DOI: 10.1002/adsc.200600639

Metallocene Sulfoxides as Precursors of Metallocenes with Planar Chirality

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Received: December 15, 2006

Dedicated to Professor M. Shibasaki for his 60th birthday anniversary.

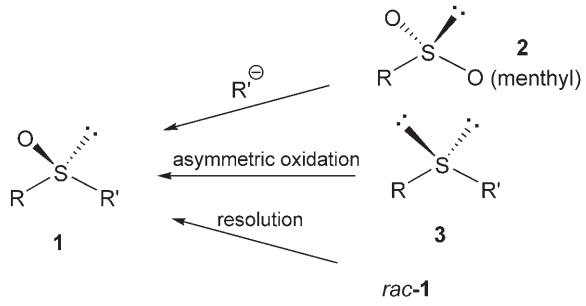
Abstract: The preparation of metallocene sulfoxides and their *ortho*-diastereoselective functionalization are described. The applications of enantiopure 1,2- and 1,3-disubstituted metallocenes are reviewed, with special emphasis on the preparation of ligands for asymmetric catalysis. The sulfoxide functionality is a useful, traceless, chiral diastereoselective *ortho*-directing group, as explained in the article. It allows one to synthesize a wide range of enantiopure metallocenes with planar chirality and predictible configuration. Most of the examples are related to the ferrocene area.

Keywords: chiral ligands; enantioselective catalysis; ferrocenes; lithiation; planar chirality; sulfoxides

1 Introduction

The sulfinyl group of sulfoxides **1** ($R \neq R'$) involves an asymmetric center which is able to control the formation of some asymmetric centers in the R and R′ moieties. A reductive cleavage of the sulfinyl group generates a chiral product, often of very high enantiomeric excess. This approach has been widely used in asymmetric synthesis.[1–5] The Andersen method[4] using the menthyl sulfinate **2** (or other types of sulfinates such as DAG sulfinates[3]) as well as the enantioselective oxidation of sulfides[6–8] are the main ways to prepare sulfoxides **1** with high enantiomeric excesses (*ee*s) (Scheme 1).

Chiral sulfites,[9] aminosulfites[10–12] and sulfinamides[13] have been used instead of sulfinates as precursors of sulfoxides in Andersen-type methodology. The sulfinyl group can act as an *ortho*-directing group in deprotonation reactions by LDA, for example.[1–4] The application of the chiral sulfoxide chemistry to metallocenes is relatively new. The first examples have been disclosed in 1993 in the ferrocene family such as **4**,[14] in 1994–1995 for some derivatives of benzenechromium tricarbonyl **5**,[15,16] in 2003 for ruthenocene **6**[17b] and in 2004 for a cobalt metallocene system **7**[18] (Scheme 2).

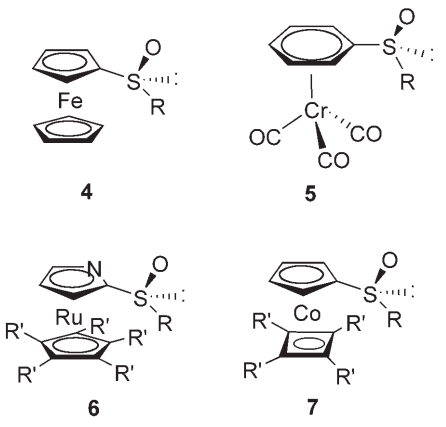


Scheme 1. Main routes to chiral sulfoxides.

Henri B. Kagan was born in Boulogne-Billancourt (France) in 1930. He graduated from the Sorbonne and Ecole Nationale Supérieure de Chimie de Paris in 1954. He prepared his Ph.D. under the supervision of Dr. J. Jacques. He joined Prof. A. Horeau at the Collège of France in Paris in 1962 as a research associate. In 1965 he worked with Prof. T. Mabry at the University of Texas, Austin. He joined in 1968 the Université Paris-Sud, Orsay. He is emeritus Professor of the Université Paris-Sud since 1999. He is member of the French Academy of Sciences. H. B. Kagan developed investigations in various areas, such as asymmetric synthesis, asymmetric catalysis, lanthanide reagents (for example, diiodosamarium). His awards include the Prelog Medal, the August-Wilhelm-von-Hofmann Medal, the Chirality Medal, the Nagoya Medal of Organic Chemistry, the Silver Medal of the RSC, the Tetrahedron Prize, the 2001 Wolf Prize for Chemistry, the 2002 Grand Prix de la Fondation de la Maison de la Chimie, the 2002 Ryoji Noyori Prize and the 2005 Bower award of the Franklin Institute.

Benoît Ferber was born in Les Lilas (France) in 1977. He studied chemistry at ESCOM (an institution specializing in chemistry and engineering) in Cergy-Pontoise where he obtained the french equivalent of B.S. Then he studied in the Université Paris 6 (Université Pierre et Marie Curie) where he obtained his M.Sc. (2002) and Ph.D. (2005) under the guidance of Prof. G. Jaouen. During his Ph.D. he worked on the synthesis of 17α-ethynylestradiol tethered by a cyclopentadienyl metal including a planar chirality and the recognition of these compounds by the estradiol α-receptor. Since then he has been working on asymmetric synthesis with Prof. H. B. Kagan at the Université Paris-Sud as a post-doctoral fellow.

In this review we describe in the first part the asymmetric synthesis of metallocene sulfoxides **4**, **5, 6** and **7**. The diastereoselective *ortho*-metallation of these compounds is developed in the next section. Finally, the removal of the sulfinyl group and the preparation of various enantiopure metallocenes with planar chirality are discussed.[19] The η^4-diene-Fe(CO)$_3$ and η^4-enone-Fe(CO)$_3$ complexes are not considered in this article. Special emphasis is given to the preparation of chiral ligands for asymmetric catalysis.

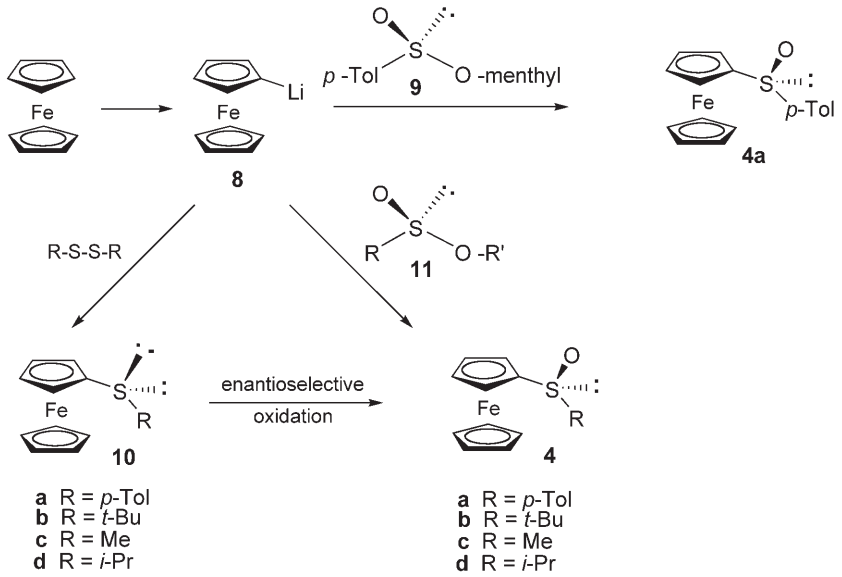


Scheme 2. Some classes of metallocene sulfoxides.

