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Iron Catalysis

Iron Cyclopentadienone Complexes: Discovery, Properties, and Catalytic Reactivity

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bifunctional catalysis · dual catalysis · hydrogenation · iron catalysis · synthetic methods

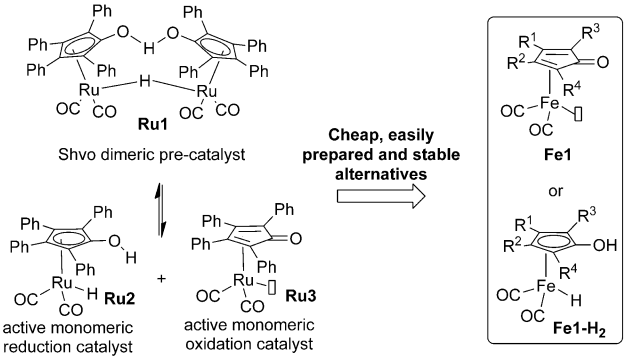
Dedicated to Professor Max Malacria in the occasion of his 65th birthday

Iron cyclopentadienone complexes have recently received particular attention in organic chemistry. This is due to their easy synthesis from simple and cheap materials, air–water stability, and most importantly for their unique catalytic features arising from the presence of a non-innocent ligand, triggering powerful redox properties. Herein we discuss the properties of such complexes from synthetic and mechanistic points of view, and their applications in original redox-neutral transformations in both racemic and enantioselective series.

1. Introduction

Metal-catalyzed redox processes, such as hydrogenations, are currently playing a crucial role in the synthesis of organic building blocks. To limit the generation of waste, greener catalytic processes have long been sought. As a result, an impressive number of hydrogenation catalysts have been successfully developed and most importantly, industrially applied.[1]

To adjust the catalysts properties, chemists have long focused on tuning the reactivity at the metal center by modulation of the electronic and steric properties of the ligands. Alternatively, bifunctional catalysts bearing a non-innocent function emerged as a pivotal concept to tune the reactivity and the catalytic activity of metal complexes.[2] Among these, the Shvo dimeric ruthenium pre-catalyst **Ru1** has been known since the mid-1980s to be efficient in a large variety of reactions and notably in hydrogenation and oxidation transformations (Scheme 1).[3] The particular ambivalent reactivity of this complex arises from its dissociation into two complementary active monomeric species bearing a non-innocent active functionalized ligand. Hydroxycyclopentadienyl ligand in **Ru2** is a proton-donor site, it is bound to a hydride-donor ruthenium center and can promote hydrogenations, while cyclopentadienone in **Ru3** is a proton-acceptor site bound to a hydride-acceptor ruthenium center and can catalyze oxidations.



Scheme 1. Shvo's ruthenium complexes and iron alternatives.

For a long time, noble metals (e.g. Ir, Rh, Ru) have dominated the field of homogeneous hydrogenation and it was only at the beginning of this century that an increased interest was given to the use of cheaper non-noble analogues notably based on abundant iron.[4] The late development of iron-based hydrogenation catalysts is rather surprising given the activity of iron hydrogenases.[5] However, in addition to the economic benefit, developing iron-based complexes produces an opportunity to access complementary chemoselectivities and discover new reactivities. In this context, cyclopentadienone iron hydride complexes, such as **Fe1-H_2** (Scheme 1) were known for half a century, long before the Shvo pre-catalyst. Surprisingly, while structurally very close, their catalytic properties remained undeveloped until 2007. Since then, given their unique catalytic behavior, easy access from abundant iron sources, and high stability, the last years have seen an explosion in the number of their applications.

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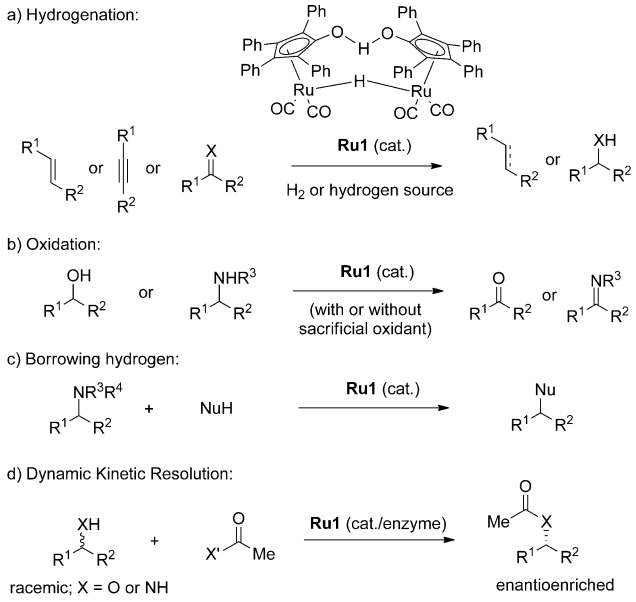
Herein we report the initial synthesis of these iron complexes, their catalytic reactivity, mechanism and recent applications in the development of enantioselective dual catalytic transformations.

2. Historical Perspective

2.1. Ruthenium Cyclopentadienone Complexes

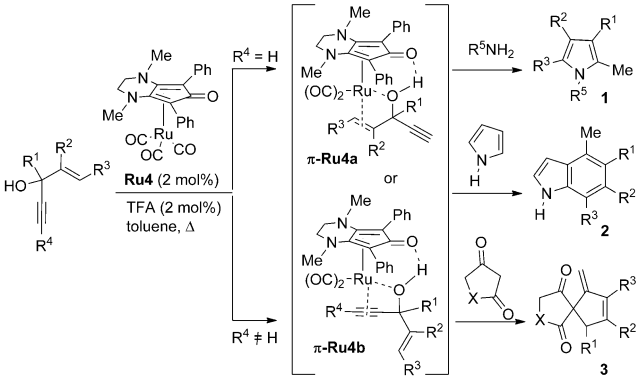
As mentioned in the introduction, Shvo complex **Ru1** was first synthesized and applied in catalysis in the 1980s.[3a,b] Since then, its catalytic properties were further demonstrated in a wide range of redox transformations (Scheme 2). This work



Scheme 2. Examples of catalytic applications of Shvo complex.

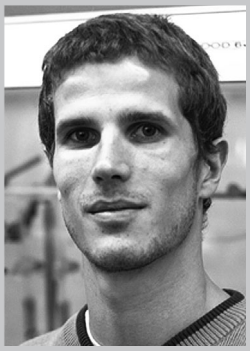
has been the topic of an excellent Review in 2010 by Williams and co-workers.[3e] These transformations include hydrogenation of alkynes, alkenes, or carbonyls (with H_2 or other hydrogen sources, such as formic acid),[6] or the reverse process: namely alcohol or amine oxidation.[7] Given the possibility to promote both reduction and oxidation, ruthenium complex **Ru1** was also applied to the so-called borrowing hydrogen strategy.[8] In addition, by taking advantage of these redox-neutral properties, Bäckvall applied this pre-catalyst in combination with enzymes in the dynamic kinetic resolution of alcohols and amines.[9]

More recently, the reactivity of parent ruthenium cylopentadienone **Ru4** was extended to other types of processes not related to hydrogen transfers, as shown in the recent work of Haak and co-workers on cascade reactions (Scheme 3).[10]



Scheme 3. Recent use of ruthenium complexes in cascade transformations.

This potent hydrogen-bond acceptor catalyst can efficiently activate various propargyl alcohols via π-complexes **π-Ru4a**,**b**, which follow different pathways depending on the substrate substitution pattern. The overall catalytic cycle, involving an internal redox isomerization process, leads to divergent substitution–cyclization sequences by reaction with various nucleophiles. Primary amines allowed the selective formation of substituted pyrroles **1**, which can also be used as nucleophiles to access indoles **2**. Alternatively, cyclic 1,3-dicarbonyl compounds behave as bis-nucleophiles giving spirocyclic skeletons **3**.



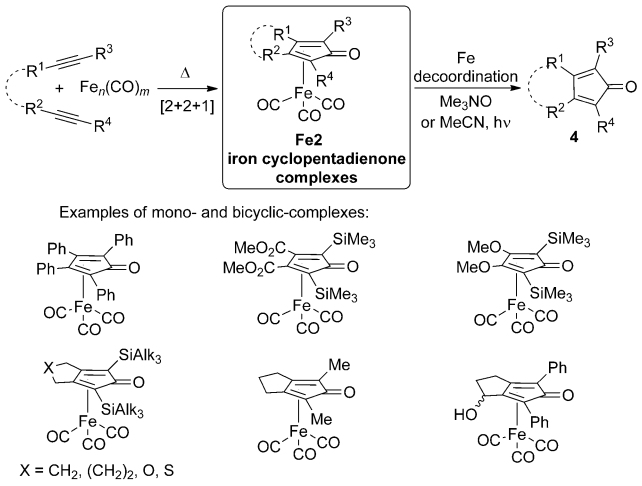
Adrien Quintard studied chemistry at the university of Toulouse and then at CPE/university of Lyon. He completed his Ph.D. in 2011 under the supervision of Prof. A. Alexakis at the university of Geneva. He subsequently moved to the university of Stanford for post-doctoral stay working with Prof. B. M. Trost. Since September 2012 He has been an associate researcher at Aix-Marseille University. His research interests include the development of organometallic/organocatalytic enantioselective methodologies and their application to natural-product synthesis.

