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MINIREVIEW

Iron bis(oxazoline) complexes in asymmetric catalysis

Thierry Ollevier

Asymmetric reactions catalyzed by iron complexes have attracted considerable attention because iron is a ubiquitous, inexpensive, and environmentally benign metal. Various chiral iron complexes can be prepared from *bis(oxazoline)* ligands and be used in asymmetric reactions. This overview charts the development and application of chiral iron *bis(oxazoline)* and *pyridine-2,6-bis(oxazoline)* catalysts through their most prominent and innovative uses in asymmetric catalysis, especially in Lewis acid and oxidation catalysis.

Born in Brussels, Thierry Ollevier obtained his B.Sc. (1991) and Ph.D. (1997) at the Université de Namur, Belgium, and was postdoctorate fellow at the Université catholique de Louvain, Belgium under István E. Markó (1997), NATO postdoctorate fellow at Stanford University under Barry M. Trost (1998–2000), then postdoctorate fellow at the Université de Montréal under André B. Charette (2000–2001). After an Assistant Professor appointment (2001) at Université Laval, he became Associate (2006) and is currently Full Professor. Current research in his group aims at designing novel catalysts, developing catalytic reactions and applying these methods to chemical synthesis. He is active in the areas of Lewis acids, asymmetric catalysis, organic chemistry in aqueous conditions, and green synthetic chemistry.

1. Introduction

Main chiral metal catalysts are key elements in the toolbox of organic chemists. Iron is one of the most abundant metals on Earth; it is inexpensive, environmentally benign, and relatively nontoxic in comparison with other metals. From a green chemistry aspect, it is interesting to develop new iron-catalyzed methods.[1] Indeed, many catalysts used in asymmetric synthesis are derived from noble and rare metals and their price or toxicity prevent their use on an industrial scale. Iron, which is ubiquitous, is thus becoming one of the most promising transition metals. Various

reviews have been published in the field of asymmetric catalysis using iron.[2] This article aims at reviewing the catalytic applications of Fe[II] and Fe[III] complexes derived from oxazoline ligands. Both *bis(oxazoline)* (*box*) and *pyridine-2,6-bis(oxazoline)* (*pybox*) have been used as chiral ligands with various metals.[3] Their use, conjointly with iron salts, is gaining increasing attention. The present review covers the most prominent uses of *bis(oxazoline)* and *pyridine-2,6-bis(oxazoline)* as chiral ligands for enantioselective iron catalysis and is primarily organized according to the type of chiral ligand used. Various *box* and *pybox* will be presented, ranging from bidentate to tetradentate oxazoline-based ligands for both Fe[II] and Fe[III]. Polydentate oxazolines have been used as highly effective chiral ligands for asymmetric catalysis. Nitrogen donor atoms with the in-plane lone pair combined with additional binding sites result in highly stereodirecting ligands. The resulting chiral iron complexes have been used in a broad range of catalytic transformations, particularly in Lewis acid catalysis. This account is an introduction to the most significant developments on the use of iron *bis(oxazoline)* complexes, including elements about the geometry of selected complexes and applications of these catalysts as Lewis acids.

2. Iron *bis(oxazoline)* catalysts

Seminal work by Corey demonstrated the efficiency of a C_2-symmetric chiral *bis(oxazoline)* Fe[III] complex for the enantioselective Diels-Alder reaction.[4] The reaction of 3-acryloyl-1,3-oxazolidin-2-one and cyclopentadiene in the presence of 10 mol % of the catalyst, which was prepared from a chiral *bis(oxazoline)*, Fe and I_2, led to an excellent yield of the *endo* product (*endo/exo* 96:4) with a very good enantioselectivity (82% *ee*) for the *endo* product (Scheme 1). The Lewis acid can either be prepared from Fe and I_2 or from $FeCl_2$ and I_2. In both cases, after complexation with **1**, the catalytic species is believed to be **1**·FeX_2^+. Reasonable models of the dienophile bound to this one were proposed based on the knowledge of the metal geometry to rationalize the stereoselectivity of the process. The geometry of **1**·FeX_2^+ is believed to be square-planar. This would lead to the

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predominant formation of the axial-equatorial chelate of the dienophile.
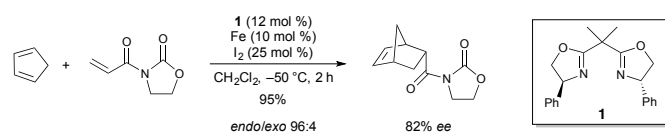
Scheme 1. Fe[III]-catalyzed enantioselective Diels-Alder reaction.

The concept of chiral relay was disclosed by Sibi in 2006. Achiral fluxional additives containing multiple sites for modification were reported to amplify the enantioselectivity of the above-mentioned Diels-Alder reaction in the presence of **1** and Fe(ClO$_4$)$_2$.[5] However, the origin of *ee* enhancements from these fluxional additives is not completely clear.