2 Asymmetric Synthesis of Metallocene Sulfoxides

2.1 Ferrocene Sulfoxides

The key ferrocene sulfoxide **4a** has been synthesized in our laboratories from (*S*)-(−)-menthyl *p*-toluenesulfinate **9** and monolithioferrocene **8** by a procedure which gives about 70% yield in enantiopure (*S*)-**4a** {[α]$_D$: 314 (*c* 0.5, chloroform)}.[20] The absolute configuration was first assigned by assuming an inversion of stereochemistry at sulfur, as generally observed in the Andersen method.[21] This assignment was later confirmed by chemical correlations.[22,23] In order to reach a high *ee* in the reaction it is necessary to avoid any excess of **8** which promotes the racemization of sulfoxide **4a**. That is why **8** has been prepared in a controlled way by transmetallation (with *n*-BuLi) of stable (tri-*n*-butylstannyl)ferrocene itself obtained at



Scheme 3. Synthesis of enantiopure ferrocene sulfoxides.

a 0.1-mol scale from $(n\text{-Bu})_3$Sn-ferrocene [*t*-BuLi followed by $(n\text{-Bu})_3$SnCl].[20] An alternate access to **4a** has been set up in 1998 by direct lithiation of ferrocene with the procedure of Mueller-Wersterhoff[24] (metallation by *t*-BuLi in the presence of a small amount of *t*-BuOK), followed by the inverse addition of the lithio compound **8** on menthyl *p*-toluenesulfinate.[23] The desired (*S*)-**4a** (>99% *ee*) was isolated in 47% yield (after crystallization). Hua et al. also used the lithiation of ferrocene by *t*-BuLi followed by addition at −78°C of sulfinate **9** to prepare **4a** in high *ee*.[22] These authors confirmed our finding[20] of the easy racemization of sulfoxide **4a** in the presence of lithiated ferrocene **8**. Bäckvall et al. reported an improved procedure giving **4a** in 80% yield (98% *ee*) by slow addition of 1 equivalent of lithiated ferrocene at −60°C on sulfinate in a more diluted system.[25] Sulfoxides **4b–d** were prepared from diastereochemically and enantiomerically pure sulfinates **11** where the chiral group R′ is derived from a chiral diol or a carbohydrate.[4,14,25,26] Thus the two enantiomers of **4c** have been prepared by the DAG technology (R = Me, R′ = DAG or diacetonideglucosyl). Sulfoxide **4b** is now easily available from the reaction between **8** and the Ellman's reagent *t*-Bu-S(O)-S-*t*-Bu.[62]

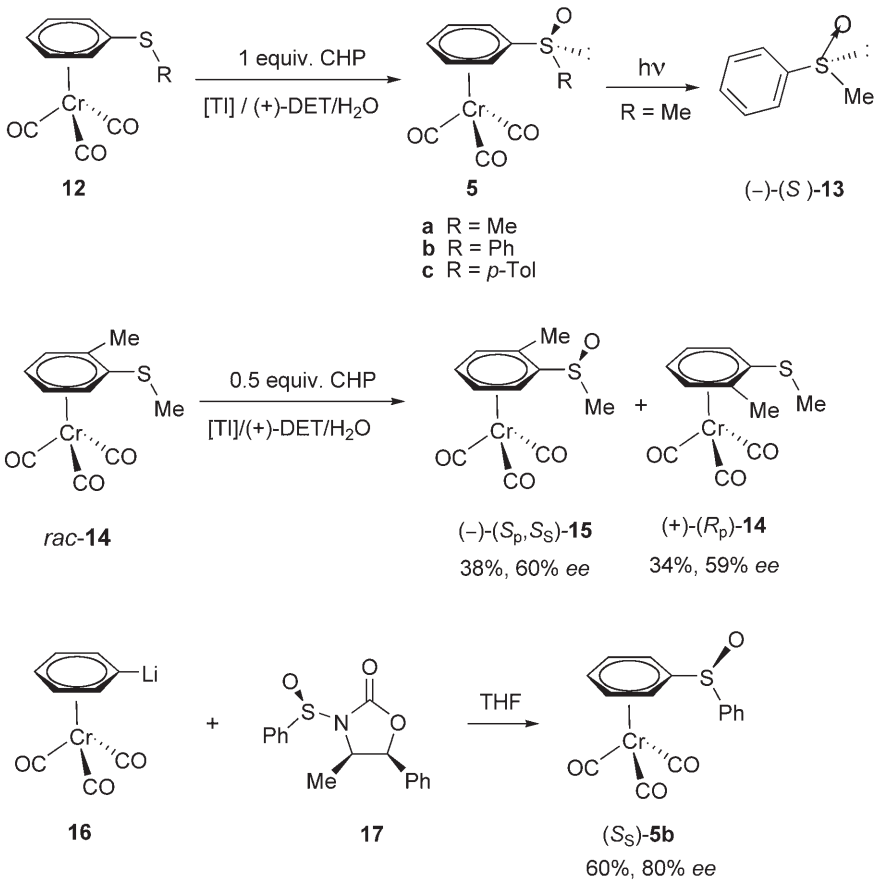
Asymmetric oxidation of sulfides **10**, easily derived from lithioferrocene **8** and disulfides R−S−S−R, gives sulfoxides **4** in high *ee*.[7–9] The oxidant system is cumyl hydroperoxide in the presence of a stoichiometric amount of Ti(O-*i*-Pr)$_4$/diethyl tartrate/water (1:2:1). The optimization of the experimental conditions provided, for example, ferrocene *p*-tolyl sulfoxide **4a** (>99% *ee*) and *tert*-butyl sulfoxide **4b** (95% *ee*) in 76% and 81% yields, respectively (Scheme 3).[8,22] The absolute configurations of (+)-(*S*)-**4a** and (+)-(*S*)-**4b** have been established by X-ray crystallography and chemical correlations.[22,14]

2.2 Arenetricarbonylchromium Sulfoxides

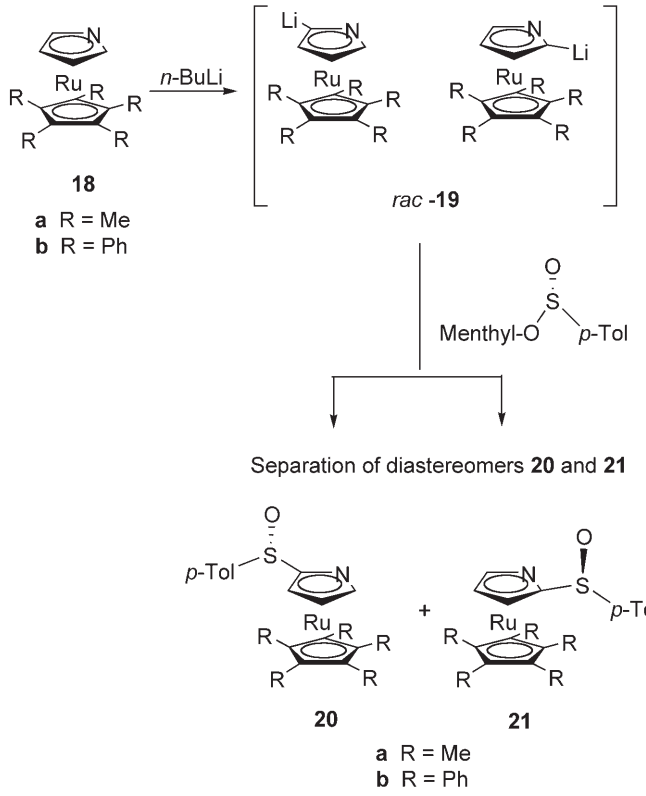
Tricarbonyl(η^6-arene)chromium(0) complexes have a very rich chemistry and allow many types of transformation in synthetic organic chemistry.[27,28] Enantioenriched **5a** has been prepared from the corresponding sulfide **12** by oxidation at −25°C using cumyl hydroperoxide (CHP) in the presence of the combination Ti(O-*i*-Pr)$_4$/(+)-diethyl tartrate (DET)/H_2O (Kagan's protocol[8]), giving after recrystallization 53% yield and *ee* >95% (Scheme 4).[15] The same methodology was used in the kinetic resolution of *rac*-**14**, allowing one to prepare the enantioenriched sulfoxide **15** (30%, >95% *ee*). Phenyl sulfoxide **5b** (80% *ee*) was prepared by Davies et al. from the reaction between the phenylsulfinamide **17**[13b] and the lithiated chromium tricarbonyl complex **16** at −100°C.[29] This low temperature is needed to avoid a racemization process at sulfur of **5b**.[29] The synthesis of the *tert*-butyl analogue (**5**, R = *t*-Bu) failed.