Jean Rodriguez was born in Cieza (Spain) in 1958 and in 1959 his family immigrated to France. He studied chemistry at the University of Aix-Marseille (France), where he completed his Ph.D. with Prof. B. Waegell and Prof. P. Brun (1987) and his Habilitation (1992). He is currently Professor and Director of the UMR-CNRS-7313-iSm2. His interests include the development of domino and multicomponent reactions, and their application in stereoselective organocatalyzed synthesis. He has been awarded ACROS prize in Organic Chemistry, the prize of the Division of Organic Chemistry from the French Chemical Society, and in 2013 became "Distinguished member" of the French Chemical Society.

2.2. Iron Cyclopentadienone Complexes

In 1953, when Reppe and Vetter described the peculiar reactivity of iron carbonyl complexes with acetylenes leading to stable but structurally non-elucidated organometallic intermediates, they could not have suspected the importance of this transformation in modern synthetic organic chemistry.[11] Subsequently, different groups reported the isolation of similar products[12] and six years later, Schrauzer disclosed the first structural elucidation of these unique iron tricarbonyl complexes bearing a cyclopentadienone motif with an iron(0) bound by π-interactions.[13]

The nature of the alkyne can be efficiently modulated including acyclic diynes, leading to a wide variety of easily synthesized mono- or bicyclic- iron tricarbonyl complexes **Fe2** (Scheme 4). Notably, it is possible to tune their electronic and

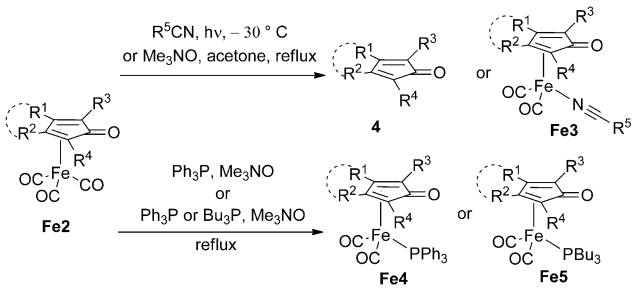


Scheme 4. Initial discovery and synthetic use of iron cyclopentadienone complexes.

steric properties by varying the substituents on the alkynes. Representative examples are the introduction of electron-withdrawing (R^1, $R^2 = CO_2R$) or electron-donating groups (R^1, $R^2 = OMe$) but also bulky R^3 and R^4 trialkylsilyl, aryl, or even alkyl substituents.[14] Unfortunately, despite their unique structural features, these complexes were for long, more regarded as scientific curiosities. It was only in the 1990s that concurrently the teams of Knölker and Pearson methodically studied the chemistry of these iron complexes.[15,16]

While missing their catalytic activities, they successfully developed elegant synthetic transformations of the valuable free cyclopentadienones ligands **4** obtained by simple oxidative decoordination of the iron, notably thanks to trimethylamine *N*-oxide (Me_3NO).

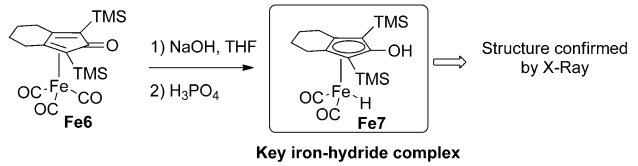
Partial decoordinations of CO ligands with concomitant ligand exchanges are also possible either under photochemical, oxidative or thermal conditions (Scheme 5). For example, UV irradiation of **Fe2** in acetonitrile at −30 °C provides the free ligand **4** under very mild conditions, after three consecutive CO to CH_3CN ligand exchanges, or the labile mono acetonitrile complex **Fe3**.[17] Alternatively, stable iron



Scheme 5. Ligand exchanges in iron tricarbonyl cyclopentadienone complexes.

mono-triphenyl- or tri-*n*-butylphosphine analogues **Fe4** and **Fe5** are also accessible by thermal exchange in refluxing di-*n*-butyl ether or in the presence of Me_3NO.[15]

The key reactivity of iron tricarbonyl cyclopentadienone complexes was discovered by Knölker and co-workers in 1999.[18] They were able to isolate the first iron hydride hydroxycyclopentadienyl complex **Fe7** by a Hieber-type reaction of **Fe6** with 1 M NaOH and subsequent treatment with H_3PO_4 (Scheme 6).[19] Crystal structures of both starting



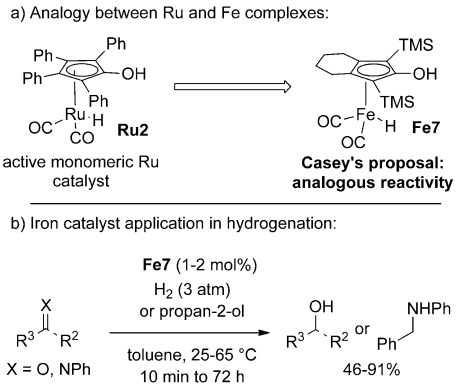
Scheme 6. First iron hydride hydroxycyclopentadienyl complex isolated in 1999 by Knölker.

complex and product confirmed the iron hydride nature of the obtained species. At this stage, all the knowledge was set for the application of these complexes in catalytic redox transformations but eight years were necessary before their successful utilization in catalytic reactions.

3. Applications as Redox Catalysts

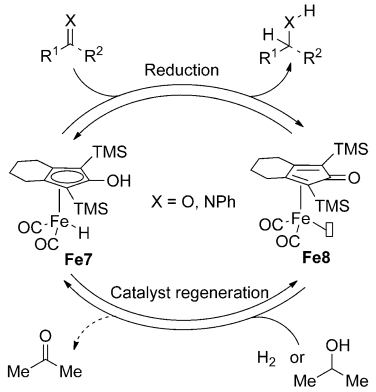
3.1. 2007 Casey and Guan Discover the Catalytic Properties of Iron Hydride Hydroxycyclopentadienyl Complexes

Casey's group at the University of Wisconsin had accumulated a strong background on the use of hydroxycyclopentadienyl ruthenium hydride catalysts **Ru2**, allowing them to bridge the gap between the formation of Knölker's hydride complex **Fe7** and its catalytic activity using dihydrogen or propan-2-ol as hydrogen donors (Scheme 7 a).[20] As expected, under mild conditions, fifteen different carbonyl compounds (ketones or aldehydes) and one imine could be efficiently reduced in good yields (Scheme 7 b). Interestingly, these conditions proved to be highly chemoselective leaving other functions, such as epoxides, esters, alkynes, and non-conjugated alkenes unchanged.



Scheme 7. 2007 Casey's initial discovery of the catalytic properties of **Fe7** in hydrogenation.

The reversibility of the reduction pathway is the crucial step of the general mechanism involving two complementary catalytic iron species **Fe7** and **Fe8** (Scheme 8). The initial hydride complex can reduce the polar group, while the resulting coordinatively unsaturated catalyst **Fe8** acts as an oxidant, activating H_2 or propan-2-ol (in that case liberating acetone).

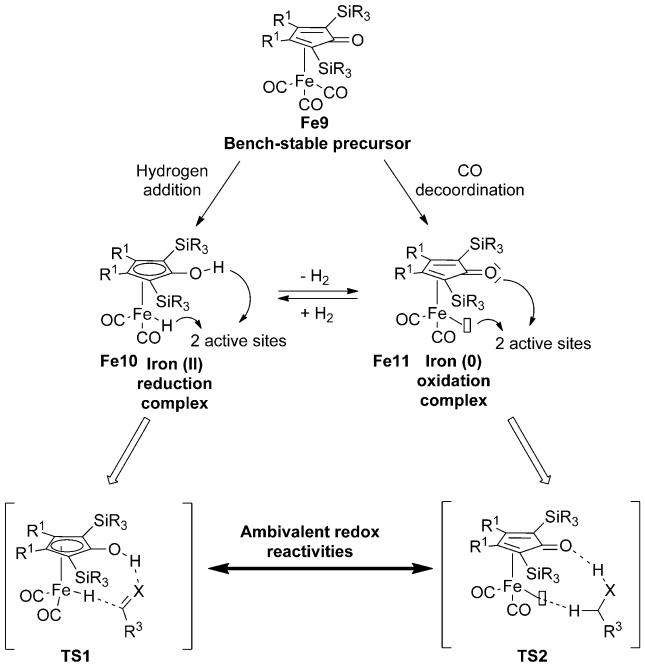


Scheme 8. 2007 Casey's initial discovery of the catalytic properties of **Fe7** in hydrogen transfer and proposed hydrogenation mechanism.