Fe catalyzed cycloisomerization reactions have been reported using an Fe catalyst obtained *in situ via* the reduction of Fe(acac)$_3$ with Et$_3$Al (3 equivalents) in the presence of a *bis(oxazoline)* ligand.[6] Only moderate levels of stereoinduction were disclosed though.

Pfaltz reported the preparation of chiral *diamino-bis(oxazoline)* ligands and their use as Fe[II] complexes.[7] When the ligands were derived from *N,N'*-dimethylcyclohexane-1,2-diamine, the resulting complexes showed different coordination modes depending on the ligand diastereoisomer used: the Fe complex adopted either a pentacoordinate (**2a**) or an hexacoordinate (**2b**) geometry (Scheme 2, a). The ionic versions of the Fe complexes with SbF$_6^-$ as weakly coordinating anion were also prepared to generate two vacant coordination sites. Ligands prepared from *N,N'*-dimethylethane-1,2-diamine reacted with FeCl$_2$ in a stereoselective manner to give an octahedral mononuclear complex **3**, after subsequent removal of the chloride anions using 2 equiv. of AgSbF$_6$ (Scheme 2, b). Preliminary catalytic tests for the epoxidation of *trans*-β-methyl-styrene showed that the Fe complexes were less active and less enantioselective than analogous Mn-based catalysts.
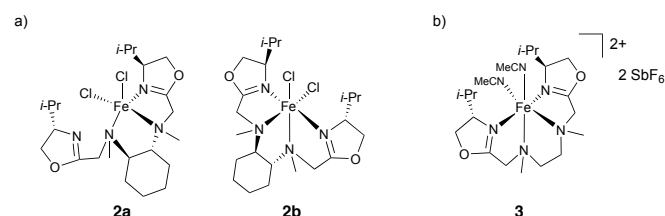
Scheme 2. Chiral Fe[II] *diamino-bis(oxazoline)* complexes prepared by Pfaltz.

Fe complexes of *spiro-bis(oxazoline)* ligands **4** and **5a** were highly efficient catalysts for asymmetric O–H bond insertion reactions.[8] Based on the lower enantioselectivities obtained with other chiral ligands in the O–H insertion reaction, the rigid *spiro* scaffold of ligands **4** and **5** appeared to be essential for a high level of chiral induction. The complexes catalyzed insertions into the O–H bond of a wide variety of alcohols with excellent enantioselectivities under mild reaction conditions (Scheme 3). Interestingly, allylic alcohols could also be used in these conditions and no competitive cyclopropanation was detected. The Fe complex also catalyzed the asymmetric O–H insertion reaction between water and methyl α-diazophenylacetate with outstanding enantioselectivities. Higher enantioselectivites were obtained

when using Fe as compared to other transition metals, including Cu and Rh, used under the same reaction conditions.
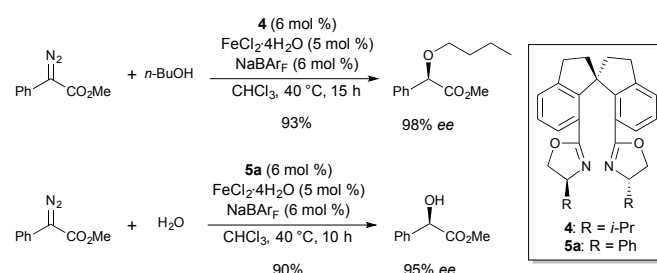
**Scheme 3.** Fe[II] catalyzed O–H bond insertion reactions.

The same authors also demonstrated that the complexes prepared *in situ* from chiral *spiro bis(oxazoline)* **5b** and an Fe[II] salt was competent to catalyze the C–H functionalization of indoles with α-aryl-α-diazoesters.[9] α-Aryl α-indolyl-acetate derivatives were isolated as the reaction products in high yields and high enantioselectivities (up to 78% *ee*) (Scheme 4). Other chiral *bis(oxazoline)* and *pyridine-2,6-bis(oxazoline)* ligands were less efficient in this reaction. The α-aryl-α-diazoester is believed to be decomposed by the Fe[II] catalyst into an Fe[II] carbene. The enantioselective proton migration on an Fe[II] zwitterionic intermediate is most likely the rate-determining step, as demonstrated by kinetic isotope effect experiments. Alternative mechanisms cannot be ruled out though. The efficiency of this Fe[II] catalytic system was also exploited in the asymmetric intramolecular cyclopropanation of α-diazoesters.[10] Using chiral ligand **5b**, Fe(ClO$_4$)$_2$·4H$_2$O in the presence of NaBAr$_F$ (sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate), [3.1.0]bi-cycloalkane lactone derivatives were obtained in high yields and excellent enantioselectivities (up to 97% *ee*) (Scheme 4). Based on the stereochemistry of the products, the authors suggested that the cyclopropanation undergoes a concerted process. According to various reaction features (higher reactivity of Fe[II] *vs.* Fe[III], higher reactivity of electron-rich alkenes and observation of fumarates and maleates as by-products), electrophilic Fe[II] carbenoids are most likely involved in the process.
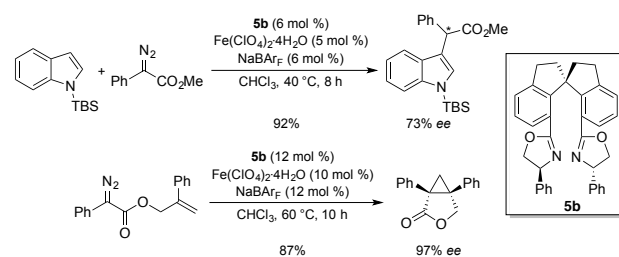
**Scheme 4.** Fe[II] catalyzed reactions with α-diazoesters.