2.3 Azaruthenocene Sulfoxides

The only case of the synthesis of an enantiopure ruthenocene sulfoxide (Scheme 5) has been reported by Hansen and Johannsen.[17] The mono-*ortho*-lithiation of achiral azaruthenocene **18a** by *n*-BuLi gave a racemic mixture of **19** which reacts with the (1*R*,2*S*,5*R*)-



Scheme 4. Synthesis of enantioenriched benzenetricarbonylchromium sulfoxides.

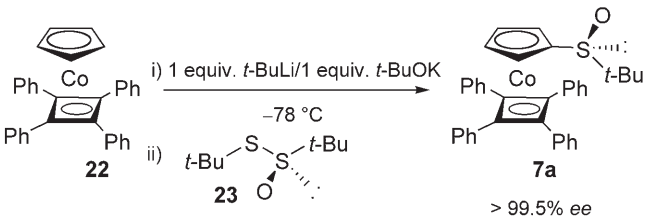


Scheme 5. Chiral azaruthenocene sulfoxides.

menthyl (S_S)-*p*-toluenesulfinate to give the mixture of diastereomers **20a** and **21a**, each one of 100% *ee*. A column chromatography provided **20a** (42%, >99.5% *de*) and **21a** (42%, >99.5% *de*). Both compounds have the S_S configuration. The configuration of the planar chirality was proposed by analogy with a similar azaferrocene where an X-ray structure of an azaferrocene sulfoxide has been obtained. The lithiation of pentaphenylruthenocene **18b** followed by addition of menthyl sulfinate provided only the diastereomer **20b** or **21b** (30% yield) presumably with the (*S*)-configuration at sulfur but of unknown configuration for the planar chirality.

2.4 (η^5-Cyclopentadienyl)(η^4-cyclobutadiene)cobalt Sulfoxides

Recently Carretero et al. studied the lithiation of (η^4-cyclobutadiene)(η^5-cyclopentadienyl)cobalt **22** by various basic systems.[18] They discovered that the Schlosser super base (*t*-BuLi + *t*-BuOK)[30] gave a clean metallation at the Cp ring. Quenching with chiral thiosulfinate (R_S)-**23** provided sulfoxide (*R*)-**7a** (>99.5% *ee*) in 30% yield (Scheme 6), the starting material was also recovered.



Scheme 6. Synthesis of an enantiopure cobaltocene sulfoxide.

3 *ortho*-Metallation of Metallocene Sulfoxides

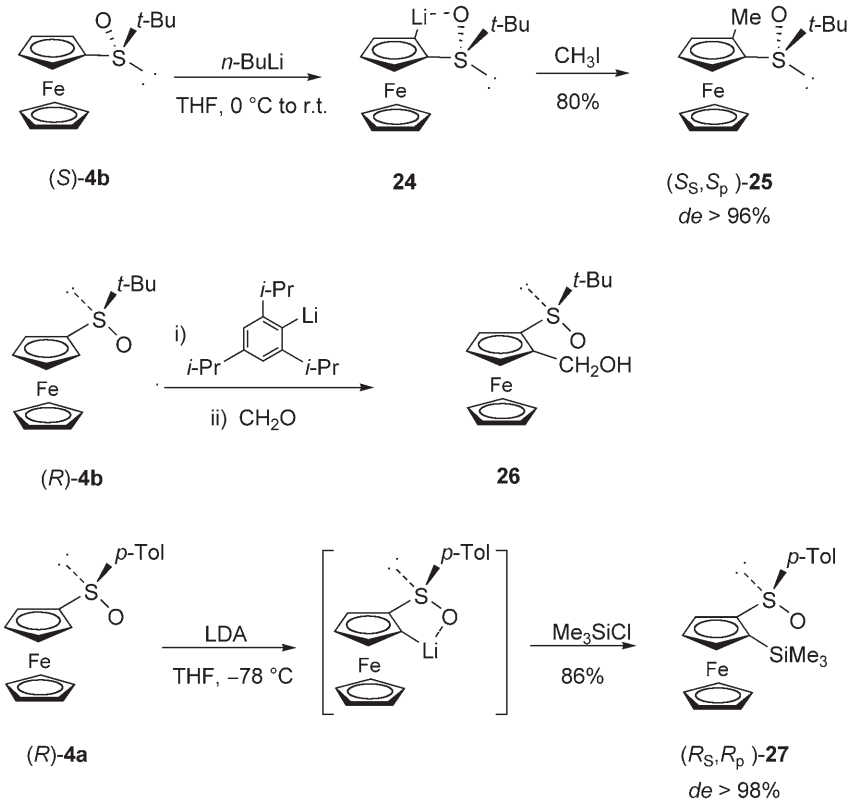
It is well known that the sulfinyl group can direct the lithiation by various agents, usually in the vicinal position with respect to the directing group. Deprotonation has been observed for a hydrogen located on an sp^3 carbon atom.[1–4] *ortho*-Lithiation has been reported for aromatic or vinylic sulfoxides.[31a]

3.1 Ferrocene Sulfoxides

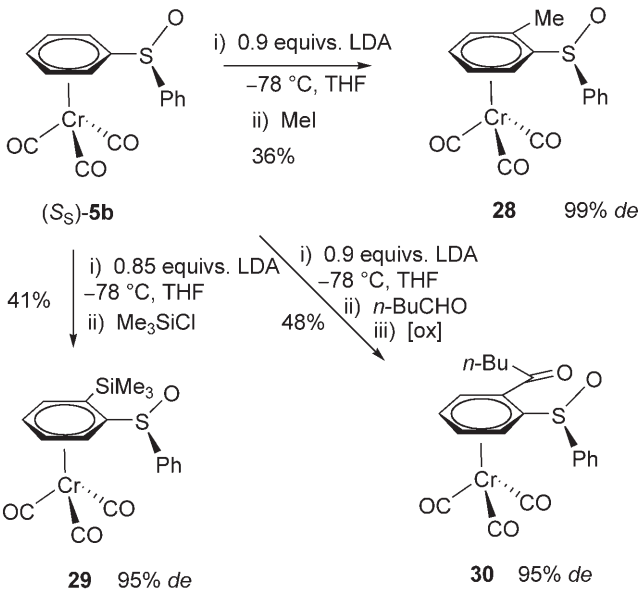
Diastereoselective *ortho*-lithiation of some ferrocenylamines was pioneered by Ugi et al. in the 1970s.[31b] The first case of diastereoselective *ortho*-lithiation of metallocene sulfoxides was described in 1993 in these laboratories on enantiopure *tert*-butyl ferrocenyl sulfoxide **4b** and *p*-tolyl ferrocenyl sulfoxide **4a** (Scheme 7).[14] The relative and absolute configurations of **25** were assigned by X-ray crystallography. The deprotonation of **4b** was conveniently done by *n*-BuLi while the same procedure applied to **4a** led to a mixture of products. However, **4a** could be easily functionalized in the *ortho*-position of the ferrocenyl ring by treatment with LDA at −78 °C followed by an electrophilic quenching. Hua et al. described similar results on the deprotonation at −40 °C of **4b** by a sterically hindered base, the (2,4,6-triisopropyl)phenyllithium.[32] The excellent diastereoselectivity was lost if the metallation was carried out at −20 °C. Quenching by formaldehyde gave alcohol **26** whose absolute and relative configurations were determined by X-ray crystallography.[32] The authors described many examples of electrophilic quenchings of the *ortho*-lithiated **4a**, for example, by ethyl formate, methyl chloroformate, allyl bromide or $ClSnMe_3$.

3.2 Tricarbonyl(arene)chromium Sulfoxides

Davies et al. investigated the *ortho*-functionalization of tricarbonyl(η^6-benzene)chromium **5** (Scheme 8).[16,29] They studied mainly the case of



Scheme 7. Diastereoselective *ortho*-deprotonation of ferrocene *tert*-butyl sulfoxide.



