 7.33 (2H, d, *J* = 8.0 Hz, ArH), 7.85 (2H, d, *J* = 8.0 Hz, ArH). δ_C ($CDCl_3$, 100MHz) 20.8, 21.5(CH_3), 39.5 (CH_2), 51.5, 67.8, 68.6, 70.7, 75.9 (CH), 92.8 (C), 119.3 (CH_2), 125.6,

127.1, 129.4, 129.8 (ArCH), 132.1 (CH), 134.7, 136.4, 138.3, 143.5 (ArC). $\nu_{max}(CCl_4)$ 3345, 1337, 1165 cm^{-1}. ESI-MS *m/z* 554 (M^++Na). $[\alpha]^{20}_D$ – 72.9 (c 0.45 $CHCl_3$). Anal. Calcd. for $C_{28}H_{29}FeNO_2S_2$ (531.10): C, 63.27; H, 5.50; N, 2.64. Found: C, 63.42; H, 5.39; N 2.81.

General procedure for the reaction of imines 3a and 3c with Grignard reagents in the presence a Lewis Acid (Table 3)

To a solution of imine **3a** or **3c** (0.2 mmol) and a Lewis Acid ($MgBr_2$ or LiCl) (0.4 mmol) in dry THF (10 mL) cooled at 0 °C under argon atmosphere, a solution of the Grignard reagent (0.6 mmol) was slowly added. The solution was stirred at the temperature reported in the Table 3. The reaction was followed by TLC analysis and then quenched with saturated NH_4Cl solution and extracted with Et_2O. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure. The diastereomeric ratio was determined by ^{1}H- and ^{13}C-NMR spectra on the reaction mixture and then the final derivative was isolated by column chromatography (hexane/EtOAc 3:1).

***N*-{(1*S*)-1-[2-(S_{Fc})-(*p*-Tolylsulfanyl)ferrocenyl]ethyl}*p*-toluenesulfonamide (2e).** (Table 3 entry 8). Following the general procedure using imine **3c** (98 mg), $MgBr_2$ (74 mg) and a 3.0 M solution in THF of MeMgBr (0.2 mL), the final product was obtained in 18 h at 0°C after chromatography as a yellow solid in 78 % yield. The d.e. was find >98% on the crude ^{1}H-NMR. M.p 150 – 151 °C (Et_2O). δ_H ($CDCl_3$, 300MHz) 0.94 (3H, d, J =6.4 Hz, CH_3), 2.11 (3H, s, CH_3), 2.29 (3H, s, CH_3), 4.08 (5H, s, FcH), 4.14 (1H, m, FcH), 4.16- 4.23 (2H, 2m, CHN, FcH), 4.31 (1H, m, FcH), 4.86 (1H, d, J = 4.8 Hz, NH), 6.72 (2H, d, *J* = 8.3 Hz, ArH), 6.83 (2H, d, *J* = 8.3 Hz, ArH), 7.17 (2H, d, *J* = 8.3 Hz, ArH), 7.78 (2H, d, *J* = 8.3 Hz, ArH). δ_C ($CDCl_3$, 75MHz) 20.9, 21.6, 29.7 (CH3), 48.3, 66.9, 68.9, 70.5, 75.7 (CH), 79.2 95.4, (C), 126.2, 127.3, 129.6, 129.8 (ArCH), 135.1. 136.1, 137.8, 143.5 (ArC). $\nu_{max}(CCl_4)$ 3331 cm^{-1}. ESI-MS *m/z* 528 (M^++Na). $[\alpha]^{20}_D$ +3 (c 0.54 $CHCl_3$). Anal. Calcd. for $C_{26}H_{27}FeNO_2S_2$ (505.08): C, 61.78; H, 5.38; N, 2.77. Found: C, 61.52; H, 5.24; N 2.99.