In 2012, Niwa and Nakada developed a Fe[II] complex bearing a carbazole-based tridentate ligand that catalyzes the asymmetric epoxidation of (*E*)-alkenes with excellent enantioselectivity (Scheme 5).[11] They found that complex **6**, which was prepared from FeCl$_2$·4H$_2$O and a tridentate carbazole ligand, in the presence of NaBAr$_F$, catalyzed the asymmetric epoxidation of *trans*-stilbene to afford the corresponding chiral epoxide in moderate yield and enantioselectivity. The use of 2 mol % of

SIPrAgCl as an additive improved both yield and enantioselectivity of the reaction (55% and 88% *ee*). The key intermediate in the epoxidation was demonstrated to be an Fe[IV]-oxo complex bearing a π-cation radical. The Fe complex bearing the carbazole ligand behaves in a similar way as Fe porphyrins in this oxidation reaction, as demonstrated by UV-vis and EPR analysis. When an Fe[III] complex derived from tridentate *bis(oxazolinylphenyl)amine* (*bopa*) ligand **7** (Scheme 6), which lacks the C–C bond between the two phenyl rings, such as in the carbazole-based tridentate system **6**, was used, no epoxidation occurred.
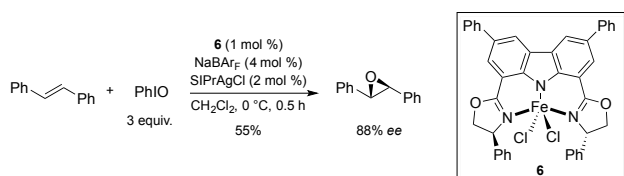

Scheme 5. Asymmetric epoxidation of an alkene with a Fe[III] carbazole-*bis(oxazoline)* complex.

In 2007, Nishiyama investigated the asymmetric hydrosilylation of ketones using iron catalysis.[12] The addition of chiral tridentate *bis(oxazoline-phenyl)amine (bopa)* **8** and **9** to Fe(OAc)$_2$ in THF at 65 °C formed *in situ* a catalytically active species to mediate the hydrosilylation of ketones with (EtO)$_2$MeSiH (Scheme 6). The isolated yields were up to 82% and the enantioselectivity of the obtained alcohols were 57 and 79% *ee* respectively. Interestingly, the use of a chiral *pyridine-2,6-bis(oxazoline)* (*pybox*) led to a lower enantioselectivity (37% *ee*, Scheme 17).
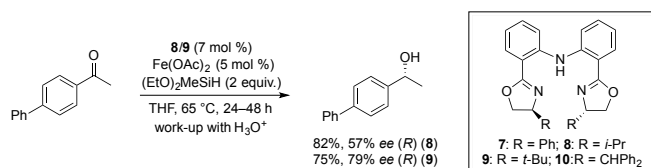

Scheme 6. Asymmetric hydrosilylation of aryl ketones catalysed by Fe *bopa* complexes.

Nishiyama was able to improve the asymmetric hydrosilylation of ketones by ligand design. Bulky substituents on the oxazoline ring led to higher enantioselectivity (up to 88% *ee*).[13] To elucidate the mechanism of the reaction, the differences between well-defined complexes and *in situ* prepared catalytic systems were investigated.[14] Interestingly, more hindered ligand **10** (Scheme 6, R = CHPh$_2$) can afford both enantiomers of the product either used as *in situ* formed catalyst (Fe(OAc)$_2$/**10**) or as well-defined iron complex **10'**, conjointly with zinc as an activator (Scheme 7). The authors suggest that zinc serves as a reducing agent for the refuction of Fe[III] to Fe[II]. Control experiments ruled out the possibility that only a Zn *bopa* complex was responsible for the asymmetric induction.
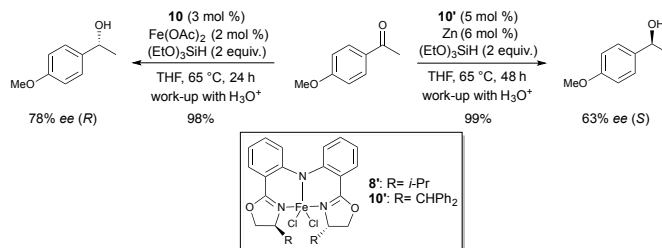

Scheme 7. Asymmetric hydrosilylation of aryl ketones catalysed by *in situ* or well-defined Fe *bopa* complexes.