Scheme 8. *ortho*-Subtitution of a benzenetricarbonylchromium sulfoxide.

phenyl sulfoxide **5b**. A very high diastereoselectivity have been observed for *ortho*-deprotonation by LDA at −78 °C (> 95–99 % *de*).

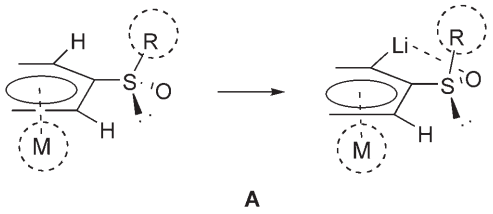
3.3 Cobalt Metallocene Sulfoxides

Sulfoxide **7a** (Scheme 6) has been deprotonated in the *ortho*-position by *t*-BuLi in THF at −78 °C, with a diastereoselectivity higher than 99 %.[18] The stereochemistry was established by transformation into a known compound (*vide infra*).

4 Applications of the Metallocene Sulfoxides

The sulfoxide methodology applied to metallocenes afffords several advantages in synthetic transformations as listed below.

i) The sulfinyl moiety is intrinsically chiral, acting as an excellent diastereoselective *ortho*-directing group in the deprotonation reactions of a metallocene ring.There are several ways to synthesize enantiopure metallocene sulfoxides (*vide supra*).



Scheme 9. Scheme of asymmetric induction.

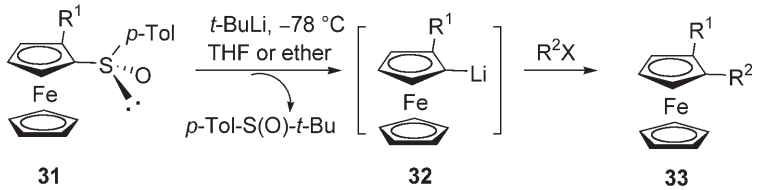
ii) The configuration of the new stereogenic unit created by the *ortho*-functionalization is predictible by a simple scheme of asymmetric induction (**A**, Scheme 9). It is rationalized by the fact the bulky group (*t*-Bu or aryl) prefers to stay away from the metal (*exo* position), thus orienting the oxygen of the sulfinyl group in the direction of only one of the two *ortho* sites. The X-ray structures of several metallocene sulfoxides clearly show this trend.[4,32]

iii) The sulfinyl group can be displaced and replaced by various types of substituents. Contrary to many chiral *ortho*-directing group it is a "traceless" *ortho*-directing group, as discussed below.

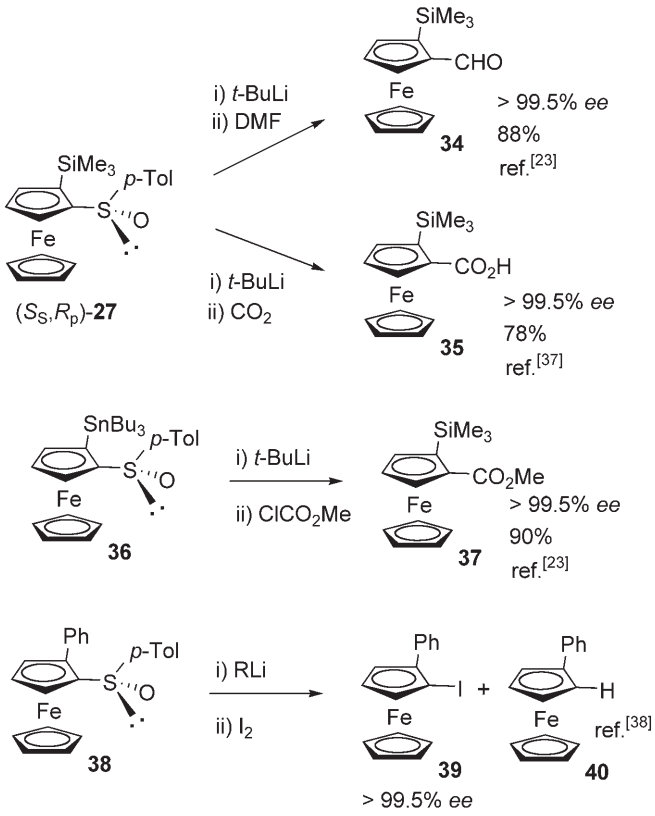
iv) The metallocene sulfoxides can be transformed into many types of metallocenes with planar chirality that are of interest for their unusual structures or as ligands in asymmetric organometallic catalysis.

4.1 The Sulfoxide-Lithium Exchange

It has been observed that some alkyllithium reagents may react with methyl *p*-tolyl sulfoxide to give alkyl *p*-tolyl sulfoxides. The yields are especially good with *t*-BuLi.[33–35] Similar reactions have been described for alkynyl sulfoxides[36] or *p*-tolyl ferrocenyl sulfoxides.[22] Obviously the substitution reaction occurs by attack of the alkyllithium at sulfur of the sulfoxide, generating also *in situ* a *p*-tolyllithium reagent which is hydrolyzed during the work-up procedure into toluene. It is possible to take advantage of the *in situ* production of a new organolithium reagent by the sulfoxide-lithium exchange. We used this procedure (Scheme 10) to transform *p*-tolylferrocene or *ortho*-

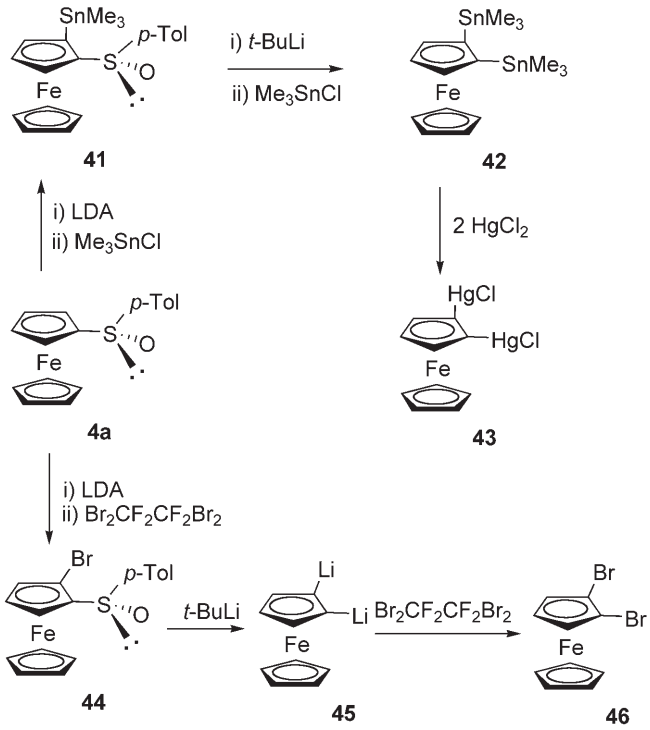


Scheme 10. The sulfoxide-lithium exchange.



t-BuLi (normal addition)	–90 °C	85:15	(73% in **39**)
t-BuLi (normal addition)	–30 °C	95:5	(86% in **39**)
t-BuLi (inverse addition)	–78 °C	94:6	(75% in **39**)
PhLi (inverse addition)	–78 °C	95:5	(87% in **39**)

Scheme 11. Synthesis of enantiopure 1,2-disubstituted ferrocene sulfoxides.



Scheme 12. Synthesis of achiral 1,2-disubtituted ferrocenes.

substituted *p*-tolylferrocenes into new ferrocene derivatives, especially with planar chirality, by electrophilic quenching of the intermediate lithioferrocene.[23] Some examples are described in Scheme 11. This procedure is now widely used in the literature to synthesize various kinds of substituted metallocenes with planar chirality.