As a result, this fundamental paper, demonstrating the potential of iron hydride hydroxycyclopentadienyl complexes in hydrogen activation paved the way for the development of various redox transformations.

3.2. Applications of the Iron Complexes in Reductions

Following Casey's breakthrough, a general ambivalent redox reactivity pattern was born (Scheme 9). From bench stable cyclopentadienone pre-catalysts **Fe9**, hydrogen addition affords the iron(II) hydride catalyst **Fe10** triggering the chemoselective reduction of polarized double bonds. The relative acidity of the hydroxy function of the resulting non-innocent ligand is crucial for the transient activation of the substrate by hydrogen-bonding donation before hydride

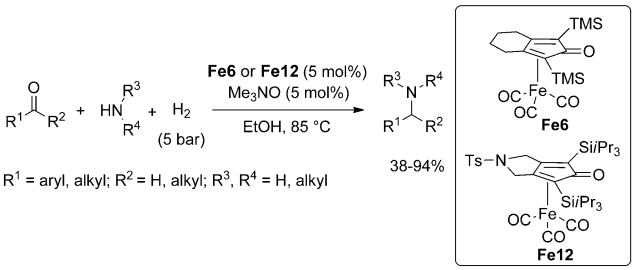


Scheme 9. General reactivity profile for the iron complexes.

transfer. On the other hand, the coordinatively unsaturated iron(0) complex **Fe11** behaves as an oxidant capable of abstracting hydrogen from alcohols thanks to the Lewis basicity of the key cyclopentanedione ligand. These two iron(0) and iron(II) catalytic species are in equilibrium depending on the reaction conditions, allowing for complementary redox catalytic processes by selective activations of the substrates through transition states **TS1** and **TS2**, respectively (reduction or oxidation). It must be pointed out that, while **Fe9** is stable in air for months and can even be purified by column chromatography, both **Fe10** and **Fe11** slowly decompose under aerobic conditions.

With the first basic set of reactivities clearly established, several groups subsequently modified initial catalyst **Fe7** and/or applied it to different redox processes.

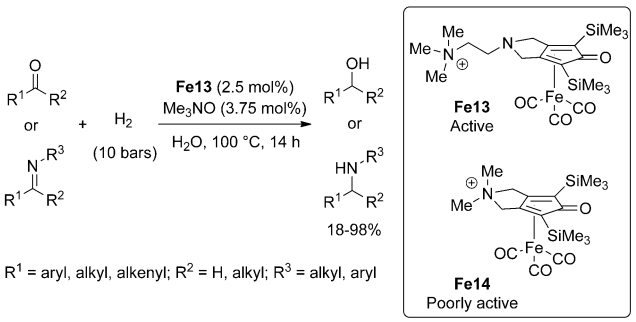
For the successful synthetic utilization of these redox properties, the selective mono-decoordination of one of the CO ligand from the Knölker pre-catalyst **Fe6** is a prerequisite. In this respect, in situ oxidative decomplexation using Me_3NO largely leads the way. Me_3NO reacts with one CO ligand on the metal center liberating the vacant site and a stoichiometric amount of CO_2 and trimethylamine as side products. For example, recently the group of Renaud reported that ketones and aldehydes could be reductively aminated using 5 mol% of **Fe6** under a positive hydrogen pressure and 5 mol% of Me_3NO (Scheme 10).[21] Mechanistically, the reduction of in situ generated imines occurs by hydrogenation in which the iron hydride catalyst is formed by activation of dihydrogen. The reaction generally proceeds with good yields and in some cases needs the addition of a catalytic amount of NH_4PF_6 to help the imine formation. Subsequent screening of 10 analogues of **Fe6** revealed that in most cases, **Fe12** with a slightly modified skeleton was more active than the initial complex.[21b]



Scheme 10. Catalytic reductive amination of aldehydes and ketones with **Fe6** and **Fe12**.

The overall amines formation is impressive since it indicates an excellent and unique selectivity of **Fe6** and **Fe12** in favor of C=N bond reduction over C=O bond reduction, which is not the case for other iron catalysts tested in this transformation.

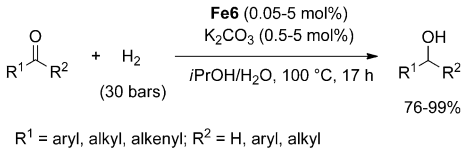
Short after, the same group synthesized different ionic-liquid-based iron complexes to evaluate their catalytic activity in water (Scheme 11).[22] The insertion of an ammonium salt



Scheme 11. Catalytic application of modified ammonium salts iron complexes.

allows for a better solubility of the iron pre-catalyst **Fe13** in water, leading to improved reactivity under these conditions as compared to complex **Fe6**. If the ammonium salt is placed too close to the reactive site as in **Fe14**, a dramatic drop in reactivity is observed. The use of Me_3NO is again essential for the formation of the active catalyst. Under optimized conditions, a whole set of ketones, aldehydes, or imines could be efficiently hydrogenated under a positive hydrogen pressure.

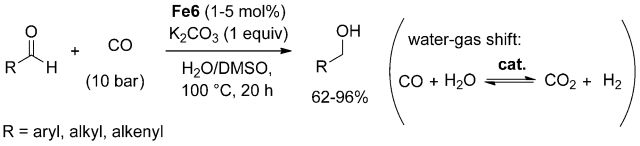
In 2011 Berkessel also showed that active iron complexes could be generated in situ from **Fe2** by UV irradiation, promoting CO ligand dissociation (see below).[32] Alternatively, Beller et al. carefully optimized the reaction conditions so that the bench stable pre-catalyst **Fe6** could also be used directly in carbonyl reduction.[23] Adding a catalytic amount of K_2CO_3, the active iron hydride **Fe7** used by Casey was formed in situ allowing the reduction of a variety of carbonyl-containing molecules with as low as 0.05 mol% loading of **Fe6** (Scheme 12). Noteworthy, water can be used as a co-solvent under these conditions, demonstrating the robustness of the active catalytic species with turnover numbers (TON) up to 3800. Modifications of the initial catalyst structure **Fe6** by



Scheme 12. Beller's reduction of ketones and aldehydes.

increasing the bulkiness on the silyl group or by replacing the cyclohexane ring by a cyclopentane ring did not bring any catalytic activity improvement.

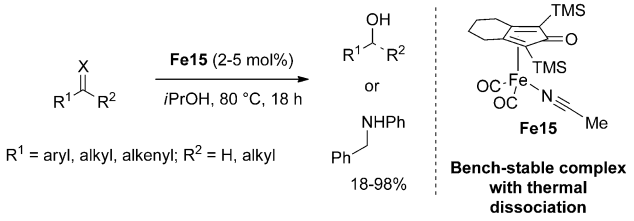
In another interesting study, Beller and co-workers also discovered that the water–gas shift reaction of carbon monoxide and water to generate hydrogen could be efficiently catalyzed by **Fe6** and applied to the reduction of aldehydes (Scheme 13).[24] In the presence of 1 equivalent of K_2CO_3,



Scheme 13. Reduction of aldehydes under water–gas shift conditions.

10 bar of CO, and water, different aliphatic, aromatic, or α,-β-unsaturated aldehydes were selectively reduced in up to 96% yield. This study extended the capacity of iron complexes to activate molecules other than hydrogen, and notably carbon monoxide. In addition, it allowed hydrogenation to be performed using less-hazardous CO and H_2O mixture as hydrogen source.

Finally, the group of Funk disclosed a new mono-acetonitrile iron dicarbonyl analogue **Fe15** as a thermally more labile pre-catalyst, in situ leading to **Fe8** having a metal vacant site (Scheme 14; see Scheme 8 for **Fe8**).[25] Efficient



Scheme 14. Reduction of polar double bonds with iron dicarbonyl acetonitrile complex **Fe15**.

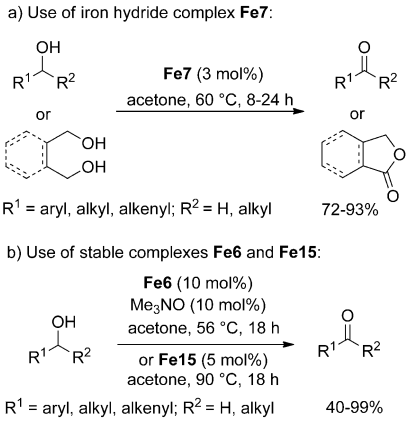
transfer hydrogenations of polar double bonds were possible at 80°C using propan-2-ol as benign hydrogen source and without assistance of Me_3NO. In this type of transfer hydrogenation, the ambivalent character of the iron cyclopentadienone acetonitrile catalyst is fully highlighted since on one side, complex **Fe8** oxidizes propan-2-ol to give **Fe7**, triggering the reduction of the polar C=X bond. It is notable that in contrast to **Fe7**, **Fe15** is unable to react under a positive hydrogen pressure. Following these results, Renaud and co-

workers have synthesized a series of related bicyclic acetonitrile complexes and evaluated their catalytic efficiency in the reductive amination of carbonyl compounds (see above Scheme 10). These catalysts were found to give activities close to those of the iron tricarbonyl species but required higher temperatures (85 °C) to promote ligand dissociation.[21b]

3.3. Applications of Iron Complexes in the Oxidation of Alcohols

The oxidation pathway of the ambivalent iron cyclopentadienone complexes has received less attention and mainly concerns the Oppenauer-type oxidation of primary and secondary alcohols.