Other *trans*-chelating tridentate ligands were reported to be efficient ligands for various metals. The resulting complexes have been characterized as cationic aqua complexes.[15] In particular, (*R,R*)-4,6-dibenzofurandiyl-2,2'(4-phenyloxazoline) **11** was reported to be an appropriate ligand for Fe[II].[15-16] The obtained complex with Fe(ClO$_4$)$_2$ was an efficient catalyst for the Diels-Alder reaction of cyclopentadiene with 3-acryloyl-2-oxazolidinone, leading to high yield and excellent stereoselectivity (Scheme 8). The absolute configuration of the product can be easily deduced from the structure of the complex coordinated to the substrate. Structural evidence was provided from the analogous Ni complex, which appeared to be a square bipyramidal structure containing an octahedral Ni[II]. Although the complex of Fe(ClO$_4$)$_2$ gave an excellent selectivity, Fe(ClO$_4$)$_3$·*n*H$_2$O (*n* = 6–9) was poorly selective (–40 °C, 67% *ee*).
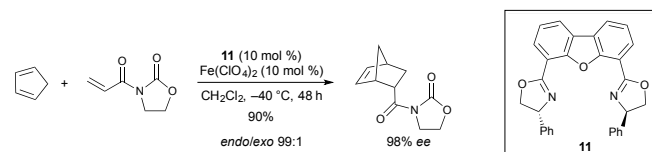
Scheme 8. Fe[III]/dibenzofuran ligand **11**-catalyzed enantioselective Diels-Alder reaction.

Yoon reported the asymmetric oxyamination reaction of alkenes using Fe[II] *bis(oxazoline)* **12**.[17] The process was highly stereoselective and regioselective using *N*-sulfonyl oxaziridines (Scheme 9). The oxyamination products were obtained with high *cis* diastereoselectivity and excellent enantioselectivity. The authors suggested that the high diastereoselectivity observed in the reaction is a consequence of a kinetic resolution process occuring with the racemic *N*-sulfonyl oxaziridines (Ns = nosyl). 1,2-Amino alcohols were prepared with high regio- and stereochemical control after clean removal of the aminal functionality in standard acid-catalyzed hydrolysis conditions.
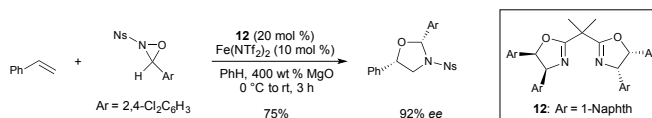
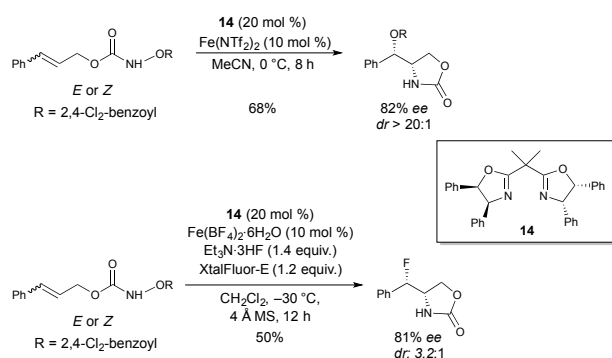**Scheme 9.** Fe[II] *bis(oxazoline)* catalyzed asymmetric oxyamination of olefins.

N-sulfonyl oxaziridines have also been rearranged into the corresponding *N*-sulfonyl imides.[18] A highly selective kinetic resolution of *N*-sulfonyl oxaziridines was promoted by Fe[II] *bis(oxazoline)* complexes (Scheme 10). Among other ligands,

cyclopropane-bridged indanyl ligand **13** gave the best yields and selectivity. A variety of substituted *N*-benzenesulfonyl groups were tolerated, and similar selectivity *s* factor values were obtained. The chiral catalyst promotes the efficient rearrangement of oxaziridines to the corresponding *N*-sulfonyl imides. Interestingly, the process was scaled up to gram quantities, which is an attractive practical method for the synthesis of enantio-enriched *N*-sulfonyl oxaziridines. The results obtained on large scale nicely demonstrated the opportunity to offset the lower intrinsic stereoselectivity of the reaction by increasing the *ee* at the expense of the yield by running the resolution to higher conversion.
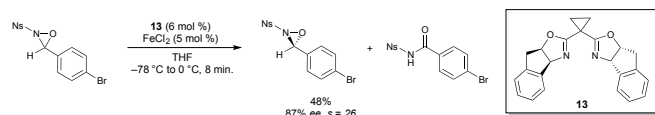

Scheme 10. Fe^{II} catalyzed kinetic resolution of *N*-sulfonyl oxaziridines.