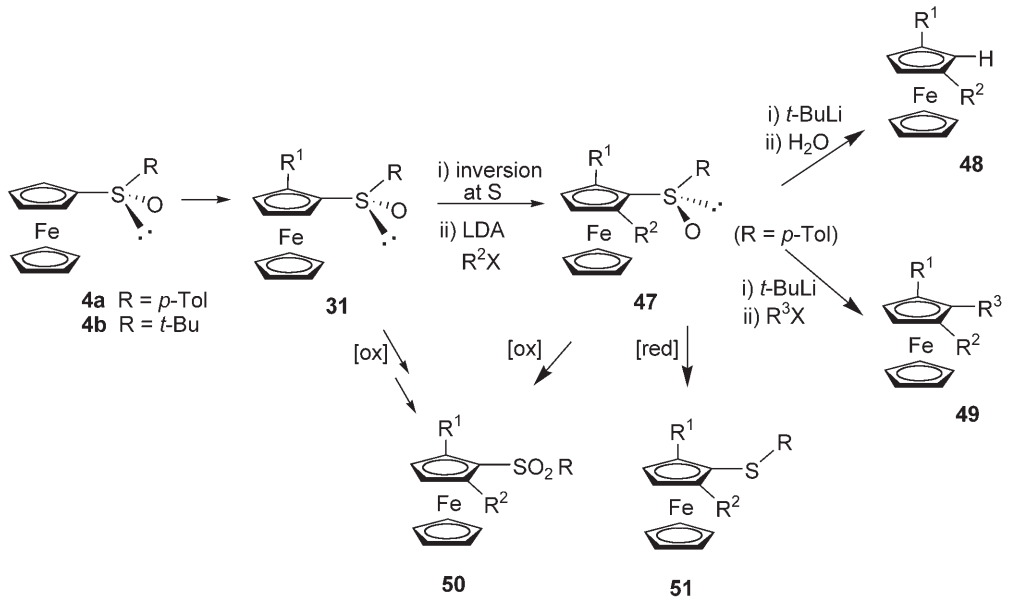
It was noticed by Knochel et al. that the yield of the expected product can be low in the case of some *ortho*-substituted ferrocene *p*-tolyl sulfoxides, such as **38** (Scheme 11), because of a competitive formation of protonated product **40**, resulting from the high reactivity of the *ortho*-lithiated intermediate.[38] Yields could be optimized with *t*-BuLi by a control of the temperature (Scheme 11) or by the use of PhLi in inverse addition.

The protocol of Scheme 10 has often been used in the literature. The absolute configuration of **33** is always predictible, since that of precursor **31** (prepared by diastereoselective *ortho*-deprotonation from **4a**) is given by model **A** of Scheme 9.

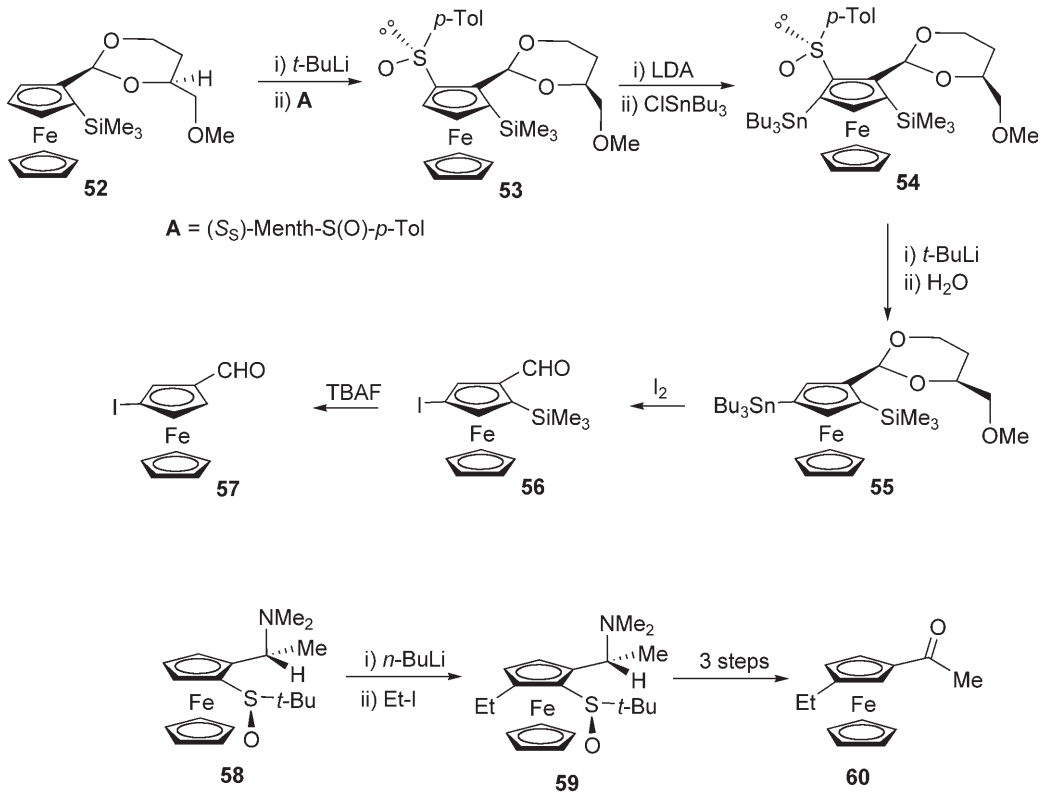
Interestingly, the sulfoxide-lithium exchange also allows one to prepare unusual *achiral* 1,2-disubstituted metallocenes. For example, a chelating redox-active bidentate Lewis acid **43** has been synthesized (Scheme 12). It chelates the oxygen of DMSO (1:1 complex) and binds the chloride anion (2:1 complex).[39] The 1,2-dilithioferrocene **45** or the 1,2-dibromoferrocene **46** may be also prepared by the sulfoxide route.[40]

The sulfoxide-lithium exchange has a great potential to prepare *polysubstituted metallocenes with planar chirality* as the only stereogenic unit, as explained in ref.[14] and in Scheme 13 in the case of ferrocene. However, there are still only few examples of such transformations.[41,42]

The sulfinyl unit, S(O)-*p*-Tol, can be introduced on chiral ferrocenes by the Andersen method and used as an *ortho*-directing group in metallation before its removal or replacement by another group, which can be also *ortho*-directing for a new metallation. This approach has been recently investigated by Jaouen et al.[42] (Scheme 14). For example, 1-formyl-3-iodoferrocene **57** (100% *ee*, R_p configuration) has been obtained by sequential diastereoselective *ortho*-lithiation/electrophilic quenchings. Ferrocene **57** was coupled with 17-α-ethynylestradiol, giving an organometallic steroid with some biological activities. The enantiomer of **57** was available by reversing the absolute configuration of the chiral *ortho*-directing groups, and its absolute configuration was established by X-ray