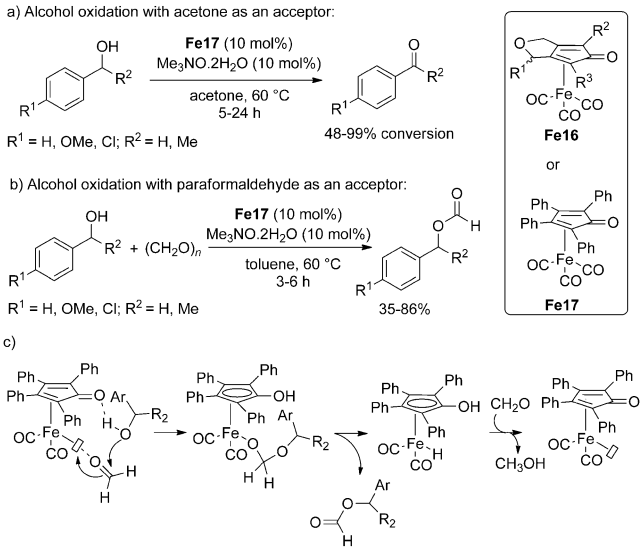
Beside a single example requiring high catalyst loading by Williams and co-workers in 2009,[26] the group of Guan reported the first efficient application of Casey's iron hydride catalyst **Fe7** to selectively oxidize secondary alcohols and cinnamyl alcohol in acetone as solvent and benign sacrificial hydrogen acceptor (Scheme 15a).[27] Interestingly, although



Scheme 15. Oppenauer-type oxidation of alcohols by iron complexes a) **Fe7**, b) **Fe6** and **Fe15**.

simple primary aliphatic alcohols are not fully oxidized under those conditions, 1,4-primary diols are effectively transformed to lactones by two successive H_2 abstractions. Soon after, Funk and Moyer reported that after in situ monodecoordination with Me_3NO, bench-stable **Fe6** also promotes the oxidation process albeit 10 mol% of catalyst was required (Scheme 15b).[28] It is worth mentioning that catalysts having phenyl instead of the TMS groups on the dienone, or a five-membered ring instead of the cyclohexane all gave decreased catalytic activity compared to **Fe6**. Finally, the previously mentioned acetonitrile modified catalyst **Fe15**, also efficiently promotes the Oppenauer-type oxidation of several alcohols in acetone without the need of Me_3NO, albeit at 90 °C in a sealed vessel (Scheme 15b).[25]

Wills and co-workers extensively modified the structure of the cyclopentadienone motif notably to obtain complexes **Fe16** and studied this effect in a related hydrogen transfer oxidation (Scheme 16a).[29] Unfortunately, these pre-catalysts gave moderate reactivity in acetone as an acceptor compared



Scheme 16. Alcohols oxidation with a) acetone or b) paraformaldehyde as hydrogen acceptors. c) Mechanism of the reaction in (b).

to complex **Fe17** with four aromatic substituents on the cyclopentanedione. $Me_3NO{\cdot}2H_2O$ was again found to be the most efficient additive for the in situ formation of the active complex, and in this case the presence of a catalytic amount of water does not affect the reactivity.

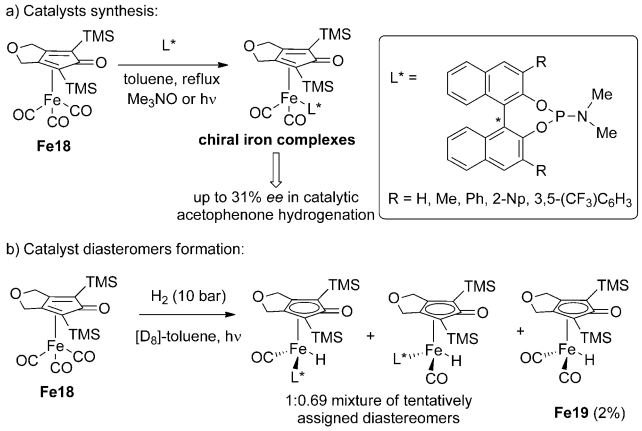
In addition to this oxidation, the same group showed that in the presence of paraformaldehyde as the hydrogen acceptor the overall oxidative process leads to formate esters as major products (Scheme 16b). This reaction goes through a particular mechanism where the alcohol first adds to paraformaldehyde and the hemiacetal obtained subsequently undergoes a hydride transfer (Scheme 16c). The final regeneration of the catalyst occurs by reduction of a sacrificial formaldehyde molecule liberating methanol.

From all these studies, it appears that only alcohols (primary or secondary) or lactols can be efficiently oxidized with iron cyclopentadienone catalysts and to date, in sharp contrast with other transition-metal catalysts, no example of amine or thiol oxidations have been reported.[30]

3.4. Chiral Iron Cyclopentadienone Complexes

Given the apparent excellent reactivity under mild conditions of the iron complexes most notably in hydrogenations, it is naturally that researchers started looking for an asymmetric version of these iron-catalyzed transformations.[31] For this purpose, two strategies were studied: 1) insertion of an extra chiral ligand directly on the iron center; 2) insertion of the chiral information on the dienone ligand. Unfortunately, to date, the success has been limited in this area and only moderate levels of enantioselective control are generally observed.

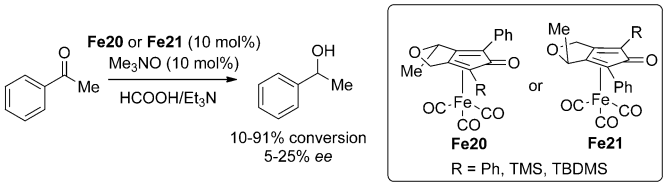
In 2011, Berkessel et al. successfully replaced a CO from **Fe18** with a chiral phosphoramidite ligand either under UV irradiation or more successfully using Me_3NO (Scheme 17a).[32] Despite the efficient introduction of a chiral



Scheme 17. Berkessel's synthesis of chiral iron complexes.

information on the iron center, these catalysts only gave at the best 31% *ee* in acetophenone hydrogenation. An NMR spectroscopic study of the activation of the iron complexes by hydrogen indicated that two diastereomeric iron hydride complexes were formed in a 1:0.69 ratio (Scheme 17b). This arises from a non-selective CO dissociation from the initial chiral iron cyclopentadienone complex leading to two different chiral iron hydride catalysts, which is probably the origin of the observed moderate enantioselective control. In addition to this, partial removal of phosphoramidite ligand also gives 2% of achiral active iron hydride complex **Fe19**, a pathway detrimental to the enantioselectivity.

In 2012, Wills and co-workers also applied chiral iron complexes to the asymmetric reduction of acetophenone by transfer hydrogenation using the system formic acid/triethylamine as hydride source and Me_3NO as decoordinating agent. Their strategy relied on the insertion of the chiral information on the cyclopentadienyl part of the complex (Scheme 18).[33]



Scheme 18. Wills' application of chiral iron complexes.

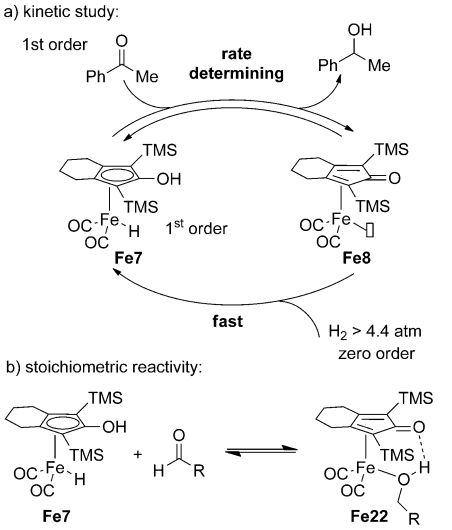
Controlled by the chirality on the cyclopentadienone ligand, two different diastereomeric iron pre-catalysts **Fe20** and **Fe21** could be synthesized with 92% *ee*. However, poor enantioselective control, with *ee* values not exceeding 25%, were observed regardless of the reaction conditions. Note that a related approach with the corresponding chiral ruthenium complexes gave the same range of enantioselective control (up to 21% *ee*).[34]

All these recent studies clearly highlight the difficulty for developing an efficient version of these chiral iron complexes, which remains the major challenge in the burgeoning field of catalytic iron chemistry. This lack of enantioselective control might be explained by the relatively important distance between the chiral information and the active site of the catalyst. Hopefully, future investigations will bring a solution to this crucial problem.