In 2013, Xu discovered a new Fe^{II} *bis(oxazoline)* **14** complex catalyzed intramolecular olefin aminohydroxylation with functionalized hydroxylamines, where both the *N* and *O* functional groups are efficiently transferred (Scheme 11).[19] Mechanistic studies revealed that an Fe nitrenoid is a possible intermediate, arising from the reductive cleavage of the N–O σ bond by the Fe^{II} complex. A stepwise cycloamination would then presumably occur, giving a carbo-radical species that would next undergo a ligand (OR) transfer, occurring faster than the competing olefin aziridination. An enantioselective intramolecular indole aminohydroxylation reaction was also reported to be catalyzed by Fe^{II} and *bis(oxazoline)* **14**.[19b] Xu also observed that the Fe^{II} catalyzed asymmetric olefin aminofluorination is stereoconvergent: isomeric olefins are converted to fluoro oxazolidinones with essentially the same *ee* (81%) and *dr* (Scheme 11).[20] Taking into account that the aminohydroxylation and aminofluorination are competing pathways, the authors suggested that, in the presence of Et$_3$N·3HF and XtalFluor-E, a facile anion metathesis process can happen to convert an Fe nitrenoid intermediate into an Fe fluoride-based nitrenoid. After subsequent cycloamination, a fluoride transfer would occur at the formed radical – or possibly cationic – center. The same authors recently reported an Fe^{II}-catalyzed enantioselective and diastereoselective intramolecular olefin aminochlorination reaction.[21] The reaction proceeds very efficiently with high stereoselectivities (up to 92% *ee*, up to 15:1 *dr*).
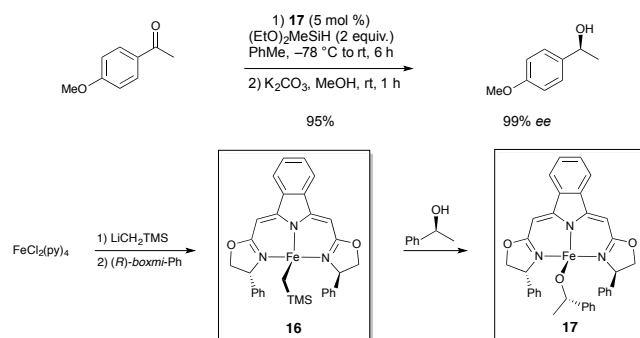

Scheme 11. Fe^{II} *bis(oxazoline)* catalyzed asymmetric aminohydroxylation and aminofluorination of olefins.

Enantioselective azidations of β-keto esters and oxindoles using complex **15'** conjointly with a readily available azidoiodinane as an N$_3$-transfer reagent were reported by Gade in 2013.[22] A number of α-azido-β-keto esters were prepared with up to 93% *ee*. 3-Azido-3-aryloxindoles were obtained with up to 94% *ee* using the catalyst prepared from iron(II) propionate and bis(oxazolinyl-methylidene)isoindoline *boxmi* ligand **15** in situ (Scheme 12).
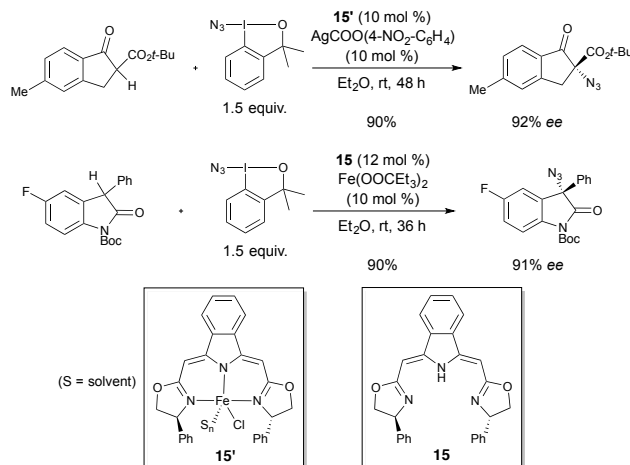
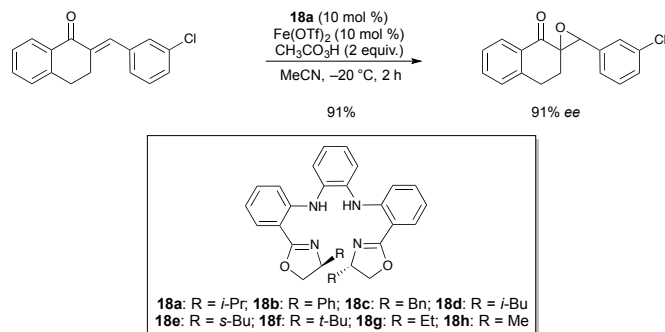**Scheme 12.** Enantioselective azidation of β-keto esters and oxindoles.

Chiral Fe alkyl and Fe alkoxide complexes prepared from *boxmi* N$_3$ ligands have been disclosed as catalysts for enantioselective hydrosilylation reactions with unprecedented activity and selectivity (up to 99% *ee* for alkyl aryl ketones), which match the performance of previously established noble-metal-derived catalysts (Scheme 13).[23] Highly reactive Fe alkyl pre-catalyst **16** was transformed into an alkoxido Fe complex **17**, which was obtained by clean alcoholytic transformation using (*S*)-1-phenyl-1-ethanol at ambient temperature. Since this species was imagined to be an important intermediate in the catalytic cycle of the studied reaction, it was believed to be an active catalyst to develop. Both of the isolated pyridine adducts of **16** and **17** were found to be as active as the *in situ* generated catalysts. The isolated complexes show a trigonal-bipyramidal coordination sphere with the ligand forming the equatorial plane of the bipyramid.