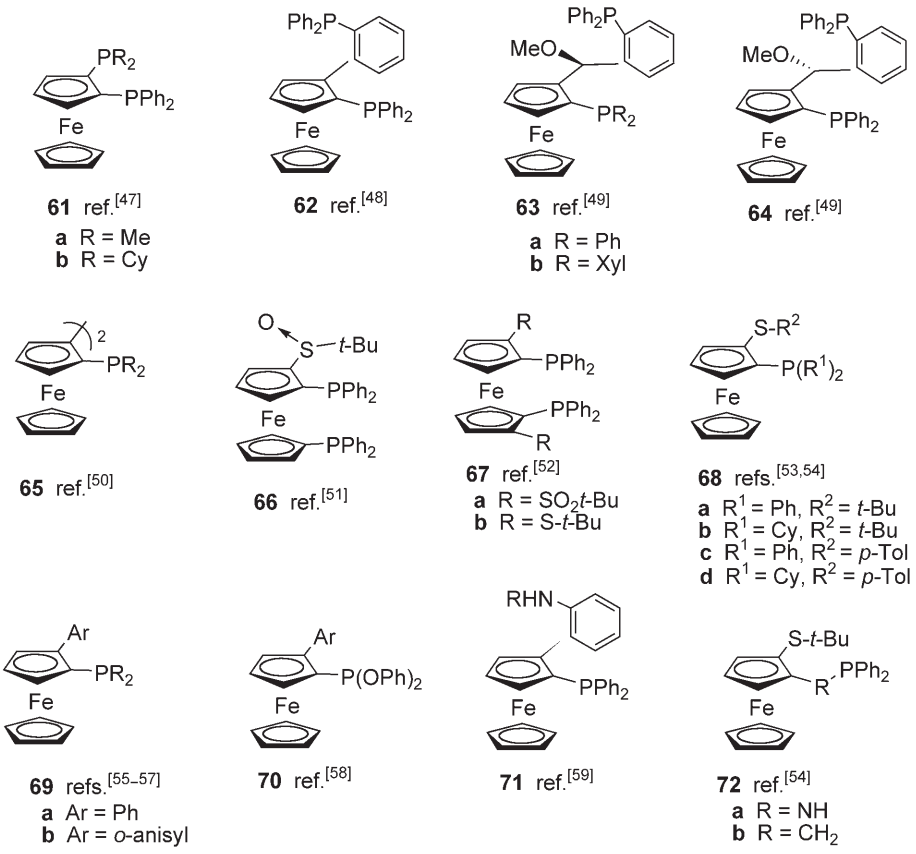
Scheme 13. Polysubstituted chiral ferrocenes.



Scheme 14. 1,3- or 1,2,3-susbtituted chiral ferrocenes.

diffraction. Nicolosi et al. prepared the *tert*-butyl sulfoxide **58** (first described by Ugi et al.[43]) and performed the *ortho*-lithiation followed by addition of ethyl iodide.[44] In three steps the authors easily converted **59** into enantiopure (S_p)-**60**.

It is interesting to point out that Weissensteiner et al. reported the transformation of (*S*)-**9a** (Scheme 3) into (R_p)-1-(S-*p*-Tol)-3-(CH_2OH)ferrocene.[41]



Scheme 15. Various chiral ferrocene phosphines.

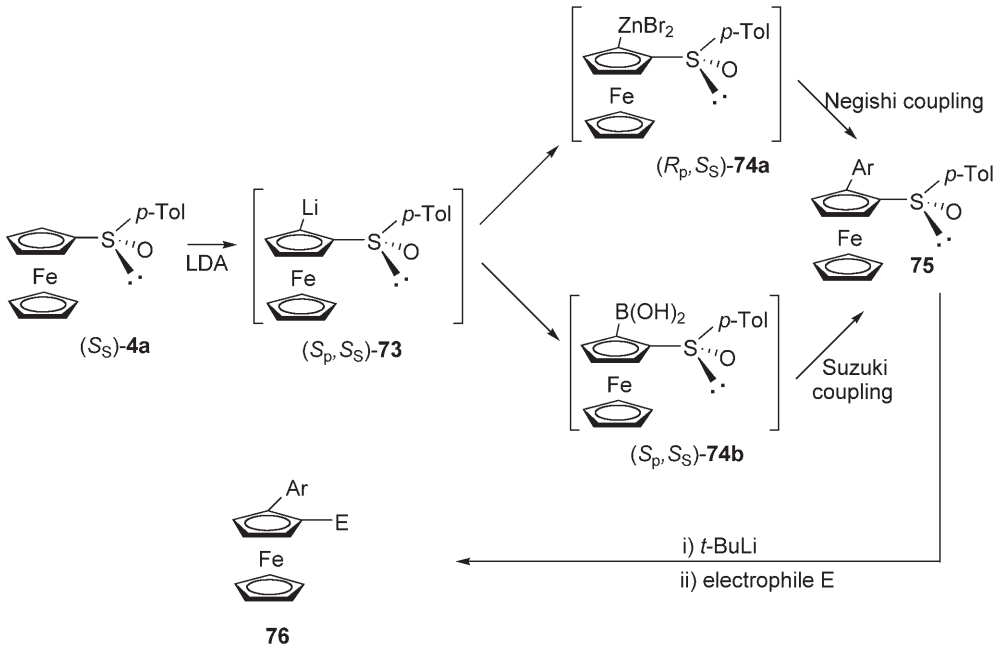
4.2 Synthesis of Chiral Ligands for Enantioselective Catalysis

Chiral ferrocenes are interesting platforms for the preparation of enantioselective catalysts,[45] Especially, ferrocenyl-mono-or diphosphines have been widely developed.[46] In this article are highlighted the synthetic approaches using the sulfoxide methodology (diastereoselective *ortho*-lithiation and sulfoxide-lithium exchange). In Scheme 15 are listed some ferrocenyl-phosphorus ligands prepared by the sulfoxide route which were screened in organometallic catalysis.

Below are shortly described the preparations of the above phosphines. In a next section the use of these compounds in asymmetric catalysis will be summarized. Except for **63** and **64**, all the phosphines of Scheme 15 possess planar chirality as the only stereogenic unit. The ferrocenyl-1,2-diphosphines **61** ($R \neq Ph$) represent a new class of ligands which has been synthesized in these laboratories.[23,47] Diphosphines **61a** and **61b** were prepared from ferrocenyl (*S*)-*p*-tolyl sulfoxide **4a** by diastereoselective *ortho*-lithiation (LDA, −78 °C) followed by quenching with $ClPPh_2$ and subsequent addition of borane (for the protection of phosphorus). The consecutive additions of *t*-BuLi and $ClPR_2$ (R = Cy or Me) followed by P deprotection (reflux in diethylamine) afforded enantiopure **61** in moderate yield. The absolute configuration of **61** is known from the synthetic scheme and was confirmed by X-ray crystallography on a rhodium complex, which also showed that **61a** behaves as a bidentate ligand.[47]

Diphosphine **62** was prepared by Knochel from the *ortho*-lithium derivative **73** of sulfoxide **4a**, and transmetallation with $ZnBr_2$ followed by a Negishi coupling with (2-iodophenyl)diphenylphosphine.[48] The subsequent sulfoxide-lithium exchange (with *t*-BuLi) and trapping by $ClPPh_2$ gave an overall yield of 60% for **62**. The two epimeric diphosphines **63** and **64** have been also synthesized by Knochel et al.[49] The *ortho*-lithiated derivative of sulfoxide **4a** was treated by 2-diphenylphosphanylbenzaldehyde, giving a mixture of epimeric alcohols, which were separated. Each alcohol was subsequently converted into a methyl ether and transformed in good yield by the sulfoxide-lithium exchange into pure **63** and **64** (after addition of $ClPR_2$).

The biferrocene diphosphines **65** have been prepared by Weissensteiner et al.[50] from the known 2-iodo-*p*-toluenesulfinylferrocene **31** ($R^1 = I$, Scheme 10).[22] This compound was heated with Cu powder and easily converted into an enantiopure bi-



Scheme 16. Suzuki or Negishi couplings on a ferrocene sulfoxide.

ferrocene disulfoxide, which was transformed into **65** by the sequential additions of *t*-BuLi and $ClPR_2$. The stepwise replacement of the sulfinyl moieties gave the possibility to prepare C_1-symmetrical diphosphines with two different phosphorus atoms (compounds not represented in Scheme 15). The diphosphine sulfoxide **66** was synthesized from ferrocene *tert*-butyl sulfoxide **4b** (Scheme 10) after diastereoselective *ortho*-lithiation by *n*-Buli (2 equivs.) and addition of 2 equivs. of $ClPPh_2$.[14,51] The 1,1′-bisphosphines **67** have been prepared by Zhang et al. from 1,1′-bis(*tert*-butylsulfinyl)-phosphinoferrocene, itself prepared by enantioselective oxidation of 1,1′-bis((*tert*-butylsulfenyl)ferrocene.[52]