3.5. Mechanisms of the Redox Transformations

Since iron cyclopentadienone complexes showed promising reactivities, numerous groups attempted to identify their exact mode of action, and notably, the hydrogenation mechanism. These mechanistic investigations include both experimental and computational studies.

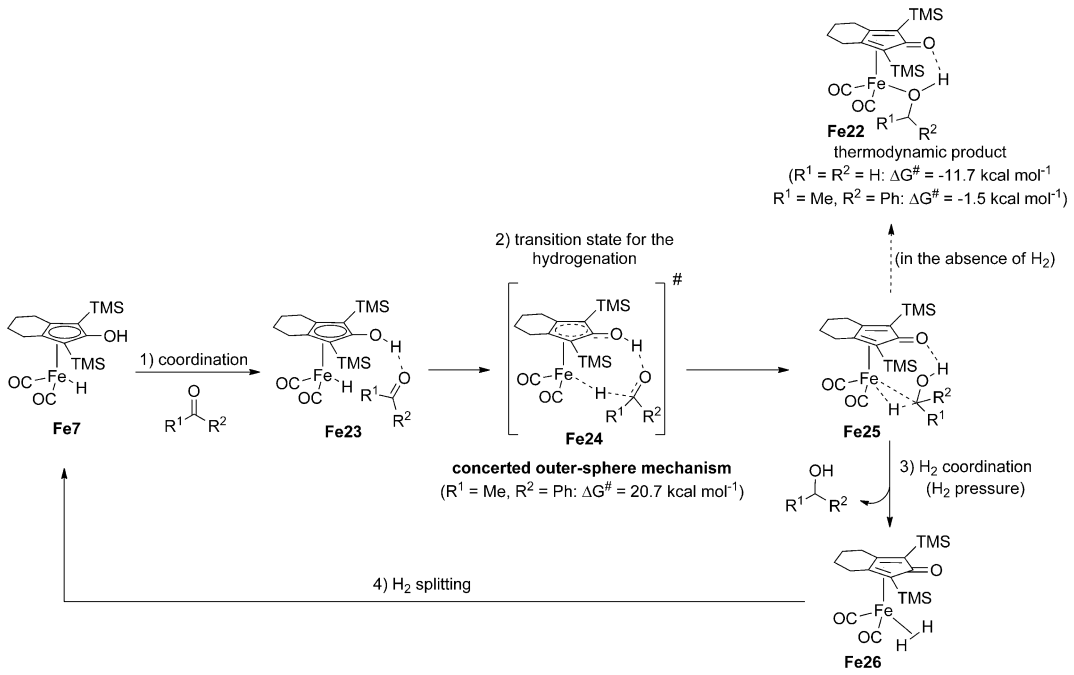
In his 2007 report, Casey gave the first evidence for the origin of the reactivity of hydroxycyclopentadienyl complex **Fe7** in the hydrogenation of carbonyl compounds through the mechanism depicted in Scheme 19.[20] Kinetic studies for the



Scheme 19. Experimental mechanistic study on **Fe7** reactivity.

reduction of acetophenone indicated that ketone reduction was the rate-determining step in the catalytic cycle. When placed under a hydrogen pressure greater than 4.4 atm, the reaction was zero order in H_2, while 1st order in **Fe7** and acetophenone (Scheme 19a). From this study, **Fe7** is able to reduce benzaldehyde eight-times faster than acetophenone. Based on the same hydroxycyclopentadienyl backbone, it seems that the reactivity profile between ruthenium and iron complexes remains in the same range of magnitude for these reductions.[35] Additional stoichiometric experiments indicated that carbonyls and notably aldehydes react rapidly and reversibly with iron hydride **Fe7** to give **Fe22** (Scheme 19b).[36] The alcohol is able to dissociate from the iron center but this dissociation rate is higher than the global reaction rate, suggesting **Fe22** as a non-viable catalytic intermediate. Analogy with ruthenium complexes and preliminary experiments seemed consistent with a concerted hydrogen transfer (see below, Scheme 20).

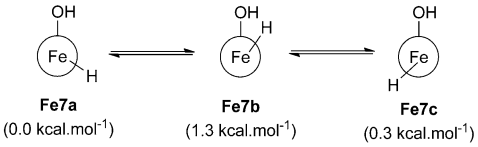
Several groups have also computationally studied the hydrogenation mechanism of carbonyl compounds involving iron hydride hydroxycyclopentadienyl complexes[37] and the



Scheme 20. Reaction mechanism for the hydrogenation of carbonyls.

results are in relative good agreement both together and with Casey's initial experiments. Using iron hydride catalyst **Fe7**, they converged to the overall reaction profile depicted in Scheme 20. Initial carbonyl activation by the acidic OH from the ligand initiates the transformation via **Fe23** (step 1). At this stage, in contrast with the corresponding ruthenium Shvo's complexes, for which the nature of the transition state was long debated,[38] a concerted outer-sphere mechanism involving transition state **Fe24** is supported by theoretical calculations with a free energy of 20.7 kcal mol^{-1} for acetophenone.[37c] Simultaneous transfer of the hydride and the proton (step 2) occurs, directly giving **Fe25** and constitutes the rate-determining step of the catalytic cycle. This intermediate is stabilized by a hydrogen bond with the ligand and an agostic interaction with the iron. In the absence of hydrogen pressure and in good agreement with Casey's observation,[36] **Fe25** can evolve to the thermodynamic alkoxy complex intermediate **Fe22**, which can exist in toluene, with free energies of −11.7 and −1.5 kcal mol^{-1} for formaldehyde and acetophenone, respectively.[37c] However, under a positive pressure of hydrogen, iron hydride hydroxycyclopentadienyl catalyst **Fe7** is regenerated with concomitant release of the expected alcohol. This process goes first through H_2 coordination to the iron (step 3) and subsequent H_2 splitting (step 4). Depending on the calculations, it was found that the dissociation of the alcohol prior to hydrogen activation could slow down the catalyst regeneration.[37] In the case of imines hydrogenation, a slightly different two-step mechanism is proposed by Berkessel and Von der Hör.[37b] Initial imine protonation gives an activated iminium ion which subsequently undergoes the key hydride transfer.

It is also interesting to note that in toluene, iron hydride catalyst **Fe7** has three conformations in equilibrium with a calculated total free-energy barrier of 7.8 kcal mol^{-1} (Scheme 21).[37c] While **Fe7a** with a dihedral angle HFeCO of 88.6° is the most thermodynamically stable, isomers **Fe7b** (HFeCO = 5.1°) and **Fe7c** (HFeCO = −100.3°) constitute more-favorable activation states, with adequate geometry of the resulting Fe–H and O–H bonds. Owing to the rapid rotation around the Fe–CpOH bond, the overall conformational equilibrium does not significantly affect the hydrogenation process; however it might partially explain the moderate chiral induction obtained by Berkessel et al. with the chiral version of their iron catalyst.[32]

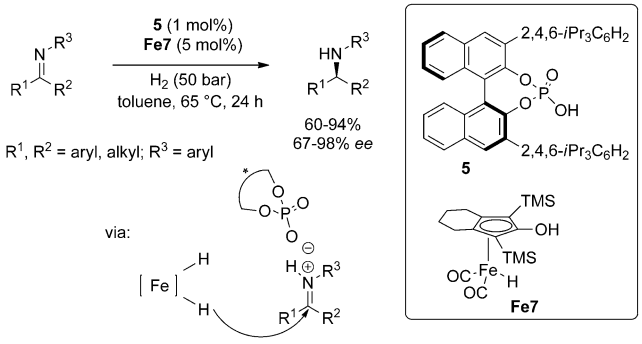


Scheme 21. Three conformations of iron hydride catalyst **Fe7**.

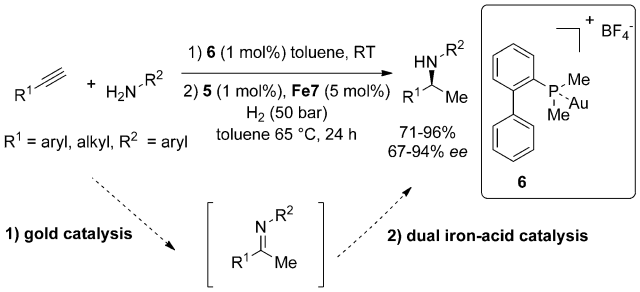
Contrary to "classical hydrogenations", no studies have been performed on the parent transfer hydrogenation where both oxidation with **Fe8** and reduction with **Fe7** are involved. The open question in such processes is whether the oxidation or the reduction is rate determining.[39]

4. Extension to Challenging Reactivities (Dual Catalysis)

With a notable reactivity in redox processes, in addition to excellent compatibility with numerous functional groups, the iron complexes appeared to be ideal to discover new transformations notably in dual catalysis.[40] Dual catalysis where two mutually compatible catalysts provide complementary



Scheme 22. Dual catalytic process for the asymmetric imine hydrogenation.