Scheme 13. Porphyrin-inspired Fe catalyzed asymmetric epoxidation of electron-deficient olefins.

A porphyrin-inspired N$_4$ ligands bearing chiral oxazolines was reported for the asymmetric epoxidation of di- and trisubstituted enones (Scheme 14).[24] The epoxidation of various enones

occurred in excellent yields and high enantioselectivities (up to 99% *ee*). The practical utility of the catalyst was demonstrated on the gram-scale preparation of an enantio-enriched epoxide. Based on Hammett analysis for the epoxidation of *para*-substituted cyclic enones, it was suggested that the transition state of the reaction is electron-demanding and the active Fe complex an electrophilic oxidant.

**Scheme 14.** Porphyrin-inspired Fe^{II} catalyzed asymmetric epoxidation of electron-deficient olefins.

3. Iron pyridine-*bis(oxazoline)* catalysts

In 2004, Shibasaki developed a catalytic enantioselective Diels-Alder reaction using a cationic Fe^{III} Ar-*pybox* **19** complex as catalyst.[25] This reaction is the first catalytic enantioselective Diels-Alder reaction of acylic 4,4-disubstituted 1,3-dienes. It allowed the efficient and rapid synthesis of chiral polysubstituted cyclohexanones, which are difficult to access using other methods (Scheme 15). The use of other *pybox* ligands, such as *i*-Pr-*pybox* and *t*-Bu-*pybox*, afforded the product in low yield and enantioselectivity. Interestingly, other Lewis acid metal salts such as Sc(OTf)$_3$, Cu(OTf)$_2$, Zn(OTf)$_2$ and cationic Fe^{II} salts gave much worse results. This methodology was used elegantly in the catalytic asymmetric total synthesis of *ent-hyperforin*.[26]
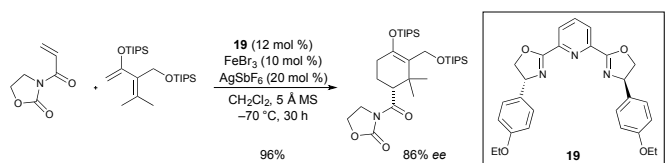

Scheme 15. Fe^{III} *pybox* catalyzed Diels-Alder reaction.

FeCl$_2$ used with *pyridine-2,6-bis(oxazoline)* ligands was reported to be an effective catalyst for the asymmetric Mukaiyama aldol in aqueous media.[27] The aldols were obtained in good yields and *syn* diastereoselectivities (Scheme 16). Moderate enantio-selectivities (up to 75% *ee*) were afforded with ligand **20**. Using bulkier ligand **21** with *O-t*-butyldiphenylsilyl groups,[28] the enantioselectivity of the process was increased (up to 92% *ee*). It is believed that, using **21**, the resulting Fe^{II} complex is more stable in the reaction conditions, affording better reproducibility of the reaction yield and *ee*. The bulky silyl groups in **21** are assumed to better shield the Fe^{II} cation against oxidation.
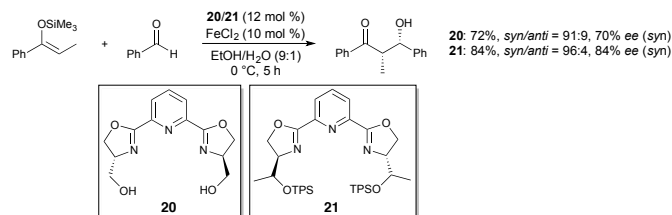

Scheme 16. Enantioselective Mukaiyama aldol reaction.

The use of *pyridine-bis(oxazoline)* was part of Nishiyama's study of the asymmetric hydrosilylation of ketones (Scheme 17).[12] The addition of *pybox* **22** to Fe(OAc)$_2$ in THF at 65 ºC allowed the preparation of enantiomerically enriched alcohols.
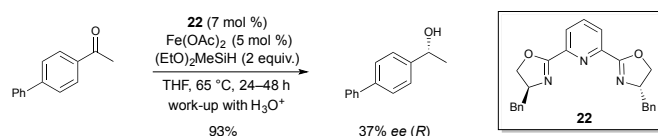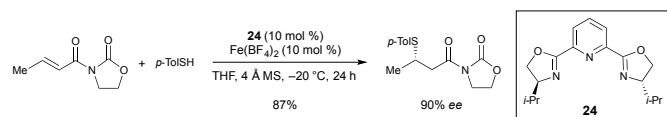

Scheme 17. Fe^{II} *pyridine-bis(oxazoline)* catalyzed hydrosilylation.