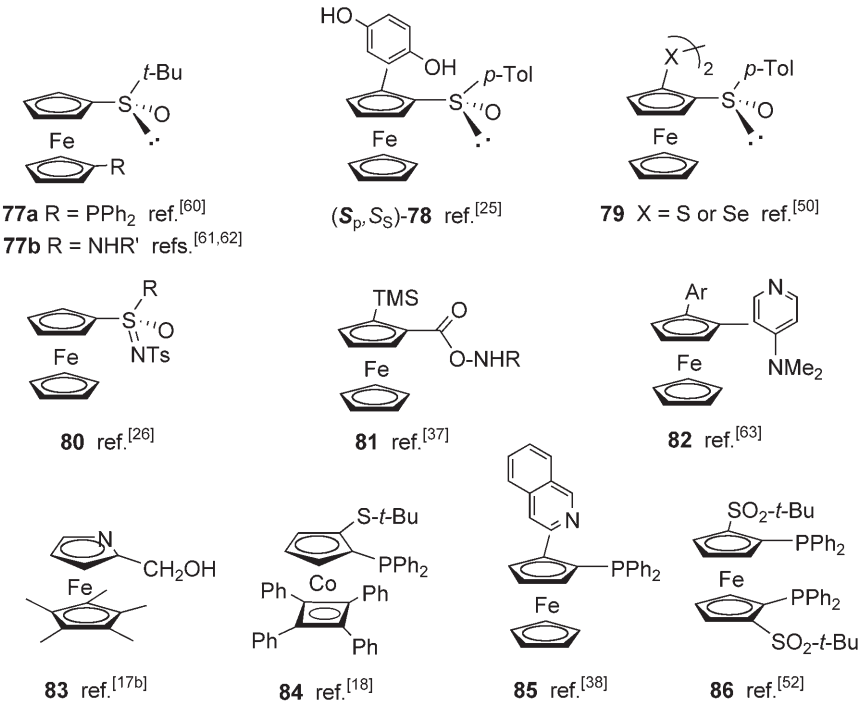
The monophosphine **68** bearing a sulfenyl group in the *ortho*-position represents a class of ligands developed by Carretero et al. and which gave rise to useful palladium catalysts.[53,54] These compounds were easily obtained from the key sulfoxides **4a** and **4b**, by *ortho*-lithiation, addition of one equiv. of $ClPh_2$ and reduction by $HSiCl_3$-Et_3N in refluxing toluene. Monophosphines **69** and **71** with an aryl group in the *ortho*-position of the Cp ring constitute another class of useful ferrocenylphosphines with planar chirality. These compounds have been elaborated from *p*-tolyl ferrocene sulfoxide **4a** *via ortho*-lithiation followed by lithium-zinc exchange with $ZnCl_2$ to give **14a** or by formation of the boronic intermediate **74b**. Then the aryl moiety was introduced by a Negishi or Suzuki coupling (Scheme 16).[55,56,59] The phosphorus group is introduced at the last stage by the sulfoxide-lithium exchange and addition of $ClPR_2$ or $ClP(OPh)_2$.[55,56,59] These phosphines have been named MOPFs (for monophosphine ferrocenes) by Johanssen et al.[55] Phosphite **70** (an aryl ferrocenephosphite) was prepared by Woodward et al.[58] Carretero et al. obtained phosphines **72** (Scheme 15) from ferrocene *tert*-butyl sulfoxide **4b** (Scheme 7) which was functionalized in the *ortho*-position before the deoxygenation of the sulfinyl group.[54]

In Scheme 17 are reported some additional metallocenes prepared by the sulfoxide route with the purpose to be used in asymmetric catalysis. Recently *t*-butyl ferrocene **4b** was transformed by the sequence *ortho*-lithiation/diastereoselective addition on imines into aminosulfoxides, which may be useful as bidentate ligands.[68]

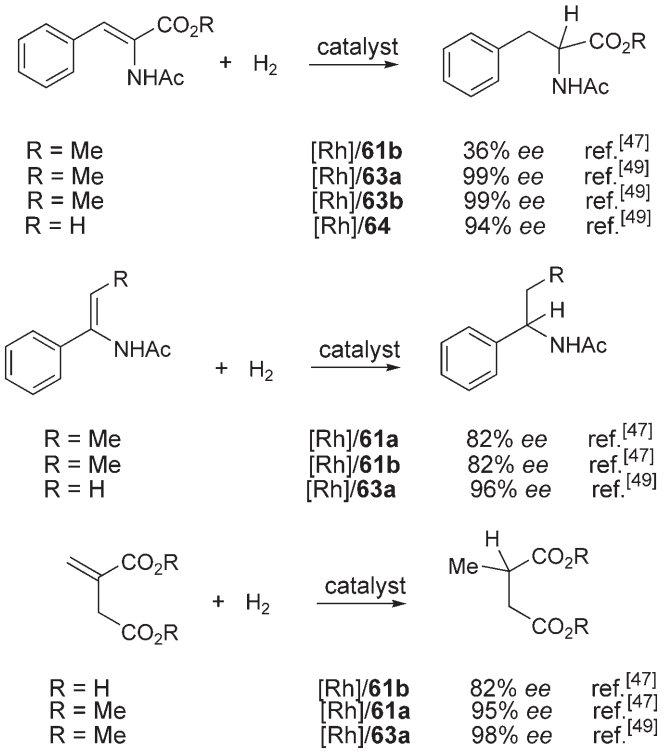
4.3 Some Results in Enantioselective Catalysis

In Scheme 18, Scheme 19, and Scheme 20 are presented selected examples of reactions catalyzed using metallocene ligands obtained by the sulfoxide route, some results will be briefly commented below.

Catalysts for *asymmetric hydrogenation of C=C bonds* (Scheme 18) were prepared with many mono- and diphosphines derived by the sulfoxide route. The most impressive ligands are the diphosphines **63** prepared by Knochel[49] (Scheme 15), very high enantioselectivities in the reduction of many types of C=C bonds with rhodium catalysts have been achieved (up to 99% *ee*). The biferrocenyl diphosphine **86** (Scheme 17) gave a rhodium catalyst for the asymmetric hydrogenation of methyl *N*-acetyldehydroalanine (93% *ee*).[52]



Scheme 17. Some chiral metallocenes used as ligands in organometallic catalysis.



Scheme 18. Asymmetric hydrogenation.

Enantioselective hydrogenation of β*-diketones or* β*-keto esters* could be realized with ruthenium catalysts and diphosphines **63a** (*ee* up to 99%).[49] A ruthenium complex with biferrocenyl diphosphine **65** catalyzed the hydrogenation of ethyl acetoacetate into β-hydroxybutyrate in 82% *ee*.[50a]

Ligands with a sulfoxide group and one or two PR_2 units gave catalysts yielding modest enantioselectivities. Moreover, these ligands are of moderate stability because of a slow transfer of oxygen from sulfur to phosphorus.