***N*-{(1*S*)-1-[2-(S_{Fc})-(*p*-Tolylsulfanyl)ferrocenyl]-2-propenyl}*p*-toluenesulfonamide (2f).** (Table 3 entry 10). Following the general procedure using imine **3c** (98 mg) $MgBr_2$ (74 mg) and a 1.0 M solution in THF of vinylMgBr (0.6 mL), the final product was obtained in 48 h at r.t. after chromatography as a yellow solid in 36 % yield and as a single diastereoisomer beside 39 % of the recovered imine **3c**. M.p 62 – 63 °C (Et_2O). δ_H ($CDCl_3$, 300MHz) 2.12 (3H, s, CH_3), 2.29 (3H, s, CH_3), 4.12 (1H, m, FcH), 4.14 (5H, s, FcH), 4.19 (1H, m, FcH), 4.32 (1H, m, FcH), 4.56 (1H, m, CHN), 4.60 (2H, m, CH=), 5.07 (1H, d, *J* = 4.6 Hz, NH), 5.50 (1H, 4d, *J* = 17.3, *J* = 9.6, J = 7.6 Hz, CH=), 6.69 (2H, d, *J* = 7.9 Hz, ArH), 6.82 (2H, d, *J* = 7.9 Hz, ArH), 7.12 (2H, d, *J* = 8.2 Hz, ArH), 7.60 (2H, d, *J* = 8.2 Hz, ArH). δ_C ($CDCl_3$, 100MHz) 20.8, 21.5(CH_3), 54.8 (CHN), 68.5, 68.9, 71.5, 75.8 (FcCH), 77.2, 92.5 (FcC), 116.35 (CH=), 126.6, 127.5, 129.3, 129.4 (ArCH), 135.0, 135.3, 137.4, 143.3 (ArC). $\nu_{max}(CCl_4)$ 1160, 1336, 3331 cm^{-1}. ESI-MS *m/z* 540 (M^++Na). $[\alpha]^{20}_D$ + 17 (c 0.44 $CHCl_3$). Anal. Calcd. for $C_{27}H_{27}FeNO_2S_2$ (517.08): C, 62.67; H, 5.26; N, 2.71. Found: C, 62.79; H, 5.41; N 2.95.

***N*-{(1*S*)-1-[2-(S_{Fc})-(*p*-Tolylsulfanyl)ferrocenyl]-2-propenyl}*p*-toluenesulfonamide (2f).** (Table 3 entry 11). Following the general procedure using imine **3c** (98 mg), LiCl (17 mg) and a 1.0 M solution in THF of vinylMgBr (0.6 mL), the final product was obtained in 5 min after chromatography as a yellow solid in 97 % yield. The d.e. was find 96% on the crude ^{1}H-NMR.

***N*-{(1*S*)-1-[2-(S_{Fc})-(*p*-Tolylsulfanyl)ferrocenyl](phenyl)methyl}*p*-toluenesulfonamide (2g).** (Table 3 entry 13). Following the general procedure using imine **3c** (98 mg), LiCl (17 mg) and a 3.0 M solution in THF of PhMgBr (0.2 mL), the final product was obtained in 20 min. The d.e. was find 77% on the crude ^{1}H-NMR. The two diastereoisomers were separated by chromatography on preparative TLC that afforded as the higher R_f product the minor diastereoisomer in 13% yield and as the second R_f product the major diastereoisomer in 84% yield. M.p 107 – 109 °C (MeOH). δ_H ($CDCl_3$, 300MHz) 2.15 (3H, s, CH_3), 2.31 (3H, s, CH_3), 4.35 (1H, m, FcH), 4.40 (5H, s, FcH), 4.46 (2H, m, FcH), 5.33 (1H, bs, CH), 5.63 (1H, bs, NH), 6.41 (2H, d, *J* = 8.1 Hz, ArH), 6.68 (2H, d, *J* = 8.1 Hz, ArH), 6.73-6.94 (5H, 2m, ArH), 7.03 (2H, d, *J* = 8.0 Hz, ArH), 7.45 (2H, d, *J* = 8.0 Hz, ArH). δ_C ($CDCl_3$, 100MHz) 20.7, 21.4 (CH_3), 56.0 (CHN), 67.6, 70.0, 71.9, 75.8 (FcCH), 77.2, 94.9 (FcC), 126.0, 126.7, 127.3, 127.7, 128.9, 129.0 (ArCH), 134.3, 135.0, 137.0, 139.1, 142.9 (ArC). ν_{max}(CCl_4) 1155, 1321, 3320 cm^{-1}. ESI-MS (-) *m/z* 566 (M^+-1). $[\alpha]^{20}_D$ + 23 (c 0.25 $CHCl_3$).Anal. Calcd. for $C_{31}H_{29}FeNO_2S_2$ (567.10): C, 65.60; H, 5.15; N, 2.47. Found: C, 65.75; H, 5.21; N 2.38.