Scheme 23. Dual catalytic process for the asymmetric alkyne reductive amination.

properties allows otherwise inconceivable transformations to be achieved. The Beller group pioneered the application of Knölker complex **Fe7** in such dual process (Scheme 22).[41] Their goal was to realize the asymmetric hydrogenation of imines by avoiding the use of precious metals. Knowing that imines could be activated by Brønsted acids, such as chiral phosphoric acids, they postulated that a metal catalyst could activate hydrogen. With the two different reactions partners activated, a synergistic transition state, in which hydrogen is transferred from the metal hydride to the protonated and thus chiral imine, would lead to the formation of the enantioenriched amine. Under a positive hydrogen pressure, the expected synergistic cooperative effect between **Fe7** and phosphoric acid **5**, allows the amine formation with *ee* values up to 98%.

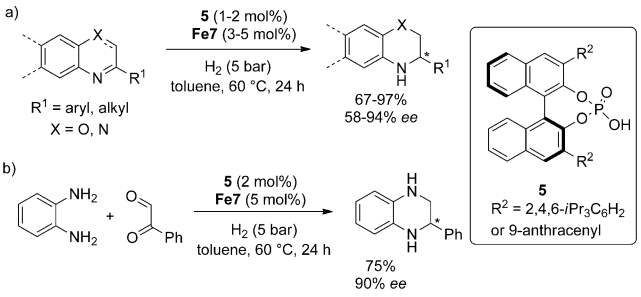
Exact nature of the bicatalytic transition state remains unclear. Preliminary mechanistic investigations indicated that the Brønsted acid and iron complex **Fe7** interact together in the absence of the imine. However, to date there is no evidence for such interactions during the hydride transfer from the iron catalyst to the iminium ion.

Use of other metal catalysts based on rhodium, palladium, or iridium in combination with binol–phosphoric acid derivatives all gave the expected product formation, albeit in a racemic form probably arising from competitive hydrogenation of the unactivated imine. Even the use of the closely related ruthenium Shvo complex provided the amine in only 8% *ee*. This result highlights again the real complementarity of iron cyclopentadienone complexes with other metal complexes and their unique reactivity profile. Overall, the synthetic utility of this process lies in the use of non-precious metals without the requirement of stoichiometric reducing agents, such as Hanztsch esters, for example.

In an extension to their work, the Beller group subsequently reported a relay cascade for the reductive hydroamination of alkynes (Scheme 23).[42] In this process, gold complex **6** is added first to promote the hydroamination of the alkyne to give the corresponding imine. Successive addition of **5** and **Fe7** followed by application of a hydrogen pressure allows the asymmetric hydrogenation leading to the enantioenriched amines in up to 94% *ee*. The only apparent limitation of the system relies on the necessary use of monosubstituted alkynes. In addition, if all the catalysts are mixed together at the beginning and not sequentially, a lower enantioselectivity is obtained (49% *ee*).

The careful optimization of the different catalysts revealed that the combination of gold complex **6**, **Fe7**, and phosphoric acid **5** was optimal to obtain both excellent yields and enantioselective control. Use of other hydroamination catalysts (e.g. Zn, Cu, Pt) or hydrogenation catalysts (Ru, Ir, Rh) was detrimental both in terms of yields and stereoselectivities. The development of this relay cascade further demonstrates the great functional tolerance of iron cyclopentadienone complexes and their ability to be accommodated in multi-catalytic systems.

The cooperative effect between Knölker complex **Fe7** and chiral phosphoric acid **5** was further applied to the enantioselective hydrogenation of six-membered nitrogen heterocycles of the quinoxaline and 2H-1,4-benzoxazine families (Scheme 24a).[43] Note that a background reaction arising

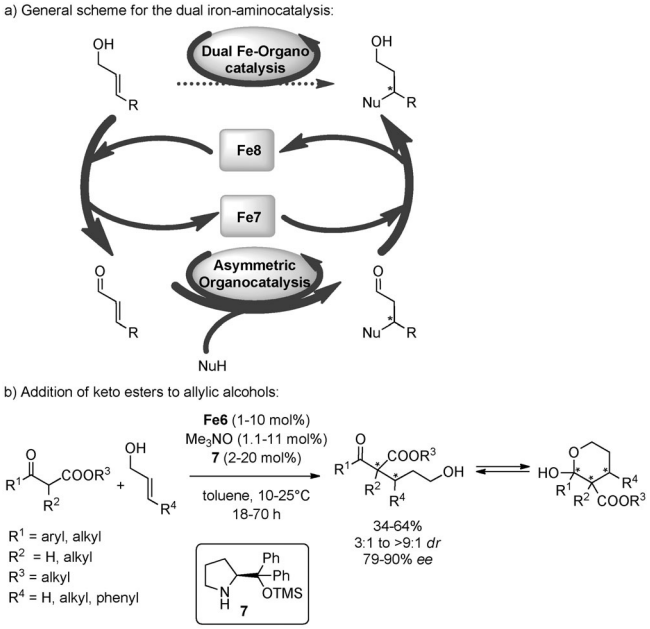


Scheme 24. Dual catalytic process for the asymmetric hydrogenation of nitrogen heterocycles.

from the direct hydrogenation of the starting heterocycles by **Fe7** exists. However, in the presence of the chiral phosphoric acid, enantioselectivities up to 94% *ee* can be obtained. The same team was also able to propose a one-pot procedure involving the in situ generation of the unsaturated heterocycle from phenyl glyoxal and 1,2-phenylenediamine, followed by enantioselective hydrogenation (Scheme 24b). In this transformation, modulating the steric hindrance of the silyl substituents of **Fe7** or modifying the original hydroxycyclopentadienyl backbone did not improve the catalytic activity. Finally, in sharp contrast to the dual catalytic imine hydrogenation, other metallic catalysts, such as [{Rh(COD)Cl}$_2$] or [{Ru(p-cymene)I$_2$}$_2$] also promoted the trans-

formation albeit with lower *ee* value of 80%, further demonstrating the utility of the iron complexes.

Recently, our group also reported an interesting dual catalytic transformation discovered thanks to iron cyclopentadienone complex **Fe6**.[44] This reaction takes full advantage of the ambivalent redox properties of this iron complex combined with an aminocatalyst **7**, triggering the enantioselective functionalization of allylic alcohols (Scheme 25a). The oxidation complex **Fe8**, formed in situ, is able to



Scheme 25. Dual catalytic process for the asymmetric functionalization of allylic alcohols.

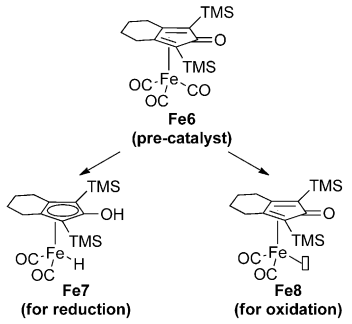
abstract hydrogen from the starting allylic alcohol leading to a reactive α,β-unsaturated aldehyde and generating **Fe7**. This aldehyde is then converted into an enantioenriched β-chiral aldehyde by an aminocatalyzed Michael addition. Subsequent selective reduction of this intermediate aldehyde, by the iron hydride complex **Fe7**, finally gives the expected saturated γ-chiral alcohol. As a result from the efficient imbrication of two different catalytic cycles, it is possible to promote the asymmetric functionalization of allylic alcohols in one single operation where traditionally three distinct stoichiometric oxydation/enantioselective addition and reduction were required. It must be pointed out that iron cyclopentadienone complexes provide unique properties for this so-called borrowing-hydrogen strategy.[45] It allows for a compatible use of a secondary amine catalyst under the mild conditions (10–25 °C) necessary to obtain a good stereocontrol. In addition, the iron complex is able to give excellent chemoselectivity in favor of the desired process, saving both the ketone function and the double bond of the starting material. As a result, the addition of β-keto esters to various allylic alcohols could be performed leading to the expected adducts in equilibrium with the lactol form in up to 90% *ee* (Scheme 25b).

5. General Selectivity and Properties

From all the described studies involving iron cyclopentadienone complexes, several general catalytic features can be highlighted.

First of all, the iron complexes are easy to prepare on multi-gram scale and from readily available starting materials. In addition to their easy preparation, the iron cyclopentadienone complexes are bench stable over months as exemplified by the possibility to purify them by chromatography. It is apparent that complex **Fe6** (Cy, TMS) gives superior activity in most catalytic processes (Table 1). A bulky substituent, such as TMS, on the dienone is crucial for the complex stability, and catalytic activity decreases considerably if lacking, probably by rapid complex decomposition.

Table 1: Indicative reactivity profile of iron complexes.[a]



Hydrogenated substrates	Oxidized substrates	Tolerated functions
aldehydes	primary alcohols	alkenes, alkynes
α-,β-unsaturated aldehydes	secondary alcohols	ethers
ketones	allylic alcohols	esters
primary and secondary imines		pyridines
quinolines		halogens (F, Br, I)
2*H*-1,4-benzoxazines		nitros
		thiophenes
		aromatics
		cyanos
		amides
		amines
		cyclopropanes

[a] This table represents the general catalytic behavior of iron cyclopentadienone complexes. However, depending on the conditions, some differences might be observed.