In connection with his work with *pybox* **22**, Nishiyama reported chiral iron *bis(oxazolinyl)phenyl* (*phebox*) complex **23** obtained by oxidative addition of Fe^0 and an aryl bromide ligand.[29] Interestingly, Fe^{II}-complex **23** showed up to 66% *ee* with full conversion of methyl(4-phenylphenyl)ketone using (EtO)$_2$MeSiH (Scheme 18). Therefore this report by Nishiyama detailing the synthesis and structural characterization of chiral iron complexes with *bis(oxazolinyl)phenyl* ligands resulting from the oxidative addition of Fe$_2$(CO)$_9$ to *phebox*-Br represents a major breakthrough in the field. The authors suggest that an active Fe–H intermediate can be generated by the initial reaction of **23** with Na(acac) and the hydrosilane.
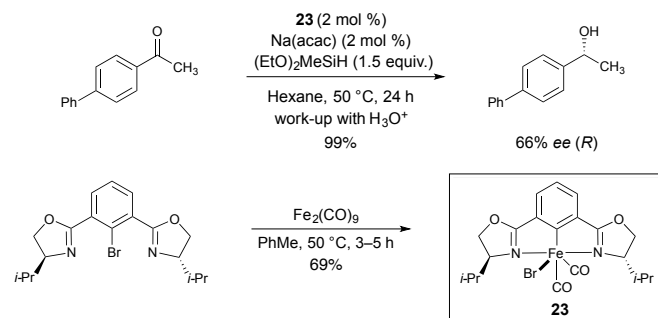

Scheme 18. Fe^{II} *bis(oxazolinyl)phenyl* catalyzed hydrosilylation.

The enantioselective conjugate addition of thiols to (*E*)-3-crotonoyloxazolidin-2-one was catalyzed by the complex prepared from *pyridine-bis(oxazoline)* **24** and Fe(BF$_4$)$_2$.[30] 1,4-Addition products were obtained in very good enantioselectivities (up to 95% *ee*) (Scheme 19). However, this catalytic system was not effective when using alkyl thiols. Using **24**, the corresponding Co(ClO$_4$)$_2$·6H$_2$O complex also catalyzed the same reaction with a high enantioselectivity.

Scheme 19. Fe^{II} catalyzed conjugate addition of thiols.

Chirik studied Fe^{II} complexes prepared from *pyridine-2,6-bis(oxazoline)* and *bis(oxazoline)* ligands in order to develop an enantioselective hydrosilylation reaction of ketones.[31] These ligands are commercially available or easily synthesized from available enantiopure amino alcohols. Following the same synthetic protocol as for the *bis(imino)pyridine* Fe-dialkyl derivatives, the corresponding *pybox* and *box* Fe-dialkyl complexes have been isolated by using the alkylation of the appropriate Fe dihalide precursor (Scheme 20). Even though high conversions were reported for the hydrosilylation of various ketones, the chiral induction of these systems was rather poor. When the hydrosilylation reactions were run for longer times, a competing catalyst deactivation pathway, *i.e.* the formation of bis(chelate) [(*S,S*)-*i*-Pr-*pybox*]$_2$Fe, was observed. Activation of these Fe-dialkyl complexes with B(C$_6$F$_5$)$_3$ resulted in catalysts able to reduce quantitatively acetophenones and α-tetralone with *ee* in the 34–54% range. Chirik also demonstrated that sodium amalgam reduction of (*S,S*)-*i*-Pr-*pybox*-FeCl$_2$ under 1 atm of CO afforded the desired Fe dicarbonyl complex (*S,S*)-*i*-Pr-*pybox*-Fe(CO)$_2$.
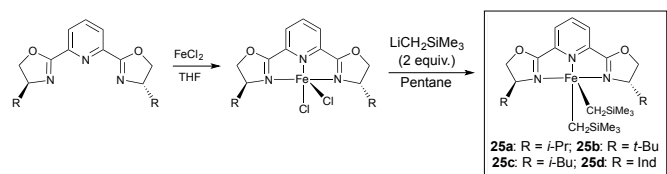
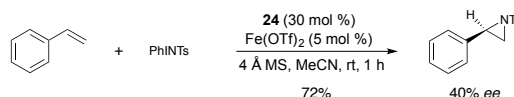**Scheme 20.** Preparation of Fe^{II} *pyridine-bis(oxazoline)* catalysts for asymmetric hydrosilylation.

Fe^{II} *pyridine-bis(oxazoline)* complexes were also used in the catalytic asymmetric aziridine forming reaction of *N*-benzylideneaniline and ethyl diazoacetate.[32] In these conditions (complex **24'** used together with an excess of ligand **24** and AgSbF$_6$), the corresponding *cis*-aziridine was obtained in poor performance – moderate yield and enantioselectivity (up to 49% *ee*) (Scheme 21).
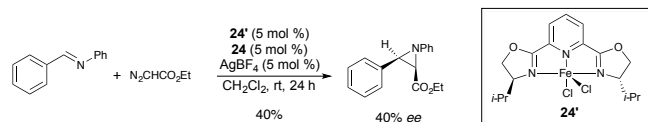
**Scheme 21.** Catalytic asymmetric aziridination reaction of arylimines.