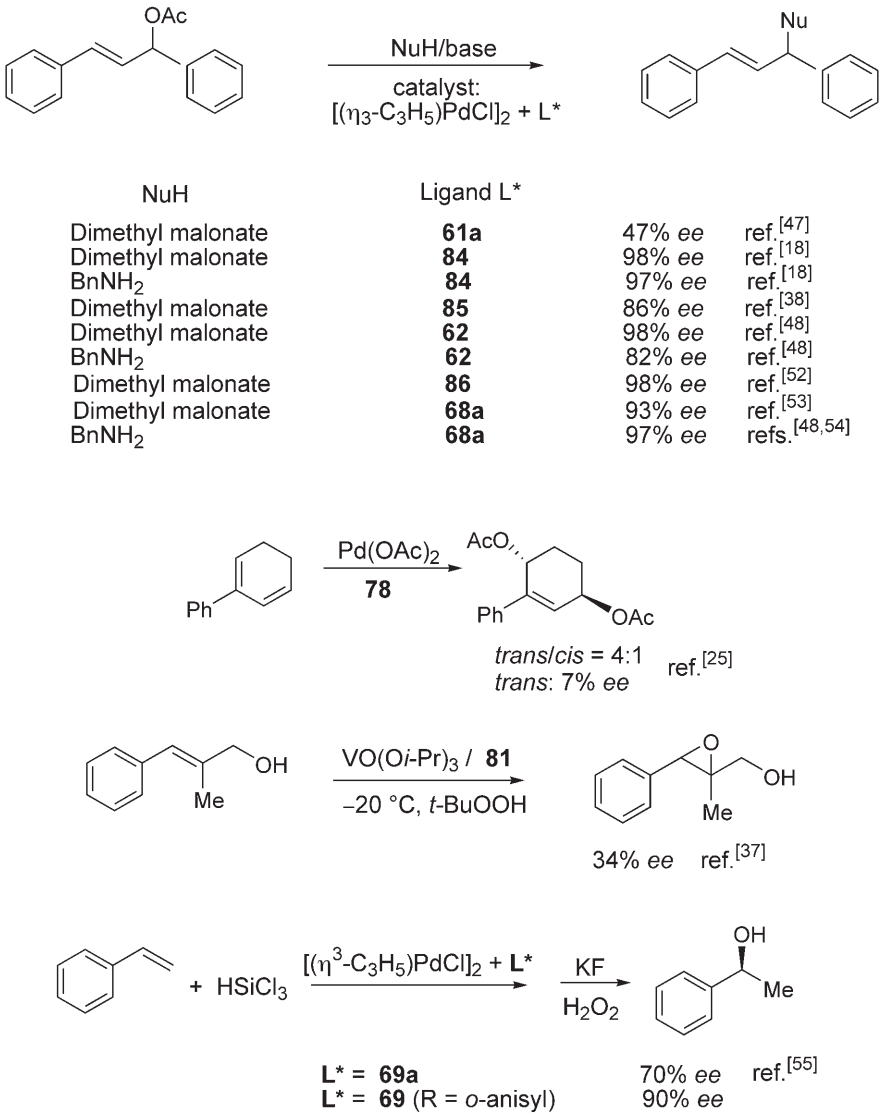
Allylic substitutions (Scheme 19) catalyzed by a palladium complex were widely studied. The best ligands are the diphosphine **62** and the sulfenyl phosphines **68, 84** and **86**, giving *ee*s of up to 98%.[18,48,54)]

Hydrosilylation of styrene (Scheme 19) catalyzed by a palladium/MOPF (**69**) complex gave up to 90% *ee*.[55] The same complex allowed one to prepare 2,2′-dimethyl-1,1′-binaphthyl by an enantioselective *Suzuki coupling* with 54% *ee*.

Allylation of an imine by $CH_2{=}CH{-}CH_2{-}SiCl_3$ (Scheme 20) could be mediated (not catalyzed) by isopropyl ferrocene sulfoxide **10d**, giving an amine in 82% *ee*, while *tert*-butyl sulfoxide **10b** was less interesting (26% *ee*).[64]

Some of the sulfenyl phosphines **68** developed by Carretero et al. are very efficient in *heterocycles rearrangement*, in *hetero-Diels–Alder reaction* or in *1,3-dipolar cycloaddition* (up to 99% *ee*) as indicated in Scheme 20.[53,64,65] The chiral DMAP analogue **82** catalyzed a dynamic kinetic resolution of azlactones with moderate enantioselectivities (*ee* < 42%).[64]

Enantioselective additions of organometallics have been catalyzed by various systems. Diethylzinc addition on aromatic aldehydes could be catalyzed by



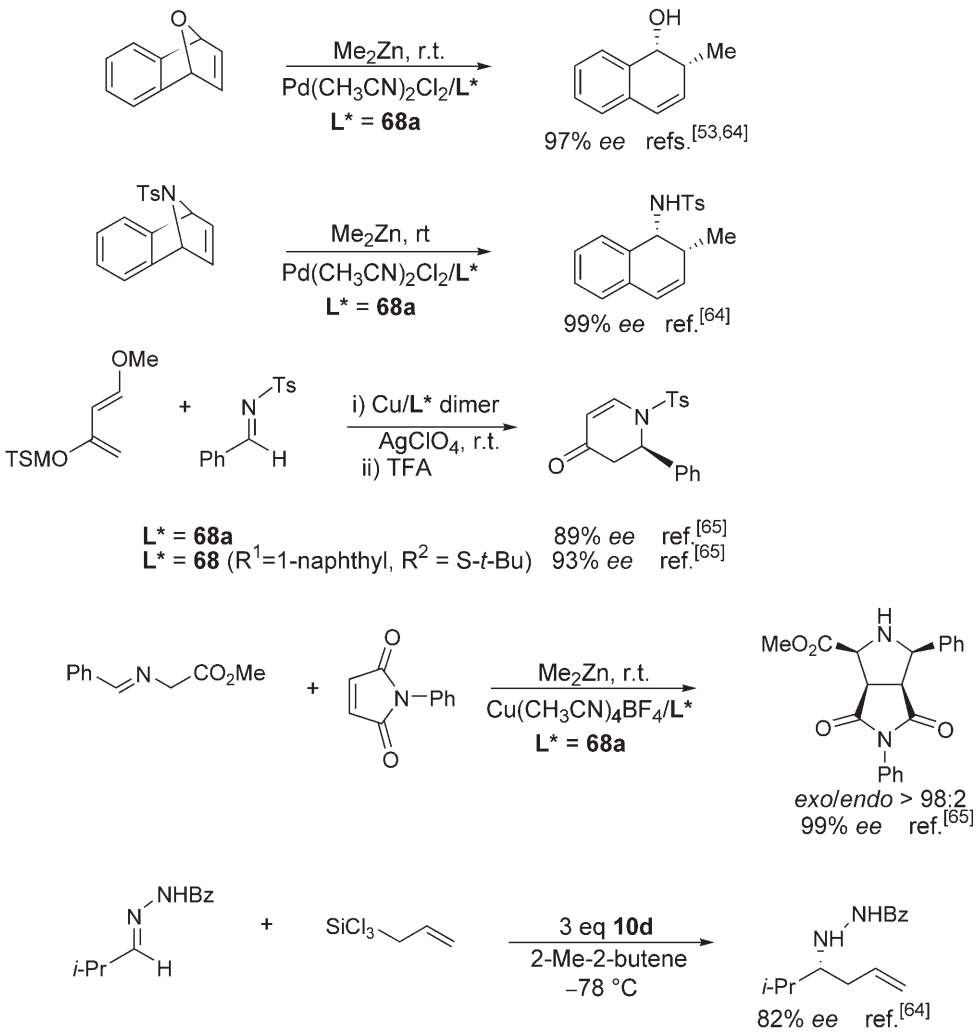
Scheme 19. Various reactions of asymmetric catalysis.

amino sulfoxide **77b** (Scheme 17), some excellent results have been reported (*ee* $<96\%$).[61,62] Aminophosphine **71** is a ligand for a Cu catalyst of the 1,4-addition of Et_2Zn on chalcone (*ee* up to 86%).[59] Phosphite **70** and analogues were used as the ligand of a copper catalyst that gave up to 92% *ee* in the conjugated addition of Et_2Zn on cyclohexenone.[58]

Most of the metallocenes with planar chirality developed as ligands for asymmetric catalysis are based on the ferrocene backbone, a new review (published after the completion of this article) details the recent applications of chiral ferrocene ligands in asymmetric synthesis.[46]

5 Conclusion

Sulfoxides connected to metallocenes with planar chirality are becoming a useful starting material for the elaboration of functionalized metallocenes.The tandem diastereoselective *ortho*-functionalization and sulfoxide-lithium exchange (Scheme 10) allowed one to prepare many classes of compounds with planar chirality. Some molecules are interesting on account of their structural features or as synthetic intermediates, others are very useful in asymmetric catalysis. Even applications to bioorganometallic chemistry may be noticed. A great flexibility in the synthetic schemes makes possible many structural variations, and one may expect that this methodology will give rise to an increased number of applications.



Scheme 20. Various reactions of asymmetric catalysis.

Acknowledgements

We thank the Université Paris-Sud and CNRS for their financial support. B.F. greatly acknowledges CNRS of Gif-sur-Yvette for financial support.

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