From this cyclopentadienone pre-catalyst, two different complementary activated reduction **Fe7** and oxidation **Fe8** catalysts can easily be generated, notably in situ, and seem in most cases to be water tolerant. The presence on the complex of the participating ligand allows for a high chemoselectivity highlighted by its great substrate tolerance (Table 1).

In terms of reactivity profile, the reduction complex gives excellent selectivity for the hydrogenation of polar double bonds, such as C=O and C=N groups. As a result and in sharp contrast to Shvo complex, other functions, such as alkenes or alkynes are poorly reactive and in addition, do not interfere with the productive reaction pathway. The most notable reactivity feature is the fact that α,β-unsaturated aldehydes

are most of the time selectively reduced at the carbonyl function. In contrast, oxidation of allylic alcohols occurs selectively without double-bond isomerization constituting an interesting property. Given the particular mechanism of action of these iron catalysts, a great substrate tolerance is observed with the possibility of using a wide variety of functional groups (e.g. cyano, halogens, amide, nitro) that will not be affected.

In comparison with ruthenium cyclopentadienone complexes, well-established for over 20 years, the number of applications of iron complexes discovered in the last 4 years still remains modest. But given the promising complementary reactivities obtained and notably in dual catalysis, time should see a growing number of unprecedented reactivities discovered thanks to these iron complexes.

6. Summary and Outlook

Iron cyclopentadienone complexes have recently appeared as potential excellent alternatives to noble metals catalysts in a wide variety of redox transformations. Their main advantages rely on their easy synthesis from abundant starting material, their stability, and their unique reactivity profile owing to the presence of the non-innocent active ligand. This particular specificity was notably recently highlighted by their applications in dual catalytic enantioselective processes. Owing to these unique features, the continual renewal of interest in this field of research will translate into an exceptional synthetic potential and many reactions should be discovered in the next years.

To further improve the catalysts properties, the modulation of the structure of these iron complexes should constitute a crucial research field in the next few years. Surprisingly, while the original syntheses of these complexes described variously electronically substituted cyclopentadienone complexes, these modifications have poorly been exploited to tune the reactivity of the catalyst. Given the importance of the non-innocent ligand on the reactivity, this should constitute a future area of research increasing the actual efficiency of this family of iron catalysts. Finally, discovery of an efficient chiral version of these catalysts will also constitute a major development in this field.

Our analysis clearly shows that the development of selective transformations with iron cyclopentadienone complexes is still in its infancy but constitutes an important window opening into many areas of chemistry that will fuel the imagination of chemists toward ingenious developments in a very close future.

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[1] For Reviews on industrial hydrogenations in the context of asymmetric catalysis : a) D. J. Ager, A. H. M. de Vries, J. G. de Vries, *Chem. Soc. Rev.* **2012**, *41*, 3340; b) H. Shimizu, I. Nagasaki, K. Matsumara, N. Sayo, T. Saito, *Acc. Chem. Res.* **2007**, *40*, 1385; c) N. B. Johnson, I. C. Lennon, P. H. Moran, J. A. Ramsden, *Acc. Chem. Res.* **2007**, *40*, 1291.

[2] a) R. Noyori, T. Ohkuma, *Angew. Chem.* **2001**, *113*, 40; *Angew. Chem. Int. Ed.* **2001**, *40*, 40; b) T. Ikariya, K. Murata, R. Noyori, *Org. Biomol. Chem.* **2006**, *4*, 393; c) V. Lyaskovskyy, B. de Bruin, *ACS Catal.* **2012**, *2*, 270; d) O. R. Luca, R. H. Crabtree, *Chem. Soc. Rev.* **2013**, *42*, 1440; e) O. Eisenstein, R. H. Crabtree, *New J. Chem.* **2013**, *37*, 21.

[3] For the first preparation of Shvo complex: a) Y. Blum, D. Czarkie, Y. Rahamim, Y. Shvo, *Organometallics* **1985**, *4*, 1459; b) Y. Shvo, D. Czierkie, Y. Rahamin, D. F. Ghodosh, *J. Am. Chem. Soc.* **1986**, *108*, 7400. For Reviews on the Shvo catalyst: c) R. Prabhakaran, *Synlett* **2004**, 2048; d) R. Karvembu, R. Prabhakaran, K. Natarajan, *Coord. Chem. Rev.* **2005**, *249*, 911; e) B. L. Conley, M. K. Pennington-Boggio, E. Boz, T. J. Williams, *Chem. Rev.* **2010**, *110*, 2294.

[4] a) S. Gaillard, J.-L. Renaud, *ChemSusChem* **2008**, *1*, 505; b) H. Nakazawa, M. Itazaki, *Top. Organomet. Chem.* **2011**, *33*, 27; c) K. Junge, K. Schröder, M. Beller, *Chem. Commun.* **2011**, *47*, 4849; d) J. Yang, X. Liu, D.-L. Meng, H.-Y. Chen, Z.-H. Zong, T.-T. Feng, K. Sun, *Adv. Synth. Catal.* **2012**, *354*, 328.

[5] a) J. C. Fontecilla-Camps, A. Volbeda, C. Cavazza, Y. Nicolet, *Chem. Rev.* **2007**, *107*, 4273; b) S. Shima, O. Pilak, S. Vogt, M. Schick, M. S. Stagni, W. Meyer-Klaucke, E. Warkentin, R. K. Thauer, U. Elmer, *Science* **2008**, *321*, 572.

[6] For examples of hydrogenations see : a) Y. Shvo, I. Goldberg, D. Czerkie, D. Reshef, Z. Stein, *Organometallics* **1997**, *16*, 133; b) N. Menashe, E. Salant, Y. Shvo, *J. Organomet. Chem.* **1996**, *514*, 97; c) J. S. M. Samec, J.-E. Bäckvall, *Chem. Eur. J.* **2002**, *8*, 2955; d) Y. Yuki, K. Takahashi, Y. Tanaka, K. Nozaki, *J. Am. Chem. Soc.* **2013**, *135*, 17393.

[7] For examples of oxidations see : a) M. L. S. Almeida, M. Beller, G.-Z. Wang, J.-E. Bäckvall, *Chem. Eur. J.* **1996**, *2*, 1533; b) M. L. S. Almeida, P. Koovsk, J.-E. Bäckvall, *J. Org. Chem.* **1996**, *61*, 6587; c) G. Csjernyik, A. H. Éll, L. Fadini, B. Pugin, J.-E. Bäckvall, *J. Org. Chem.* **2002**, *67*, 1657; d) A. H. Éll, J. S. M. Samec, C. Brasse, J.-E. Bäckvall, *Chem. Commun.* **2002**, 1144; e) E. Haak, *Synlett* **2006**, 1847; f) E. Haak, *Eur. J. Org. Chem.* **2007**, 2815; g) S. Muthaiah, S. H. Hong, *Adv. Synth. Catal.* **2012**, *354*, 3045.

[8] For examples of borrowing hydrogen: a) D. Hollmann, S. Bähn, A. Tillack, M. Beller, *Angew. Chem.* **2007**, *119*, 8440; *Angew. Chem. Int. Ed.* **2007**, *46*, 8291; b) L. Neubert, D. Michalik, S. Bähn, S. Imm, H. Neumann, J. Atzrodt, V. Derdau, W. Holla, M. Beller, *J. Am. Chem. Soc.* **2012**, *134*, 12239.

[9] See for example: a) A. L. E. Larsson, B. A. Perssonn, J. E. Bäckvall, *Angew. Chem.* **1997**, *109*, 1256; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1211; b) B. Martín-Matute, J. E. Backvall, *Curr. Opin. Chem. Biol.* **2007**, *11*, 226.

[10] See for example: a) A. Jonek, S. Berger, E. Haak, *Chem. Eur. J.* **2012**, *18*, 15504; b) N. Thies, C. G. Hrib, E. Haak, *Chem. Eur. J.* **2012**, *18*, 6302; c) N. Thies, M. Gerlach, E. Haak, *Eur. J. Org. Chem.* **2013**, 7354.

[11] W. Reppe, H. Vetter, *Liebigs Ann. Chem.* **1953**, *582*, 133.

[12] a) I. Wender, R. A. Friedel, R. Markby, H. W. Sternberg, *J. Am. Chem. Soc.* **1955**, *77*, 4946; b) I. Wender, R. A. Friedel, R. Markby, H. W. Sternberg, *J. Am. Chem. Soc.* **1956**, *78*, 3621; c) G. N. Schrauzer, *Chem. Ind.* **1958**, 1403; d) E. Weiss, R. Merenyi, W. Hubel, *Chem. Ind.* **1960**, 407.