***N*-{(1*S*)-1-[2-(S_{Fc})-(*p*-Tolylsulfanyl)ferrocenyl]propyl}*p*-toluenesulfonamide (2h).** (Table 4 entry 3). Following the general procedure using imine **3c** (98 mg) $MgBr_2$ (74 mg) and a 3.0 M solution in THF of EtMgBr (0.2 mL), after 48 h at r.t. the column chromatography afforded a fraction containing product **2h** as a single diastereoisomer and product **7b** a 1:3 ratio in a 35% yield. The separation of the two product was attempted by preparative thin layer chromatography and afford as the first R_f fraction a mixture of **2h** and **7** in a 1:1 ratio and as the second R_f fraction product **7** with a purity of 90%.

2h. δ_H ($CDCl_3$, 300MHz) 0.43 (3H, t, *J* = 7.5 Hz, CH_3), 2.23 (3H, s, CH_3), 2.42 (3H, s, CH_3), 3.92 (2H, m, CH_2), 4.18 (5H, s, FcH), 4.22 (1H, brm, CHN), 4.30 (1H, m, FcH), 4.38 (1H, m, FcH), 4.46 (1H, m, FcH), 4.84 (H, brd, *J* = 5.4 Hz, NH), 6.73 (2H, d, *J* = 8.3 Hz, ArH), 6.83 (2H, d, *J* = 8.3 Hz, ArH), 7.20 (2H, d, *J* = 8.5 Hz, ArH), 7.69 (2H, d, *J* = 8.5 Hz, ArH). MS *m/z* 542 (M^++Na).

7b. δ_H ($CDCl_3$, 300MHz) 2.27 (3H, s, CH_3), 2.41 (3H, s, CH_3), 3.92 (2H, m, CH_2), 4.19 (5H, s, FcH), 4.28 (1H, m, FcH), 4.34 (1H, m, FcH), 4.42 (1H, m, FcH), 6.82 (2H, d, *J* = 8.0 Hz, ArH), 6.99 (2H, d, *J* = 8.0 Hz, ArH), 7.23 (2H, d, *J* = 8.3 Hz, ArH), 7.55 (2H, d, *J* = 8.2 Hz, ArH). δ_C ($CDCl_3$, 75MHz) 20.9, 21.5 (CH_3), 41.4 (CH_2), 69.5, 69.9, 70.7, 75.4 (FcCH), 77.8, 86.6 (FcC), 126.3, 127.0, 129.5, 129.7 (ArCH), 135.4, 136.1, 136.8, 143.2 (ArC). MS *m/z* 514 (M^++Na).

***N*-{(1*S*)-1-[2-(S_{Fc})-(*p*-Tolylsulfanyl)ferrocenyl]propyl}*p*-toluenesulfonamide (2h).** (Table 4 entry 4). Following the general procedure using imine **3c** (98 mg), LiCl (17 mg) and a 3.0 M solution in THF of EtMgBr (0.3 mL), after 18 h at r.t. the column chromatography afforded as the first R_f fraction a mixture containing product **2h** and product **7b** in a 1:1 ratio in 62% yield and as the second R_f fraction the unreacted imine **3c** in 20% yield.

General procedure for the reaction of imine 3c with EtMgBr in the presence of Cp_2ZrCl_2 (Table 4, entries 5-7)

To a solution of imine **3c** (98 mg, 0.2 mmol) and Cp_2ZrCl_2 (6 mg, 0.02 mmol) in dry THF (5 mL) under argon atmosphere, the EtMgBr (3M in THF) was added and the reaction mixture was stirred until disappearance of the starting imine. The reaction was quenched with 5% NaOH (1.5 mL) and then diluted with water and extracted with Et_2O. The combined organic layer were dried ($MgSO_4$) and concentrated. Chromatography of the crude reaction mixture furnished a fraction containing the alkylated product **2h** and the reduction product **7b** in variable ratio depending on the amount of EtMgBr used. (3 equivalents of EtMgBr: ratio **2h** : **7b** = 1:3 total yield 88%; 10 equivalents of EtMgBr: ratio **2h** : **7b** = 1:2 total yield 89%; 25 equivalents of EtMgBr: ratio **2h** : **7b** = 1.2:1 total yield 89%)

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