Asymmetric aziridination reaction of styrene was studied using various Fe^{II} derived catalysts.[33] Among various tridentate ligands tested with Fe(OTf)$_2$ and *N*-(*p*-tolyl-sulfonyl)imino phenyliodinane (Scheme 22), ligand **24** was found to be the most effective leading to the product with up to 40% *ee* in 72% yield. When studying the aziridination of *cis*-stilbene using Fe(OTf)$_2$ as a catalyst, Bolm suggested that a concerted mechanism was unlikely, and that the

formation of a radical intermediate during the nitrogen transfer process can be invoked.

Scheme 22. Fe^{II} *pyridine-bis(oxazoline)* catalyzed aziridination.

In 2010, Itoh disclosed an asymmetric Nazarov cyclization of divinyl ketones catalyzed by Fe^{II} complexes, which were prepared from Fe(ClO$_4$)$_2$·6H$_2$O and Fe(OTf)$_2$ (Scheme 23).[34] Such Fe^{II} complexes also catalyzed the tandem Nazarov cyclization-fluorination reaction of divinyl ketones in good yields but no enantiomeric excess could be observed.
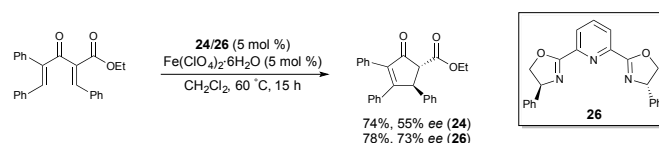
Scheme 23. Asymmetric Nazarov cyclization catalyzed by a Fe^{II} *pyridine-bis(oxazoline)* complex.

Bolm reported the first Fe^{III} catalyzed enantioselective sulfimidation reaction using Fe^{III} salts and *pyridine-bis(oxazoline)* ligand **26**, in combination with *N*-(*p*-tolylsulfonyl)imino phenyliodinane as the nitrene precursor.[35] A variety of optically active sulfimides were afforded in good yields and enantioselectivities (Scheme 24). Interestingly, the reactions could be performed in air, without exclusion of moisture.
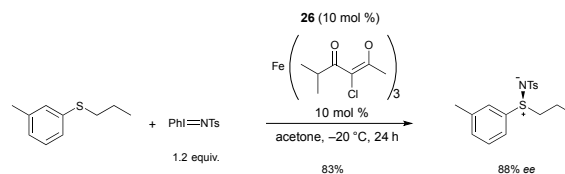
Scheme 24. Fe^{III} catalyzed enantioselective sulfimidation.

Following on from this, Bolm reported a catalyst, prepared *in situ* from an Fe^{III} salt and the same ligand **26**, allowing the resolution of racemic sulfoxides through catalytic asymmetric nitrene-transfer reactions (Scheme 25).[36] This method provides a synthetically useful approach for the synthesis of enantiomerically enriched sulfoximines. In most cases the reaction proceeded smoothly to give the desired product using various sulfides as substrates, Fe^{+3} 4-chloro-2,6-dimethyl-3,5-heptanedionate as the Fe^{III} source, and **26** as chiral ligand. A large variety of enantioenriched sulfimides were prepared in good yields and good enantioselectivities (up to 88% *ee*). Both iron pre-catalyst and chiral ligand are commercially available. Catalytic loadings of iron source and ligand were used at 10 mol % but a reduction of the catalyst loading from 10 mol % to 5 mol % was possible. Interestingly, the reactions could be performed in air, without exclusion of moisture. Another major advantage of the method is the choice of solvent. Acetone was used as a cheap and environmentally-benign solvent.
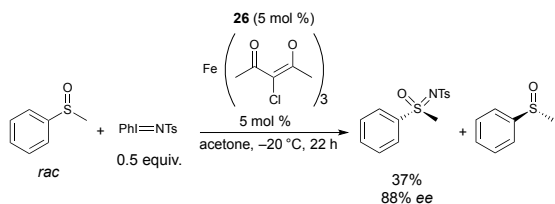
Scheme 25. Resolution of racemic sulfoxides through catalytic asymmetric nitrene-transfer reactions.

4. Conclusions

This minireview summarizes many of the important advances in the field of asymmetric catalysis using chiral iron *bis(oxazoline)* and *pyridine-2,6-bis(oxazoline)* catalysts. Efficient catalytic asymmetric transformations using iron are definitively high potential processes and demonstrate the future challenges that will need to be addressed in this field. A deeper understanding of iron complex geometries and their influences on enantioselectivity is required for future rational development of new catalysts in enantioselective reactions. Iron catalysts have definitively contributed to the area of environmentally benign catalysts, known as green catalysts. The study of asymmetric catalysis using iron has been garnering increased attention, particularly over the last five years. Given the ongoing need for new economical and green reactions, asymmetric catalysis using iron salts will clearly be a prominent area in the forthcoming years.

Acknowledgements

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