[13] G. N. Schrauzer, *J. Am. Chem. Soc.* **1959**, *81*, 5307.

[14] a) J. L. Boston, D. W. A. Sharp, G. Wilkinson, *J. Chem. Soc.* **1962**, 3488; b) C. G. Krespan, *J. Org. Chem.* **1975**, *40*, 261; c) R. S.

Dickson, C. Mok, G. Connor, *Aust. J. Chem.* **1977**, *30*, 2143; d) R. J. Kazlauskas, M. S. Wrighton, *Organometallics* **1982**, *1*, 602; e) D. Fornals, M. A. Pericàs, F. Serratosa, J. Vinaixa, M. Font-Altaba, X. Solans, *J. Chem. Soc. Perkin Trans. 1* **1987**, 2749; f) A. J. Pearson, J. B. Kim, *Org. Lett.* **2002**, *4*, 2837; g) J. D. Rainier, J. E. Imbriglio, *J. Org. Chem.* **2000**, *65*, 7272.

[15] a) H.-J. Knölker, J. Heber, C. H. Mahler, *Synlett* **1992**, 1002; b) H.-J. Knölker, J. Heber, *Synlett* **1993**, 924; c) H.-J. Knölker, E. Baum, R. Klauss, *Tetrahedron Lett.* **1995**, *36*, 7647.

[16] a) A. J. Pearson, R. A. Dubbert, *J. Chem. Soc. Chem. Commun.* **1991**, 202; b) A. J. Pearson, R. J. Shively, Jr., R. A. Dubbert, *Organometallics* **1992**, *11*, 4096; c) A. J. Pearson, R. J. Shively, Jr., *Organometallics* **1994**, *13*, 578; d) A. J. Pearson, A. Perosa, *Organometallics* **1995**, *14*, 5178; e) A. J. Pearson, X. Yao, *Synlett* **1997**, 1281.

[17] H.-J. Knölker, H. Goesmann, R. Klauss, *Angew. Chem.* **1999**, *111*, 727; *Angew. Chem. Int. Ed.* **1999**, *38*, 702.

[18] H.-J. Knölker, E. Baum, H. Goesmann, R. Klauss, *Angew. Chem.* **1999**, *111*, 2196; *Angew. Chem. Int. Ed.* **1999**, *38*, 2064.

[19] For a related cyclopentadienyl iron hydride complex, see: T. A. Shackleton, S. C. Mackie, S. B. Fergusson, L. J. Johnston, M. C. Baird, *Organometallics* **1990**, *9*, 2248.

[20] a) C. P. Casey, H. Guan, *J. Am. Chem. Soc.* **2007**, *129*, 5816; For an Highlight on this discovery: b) R. M. Bullock, *Angew. Chem.* **2007**, *119*, 7504; *Angew. Chem. Int. Ed.* **2007**, *46*, 7360.

[21] a) A. Pagnoux-Ozherelyeva, N. Pannetier, M. D. Mbaye, S. Gaillard, J.-L. Renaud, *Angew. Chem.* **2012**, *124*, 5060; *Angew. Chem. Int. Ed.* **2012**, *51*, 4976. For a recent Full Paper on this work: b) S. Moulin, H. Dentel, A. Pagnoux-Ozherelyeva, S. Gaillard, A. Poater, L. Cavallo, J.-F. Lohier, J.-L. Renaud, *Chem. Eur. J.* **2013**, DOI: 10.1002/chem.201302432.

[22] D. S. Mérel, M. Elie, J.-F. Lohier, S. Gaillard, J.-L. Renaud, *ChemCatChem* **2013**, *5*, 2939.

[23] S. Fleischer, S. S. Zhou, K. Junge, M. Beller, *Angew. Chem.* **2013**, *125*, 5224; *Angew. Chem. Int. Ed.* **2013**, *52*, 5120.

[24] A. Tlili, J. Schranck, H. Neumann, M. Beller, *Chem. Eur. J.* **2012**, *18*, 15935.

[25] T. N. Plank, J. L. Drake, D. K. Kim, T. W. Funk, *Adv. Synth. Catal.* **2012**, *354*, 597. For a similar activation by acetonitrile complex formation see Ref. [17].

[26] M. K. Thorson, K. L. Klinkel, J. Wang, T. J. Williams, *Eur. J. Inorg. Chem.* **2009**, 295.

[27] M. G. Coleman, A. N. Brown, B. A. Bolton, H. Guan, *Adv. Synth. Catal.* **2010**, *352*, 967.

[28] S. A. Moyer, T. Funk, *Tetrahedron Lett.* **2010**, *51*, 5430.

[29] T. C. Johnson, G. J. Clarkson, M. Wills, *Organometallics* **2011**, *30*, 1859.

[30] For a recent Palladium-catalyzed borrowing hydrogen oxidation of thiols, see: A. Corma, J. Navas, T. Rodenas, M. J. Sabater, *Chem. Eur. J.* **2013**, *19*, 17464.

[31] For Reviews on the development of chiral iron catalysts: a) M. Darwish, M. Wills, *Catal. Sci. Technol.* **2012**, *2*, 243; b) K. Gopalaiah, *Chem. Rev.* **2013**, *113*, 3248. For a recent report of an efficient chiral iron catalyst see, c) W. Zuo, A. J. Lough, Y. F. Li, R. H. Morris, *Science* **2013**, *342*, 1080.

[32] A. Berkessel, S. Reichau, A. von der Höh, N. Leconte, J.-M. Neudörfl, *Organometallics* **2011**, *30*, 3880.

[33] J. P. Hopewell, J. E. D. Martins, T. C. Johnson, J. Godfrey, M. Wills, *Org. Biomol. Chem.* **2012**, *10*, 134.

[34] Y. Yamamoto, K. Yamashita, M. Nakamura, *Organometallics* **2010**, *29*, 18472.

[35] C. P. Casey, H. Guan, *Organometallics* **2012**, *31*, 2631.

[36] C. P. Casey, H. Guan, *J. Am. Chem. Soc.* **2009**, *131*, 2499.

[37] a) H. Zhang, D. Chen, Y. Zhang, G. Zhang, J. Liu, *Dalton Trans.* **2010**, *39*, 1972; b) A. Von der Hör, A. Berkessel, *ChemCatChem* **2011**, *3*, 861; c) X. Lu, Y. Zhang, P. Yun, M. Zhang, T. Li, *Org. Biomol. Chem.* **2013**, *11*, 5264.

[38] a) C. P. Casey, S. W. Singer, D. R. Powell, R. K. Hayashi, M. Kavana, *J. Am. Chem. Soc.* **2001**, *123*, 1090; b) J. B. Johnson, J. E. Bäckvall, *J. Org. Chem.* **2003**, *68*, 7681; c) C. P. Casey, G. A. Bikzhanova, Q. Cui, I. A. Guzei, *J. Am. Chem. Soc.* **2005**, *127*, 14062; d) A. Comas-Vives, G. Ujaque, A. Lledós, *Organometallics* **2007**, *26*, 4135; and Ref. [3c]. In an inner-sphere mechanism the substrate coordinates to the metal center prior to reacting, whereas in an outer-sphere mechanism the substrate reacts outside of the metal coordination sphere.

[39] Williams has reported a 3.9 isotope effect in an oxidation of alcohol by iron cyclopentadienone complex probably suggesting a C–H bond cleavage rate-determining step. See ref. [26].

[40] For selected Reviews on dual catalysis: a) A. E. Allen, D. W. C. MacMillan, *Chem. Sci.* **2012**, *3*, 633; b) C. Zhong, X. Shi, *Eur. J. Org. Chem.* **2010**, 2999 – 3025; c) Z. Du, Z. Shao, *Chem. Soc. Rev.* **2013**, *42*, 1337.

[41] S. Zhou, S. Fleischer, K. Junge, M. Beller, *Angew. Chem.* **2011**, *123*, 5226; *Angew. Chem. Int. Ed.* **2011**, *50*, 5120.

[42] S. Fleischer, S. Werkmeister, S. Zhou, K. Junge, M. Beller, *Chem. Eur. J.* **2012**, *18*, 9005.

[43] S. Fleischer, S. Zhou, S. Wermeister, K. Junge, M. Beller, *Chem. Eur. J.* **2013**, *19*, 4997.

[44] A. Quintard, T. Constantieux, J. Rodriguez, *Angew. Chem.* **2013**, *125*, 13121; *Angew. Chem. Int. Ed.* **2013**, *52*, 12883.

[45] For selected Reviews on borrowing hydrogen: a) M. H. S. A. Hamid, P. A. Slatford, J. M. J. Williams, *Adv. Synth. Catal.* **2007**, *349*, 1555; b) A. J. A. Watson, J. M. J. Williams, *Science* **2010**, *329*, 635 – 636; c) G. E. Dobereiner, R. H. Crabtree, *Chem. Rev.* **2010**, *110*, 681 – 703; d) C. Gunanathan, D. Milstein, *Science* **2013**, *341*, 1229712.

